Highly Enantioselective [3+2] Annulation of 3-Butynoates with β-Trifluoromethyl Enones Promoted by an Amine–Phosphine Binary Catalytic System

Huanzhen Ni,[†] Yee Lin Wong,[†] Mingyue Wu,[†] Zhaobin Han,[⊥] Kuiling Ding,*[⊥] and Yixin Lu*[,†,‡,§]

[†]*Department of Chemistry, National University of Singapore, 3 Science Drive 3, 117543 Singapore.*

[⊥]State Key Laboratory of Organometallic Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032 (China)

Email: kding@mail.sioc.ac.cn

[‡] *Joint School of National University of Singapore and Tianjin University, International Campus of Tianjin Univer-sity, Binhai New City, Fuzhou, Fujian, 359297, PR China.*

[§] *National University of Singapore (Suzhou) Research Institute, 377 Lin Quan Street, Suzhou Industrial Park, Suzhou, Jiangsu, PR China, 215123*

Email: chmlyx@nus.edu.sg

Supporting Information

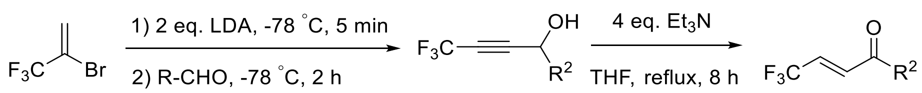
A. General Information

Unless otherwise specified, all reactions were carried out under a nitrogen atmosphere in anhydrous conditions. All the solvents were purified according to the standard procedures. All chemicals which are commercially available were used without further purification unless otherwise noted. Thin-layer chromatography (TLC) was performed on silica gel plates (60F-254) using UV-light (254 and 365 nm). Flash chromatography was conducted on silica gel (200–300 mesh). ^{1}H and ^{13}C NMR spectra were recorded at ambient temperature in $CDCl_3$ on a Bruker AMX500 (500 MHz) or AMX400 (400 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm). All high resolution mass spectra were obtained on a Finnigan/MAT 95XL-T spectrometer. Optical rotations were measured using a Jasco DIP-1000 polarimeter. Enantiomeric excesses were determined by HPLC analysis on a chiral stationary phase.

Catalyst **3** and **4** were synthesized by following our previously reported procedures.[1] β-Perfluoroalkyl enones **2** were synthesized according to literature reported procedures.[2] Enones **7** were synthesized according to previous reported procedures.[3] 3-Butynoate **1** was synthesized according to the method established by the Fu group.[4]

B. Representative Procedures

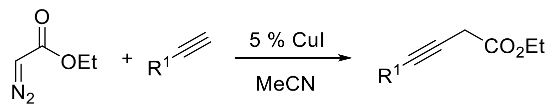
1. Preparation of enone **2**



Enone **2** was synthesized according to literature reported procedures.[2] To a solution of LDA (2.6 mmol) in THF (5 mL) was added dropwise 2-bromo-3,3,3-trifluoropropene (0.13 mL, 1.3 mmol) at -78 °C. After stirring for 5 min, a THF solution (1 mL) of respective aldehyde (1 mmol) was added and the mixture was stirred for 2 h at -78 °C. Subsequent extraction with ethyl acetate, drying over Na_2SO_4

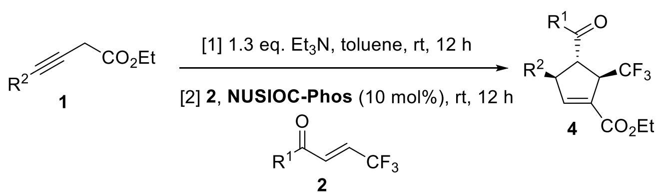
and concentration in vacuo afforded the crude product, which was then dissolved in 5 mL THF. To this solution was added triethylamine (0.56 mL, 4 mmol), and the mixture was refluxed for 8 h. Subsequently, 5 mL of 1M HCl was added to the mixture, and the crude product was extracted by ethyl acetate for three times, dried, and concentrated in vacuo. The crude product was then purified by column chromatography using 20% EtOAc/Hexane to afford enone **2**.

2. Preparation of 3-butynoate **1**



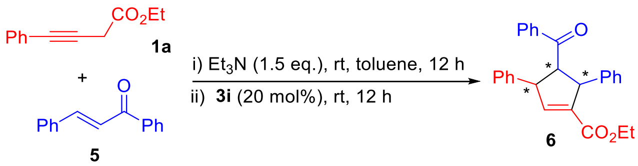
3-Butynoate **1** was synthesized according to literature reported procedures.[4] To a solution of alkyne (1 mmol) and CuI (15 mg) in MeCN (2 mL) were added ethyl diazoacetate (1 mmol). The resulting mixture was stirred at room temperature for 12 h, and the solvent was removed in vacuo. The crude product was then purified by column chromatography using 5–10% EtOAc/Hexane to afford 3-butynoate **1**.

3. [3+2] Annulation of 3-Butynoates with β-Trifluoromethyl Enones Promoted by Et_3N and **NUSIOC-Phos**



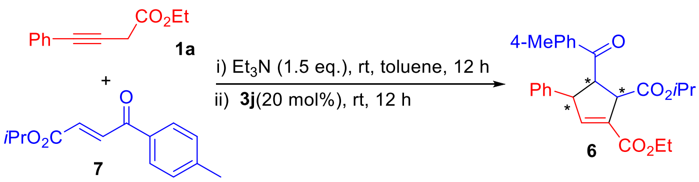
To a dried round bottle flask with a magnetic stirring bar under N_2 at room temperature was added 3-butynoate **1** (0.12 mmol) in toluene (1 mL), followed by the addition of Et_3N (0.13 mmol), and the mixture was stirred for 12 h. Catalyst **NUSIOC-Phos** (0.01 mmol, 4 mg) and enone **2** were then introduced, and the reaction mixture was stirred for another 12 h. The solvent was then removed under reduced pressure and crude ^1H NMR analysis of the residue was performed to identify the diastereomeric ratio of the product. The crude product was subsequently purified by column chromatography (10%–20% EtOAc/Hexane) on silica gel to afford annulation adduct **4.**

4. [3+2] Annulation of 3-Butynoate **1a** with Enones **5** Promoted by Et_3N and Bifunctional Chiral Phosphine **3i**



To a dried round bottle flask with a magnetic stirring bar under N_2 at room temperature was added 3-butynoate **1a** (0.12 mmol) in toluene (1 mL), followed by the addition of Et_3N (0.15 mmol), and the mixture was stirred for 12 h. Catalyst **3i** (0.02 mmol, 19 mg) and enone **5** were then introduced, and the reaction mixture was stirred for another 12 h. The solvent was then removed under reduced pressure and crude ^1H NMR analysis of the residue was performed to identify the diastereomeric ratio of the product. The crude product was subsequently purified by column chromatography (10%–20% EtOAc/Hexane) on silica gel to afford annulation adduct **6.**

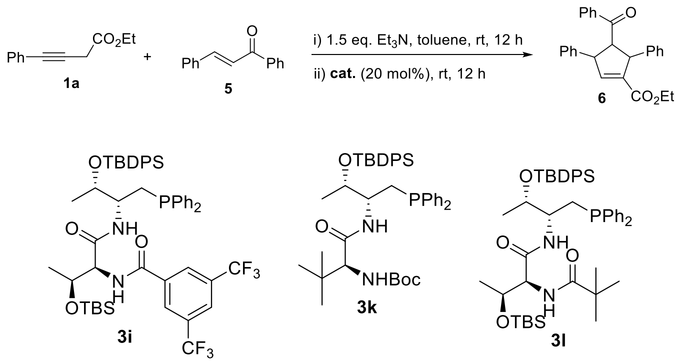
5. [3+2] Annulation of 3-Butynoate **1a** with Enones **7** Promoted by Et_3N and Bifunctional Chiral Phosphine **3j**



To a dried round bottle flask with a magnetic stirring bar under N_2 at room temperature was added 3-butynoate **1a** (0.12 mmol) in toluene (1 mL), followed by the addition of Et_3N (0.15 mmol), and the mixture was stirred for 12 h. Catalyst **3j** (0.02 mmol, 16 mg) and enone **7** were then introduced, and the reaction mixture was stirred for another 12 h. The solvent was then removed under reduced pressure and crude ^1H NMR analysis of the residue was performed to identify the diastereomeric ratio of the product. The crude product was subsequently purified by column chromatography (10%–20% EtOAc/Hexane) on silica gel to afford annulation adduct **8.**

C. Preliminary further investigation

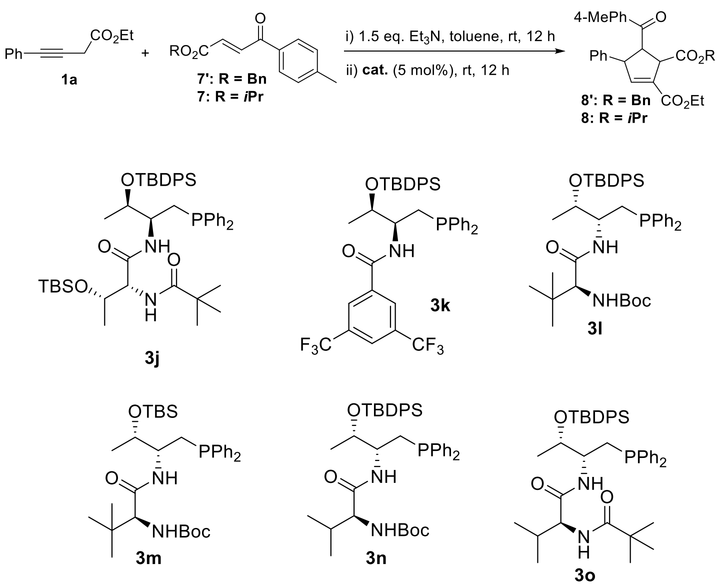
1. Catalyst screening[a]



entry	phosphine	dr[b]	yield (%)[c]	ee (%)[d]
1	**3i**	**>99:1**	**92**	**92**
2	**3k**	9:1	88	93
3	**3l**	19:1	95	89

[a]Reactions were performed by treating **1a** (0.12 mmol) in toluene (1 mL) with Et_3N (0.15mmol) and stirred for 12 h at room temperature, followed by the addition of **5** (0.10 mmol) and the catalyst (20 mol%). [b]Determined by crude ^1H NMR analysis. [c]Isolated yield of the major diastereomer. [d]Determined by HPLC analysis on a chiral stationary phase.

2. Examining another annulation[a]



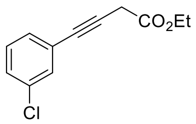
entry	phosphine	**7 / 7'**	**8 / 8'**	dr[b]	yield (%)[c]	ee (%)[d]

1	**3j**	**7'**	**8'**	7:1	85	93
2	**3k**	**7'**	**8'**	10:1	78	-37
3	**3l**	**7'**	**8'**	3:1	70	88
4	**3m**	**7'**	**8'**	4:1	77	89
5	**3n**	**7'**	**8'**	5:1	80	91
6	**3o**	**7'**	**8'**	4:1	76	93
7	**3j**	**7**	**8**	**13:1**	**88**	**94**

[a]Reactions were performed by treating **1a** (0.12 mmol) in toluene (1 mL) with Et_3N (0.15mmol) and stirred for 12 h at room temperature, followed by the addition of **7 or 7'** (0.10 mmol) and the catalyst (5 mol%). [b]Determined by crude ^{1}H NMR analysis. [c]Isolated yield of the major diastereomer. [d]Determined by HPLC analysis on a chiral stationary phase.

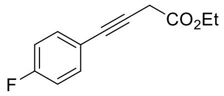
D. Analytical Data and HPLC Chromatograms of Substrates and Products

Ethyl 4-(3-chlorophenyl)but-3-ynoate **1c**



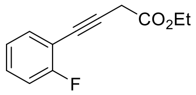
Prepared according to Representative Procedure **B-2**. Flash column chromatography (eluent: 5%-10% EtoAc/Hexane) to afford **1c** as colorless oil (150 mg, 68%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (t, *J* = 1.7 Hz, 1H), 7.31 (dt, *J* = 7.5 Hz, 1.4 Hz, 1H), 7.27–7.25 (m, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 3H), 3.49 (s, 2H), 1.31 (t, *J* = 7.1 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 134.1, 131.7, 129.9, 129.5, 128.5, 124.7, 82.6, 82.2, 61.8, 26.7, 14.1; ; HRMS (ESI) m/z calcd for $C_{12}H_{11}ClNaO_2$ $[M + Na]^+$ = 245.0340, found = 245.0345.

Ethyl 4-(4-fluorophenyl)but-3-ynoate **1d**



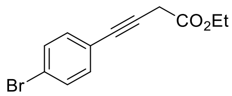
Prepared according to Representative Procedure **B-2**. Flash column chromatography (eluent: 5%-10% EtoAc/Hexane) to afford **1d** as colorless oil (134 mg, 65%);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.34 (m, 2H), 6.98 (t, *J* = 8.8 Hz, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.47 (s, 2H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.17, 133.67, 133.59, 115.58, 115.36, 82.41, 61.68, 26.67, 14.12; HRMS (ESI) m/z calcd for $C_{12}H_{11}FNaO_2$ $[M + Na]^+$ = 229.0635, found = 229.0630.

Ethyl 4-(2-fluorophenyl)but-3-ynoate **1e**



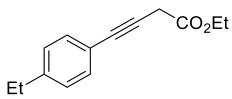
Prepared according to Representative Procedure **B-2**. Flash column chromatography (eluent: 5%-10% EtoAc/Hexane) to afford **1e** as colorless oil (144 mg, 70%);[1]H NMR (400 MHz, $CDCl_3$) δ 7.29–7.19 (m, 2H), 7.13 (ddd, *J* = 9.3 Hz, 2.4 Hz, 1.2 Hz, 1H), 7.05–6.97 (m, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.49 (s, 2H), 1.31 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 129.8, 129.7, 127.7, 127.6, 118.7, 118.5, 115.7, 115.5, 82.4, 61.8, 26.7, 14.1; HRMS (ESI) m/z calcd for $C_{12}H_{11}FNaO_2$ $[M + Na]^+$ = 229.0635, found = 229.0627.

Ethyl 4-(4-bromophenyl)but-3-ynoate **1f**



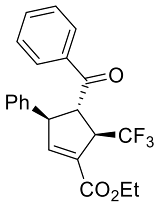
Prepared according to Representative Procedure **B-2**. Flash column chromatography (eluent: 5%-10% EtoAc/Hexane) to afford **1f** as colorless oil (160 mg, 60%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.38 (m, 1H), 7.30–7.25 (m, 1H), 4.20 (q, *J* = 7.1 Hz, 1H), 3.46 (s, 1H), 1.28 (t, *J* = 7.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 133.2, 131.5, 122.4, 122.0, 82.6, 61.7, 26.8, 14.1; HRMS (ESI) m/z calcd for $C_{12}H_{11}BrNaO_2$ $[M + Na]^+$ = 288.9835, found = 288.9831.

Ethyl 4-(4-ethylphenyl)but-3-ynoate **1g**

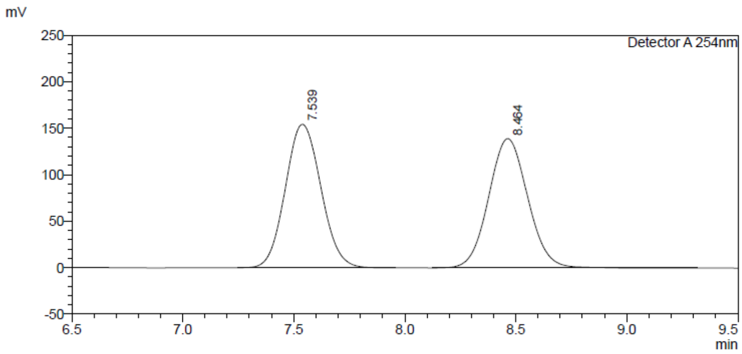


Prepared according to Representative Procedure **B-2**. Flash column chromatography (eluent: 5%-10% EtoAc/Hexane) to afford **1g** as colorless oil (108 mg, 50%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.32 (m, 1H), 7.14–7.07 (m, 2H), 4.21 (q, *J* = 7.0 Hz, 2H), 3.48 (s, 2H), 2.62 (q, *J* = 7.6 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 144.5, 131.7, 127.8, 120.2, 83.6, 80.4, 61.6, 28.8, 26.8, 15.3, 14.1; HRMS (ESI) m/z calcd for $C_{14}H_{16}NaO_2$ $[M + Na]^+$ = 239.1043, found = 239.1044.

Ethyl (3*R*,4*S*,5*R*)-4-benzoyl-3-phenyl-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4a**



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4a** as colorless oil (33.8 mg, 87%); $[\alpha]^{25}{}_{D}$ = -28.9 (c 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.73–7.65 (m, 2H), 7.58–7.51 (m, 1H), 7.41–7.28 (m, 6H), 7.08 (dd, J = 6.4, 3.1 Hz, 2H), 6.82 (s, 1H), 4.63–4.52 (m, 1H), 4.37–4.21 (m, 3H), 4.03–3.96 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.2, 163.3, 147.5, 140.2, 135.3, 133.9, 131.9, 129.2, 129.0, 128.7, 128.1, 127.9, 126.3 (q, *J* = 279.9 Hz), 61.1, 55.5, 54.1, 51.4 (q, *J* = 28.9 Hz), 14.1; HRMS (ESI) m/z calcd for $C_{22}H_{19}F_3NaO_3$ $[M + Na]^+$ = 411.1179, found = 411.1187; The ee value was 99%, t_R (minor) = 7.552 min, t_R (major) = 8.476 min (Chiralpak IC, λ = 254 nm, 5% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

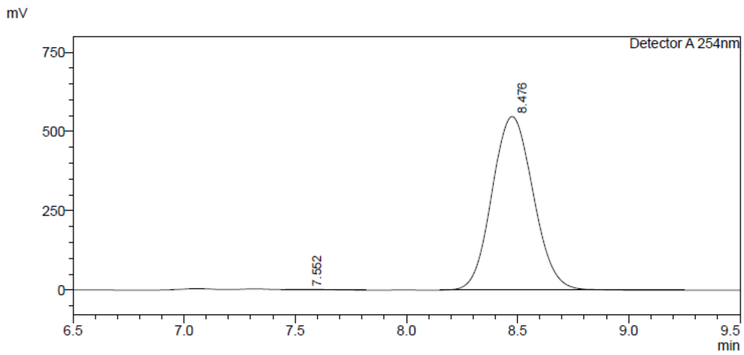


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.539	1724460	154266	50.334		M	
2	8.464	1701605	139056	49.666			
Total		3426065	293322	100.000			

Racemic **4a**



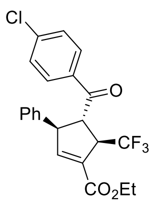
<Peak Table>

Detector A 254nm

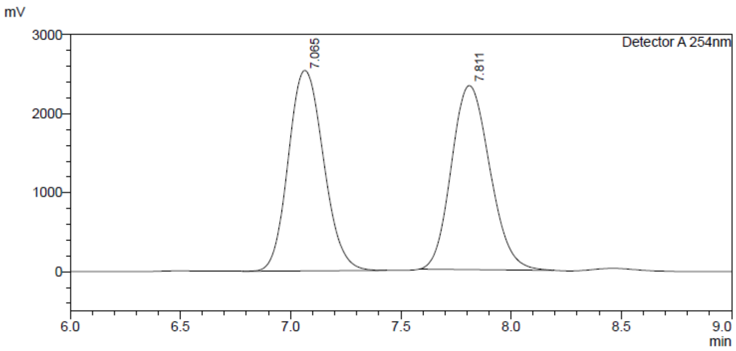
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.552	28000	2307	0.395		M	
2	8.476	7055370	547507	99.605		M	
Total		7083369	549814	100.000			

Enantiomeric enriched **4a**

<u>Ethyl (3*R*,4*S*,5*R*)-4-(4-chlorobenzoyl)-3-phenyl-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4b**</u>



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4b** as colorless oil (37.6 mg, 89%); $[\alpha]^{25}{}_{D}$ = -71.4 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65–7.56 (m, 2H), 7.37–7.28 (m, 2H), 7.13–7.05 (m, 1H), 6.80 (s, 1H), 4.62–4.49 (m, 1H), 4.39–4.20 (m, 2H), 4.17 (t, *J* = 5.5 Hz, 1H), 4.01–3.87 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 163.2, 147.3, 140.6, 140.0, 133.6, 131.9, 130.5, 129.1, 129.0, 128.1, 128.0, 126.2 (q, *J* = 279.7 Hz), 61.2, 55.5, 54.3, 51.4 (q, *J* = 29.5 Hz), 14.1; HRMS (ESI) m/z calcd for $C_{22}H_{18}ClF_3NaO_3$ $[M + Na]^+$ = 445.0789, found = 445.0795; The ee value was 99%, t_R (minor) = 7.381 min, t_R (major) = 8.225 min (Chiralpak IC, λ = 254 nm, 5% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

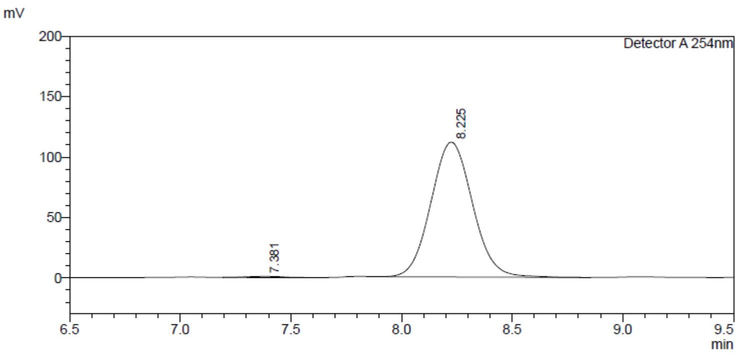


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.065	28241786	2539396	49.926		M	
2	7.811	28325629	2329923	50.074		M	
Total		56567416	4869319	100.000			

Racemic **4b**



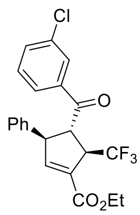
<Peak Table>

Detector A 254nm

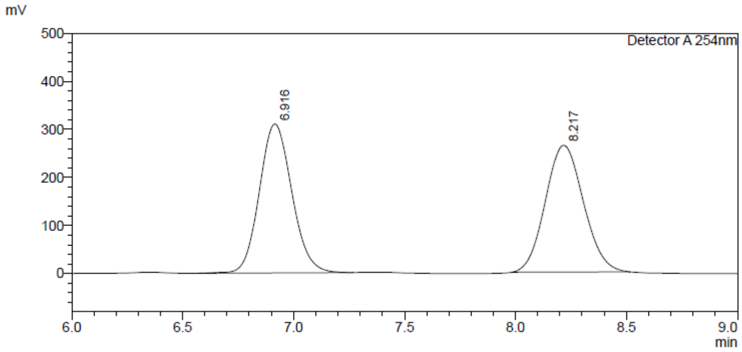
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.381	9838	914	0.669			
2	8.225	1461655	111629	99.331			
Total		1471493	112543	100.000			

Enantioenriched **4b**

<u>Ethyl (3*R* ,4S,5R)-4-(3-chlorobenzoyl)-3-phenyl-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4c**</u>



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4c** as colorless oil (38.1 mg, 90%); $[\alpha]^{25}{}_{D}$ = -39.6 (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.54–7.46 (m, 2H), 7.37–7.24 (m, 4H), 7.12–7.03 (m, 2H), 6.79 (s, 1H), 4.64–4.52 (m, 1H), 4.37–4.20 (m, 2H), 4.15 (t, *J* = 5.5 Hz, 1H), 3.97–3.89 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.8, 163.2, 147.2, 139.9, 136.8, 135.1, 133.8, 131.9, 129.9, 129.3, 129.2, 128.1, 128.0, 127.2, 126.2 (q, *J* = 279.7 Hz), 125.1, 122.9, 61.2, 55.4, 54.6, 51.2 (q, *J* = 29.3 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.51; HRMS (ESI) m/z calcd for $C_{22}H_{18}ClF_3NaO_3$ $[M + Na]^+$ = 445.0789, found = 445.0785; The ee value was 99%, t_R (minor) = 6.955 min, t_R (major) = 8.230 min (Chiralpak IC, λ = 254 nm, 5% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

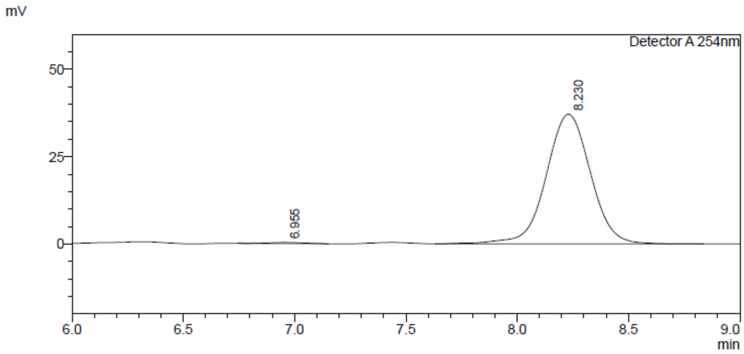


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.916	3161064	310350	50.040			
2	8.217	3155968	264011	49.960		M	
Total		6317032	574361	100.000			

Racemic **4c**



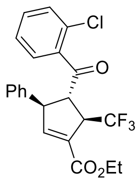
<Peak Table>

Detector A 254nm

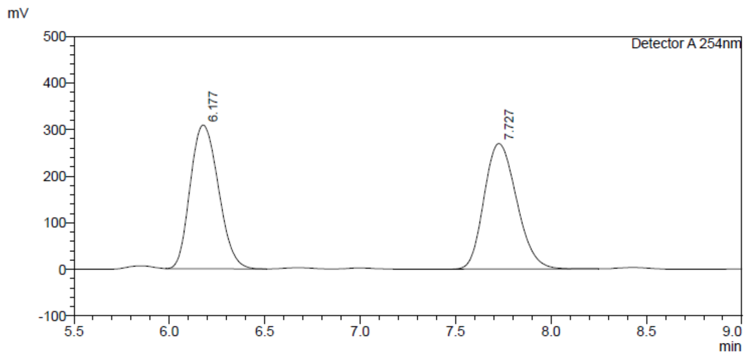
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.955	3244	308	0.627		M	
2	8.230	514148	37049	99.373			
Total		517392	37357	100.000			

Enantioenriched **4c**

Ethyl (3*R*,4*S*,5*R*)-4-(2-chlorobenzoyl)-3-phenyl-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4d**



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4d** as colorless oil (31.7 mg, 75%); $[\alpha]^{25}{}_{D}$ = -70.5 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.40 (m, 2H), 7.28–7.24 (m, 2H), 7.23–7.18 (m, 3H), 6.88 (dd, *J* = 6.6 Hz, 2.9 Hz, 2H), 6.83 (s, 1H), 4.58–4.48 (m, 1H), 4.39–4.21 (m, 2H), 4.19–4.12 (m, 2H), 1.34 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6, 163.2, 147.2, 140.3, 137.8, 132.2, 131.9, 131.4, 130.7, 129.1, 128.8, 127.6, 127.5, 126.9, 126.2 (q, *J* = 279.7 Hz), 122.0, 61.2, 58.4, 53.5, 49.9 (q, *J* = 29.3 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.01; HRMS (ESI) m/z calcd for $C_{22}H_{18}ClF_3NaO_3$ $[M + Na]^+$ = 445.0789, found = 445.0784; The ee value was 91%, t_R (major) = 6.161 min, t_R (minor) = 7.719 min (Chiralpak IE, λ = 254 nm, 10% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

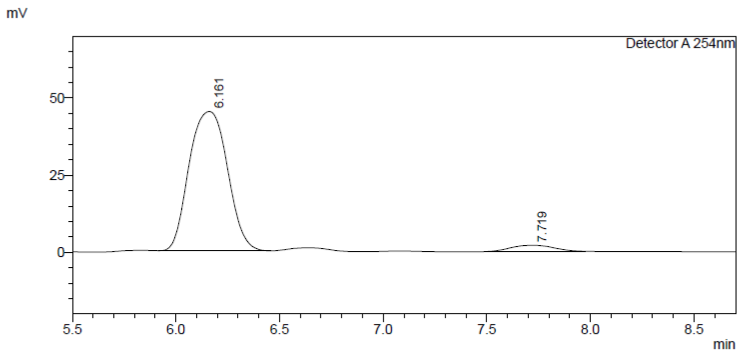


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.177	3173713	308104	49.740			
2	7.727	3206929	269473	50.260			
Total		6380642	577577	100.000			

Racemic **4d**



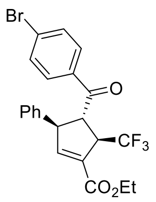
<Peak Table>

Detector A 254nm

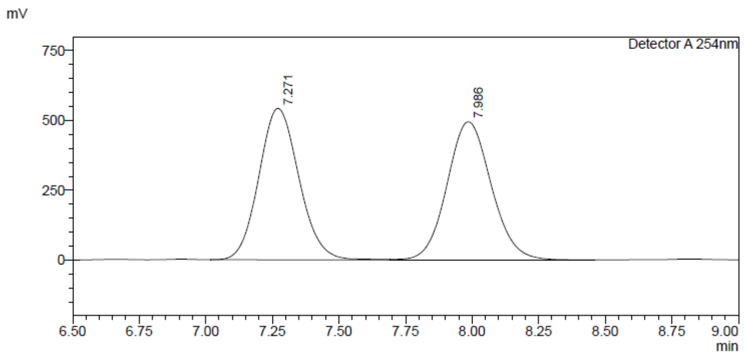
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.161	581095	45119	95.408			
2	7.719	27965	1978	4.592		M	
Total		609059	47097	100.000			

Enantioenriched **4d**

Ethyl (3*R*,4*S*,5*R*)-4-(4-bromobenzoyl)-3-phenyl-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4e**



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4e** as colorless oil (37.4 mg, 80%); $[\alpha]^{25}_{D}$ = -65.5 (c 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55–7.45 (m, 4H), 7.36–7.30 (m, 3H), 7.11–7.05 (m, 2H), 6.80 (s, 1H), 4.60–4.51 (m, 1H), 4.38–4.20 (m, 2H), 4.17 (t, *J* = 5.5 Hz, 1H), 3.99–3.92 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.2, 163.2, 147.3, 140.0, 133.9, 132.0, 131.9, 130.6, 129.4, 129.1, 128.1, 128.0, 126.2 (q, *J* = 279.7 Hz), 61.2, 55.5, 54.2, 51.4 (q, *J* = 29.2 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.49; HRMS (ESI) m/z calcd for $C_{22}H_{18}BrF_3NaO_3$ $[M + Na]^+$ = 489.0284, found = 489.0286; The ee value was 98%, t_R (minor) = 7.220 min, t_R (major) = 8.013 min (Chiralpak IC, λ = 254 nm, 5% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

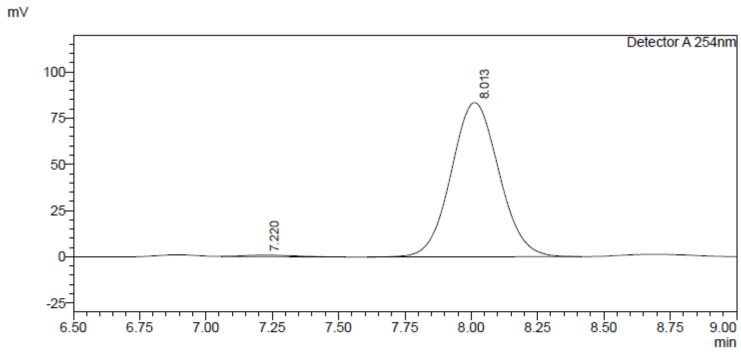


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.271	5688314	541923	49.852			
2	7.986	5722055	494810	50.148		V	
Total		11410369	1036733	100.000			

Racemic **4e**



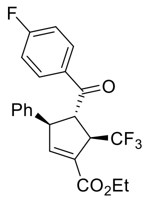
<Peak Table>

Detector A 254nm

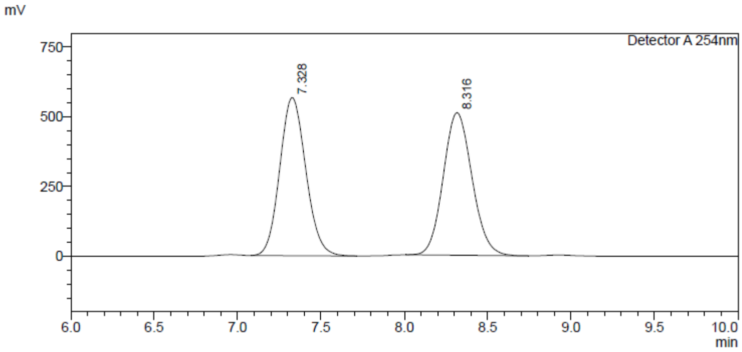
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.220	10015	792	0.948			
2	8.013	1046486	83430	99.052			
Total		1056500	84221	100.000			

Enantioenriched **4e**

<u>Ethyl (3*R*,4*S*,5*R*)-4-(4-fluorobenzoyl)-3-phenyl-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4f**</u>



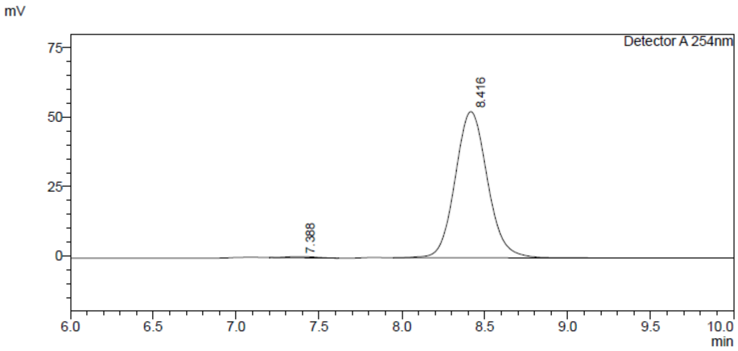
Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4f** as colorless oil (92%, 37.4 mg); $[\alpha]^{25}{}_{D}$ = -56.2 (c 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73–7.66 (m, 2H), 7.33 (dd, *J* = 5.4 Hz, 1.6 Hz, 3H), 7.09 (dd, *J* = 7.1 Hz, 2.1 Hz, 2H), 7.02 (t, *J* = 8.5 Hz, 2H), 6.81 (s, 1H), 4.63–4.50 (m, 1H), 4.37–4.21 (m, 2H), 4.19 (t, *J* = 5.5 Hz, 1H), 4.01–3.91 (m, 1H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.6, 167.3, 164.2 (d, *J* = 248.3 Hz), 147.3, 140.1, 131.9 (d, *J* = 9.6 Hz), 131.7 (d, *J* = 3 Hz), 129.1, 128.0, 126.3 (q, *J* = 279.5 Hz), 115.8 (d, *J* = 22.0 Hz), 61.1, 55.6, 54.2, 51.5 (q. *J* = 29.0 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.52, -103.63; HRMS (ESI) m/z calcd for $C_{22}H_{18}F_4NaO_3$ $[M + Na]^+$ = 429.1084, found = 429.1088; The ee value was 99%, t_R (minor) = 7.388 min, t_R (major) = 8.416 min (Chiralpak IC, λ = 254 nm, 5% *i*-PrOH/hexane, flow rate = 1.0 mL/min).



<Peak Table>
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.328	6171797	567251	50.102		M	
2	8.316	6146660	511396	49.898		M	
Total		12318457	1078647	100.000			

Racemic **4f**

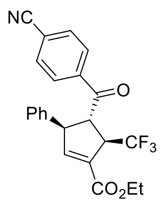


<Peak Table>
Detector A 254nm

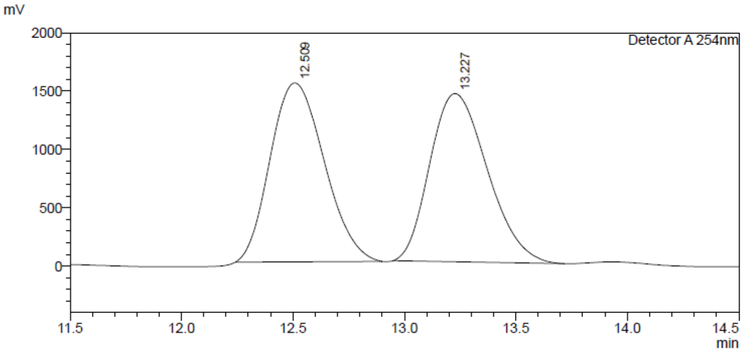
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.388	4880	405	0.677			
2	8.416	715756	52761	99.323		S	
Total		720636	53166	100.000			

Enantioenriched **4f**

Ethyl (3*R*,4*S*,5*R*)-4-(4-cyanobenzoyl)-3-phenyl-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4g**



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4g** as colorless oil (90%, 37.2 mg); $[\alpha]^{25}{}_{D}$ = -62.0 (c 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75–7.70 (m, 2H), 7.67–7.61 (m, 2H), 7.34–7.32 (m, 3H), 7.09 – 7.03 (m, 2H), 6.79 (s, 1H), 4.62–4.49 (m, 1H), 4.37–4.22 (m, 2H), 4.20 (t, *J* = 5.8 Hz, 1H), 3.99–3.91 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 163.1, 147.0, 139.7, 138.3, 132.4, 129.4, 129.3, 128.3, 127.9, 126.1 (q, J = 279.7 Hz), 61.2, 55.3, 54.8, 51.4 (q, J = 29.4 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.51; HRMS (ESI) m/z calcd for $C_{23}H_{18}F_3NNaO_3$ $[M + Na]^+$ = 436.1131, found = 436.1128; The ee value was 95%, t_R (minor) = 11.518 min, t_R (major) = 12.479 min (Chiralpak IE, λ = 254 nm, 40% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

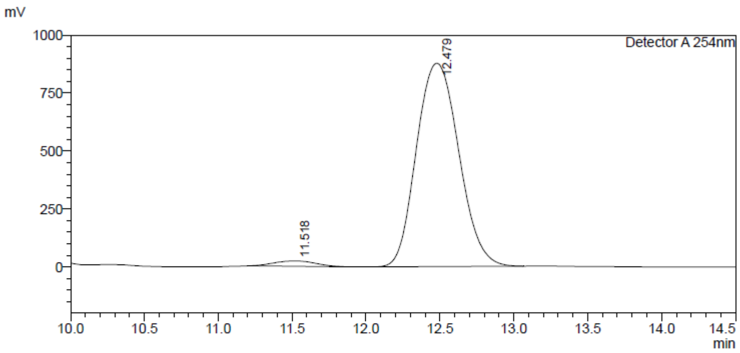


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	12.509	25866535	1534069	49.991		M	
2	13.227	25875574	1441451	50.009		M	
Total		51742109	2975520	100.000			

Racemic **4g**



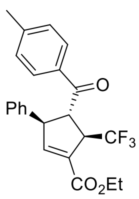
<Peak Table>

Detector A 254nm

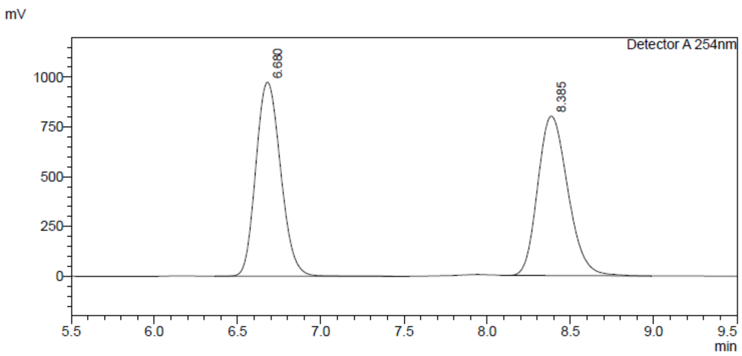
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.518	448982	22981	2.500		M	
2	12.479	17511087	876673	97.500			
Total		17960069	899654	100.000			

Enantioenriched **4g**

<u>Ethyl (3*R*,4*S*,5*R*)-4-(4-methylbenzoyl)-3-phenyl-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4h**</u>



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4h** as colorless oil (91%, 36.6 mg); $[\alpha]^{25}{}_{D}$ = -61.3 (c 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.2 Hz, 2H), 7.34–7.29 (m, 3H), 7.16 (d, *J* = 8.1 Hz, 2H), 7.12–7.08 (m, 2H), 6.82 (s, 1H), 4.60–4.50 (m, 1H), 4.38–4.18 (m, 3H), 4.04–3.95 (m, 1H), 2.39 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.8, 163.4, 147.6, 144.9, 140.3, 132.7, 132.0, 129.4, 129.3, 129.0, 128.1, 127.8, 126.4 (q, *J* = 279.9 Hz), 61.1, 55.6, 53.9, 51.5 (q, *J* = 28.6 Hz), 21.7, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.47.; HRMS (ESI) m/z calcd for $C_{23}H_{21}F_3NaO_3$ $[M + Na]^+$ = 425.1335, found = 425.1347; The ee value was 99%, t_R (major) = 6.655 min, t_R (major) = 8.377 min (Chiralpak IE, λ = 254 nm, 10% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

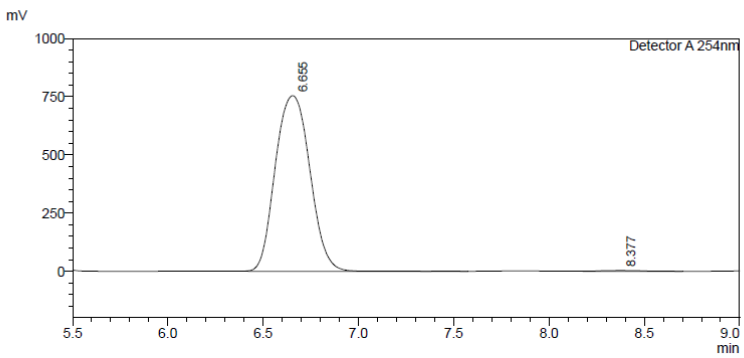


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.680	10091693	973339	49.981			
2	8.385	10099385	801342	50.019			
Total		20191077	1774681	100.000			

Racemic **4h**



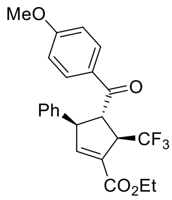
<Peak Table>

Detector A 254nm

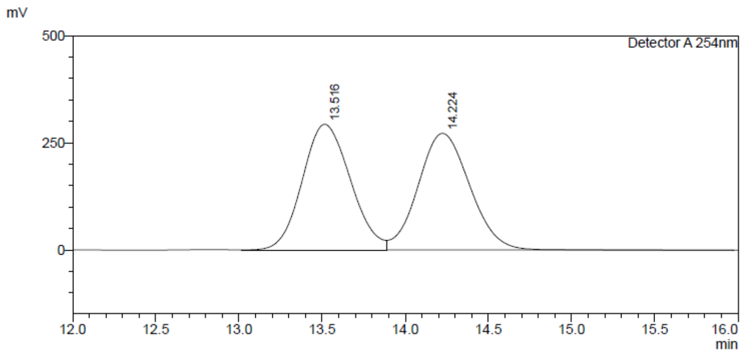
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.655	9543615	754393	99.385		S	
2	8.377	59101	3983	0.615		M	
Total		9602716	758376	100.000			

Enantioenriched **4h**

Ethyl (3*R*,4*S*,5*R*)-4-(4-methoxybenzoyl)-3-phenyl-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4i**



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4i** as colorless oil (91%, 38 mg); $[\alpha]^{25}{}_{D}$ = -72.5 (c 1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.70–7.65 (m, 2H), 7.36–7.29 (m, 3H), 7.13–7.08 (m, 2H), 6.85–6.79 (m, 3H), 4.61–4.48 (m, 1H), 4.38–4.21 (m, 2H), 4.19 (t, *J* = 5.4 Hz, 1H), 4.02–3.96 (m, 1H), 3.84 (s, 3H); 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 164.2, 163.4, 147.6, 140.4, 132.0, 131.6, 129.0, 128.2, 128.1, 127.8, 126.4 (q, J = 279.9 Hz), 113.8, 61.1, 55.7, 55.5, 53.7, 51.6 (q, *J* = 29.1 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.49; HRMS (ESI) m/z calcd for $C_{23}H_{21}F_3NaO_4$ $[M + Na]^+$ = 441.1284, found = 441.1289; The ee value was 99%, t_R (minor) = 14.633 min, t_R (major) = 15.327 min (Chiralpak IC, λ = 254 nm, 5% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

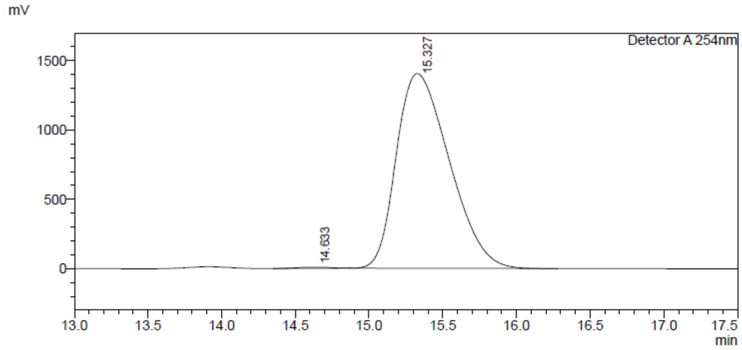


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.516	5906003	293420	50.125			
2	14.224	5876593	272287	49.875		V	
Total		11782597	565707	100.000			

