

Supporting Information
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Supporting Information

Palladium-Catalyzed Asymmetric Allylic Alkylation of Azlactones: An Efficient Access to Unsaturated Trifluoromethylated α -Amino Acid Derivatives Possessing α -Quaternary Stereogenic Centers

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Table of contents

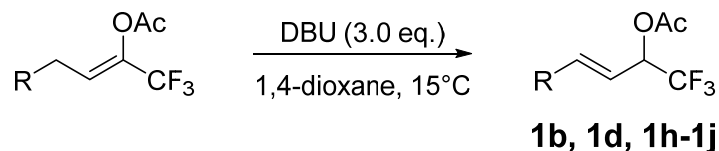
1. General Information.....	S2
2. Experimental procedure	S3
3. Crystal data and structure refinement for 3v	S6
4. Experimental characterization data for new products	S7
5. References.....	S36
6. Copy of NMR spectra for the products	S37

1. General Information

Unless otherwise noted, all reactions were performed under an argon atmosphere in glassware with magnetic stirring. Other reagents were purchased from commercial sources and used without further purification. All solvents used were treated prior to use according to the standard methods. Column chromatography was performed on silica gel (200 - 300 mesh) using petroleum ether/ethyl acetate as eluent. ¹H NMR, ¹⁹F NMR and ¹³C NMR were obtained on a Bruker Avance II 400 MHz, Varian DLG 400, Bruker AVANCE II 500 and Bruker Avance NEO 600M NMR Spectroscopy recorded in ppm (δ) downfield of TMS ($\delta = 0$) in CDCl₃ unless noted otherwise. Melting points were recorded on a Novel X-4 spectrometer. HRMS (ESI) were recorded on a Waters Synapt G2 Si. 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 D8 Venture diffractometer. **1b**, **1d** and **1h–1j** were synthesized through isomerization of corresponding α -(trifluoromethyl)alkenyl esters in the presence of 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) according to our previous work.^[1] Other α -(trifluoromethyl)allyl esters were prepared by the reaction of corresponding allylic alcohols with AcCl, Boc₂O or methyl chloroformate,^[2] and substituted azlactones were prepared according to the literature.^[3]

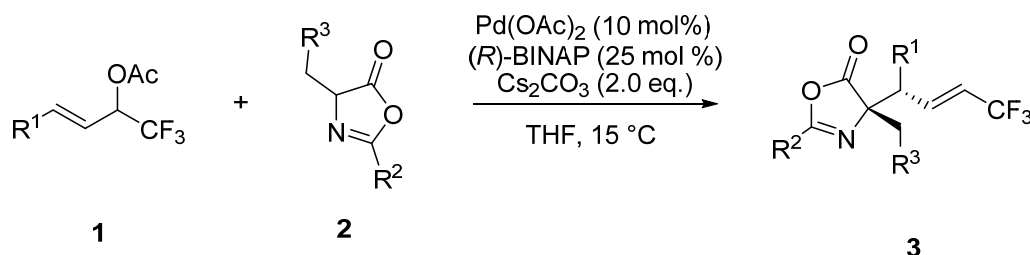
2. Experimental procedure

2.1 Procedure for the synthesis of α -(trifluoromethyl)allyl esters



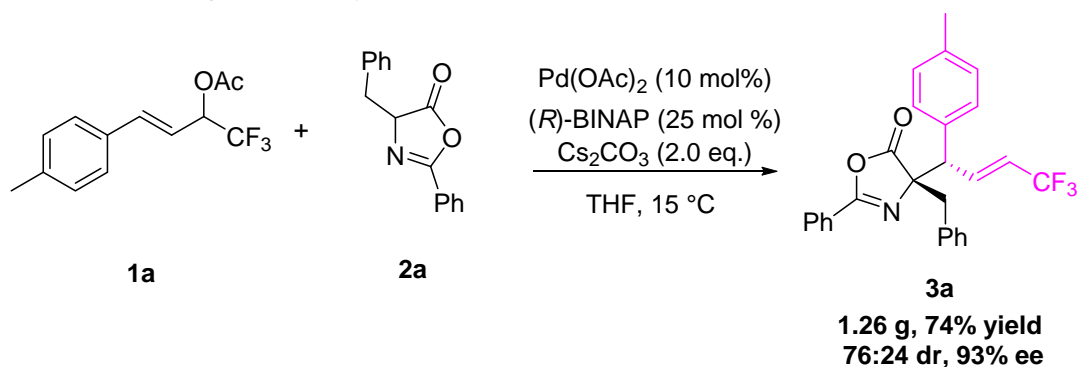
Dissolving the corresponding α -(trifluoromethyl)alkenyl esters (20 mmol) in 1,4-dioxane (40 mL) at 15 °C under argon atmosphere, and DBU (60 mmol, 3.0 equiv.) was added slowly. The reaction mixture was stirred at 15 °C for 24 h. After the reaction was completed (monitored by TLC), the solution was concentrated under reduced pressure and the crude was purified by column chromatography on silica gel to afford the products **1b, 1d and 1h-1j**.

2.2 General procedure for the asymmetric trifluoromethylated allylic alkylation of substituted azlactones



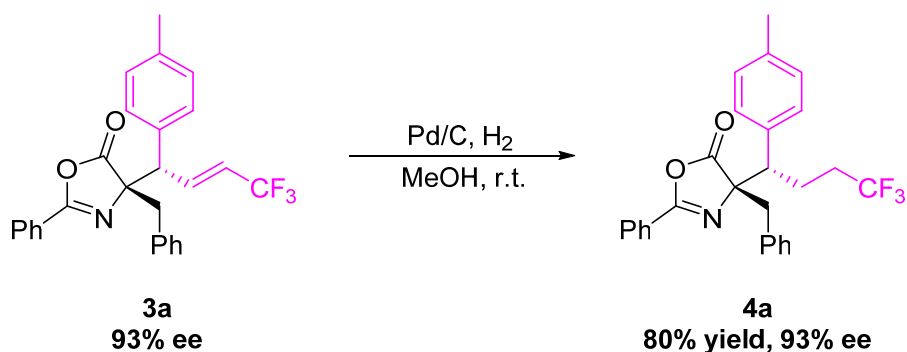
A flame-dried 25 mL Schlenk tube with a stirring bar was charged with Pd(OAc)₂ (0.02 mmol, 10 mol%), (*R*)-BINAP (0.05 mmol, 25 mol%) and THF (2.0 mL) under argon atmosphere, then the mixture was stirred at 15 °C for 20 min. Subsequently, allyl esters **1** (0.6 mmol, 3.0 equiv.), **2** (0.2 mmol, 1.0 equiv.), Cs₂CO₃ (0.4 mmol, 2.0 equiv.) and THF (2.0 mL) were added. The mixture was stirred at 15 °C for 96-144 h (monitored by TLC). After the reaction was completed, the solution was filtered and filtrate was concentrated under reduced pressure, the crude was purified by column chromatography on silica gel to afford the desired products **3**.

2.3 Procedure for gram-scale synthesis of 3a

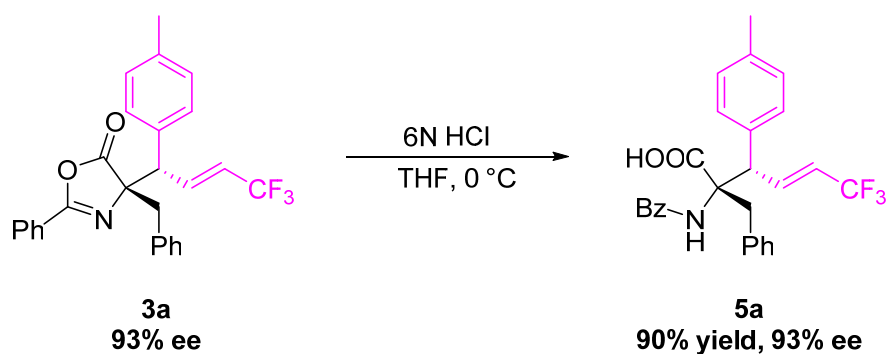


A flame-dried 200 mL Schlenk tube with a stirring bar was charged with Pd(OAc)₂ (85.3 mg, 0.38 mmol, 10 mol%), (*R*)-BINAP (591.5 mg, 0.95 mmol, 25 mol%) and THF (38.0 mL) under argon atmosphere, then the mixture was stirred at 15 °C for 20 min. Subsequently, allyl esters **1** (2942 mg, 11.4 mmol, 3.0 equiv.), **2** (954 mg, 3.8 mmol, 1.0 equiv.), Cs₂CO₃ (2476 mg, 7.6 mmol, 2.0 equiv.) and THF (38 mL) were added. The mixture was stirred at 15 °C for 96 h (monitored by TLC). After the reaction was completed, the solution was filtered and filtrate was concentrated under reduced pressure, the crude was purified by column chromatography on silica gel to afford the desired products **3a** (1.26 g, 74% yield, 76:24 dr, 93% ee for the major diastereoisomer).

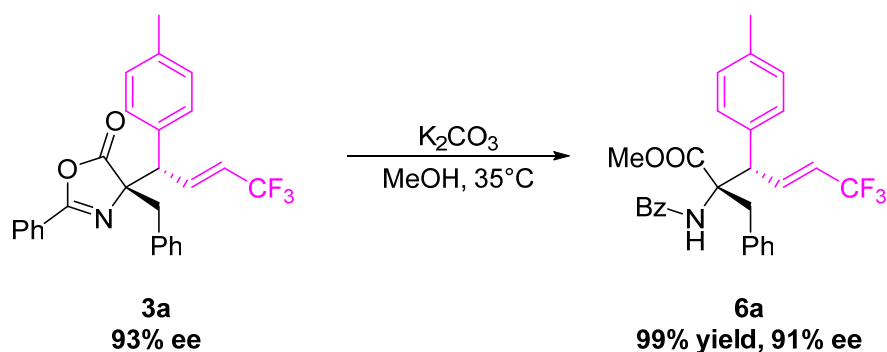
2.5 Procedure for the transformations of **3a**



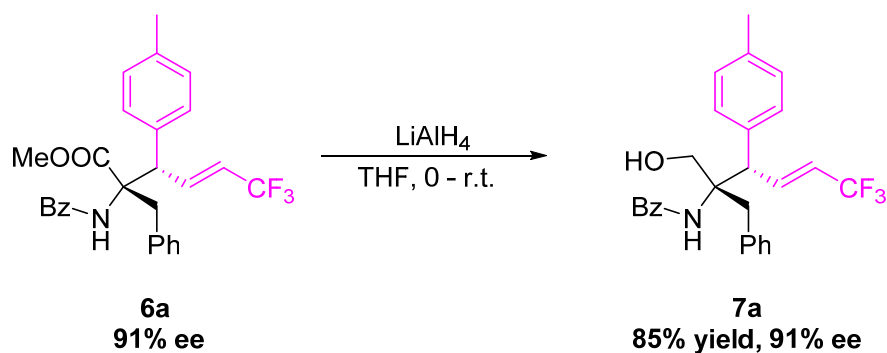
To a solution of **3a** (50 mg, 0.11 mmol) in CH₃OH (2.0 mL) was added 5% Pd/C (10 mg, 20% w/w). The resulting mixture was degassed and stirred under hydrogen gas balloon pressure at 25 °C. After the completion of hydrogenation (monitored by TLC), the mixture was filtered, concentrated under reduced pressure, and the crude was purified by column chromatography on silica gel to afford the desired product **4a** (80% yield, 93% ee).



To a solution of **3a** (60 mg, 0.13 mmol) in THF (2.0 mL) was added 6 N HCl (1 mL), the reaction mixture was stirred at 0 °C until **3a** was completely consumed. Then, water (20 mL) was added to the reaction system and extracted with CH₂Cl₂ (3 × 10 mL). The organics were combined and dried over Na₂SO₄ and concentrated under vacuum and purified by silica-gel column chromatography to give **5a** (90% yield, 93% ee).



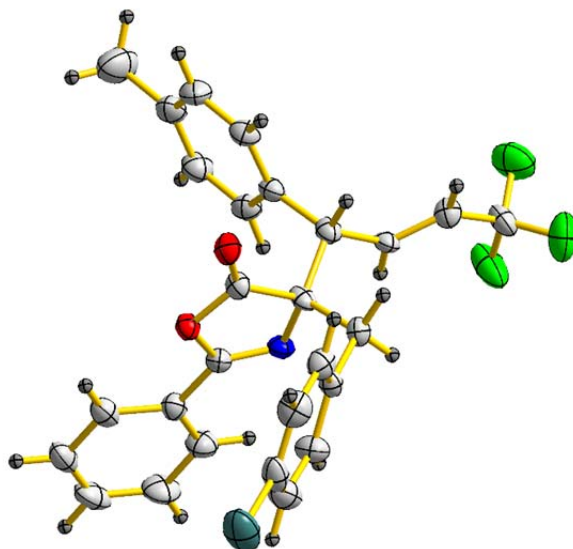
To a solution of **3a** (202 mg, 0.45 mmol) in MeOH (5.0 mL) was added K_2CO_3 (25 mg, 0.18 mmol, 40 mol%) at 35 °C and the reaction mixture was stirred overnight before concentrated in vacuo and purified by silica-gel column chromatography to give **6a** (99% yield, 91% ee).



A flame-dried 25 mL Schlenk tube with a stirring bar was charged with LiAlH_4 (17 mg, 0.45 mmol, 3.0 equiv.) and THF (1.5 mL) under argon atmosphere, then the mixture was cooled to 0 °C, and **6a** (72 mg, 0.15 mmol, 1.0 equiv.) was added in portions, then the reaction was warmed to room temperature. After the reaction was completed, sodium hydroxide solution (15%, 2 mL) was added to quench the reaction. Then, water (20 mL) was added to the reaction system and extracted with CH_2Cl_2 (3 × 20 mL). 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 product **7a** (85% yield, 91% ee).

3. Crystal data and structure refinement for 3v

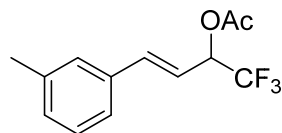
The crystals of **3v** were obtained by slow evaporation of the solution (in Et₂O) in the refrigerator.



Empirical formula	C ₂₇ H ₂₁ ClF ₃ NO ₂
Formula weight	483.12
Temperature/K	120
Crystal system	orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
a/Å	27.5771(16)
b/Å	6.7609(4)
c/Å	15.3198(9)
α/°	90
β/°	90
γ/°	90
Volume/Å ³	2613.9(3)
Z	4
ρ _{calc} /cm ³	1.230
μ/mm ⁻¹	0.190
F(000)	1000.0
Crystal size/mm ³	0.2 × 0.15 × 0.1
Radiation	MoKα (λ = 0.71073)
2θ range for data collection/°	5.812 to 50
Index ranges	-32 ≤ h ≤ 32, -8 ≤ k ≤ 8, -18 ≤ l ≤ 18
Reflections collected	23905
Independent reflections	4443 [R _{int} = 0.0802, R _{sigma} = 0.0695]
Data/restraints/parameters	4443/1/309
Goodness-of-fit on F ²	1.024
Final R indexes [I ≥ 2σ(I)]	R ₁ = 0.0571, wR ₂ = 0.1358
Final R indexes [all data]	R ₁ = 0.0838, wR ₂ = 0.1470
Largest diff. peak/hole / e Å ⁻³	0.23/-0.27

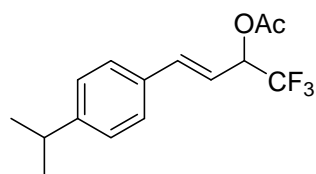
4. Experimental characterization data for new products

(*E*)-1,1,1-Trifluoro-4-(*m*-tolyl)but-3-en-2-yl acetate (**1b**)



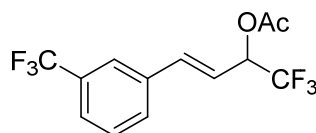
Purified using a Biotage flash chromatography system (PE/EtOAc, 10:1). Yield: 4.4 g (85%); pale yellow oil. ^1H NMR (500 MHz, CDCl_3) δ = 7.25 – 7.17 (m, 3H), 7.13 – 7.09 (m, 1H), 6.82 (d, J = 15.9 Hz, 1H), 6.10 (dd, J = 15.9, 7.8 Hz, 1H), 5.86 – 5.77 (m, 1H), 2.33 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ = 168.8, 138.9, 138.4, 135.0, 129.9, 128.7, 127.7, 124.2, 123.3 (q, J = 280.4 Hz), 117.1, 71.2 (q, J = 33.5 Hz), 21.3, 20.6. ^{19}F NMR (376 MHz, CDCl_3) δ = -76.50 (d, J = 6.7 Hz). HRMS (EI) m/z : calcd for $\text{C}_{13}\text{H}_{13}\text{F}_3\text{O}_2$ [$\text{M}^{+\bullet}$] 258.0868, found: 258.0866.

(*E*)-1,1,1-Trifluoro-4-(4-isopropylphenyl)but-3-en-2-yl acetate (**1d**)



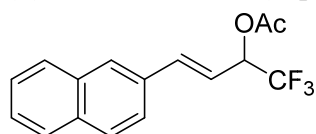
Purified using a Biotage flash chromatography system (PE/EtOAc, 10:1). Yield: 4.7 g (83%); pale yellow oil. ^1H NMR (500 MHz, CDCl_3) δ = 7.34 (m, 2H), 7.20 (m, 2H), 6.84 (d, J = 15.9 Hz, 1H), 6.07 (dd, J = 15.9, 7.9 Hz, 1H), 5.86 – 5.77 (m, 1H), 2.94 – 2.85 (m, 1H), 2.15 (s, 3H), 1.24 (d, J = 7.0 Hz, 6H). ^{13}C NMR (126 MHz, CDCl_3) δ = 168.8, 150.2, 138.8, 132.7, 127.1, 126.8, 123.3 (q, J = 280.3 Hz), 116.3, 71.2 (q, J = 33.5 Hz), 34.0, 23.8, 20.6. ^{19}F NMR (470 MHz, CDCl_3) δ = -76.54 (d, J = 6.9 Hz). HRMS (EI) m/z : calcd for $\text{C}_{15}\text{H}_{17}\text{F}_3\text{O}_2$ [$\text{M}^{+\bullet}$] 286.1181, found: 286.1182.

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



Purified using a Biotage flash chromatography system (PE/EtOAc, 10:1). Yield: 5.0 g (80%); yellow oil. ^1H NMR (400 MHz, CDCl_3) δ = 7.66 (s, 1H), 7.62 – 7.54 (m, 2H), 7.52 – 7.44 (m, 1H), 6.89 (d, J = 15.9 Hz, 1H), 6.19 (dd, J = 15.9, 7.5 Hz, 1H), 5.89 – 5.78 (m, 1H), 2.20 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ = 168.8, 137.0, 135.8, 131.3 (q, J = 32.4 Hz), 130.1, 129.2, 125.5 (q, J = 3.8 Hz), 123.9 (q, J = 272.3 Hz), 123.6 (q, J = 3.9 Hz), 123.0 (q, J = 280.5 Hz), 119.4, 70.7 (q, J = 33.6 Hz), 20.5. ^{19}F NMR (470 MHz, CDCl_3) δ = -62.97 (s, 3F), -76.49 (d, J = 6.8 Hz, 3F). HRMS (EI) m/z : calcd for $\text{C}_{13}\text{H}_{10}\text{F}_6\text{O}_2$ [$\text{M}^{+\bullet}$] 312.0585, found: 312.0586.

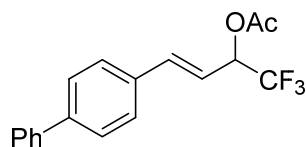
(*E*)-1,1,1-Trifluoro-4-(naphthalen-2-yl)but-3-en-2-yl acetate (**1i**)



Purified using a Biotage flash chromatography system (PE/EtOAc, 10:1). Yield: 5.0 g (85%); white solid; mp 111–112 °C. ^1H NMR (400 MHz, CDCl_3) δ = 7.88 – 7.81 (m, 4H), 7.65 – 7.59 (m, 1H), 7.55 – 7.48 (m, 2H), 7.05 (d, J = 15.9 Hz, 1H), 6.26 (dd, J = 15.9, 7.8 Hz, 1H), 5.97 – 5.86 (m, 1H), 2.23 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ = 168.9, 138.9, 133.7, 133.4, 132.5, 128.5, 128.3, 127.9, 127.8, 126.7, 126.6, 123.3 (q, J = 280.5 Hz), 123.3, 117.6, 71.2 (q, J = 33.5 Hz), 20.7. ^{19}F NMR (470 MHz, CDCl_3) δ = -76.34 (d, J = 6.7 Hz). HRMS

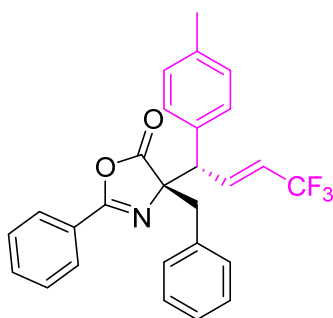
(EI) m/z : calcd for $C_{16}H_{13}F_3O_2 [M^+]$ 294.0868, found: 294.0864.

(E)-4-([1,1'-Biphenyl]-4-yl)-1,1,1-trifluorobut-3-en-2-yl acetate (1j)

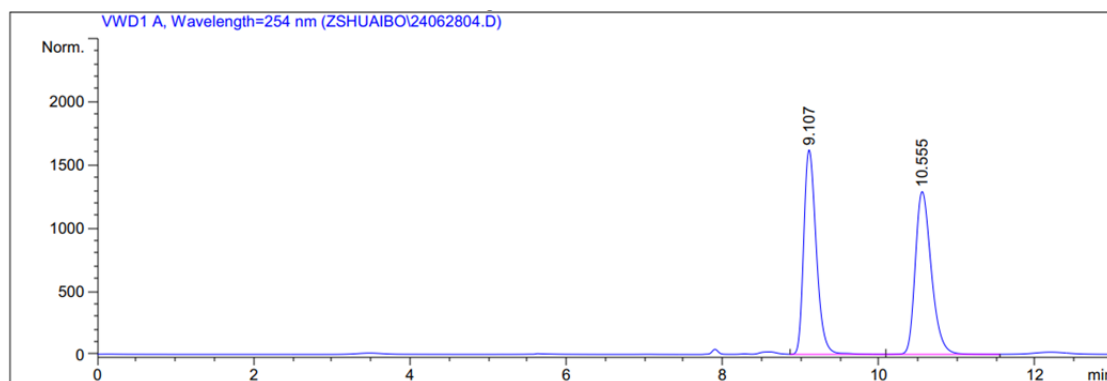


Purified using a Biotage flash chromatography system (PE/EtOAc, 10:1). Yield: 5.6 g (87%); white solid; mp 157–158 °C. 1H NMR (400 MHz, $CDCl_3$) δ = 7.65 – 7.59 (m, 4H), 7.55 – 7.43 (m, 4H), 7.43 – 7.35 (m, 1H), 6.93 (d, J = 15.9 Hz, 1H), 6.18 (dd, J = 15.9, 7.8 Hz, 1H), 5.93 – 5.82 (m, 1H), 2.22 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 168.9, 141.9, 140.4, 138.4, 134.0, 128.9, 127.7, 127.5, 127.4, 127.0, 123.3 (q, J = 280.5 Hz), 117.3, 71.1 (q, J = 33.5 Hz), 20.7. ^{19}F NMR (470 MHz, $CDCl_3$) δ = -76.39 (d, J = 6.8 Hz). HRMS (EI) m/z : calcd for $C_{18}H_{15}F_3O_2 [M^+]$ 320.1024, found: 320.1021.

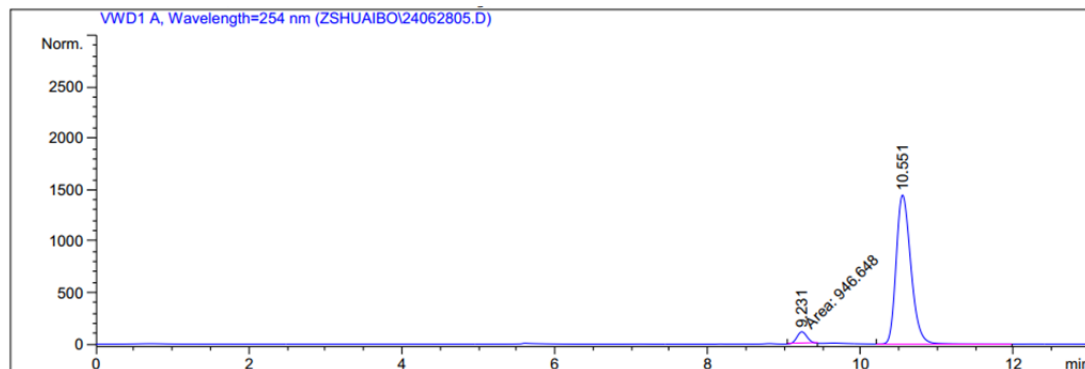
(S)-4-Benzyl-2-phenyl-4-((S,E)-4,4,4-trifluoro-1-(p-tolyl)but-2-en-1-yl)oxazol-5(4H)-one (3a)



Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1). Yield: 70.1 mg (78%); white solid; mp 137–138 °C; 75:25 dr; 91% ee (major diastereoisomer); $[\alpha]_D^{20}$ = +5.29 (c 0.12, CH_2Cl_2). The major diastereoisomer: 1H NMR (400 MHz, $CDCl_3$) δ = 7.75 (m, 2H), 7.58 – 7.49 (m, 1H), 7.41 (m, 2H), 7.20 – 7.03 (m, 8H), 7.05 – 6.99 (m, 2H), 6.07 – 5.92 (m, 1H), 4.02 (d, J = 9.9 Hz, 1H), 3.38 (d, J = 13.3 Hz, 1H), 3.18 (d, J = 13.3 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 177.7, 160.9, 137.9, 137.7 (q, J = 6.6 Hz), 133.8, 133.1, 132.6, 130.2, 129.4, 128.7, 128.6, 128.2, 127.8, 127.3, 125.4, 122.7 (q, J = 270.2 Hz), 122.1 (q, J = 33.9 Hz), 77.9, 54.3, 42.4, 21.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -63.97 (d, J = 6.2 Hz). HPLC analysis: Daicel CHIRALPAK OD-H, n -hexane/ i -PrOH = 50/1, flow rate = 0.6 mL/min, λ = 254 nm, retention time: t_{major} = 10.55 min, t_{minor} = 9.23 min. HRMS (ESI) m/z : calcd for $C_{27}H_{23}F_3NO_2 [M + H]^+$ 450.1675, found: 450.1672.

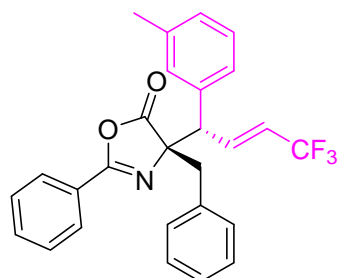


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.107	VV	0.1728	1.81061e4	1618.20239	49.6208
2	10.555	VB	0.2203	1.83828e4	1288.32617	50.3792



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.231	MM	0.1446	946.64771	109.07423	4.6502
2	10.551	VV	0.2091	1.94103e4	1445.53406	95.3498

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



Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1). Yield: 66.5 mg (74%); white solid; mp 157–

158 °C; 77:23 dr; 90% ee (major diastereoisomer); $[\alpha]_D^{20} = +7.69$

(*c* 0.13, CH₂Cl₂). The major diastereoisomer: ¹H NMR (400 MHz, CDCl₃) $\delta = 7.73 - 7.67$ (m, 2H), 7.53 – 7.44 (m, 1H), 7.41 – 7.32 (m, 2H), 7.17 – 7.01 (m, 7H), 7.01 – 6.93 (m, 3H), 6.02 – 5.89 (m,

1H), 3.95 (d, *J* = 9.9 Hz, 1H), 3.34 (d, *J* = 13.3 Hz, 1H), 3.13 (d, *J* = 13.3 Hz, 1H), 2.13 (s, 3H).

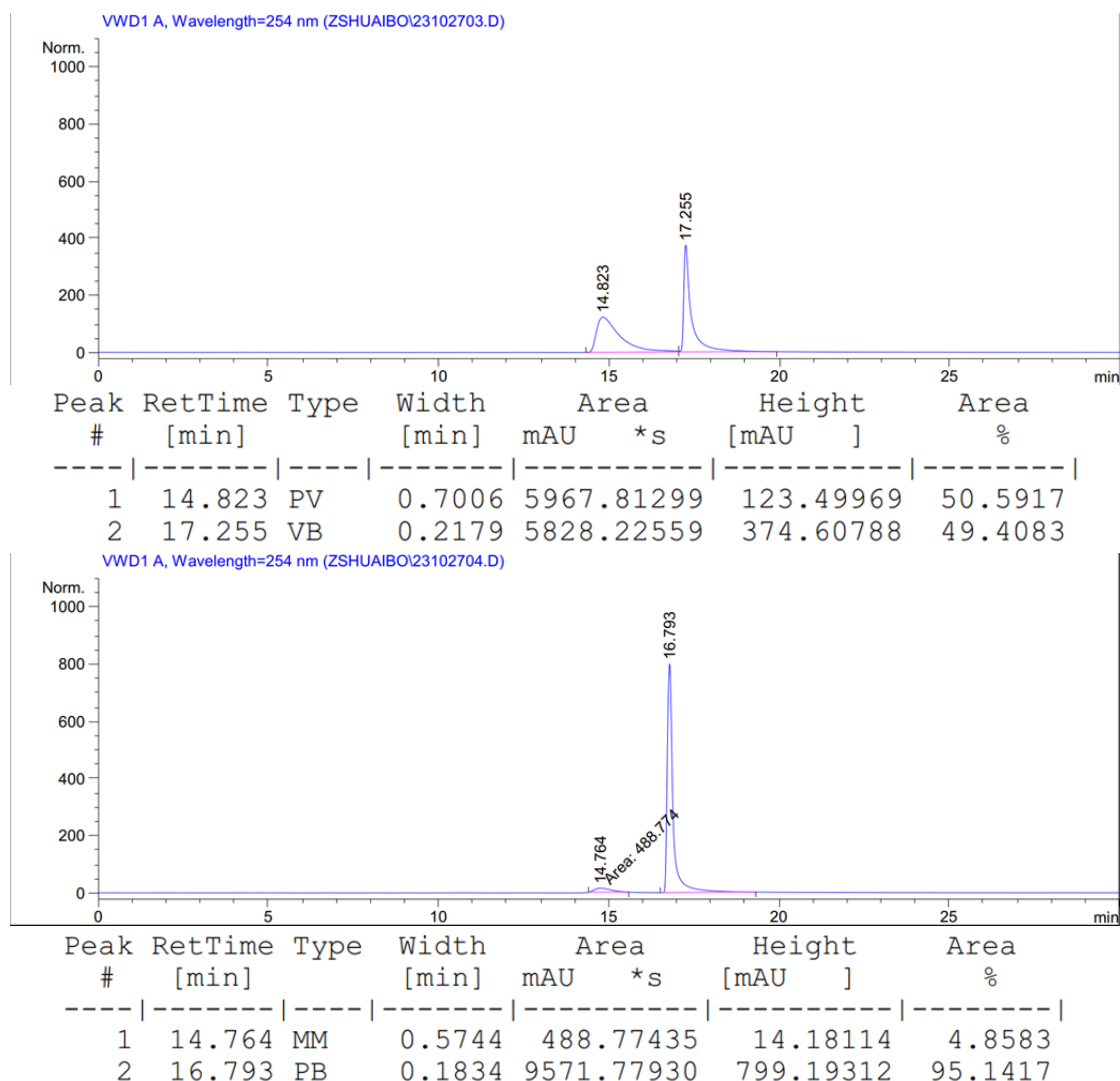
¹³C NMR (101 MHz, CDCl₃) $\delta = 177.7, 160.9, 138.2, 137.6$ (q, *J* = 6.5 Hz), 135.9, 133.9, 132.6, 130.2, 129.7, 128.9, 128.6, 128.5, 128.2, 127.8, 127.3, 125.9, 125.4, 122.6 (q, *J* = 269.8 Hz),

122.2 (q, *J* = 33.9 Hz), 77.8, 54.8, 42.2, 21.2. ¹⁹F NMR (376 MHz, CDCl₃) $\delta = -63.96$ (d, *J* = 5.9

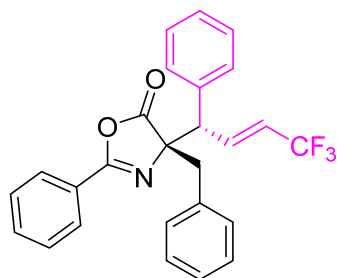
Hz). HPLC analysis: Daicel CHIRALPAK IE, *n*-hexane/*i*-PrOH = 500/1, flow rate = 0.8 mL/min,

$\lambda = 254$ nm, retention time: $t_{\text{major}} = 16.79$ min, $t_{\text{minor}} = 14.76$ min. HRMS (ESI) *m/z*: calcd for

C₂₇H₂₃F₃NO₂ [M + H]⁺ 450.1675, found: 450.1674.



(S)-4-Benzyl-2-phenyl-4-((S,E)-4,4,4-trifluoro-1-phenylbut-2-en-1-yl)oxazol-5(4H)-one (3c)

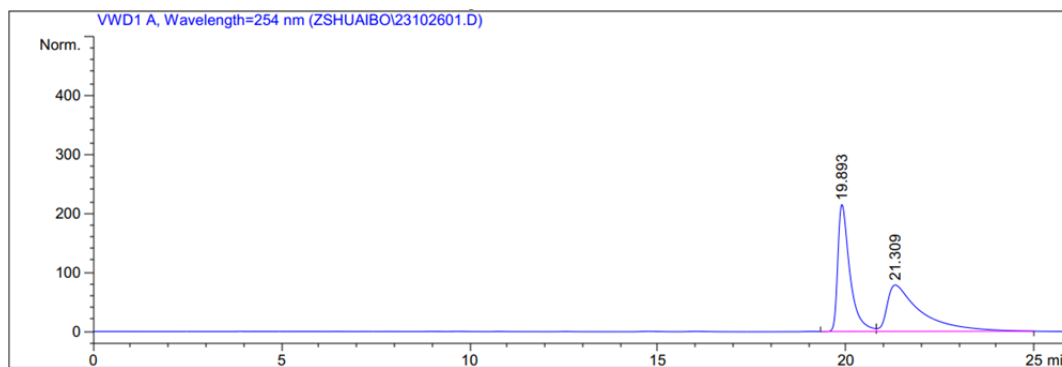


Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1). Yield: 60.9 mg (70%); white solid; mp 167–

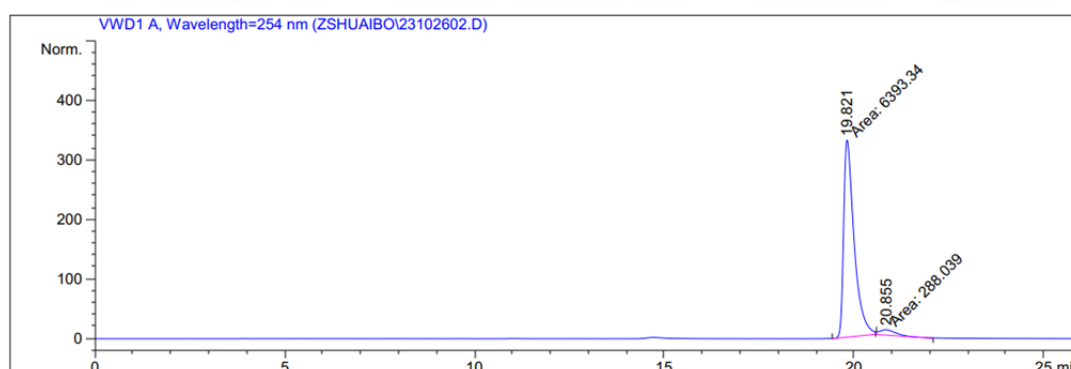
168 °C; 72:28 dr; 91% ee (major diastereoisomer); $[\alpha]_D^{20} = -3.85$

(*c* 0.13, CH₂Cl₂). The major diastereoisomer: ¹H NMR (400 MHz, CDCl₃) $\delta = 7.77 - 7.70$ (m, 2H), 7.57 – 7.49 (m, 1H), 7.45 – 7.37 (m, 2H), 7.26 – 7.18 (m, 5H), 7.19 – 7.14 (m, 5H), 7.13 – 7.07 (m, 1H), 6.08 – 5.95 (m, 1H), 4.05 (d, *J* = 9.9 Hz, 1H), 3.39 (d, *J* =

13.3 Hz, 1H), 3.19 (d, *J* = 13.3 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) (one aromatic carbon missing) $\delta = 177.7, 160.9, 137.5$ (q, *J* = 6.6 Hz), 136.1, 133.8, 132.7, 130.2, 128.9, 128.6, 128.20, 128.16, 127.8, 127.4, 125.3, 122.6 (q, *J* = 269.8 Hz), 122.4 (q, *J* = 33.9 Hz), 77.8, 54.7, 42.3. ¹⁹F NMR (376 MHz, CDCl₃) $\delta = -64.00$ (d, *J* = 5.9 Hz). HPLC analysis: Daicel CHIRALPAK IA, *n*-hexane/*i*-PrOH= 500/1, flow rate = 0.8 mL/min, $\lambda = 254$ nm, retention time: $t_{\text{major}} = 19.82$ min, $t_{\text{minor}} = 20.86$ min. HRMS (ESI) *m/z*: calcd for C₂₆H₂₁F₃NO₂ [M + H]⁺ 436.1519, found: 436.1519.

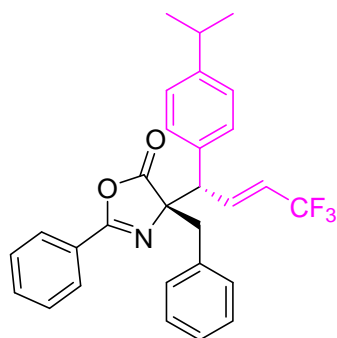


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.893	VV	0.3311	4824.42578	215.51682	49.5133
2	21.309	VB	0.8597	4919.27686	78.91841	50.4867



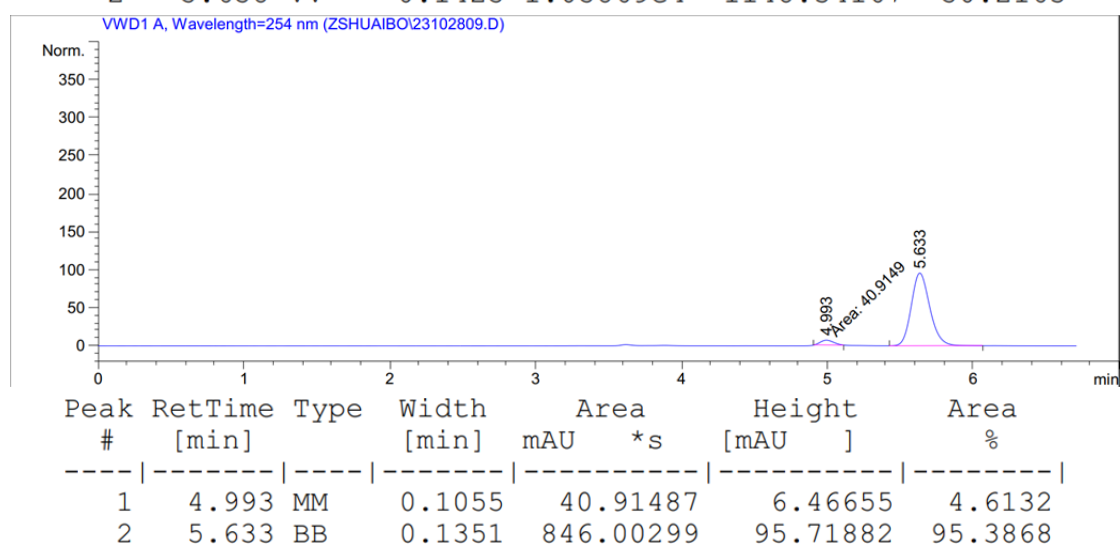
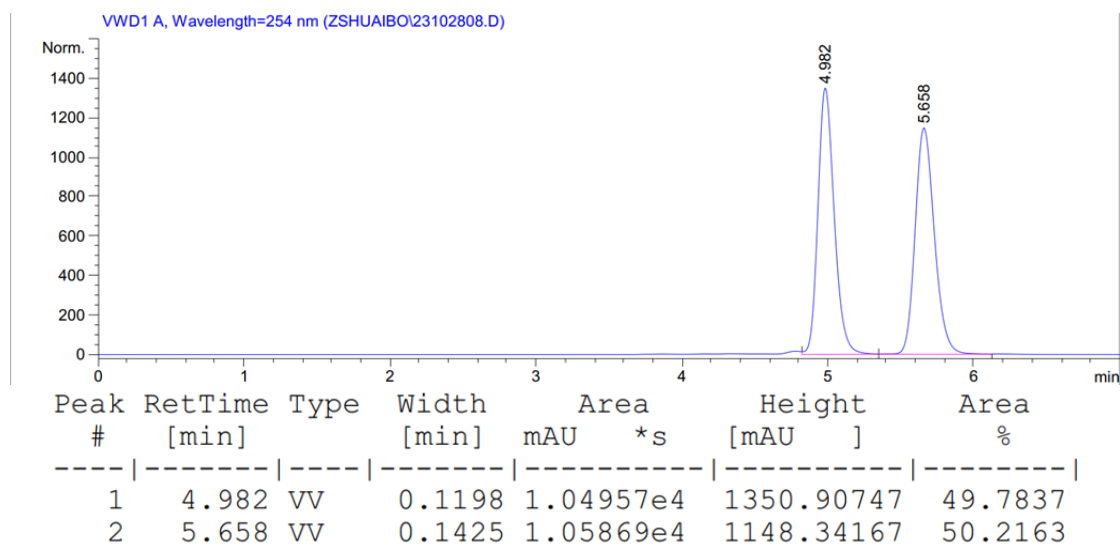
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.821	MM	0.3212	6393.34082	331.76263	95.6889
2	20.855	MM	0.5255	288.03860	9.13458	4.3111

(S)-4-Benzyl-2-phenyl-4-((S,E)-4,4,4-trifluoro-1-(4-isopropylphenyl)but-2-en-1-yl)oxazol-5(4H)-one (3d)

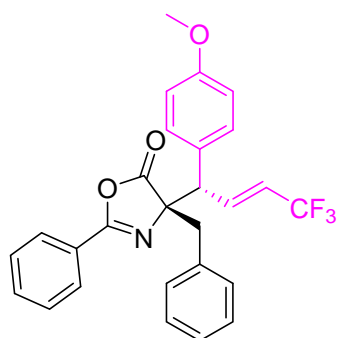


Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1). Yield: 74.4 mg (78%); white solid; mp 134–135 °C; 77:23 dr; 91% ee (major diastereoisomer); $[\alpha]_D^{20} = -0.71$ (c 0.12, CH₂Cl₂). The major diastereoisomer: ¹H NMR (400 MHz, CDCl₃) $\delta = 7.71 - 7.65$ (m, 2H), 7.52 – 7.44 (m, 1H), 7.44 – 7.32 (m, 2H), 7.17 – 7.08 (m, 7H), 7.08 – 6.98 (m, 3H), 6.02 – 5.88 (m, 1H), 3.98 (d, $J = 10.0$ Hz, 1H), 3.33 (d, $J = 13.3$ Hz, 1H), 3.13 (d, $J = 13.3$ Hz, 1H), 2.83 – 2.68 (m, 1H), 1.12 (d, $J = 7.0$ Hz, 3H), 1.11 (d, $J = 7.0$ Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) $\delta = 177.8$,

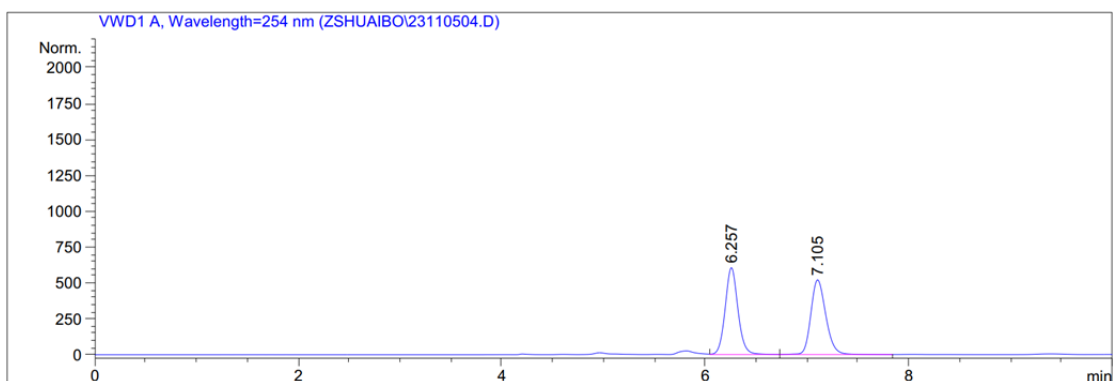
160.9, 148.8, 137.7 (q, $J = 6.4$ Hz), 133.9, 133.3, 132.6, 130.2, 128.8, 128.6, 128.2, 127.8, 127.3, 126.7, 125.5, 122.7 (q, $J = 269.7$ Hz), 122.1 (q, $J = 33.9$ Hz), 77.9, 54.4, 42.3, 33.6, 23.8. ¹⁹F NMR (377 MHz, CDCl₃) $\delta = -63.96$ (d, $J = 6.1$ Hz). HPLC analysis: Daicel CHIRALPAK OD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, $\lambda = 254$ nm, retention time: $t_{\text{major}} = 5.63$ min, $t_{\text{minor}} = 4.99$ min. HRMS (ESI) m/z : calcd for C₂₉H₂₇F₃NO₂ [M + H]⁺ 478.1988, found: 478.1982.



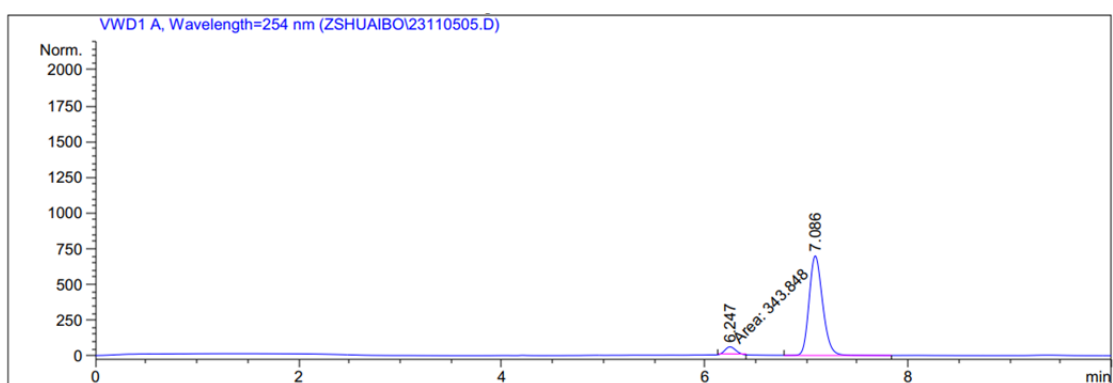
(S)-4-Benzyl-2-phenyl-4-((S,E)-4,4,4-trifluoro-1-(4-methoxyphenyl)but-2-en-1-yl)oxazol-5(4H)-one (3e)



Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1). Yield: 74.4 mg (80%); yellow solid; mp 151–152 °C; 75:25 dr; 90% ee (major diastereoisomer); $[\alpha]_D^{20} = +12.50$ (*c* 0.15, CH₂Cl₂). The major diastereoisomer: ¹H NMR (400 MHz, CDCl₃) δ = 7.75 (d, *J* = 7.6 Hz, 2H), 7.57 – 7.49 (m, 1H), 7.45 – 7.37 (m, 2H), 7.21 – 7.02 (m, 8H), 6.74 (d, *J* = 8.4 Hz, 2H), 6.06 – 5.93 (m, 1H), 4.02 (d, *J* = 9.8 Hz, 1H), 3.72 (s, 3H), 3.38 (d, *J* = 13.3 Hz, 1H), 3.18 (d, *J* = 13.3 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ = 177.8, 160.9, 159.3, 137.7 (q, *J* = 6.4 Hz), 133.9, 132.7, 130.2, 130.0, 128.6, 128.2, 128.1, 127.8, 127.3, 125.4, 122.7 (q, *J* = 270.0 Hz), 122.0 (q, *J* = 33.9 Hz), 114.0, 78.0, 55.1, 53.9, 42.3. ¹⁹F NMR (376 MHz, CDCl₃) δ = -63.93 (d, *J* = 6.1 Hz). HPLC analysis: Daicel CHIRALPAK IE, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: $t_{\text{major}} = 7.09$ min, $t_{\text{minor}} = 6.25$ min. HRMS (ESI) *m/z*: calcd for C₂₇H₂₃F₃NO₃ [M + H]⁺ 466.1625, found: 466.1621.

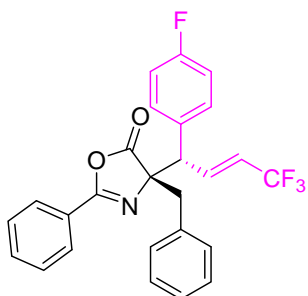


Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	6.257	VV	0.1330	5315.22168		605.40643	49.8786
2	7.105	VV	0.1591	5341.09717		520.33978	50.1214



Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	6.247	MM	0.1135	343.84763		50.47368	5.0214
2	7.086	BB	0.1453	6503.78955		696.84259	94.9786

(S)-4-Benzyl-2-phenyl-4-((S,E)-4,4,4-trifluoro-1-(4-fluorophenyl)but-2-en-1-yl)oxazol-5(4H)-one (3f)



Purified using a Biotage flash chromatography system (PE/EtOAc,

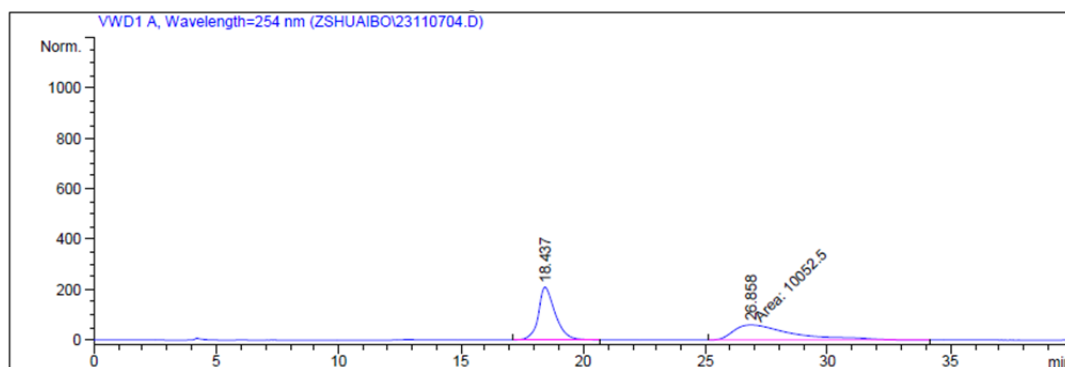
20:1). Yield: 45.3 mg (50%); white solid; mp 148–149 °C; 78:22 dr;

90% ee (major diastereoisomer); $[\alpha]_D^{20} = -16.67$ (*c* 0.13, CH₂Cl₂).

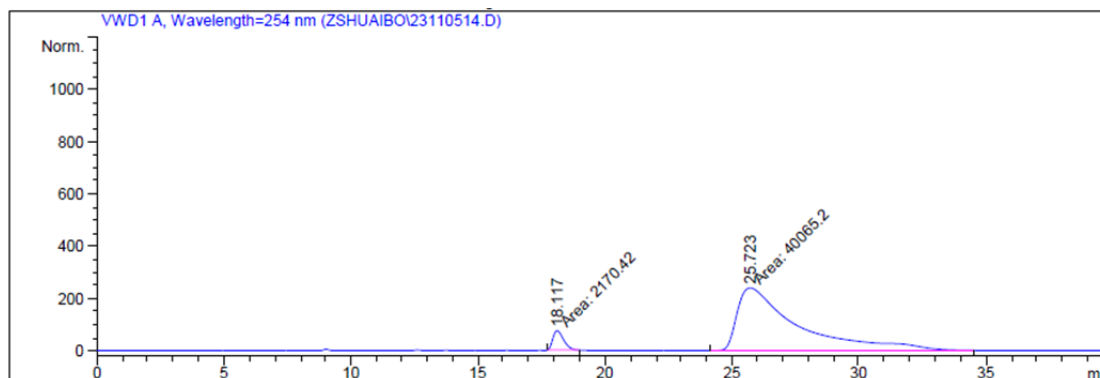
The major diastereoisomer: ¹H NMR (600 MHz, CDCl₃) δ = 7.72 – 7.68 (m, 2H), 7.53 – 7.47 (m, 1H), 7.40 – 7.36 (m, 2H), 7.20 – 7.08 (m, 7H), 7.05 – 6.98 (m, 1H), 6.90 – 6.80 (m, 2H), 6.02 – 5.93 (m, 1H), 4.01 (d, *J* = 9.8 Hz, 1H), 3.33 (d, *J* = 13.4 Hz, 1H), 3.13 (d, *J* =

13.4 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ = 177.6, 162.4 (d, *J* = 247.5 Hz), 161.0, 137.2 (q, *J* = 6.5 Hz), 133.6, 132.8, 131.9 (d, *J* = 3.0 Hz), 130.6 (d, *J* = 8.2 Hz), 130.2, 128.7, 128.2, 127.8, 127.4, 125.1, 122.6 (q, *J* = 34.0 Hz), 122.5 (q, *J* = 270.1 Hz), 115.6 (d, *J* = 21.5 Hz), 77.8, 53.7, 42.2. ¹⁹F NMR (376 MHz, CDCl₃) δ = -64.07 (d, *J* = 6.4 Hz, 3F), -113.41 – -113.56 (m, 1F). HPLC analysis: Daicel CHIRALPAK OD-H, *n*-hexane/*i*-PrOH = 500/1, flow rate = 0.8 mL/min, λ = 254 nm, retention time: *t*_{major} = 25.72 min, *t*_{minor} = 18.12 min. HRMS (ESI) *m/z*: calcd for

C₂₆H₂₀F₄NO₂ [M + H]⁺ 454.1425, found: 454.1427.

