Palladium-Catalyzed Asymmetric Trifluoromethylated Allylic Alkylation of Pyrazolones Enabled by *α*-(Trifluoromethyl)alkenyl Acetates

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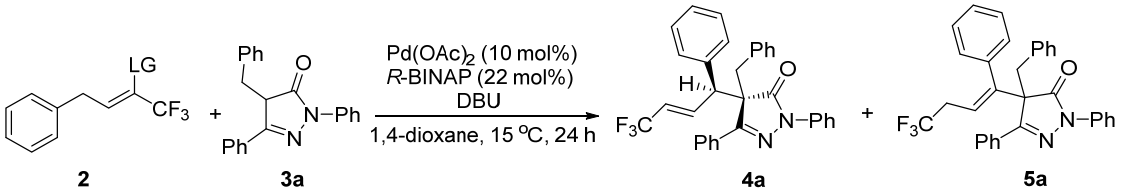
1. General information

Unless otherwise noted, all reactions were performed under an argon atmosphere in glassware with magnetic stirring. NaH (60% in mineral oil) was washed with anhydrous *n*-hexane to remove mineral oil prior to use. Other reagents were purchased from commercial sources and used without further purification. All solvents were treated with molecular sieve. Column chromatography was performed on silica gel (200–300 mesh) using petroleum ether/ethyl acetate as eluent. All ^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (377 MHz or 470 MHz) were recorded on Bruker AVANCE II-400 or Bruker AVANCE III-500 spectrometers (in $CDCl_3$ with TMS as internal standard). Melting points were recorded on a Novel X-4 spectrometer. HRMS (ESI) were recorded on a Thermo LTQ Orbitrap XL spectrometer. HRMS (EI) were recorded on a Micromass GCT spectrometer. The enantiomeric excess was determined by chiral HPLC with *n*-hexane and *i*-propanol as eluents. Optical rotations were measured on a Rudolph AUTOPOL IV polarimeter. X-ray analysis was performed on a Bruker SMART APEX CCD diffractometer. Pyrazolones were prepared from *β*-keto esters according to the literature.[1-3]

2. Optimization of reaction conditions and control experiments

Table S1. Optimization of leaving groups. [a]



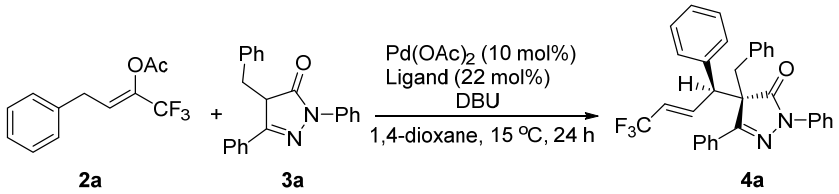
Entry	LG	Yield of **4a** (%) [b]	Yield of **5a** (%) [b]	dr of **4a** [c]	ee of **4a** (%) [d]
1	OTf	0	0	--	--
2	OTs	0	0	--	--
3	OBoc	63	12	> 20:1	87
4	OAc	44	<5	> 20:1	94
5	OBz	47	8	> 20:1	90

[a] Reactions were performed with **2** (0.375 mmol), **3a** (0.25 mmol), $Pd(OAc)_2$ (10 mol %), *R*-BINAP (22 mol %) and DBU (0.75 mmol) in 3.0 mL of 1,4-dioxane at 15 °C for 24 h. [b] Yield of isolated product. [c] Determined by ^{1}H NMR. [d] Determined by chiral HPLC. LG = leaving group.

4-Phenyl-1,1,1-trifluorobut-2-en-2-yl trifluoromethanesulfonate was first investigated owing to our continuous study on this molecular but the desired product was failed to detected (Table S1, entry 1). 4-Phenyl-1,1,1-trifluorobut-2-en-2-yl 4-methylbenzenesulfonate was next examed and the desired product was failed to detected too (Table S1, entry 2). We speculate that sulfonyloxy as a substrate for the leaving group is not suitable for this reaction. So next we looked at the

substrate with carbonyloxy as the leaving group. As shown in Table S1, entries 3-5, substrates with tert-butyl carbonate, acetoxy and benzoyloxy as leaving group all fitted well for this reaction and the desired product was obtained in middle yields amd excellent stereoselectivity. At the same time, **5a** was detected as by-product. Specially, the reaction took place smoothly with optimal control of regio-/stereochemistry when acetoxy was used as the leaving group (Table S1, entry 4, 44% yield, >20:1 dr, 94% ee in 24 h).

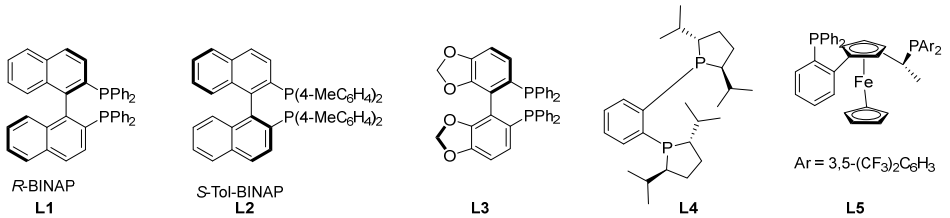
Table S2. Optimization of ligands. [a]

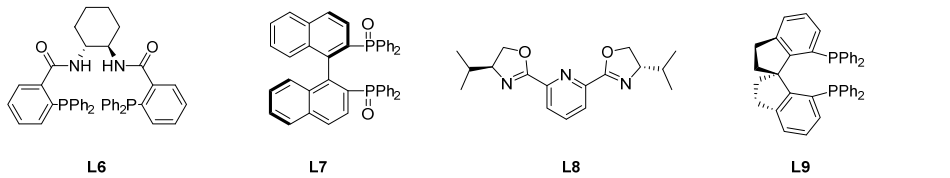


2a **3a** **4a**

Entry	Ligand	Yield of **4a** (%) [b]	dr of **4a** [c]	ee of **4a** (%) [d]
1	L1	44	> 20:1	94
2	L2	40	> 20:1	-86
3	L3	30	> 20:1	78
4	L4	0	--	--
5	L5	0	--	--
6	L6	0	--	--
7	L7	0	--	--
8	L8	0	--	--
9	L9	0	--	--

[a] Reactions were performed with **2a** (0.375 mmol), **3a** (0.25 mmol), $Pd(OAc)_2$ (10 mol %), Ligand (22 mol %) and DBU (0.75 mmol) in 3.0 mL of 1,4-dioxane at 15 °C for 24 h. [b] Yield of isolated product. [c] Determined by ^1H NMR. [d] Determined by chiral HPLC.

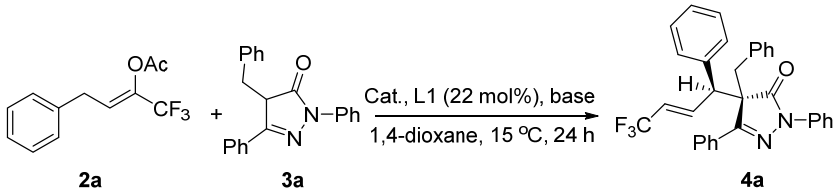




As shown in Table S2, several chiral ligands were investigated and the reaction took place when L1 (*R*-BINAP), L2 (*S*-Tol-BINAP), and L3 were used. The enantioselectives of **4a** was decreased when switching L1 to L2 or L3 (-86% ee and 78% ee respectively). Ligands L4-L9 are

not suitable for this reaction because the reaction did not occur when they were used.

Table S3. Optimization of catalysts and bases. [a]



2a **3a** **4a**

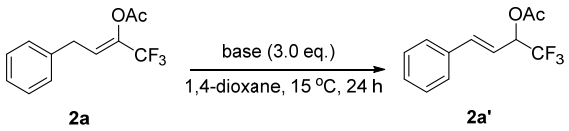
Entry	Cat. (mol%)	Base	Yield of **4a** (%) [b]	dr of **4a** [c]	ee of **4a** (%)[d]
1	$Pd(OAc)_2$ (10 mol%)	DBU	44	> 20:1	94
2	$PdCl_2$ (10 mol%)	DBU	0	--	--
3	$PdCl_2(PPh_3)_2$ (10 mol%)	DBU	0	--	--
4	$Pd_2(dba)_3$ (5 mol%)	DBU	0	--	--
5	$[Pd(allyl)Cl]_2$ (5 mol%)	DBU	52	> 20:1	91
6	$Pd(OAc)_2$ (10 mol%)	TBD	0	--	--
7	$Pd(OAc)_2$ (10 mol%)	Et_3N	0	--	--
8	$Pd(OAc)_2$ (10 mol%)	TMG	0	--	--
9	$Pd(OAc)_2$ (10 mol%)	DABCO	0	--	--
10	$Pd(OAc)_2$ (10 mol%)	DMAP	0	--	--
11	$Pd(OAc)_2$ (10 mol%)	DIPEA	0	--	--
12	$Pd(OAc)_2$ (10 mol%)	pyiridine	0	--	--
13	$Pd(OAc)_2$ (10 mol%)	piperidine	0	--	--

[a] Reactions were performed with **2a** (0.375 mmol), **3a** (0.25 mmol), Cat., *R*-BINAP (22 mol %) and base (0.75 mmol) in 3.0 mL of 1,4-dioxane at 15 °C for 24 h. [b] Yield of isolated product. [c] Determined by ^{1}H NMR. [d] Determined by chiral HPLC.

Then the palladium-catalysts were explored (Table S3, entries 1-5) and $Pd(OAc)_2$ was proved to be the best catalyst with slightly higher enantioselectivity than $[Pd(ally)Cl]_2$ (Table S1, entry 1 and entry 5, 94% ee and 91% ee respectively). The reaction did not occur when $PdCl_2$, $Pd_2(dba)_3$ and $PdCl_2(PPh_3)_2$ were used.

The screening of bases showed that the reaction did not occur when switching DBU to other organobases (Table S3, entries 6-13), indicating that DBU was more efficient for the double-bond migration of *α*-(trifluoromethyl)alkenyl acetates. So experiments were next performed to detect whether the double bond of *α*-(trifluoromethyl)alkenyl acetates is isomerized in the presence of different organobases. As shown in Table S4, DBU is the most suitable base for the double-bond migration of *α*-(trifluoromethyl)alkenyl acetates.

Table S4. Double-bond migration of **2a** with different bases. [a]

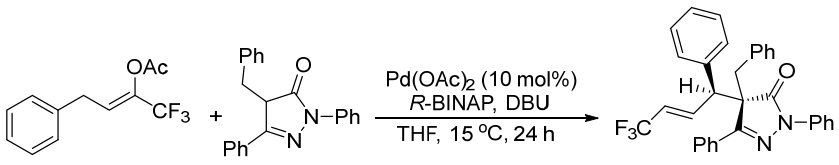


2a **2a'**

Entry	Base	Conversion of **2a** (%) [b]	Yield of **2a'** (%) [b]
1	DBU	100	100
2	TBD	0	0
3	Et_3N	8	8
4	TMG	0	0
5	DABCO	17	17
6	DMAP	0	0
7	DIPEA	0	0
8	pyiridine	0	0
9	piperidine	0	0

[a] Reactions were performed with **2a** (0.25 mmol), base (0.75 mmol) in 2.0 mL of 1,4-dioxane at 15 °C for 24 h.
[b] Yield and conversion were determined by ^{1}H NMR.

Table S5. Optimization of equivalents of ligand, DBU and **2a**. [a]



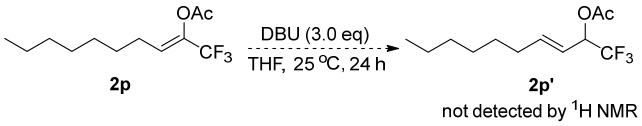
2a **3a** **4a**

Entry	**2a**	*R*-BINAP	DBU	Yield of **4a** (%) [b]	dr of **4a** [c]	ee of **4a** (%) [d]
1	1.5 eq.	22 mol%	3.0 eq.	40	> 20:1	96
2	1.5 eq.	16 mol%	3.0 eq.	46	> 20:1	95
3	1.5 eq.	12 mol%	3.0 eq.	51	> 20:1	96
4	1.5 eq.	10 mol%	3.0 eq.	49	>20:1	93
5	1.2 eq.	12 mol%	3.0 eq.	50	>20:1	94
6	1.5 eq.	12 mol%	2.0 eq.	50	>20:1	95
7	1.5 eq.	12 mol%	1.5 eq.	52	>20:1	96
8	1.5 eq.	12 mol%	1.2 eq.	44	>20:1	96
9 [e]	1.5 eq.	12 mol%	1.5 eq.	80	>20:1	96

[a] Reactions were performed with **2a**, **3a** (0.25 mmol), $Pd(OAc)_2$ (10 mol %), *R*-BINAP and DBU in 3.0 mL of THF at 15 °C for 24 h. [b] Yield of isolated product **4a**. [c] Determined by ^1H NMR. [d] Determined by chiral HPLC. [e] 52 h.

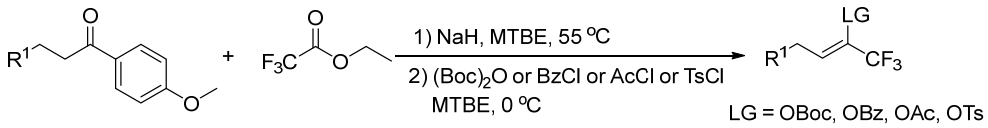
The equivalents of ligand, DBU and **2a** were next optimized. As shown in Table S5, entires 1-3, both the yield and stereoselectivity of **4a** were maintained when the equivalent of *R*-BINAP was gradually reduced from 22 mol% to 12 mol%. However, the stereoselectivity of **4a** was decreased when the amount of *R*-BINAP was reduced to 10 mol%. The stereoselectivity of **4a** is slightly lower when the amount of **2a** was reduced to 1.2 equivalents (Table S5, entry 5, 94% ee). Both the yield and stereoselectivity of **4a** were maintained when the equivalent of DBU was reduced form 3.0 equivalent to 1.5 equivalent but the yield of **4a** was decreased when 1.2 equivalent of DBU was used (Table S5, entires 3, 6-8). At last, the yield of **4a** was increased to 80% with maintained stereoselectivity when the reaction time was exented to 52 h.

Scheme S1. The experiment of double-bond migration in **2p**.



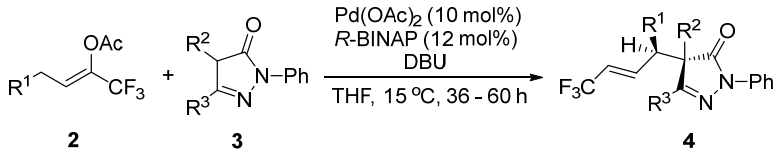
3. General procedure for the synthesis of *α*-(trifluoromethyl)alkenyl esters

α-(Trifluoromethyl)alkenyl esters were preparated following our previous works on synthesizing of *α*-trifluoromethyl alkenyl triflates.[4]



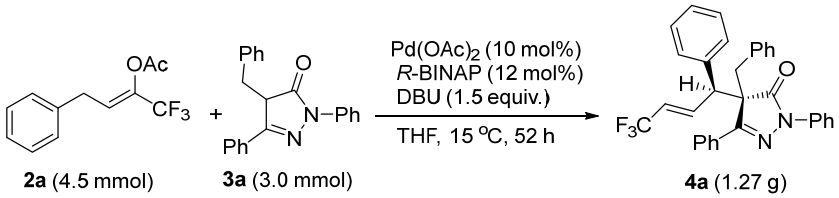
To a suspension of NaH (480 mg, 20.0 mmol) in MTBE (50 mL) was added ethyl trifluoroacetate (2.4 mL, 20.0 mmol) at room temperature under argon atmosphere. After about 1 min of stirring, enolizable ketone (10.0 mmol) was added, and the mixture was refluxed for 6-12 h. After the reaction was complete (monitored by TLC or GC analyses), the reaction solution was cooled to 0 °C. Di-tert-butyl dicarbonate ($(Boc)_2O$, 20.0 mmol) or benzoyl chloride (BzCl, 20.0 mmol) or acetyl chloride (AcCl, 20.0 mmol) or tosyl chloride (TsCl, 20.0 mmol) was added slowly into the reaction mixture. After the reaction was complete (5-15 min, monitored by TLC or GC analyses), the reaction was quenched with ice-water. The aqueous layer was separated and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel to afford the products.

4. General procedure for Pd-catalyzed asymmetric trifluoromethylated allylic alkylation



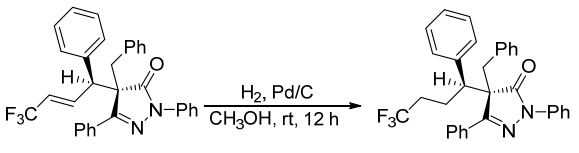
Dissolving the $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 10 mol%) and *R*-BINAP (37.4 mg, 0.06 mmol, 12 mol%) in THF at 15 °C under argon atmosphere and the mixture was stirred for 5 min. Subsequently, *α*-(trifluoromethyl)alkenyl acetates **2** (0.75 mmol, 1.5 equiv.), pyrazolones **3** (0.5 mmol, 1.0 equiv.) and DBU (114 mg, 0.75 mmol, 1.5 equiv.) were added. The reaction mixture was stirred at at 15 °C for 36-60 h. The solution was concentrated under reduced pressure and the crude was purified by column chromatography on silica gel to afford the pyrazolone-derived products **4**.

5. Procedure for gram-scale synthesis of 4a

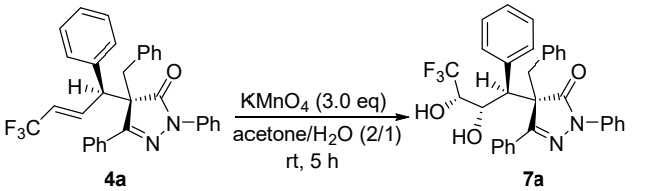


Dissolving the $Pd(OAc)_2$ (67.4 mg, 0.3 mmol, 10 mol%) and *R*-BINAP (224.2 mg, 0.36 mmol, 12 mol%) in 6 mL THF at 15 °C under argon atmosphere and the mixture was stirred for 5 min. Subsequently, *α*-(trifluoromethyl)alkenyl acetates **2** (1.10 g, 4.5 mmol, 1.5 equiv.), pyrazolones **3** (0.98 g, 3.0 mmol, 1.0 equiv.) and DBU (684.0 mg, 4.5 mmol, 1.5 equiv.) were added. The reaction mixture was stirred at at 15 °C for 52 h. The solution was concentrated under reduced pressure and the crude was purified by column chromatography on silica gel to afford the products **4a** (1.27 g, 83%, > 20:1 dr, 95% ee).

6. General procedures for the transformation of product 4a



A solution of **4a** (255.0 mg, 0.5 mmol) and 10% Pd/C (25.5 mg, 10% w/w) in 3.0 mL CH_3OH was stirred at room temperature under a hydrogen atmosphere. The reaction mixture was stirred for about 12 h till completion (monitored by TLC). Then the mixture was filtered, concentrated under reduced pressure, and the crude was purified by column chromatography on silica gel to afford the desired product **6a** (87% yield, > 20: 1 dr, 95% ee).



4a
> 20:1 dr, 95% ee

7a
49%, >20:1 d.r., 95% ee

To a solution of **4a** (204.0 mg, 0.4 mmol) in acetone/H_2O (2:1, v/v, 12 mL) was added $KMnO_4$ (189.6 mg, 1.2 mmol) at room temperature, and the mixture was stirred for 5 h. The reaction mixture was concentrated under reduced pressure to remove acetone and extracted with CH_2Cl_2 for 3 times. The combined organic extracts were dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel to afford the desired products **7a** (49% yield, > 20:1 dr, 95% ee).

7. Reference

[1] H. Nakagawa, R. Ohyama, A. Kimata, T. Suzuki, N. Miyata, *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5939-5942.

[2] A. Rioz-Martínez, A. Cuetos, C. Rodríguez, G. de Gonzalo, I. Lavandera, M. W. Fraaije, V. Gotor, *Ange. Chem. Int.Ed.* **2011**, *50*, 8387-8390.

[3] M. Kamlar, I. Císařová, J. Veselý, *Org. Biomol. Chem.* **2015**, *13*, 2884-2889.

[4] Y. Zhao, Y. Zhou, J. Liu, D. Yang, L. Tao, Y. Liu, X. Dong, J. Liu, J. Qu, *J. Org. Chem.* **2016**, *81*, 4797-4806.

8. Crystal data and structure refinement for 4ab

The crystals of **4ab** were obtained by slow evaporation of the solution (in CH_2Cl_2/ *n*-hexane (1:3) at 0 °C.

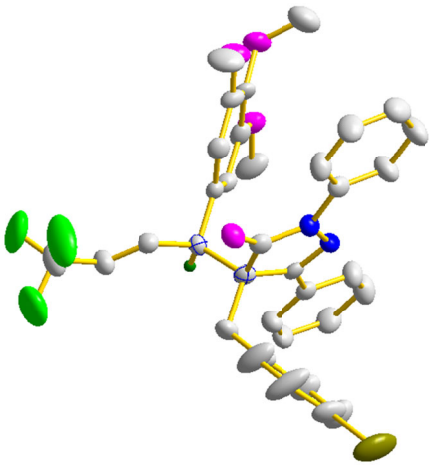
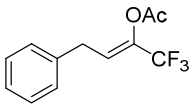


Figure S1. ORTEP diagrams of **4ab** with thermal ellipsoids shown at a 50% probability level. Hydrogen atoms except for substituted on a chiral carbon atom are omitted for the sake of clarity.

Identification code	4ab
Empirical formula	$C_{39}H_{38}BrF_3N_2O_5$
Formula weight	751.62
Temperature	173(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 11.3086(4) A alpha = 90 deg. b = 11.5305(3) A beta = 90 deg. c = 29.2389(9) A gamma = 90 deg.
Volume	3812.6(2) A^3
Z, Calculated density	4, 1.309 Mg/m^3
Absorption coefficient	1.136 mm^-1
F(000)	1552
Crystal size	0.30 x 0.04 x 0.03 mm
Theta range for data collection	1.931 to 24.999 deg.
Limiting indices	-12<=h<=13, -13<=k<=13, -34<=l<=34
Reflections collected / unique	33979 / 6716 [R(int) = 0.0843]
Completeness to theta = 24.999	99.9 %
Absorption correction	Empirical
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6716 / 0 / 406
Goodness-of-fit on F^2	0.853
Final R indices [I>2sigma(I)]	R1 = 0.0460, wR2 = 0.1258
R indices (all data)	R1 = 0.0667, wR2 = 0.1361
Absolute structure parameter	0.087(7)
Largest diff. peak and hole	0.339 and -0.420 e.A^-3

9. Experimental characterization data for new products

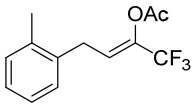
1,1,1-Trifluoro-4-phenylbut-2-en-2-yl acetate (**2a**)



Column chromatography elution: petroleum ether/ethyl acetate = 100:1 (v/v), colorless oil, 2.10 g, 86% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 2H), 7.30 – 7.28 (m, 1H), 7.22 (d, *J* = 7.2 Hz, 2H), 6.26 (t, *J* = 7.4 Hz, 1H), 3.39 (dd, *J* = 7.3, 1.3 Hz, 2H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 137.2, 135.24 (q, *J* = 36.4 Hz), 128.8, 128.6, 126.9, 124.8 (q, *J* = 3.0 Hz), 119.8 (q, *J* = 273.7 Hz), 31.7, 20.1. ^{19}F NMR (470 MHz, $CDCl_3$) δ -70.85 (s). HRMS (EI) *m/z*: calcd for $C_{12}H_{11}F_3O_2$ [$M^{+\bullet}$] 244.0711, found: 244.0710.

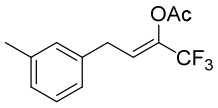
1,1,1-Trifluoro-4-(*o*-tolyl)but-2-en-2-yl acetate (**2b**)



Column chromatography elution: petroleum ether/ethyl acetate = 100:1 (v/v), colorless oil, 2.14 g, 83% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.18 (m, 3H), 7.17 – 7.12 (m, 1H), 6.20 (t, *J* = 7.2 Hz, 1H), 3.37 (dd, *J* = 7.1, 1.7 Hz, 2H), 2.31 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 136.3, 135.6, 135.2 (q, *J* = 35.8 Hz), 130.5, 129.1, 127.2, 126.4, 124.4 (q, *J* = 3.3 Hz), 119.8 (q, *J* = 272.8 Hz), 29.5, 20.1, 19.4. ^{19}F NMR (470 MHz, $CDCl_3$) δ -70.78 (s). HRMS (EI) *m/z*: calcd for $C_{13}H_{13}F_3O_2$ [$M^{+\bullet}$] 258.0868, found: 258.0874.

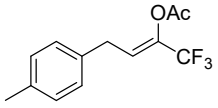
1,1,1-Trifluoro-4-(*m*-tolyl)but-2-en-2-yl acetate (**2c**)



Column chromatography elution: petroleum ether/ethyl acetate = 100:1 (v/v), colorless oil, 2.17 g, 84% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.15 (m, 1H), 7.04 (d, *J* = 7.6 Hz, 1H), 6.97 – 6.95 (m, 2H), 6.20 (t, *J* = 7.4 Hz, 1H), 3.30 (dd, *J* = 7.4, 1.7 Hz, 2H), 2.31 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 138.5, 137.1, 135.1 (q, *J* = 36.4 Hz), 129.3, 128.7, 127.7, 125.6, 124.9 (q, *J* = 3.0 Hz), 119.8 (q, *J* = 272.5 Hz), 31.6, 21.3, 20.2. ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.83 (s). HRMS (EI) *m/z*: calcd for $C_{13}H_{13}F_3O_2$ [$M^{+\bullet}$] 258.0868, found: 258.0863.

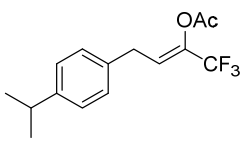
1,1,1-Trifluoro-4-(*p*-tolyl)but-2-en-2-yl acetate (**2d**)



Column chromatography elution: petroleum ether/ethyl acetate = 100:1 (v/v), colorless oil, 2.22 g, 86% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.21 (t, *J* = 7.4 Hz, 1H), 3.32 (dd, *J* = 7.4, 1.5 Hz, 2H), 2.32 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 136.5, 135.0 (q, *J* = 36.3 Hz), 134.1, 129.5, 128.4, 125.1 (q, *J* = 3.5 Hz), 119.9 (q, *J* = 272.5 Hz), 31.3, 21.0, 20.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.84 (s). HRMS (EI) *m/z*: calcd for $C_{13}H_{13}F_3O_2$ [$M^{+\bullet}$] 258.0868, found: 258.0871.

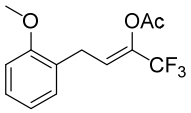
1,1,1-Trifluoro-4-(4-isopropylphenyl)but-2-en-2-yl acetate (**2e**)



Column chromatography elution: petroleum ether/ethyl acetate = 100:1 (v/v), colorless oil, 2.57 g, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19

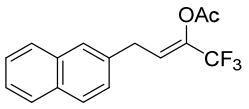
(d, J = 8.1 Hz, 2H), 7.12 (d, J = 8.1 Hz, 2H), 6.24 (t, J = 7.2 Hz, 1H), 3.34 (dd, J = 7.3, 1.6 Hz, 2H), 2.89 (heptet, J = 6.9 Hz, 1H), 2.27 (s, 3H), 1.25 (d, J = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 147.6, 135.1 (q, J = 36.3 Hz), 134.5, 128.5, 126.9, 125.0 (q, J = 3.5 Hz), 119.9 (q, J = 272.4 Hz), 33.8, 31.3, 24.0, 20.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.82 (s). HRMS (EI) *m/z*: calcd for $C_{15}H_{17}F_3O_2$ [$M^{+\bullet}$] 286.1181, found: 286.1187.

1,1,1-Trifluoro-4-(2-methoxyphenyl)but-2-en-2-yl acetate (**2f**)



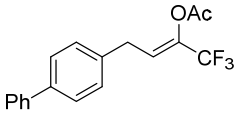
Column chromatography elution: petroleum ether/ethyl acetate = 100:1 (v/v), light yellow oil, 2.19 g, 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, J = 7.8 Hz, 1H), 7.09 (d, J = 7.2 Hz, 1H), 6.91 – 6.84 (m, 2H), 6.24 (t, J = 7.1 Hz, 1H), 3.82 (s, 3H), 3.33 (d, J = 7.1 Hz, 2H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 157.3, 134.9 (q, J = 36.4 Hz), 129.9, 128.3, 125.5, 124.7 (q, J = 3.6 Hz), 120.7, 120.0 (q, J = 273.7 Hz), 110.4, 55.3, 26.5, 20.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.69 (s). HRMS (EI) *m/z*: calcd for $C_{13}H_{13}F_3O_3$ [$M^{+\bullet}$] 274.0817, found: 274.0824.

1,1,1-Trifluoro-4-(naphthalen-2-yl)but-2-en-2-yl acetate (**2g**)



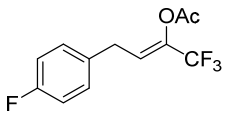
Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), light yellow oil, 2.50 g, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.81 (m, 3H), 7.64 (s, 1H), 7.51 – 7.47 (m, 2H), 7.32 (d, J = 8.3 Hz, 1H), 6.33 (t, J = 7.1 Hz, 1H), 3.54 (d, J = 7.1 Hz, 2H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 135.4 (q, J = 36.3 Hz), 134.7, 133.6, 132.4, 128.6, 127.7, 127.6, 127.0, 126.8, 126.3, 125.8, 124.7 (d, J = 3.6 Hz), 119.9 (d, J = 272.7 Hz), 31.9, 20.2. ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.78 (s). HRMS (EI) *m/z*: calcd for $C_{16}H_{13}F_3O_2$ [$M^{+\bullet}$] 294.0868, found: 294.0875.

1,1,1-Trifluoro-4-([1,1'-biphenyl]-4-yl)but-2-en-2-yl acetate (**2h**)



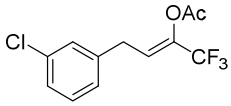
Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), white solid, mp 45 – 46 °C, 2.75 g, 86% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.56 (m, 4H), 7.50 – 7.46 (m, 2H), 7.40 – 7.37 (m, 1H), 7.32 – 7.30 (m, 2H), 6.31 (t, J = 7.2 Hz, 1H), 3.45 (dd, J = 7.3, 1.6 Hz, 2H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 140.8, 140.0, 136.3, 135.4 (q, J = 36.3 Hz), 129.0, 128.9, 127.6, 127.4, 127.1, 124.7 (q, J = 3.6 Hz), 119.9 (q, J = 271.3 Hz), 31.4, 20.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.75 (s). HRMS (EI) *m/z*: calcd for $C_{18}H_{15}F_3O_2$ [$M^{+\bullet}$] 320.1024, found: 320.1032.

1,1,1-Trifluoro-4-(4-fluorophenyl)but-2-en-2-yl acetate (**2i**)



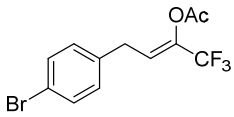
Column chromatography elution: petroleum ether/ethyl acetate = 100:1 (v/v), colorless oil, 2.33 g, 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 – 7.13 (m, 2H), 7.04 – 6.97 (m, 2H), 6.19 (t, *J* = 7.4 Hz, 1H), 3.34 (d, *J* = 7.4 Hz, 2H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 161.9 (d, *J* = 245.2 Hz), 135.3 (q, *J* = 36.4 Hz), 132.9, 130.0 (d, *J* = 8.0 Hz), 124.5 (q, *J* = 3.5 Hz), 119.8 (q, *J* = 272.5 Hz), 115.6 (d, *J* = 21.4 Hz), 30.9, 20.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.93 (s, 3F), -115.88 – -116.04 (m, 1F). HRMS (EI) *m/z*: calcd for $C_{12}H_{10}F_4O_2$ [$M^{+\bullet}$] 262.0617, found: 262.0620.

1,1,1-Trifluoro-4-(3-chlorophenyl)but-2-en-2-yl acetate (**2j**)



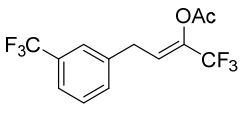
Column chromatography elution: petroleum ether/ethyl acetate = 100:1 (v/v), colorless oil, 2.42 g, 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.21 (m, 2H), 7.16 (s, 1H), 7.09 – 7.03 (m, 1H), 6.18 (t, *J* = 7.3 Hz, 1H), 3.32 (dd, *J* = 7.4, 1.7 Hz, 2H), 2.26 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 139.2, 135.7 (q, *J* = 36.5 Hz), 134.5, 130.0, 128.7, 127.2, 126.7, 123.9 (q, *J* = 3.6 Hz), 119.7 (q, *J* = 272.6 Hz), 31.3, 20.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.94 (s). HRMS (EI) *m/z*: calcd for $C_{12}H_{10}ClF_3O_2$ [$M^{+\bullet}$] 278.0321, found: 278.0324.

1,1,1-Trifluoro-4-(4-bromophenyl)but-2-en-2-yl acetate (**2k**)



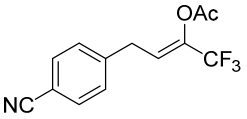
Column chromatography elution: petroleum ether/ethyl acetate = 100:1 (v/v), light yellow oil, 2.75 g, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.2 Hz, 2H), 7.07 (d, *J* = 8.2 Hz, 2H), 6.18 (t, *J* = 7.4 Hz, 1H), 3.32 (d, *J* = 7.3 Hz, 2H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 136.2, 135.6 (q, *J* = 36.5 Hz), 131.9, 130.3, 124.0 (q, *J* = 3.5 Hz), 120.8, 119.7 (q, *J* = 273.7 Hz), 31.1, 20.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.93 (s). HRMS (EI) *m/z*: calcd for $C_{12}H_{10}BrF_3O_2$ [$M^{+\bullet}$] 321.9816, found: 321.9819.

1,1,1-Trifluoro-4-(3-(trifluoromethyl)phenyl)but-2-en-2-yl acetate (**2l**)



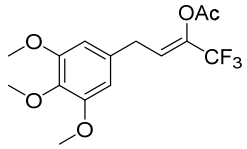
Column chromatography elution: petroleum ether/ethyl acetate = 100:1 (v/v), colorless oil, 2.81 g, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.6 Hz, 1H), 7.47 – 7.42 (m, 2H), 7.39 (d, *J* = 7.6 Hz, 1H), 6.21 (t, *J* = 7.3 Hz, 1H), 3.42 (d, *J* = 7.2 Hz, 2H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 138.2, 135.9 (q, *J* = 36.6 Hz), 131.9, 131.1 (q, *J* = 32.2 Hz), 129.3, 125.3 (q, *J* = 3.8 Hz), 124.0 (q, *J* = 272.7 Hz), 123.8 (q, *J* = 3.8 Hz), 123.6 (q, *J* = 3.5 Hz), 119.7 (q, *J* = 272.7 Hz), 31.4, 20.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.72 (s, 3F), -71.01 (s, 3F). HRMS (EI) *m/z*: calcd for $C_{13}H_{10}F_6O_2$ [$M^{+\bullet}$] 312.0585, found: 312.0587.

1,1,1-Trifluoro-4-(4-cyanophenyl)but-2-en-2-yl acetate (**2m**)



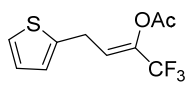
Column chromatography elution: petroleum ether/ethyl acetate = 20:1 (v/v), white solid, mp 67 – 68 °C, 1.67 g, 62% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.18 (t, *J* = 7.4 Hz, 1H), 3.42 (d, *J* = 7.4 Hz, 2H), 2.24 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 142.7, 136.1 (q, *J* = 36.3 Hz), 132.4, 129.4, 123.1 (q, *J* = 3.5 Hz), 119.6 (q, *J* = 273.7 Hz), 118.6, 110.8, 31.5, 20.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ -71.00 (s). HRMS (EI) *m/z*: calcd for $C_{13}H_{10}F_3NO_2$ [$M^{+\bullet}$] 269.0664, found: 269.0658.

1,1,1-Trifluoro-4-(3,4,5-trimethoxyphenyl)but-2-en-2-yl acetate (**2n**)



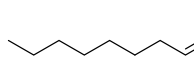
Column chromatography elution: petroleum ether/ethyl acetate = 30:1 (v/v), light yellow oil, 3.04 g, 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.40 (s, 2H), 6.20 (t, *J* = 7.3 Hz, 1H), 3.84 (s, 6H), 3.82 (s, 3H), 3.29 (d, *J* = 7.3 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 153.4, 136.9, 135.2 (q, *J* = 36.4 Hz), 132.8, 124.7 (q, *J* = 3.5 Hz), 119.8 (q, *J* = 272.7 Hz), 105.5, 60.8, 56.1, 31.9, 20.2. ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.82 (s). HRMS (EI) *m/z*: calcd for $C_{15}H_{17}F_3O_5$ [$M^{+\bullet}$] 334.1028, found: 334.1038.

1,1,1-Trifluoro-4-(thiophen-2-yl)but-2-en-2-yl acetate (**2o**)



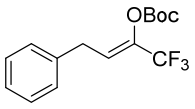
Column chromatography elution: petroleum ether/ethyl acetate = 100:1 (v/v), light yellow oil, 2.20 g, 88% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 5.2, 1.1 Hz, 1H), 6.96 – 6.94 (m, 1H), 6.87 – 6.84 (m, 1H), 6.26 (t, *J* = 7.3 Hz, 1H), 3.57 (dd, *J* = 7.3, 1.6 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 139.1, 135.3 (q, *J* = 36.6 Hz), 127.2, 125.7, 124.4, 123.9 (q, *J* = 3.5 Hz), 119.7 (q, *J* = 272.6 Hz), 25.9, 20.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -71.00 (s). HRMS (EI) *m/z*: calcd for $C_{10}H_9F_3O_2S$ [$M^{+\bullet}$] 250.0275, found: 250.0277.

1,1,1-Trifluorodec-2-en-2-yl acetate (**2p**)



Column chromatography elution: petroleum ether/ethyl acetate = 100:1 (v/v), colorless oil, 2.12 g, 84% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.04 (t, *J* = 7.5 Hz, 1H), 2.23 (s, 3H), 2.04 – 1.95 (m, 2H), 1.43 – 1.38 (m, 2H), 1.34 – 1.21 (m, 8H), 0.91 – 0.81 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 134.7 (q, *J* = 36.1 Hz), 126.2 (q, *J* = 3.5 Hz), 119.9 (q, *J* = 272.1 Hz), 31.7, 29.1, 28.9, 27.8, 25.4, 22.6, 20.1, 14.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.95 (s). HRMS (EI) *m/z*: calcd for $C_{12}H_{19}F_3O_2$ [$M^{+\bullet}$] 252.1337, found: 252.1339.

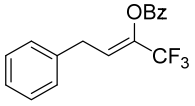
Tert-butyl (1,1,1-trifluoro-4-phenylbut-2-en-2-yl) carbonate (**2-OBoc**)



Column chromatography elution: petroleum ether/ethyl acetate = 100:1 (v/v), colorless oil, 2.51 g, 83% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.30 (m, 2H), 7.29 – 7.23 (m, 1H), 7.21 (d, *J* = 7.2 Hz, 2H), 6.20 (t, *J* = 7.5 Hz, 1H), 3.44 (dd, *J* = 7.5, 1.5 Hz, 2H), 1.55 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.9, 137.2, 135.7 (q, *J* = 36.5 Hz), 128.8, 128.6, 126.9, 124.8 (q, *J* = 3.3 Hz), 119.8 (q, *J* = 272.6 Hz), 84.9, 31.4, 27.5. ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.68 (s). HRMS (EI) m/z: calcd for $C_{11}H_8F_3O_2$ $[M - OBu]^+$ 229.0476, found: 229.0478.

1,1,1-Trifluoro-4-phenylbut-2-en-2-yl benzoate (**2-OBz**)

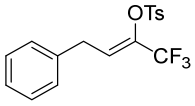


Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 2.48 g, 81% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 7.97 (m, 2H), 7.75 – 7.67 (m, 1H), 7.58 (dd, *J* = 10.8, 4.9 Hz, 2H), 7.33 (dd, *J* = 9.9, 4.5 Hz, 2H), 7.29 – 7.19 (m, 3H), 6.34 (t, *J* = 7.5 Hz, 1H), 3.70 (dd, *J* = 7.5, 1.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 137.3, 135.4 (d, *J* = 36.6 Hz), 134.3, 130.5, 130.3, 128.8, 128.6, 127.9, 126.9, 125.1 (d, *J* = 3.5 Hz), 119.9 (d, *J* = 272.8 Hz), 31.8. ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.59 (s).

HRMS (EI) *m/z*: calcd for $C_{17}H_{13}F_3O_2$ $[M^{+\bullet}]$ 306.0868, found: 306.0865.

1,1,1-Trifluoro-4-phenylbut-2-en-2-yl 4-methylbenzenesulfonate (**2-OTs**)

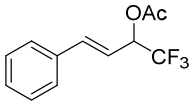


Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 2.74 g, 77% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.6 Hz, 2H), 7.39 – 7.30 (m, 4H), 7.26 – 7.20 (m, 3H), 6.33 (t, *J* = 7.4 Hz, 1H), 3.69 (d, *J* = 7.3 Hz, 2H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.9, 137.1, 134.7 (d, *J* = 37.3 Hz), 133.2, 129.9, 128.8, 128.65 (q, *J* = 3.3 Hz), 128.6, 128.2, 127.0, 119.4 (d, *J* = 273.2 Hz), 32.3, 21.7. ^{19}F NMR (377 MHz, $CDCl_3$) δ -69.02 (s).

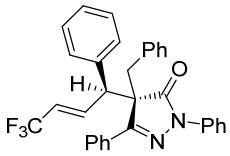
HRMS (EI) *m/z*: calcd for $C_{17}H_{15}F_3O_3S$ $[M^{+\bullet}]$ 356.0694, found: 356.0704.

(*E*)-1,1,1-Trifluoro-4-phenylbut-3-en-2-yl acetate (**2a'**)



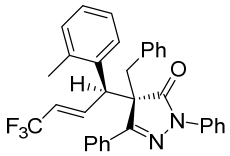
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 7.9, 1.3 Hz, 2H), 7.40 – 7.30 (m, 3H), 6.87 (d, *J* = 15.9 Hz, 1H), 6.13 (dd, *J* = 15.9, 7.8 Hz, 1H), 5.90 – 5.78 (m, 1H), 2.19 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 138.8, 135.0, 129.1, 128.8, 127.0, 123.2 (q, *J* = 280.4 Hz), 117.3 (q, *J* = 1.5 Hz), 71.1 (q, *J* = 33.5 Hz), 20.6. ^{19}F NMR (377 MHz, $CDCl_3$) δ -76.50 (d, *J* = 6.6 Hz). HRMS (EI) *m/z*: calcd for $C_{12}H_{11}F_3O_2$ $[M^{+\bullet}]$ 244.0711, found: 244.0704.

(*S*)-4-Benzyl-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-phenylbut-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4a**)



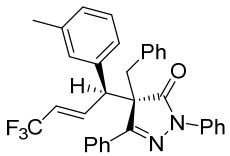
Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 204.2 mg, 80% yield, > 20:1 dr, 94% ee.
$[\alpha]_D^{20}$ = +67.08 (c 0.40, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.82 (m, 2H), 7.63 – 7.56 (m, 1H), 7.54 – 7.45 (m, 3H), 7.42 – 7.39 (m, 2H), 7.31 – 7.28 (m, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.12 – 7.07 (m, 1H), 7.07 – 6.96 (m, 7H), 6.85 (d, *J* = 7.3 Hz, 2H), 5.92 (dq, *J* = 15.6, 6.2 Hz, 1H), 4.23 (d, *J* = 10.0 Hz, 1H), 3.60 (d, *J* = 13.6 Hz, 1H), 3.46 (d, *J* = 13.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 157.3, 137.1, 137.0 (q, *J* = 7.1 Hz), 136.5, 134.2, 131.7, 130.4, 129.3, 128.9, 128.7, 128.5, 128.2, 128.1, 127.8, 127.3, 126.7, 125.9, 122.7 (q, *J* = 270.7 Hz), 121.7 (q, *J* = 33.9 Hz), 120.4, 63.6, 53.5, 41.5. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.80 (d, *J* = 6.3 Hz).
HPLC analysis: Daicel CHIRALPAK OD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{minor} = 6.14 min, t_{major} = 6.78 min.
HRMS (ESI) *m/z*: calcd for $C_{32}H_{26}F_3N_2O$ $[M + H]^+$ 511.1997, found: 511.1989.

(*S*)-4-Benzyl-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(*o*-tolyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4b**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 236.1 mg, 90% yield, > 20:1 dr, 99% ee.
$[\alpha]_D^{20}$ = +68.45 (c 0.50, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.83 (m, 2H), 7.66 – 7.55 (m, 1H), 7.54 – 7.40 (m, 5H), 7.32 (t, *J* = 7.4 Hz, 2H), 7.17 (t, *J* = 7.2 Hz, 1H), 7.09 – 6.93 (m, 5H), 6.84 (d, *J* = 7.4 Hz, 2H), 6.76 (d, *J* = 7.4 Hz, 2H), 5.94 – 5.89 (m, 1H), 4.22 (d, *J* = 9.9 Hz, 1H), 3.60 (d, *J* = 13.5 Hz, 1H), 3.46 (d, *J* = 13.5 Hz, 1H), 2.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) (one aromatic carbon missing) δ 174.1, 157.5, 137.8, 137.2 (q, *J* = 6.1 Hz), 137.13, 137.11, 134.3, 133.5, 131.7, 130.4, 129.3, 129.2, 128.9, 128.7, 128.2, 127.7, 127.3, 126.7, 125.9, 122.8 (q, *J* = 271.7 Hz), 121.4 (q, *J* = 33.8, 1H), 120.4, 63.7, 53.2, 41.6, 21.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.81 (d, *J* = 6.3 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{minor} = 5.19 min, t_{major} = 6.45 min.
HRMS (ESI) *m/z*: calcd for $C_{33}H_{28}F_3N_2O$ $[M + H]^+$ 525.2154, found: 525.2142.

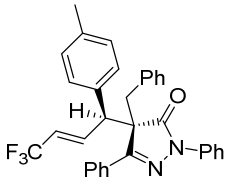
(*S*)-4-Benzyl-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(*m*-tolyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4c**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 215.1 mg, 82% yield, > 20:1 dr, 94% ee.
$[\alpha]_D^{20}$ = +83.61 (c 0.77, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.84 (m, 2H), 7.65 – 7.55 (m, 1H),

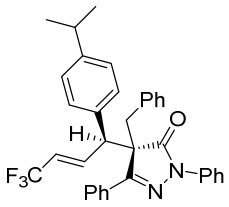
7.55 – 7.49 (m, 3H), 7.49 – 7.44 (m, 2H), 7.37 – 7.30 (m, 2H), 7.22 – 7.16 (m, 1H), 7.10 – 7.02 (m, 5H), 6.96 – 6.89 (m, 2H), 6.70 – 6.63 (m, 2H), 5.94 (dq, J = 15.6, 6.2 Hz, 1H), 4.19 (d, J = 10.0 Hz, 1H), 3.63 (d, J = 13.6 Hz, 1H), 3.49 (d, J = 13.6 Hz, 1H), 2.03 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 157.5, 138.2, 137.1, 137.0 (q, J = 6.5 Hz), 136.3, 134.3, 131.8, 130.4, 129.3, 128.9, 128.8, 128.7, 128.5, 128.3, 128.2, 127.3, 126.8, 125.9, 124.9, 122.7 (q, J = 270.7 Hz), 121.5 (q, J = 33.8 Hz), 120.3, 63.7, 53.6, 41.4, 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.75 (d, J = 6.3 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 8.77 min, t_{minor} = 10.56 min.
HRMS (ESI) *m/z*: calcd for $C_{33}H_{28}F_3N_2O$ $[M + H]^+$ 525.2154, found: 525.2143.

(*S*)-4-Benzyl-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(*p*-tolyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4d**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 212.5 mg, 81% yield, > 20:1 dr, 91% ee.
$[\alpha]_D^{20}$ = +62.83 (c 0.67, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.84 (m, 2H), 7.62 – 7.55 (m, 1H), 7.53 – 7.46 (m, 3H), 7.43 (dd, J = 8.6, 1.0 Hz, 2H), 7.36 – 7.28 (m, 2H), 7.19 – 7.15 (m, 1H), 7.10 – 6.95 (m, 5H), 6.84 (d, J = 8.0 Hz, 2H), 6.75 (d, J = 8.2 Hz, 2H), 5.91 (dq, J = 15.6, 6.2 Hz, 1H), 4.21 (d, J = 10.0 Hz, 1H), 3.59 (d, J = 13.5 Hz, 1H), 3.45 (d, J = 13.5 Hz, 1H), 2.17 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 157.5, 137.8, 137.2 (q, J = 6.1 Hz), 137.1, 134.2, 133.5, 131.7, 130.4, 129.3, 129.2, 128.9, 128.7, 128.2, 127.7, 127.3, 126.7, 125.9, 122.7 (q, J = 270.7 Hz), 121.4 (q, J = 33.9 Hz), 120.4, 63.7, 53.2, 41.6, 21.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.80 (d, J = 6.2 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 9.57 min, t_{minor} = 10.79 min.
HRMS (ESI) *m/z*: calcd for $C_{33}H_{28}F_3N_2O$ $[M + H]^+$ 525.2154, found: 525.2149.

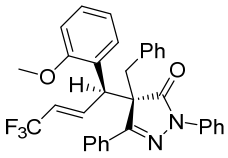
(*S*)-4-Benzyl-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(4-isopropylphenyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4e**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 229.3 mg, 83% yield, > 20:1 dr, 99% ee.
$[\alpha]_D^{20}$ = +59.70 (c 0.41, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 4.6 Hz, 2H), 7.55 – 7.45 (m, 1H), 7.44 – 7.37 (m, 3H), 7.27 (d, J = 8.0 Hz, 2H), 7.20 (t, J = 7.6 Hz, 2H), 7.07 (t, J = 7.2 Hz,1H), 6.99 – 6.85 (m, 5H), 6.79 (d, J = 7.7 Hz, 2H), 6.70 (d, J = 7.7 Hz, 2H), 5.83 (dq, J = 12.3, 6.0 Hz, 1H), 4.14 (d, J = 10.1 Hz, 1H), 3.50 (d, J = 13.5 Hz, 1H), 3.35 (d, J = 13.5 Hz, 1H), 2.63 (heptet, J = 6.9 Hz, 1H), 1.00 (d, J = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 157.4, 148.7, 137.08 (q, J = 7.1 Hz), 137.07, 134.3, 133.6, 131.8, 130.4, 129.3, 128.9, 128.6,

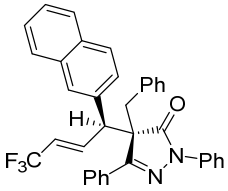
128.2, 127.8, 127.3, 126.7, 126.4, 125.9, 122.7 (q, J = 270.7 Hz), 121.4 (q, J = 34.0 Hz), 120.5, 63.8, 53.1, 41.3, 33.6, 23.9, 23.7. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.73 (d, J = 6.0 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 7.04 min, t_{minor} = 8.75 min.
HRMS (ESI) *m/z*: calcd for $C_{35}H_{32}F_3N_2O$ $[M + H]^+$ 553.2467, found: 553.2457.

(*S*)-4-Benzyl-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(2-methoxyphenyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4f**)



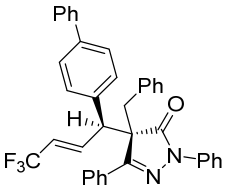
Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 221.6 mg, 82% yield, > 20:1 dr, 97% ee.
$[\alpha]_D^{20}$ = +90.33 (c 0.33, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.81 (m, 2H), 7.55 – 7.46 (m, 3H), 7.45 – 7.39 (m, 3H), 7.31 (t, J = 7.9 Hz, 2H), 7.19 – 7.12 (m, 2H), 7.07 – 6.97 (m, 6H), 6.66 (t, J = 7.6 Hz, 1H), 6.53 (d, J = 8.1 Hz, 1H), 5.96 – 5.84 (m, 1H), 4.95 (d, J = 9.8 Hz, 1H), 3.63 (d, J = 13.5 Hz, 1H), 3.50 (d, J = 13.5 Hz, 1H), 3.14 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.4, 157.8, 155.8, 137.4 (q, J = 6.5 Hz), 137.2, 134.3, 131.7, 129.9, 129.4, 128.9, 128.7, 128.3, 128.1, 128.0, 127.2, 126.9, 125.7, 125.1, 122.8 (q, J = 269.9 Hz), 121.0 (q, J = 33.7 Hz), 120.5, 120.2, 110.2, 63.3, 54.3, 44.6, 41.9. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.66 (d, J = 6.2 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 7.28 min, t_{minor} = 14.43 min.
HRMS (ESI) *m/z*: calcd for $C_{33}H_{28}F_3N_2O_2$ $[M + H]^+$ 541.2103, found: 541.2094.

(*S*)-4-Benzyl-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(naphthalen-2-yl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4g**)



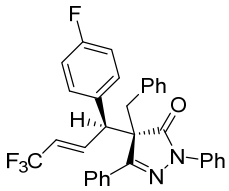
Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 246.7 mg, 88% yield, > 20:1 dr, 94% ee.
$[\alpha]_D^{20}$ = +83.53 (c 0.16, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 6.9 Hz, 2H), 7.77 – 7.66 (m, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.55 – 7.44 (m, 4H), 7.43 – 7.28 (m, 5H), 7.28 – 7.19 (m, 3H), 7.12 (t, J = 7.3 Hz, 1H), 7.03 (d, J = 3.6 Hz, 6H), 5.95 (dq, J = 15.6, 6.1 Hz, 1H), 4.39 (d, J = 9.6 Hz, 1H), 3.67 (d, J = 13.5, 1H), 3.54 (d, J = 13.5, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) (one aromatic carbon missing) δ 174.1, 157.5, 137.0, 136.9 (q, J = 6.1 Hz), 134.1, 133.9, 133.0, 132.8, 131.8, 130.5, 129.3, 128.9, 128.7, 128.33, 128.31, 127.8, 127.5, 127.4, 127.3, 126.8, 126.3, 126.0, 125.3, 122.7 (q, J = 270.7 Hz), 121.82 (q, J = 33.8 Hz), 120.4, 63.7, 53.7, 41.7. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.83 (d, J = 5.9 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 100/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 16.38 min, t_{minor} = 21.72 min.
HRMS (ESI) *m/z*: calcd for $C_{36}H_{28}F_3N_2O$ $[M + H]^+$ 561.2154, found: 561.2144.

(*S*)-4-((*S*,*E*)-1-([1,1'-Biphenyl]-4-yl)-4,4,4-trifluorobut-2-en-1-yl)-4-benzyl-1,3-diphenyl-1*H*-pyrazol-5(4*H*)-one (**4h**)



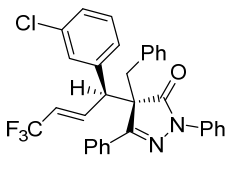
Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 249.3 mg, 85% yield, > 20:1 dr, 94% ee.
$[\alpha]_D^{20}$ = +53.86 (c 0.44, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 5.4 Hz, 2H), 7.68 – 7.58 (m, 1H), 7.54 – 7.49 (m, 3H), 7.45 – 7.40 (m, 4H), 7.39 – 7.23 (m, 8H), 7.16 (t, *J* = 7.3 Hz, 1H), 7.10 – 6.98 (m, 5H), 6.93 (d, *J* = 7.6 Hz, 2H), 6.03 – 5.90 (m, 1H), 4.29 (d, *J* = 9.9 Hz, 1H), 3.62 (d, *J* = 13.5Hz, 1H), 3.49 (d, *J* = 13.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) (one aromatic carbon missing) δ 174.0, 157.3, 140.8, 140.2, 137.0, 136.9 (q, *J* = 6.7 Hz), 135.5, 134.2, 131.7, 130.5, 129.3, 129.0, 128.74, 128.73, 128.3, 127.5, 127.4, 127.1, 127.0, 126.7, 126.0, 122.7 (q, *J* = 270.7 Hz), 121.7 (q, *J* = 34.0 Hz), 120.4, 63.7, 53.2, 41.5. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.73 (d, *J* = 6.1 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 9.53 min, t_{minor} = 11.93 min.
HRMS (ESI) *m/z*: calcd for $C_{38}H_{30}F_3N_2O$ $[M + H]^+$ 587.2310, found: 587.2309.

(*S*)-4-Benzyl-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(4-fluorophenyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4i**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 222.0 mg, 84% yield, > 20:1 dr, 95% ee.
$[\alpha]_D^{20}$ = +62.40 (c 0.53, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.86 (m, 2H), 7.64 – 7.54 (m, 1H), 7.54 – 7.47 (m, 3H), 7.42 (d, *J* = 8.1 Hz, 2H), 7.31 (dd, *J* = 10.7, 5.1 Hz, 2H), 7.18 – 7.14 (m, 1H), 7.07 – 6.96 (m, 5H), 6.85 – 6.79 (m, 2H), 6.76 – 6.68 (m, 2H), 5.91 (dq, *J* = 15.6, 6.1 Hz, 1H), 4.23 (d, *J* = 9.9 Hz, 1H), 3.58 (d, *J* = 13.5 Hz, 1H), 3.45 (d, *J* = 13.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 162.2 (d, *J* = 247.5 Hz), 157.2, 136.9, 136.6 (q, *J* = 6.6 Hz), 134.0, 132.3, 131.5, 130.5, 129.5 (d, *J* = 8.1Hz), 129.2, 129.0, 128.8, 128.3, 127.4, 126.6, 126.0, 122.6 (q, *J* = 270.7 Hz), 121.85 (q, *J* = 34.0 Hz), 120.2, 115.4 (d, *J* = 21.5 Hz), 63.6, 52.6, 41.4. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.85 (d, *J* = 6.0 Hz, 3F), -113.49 – -113.56 (m, 1F).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 100/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 14.74 min, t_{minor} = 18.59 min.
HRMS (ESI) *m/z*: calcd for $C_{32}H_{25}F_4N_2O$ $[M + H]^+$ 529.1903, found: 529.1896.

(*S*)-4-Benzyl-4-((*S*,*E*)-1-(3-chlorophenyl)-4,4,4-trifluorobut-2-en-1-yl)-1,3-diphenyl-1*H*-pyrazol-5(4*H*)-one (**4j**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), white solid, mp 54 – 55 °C, 234.3 mg, 86% yield, > 20:1 dr, 92% ee.

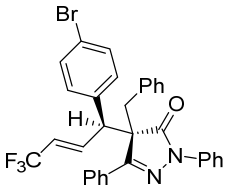
$[\alpha]_D^{20}$ = +75.27 (c 0.64, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 7.2, 2.4 Hz, 2H), 7.61 – 7.47 (m, 4H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.37 – 7.28 (m, 2H), 7.22 – 7.14 (m, 1H), 7.09 – 6.95 (m, 7H), 6.81 – 6.74 (m, 2H), 5.93 (dq, *J* = 15.6, 6.1 Hz, 1H), 4.17 (d, *J* = 10.0 Hz, 1H), 3.58 (d, *J* = 13.6 Hz, 1H), 3.46 (d, *J* = 13.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 157.2, 138.4, 136.8, 136.1 (q, *J* = 7.1 Hz), 134.3, 133.9, 131.5, 130.6, 129.8, 129.2, 129.1, 128.8, 128.3, 128.28, 128.22, 127.5, 126.7, 126.2, 125.8, 122.5 (q, *J* = 271.7 Hz), 122.2 (q, *J* = 34.0 Hz), 120.5, 63.4, 53.0, 41.4. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.93 (d, *J* = 5.9 Hz).

HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 7.08 min, t_{minor} = 7.93 min.

HRMS (ESI) *m/z*: calcd for $C_{32}H_{25}ClF_3N_2O$ $[M + H]^+$ 545.1608, found: 545.1599.

(*S*)-4-Benzyl-4-((*S*,*E*)-1-(4-bromophenyl)-4,4,4-trifluorobut-2-en-1-yl)-1,3-diphenyl-1*H*-pyrazol-5(4*H*)-one (**4k**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), white solid, mp 71 – 72 °C, 232.8 mg, 79% yield, > 20:1 dr, 94% ee.

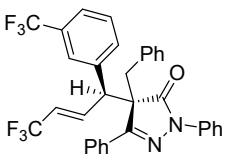
$[\alpha]_D^{20}$ = +61.62 (c 0.56, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.84 (m, 2H), 7.62 – 7.54 (m, 1H), 7.54 – 7.46 (m, 3H), 7.45 – 7.39 (m, 2H), 7.35 – 7.27 (m, 2H), 7.21 – 7.13 (m, 3H), 7.07 – 6.95 (m, 5H), 6.75 – 6.69 (m, 2H), 5.91 (dq, *J* = 15.6, 6.1 Hz, 1H), 4.20 (d, *J* = 10.0 Hz, 1H), 3.57 (d, *J* = 13.5 Hz, 1H), 3.45 (d, *J* = 13.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 157.1, 136.9, 136.3 (q, *J* = 6.5 Hz), 135.6, 133.9, 131.6, 131.4, 130.6, 129.5, 129.2, 129.1, 128.8, 128.3, 127.4, 126.6, 126.1, 122.5 (q, *J* = 270.7 Hz), 122.2, 122.1 (q, *J* = 34.3 Hz), 120.3, 63.4, 52.8, 41.5. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.93 (d, *J* = 6.1 Hz).

HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 10.38 min, t_{minor} = 12.90 min.

HRMS (ESI) *m/z*: calcd for $C_{32}H_{25}BrF_3N_2O$ $[M + H]^+$ 589.1102, found: 589.1094.

(*S*)-4-Benzyl-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(3-(trifluoromethyl)phenyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4l**)



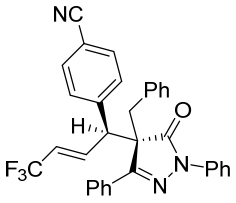
Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 245.9 mg, 85% yield, > 20:1 dr, 96% ee.

$[\alpha]_D^{20}$ = +94.57 (c 0.41, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 5.5 Hz, 2H), 7.65 – 7.57 (m, 1H), 7.55 – 7.46 (m, 3H), 7.44 – 7.33 (m, 3H), 7.32 – 7.26 (m, 2H), 7.20 – 7.11 (m, 3H), 7.09 – 6.98 (m, 5H), 6.97 – 6.91 (m, 1H), 5.98 – 5.93 (m, 1H), 4.26 (d, *J* = 9.8 Hz, 1H), 3.62 (d, *J* = 13.6 Hz, 1H), 3.50 (d, *J* = 13.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 157.2, 137.5, 136.8, 135.9 (q, *J* = 6.5 Hz), 133.8, 131.3, 130.9, 130.8 (q, *J* = 32.3 Hz), 130.7, 129.2, 129.1, 129.0, 128.7, 128.3, 127.5, 126.6, 126.1, 125.1 (q, *J* = 4.0 Hz), 124.9 (q, *J* = 4.0 Hz), 123.5 (q, *J* = 272.7 Hz), 122.5 (q, *J* = 34.2 Hz, 1H), 122.4 (q, *J* = 270.7 Hz), 120.2, 63.4, 53.1, 41.5. ^{19}F NMR (377 MHz, $CDCl_3$) δ

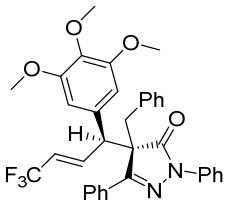
-62.92 (s, 3F), -63.94 (d, J = 5.9 Hz, 3F).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 7.74 min, t_{minor} = 10.81 min.
HRMS (ESI) *m/z*: calcd for $C_{33}H_{25}F_6N_2O$ $[M + H]^+$ 579.1871, found: 579.1862.

(*S*)-4-Benzyl-4-((*S*,*E*)-1-(4-cyanophenyl)-4,4,4-trifluorobut-2-en-1-yl)-1,3-diphenyl-1*H*-pyrazol-5(4*H*)-one (**4m**)



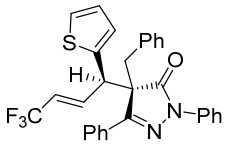
Column chromatography elution: petroleum ether/ethyl acetate = 30:1 (v/v), colorless oil, 187.3 mg, 70% yield, > 20:1 dr, 95% ee.
$[\alpha]_D^{20}$ = +72.50 (c 0.28, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 5.6 Hz, 2H), 7.66 – 7.53 (m, 4H), 7.46 – 7.42 (m, 2H), 7.40 – 7.32 (m, 4H), 7.26 – 7.19 (m, 1H), 7.11 – 6.97 (m, 7H), 6.01 (dq, J = 12.1, 6.0 Hz, 1H), 4.34 (d, J = 9.9 Hz, 1H), 3.64 (d, J = 13.5 Hz, 1H), 3.52 (d, J = 13.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) (one aromatic carbon missing) δ 173.5, 156.8, 141.9, 136.7, 135.5 (d, J = 6.6 Hz), 133.6, 132.2, 131.2, 130.8, 129.2, 128.9, 128.7, 128.3, 127.6, 126.5, 126.2, 122.9 (d, J = 34.3 Hz), 122.4 (d, J = 271.7 Hz), 120.0, 118.2, 112.1, 63.2, 53.1, 41.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.05 (d, J = 6.0 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 9/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 7.75 min, t_{minor} = 9.36 min.
HRMS (ESI) *m/z*: calcd for $C_{33}H_{25}F_3N_3O$ $[M + H]^+$ 536.1950, found: 536.1944.

(*S*)-4-Benzyl-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(3,4,5-trimethoxyphenyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4n**)



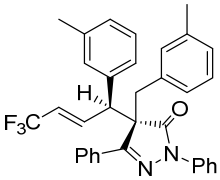
Column chromatography elution: petroleum ether/ethyl acetate = 20:1 (v/v), white solid, mp 194 – 195 °C, 270.3 mg, 90% yield, > 20:1 dr, 94% ee.
$[\alpha]_D^{20}$ = +76.95 (c 0.56, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ7.93 – 7.87 (m, 2H), 7.60 – 7.48 (m, 6H), 7.34 – 7.28 (m, 2H), 7.20 – 7.12 (m, 1H), 7.09 – 7.01 (m, 5H), 5.99 (s, 2H), 5.97 – 5.91 (m, 1H), 4.13 (d, J = 9.9 Hz, 1H), 3.69 (s, 3H), 3.61 (d, J = 13.7 Hz, 1H), 3.48 (d, J = 13.7 Hz, 1H), 3.31 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 157.3, 152.9, 137.4, 137.2, 136.5 (q, J = 6.1 Hz), 134.1, 131.9, 131.8, 130.3, 129.2, 128.9, 128.7, 128.3, 127.4, 126.7, 125.8, 122.7 (q, J = 270.7 Hz), 121.6 (q, J = 33.8 Hz), 119.7, 104.5, 63.8, 60.7, 55.5, 53.9, 41.5. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.77 (d, J = 5.8 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 9.93 min, t_{minor} = 12.22 min.
HRMS (ESI) *m/z*: calcd for $C_{35}H_{32}F_3N_2O_4$ $[M + H]^+$ 601.2314, found: 601.2306.

(*S*)-4-Benzyl-1,3-diphenyl-4-((*R*,*E*)-4,4,4-trifluoro-1-(thiophen-2-yl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4o**)



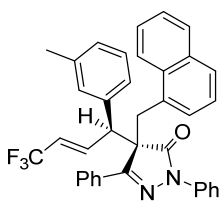
Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), white solid, mp 118 – 120 °C, 209.2 mg, 81% yield, > 20:1 dr, 85% ee.
$[\alpha]_D^{20}$ = +95.65 (c 0.12, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.59 – 7.46 (m, 6H), 7.36 – 7.30 (m, 2H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.11 – 6.97 (m, 6H), 6.73 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.59 (d, *J* = 3.1 Hz, 1H), 5.96 (dq, *J* = 15.5, 6.1 Hz, 1H), 4.58 (d, *J* = 9.9 Hz, 1H), 3.57 (d, *J* = 13.4 Hz, 1H), 3.46 (d, *J* = 13.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 157.2, 138.1, 137.1, 136.5 (q, *J* = 6.5 Hz), 133.9, 131.4, 130.5, 129.2, 129.0, 128.7, 128.2, 127.4, 126.7, 126.6, 125.9, 125.7, 124.9, 122.7 (q, *J* = 271.7 Hz), 121.6 (q, *J* = 34.1 Hz), 120.2, 63.8, 48.5, 41.6. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.91 (d, *J* = 6.1 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{minor} = 19.75 min, t_{major} = 21.71 min.
HRMS (ESI) *m/z*: calcd for $C_{30}H_{24}F_3N_2OS$ $[M + H]^+$ 517.1561, found: 517.1554.

(*S*)-4-(3-Methylbenzyl)-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(*m*-tolyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4q**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 237.0 mg, 88% yield, > 20:1 dr, 95% ee.
$[\alpha]_D^{20}$ = +69.33 (c 0.53, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.81 (m, 2H), 7.65 – 7.56 (m, 1H), 7.55 – 7.45 (m, 5H), 7.38 – 7.31 (m, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 6.97 – 6.79 (m, 6H), 6.71 – 6.67 (m, 1H), 6.65 (s, 1H), 5.93 (dq, *J* = 15.6, 6.2 Hz, 1H), 4.19 (d, *J* = 10.0 Hz, 1H), 3.61 (d, *J* = 13.6 Hz, 1H), 3.43 (d, *J* = 13.6 Hz, 1H), 2.06 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) (one aromatic carbon missing) δ 174.2, 157.7, 138.2, 137.8, 137.1, 137.0 (q, *J* = 6.1 Hz), 136.3, 134.1, 131.9, 130.3, 130.0, 128.8, 128.7, 128.6, 128.5, 128.3, 128.1, 128.0, 126.8, 126.2, 125.9, 124.9, 122.7 (q, *J* = 270.7 Hz), 121.4 (q, *J* = 34.3 Hz), 120.3, 63.6, 53.7, 41.5, 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.76 (d, *J* = 6.2 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 8.11 min, t_{minor} = 10.20 min.
HRMS (ESI) *m/z*: calcd for $C_{34}H_{30}F_3N_2O$ $[M + H]^+$ 539.2310, found: 539.2301.

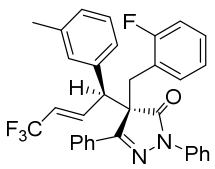
(*S*)-4-(Naphthalen-1-ylmethyl)-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(*m*-tolyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4r**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 229.8 mg, 80% yield, > 20:1 dr, 96% ee.
$[\alpha]_D^{20}$ = +87.55 (c 0.25, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.3 Hz, 1H), 7.79 (d, *J* = 7.4 Hz, 2H), 7.76 – 7.65 (m, 2H), 7.61 (d, *J* = 7.0 Hz, 1H), 7.51 – 7.40 (m, 5H), 7.34 – 7.23 (m, 4H), 7.17 – 7.09 (m, 3H), 6.98 – 6.92 (m, 2H), 6.74 – 6.66 (m, 2H), 6.09 – 5.97 (m,

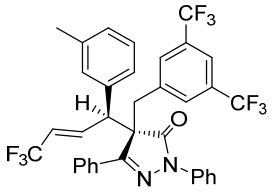
1H), 4.28 (d, J = 10.1 Hz, 1H), 4.23 (d, J = 15.0 Hz, 1H), 3.90 (d, J = 15.0 Hz, 1H), 2.02 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 158.0, 138.2, 137.1 (q, J = 6.3 Hz), 137.0, 136.0, 133.7, 131.8, 131.7, 130.8, 130.3, 128.82, 128.80, 128.62, 128.60, 128.5, 128.3, 128.1, 126.9, 126.5, 125.84, 125.80, 125.6, 125.1, 124.9, 123.7, 122.7 (q, J = 270.7 Hz), 121.7 (q, J = 34.0 Hz), 120.1, 62.6, 54.5, 36.2, 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.72 (d, J = 5.9 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 8.29 min, t_{minor} = 26.40 min.
HRMS (ESI) *m/z*: calcd for $C_{37}H_{30}F_3N_2O$ $[M + H]^+$ 575.2310, found: 575.2304.