Racemic **4i**



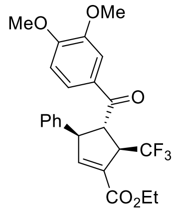
<Peak Table>

Detector A 254nm

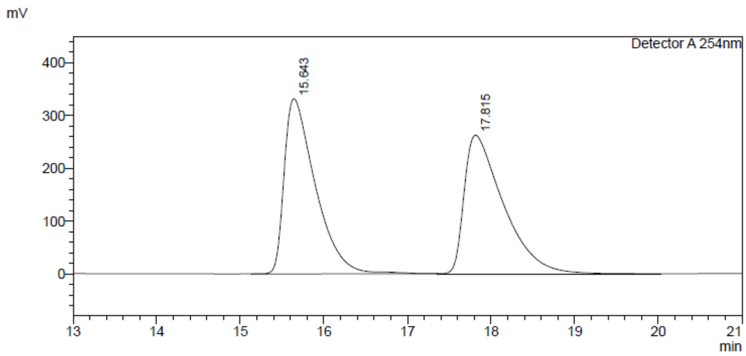
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	14.633	129250	8013	0.366		M	
2	15.327	35139960	1405263	99.634			
Total		35269210	1413276	100.000			

Enantioenriched **4i**

Ethyl (3*R*,4*S*,5*R*)-4-(3,4-dimethoxybenzoyl)-3-phenyl-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4j**



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4j** as colorless oil (72%, 32.3 mg); $[\alpha]^{25}_{D}$ = -52.4 (c 1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.23 (m, 5H), 7.17–7.11 (m, 2H), 6.80 (s, 1H), 6.75 (d, *J* = 8.4 Hz, 1H), 4.66–4.56 (m, 1H), 4.37–4.19 (m, 3H), 4.00–3.95 (m, 1H), 3.90 (s, 3H), 3.69 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.5, 163.3, 154.0, 149.0, 147.6, 140.5, 131.8, 129.1, 128.2, 128.1, 127.9, 126.4 (q, *J* = 279.8 Hz), 124.0, 111.1, 110.1, 61.1, 56.1, 55.8, 55.6, 53.7, 51.5 (q, *J* = 29.1 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.45; HRMS (ESI) m/z calcd for $C_{24}H_{23}F_3NaO_5$ $[M + Na]^+$ = 471.1390, found = 471.1403; The ee value was 99%, t_R (major) = 15.774 min, t_R (minor) = 18.211 min (Chiralpak IE, λ = 254 nm, 10% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

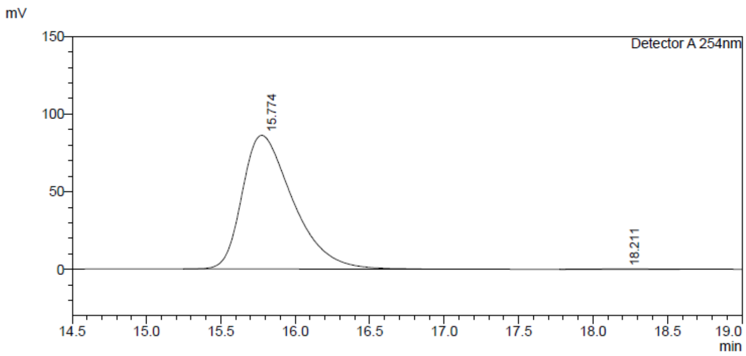


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	15.643	8597338	331807	50.107			
2	17.815	8560515	262535	49.893		V	
Total		17157853	594342	100.000			

Racemic **4j**



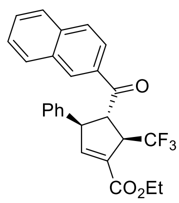
<Peak Table>

Detector A 254nm

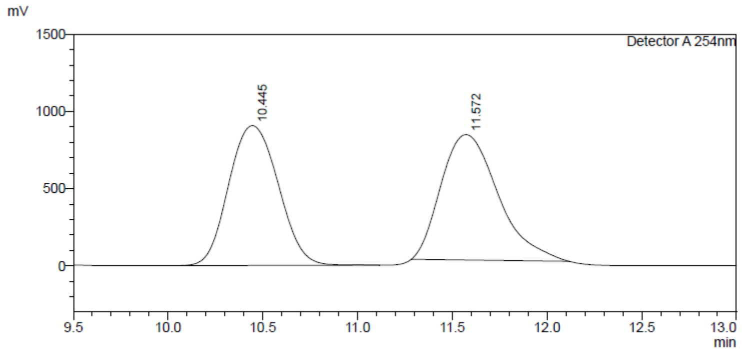
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	15.774	2043576	86049	99.595			
2	18.211	8315	338	0.405		M	
Total		2051891	86386	100.000			

Enantioenriched **4j**

Ethyl (3*R*,4*S*,5*R*)-4-(2-naphthoyl)-3-phenyl-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4k**



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4k** as colorless oil (95%, 41.6 mg); $[\alpha]^{25}{}_{D}$ = 29.4 (c 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 8.7 Hz, 1.8 Hz, 1H), 7.91 (s, 1H), 7.85 (d, *J* = 8.5 Hz, 2H), 7.63–7.53 (m, 2H), 7.53–7.46 (m, 1H), 7.36–7.30 (m, 3H), 7.13 (dd, *J* = 7.6 Hz, 1.7 Hz, 2H), 6.84 (s, 1H), 4.78–4.64 (m, 1H), 4.43–4.23 (m, 3H), 4.05–3.97 (m, 1H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 163.4, 147.3, 140.4, 135.9, 132.3, 132.1, 132.1, 131.8, 129.7, 129.1, 129.0, 128.6, 128.3, 128.0, 127.7, 126.9, 126.4 (q, J = 279.7 Hz), 124.4, 61.1, 55.7, 54.6, 51.2 (q, J = 29.1 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.43; HRMS (ESI) m/z calcd for $C_{26}H_{21}F_3NaO_3$ $[M + Na]^+$ = 461.1335, found = 461.1342; The ee value was 97%, t_R (minor) = 10.466 min, t_R (minor) = 11.643 (Chiralpak IC, λ = 254 nm, 5% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

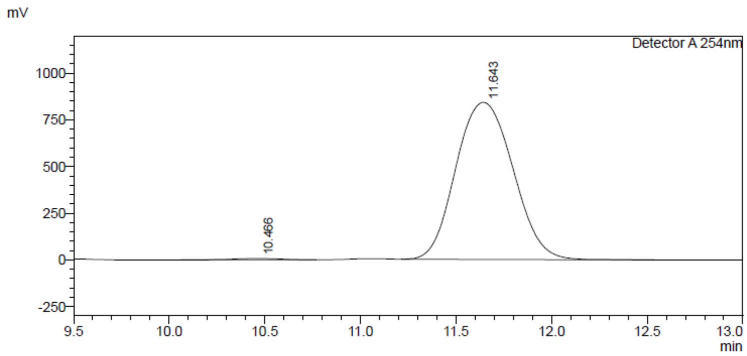


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.445	16507736	905545	49.157		M	
2	11.572	17074131	811842	50.843		M	
Total		33581867	1717387	100.000			

Racemic **4k**



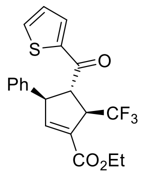
<Peak Table>

Detector A 254nm

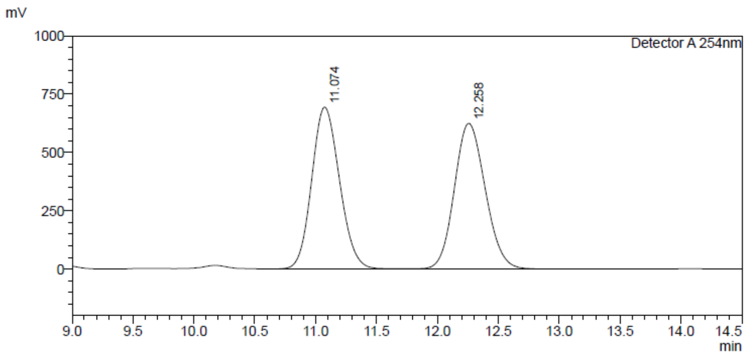
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.466	140455	7768	0.796			
2	11.643	17497104	841421	99.204			
Total		17637559	849188	100.000			

Enantioenriched **4k**

Ethyl (3*R*,4*S*,5*R*)-3-phenyl-4-(thiophene-2-carbonyl)-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4l**



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4l** as colorless oil (93%, 36.6 mg); $[\alpha]^{25}{}_{D}$ = -80 (c 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 4.9 Hz, 1.0 Hz, 1H), 7.36–7.30 (m, 3H), 7.17 (dd, *J* = 3.9 Hz, 1.0 Hz, 1H), 7.16–7.11 (m, 2H), 6.99 (dd, *J* = 4.9 Hz, 3.9 Hz, 1H), 6.84 (s, 1H), 4.56–4.44 (m, 1H), 4.37–4.20 (m, 2H), 4.12–4.08 (m, 1H), 4.03 (t, *J* = 5.6 Hz, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.0, 163.2, 147.6, 142.8, 140.3, 135.7, 133.6, 131.9, 129.0, 128.3, 128.0, 127.9, 126.2 (q, *J* = 279.8 Hz), 122.0, 61.1, 55.7, 55.6, 51.7 (q, *J* = 29.2 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.60; HRMS (ESI) m/z calcd for $C_{20}H_{17}F_3NaO_3S$ $[M + Na]^+$ = 417.0743, found = 417.0746; The ee value was 98%, t_R (minor) = 10.884 min, t_R (major) = 12.141 (Chiralpak IC, λ = 254 nm, 5% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

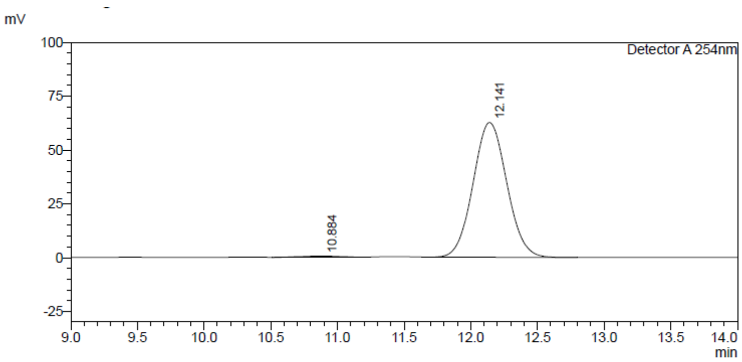


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.074	11037163	693561	50.002			
2	12.258	11036175	624449	49.998		V	
Total		22073338	1318010	100.000			

Racemic **4l**



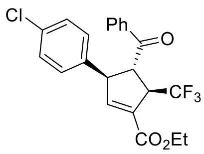
<Peak Table>

Detector A 254nm

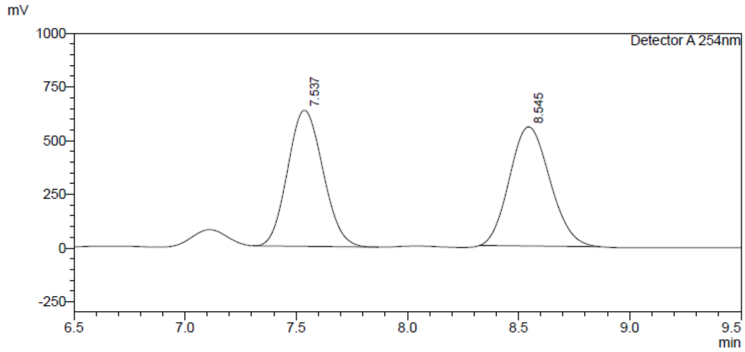
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.884	9657	477	0.869			
2	12.141	1101889	62668	99.131			
Total		1111546	63145	100.000			

Enantioenriched **4l**

Ethyl (3*R*,4*S*,5*R*)-4-benzoyl-3-(4-chlorophenyl)-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4m**



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4m** as colorless oil (78%, 33.0 mg); $[\alpha]^{25}{}_{D}$ = -91.2 (c 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 8.3 Hz, 1.2 Hz, 2H), 7.62–7.55 (m, 1H), 7.43–7.37 (m, 2H), 7.32–7.27 (m, 2H), 7.04–6.98 (m, 2H), 6.78 (s, 1H), 4.58–4.48 (m, 1H), 4.38–4.21 (m, 2H), 4.18 (t, *J* = 5.1 Hz, 1H), 4.02–3.96 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 163.1, 146.8, 138.7, 135.1, 134.0, 133.8, 132.4, 129.4, 129.2, 129.1, 128.8, 126.2 (q, *J* = 279.7 Hz), 61.2, 54.7, 53.9, 51.3 (q, *J* = 29.4 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.55; HRMS (ESI) m/z calcd for $C_{22}H_{18}ClF_3NaO_3$ $[M + Na]^+$ = 445.0789, found = 445.0791; The ee value was 99%, t_R (minor) = 7.497 min, t_R (major) = 8.511 min (Chiralpak IC, λ = 254 nm, 5% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

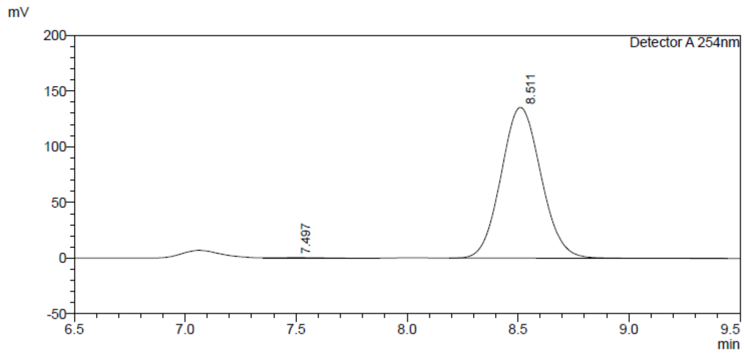


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.537	7029566	634128	49.954			
2	8.545	7042476	554725	50.046		M	
Total		14072042	1188854	100.000			

Racemic **4m**



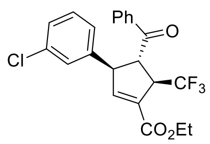
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.497	7596	617	0.446		M	
2	8.511	1696175	135247	99.554			
Total		1703771	135864	100.000			

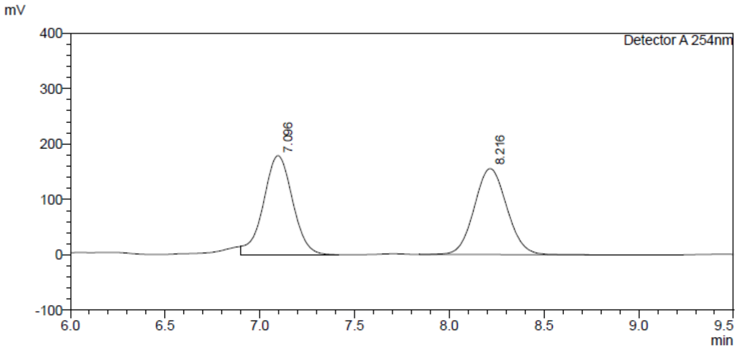
Enantioenriched **4m**

Ethyl (3*R*,4*S*,5*R*)-4-benzoyl-3-(3-chlorophenyl)-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4n**



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4n** as colorless oil (73%, 30.9 mg); $[\alpha]^{25}_{D}$ = -61.7 (c 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8.3 Hz, 1.1 Hz, 2H), 7.62–7.56 (m, 1H), 7.40 (dd, *J* = 8.1 Hz, 7.6 Hz, 2H), 7.29–7.22 (m, 2H), 7.04 (t, *J* = 1.7 Hz, 1H), 6.96 (dt, *J* = 7.2 Hz, 1.4 Hz, 1H), 6.80 (s, 1H), 4.60–4.48 (m, 1H), 4.37–4.18 (m, 3H), 4.02–3.96 (m, 1H), 1.34 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.8, 163.1, 146.5, 142.2, 135.1, 134.9, 134.1, 132.6, 130.2, 129.1, 128.8, 128.2, 128.1, 126.2 (q, *J* = 279.8

Hz), 126.2, 61.2, 54.8, 53.8, 51.3 (q, *J* = 29.3 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.53; HRMS (ESI) m/z calcd for $C_{22}H_{18}ClF_3NaO_3$ $[M + Na]^+$ = 445.0789, found = 445.0785; The ee value was 98%, t_R (minor) = 7.104 min, t_R (major) = 8.214 min (Chiralpak IC, λ = 254 nm, 5% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

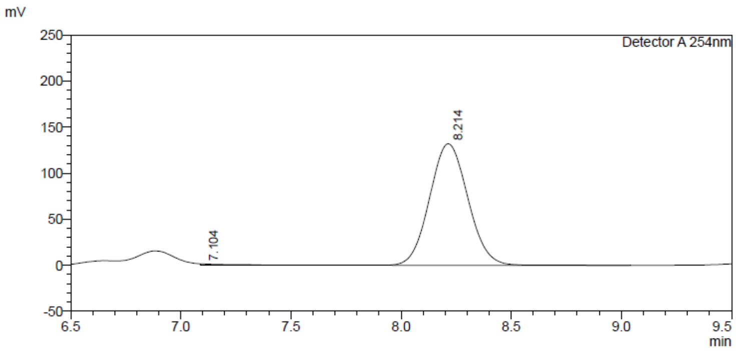


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.096	1909715	178457	50.680		M	
2	8.216	1858455	155247	49.320			
Total		3768170	333705	100.000			

Racemic **4n**



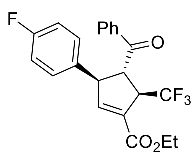
<Peak Table>

Detector A 254nm

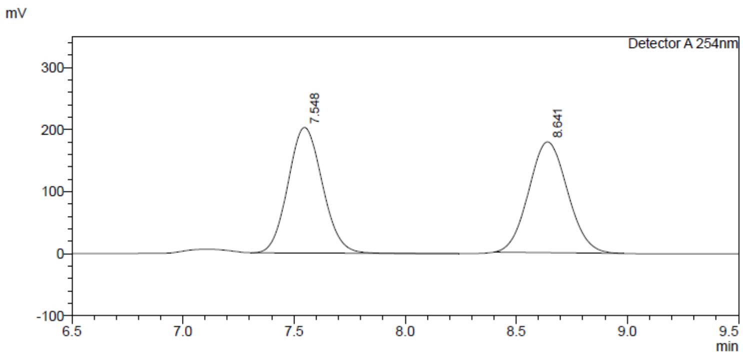
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.104	20283	1674	1.255		M	
2	8.214	1595629	131927	98.745			
Total		1615912	133601	100.000			

Enantioenriched **4n**

<u>Ethyl (3*R*,4*S*,5*R*)-4-benzoyl-3-(4-fluorophenyl)-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4o**</u>



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4o** as colorless oil (81%, 32.9 mg); $[\alpha]^{25}_{D}$ = -51.7 (c 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 8.3 Hz, 1.1 Hz, 2H), 7.60–7.55 (m, 1H), 7.39 (t, *J* = 7.8 Hz, 2H), 7.08–6.98 (m, 4H), 6.78 (s, 1H), 4.60–4.49 (m, 1H), 4.38–4.21 (m, 2H), 4.18 (t, *J* = 5.2 Hz, 1H), 4.02–3.94 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.0, 163.2, 162.3 (d, *J* = 247.1 Hz), 147.0, 136.0 (d, *J* = 3.3 Hz), 135.2, 134.0, 132.2, 129.7 (d, *J* = 8.2 Hz), 129.1, 128.7, 126.3 (q, *J* = 279.9 Hz), 115.9 (d, *J* = 21.5 Hz), 61.2, 54.7, 54.1, 51.3 (q, *J* = 29.2 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.56, -114.10; HRMS (ESI) m/z calcd for $C_{22}H_{18}F_4NaO_3$ $[M + Na]^+$ = 429.1084, found = 429.1087; The ee value was 99%, t_R (minor) = 7.594 min, t_R (major) = 8.640 min (Chiralpak IC, λ = 254 nm, 5% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

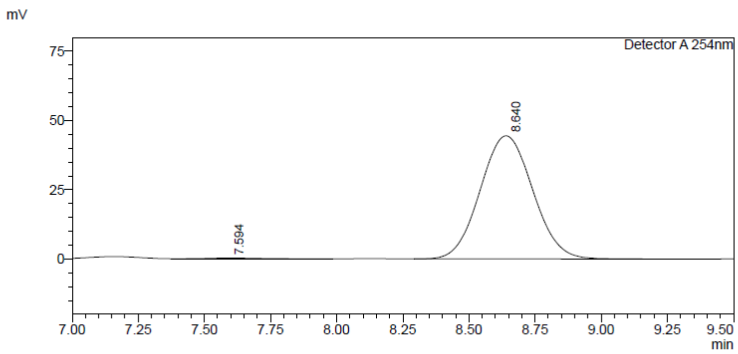


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.548	2172585	202221	49.957		S	
2	8.641	2176354	178434	50.043		M	
Total		4348938	380655	100.000			

Racemic **4o**



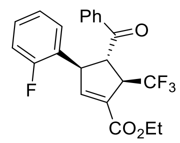
<Peak Table>

Detector A 254nm

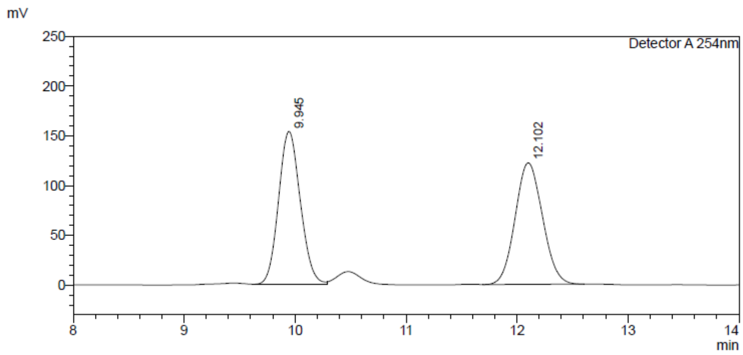
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.594	3535	246	0.570		M	
2	8.640	616308	44502	99.430			
Total		619843	44747	100.000			

Enantioenriched **4o**

<u>Ethyl (3*R*,4*S*,5*R*)-4-benzoyl-3-(2-fluorophenyl)-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4p**</u>



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4p** as colorless oil (70%, 28.4 mg); $[\alpha]^{25}{}_{D}$ = -57.8 (c 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75–7.67 (m, 2H), 7.61–7.56 (m, 1H), 7.43–7.36 (m, 2H), 7.28 (td, *J* = 8.0 Hz, 6.0 Hz, 1H), 7.00 (tdd, *J* = 8.4 Hz, 2.6 Hz, 0.8 Hz, 1H), 6.86 (d, *J* = 7.7 Hz, 1H), 6.80 (ddd, *J* = 5.2 Hz, 4.4 Hz, 2.3 Hz, 2H), 4.60–4.48 (m, 1H), 4.38–4.20 (m, 3H), 4.03–4.00 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 163.1, 163.0 (d, *J* = 247.5 Hz), 146.6, 142.7 (d, *J* = 6.9 Hz), 135.1, 134.0, 132.5, 130.5 (d, *J* = 8.3 Hz), 129.1, 128.8, 126.2 (q, *J* = 279.7 Hz), 123.7 (d, *J* = 2.5 Hz), 115.0 (d, *J* = 22.0 Hz), 114.9 (d, *J* = 21.1 Hz), 61.2, 54.9, 53.8, 51.4 (q, *J* = 29.3 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.53, -111.79; HRMS (ESI) m/z calcd for $C_{22}H_{18}F_4NaO_3$ $[M + Na]^+$ = 429.1084, found = 429.1083; The ee value was 99%, t_R (minor) = 10.006 min, t_R (major) = 12.153 min (Chiralpak IC, λ = 254 nm, 2% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

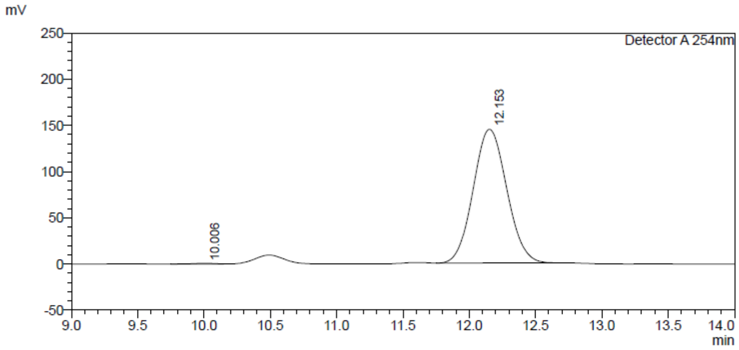


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.945	2090819	153543	49.987		M	
2	12.102	2091894	122031	50.013			
Total		4182713	275573	100.000			

Racemic **4p**

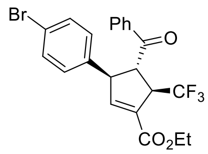


<Peak Table>
Detector A 254nm

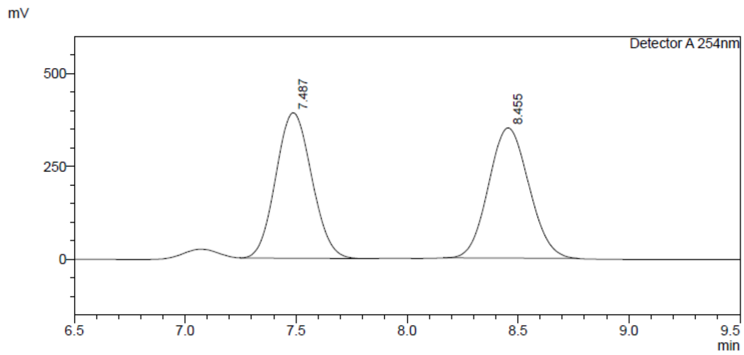
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.006	7827	661	0.306			
2	12.153	2546893	144657	99.694			
Total		2554720	145319	100.000			

Enantioenriched **4p**

Ethyl (3*R*,4*S*,5*R*)-4-benzoyl-3-(4-bromophenyl)-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4q**



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4q** as colorless oil (71%, 33.2 mg); $[\alpha]^{25}{}_D$ = -99.1 (c 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8.3 Hz, 1.2 Hz, 2H), 7.62–7.55 (m, 1H), 7.46–7.37 (m, 4H), 6.98–6.92 (m, 2H), 6.78 (s, 1H), 4.57–4.49 (m, 1H), 4.38–4.20 (m, 2H), 4.17 (t, *J* = 5.1 Hz, 1H), 4.01–3.95 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 163.1, 146.7, 139.2, 135.1, 132.5, 132.1, 129.7, 129.1, 128.8, 126.2 (q, *J* = 279.8 Hz), 121.9, 61.2, 54.7, 53.8, 51.3 (q, *J* = 29.1 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.55; HRMS (ESI) m/z calcd for $C_{22}H_{18}BrF_3NaO_3$ $[M + Na]^+$ = 489.0284, found = 489.0293; The ee value was 98%, t_R (minor) = 7.304 min, t_R (major) = 8.510 min (Chiralpak IC, λ = 254 nm, 5% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

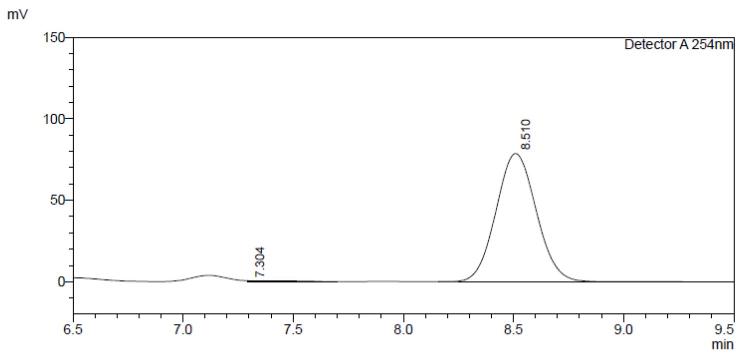


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.487	4406739	390724	49.802			
2	8.455	4441848	350047	50.198		M	
Total		8848587	740771	100.000			

Racemic **4q**



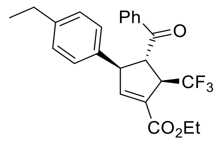
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.304	12607	691	1.240		M	
2	8.510	1004084	78761	98.760			
Total		1016691	79452	100.000			

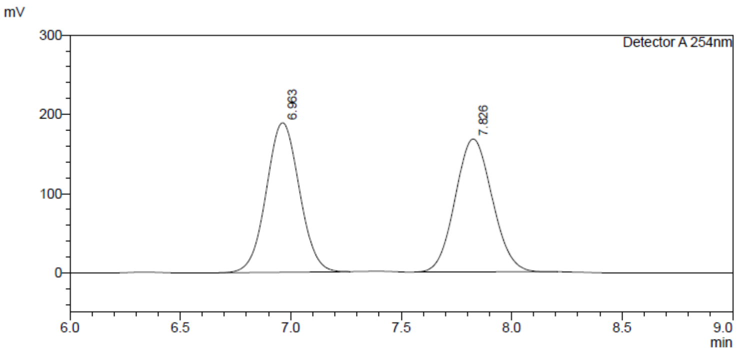
Enantioenriched **4q**

<u>Ethyl (3*R*,4*S*,5*R*)-4-benzoyl-3-(4-ethylphenyl)-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4r**</u>



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4r** as a white solid (89%, 37.0 mg); $[\alpha]^{25}_{D}$ = -74.2 (c 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8.3 Hz, 1.1 Hz, 2H), 7.60–7.53 (m, 1H), 7.36 (dd, *J* = 10.8 Hz, 4.9 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 8.1 Hz, 2H), 6.81 (s, 1H), 4.62–4.51 (m, 1H), 4.37–4.20 (m, 3H), 3.99–3.93 (m, 1H), 2.65 (q, *J* = 7.6 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 198.3, 163.4, 147.7, 144.0, 137.4, 135.3, 133.8, 131.7, 129.2, 128.6, 128.4, 128.0, 126.3 (q, *J* = 279.8 Hz), 61.1, 55.2, 54.2, 51.3 (q, *J* = 28.9 Hz), 28.5, 15.6, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.46; HRMS (ESI) m/z calcd for $C_{24}H_{23}F_3NaO_3$ $[M + Na]^+$ = 439.1492, found = 439.1502; The ee value was 99%, t_R (minor) = 7.153 min, t_R (major) = 8.081 min (Chiralpak IC, λ = 254 nm, 5% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

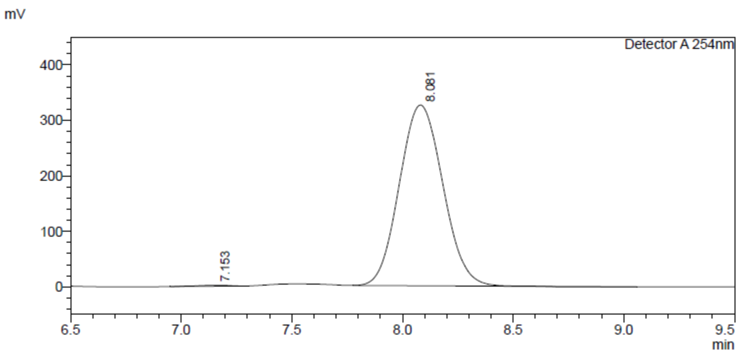


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.963	1967492	188649	50.166			
2	7.826	1954505	167863	49.834		M	
Total		3921997	356512	100.000			

Racemic **4r**



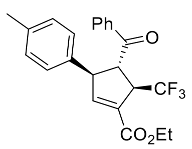
<Peak Table>

Detector A 254nm

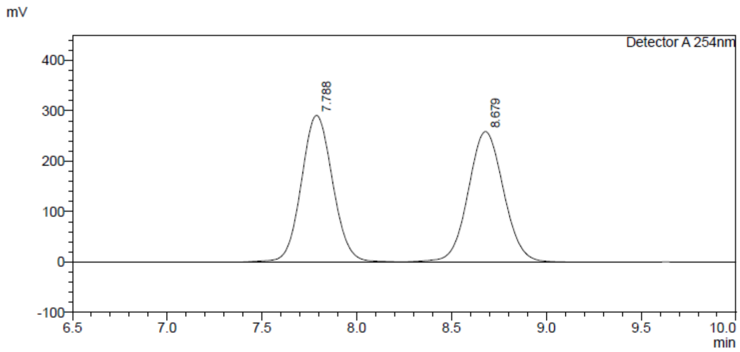
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.153	16156	1631	0.361		M	
2	8.081	4453186	325680	99.639		S	
Total		4469343	327311	100.000			

Enantioenriched **4r**

<u>Ethyl (3*R*,4*S*,5*R*)-4-benzoyl-3-(p-tolyl)-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4s**</u>



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4s** as a white solid (88%, 35.4 mg); $[\alpha]^{25}{}_{D}$ = -66.6 (c 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8.4 Hz, 1.2 Hz, 2H), 7.59–7.53 (m, 1H), 7.41–7.33 (m, 2H), 7.12 (d, *J* = 7.8 Hz, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.80 (s, 1H), 4.63–4.50 (m, 1H), 4.37–4.19 (m, 3H), 3.99–3.92 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3, 163.3, 147.7, 137.6, 137.2, 135.3, 133.8, 131.7, 129.6, 129.2, 128.6, 128.0, 126.3 (q, *J* = 279.8 Hz), 61.1, 55.2, 54.1, 51.3 (q, *J* = 29.0 Hz), 21.1, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.48; HRMS (ESI) m/z calcd for $C_{23}H_{21}F_3NaO_3$ $[M + Na]^+$ = 425.1335, found = 425.1344; The ee value was 99%, t_R (minor) = 7.807 min, t_R (major) = 8.686 min (Chiralpak IC, λ = 254 nm, 5% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

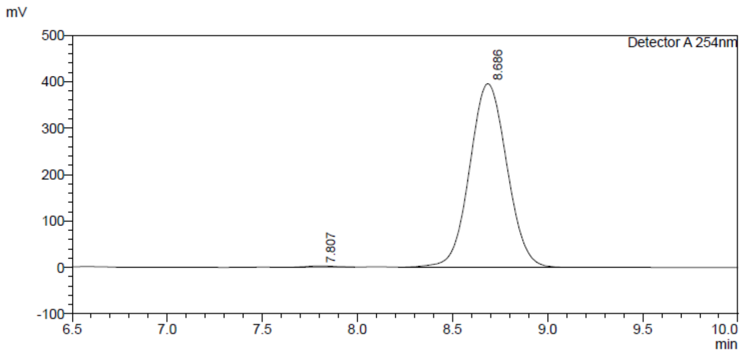


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.788	3349975	290641	49.886			
2	8.679	3365327	258393	50.114		V	
Total		6715302	549034	100.000			

Racemic **4s**



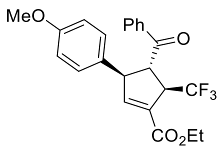
<Peak Table>

Detector A 254nm

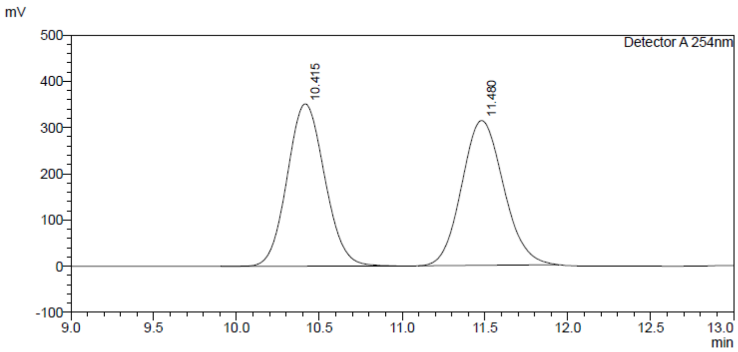
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.807	24950	2455	0.461			
2	8.686	5383923	395209	99.539			
Total		5408873	397663	100.000			

Enantioenriched **4s**

Ethyl (3*R*,4*S*,5*R*)-4-benzoyl-3-(4-methoxyphenyl)-5-(trifluoromethyl)cyclopent-1-ene-1-carboxylate **4t**



Prepared according to Representative Procedure **B-3**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **4t** as colorless oil (82%, 34.3 mg); $[\alpha]^{25}_{D}$ = -113.5 (c 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8.4 Hz, 1.2 Hz, 2H), 7.60–7.53 (m, 1H), 7.40–7.35 (m, 2H), 7.03–6.97 (m, 2H), 6.87–6.82 (m, 2H), 6.78 (s, 1H), 4.63–4.51 (m, 1H), 4.38–4.22 (m, 2H), 4.19 (t, *J* = 5.2 Hz, 1H), 3.95–3.90 (m, 1H), 3.81 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.2, 163.4, 159.2, 147.7, 135.3, 133.8, 132.2, 131.6, 129.2, 128.7, 126.4 (q, *J* = 279.7 Hz), 114.3, 61.1, 55.3, 54.9, 54.3, 51.1 (q, *J* = 29.0 Hz), 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.52; HRMS (ESI) m/z calcd for $C_{23}H_{21}F_3NaO_4$ $[M + Na]^+$ = 441.1284, found = 441.1296; The ee value was 99%, t_R (minor) = 10.413 min, t_R (major) = 11.465 min (Chiralpak IC, λ = 254 nm, 5% *i*-PrOH/hexane, flow rate = 1.0 mL/min).

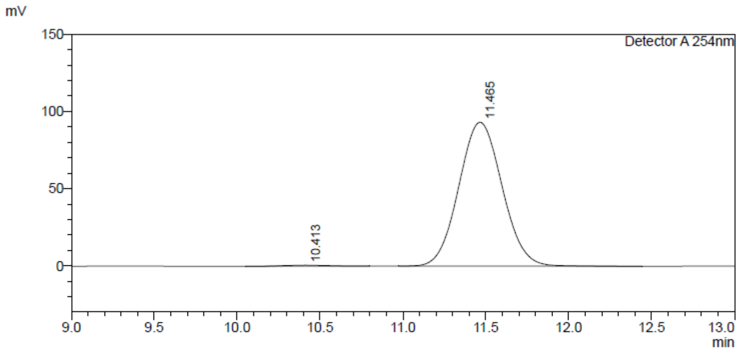


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.415	5535079	351296	50.170			
2	11.480	5497644	313090	49.830		M	
Total		11032722	664385	100.000			

Racemic **4t**



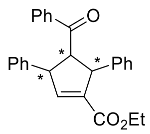
<Peak Table>

Detector A 254nm

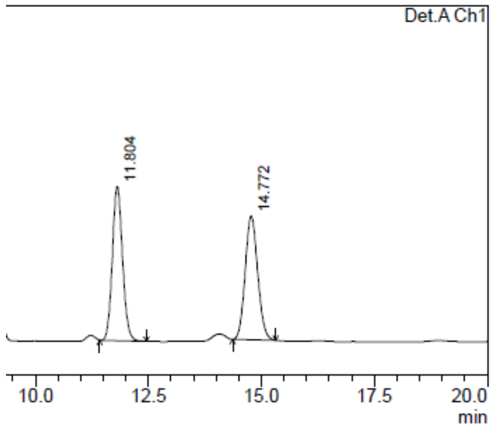
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.413	9477	592	0.557		M	
2	11.465	1693094	93130	99.443			
Total		1702572	93721	100.000			

Enantioenriched **4t**

<u>Ethyl 4-benzoyl-3,5-diphenylcyclopent-1-ene-1-carboxylate **6**</u>



Prepared according to Representative Procedure **B-4**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **6** as colourless oil (88%, 34.8 mg); $[\alpha]_D^{25}$= +5.2 (c 0.5, $CHCl_3$); The ^1H NMR was in agreement with literature reported values.[5] ^1H NMR (400 MHz, $CDCl_3$) δ 7.43-7.42 (m, 3H), 7.31–6.96 (m, 12H), 6.95 (t, *J* = 2.4 Hz, 1H), 4.64 (dt, *J* = 7.2 Hz, 2.4 Hz, 1H), 4.48 (dt, *J* = 7.2 Hz, 2.4 Hz, 1H), 4.12–3.97 (m, 3H), 1.07 (t, *J* = 7.2 Hz, 3H); The ee value was 92%, t_R (major) = 14.1 min, t_R (minor) = 11.4 min (Chiralcel IF, λ = 254 nm, 20% *i*-PrOH/hexanes, flow rate = 1.0 mL/min).

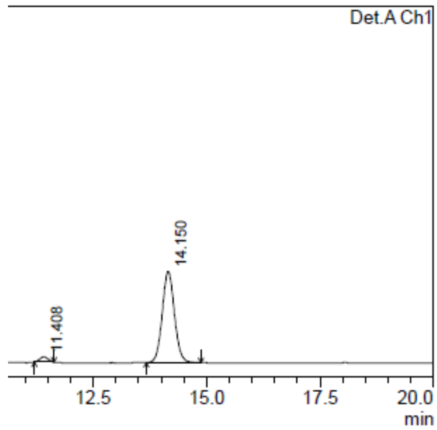


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.804	1440411	91815	50.300	55.501
2	14.772	1423213	73614	49.700	44.499
Total		2863623	165429	100.000	100.000

Racemic **6**



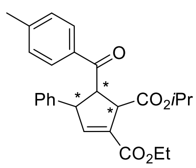
PeakTable

Detector A Ch1 254nm

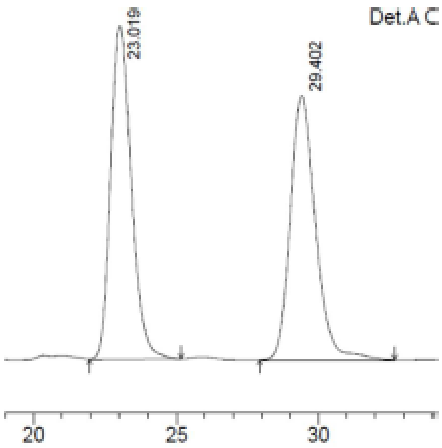
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.408	40316	3056	3.980	5.561
2	14.150	972561	51897	96.020	94.439
Total		1012877	54953	100.000	100.000

Enantioenriched **6**

<u>2-Ethyl 1-isopropyl 5-(4-methylbenzoyl)-4-phenylcyclopent-2-ene-1,2-dicarboxylate **8**</u>



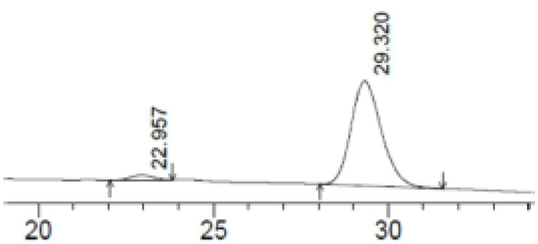
Prepared according to Representative Procedure **B-5**. Flash column chromatography (eluent: 10%-20% EtoAc/Hexane) to afford **8** as colorless oil (88%, 37.0 mg); $[\alpha]_D^{25}$= +9.2 (c 2.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J*= 8.5 Hz, 2H), 7.30-7.21 (m, 6H), 7.17 (d, *J*= 8.0 Hz, 2H), 6.81 (t, *J*= 2.5 Hz, 1H), 4.99 (sep, *J*= 6.5, 6.0 Hz, 1H), 4.39-4.37 (m, 1H), 4.24-4.19 (m, 4H), 2.37 (s, 3H), 1.28 (t, *J*=7.0 Hz, 3H), 1.24 (d, *J*= 6.5 Hz, 3H), 1.06 (d, *J*=6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.3, 172.8, 163.7, 145.6, 144.5, 141.4, 134.3, 133.3, 129.3, 129.1, 128.8, 128.0, 127.4, 68.7, 60.7, 58.1, 54.8, 53.4, 29.7, 21.6, 21.6, 21.5, 14.1; HRMS (ESI) m/z calcd for $C_{26}H_{28}O_5$ $[M+Na]^+$ = 443.1835, found = 443.1829; The ee value was 93%, t_R (major) = 29.3 min, t_R (minor) = 22.9 min (Chiralcel IC, λ = 254 nm, 10% *i*-PrOH/hexanes, flow rate = 1.0 mL/min).