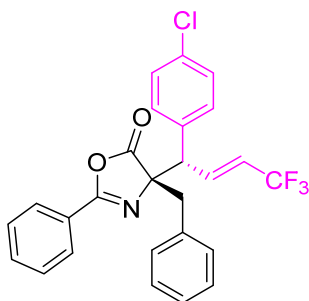


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	18.437	VB	0.7003	1.00564e4	209.87260	50.0095
2	26.858	MM	2.7976	1.00525e4	59.88881	49.9905



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	18.117	MM	0.4869	2170.42188	74.30031	5.1388
2	25.723	MM	2.7740	4.00652e4	240.71820	94.8612

(S)-4-Benzyl-4-((S,E)-1-(4-chlorophenyl)-4,4,4-trifluorobut-2-en-1-yl)-2-phenyloxazol-5(4H)-one (3g)



Purified using a Biotage flash chromatography system (PE/EtOAc,

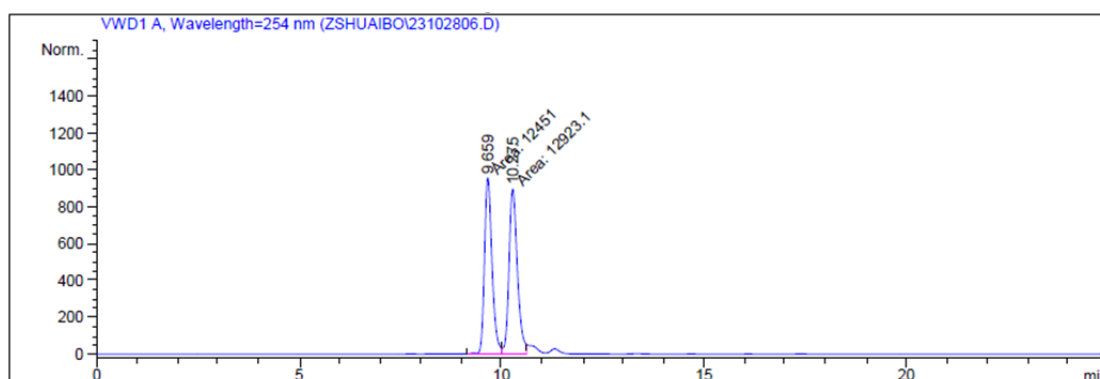
20:1). Yield: 63.8 mg (68%); white solid; mp 135–136 °C; 76:24 dr;

90% ee (major diastereoisomer); $[\alpha]_D^{20} = +10.00$ (*c* 0.12, CH₂Cl₂).

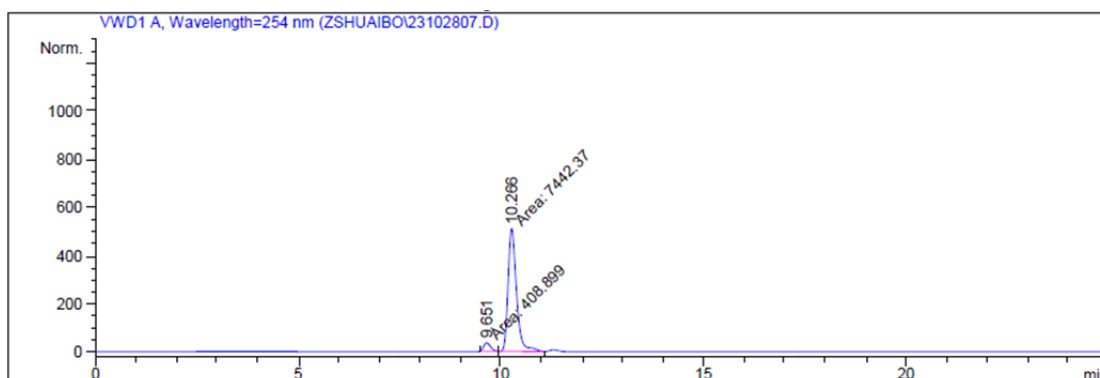
The major diastereoisomer: ¹H NMR (600 MHz, CDCl₃) δ = 7.66 – 7.61 (m, 2H), 7.47 – 7.41 (m, 1H), 7.34 – 7.26 (m, 2H), 7.11 – 7.01 (m, 9H), 6.98 – 6.90 (m, 1H), 5.94 – 5.85 (m, 1H), 3.92 (d, *J* = 9.8 Hz, 1H), 3.25 (d, *J* = 13.4 Hz, 1H), 3.05 (d, *J* = 13.4 Hz, 1H). ¹³C

NMR (151 MHz, CDCl₃) δ = 177.5, 161.1, 137.0 (q, *J* = 6.4 Hz), 134.7, 134.2, 133.5, 132.9, 130.21, 130.19, 128.9, 128.7, 128.2, 127.8, 127.5, 125.1, 122.7 (q, *J* = 34.0 Hz), 122.5 (q, *J* = 270.0 Hz), 77.7, 53.8, 42.3. ¹⁹F NMR (376 MHz, CDCl₃) δ = -64.09 (d, *J* = 6.4 Hz). HPLC analysis: Daicel CHIRALPAK OD-H, *n*-hexane/*i*-PrOH = 8/2, flow rate = 0.4 mL/min, λ = 254 nm, retention time: *t*_{major} = 10.27 min, *t*_{minor} = 9.65 min. HRMS (ESI) *m/z*: calcd for

C₂₆H₂₀ClF₃NO₂ [M + H]⁺ 470.1129, found: 470.1129.

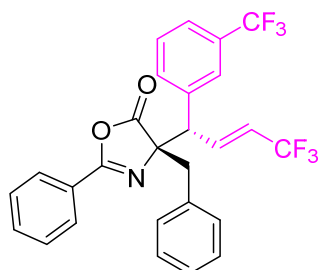


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.659	MM	0.2169	1.24510e4	956.65381	49.0696
2	10.275	MM	0.2408	1.29231e4	894.29041	50.9304



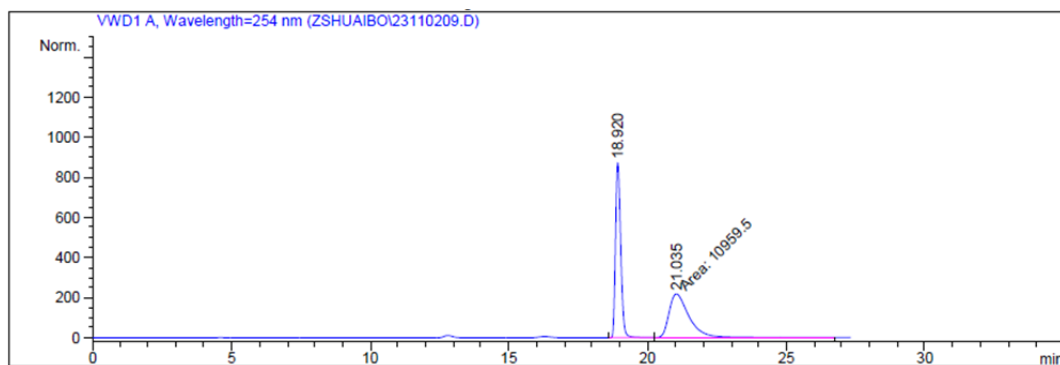
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.651	MM	0.1970	408.89899	34.59780	5.2081
2	10.266	MM	0.2429	7442.36572	510.74994	94.7919

(S)-4-Benzyl-2-phenyl-4-((S,E)-4,4,4-trifluoro-1-(3-(trifluoromethyl)phenyl)but-2-en-1-yl)oxazol-5(4H)-one (3h)

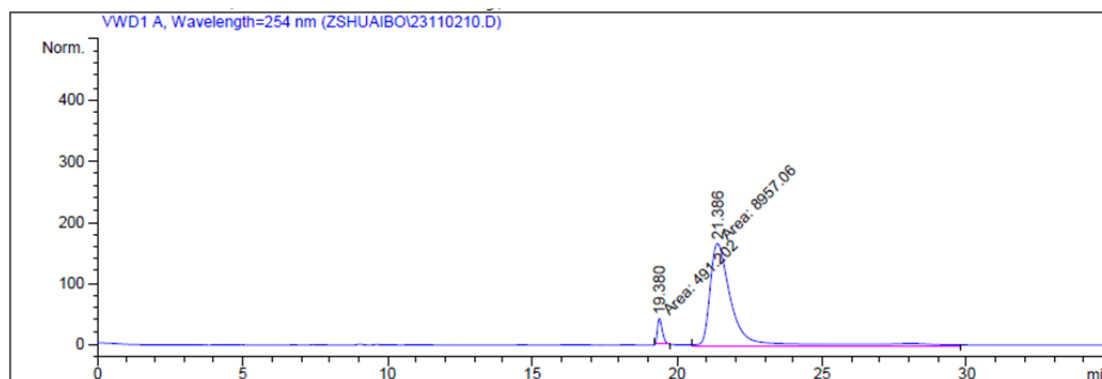


Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1). Yield: 64.4 mg (64%); yellow solid; mp 135–136 °C; 71:29 dr; 90% ee (major diastereoisomer); $[\alpha]_D^{20} = +5.56$ (*c* 0.18, CHCl₃). The major diastereoisomer: ¹H NMR (400 MHz, CDCl₃) δ = 7.71 – 7.64 (m, 2H), 7.54 – 7.27 (m, 7H), 7.19 – 6.98 (m, 6H), 6.15 – 5.88 (m, 1H), 4.07 (d, *J* = 9.9 Hz, 1H), 3.34 (d, *J* = 13.3 Hz, 1H), 3.14 (d, *J* = 13.3 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ = 177.5, 161.3, 137.1, 136.5 (q, *J* = 6.6 Hz), 133.4, 132.9, 132.4, 130.9 (q, *J* = 32.4 Hz), 130.2, 129.3, 128.7, 128.3, 127.8, 127.5, 125.7 (q, *J* = 3.7 Hz), 125.1 (q, *J* = 3.9 Hz), 124.9, 123.6 (q, *J* = 272.5 Hz), 123.2 (q, *J* = 34.2 Hz), 122.4 (q, *J* = 269.9 Hz), 77.6, 54.3, 42.2. ¹⁹F NMR (377 MHz, None) δ = -62.78 – -63.16 (m, 3F), -64.21 (d, *J* =

6.4 Hz, 3F). HPLC analysis: Daicel CHIRALPAK OD-H, *n*-hexane/*i*-PrOH= 500/1, flow rate = 0.8 mL/min, $\lambda = 254$ nm, retention time: $t_{\text{major}} = 21.39$ min, $t_{\text{minor}} = 19.38$ min. HRMS (ESI) m/z : calcd for $C_{27}H_{20}F_6NO_2$ $[M + H]^+$ 504.1393, found: 504.1391.

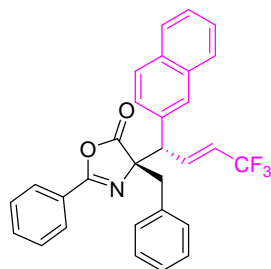


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	18.920	PB	0.2049	1.15129e4	872.58466	51.2312
2	21.035	MM	0.8390	1.09595e4	217.70723	48.7688



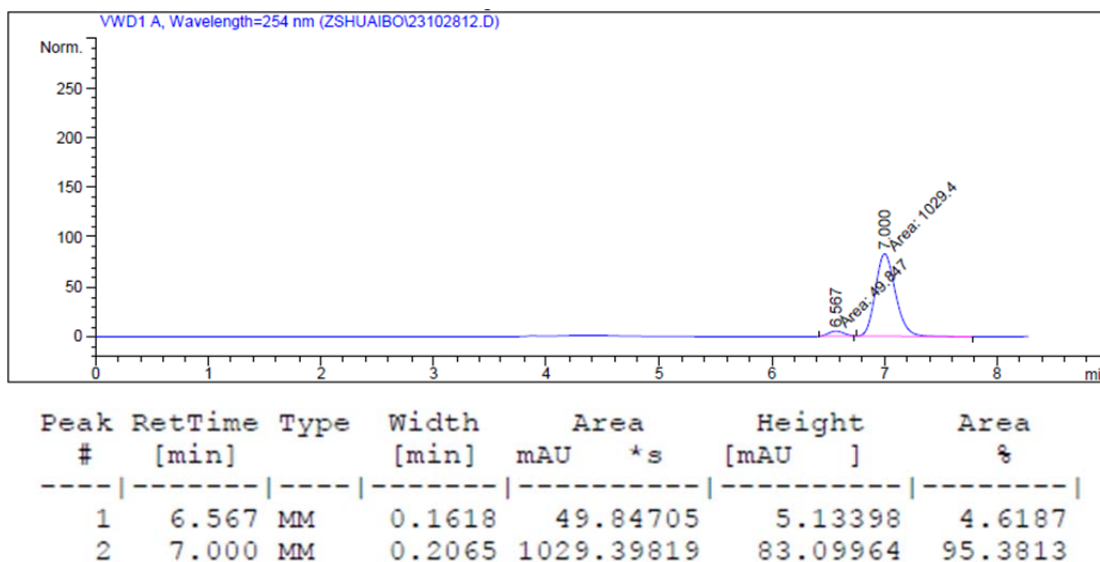
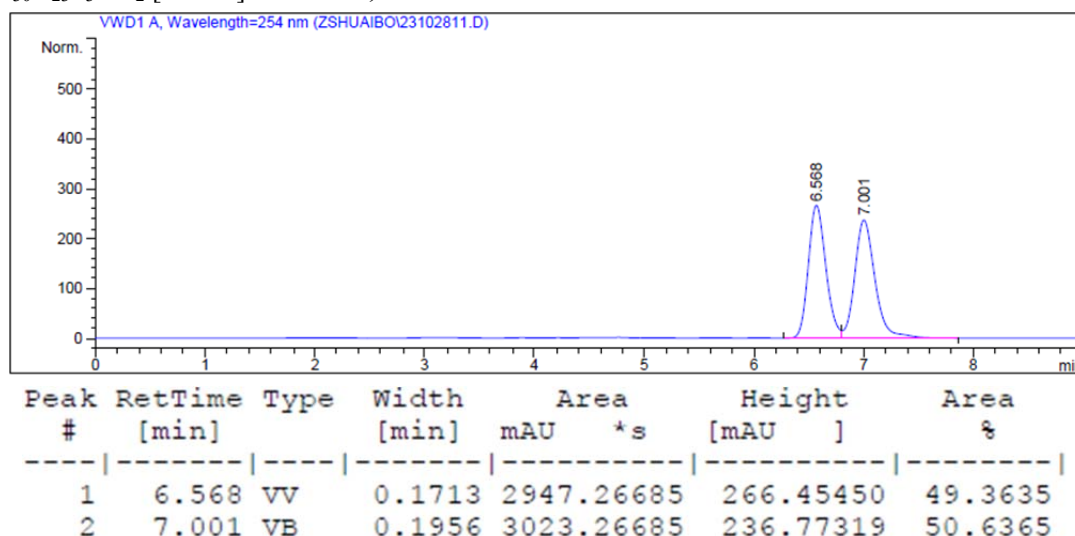
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.380	MM	0.1952	491.20242	41.93858	5.1989
2	21.386	MM	0.8930	8957.06055	167.16779	94.8011

(*S*)-4-Benzyl-2-phenyl-4-((*S,E*)-4,4,4-trifluoro-1-(naphthalen-2-yl)but-2-en-1-yl)oxazol-5(*4H*)-one (3i)

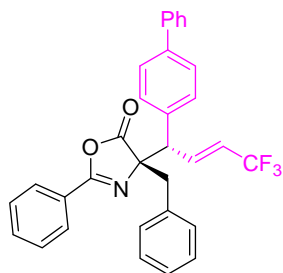


Purified using a Biotage flash chromatography system (PE/EtOAc, 10:1). Yield: 67.9 mg (70%); white solid; mp 212–213 °C; 79:21 dr; 91% ee (major diastereoisomer); $[\alpha]_D^{20} = +61.33$ (c 0.14, CH_2Cl_2). The major diastereoisomer: 1H NMR (600 MHz, $CDCl_3$) $\delta = 7.72 - 7.65$ (m, 5H), 7.63 (d, $J = 8.6$ Hz, 1H), 7.50 – 7.43 (m, 1H), 7.41 – 7.36 (m, 2H), 7.35 – 7.30 (m, 3H), 7.20 – 7.07 (m, 6H), 6.04 – 5.96 (m, 1H), 4.18 (d, $J = 9.8$ Hz, 1H), 3.39 (d, $J = 13.4$ Hz, 1H), 3.19 (d, $J = 13.4$ Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) $\delta = 177.7, 161.1, 137.5$ (q, $J = 6.5$ Hz), 133.72, 133.68, 133.2, 132.9, 132.7, 130.3, 128.6, 128.5, 128.3, 128.2, 128.0, 127.8, 127.6, 127.4, 126.4, 126.3, 126.1, 125.3, 122.7 (q, $J = 270.0$ Hz),

122.6 (q, $J = 33.8$ Hz), 77.9, 54.8, 42.5. ^{19}F NMR (377 MHz, CDCl_3) $\delta = -63.96$ (d, $J = 5.2$ Hz). HPLC analysis: Daicel CHIRALPAK OD-H, n -hexane/ i -PrOH = 95/5, flow rate = 0.8 mL/min, $\lambda = 254$ nm, retention time: $t_{\text{major}} = 7.00$ min, $t_{\text{minor}} = 6.57$ min. HRMS (ESI) m/z : calcd for $\text{C}_{30}\text{H}_{23}\text{F}_3\text{NO}_2$ $[\text{M} + \text{H}]^+$ 486.1675, found: 486.1677.



(S)-4-((S,E)-1-([1,1'-Biphenyl]-4-yl)-4,4,4-trifluorobut-2-en-1-yl)-4-benzyl-2-phenyloxazol-5(4H)-one (3j)



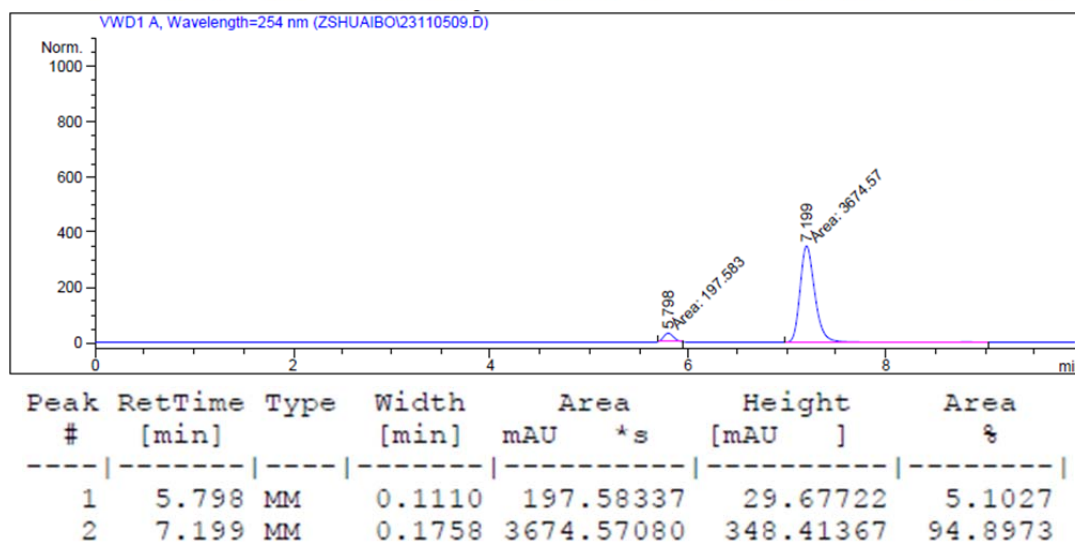
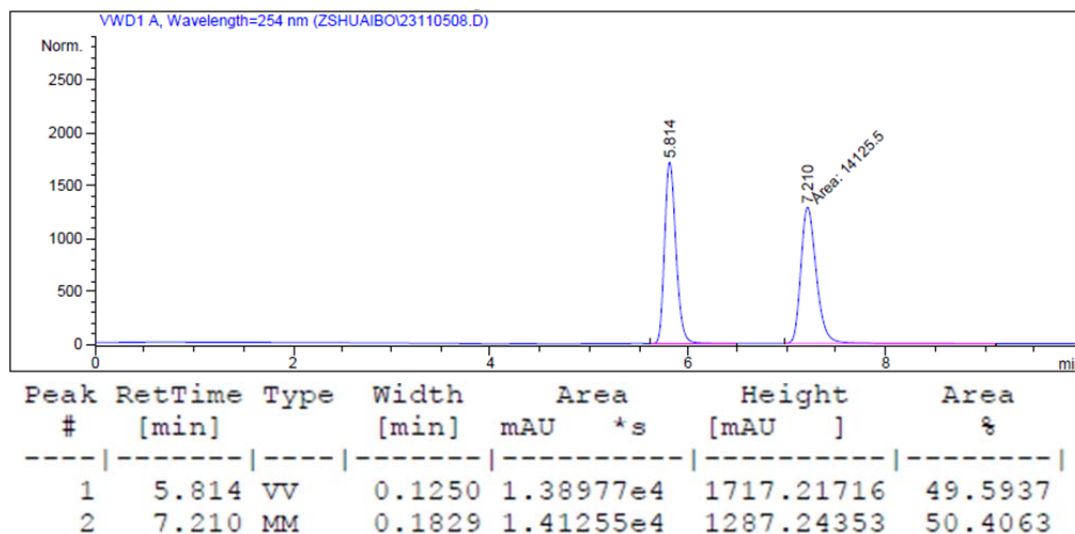
Purified using a Biotage flash chromatography system (PE/EtOAc,

10:1). Yield: 72.6 mg (71%); white solid; mp 180–181 °C; 77:23 dr;

90% ee (major diastereoisomer); $[\alpha]_{\text{D}}^{20} = +42.35$ (c 0.14, CH_2Cl_2). The major diastereoisomer: ^1H NMR (400 MHz, CDCl_3) $\delta = 7.74 - 7.68$ (m, 2H), 7.53 – 7.32 (m, 9H), 7.32 – 7.21 (m, 3H), 7.20 – 7.03 (m, 6H), 6.15 – 5.87 (m, 1H), 4.05 (d, $J = 9.9$ Hz, 1H), 3.36 (d, $J = 13.3$ Hz,

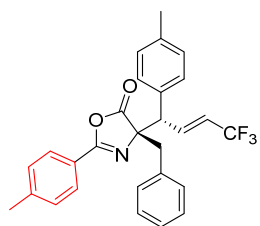
1H), 3.17 (d, $J = 13.3$ Hz, 1H). ^{13}C NMR (151 MHz, CDCl_3) $\delta = 177.8, 161.1, 140.9, 140.3, 137.5$ (q, $J = 6.6$ Hz), 135.1, 133.8, 132.7, 130.3, 129.3, 128.8, 128.7, 128.3, 127.8, 127.5, 127.4, 127.3, 127.0, 125.3, 122.7 (q, $J = 270.1$ Hz), 122.4 (q, $J = 33.9$ Hz), 77.9, 54.4, 42.4. ^{19}F NMR (377

MHz, CDCl₃) δ = -63.96 (d, J = 6.0 Hz). HPLC analysis: Daicel CHIRALPAK IE, *n*-hexane/*i*-PrOH= 95/5, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 7.20 min, t_{minor} = 5.80 min. HRMS (ESI) m/z : calcd for C₃₂H₂₅F₃NO₂ [M + H]⁺ 512.1832, found: 512.1827.



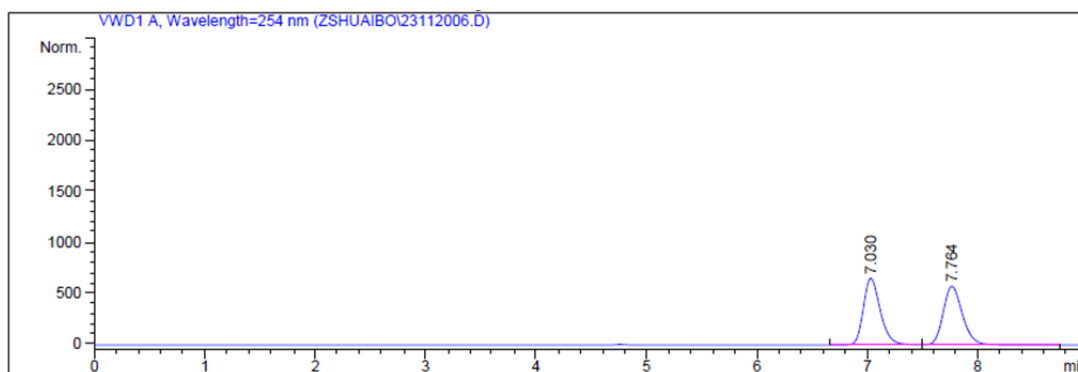
(S)-4-Benzyl-2-(*p*-tolyl)-4-((S,E)-4,4,4-trifluoro-1-(*p*-tolyl)but-2-en-1-yl)oxazol-5(4H)-one (3k)

Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1).

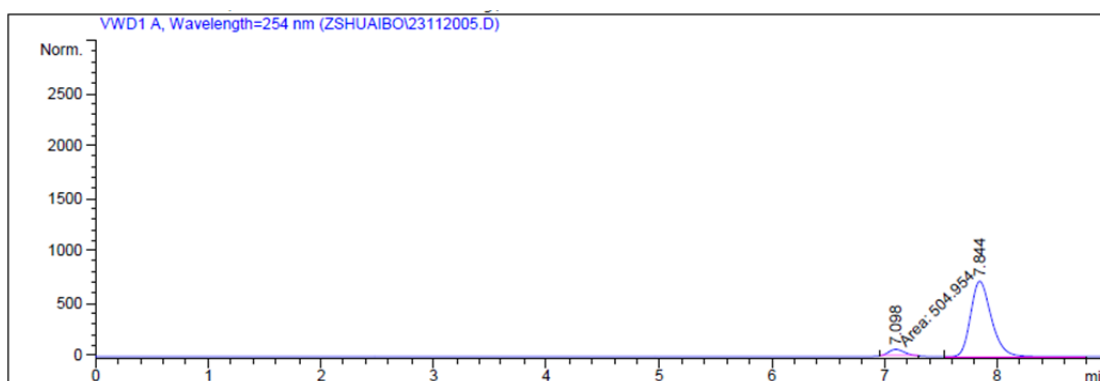


Yield: 71.3 mg (77%); white solid; mp 143–144 °C; 75:25 dr; 90% ee

(major diastereoisomer); $[\alpha]_{\text{D}}^{20}$ = +4.17 (c 0.12, CH₂Cl₂). The major diastereoisomer: ¹H NMR (500 MHz, CDCl₃) δ = 7.60 (d, J = 7.7 Hz, 2H), 7.16 (d, J = 7.8 Hz, 2H), 7.13 – 7.01 (m, 8H), 6.97 (d, J = 7.5 Hz, 2H), 5.97 - 5.90 (m, 1H), 3.95 (d, J = 9.7 Hz, 1H), 3.32 (d, J = 13.5 Hz, 1H), 3.12 (d, J = 13.5 Hz, 1H), 2.36 (s, 3H), 2.19 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ = 177.9, 160.9, 143.4, 137.9, 137.8 (q, J = 6.6 Hz), 133.9, 133.1, 130.2, 129.4, 129.3, 128.7, 128.2, 127.8, 127.3, 122.7 (q, J = 270.1 Hz), 122.6, 122.0 (q, J = 34.0 Hz), 77.8, 54.4, 42.4, 21.7, 21.0. ¹⁹F NMR (376 MHz, CDCl₃) δ = -63.93 (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_{major} = 7.84 min, t_{minor} = 7.10 min. HRMS (ESI) m/z : calcd for C₂₈H₂₅F₃NO₂ [M + H]⁺ 464.1832, found: 464.1837.

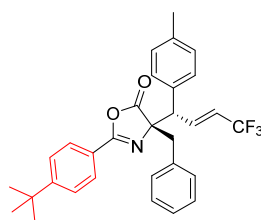


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.030	VV	0.1630	7026.96875	654.95538	50.0871
2	7.764	VB	0.1870	7002.51807	575.90479	49.9129



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.098	MM	0.1488	504.95441	56.54668	5.2194
2	7.844	VB	0.1955	9169.60059	718.35303	94.7806

(S)-4-Benzyl-2-(4-(tert-butyl)phenyl)-4-((S,E)-4,4,4-trifluoro-1-(p-tolyl)but-2-en-1-yl)oxazol-5(4H)-one (3l)

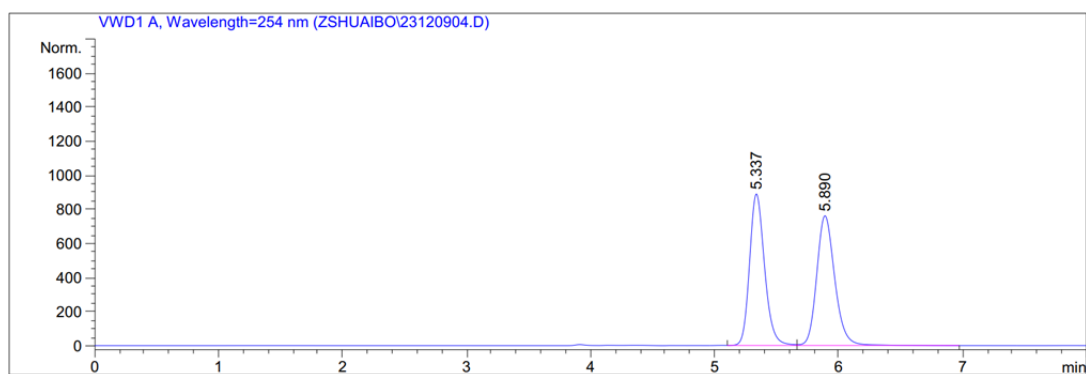


Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1).

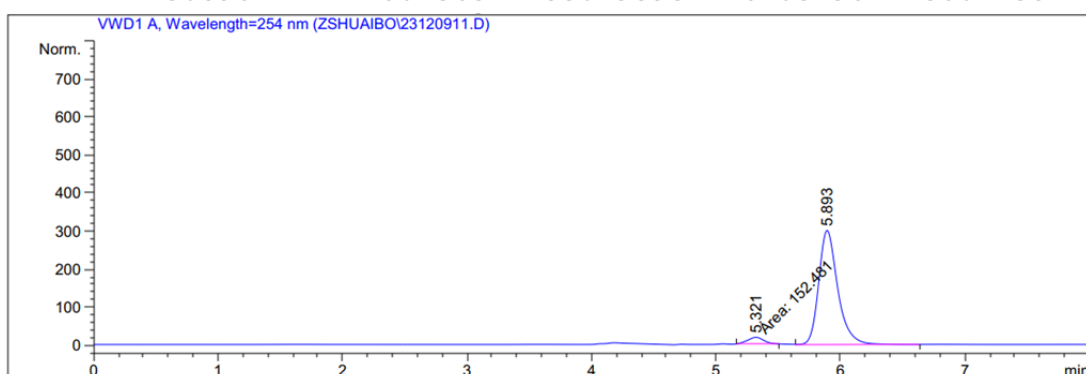
Yield: 75.8 mg (75%); white solid; mp 217–218 °C; 81:19 dr; 91% ee

(major diastereoisomer); $[\alpha]_D^{20} = +5.93$ (*c* 0.15, CH₂Cl₂). The major diastereoisomer: ¹H NMR (500 MHz, CDCl₃) δ = 7.63 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.16 – 6.95 (m, 10H), 5.98 – 5.88 (m, 1H),

3.95 (d, *J* = 9.8 Hz, 1H), 3.32 (d, *J* = 13.4 Hz, 1H), 3.12 (d, *J* = 13.4 Hz, 1H), 2.21 (s, 3H), 1.32 (s, 9H). ¹³C NMR (126 MHz, CDCl₃) δ = 177.9, 160.9, 156.3, 137.84, 137.83 (q, *J* = 6.4 Hz), 133.9, 133.2, 130.2, 129.4, 128.7, 128.2, 127.7, 127.3, 125.6, 122.7 (q, *J* = 269.9 Hz), 122.6, 122.0 (q, *J* = 33.7 Hz), 77.8, 54.4, 42.4, 35.1, 31.1, 21.0. ¹⁹F NMR (376 MHz, CDCl₃) δ = -63.94 (d, *J* = 6.2 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*_{major} = 5.89 min, *t*_{minor} = 5.32 min. HRMS (ESI) *m/z*: calcd for C₃₁H₃₁F₃NO₂ [M + H]⁺ 506.2301, found: 506.2301.

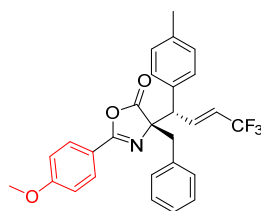


Peak #	RetTime [min]	Type	Width [min]	Area mAU * s	Height [mAU]	Area %
1	5.337	VV	0.1305	7505.99512	889.35992	49.2542
2	5.890	VB	0.1563	7733.29395	761.54907	50.7458



Peak #	RetTime [min]	Type	Width [min]	Area mAU * s	Height [mAU]	Area %
1	5.321	MM	0.1474	152.48093	17.24311	4.5501
2	5.893	VB	0.1609	3198.64307	299.77966	95.4499

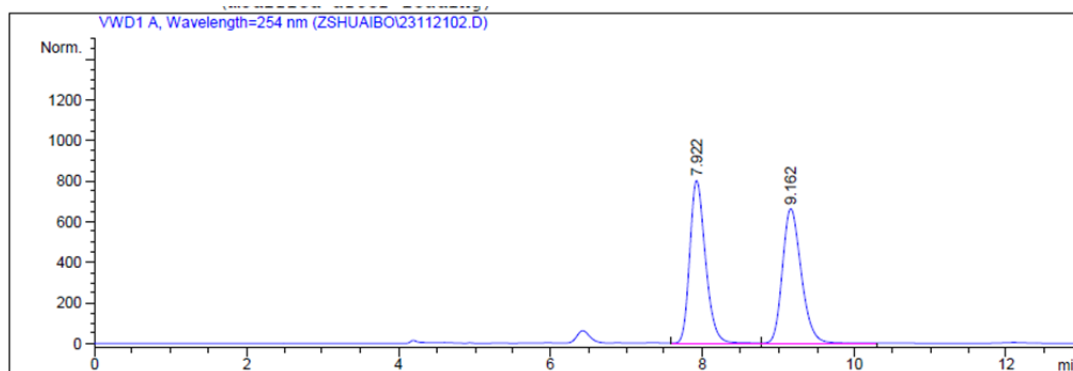
(S)-4-Benzyl-2-(4-methoxyphenyl)-4-((S,E)-4,4,4-trifluoro-1-(p-tolyl)but-2-en-1-yl)oxazol-5(4H)-one(3m)



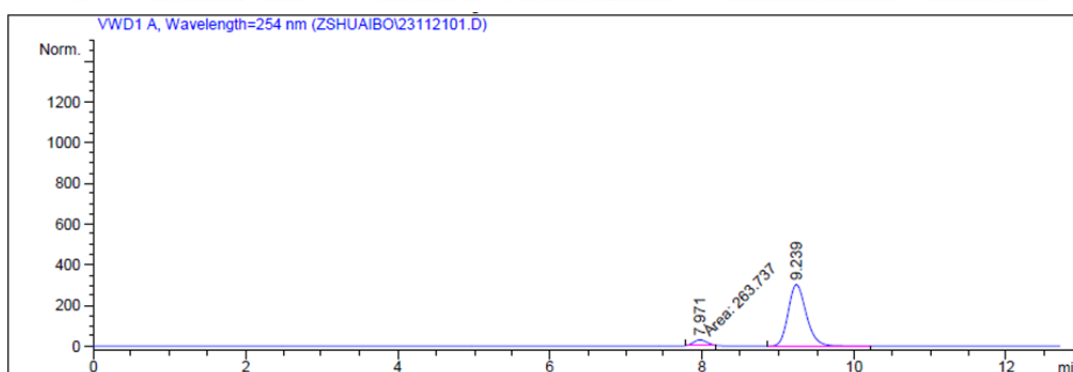
Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1).

Yield: 70.9 mg (74%); white solid; mp 97–98 °C; 76:24 dr; 90% ee

(major diastereoisomer); $[\alpha]_D^{20} = -3.64$ (*c* 0.12, CH₂Cl₂). The major diastereoisomer: ¹H NMR (500 MHz, CDCl₃) $\delta = 7.66$ (d, *J* = 8.4 Hz, 2H), 7.16 – 7.00 (m, 8H), 6.97 (d, *J* = 7.7 Hz, 2H), 6.85 (d, *J* = 8.3 Hz, 2H), 5.97 - 5.90 (m, 1H), 3.95 (d, *J* = 9.8 Hz, 1H), 3.80 (s, 3H), 3.31 (d, *J* = 13.3 Hz, 1H), 3.11 (d, *J* = 13.3 Hz, 1H), 2.19 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) $\delta = 177.9, 163.1, 160.5, 137.9$ (q, *J* = 6.4 Hz), 137.8, 134.0, 133.2, 130.2, 129.7, 129.3, 128.8, 128.1, 127.3, 122.7 (q, *J* = 269.8 Hz), 121.9 (q, *J* = 33.7 Hz), 117.7, 114.1, 77.8, 55.4, 54.4, 42.4, 21.0. ¹⁹F NMR (376 MHz, CDCl₃) $\delta = -63.92$ (d, *J* = 7.5 Hz). HPLC analysis: Daicel CHIRALPAK OD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, $\lambda = 254$ nm, retention time: $t_{\text{major}} = 9.24$ min, $t_{\text{minor}} = 7.97$ min. HRMS (ESI) *m/z*: calcd for C₂₈H₂₅F₃NO₃ [M + H]⁺ 480.1781, found: 480.1779.

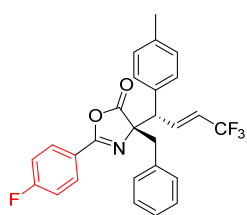


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.922	VV	0.2200	1.15057e4	801.18945	50.2499
2	9.162	VB	0.2661	1.13912e4	662.40527	49.7501



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.971	MM	0.1778	263.73676	24.71680	5.0422
2	9.239	PB	0.2532	4966.82764	301.77536	94.9578

(S)-4-Benzyl-2-(4-fluorophenyl)-4-((S,E)-4,4,4-trifluoro-1-(p-tolyl)but-2-en-1-yl)oxazol-5(4H)-one (3n)

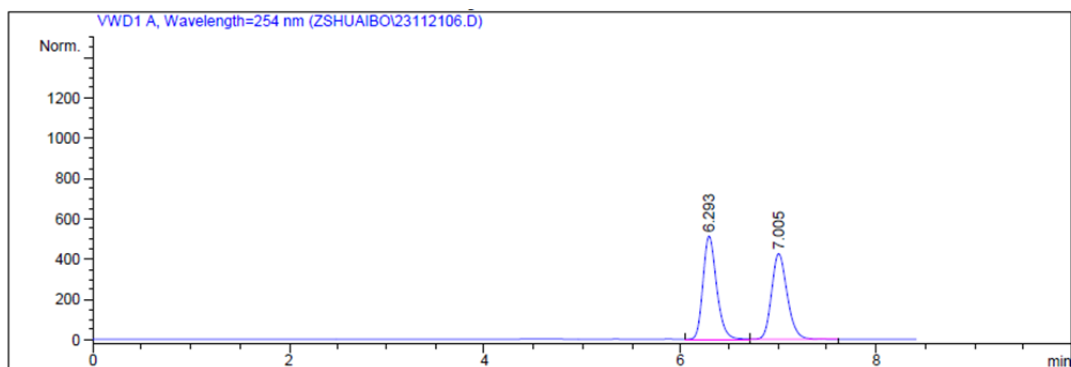


Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1).

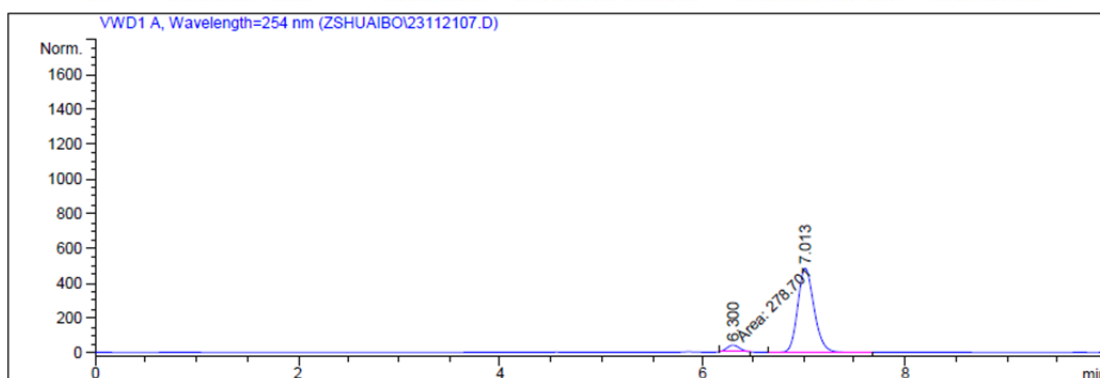
Yield: 72.9 mg (78%); white solid; mp 161–162 °C; 75:25 dr; 90% ee

(major diastereoisomer); $[\alpha]_D^{20} = -1.82$ (*c* 0.14, CH₂Cl₂). The major diastereoisomer: ¹H NMR (400 MHz, CDCl₃) $\delta = 7.81 - 7.72$ (m, 2H), 7.19 – 7.13 (m, 5H), 7.13 – 7.06 (m, 5H), 7.04 - 7.01 (m, 2H), 6.03 - 5.95

(m, 1H), 4.01 (d, *J* = 9.9 Hz, 1H), 3.37 (d, *J* = 13.3 Hz, 1H), 3.17 (d, *J* = 13.3 Hz, 1H), 2.25 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) $\delta = 177.5, 165.5$ (d, *J* = 254.4 Hz), 159.9, 138.0, 137.6 (q, *J* = 6.5 Hz), 133.8, 133.0, 130.2, 130.19 (d, *J* = 9.1 Hz), 129.4, 128.7, 128.2, 127.4, 122.6 (q, *J* = 270.0 Hz), 122.2 (q, *J* = 33.8 Hz), 121.6 (d, *J* = 3.1 Hz), 116.0 (d, *J* = 22.3 Hz), 78.0, 54.3, 42.3, 21.0. ¹⁹F NMR (376 MHz, CDCl₃) $\delta = -64.00$ (d, *J* = 4.3 Hz, 3F), -105.29 – -105.43 (m, 1F). HPLC analysis: Daicel CHIRALPAK OD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, $\lambda = 254$ nm, retention time: $t_{\text{major}} = 7.01$ min, $t_{\text{minor}} = 6.30$ min. HRMS (ESI) *m/z*: calcd for C₂₇H₂₂F₄NO₂ [M + H]⁺ 468.1581, found: 468.1581.



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.293	VV	0.1480	4963.71729	512.23083	51.1731
2	7.005	VB	0.1708	4736.13086	425.00290	48.8269

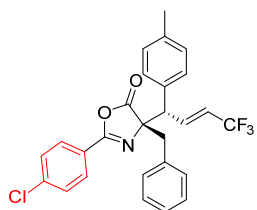


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.300	MM	0.1339	278.70081	34.68824	4.8751
2	7.013	VB	0.1733	5438.12061	483.94510	95.1249

(S)-4-Benzyl-2-(4-chlorophenyl)-4-((S,E)-4,4,4-trifluoro-1-(p-tolyl)but-2-en-1-yl)oxazol-5(4H)-one (3o)

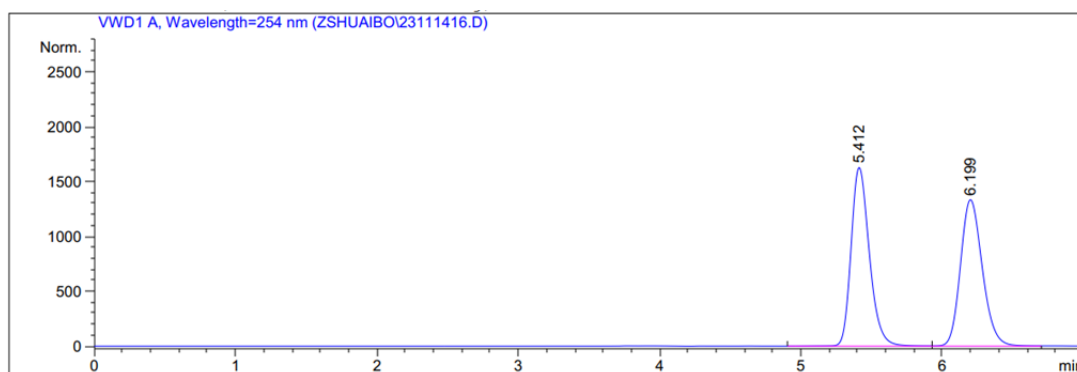
Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1).

Yield: 72.5 mg (75%); white solid; mp 168–169 °C; 73:27 dr; 90% ee

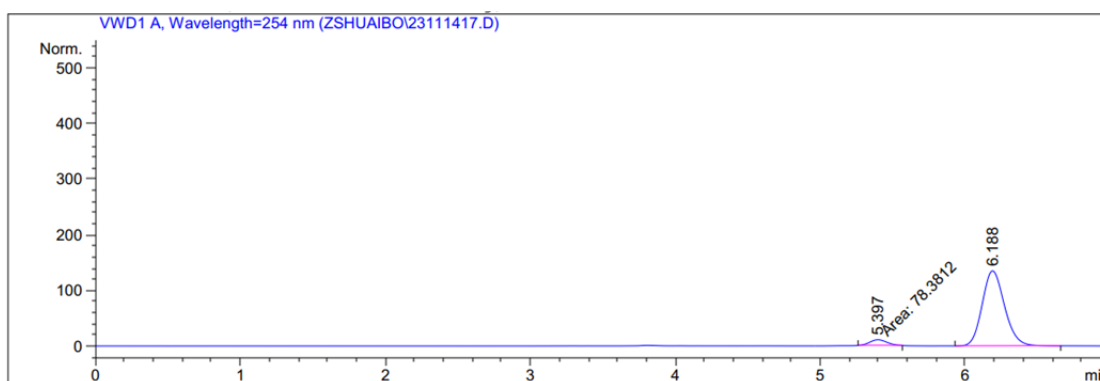


(major diastereoisomer); $[\alpha]_D^{20} = -1.67$ (*c* 0.15, CH₂Cl₂). The major diastereoisomer: ¹H NMR (600 MHz, CDCl₃) $\delta = 7.57$ (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.08 – 7.00 (m, 5H), 6.99 – 6.92 (m, 3H),

6.90 (d, *J* = 7.8 Hz, 2H), 5.92 - 5.84 (m, 1H), 3.89 (d, *J* = 9.9 Hz, 1H), 3.24 (d, *J* = 13.4 Hz, 1H), 3.05 (d, *J* = 13.4 Hz, 1H), 2.13 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) $\delta = 176.4, 158.9, 138.0, 137.0, 136.4$ (q, *J* = 6.4 Hz), 132.7, 131.9, 129.1, 128.3, 128.1, 128.0, 127.6, 127.2, 126.3, 122.7, 121.6 (q, *J* = 269.8 Hz), 121.1 (q, *J* = 33.8 Hz), 77.0, 53.2, 41.3, 20.0. ¹⁹F NMR (376 MHz, CDCl₃) $\delta = -64.00$ (d, *J* = 6.0 Hz). HPLC analysis: Daicel CHIRALPAK OD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, $\lambda = 254$ nm, retention time: $t_{\text{major}} = 7.13$ min, $t_{\text{minor}} = 6.30$ min. HRMS (ESI) *m/z*: calcd for C₂₇H₂₂ClF₃NO₂ [M + H]⁺ 484.1286, found: 484.1283.

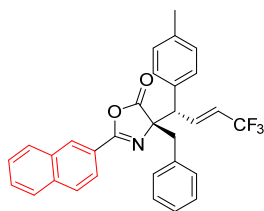


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.412	VV	0.1383	1.46248e4	1627.43005	50.4504
2	6.199	VV	0.1663	1.43637e4	1334.55847	49.5496



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.397	MM	0.1317	78.38120	9.92254	5.1427
2	6.188	PB	0.1644	1445.73193	134.84421	94.8573

(S)-4-Benzyl-2-(naphthalen-2-yl)-4-((S,E)-4,4,4-trifluoro-1-(p-tolyl)but-2-en-1-yl)oxazol-5(4H)-one (3p)



Purified using a Biotage flash chromatography system (PE/EtOAc,

10:1). Yield: 66.9 mg (67%); white solid; mp 188–189 °C; 73:27 dr;

90% ee (major diastereoisomer); $[\alpha]_D^{20} = -8.33$ (*c* 0.17, CH₂Cl₂). The

major diastereoisomer: ¹H NMR (600 MHz, CDCl₃) $\delta = 7.69 - 7.63$ (m, 4H), 7.62 – 7.57 (m, 2H), 7.45 – 7.40 (m, 1H), 7.38 – 7.28 (m, 4H), 7.26

(dd, *J* = 8.5, 1.7 Hz, 1H), 7.12 – 7.06 (m, 3H), 6.97 (d, *J* = 7.9 Hz, 2H), 6.01 - 5.94 (m, 1H), 4.01

(d, *J* = 9.9 Hz, 1H), 3.50 (d, *J* = 13.5 Hz, 1H), 3.30 (d, *J* = 13.5 Hz, 1H), 2.18 (s, 3H). ¹³C NMR

(151 MHz, CDCl₃) $\delta = 176.6, 160.0, 136.9, 136.6$ (q, *J* = 6.5 Hz), 132.1, 131.9, 131.6, 131.4,

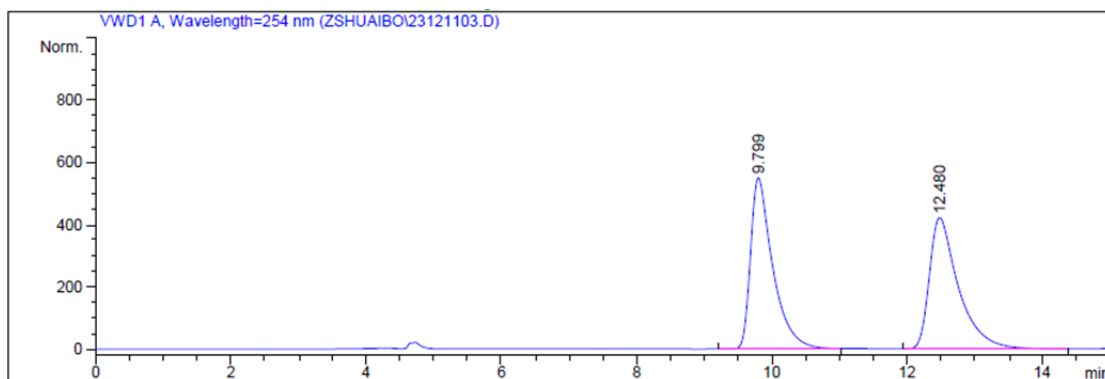
130.5, 128.3, 128.2, 127.7, 127.5, 127.1, 126.8, 126.7, 126.6, 126.4, 124.9, 124.7, 124.2, 121.6 (q,

J = 270.1 Hz), 121.1 (q, *J* = 33.9 Hz), 76.9, 53.4, 41.3, 19.9. ¹⁹F NMR (376 MHz, CDCl₃) $\delta = -$

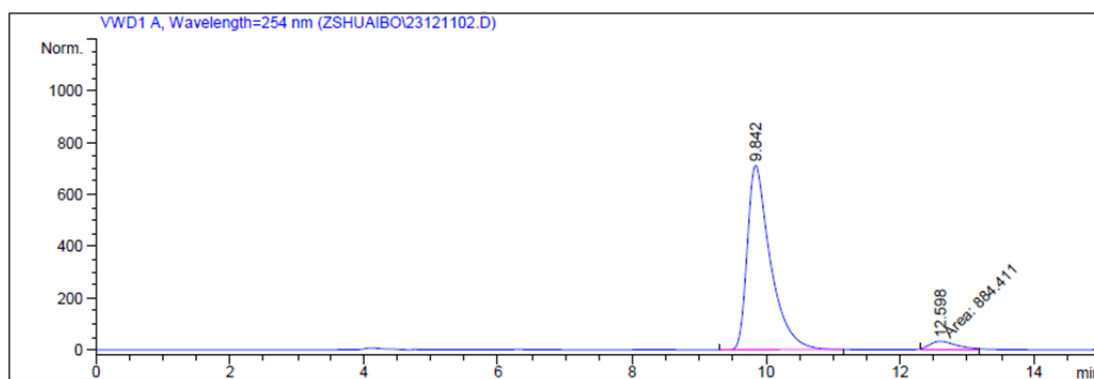
63.89 (d, *J* = 6.3 Hz). HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 95/5, flow

rate = 0.8 mL/min, $\lambda = 254$ nm, retention time: $t_{\text{major}} = 9.84$ min, $t_{\text{minor}} = 12.60$ min. HRMS (ESI)

m/z: calcd for C₃₁H₂₅F₃NO₂ [M + H]⁺ 500.1832, found: 500.1830.