(*S*)-4-(2-Fluorobenzyl)-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(*m*-tolyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4s**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 195.3 mg, 72% yield, > 20:1 dr, 97% ee.
$[\alpha]_D^{20}$ = +73.09 (c 0.20, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 7.4 Hz, 2H), 7.63 – 7.52 (m, 3H), 7.51 – 7.41 (m, 3H), 7.38 – 7.31 (m, 2H), 7.20 (t, J = 7.4 Hz, 1H), 7.14 – 7.01 (m, 2H), 6.95 – 6.87 (m, 2H), 6.87 – 6.77 (m, 2H), 6.67 – 6.57 (m, 2H), 5.94 (dq, J = 15.5, 6.2 Hz, 1H), 4.17 (d, J = 10.1 Hz, 1H), 3.68 (d, J = 14.2 Hz, 1H), 3.54 (d, J = 14.2 Hz, 1H), 2.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 160. 6 (d, J = 246.6 Hz), 157.8, 138.1, 137.1, 136.7 (q, J = 6.5 Hz), 136.0, 131.2, 130.7 (d, J = 3.7 Hz), 130.3, 129.1 (d, J = 8.4 Hz), 128.8, 128.7, 128.55, 128.53, 128.3, 126.8 (d, J = 1.7 Hz), 125.9, 124.9, 124.0 (d, J = 3.7 Hz), 122.6 (q, J = 271.7 Hz), 121.6 (q, J = 34.0 Hz), 121.5, 120.1, 115.4 (d, J = 22.9 Hz), 62.6, 54.0, 33.7, 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.83 (d, J = 6.2 Hz, 3F), -114.58 – -114.68 (m, 1F).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 8.85 min, t_{minor} = 10.14 min.
HRMS (ESI) *m/z*: calcd for $C_{33}H_{27}F_4N_2O$ $[M + H]^+$ 543.2060, found: 543.2051.

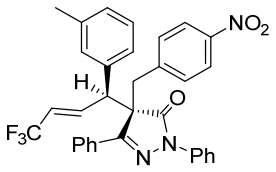
(*S*)-4-(3,5-Bis(trifluoromethyl)benzyl)-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(*m*-tolyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4t**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 287.3 mg, 87% yield, 10:1 dr, 95% ee.
$[\alpha]_D^{20}$ = +71.67 (c 0.60, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 6.1 Hz, 2H), 7.62 – 7.50 (m, 5H), 7.44 – 7.35 (m, 4H), 7.36 – 7.29 (m, 2H), 7.20 (t, J = 7.4 Hz, 1H), 6.98 – 6.90 (m, 2H), 6.76 – 6.68 (m, 2H), 5.98 (dq, J = 14.7, 6.3 Hz, 1H), 4.30 (d, J = 9.9 Hz, 1H), 3.71 (d, J = 13.5 Hz, 1H), 3.52 (d, J = 13.5 Hz, 1H), 2.02 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 156.6, 138.4, 136.9, 136.6, 136.3 (q, J = 6.3 Hz), 135.7, 131.5 (q, J = 33.3 Hz), 131.1, 130.9, 129.7, 129.1, 129.0, 128.7, 128.5, 128.3, 126.3, 126.2, 124.8, 122.6 (q, J = 270.7 Hz), 122.9 (q, J = 273.7 Hz), 121.9 (q, J = 34.0 Hz), 121.2 (q, J = 9.1 Hz), 120.1, 63.4, 53.6, 40.5, 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.20 (s, 6F), -63.91 (d, J = 6.2 Hz, 3F).

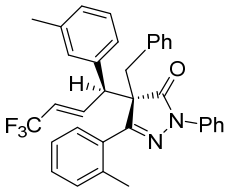
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 99/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 7.25 min, t_{minor} = 7.58 min.
HRMS (ESI) *m/z*: calcd for $C_{35}H_{26}F_9N_2O$ $[M + H]^+$ 661.1901, found: 661.1901.

(*S*)-4-(4-Nitrobenzyl)-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(*m*-tolyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4u**)



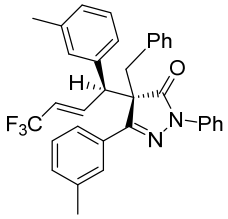
Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 196.5 mg, 69% yield, > 20:1 dr, 77% ee.
$[\alpha]_D^{20}$ = +46.93 (c 0.41, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.6 Hz, 2H), 7.89 – 7.80 (m, 2H), 7.62 – 7.50 (m, 4H), 7.47 (d, *J* = 8.3 Hz, 2H), 7.36 – 7.31 (m, 2H), 7.25 – 7.15 (m, 3H), 6.97 – 6.89 (m, 2H), 6.72 – 6.58 (m, 2H), 6.05 – 5.92 (m, 1H), 4.24 (d, *J* = 10.0 Hz, 1H), 3.69 (d, *J* = 13.5 Hz, 1H), 3.57 (d, *J* = 13.5 Hz, 1H), 2.01 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 156.8, 147.2, 142.0, 138.3, 136.7, 136.4 (q, *J* = 6.7 Hz), 135.7, 131.3, 130.8, 130.3, 129.1, 129.0, 128.8, 128.4, 128.3, 126.5, 126.2, 124.8, 123.4, 122.6 (q, *J* = 270.7 Hz), 121.9 (q, *J* = 33.9 Hz), 119.9, 63.3, 53.7, 40.7, 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.82 (d, *J* = 5.9 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 13.37 min, t_{minor} = 16.54 min.
HRMS (ESI) *m/z*: calcd for $C_{33}H_{27}F_3N_3O_3$ $[M + H]^+$ 570.2005, found: 570.1993.

(*S*)-4-Benzyl-1-phenyl-3-(o-tolyl)-4-((*S*,*E*)-4,4,4-trifluoro-1-(*m*-tolyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4v**)



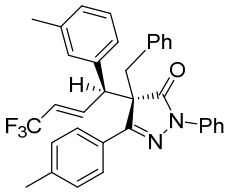
Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 239.7 mg, 89% yield, > 20:1 dr, 94% ee.
$[\alpha]_D^{20}$ = +97.13 (c 0.21, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.8 Hz, 1H), 7.59 (s, 1H), 7.58 – 7.51 (m, 1H), 7.48 – 7.39 (m, 3H), 7.36 – 7.29 (m, 3H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.11 – 6.99 (m, 5H), 6.97 – 6.88 (m, 2H), 6.67 (d, *J* = 6.7 Hz, 1H), 6.63 (s, 1H), 5.92 (dq, *J* = 15.6, 6.2 Hz, 1H), 4.16 (d, *J* = 10.0 Hz, 1H), 3.59 (d, *J* = 13.6 Hz, 1H), 3.47 (d, *J* = 13.6 Hz, 1H), 2.43 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 157.7, 138.7, 138.1, 137.04, 137.00 (q, *J* = 6.7 Hz), 136.3, 134.3, 131.7, 131.2, 129.3, 128.7, 128.67, 128.60, 128.5, 128.3, 128.2, 127.4, 127.3, 125.9, 125.0, 123.9, 123.0 (q, *J* = 208.1 Hz), 121.5 (q, *J* = 33.9 Hz), 120.4, 63.6, 53.6, 41.4, 21.6, 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.78 (d, *J* = 6.1 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 7.62 min, t_{minor} = 10.52 min.
HRMS (ESI) *m/z*: calcd for $C_{34}H_{30}F_3N_2O$ $[M + H]^+$ 539.2310, found: 539.2311.

(*S*)-4-Benzyl-1-phenyl-3-(*m*-tolyl)-4-((*S*,*E*)-4,4,4-trifluoro-1-(*m*-tolyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4w**)



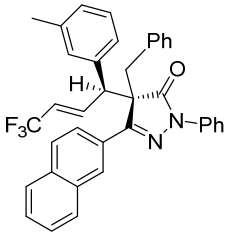
Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 237.0 mg, 88% yield, > 20:1 dr, 92% ee.
$[\alpha]_D^{20}$ = +72.00 (c 0.43, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.6 Hz, 1H), 7.64 – 7.52 (m, 2H), 7.47 – 7.38 (m, 3H), 7.36 – 7.28 (m, 3H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.11 – 6.99 (m, 5H), 6.99 – 6.88 (m, 2H), 6.74 – 6.60 (m, 2H), 6.01 – 5.86 (m, 1H), 4.17 (d, *J* = 10.0 Hz, 1H), 3.60 (d, *J* = 13.5 Hz, 1H), 3.48 (d, *J* = 13.5 Hz, 1H), 2.43 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 157.8, 138.7, 138.1, 137.1, 137.0 (q, *J* = 6.7 Hz), 136.4, 134.3, 131.8, 131.3, 129.3, 128.8, 128.7, 128.66, 128.65, 128.3, 128.2, 127.5, 127.3, 125.9, 125.0, 123.9, 122.8 (q, *J* = 270.7 Hz), 121.5 (q, *J* = 34.3 Hz), 120.4, 63.7, 53.6, 41.4, 21.6, 21.2. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.77 (d, *J* = 5.9 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 7.28 min, t_{minor} = 10.17 min.
HRMS (ESI) *m/z*: calcd for $C_{34}H_{30}F_3N_2O$ $[M + H]^+$ 539.2310, found: 539.2310.

(*S*)-4-Benzyl-1-phenyl-3-(p-tolyl)-4-((*S*,*E*)-4,4,4-trifluoro-1-(*m*-tolyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4x**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), white solid, mp 61 – 62 °C, 223.5 mg, 83% yield, > 20:1 dr, 94% ee.
$[\alpha]_D^{20}$ = +77.90 (c 0.44, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.6 Hz, 2H), 7.66 – 7.54 (m, 1H), 7.50 – 7.41 (m, 2H), 7.37 – 7.28 (m, 4H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.11 – 7.01 (m, 5H), 6.97 – 6.88 (m, 2H), 6.66 (d, *J* = 6.5 Hz, 2H), 5.93 (dq, *J* = 12.4, 6.0 Hz, 1H), 4.18 (d, *J* = 10.0 Hz, 1H), 3.60 (d, *J* = 13.6 Hz, 1H), 3.46 (d, *J* = 13.6 Hz, 1H), 2.48 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 157.6, 140.7, 138.1, 137.2, 137.1 (q, *J* = 6.7 Hz), 136.3, 134.4, 129.6, 129.3, 129.1, 128.7, 128.6, 128.5, 128.3, 128.2, 127.3, 126.7, 125.8, 125.0, 122.8 (q, *J* = 271.7 Hz), 121.4 (q, *J* = 33.3 Hz), 120.3, 63.6, 53.7, 41.3, 21.6, 21.2. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.75 (d, *J* = 6.0 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 8.74 min, t_{minor} = 10.30 min.
HRMS (ESI) *m/z*: calcd for $C_{34}H_{30}F_3N_2O$ $[M + H]^+$ 539.2310, found: 539.2298.

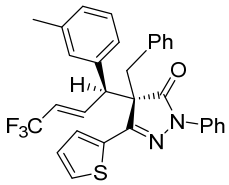
(*S*)-4-Benzyl-3-(naphthalen-2-yl)-1-phenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(*m*-tolyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4y**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), white solid, mp 88 – 89 °C, 232.7 mg, 81% yield, > 20:1 dr, 96% ee.
$[\alpha]_D^{20}$ = +72.74 (c 0.58, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.04 – 7.97 (m, 1H), 7.96 – 7.87 (m, 3H), 7.66 – 7.54 (m, 3H), 7.49 (d, *J* = 7.9 Hz, 2H), 7.38 – 7.33 (m,

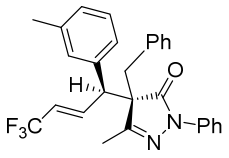
2H), 7.24 – 7.17 (m, 1H), 7.07 – 6.96 (m, 5H), 6.93 – 6.84 (m, 2H), 6.71 – 6.60 (m, 2H), 5.98 (dq, *J* = 12.4, 6.0 Hz, 1H), 4.30 (d, *J* = 9.9 Hz, 1H), 3.69 (d, *J* = 13.5 Hz, 1H), 3.61 (d, *J* = 13.5 Hz, 1H), 1.96 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) (two aromatic carbons missing) δ 174.1, 157.4, 138.2, 137.1, 137.0 (q, *J* = 6.5 Hz), 136.3, 134.3, 134.1, 132.9, 129.5, 129.3, 128.8, 128.7, 128.5, 128.4, 128.3, 128.0, 127.6, 127.3, 127.0, 126.6, 126.0, 125.1, 123.9, 122.8 (q, *J* = 270.7 Hz), 121.6 (q, *J* = 33.9 Hz), 120.4, 63.8, 53.8, 41.5, 21.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.74 (d, *J* = 5.9 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 10.16 min, t_{minor} = 16.43 min.
HRMS (ESI) *m/z*: calcd for $C_{37}H_{30}F_3N_2O$ $[M + H]^+$ 575.2310, found: 575.2299.

(*S*)-4-Benzyl-1-phenyl-3-(thiophen-2-yl)-4-((*S*,*E*)-4,4,4-trifluoro-1-(*m*-tolyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4z**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), white solid, mp 48 – 49 °C, 222.9 mg, 84% yield, 10:1 dr, 97% ee.
$[\alpha]_D^{20}$ = +59.42 (c 0.31, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 3.4 Hz, 1H), 7.62 – 7.53 (m, 1H), 7.49 (d, *J* = 5.1 Hz, 1H), 7.42 – 7.35 (m, 2H), 7.33 – 7.27 (m, 2H), 7.25 – 7.21 (m, 1H), 7.16 (t, *J* = 7.4 Hz, 1H), 7.12 – 7.00 (m, 5H), 7.00 – 6.90 (m, 2H), 6.74 (d, *J* = 6.0 Hz, 2H), 5.93 (dq, *J* = 12.3, 6.1 Hz, 1H), 4.14 (d, *J* = 9.9 Hz, 1H), 3.58 (d, *J* = 13.5 Hz, 1H), 3.34 (d, *J* = 13.5 Hz, 1H), 2.06 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) (one aromatic carbon missing) δ 173.4, 154.0, 138.3, 136.9, 136.8 (q, *J* = 6.5 Hz), 136.2, 135.4, 134.1, 129.4, 128.8, 128.6, 128.43, 128.41, 128.3, 127.6, 127.3, 127.2, 125.9, 124.9, 122.6 (q, *J* = 271.7 Hz), 121.6 (q, *J* = 34.0 Hz), 120.4, 63.7, 54.1, 41.1, 21.2. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.79 (d, *J* = 6.1 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 14.32 min, t_{minor} = 16.49 min.
HRMS (ESI) *m/z*: calcd for $C_{31}H_{26}F_3N_2OS$ $[M + H]^+$ 531.1718, found: 531.1711.

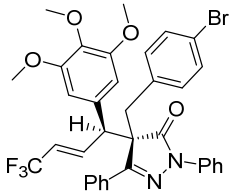
(*S*)-4-Benzyl-3-methyl-1-phenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(*m*-tolyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4aa**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 208.1 mg, 90% yield, 3:1 dr, 92% ee.
$[\alpha]_D^{20}$ = +32.47 (c 0.65, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ7.43 – 7.32 (m, 3H), 7.31 – 7.23 (m, 2H), 7.20 – 7.04 (m, 7H), 7.02 – 6.90 (m, 3H), 5.79 (dq, *J* = 12.3, 6.0 Hz, 1H), 3.65 (d, *J* = 9.9 Hz, 1H), 3.44 (d, *J* = 13.5 Hz, 1H), 2.81 (d, *J* = 13.5 Hz, 1H), 2.14 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 159.9, 138.8, 137.1, 136.9 (q, *J* = 6.6 Hz), 136.6, 134.3, 129.1, 129.0, 128.9, 128.7, 128.5, 128.1, 127.5, 125.6, 124.8, 122.6 (q, *J* = 270.7 Hz), 121.3 (q, *J* = 33.3 Hz), 120.0, 63.4, 53.6, 40.6, 21.3, 14.9. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.85 (d, *J* = 6.0 Hz).

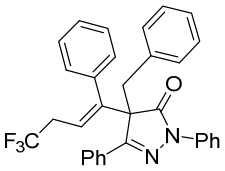
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 50/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 12.39 min, t_{minor} = 16.49 min.
HRMS (ESI) *m/z*: calcd for $C_{28}H_{26}F_3N_2O$ $[M + H]^+$ 463.1997, found: 463.1986.

(*S*)-4-(4-Bromobenzyl)-1,3-diphenyl-4-((*S*,*E*)-4,4,4-trifluoro-1-(3,4,5-trimethoxyphenyl)but-2-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**4ab**)



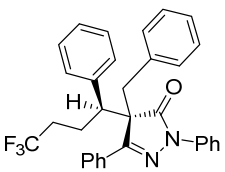
Column chromatography elution: petroleum ether/ethyl acetate = 20:1 (v/v), white solid, mp 194 – 195 °C, 302.4 mg, 89% yield, > 20:1 dr, 98% ee.
$[\alpha]_D^{20}$ = +64.80 (c 0.25, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 1.8 Hz, 2H), 7.61 – 7.43 (m, 6H), 7.38 – 7.29 (m, 2H), 7.22 – 7.14 (m, 3H), 6.89 (d, *J* = 7.6 Hz, 2H), 5.98 (s, 2H), 5.97 – 5.90 (m, 1H), 4.12 (d, *J* = 9.8 Hz, 1H), 3.69 (s, 3H), 3.55 (d, *J* = 13.5 Hz, 1H), 3.43 (q, *J* = 13.5 Hz, 1H), 3.30 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 157.0, 152.9, 137.5, 137.0, 136.3 (q, *J* = 6.4 Hz), 133.1, 131.7, 131.5, 131.4, 130.9, 130.5, 129.0, 128.8, 126.6, 126.0, 122.6 (q, *J* = 270.7 Hz), 121. 8 (q, *J* = 34.0 Hz), 121.5, 119.6, 104.5, 63.6, 60.7, 55.5, 53.9, 40.7. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.79 (d, *J* = 5.9 Hz).
HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 19.54 min, t_{minor} = 26.65 min.
HRMS (ESI) *m/z*: calcd for $C_{35}H_{31}BrF_3N_2O_4$ $[M + H]^+$ 679.1419, found: 679.1416.

4-Benzyl-1,3-diphenyl-4-(4,4,4-trifluoro-1-phenylbut-1-en-1-yl)-1*H*-pyrazol-5(4*H*)-one (**5a**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.48 – 7.40 (m, 3H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.22 (t, *J* = 7.9 Hz, 2H), 7.16 – 7.05 (m, 4H), 7.02 – 6.99 (m, 1H), 6.98 – 6.91 (m, 4H), 6.79 (d, *J* = 7.8 Hz, 2H), 6.18 (t, *J* = 15.6 Hz, 1H), 3.63 (d, *J* = 12.6 Hz, 1H), 3.54 (d, *J* = 12.6 Hz, 1H), 2.85 – 2.62 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 156.9, 144.1, 137.1, 135.5, 133.7, 131.8, 130.5, 129.7, 128.9, 128.8, 128.6, 128.5 (q, *J* = 259.7 Hz), 128.4, 128.3, 128.0, 127.3, 126.4, 125.9, 120.4, 119.7 (q, *J* = 3.5 Hz), 66.0, 39.2, 34.4 (q, *J* = 29.7 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ -65.23 (td, *J* = 10.6, 0.9 Hz).
HRMS (ESI) *m/z*: calcd for $C_{32}H_{26}F_3N_2O$ $[M + H]^+$ 511.1997, found: 511.1987.

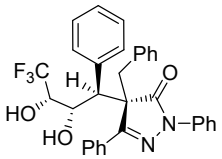
(*S*)-4-Benzyl-1,3-diphenyl-4-((*S*)-4,4,4-trifluoro-1-phenylbutyl)-1*H*-pyrazol-5(4*H*)-one (**6a**)



Column chromatography elution: petroleum ether/ethyl acetate = 50:1 (v/v), colorless oil, 222.7 mg, 87% yield, > 20:1 dr, 95% ee.
$[\alpha]_D^{20}$ = +19.00 (c 0.30, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.0 Hz, 2H), 7.53 – 7.39 (m, 5H), 7.35 – 7.28 (m, 2H), 7.20 – 7.13 (m, 1H), 7.12 – 6.94 (m, 8H), 6.80 (d, *J* =

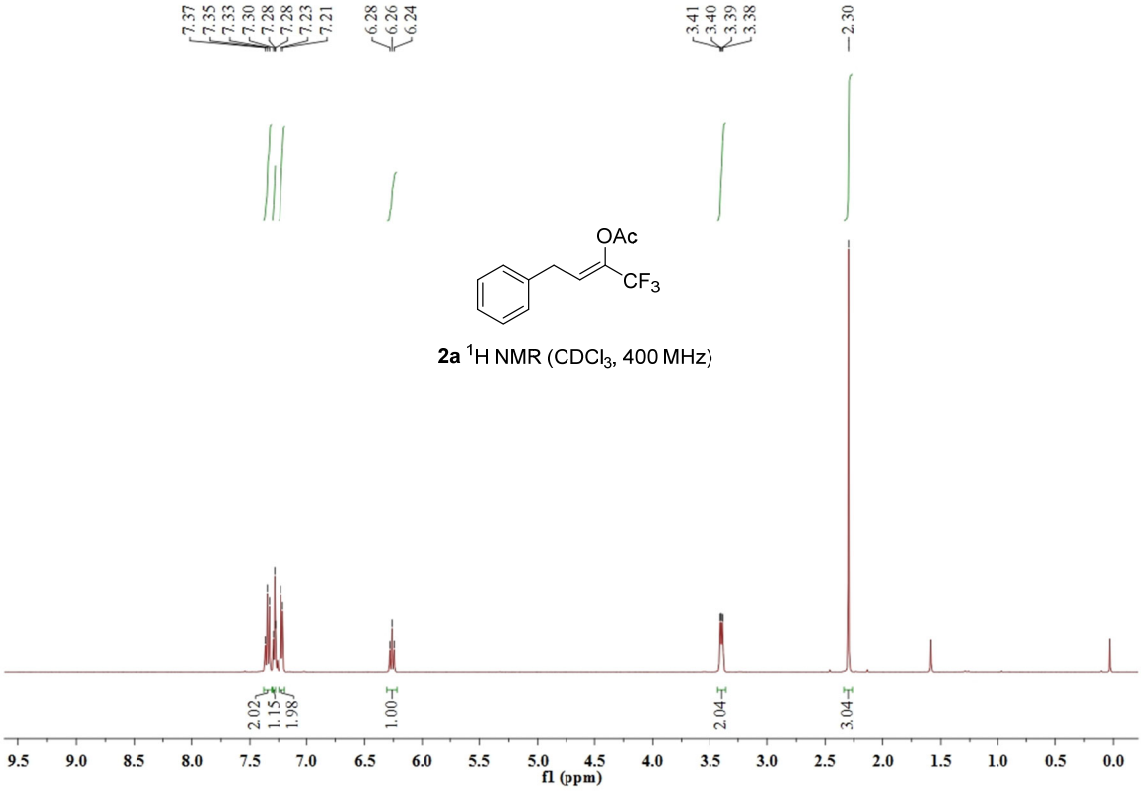
7.4 Hz, 2H), 3.84 (d, *J* = 13.3 Hz, 1H), 3.56 (d, *J* = 10.1 Hz, 1H), 3.50 (d, *J* = 13.3 Hz, 1H), 2.89 – 2.77 (m, 1H), 2.55 – 2.43 (m, 1H),1.94 – 1.75 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) (one aromatic carbon missing) δ 174.5, 158.3, 137.2, 136.8, 134.5, 131.9, 130.1, 129.2, 128.7, 128.6, 128.3 (q, *J* = 258.6 Hz), 128.28, 128.1, 127.8, 127.2, 126.8, 125.8, 120.4, 63.6, 50.2, 40.6, 32.1 (q, *J* = 28.7 Hz), 20.1 (q, *J* = 3.0 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ -65.75 (t, *J* = 10.8 Hz).
HPLC analysis: Daicel CHIRALPAK OD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{minor} = 6.11 min, t_{major} = 6.56 min.
HRMS (ESI) *m/z*: calcd for $C_{32}H_{28}F_3N_2O$ $[M + H]^+$ 513.2154, found: 513.2145.

(S)-4-Benzyl-1,3-diphenyl-4-((1*S*,2*S*,3*S*)-4,4,4-trifluoro-2,3-dihydroxy-1-phenylbutyl)-1*H*-pyrazol -5(4*H*)-one (**7a**)

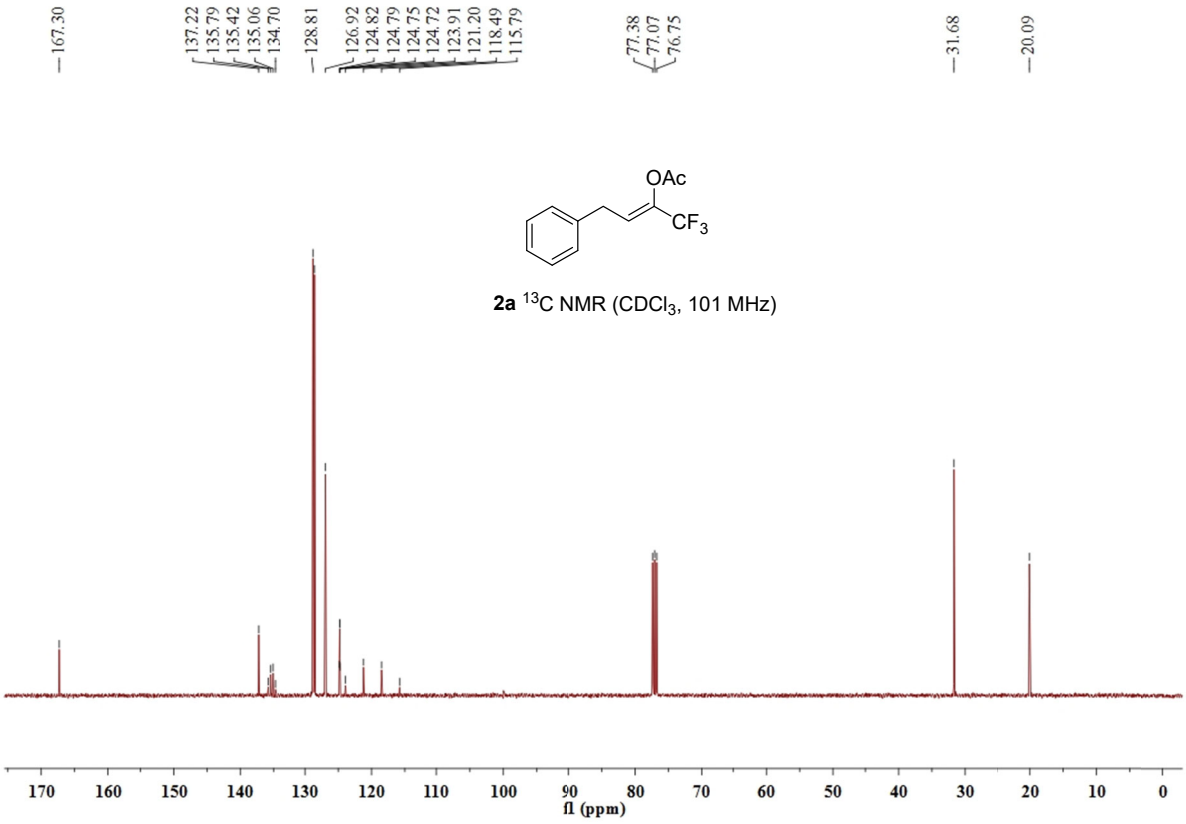


Column chromatography elution: petroleum ether/ethyl acetate = 10:1 (v/v), white solid, mp 234 – 235 °C, 106.7 mg, 49% yield, > 20:1 dr, 95% ee.
$[\alpha]_D^{20}$ = +31.11 (c 0.27, CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.71 (m, 2H), 7.56 – 7.49 (m, 2H), 7.43 – 7.33 (m, 5H), 7.26 – 7.21 (m, 1H), 7.09 – 7.00 (m, 5H), 7.00 – 6.92 (m, 3H), 6.80 (d, *J* = 7.1 Hz, 2H), 5.30 (d, *J* = 5.0 Hz,1H), 4.83 (dd, *J* = 10.3, 5.0 Hz, 1H), 4.33 (d, *J* = 13.7 Hz, 1H), 3.92 (d, *J* = 10.3 Hz, 1H), 3.67 (d, *J* = 13.7 Hz, 1H), 3.60 – 3.51 (m, 1H), 3.40 (d, *J* = 11.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) (two aromatic carbons missing) δ 176.1, 159.9, 136.9, 136.7, 134.2, 131.3, 130.3, 129.5, 128.9, 128.6, 128.5, 128.1, 127.4, 126.8, 126.5, 124.5 (q, *J* = 283.7 Hz), 120.7, 70.7, 69.6 (q, *J* = 30.4 Hz), 64.5, 53.1, 43.5. ^{19}F NMR (377 MHz, $CDCl_3$) δ -77.05 (d, *J* = 4.5 Hz).
HPLC analysis: Daicel CHIRALPAK OD-H, *n*-hexane/*i*-PrOH = 9/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{minor} = 7.51 min, t_{major} = 15.90 min.
HRMS (ESI) *m/z*: calcd for $C_{32}H_{28}F_3N_2O_3$ $[M + H]^+$ 545.2052, found: 545.2052.

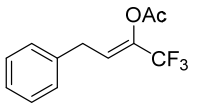
10. Copies of ^{1}H, ^{13}C and ^{19}F NMR spectrum



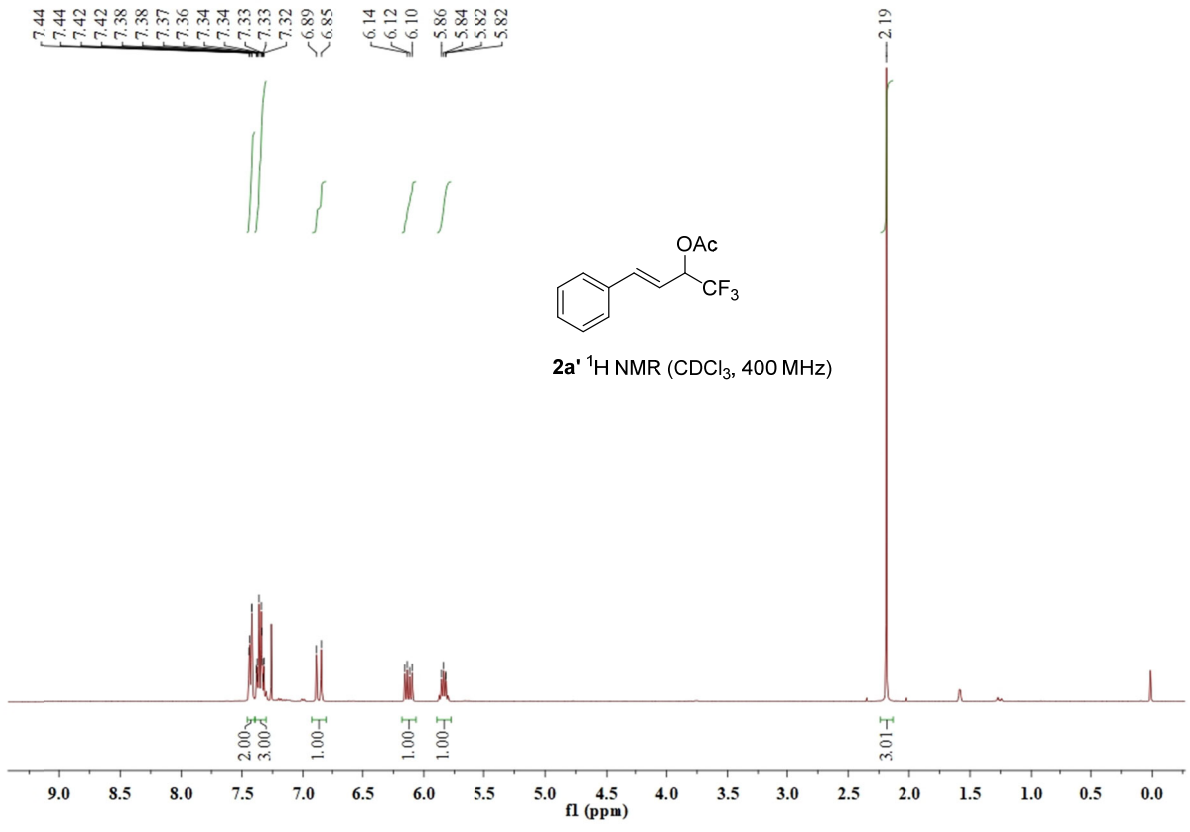
2a ^{1}H NMR ($CDCl_3$, 400 MHz)



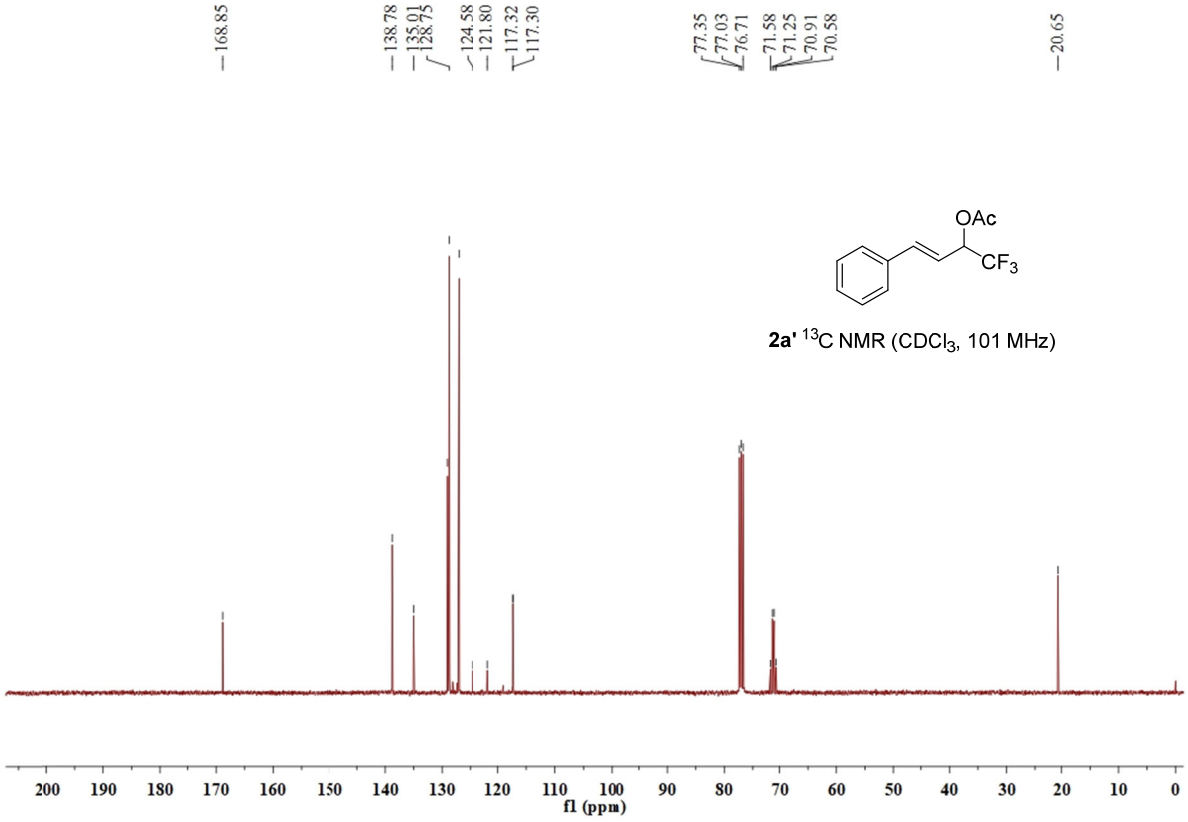
2a ^{13}C NMR ($CDCl_3$, 101 MHz)



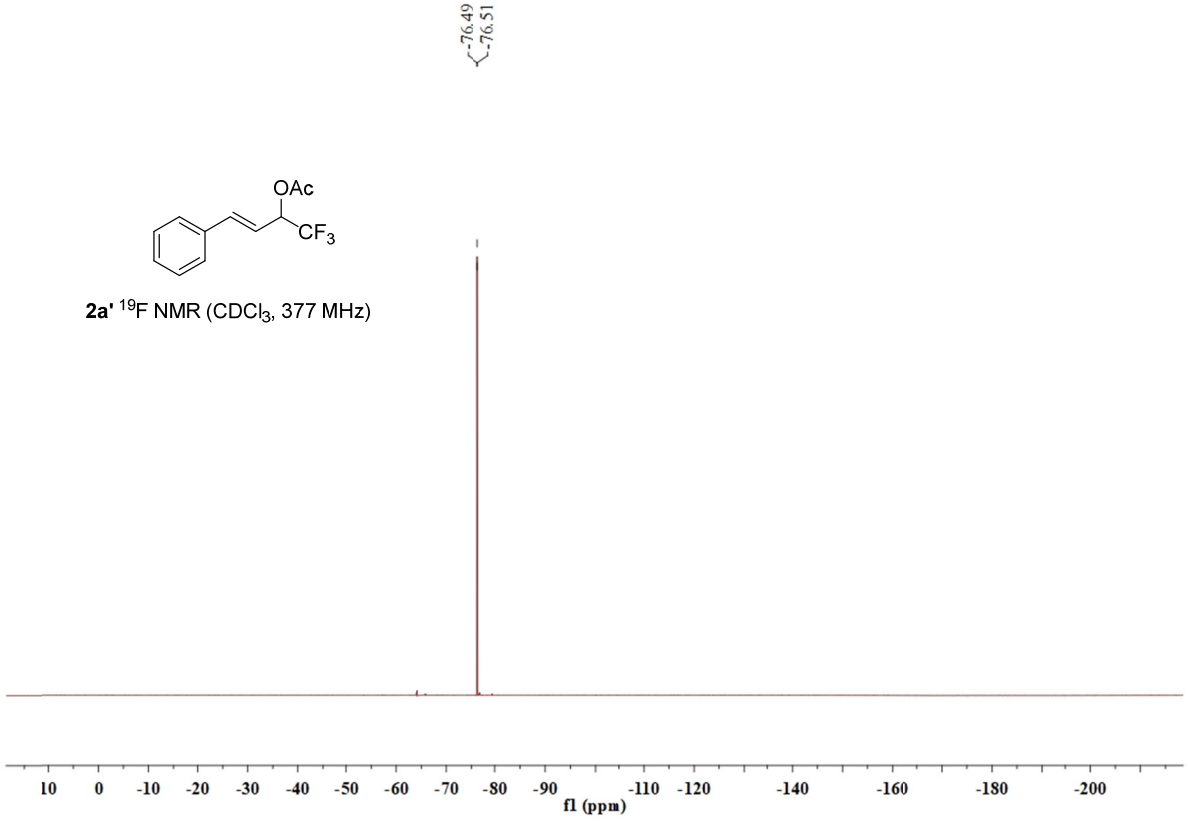
2a ^{19}F NMR ($CDCl_3$, 470 MHz)



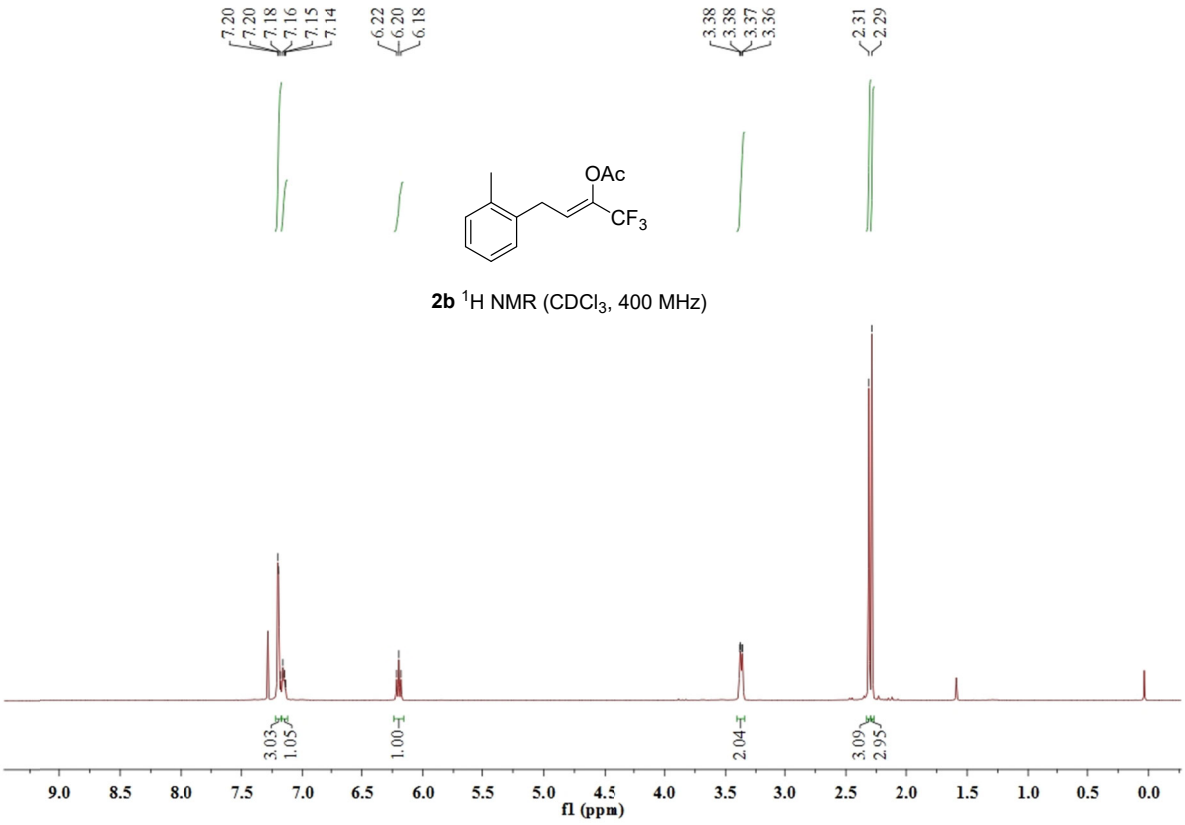
2a' ^{1}H NMR ($CDCl_3$, 400 MHz)



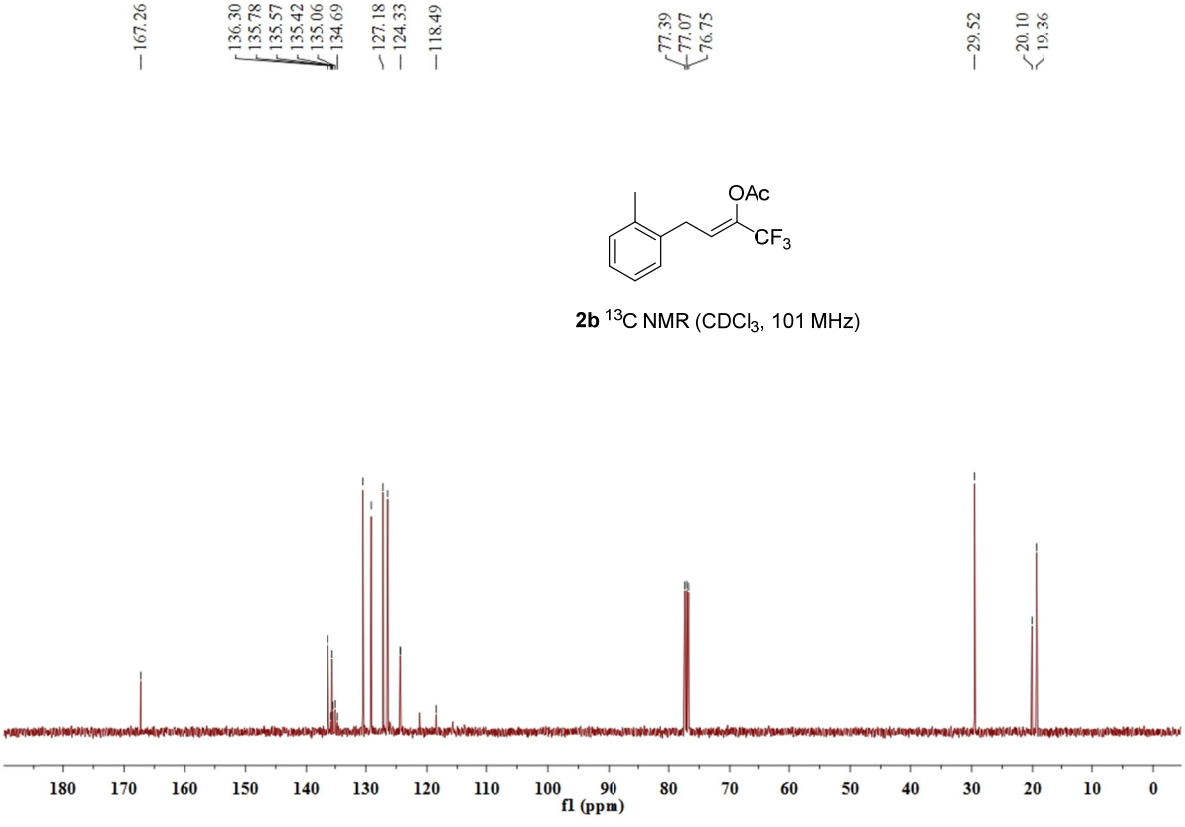
2a' ^{13}C NMR ($CDCl_3$, 101 MHz)



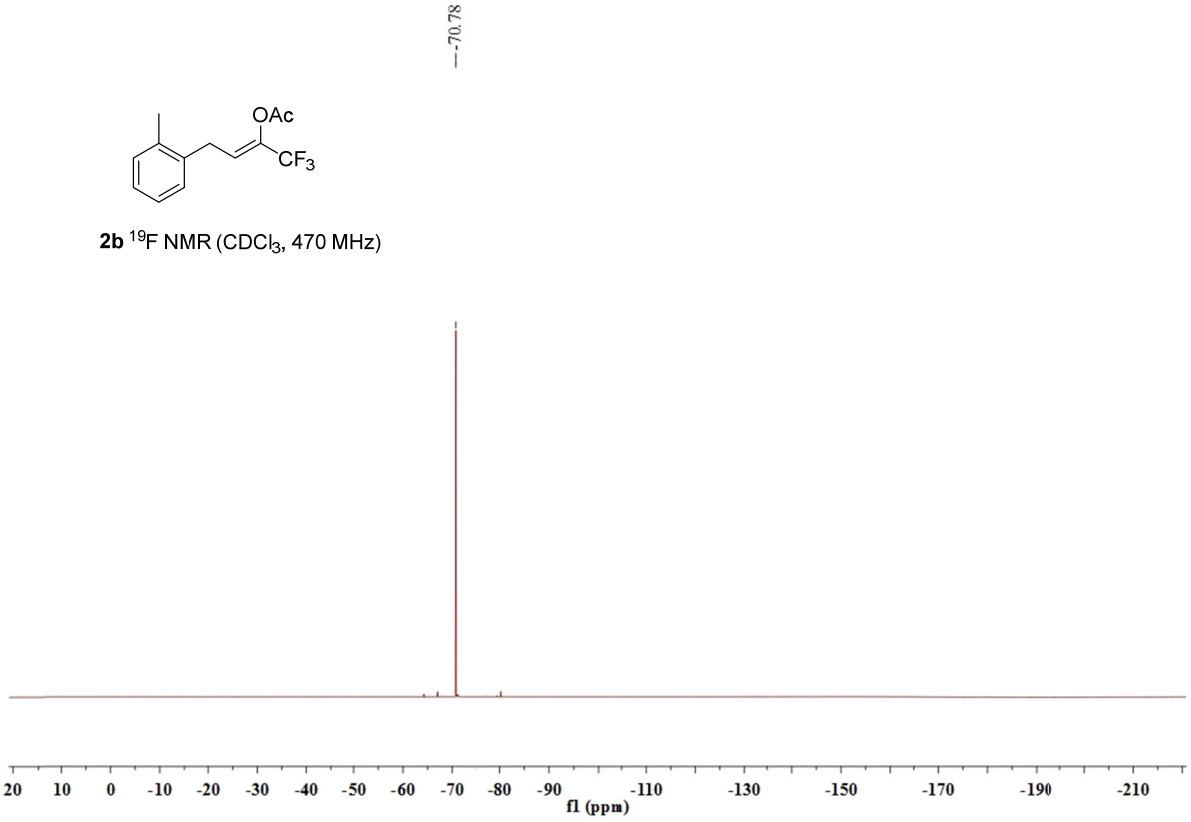
2a' ^{19}F NMR ($CDCl_3$, 377 MHz)



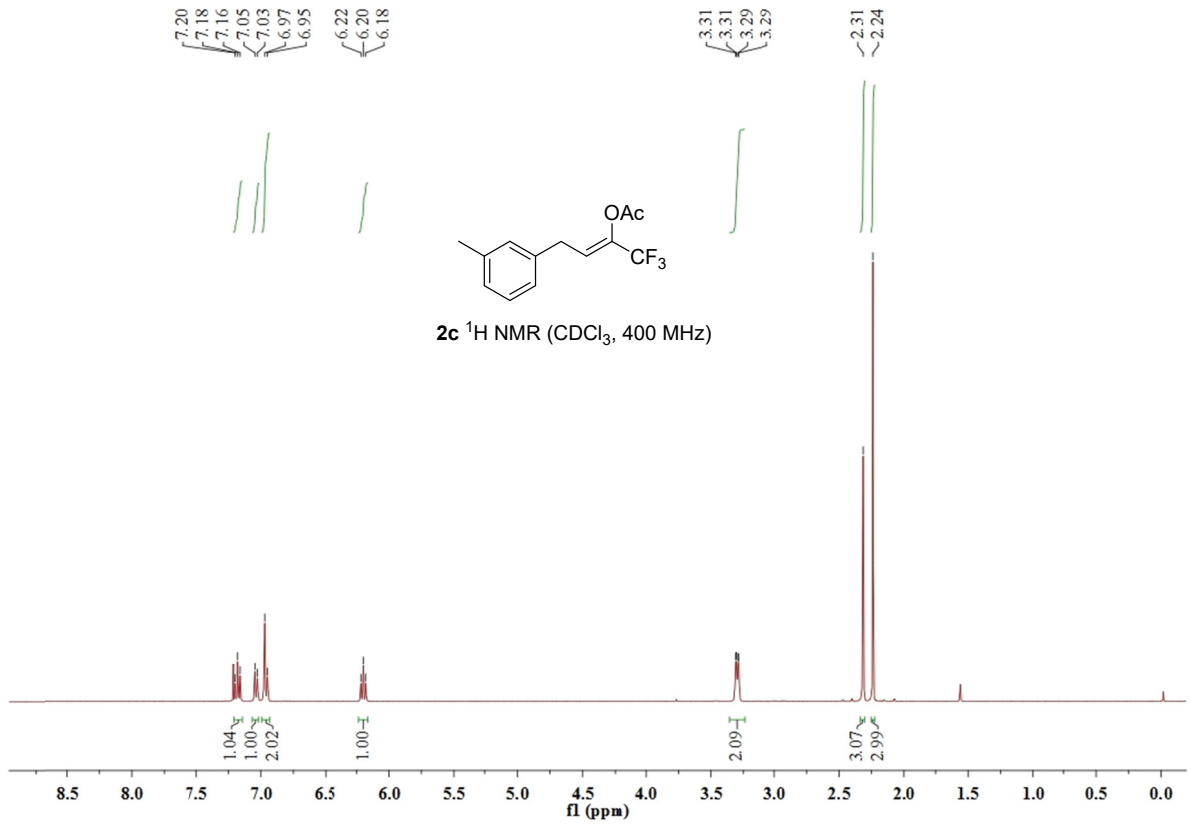
2b ^{1}H NMR ($CDCl_3$, 400 MHz)



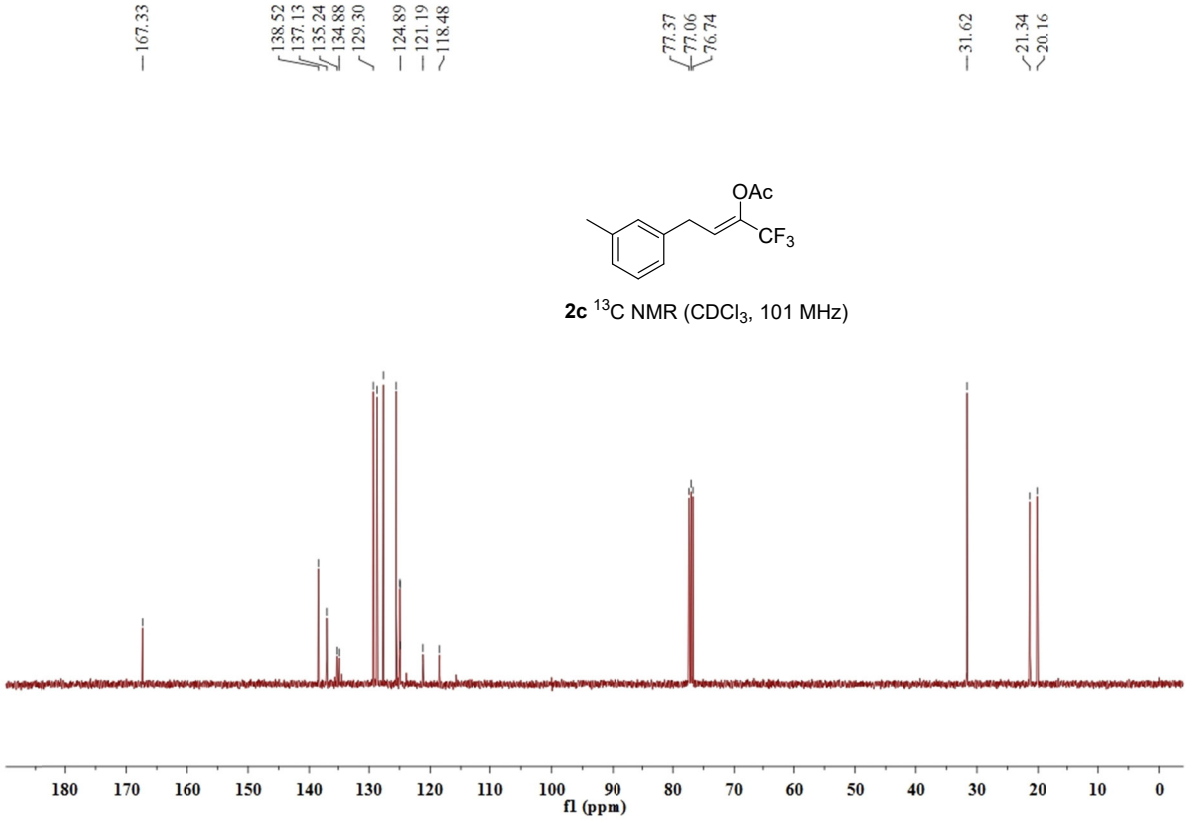
2b ^{13}C NMR ($CDCl_3$, 101 MHz)



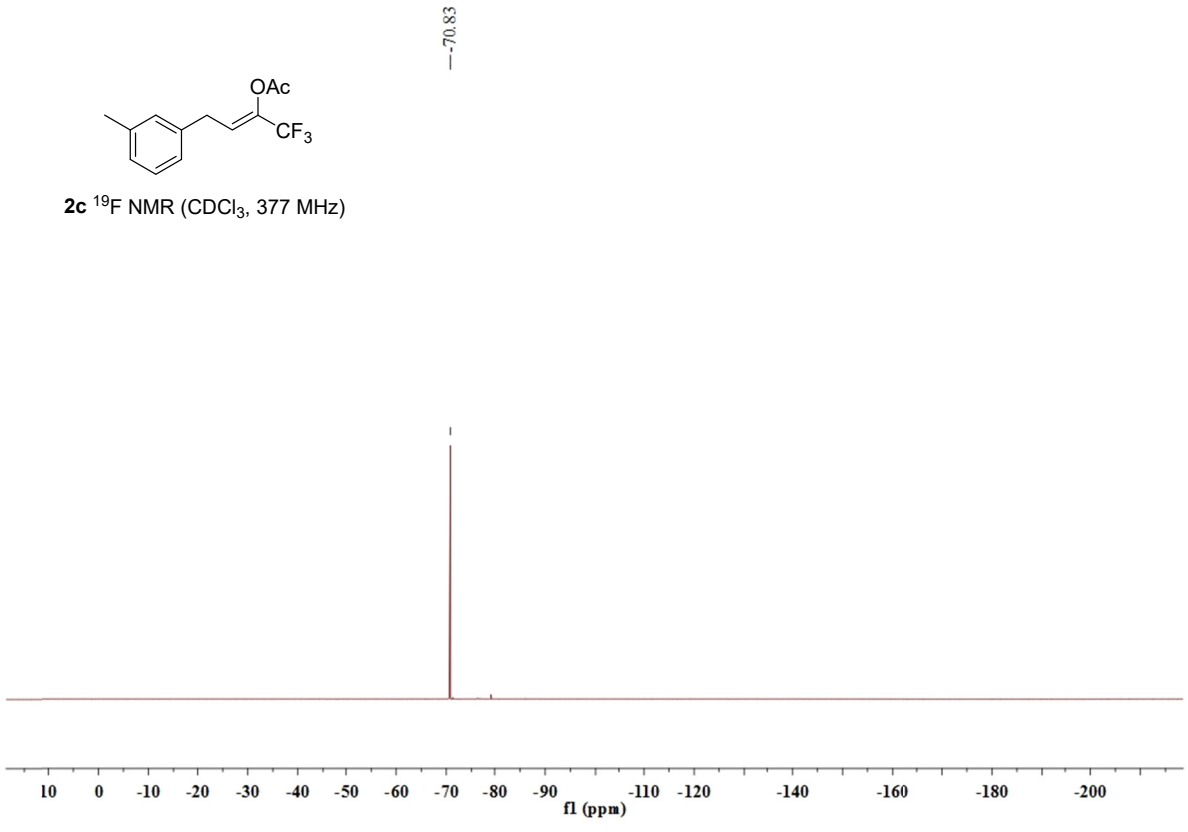
2b ^{19}F NMR ($CDCl_3$, 470 MHz)



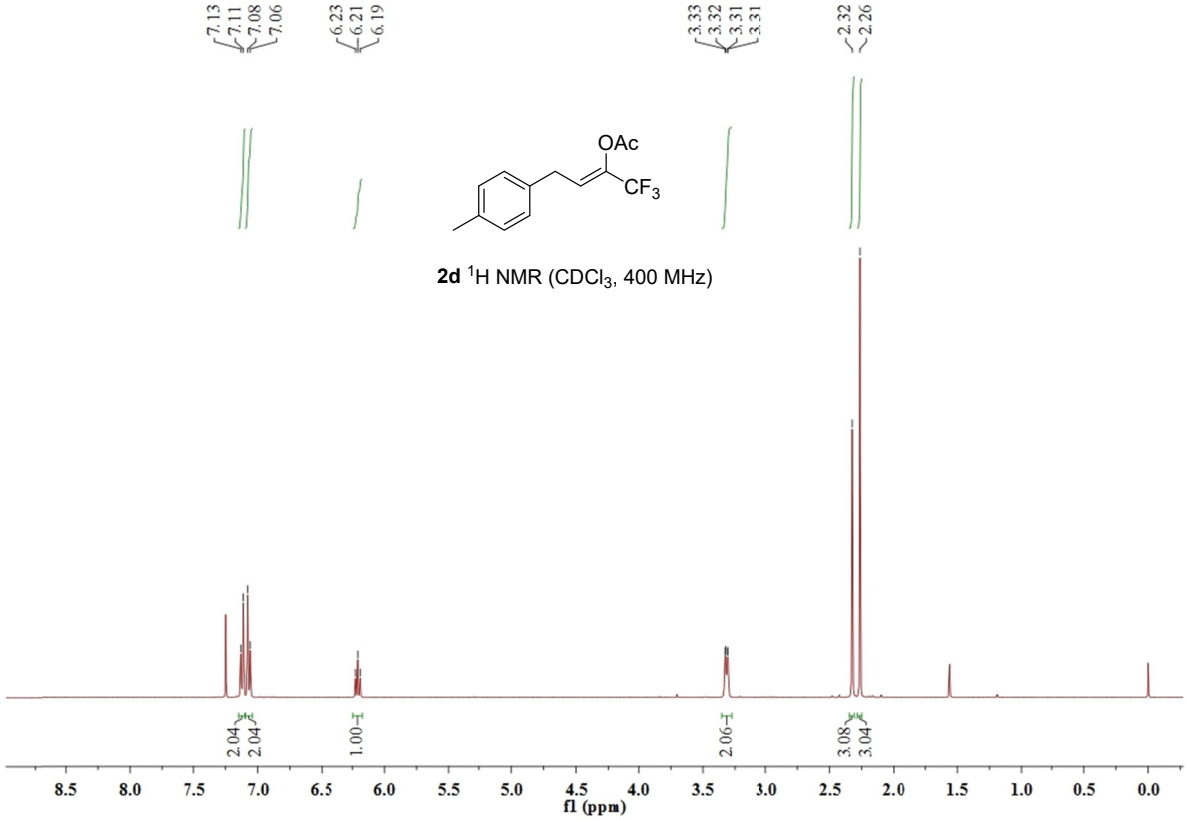
2c ^{1}H NMR ($CDCl_3$, 400 MHz)



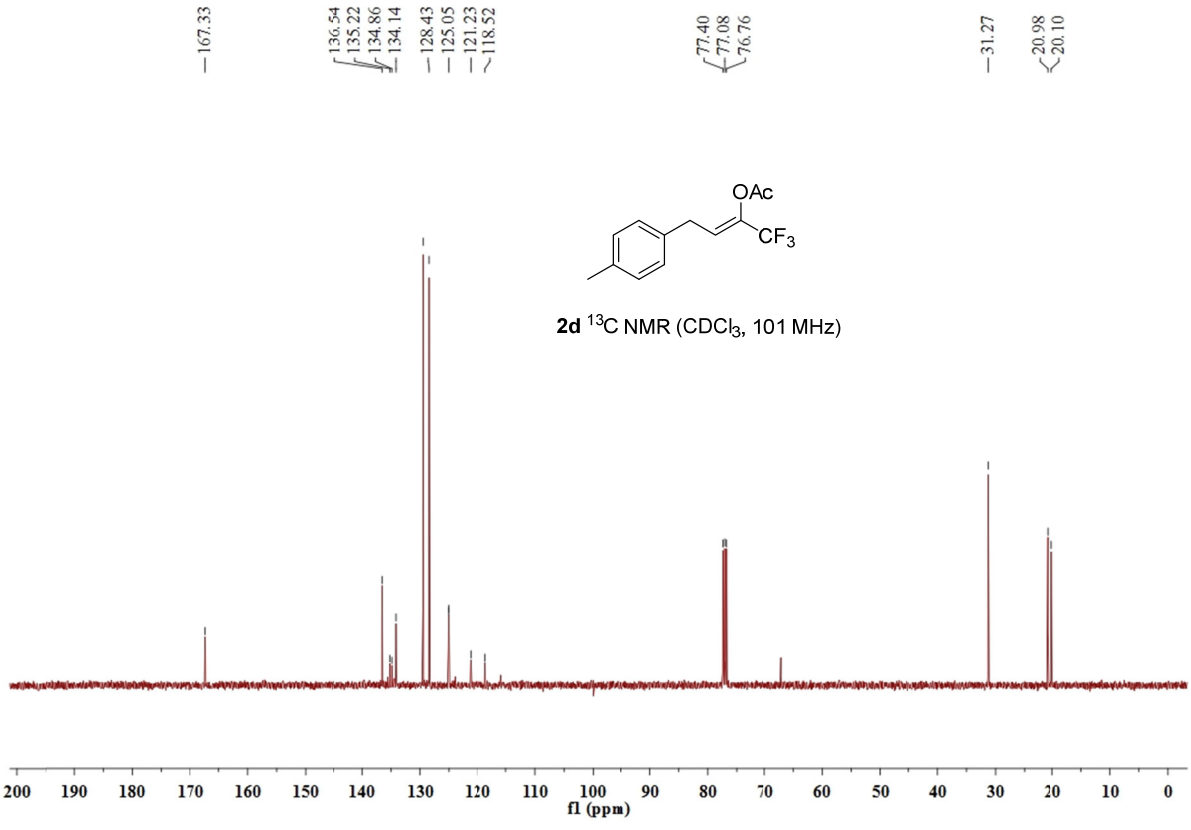
2c ^{13}C NMR ($CDCl_3$, 101 MHz)



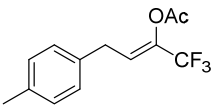
2c ^{19}F NMR ($CDCl_3$, 377 MHz)



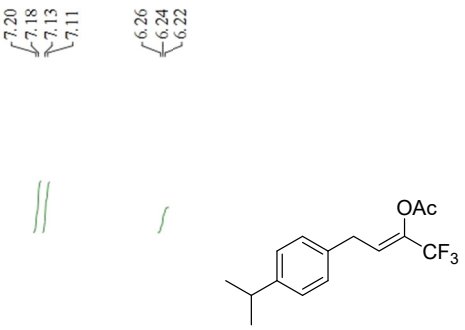
2d ^{1}H NMR ($CDCl_3$, 400 MHz)



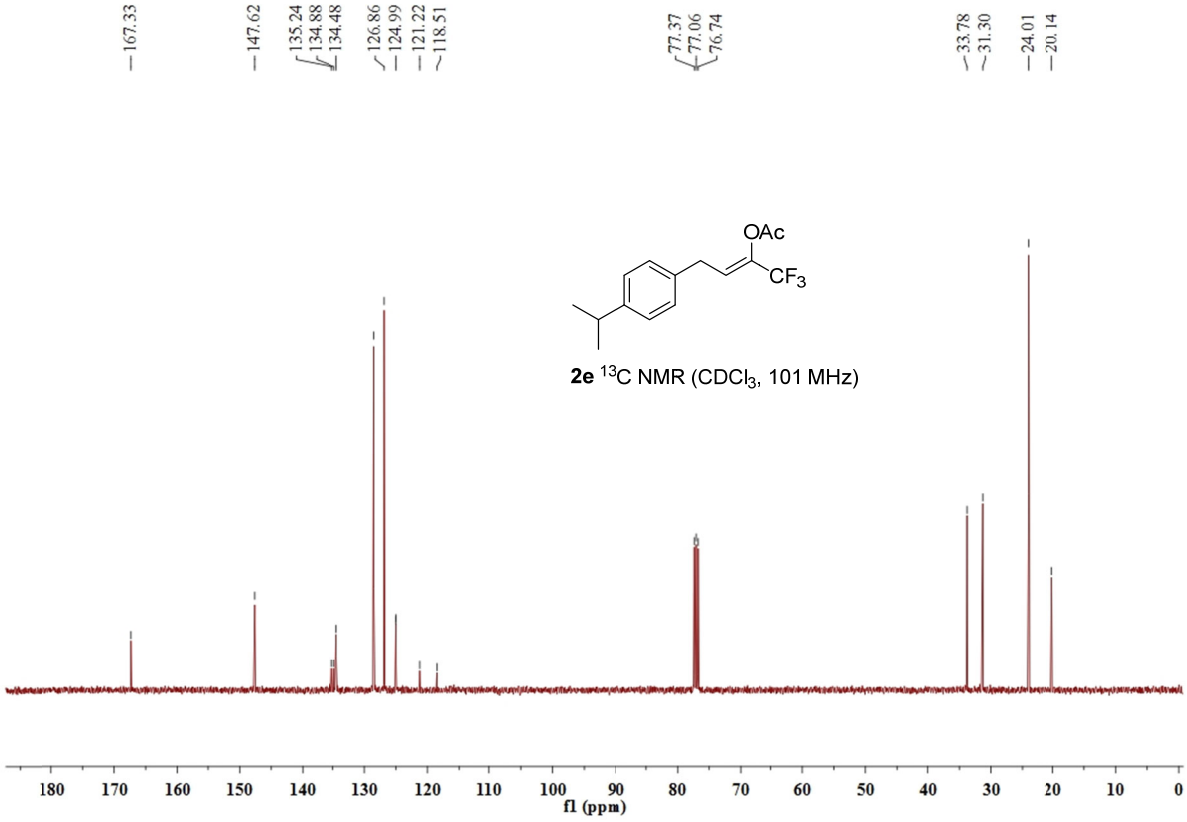
2d ^{13}C NMR ($CDCl_3$, 101 MHz)



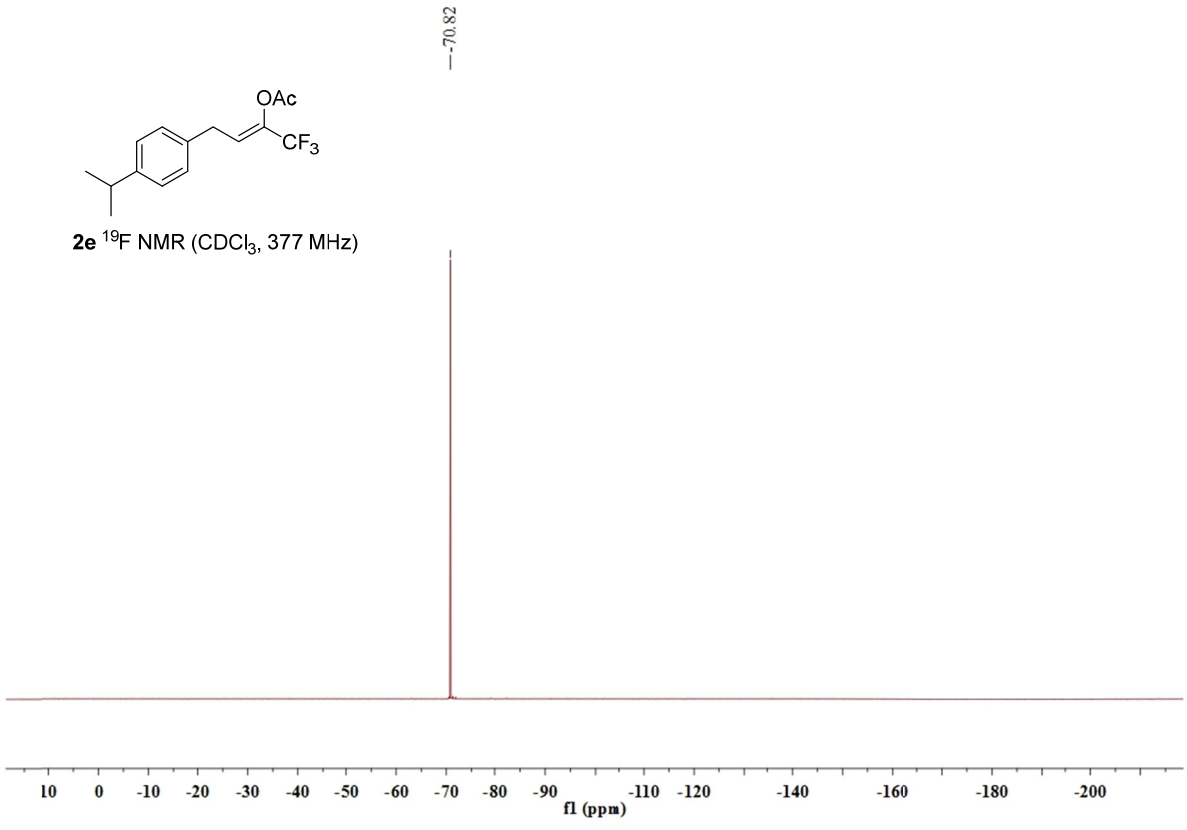
2d ^{19}F NMR ($CDCl_3$, 377 MHz)



