Supporting Information

Copper-Catalyzed Enantioselective Fluoroalkenylation of Cyclic Imino Esters

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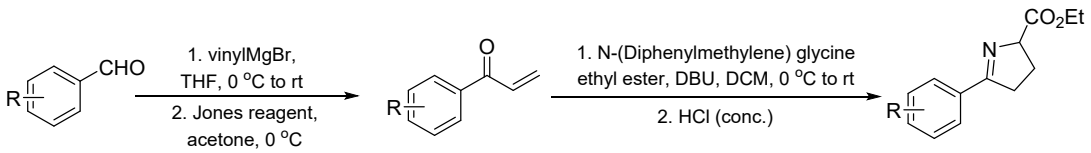
1. General information

All reactions were generally performed in dried glassware under an atmosphere of dry Ar. Reaction mixtures were monitored by thin layer chromatography (TLC) with visualization by fluorescence quenching at 254 nm. TLC was performed on SGF254 glass plates percolated with 0.15 – 0.20 mm thickness of silica gel. Flash chromatography was performed with silica gel (300-400 mesh). The substrates **1**[1], and **2** [2] were synthesized according to published procedures and the spectral data of the substrates were consisted with that reported in the literature. The others commercially available reagents were used as received without further purification. Solvents used in the catalysis were distilled from appropriate drying agents. NMR spectra were recorded on a Bruker 400 spectrometer operating at 400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR and 376 MHz for ^{19}F NMR. Chemical shifts were reported in ppm relative to the central line of $CHCl_3$ (δ 7.28) for ^{1}H NMR, for ^{13}C NMR, the residual $CDCl_3$ (δ 77.2) were used as the internal standards. The coupling constants are in Hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, dd = doublet of doublet, dq = doublet of quartet, dt = doublet of quartet, t = triplet, q = quartet, m = multiplet and brs = broad singlet. Optical rotation were measured on PE polarmeter 341 and reported as $[\alpha]_D$. Enantiomeric excess was determined by HPLC analysis on Chiralpak IC column (Daicel Chemical Industries, LTD). Melting points were measured on X-4 Micro melting point apparatus. Electrospray ionization high-resolution mass spectra (ESI-HRMS) were recorded on a Waters Vion® IMS Q-TOF mass spectrometer. X-ray crystal structure analyses were performed on a Bruker D8 Venture Photon II using Cu-Kα radiation.

2. Preparation of Substrates

General procedure for 5-membered cyclic imino esters[1a]:



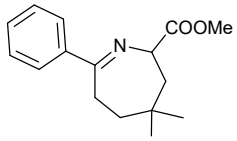
The mixture of aldehyde (8 mmol) in dry THF (10 mL) was cooled to 0 ºC in an ice-water bath and vinylmagnesium bromide (9.6 mmol, 1.0 M solution in THF) was added dropwise. The mixture was warmed to room temperature and stirred overnight. Saturated NH_4Cl solution (20 mL) was added to quench the reaction and the aqueous layer was extracted with EtOAc (20 mL×2). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was dissolved in acetone (20 mL) and cooled to 0 ºC in an ice-water bath, and then Jones reagent (2.5 M, 1.0 eq.) was added dropwise. The mixture was stirred at 0 ºC for 5 mins before isopropyl alcohol (1 mL) was added to quench the reaction. Water (50 ml) was added and the mixture was extracted with DCM (20 mL×2). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography to afford the desired vinyl ketone.

To a solution of vinyl ketone (1.1 eq.) and Schiff base (1.0 eq.) in DCM (1 M) at 0 °C was added DBU (0.1 eq.). After stirring at rt for 6 h, HCl 12 N (0.3 eq.) was added and the reaction mixture was stirred at rt overnight. Then, water was added and the mixture was extracted with DCM. The organic layers were combined, dried over Na_2SO_4, filtered and concentrated in vacuo. The crude residue was then purified by flash chromatography over silica gel.

All cyclic imino esters are known compounds and identical in the spectrum data reported by literatures.

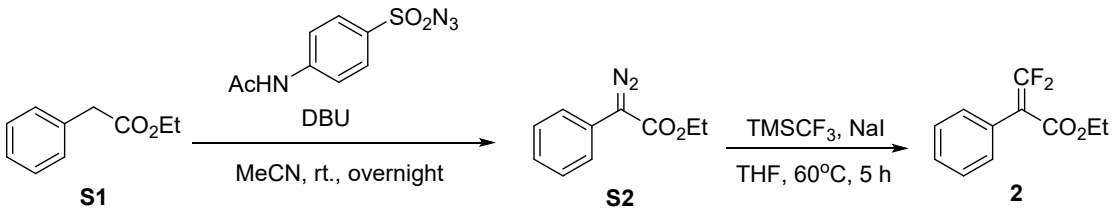
7-membered cyclic imino ester **1l** was synthesized according to the literature[1b].

methyl 4,4-dimethyl-7-phenyl-3,4,5,6-tetrahydro-2H-azepine-2-carboxylate (1l)



^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 – 7.77 (m, 2H), 7.40 – 7.28 (m, 3H), 4.38 – 4.35 (d, *J* = 10.4 Hz, 1H), 3.83 (s, 3H), 2.98 – 2.93 (m, 1H), 2.68 – 2.61 (m, 1H), 1.80 – 1.77 (m, 1H), 1.59 – 1.53 (m, 2H), 1.38 – 1.31 (m, 1H), 1.18 (s, 3H), 0.99 (s, 3H).

General procedures for difluoroacrylates 2[2]



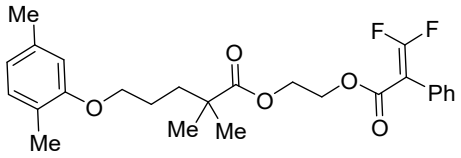
The mixture of ethyl phenylacetate **S1** (15 mmol, 1.0 eq) and 4-acetamidobenzenesulfonyl azide (2.25 mmol, 1.5 eq) in MeCN (0.25 M) was cooled to 0 ºC in an ice-water bath, then DBU (2.25 mmol, 1.5 eq) was added slowly. The mixture was warmed to room temperature and stirred overnight. Saturated NH_4Cl solution (15 mL) was added to quench the reaction and the aqueous layer was extracted with EtOAc (20 mL×2). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography to afford the desired phenyl diazoacetate **S2** (1.5 g, 53% yield).

To an oven-dried 100 mL flask equipped with a stir bar was added NaI (3.0 eq), the solid was heated at 60 °C in vacuo for 30 min (remove H_2O). Then NaI was cooled down to room temperature followed by the addition of ethyl phenyl diazoacetate **S2** (1.5 g, 1.0 eq) and $TMSCF_3$ (3.0 eq) in anhydrous THF (0.3 M) under argon. The resulting mixture was heated at 60 °C for 5 h with vigorous stirring. After cooling to room temperature, the reaction mixture was extracted with 20 mL Et_2O, washed with H_2O (20 mL) and brine (20 mL), dried over Na_2SO_4 and concentrated in

vacuo. The residue was purified by flash column chromatography on silica gel (hexane : EA = 75 : 1) to afford difluoroacrylate **2a** as a yellow oil (820 mg, 48% yield).

All difluoroacrylates except **2l** are known compounds and identical in the spectrum data reported by literatures.

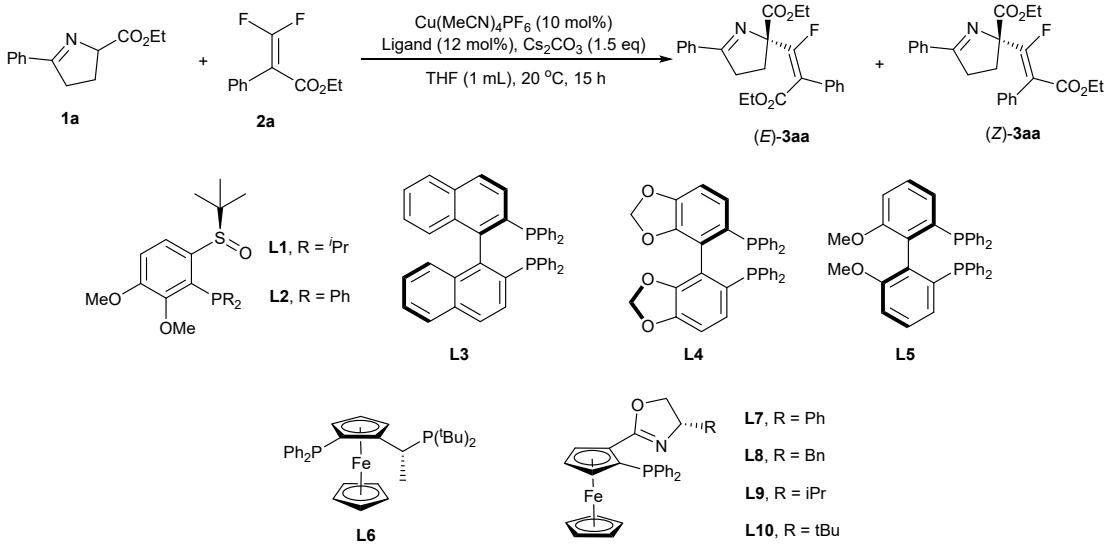
2-((2,2-dimethyl-5-(2,5-dimethylphenoxy)pentanoyl)oxy)ethyl 3,3-difluoro-2-phenylacrylate (2l)



^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.30 (m, 5H), 7.04 (d, *J* = 7.4 Hz, 1H), 6.70 (d, *J* = 7.4 Hz, 1H), 6.64 (s, 1H), 4.49 – 4.41 (m, 2H), 4.36 – 4.28 (m, 2H), 3.93 (brs, 2H), 2.35 (s, 3H), 2.21 (s, 3H), 1.75 (brs, 4H), 1.24 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.5, 163.8 (dd, *J* = 11.1, 7.1 Hz), 159.8 (dd, *J* = 314.1, 300.0 Hz), 156.9, 136.5, 130.3, 130.03 (dd, *J* = 3.0, 2.0 Hz), 128.5, 128.4, 123.6, 120.7, 111.9, 92.0 (dd, *J* = 22.2, 10.1 Hz), 67.8, 63.1, 61.9, 42.1, 37.0, 25.11, 25.07, 21.4, 15.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -68.5 (d, *J* = 12.5 Hz), -70.3 (d, *J* = 12.8 Hz). HRMS (m/z, ESI): Calcd. for $C_{26}H_{30}F_2NaO_5$ $[M+H]^+$: 483.1954, Found: 483.1951.

3. Optimization of Reaction Conditions

Table S1. Screening of ligands[a]

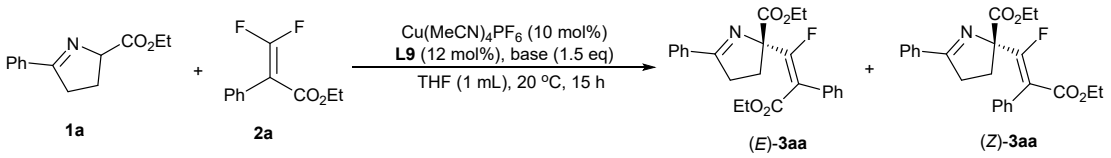


Entry	ligand	Yield (*E*/*Z*)[b]	ee/% (*E*/*Z*)[c]
1	**L1**	88% (6.3/1)	31/10
2	**L2**	88% (7.8/1)	8/27
3	**L3**	99% (2.4/1)	42/50
4	**L4**	92% (4.4/1)	36/30
5	**L5**	91% (5.1/1)	12/41
6	**L6**	88% (6.3/1)	83/91
7	**L7**	91% (3.8/1)	98/98
8	**L8**	99% (13.1/1)	95/87
9	**L9**	**95% (12.6/1)**	**98/94**
10	**L10**	95% (7.6/1)	98/99

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.12 mmol), Cs_2CO_3 (0.15 mmol), $Cu(MeCN)_4PF_6$ (10 mol %) and **Ligand** (12 mol %) in 1 mL THF at 20 °C for 15 h. [b]Yields (*E* + *Z*) and *E*/*Z* ratio were

determined by ^{1}H-NMR using 1,1,2,2-Tetrachloroethane as an internal standard; [c]The ee values were determined by chiral HPLC analysis.

Table S2. Screening of bases[a]

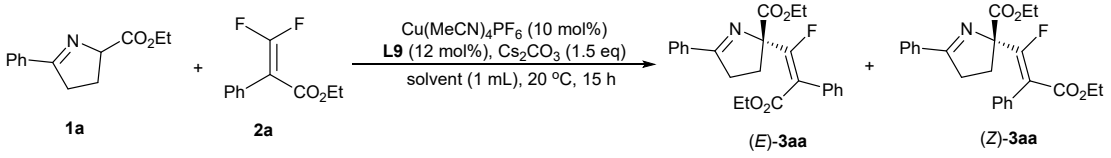


1a 2a (*E*)-3aa (*Z*)-3aa

Entry	base	Yield (*E*/*Z*)[b]	ee/% (*E*)[c]
1	K_2CO_3	87% (11.4/1)	98
2	Na_2CO_3	39% (6.8/1)	98
3	$NaHCO_3$	26% (5.5/1)	98
4	K_3PO_4	90% (9.5/1)	98
5	**Cs_2CO_3**	**95% (12.6/1)**	**98**
6	TEA	43% (4.4/1)	97
7	DBU	N.R.	/

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.12 mmol), base (0.15 mmol), $Cu(MeCN)_4PF_6$ (10 mol %) and **L9** (12 mol %) in 1 mL THF at 20 °C for 15 h. [b]Yields (*E* + *Z*) and *E*/*Z* ratio were determined by ^{1}H-NMR using 1,1,2,2-Tetrachloroethane as an internal standard; N.R.= no reaction. [c]The ee values were determined by chiral HPLC analysis.

Table S3. Screening of solvents[a]



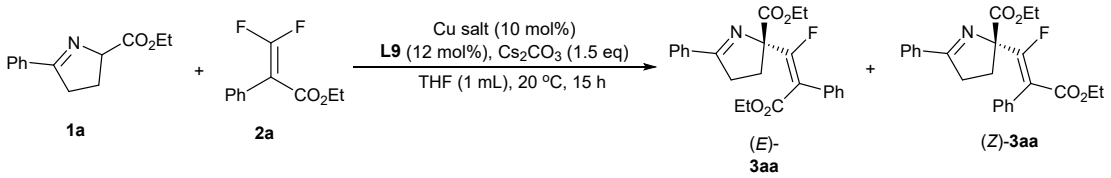
1a 2a (*E*)-3aa (*Z*)-3aa

Entry	solvent	Yield (*E*/*Z*)[b]	ee/% (*E*)[c]
1	DCM	90% (2.8/1)	97
2	DCE	53% (3.8/1)	98

3	MeCN	46% (4.4/1)	94
4	CPME	93% (13.2/1)	98
5	DME	94% (10/1)	98
6	1,4-dioxane	85% (7.9/1)	98
7	2-Me-THF	96% (12.2/1)	96
8	**THF**	**95% (12.6/1)**	**98**

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.12 mmol), Cs_2CO_3 (0.15 mmol), $Cu(MeCN)_4PF_6$ (10 mol %) and **L9** (12 mol %) in 1 mL solvent at 20 °C for 15 h. [b]Yields (*E* + *Z*) and *E*/*Z* ratio were determined by ^{1}H-NMR using 1,1,2,2-Tetrachloroethane as an internal standard. [c]The ee values were determined by chiral HPLC analysis.

Table S4. Screening of Cu salts[a]



Entry	Cu salt	Yield (*E*/*Z*)[b]	ee/% (*E*)[c]
1	CuCl	52% (12/1)	98
2	CuI	N.R.	/
3	CuBr	43% (8.4/1)	98
4	CuOAc	66% (12.2/1)	98
5	$Cu(OTf)_2$	81% (6.4/1)	98
6	$Cu(MeCN)_4PF_6$	95% (12.6/1) (66%)[d]	98
7[e]	**$Cu(MeCN)_4PF_6$**	**78%[d] (12.9/1)**	**98**

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.12 mmol), Cs_2CO_3 (0.15 mmol), Cu salt (10 mol %) and **L9** (12 mol %) in 1 mL THF at 20 °C for 15 h. [b]Yields (*E* + *Z*) and *E*/*Z* ratio were determined by ^{1}H-NMR using 1,1,2,2-Tetrachloroethane as an internal standard; N.R.= no reaction. [c]The ee values were determined by chiral HPLC analysis; [d]Isolated yield; [e]**2a** (0.15 mmol) was used.

4. General Procedure for the Copper-Catalyzed Enantioselective Nucleophilic Vinylic Substitution (S_NV) Reaction of Difluoroacrylates

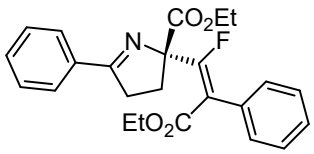
In the glove box, to a dried tube with a magnetic stir bar was added $Cu(MeCN)_4PF_6$ (10 mol %, 0.01 mmol, 3.7 mg), **L9** (12 mol %, 0.012 mmol, 5.8 mg) and 0.5 mL anhydrous THF, the mixture was stirred for 0.5 hour at 25 ^oC. Then, the mixture was successively added cyclic imino ester **1** (0.1 mmol), difluoroacrylate **2** (0.15 mmol), and Cs_2CO_3 (0.15 mmol, 48.8 mg). After that, another 0.5 mL THF was added into the mixture. The tube was sealed by the rubber stopper, removed out of the glove box and stirred at 20 ^oC for 15 h. When the reaction was completed, the mixture was filtered through celite and the filtrate was concentrated in vacuo. The E/Z ratio was determined by ^{1}HNMR analysis of the crude product. Then the recovered residue was purified by flash chromatography over silica gel with petro ether/Ethyl acetate (6:1 – 4:1) as the eluent to give the product **3**, the ee was determined by HPLC analysis. The isolated yields and ee values given in the text were all refer to *E*-isomer of **3**.

5. 1 mmol-scale synthesis

In the glove box, to a dried 50 ml round-bottom flask with a magnetic stir bar was added $Cu(MeCN)_4PF_6$ (10 mol %, 0.1 mmol, 37 mg), **L9** (12 mol %, 0.12 mmol, 58 mg) and 5 mL anhydrous THF, the mixture was stirred for 0.5 hour at 25 ^oC. Then to the mixture was successively added cyclic imino ester **1k** (1.0 mmol, 203 mg), difluoroacrylate **2a** (1.5 mmol, 318 mg), and Cs_2CO_3 (1.5 mmol, 487 mg). After that, another 5.0 mL THF was added into the mixture. The flask was sealed by the rubber stopper, removed out of the glove box and stirred at 20 ^oC for 20 h. When the reaction was completed, the mixture was filtered through celite and silica gel and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography over silica gel with petro ether/ethyl acetate (15:1 – 6:1) as the eluent to give the product (*E*)-**3ka** as white solid, 316 mg, 80% yield, 99% ee.

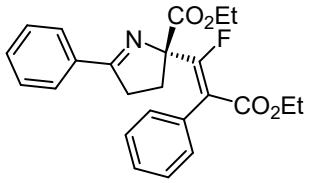
6. Characterization data for Products (*E*)-3aa – (*E*)-3al

(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-phenylacrylate (*E*)-(3aa)



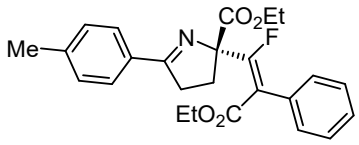
Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 32 mg, 78% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 8.84 min (major) and 11.68 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.92 (d, *J* = 6.8 Hz, 2H), 7.58 – 7.29 (m, 8H), 4.29 (q, *J* = 7.1 Hz, 2H), 4.23 – 4.12 (m, 2H), 3.34 – 3.12 (m, 2H), 2.91 – 2.85 (m, 1H), 2.55 – 2.40 (m, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.7, 170.2, 166.9 (d, *J* = 15.2 Hz), 161.2 (d, *J* = 271.7 Hz), 133.6, 132.0, 1314, 129.0 (d, *J* = 4.0 Hz), 128.5 (d, *J* = 4.0 Hz), 128.2, 128.0, 116.3 (d, *J* = 17.2 Hz), 84.6 (d, *J* = 28.3 Hz), 62.0, 61.4, 35.6, 31.8 (d, *J* = 3.0 Hz), 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -104.7. HRMS (m/z, ESI): Calcd. for $C_{24}H_{25}FNO_4$ $[M+H]^+$: 410.1762, Found: 410.1772. $[\alpha]_D^{20}$= -102.6 (c 1.8, $CHCl_3$).

ethyl (*R, Z*)-3-(2-((ethylperoxy)-l2-methyl)-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-3-fluoro-2-phenylacrylate (*Z*)-(3aa)



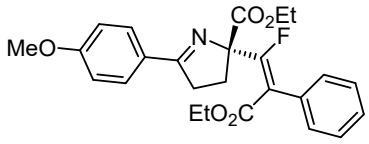
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 8 Hz, 2H), 7.58 – 7.29 (m, 8H), 4.27 – 4.22 (m, 2H), 3.95 –3.83 (m, 2H), 3.14 – 3.03 (m, 2H), 2.64 – 2.48 (m, 2H), 1.28 (t, *J* = 8 Hz, 3H), 1.21 (t, *J* = 8 Hz, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -99.9.

(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-(4-methyl)phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-phenylacrylate (*E*)-(3ba)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 37 mg, 88% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 11.24 min (major) and 14.87 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 (d, *J* = 8.1 Hz, 2H), 7.47 (d, *J* = 8.9 Hz, 2H), 7.42 – 7.30 (m, 3H), 7.25 (d, *J* = 7.9 Hz, 2H), 4.28 (qd, *J* = 7.1, 1.9 Hz, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.32 – 3.09 (m, 2H), 2.91 – 2.84 (m, 1H), 2.49 – 2.40 (m, 4H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.6, 170.3, 166.8 (d, *J* = 16.2 Hz), 161.4 (d, *J* = 271.7 Hz), 141.8, 132.0, 131.0, 129.2, 129.0 (d, *J* = 4.0 Hz), 128.4, 128.2, 128.0, 116.2 (d, *J* = 17.2 Hz), 84.6 (d, *J* = 28.3 Hz), 62.0, 61.4, 35.6, 31.8 (d, *J* = 3.0 Hz), 21.6, 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -104.6. HRMS (m/z, ESI): Calcd. for $C_{25}H_{27}FNO_4$ $[M+H]^+$: 424.1919, Found: 424.1916. $[\alpha]_D^{20}$= -112.0 (c 1.5, $CHCl_3$).

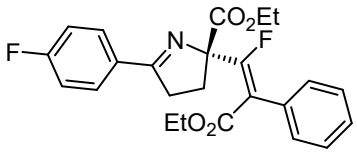
(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-(4-methyloxy)phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-phenylacrylate (*E*)-(3ca)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 26 mg, 82% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 18.16 min (major) and 23.36 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 (d, *J* = 8.9 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 2H), 7.43 – 7.29 (m, 3H), 6.94 (d, *J* = 8.8 Hz, 2H), 4.34 – 4.22 (m, 2H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.87 (s, 3H), 3.30 – 3.08 (m, 2H), 2.87 (ddd, *J* = 13.3, 8.8, 4.3 Hz, 1H), 2.51 – 2.38 (m,

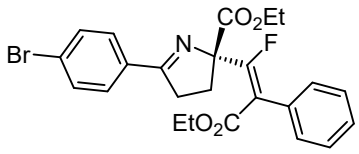
1H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.9, 170.4, 166.9 (d, *J* = 15.2 Hz), 162.2, 161.4 (d, *J* = 271.7 Hz), 132.0, 130.2, 129.0 (d, *J* = 4.0 Hz), 128.2, 128.0, 126.5, 116.1 (d, *J* = 18.2 Hz), 113.8, 84.5 (d, *J* = 28.3 Hz), 62.0, 61.4, 55.4, 35.5, 31.8 (d, *J* = 2.0 Hz), 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -104.7. HRMS (m/z, ESI): Calcd. for $C_{25}H_{27}FNO_5$ $[M+H]^+$: 440.1868, Found: 440.1869. $[\alpha]_D^{20}$= -111.4 (c 1.7, $CHCl_3$).

(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-(4-fluoro)phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-phenylacrylate (*E*)-(3da)



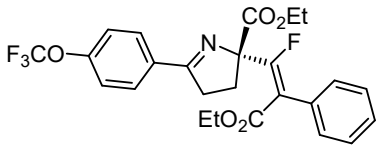
Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 25 mg, 59% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 8.49 min (major) and 10.34 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 (dd, *J* = 8.7, 5.5 Hz, 2H), 7.47 (d, *J* = 8.3 Hz, 2H), 7.43 – 7.29 (m, 3H), 7.13 (t, *J* = 8.6 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 4.22 – 4.12 (m, 2H), 3.31 – 3.09 (m, 2H), 2.91– 2.81 (m, 1H), 2.55 – 2.41 (m, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.4, 170.2, 166.9 (d, *J* = 15.2 Hz), 164.7 (d, *J* = 253.5 Hz), 161.1 (d, *J* = 271.7 Hz), 131.9, 130.7, 130.6, 129.9 (d, *J* = 3.0 Hz), 129.0 (d, *J* = 4.0 Hz), 128.3, 128.0, 116.3 (d, *J* = 17.2 Hz), 115.6 (d, *J* = 22.2 Hz), 84.6 (d, *J* = 28.3 Hz), 62.1, 61.4, 35.6, 31.9 (d, *J* = 4.0 Hz), 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -104.8, -108.3. HRMS (m/z, ESI): Calcd. for $C_{24}H_{24}F_2NO_4$ $[M+H]^+$: 428.1668, Found: 428.1667. $[\alpha]_D^{20}$= -99.2 (c 1.7, $CHCl_3$).

(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-(4-bromo)phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-phenylacrylate (*E*)-(3ea)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 30 mg, 61% yield, 97% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 9.20 min (major) and 11.42 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 8.5 Hz, 2H), 7.58 (d, *J* = 8.5 Hz, 2H), 7.46 (d, *J* = 7.2 Hz, 2H), 7.42 – 7.30 (m, 3H), 4.29 (q, *J* = 7.1 Hz, 2H), 4.22 – 4.12(m, 2H), 3.30 – 3.07 (m, 2H), 2.87 (dt, *J* = 13.2, 9.0 Hz, 1H), 2.48 (dt, *J* = 13.4, 9.0 Hz, 1H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.7, 170.0, 166.8 (d, *J* = 16.2 Hz), 161.0 (d, *J* = 271.7 Hz), 132.5, 1319, 131.8, 129.9, 129.0 (d, *J* = 4.0 Hz), 128.3, 128.1, 126.1, 116.4 (d, *J* = 18.2 Hz), 84.7 (d, *J* = 28.3 Hz), 62.1, 61.4, 35.6, 31.8 (d, *J* = 4.0 Hz), 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -104.7. HRMS (m/z, ESI): Calcd. for $C_{24}H_{24}BrFNO_4$ $[M+H]^+$: 488.0867, Found: 488.0867. $[\alpha]_D^{20}$= -97.0 (c 2.0, $CHCl_3$).

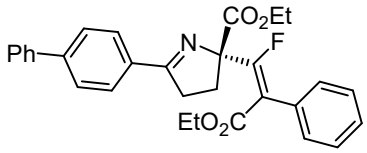
(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-(4-trifluoromethyloxy)phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-phenylacrylate (*E*)-(3fa)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 36 mg, 73% yield, 97% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 6.00 min (major) and 7.46 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.95 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.36 – 7.26 (m, 3H), 4.30 (q, *J* = 7.1 Hz, 2H), 4.24 – 4.11 (m, 2H), 3.33 – 3.10 (m, 2H), 2.87 (dt, *J* = 13.2, 9.0 Hz, 1H), 2.50 (dt, *J* = 14.7, 8.9 Hz, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.3, 170.1, 166.9 (d, *J* = 15.2 Hz), 161.0 (d, *J* = 271.7 Hz), 151.4 (d, *J* = 1.0 Hz), 132.2,

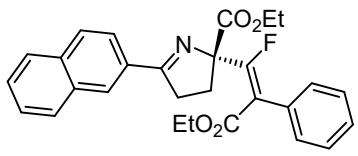
131.9, 130.1, 129.0 (d, J = 4.0 Hz), 128.3, 128.1, 121.7, 120.6, 119.1, 116.4 (d, J = 17.2 Hz), 84.6 (d, J = 18.2 Hz), 62.1, 61.4, 35.6, 31.8 (d, J = 4.0 Hz), 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -57.7, -104.8. HRMS (m/z, ESI): Calcd. for $C_{25}H_{24}F_4NO_5$ $[M+H]^+$: 494.1585, Found: 494.1587. $[\alpha]_D^{20}$= -93.6 (c 2.4, $CHCl_3$).

(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-(4-phenyl)phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-phenylacrylate (*E*)-(3ga)



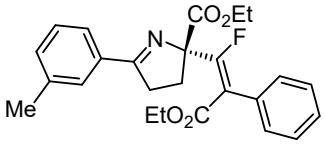
Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 29 mg, 60% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 13.98 min (major) and 20.15 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.00 (d, J = 7.9 Hz, 2H), 7.68 (dd, J = 11.4, 8.0 Hz, 4H), 7.55 – 7.45 (m, 4H), 7.45 – 7.31 (m, 4H), 4.31 (q, J = 7.1 Hz, 2H), 4.22 (q, J = 7.1 Hz, 2H), 3.38 – 3.15 (m, 2H), 2.91 (dt, J = 13.2, 8.7 Hz, 1H), 2.50 (dt, J = 13.4, 8.9 Hz, 1H), 1.36 (t, J = 6.4 Hz, 3H), 1.23 (t, J = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.4, 170.2, 166.9 (d, J = 15.2 Hz), 161.3 (d, J = 271.7 Hz), 144.1, 140.2, 132.5, 132.0, 129.01 (d, J = 4.0 Hz), 129.0, 128.9, 128.3, 128.0, 127.9, 127.2, 127.1, 116.3 (d, J = 17.2 Hz), 84.7 (d, J = 28.3 Hz), 62.1, 61.5, 35.7, 31.8 (d, J = 3.0 Hz), 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -104.6. HRMS (m/z, ESI): Calcd. for $C_{30}H_{29}FNO_4$ $[M+H]^+$: 486.2075, Found: 486.2074. $[\alpha]_D^{20}$= -135.5 (c 1.9, $CHCl_3$).

(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-(2-napthyl)-3,4-dihydro-2H-pyrrol-2-yl)-2-phenylacrylate (*E*)-(3ha)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 32 mg, 70% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 13.20 min (major) and 16.55 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.26 (s, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 7.98 – 7.85 (m, 3H), 7.64 – 7.46 (m, 4H), 7.45 – 7.31 (m, 3H), 4.36 – 4.25 (m, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.47 – 3.27 (m, 2H), 2.96 (dt, *J* = 13.1, 8.6 Hz, 1H), 2.53 (dt, *J* = 13.4, 9.0 Hz, 1H), 1.36 (t, *J* = 7.0 Hz, 3H), 1.20 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.7, 170.2, 166.9 (d, *J* = 15.2 Hz), 161.4 (d, *J* = 270.7 Hz), 134.8, 132.8, 132.0, 131.2, 129.4, 129.1 (d, *J* = 3.0 Hz), 128.9, 128.3, 128.2, 128.0, 127.8, 127.6, 126.6, 124.9, 116.3 (d, *J* = 18.2 Hz), 84.8 (d, *J* = 28.3 Hz), 62.1, 61.5, 35.7, 31.9 (d, *J* = 3.0 Hz), 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -104.5. HRMS (m/z, ESI): Calcd. for $C_{28}H_{27}FNO_4$ $[M+H]^+$: 460.1919, Found: 460.1911. $[\alpha]_D^{20}$= -117.9 (c 2.1, $CHCl_3$).

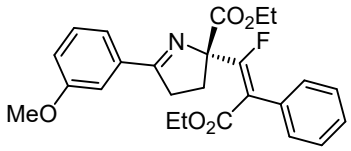
(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-(3-methyl)phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-phenylacrylate (*E*)-(3ia)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 35 mg, 83% yield, 97% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 9.50 min (major) and 13.64 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (s, 1H), 7.68 (d, *J* = 7.1 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 2H), 7.43 – 7.29 (m, 5H), 4.33 – 4.24 (m, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.32 – 3.13 (m, 2H), 2.91 (dt, *J* = 13.3, 8.9 Hz, 1H), 2.50 – 2.37 (m, 4H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.9, 170.1, 166.8 (d, *J* = 16.2 Hz), 161.5 (d, *J* = 270.7 Hz), 138.1, 133.6, 132.2, 132.0, 129.1 (d, *J* = 4.0 Hz), 128.9, 128.4, 128.2, 128.0, 125.7, 116.2 (d, *J* = 17.2 Hz), 84.7 (d, *J* = 28.3 Hz), 62.0, 61.4, 35.8, 31.8 (d, *J* = 3.0 Hz), 21.4, 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -

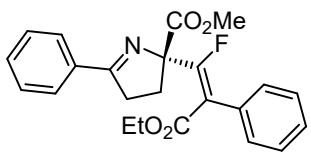
104.2. HRMS (m/z, ESI): Calcd. for $C_{25}H_{27}FNO_4$ $[M+H]^+$: 424.1919, Found: 424.1917. $[\alpha]_D^{20}$= -87.6 (c 2.3, $CHCl_3$).

(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-(3-methyloxy)phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-phenylacrylate (*E*)-(3ja)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 27 mg, 62% yield, 97% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 10.96 min (major) and 16.23 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (s, 1H), 7.48 (d, *J* = 7.3 Hz, 2H), 7.44 – 7.29 (m, 5H), 7.05 (dd, *J* = 8.3, 2.6 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 4.24 – 4.15 (m, 2H), 3.89 (s, 3H), 3.33 – 3.10 (m, 2H), 2.84 (dt *J* = 13.2, 9.0 Hz, 1H), 2.48 (dt, *J* = 13.5, 9.0 Hz, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.5, 170.2, 167.0 (d, *J* = 15.2 Hz), 161.1 (d, *J* = 271.7 Hz), 159.6, 135.0, 132.0, 129.4, 129.0 (d, *J* = 4.0 Hz), 128.2, 128.0, 121.1, 118.0, 116.4 (d, *J* = 17.2 Hz), 112.7, 84.4 (d, *J* = 28.3 Hz), 62.0, 61.34, 55.5, 35.7, 31.8 (d, *J* = 4.0 Hz), 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -105.1. HRMS (m/z, ESI): Calcd. for $C_{25}H_{27}FNO_5$ $[M+H]^+$: 440.1868, Found: 424.1868. $[\alpha]_D^{20}$= -76.7 (c 1.8, $CHCl_3$).

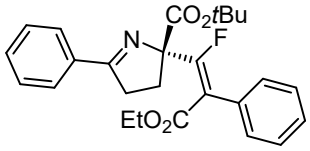
(*R, E*)-Ethyl 3-F-3-(2-methyloxycarbonyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-phenylacrylate (*E*)-(3ka)



Eluent: petroleum ether/ethyl acetate (6/1), white solid, 30 mg, 76% yield, 97% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 10.63min (major) and 14.21 min (minor). ^{1}H NMR (400 MHz,

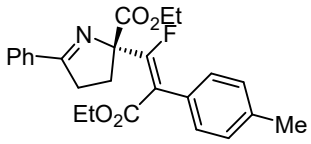
Chloroform-*d*) δ 7.98 – 7.86 (m, 2H), 7.55 – 7.29 (m, 8H), 4.16 (q, *J* = 7.2 Hz, 2H), 3.84 (s, 3H), 3.37 – 3.14 (m, 2H), 2.91 (dt, *J* = 13.3, 8.8 Hz, 1H), 2.57 – 2.41 (m, 1H), 1.19 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.9, 170.7, 166.8 (d, *J* = 15.2 Hz), 161.0 (d, *J* = 271.7 Hz), 133.5, 131.9, 131.5, 129.0 (d, *J* = 4.0 Hz), 128.5 (d, *J* = 4.0 Hz), 128.3, 128.1, 116.4 (d, *J* = 18.2 Hz), 84.6 (d, *J* = 29.3 Hz), 61.5, 53.1, 35.7, 31.8 (d, *J* = 3.0 Hz), 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -105.1. HRMS (m/z, ESI): Calcd. for $C_{23}H_{23}FNO_4$ $[M+H]^+$: 396.1606, Found: 396.1604. $[\alpha]_D^{20}$= -100.6 (c 2.0, $CHCl_3$).