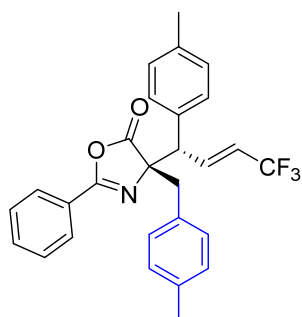


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.799	BB	0.3321	1.25783e4	550.39056	49.9319
2	12.480	BB	0.4358	1.26126e4	422.35965	50.0681



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.842	PB	0.3495	1.70940e4	713.11737	95.0807
2	12.598	MM	0.4572	884.41064	32.23820	4.9193

(S)-4-(4-Methylbenzyl)-2-phenyl-4-((S,E)-4,4,4-trifluoro-1-(p-tolyl)but-2-en-1-yl)oxazol-5(4H)-one (3q)



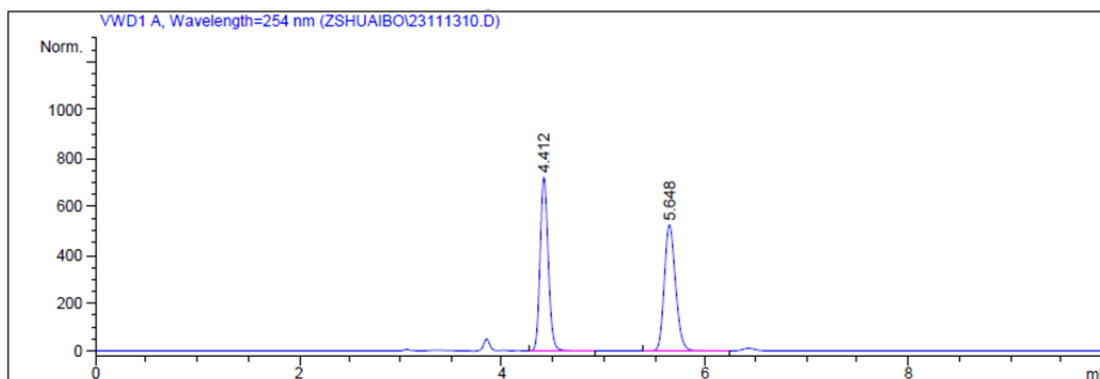
Purified using a Biotage flash chromatography system (PE/EtOAc,

20:1). Yield: 74.1 mg (80%); white solid; mp 97–98 °C; 75:25 dr;

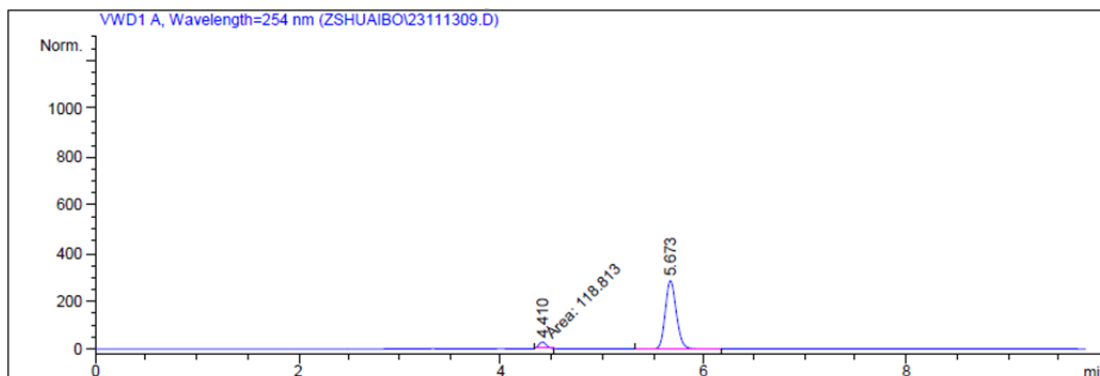
90% ee (major diastereoisomer); $[\alpha]_D^{20} = +2.50$ (*c* 0.14, CH₂Cl₂). The major diastereoisomer: ¹H NMR (500 MHz, CDCl₃) δ = 7.72 (d, *J* = 7.7 Hz, 2H), 7.52 – 7.45 (m, 1H), 7.40 – 7.34 (m, 2H), 7.11 – 6.87 (m, 9H), 5.98 – 5.88 (m, 1H), 3.95 (d, *J* = 9.7 Hz, 1H), 3.29 (d, *J* = 13.3 Hz, 1H), 3.09 (d, *J* = 13.3 Hz, 1H), 2.19 (s, 3H), 2.17 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) (one alkyl carbon missing) δ = 177.8,

160.8, 137.9, 137.7 (q, *J* = 6.5 Hz), 136.9, 133.1, 132.6, 130.7, 130.1, 129.3, 128.9, 128.7, 128.6, 127.8, 125.5, 122.7 (q, *J* = 269.5 Hz), 122.0 (q, *J* = 33.9 Hz), 78.0, 54.4, 41.9, 21.0. ¹⁹F NMR (376 MHz, CDCl₃) δ = -63.96 (d, *J* = 6.3 Hz). HPLC analysis: Daicel CHIRALPAK IE, *n*-hexane/*i*-PrOH = 95/5, flow rate = 1.0 mL/min, λ = 254 nm, retention time: *t*_{major} = 5.67 min, *t*_{minor} = 4.41 min. HRMS (ESI) *m/z*: calcd for C₂₈H₂₅F₃NO₂ [M + H]⁺ 464.1832, found: 464.1832.

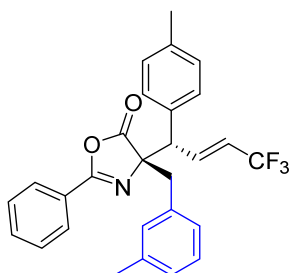


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.412	VB	0.0871	4029.85449	720.75336	49.9265
2	5.648	VB	0.1207	4041.72607	523.12555	50.0735



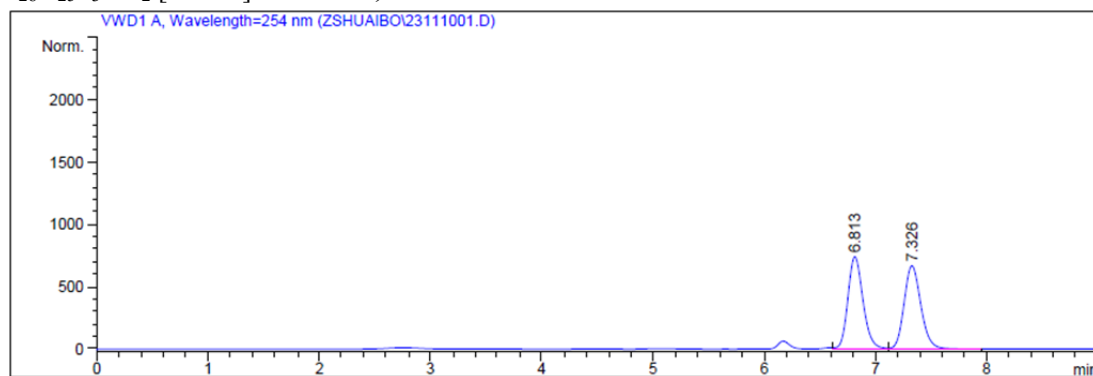
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.410	MM	0.0791	118.81348	25.01951	5.2301
2	5.673	VB	0.1176	2152.90186	283.92130	94.7699

(S)-4-(3-Methylbenzyl)-2-phenyl-4-((S,E)-4,4,4-trifluoro-1-(p-tolyl)but-2-en-1-yl)oxazol-5(4H)-one (3r)

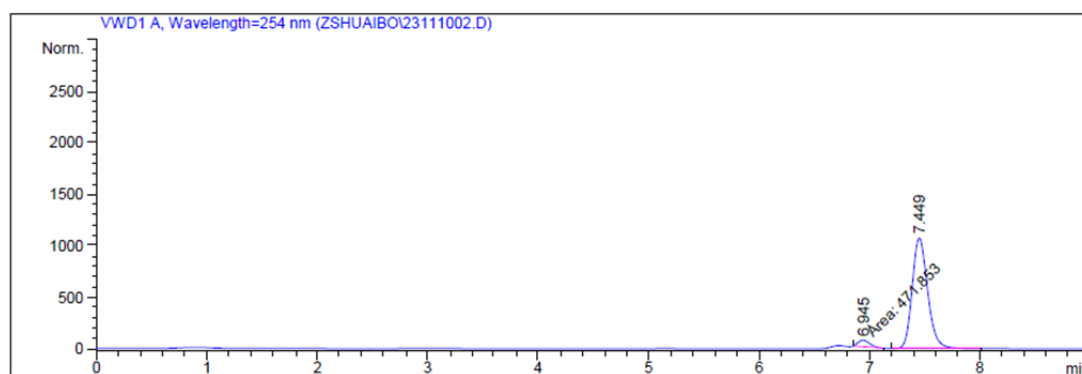


Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1). Yield: 75.0 mg (81%); white solid; mp 137–138 °C; 75:25 dr; 92% ee (major diastereoisomer); $[\alpha]_D^{20} = +1.29$ (*c* 0.31, CHCl₃). The major diastereoisomer: ¹H NMR (600 MHz, CDCl₃) δ = 7.74 – 7.69 (m, 2H), 7.52 – 7.47 (m, 1H), 7.42 – 7.35 (m, 2H), 7.10 – 6.96 (m, 6H), 6.95 – 6.88 (m, 3H), 5.98 – 5.89 (m, 1H), 3.96 (d, *J* = 9.8 Hz, 1H), 3.30 (d, *J* = 13.4 Hz, 1H), 3.08 (d, *J* = 13.4 Hz, 1H), 2.21 (s, 3H), 2.14 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ = 177.7, 160.9, 137.9, 137.8 (q, *J* = 6.5 Hz), 137.7, 133.7, 133.2, 132.6, 131.1, 129.4, 128.7, 128.6, 128.07, 128.05, 127.8, 127.2, 125.5, 122.7 (q, *J* = 269.8 Hz), 122.1 (q, *J* = 33.9 Hz), 77.9, 54.3, 42.4, 21.2, 21.0. ¹⁹F NMR (376 MHz, CDCl₃) δ = -63.94 (d, *J* = 6.4 Hz). HPLC analysis: Daicel CHIRALPAK OD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.6 mL/min, λ = 254 nm, retention time: $t_{\text{major}} = 7.45$ min, $t_{\text{minor}} = 6.95$ min. HRMS (ESI) *m/z*: calcd for

C₂₈H₂₅F₃NO₂ [M + H]⁺ 464.1832, found: 464.1827.

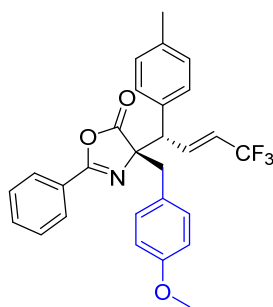


Peak #	RetTime [min]	Type	Width [min]	Area mAU * s	Height [mAU]	Area %
1	6.813	VV	0.1474	7065.51904	742.61780	49.8786
2	7.326	VV	0.1645	7099.91650	669.66266	50.1214



Peak #	RetTime [min]	Type	Width [min]	Area mAU * s	Height [mAU]	Area %
1	6.945	MM	0.1237	471.85291	63.57877	4.2951
2	7.449	VV	0.1506	1.05141e4	1074.12952	95.7049

(S)-4-(4-Methoxybenzyl)-2-phenyl-4-((S,E)-4,4,4-trifluoro-1-(p-tolyl)but-2-en-1-yl)oxazol-5(4H)-one (3s)

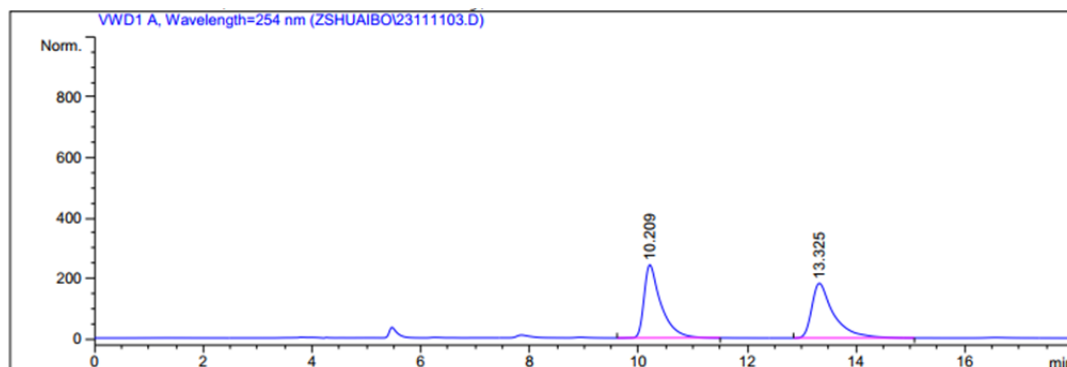


Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1). Yield: 73.8 mg (77%); yellow solid; mp 124–125 °C; 76:24 dr;

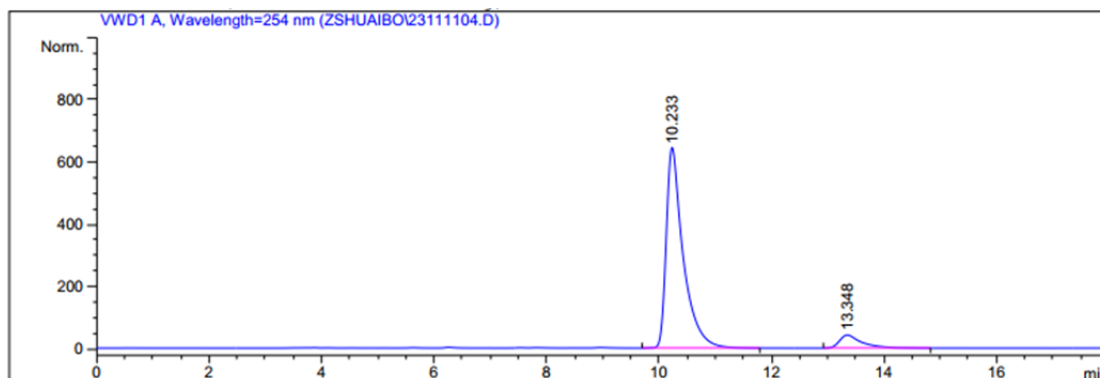
84% ee (major diastereoisomer); $[\alpha]_D^{20} = -0.91$ (*c* 0.33, CHCl₃). The major diastereoisomer: ¹H NMR (500 MHz, CDCl₃) $\delta = 7.66$ (d, *J* = 8.4 Hz, 2H), 7.16 – 7.00 (m, 8H), 6.97 (d, *J* = 7.7 Hz, 2H), 6.85 (d, *J* = 8.3 Hz, 2H), 5.99 – 5.88 (m, 1H), 3.95 (d, *J* = 9.8 Hz, 1H), 3.80 (s, 3H), 3.31 (d, *J* = 13.3 Hz, 1H), 3.11 (d, *J* = 13.3 Hz, 1H), 2.19 (s, 3H). ¹³C

NMR (151 MHz, CDCl₃) $\delta = 177.8, 160.9, 158.8, 137.9, 137.8$ (q, *J* = 6.5 Hz), 133.2, 132.6, 131.3, 129.4, 128.72, 128.66, 127.9, 125.8, 125.5, 122.7 (q, *J* = 269.7 Hz), 122.0 (q, *J* = 33.8 Hz), 113.6, 78.1, 55.0, 54.3, 41.6, 21.0. ¹⁹F NMR (376 MHz, CDCl₃) $\delta = -63.91$ (d, *J* = 6.2 Hz). HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate = 0.8 mL/min, $\lambda = 254$ nm, retention time: *t*_{major} = 10.23 min, *t*_{minor} = 13.35 min. HRMS (ESI) *m/z*: calcd for C₂₈H₂₅F₃NO₃

$[M + H]^+$ 480.1781, found: 480.1780.

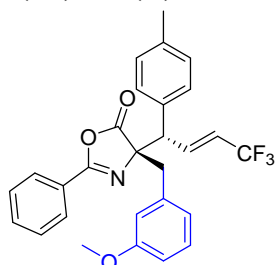


Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	10.209	VB	0.3088	5234.41162		242.32962	50.8487
2	13.325	BB	0.4015	5059.67871		181.21222	49.1513



Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	10.233	BB	0.3015	1.34372e4		644.39783	92.0716
2	13.348	BB	0.3979	1157.09241		41.90150	7.9284

(S)-4-(3-Methoxybenzyl)-2-phenyl-4-((S,E)-4,4,4-trifluoro-1-(p-tolyl)but-2-en-1-yl)oxazol-5(4H)-one (3t)

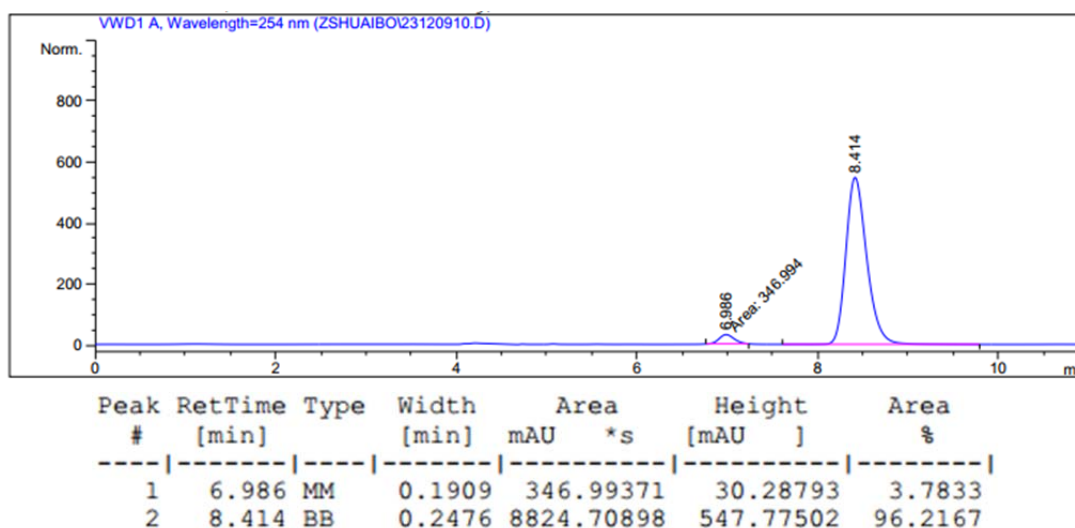
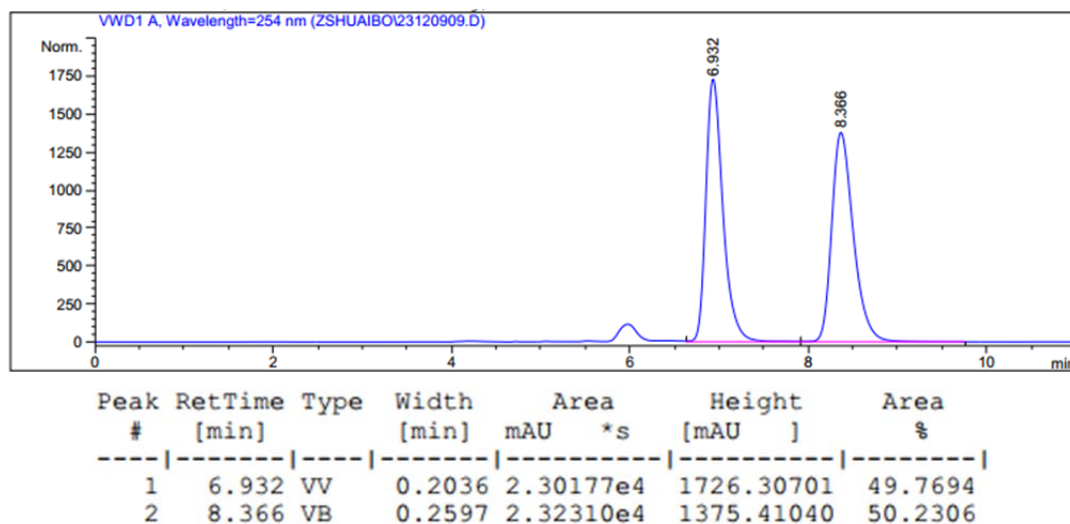


Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1). Yield: 67.1 mg (70%); white solid; mp 84–85 °C; 78:22 dr; 93%

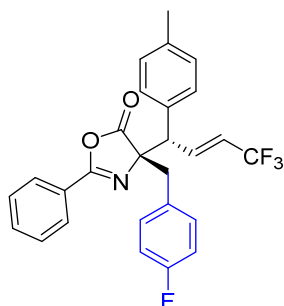
ee (major diastereoisomer); $[\alpha]_D^{20} = +3.6$ (*c* 0.13, CH₂Cl₂). The major diastereoisomer: ¹H NMR (600 MHz, CDCl₃) $\delta = 7.73$ (d, *J* = 7.7 Hz, 2H), 7.52 – 7.47 (m, 1H), 7.40 – 7.30 (m, 2H), 7.11 – 7.00 (m, 4H), 6.97 (d, *J* = 7.8 Hz, 2H), 6.72 (d, *J* = 7.6 Hz, 1H), 6.68 – 6.63 (m, 2H),

5.98 – 5.90 (m, 1H), 3.96 (d, *J* = 9.9 Hz, 1H), 3.59 (s, 3H), 3.31 (d, *J* = 13.4 Hz, 1H), 3.10 (d, *J* = 13.4 Hz, 1H), 2.20 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) $\delta = 177.6$, 161.0, 159.2, 137.9, 137.7 (q, *J* = 6.4 Hz), 135.3, 133.1, 132.7, 129.4, 129.2, 128.7, 128.6, 127.8, 125.4, 122.7 (q, *J* = 270.2 Hz), 122.6, 122.1 (q, *J* = 33.9 Hz), 115.2, 113.7, 77.8, 55.0, 54.4, 42.4, 21.0. ¹⁹F NMR (470 MHz, None) $\delta = -64.02$ (d, *J* = 6.8 Hz). HPLC analysis: Daicel CHIRALPAK OD-H, *n*-hexane/*i*-PrOH=

95/5, flow rate = 0.8 mL/min, $\lambda = 254$ nm, retention time: $t_{\text{major}} = 8.41$ min, $t_{\text{minor}} = 6.99$ min.
 HRMS (ESI) m/z: calcd for $\text{C}_{28}\text{H}_{25}\text{F}_3\text{NO}_3$ $[\text{M} + \text{H}]^+$ 480.1781, found: 480.1778.

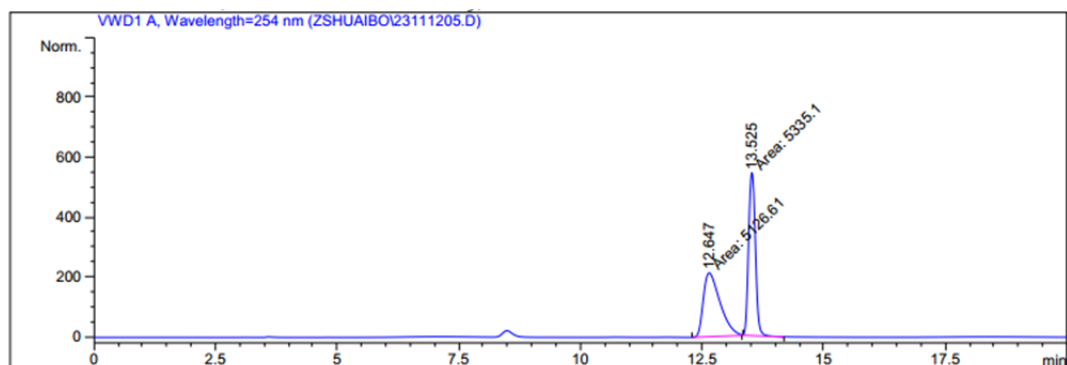


(S)-4-(4-Fluorobenzyl)-2-phenyl-4-((S,E)-4,4,4-trifluoro-1-(p-tolyl)but-2-en-1-yl)oxazol-5(4H)-one (3u)

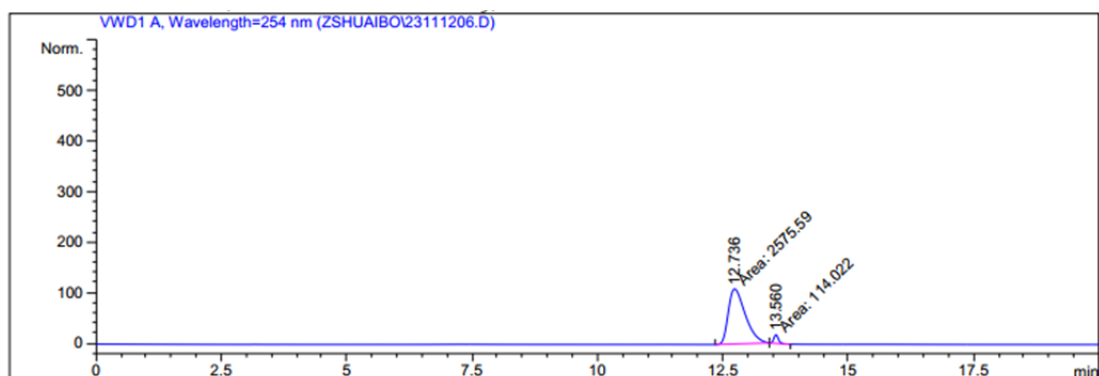


Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1). Yield: 71.9 mg (77%); white solid; mp 130–131 °C; 72:28 dr; 92% ee (major diastereoisomer); $[\alpha]_{\text{D}}^{20} = +6.67$ (c 0.15, CH_2Cl_2). The major diastereoisomer: ^1H NMR (600 MHz, CDCl_3) $\delta = 7.67 - 7.62$ (m, 2H), 7.47 – 7.41 (m, 1H), 7.34 – 7.29 (m, 2H), 7.07 – 6.87 (m, 7H), 6.78 – 6.71 (m, 2H), 5.91 - 5.84 (m, 1H), 3.87 (d, $J = 9.9$ Hz, 1H), 3.22 (d, $J = 13.6$ Hz, 1H), 3.03 (d, $J = 13.6$ Hz, 1H), 2.13 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) $\delta = 177.7$, 162.1 (d, $J = 246.1$ Hz), 161.0, 138.0, 137.6 (q, $J = 6.5$ Hz), 133.0, 132.8, 131.8 (d, $J = 7.9$ Hz), 129.6 (d, $J = 3.3$ Hz), 129.4, 128.71, 128.68, 127.8, 125.2, 122.6 (q, $J = 270.1$ Hz), 122.2 (q, $J = 33.9$ Hz), 115.1 (d, $J = 21.3$ Hz), 77.9, 54.3, 41.5, 21.0. ^{19}F NMR (376 MHz, CDCl_3) $\delta = -63.98$ (d, $J = 5.9$ Hz, 3F), -114.98 – -115.14 (m, 1F). HPLC analysis: Daicel

CHIRALPAK OD-H, *n*-hexane/*i*-PrOH = 500/1, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 12.74 min, t_{minor} = 13.56 min. HRMS (ESI) m/z : calcd for $C_{27}H_{22}F_4NO_2$ $[M + H]^+$ 468.1581, found: 468.1583.

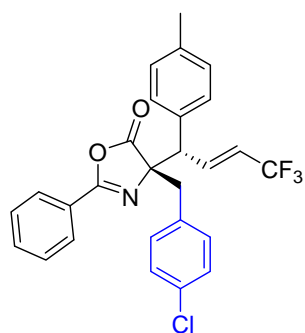


Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	12.647	MM	0.3998	5126.61328		213.74001	49.0036
2	13.525	MM	0.1632	5335.10352		544.77014	50.9964



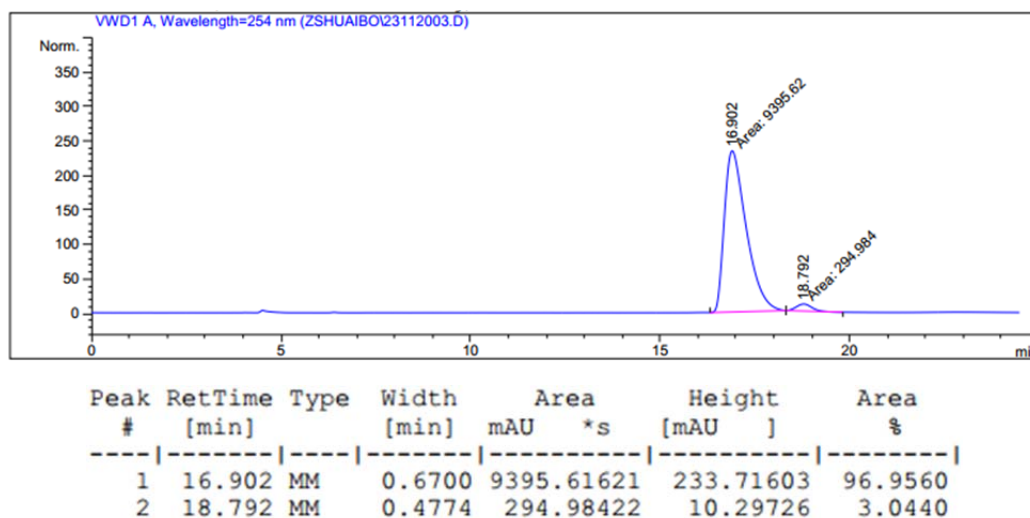
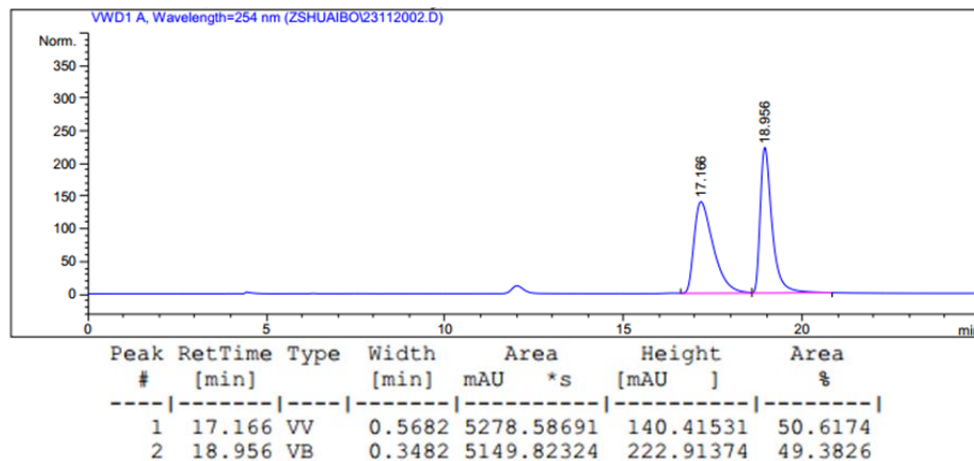
Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	12.736	MM	0.3937	2575.58643		109.02177	95.7606
2	13.560	MM	0.1117	114.02214		17.01612	4.2394

(*S*)-4-(4-Chlorobenzyl)-2-phenyl-4-((*S,E*)-4,4,4-trifluoro-1-(*p*-tolyl)but-2-en-1-yl)oxazol-5(*4H*)-one (3v)

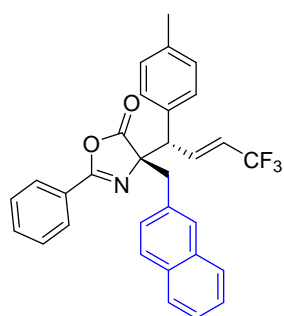


Purified using a Biotage flash chromatography system (PE/EtOAc, 20:1). Yield: 72.5 mg (75%); white solid; mp 96–97 °C; 73:27 dr; 94% ee (major diastereoisomer); $[\alpha]_D^{20}$ = -6.36 (*c* 0.14, CH_2Cl_2). The major diastereoisomer: 1H NMR (600 MHz, $CDCl_3$) δ = 7.67 – 7.63 (m, 2H), 7.46 – 7.41 (m, 1H), 7.34 – 7.29 (m, 2H), 7.05 – 7.01 (m, 2H), 7.00 – 6.92 (m, 5H), 6.90 (d, J = 7.9 Hz, 2H), 5.89 – 5.84 (m, 1H), 3.87 (d, J = 9.9 Hz, 1H), 3.22 (d, J = 13.5 Hz, 1H), 3.02 (d, J = 13.5 Hz, 1H), 2.13 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 176.5, 160.0, 137.0, 136.4 (q, J = 6.4 Hz), 132.3, 131.80, 131.78, 131.3, 130.5, 128.3, 127.7, 127.6,

127.4, 126.8, 124.1, 121.6 (q, $J = 269.9$ Hz), 121.2 (q, $J = 33.9$ Hz), 76.7, 53.3, 40.5, 20.0. ^{19}F NMR (376 MHz, CDCl_3) $\delta = -63.98$ (d, $J = 5.8$ Hz). HPLC analysis: Daicel CHIRALPAK OD-H, n -hexane/ i -PrOH = 500/1, flow rate = 0.8 mL/min, $\lambda = 254$ nm, retention time: $t_{\text{major}} = 16.90$ min, $t_{\text{minor}} = 18.79$ min. HRMS (ESI) m/z : calcd for $\text{C}_{27}\text{H}_{22}\text{ClF}_3\text{NO}_2$ $[\text{M} + \text{H}]^+$ 484.1286, found: 484.1288.

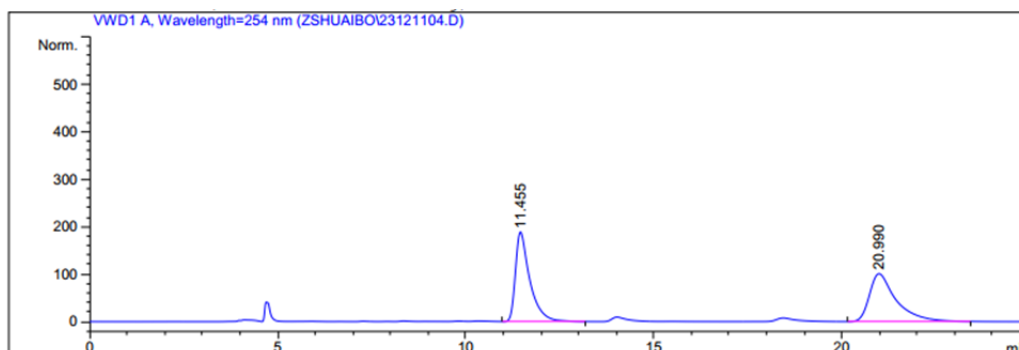


(*S*)-4-(Naphthalen-2-ylmethyl)-2-phenyl-4-((*S,E*)-4,4,4-trifluoro-1-(*p*-tolyl)but-2-en-1-yl)oxazol-5(4*H*)-one (3w)

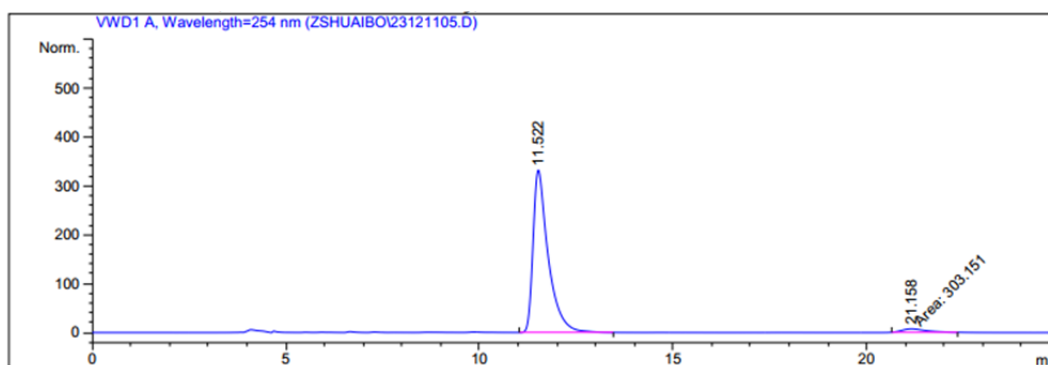


Purified using a Biotage flash chromatography system (PE/EtOAc, 10:1). Yield: 73.9 mg (74%); white solid; mp 186–187 °C; 79:21 dr; 94% ee (major diastereoisomer); $[\alpha]_{\text{D}}^{20} = -51.82$ (c 0.16, CH_2Cl_2). The major diastereoisomer: ^1H NMR (600 MHz, CDCl_3) $\delta = 8.07$ (s, 1H), 7.95 (dd, $J = 8.6, 1.7$ Hz, 1H), 7.84 (m, 2H), 7.79 (d, $J = 8.1$ Hz, 1H), 7.58 – 7.52 (m, 1H), 7.52 – 7.46 (m, 1H), 7.19 – 7.13 (m, 2H), 7.14 – 7.03 (m, 6H), 6.95 (d, $J = 7.9$ Hz, 2H), 6.02 – 5.94 (m, 1H), 4.01 (d, $J = 9.9$ Hz, 1H), 3.37 (d, $J = 13.5$ Hz, 1H), 3.17 (d, $J = 13.5$ Hz, 1H), 2.16 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) $\delta = 177.7, 161.0, 137.9, 137.8$ (q, $J = 6.6$ Hz), 135.3, 133.9, 133.1, 132.5, 130.2, 129.4, 129.3, 129.1, 128.7, 128.7, 128.4, 128.2, 127.9, 127.4, 126.9, 123.4, 122.7 (q, $J = 270.1$

Hz), 122.5, 122.1 (q, $J = 33.8$ Hz), 78.1, 54.4, 42.4, 21.0. ^{19}F NMR (376 MHz, CDCl_3) $\delta = -63.89$ (d, $J = 6.6$ Hz). HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH= 95/5, flow rate = 0.8 mL/min, $\lambda = 254$ nm, retention time: $t_{\text{major}} = 11.52$ min, $t_{\text{minor}} = 21.16$ min. HRMS (ESI) m/z : calcd for $\text{C}_{31}\text{H}_{25}\text{F}_3\text{NO}_2$ $[\text{M} + \text{H}]^+$ 500.1832, found: 500.1831.

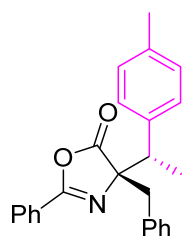


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.455	VB	0.3844	5014.40527	188.61124	50.2275
2	20.990	BB	0.7165	4968.98047	100.77014	49.7725



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.522	BB	0.3937	9047.47852	331.90924	96.7580
2	21.158	MM	0.7149	303.15149	7.06756	3.2420

(S)-4-Benzyl-2-phenyl-4-((S)-4,4,4-trifluoro-1-(*p*-tolyl)butyl)oxazol-5(4H)-one (4a)



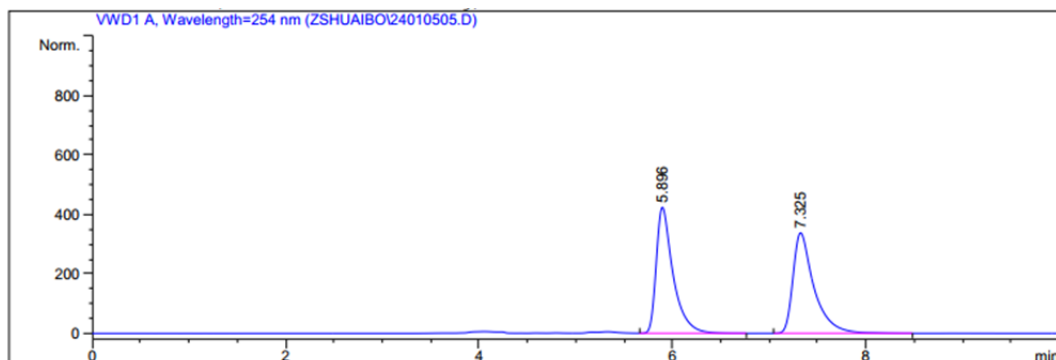
Purified using a Biotage flash chromatography system (PE/EtOAc,

10:1). Yield: 39.7 mg (80%); white solid; mp 150–151 °C; 93% ee;

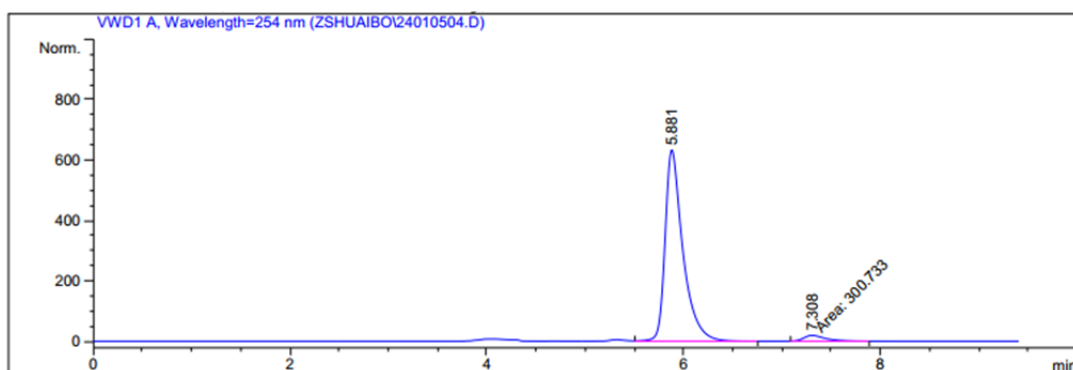
$[\alpha]_{\text{D}}^{20} = +10.44$ (c 0.2, CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3) $\delta = 7.74$ – 7.68 (m, 2H), 7.54 – 7.45 (m, 1H), 7.42 – 7.34 (m, 2H), 7.16 – 7.04 (m, 7H), 7.00 (d, $J = 8.0$ Hz, 2H), 3.48 (d, $J = 13.1$ Hz, 1H), 3.24 (dd, $J = 12.1$, 3.9 Hz, 1H), 3.13 (d, $J = 13.1$ Hz, 1H), 2.49 – 2.28 (m, 2H),

2.23 (s, 3H), 1.94 – 1.80 (m, 2H). ^{13}C NMR (126 MHz, CDCl_3) $\delta = 178.1$, 160.5, 137.7, 134.1, 133.5, 132.5, 130.3, 129.3, 129.0, 128.6, 128.1, 127.7, 127.2, 127.1 (q, $J = 276.5$ Hz), 125.6, 78.3, 50.9, 42.0, 32.0 (q, $J = 28.7$ Hz), 22.1 (q, $J = 3.2$ Hz), 21.0. ^{19}F NMR (376 MHz, CDCl_3) $\delta = -66.08$ (t, $J = 10.8$ Hz). HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH= 9/1, flow

rate = 0.8 mL/min, $\lambda = 254$ nm, retention time: $t_{\text{major}} = 5.88$ min, $t_{\text{minor}} = 7.31$ min. HRMS (ESI) m/z : calcd for $C_{27}H_{25}F_3NO_2$ $[M + H]^+$ 452.1832, found: 452.1835.

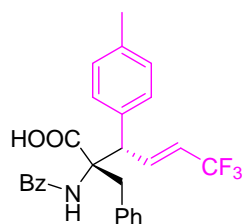


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.896	VB	0.1789	5127.61816	424.04434	50.1108
2	7.325	BB	0.2198	5104.94678	338.15970	49.8892



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.881	VB	0.1847	7970.98828	633.22235	96.3643
2	7.308	MM	0.2610	300.73306	19.20419	3.6357

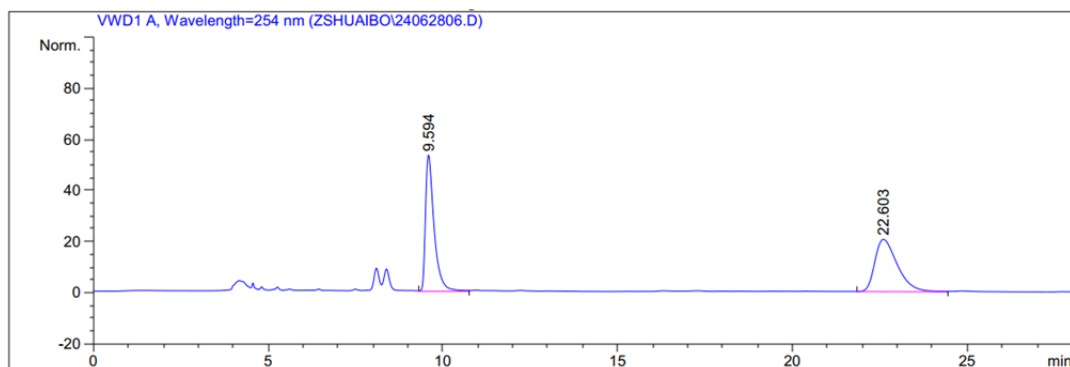
(2*S*,3*S*,*E*)-2-Benzamido-2-benzyl-6,6,6-trifluoro-3-(*p*-tolyl)hex-4-enoic acid (5a)



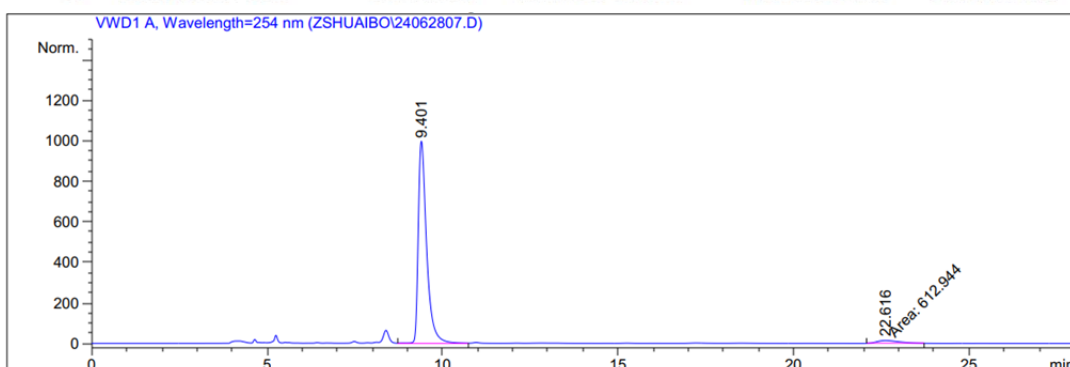
Purified using a Biotage flash chromatography system (PE/EtOAc, 1:2).

Yield: 54.7 mg (90%); white solid; mp 158–159 °C; 93% ee; $[\alpha]_D^{20} = -$

21.67 (*c* 0.2, CH_2Cl_2). 1H NMR (400 MHz, $CDCl_3$) $\delta = 10.92$ (brs, 1H), 7.60 (d, $J = 7.6$ Hz, 2H), 7.55 – 7.49 (m, 1H), 7.45 – 7.38 (m, 2H), 7.20 – 7.03 (m, 11H), 5.86 – 5.73 (m, 1H), 4.73 (d, $J = 9.9$ Hz, 1H), 4.14 (d, $J = 13.6$ Hz, 1H), 3.15 (d, $J = 13.6$ Hz, 1H), 2.30 (s, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) (one aromatic carbon missing) $\delta = 174.5, 169.1, 138.5$ (q, $J = 6.7$ Hz), 137.7, 135.7, 134.8, 134.0, 132.1, 129.9, 129.3, 128.9, 128.3, 127.1, 126.9, 122.8 (q, $J = 269.7$ Hz), 121.5 (q, $J = 33.5$ Hz), 69.4, 53.9, 38.0, 21.1. ^{19}F NMR (470 MHz, $CDCl_3$) $\delta = -63.87$ (d, $J = 6.1$ Hz). HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 9/1, flow rate = 0.8 mL/min, $\lambda = 254$ nm, retention time: $t_{\text{major}} = 9.40$ min, $t_{\text{minor}} = 22.62$ min. HRMS (ESI) m/z : calcd for $C_{27}H_{25}F_3NO_3$ $[M + H]^+$ 468.1781, found: 468.1783.

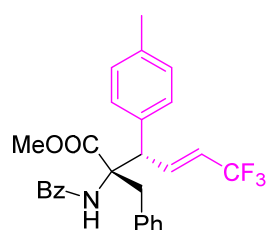


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.594	BV	0.2611	921.82806	53.02539	49.9697
2	22.603	BV	0.6997	922.94543	20.51193	50.0303



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.401	VV	0.2525	1.65304e4	992.67407	96.4246
2	22.616	MM	0.7378	612.94434	13.84529	3.5754

Methyl (2*S*,3*S*,*E*)-2-benzamido-2-benzyl-6,6,6-trifluoro-3-(*p*-tolyl)hex-4-enoate (6a)

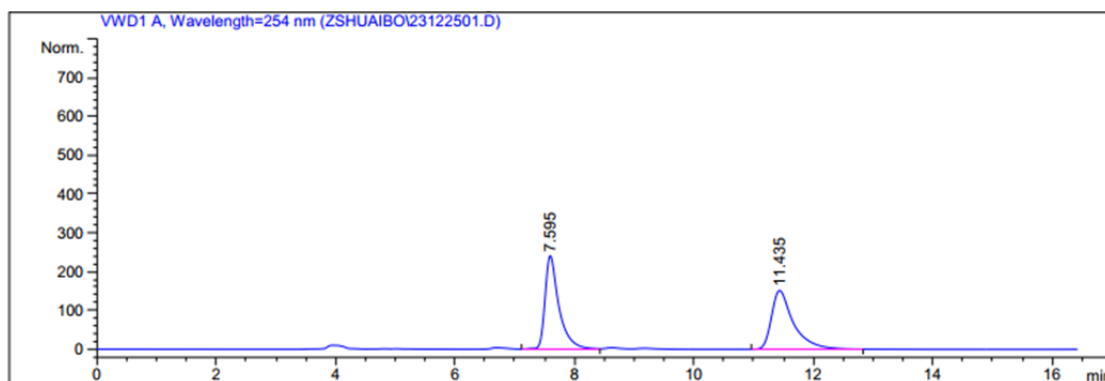


Purified using a Biotage flash chromatography system (PE/EtOAc,

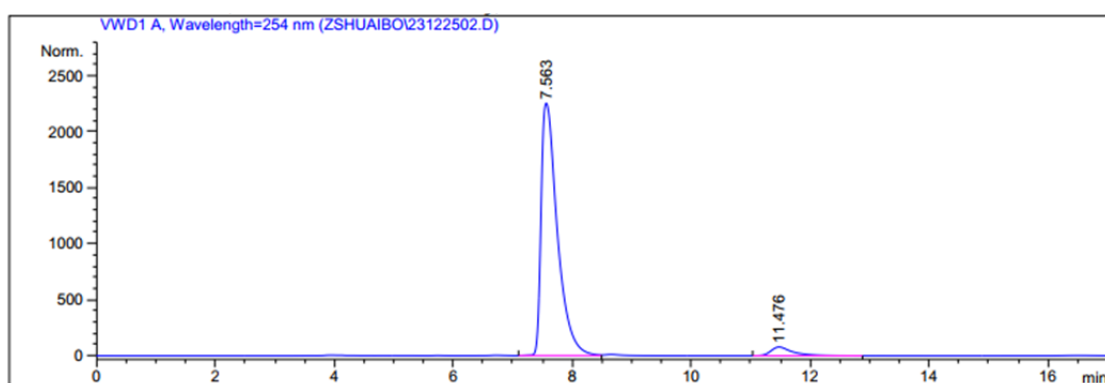
10:1). Yield: 214.0 mg (99%); white solid; mp 84–85 °C; 91% ee; $[\alpha]_D^{20}$

= -9.17 (*c* 0.19, CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃) δ = 7.64 (d, *J* = 7.6 Hz, 2H), 7.51 – 7.44 (m, 1H), 7.42 – 7.36 (m, 2H), 7.16 – 7.08 (m, 8H), 7.07 – 7.02 (m, 2H), 7.00 (s, 1H), 5.82 – 5.72 (m, 1H), 4.67 (d, *J* =

9.9 Hz, 1H), 4.22 (d, *J* = 13.6 Hz, 1H), 3.76 (s, 3H), 3.10 (d, *J* = 13.6 Hz, 1H), 2.32 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ = 172.2, 167.8, 138.8 (q, *J* = 6.5 Hz), 137.7, 136.0, 135.4, 134.3, 131.7, 129.8, 129.3, 129.1, 128.7, 128.3, 127.0, 126.8, 122.8 (q, *J* = 269.7 Hz), 121.1 (q, *J* = 33.6 Hz), 69.4, 54.5, 52.7, 37.9, 21.1. ¹⁹F NMR (470 MHz, CDCl₃) δ = -63.90 (d, *J* = 6.5 Hz). HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 8/2, flow rate = 0.8 mL/min, λ = 254 nm, retention time: *t*_{major} = 7.56 min, *t*_{minor} = 11.48 min. HRMS (ESI) *m/z*: calcd for C₂₈H₂₇F₃NO₃ [M + H]⁺ 482.1938, found: 482.1930.

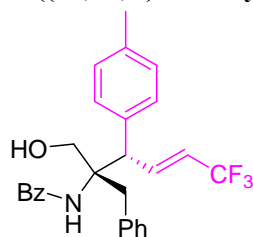


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.595	VV	0.2386	3932.52393	240.74437	50.4627
2	11.435	PB	0.3729	3860.40820	151.52843	49.5373



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.563	VV	0.2834	4.26707e4	2255.20825	95.5570
2	11.476	BB	0.3711	1983.99829	77.96616	4.4430

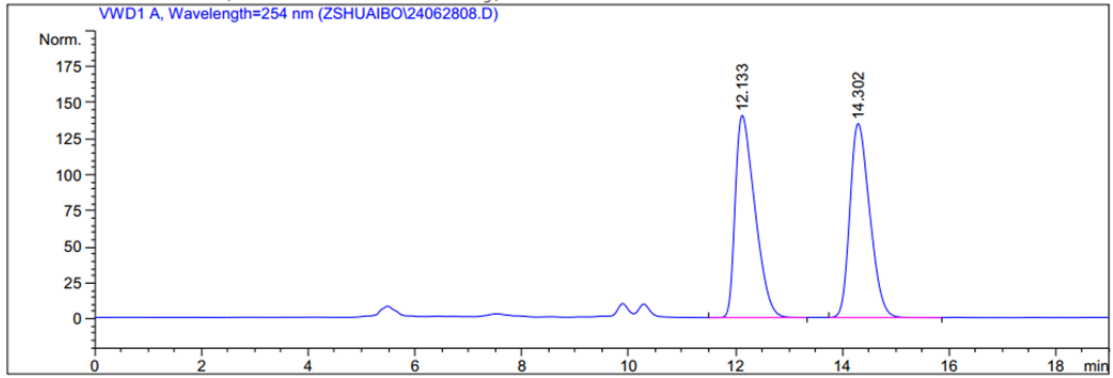
***N*-((2*S*,3*S*,*E*)-2-benzyl-6,6,6-trifluoro-1-hydroxy-3-(*p*-tolyl)hex-4-en-2-yl)benzamide (7a)**



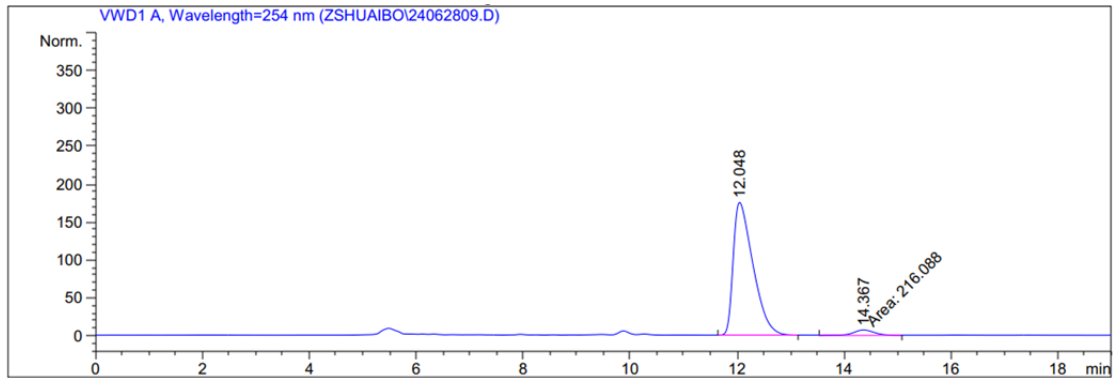
Purified using a Biotage flash chromatography system (PE/EtOAc, 5:1).

Yield: 57.8 mg (85%); white solid; mp 109–110 °C; 91% ee; $[\alpha]_D^{20} = -$

60.53 (*c* 0.22, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ = 7.59 – 7.52 (m, 2H), 7.50 – 7.43 (m, 1H), 7.40 – 7.34 (m, 2H), 7.29 – 7.24 (m, 2H), 7.23 – 7.15 (m, 5H), 7.13 – 7.00 (m, 3H), 6.31 (s, 1H), 5.86 – 5.73 (m, 1H), 4.64 (d, *J* = 9.4 Hz, 1H), 3.85 (d, *J* = 11.6 Hz, 1H), 3.70 (d, *J* = 11.6 Hz, 1H), 3.58 (d, *J* = 13.8 Hz, 2H), 2.68 (d, *J* = 13.8 Hz, 1H), 2.36 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ = 168.9, 139.2 (q, *J* = 6.6 Hz), 137.5, 136.0, 135.2, 134.6, 131.6, 130.2, 129.8, 129.5, 128.7, 128.6, 127.1, 126.7, 123.0 (q, *J* = 269.6 Hz), 121.0 (q, *J* = 33.3 Hz), 65.5, 63.3, 52.1, 39.4, 21.1. ¹⁹F NMR (377 MHz, CDCl₃) δ = -63.86 (d, *J* = 7.0 Hz). HPLC analysis: Daicel CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 7/3, flow rate = 0.8 mL/min, λ = 254 nm, retention time: t_{major} = 12.05 min, t_{minor} = 14.37 min. HRMS (ESI) *m/z*: calcd for C₂₇H₂₅F₃NO₂ [M - H]⁻ 452.1843, found: 452.1849.



