SUPPORTING INFORMATION

Organocatalytic Enantioselective [2 + 2] Cycloadditions towards Chiral Fused α-Trifluoromethyl Azetidines

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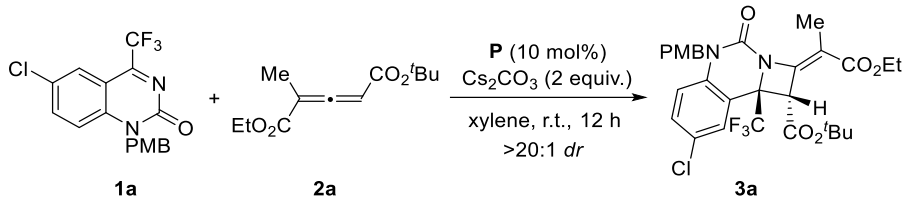
1. General information

All the starting materials were obtained from commercial sources and used without further purification unless otherwise stated. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AVANCE III HD (400 MHz) spectrometer in $CDCl_3$. Chemical shifts (δ) are reported in ppm, and the residual solvent peak was used as an internal reference $CDCl_3$ [δ (^{1}H) = 7.26 ppm, δ (^{13}C) = 77.16 ppm], CD_3OD [δ (^{1}H) = 2.05 ppm, δ (^{13}C) = 206.26, 29.84 ppm], $(CD_3)_2CO$ [δ (^{1}H) = 3.31 ppm, δ (^{13}C) = 49.00 ppm]. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), br s (broad singlet). Coupling constants (*J*) were reported in Hertz (Hz). All high resolution mass spectra were obtained on a Thermo LTQ mass spectrometer. For thin layer chromatography (TLC), Merck pre-coated TLC plates (Merck 60 F254) were used, and compounds were visualized with a UV light at 254 nm. Further visualization was achieved by staining with iodine, followed by heating on a hot plate. Flash chromatographic separations were performed on Merck 60 (0.040-0.063 mm) mesh silica gel. Enantiomeric excesses were determined by HPLC analysis using chiral column described below in detail. Optical rotations were measured with polarimeter.

All the phosphonium salt catalysts **P1-P8** used in this study were prepared via a P-alkylation reaction of our previously reported organophosphines according to the known procedures.[1] All the cyclic trifluoroketimines **1** and Allene **2** were synthesized following the methods reported in the literature.[2-3] The structure and absolute configurations of chiral fused Azetidines scaffolds were assigned by X-ray crystallographic analysis of the single crystal of chiral product **3f** (Table S5).

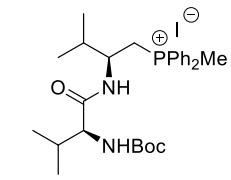
2. Optimization of reaction conditions

Table S1. Screening of the chiral phosphonium salt catalysts.[a]

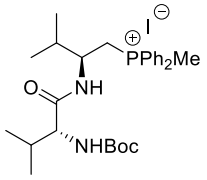


1a **2a** **3a**

Entry	**P**	yield (%)[b]	ee (%)[c]
1	**P1**	81	5
2	**P2**	82	8
3	**P3**	79	4
4	**P4**	85	5
5	**P5**	78	12
6	**P6**	73	23
7	**P7**	74	34
8	**P8**	80	52



P1



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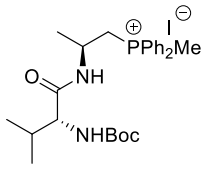

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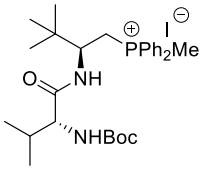

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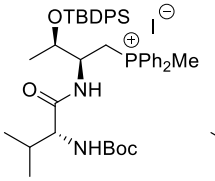

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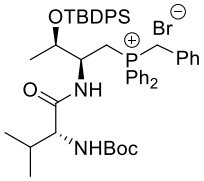

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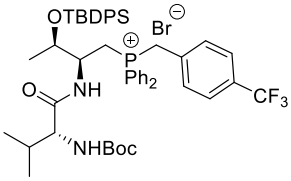

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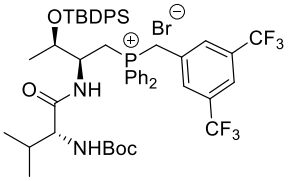
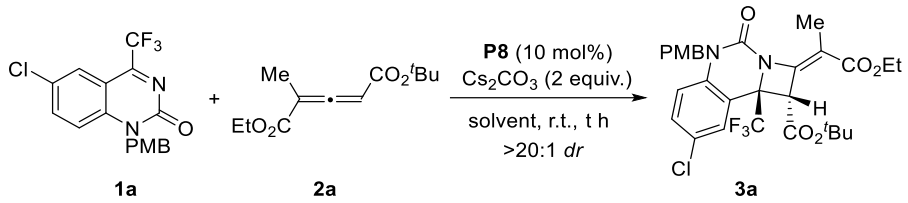


P8

[a] Reaction condition: substrates **1a** (0.1 mmol), **2a** (0.11 mmol), Cs_2CO_3 (0.2 mmol) and **P** (0.001 mmol) in 1 mL xylene at room temperature for 12 h. [b] Isolated yields based on **1a**. [c] The ee values were determined by chiral HPLC analysis. *dr* values were analyzed by ^{1}H NMR spectroscopy. TBDPS = *tert*-butyldiphenylsilyl.

Table S2. Screening of the solvents.[a]

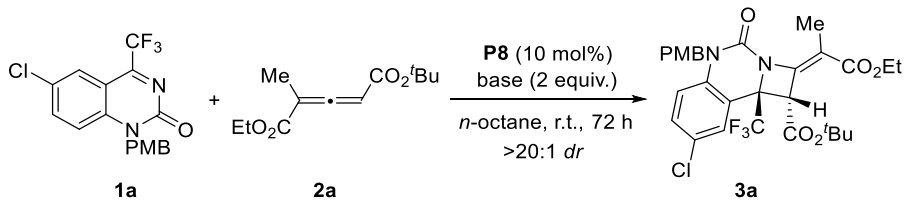


1a 2a 3a

Entry	**solvent**	t (h)	yield (%)[b]	ee (%)[c]
1	xylene	12	80	52
2	toluene	12	72	37
3	CH_2Cl_2	12	81	6
4	$CHCl_3$	12	77	3
5	Et_2O	12	79	21
6	*n*-hexane	72	82	72
7	PE	72	83	82
8	*n*-pentane	72	80	86
9	*c*-pentane	72	87	78
10	*n*-heptane	72	92	91
11	*n*-octane	72	96	98

[a] Reaction condition: substrates **1a** (0.1 mmol), **2a** (0.11 mmol), Cs_2CO_3 (0.2 mmol) and **P8** (0.001 mmol) in 1 mL solvent at room temperature for 12-72 h. [b] Isolated yields based on **1a**. [c] The ee values were determined by chiral HPLC analysis. *dr* values were analyzed by ^{1}H NMR spectroscopy.

Table S3. Screening of the bases.[a]



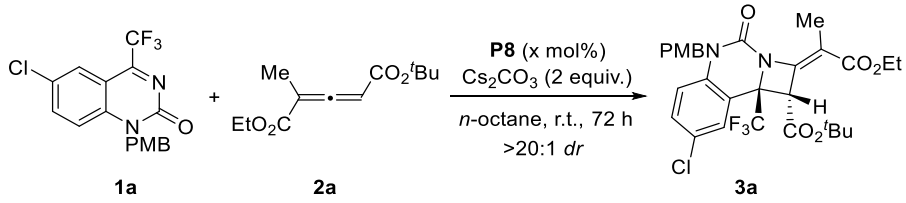
1a 2a 3a

Entry	**base**	yield (%)[b]	ee (%)[c]
1	Cs_2CO_3	96	98
2	Na_2CO_3	trace	-
3	K_2CO_3	86	82

4	K_3PO_4	76	16
5	K_3PO_4▪$7H_2O$	81	26
6	NaOH	73	32
7	KOH	65	0
8	DBU	78	0
9[d]	Cs_2CO_3	56	92
10[e]	Cs_2CO_3	94	96
11[f]	Cs_2CO_3	91	86

[a] Reaction condition: substrates **1a** (0.1 mmol), **2a** (0.11 mmol), base (0.2 mmol) and **P8** (0.001 mmol) in 1 mL *n*-octane at room temperature for 72 h. [b] Isolated yields based on **1a**. [c] The ee values were determined by chiral HPLC analysis. *dr* values were analyzed by ^{1}H NMR spectroscopy. [d] Cs_2CO_3 (0.1 mmol) was used. [e] Cs_2CO_3 (0.4 mmol). [f] Cs_2CO_3 (0.8 mmol).

Table S4. Screening of the catalyst loading and temperature.[a]



1a **2a** **3a**

Entry	**P8 (**mol%**)**	yield (%)[b]	ee (%)[c]
1	10	96	98
2[d]	10	trace	-
3	5	95	98
4	2.5	96	98
5	1	96	98

[a] Reaction condition: substrates **1a** (0.1 mmol), **2a** (0.11 mmol), Cs_2CO_3 (0.2 mmol) and **P8** (x mmol) in 1 mL *n*-octane at room temperature for 72 h. [b] Isolated yields based on **1a**. [c] The ee values were determined by chiral HPLC analysis. *dr* values were analyzed by ^{1}H NMR spectroscopy. [d] At 0 °C.

3. Preparation of phosphonium salt catalysts

All the phosphonium salt catalysts in this study were listed in **Figure S1**, which

were prepared by following our previously reported procedures.[1]

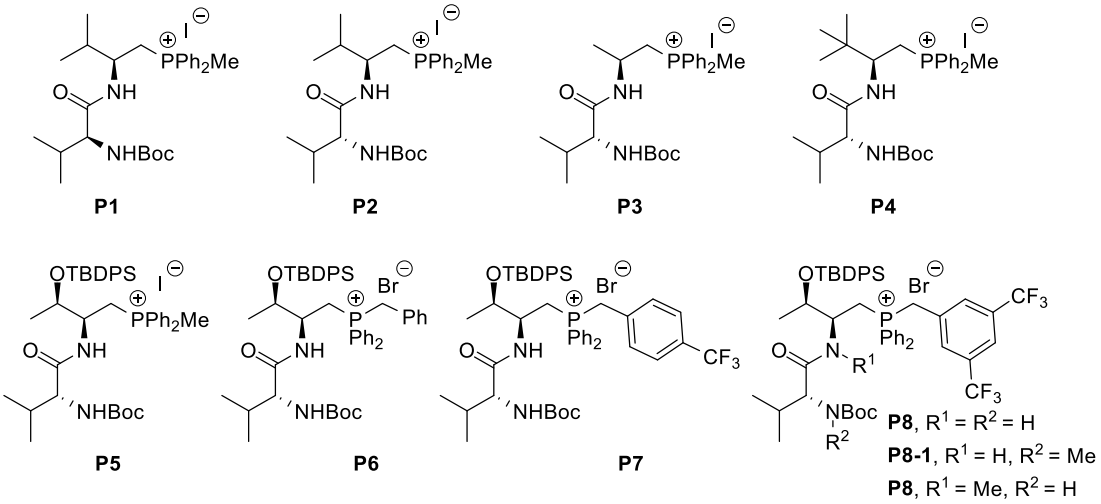
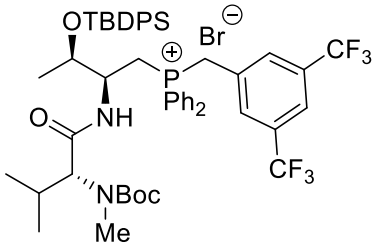


Figure S1. Bifunctional phosphonium salt catalysts in this study.

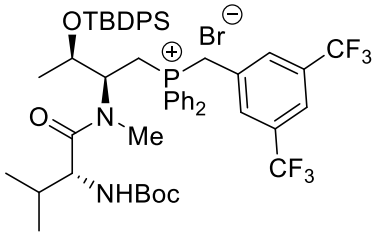
Characterization of the unknown phosphonium salts：

(3,5-bis(trifluoromethyl)benzyl)((2*S*,3*R*)-2-((*R*)-2-((tert-butoxycarbonyl)(methyl)amino)-3-methylbutanamido)-3-((tert-butyldiphenylsilyl)oxy)butyl)diphenylphosphonium bromide (P8-1)



A white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 8.4 Hz, 1H), 7.90-7.79 (m, 3H), 7.76-7.70 (m, 1H), 7.67-7.45 (m, 11H), 7.42 (d, *J* = 7.2 Hz, 1H), 7.39-7.21 (m, 7H), 6.18 (t, *J* = 16.0 Hz, 1H), 5.53 (t, *J* = 14.4 Hz, 1H), 5.21-5.07 (m, 1H), 4.18-4.01 (m, 3H), 2.99 (s, 3H), 2.90 (t, *J* = 14.0 Hz, 2H), 1.48 (s, 9H), 1.19 (d, *J* = 6.2 Hz, 3H), 1.03 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 6.5 Hz, 3H), 0.81 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.50, 157.52, 135.70, 135.59, 135.32 (d, *J* = 26.9 Hz), 133.55 (d, *J* = 9.3 Hz), 132.83, 131.04, 130.67 (d, *J* = 12.2 Hz), 130.20 (d, *J* = 12.1 Hz), 129.83, 127.71 (d, *J* = 9.8 Hz), 122.70 (q, *J* = 272.7 Hz), 115.69, 114.88, 79.78, 69.45 (d, *J* = 13.7 Hz), 65.05, 49.91, 31.56, 28.39, 28.00, 27.01, 20.96, 20.11, 19.22, 17.65; ^{31}P NMR (162 MHz, $CDCl_3$) δ 31.16; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.90; HRMS (ESI) *m/z* calcd for $C_{52}H_{62}BrF_6N_2O_4PSi$ $[M\text{-}Br]^+$ = 951.4115, found = 951.4108.

(3,5-bis(trifluoromethyl)benzyl)((2*S*,3*R*)-2-((*R*)-2-((tert-butoxycarbonyl)amino)-N,3-dimethylbutanamido)-3-((tert-butyldiphenylsilyl)oxy)butyl)diphenylphosphonium bromide (P8-2)

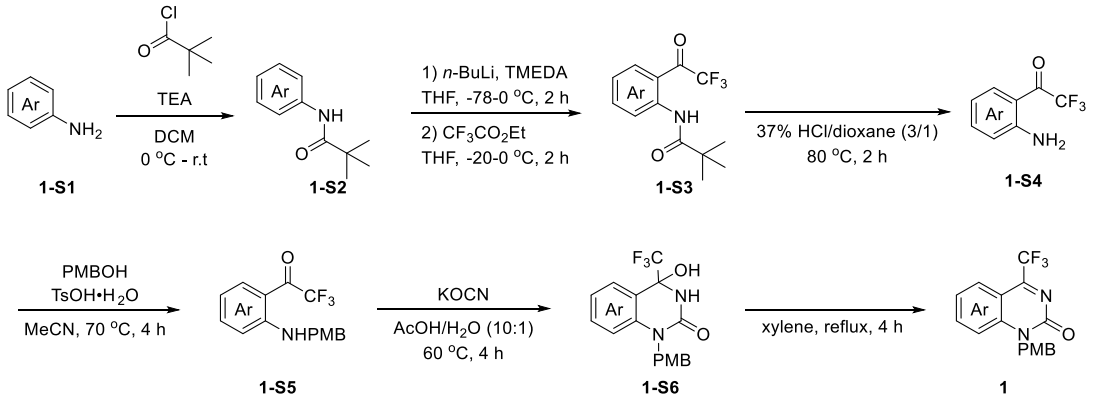


A white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 12.8, 7.8 Hz, 2H), 7.78-7.68 (m, 2H), 7.67-7.43 (m, 13H), 7.41-7.26 (m, 6H), 5.96 (t, *J* = 15.2 Hz, 1H), 5.25-5.05 (m, 2H), 4.88 (t, *J* = 14.8 Hz, 1H), 4.58 (p, *J* = 12.3 Hz, 1H), 3.87 (dd, *J* = 8.4, 3.4 Hz, 2H), 3.02 (t, *J* = 15.4 Hz, 1H), 2.79 (s, 3H), 1.78-1.67 (m, 1H), 1.49 (s, 9H), 0.98 (s, 9H), 0.96 (s, 3H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.59 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.87, 155.58, 135.83 (d, *J* = 6.1 Hz), 135.63, 135.42, 134.22 (d, *J* = 10.1 Hz), 133.61 (d, *J* = 8.9 Hz), 133.10, 132.81, 131.84 (d, *J* = 34.8 Hz), 131.46 (d, *J* = 8.8 Hz), 131.07, 130.23 (d, *J* = 12.1 Hz), 130.06 (d, *J* = 4.3 Hz), 129.93 (d, *J* = 13.0 Hz), 128.01, 127.82, 122.69 (q, *J* = 273.1 Hz), 121.86, 116.31 (d, *J* = 11.8 Hz), 115.43, 79.65, 72.28 (d, *J* = 14.2 Hz), 55.21, 52.01, 32.44, 30.33, 29.26 (d, *J* = 46.3 Hz), 28.39, 27.12, 20.00, 19.44, 19.22, 15.77; ^{31}P NMR (162 MHz, $CDCl_3$) δ 31.16; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.93; HRMS (ESI) *m/z* calcd for $C_{52}H_{62}BrF_6N_2O_4PSi$ $[M\text{-}Br]^+$ = 951.4115, found = 951.4110.

4. Preparation of both types of substrates

A. Preparation of cyclic trifluoroketimines **1**

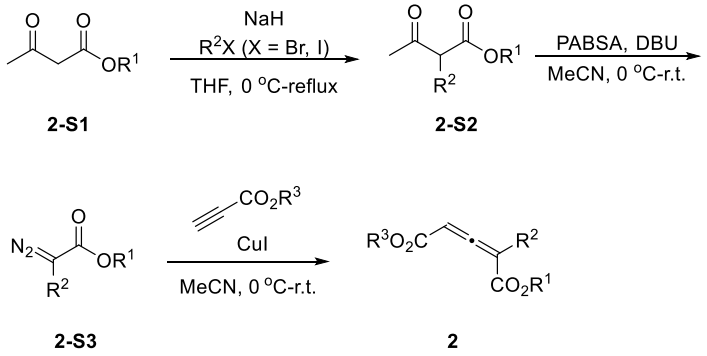
The all of cyclic trifluoroketimines **1** were synthesized according to the literature reports.[2]



The **1a-1d** are known compounds.

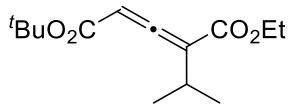
B. Preparation of Allene **2**

Allene **2** were prepared from corresponding benzyl bromide in quantitative yields following the literature procedure.[3]



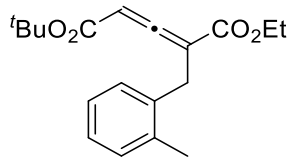
Unknown compounds **2c, 2f-2g**, **2l**, **2n-2u**, **2r**, **2s**, **2x** were fully characterized.

5-(*tert*-butyl) 1-ethyl 2-isopropylpenta-2,3-dienedioate (2c)



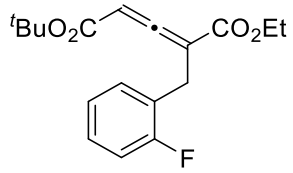
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 (d, *J* = 2.2 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.84-2.72 (m, 1H), 1.47 (s, 9H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 217.41, 165.28, 163.69, 111.30, 94.70, 81.59, 61.40, 28.18, 21.93, 21.85, 14.32, 1.16; HRMS (ESI^+) *m/z* calcd for $C_{14}H_{22}O_4$ $[M+Na]^+$ = 277.1416, found = 277.1407.

5-(*tert*-butyl) 1-ethyl 2-(2-methylbenzyl)penta-2,3-dienedioate (2f)



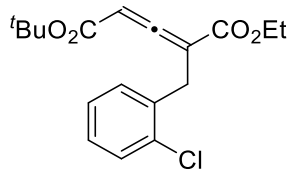
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23-7.16 (m, 1H), 7.15-7.07 (m, 3H), 5.68 (t, *J* = 3.0 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.65 (ddd, *J* = 47.8, 15.8, 3.0 Hz, 2H), 2.32 (s, 3H), 1.43 (s, 9H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.38, 165.29, 163.12, 136.68, 135.84, 130.25, 129.74, 126.99, 125.99, 104.14, 93.99, 81.75, 61.71, 32.31, 28.12, 19.59, 14.30; HRMS (ESI) *m/z* calcd for $C_{19}H_{24}O_4$ $[M+Na]^+$ = 339.1572, found = 339.1574.

5-(*tert*-butyl) 1-ethyl 2-(2-fluorobenzyl)penta-2,3-dienedioate (2g)



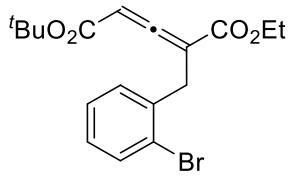
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.24 (m, 1H), 7.21-7.16 (m, 1H), 7.06-6.97 (m, 2H), 5.74 (t, *J* = 2.7 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.68 (ddd, *J* = 45.2, 15.5, 2.3 Hz, 2H), 1.43 (s, 9H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.26, 164.83, 162.85, 161.04 (d, *J* = 245.0 Hz), 131.15 (d, *J* = 4.2 Hz), 128.50 (d, *J* = 8.0 Hz), 124.62 (d, *J* = 15.5 Hz), 123.84 (d, *J* = 3.6 Hz), 115.20 (d, *J* = 21.7 Hz), 103.25, 94.00, 81.61, 61.57, 27.96, 14.13; ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.47; HRMS (APCI$^+$): calcd for $C_{18}H_{21}FO_4$ $[M+H]^+$ = 321.1502, found = 321.1508.

5-(*tert*-butyl) 1-ethyl 2-(2-chlorobenzyl)penta-2,3-dienedioate (2h)



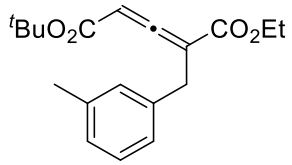
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.31 (m, 2H), 7.20-7.11 (m, 2H), 5.73 (t, *J* = 2.8 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.79 (ddd, *J* = 38.1, 15.6, 2.7 Hz, 2H), 1.42 (s, 9H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.34, 164.89, 162.84, 135.37, 134.33, 130.98, 129.39, 128.14, 126.65, 103.07, 94.07, 81.62, 61.60, 32.33, 27.98, 14.15; HRMS (APCI$^+$): calcd for $C_{18}H_{21}ClO_4$ $[M+H]^+$ = 337.1207, found = 337.1202.

5-(*tert*-butyl) 1-ethyl 2-(2-bromobenzyl)penta-2,3-dienedioate (2i)



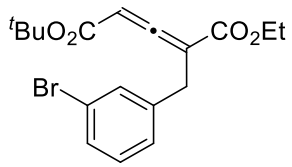
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.0 Hz, 1H), 7.32 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 5.73 (t, *J* = 2.8 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.80 (ddd, *J* = 34.8, 15.7, 2.8 Hz, 2H), 1.42 (s, 9H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.35, 164.86, 162.81, 137.14, 132.72, 130.94, 128.35, 127.30, 124.78, 103.17, 94.19, 81.63, 61.62, 34.89, 28.00, 14.16; HRMS (APCI$^+$): calcd for $C_{18}H_{21}BrO_4$ $[M+H]^+$ = 381.0701, found = 381.0703.

5-(*tert*-butyl) 1-ethyl 2-(3-bromobenzyl)penta-2,3-dienedioate (2j)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (t, *J* = 7.8 Hz, 1H), 7.10-7.05 (m, 2H), 7.02 (d, *J* = 7.4 Hz, 1H), 5.77 (t, *J* = 2.5 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.61 (ddd, *J* = 34.0, 15.2, 2.5 Hz, 2H), 2.32 (s, 3H), 1.47 (s, 9H), 1.24 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.63, 165.19, 163.22, 137.97, 137.73, 129.85, 128.30, 127.53, 126.05, 104.48, 93.74, 81.78, 61.66, 34.92, 28.16, 21.52, 14.27; HRMS (ESI) *m/z* calcd for $C_{19}H_{24}O_4$ $[M+Na]^+$ = 339.1572, found = 339.1575.

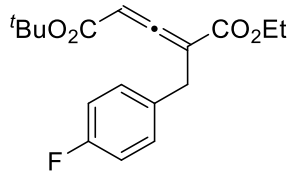
5-(*tert*-butyl) 1-ethyl 2-(3-bromobenzyl)penta-2,3-dienedioate (2l)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.23-7.11 (m, 2H), 5.79 (s, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 3.60 (ddd, *J* = 40.4, 15.2, 2.2 Hz, 2H), 1.47 (s, 9H), 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.27, 164.75, 162.80, 139.97, 138.35, 133.08, 131.89, 130.15, 129.83, 129.81, 128.61, 127.63, 122.32,

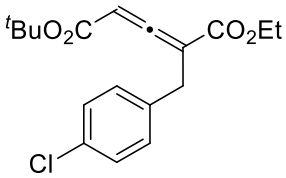
122.28, 103.71, 93.92, 81.89, 61.66, 39.48, 34.49, 28.01, 14.12; HRMS (APCI$^+$): calcd for $C_{18}H_{21}BrO_4$ $[M+H]^+$ = 381.0701, found = 381.0705.

5-(*tert*-butyl) 1-ethyl 2-(4-fluorobenzyl)penta-2,3-dienedioate (2n)



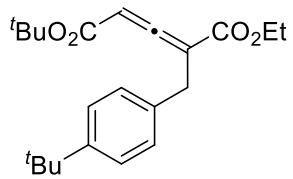
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.20 (m, 2H), 6.95 (t, *J* = 8.7 Hz, 2H), 5.78 (t, *J* = 2.5 Hz, 1H), 4.20 (qd, *J* = 7.1, 1.2 Hz, 2H), 3.61 (ddd, *J* = 41.6, 15.2, 2.6 Hz, 2H), 1.46 (s, 9H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.31, 164.87, 162.90, 161.74 (d, *J* = 243.0 Hz), 133.40 (d, *J* = 3.2 Hz), 130.44 (d, *J* = 7.9 Hz), 115.08 (d, *J* = 21.2 Hz), 104.29, 93.76, 81.79, 61.58, 34.17, 28.04, 14.12; ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.48; HRMS (APCI$^+$): calcd for $C_{18}H_{21}FO_4$ $[M+H]^+$ = 321.1502, found = 321.1503.

5-(*tert*-butyl) 1-ethyl 2-(4-chlorobenzyl)penta-2,3-dienedioate (2o)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.19 (m, 4H), 5.79 (t, *J* = 2.4 Hz, 1H), 4.20 (qd, *J* = 7.1, 1.1 Hz, 2H), 3.61 (ddd, *J* = 41.3, 15.2, 2.6 Hz, 2H), 1.47 (s, 9H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.29, 164.81, 162.85, 136.25, 132.48, 130.30, 128.43, 103.94, 93.81, 81.87, 61.63, 34.33, 28.05, 14.13; HRMS (APCI$^+$): calcd for $C_{18}H_{21}ClO_4$ $[M+H]^+$ = 337.1207, found = 337.1205.

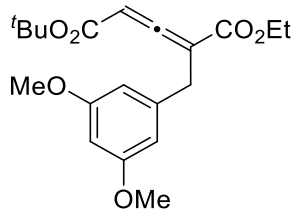
5-(*tert*-butyl) 1-ethyl 2-(4-(*tert*-butyl)benzyl)penta-2,3-dienedioate (2p)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 5.78 (t, *J* = 2.4 Hz, 1H), 4.21 (q, *J* = 7.0 Hz, 2H), 3.62 (ddd, *J* = 37.1, 18.6, 2.4 Hz, 2H), 1.46

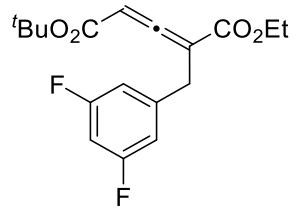
(s, 9H), 1.30 (s, 9H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.54, 165.06, 163.07, 149.38, 134.74, 128.57, 125.19, 104.32, 93.53, 81.59, 61.48, 34.40, 34.36, 31.36, 28.05, 14.15; HRMS (APCI$^+$): calcd for $C_{22}H_{31}O_4$ $[M+H]^+$ = 359.2222, found = 359.2225.

5-(*tert*-butyl) 1-ethyl 2-(3,5-dimethoxybenzyl)penta-2,3-dienedioate (2r)



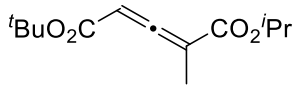
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.43 (d, J = 2.2 Hz, 2H), 6.31 (t, J = 2.2 Hz, 1H), 5.79 (t, J = 2.5 Hz, 1H), 4.21 (q, J = 7.0 Hz, 1H), 3.76 (s, 6H), 3.58 (ddd, J = 36.3, 15.2, 2.6 Hz, 2H), 1.45 (s, 9H), 1.25 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.55, 165.01, 163.02, 160.72, 139.99, 107.03, 104.22, 98.70, 93.74, 81.75, 61.57, 55.24, 35.05, 27.98, 14.15; HRMS (APCI$^+$): calcd for $C_{20}H_{26}O_6$ $[M+H]^+$ = 363.1808, found = 363.1813.

5-(*tert*-butyl) 1-ethyl 2-(3,5-difluorobenzyl)penta-2,3-dienedioate (2s)



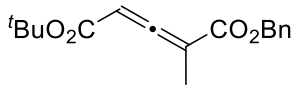
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.91-6.73 (m, 2H), 6.65 (t, J = 9.0 Hz, 1H), 5.82 (t, J = 2.3 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.61 (ddd, J = 49.5, 15.3, 2.2 Hz, 2H), 1.47 (s, 9H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.24, 164.63, 162.97 (d, J = 246.7 Hz), 162.84 (d, J = 246.6 Hz), 162.69, 141.68 (t, J = 9.2 Hz), 111.78 (d, J = 11.6 Hz), 111.78 (d, J = 24.9 Hz), 103.11, 102.21 (t, J = 25.2 Hz), 94.02, 82.14, 61.74, 34.64, 27.97, 14.11; ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.22; HRMS (APCI$^+$): calcd for $C_{18}H_{21}F_2O_4$ $[M+H]^+$ = 339.1408, found = 339.1405.

5-(*tert*-butyl) 1-isopropyl 2-methylpenta-2,3-dienedioate (2t)



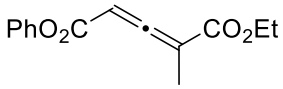
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (q, *J* = 2.9 Hz, 1H), 5.13-4.98 (m, 1H), 1.95 (d, *J* = 2.9 Hz, 3H), 1.47 (s, 9H), 1.25 (d, *J* = 2.7 Hz, 3H), 1.24 (d, *J* = 2.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.10, 165.38, 163.60, 100.38, 92.46, 81.69, 69.13, 28.18, 21.89, 21.85, 14.37; HRMS (ESI) *m/z* calcd for $C_{13}H_{20}O_4$ $[M+Na]^+$ = 263.1259, found = 263.1259.

1-benzyl 5-(*tert*-butyl) 2-methylpenta-2,3-dienedioate (2u)



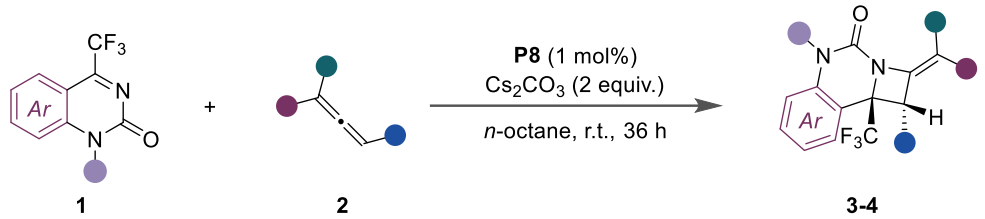
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.29 (m, 5H), 5.82 (q, *J* = 2.9 Hz, 1H), 5.22 (dd, *J* = 12.7, 19.3 Hz, 2H), 1.98 (d, *J* = 3.0 Hz, 3H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.36, 165.70, 163.38, 136.00, 128.63, 128.23, 127.76, 99.87, 92.78, 81.88, 66.93, 28.16, 14.37; HRMS (ESI) *m/z* calcd for $C_{17}H_{20}O_4$ $[M+Na]^+$ = 311.1259, found = 311.1252.

1-ethyl 5-phenyl 2-methylpenta-2,3-dienedioate (2x)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (t, *J* = 7.9 Hz, 2H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.14 (d, *J* = 7.6 Hz, 2H), 6.08 (q, *J* = 3.0 Hz, 1H), 4.26 (qd, *J* = 7.1, 1.3 Hz, 2H), 2.03 (d, *J* = 2.9 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 219.19, 165.21, 162.63, 150.57, 129.42, 126.01, 121.46, 100.77, 90.49, 61.77, 14.32, 14.20; HRMS ($APCI^+$): calcd for $C_{14}H_{24}O_4$ $[M+H]^+$ = 247.0970, found = 247.0978.

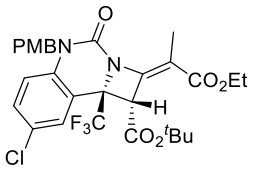
5. General procedure for the asymmetric [2 + 2] cycloaddition.



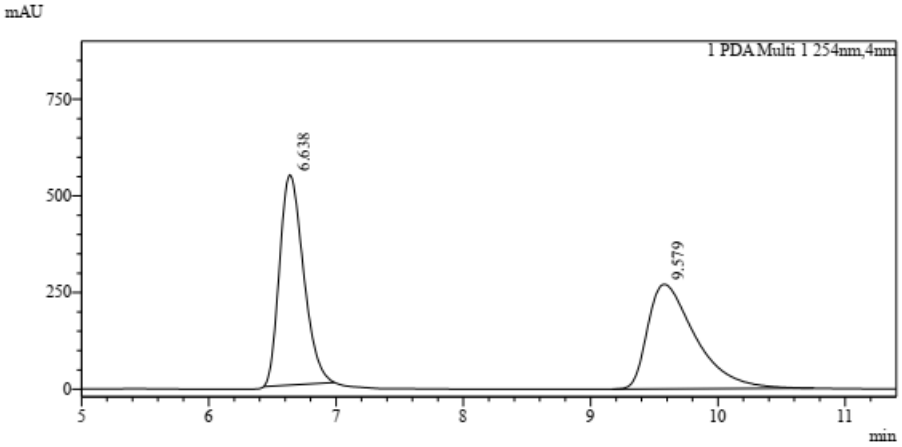
1 2 3-4

Representative procedure for the fused azetidines 3a: To a round bottle flask with a magnetic stirring bar were added **1a** (36.8 mg, 0.1 mmol) and Cs_2CO_3 (65.2 mg, 0.2 mmol) and catalyst **P8** (1.0 mg, 0.001 mmol), followed by the addition of **2a** (24.9 mg, 0.11 mmol) in *n*-octane (1 mL). The reaction mixture was stirred at rt for 72 h, and TLC show that the reaction was completed. Then, the residue was purified by column chromatography on silica gel (PE/EtOAc = 20:1-10:1) to afford the corresponding products **3a** (57 mg, 96% yield, 98% ee) as a white solid.

***tert*-butyl (*1S,9bR,E*)-8-chloro-2-(1-ethoxy-1-oxopropan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3a)**



A white solid; 96% yield; m.p. = 153-156 °C; $[\alpha]^{25}_D$ = -67.5 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17-7.10 (m, 2H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.79-6.74 (m, 2H), 6.72 (d, *J* = 9.4 Hz, 1H), 4.97 (dd, *J* = 53.7, 16.4 Hz, 2H), 4.44 (s, 1H), 4.24-3.99 (m, 2H), 3.70 (s, 3H), 2.26 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.17 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.70, 164.84, 158.95, 148.90, 148.78, 137.65, 130.82, 128.32, 127.56, 127.41, 126.26, 116.94, 116.15, 114.35, 109.47, 83.07, δ 68.58 (q, *J* = 31.9 Hz)60.80, 58.87, 55.24, 46.65, 27.62, 14.26, 14.04; ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.00; HRMS (ESI^+): calcd for $C_{29}H_{30}ClF_3N_2O_6$ $[M+H]^+$ = 595.1823, found = 595.1823; The ee value was 98%, t_R (major) = 7.2 min, t_R (minor) = 11.1 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

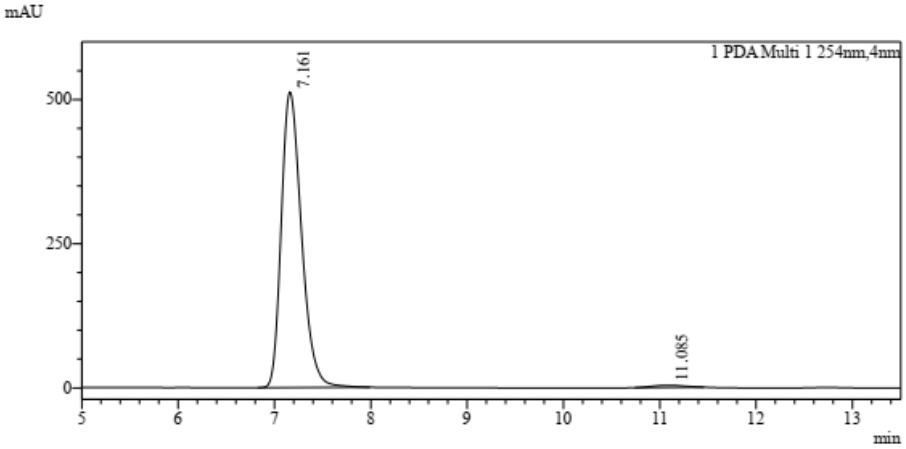


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	6.638	543298	66.749	7120786	50.176
2	9.579	270641	33.251	7070939	49.824
Total		813940	100.000	14191726	100.000

Racemic **3a**



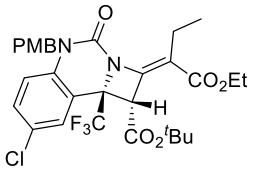
Peak Table

PDA Ch1 254nm

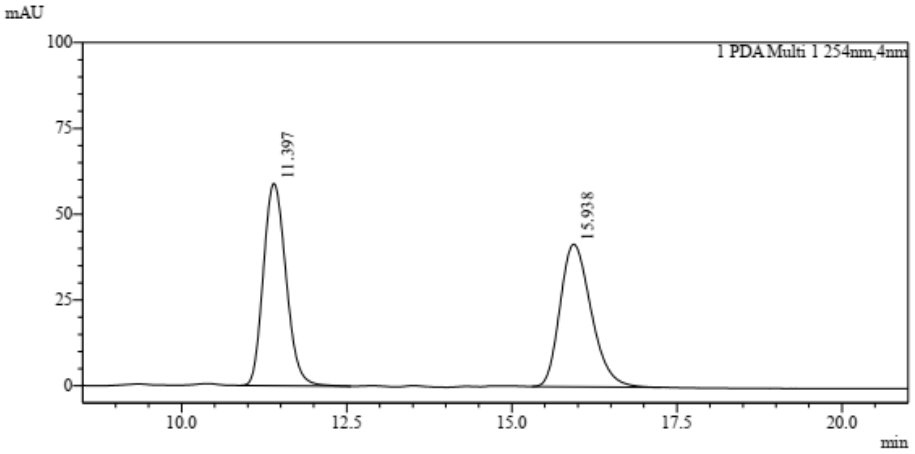
Peak#	Ret. Time	Height	Height%	Area	Area%
1	7.161	512317	99.277	7460435	98.853
2	11.085	3732	0.723	86569	1.147
Total		516049	100.000	7547004	100.000

Enantiomerically enriched **3a**

<u>*tert*-butyl (*1S,9bR,E*)-8-chloro-2-(1-ethoxy-1-oxobutan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3b)</u>



A white solid; 90% yield; m.p. = 136-138 °C; $[\alpha]^{25}_{D}$ = -57.6 (c 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.23-7.18 (m, 2H), 7.13 (d, *J* = 8.7 Hz, 2H), 6.85-6.77 (m, 3H), 5.05 (dd, *J* = 21.4, 16.6 Hz, 2H), 4.48 (s, 1H), 4.28-4.10 (m, 2H), 3.01-2.70 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.20 (s, 9H), 1.10 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.41, 164.73, 158.94, 148.88, 148.38, 137.60, 130.81, 128.44, 127.54, 127.44, 126.32, 116.89, 116.32, 115.22, 114.33, 82.77, 68.49 (q, *J* = 43.7 Hz), 60.72, 58.57, 55.29, 46.78, 27.53, 21.43, 15.53, 14.28; ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.02; HRMS (ESI^+): calcd for $C_{30}H_{32}ClF_3N_2O_6$ $[M+Na]^+$ = 631.1799, found = 631.1802; The ee value was 96%, t_R (major) = 12.1 min, t_R (minor) = 16.2 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

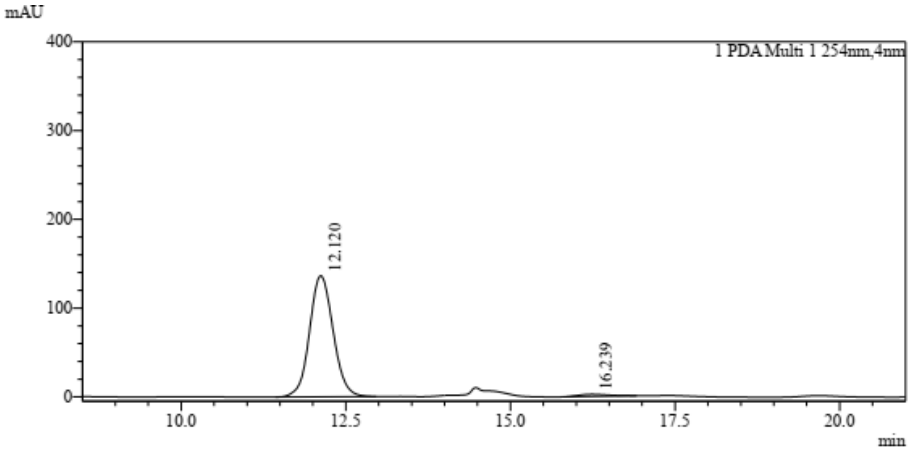


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	11.397	58889	58.651	1406232	50.725
2	15.938	41517	41.349	1366053	49.275
Total		100406	100.000	2772285	100.000

Racemic **3b**



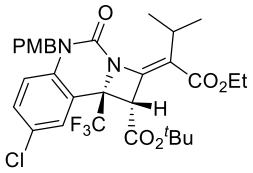
Peak Table

PDA Ch1 254nm

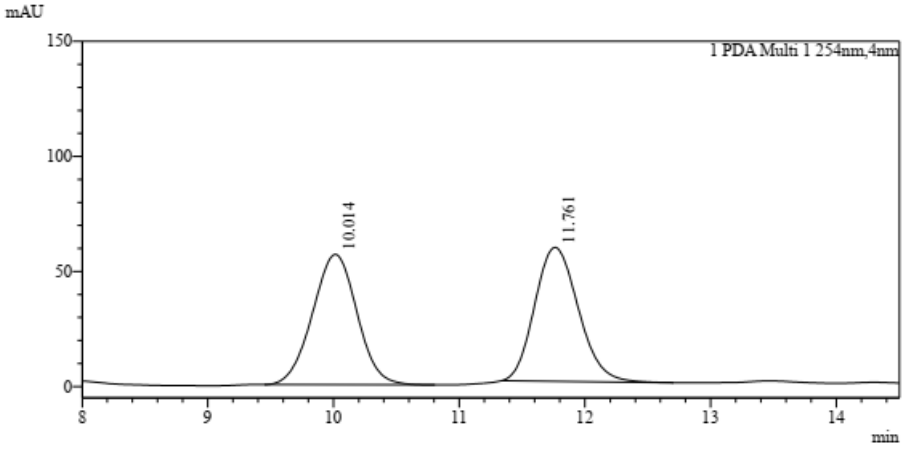
Peak#	Ret. Time	Height	Height%	Area	Area%
1	12.120	136424	98.309	3412155	97.792
2	16.239	2347	1.691	77047	2.208
Total		138770	100.000	3489201	100.000

Enantiomerically enriched **3b**

tert-butyl (_1S,9bR,E_)-8-chloro-2-(1-ethoxy-3-methyl-1-oxobutan-2-ylidene)-5- (4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3c)



A white solid; 95% yield; m.p. = 129-131 °C; $[\alpha]^{25}_{D}$ = -103.2 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22-7.16 (m, 2H), 7.13 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 6.78 (d, *J* = 9.6 Hz, 1H), 5.05 (dd, *J* = 69.3, 16.4 Hz, 2H), 4.50 (s, 1H), 4.29-4.08 (m, 2H), 4.06-3.97 (m, 1H), 3.76 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.26 (d, *J* = 6.9 Hz, 3H), 1.23 (d, *J* = 7.0 Hz, 3H), 1.18 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.73, 164.73, 158.96, 148.70, 148.15, 137.57, 130.79, 128.31, 127.56, 127.47, 126.35, 119.88, 116.78, 116.01, 114.33, 82.82, 68.44 (q, *J* = 32.0 Hz), 60.33, 59.35, 55.25, 46.76, 28.40, 27.49, 22.05, 20.80, 14.20; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.92; HRMS (ESI^+): calcd for $C_{31}H_{34}ClF_3N_2O_6$ $[M+Na]^+$ = 645.1955, found = 645.1956; The ee value was 94%, t_R (major) = 10.6 min, t_R (minor) = 12.3 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

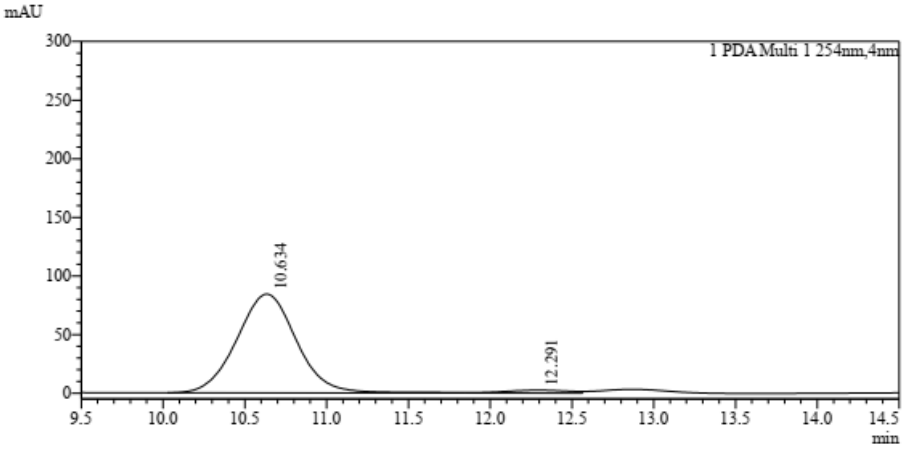


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	10.014	56636	49.336	1395093	49.801
2	11.761	58160	50.664	1406250	50.199
Total		114796	100.000	2801343	100.000