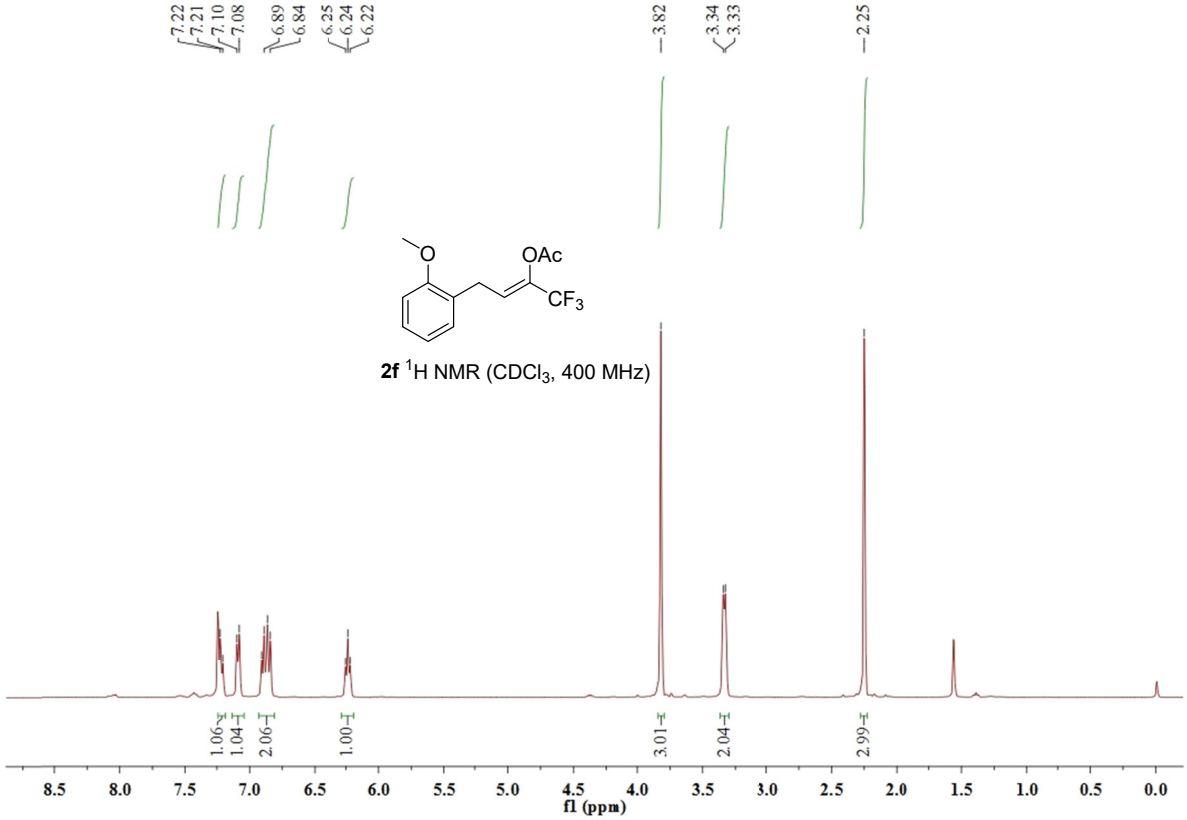
2e ^{1}H NMR ($CDCl_3$, 400 MHz)



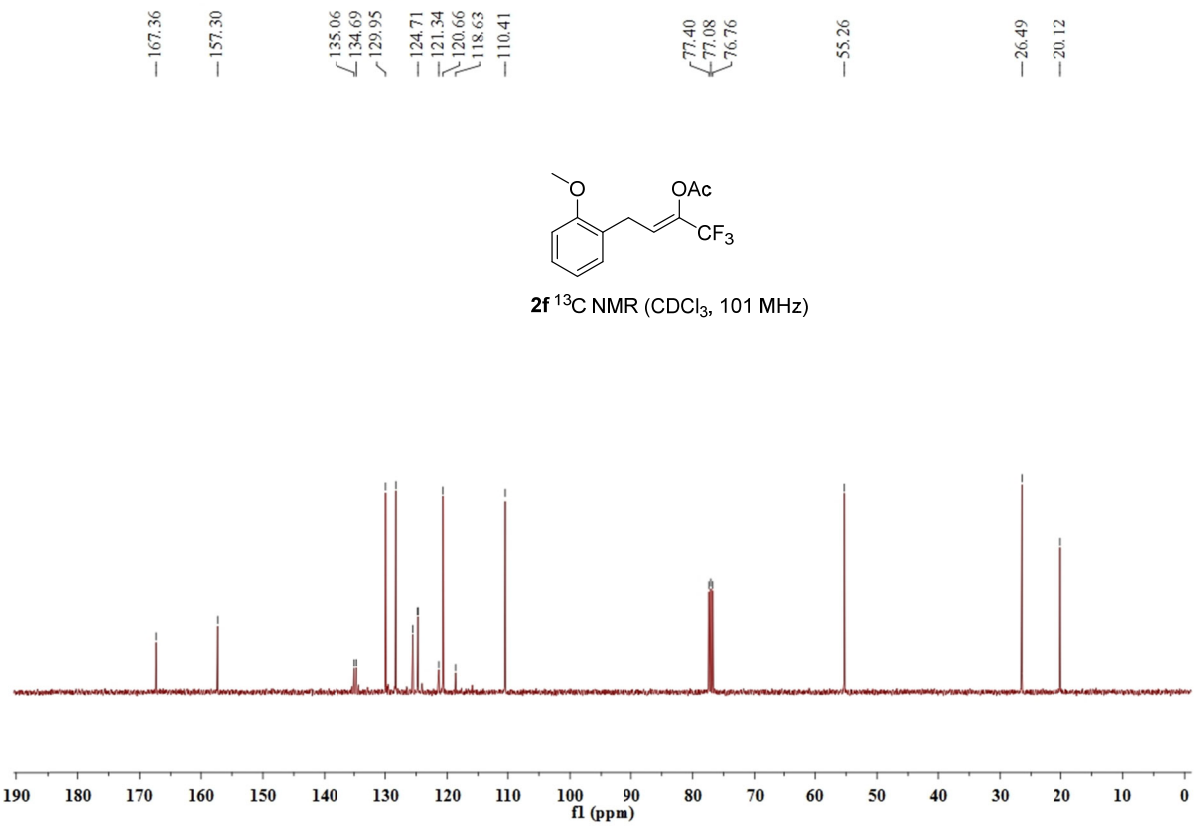
2e ^{13}C NMR ($CDCl_3$, 101 MHz)



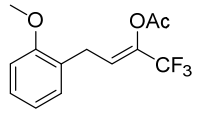
2e ^{19}F NMR ($CDCl_3$, 377 MHz)



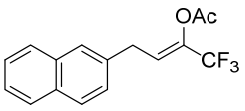
2f ^{1}H NMR ($CDCl_3$, 400 MHz)



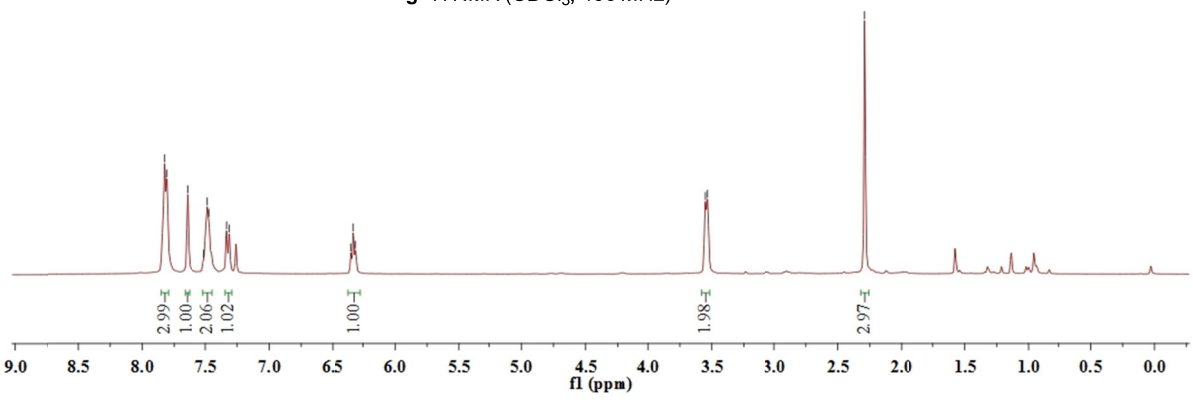
2f ^{13}C NMR ($CDCl_3$, 101 MHz)

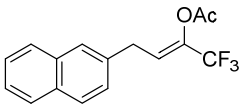


2f ^{19}F NMR ($CDCl_3$, 377 MHz)

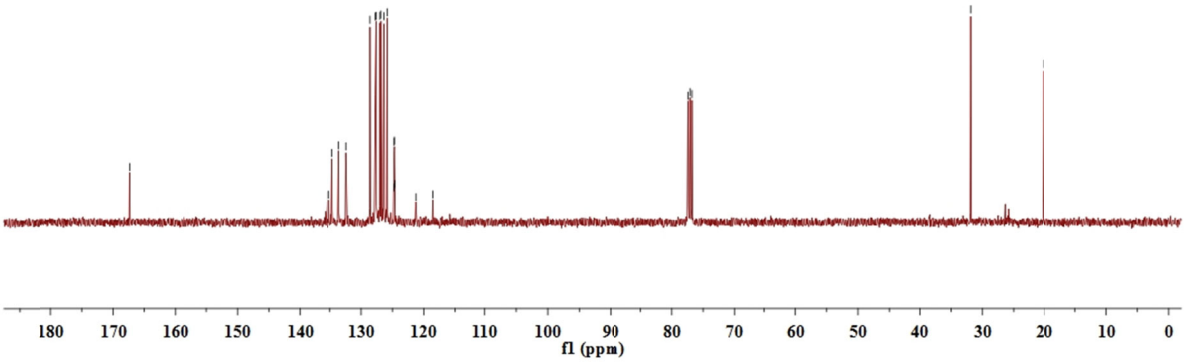


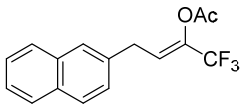
2g ^{1}H NMR ($CDCl_3$, 400 MHz)



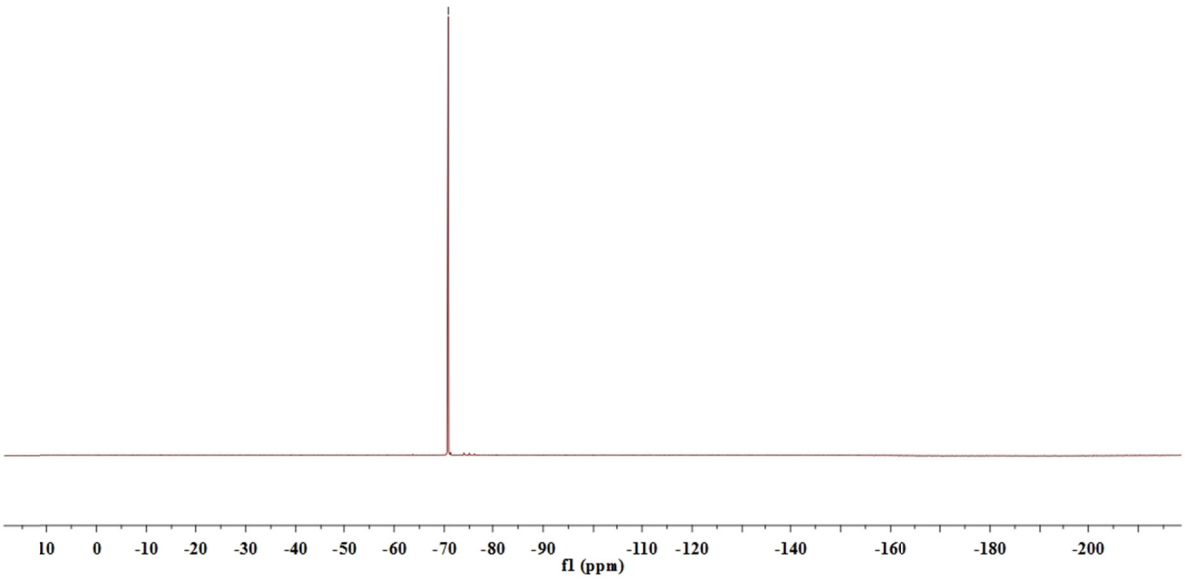


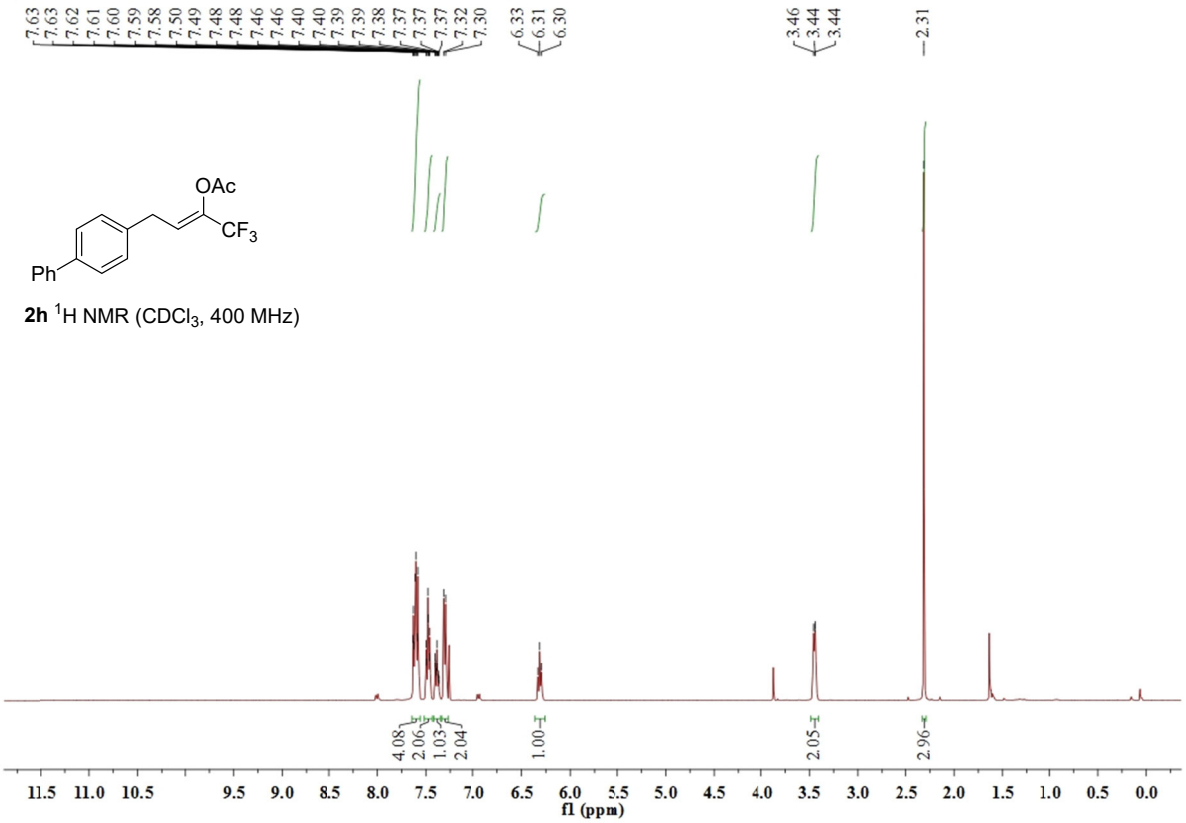
2g ^{13}C NMR ($CDCl_3$, 101 MHz)



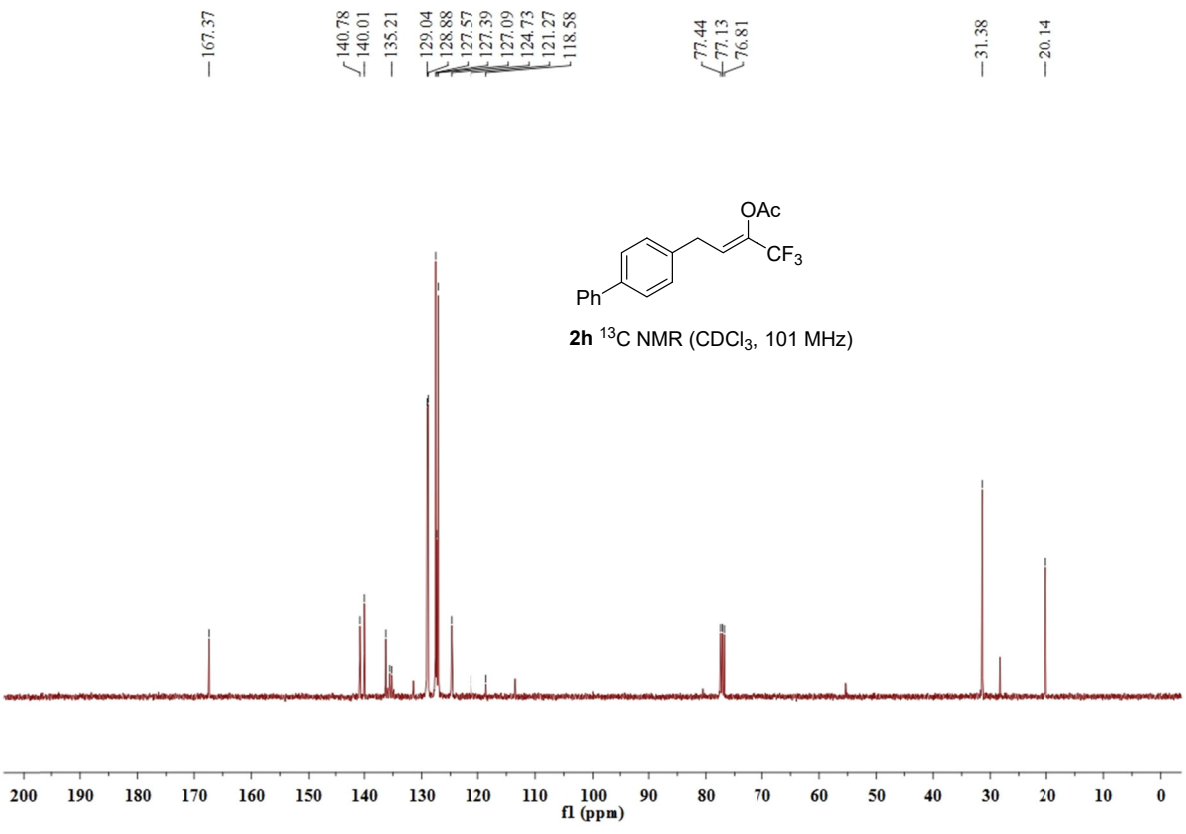


2g ^{19}F NMR ($CDCl_3$, 377 MHz)

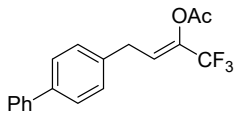




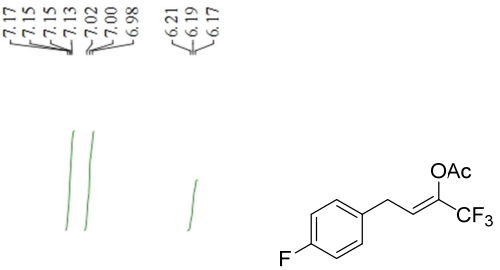
2h ^{1}H NMR ($CDCl_3$, 400 MHz)



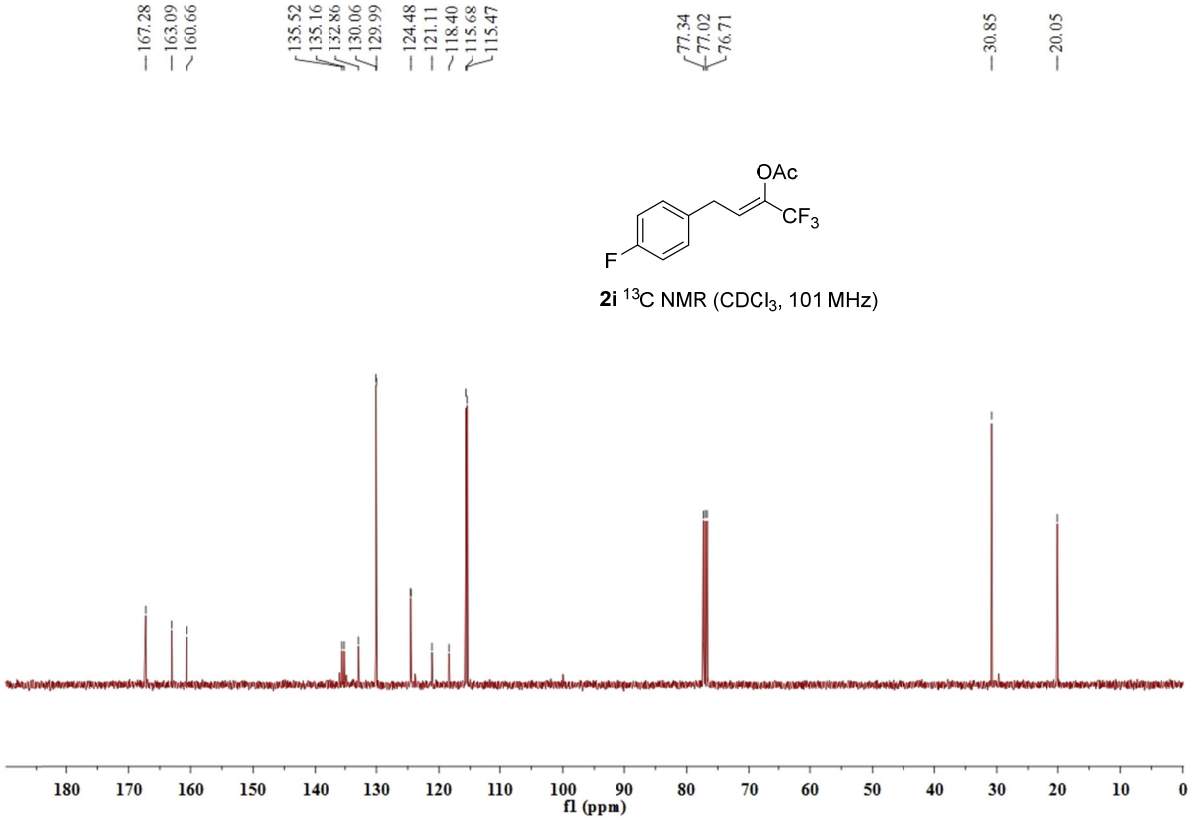
2h ^{13}C NMR ($CDCl_3$, 101 MHz)



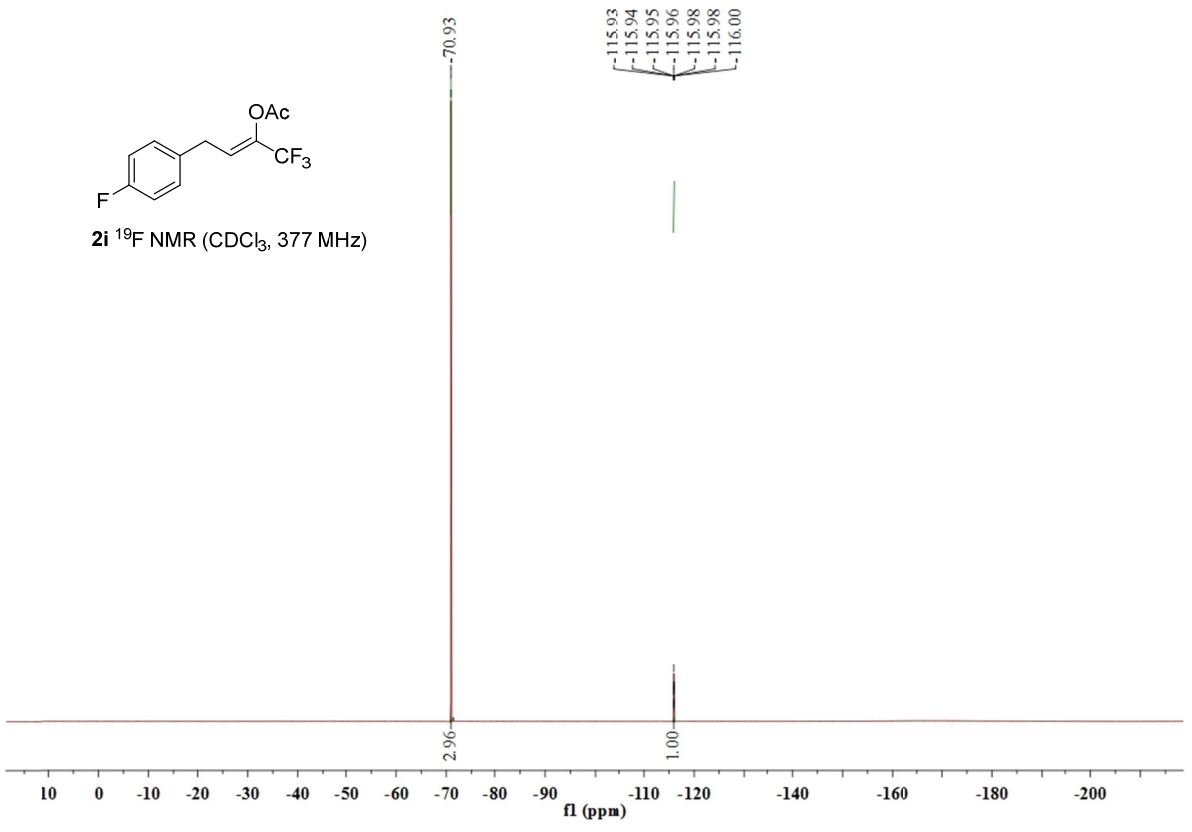
2h ^{19}F NMR ($CDCl_3$, 377 MHz)



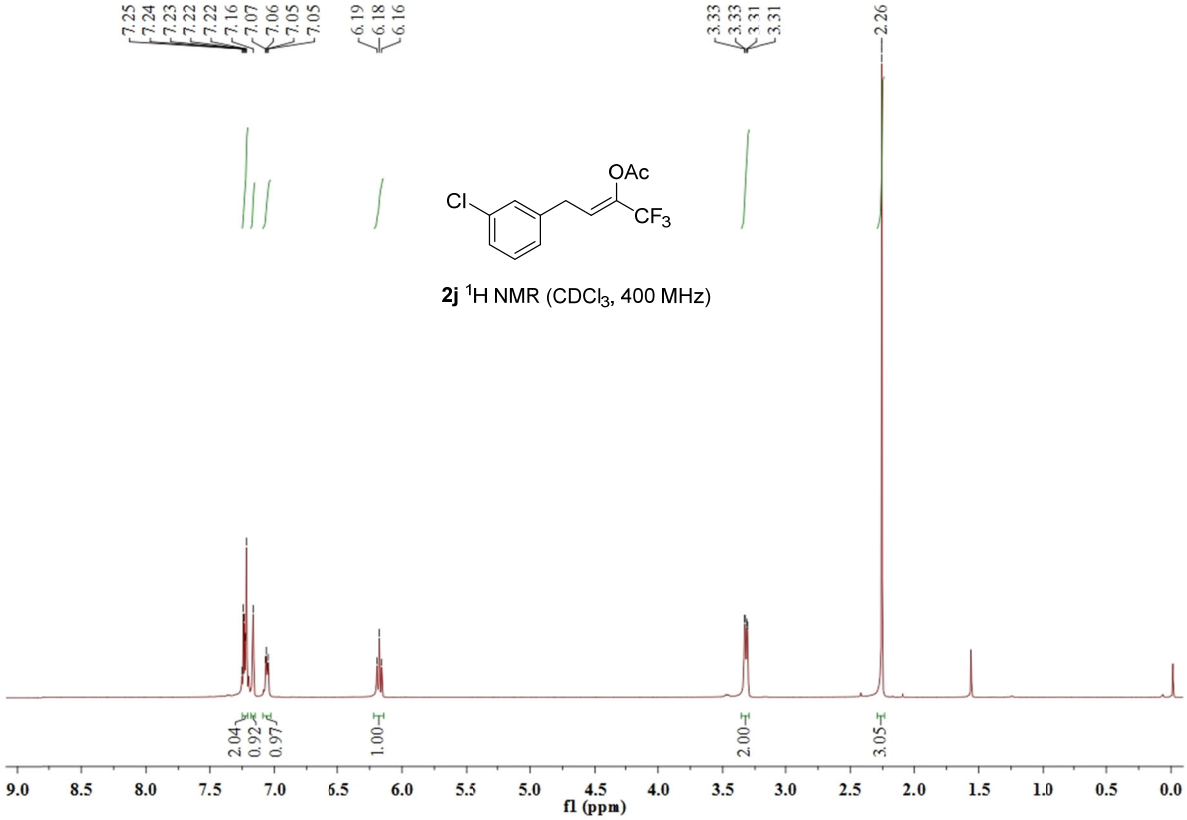
2i ^{1}H NMR ($CDCl_3$, 400 MHz)



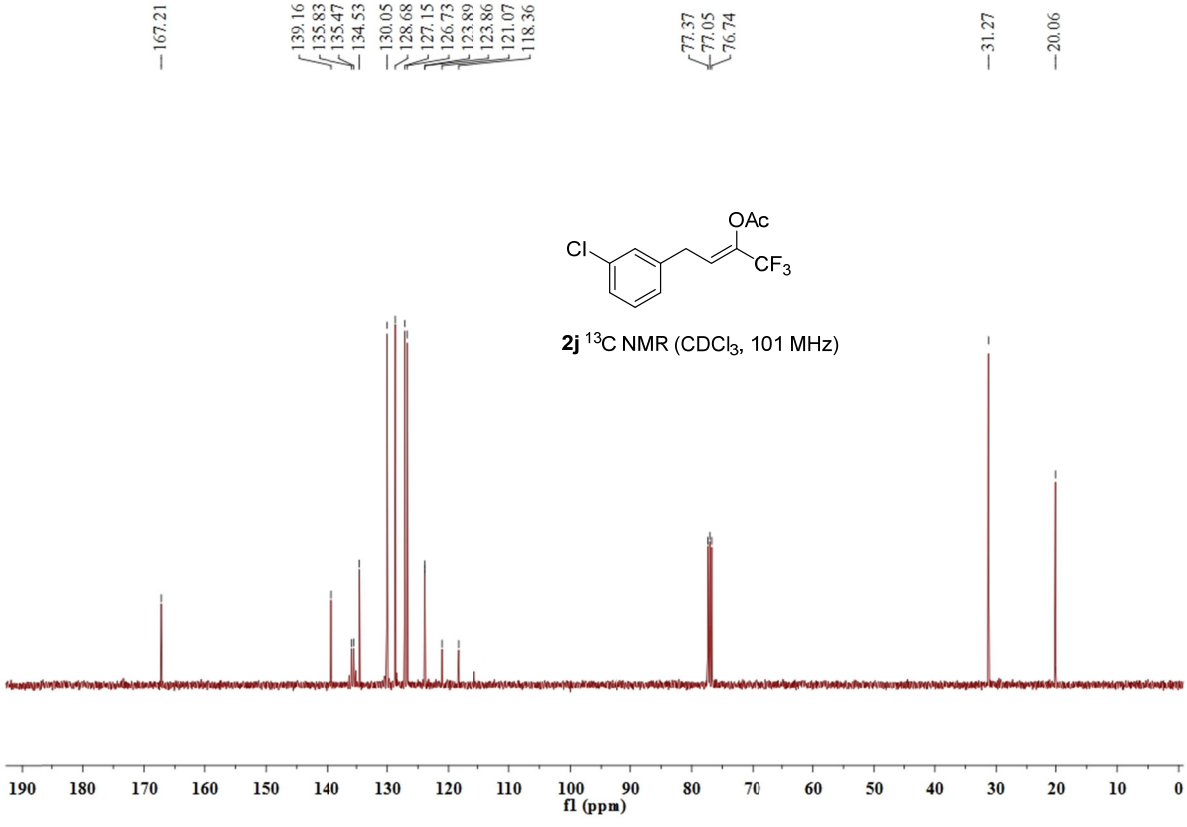
2i ^{13}C NMR ($CDCl_3$, 101 MHz)



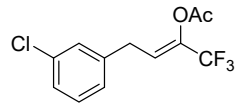
2i ^{19}F NMR ($CDCl_3$, 377 MHz)



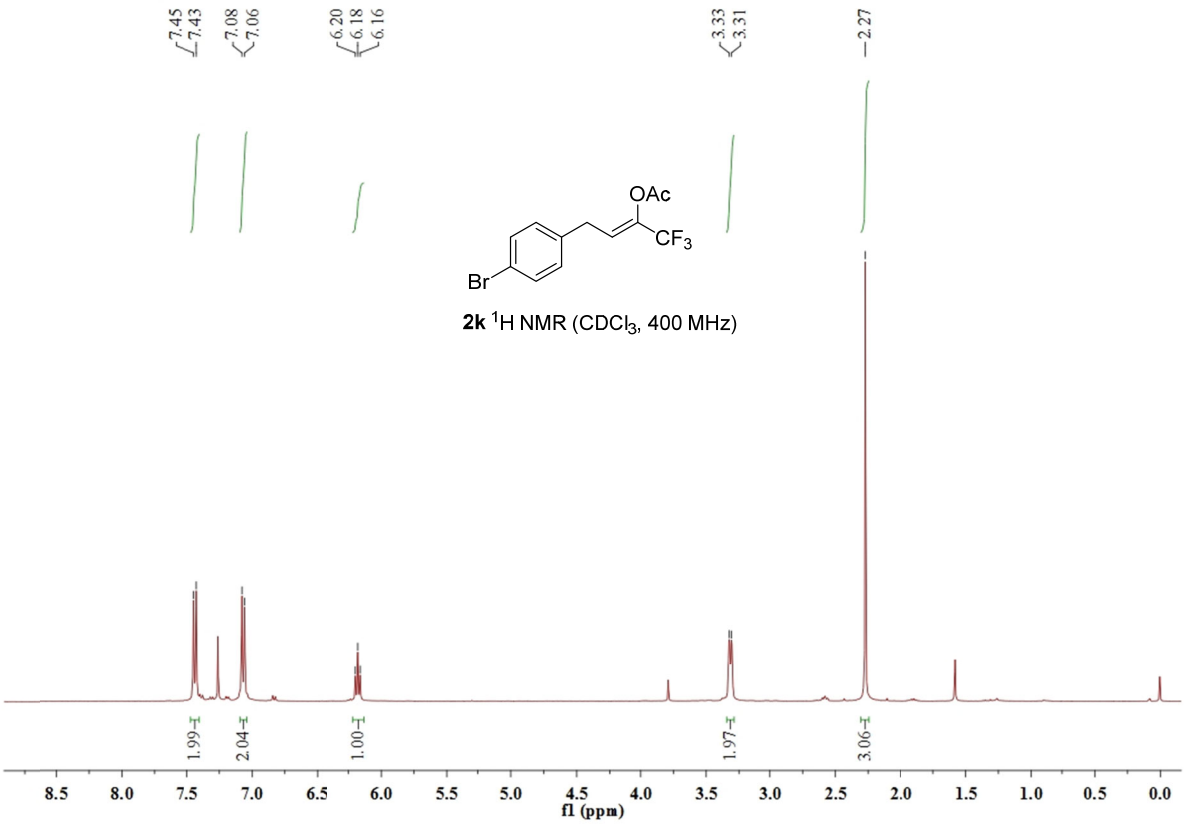
2j ^{1}H NMR ($CDCl_3$, 400 MHz)



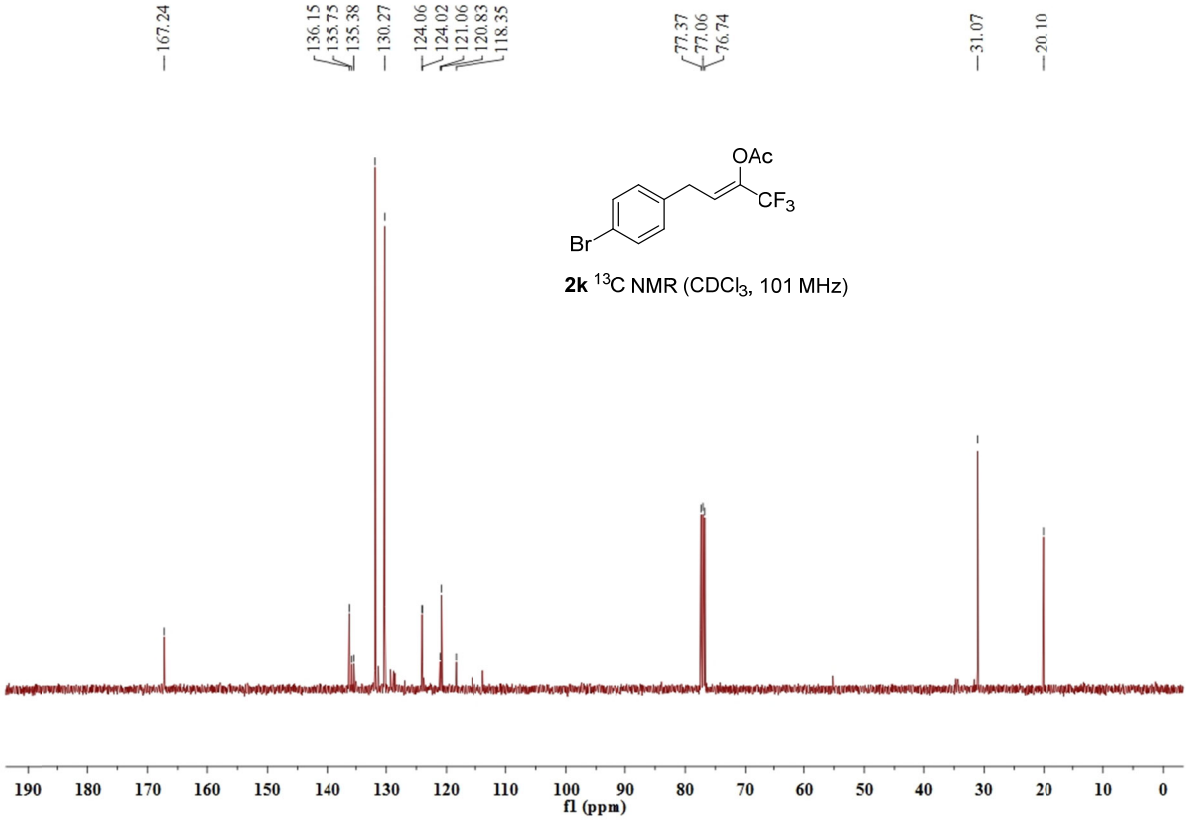
2j ^{13}C NMR ($CDCl_3$, 101 MHz)



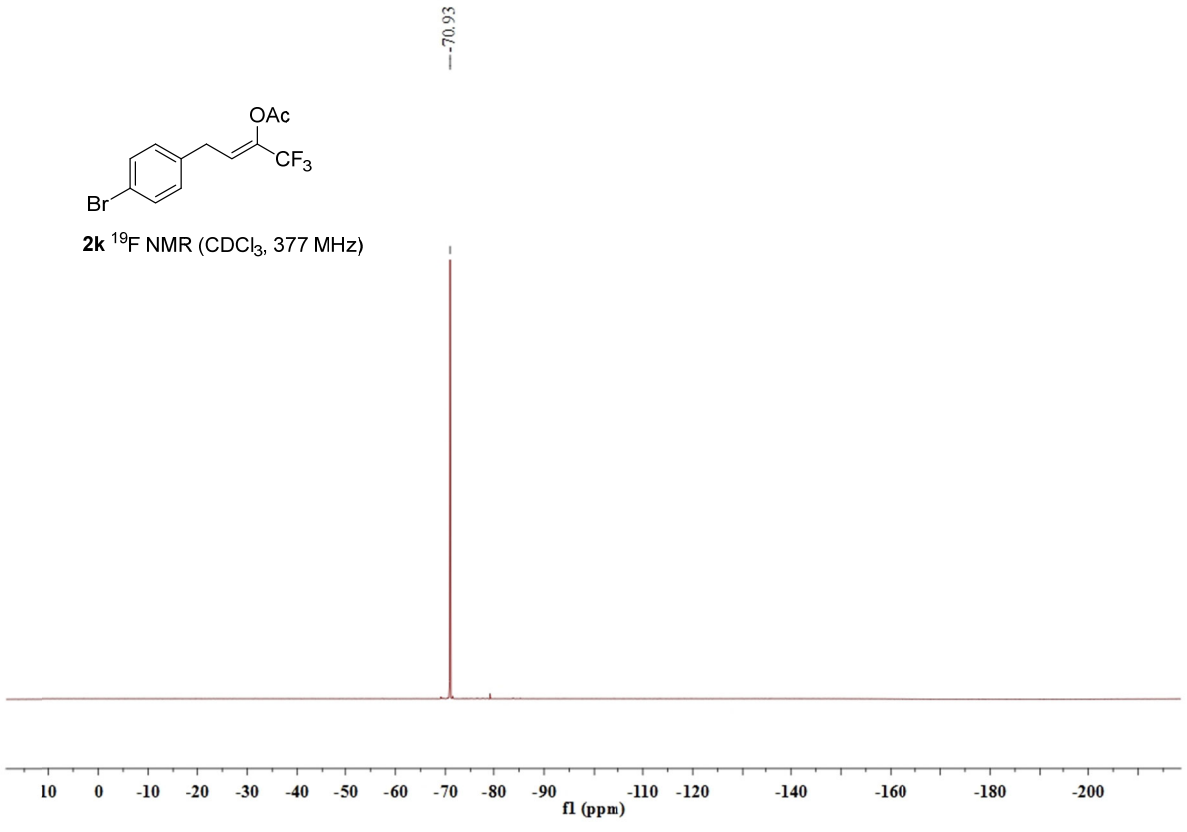
2j ^{19}F NMR ($CDCl_3$, 377 MHz)



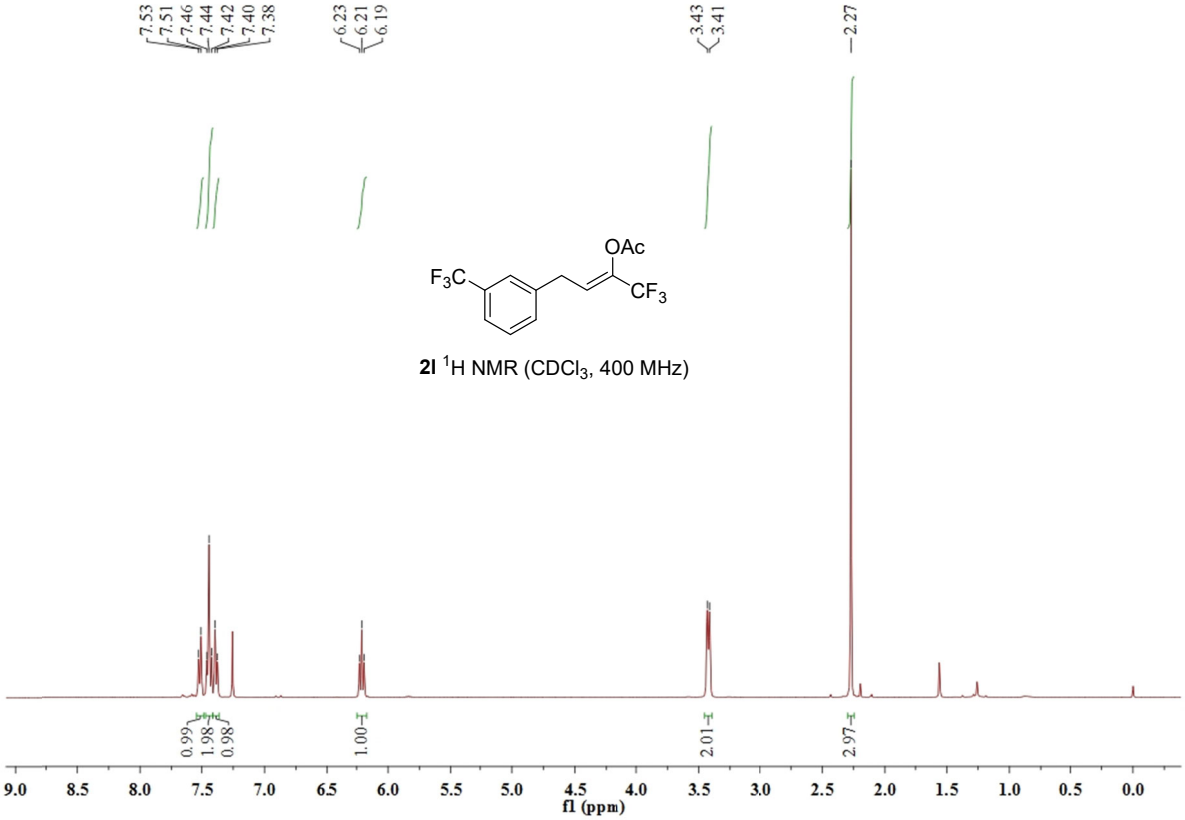
2k ^{1}H NMR ($CDCl_3$, 400 MHz)



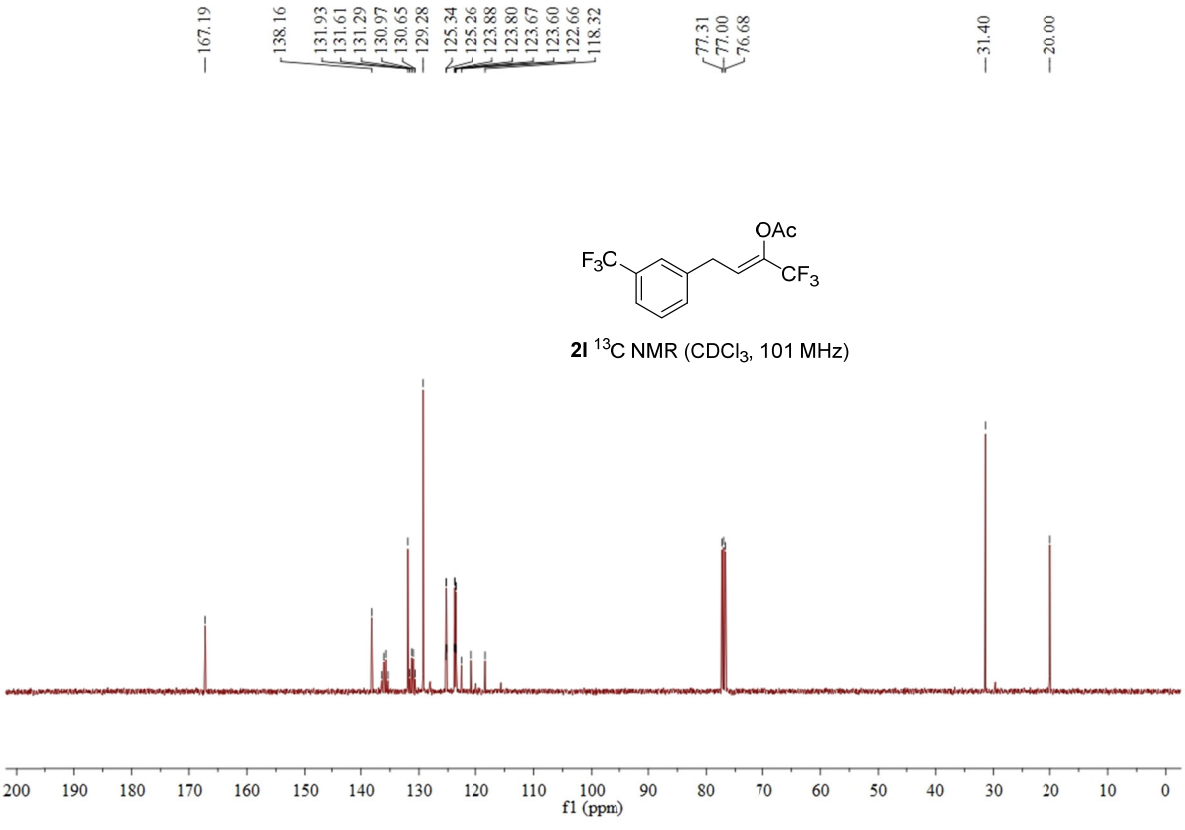
2k ^{13}C NMR ($CDCl_3$, 101 MHz)



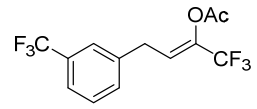
2k ^{19}F NMR ($CDCl_3$, 377 MHz)



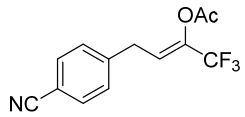
2l ^{1}H NMR ($CDCl_3$, 400 MHz)



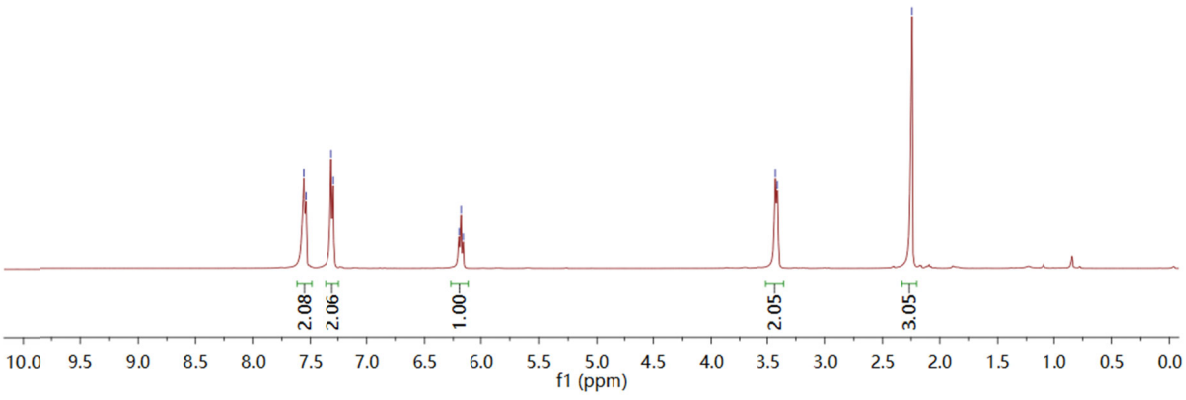
2l ^{13}C NMR ($CDCl_3$, 101 MHz)

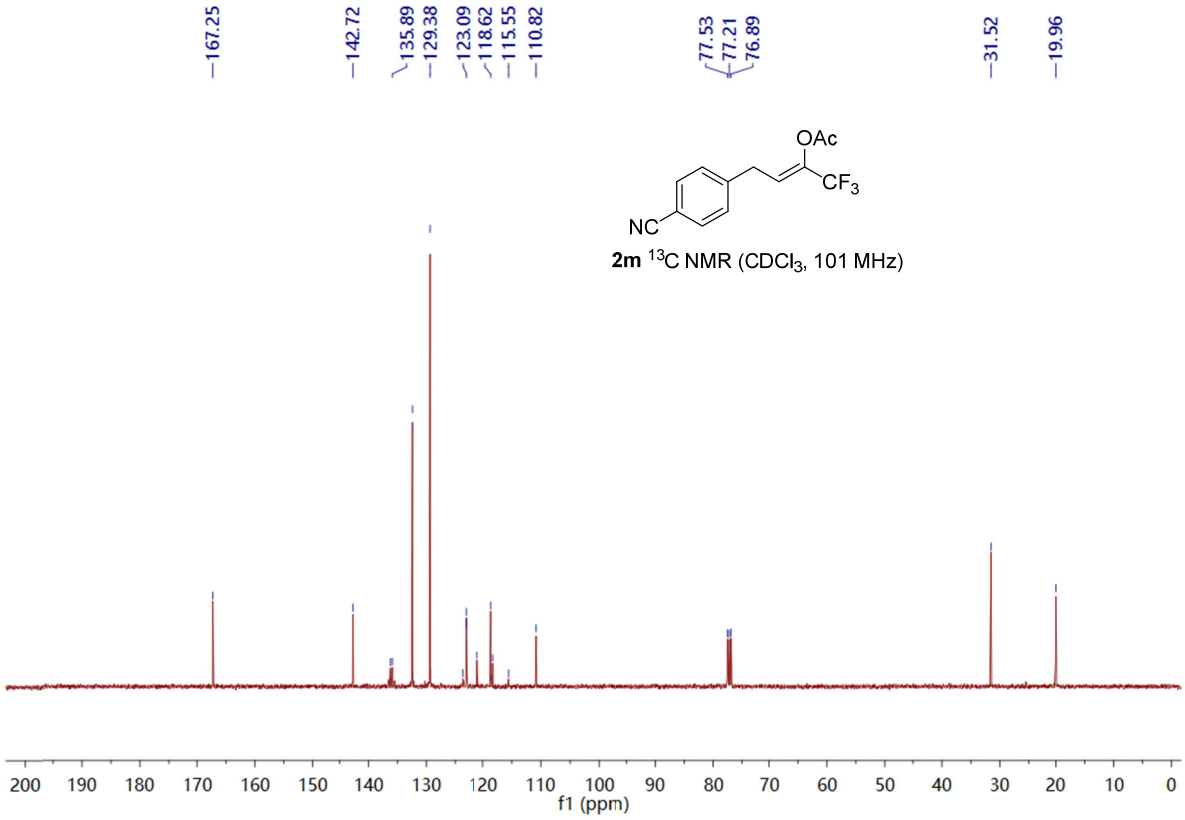


2l ^{19}F NMR ($CDCl_3$, 377 MHz)

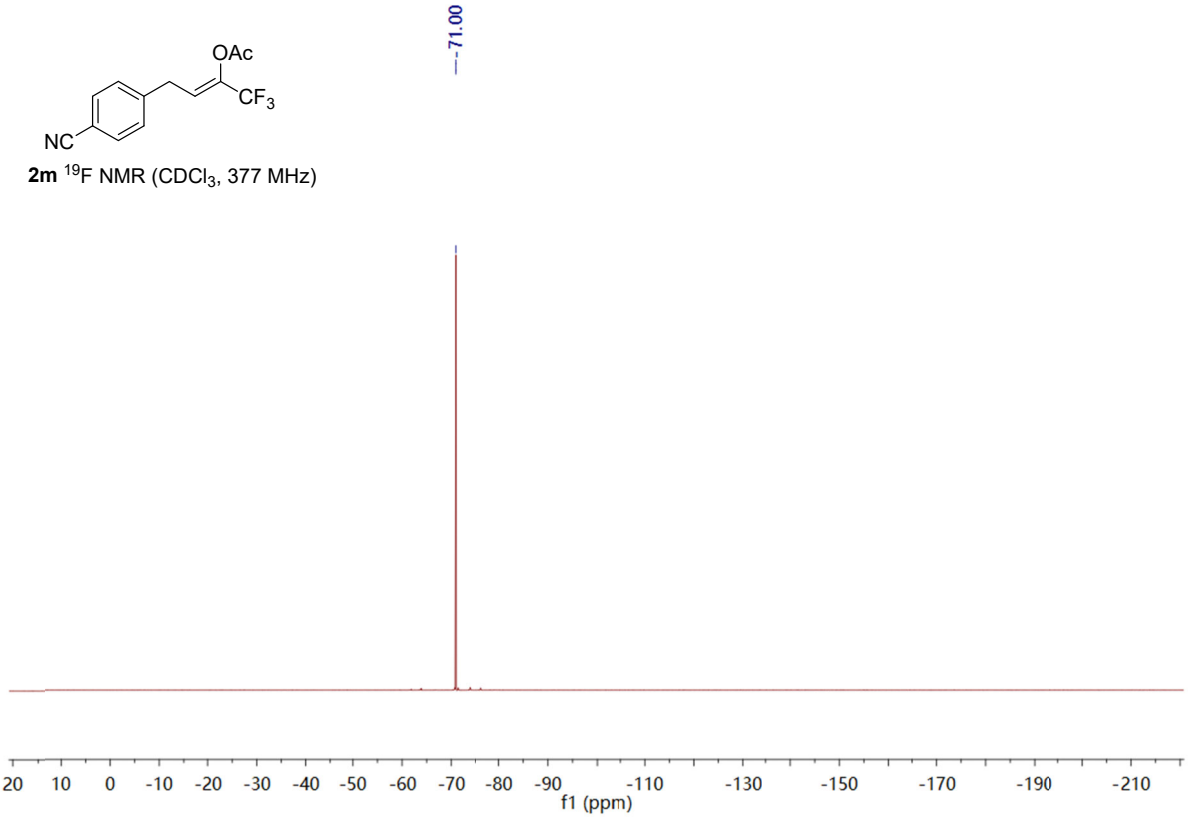


2m ^{1}H NMR ($CDCl_3$, 400 MHz)

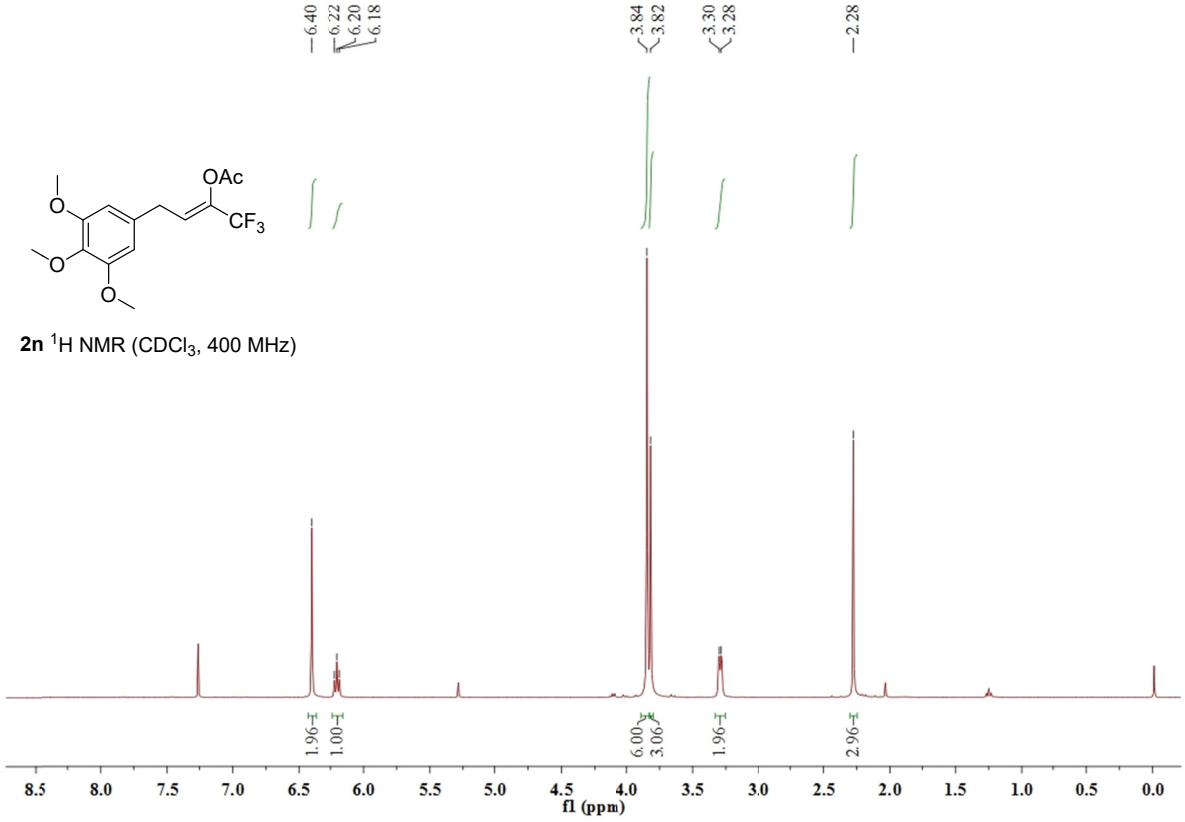




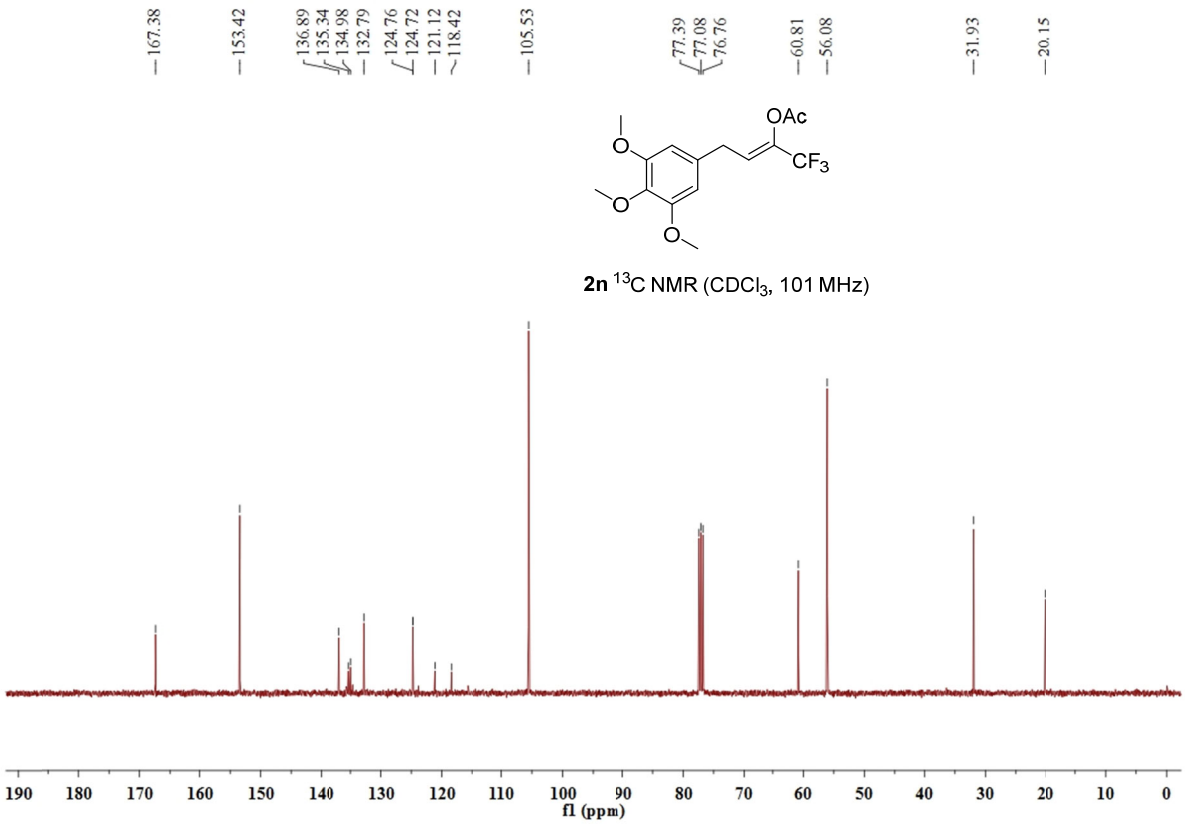
2m ^{13}C NMR ($CDCl_3$, 101 MHz)



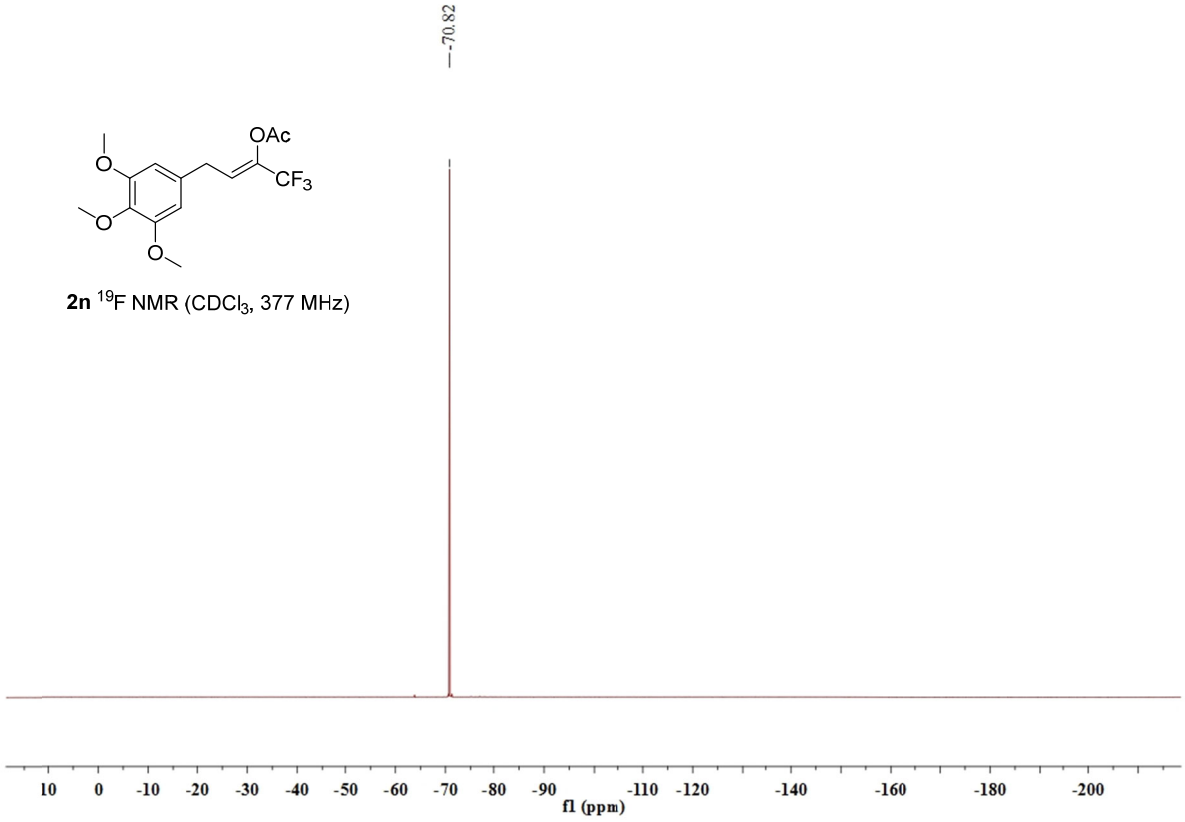
2m ^{19}F NMR ($CDCl_3$, 377 MHz)



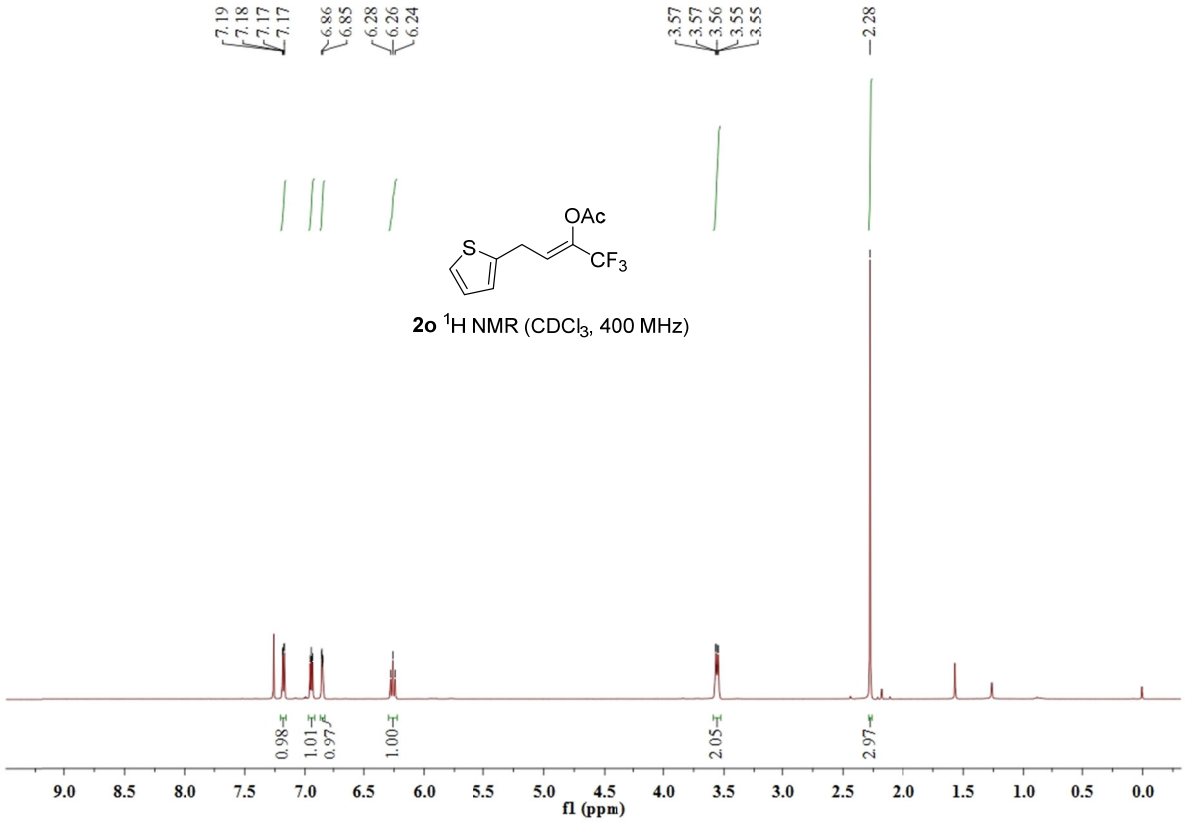
2n ^{1}H NMR ($CDCl_3$, 400 MHz)



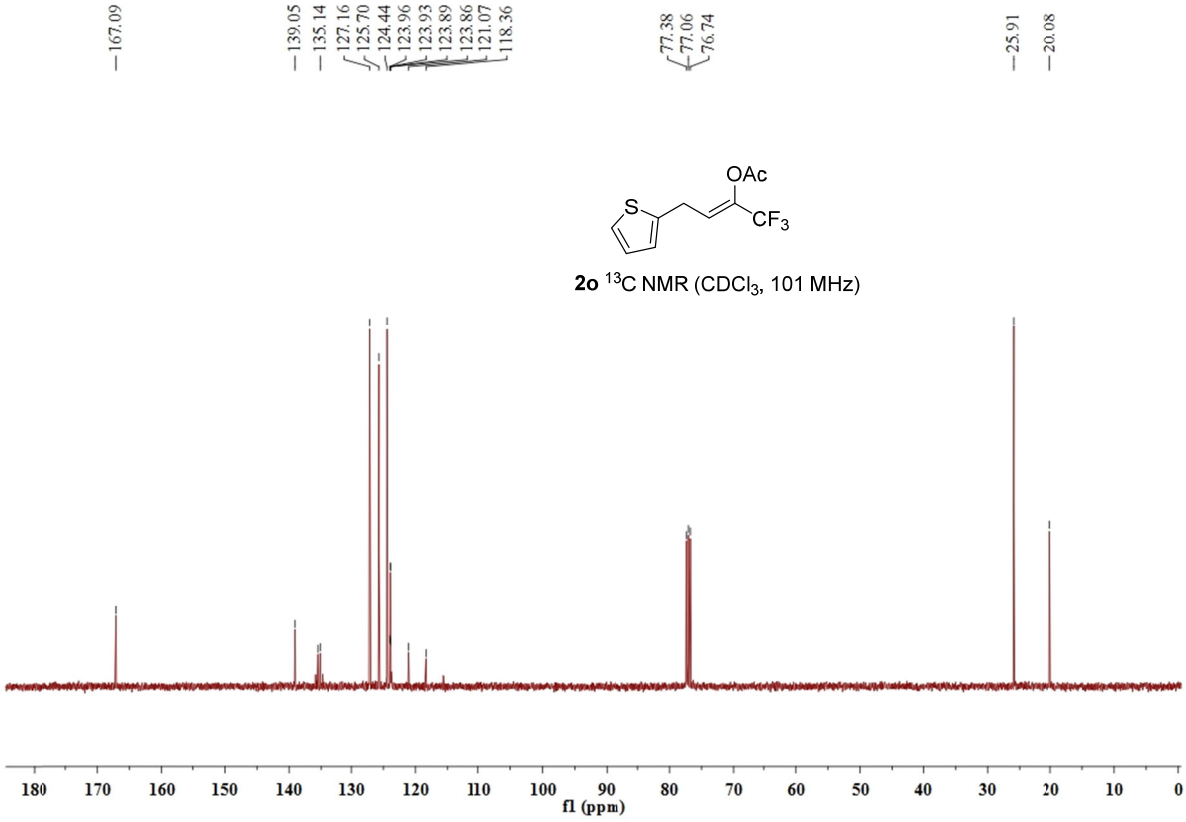
2n ^{13}C NMR ($CDCl_3$, 101 MHz)