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.133	VB	0.3936	3603.96289	139.97615	50.7656
2	14.302	BB	0.3958	3495.25952	134.73459	49.2344



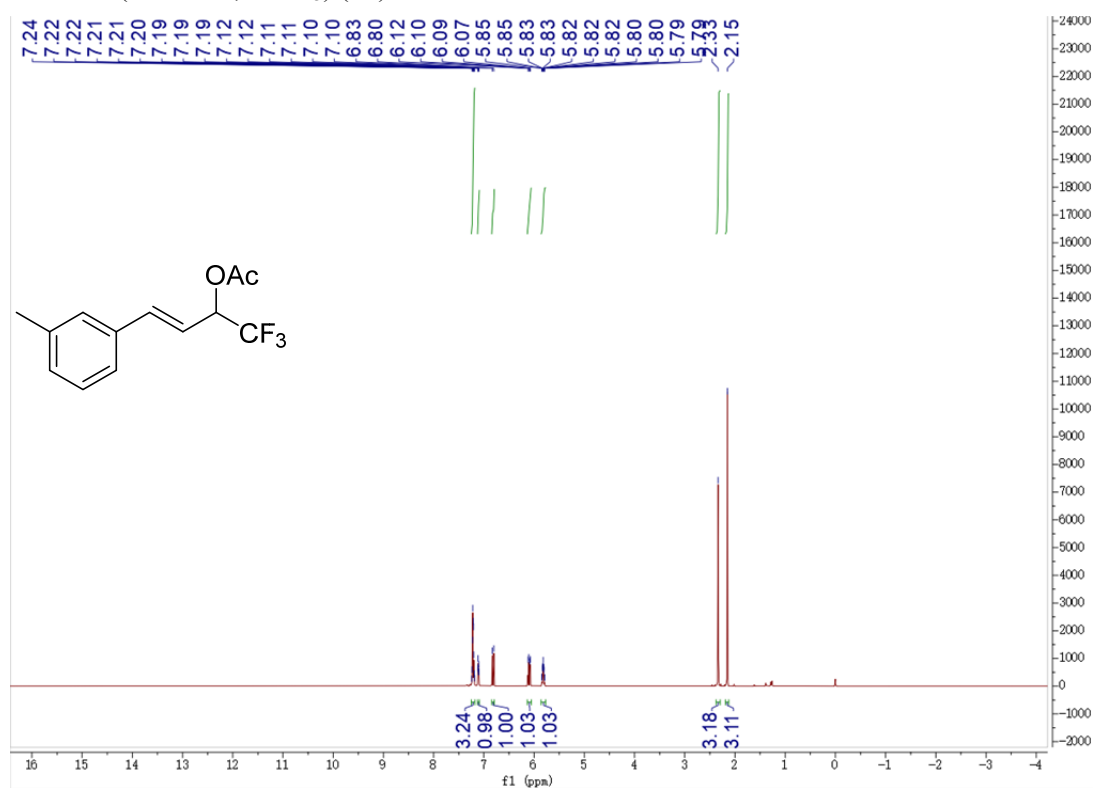
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.048	BB	0.3869	4492.23828	174.96991	95.4105
2	14.367	MM	0.4946	216.08801	7.28102	4.5895

5. References

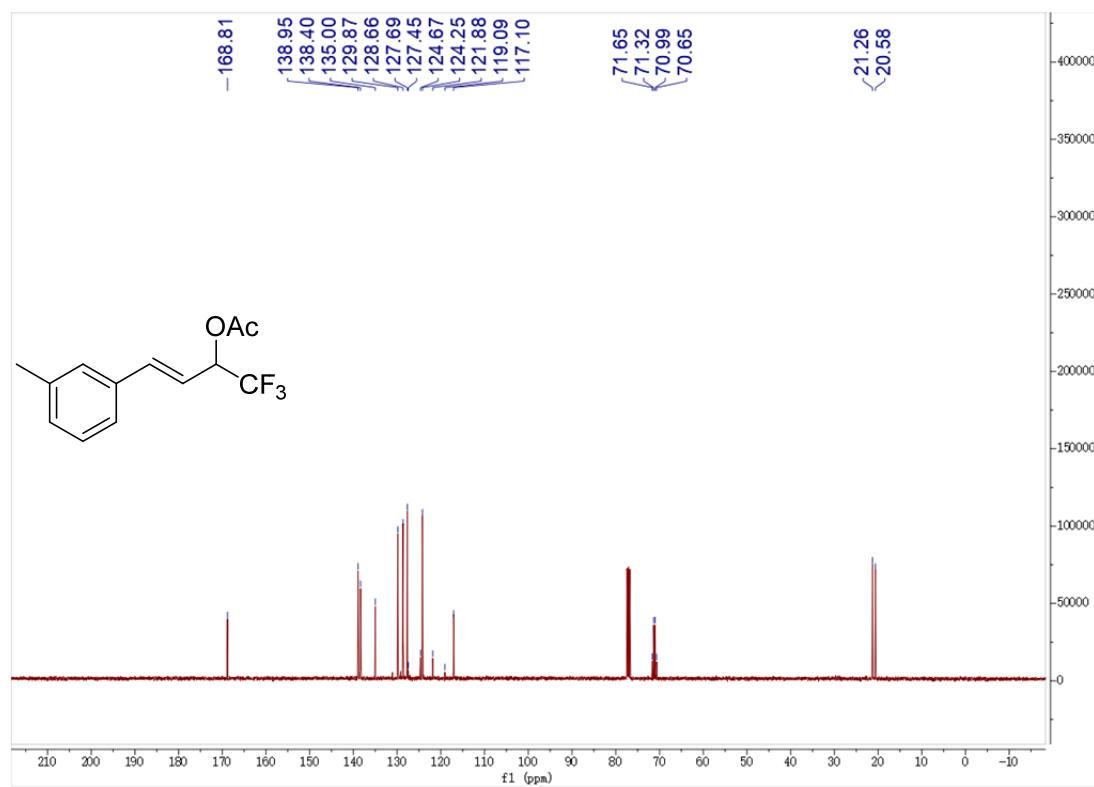
- [1] S. Zhang, D. Li, B. Wang, W. Sun, H. Ma, K. Di, L. Sun, J. Zhao, J. Qu, Y. Zhou, *Eur. J. Org. Chem.* **2023**, 26, e202300593.
- [2] a) M. Kawatsura, S. Terasaki, M. Minakawa, T. Hirakawa, K. Ikeda, T. Itoh, *Org. Lett.* **2014**, 16, 2442-2445; b) M. Zhou, J. Zhang, X.-G. Zhang, X. Zhang, *Org. Lett.* **2019**, 21, 671-674.
- [3] M. Sicignano, R. I. Rodríguez, V. Capaccio, F. Borello, R. Cano, F. De Riccardis, L. Bernardi, S. Díaz-Tendero, G. Della Sala, J. Alemán, *Org. Biomol. Chem.* **2020**, 18, 2914-2920.

6. Copy of NMR spectra for the products

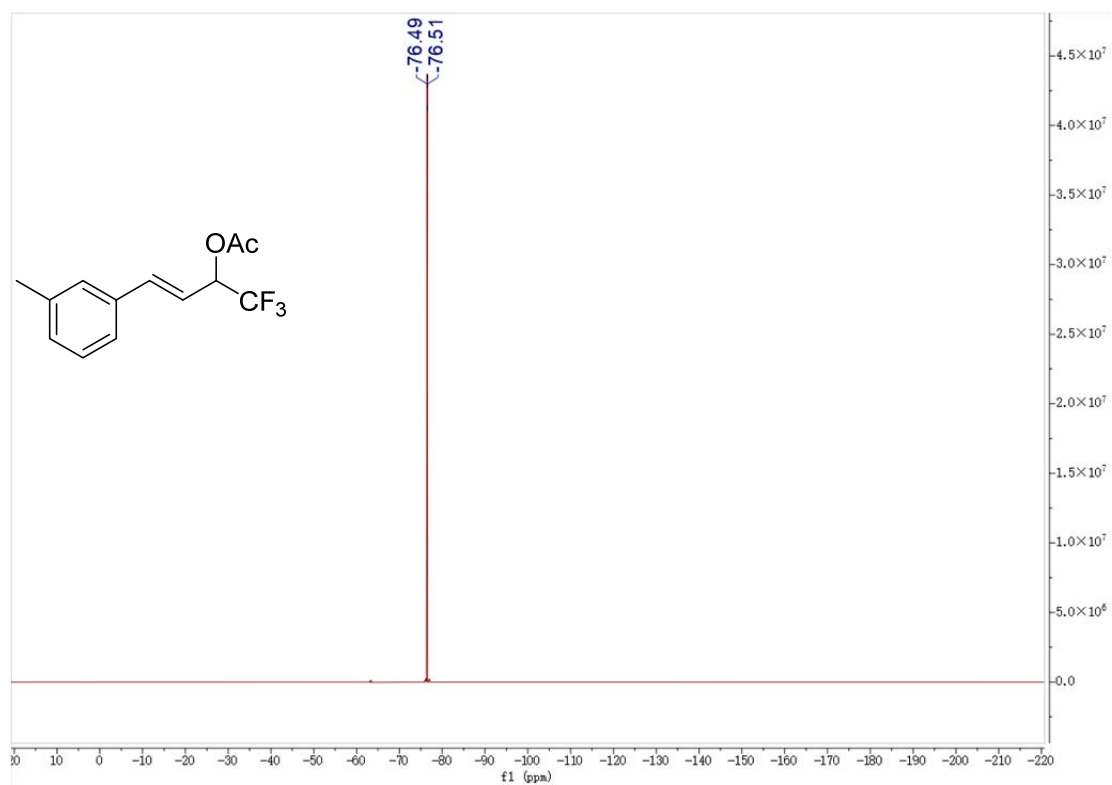
^1H NMR (500 MHz, CDCl_3) (**1b**)



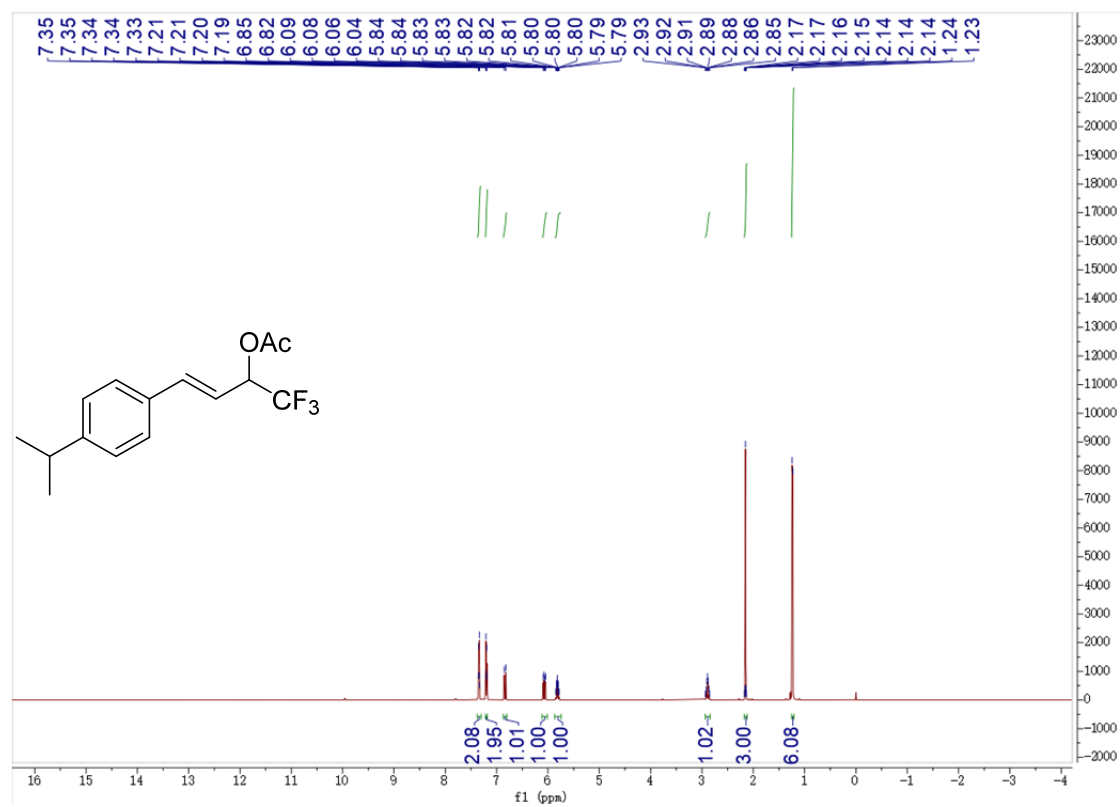
^{13}C NMR (101 MHz, CDCl_3) (**1b**)



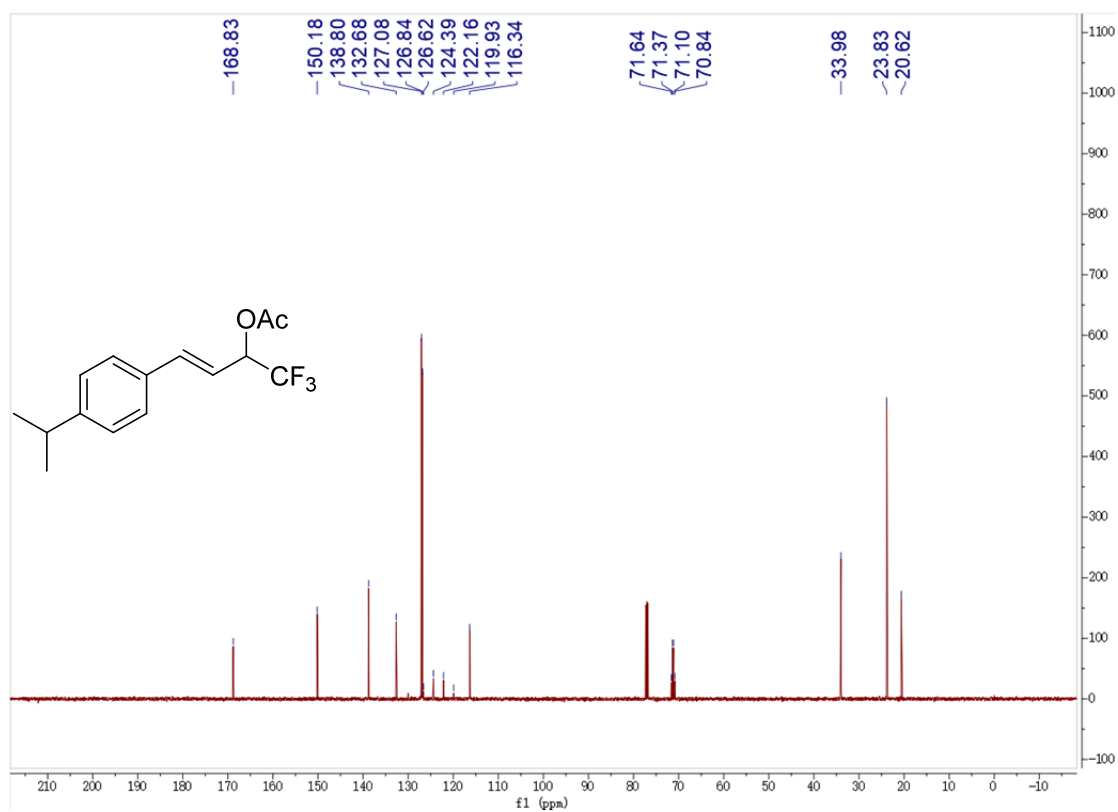
^{19}F NMR (376 MHz, CDCl_3) (**1b**)



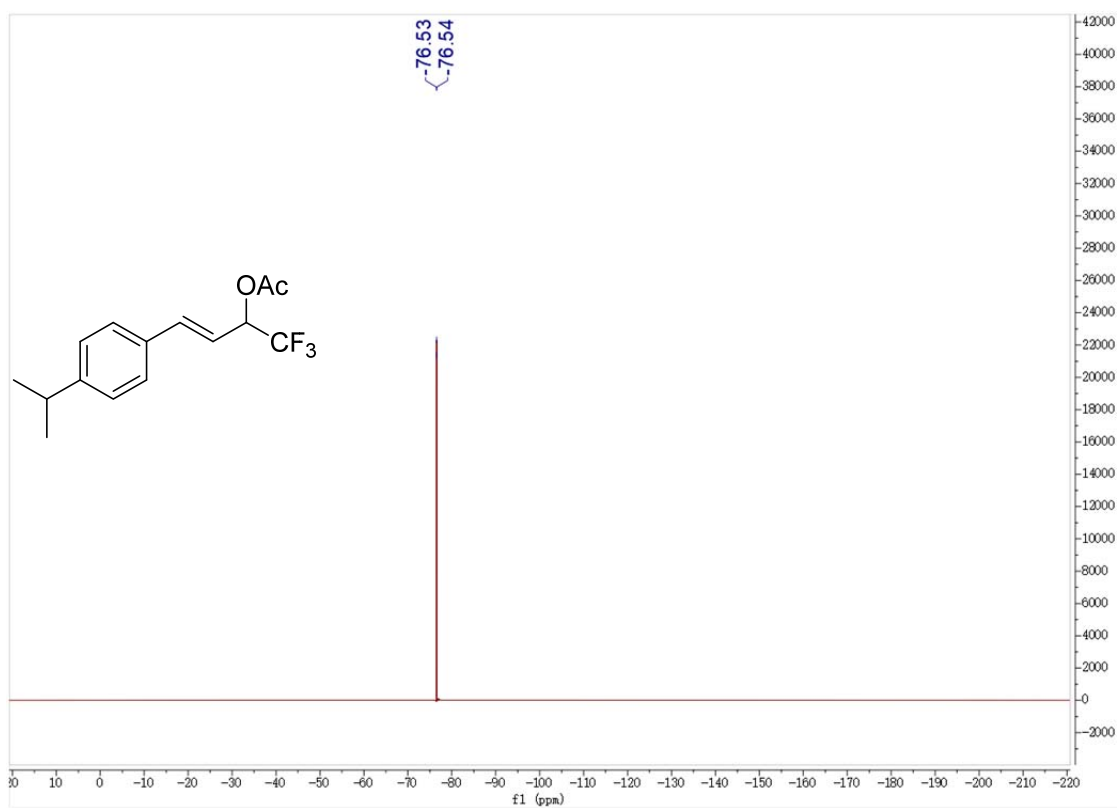
^1H NMR (500 MHz, CDCl_3) (**1d**)



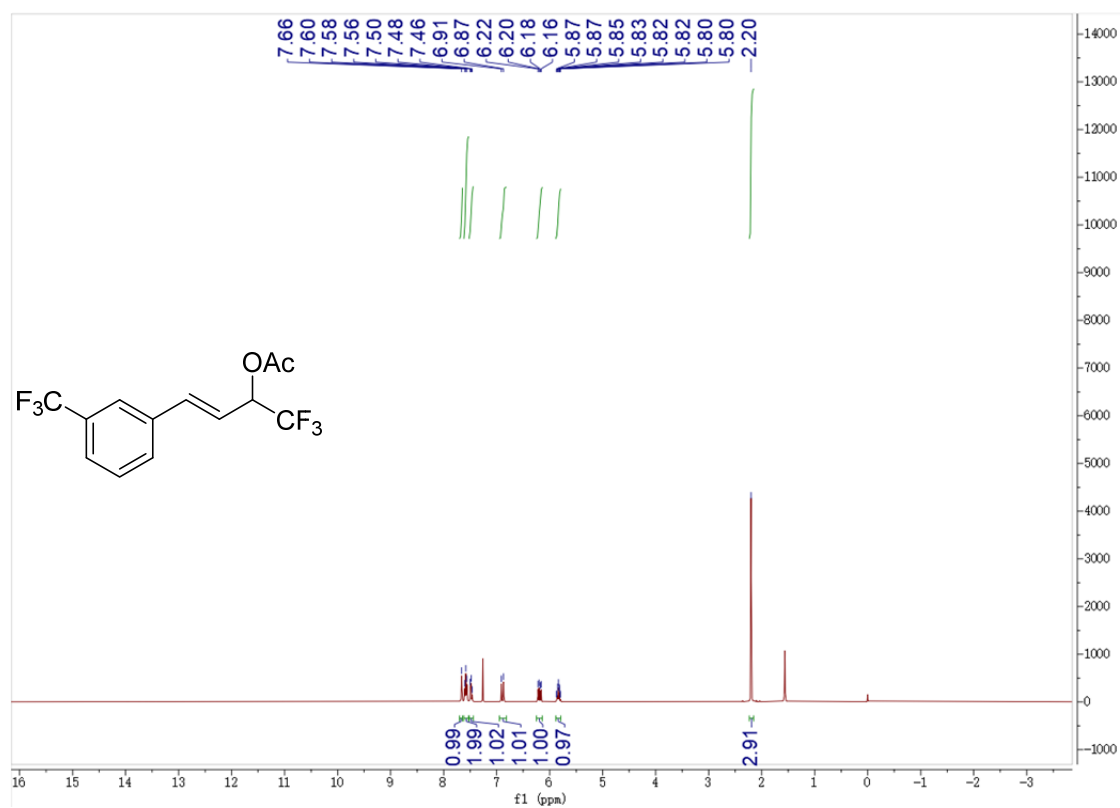
^{13}C NMR (126 MHz, CDCl_3) (**1d**)



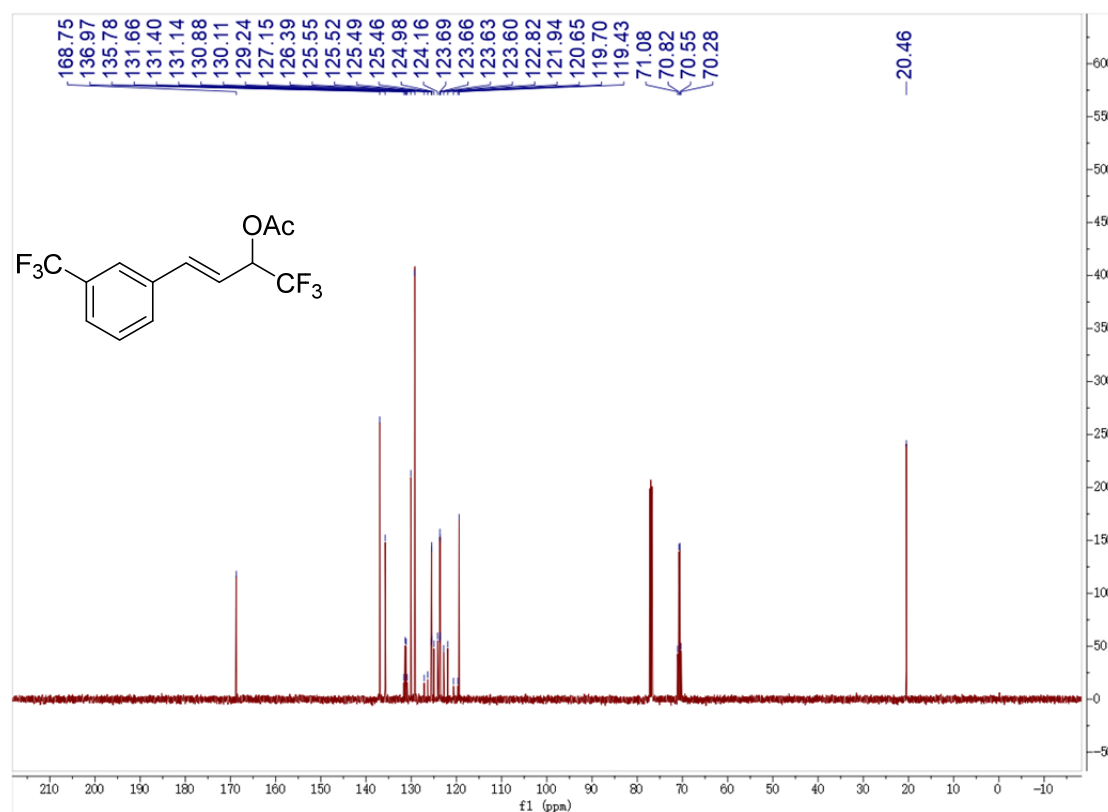
^{19}F NMR (470 MHz, CDCl_3) (**1d**)



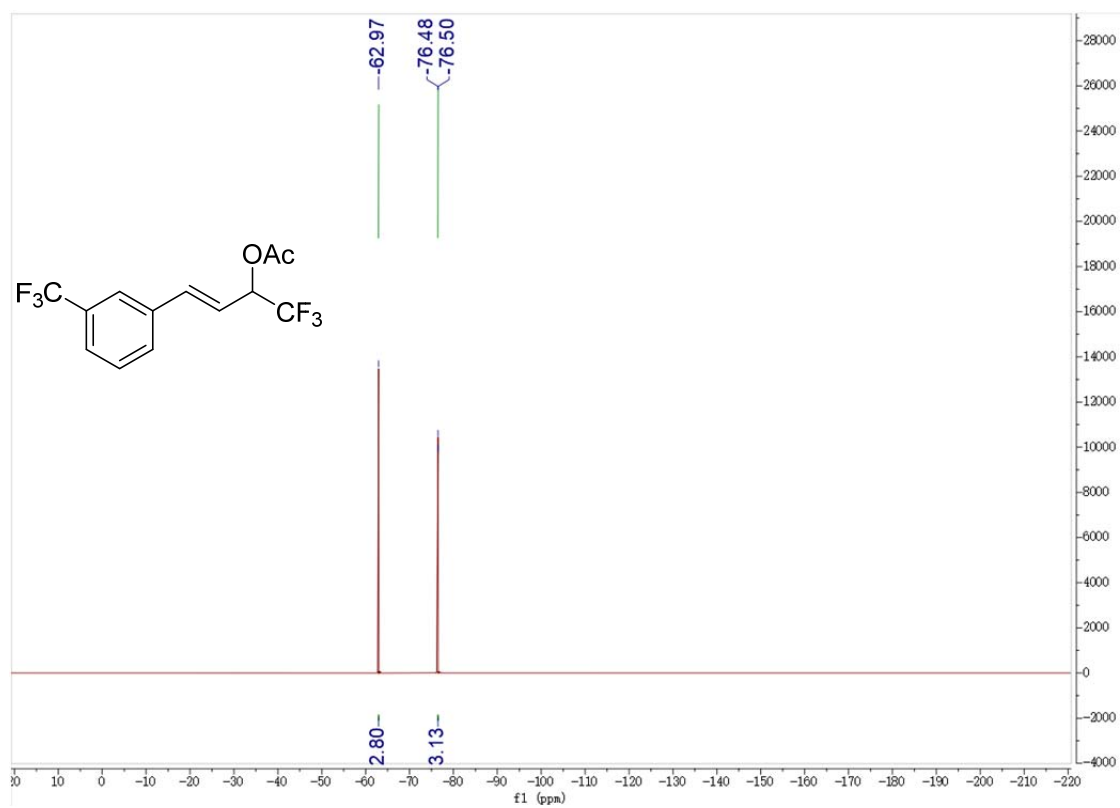
¹H NMR (400 MHz, CDCl₃) (**1h**)



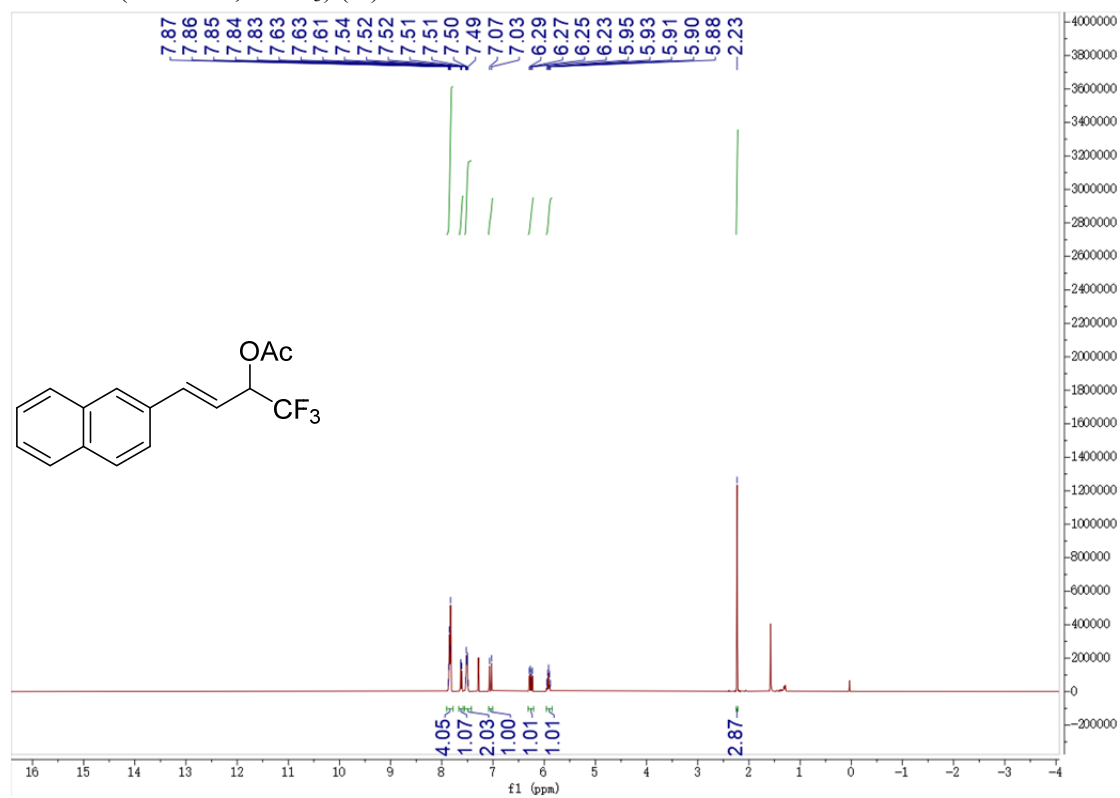
¹³C NMR (126 MHz, CDCl₃) (**1h**)



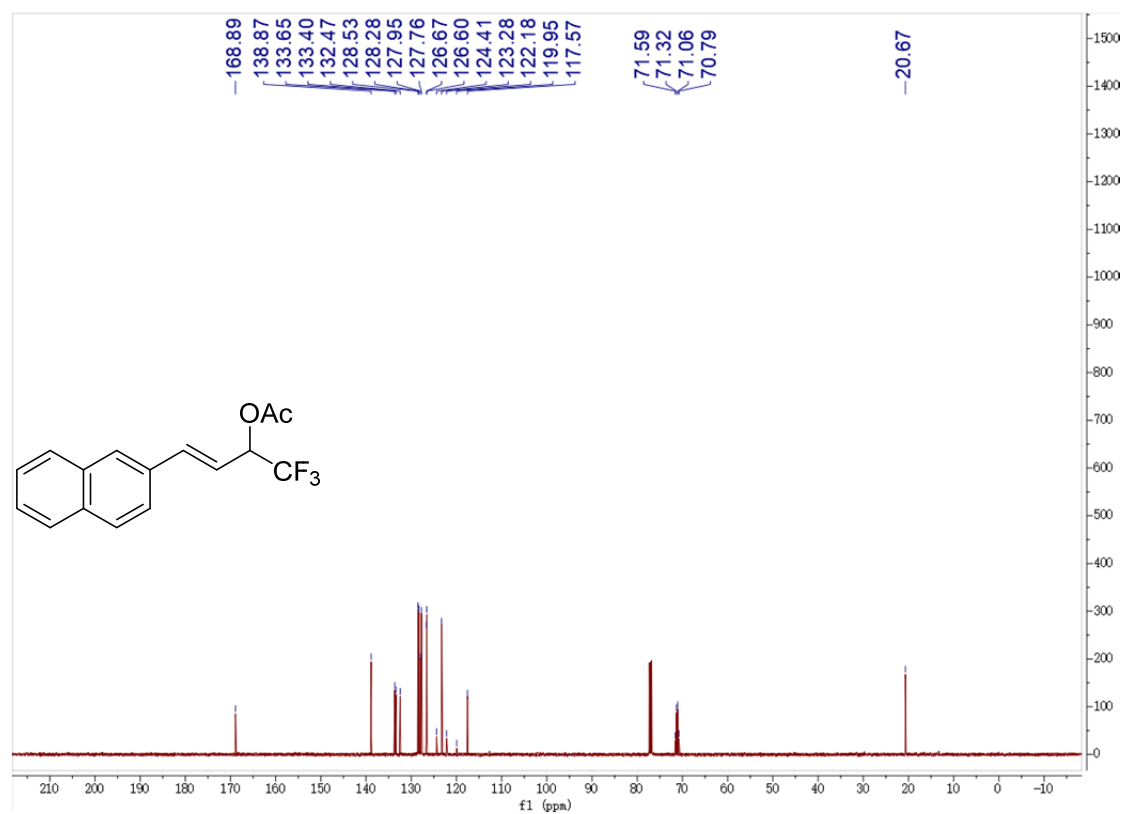
^{19}F NMR (470 MHz, CDCl_3) (**1h**)



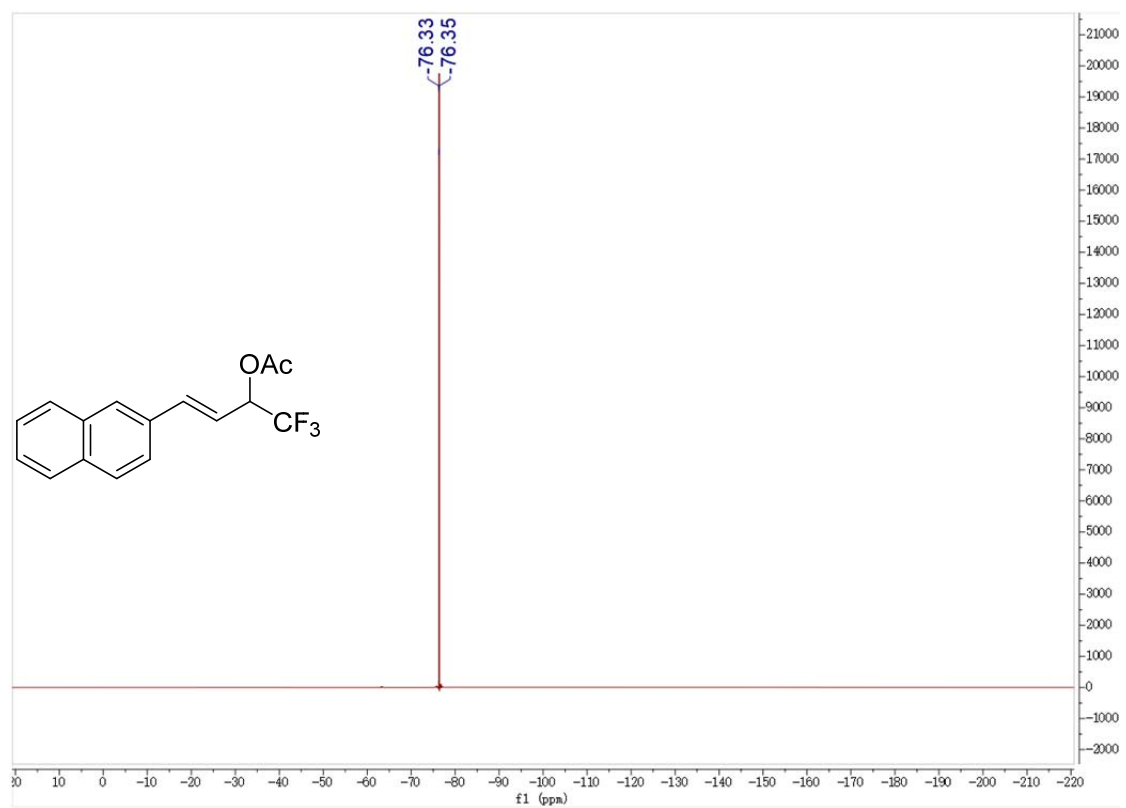
^1H NMR (400 MHz, CDCl_3) (**1i**)



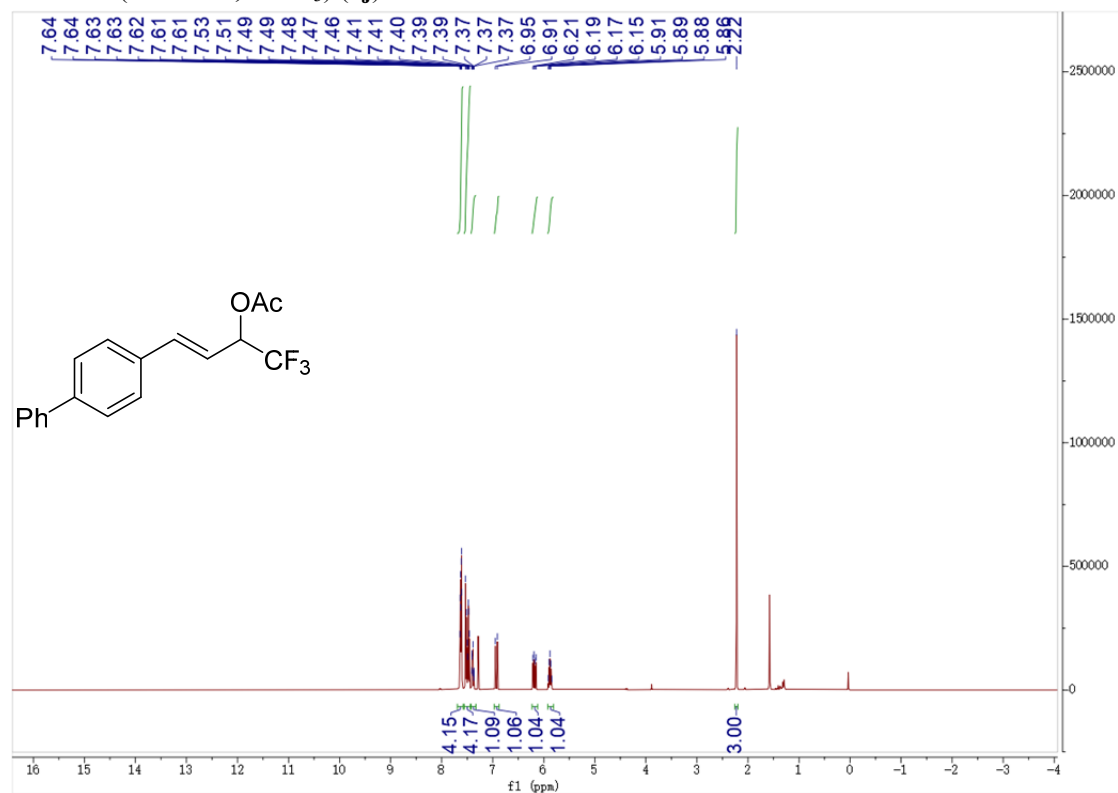
^{13}C NMR (126 MHz, CDCl_3) (**1i**)



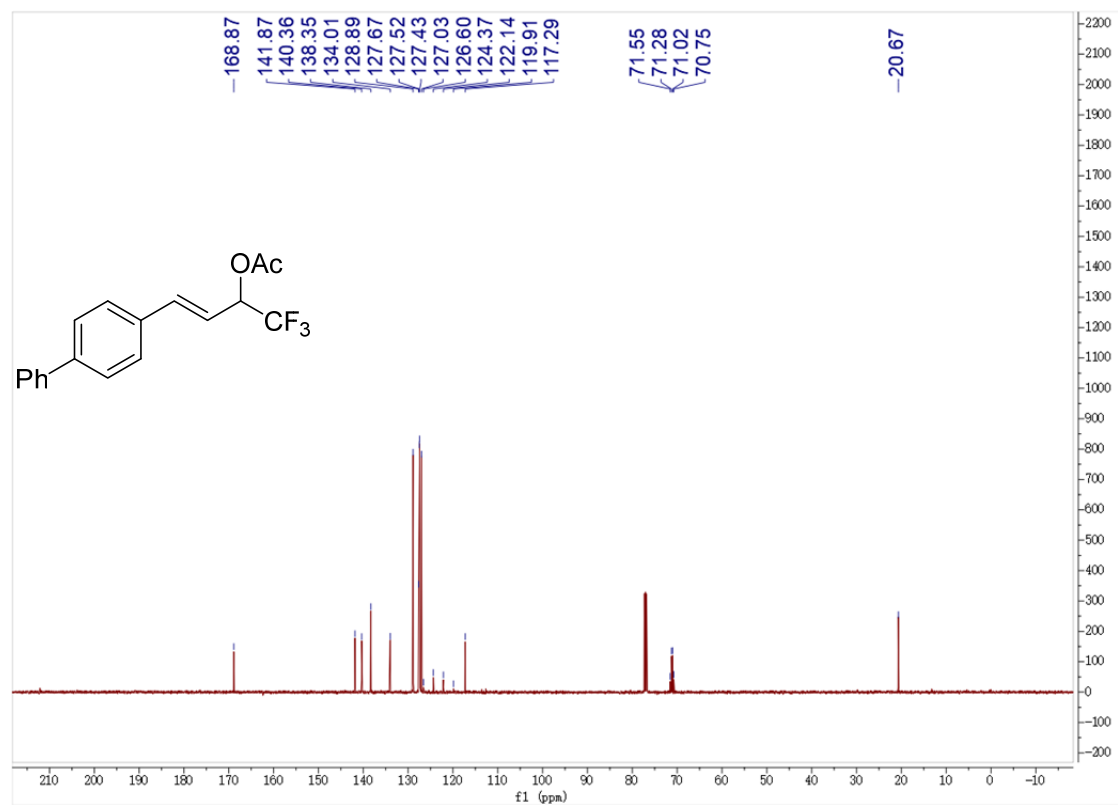
^{19}F NMR (470 MHz, CDCl_3) (**1i**)



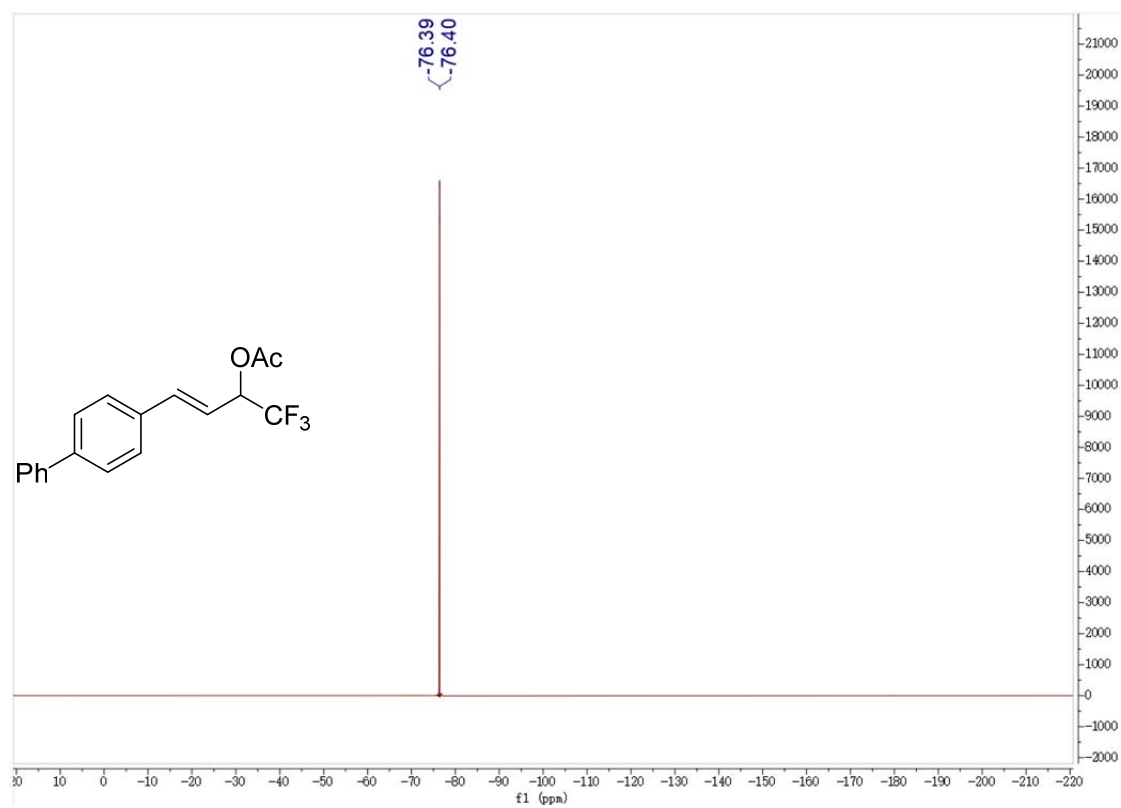
¹H NMR (400 MHz, CDCl₃) (**1j**)



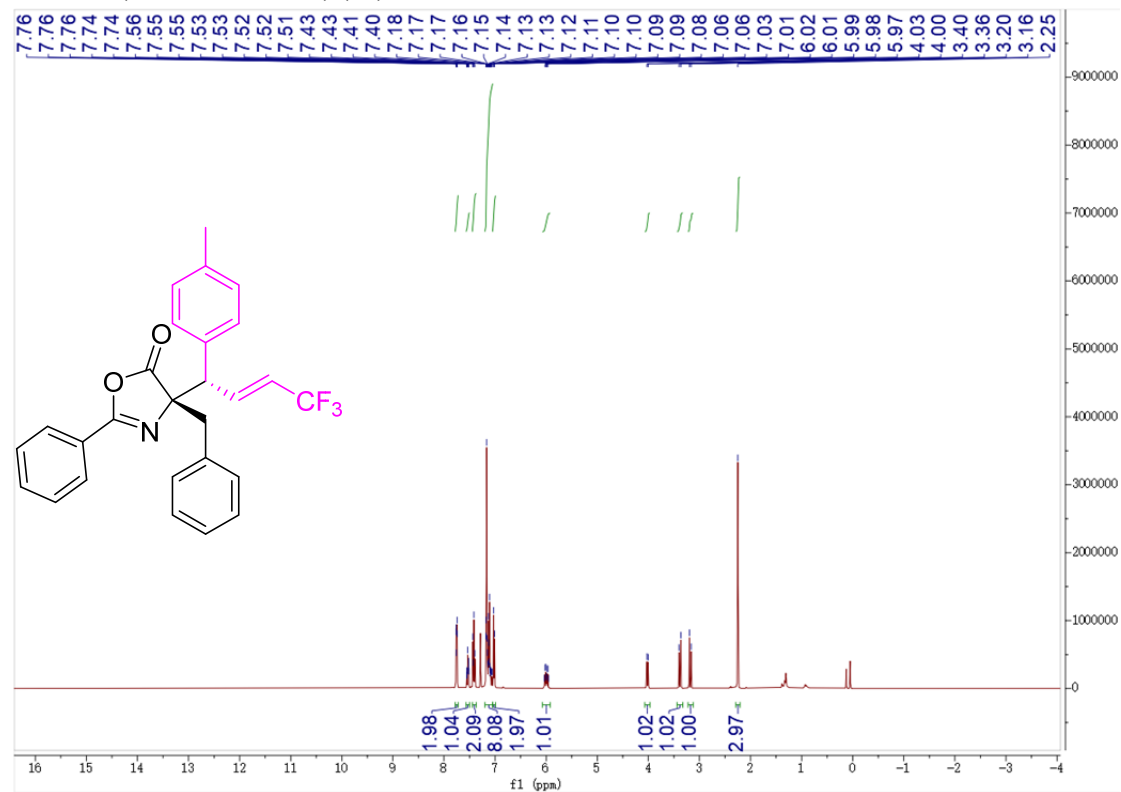
¹³C NMR (126 MHz, CDCl₃) (**1j**)



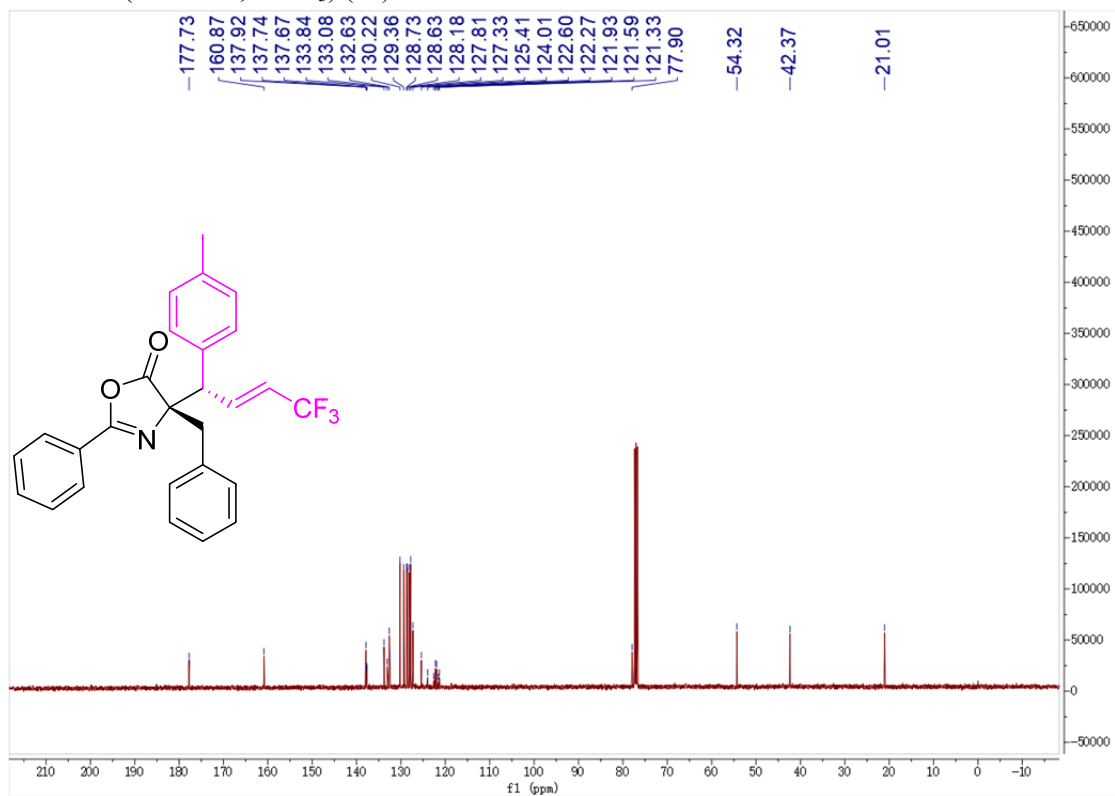
^{19}F NMR (470 MHz, CDCl_3) (**1j**)



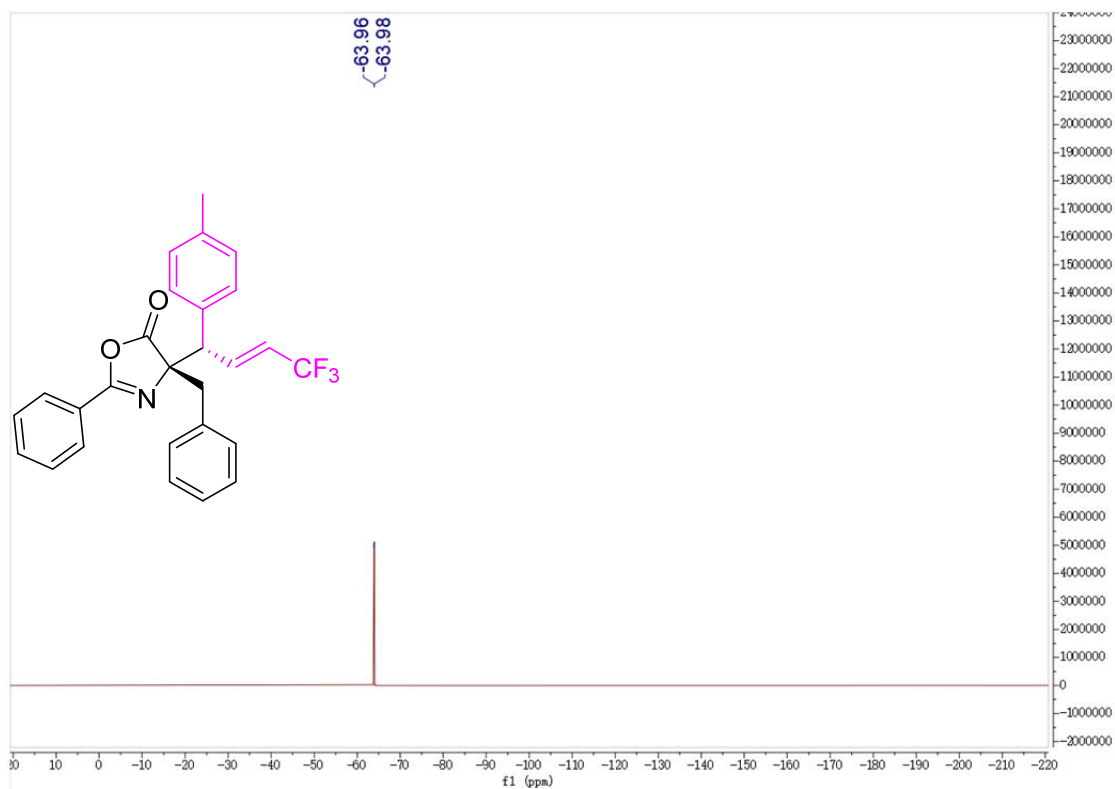
^1H NMR (400 MHz, CDCl_3) (**3a**)



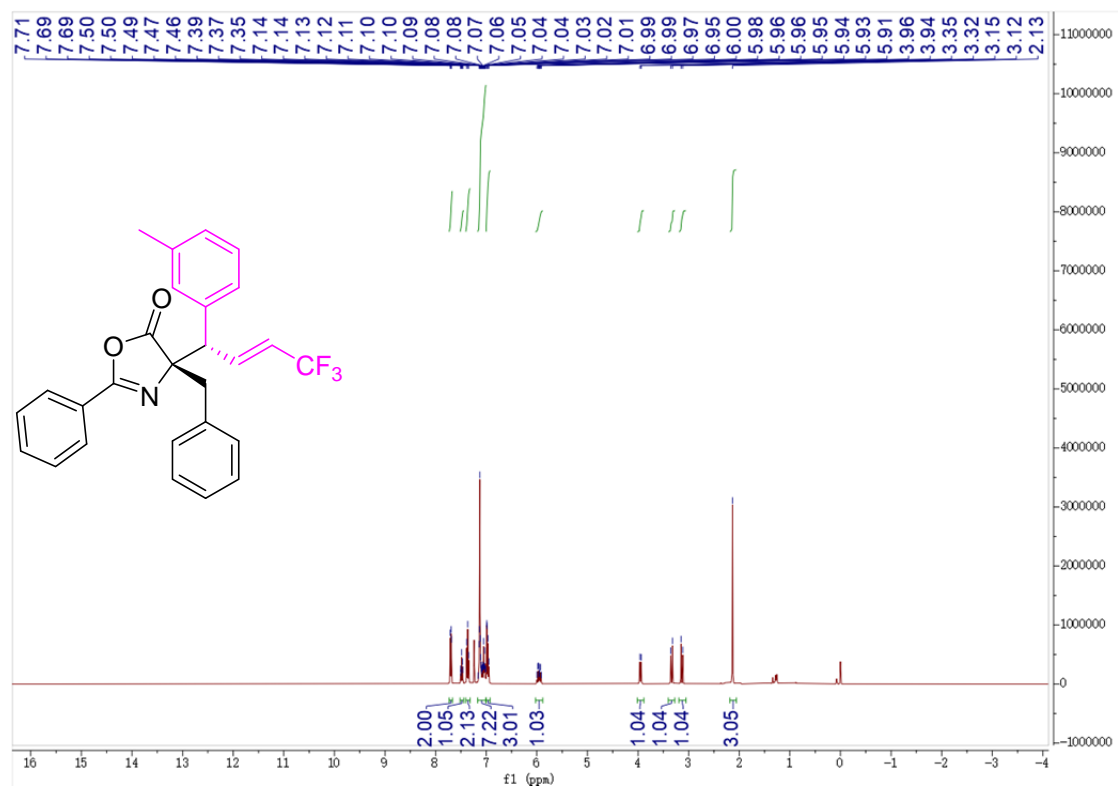
^{13}C NMR (101 MHz, CDCl_3) (**3a**)