Racemic **3c**



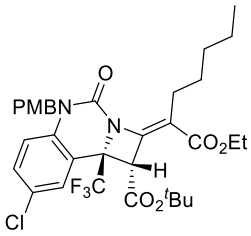
Peak Table

PDA Ch1 254nm

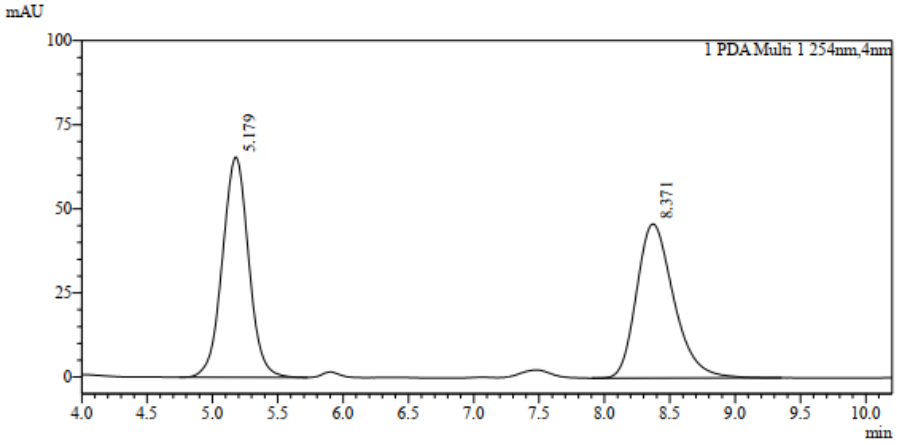
Peak#	Ret. Time	Height	Height%	Area	Area%
1	10.634	84208	97.040	2144126	96.765
2	12.291	2568	2.960	71683	3.235
Total		86776	100.000	2215809	100.000

Enantiomerically enriched **3c**

<u>*tert*-butyl (*1S,9bR,E*)-8-chloro-2-(1-ethoxy-1-oxoheptan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3d)</u>



A white solid; 90% yield; m.p. = 138-142 ºC; $[\alpha]^{25}_{D}$ = -91.5 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23-7.16 (m, 2H), 7.14 (d, *J* = 8.7 Hz, 2H), 6.86-6.76 (m, 3H), 5.04 (dd, *J* = 16.4, 34.2 Hz, 2H), 4.49 (s, 1H), 4.28-4.09 (m, 2H), 3.77 (s, 3H), 3.01-2.71 (m, 2H), 1.57-1.42 (m, 4H), 1.34-1.27 (m, 7H), 1.19 (s, 9H), 0.87 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.59, 164.76, 158.92, 148.93, 148.26, 137.66, 130.77, 128.42, 127.56, 126.29, 116.93, 116.49, 114.29, 113.77, 82.82, 68.22 (q, *J* = 32.2 Hz), 60.70, 58.40, 55.27, 46.90, 31.39, 30.39, 27.55, 22.65, 14.27, 14.09; ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.06; HRMS (ESI^+): calcd for $C_{33}H_{38}ClF_3N_2O_6$ $[M+Na]^+$ = 673.2268, found = 673.2263; The ee value was 89%, t_R (major) = 5.1 min, t_R (minor) = 8.1 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

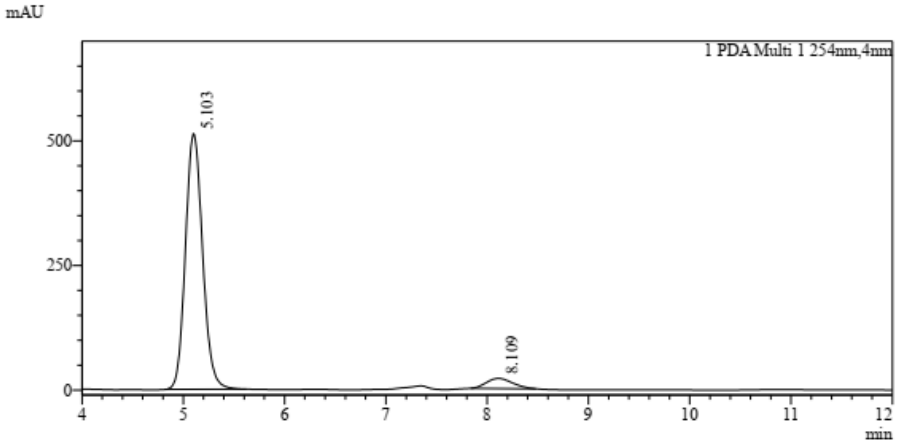


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	5.179	65422	58.815	914199	50.203
2	8.371	45810	41.185	906811	49.797
Total		111232	100.000	1821010	100.000

Racemic **3d**



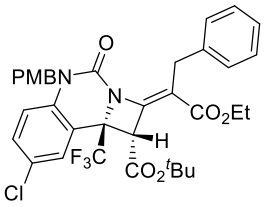
Peak Table

PDA Ch1 254nm

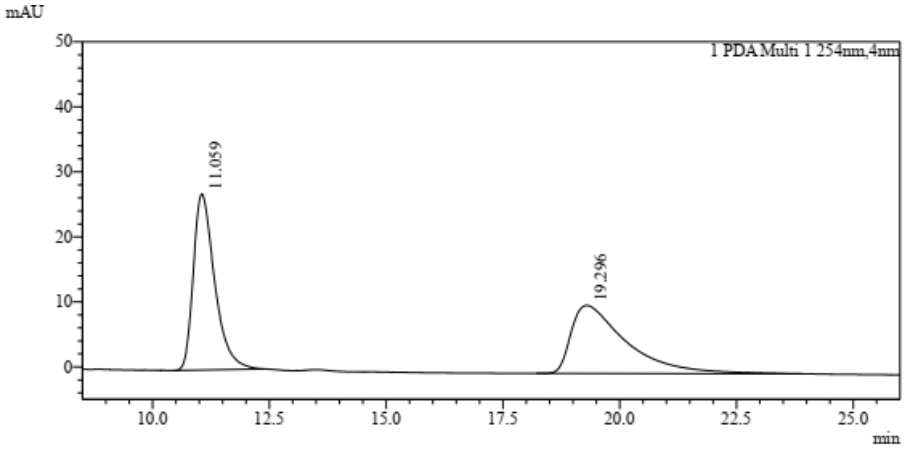
Peak#	Ret. Time	Height	Height%	Area	Area%
1	5.103	512866	96.208	6052891	94.354
2	8.109	20213	3.792	362192	5.646
Total		533079	100.000	6415083	100.000

Enantiomerically enriched **3d**

tert-butyl (_1S,9bR,E_)-8-chloro-2-(1-ethoxy-1-oxo-3-phenylpropan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3e)



A white solid; 91% yield; m.p. = 138-140 °C; $[\alpha]^{25}_{D}$ = -72.8 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.20 (m, 6H), 7.18-7.12 (m, 1H), 7.09 (d, *J* = 8.6 Hz, 2H), 6.82 (t, *J* = 8.4 Hz, 3H), 5.01 (dd, *J* = 76.2, 16.3 Hz, 2H), 4.59 (s, 1H), 4.47 (d, *J* = 14.9 Hz, 1H), 4.20-4.02 (m, 3H), 3.78 (s, 3H), 1.21 (s, 9H), 1.17 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.13, 163.48, 157.87, 148.91, 147.12, 140.10, 136.54, 129.85, 127.61, 127.45, 126.93, 126.57, 126.40, 125.31, 124.63, 115.99, 115.46, 113.25, 110.28, 82.14, 67.28 (q, *J* = 49.20 Hz), 59.78, 57.27, 54.24, 46.05, 32.23, 26.39, 12.87; ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.06; HRMS (ESI^+): calcd for $C_{35}H_{33}Cl_2F_3N_2O_6$ $[M+Na]^+$ = 693.1955, found = 693.1955; The ee value was 97%, t_R (major) = 12.6 min, t_R (minor) = 23.2 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

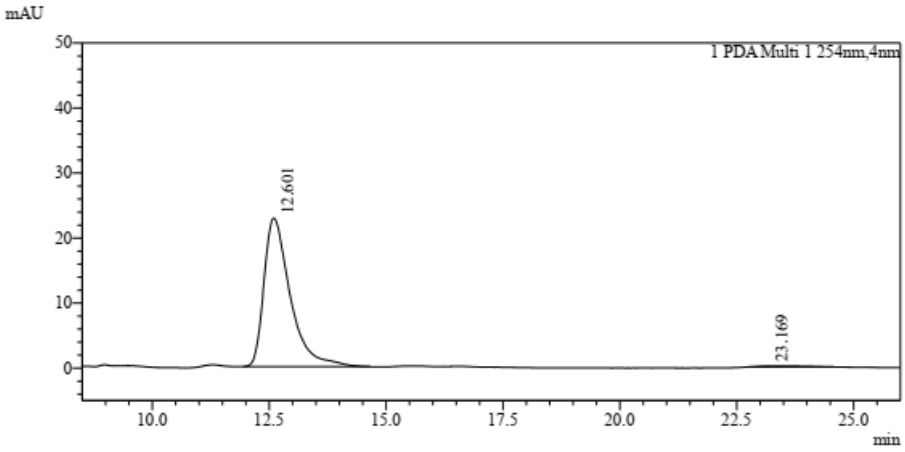


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	11.059	27092	72.131	862831	50.101
2	19.296	10468	27.869	859351	49.899
Total		37560	100.000	1722182	100.000

Racemic **3e**



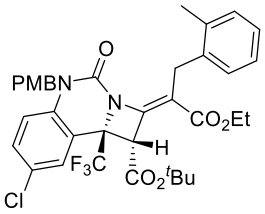
Peak Table

PDA Ch1 254nm

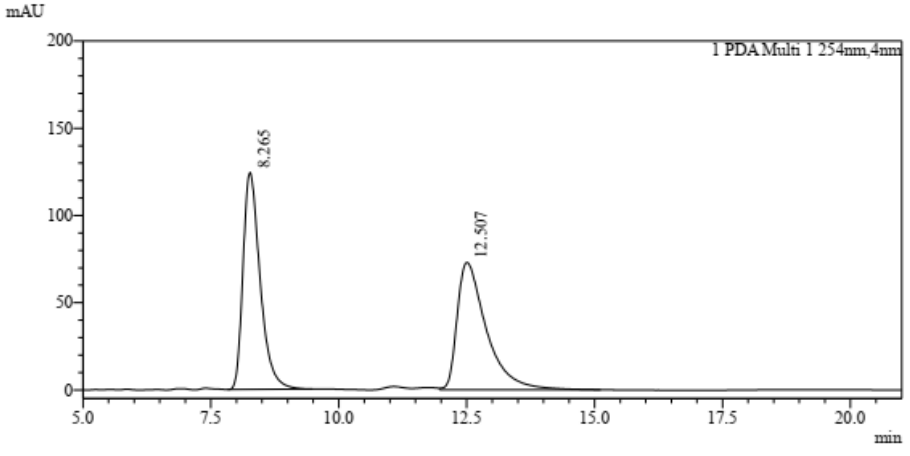
Peak#	Ret. Time	Height	Height%	Area	Area%
1	12.601	22826	99.202	893601	98.698
2	23.169	184	0.798	11788	1.302
Total		23010	100.000	905389	100.000

Enantiomerically enriched **3e**

<u>*tert*-butyl (*1S,9bR,E*)-8-chloro-2-(1-ethoxy-1-oxo-3-(o-tolyl)propan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3f)</u>



A white solid; 96% yield; m.p. = 148-152 ºC; $[\alpha]^{25}_{D}$ = -55.7 (c 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.26-7.24 (m, 1H), 7.22 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.15-7.10 (m, 1H), 7.06 (d, *J* = 3.2 Hz, 3H), 7.00 (d, *J* = 8.6 Hz, 2H), 6.83-6.73 (m, 3H), 4.94 (dd, *J* = 16.3, 104.3 Hz, 2H), 4.65 (s, 1H), 4.25 (dd, *J* = 89.7, 15.7 Hz, 2H), 4.24-3.97 (m, 2H), 3.77 (s, 3H), 2.39 (s, 3H), 1.25 (s, 9H), 1.15 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.30, 164.55, 158.88, 150.47, 147.98, 139.68, 137.63, 136.03, 130.89, 129.8, 128.63, 127.59, 127.52, 127.24, 126.36, 125.49, 125.37, 117.04, 116.53, 114.28, 110.68, 83.37, 68.34(q, J = 30.3 Hz), 60.83, 58.18, 55.27, 47.09, 30.48, 27.72, 19.83, 14.08; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.72; HRMS (ESI^+): calcd for $C_{36}H_{36}ClF_3N_2O_6$ $[M+Na]^+$ = 707.2112, found = 707.2111; The ee value was >99.9%, t_R (major) = 8.5 min, t_R (minor) = 12.9 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

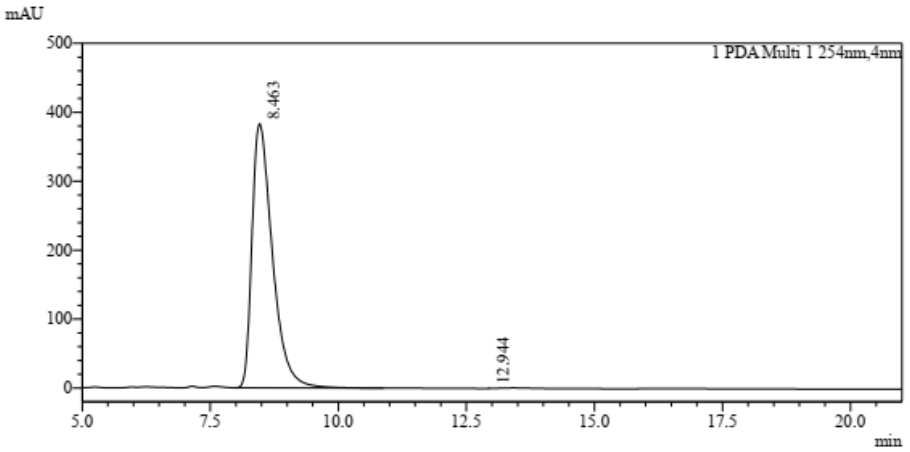


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	8.265	124307	62.981	2902381	49.867
2	12.507	73066	37.019	2917805	50.133
Total		197373	100.000	5820187	100.000

Racemic **3f**



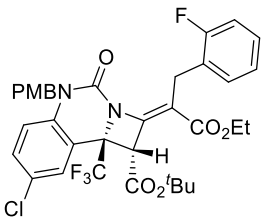
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	8.463	382987	100.001	10648127	100.000
2	12.944	-5	-0.001	9	0.000
Total		382982	100.000	10648136	100.000

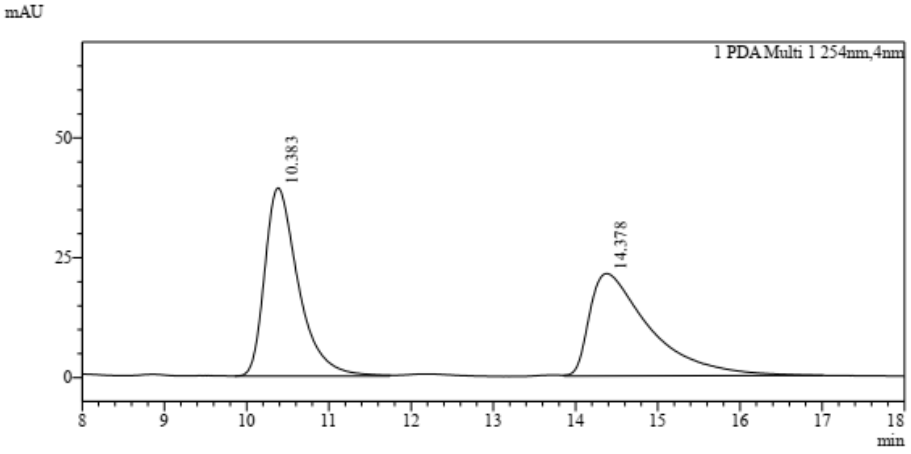
Enantiomerically enriched **3f**

tert-butyl (_1S,9bR,E_)-8-chloro-2-(1-ethoxy-3-(2-fluorophenyl)-1-oxopropan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3g)



A white solid; 86% yield; m.p. = 99-102 °C; $[\alpha]^{25}_D$ = 15.7 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ7.26-7.21 (m, 2H), 7.20-7.10 (m, 2H), 7.07 (d, *J* = 8.7 Hz, 2H), 7.03-6.94 (m, 2H), 6.83 (d, *J* = 8.8 Hz, 1H), 6.80 (d, *J* = 8.7 Hz, 2H), 5.00 (dd, *J* = 66.6, 16.3 Hz, 2H), 4.63 (s, 1H), 4.35 (dd, *J* = 69.4, 15.5 Hz, 2H), 4.17-3.97 (m, 2H), 3.77 (s, 3H), 1.24 (s, 9H), 1.15 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.00, 164.46, 160.88 (d, *J* = 244.2 Hz), 158.95, 150.80, 148.16, 137.65, 130.90, 130.05 (d, *J* = 4.6 Hz), 128.66, 128.18 (d, *J* = 15.2 Hz), 127.64, 127.46, 127.20 (d, *J* = 8.0 Hz), 126.36, 123.42 (d, *J* = 3.5 Hz), 117.09, 116.52, 114.96 (d, *J* = 22.1 Hz), 114.31, 109.76, 83.25, 68.46 (q, *J* = 32.5 Hz), 60.81, 58.23, 55.27, 47.04, 27.67, 26.67, 26.63, 13.98; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.98, -118.22; HRMS (ESI^+): calcd for $C_{35}H_{33}ClF_4N_2O_6$ $[M+Na]^+$ = 711.1861, found = 711.1858; The ee value was 91%, t_R (major) = 10.2 min, t_R (minor) = 14.6 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate

= 1.0 mL/min).

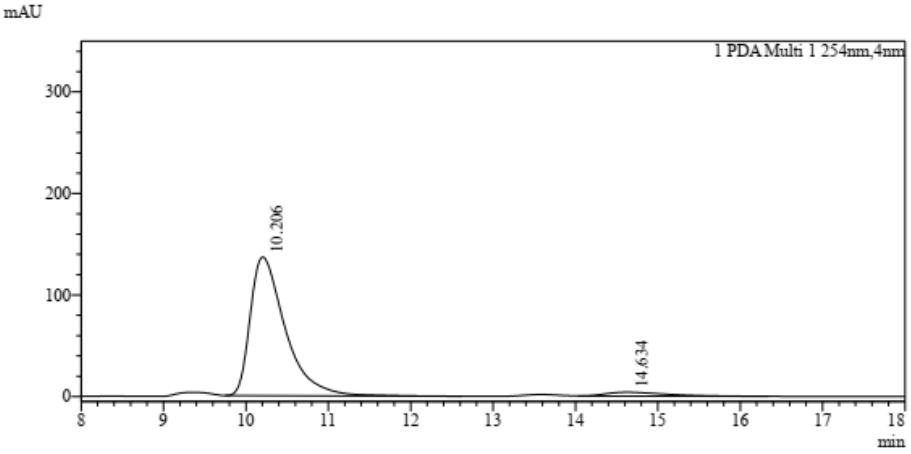


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	10.383	39255	64.745	1119687	50.648
2	14.378	21375	35.255	1091045	49.352
Total		60631	100.000	2210732	100.000

Racemic **3g**



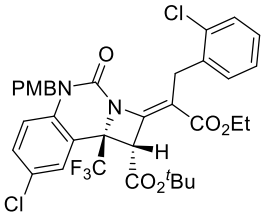
Peak Table

PDA Ch1 254nm

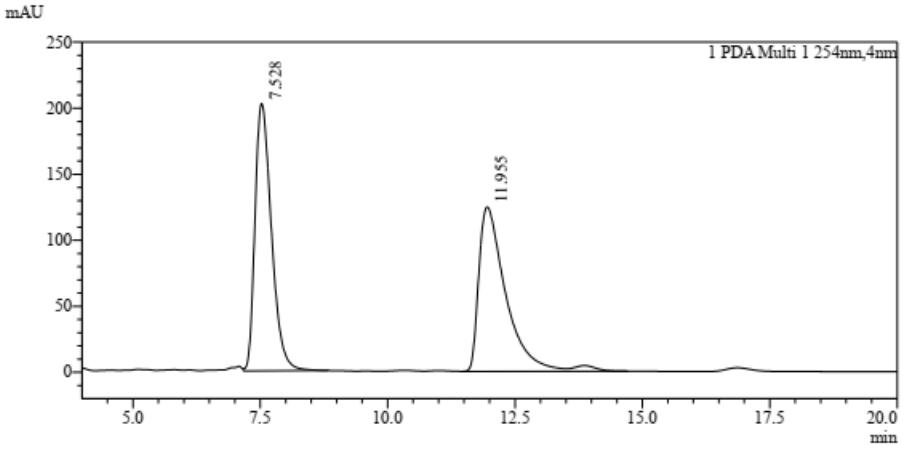
Peak#	Ret. Time	Height	Height%	Area	Area%
1	10.206	136532	97.322	4043914	95.533
2	14.634	3757	2.678	189082	4.467
Total		140289	100.000	4232997	100.000

Enantiomerically enriched **3g**

***tert*-butyl (*1S,9bR,E*)-8-chloro-2-(3-(2-chlorophenyl)-1-ethoxy-1-oxopropan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3h)**



A white solid; 88% yield; m.p. = 110-116 ºC; $[\alpha]^{25}_{D}$ = -81.7 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.31 (m, 1H), 7.25-7.06 (m, 5H), 7.01 (d, *J* = 8.7 Hz, 2H), 6.81 (d, *J* = 8.9 Hz, 1H), 6.77 (d, *J* = 8.7 Hz, 2H), 4.95 (dd, *J* = 63.5, 16.3 Hz, 2H), 4.66 (s, 1H), 4.41 (dd, J = 63.5, 16.2 Hz, 2H), 4.16-4.00 (m, 2H), 3.77 (s, 3H), 1.27 (s, 9H), 1.13 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.02, 164.46, 158.93, 151.26, 148.00, 139.16, 137.60, 133.86, 130.93, 129.18, 128.95, 128.65, 127.67, 127.44, 126.80, 126.37, 126.16, 117.08, 116.38, 114.28, 109.74, 83.34, 68.52 (q, *J* = 32.1 Hz), 60.85, 58.27, 55.26, 47.00, 31.19, 27.73, 14.02; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.95; HRMS (ESI^+): calcd for $C_{35}H_{33}Cl_2F_3N_2O_6$ $[M+Na]^+$ = 727.1565, found = 727.1568; The ee value was 85%, t_R (major) = 7.9 min, t_R (minor) = 13.5 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

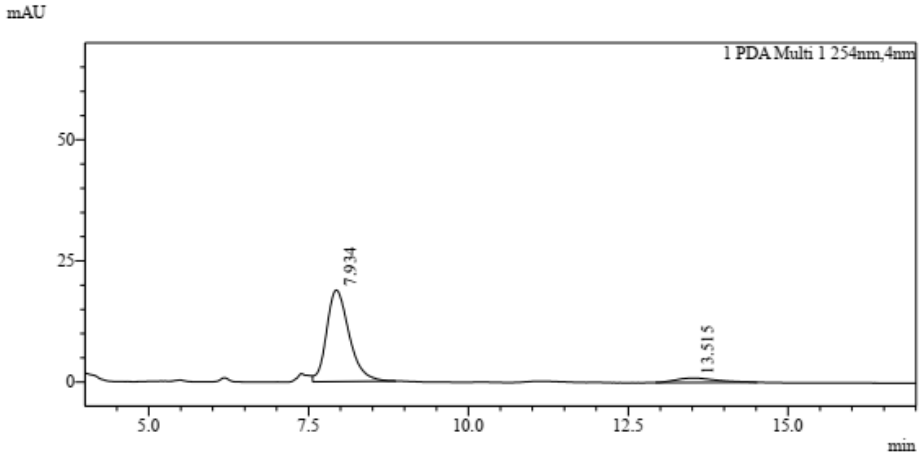


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	7.528	202403	61.941	4551498	49.464
2	11.955	124364	38.059	4650138	50.536
Total		326767	100.000	9201636	100.000

Racemic **3h**



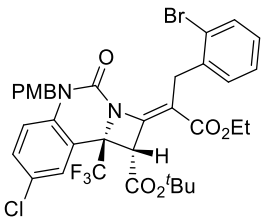
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	7.934	18888	95.463	465018	92.310
2	13.515	898	4.537	38741	7.690
Total		19785	100.000	503758	100.000

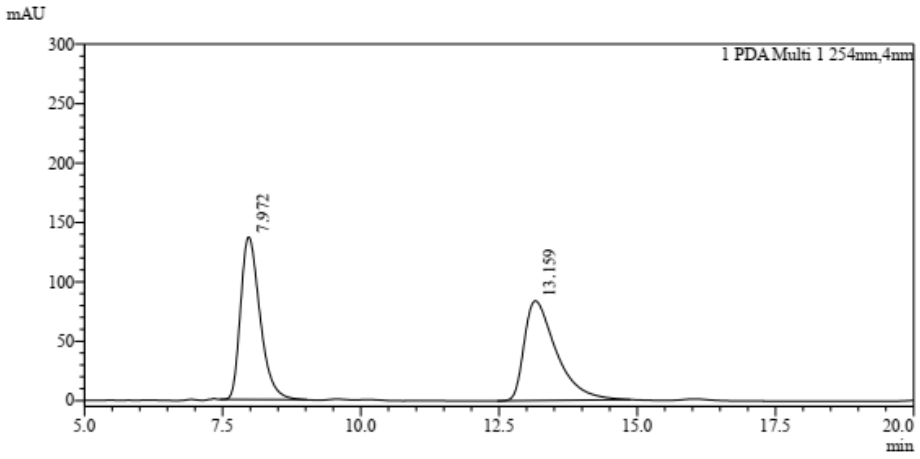
Enantiomerically enriched **3h**

***tert*-butyl (*1S,9bR,E*)-2-(3-(2-bromophenyl)-1-ethoxy-1-oxopropan-2-ylidene)- 8-chloro-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3i)**



A white solid; 91% yield; m.p. = 100-105 °C; $[\alpha]^{25}_{D}$ = -103.5 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.26-7.12 (m, 4H), 7.07-6.96 (m, 3H), 6.81 (d, *J* = 8.9 Hz, 1H), 6.77 (d, *J* = 8.7 Hz, 2H), 4.95 (dd, *J* = 63.8, 16.4 Hz, 2H), 4.67 (s, 1H), 4.40 (dd, *J* = 86.4, 16.2 Hz, 2H), 4.19-3.98 (m, 2H), 3.77 (s, 3H), 1.27 (s, 9H), 1.14 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.01, 164.44, 158.93, 151.32, 147.97, 140.90, 137.59, 132.50, 130.93, 128.87, 128.65, 127.68, 127.45, 127.08, 126.81, 126.37, 124.55, 117.08, 116.36, 114.27, 109.86, 83.35, 68.65 (q, J = 32.3 Hz), 60.86, 58.27, 55.26, 46.99, 34.04, 27.73, 14.05; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.94; HRMS (ESI^+): calcd for $C_{35}H_{33}BrClF_3N_2O_6$ $[M+Na]^+$ = 771.1060, found =

771.1060; The ee value was 97%, t_R (major)= 8.6 min, t_R (minor) = 14.7 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

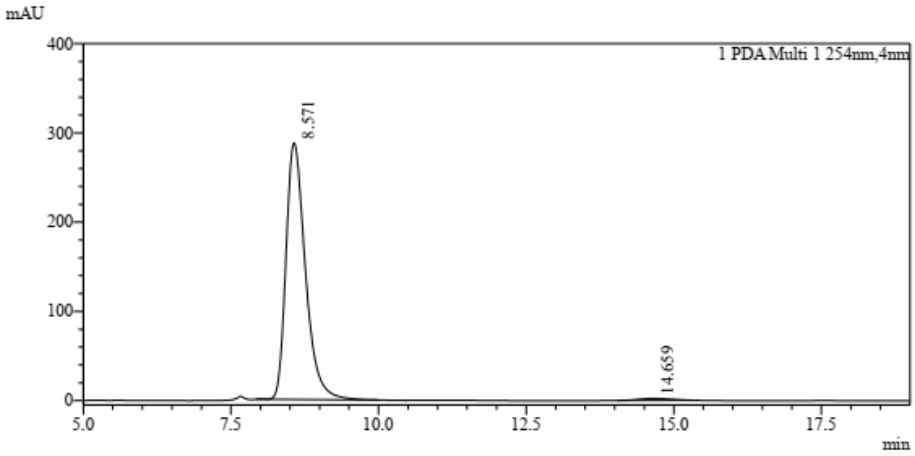


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	7.972	136744	61.970	3351663	49.728
2	13.159	83916	38.030	3388351	50.272
Total		220660	100.000	6740014	100.000

Racemic **3i**



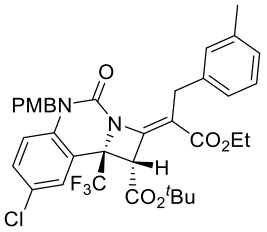
Peak Table

PDA Ch1 254nm

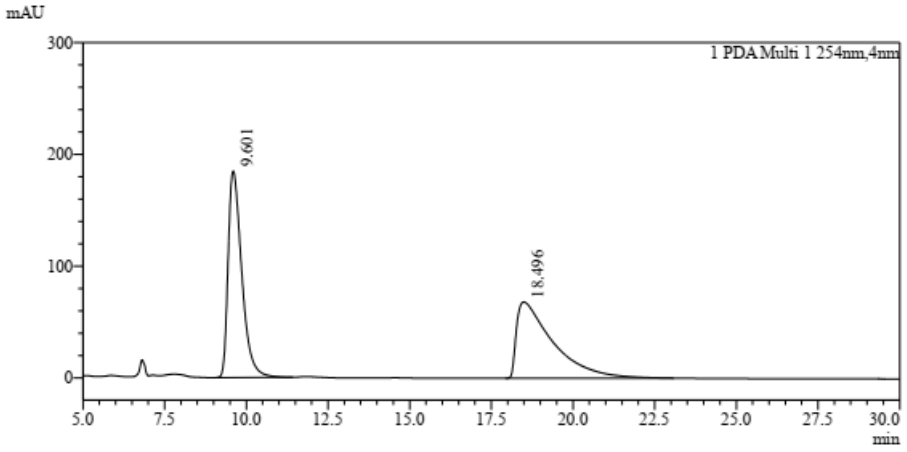
Peak#	Ret. Time	Height	Height%	Area	Area%
1	8.571	287331	99.262	6579154	98.697
2	14.659	2135	0.738	86828	1.303
Total		289467	100.000	6665982	100.000

Enantiomerically enriched **3i**

<u>*tert*-butyl (*1S,9bR,E*)-8-chloro-2-(1-ethoxy-1-oxo-3-(m-tolyl)propan-2-ylidene)- 5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3j)</u>



A white solid; 93% yield; m.p. = 118-122 ºC; $[\alpha]^{25}_{D}$ = -57.3 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.20 (m, 2H), 7.16-7.06 (m, 4H), 7.04 (d, *J* = 7.6 Hz, 1H), 6.97 (d, *J* = 7.4 Hz, 1H), 6.87-6.78 (m, 3H), 5.02 (dd, *J* = 80.0, 16.4 Hz, 2H), 4.59 (s, 1H), 4.29 (dd, *J* = 81.4, 14.8 Hz, 2H), 4.25-3.98 (m, 2H), 3.78 (s, 3H), 2.30 (s, 3H), 1.21 (s, 9H), 1.18 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.13, 163.49, 157.86, 148.74, 147.20, 139.82, 136.56, 136.33, 129.83, 128.35, 127.56, 126.75, 126.56, 126.45, 125.41, 125.28, 124.49, 115.97, 115.37, 113.25, 110.64, 82.05, 67.31 (q, *J* = 32.2 Hz), 59.76, 57.45, 54.21, 46.00, 32.26, 26.57, 20.46, 13.03; ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.07; HRMS (ESI^+): calcd for $C_{36}H_{36}ClF_3N_2O_6$ $[M+Na]^+$ = 707.2112, found = 707.2119; The ee value was >99.9%, t_R (major) = 12.1 min, t_R (minor) = 23.1 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

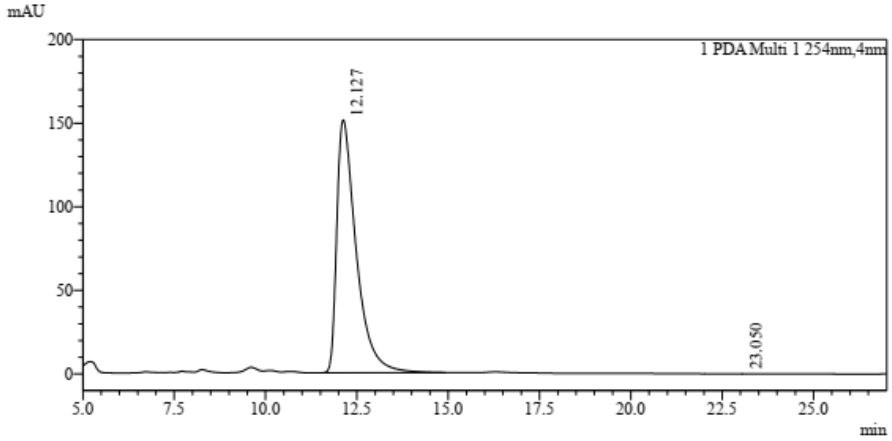


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	9.601	184874	73.031	5372403	50.305
2	18.496	68271	26.969	5307188	49.695
Total		253145	100.000	10679591	100.000

Racemic **3j**



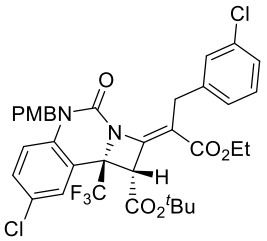
Peak Table

PDA Ch1 254nm

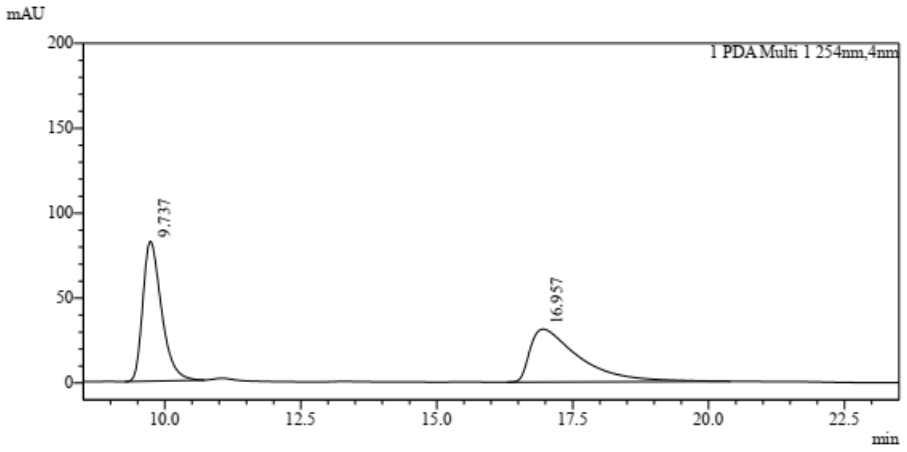
Peak#	Ret. Time	Height	Height%	Area	Area%
1	12.127	151255	99.997	5599489	100.000
2	23.050	4	0.003	0	0.000
Total		151259	100.000	5599489	100.000

Enantiomerically enriched **3j**

tert-butyl (_1S,9bR,E_)-8-chloro-2-(3-(3-chlorophenyl)-1-ethoxy-1-oxopropan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3k)



A white solid; 90% yield; m.p. = 138-141 °C; $[\alpha]^{25}_D$ = -95.4 (c 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.26-7.20 (m, 3H), 7.13 (m, 5H), 6.84 (d, *J* = 8.7 Hz, 3H), 5.02 (dd, *J* = 103.2, 16.4 Hz, 2H), 4.58 (s, 1H), 4.30 (dd, *J* = 175.0, 15.0 Hz, 2H), 4.24-3.99 (m, 2H), 3.78 (s, 3H), 1.21 (s, 9H), 1.17 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.86, 163.29, 157.91, 149.42, 147.20, 142.19, 136.47, 132.75, 129.92, 128.17, 127.72, 127.42, 126.51, 126.28, 125.93, 125.29, 124.88, 116.04, 115.25, 113.35, 109.63, 82.26, 67.35 (q, *J* = 32.1 Hz), 59.92, 57.58, 54.22, 46.13, 32.28, 26.53, 13.03; ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.07; HRMS (ESI^+): calcd for $C_{35}H_{33}Cl_2F_3N_2O_6$ $[M+Na]^+$ = 727.1565, found = 727.1566; The ee value was 94%, t_R (major) = 9.7 min, t_R (minor) = 17.9 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

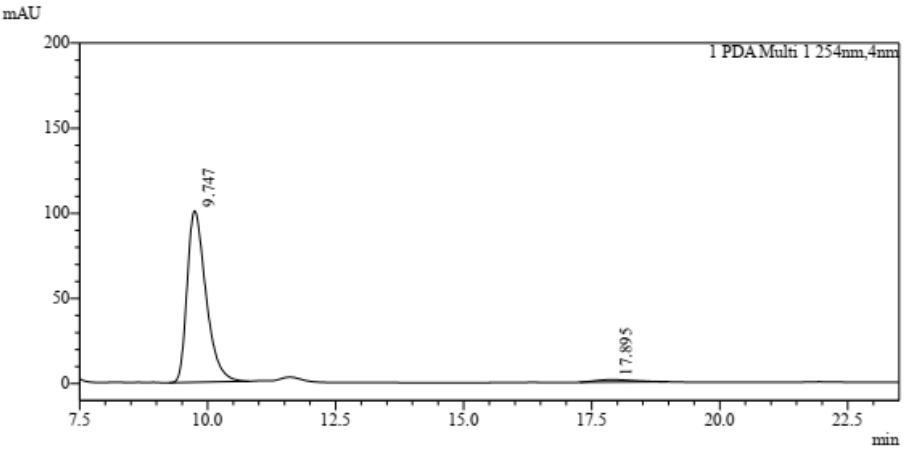


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	9.737	82264	72.584	1976317	50.397
2	16.957	31072	27.416	1945202	49.603
Total		113336	100.000	3921519	100.000

Racemic **3k**



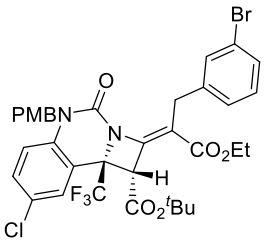
Peak Table

PDA Ch1 254nm

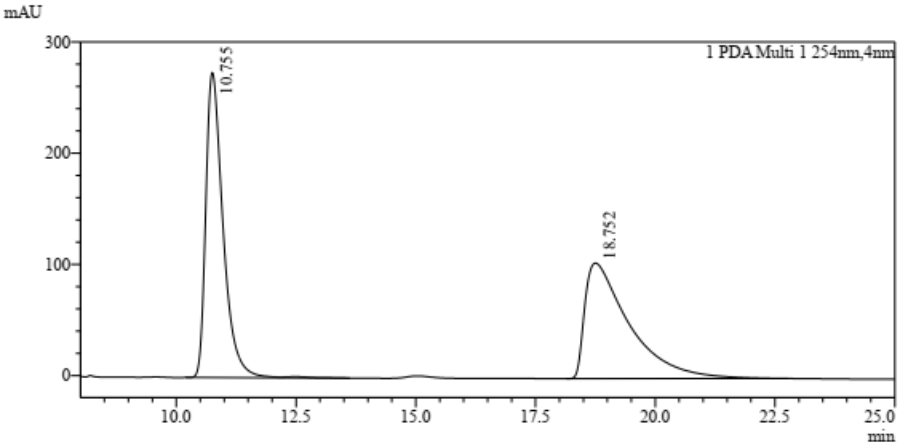
Peak#	Ret. Time	Height	Height%	Area	Area%
1	9.747	100669	98.597	2582120	97.156
2	17.895	1433	1.403	75584	2.844
Total		102102	100.000	2657704	100.000

Enantiomerically enriched **3k**

tert-butyl (*1S,9bR,E*)-2-(3-(3-bromophenyl)-1-ethoxy-1-oxopropan-2-ylidene)-8-chloro-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3l)



A white solid; 87% yield; m.p. = 138-141 ºC; $[\alpha]^{25}_{D}$ = -67.5 (c 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (s, 1H), 7.31-7.16 (m, 3H), 7.14-7.07 (m, 4H), 6.85 (d, *J* = 8.7 Hz, 3H), 5.02 (dd, *J* = 87.6, 16.4 Hz, 2H), 4.58 (s, 1H), 4.30 (dd, *J* = 151.5, 15.0 Hz, 2H), 4.21-3.98 (m, 2H), 3.77 (s, 3H), 1.22 (s, 9H), 1.19 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.89, 164.33, 159.00, 150.46, 148.29, 143.53, 137.57, 131.46, 130.97, 129.54, 128.86, 128.76, 127.60, 127.43, 127.37, 126.35, 122.20, 117.09, 116.33, 114.44, 110.77, 83.31, 68.46 (q, *J* = 32.5 Hz), 60.95, 58.58, 55.28, 47.16, 33.29, 27.68, 14.09; HRMS (ESI^+): calcd for $C_{35}H_{33}BrClF_3N_2O_6$ $[M+Na]^+$ = 771.1060, found = 771.1061; The ee value was 88%, t_R (major) = 10.8 min, t_R (minor) = 21.4 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

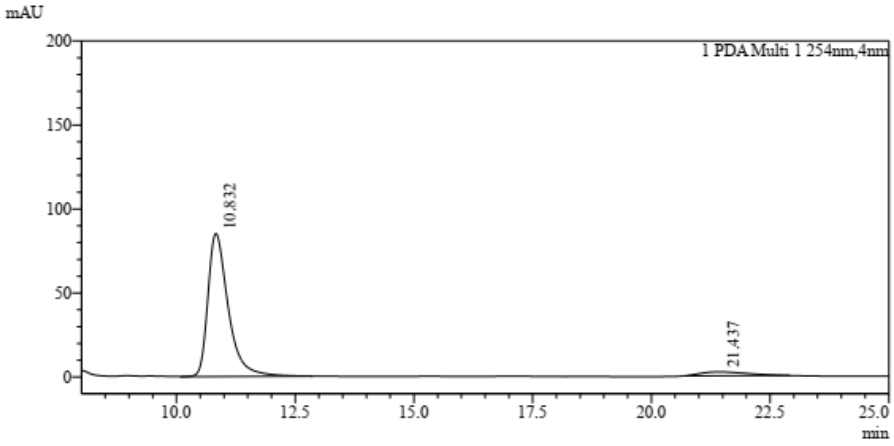


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	10.755	274407	72.506	6893971	50.616
2	18.752	104055	27.494	6726246	49.384
Total		378462	100.000	13620217	100.000

Racemic **3l**



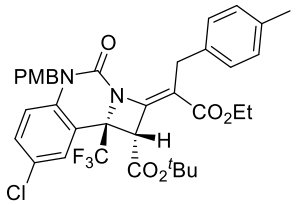
Peak Table

PDA Ch1 254nm

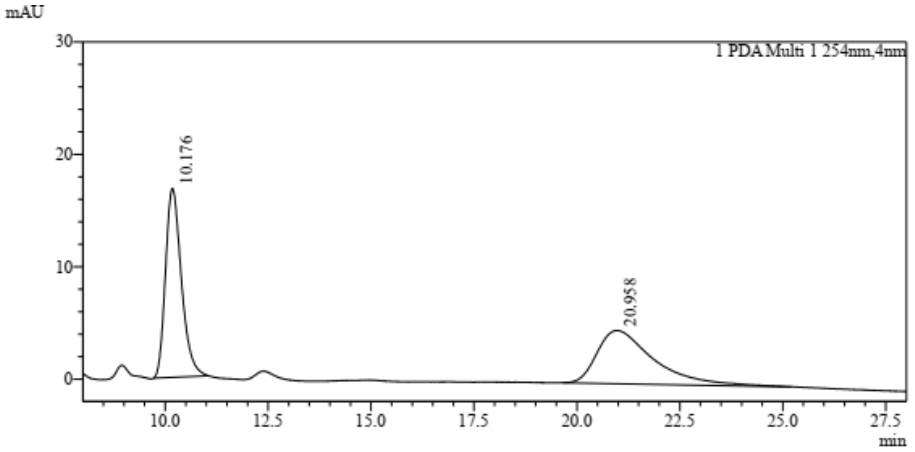
Peak#	Ret. Time	Height	Height%	Area	Area%
1	10.832	85066	97.304	2529357	93.967
2	21.437	2357	2.696	162389	6.033
Total		87422	100.000	2691746	100.000

Enantiomerically enriched **3l**

<u>*tert*-butyl (*1S,9bR,E*)-8-chloro-2-(1-ethoxy-1-oxo-3-(p-tolyl)propan-2-ylidene)- 5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3m)</u>



A white solid; 90% yield; m.p. = 119-122 ºC; $[\alpha]^{25}_{D}$ = -77.6 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.20 (m, 2H), 7.16-7.01 (m, 6H), 6.82 (t, *J* = 8.0 Hz, 3H), 5.01 (dd, *J* = 73.3, 16.6 Hz, 2H), 4.59 (s, 1H), 4.42 (dd, *J* = 116.9, 14.9 Hz, 2H), 4.22-3.96 (m, 2H), 3.78 (s, 3H), 2.30 (s, 3H), 1.21 (s, 9H), 1.19 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.14, 163.51, 157.86, 148.76, 147.09, 136.96, 136.55, 133.86, 129.82, 127.65, 127.56, 127.30, 126.59, 126.43, 125.29, 115.97, 115.43, 113.23, 110.49, 82.10, 67.26 (q, *J* = 32.2 Hz), 59.77, 57.32, 54.22, 45.96, 31.87, 26.58, 20.04, 13.05; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.72; HRMS (ESI^+): calcd for $C_{36}H_{36}ClF_3N_2O_6$ $[M+Na]^+$ = 707.2112, found = 707.2113; The ee value was 94%, t_R (major) = 9.0 min, t_R (minor) = 17.9 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

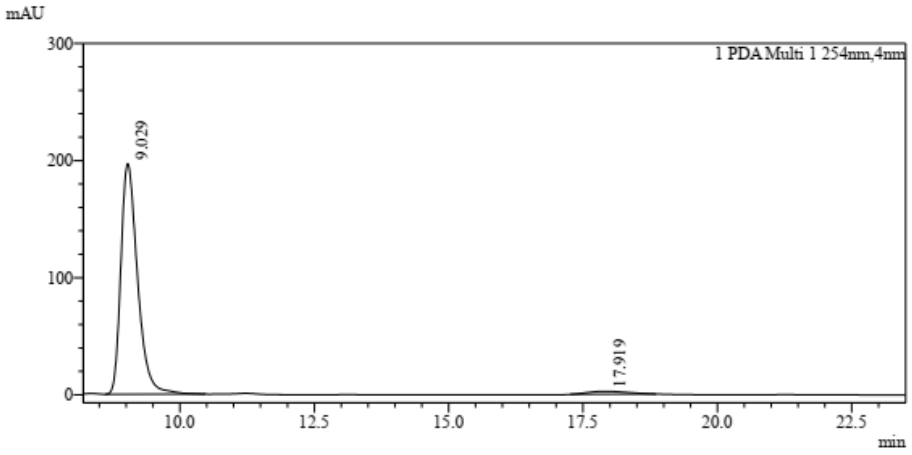


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	10.176	16827	78.060	452570	50.124
2	20.958	4730	21.940	450332	49.876
Total		21556	100.000	902902	100.000