(*R, E*)-Ethyl 3-F-3-(2-*tert*-butyloxycarbonyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-phenylacrylate (*E*)-(3la)



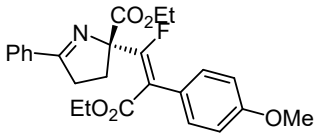
Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 21 mg, 48% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 5.60 min (major) and 7.26 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 – 7.83 (m, 2H), 7.60 – 7.29 (m, 8H), 4.30 – 4.16 (m, 2H), 3.30 – 3.07 (m, 2H), 2.75 (dt, *J* = 12.9, 8.7 Hz, 1H), 2.49 – 2.37 (m, 1H), 1.54 (s, 9H), 1.23 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.1, 169.2, 167.0 (d, *J* = 15.2 Hz), 161.2 (d, *J* = 271.7 Hz), 133.86, 132.2, 131.2, 129.0, 128.9, 128.4 (d, *J* = 5.0 Hz), 128.2, 127.9, 115.8 (d, *J* = 18.2 Hz), 85.1 (d, *J* = 28.3 Hz), 61.4, 35.4, 31.6 (d, *J* = 5.0 Hz), 27.9, 13.9. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -105.2. HRMS (m/z, ESI): Calcd. for $C_{26}H_{29}FNO_4$ $[M+H]^+$: 438.2075, Found: 438.2066. $[\alpha]_D^{20}$= -106.0 (c 1.4, $CHCl_3$).

(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-(4-methylphenyl)acrylate (*E*)-(3ab)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 29 mg, 69% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 10.04 min (major) and 15.85 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 (d, *J* = 9.4 Hz, 2H), 7.51 – 7.42 (m, 3H), 7.36 (d, *J* = 7.8 Hz, 2H), 7.20 (d, *J* = 7.8 Hz, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.32 – 3.12 (m, 2H), 2.91 – 2.84 (m, 1H), 2.51 – 2.43 (m , 1H), 2.38 (s, 3H), 1.34 (t, *J* = 8.0 Hz, 3H), 1.20 (t, *J* = 8.0 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.6, 170.3, 167.0 (d, *J* = 15.2 Hz), 160.9 (d, *J* = 270.7 Hz), 137.9, 133.7, 131.4, 129.0, 129.0, 128.9 (d, *J* = 4.0 Hz), 128.4 (d, *J* = 3.0 Hz), 116.2 (d, *J* = 17.2 Hz), 84.7 (d, *J* = 28.3 Hz), 62.0, 61.4, 35.6, 31.8 (d, *J* =4.0 Hz), 21.3, 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -105.4. HRMS (m/z, ESI): Calcd. for $C_{25}H_{27}FNO_4$ $[M+H]^+$: 424.1919, Found: 424.1916. $[\alpha]_D^{20}$= -101.6 (c 1.9, $CHCl_3$).

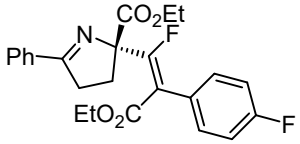
(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-(4-methyloxyphenyl)acrylate (*E*)-(3ac)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 33 mg, 75% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 15.56 min (major) and 26.21 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 (d, *J* = 7.4 Hz, 2H), 7.66 – 7.32 (m, 5H), 6.92 (d, *J* = 10.9 Hz, 2H), 4.37 – 4.23 (m, 2H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.83 (s, 3H), 3.33 – 3.09 (m, 2H), 2.93 – 2.76 (m, 1H), 2.51– 2.43 (m, 1H), 1.34 (t, *J* = 8.1 Hz, 3H), 1.20 (t, *J* = 6.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.6, 170.3, 167.1 (d, *J* = 15.2 Hz), 160.5 (d, *J* = 270.7 Hz), 159.24, 133.7, 131.4, 130.2 (d, *J* = 4.0 Hz), 128.4 (d, *J* = 4.0

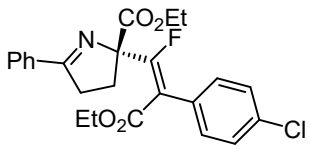
Hz), 124.2, 115.9 (d, J =17.2 Hz), 113.7, 84.6 (d, J = 29.3 Hz), 62.0, 61.4, 55.3, 35.6, 31.8 (d, J =4.0 Hz), 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -106.3. HRMS (m/z, ESI): Calcd. for $C_{25}H_{27}FNO_5$ $[M+H]^+$: 440.1868, Found: 440.1867. $[\alpha]_D^{20}$= -109.5 (c 2.2, $CHCl_3$).

(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-(4-fluorophenyl)acrylate (*E*)-(3ad)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 20 mg, 47% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 6.85 min (major) and 8.79 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 (d, J = 8.1 Hz, 2H), 7.55 – 7.40 (m, 5H), 7.08 (t, J = 8.7 Hz, 2H), 4.29 (q, J = 7.1 Hz, 2H), 4.22 – 4.14 (m, 2H), 3.33 – 3.14 (m, 2H), 2.90 – 2.83 (m, 1H), 2.53 – 2.40 (m, 1H), 1.34 (t, J = 7.1 Hz, 3H), 1.20 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.7, 170.1, 166.8 (d, J = 15.2 Hz), 162.3 (d, J = 248.5 Hz), 161.6 (d, J = 271.7 Hz), 133.6, 131.4, 130.9 (q, J = 4.0 Hz), 128.5, 128.4, 115.4, 115.1, 84.6 (d, J = 17.2 Hz), 62.1, 61.5, 35.63, 31.8 (d, J = 3.0 Hz), 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -104.2, -113.6. HRMS (m/z, ESI): Calcd. for $C_{24}H_{24}FNO_4$ $[M+H]^+$: 428.1668, Found: 428.1669. $[\alpha]_D^{20}$= -133.7 (c 1.3, $CHCl_3$).

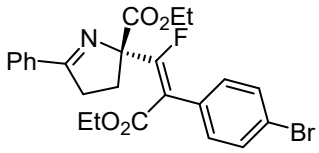
(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-(4-chlorophenyl)acrylate (*E*)-(3ae)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 31 mg, 70% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ=

254 nm, retention time: 6.74 min (major) and 8.97 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.90 (d, *J* = 9.0 Hz, 2H), 7.57 – 7.33 (m, 7H), 4.35 – 4.25 (m, 2H), 4.24 – 4.12 (m, 2H), 3.30 – 3.15 (m, 2H), 2.90 – 2.84 (m, 1H), 2.54 – 2.42 (m, 1H), 1.34 (t, *J* = 7.3 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.8, 170.0, 166.6 (d, *J* = 15.0 Hz), 161.9 (d, *J* = 272.7 Hz), 133.9, 133.5, 131.5, 130.43, 130.39, 128.50, 128.47, 128.4, 115.4 (d, *J* = 18.2 Hz), 84.6 (d, *J* = 28.3 Hz), 62.1, 61.6, 35.64, 31.8 (d, *J* = 3.0 Hz), 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -103.3. HRMS (m/z, ESI): Calcd. for $C_{24}H_{24}ClFNO_4$ $[M+H]^+$: 444.1372, Found: 444.1370. $[\alpha]_D^{20}$= -96.2 (c 2.1, $CHCl_3$).

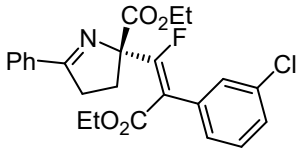
(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-(4-bromophenyl)acrylate (*E*)-(3af)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 39 mg, 80% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 7.20 min (major) and 9.80 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.90 (d, *J* = 8.9 Hz, 2H), 7.58 – 7.40 (m, 5H), 7.34 (d, *J* = 10.9 Hz, 2H), 4.28 (q, *J* = 8.1, 6.8 Hz, 2H), 4.23 – 4.11 (m, 2H), 3.35 – 3.10 (m, 2H), 2.95 – 2.79 (m, 1H), 2.54 – 2.39 (m, 1H), 1.34 (t, *J* = 9.0 Hz, 3H), 1.20 (t, *J* = 8.5 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.8, 170.0, 166.5 (d, J =14.1 Hz), 161.9 (d, *J* = 272.7 Hz), 133.5, 131.5 (d, *J* = 4.0 Hz), 131.4, 130.9, 130.7 (d, *J* = 4.0 Hz), 128.5, 128.4, 122.17, 115.4 (d, *J* = 17.2 Hz), 84.6 (d, *J* = 18.2 Hz), 62.1, 61.6, 35.6, 31.8 (d, *J* = 3.0 Hz), 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -103.15. HRMS (m/z, ESI): Calcd. for $C_{24}H_{24}BrFNO_4$ $[M+H]^+$: 488.0867, Found: 488.0868. $[\alpha]_D^{20}$= -75.8 (c 2.6, $CHCl_3$).

(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-

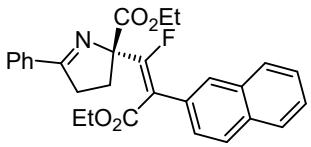
2-(3-chlorophenyl)acrylate (*E*)-(3ag)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 25 mg, 56% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 6.90 min (major) and 8.91 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 (d, *J* = 6.8 Hz, 2H), 7.55 – 7.41 (m, 4H), 7.39 – 7.29 (m, 3H), 4.29 (q, *J* = 7.1 Hz, 2H), 4.23 – 4.15 (m, 2H), 3.33 – 3.12 (m, 2H), 2.92 – 2.81 (m, 1H), 2.54 – 2.40 (m, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.8, 170.0, 166.4 (d, *J* = 15.2 Hz), 162.2 (d, *J* = 273.7 Hz), 134.1, 133.6, 133.5, 131.5, 129.5, 129.2 (d, *J* = 4.0 Hz), 128.5, 128.4, 128.2, 127.2 (d, *J* = 4.0 Hz), 115.3 (d, *J* = 17.2 Hz), 84.6 (d, *J* = 28.3 Hz), 62.1, 61.6, 35.6, 31.8 (d, *J* = 3.0 Hz), 14.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -102.5. HRMS (m/z, ESI): Calcd. for $C_{24}H_{24}ClFNO_4$ $[M+H]^+$: 444.1372, Found: 444.1373. $[\alpha]_D^{20}$= -88.6 (c 1.7, $CHCl_3$).

(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-

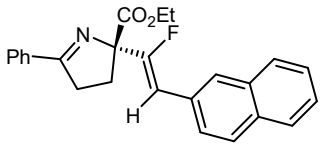
2-(2-napthyl)acrylate (*E*)-(3ah)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 35 mg, 76% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 10.73 min (major) and 21.04 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.02 – 7.91 (m, 3H), 7.91 – 7.82 (m, 3H), 7.60 (d, *J* = 8.6 Hz, 1H), 7.55 – 7.42 (m, 5H), 4.33 (q, *J* = 7.1 Hz, 2H), 4.23 (q, *J* = 6.6, 6.1 Hz, 2H), 3.36 – 3.17 (m, 2H), 2.96 – 2.89 (m, 1H), 2.57 – 2.49 (m, 1H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.8, 170.2, 166.9 (d,

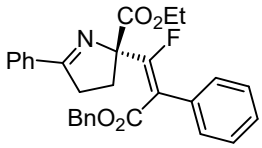
J = 15.0 Hz), 161.7 (d, *J* = 271.7 Hz), 133.6, 133.1, 132.8, 131.4, 128.5 (d, *J* = 4.0 Hz), 128.4 (d, *J* = 4.0 Hz), 128.3, 127.8, 127.6, 126.8 (d, *J* = 4.0 Hz), 126.4, 126.2, 116.4 (d, *J* = 18.2 Hz), 84.7 (d, *J* = 28.3 Hz), 62.1, 61.5, 35.7, 31.8 (d, *J* = 3.0 Hz), 14.2, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -104.2. HRMS (m/z, ESI): Calcd. for $C_{28}H_{27}FNO_4$ $[M+H]^+$: 460.1919, Found: 460.1918. $[\alpha]_D^{20}$= -125.5 (c 2.3, $CHCl_3$).

(*R*, *Z*)-1-F-1-(2-ethyloxycarbonyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-(2-napthyl)ethylene (*Z*)-(3ah')



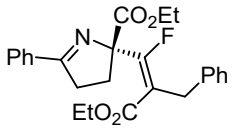
Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 17 mg, 43% yield, 99% ee, HPLC analysis: Daicel Chiralpak OJ-H, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 33.15 min (major) and 45.16 min (minor).^{1}H NMR (400 MHz, Chloroform-d) δ 8.08 – 7.94 (m, 3H), 7.86 – 7.76 (m, 3H), 7.72 (d, J = 8.7 Hz, 1H), 7.62 – 7.38 (m, 5H), 6.14 (d, J = 40.2 Hz, 1H), 4.46 – 4.21 (m, 2H), 3.38 – 3.12 (m, 2H), 3.01 – 2.87 (m, 1H), 2.51 – 2.38 (m, 1H), 1.35 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.6, 170.8, 159.0 (d, *J* = 268.7 Hz), 133.6 (d, *J* = 1.0 Hz), 133.5, 132.5 (d, *J* = 2.0 Hz), 131.5, 130.6 (d, *J* = 3.0 Hz), 128.6, 128.4, 128.1, 128.0 (d, *J* = 8.0 Hz), 127.9, 127.6, 126.8 (d, *J* = 8.0 Hz), 126.1, 126.0, 106.3 (d, *J* = 5.0 Hz), 84.5 (d, *J* = 30.0 Hz), 62.3, 35.9, 30.8, 14.2. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -110.6. HRMS (m/z, ESI): Calcd. for $C_{25}H_{23}FNO_2$ $[M+H]^+$: 388.1707, Found: 388.1713.

(*R, E*)-Benzyl 3-F-3-(2-ethyloxycarbonyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-phenylacrylate (*E*)-(3ai)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 27 mg, 57% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 8.60 min (major) and 11.42 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.92 (d, *J* = 6.9 Hz, 2H), 7.56 – 7.42 (m, 5H), 7.42 – 7.21 (m, 8H), 5.25 – 5.08 (m, 2H), 4.20 – 4.12 (m, 2H), 3.37 – 3.08 (m, 2H), 2.91– 2.84 (m, 1H), 2.49– 2.42 (m, 1H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.9, 170.1, 166.7 (d, *J* = 16.2 Hz), 161.3 (d, *J* = 270.7 Hz), 135.5, 133.6, 131.8, 131.5, 129.0 (d, *J* = 4.0 Hz), 128.5 (d, *J* = 4.0 Hz), 128.34, 128.31, 128.27, 128.1, 116.1 (d, *J* = 18.2 Hz), 84.7 (d, *J* = 29.3 Hz), 67.1, 62.1, 35.7, 31.8 (d, *J* = 3.0 Hz), 14.0. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -104.7. HRMS (m/z, ESI): Calcd. for $C_{29}H_{27}FNO_4$ $[M+H]^+$: 472.1919, Found: 472.1919. $[\alpha]_D^{20}$= -101.2 (c 1.8, $CHCl_3$).

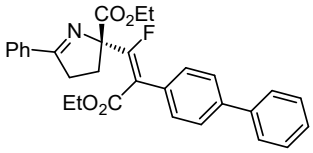
(*R, E*)-ethyl 3-F-3-(2-ethyloxycarbonyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-benzylacrylate (*E*)-(3aj)



Eluent: petroleum ether/ethyl acetate (6/1), pale yellow oil, 28 mg, 66% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 9.13 min (major) and 12.64 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.90 (d, *J* = 6.8 Hz, 2H), 7.51 – 7.42(m, 3H), 7.33 – 7.25 (m, 4H), 7.24 – 7.19 (m, 1H), 4.23 (qd, *J* = 7.2, 1.7 Hz, 2H), 4.17 – 4.02 (m, 2H), 3.88 – 3.68 (m, 2H), 3.34 – 3.11 (m, 2H), 3.04 (ddd, *J* = 13.5, 9.4, 4.1 Hz, 1H), 2.41 – 2.26 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.15 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.6, 170.0 (d, *J* = 3.0 Hz), 167.1 (d, *J* = 17.2 Hz), 165.9 (d, *J* = 272.7 Hz), 138.7 (d, *J* = 2.0 Hz), 133.6, 131.3, 128.50, 128.45, 128.34, 128.3, 126.2,

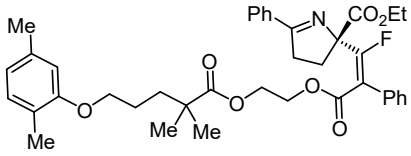
113.6 (d, *J* = 22.2 Hz), 85.1 (d, *J* = 25.3 Hz), 61.9, 61.0, 35.9, 32.4, 32.0 (d, *J* = 6.0 Hz), 14.0, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -97.1. HRMS (m/z, ESI): Calcd. for $C_{25}H_{27}FNO_4$ $[M+H]^+$: 424.1919, Found: 424.1917. $[\alpha]_D^{20}$= -94.5 (c 1.9, $CHCl_3$).

(*R, E*)-Ethyl 3-F-3-(2-ethyloxycarbonyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-(4-phenylphenyl)acrylate (*E*)-(3ak)



Eluent: petroleum ether/ethyl acetate (4/1), pale yellow oil, 41 mg, 84% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 12.12 min (major) and 15.75 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.94 (d, *J* = 6.7 Hz, 2H), 7.65 – 7.58(m, 4H), 7.57 (d, *J* = 8.1 Hz, 2H), 7.52 – 7.43 (m, 5H), 7.39 (d, *J* = 7.3 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 4.22 (qd, *J* = 7.2, 2.0 Hz, 2H), 3.34 – 3.16 (m, 2H), 2.93 – 2.86 (m, 1H), 2.55 – 2.47 (m, 1H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.8, 170.3, 167.0 (d, *J* = 15.2 Hz), 161.4 (d, *J* = 276.5 Hz), 140.9, 140.7, 133.7, 131.5, 131.1, 129.5 (d, *J* = 4.0 Hz), 128.9, 128.55 (d, *J* = 4.0 Hz), 127.5, 127.2, 127.1, 116.1 (d, *J* = 17.2 Hz), 84.7 (d, *J* = 28.3 Hz), 62.2, 61.6, 35.7, 31.9 (d, *J* = 3.0 Hz), 14.2, 13.9. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -109.8. HRMS (m/z, ESI): Calcd. for $C_{30}H_{29}FNO_4$ $[M+H]^+$: 486.2075, Found: 486.2073. $[\alpha]_D^{20}$= -86.9 (c 2.7, $CHCl_3$).

(*R, E*)-2-((2,2-dimethyl-5-(2,5-dimethylphenoxy)pentanoyl)oxy)ethyl 3-F-3-(2-ethyloxycarbonyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-yl)-2-phenylacrylate (*E*)-(3al)



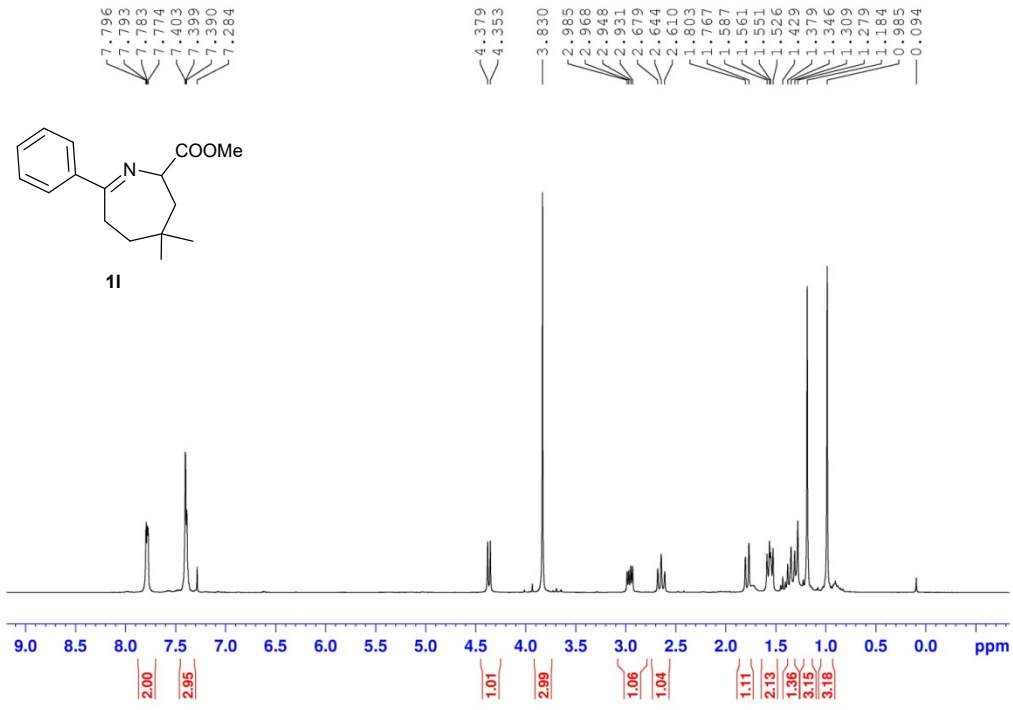
Eluent: petroleum ether/ethyl acetate (6/1), colorless oil, 38 mg, 58% yield, 98% ee, HPLC analysis: Daicel Chiralpak IC, hexane/iso-propanol = 90:10, 1.0 mL/min, λ= 254 nm, retention time: 14.12 min (major) and 17.81 min (minor). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 (d, *J* = 6.7 Hz, 2H), 7.60 – 7.41 (m, 5H), 7.41 – 7.24 (m, 3H), 7.03 (d, *J* = 7.4 Hz, 1H), 6.69 (d, *J* = 7.5 Hz, 1H), 6.60 (s, 1H), 4.42 – 4.14 (m, 6H), 3.86 (s, 2H), 3.33 – 3.14 (m, 2H), 2.95 – 2.81 (m, 1H), 2.54 – 2.40 (m, 1H), 2.34 (s, 3H), 2.18 (s, 3H), 1.76 – 1.61 (m, 4H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.17 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.9, 177.5, 170.1, 166.6 (d, *J* = 15.2 Hz), 161.5 (d, *J* = 271.7 Hz), 156.9, 136.5, 133.5, 131.7, 131.5, 130.3, 129.0, 128.9 (d, *J* = 3.0 Hz) , 128.6, 128.4, 128.3, 128.1, 123.5, 120.7, 115.9 (d, *J* = 18.2 Hz), 111.9, 84.6 (d, *J* = 28.3 Hz), 67.8, 63.1, 62.1, 61.7, 42.0, 37.0, 35.6, 31.7 (d, *J* = 2.0 Hz), 25.1, 25.0, 21.4, 15.8, 14.1. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -103.96. HRMS (m/z, ESI): Calcd. for $C_{39}H_{45}FNO_7$ $[M+H]^+$: 658.3175, Found: 658.3180. $[\alpha]_D^{20}$= -79.0 (c 2.5, $CHCl_3$).

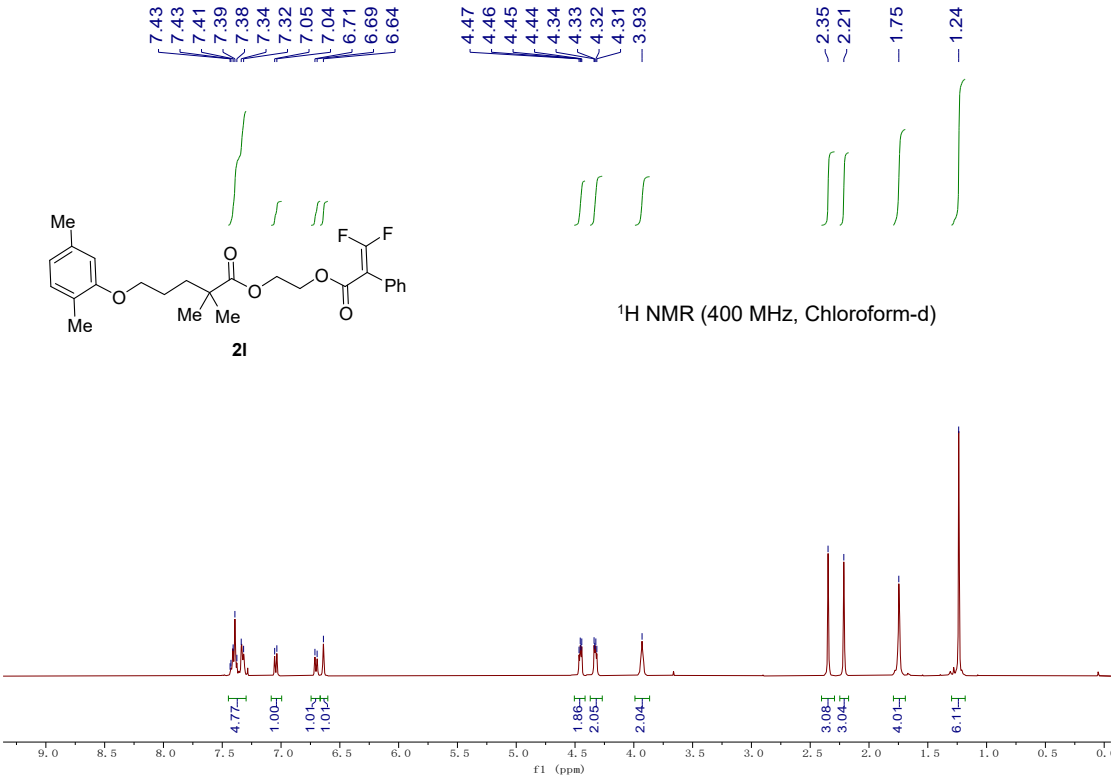
7. References

1. (a) Penglin Liu, Xiaohong Huo, Bowen Li, Rui He, Jiacheng Zhang, Tianhong Wang, Fang Xie and Wanbin Zhang, Stereoselective Allylic Alkylation of 1-Pyrroline-5-carboxylic Esters via a Pd/Cu Dual Catalysis, *Org. Lett.* **2018**, *20*, 6564−6568; (b) Wu Liang, Kun Jiang, Fei Du, Jie Yang, Li Shuai, Qin Ouyang, Ying-Chun Chen, and Ye Wei, Iron-Catalyzed, Iminyl Radical-Triggered Cascade 1,5-Hydrogen Atom Transfer/(5+2) or (5+1) Annulation: Oxime as a Five-Atom Assembling Unit, *Angew. Chem. Int. Ed.* **2020**, *59*, 19222–19228.

2. (a) Q. Ma, Y. H. Wang and G. C. Tsui, Stereoselective Palladium Catalyzed C-F Bond Alkynylation of Tetrasubstituted gem-Difluoroalkenes, *Angew. Chem., Int. Ed*., 2020, 59, 11293−11297; (b) Q. Ma, C. Liu, and G. C. Tsui, Palladium-Catalyzed Stereoselective Hydrodefluorination of Tetrasubstituted gem-Difluoroalkenes, *Org. Lett*., 2020, 22, 5193−5197; (c) M. Li, Y. H. Wang, and G. C. Tsui, Palladium-Catalyzed Stereoselective C−F Bond Vinylation and Allylation of Tetrasubstituted gem-Difluoroalkenes via Stille Coupling: Synthesis of Monofluorinated 1,3- and 1,4-Dienes, *Org. Lett.,* 2021, 23,

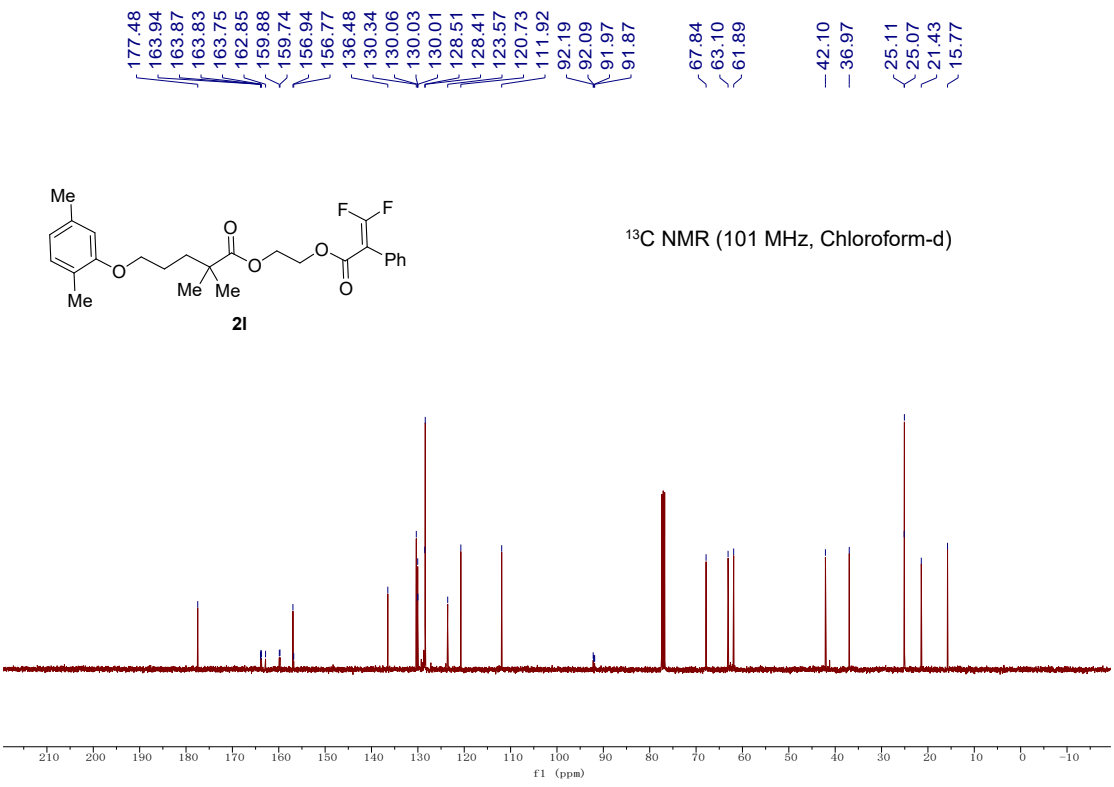
8. NMR and HPLC Spectra for The New Compounds





2l

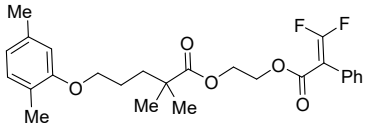
^{1}H NMR (400 MHz, Chloroform-d)



2l

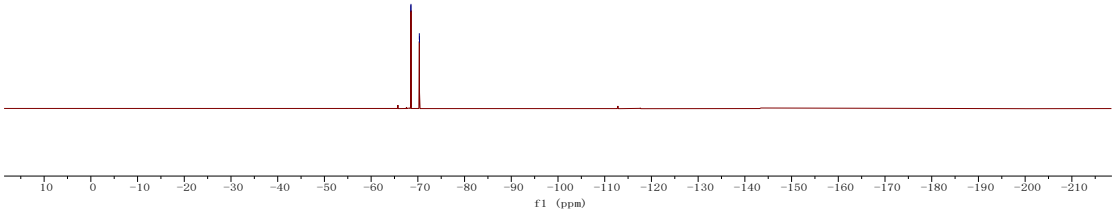
^{13}C NMR (101 MHz, Chloroform-d)

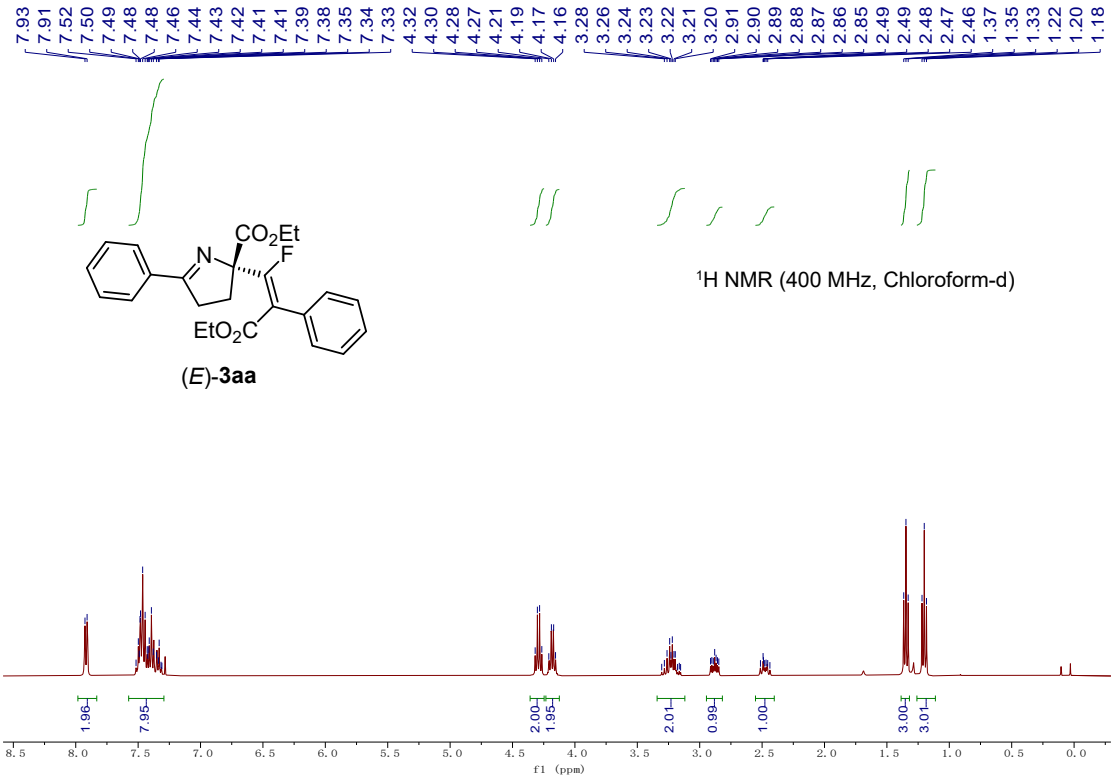
-68.49
-68.53
-70.32
-70.35

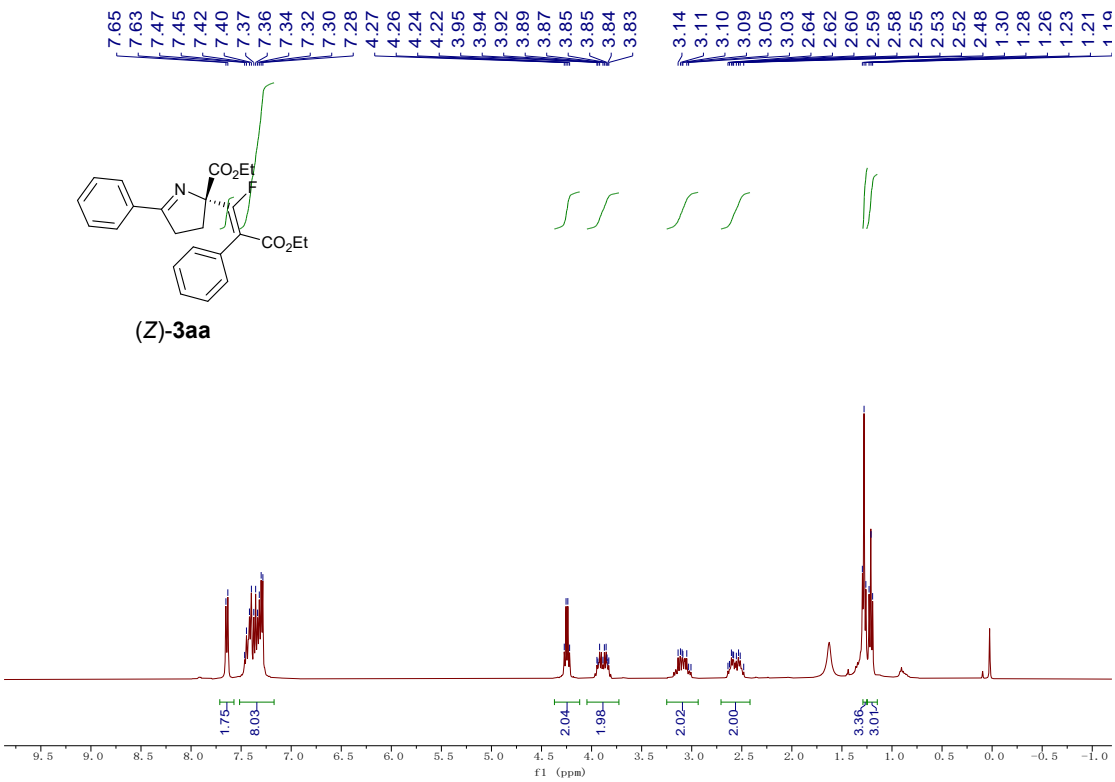


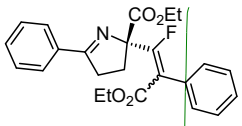
2l

^{19}F NMR (376 MHz, Chloroform-d)