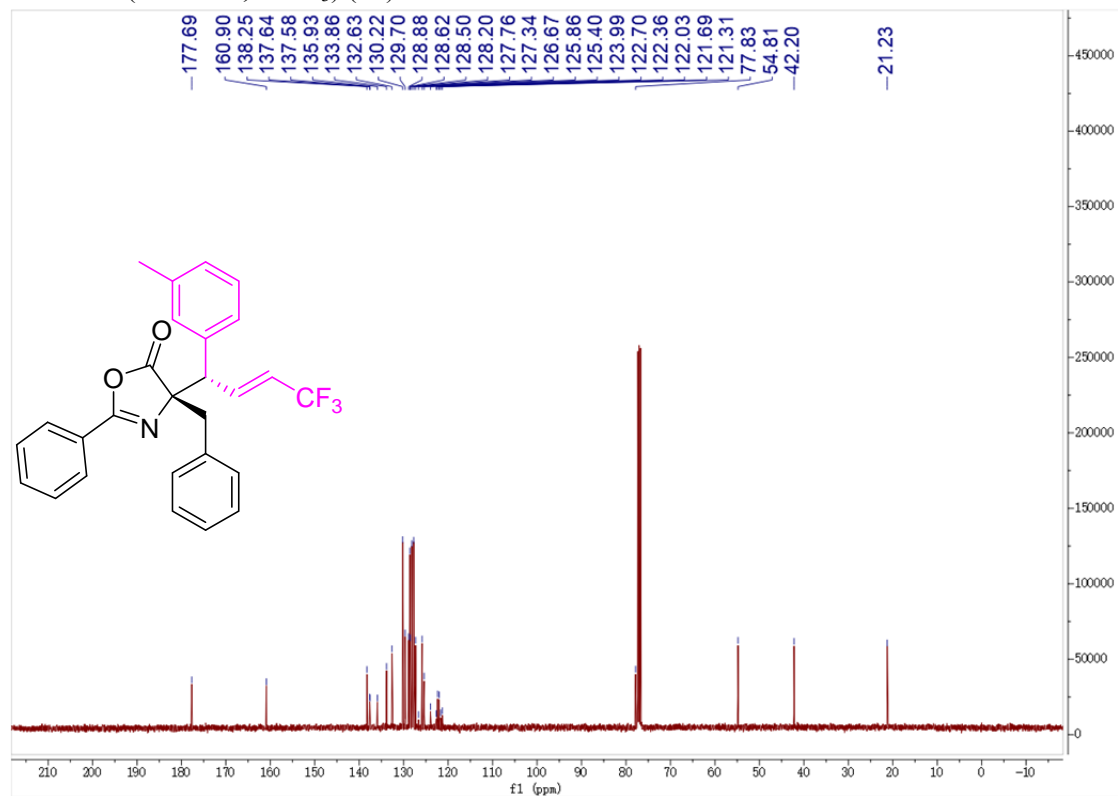
^{19}F NMR (376 MHz, CDCl_3) (**3a**)



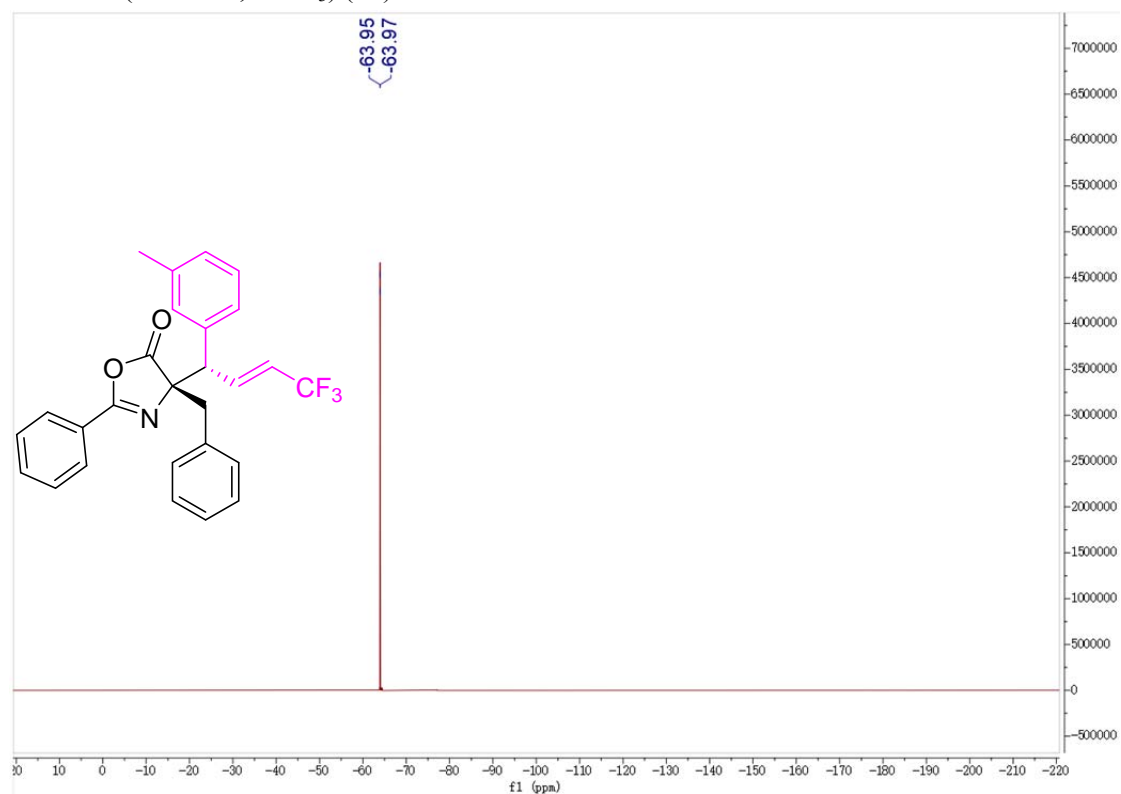
^1H NMR (400 MHz, CDCl_3) (**3b**)



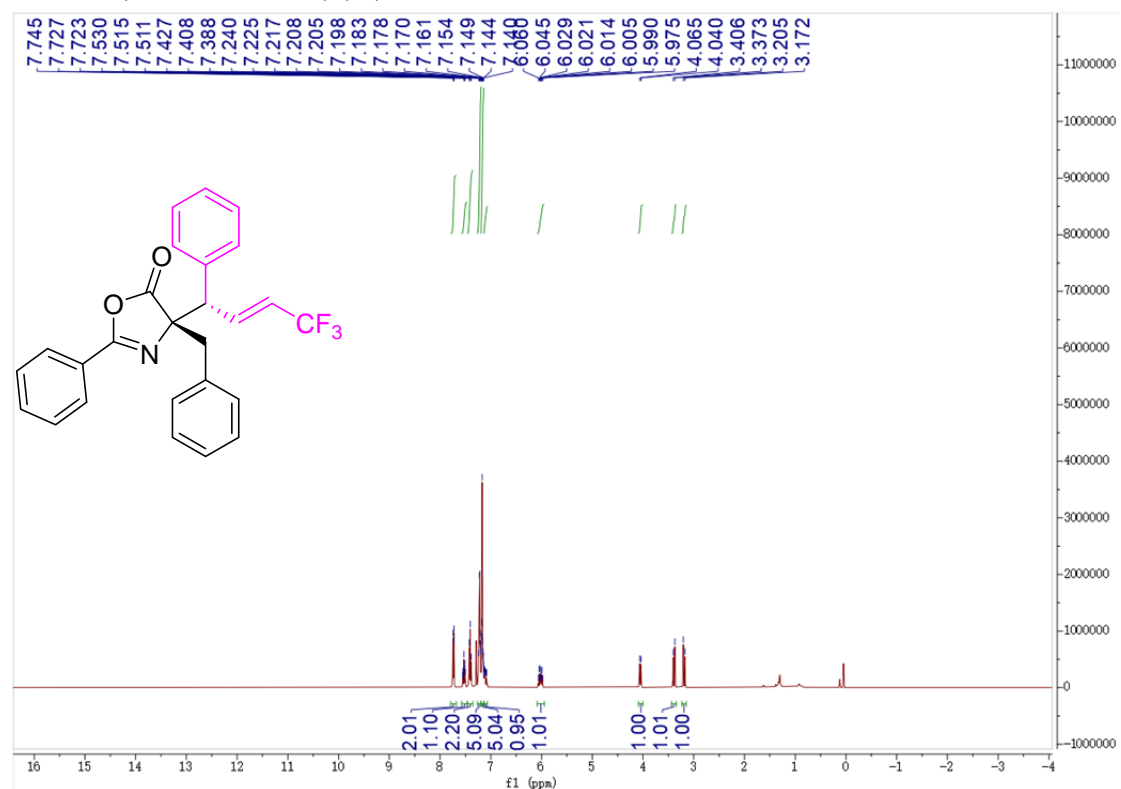
^{13}C NMR (101 MHz, CDCl_3) (**3b**)



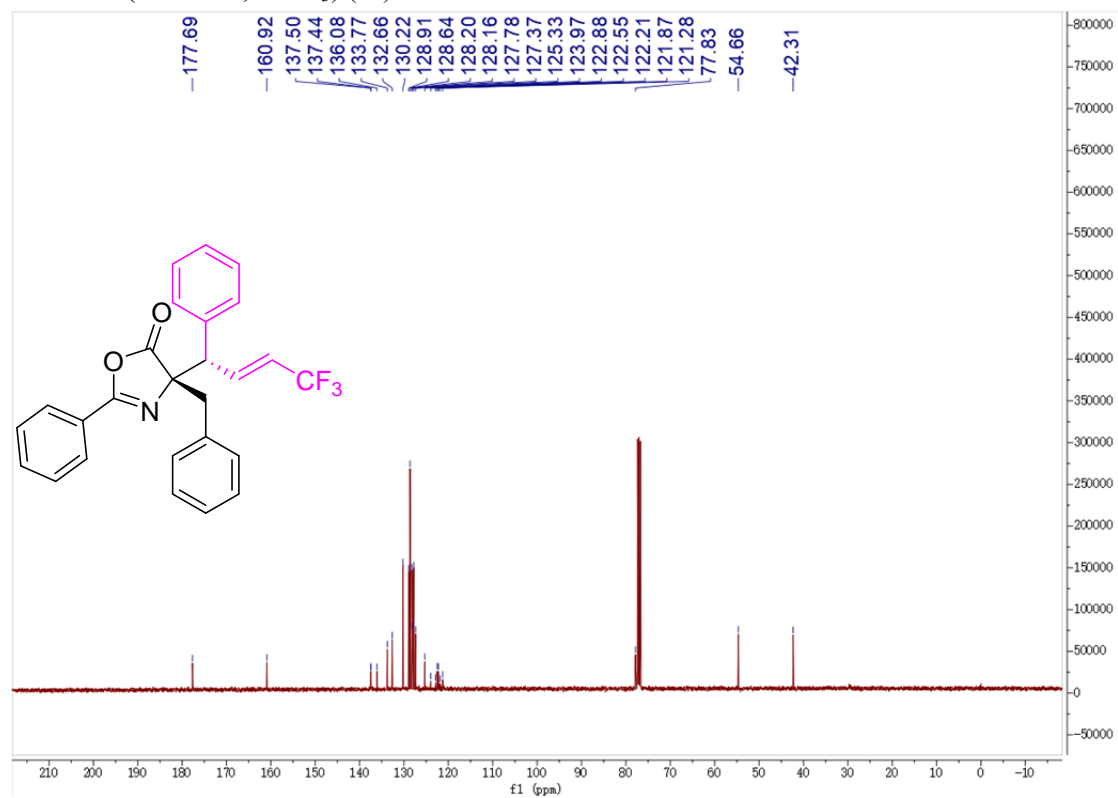
¹⁹F NMR (376 MHz, CDCl₃) (**3b**)



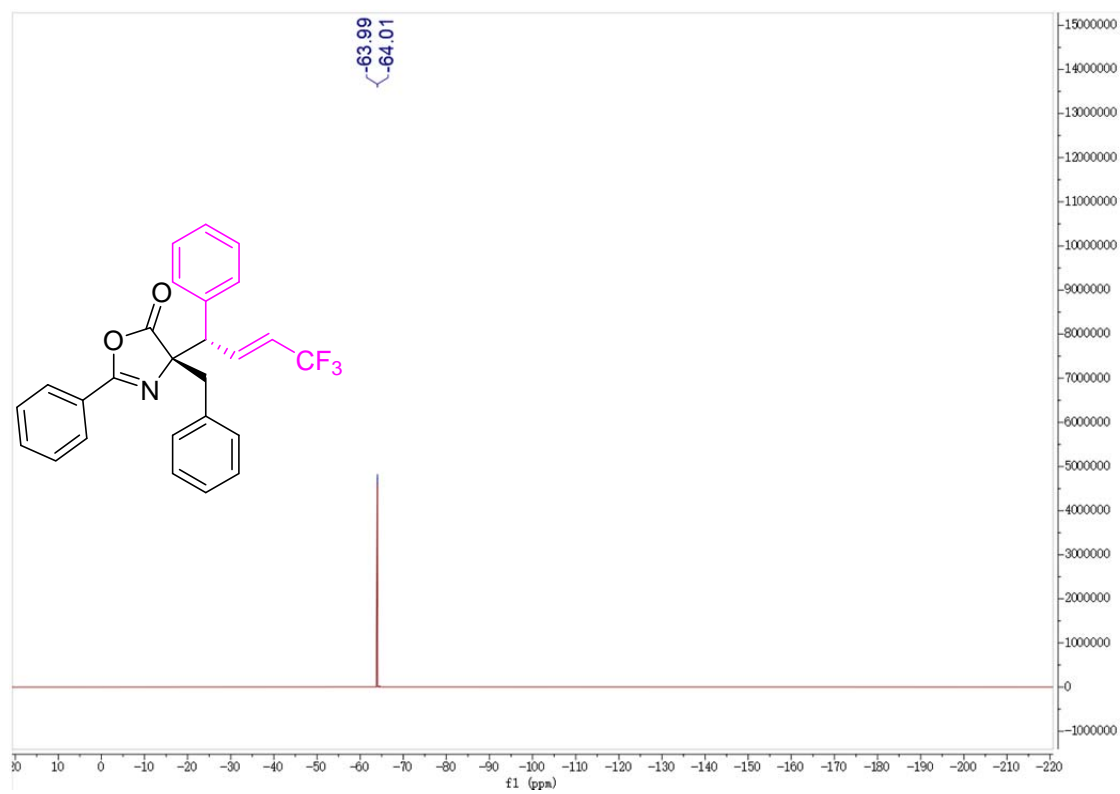
¹H NMR (400 MHz, CDCl₃) (**3c**)



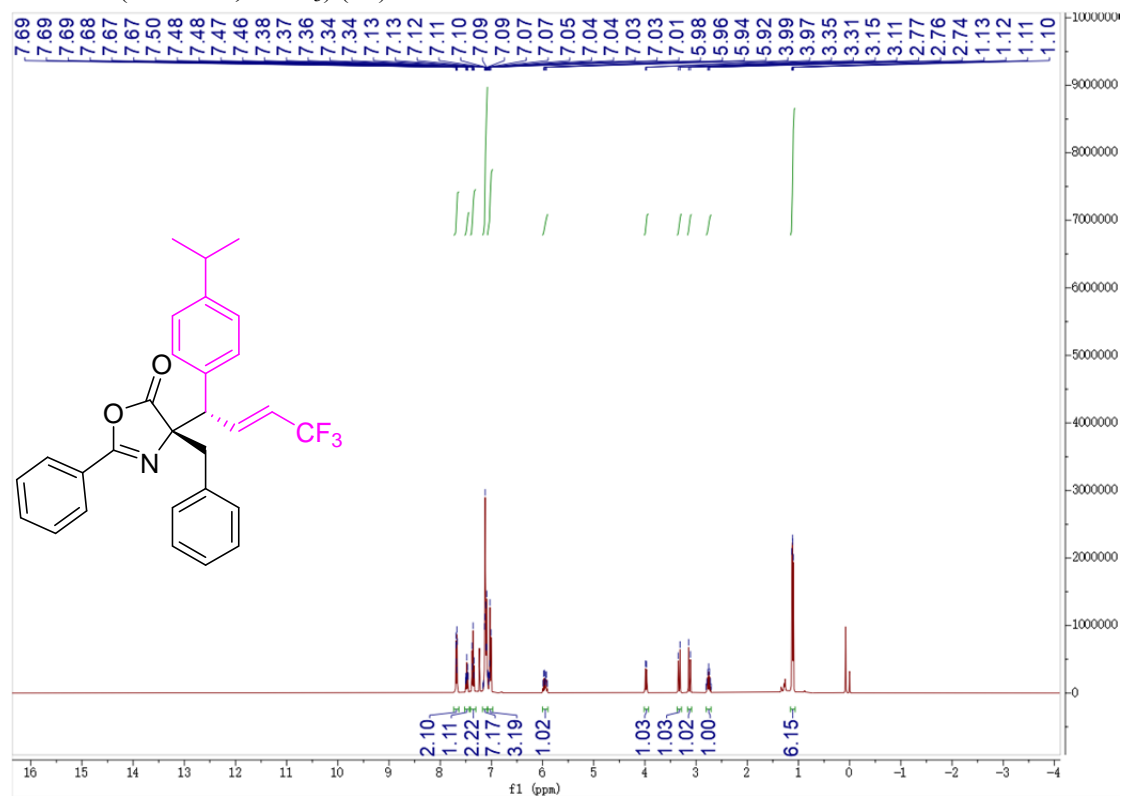
^{13}C NMR (101 MHz, CDCl_3) (**3c**)



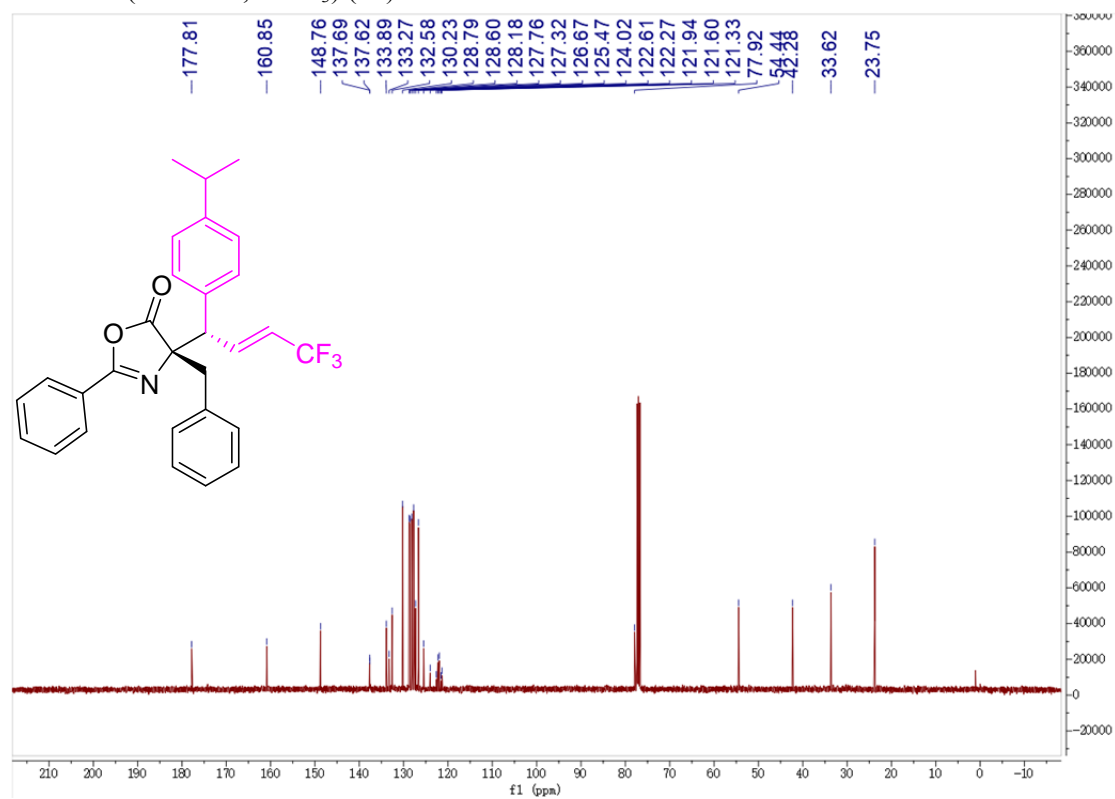
^{19}F NMR (376 MHz, CDCl_3) (**3c**)



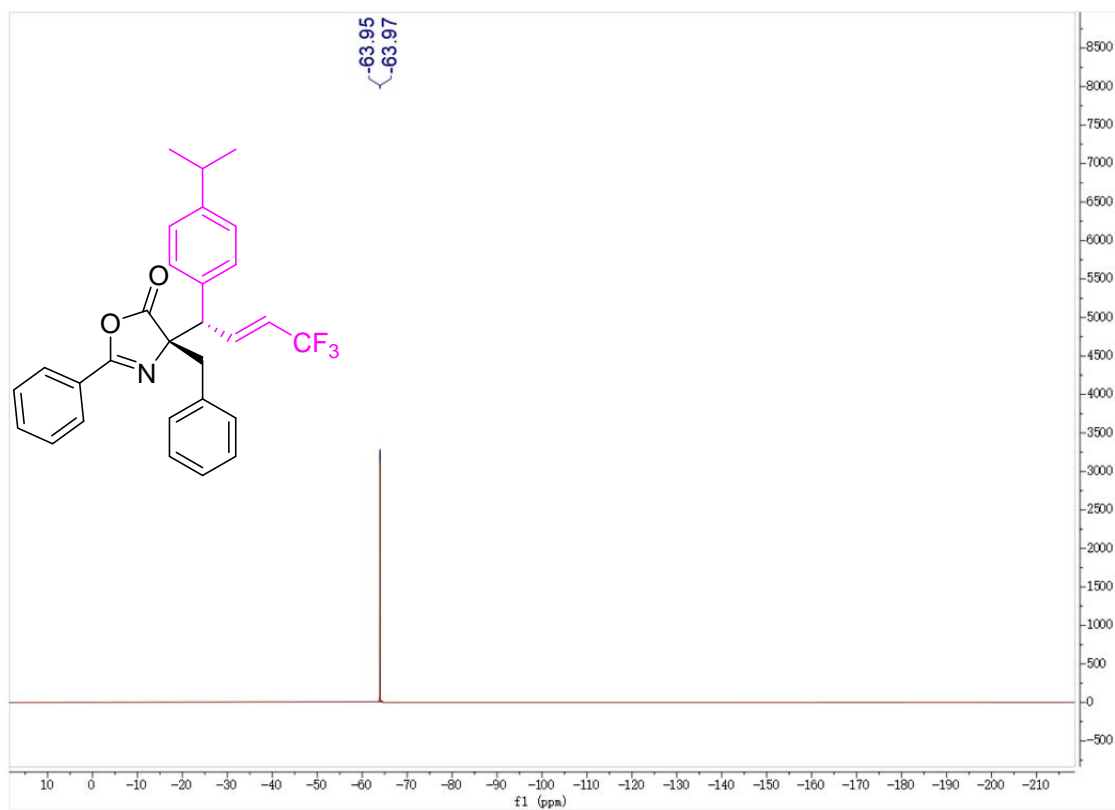
¹H NMR (400 MHz, CDCl₃) (3d)



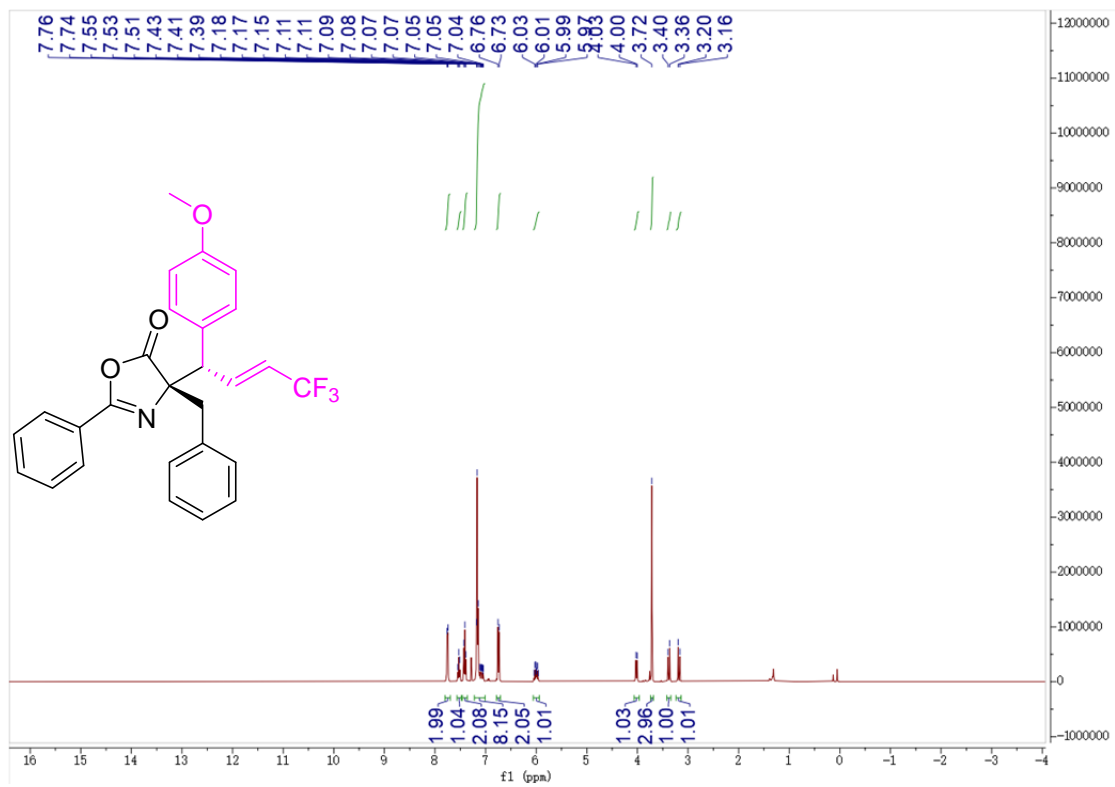
¹³C NMR (101 MHz, CDCl₃) (3d)



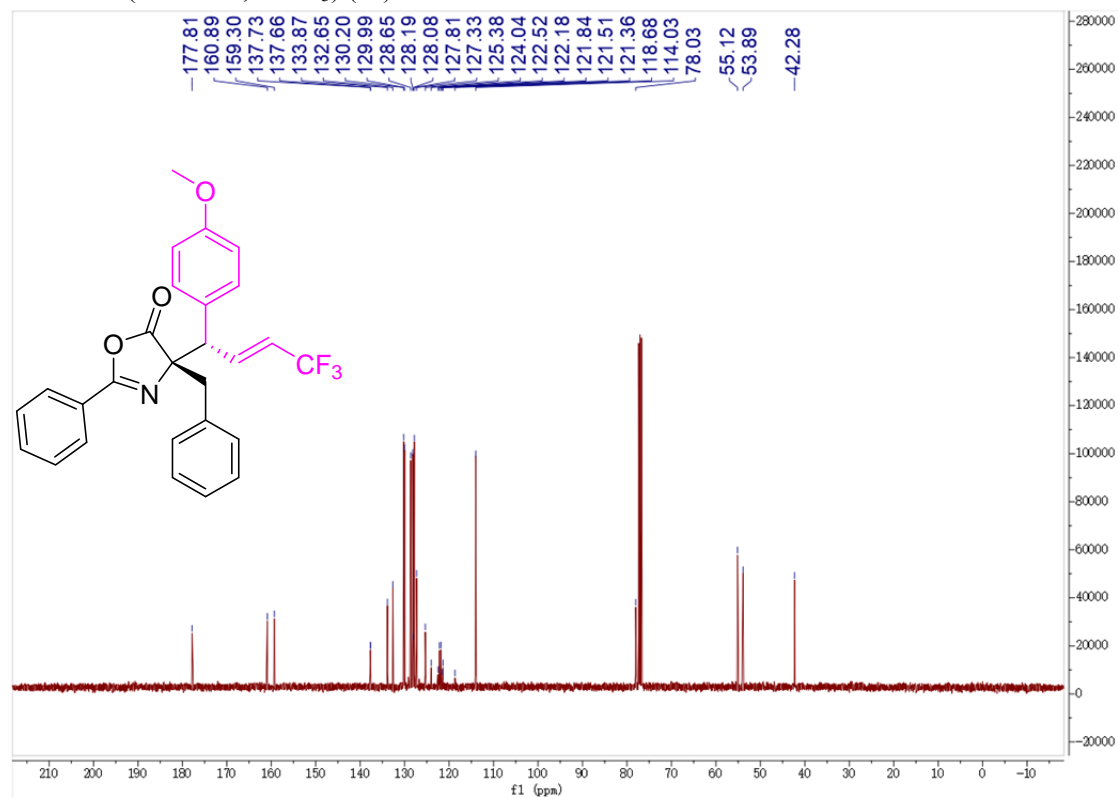
^{19}F NMR (377 MHz, CDCl_3) (**3d**)



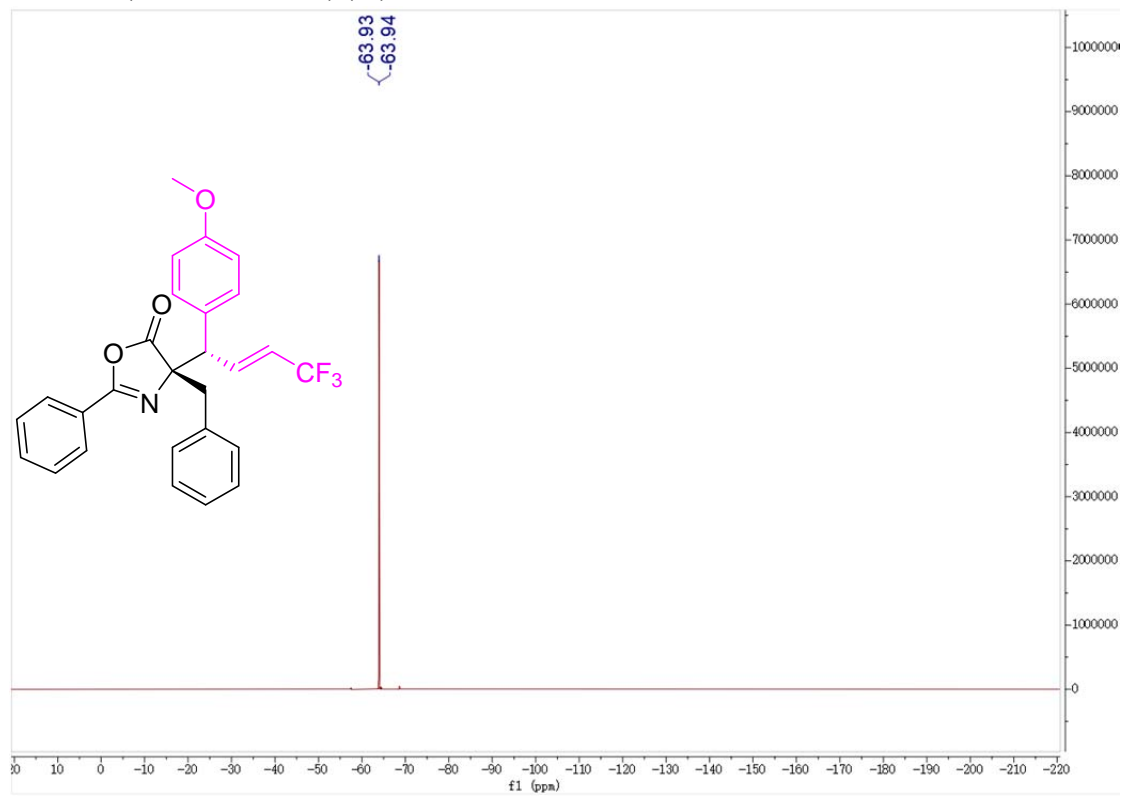
^1H NMR (400 MHz, CDCl_3) (**3e**)



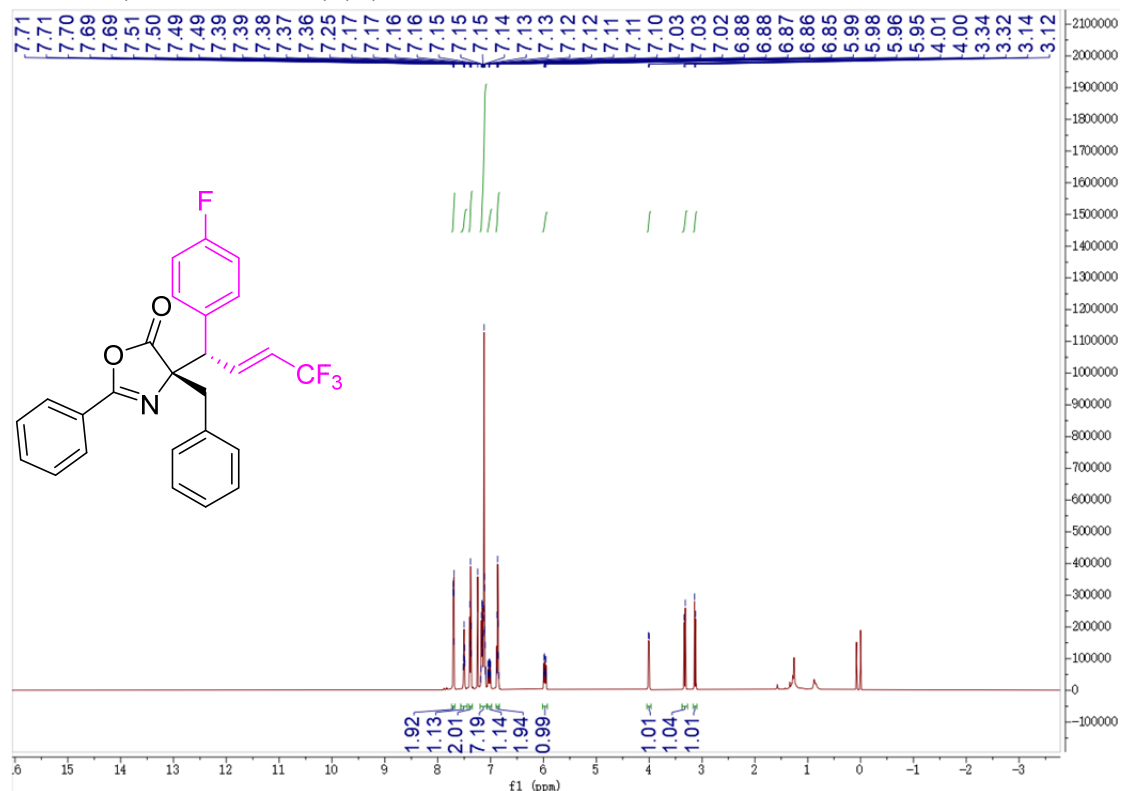
^{13}C NMR (101 MHz, CDCl_3) (**3e**)



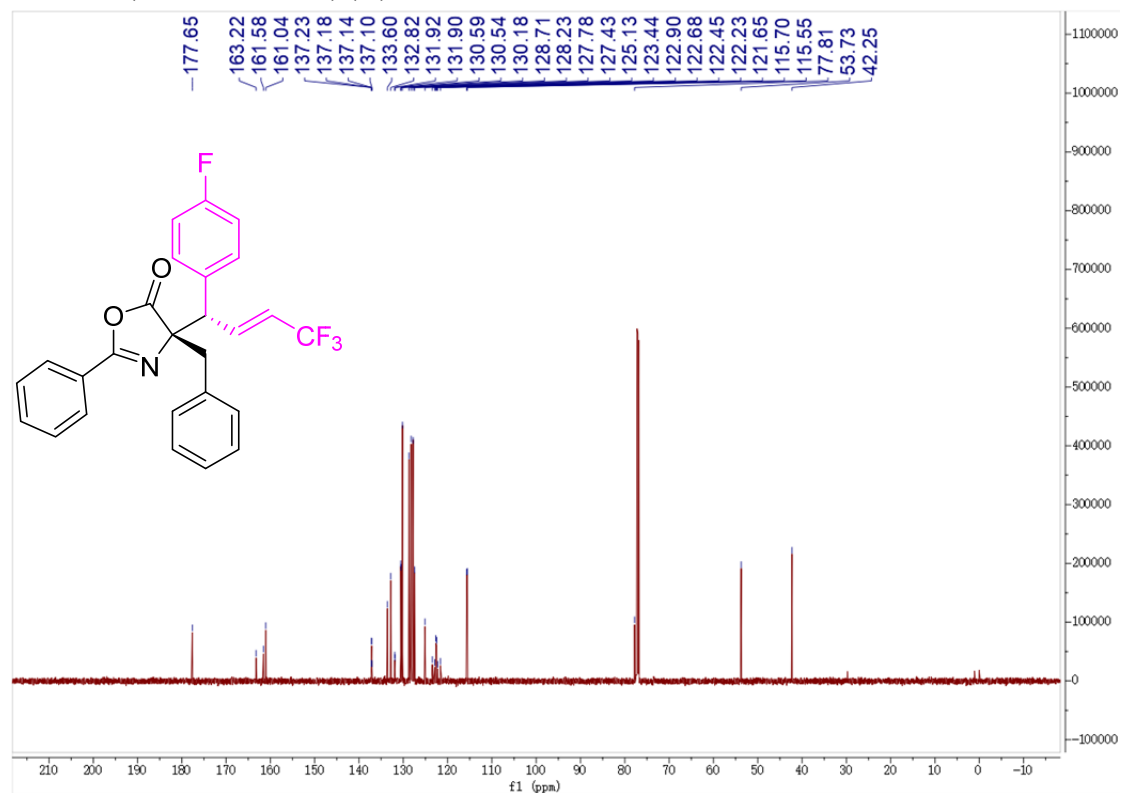
^{19}F NMR (376 MHz, CDCl_3) (**3e**)



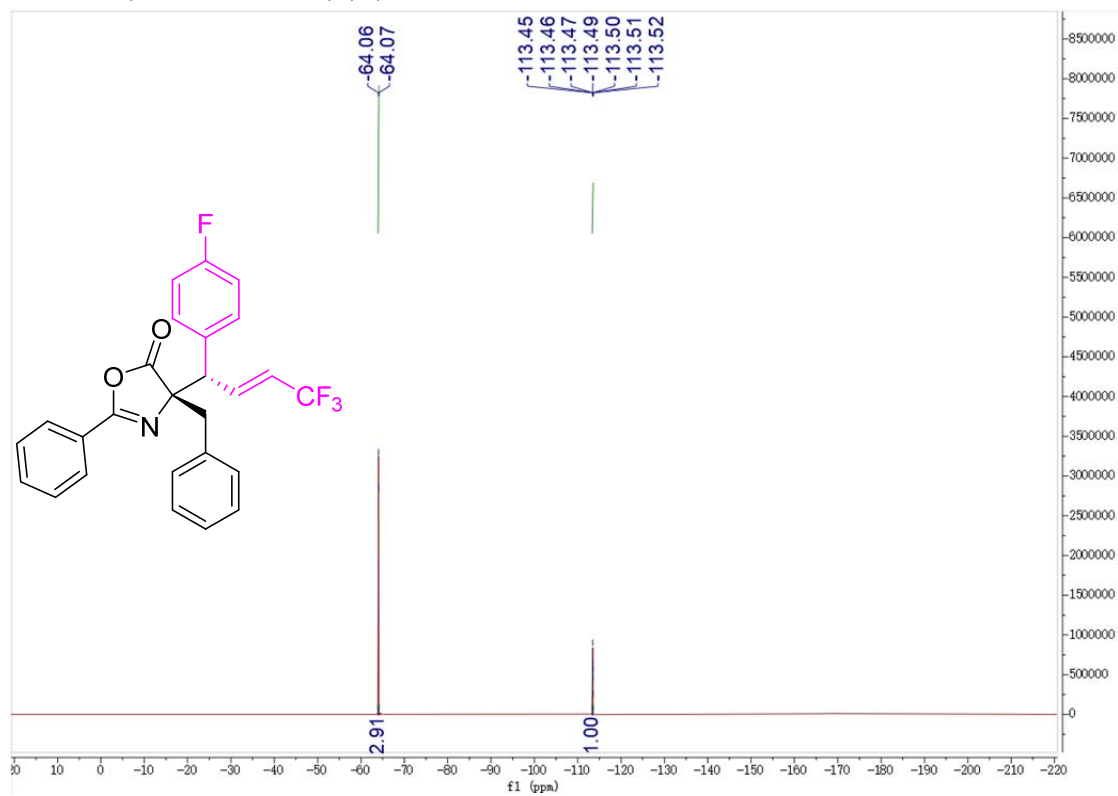
¹H NMR (600 MHz, CDCl₃) (3f)



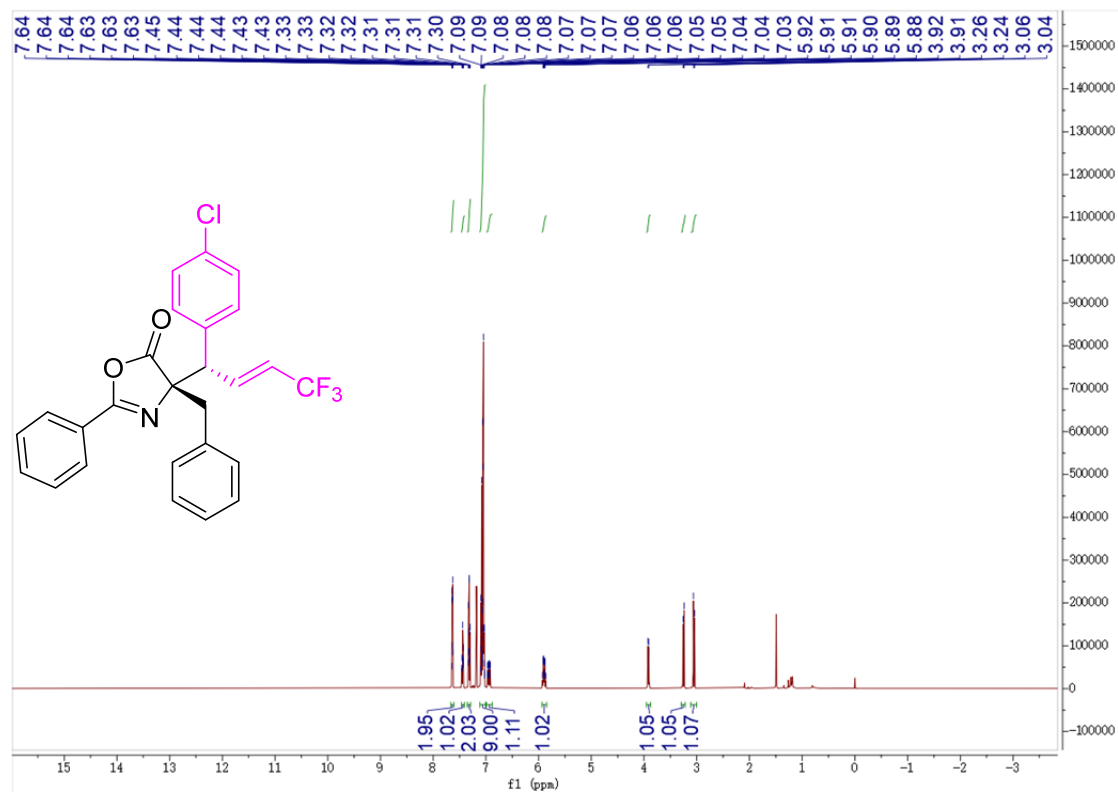
¹³C NMR (151 MHz, CDCl₃) (3f)



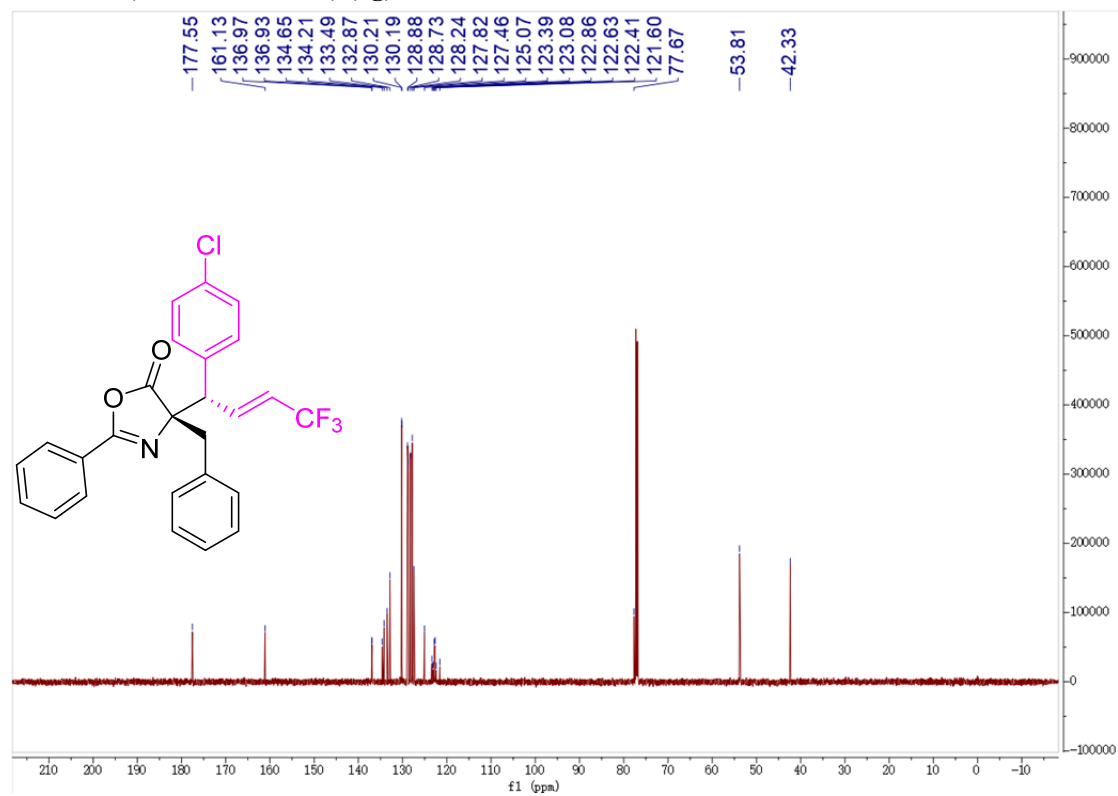
^{19}F NMR (376 MHz, CDCl_3) (**3f**)



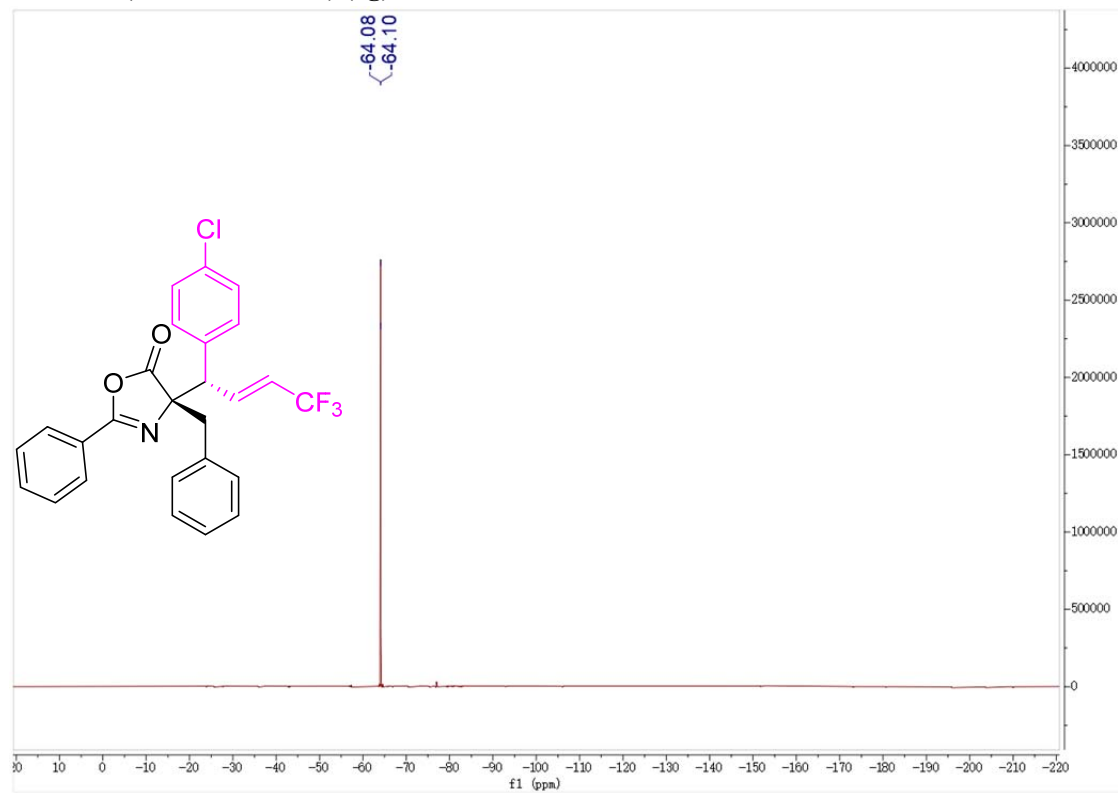
^1H NMR (600 MHz, CDCl_3) (**3g**)



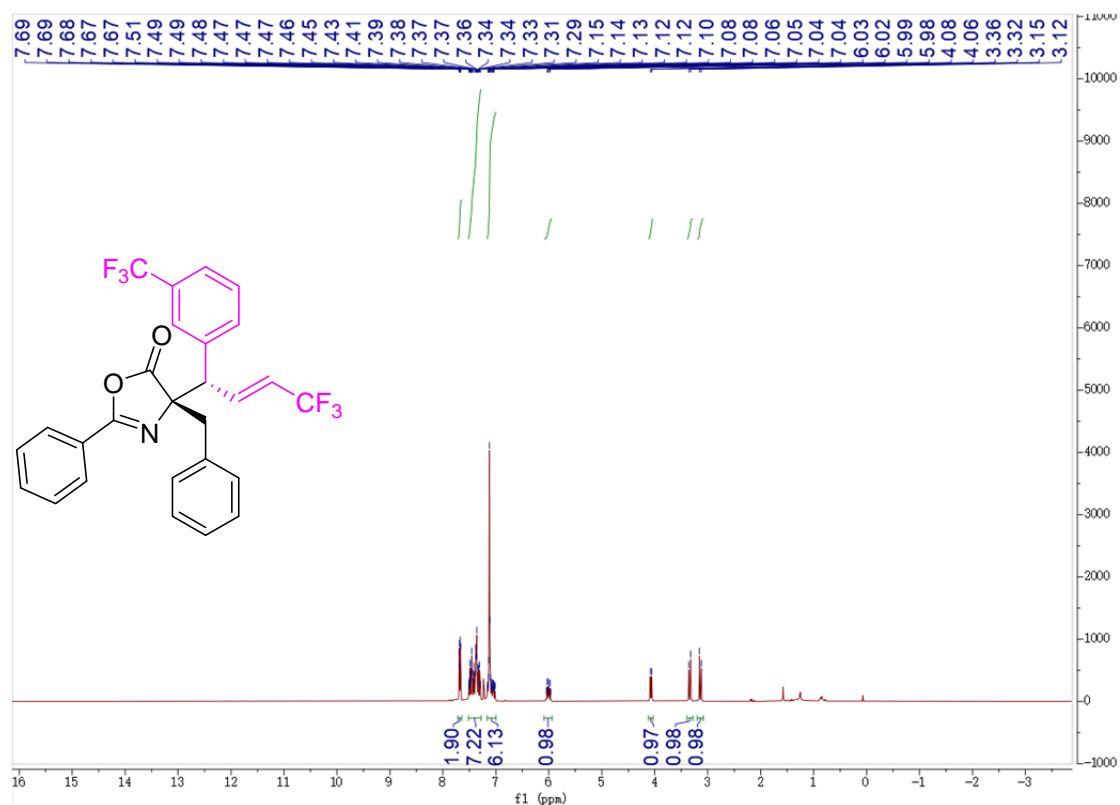
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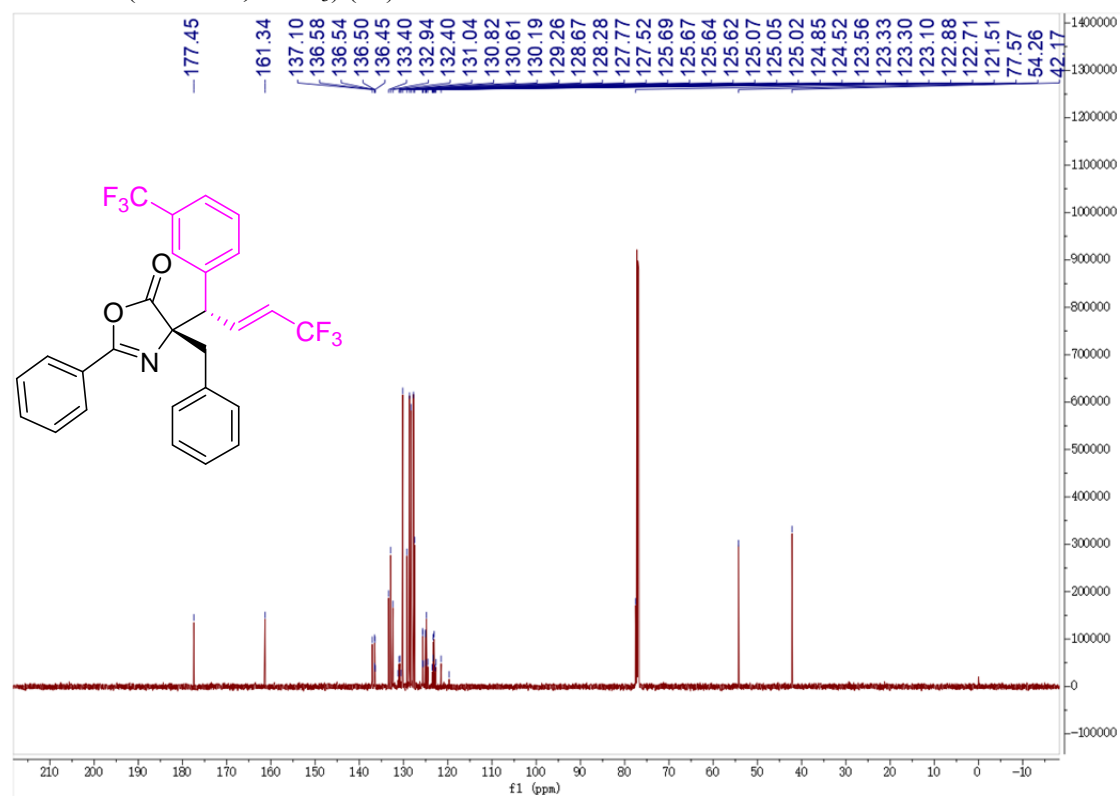
^{19}F NMR (376 MHz, CDCl_3) (**3g**)