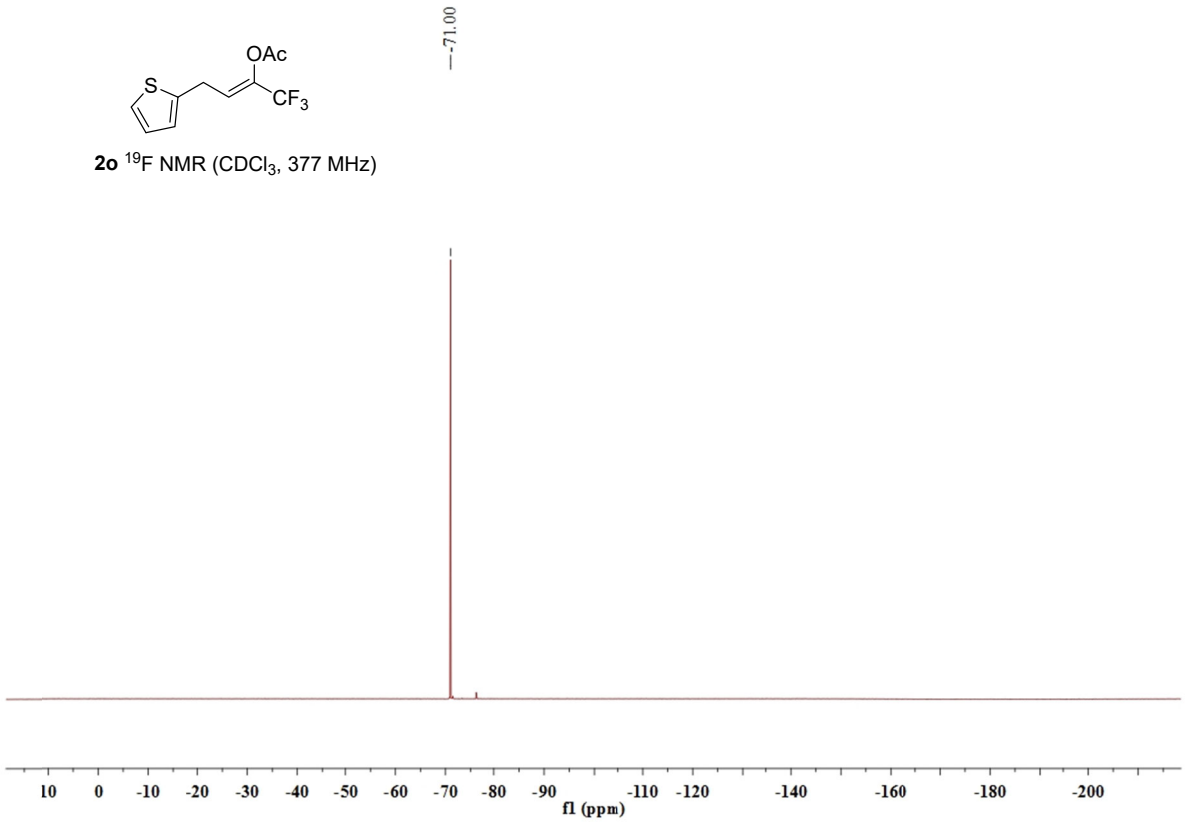
2n ^{19}F NMR ($CDCl_3$, 377 MHz)



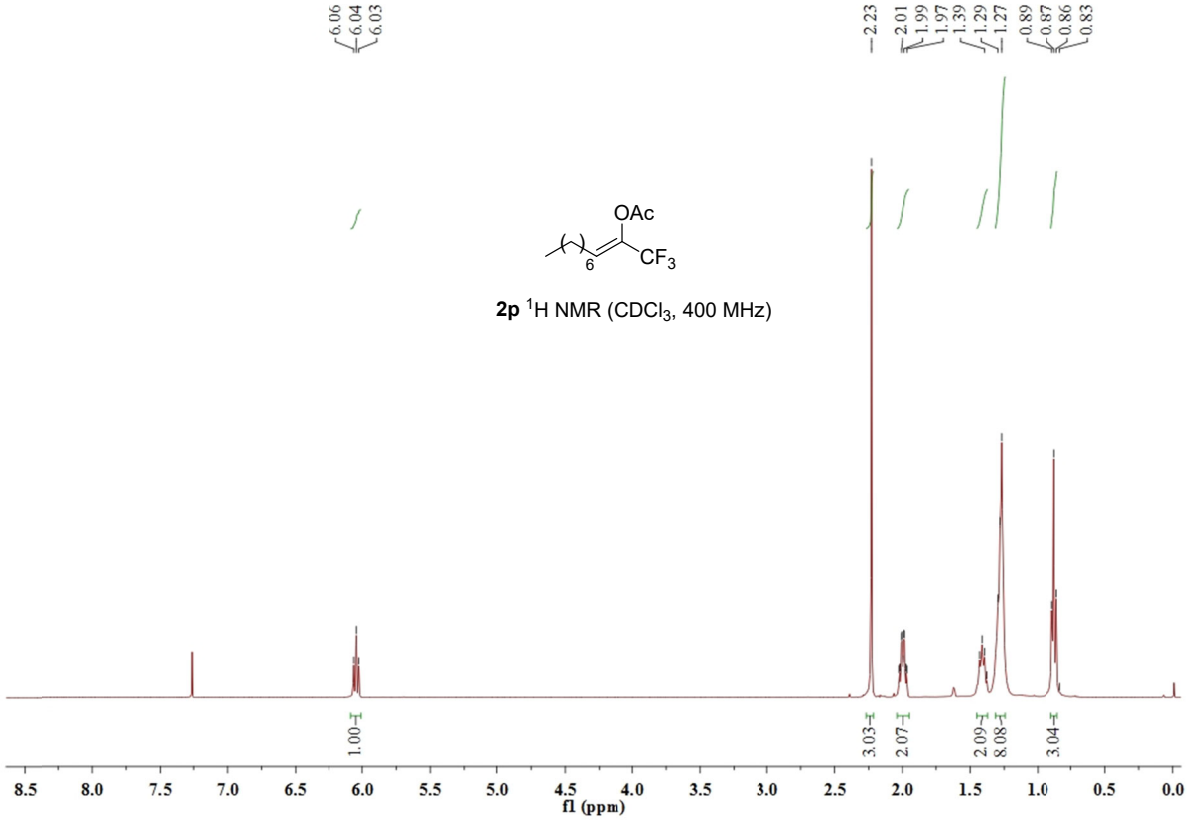
2o ^{1}H NMR ($CDCl_3$, 400 MHz)



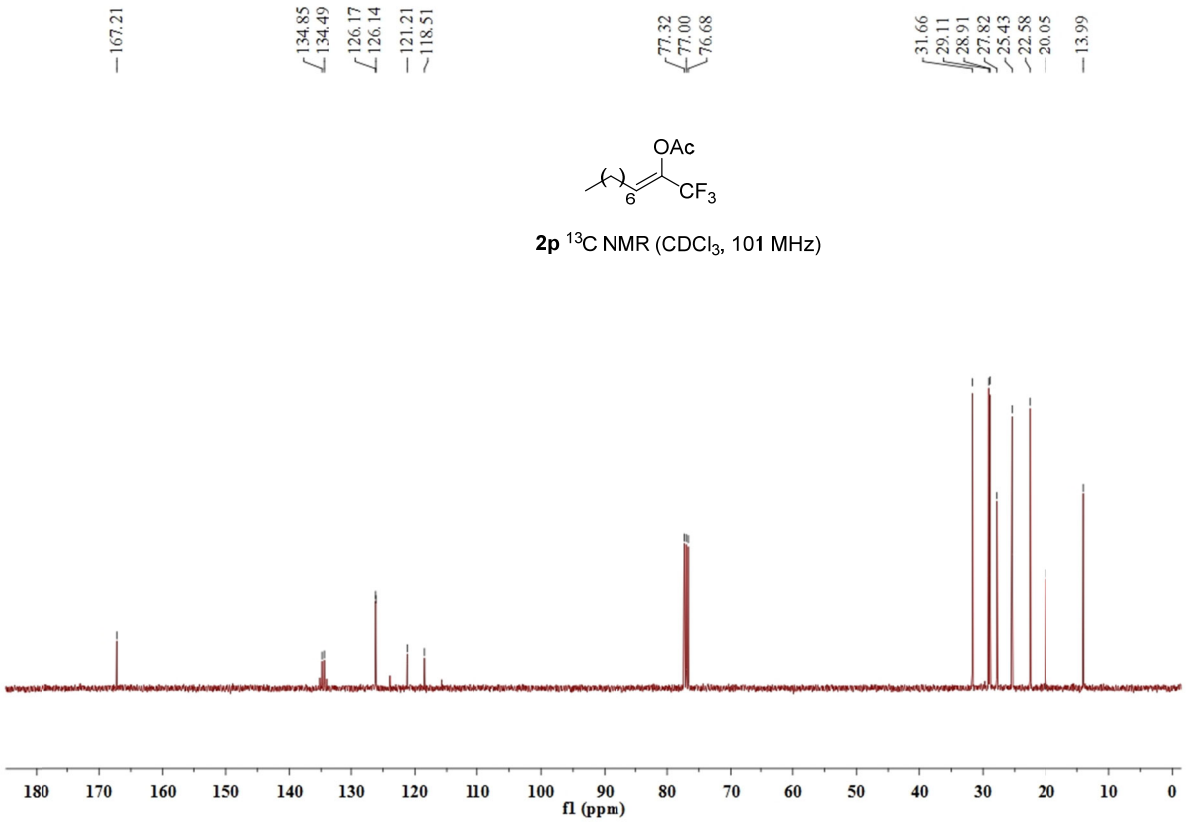
2o ^{13}C NMR ($CDCl_3$, 101 MHz)



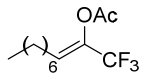
2o ^{19}F NMR ($CDCl_3$, 377 MHz)



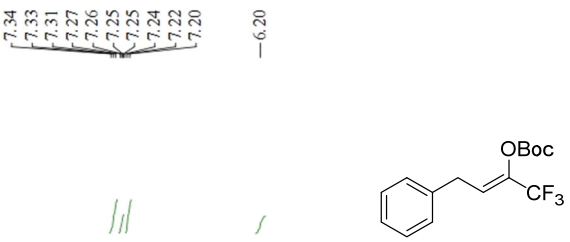
2p ^{1}H NMR ($CDCl_3$, 400 MHz)



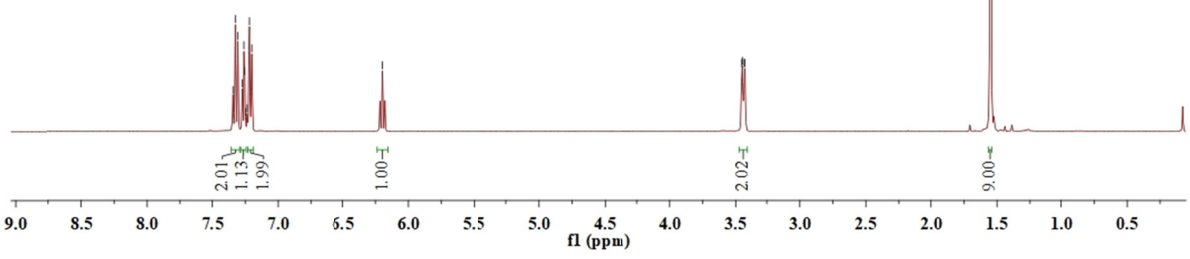
2p ^{13}C NMR ($CDCl_3$, 101 MHz)

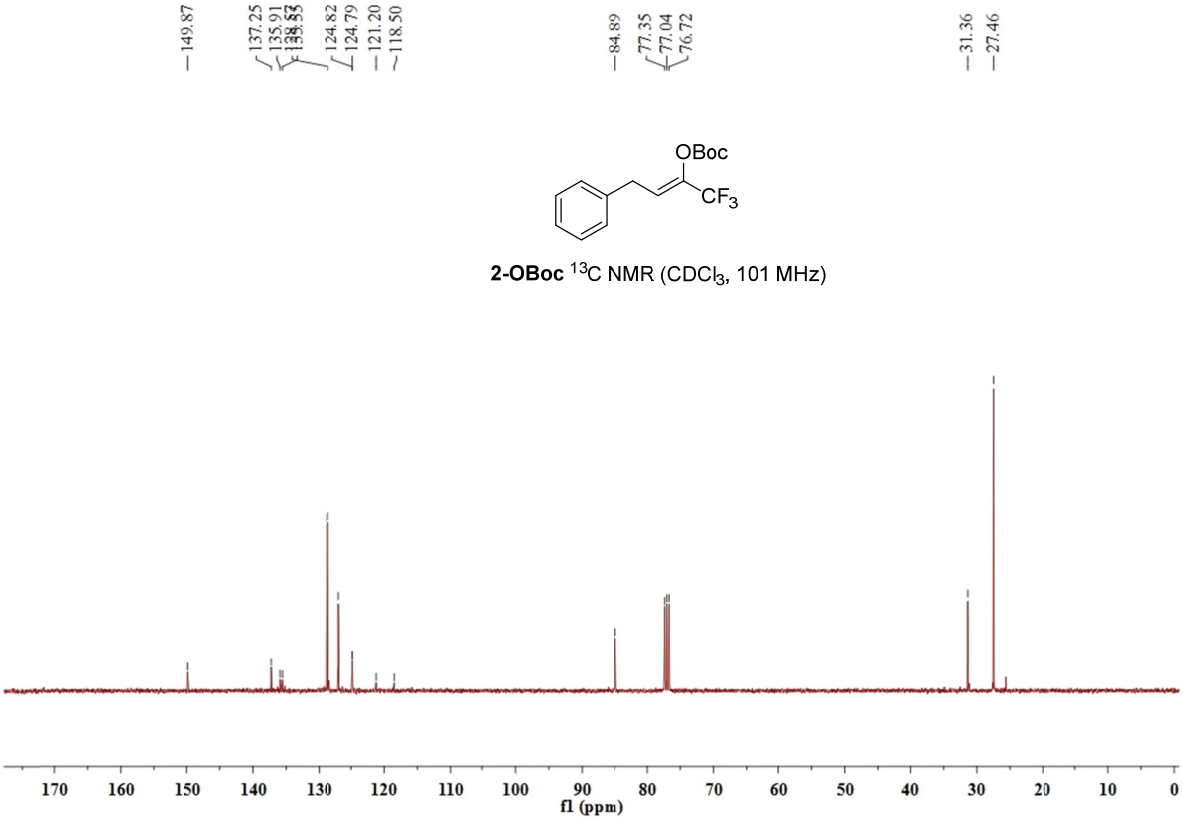


2p ^{19}F NMR ($CDCl_3$, 377 MHz)

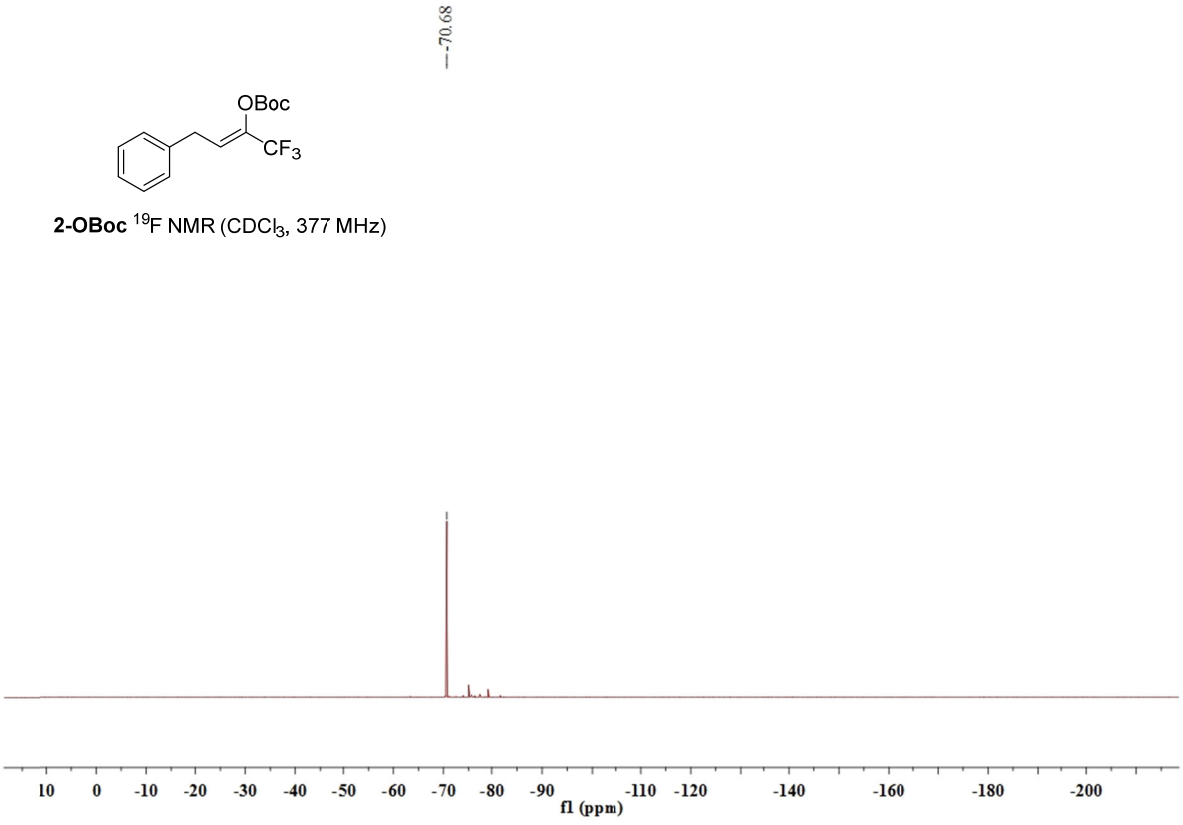


2-OBoc ^{1}H NMR ($CDCl_3$, 400 MHz)

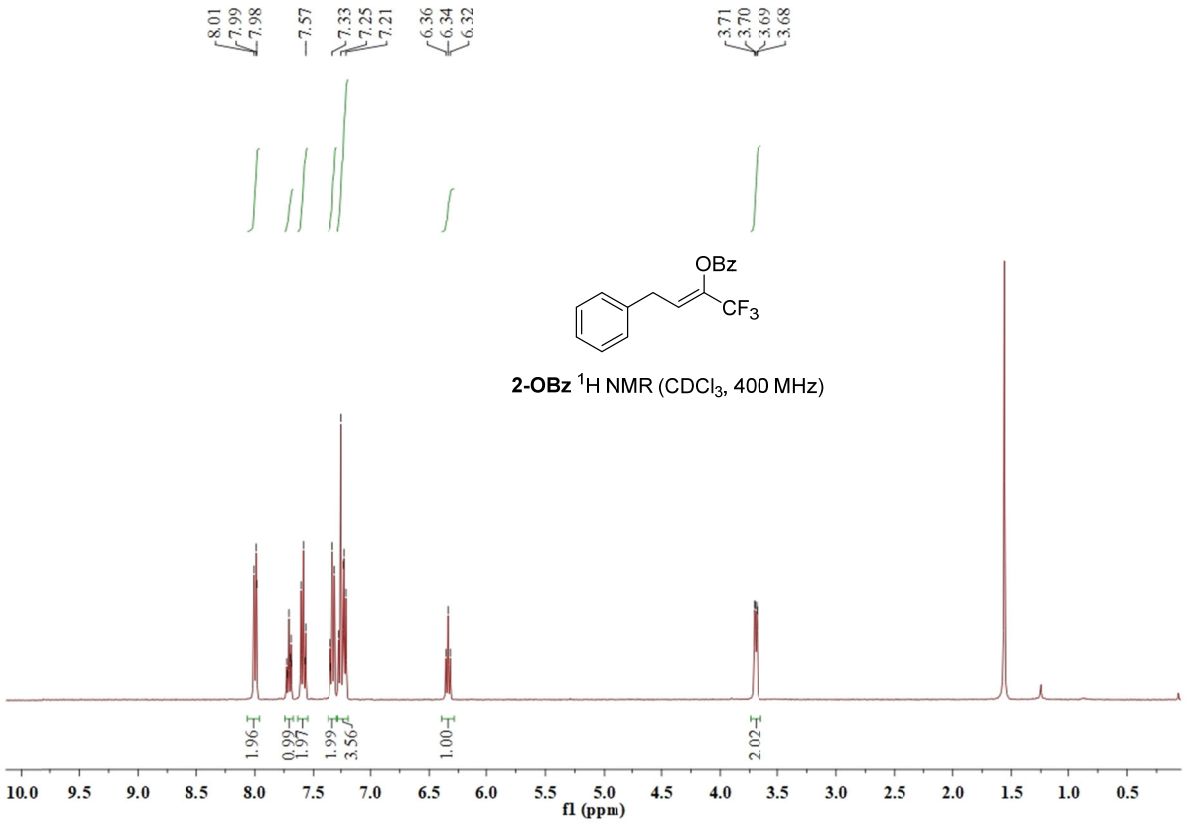




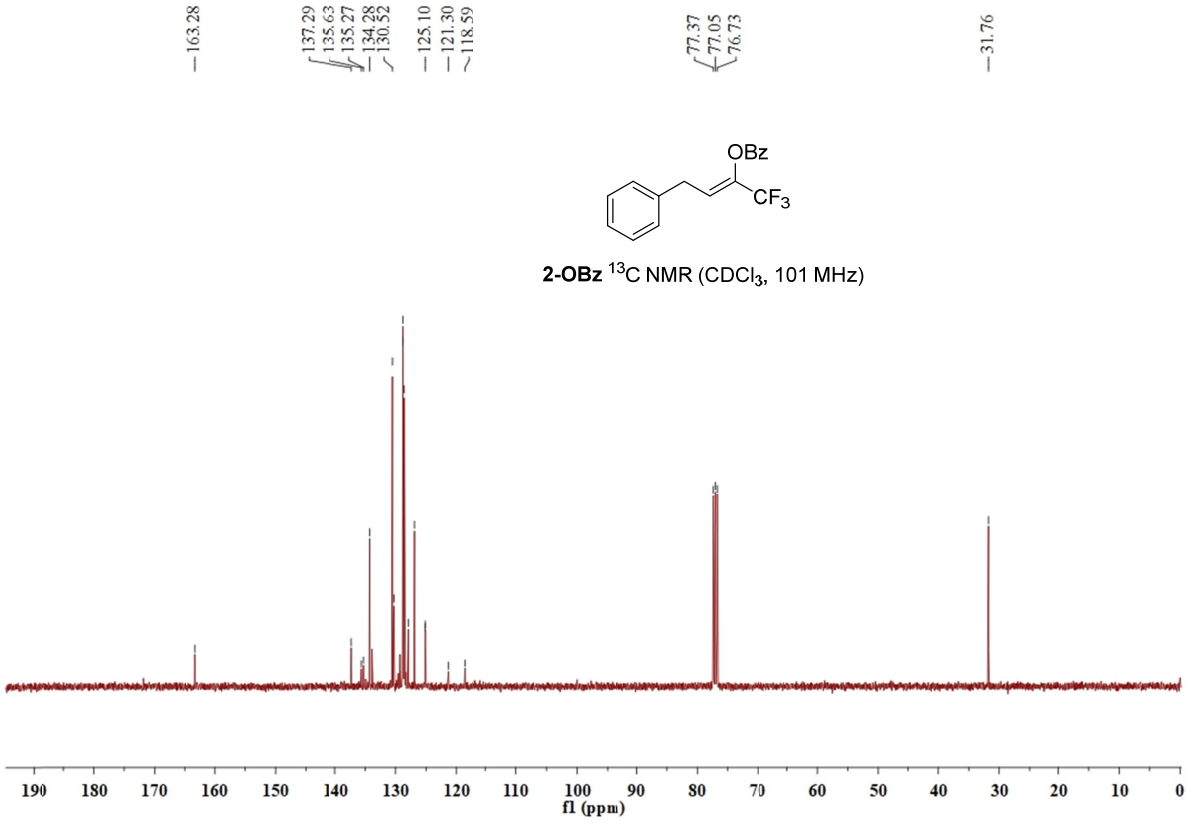
2-OBoc ^{13}C NMR ($CDCl_3$, 101 MHz)



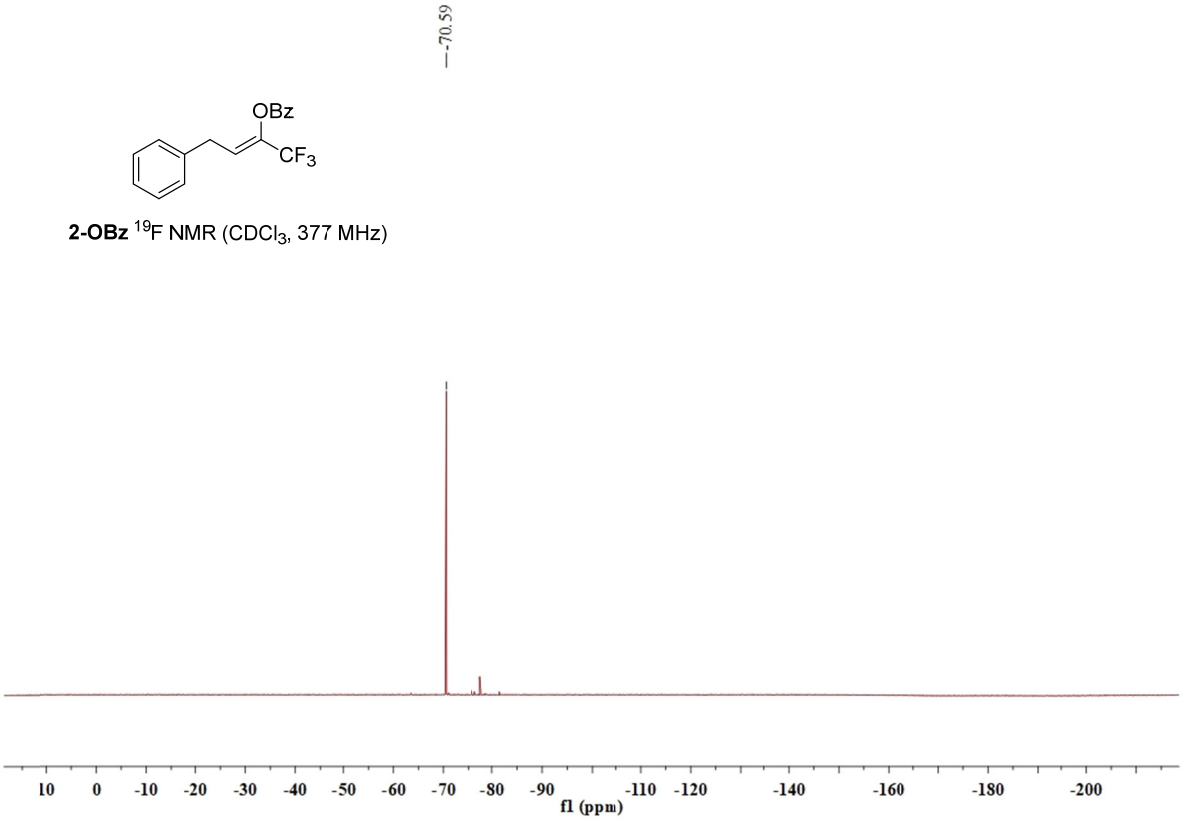
2-OBoc ^{19}F NMR ($CDCl_3$, 377 MHz)



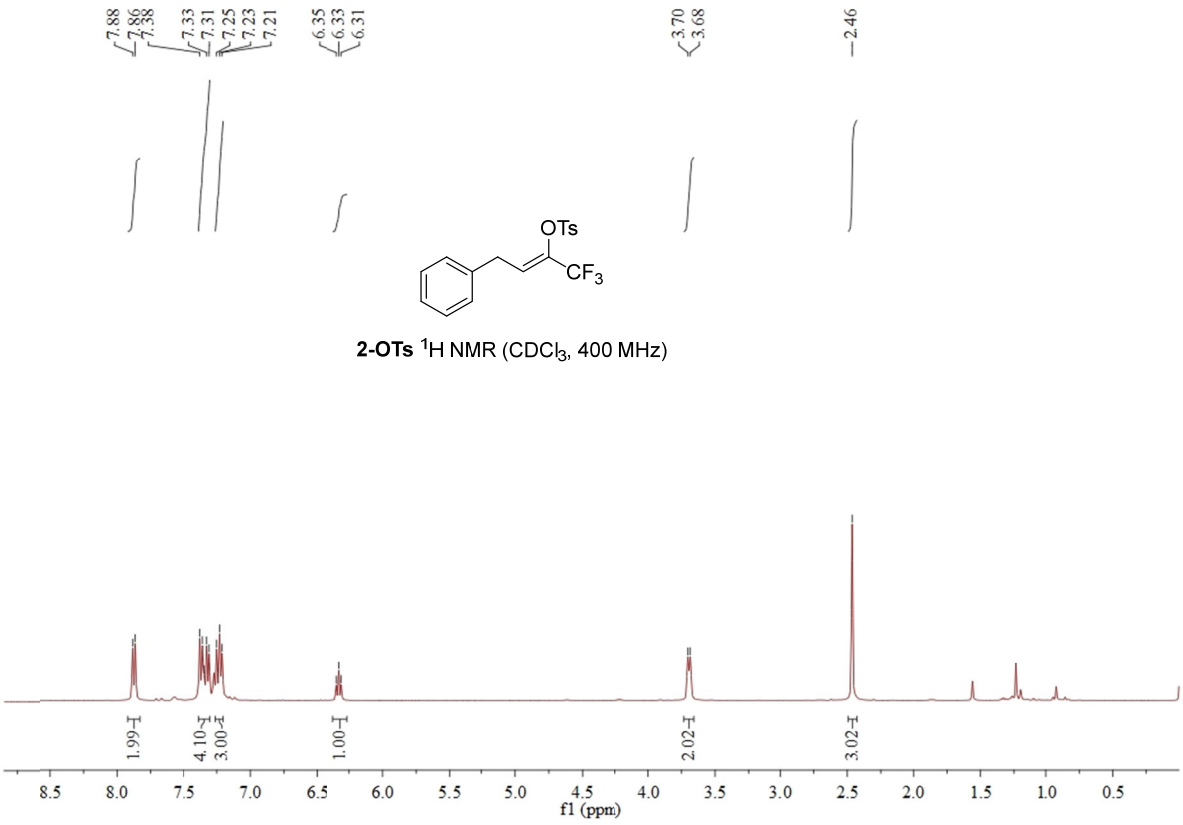
2-OBz ^{1}H NMR ($CDCl_3$, 400 MHz)



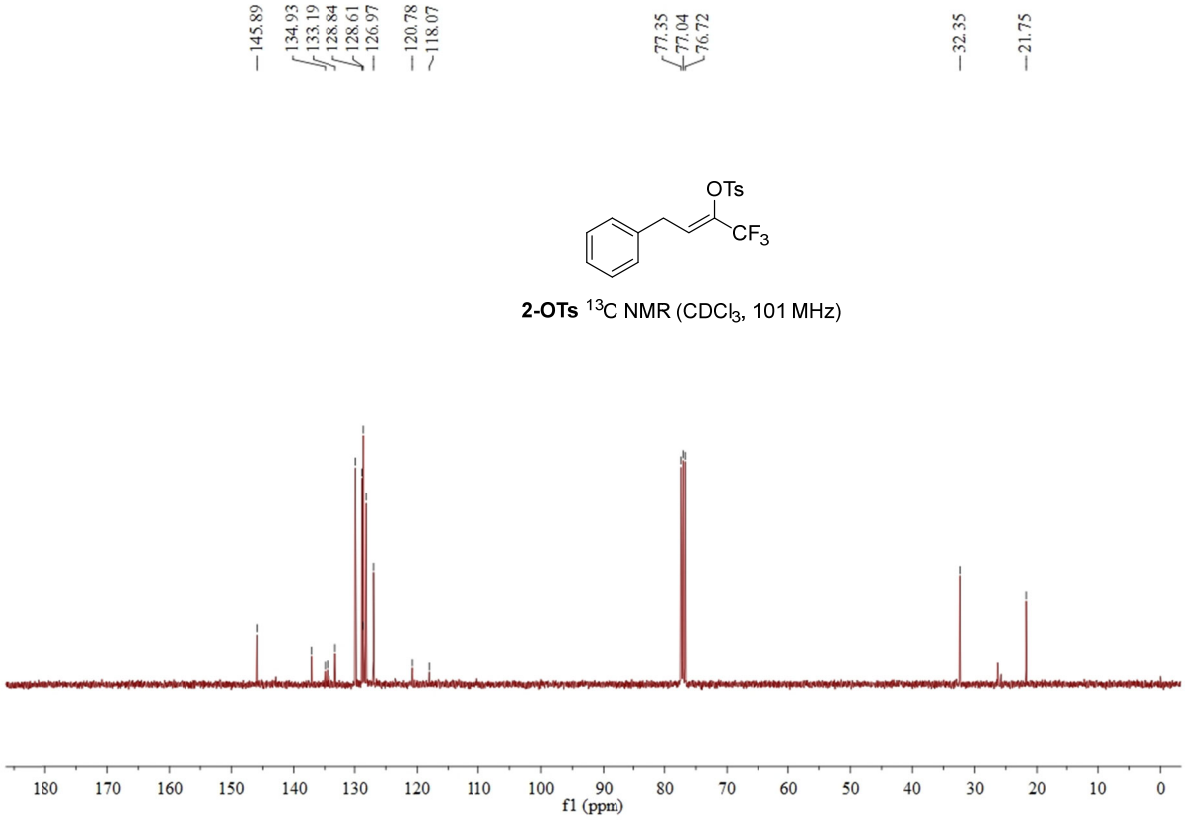
2-OBz ^{13}C NMR ($CDCl_3$, 101 MHz)



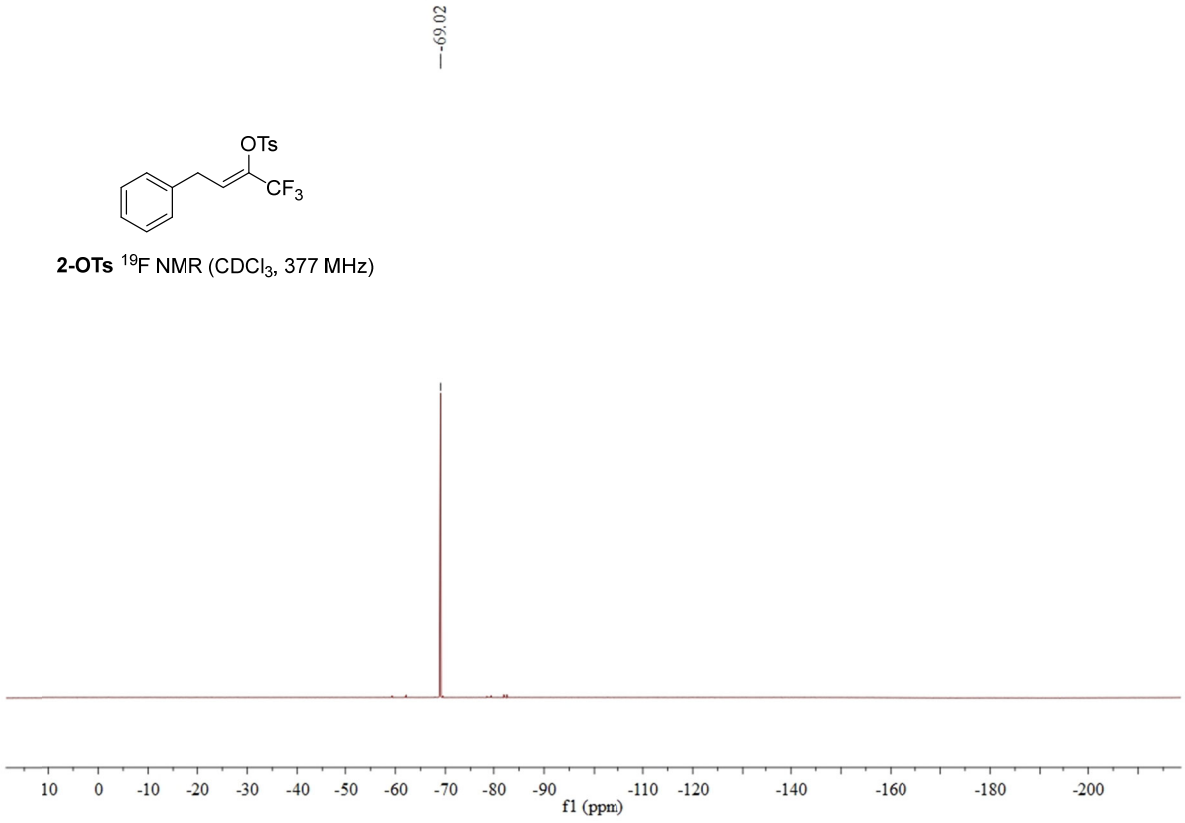
2-OBz ^{19}F NMR ($CDCl_3$, 377 MHz)



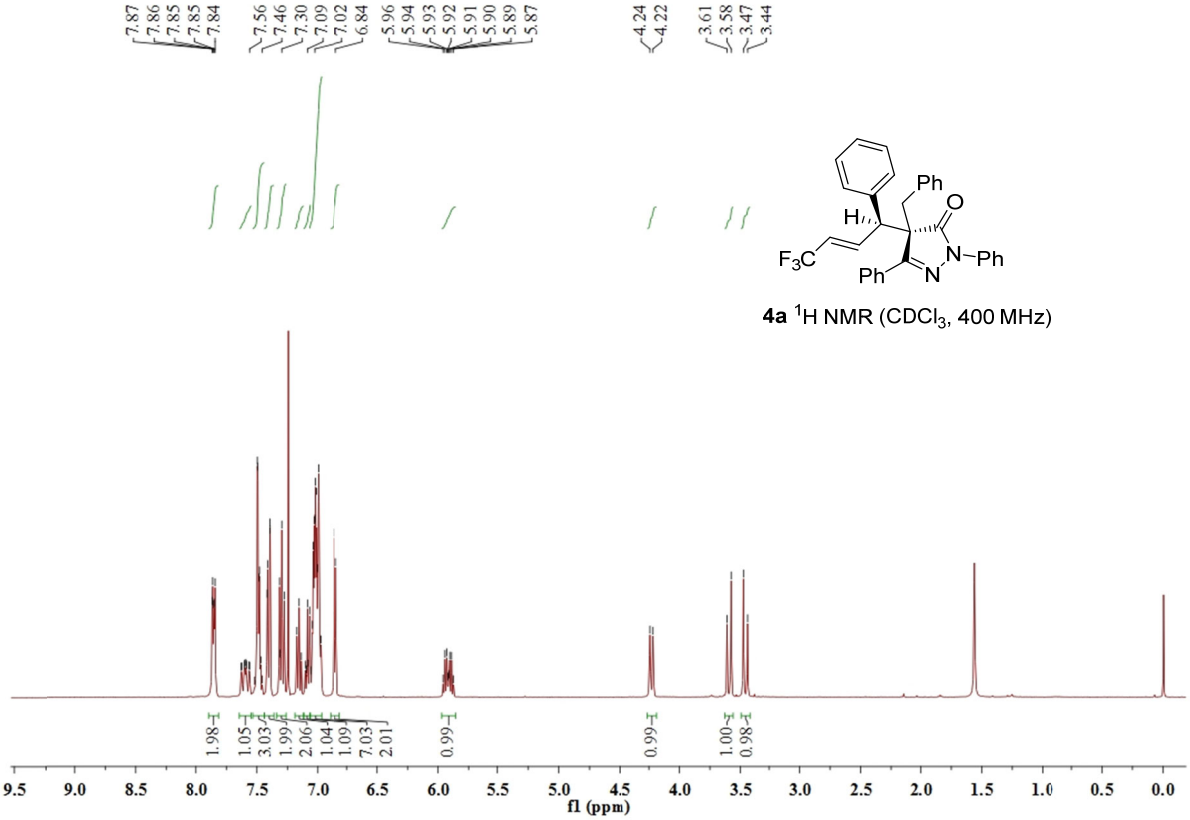
2-OTs ^{1}H NMR ($CDCl_3$, 400 MHz)



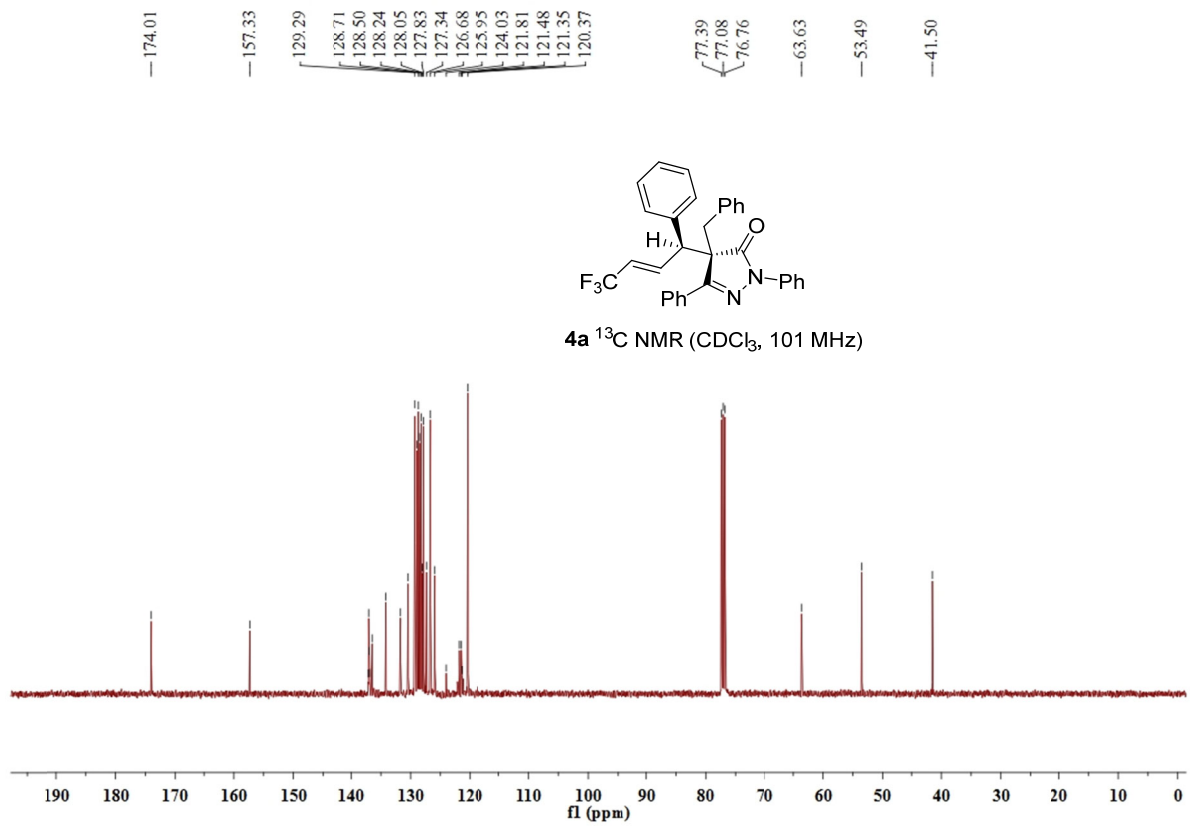
2-OTs ^{13}C NMR ($CDCl_3$, 101 MHz)



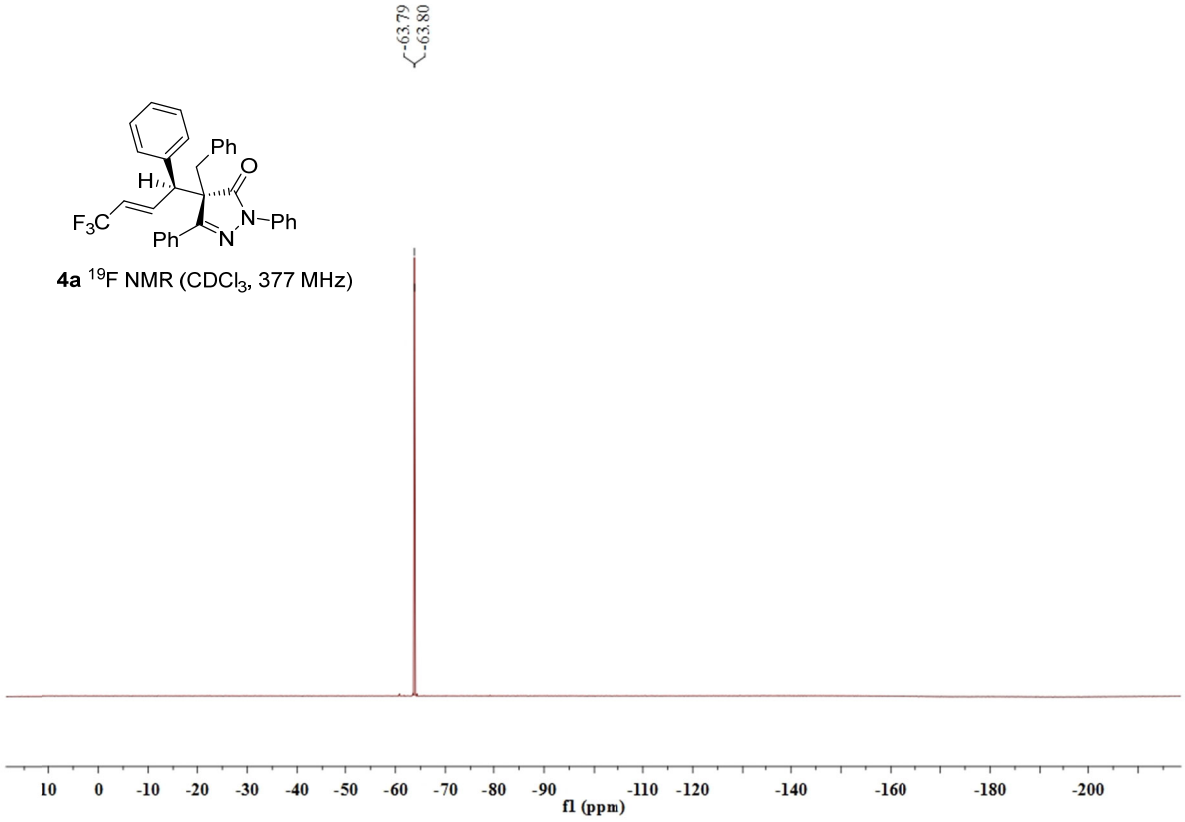
2-OTs ^{19}F NMR ($CDCl_3$, 377 MHz)



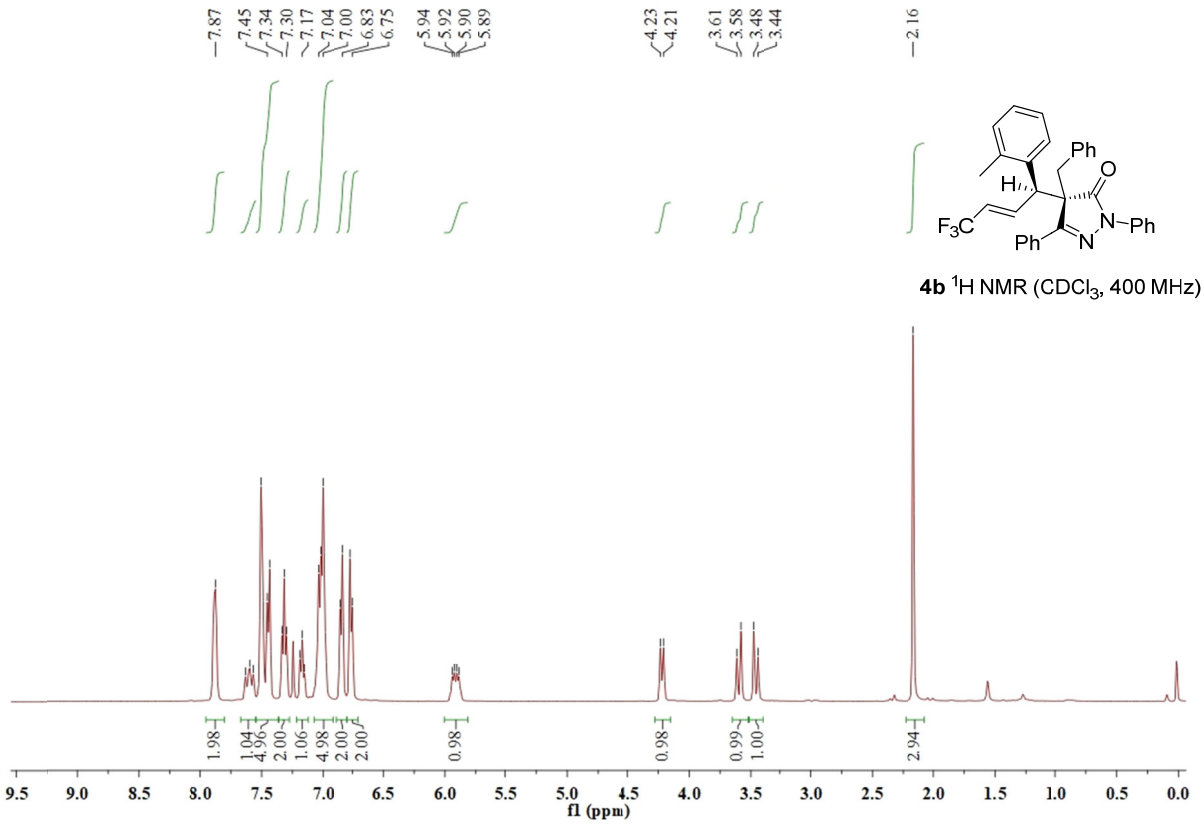
4a ^{1}H NMR ($CDCl_3$, 400 MHz)



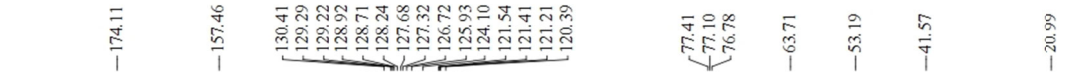
4a ^{13}C NMR ($CDCl_3$, 101 MHz)

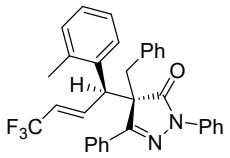


4a ^{19}F NMR ($CDCl_3$, 377 MHz)

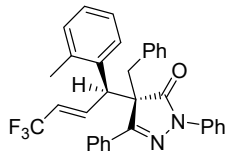


4b ^{1}H NMR ($CDCl_3$, 400 MHz)

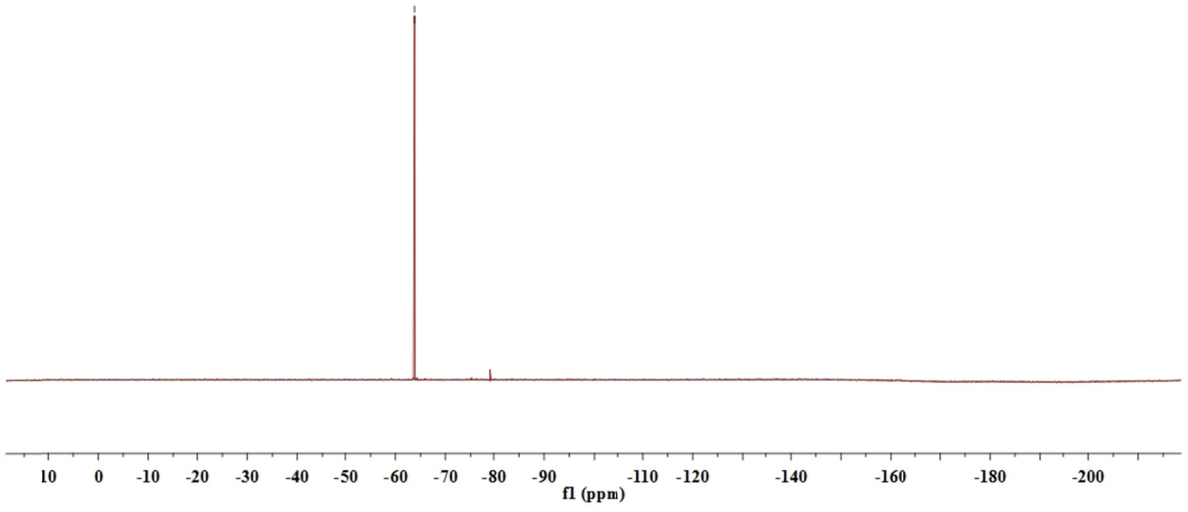


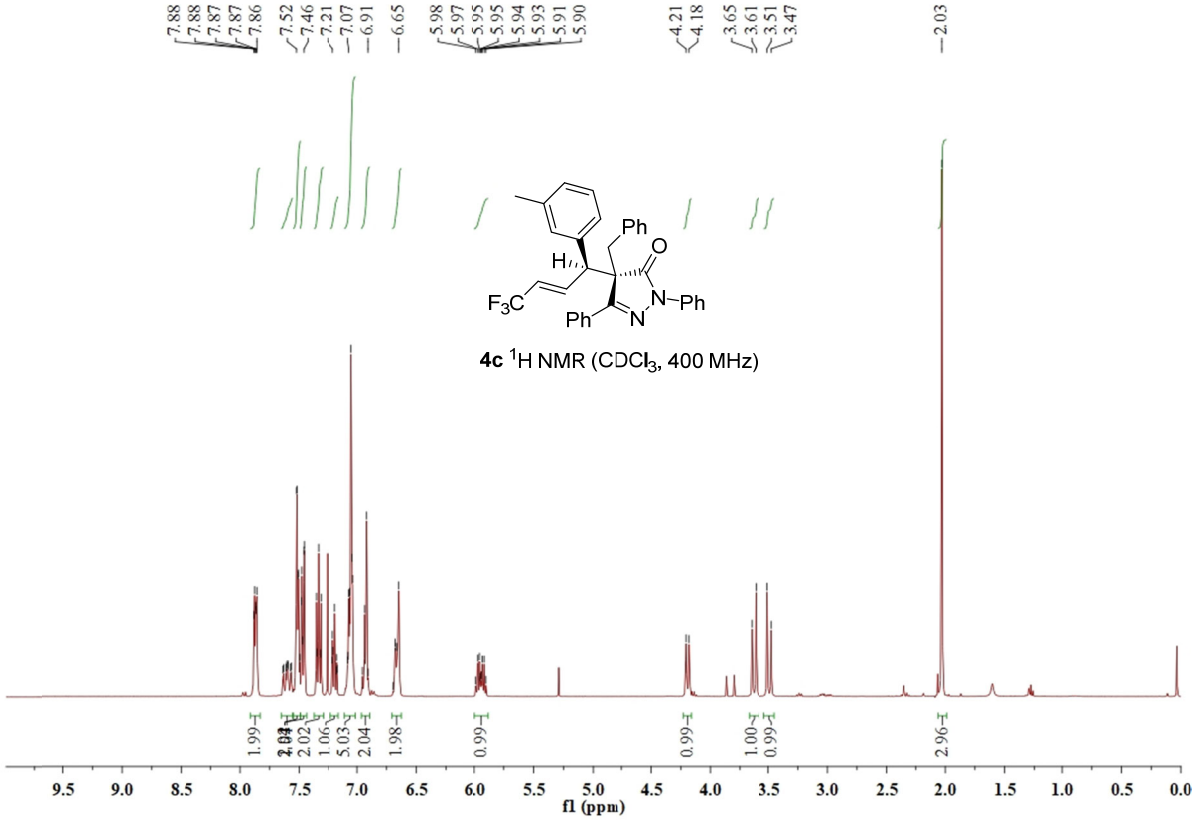


4b ^{13}C NMR ($CDCl_3$, 101 MHz)

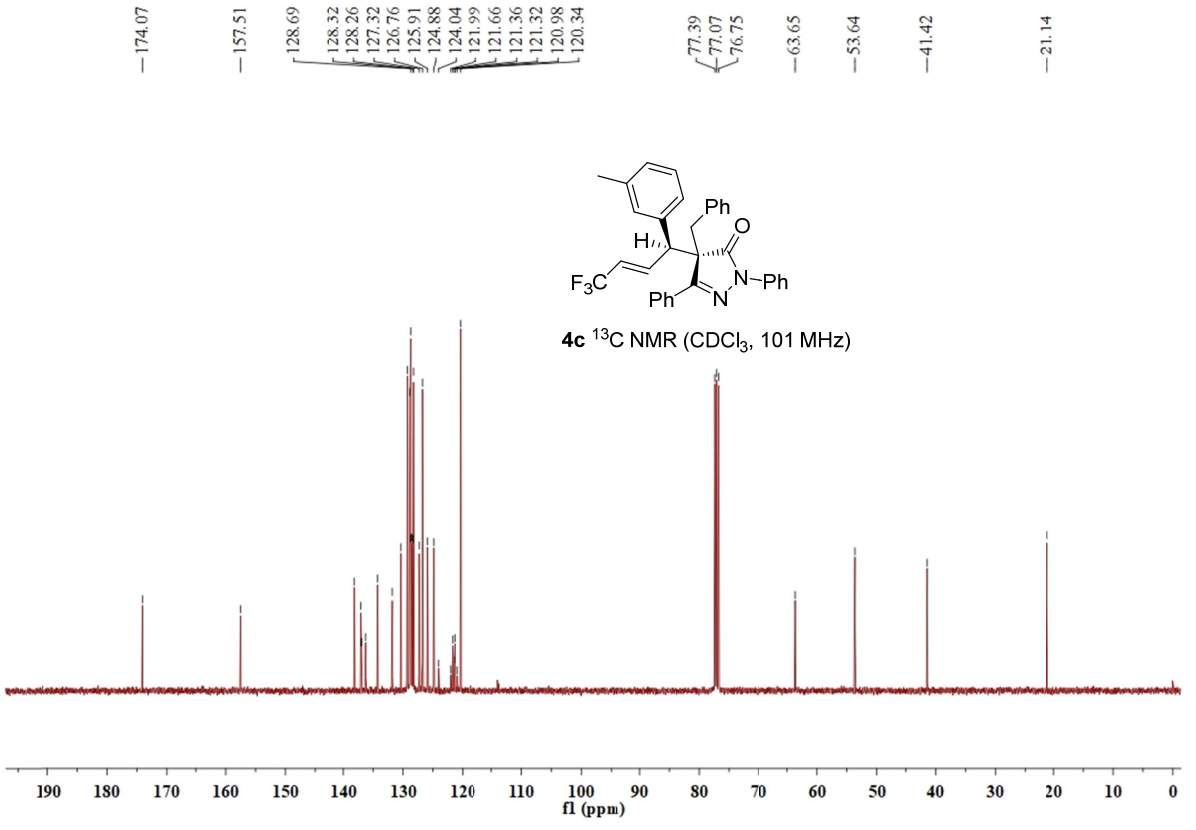


4b ^{19}F NMR ($CDCl_3$, 377 MHz)

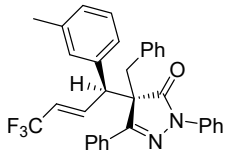




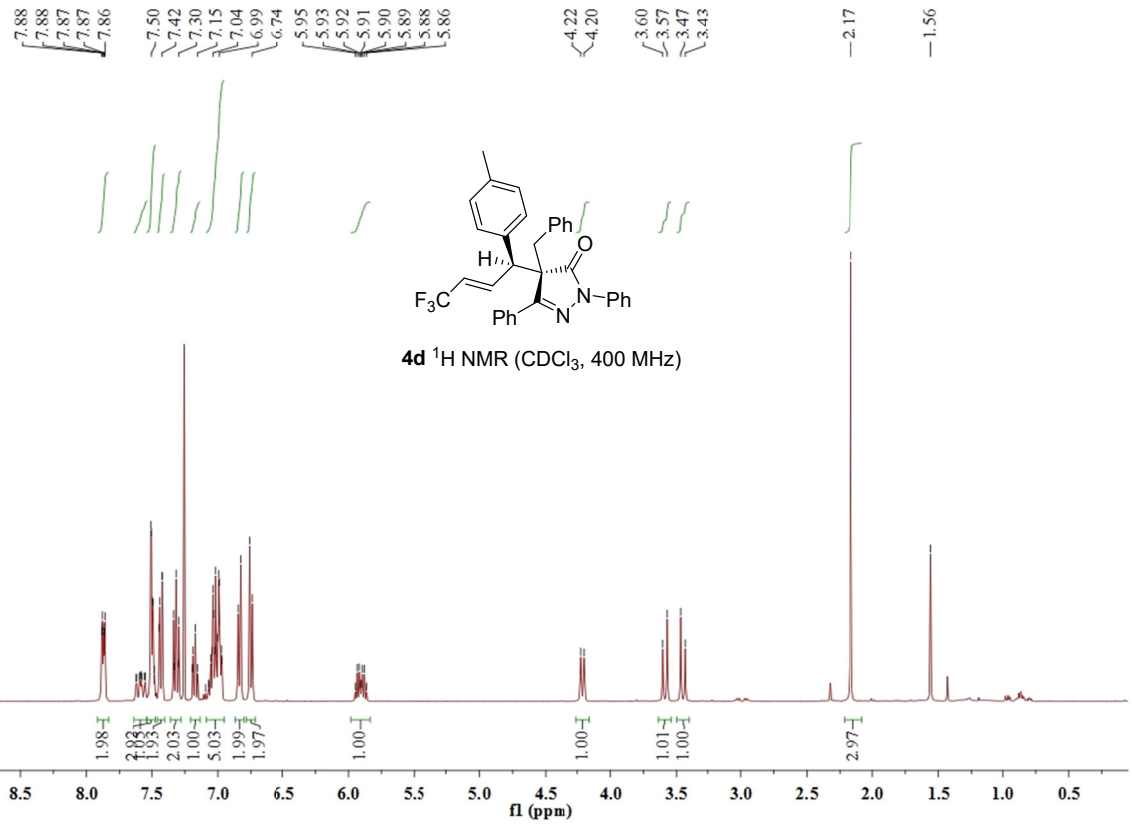
4c ^{1}H NMR ($CDCl_3$, 400 MHz)



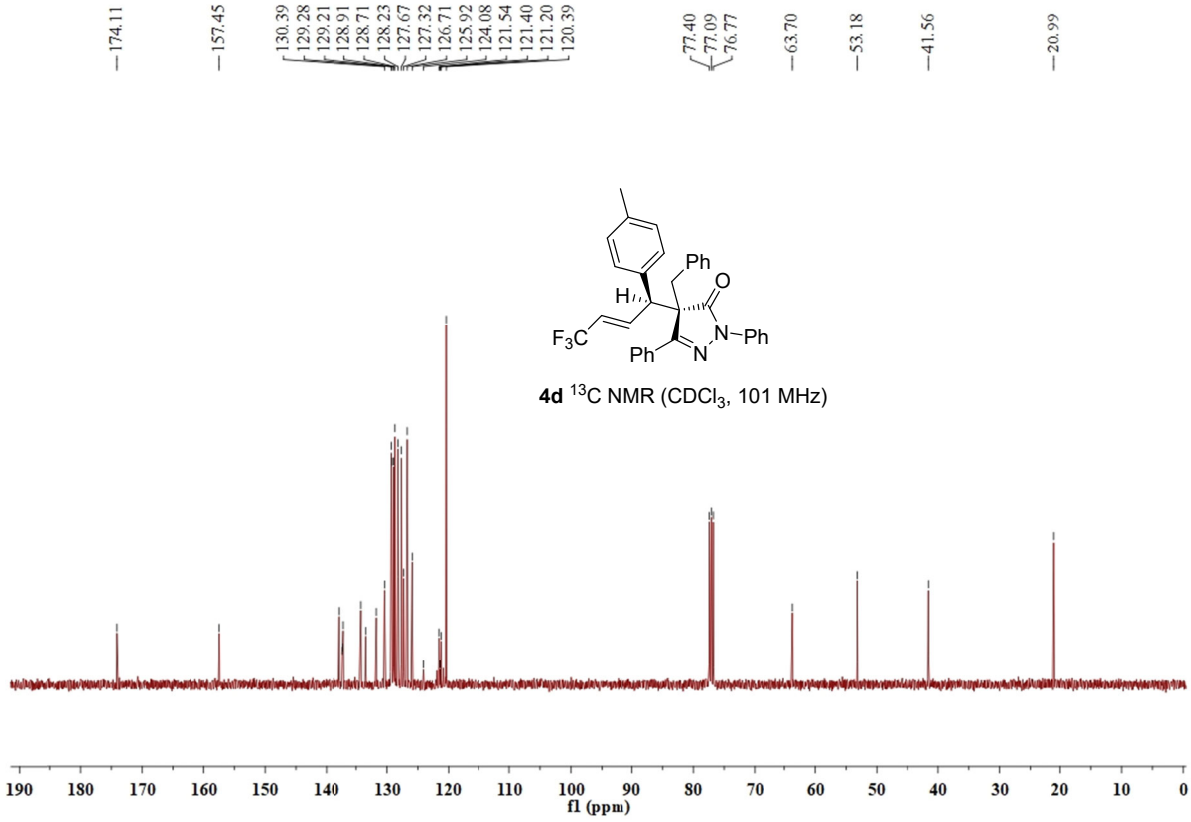
4c ^{13}C NMR ($CDCl_3$, 101 MHz)



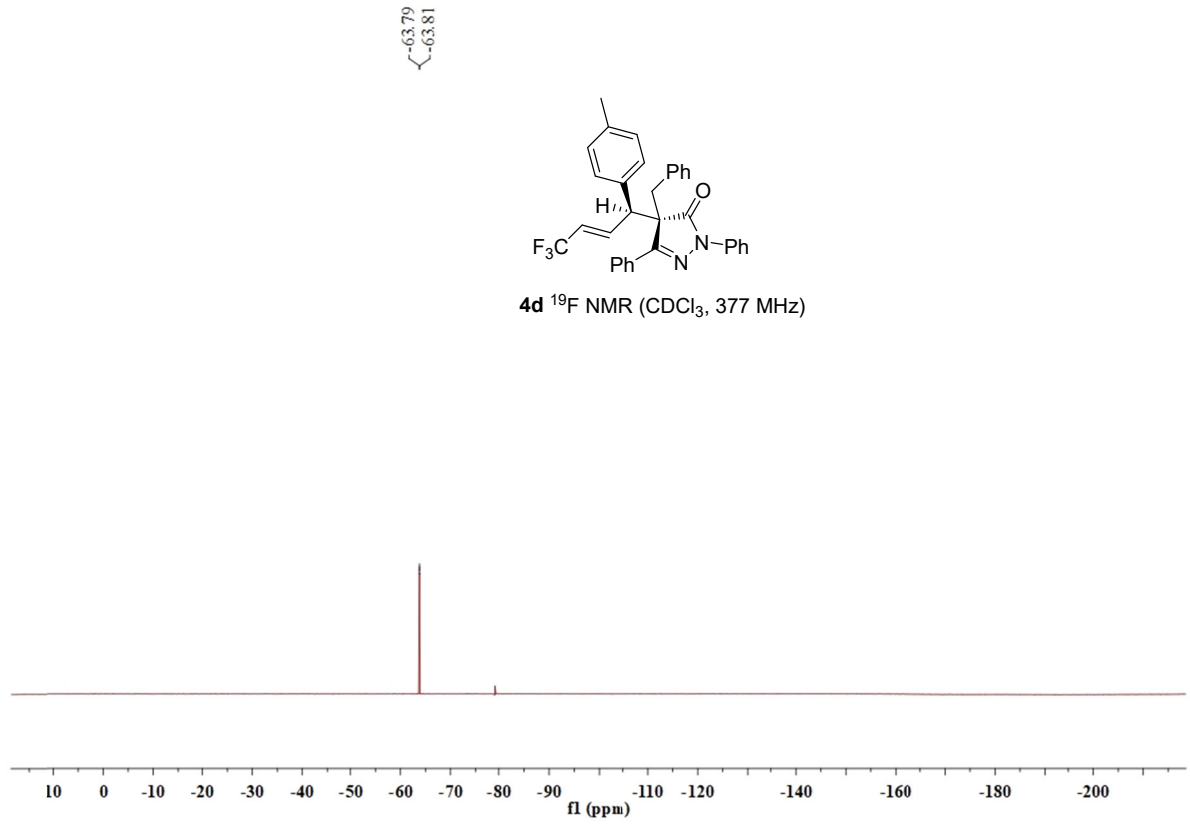
4c ^{19}F NMR ($CDCl_3$, 377 MHz)



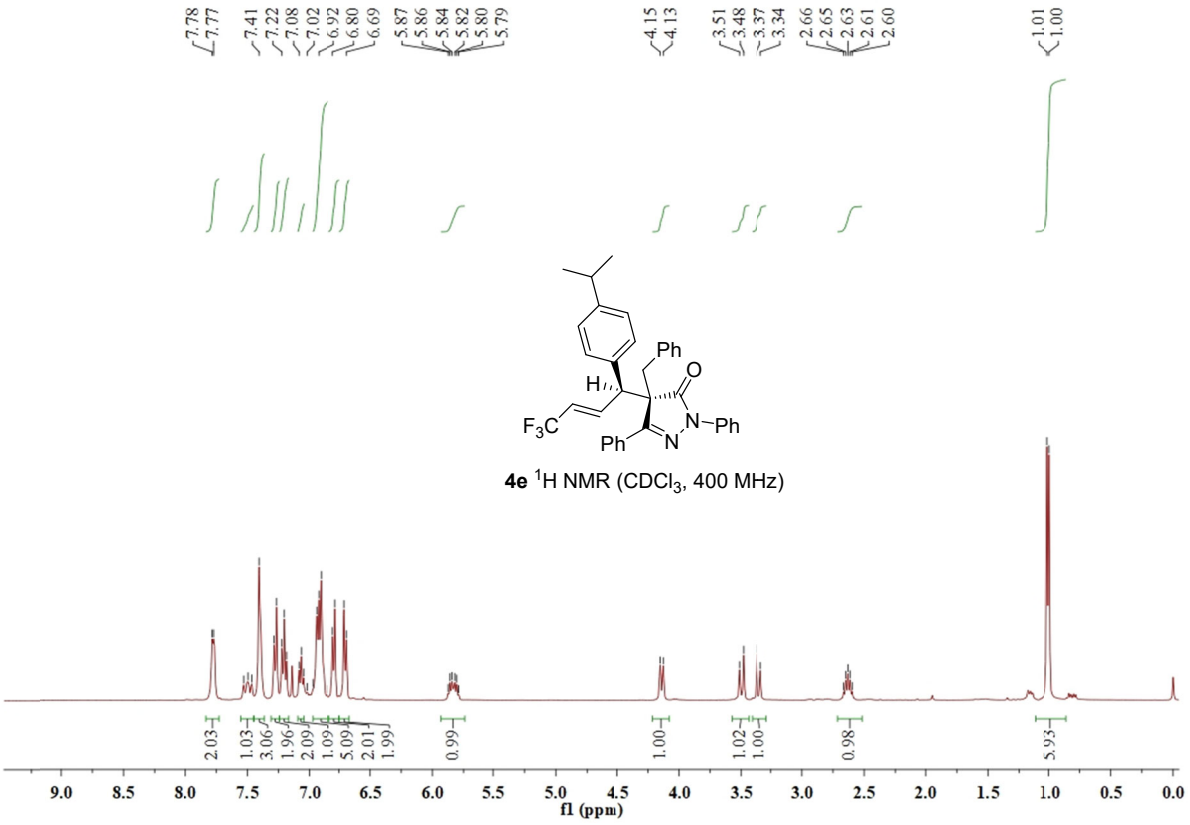
4d ^{1}H NMR ($CDCl_3$, 400 MHz)