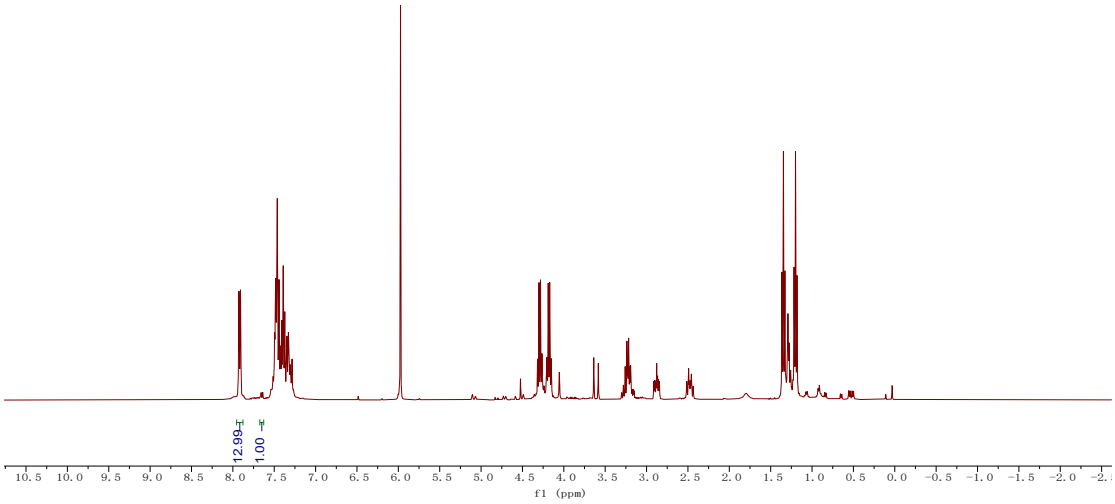



7.93 7.91 7.52 7.50 7.49 7.48 7.48 7.46 7.44 7.43 7.42 7.41 7.41 7.39 7.38 7.35 7.34 7.33 4.32 4.30 4.28 4.27 4.21 4.19 4.17 4.16 3.28 3.26 3.24 3.23 3.22 3.21 3.20 2.91 2.90 2.89 2.88 2.87 2.86 2.85 2.49 2.49 2.48 2.47 2.46 1.37 1.35 1.33 1.22 1.20 1.18
CO2Et
N
F
EtO2C
1H NMR (400 MHz, Chloroform-d)
(E)-3aa
1.96 7.95 2.00 1.95 2.01 0.99 1.00 3.00 3.01
f1 (ppm)

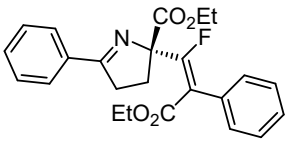

7.65 7.63 7.47 7.45 7.42 7.40 7.37 7.36 7.34 7.32 7.30 7.28 4.27 4.26 4.24 4.22 3.95 3.94 3.92 3.89 3.87 3.85 3.85 3.84 3.83 3.14 3.11 3.10 3.09 3.05 3.03 2.64 2.62 2.60 2.59 2.58 2.55 2.53 2.52 2.48 1.30 1.28 1.26 1.23 1.21
CO2Et
N
F
CO2Et
(Z)-3aa
1.75 8.03 2.04 1.98 2.02 2.00 3.36 3.01
f1 (ppm)



crude product of **3aa**
E/*Z* = 12.99:1

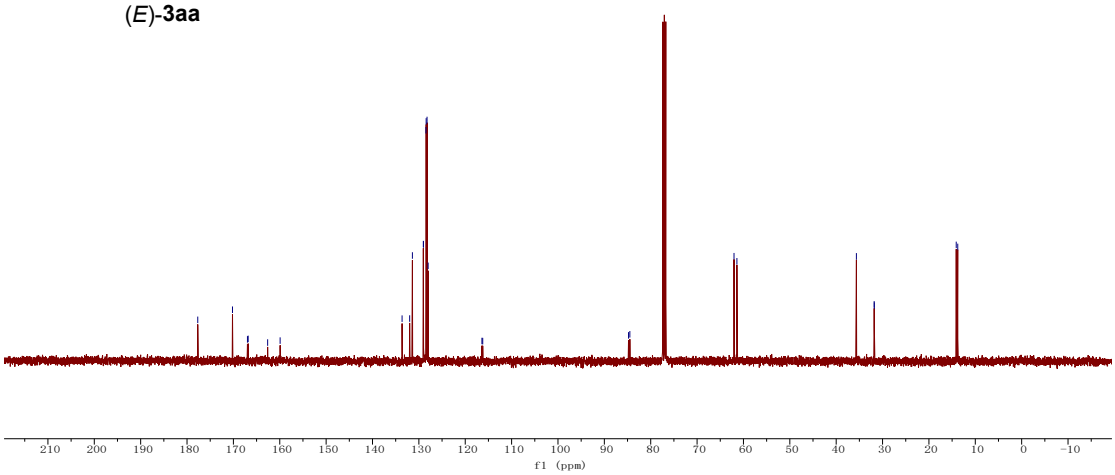


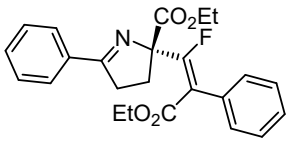
177.69
170.19
166.97
166.82
162.61
159.92
133.62
131.99
131.39
129.04
129.00
128.47
128.43
128.24
128.00
116.40
116.23
84.78
84.50
62.04
61.41
35.64
31.81
31.78
14.11
13.78



(*E*)-**3aa**

^{13}C NMR (101 MHz, Chloroform-d)

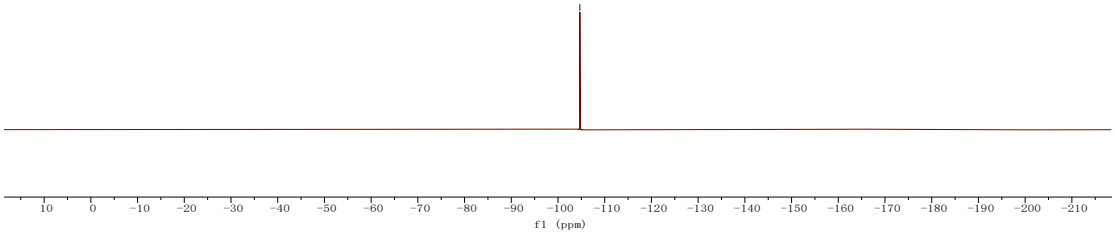


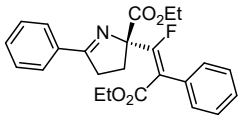


(*E*)-**3aa**

-104.68

^{19}F NMR (376 MHz, Chloroform-d)

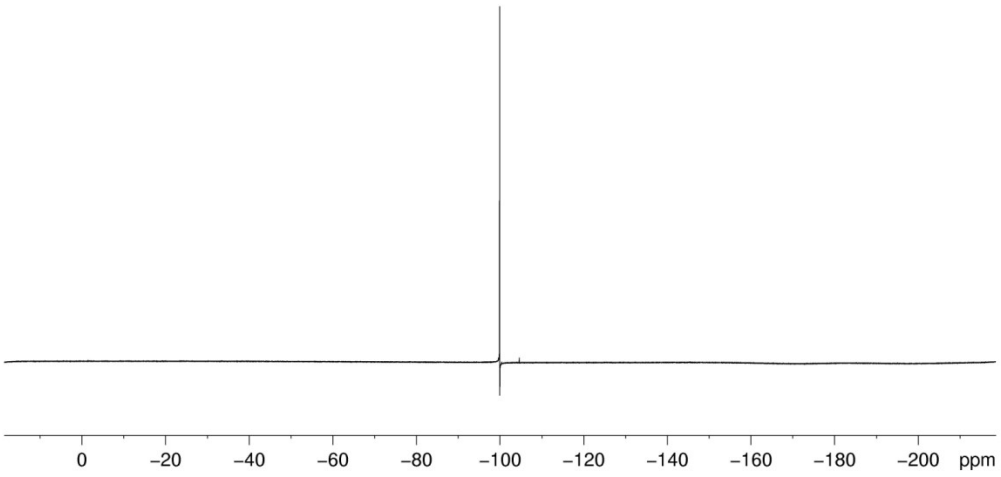


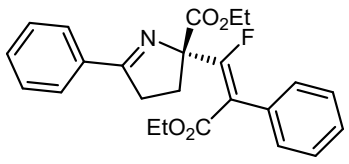


(*Z*)-**3aa**

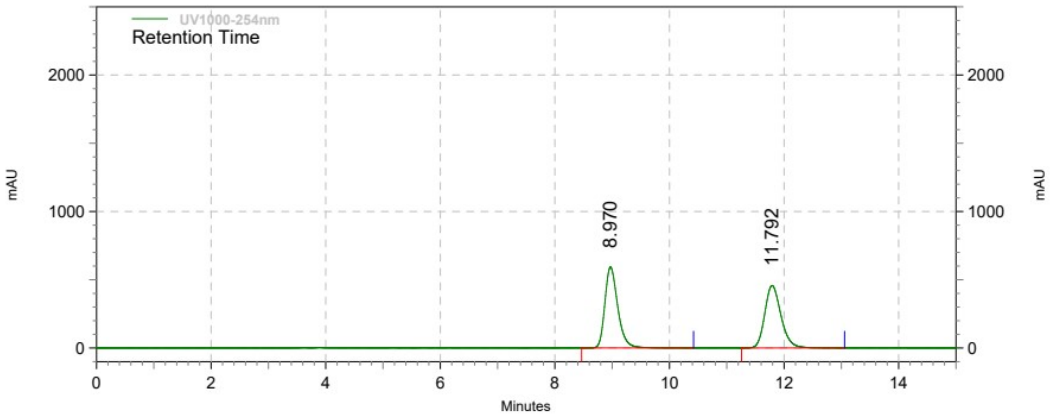
−99.954

^{19}F NMR (376 MHz, Chloroform-d)



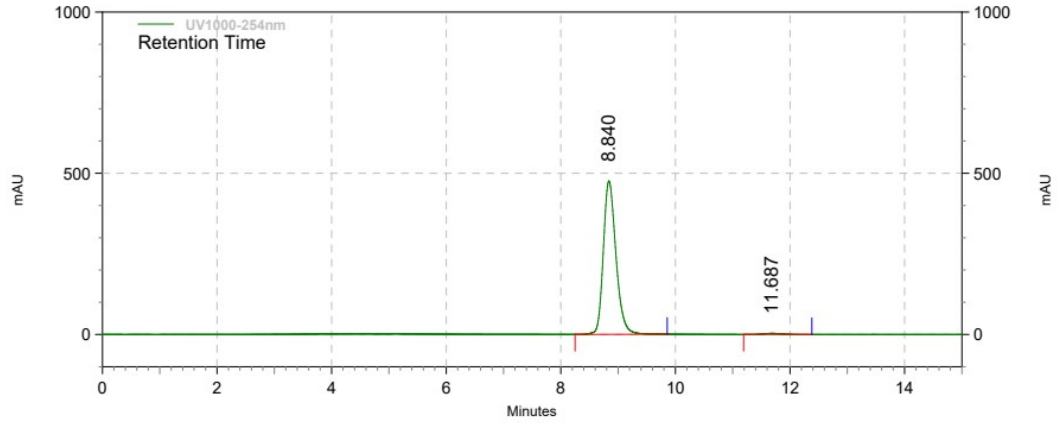


(*E*)-**3aa**



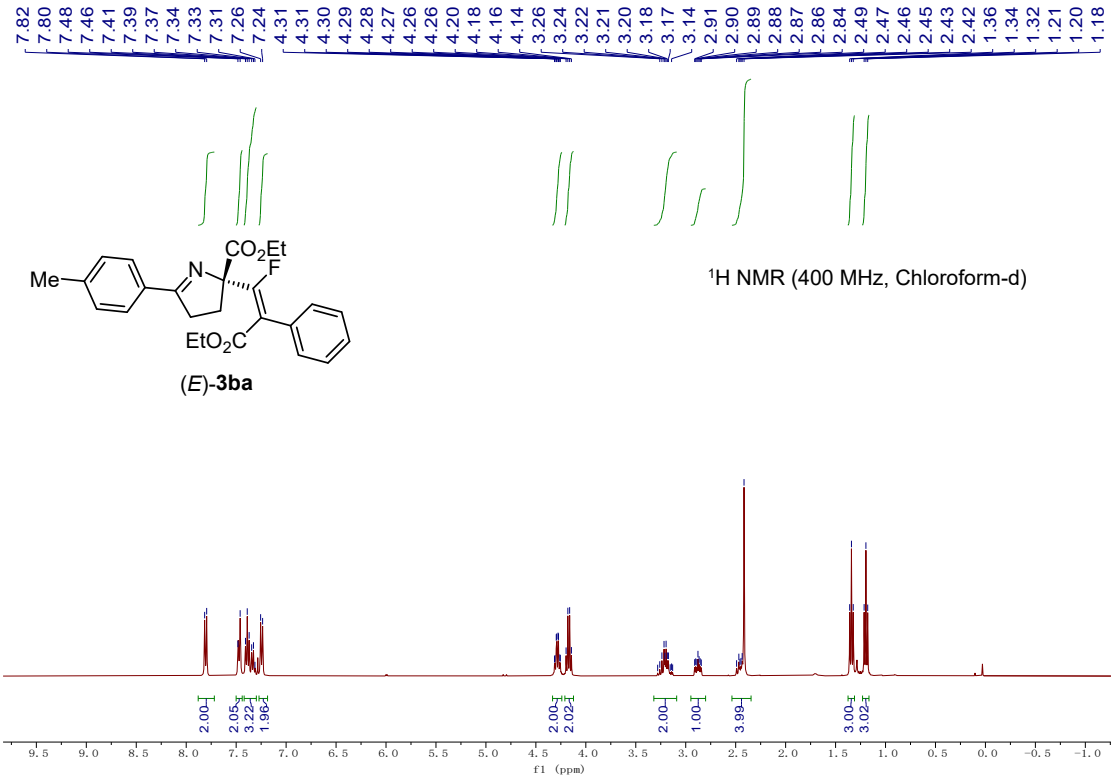
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
8.970	9256250	50.76	592780	56.44
11.792	8980866	49.24	457541	43.56
Totals	18237116	100.00	1050321	100.00



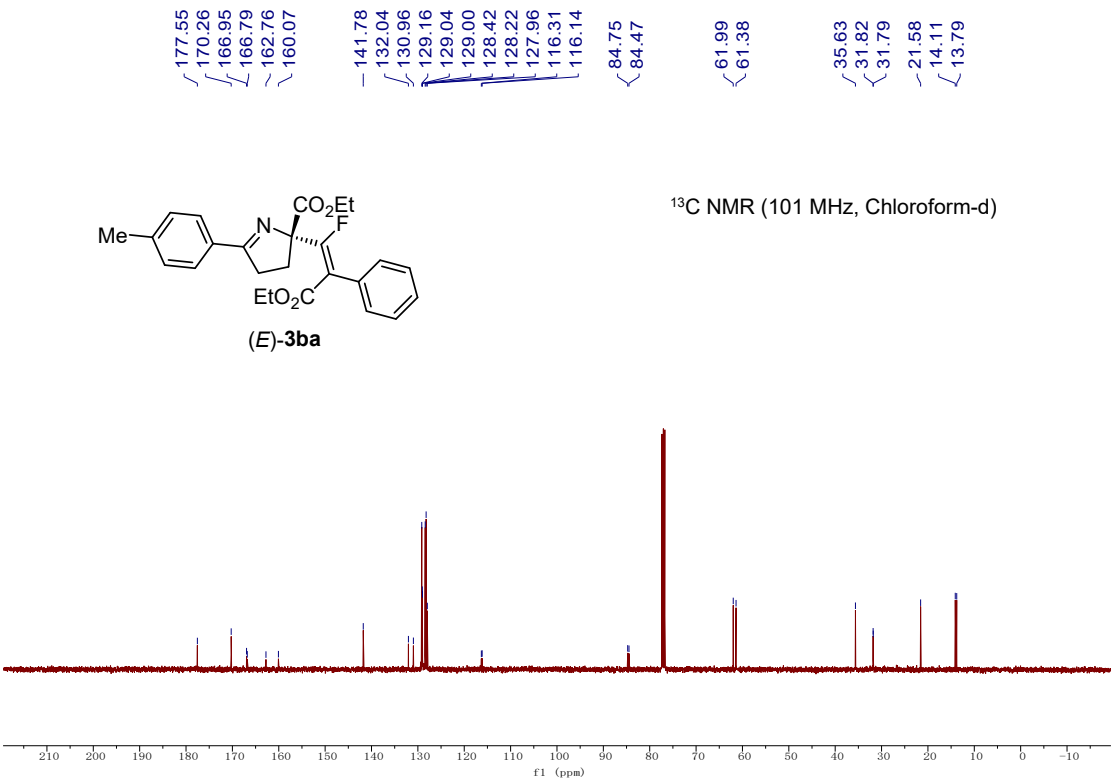
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
8.840	7288934	99.01	475776	99.26
11.687	73052	0.99	3550	0.74
Totals	7361986	100.00	479326	100.00



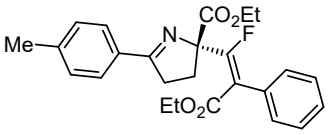
(*E*)-**3ba**

^{1}H NMR (400 MHz, Chloroform-d)



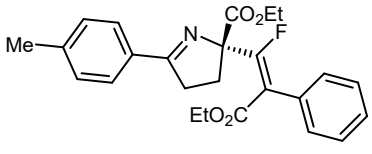
(*E*)-**3ba**

^{13}C NMR (101 MHz, Chloroform-d)

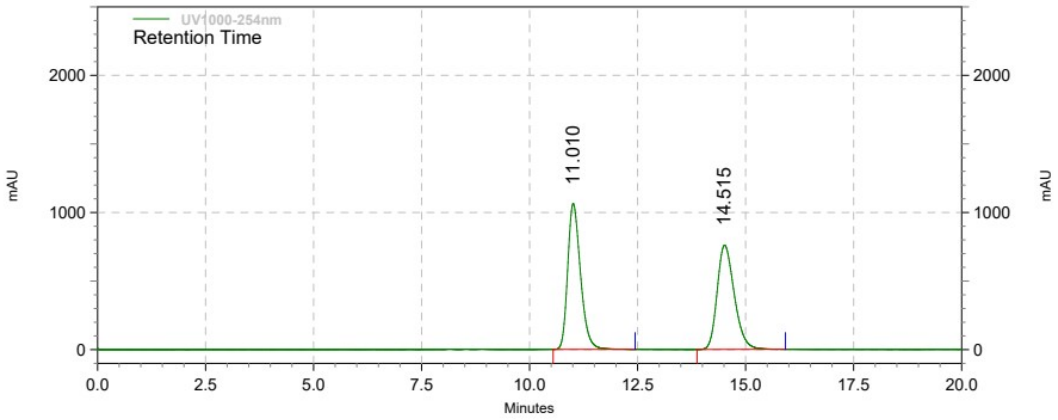


(*E*)-**3ba**

^{19}F NMR (376 MHz, Chloroform-d)



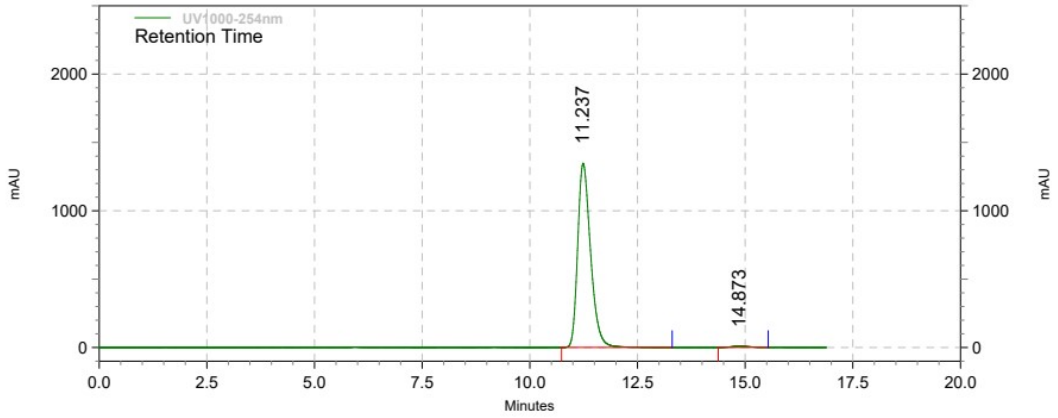
(*E*)-**3ba**



UV1000-254nm

Results

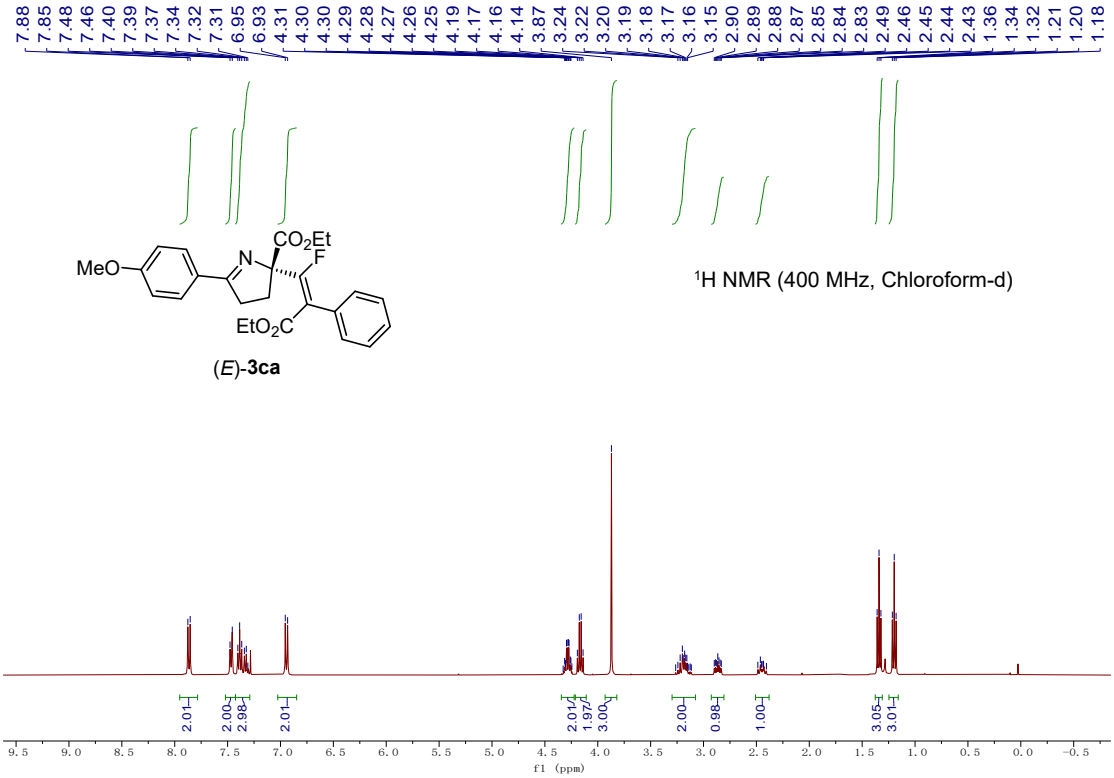
Retention Time	Area	Area %	Height	Height %
11.010	21919399	51.08	1063652	58.31
14.515	20990253	48.92	760440	41.69
Totals	42909652	100.00	1824092	100.00



UV1000-254nm

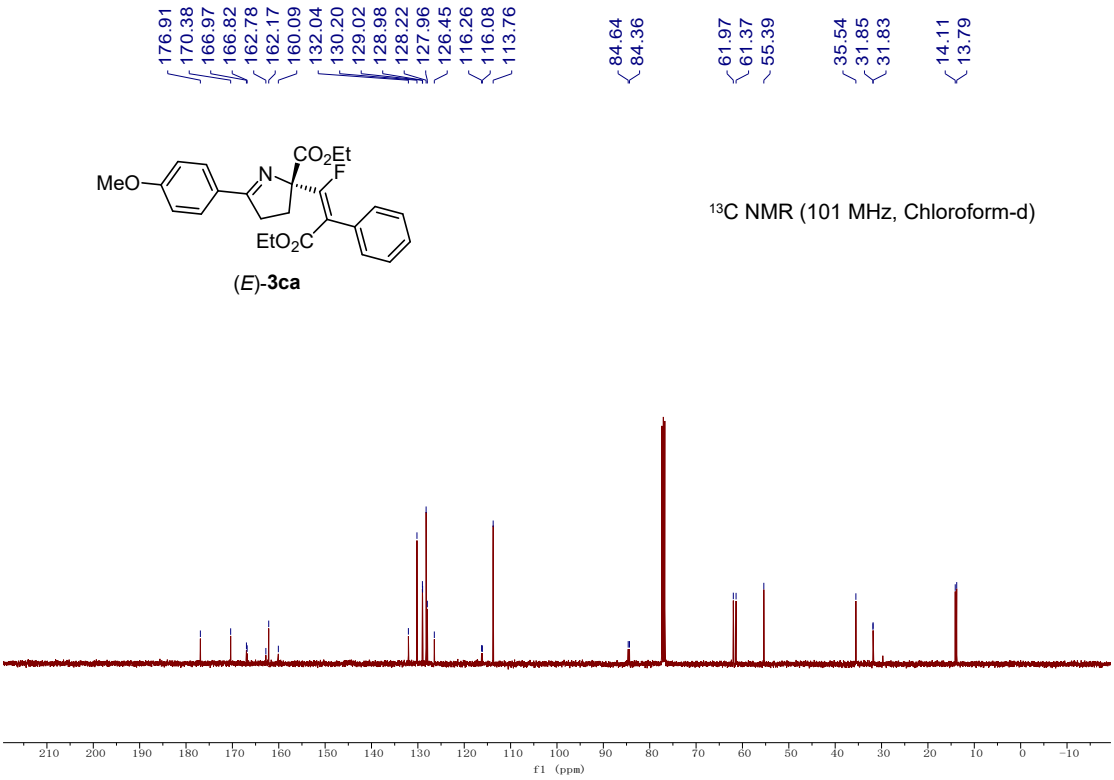
Results

Retention Time	Area	Area %	Height	Height %
11.237	28022717	99.13	1347320	99.34
14.873	246874	0.87	8986	0.66
Totals	28269591	100.00	1356306	100.00



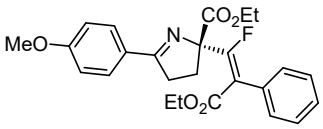
(*E*)-**3ca**

^{1}H NMR (400 MHz, Chloroform-d)



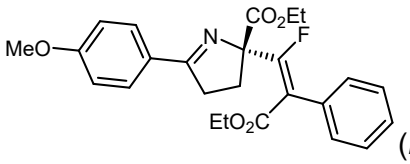
(*E*)-**3ca**

^{13}C NMR (101 MHz, Chloroform-d)

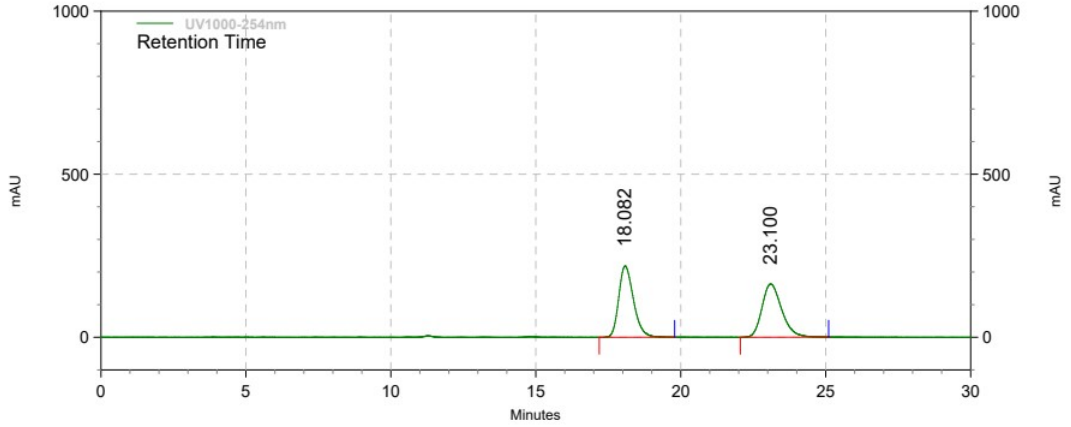


(*E*)-**3ca**

^{19}F NMR (376 MHz, Chloroform-d)

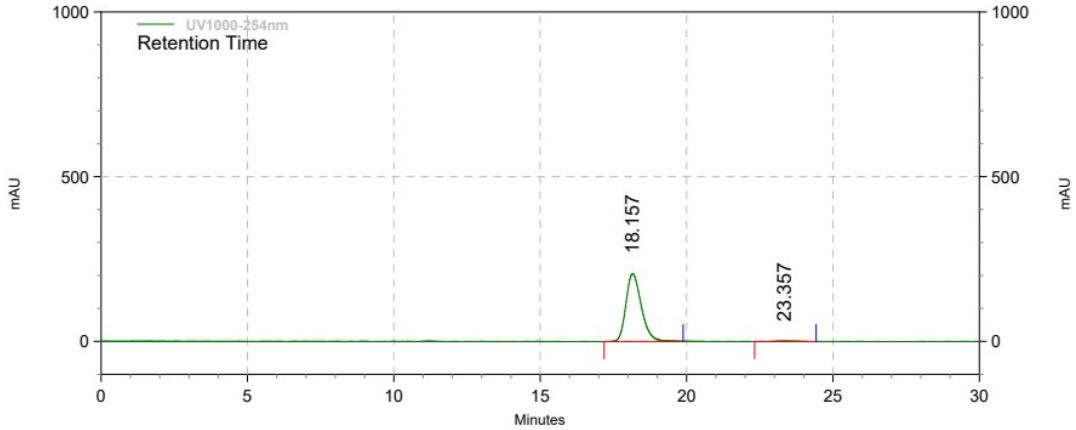


(*E*)-**3ca**



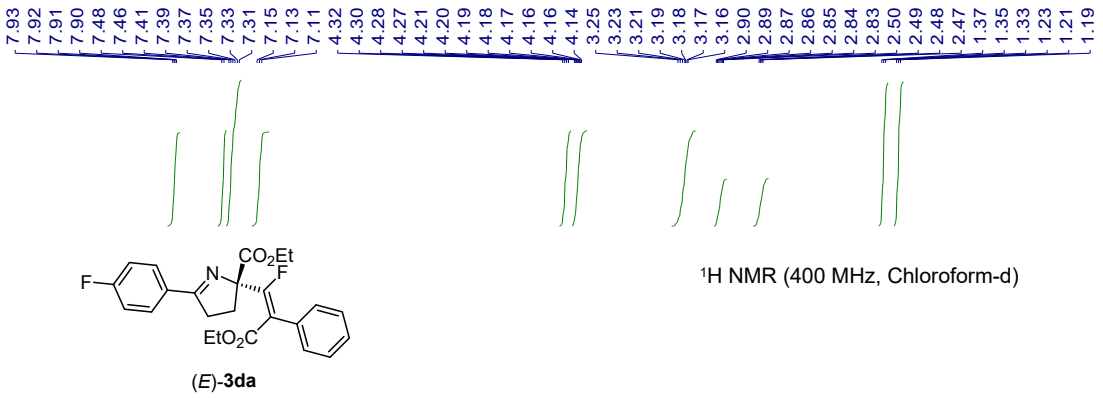
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
18.082	7728630	50.08	218499	57.24
23.100	7702631	49.92	163248	42.76
Totals	15431261	100.00	381747	100.00



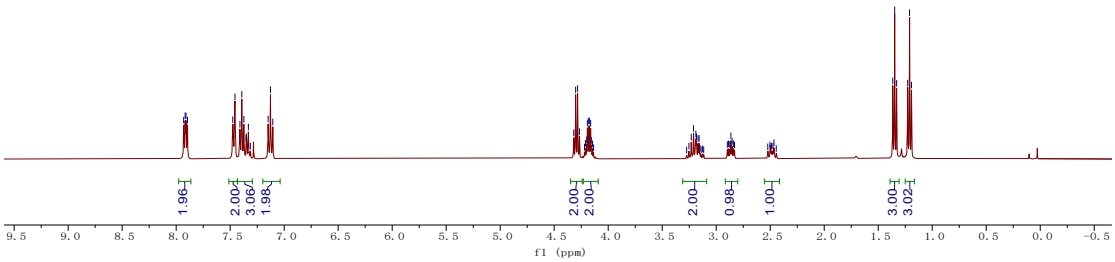
UV1000-254nm
Results

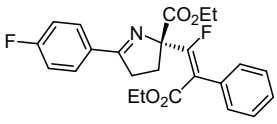
Retention Time	Area	Area %	Height	Height %
18.157	7496991	99.21	206341	99.46
23.357	59921	0.79	1116	0.54
Totals	7556912	100.00	207457	100.00



(*E*)-**3da**

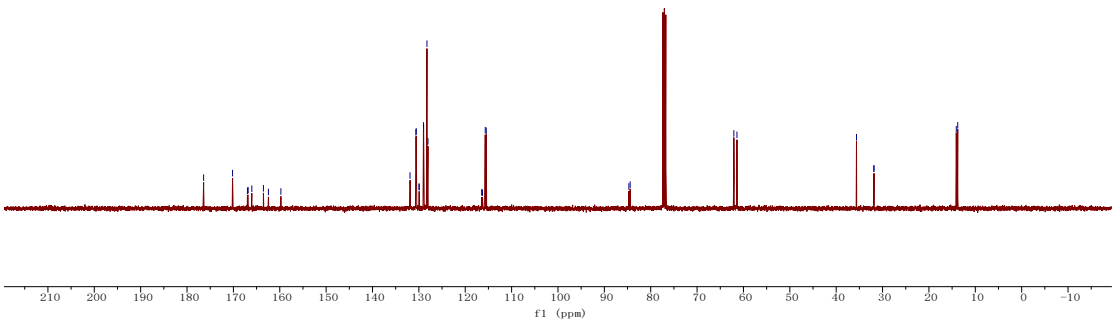
^{1}H NMR (400 MHz, Chloroform-d)

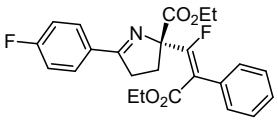




(*E*)-**3da**

^{13}C NMR (101 MHz, Chloroform-d)

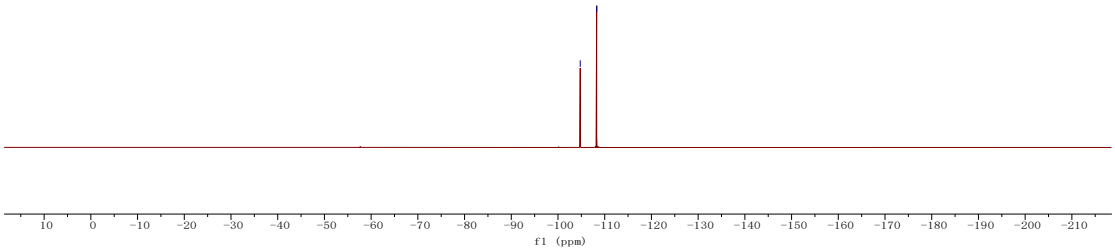


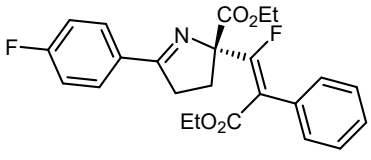


(*E*)-**3da**

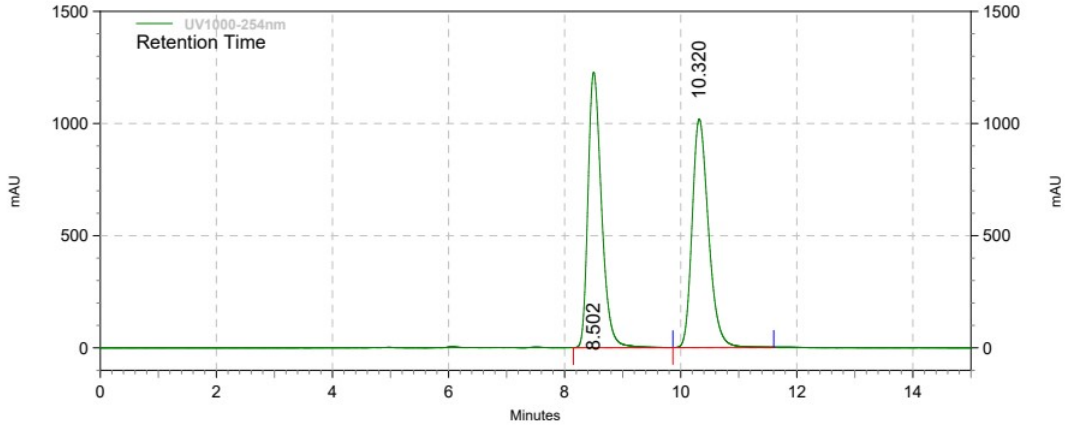
-104.76
-108.28

^{19}F NMR (376 MHz, Chloroform-d)



