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Supplementary Materials for

Ligand-Controlled C(sp^3)–H Arylation and Olefination in Synthesis of Unnatural Chiral α–Amino Acids

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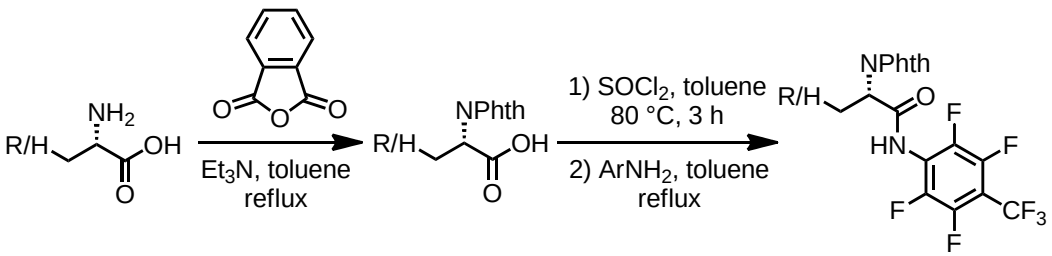
General Information: Solvents were obtained from Sigma-Aldrich, Alfa-Aesar and Acros and used directly without further purification. Amino acids and 2,3,5,6-tetrafluoro-4-(trifluoromethyl)aniline were obtained from the commercial sources or synthesized following literature procedures, and used to prepare 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). Chemical shifts were quoted in parts per million (ppm) referenced to 0.0 ppm for tetramethylsilane. 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 AMX-400 instrument (100 MHz) or Bruker DRX-600 instrument (150 MHz), and were fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to the center line of a triplet at 77.0 ppm of chloroform-*d*. In the ^{13}C NMR analysis, peaks that correspond to those of the polyfluoroarylamide auxiliary appeared as nearly invisible, complex sets of multiplets; they are omitted in the following spectroscopic analysis. High-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight). Enantiomeric excesses values were determined on a Hitachi LaChrom Elite HPLC system using commercially available chiral columns. Optical rotation data were obtained on a Perkin-Elmer 341 polarimeter. Melting points were recorded on a Fisher-Johns 12-144 melting point apparatus.

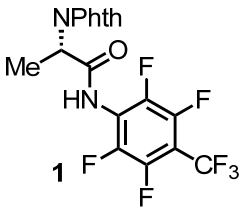
Experimental Section

A. Substrate Preparation



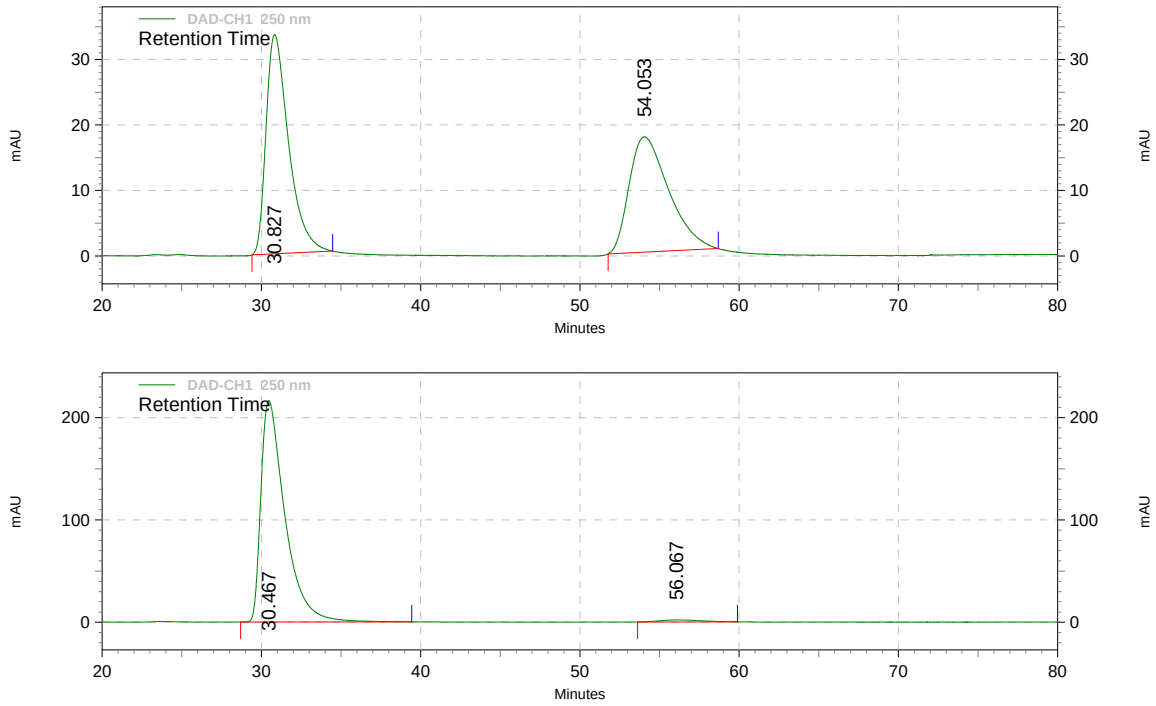
General Procedure for the Preparation of Amide Substrates: To a 100 mL round-bottom flask were added the appropriate amino acid (20 mmol), finely ground phthalic anhydride (20 mmol or 40 mmol in the synthesis of lysine derivatives), toluene (45 mL), and triethylamine (2 mmol, 0.28 mL). After refluxing the reaction mixture overnight, the crude product was evacuated and dissolved in DCM. After adding concentrated hydrochloric acid (0.4 mL), the mixture was washed by water (50 mL) and dried over anhydrous Na_2SO_4. The organic solvent was removed and recrystallized to give the *N*-phthalimido-protected amino acid.

N-Phthalimido-protected amino acid (10 mmol), thionyl chloride (25 mmol) and several drops of DMF were added in toluene at 80 °C for 3 h. After the reaction, the excess of thionyl chloride was removed *in vacuo*, and the crude acid chloride was added to a vigorously stirring solution of 2,3,5,6-tetrafluoro-4-(trifluoromethlyl)aniline (10 mmol) in toluene (8 mL). The reaction mixture was stirred for 12 h under reflux, and then stirred at room temperature for 0.5 h. The product mixture was concentrated *in vacuo* and was recrystallized from ethyl acetate/hexane to give the amide.



(S)-2-Phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (1)

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.39 (br s, 1H), 7.87-7.84 (m, 2H), 7.78-7.75 (m, 2H), 5.15 (q, *J* = 7.2 Hz, 1H), 1.79 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.7, 167.5, 134.6, 131.4, 123.8, 49.9, 15.5; HRMS (ESI-TOF) Calcd for $C_{18}H_{10}F_7N_2O_3$ $[M+H]^+$: 435.0574; found: 435.0574. The ee value was determined by HPLC analysis on a Chiralcel OD-H column (20% isopropanol/hexanes, 0.5 mL/min) with t_r 30.5 min (major), 56.1 min (minor): 97% ee.



DAD-CH1 250 nm Results

Retention Time	Area	Area %	Height	Height %
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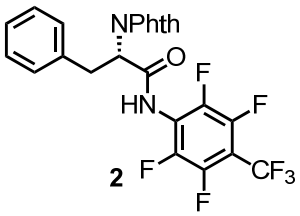
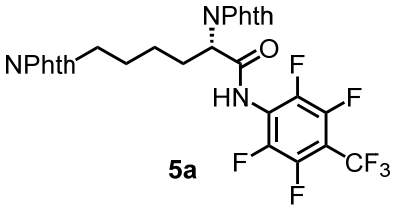
56.067	1392244	1.51	7815	0.89
Totals	91941565	100.00	873832	100.00



2

(S)-3-Phenyl-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2)

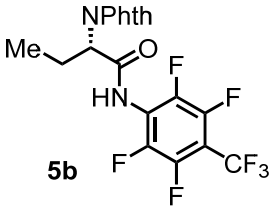
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (br s, 1H), 7.83-7.78 (m, 2H), 7.75-7.71 (m, 2H), 7.23-7.13 (m, 5H), 5.34 (dd, J_1 = 6.4 Hz, J_2 = 10.4 Hz, 1H), 3.64 (ABqd, J_1 = 6.4 Hz, J_2 = 14.2 Hz, 1H), 3.58 (ABqd, J_1 = 10.4 Hz, J_2 = 14.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 166.6, 135.4, 134.7, 131.0, 128.9, 128.8, 127.4, 123.8, 56.6, 35.3; HRMS (ESI-TOF) Calcd for $C_{24}H_{14}F_7N_2O_3$ $[M+H]^+$: 511.0887; found: 511.0883.



5a

(S)-2,6-Bis(phthalimido)-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)hexanamide (5a)

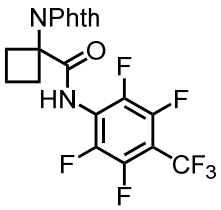
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (br s, 1H), 7.91-7.87 (m, 2H), 7.82-7.77 (m, 4H), 7.73-7.70 (m, 2H), 5.04 (dd, J_1 = 6.4 Hz, J_2 = 9.6 Hz, 1H), 3.70 (t, J = 7.0 Hz, 2H), 2.49-2.32 (m, 2H), 1.82-1.74 (m, 2H), 1.50-1.38 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.5, 168.2, 166.8, 134.7, 134.0, 131.9, 131.3, 124.0, 123.2, 55.3, 36.9, 28.6, 27.5, 23.2; HRMS (ESI-TOF) Calcd for $C_{29}H_{19}F_7N_3O_5$ $[M+H]^+$: 622.1207; found: 622.1203.



5b

(S)-2-Phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)butanamide (5b)

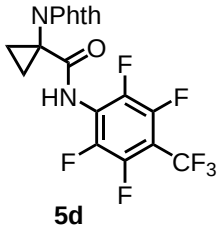
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (br s, 1H), 7.95-7.91 (m, 2H), 7.83-7.79 (m, 2H), 5.00 (dd, J_1 = 6.8 Hz, J_2 = 9.6 Hz, 1H), 2.42-2.25 (m, 2H), 1.02 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 167.1, 134.8, 131.2, 123.9, 57.1, 22.9, 10.6; HRMS (ESI-TOF) Calcd for $C_{19}H_{12}F_7N_2O_3$ $[M+H]^+$: 449.0731; found: 449.0733.



5c

1-Phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)cyclobutanecarboxamide (5c)

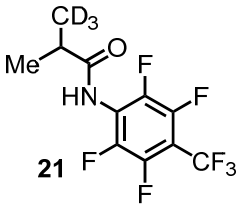
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (br s, 1H), 7.89-7.85 (m, 2H), 7.79-7.76 (m, 2H), 3.14-3.09 (m, 2H), 2.84-2.75 (m, 2H), 2.19-2.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 168.0, 134.6, 131.5, 123.5, 60.8, 31.6, 17.3; HRMS (ESI-TOF) Calcd for $C_{20}H_{12}F_7N_2O_3$ $[M+H]^+$: 461.0731; found: 461.0727.



5d

1-Phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)cyclopropanecarboxamide (5d)

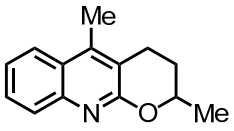
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94-7.91 (m, 2H), 7.84-7.80 (m, 2H), 7.50 (br s, 1H), 1.97 (dd, J_1 = 5.4 Hz, J_2 = 9.0 Hz, 2H), 1.50 (dd, J_1 = 5.4 Hz, J_2 = 9.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.0, 135.0, 131.2, 124.0, 33.5, 17.3; HRMS (ESI-TOF) Calcd for $C_{19}H_9F_7N_2O_3Na$ $[M+Na]^+$: 469.0394; found: 469.0389.



21

3,3,3-Trideuterio-2-methyl-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propionamide (21)

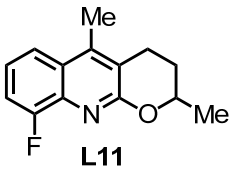
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.00 (br s, 1H), 2.67 (q, J = 7.2 Hz, 1H), 1.31 (d, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.6, 35.6, 19.3; HRMS (ESI-TOF) Calcd for $C_{11}H_6D_3F_7NO$ $[M+H]^+$: 307.0752; found: 307.0754.



L10

2,5-Dimethyl-3,4-dihydro-2*H*-pyrano[2,3-*b*]quinoline (L10)

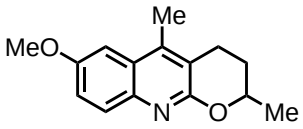
L10 was synthesized according to the literature procedure (*27*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 7.59-7.55 (m, 1H), 7.39-7.35 (m, 1H), 4.42-4.35 (m, 1H), 3.04-2.98 (m, 1H), 2.92-2.83 (m, 1H), 2.56 (s, 3H), 2.18-2.12 (m, 1H), 1.90-1.76 (m, 1H), 1.52 (d, J = 6.4 Hz, 3H).



L11

9-Fluoro-2,5-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-b]quinoline (L11)

L11 was synthesized according to the literature procedure (*27*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.61 (m, 1H), 7.31-7.25 (m, 2H), 4.44-4.36 (m, 1H), 3.04-2.98 (m, 1H), 2.92-2.84 (m, 1H), 2.55 (s, 3H), 2.19-2.13 (m, 1H), 1.91-1.76 (m, 1H), 1.52 (d, *J* = 6.4 Hz, 3H).



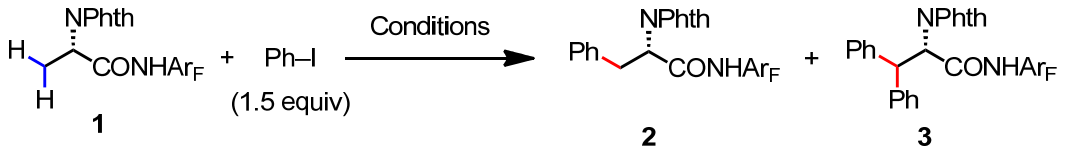
L12

7-Methoxy-2,5-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-b]quinoline (L12)

L12 was synthesized according to the literature procedure (*27*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.8 Hz, 1H), 7.24 (d, *J* = 8.8 Hz, 1H), 7.12 (s, 1H), 4.40-4.34 (m, 1H), 3.93 (s, 3H), 3.02-2.96 (m, 1H), 2.90-2.82 (m, 1H), 2.53 (s, 3H), 2.18-2.11 (m, 1H), 1.90-1.75 (m, 1H), 1.52 (d, *J* = 6.4 Hz, 3H).

B. Ligand-Promoted Primary C(sp^3)–H Arylation

Condition Screening Scheme

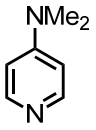
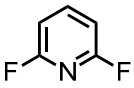
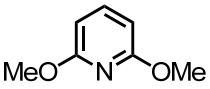
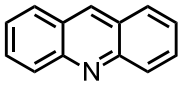


Ar$_F$ = 4-(CF$_3$)C$_6$F$_4$

Condition Screening Tables

Screening experiments were carried out using (S)-2-Phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (**1**) (43.4 mg, 0.1 mmol) as the substrate and iodobenzene. The conditions for each trial are specified in the tables below. All yields were determined by analysis of the crude ^{1}H NMR ($CDCl_3$) spectrum using CH_2Br_2 as the internal standard after filtration of the reaction mixture through a pad of silica gel.

***Table S1*: Ligand Screening**

	—					
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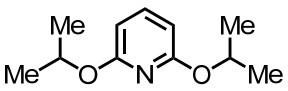
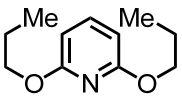
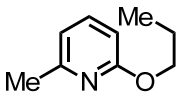
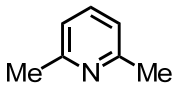
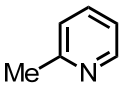
3:	1%	0%	0%	2%	13%	12%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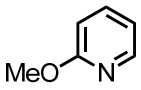
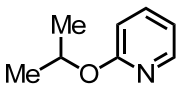
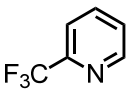
3:	5%	23%	21%	9%	2%

			
2:	59%	83%	66%
3:	1%	17%	3%

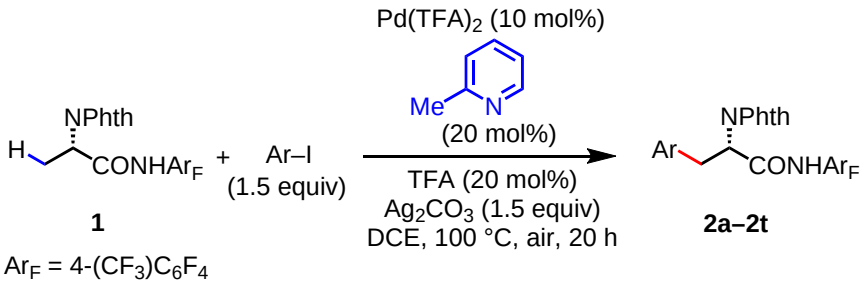
Pd(TFA)$_2$ (10 mol%), ligand (20 mol%), TFA (20 mol%), Ag_2CO_3 (1.5 equiv), DCE, 100 °C, 20 h

***Table S2*: Further Optimization and Control Experiments**

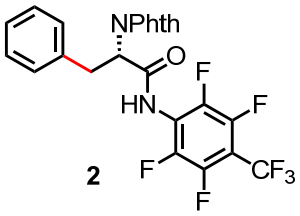
Entry	Pd catalyst (mol%)	**L7** (mol%)	Ag salt (equiv)	Temp. (°C)	^{1}H NMR yield (%) **2**	**3**
1	none	20	Ag_2CO_3 (1.5)	100	0	0
2	$Pd(TFA)_2$ (10)	20	Ag_2CO_3 (1.5)	100	94	2
3	$Pd(TFA)_2$ (10)	40	Ag_2CO_3 (1.5)	100	60	0
4	$Pd(TFA)_2$ (5)	10	Ag_2CO_3 (1.5)	100	79	2
5	$Pd(OAc)_2$ (10)	20	Ag_2CO_3 (1.5)	100	80	10
6	$Pd(TFA)_2$ (10)	20	Ag_3PO_4 (1.5)	100	82	2
7	$Pd(TFA)_2$ (10)	20	Ag_2CO_3 (1)	100	75	2
8	$Pd(TFA)_2$ (10)	20	AgOAc (3)	100	45	1
9	$Pd(TFA)_2$ (10)	20	AgTFA (3)	100	0	0
10	$Pd(TFA)_2$ (10)	20	none	100	0	0
11	$Pd(TFA)_2$ (10)	20	Ag_2CO_3 (1.5)	90	53	1
12	$Pd(TFA)_2$ (10)	20	Ag_2CO_3 (1.5)	80	32	0
13	$Pd(TFA)_2$ (10)	0	Ag_2CO_3 (1.5)	100	47	1
14	$Pd(TFA)_2$ (20)	0	Ag_2CO_3 (1.5)	100	55	1
15	$Pd(TFA)_2$ (30)	0	Ag_2CO_3 (1.5)	100	52	1
16	$Pd(TFA)_2$ (10)	0	Ag_2CO_3 (1.5)	100	32*	N/A

Ph–I (1.5 equiv), TFA (20 mol%), DCE, air, 20 h. *__1__ (1.0 equiv) and **2** (0.5 equiv) were added, and the yield was based on the crude ^{1}H NMR (minus 50% of **2**).

General Procedure Scheme A



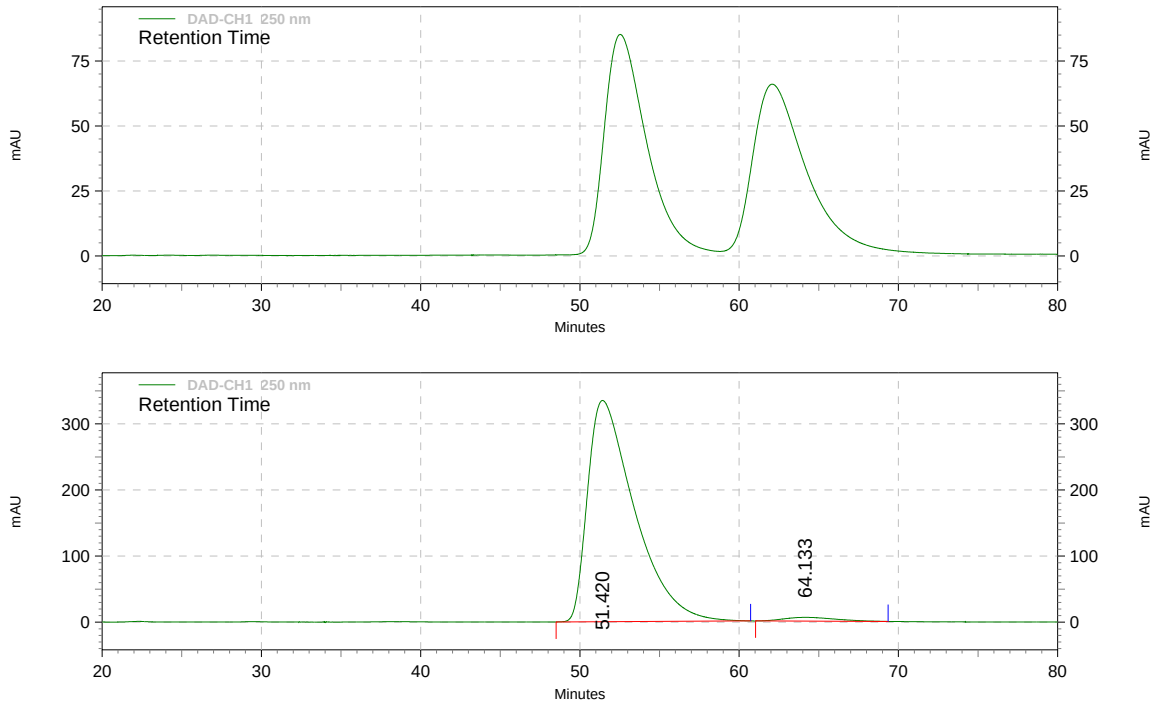
General Arylation Procedure A: Substrate **1** (0.1 mmol, 43.4 mg), $Pd(TFA)_2$ (0.01 mmol, 3.3 mg), and Ag_2CO_3 (0.15 mmol, 41.4 mg) were weighed out open to air and placed in a microwave tube (5 mL) with a magnetic stir bar. The aryl iodide (0.15 mmol), 2-picoline (0.02 mmol, 2 μL), TFA (0.02 mmol, 2 μL), and DCE (0.5 mL) were added. The reaction vessel was sealed and the mixture was first stirred at room temperature for 10 min and then heated to 100 °C for 20 hours with vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using toluene/EtOAc or hexane/EtOAc as the eluent.



(S)-3-Phenyl-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2)

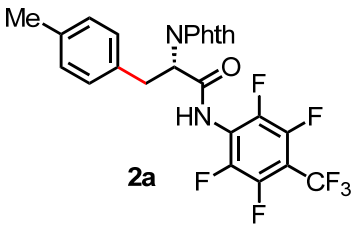
Substrate **1** was arylated following the general arylation procedure A. Analysis of crude reaction mixture by ^1H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using toluene/EtOAc mixtures (30/1) as the eluent, **2** was obtained as a white solid (45.2 mg, 89%, 97% ee). The ee value was determined by HPLC analysis on a Chiralcel OD-H column (20% isopropanol/hexanes, 0.5 mL/min) with t_r 51.4 min (major), 64.1 min (minor). ^1H NMR (600 MHz, $CDCl_3$) δ 8.48 (br s, 1H), 7.84-

7.81 (m, 2H), 7.76-7.73 (m, 2H), 7.23-7.18 (m, 4H), 7.17-7.15 (m, 1H), 5.35 (dd, J_1 = 6.6 Hz, J_2 = 10.8 Hz, 1H), 3.64 (ABqd, J_1 = 6.6 Hz, J_2 = 14.2 Hz, 1H), 3.59 (ABqd, J_1 = 10.8 Hz, J_2 = 14.2 Hz, 1H).



DAD-CH1 250 nm Results

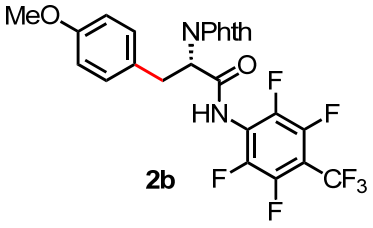
Retention Time	Area	Area %	Height	Height %
51.420	273651794	98.32	1338720	98.42
64.133	4670962	1.68	21523	1.58
Totals	278322756	100.00	1360243	100.00



2a

(S)-2-Phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-3-(*p*-tolyl)propanamide (2a)

Substrate **1** was arylated following the general arylation procedure A. 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 toluene/EtOAc (30/1) as the eluent, **2a** was obtained as a white solid (48.1 mg, 92%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.46 (br s, 1H), 7.83-7.81 (m, 2H), 7.76-7.73 (m, 2H), 7.09 (d, J = 7.8 Hz, 2H), 7.02 (d, J = 7.8 Hz, 2H), 5.32 (dd, J_1 = 6.6 Hz, J_2 = 10.2 Hz, 1H), 3.60 (ABqd, J_1 = 6.6 Hz, J_2 = 14.4 Hz, 1H), 3.54 (ABqd, J_1 = 10.2 Hz, J_2 = 14.4 Hz, 1H), 2.23 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.1, 166.7, 137.1, 134.7, 132.2, 131.1, 129.6, 128.7, 123.8, 56.7, 34.9, 21.0; HRMS (ESI-TOF) Calcd for $C_{25}H_{16}F_7N_2O_3$ $[M+H]^+$: 525.1044; found: 525.1049.

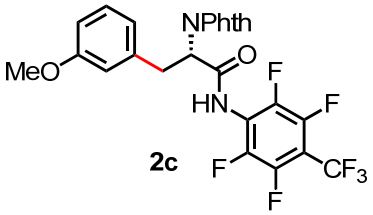


2b

(S)-3-(4-Methoxyphenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2b)

Substrate **1** was arylated following the general arylation procedure A. 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 toluene/EtOAc (30/1) as the eluent, **2b** was obtained as a white solid (48.2 mg, 89%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.52 (br s, 1H), 7.81-7.80 (m, 2H), 7.74-7.72 (m, 2H), 7.11 (d, J = 7.8 Hz, 2H), 6.73 (d, J = 7.8 Hz, 2H),

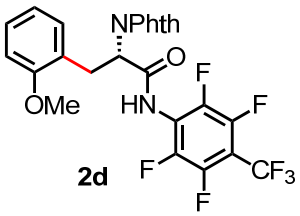
5.29 (dd, J_1 = 6.6 Hz, J_2 = 10.2 Hz, 1H), 3.71 (s, 3H), 3.57 (ABqd, J_1 = 6.6 Hz, J_2 = 14.4 Hz, 1H), 3.52 (ABqd, J_1 = 10.2 Hz, J_2 = 14.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.1, 166.7, 158.7, 134.7, 131.1, 129.9, 127.3, 123.8, 114.2, 56.7, 55.1, 34.5; HRMS (ESI-TOF) Calcd for $C_{25}H_{16}F_7N_2O_4$ $[M+H]^+$: 541.0993; found: 541.0994.



(S)-3-(3-Methoxyphenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2c)

Substrate **1** was arylated following the general arylation procedure A. 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 toluene/EtOAc (30/1) as the eluent, **2c** was obtained as a white solid (46.6 mg, 86%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.49 (br s, 1H), 7.82-7.79 (m, 2H), 7.75-7.73 (m, 2H), 7.12-7.09 (m, 1H), 6.77 (d, J = 7.2 Hz, 1H), 6.73-6.72 (m, 1H), 6.70-6.68 (m, 1H), 5.35 (dd, J_1 = 6.3 Hz, J_2 = 10.5 Hz, 1H), 3.67 (s, 3H), 3.61 (ABqd, J_1 = 6.3 Hz, J_2 = 14.4 Hz, 1H), 3.56 (ABqd, J_1 = 10.5 Hz, J_2 = 14.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.0, 166.6, 159.8, 137.0, 134.7, 131.1, 129.9, 123.8, 121.1, 114.1, 113.3, 56.4, 55.1, 35.3; HRMS (ESI-TOF) Calcd for $C_{25}H_{16}F_7N_2O_4$ $[M+H]^+$: 541.0993; found: 541.0989.

Large scale reaction: Substrate **1** (10 mmol, 4.34 g), $Pd(TFA)_2$ (1.0 mmol, 0.33 g), and Ag_2CO_3 (15 mmol, 4.14 g) were weighed in air and placed in a round-bottom flask (100 mL) with a magnetic stir bar. 3-Iodoanisole (15 mmol, 3.51 g), 2-picoline (2.0 mmol, 0.19 g), TFA (2.0 mmol, 0.23 g), and DCE (35 mL) were added. The pressure vessel was sealed. The reaction mixture was first stirred at room temperature for 10 min and then heated to 100 °C. Upon completion, the reaction mixture was purified by a silica gel-packed flash chromatography column, and **2c** was obtained in 87% yield (4.69 g).

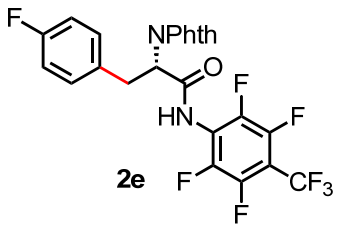


2d

(S)-3-(2-Methoxyphenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2d)

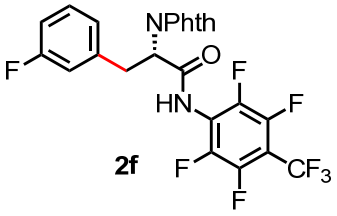
Substrate **1** was arylated following the general arylation procedure A. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using toluene/EtOAc (30/1) as the eluent, **2d** was obtained as a white solid (47.3 mg, 88%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.53 (br s, 1H), 7.80-7.78 (m, 2H), 7.73-7.70 (m, 2H), 7.17-7.14 (m, 1H), 7.08-7.06 (m, 1H), 6.78 (d, J = 7.8 Hz, 1H), 6.76-6.74 (m, 1H), 5.47 (dd, J_1 = 5.7 Hz, J_2 = 9.9 Hz, 1H), 3.77 (s, 3H), 3.65 (ABqd, J_1 = 5.7 Hz, J_2 = 14.1 Hz, 1H), 3.50 (ABqd, J_1 = 9.9 Hz, J_2 = 14.1 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.9, 166.9, 157.3, 134.4, 131.3, 130.9, 128.9, 124.0, 123.6, 120.7, 110.4, 55.2, 54.6, 30.9; HRMS (ESI-TOF) Calcd for $C_{25}H_{16}F_7N_2O_4$ $[M+H]^+$: 541.0993; found: 541.0993.

Large scale reaction: Substrate **1** (15 mmol, 6.51 g), $Pd(TFA)_2$ (1.5 mmol, 0.50 g), and Ag_2CO_3 (22.5 mmol, 6.12 g) were weighed in air and placed in a round-bottom flask (100 mL) with a magnetic stir bar. 2-Iodoanisole (22.5 mmol, 5.27 g), 2-picoline (3.0 mmol, 0.28 g), TFA (3.0 mmol, 0.34 g), and DCE (50 mL) were added. The pressure vessel was sealed. The reaction mixture was first stirred at room temperature for 10 min and then heated to 100 °C. Upon completion, the reaction mixture was purified by a silica gel-packed flash chromatography column, and **2d** was obtained in 80% yield (6.48 g).



(S)-3-(4-Fluorophenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2e)

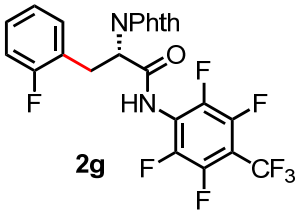
Substrate **1** was arylated following the general arylation procedure A. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using toluene/EtOAc (30/1) mixtures as the eluent, **2e** was obtained as a white solid (47.4 mg, 90%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.54 (br s, 1H), 7.82-7.79 (m, 2H), 7.76-7.73 (m, 2H), 7.16-7.13 (m, 2H), 6.90-6.86 (m, 2H), 5.29 (dd, J_1 = 6.6 Hz, J_2 = 10.2 Hz, 1H), 3.60 (ABqd, J_1 = 6.6 Hz, J_2 = 14.4 Hz, 1H), 3.56 (ABqd, J_1 = 10.2 Hz, J_2 = 14.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.0, 166.5, 162.0 (d, J_{FC} = 244.5 Hz), 134.8, 131.1 (d, J_{FC} = 3.3 Hz), 130.9, 130.5 (d, J_{FC} = 8.0 Hz), 123.9, 115.7 (d, J_{FC} = 21.2 Hz), 56.4, 34.4; HRMS (ESI-TOF) Calcd for $C_{24}H_{13}F_8N_2O_3$ $[M+H]^+$: 529.0793; found: 529.0793.



(S)-3-(3-Fluorophenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2f)

Substrate **1** was arylated following the general arylation procedure A. 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 toluene/EtOAc (30/1) as the eluent, **2f** was

obtained as a white solid (44.1 mg, 84%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.51 (br s, 1H), 7.82-7.79 (m, 2H), 7.76-7.73 (m, 2H), 7.19-7.15 (m, 1H), 6.97 (d, J = 7.2 Hz, 1H), 6.91-6.89 (m, 1H), 6.87-6.83 (m, 1H), 5.32 (dd, J_1 = 6.0 Hz, J_2 = 10.8 Hz, 1H), 3.63 (ABqd, J_1 = 6.0 Hz, J_2 = 14.4 Hz, 1H), 3.58 (ABqd, J_1 = 10.8 Hz, J_2 = 14.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.9, 166.4, 162.8 (d, J_{FC} = 245.4 Hz), 138.0 (d, J_{FC} = 7.4 Hz), 134.8, 130.9, 130.3 (d, J_{FC} = 8.3 Hz), 124.6 (d, J_{FC} = 2.9 Hz), 123.9, 115.9 (d, J_{FC} = 21.3 Hz), 114.4 (d, J_{FC} = 20.7 Hz), 56.1, 34.8; HRMS (ESI-TOF) Calcd for $C_{24}H_{13}F_8N_2O_3$ $[M+H]^+$: 529.0793; found: 529.0794.

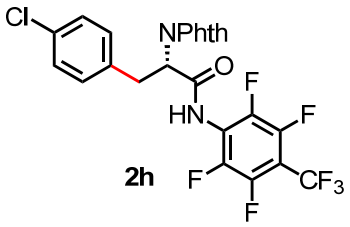


(S)-3-(2-Fluorophenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2g)

Substrate **1** was arylated following the general arylation procedure A. 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 toluene/EtOAc (30/1) as the eluent, **2g** was obtained as a white solid (45.0 mg, 85%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.46 (br s, 1H), 7.81-7.78 (m, 2H), 7.74-7.71 (m, 2H), 7.18-7.13 (m, 2H), 6.96-6.93 (m, 2H), 5.36 (dd, J_1 = 5.7 Hz, J_2 = 10.5 Hz, 1H), 3.67 (ABqd, J_1 = 5.7 Hz, J_2 = 14.1 Hz, 1H), 3.60 (ABqd, J_1 = 10.5 Hz, J_2 = 14.1 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.8, 166.3, 161.3 (d, J_{FC} = 244.7 Hz), 134.7, 131.3 (d, J_{FC} = 4.5 Hz), 131.0, 129.4 (d, J_{FC} = 8.1 Hz), 124.4 (d, J_{FC} = 3.5 Hz), 123.8, 122.7 (d, J_{FC} = 15.5 Hz), 115.5 (d, J_{FC} = 21.6 Hz), 54.8, 29.2 (d, J_{FC} = 2.1 Hz); HRMS (ESI-TOF) Calcd for $C_{24}H_{13}F_8N_2O_3$ $[M+H]^+$: 529.0793; found: 529.0789.

Large scale reaction: Substrate **1** (10 mmol, 4.34 g), $Pd(TFA)_2$ (1.0 mmol, 0.33 g), and Ag_2CO_3 (15 mmol, 4.14 g) were weighed in air and placed in a round-bottom flask (100

mL) with a magnetic stir bar. 1-Fluoro-2-iodobenzene (15 mmol, 3.33 g), 2-picoline (2.0 mmol, 0.19 g), TFA (2.0 mmol, 0.23 g), and DCE (35 mL) were added. The pressure vessel was sealed. The reaction mixture was first stirred at room temperature for 10 min and then heated to 100 °C. Upon completion, the reaction mixture was purified by a silica gel-packed flash chromatography column, and **2g** was obtained in 78% yield (4.11 g).

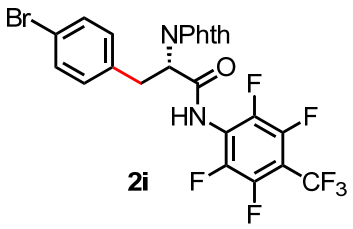


2h

(S)-3-(4-Chlorophenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2h)

Substrate **1** was arylated following the general arylation procedure A. 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 toluene/EtOAc (30/1) as the eluent, **2h** was obtained as a white solid (46.1 mg, 85%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.51 (br s, 1H), 7.82-7.79 (m, 2H), 7.76-7.73 (m, 2H), 7.17 (d, J = 8.4 Hz, 2H), 7.12 (d, J = 7.8 Hz, 2H), 5.30 (dd, J_1 = 6.6 Hz, J_2 = 10.2 Hz, 1H), 3.61-3.54 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.0, 166.4, 134.8, 133.9, 133.3, 130.9, 130.2, 129.0, 123.9, 56.1, 34.5; HRMS (ESI-TOF) Calcd for $C_{24}H_{13}ClF_7N_2O_3$ $[M+H]^+$: 545.0497; found: 545.0496.

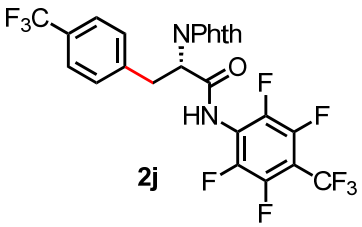
Large scale reaction: Substrate **1** (10 mmol, 4.34 g), $Pd(TFA)_2$ (1.0 mmol, 0.33 g), and Ag_2CO_3 (15 mmol, 4.14 g) were weighed in air and placed in a round-bottom flask (100 mL) with a magnetic stir bar. 1-Chloro-2-iodobenzene (15 mmol, 3.58 g), 2-picoline (2.0 mmol, 0.19 g), TFA (2.0 mmol, 0.23 g), and DCE (35 mL) were added. The pressure vessel was sealed. The reaction mixture was first stirred at room temperature for 10 min and then heated to 100 °C. Upon completion, the reaction mixture was purified by a silica gel-packed flash chromatography column, and **2h** was obtained in 78% yield (4.24 g).



2i

(S)-3-(4-Bromophenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2i)

Substrate **1** was arylated following the general arylation procedure A. 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 toluene/EtOAc (30/1) as the eluent, **2i** was obtained as a white solid (50.7 mg, 86%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.50 (br s, 1H), 7.82-7.80 (m, 2H), 7.76-7.74 (m, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.4 Hz, 2H), 5.30 (dd, J_1 = 6.9 Hz, J_2 = 9.9 Hz, 1H), 3.60-3.53 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.9, 166.4, 134.9, 134.4, 131.9, 130.9, 130.6, 123.9, 121.4, 56.1, 34.6; HRMS (ESI-TOF) Calcd for $C_{24}H_{13}BrF_7N_2O_3$ $[M+H]^+$: 588.9992; found: 588.9999.

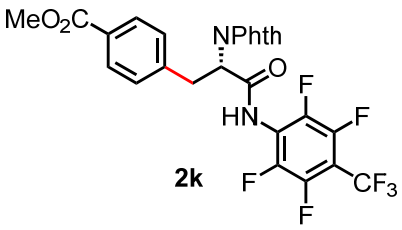


2j

(S)-2-Phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-3-(4-(trifluoromethyl)phenyl)propanamide (2j)

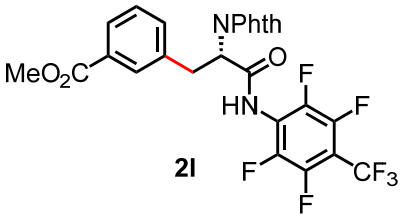
Substrate **1** was arylated following the general arylation procedure A. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using toluene/EtOAc (30/1) as the eluent, **2j** was obtained as a white solid (49.5 mg, 86%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.45 (br s, 1H), 7.83-7.81 (m, 2H), 7.77-7.75 (m, 2H), 7.47 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 5.30 (dd, J_1 = 6.6 Hz, J_2 = 10.2 Hz, 1H), 3.72-3.64 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$)

δ 167.9, 166.2, 139.6, 134.9, 130.8, 129.7 (q, J_{FC} = 32.3 Hz), 129.3, 125.7 (q, J_{FC} = 3.8 Hz), 124.0, 123.9 (q, J_{FC} = 270.5 Hz), 55.9, 34.9; HRMS (ESI-TOF) Calcd for $C_{25}H_{13}F_{10}N_2O_3$ $[M+H]^+$: 579.0761; found: 579.0767.



(S)-Methyl 4-(3-oxo-2-phthalimido-3-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)amino)propyl)benzoate (2k)

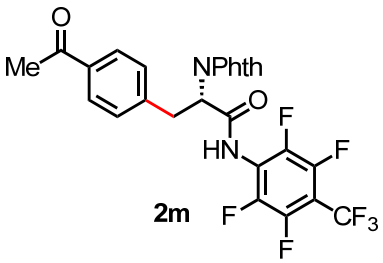
Substrate **1** was arylated following the general arylation procedure A. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using hexane/EtOAc (4/1) as the eluent, **2k** was obtained as a white solid (49.5 mg, 87%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.50 (br s, 1H), 7.86 (d, J = 7.8 Hz, 2H), 7.81-7.79 (m, 2H), 7.74-7.73 (m, 2H), 7.27 (d, J = 7.8 Hz, 2H), 5.36 (dd, J_1 = 7.5 Hz, J_2 = 9.3 Hz, 1H), 3.85 (s, 3H), 3.72-3.64 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.9, 166.7, 166.3, 140.8, 134.9, 130.9, 130.1, 129.2, 129.0, 124.0, 56.0, 52.1, 35.1; HRMS (ESI-TOF) Calcd for $C_{26}H_{16}F_7N_2O_5$ $[M+H]^+$: 569.0942; found: 569.0940.



(S)-Methyl 3-(3-oxo-2-phthalimido-3-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)amino)propyl)benzoate (2l)

Substrate **1** was arylated following the general arylation procedure A. 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 hexane/EtOAc (5/1) as the eluent, **2l** was obtained as a white solid (50.0 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (br s, 1H), 7.85-7.77 (m, 4H), 7.75-7.70 (m, 2H), 7.41-7.38 (m, 1H), 7.30-7.26 (m, 1H), 5.34 (dd, J_1 = 6.0 Hz, J_2 = 10.4 Hz, 1H), 3.80 (s, 3H), 3.69 (ABqd, J_1 = 6.2 Hz, J_2 = 14.3 Hz, 1H), 3.63 (ABqd, J_1 = 10.4 Hz, J_2 = 14.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 166.6, 166.4, 136.0, 134.7, 133.5, 131.0, 130.5, 130.0, 128.9, 128.6, 123.9, 56.2, 52.1, 34.9; HRMS (ESI-TOF) Calcd for $C_{26}H_{16}F_7N_2O_5$ $[M+H]^+$: 569.0942; found: 569.0941.

Large scale reaction: Substrate **1** (10 mmol, 4.34 g), $Pd(TFA)_2$ (1.0 mmol, 0.33 g), and Ag_2CO_3 (15 mmol, 4.14 g) were weighed in air and placed in a round-bottom flask (100 mL) with a magnetic stir bar. Methyl 3-iodobenzoate (15 mmol, 3.93 g), 2-picoline (2.0 mmol, 0.19 g), TFA (2.0 mmol, 0.23 g), and DCE (35 mL) were added. The pressure vessel was sealed. The reaction mixture was first stirred at room temperature for 10 min and then heated to 100 °C. Upon completion, the reaction mixture was purified by a silica gel-packed flash chromatography column, and **2l** was obtained in 78% yield (4.43 g).

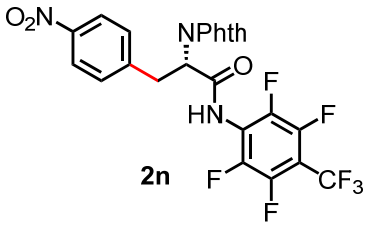


2m

(S)-3-(4-Acetylphenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2m)

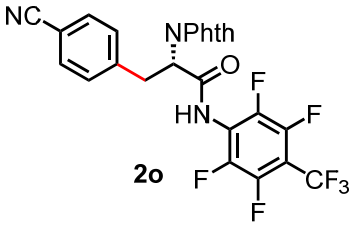
Substrate **1** was arylated following the general arylation procedure A. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using hexane/EtOAc (3/1) as the eluent, **2m** was obtained as a white solid (45.8 mg, 83%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.59 (br s, 1H),

7.81-7.73 (m, 6H), 7.29 (d, J = 7.8 Hz, 2H), 5.37 (dd, J_1 = 6.6 Hz, J_2 = 10.2 Hz, 1H), 3.72-3.65 (m, 2H), 2.50 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.8, 167.9, 166.3, 141.2, 136.0, 134.8, 130.9, 129.2, 128.8, 123.9, 55.8, 35.0, 26.5; HRMS (ESI-TOF) Calcd for $C_{26}H_{16}F_7N_2O_4$ $[M+H]^+$: 553.0993; found: 553.0992.



(S)-3-(4-Nitrophenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2n)

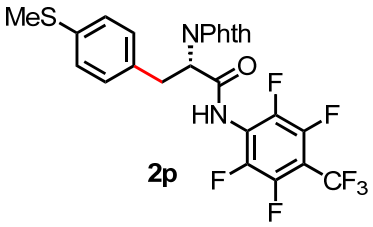
Substrate **1** was arylated following the general arylation procedure A. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using hexane/EtOAc (4/1) as the eluent, **2n** was obtained as a white solid (45.6 mg, 82%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.41 (br s, 1H), 8.06 (d, J = 7.8 Hz, 2H), 7.83-7.81 (m, 2H), 7.78-7.76 (m, 2H), 7.38 (d, J = 7.8 Hz, 2H), 5.37 (dd, J_1 = 6.6 Hz, J_2 = 10.2 Hz, 1H), 3.76-3.69 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.7, 166.0, 147.2, 143.3, 135.1, 130.7, 129.9, 124.1, 124.0, 55.4, 34.8; HRMS (ESI-TOF) Calcd for $C_{24}H_{13}F_7N_3O_5$ $[M+H]^+$: 556.0738; found: 556.0732.



(S)-3-(4-Cyanophenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2o)

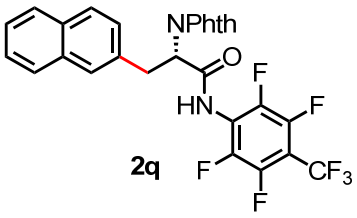
Substrate **1** was arylated following the general arylation procedure A. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After

purification by column chromatography using hexane/EtOAc (5/1) as the eluent, **2o** was obtained as a white solid (45.9 mg, 86%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (br s, 1H), 7.84-7.81 (m, 2H), 7.78-7.75 (m, 2H), 7.48 (d, J = 7.8 Hz, 2H), 7.32 (d, J = 7.8 Hz, 2H), 5.33 (dd, J_1 = 6.0 Hz, J_2 = 10.8 Hz, 1H), 3.70 (ABqd, J_1 = 6.0 Hz, J_2 = 14.3 Hz, 1H), 3.65 (ABqd, J_1 = 10.8 Hz, J_2 = 14.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.7, 166.0, 141.3, 135.0, 132.5, 130.8, 129.8, 124.0, 118.4, 111.2, 55.4, 35.1; HRMS (ESI-TOF) Calcd for $C_{25}H_{13}F_7N_3O_3$ $[M+H]^+$: 536.0840; found: 536.0838.



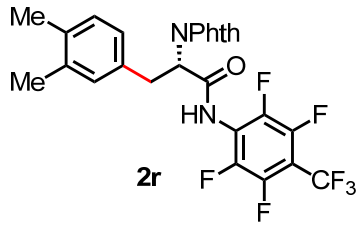
(S)-(4-(Methylthio)phenyl)-2-phthalimido-3-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2p)

Substrate **1** was arylated following the general arylation procedure A. 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 toluene/EtOAc (30/1) as the eluent, **2p** was obtained as a white solid (39.8 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (br s, 1H), 7.83-7.79 (m, 2H), 7.76-7.71 (m, 2H), 7.12-7.06 (m, 4H), 5.31 (dd, J_1 = 6.8 Hz, J_2 = 10.0 Hz, 1H), 3.62-3.52 (m, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 166.6, 137.6, 134.7, 132.0, 131.0, 129.3, 126.7, 123.9, 56.3, 34.7, 15.6; HRMS (ESI-TOF) Calcd for $C_{25}H_{16}F_7N_2O_3S$ $[M+H]^+$: 557.0764; found: 557.0765.