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.019	1647484	33833	49.830	55.781
2	29.402	1658725	26820	50.170	44.219
Total		3306208	60653	100.000	100.000

Racemic **8**



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.957	92374	2140	3.378	4.671
2	29.320	2642121	43673	96.622	95.329
Total		2734495	45812	100.000	100.000

Enantioenriched **8**

E. X-Ray Crystallographic Analysis and Determination of the Absolute Configurations of the Products

X-Ray Crystallographic Analysis of 4s

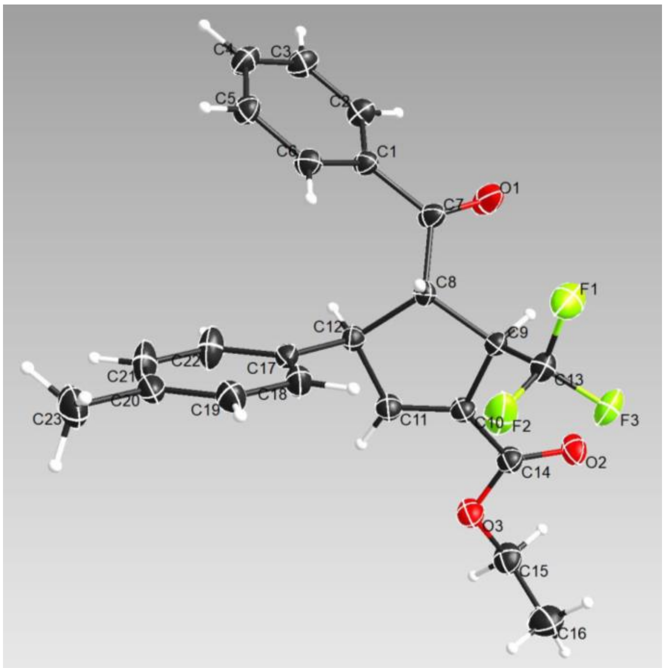


Figure S1. X ray structure of **4s**

Table 1. Crystal data and structure refinement for I677.

Identification code	I677
Empirical formula	C23 H21 F3 O3
Formula weight	402.40
Temperature	100(2) K
Wavelength	1.54178 Å

Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 9.5725(10) Å	α= 90°.
	b = 14.2327(14) Å	β= 90°.
	c = 14.4772(14) Å	γ = 90°.
Volume	1972.4(3) $Å^3$	
Z	4	
Density (calculated)	1.355 Mg/m^3	
Absorption coefficient	0.910 mm^{-1}	
F(000)	840	
Crystal size	0.351 x 0.345 x 0.172 mm^3	
Theta range for data collection	4.356 to 80.049°.	
Index ranges	-12<=h<=10, -18<=k<=18, -18<=l<=17	
Reflections collected	30482	
Independent reflections	4253 [R(int) = 0.0341]	
Completeness to theta = 67.679°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7543 and 0.6697	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4253 / 0 / 264	
Goodness-of-fit on F^2	1.090	
Final R indices [I>2sigma(I)]	R1 = 0.0331, wR2 = 0.0936	
R indices (all data)	R1 = 0.0346, wR2 = 0.0997	
Absolute structure parameter	0.094(19)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.560 and -0.477 e.$Å^{-3}$	

F. References

[1] a) Han, X.; Wang, Y.; Zhong, F.; Lu, Y. *J. Am. Chem. Soc.* **2011**, *133*, 1726; b) Han, X.; Zhong, F.; Wang, Y.; Lu, Y. *Angew. Chem. Int. Ed.* **2012**, *51*, 767; c) Zhong, F.; Han, X.; Wang, Y.; Lu, Y. *Chem. Sci.* **2012**, *3*, 1231; d) Zhong, F.; Han, X.; Wang, Y.; Lu, Y. *Angew. Chem. Int. Ed.* **2011**, *50*, 7837; e) Zhong, F.; Luo, J.; Chen, G.–Y.; Dou, X.; Lu, Y. *J. Am. Chem. Soc.* **2012**, *134*, 10222; f) Zhong, F.; Dou, X.; Han, X.; Yao, W.; Zhu, Q.; Meng, Y.; Lu, Y. *Angew. Chem. Int. Ed.* **2013**, *52*, 943; g) Yao, W.; Dou, X.; Lu, Y. *J. Am. Chem. Soc.* **2015**, *137*, 54.

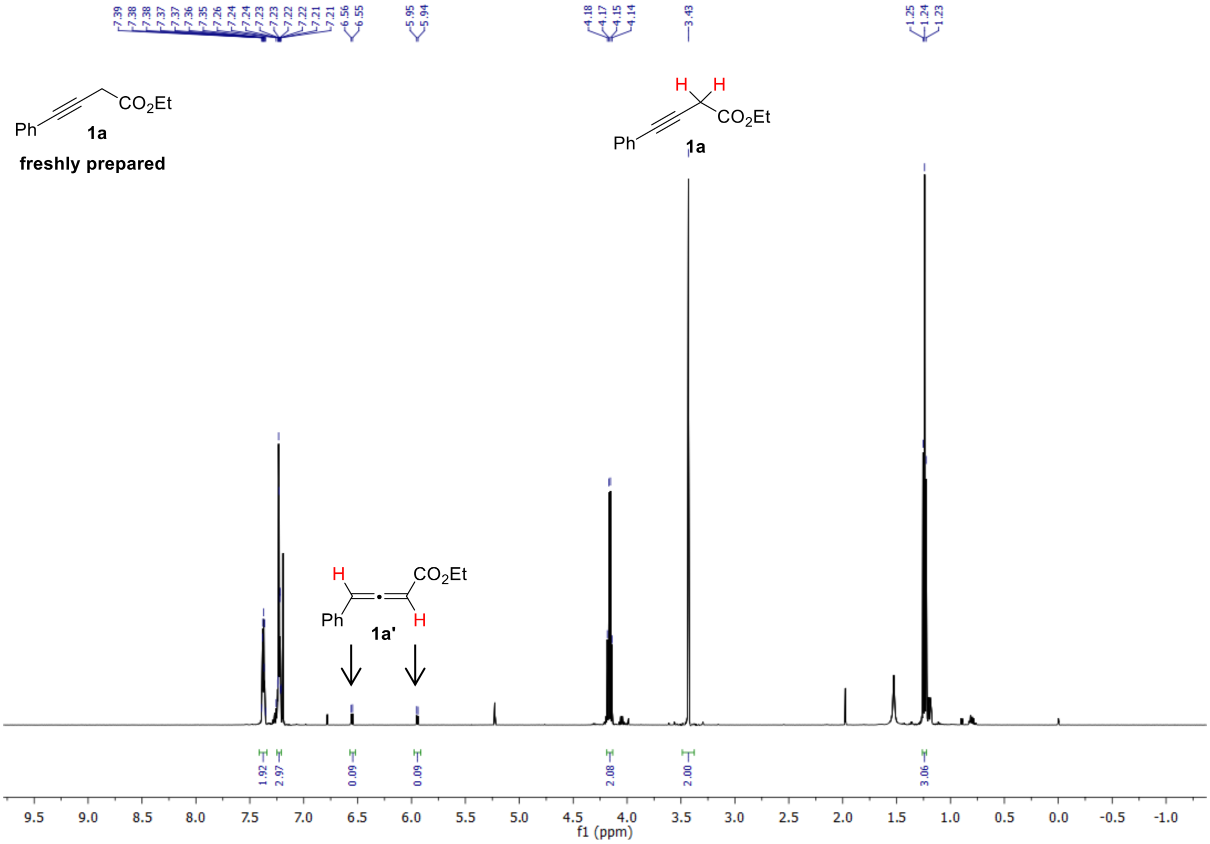
[2] a) Yamazaki, T.; Kawasaki-Takasuka, T.; Furuta, A.; Sakamoto, S. *Tetrahedron*, **2009**, *65*, 5945. b) Zhou, W.; Wang, H.; Tao, M.; Zhu, C.-Z.; Lin, T.-Y.; Zhang, J. *Chem. Sci.* **2017**, *8*, 4660.

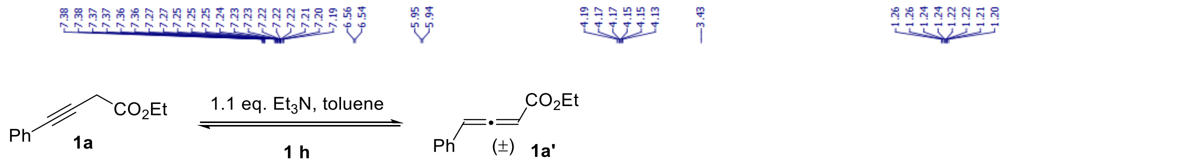
[3] Xu, C.; Bai, X.; Xu, J.; Ren, J.; Xing, Y.; Li, Z.; Wang, J.; Shi, J.; Yu, L.; Wang, Y. *RSC Adv.* **2017**, *7*, 4763.

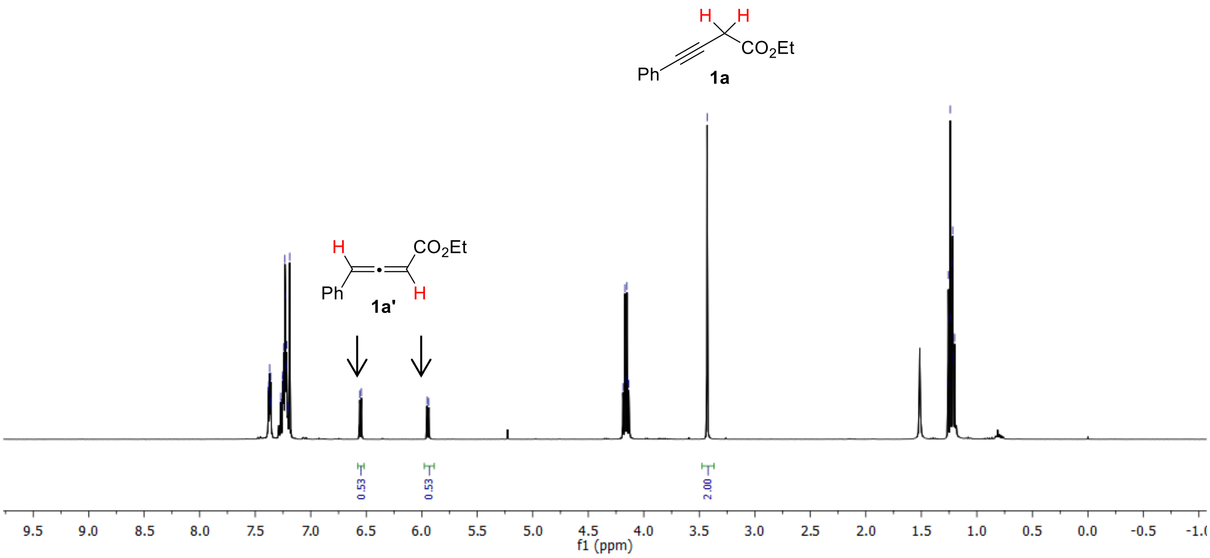
[4] a) Suárez,A.; Fu, G. C. *Angew. Chem. Int. Ed.* **2004**, *43*, 3580. b) Liao, L.; Zhang. H.; Zhao. X. *ACS Catal.* **2018**, *8*, 6745.

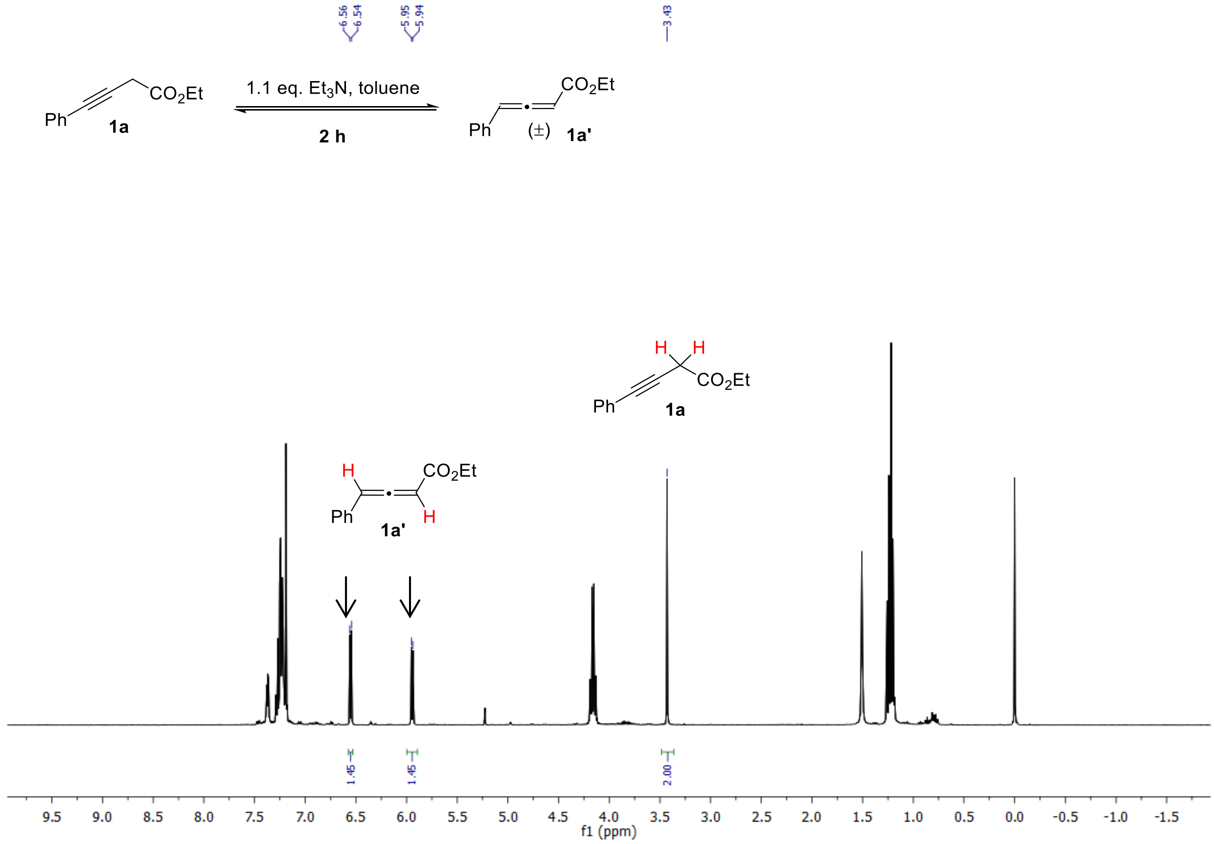
[5] Sampath, M.; Loh, T.-P. *Chem. Sci.*, **2010**, *1*, 739.

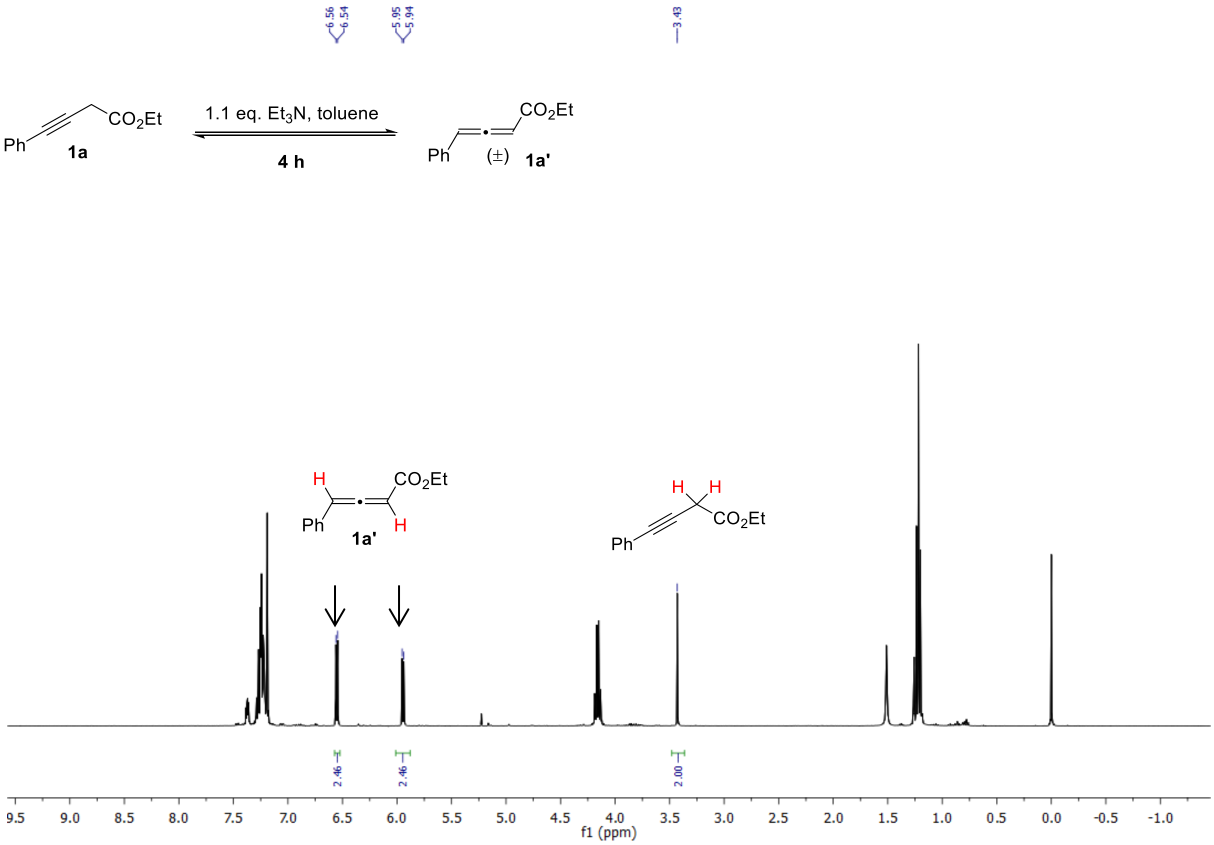
G. NMR Analysis of the Isomerization Process of 3-Butynoate 1a

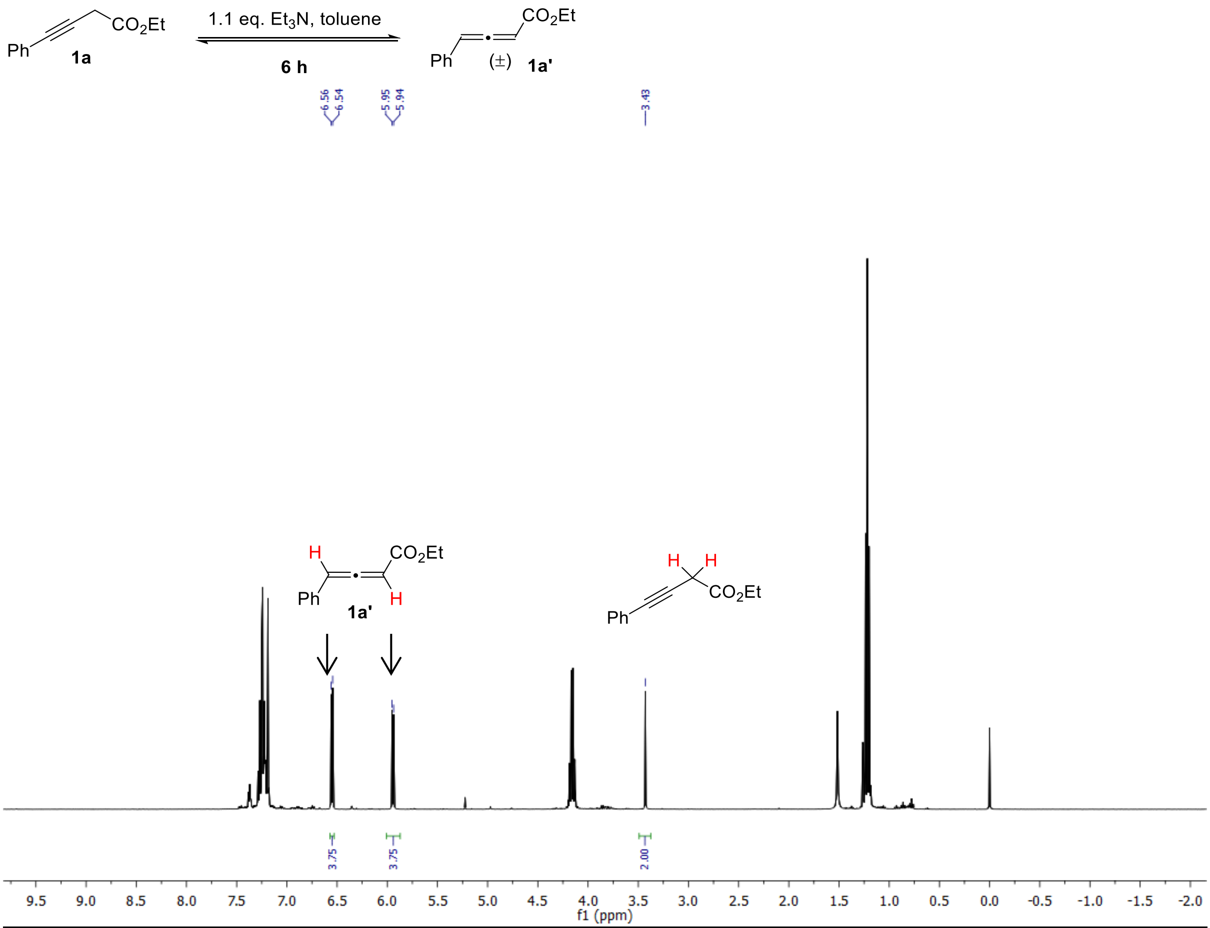




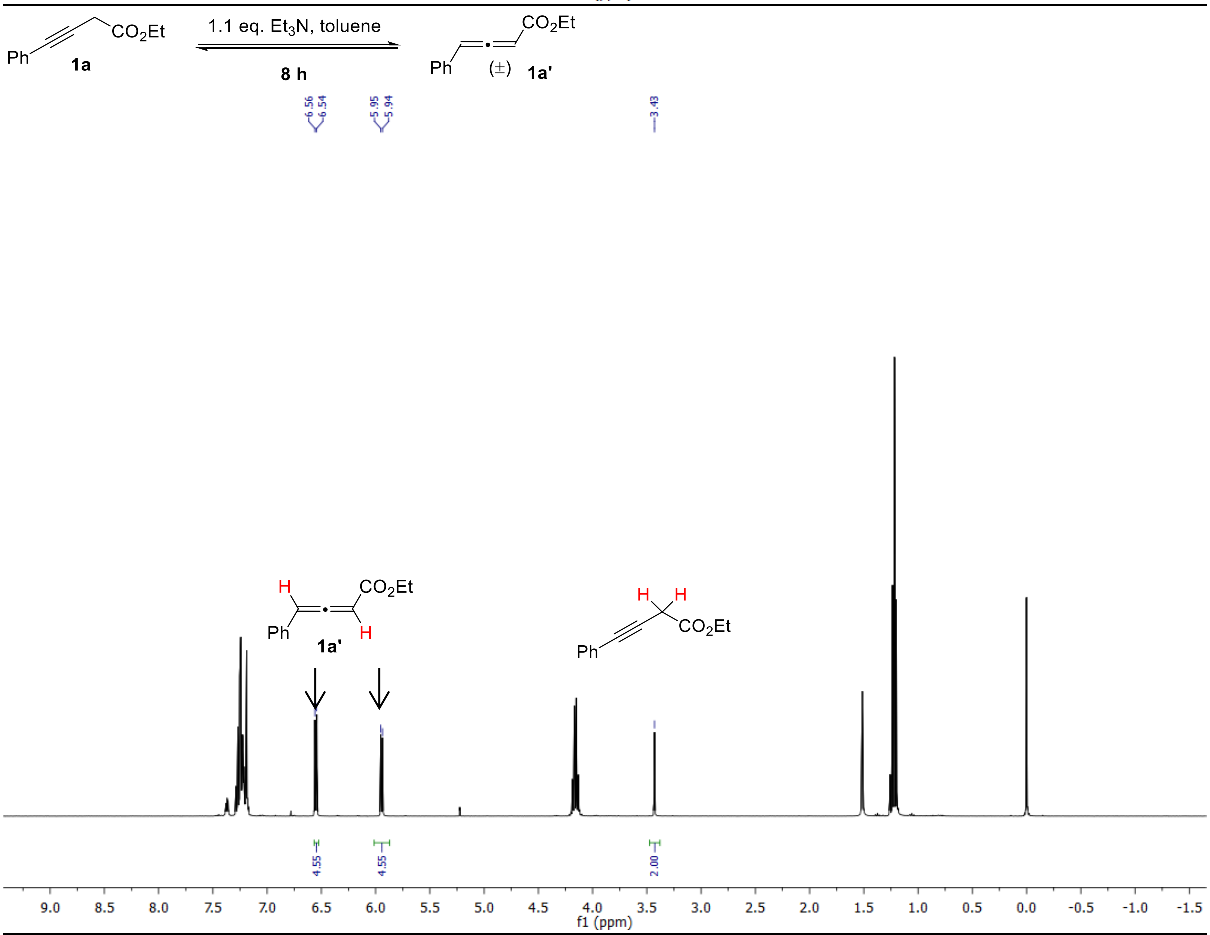



1.1 eq. Et3N, toluene
2 h
1a
1a'
(±)
f1 (ppm)

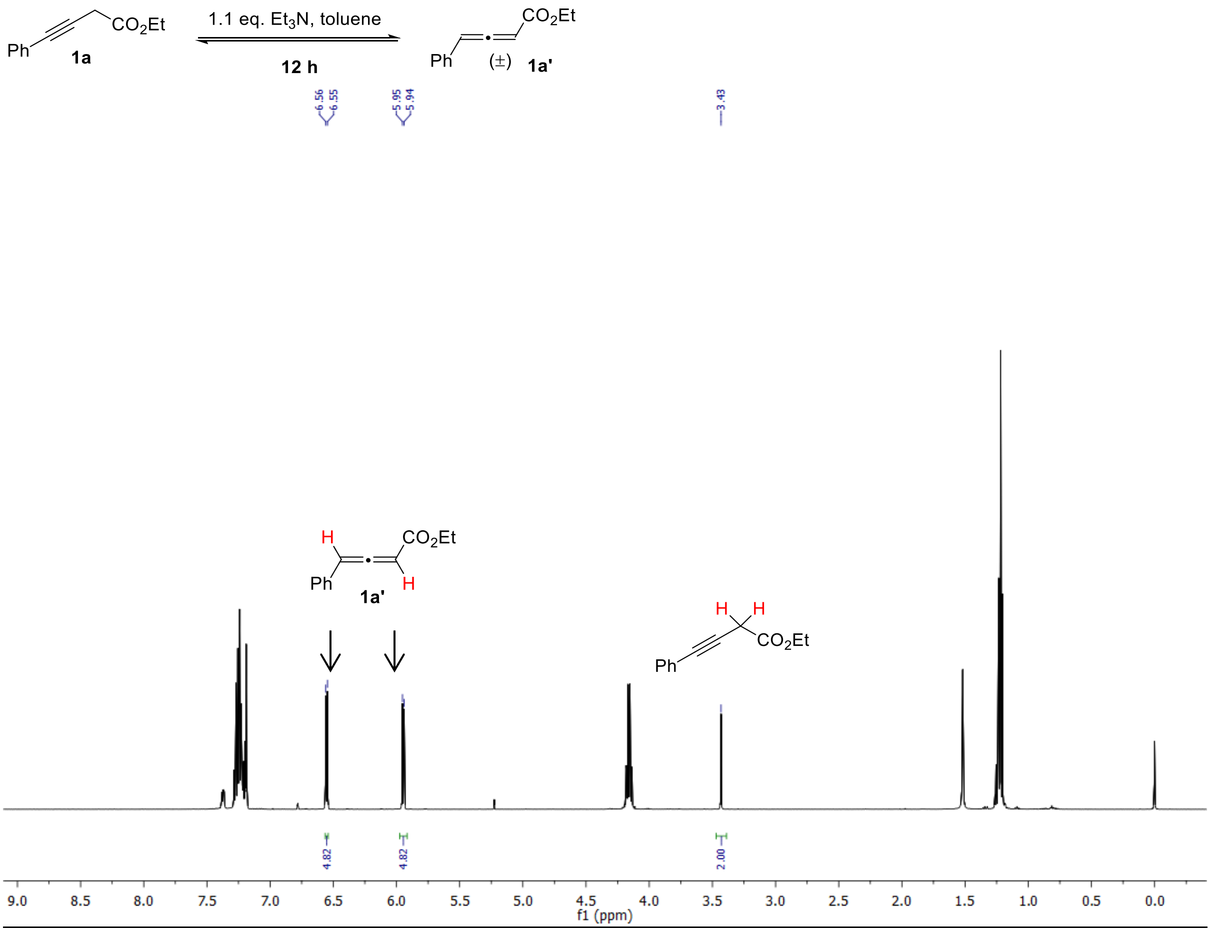

1.1 eq. Et3N, toluene
4 h
1a
1a'
(±)
f1 (ppm)

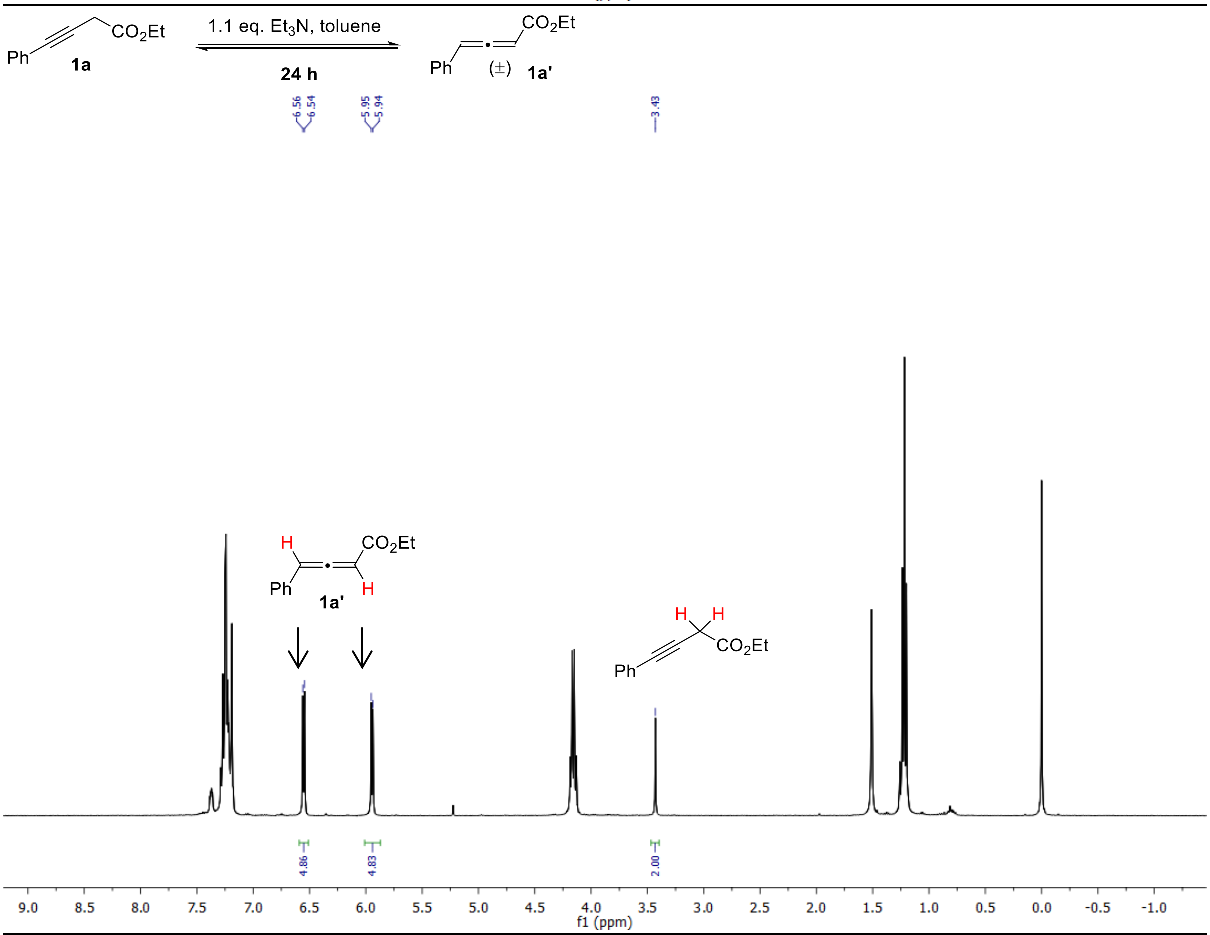


1.1 eq. Et_3N, toluene
6 h
CO_2Et
Ph
1a
(±)
1a'
6.56
6.54
5.95
5.94
3.43
3.75
3.75
2.00
f1 (ppm)

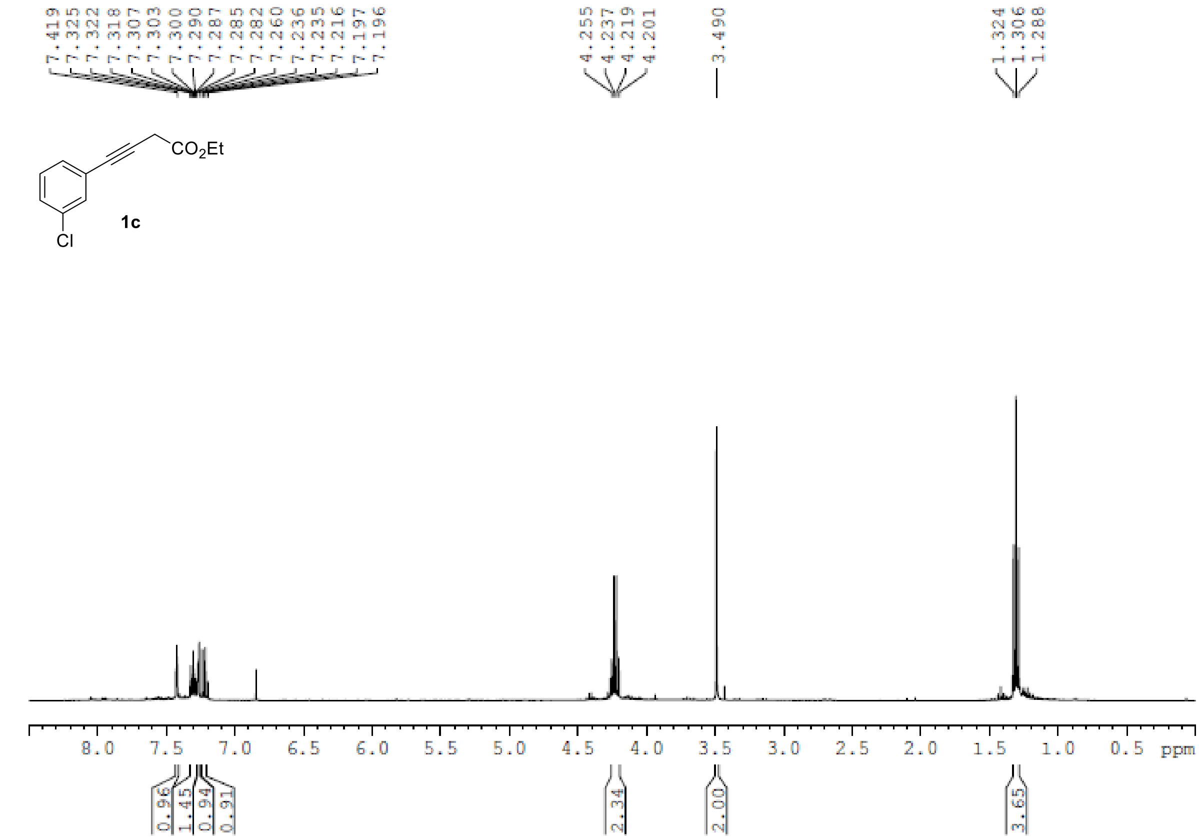


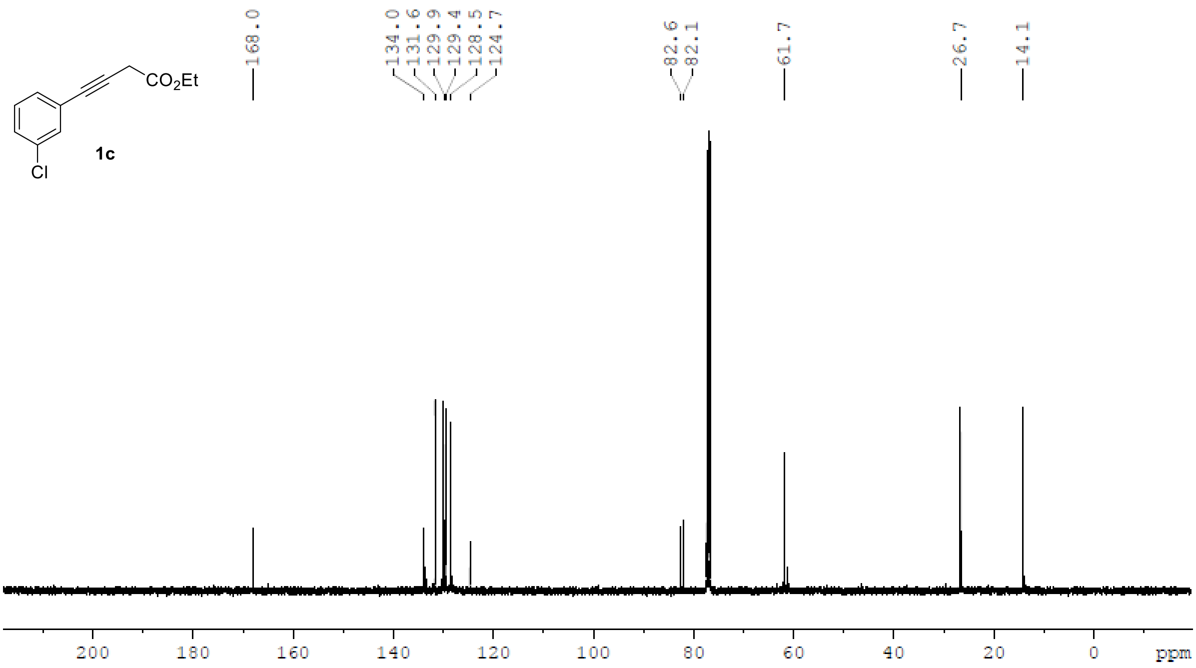
1.1 eq. Et_3N, toluene
8 h
CO_2Et
Ph
1a
(±)
1a'
6.56
6.54
5.95
5.94
3.43
4.55
4.55
2.00
f1 (ppm)

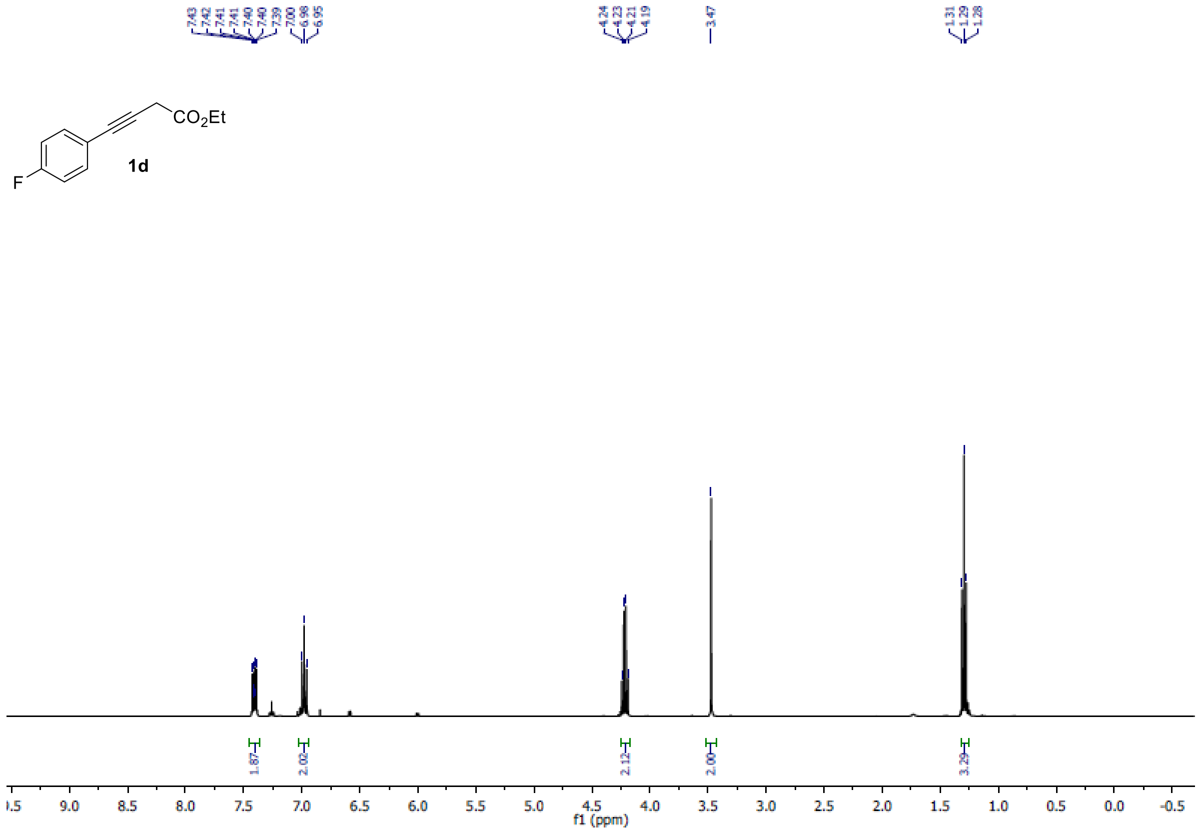

CO2Et
Ph
1a
1.1 eq. Et3N, toluene
12 h
CO2Et
Ph
(±)
1a'
6.56
6.55
5.95
5.94
3.43
H
CO2Et
Ph
1a'
H
H
H
CO2Et
Ph
4.82
4.82
2.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

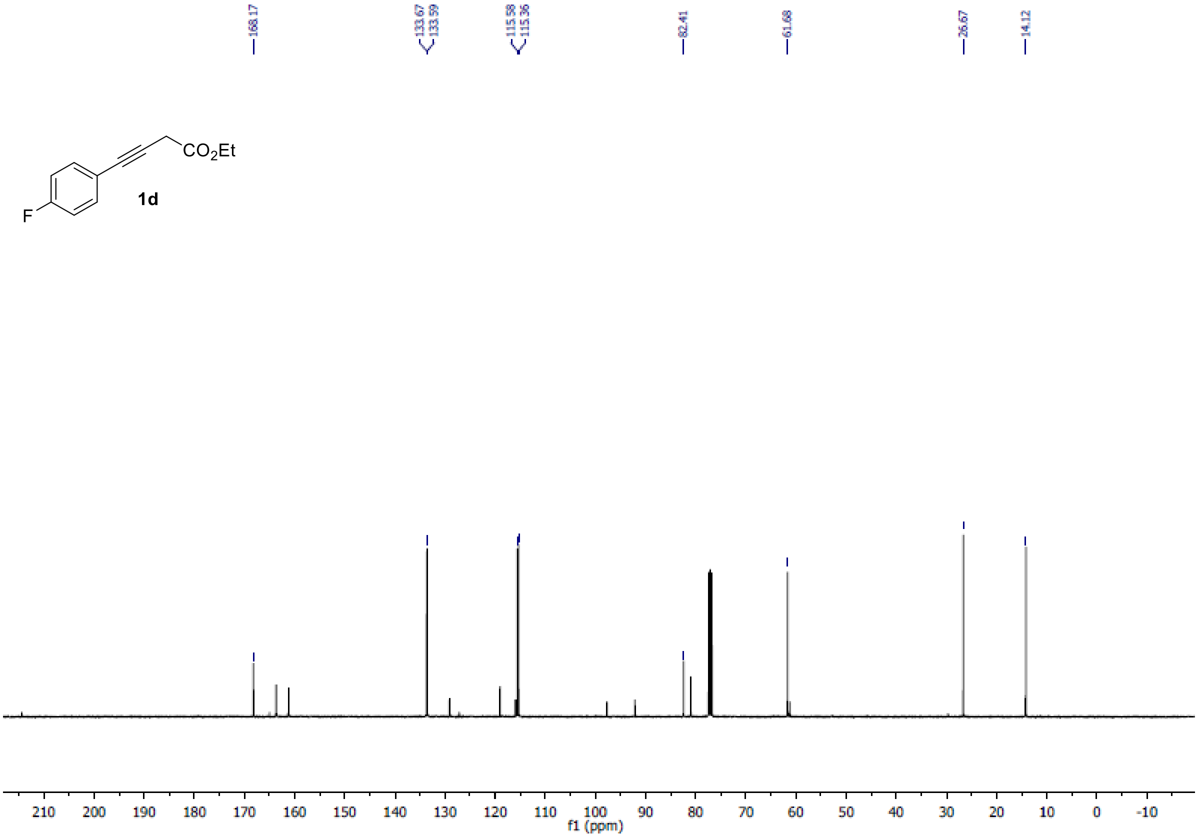

CO2Et
Ph
1a
1.1 eq. Et3N, toluene
24 h
CO2Et
Ph
(±)
1a'
6.56
6.54
5.95
5.94
3.43
H
CO2Et
Ph
1a'
H
H
H
CO2Et
Ph
4.86
4.83
2.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