Racemic **3m**



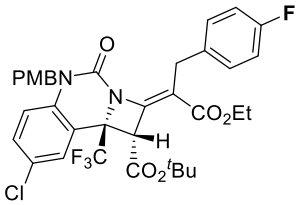
Peak Table

PDA Ch1 254nm

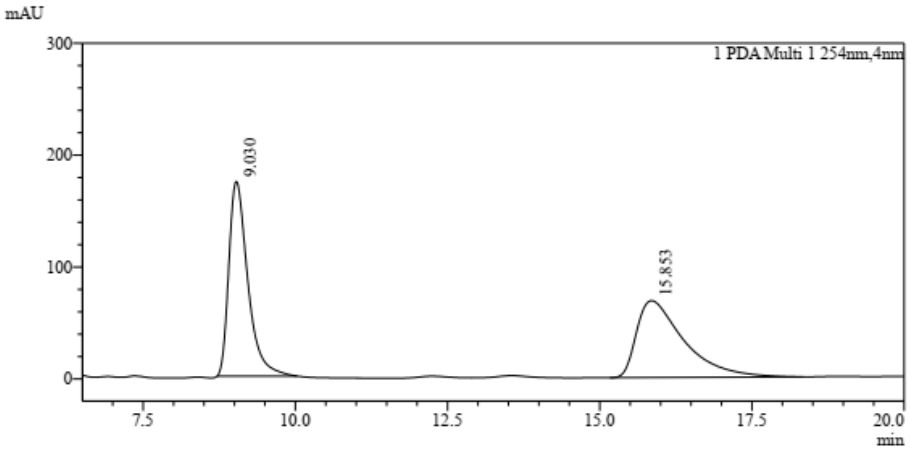
Peak#	Ret. Time	Height	Height%	Area	Area%
1	9.029	196813	98.760	4258884	97.107
2	17.919	2470	1.240	126875	2.893
Total		199283	100.000	4385759	100.000

Enantiomerically enriched **3m**

<u>*tert*-butyl (*1S,9bR,E*)-8-chloro-2-(1-ethoxy-3-(4-fluorophenyl)-1-oxopropan- 2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3n)</u>



A white solid; 82% yield; m.p. = 103-108 ºC; $[\alpha]^{25}_D$ = -112.8 (c 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.26-7.18 (m, 4H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.95-6.88 (m, 2H), 6.86-6.79 (m, 3H), 5.02 (dd, *J* = 67.3, 16.4 Hz, 2H), 4.59 (s, 1H), 4.27 (dd, *J* = 123.1, 14.9 Hz, 2H), 4.19-4.01 (m, 2H), 3.78 (s, 3H), 1.22 (s, 9H), 1.18 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.05, 164.48, 161.22 (d, *J* = 241.3 Hz), 159.03, 150.09, 148.16, 137.59, 136.80, 136.77, 130.96, 129.91, 129.83, 128.72, 127.57, 127.34, 126.37, 117.10, 116.44, 114.70 (d, *J* = 21.0 Hz), 114.33, 111.23, 83.26, 68.37 (q, *J* = 32.2 Hz), 60.87, 58.29, 55.27, 47.05, 32.55, 27.64, 14.09; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.98, -118.22; HRMS (ESI^+): calcd for $C_{35}H_{33}ClF_4N_2O_6$ $[M+Na]^+$ = 711.1861, found = 711.1868; The ee value was 84%, t_R (major) = 8.9 min, t_R (minor) = 15.7 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

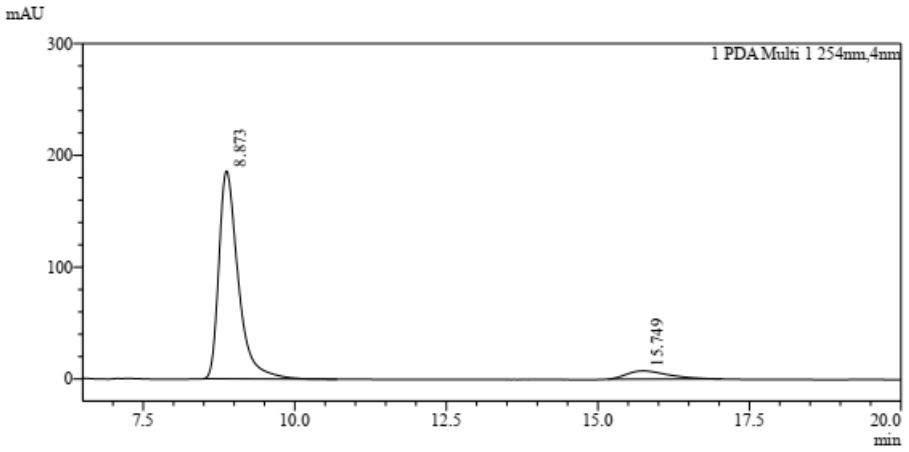


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	9.030	173925	71.668	3772649	50.343
2	15.853	68755	28.332	3721210	49.657
Total		242680	100.000	7493859	100.000

Racemic **3n**



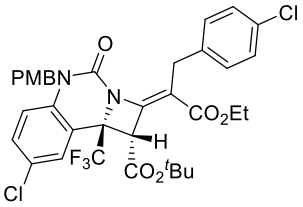
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	8.873	185986	96.183	4143842	92.154
2	15.749	7381	3.817	352831	7.846
Total		193367	100.000	4496673	100.000

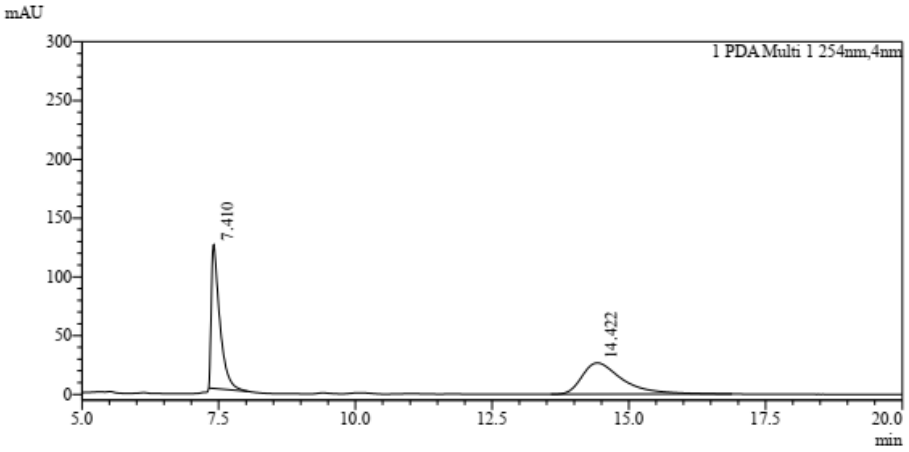
Enantiomerically enriched **3n**

tert-butyl (_1S,9bR,E_)-8-chloro-2-(3-(4-chlorophenyl)-1-ethoxy-1-oxopropan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3o)



A white solid; 93% yield; m.p. = 125-130 ^{o}C; $[\alpha]^{25}_{D}$ = -21.5 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (s, 1H), 7.25-7.15 (m, 5H), 7.05 (d, *J* = 8.7 Hz, 2H), 6.83 (t, *J* = 9.3 Hz, 3H), 5.00 (dd, *J* = 85.9, 16.4 Hz, 2H), 4.60 (s, 1H), 4.28 (dd, *J* = 146.9, 15.1 Hz, 2H), 4.20-4.01 (m, 2H), 3.79 (s, 3H), 1.23 (s, 9H), 1.18 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.00, 164.44, 159.05, 150.41, 148.07, 139.82, 137.60, 131.39, 131.32, 130.98, 129.80, 128.76, 128.50, 128.11, 127.59, 127.32, 126.36, 117.12, 116.44, 114.36, 110.64, 83.32, 68.36 (q, *J* = 32.2 Hz), 60.92, 58.20, 55.31, 47.12, 32.74, 27.67, 14.10; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.99; HRMS (ESI^+): calcd for $C_{35}H_{33}Cl_2F_3N_2O_6$ $[M+Na]^+$ = 727.1565, found = 727.1561; The ee value was 98%,

t_R (major) = 7.3 min, t_R (minor) = 14.4 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

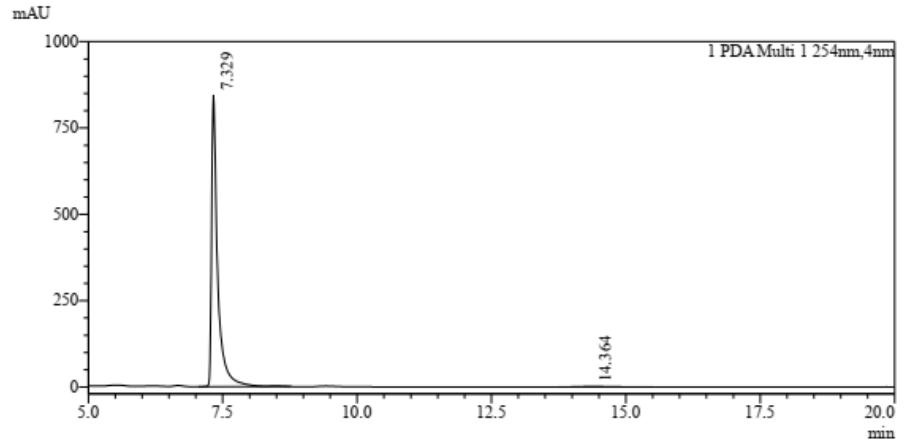


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	7.410	122254	82.140	1319479	49.003
2	14.422	26583	17.860	1373173	50.997
Total		148837	100.000	2692652	100.000

Racemic **3o**



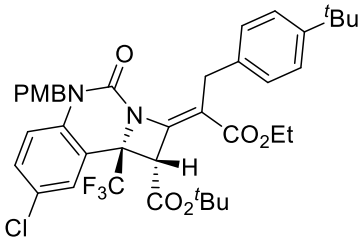
Peak Table

PDA Ch1 254nm

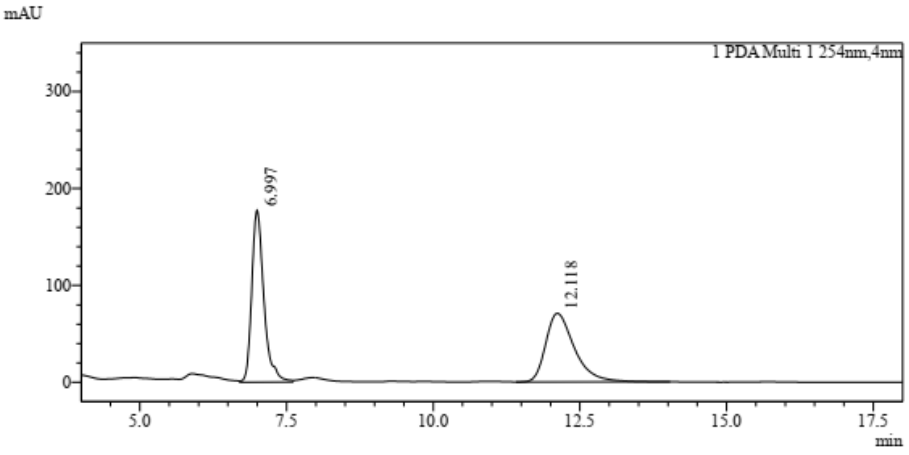
Peak#	Ret. Time	Height	Height%	Area	Area%
1	7.329	844944	99.838	6678618	99.115
2	14.364	1371	0.162	59667	0.885
Total		846315	100.000	6738285	100.000

Enantiomerically enriched **3o**

<u>*tert*-butyl (*1S,9bR,E*)-2-(3-(4-(*tert*-butyl)phenyl)-1-ethoxy-1-oxopropan-2-ylidene)-8-chloro-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3p)</u>



A white solid; 94% yield; m.p. = 108-113 ºC; $[\alpha]^{25}_{D}$ = -127.3 (c 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.26-7.10 (m, 8H), 6.88-6.79 (m, 3H), 5.04 (dd, *J* = 63.1, 16.4 Hz, 2H), 4.59 (s, 1H), 4.29 (dd, *J* = 75.8, 14.4 Hz, 2H), 4.24-3.98 (m, 2H), 3.77 (s, 3H), 1.29 (s, 9H), 1.21 (s, 9H), 1.18 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.25, 164.60, 158.99, 149.67, 148.21, 148.18, 137.88, 137.67, 130.89, 128.61, 128.18, 127.67, 127.52, 126.36, 124.87, 117.07, 116.52, 114.33, 111.81, 83.12, 68.33 (d, *J* = 32.2 Hz), 60.80, 58.39, 55.25, 47.02, 34.30, 32.80, 31.46, 27.63, 14.08; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.93; HRMS (ESI^+): calcd for $C_{39}H_{42}ClF_3N_2O_6$ $[M+Na]^+$ = 749.2581, found = 749.2582; The ee value was 98%, t_R (major) = 6.9 min, t_R (minor) = 12.0 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

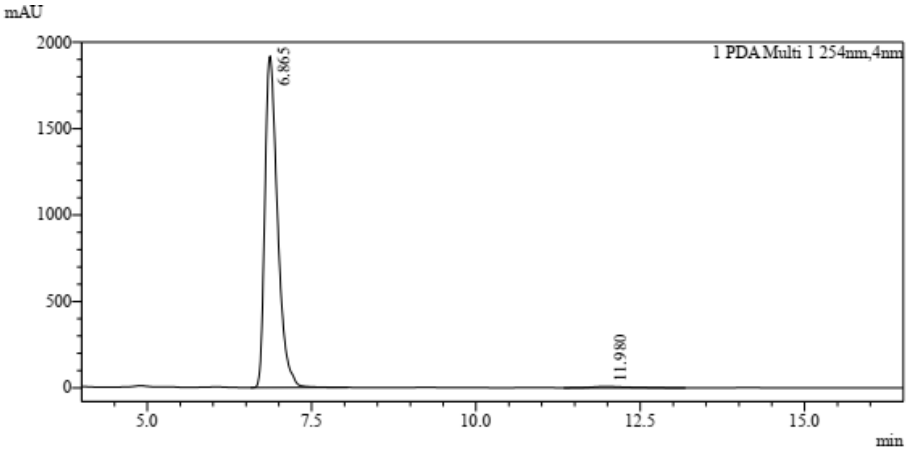


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	6.997	177237	71.458	2559718	51.548
2	12.118	70791	28.542	2405989	48.452
Total		248028	100.000	4965708	100.000

Racemic **3p**



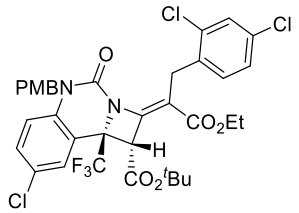
Peak Table

PDA Ch1 254nm

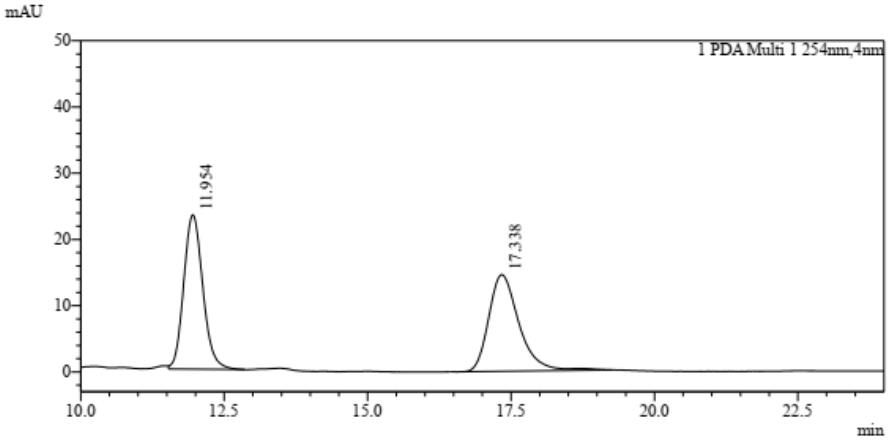
Peak#	Ret. Time	Height	Height%	Area	Area%
1	6.865	1916572	99.629	25752290	98.905
2	11.980	7143	0.371	284979	1.095
Total		1923715	100.000	26037269	100.000

Enantiomerically enriched **3p**

tert-butyl (_1S,9bR,E_)-8-chloro-2-(3-(2,4-dichlorophenyl)-1-ethoxy-1-oxopropan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3q)



A white solid; 95% yield; m.p. = 115-117 °C; $[\alpha]^{25}_D$ = -123.5 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 1.4 Hz, 1H), 7.25-7.20 (m, 2H), 7.12-7.09 (m, 2H), 6.97 (d, *J* = 8.6 Hz, 2H), 6.83-6.75 (m, 3H), 4.93 (dd, *J* = 90.7, 16.3 Hz, 2H), 4.67 (s, 1H), 4.33 (dd, *J* = 95.5, 16.4 Hz, 2H), 4.18-4.01 (m, 2H), 3.78 (s, 3H), 1.28 (s, 9H), 1.16 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.85, 164.42, 159.02, 151.67, 147.88, 138.14, 137.58, 134.47, 131.69, 131.02, 129.72, 128.95, 128.74, 127.63, 127.31, 126.50, 126.35, 117.14, 116.31, 114.31, 108.97, 83.50, 68.53 (q, *J* = 33.3 Hz), 60.98, 58.06, 55.30, 47.13, 30.88, 27.76, 14.06; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.73; HRMS (ESI^+): calcd for $C_{35}H_{32}Cl_3F_3N_2O_6$ $[M+Na]^+$ = 761.1176, found = 761.1176; The ee value was 95%, t_R (major) = 14.3 min, t_R (minor) = 19.8 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

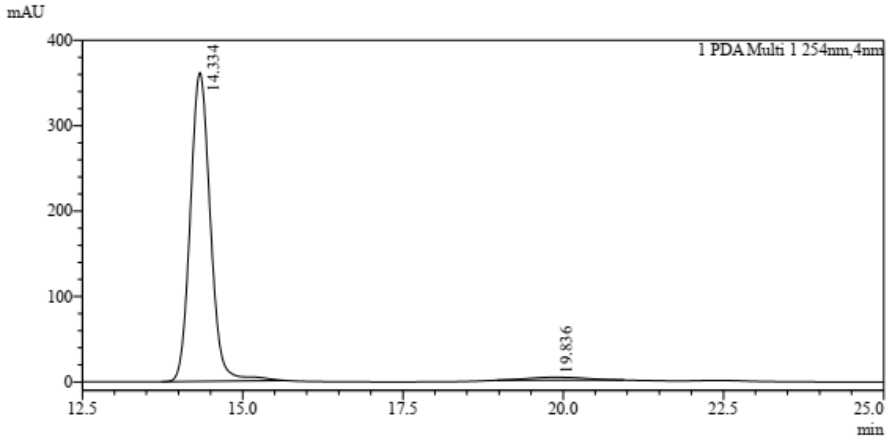


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	11.954	23310	61.504	540587	50.123
2	17.338	14590	38.496	537937	49.877
Total		37900	100.000	1078524	100.000

Racemic **3q**



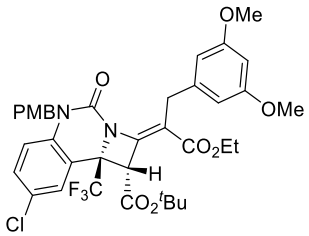
Peak Table

PDA Ch1 254nm

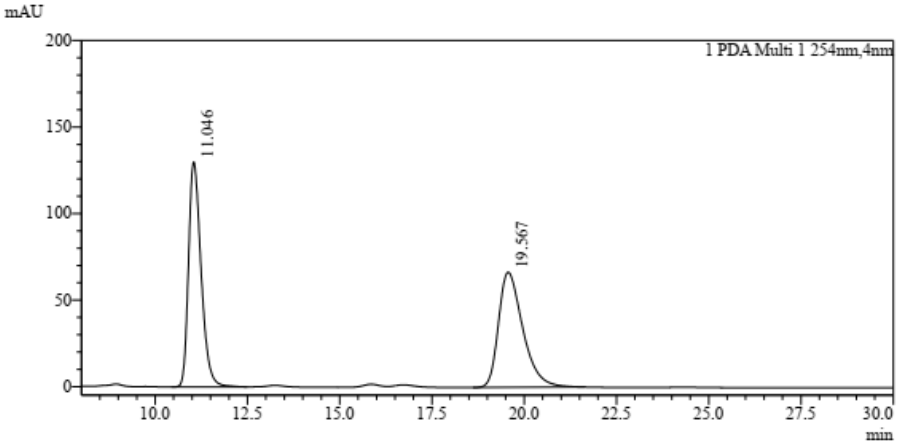
Peak#	Ret. Time	Height	Height%	Area	Area%
1	14.334	361413	99.068	7875347	97.347
2	19.836	3399	0.932	214632	2.653
Total		364811	100.000	8089978	100.000

Enantiomerically enriched **3q**

<u>*tert*-butyl (*1S,9bR,E*)-8-chloro-2-(3-(3,5-dimethoxyphenyl)-1-ethoxy-1-oxopropan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3r)</u>



A white solid; 84% yield; m.p. = 113-117 ºC; $[\alpha]^{25}_{D}$ = -91.3 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.18 (m, 3H), 7.10 (d, *J* = 8.7 Hz, 2H), 6.86-6.78 (m, 3H), 6.45 (d, *J* = 2.2 Hz, 2H), 6.27 (t, *J* = 2.3 Hz, 1H), 5.01 (dd, *J* = 94.1, 16.3 Hz, 2H), 4.60 (s, 1H), 4.27 (dd, *J* = 50.7, 15.3 Hz, 2H), 4.25-4.00 (m, 2H), 3.77 (s, 3H), 3.73 (s, 6H), 1.24 (s, 9H), 1.19 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.13, 164.61, 160.55, 158.95, 150.11, 148.22, 143.43, 137.65, 130.89, 128.57, 127.60, 127.43, 126.31, 117.04, 116.44, 114.37, 111.28, 106.62, 97.87, 83.35, 68.40 (q, *J* = 28.2 Hz), 60.81, 58.37, 55.24, 55.15, 47.09, 33.50, 27.65, 14.13; HRMS (ESI^+): calcd for $C_{37}H_{38}ClF_3N_2O_8$ $[M+Na]^+$ = 753.2166, found = 753.2160; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.93; The ee value was 86%, t_R (major) = 10.8 min, t_R (minor) = 19.1 min (Chiralcel IA, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

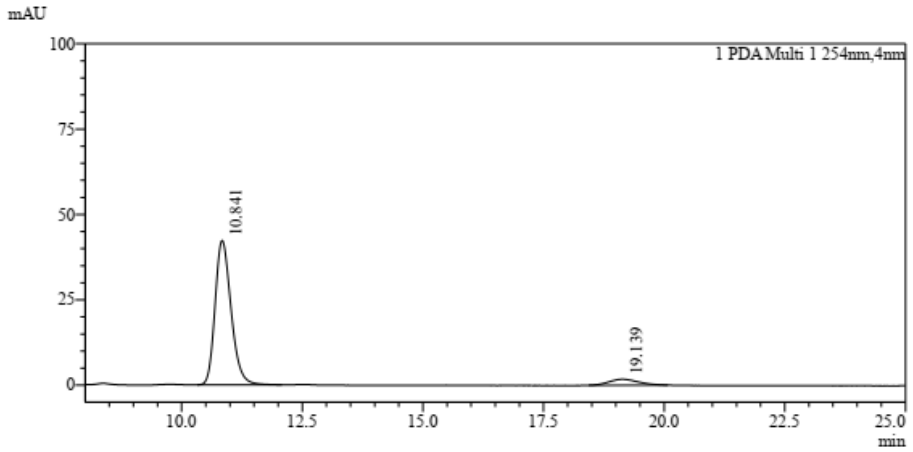


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	11.046	130060	66.155	3087775	50.307
2	19.567	66539	33.845	3050052	49.693
Total		196599	100.000	6137827	100.000

Racemic **3r**



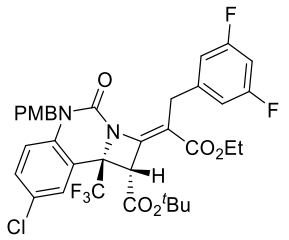
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	10.841	42289	96.042	975695	92.973
2	19.139	1743	3.958	73741	7.027
Total		44032	100.000	1049437	100.000

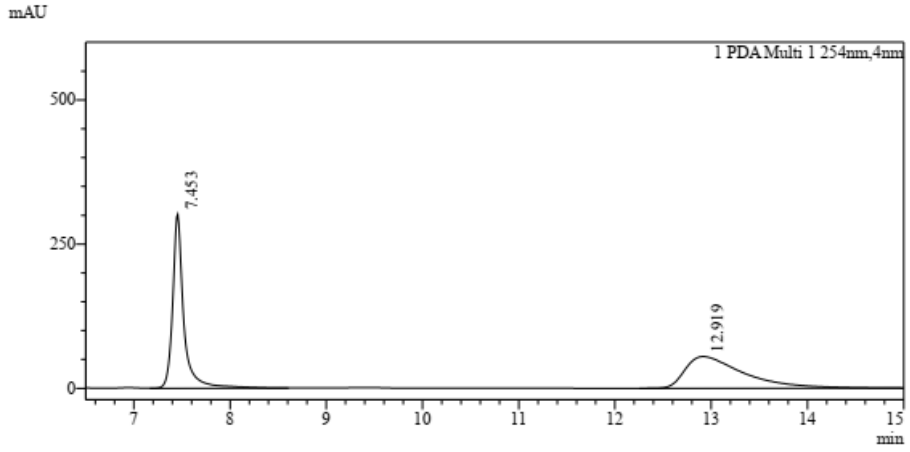
Enantiomerically enriched **3r**

<u>*tert*-butyl (*1S,9bR,E*)-8-chloro-2-(3-(3,5-difluorophenyl)-1-ethoxy-1-oxopropan- 2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3s)</u>



A white solid; 90% yield; m.p. = 83-88 °C; $[\alpha]^{25}_{D}$ = -36.0 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.22 (m, 2H), 7.10 (d, *J* = 8.7 Hz, 2H), 6.88-6.83 (m, 3H), 6.83-6.73 (m, 2H), 6.60 (tt, *J* = 9.0, 2.3 Hz, 1H), 5.02 (dd, *J* = 118.9, 16.4 Hz, 2H), 4.60 (s, 1H), 4.29 (dd, *J* = 220.4, 14.9 Hz, 2H), 4.26-4.04 (m, 2H), 3.78 (s, 3H), 1.21 (s, 9H), 1.20 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.75, 164.21, 162.91 (d, *J* = 245.5 Hz), 162.78 (d, *J* = 245.5 Hz), 159.06, 150.92, 148.14, 145.48 (t, *J* = 18.0 Hz), 137.48, 131.02, 128.89, 127.44, 126.79 (d, *J* = 76.6 Hz), 116.71 (d, *J* = 86.71 Hz), 114.41, 111.29 (d, *J* = 24.7 Hz), 111.29 (d, *J* = 12.0 Hz), 109.92, 101.17 (t, *J* = 51.0 Hz), 83.48, 68.57, 68.25, 61.05, 58.45, 55.25, 47.20, 33.44, 27.61, 14.08; ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.00, -111.20; HRMS (ESI^+): calcd for $C_{35}H_{32}ClF_5N_2O_6$ $[M+Na]^+$ = 729.1767, found = 729.1770; The ee value was 89%, t_R (major) = 7.3 min, t_R (minor) =

9.3 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

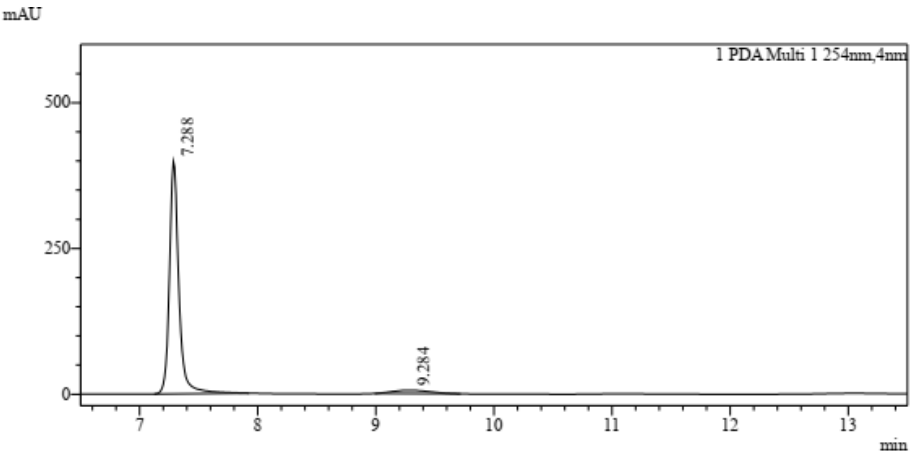


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	7.453	301729	84.587	2431236	50.942
2	12.919	54979	15.413	2341311	49.058
Total		356708	100.000	4772547	100.000

Racemic **3s**



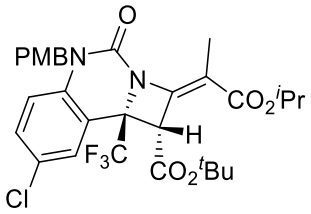
Peak Table

PDA Ch1 254nm

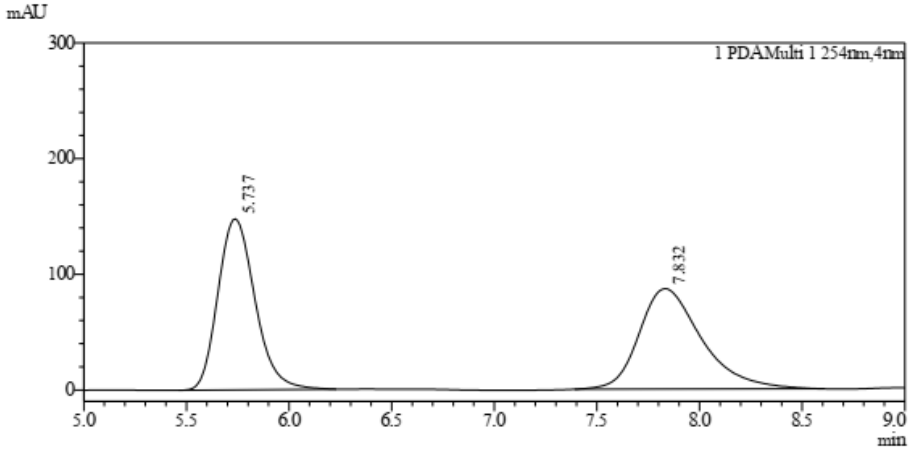
Peak#	Ret. Time	Height	Height%	Area	Area%
1	7.288	398360	98.593	2218991	94.689
2	9.284	5685	1.407	124469	5.311
Total		404045	100.000	2343459	100.000

Enantiomerically enriched **3s**

<u>*tert*-butyl (*1S,9bR,E*)-8-chloro-2-(1-isopropoxy-1-oxopropan-2-ylidene)-5- (4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3t)</u>



A white solid; 89% yield; m.p. = 132-135 °C; $[\alpha]^{25}_D$ = -123.7 (c 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.22-7.11 (m, 2H), 7.14 (d, *J* = 8.6 Hz, 2H), 6.86-6.76 (m, 3H), 5.22-4.87 (m, 3H), 4.51 (s, 1H), 3.76 (s, 3H), 2.30 (s, 3H), 1.26 (d, *J* = 6.3 Hz, 6H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.30, 164.86, 158.93, 148.86, 148.76, 137.67, 130.83, 128.33, 127.57, 127.44, 126.29, 116.85, 116.12, 114.34, 109.85, 83.07, 68.73 (q, *J* = 32.2 Hz), 68.39, 59.00, 55.27, 46.67, 27.50, 21.91, 14.09; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.44; HRMS (ESI^+): calcd for $C_{30}H_{32}ClF_3N_2O_6$ $[M+Na]^+$ = 631.1799, found = 631.1795; The ee value was 97%, t_R (major) = 5.8 min, t_R (minor) = 7.8 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

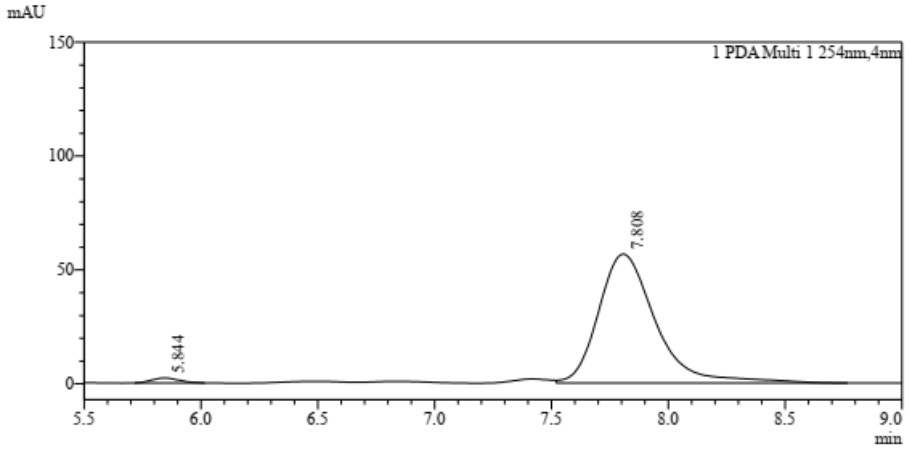


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	5.737	147933	63.003	1859208	50.221
2	7.832	86872	36.997	1842826	49.779
Total		234805	100.000	3702034	100.000

Racemic **3j**



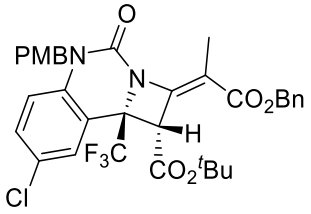
Peak Table

PDA Ch1 254nm

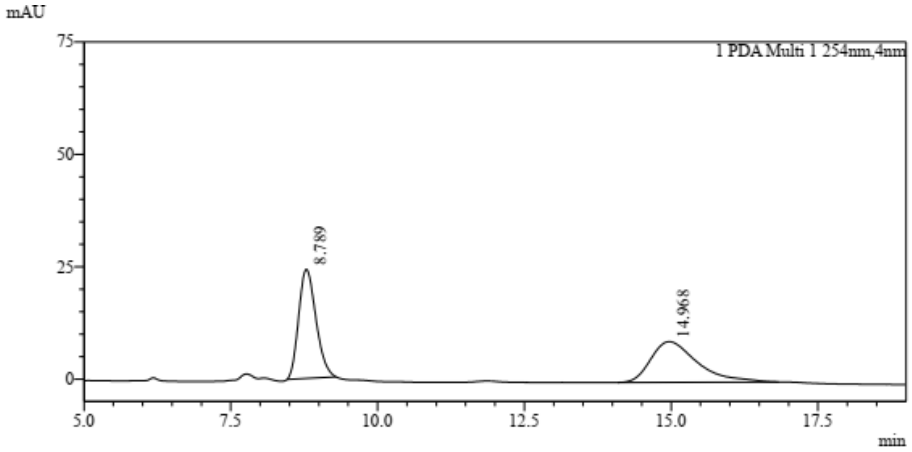
Peak#	Ret. Time	Height	Height%	Area	Area%
1	5.844	2096	3.569	17351	1.776
2	7.808	56623	96.431	959509	98.224
Total		58719	100.000	976860	100.000

Enantiomerically enriched **3t**

***tert*-butyl (*1S,9bR,E*)-2-(1-(benzyloxy)-1-oxopropan-2-ylidene)-8-chloro-5- (4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3u)**



A white solid; 94% yield; m.p. = 111-114 ºC; $[\alpha]^{25}_{D}$ = -85.2 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.29 (m, 5H), 7.22-7.17 (m, 2H), 7.13 (d, *J* = 8.6 Hz, 2H), 6.86-6.81 (m, 2H), 6.79 (d, *J* = 9.6 Hz, 1H), δ 5.17 (dd, *J* = 63.5, 12.5 Hz, 2H), δ 5.04 (dd, *J* = 58.4, 16.6 Hz, 2H), 4.54 (s, 1H), 3.77 (s, 3H), 2.36 (s, 3H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.63, 164.74, 158.97, 149.53, 148.71, 137.62, 136.06, 130.85, 128.55, 128.37, 128.19, 128.15, 127.57, 127.37, 126.26, 117.00, 116.22, 114.37, 108.91, 83.17, 68.70(q, *J* = 32.0 Hz), 66.29, 58.64, 55.27, 46.67, 27.64, 13.96; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.72; HRMS (ESI^+): calcd for $C_{29}H_{30}ClF_3N_2O_6$ $[M+H]^+$ = 595.1823, found = 595.1825; The ee value was 98%, t_R (major) = 7.8 min, t_R (minor) = 14.8 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

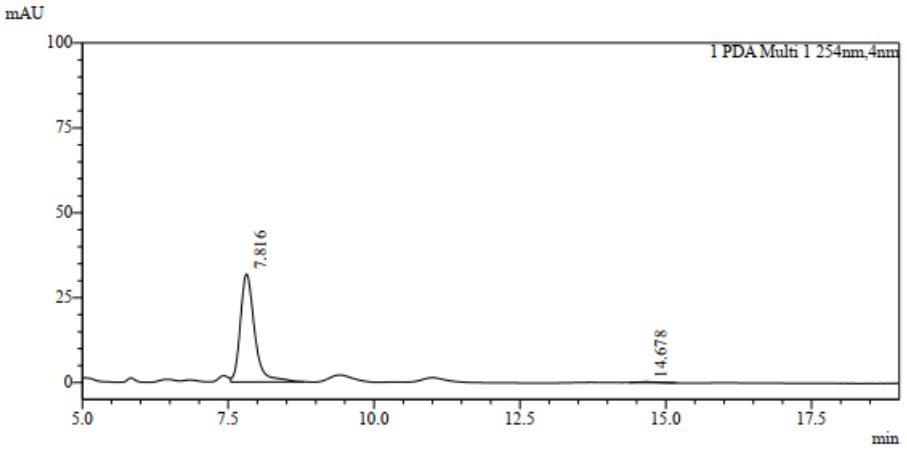


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	8.789	24277	72.841	498098	49.944
2	14.968	9052	27.159	499209	50.056
Total		33329	100.000	997307	100.000

Racemic **3u**



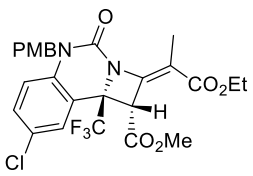
Peak Table

PDA Ch1 254nm

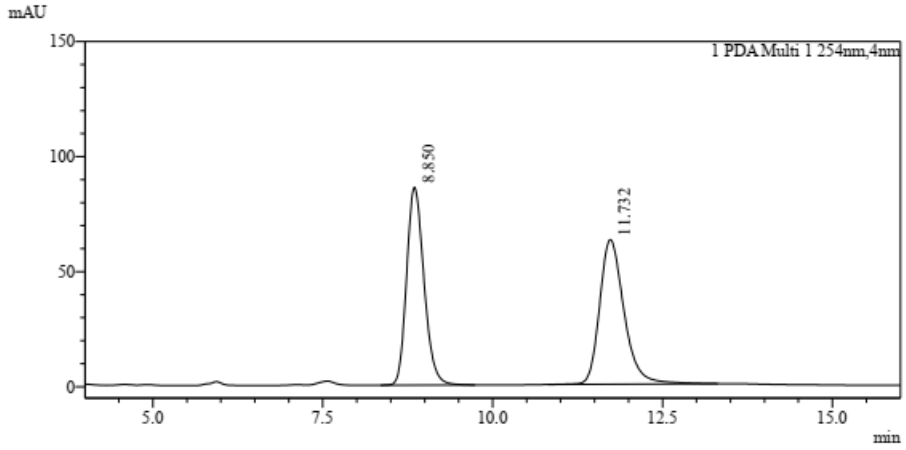
Peak#	Ret. Time	Height	Height%	Area	Area%
1	7.816	31788	99.251	540023	98.954
2	14.678	240	0.749	5707	1.046
Total		32028	100.000	545731	100.000

Enantiomerically enriched **3u**

methyl (*1S,9bR,E*)-8-chloro-2-(1-ethoxy-1-oxopropan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3v)



A white solid; 92% yield; m.p. = 129-132 °C; $[\alpha]^{25}_{D}$ = -91.5 (c 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.21 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.16-7.08 (m, 3H), 6.87-6.77 (m, 3H), 5.05 (dd, *J* = 108.0, 16.5 Hz, 2H), 4.70 (s, 1H), 4.24-4.10 (m, 2H), 3.76 (s, 3H), 3.61 (s, 3H), 2.34 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.81, 166.64, 158.95, 148.71, 147.91, 137.57, 131.01, 128.52, 127.61, 127.17, 125.28, 117.35, 116.31, 114.37, 109.79, 68.56 (q, *J* = 32.5 Hz), 60.91, 57.45, 55.26, 52.64, 46.50, 14.20, 13.97; ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.07; HRMS (ESI^+): calcd for $C_{26}H_{24}ClF_3N_2O_6$ $[M+Na]^+$ = 575.1173, found = 575.1176; The ee value was 77%, t_R (major) = 8.7 min, t_R (minor) = 11.6 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

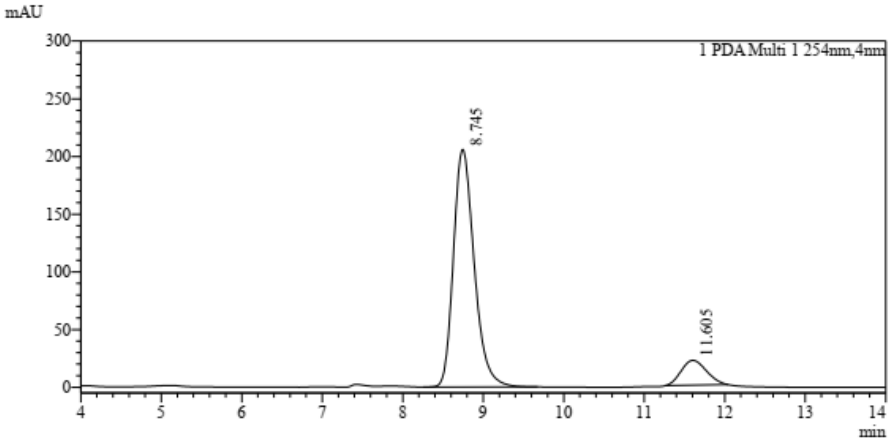


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	8.850	85928	57.751	1533706	49.341
2	11.732	62862	42.249	1574698	50.659
Total		148789	100.000	3108404	100.000

Racemic **3v**



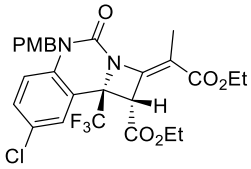
Peak Table

PDA Ch1 254nm

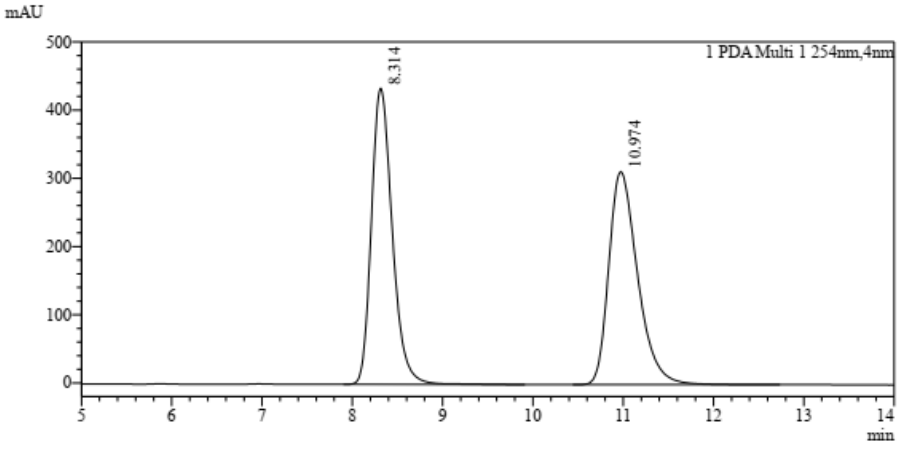
Peak#	Ret. Time	Height	Height%	Area	Area%
1	8.745	205931	90.522	3703215	88.686
2	11.605	21563	9.478	472417	11.314
Total		227493	100.000	4175631	100.000

Enantiomerically enriched **3v**

ethyl (*1S,9bR,E*)-8-chloro-2-(1-ethoxy-1-oxopropan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3w)



A white solid; 92% yield; m.p. = 132-134 ºC; $[\alpha]^{25}_{D}$ = -83.4 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.12 (d, *J* = 8.8 Hz, 3H), 6.87-6.81 (m, 2H), 6.79 (d, *J* = 8.9 Hz, 1H), 5.05 (dd, *J* = 83.6, 16.5 Hz, 2H), 4.65 (s, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 4.12-4.01 (m, 2H), 3.76 (s, 3H), 2.34 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.74, 166.09, 158.94, 148.73, 148.13, 137.60, 130.97, 128.43, 127.57, 127.20, 125.59, 117.23, 116.17, 114.36, 109.87, 68.57 (q, *J* = 32.3 Hz), 62.00, 60.87, 57.75, 55.27, 46.53, 14.22, 14.07, 13.87; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.72; HRMS (ESI^+): calcd for $C_{27}H_{26}ClF_3N_2O_6$ $[M+Na]^+$ = 589.1329, found = 589.1329; The ee value was 97%, t_R (major) = 8.9 min, t_R (minor) = 11.8 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

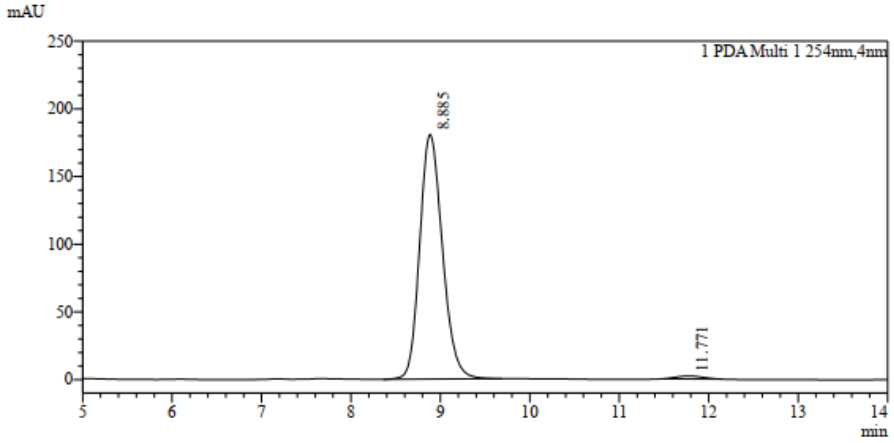


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	8.314	433822	58.162	6978251	50.190
2	10.974	312057	41.838	6925397	49.810
Total		745879	100.000	13903648	100.000

Racemic **3w**



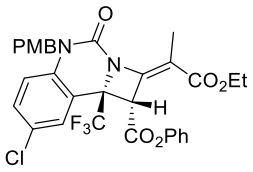
Peak Table

PDA Ch1 254nm

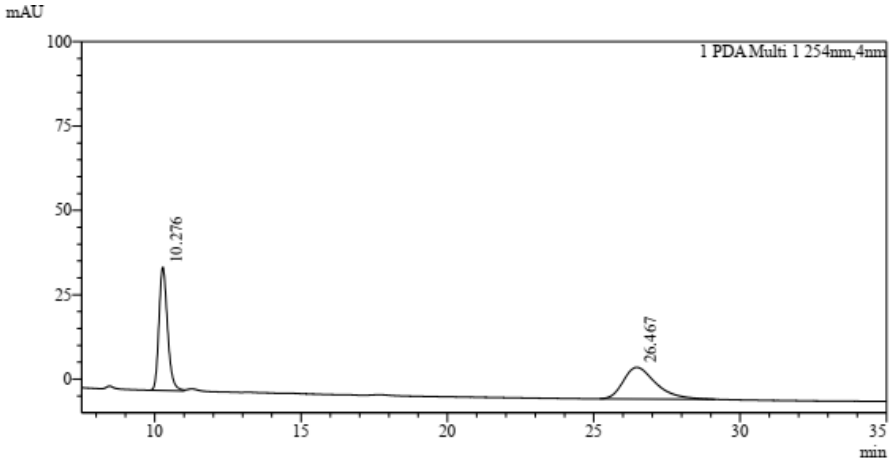
Peak#	Ret. Time	Height	Height%	Area	Area%
1	8.885	180643	98.771	3195573	98.517
2	11.771	2249	1.229	48098	1.483
Total		182891	100.000	3243671	100.000