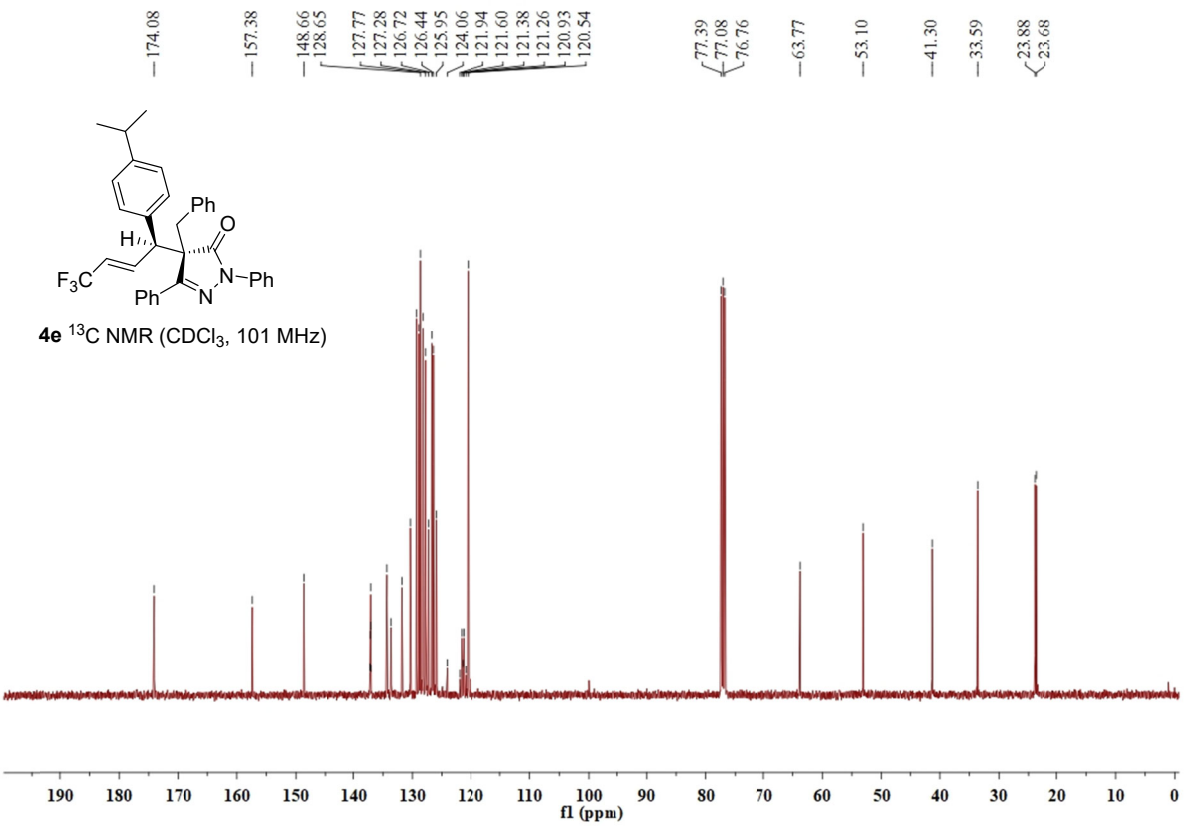
4d ^{13}C NMR ($CDCl_3$, 101 MHz)



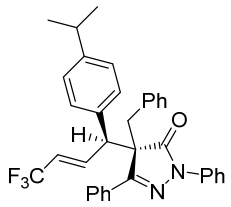
4d ^{19}F NMR ($CDCl_3$, 377 MHz)



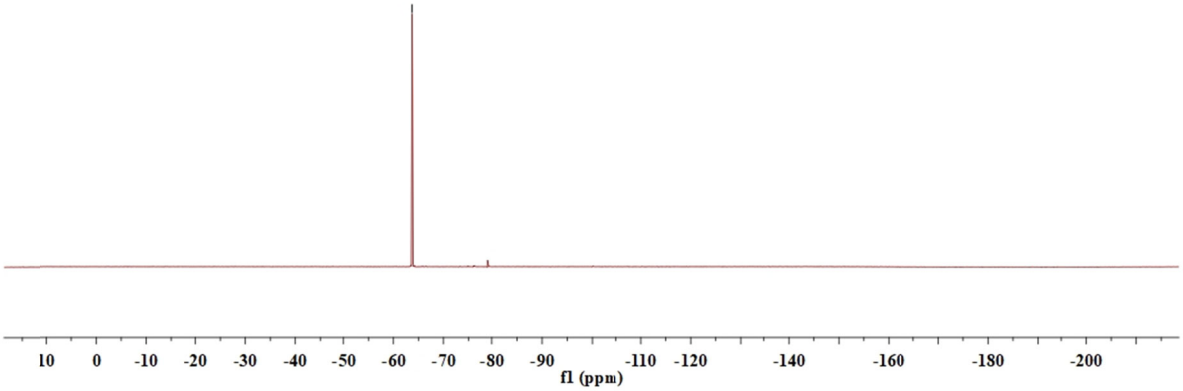
4e ^{1}H NMR ($CDCl_3$, 400 MHz)

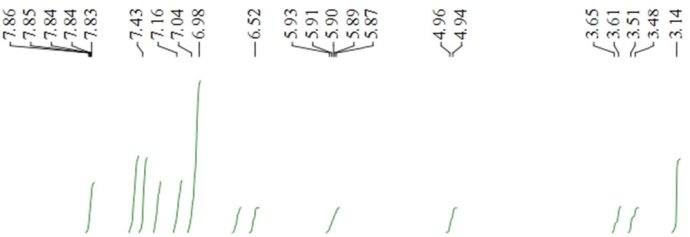


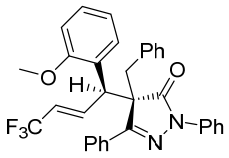
4e ^{13}C NMR ($CDCl_3$, 101 MHz)



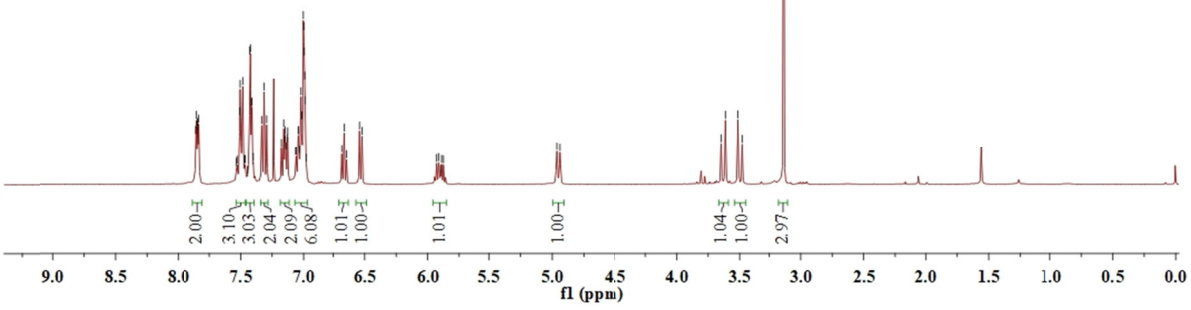
4e ^{19}F NMR ($CDCl_3$,377 MHz)

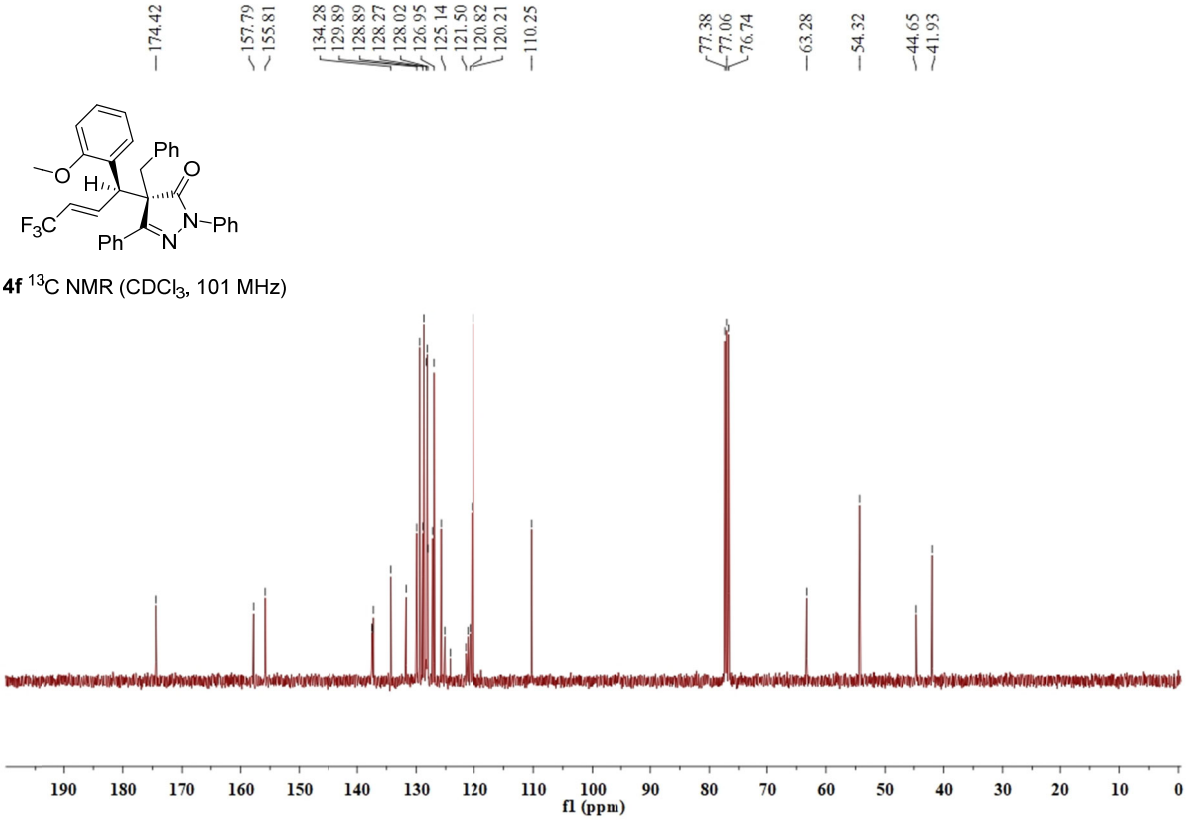




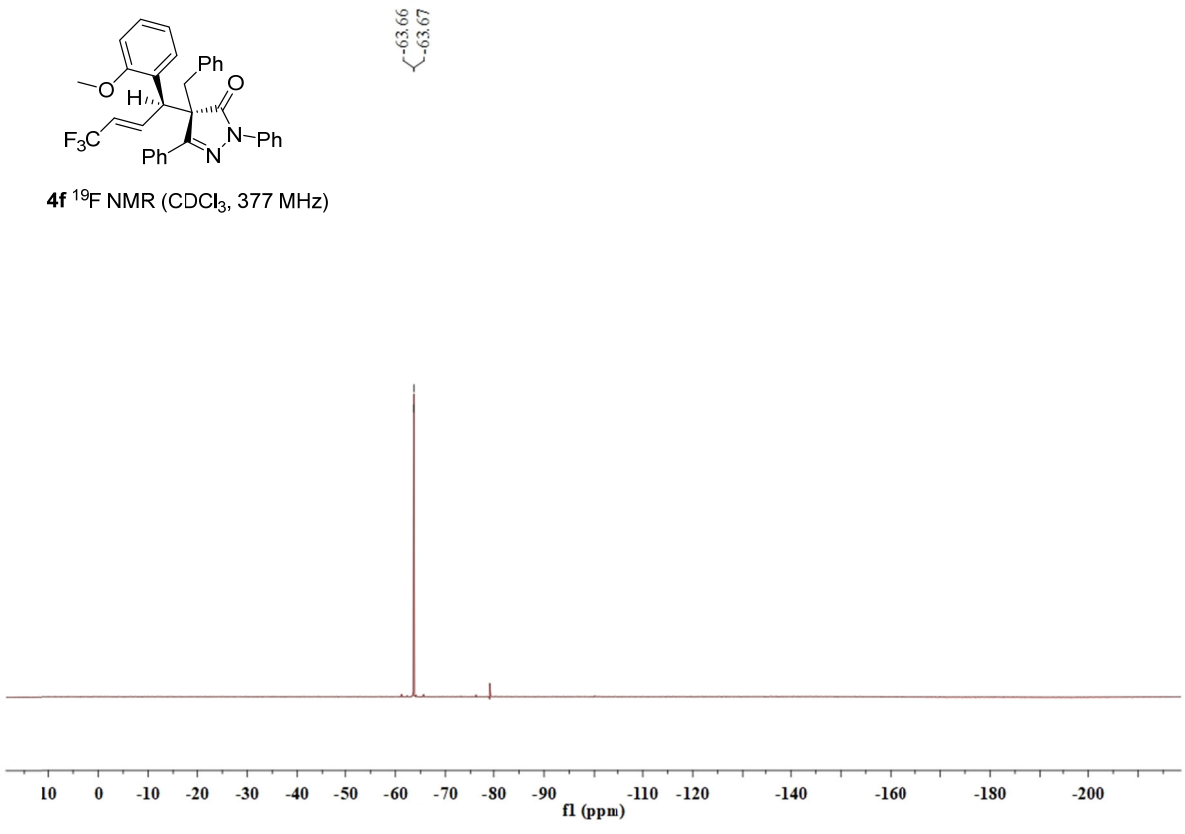


4f ^{1}H NMR ($CDCl_3$, 400 MHz)

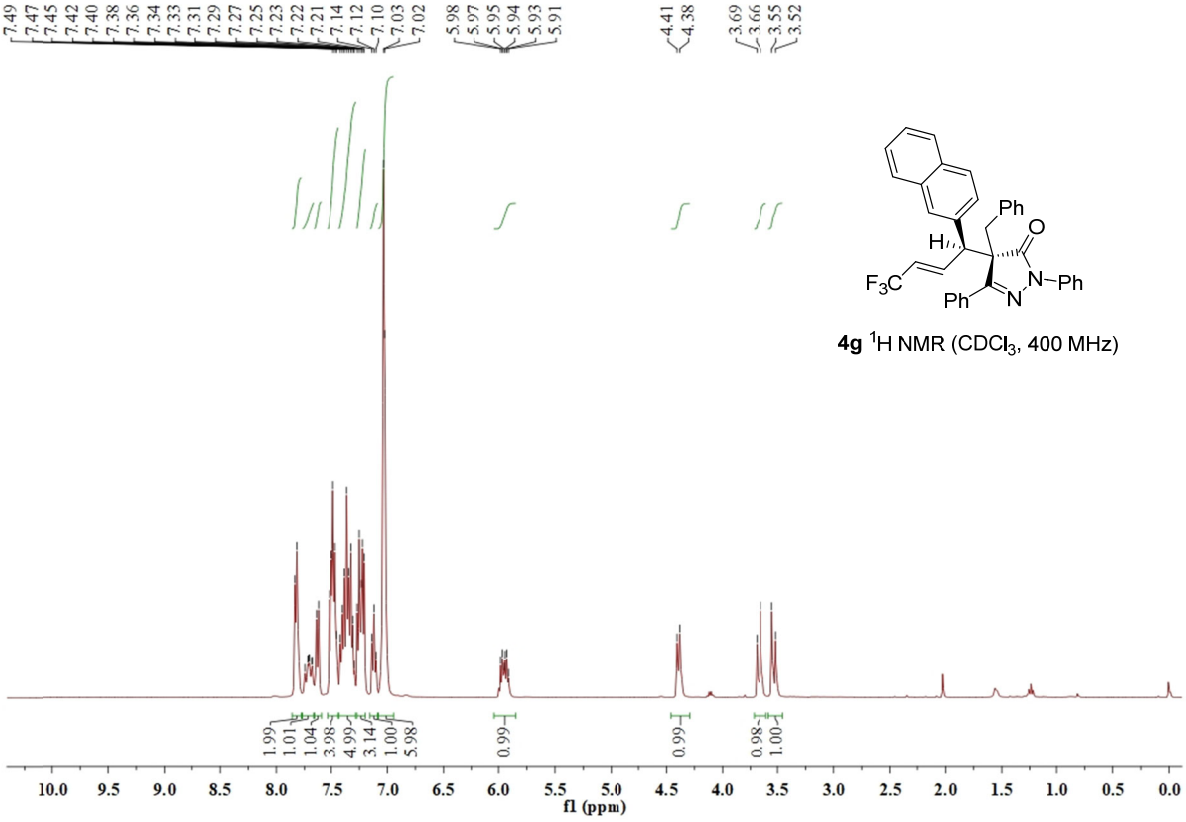




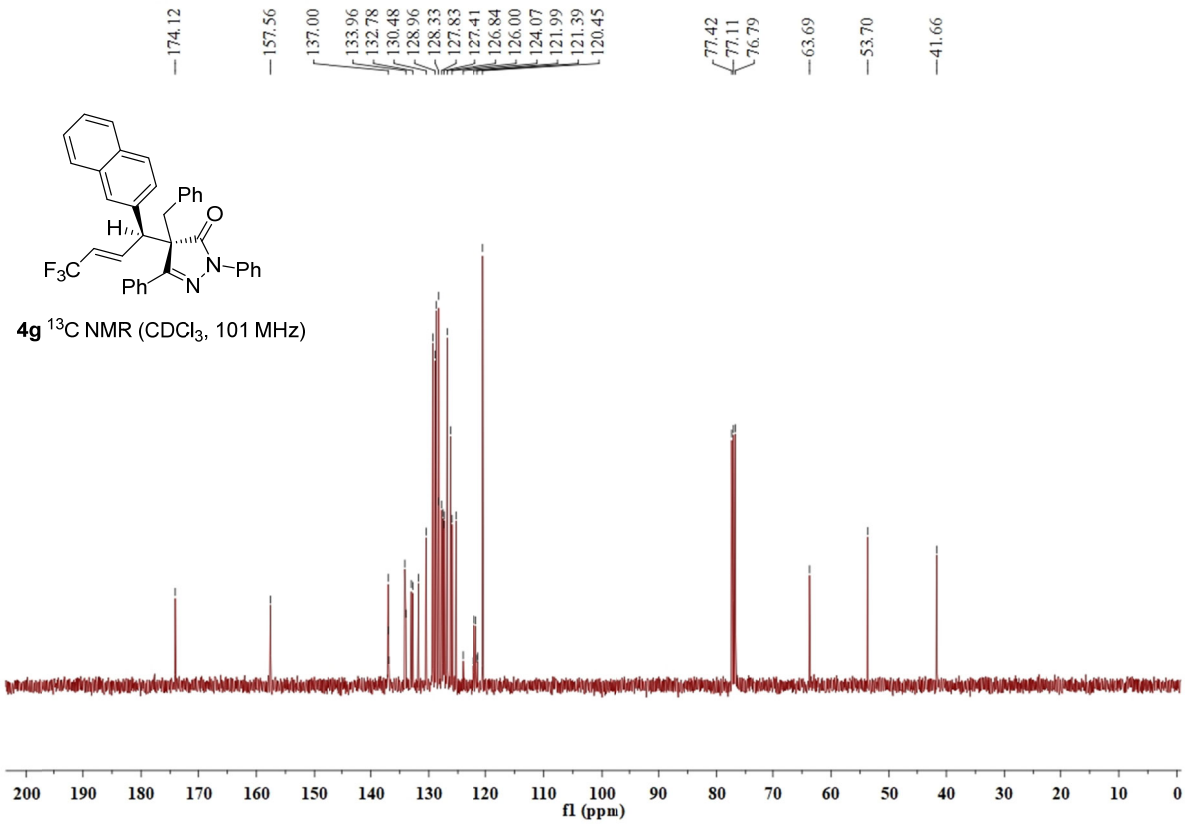
4f ^{13}C NMR ($CDCl_3$, 101 MHz)



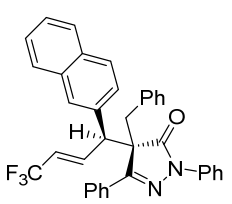
4f ^{19}F NMR ($CDCl_3$, 377 MHz)



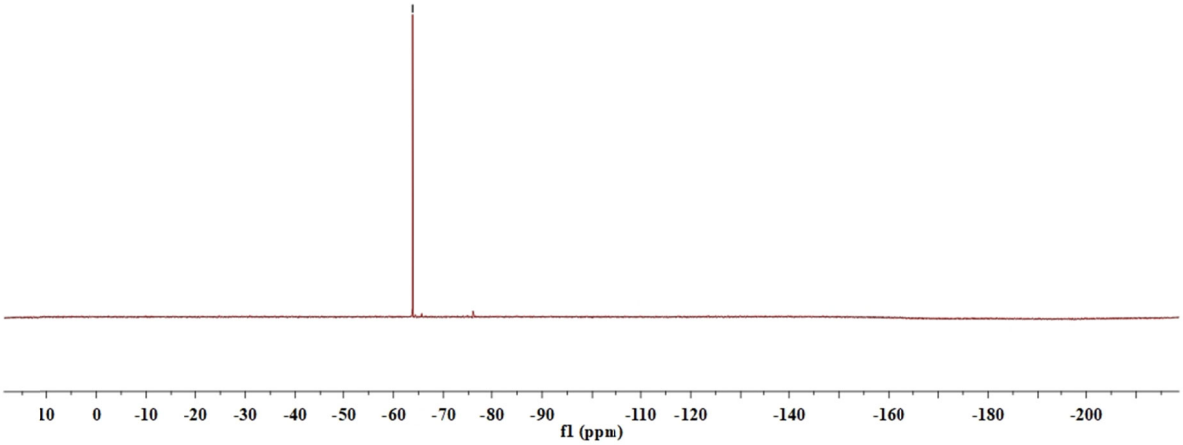
4g ^{1}H NMR ($CDCl_3$, 400 MHz)

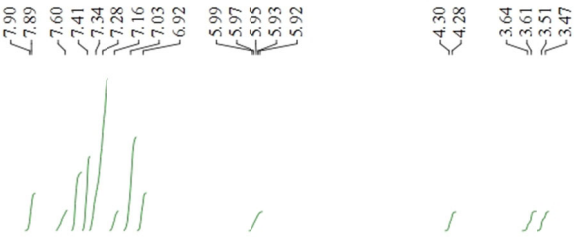


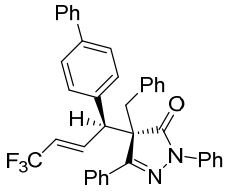
4g ^{13}C NMR ($CDCl_3$, 101 MHz)



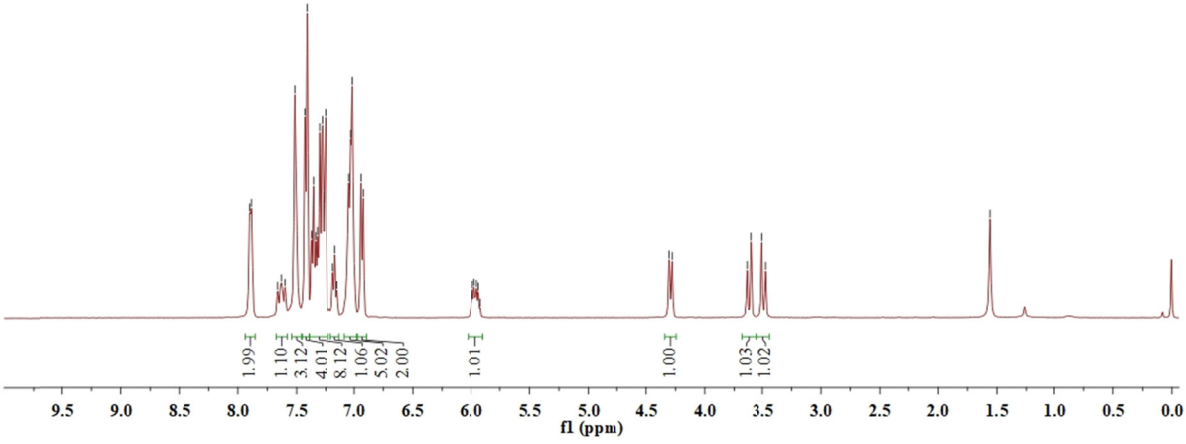
4g ^{19}F NMR ($CDCl_3$, 377 MHz)

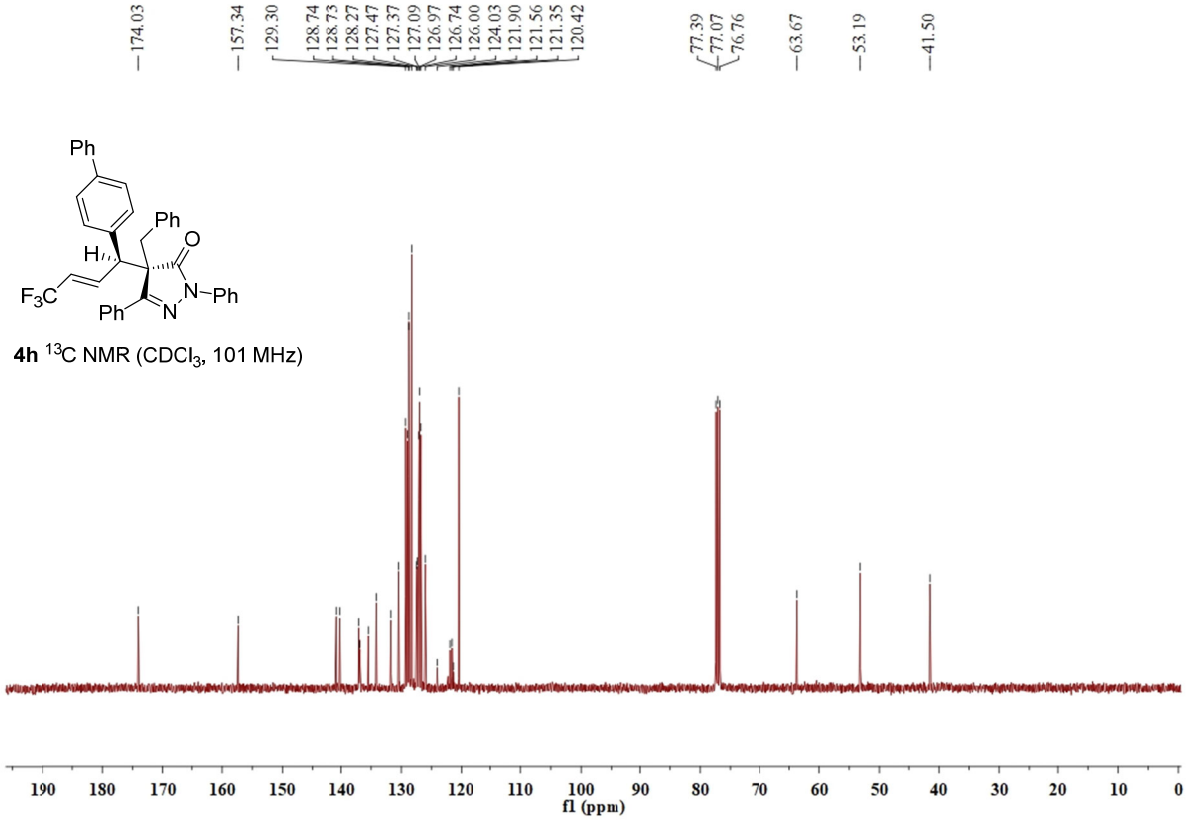




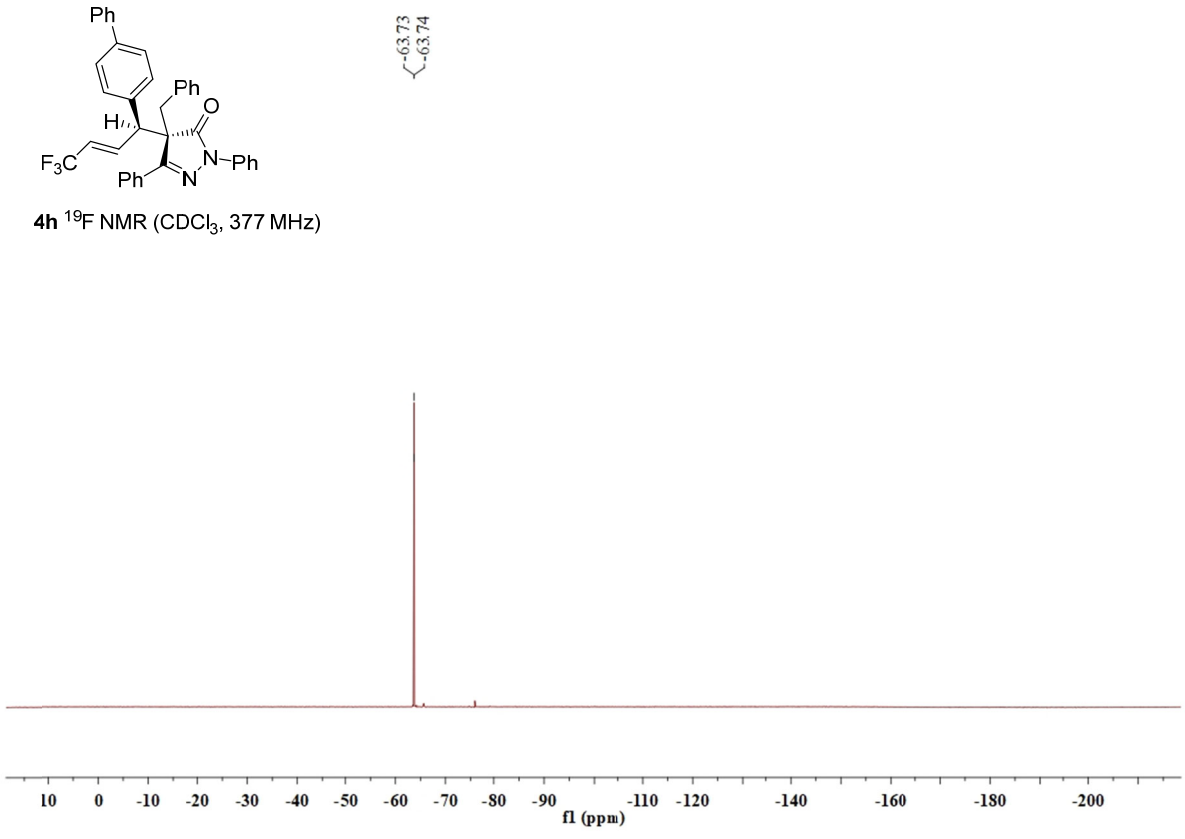


4h ^{1}H NMR ($CDCl_3$, 400 MHz)

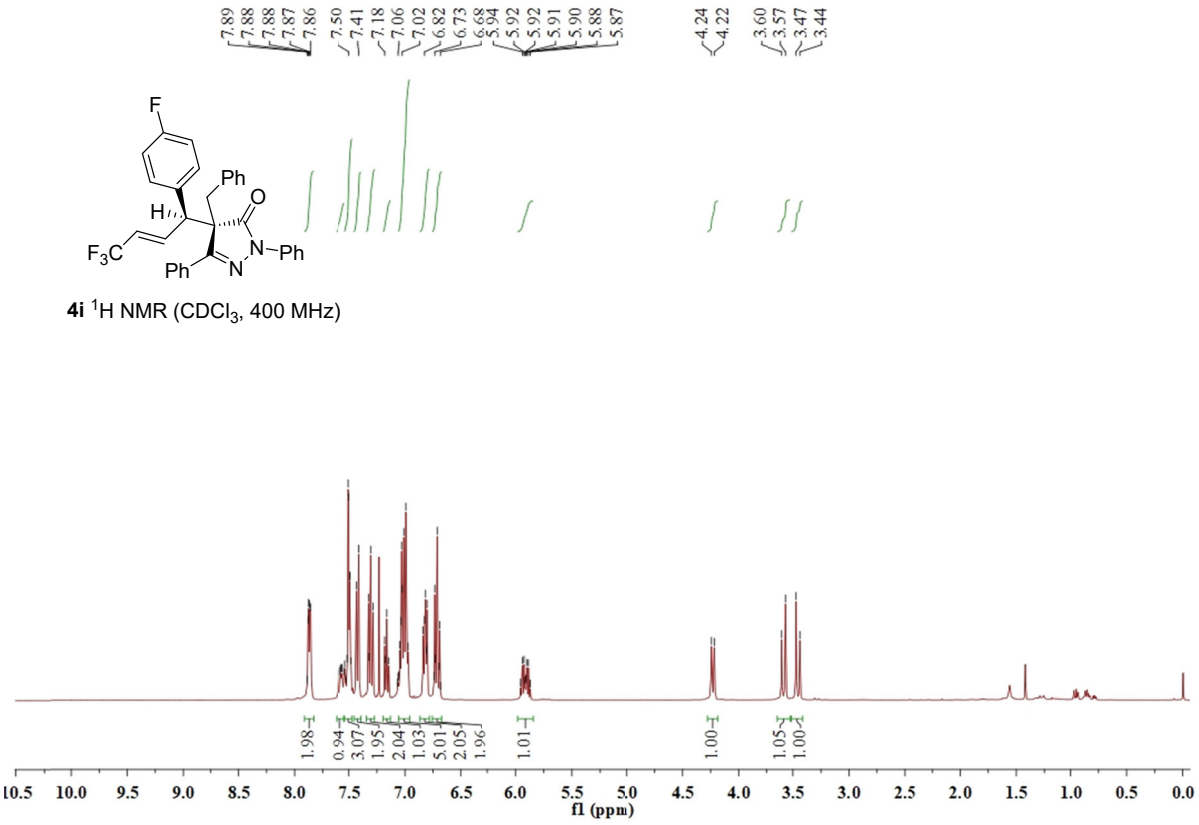




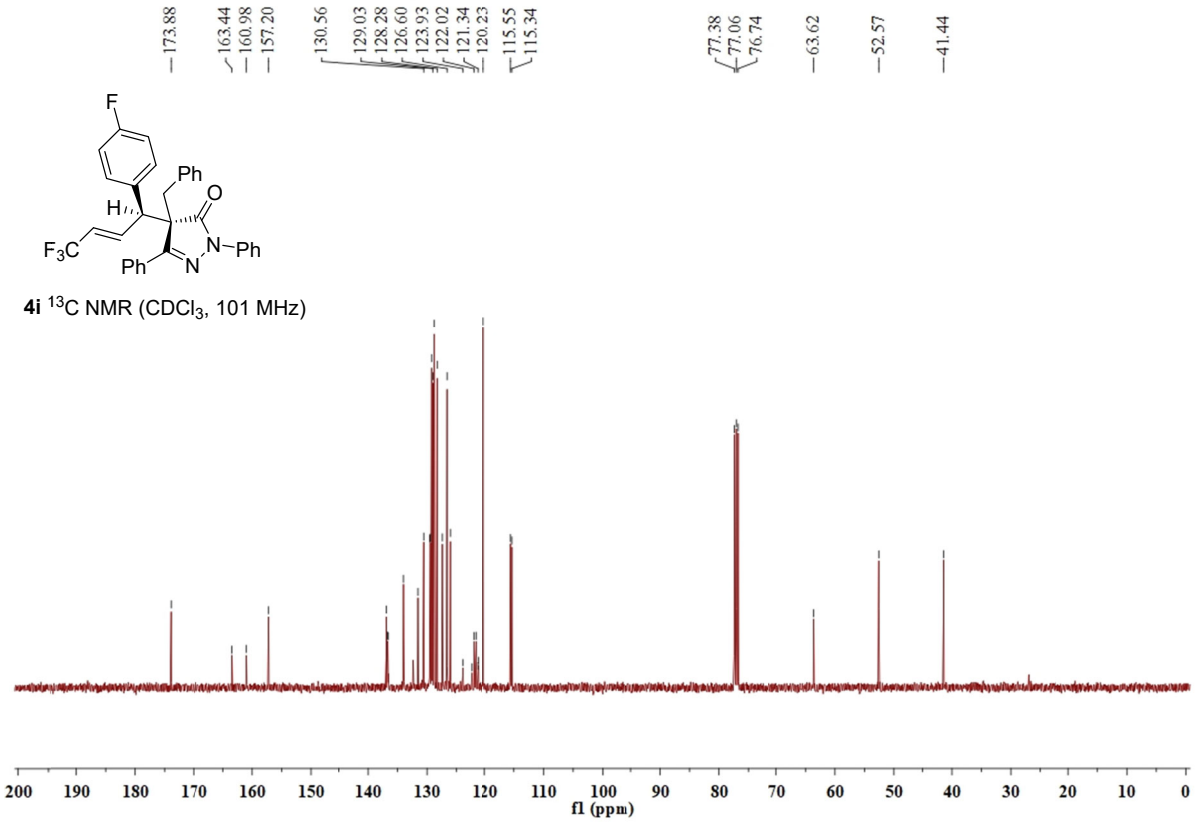
4h ^{13}C NMR ($CDCl_3$, 101 MHz)



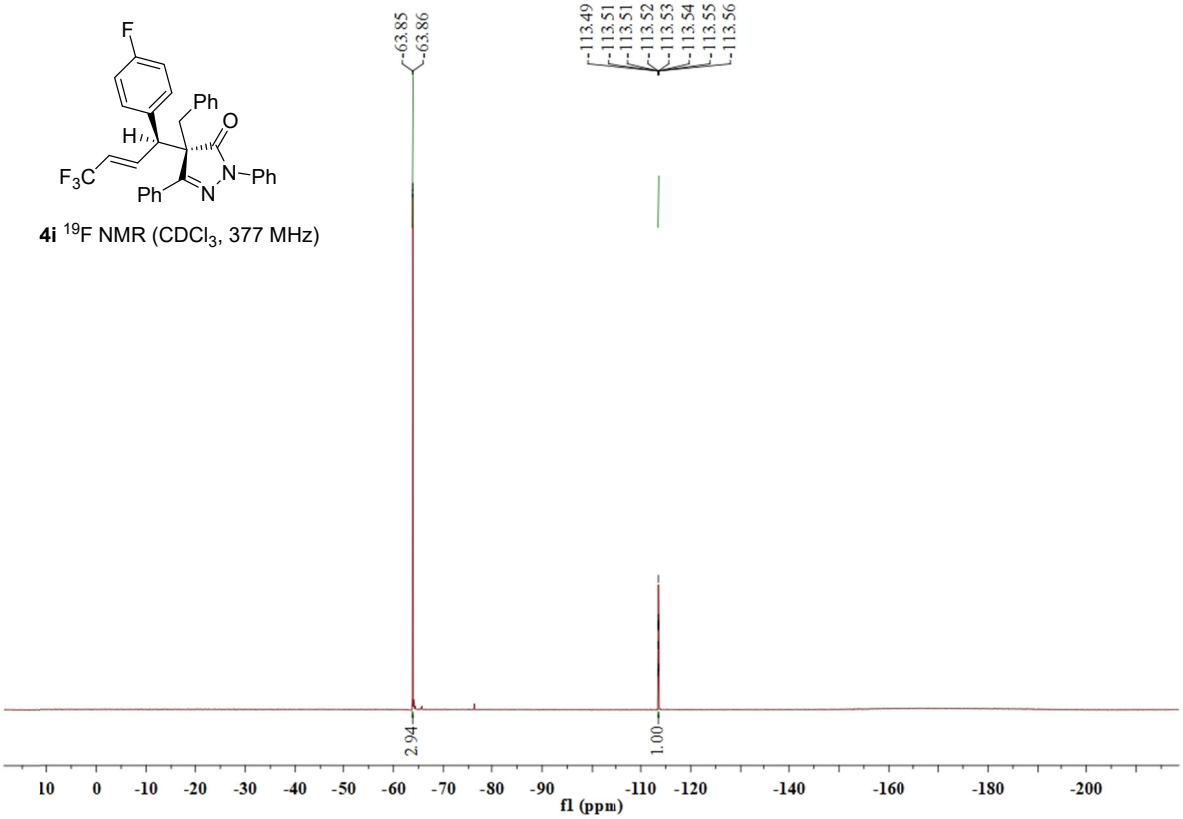
4h ^{19}F NMR ($CDCl_3$, 377 MHz)



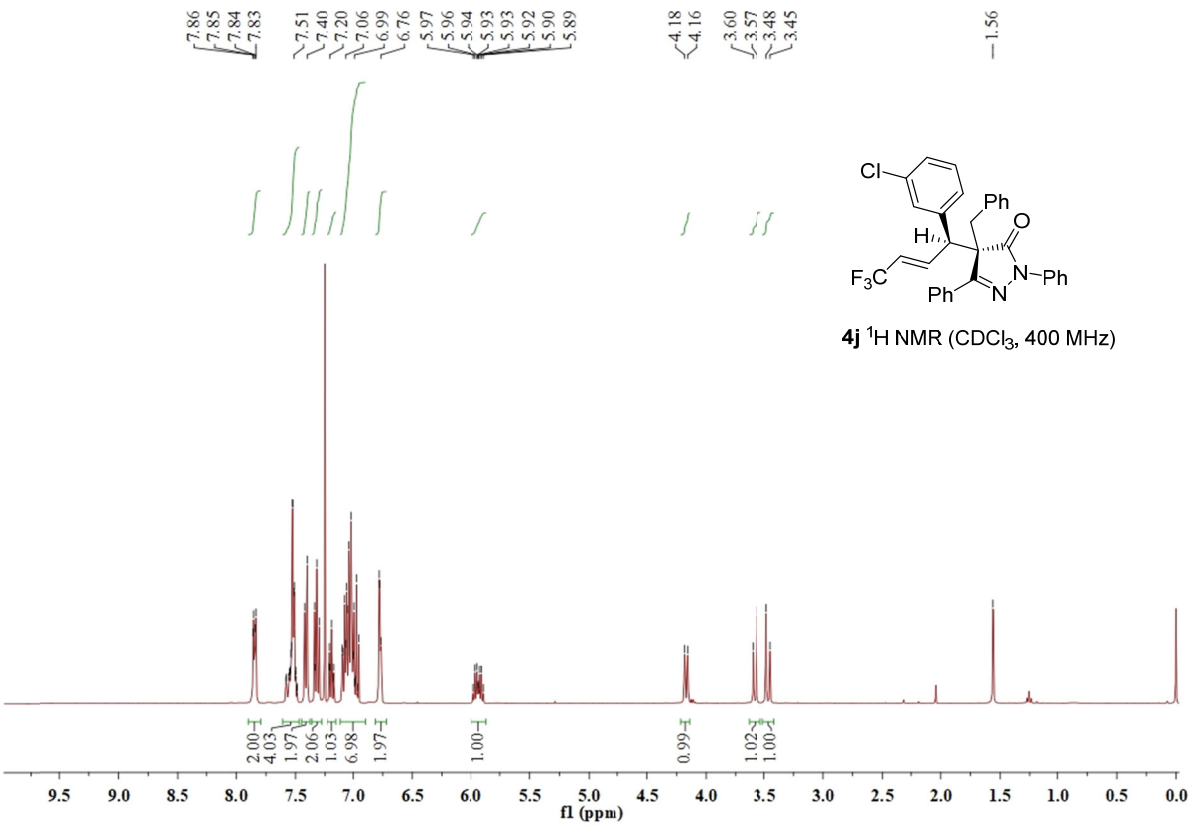
4i ^{1}H NMR ($CDCl_3$, 400 MHz)



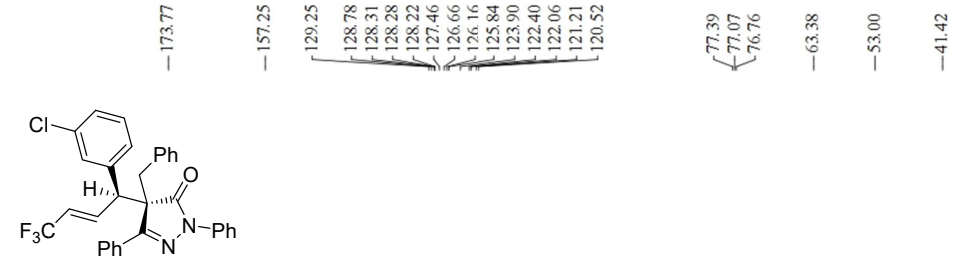
4i ^{13}C NMR ($CDCl_3$, 101 MHz)



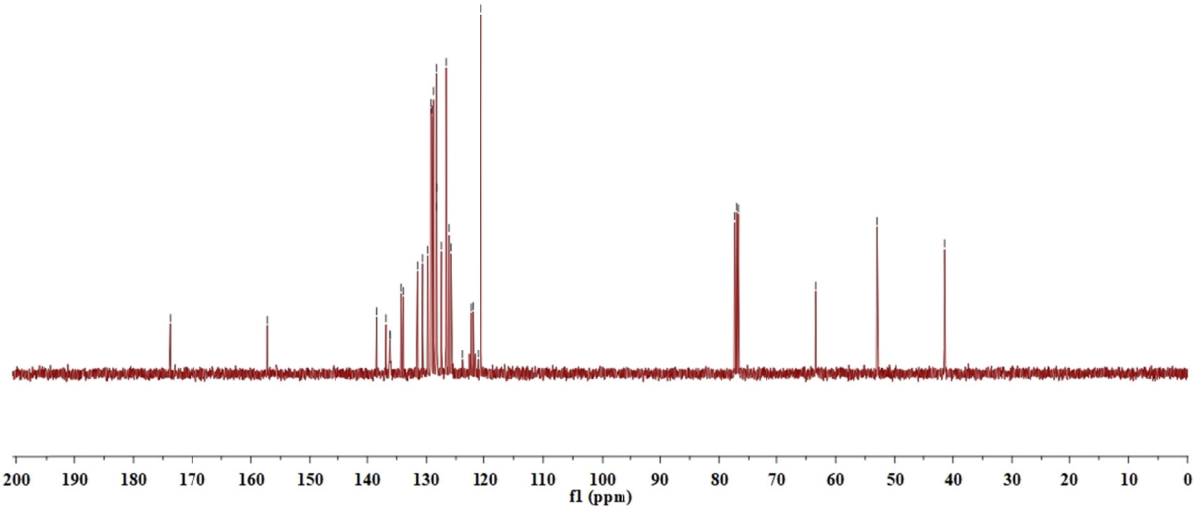
4i ^{19}F NMR ($CDCl_3$, 377 MHz)

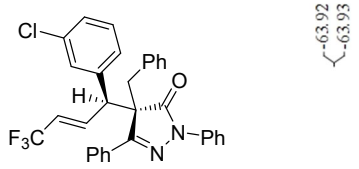


4j ^{1}H NMR ($CDCl_3$, 400 MHz)

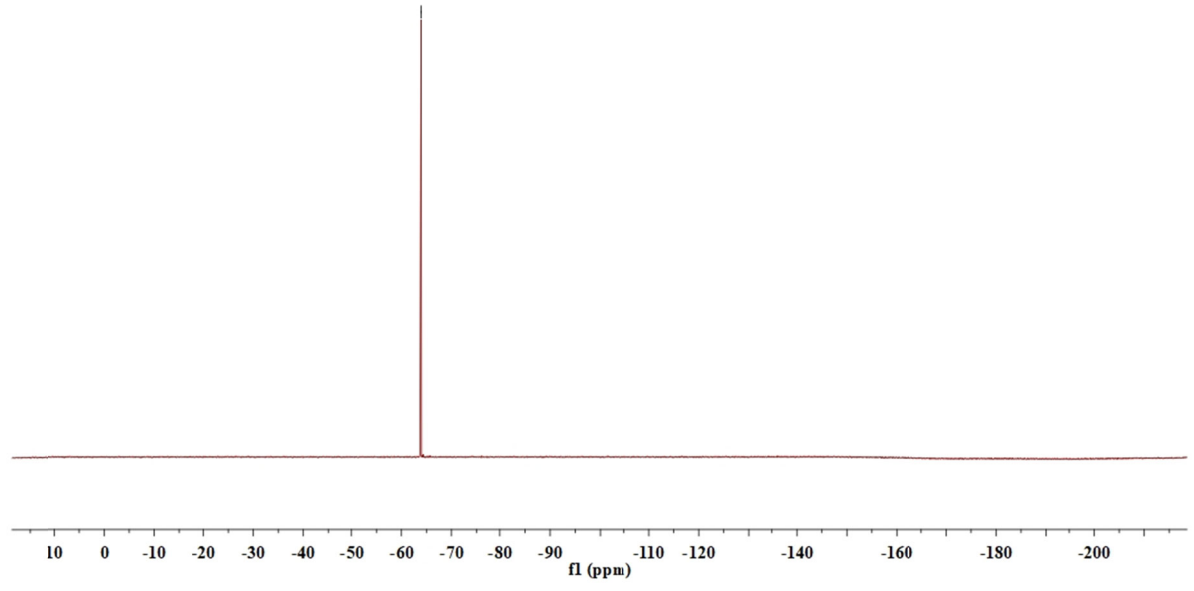


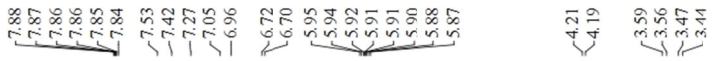
4j ^{13}C NMR ($CDCl_3$, 101 MHz)

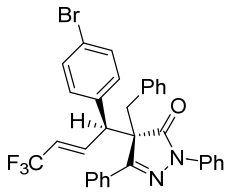




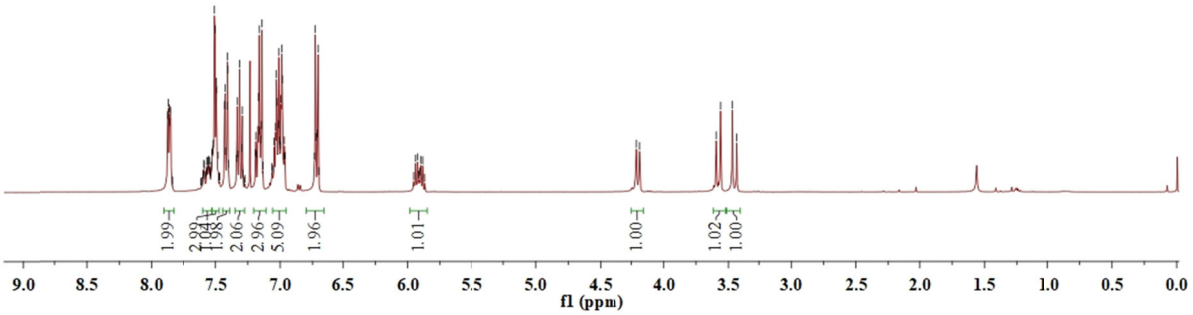
4j ^{19}F NMR ($CDCl_3$, 377 MHz)

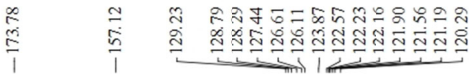


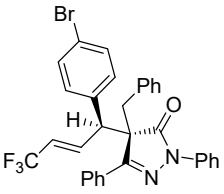




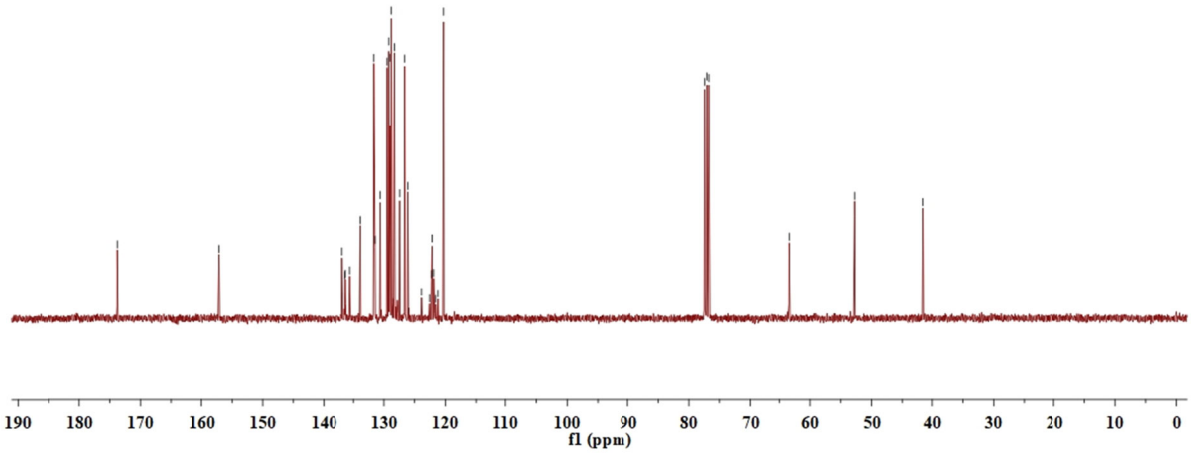
4k ^{1}H NMR ($CDCl_3$, 400 MHz)

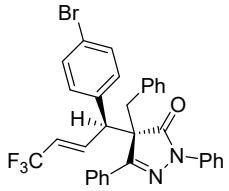




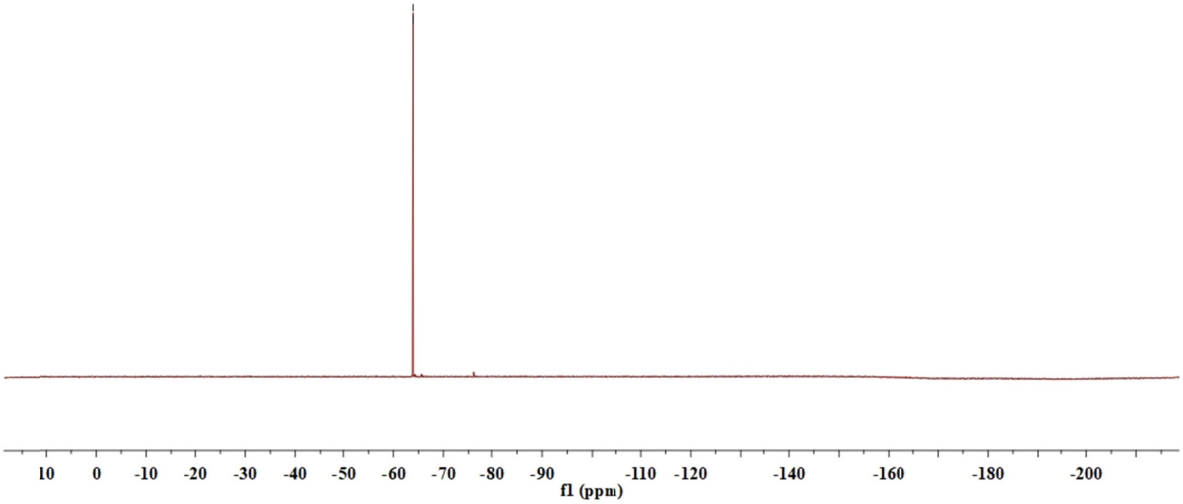


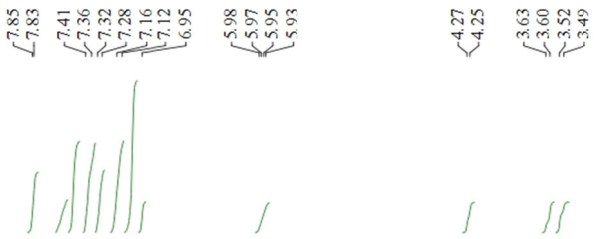
4k ^{13}C NMR ($CDCl_3$, 101 MHz)

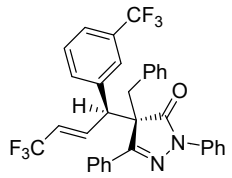




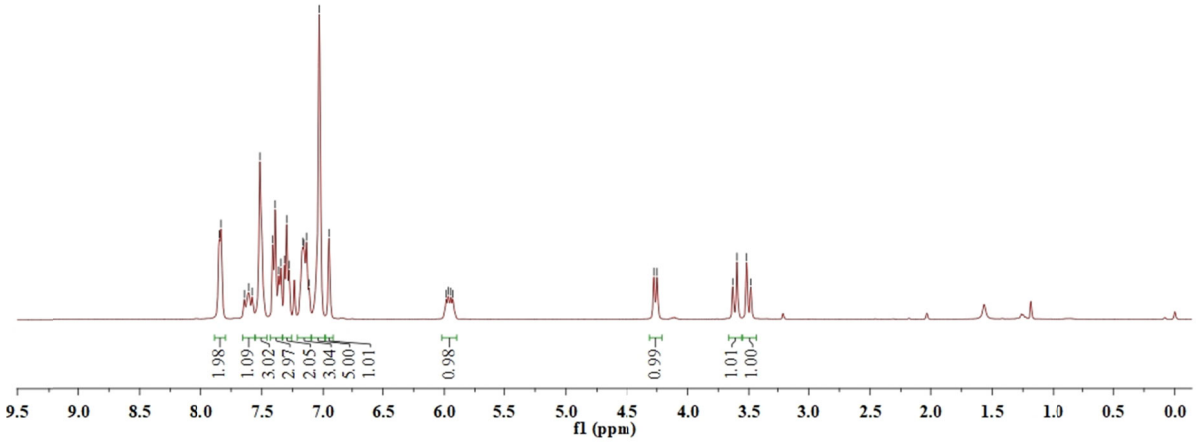
4k ^{19}F NMR ($CDCl_3$, 377 MHz)

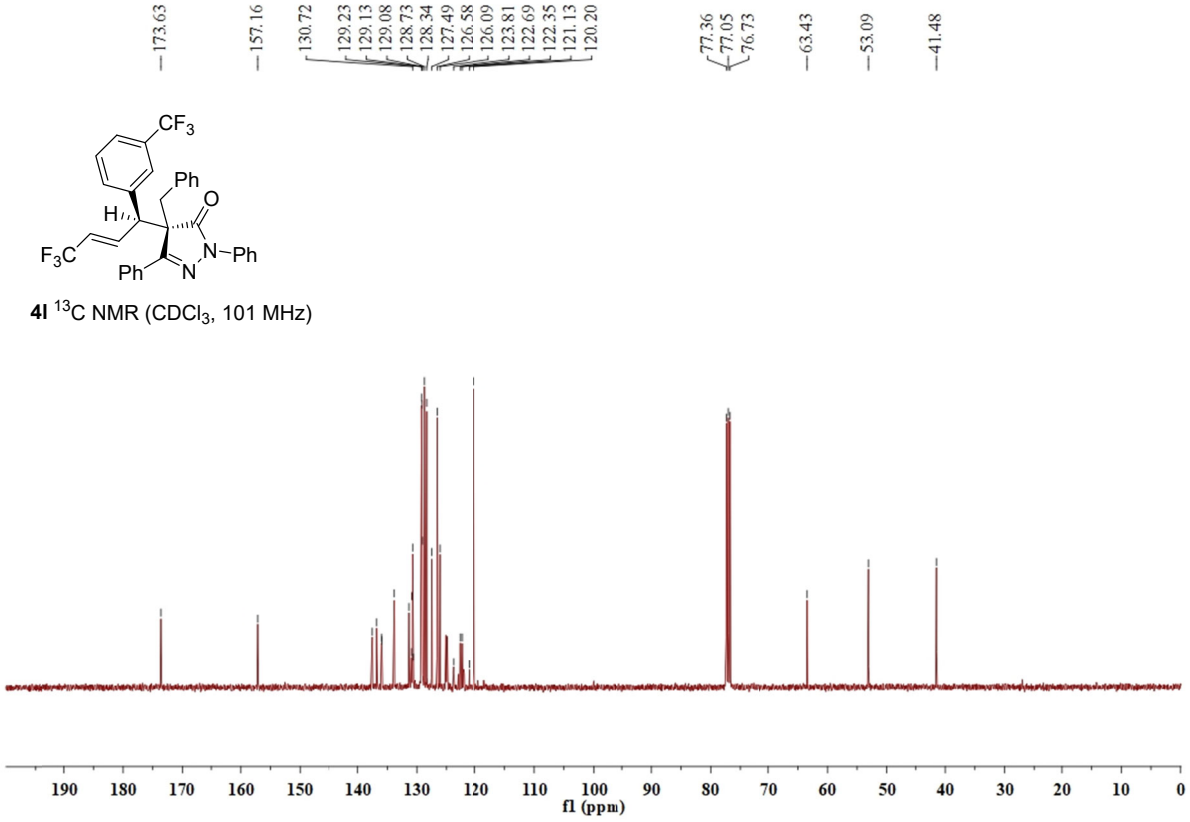




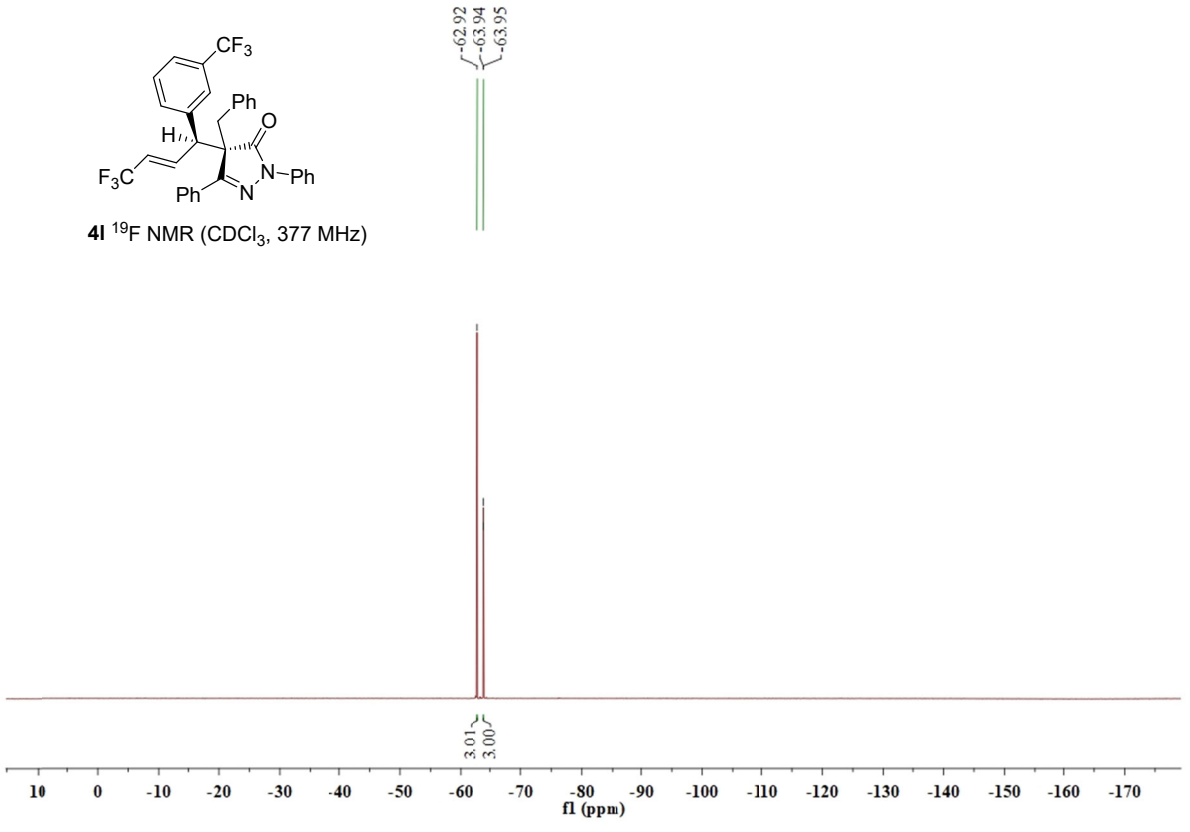


4l ^{1}H NMR ($CDCl_3$, 400 MHz)

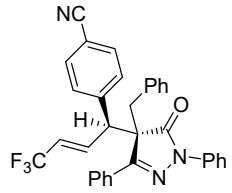




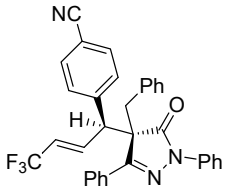
4l ^{13}C NMR ($CDCl_3$, 101 MHz)



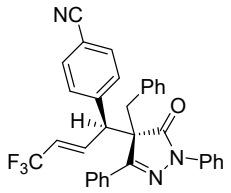
4l ^{19}F NMR ($CDCl_3$, 377 MHz)



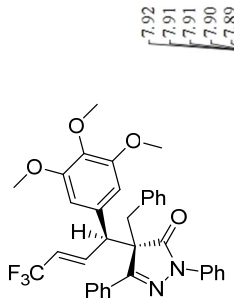
4m ^{1}H NMR ($CDCl_3$, 400 MHz)



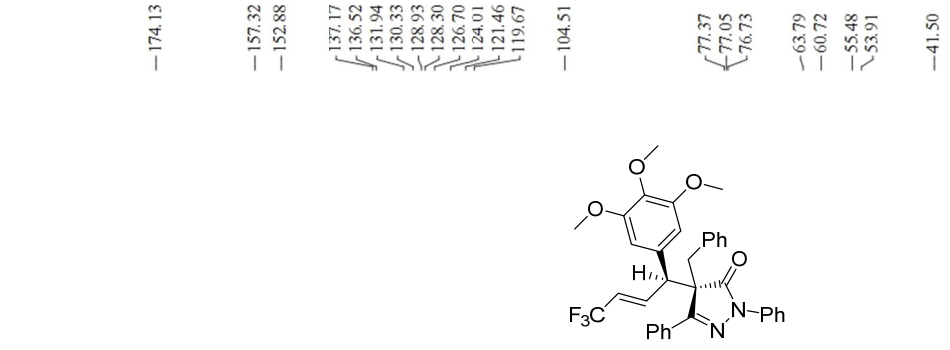
4m ^{13}C NMR ($CDCl_3$, 101 MHz)



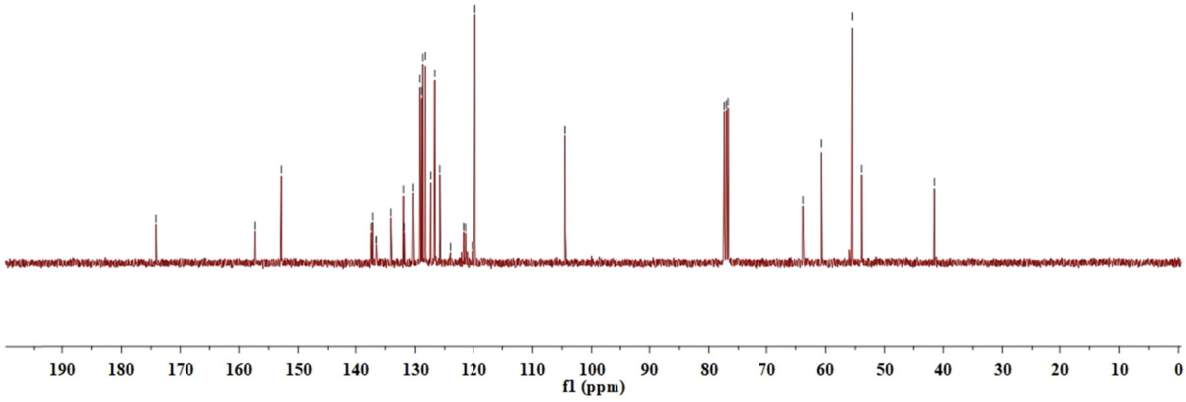
4m ^{19}F NMR ($CDCl_3$, 377 MHz)

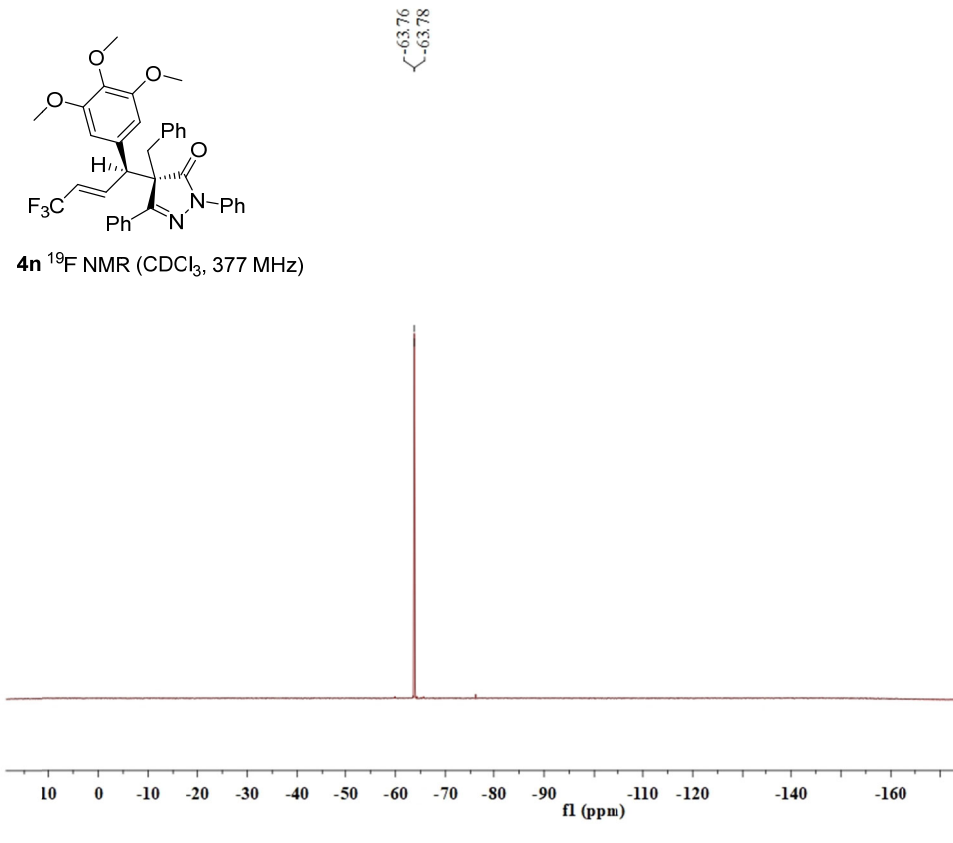


4n ^{1}H NMR ($CDCl_3$, 400 MHz)

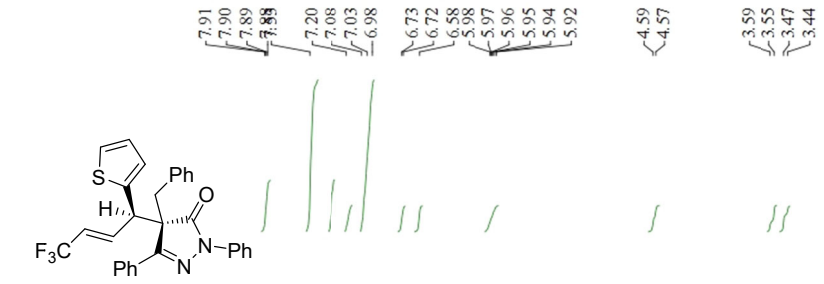


4n ^{13}C NMR ($CDCl_3$, 101 MHz)