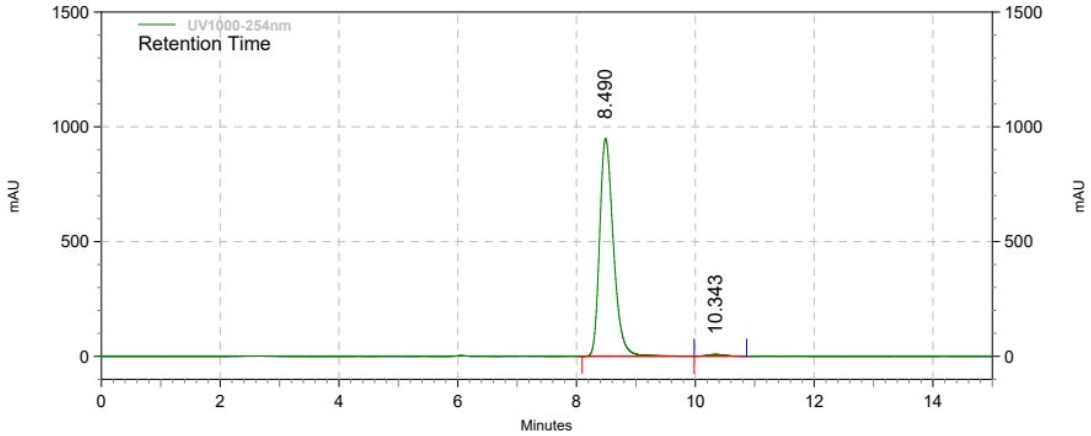


(*E*)-**3da**



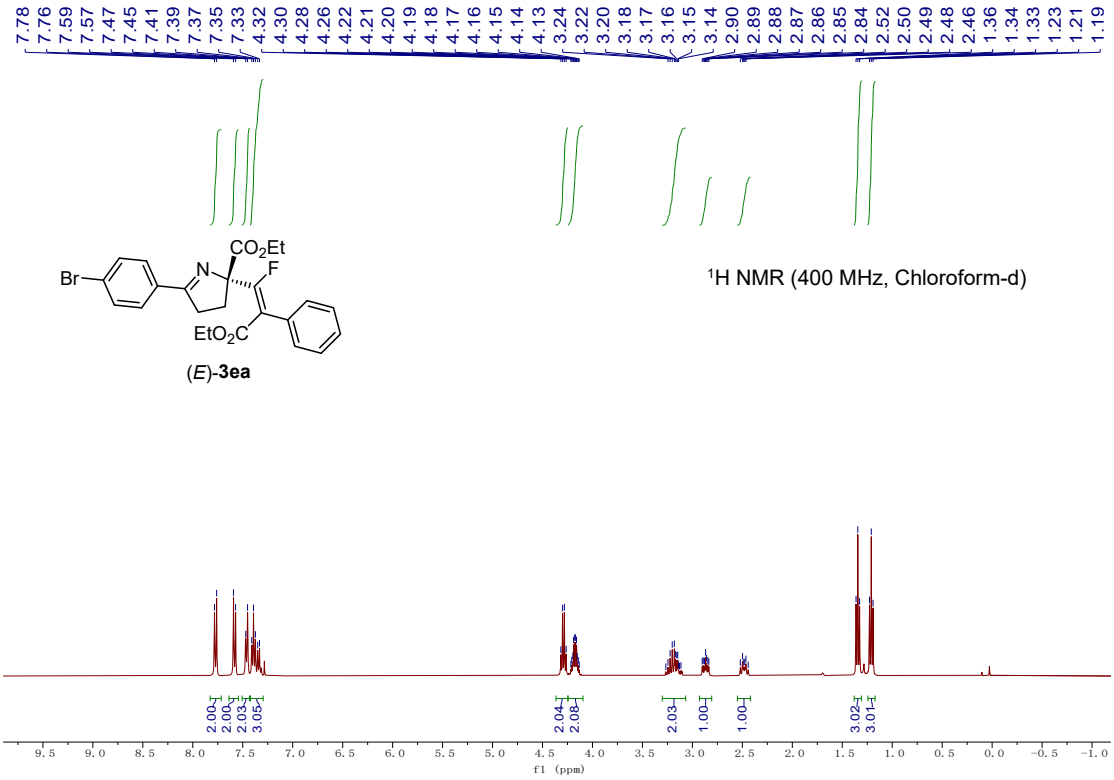
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
8.502	19879103	49.99	1228473	54.66
10.320	19890191	50.01	1019024	45.34
Totals	39769294	100.00	2247497	100.00



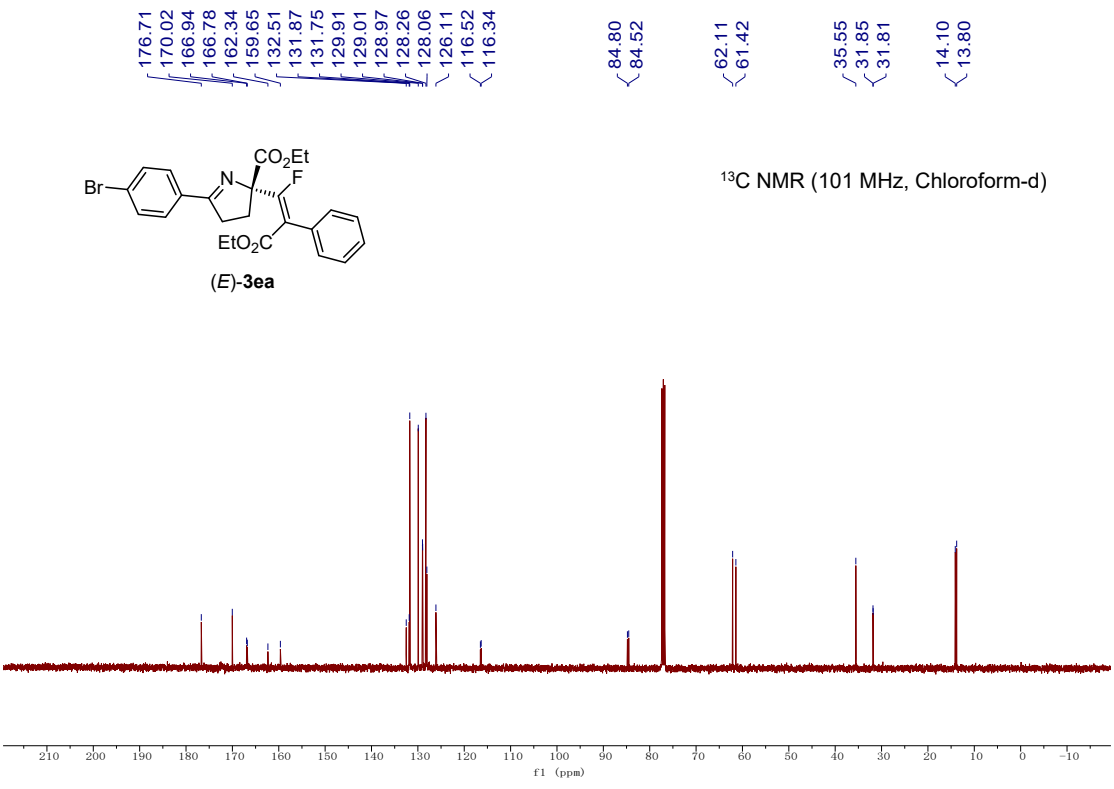
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
8.490	15294138	98.98	949039	99.18
10.343	156889	1.02	7859	0.82
Totals	15451027	100.00	956898	100.00



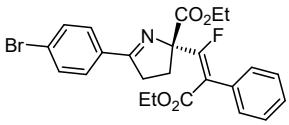
(*E*)-**3ea**

^{1}H NMR (400 MHz, Chloroform-d)



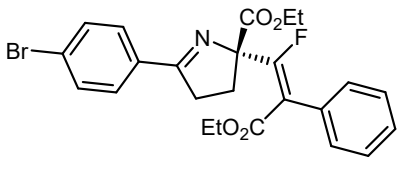
(*E*)-**3ea**

^{13}C NMR (101 MHz, Chloroform-d)

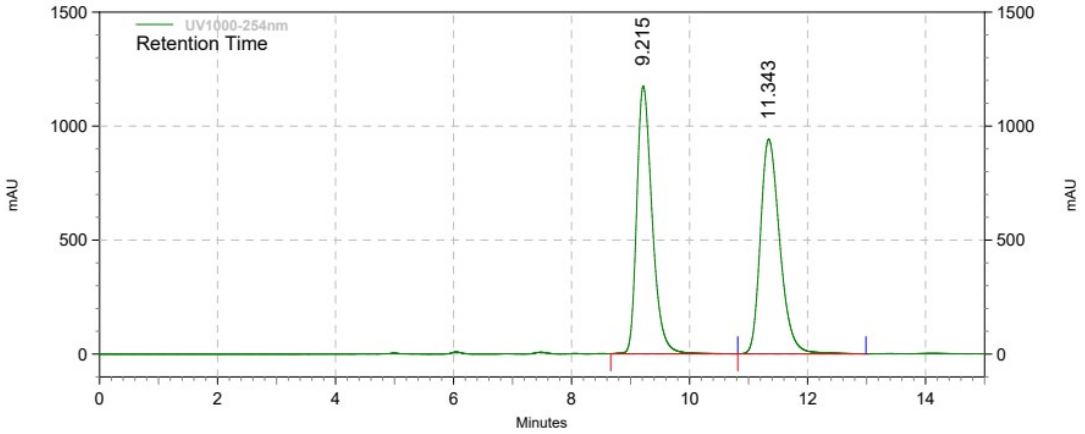


(*E*)-**3ea**

^{19}F NMR (376 MHz, Chloroform-d)

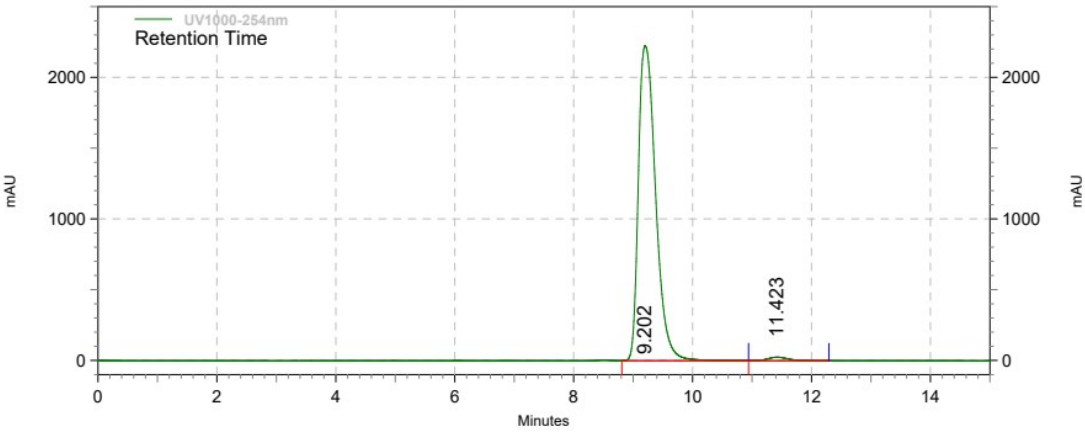


(*E*)-**3ea**



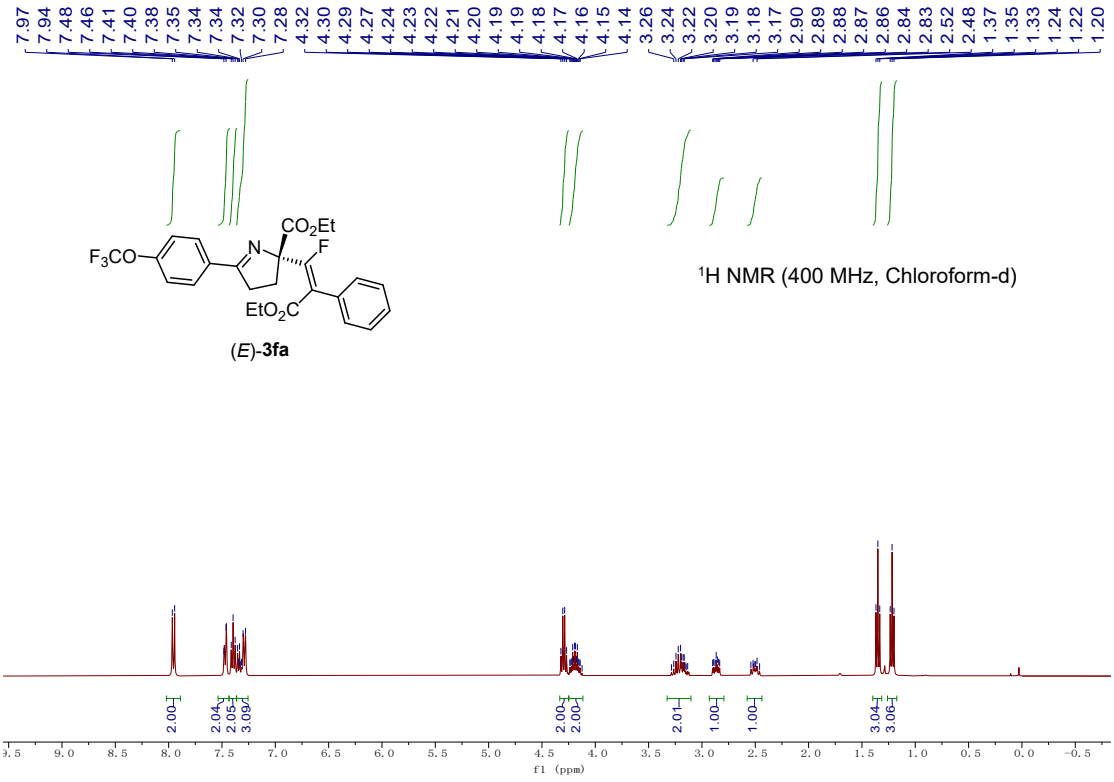
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
9.215	21301173	49.76	1175177	55.52
11.343	21504223	50.24	941609	44.48
Totals	42805396	100.00	2116786	100.00



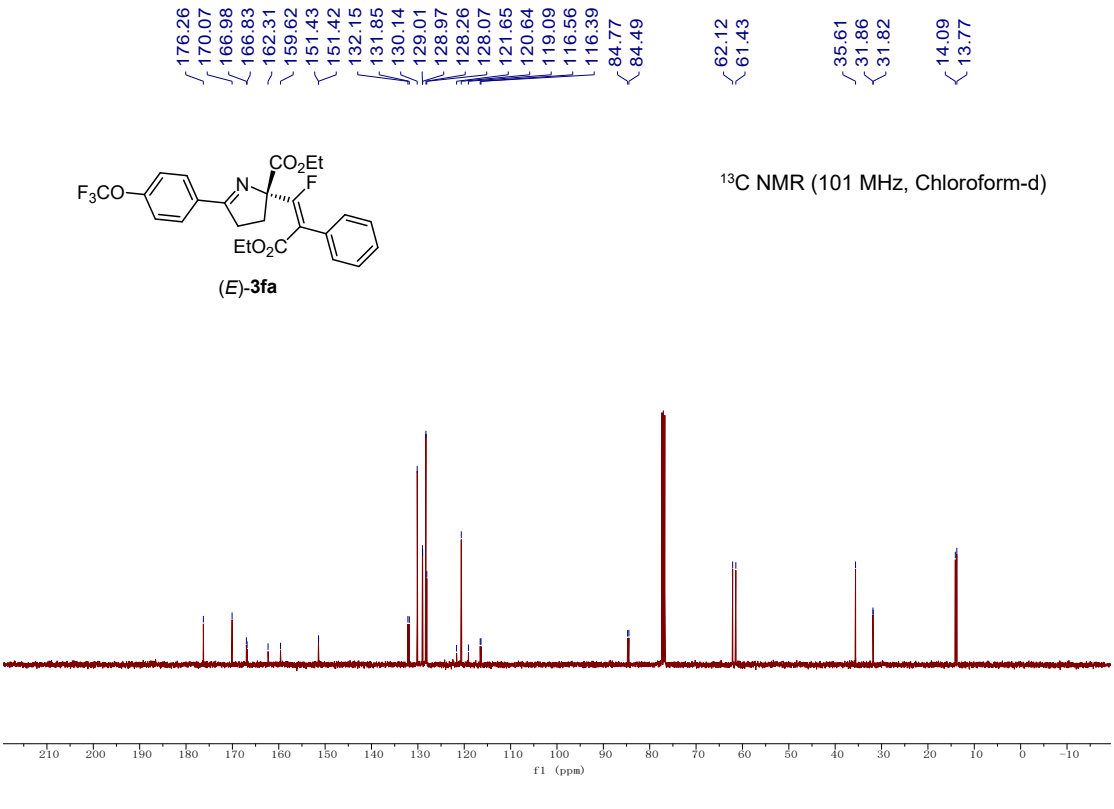
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
9.202	44888471	98.70	2225917	98.89
11.423	589685	1.30	24947	1.11
Totals	45478156	100.00	2250864	100.00



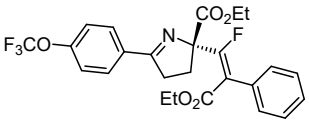
(*E*)-**3fa**

^{1}H NMR (400 MHz, Chloroform-d)



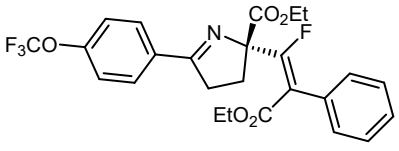
(*E*)-**3fa**

^{13}C NMR (101 MHz, Chloroform-d)

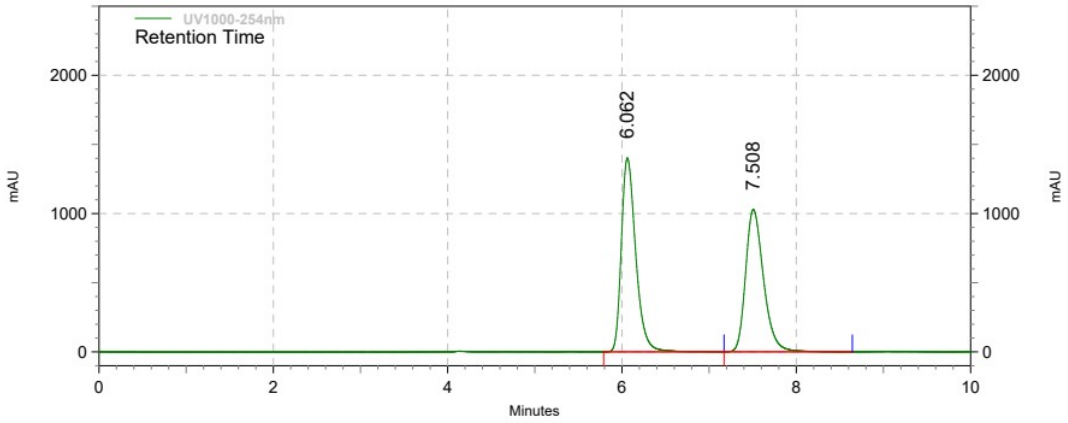


(*E*)-**3fa**

^{19}F NMR (376 MHz, Chloroform-d)

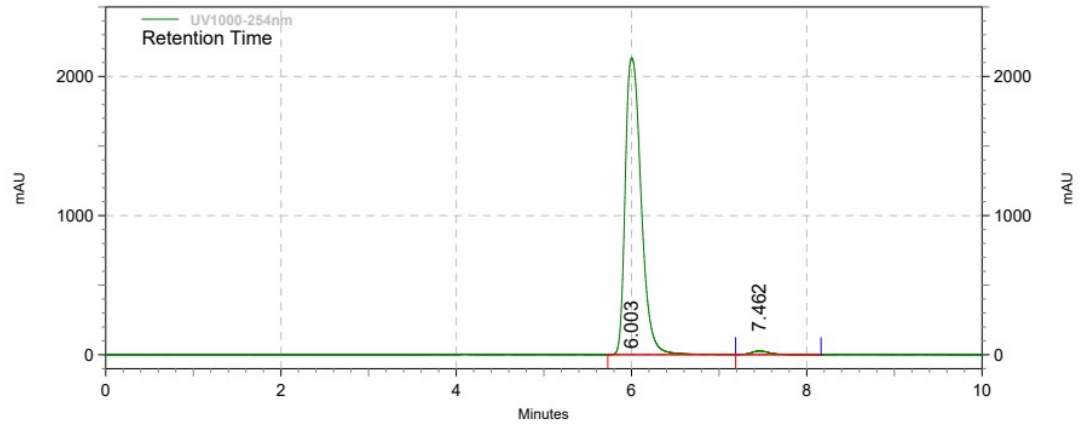


(*E*)-**3fa**



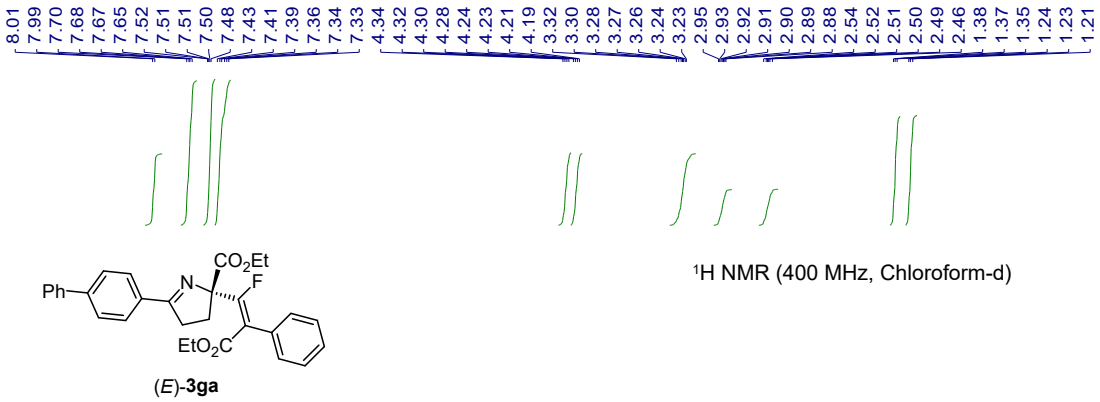
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
6.062	16078693	52.18	1401932	57.66
7.508	14736008	47.82	1029494	42.34
Totals	30814701	100.00	2431426	100.00



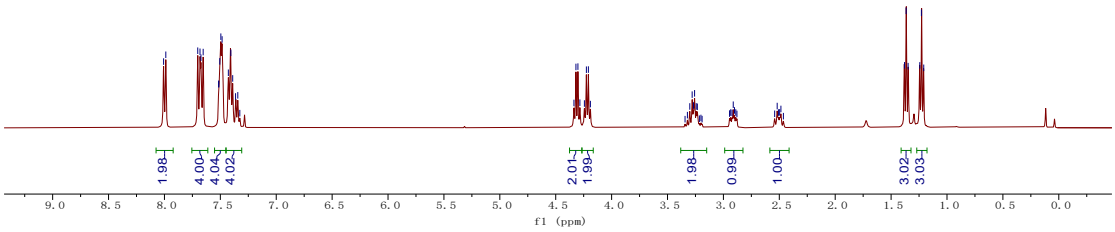
UV1000-254nm
Results

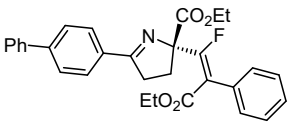
Retention Time	Area	Area %	Height	Height %
6.003	26886616	98.58	2132424	98.78
7.462	387119	1.42	26434	1.22
Totals	27273735	100.00	2158858	100.00



(*E*)-**3ga**

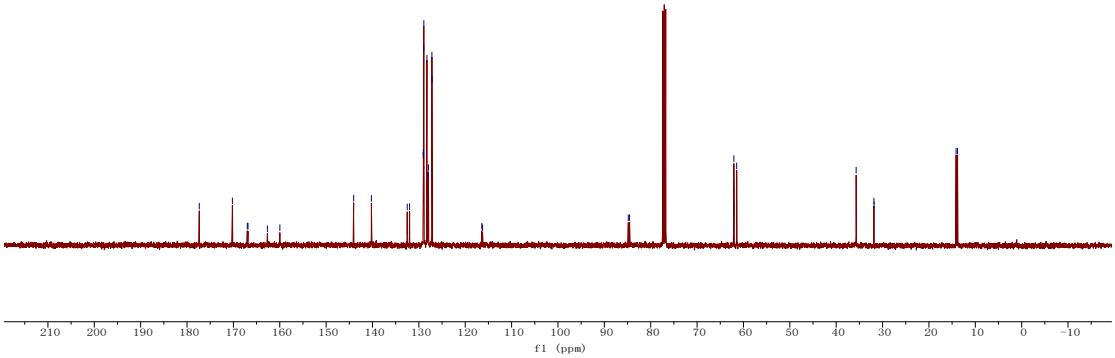
^{1}H NMR (400 MHz, Chloroform-d)

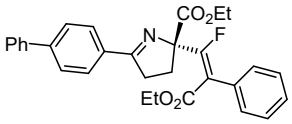




(*E*)-**3ga**

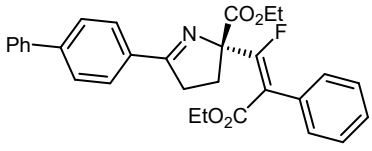
^{13}C NMR (101 MHz, Chloroform-d)



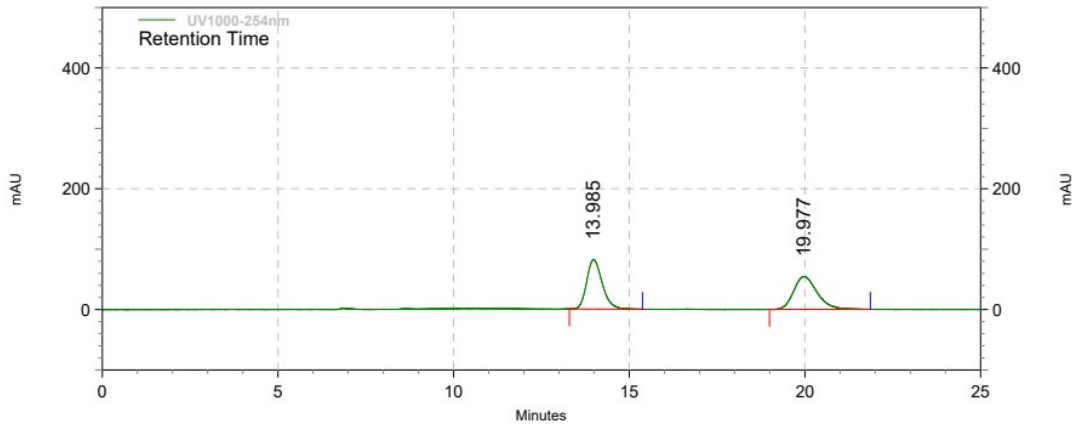


(*E*)-**3ga**

^{19}F NMR (376 MHz, Chloroform-d)

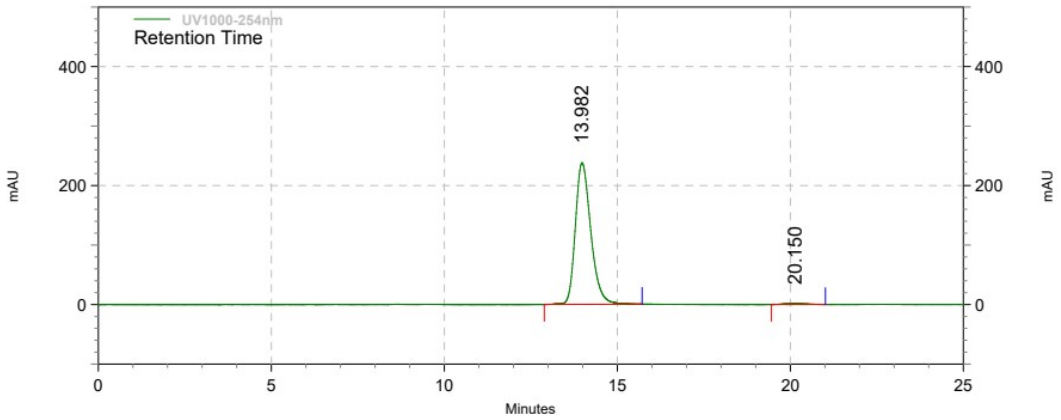


(*E*)-**3ga**



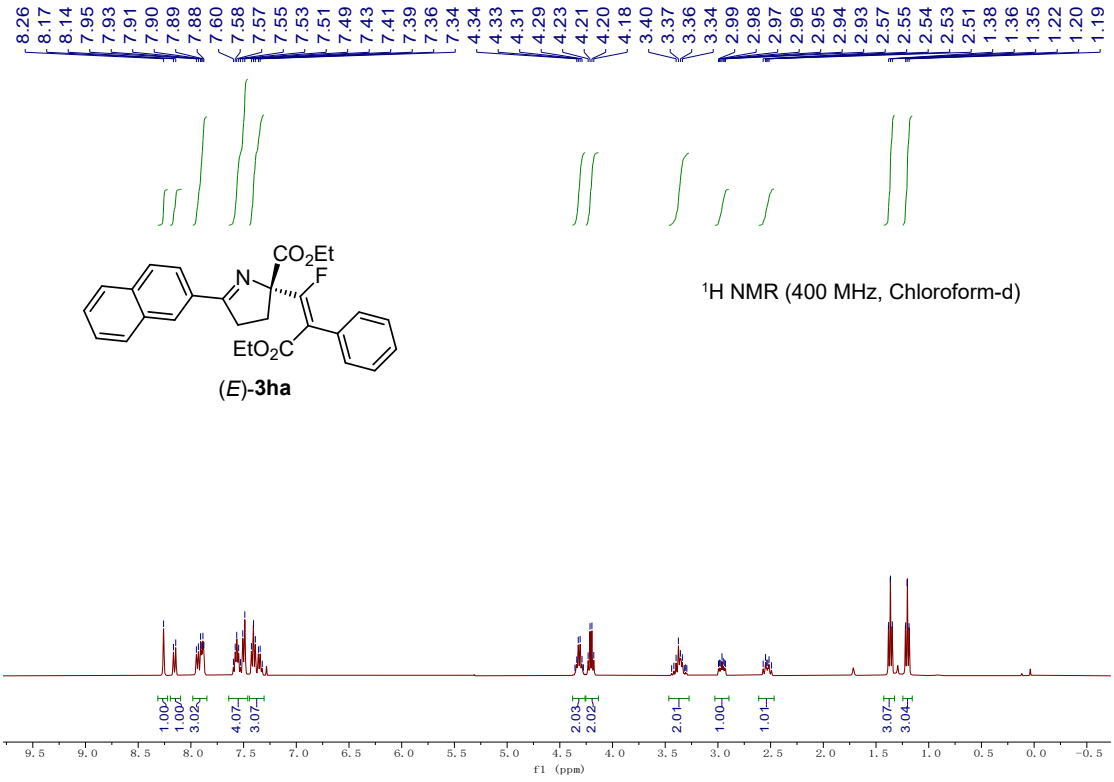
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
13.985	2521897	50.01	82015	60.14
19.977	2521283	49.99	54358	39.86
Totals	5043180	100.00	136373	100.00



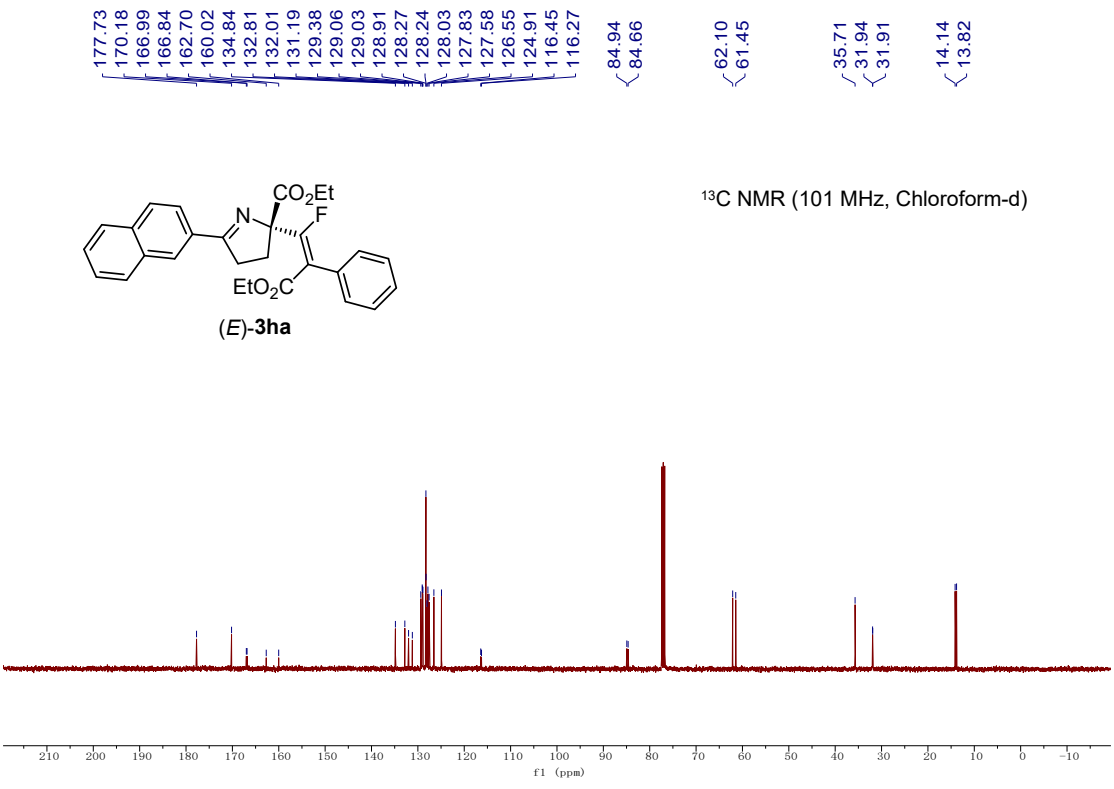
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
13.982	7391656	99.07	237912	99.34
20.150	69224	0.93	1571	0.66
Totals	7460880	100.00	239483	100.00



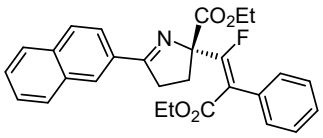
(*E*)-**3ha**

^{1}H NMR (400 MHz, Chloroform-d)



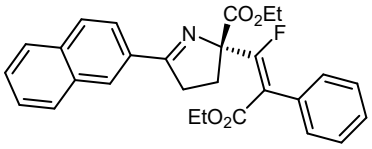
(*E*)-**3ha**

^{13}C NMR (101 MHz, Chloroform-d)

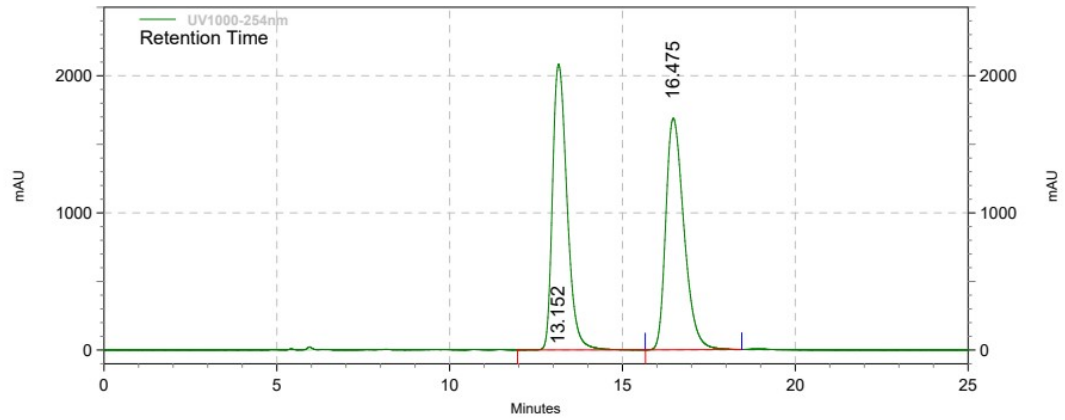


(*E*)-**3ha**

^{19}F NMR (376 MHz, Chloroform-d)