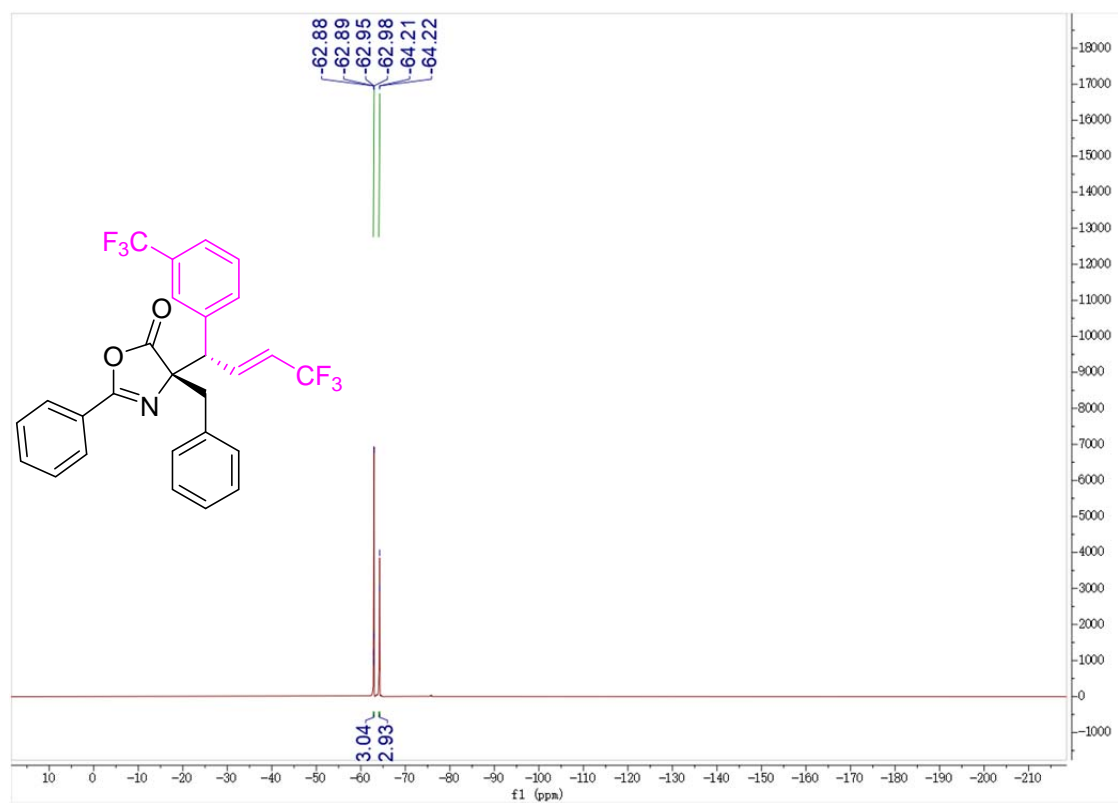
¹H NMR (400 MHz, CDCl₃) (3h)



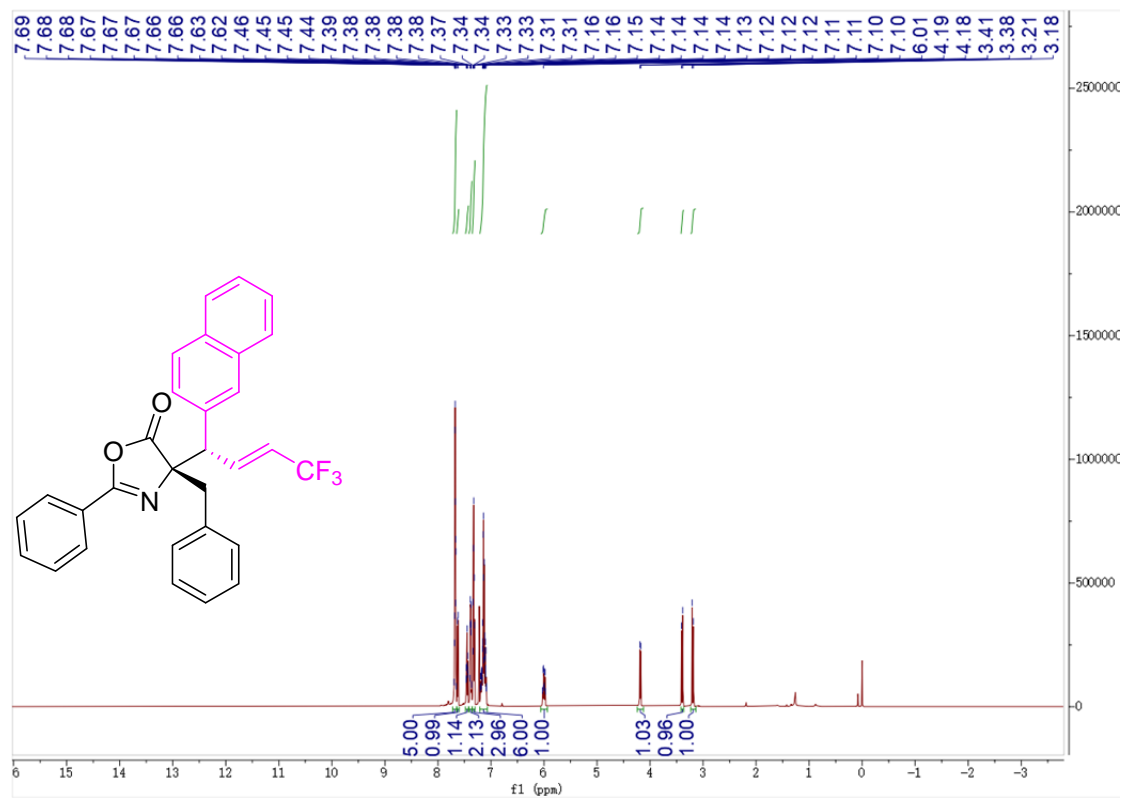
¹³C NMR (151 MHz, CDCl₃) (3h)



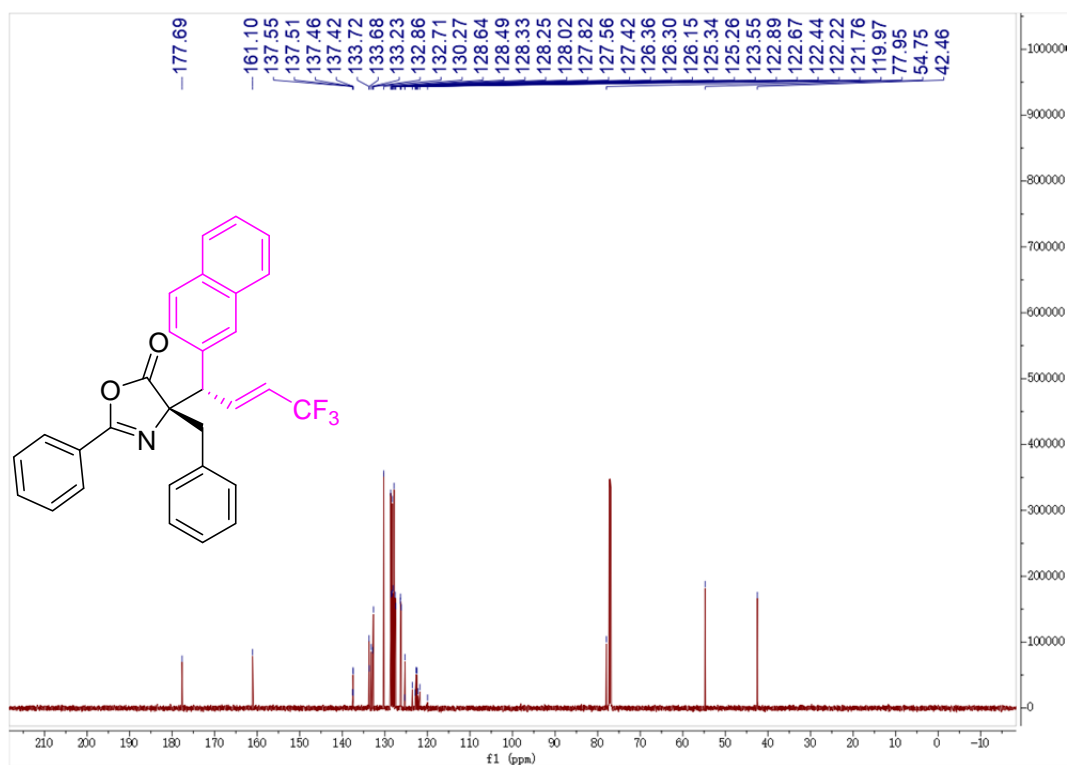
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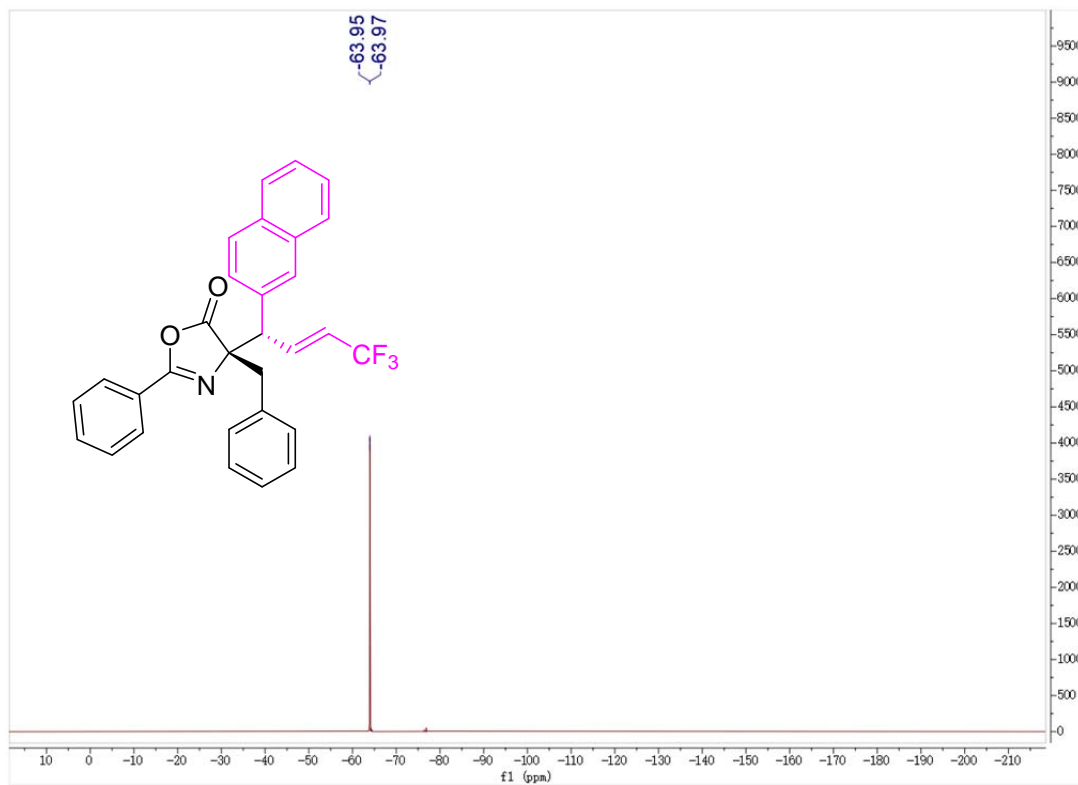
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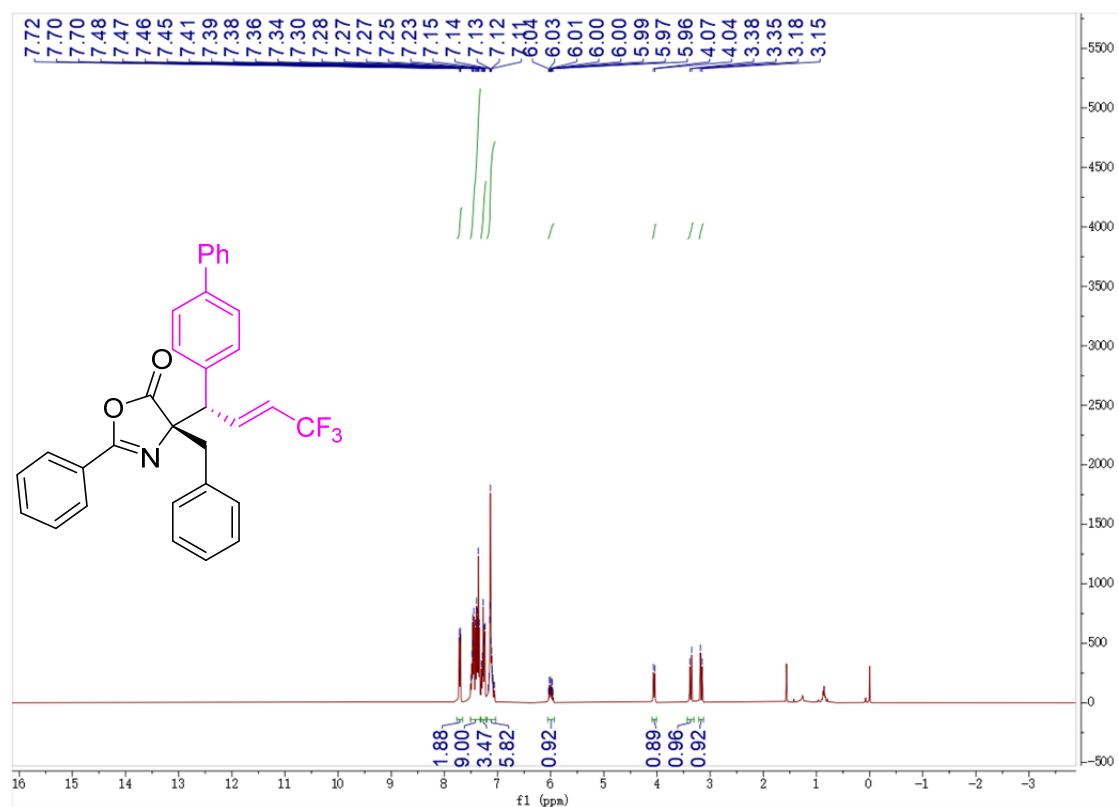
^{13}C NMR (151 MHz, CDCl_3) (**3i**)



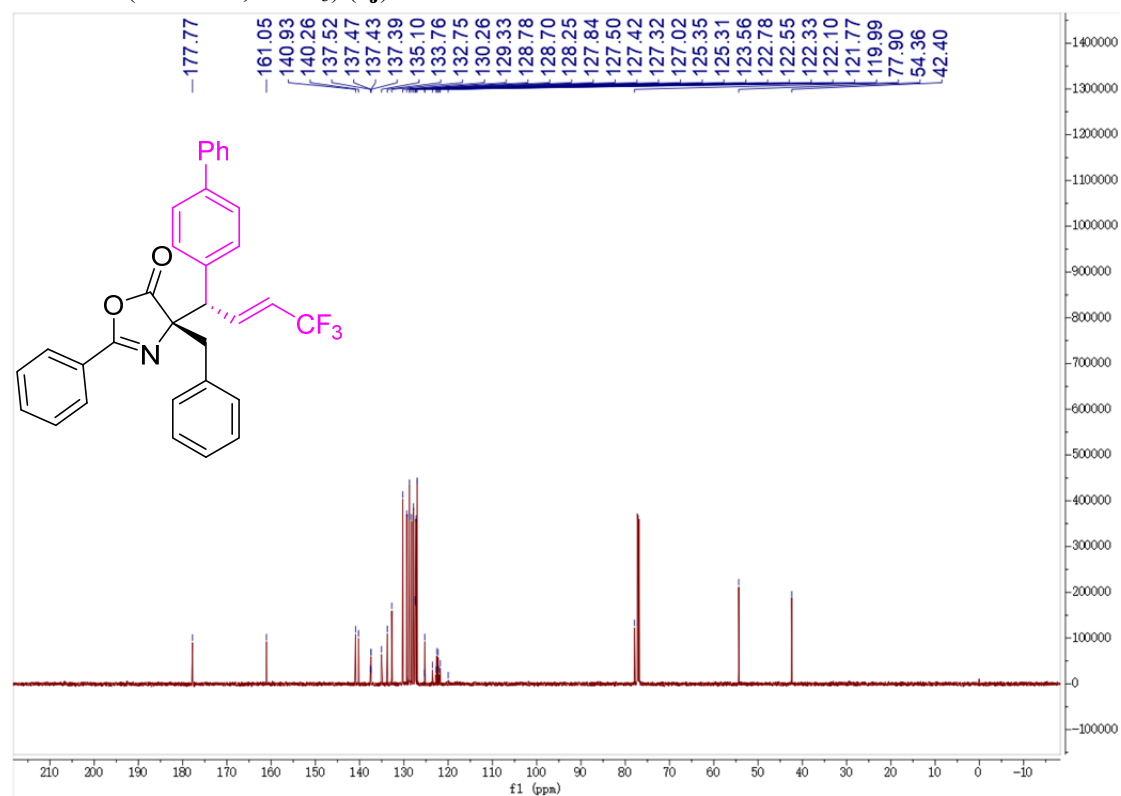
^{19}F NMR (377 MHz, CDCl_3) (**3i**)



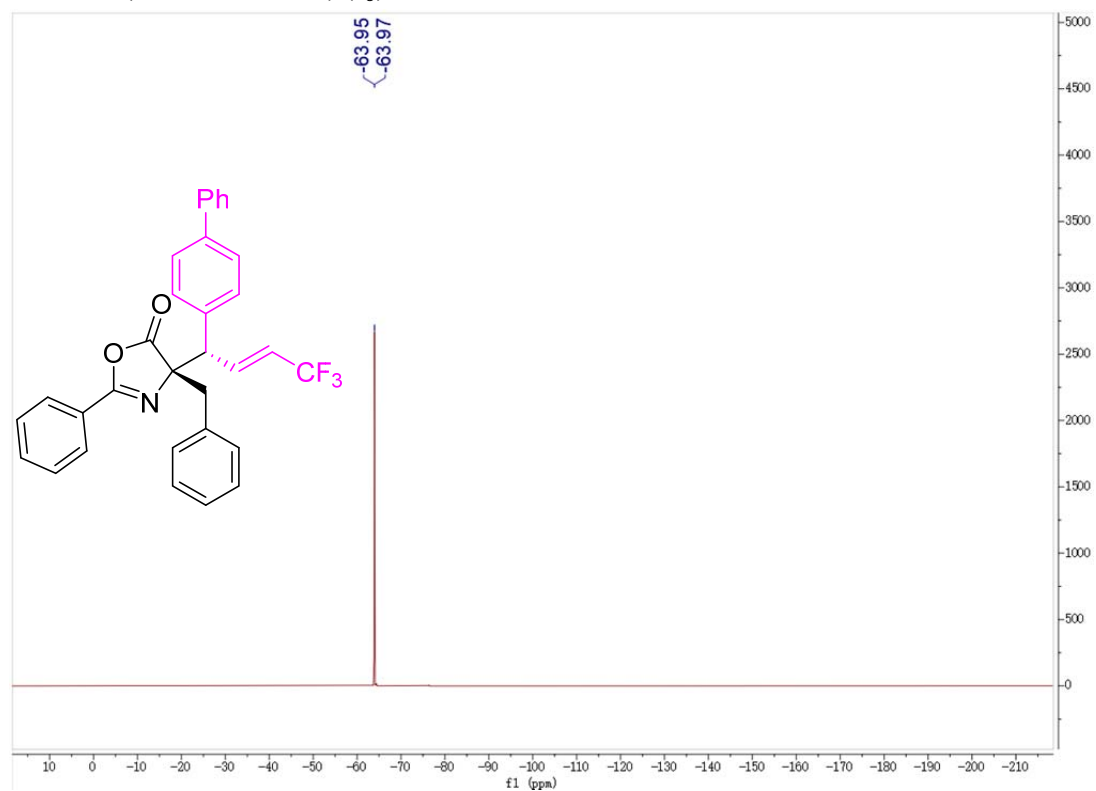
¹H NMR (400 MHz, CDCl₃) (**3j**)



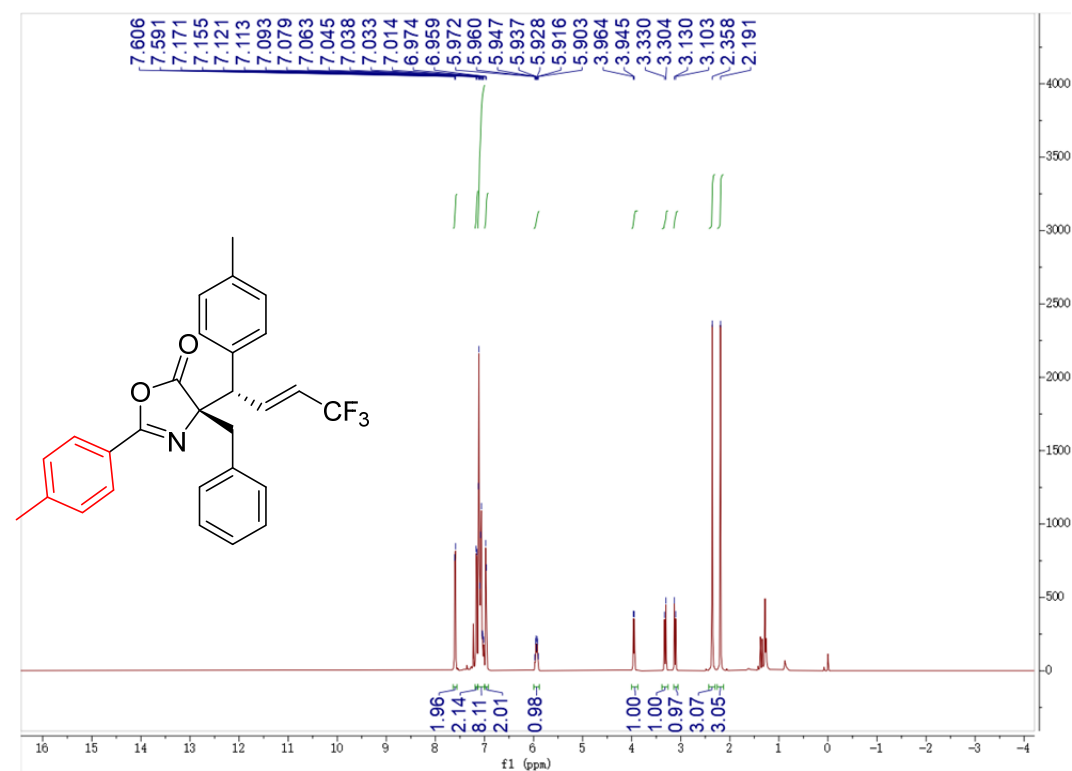
¹³C NMR (151 MHz, CDCl₃) (**3j**)



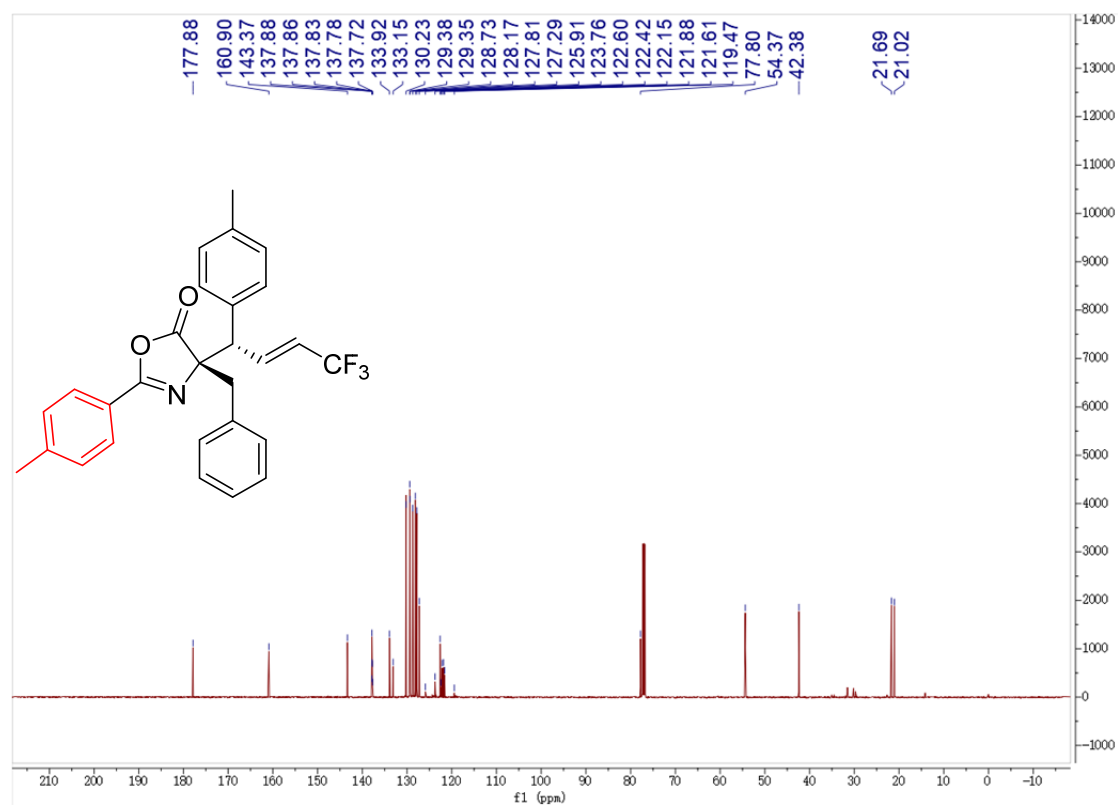
^{19}F NMR (377 MHz, CDCl_3) (**3j**)



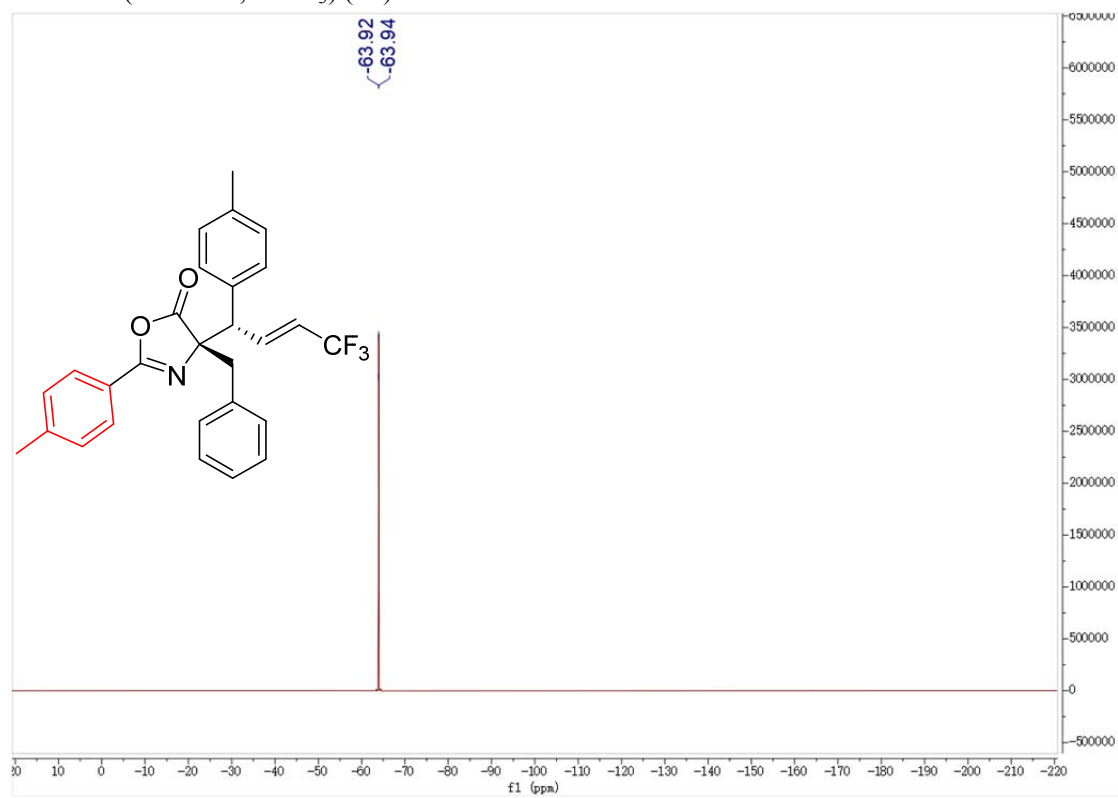
^1H NMR (500 MHz, CDCl_3) (**3k**)



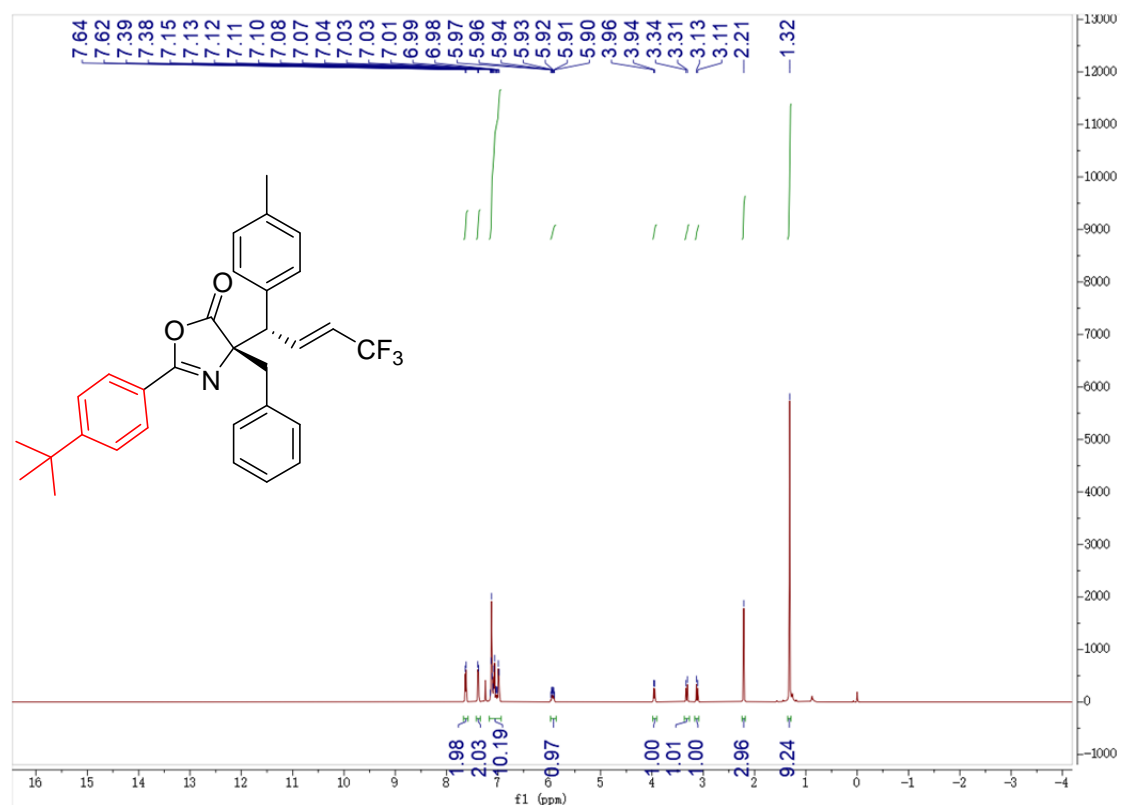
^{13}C NMR (126 MHz, CDCl_3) (**3k**)



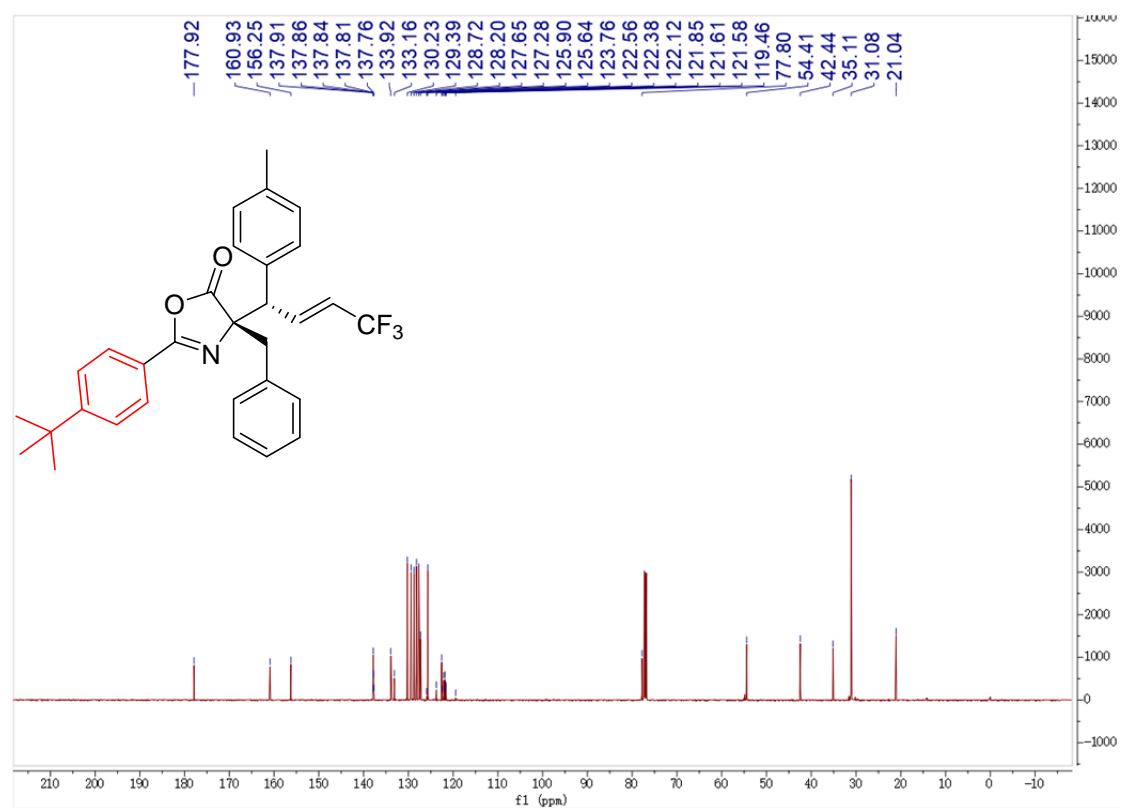
^{19}F NMR (376 MHz, CDCl_3) (**3k**)



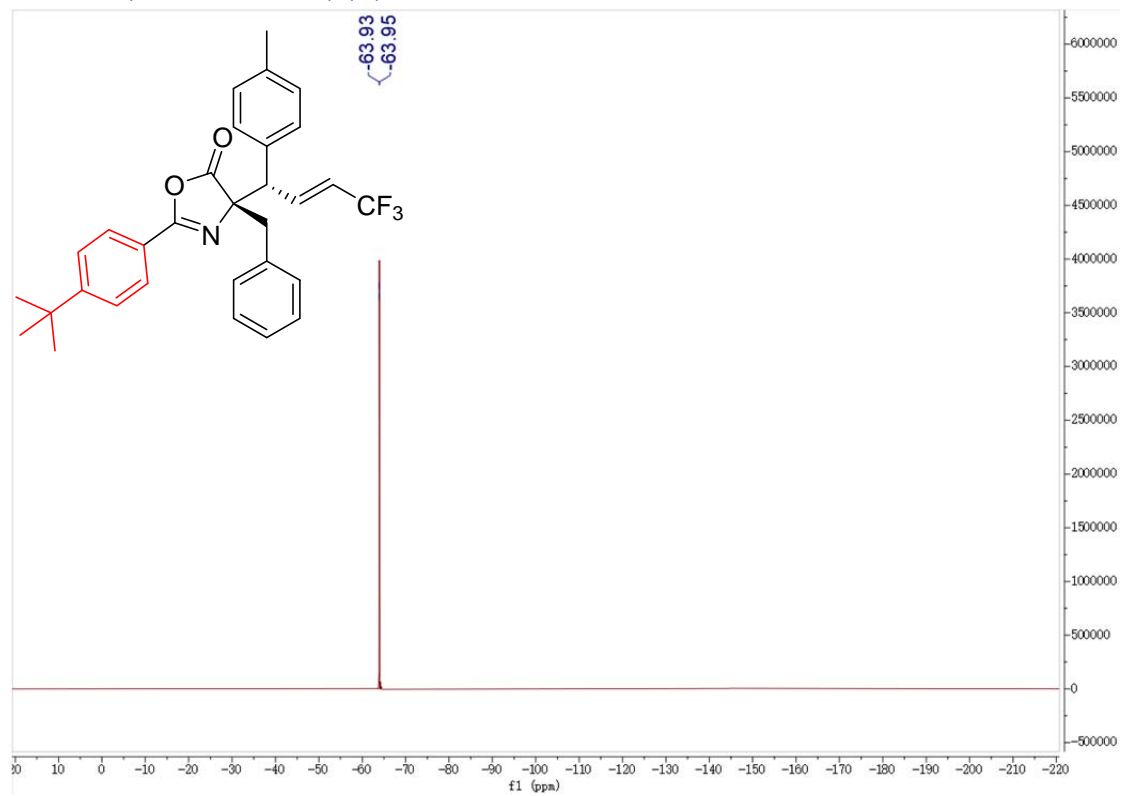
¹H NMR (500 MHz, CDCl₃) (31)



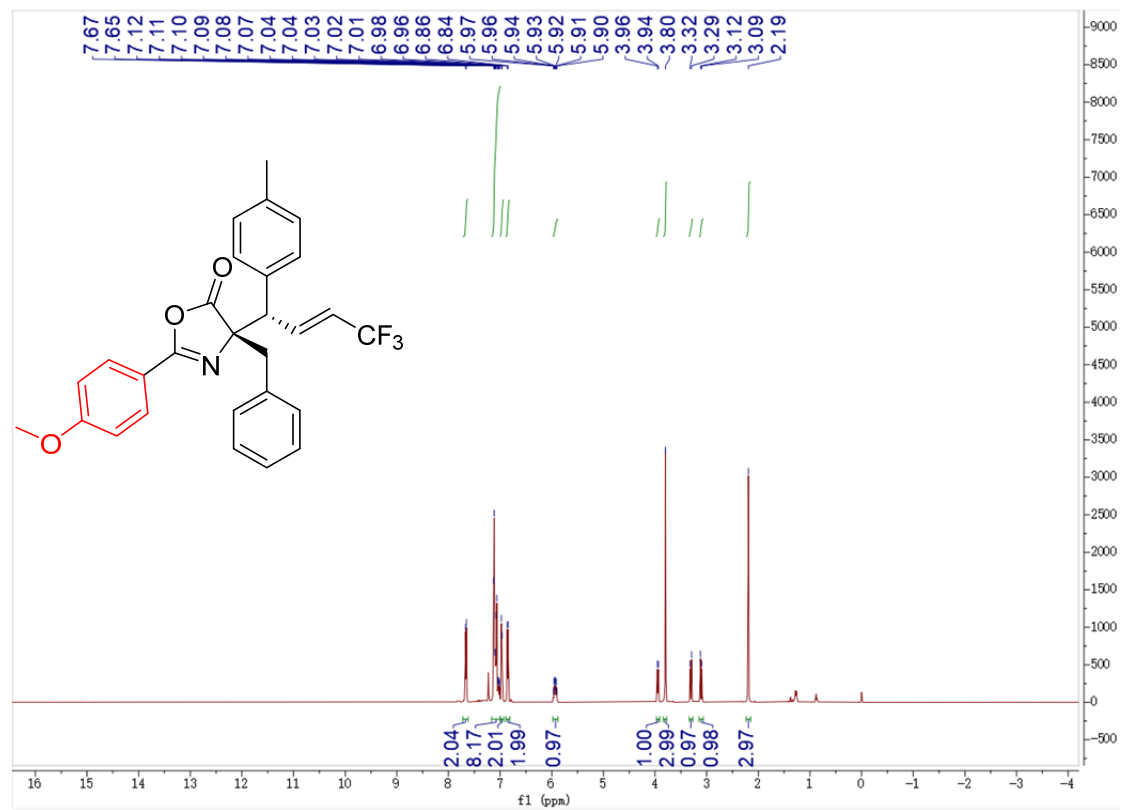
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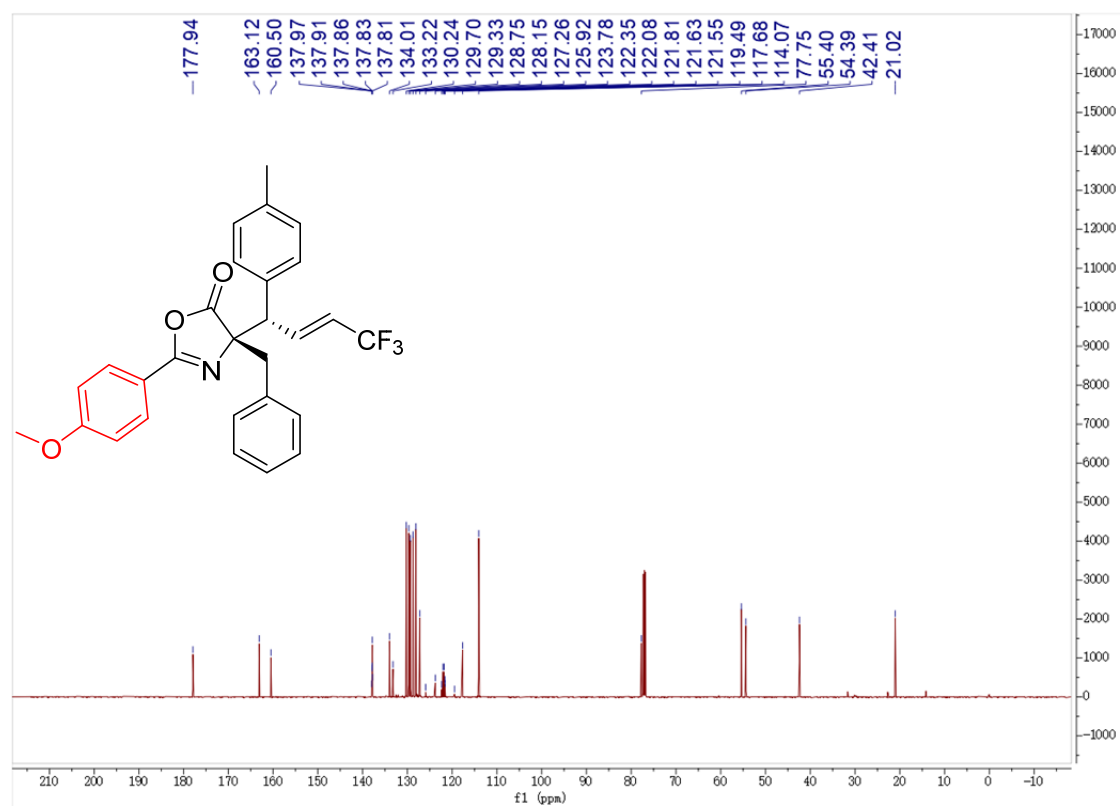
^{19}F NMR (376 MHz, CDCl_3) (**3l**)



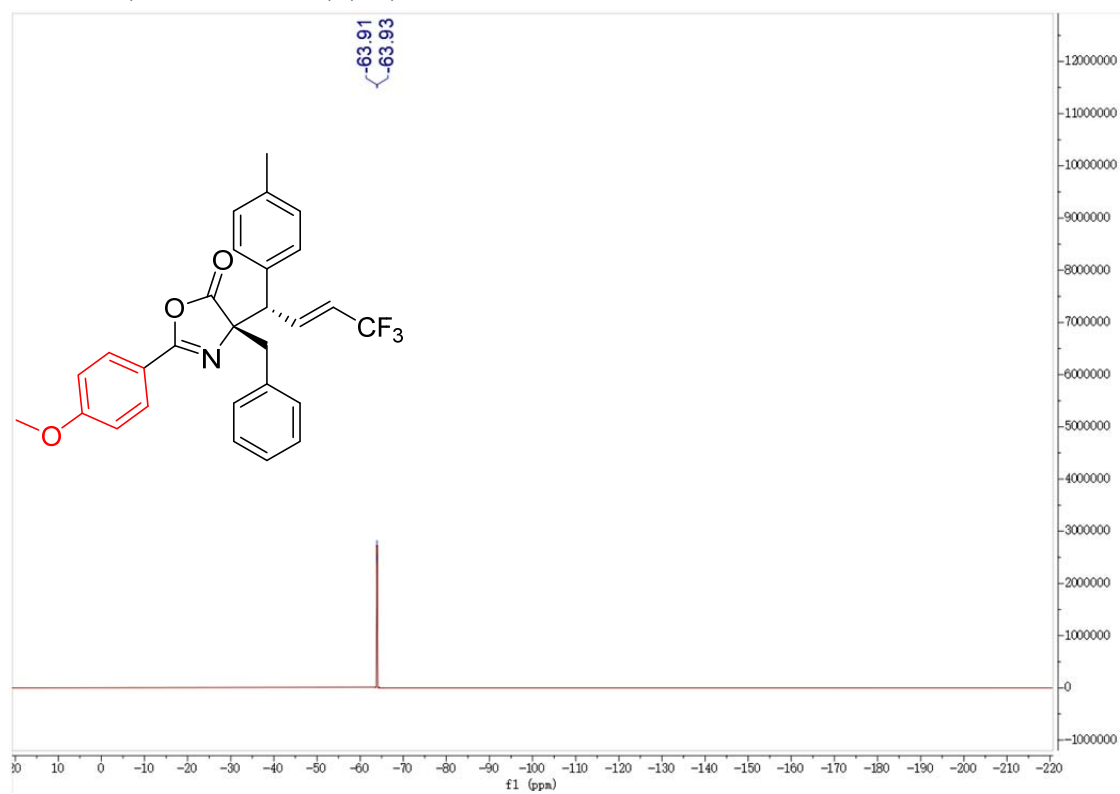
^1H NMR (500 MHz, CDCl_3) (**3m**)



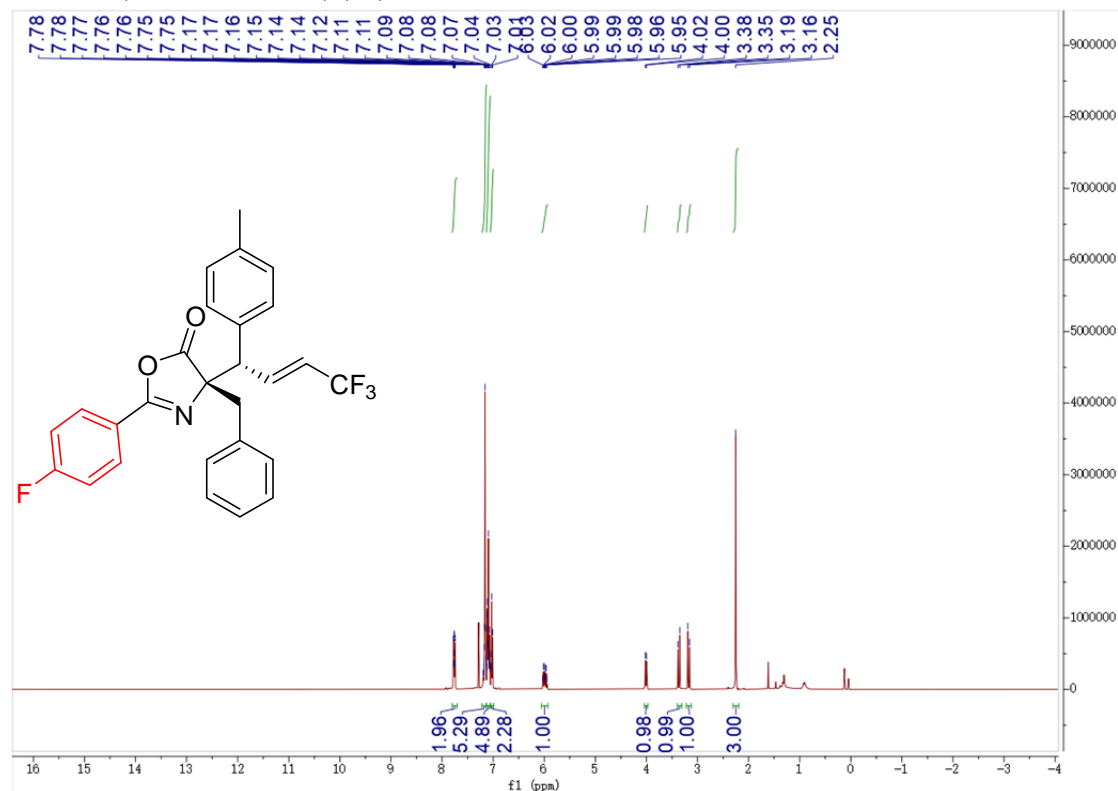
^{13}C NMR (126 MHz, CDCl_3) (**3m**)



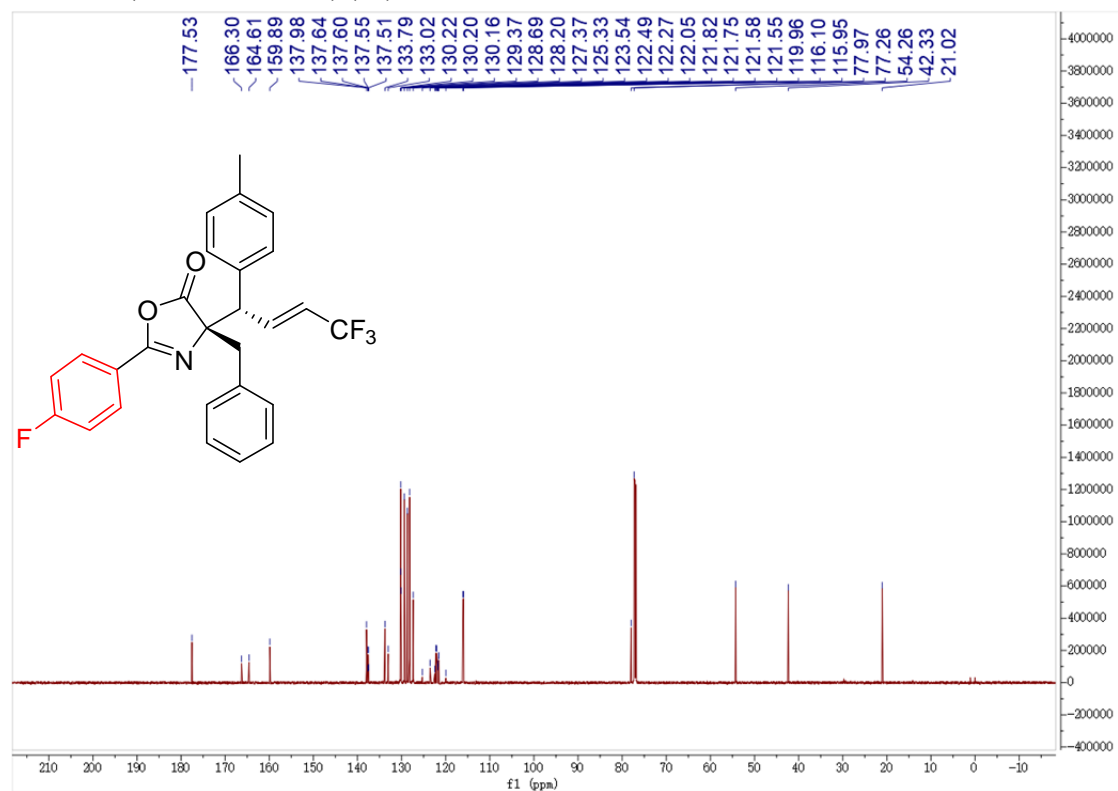
^{19}F NMR (376 MHz, CDCl_3) (**3m**)



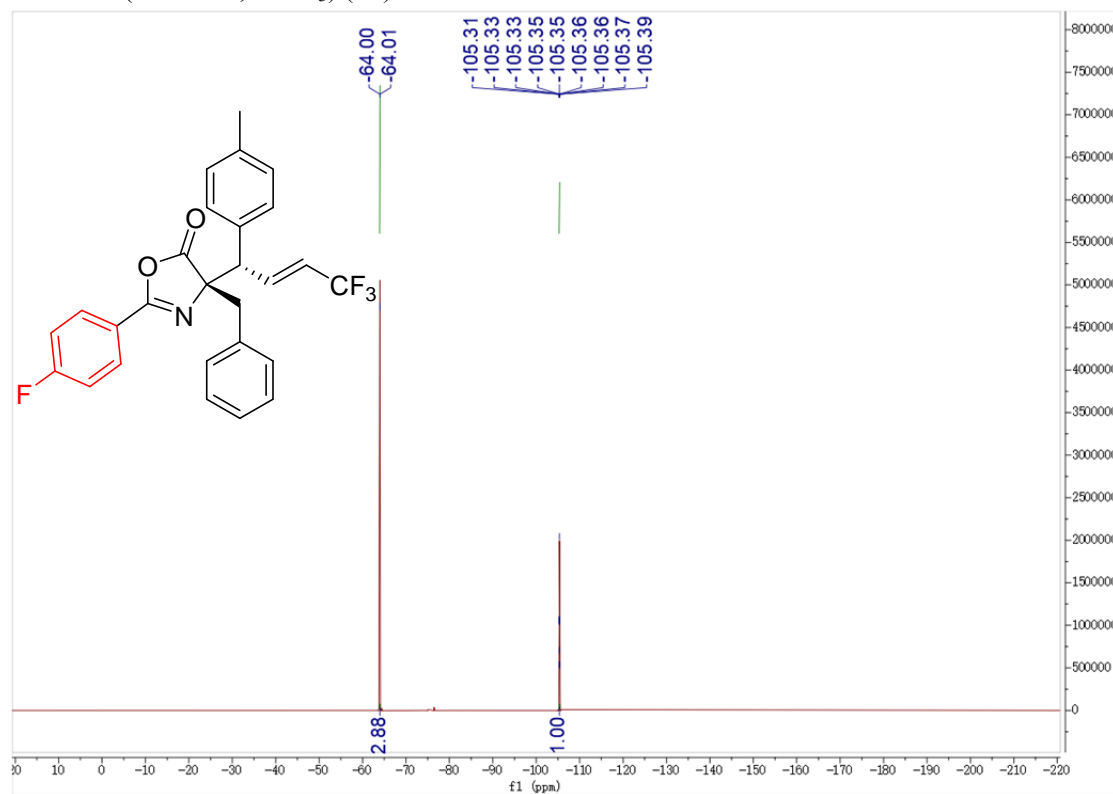
¹H NMR (400 MHz, CDCl₃) (3n)