(S)-3-(Naphthalen-2-yl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2q)

Substrate **1** was arylated following the general arylation procedure A. Analysis of crude reaction mixture by ^{1}H NMR showed a 14:1 ratio of mono- and diarylated products. After purification by column chromatography using toluene/EtOAc (30/1) as the eluent, **2q** was obtained as a light yellow solid (50.7 mg, 91%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.52 (br s, 1H), 7.77-7.71 (m, 4H), 7.68-7.62 (m, 4H), 7.41-7.37 (m, 2H), 7.36-7.34 (m, 1H), 5.47 (dd, J_1 = 6.6 Hz, J_2 = 10.2 Hz, 1H), 3.82-3.74 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.1, 166.7, 134.6, 133.3, 132.9, 132.5, 131.0, 128.7, 127.9, 127.6, 127.5, 126.5, 126.2, 125.9, 123.8, 56.3, 35.4; HRMS (ESI-TOF) Calcd for $C_{28}H_{16}F_7N_2O_3$ $[M+H]^+$: 561.1044; found: 561.1048.

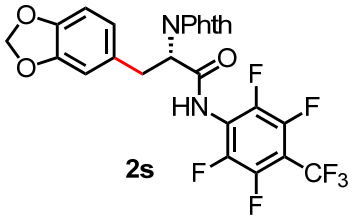


2r

(S)-3-(3,4-Dimethylphenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2r)

Substrate **1** was arylated following the general arylation procedure A. 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 toluene/EtOAc (30/1) as the eluent, **2r** was obtained as a white solid (47.0 mg, 87%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (br s, 1H), 7.83-7.80 (m, 2H), 7.75-7.72 (m, 2H), 6.97-6.96 (m, 2H), 6.94-6.92 (m, 1H), 5.31 (dd, J_1 = 6.6 Hz, J_2 = 10.2 Hz, 1H), 3.58 (ABqd, J_1 = 6.6 Hz, J_2 = 14.4 Hz, 1H), 3.48 (ABqd, J_1 = 10.2 Hz, J_2 = 14.4 Hz, 1H), 2.14 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.1, 166.7, 137.2, 135.7, 134.6, 132.7, 131.2, 130.13, 130.09, 126.1, 123.8, 56.6, 34.9, 19.5, 19.3; HRMS (ESI-TOF) Calcd for $C_{26}H_{18}F_7N_2O_3$ $[M+H]^+$: 539.1200; found: 539.1195.

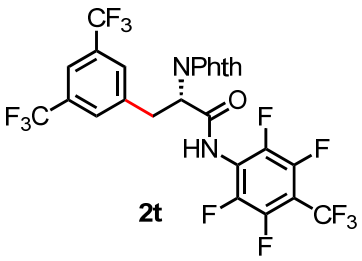
Large scale reaction: Substrate **1** (15 mmol, 6.51 g), $Pd(TFA)_2$ (1.5 mmol, 0.50 g), and Ag_2CO_3 (22.5 mmol, 6.12 g) were weighed in air and placed in a round-bottom flask (100 mL) with a magnetic stir bar. 4-Iodo-*o*-xylene (22.5 mmol, 5.22 g), 2-picoline (3.0 mmol, 0.28 g), TFA (3.0 mmol, 0.34 g), and DCE (50 mL) were added. The pressure vessel was sealed. The reaction mixture was first stirred at room temperature for 10 min and then heated to 100 °C. Upon completion, the reaction mixture was purified by a silica gel-packed flash chromatography column, and **2r** was obtained in 79% yield (6.38 g).



2s

(S)-3-(3,4-Methylenedioxyphenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2s)

Substrate **1** was arylated following the general arylation procedure A. 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 toluene/EtOAc (30/1) as the eluent, **2s** was obtained as a white solid (47.3 mg, 85%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.50 (br s, 1H), 7.85-7.81 (m, 2H), 7.77-7.73 (m, 2H), 6.70 (s, 1H), 6.63-6.60 (m, 2H), 5.88 (ABq, J = 1.5 Hz, 1H), 5.86 (ABq, J = 1.5 Hz, 1H), 5.27 (dd, J_1 = 6.0 Hz, J_2 = 10.2 Hz, 1H), 3.55 (ABqd, J_1 = 6.0 Hz, J_2 = 14.4 Hz, 1H), 3.49 (ABqd, J_1 = 10.2 Hz, J_2 = 14.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.1, 166.6, 148.0, 146.8, 134.7, 131.1, 129.0, 123.9, 122.1, 109.1, 108.5, 101.0, 56.6, 35.0; HRMS (ESI-TOF) Calcd for $C_{25}H_{14}F_7N_2O_5$ $[M+H]^+$: 555.0785; found: 555.0776.

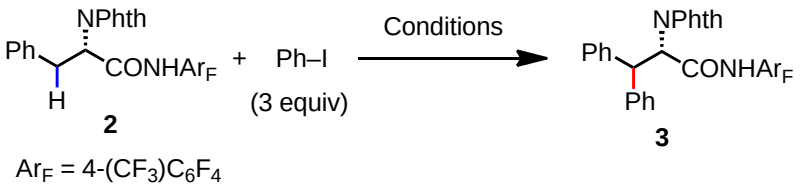


(S)-3-(3,5-Bis(trifluoromethyl)phenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2t)

Substrate **1** was arylated following the general arylation procedure A. 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 toluene/EtOAc (30/1) as the eluent, **2t** was obtained as a white solid (55.4 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (br s, 1H), 7.83-7.73 (m, 4H), 7.68 (s, 1H), 7.63 (s, 2H), 5.31 (dd, J_1 = 6.0 Hz, J_2 = 10.4 Hz, 1H), 3.78 (ABqd, J_1 = 6.0 Hz, J_2 = 14.4 Hz, 1H), 3.68 (ABqd, J_1 = 10.4 Hz, J_2 = 14.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.8, 165.8, 138.3, 135.1, 132.0 (q, J_{FC} = 33.3 Hz), 130.7, 129.3 (q, J_{FC} = 3.6 Hz), 124.0, 122.9 (q, J_{FC} = 271.2 Hz), 121.4-121.3, 55.4, 34.6; HRMS (ESI-TOF) Calcd for $C_{26}H_{12}F_{13}N_2O_3$ $[M+H]^+$: 647.0635; found: 647.0630.

C. Ligand-Promoted Secondary C(sp^3)–H Arylation

Condition Screening Scheme

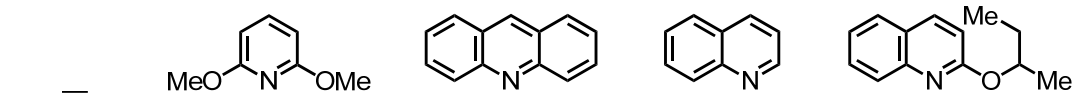


Ar$_F$ = 4-(CF$_3$)C$_6$F$_4$

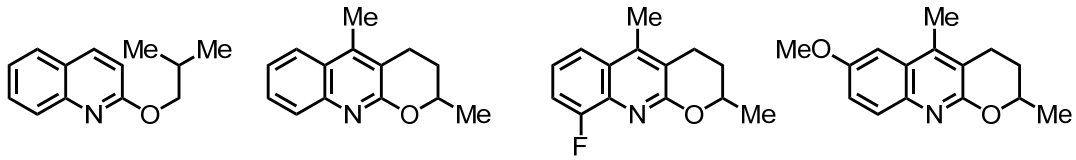
Condition Screening Table

Screening experiments were carried out using (S)-3-Phenyl-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (**2**) (51.0 mg, 0.1 mmol) as the substrate and iodobenzene. The conditions for each trial are specified in the tables below. All yields were determined by analysis of the crude ^{1}H NMR ($CDCl_3$) spectrum using CH_2Br_2 as the internal standard after filtration of the reaction mixture through a pad of silica gel.

***Table S3*: Ligand Screening**



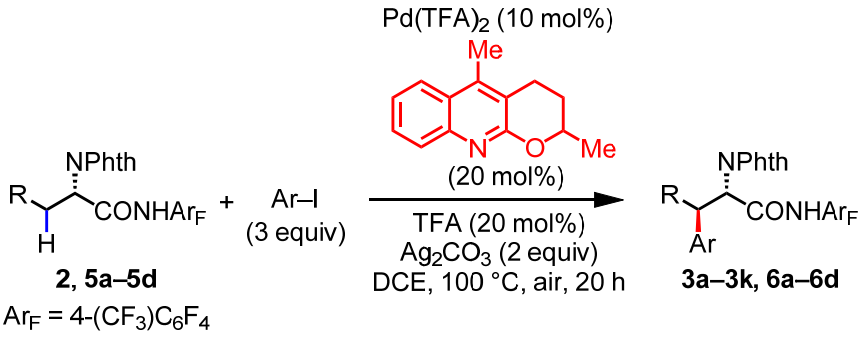
	—				
3:	4%	47%	53%	29%	55%



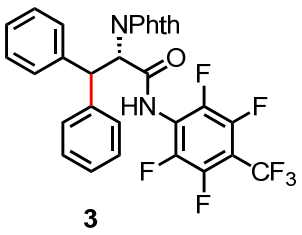
3:	67%	92%	83%	68%

Pd(TFA)$_2$ (10 mol%), ligand (20 mol%), TFA (20 mol%), Ag_2CO_3 (2 equiv), DCE, 100 °C, 20 h

General Procedure Scheme B



General Arylation Procedure B: Substrate **2** or **5a–5d** (0.1 mmol), $Pd(TFA)_2$ (0.01 mmol, 3.3 mg), **L10** (0.02 mmol, 4.3 mg) and Ag_2CO_3 (0.2 mmol, 55.0 mg) were weighed out open to air and placed in a microwave tube (5 mL) with a magnetic stir bar. The aryl iodide (0.3 mmol), TFA (0.02 mmol, 2 μL), and DCE (0.5 mL) were added. The reaction vessel was sealed and the mixture was first stirred at room temperature for 10 min and then heated to 100 °C for 20 hours with vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using toluene/EtOAc or hexane/EtOAc as the eluent.

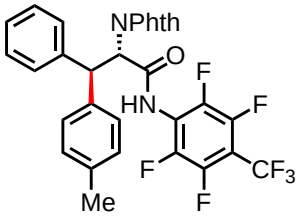


3

(S)-3,3-Diphenyl-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (3)

Substrate **2** was arylated following the general arylation procedure B. After purification by column chromatography using toluene/EtOAc (30/1) as the eluent, **3** was obtained as a white solid (52.7 mg, 90%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.70 (br s, 1H), 7.78-7.76 (m, 2H), 7.70-7.67 (m, 2H), 7.57 (d, *J* = 7.2 Hz, 2H), 7.38-7.36 (m, 2H), 7.32-7.26 (m, 3H), 7.16-7.14 (m, 2H), 7.06-7.04 (m, 1H), 5.90 (d, *J* = 12.6 Hz, 1H), 5.33 (d, *J* = 12.6 Hz, 1H);

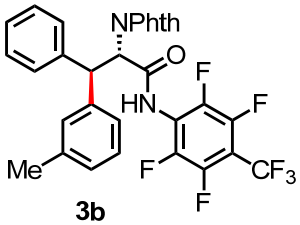
^{13}C NMR (150 MHz, $CDCl_3$) δ 165.3, 139.3, 138.8, 134.6, 130.9, 129.3, 128.8, 128.0, 127.5, 127.4, 123.8, 59.1, 50.9; HRMS (ESI-TOF) Calcd for $C_{30}H_{18}F_7N_2O_3$ $[M+H]^+$: 587.1200; found: 587.1193.



3a

(2S,3R)-3-Phenyl-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-3-(*p*-tolyl)propanamide (3a)

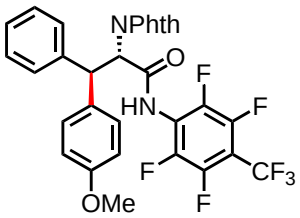
Substrate **2** was arylated following the general arylation procedure B. Analysis of crude reaction mixture by ^{1}H NMR showed a 20:1 diastereomer ratio. After purification by column chromatography using toluene/EtOAc (30/1) as the eluent, **3a** was obtained as a white solid (53.5 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (br s, 1H), 7.78-7.74 (m, 2H), 7.70-7.67 (m, 2H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.31-7.29 (m, 2H), 7.19-7.12 (m, 4H), 7.06-7.02 (m, 1H), 5.89 (d, *J* = 12.8 Hz, 1H), 5.28 (d, *J* = 12.8 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 139.6, 137.8, 135.8, 134.5, 130.9, 130.0, 128.8, 127.8, 127.4, 127.3, 123.7, 59.0, 50.6, 21.1; HRMS (ESI-TOF) Calcd for $C_{31}H_{20}F_7N_2O_3$ $[M+H]^+$: 601.1357; found: 601.1349.



3b

(2S,3R)-3-Phenyl-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-3-(*m*-tolyl)propanamide (3b)

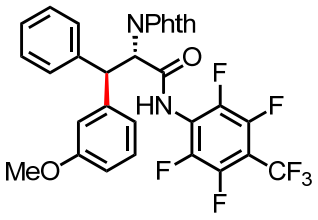
Substrate **2** was arylated following the general arylation procedure B. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 diastereomer ratio. After purification by column chromatography using toluene/EtOAc (30/1) as the eluent, **3b** was obtained as a white solid (51.5 mg, 86%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.54 (br s, 1H), 7.78-7.75 (m, 2H), 7.69-7.66 (m, 2H), 7.39-7.36 (m, 2H), 7.31 (d, *J* = 7.8 Hz, 2H), 7.28-7.25 (m, 1H), 7.16-7.14 (m, 2H), 7.09 (d, *J* = 7.8 Hz, 1H), 7.06-7.03 (m, 1H), 5.89 (d, *J* = 12.6 Hz, 1H), 5.29 (d, *J* = 12.6 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.3, 139.5, 139.1, 138.8, 134.5, 130.9, 129.2, 128.83, 128.80, 128.76, 127.5, 127.3, 124.9, 123.7, 58.9, 50.8, 21.5; HRMS (ESI-TOF) Calcd for $C_{31}H_{20}F_7N_2O_3$ $[M+H]^+$: 601.1357; found: 601.1355.



3c

(2S,3R)-3-(4-Methoxyphenyl)-3-phenyl-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (3c)

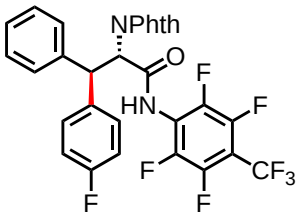
Substrate **2** was arylated following the general arylation procedure B. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 diastereomer ratio. After purification by column chromatography using toluene/EtOAc (30/1) as the eluent, **3c** was obtained as a white solid (52.5 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (br s, 1H), 7.80-7.75 (m, 2H), 7.71-7.66 (m, 2H), 7.50-7.47 (m, 2H), 7.30-7.28 (m, 2H), 7.17-7.13 (m, 2H), 7.06-7.02 (m, 1H), 6.92-6.88 (m, 2H), 5.85 (d, *J* = 12.8 Hz, 1H), 5.28 (d, *J* = 12.8 Hz, 1H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 159.2, 139.7, 134.6, 130.9, 130.8, 129.1, 128.8, 127.4, 127.3, 123.8, 114.7, 59.2, 55.2, 50.2; HRMS (ESI-TOF) Calcd for $C_{31}H_{20}F_7N_2O_4$ $[M+H]^+$: 617.1306; found: 617.1295.



3d

(2S,3R)-3-(3-Methoxyphenyl)-3-phenyl-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (3d)

Substrate **2** was arylated following the general arylation procedure B. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 diastereomer ratio. After purification by column chromatography using toluene/EtOAc (30/1) as the eluent, **3d** was obtained as a white solid (49.6 mg, 81%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (br s, 1H), 7.78-7.76 (m, 2H), 7.70-7.67 (m, 2H), 7.32-7.29 (m, 3H), 7.18-7.14 (m, 3H), 7.09-7.08 (m, 1H), 7.07-7.04 (m, 1H), 6.82-6.80 (m, 1H), 5.89 (d, J = 12.6 Hz, 1H), 5.30 (d, J = 12.6 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.2, 160.1, 140.5, 139.3, 134.6, 130.9, 130.4, 128.8, 127.5, 127.4, 123.8, 120.0, 114.1, 113.1, 58.8, 55.2, 50.8; HRMS (ESI-TOF) Calcd for $C_{31}H_{20}F_7N_2O_4$ $[M+H]^+$: 617.1306; found: 617.1300.

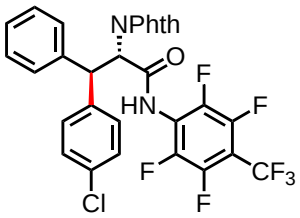


3e

(2S,3R)-3-(4-Fluorophenyl)-3-phenyl-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (3e)

Substrate **2** was arylated following the general arylation procedure B. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 diastereomer ratio. After purification by column chromatography using toluene/EtOAc (30/1) as the eluent, **3e** was obtained as a white solid (46.2 mg, 76%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.93 (br s, 1H), 7.80-7.77 (m,

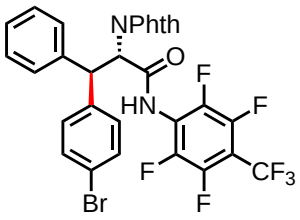
2H), 7.72-7.69 (m, 2H), 7.53-7.51 (m, 2H), 7.29-7.26 (m, 2H), 7.18-7.15 (m, 2H), 7.08-7.03 (m, 3H), 5.83 (d, J = 12.6 Hz, 1H), 5.32 (d, J = 12.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.2, 162.2 (d, J_{FC} = 245.7 Hz), 139.0, 134.7, 134.5 (d, J_{FC} = 3.2 Hz), 130.7, 129.7 (d, J_{FC} = 8.1 Hz), 128.9, 127.6, 127.4, 123.9, 116.1 (d, J_{FC} = 21.5 Hz), 59.4, 50.2; HRMS (ESI-TOF) Calcd for $C_{30}H_{17}F_8N_2O_3$ $[M+H]^+$: 605.1106; found: 605.1097.



3f

(2S,3R)-3-(4-Chlorophenyl)-3-phenyl-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (3f)

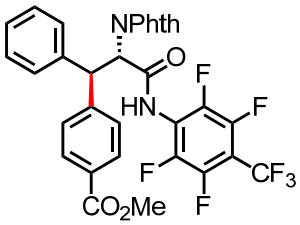
Substrate **2** was arylated following the general arylation procedure B. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 diastereomer ratio. After purification by column chromatography using toluene/EtOAc (30/1) as the eluent, **3f** was obtained as a white solid (45.7 mg, 74%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.92 (br s, 1H), 7.79-7.76 (m, 2H), 7.72-7.69 (m, 2H), 7.48 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.27-7.26 (m, 2H), 7.17-7.14 (m, 2H), 7.08-7.05 (m, 1H), 5.84 (d, J = 12.6 Hz, 1H), 5.31 (d, J = 12.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.2, 138.7, 137.3, 134.8, 133.8, 130.7, 129.4, 129.3, 129.0, 127.7, 127.5, 123.9, 59.2, 50.3; HRMS (ESI-TOF) Calcd for $C_{30}H_{17}ClF_7N_2O_3$ $[M+H]^+$: 621.0810; found: 621.0803.



3g

(2S,3R)-3-(4-Bromophenyl)-3-phenyl-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (3g)

Substrate **2** was arylated following the general arylation procedure B. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 diastereomer ratio. After purification by column chromatography using toluene/EtOAc (30/1) as the eluent, **3g** was obtained as a white solid (47.7 mg, 72%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.91 (br s, 1H), 7.79-7.77 (m, 2H), 7.72-7.70 (m, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.27-7.26 (m, 2H), 7.17-7.14 (m, 2H), 7.08-7.06 (m, 1H), 5.83 (d, *J* = 12.6 Hz, 1H), 5.30 (d, *J* = 12.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.1, 138.6, 137.8, 134.8, 132.2, 130.7, 129.7, 129.0, 127.7, 127.5, 123.9, 121.9, 59.1, 50.4; HRMS (ESI-TOF) Calcd for $C_{30}H_{17}BrF_7N_2O_3$ $[M+H]^+$: 665.0305; found: 665.0290.

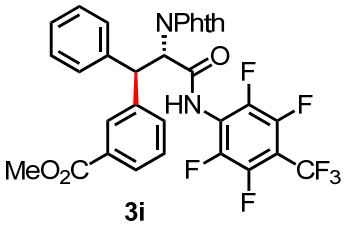


3h

Methyl 4-((1R,2S)-3-oxo-1-phenyl-2-phthalimido-3-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)amino)propyl)benzoate (3h)

Substrate **2** was arylated following the general arylation procedure B. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 diastereomer ratio. After purification by column chromatography using hexane/EtOAc (5/1) as the eluent, **3h** was obtained as a

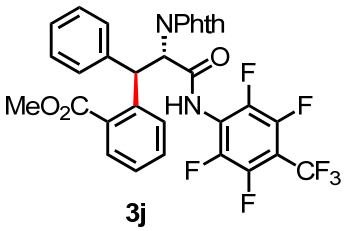
white solid (52.8 mg, 82%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.92 (br s, 1H), 8.02 (d, *J* = 7.8 Hz, 2H), 7.79-7.77 (m, 2H), 7.71-7.69 (m, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.30-7.28 (m, 2H), 7.17-7.15 (m, 2H), 7.08-7.06 (m, 1H), 5.91 (d, *J* = 12.6 Hz, 1H), 5.40 (d, *J* = 12.6 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.6, 165.1, 143.9, 138.4, 134.8, 130.7, 130.4, 129.6, 129.0, 128.1, 127.7, 127.6, 123.9, 58.9, 52.1, 50.8; HRMS (ESI-TOF) Calcd for $C_{32}H_{20}F_7N_2O_5$ $[M+H]^+$: 645.1255; found: 645.1246.



3i

Methyl 3-((1R,2S)-3-oxo-1-phenyl-2-phthalimido-3-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)amino)propyl)benzoate (3i)

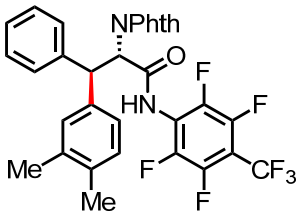
Substrate **2** was arylated following the general arylation procedure B. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 diastereomer ratio. After purification by column chromatography using hexane/EtOAc (5/1) as the eluent, **3i** was obtained as a white solid (50.2 mg, 78%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.97 (br s, 1H), 8.21-8.20 (m, 1H), 7.95-7.93 (m, 1H), 7.80-7.77 (m, 3H), 7.72-7.69 (m, 2H), 7.46-7.44 (m, 1H), 7.33-7.31 (m, 2H), 7.18-7.15 (m, 2H), 7.09-7.06 (m, 1H), 5.92 (d, *J* = 12.6 Hz, 1H), 5.42 (d, *J* = 12.6 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.6, 165.1, 139.3, 138.6, 134.7, 132.5, 130.9, 130.8, 129.25, 129.23, 129.1, 129.0, 127.7, 127.6, 123.9, 59.1, 52.2, 50.6; HRMS (ESI-TOF) Calcd for $C_{32}H_{20}F_7N_2O_5$ $[M+H]^+$: 645.1255; found: 645.1264.



3j

Methyl 2-((1R,2S)-3-oxo-1-phenyl-2-phthalimido-3-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)amino)propyl)benzoate (3j)

Substrate **2** was arylated following the general arylation procedure B. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 diastereomer ratio. After purification by column chromatography using hexane/EtOAc (5/1) as the eluent, **3j** was obtained as a white solid (43.8 mg, 68%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.76 (br s, 1H), 7.90 (d, J = 7.8 Hz, 1H), 7.84-7.80 (m, 3H), 7.72-7.69 (m, 2H), 7.62-7.59 (m, 1H), 7.35-7.33 (m, 3H), 7.17-7.14 (m, 2H), 7.08-7.06 (m, 1H), 6.75 (d, J = 12.6 Hz, 1H), 6.01 (d, J = 12.6 Hz, 1H), 4.01 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 165.2, 140.0, 138.9, 134.5, 132.8, 131.0, 130.9, 129.6, 128.9, 128.0, 127.6, 127.52, 127.49, 123.8, 58.9, 52.9, 42.6; HRMS (ESI-TOF) Calcd for $C_{32}H_{20}F_7N_2O_5$ $[M+H]^+$: 645.1255; found: 645.1248.

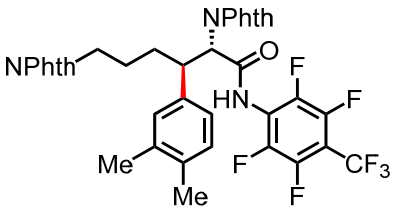


3k

(2S,3R)-3-(3,4-Dimethylphenyl)-3-phenyl-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (3k)

Substrate **2** was arylated following the general arylation procedure B. Analysis of crude reaction mixture by ^{1}H NMR showed a 19:1 diastereomer ratio. After purification by column chromatography using toluene/EtOAc (30/1) as the eluent, **3k** was obtained as a white solid (54.2 mg, 88%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.48 (br s, 1H), 7.77-7.75 (m,

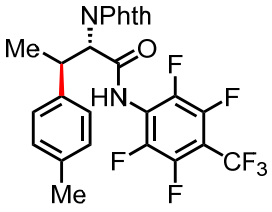
2H), 7.69-7.66 (m, 2H), 7.32-7.30 (m, 4H), 7.15-7.13 (m, 3H), 7.04-7.02 (m, 1H), 5.88 (d, J = 12.6 Hz, 1H), 5.25 (d, J = 12.6 Hz, 1H), 2.25 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.4, 139.8, 137.8, 136.5, 136.3, 134.5, 131.0, 130.6, 129.2, 128.8, 127.4, 127.2, 125.1, 123.7, 58.8, 50.6, 19.9, 19.4; HRMS (ESI-TOF) Calcd for $C_{32}H_{22}F_7N_2O_3$ $[M+H]^+$: 615.1513; found: 615.1512.



6a

(2S,3R)-3-(3,4-Dimethylphenyl)-2,6-bis(phthalimido)-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)hexanamide (6a)

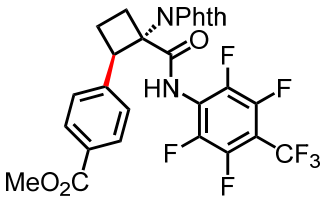
Substrate **5a** was arylated following the general arylation procedure B. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 diastereomer ratio. After purification by column chromatography using hexane/EtOAc (3/1) as the eluent, **6a** was obtained as a white solid (47.8 mg, 66%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30 (br s, 1H), 7.92-7.89 (m, 2H), 7.82-7.79 (m, 2H), 7.73-7.70 (m, 2H), 7.68-7.65 (m, 2H), 7.14-7.11 (m, 3H), 5.24 (d, J = 11.4 Hz, 1H), 3.87-3.83 (m, 1H), 3.51 (t, J = 7.5 Hz, 2H), 2.25 (s, 3H), 2.22 (s, 3H), 1.68-1.56 (m, 2H), 1.46-1.41 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.1, 165.3, 137.8, 136.7, 135.3, 134.7, 133.8, 131.9, 131.3, 130.6, 129.4, 125.6, 124.0, 123.1, 60.6, 43.9, 37.3, 30.1, 25.6, 19.8, 19.5; HRMS (ESI-TOF) Calcd for $C_{37}H_{27}F_7N_3O_5$ $[M+H]^+$: 726.1833; found: 726.1826.



6b

(2S,3R)-2-Phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-3-(*p*-tolyl)butanamide (6b)

Substrate **5b** was arylated following the general arylation procedure B. Analysis of crude reaction mixture by ^{1}H NMR showed a 15:1 diastereomer ratio. After purification by column chromatography using hexane/EtOAc (4/1) as the eluent, **6b** was obtained as a white solid (47.6 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (br s, 1H), 7.98-7.93 (m, 2H), 7.84-7.80 (m, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 5.22 (d, *J* = 12.0 Hz, 1H), 4.07-3.99 (m, 1H), 2.34 (s, 3H), 1.26 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 165.5, 137.79, 137.77, 134.8, 131.2, 130.0, 127.4, 124.0, 61.4, 39.0, 21.1, 20.0; HRMS (ESI-TOF) Calcd for $C_{26}H_{18}F_7N_2O_3$ $[M+H]^+$: 539.1200; found: 539.1196.

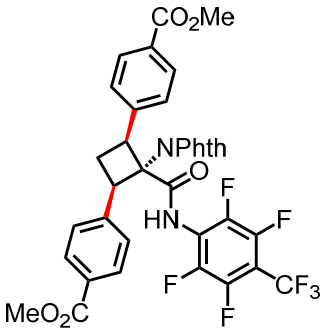


6c-mono

Methyl 4-(2-phthalimido-2-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)carbamoyl)cyclobutyl)benzoate (6c-mono)

Substrate **5c** was arylated following the general arylation procedure B. After purification by column chromatography using hexane/EtOAc (4/1) as the eluent, **6c-mono** was obtained as a white solid (35.6 mg, 60%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.4 Hz, 2H), 7.91-7.87 (m, 2H), 7.81-7.78 (m, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.29 (br s, 1H), 4.75 (t, *J* = 9.9

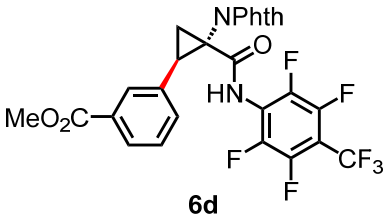
Hz, 1H), 3.84 (s, 3H), 3.45-3.42 (m, 1H), 2.64-2.57 (m, 1H), 2.55-2.50 (m, 1H), 2.43-2.38 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.0, 167.0, 166.9, 143.2, 134.8, 131.5, 129.42, 129.39, 129.0, 123.7, 67.5, 52.0, 47.4, 28.3, 23.1; HRMS (ESI-TOF) Calcd for $C_{28}H_{18}F_7N_2O_5$ $[M+H]^+$: 595.1098; found: 595.1101.



6c-di

Dimethyl 4,4'-(2-phthalimido-2-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)carbamoyl)cyclobutane-1,3-diyl)dibenzoate (6c-di)

6c-di was obtained as a yellow solid (22.0 mg, 30%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97-7.92 (m, 6H), 7.83-7.81 (m, 2H), 7.56 (d, *J* = 8.4 Hz, 4H), 7.36 (br s, 1H), 4.90-4.87 (m, 2H), 3.84 (s, 6H), 3.24-3.19 (m, 1H), 2.80-2.75 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.4, 167.0, 164.6, 142.6, 135.0, 131.4, 129.2, 129.0, 128.9, 123.9, 72.6, 52.0, 45.7, 26.8; HRMS (ESI-TOF) Calcd for $C_{36}H_{24}F_7N_2O_7$ $[M+H]^+$: 729.1466; found: 729.1453.



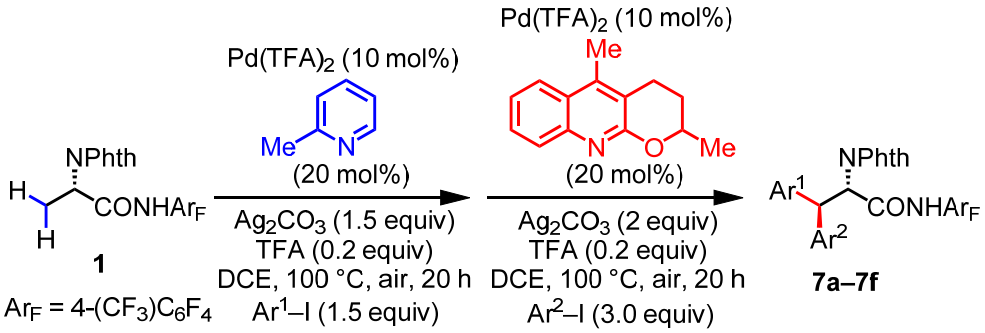
6d

Methyl 3-(2-phthalimido-2-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)carbamoyl)cyclopropyl)benzoate (6d)

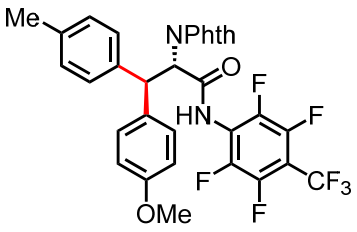
Substrate **5d** was arylated following the general arylation procedure B. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using hexane/EtOAc (2/1) as the eluent, **6d** was obtained as a yellow solid (40.5 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (br s, 1H), 7.95-7.91 (m, 3H), 7.84-7.78 (m, 4H), 7.45 (t, J = 7.6 Hz, 1H), 3.90 (s, 3H), 3.08 (t, J = 9.6 Hz, 1H), 2.76 (dd, J_1 = 7.2 Hz, J_2 = 9.2 Hz, 1H), 2.05 (dd, J_1 = 7.2 Hz, J_2 = 10.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.8, 164.3, 135.0, 133.8, 131.2, 130.4, 130.1, 129.2, 128.7, 124.0, 52.2, 40.5, 33.8, 17.4; HRMS (ESI-TOF) Calcd for $C_{27}H_{16}F_7N_2O_5$ $[M+H]^+$: 581.0942; found: 581.0943.

D. Sequential C(sp^3)–H Arylation Reactions

General Procedure Scheme C



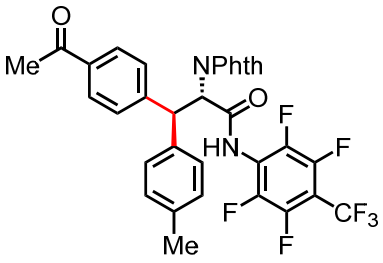
General Arylation Procedure C: Substrate **1** (0.1 mmol, 43.4 mg), $Pd(TFA)_2$ (0.01 mmol, 3.3 mg), and Ag_2CO_3 (0.15 mmol, 41.4 mg) were weighed out open to air and placed in a microwave tube (5 mL) with a magnetic stir bar. Ar^1–I (0.15 mmol), 2-picoline (0.02 mmol, 2 μL), TFA (0.02 mmol, 2 μL), and DCE (0.5 mL) were added and the reaction vessel was sealed. The reaction mixture was first stirred at room temperature for 10 min and then heated to 100 °C for 20 hours with vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. $Pd(TFA)_2$ (0.01 mmol, 3.3 mg), **L10** (0.02 mmol, 4.3 mg), and Ag_2CO_3 (0.2 mmol, 55.0 mg) were weighed open to air and added in the reaction mixture. Ar^2–I (0.3 mmol) and TFA (0.02 mmol, 2 μL) were then added. The reaction vessel was sealed. The mixture was first stirred at room temperature for 10 min and then heated to 100 °C for 20 hours with vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using toluene/EtOAc or hexane/EtOAc as the eluent.



7a

(2S,3R)-3-(4-Methoxyphenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-3-(*p*-tolyl)propanamide (7a)

Substrate **1** was arylated following the general arylation procedure C. Analysis of crude reaction mixture by ^{1}H NMR showed a 19:1 diastereomer ratio. 19% of monoarylated products were observed. After purification by column chromatography using toluene/EtOAc (30/1) as the eluent, **7a** was obtained as a white solid (42.9 mg, 68%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.68 (br s, 1H), 7.79-7.78 (m, 2H), 7.70-7.69 (m, 2H), 7.46 (d, *J* = 7.8 Hz, 2H), 7.17 (d, *J* = 7.8 Hz, 2H), 6.95 (d, *J* = 7.8 Hz, 2H), 6.89 (d, *J* = 7.8 Hz, 2H), 5.83 (d, *J* = 12.6 Hz, 1H), 5.24 (d, *J* = 12.6 Hz, 1H), 3.77 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.5, 159.1, 136.9, 136.7, 134.5, 131.1, 131.0, 129.5, 129.0, 127.2, 123.8, 114.7, 59.2, 55.2, 49.8, 20.9; HRMS (ESI-TOF) Calcd for $C_{32}H_{22}F_7N_2O_4$ $[M+H]^+$: 631.1462; found: 631.1460.

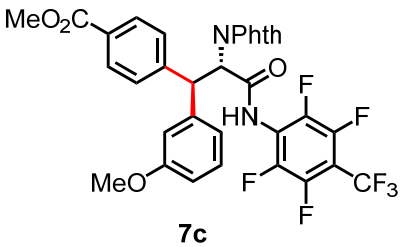


7b

(2S,3S)-3-(4-Acetylphenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-3-(*p*-tolyl)propanamide (7b)

Substrate **1** was arylated following the general arylation procedure C. Analysis of crude reaction mixture by ^{1}H NMR showed a 19:1 diastereomer ratio. 23% of monoarylated products were observed. After purification by column chromatography using hexane/EtOAc (3/1) as the eluent, **7b** was obtained as a white solid (39.7 mg, 62%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.54 (br s, 1H), 7.76-7.73 (m, 4H), 7.69-7.66 (m, 2H), 7.44-7.40 (m, 4H), 7.17 (d, *J* = 7.8 Hz, 2H), 5.91 (d, *J* = 12.6 Hz, 1H), 5.41 (d, *J* = 12.6 Hz, 1H), 2.43 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.5, 165.0, 145.1, 138.2, 136.0, 135.1, 134.7, 130.8, 130.2, 128.9, 127.8, 127.7, 123.9, 58.4, 50.3, 26.5, 21.0; HRMS (ESI-TOF) Calcd for $C_{33}H_{22}F_7N_2O_4$ $[M+H]^+$: 643.1462; found: 643.1458.

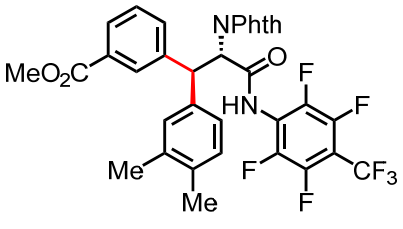
Large scale reaction: Substrate **1** (5 mmol, 2.17 g), $Pd(TFA)_2$ (0.5 mmol, 0.17 g), and Ag_2CO_3 (7.5 mmol, 2.07 g) were weighed out open to air and added in a round-bottom flask (100 mL) with a magnetic stir bar. 4'-Iodoacetophenone (7.5 mmol, 1.85 g), 2-picoline (1 mmol, 100 μL), TFA (1 mmol, 0.11 g), and DCE (25 mL) were added and the pressure vessel was sealed. The reaction mixture was first stirred at room temperature for 10 min and then heated to 100 °C for 20 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. $Pd(TFA)_2$ (0.5 mmol, 0.17 g), **L10** (1 mmol, 0.21 g), Ag_2CO_3 (10 mmol, 2.75 g), and 4-iodotoluene (15 mmol, 3.27 g) were weighed out open to air and added in the reaction vessel, and TFA (1 mmol, 0.11 g) was then added. The vessel was sealed. The reaction mixture was first stirred at room temperature for 10 min and then heated to 100 °C for 20 hours under vigorous stirring. Upon completion, the resulting mixture was purified by a silica gel-packed flash chromatography column, and **7b** was obtained in 60% yield (1.92 g).



7c

Methyl 4-((1R,2S)-1-(3-methoxyphenyl)-3-oxo-2-phthalimido-3-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)amino)propyl)benzoate (7c)

Substrate **1** was arylated following the general arylation procedure C. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 diastereomer ratio. 25% of monoarylated products were observed. After purification by column chromatography using hexane/EtOAc (5/1) as the eluent, **7c** was obtained as a white solid (43.5 mg, 65%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.45 (br s, 1H), 7.84 (d, *J* = 7.8 Hz, 2H), 7.78-7.77 (m, 2H), 7.71-7.69 (m, 2H), 7.40 (d, *J* = 7.8 Hz, 2H), 7.33-7.30 (m, 1H), 7.16 (d, *J* = 7.8 Hz, 1H), 7.07 (s, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 5.90 (d, *J* = 12.6 Hz, 1H), 5.41 (d, *J* = 12.6 Hz, 1H), 3.80 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.5, 164.9, 160.2, 144.5, 139.7, 134.7, 130.8, 130.6, 130.2, 129.3, 127.6, 123.9, 120.0, 114.2, 113.3, 58.3, 55.3, 52.1, 50.6; HRMS (ESI-TOF) Calcd for $C_{33}H_{22}F_7N_2O_6$ $[M+H]^+$: 675.1361; found: 675.1358.

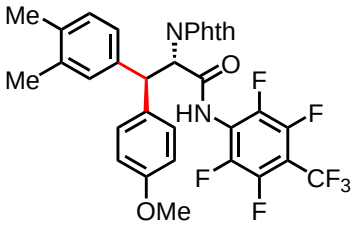


7d

Methyl 3-((1S,2S)-1-(3,4-dimethylphenyl)-3-oxo-2-phthalimido-3-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)amino)propyl)benzoate (7d)

Substrate **1** was arylated following the general arylation procedure C. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 diastereomer ratio. 16% of monoarylated products were observed. After purification by column chromatography using

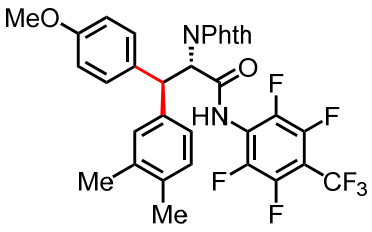
hexane/EtOAc (3/1) as the eluent, **7d** was obtained as a white solid (44.1 mg, 66%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (br s, 1H), 7.97 (s, 1H), 7.79-7.76 (m, 2H), 7.75-7.73 (m, 1H), 7.70-7.67 (m, 2H), 7.55-7.53 (m, 1H), 7.33-7.31 (m, 2H), 7.27-7.24 (m, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 5.90 (d, *J* = 12.6 Hz, 1H), 5.34 (d, *J* = 12.6 Hz, 1H), 3.84 (s, 3H), 2.26 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.5, 165.2, 140.3, 138.0, 136.8, 135.8, 134.6, 131.6, 130.9, 130.7, 130.6, 129.2, 129.0, 128.9, 128.6, 125.1, 123.8, 58.6, 52.1, 50.3, 19.9, 19.4; HRMS (ESI-TOF) Calcd for $C_{34}H_{24}F_7N_2O_5$ $[M+H]^+$: 673.1568; found: 673.1566.



7e

(2S,3S)-3-(3,4-Dimethylphenyl)-3-(4-methoxyphenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (7e)

Substrate **1** was arylated following the general arylation procedure C. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 diastereomer ratio. 19% of monoarylated products were observed. After purification by column chromatography using toluene/EtOAc (30/1) as the eluent, **7e** was obtained as a white solid (37.8 mg, 59%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.69 (br s, 1H), 7.80-7.78 (m, 2H), 7.70-7.69 (m, 2H), 7.46 (d, *J* = 7.8 Hz, 2H), 7.02-7.01 (m, 2H), 6.90-6.87 (m, 3H), 5.82 (d, *J* = 12.6 Hz, 1H), 5.20 (d, *J* = 12.6 Hz, 1H), 3.76 (s, 3H), 2.07 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.6, 159.1, 137.03, 136.99, 135.5, 134.5, 131.2, 131.0, 130.0, 129.0, 128.8, 124.3, 123.8, 114.6, 59.3, 55.2, 49.7, 19.7, 19.2; HRMS (ESI-TOF) Calcd for $C_{33}H_{24}F_7N_2O_4$ $[M+H]^+$: 645.1619; found: 645.1618.



7f

(2S,3R)-3-(3,4-Dimethylphenyl)-3-(4-methoxyphenyl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (7f)

Substrate **1** was arylated following the general arylation procedure C. Analysis of crude reaction mixture by ^{1}H NMR showed a 16:1 diastereomer ratio. 15% of monoarylated products were observed. After purification by column chromatography using toluene/EtOAc (30/1) as the eluent, **7f** was obtained as a white solid (38.8 mg, 60%). **7f** was recrystallized in EtOAc/hexane, and the structure was determined by X-ray diffraction. $[\alpha]_D^{20}$ = -31.5 (c = 1.00, $CHCl_3$); m.p. 192-193 °C (EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (br s, 1H), 7.81-7.76 (m, 2H), 7.71-7.69 (m, 2H), 7.30-7.28 (m, 2H), 7.23-7.20 (m, 2H), 7.14-7.12 (m, 1H), 6.69-6.65 (m, 2H), 5.83 (d, *J* = 12.4 Hz, 1H), 5.19 (d, *J* = 12.4 Hz, 1H), 3.63 (s, 3H), 2.25 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.5, 158.5, 137.7, 136.7, 136.4, 134.5, 131.9, 131.0, 130.6, 129.1, 128.5, 125.0, 123.8, 114.2, 58.9, 55.1, 49.8, 19.9, 19.4; HRMS (ESI-TOF) Calcd for $C_{33}H_{24}F_7N_2O_4$ $[M+H]^+$: 645.1619; found: 645.1622.

Figure S1. X-ray Crystallographic Data of **7f**

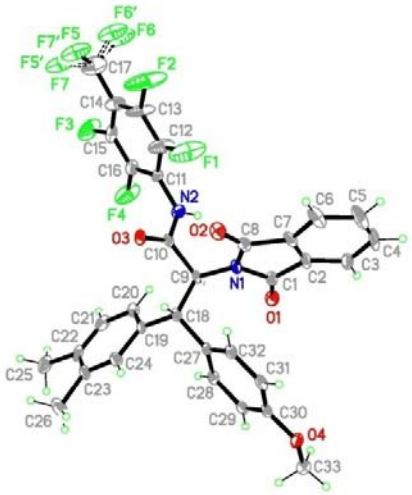


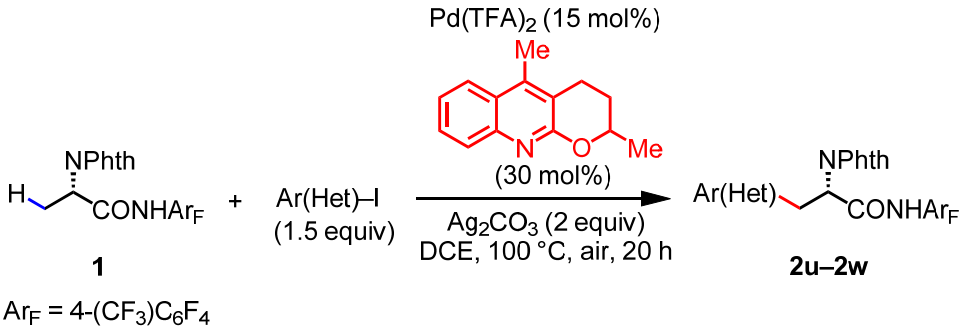
***Table S4*: Crystal Data and Structure Refinement for 7f**

CCDC-985675		
Identification code	**7f**	
Empirical formula	$C_{33}H_{23}F_7N_2O_4$	
Molecular formula	$C_{33}H_{23}F_7N_2O_4$	
Formula weight	644.53	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2	
Unit cell dimensions	a = 47.544(18) Å	α = 90°.
	b = 5.5459(19) Å	β = 92.544(9)°.
	c = 21.860(7) Å	γ = 90°.
Volume	5758(3) $Å^3$	

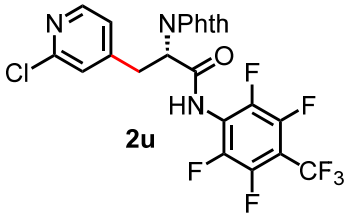
Z	8
Density (calculated)	1.487 Mg/m^3
Absorption coefficient	0.128 mm^{-1}
F(000)	2640
Crystal size	0.18 x 0.05 x 0.02 mm^3
Crystal color, habit	colourless PLATE
Theta range for data collection	1.71 to 25.71°.
Index ranges	-50<=h<=58, -6<=k<=6, -26<=l<=26
Reflections collected	18316
Independent reflections	10714 [R(int) = 0.0343]
Completeness to theta = 25.00°	99.8 %
Absorption correction	multi-scan / sadabs
Max. and min. transmission	0.9974 and 0.9773
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	10714 / 35 / 954
Goodness-of-fit on F^2	1.005
Final R indices [I>2sigma(I)]	R1 = 0.0597, wR2 = 0.1179
R indices (all data)	R1 = 0.1199, wR2 = 0.1407
Absolute structure parameter	-1.2(8)
Largest diff. peak and hole	0.314 and -0.371 $e.Å^{-3}$

E. Ligand-Enabled C(sp^3)–H Arylation with Heteroaryl Iodides

General Procedure Scheme D



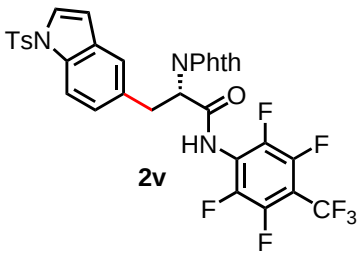
General Arylation Procedure D: Substrate **1** (0.1 mmol), $Pd(TFA)_2$ (0.015 mmol, 5.0 mg), **L10** (0.03 mmol, 6.5 mg) and Ag_2CO_3 (0.2 mmol, 55 mg) were weighed out open to air and placed in a microwave tube (5 mL) with a magnetic stir bar. The heteroaryl iodide (0.15 mmol) and DCE (0.5 mL) were added. The reaction vessel was sealed and the mixture was first stirred at room temperature for 10 min and then heated to 100 °C for 20 hours with vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using hexane/EtOAc as the eluent.