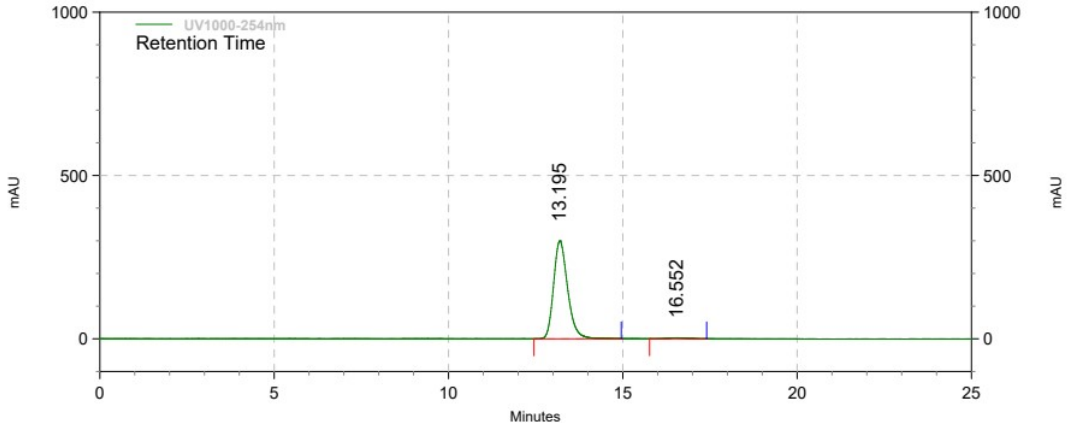


(*E*)-**3ha**



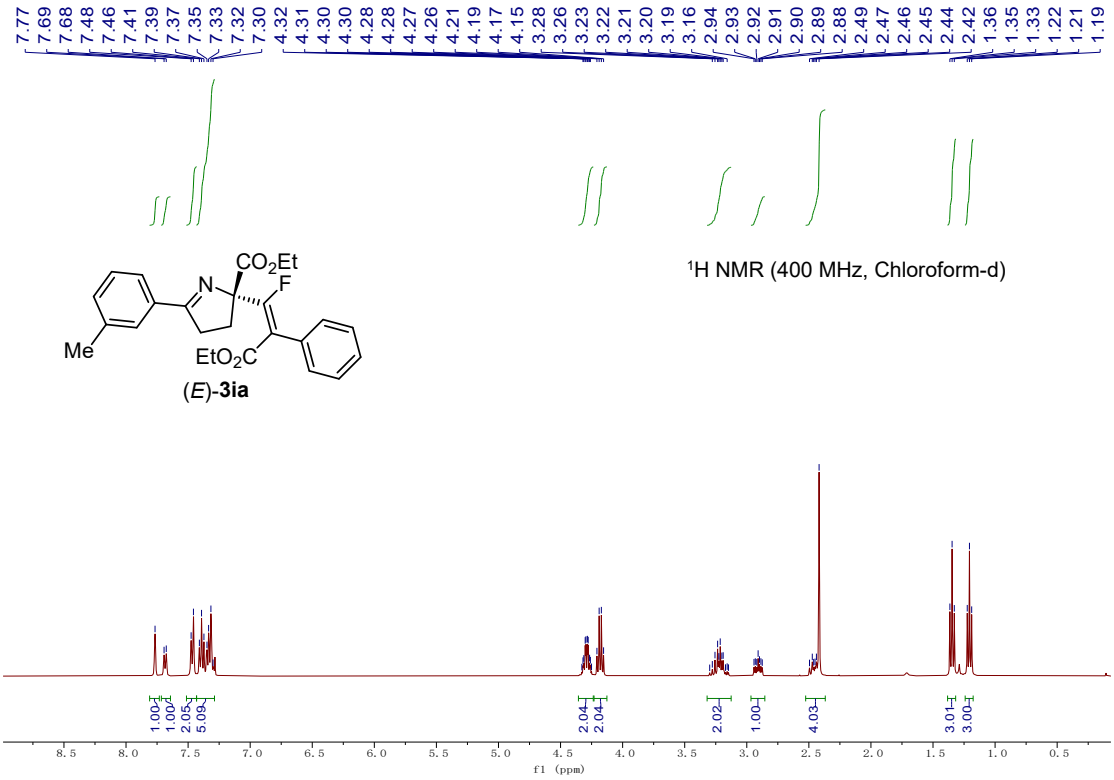
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
13.152	60892321	49.61	2083670	55.25
16.475	61850094	50.39	1687990	44.75
Totals	122742415	100.00	3771660	100.00



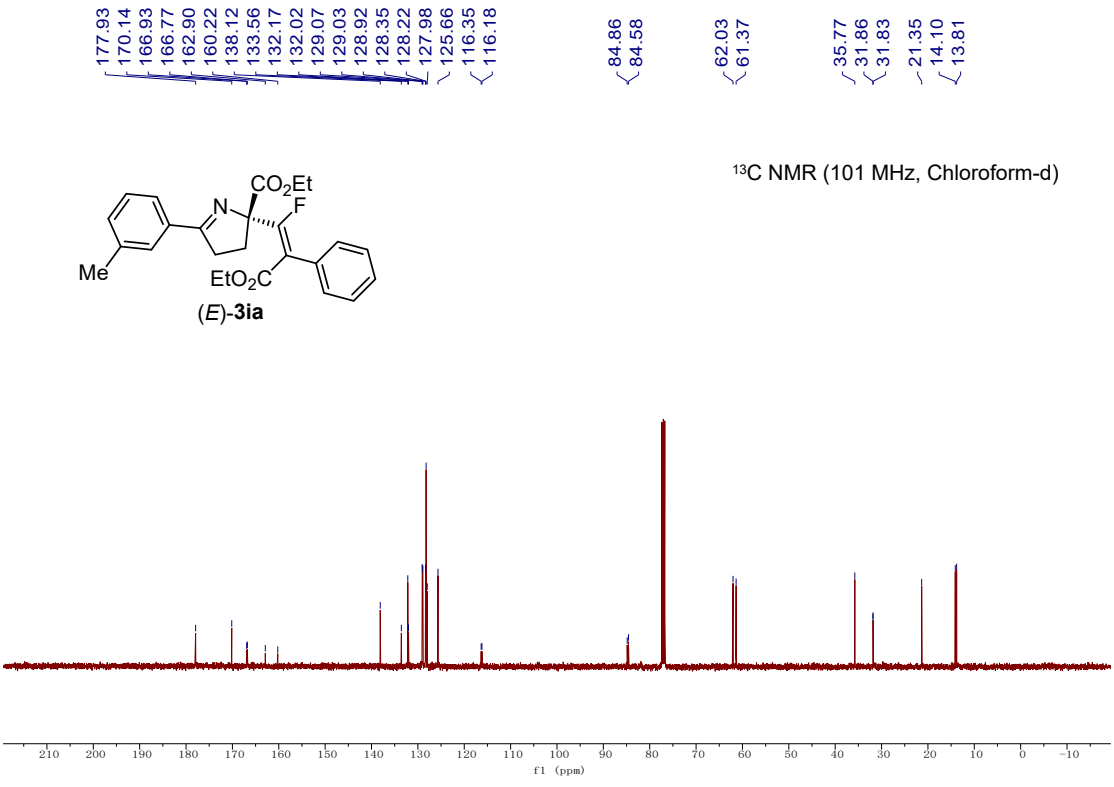
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
13.195	8392558	98.76	299771	99.01
16.552	105095	1.24	2996	0.99
Totals	8497653	100.00	302767	100.00



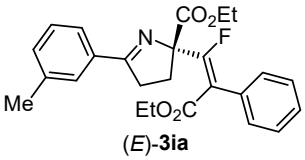
(*E*)-**3ia**

^{1}H NMR (400 MHz, Chloroform-d)



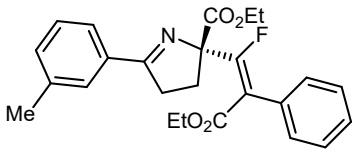
(*E*)-**3ia**

^{13}C NMR (101 MHz, Chloroform-d)

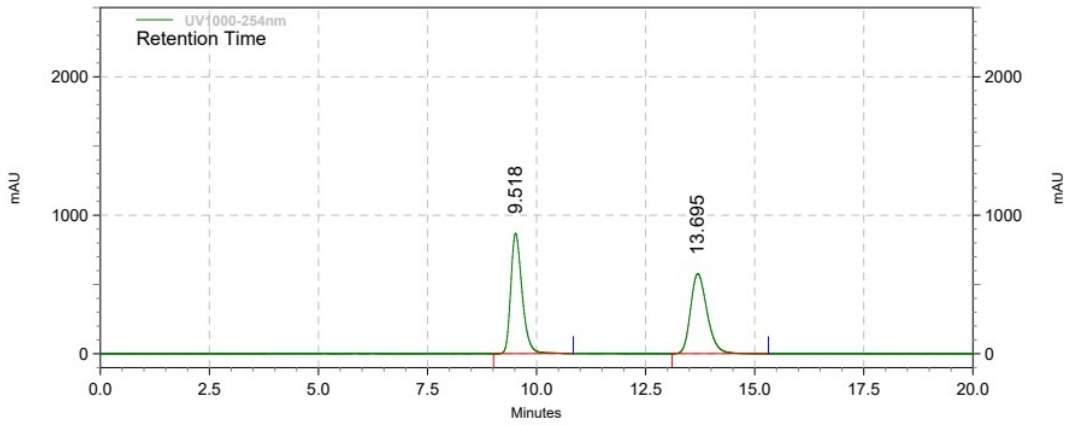


(*E*)-**3ia**

^{19}F NMR (376 MHz, Chloroform-d)

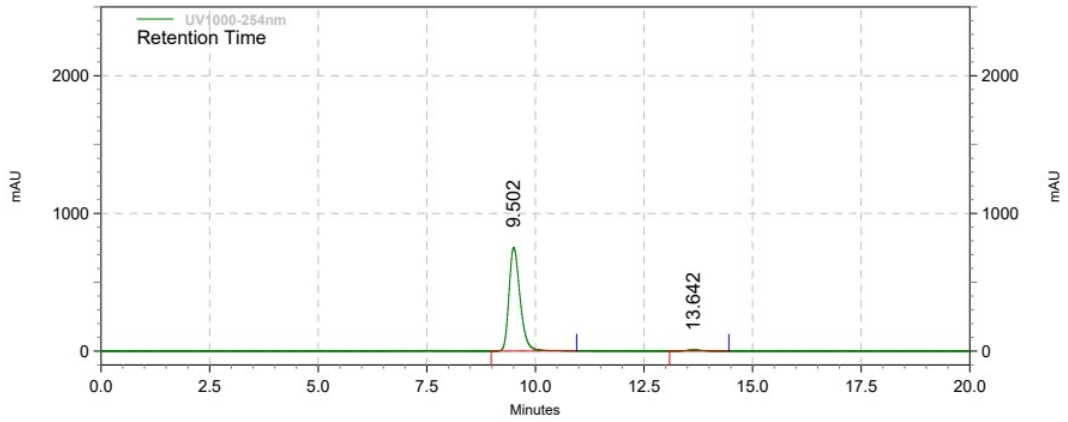


(*E*)-**3ia**



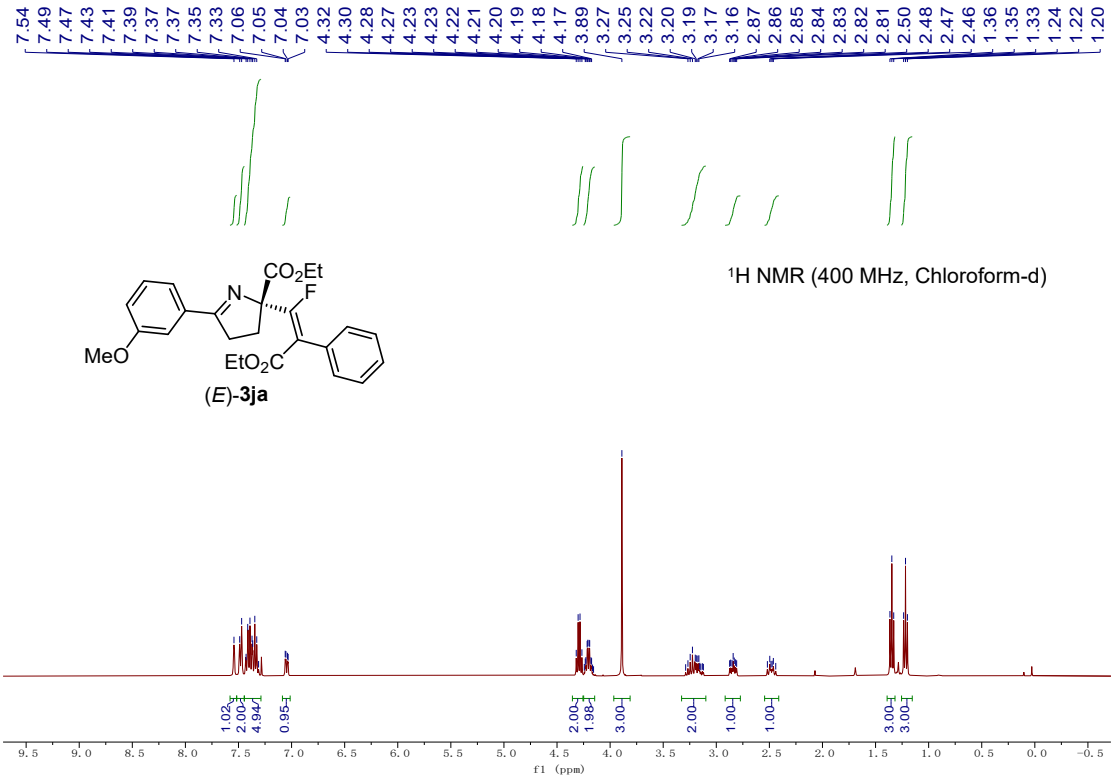
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
9.518	15695311	50.79	868855	60.08
13.695	15210019	49.21	577230	39.92
Totals	30905330	100.00	1446085	100.00



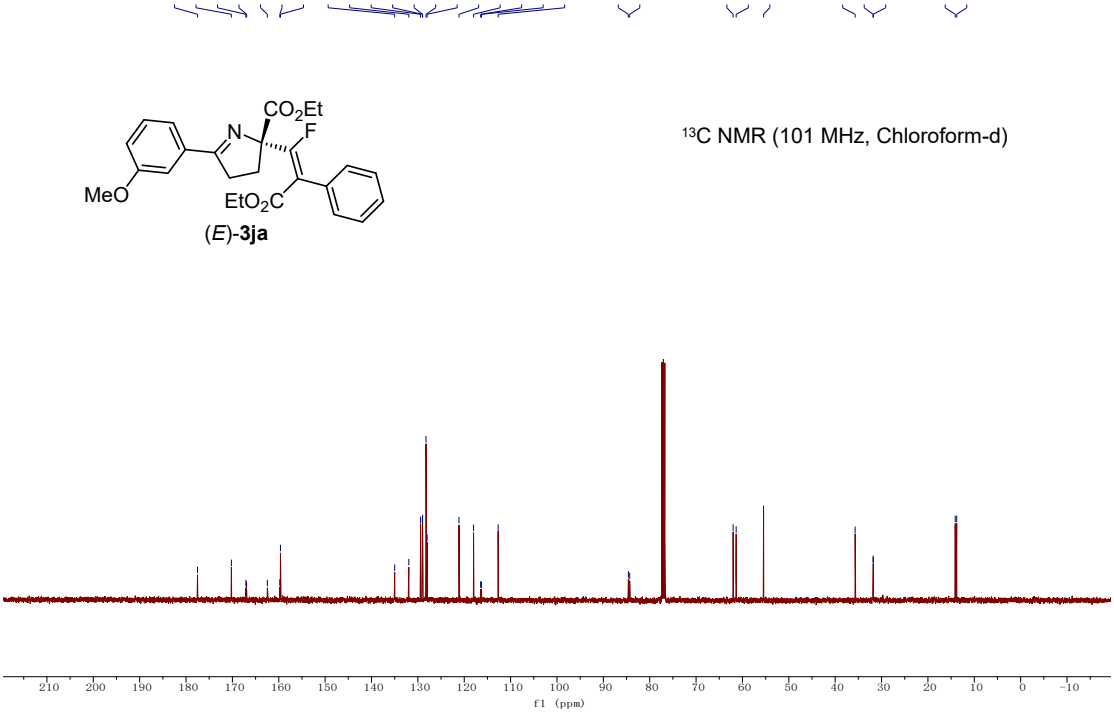
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
9.502	13362108	98.56	752222	99.00
13.642	195619	1.44	7579	1.00
Totals	13557727	100.00	759801	100.00



(*E*)-**3ja**

^{1}H NMR (400 MHz, Chloroform-d)

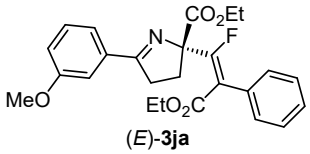


(*E*)-**3ja**

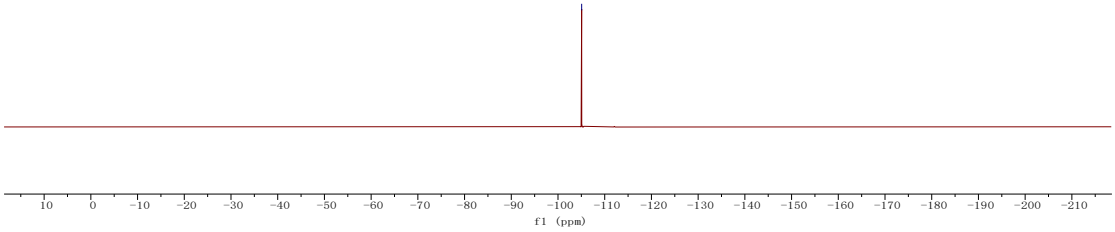
^{13}C NMR (101 MHz, Chloroform-d)

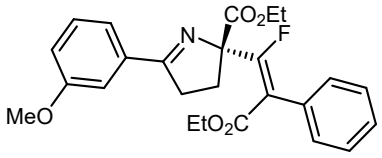
-105.06

^{19}F NMR (376 MHz, Chloroform-d)

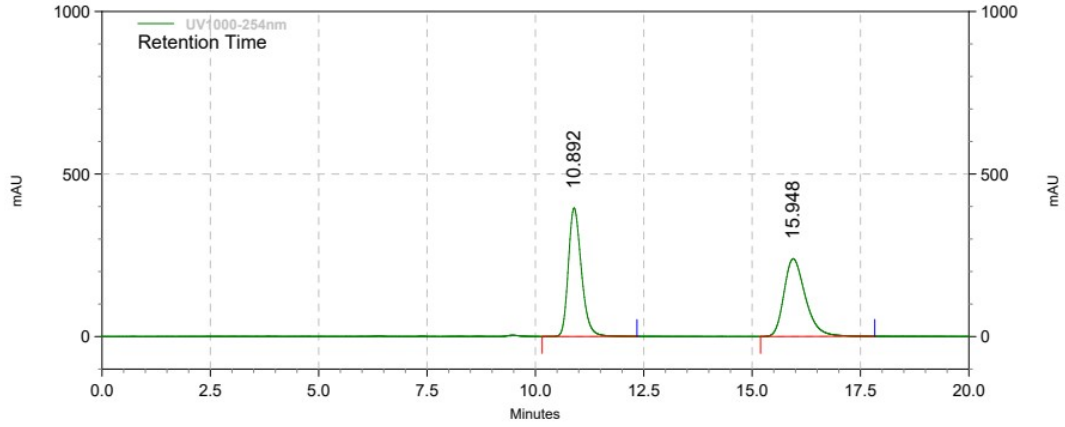


(*E*)-**3ja**



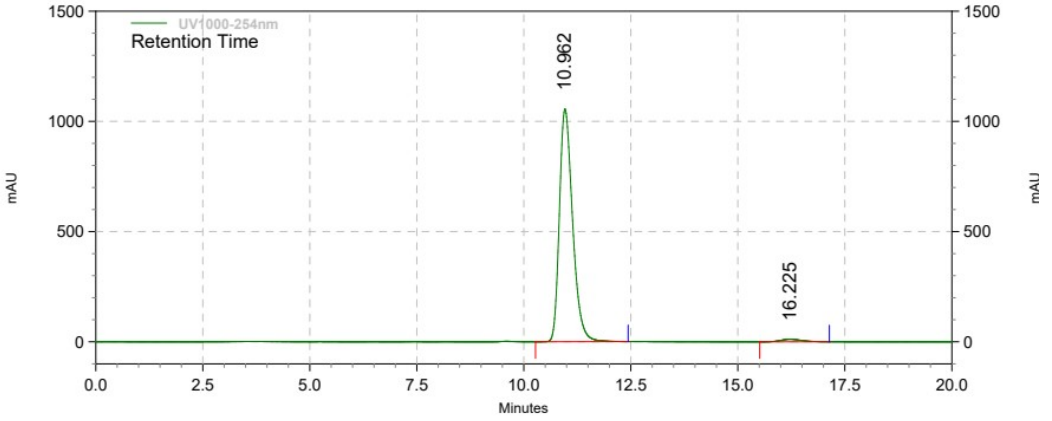


(*E*)-**3ja**



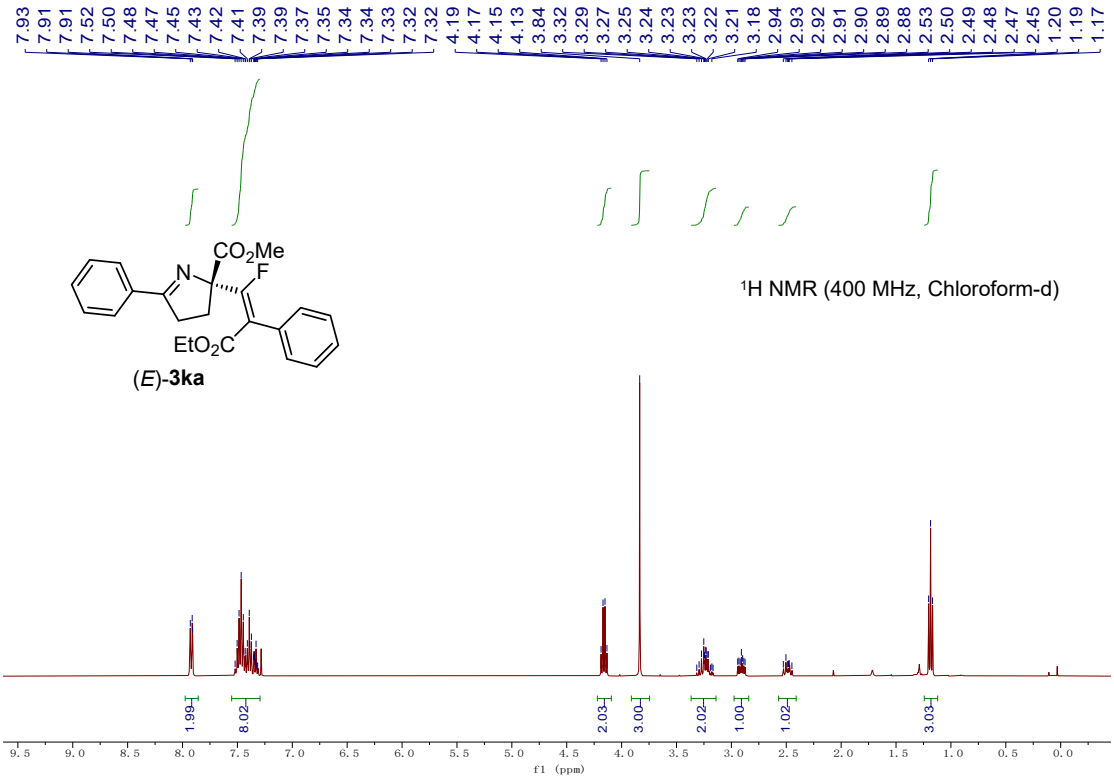
UV1000-254nm
Results

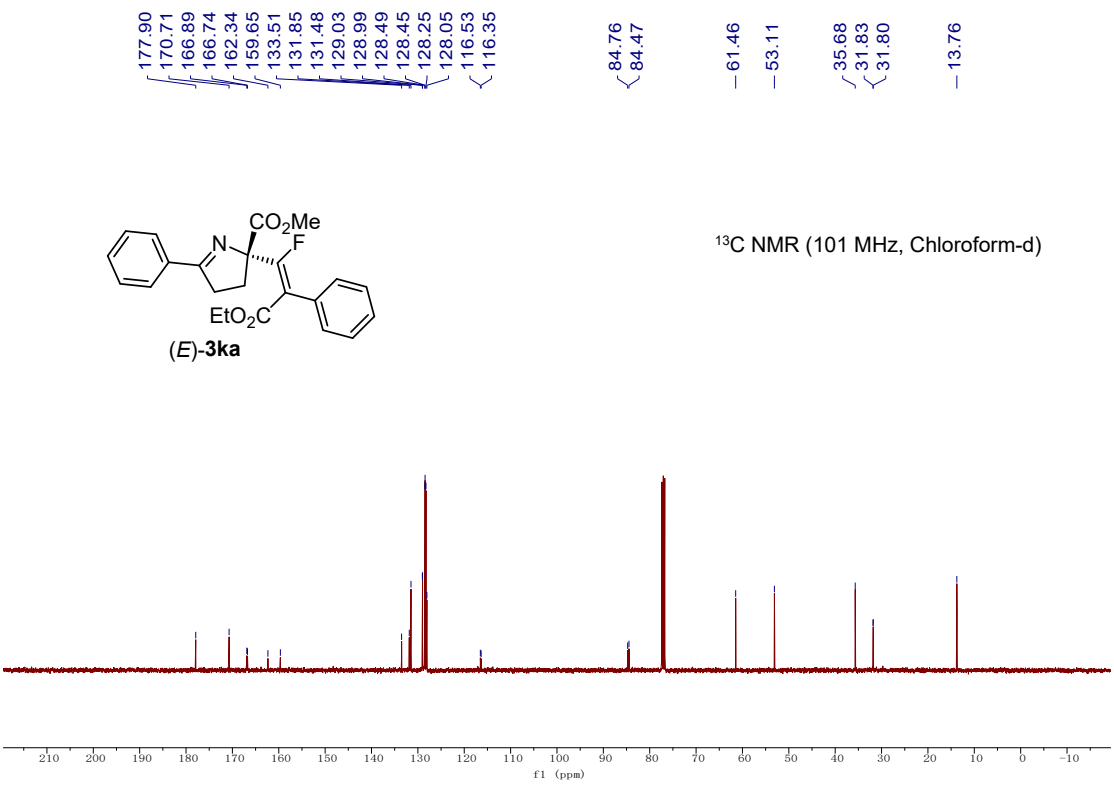
Retention Time	Area	Area %	Height	Height %
10.892	8286267	50.18	395204	62.29
15.948	8226441	49.82	239214	37.71
Totals	16512708	100.00	634418	100.00

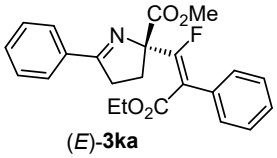


UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
10.962	22642096	98.28	1055688	98.92
16.225	396247	1.72	11482	1.08
Totals	23038343	100.00	1067170	100.00

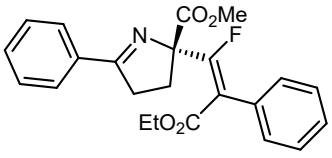

7.93 7.91 7.91 7.52 7.50 7.48 7.47 7.45 7.43 7.42 7.41 7.39 7.39 7.37 7.35 7.34 7.34 7.33 7.32 7.32
4.19 4.17 4.15 4.13 3.84 3.32 3.29 3.27 3.25 3.24 3.23 3.23 3.22 3.21 3.18 2.94 2.93 2.92 2.91 2.90 2.89 2.88 2.53 2.50 2.49 2.48 2.47 2.45 1.20 1.19 1.17
CO2Me
F
N
EtO2C
(E)-3ka
1H NMR (400 MHz, Chloroform-d)
1.99 8.02 2.03 3.00 2.02 1.00 1.02 3.03
f1 (ppm)


177.90 170.71 166.89 166.74 162.34 159.65 133.51 131.85 131.48 129.03 128.99 128.49 128.45 128.25 128.05 116.53 116.35
84.76 84.47
61.46
53.11
35.68 31.83 31.80
13.76
CO2Me
F
N
EtO2C
(E)-3ka
13C NMR (101 MHz, Chloroform-d)
f1 (ppm)

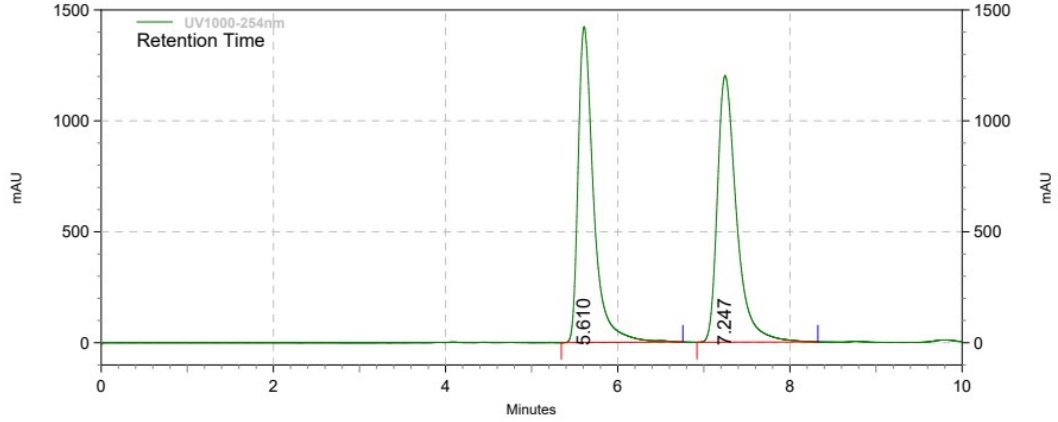


(*E*)-**3ka**

^{19}F NMR (376 MHz, Chloroform-d)

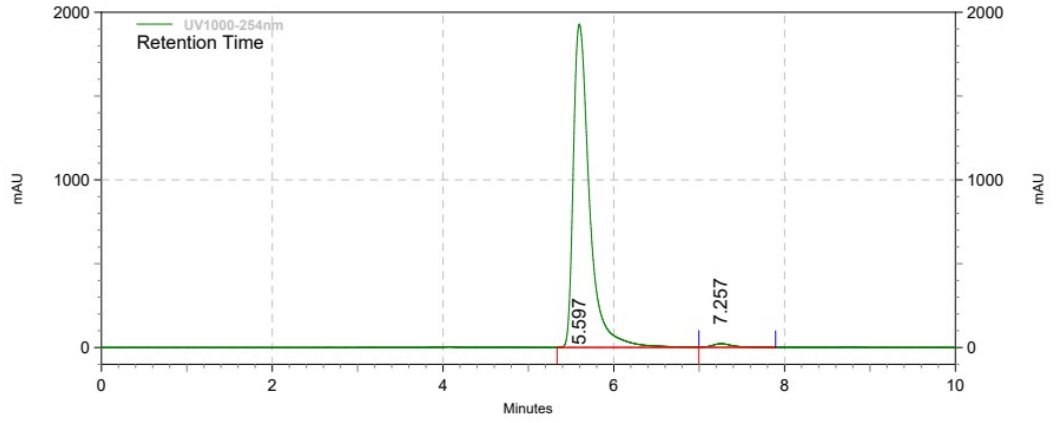


(*E*)-**3ka**



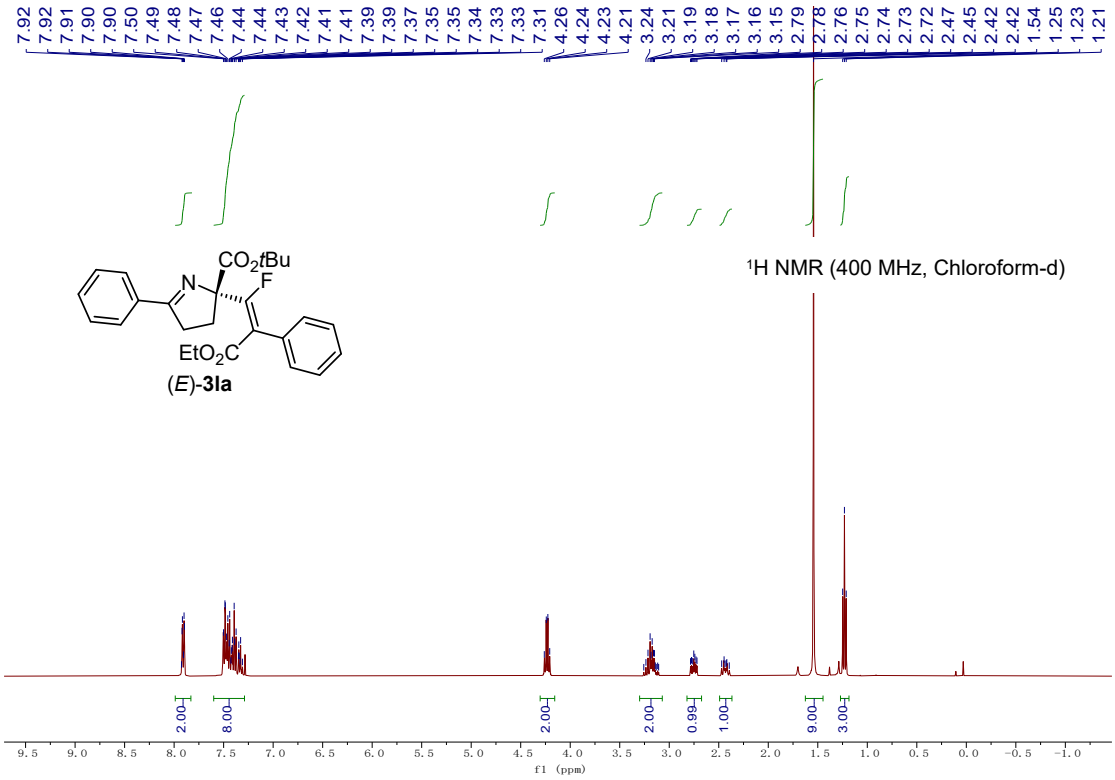
UV1000-254nm
Results

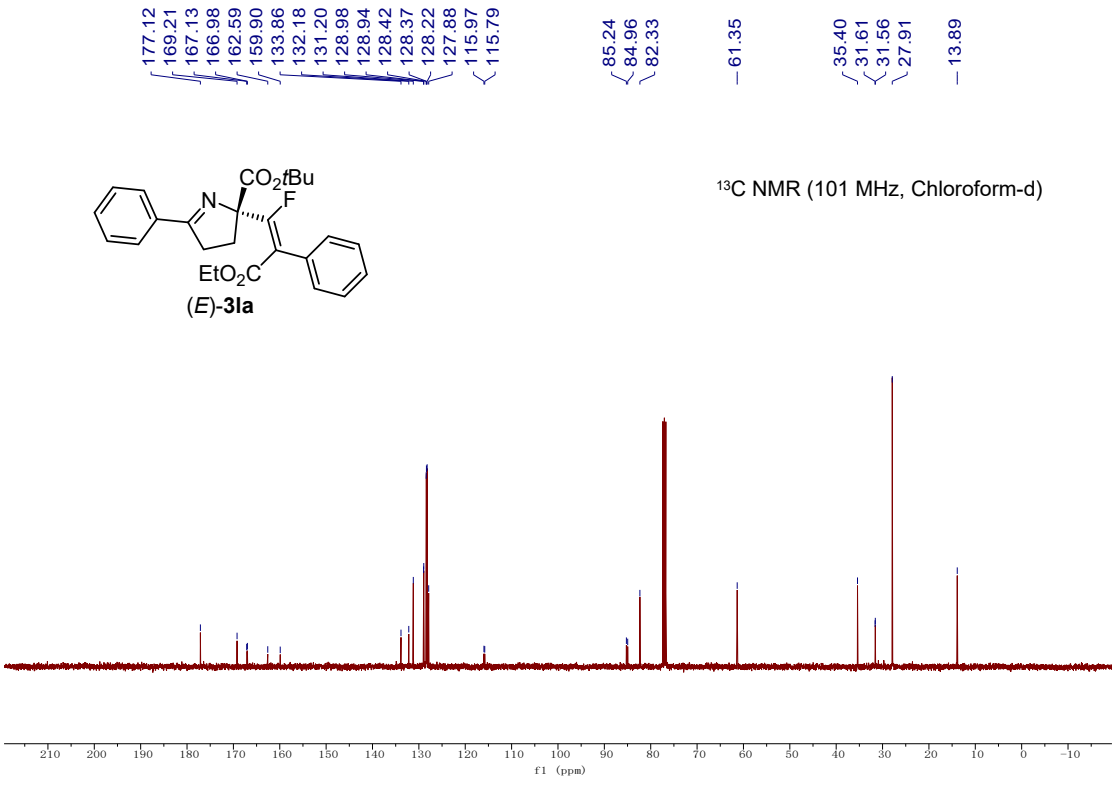
Retention Time	Area	Area %	Height	Height %
5.610	17827276	48.95	1423125	54.22
7.247	18593385	51.05	1201587	45.78
Totals	36420661	100.00	2624712	100.00