Enantiomerically enriched **3w**

phenyl (*1S,9bR,E*)-8-chloro-2-(1-ethoxy-1-oxopropan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3x)



A white solid; 86% yield; m.p. = 134-136 °C; $[\alpha]^{25}_{D}$ = -101.9 (c 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.34-7.29 (m, 3H), 7.28-7.25 (m, 1H), 7.24-7.18 (m, 1H), 7.09 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 1H), 6.79-6.71 (m, 4H), 5.07 (dd, *J* = 61.9, 16.5 Hz, 2H), 4.88 (s, 1H), 4.32-4.20 (m, 2H), 3.73 (s, 3H), 2.38 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.89, 164.69, 158.84, 149.89, 148.67, 147.85, 137.57, 131.17, 129.52, 128.63, 127.42, 126.89, 126.39, 125.73, 121.09, 117.45, 115.94, 114.29, 109.94, 68.71 (q, *J* = 32.2 Hz), 61.03, 57.56, 55.16, 46.47, 14.25, 13.95; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.72; HRMS (ESI^+): calcd for $C_{31}H_{26}ClF_3N_2O_6$ $[M+Na]^+$ = 637.1329, found = 637.1328; The ee value was 92%, t_R (major) = 10.3 min, t_R (minor) = 27.3 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

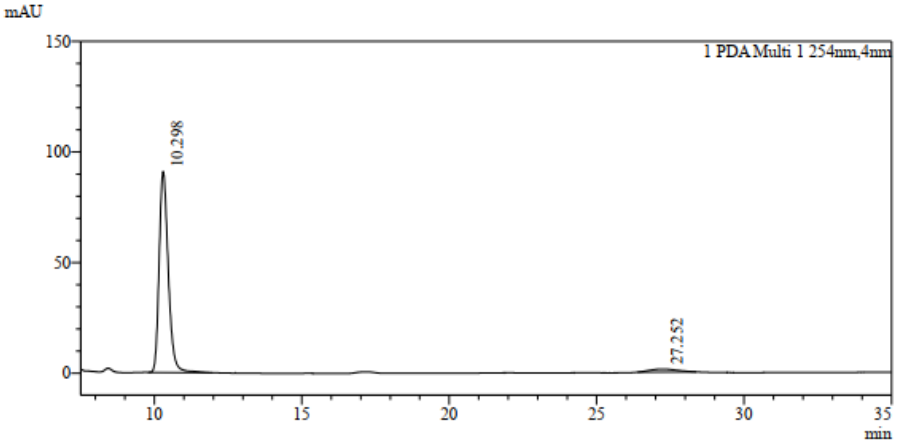


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	10.276	36561	79.614	746991	50.772
2	26.467	9362	20.386	724283	49.228
Total		45923	100.000	1471274	100.000

Racemic **3x**



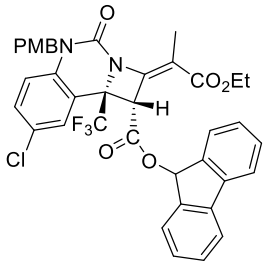
Peak Table

PDA Ch1 254nm

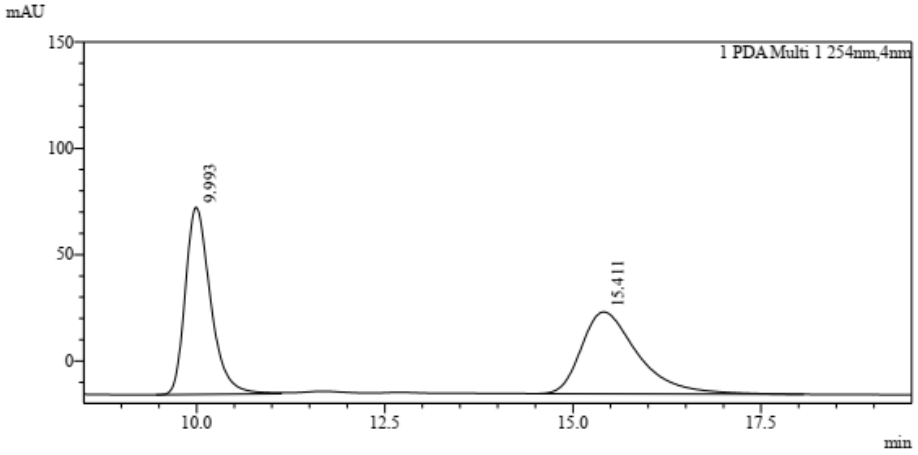
Peak#	Ret. Time	Height	Height%	Area	Area%
1	10.298	90859	98.556	1957107	95.821
2	27.252	1331	1.444	85346	4.179
Total		92190	100.000	2042453	100.000

Enantiomerically enriched **3x**

9H-fluoren-9-yl (*1S,9bR,E*)-8-chloro-2-(1-ethoxy-1-oxopropan-2-ylidene)-5- (4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3y)



A white solid; 92% yield; m.p. = 171 175 ºC; $[\alpha]^{25}_{D}$ = -71.1 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.59 (m, 2H), 7.43-7.37 (m, 2H), 7.33 (m, 2H), 7.25-7.22 (m, 2H), 7.10 (t, *J* = 7.4 Hz, 1H), 7.02-6.93 (m, 3H), 6.78-6.72 (m, 3H), 6.68 (s, 1H), 4.99 (dd, *J* = 31.7, 16.6 Hz, 2H), 4.84 (s, 1H), 4.31-4.08 (m, 2H), 3.77 (s, 3H), 2.31 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.94, 167.00, 158.80, 148.34, 148.30, 140.99, 140.88, 137.79, 131.22, 129.68, 128.77, 128.08, 127.75, 127.24, 126.96, 125.99, 125.82, 120.00, 117.30, 115.90, 114.42, 109.62, 76.62, 68.80 (q, *J* = 31.9 Hz), 60.96, 57.97, 55.28, 46.61, 14.27, 13.94; ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.07; HRMS (ESI^+): calcd for $C_{38}H_{30}ClF_3N_2O_6$ $[M+Na]^+$ = 725.1642, found = 725.1648; The ee value was 92%, t_R (major) = 9.8 min, t_R (minor) = 15.1 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

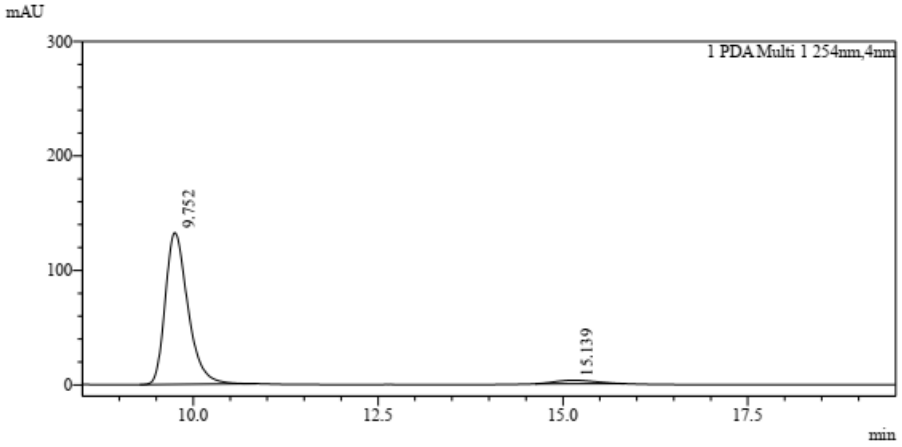


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	9.993	88042	69.562	2059030	50.522
2	15.411	38523	30.438	2016505	49.478
Total		126565	100.000	4075535	100.000

Racemic **3i**



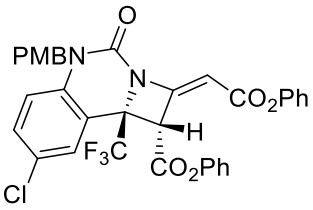
Peak Table

PDA Ch1 254nm

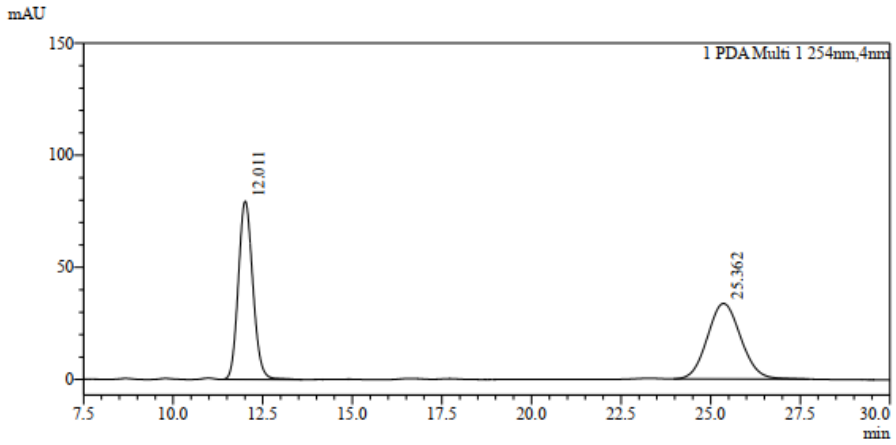
Peak#	Ret. Time	Height	Height%	Area	Area%
1	9.752	132572	97.731	2834581	96.039
2	15.139	3078	2.269	116896	3.961
Total		135650	100.000	2951477	100.000

Enantiomerically enriched **3i**

phenyl (*1S,9bR,E*)-8-chloro-5-(4-methoxybenzyl)-4-oxo-2-(2-oxo-2-phenoxyethylidene)-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (3z)



A white solid; 81% yield; m.p. = 168-171 ºC; $[\alpha]^{25}_{D}$ = -103.6 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (t, *J* = 7.9 Hz, 2H), 7.34-7.25 (m, 4H), 7.25-7.16 (m, 2H), 7.15-7.09 (m, 4H), 6.89 (d, *J* = 9.0 Hz, 1H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.72-6.65 (m, 2H), 6.43 (d, *J* = 1.5 Hz, 1H), 5.10 (dd, *J* = 103.3, 16.5 Hz, 2H), 5.04 (d, *J* = 1.6 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.08, 163.26, 159.10, 154.24, 150.40, 149.83, 148.64, 137.60, 131.56, 129.59, 129.47, 129.21, 127.52, 126.62, 126.57, 126.07, 125.96, 121.60, 121.10, 117.97, 115.59, 114.52, 98.39, 69.36 (q, *J* = 32.9 Hz), 55.79, 55.27, 46.24; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.72; HRMS (ESI^+): calcd for $C_{34}H_{24}ClF_3N_2O_6$ $[M+Na]^+$ = 671.1173, found = 671.1175; The ee value was 97%, t_R (major) = 12.7 min, t_R (minor) = 28.7 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

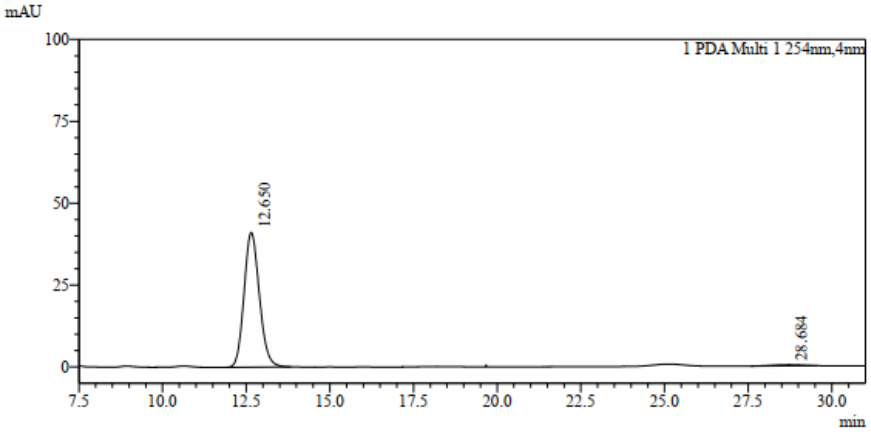


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	12.011	79544	70.245	2244545	50.628
2	25.362	33694	29.755	2188861	49.372
Total		113238	100.000	4433405	100.000

Racemic **3z**



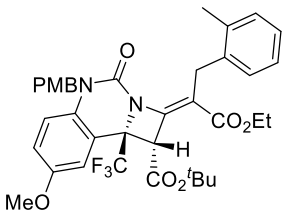
Peak Table

PDA Ch1 254nm

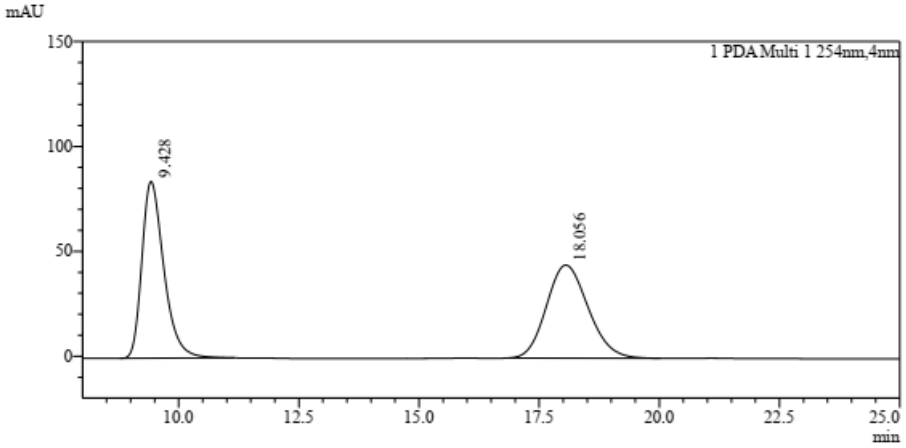
Peak#	Ret. Time	Height	Height%	Area	Area%
1	12.650	41121	99.196	1310158	98.426
2	28.684	333	0.804	20956	1.574
Total		41454	100.000	1331113	100.000

Enantiomerically enriched **3z**

<u>*tert*-butyl (*1S,9bR,E*)-2-(1-ethoxy-1-oxo-3-(o-tolyl)propan-2-ylidene)-8-methoxy -5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (4a)</u>



A white solid; 84% yield; m.p. = 134-136 ºC; $[\alpha]^{25}_{D}$ = -81.7 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13-6.99 (m, 6H), 6.86-6.70 (m, 5H), 4.93 (dd, *J* = 119.6, 16.3 Hz, 2H), 4.62 (s, 1H), 4.27 (dd, *J* = 100.3, 9.9 Hz, 2H), 4.18-3.98 (m, 2H), 3.76 (s, 3H), 3.73 (s, 3H), 2.39 (s, 3H), 1.18 (s, 9H), 1.15 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.42, 164.78, 158.75, 155.24, 150.91, 148.23, 139.86, 136.05, 132.35, 129.76, 128.25, 127.69, 127.31, 125.38, 125.25, 116.80, 116.45, 115.93, 114.17, 111.69, 110.06, 82.74, 68.64 (q, 32.3 Hz), 60.71, 58.46, 55.61, 55.24, 47.03, 30.56, 27.64, 19.80, 14.09; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.79; HRMS (ESI^+): calcd for $C_{37}H_{39}F_3N_2O_7$ $[M+Na]^+$ = 703.2607, found = 703.2603; The ee value was 99.7%, t_R (major) = 9.3 min, t_R (minor) = 20.0 min (Chiralcel IG, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

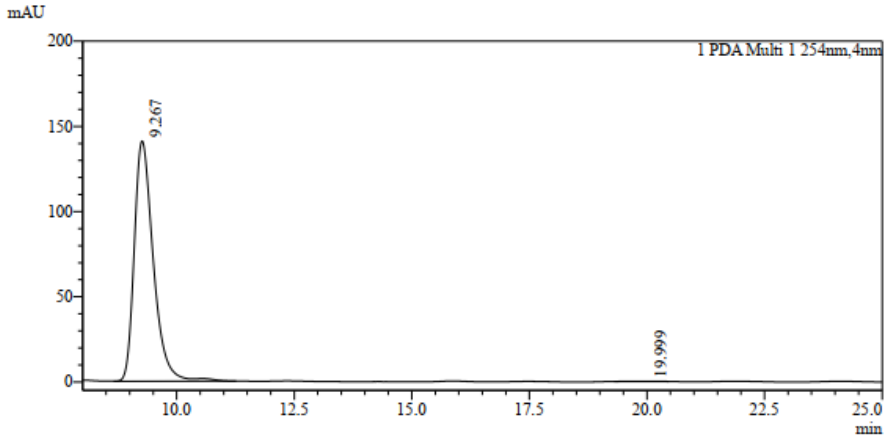


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	9.428	84260	65.495	2680354	49.956
2	18.056	44392	34.505	2685048	50.044
Total		128653	100.000	5365402	100.000

Racemic **4a**



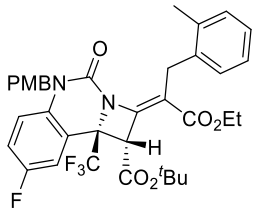
Peak Table

PDA Ch1 254nm

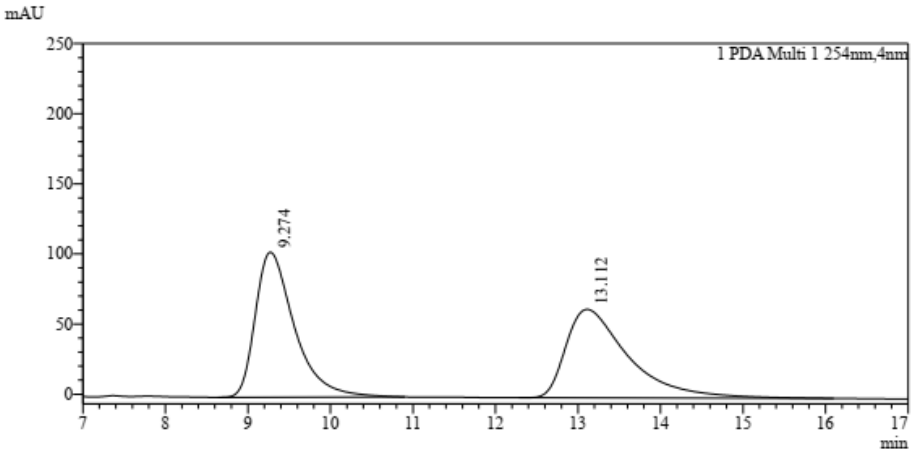
Peak#	Ret. Time	Height	Height%	Area	Area%
1	9.267	140984	99.877	3969780	99.821
2	19.999	173	0.123	7110	0.179
Total		141157	100.000	3976889	100.000

Enantiomerically enriched **4a**

<u>*tert*-butyl (*1S,9bR,E*)-2-(1-ethoxy-1-oxo-3-(o-tolyl)propan-2-ylidene)-8-fluoro-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (4b)</u>



A white solid; 92% yield; m.p. = 131 137 ºC; $[\alpha]^{25}_{D}$ = -124.3 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21-6.92 (m, 8H), 6.87 (dd, *J* = 9.1, 4.3 Hz, 1H), 6.81 (d, *J* = 8.6 Hz, 2H), 4.98 (dd, *J* = 107.9, 16.7 Hz, 2H), 4.68 (s, 1H), 4.29 (dd, *J* = 87.3, 15.7 Hz, 2H), 4.19-4.01 (m, 2H), 3.80 (s, 3H), 2.43 (s, 3H), 1.27 (s, 9H), 1.18 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.30, 164.55, 158.91, 158.13 (d, *J* = 245.0 Hz), 150.49, 148.08, 139.65, 136.02, 135.35, 129.78, 127.67, 127.29, 125.39 (d, *J* = 12.3 Hz), 117.65 (d, *J* = 22.3 Hz), 117.16 (d, *J* = 7.6 Hz), 116.45 (d, *J* = 7.6 Hz), 114.29, 113.77 (d, *J* = 24.6 Hz), 110.61, 83.11, 68.39 (q, *J* = 32.2 Hz), 60.76, 58.31, 55.24, 47.19, 30.54, 27.69, 19.77, 14.07; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.94, -119.20; The ee value was 99.5%, t_R (major) = 9.2 min, t_R (minor) = 12.0 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 0.5 mL/min).

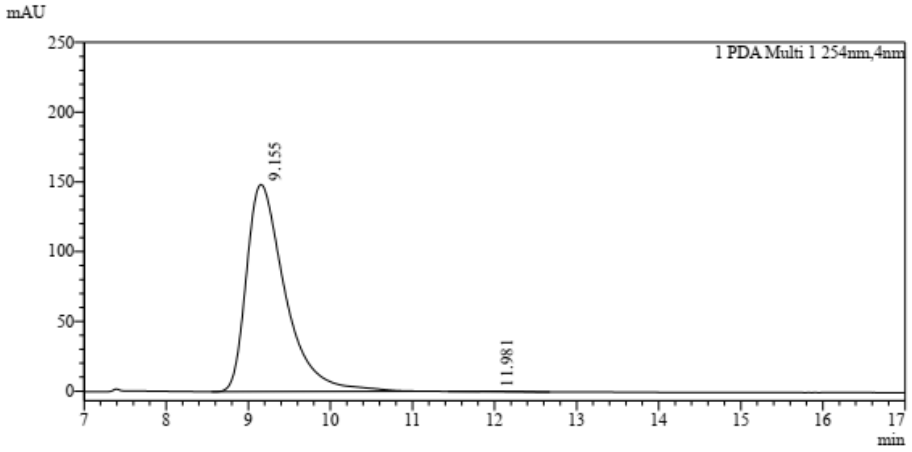


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	9.274	103372	62.099	3412990	50.660
2	13.112	63092	37.901	3323996	49.340
Total		166465	100.000	6736986	100.000

Racemic **4b**



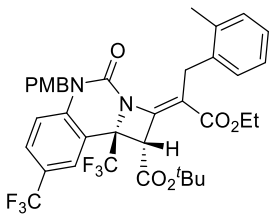
Peak Table

PDA Ch1 254nm

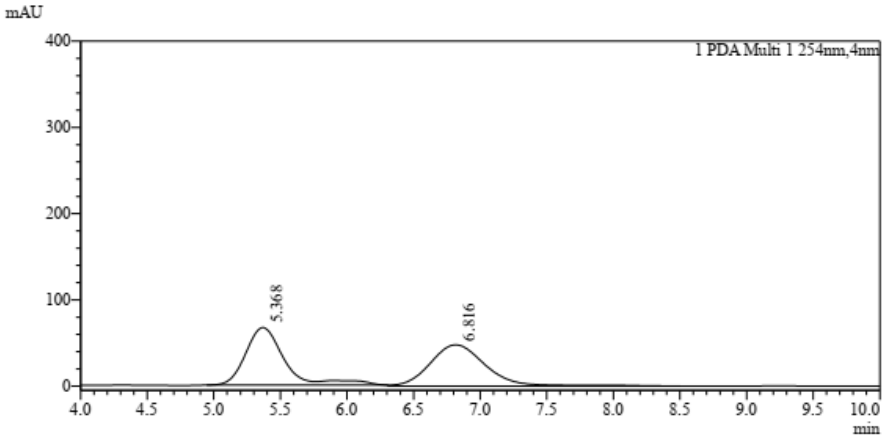
Peak#	Ret. Time	Height	Height%	Area	Area%
1	9.155	148473	99.767	4867007	99.758
2	11.981	346	0.233	11805	0.242
Total		148820	100.000	4878813	100.000

Enantiomerically enriched **4b**

tert-butyl (_1S,9bR,E_)-2-(1-ethoxy-1-oxo-3-(o-tolyl)propan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-8,9b-bis(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (4c)



A white solid; 92% yield; m.p. = 151 154 °C; $[\alpha]^{25}_{D}$ = -108.9 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.1 Hz, 2H), 7.13-6.97 (m, 7H), 6.79 (d, *J* = 8.7 Hz, 2H), 5.00 (dd, *J* = 95.7, 16.3 Hz, 2H), 4.69 (s, 1H), 4.25 (dd, *J* = 70.1, 16.0 Hz, 2H), 4.21-4.01 (m, 2H), 3.77 (s, 3H), 2.40 (s, 3H), 1.20 (s, 9H), 1.16 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.11, 164.46, 159.01, 150.28, 147.87, 141.90, 139.53, 136.03, 129.83, 128.21 (q, *J* = 31.9 Hz), 127.70, 127.30, 127.24, 125.54, 125.34, 123.74, 115.88, 115.24, 114.37, 111.47, 83.31, 69.37-67.79 (q, *J* = 32.5 Hz), 60.90, 58.63, 55.26, 47.17, 30.68, 27.60, 19.78, 14.04; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.28, -81.13; HRMS (ESI^+): calcd for $C_{37}H_{36}F_6N_2O_6$ $[M+H]^+$ = 719.2556, found = 719.2555; The ee value was 81%, t_R (major) = 5.4 min, t_R (minor) = 6.9 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

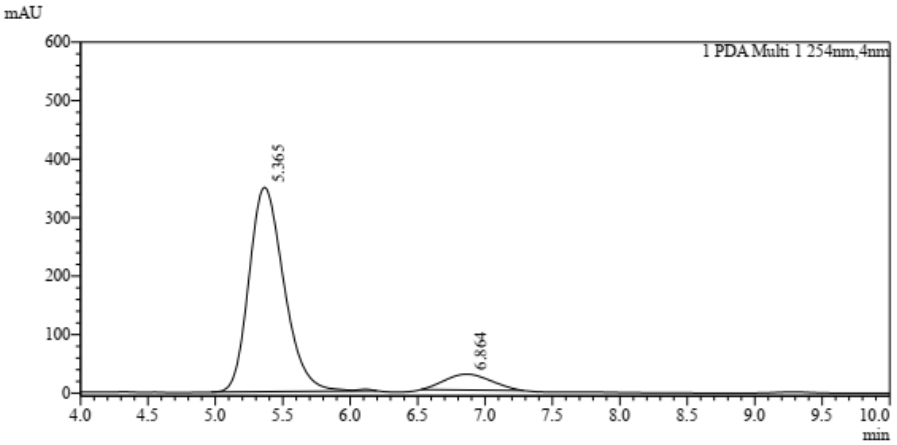


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	5.368	66709	58.223	1367750	49.669
2	6.816	47867	41.777	1385971	50.331
Total		114575	100.000	2753721	100.000

Racemic **4c**



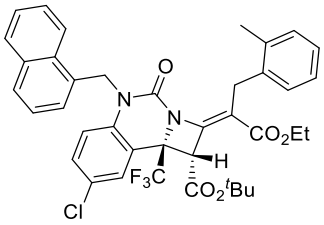
Peak Table

PDA Ch1 254nm

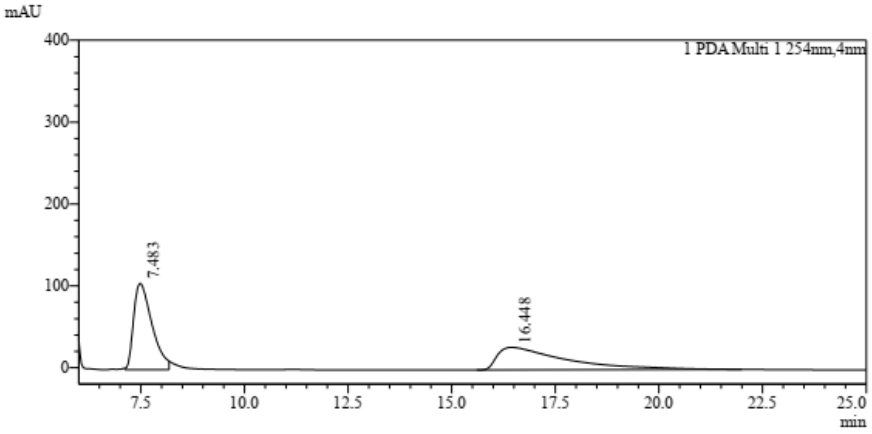
Peak#	Ret. Time	Height	Height%	Area	Area%
1	5.365	349549	92.847	6320583	90.755
2	6.864	26929	7.153	643901	9.245
Total		376478	100.000	6964483	100.000

Enantiomerically enriched **4c**

<u>*tert*-butyl (*1S,9bR,E*)-8-chloro-2-(1-ethoxy-1-oxo-3-(o-tolyl)propan-2-ylidene)-5-(naphthalen-1-ylmethyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (4d)</u>



A white solid; 89% yield; m.p. = 121 123 ºC; $[\alpha]^{25}_{D}$ = -91.4 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.2 Hz, 1H), 7.93-7.87 (m, 1H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.62-7.50 (m, 2H), 7.36-7.25 (m, 2H), 7.17-7. 01 (m, 5H), 6.97 (d, *J* = 7.1 Hz, 1H), 6.59 (d, *J* = 8.9 Hz, 1H), 5.49 (dd, *J* = 29.2, 17.3 Hz, 2H), 4.72 (s, 1H), 4.26 (dd, *J* = 53.7, 15.8 Hz, 2H), 4.18-3.99 (m, 2H), 2.36 (s, 3H), 1.34 (s, 9H), 1.16 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.27, 164.63, 150.30, 147.91, 139.40, 137.73, 136.01, 133.88, 130.99, 130.32, 129.80, 129.42, 129.13, 128.78, 127.92, 127.36, 126.53, 126.43, 126.00, 125.54, 125.39, 122.63, 122.06, 117.21, 116.46, 111.13, 83.36, 68.53 (q, *J* = 32.5 Hz), 60.82, 58.33, 45.38, 30.50, 27.80, 19.77, 14.06; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.72; HRMS (ESI^+): calcd for $C_{39}H_{36}ClF_3N_2O_6$ $[M+Na]^+$ = 727.2163, found = 727.2168; The ee value was 92%, t_R (major) = 7.8 min, t_R (minor) = 18.2 min (Chiralcel ID, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 1.0 mL/min).

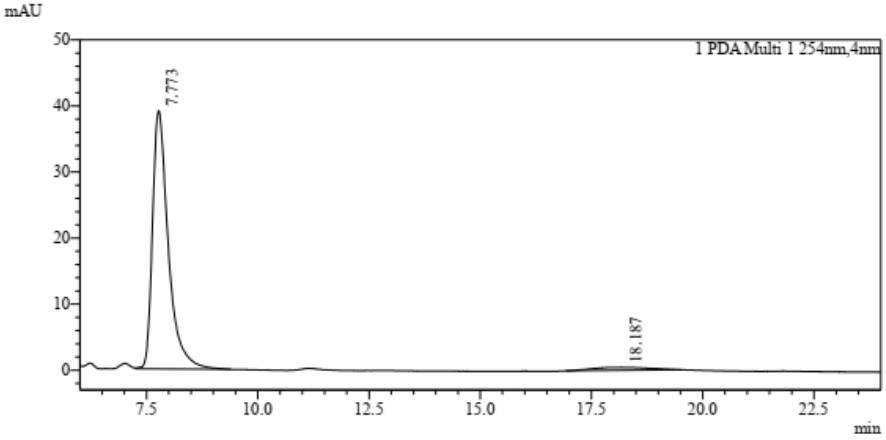


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	7.483	105199	79.310	3244453	50.854
2	16.448	27443	20.690	3135482	49.146
Total		132642	100.000	6379935	100.000

Racemic **4d**



Peak Table

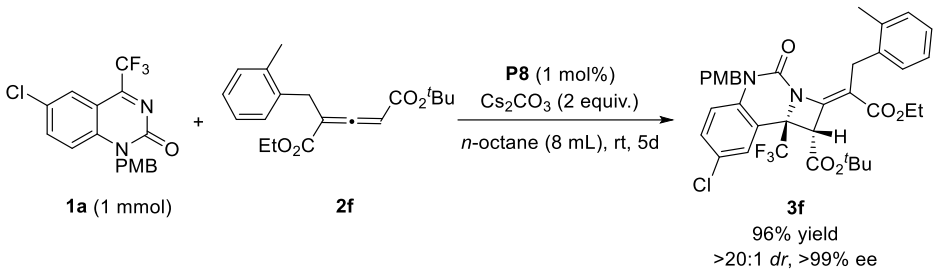
PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	7.773	39076	98.884	969213	96.028
2	18.187	441	1.116	40090	3.972
Total		39517	100.000	1009302	100.000

Enantiomerically enriched **4d**

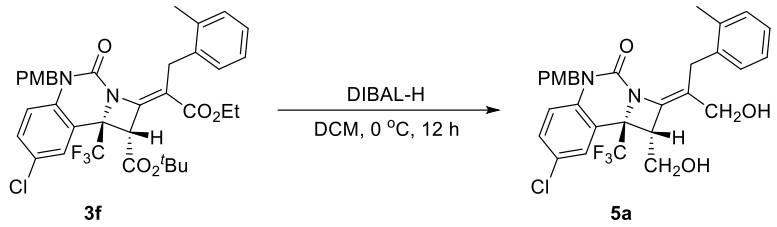
6. Gram-scale preparations and transformations

A. Procedure for the scale-up synthesis and transformations of **3f**



To a round bottle flask with a magnetic stirring bar were added cyclic trifluoroketimine **1a** (1 mmol), phosphonium salt **P8** (10.2 mg, 0.01 mmol) and Cs_2CO_3 (65.2 mg, 2 mmol), allene **2p** was dissolved by *n*-octane (8.0 mL) and added in. The reaction mixture was stirred at room temperature for 5 d and TLC show that the reaction was completed. Purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to afforded product **3f** (96% yield, 656.9 mg, >20:1*dr*, >99% ee).

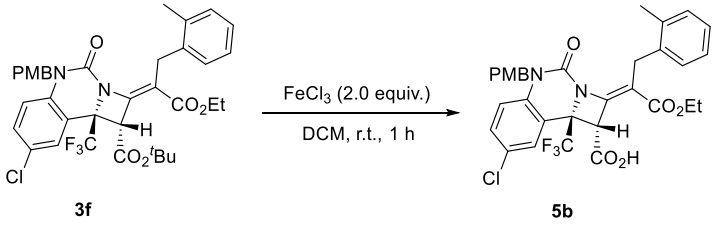
(*1S,9bR,E*)-8-chloro-2-(1-hydroxy-3-(o-tolyl)propan-2-ylidene)-1-(hydroxyl methyl)-5-(4-methoxybenzyl)-9b-(trifluoromethyl)-1,2,5,9b-tetrahydro-4H-azeto[1,2-c]quinazolin-4-one (5a)



3f **5a**

Under nitrogen atmosphere, a round bottle flask with a magnetic stirring bar were added **3f** (>20:1*dr*, >99% ee, 68.5 mg, 0.1 mmol), and dry DCM (2 mL), (*i*Bu)$_2$AlH (0.7 mL, 0.7 mmol), after stired for 12 h at 0 °C. H_2O (3 mL) was added, the mixture was extracted with DCM (5 mL × 3), dried over Na_2SO_4, and the solvent was removed under reduced pressure, the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2 : 1) to give **5a** (>20:1 *dr*, 81% yield, 46.4 mg) as a white solid; m.p. = 132-136 °C; $[\alpha]^{25}_D$ = -94.2 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, CD_3OD) δ 7.55 (s, 1H), 7.28 (dd, *J* = 8.9, 2.3 Hz, 1H), 7.25-7.21 (m, 1H), 7.19-7.09 (m, 5H), 6.90 (d, *J* = 9.0 Hz, 1H), 6.86 (d, *J* = 8.7 Hz, 2H), 5.06 (s, 2H), 4.79-4.48 (m, 1H), 3.99-3.89 (m, 3H), 3.87 (t, *J* = 4.6 Hz, 1H), 3.81 (m, 1H), 3.76 (s, 3H), 3.70 (m, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.95, 150.11, 138.33, 138.03, 137.70, 136.67, 129.85, 129.61, 129.31, 127.96, 127.35, 127.31, 126.76, 125.76, 125.34, 119.91, 116.80, 115.90, 113.76, 68.61 (q, *J* = 24.6 Hz), 58.88, 58.06, 54.30, 52.57, 45.71, 31.91, 18.30; ^{19}F NMR (376 MHz, CD_3OD) δ -82.01. HRMS (ESI$^+$): calcd for $C_{30}H_{28}ClF_3N_2O_4$ $[M+H]^+$ = 573.1768, found = 573.1776.

(*1S,9bR,E*)-8-chloro-2-(1-ethoxy-1-oxo-3-(o-tolyl)propan-2-ylidene)-5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylic acid (5b)

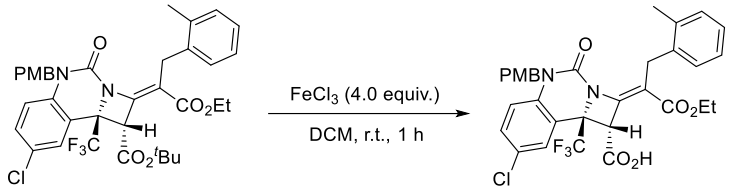


3f **5b**

A round bottle flask with a magnetic stirring bar were added **3f** (>20:1*dr*, >99% ee, 68.5 mg, 0.1 mmol), and dry DCM (2 mL), $FeCl_3$ (32.4 mg, 0.2 mmol), after stired for 1 h at room temperature, the mixture was filtrated and purified by column chromatography on silica gel (ethyl acetate) to give **5b** (>20:1*dr*, 56.6 mg, 91% yield) as a white solid; m.p. = 181-183 °C; $[\alpha]^{25}_D$ = -61.2 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, CD_3OD) δ 7.36

(s, 1H), 7.35-7.29 (m, 1H), 7.14-6.94 (m, 7H), 6.77 (d, J = 8.6 Hz, 2H), 5.11-4.78 (m, 2H), 4.24 (dd, J = 70.6, 15.9 Hz, 3H), 4.13-4.06 (m, 2H), 3.73 (s, 3H), 3.37 (s, 1H), 2.36 (s, 3H), 1.17 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 167.57, 167.34, 158.96, 150.50, 147.92, 139.19, 137.67, 135.63, 130.74, 129.28, 128.32, 127.43, 126.87, 125.33, 125.27, 125.22, 117.68, 116.58, 113.84, 110.29, 67.95 (q, J = 32.3 Hz), 60.59, 56.82, 54.28, 46.25, 30.03, 18.45, 12.99; ^{19}F NMR (376 MHz, CD_3OD) δ -82.01; HRMS (ESI^+): calcd for $C_{32}H_{28}ClF_3N_2O_6$ $[M+Na]^+$ = 651.1486, found = 651.1486.

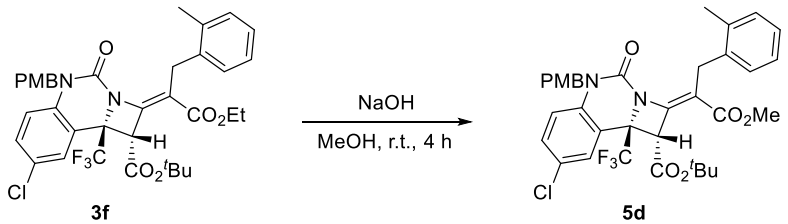
(*1S,9bR,E*)-8-chloro-2-(1-ethoxy-1-oxo-3-(o-tolyl)propan-2-ylidene)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylic acid (5c)



3f **5c**

5c (>20:1 *dr*, 44.3 mg, 87% yield) was gained under similar condition of **5b**, by used $FeCl_3$ (64.8 mg, 0.4 mmol). As a white solid; m.p. = 173-176 °C; $[\alpha]^{25}_D$ = -84.6 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, CD_3OD) δ 7.40 (dd, J = 8.7, 2.3 Hz, 1H), 7.31 (s, 1H), 7.10-6.98 (m, 4H), 6.94 (d, J = 8.6 Hz, 1H), 4.76 (s, 1H), 4.21 (dd, J = 71.2, 15.6 Hz, 1H), 4.09-4.03 (m, 2H), 2.35 (s, 3H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 167.63, 167.29, 150.45, 148.04, 138.90, 137.19, 135.64, 131.10, 129.22, 127.76, 127.27, 125.68, 125.23, 116.89, 114.01, 110.84, 69.30 (q, J = 32.2 Hz), 60.50, 57.01, 30.45, 30.17, 18.44, 12.94; ^{19}F NMR (376 MHz, CD_3OD) δ -82.82. HRMS (ESI^+): calcd for $C_{24}H_{20}ClF_3N_2O_5$ $[M+Na]^+$ = 509.1091, found = 509.1093.

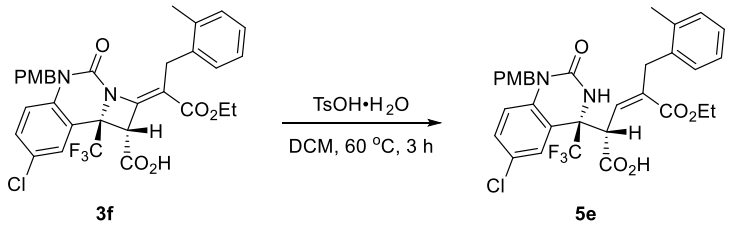
***tert*-butyl (*1S,9bR,E*)-8-chloro-2-(1-methoxy-1-oxo-3-(o-tolyl)propan-2-ylidene) -5-(4-methoxybenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydro-2H-azeto[1,2-c]quinazoline-1-carboxylate (5d)**



3f **5d**

A round bottle flask with a magnetic stirring bar were added **3f** (>20:1 *dr*, >99% ee, 68.5 mg, 0.1 mmol), and MeOH (1 mL), NaOH (32 mg, 0.2 mmol), after stired for 4 h at ambient temperature, H_2O (3 mL) was added, methanol was removed by evaporation under reduced pressure, the mixture was extracted with DCM (3 mL × 3), dried over Na_2SO_4, the solvent was removed by evaporation under reduced pressure, and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **5d** (>20:1*dr*, 46.5 mg, 80% yield) as a white solid; m.p. = 115-117 °C; $[\alpha]^{25}_D$ = -95.8 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (s, 1H), 7.22 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.16-7.05 (m, 4H), 6.98 (d, *J* = 8.6 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 1H), 6.77 (d, *J* = 8.7 Hz, 2H), 4.93 (dd, *J* = 107.3, 16.3 Hz, 2H), 4.66 (s, 1H), 4.25 (dd, *J* = 86.0, 15.8 Hz, 2H), 3.77 (s, 3H), 3.64 (s, 3H), 2.39 (s, 3H), 1.28 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.11, 164.89, 158.96, 149.11, 148.75, 137.62, 130.85, 128.35, 127.56, 127.36, 126.19, 117.02, 116.19, 114.36, 109.19, 83.14, 68.66 (q, *J* = 31.9 Hz), 58.72, 55.27, 51.68, 46.65, 27.66, 14.07; ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.04; HRMS (ESI^+): calcd for $C_{35}H_{34}ClF_3N_2O_6$ $[M+H]^+$ = 671.2136, found = 671.2133.

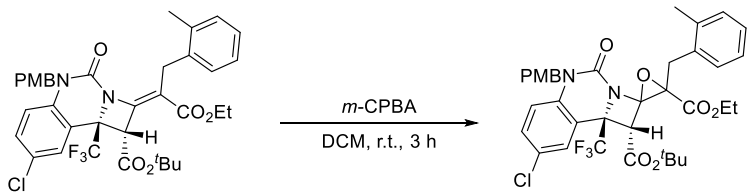
(*S*,*Z*)-2-((*R*)-6-chloro-1-(4-methoxybenzyl)-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-4-yl)-5-ethoxy-4-(2-methylbenzyl)-5-oxopent-3-enoic acid (5e)



Under nitrogen atmosphere, a round bottle flask with a magnetic stirring bar were added **3f** (>20:1 *dr*, >99% ee, 68.5 mg, 0.1 mmol), and DCE (2 mL), TsOH·H_2O (5.2 mg, 0.02 mmol), after stired for 3 h at 60 °C. H_2O (3 mL) was added, the mixture was extracted with DCM (3 mL × 3), dried over Na_2SO_4, and the solvent was removed under reduced pressure, the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2 : 1) to give **5e** (>20:1 *dr*, 94% yield, 59.2 mg). ^{1}H NMR (400 MHz, CD_3OD) δ 7.35 (s, 1H), 7.32-7.21 (m, 1H), 7.18-6.98 (m, 4H), 6.97-6.87 (m, 3H), 6.81-6.67 (m, 2H), 4.98-4.80 (m, 6H), 4.23 (dd, *J* = 69.5, 16.0 Hz, 2H), 4.14-3.98 (m, 1H), 3.68 (s, 3H), 2.32 (s, 3H), 1.13 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 171.51, 171.28, 162.90, 154.44, 151.86, 143.14, 141.60, 139.58, 134.68, 133.23,

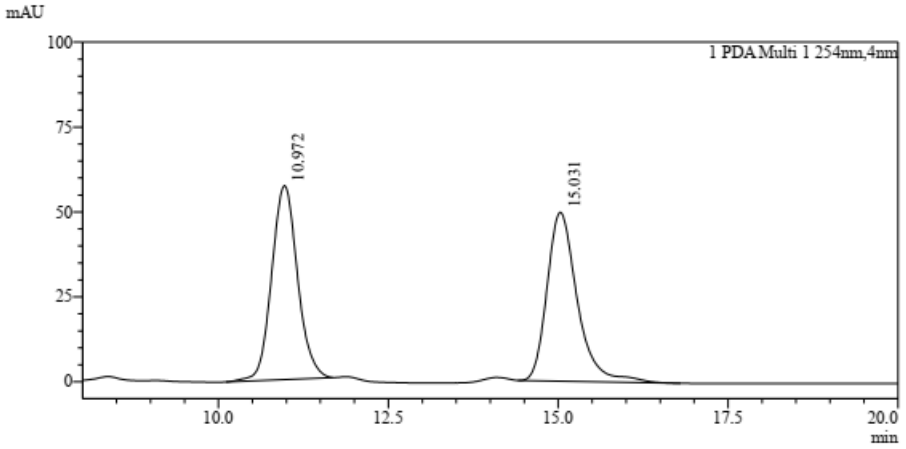
132.26, 131.38, 131.36, 130.81, 129.27, 129.17, 121.62, 120.51, 117.78, 114.24, 71.89 (q, J = 32.5 Hz), 64.53, 60.76, 58.22, 50.17, 33.99, 22.42, 16.94; ^{19}F NMR (376 MHz, CD_3OD) δ -82.49.

1-(*tert*-butyl) 3'-ethyl (*1R,3'S,9bS*)-8-chloro-5-(4-methoxybenzyl)-3'-(2-methylbenzyl)-4-oxo-9b-(trifluoromethyl)-1,4,5,9b-tetrahydrospiro[azeto[1,2-c]quinazoline-2,2'-oxirane]-1,3'-dicarboxylate (5f)



3f **5f**

A round bottle flask with a magnetic stirring bar were added **3f** (>20:1 *dr*, >99% ee, 68.5 mg, 0.1 mmol), and DCE (2 mL), *m*-CPBA (121.8 mg, 0.6 mmol), after stired for 3 h at room temperature. H_2O (3 mL) was added, the mixture was extracted with DCM (3 mL × 3), dried over Na_2SO_4, and the solvent was removed under reduced pressure, the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10 : 1) to give **5f (**>20:1 *dr*, 96% ee, 83% yield, 59.1 mg). m.p. = 91-96 °C; $[\alpha]^{25}_D$ = -103.1 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, Acetone-d6) δ 7.55-7.41 (m, 2H), 7.32-7.10 (m, 7H), 6.93 (d, J = 8.7 Hz, 2H), 5.13 (dd, J = 37.1, 16.4 Hz, 2H), 4.20 (s, 1H), 4.07 (dd, J = 201.9, 16.2 Hz, 2H), 4.11-4.02 (m, 2H), 3.81 (s, 3H), 2.43 (s, 3H), 1.33 (s, 9H), 1.08 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, Acetone-d6) δ 166.70, 164.53, 159.14, 149.38, 138.10, 136.53, 135.72, 131.20, 130.01, 128.03, 127.93, 127.72, 126.35, 125.72, 117.96, 116.06, 114.09, 84.15, 83.96, 66.34, 62.01, 57.03, 54.62, 45.65, 31.79, 26.91, 19.27, 12.96; ^{19}F NMR (376 MHz, Acetone-d6) δ -82.06; The ee value was 96%, t_R (major) = 11.3 min, t_R (minor) = 15.0 min (Chiralcel IA, λ = 254 nm, hexane/2-propanol = 90/10, flow rate = 0.5 mL/min).