(S)-3-(2-Chloropyridin-4-yl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2u)

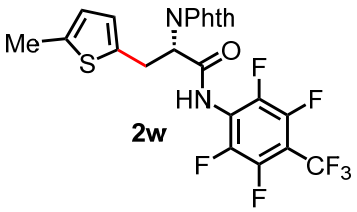
Substrate **1** was arylated following the general arylation procedure D. Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using hexane/EtOAc (4/1) as the eluent, **2u** was obtained as a white solid (29.8 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (br s, 1H),

8.21-8.20 (m, 1H), 7.85-7.80 (m, 2H), 7.79-7.74 (m, 2H), 7.17-7.16 (m, 1H), 7.09-7.07 (m, 1H), 5.35 (dd, J_1 = 6.4 Hz, J_2 = 10.4 Hz, 1H), 3.66 (ABqd, J_1 = 6.4 Hz, J_2 = 14.4 Hz, 1H), 3.59 (ABqd, J_1 = 10.4 Hz, J_2 = 14.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 165.8, 152.0, 149.9, 148.4, 135.0, 130.8, 124.7, 124.1, 122.8, 54.5, 34.0; HRMS (ESI-TOF) Calcd for $C_{23}H_{12}ClF_7N_3O_3$ $[M+H]^+$: 546.0450; found: 546.0451.



(S)-2-Phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-3-(1-tosyl-1*H*-indol-5-yl)propanamide (2v)

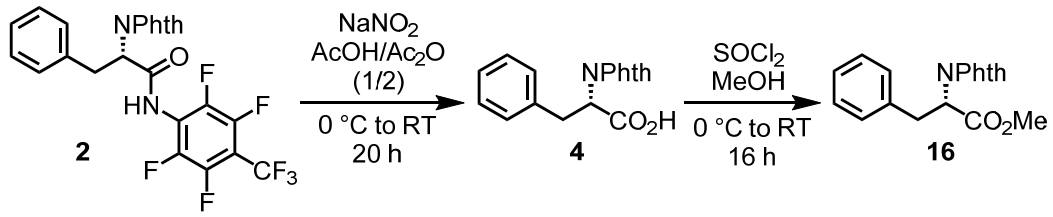
Substrate **1** was arylated following the general arylation procedure D. Analysis of crude reaction mixture by ^{1}H NMR showed a 12:1 ratio of mono- and diarylated products. After purification by column chromatography using hexane/EtOAc (3/1) as the eluent, **2v** was obtained as a white solid (45.5 mg, 65%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.40 (br s, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.79-7.76 (m, 2H), 7.72-7.70 (m, 2H), 7.68 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 3.6 Hz, 1H), 7.37-7.36 (m, 1H), 7.18 (d, J = 7.8 Hz, 2H), 7.14-7.13 (m, 1H), 6.50 (d, J = 3.6 Hz, 1H), 5.35 (dd, J_1 = 6.6 Hz, J_2 = 10.2 Hz, 1H), 3.70 (ABqd, J_1 = 6.6 Hz, J_2 = 14.4 Hz, 1H), 3.61 (ABqd, J_1 = 10.2 Hz, J_2 = 14.4 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.1, 166.6, 145.0, 135.1, 134.7, 134.0, 131.2, 131.0, 130.5, 129.8, 126.9, 126.7, 125.3, 123.9, 121.7, 113.9, 108.8, 56.7, 35.1, 21.5; HRMS (ESI-TOF) Calcd for $C_{33}H_{21}F_7N_3O_5S$ $[M+H]^+$: 704.1085; found: 704.1085.



(S)-3-(5-Methylthiophen-2-yl)-2-phthalimido-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (2w)

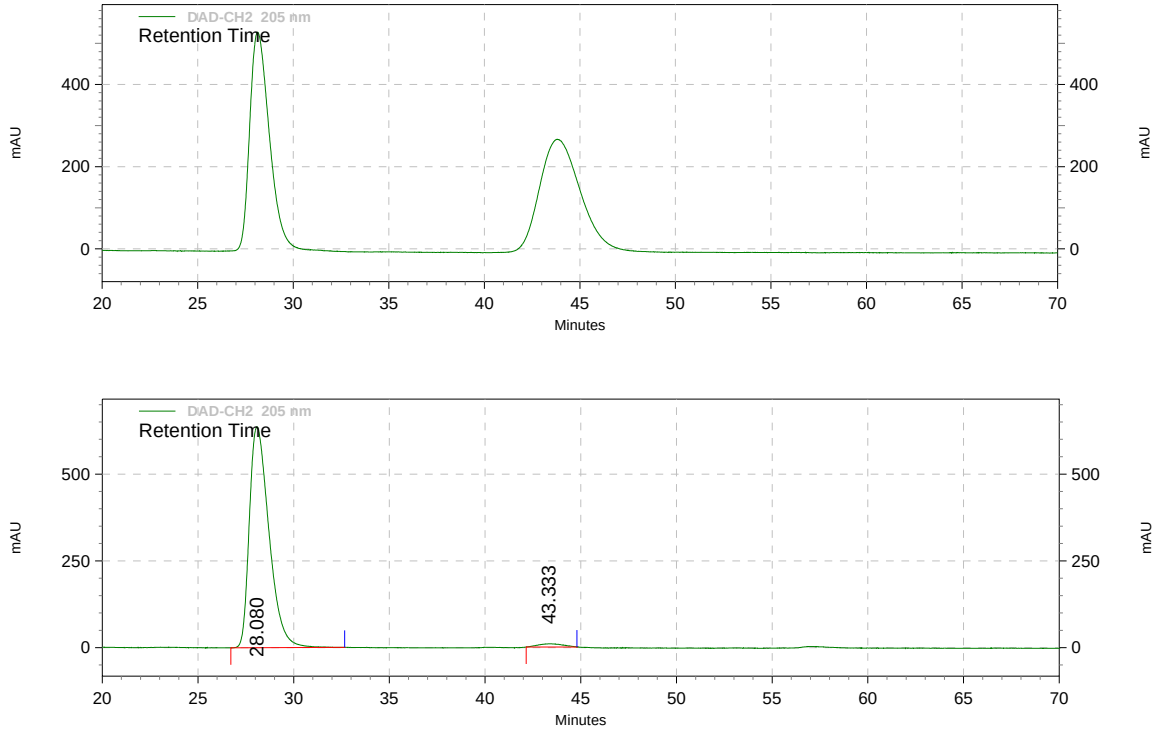
Substrate **1** was arylated following the general arylation procedure D. Analysis of crude reaction mixture by ^{1}H NMR showed > 20:1 ratio of mono- and diarylated products. After purification by column chromatography using hexane/EtOAc (4/1) as the eluent, **2w** was obtained as a white solid (38.3 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (br s, 1H), 7.88-7.84 (m, 2H), 7.79-7.74 (m, 2H), 6.63 (d, *J* = 3.6 Hz, 1H), 6.47-6.46 (m, 1H), 5.35 (t, *J* = 8.0 Hz, 1H), 3.66 (d, *J* = 8.0 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 166.2, 139.9, 135.0, 134.7, 131.2, 126.8, 125.1, 123.9, 56.4, 29.7, 15.3; HRMS (ESI-TOF) Calcd for $C_{23}H_{14}F_7N_2O_3S$ $[M+H]^+$: 531.0608; found: 531.0606.

F. Auxiliary Cleavage



The mono-arylated product **2** (153mg, 0.3 mmol) 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 hours 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 **4** (84.5 mg, 95%) (*28*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (br s, 1H), 7.80-7.75 (m, 2H), 7.70-7.65 (m, 2H), 7.21-7.11 (m, 5H), 5.22 (dd, J_1 = 7.6 Hz, J_2 = 8.8 Hz, 1H), 3.60-3.58 (m, 2H).

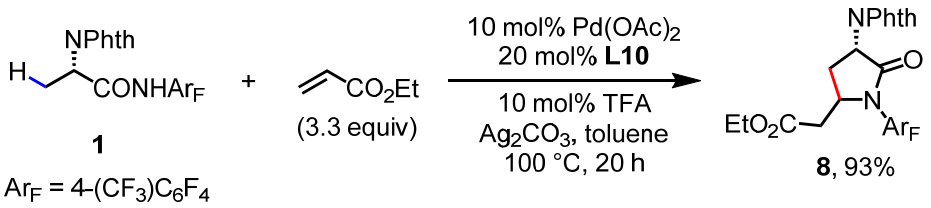
To a solution of **4** (29.5 mg, 0.1 mmol) in anhydrous methanol (5 mL) was added thionyl chloride (44 μL, 0.6 mmol) dropwise at 0 °C. The solution was stirred overnight at room temperature. After concentration, the mixture was purified by column chromatography using hexane/EtOAc (5/1) as the eluent, and the product **16** was obtained as white solid (27.8 mg, 90%, 97% ee) (*29*). The ee value was determined by HPLC analysis on a Chiralcel OJ column (25% isopropanol/hexanes, 0.5 mL/min) with t_r = 28.1 min (major), 43.3 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80-7.76 (m, 2H), 7.71-7.66 (m, 2H), 7.21-7.11 (m, 5H), 5.16 (dd, J_1 = 5.2 Hz, J_2 = 11.2 Hz, 1H), 3.78 (s, 3H), 3.60 (ABqd, J_1 = 5.2 Hz, J_2 = 14.4 Hz, 1H), 3.54 (ABqd, J_1 = 11.2 Hz, J_2 = 14.4 Hz, 1H).



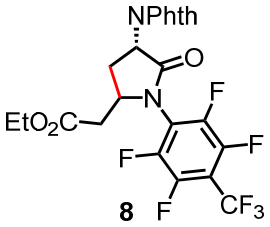
DAD-CH2 205 nm Results

Retention Time	Area	Area %	Height	Height %
28.080	275406923	98.45	3486673	98.39
43.333	4336862	1.55	56903	1.61
Totals	279743785	100.00	3543576	100.00

G. Synthesis of *N*-Boc-Protected Unnatural Amino Acid Derivatives *via* C(sp^3)–H Olefination



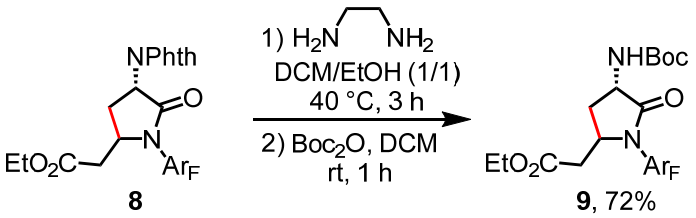
Substrate **1** (0.1 mmol, 43.4 mg), $Pd(OAc)_2$ (0.01 mmol, 2.3 mg), **L10** (0.02 mmol, 4.3 mg), and Ag_2CO_3 (0.15 mmol, 41.4 mg) were weighed out open to air and placed in a microwave tube (5 mL) with a magnetic stir bar. Ethyl acrylate (0.33 mmol, 35 μL), TFA (0.01 mmol, 1 μL), and toluene (0.5 mL) were added. The reaction vessel was sealed and the mixture was first stirred at room temperature for 10 min and then heated to 100 °C for 20 hours with vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using toluene/Et_2O (5/1) as the eluent.



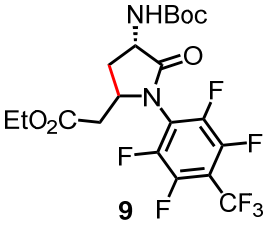
Ethyl 2-((4S)-5-oxo-4-phthalimido-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidin-2-yl)acetate (8)

Analysis of crude reaction mixture by ^{1}H NMR showed a 2.2:1 average diastereomer ratio. After purification, **8** was obtained as a white solid (49.6 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91-7.85 (m, 2H), 7.79-7.75 (m, 2H), 5.36-5.20 (m, 1H), 4.80-4.60 (m, 1H), 4.13-4.04 (m, 2H), 3.06-2.93 (m, 1H), 2.77-2.63 (m, 2H), 2.60-2.41 (m, 1H), 1.25-1.19 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 169.2, 169.1, 168.9, 167.1, 167.0, 134.4, 131.6,

123.7, 61.2, 54.1, 53.2, 48.6, 47.7, 39.2, 38.6, 31.2, 30.3, 13.91, 13.89; HRMS (ESI-TOF) Calcd for $C_{23}H_{16}F_7N_2O_5$ $[M+H]^+$: 533.0942; found: 533.0941.



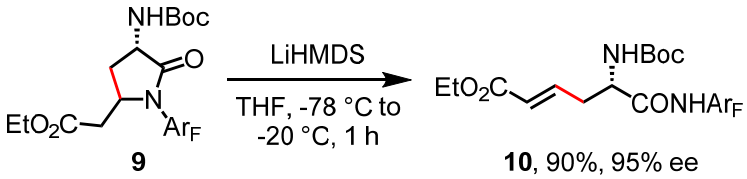
Substrate **8** (0.5 mmol, 266 mg) was weighed and placed in a round-bottom flask (25 mL) with a magnetic stir bar. DCM (1.5 mL), EtOH (1.5 mL), and ethylenediamine (2.5 mmol, 0.17 mL) were added. The reaction vessel was capped and the mixture was heated to 40 °C for 3 hours with vigorous stirring. Upon completion, the solvents were removed under reduced pressure. $CuCl_2$ (1.25 mmol, 168 mg) and deionized water (15 mL) were added into the resulting mixture. The aqueous solution was extracted with EtOAc (3 × 20 mL). The organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was dissolved in DCM (1.5 mL) without purification, and di-*t*-butyl dicarbonate (1.5 mmol, 0.35 mL) was added in the solution. The solvent was removed after one-hour reaction, and the mixture was purified by a silica gel-packed flash chromatography column using hexane/EtOAc (4/1 to 3/1) as the eluent.



Ethyl 2-((4S)-4-((*t*-butoxycarbonyl)amino)-5-oxo-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidin-2-yl)acetate (9)

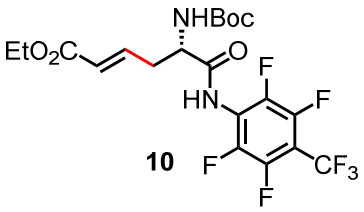
After purification, **9** was obtained as a white solid (181 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.27-5.16 (m, 1H), 4.62-4.44 (m, 2H), 4.08-4.00 (m, 2H), 3.15-3.07 and 2.72-

2.66 (m, 1H), 2.63-2.60 (m, 1H), 2.57-2.43 and 2.00-1.92 (m, 2H), 1.471-1.465 (m, 9H), 1.22-1.17 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.9, 169.6, 169.1, 155.6, 155.5, 80.5, 80.4, 61.24, 61.22, 54.2, 53.4, 51.7, 50.1, 38.8, 38.5, 35.1, 34.2, 28.2, 13.9; HRMS (ESI-TOF) Calcd for $C_{20}H_{22}F_7N_2O_5$ $[M+H]^+$: 503.1411; found: 503.1415.



9 **10**, 90%, 95% ee

To a dried Schlenk tube (50 mL) equipped with a magnetic stir bar were added lactam **9** (50.2 mg, 0.1mmol) and 1 mL of anhydrous THF. After cooling to -78 °C, LiHMDS (0.5 M in 2-methyltetrahydrofuran, 0.5 mL, 0.5 mmol) was added dropwise within 5 minutes. The mixture was warmed up to -20 °C naturally in one hour. The reaction was then quenched with saturated NH_4Cl/AcOH (v/v = 20/1) at -78 °C and exacted with EtOAc (3 × 6 mL). The combined organic layer was washed with brine and dried over anhydrous $MgSO_4$, filtrated and concentrated. The crude product was purified by a silica gel-packed flash chromatography column using DCM/EtOAc (10/1) as the eluent.

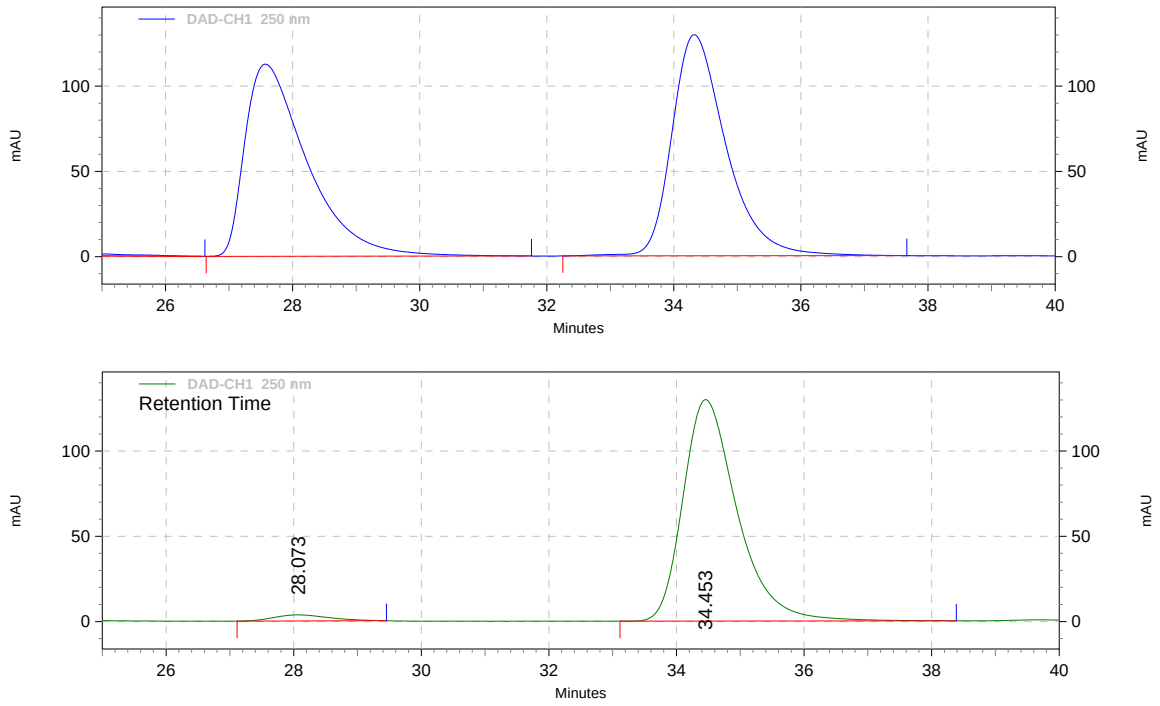


10

Ethyl (S,E)-5-((*t*-butoxycarbonyl)amino)-6-oxo-6-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)amino)hex-2-enoate (10)

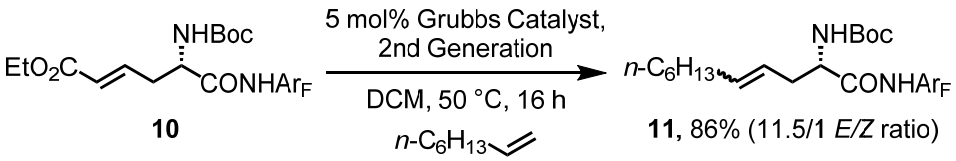
After purification, **10** was obtained as a white solid (45.2 mg, 90%, 95% ee). The ee value was determined by HPLC analysis on a Chiralpak AD-H column (20% isopropanol/hexanes, 0.2 mL/min) with t_r = 28.1 min (minor), 34.5 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (br s, 1H), 6.97-6.89 (m, 1H), 5.98 (d, *J* = 16.0 Hz, 1H), 5.25-

5.12 (m, 1H), 4.56-4.44 (m, 1H), 4.20 (q, J = 7.2 Hz, 2H), 2.86-2.79 (m, 1H), 2.76-2.68 (m, 1H), 1.47 (s, 9H), 1.29 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.1, 165.8, 156.5, 141.9, 125.5, 81.8, 60.6, 53.3, 33.5, 28.2, 14.2; HRMS (ESI-TOF) Calcd for $C_{20}H_{21}F_7N_2O_5Na$ $[M+Na]^+$: 525.1231; found: 525.1231.

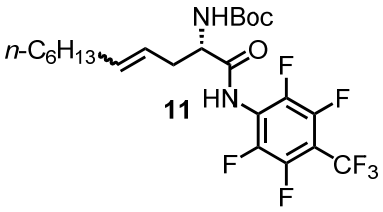


DAD-CH1 250 nm Results

Retention Time	Area	Area %	Height	Height %
28.073	3493348	2.36	66710	2.57
34.453	144495133	97.64	2527818	97.43
Totals	147988481	100.00	2594528	100.00

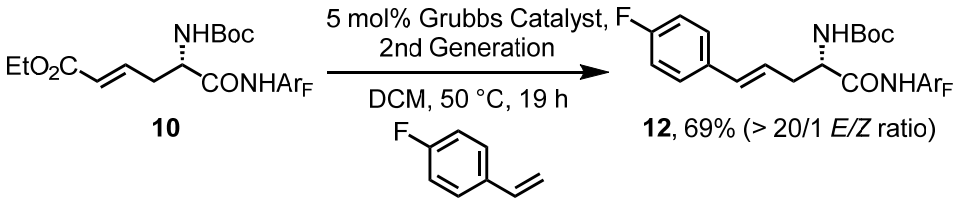


To a dried Schlenk tube (25 mL) were added Grubbs Catalyst, 2nd Generation (2.8 mg, 0.0035 mmol), amide **10** (35.1mg, 0.07 mmol), DCM (1.5 mL), and 1-octene (71.5 mg, d = 0.715 g/mL, 0.1 mL, 0.64 mmol). The mixture refluxed under N_2 atmosphere (oil bath, 50 °C) for 16 h. The mixture was filtered through a small pad of Celite. The solvents were removed under reduced pressure and the resulting mixture was purified by preparative TLC using hexane/EtOAc (5/1) as the eluent to afford product **11** as colorless oil (31.0 mg, 86%).

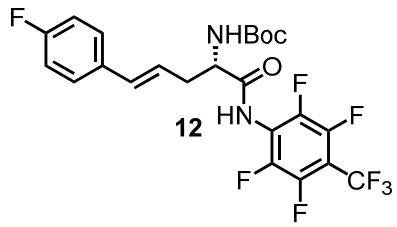


***t*-Butyl (S)-(1-oxo-1-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)amino)undec-4-en-2-yl)carbamate (11)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (br s, 1H), 5.96-5.89 and 5.66-5.59 (m, 1H), 5.51-5.34 (m, 1H), 5.22-5.04 (m, 1H), 4.38 (br s, 1H), 2.74-2.49 (m, 2H), 2.09-1.97 (m, 2H), 1.46 (s, 9H), 1.35-1.27 (m, 8H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.9, 156.5, 136.4, 123.2, 81.3, 54.1, 34.5, 32.5, 31.7, 29.2, 28.8, 28.2, 22.6, 14.1; HRMS (ESI-TOF) Calcd for $C_{23}H_{30}F_7N_2O_3$ $[M+H]^+$: 515.2139; found: 515.2137.



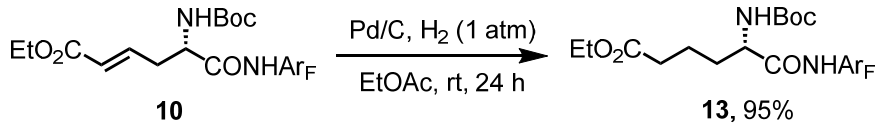
The reaction of Grubbs Catalyst, 2nd Generation (2.8 mg, 0.0035 mmol), amide **10** (35.3 mg, 0.07 mmol), DCM (1.5 mL), and 4-fluorostyrene (153.6 mg, d = 1.024 g/mL, 0.15 mL, 0.80 mmol) afforded **12** as a white solid (25.3 mg, 69%).



12

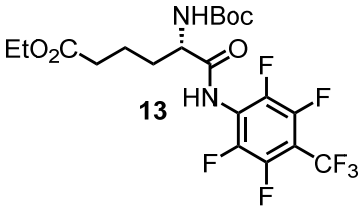
***t*-Butyl (S,E)-(5-(4-fluorophenyl)-1-oxo-1-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)amino)pent-4-en-2-yl)carbamate (12)**

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.87 (br s, 1H), 7.34-7.29 (m, 2H), 7.02-6.97 (m, 2H), 6.50 (d, J = 15.6 Hz, 1H), 6.11 (dt, J_1 = 7.2 Hz, J_2 = 15.6 Hz, 1H), 5.19 (d, J = 7.8 Hz, 1H), 4.51 (br s, 1H), 2.79-2.72 (m, 2H), 1.43 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.7, 162.4 (d, J_{FC} = 245.7 Hz), 156.5, 133.5, 132.7, 127.8 (d, J_{FC} = 8.0 Hz), 123.1, 115.5 (d, J_{FC} = 21.5 Hz), 81.6, 54.1, 34.8, 28.2; HRMS (ESI-TOF) Calcd for $C_{23}H_{20}F_8N_2O_3Na$ $[M+Na]^+$: 547.1238; found: 547.1234.



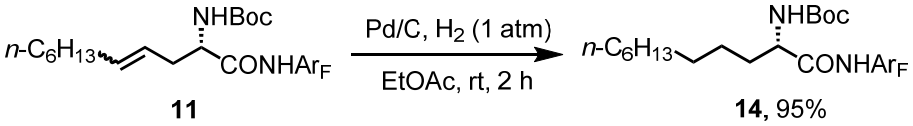
10 **13**, 95%

To a round-bottom flask (25 mL) was added Pd/C (10 wt. % loading on carbon, 5.0 mg), amide **10** (35.2 mg, 0.07 mmol), and EtOAc (1 mL). The reaction tube was evacuated and back-filled with H_2 (3 times, balloon). After stirring at room temperature for 24 hours, the mixture was filtered through a small pad of Celite. The solvents were removed under reduced pressure and the resulting mixture was purified by preparative TLC using hexane/EtOAc (3/1) as the eluent to afford **13** as colorless oil (33.4 mg, 95%).

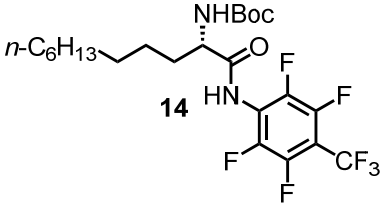


Ethyl (S)-5-((*t*-butoxycarbonyl)amino)-6-oxo-6-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)amino)hexanoate (13)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (br s, 1H), 5.24 (br s, 1H), 4.33 (br s, 1H), 4.15 (q, J = 7.2 Hz, 2H), 2.48-2.35 (m, 2H), 2.04-1.93 (m, 1H), 1.87-1.76 (m, 3H), 1.47 (s, 9H), 1.27 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.5, 170.0, 156.6, 81.3, 60.7, 54.1, 33.4, 30.4, 28.2, 20.7, 14.2; HRMS (ESI-TOF) Calcd for $C_{20}H_{24}F_7N_2O_5$ $[M+H]^+$: 505.1568; found: 505.1567.



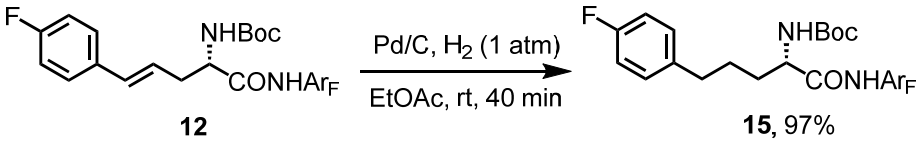
The reaction of Pd/C (10 wt. % loading on carbon, 5.0 mg), amide **11** (31.0 mg), and EtOAc (1 mL) afforded **14** as colorless oil (29.5 mg, 95%).



***t*-Butyl (S)-(1-oxo-1-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)amino)undecan-2-yl)carbamate (14)**

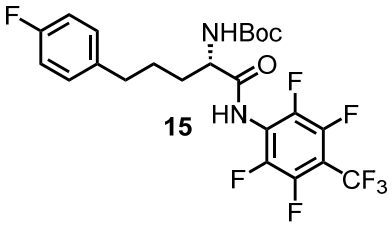
^{1}H NMR (600 MHz, $CDCl_3$) δ 9.00 (br s, 1H), 5.22-5.20 (m, 1H), 4.38-4.37 (m, 1H), 1.95-1.89 (m, 1H), 1.75-1.66 (m, 1H), 1.45-1.40 (m, 11H), 1.34-1.26 (m, 12H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.6, 156.6, 81.2, 54.6, 31.8, 31.5, 29.44, 29.38,

29.2, 28.2, 25.6, 22.7, 14.1; HRMS (ESI-TOF) Calcd for $C_{23}H_{31}F_7N_2O_3Na$ $[M+Na]^+$: 539.2115; found: 539.2111.



12 **15**, 97%

The reaction of Pd/C (10 wt. % loading on carbon, 5.0 mg), amide **12** (25.3 mg), and EtOAc (1 mL) afforded **15** as colorless oil (24.6 mg, 97%).

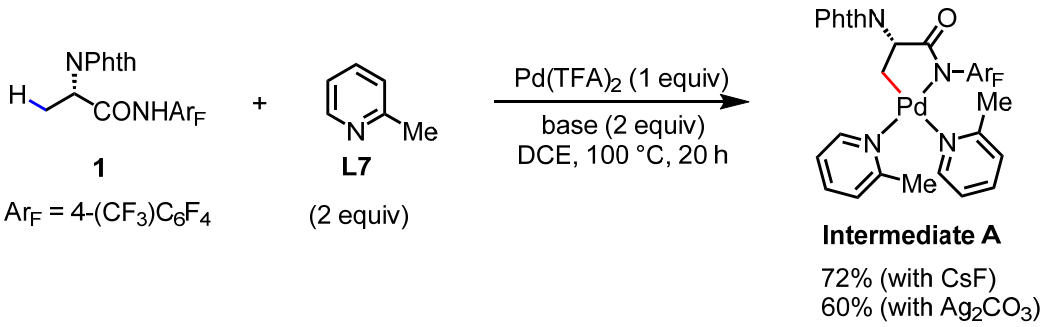


15

***t*-Butyl (S)-(5-(4-fluorophenyl)-1-oxo-1-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)amino)pentan-2-yl)carbamate (15)**

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.88 (br s, 1H), 7.13-7.10 (m, 2H), 6.98-6.94 (m, 2H), 5.14-5.12 (m, 1H), 4.36 (br s, 1H), 2.69-2.59 (m, 2H), 2.00-1.94 (m, 1H), 1.76-1.70 (m, 3H), 1.44 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.2, 161.3 (d, J_{FC} = 242.3 Hz), 156.6, 136.9 (d, J_{FC} = 3.5 Hz), 129.6 (d, J_{FC} = 7.7 Hz), 115.2 (d, J_{FC} = 21.0 Hz), 81.4, 54.4, 34.5, 30.6, 28.2, 27.5; HRMS (ESI-TOF) Calcd for $C_{23}H_{22}F_8N_2O_3Na$ $[M+Na]^+$: 549.1395; found: 549.1394.

H. Synthesis and Reactivity of Palladacycle Intermediates in C(sp^3)–H Arylation



In a sealable tube (20 mL), amide **1** (43.4 mg, 0.10 mmol), $Pd(TFA)_2$ (33.2 mg, 0.10 mmol), 2-picoline (18.6 mg, 0.2 mmol), and CsF (30.4 mg, 0.20 mmol) were dissolved in DCE (2 mL). The reaction mixture was then tightly capped and stirred for 10 minutes at room temperature, and then heated up to 100 °C with vigorous stirring for 20 hours. The reaction mixture was then cooled to room temperature, and filtered through a small pad of Celite. The residue was purified by preparative TLC using hexane/EtOAc (1/2) as the eluent to afford **Intermediate A** as a yellow solid (52.0 mg, 72%). HRMS (ESI-TOF) Calcd for $C_{30}H_{22}F_7N_4O_3Pd$ $[M+H]^+$: 725.0609; found: 725.0621. **Intermediate A** was recrystallized in DCM/hexane, and the structure was determined by X-ray diffraction.

Figure S2. X-ray Crystallographic Data of **Intermediate A**

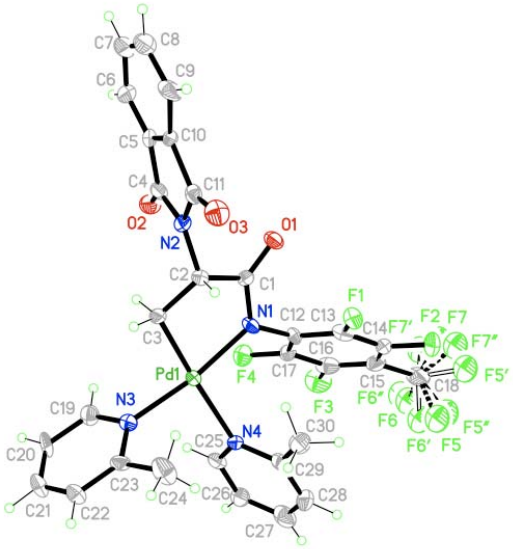
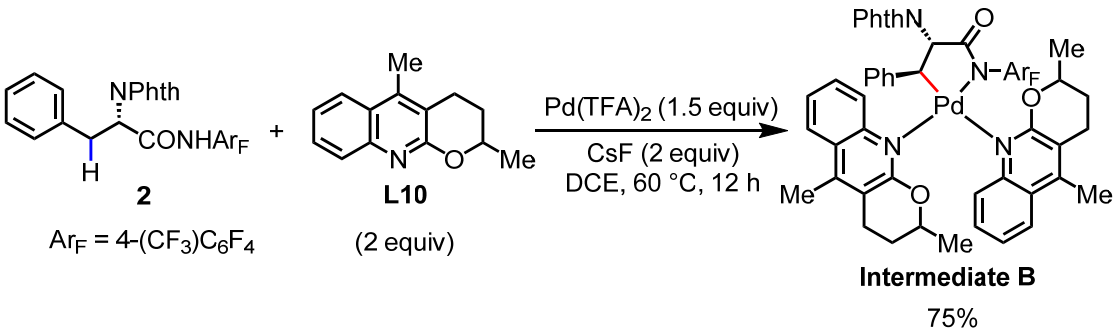


***Table S5*: Crystal Data and Structure Refinement for Intermediate A**

CCDC-985676		
Identification code	**Intermediate A**	
Empirical formula	$C_{31}H_{23}Cl_2F_7N_4O_3Pd$	
Molecular formula	$C_{30}H_{21}F_7N_4O_3Pd$, CH_2Cl_2	
Formula weight	809.83	
Temperature	200(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 10.9436(12) Å	α = 110.701(3)°.
	b = 12.9351(14) Å	β = 108.032(3)°.
	c = 13.8591(16) Å	γ = 103.155(3)°.
Volume	1614.9(3) $Å^3$	
Z	2	
Density (calculated)	1.665 Mg/m^3	

Absorption coefficient	0.820 mm^{-1}
F(000)	808
Crystal size	0.28 × 0.12 × 0.10 mm^3
Crystal color, habit	COLORLESS BLOCK
Theta range for data collection	1.74 to 26.43°.
Index ranges	-13<=h<=13, -16<=k<=16, -17<=l<=16
Reflections collected	14965
Independent reflections	9256 [R(int) = 0.0366]
Completeness to theta = 25.00°	99.9 %
Absorption correction	multi-scan / sadabs
Max. and min. transmission	0.9225 and 0.8029
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9256 / 94 / 876
Goodness-of-fit on F^2	1.038
Final R indices [I>2sigma(I)]	R1 = 0.0417, wR2 = 0.0927
R indices (all data)	R1 = 0.0592, wR2 = 0.0986
Absolute structure parameter	-0.01(2)
Largest diff. peak and hole	1.240 and -0.704 e.$Å^{-3}$



In a sealable tube (20 mL), amide **1** (43.4 mg, 0.10 mmol), $Pd(TFA)_2$ (49.8 mg, 0.15 mmol), L10 (42.6 mg, 0.20 mmol), and CsF (30.4 mg, 0.20 mmol) were dissolved in DCE (2 mL). The reaction mixture was then tightly capped and stirred for 10 minutes at room temperature, and then heated up to 60 °C with vigorous stirring for 12 hours. The reaction mixture was then cooled to room temperature, and filtered through a small pad of Celite. The residue was purified by preparative TLC using hexane/EtOAc (1/2) as the eluent to afford **Intermediate B** as a yellow solid (78.0 mg, 75%). HRMS (ESI-TOF) Calcd for $C_{52}H_{42}F_7N_4O_5Pd$ $[M+H]^+$: 1041.2073; found: 1041.2070. **Intermediate B** was recrystallized in DCM/hexane, and the structure was determined by X-ray diffraction.

Figure S3. X-ray Crystallographic Data of **Intermediate B**

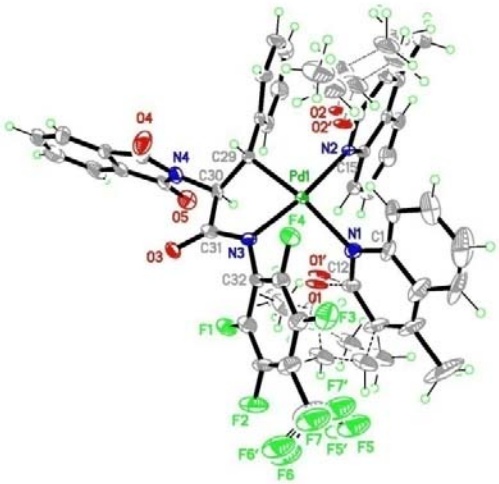


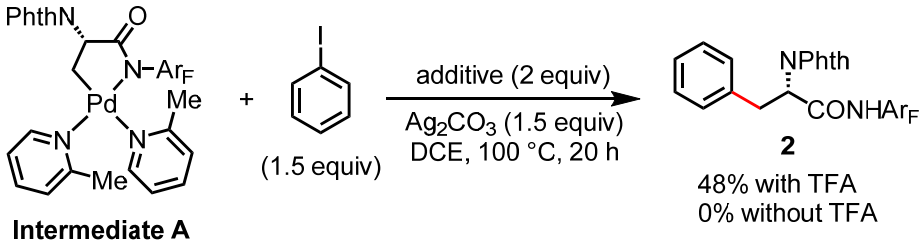
***Table S6*: Crystal Data and Structure Refinement for Intermediate B**

CCDC-985677

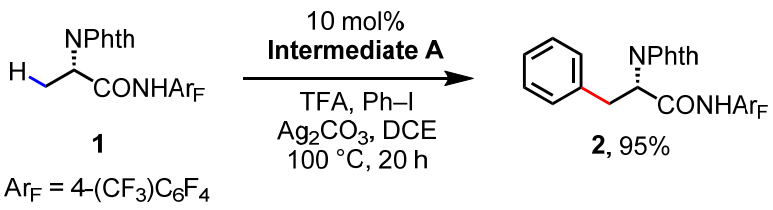
Identification code	**Intermediate B**	
Empirical formula	$C_{52.50}H_{42}ClF_7N_4O_5Pd$	
Molecular formula	$C_{52}H_{41}F_7N_4O_5Pd$, $0.5(CH_2Cl_2)$	
Formula weight	1083.75	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2	
Unit cell dimensions	a = 34.9648(19) Å	α = 90°.
	b = 15.3694(7) Å	β = 125.823(3)°.
	c = 23.2457(13) Å	γ = 90°.
Volume	10128.8(9) $Å^3$	
Z	8	
Density (calculated)	1.421 Mg/m^3	
Absorption coefficient	0.495 mm^{-1}	
F(000)	4408	
Crystal size	0.20 × 0.16 × 0.12 mm^3	
Crystal color, habit	orange / block	
Theta range for data collection	1.76 to 26.45°.	
Index ranges	-43<=h<=35, -19<=k<=19, 0<=l<=28	
Reflections collected	20613	
Independent reflections	20613 [R(int) = 0.0000]	
Completeness to theta = 25.00°	99.9 %	
Absorption correction	multi-scan / sadabs	
Max. and min. transmission	0.9430 and 0.9075	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	20613 / 82 / 1227	

Goodness-of-fit on F^2	1.049
Final R indices [I>2sigma(I)]	R1 = 0.0459, wR2 = 0.1080
R indices (all data)	R1 = 0.0652, wR2 = 0.1137
Absolute structure parameter	0.043(18)

Largest diff. peak and hole 0.522 and -0.652 e.Å^{-3}

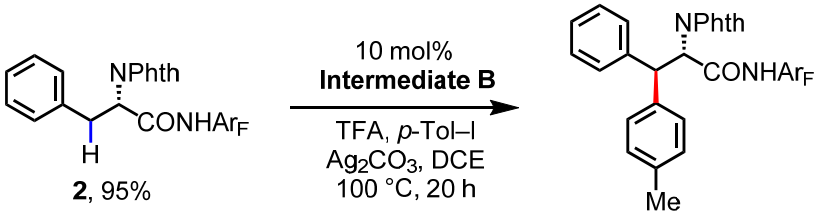


Intermediate A (0.1 mmol, 72.4 mg), and Ag_2CO_3 (0.15 mmol, 41.4 mg) were weighed out open to air and placed in a sealable tube (50 mL) with a magnetic stir bar. Iodobenzene (30.6 mg, 0.15 mmol), TFA (0.2 mmol, 22.8 mg), and DCE (2 mL) were added. The reaction vessel was sealed and the mixture was first stirred at room temperature for 10 min and then heated to 100 °C for 20 hours with vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using hexane/EtOAc mixtures (3/1) as the eluent to afford **2** (24.6 mg, 48%).



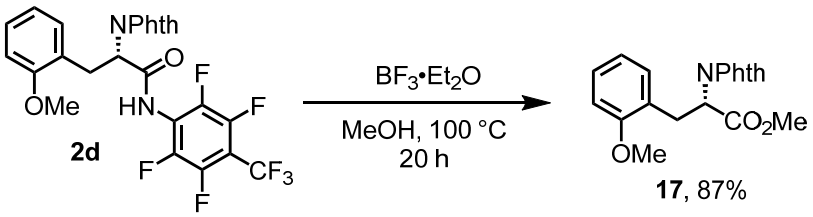
Substrate **1** (0.1 mmol, 43.4 mg), **Intermediate A** (0.01 mmol, 7.2 mg), and Ag_2CO_3 (0.15 mmol, 41.4 mg) were weighed out open to air and placed in a microwave tube (5 mL) with

a magnetic stir bar. Iodobenzene (30.6 mg, 0.15 mmol), TFA (0.02 mmol, 2 μL), and DCE (0.5 mL) were added. The reaction vessel was sealed and the mixture was first stirred at room temperature for 10 min and then heated to 100 °C for 20 hours with vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using toluene/EtOAc mixtures (30/1) as the eluent to afford **2** (53.1 mg, 95% based on **1** and **Intermediate A**).

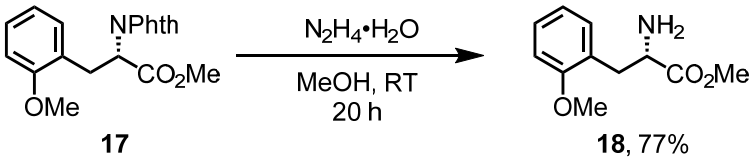


Substrate **2** (0.1 mmol, 51.0 mg), **Intermediate B** (0.01 mmol, 10.4 mg), 4-iodotoluene (0.3 mmol, 65.4 mg), and Ag_2CO_3 (0.2 mmol, 55.0 mg) were weighed out open to air and placed in a microwave tube (5 mL) with a magnetic stir bar. TFA (0.02 mmol, 2 μL) and DCE (0.5 mL) were added. The reaction vessel was sealed and the mixture was first stirred at room temperature for 10 min and then heated to 100 °C for 20 hours with vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The solvents were removed under reduced pressure and the resulting mixture was purified by a silica gel-packed flash chromatography column using toluene/EtOAc mixtures (30/1) as the eluent to afford **3a** (39.8 mg, 60% based on **2** and **Intermediate B**). Analysis of crude reaction mixture by ^{1}H NMR showed a > 20:1 diastereomer ratio.

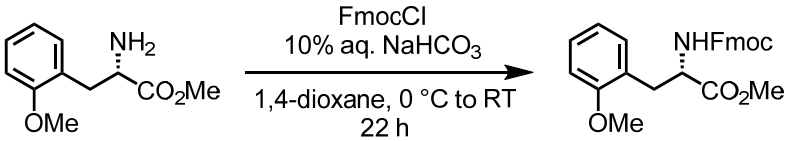
I. Synthesis of *N*-Fmoc-Protected Unnatural Amino Acid



A sealable pressure flask was charged with MeOH (99 mL) and the amide **2d** (6.46 mmol, 3.49 g). $BF_3 \cdot Et_2O$ (6 equiv) was added dropwise via syringe, and the reaction vessel sealed. The mixture was heated to 100 °C for 20 h, and then cooled to room temperature. Triethylamine (6 equiv) was then carefully added via syringe, and stirred for 10 min. The solvent was removed *in vacuo*, and the residue purified by column chromatography using hexane/EtOAc (5/1) as the eluent to afford the desired product **17** (87%, 1.91 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76-7.74 (m, 2H), 7.67-7.66 (m, 2H), 7.12-7.09 (m, 1H), 6.99-6.98 (m, 1H), 6.76-6.75 (m, 1H), 6.70-6.67 (m, 1H), 5.39-5.36 (m, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.66-3.63 (m, 1H), 3.44-3.40 (m, 1H).

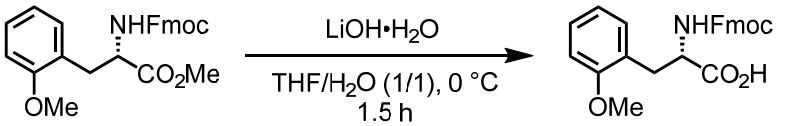


N-Phthalimido-protected amino ester **17** (4.60 mmol, 1.56 g) was dissolved in MeOH (88 mL), and $N_2H_4 \cdot H_2O$ (4 equiv) was added. The reaction was stirred at room temperature for 20 h, after which, the solvent was removed *in vacuo*. Saturated aqueous $NaHCO_3$ was added, and the solution extracted with EtOAc (3 × 50 mL). The organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography using hexane/EtOAc (1/1) as the eluent to afford the desired product **18** (77%, 0.74 g) (*30*). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24-7.21 (m, 1H), 7.13-7.11 (m, 1H), 6.91-6.85 (m, 2H), 3.83-3.79 (m, 4H), 3.70 (s, 3H), 3.12 (dd, J_1 = 5.6 Hz, J_2 = 13.3 Hz, 1H), 2.85 (dd, J_1 = 8.2 Hz, J_2 = 13.3 Hz, 1H), 1.64 (br s, 2H).



18 **19**, 75%

Amino ester **18** (3.54 mmol, 0.74 g) was taken up in 1,4-dioxane (18 mL), and 10% aqueous $NaHCO_3$ (11 mL) was added. The mixture was cooled to 0 °C and FmocCl (3.54 mmol, 1 equiv) was added. The ice bath was allowed to warm to room temperature overnight, after which H_2O and EtOAc were added to the reaction mixture. The aqueous layer was then extracted with EtOAc (3 × 50 mL) and the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography using hexane/EtOAc (5/1) as the eluent to afford the desired product **19** (75%, 1.15 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 2H), 7.56-7.51 (m, 2H), 7.41-7.37 (m, 2H), 7.31-7.22 (m, 3H), 7.10-7.08 (m, 1H), 6.92-6.86 (m, 2H), 5.61 (d, *J* = 7.8 Hz, 1H), 4.61-4.56 (m, 1H), 4.32 (d, *J* = 6.7 Hz, 2H), 4.18 (t, *J* = 7.1 Hz, 1H), 3.82 (s, 3H), 3.73 (s, 3H), 3.17-3.08 (m, 2H).