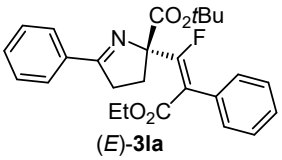


UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
5.597	25325696	98.65	1927803	98.89
7.257	346223	1.35	21727	1.11
Totals	25671919	100.00	1949530	100.00

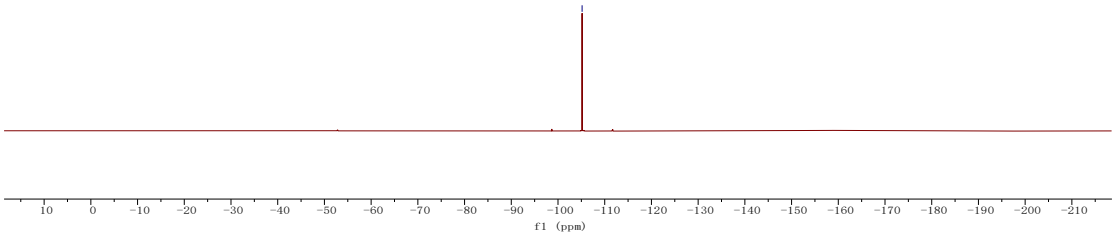

7.92 7.92 7.91 7.90 7.90 7.50 7.49 7.48 7.47 7.46 7.44 7.44 7.43 7.42 7.41 7.41 7.39 7.39 7.37 7.35 7.35 7.34 7.33 7.33 7.31 4.26 4.24 4.23 4.21 3.24 3.21 3.19 3.18 3.17 3.16 3.15 2.79 2.78 2.76 2.75 2.74 2.73 2.72 2.47 2.45 2.42 2.42 1.54 1.25 1.23 1.21
CO2tBu
N
F
EtO2C
(E)-3la
1H NMR (400 MHz, Chloroform-d)
2.00 8.00 2.00 2.00 0.99 1.00 9.00 3.00
f1 (ppm)

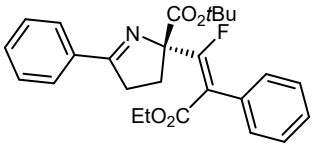

177.12 169.21 167.13 166.98 162.59 159.90 133.86 132.18 131.20 128.98 128.94 128.42 128.37 128.22 127.88 115.97 115.79
85.24 84.96 82.33
61.35
35.40 31.61 31.56 27.91
13.89
CO2tBu
N
F
EtO2C
(E)-3la
13C NMR (101 MHz, Chloroform-d)
f1 (ppm)



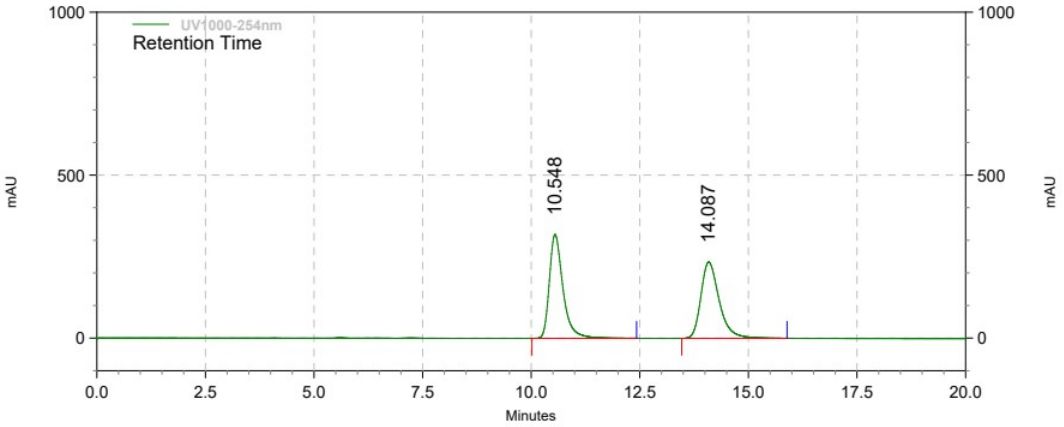
(*E*)-**3la**

^{19}F NMR (376 MHz, Chloroform-d)



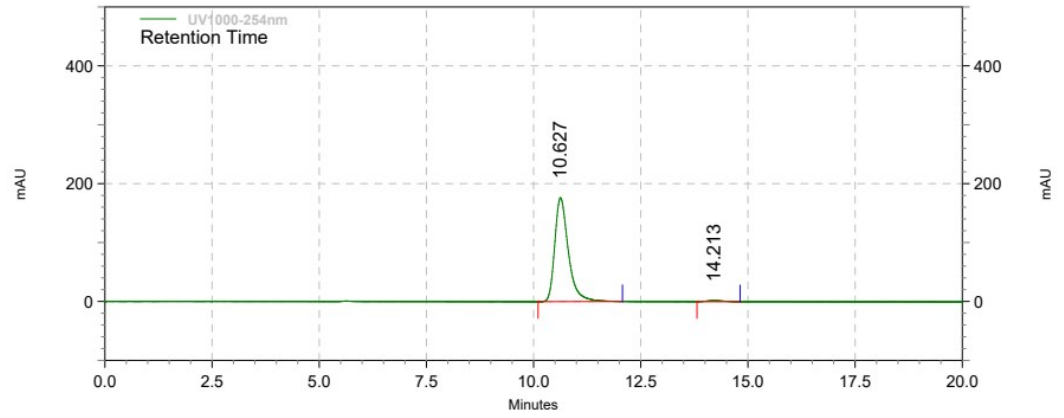


(*E*)-**3la**



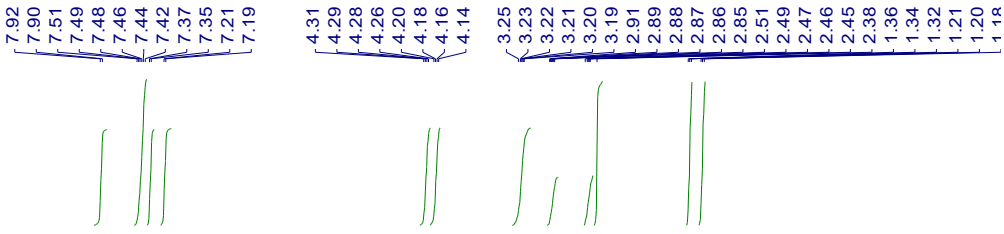
UV1000-254nm
Results

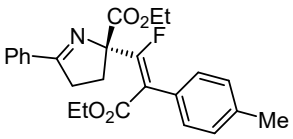
Retention Time	Area	Area %	Height	Height %
10.548	6958938	50.31	318779	57.65
14.087	6873772	49.69	234159	42.35
Totals	13832710	100.00	552938	100.00



UV1000-254nm
Results

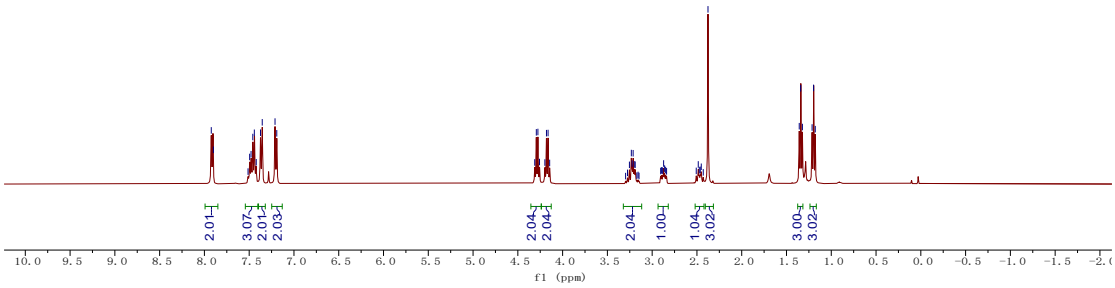
Retention Time	Area	Area %	Height	Height %
10.627	3894862	98.79	176370	99.02
14.213	47789	1.21	1745	0.98
Totals	3942651	100.00	178115	100.00

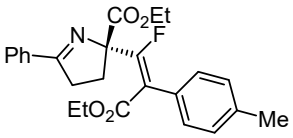




(*E*)-**3ab**

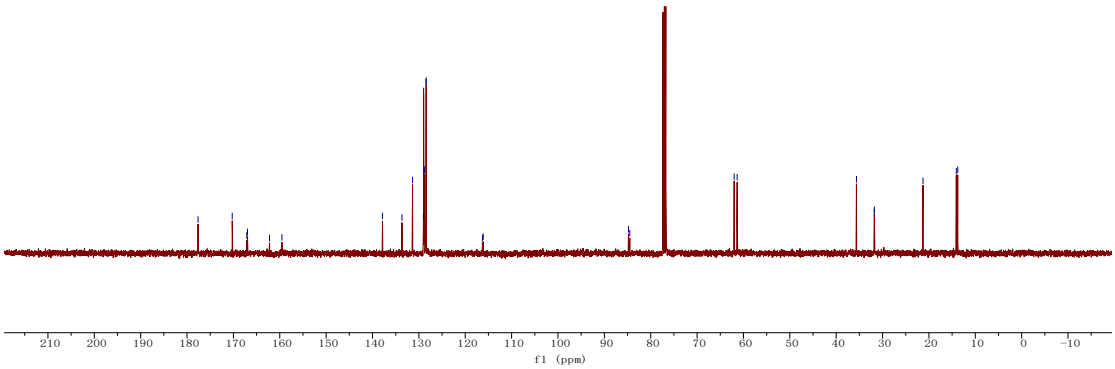
^{1}H NMR (400 MHz, Chloroform-d)

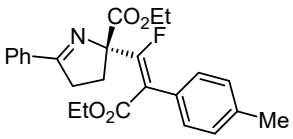




(*E*)-**3ab**

^{13}C NMR (101 MHz, Chloroform-d)

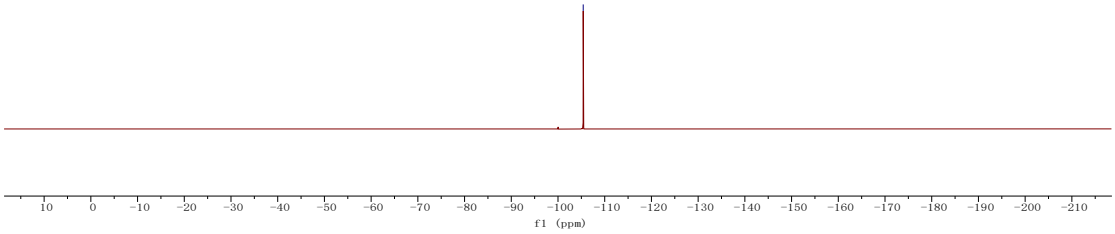


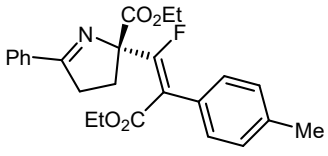


(*E*)-**3ab**

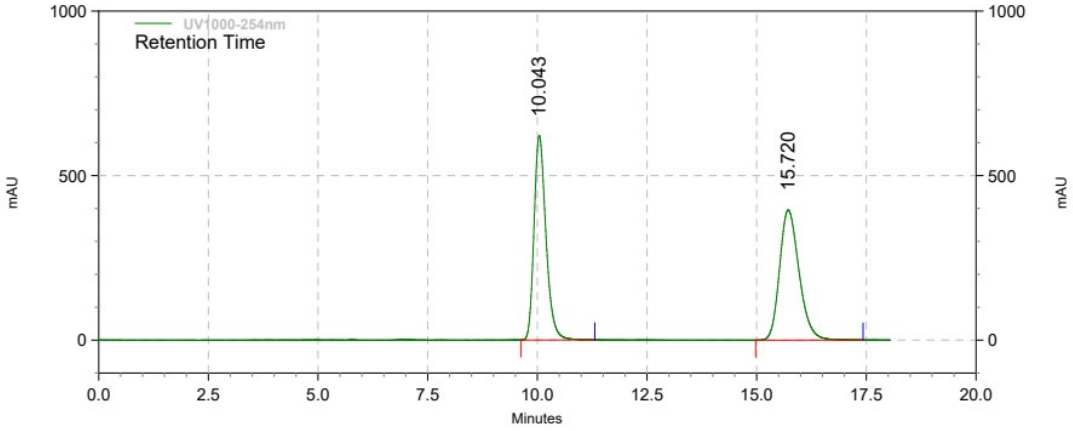
-105.40

^{19}F NMR (376 MHz, Chloroform-d)



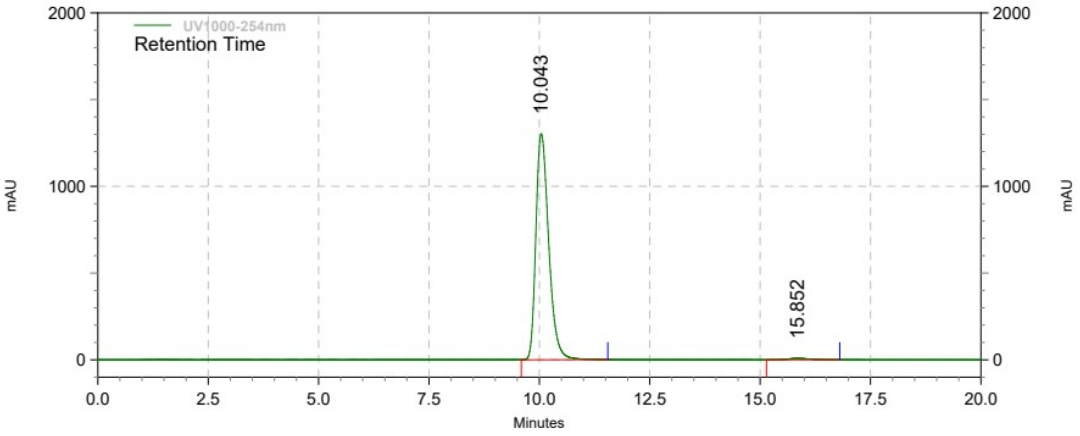


(*E*)-**3ab**



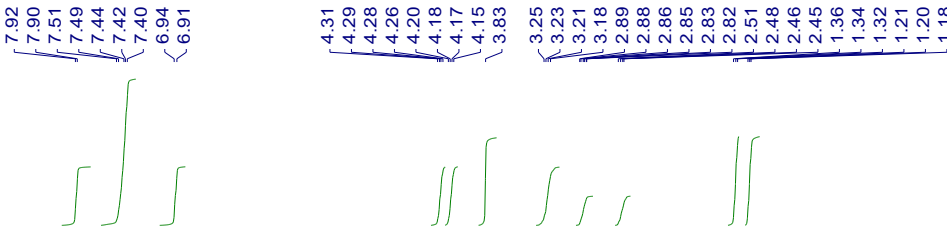
UV1000-254nm
Results

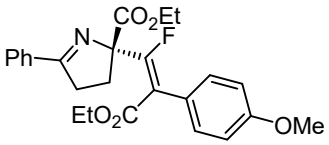
Retention Time	Area	Area %	Height	Height %
10.043	11759869	49.06	621358	61.10
15.720	12211479	50.94	395648	38.90
Totals	23971348	100.00	1017006	100.00



UV1000-254nm
Results

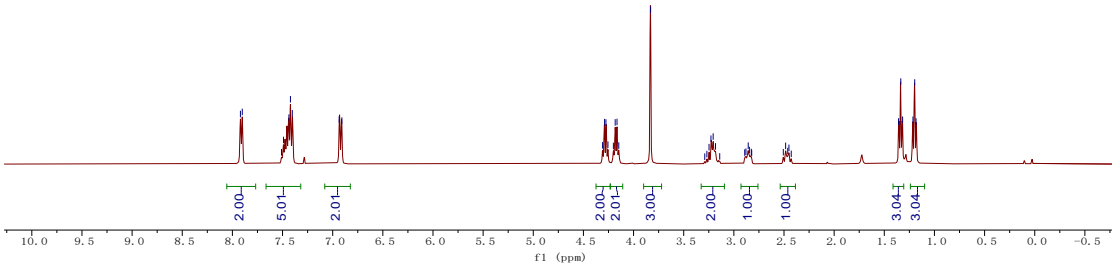
Retention Time	Area	Area %	Height	Height %
10.043	26298178	99.00	1302055	99.38
15.852	266054	1.00	8182	0.62
Totals	26564232	100.00	1310237	100.00

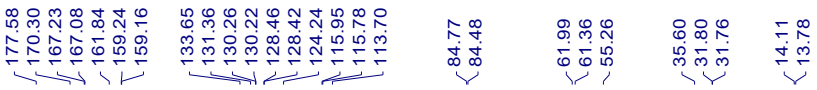


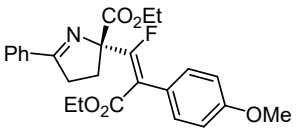


(*E*)-**3ac**

^{1}H NMR (400 MHz, Chloroform-d)

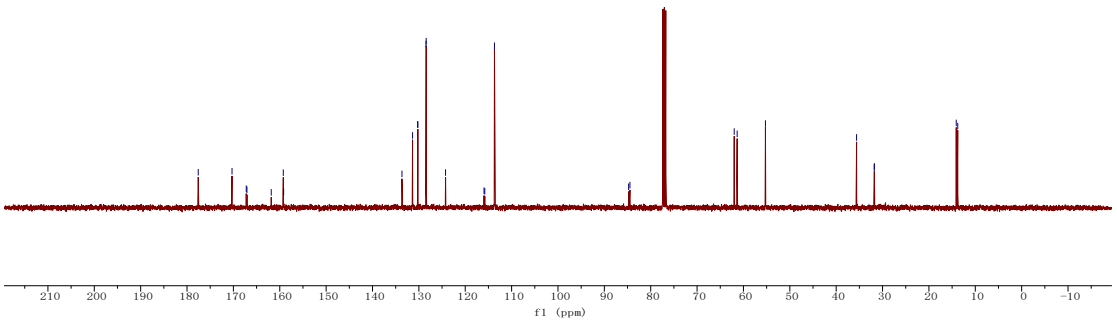


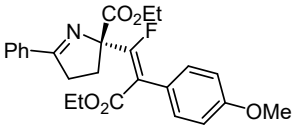




(*E*)-**3ac**

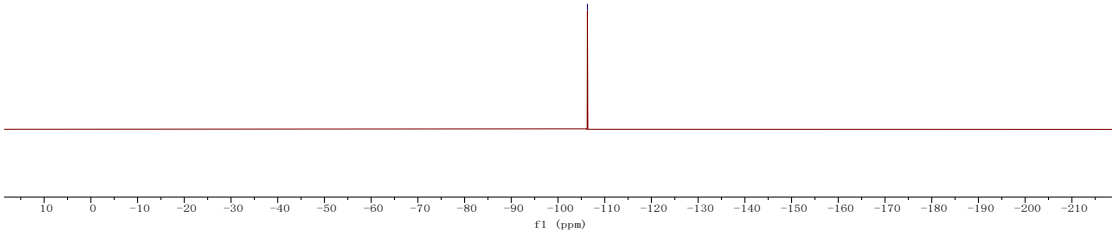
^{13}C NMR (101 MHz, Chloroform-d)

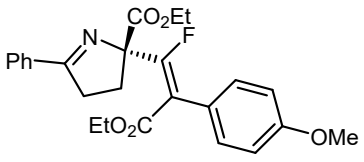




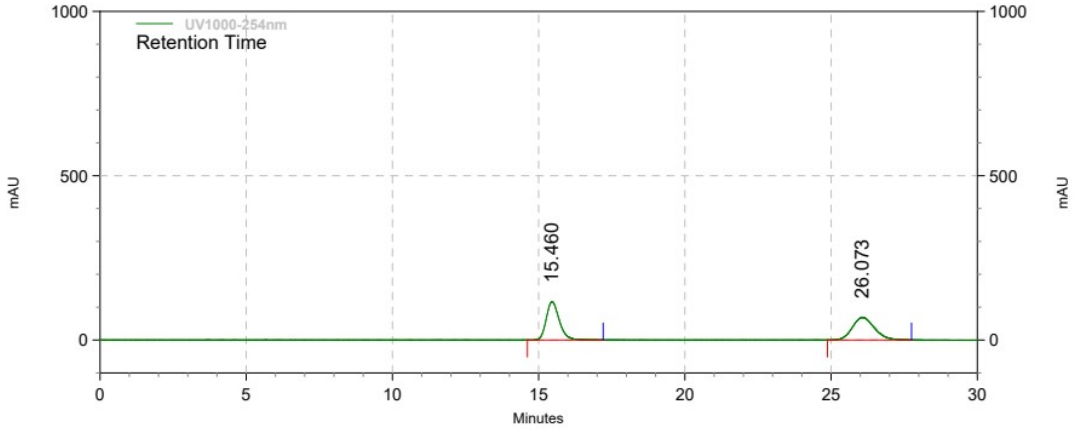
(*E*)-**3ac**

^{19}F NMR (376 MHz, Chloroform-d)



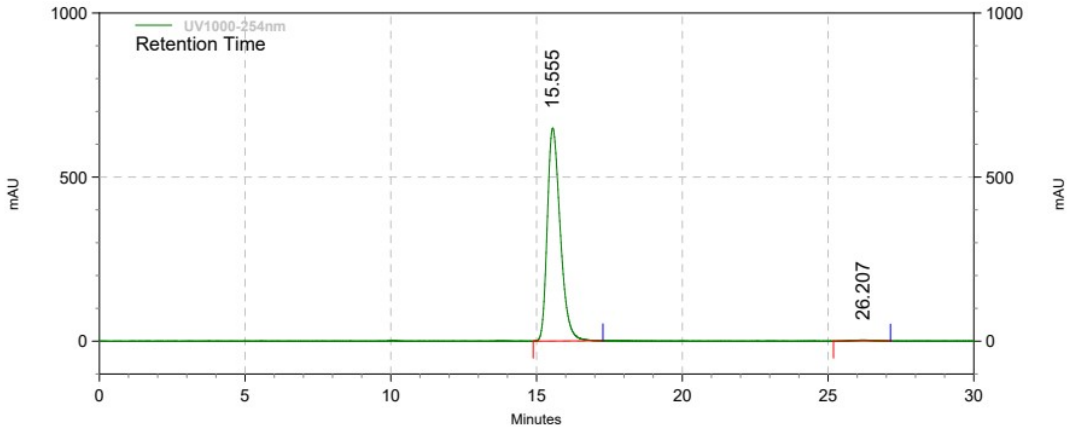


(*E*)-**3ac**



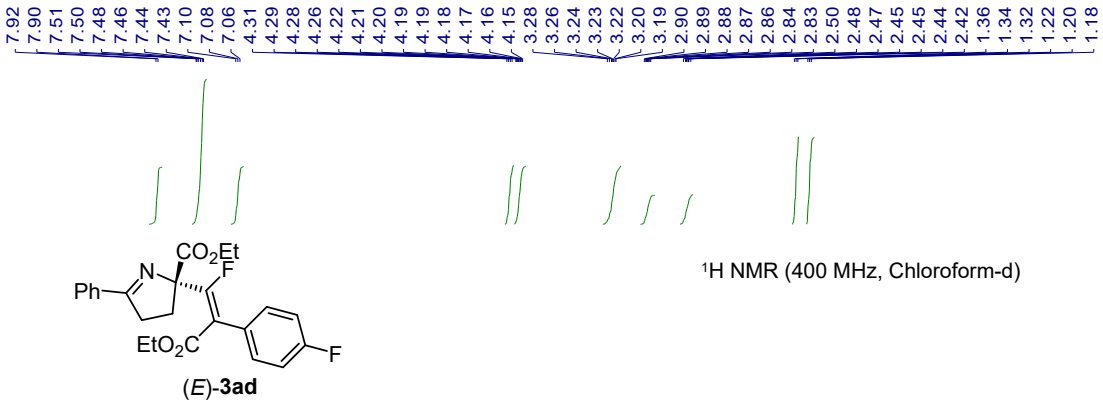
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
15.460	3610337	50.00	116731	63.04
26.073	3610146	50.00	68436	36.96
Totals	7220483	100.00	185167	100.00



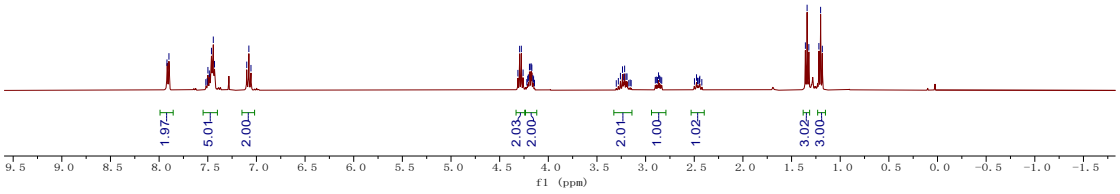
UV1000-254nm
Results

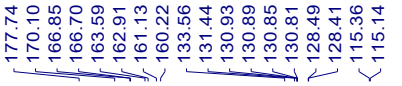
Retention Time	Area	Area %	Height	Height %
15.555	20039207	99.23	648878	99.53
26.207	155713	0.77	3036	0.47
Totals	20194920	100.00	651914	100.00

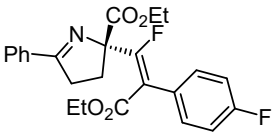


(*E*)-**3ad**

^{1}H NMR (400 MHz, Chloroform-d)

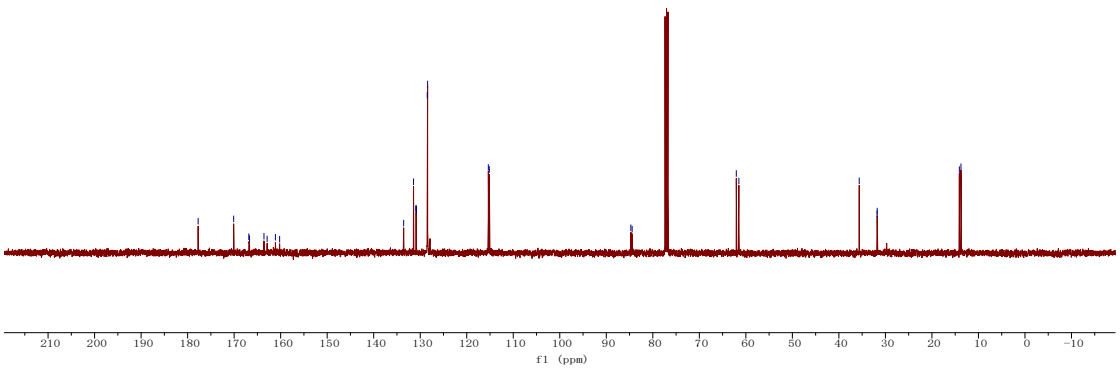


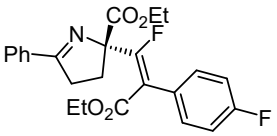




(*E*)-**3ad**

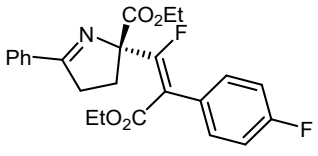
^{13}C NMR (101 MHz, Chloroform-d)



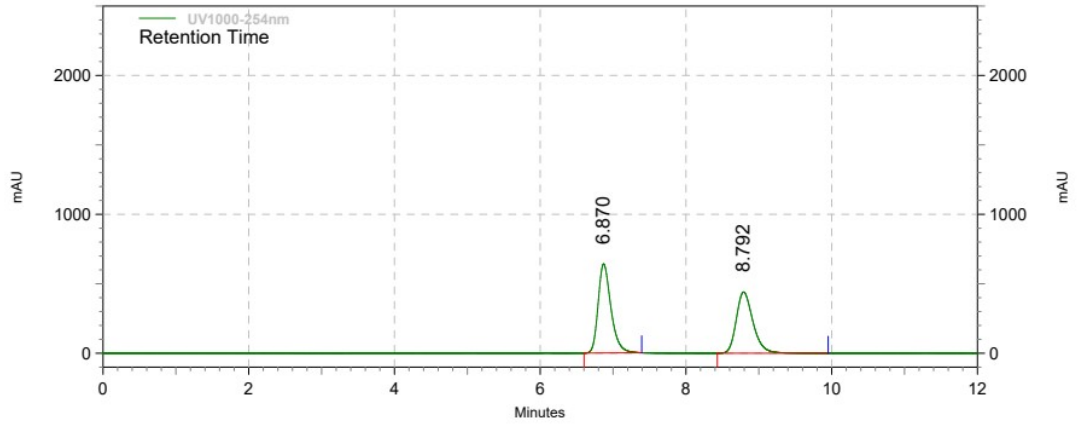


(*E*)-**3ad**

^{19}F NMR (376 MHz, Chloroform-d)

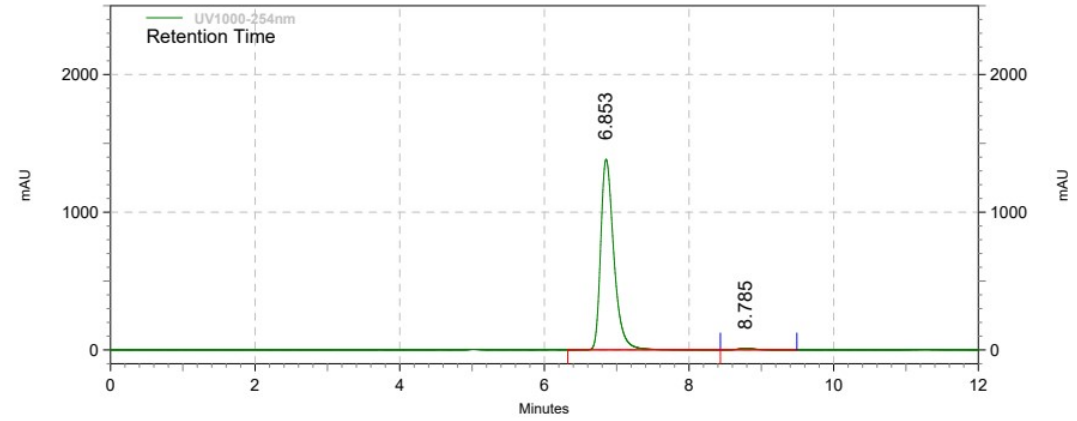


(*E*)-**3ad**



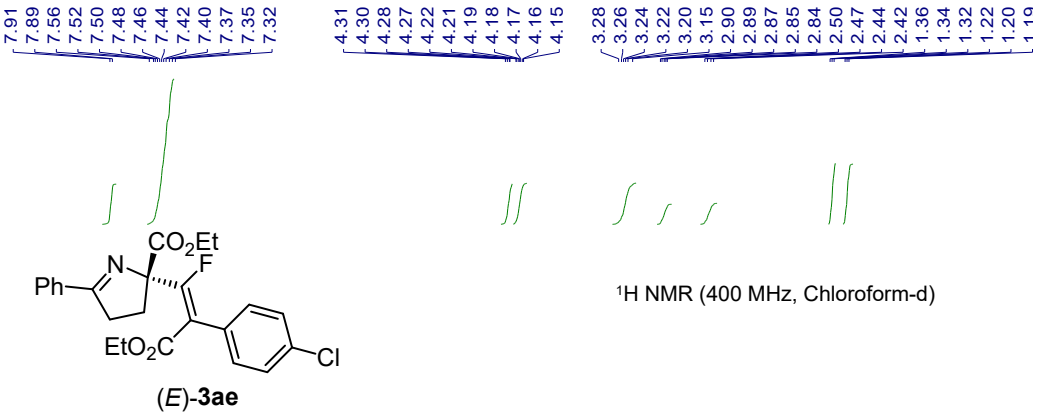
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
6.870	7848823	52.82	641352	59.28
8.792	7011089	47.18	440540	40.72
Totals	14859912	100.00	1081892	100.00



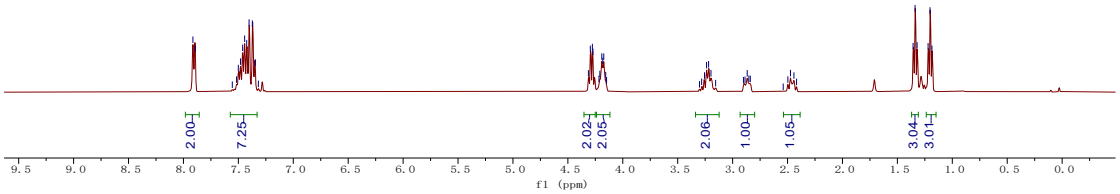
UV1000-254nm
Results

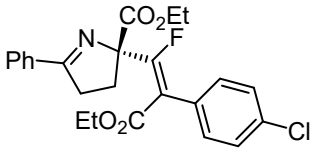
Retention Time	Area	Area %	Height	Height %
6.853	17490845	99.03	1383435	99.26
8.785	170720	0.97	10351	0.74
Totals	17661565	100.00	1393786	100.00



(*E*)-**3ae**

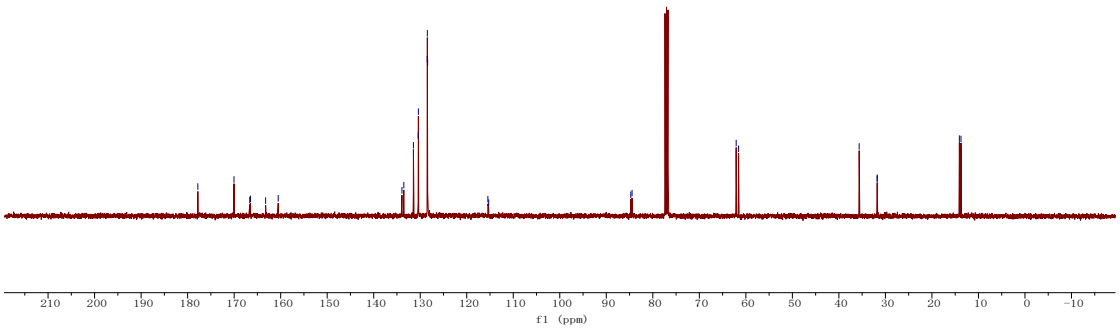
^{1}H NMR (400 MHz, Chloroform-d)

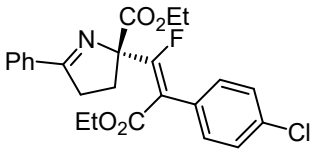




(*E*)-**3ae**

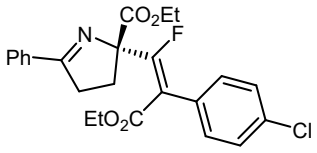
^{13}C NMR (101 MHz, Chloroform-d)



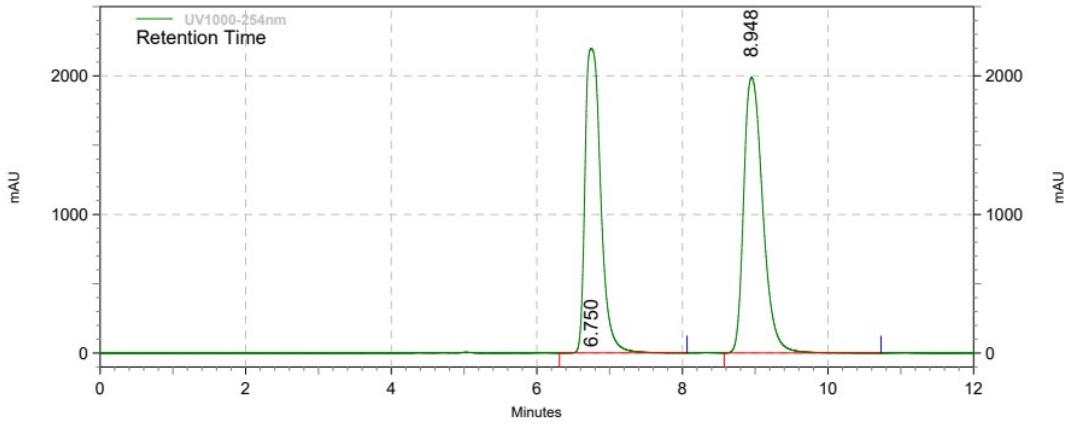


(*E*)-**3ae**

^{19}F NMR (376 MHz, Chloroform-d)