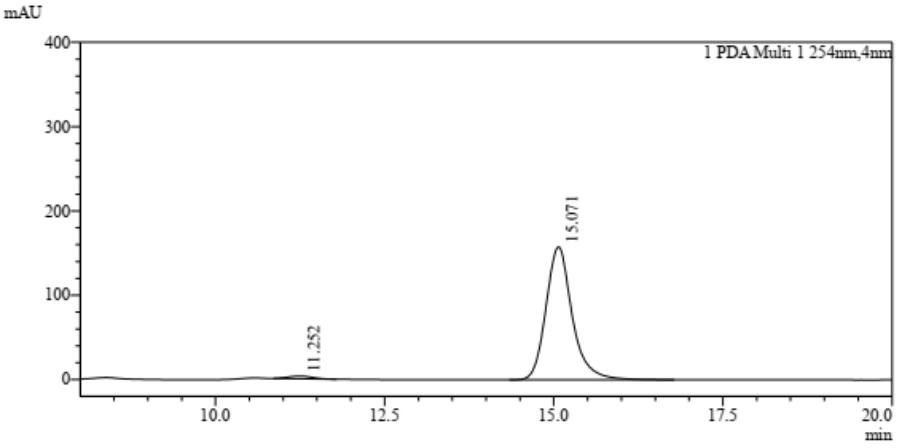


Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	10.972	57073	53.447	1513798	49.515
2	15.031	49712	46.553	1543467	50.485
Total		106785	100.000	3057265	100.000

Racemic **5f**



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	11.252	3179	1.976	78645	1.811
2	15.071	157699	98.024	4263187	98.189
Total		160878	100.000	4341832	100.000

Enantiomerically enriched **5f**

7. Determination of absolute configuration of products

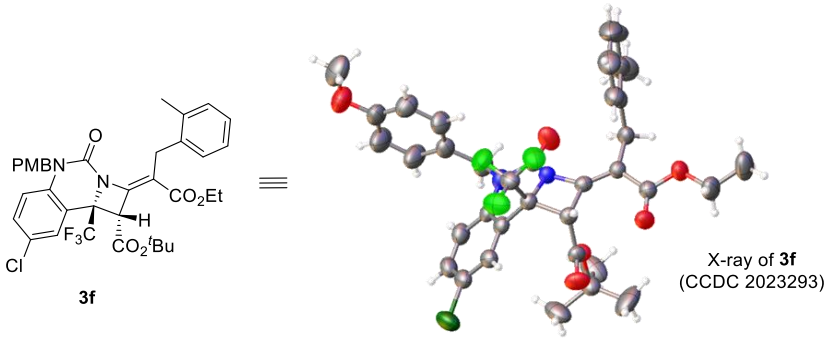


Figure S2. X-ray structure of **3f**.

Table S5. Crystal data and structure refinement for **3f.**

Identification code	wtl-zs-1429
Empirical formula	C36H36ClF3N2O6
Formula weight	685.12
Temperature/K	294.5(7)
Crystal system	monoclinic
Space group	P21
a/Å	8.08272(16)
b/Å	9.84747(16)
c/Å	21.8501(4)
α/°	90
β/°	95.1500(19)
γ/°	90
Volume/Å3	1732.13(6)
Z	2
ρcalcg/cm3	1.314
μ/mm-1	1.520
F(000)	716.0
Crystal size/mm3	0.5 × 0.3 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.126 to 143.836
Index ranges	-6 ≤ h ≤ 9, -12 ≤ k ≤ 12, -26 ≤ l ≤ 24
Reflections collected	11907
Independent reflections	6345 [Rint = 0.0424, Rsigma = 0.0539]
Data/restraints/parameters	6345/1/439

Goodness-of-fit on F2	1.076
Final R indexes [I>=2σ (I)]	R1 = 0.0627, wR2 = 0.1616
Final R indexes [all data]	R1 = 0.0681, wR2 = 0.1711
Largest diff. peak/hole / e Å-3	0.28/-0.29
Flack parameter	0.003(17)

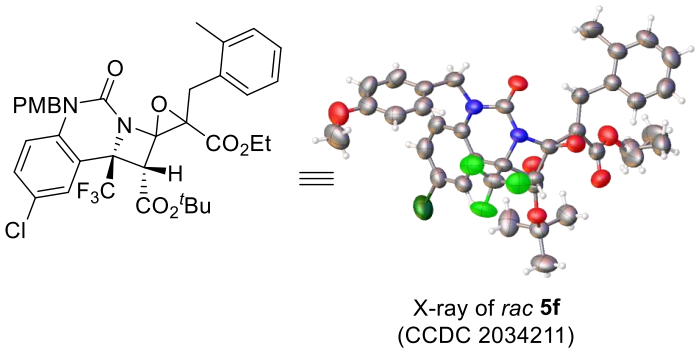


Figure S3. X-ray structure of racemic **5f**.

Table S6. Crystal data and structure refinement for **5f**.

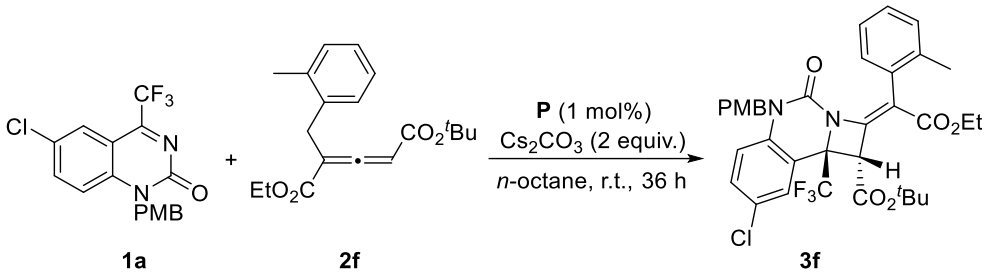
Identification code	wtl-zs-4-O
Empirical formula	C36H36ClF3N2O7
Formula weight	701.12
Temperature/K	295.2(4)
Crystal system	triclinic
Space group	P-1
a/Å	12.0254(7)
b/Å	12.2134(8)
c/Å	13.7083(7)
α/°	104.703(5)
β/°	91.687(5)
γ/°	116.424(6)
Volume/Å3	1720.23(19)
Z	2
ρcalcg/cm3	1.354
μ/mm-1	1.566
F(000)	732.0
Crystal size/mm3	0.3 × 0.2 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	6.758 to 143.03
Index ranges	-13 ≤ h ≤ 14, -14 ≤ k ≤ 14, -16 ≤ l ≤ 16

Reflections collected	18459
Independent reflections	6584 [Rint = 0.0372, Rsigma = 0.0315]
Data/restraints/parameters	6584/0/469
Goodness-of-fit on F2	1.035
Final R indexes [I>=2σ (I)]	R1 = 0.0575, wR2 = 0.1629
Final R indexes [all data]	R1 = 0.0695, wR2 = 0.1793
Largest diff. peak/hole / e Å-3	0.25/-0.25

8. Mechanistic studies

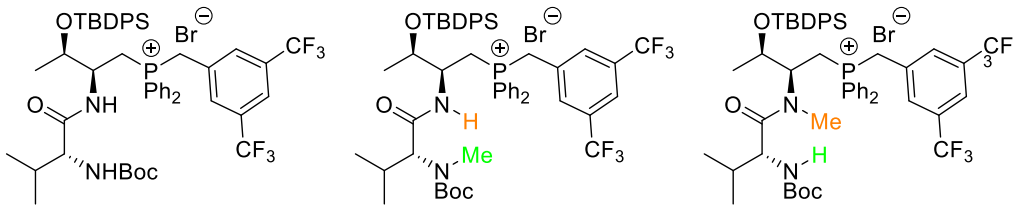
A. Reaction catalyzed by different phosphonium salts

Table S7. Reaction catalyzed by different phosphonium salts[a]



1a 2f 3f

Entry	P	yield (%)[b]	ee (%)[c]
1	**P8**	96	>99
2	**P8-1**	35	2
3	**P8-2**	30	3
4[d]	**P8**	messy	-



P8 P8-1 P8-2

Reaction condition: [a] **1a** (0.05 mmol), **2f** (0.055 mmol), **P** (0.0005 mmol) and Cs_2CO_3 (0.1 mmol) in *n*-octane (0.5 mL) at room temperature for 36 h. All >20:1 *dr*, and *dr* values were analyzed by ^1H NMR spectroscopy. [b] Isolated yields. [c] The ee values were determined by HPLC. [d] Solvent is MeOH.

We also prepared the methylated phosphonium salt catalysts **P8-1** and **P8-2**. When methylated phosphonium salts **P8-1** and **P8-2** was used, the racemic product was

obtained with loss of yield (Table S7, entries 2-3). Of note, when the reaction was performed in methanol, we did not obtain the expected product. These preliminary results indicated the importance of both hydrogen-bonding and ion-pair interactions and steric hindrance provide by phosphonium salt catalysts (Table S7).

B. Proposed mechanism

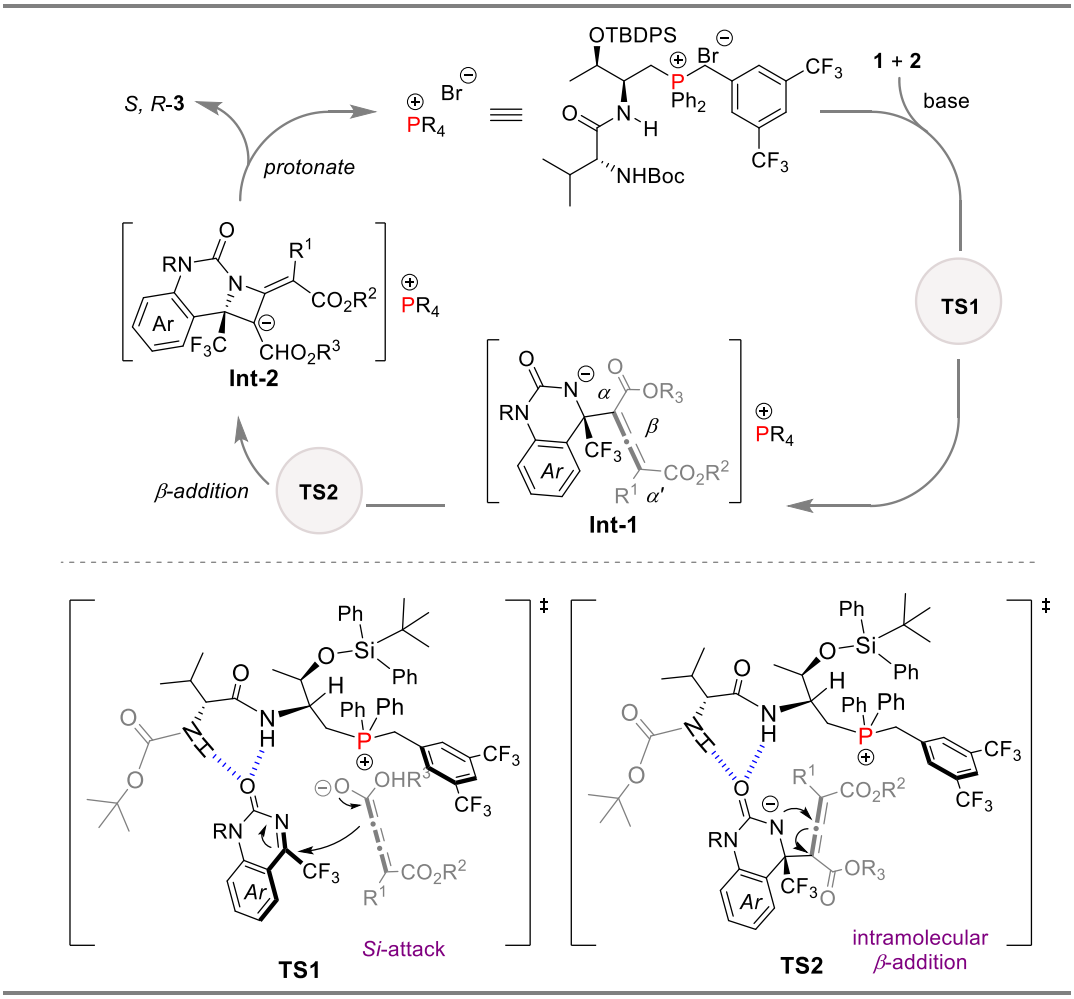


Figure S4. Proposed catalytic cycle.

9. References

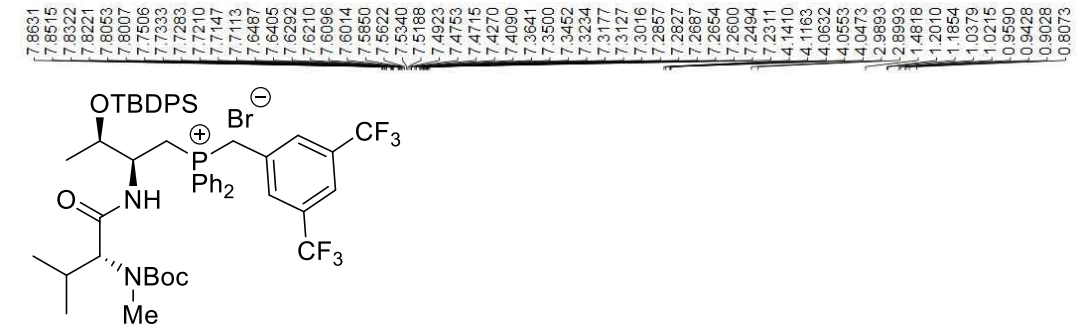
[1] a) J. Pan, J.-H. Wu, H. Zhang, X. Ren, J.-P. Tan, L. Zhu, H.-S. Zhang, C. Jiang, T. Wang, *Angew. Chem. Int. Ed*. **2019**, *58*, 7425-7430; b) H. Zhang, J. He, Y. Chen, C. Zhuang, C. Jiang, K.Xiao, Z. Su, X. Ren, T. Wang, *Angew. Chem. Int. Ed*. **2021**, *60*, 19860-19870.

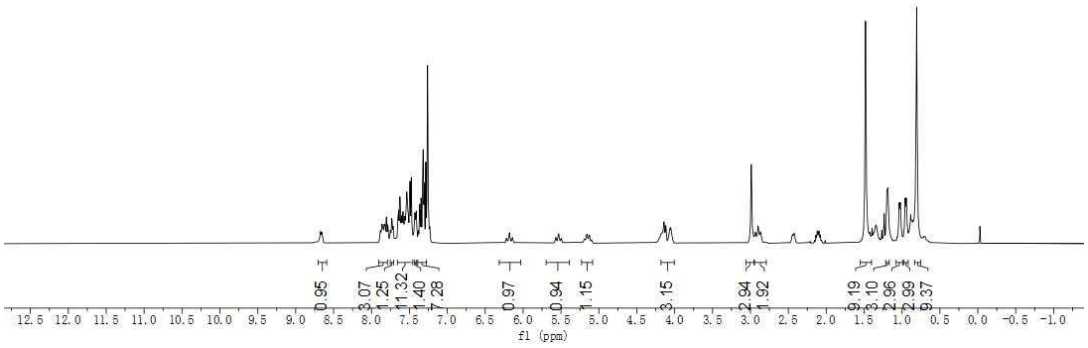
[2] L.-J. Yang, S. Li, S. Wang, J. Nie, J.-A. Ma, *J. Org. Chem*. **2014**, *79*, 3547-3558.

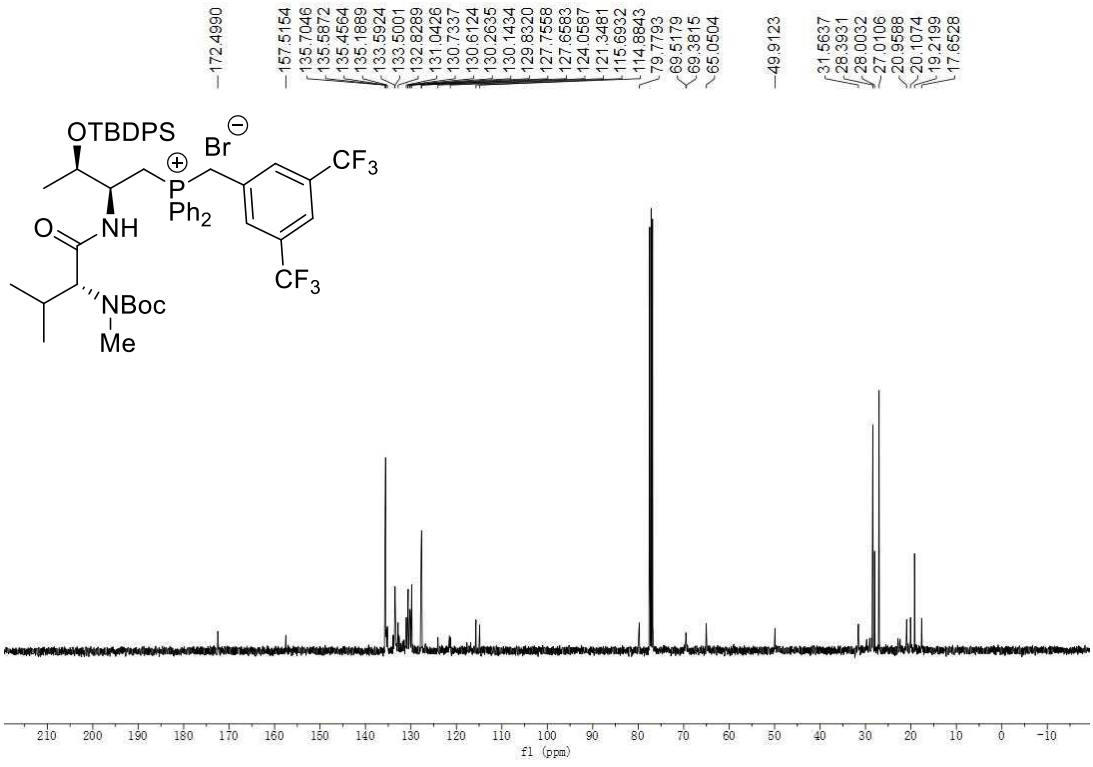
[3] T. Hashimoto, K. Sakata, F. Tamakuni, M. J. Dutton, K. Maruoka, *Nat. Chem.* **2013**, *5*, 240-244.

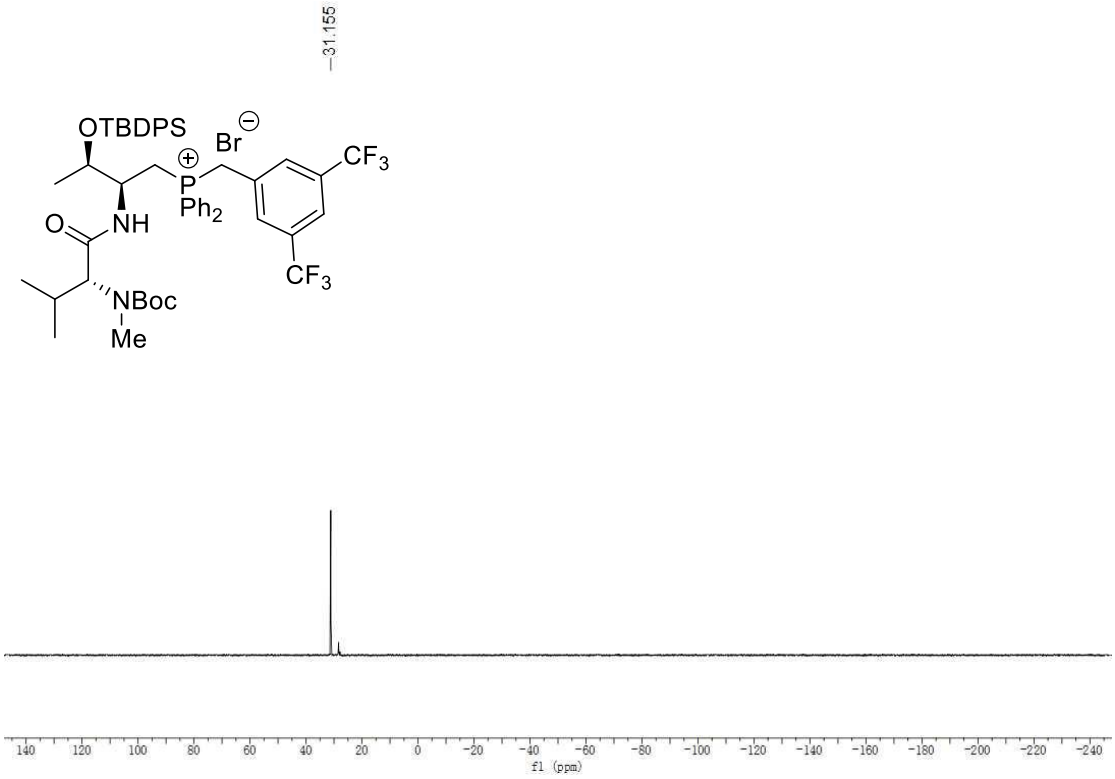
11. NMR spectra

NMR of **P8-1** ($CDCl_3$)





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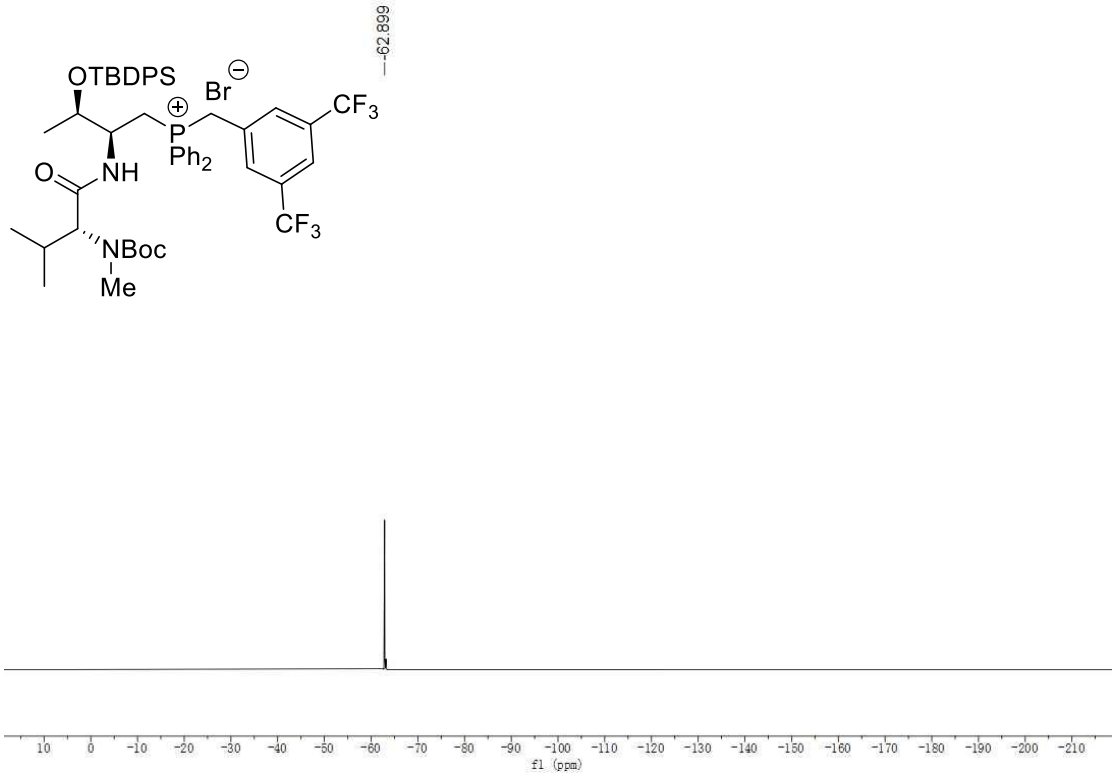
Br
CF3
P
Ph2
O
NH
CF3
NBoc
Me
140 120 100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240
f1 (ppm)


62.899
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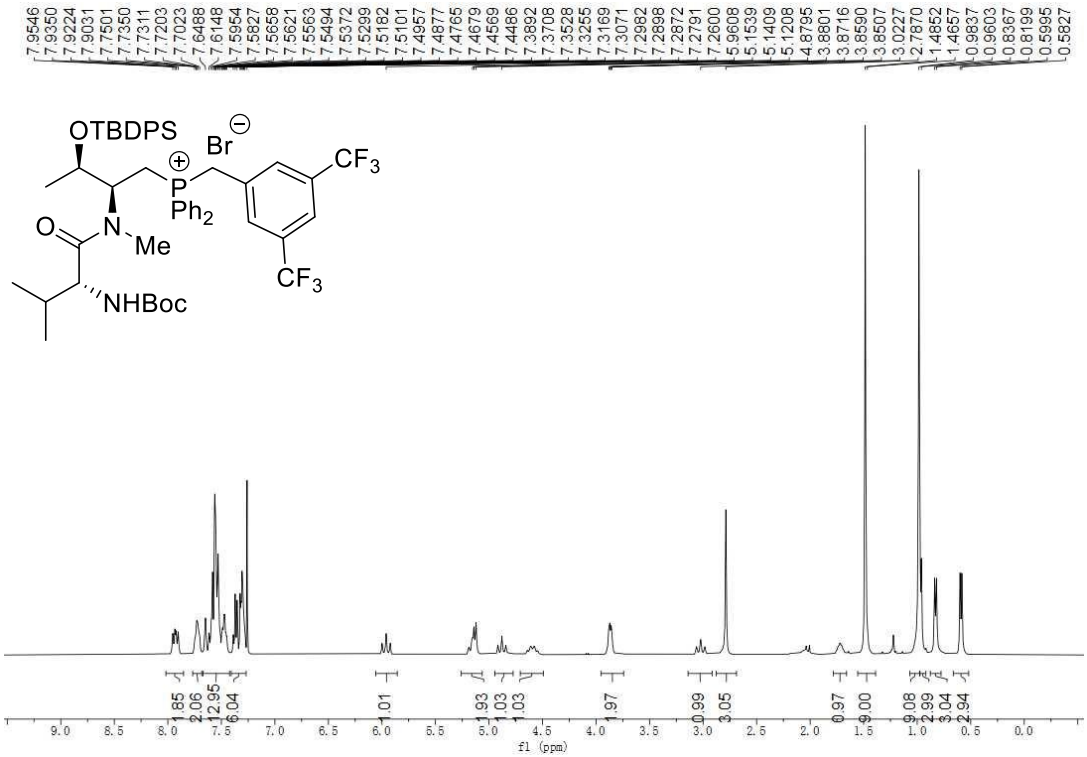
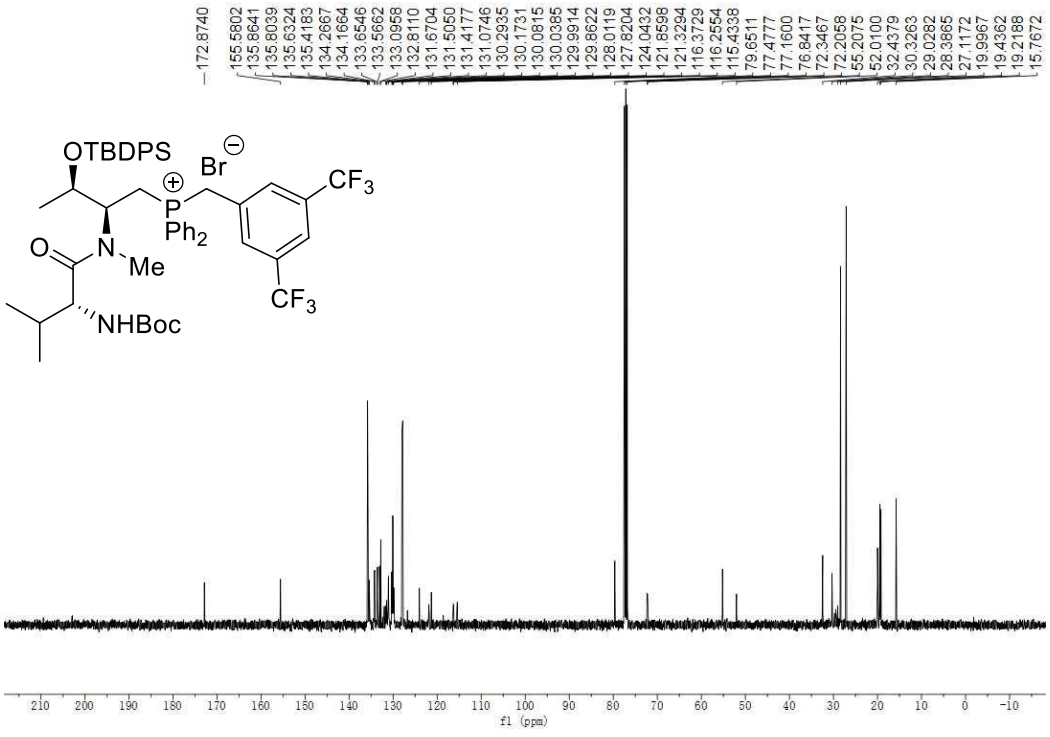
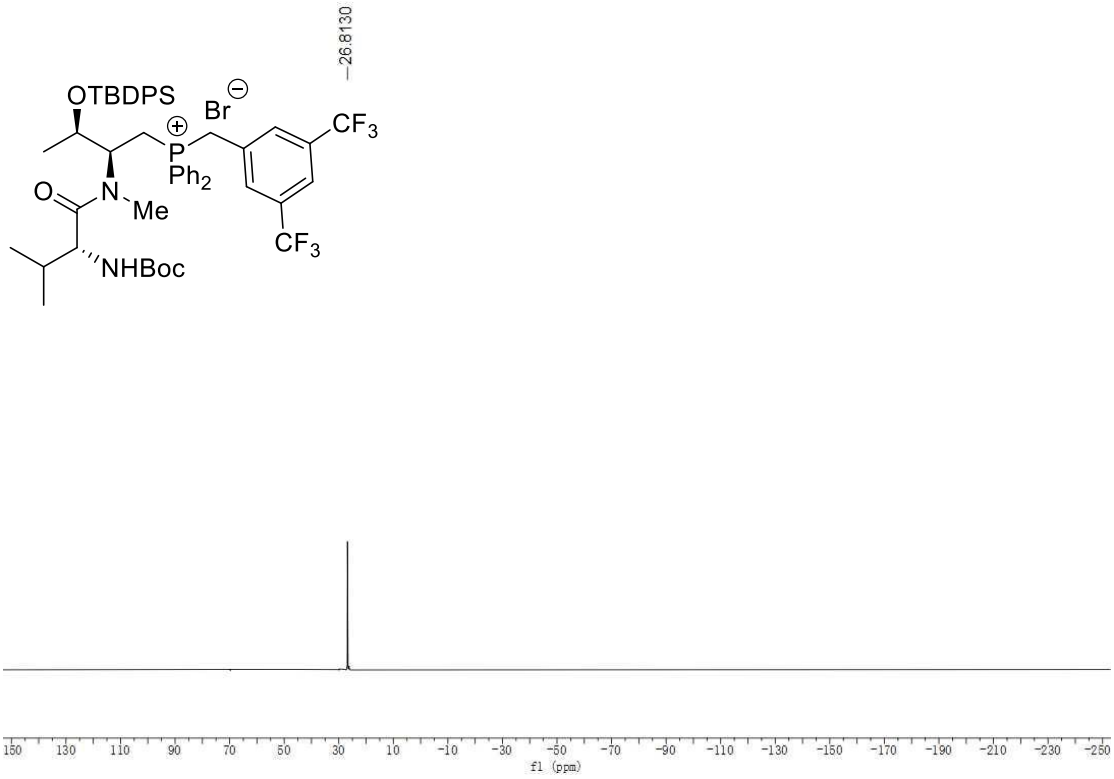
Br
CF3
P
Ph2
O
NH
CF3
NBoc
Me
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

NMR of **P8-2** ($CDCl_3$)



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P
Ph2
O
N
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CF3
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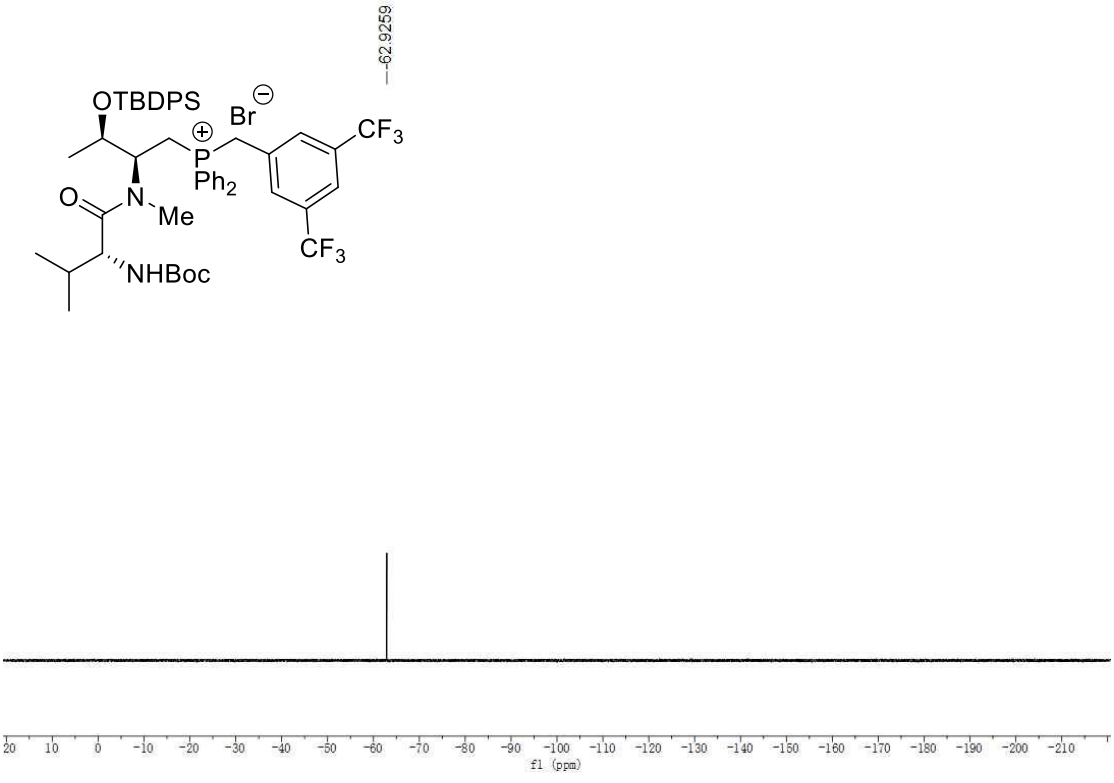
150 130 110 90 70 50 30 10 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210 -230 -250
f1 (ppm)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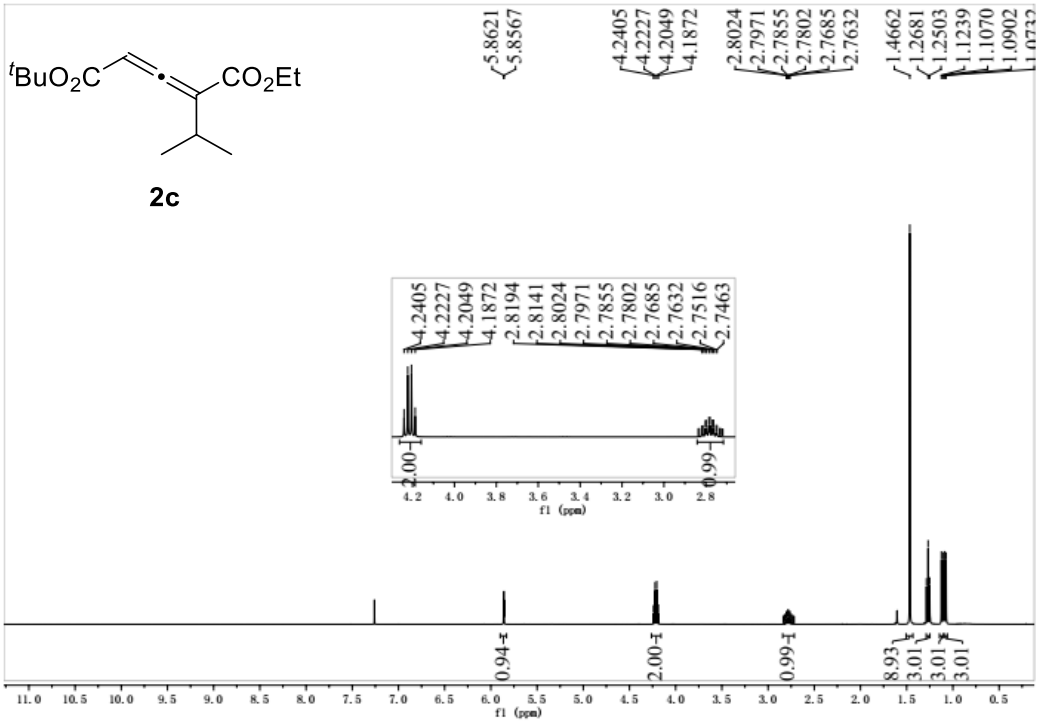
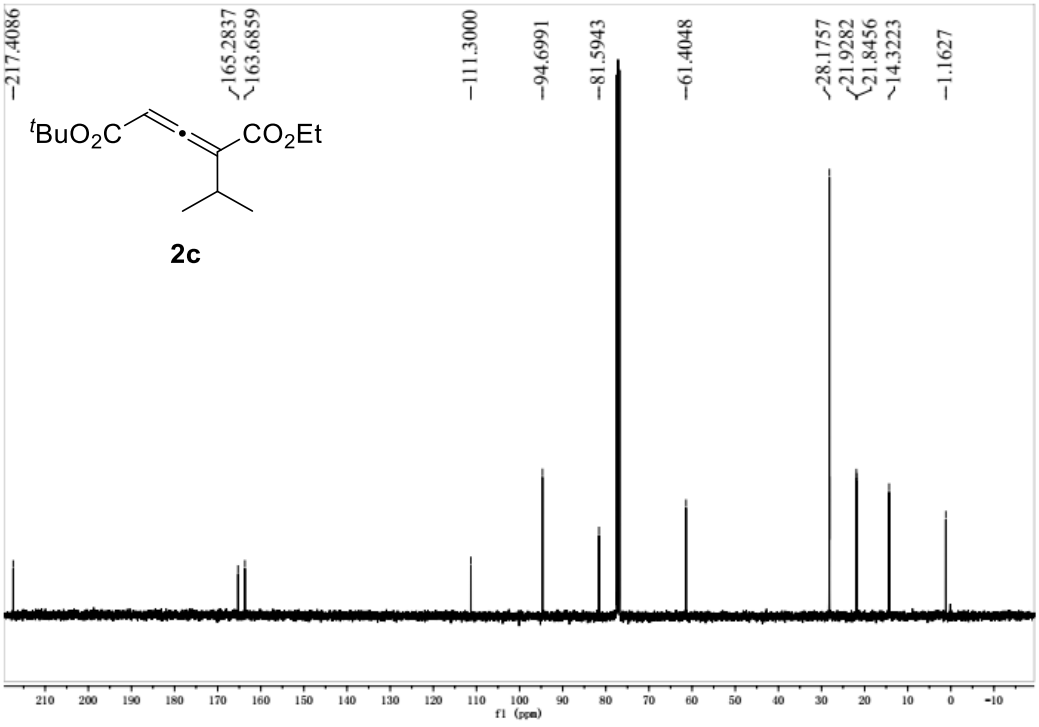
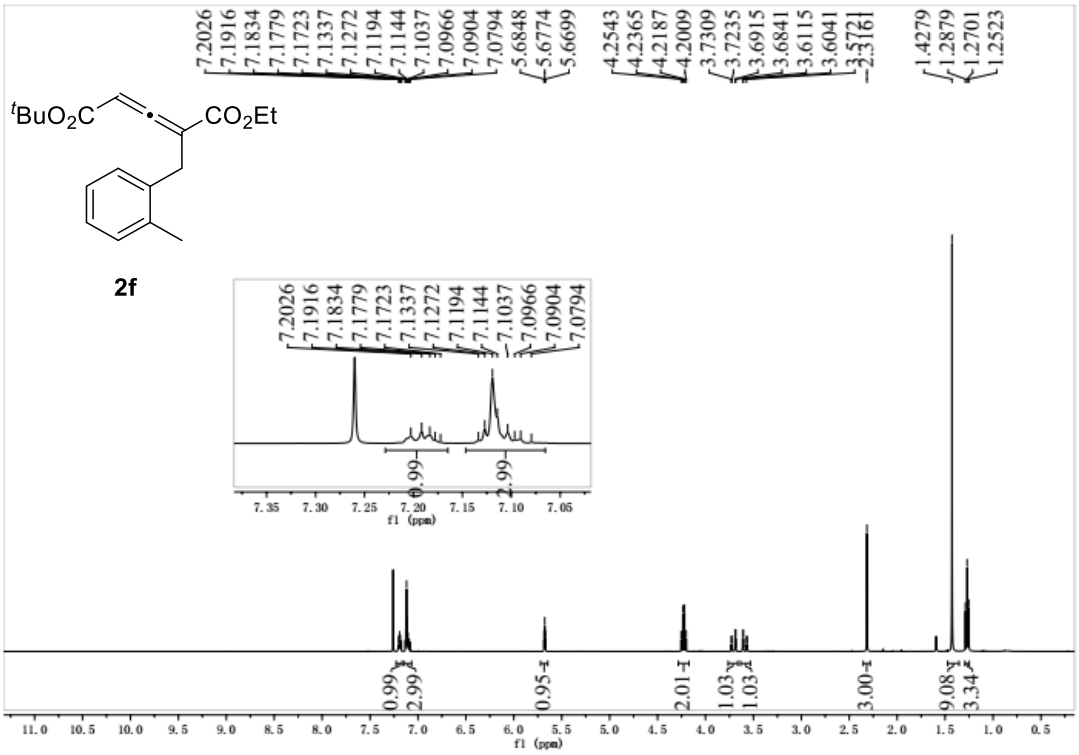
CF3
P
Ph2
O
N
Me
CF3
NHBoc
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

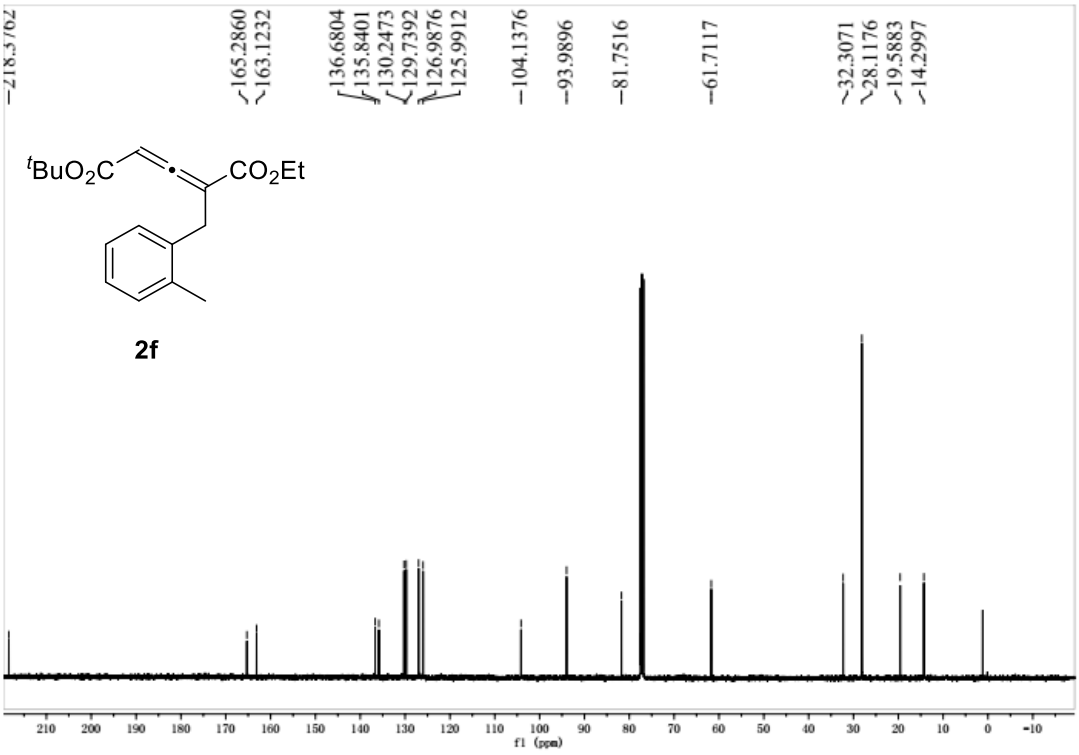
NMR of **2c** ($CDCl_3$)



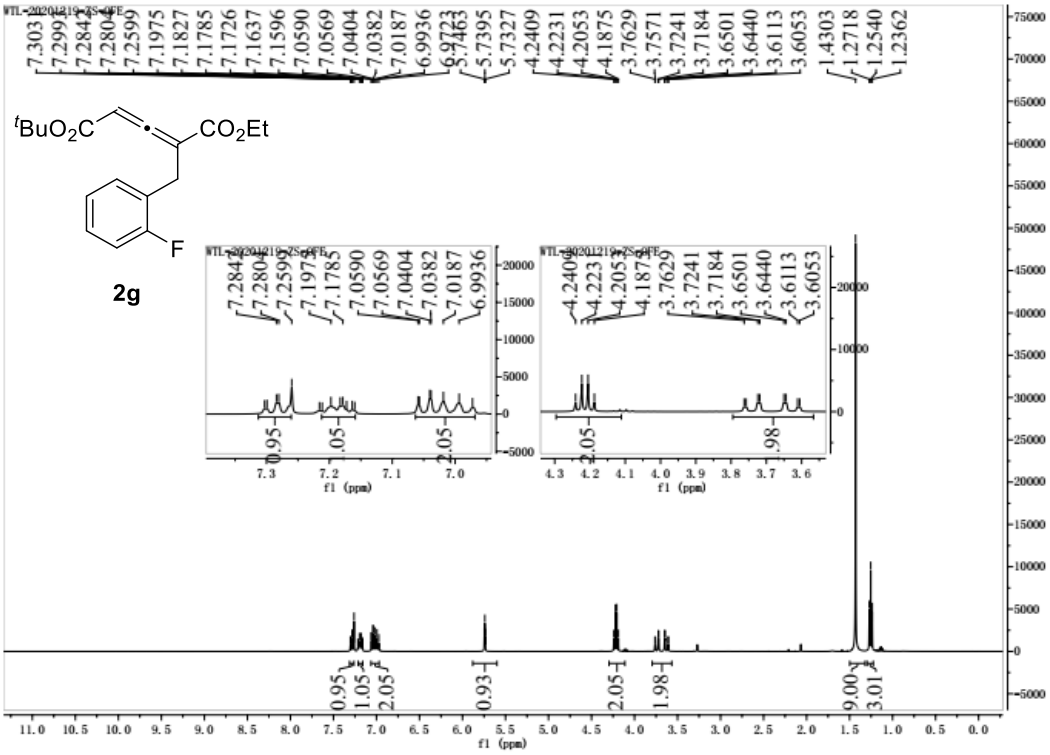


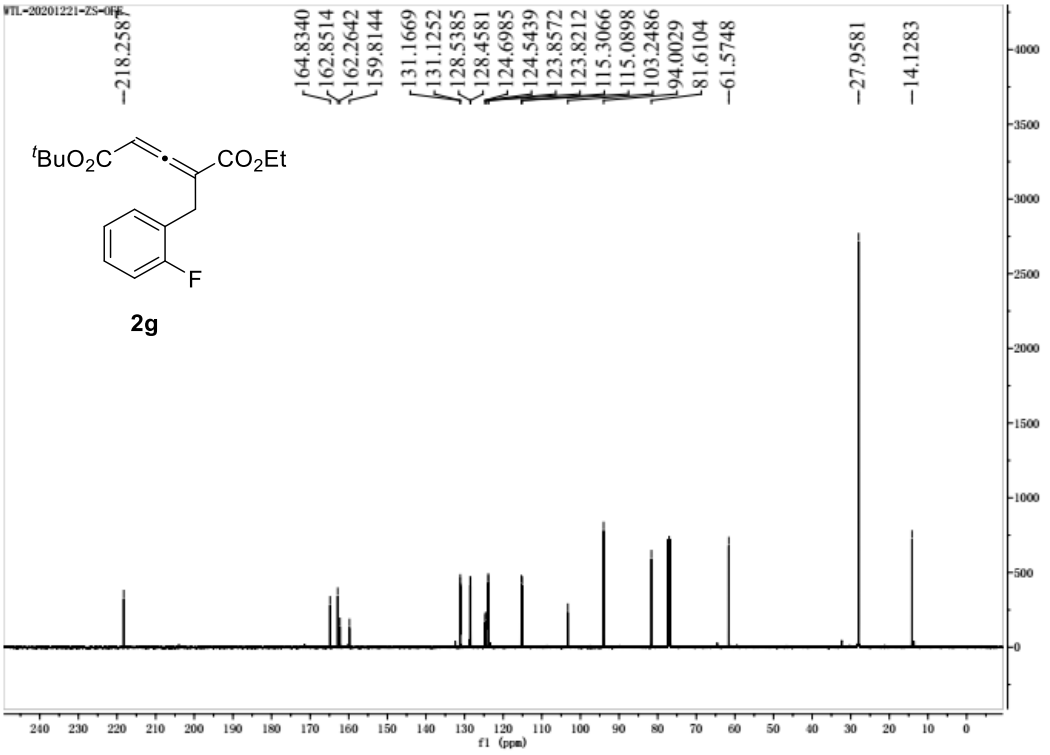
NMR of **2f** ($CDCl_3$)