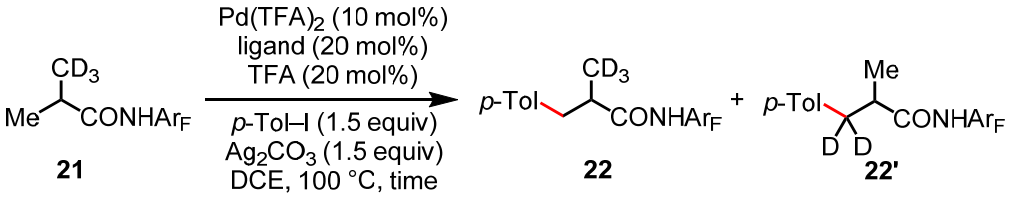
19 **20**, 70%

Methyl ester **19** (2.55 mmol, 1.10 g) was dissolved in THF (18 mL). The solution was cooled to 0 °C, and a cold solution of $LiOH{\cdot}H_2O$ (5.10 mmol, 2 equiv) in H_2O (18 mL) were added. The reaction was maintained at 0 °C and monitored by TLC. After consumption of starting material, the reaction was acidified with HCl (2 N) and extracted with EtOAc (4 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography using hexane/EtOAc/MeOH (3/2/0.1) as the eluent to afford the desired product **20** (70%, 0.74 g). Spectral data agree with literature (*31*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 2H), 7.54-7.49 (m, 2H), 7.41-7.37 (m, 2H), 7.31-7.24 (m, 3H), 7.14 (d, *J* = 7.2 Hz, 1H),

6.93-6.87 (m, 2H), 5.68 (d, *J* = 7.3 Hz, 1H), 4.60-4.54 (m, 1H), 4.34 (d, *J* = 7.0 Hz, 2H), 4.18 (t, *J* = 7.1 Hz, 1H), 3.80 (s, 3H), 3.23-3.13 (m, 2H).

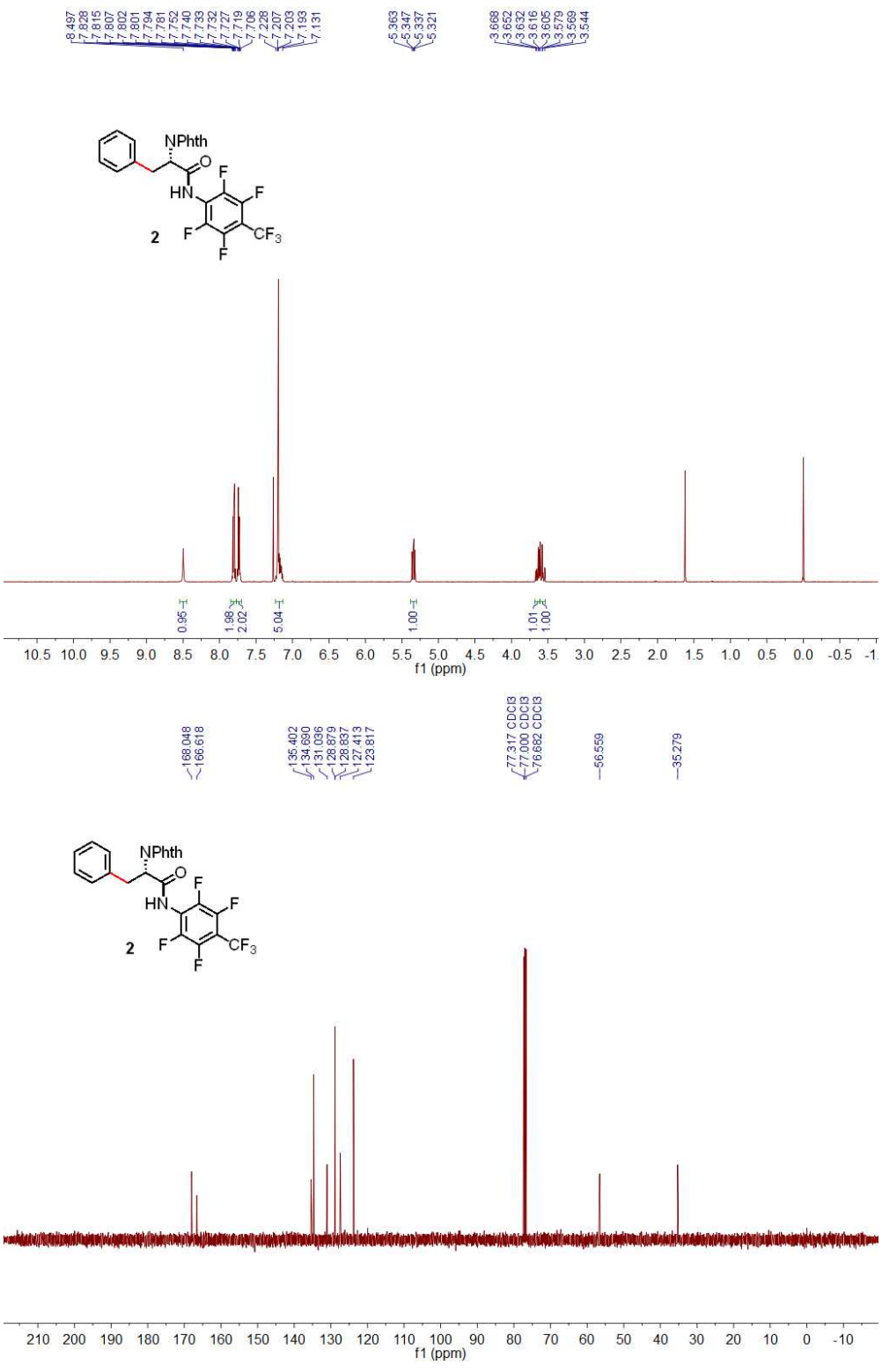
J. Intramolecular Isotope Effect and Ligand Acceleration

General Procedure: Substrate **21** (0.1 mmol, 30.6 mg), $Pd(TFA)_2$ (0.01 mmol, 3.3 mg), and Ag_2CO_3 (0.15 mmol, 41.4 mg) were weighed out open to air and placed in a microwave tube (5 mL) with a magnetic stir bar. 4-Iodotoluene (0.15 mmol, 32.7 mg), ligand (0.02 mmol), TFA (0.02 mmol, 2 μL), and DCE (0.5 mL) were added. The reaction vessel was sealed. The reaction mixture was first stirred at room temperature for 10 min and then heated to 100 °C under vigorous stirring. After a certain amount of time, the reaction mixture was cooled to room temperature. The solvents were removed under reduced pressure. All conversions were determined by analysis of the crude ^{1}H NMR ($CDCl_3$) spectrum using CH_2Br_2 as the internal standard. The ratio of the arylated products was determined by ^{1}H NMR ($CDCl_3$) spectrum after the reaction mixture was purified by a silica gel-packed flash chromatography column using hexane/EtOAc (5/1) as the eluent.



Entry	Ligand	Time (h)	Conversion (%)*	Ratio (**22/22'**)*
1	—	10	13	6.0
2	**L7**	10	45	8.1
3	**L7**	24	80	8.1
4	**L10**	5	100	10.7

*Conversions and ratios are the averaged results of three reproducible experiments.


8.497
7.828
7.815
7.807
7.802
7.801
7.794
7.781
7.752
7.740
7.733
7.732
7.727
7.719
7.706
7.228
7.207
7.203
7.193
7.131
5.363
5.347
5.337
5.321
3.668
3.652
3.632
3.616
3.605
3.579
3.569
3.544
NPhth
O
HN
F
F
F
F
CF3
2
0.95
1.98
2.02
5.04
1.00
1.01
1.00
f1 (ppm)
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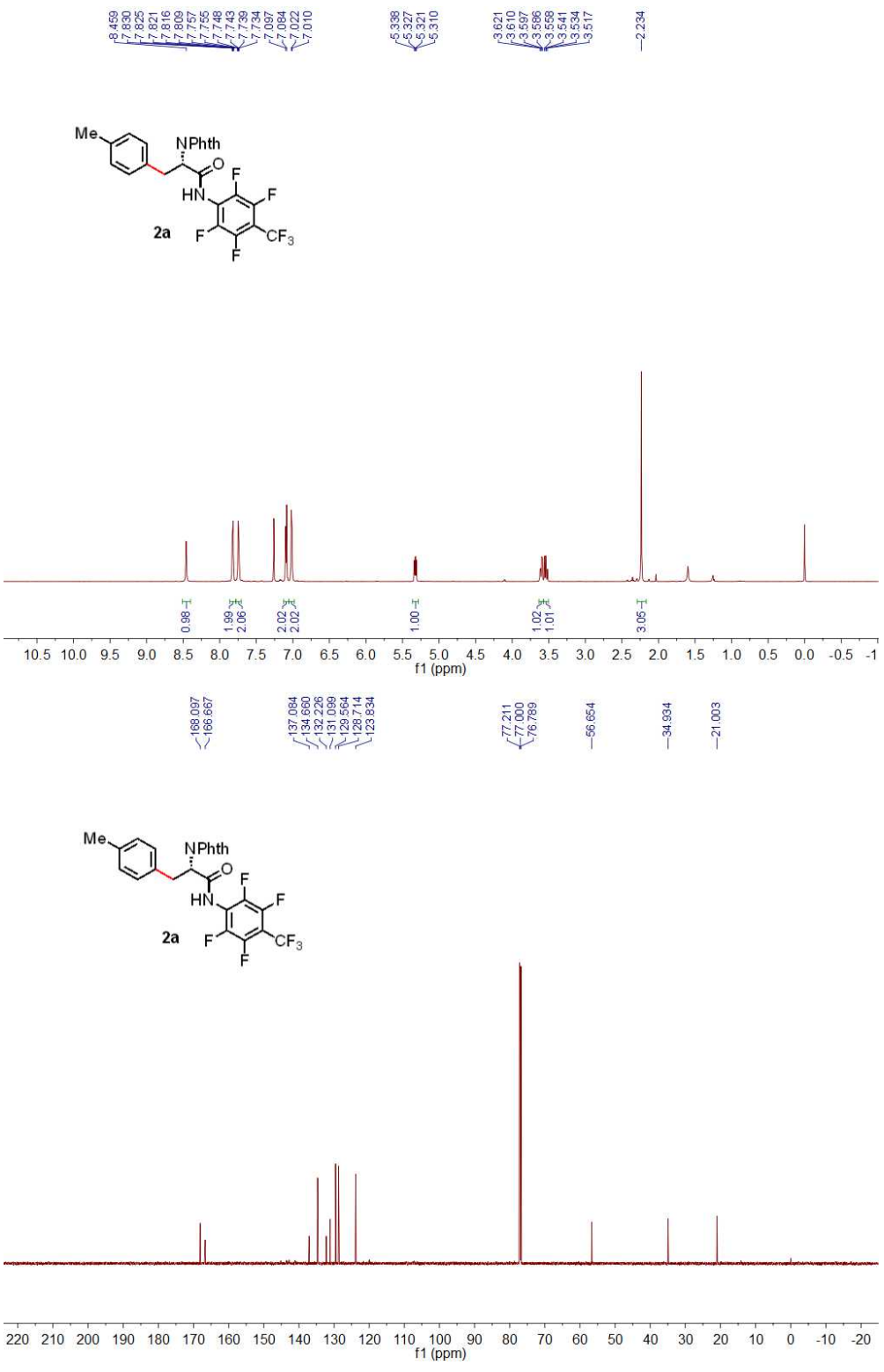
166.618
135.402
134.690
131.036
129.879
129.837
127.413
123.817
77.317 CDCl3
77.000 CDCl3
76.682 CDCl3
56.559
35.279
f1 (ppm)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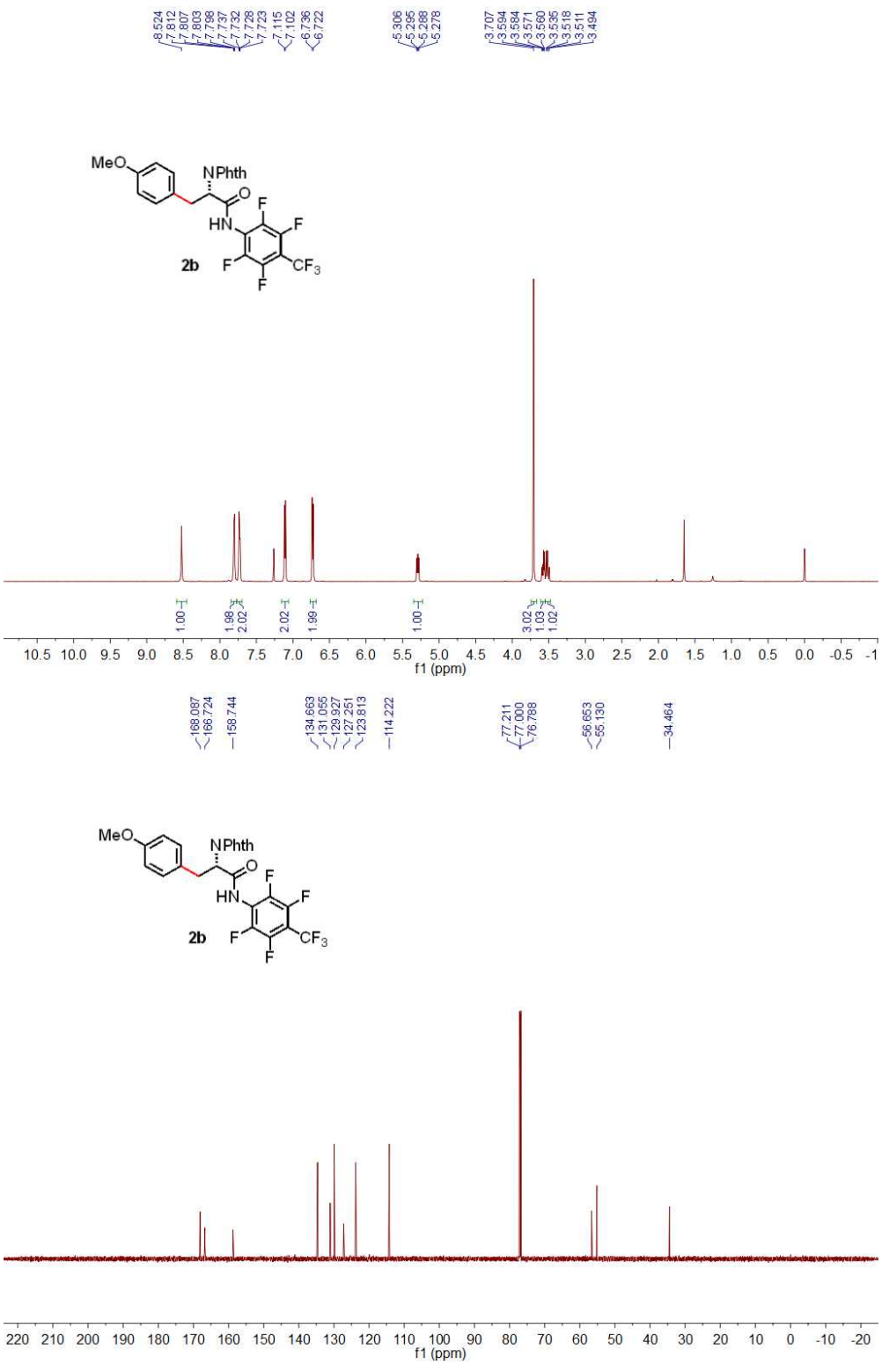
7.825
7.821
7.816
7.809
7.757
7.755
7.748
7.743
7.739
7.734
7.097
7.084
7.022
7.010
5.338
5.327
5.321
5.310
3.621
3.610
3.597
3.586
3.558
3.541
3.534
3.517
2.234
Me
NPhth
O
HN
F
F
F
F
CF3
2a
0.98
1.99
2.06
2.02
2.02
1.00
1.02
1.01
3.05
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)
168.097
166.667
137.094
134.660
132.226
131.089
129.564
128.714
123.834
77.211
77.000
76.789
56.654
34.934
21.003
Me
NPhth
O
HN
F
F
F
F
CF3
2a
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


8.524
7.812
7.807
7.803
7.798
7.737
7.732
7.728
7.723
7.115
7.102
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5.306
5.295
5.288
5.278
3.707
3.594
3.584
3.571
3.560
3.535
3.518
3.511
3.494
MeO
NPhth
O
HN
F
F
F
F
CF3
2b
1.00
1.98
2.02
2.02
1.99
1.00
3.02
1.03
1.02
f1 (ppm)
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166.724
158.744
134.663
131.055
129.927
127.251
123.813
114.222
77.211
77.000
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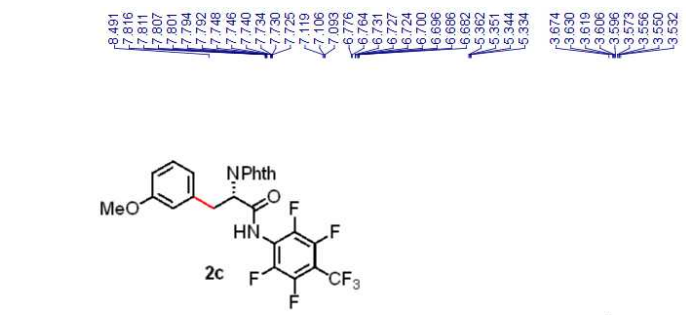
HN
F
F
F
F
CF3
2b
f1 (ppm)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7.801
7.794
7.792
7.748
7.746
7.740
7.734
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7.106
7.093
6.776
6.764
6.731
6.727
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6.696
6.686
6.682
5.362
5.351
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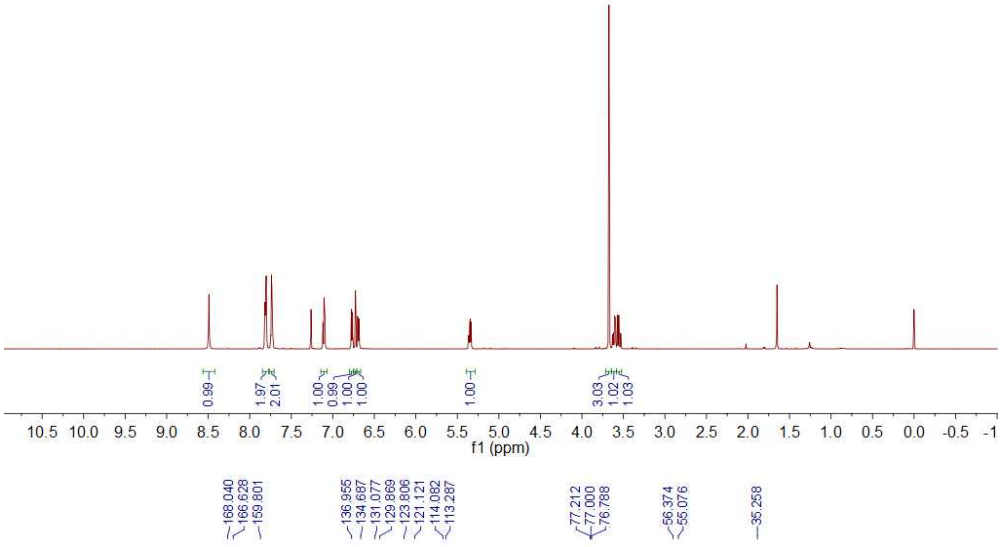
O
HN
F
F
F
F
CF3
2c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1.97
2.01
1.00
0.99
1.00
1.00
1.00
3.03
1.02
1.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

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166.628
159.801
136.955
134.687
131.077
129.869
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121.121
114.082
113.267
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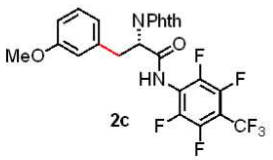
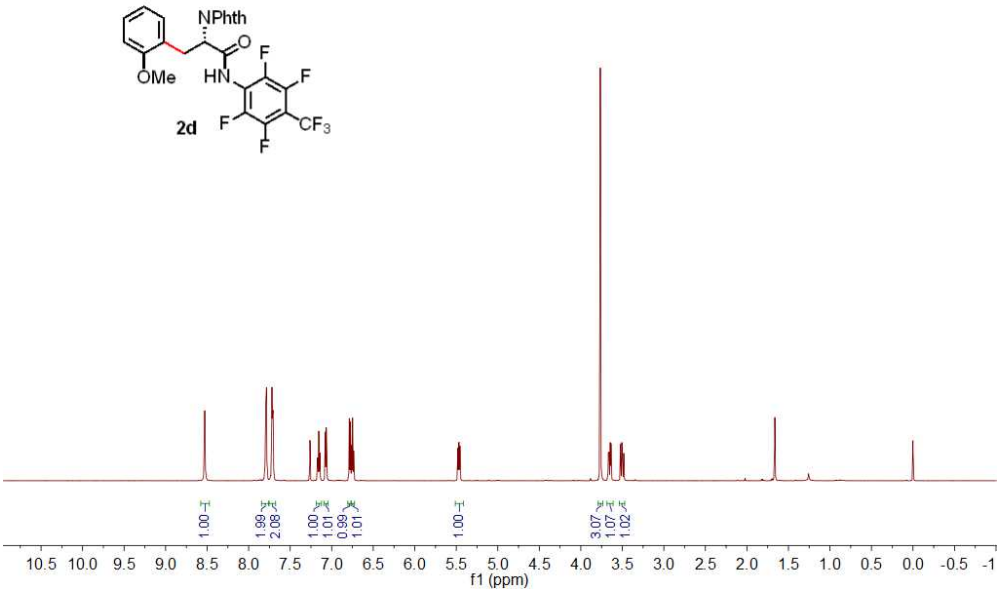
77.000
76.788
56.374
55.076
35.258


NPhth
MeO
O
HN
F
F
F
F
CF3
2c

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


8.529
7.800
7.794
7.790
7.785
7.778
7.728
7.727
7.720
7.715
7.711
7.705
7.699
7.170
7.168
7.157
7.156
7.154
7.144
7.142
7.141
7.079
7.077
7.075
7.066
7.063
6.788
6.775
6.760
6.748
6.736
5.481
5.472
5.465
5.455
3.765
3.669
3.660
3.646
3.636
3.522
3.506
3.499
3.482


NPhth
O
HN
OMe
F
F
F
F
CF3
2d
1.00
1.99
2.08
1.00
1.01
0.99
1.01
1.00
3.07
1.07
1.02
10.5 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 -1
f1 (ppm)


167.917
166.893
157.346
134.426
131.307
130.942
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76.788
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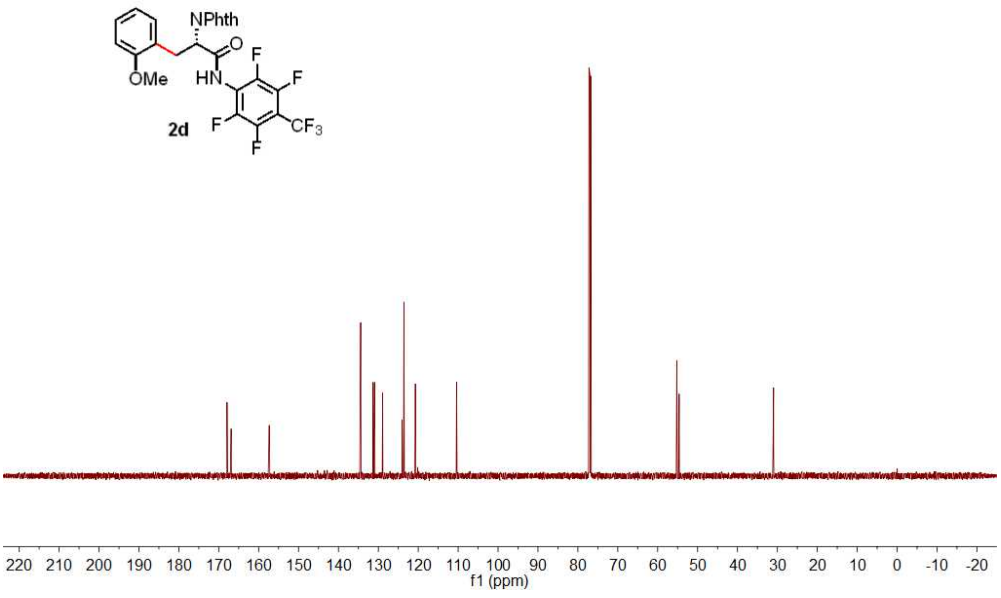
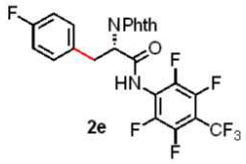
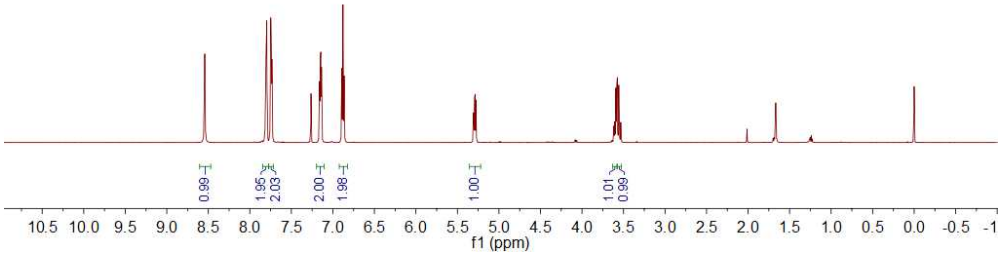
30.941


NPhth
O
HN
OMe
F
F
F
F
CF3
2d
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


8.543
7.817
7.810
7.805
7.801
7.796
7.788
7.756
7.755
7.748
7.743
7.739
7.734
7.727
7.159
7.150
7.145
7.137
7.131
6.898
6.893
6.889
6.878
6.867
6.864
5.304
5.294
5.287
5.276
3.616
3.605
3.592
3.581
3.574
3.557
3.550
3.533


F
NPhth
O
HN
F
F
F
F
CF3
2e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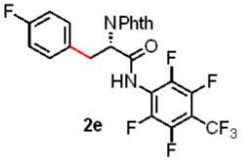
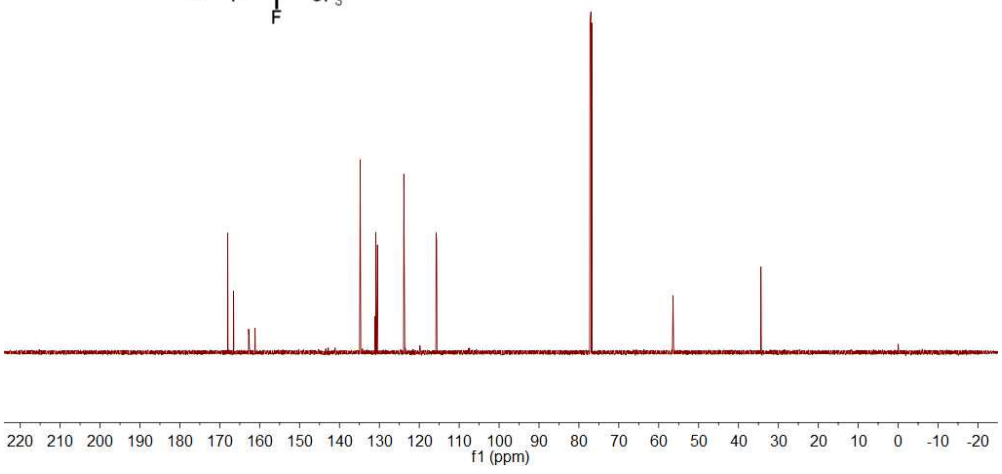
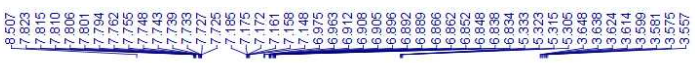
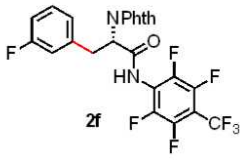
1.95
2.03
2.00
1.98
1.00
1.01
0.99
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

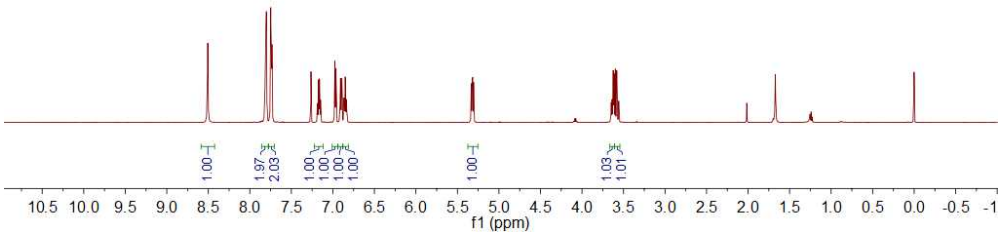

167.992
166.525
162.768
161.138
134.808
131.138
131.116
130.908
130.490
130.437
123.869
115.785
115.644
77.212
77.000
76.788
56.403
34.379


F
NPhth
O
HN
F
F
F
F
CF3
2e

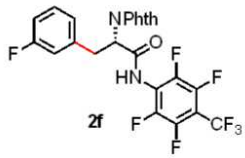

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

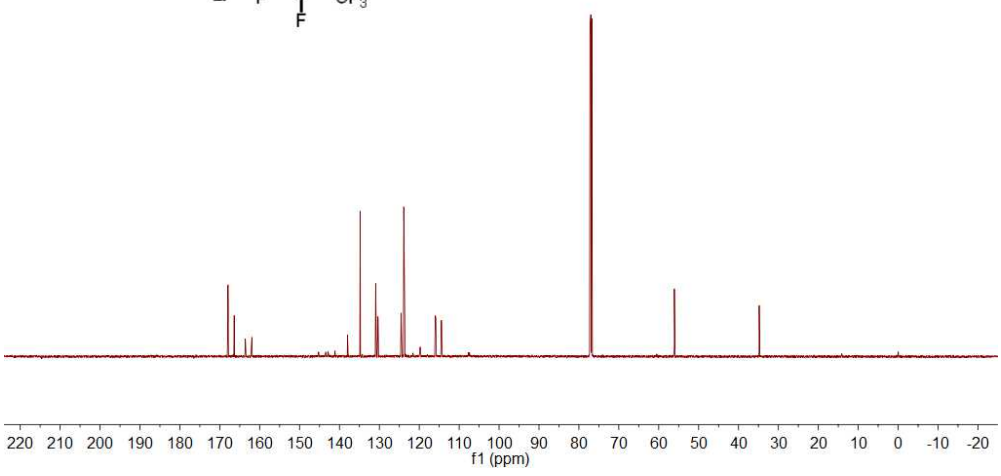

8.507
7.823
7.815
7.810
7.806
7.801
7.794
7.762
7.755
7.748
7.743
7.739
7.733
7.727
7.725
7.185
7.175
7.172
7.161
7.158
7.148
6.975
6.963
6.912
6.908
6.905
6.896
6.892
6.889
6.866
6.862
6.852
6.848
6.838
6.834
5.333
5.323
5.315
5.305
3.648
3.638
3.624
3.614
3.599
3.581
3.575
3.557


NPhth
O
F
HN
F
F
F
F
F
CF3
2f

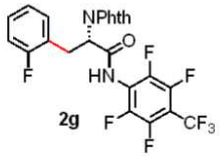

1.00
1.97
2.03
1.00
1.00
1.00
1.00
1.00
1.03
1.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

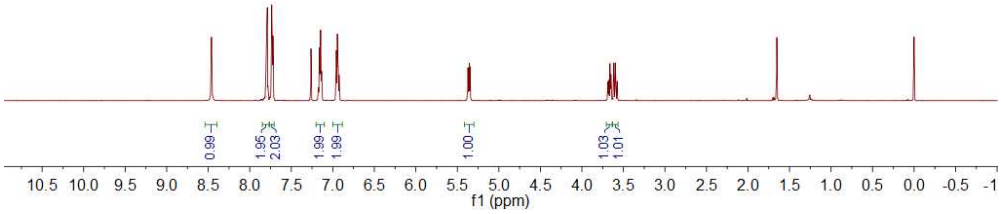

167.939
166.387
163.589
161.953
137.989
137.940
134.814
130.924
130.370
130.315
124.562
124.543
123.886
115.987
115.845
114.456
114.318
77.211
77.000
76.788
56.071
34.816


NPhth
O
F
HN
F
F
F
F
F
CF3
2f

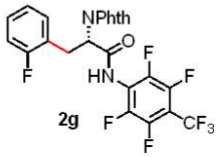

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


8.461
7.812
7.810
7.803
7.797
7.794
7.788
7.781
7.742
7.735
7.730
7.726
7.721
7.714
7.175
7.172
7.166
7.163
7.159
7.151
7.146
7.137
7.134
7.131
6.957
6.954
6.946
6.939
6.933
6.925
5.372
5.363
5.355
5.345
3.685
3.675
3.661
3.652
3.616
3.598
3.592
3.575

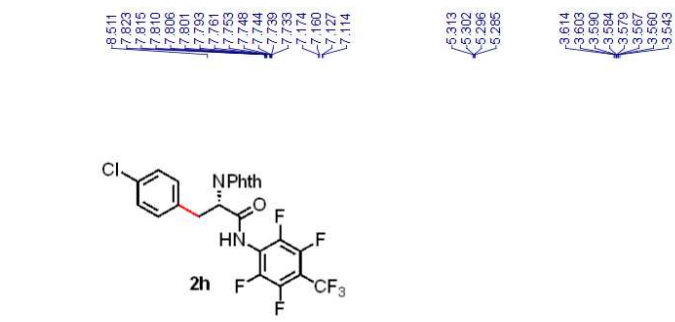

NPhth
O
HN
F
F
F
F
F
F
CF3
2g

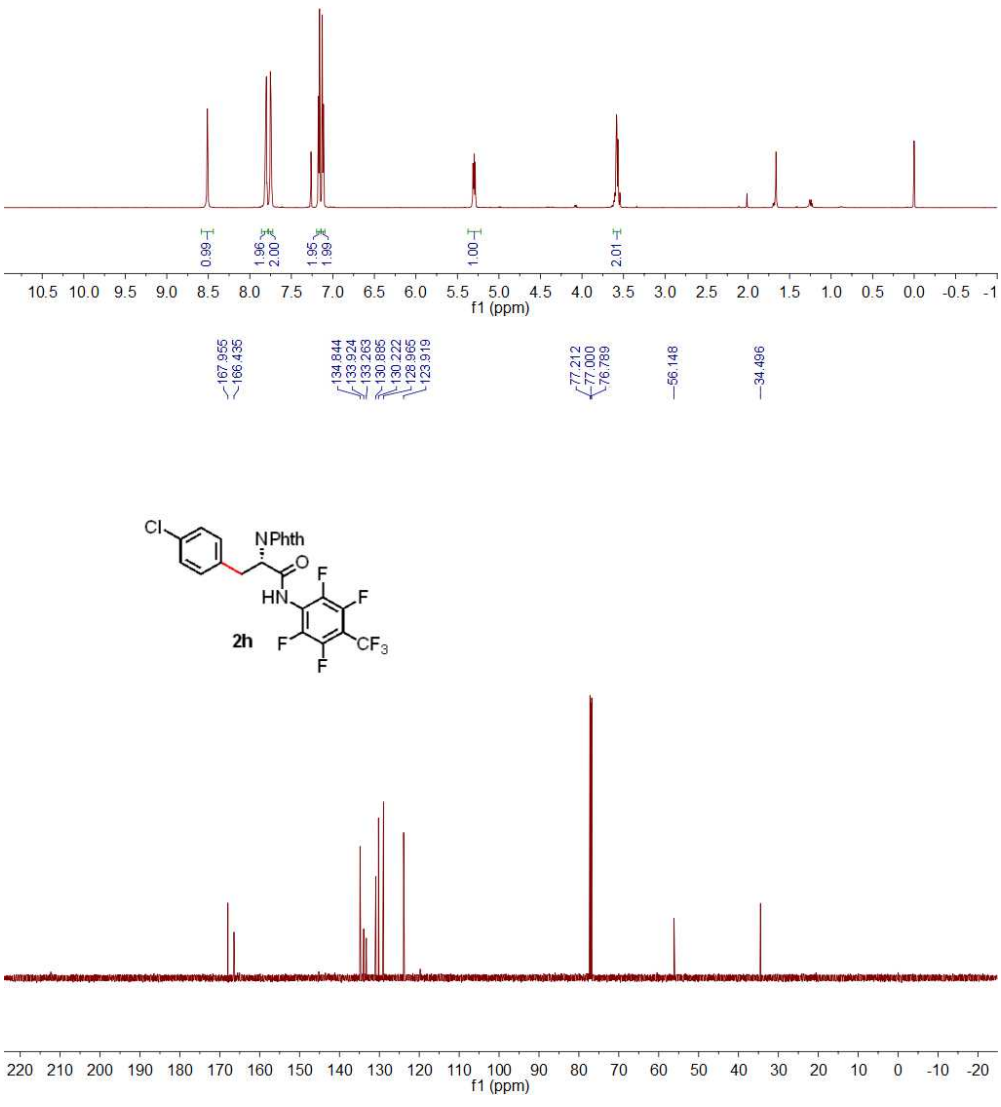

0.99
1.95
2.03
1.99
1.99
1.00
1.03
1.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


167.785
166.278
162.092
160.451
134.691
131.339
131.309
131.049
129.425
129.371
124.383
124.360
123.800
122.745
122.642
115.567
115.423
77.211
77.000
76.788
54.802
29.158
29.144


NPhth
O
HN
F
F
F
F
F
F
CF3
2g

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


8.511
7.823
7.815
7.810
7.806
7.801
7.793
7.761
7.753
7.748
7.744
7.739
7.733
7.174
7.160
7.127
7.114
5.313
5.302
5.296
5.285
3.614
3.603
3.590
3.584
3.579
3.567
3.560
3.543
Cl
NPhth
O
HN
F
F
F
F
CF3
2h
0.99
1.96
2.00
1.95
1.99
1.00
2.01
10.5 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 -1
f1 (ppm)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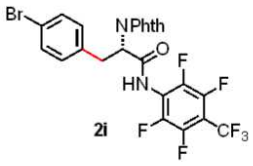
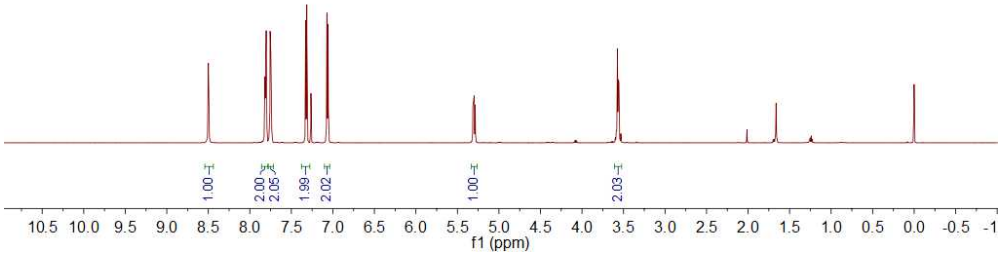
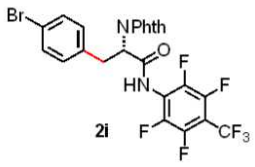
134.844
133.924
133.263
130.885
130.222
128.965
123.919
77.212
77.000
76.789
56.148
34.496
Cl
NPhth
O
HN
F
F
F
F
CF3
2h
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

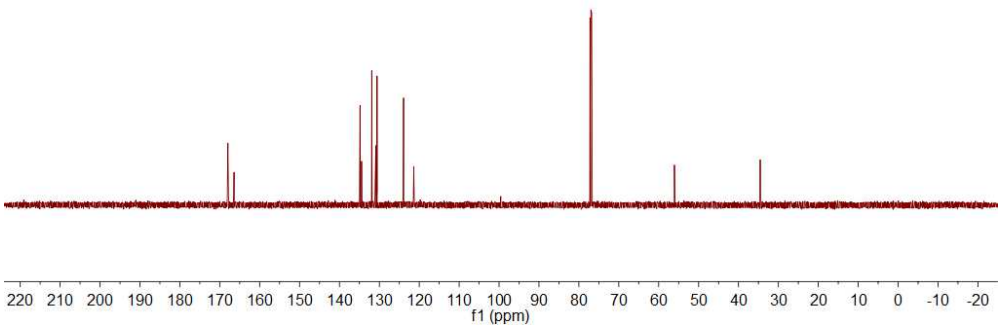

8.499
7.823
7.817
7.812
7.808
7.802
7.795
7.764
7.762
7.756
7.751
7.746
7.741
7.735
7.328
7.314
7.072
7.058
5.314
5.302
5.297
5.286
3.598
3.587
3.575
3.572
3.563
3.555
3.548
3.532

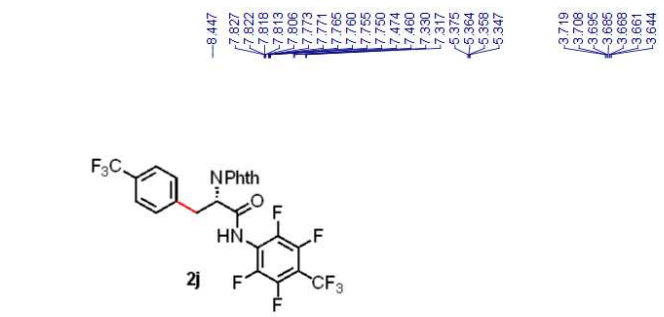

Br
NPhth
O
HN
F
F
F
F
CF3
2i

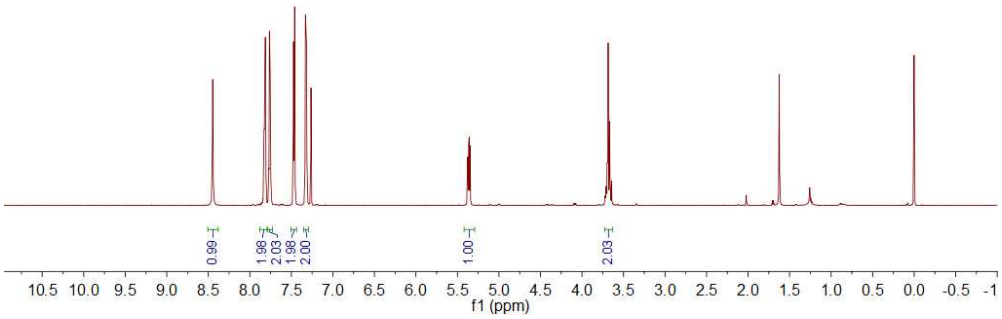

1.00
2.00
2.05
1.99
2.02
1.00
2.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


167.949
166.415
134.852
134.449
131.916
130.878
130.569
123.931
121.377
77.211
77.000
76.788
56.051
34.555