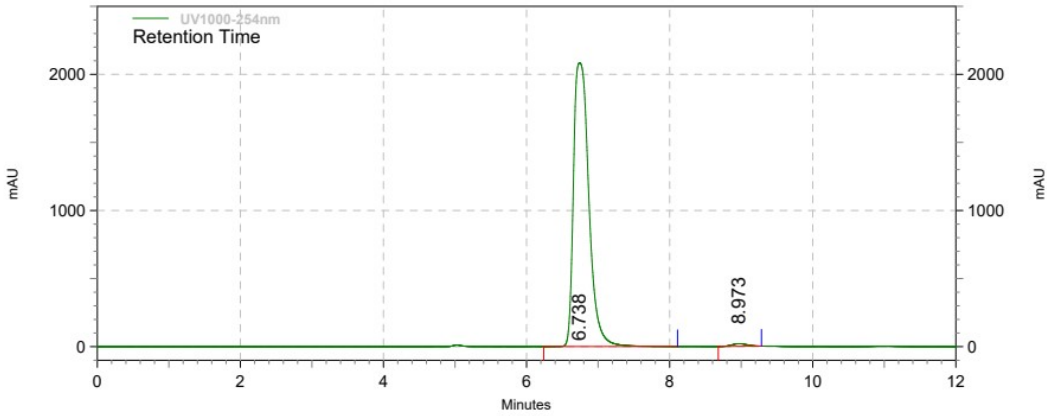


(*E*)-**3ae**



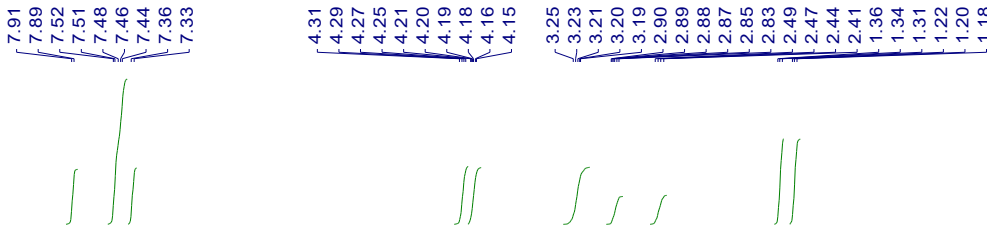
UV1000-254nm
Results

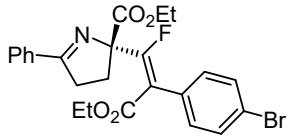
Retention Time	Area	Area %	Height	Height %
6.750	32975745	47.69	2195273	52.47
8.948	36165906	52.31	1988233	47.53
Totals	69141651	100.00	4183506	100.00



UV1000-254nm
Results

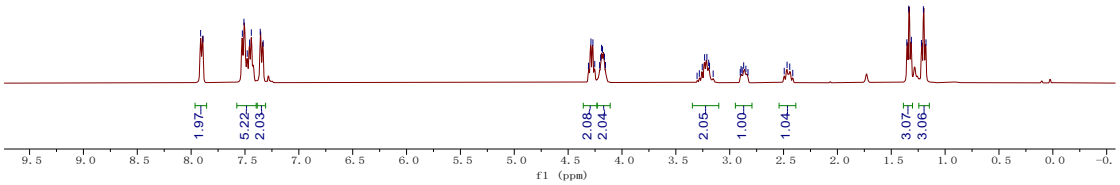
Retention Time	Area	Area %	Height	Height %
6.738	31122844	99.10	2083874	99.09
8.973	284008	0.90	19155	0.91
Totals	31406852	100.00	2103029	100.00

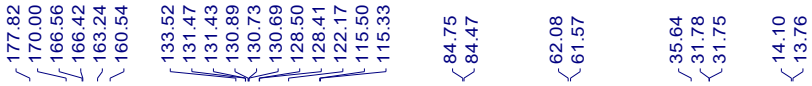


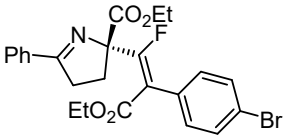


(*E*)-**3af**

^{1}H NMR (400 MHz, Chloroform-d)

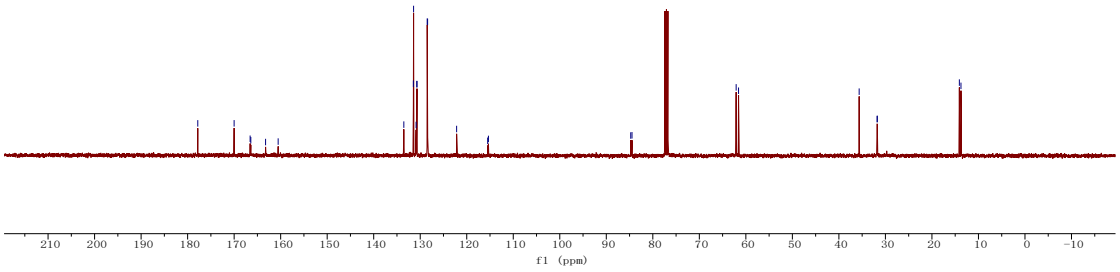


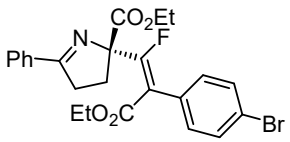




(*E*)-**3af**

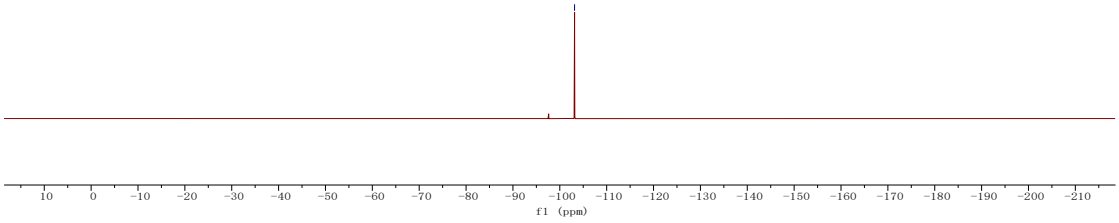
^{13}C NMR (101 MHz, Chloroform-d)

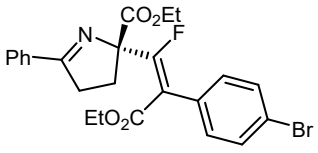




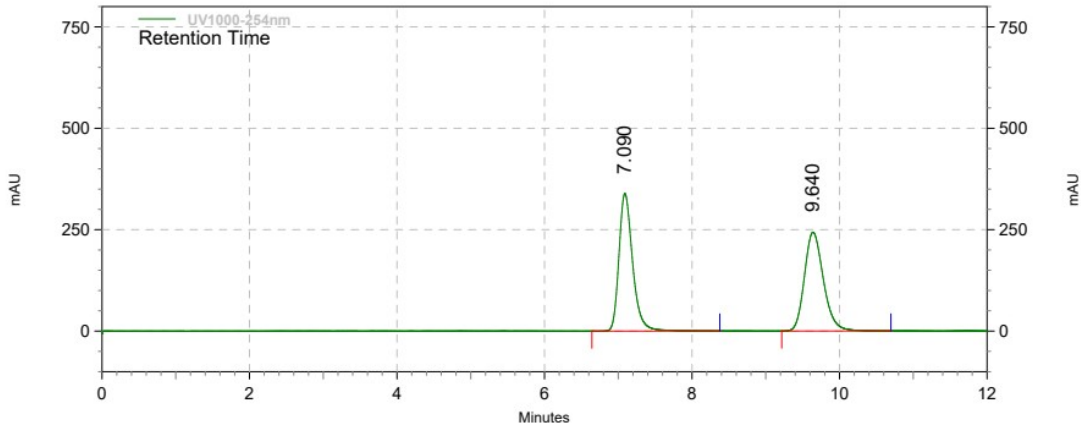
(*E*)-**3af**

^{19}F NMR (376 MHz, Chloroform-d)



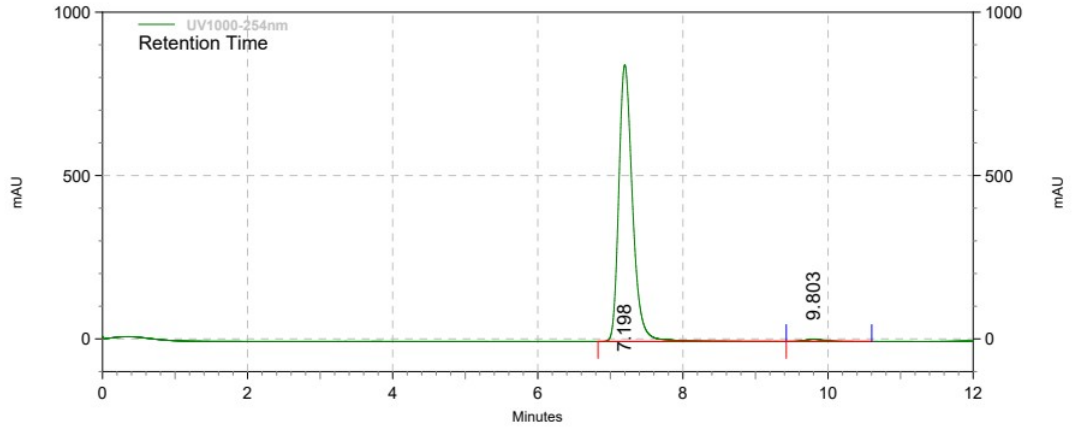


(*E*)-**3af**



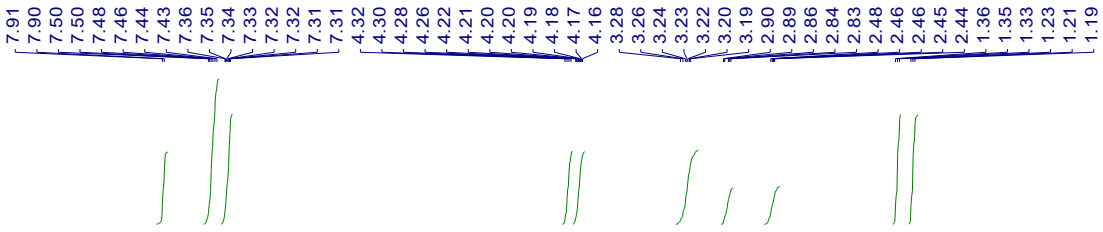
UV1000-254nm
Results

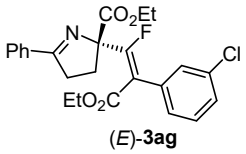
Retention Time	Area	Area %	Height	Height %
7.090	4370569	50.11	339164	58.19
9.640	4351437	49.89	243686	41.81
Totals	8722006	100.00	582850	100.00



UV1000-254nm
Results

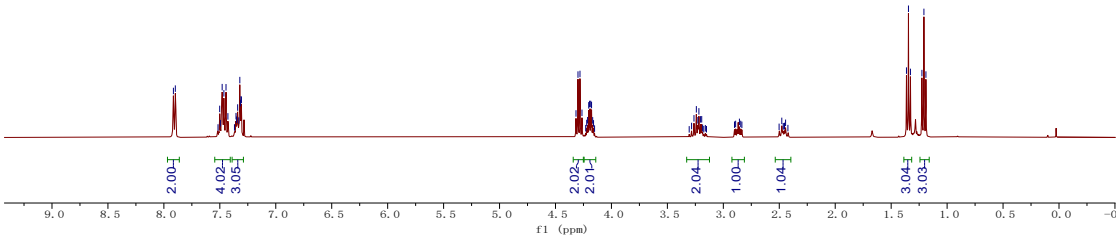
Retention Time	Area	Area %	Height	Height %
7.198	11135679	98.87	846548	99.21
9.803	127502	1.13	6780	0.79
Totals	11263181	100.00	853328	100.00

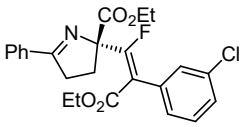




(*E*)-**3ag**

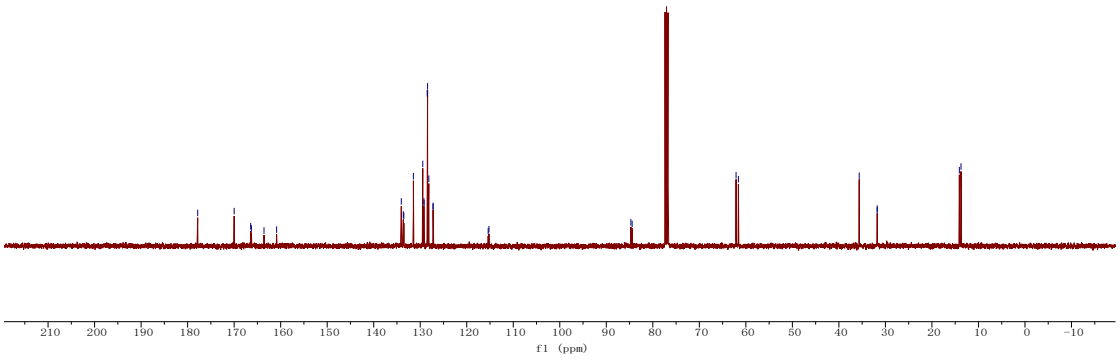
^{1}H NMR (400 MHz, Chloroform-d)

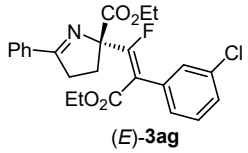




(*E*)-**3ag**

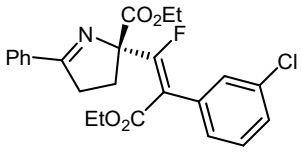
^{13}C NMR (101 MHz, Chloroform-d)



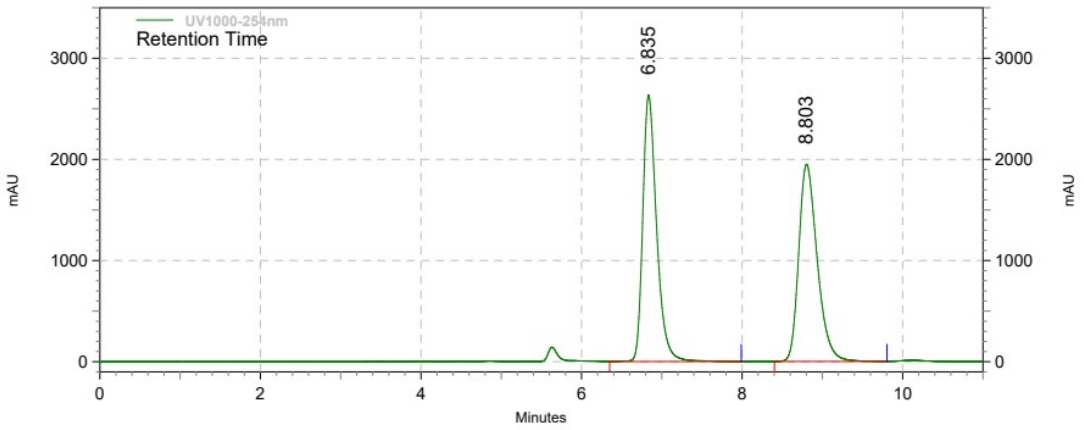


(*E*)-**3ag**

^{19}F NMR (376 MHz, Chloroform-d)

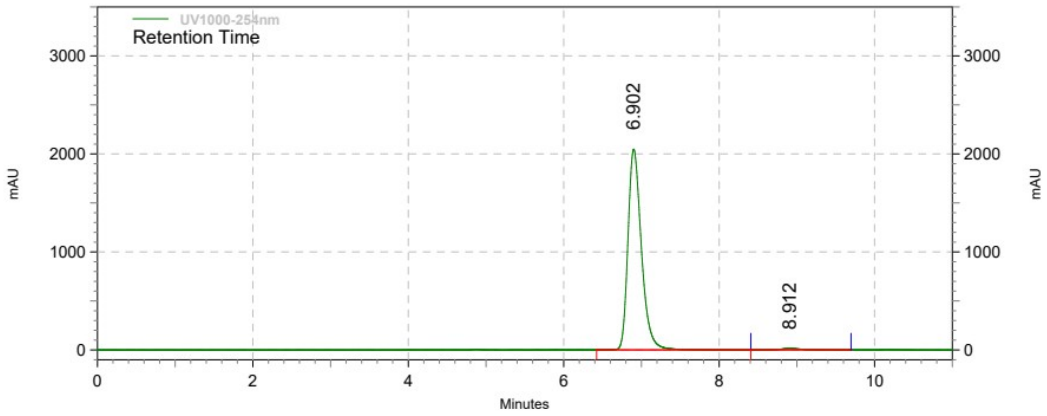


(*E*)-**3ag**



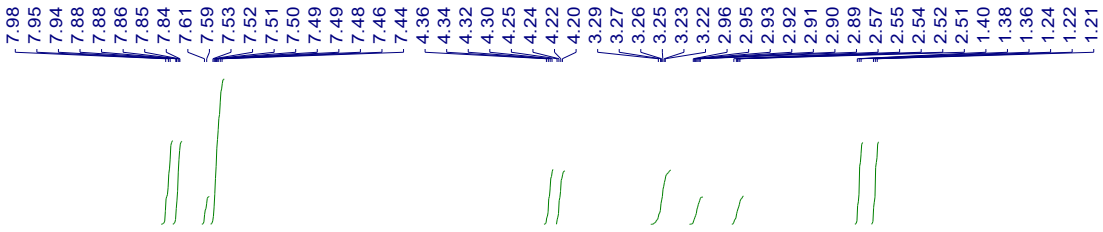
UV1000-254nm
Results

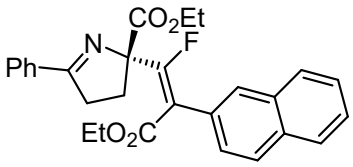
Retention Time	Area	Area %	Height	Height %
6.835	31580079	50.30	2636344	57.49
8.803	31198195	49.70	1949194	42.51
Totals	62778274	100.00	4585538	100.00



UV1000-254nm
Results

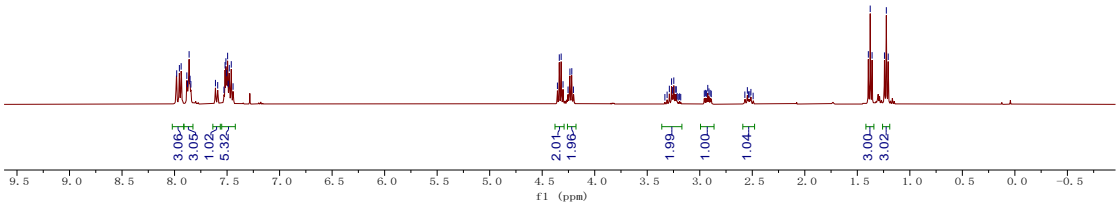
Retention Time	Area	Area %	Height	Height %
6.902	24608548	98.90	2048091	99.28
8.912	274153	1.10	14920	0.72
Totals	24882701	100.00	2063011	100.00

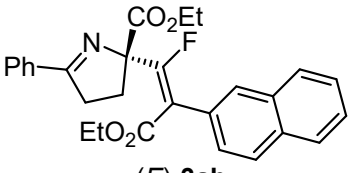




(*E*)-**3ah**

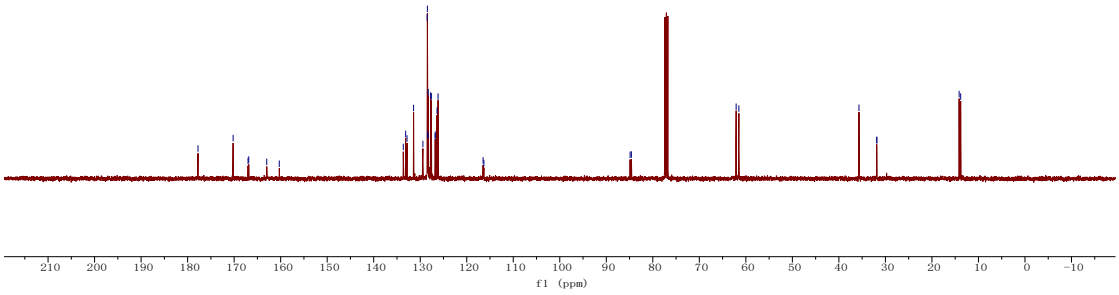
^{1}H NMR (400 MHz, Chloroform-d)

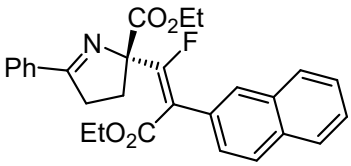




(*E*)-**3ah**

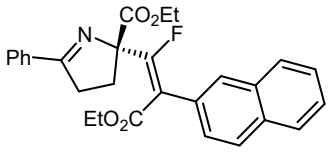
^{13}C NMR (101 MHz, Chloroform-d)



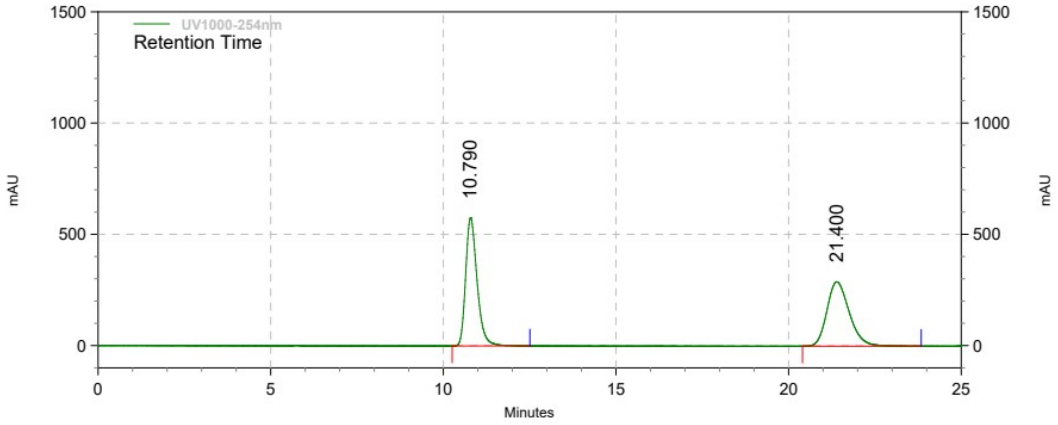


(*E*)-**3ah**

^{19}F NMR (376 MHz, Chloroform-d)

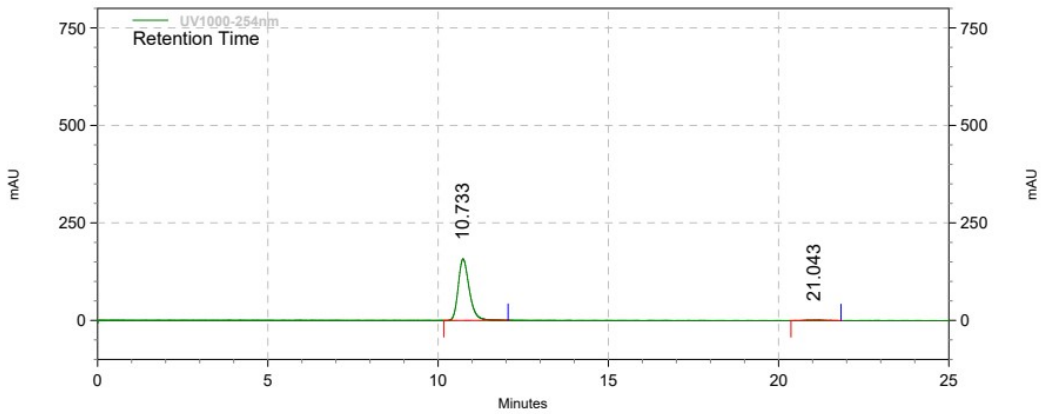


(*E*)-**3ah**



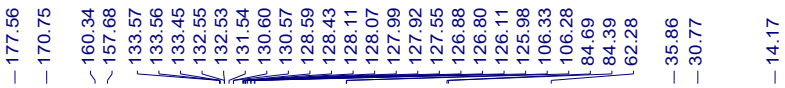
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
10.790	13253242	50.47	576409	66.59
21.400	13006407	49.53	289172	33.41
Totals	26259649	100.00	865581	100.00

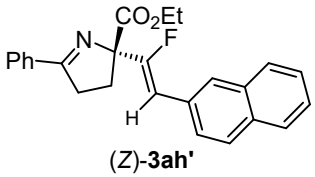


UV1000-254nm
Results

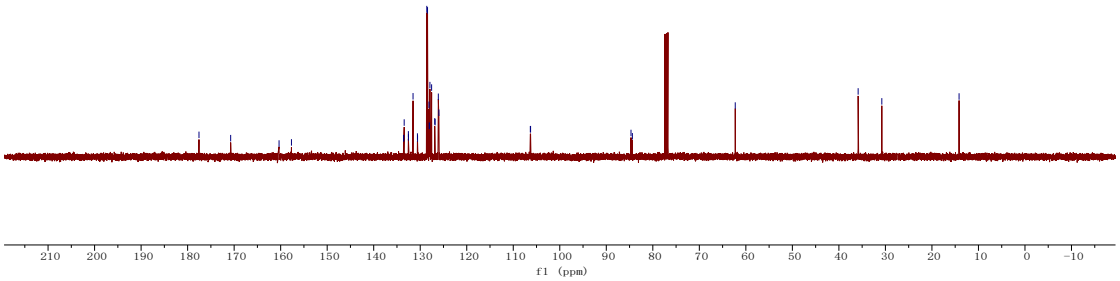
Retention Time	Area	Area %	Height	Height %
10.733	3563717	98.88	157739	99.40
21.043	40189	1.12	960	0.60
Totals	3603906	100.00	158699	100.00

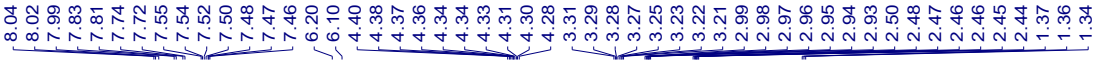


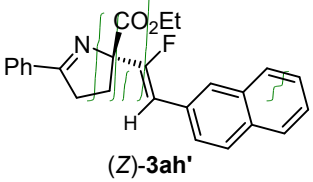
^{13}C NMR (101 MHz, Chloroform-d)



(*Z*)-**3ah'**

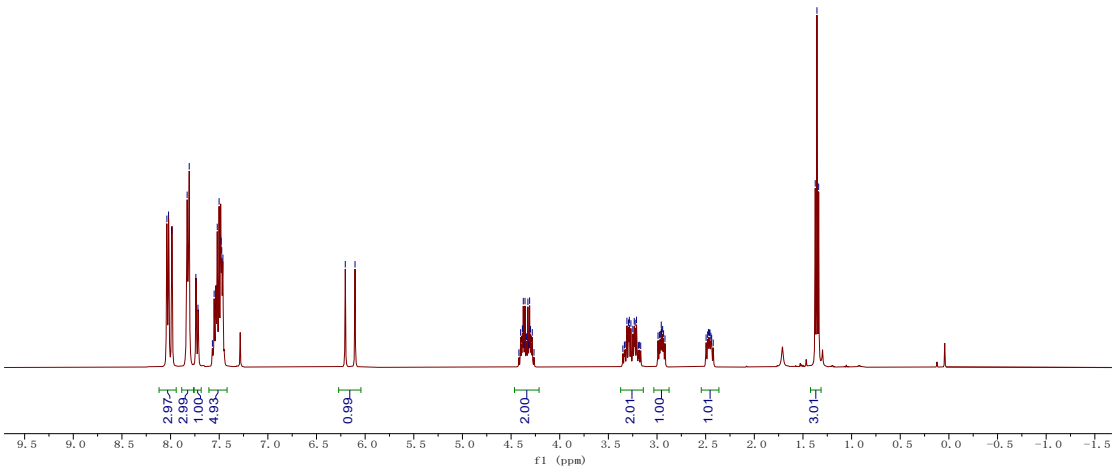


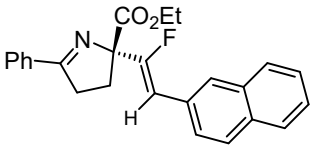




(*Z*)-**3ah'**

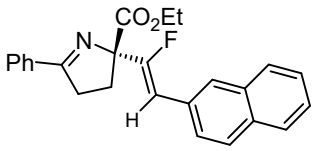
^{1}H NMR (400 MHz, Chloroform-*d*)



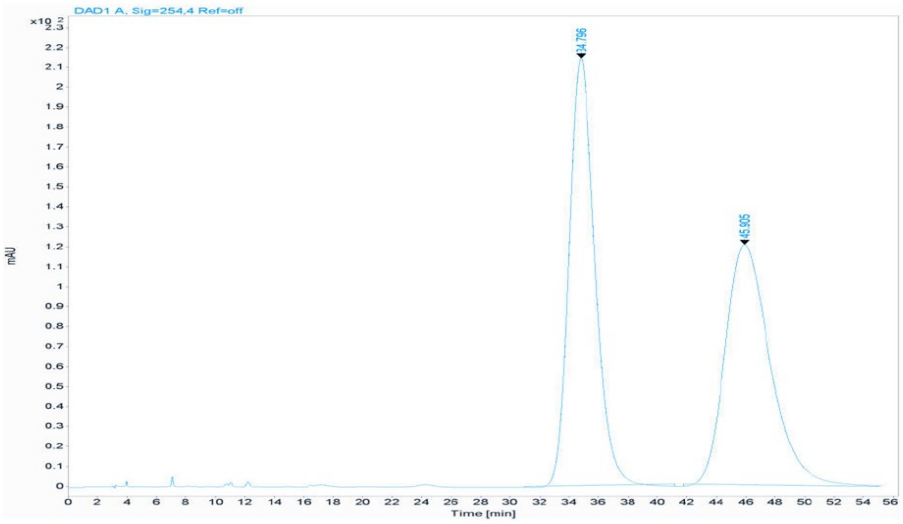


(*Z*)-**3ah'**

^{19}F NMR (376 MHz, Chloroform-d)

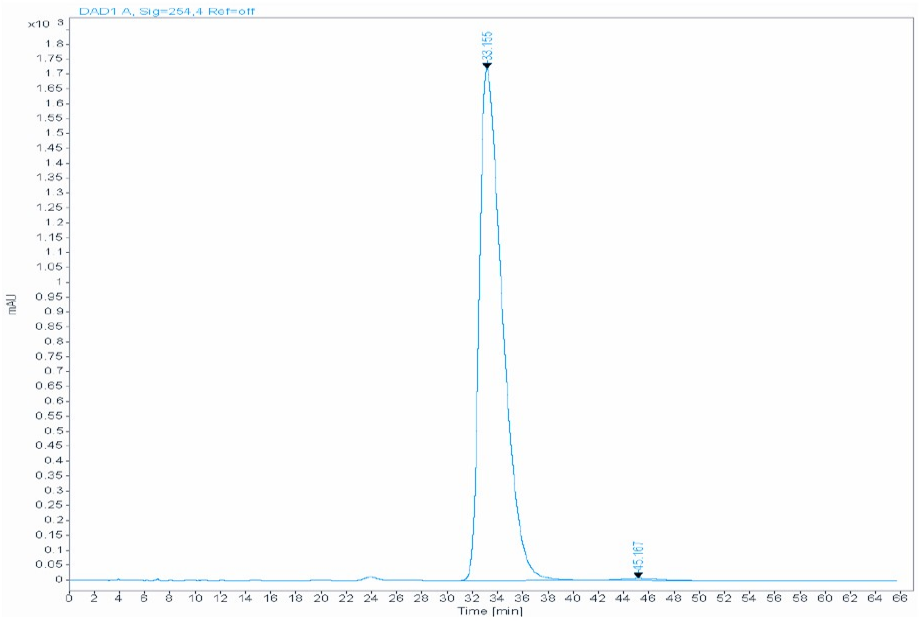


(*Z*)-**3ah'**



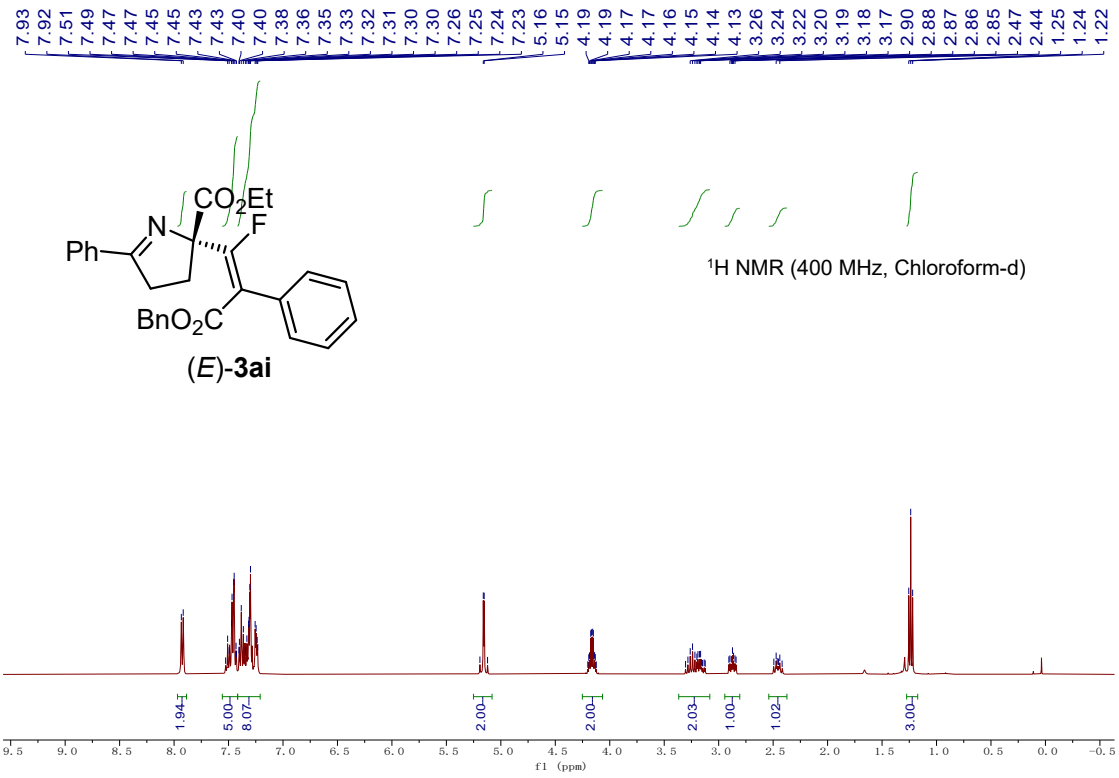
Signal: DAD1 A, Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
34.796	MM R	2.0289	26046.5664	213.9592	50.5778	
45.905	MM R	3.5245	25451.4199	120.3549	49.4222	
		Sum	51497.9863			



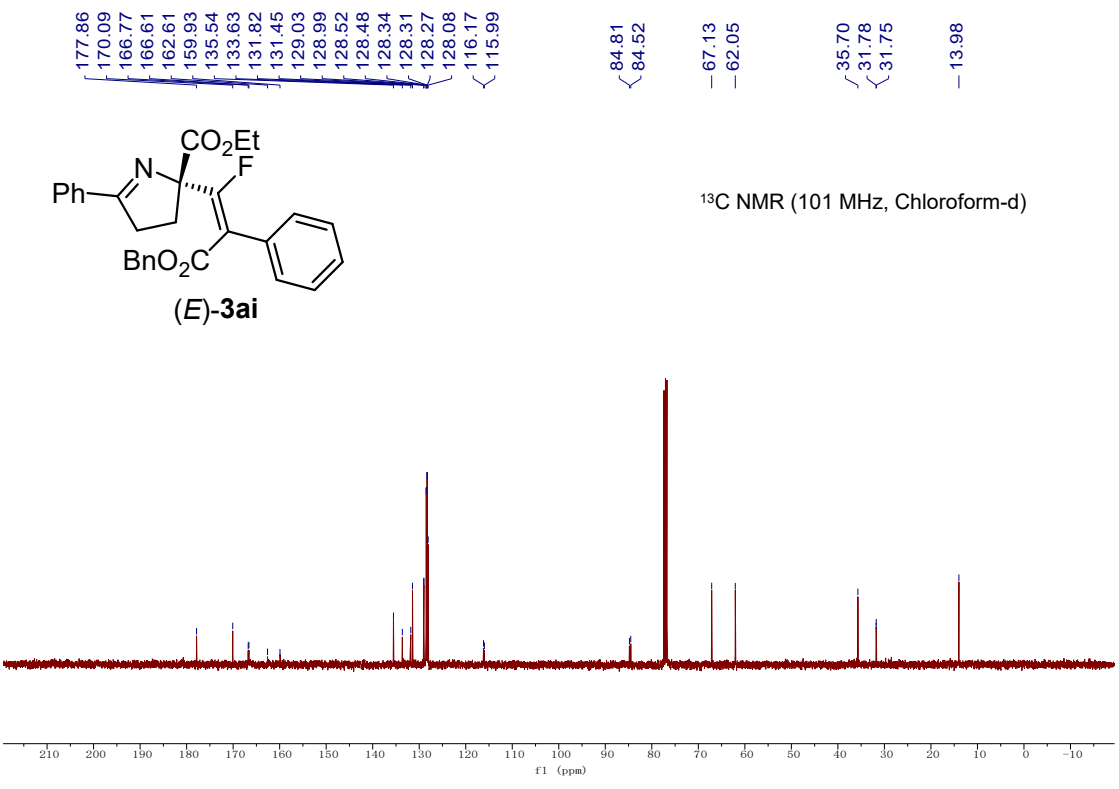
Signal: DAD1 A, Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
33.155	BB	1.8886	218624.5156	1718.0828	99.4716	
45.167	BB	2.4769	1161.4430	5.5106	0.5284	
		Sum	219785.9586			