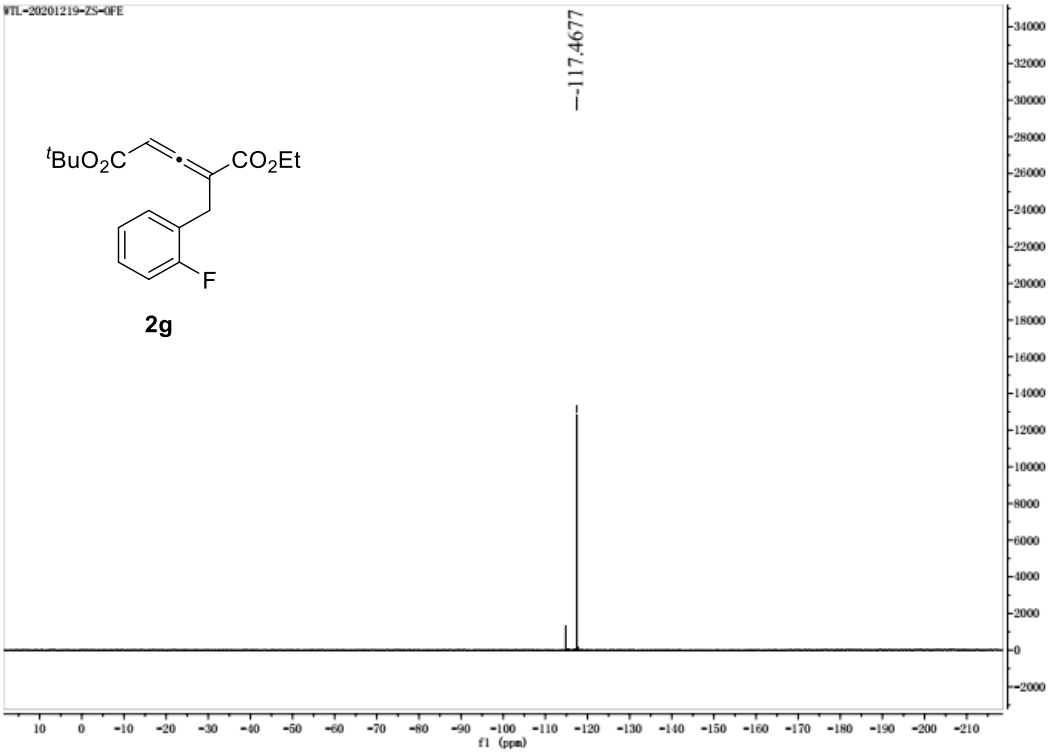




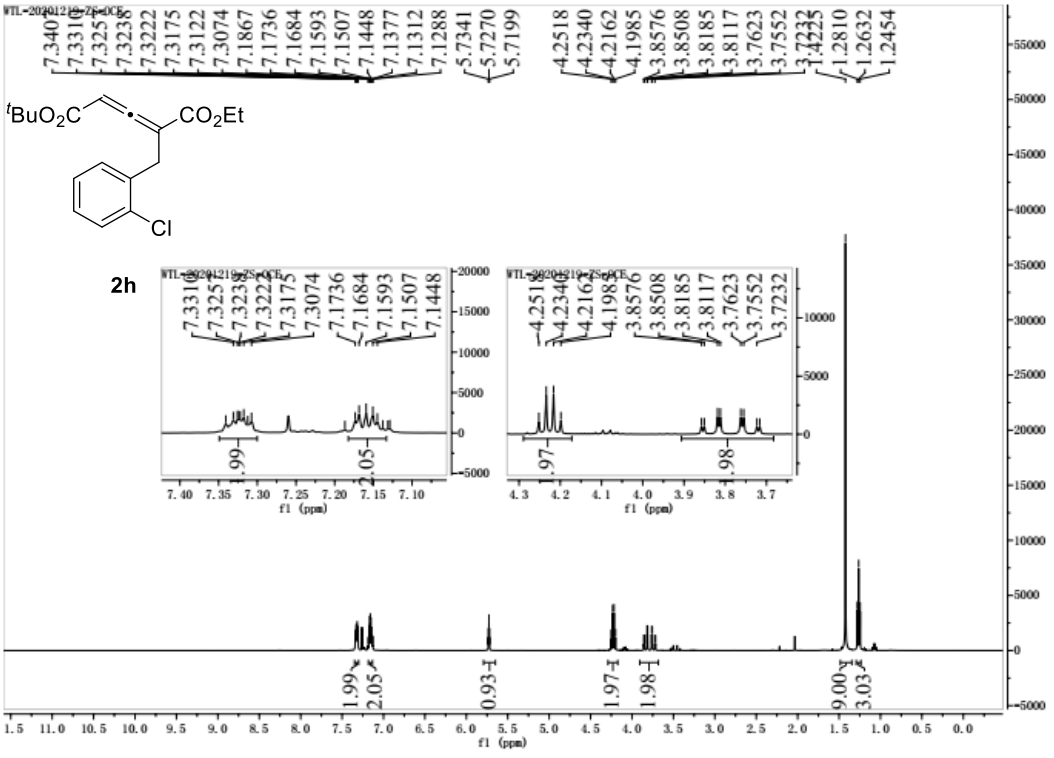
NMR of **2g** ($CDCl_3$)

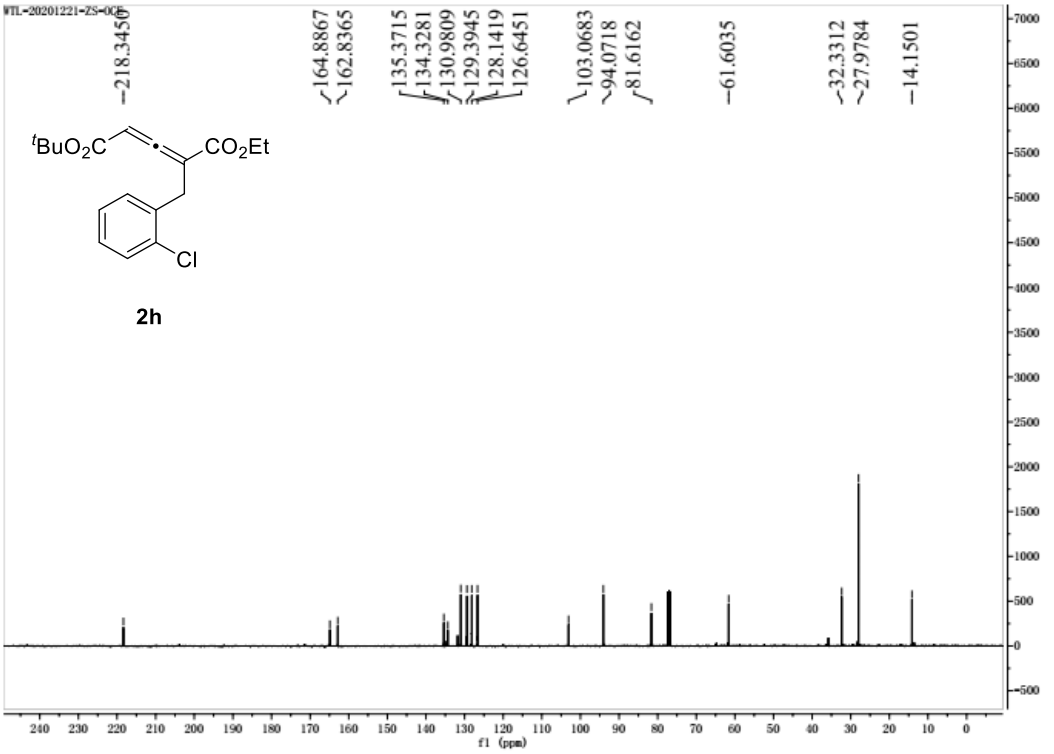






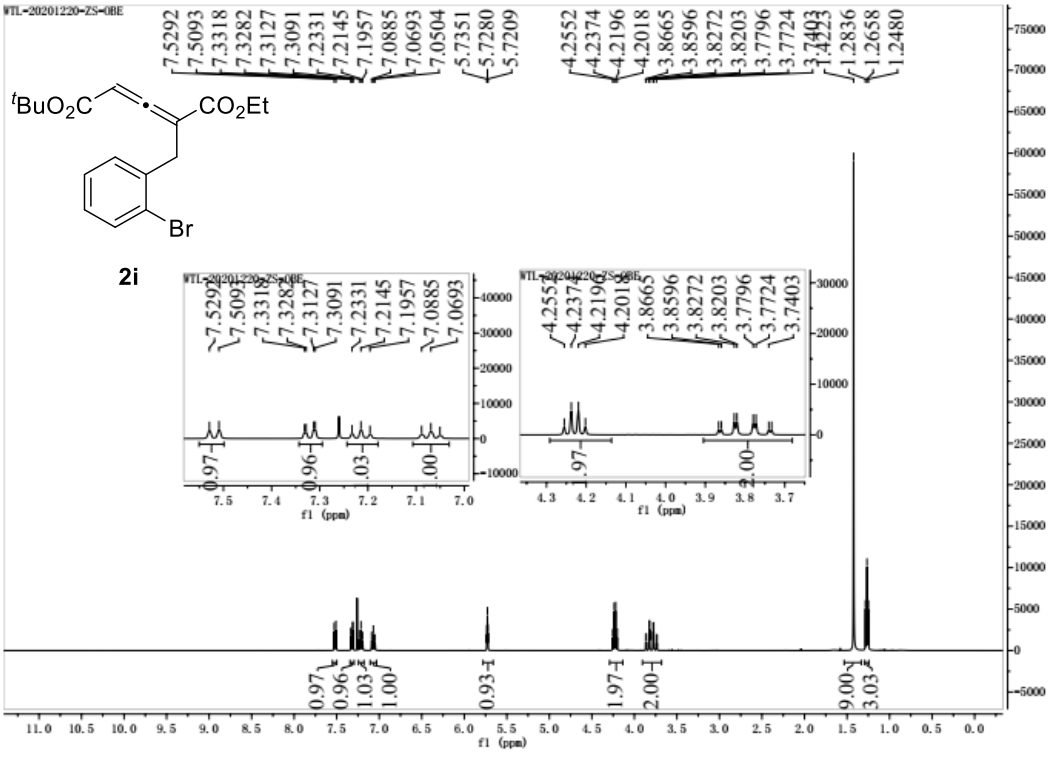
NMR of **2h** ($CDCl_3$)



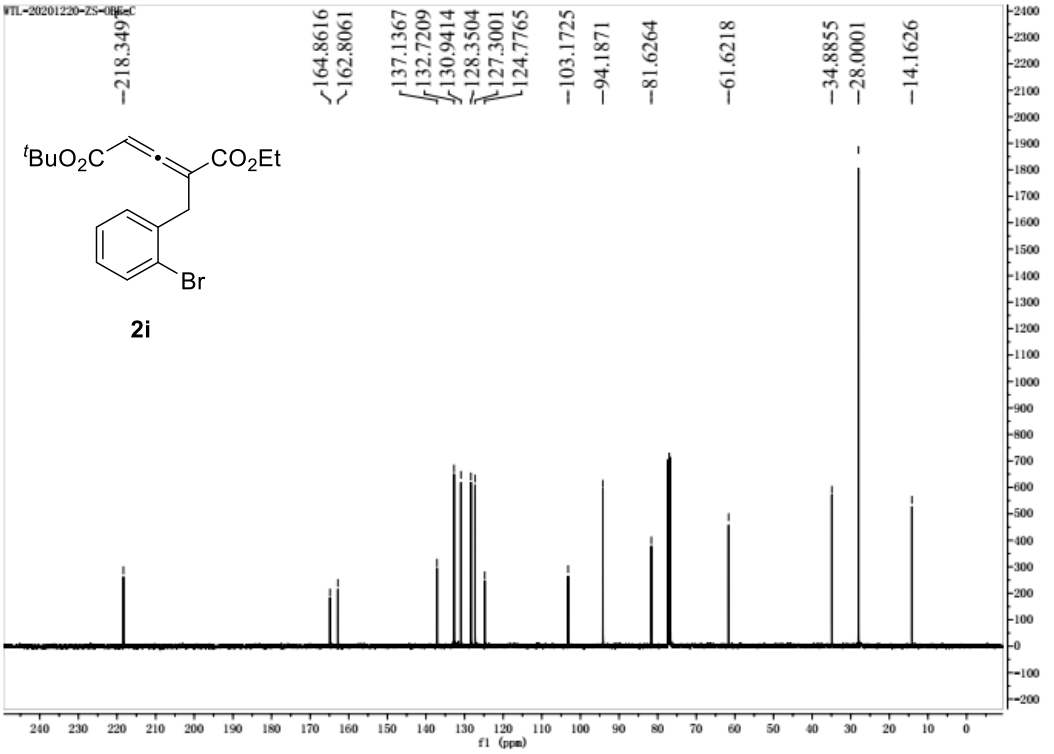


2h

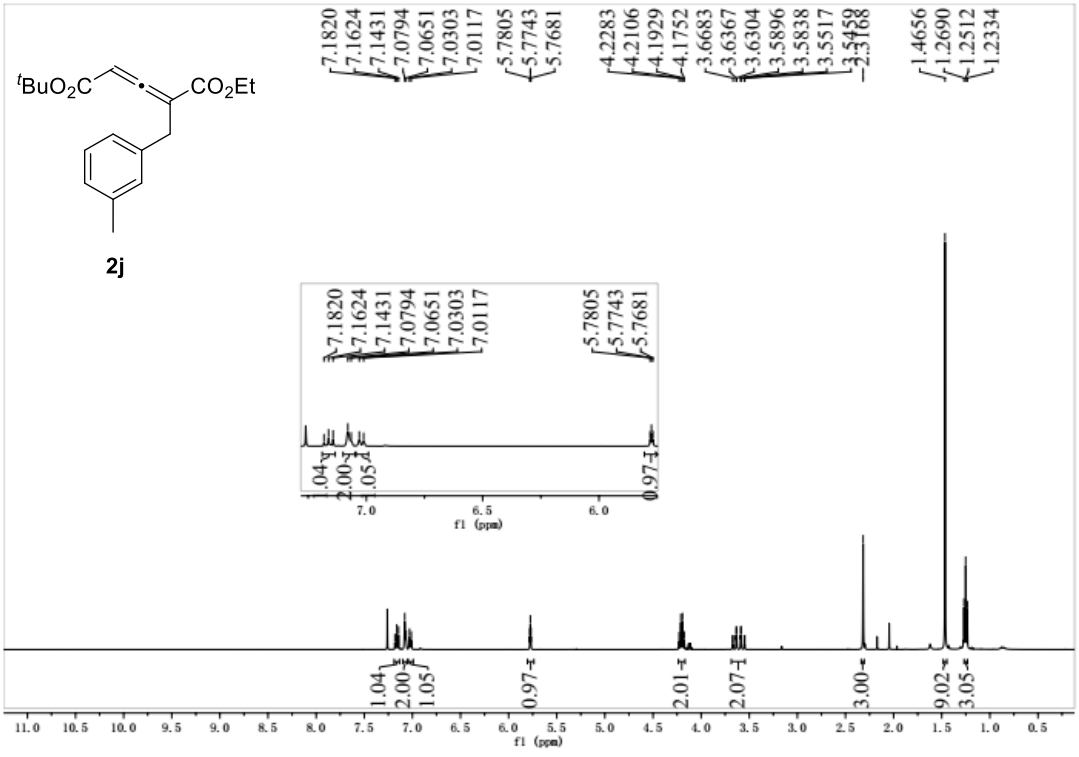
NMR of **2i** ($CDCl_3$)

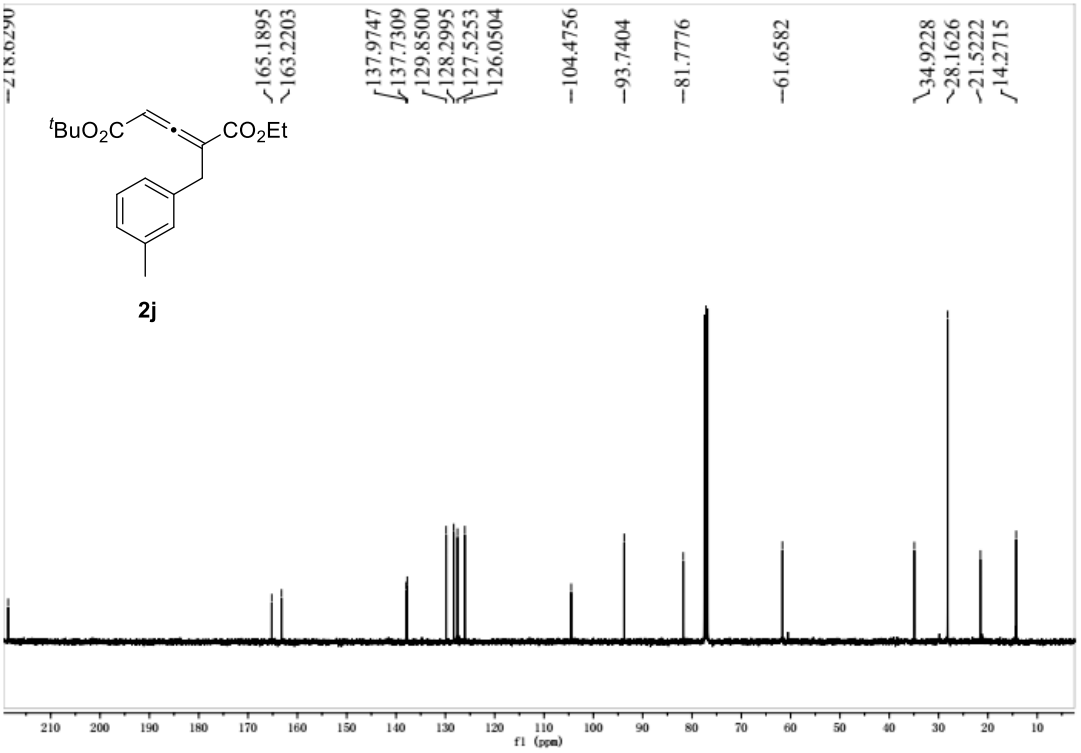


2i

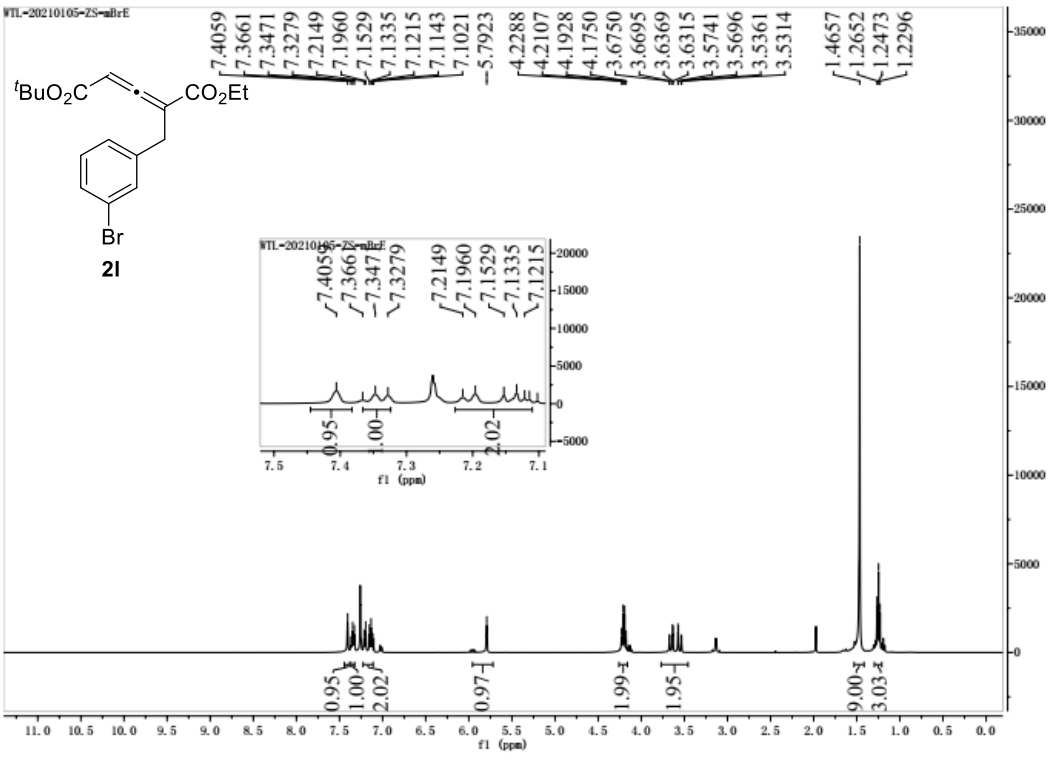


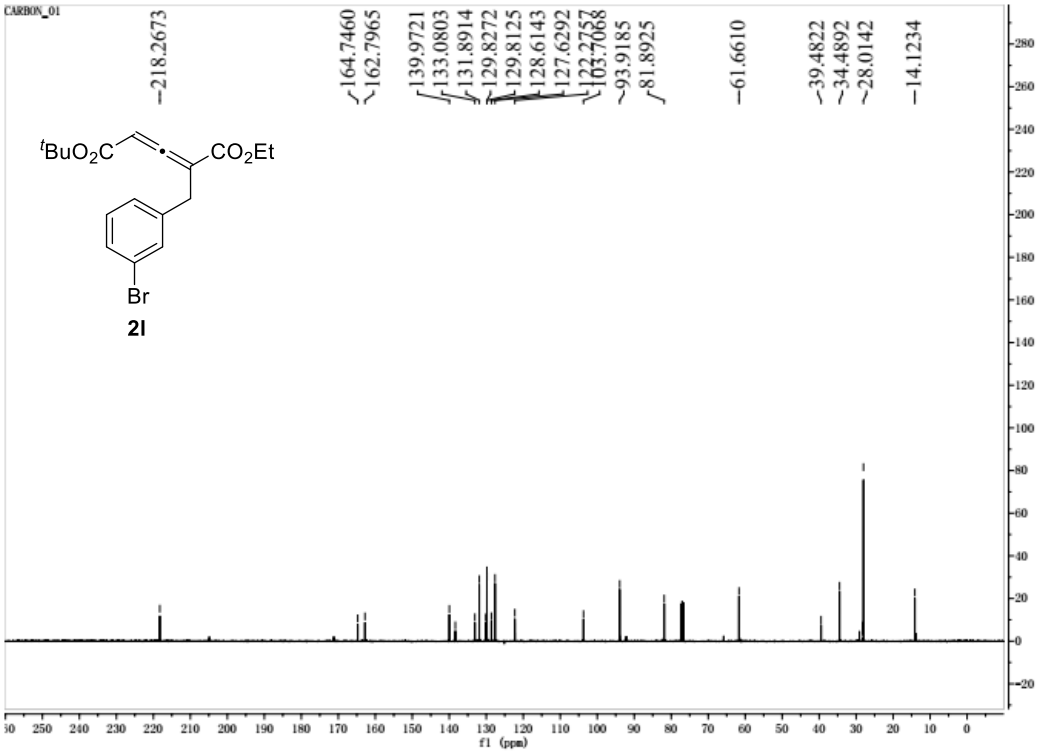
NMR of **2j** ($CDCl_3$)



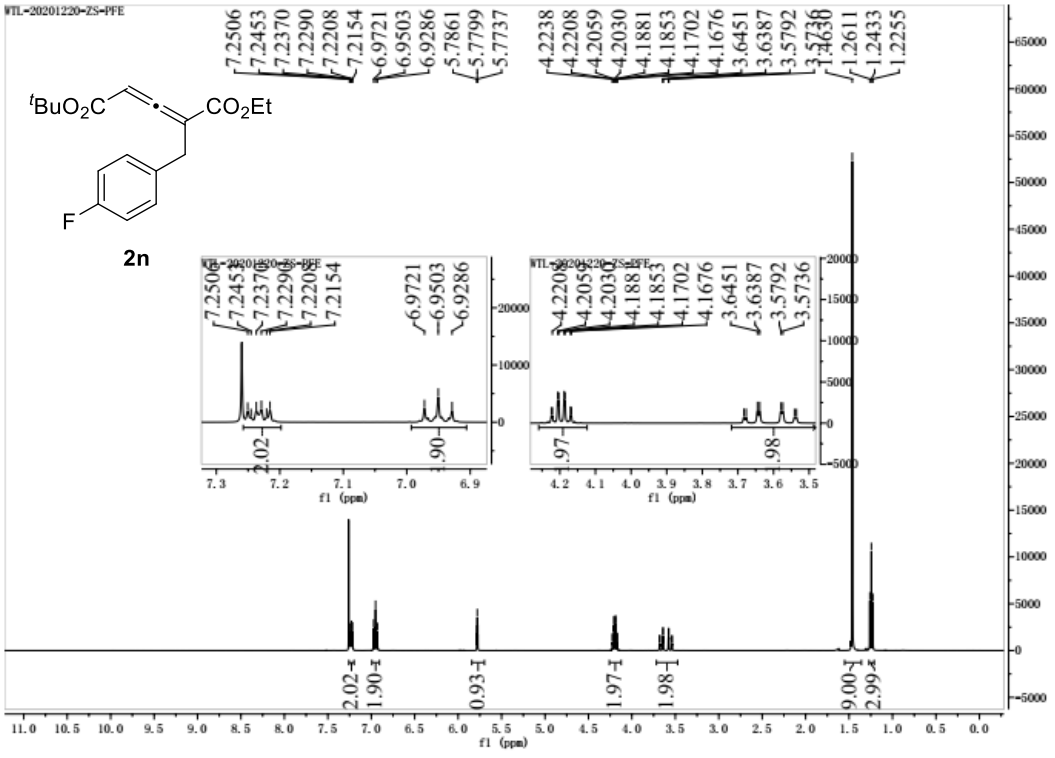


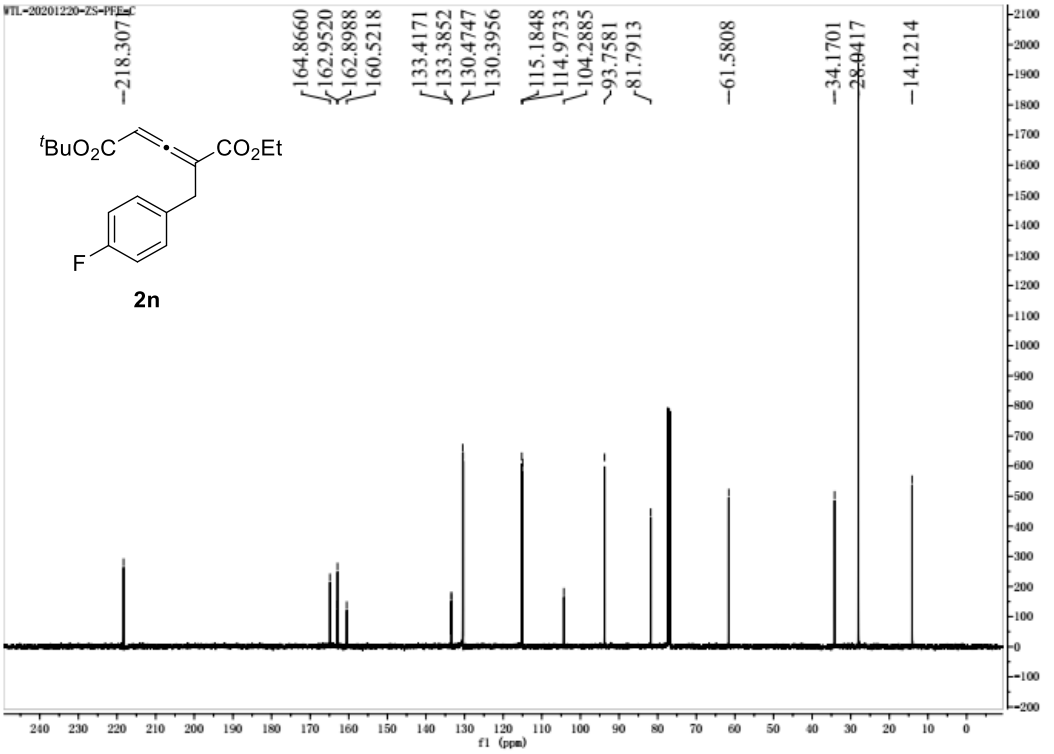
NMR of **2l** ($CDCl_3$)





NMR of **2n** ($CDCl_3$)

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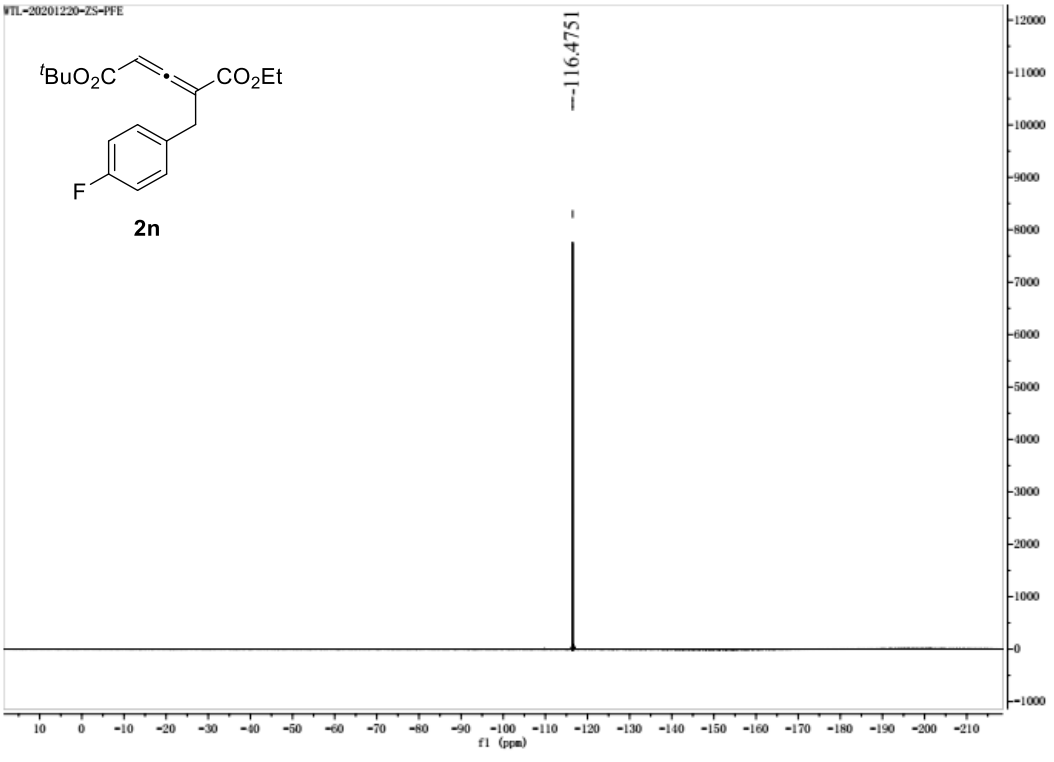
162.9520
162.8988
160.5218
133.4171
133.3852
130.4747
130.3956
115.1848
114.9733
104.2885
93.7581
81.7913
61.5808
34.1701
28.0417
14.1214
tBuO2C
CO2Et
F
2n
f1 (ppm)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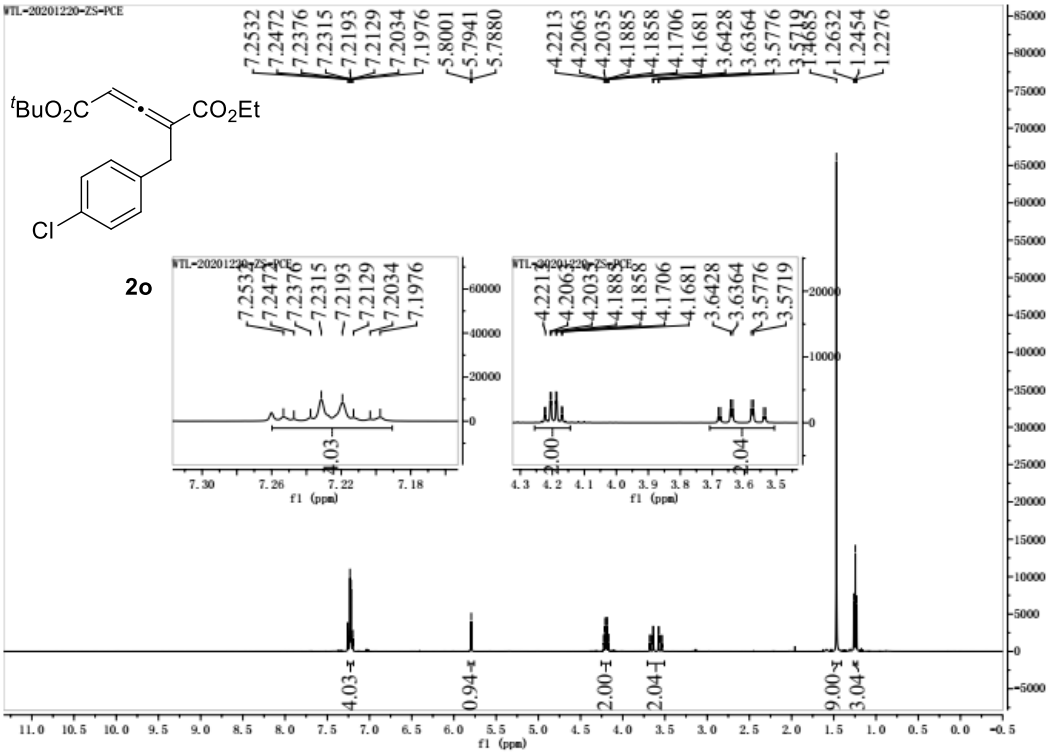
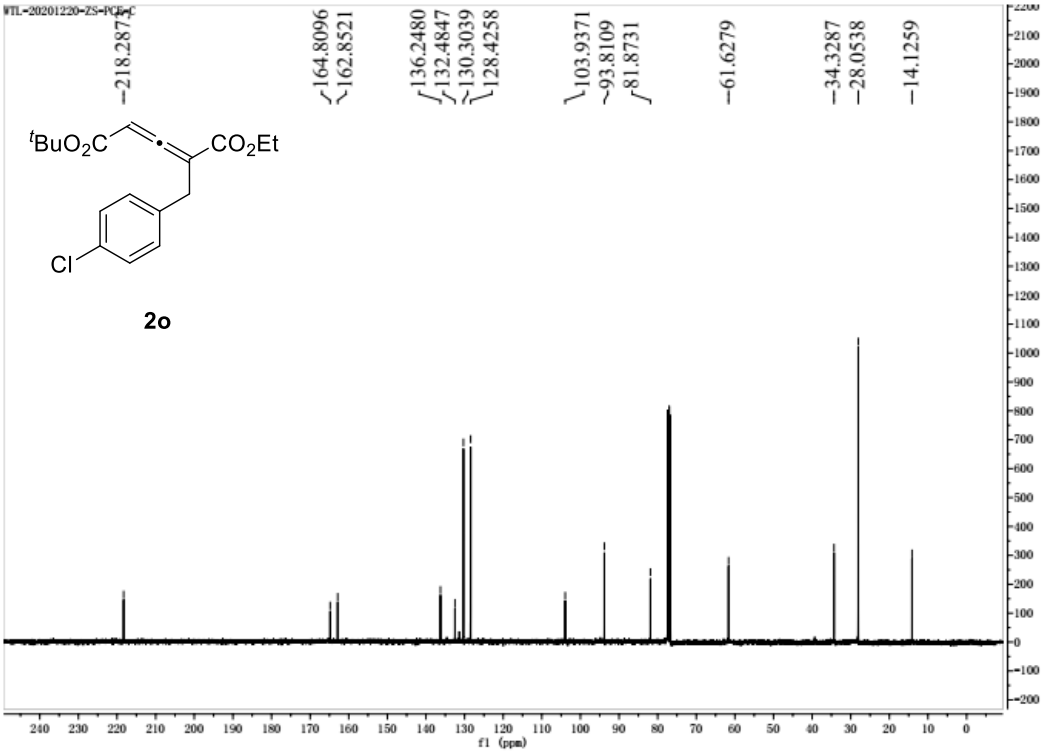
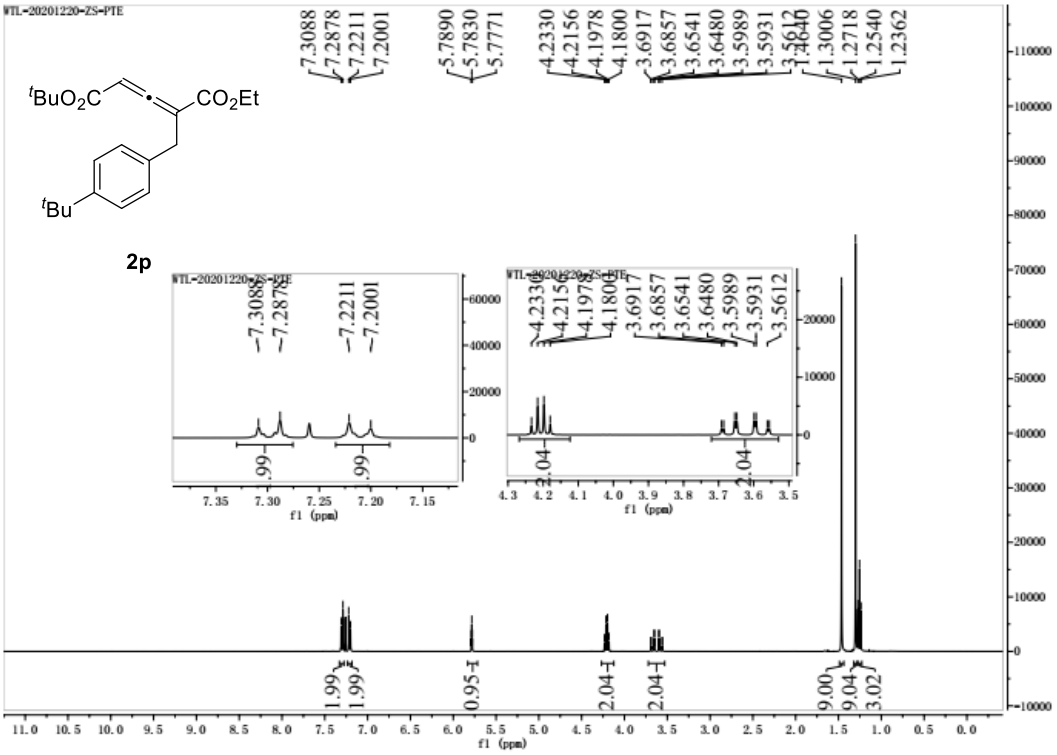
F
2n
f1 (ppm)

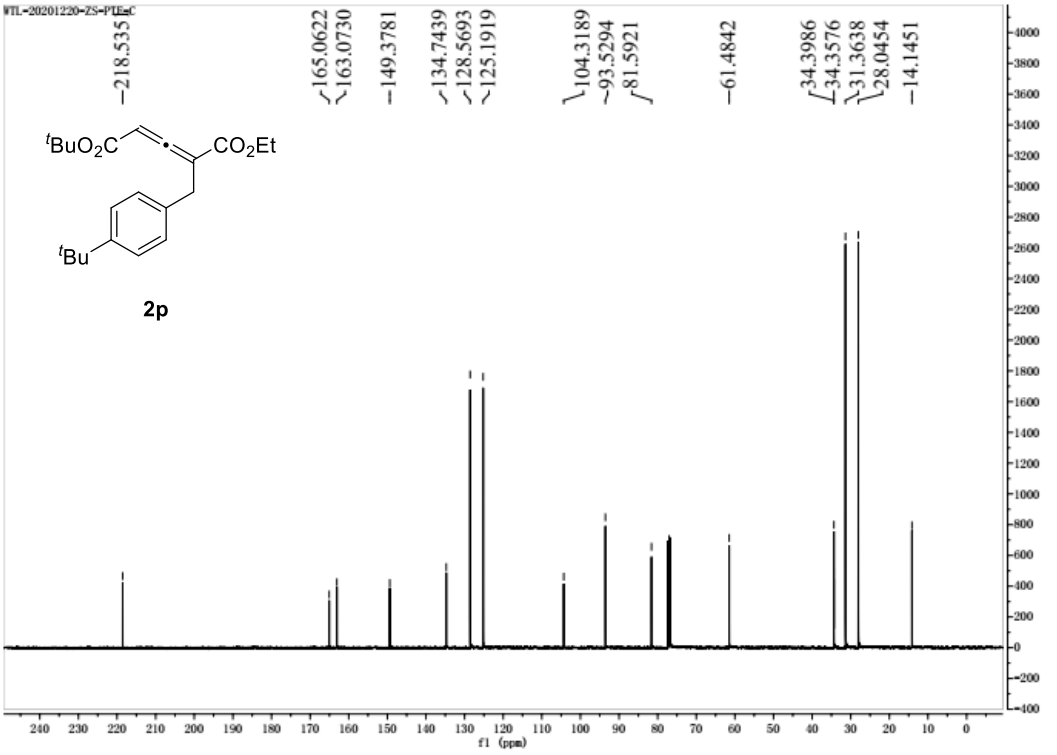
NMR of **2o** ($CDCl_3$)



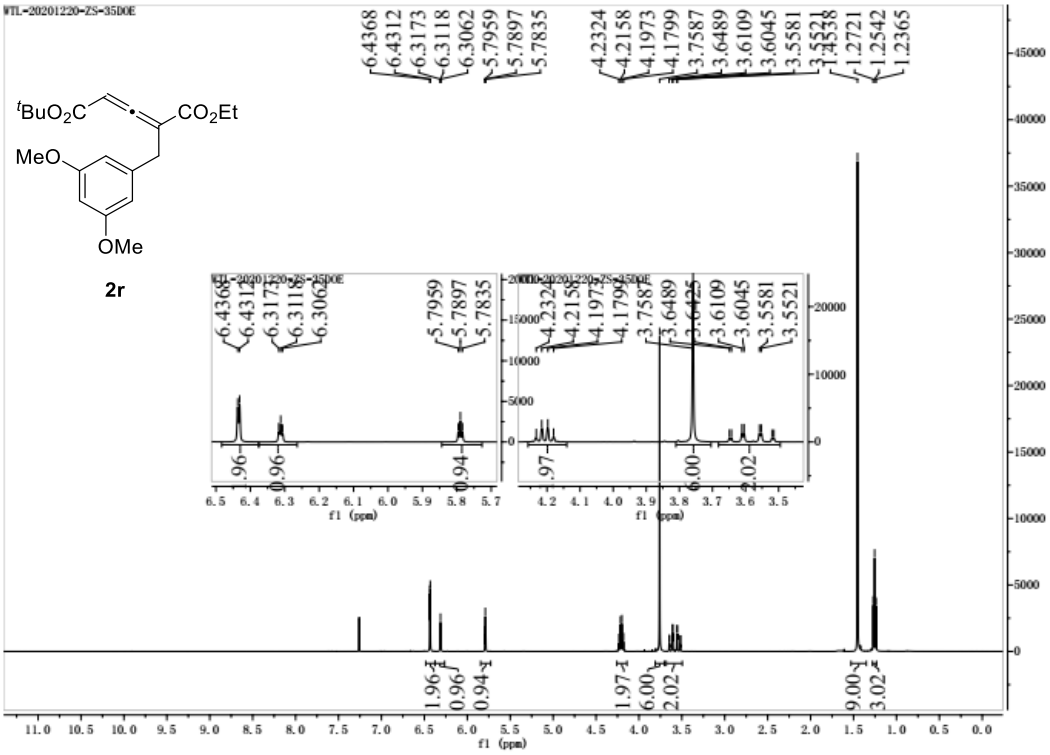


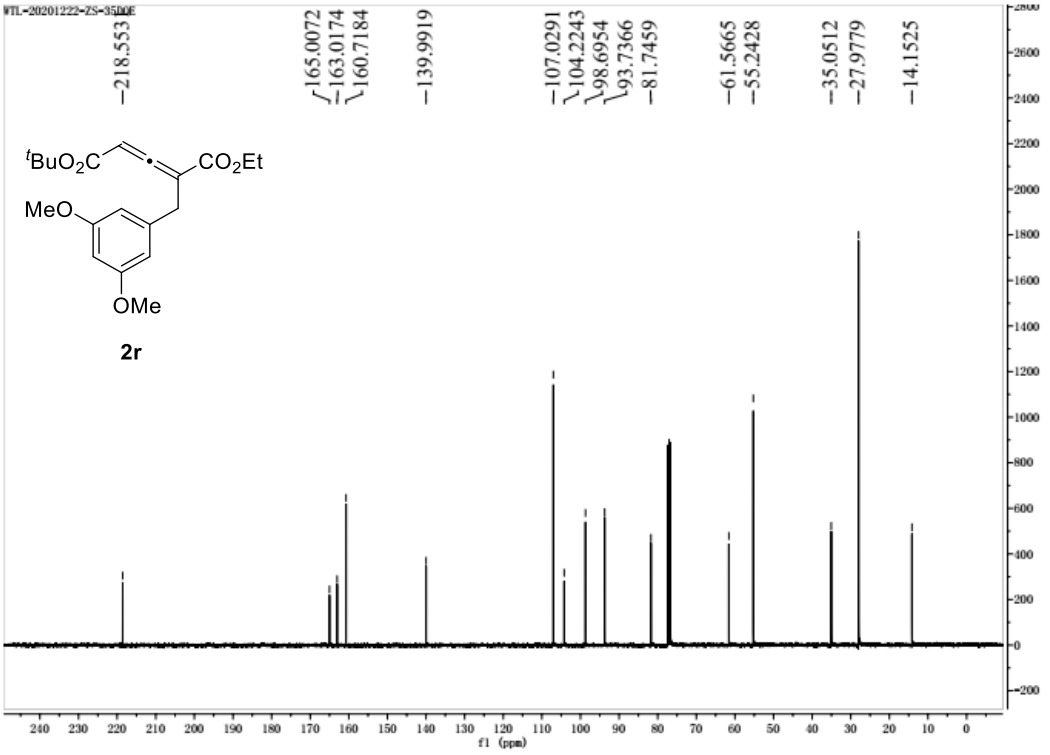
NMR of **2p** ($CDCl_3$)