Br
NPhth
O
HN
F
F
F
F
CF3
2i


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


8.447
7.827
7.822
7.818
7.813
7.806
7.773
7.771
7.765
7.760
7.755
7.750
7.474
7.460
7.330
7.317
5.375
5.364
5.358
5.347
3.719
3.708
3.695
3.685
3.668
3.661
3.644
F3C
NPhth
O
HN
F
F
F
F
CF3
2j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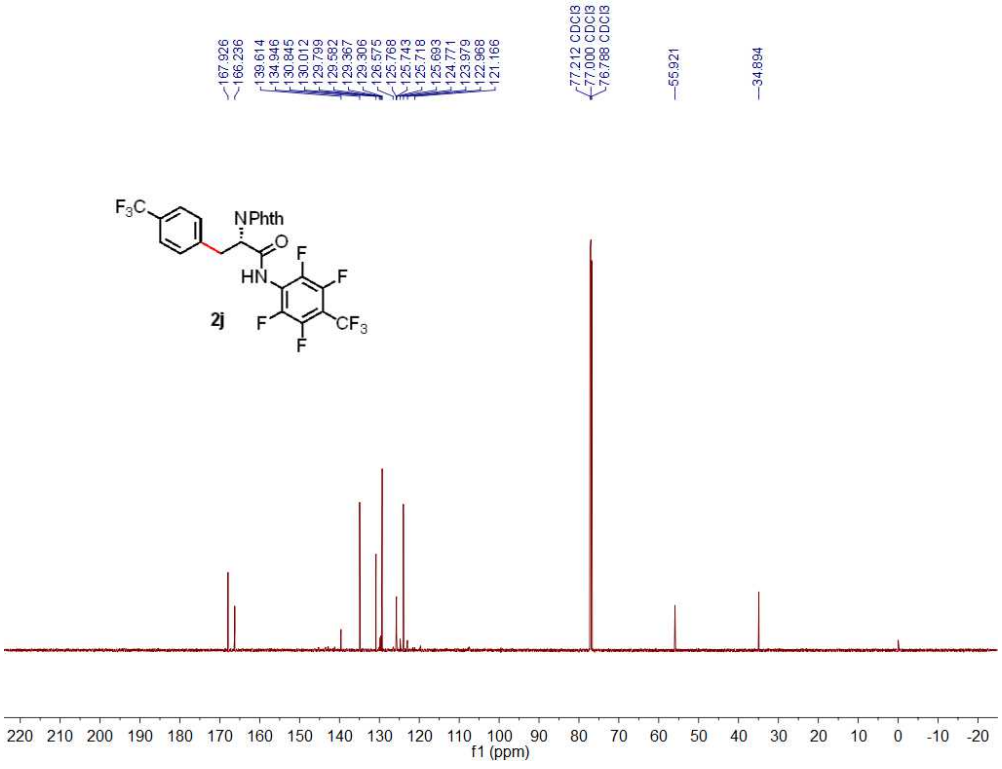
1.98
2.03
1.98
2.00
1.00
2.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)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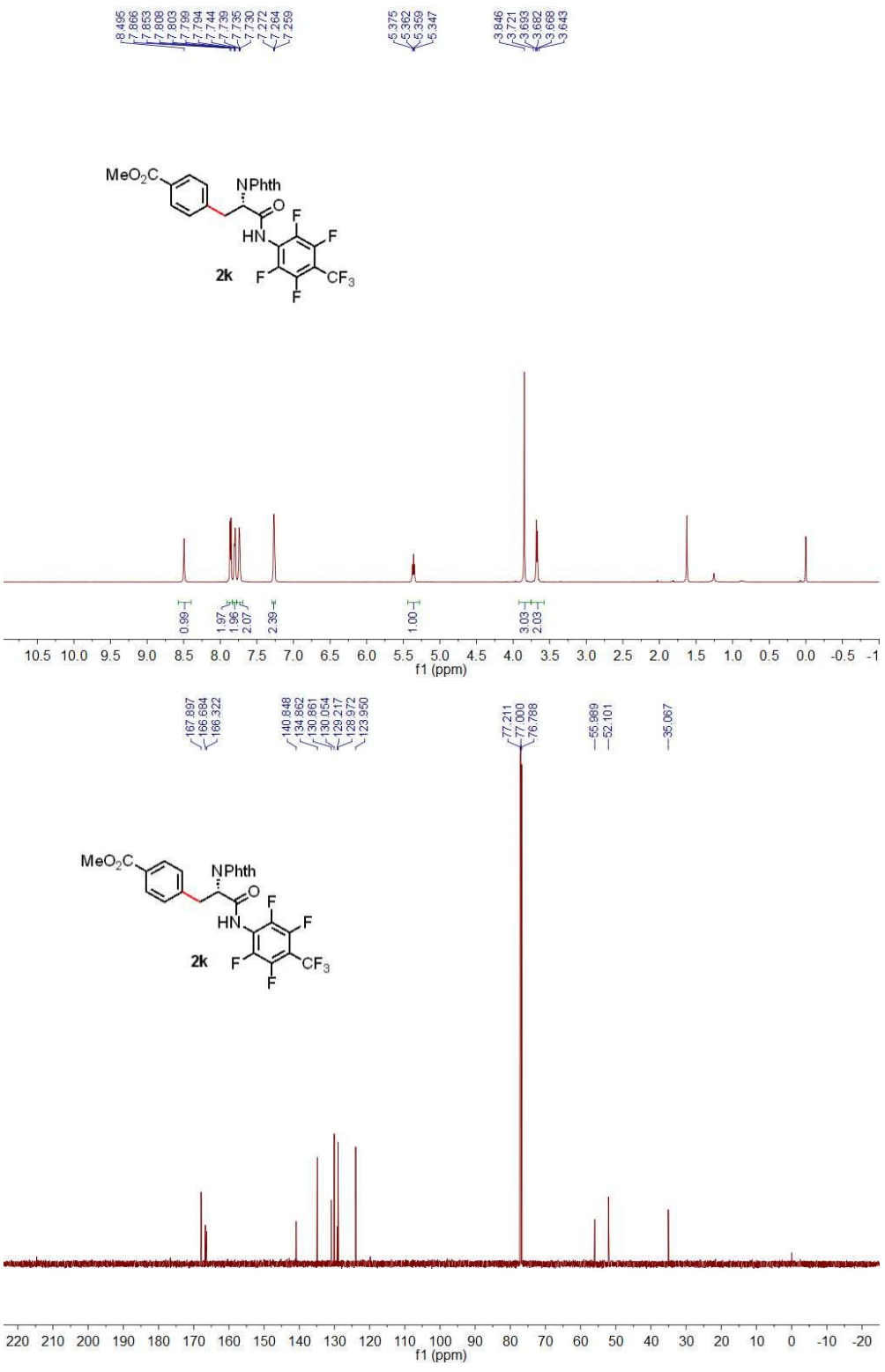
139.614
134.946
130.845
130.012
129.799
129.582
129.367
129.306
126.575
125.768
125.743
125.718
125.693
124.771
123.979
122.968
121.166
77.212 CDCl3
77.000 CDCl3
76.788 CDCl3
55.921
34.894
F3C
NPhth
O
HN
F
F
F
F
CF3
2j
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)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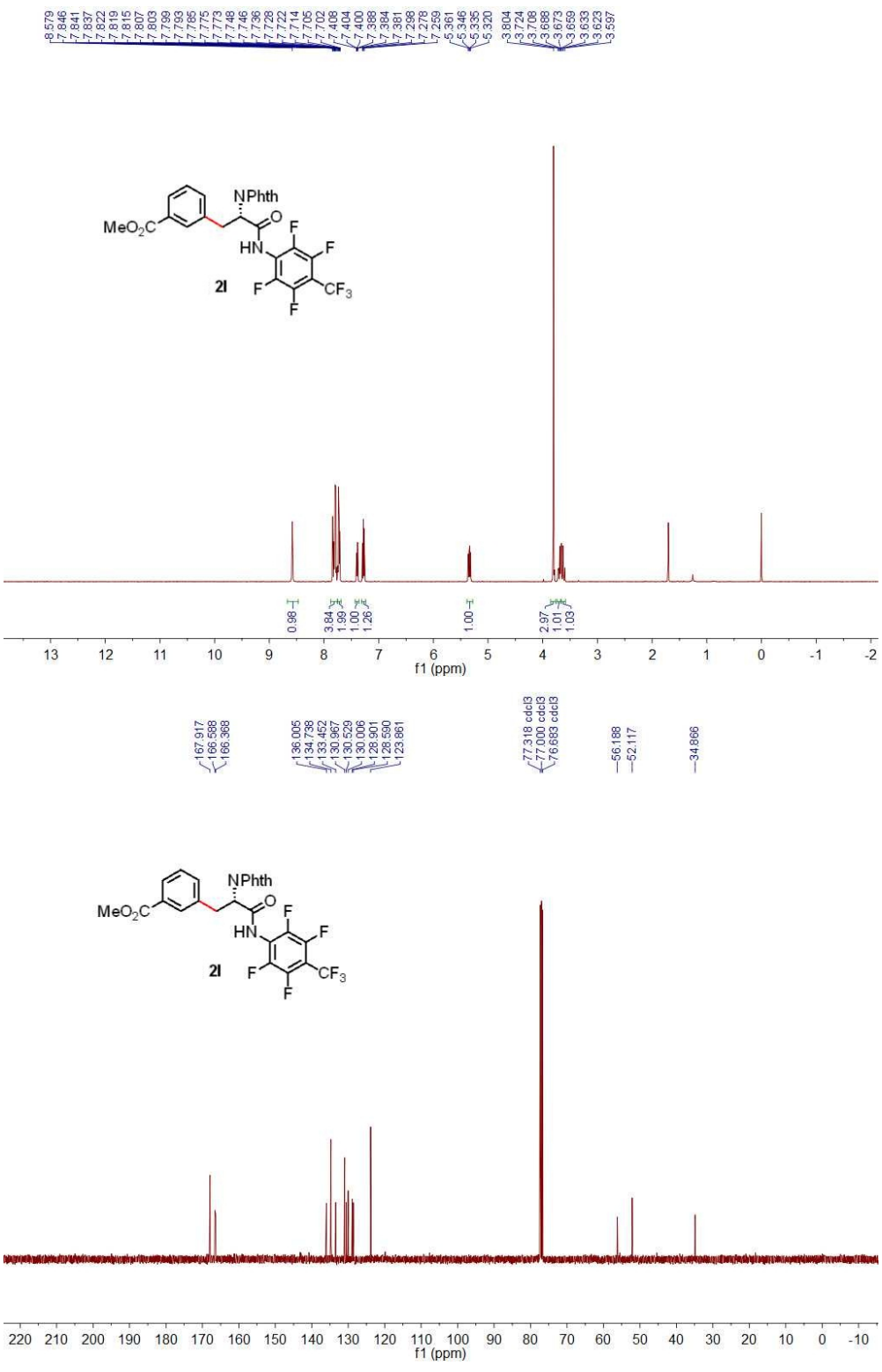
7.803
7.799
7.794
7.744
7.739
7.735
7.730
7.272
7.264
7.259
5.375
5.362
5.359
5.347
3.846
3.721
3.693
3.682
3.668
3.643
MeO2C
NPhth
O
HN
F
F
F
F
CF3
2k
0.99
1.97
1.96
2.07
2.39
1.00
3.03
2.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)
167.897
166.684
166.322
140.848
134.862
130.861
130.054
129.217
128.972
123.950
77.211
77.000
76.788
55.989
52.101
35.067
MeO2C
NPhth
O
HN
F
F
F
F
CF3
2k
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)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7.799
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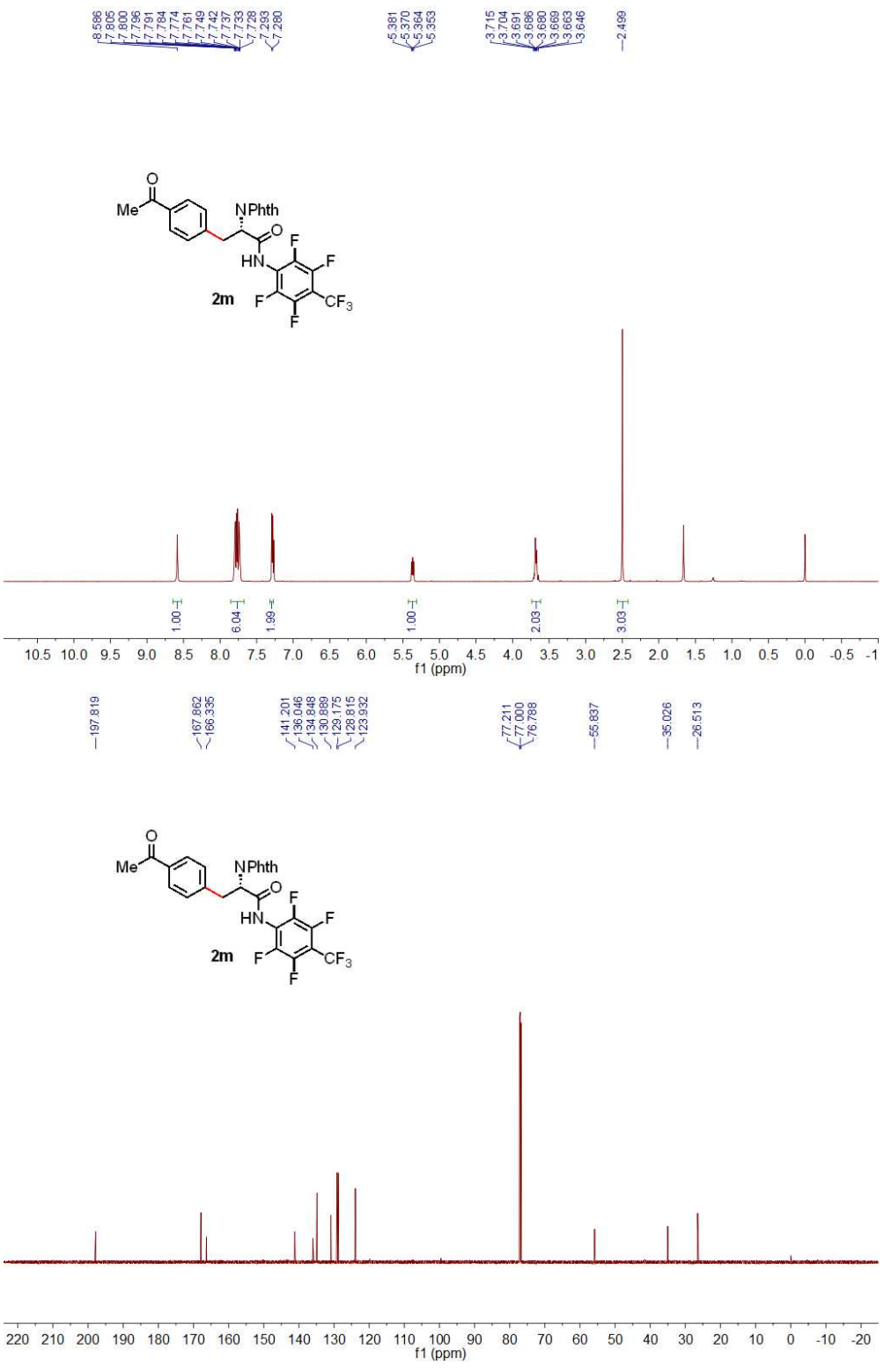
7.785
7.775
7.773
7.748
7.746
7.736
7.728
7.722
7.714
7.705
7.702
7.408
7.404
7.400
7.388
7.384
7.381
7.298
7.278
7.259
5.361
5.346
5.335
5.320
3.804
3.724
3.708
3.688
3.673
3.659
3.633
3.623
3.597
NPhth
MeO2C
O
HN
F
F
F
F
CF3
2l
0.98
3.84
1.99
1.00
1.26
1.00
2.97
1.01
1.03
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)
167.917
166.588
166.368
136.005
134.738
133.452
130.967
130.529
130.006
128.901
128.590
123.861
77.318 cdcl3
77.000 cdcl3
76.683 cdcl3
56.188
52.117
34.866
NPhth
MeO2C
O
HN
F
F
F
F
CF3
2l
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.774
7.761
7.749
7.742
7.737
7.733
7.728
7.293
7.280
5.381
5.370
5.364
5.353
3.715
3.704
3.691
3.686
3.680
3.669
3.663
3.646
2.499
Me
O
NPhth
HN
O
F
F
F
F
CF3
2m
1.00
6.04
1.99
1.00
2.03
3.03
f1 (ppm)
197.819
167.862
166.335
141.201
136.046
134.848
130.889
129.175
128.815
123.932
77.211
77.000
76.788
55.837
35.026
26.513
f1 (ppm)


8.413
8.063
8.050
7.828
7.822
7.819
7.814
7.806
7.781
7.773
7.769
7.765
7.759
7.388
7.374
5.383
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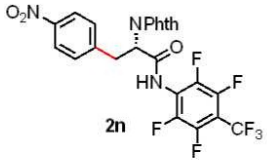
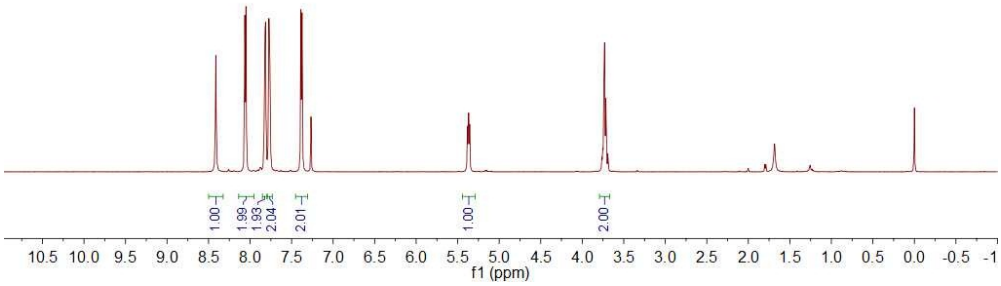
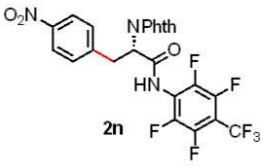
5.366
5.355
3.764
3.753
3.740
3.731
3.715
3.708
3.691

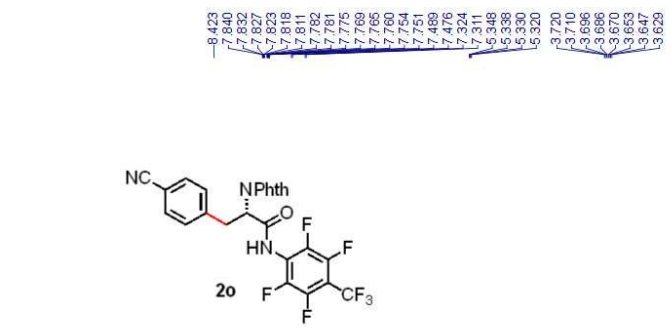

O2N
NPhth
O
HN
F
F
F
F
CF3
2n

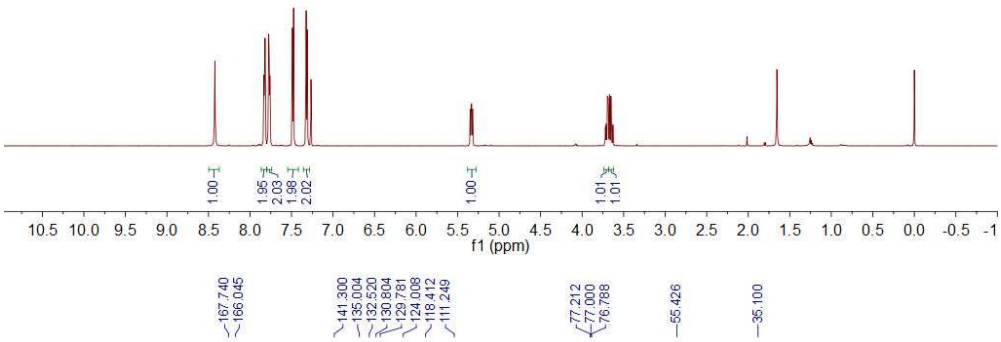

1.00
1.99
1.93
2.04
2.01
1.00
2.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

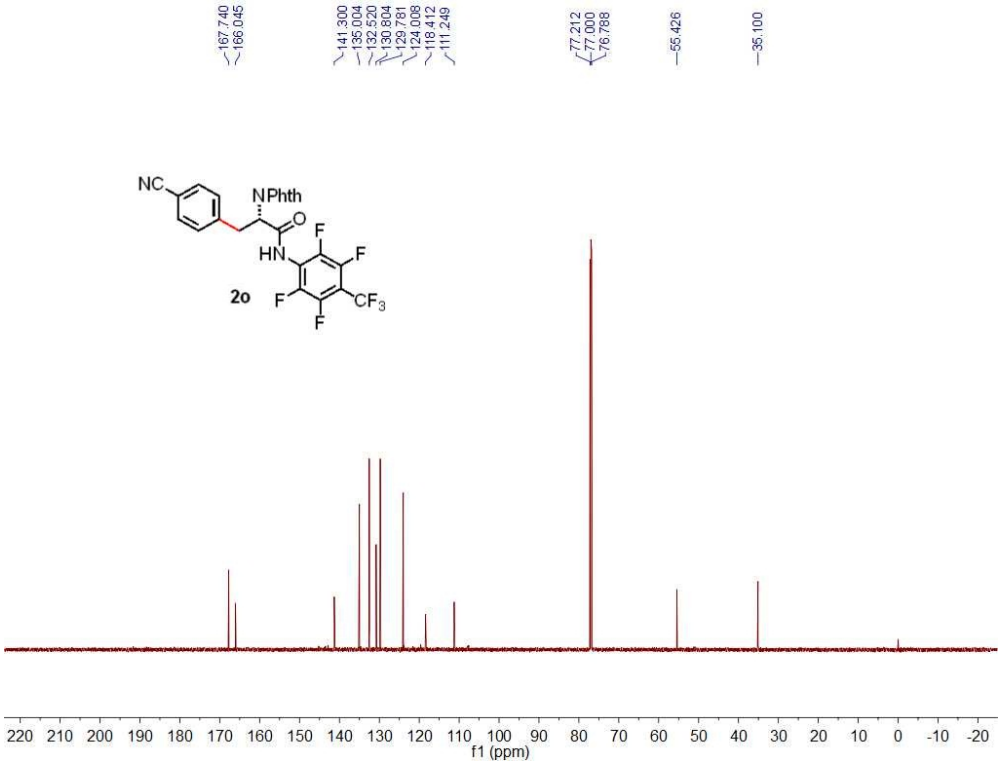

167.740
166.001
147.168
143.314
135.054
130.740
129.910
124.055
123.954
77.211
77.000
76.788
55.391
34.819


O2N
NPhth
O
HN
F
F
F
F
CF3
2n

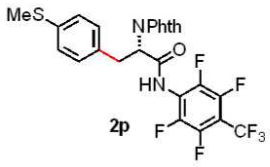
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


8.423
7.840
7.832
7.827
7.823
7.818
7.811
7.782
7.781
7.775
7.769
7.765
7.760
7.754
7.751
7.489
7.476
7.324
7.311
5.348
5.338
5.330
5.320
3.720
3.710
3.696
3.686
3.670
3.653
3.647
3.629
NC
NPhth
O
HN
F
F
F
F
CF3
2o


1.00
1.95
2.03
1.98
2.02
1.00
1.01
1.01
10.5 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 -1
f1 (ppm)

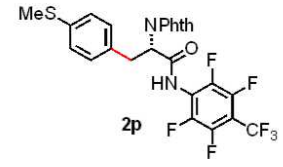

167.740
166.045
141.300
135.004
132.520
130.804
129.781
124.008
118.412
111.249
77.212
77.000
76.788
55.426
35.100
NC
NPhth
O
HN
F
F
F
F
CF3
2o
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

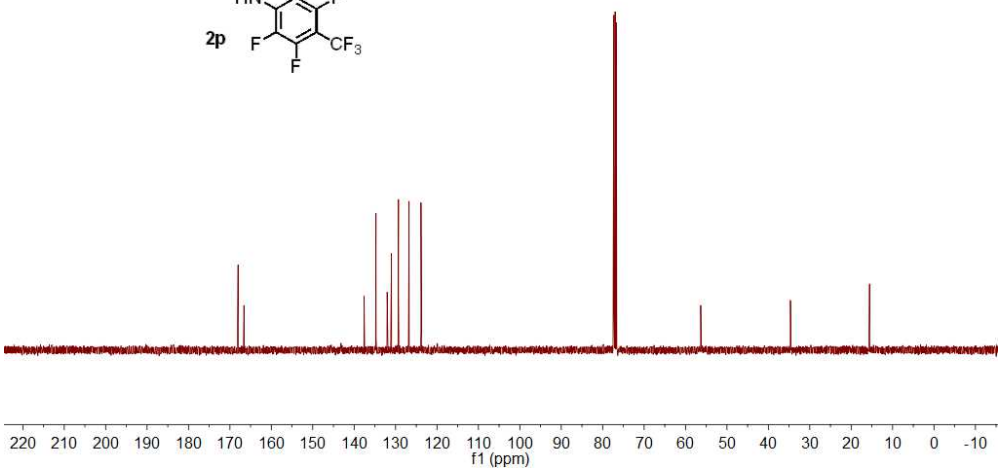

8.529
7.833
7.830
7.820
7.813
7.808
7.806
7.799
7.789
7.787
7.761
7.758
7.749
7.741
7.735
7.727
7.718
7.714
7.124
7.109
7.103
7.099
7.088
7.084
7.078
7.063
5.333
5.316
5.308
5.291
3.620
3.603
3.584
3.577
3.567
3.553
3.542
3.517
2.389


MeS
NPhth
O
HN
F
F
F
F
F
CF3
2p

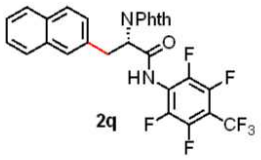
0.98
1.92
2.07
3.99
1.00
2.04
2.92
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)

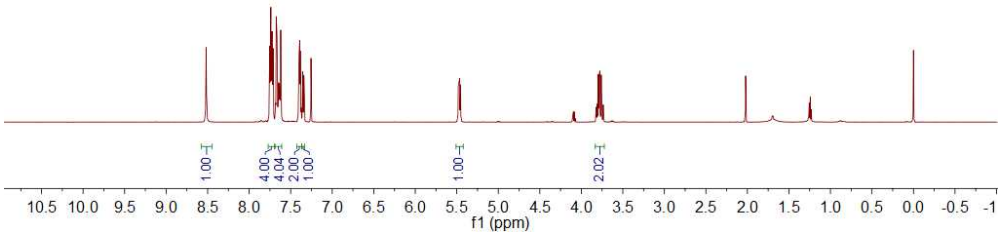

168.032
166.608
137.603
134.728
132.035
130.992
129.298
126.741
123.864
77.318 cdcl3
77.000 cdcl3
76.682 cdcl3
56.323
34.666
15.570


MeS
NPhth
O
HN
F
F
F
F
F
CF3
2p

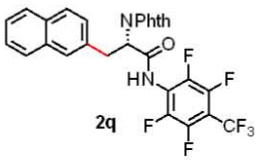

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


8.518
7.767
7.753
7.743
7.738
7.724
7.710
7.681
7.674
7.669
7.665
7.660
7.646
7.630
7.620
7.412
7.408
7.400
7.397
7.391
7.385
7.382
7.374
7.371
7.357
7.354
7.342
7.339
5.482
5.471
5.465
5.454
3.820
3.810
3.796
3.786
3.777
3.760
3.753
3.736

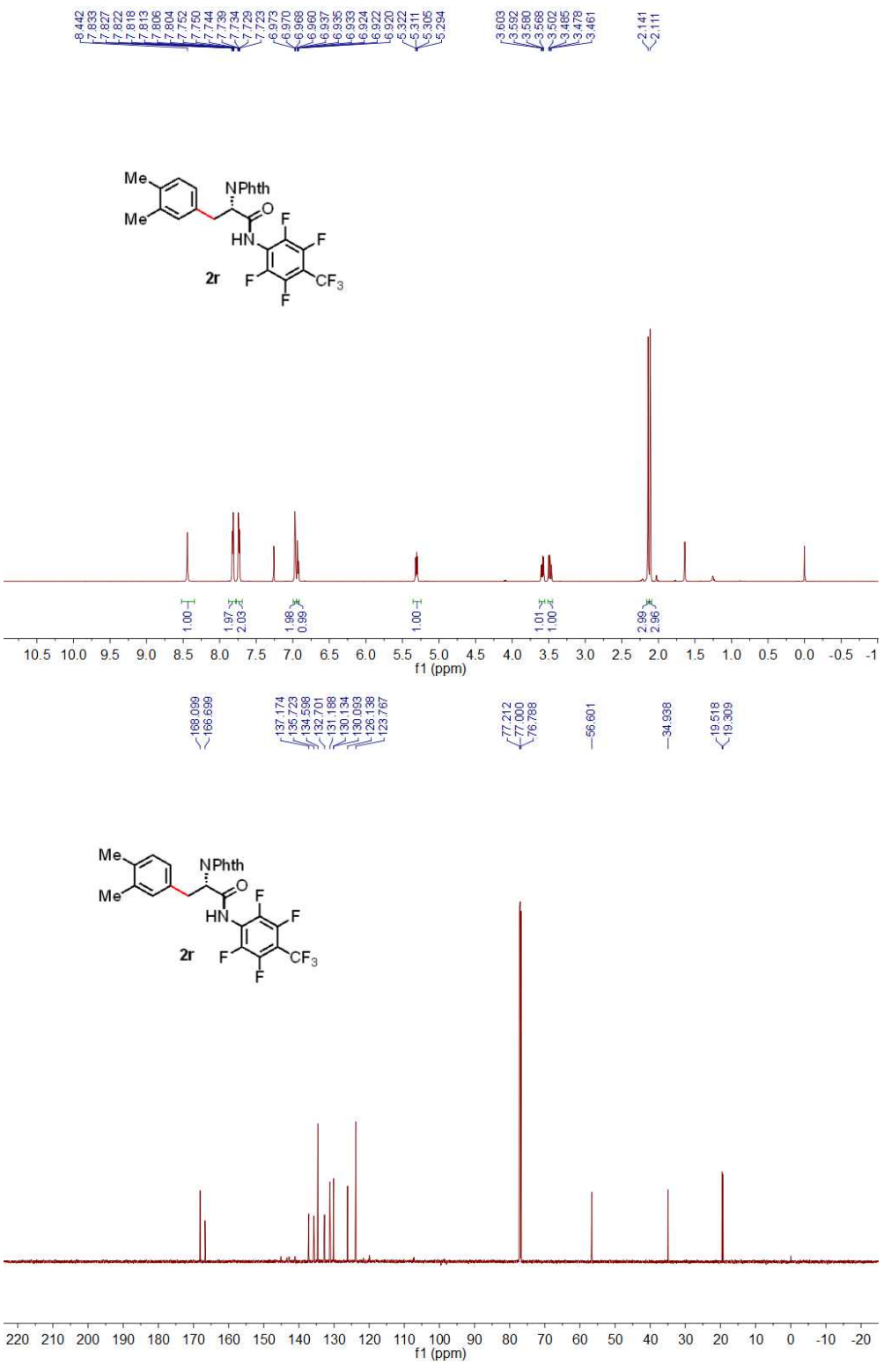

NPhth
O
HN
F
F
F
F
CF3
2q

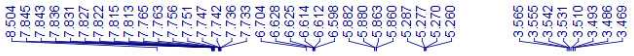

1.00
4.00
4.04
2.00
1.00
1.00
2.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


168.053
166.654
134.646
133.335
132.929
132.459
130.987
128.727
127.942
127.583
127.475
126.467
126.224
125.905
123.797
77.211
77.000
76.788
56.252
35.417


NPhth
O
HN
F
F
F
F
CF3
2q

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


8.442
7.833
7.827
7.822
7.818
7.813
7.806
7.804
7.752
7.750
7.744
7.739
7.734
7.729
7.723
6.973
6.970
6.968
6.960
6.937
6.935
6.933
6.924
6.922
6.920
5.322
5.311
5.305
5.294
3.603
3.592
3.580
3.568
3.502
3.485
3.478
3.461
2.141
2.111
Me
Me
NPhth
O
HN
F
F
F
F
F
CF3
2r
1.00
1.97
2.03
1.98
0.99
1.00
1.01
1.00
2.99
2.96
10.5 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 -1
f1 (ppm)
168.099
166.699
137.174
135.723
134.598
132.701
131.188
130.134
130.093
126.138
123.767
77.212
77.000
76.788
56.601
34.938
19.518
19.309
Me
Me
NPhth
O
HN
F
F
F
F
F
CF3
2r
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


8.504
7.845
7.843
7.836
7.831
7.827
7.822
7.815
7.813
7.765
7.763
7.756
7.751
7.747
7.742
7.736
7.733
6.704
6.628
6.625
6.614
6.612
6.598
5.882
5.880
5.863
5.860
5.287
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5.260
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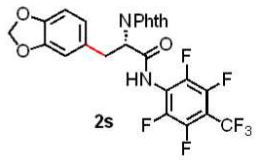
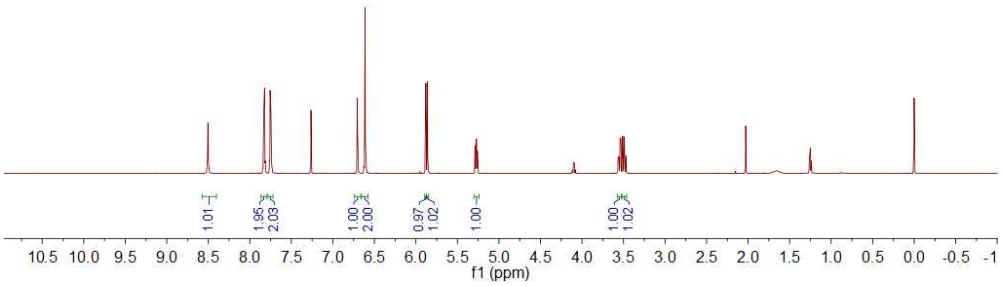
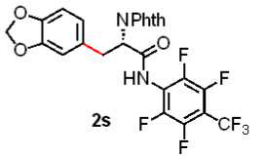
3.555
3.542
3.531
3.510
3.493
3.486
3.469


NPhth
O
HN
F
F
F
F
CF3

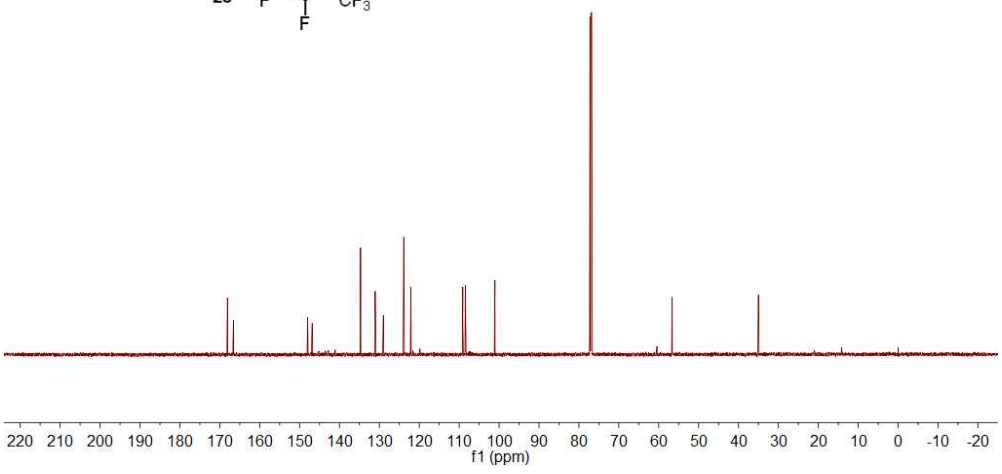
2s


1.01
1.95
2.03
1.00
2.00
0.97
1.02
1.00
1.00
1.02
10.5 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 -1
f1 (ppm)


168.071
166.579
147.975
146.835
134.726
131.061
129.000
123.880
122.104
109.092
108.451
101.039
77.211
77.000
76.788
56.633
35.001


NPhth
O
HN
F
F
F
F
CF3

2s


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


8.440
7.826
7.816
7.808
7.804
7.801
7.794
7.784
7.776
7.766
7.759
7.756
7.752
7.744
7.735
7.732
7.675
7.653
5.330
5.315
5.304
5.289
3.809
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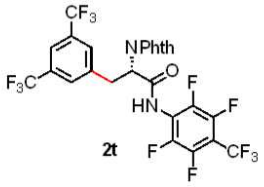
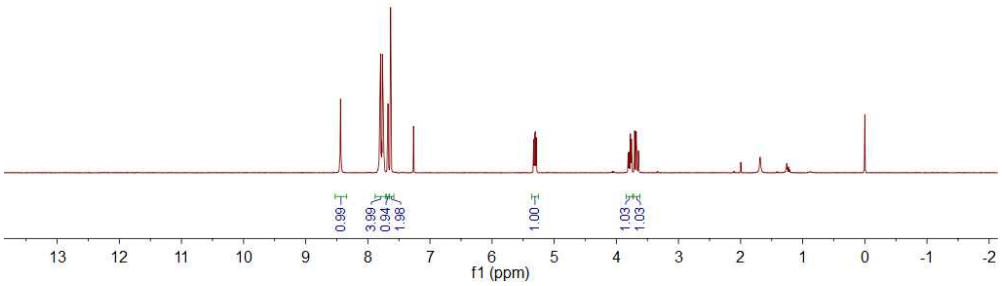
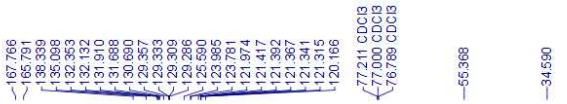
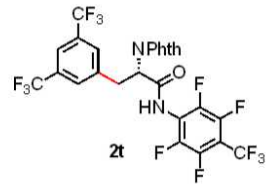
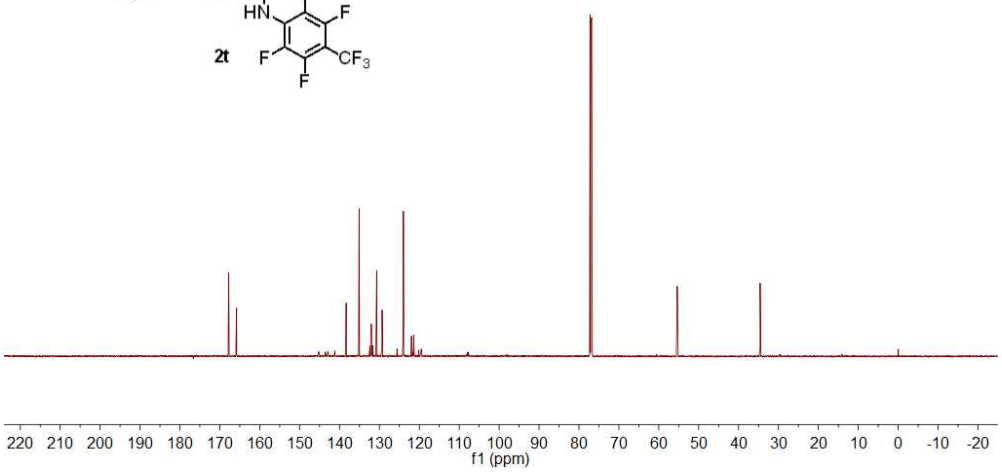
3.773
3.758
3.706
3.680
3.670
3.644

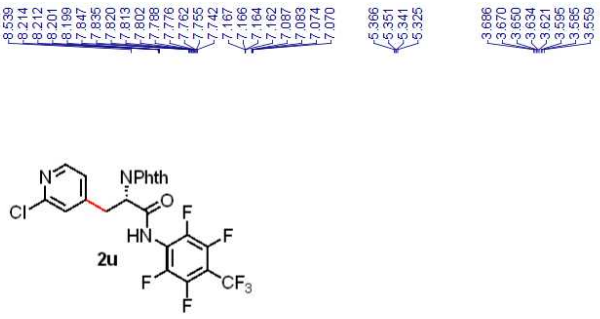

CF3
NPhth
F3C
O
HN
F
F
F
CF3
F
2t

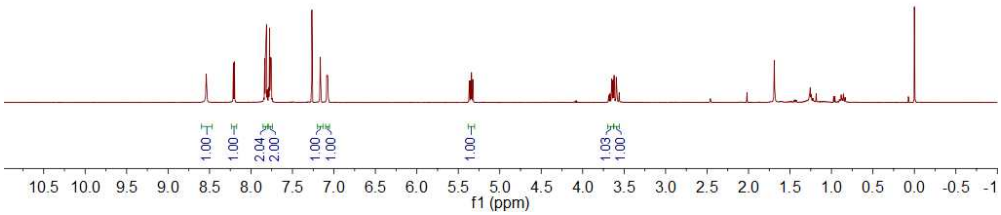

0.99
3.99
0.94
1.98
1.00
1.03
1.03
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)

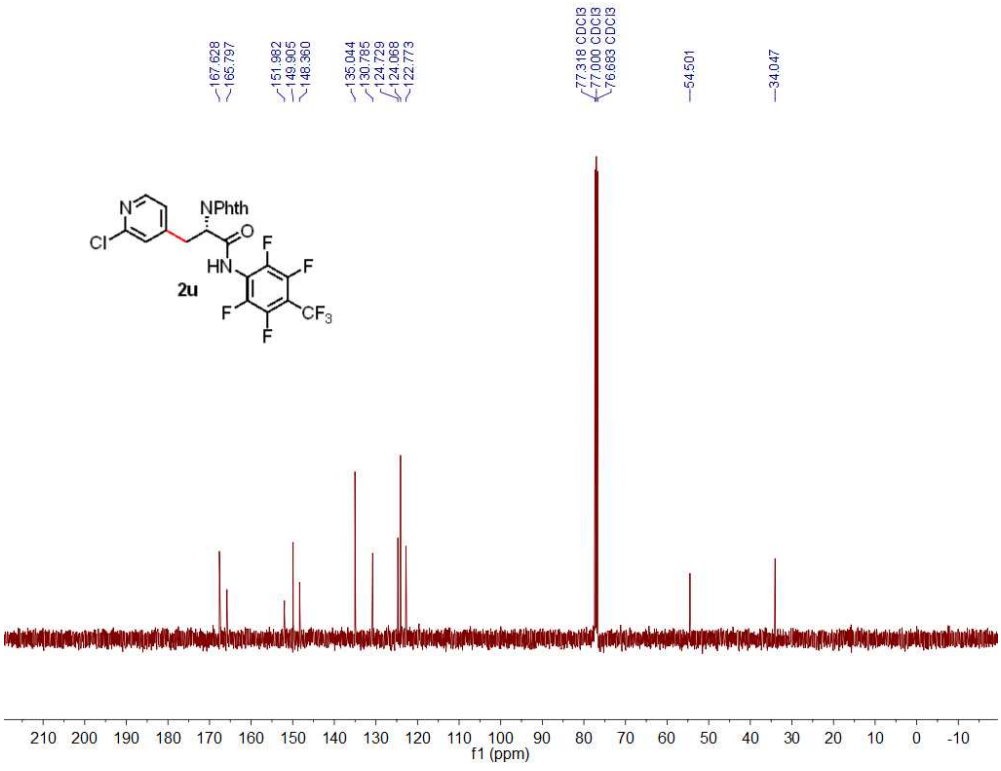

167.766
165.791
138.339
135.098
132.353
132.132
131.910
131.888
130.690
129.357
129.333
129.309
129.286
125.590
123.985
123.781
121.974
121.417
121.392
121.367
121.341
121.315
120.166
77.211 CDCl3
77.000 CDCl3
76.789 CDCl3
55.368
34.590

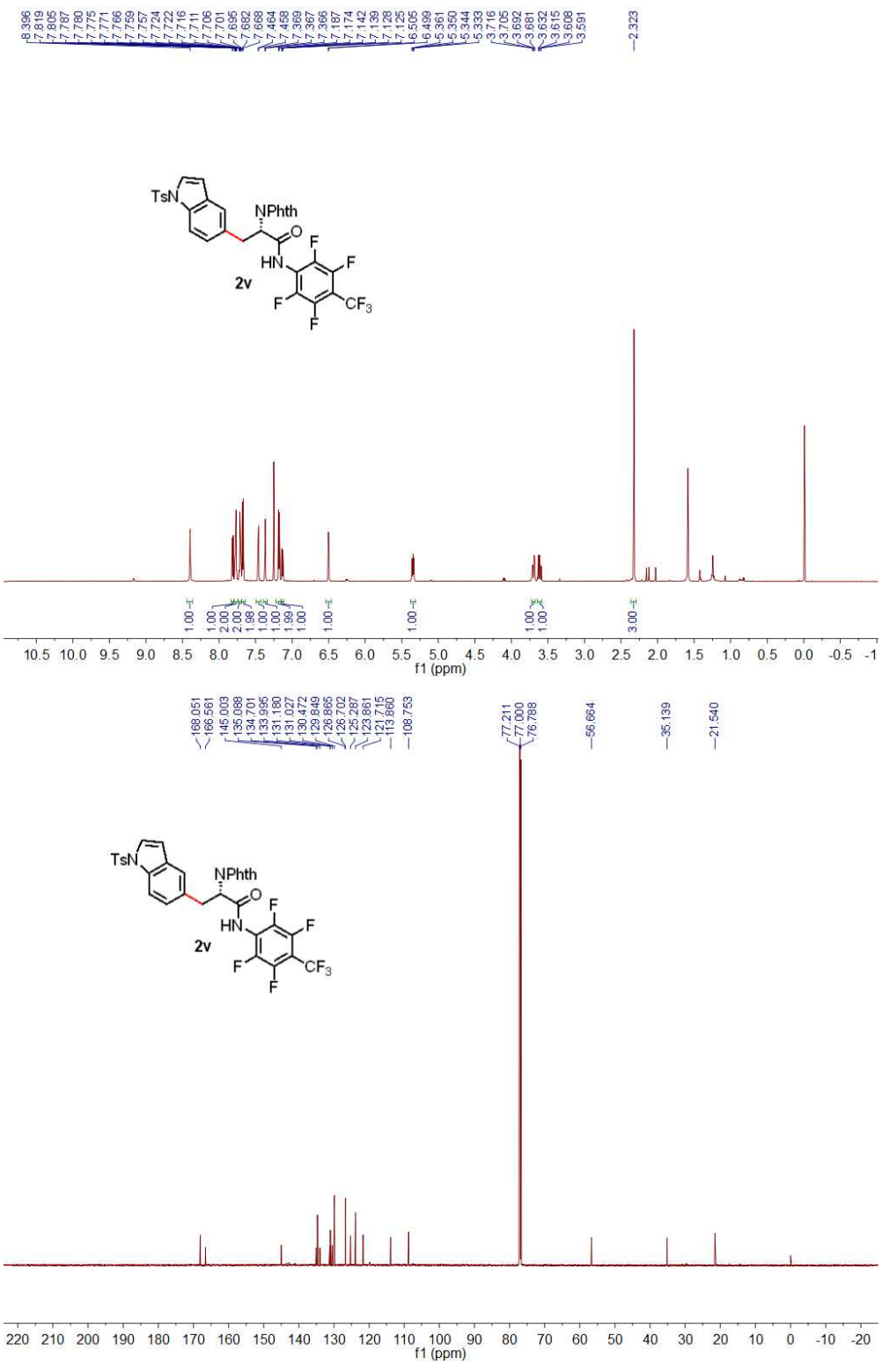

CF3
NPhth
F3C
O
HN
F
F
F
CF3
F
2t


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


8.539
8.214
8.212
8.201
8.199
7.847
7.835
7.820
7.813
7.802
7.788
7.776
7.762
7.755
7.742
7.167
7.166
7.164
7.162
7.087
7.083
7.074
7.070
5.366
5.351
5.341
5.325
3.686
3.670
3.650
3.634
3.621
3.595
3.585
3.559
NPhth
Cl
HN
O
F
F
F
F
CF3
2u


1.00
1.00
2.04
2.00
1.00
1.00
1.00
1.03
1.00
10.5 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 -1
f1 (ppm)


167.628
165.797
151.982
149.905
148.360
135.044
130.785
124.729
124.068
122.773
77.318 CDCl3
77.000 CDCl3
76.683 CDCl3
54.501
34.047
NPhth
Cl
HN
O
F
F
F
F
CF3
2u
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.787
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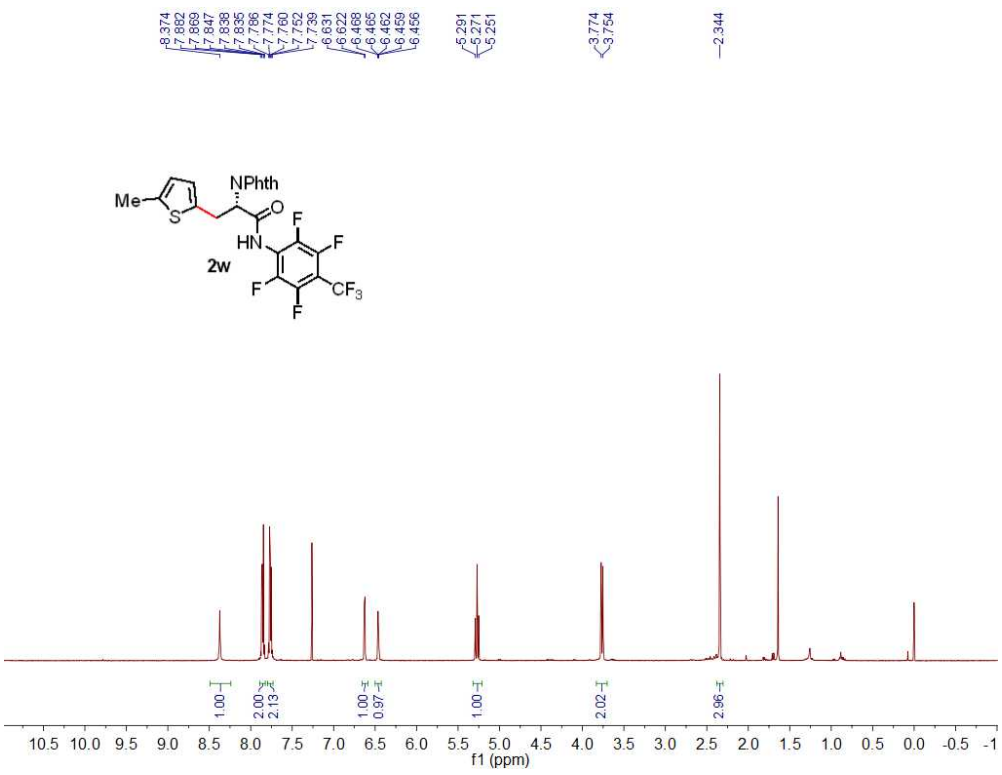
7.775
7.771
7.766
7.759
7.757
7.724
7.722
7.716
7.711
7.706
7.701
7.695
7.682
7.668
7.464
7.458
7.369
7.367
7.366
7.187
7.174
7.142
7.139
7.128
7.125
6.505
6.499
5.361
5.350
5.344
5.333
3.716
3.705
3.692
3.681
3.632
3.615
3.608
3.591
2.323
TsN
NPhth
O
HN
F
F
F
F
CF3
2v
1.00
1.00
2.00
2.00
1.98
1.00
1.99
1.00
1.00
1.00
1.00
1.00
3.00
10.5 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 -1
f1 (ppm)
168.051
166.561
145.003
135.088
134.701
133.995
131.180
131.027
130.472
129.849
126.865
126.702
125.287
123.861
121.715
113.860
108.753
77.211
77.000
76.788
56.664
35.139
21.540
TsN
NPhth
O
HN
F
F
F
F
CF3
2v
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


8.374
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7.847
7.838
7.835
7.786
7.774
7.760
7.752
7.739
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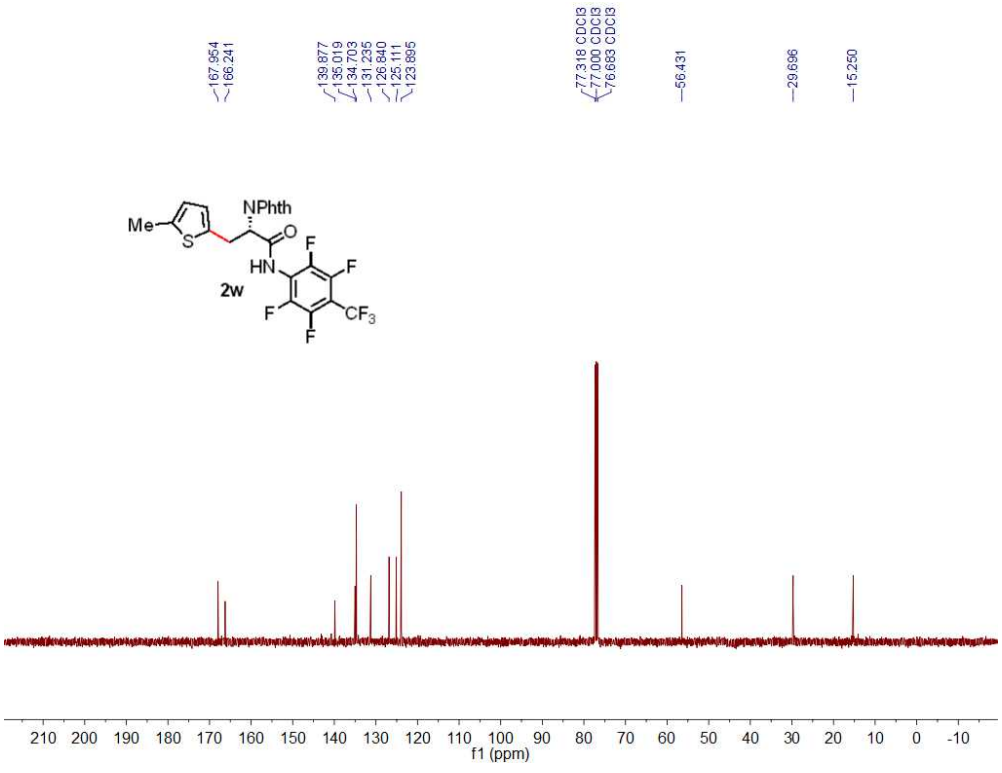
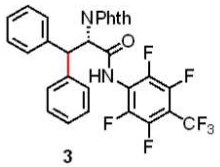
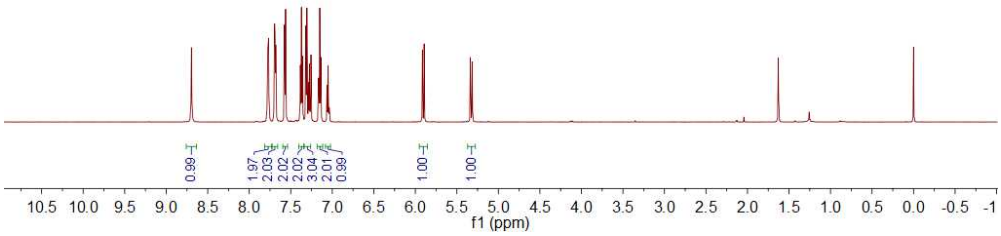
6.622
6.468
6.465
6.462
6.459
6.456
5.291
5.271
5.251
3.774
3.754
2.344
NPhth
Me
S
O
HN
F
F
F
F
CF3
2w
1.00
2.00
2.13
1.00
0.97
1.00
2.02
2.96
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