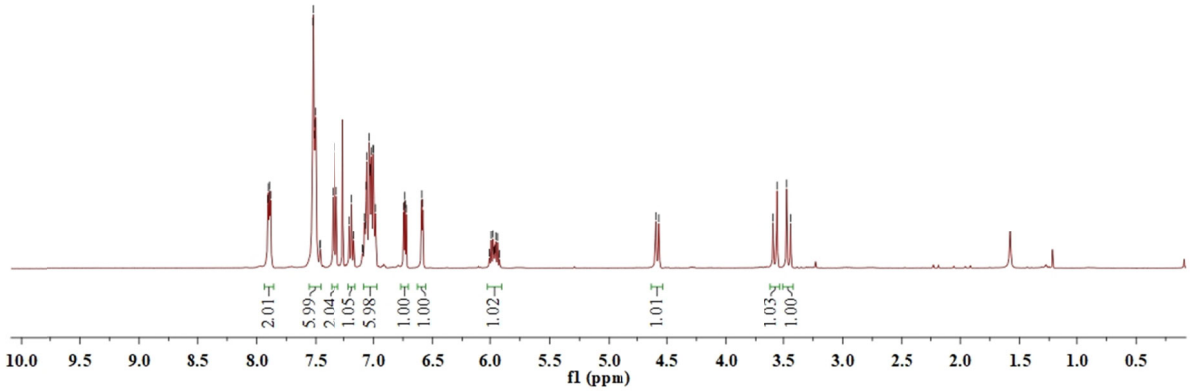


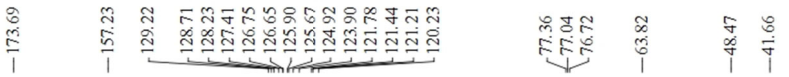


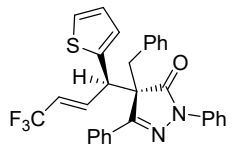
4n ^{19}F NMR ($CDCl_3$, 377 MHz)



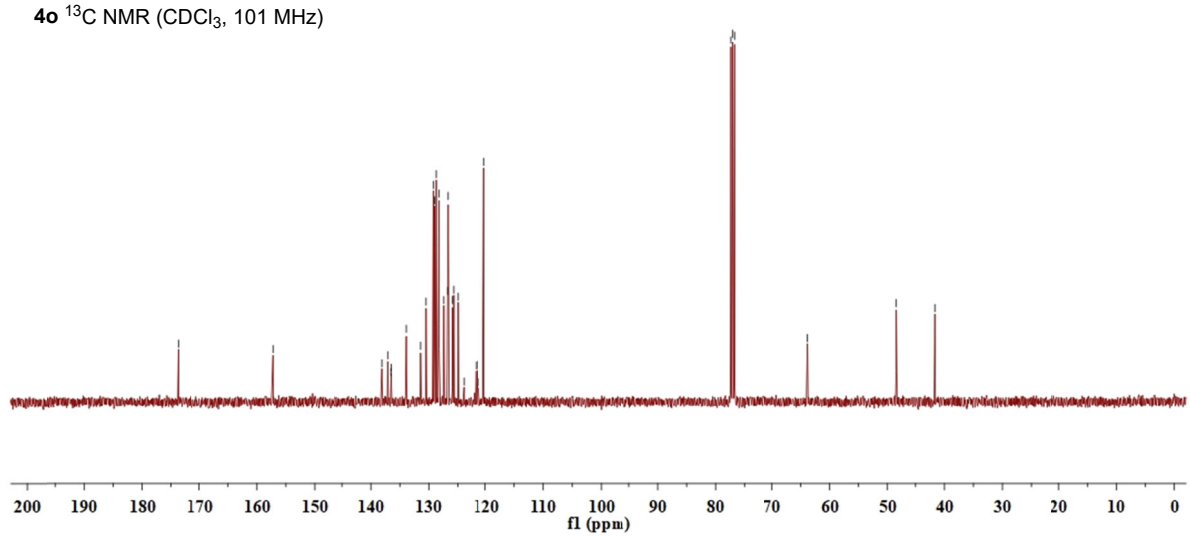
4o ^{1}H NMR ($CDCl_3$, 400 MHz)

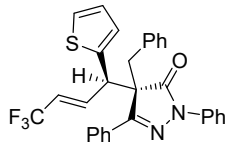




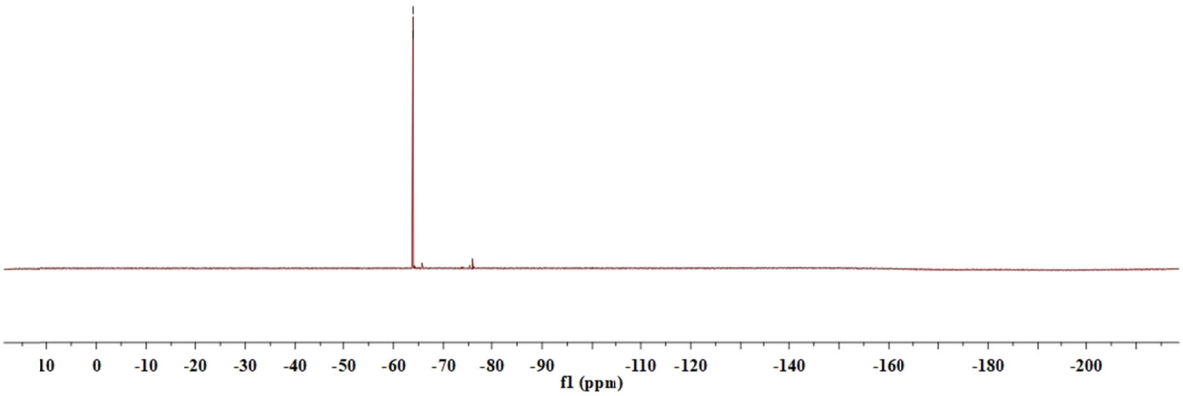


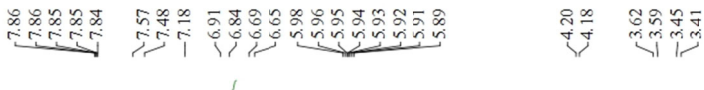
4o ^{13}C NMR ($CDCl_3$, 101 MHz)

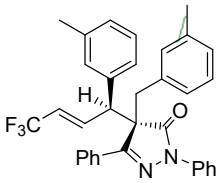




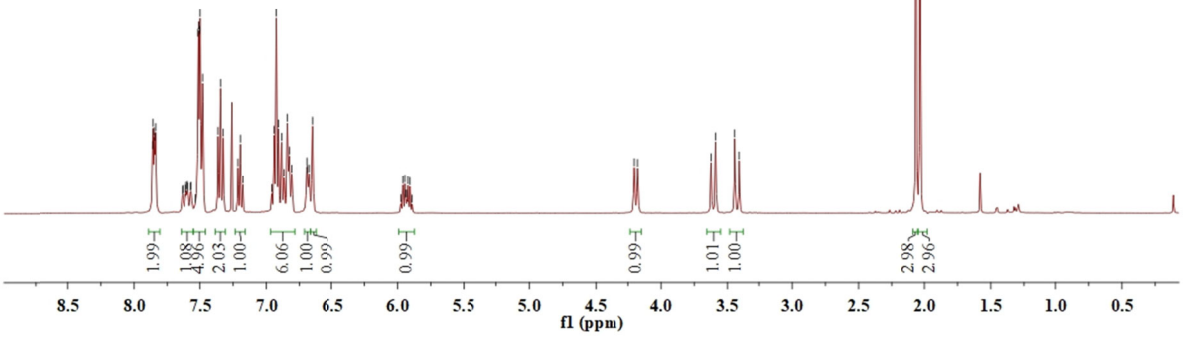
4o ^{19}F NMR ($CDCl_3$, 377 MHz)

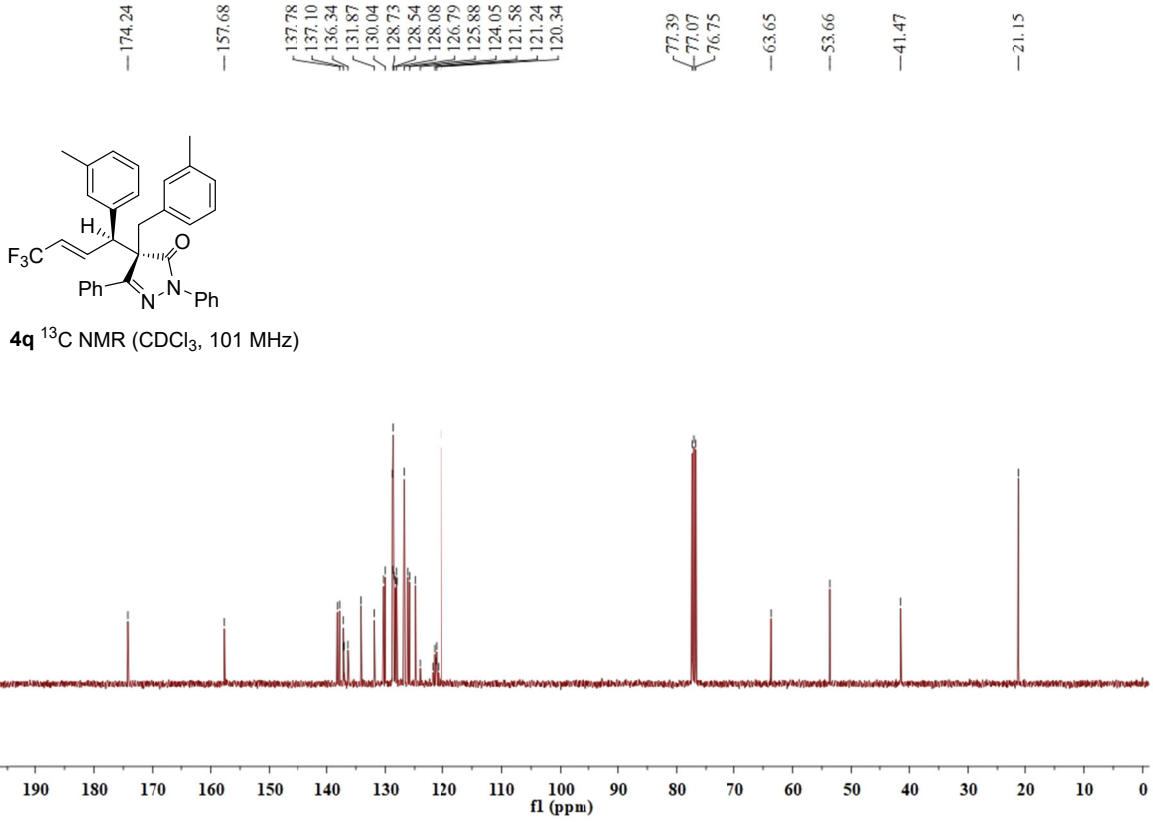




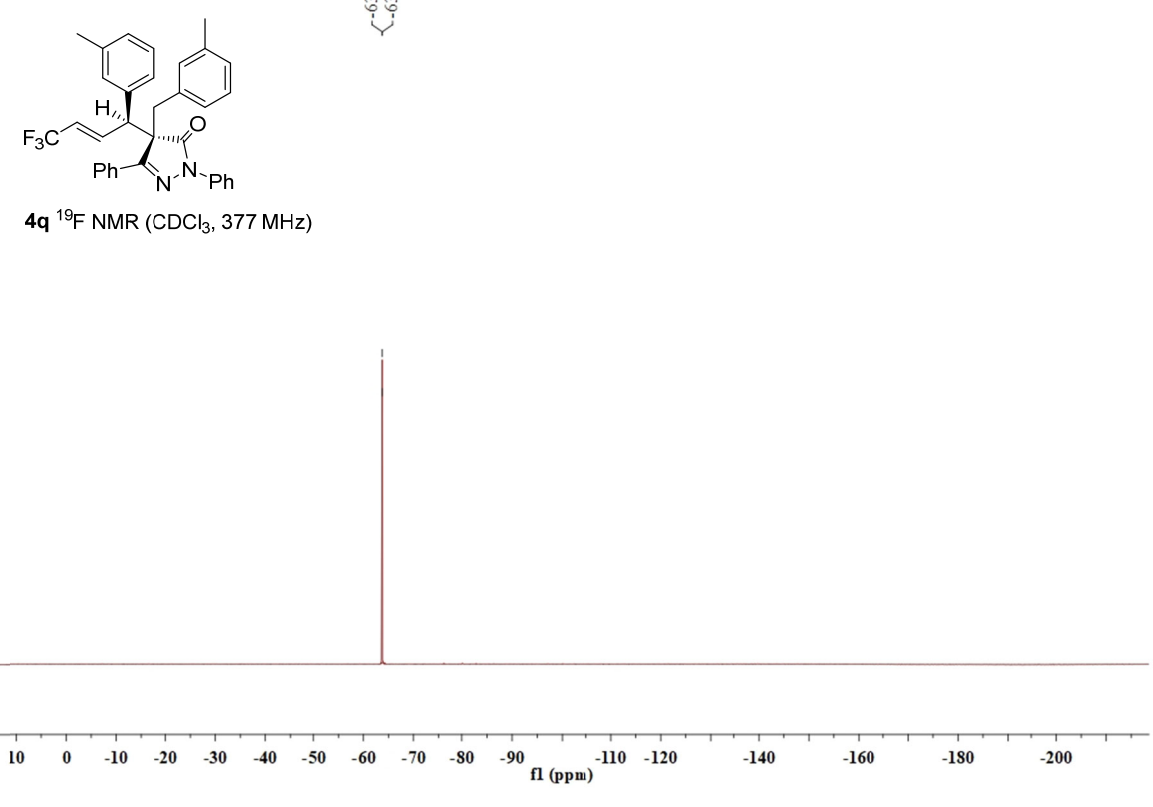


4q ^{1}H NMR ($CDCl_3$, 400 MHz)

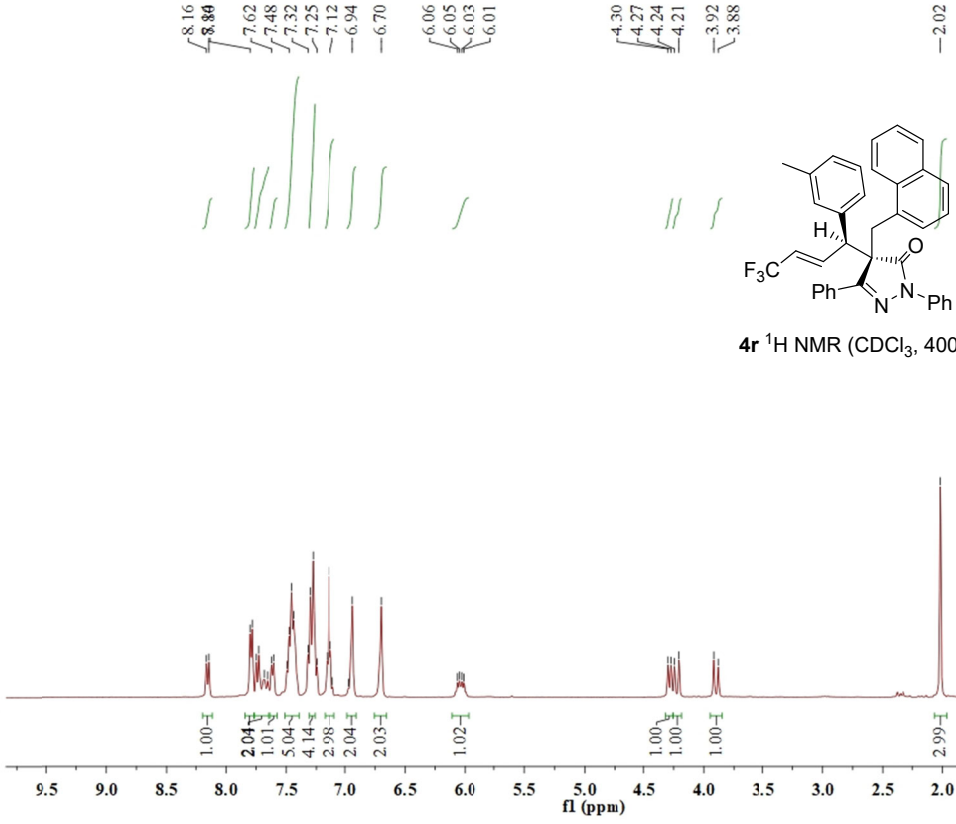




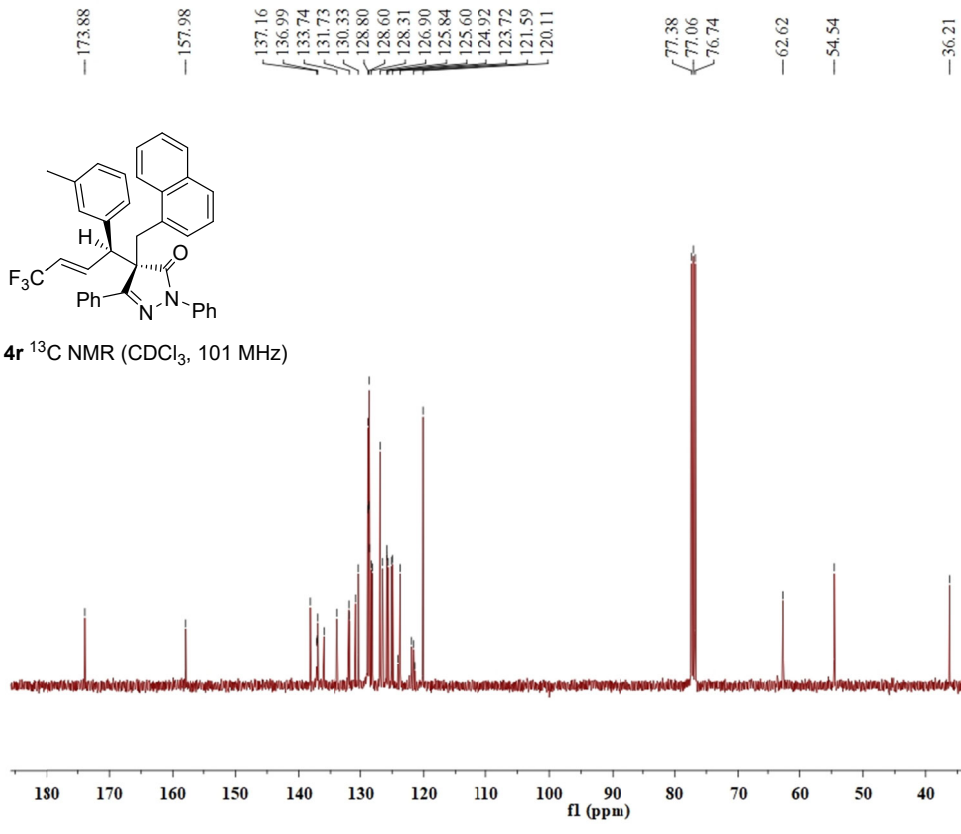
4q ^{13}C NMR ($CDCl_3$, 101 MHz)



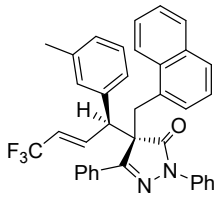
4q ^{19}F NMR ($CDCl_3$, 377 MHz)



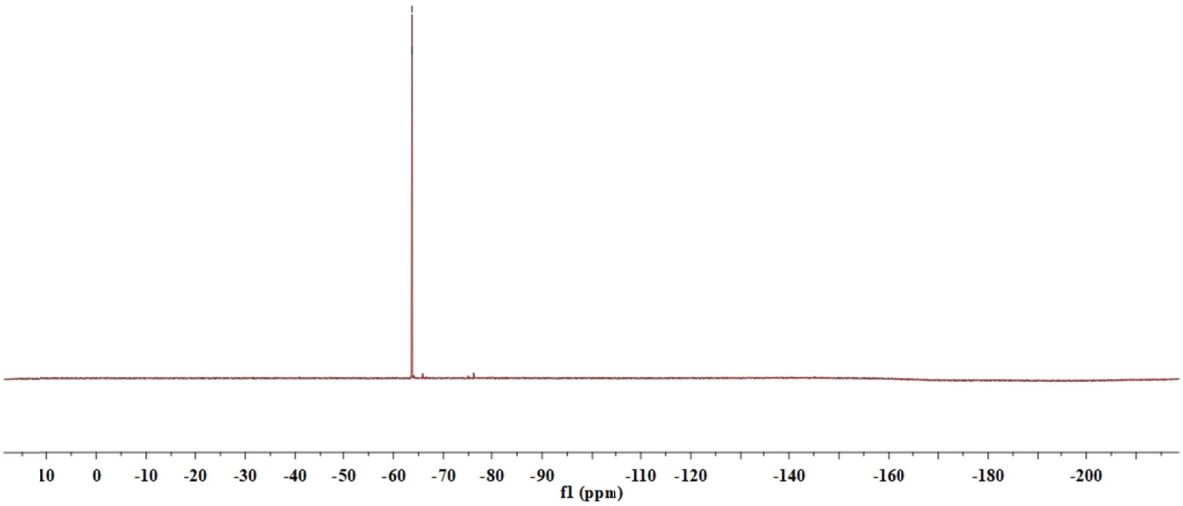
4r ^{1}H NMR ($CDCl_3$, 400 MHz)

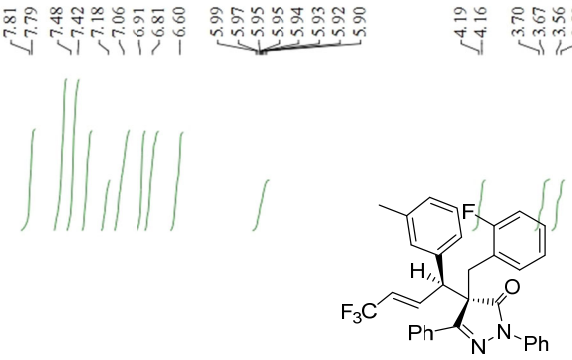


4r ^{13}C NMR ($CDCl_3$, 101 MHz)

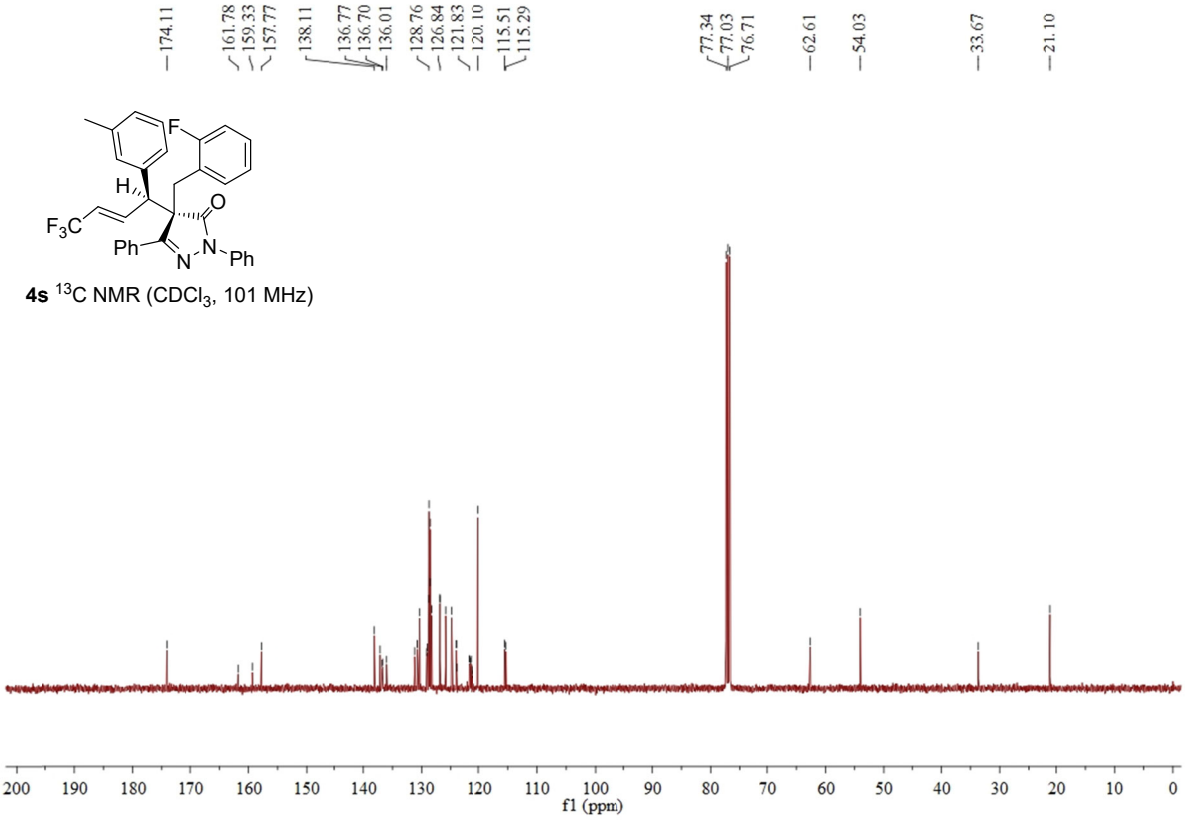


4r ^{19}F NMR ($CDCl_3$, 377 MHz)

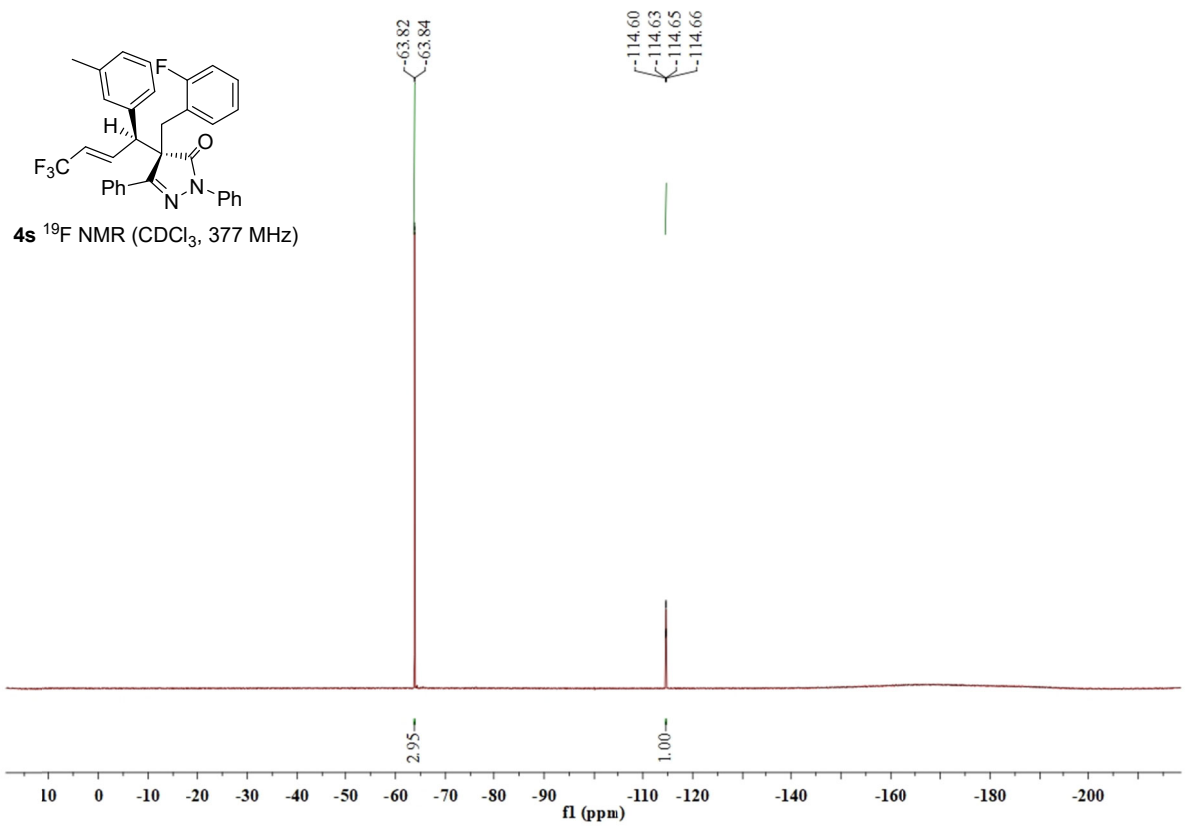




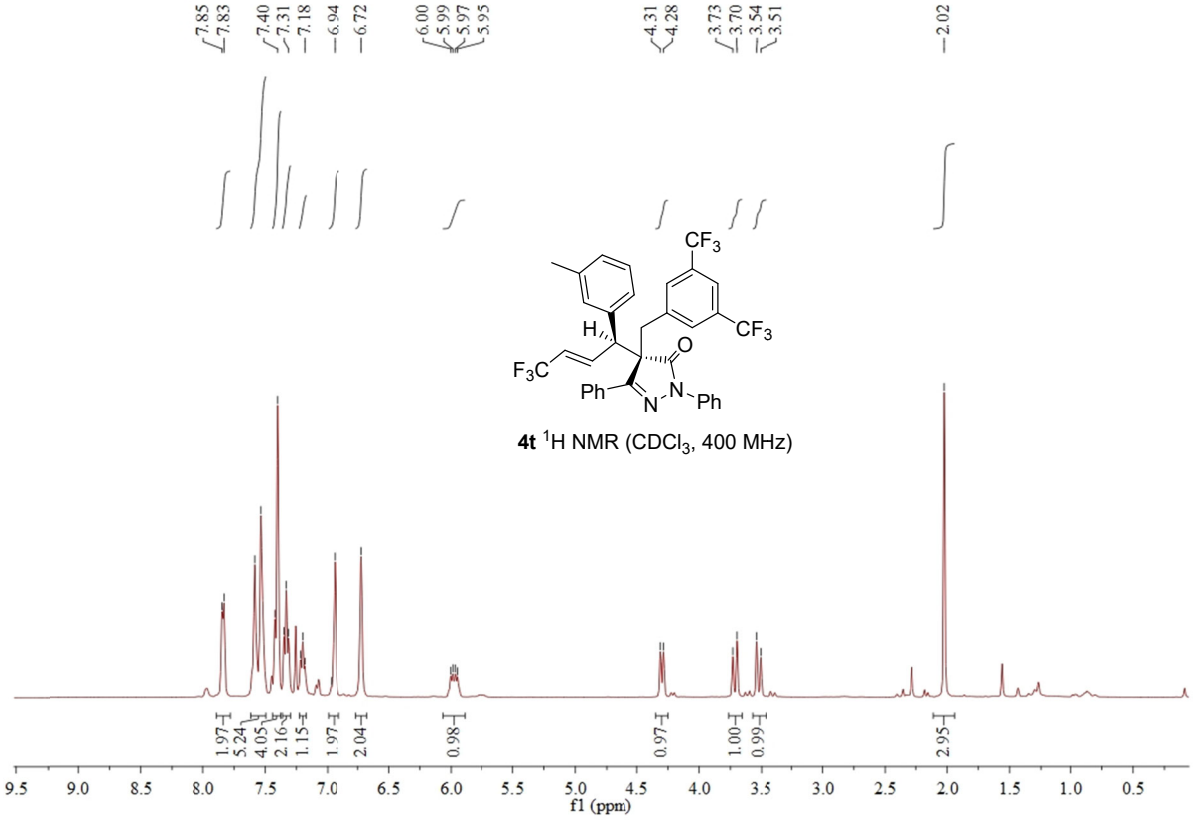
4s ^{1}H NMR ($CDCl_3$, 400 MHz)



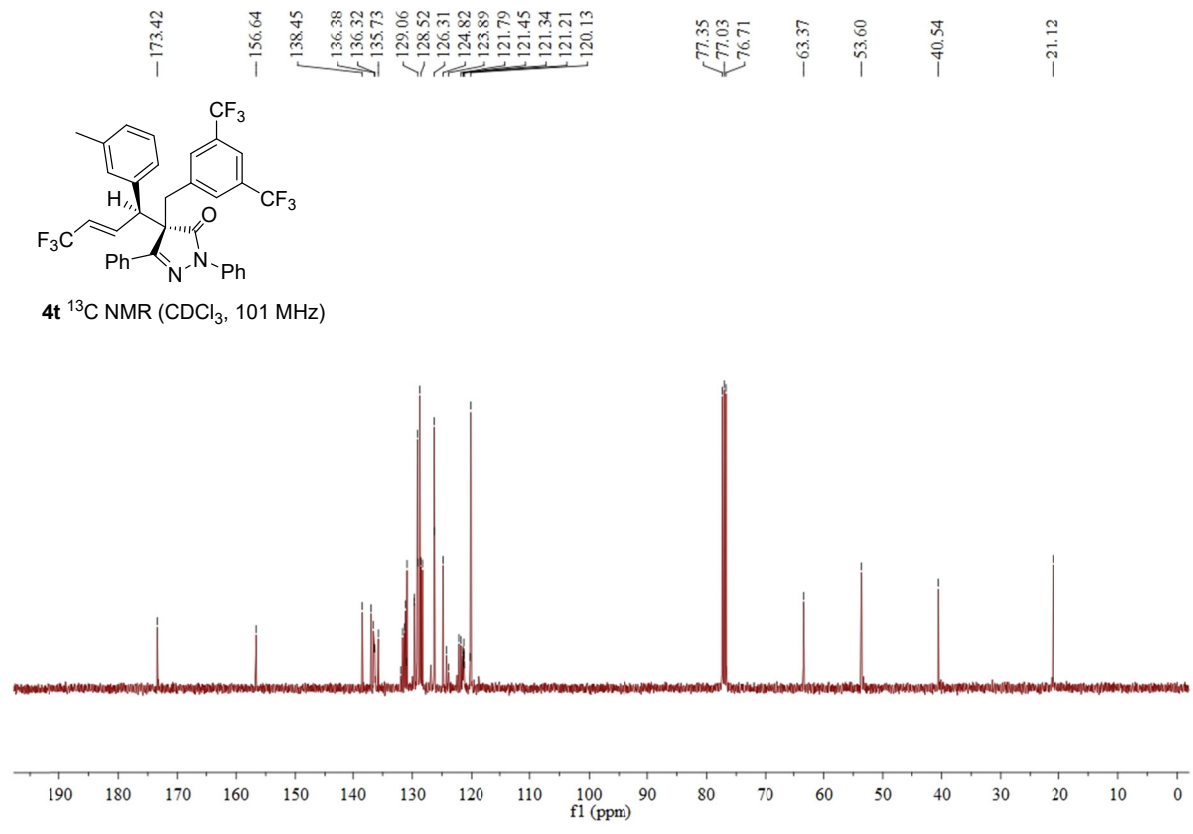
4s ^{13}C NMR ($CDCl_3$, 101 MHz)



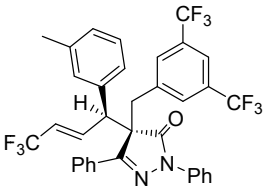
4s ^{19}F NMR ($CDCl_3$, 377 MHz)



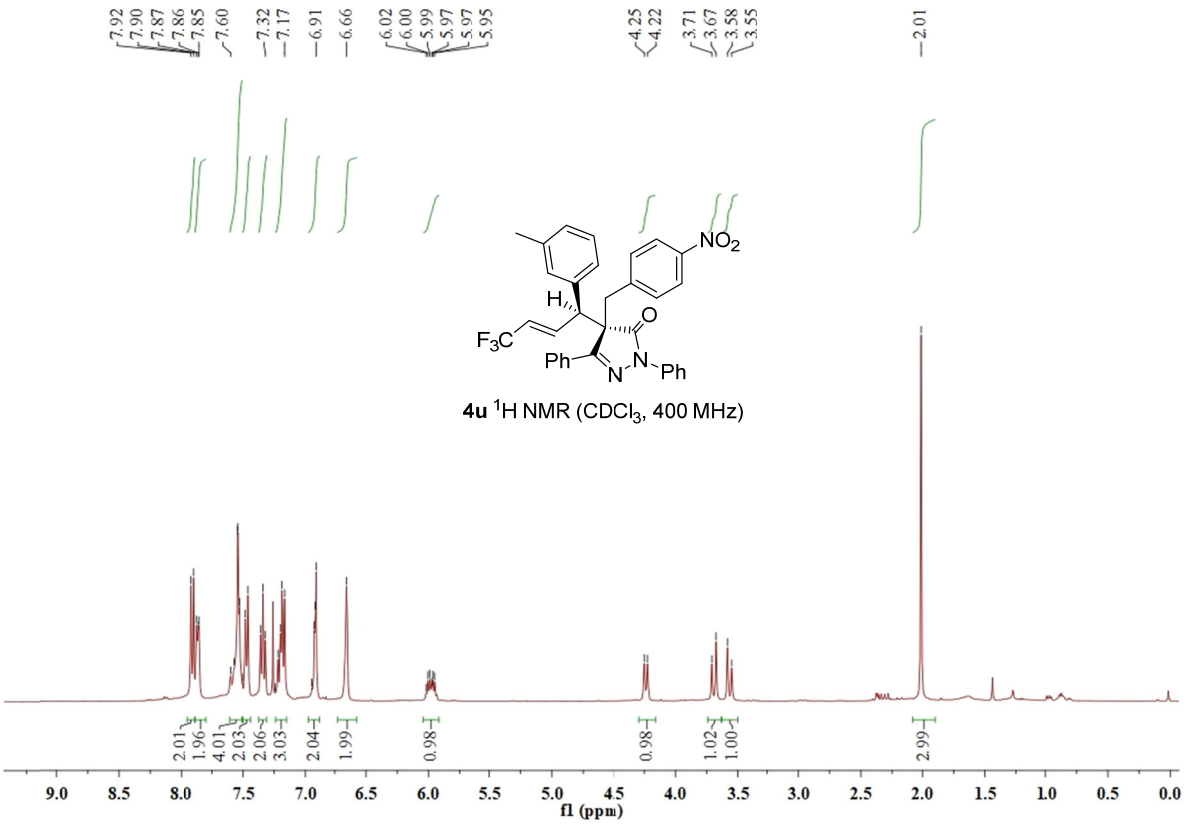
4t ^{1}H NMR ($CDCl_3$, 400 MHz)



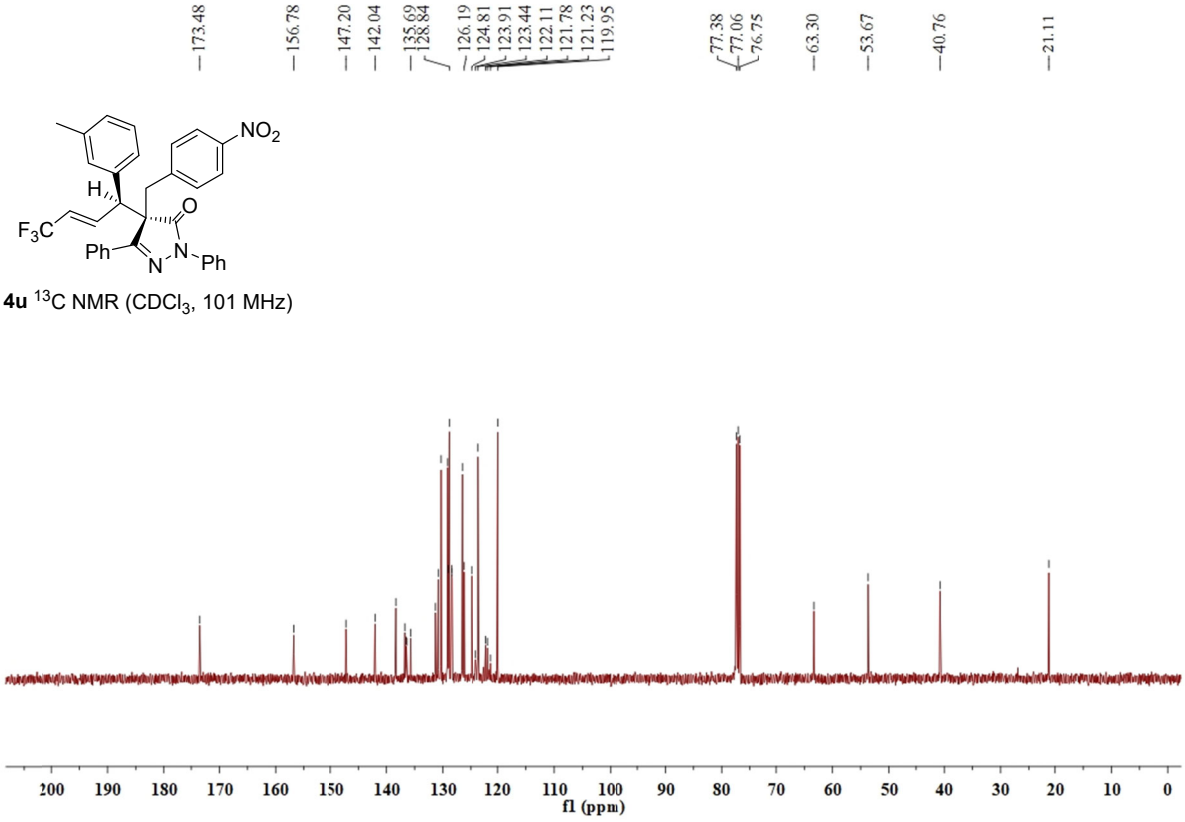
4t ^{13}C NMR ($CDCl_3$, 101 MHz)



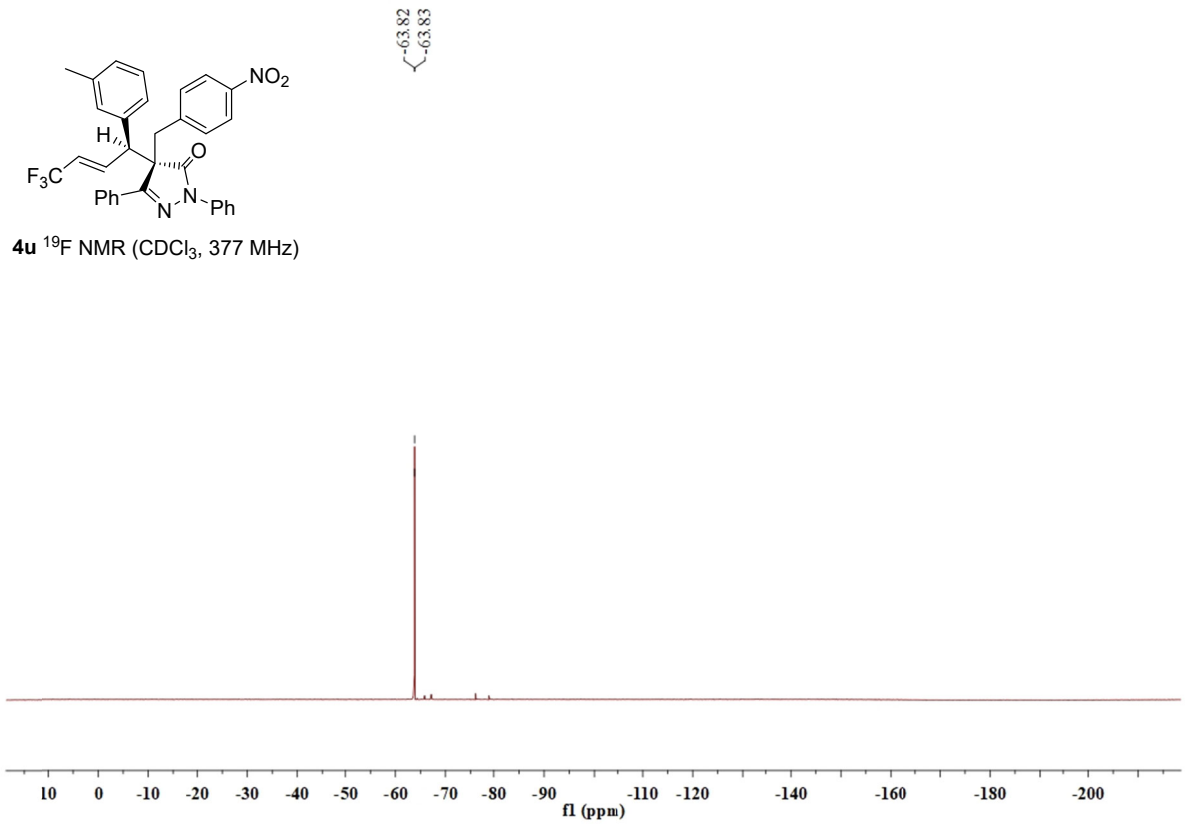
4t ^{19}F NMR ($CDCl_3$, 377 MHz)



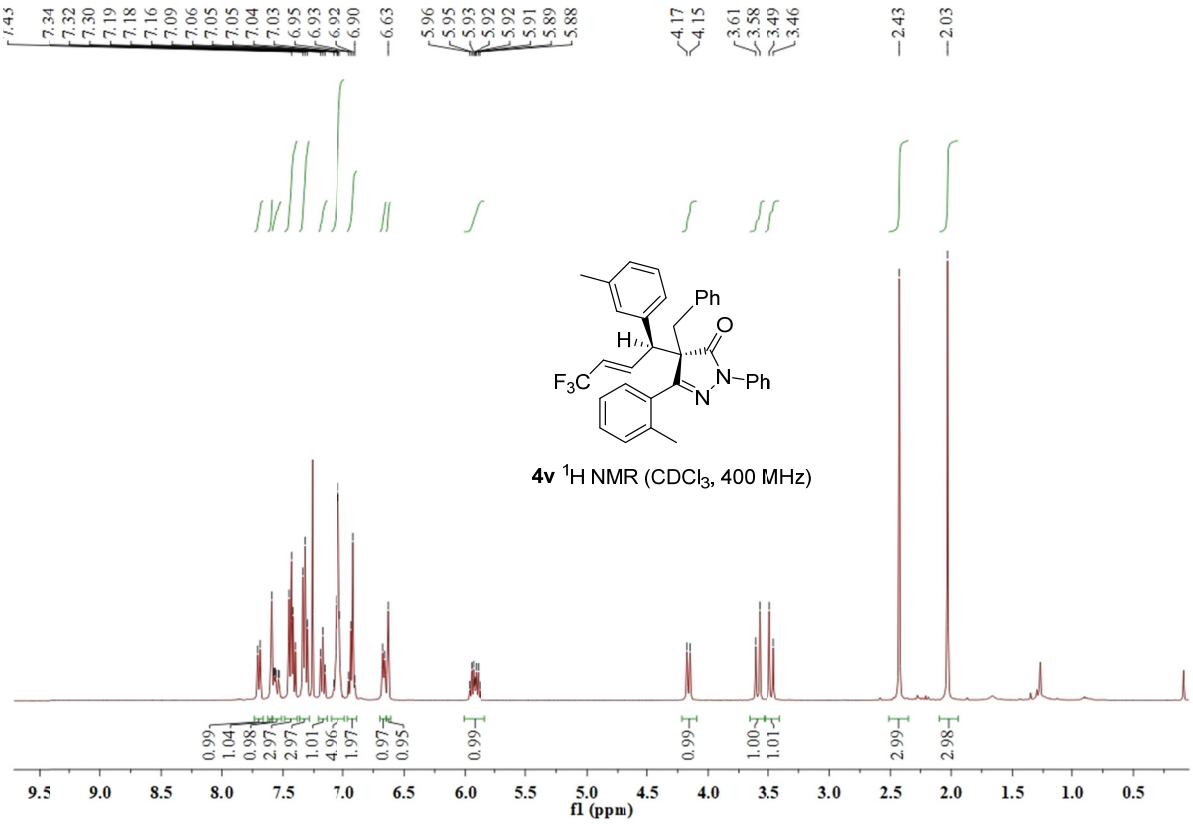
4u ^{1}H NMR ($CDCl_3$, 400 MHz)



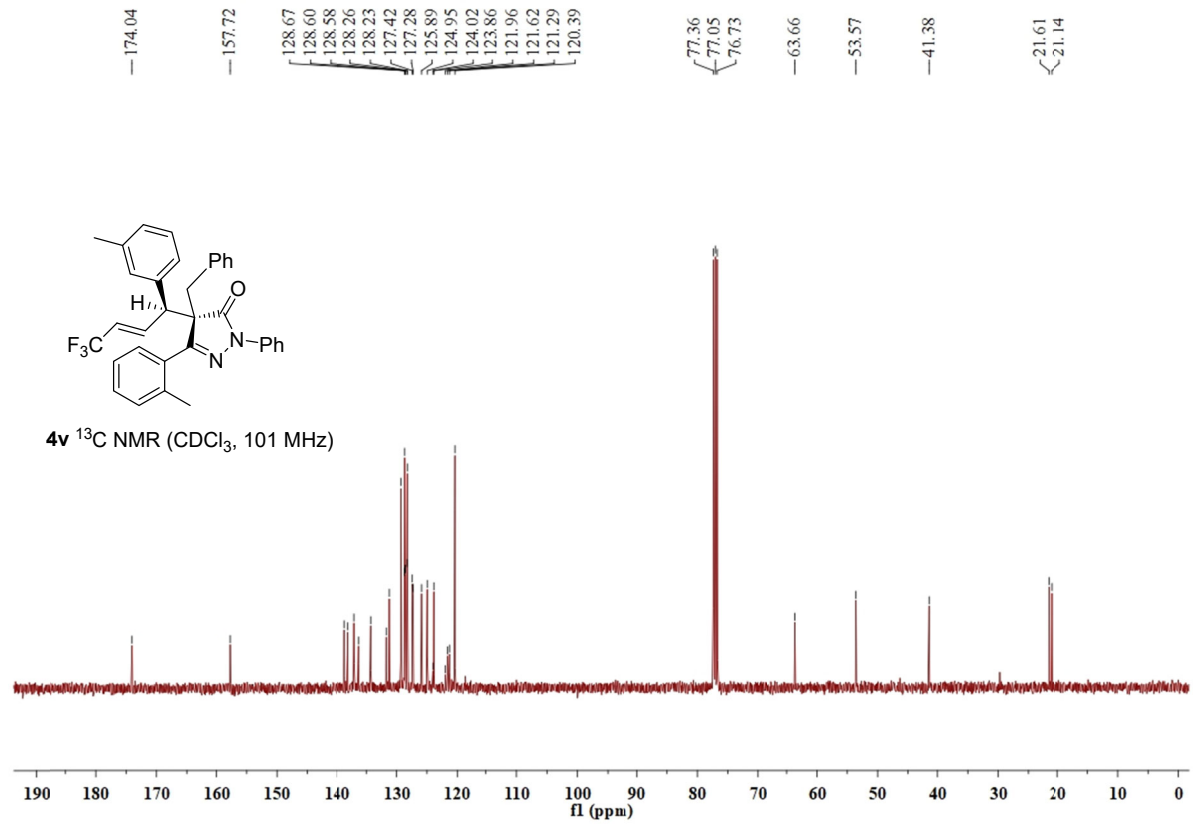
4u ^{13}C NMR ($CDCl_3$, 101 MHz)



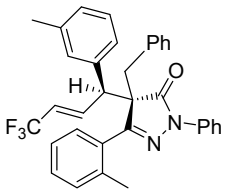
4u ^{19}F NMR ($CDCl_3$, 377 MHz)



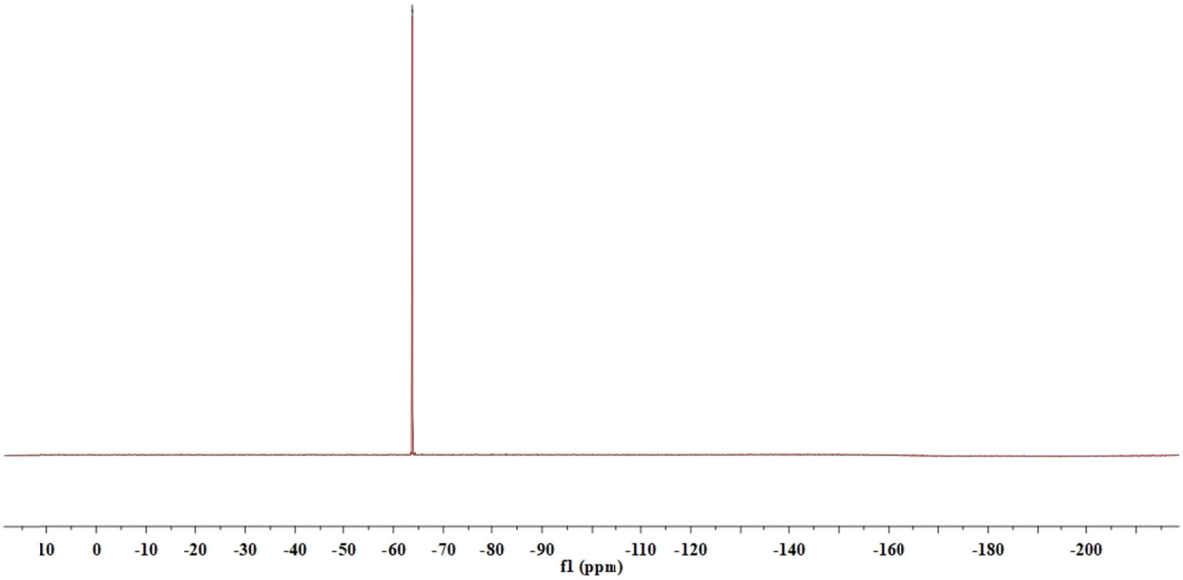
4v ^{1}H NMR ($CDCl_3$, 400 MHz)

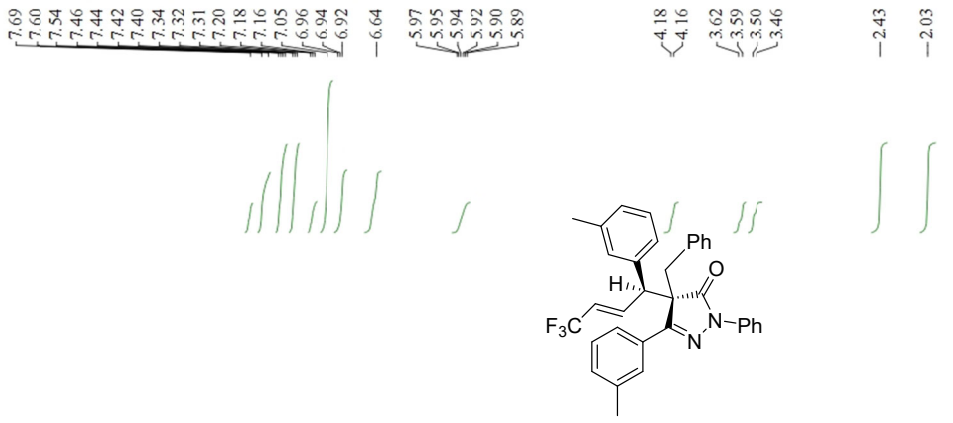


4v ^{13}C NMR ($CDCl_3$, 101 MHz)

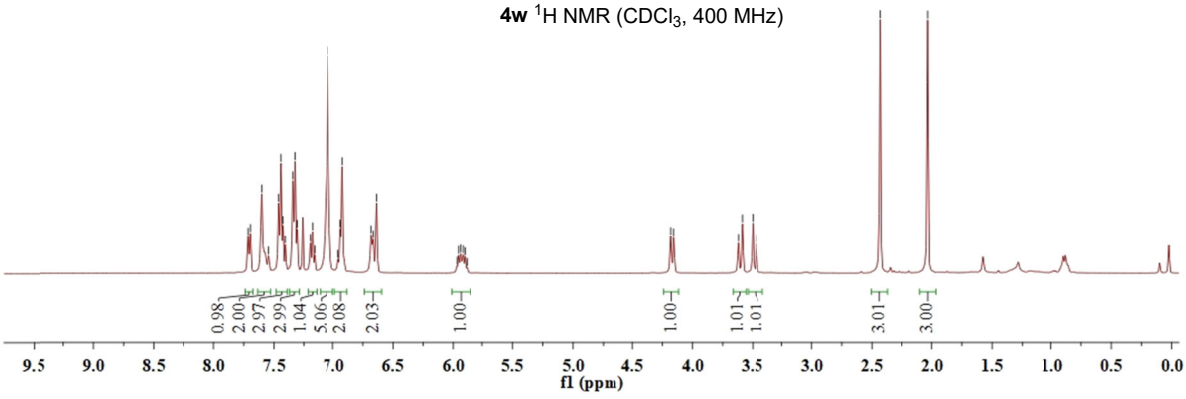


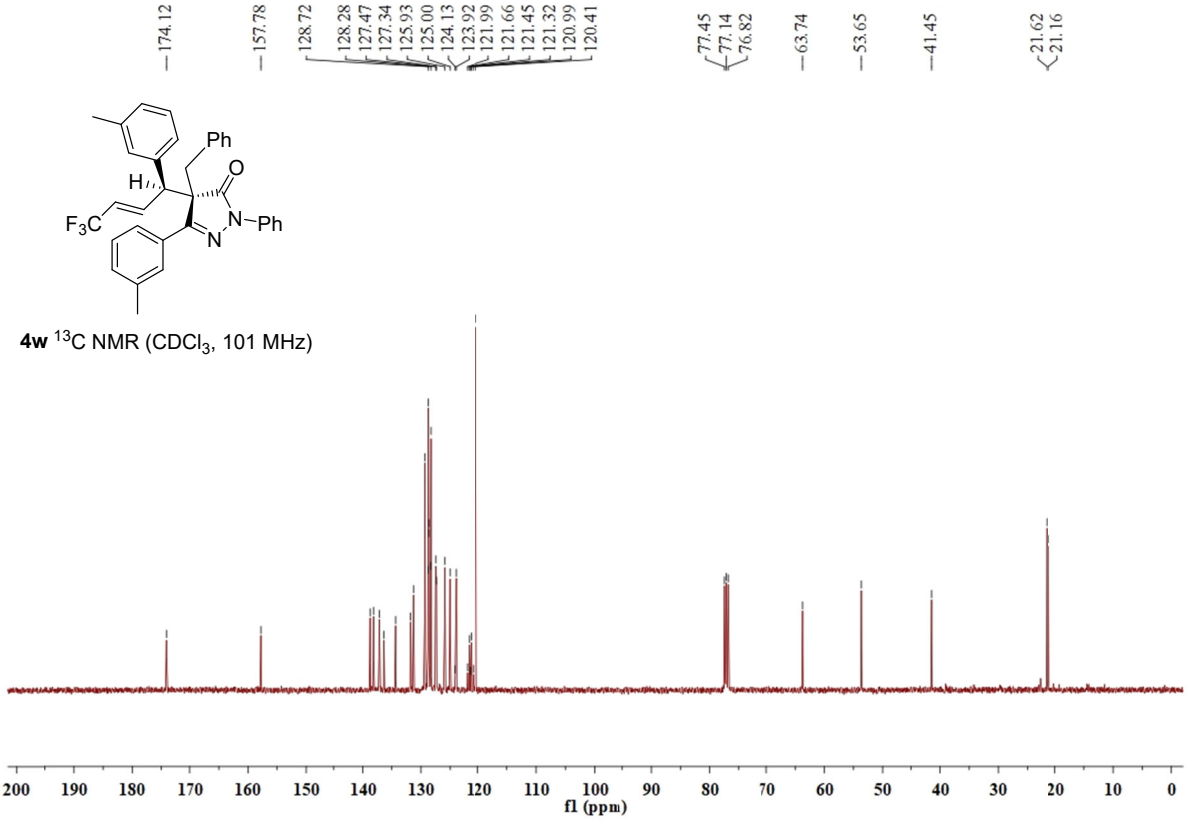
4v ^{19}F NMR ($CDCl_3$, 377 MHz)



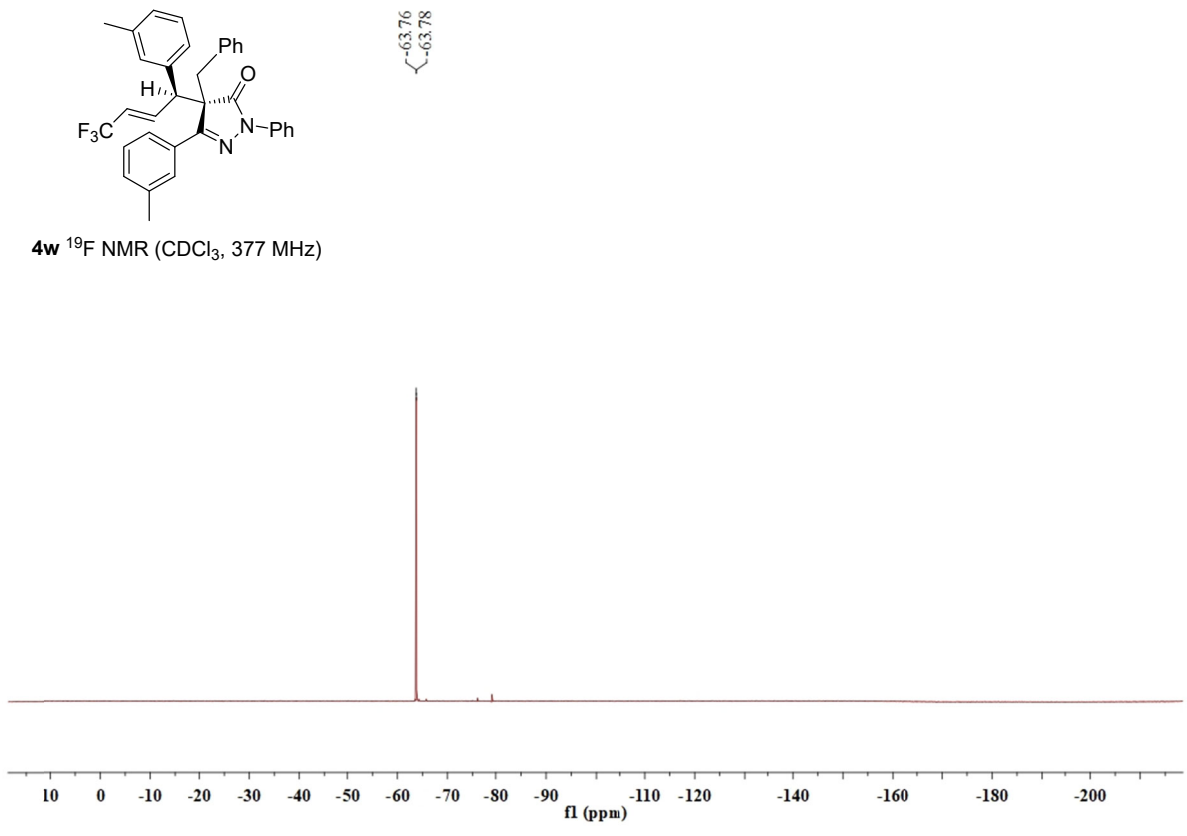


4w ^{1}H NMR ($CDCl_3$, 400 MHz)

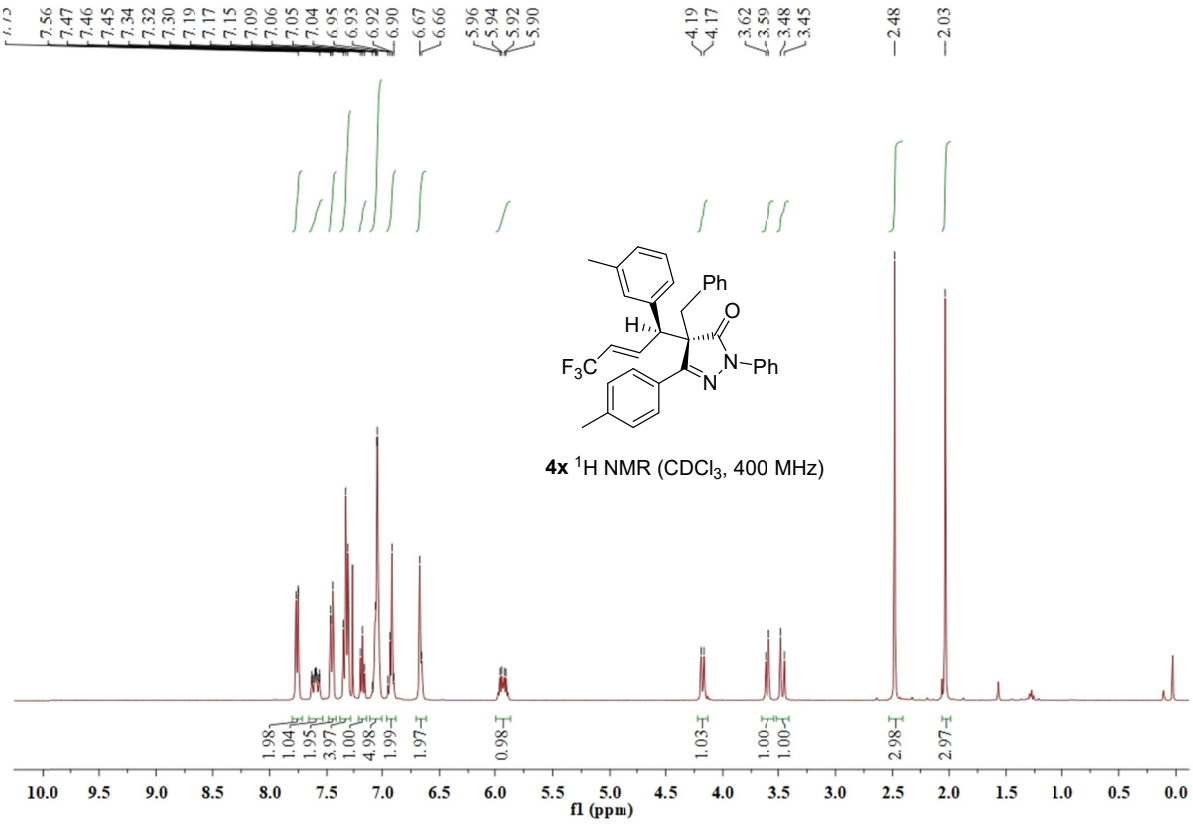




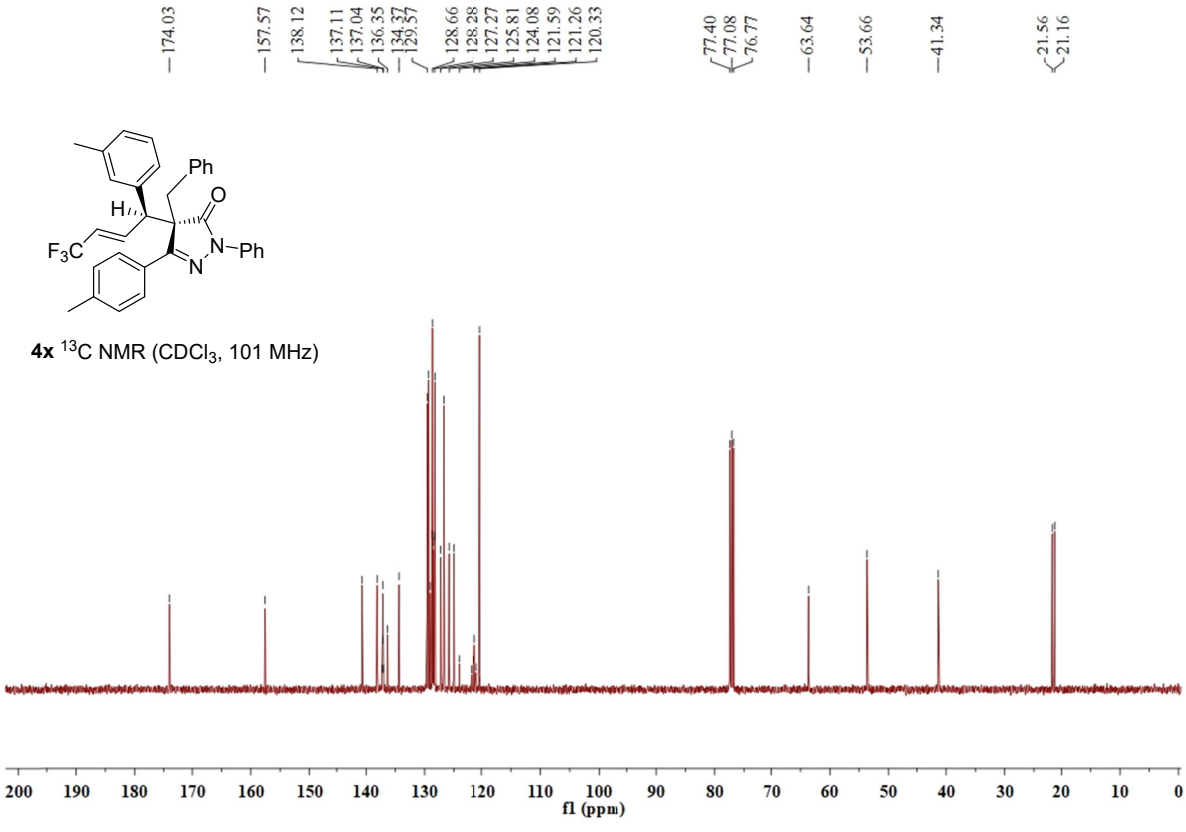
4w ^{13}C NMR ($CDCl_3$, 101 MHz)



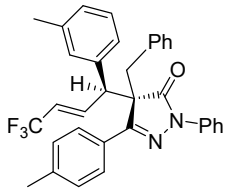
4w ^{19}F NMR ($CDCl_3$, 377 MHz)



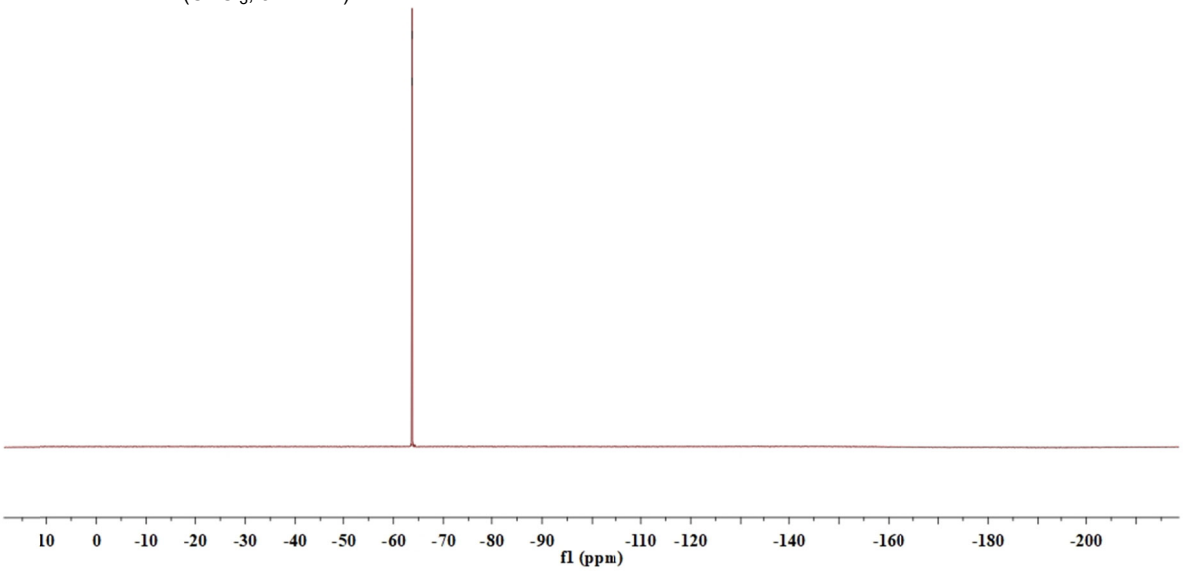
4x ^{1}H NMR ($CDCl_3$, 400 MHz)

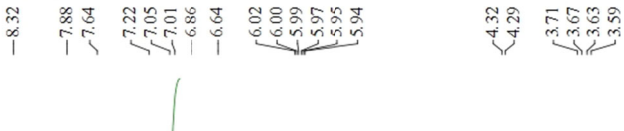


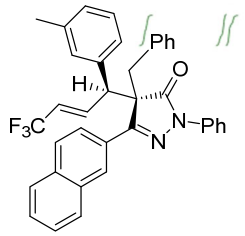
4x ^{13}C NMR ($CDCl_3$, 101 MHz)