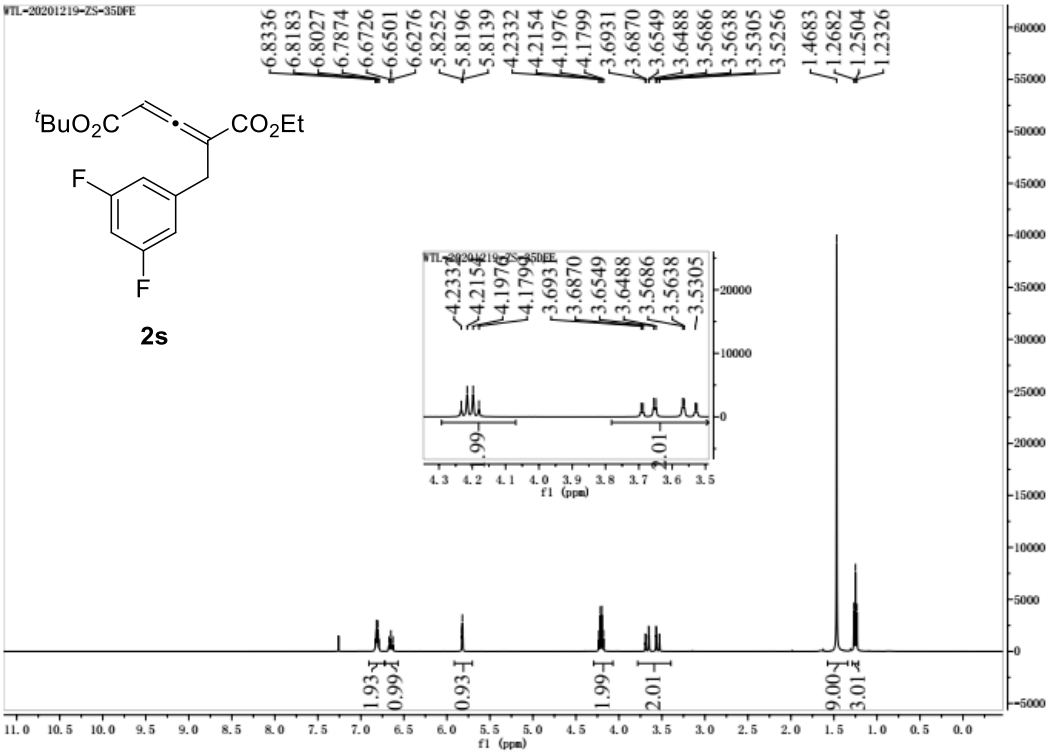


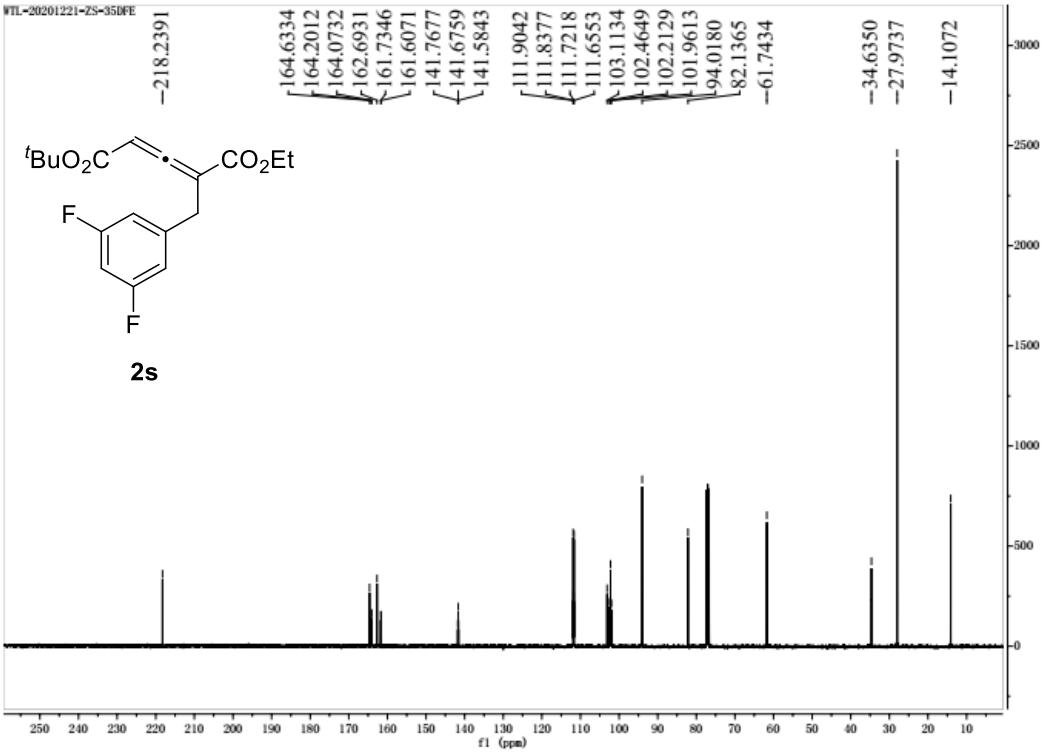
NMR of **2r** ($CDCl_3$)

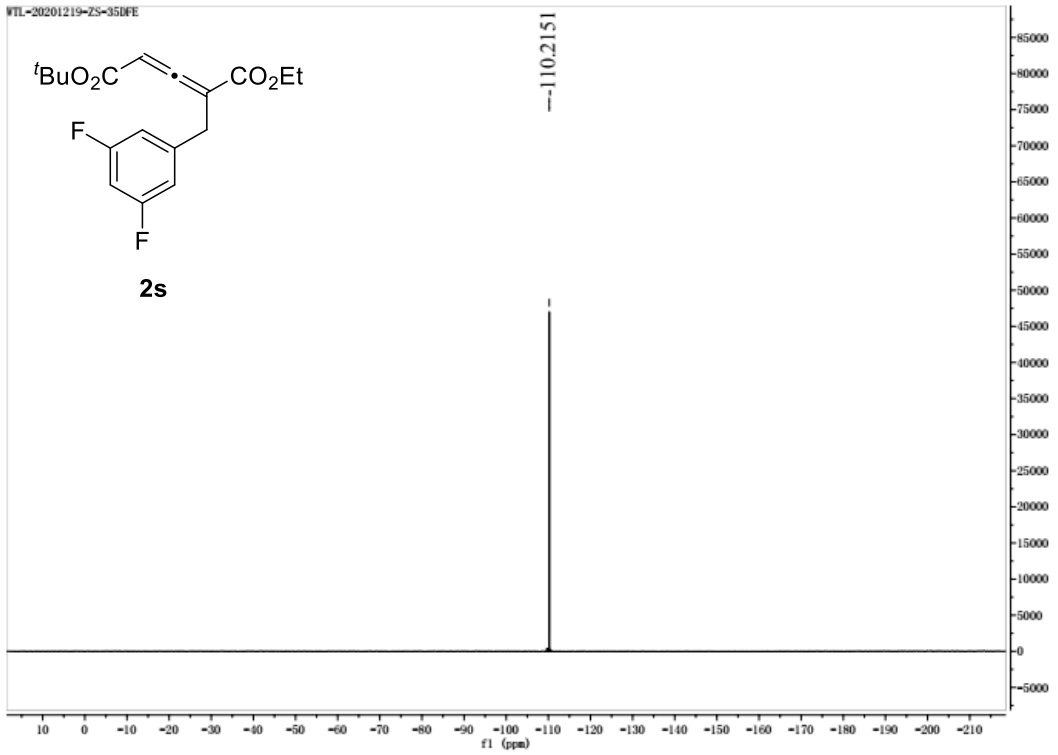




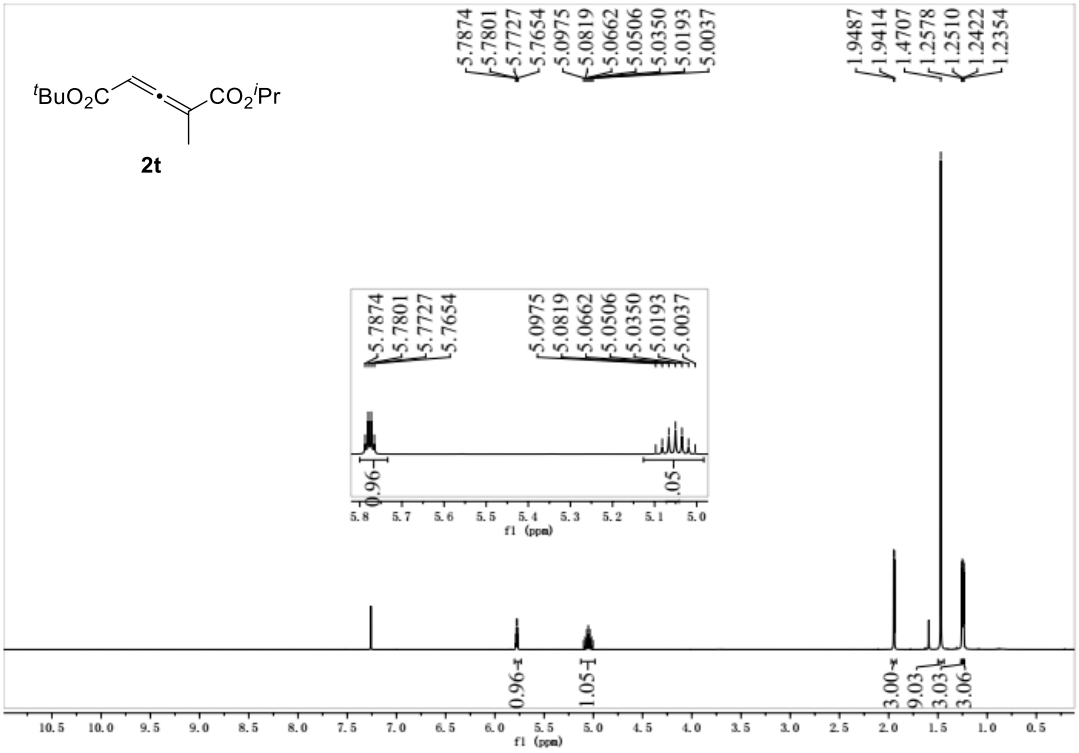
NMR of **2s** ($CDCl_3$)

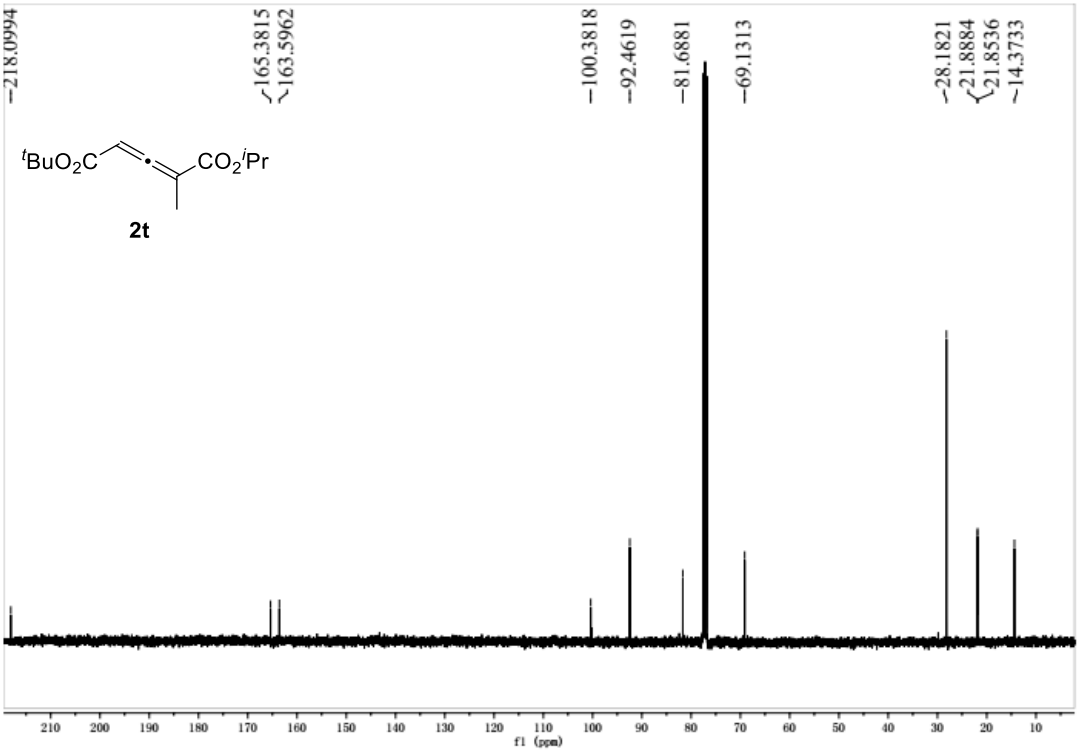




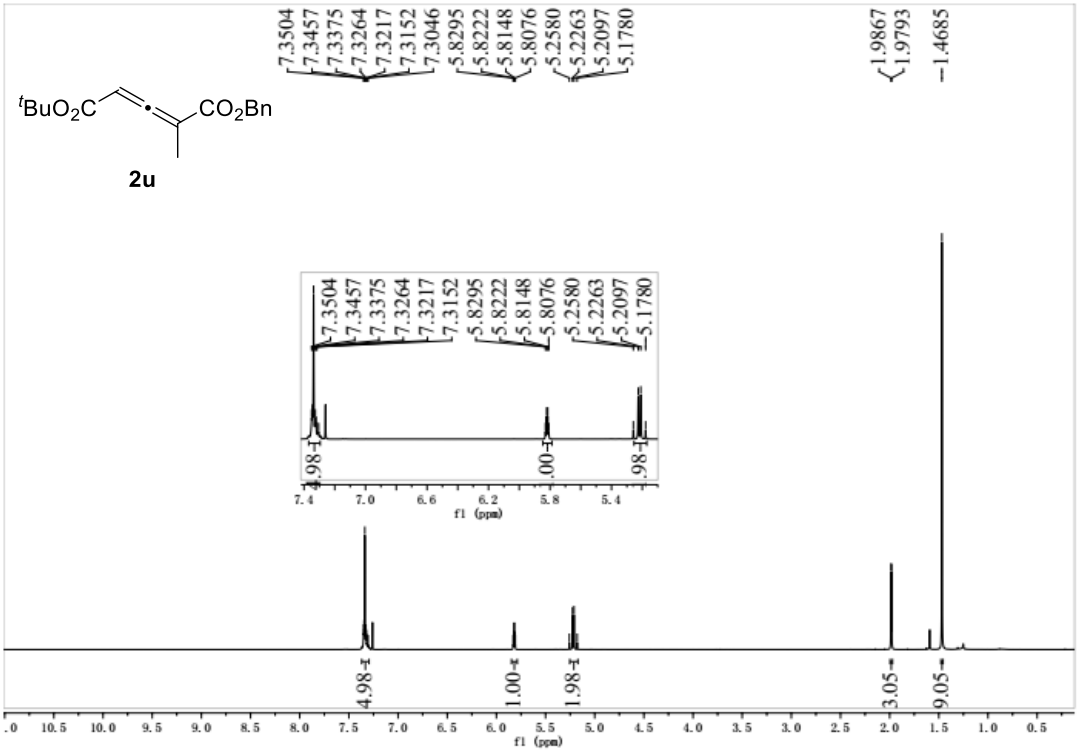


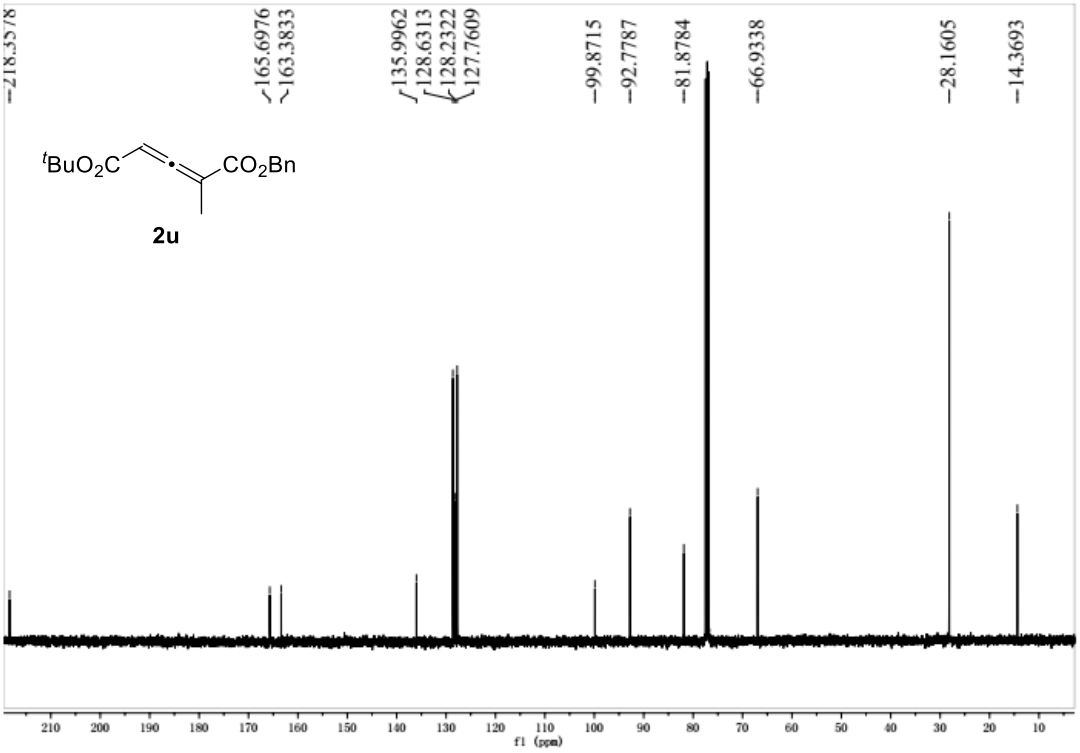
NMR of **2t** ($CDCl_3$)



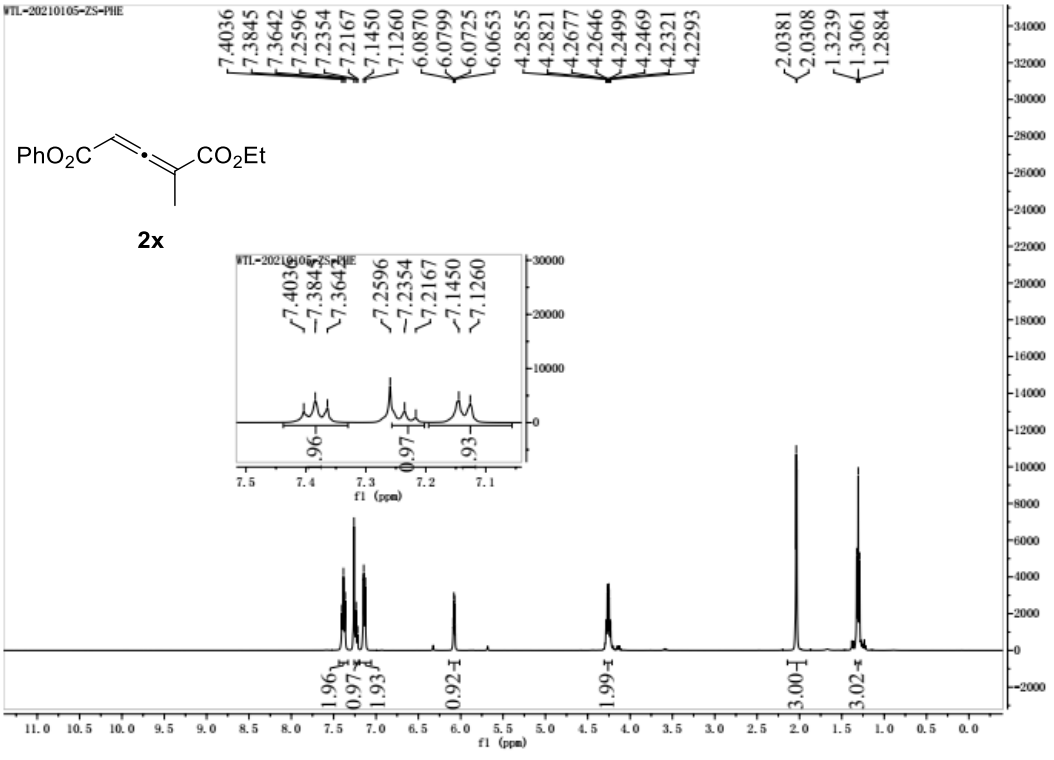


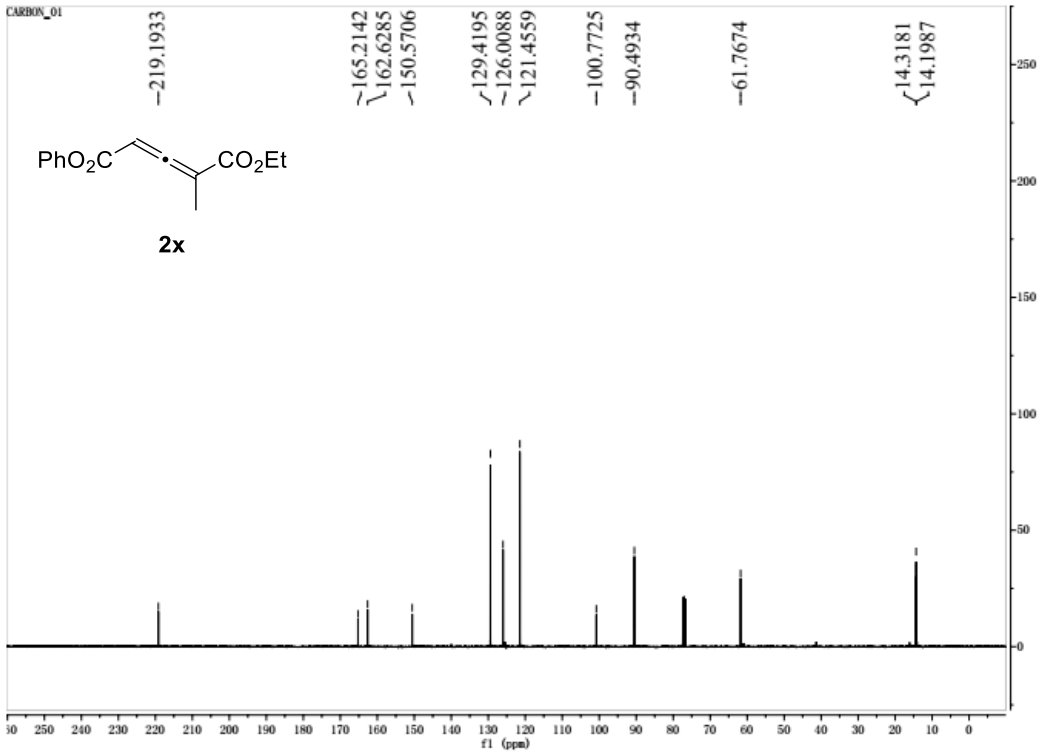
NMR of **2u** ($CDCl_3$)



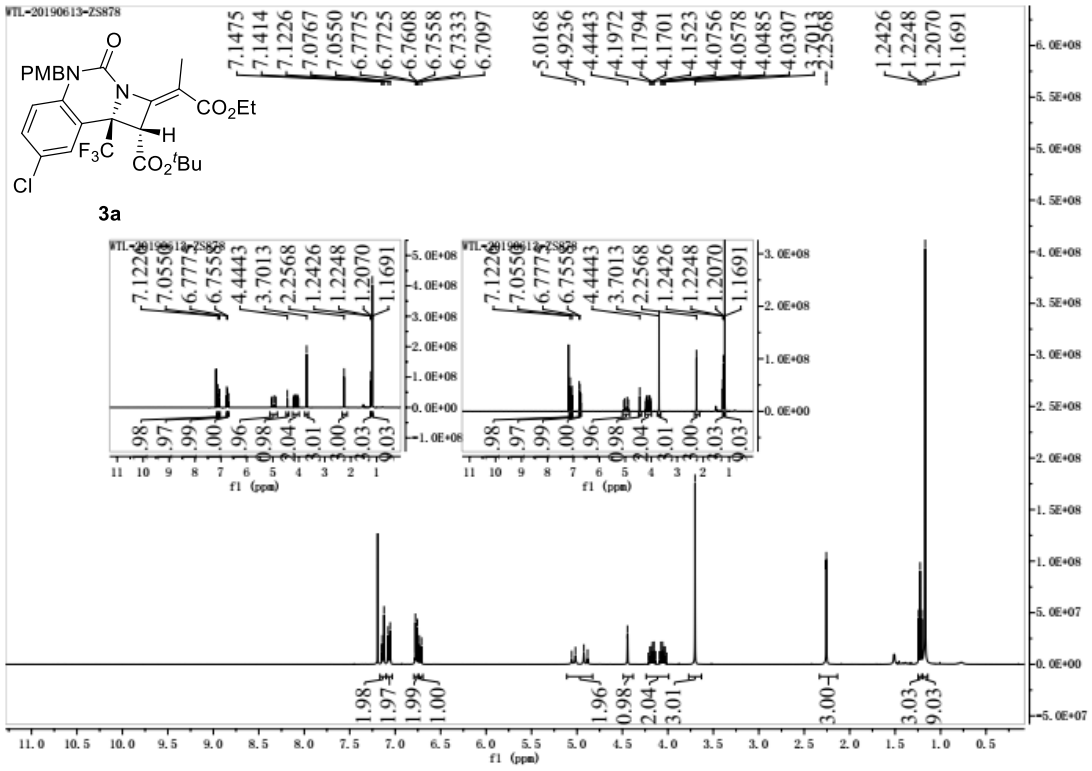


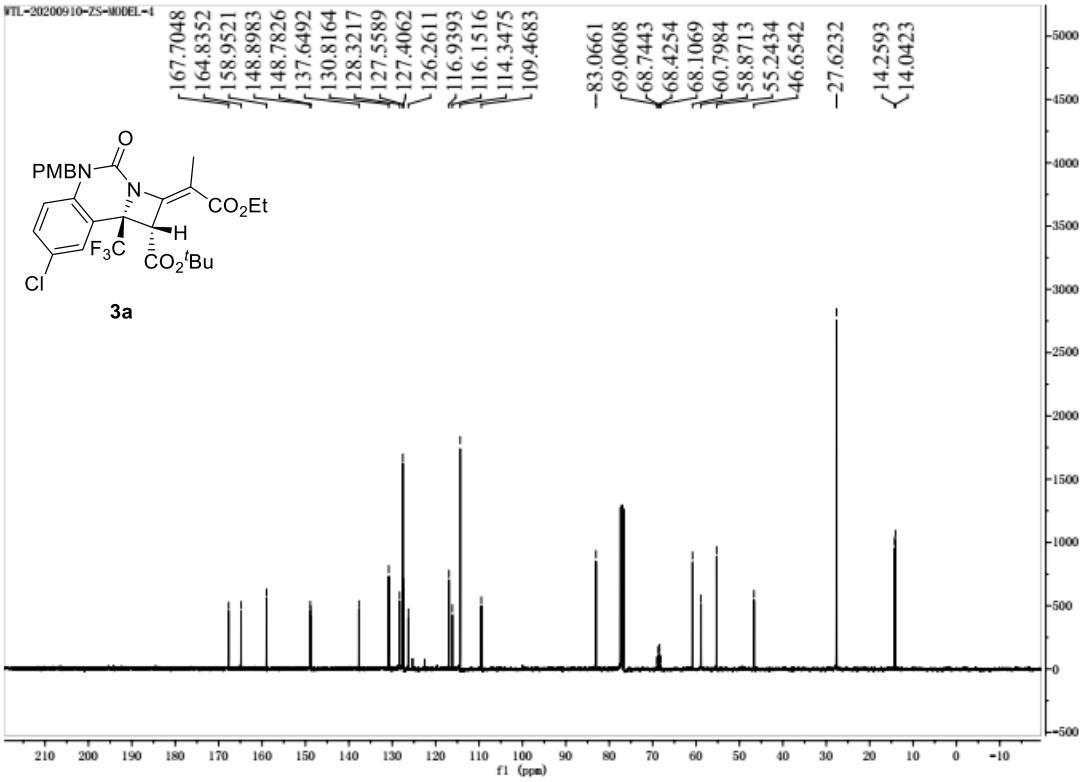
NMR of **2x** ($CDCl_3$)





NMR of **3a** ($CDCl_3$)

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127.5589
127.4062
126.2611
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116.1516
114.3475
109.4683
83.0661
69.0608
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68.4254
68.1069
60.7984
58.8713
55.2434
46.6542
27.6232
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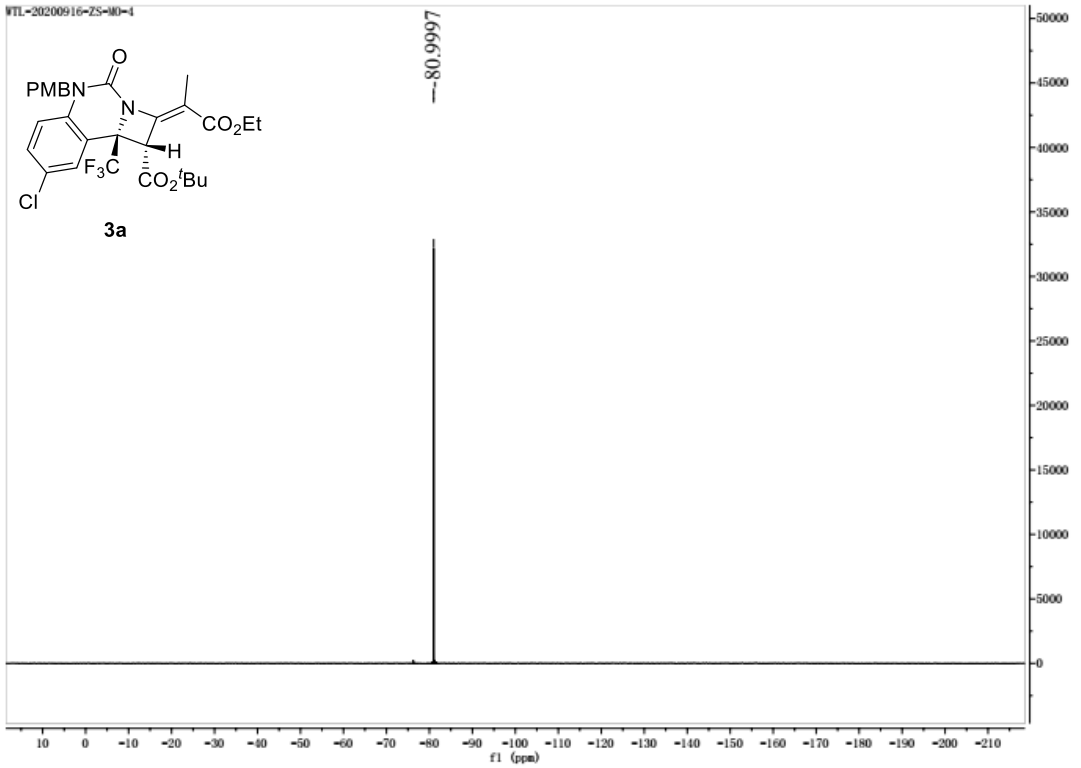
14.0423
PMBN
O
N
CO2Et
H
F3C
CO2tBu
Cl
3a
f1 (ppm)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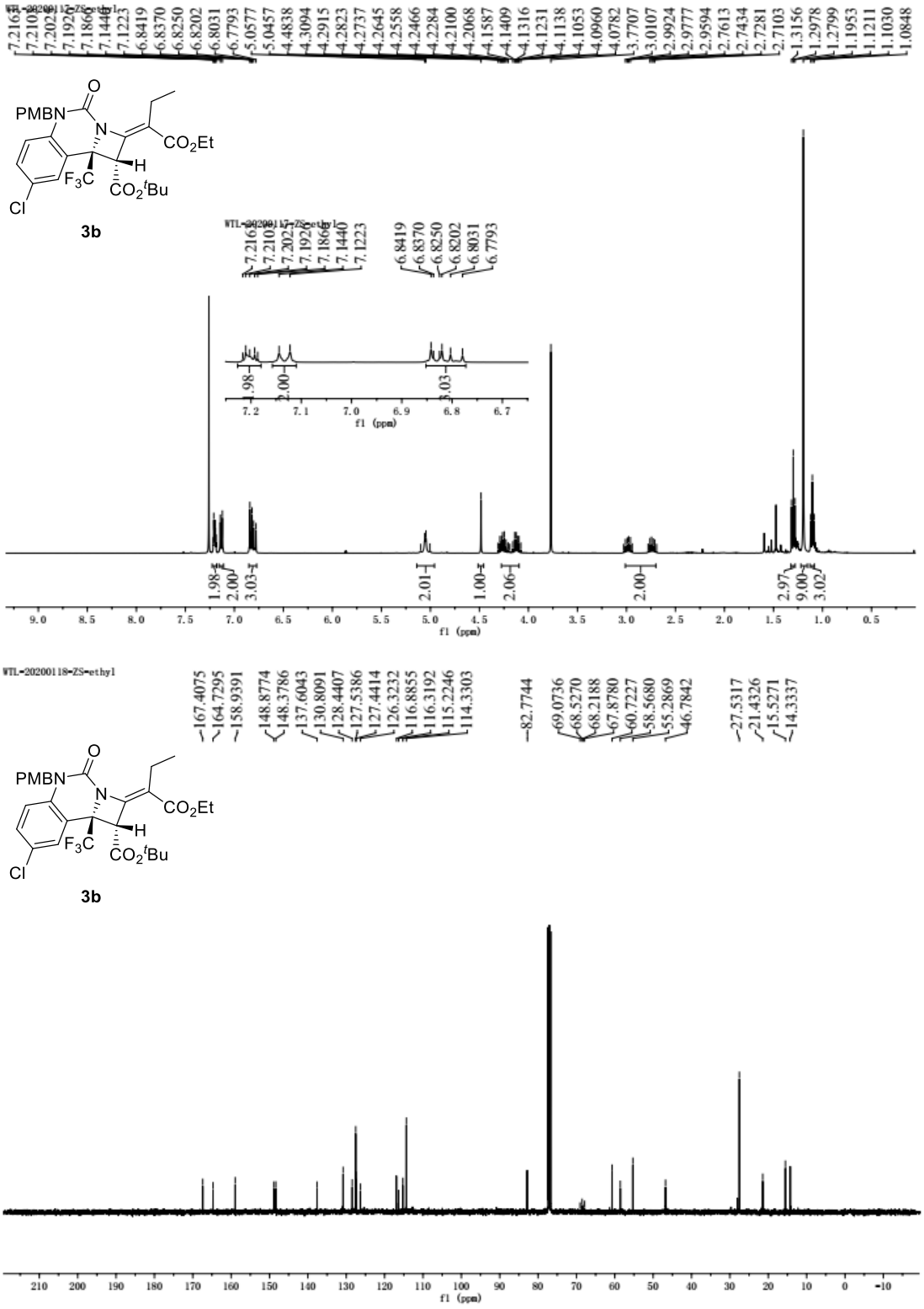
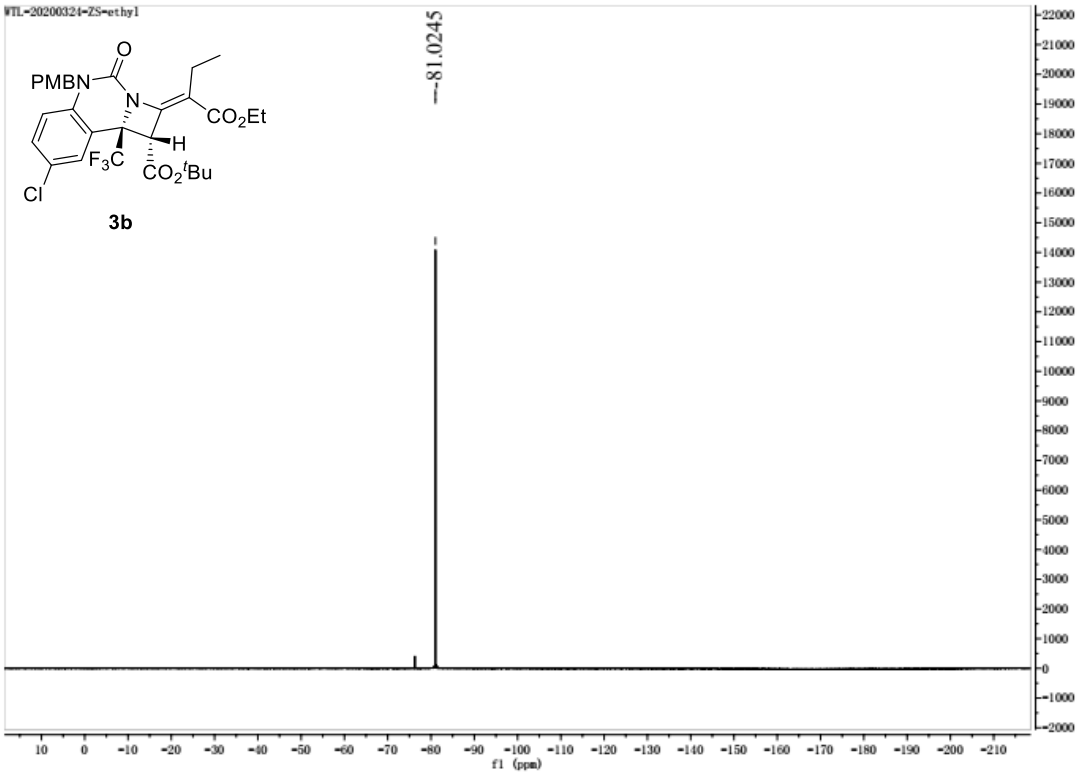
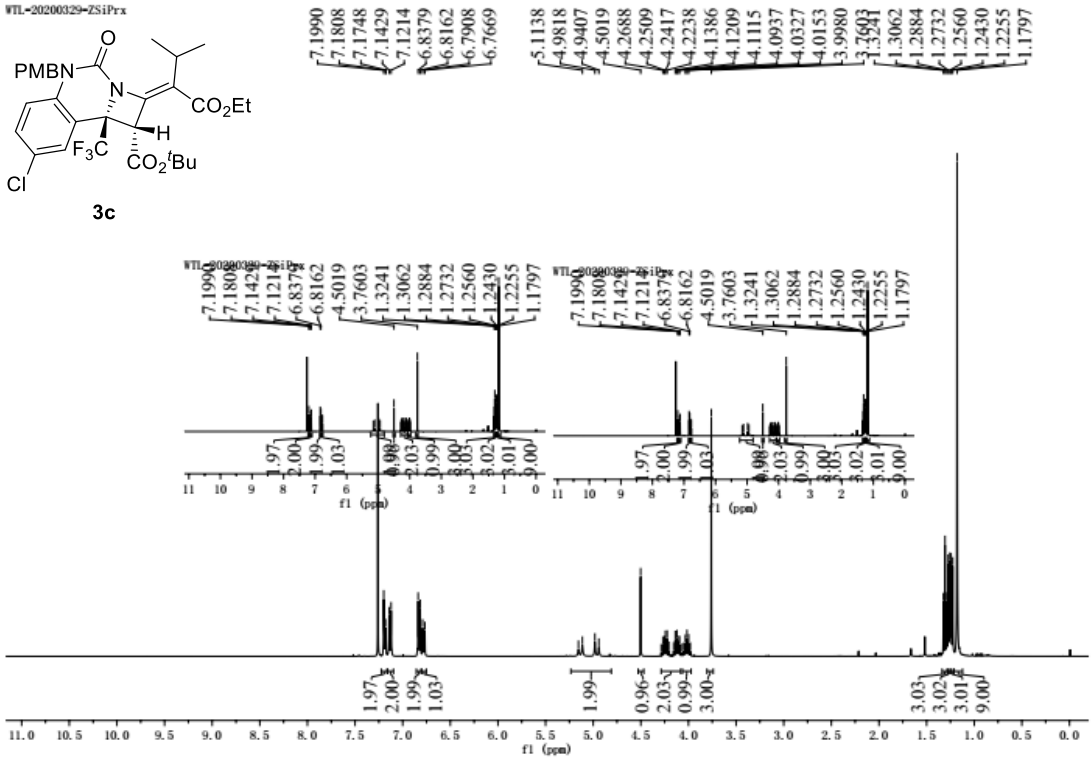
3a
f1 (ppm)

NMR of **3b** ($CDCl_3$)



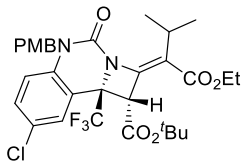


NMR of **3c** ($CDCl_3$)

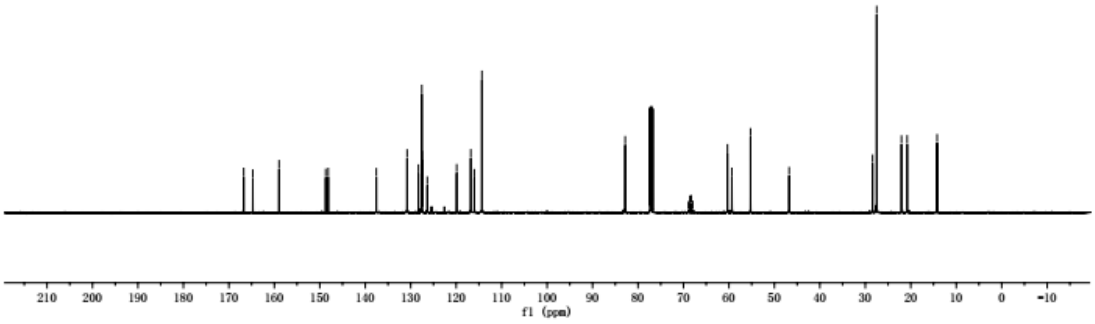


WTL-20200329-ZSiPrx-C

166.7326
164.7295
158.9614
148.7023
148.1465
137.5742
130.7920
128.3069
127.5566
127.4730
126.3519
119.8843
116.7813
116.0092
114.3342
82.8186
68.9159
68.5988
68.2799
67.9600
60.3252
59.3543
55.2462
46.7578
28.4047
27.4907
22.0457
20.7952
14.2028