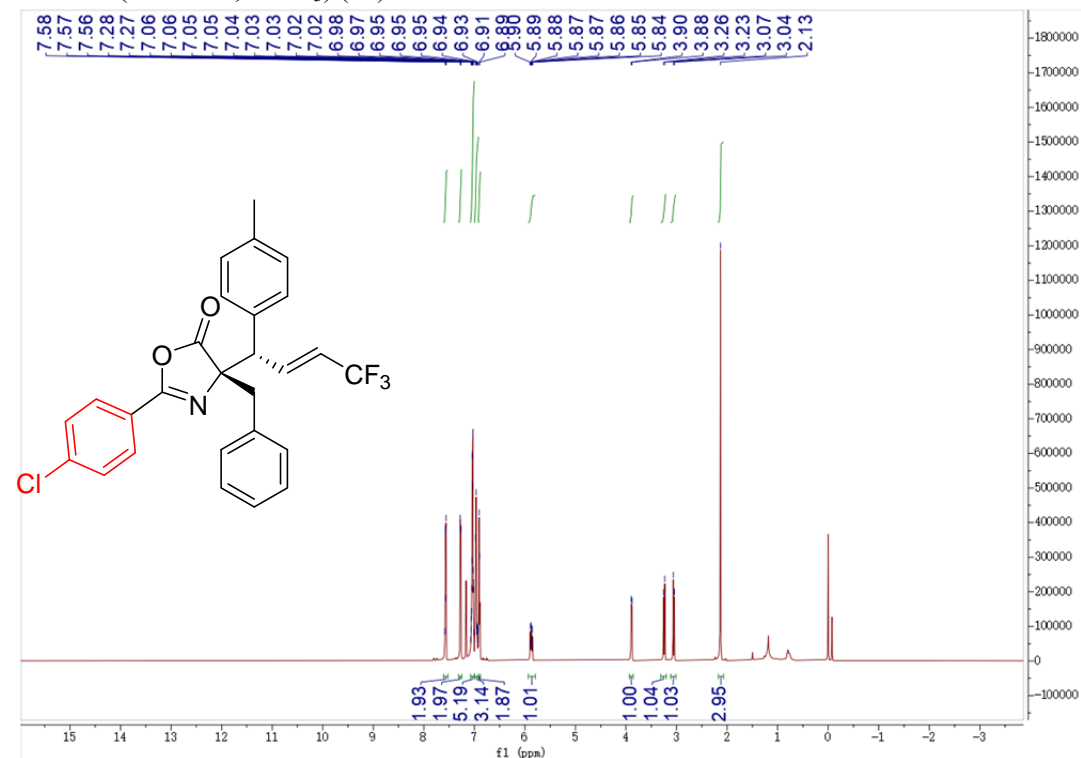
¹³C NMR (151 MHz, CDCl₃) (3n)



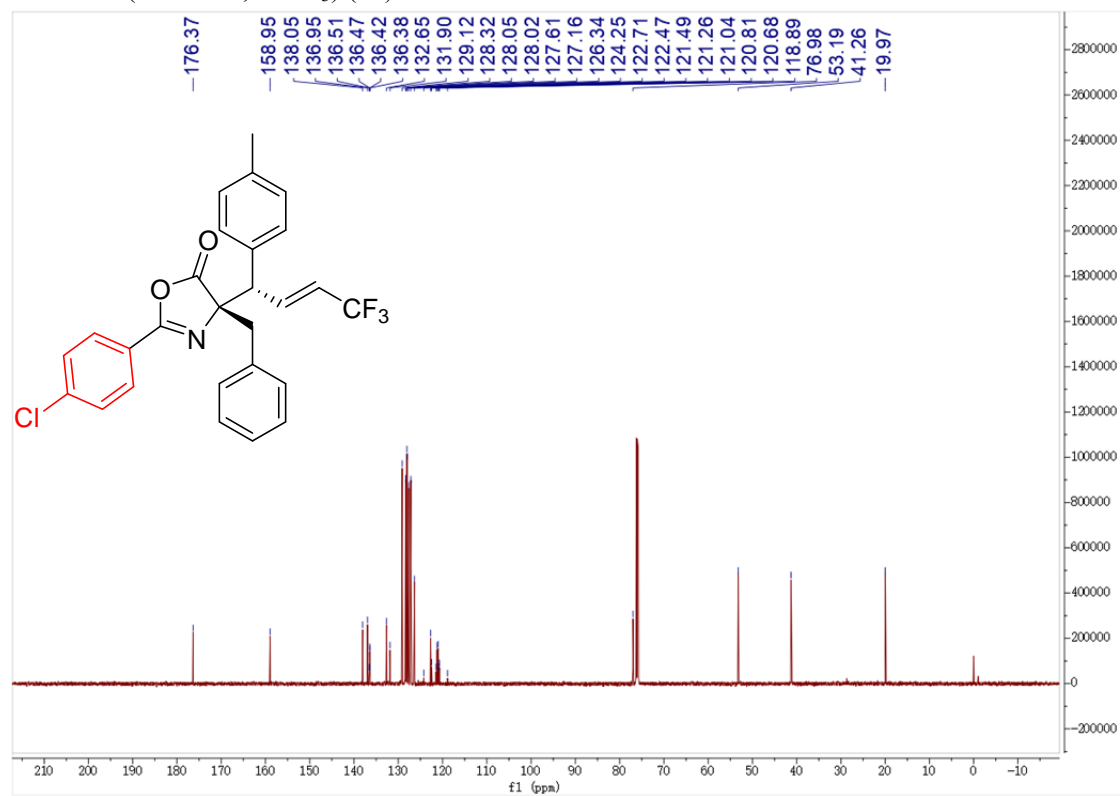
^{19}F NMR (376 MHz, CDCl_3) (**3n**)



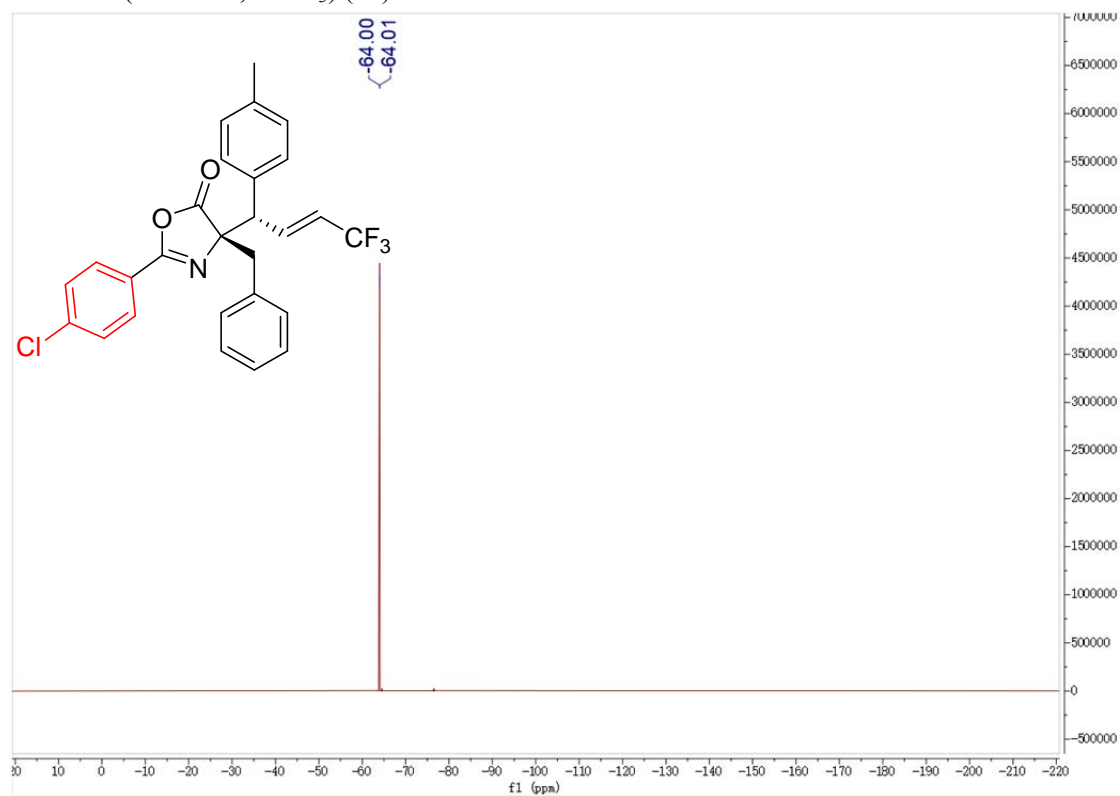
^1H NMR (600 MHz, CDCl_3) (**3o**)



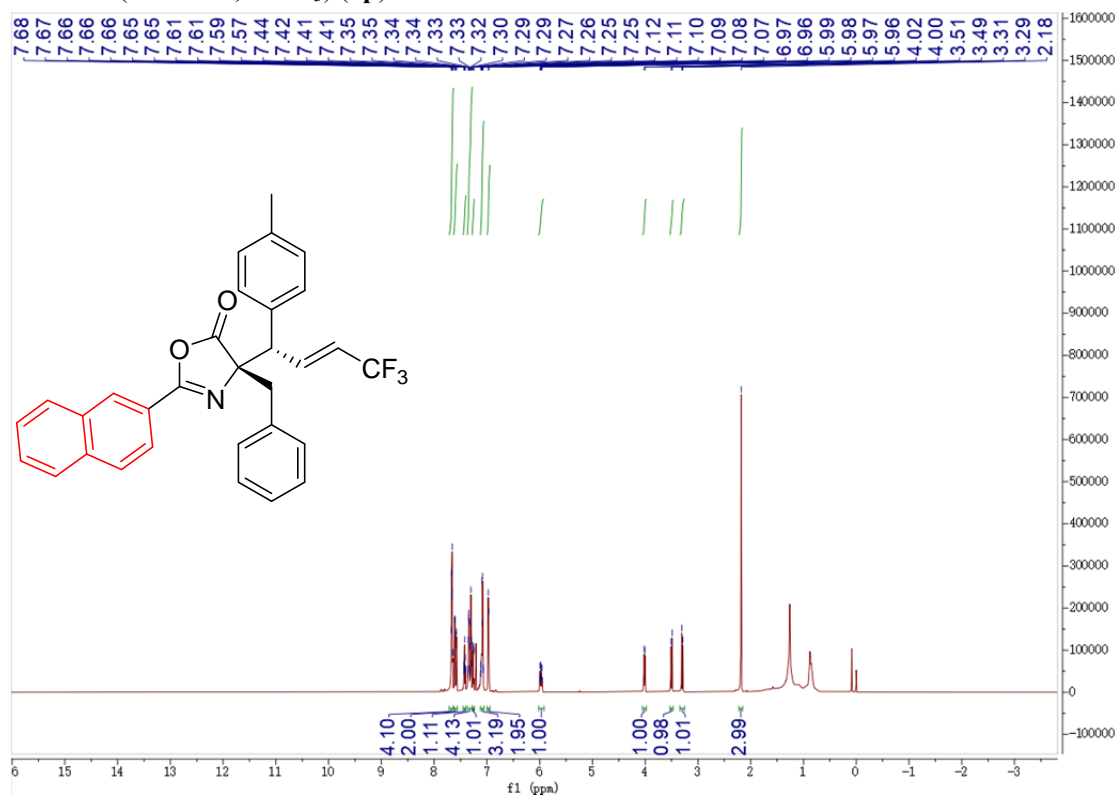
^{13}C NMR (151 MHz, CDCl_3) (**30**)



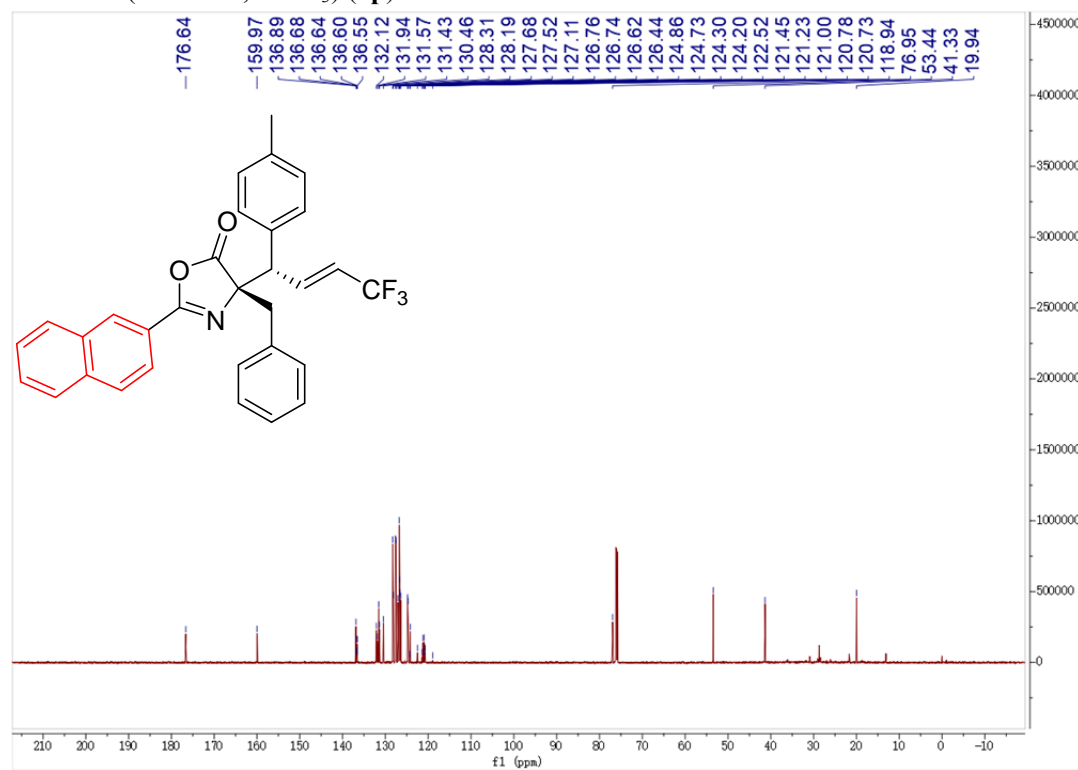
^{19}F NMR (376 MHz, CDCl_3) (**30**)



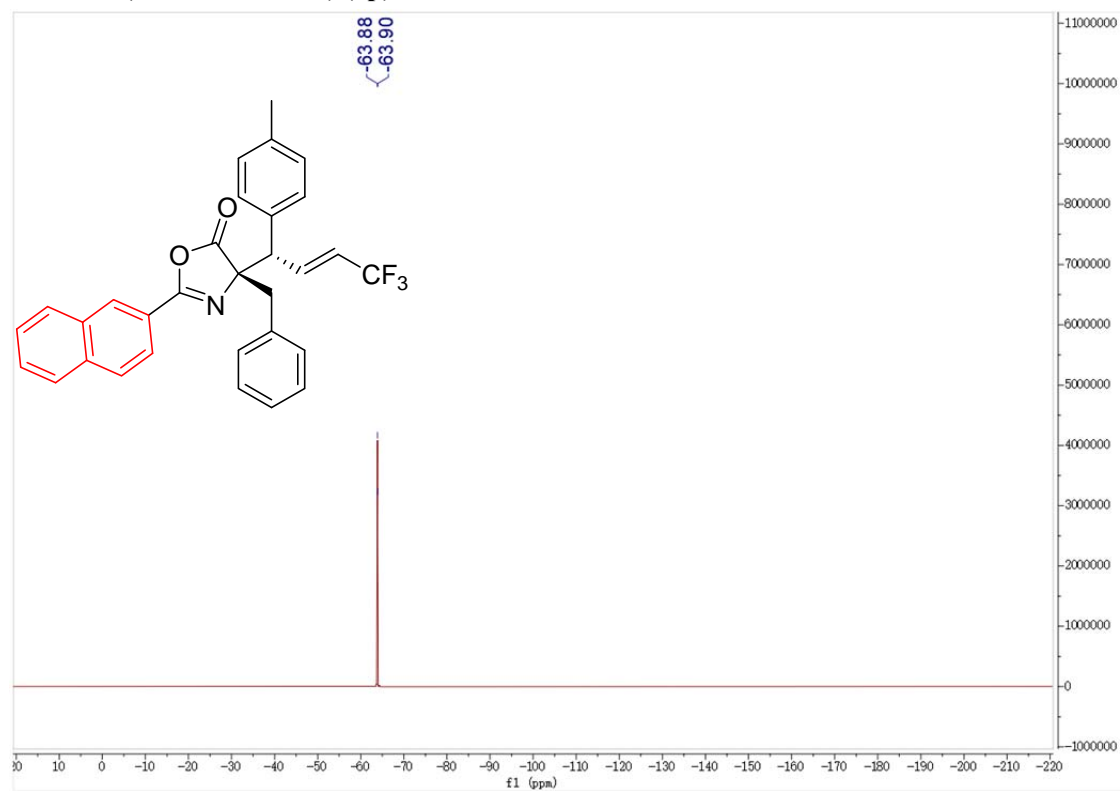
¹H NMR (600 MHz, CDCl₃) (**3p**)



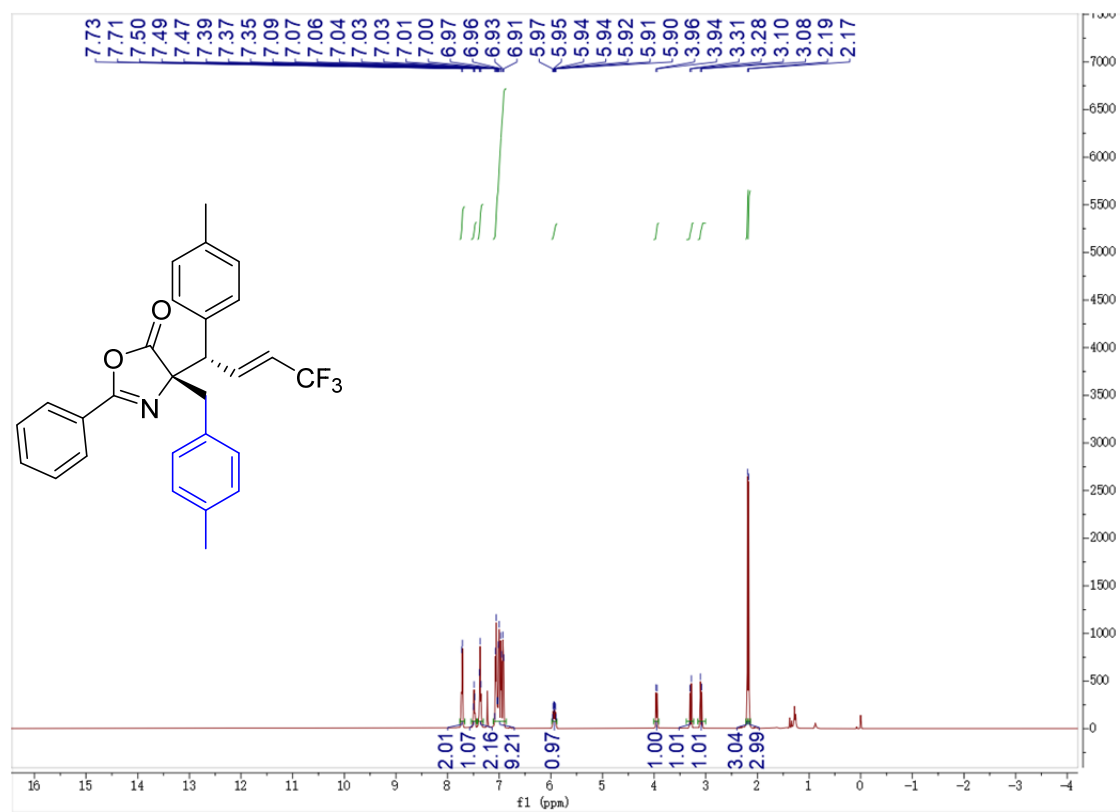
¹³C NMR (151 MHz, CDCl₃) (**3p**)



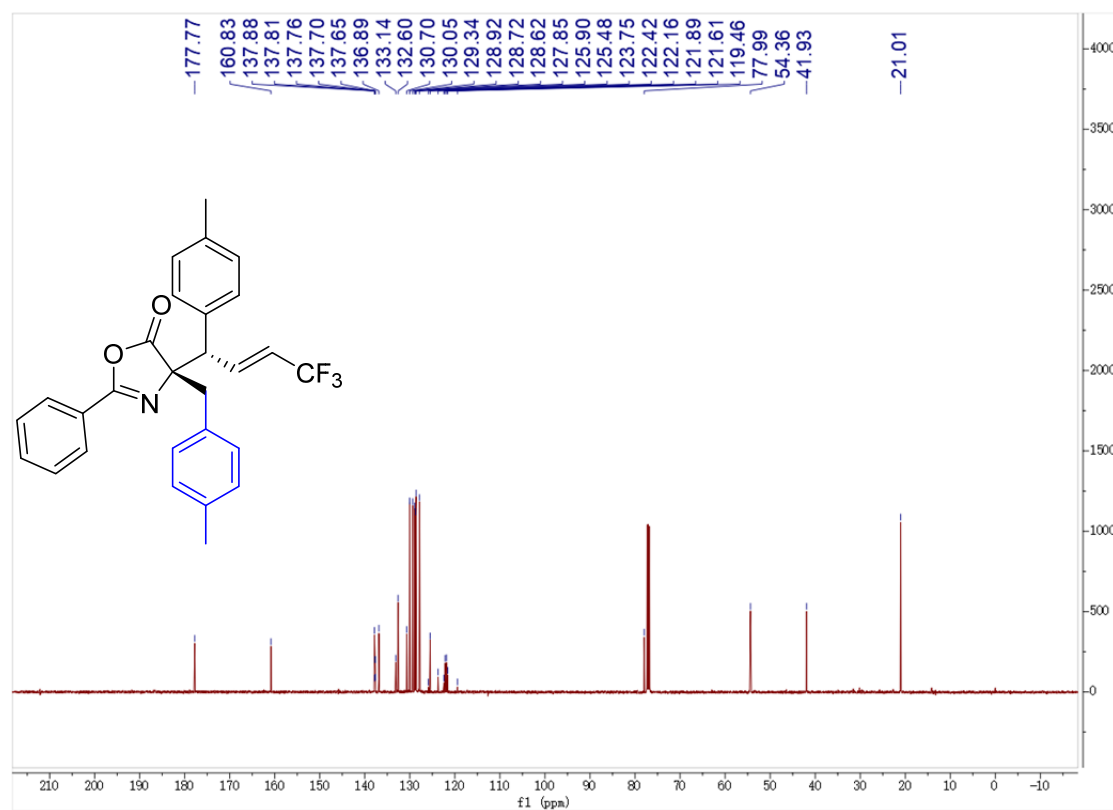
^{19}F NMR (376 MHz, CDCl_3) (**3p**)



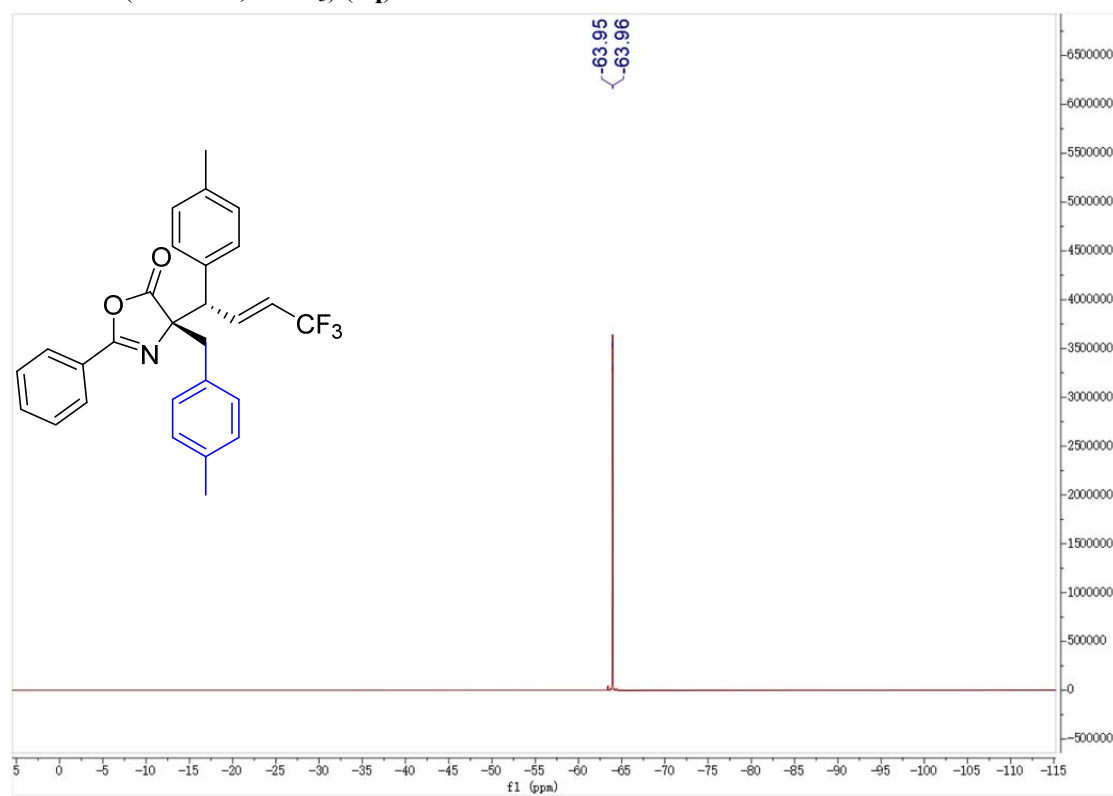
^1H NMR (500 MHz, CDCl_3) (**3q**)



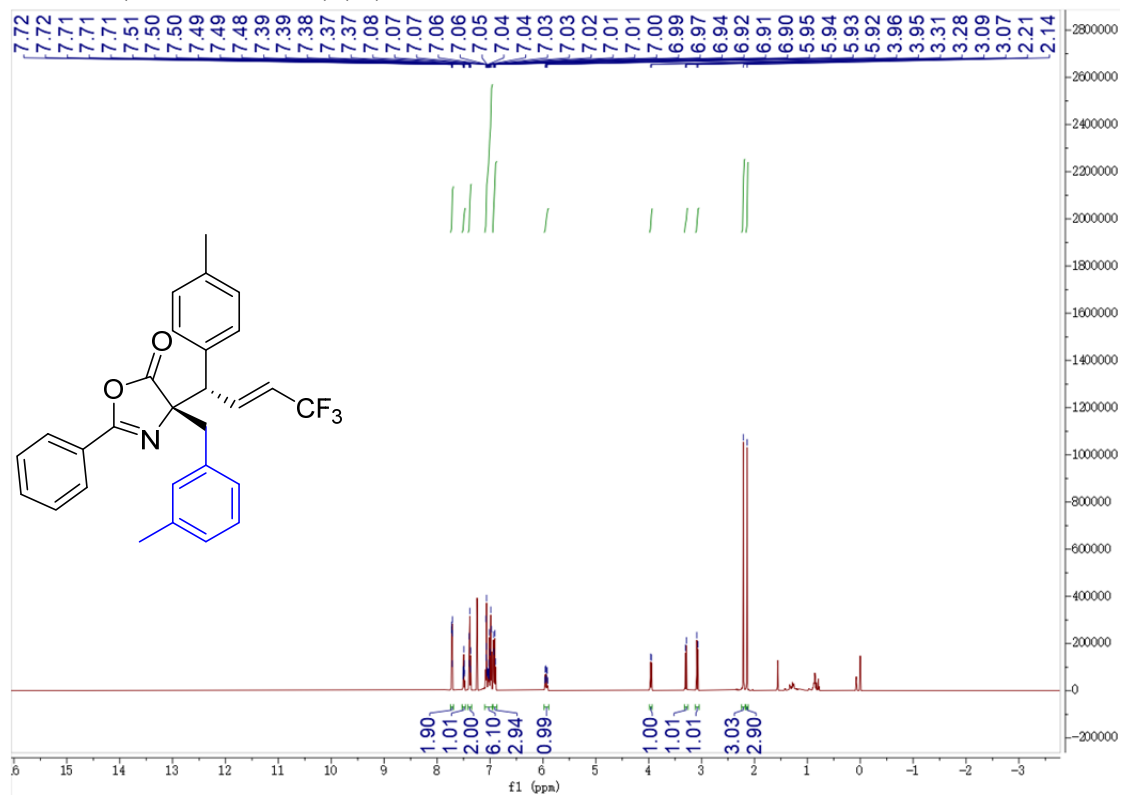
^{13}C NMR (126 MHz, CDCl_3) (**3q**)



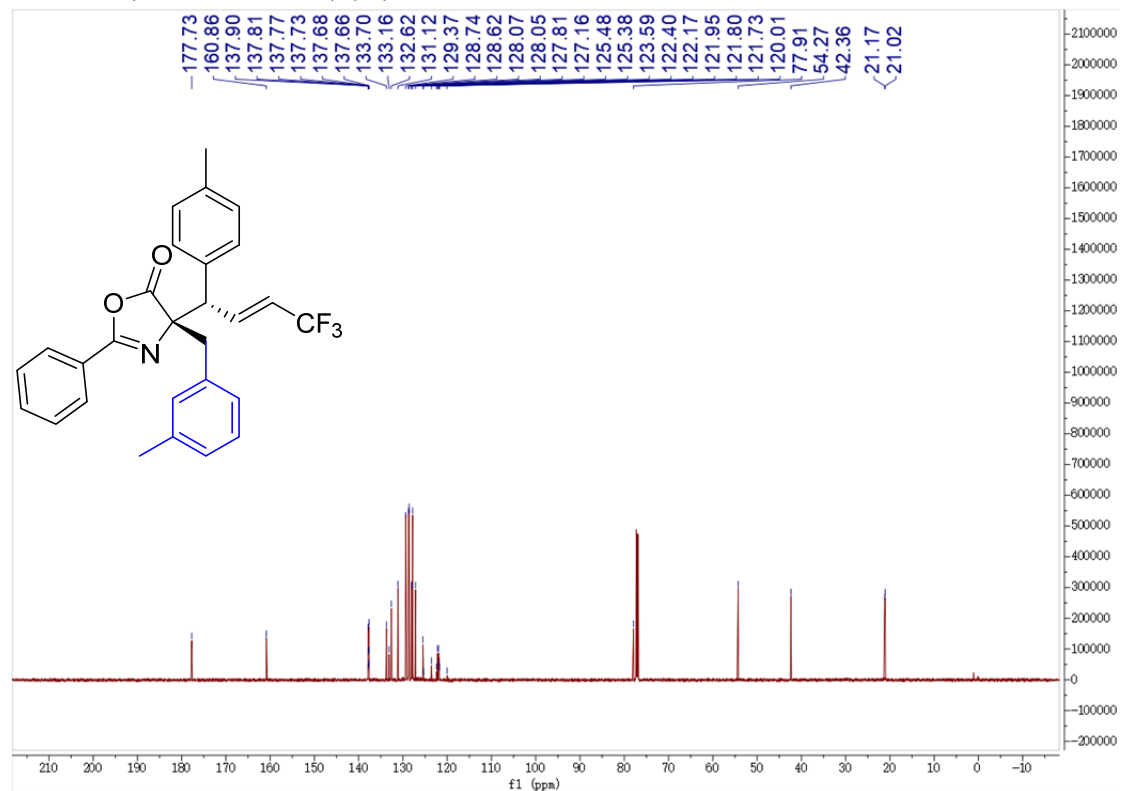
^{19}F NMR (376 MHz, CDCl_3) (**3q**)



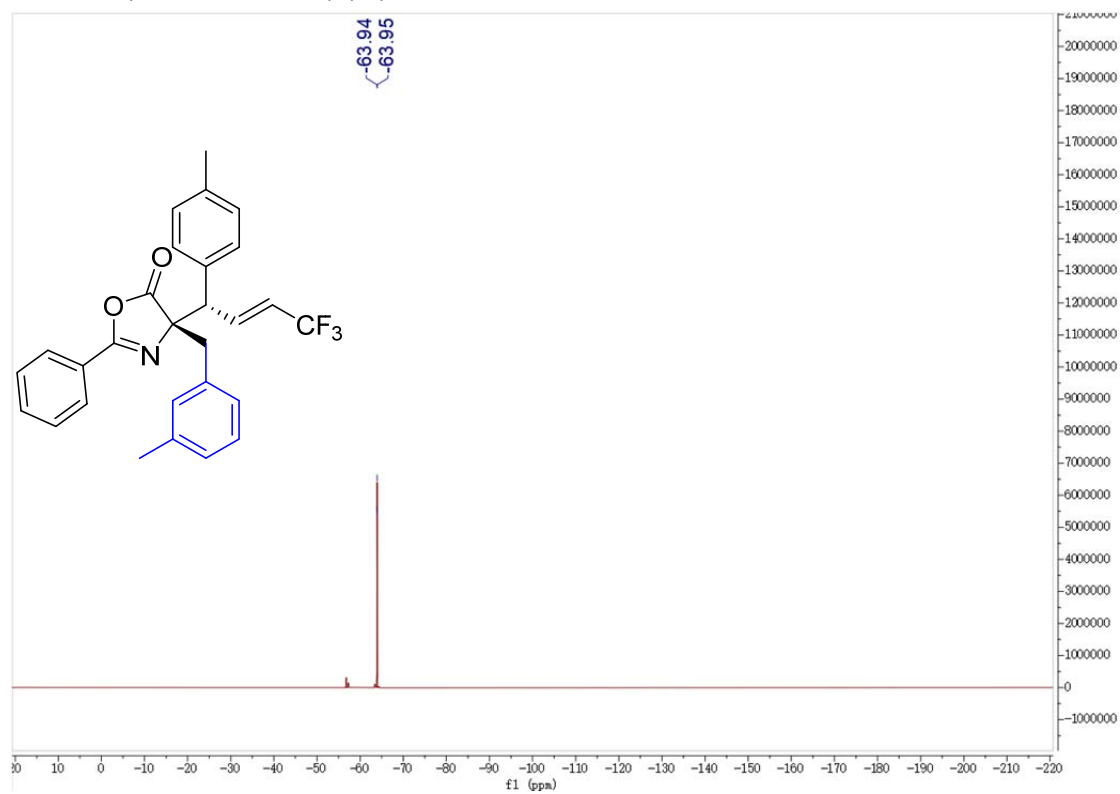
¹H NMR (600 MHz, CDCl₃) (**3r**)



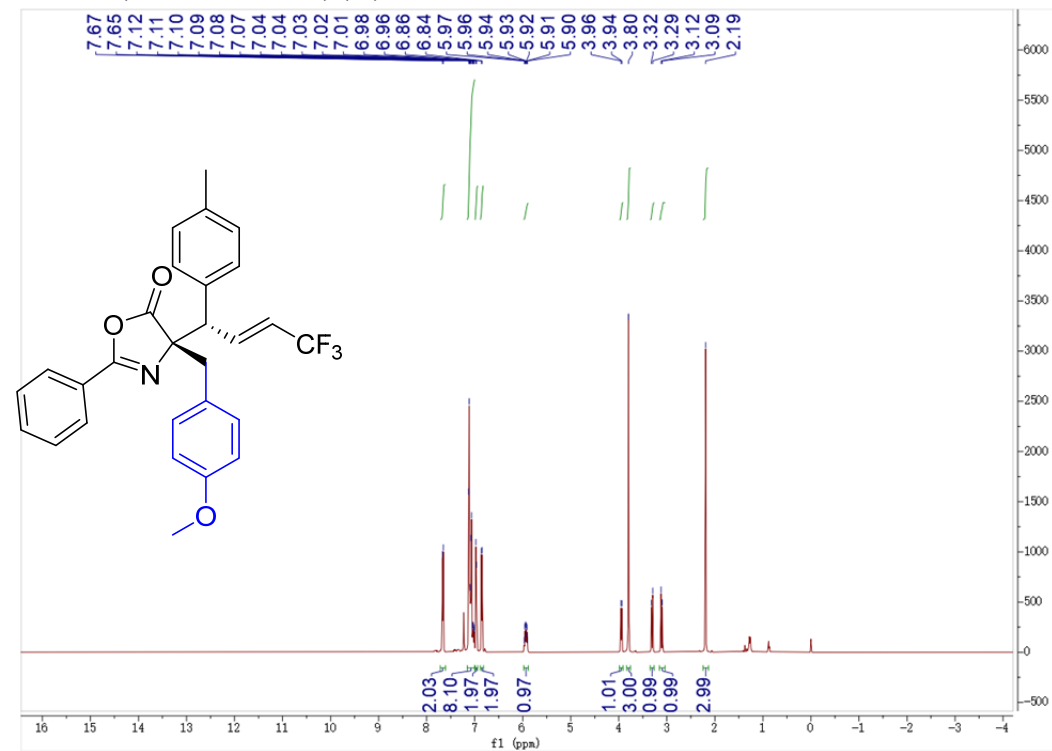
¹³C NMR (151 MHz, CDCl₃) (**3r**)



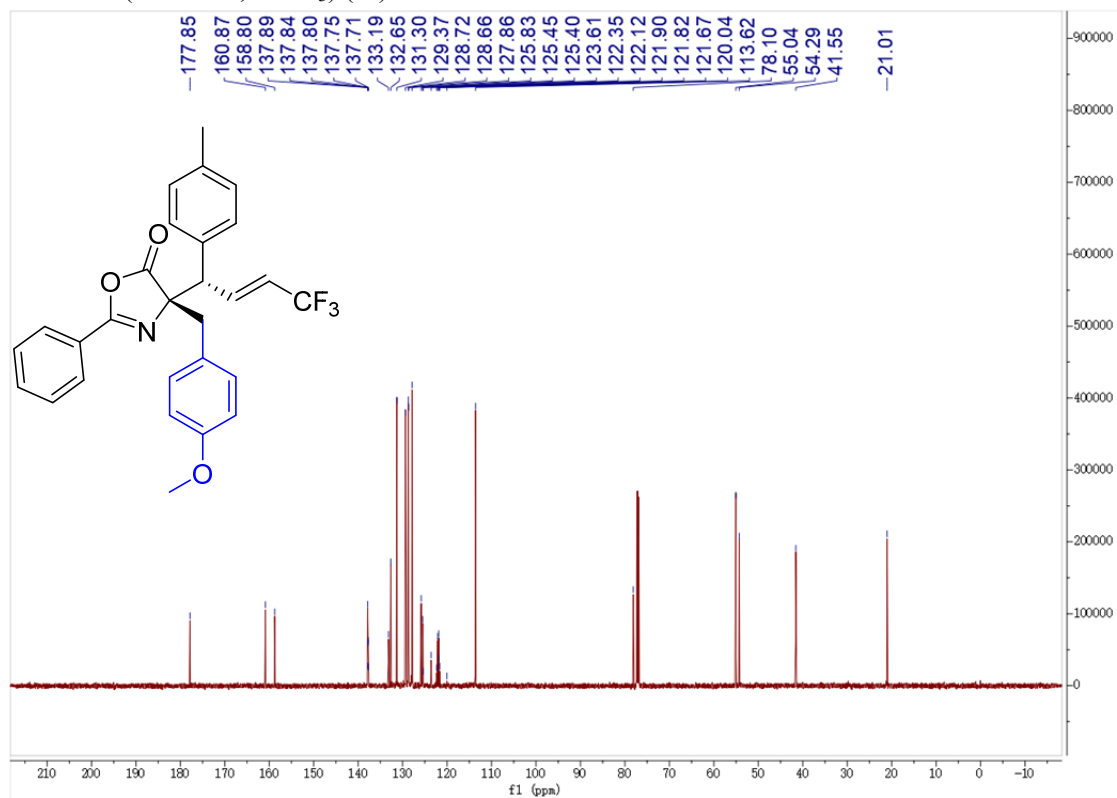
^{19}F NMR (376 MHz, CDCl_3) (**3r**)



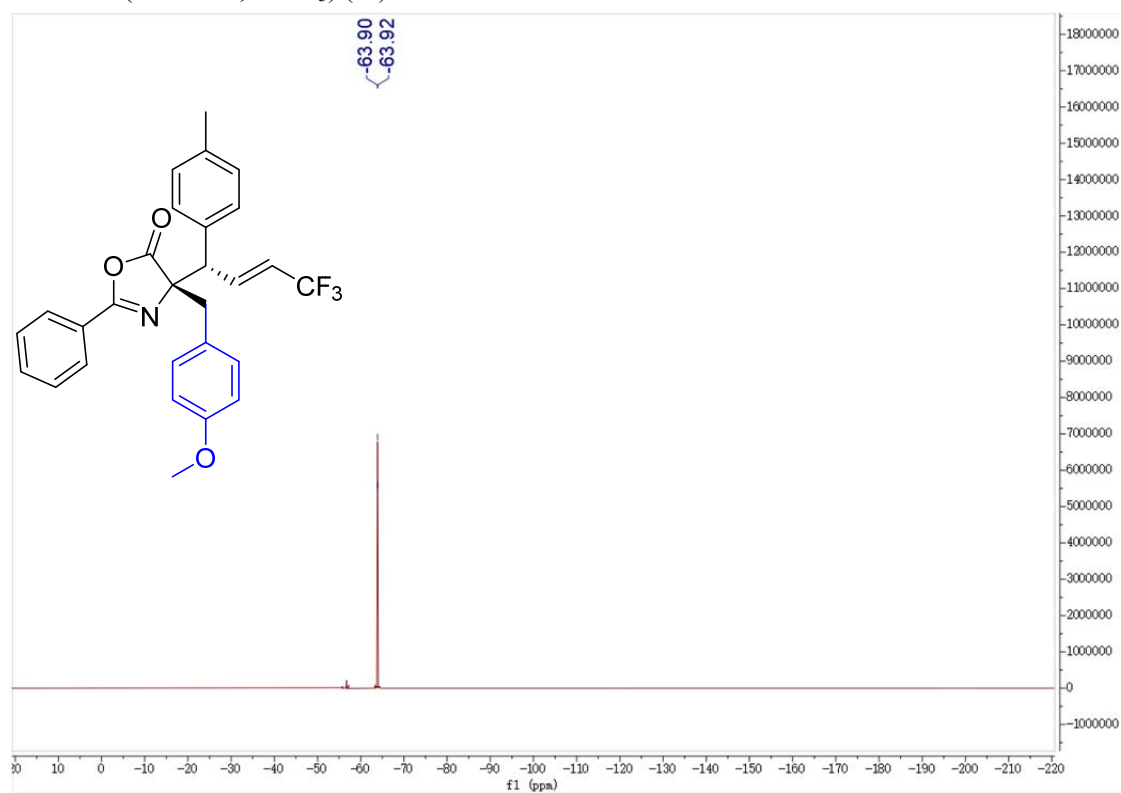
^1H NMR (500 MHz, CDCl_3) (**3s**)



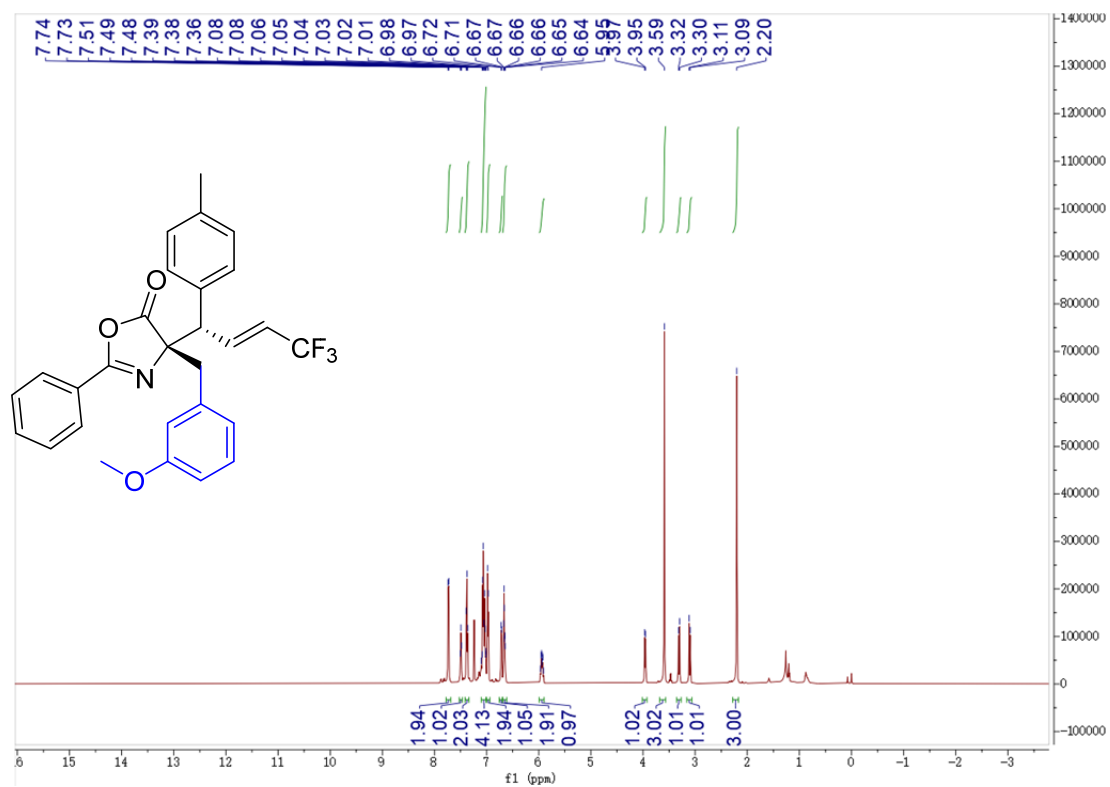
¹³C NMR (151 MHz, CDCl₃) (**3s**)



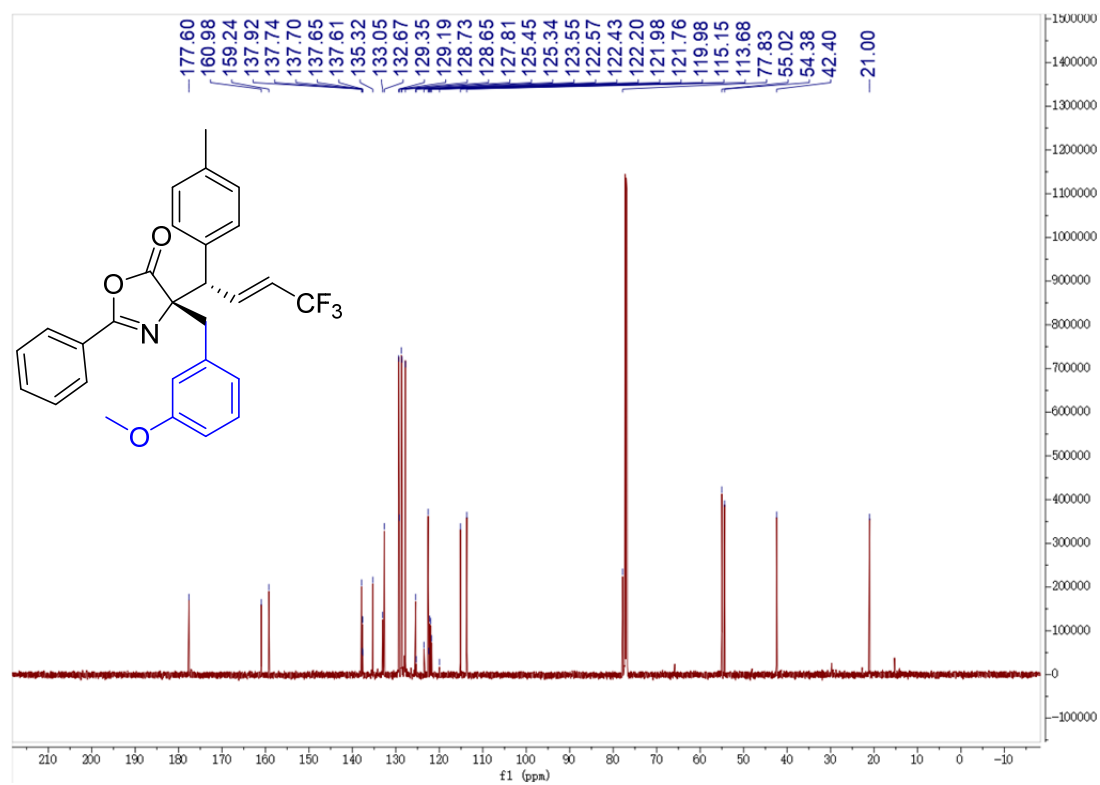
¹⁹F NMR (376 MHz, CDCl₃) (**3s**)



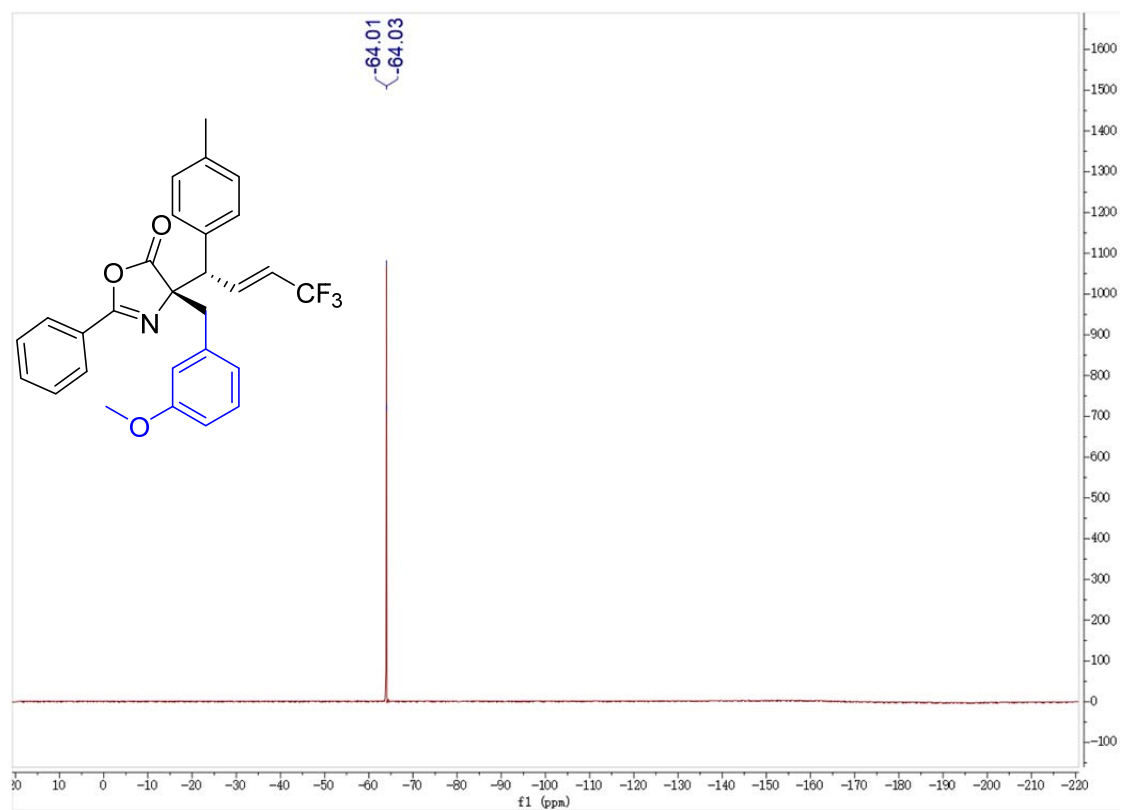
¹H NMR (600 MHz, CDCl₃) (3t)



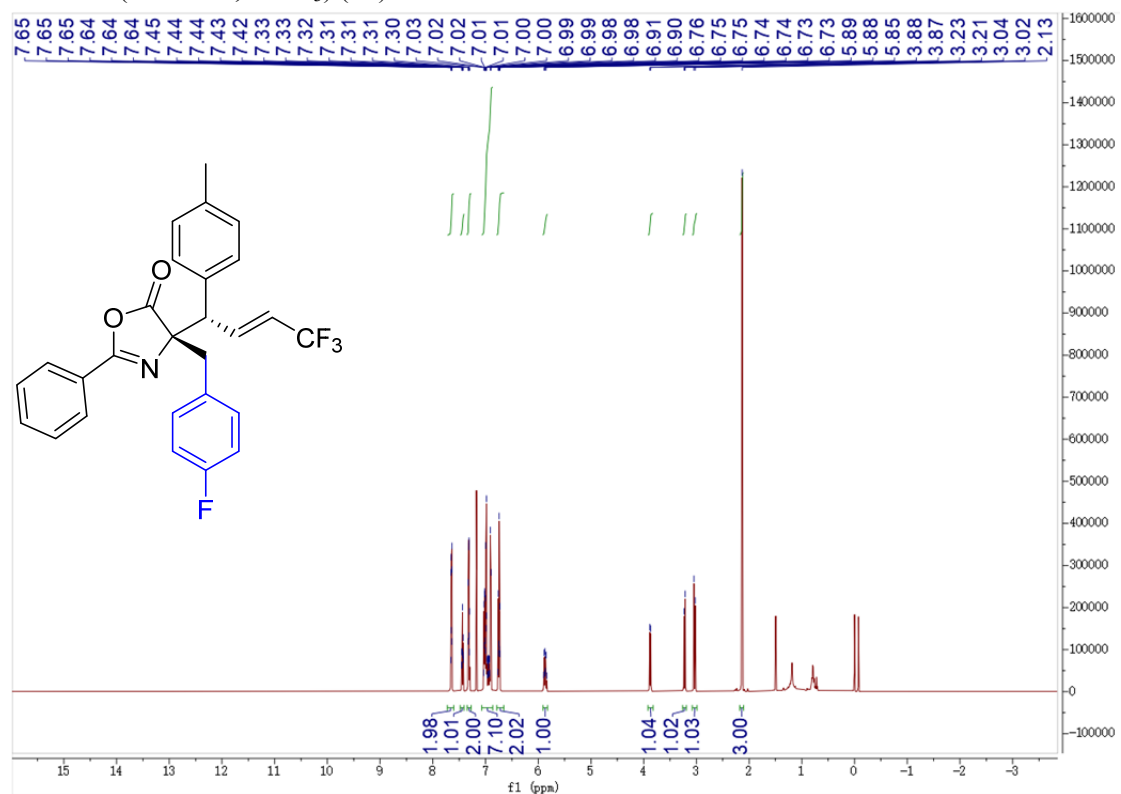
¹³C NMR (151 MHz, CDCl₃) (3t)