167.954
166.241
139.877
135.019
134.703
131.235
126.840
125.111
123.895
77.318 CDCl3
77.000 CDCl3
76.683 CDCl3
56.431
29.696
15.250
NPhth
Me
S
O
HN
F
F
F
F
CF3
2w
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

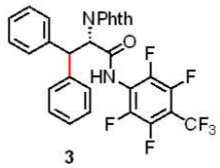

8.896
7.781
7.776
7.772
7.767
7.760
7.702
7.695
7.690
7.686
7.681
7.673
7.574
7.562
7.384
7.372
7.359
7.320
7.318
7.306
7.287
7.275
7.262
7.164
7.151
7.138
7.063
7.061
7.050
7.038
5.915
5.894
5.337
5.315


NPhth
O
HN
F
F
F
F
CF3

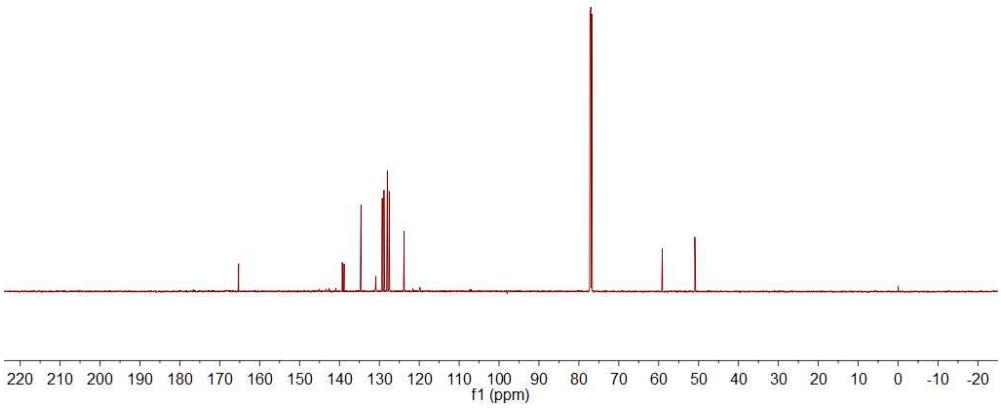
3

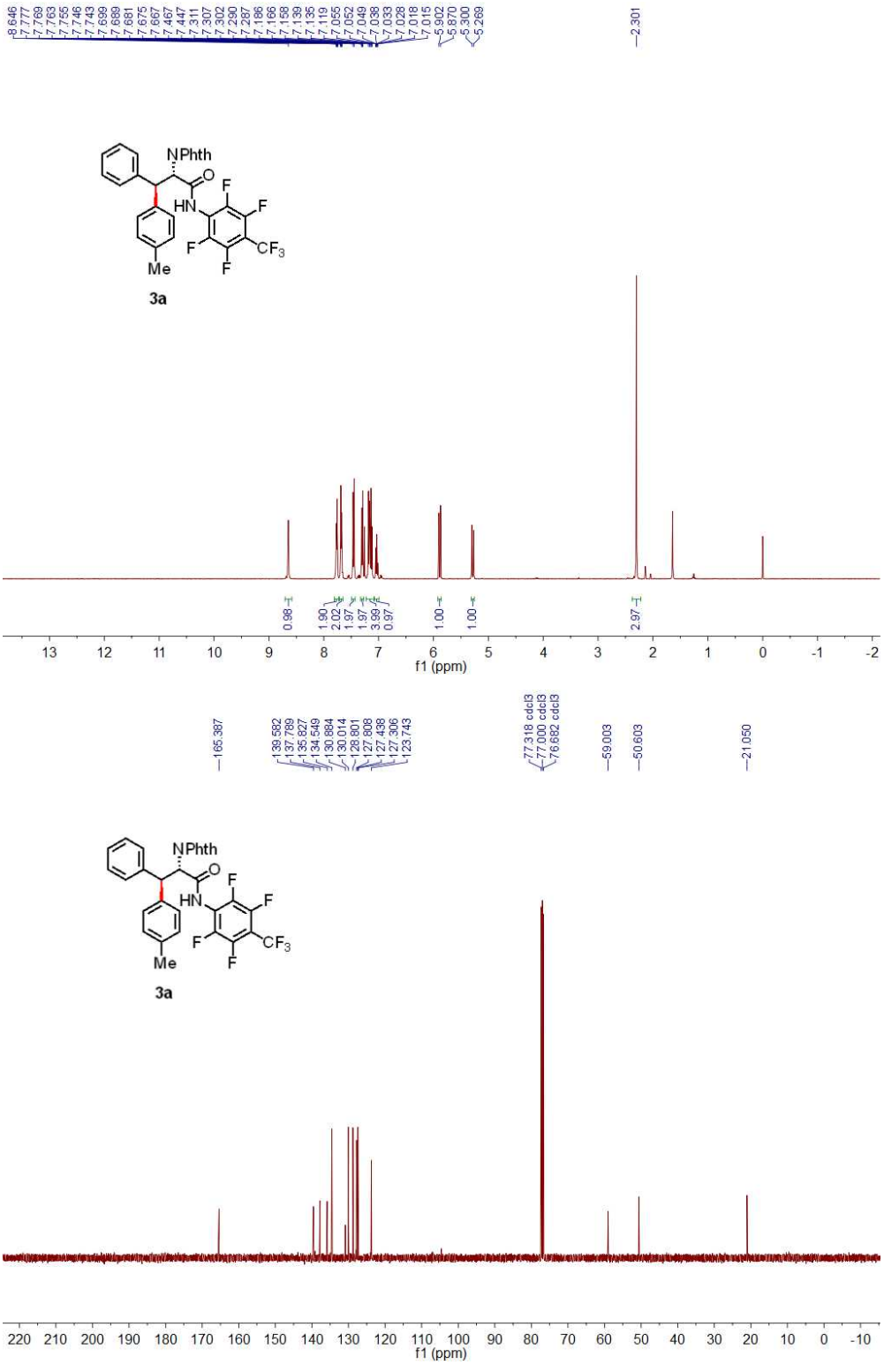

0.99
1.97
2.03
2.02
2.02
3.04
2.01
0.99
1.00
1.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

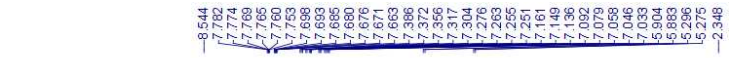

165.268
139.299
138.820
134.605
130.858
129.278
128.838
128.003
127.530
127.420
123.787
77.212
77.000
76.788
59.095
50.936

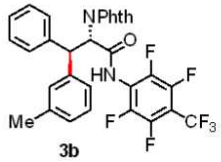

NPhth
O
HN
F
F
F
F
CF3

3

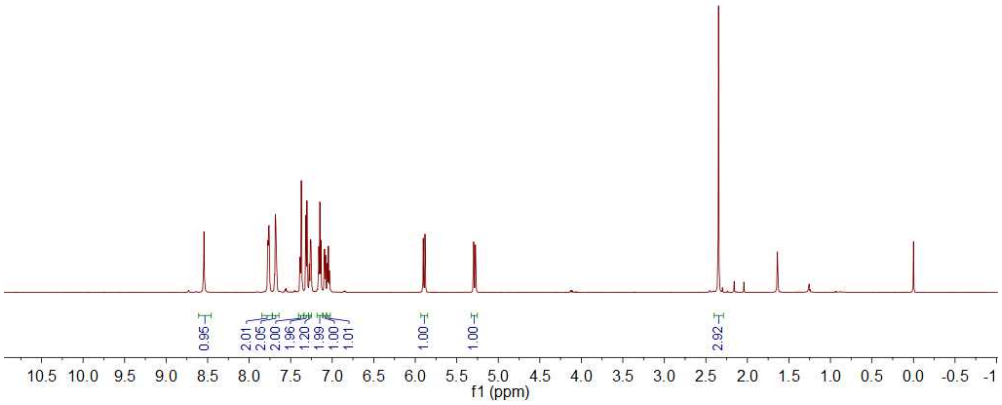

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


8.646
7.777
7.769
7.763
7.755
7.746
7.743
7.699
7.689
7.681
7.675
7.667
7.467
7.447
7.311
7.307
7.302
7.290
7.287
7.186
7.166
7.158
7.139
7.135
7.119
7.055
7.052
7.049
7.038
7.033
7.028
7.018
7.015
5.902
5.870
5.300
5.269
2.301
NPhth
O
HN
F
F
F
F
CF3
Me
3a
0.98
1.90
2.02
1.97
1.97
3.99
0.97
1.00
1.00
2.97
f1 (ppm)
165.387
139.582
137.789
135.827
134.549
130.884
130.014
128.801
127.808
127.438
127.306
123.743
77.318 cdcl3
77.000 cdcl3
76.682 cdcl3
59.003
50.603
21.050
f1 (ppm)

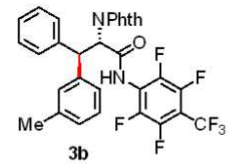

8.544
7.782
7.774
7.769
7.765
7.760
7.753
7.698
7.693
7.685
7.680
7.676
7.671
7.663
7.386
7.372
7.356
7.317
7.304
7.276
7.263
7.255
7.251
7.161
7.149
7.136
7.092
7.079
7.058
7.046
7.033
5.904
5.883
5.296
5.275
2.348


NPhth
O
HN
F
F
F
F
Me
CF3

3b


0.95
2.01
2.05
2.00
1.96
1.20
1.99
1.00
1.01
1.00
1.00
2.92
10.5 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 -1
f1 (ppm)

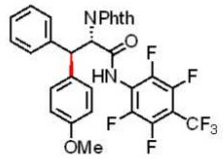

165.321
139.467
139.123
138.811
134.534
130.908
129.215
128.832
128.800
128.762
127.521
127.345
124.864
123.740
77.211
77.000
76.788
58.891
50.842
21.465


NPhth
O
HN
F
F
F
F
Me
CF3

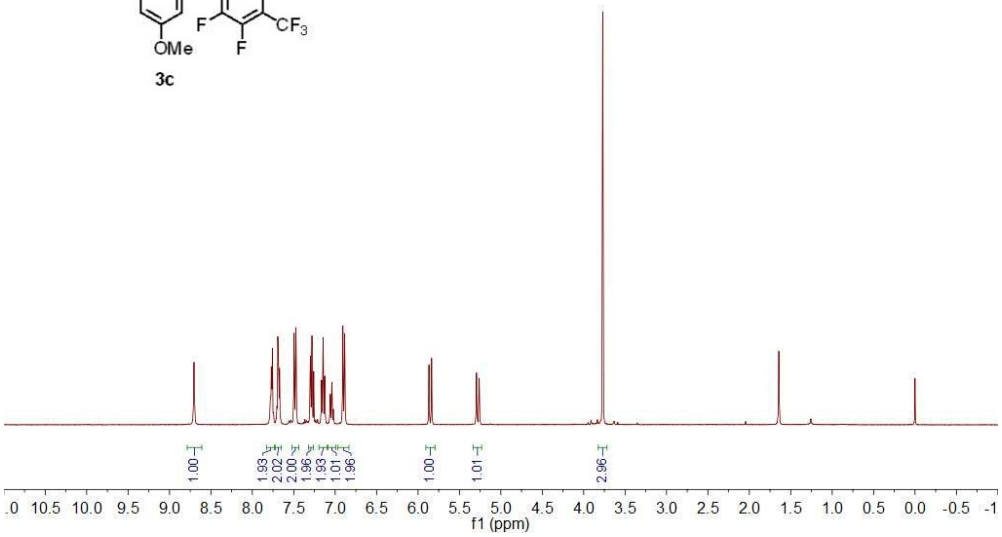
3b

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

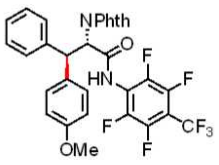

8.704
7.800
7.791
7.779
7.771
7.765
7.758
7.748
7.745
7.712
7.704
7.693
7.685
7.679
7.671
7.661
7.504
7.496
7.490
7.479
7.474
7.466
7.302
7.298
7.284
7.280
7.278
7.165
7.159
7.146
7.130
7.126
7.062
7.059
7.055
7.045
7.040
7.035
7.025
7.022
7.018
6.916
6.907
6.902
6.890
6.886
6.877
5.668
5.636
5.294
5.262
3.770


NPhth
O
HN
F
F
F
F
CF3
OMe

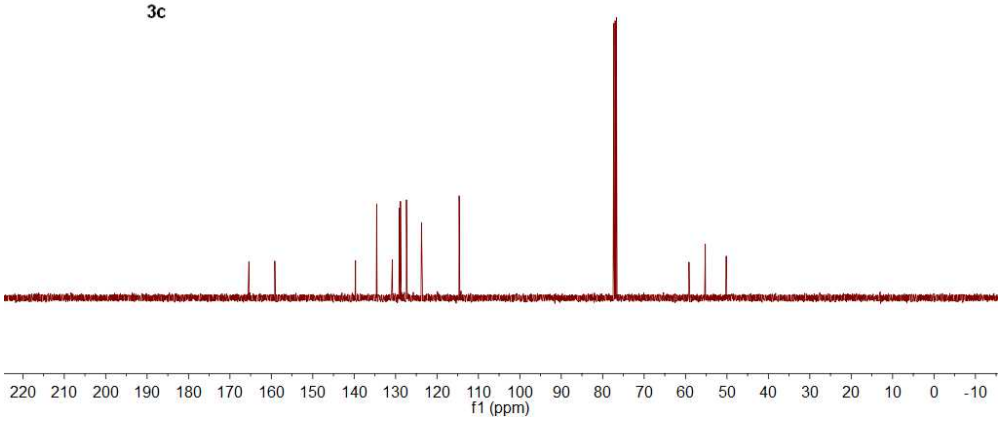
3c


1.00
1.93
2.02
2.00
1.96
1.93
1.01
1.96
1.00
1.01
2.96
.0 10.5 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 -1
f1 (ppm)

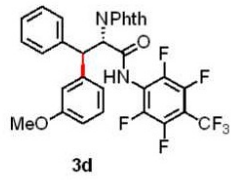

165.418
159.158
139.673
134.570
130.869
130.786
129.083
128.813
127.377
127.295
123.756
114.656
77.318 cdcl3
77.000 cdcl3
76.683 cdcl3
59.159
55.220
50.176


NPhth
O
HN
F
F
F
F
CF3
OMe

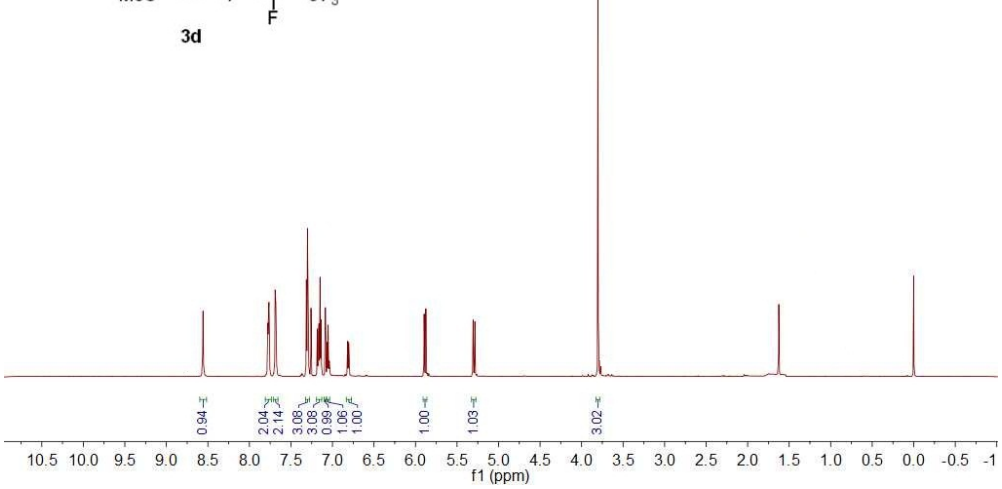
3c


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

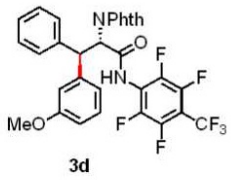

8.558
7.778
7.773
7.769
7.764
7.756
7.698
7.691
7.686
7.682
7.677
7.669
7.315
7.313
7.301
7.299
7.289
7.184
7.181
7.170
7.162
7.150
7.137
7.089
7.085
7.081
7.066
7.064
7.062
7.052
7.042
7.040
7.038
6.820
6.816
6.807
6.805
6.802
5.896
5.875
5.306
5.285
3.802


NPhth
O
HN
F
F
F
F
MeO
CF3

3d


0.94
2.04
2.14
3.08
3.08
0.99
1.06
1.00
1.00
1.03
3.02
10.5 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 -1
f1 (ppm)

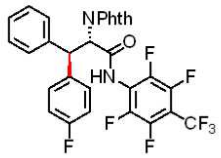

165.248
160.128
140.459
139.262
134.560
130.894
130.400
128.821
127.518
127.431
123.763
120.014
114.148
113.092
77.212
77.000
76.789
58.824
55.249
50.830


NPhth
O
HN
F
F
F
F
MeO
CF3

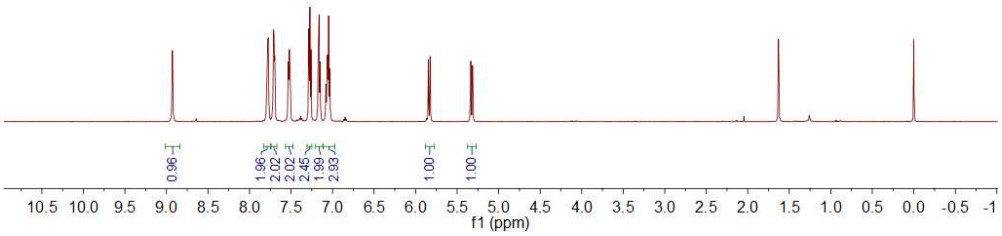
3d

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

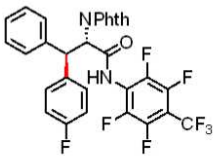

8.928
7.797
7.788
7.782
7.779
7.774
7.766
7.718
7.710
7.705
7.701
7.696
7.689
7.533
7.524
7.519
7.510
7.285
7.272
7.259
7.175
7.162
7.149
7.081
7.068
7.061
7.056
7.047
7.033
5.845
5.824
5.335
5.314


NPhth
O
HN
F
F
F
F
F
CF3

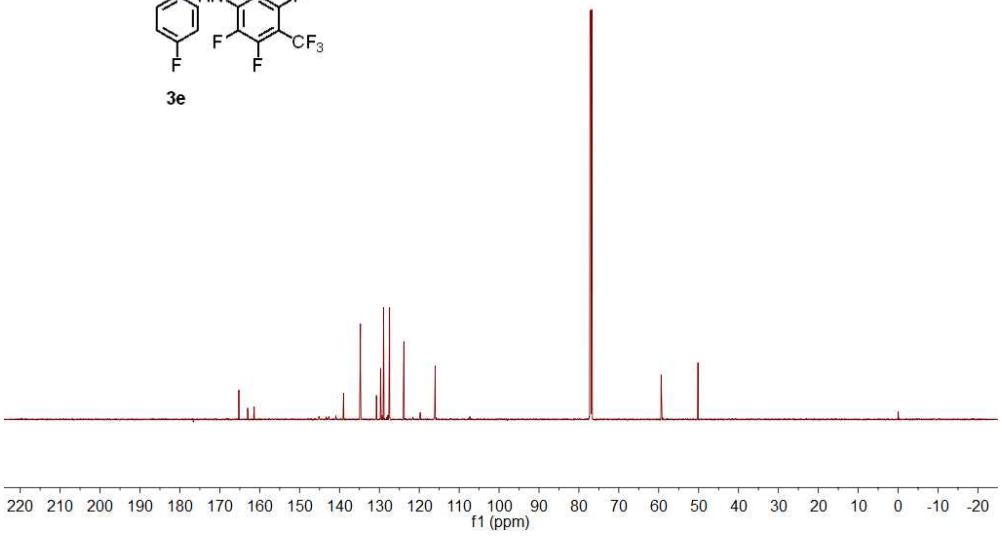
3e


0.96
1.96
2.02
2.02
2.45
1.99
2.93
1.00
1.00
10.5 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 -1
f1 (ppm)


165.218
163.016
161.378
138.977
134.734
134.548
134.527
130.747
129.710
129.656
128.943
127.583
127.446
123.868
116.146
116.003
77.211
77.000
76.788
59.398
50.164


NPhth
O
HN
F
F
F
F
F
CF3

3e


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


8.919
7.792
7.785
7.780
7.776
7.771
7.764
7.717
7.710
7.705
7.700
7.695
7.688
7.488
7.474
7.331
7.317
7.272
7.259
7.170
7.157
7.144
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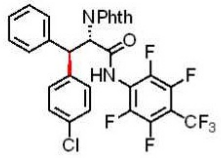
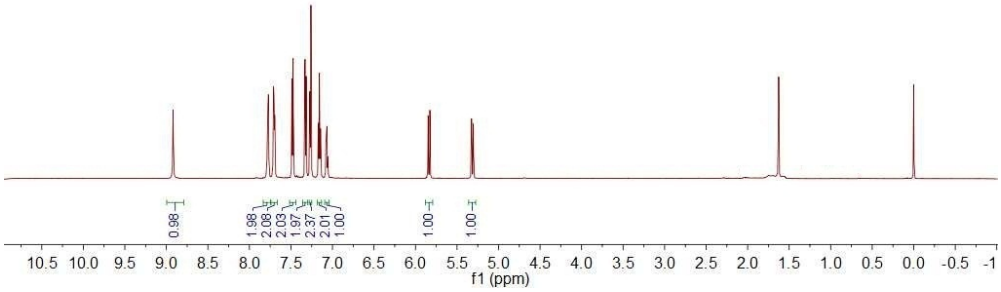
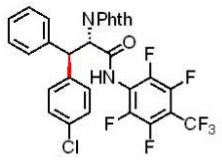
7.067
7.054
5.847
5.826
5.325
5.303


NPhth
O
HN
F
F
F
F
CF3
Cl

3f


0.98
1.98
2.08
2.03
1.97
2.37
2.01
1.00
1.00
1.00
10.5 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 -1
f1 (ppm)


165.155
138.721
137.274
134.754
133.778
130.726
129.358
129.280
128.969
127.660
127.475
123.880
77.211
77.000
76.789
59.163
50.282


NPhth
O
HN
F
F
F
F
CF3
Cl

3f

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


8.909
7.789
7.785
7.780
7.776
7.772
7.765
7.719
7.714
7.711
7.705
7.702
7.699
7.697
7.485
7.471
7.427
7.413
7.270
7.267
7.260
7.255
7.169
7.156
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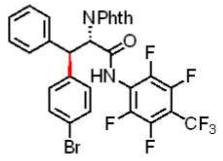
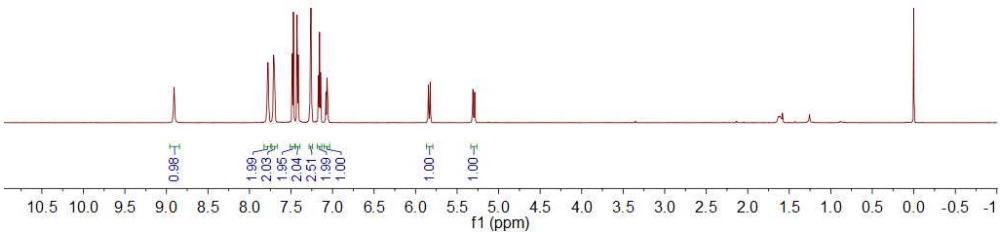
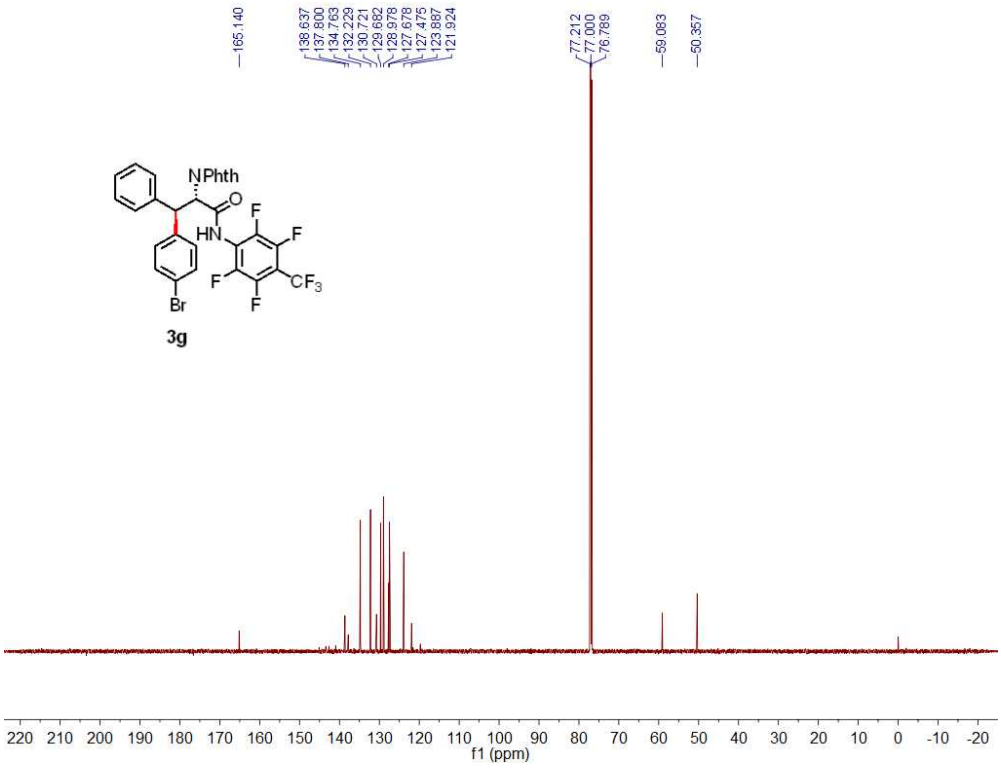
7.057
7.055
5.845
5.824
5.309
5.288

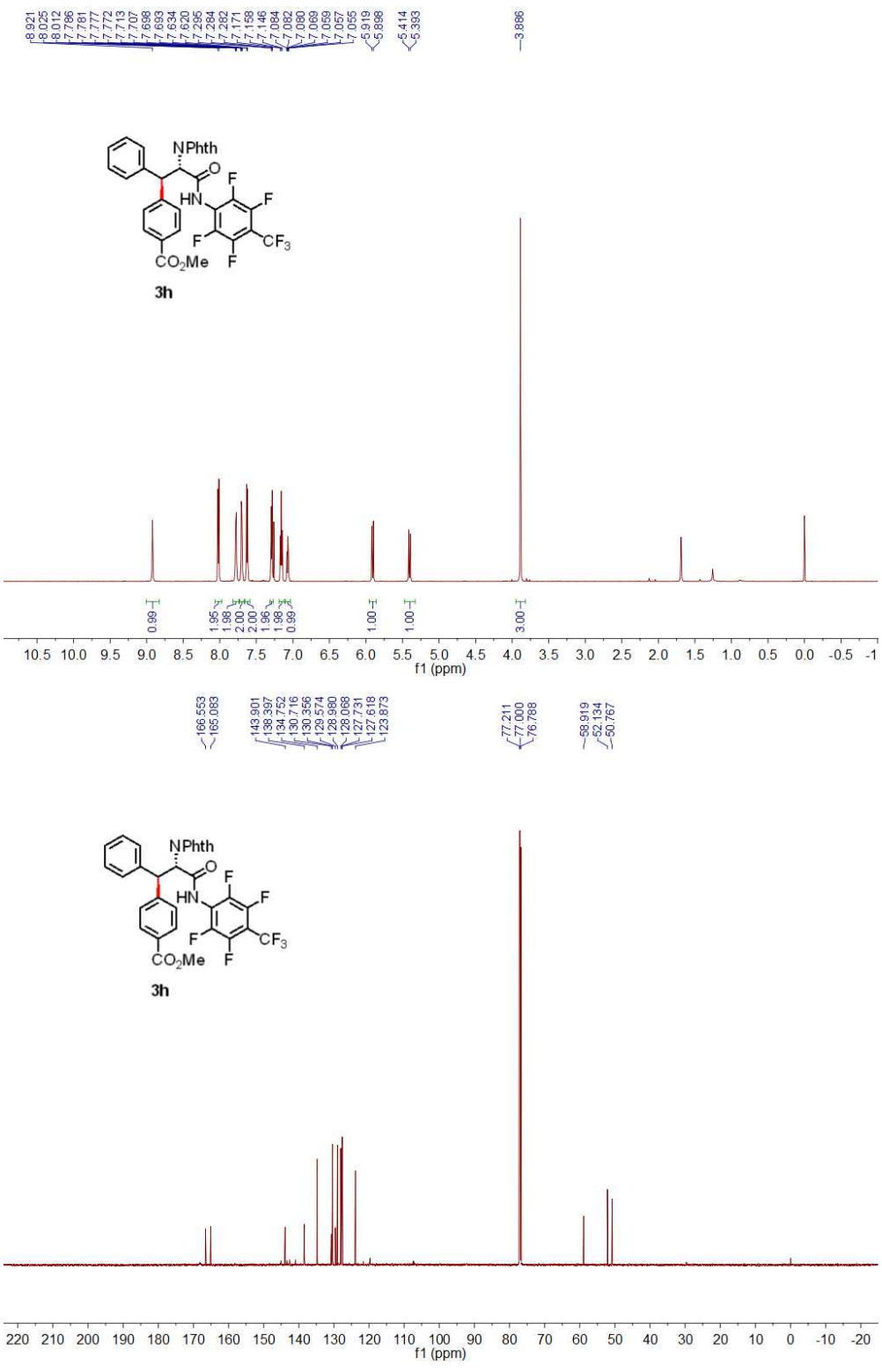

NPhth
O
HN
F
F
F
F
CF3
Br

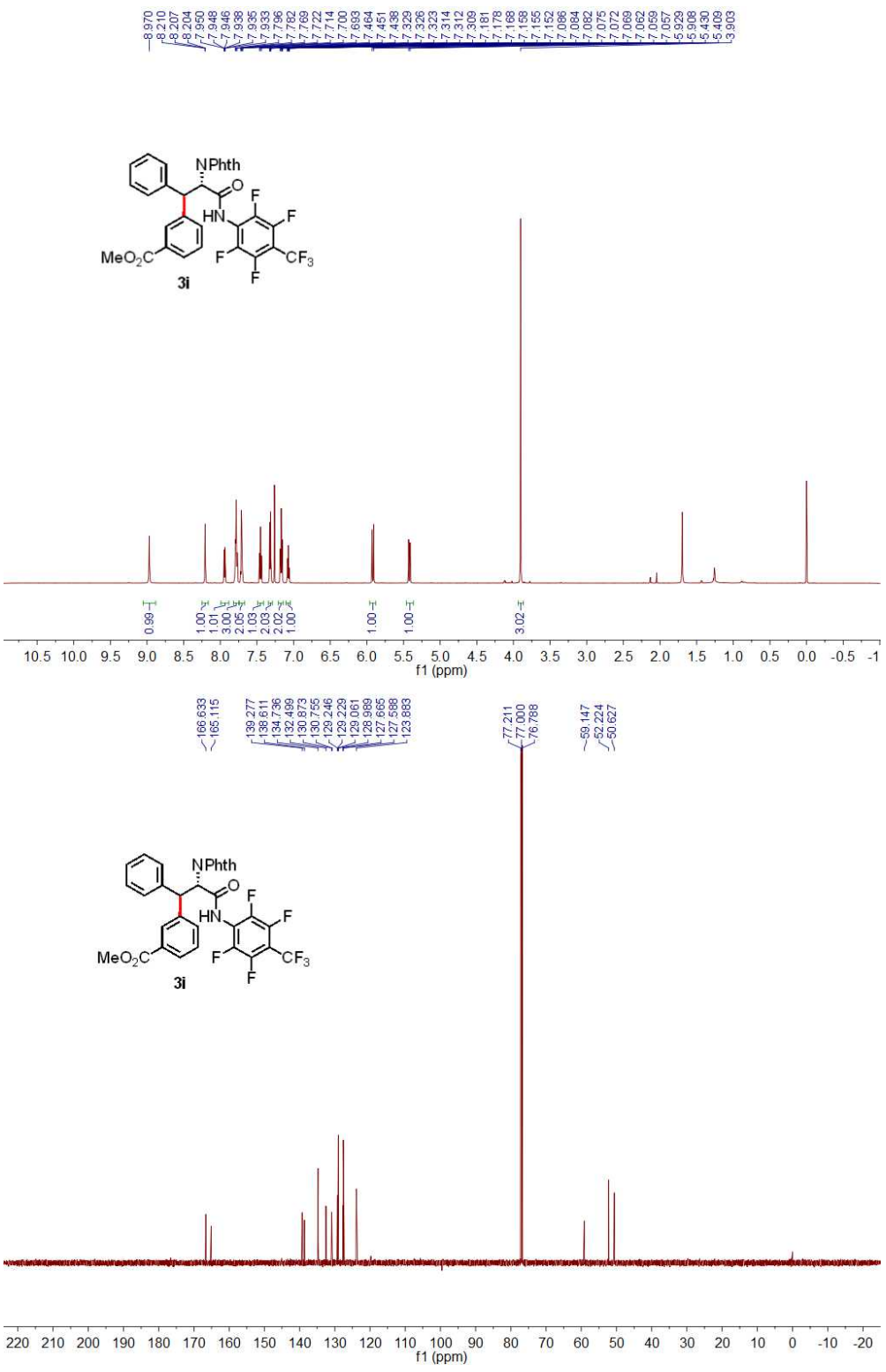
3g

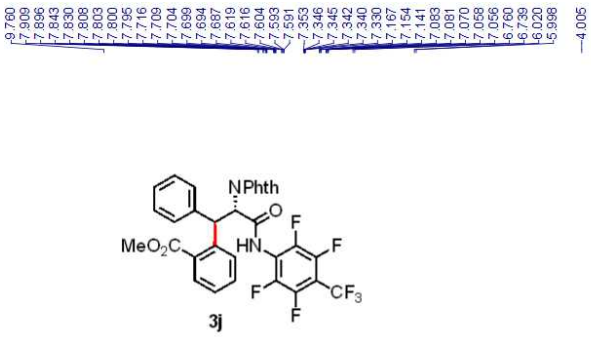

0.98
1.99
2.03
1.95
2.04
2.51
1.99
1.00
1.00
1.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

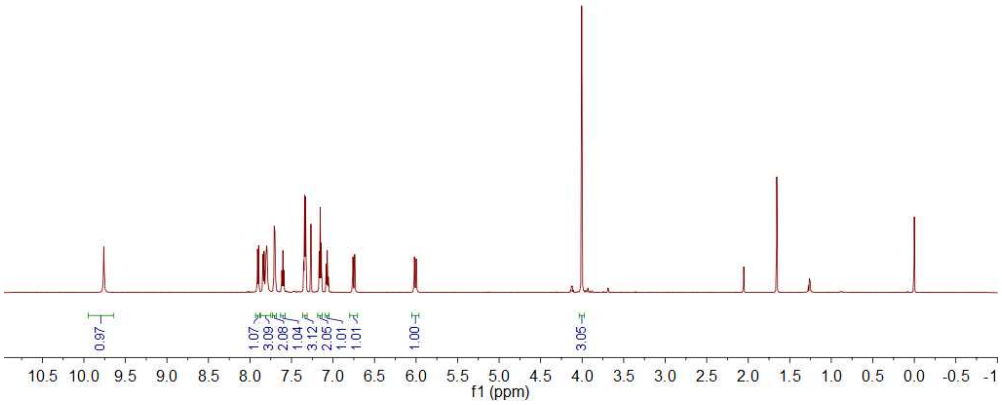

165.140
138.637
137.800
134.763
132.229
130.721
129.652
128.978
127.678
127.475
123.887
121.924
77.212
77.000
76.789
59.083
50.357
NPhth
O
HN
F
F
F
F
CF3
Br
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

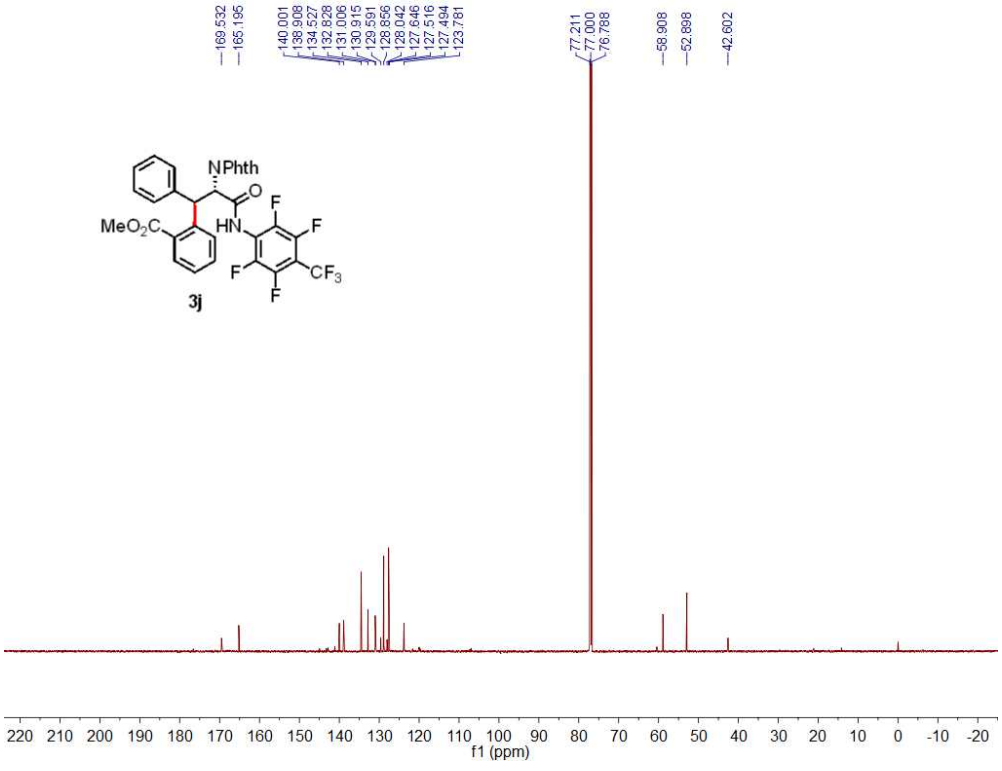
3g

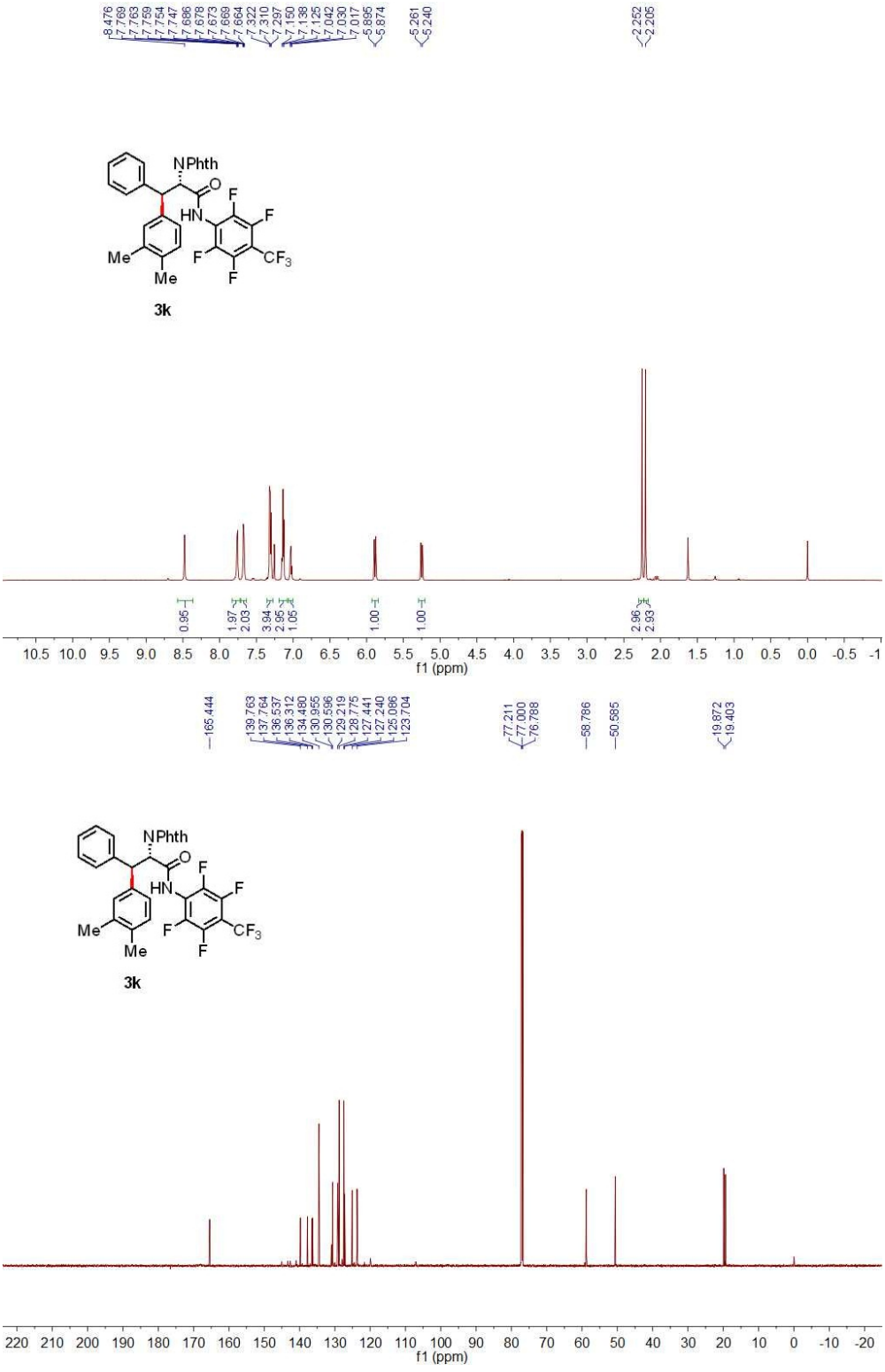

8.921
8.025
8.012
7.786
7.781
7.777
7.772
7.713
7.707
7.698
7.693
7.634
7.620
7.295
7.284
7.282
7.171
7.158
7.146
7.084
7.082
7.080
7.069
7.059
7.057
7.055
5.919
5.898
5.414
5.393
3.886
NPhth
O
HN
F
F
F
F
CF3
CO2Me
3h
0.99
1.95
1.98
2.00
2.00
1.96
1.98
0.99
1.00
1.00
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 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 -1
f1 (ppm)
166.553
165.083
143.901
138.397
134.752
130.716
130.356
129.574
128.980
128.088
127.731
127.618
123.873
77.211
77.000
76.788
58.919
52.134
50.767
NPhth
O
HN
F
F
F
F
CF3
CO2Me
3h
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


8.970
8.210
8.207
8.204
7.950
7.948
7.946
7.938
7.935
7.933
7.796
7.782
7.769
7.722
7.714
7.700
7.693
7.464
7.451
7.438
7.329
7.326
7.323
7.314
7.312
7.309
7.181
7.178
7.168
7.158
7.155
7.152
7.086
7.084
7.082
7.075
7.072
7.069
7.062
7.059
7.057
5.929
5.908
5.430
5.409
5.403
NPhth
O
HN
F
F
F
F
CF3
MeO2C
3i
0.99
1.00
1.01
3.00
2.05
1.03
2.03
2.02
1.00
1.00
1.00
3.02
10.5 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 -1
f1 (ppm)
166.633
165.115
139.277
138.611
134.736
132.499
130.873
130.755
129.246
129.229
129.061
128.989
127.665
127.598
123.883
77.211
77.000
76.788
59.147
52.224
50.627
NPhth
O
HN
F
F
F
F
CF3
MeO2C
3i
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


9.760
7.909
7.896
7.843
7.830
7.808
7.803
7.800
7.795
7.716
7.709
7.704
7.699
7.694
7.687
7.619
7.616
7.604
7.593
7.591
7.353
7.346
7.345
7.342
7.340
7.330
7.167
7.154
7.141
7.083
7.081
7.070
7.058
7.056
6.760
6.739
6.020
5.998
4.005
NPhth
O
HN
MeO2C
F
F
F
F
CF3
3j

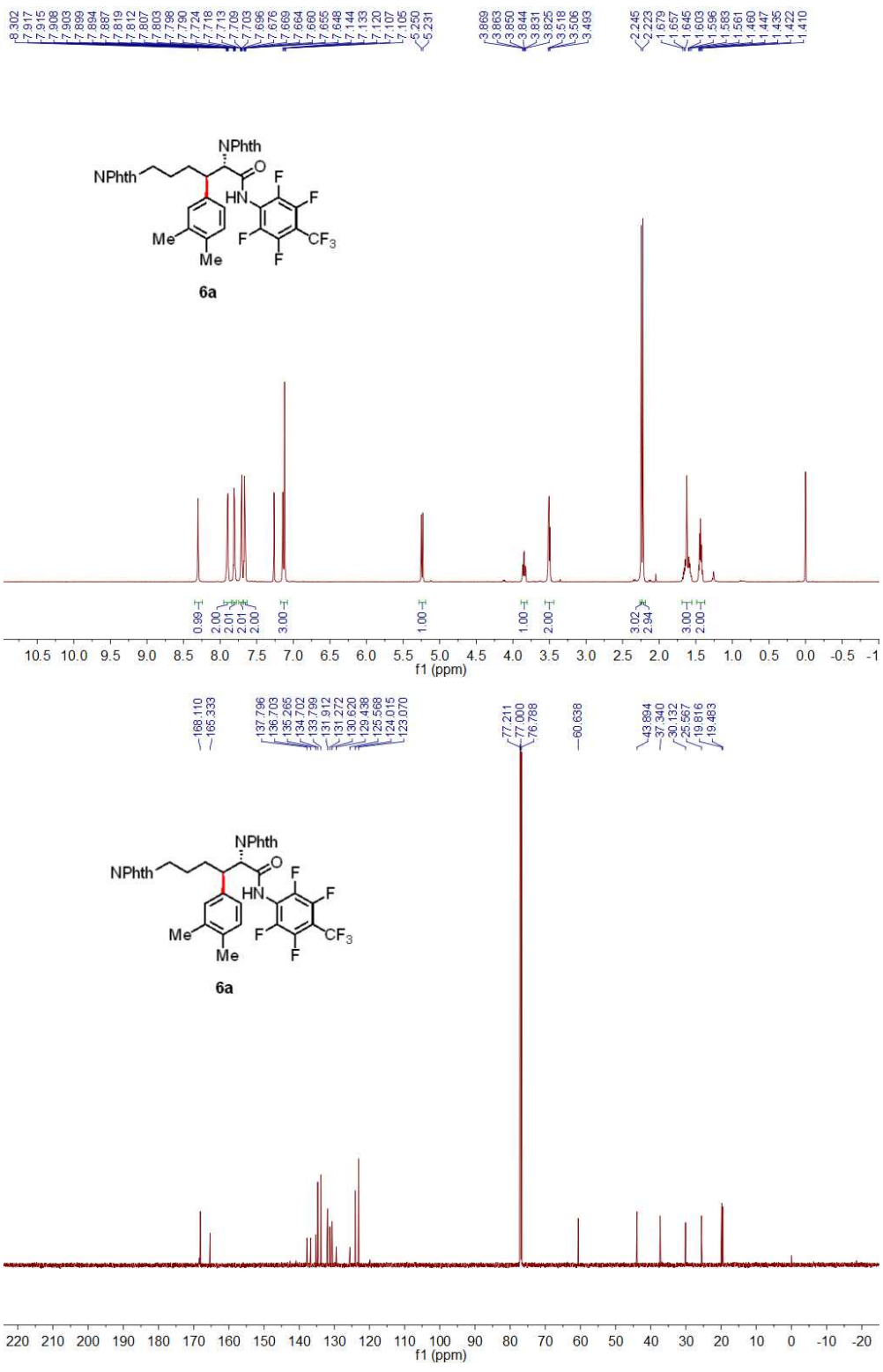

0.97
1.07
3.09
2.08
1.04
3.12
2.05
1.01
1.01
1.00
3.05
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