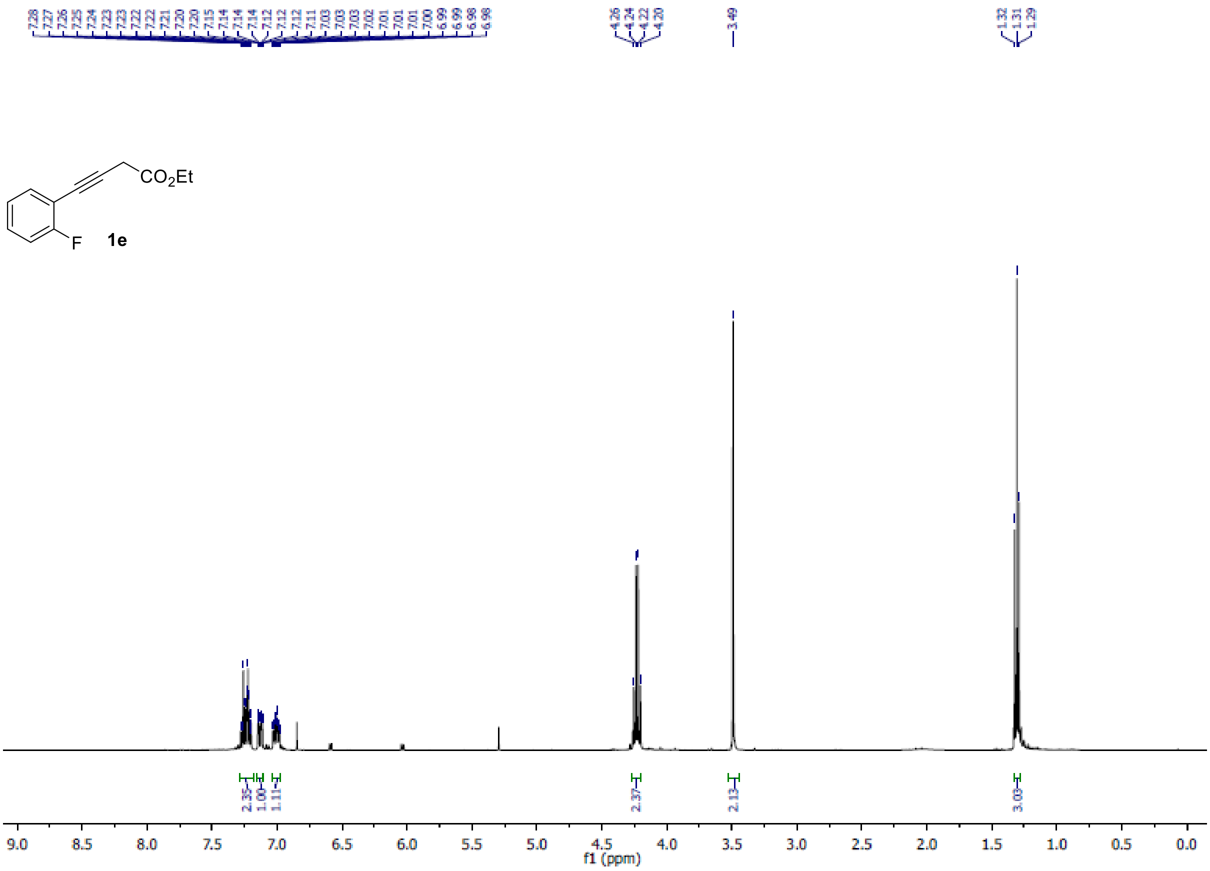
H. NMR Spectra of the Substrates and Products

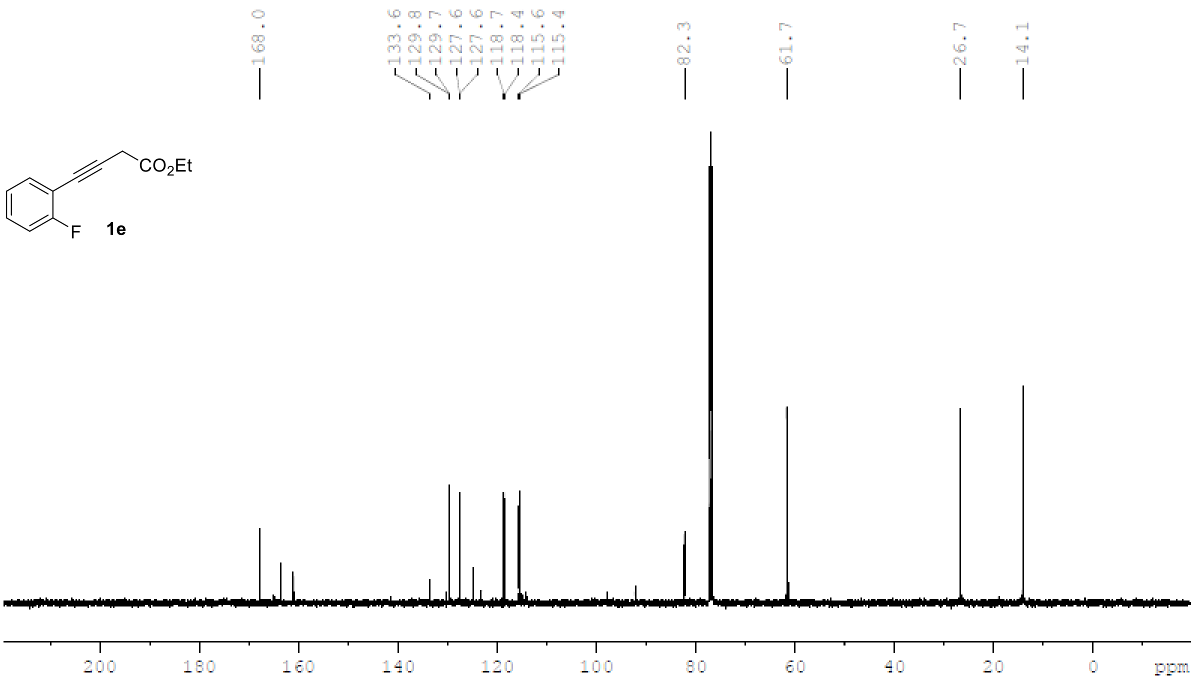


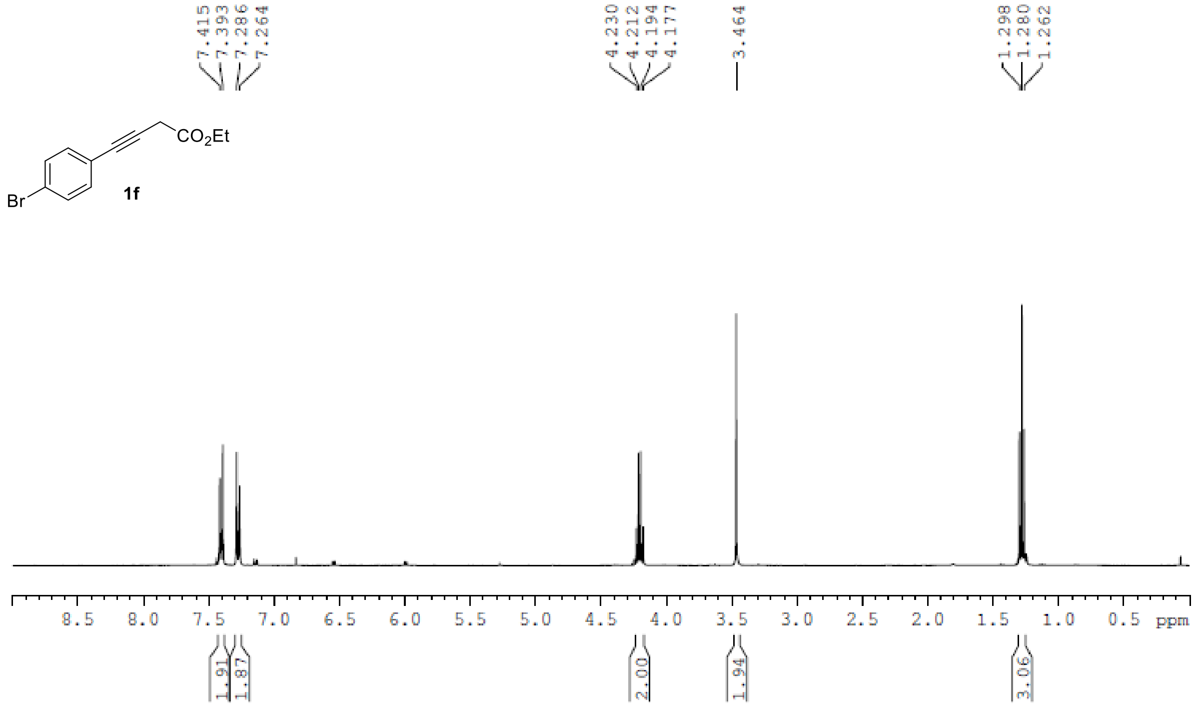


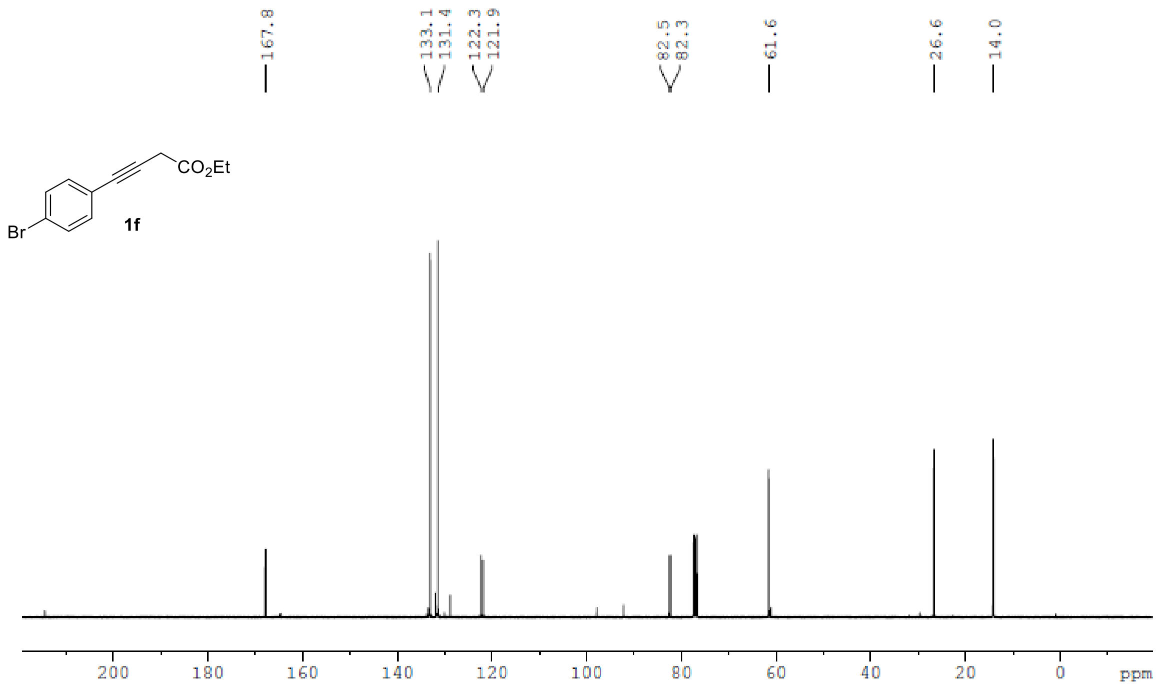

7.43
7.42
7.41
7.41
7.40
7.40
7.39
7.00
6.98
6.95
4.24
4.23
4.21
4.19
3.47
1.31
1.29
1.28
CO2Et
F
1d
1.87
2.02
2.12
2.00
3.29
f1 (ppm)

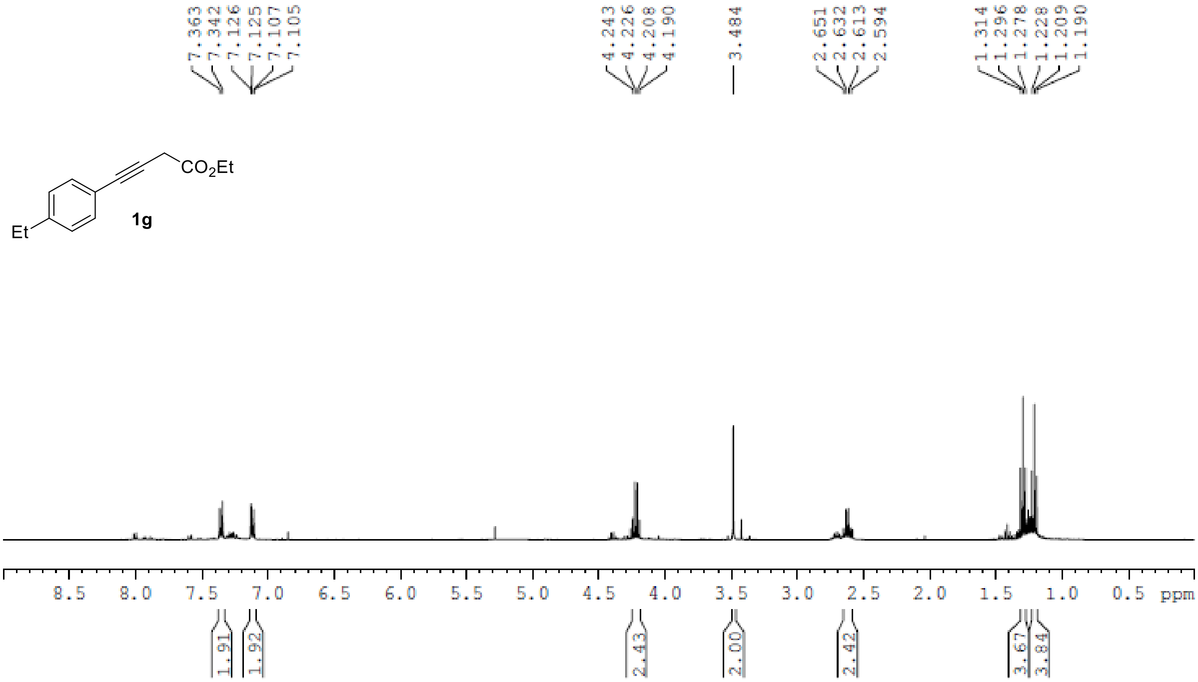

168.17
133.67
133.59
115.58
115.36
82.41
61.68
26.67
14.12
CO2Et
F
1d
f1 (ppm)

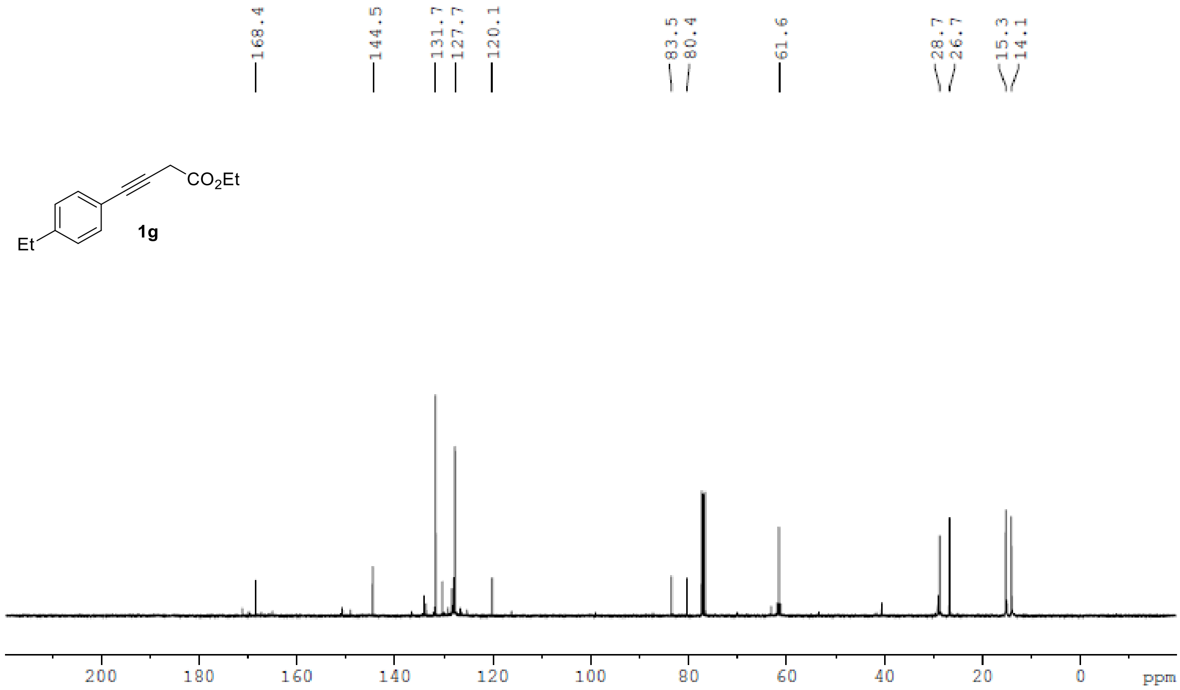

7.28 7.27 7.26 7.25 7.24 7.23 7.23 7.22 7.22 7.21 7.20 7.20 7.15 7.14 7.14 7.14 7.12 7.12 7.12 7.11 7.03 7.03 7.02 7.01 7.01 7.01 7.00 6.99 6.99 6.98 6.98
4.26 4.24 4.22 4.20
3.49
1.32 1.31 1.29
CO_2Et
F
1e
2.35 1.00 1.11
2.37
2.13
3.03
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

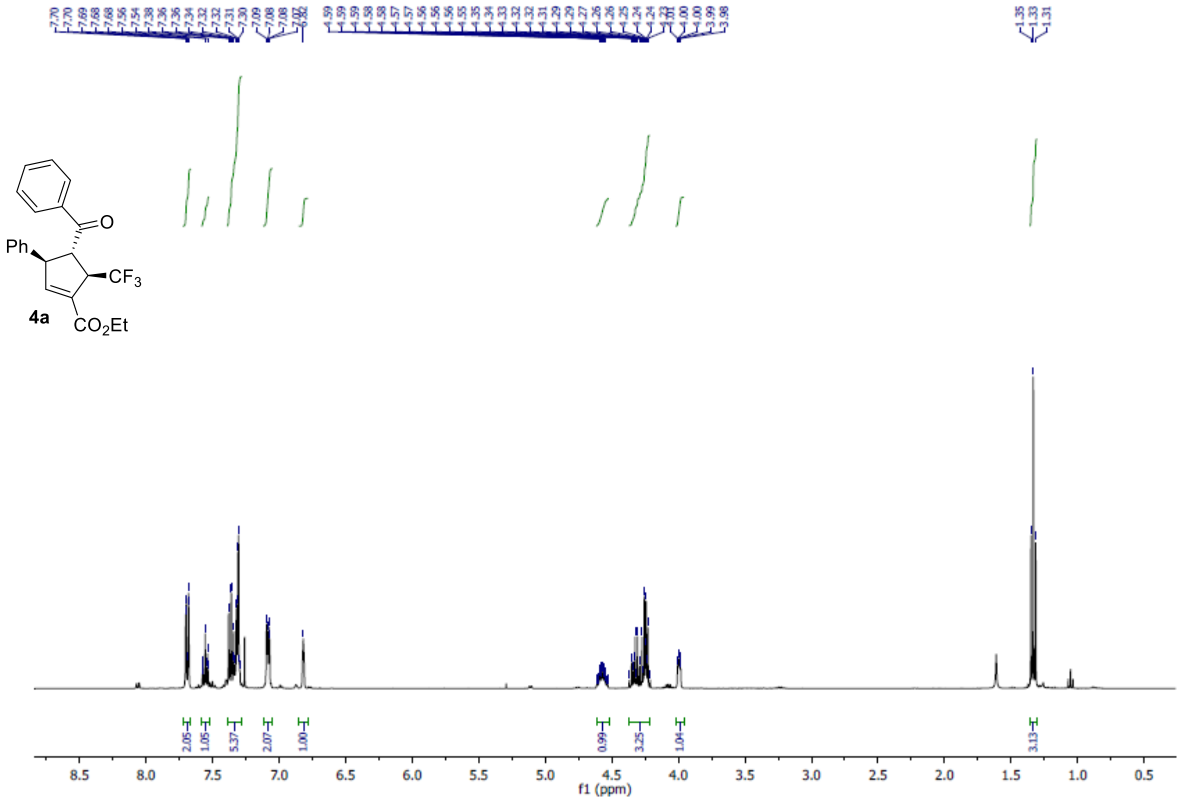

168.0
133.6 129.8 129.7 127.6 127.6 118.7 118.4 115.6 115.4
82.3
61.7
26.7
14.1
CO_2Et
F
1e
200 180 160 140 120 100 80 60 40 20 0 ppm

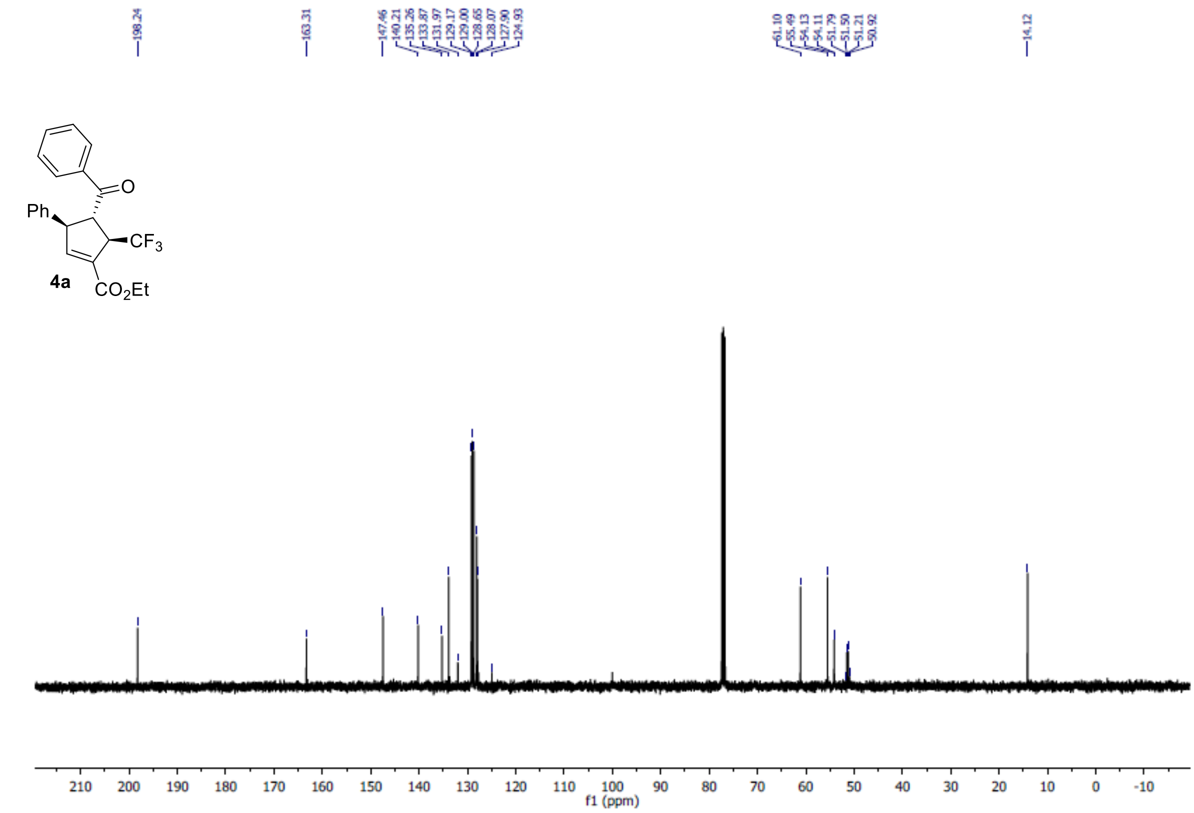

7.415
7.393
7.286
7.264
4.230
4.212
4.194
4.177
3.464
1.298
1.280
1.262
CO2Et
Br
1f
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.91
1.87
2.00
1.94
3.06

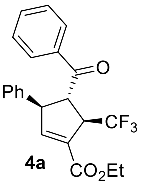

167.8
133.1
131.4
122.3
121.9
82.5
82.3
61.6
26.6
14.0
CO2Et
Br
1f
200
180
160
140
120
100
80
60
40
20
0
ppm


7.363
7.342
7.126
7.125
7.107
7.105
4.243
4.226
4.208
4.190
3.484
2.651
2.632
2.613
2.594
1.314
1.296
1.278
1.228
1.209
1.190
CO2Et
Et
1g
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
ppm
1.91
1.92
2.43
2.00
2.42
3.67
3.84

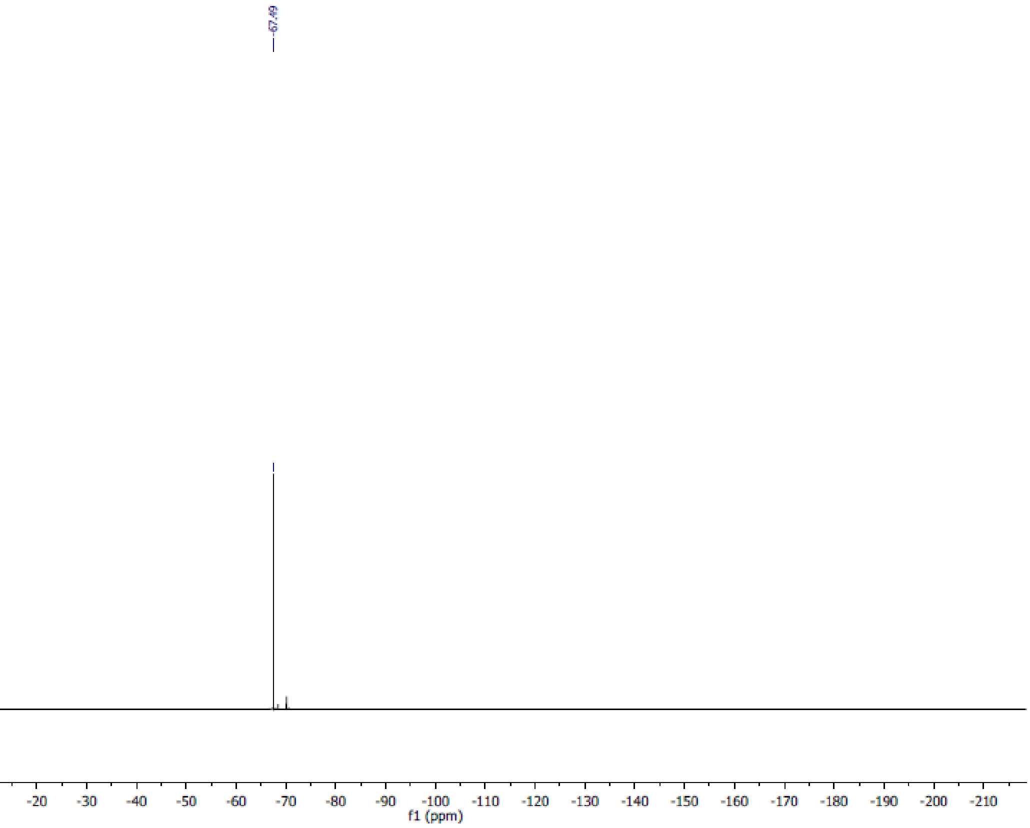

168.4
144.5
131.7
127.7
120.1
83.5
80.4
61.6
28.7
26.7
15.3
14.1
CO2Et
Et
1g
200
180
160
140
120
100
80
60
40
20
0
ppm

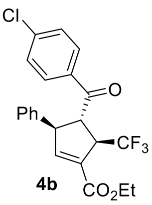

Ph
CF3
4a
CO2Et
O
1.35
1.33
1.31
2.05
1.05
5.37
2.07
1.00
0.99
3.25
1.04
3.13
f1 (ppm)


198.24
163.31
147.46
140.21
135.26
133.87
131.97
129.17
129.00
128.65
128.07
127.90
124.93
61.10
55.49
54.13
54.11
51.79
51.50
51.21
50.92
14.12
Ph
CF3
4a
CO2Et
O
f1 (ppm)

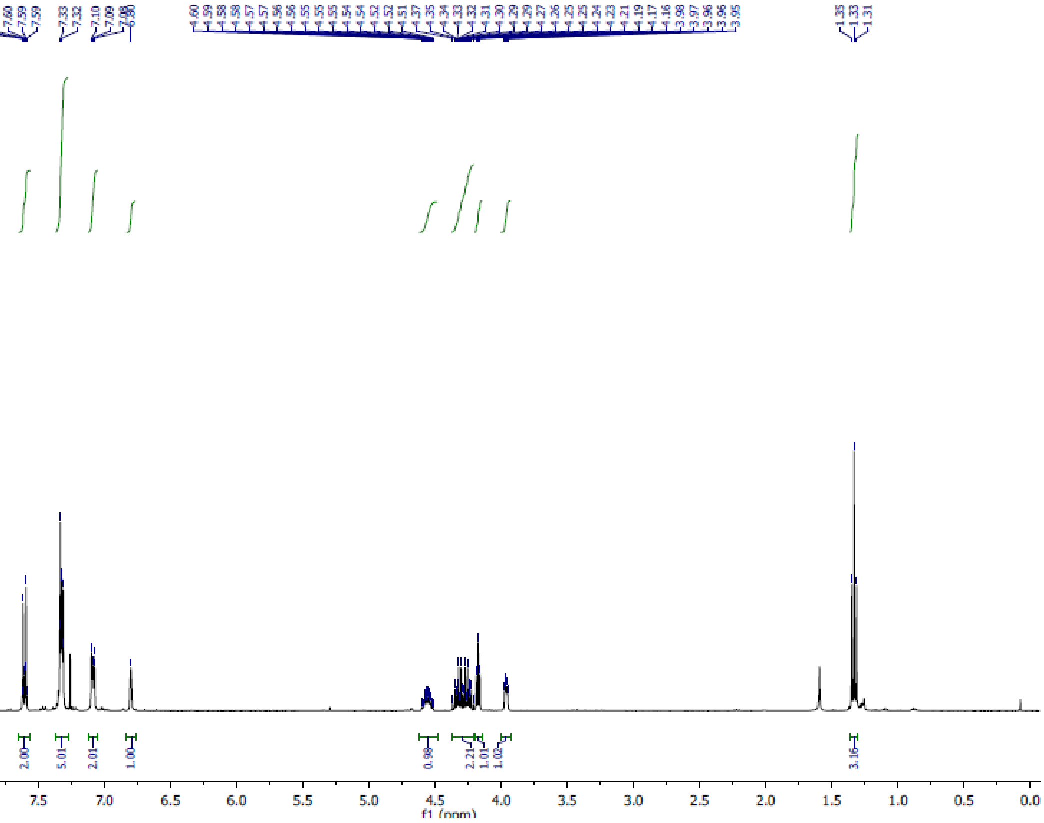


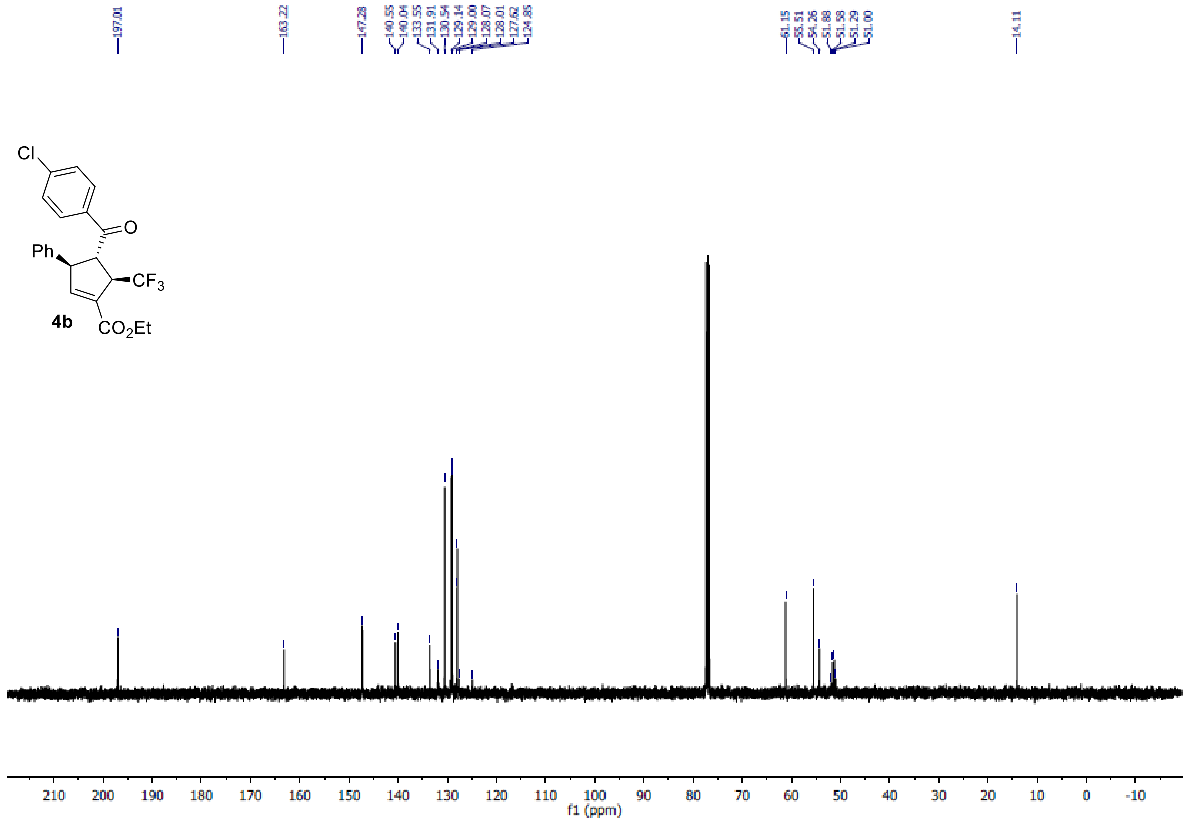
4a

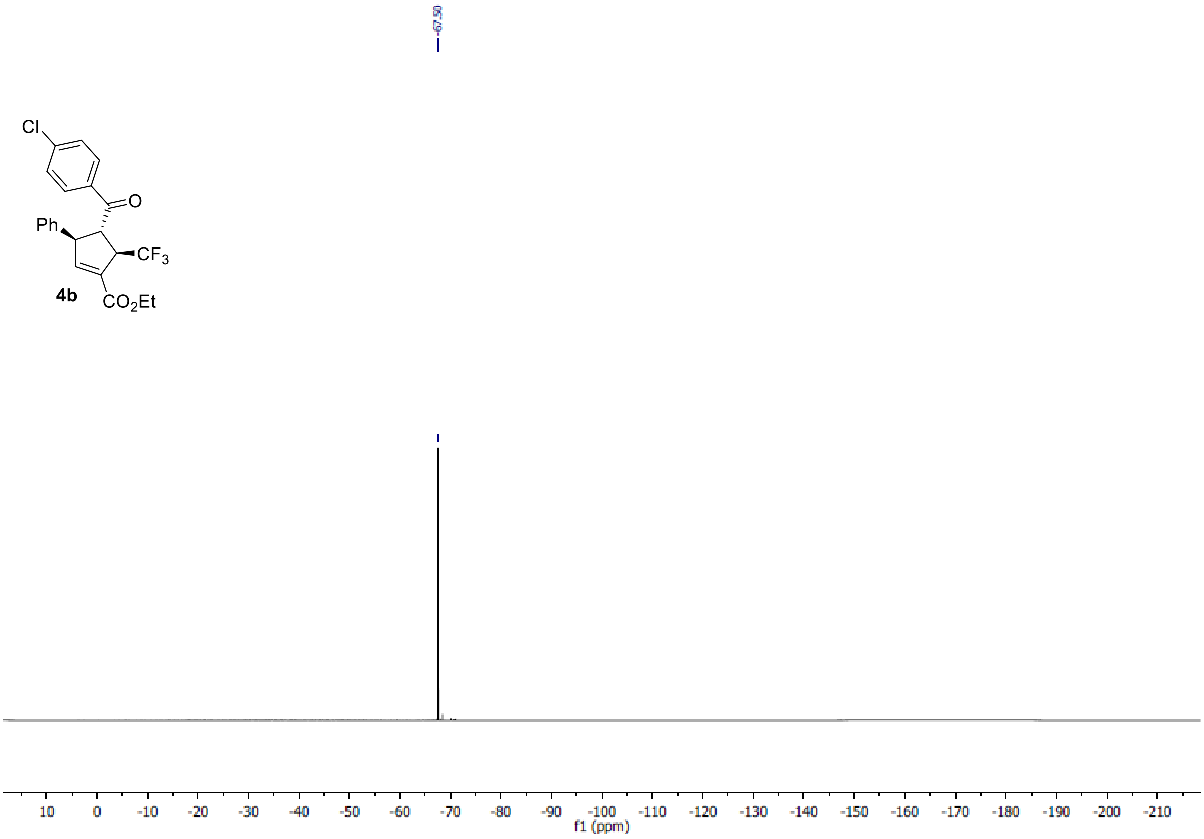


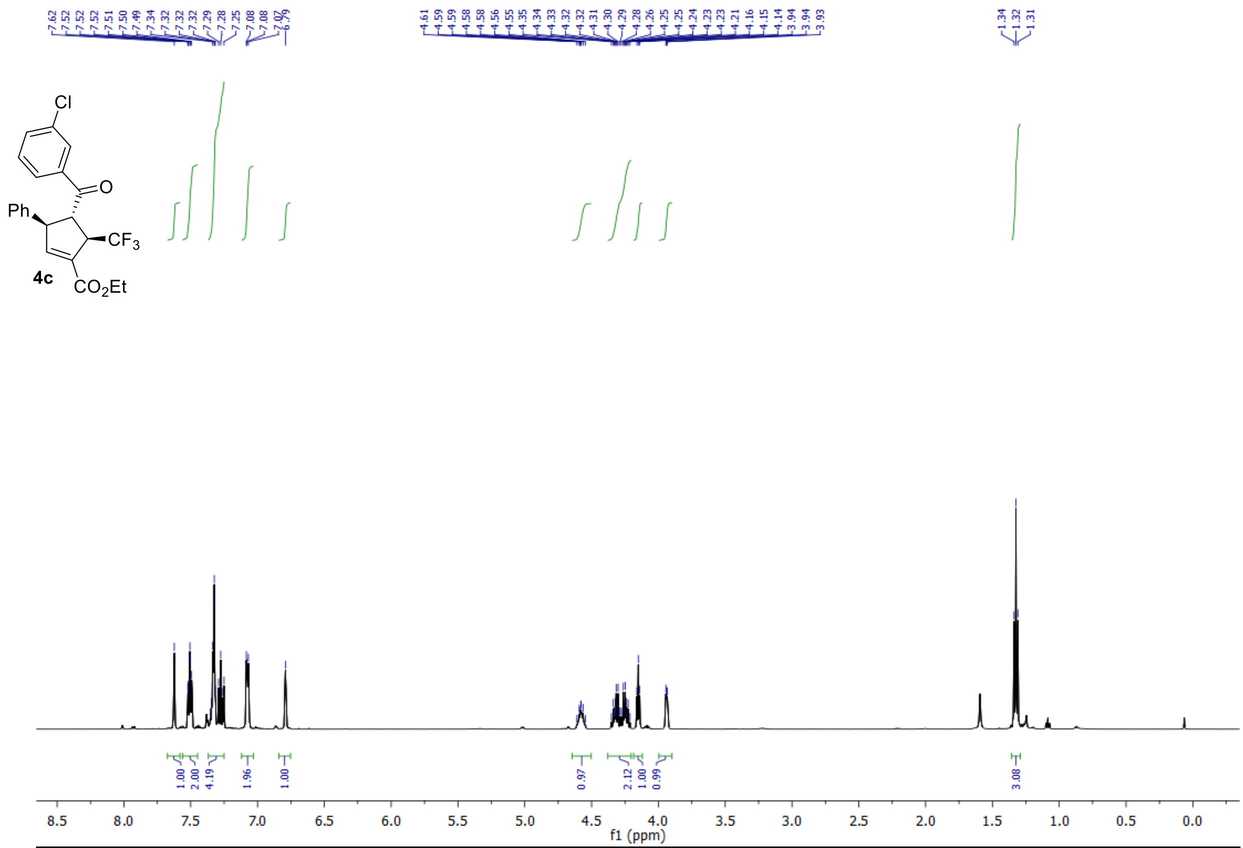


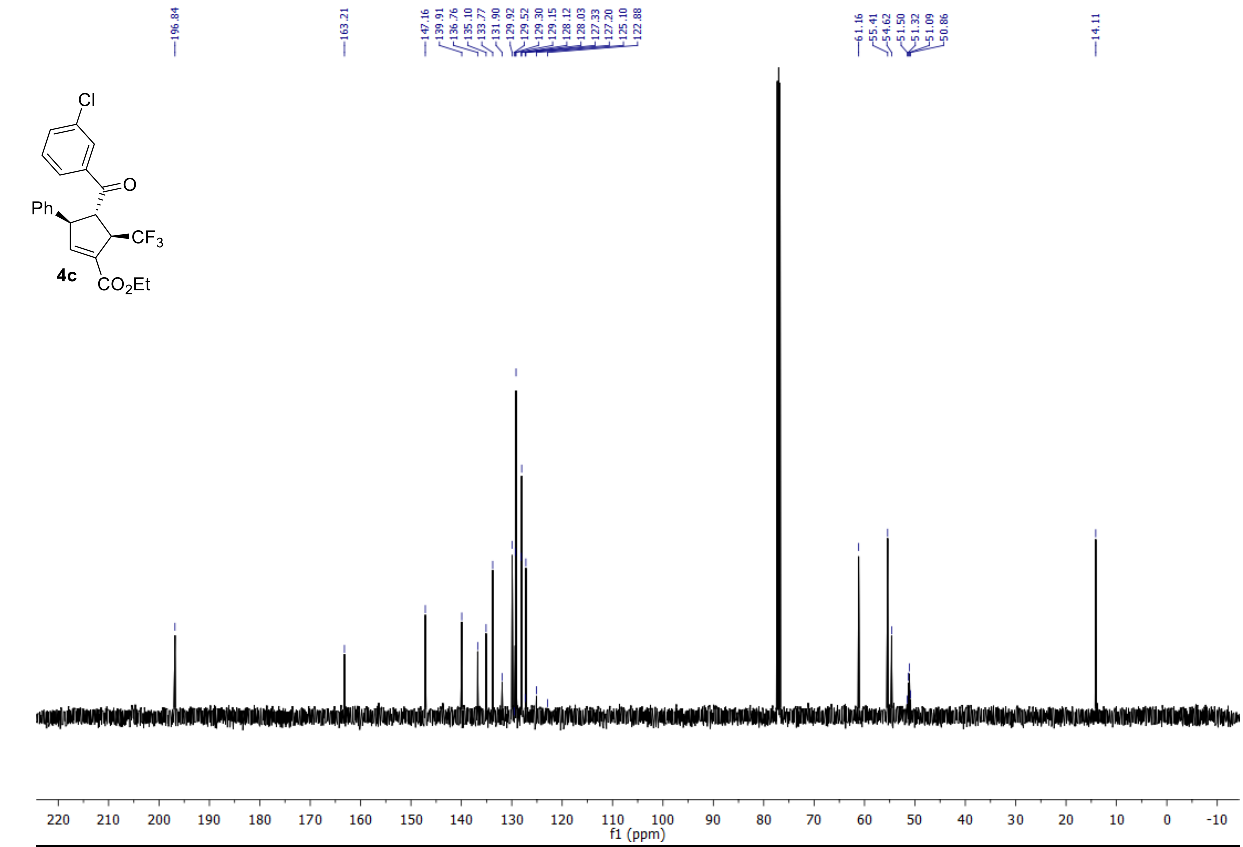
4b

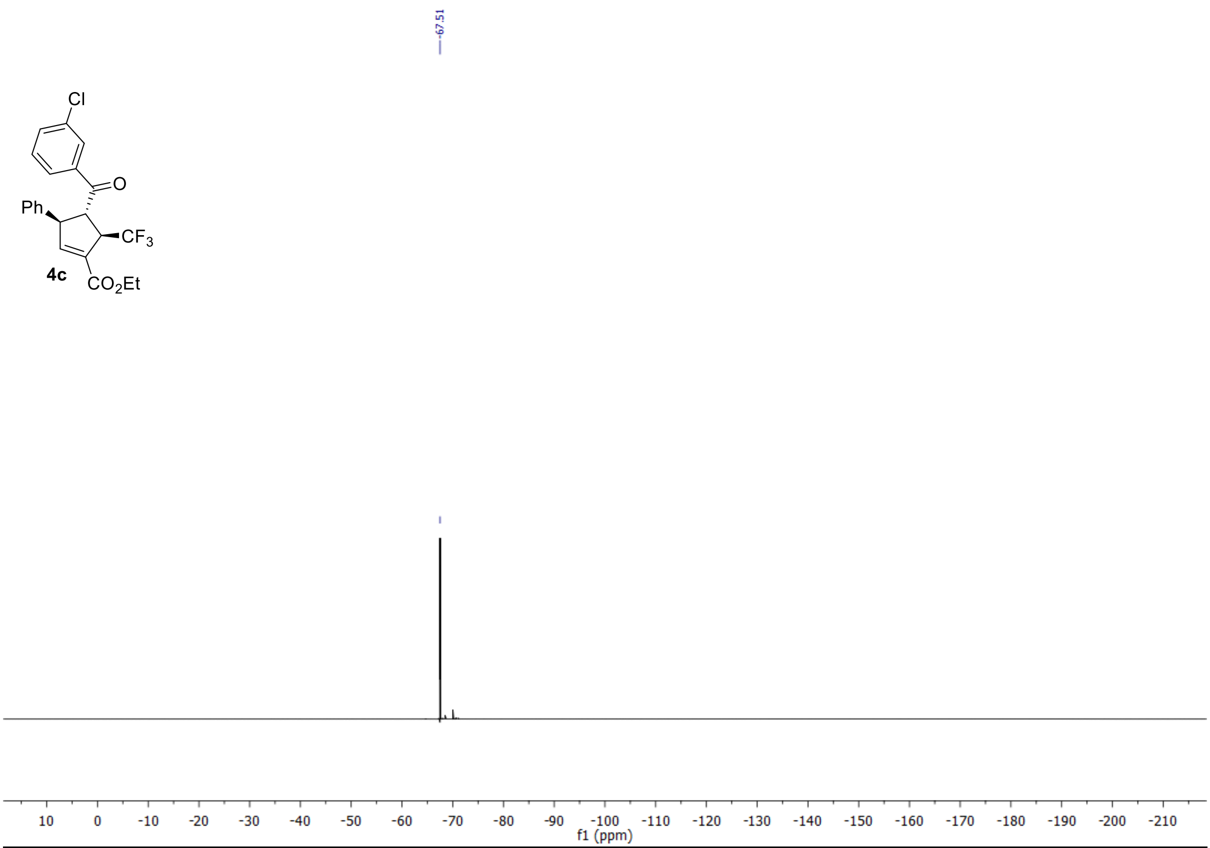


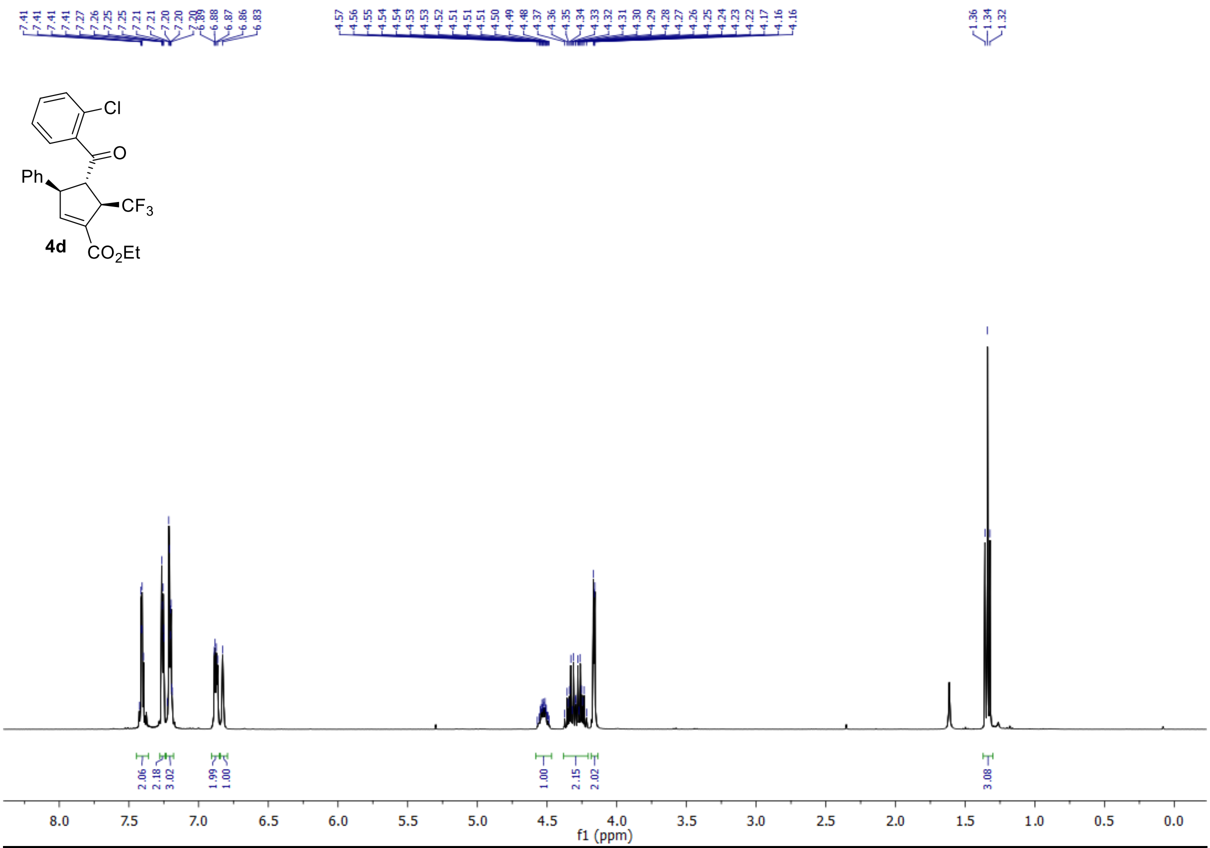

197.01
163.22
147.28
140.55
140.04
133.55
131.91
130.54
129.14
129.00
128.07
128.01
127.62
124.85
61.15
55.51
54.26
51.88
51.58
51.29
51.00
14.11
Cl
O
Ph
CF3
4b
CO2Et
f1 (ppm)