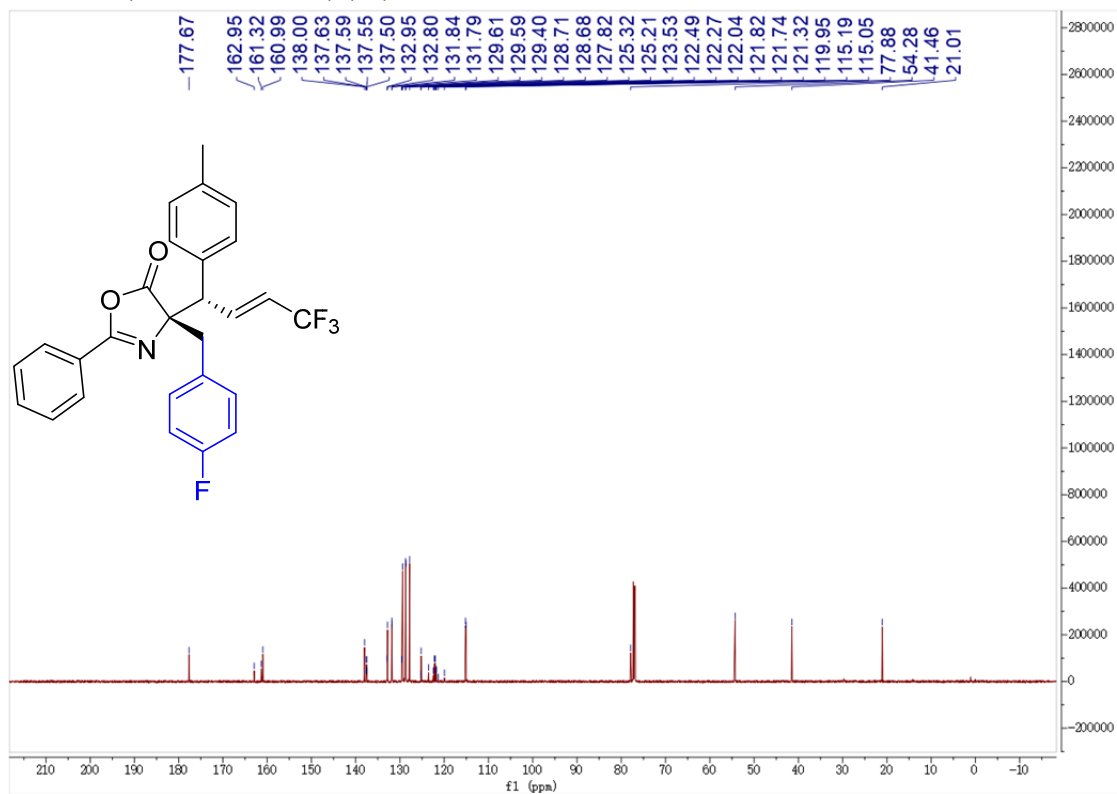
^{19}F NMR (470 MHz, CDCl_3) (**3t**)



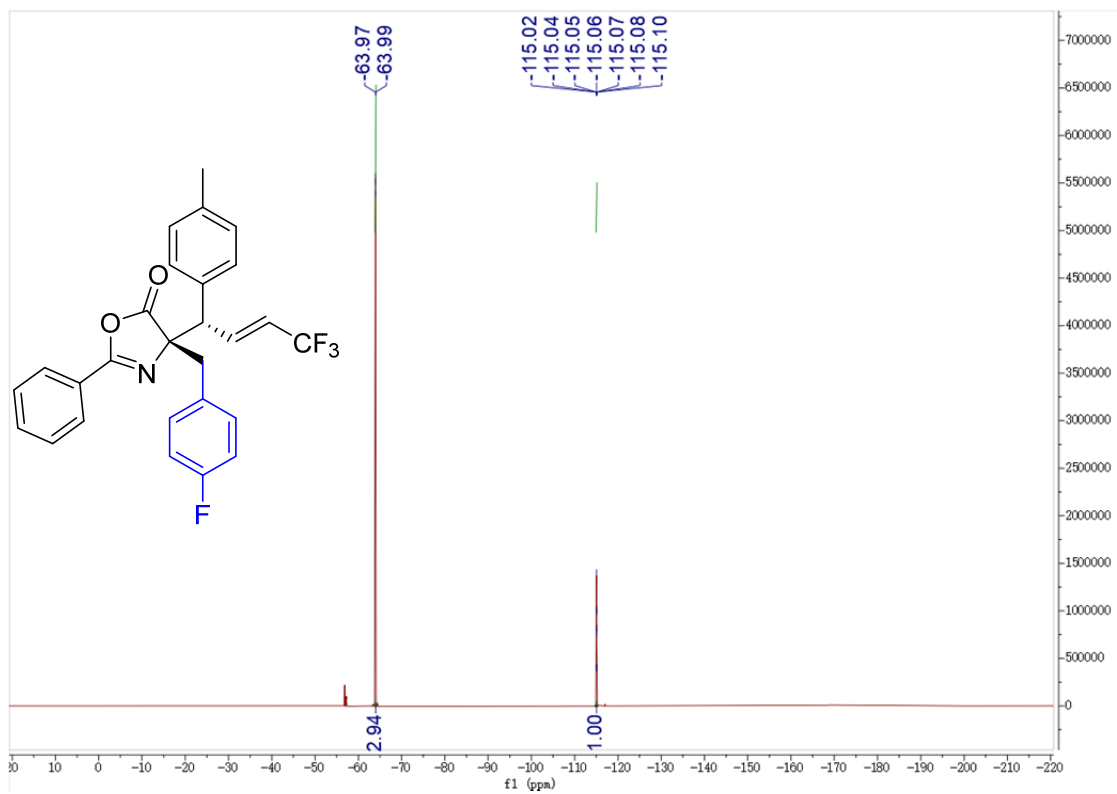
^1H NMR (600 MHz, CDCl_3) (**3u**)



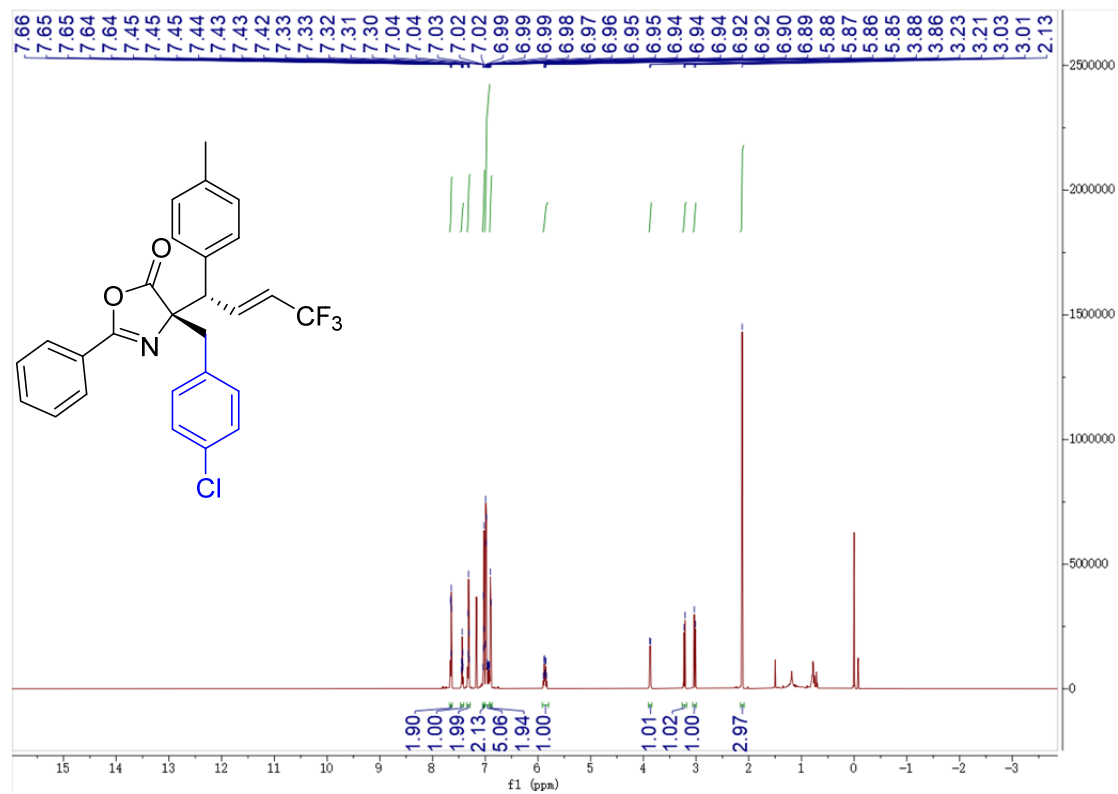
¹³C NMR (151 MHz, CDCl₃) (**3u**)



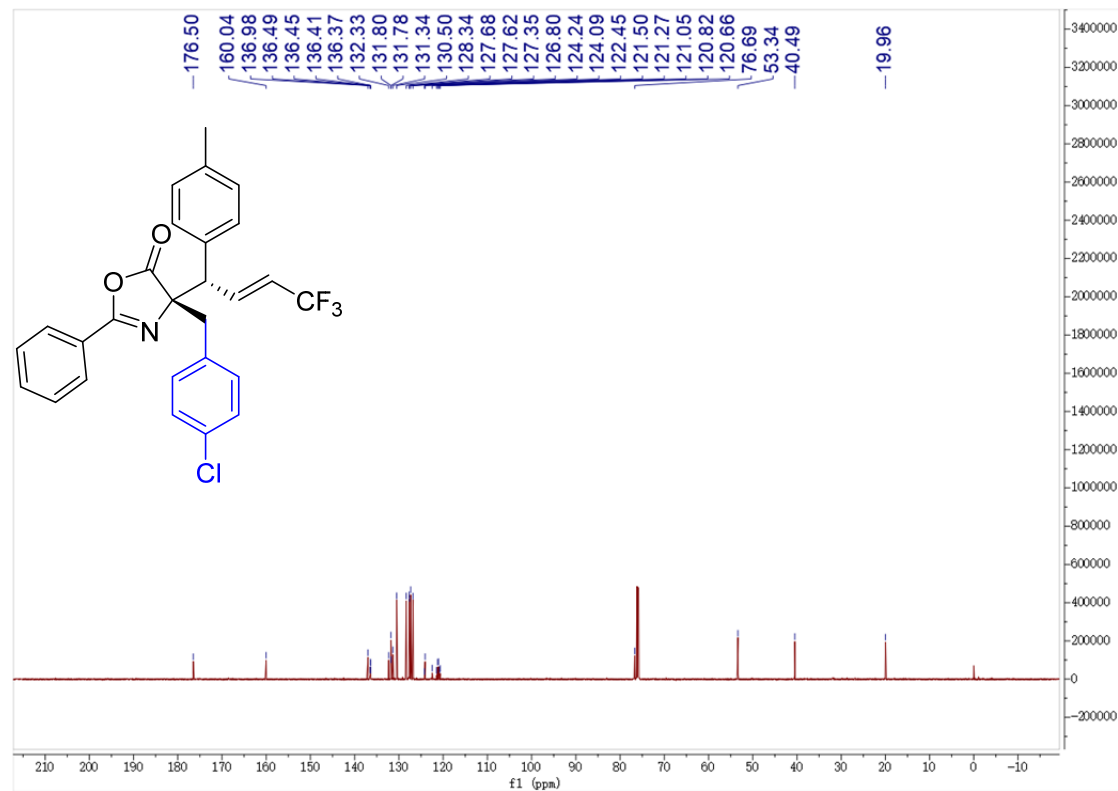
¹⁹F NMR (376 MHz, CDCl₃) (**3u**)



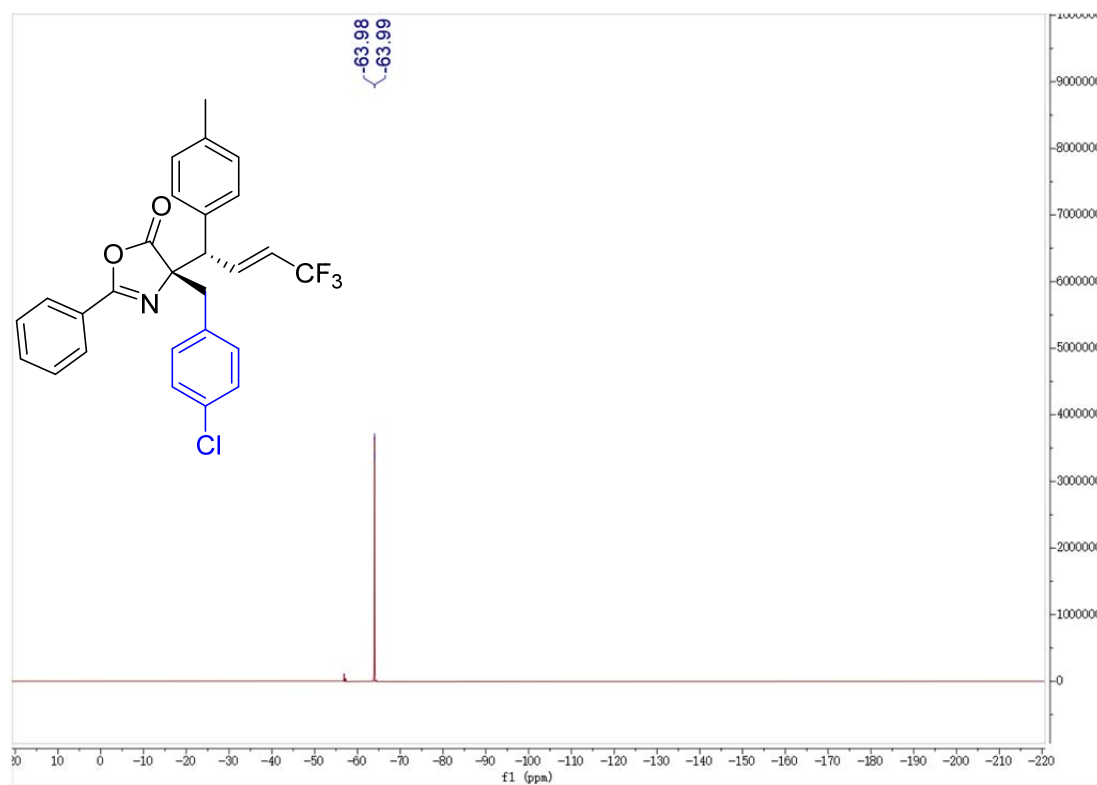
¹H NMR (600 MHz, CDCl₃) (**3v**)



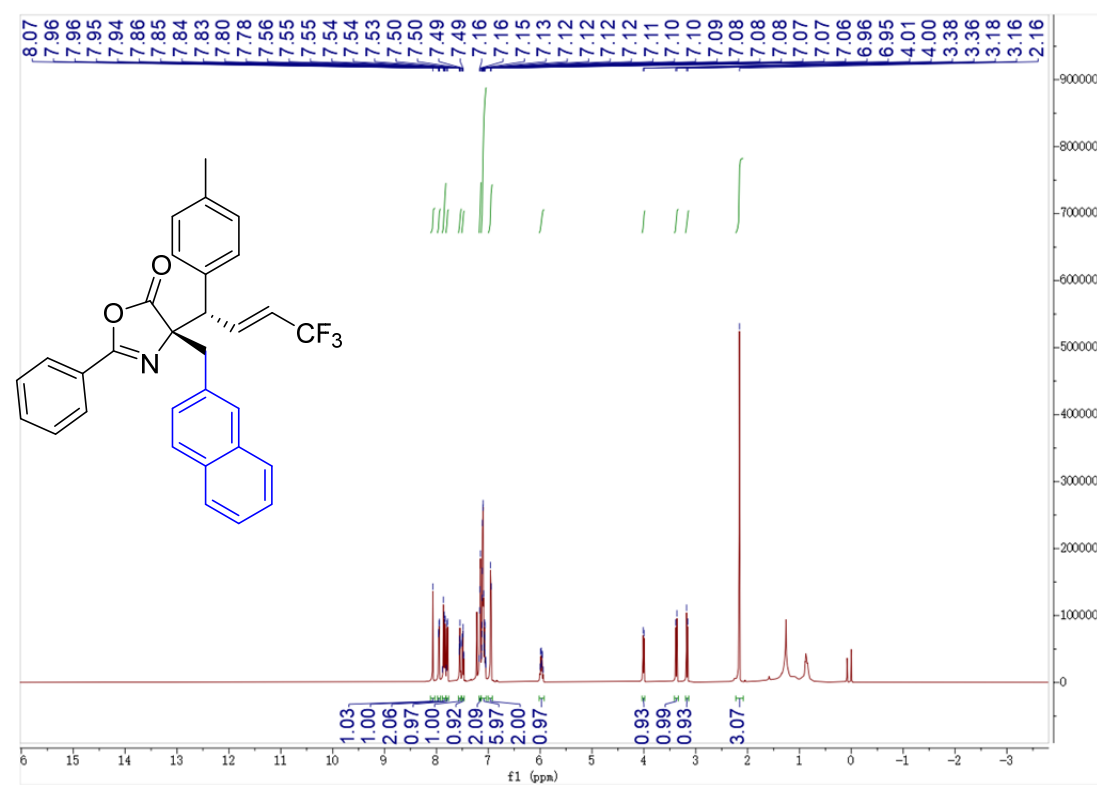
¹³C NMR (151 MHz, CDCl₃) (**3v**)



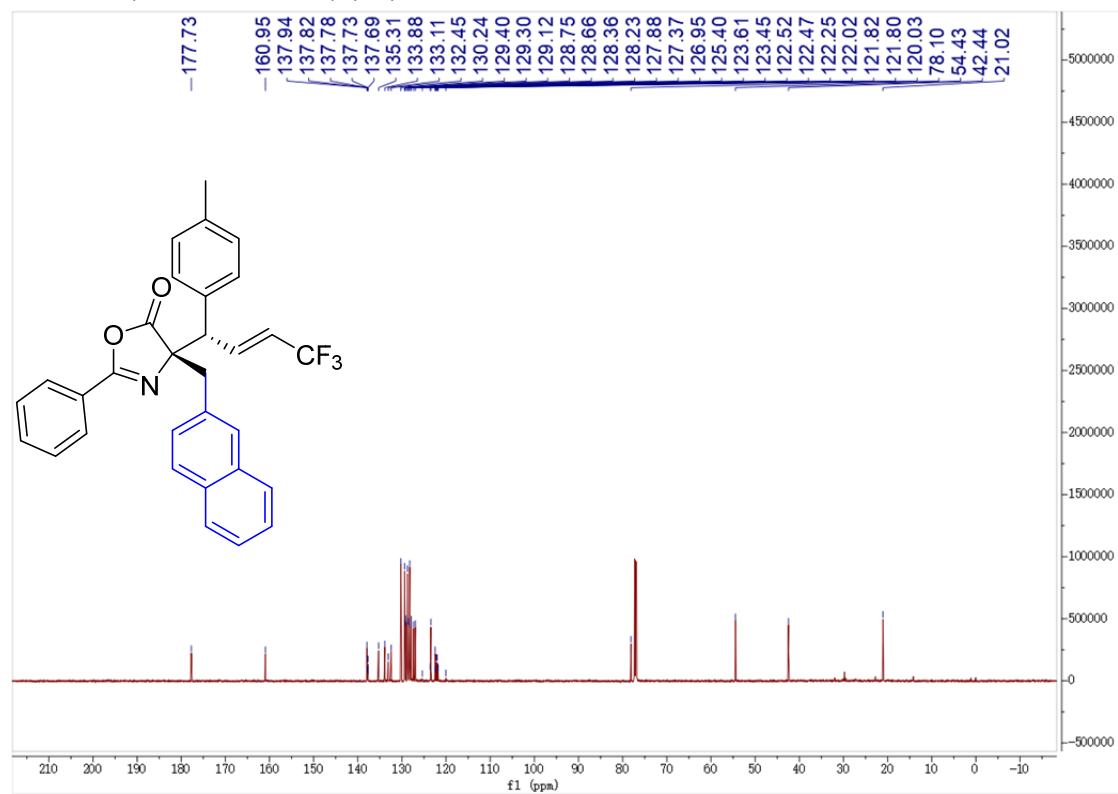
^{19}F NMR (376 MHz, CDCl_3) (**3v**)



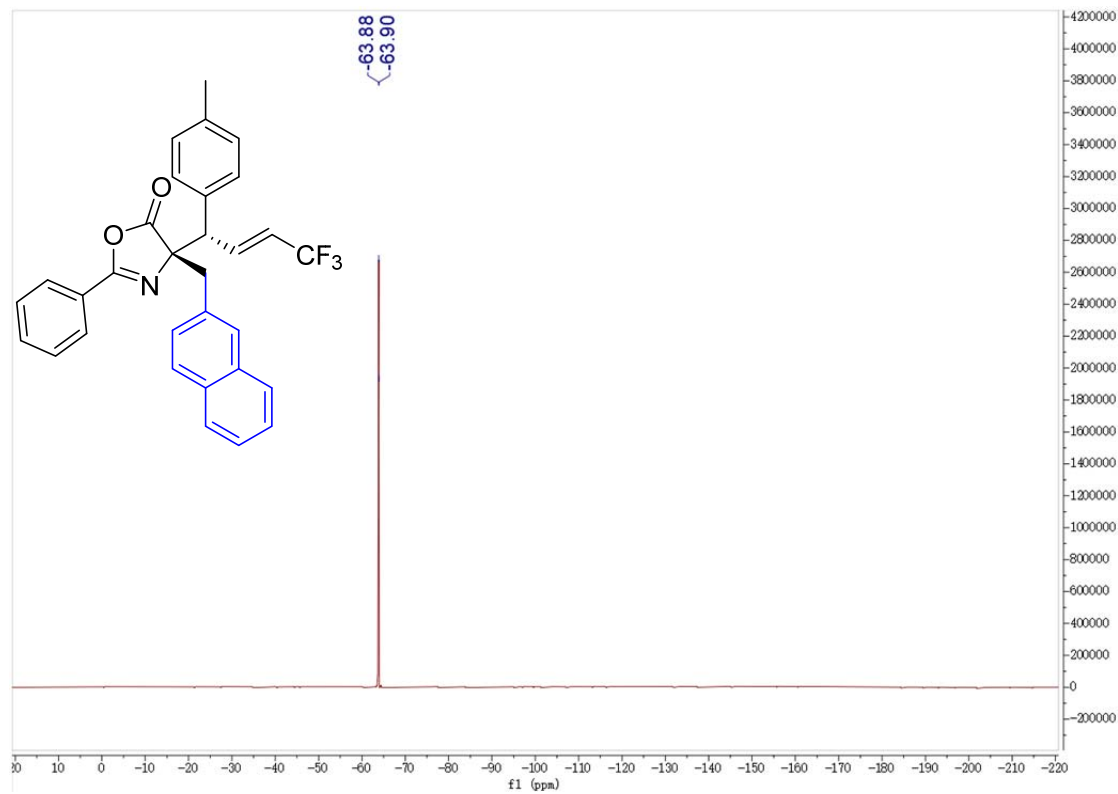
^1H NMR (600 MHz, CDCl_3) (**3w**)



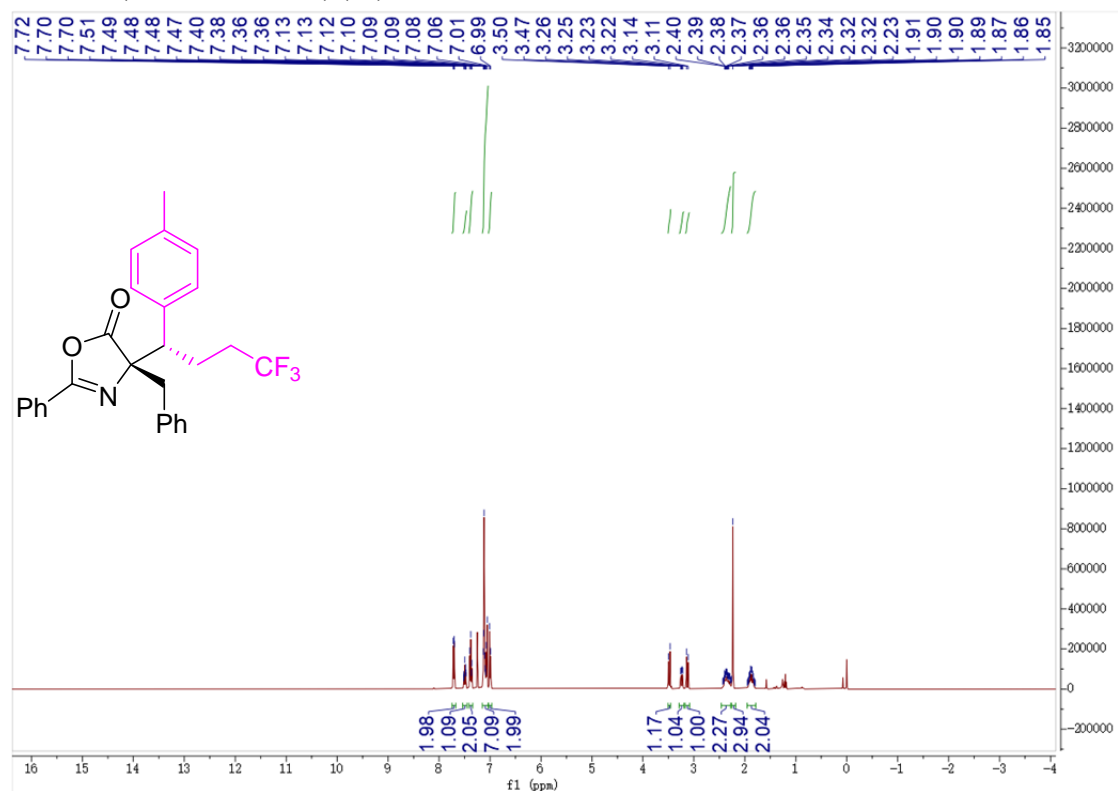
¹³C NMR (151 MHz, CDCl₃) (**3w**)



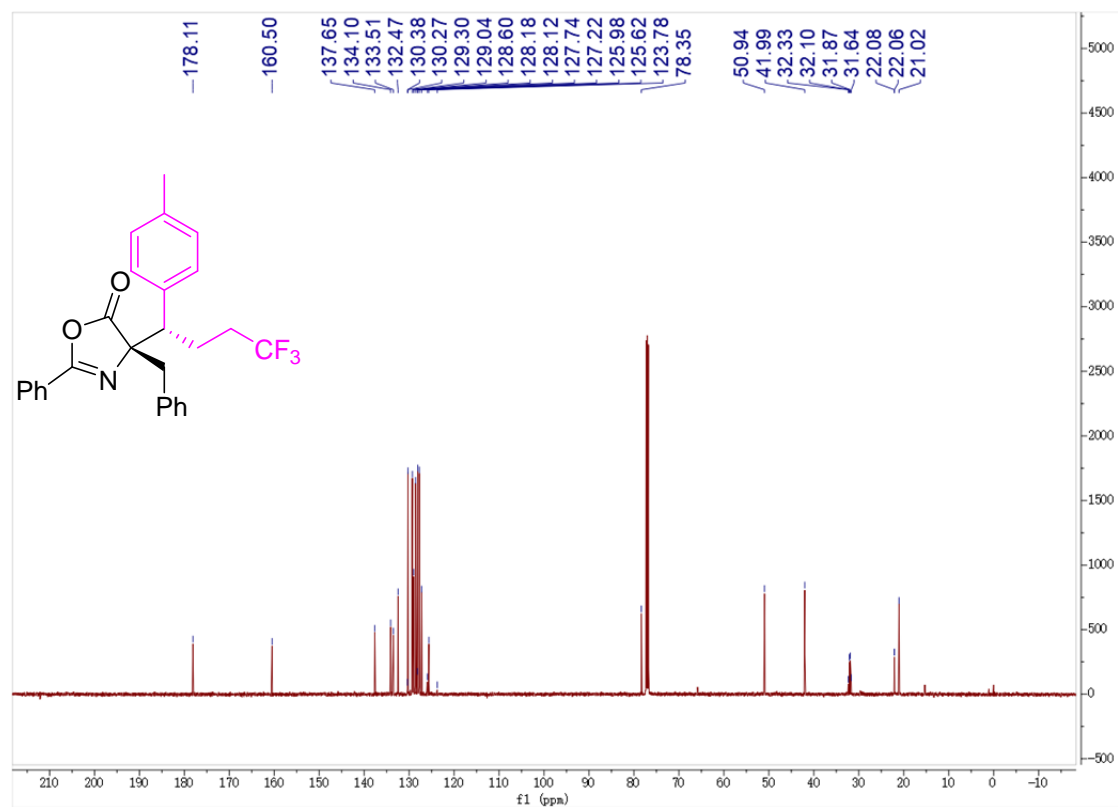
¹⁹F NMR (376 MHz, CDCl₃) (**3w**)



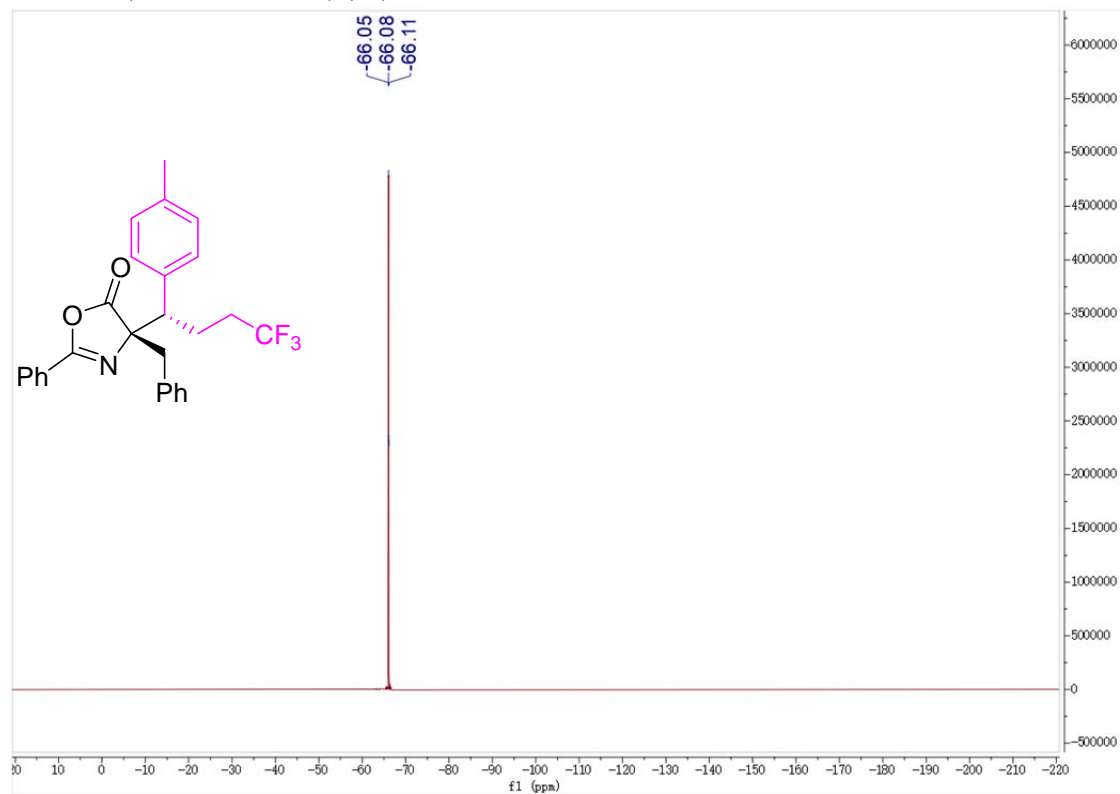
¹H NMR (400 MHz, CDCl₃) (4a)



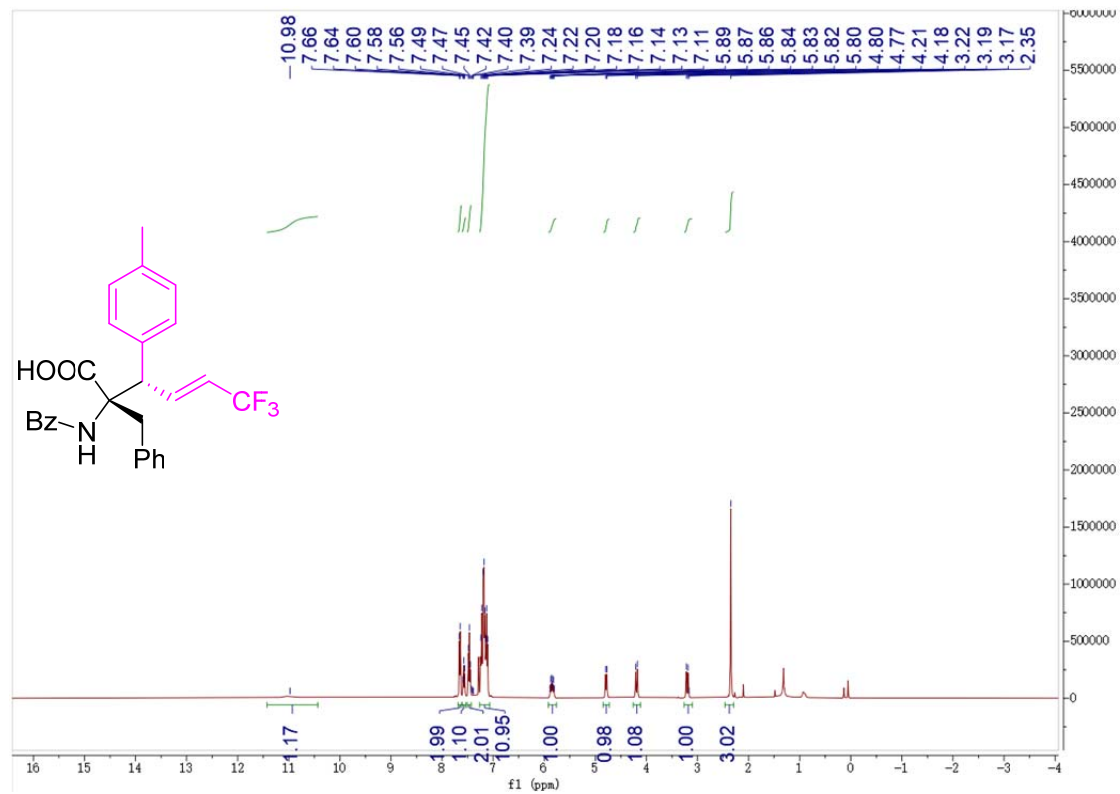
¹³C NMR (126 MHz, CDCl₃) (4a)



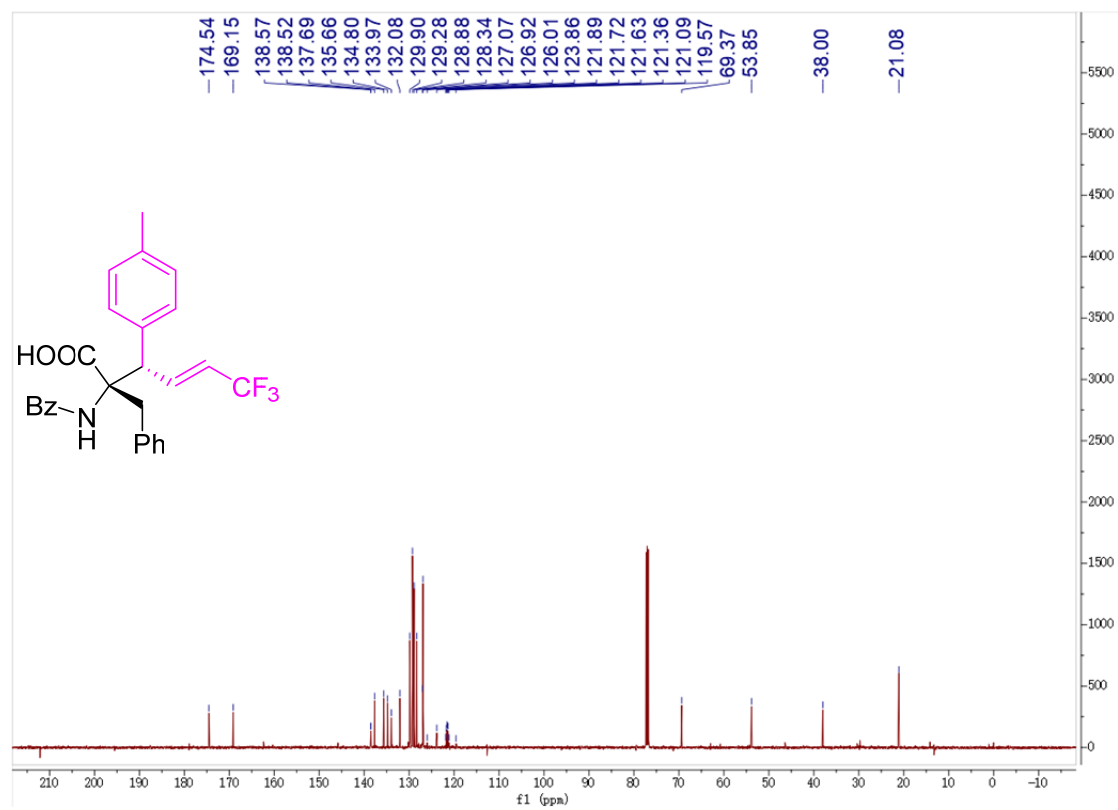
^{19}F NMR (376 MHz, CDCl_3) (**4a**)



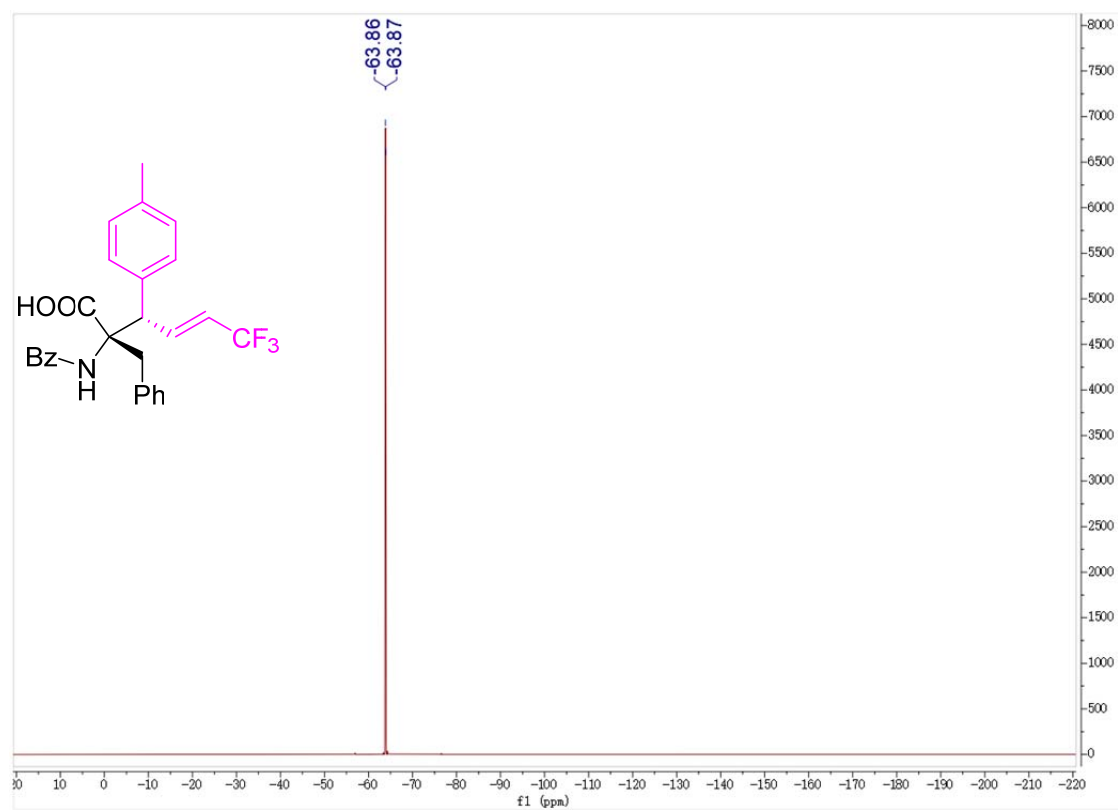
^1H NMR (400 MHz, CDCl_3) (**5a**)



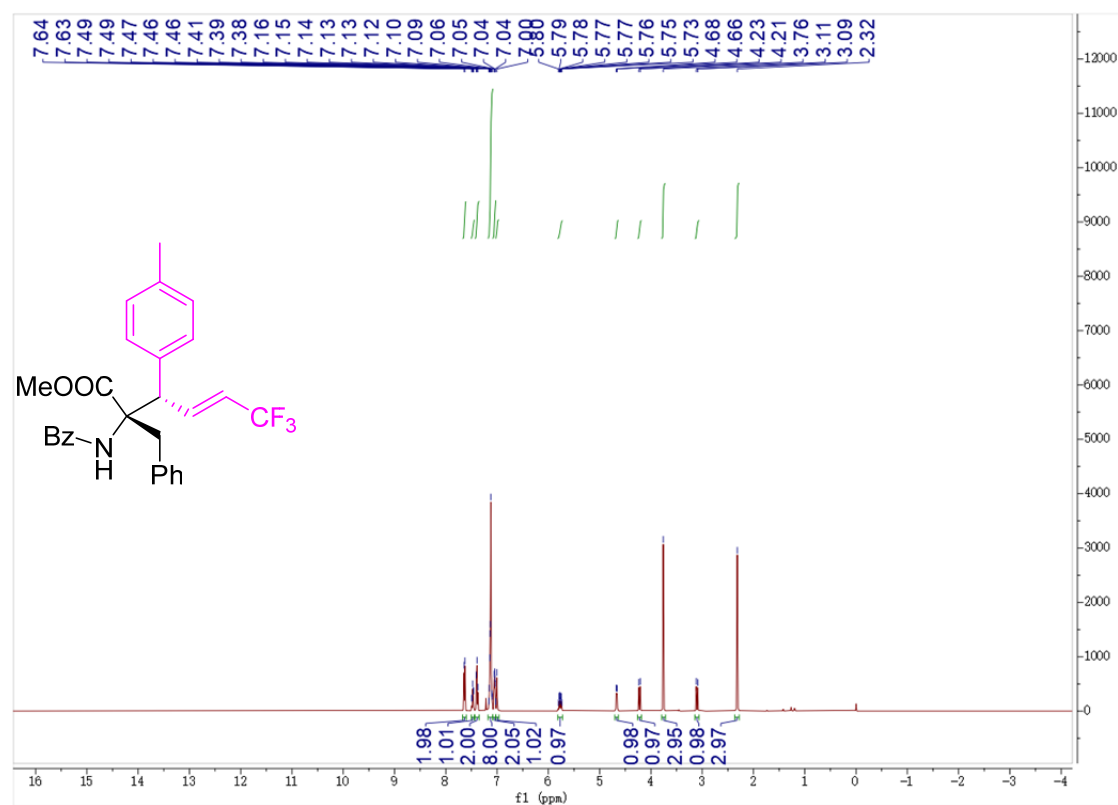
^{13}C NMR (126 MHz, CDCl_3) (**5a**)



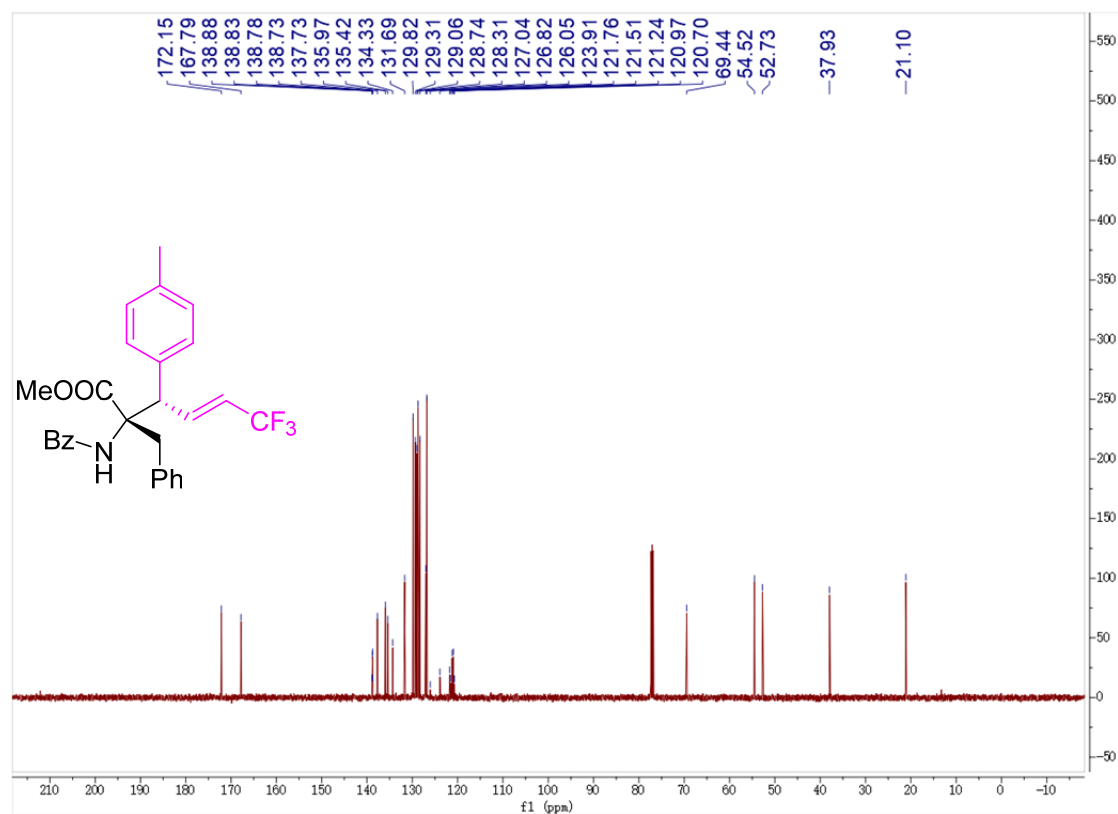
^{19}F NMR (470 MHz, CDCl_3) (**5a**)



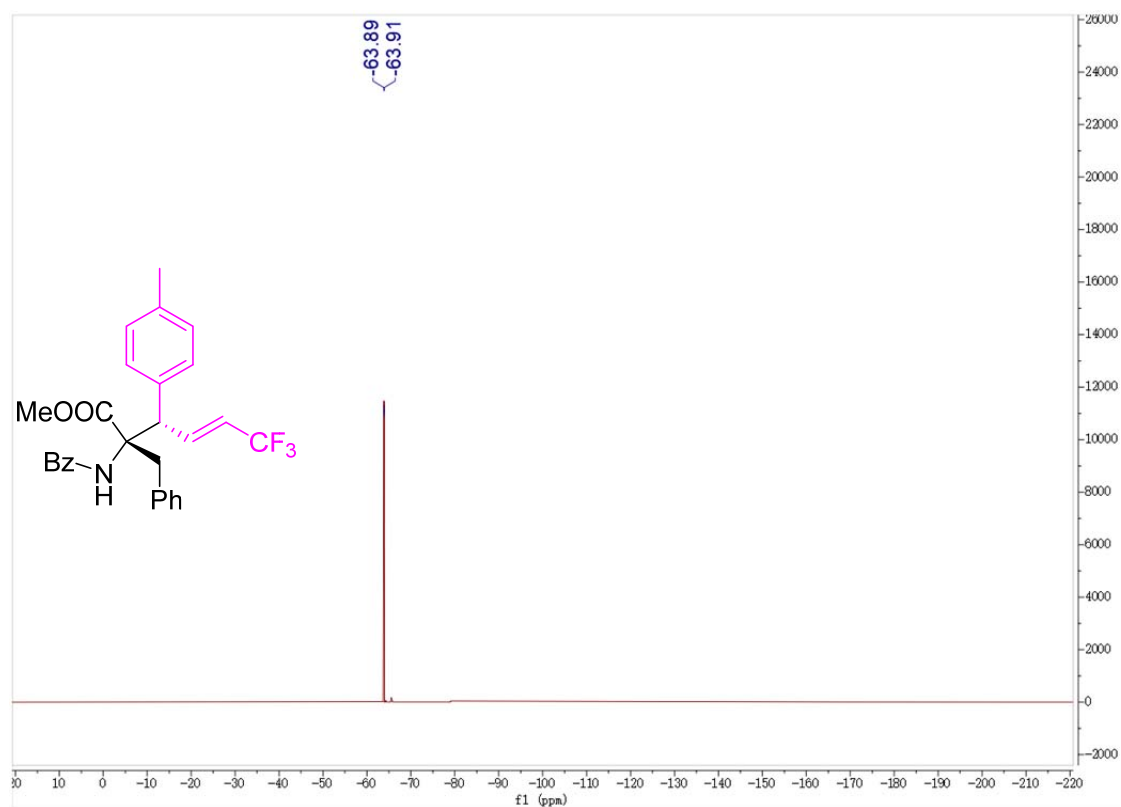
¹H NMR (500 MHz, CDCl₃) (**6a**)



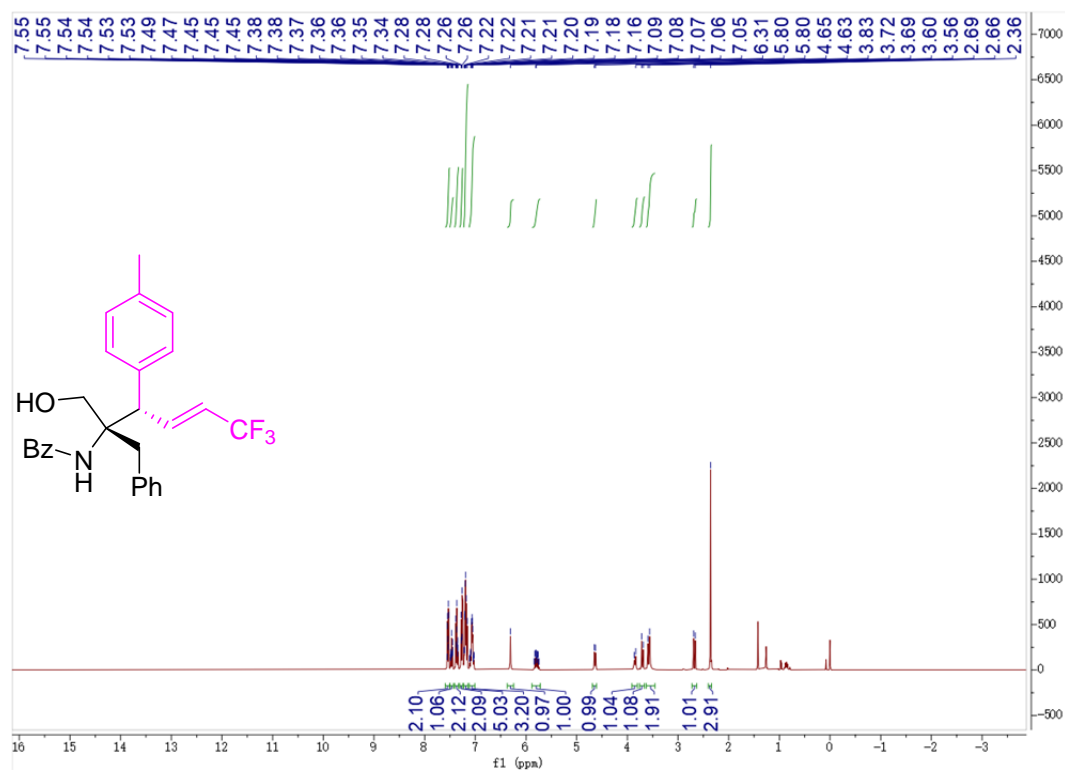
¹³C NMR (126 MHz, CDCl₃) (**6a**)



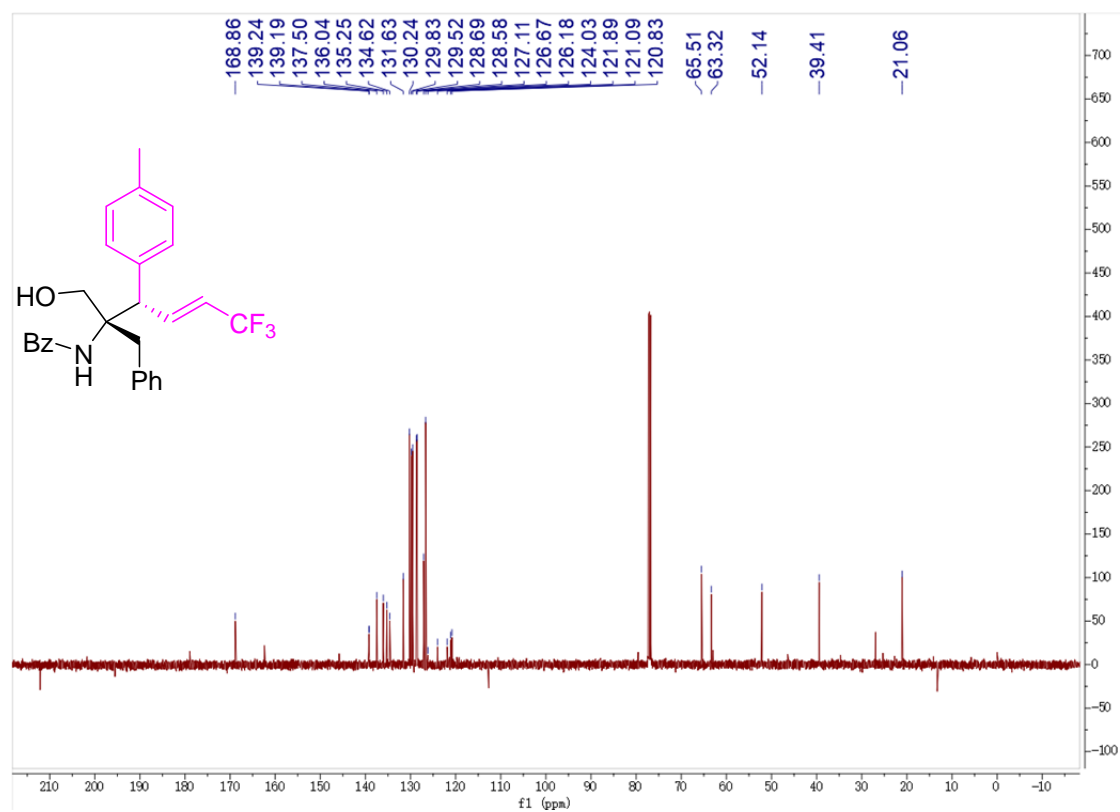
^{19}F NMR (470 MHz, CDCl_3) (**6a**)



^1H NMR (400 MHz, CDCl_3) (**7a**)



^{13}C NMR (126 MHz, CDCl_3) (**7a**)



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