169.532
165.195
140.001
138.908
134.527
132.828
131.006
130.915
129.591
128.856
128.042
127.646
127.516
127.494
123.781
77.211
77.000
76.788
58.908
52.898
42.602
NPhth
O
HN
MeO2C
F
F
F
F
CF3
3j
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

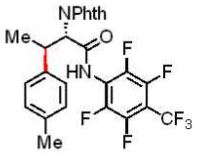

8.476
7.769
7.763
7.759
7.754
7.747
7.686
7.678
7.673
7.669
7.664
7.322
7.310
7.297
7.150
7.138
7.125
7.042
7.030
7.017
5.895
5.874
5.261
5.240
2.252
2.205
NPhth
O
HN
F
F
F
F
CF3
Me
Me
0.95
1.97
2.03
3.94
2.95
1.05
1.00
1.00
2.96
2.93
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)
165.444
139.763
137.764
136.537
136.312
134.480
130.955
130.596
129.219
128.775
127.441
127.240
125.086
123.704
77.211
77.000
76.788
58.786
50.585
19.872
19.403
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

3k

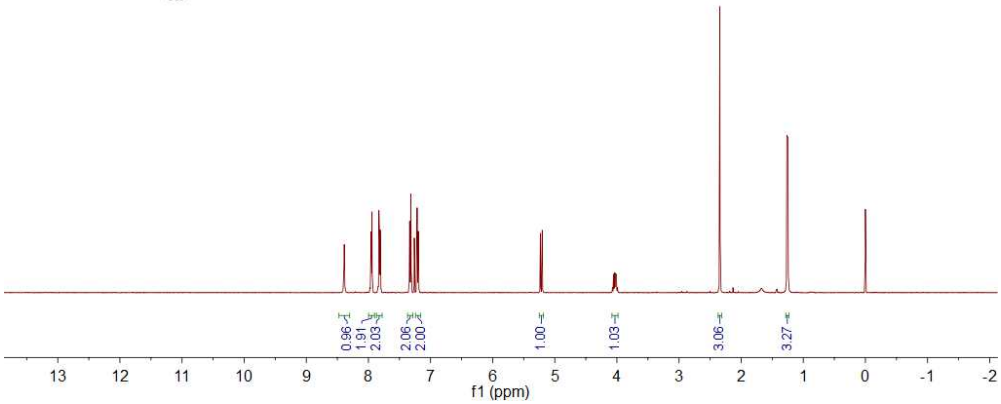
3k


8.302
7.917
7.915
7.908
7.903
7.899
7.894
7.887
7.819
7.812
7.807
7.803
7.798
7.790
7.724
7.718
7.713
7.709
7.703
7.696
7.676
7.669
7.664
7.660
7.655
7.648
7.144
7.133
7.120
7.107
7.105
5.250
5.231
3.869
3.863
3.850
3.844
3.831
3.825
3.518
3.506
3.493
2.245
2.223
1.679
1.657
1.645
1.603
1.596
1.583
1.561
1.460
1.447
1.435
1.422
1.410
NPhth
NPhth
O
HN
F
F
F
CF3
F
Me
Me
6a
0.99
2.00
2.01
2.01
2.00
3.00
1.00
1.00
2.00
3.02
2.94
3.00
2.00
f1 (ppm)
168.110
165.333
137.796
136.703
135.265
134.702
133.799
131.912
131.272
130.620
129.438
125.588
124.015
123.070
77.211
77.000
76.788
60.638
43.894
37.340
30.132
25.567
19.816
19.483
NPhth
NPhth
O
HN
F
F
F
CF3
F
Me
Me
6a
f1 (ppm)

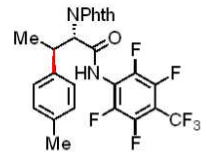

8.389
7.976
7.973
7.963
7.955
7.950
7.942
7.932
7.929
7.844
7.841
7.831
7.824
7.818
7.810
7.801
7.797
7.336
7.316
7.216
7.196
5.232
5.202
4.071
4.054
4.042
4.037
4.024
4.019
4.007
3.990
2.344
1.264
1.247


NPhth
Me
O
HN
F
F
F
F
CF3
Me

6b

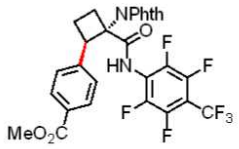

0.96
1.91
2.03
2.06
2.00
1.00
1.03
3.06
3.27
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)


168.440
165.504
137.785
137.770
134.808
131.231
130.022
127.407
124.030
77.318 cdcl3
77.000 cdcl3
76.682 cdcl3
61.366
39.047
21.116
19.985

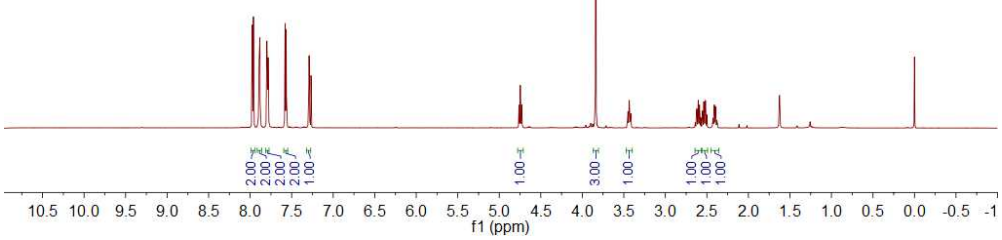

NPhth
Me
O
HN
F
F
F
F
CF3
Me

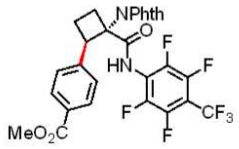
6b

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

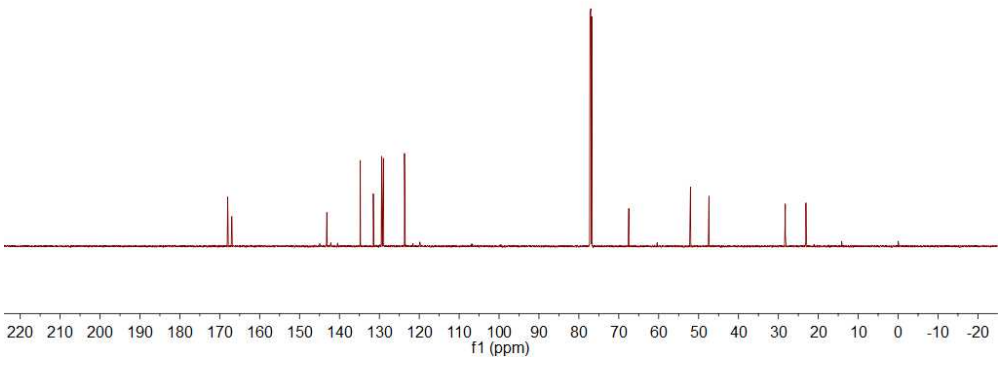


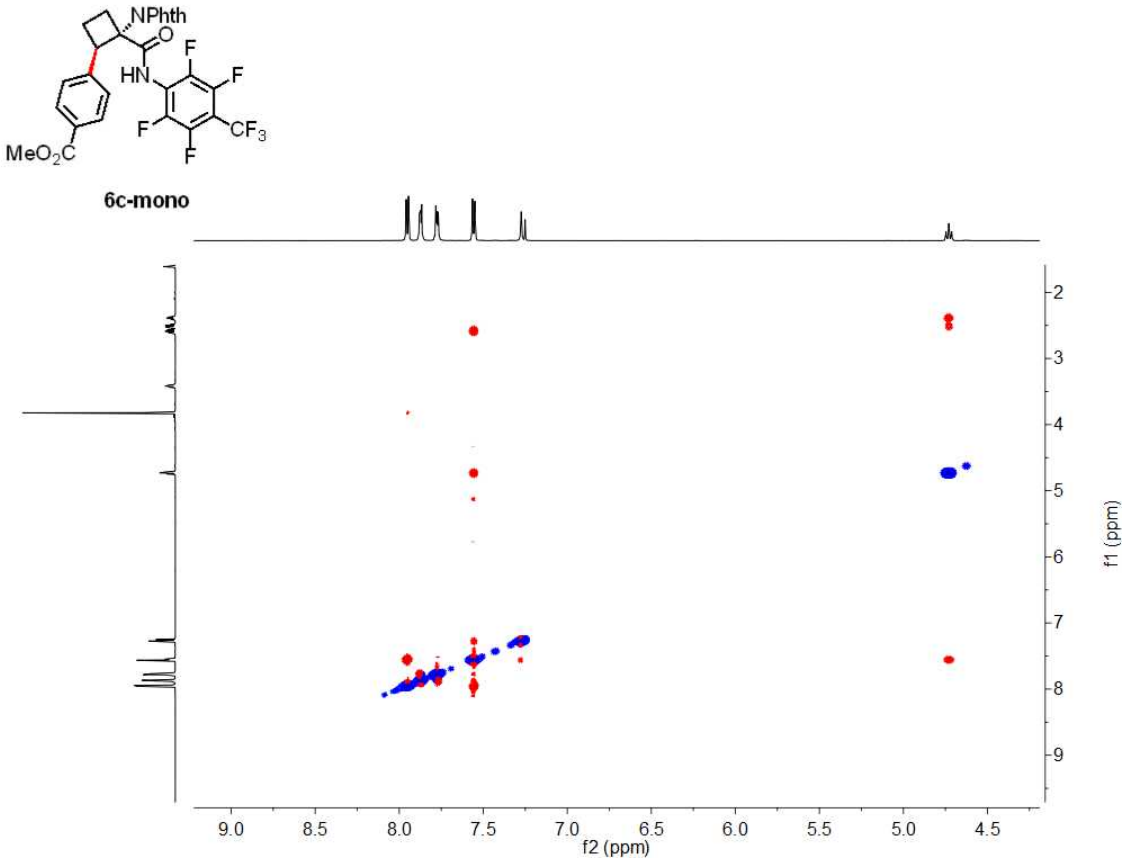
6c-mono

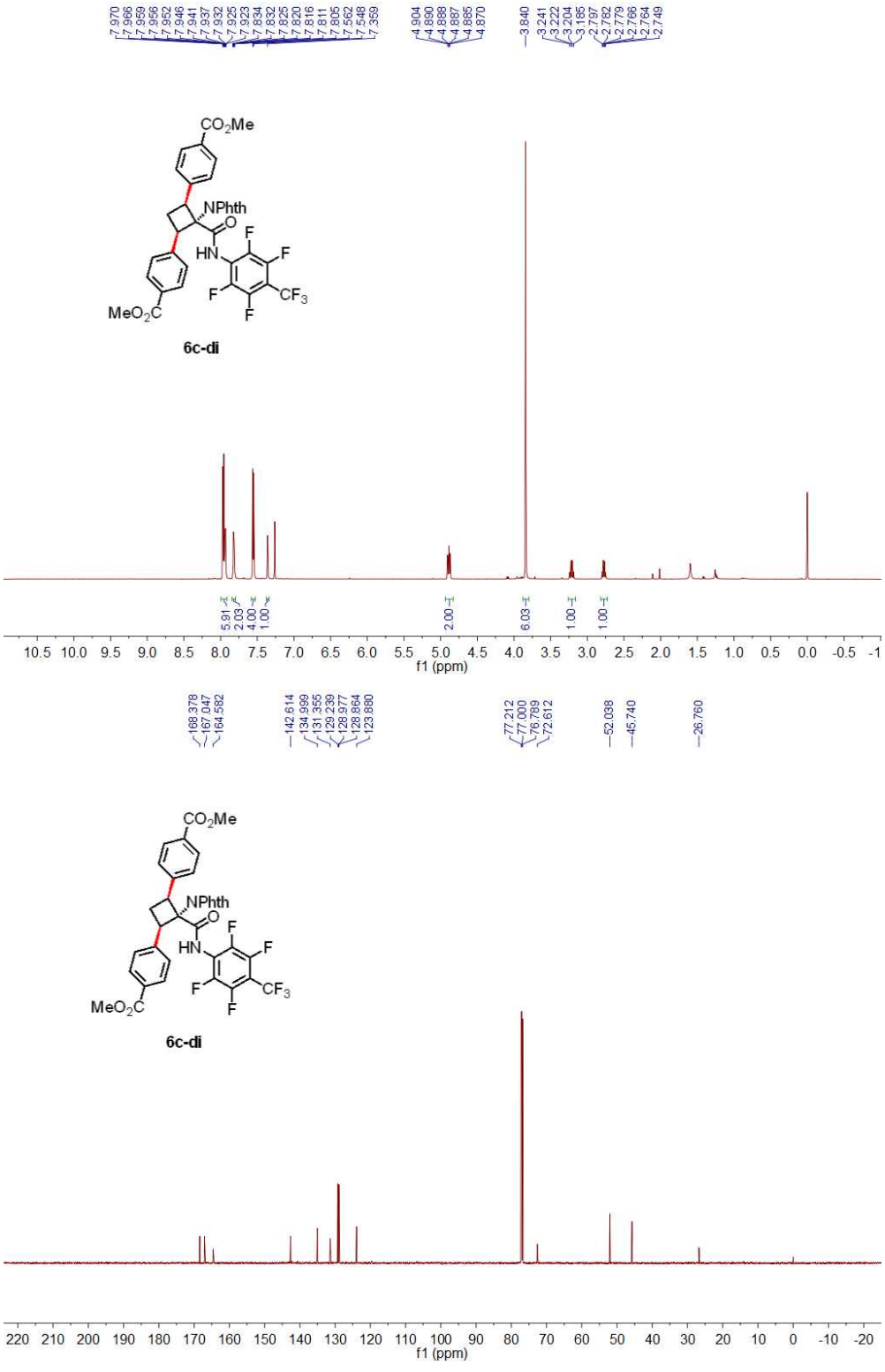


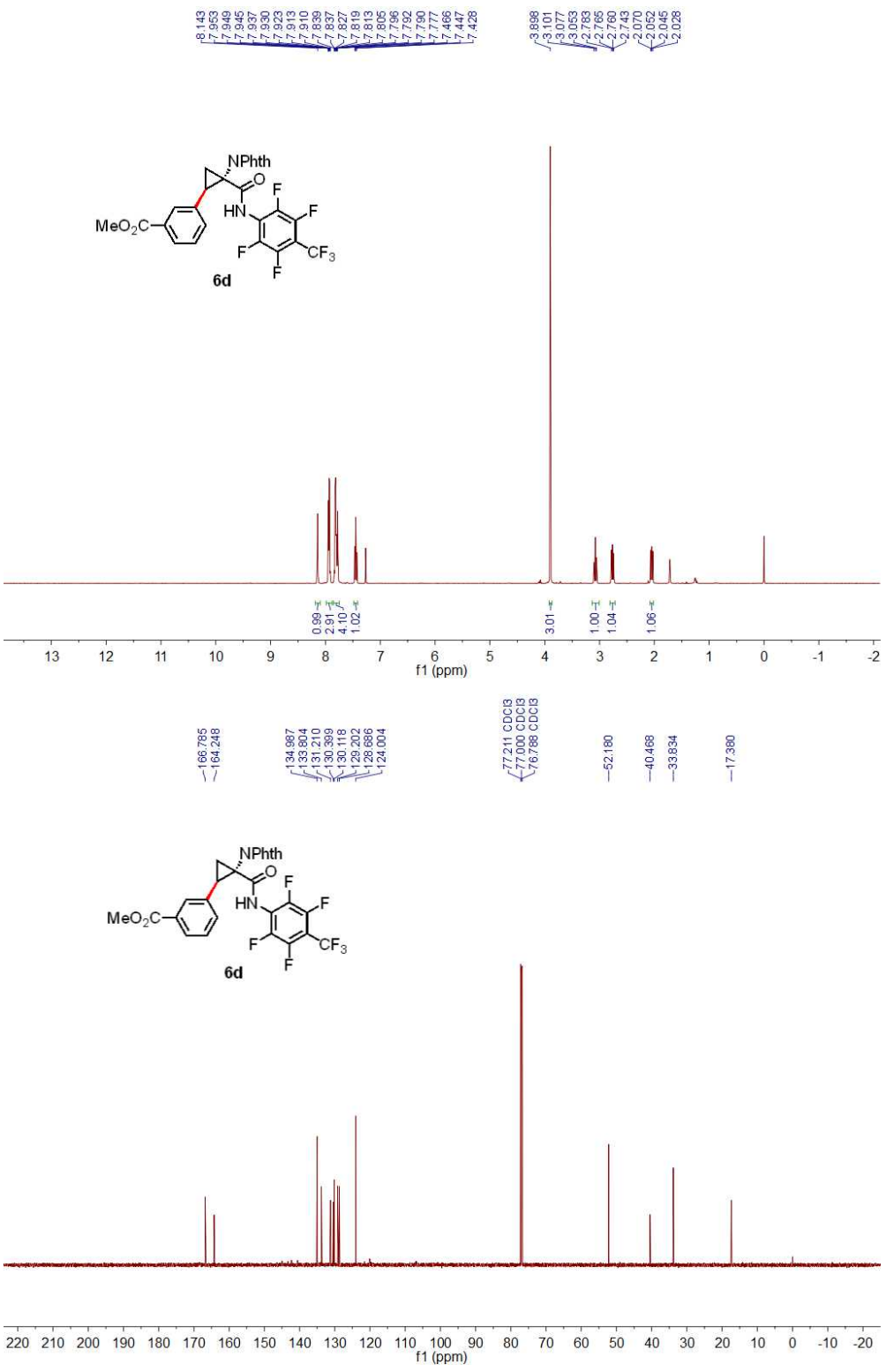


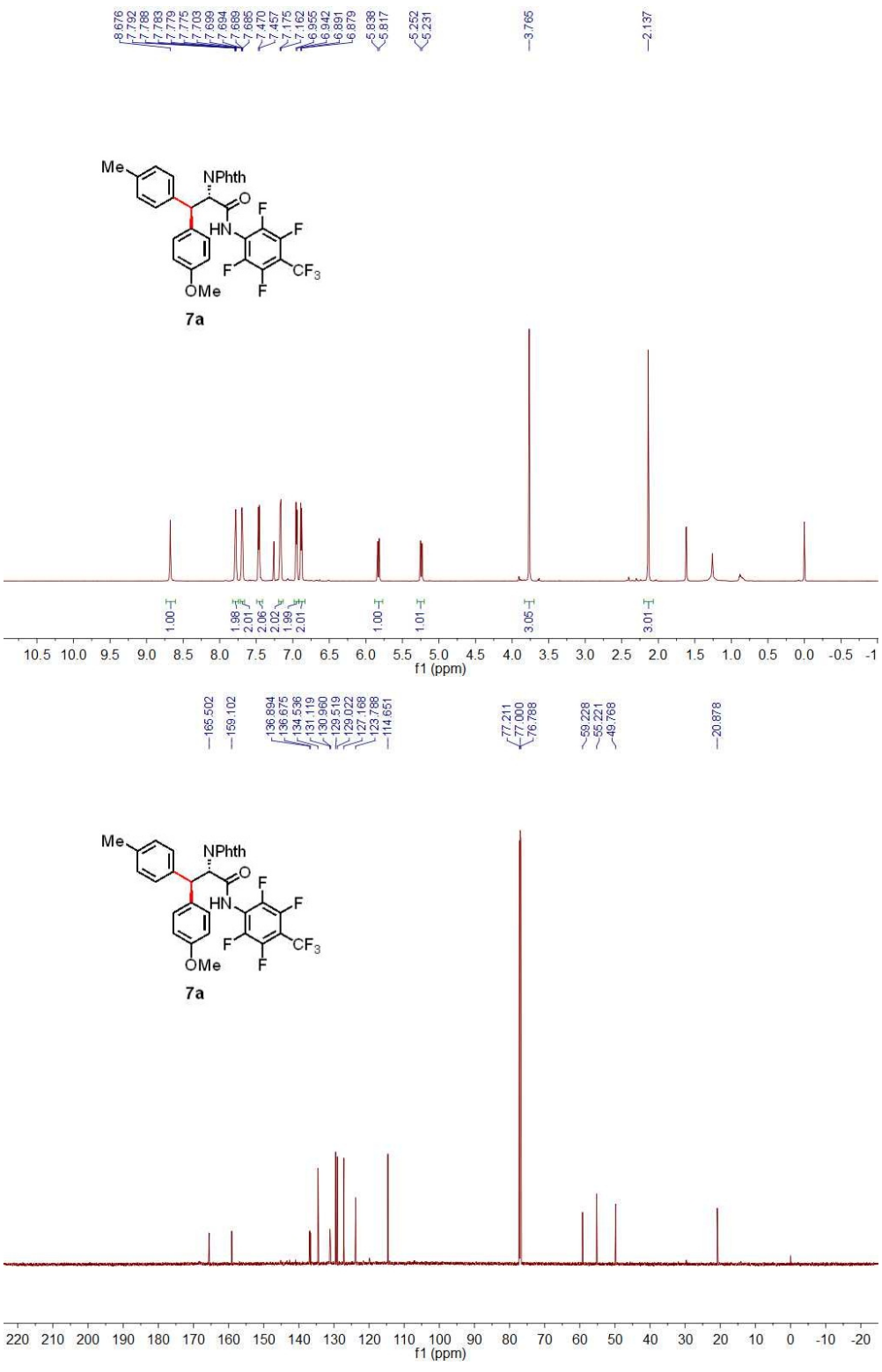
6c-mono

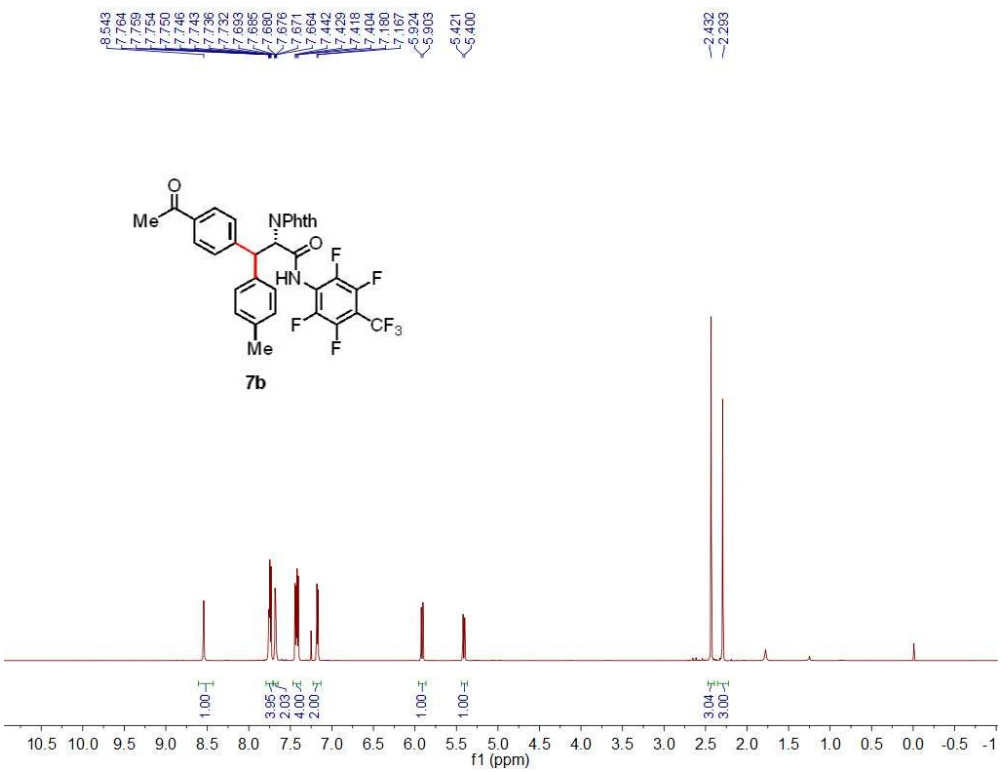


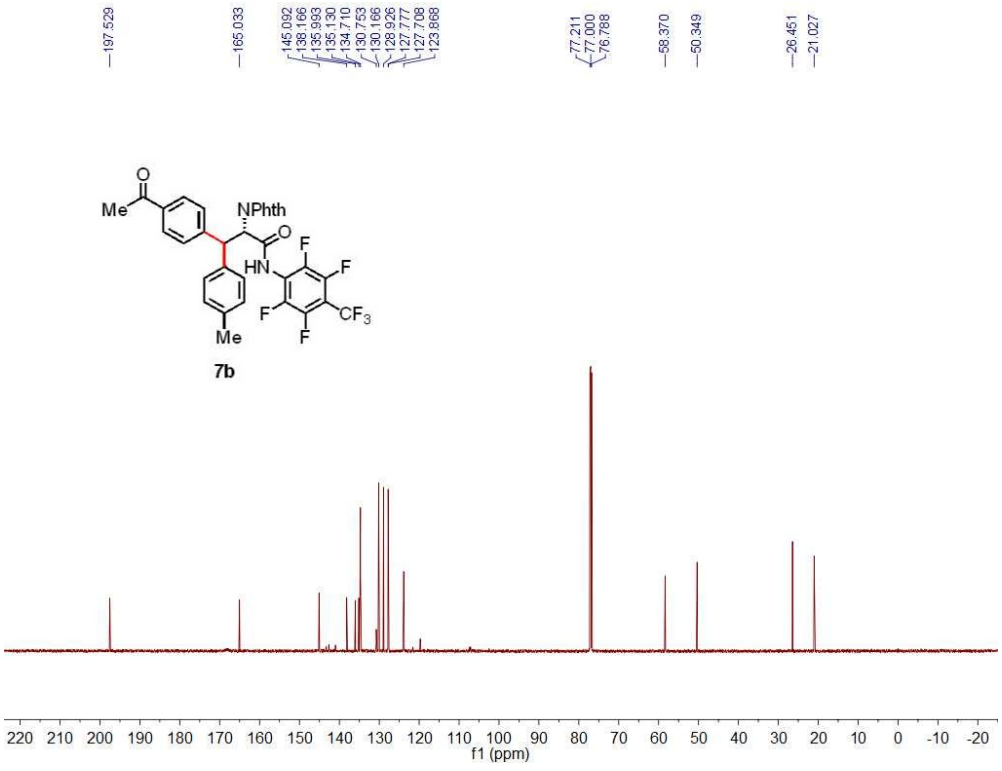

NPhth
O
HN
F
F
F
F
CF3
MeO2C
6c-mono
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
f2 (ppm)
2
3
4
5
6
7
8
9
f1 (ppm)

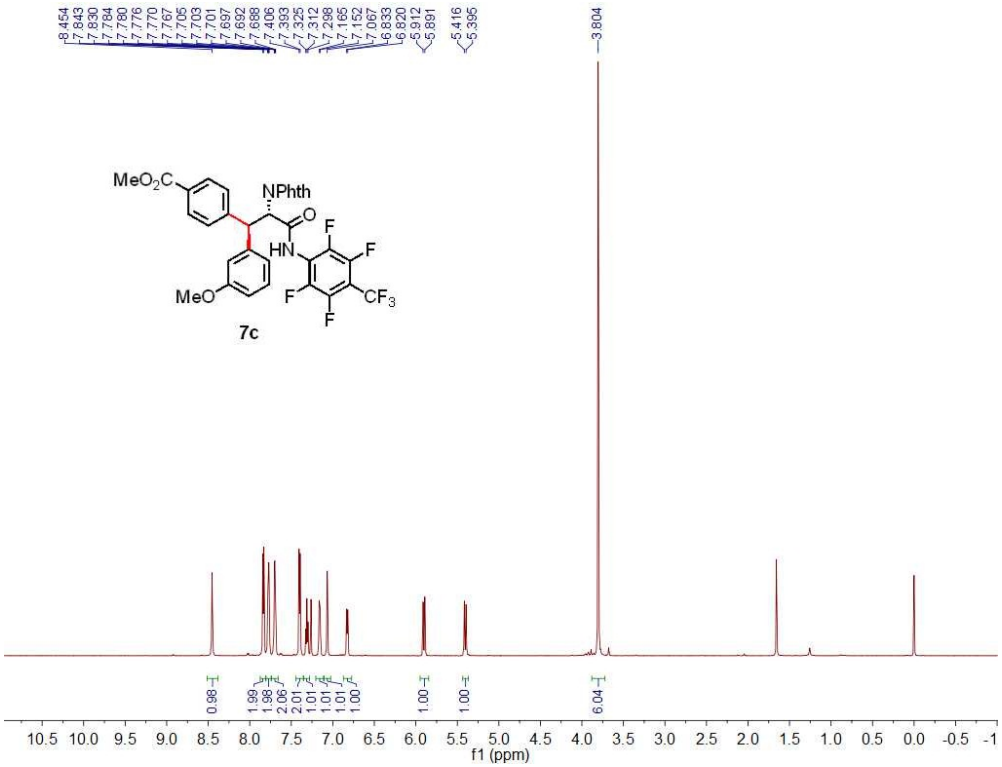

7.970
7.966
7.959
7.956
7.952
7.946
7.941
7.937
7.932
7.925
7.923
7.834
7.832
7.825
7.820
7.816
7.811
7.805
7.562
7.548
7.359
4.904
4.890
4.888
4.887
4.885
4.870
3.840
3.241
3.222
3.204
3.185
2.797
2.782
2.779
2.766
2.764
2.749
CO2Me
NPhth
O
HN
F
F
F
F
CF3
MeO2C
6c-di
5.91
2.03
4.00
1.00
2.00
6.03
1.00
1.00
f1 (ppm)
188.378
167.047
164.582
142.614
134.999
131.355
129.239
128.977
128.864
123.880
77.212
77.000
76.789
72.612
52.038
45.740
26.760
f1 (ppm)

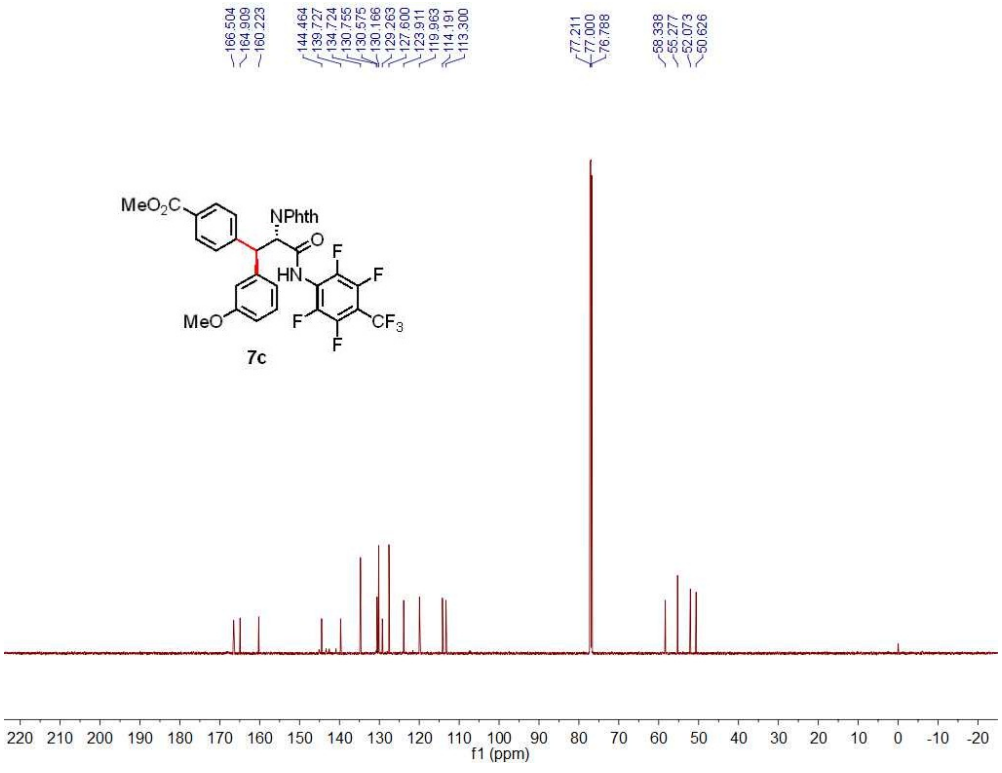

8.143
7.953
7.949
7.945
7.937
7.930
7.923
7.913
7.910
7.839
7.837
7.827
7.819
7.813
7.805
7.796
7.792
7.790
7.777
7.466
7.447
7.428
3.898
3.101
3.077
3.053
2.783
2.765
2.760
2.743
2.070
2.052
2.045
2.028
NPhth
O
HN
F
F
F
F
CF3
MeO2C
6d
0.99
2.91
4.10
1.02
3.01
1.00
1.04
1.06
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)
166.785
164.248
134.987
133.804
131.210
130.399
130.118
129.202
128.686
124.004
77.211 CDCl3
77.000 CDCl3
76.788 CDCl3
52.180
40.488
33.834
17.380
NPhth
O
HN
F
F
F
F
CF3
MeO2C
6d
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


8.676
7.792
7.788
7.783
7.779
7.775
7.703
7.699
7.694
7.689
7.685
7.470
7.457
7.175
7.162
6.955
6.942
6.891
6.879
5.838
5.817
5.252
5.231
3.765
2.137
Me
NPhth
O
HN
F
F
F
F
CF3
OMe
7a
1.00
1.98
2.01
2.06
2.02
1.99
2.01
1.00
1.01
3.05
3.01
10.5 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 -1
f1 (ppm)
165.502
159.102
136.894
136.675
134.536
131.119
130.960
129.519
129.022
127.188
123.788
114.651
77.211
77.000
76.788
59.228
55.221
49.768
20.878
Me
NPhth
O
HN
F
F
F
F
CF3
OMe
7a
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

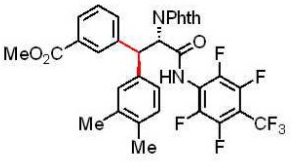

8.543
7.764
7.759
7.754
7.750
7.746
7.743
7.736
7.732
7.693
7.685
7.680
7.676
7.671
7.664
7.442
7.429
7.418
7.404
7.180
7.167
5.924
5.903
5.421
5.400
2.432
2.293
Me
NPhth
O
HN
F
F
F
F
CF3
Me
7b
1.00
3.95
2.03
4.00
2.00
1.00
1.00
3.04
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


197.529
165.033
145.092
138.166
135.993
135.130
134.710
130.753
130.166
128.926
127.777
127.708
123.868
77.211
77.000
76.788
58.370
50.349
26.451
21.027
Me
NPhth
O
HN
F
F
F
F
CF3
Me
7b
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

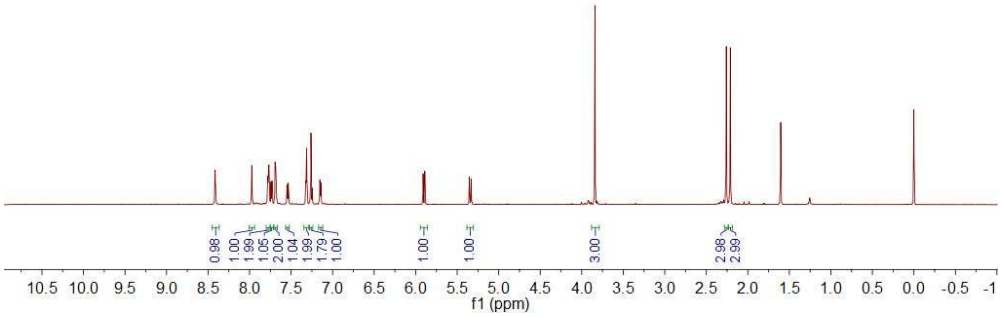

8.454
7.843
7.830
7.784
7.780
7.776
7.770
7.767
7.765
7.703
7.701
7.697
7.692
7.688
7.406
7.393
7.325
7.312
7.298
7.165
7.152
7.067
6.833
6.820
5.912
5.891
5.416
5.395
3.804
MeO2C
NPhth
O
HN
F
F
F
F
CF3
MeO
7c
0.98
1.99
1.98
2.06
2.01
1.01
1.01
1.01
1.00
1.00
1.00
6.04
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 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 -1
f1 (ppm)

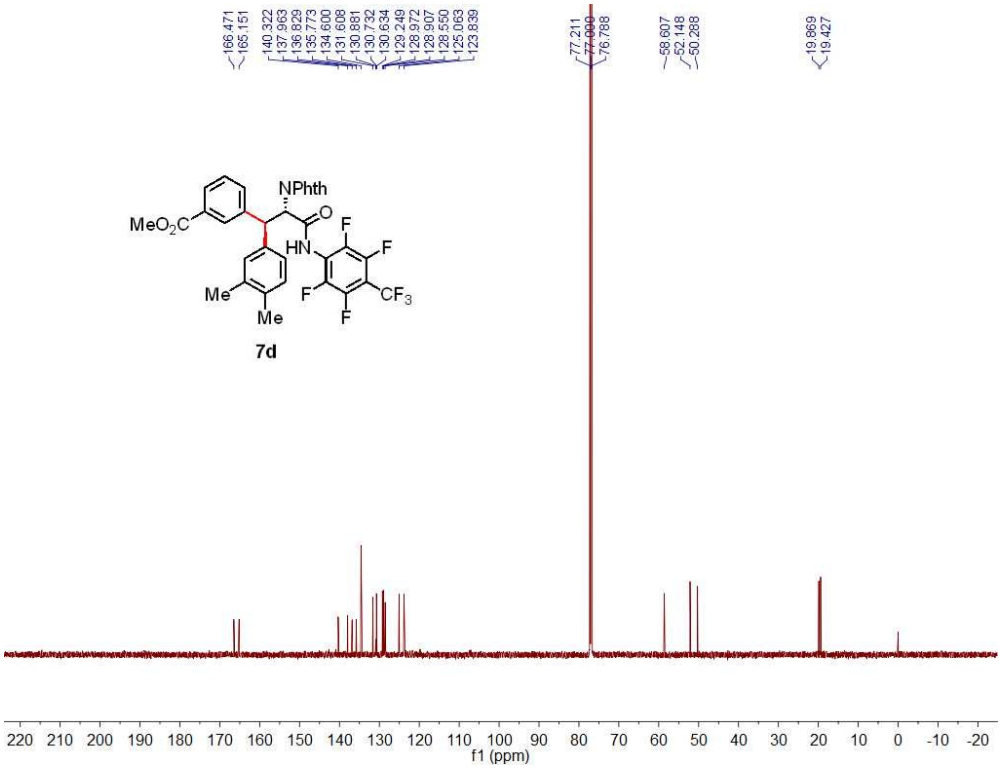

166.504
164.909
160.223
144.464
139.727
134.724
130.755
130.575
130.166
129.263
127.600
123.911
119.963
114.191
113.300
77.211
77.000
76.788
58.338
55.277
52.073
50.626
MeO2C
NPhth
O
HN
F
F
F
F
CF3
MeO
7c
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


8.415
7.973
7.788
7.781
7.776
7.772
7.767
7.760
7.745
7.743
7.740
7.732
7.730
7.727
7.701
7.694
7.689
7.684
7.679
7.672
7.550
7.547
7.545
7.537
7.534
7.532
7.326
7.323
7.317
7.313
7.270
7.261
7.258
7.244
7.153
7.140
5.910
5.889
5.352
5.331
3.841
2.259
2.211


NPhth
MeO2C
O
F
HN
F
Me
F
CF3
Me
F

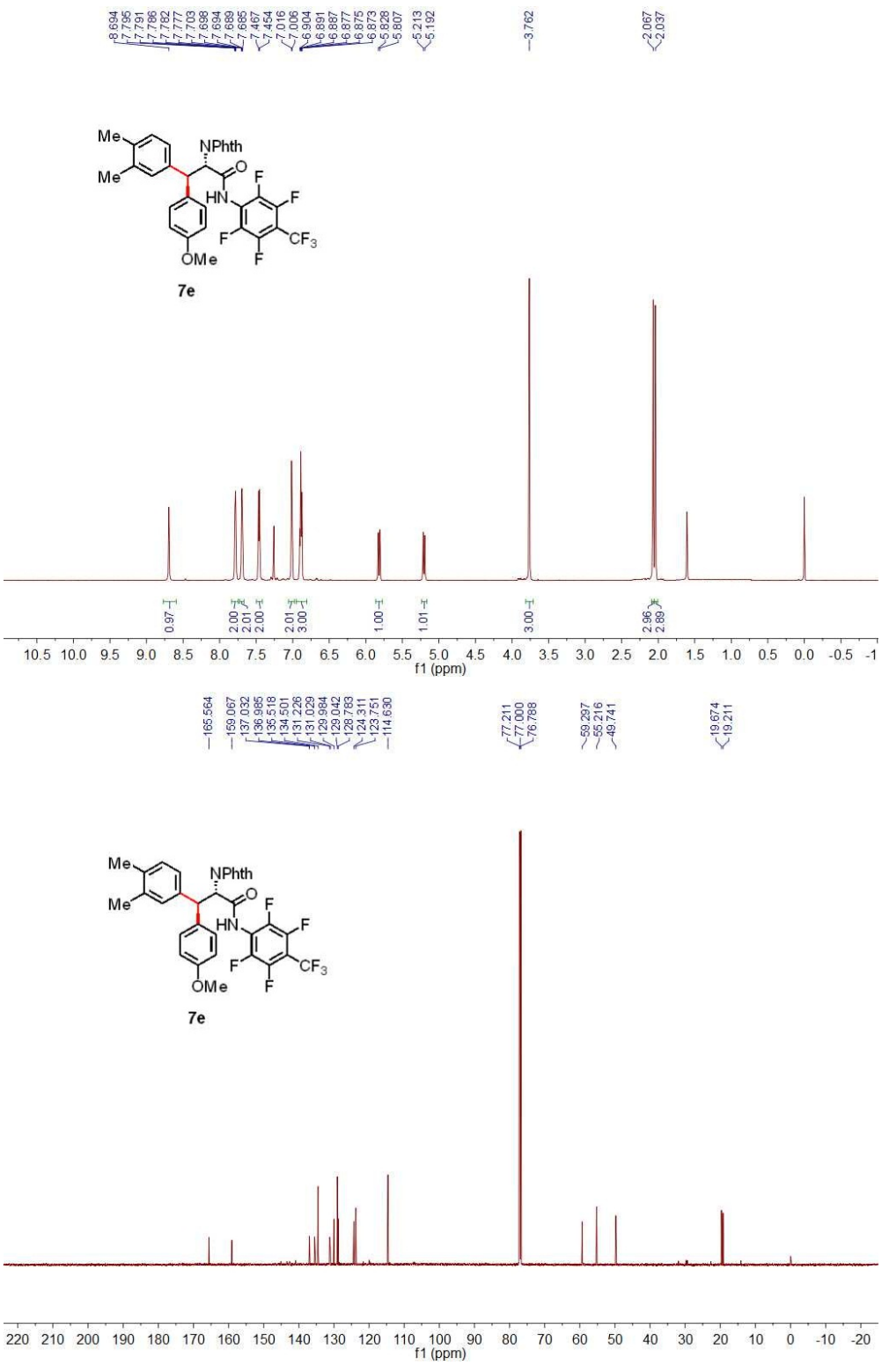
7d

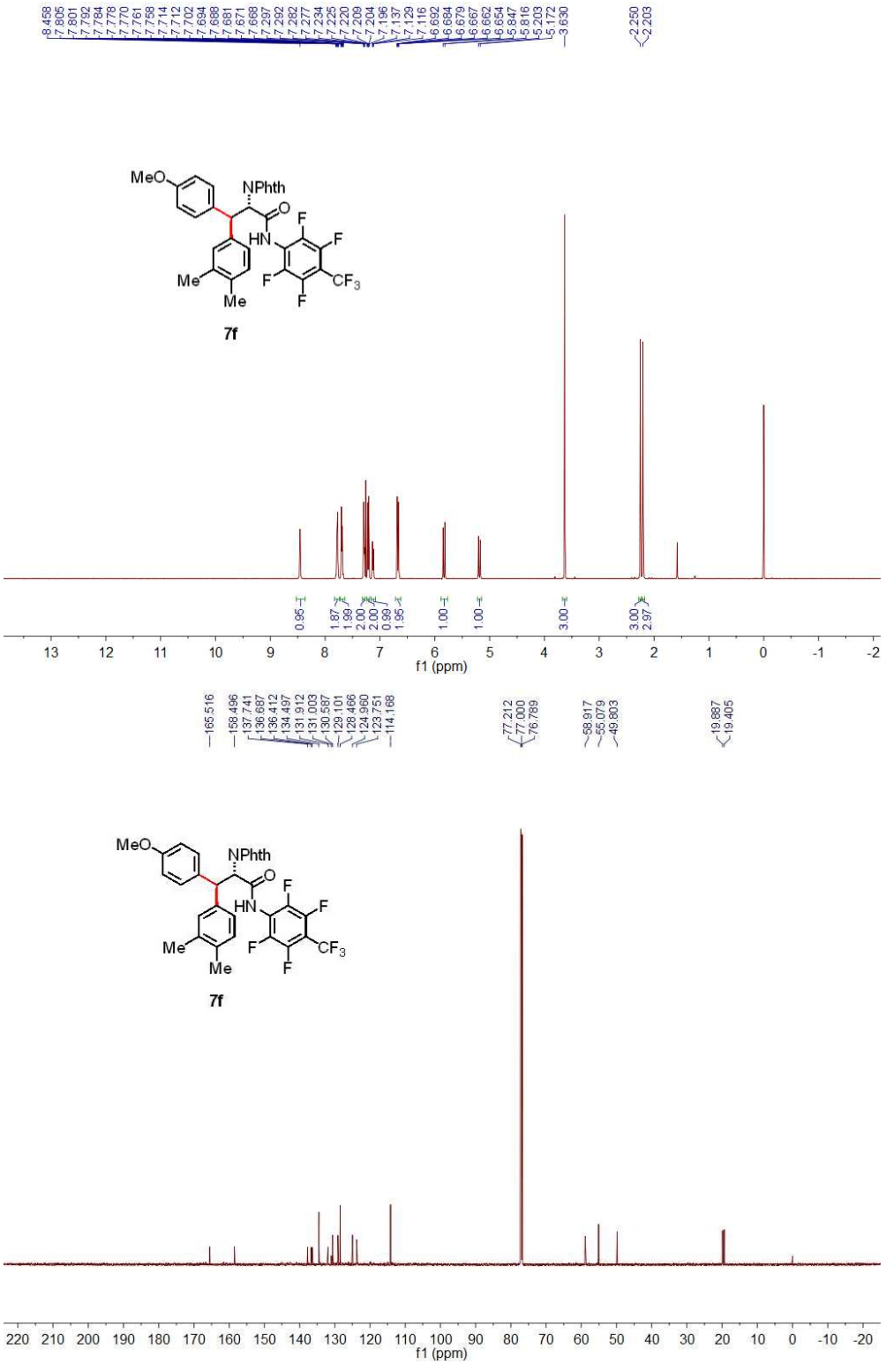

0.98
1.00
1.99
1.05
2.00
1.04
1.99
1.79
1.00
1.00
1.00
3.00
2.98
2.99
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