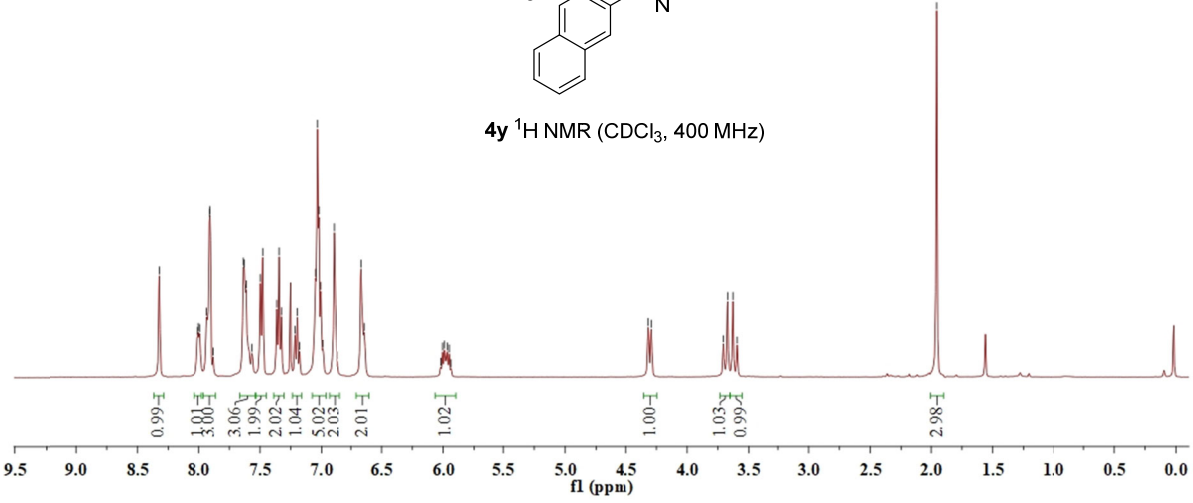
4x ^{19}F NMR ($CDCl_3$, 377 MHz)

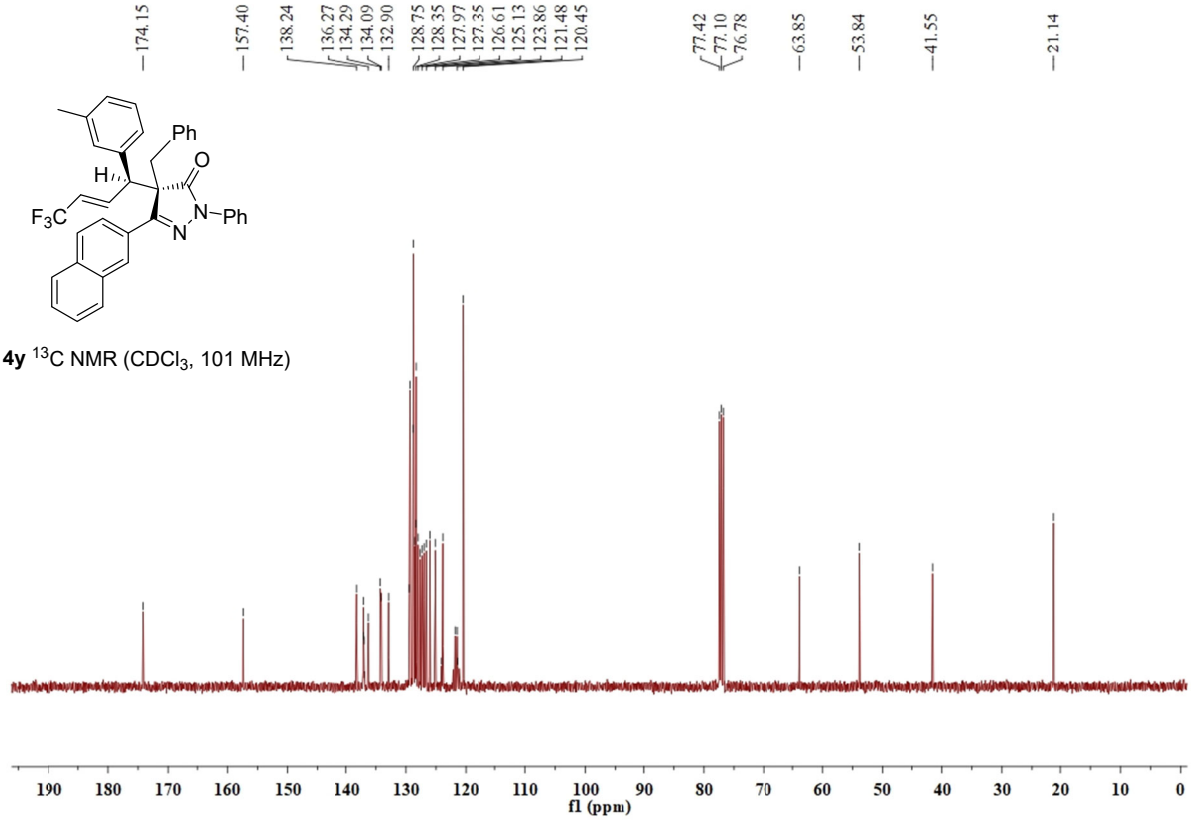




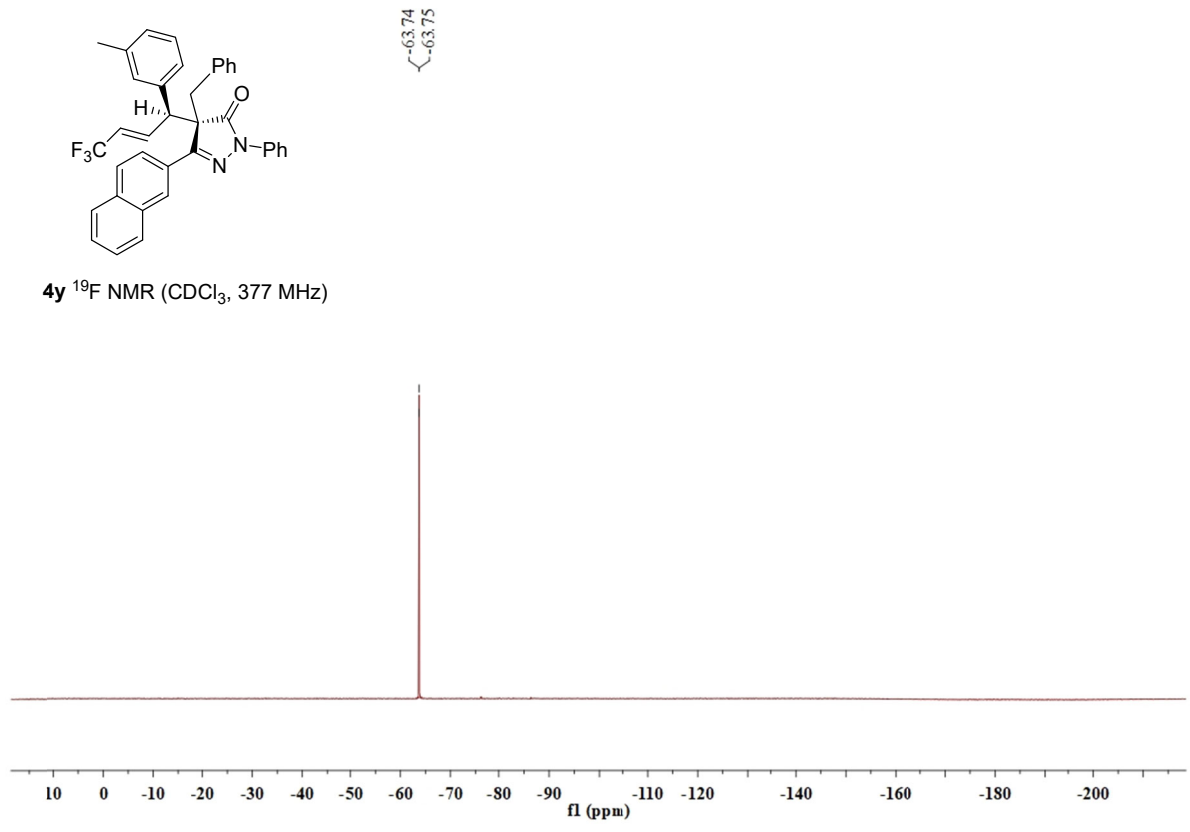


4y ^{1}H NMR ($CDCl_3$, 400 MHz)

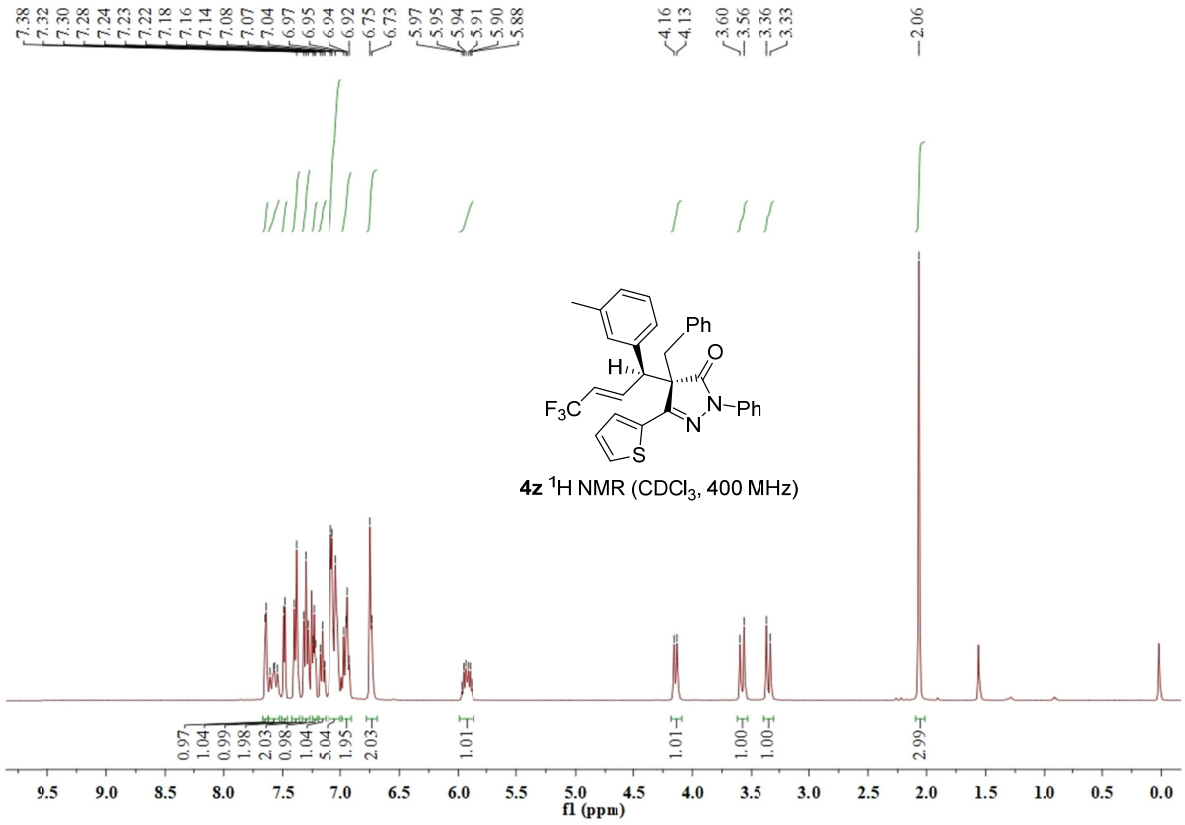




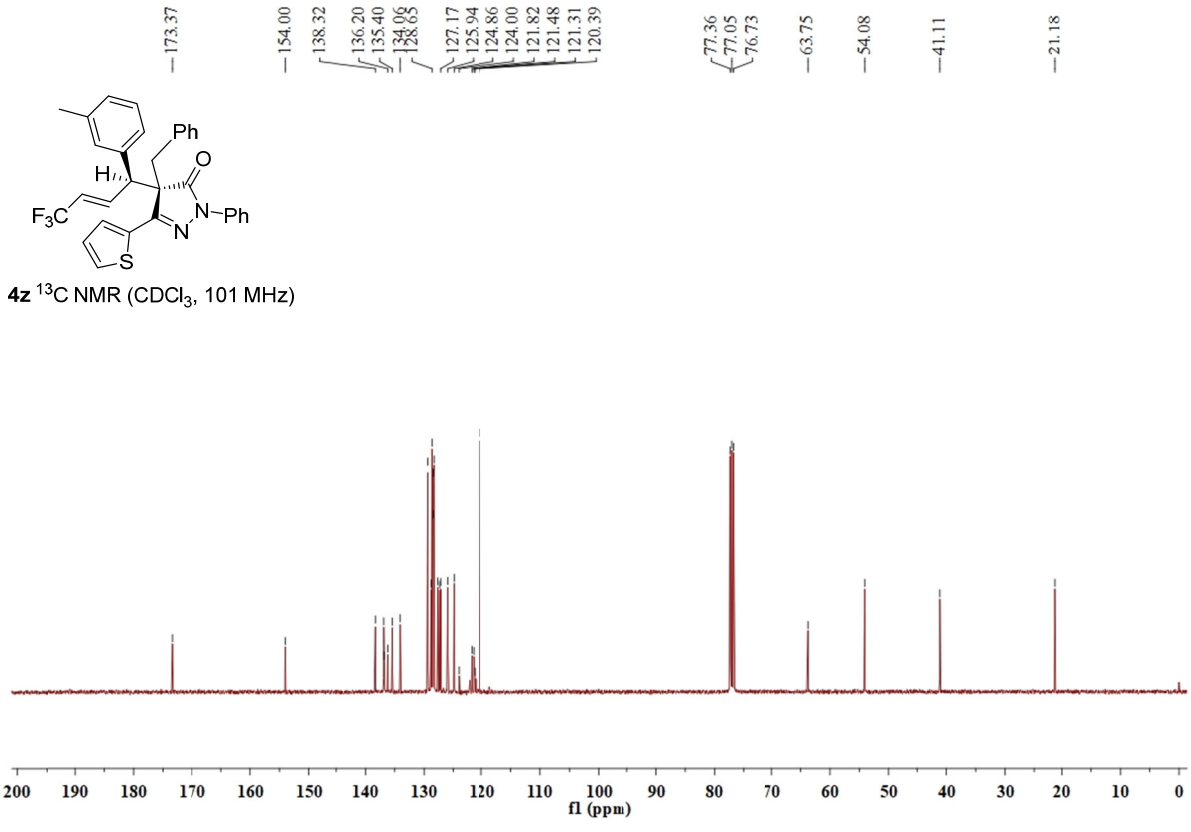
4y ^{13}C NMR ($CDCl_3$, 101 MHz)



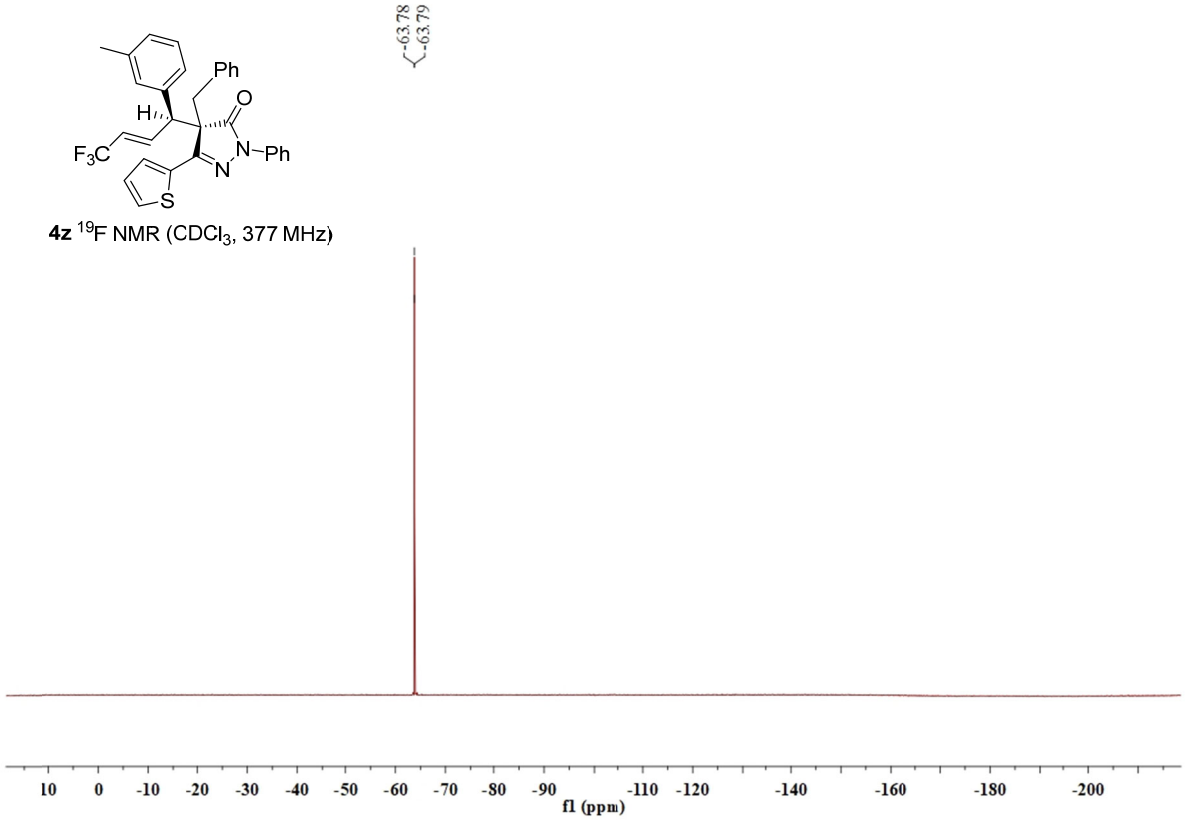
4y ^{19}F NMR ($CDCl_3$, 377 MHz)



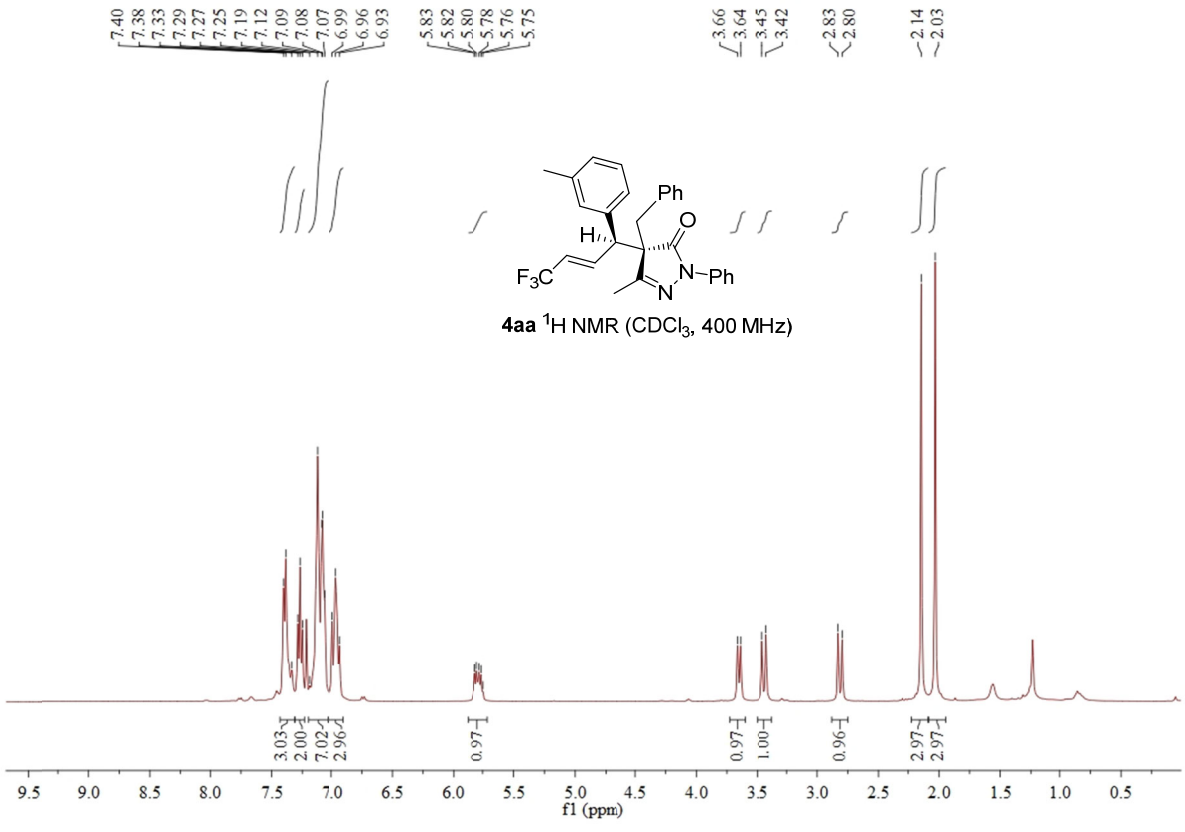
4z ^{1}H NMR ($CDCl_3$, 400 MHz)



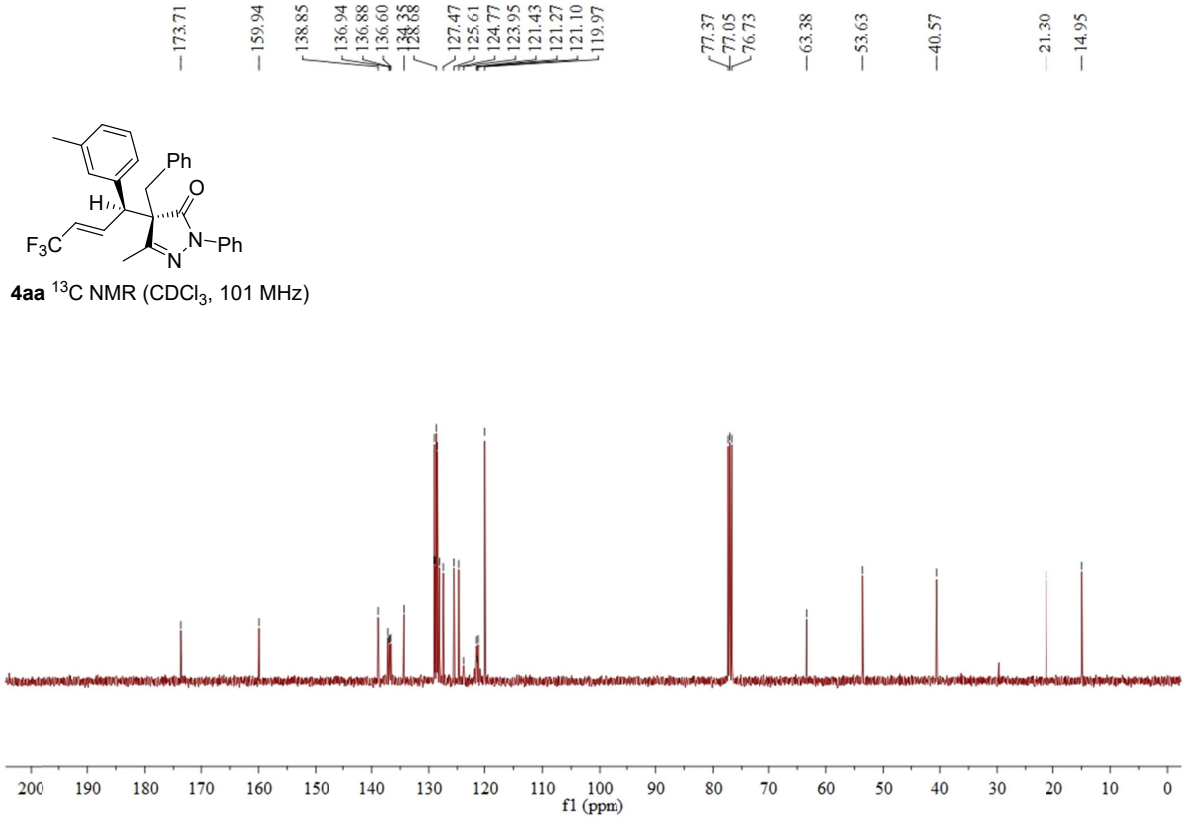
4z ^{13}C NMR ($CDCl_3$, 101 MHz)



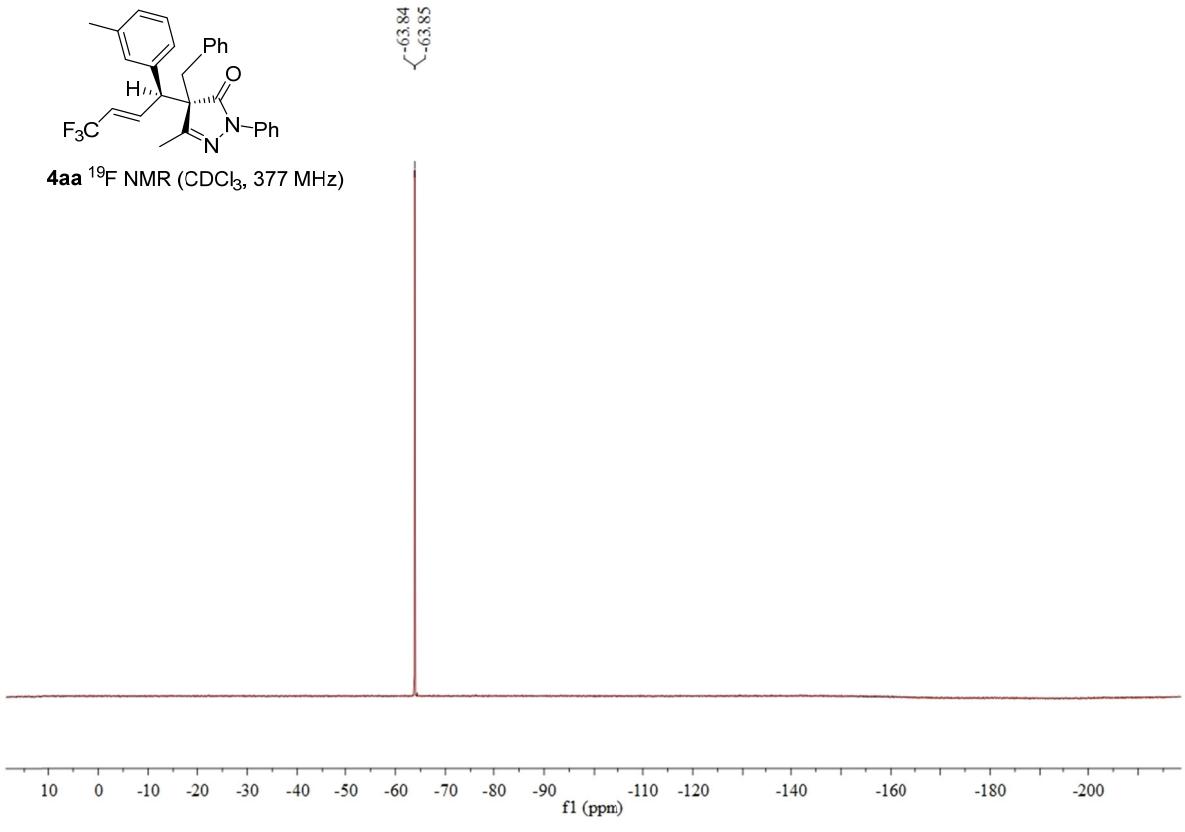
4z ^{19}F NMR ($CDCl_3$, 377 MHz)



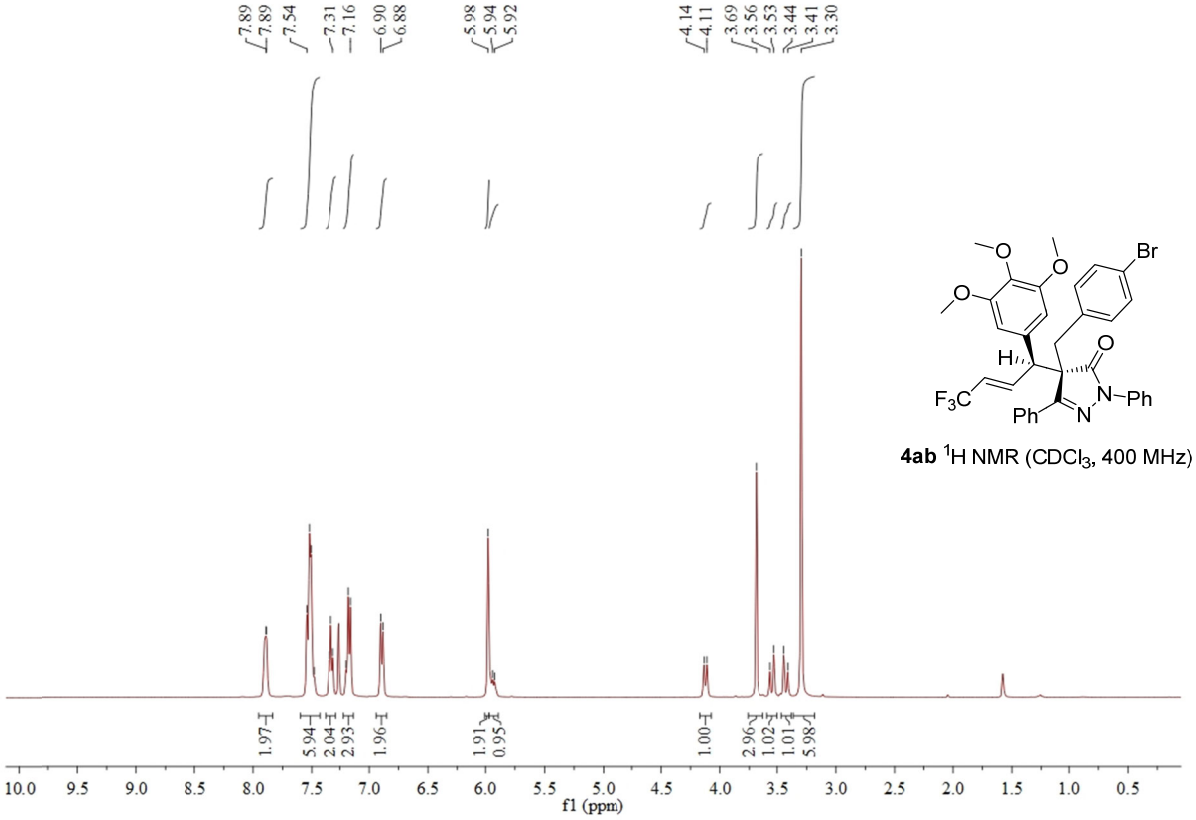
4aa ^{1}H NMR ($CDCl_3$, 400 MHz)



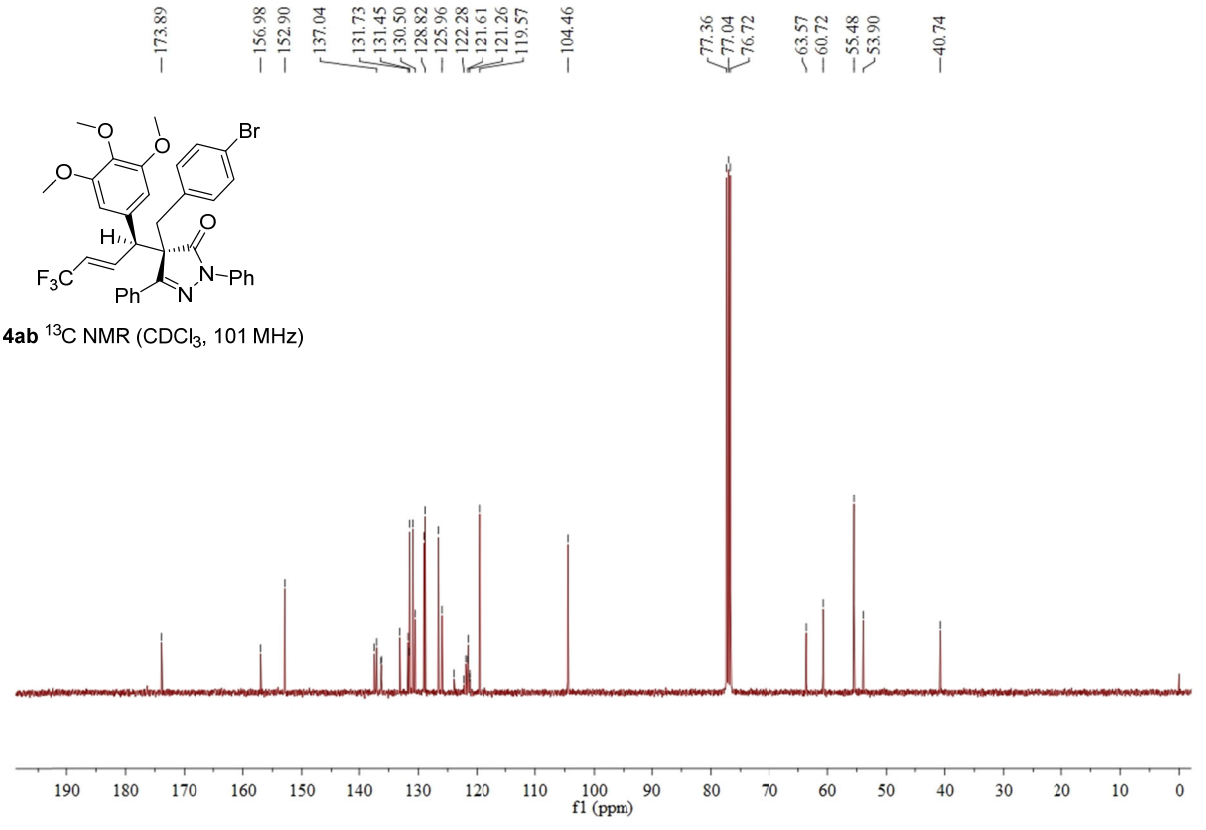
4aa ^{13}C NMR ($CDCl_3$, 101 MHz)



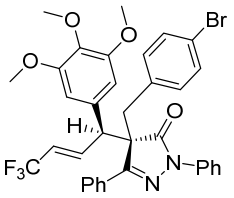
4aa ^{19}F NMR ($CDCl_3$, 377 MHz)



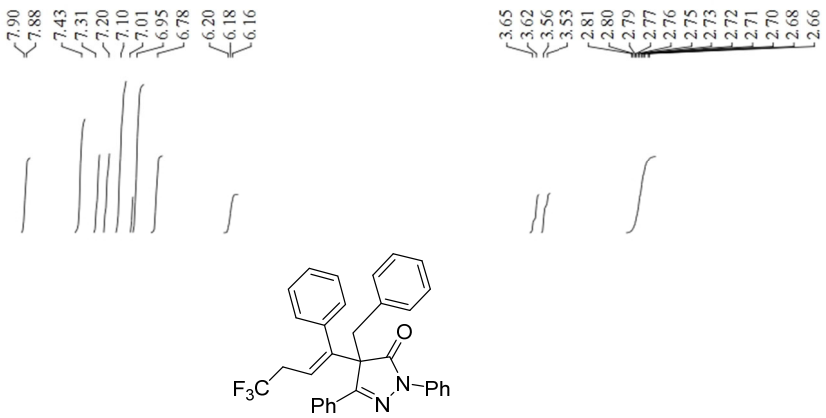
4ab ^{1}H NMR ($CDCl_3$, 400 MHz)



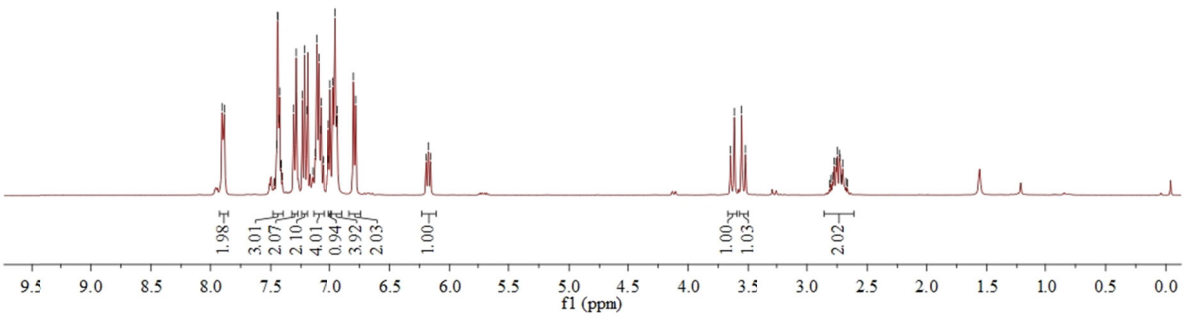
4ab ^{13}C NMR ($CDCl_3$, 101 MHz)

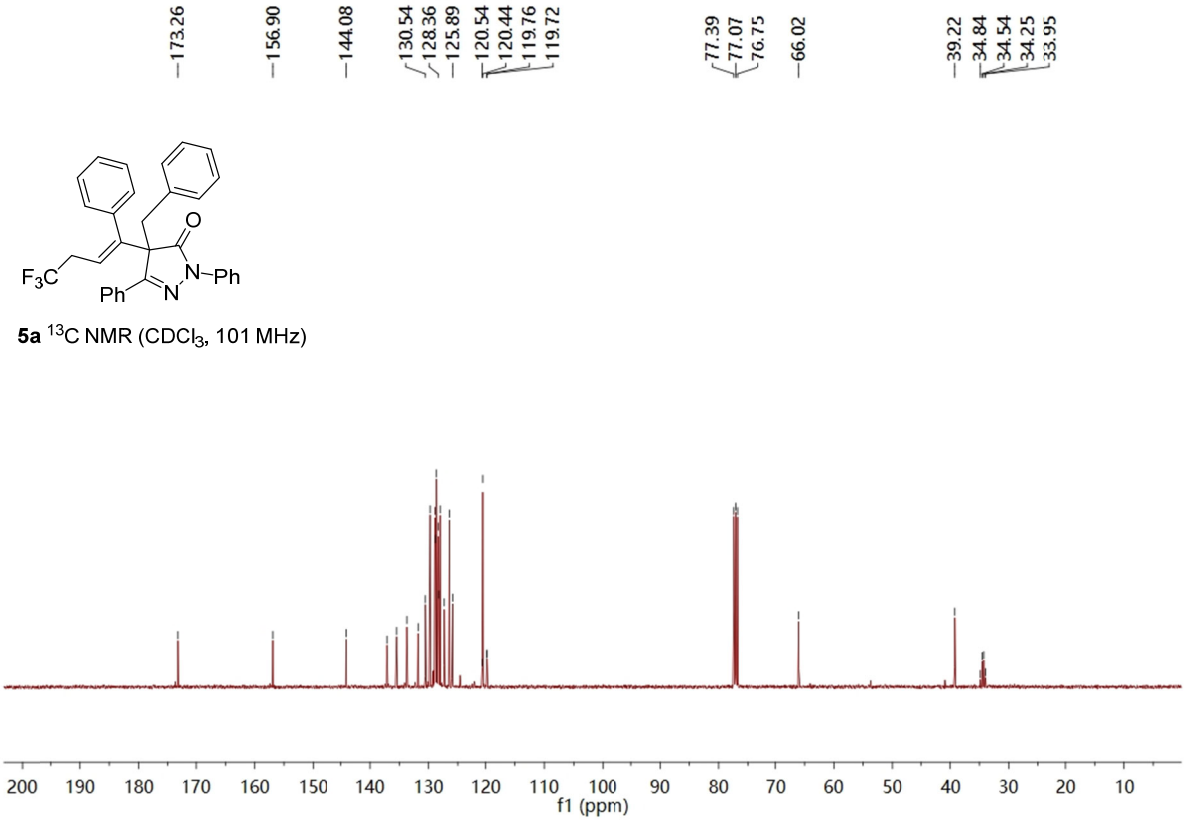


4ab ^{19}F NMR ($CDCl_3$, 377 MHz)

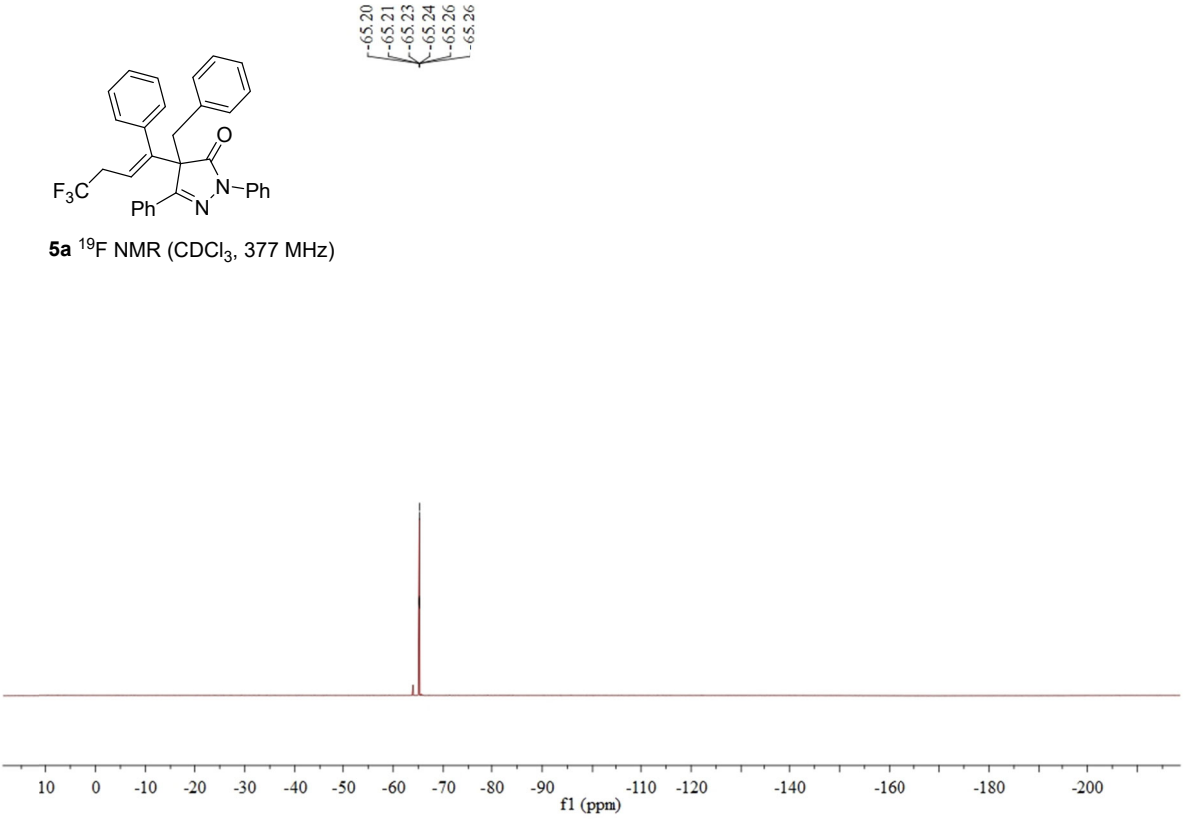


5a ^{1}H NMR ($CDCl_3$, 400 MHz)

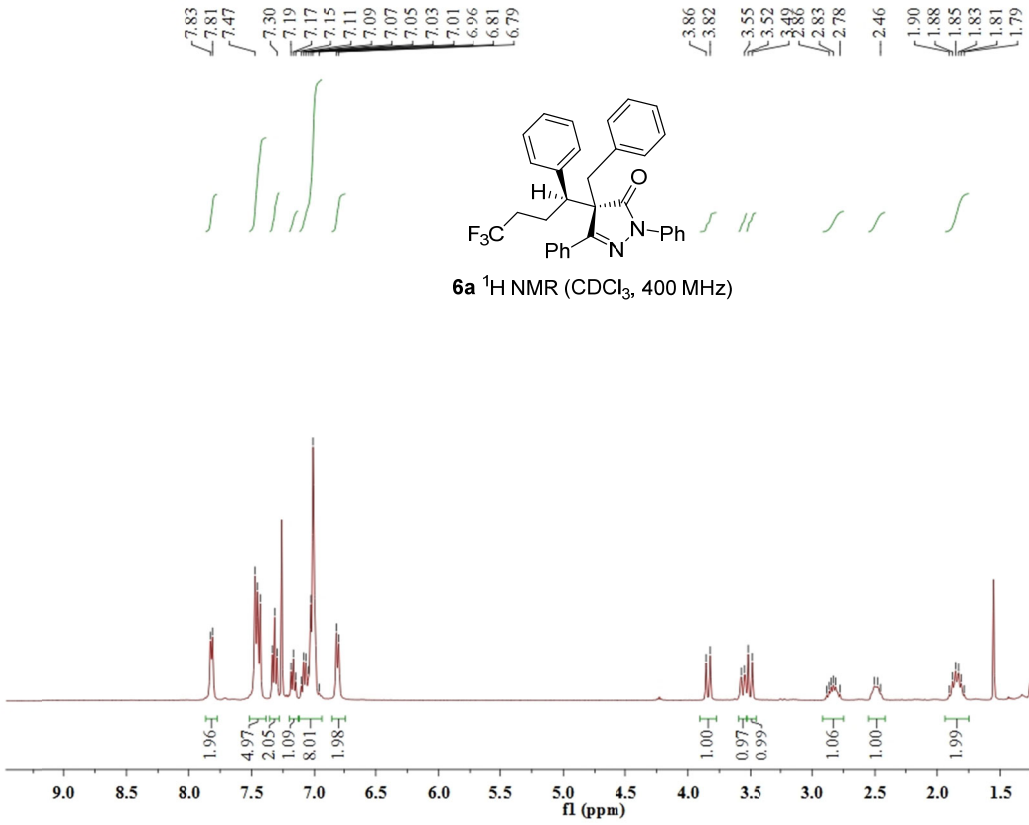




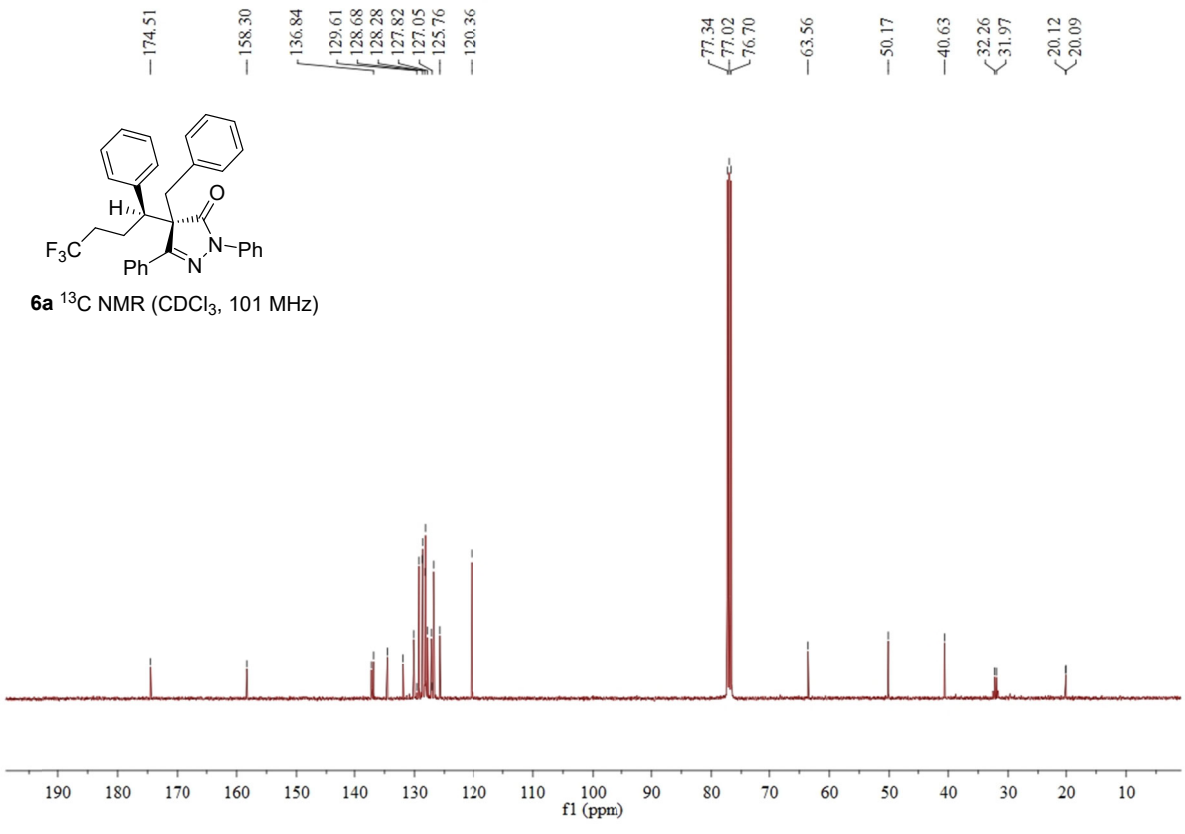
5a ^{13}C NMR ($CDCl_3$, 101 MHz)



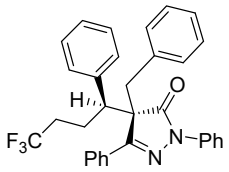
5a ^{19}F NMR ($CDCl_3$, 377 MHz)



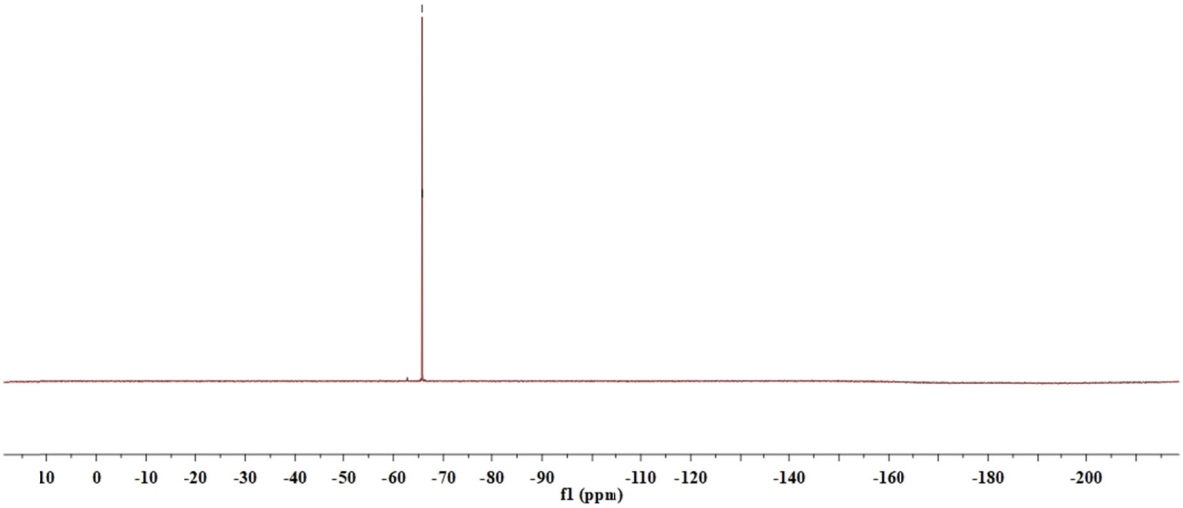
6a ^{1}H NMR ($CDCl_3$, 400 MHz)

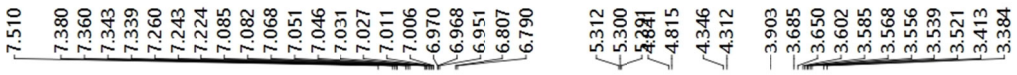


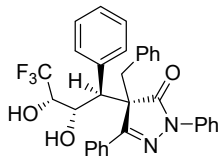
6a ^{13}C NMR ($CDCl_3$, 101 MHz)



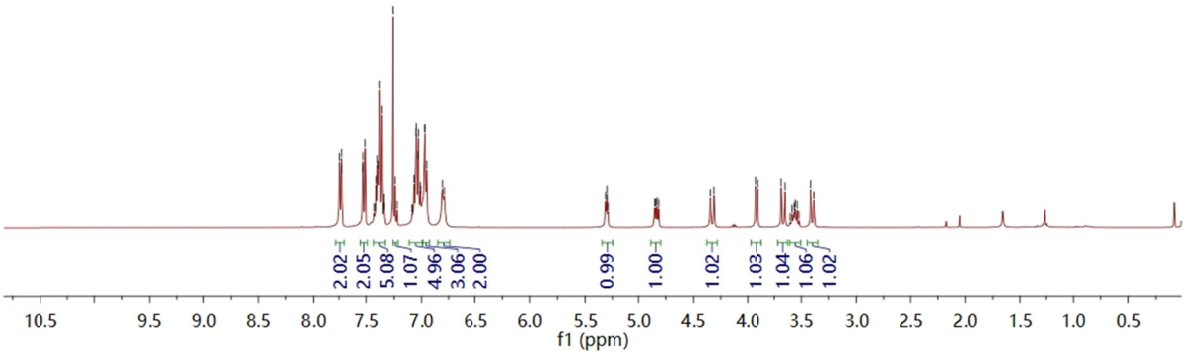
6a ^{19}F NMR ($CDCl_3$, 377 MHz)

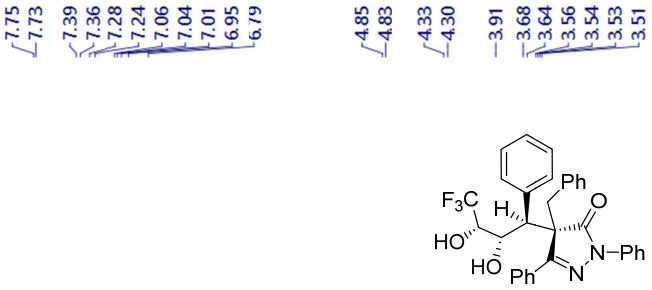




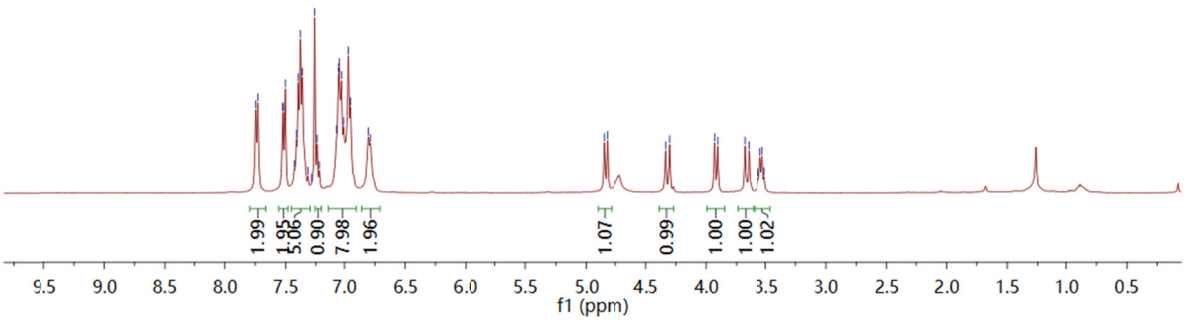


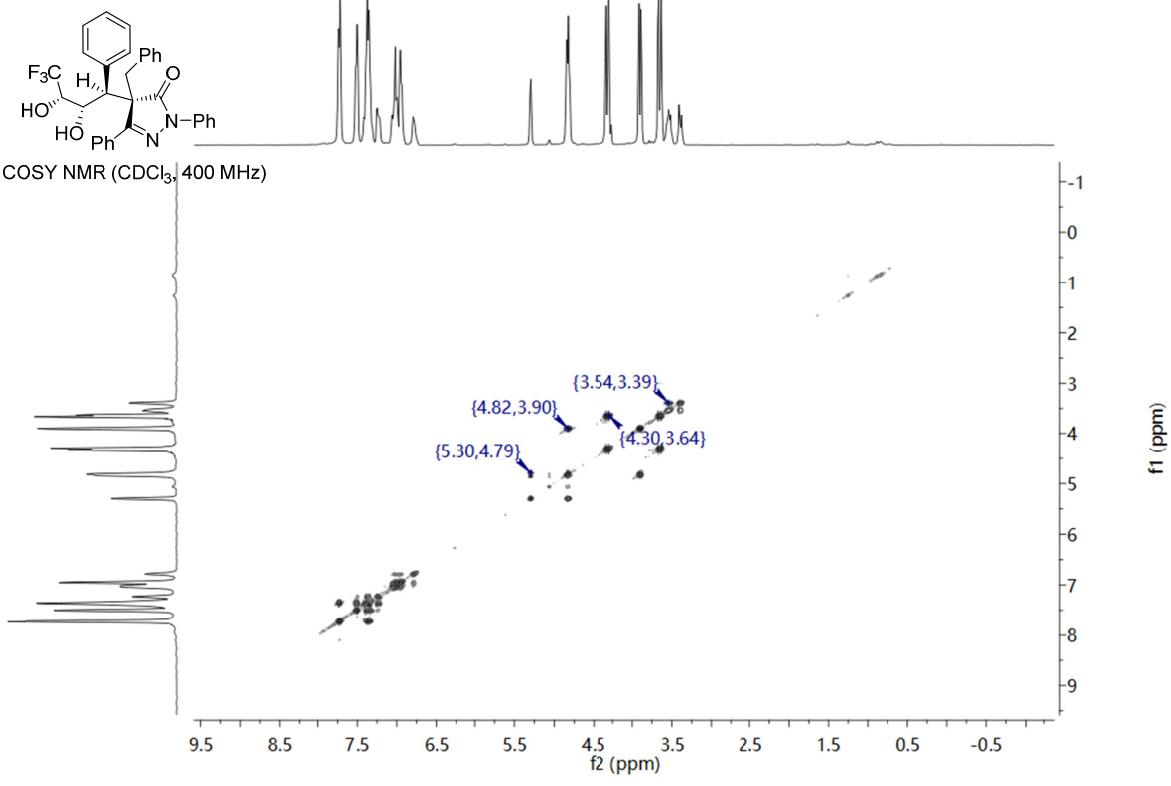
7a ^{1}H NMR ($CDCl_3$, 400 MHz)



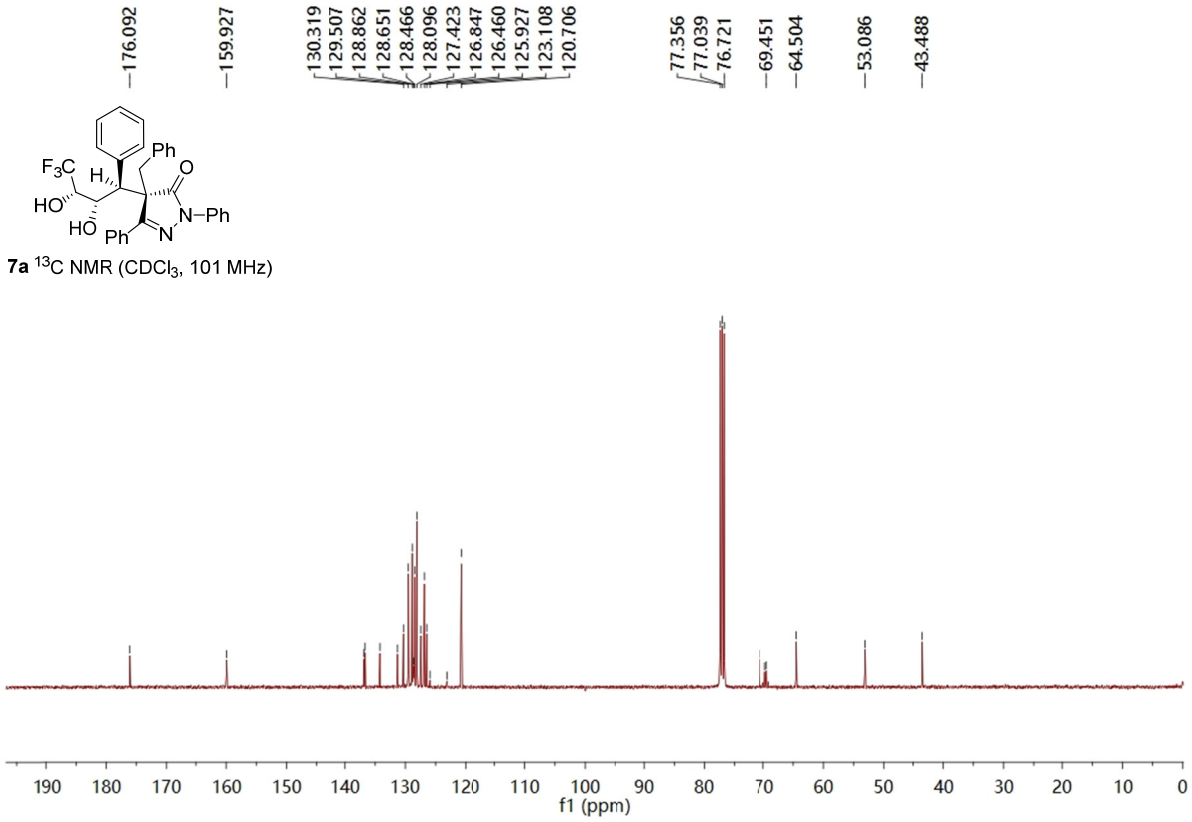


7a Hydrogen-deuterium exchange
^{1}H NMR ($CDCl_3$, 400 MHz)

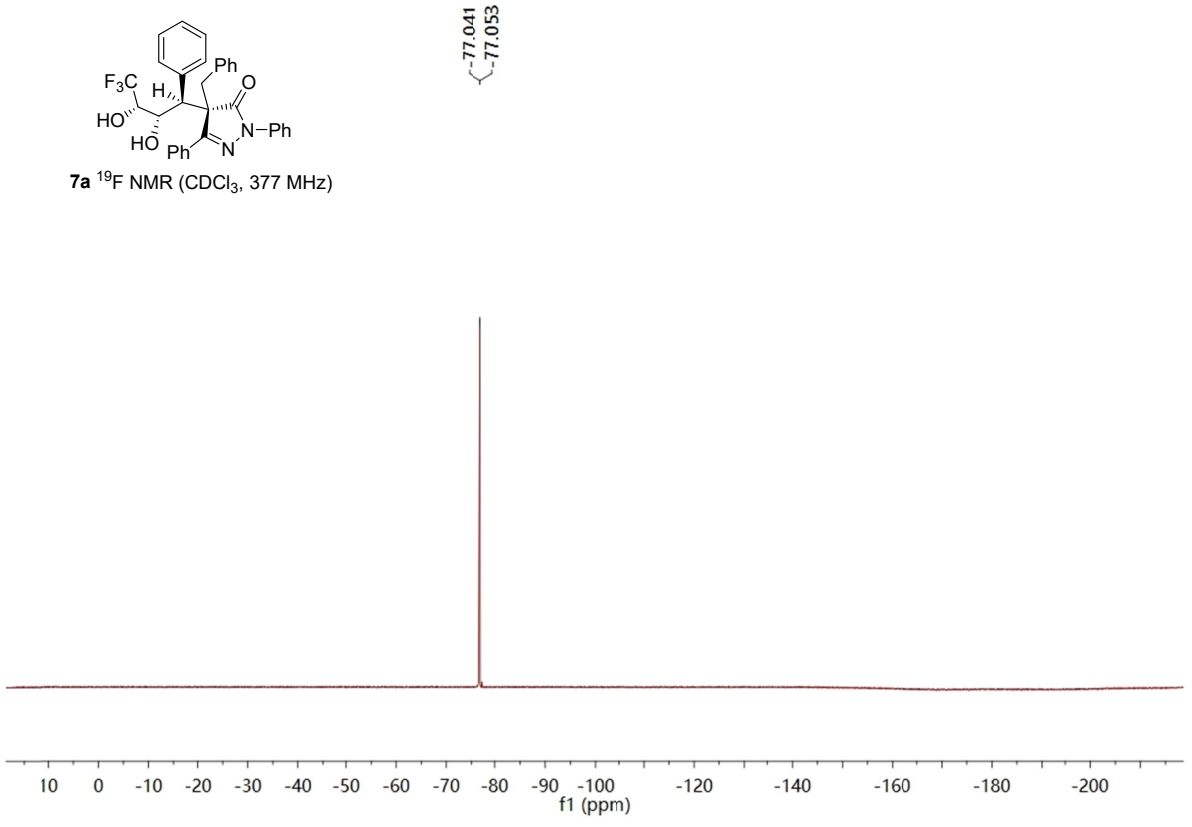




7a COSY NMR ($CDCl_3$, 400 MHz)

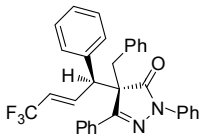


7a ^{13}C NMR ($CDCl_3$, 101 MHz)

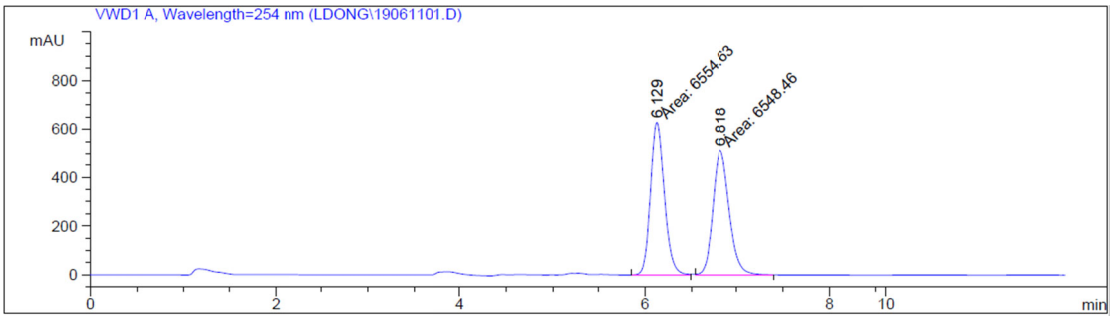


7a ^{19}F NMR ($CDCl_3$, 377 MHz)

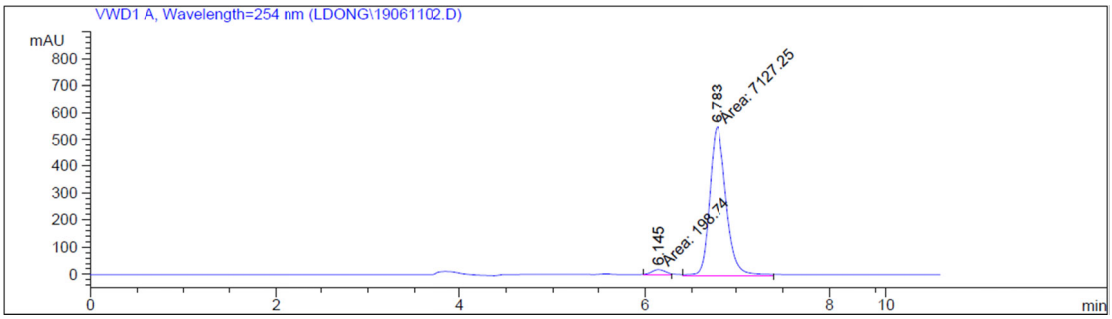
11. Copies of HPLC spectrum



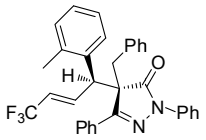
4a



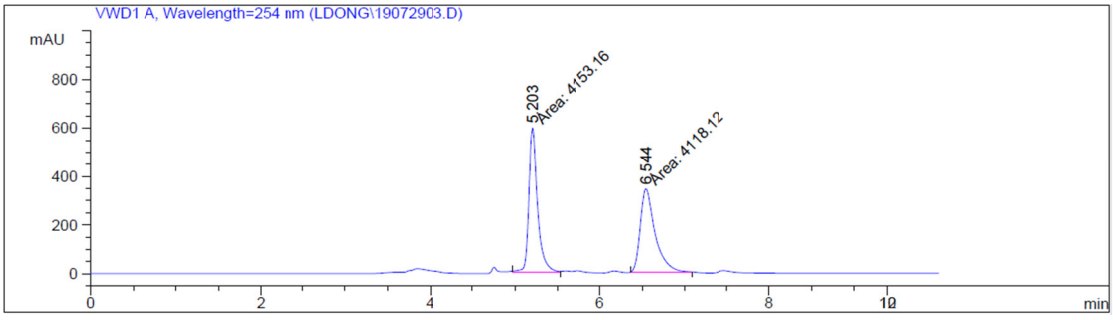
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.129	MM	0.1735	6554.63281	629.64233	50.0236
2	6.818	MM	0.2118	6548.45752	515.21313	49.9764



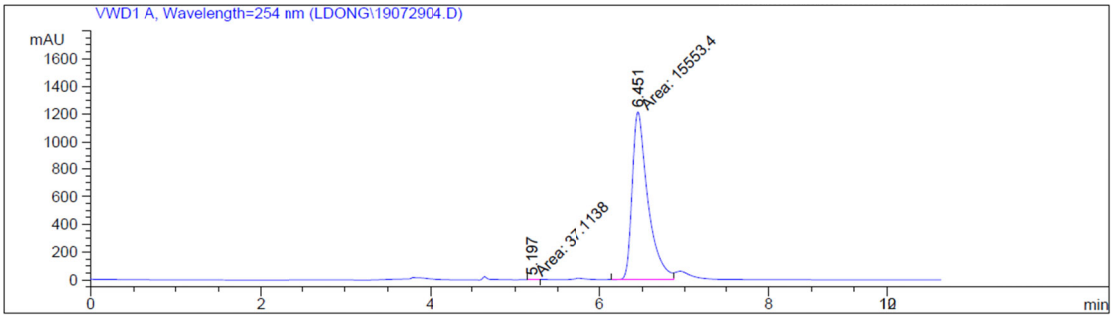
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.145	MM	0.1718	198.74040	19.27572	2.7128
2	6.783	MM	0.2149	7127.25439	552.66766	97.2872



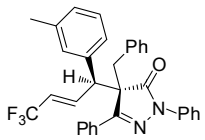
4b



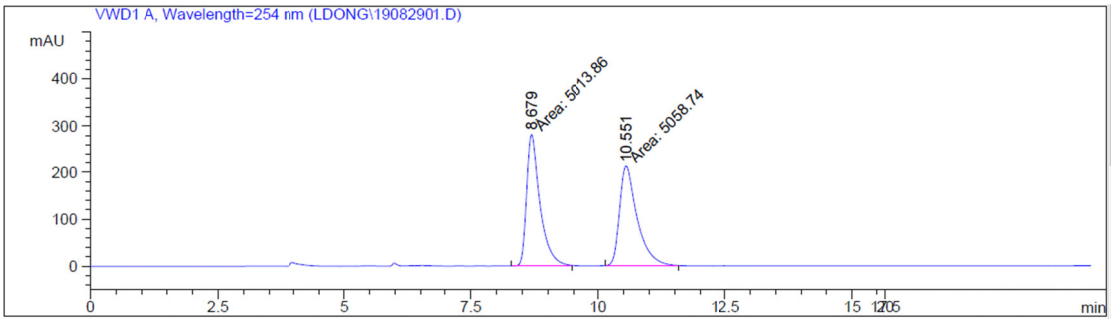
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.203	MM	0.1163	4153.15771	595.39893	50.2118
2	6.544	MM	0.2007	4118.11719	341.95682	49.7882



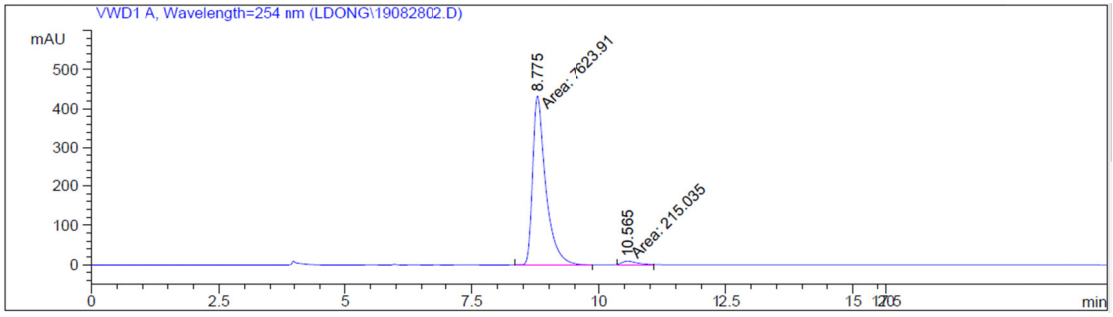
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.197	MM	0.1315	37.11379	4.70449	0.2381
2	6.451	MM	0.2130	1.55534e4	1217.22668	99.7619