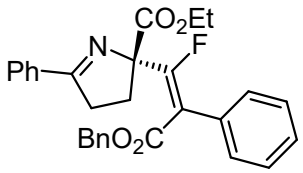
(*E*)-**3ai**

^{1}H NMR (400 MHz, Chloroform-d)



(*E*)-**3ai**

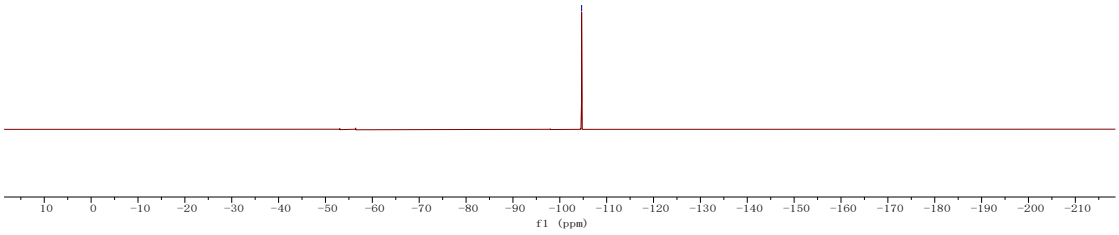
^{13}C NMR (101 MHz, Chloroform-d)

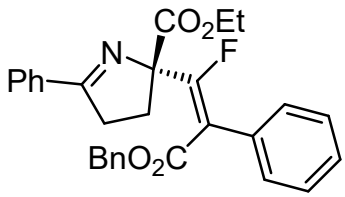


(*E*)-**3ai**

-104.66

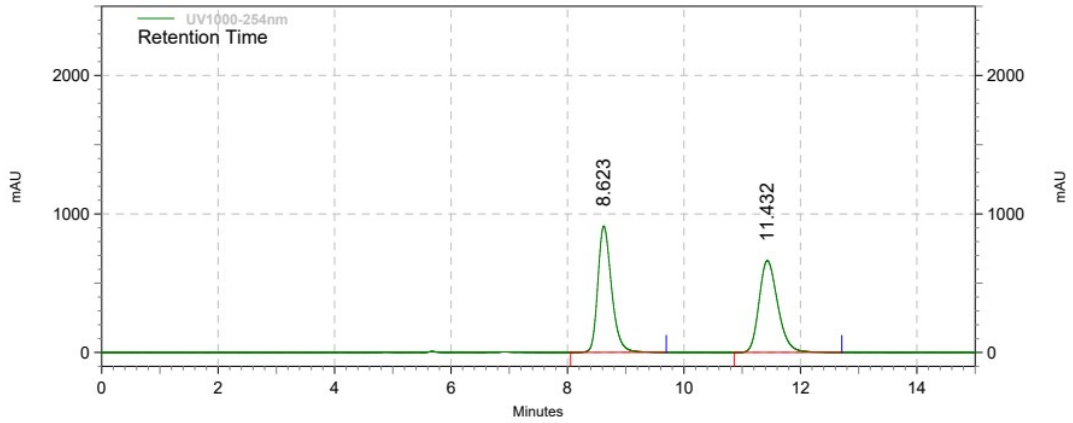
^{19}F NMR (376 MHz, Chloroform-d)





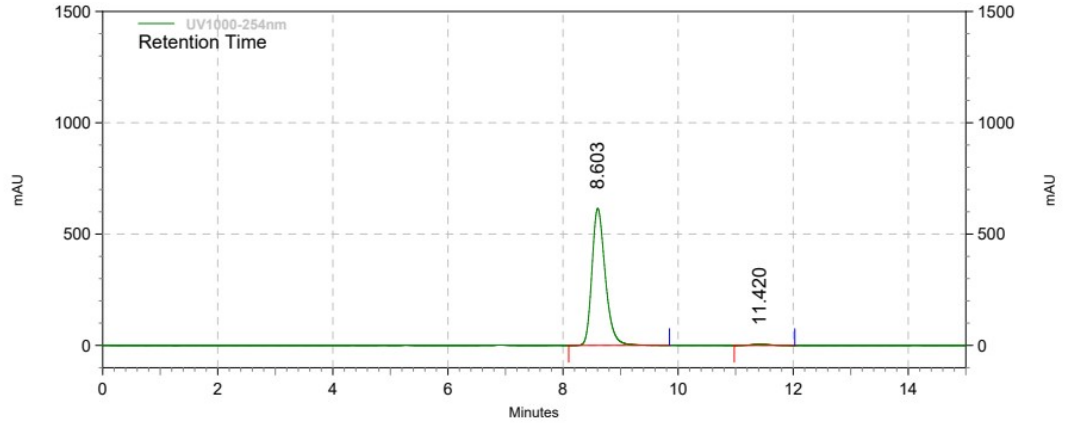
(*E*)-**3ai**

(*E*)-**3ai**



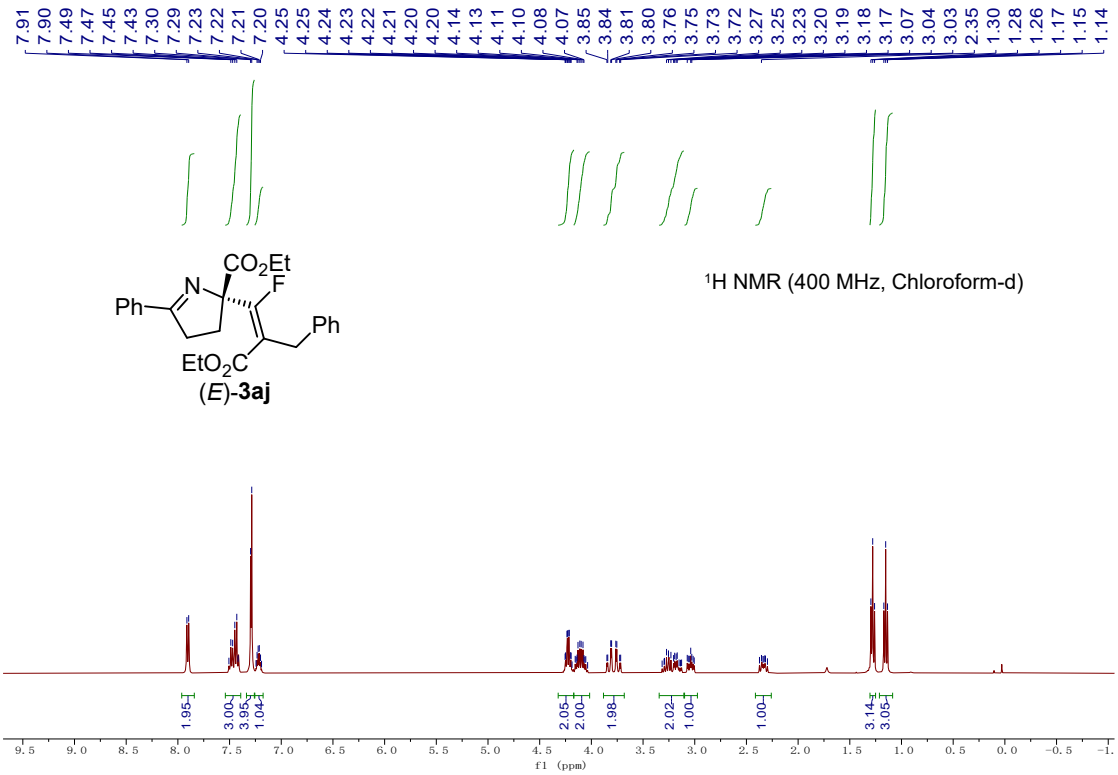
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
8.623	14952916	50.29	912088	57.92
11.432	14782443	49.71	662606	42.08
Totals	29735359	100.00	1574694	100.00



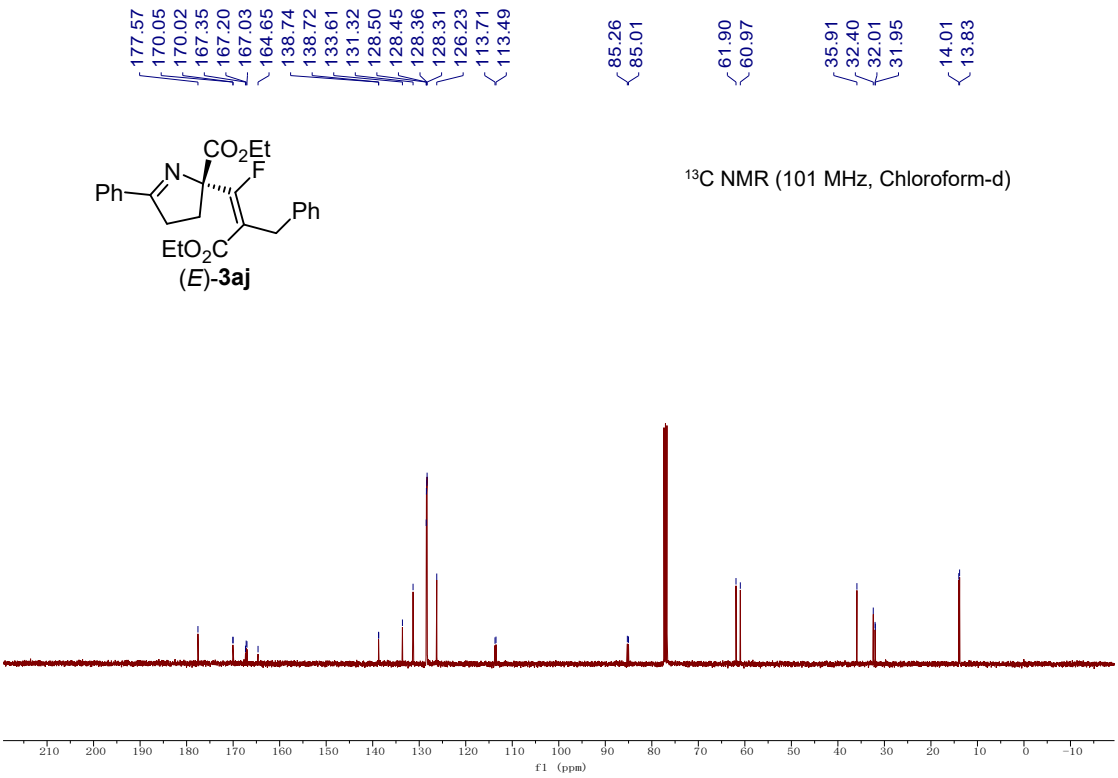
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
8.603	9920804	98.91	615144	99.19
11.420	109206	1.09	5014	0.81
Totals	10030010	100.00	620158	100.00



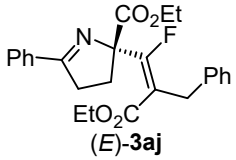
(*E*)-**3aj**

^{1}H NMR (400 MHz, Chloroform-d)



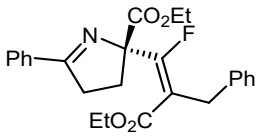
(*E*)-**3aj**

^{13}C NMR (101 MHz, Chloroform-d)

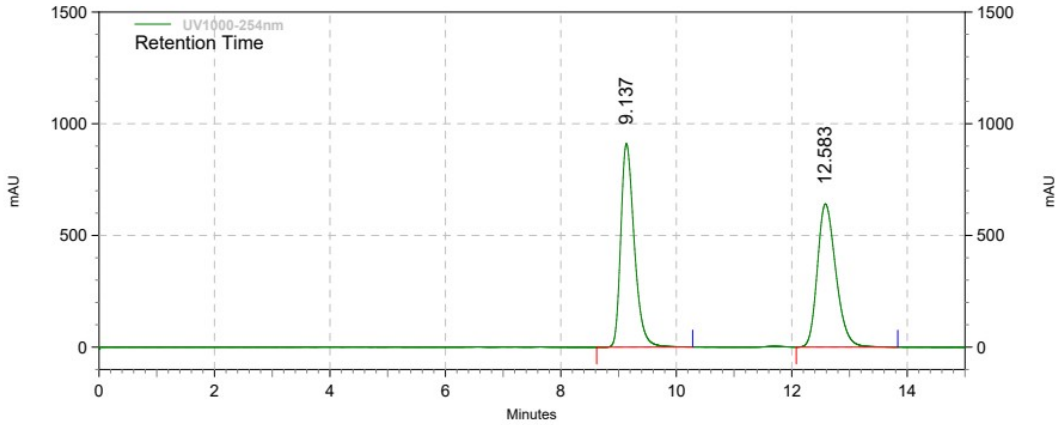


(*E*)-**3aj**

^{19}F NMR (376 MHz, Chloroform-d)

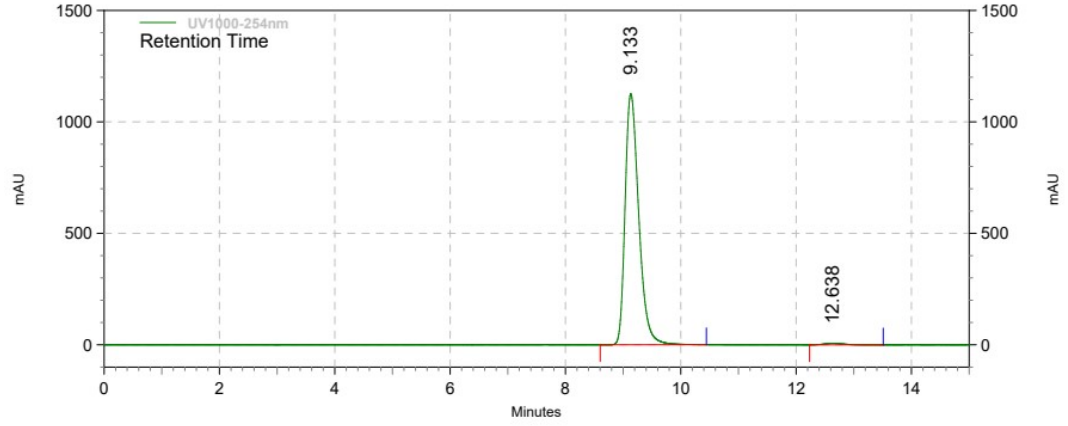


(*E*)-**3aj**



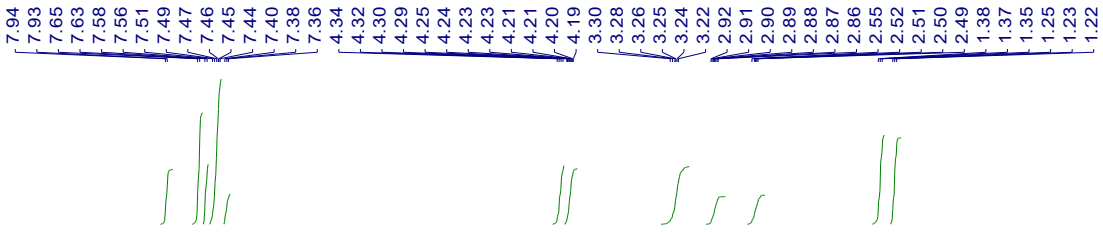
UV1000-254nm
Results

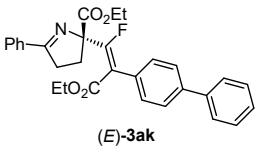
Retention Time	Area	Area %	Height	Height %
9.137	14761827	50.86	910989	58.71
12.583	14259955	49.14	640641	41.29
Totals	29021782	100.00	1551630	100.00



UV1000-254nm
Results

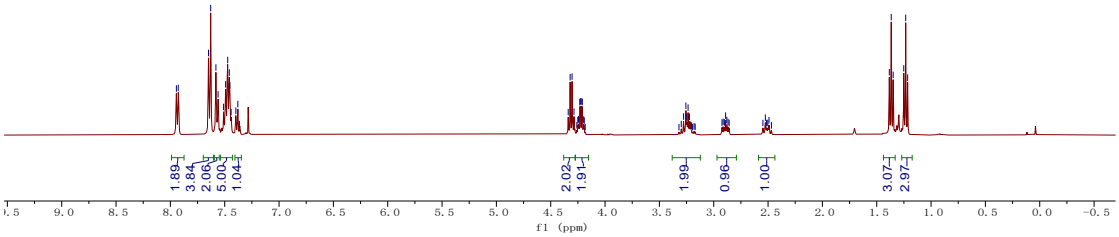
Retention Time	Area	Area %	Height	Height %
9.133	18499042	99.20	1125988	99.42
12.638	148752	0.80	6586	0.58
Totals	18647794	100.00	1132574	100.00

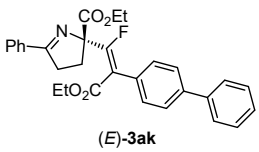




(*E*)-**3ak**

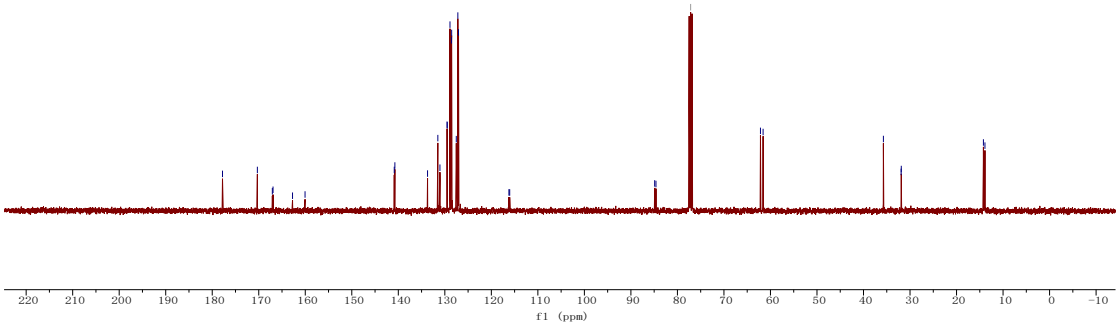
^{1}H NMR (400 MHz, Chloroform-d)

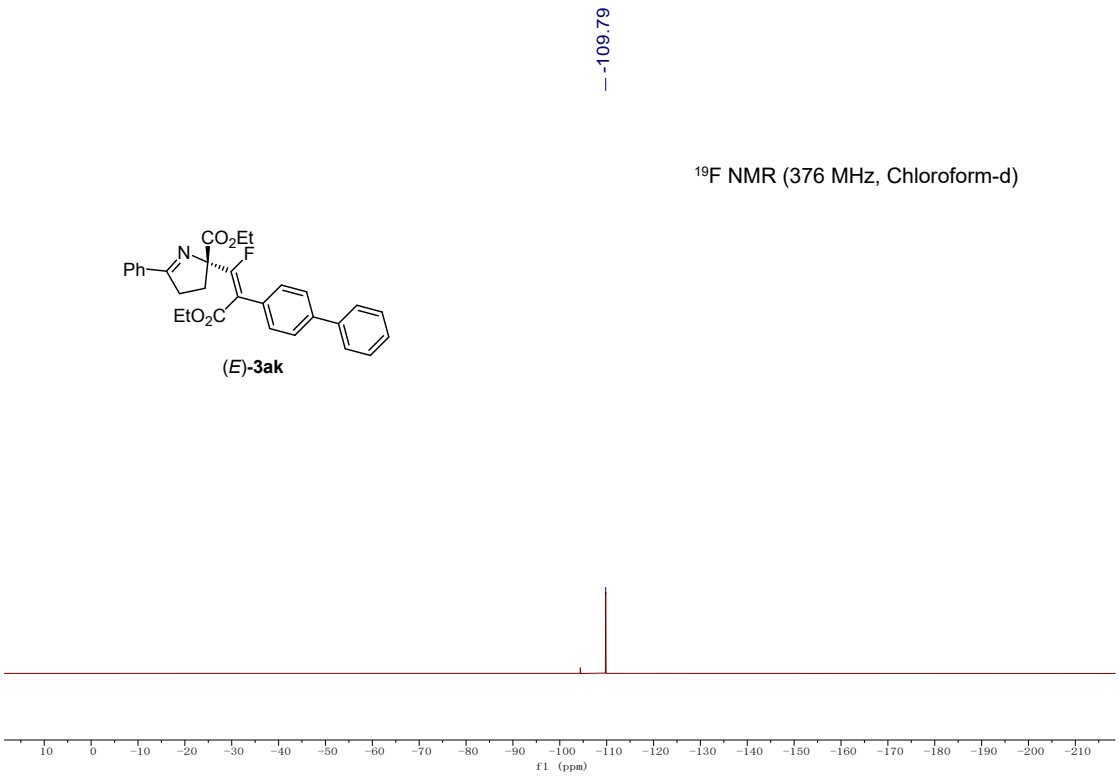




(*E*)-**3ak**

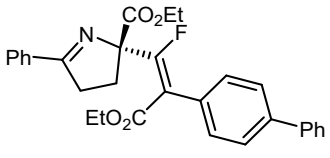
^{13}C NMR (101 MHz, Chloroform-d)



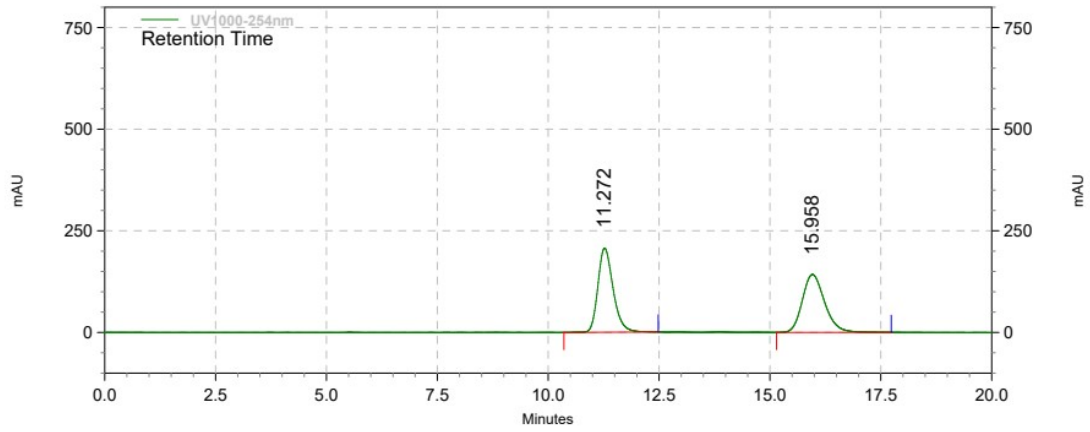


^{19}F NMR (376 MHz, Chloroform-d)

(*E*)-**3ak**

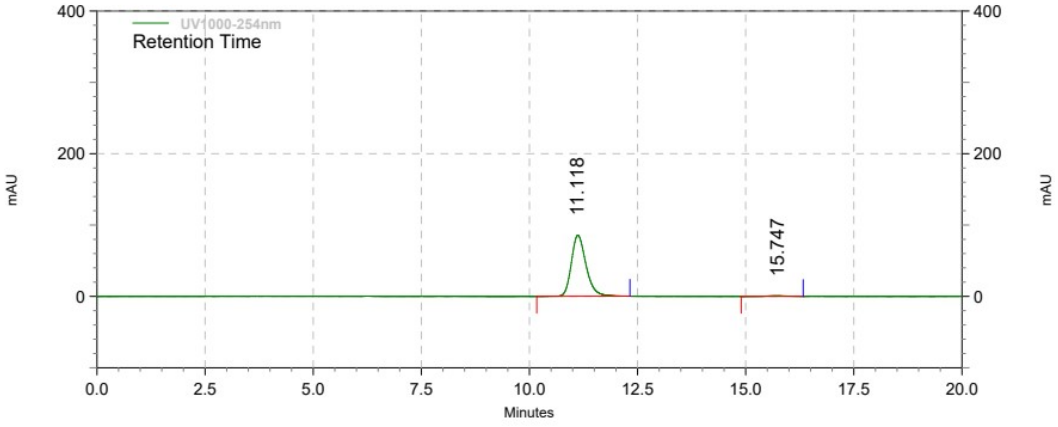


(*E*)-**3ak**



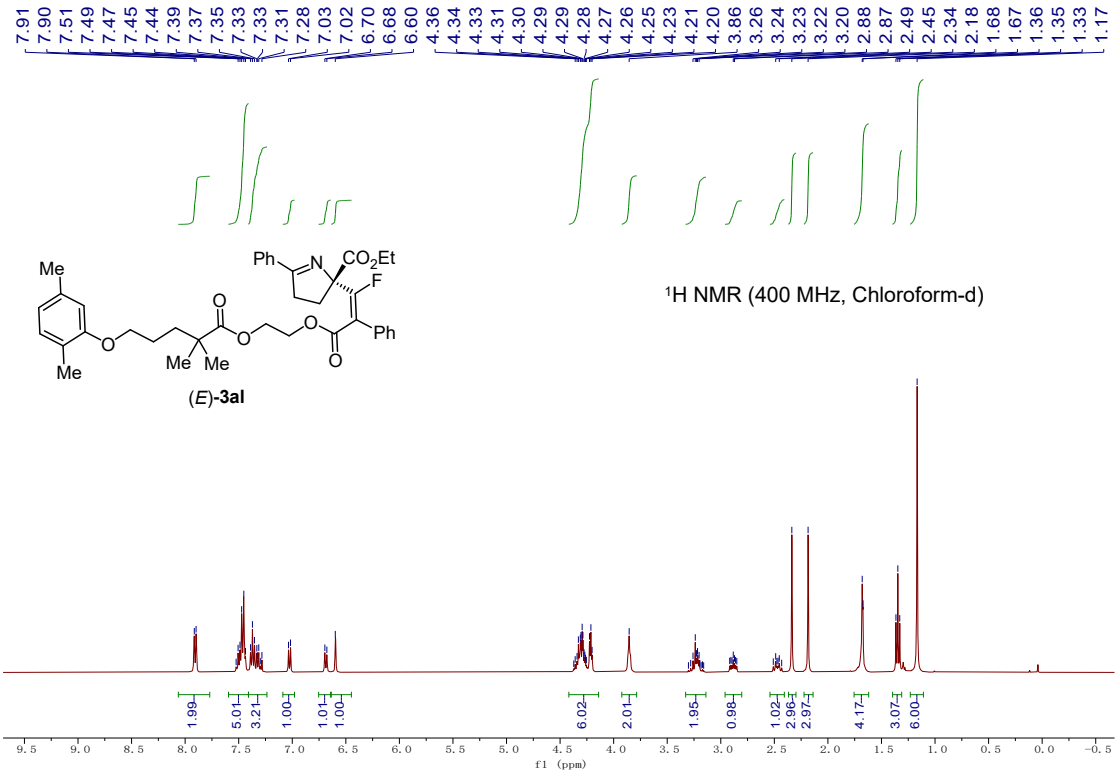
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
11.272	4947132	49.89	207166	59.24
15.958	4969697	50.11	142564	40.76
Totals	9916829	100.00	349730	100.00



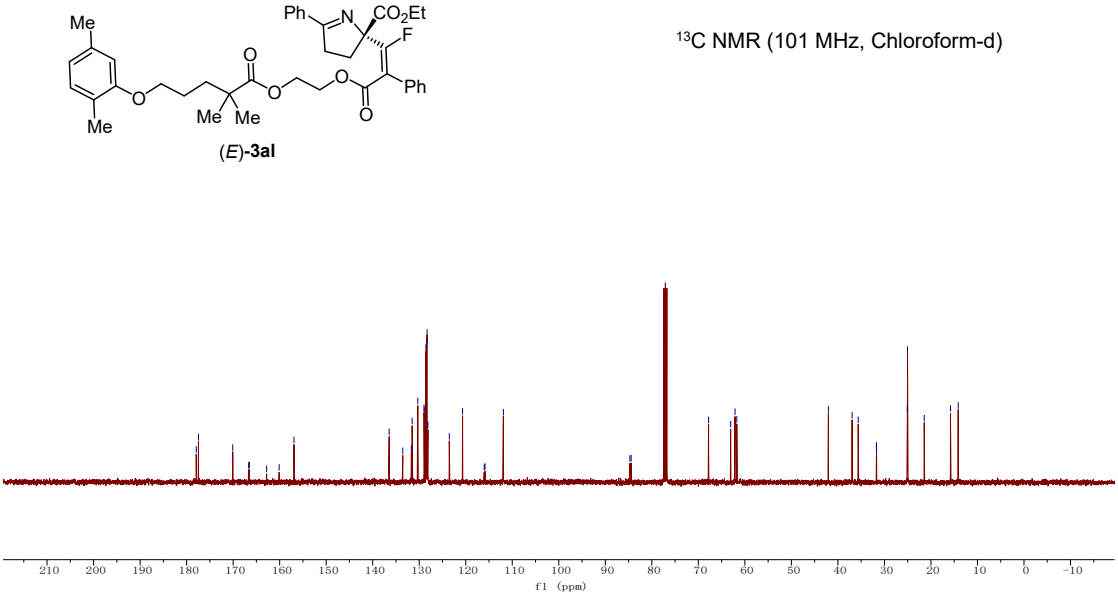
UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
11.118	2022444	98.76	85623	99.16
15.747	25338	1.24	724	0.84
Totals	2047782	100.00	86347	100.00



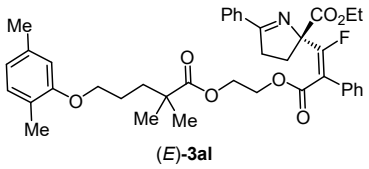
(*E*)-**3al**

^{1}H NMR (400 MHz, Chloroform-d)



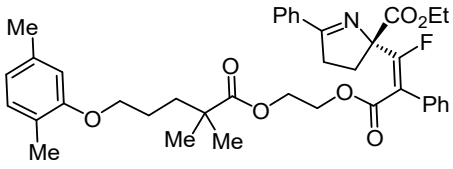
(*E*)-**3al**

^{13}C NMR (101 MHz, Chloroform-d)

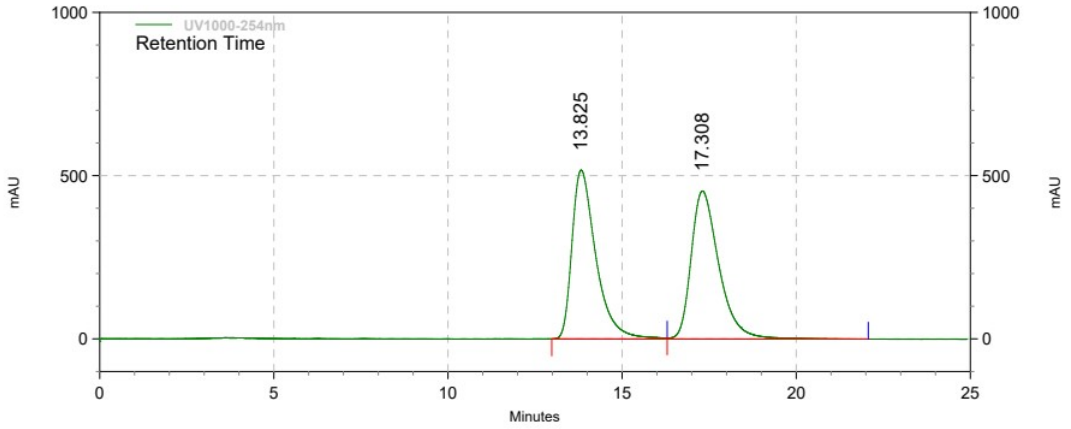


(*E*)-**3al**

^{19}F NMR (376 MHz, Chloroform-d)

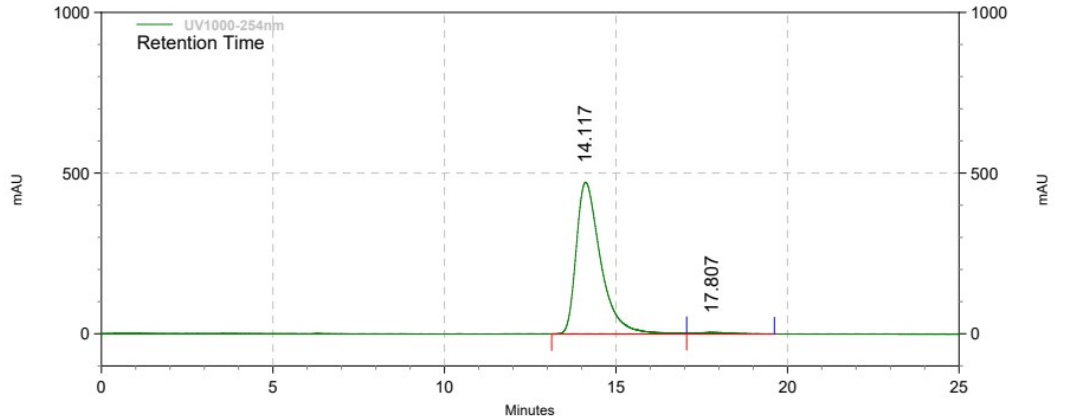


(*E*)-**3al**



UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
13.825	24743562	49.63	517326	53.29
17.308	25109136	50.37	453359	46.71
Totals	49852698	100.00	970685	100.00



UV1000-254nm
Results

Retention Time	Area	Area %	Height	Height %
14.117	23328910	98.72	472177	99.01
17.807	301569	1.28	4743	0.99
Totals	23630479	100.00	476920	100.00

9. X-ray Crystal structure of Compounds (*E*)-3ka (CCDC 2151837)

The single crystal for compound (*E*)-**3ka** were prepared from a mixture solvent of hexane and ethyl acetate (v/v = 3:1) at 14 °C. The data were collected on a Bruker D8 Venture Photon II instrument using Cu-Kα radiation (λ = 1.54178 Å) at 170 K. The crystal structures were solved and refined using the SHELXTL software package. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were added in the riding model and refined with isotropicthermal parameters. The crystallographic data have already been deposited at the Cambridge Crystallographic Data Centre. CCDC numbers: 2151837

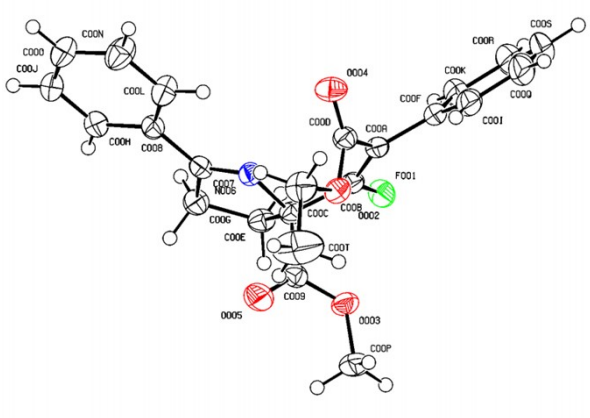


Figure S1 X-ray derived ORTEP of (*E*)-**3ka** with thermal ellipsoids shown at 50% probability level

Table S5 Crystal data and structure refinement for (*E*)-**3ka**

Identification code	**(*E*)-**3ka
Empirical formula	$C_{23}H_{22}FNO_4$
Formula weight	395.41
Temperature/K	169.99
Crystal system	orthorhombic
Space group	$P2_12_12_1$

a/Å	9.4819(3)
b/Å	11.7917(3)
c/Å	18.3290(5)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2049.32(10)
Z	4
ρ_{calc}g/cm^3	1.282
μ/mm^{-1}	0.775
F(000)	832.0
Crystal size/mm^3	0.09 × 0.08 × 0.08
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	8.916 to 133.476
Index ranges	-11 ≤ h ≤ 9, -14 ≤ k ≤ 14, -20 ≤ l ≤ 21
Reflections collected	19517
Independent reflections	3586 [R_{int} = 0.0428, R_{sigma} = 0.0283]
Data/restraints/parameters	3586/0/265
Goodness-of-fit on F^2	1.052
Final R indexes [I>=2σ (I)]	R_1 = 0.0278, wR_2 = 0.0716
Final R indexes [all data]	R_1 = 0.0285, wR_2 = 0.0721
Largest diff. peak/hole / e Å^{-3}	0.17/-0.13