166.471
165.151
140.322
137.963
136.829
135.773
134.600
131.608
130.881
130.732
130.634
129.249
128.972
128.907
128.550
125.063
123.839
77.211
77.000
76.788
58.607
52.148
50.288
19.869
19.427
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

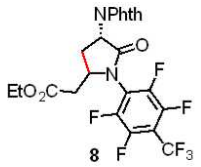
NPhth
MeO2C
O
F
HN
F
Me
F
CF3
Me
F

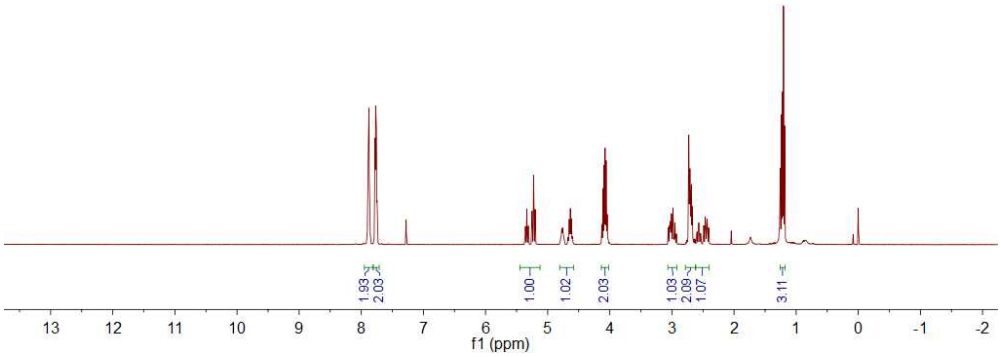
7d


8.694
7.795
7.791
7.786
7.782
7.777
7.703
7.698
7.694
7.689
7.685
7.467
7.454
7.016
7.006
6.904
6.891
6.887
6.877
6.875
6.873
5.828
5.807
5.213
5.192
3.762
2.067
2.037
Me
Me
NPhth
O
HN
F
F
F
F
CF3
OMe
7e
0.97
2.00
2.01
2.00
2.01
3.00
1.00
1.01
3.00
2.96
2.89
10.5 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 -1
f1 (ppm)
165.564
159.067
137.032
136.985
135.518
134.501
131.226
131.029
129.984
129.042
128.783
124.311
123.751
114.630
77.211
77.000
76.788
59.297
55.216
49.741
19.674
19.211
Me
Me
NPhth
O
HN
F
F
F
F
CF3
OMe
7e
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

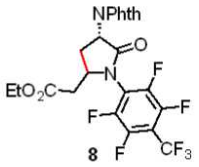

8.458
7.805
7.801
7.792
7.784
7.778
7.770
7.761
7.758
7.714
7.712
7.702
7.694
7.688
7.681
7.671
7.668
7.297
7.292
7.282
7.277
7.234
7.225
7.220
7.209
7.204
7.196
7.137
7.129
7.116
6.692
6.684
6.679
6.667
6.662
6.654
5.847
5.816
5.203
5.172
3.630
2.250
2.203
MeO
NPhth
O
HN
F
F
F
F
CF3
Me
Me
7f
0.95
1.87
1.99
2.00
2.00
0.99
1.95
1.00
1.00
3.00
3.00
2.97
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)
165.516
158.496
137.741
136.687
136.412
134.497
131.912
131.003
130.587
129.101
128.466
124.960
123.751
114.168
77.212
77.000
76.789
58.917
55.079
49.803
19.887
19.405
MeO
NPhth
O
HN
F
F
F
F
CF3
Me
Me
7f
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

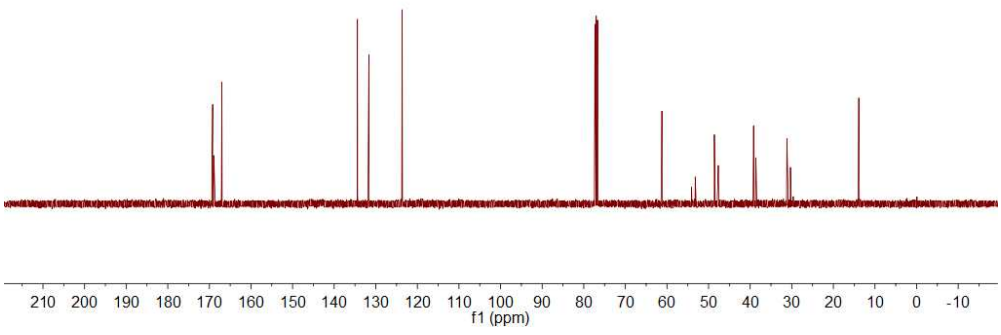

7.909
7.897
7.889
7.884
7.876
7.864
7.852
7.788
7.777
7.769
7.762
7.755
7.747
5.359
5.335
5.311
5.252
5.226
5.201
4.795
4.789
4.779
4.772
4.764
4.756
4.749
4.741
4.734
4.671
4.653
4.635
4.617
4.599
4.127
4.109
4.092
4.075
4.058
4.040
3.057
3.007
2.983
2.927
2.771
2.728
2.686
2.629
2.599
2.567
2.463
2.408
1.253
1.220
1.203
1.185

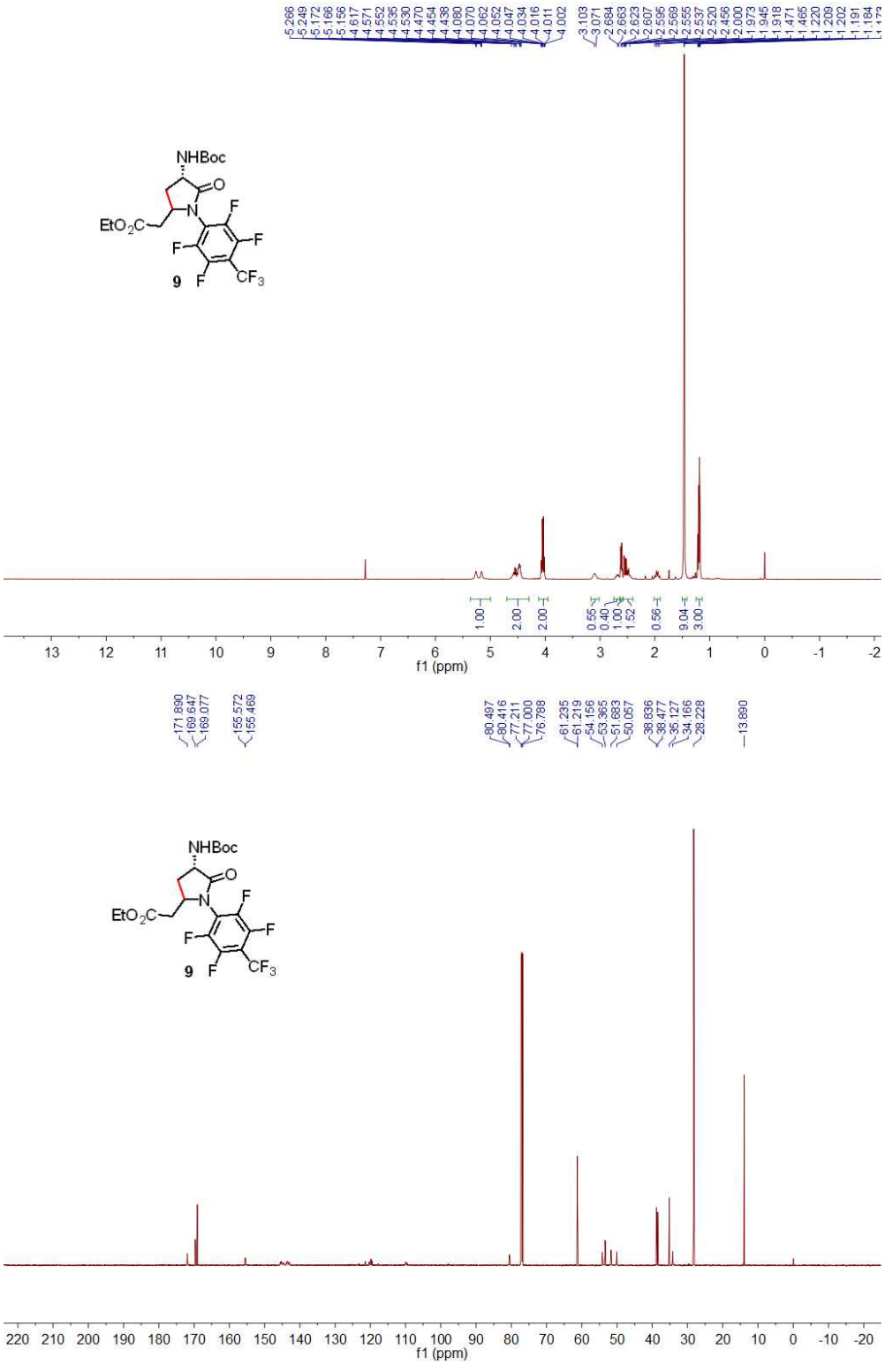

NPhth
O
N
EtO2C
F
F
F
F
CF3
8

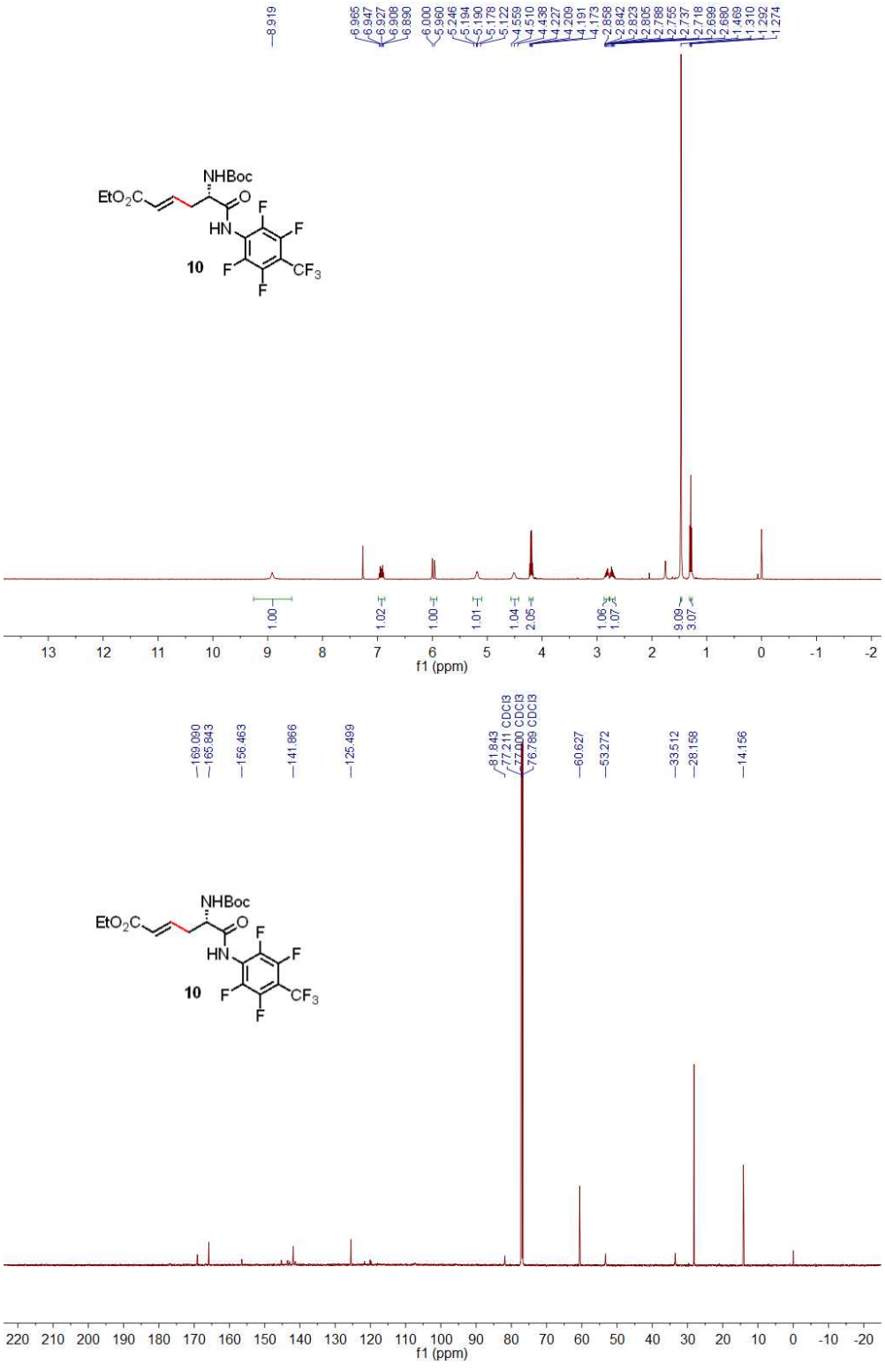

1.93
2.03
1.00
1.02
2.03
1.03
2.09
1.07
3.11
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)

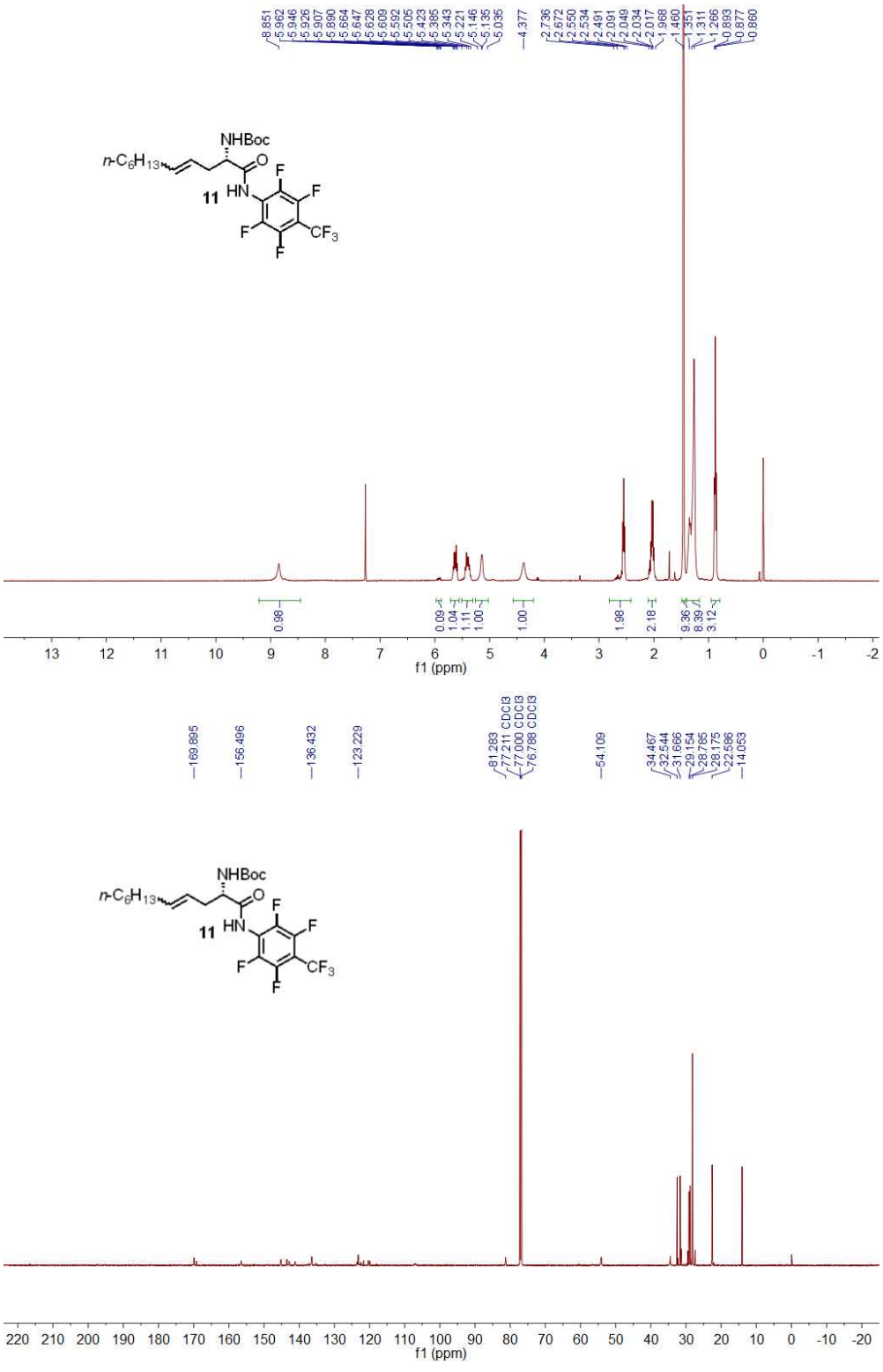

169.373
169.208
169.086
168.942
167.050
167.000
134.409
131.649
123.661
77.318 CDCl3
77.000 CDCl3
76.682 CDCl3
61.219
54.067
53.210
48.605
47.650
39.174
38.624
31.167
30.310
13.905
13.885

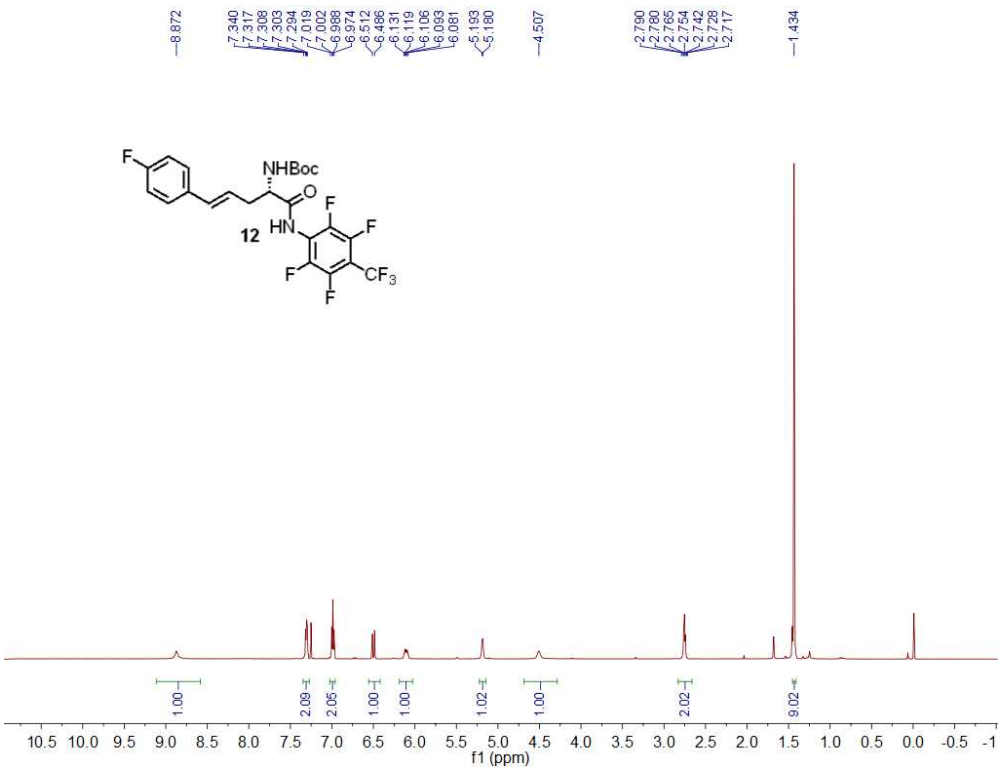

NPhth
O
N
EtO2C
F
F
F
F
CF3
8

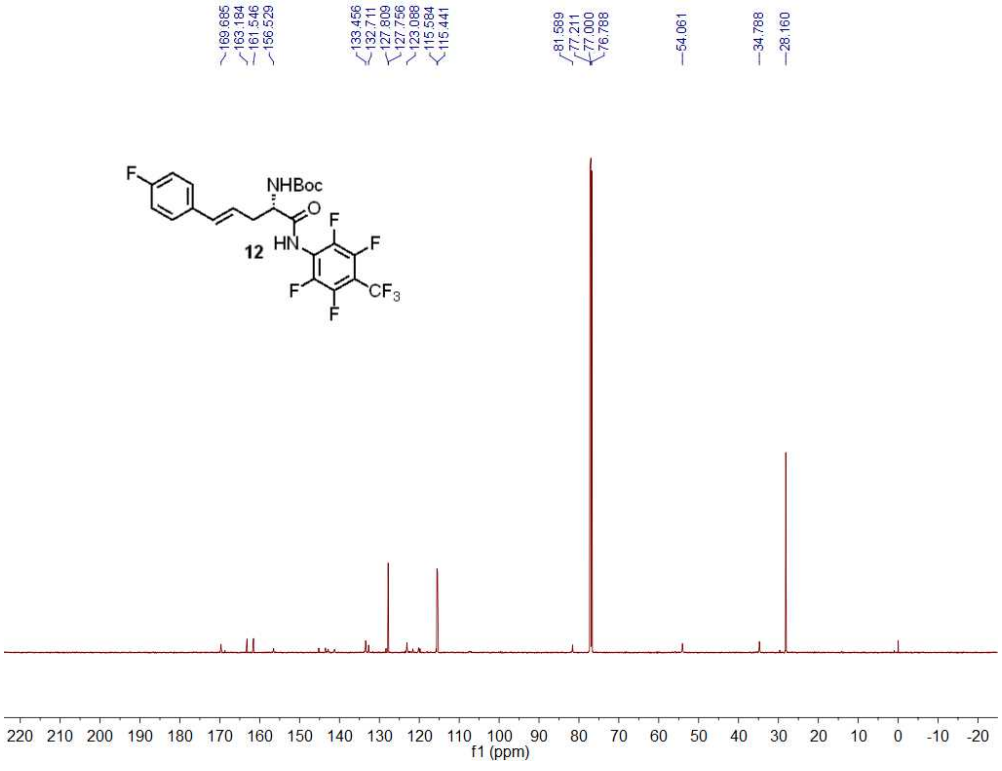

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

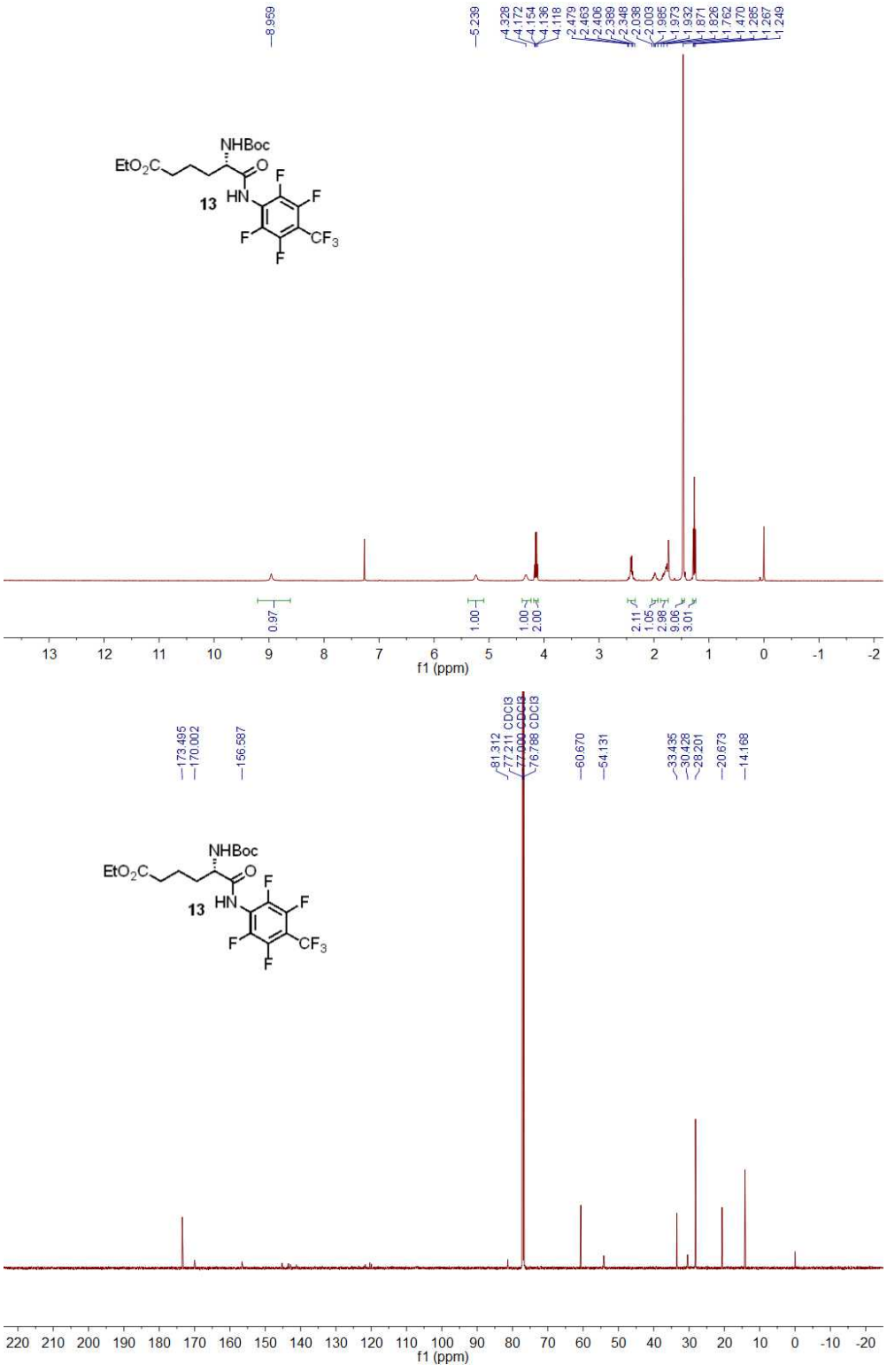

NHBoc
EtO2C
F
F
F
F
CF3
9
f1 (ppm)
NHBoc
EtO2C
F
F
F
F
CF3
9
f1 (ppm)

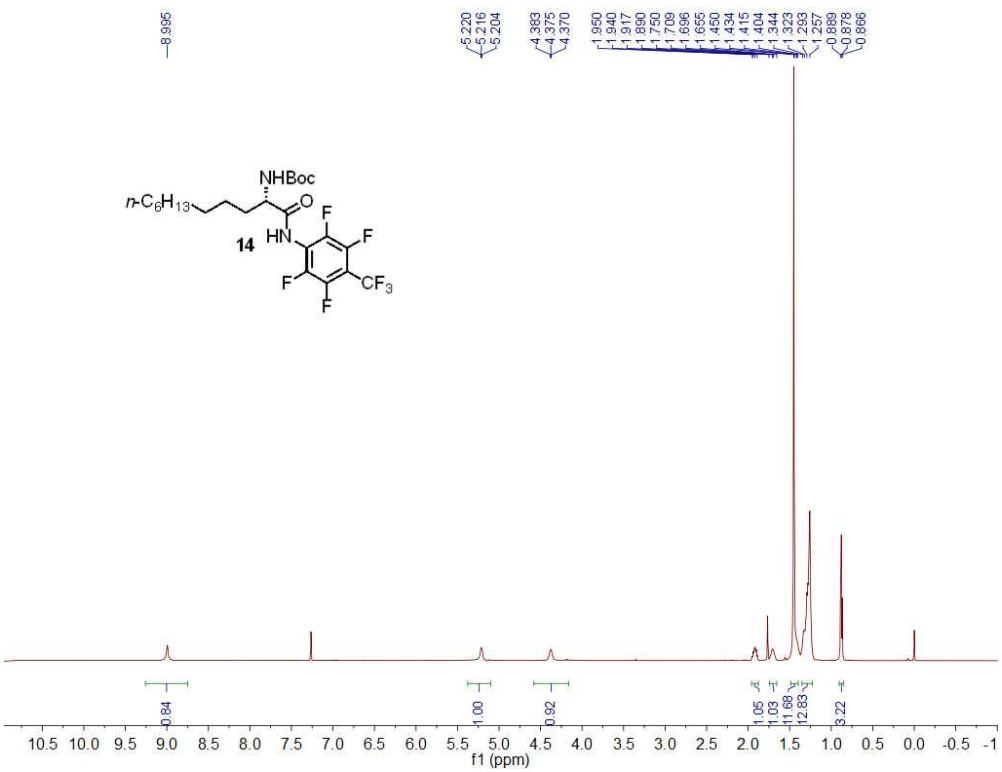

8.919
6.965
6.947
6.927
6.906
6.890
6.000
5.960
5.246
5.194
5.190
5.178
5.122
4.559
4.510
4.438
4.227
4.209
4.191
4.173
2.858
2.842
2.823
2.805
2.788
2.755
2.737
2.718
2.699
2.680
1.469
1.310
1.292
1.274
NHBoc
EtO2C
O
HN
F
F
F
F
CF3
10
1.00
1.02
1.00
1.01
1.04
2.05
1.06
1.07
9.09
3.07
f1 (ppm)
169.090
165.843
156.463
141.866
125.499
81.843
77.211 CDCl3
77.000 CDCl3
76.789 CDCl3
60.627
53.272
33.512
28.158
14.156
f1 (ppm)

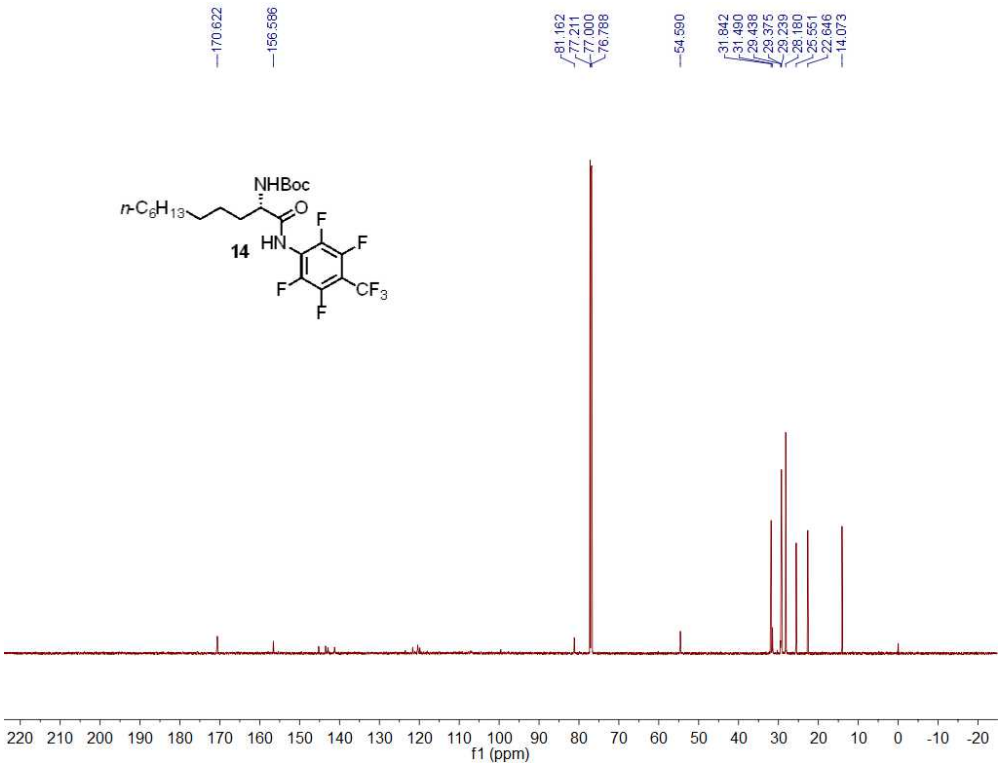

8.851
5.962
5.946
5.926
5.907
5.890
5.664
5.647
5.628
5.609
5.592
5.505
5.423
5.385
5.343
5.221
5.146
5.135
5.035
4.377
2.736
2.672
2.550
2.534
2.491
2.091
2.049
2.034
2.017
1.968
1.460
1.351
1.311
1.266
0.893
0.877
0.860
NHBoc
n-C6H13
O
HN
11
F
F
F
F
CF3
0.98
0.09
1.04
1.11
1.00
1.00
1.98
2.18
9.36
8.39
3.12
f1 (ppm)
169.895
156.496
136.432
123.229
81.283
77.211 CDCl3
77.000 CDCl3
76.788 CDCl3
54.109
34.467
32.544
31.686
29.154
28.765
28.175
22.586
14.053
f1 (ppm)

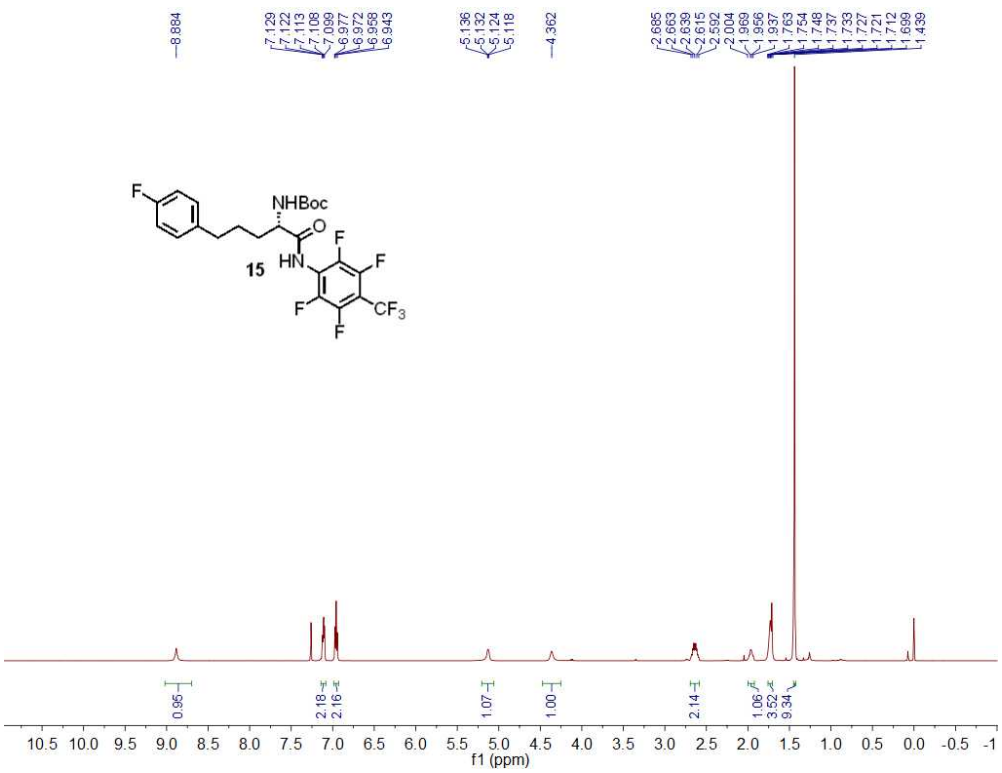

8.872
7.340
7.317
7.308
7.303
7.294
7.019
7.002
6.988
6.974
6.512
6.486
6.131
6.119
6.106
6.093
6.081
5.193
5.180
4.507
2.790
2.780
2.765
2.754
2.742
2.728
2.717
1.434
NHBoc
O
HN
12
F
F
F
F
F
CF3
1.00
2.09
2.05
1.00
1.00
1.02
1.00
2.02
9.02
f1 (ppm)

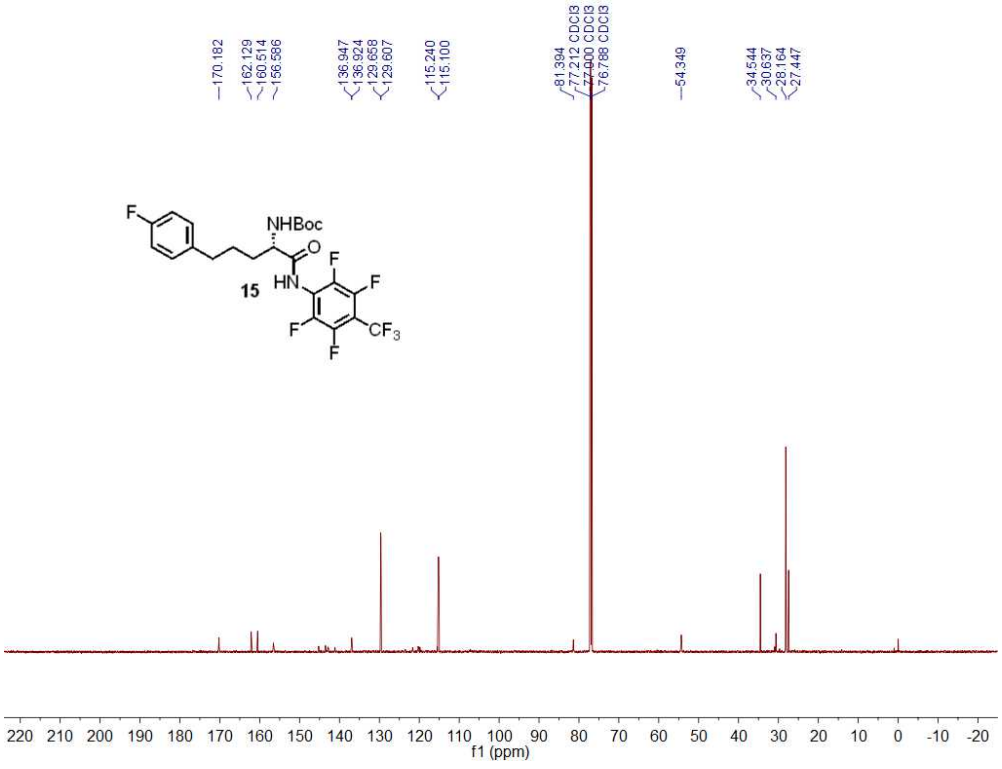

169.685
163.184
161.546
156.529
133.456
132.711
127.809
127.756
123.088
115.584
115.441
81.589
77.211
77.000
76.788
54.061
34.788
28.160
NHBoc
O
HN
12
F
F
F
F
F
CF3
f1 (ppm)

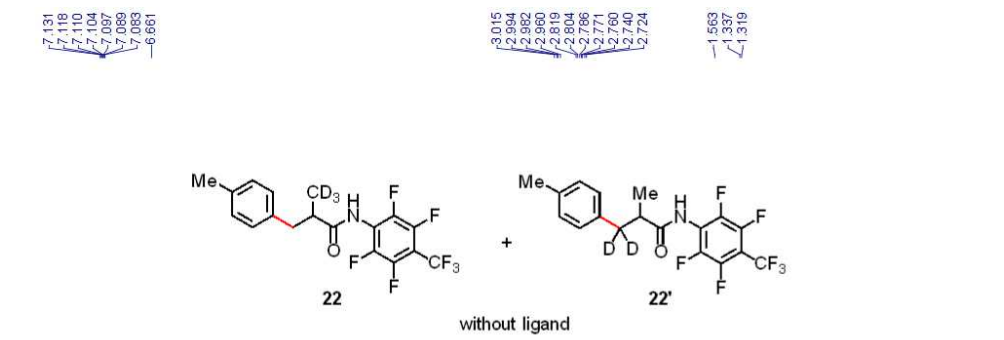

8.959
5.239
4.328
4.172
4.154
4.136
4.118
2.479
2.463
2.406
2.389
2.348
2.038
2.003
1.985
1.973
1.932
1.871
1.826
1.762
1.470
1.285
1.267
1.249
NHBoc
EtO2C
O
HN
13
F
F
F
F
CF3
0.97
1.00
1.00
2.00
2.11
1.05
2.98
9.06
3.01
f1 (ppm)
173.495
170.002
156.587
81.312
77.211 CDCl3
77.000 CDCl3
76.788 CDCl3
60.670
54.131
33.435
30.428
28.201
20.673
14.168
f1 (ppm)

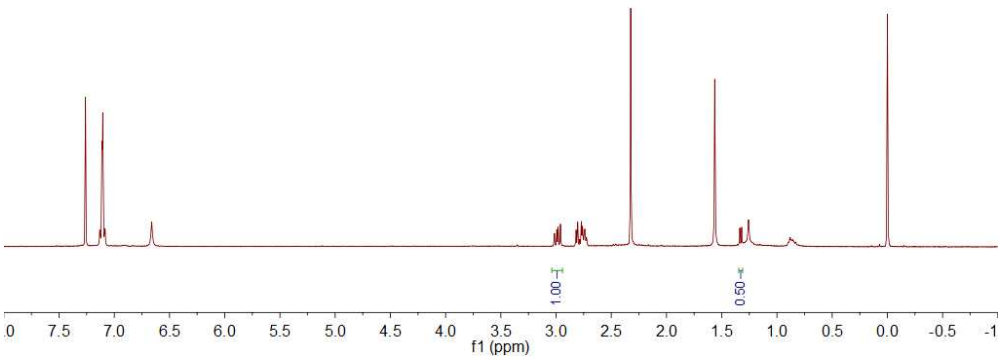

8.995
5.220
5.216
5.204
4.383
4.375
4.370
1.950
1.940
1.917
1.890
1.750
1.709
1.696
1.655
1.450
1.434
1.415
1.404
1.344
1.323
1.293
1.257
0.889
0.878
0.866
NHBoc
n-C6H13
O
HN
F
F
F
F
CF3
14
0.84
1.00
0.92
1.05
1.03
11.68
12.83
3.22
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

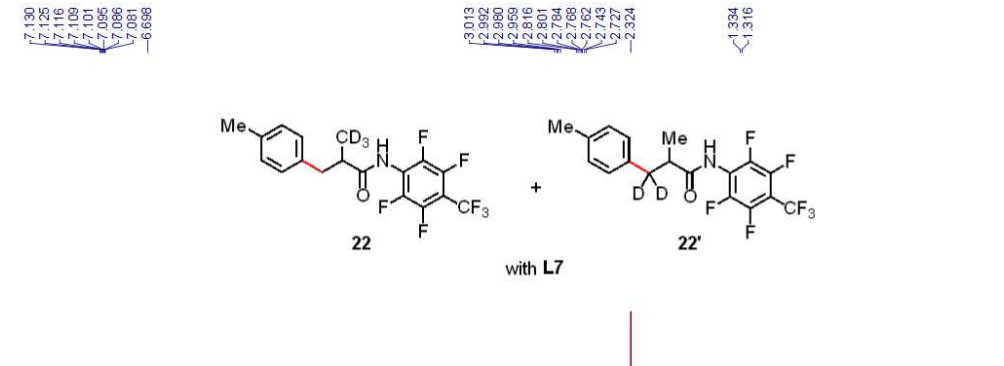

170.622
156.586
81.162
77.211
77.000
76.788
54.590
31.842
31.490
29.438
29.375
29.239
28.180
25.551
22.646
14.073
NHBoc
n-C6H13
O
HN
F
F
F
F
CF3
14
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

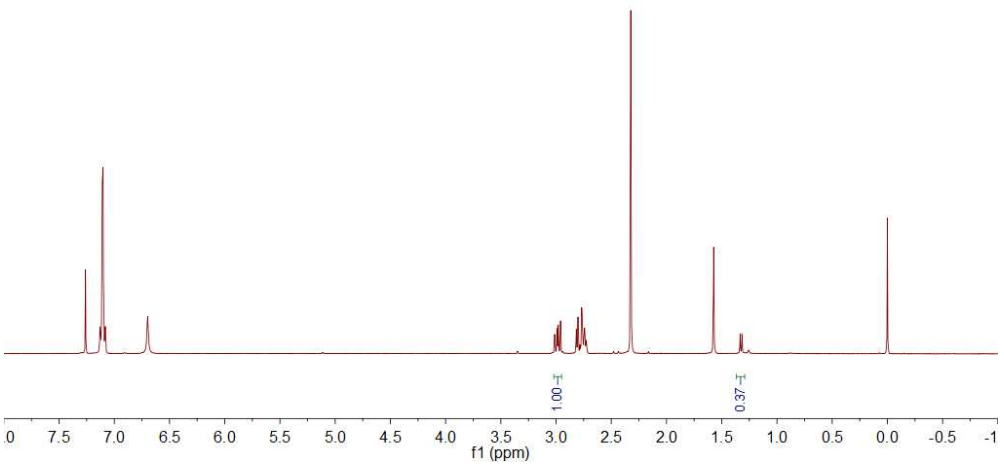

8.884
7.129
7.122
7.113
7.108
7.099
6.977
6.972
6.958
6.943
5.136
5.132
5.124
5.118
4.362
2.685
2.663
2.639
2.615
2.592
2.004
1.969
1.956
1.937
1.763
1.754
1.748
1.737
1.733
1.727
1.721
1.712
1.699
1.439
NHBoc
HN
O
F
F
F
F
F
CF3
15
0.95
2.18
2.16
1.07
1.00
2.14
1.06
3.52
9.34
f1 (ppm)

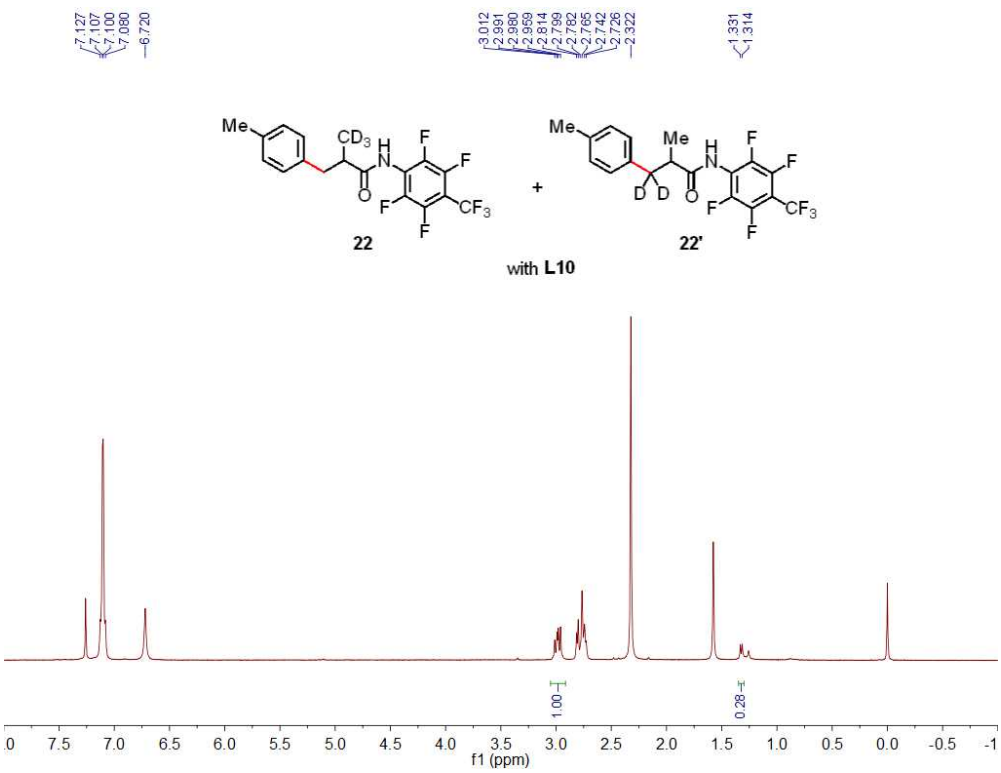

170.182
162.129
160.514
156.586
136.947
136.924
129.658
129.607
115.240
115.100
81.394
77.212 CDCl3
77.000 CDCl3
76.788 CDCl3
54.349
34.544
30.637
28.164
27.447
NHBoc
HN
O
F
F
F
F
F
CF3
15
f1 (ppm)


7.131
7.118
7.110
7.104
7.097
7.089
7.083
6.661
3.015
2.994
2.982
2.960
2.819
2.804
2.786
2.771
2.760
2.740
2.724
1.563
1.337
1.319
Me
CD3
H
N
F
F
F
F
CF3
O
22
+
Me
Me
D
D
22'
without ligand


1.00
0.50
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
-1
f1 (ppm)


7.130
7.125
7.116
7.109
7.101
7.095
7.086
7.081
6.698
3.013
2.992
2.980
2.959
2.816
2.801
2.784
2.768
2.762
2.743
2.727
2.324
1.334
1.316
Me
CD3
H
N
F
F
F
F
CF3
O
22
+
Me
Me
D
D
22'
with L7


1.00
0.37
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
-1
f1 (ppm)


7.127
7.107
7.100
7.080
6.720
3.012
2.991
2.980
2.959
2.814
2.799
2.782
2.765
2.742
2.726
2.322
1.331
1.314
Me
CD3
H
N
O
F
F
F
F
CF3
22
+
Me
Me
H
N
D
D
O
F
F
F
F
CF3
22'
with L10
1.00
0.28
f1 (ppm)

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