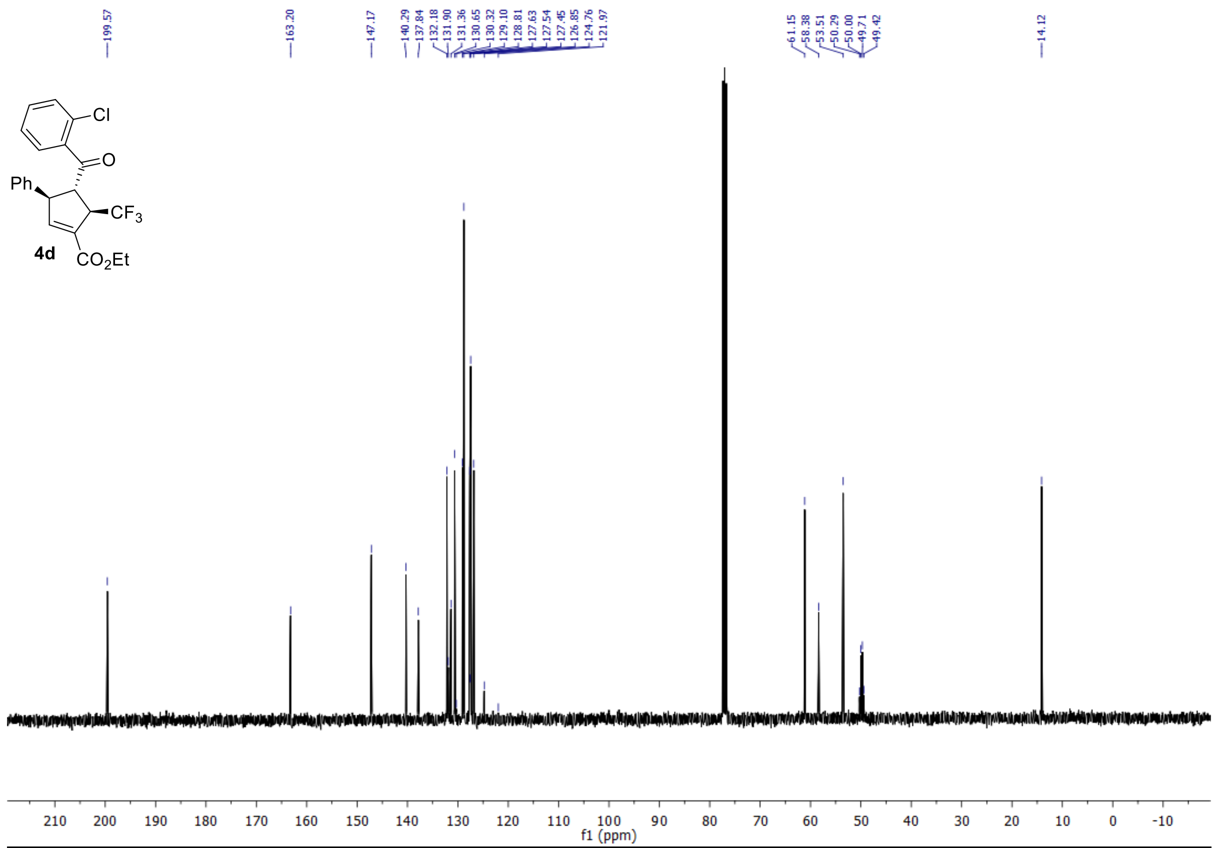

-67.50
Cl
O
Ph
CF3
4b
CO2Et
f1 (ppm)

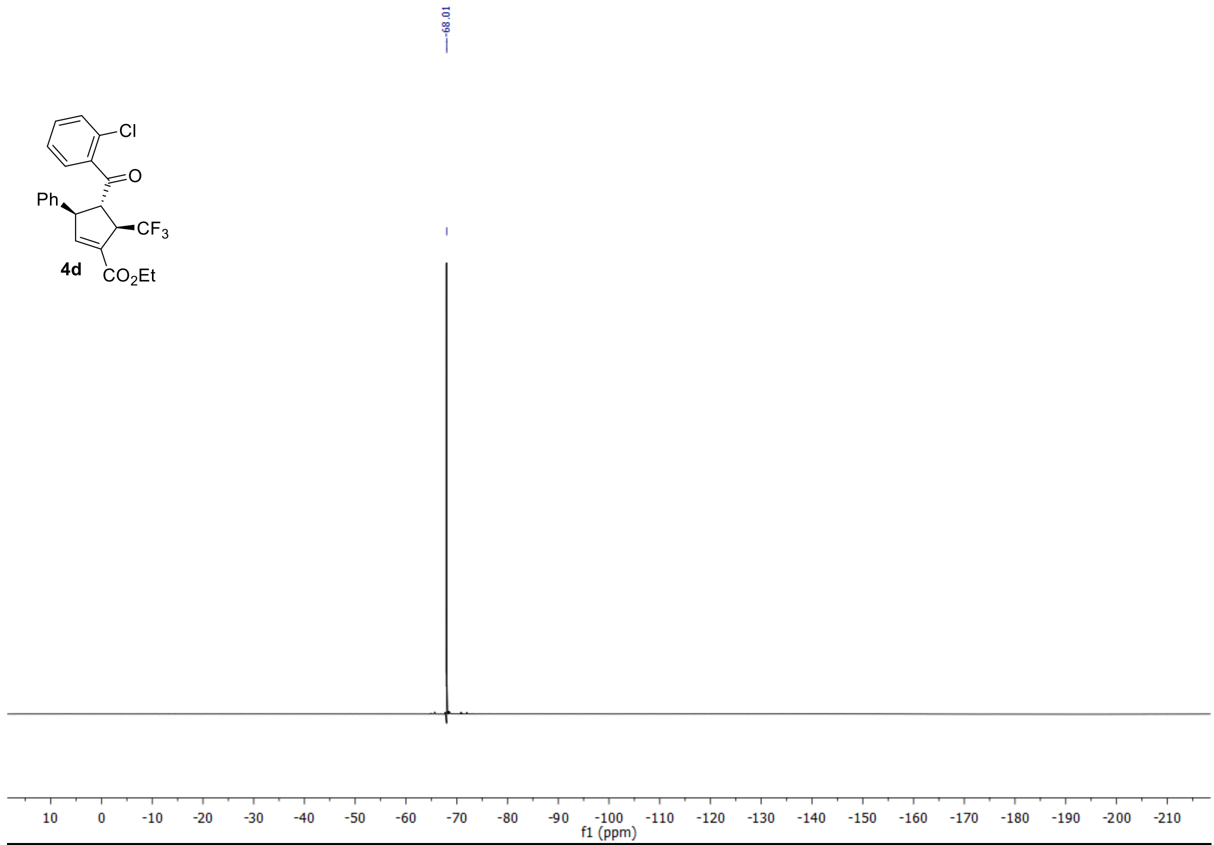

Cl
O
Ph
CF_3
4c
CO_2Et
f1 (ppm)

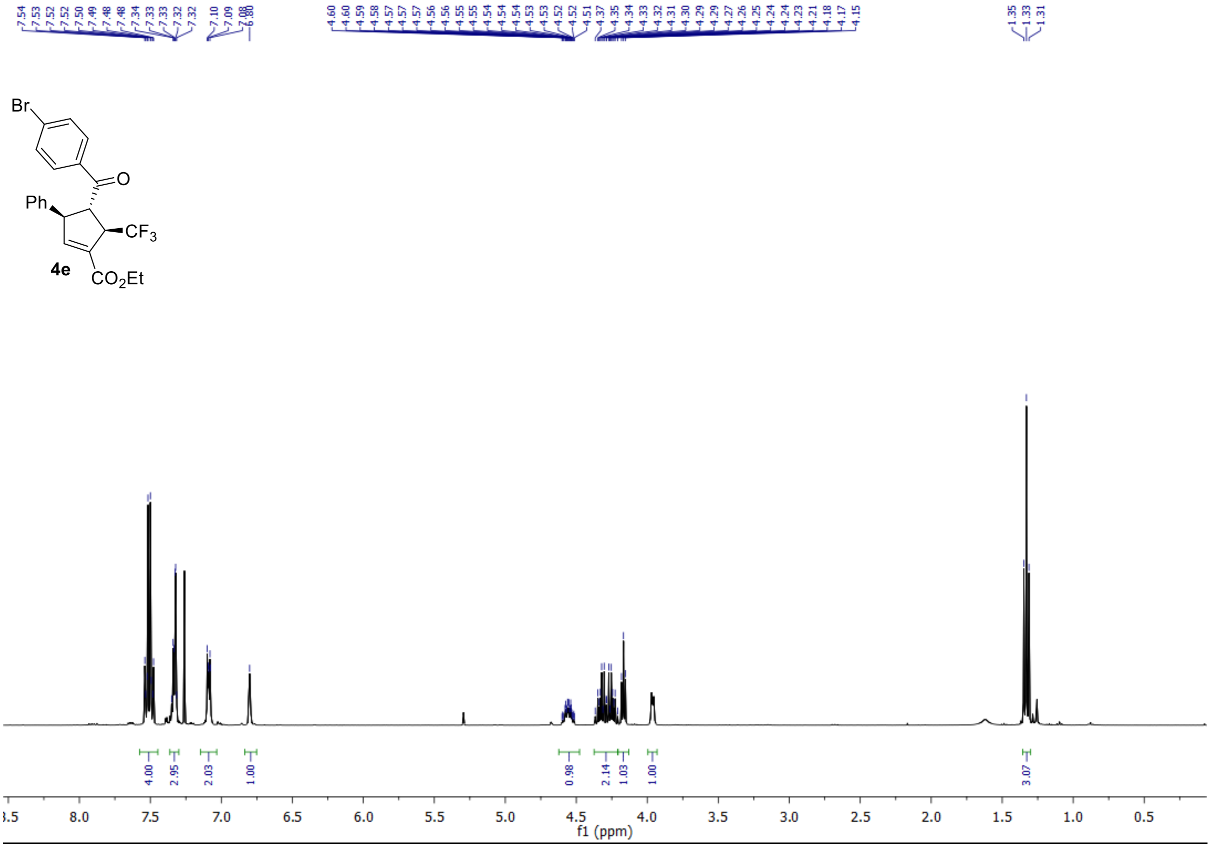

Cl
O
Ph
CF_3
4c
CO_2Et
f1 (ppm)

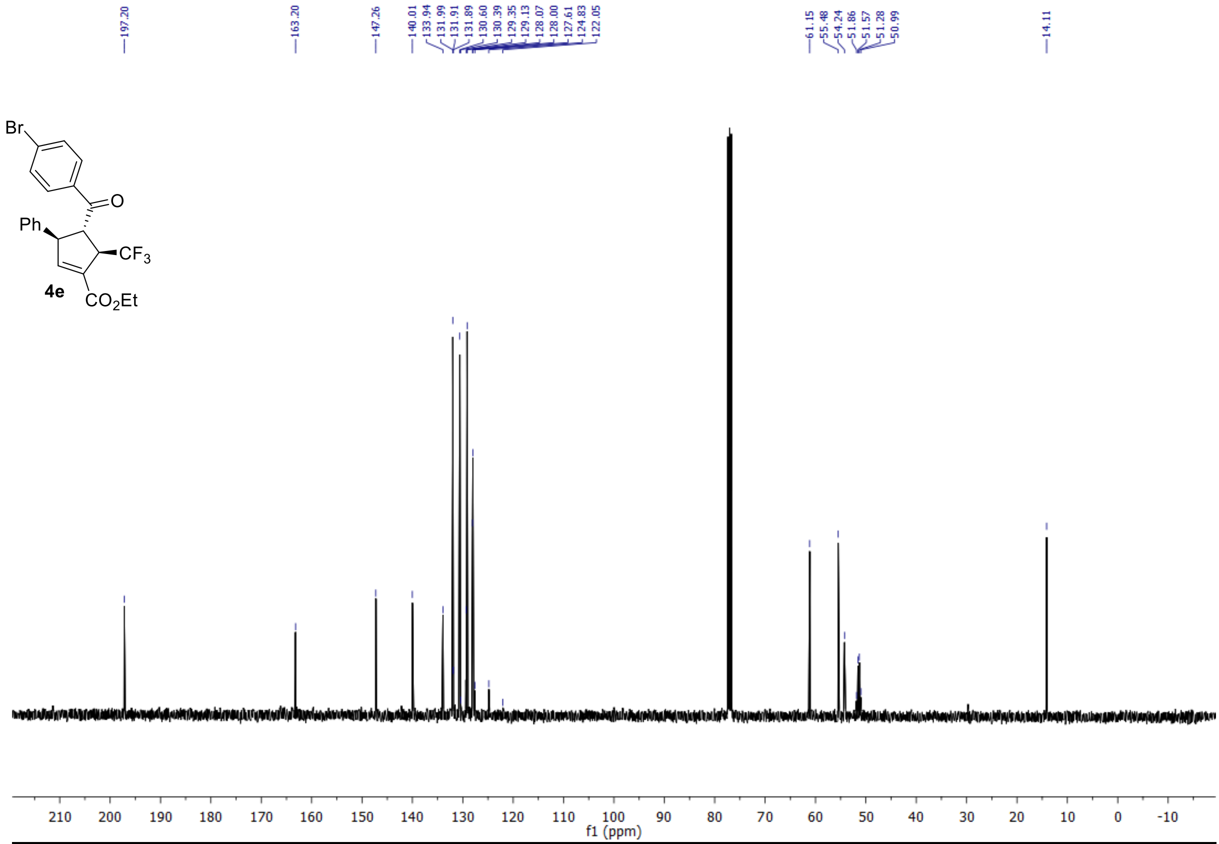

-67.51
Cl
O
Ph
CF3
4c
CO2Et
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

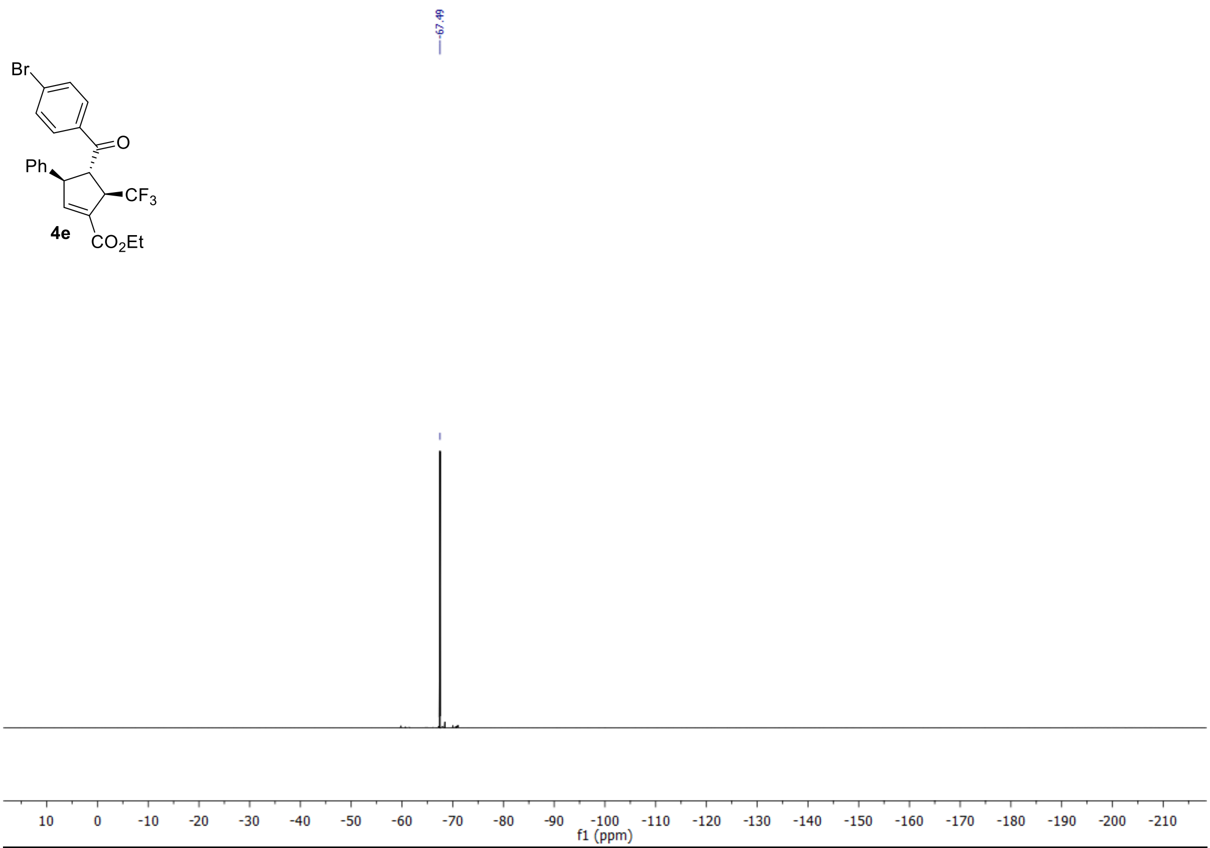

Cl
O
Ph
CF3
4d
CO2Et
2.06 2.18 3.02 1.99 1.00 1.00 2.15 2.02 3.08
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


199.57
163.20
147.17
140.29
137.84
132.18
131.90
131.36
130.65
130.32
129.10
128.81
127.63
127.54
127.45
126.85
124.76
121.97
61.15
58.38
53.51
50.29
50.00
49.71
49.42
14.12
Cl
O
Ph
CF_3
4d
CO_2Et
f1 (ppm)

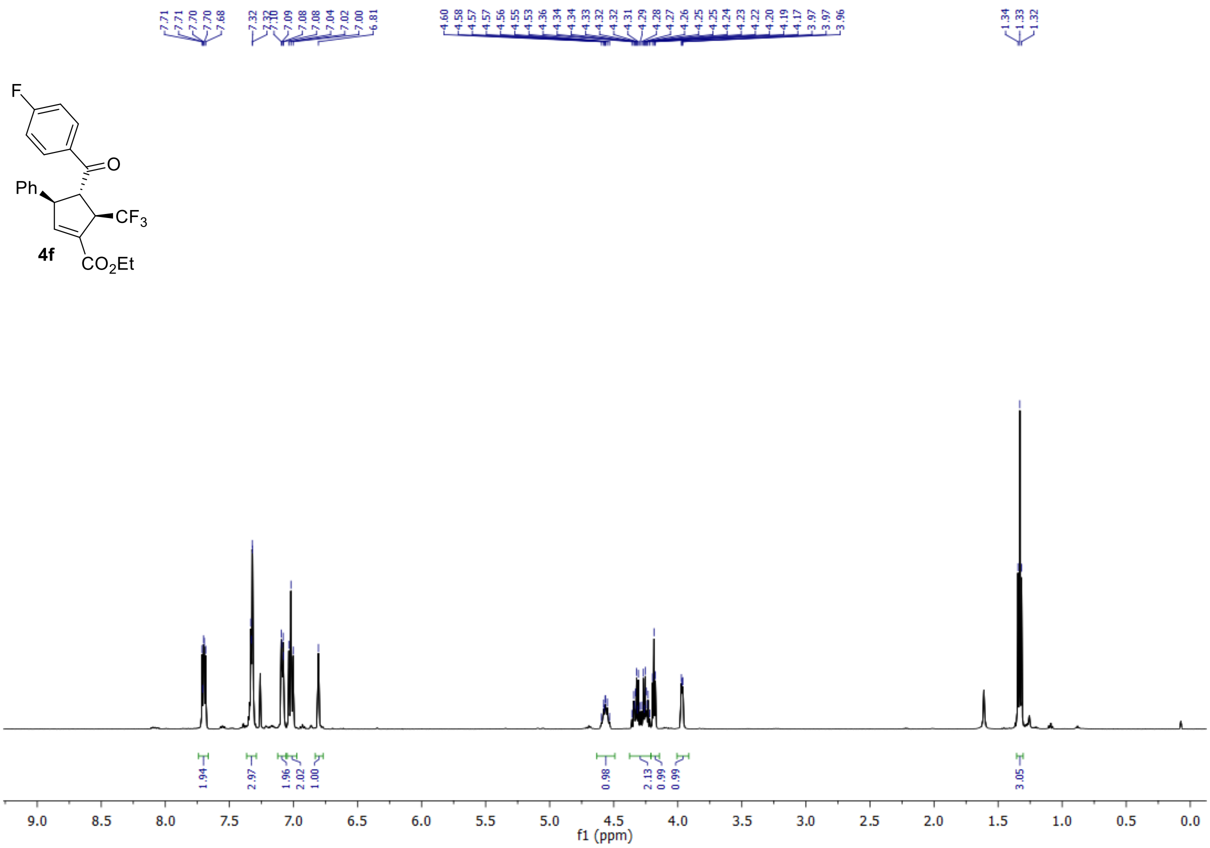

-68.01
Cl
O
Ph
CF_3
4d
CO_2Et
f1 (ppm)


Br
O
Ph
CF3
4e
CO2Et
f1 (ppm)

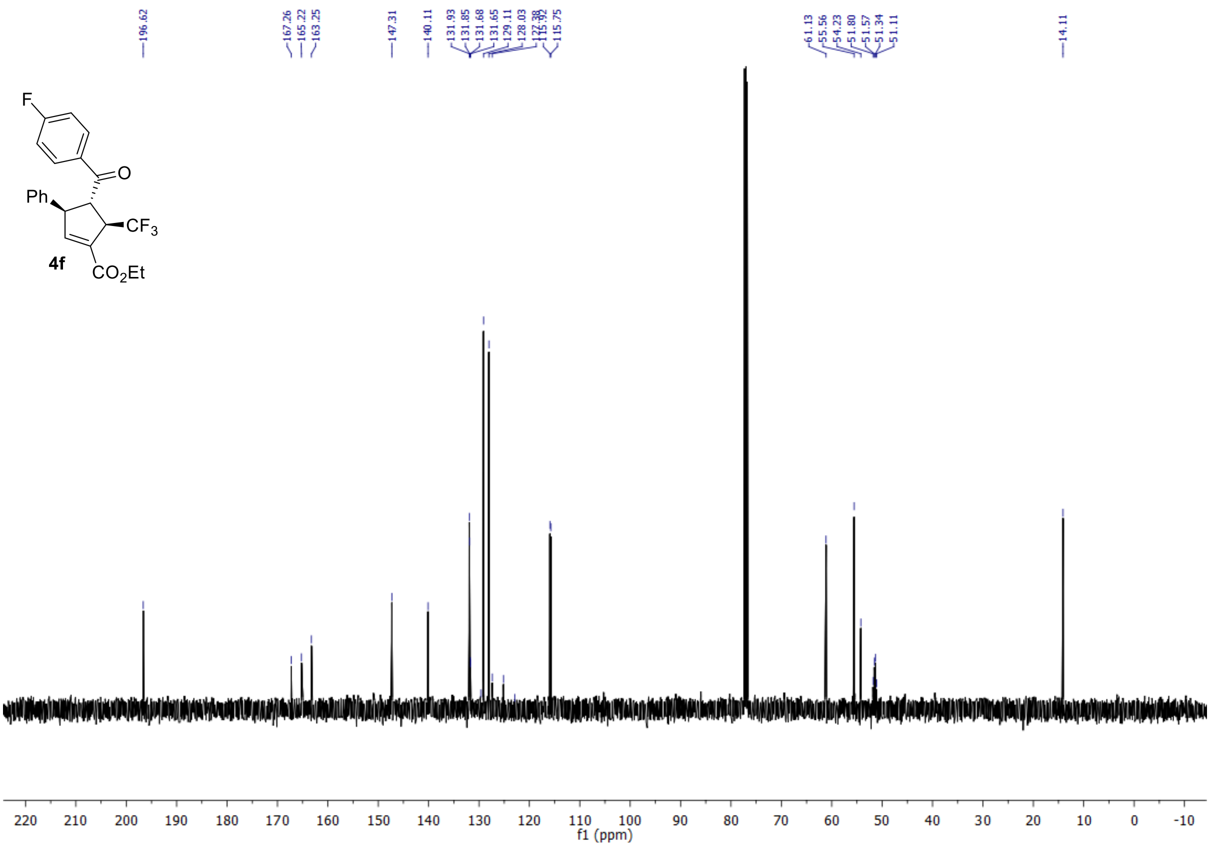

Br
O
Ph
CF3
4e
CO2Et
f1 (ppm)

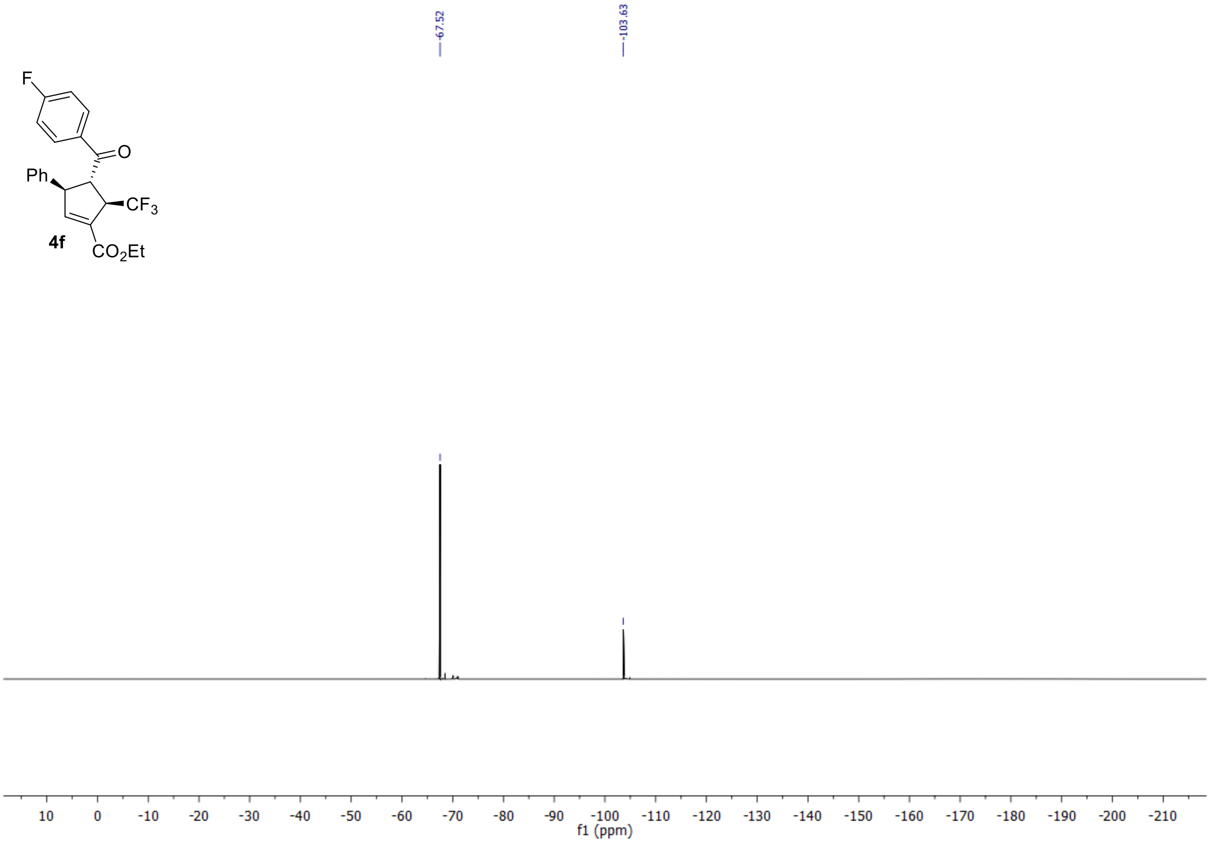


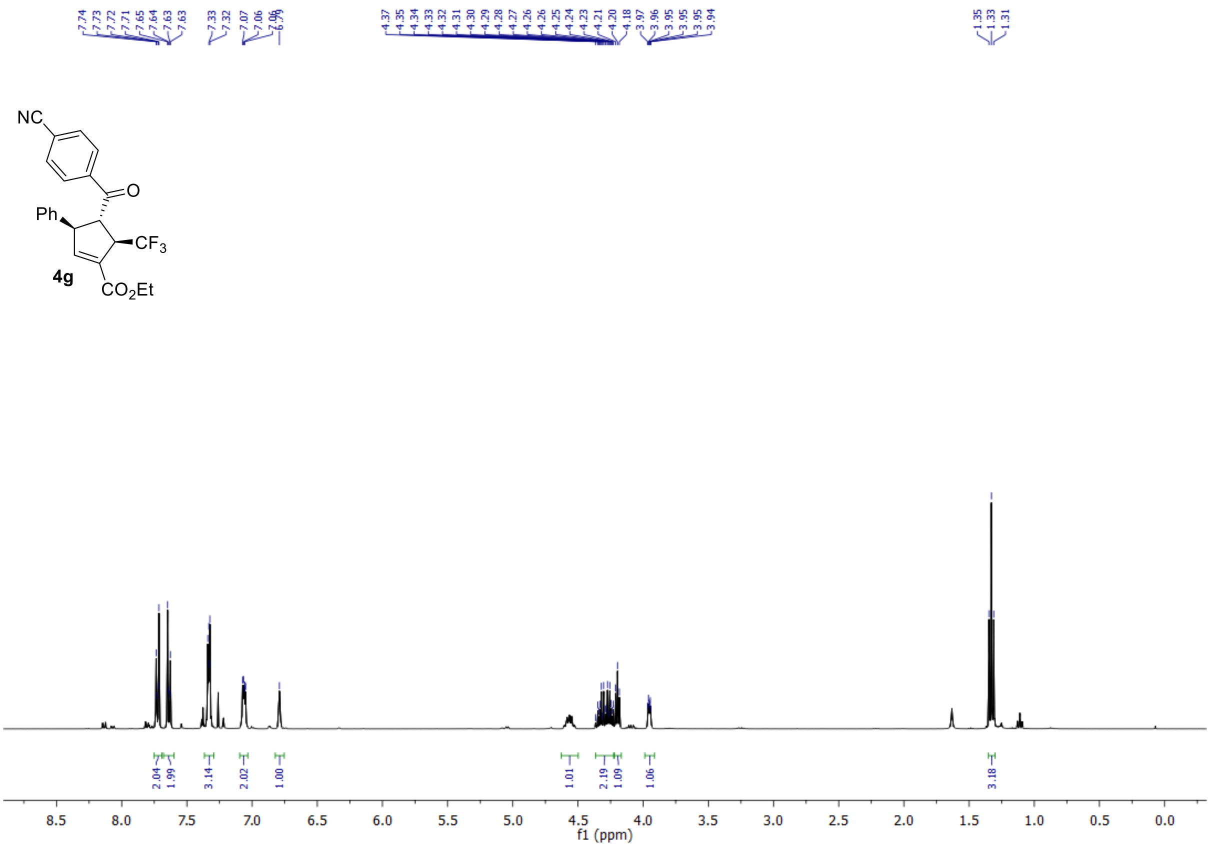
4e

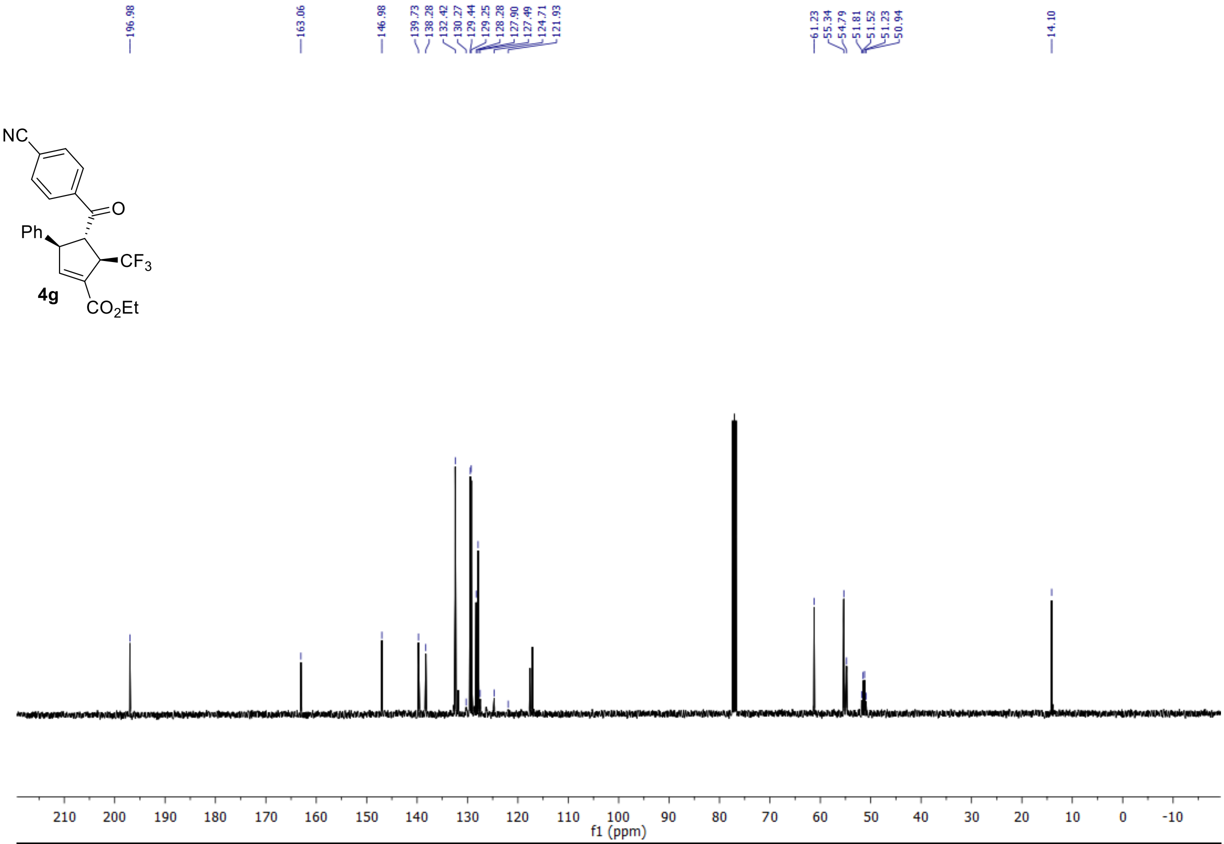


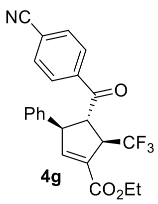
4f


196.62
167.26
165.22
163.25
147.31
140.11
131.93
131.85
131.68
131.65
129.11
128.03
127.38
115.92
115.75
61.13
55.56
54.23
51.80
51.57
51.34
51.11
14.11
F
O
Ph
CF3
4f
CO2Et
f1 (ppm)

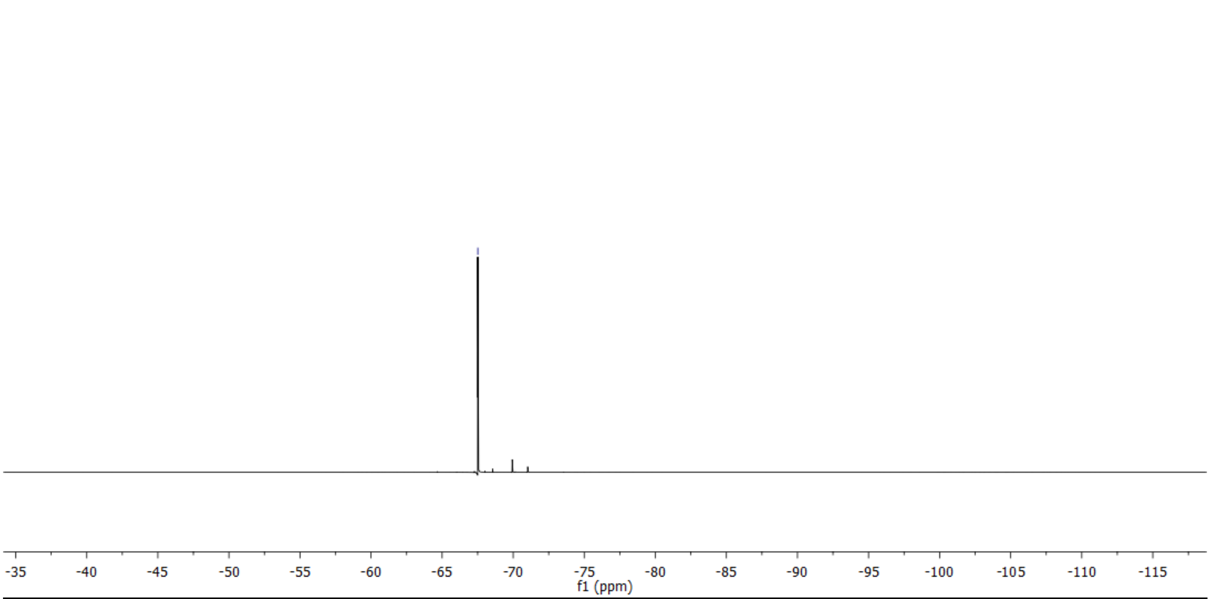

-67.52
-103.63
F
O
Ph
CF3
4f
CO2Et
f1 (ppm)

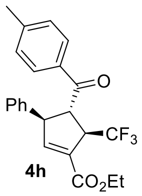

NC
O
Ph
CF_3
4g
CO_2Et
f1 (ppm)


NC
O
Ph
CF_3
4g
CO_2Et
f1 (ppm)