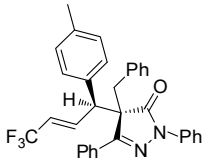
4c



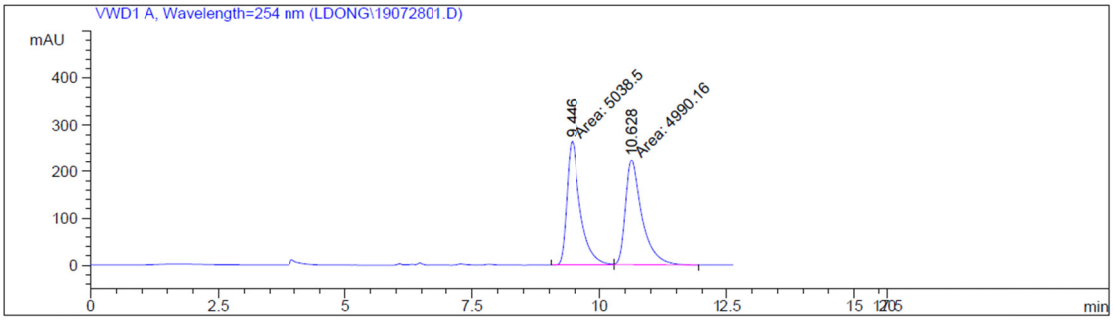
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.679	MM	0.2977	5013.86475	280.71616	49.7772
2	10.551	MM	0.3975	5058.74463	212.08707	50.2228



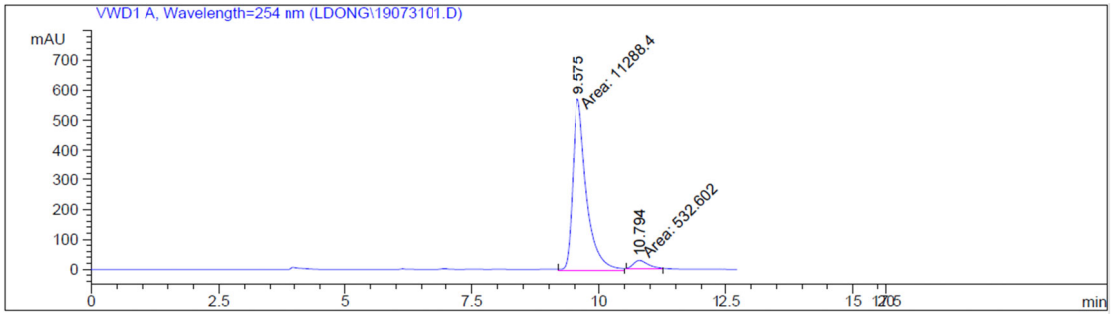
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.775	MM	0.2932	7623.91357	433.36597	97.2568
2	10.565	MM	0.3651	215.03452	9.81545	2.7432



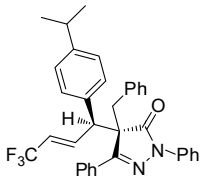
4d



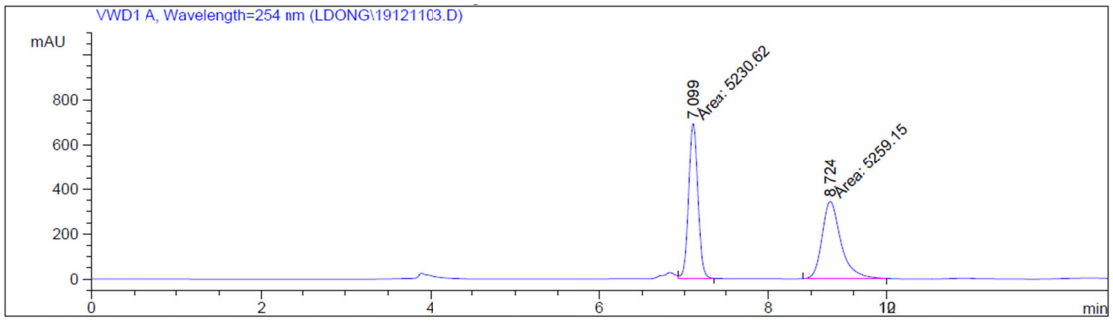
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.446	MM	0.3166	5038.49805	265.26724	50.2410
2	10.628	MM	0.3721	4990.15918	223.51845	49.7590



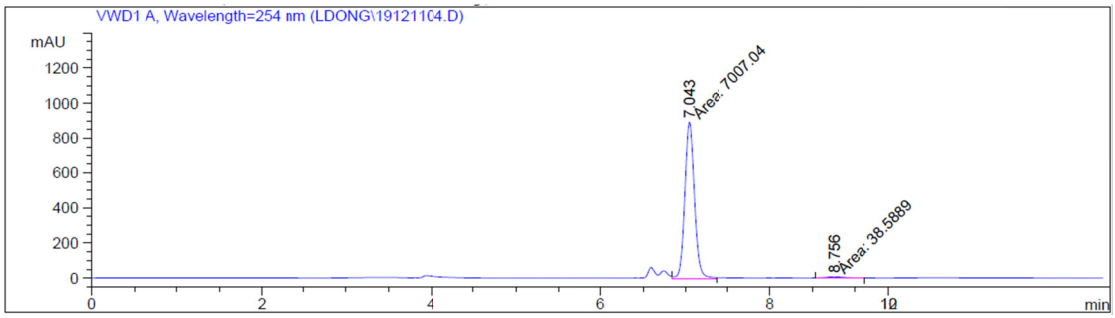
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.575	MM	0.3273	1.12884e4	574.82489	95.4945
2	10.794	MM	0.3242	532.60217	27.37759	4.5055



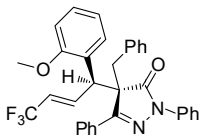
4e



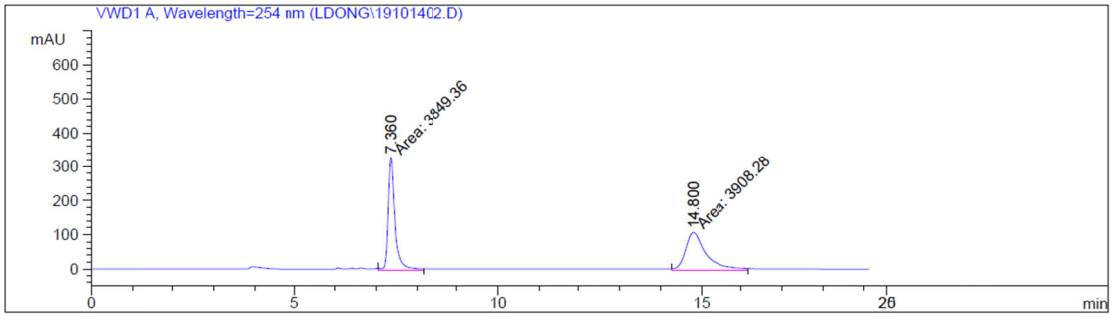
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.099	MM	0.1256	5230.62158	693.94574	49.8640
2	8.724	MM	0.2559	5259.14746	342.47577	50.1360



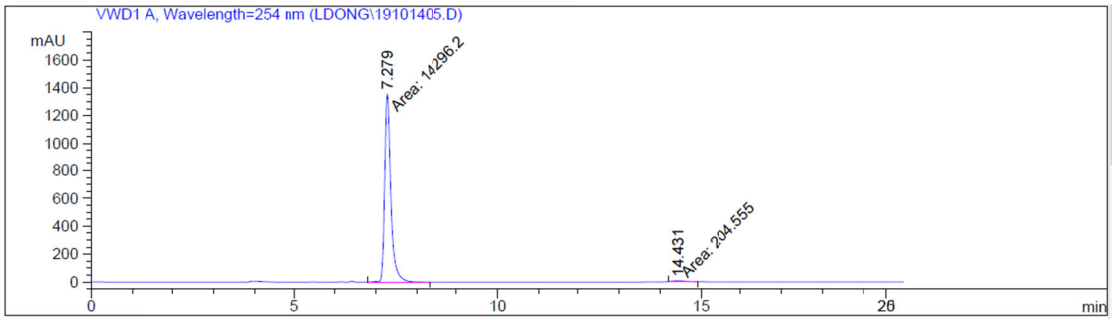
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.043	MM	0.1303	7007.04053	896.22119	99.4523
2	8.756	MM	0.1589	38.58890	4.04718	0.5477



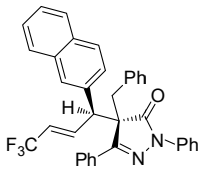
4f



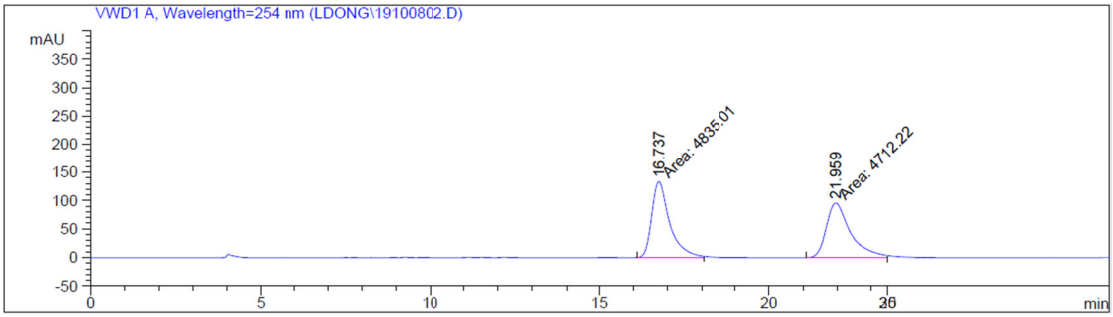
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.360	MM	0.1940	3849.36182	330.65579	49.6202
2	14.800	MM	0.5924	3908.28418	109.96266	50.3798



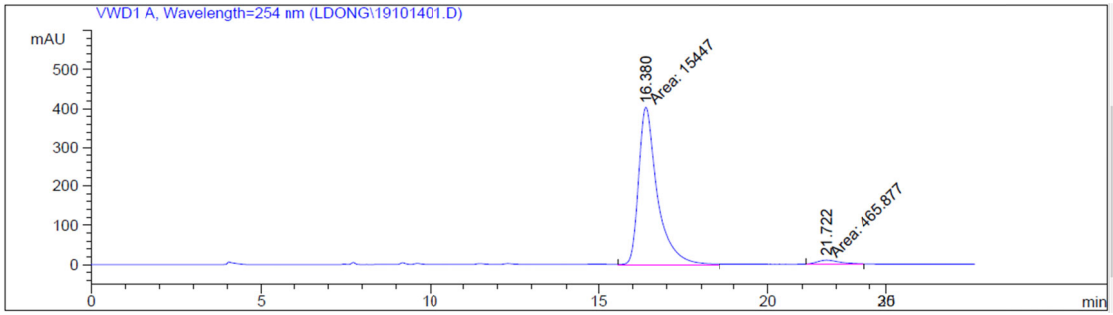
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.279	MM	0.1754	1.42962e4	1358.75342	98.5893
2	14.431	MM	0.4237	204.55542	8.04687	1.4107



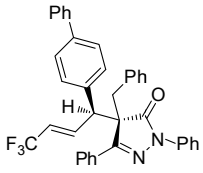
4g



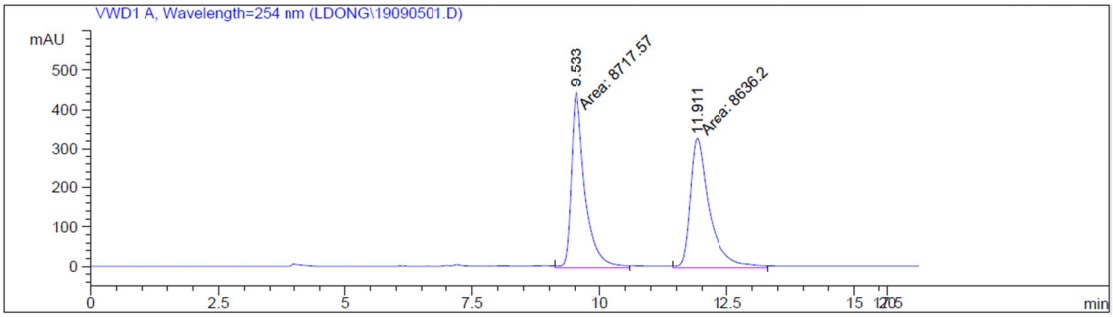
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.737	MM	0.6049	4835.01074	133.22649	50.6431
2	21.959	MM	0.8236	4712.21973	95.35827	49.3569



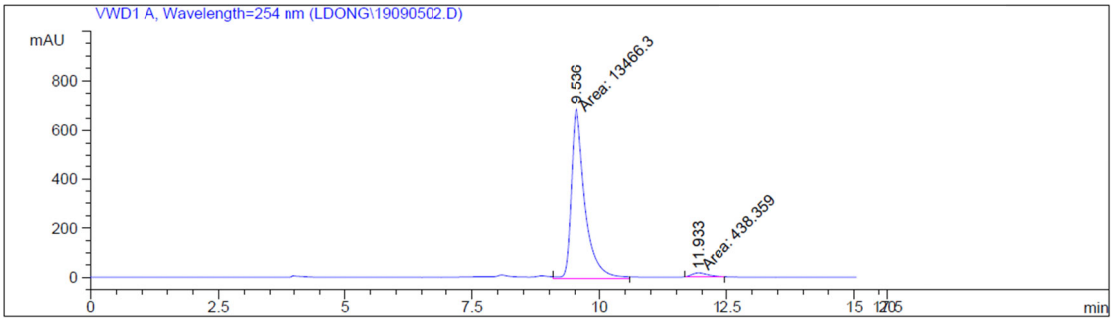
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.380	MM	0.6370	1.54470e4	404.18604	97.0723
2	21.722	MM	0.7810	465.87695	9.94179	2.9277



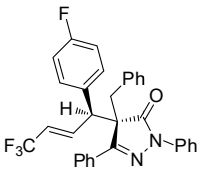
4h



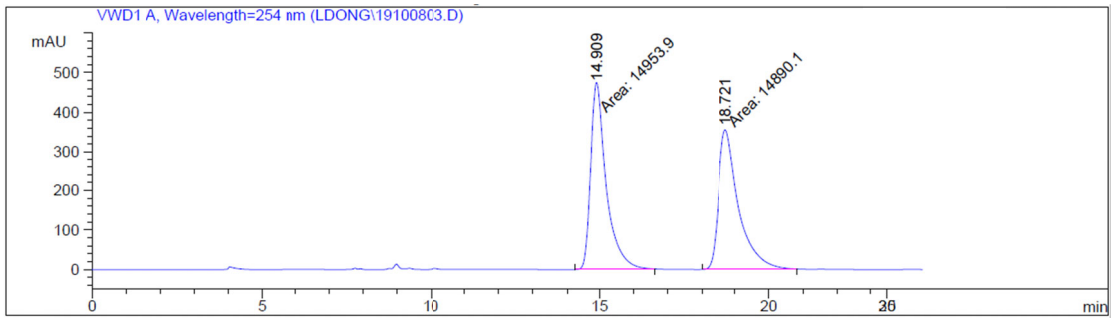
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.533	MM	0.3227	8717.57031	450.30133	50.2344
2	11.911	MM	0.4366	8636.20410	329.67978	49.7656



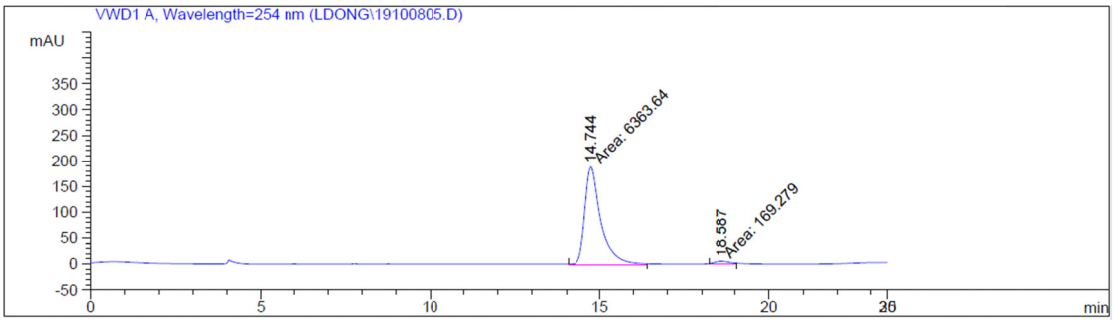
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.536	MM	0.3237	1.34663e4	693.35876	96.8474
2	11.933	MM	0.4063	438.35886	17.98360	3.1526



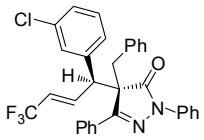
4i



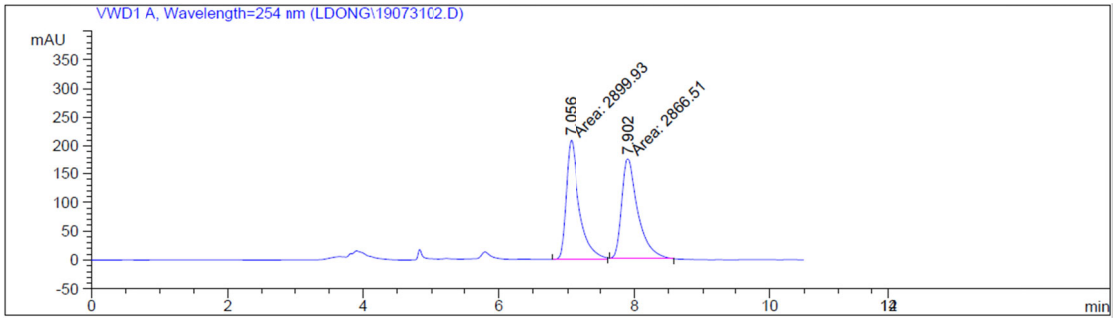
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.909	MM	0.5258	1.49539e4	474.03000	50.1069
2	18.721	MM	0.6988	1.48901e4	355.12781	49.8931



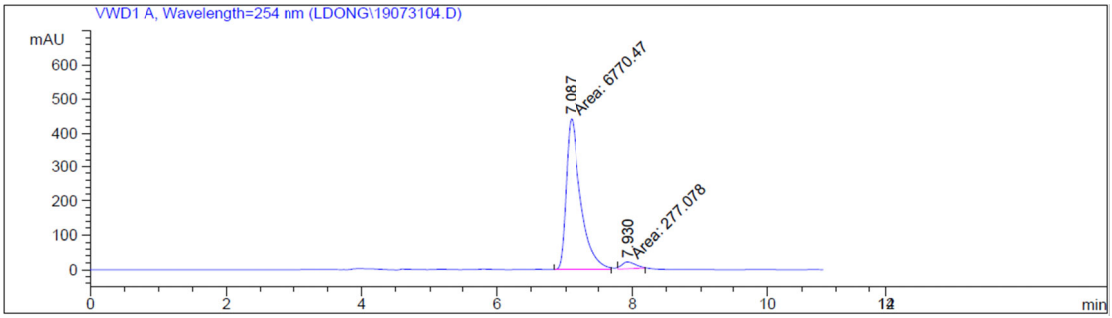
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.744	MM	0.5575	6363.64355	190.26044	97.4088
2	18.587	MM	0.5384	169.27898	5.24039	2.5912



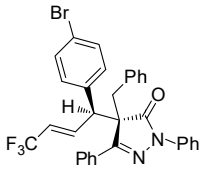
4j



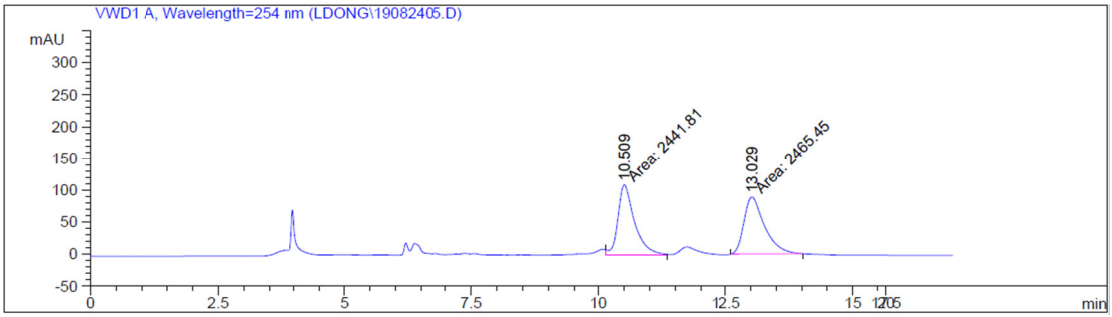
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.056	MM	0.2314	2899.92603	208.82416	50.2898
2	7.902	MM	0.2726	2866.50806	175.23656	49.7102



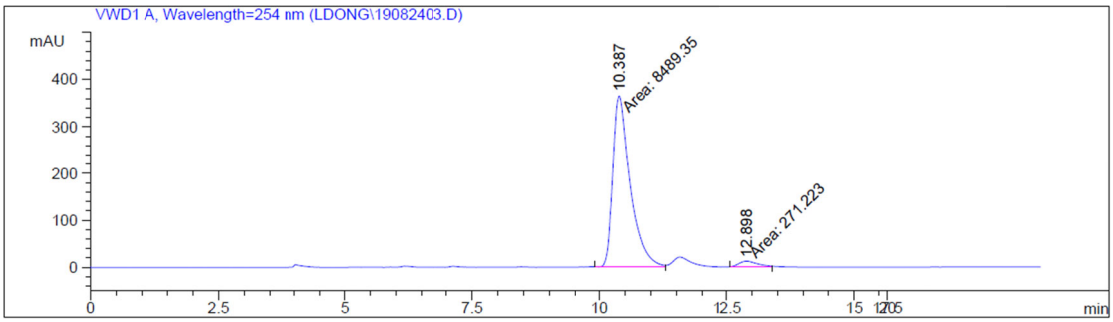
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.087	MM	0.2558	6770.47070	441.08014	96.0684
2	7.930	MM	0.2308	277.07325	20.01131	3.9316



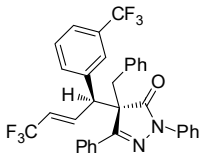
4k



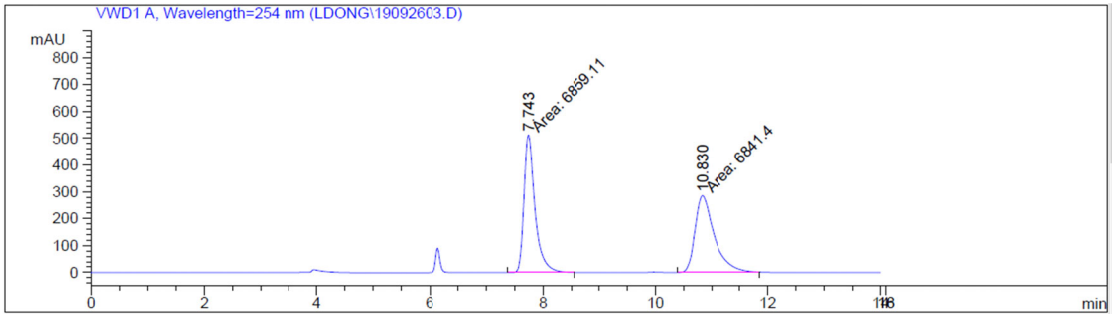
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.509	MM	0.3726	2441.81152	109.22926	49.7592
2	13.029	MM	0.4619	2465.44678	88.95197	50.2408



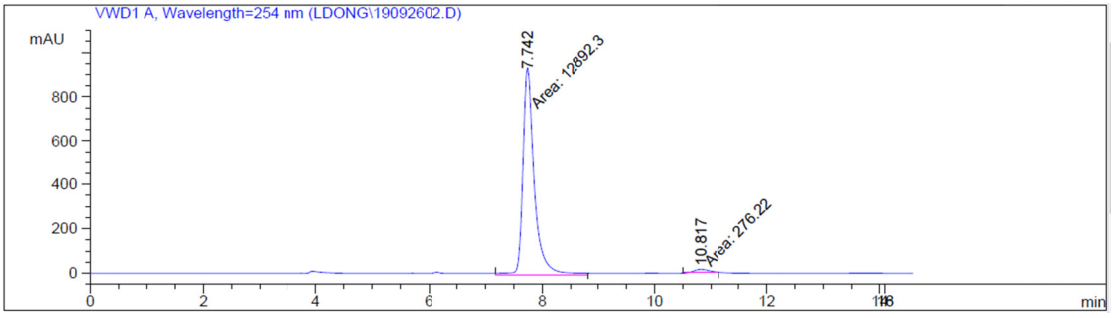
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.387	MM	0.3389	8489.34863	363.80173	96.9041
2	12.898	MM	0.3985	271.22260	11.34391	3.0959



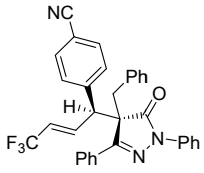
4l



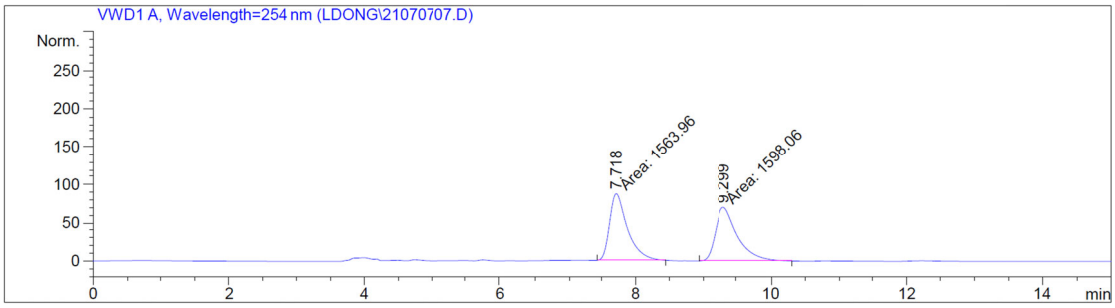
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.743	MM	0.2233	6859.10693	512.00098	50.0646
2	10.830	MM	0.4002	6841.40039	284.88446	49.9354



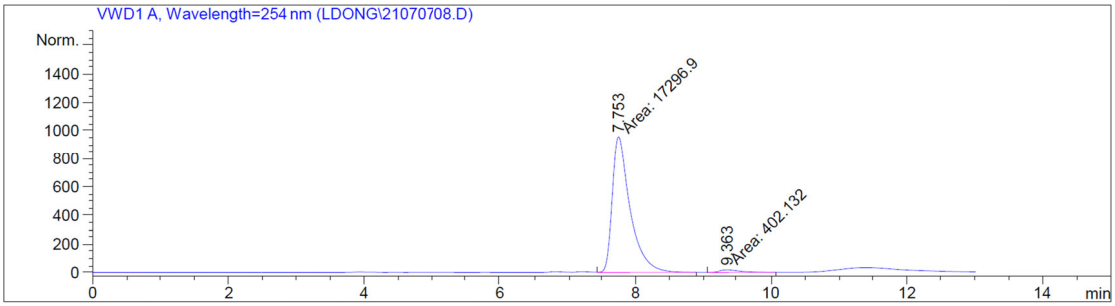
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.742	MM	0.2295	1.28923e4	936.31647	97.9024
2	10.817	MM	0.3079	276.22025	14.95183	2.0976



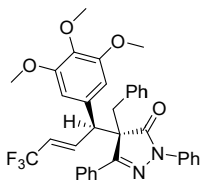
4m



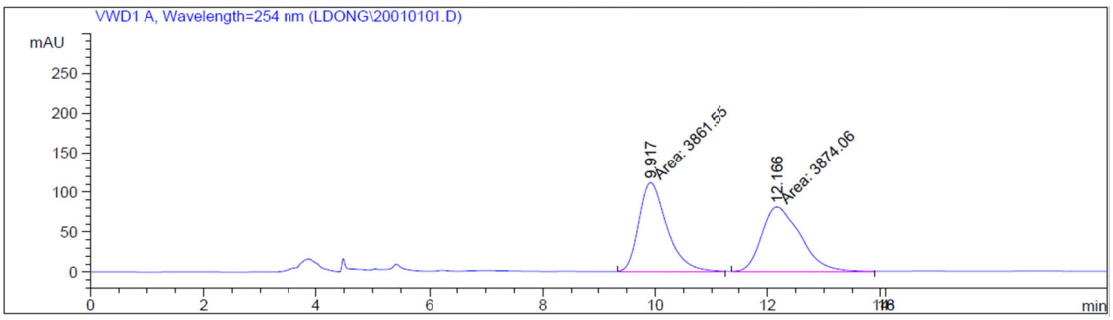
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.718	MM	0.2993	1563.96289	87.07621	49.4608
2	9.299	MM	0.3791	1598.05920	70.25195	50.5392



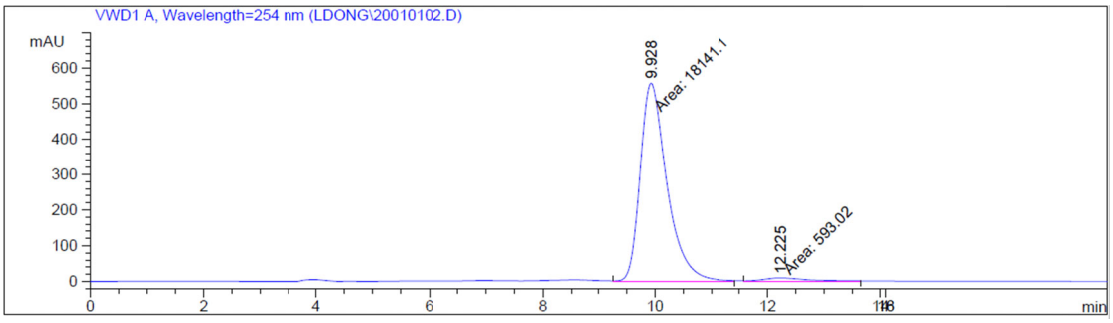
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.753	MM	0.3005	1.72969e4	959.26813	97.7279
2	9.363	MM	0.3638	402.13174	18.42396	2.2721



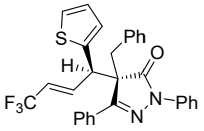
4n



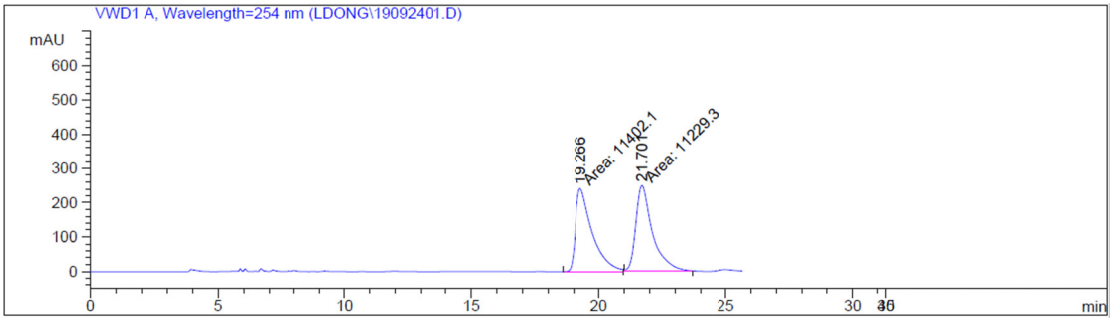
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.917	MM	0.5762	3861.55029	111.70404	49.9191
2	12.166	MM	0.7957	3874.06348	81.14972	50.0809



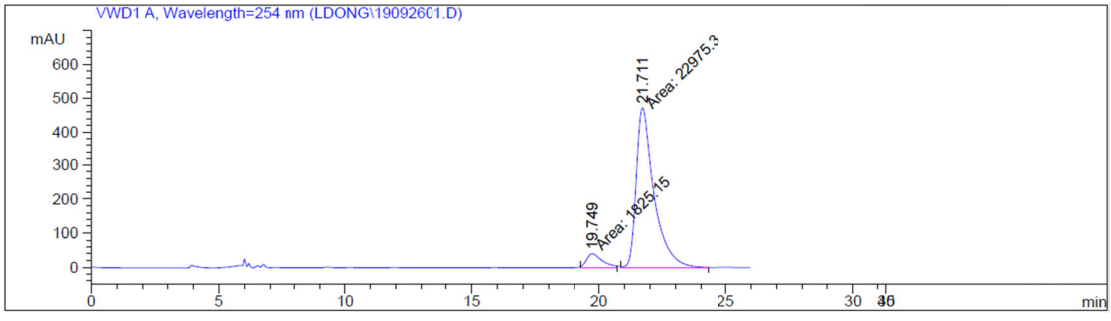
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.928	MM	0.5441	1.81411e4	555.65094	96.8345
2	12.225	MM	0.9881	593.01978	10.00281	3.1655



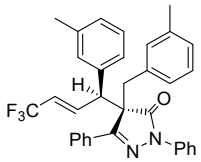
4o



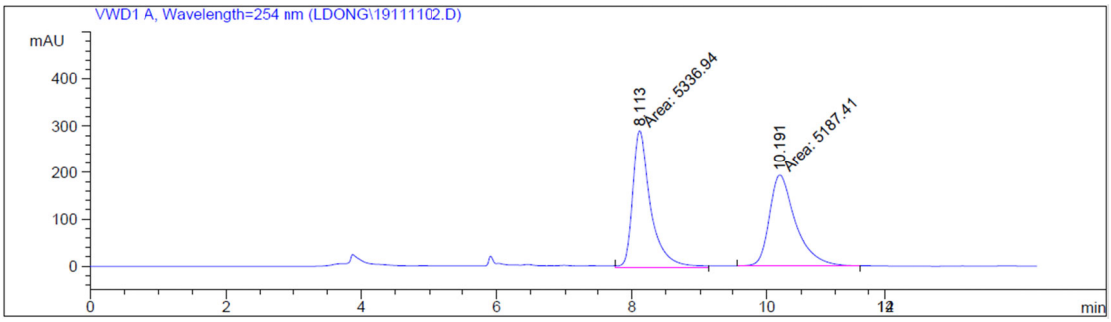
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.266	MM	0.7815	1.14021e4	243.17046	50.3818
2	21.701	MM	0.7538	1.12293e4	248.27692	49.6182



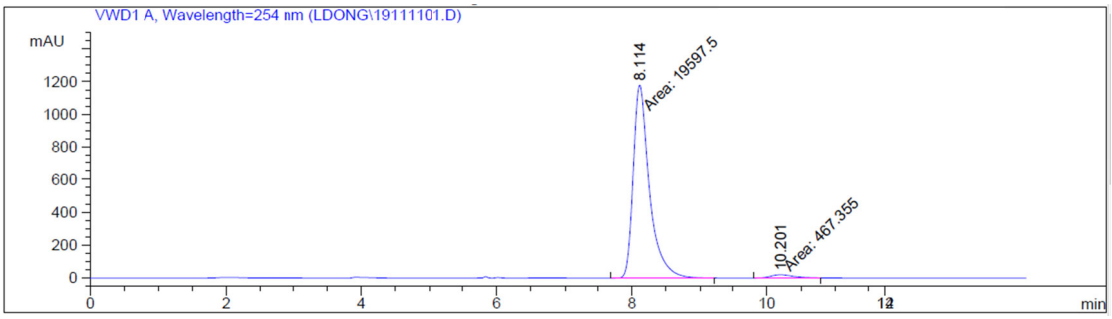
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.749	MM	0.7281	1825.14819	41.78017	7.3593
2	21.711	MM	0.8078	2.29753e4	474.00711	92.6407



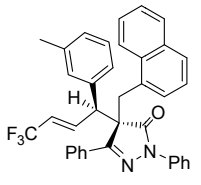
4q



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.113	MM	0.3043	5336.94043	292.29111	50.7104
2	10.191	MM	0.4461	5187.41455	193.81909	49.2896



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.114	MM	0.2766	1.95975e4	1180.65503	97.6708
2	10.201	MM	0.3912	467.35510	19.91253	2.3292



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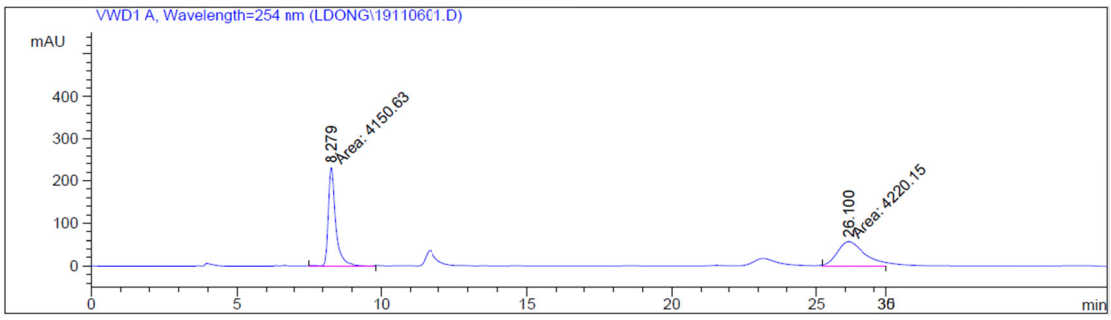
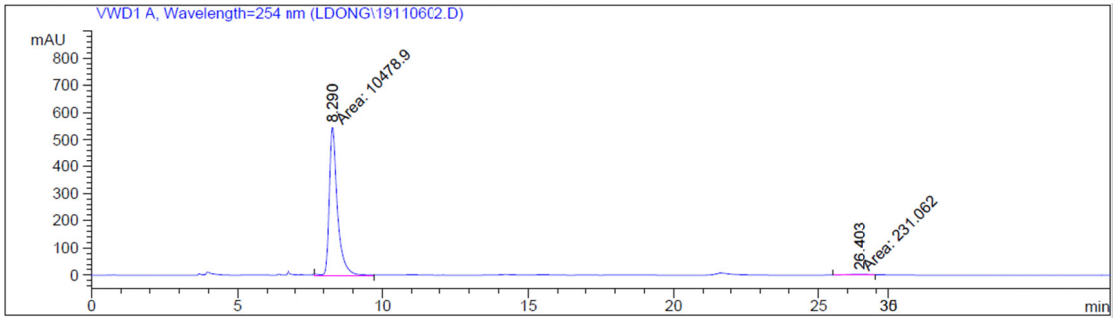
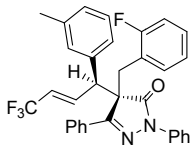


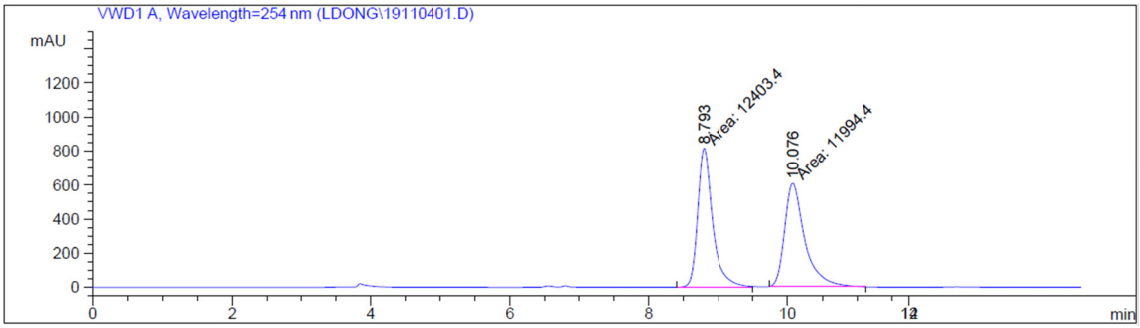
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.279	MM	0.2987	4150.63428	231.60814	49.5848
2	26.100	MM	1.2142	4220.14795	57.92579	50.4152



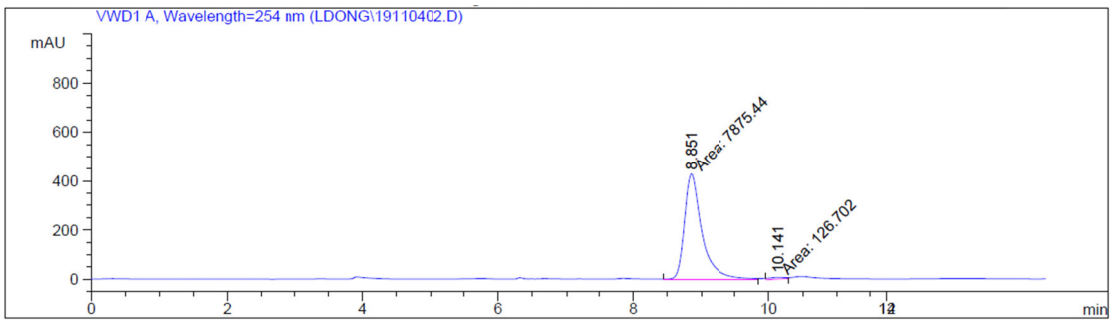
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.290	MM	0.3193	1.04789e4	547.00635	97.8426
2	26.403	MM	1.0012	231.06213	3.84634	2.1574



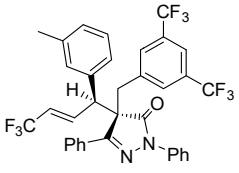
4s



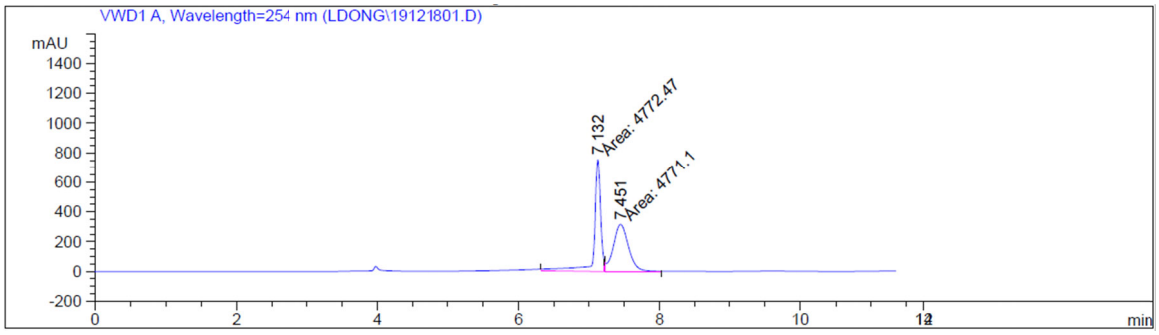
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.793	MM	0.2530	1.24034e4	817.23547	50.8380
2	10.076	MM	0.3312	1.19944e4	603.66272	49.1620



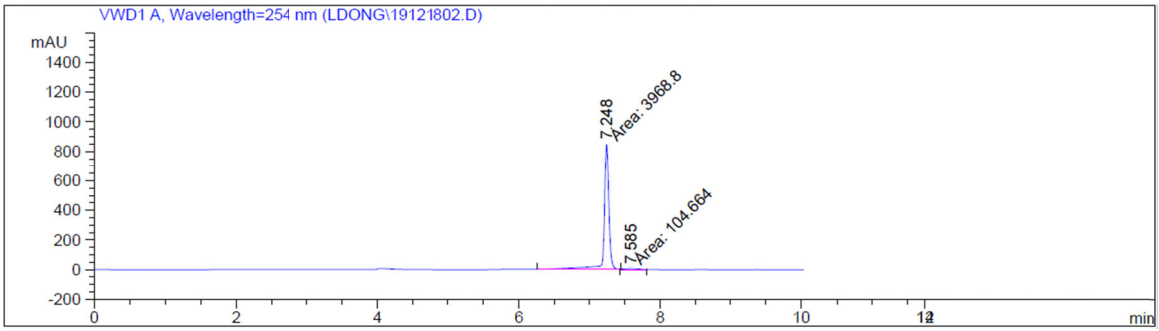
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.851	MM	0.3046	7875.43750	430.93393	98.4167
2	10.141	MM	0.2912	126.70174	7.25188	1.5833



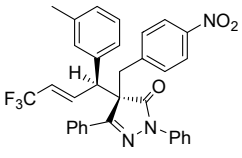
4t



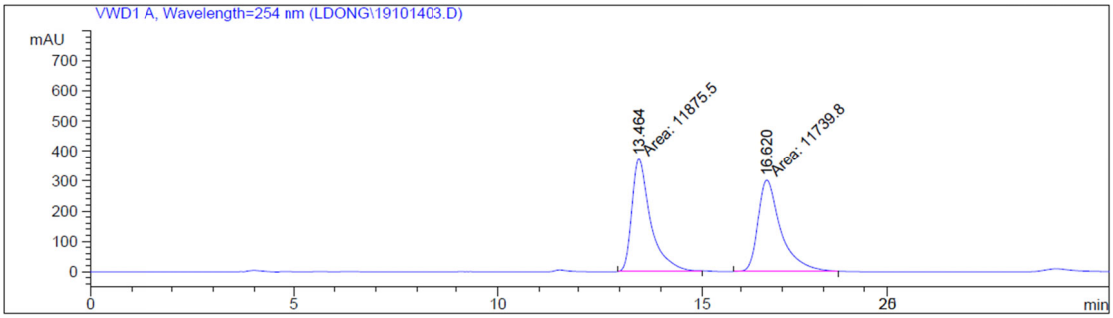
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.132	MM	0.1050	4772.47119	757.55859	50.0072
2	7.451	MM	0.2506	4771.10254	317.29169	49.9928



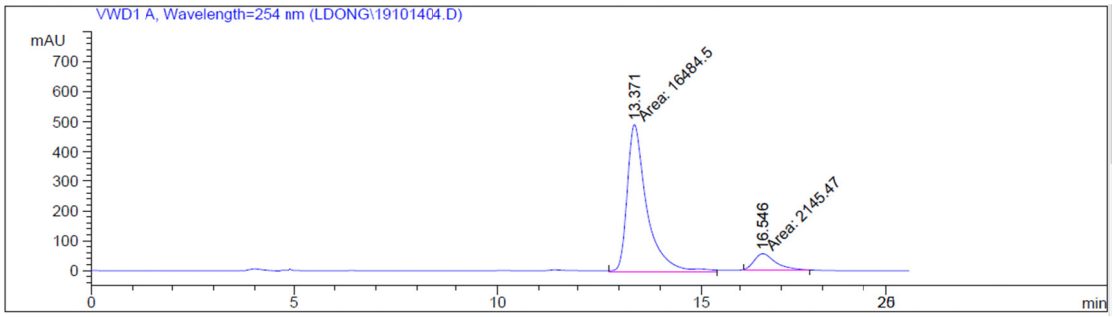
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.248	MM	0.0780	3968.80078	848.53668	97.4306
2	7.585	MM	0.2470	104.66351	7.06332	2.5694



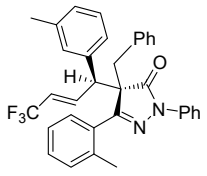
4u



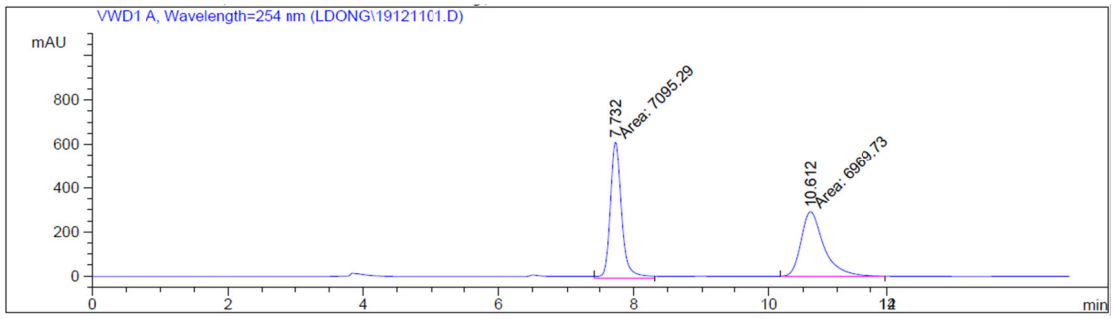
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.464	MM	0.5320	1.18755e4	372.02515	50.2872
2	16.620	MM	0.6476	1.17398e4	302.14951	49.7128



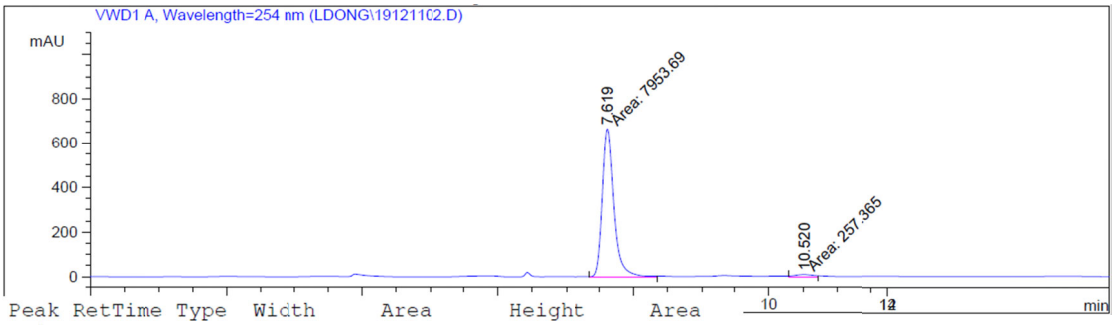
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.371	MM	0.5555	1.64845e4	494.60312	88.4837
2	16.546	MM	0.6357	2145.47119	56.25146	11.5163



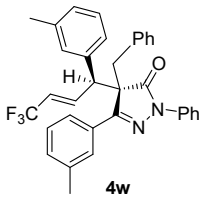
4v



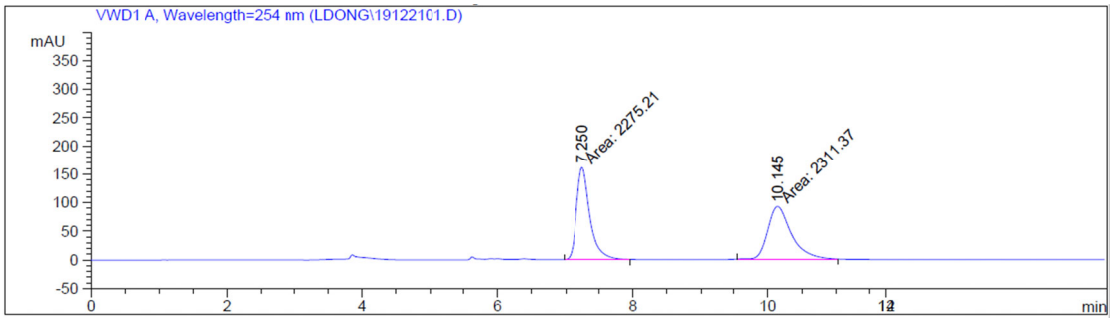
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.732	MM	0.1913	7095.28906	618.04041	50.4463
2	10.612	MM	0.3949	6969.73193	294.17920	49.5537



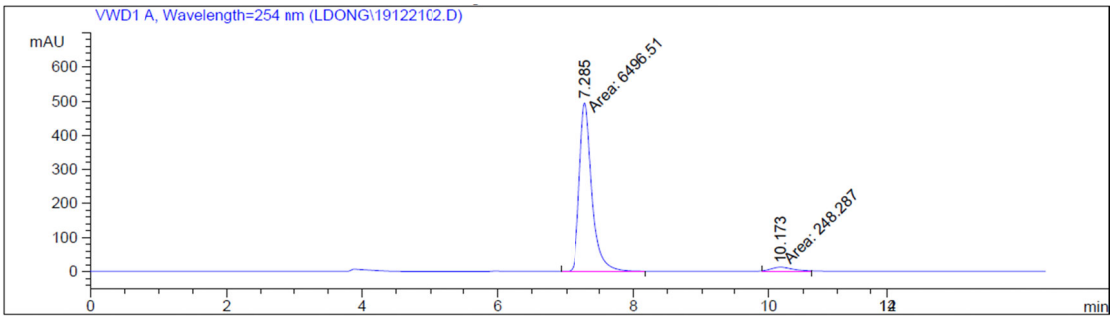
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.619	MM	0.1985	7953.69385	667.82977	96.8656
2	10.520	MM	0.3375	257.36545	12.70885	3.1344



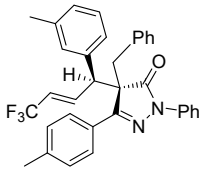
4w



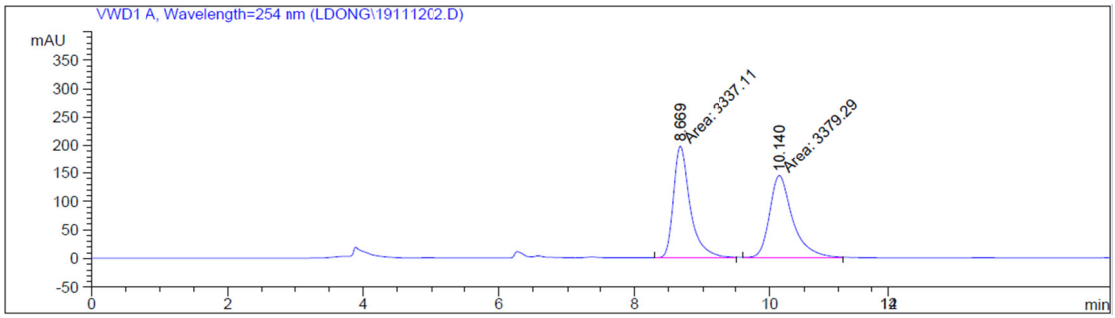
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.250	MM	0.2347	2275.20728	161.60056	49.6058
2	10.145	MM	0.4143	2311.36890	92.97404	50.3942



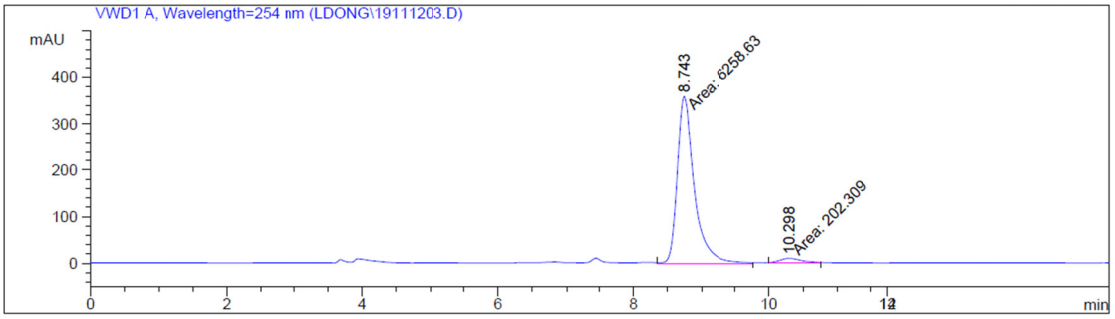
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.285	MM	0.2181	6496.51025	496.43604	96.3188
2	10.173	MM	0.3570	248.28709	11.59224	3.6812



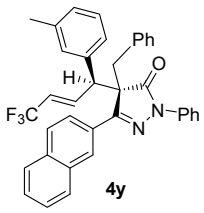
4x



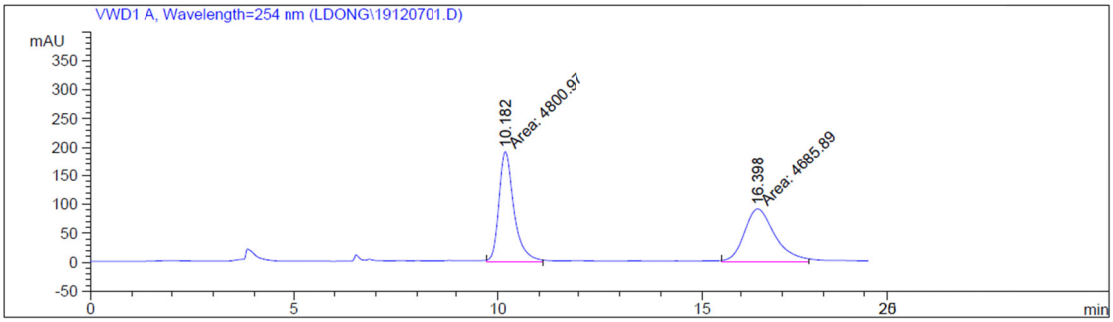
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.669	MM	0.2819	3337.10986	197.28165	49.6860
2	10.140	MM	0.3907	3379.28833	144.16446	50.3140



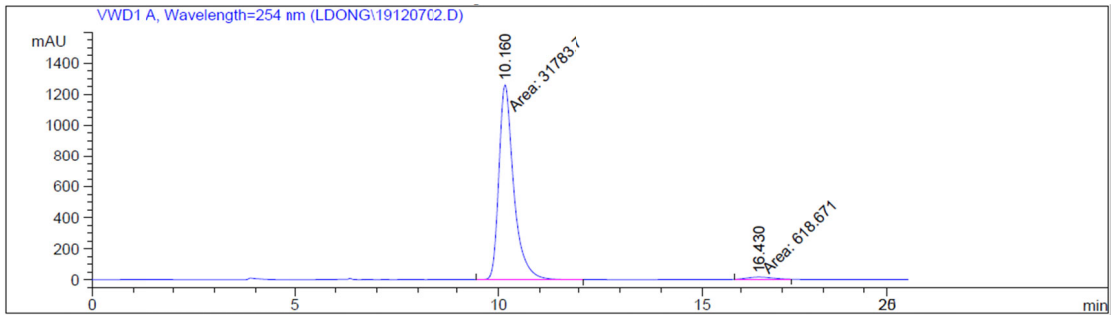
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.743	MM	0.2896	6258.62939	360.14124	96.8687
2	10.298	MM	0.3583	202.30896	9.41040	3.1313



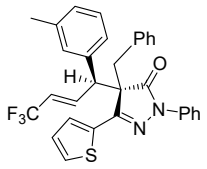
4y



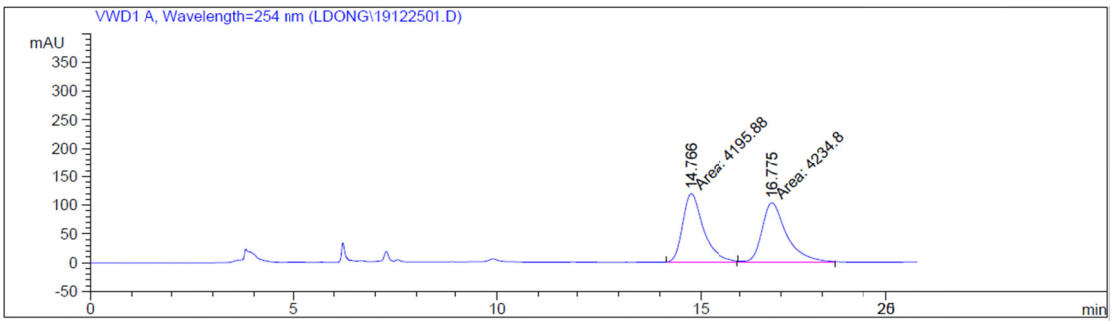
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.182	MM	0.4179	4800.97119	191.49046	50.6065
2	16.398	MM	0.8620	4685.88818	90.60236	49.3935



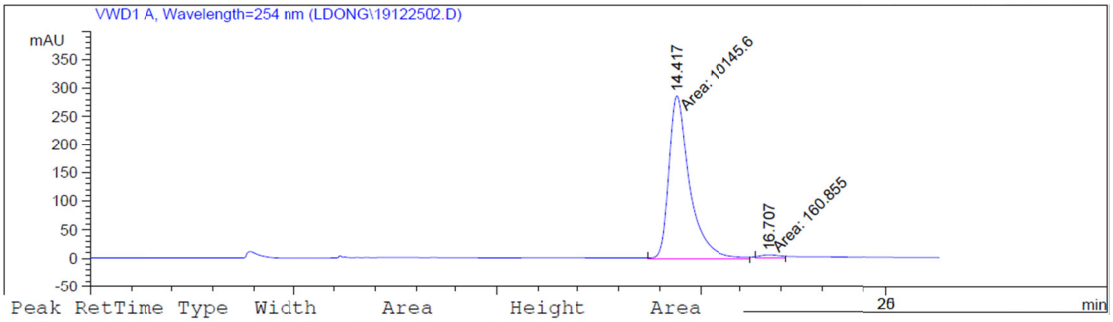
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.160	MM	0.4195	3.17837e4	1262.82141	98.0907
2	16.430	MM	0.7177	618.67133	14.36599	1.9093



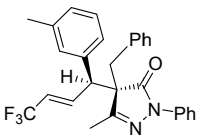
4z



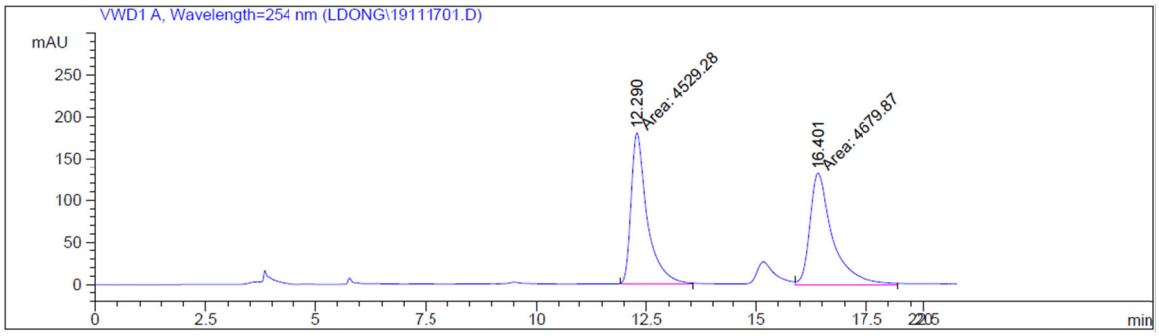
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.766	MM	0.5891	4195.87744	118.70083	49.7692
2	16.775	MM	0.6867	4234.79639	102.78461	50.2308



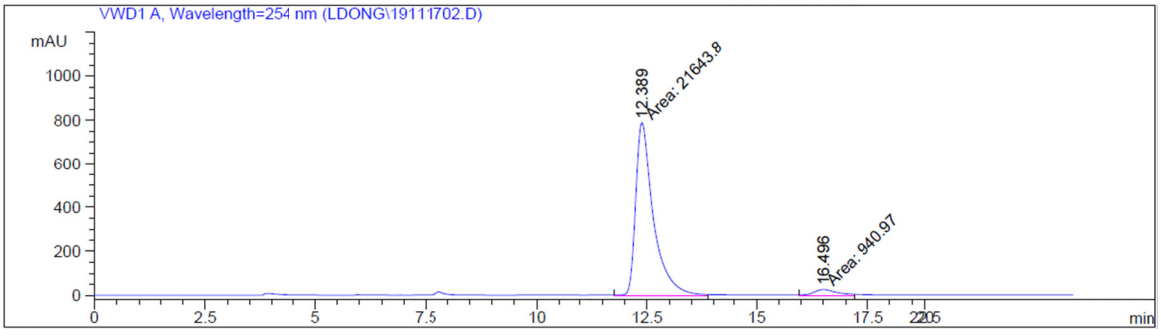
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.417	MM	0.5887	1.01456e4	287.22839	98.4393
2	16.707	MM	0.5511	160.85460	4.86477	1.5607



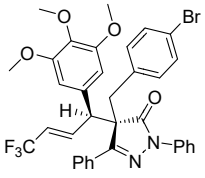
4aa



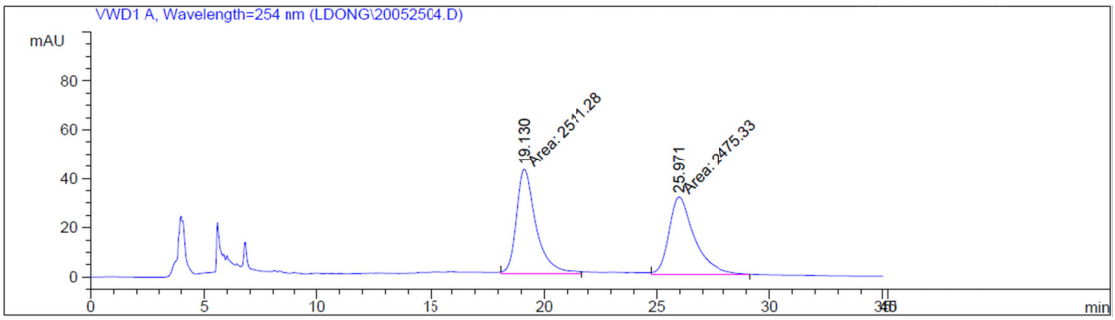
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.290	MM	0.4185	4529.28076	180.38916	49.1824
2	16.401	MM	0.5901	4679.87451	132.17416	50.8176



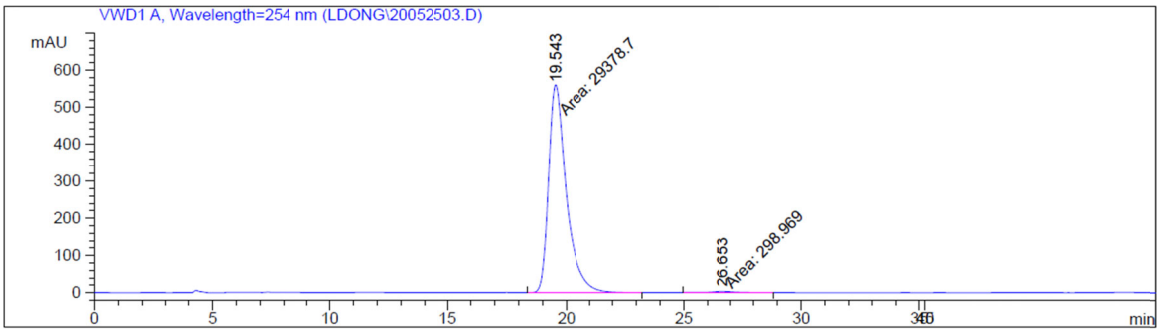
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.389	MM	0.4574	2.16438e4	788.71881	95.8336
2	16.496	MM	0.5952	940.96979	26.35018	4.1664



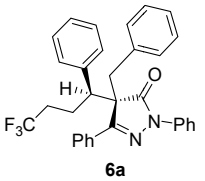
4ab



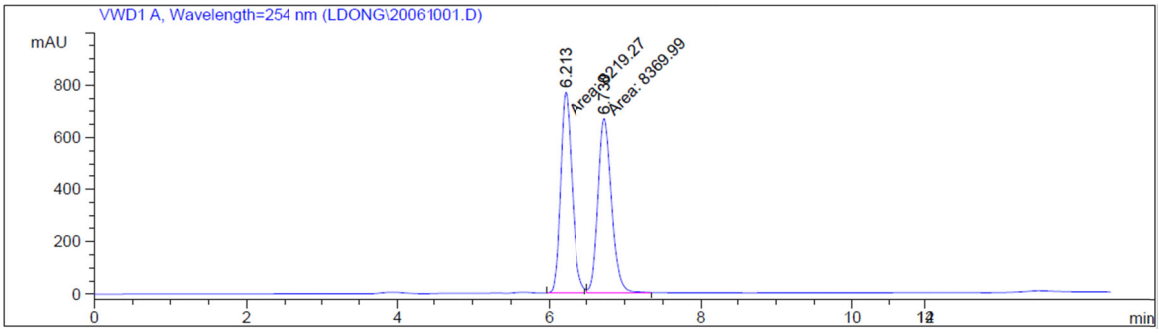
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.130	MM	0.9900	2511.27832	42.27901	50.3604
2	25.971	MM	1.3115	2475.33276	31.45665	49.6396



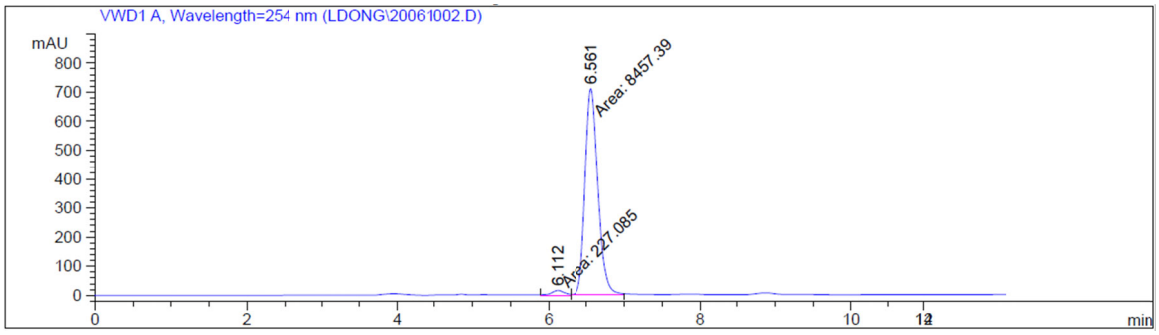
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.543	MM	0.8742	2.93787e4	560.11731	98.9926
2	26.653	MM	1.4432	298.96918	3.45267	1.0074



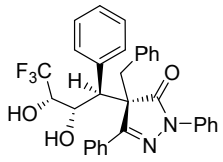
6a



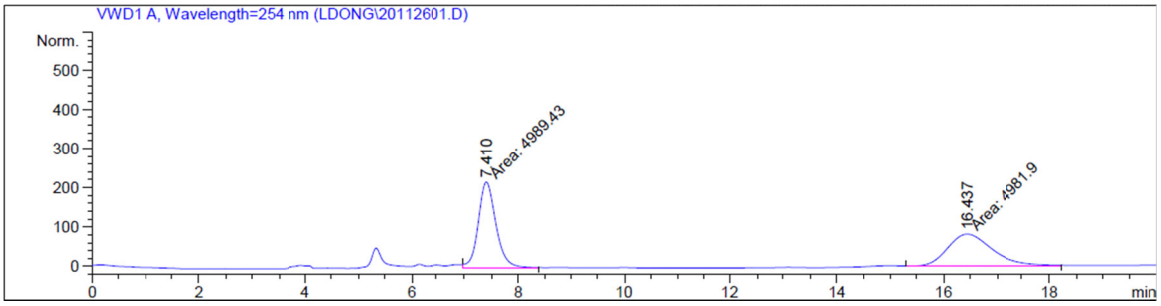
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.213	MM	0.1779	8219.27441	769.93646	49.5457
2	6.730	MM	0.2085	8369.98926	669.07452	50.4543



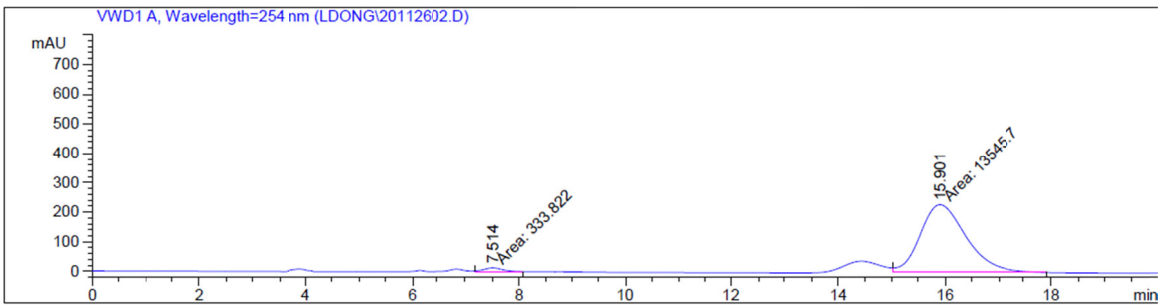
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.112	MM	0.2124	227.08501	17.82021	2.6148
2	6.561	MM	0.1983	8457.39355	710.87885	97.3852



7a



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.410	MM	0.3798	4989.42871	218.92755	50.0378
2	16.437	MM	1.0071	4981.89648	82.44707	49.9622



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.514	MM	0.4199	333.82156	13.24872	2.4051
2	15.901	MM	0.9913	1.35457e4	227.74120	97.5949