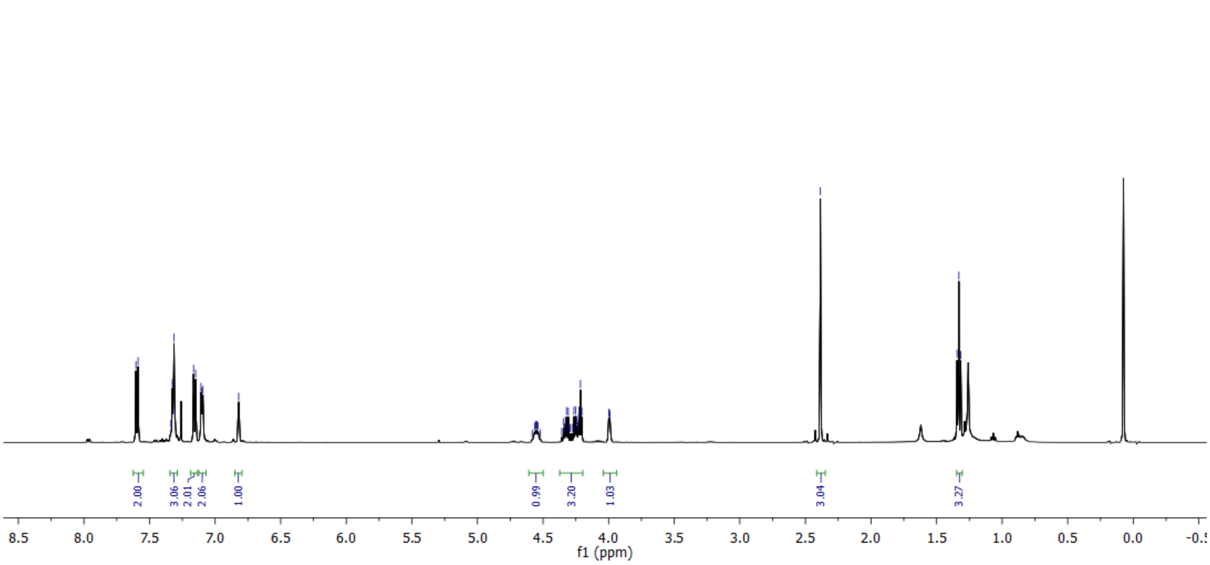


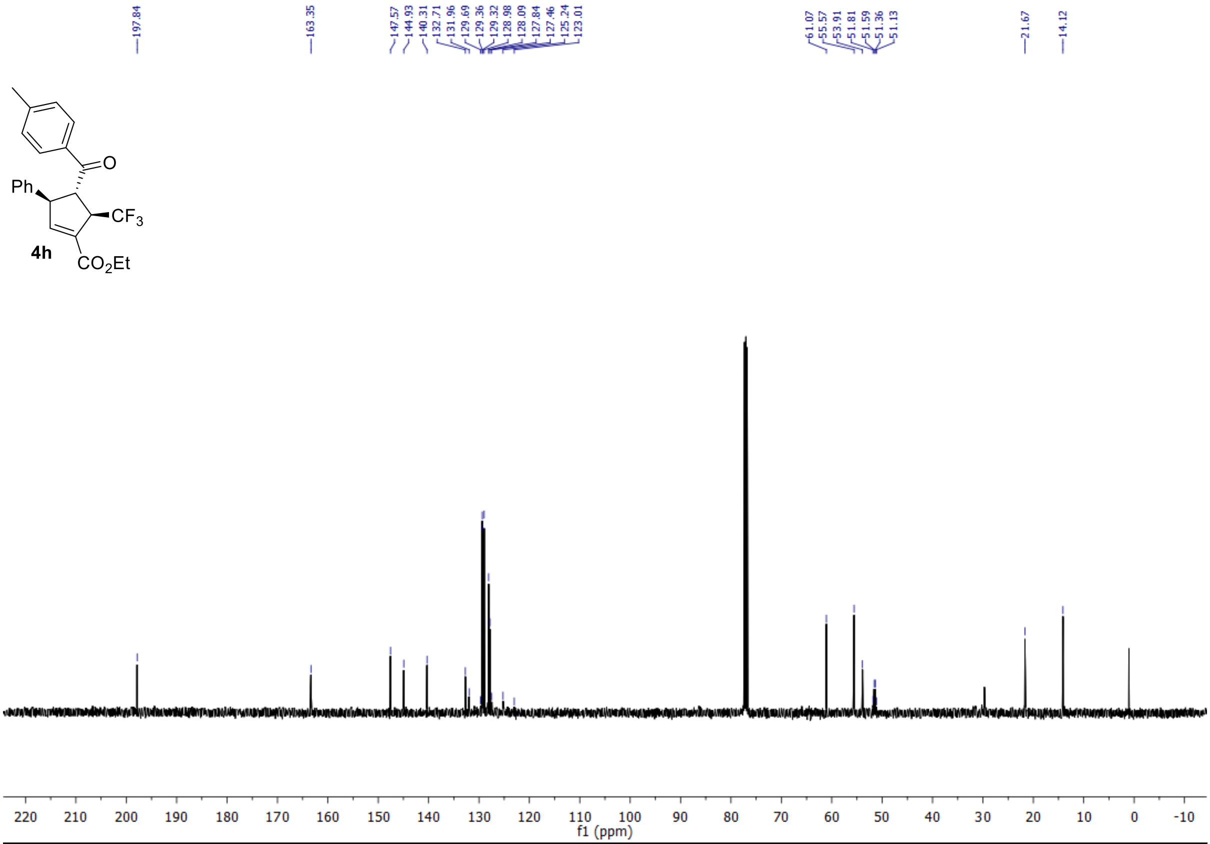
4g

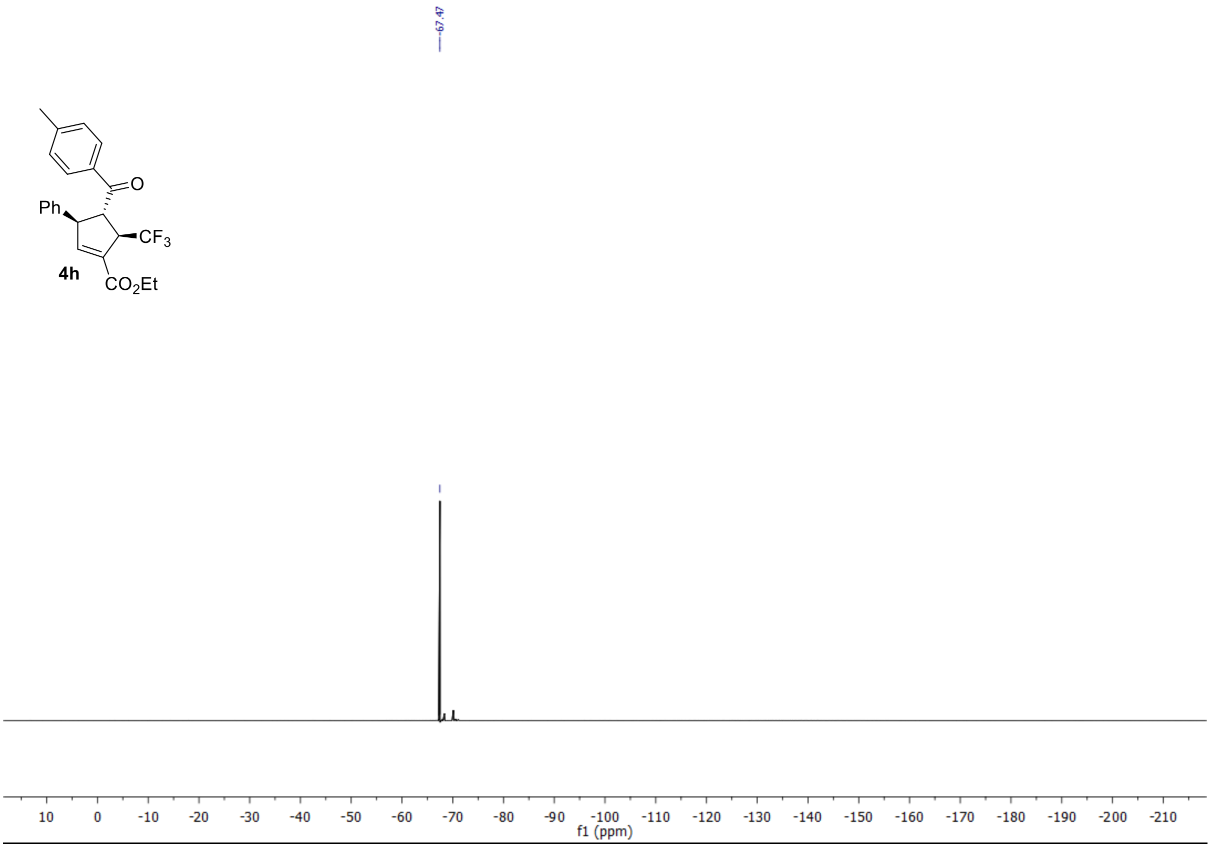


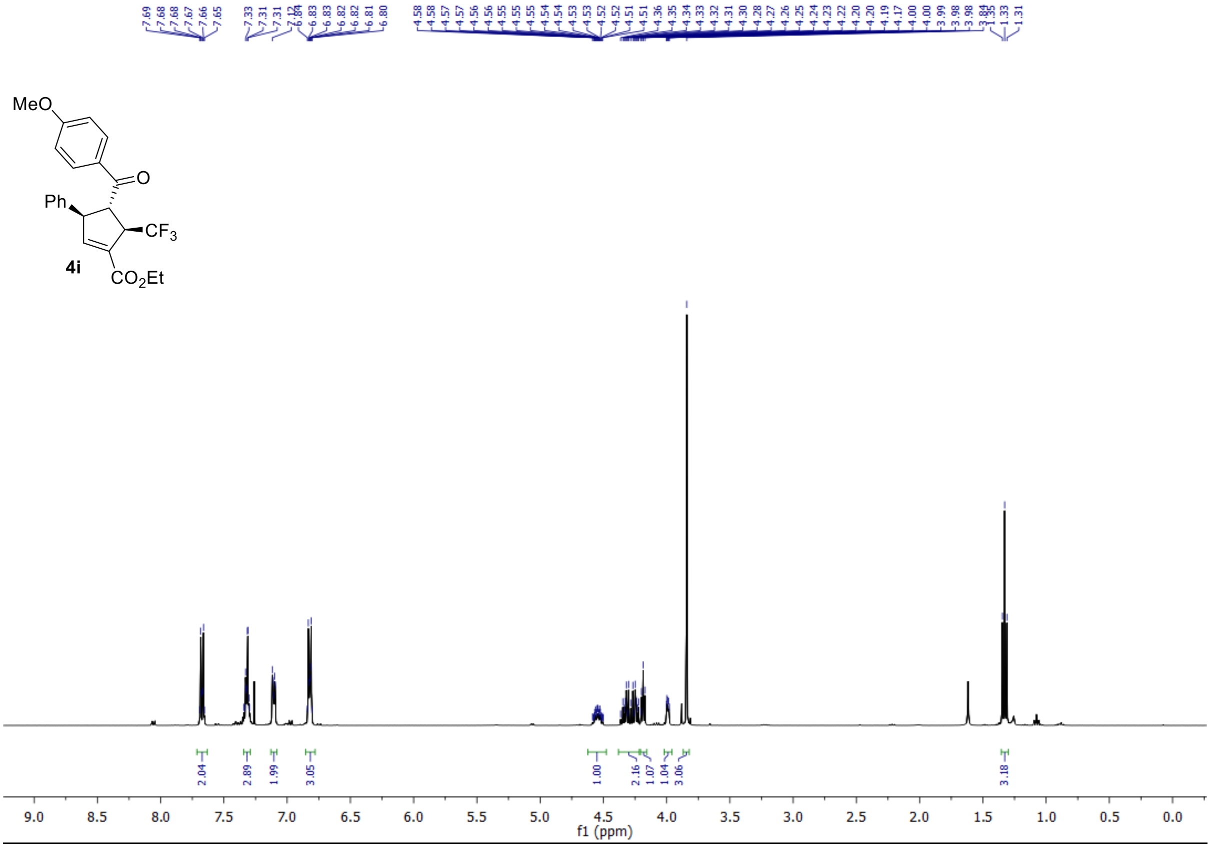


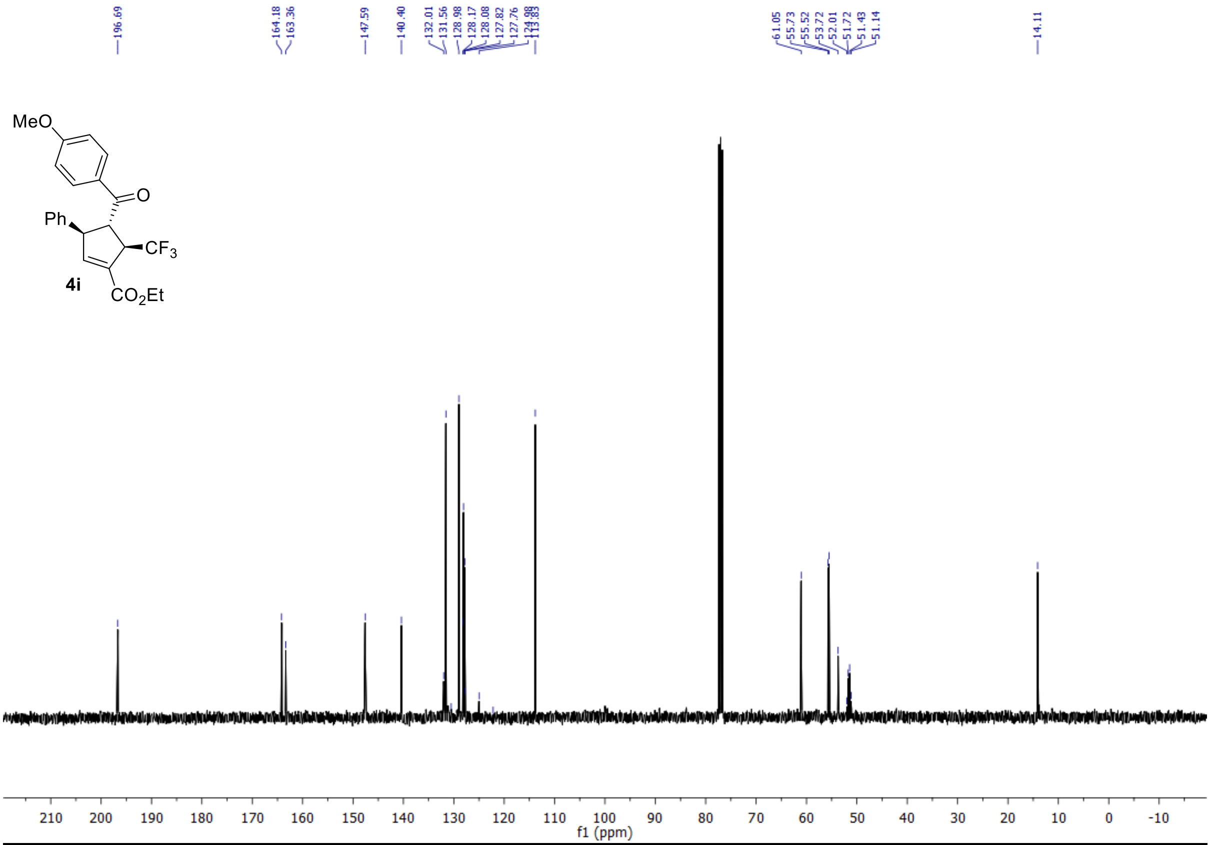
4h

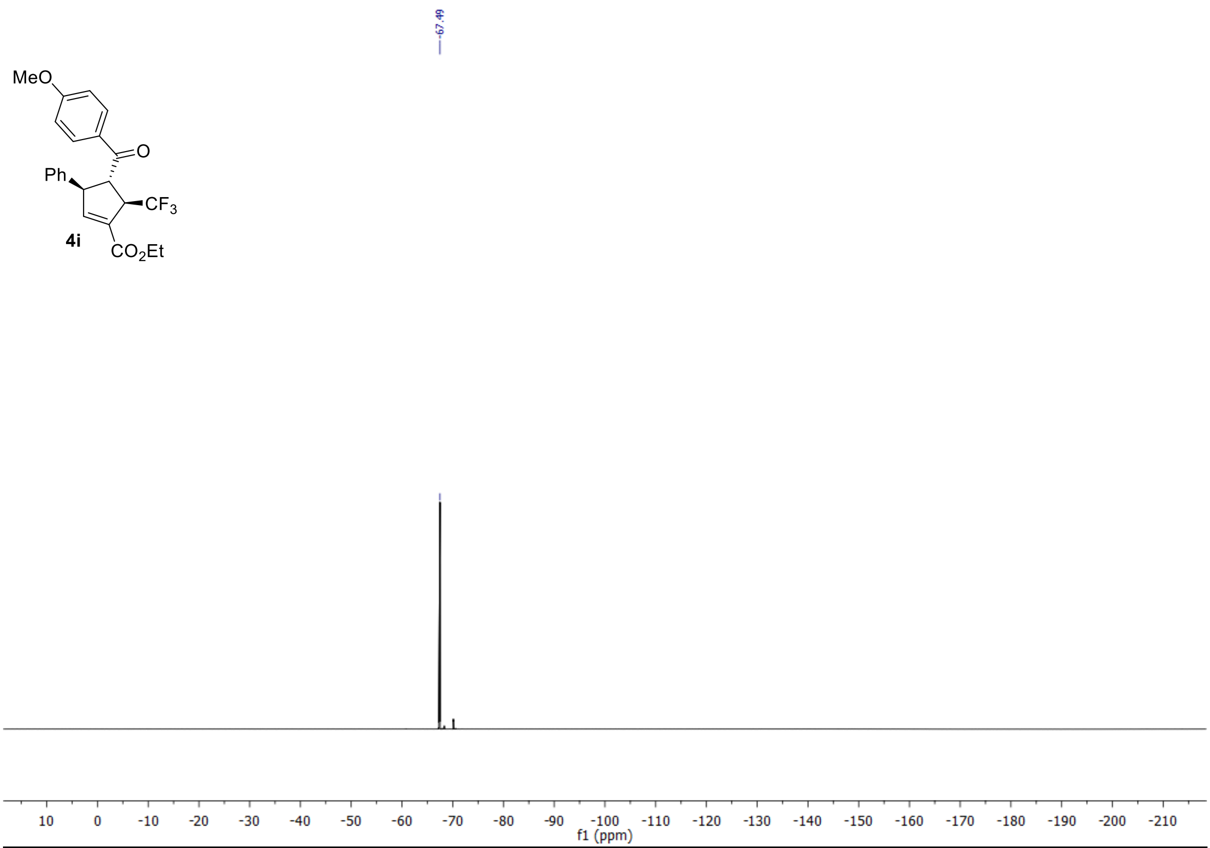


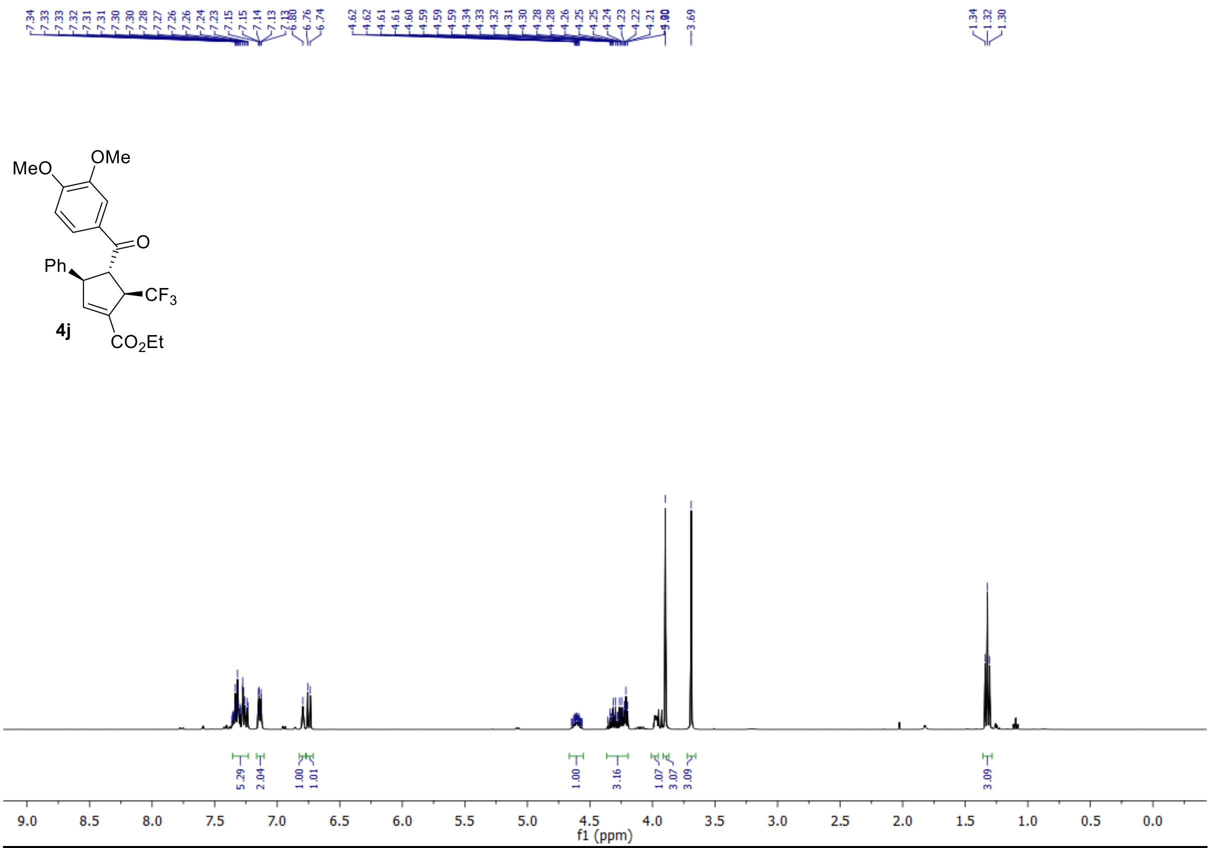

197.84
163.35
147.57
144.93
140.31
132.71
131.96
129.69
129.36
129.32
128.98
128.09
127.84
127.46
125.24
123.01
61.07
55.57
53.91
51.81
51.59
51.36
51.13
21.67
14.12
Ph
O
CF_3
4h
CO_2Et
f1 (ppm)

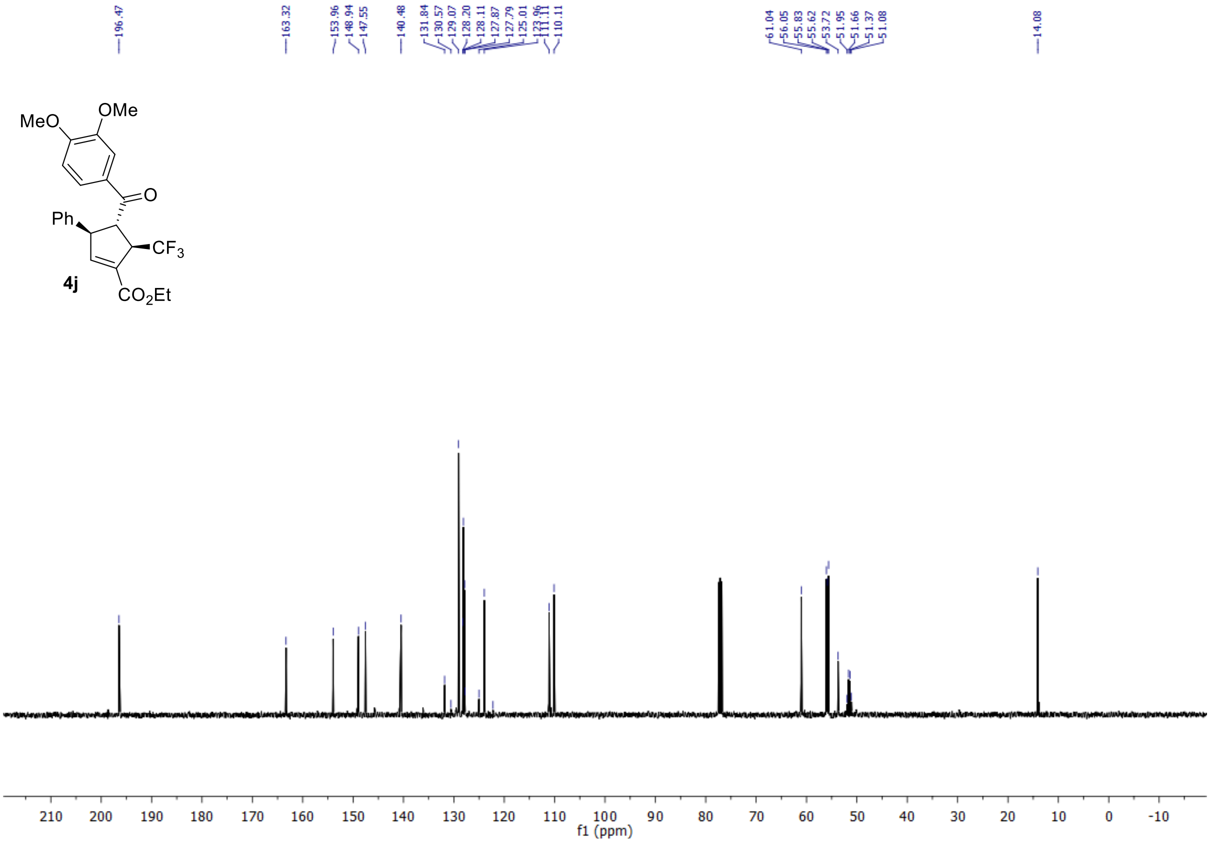

-67.47
Ph
O
CF_3
4h
CO_2Et
f1 (ppm)

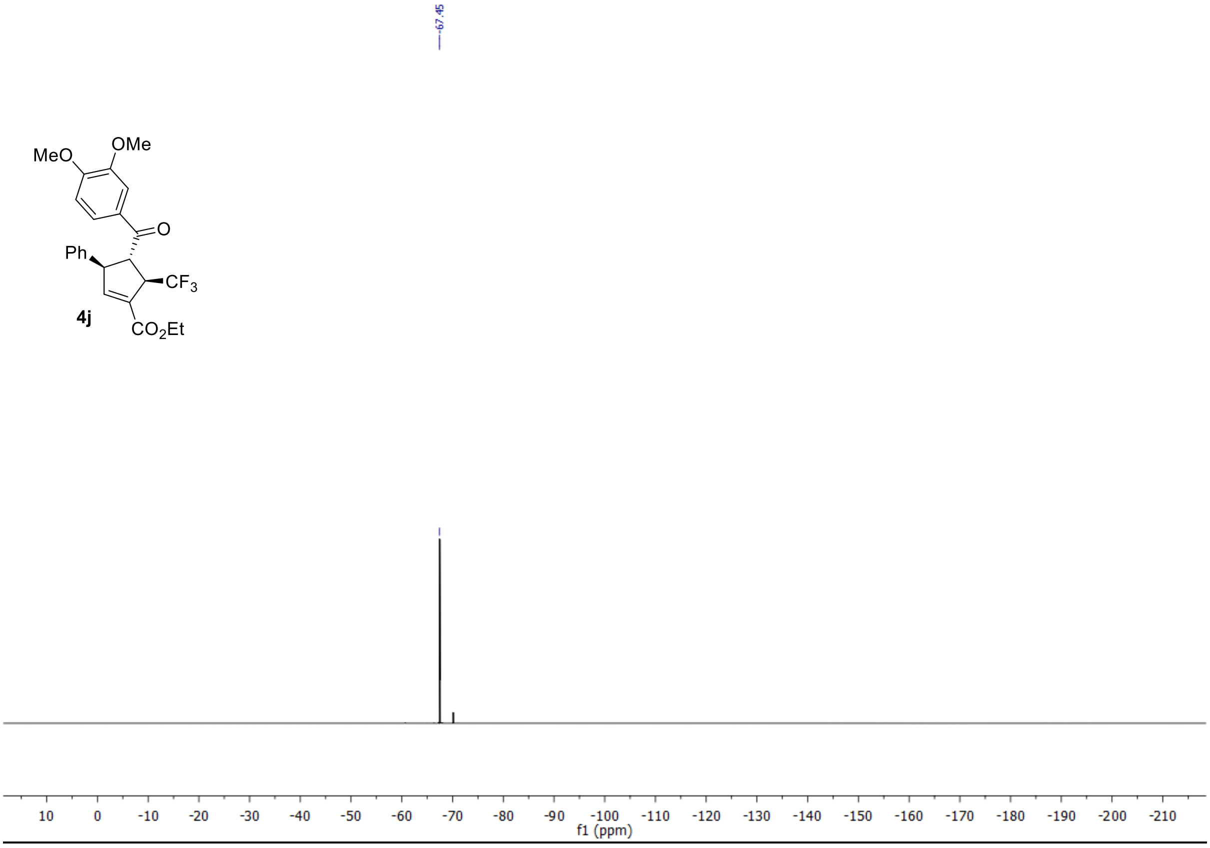


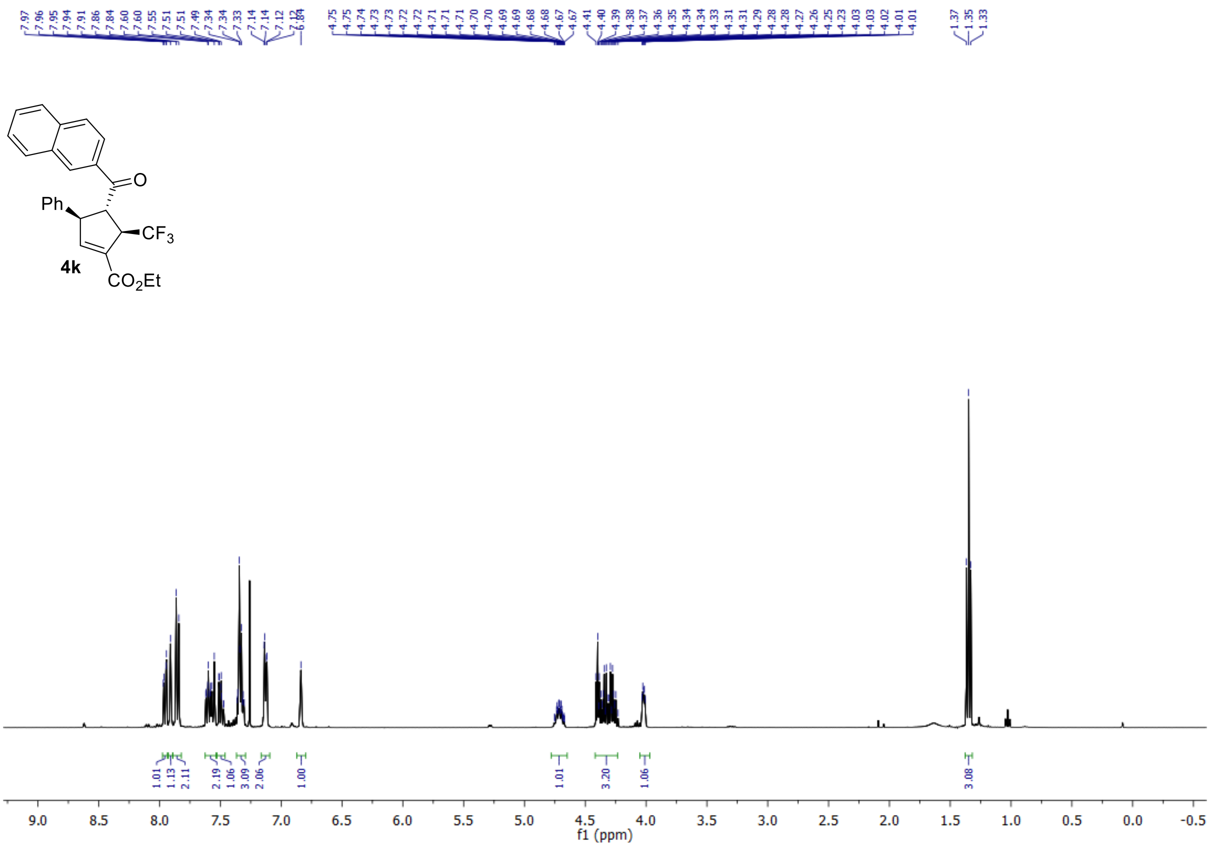


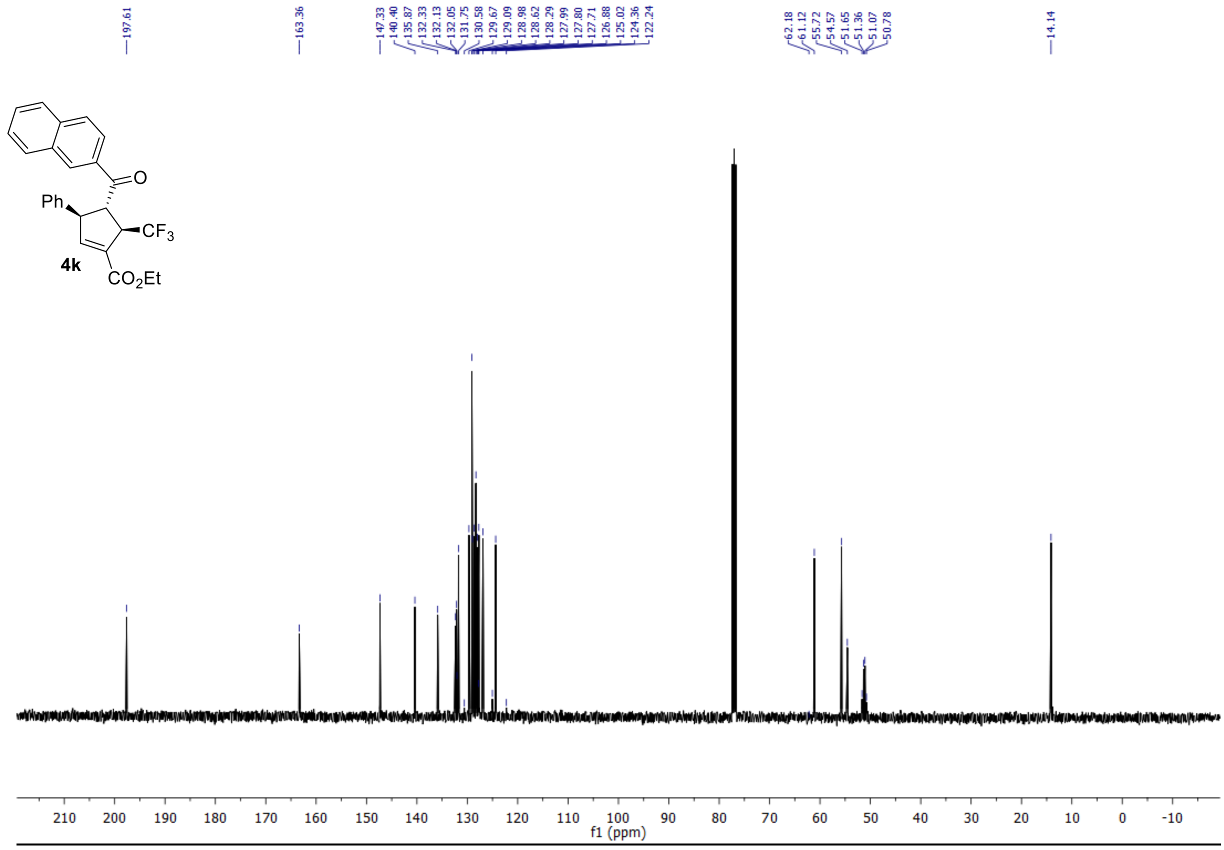

MeO
Ph
CF3
4i
CO2Et
f1 (ppm)

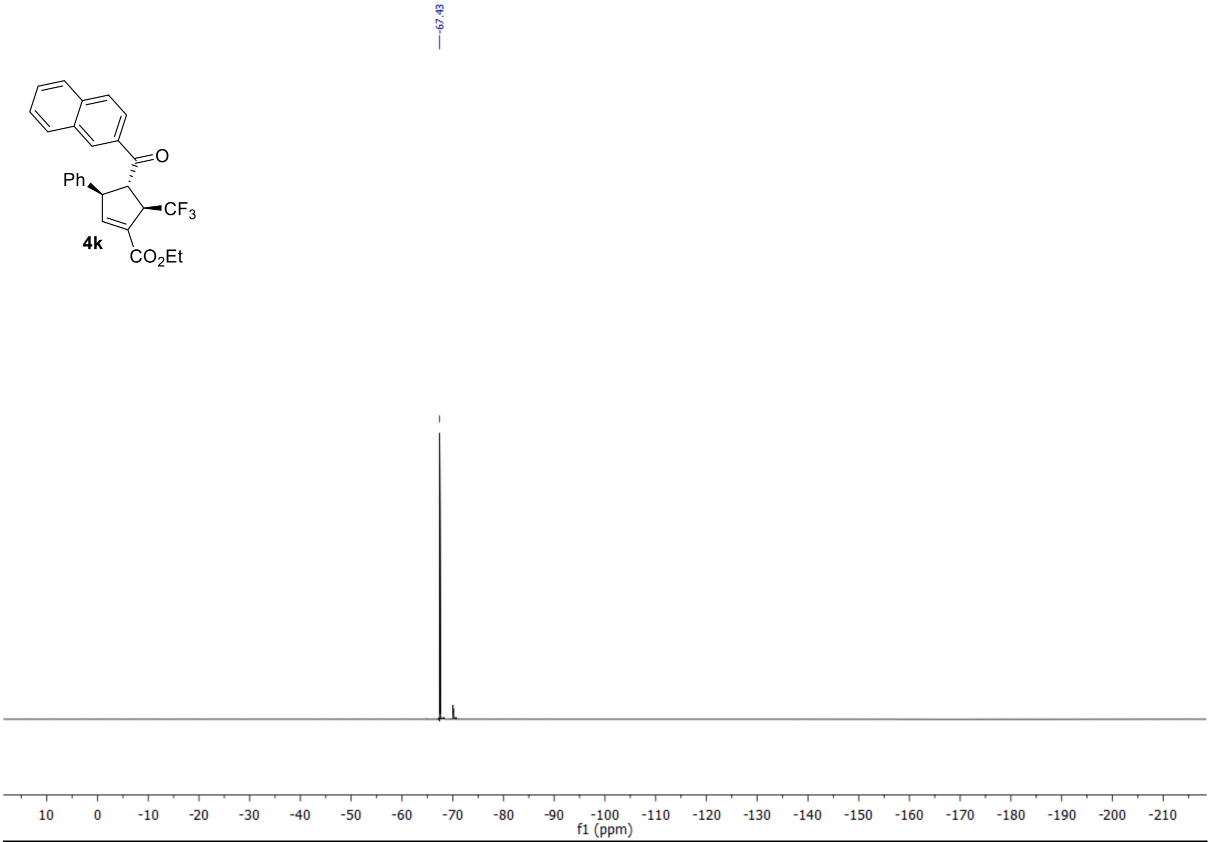

MeO
OMe
Ph
CF3
4j
CO2Et
f1 (ppm)

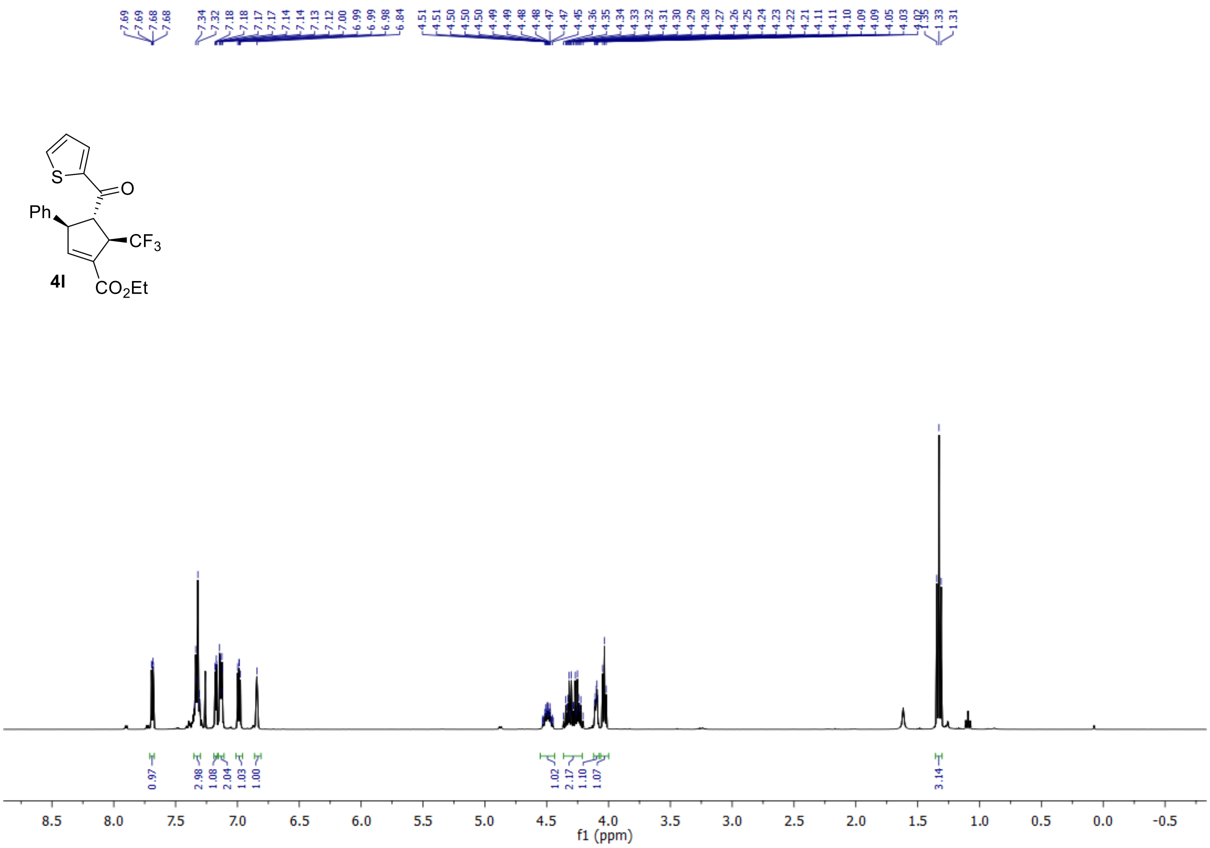

196.47
163.32
153.96
148.94
147.55
140.48
131.84
130.57
129.07
128.20
128.11
127.87
127.79
125.01
123.96
111.11
110.11
61.04
56.05
55.83
55.62
53.72
51.95
51.66
51.37
51.08
14.08
MeO
OMe
O
Ph
CF_3
4j
CO_2Et
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

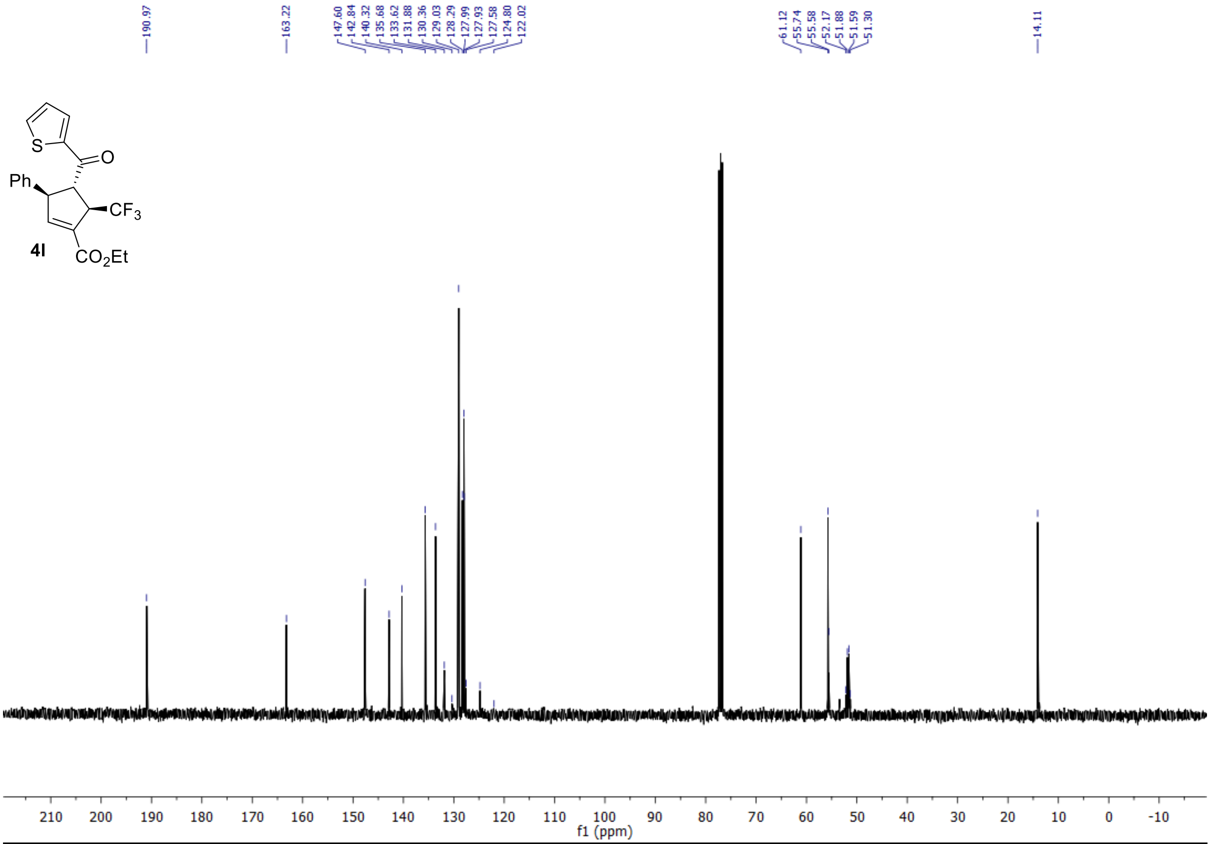

-67.45
MeO
OMe
O
Ph
CF_3
4j
CO_2Et
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

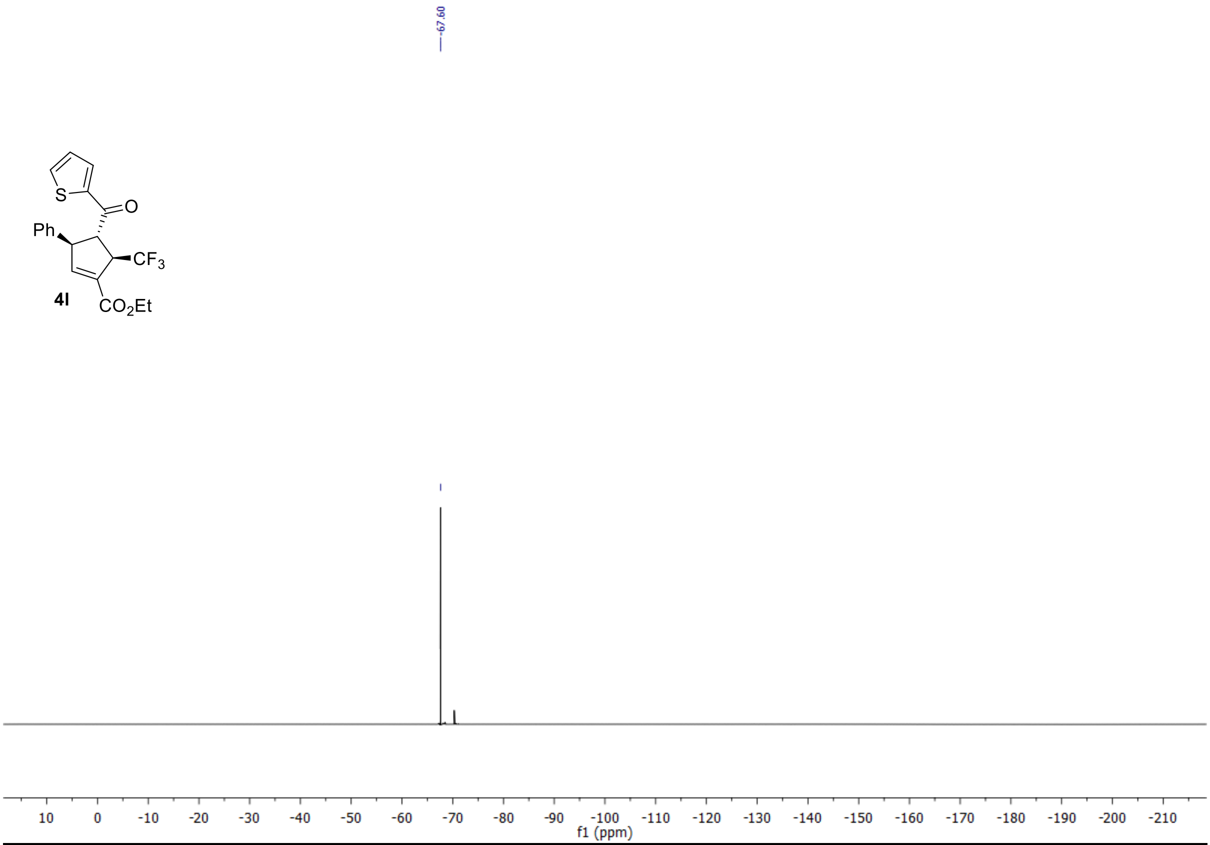


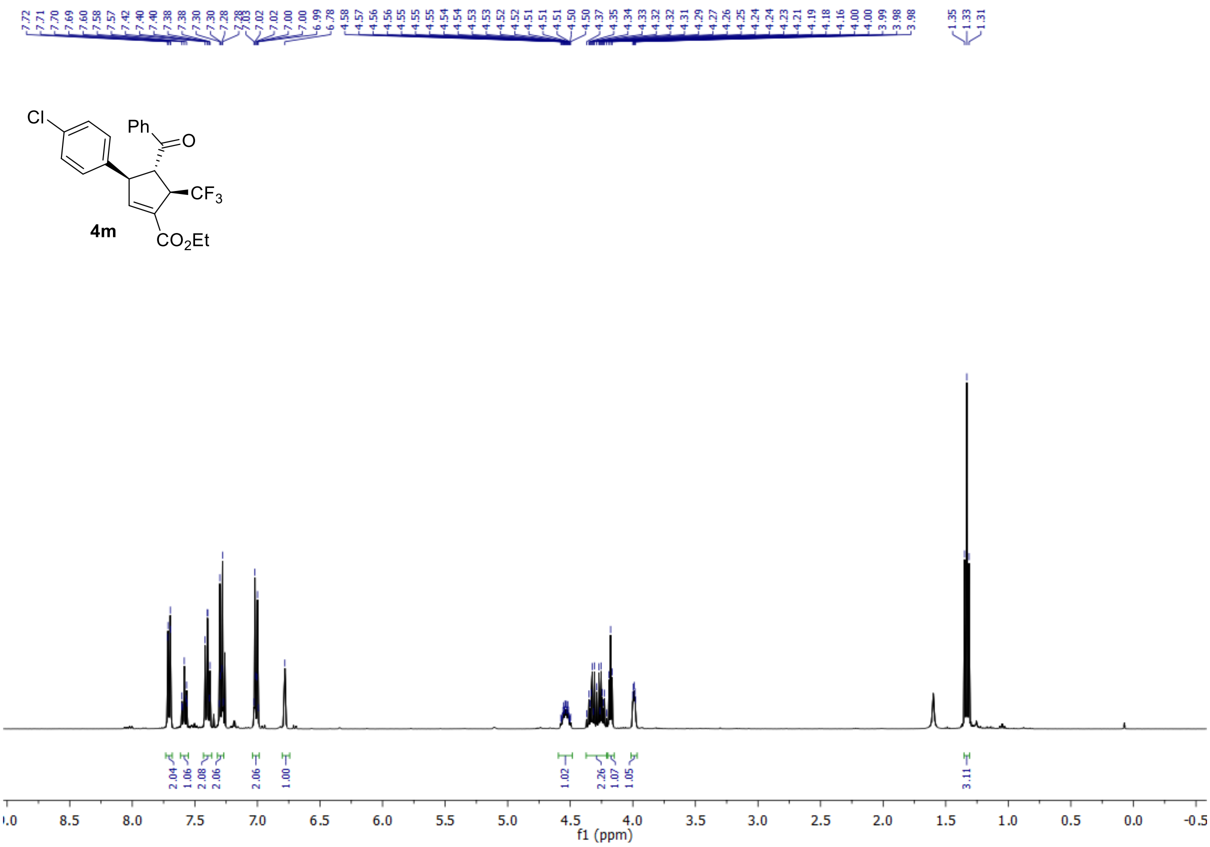


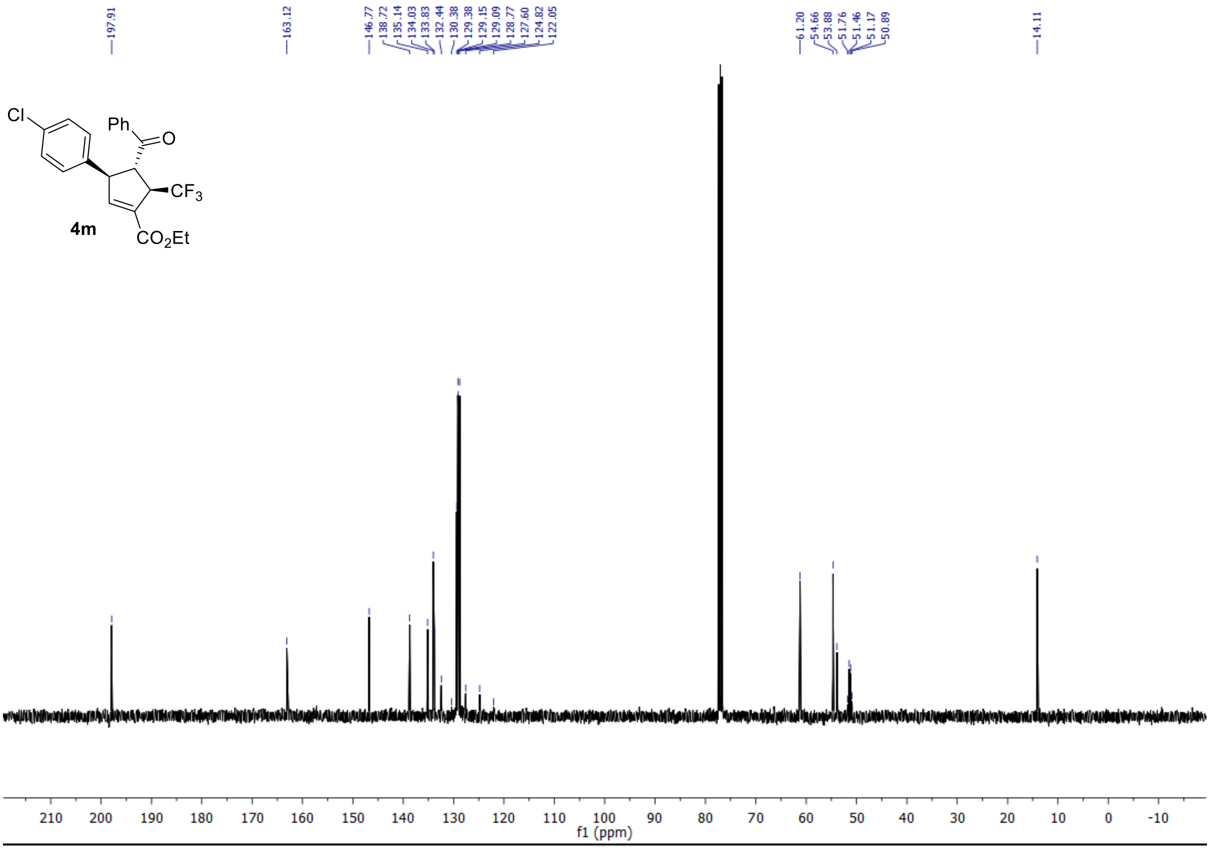

-67.43
Ph
O
CF_3
4k
CO_2Et
f1 (ppm)

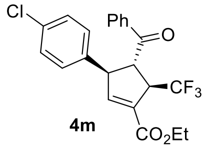

S
O
Ph
CF_3
4l
CO_2Et
f1 (ppm)


190.97
163.22
147.60
142.84
140.32
135.68
133.62
131.88
130.36
129.03
128.29
127.99
127.93
127.58
124.80
122.02
61.12
55.74
55.58
52.17
51.88
51.59
51.30
14.11
Ph
S
O
CF3
4l
CO2Et
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)

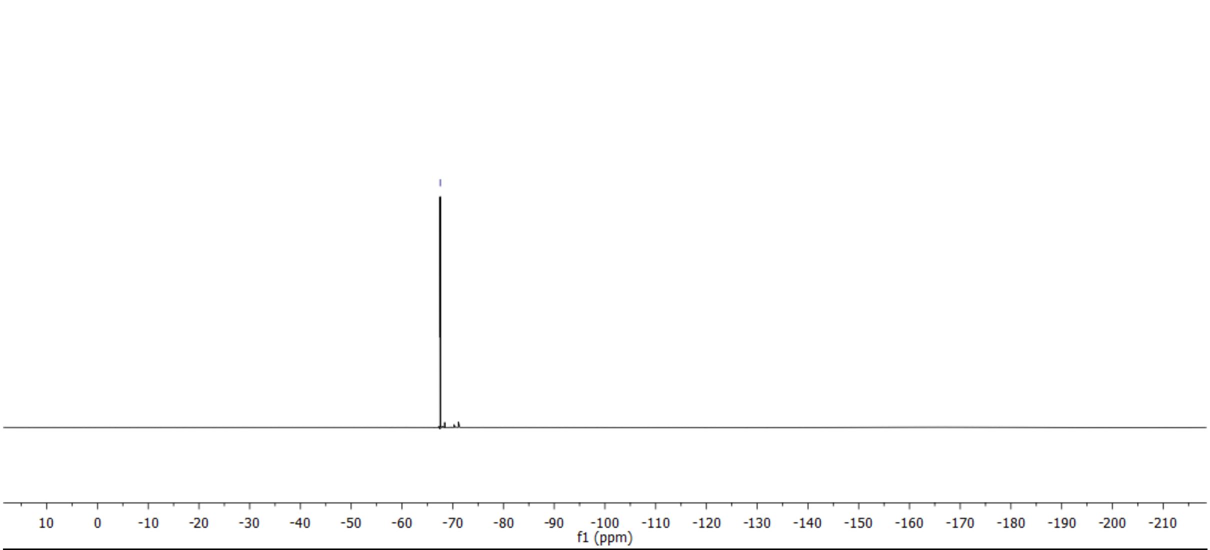

-67.60
Ph
S
O
CF3
4l
CO2Et
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

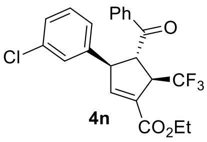




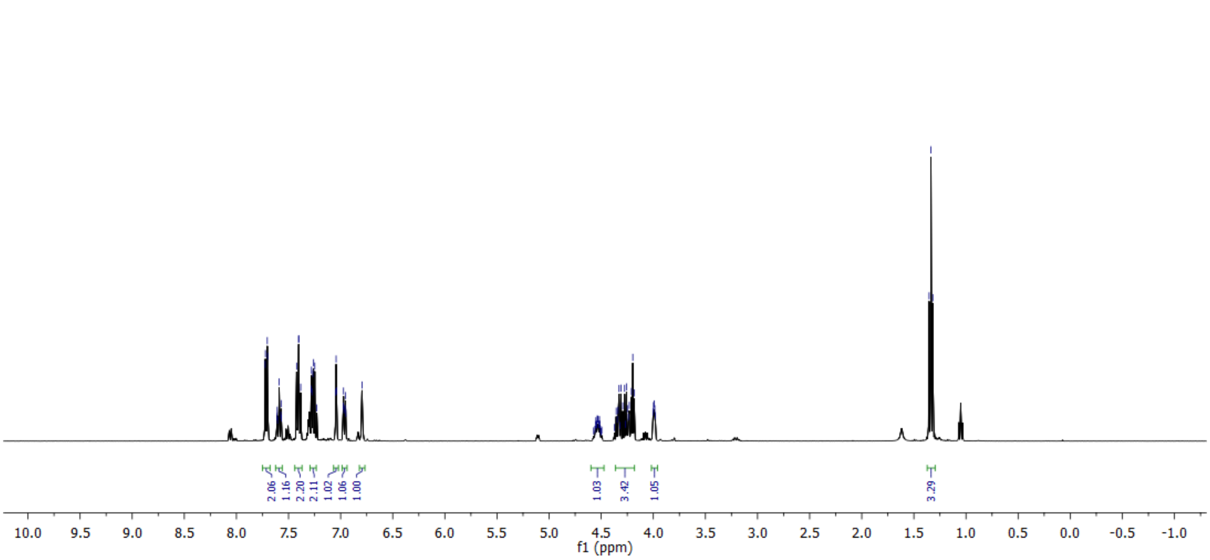


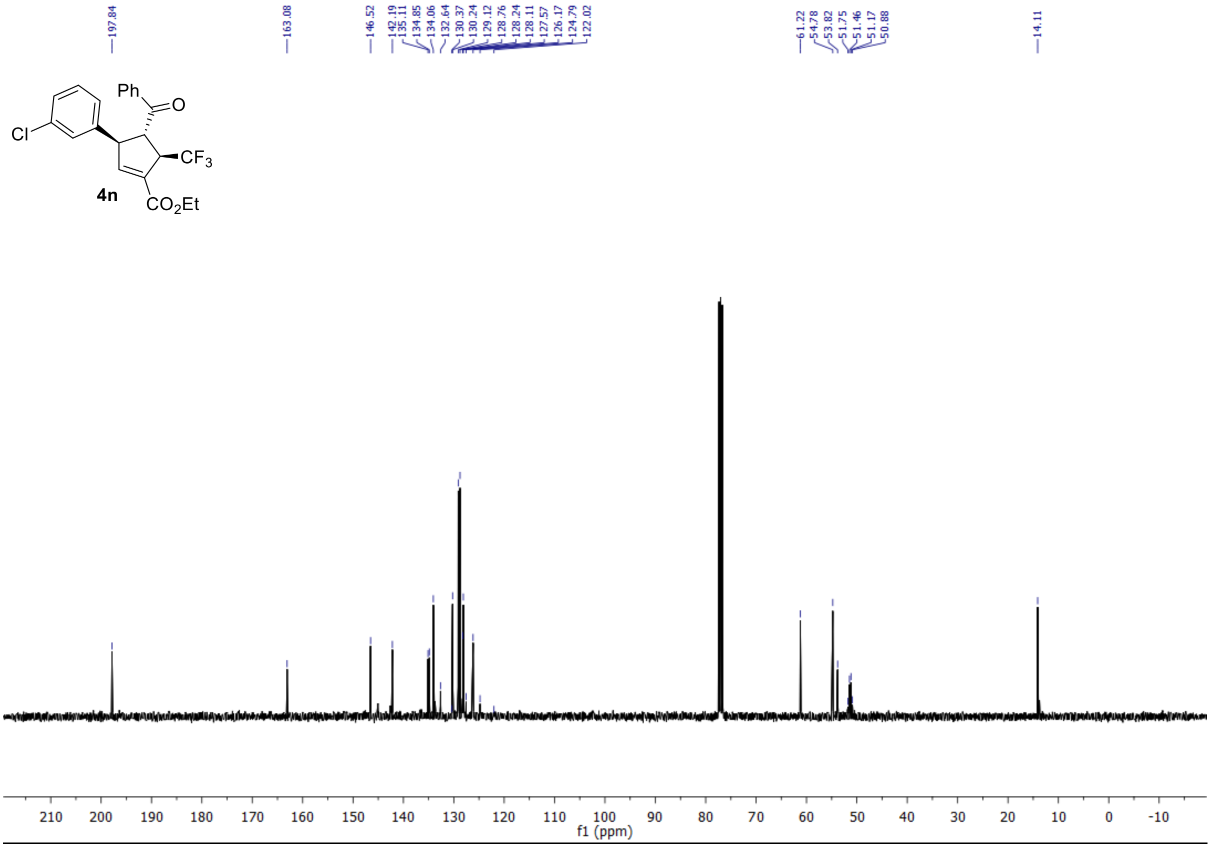
4m

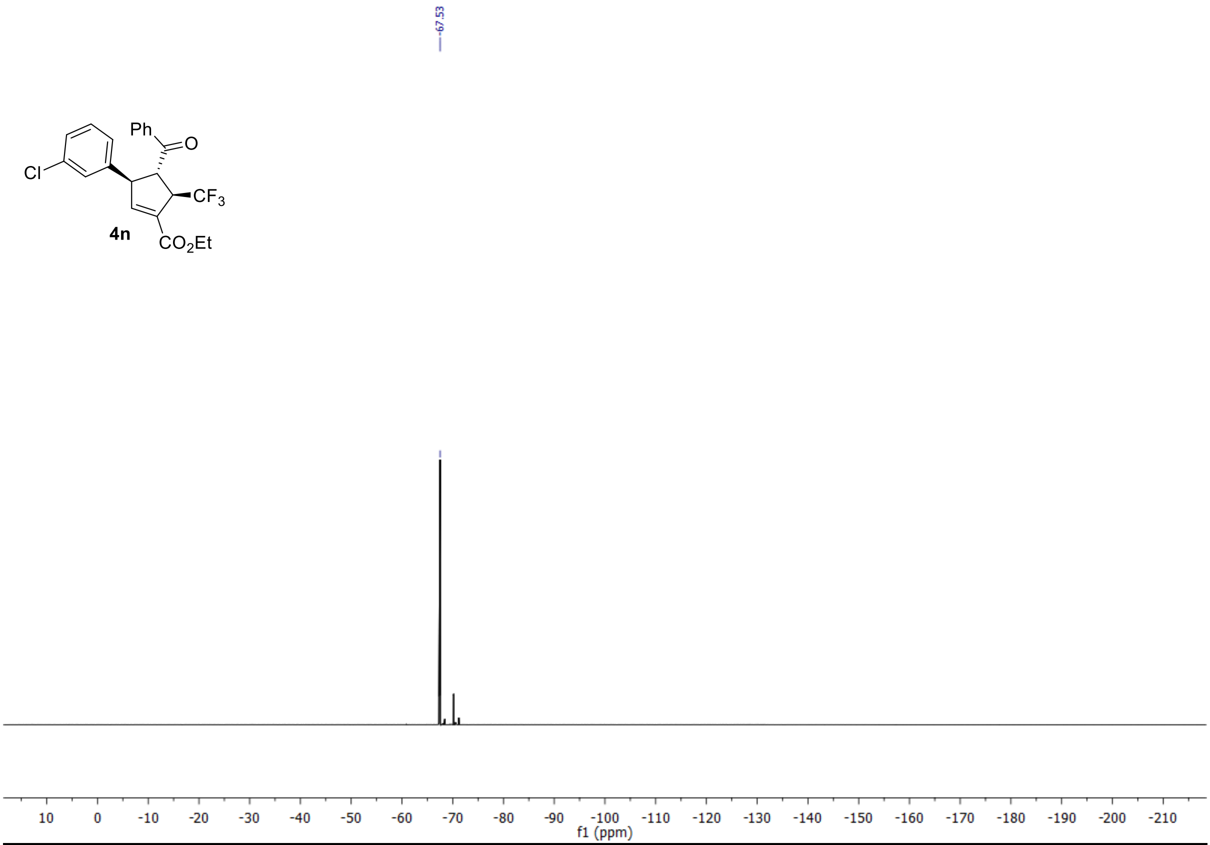


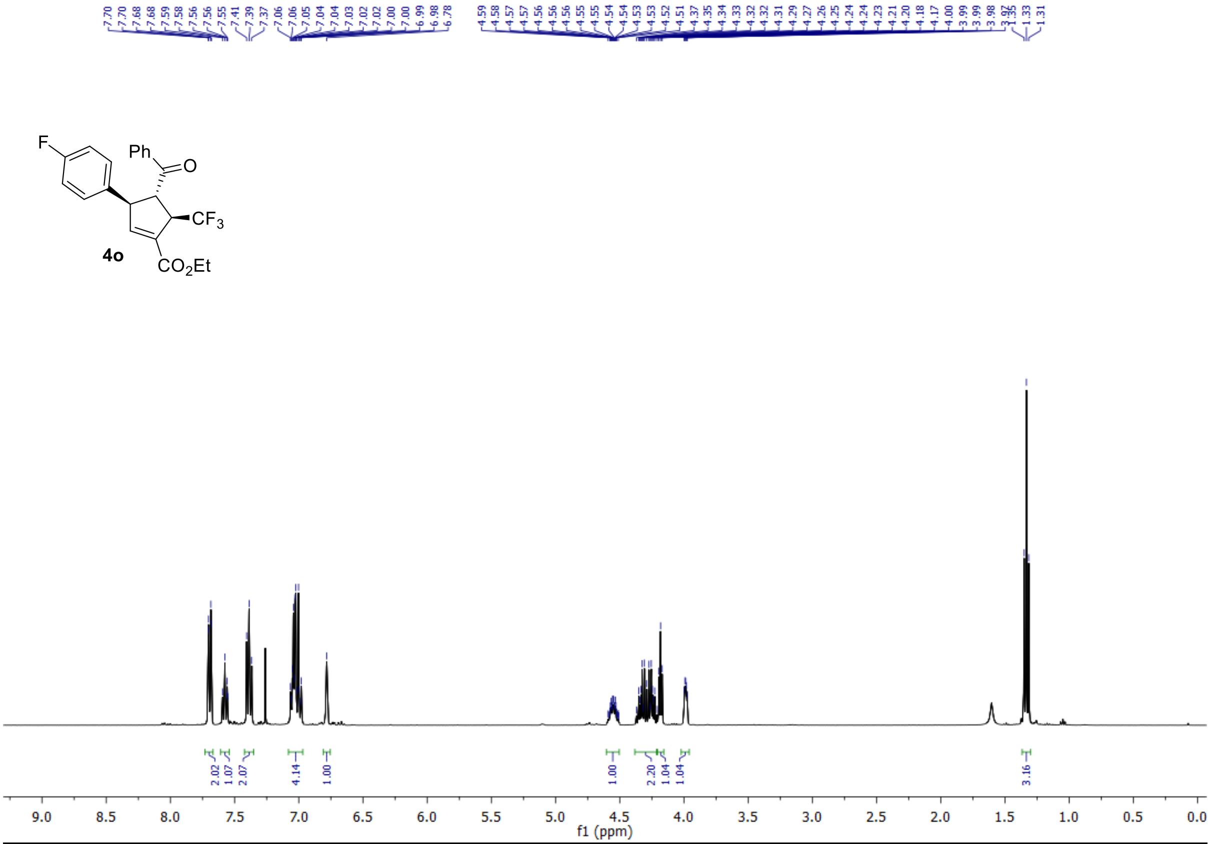


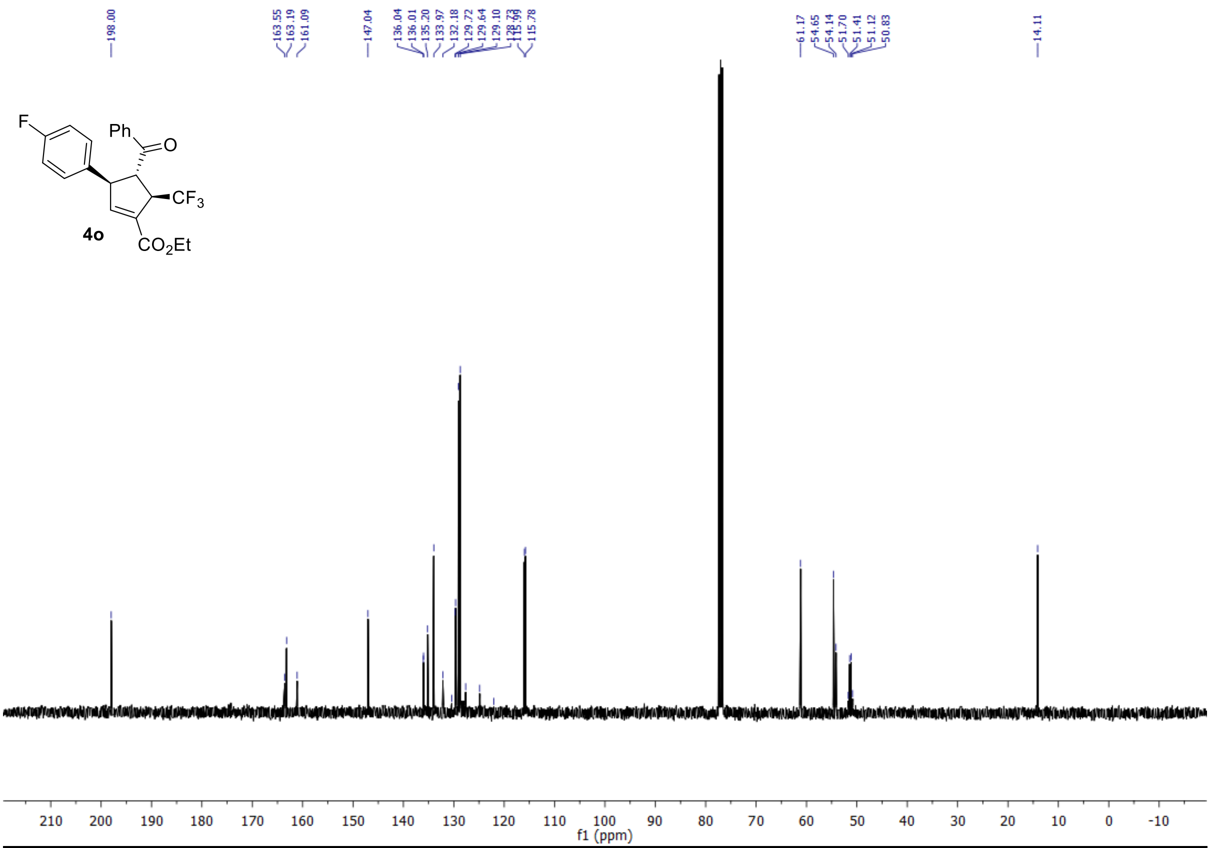
4n

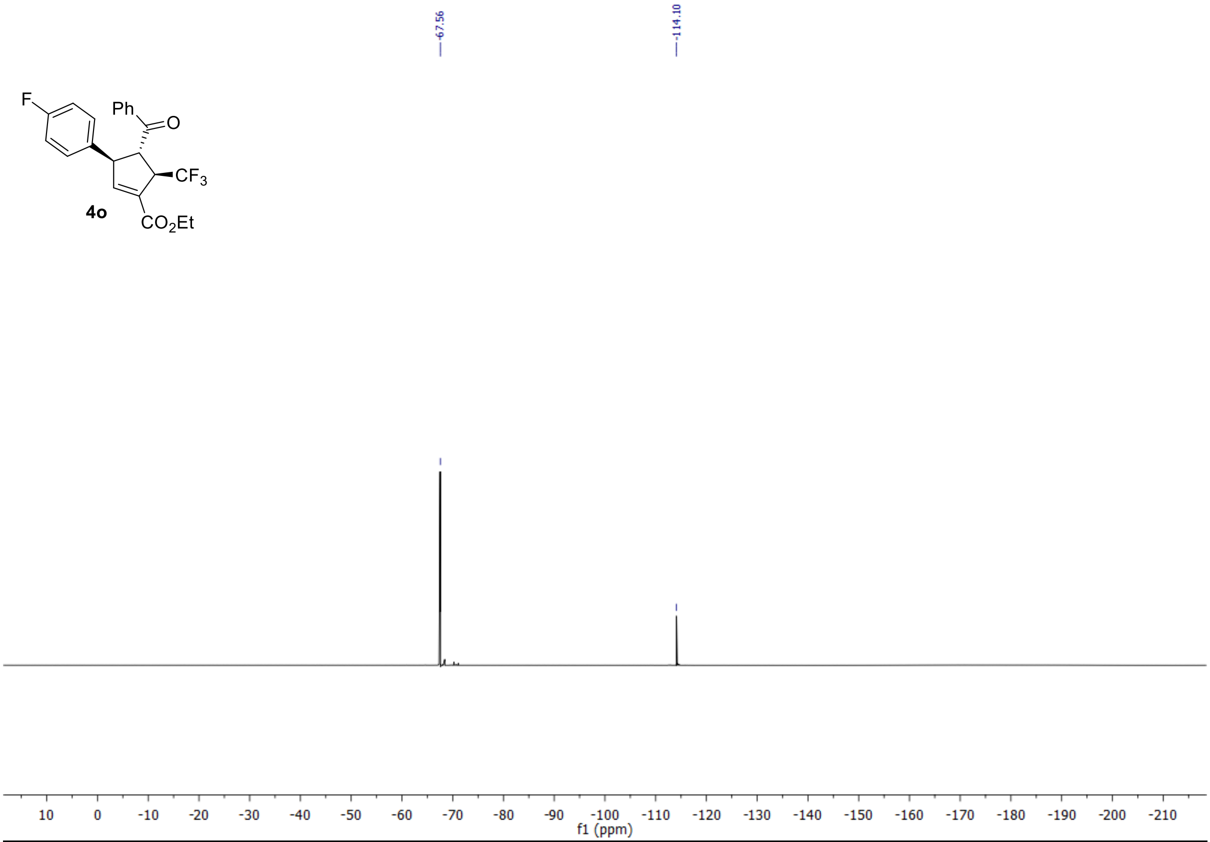


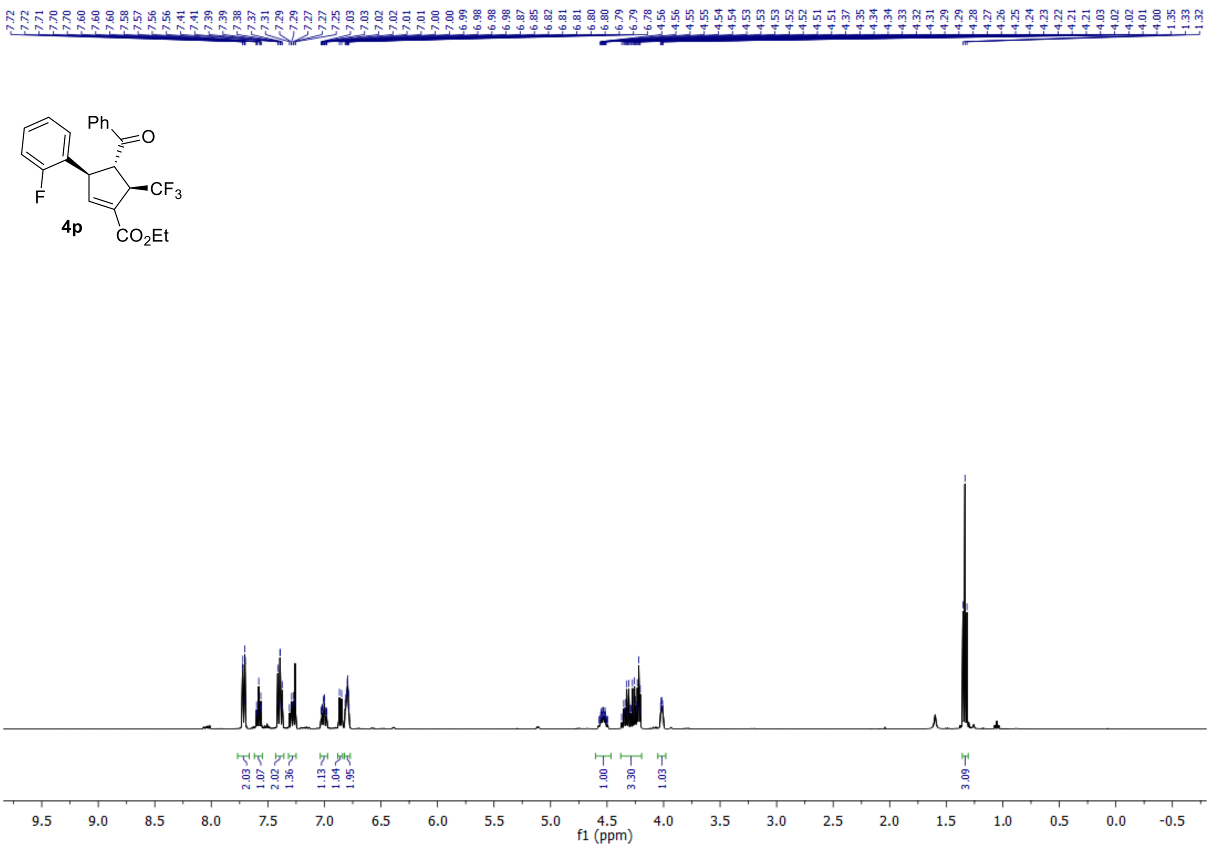

197.84
163.08
146.52
142.19
135.11
134.85
134.06
132.64
130.37
130.24
129.12
128.76
128.24
128.11
127.57
126.17
124.79
122.02
61.22
54.78
53.82
51.75
51.46
51.17
50.88
14.11
Ph
O
Cl
CF_3
4n
CO_2Et
f1 (ppm)

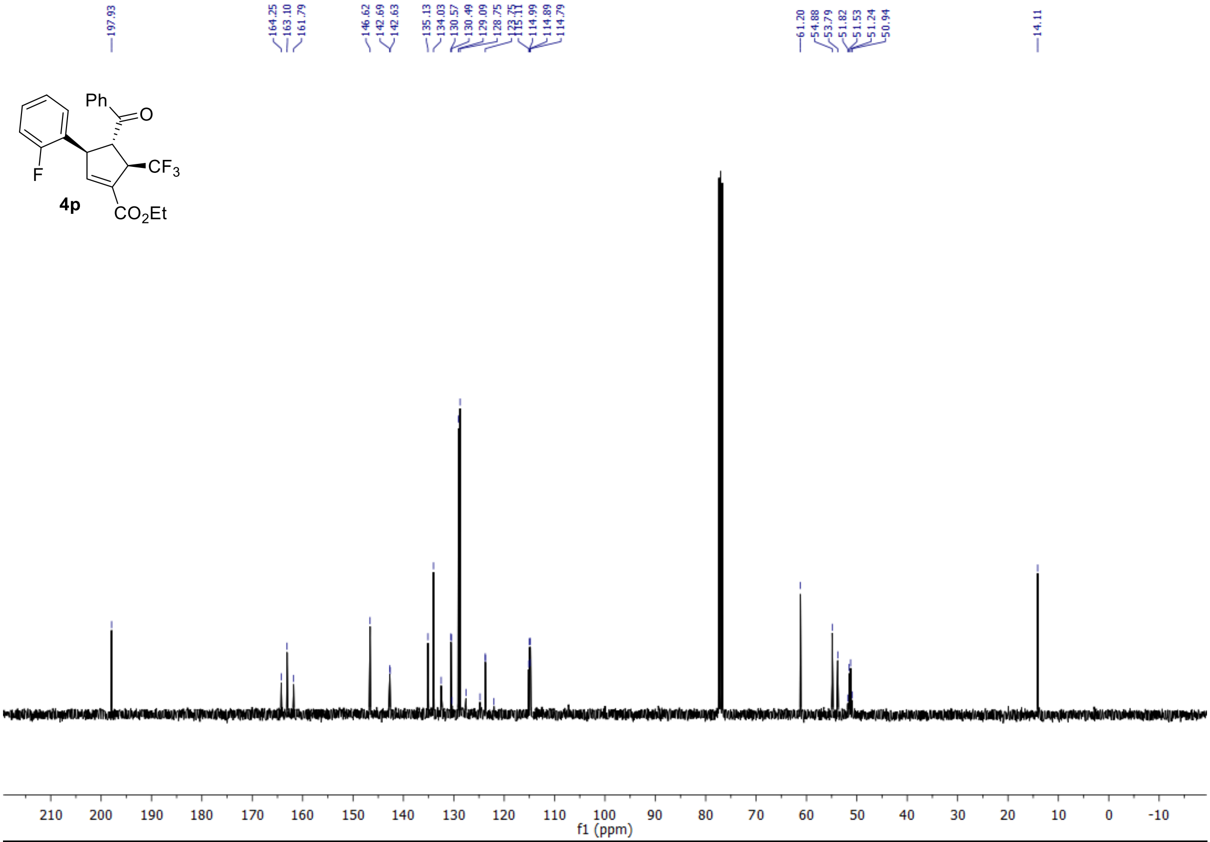

-67.53
Ph
O
Cl
CF_3
4n
CO_2Et
f1 (ppm)

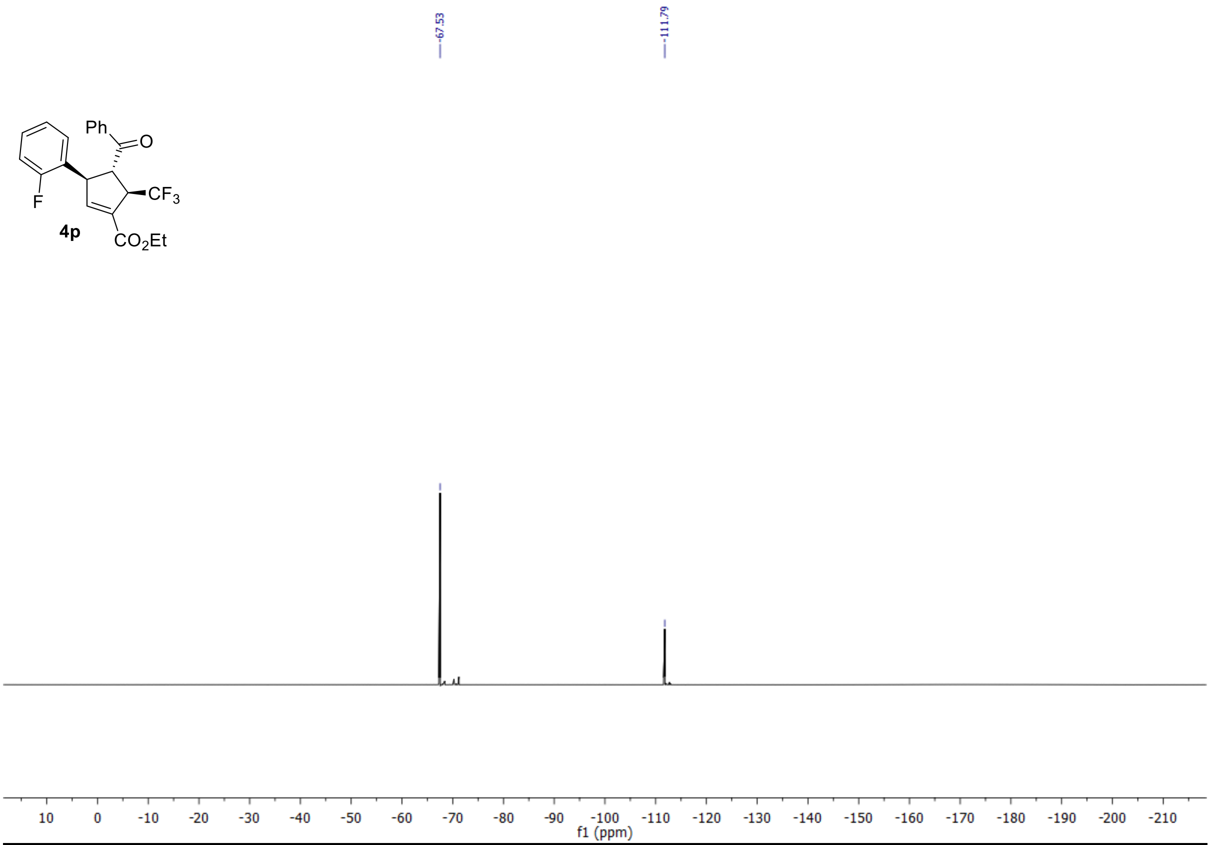

F
Ph
O
CF3
4o
CO2Et
f1 (ppm)

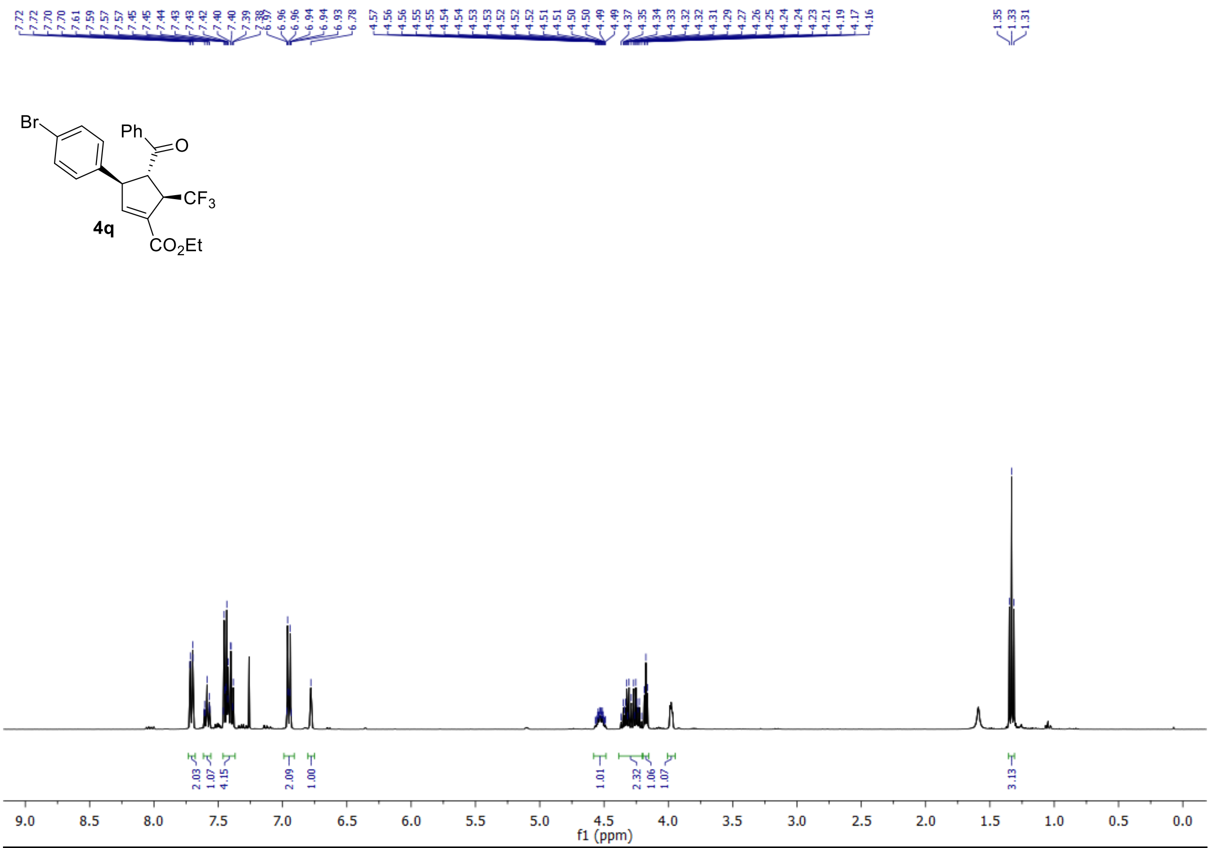

F
Ph
O
CF3
4o
CO2Et
f1 (ppm)

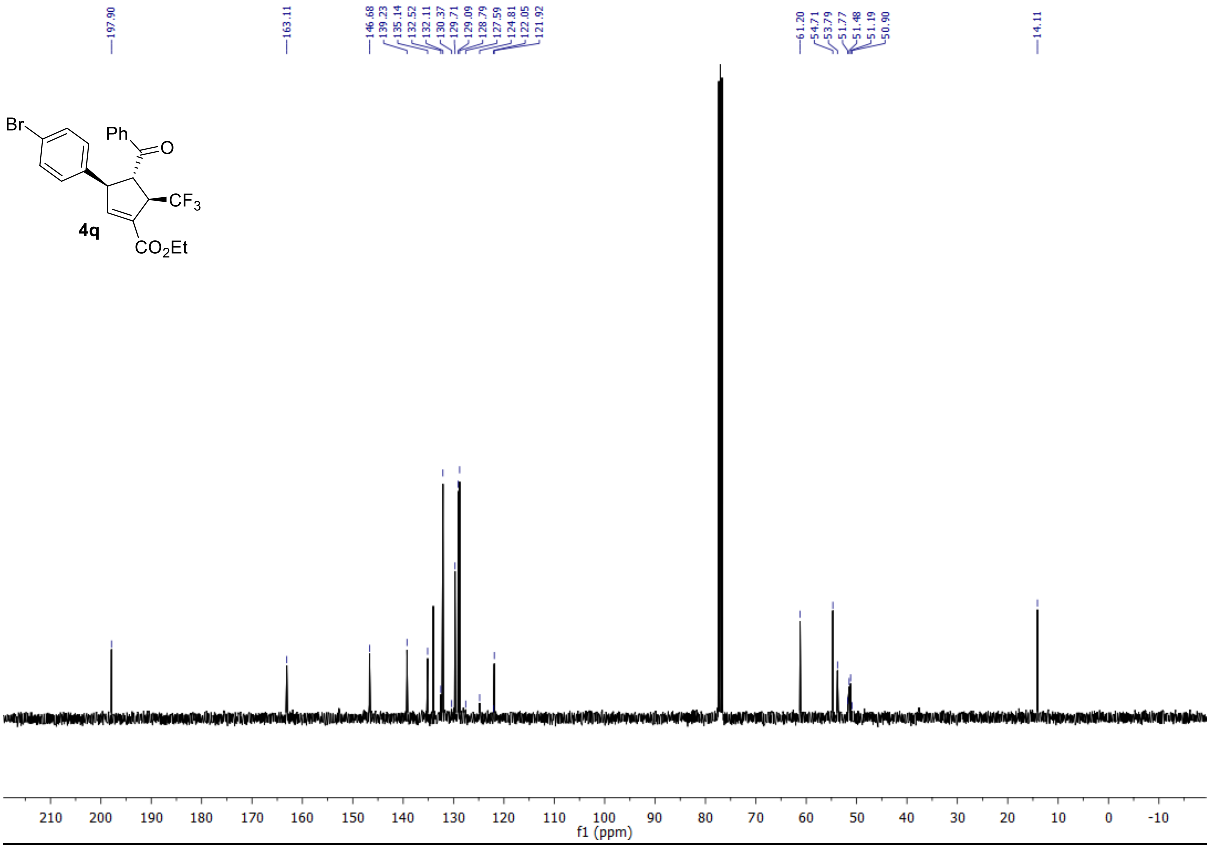

-67.56
-114.10
F
Ph
O
CF3
4o
CO2Et
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

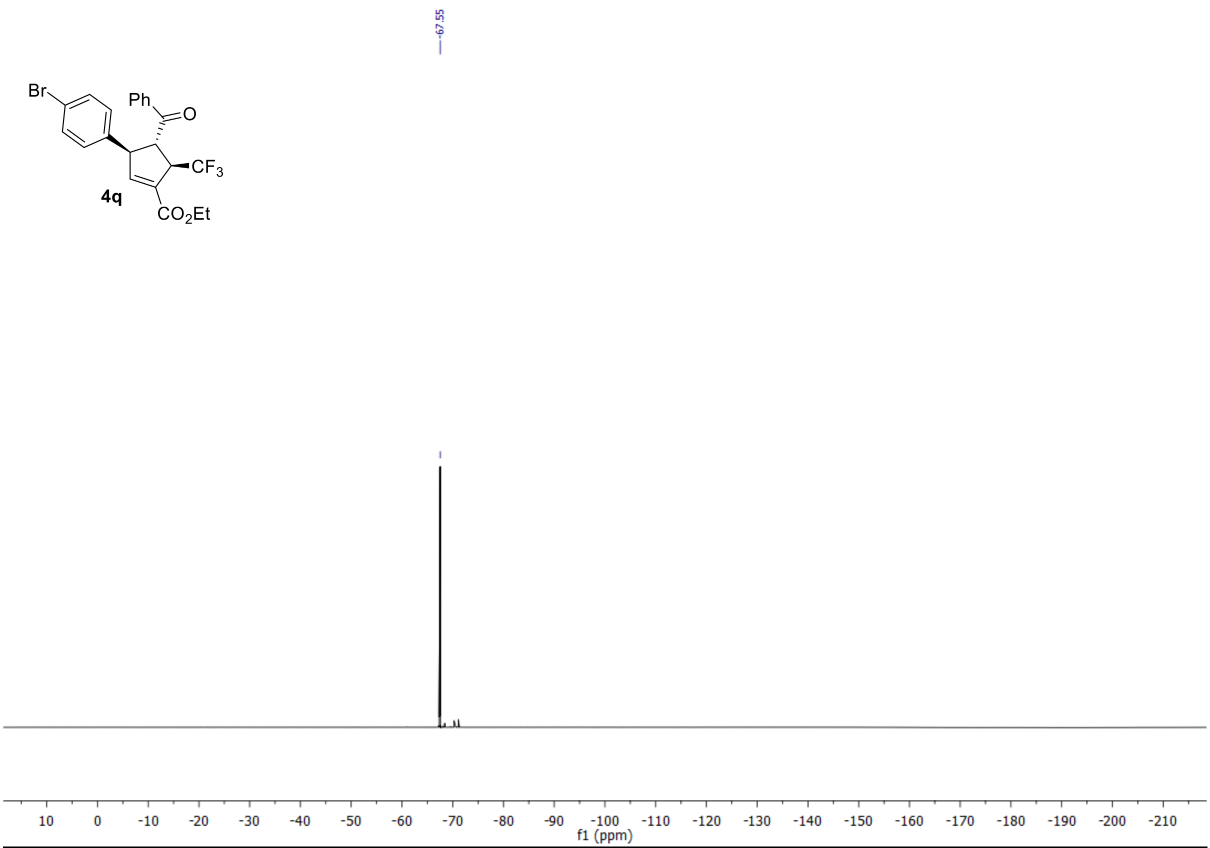

7.72 7.72 7.71 7.70 7.70 7.60 7.60 7.58 7.57 7.56 7.56 7.41 7.41 7.39 7.39 7.38 7.37 7.31 7.29 7.29 7.27 7.27 7.25 7.03 7.03 7.02 7.02 7.01 7.01 7.00 7.00 6.99 6.98 6.98 6.87 6.85 6.82 6.81 6.81 6.80 6.80 6.79 6.79 6.78 4.56 4.56 4.55 4.55 4.54 4.54 4.53 4.53 4.53 4.52 4.52 4.51 4.51 4.37 4.35 4.34 4.34 4.33 4.32 4.31 4.29 4.29 4.28 4.27 4.26 4.25 4.24 4.23 4.22 4.21 4.21 4.03 4.02 4.02 4.01 4.00 1.35 1.33 1.32
Ph
O
CF3
F
4p
CO2Et
2.03 1.07 2.02 1.36 1.13 1.04 1.95 1.00 3.30 1.03 3.09
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

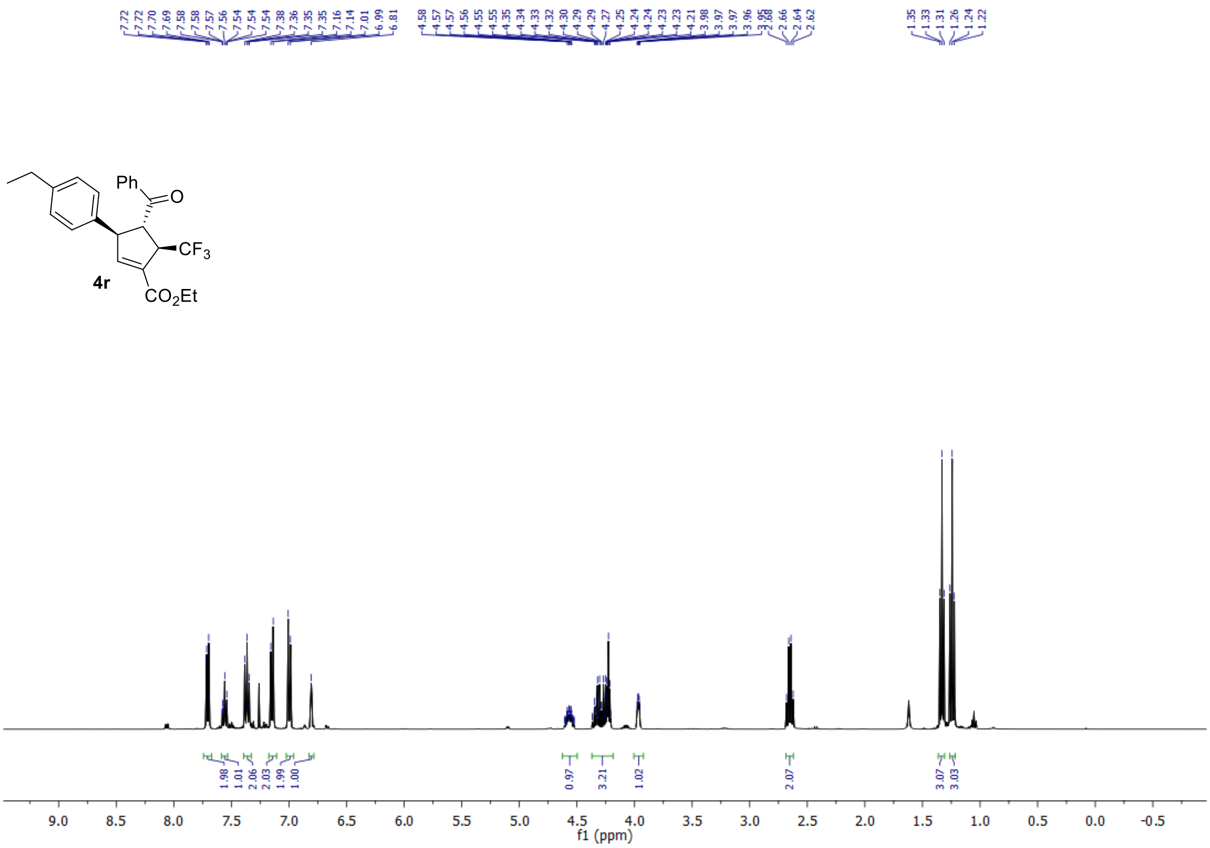

197.93
164.25
163.10
161.79
146.62
142.69
142.63
135.13
134.03
130.57
130.49
129.09
128.75
114.99
114.89
114.79
61.20
54.88
53.79
51.82
51.53
51.24
50.94
14.11
Ph
O
F
CF_3
4p
CO_2Et
f1 (ppm)

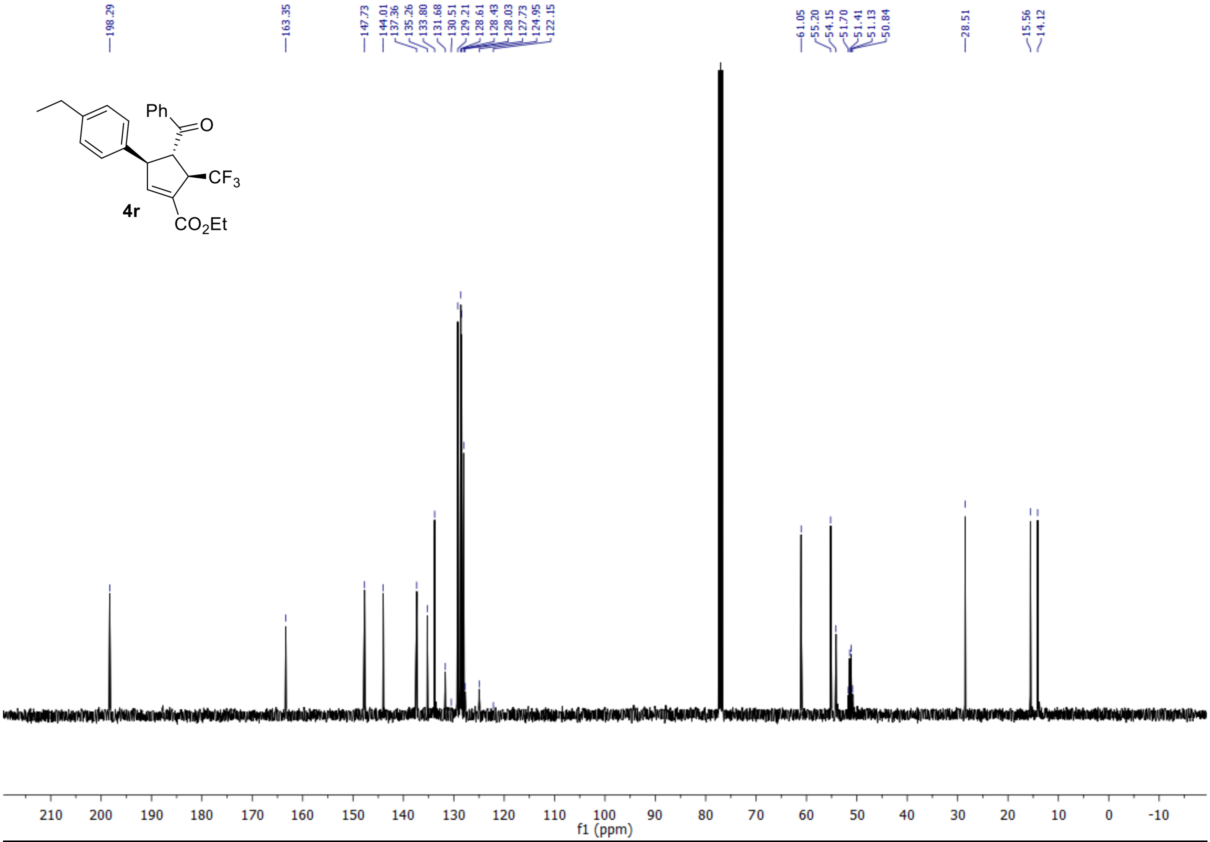

-67.53
-111.79
Ph
O
F
CF_3
4p
CO_2Et
f1 (ppm)

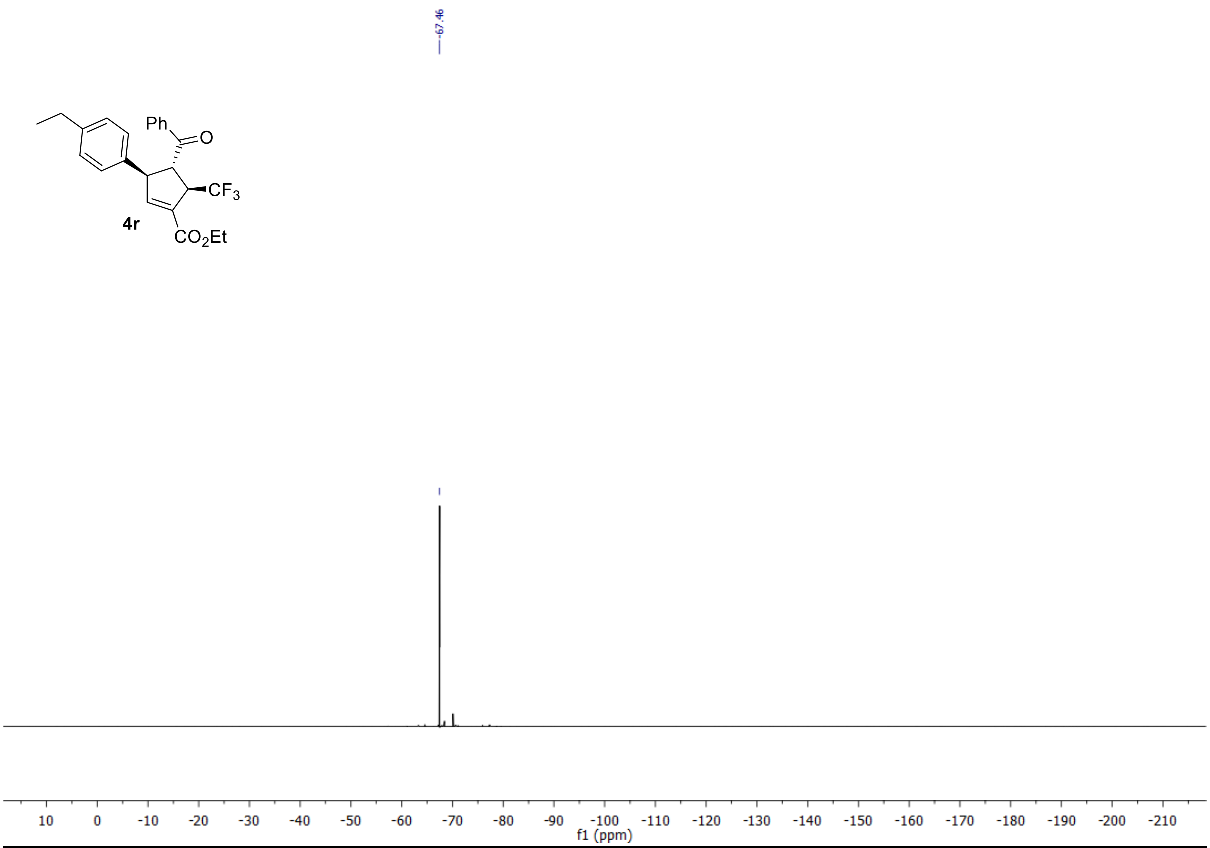

Br
Ph
O
CF3
4q
CO2Et
2.03
1.07
4.15
2.09
1.00
1.01
2.32
1.06
1.07
3.13
f1 (ppm)

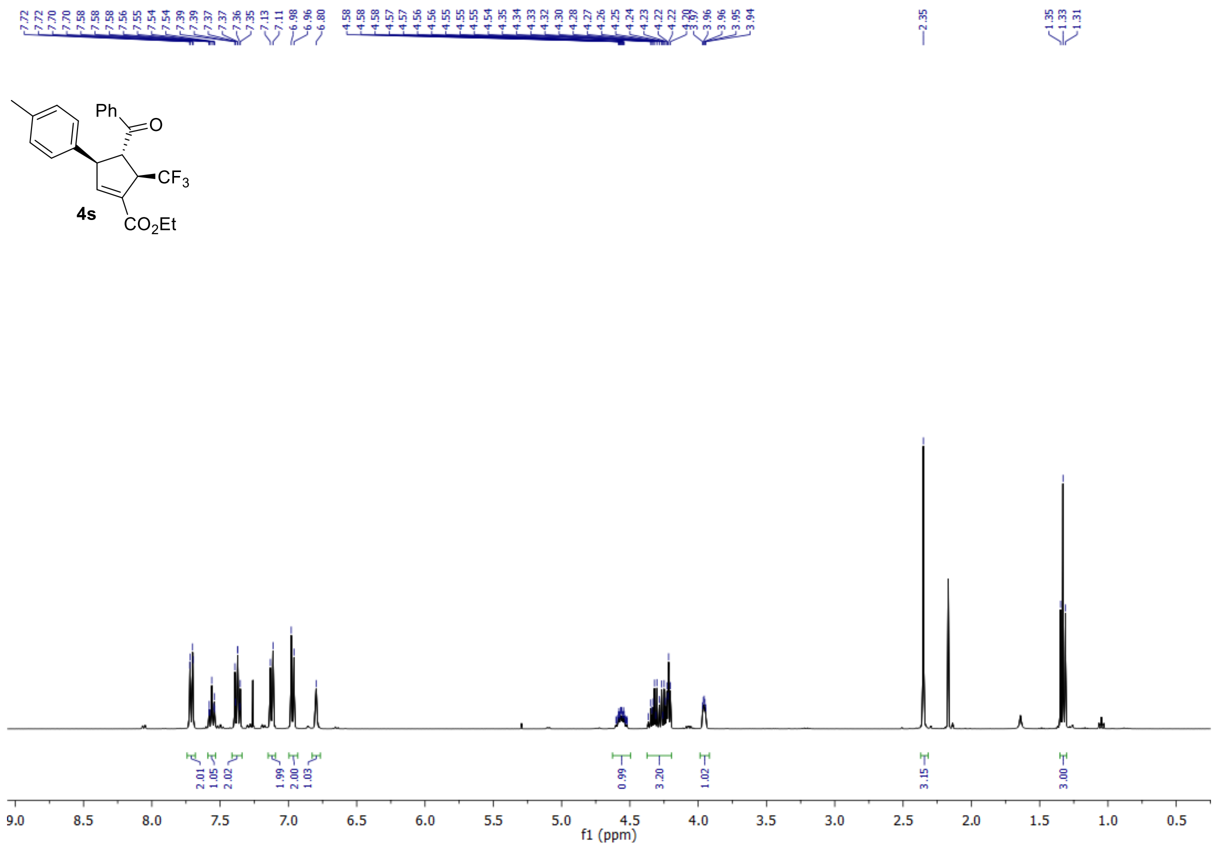

197.90
163.11
146.68
139.23
135.14
132.52
132.11
130.37
129.71
129.09
128.79
127.59
124.81
122.05
121.92
61.20
54.71
53.79
51.77
51.48
51.19
50.90
14.11
Br
Ph
O
CF3
4q
CO2Et
f1 (ppm)


-67.55
Br
Ph
O
CF3
4q
CO2Et
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

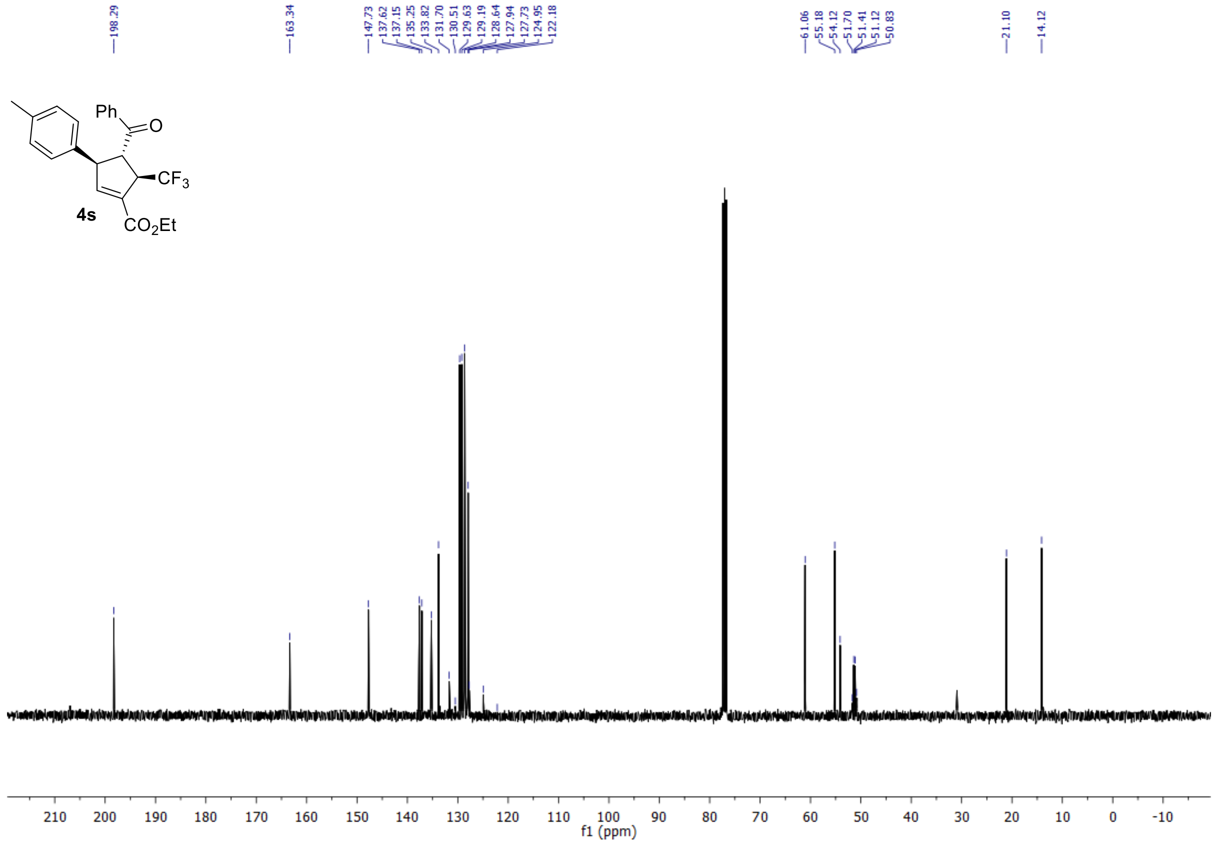

7.72 7.72 7.70 7.69 7.58 7.58 7.57 7.56 7.54 7.54 7.54 7.38 7.36 7.35 7.35 7.16 7.14 7.01 6.99 6.81
4.58 4.57 4.57 4.56 4.55 4.35 4.34 4.33 4.32 4.30 4.29 4.27 4.25 4.24 4.24 4.23 4.21 3.98 3.97 3.96 3.95 2.68 2.66 2.64 2.62
1.35 1.33 1.31 1.26 1.24 1.22
Ph
O
CF3
4r
CO2Et
1.98 1.01 2.06 2.03 1.99 1.00
0.97 3.21 1.02
2.07
3.07 3.03
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


198.29
163.35
147.73
144.01
137.36
135.26
133.80
131.68
130.51
129.21
128.61
128.43
128.03
127.73
124.95
122.15
61.05
55.20
54.15
51.70
51.41
51.13
50.84
28.51
15.56
14.12
Ph
O
CF_3
4r
CO_2Et
f1 (ppm)

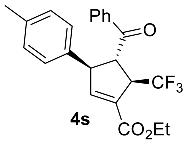

-67.46
Ph
O
CF_3
4r
CO_2Et
f1 (ppm)



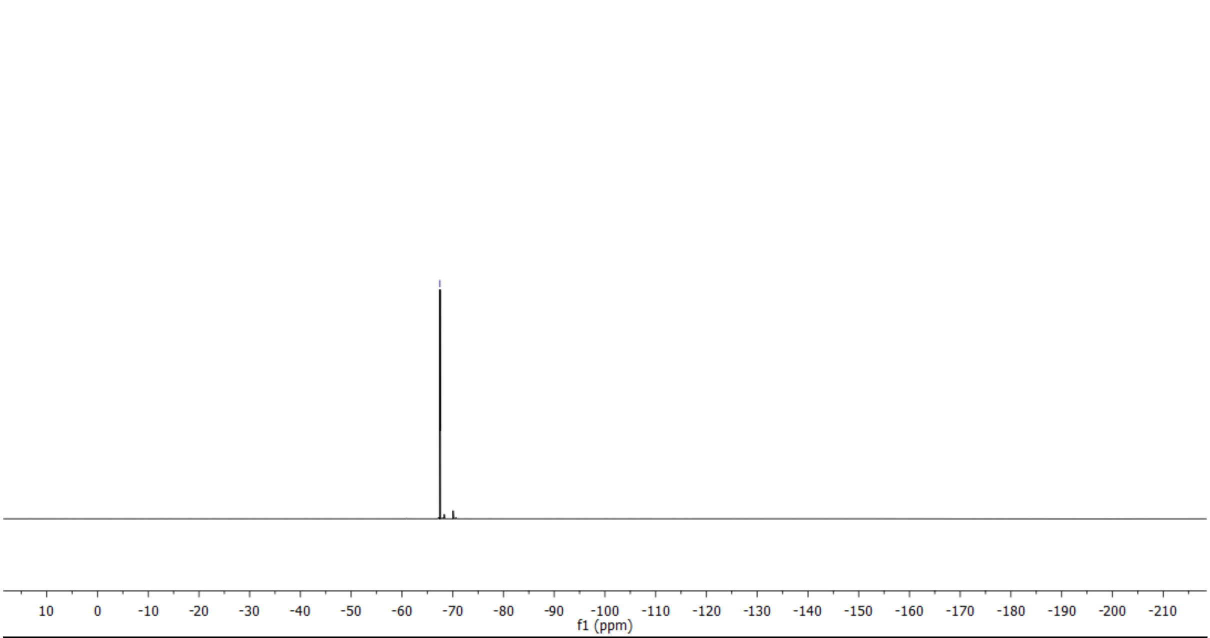
7.72 7.72 7.70 7.70 7.58 7.58 7.58 7.56 7.55 7.54 7.54 7.39 7.39 7.37 7.37 7.36 7.35 7.13 7.11 6.98 6.96 6.80 4.58 4.58 4.58 4.57 4.57 4.56 4.56 4.55 4.55 4.55 4.54 4.35 4.34 4.33 4.32 4.30 4.28 4.27 4.26 4.25 4.24 4.23 4.22 4.22 4.20 3.97 3.96 3.96 3.95 3.94 2.35 1.35 1.33 1.31
Ph
O
CF3
4s
CO2Et
2.01 1.05 2.02 1.99 2.00 1.03 0.99 3.20 1.02 3.15 3.00
f1 (ppm)

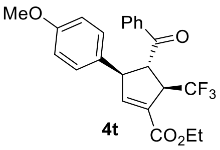


198.29 163.34 147.73 137.62 137.15 135.25 133.82 131.70 130.51 129.63 129.19 128.64 127.94 127.73 124.95 122.18 61.06 55.18 54.12 51.70 51.41 51.12 50.83 21.10 14.12
Ph
O
CF3
4s
CO2Et
f1 (ppm)

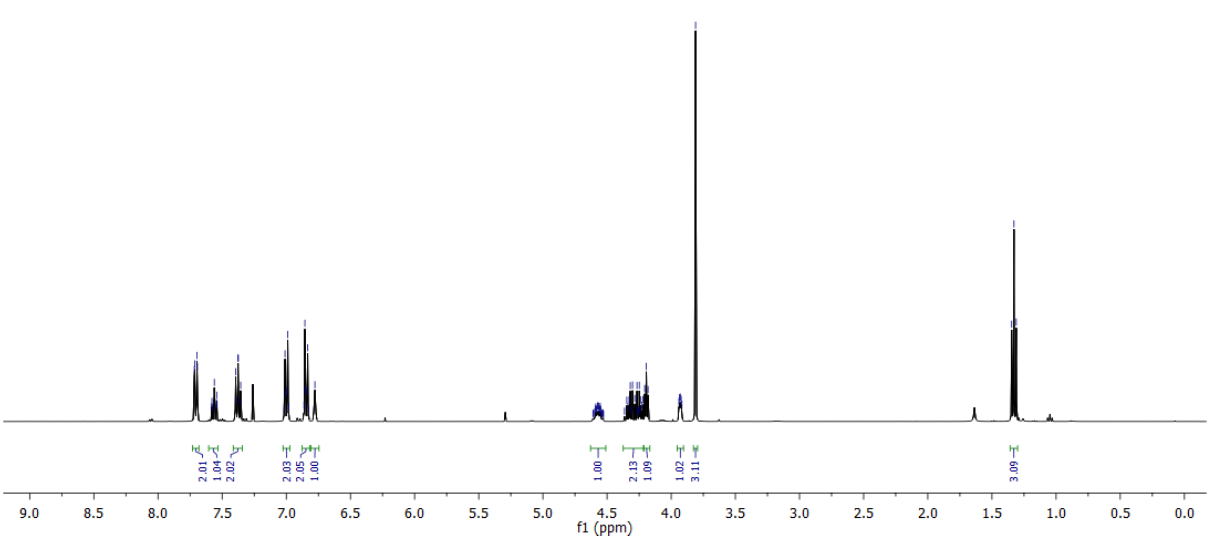

Ph
O
CF3
CO2Et

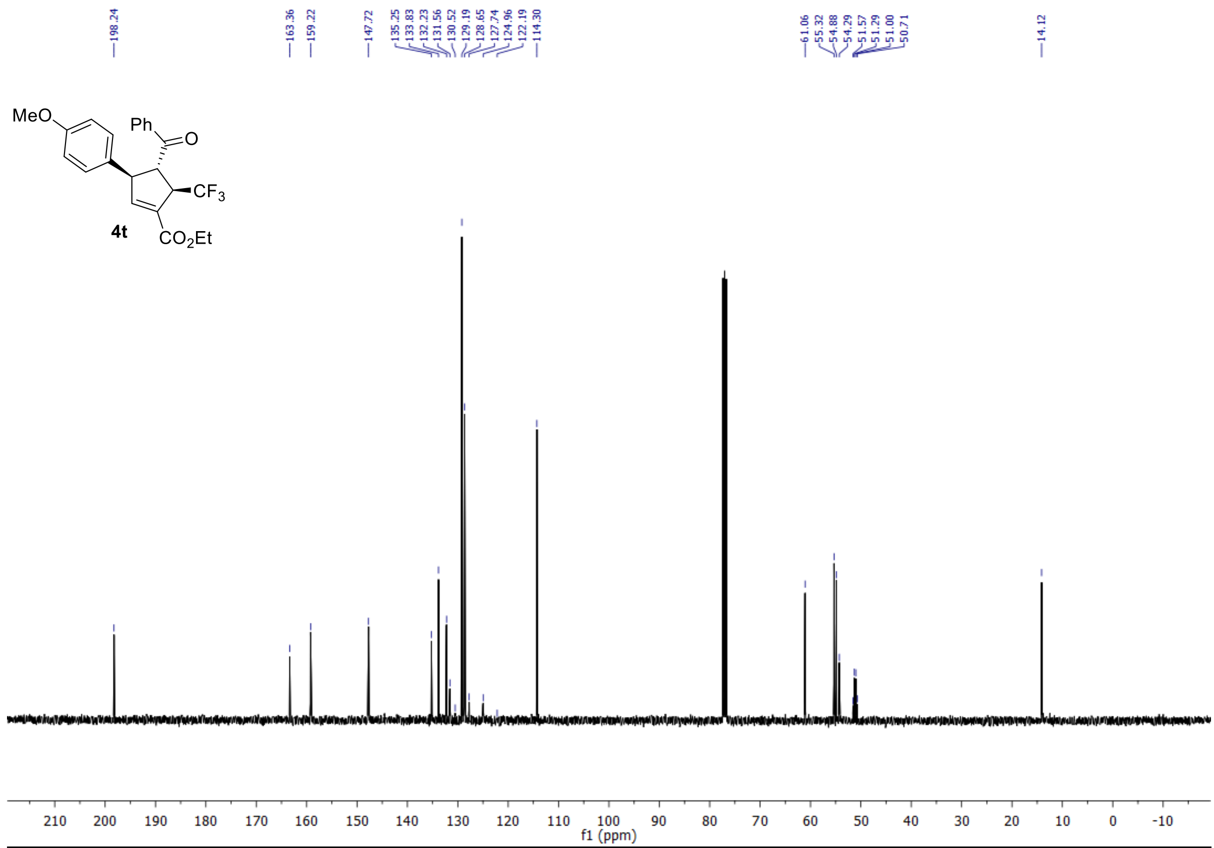
4s

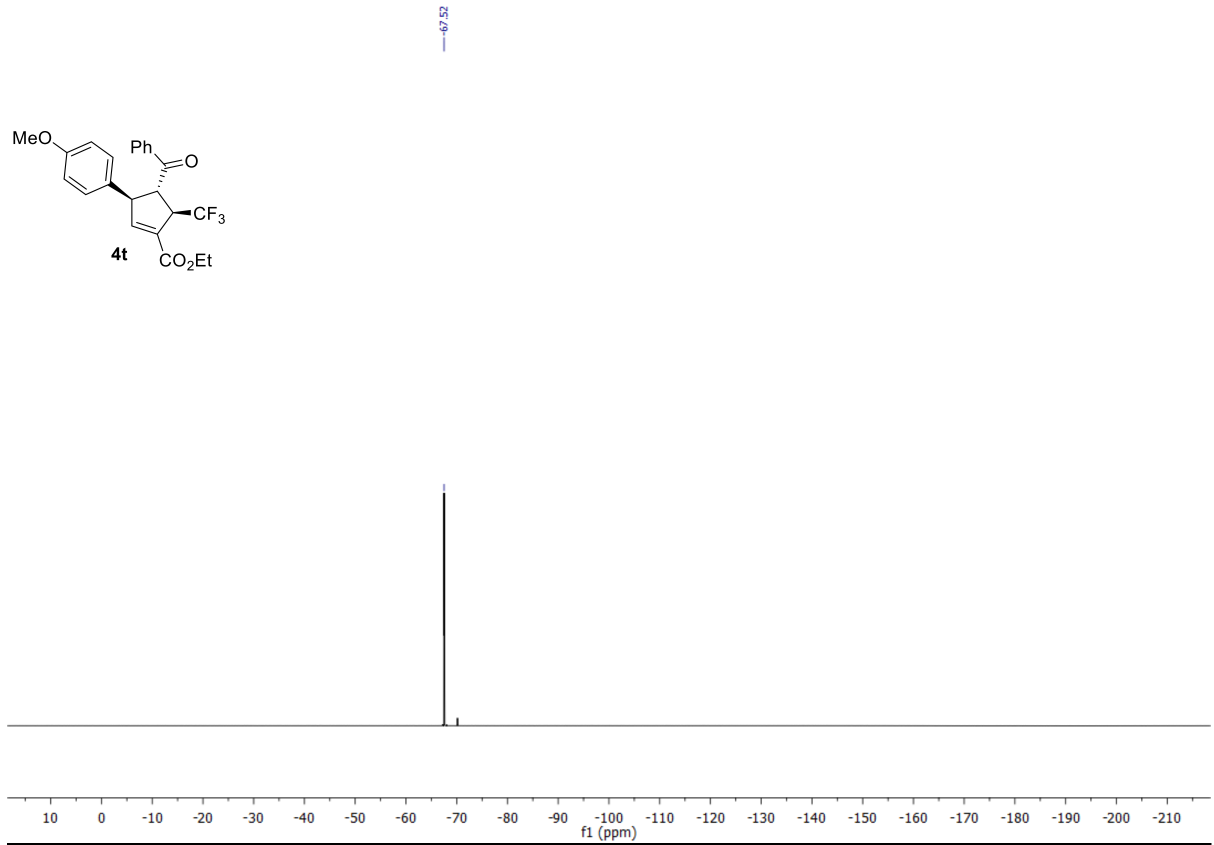

-67.48
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

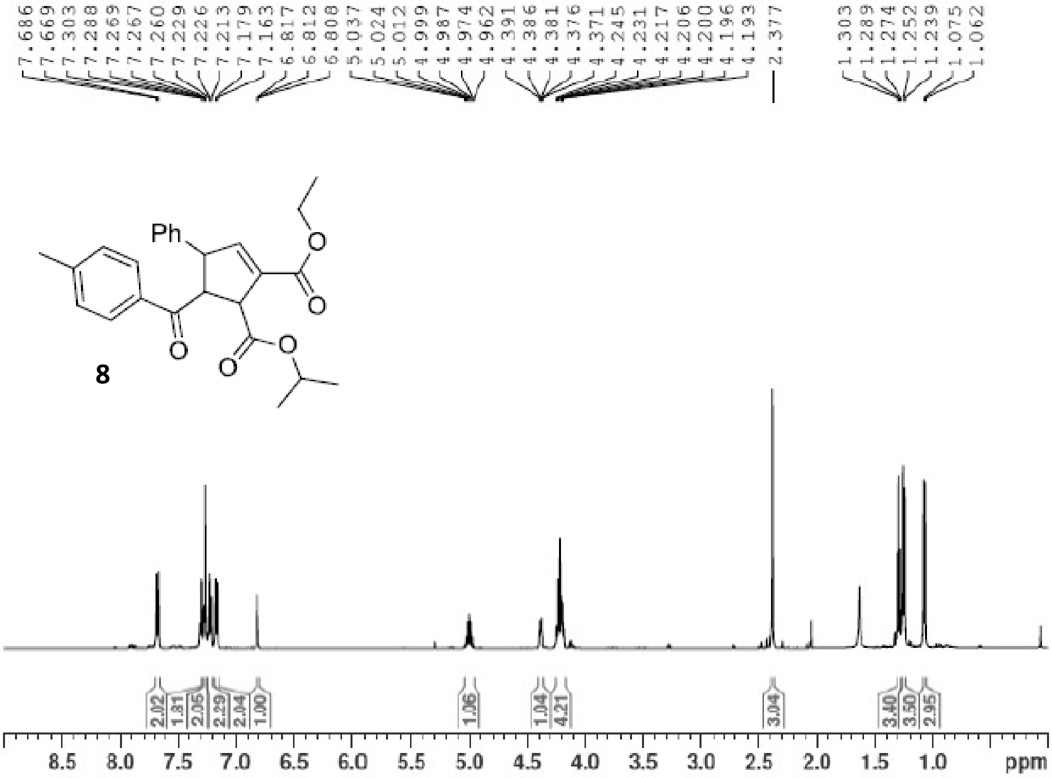

MeO
Ph
O
CF3
CO2Et

4t

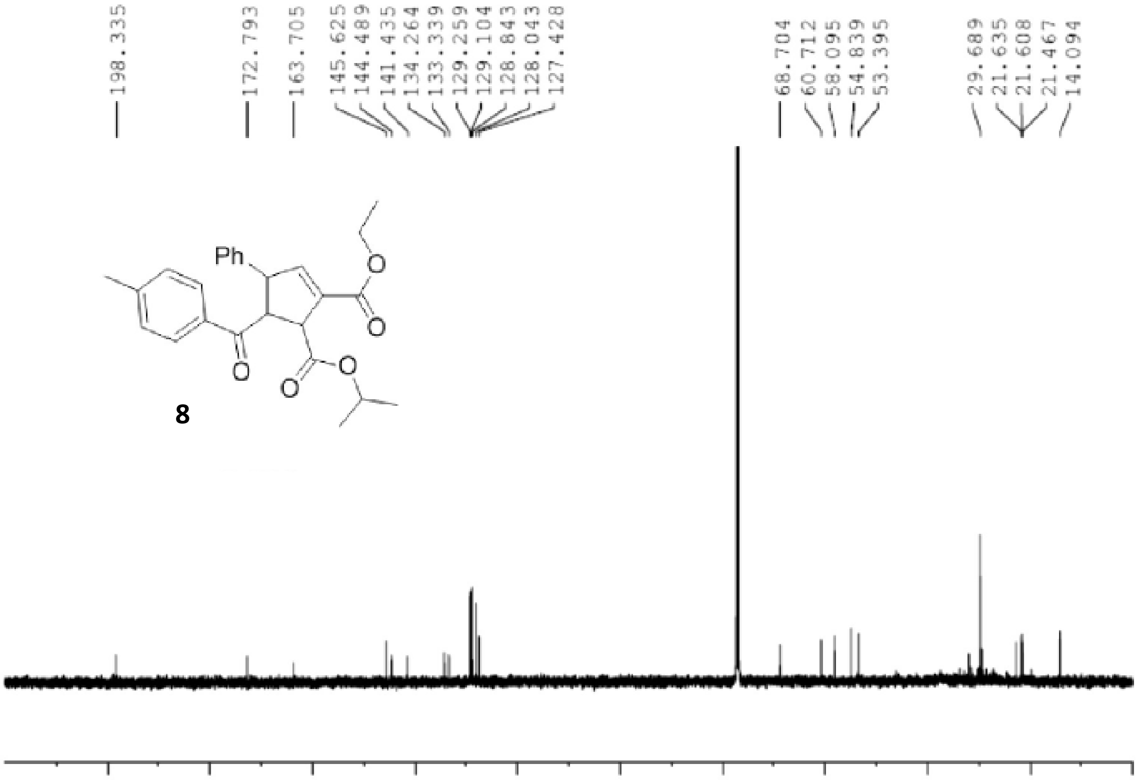

7.72 7.71 7.70 7.69 7.58 7.58 7.58 7.56 7.55 7.54 7.54 7.39 7.38 7.37 7.36 7.36 7.02 7.01 7.00 6.99 6.99 6.98 6.86 6.85 6.85 6.84 6.83 6.83 6.78 4.58 4.57 4.35 4.33 4.32 4.30 4.28 4.27 4.25 4.24 4.23 4.22 4.21 4.19 4.18 3.94 3.93 3.93 3.92 3.92 3.81 1.35 1.33 1.31
2.01 1.04 2.02 2.03 2.05 1.00 1.00 2.13 1.09 1.02 3.11 3.09
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


198.24
163.36
159.22
147.72
135.25
133.83
132.23
131.56
130.52
129.19
128.65
127.74
124.96
122.19
114.30
61.06
55.32
54.88
54.29
51.57
51.29
51.00
50.71
14.12
MeO
Ph
O
CF3
4t
CO2Et
f1 (ppm)


-67.52
MeO
Ph
O
CF3
4t
CO2Et
f1 (ppm)


7.686
7.669
7.303
7.288
7.269
7.267
7.260
7.229
7.226
7.213
7.179
7.163
6.817
6.812
6.808
5.037
5.024
5.012
4.999
4.987
4.974
4.962
4.391
4.386
4.381
4.376
4.371
4.245
4.231
4.217
4.206
4.200
4.196
4.193
2.377
1.303
1.289
1.274
1.252
1.239
1.075
1.062
Ph
2.02
1.81
2.05
2.29
2.04
1.00
1.06
1.04
4.21
3.04
3.40
3.50
2.95
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

8


198.335
172.793
163.705
145.625
144.489
141.435
134.264
133.339
129.259
129.104
128.843
128.043
127.428
68.704
60.712
58.095
54.839
53.395
29.689
21.635
21.608
21.467
14.094
Ph
200
180
160
140
120
100
80
60
40
20
ppm

8