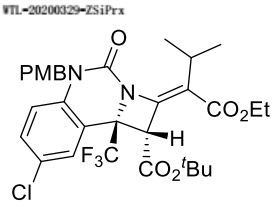


3c

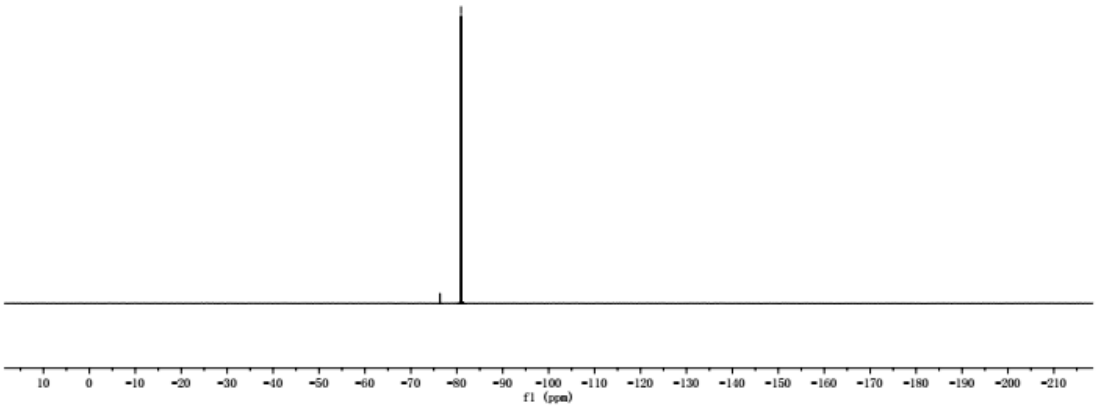


WTL-20200329-ZSiPrx

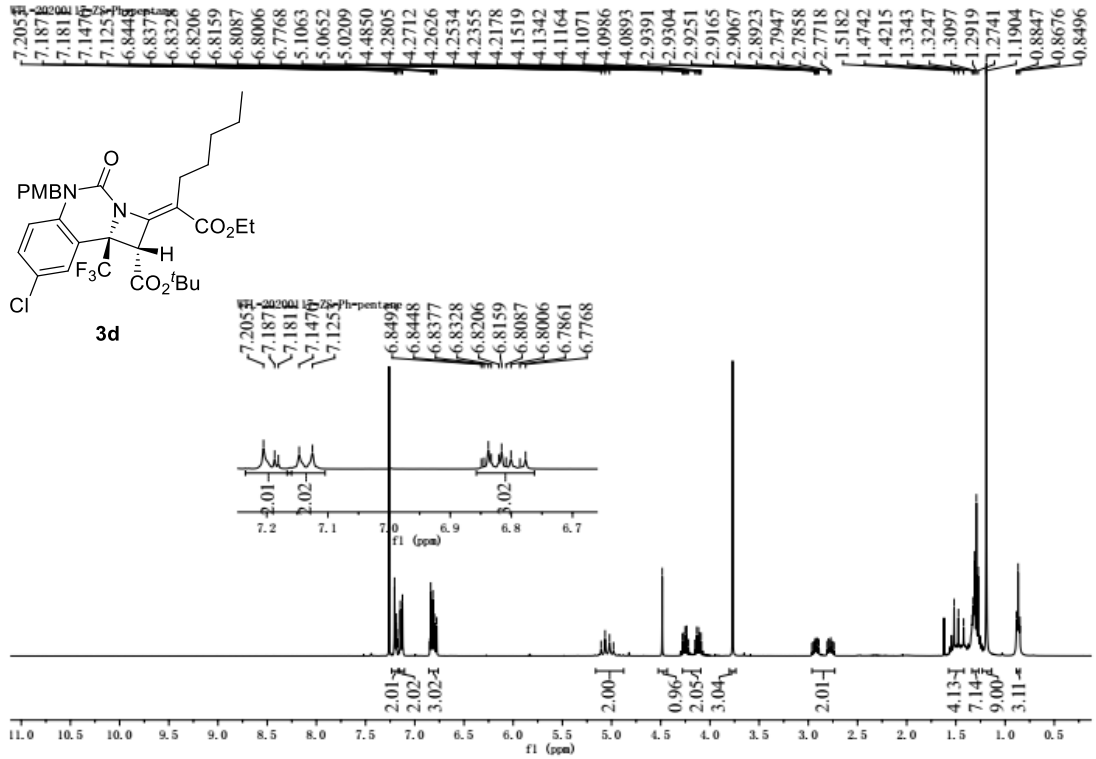
-80.9193

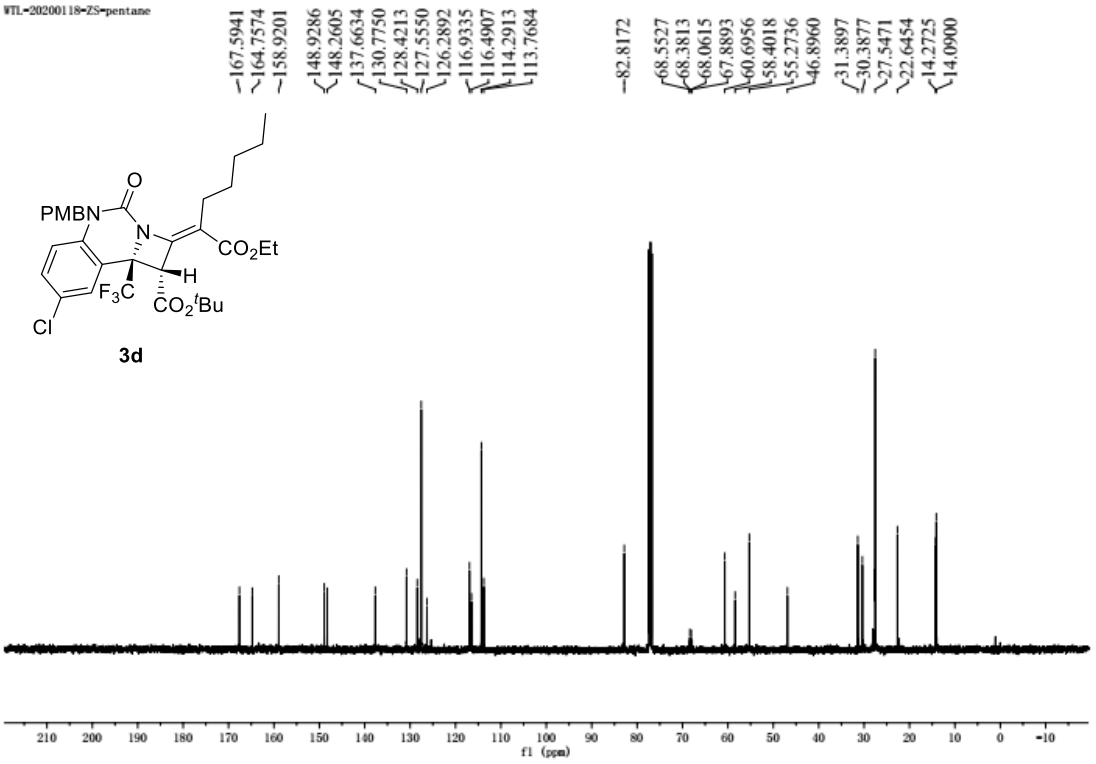


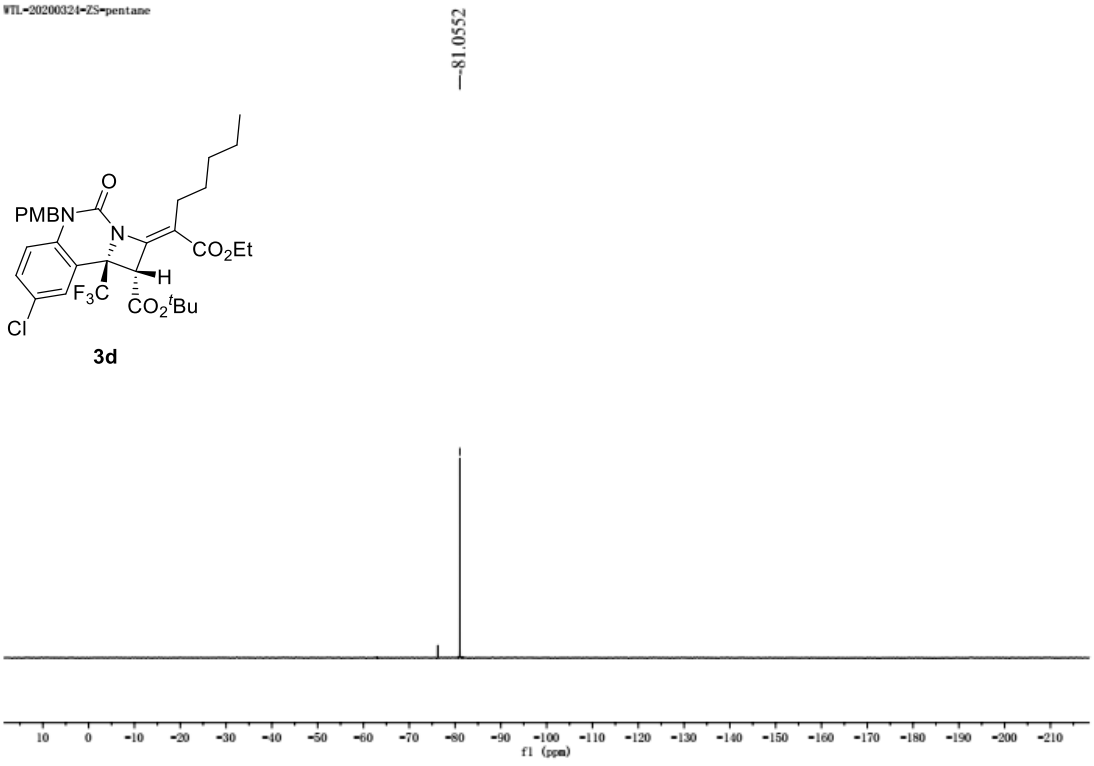
3c



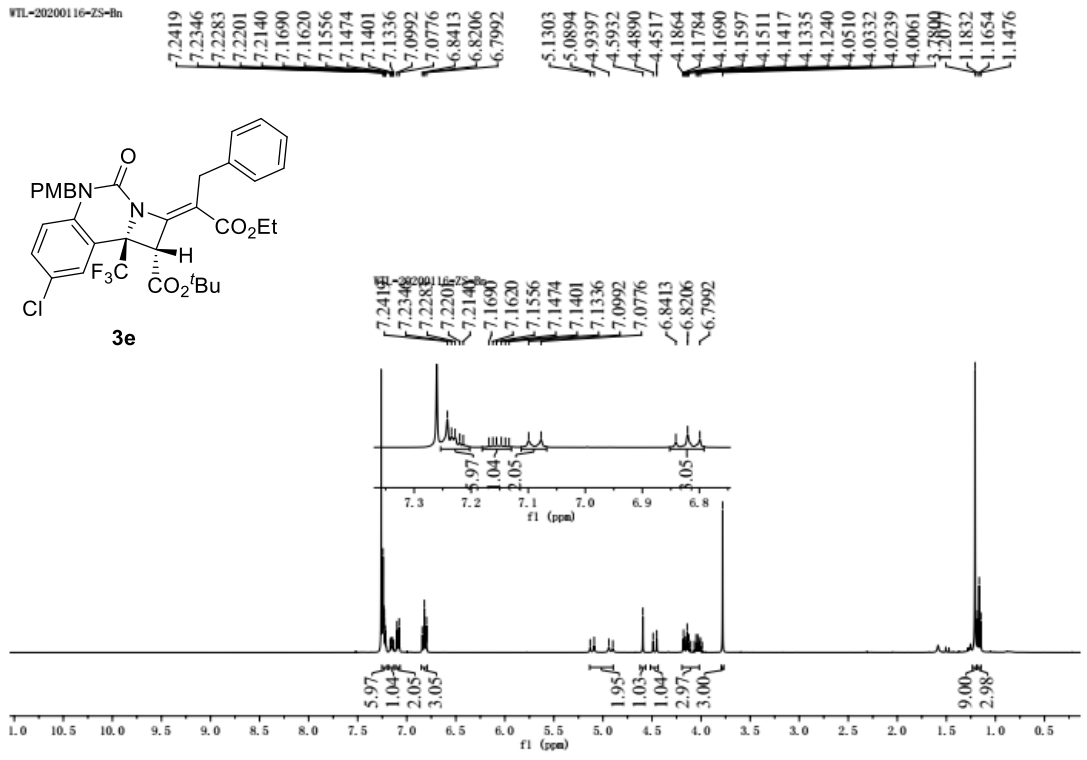
NMR of **3d** ($CDCl_3$)

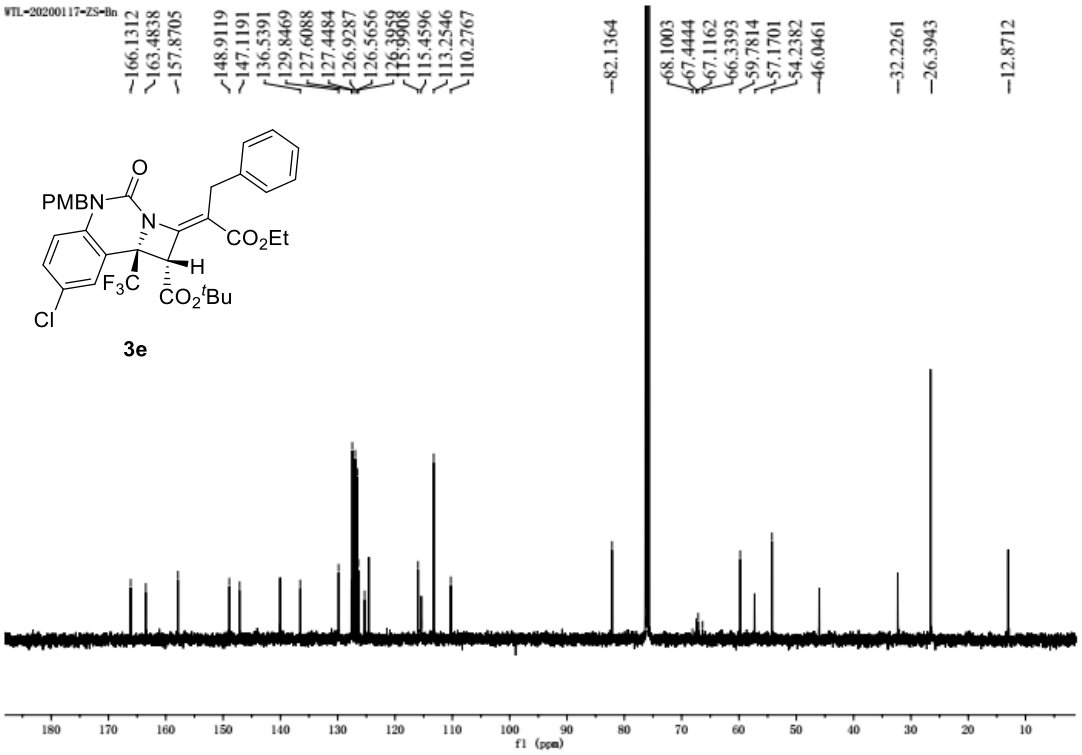


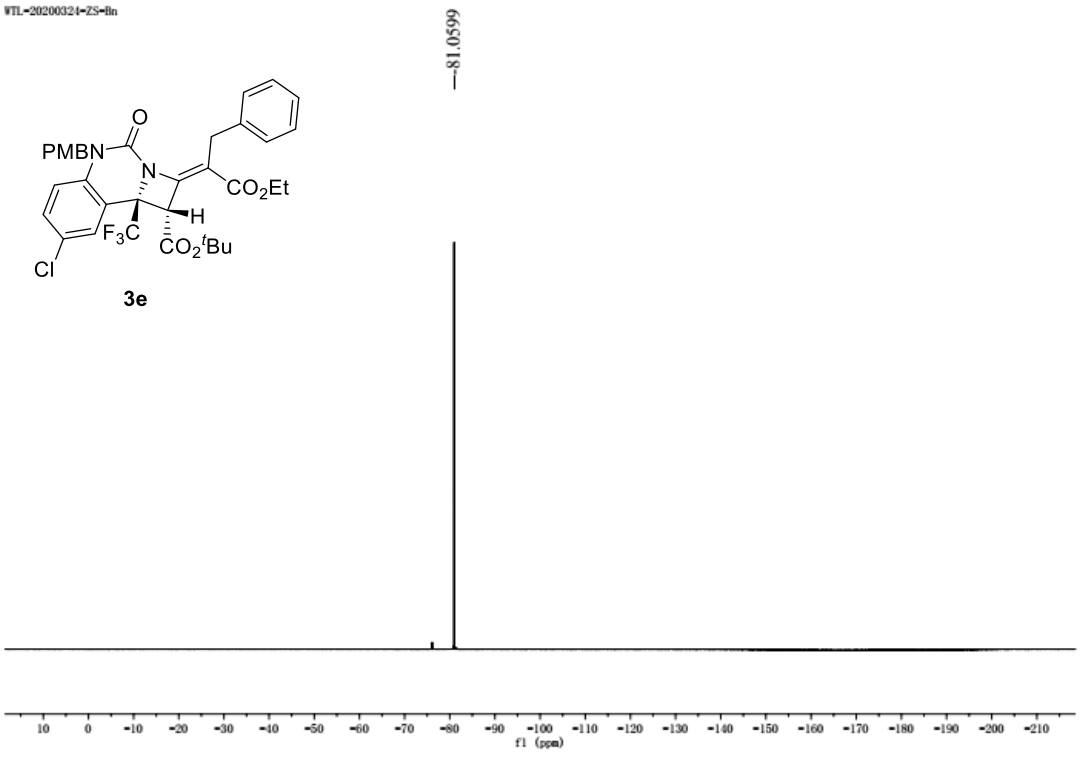




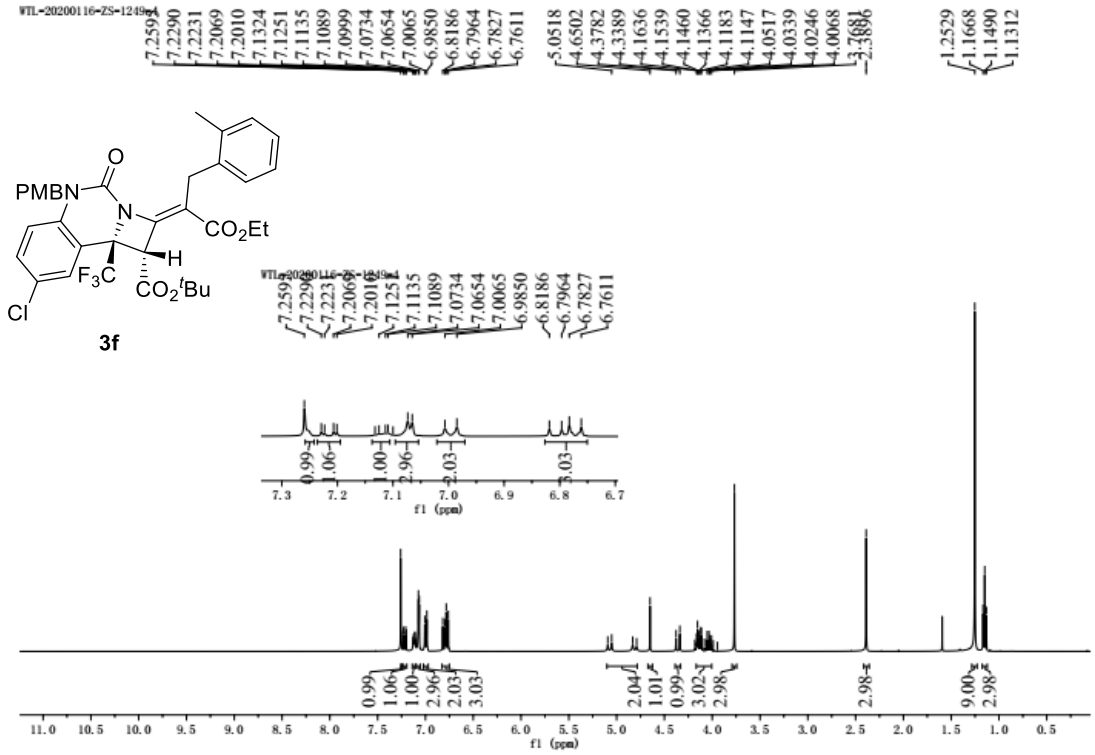
NMR of **3e** ($CDCl_3$)

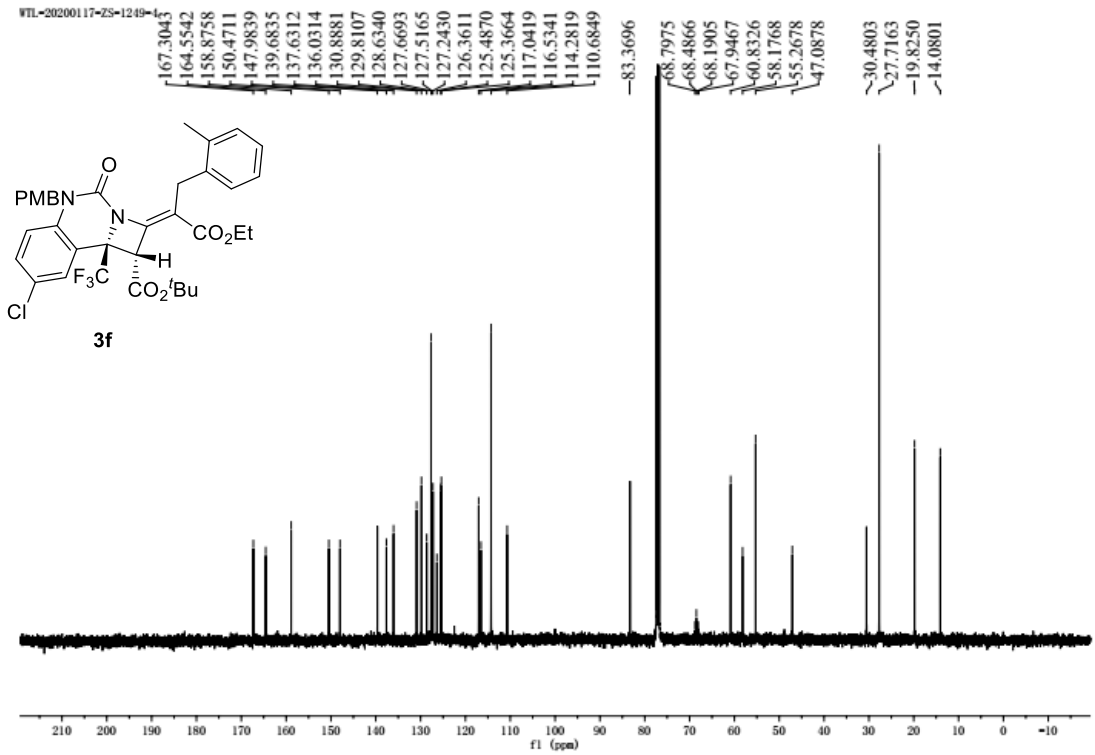


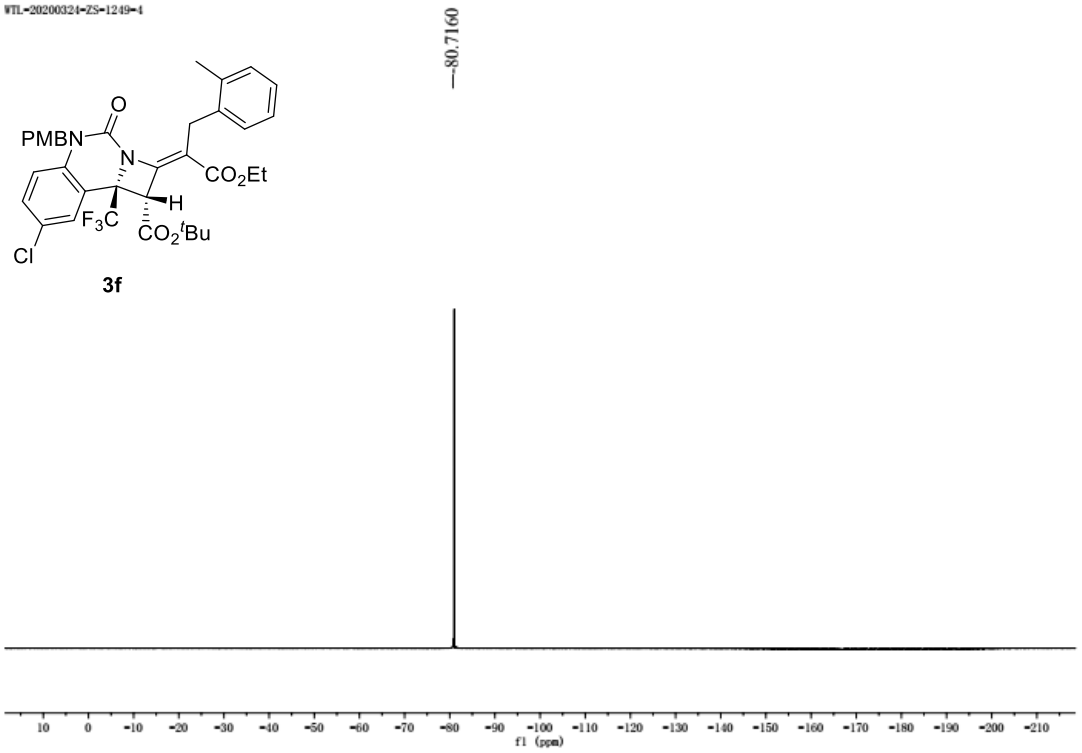

WTL-20200117-ZS-Bn
166.1312
163.4838
157.8705
148.9119
147.1191
136.5391
129.8469
127.6088
127.4484
126.9287
126.5656
115.4596
113.2546
110.2767
82.1364
68.1003
67.4444
67.1162
66.3393
59.7814
57.1701
54.2382
46.0461
32.2261
26.3943
12.8712
O
PMBN
N
CO2Et
H
F3C
CO2tBu
Cl
3e
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


WTL-20200324-ZS-Bn
81.0599
O
PMBN
N
CO2Et
H
F3C
CO2tBu
Cl
3e
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

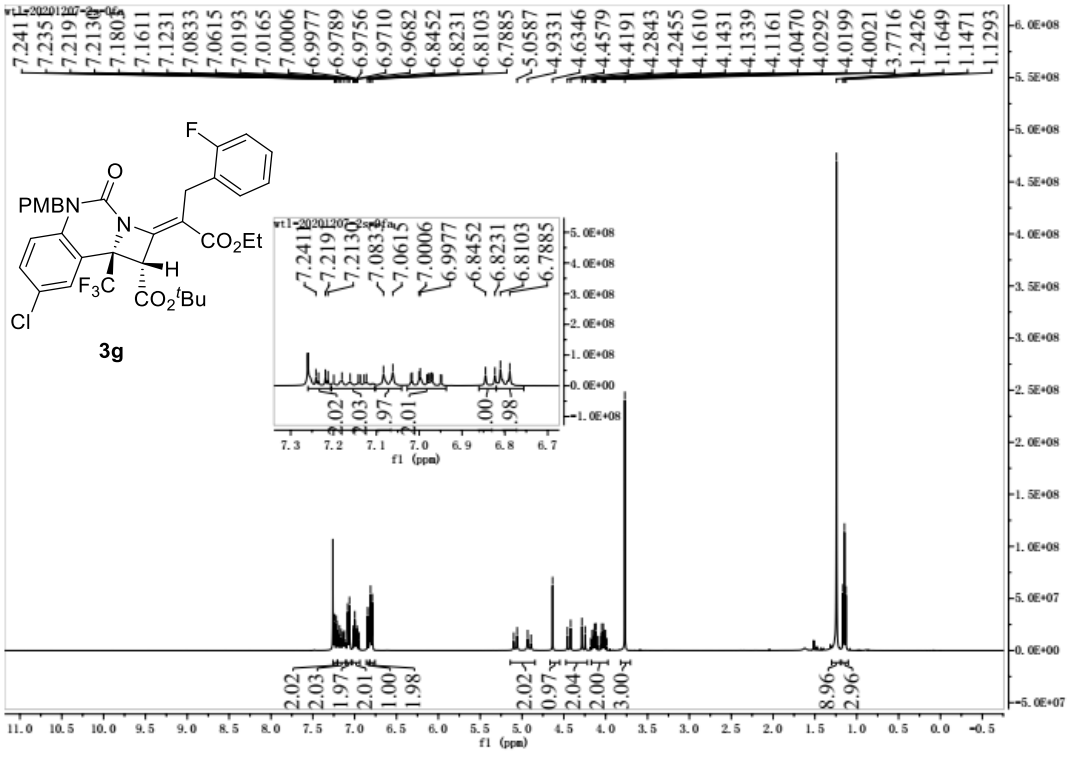
NMR of **3f** ($CDCl_3$)

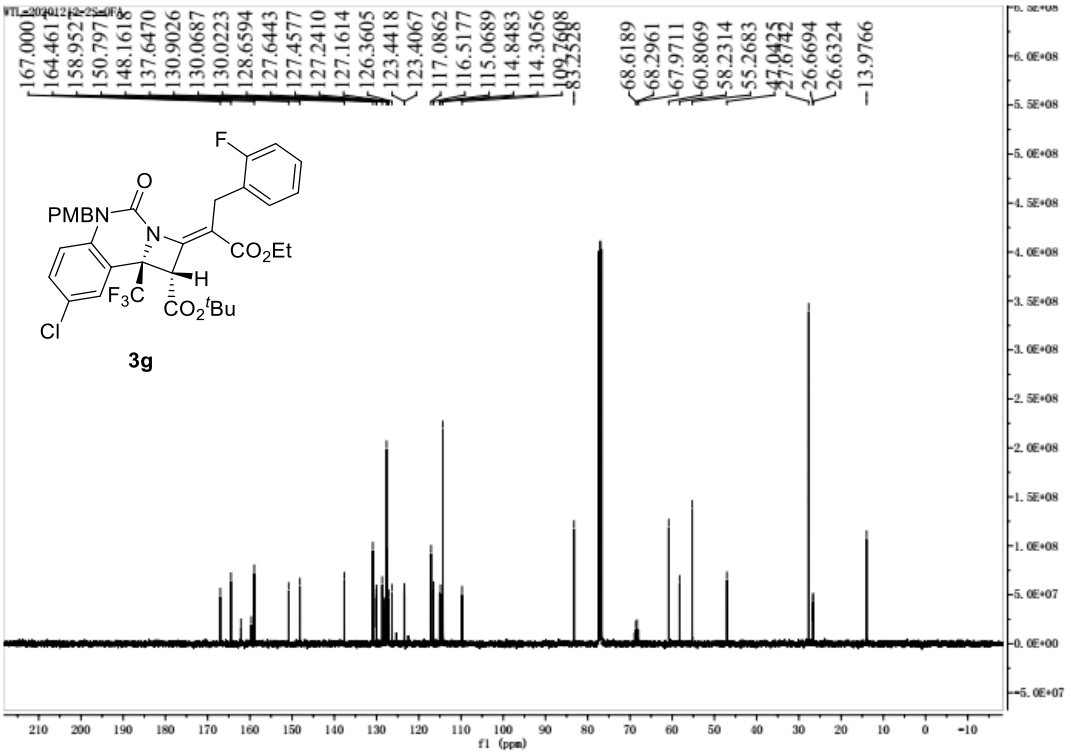


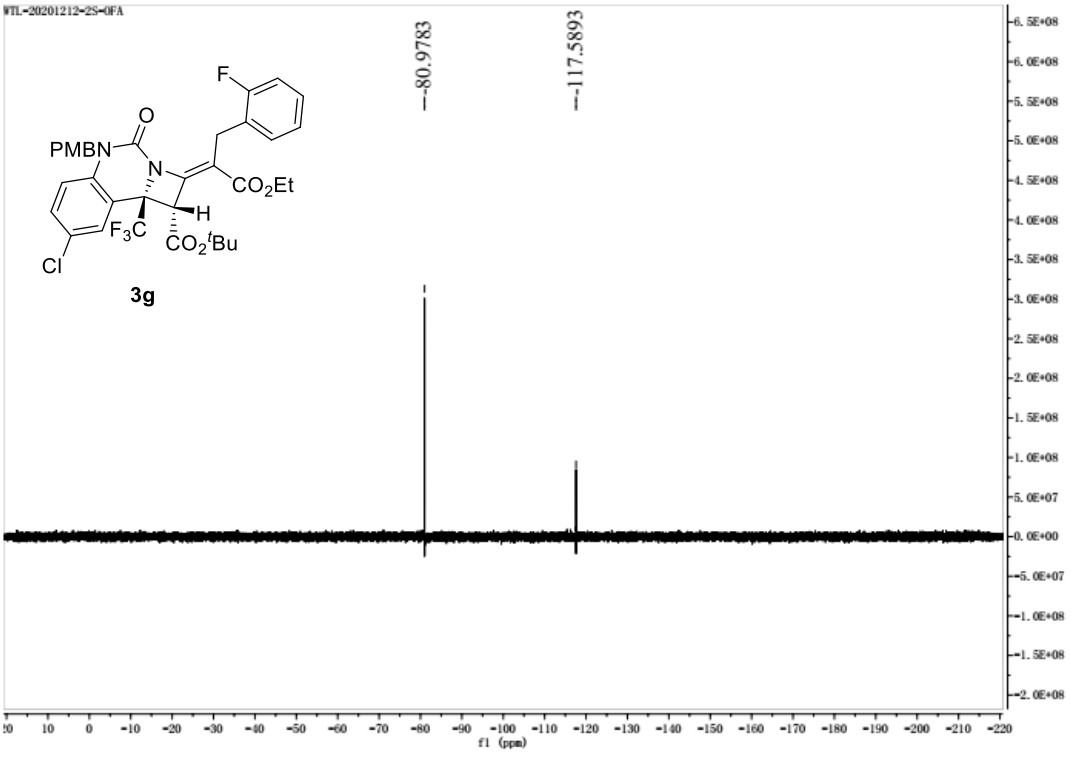




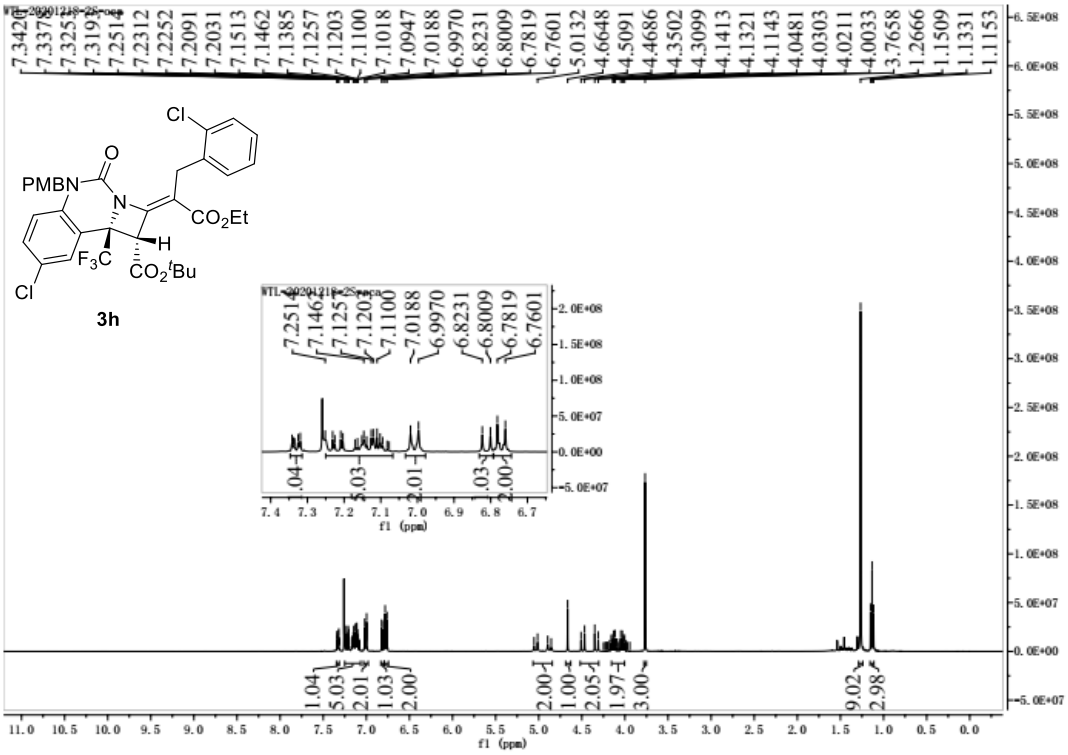
NMR of **3g** ($CDCl_3$)

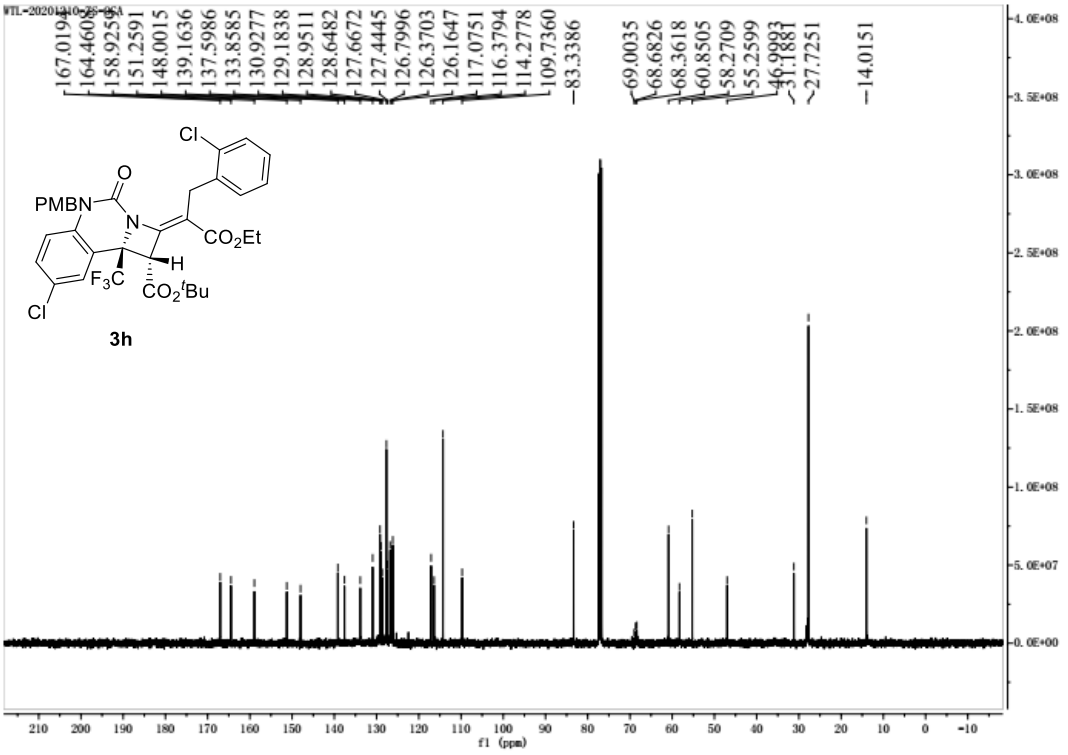


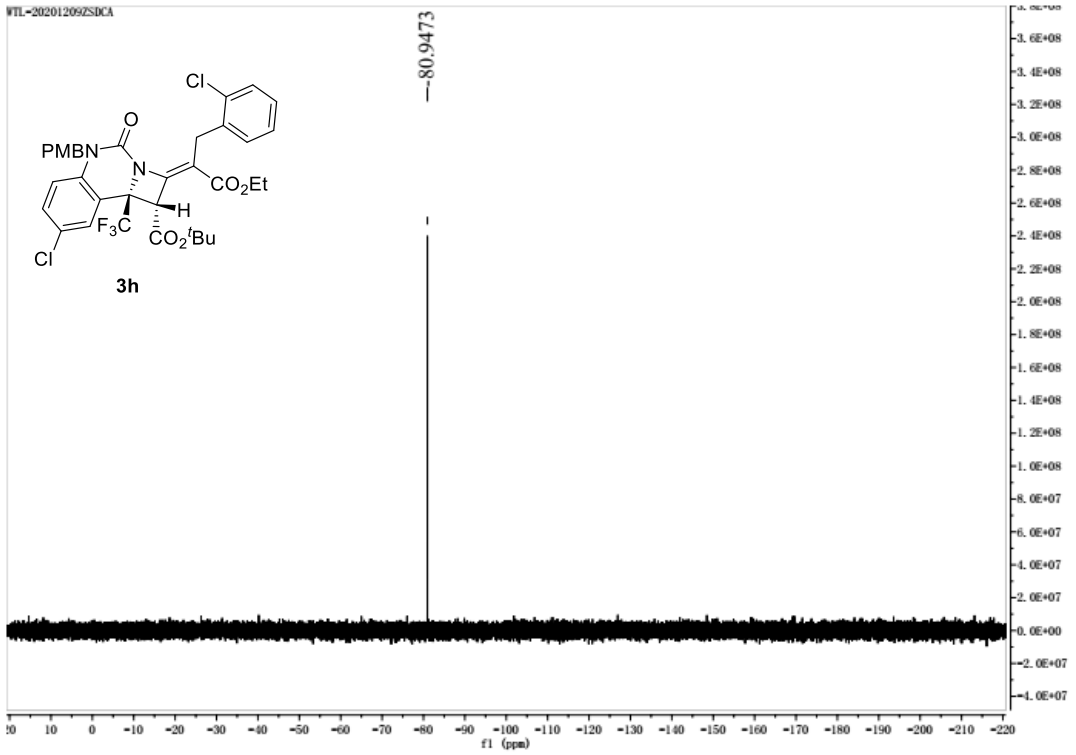

167.0007
164.4617
158.9527
150.7971
148.1618
137.6470
130.9026
130.0687
130.0223
128.6594
127.6443
127.4577
127.2410
127.1614
126.3605
123.4418
123.4067
117.0862
116.5177
115.0689
114.8483
114.3056
109.7608
83.2528
68.6189
68.2961
67.9711
60.8069
58.2314
55.2683
47.0425
27.6742
26.6694
26.6324
13.9766
F
O
PMBN
N
CO2Et
H
F3C
CO2tBu
Cl
3g
f1 (ppm)


-80.9783
-117.5893
F
O
PMBN
N
CO2Et
H
F3C
CO2tBu
Cl
3g
f1 (ppm)

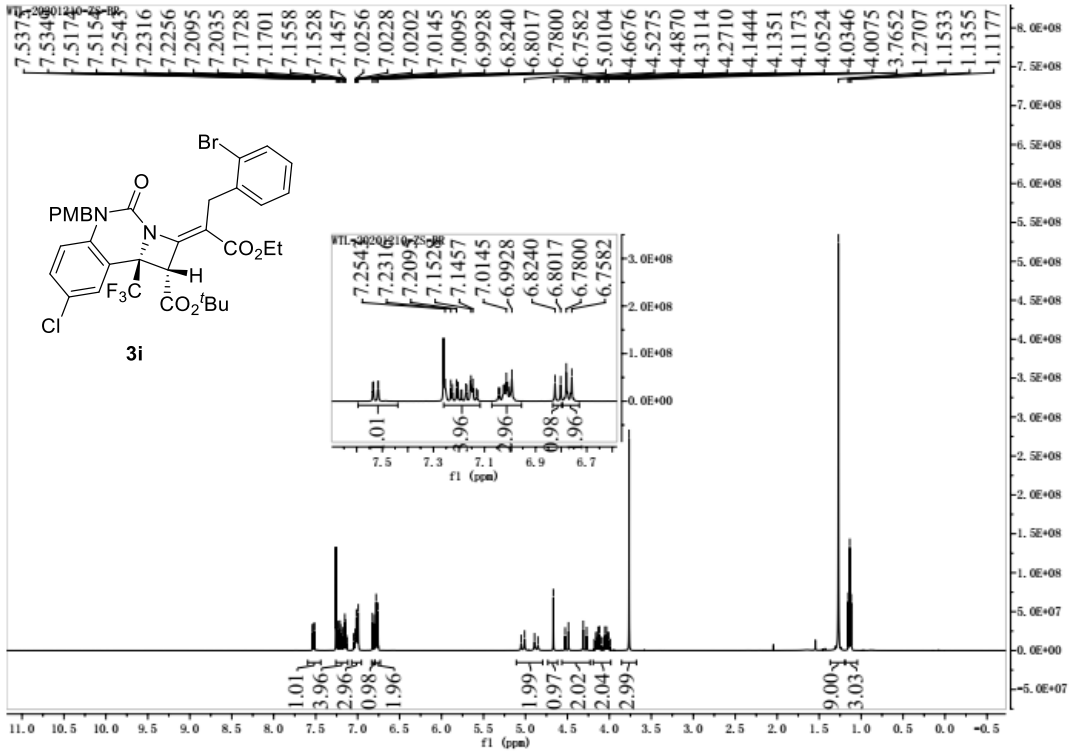
NMR of **3h** ($CDCl_3$)

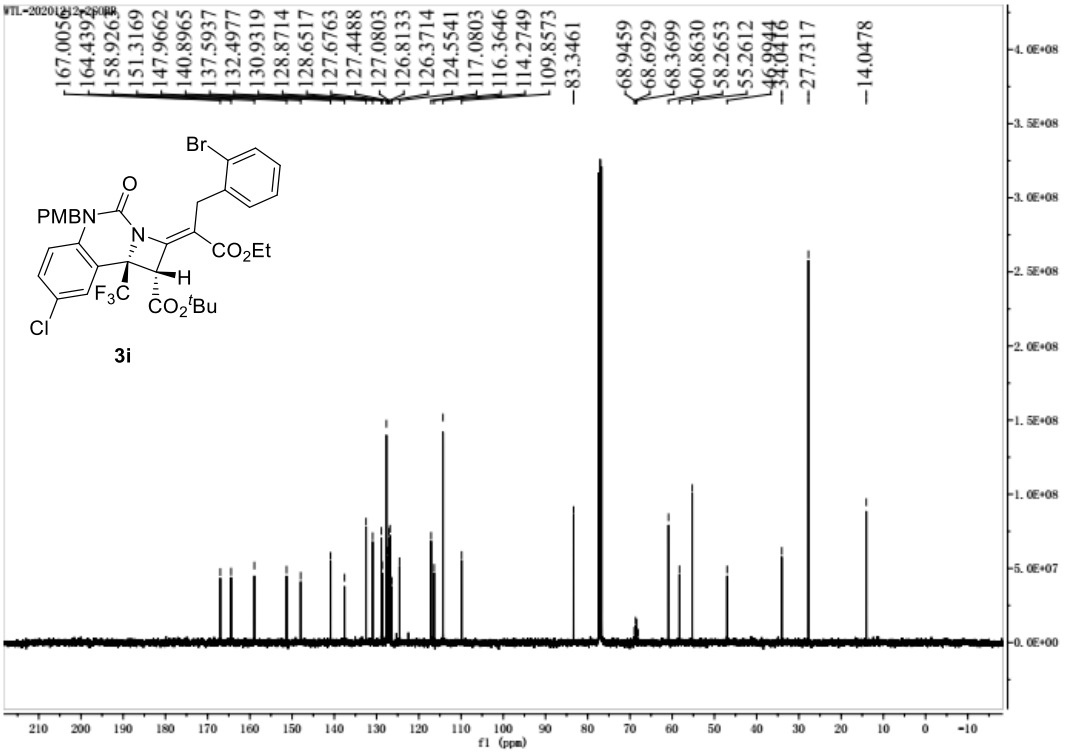


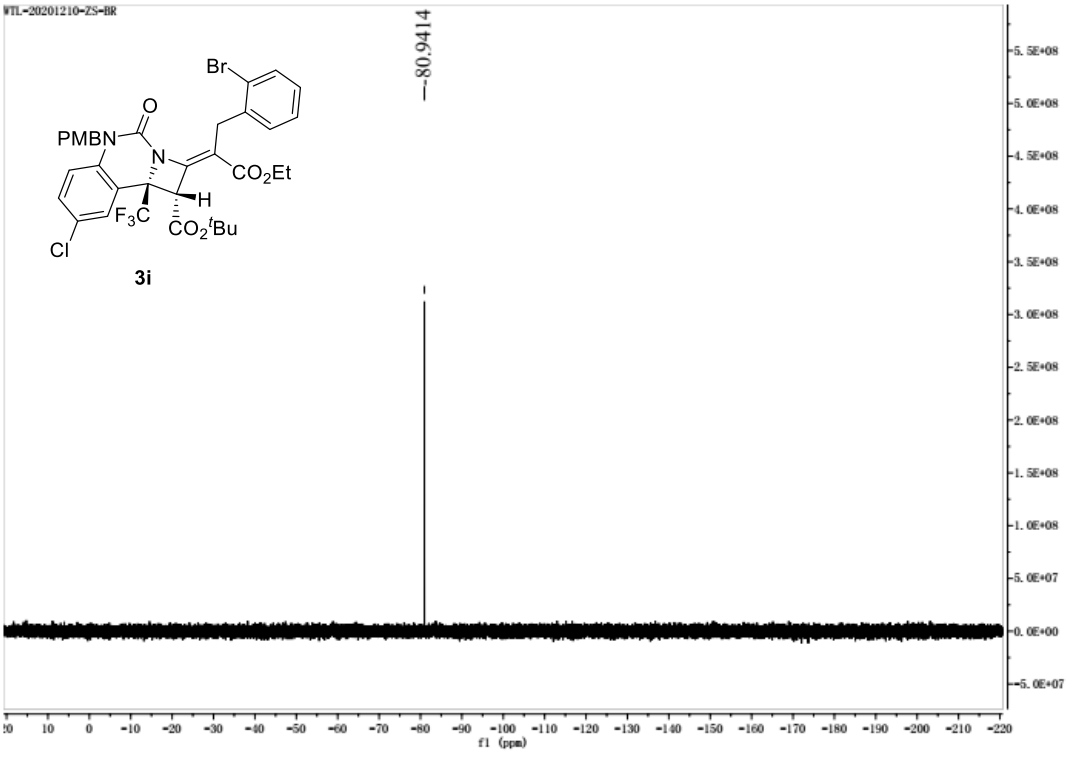




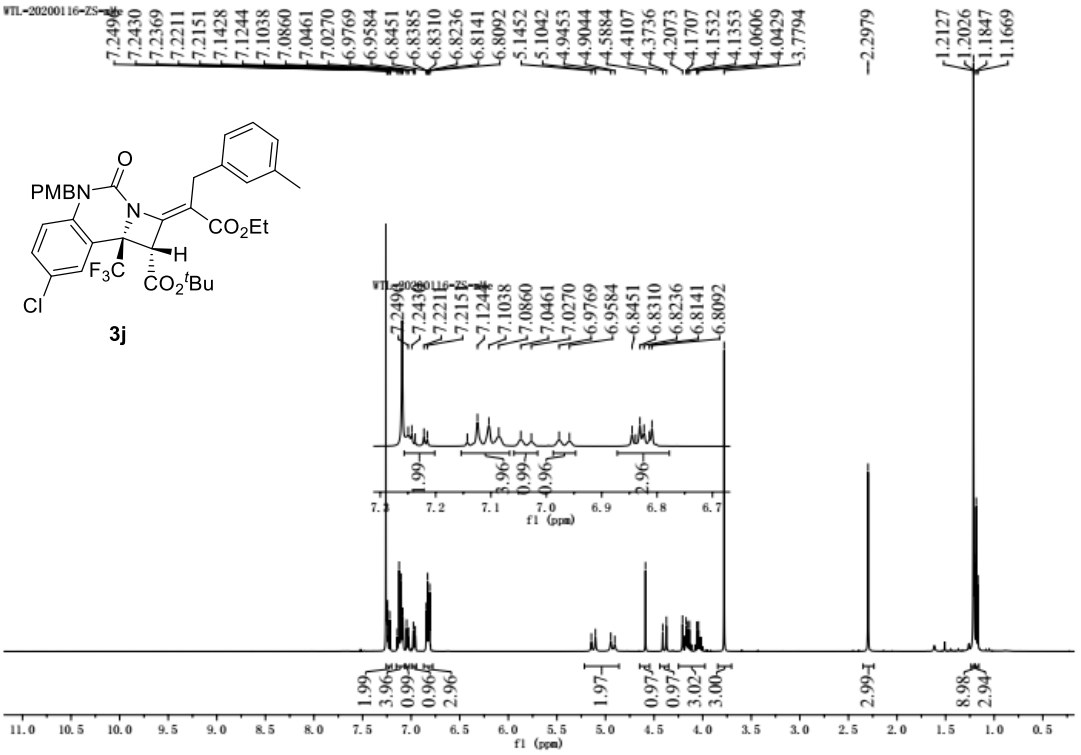
NMR of **3i** ($CDCl_3$)

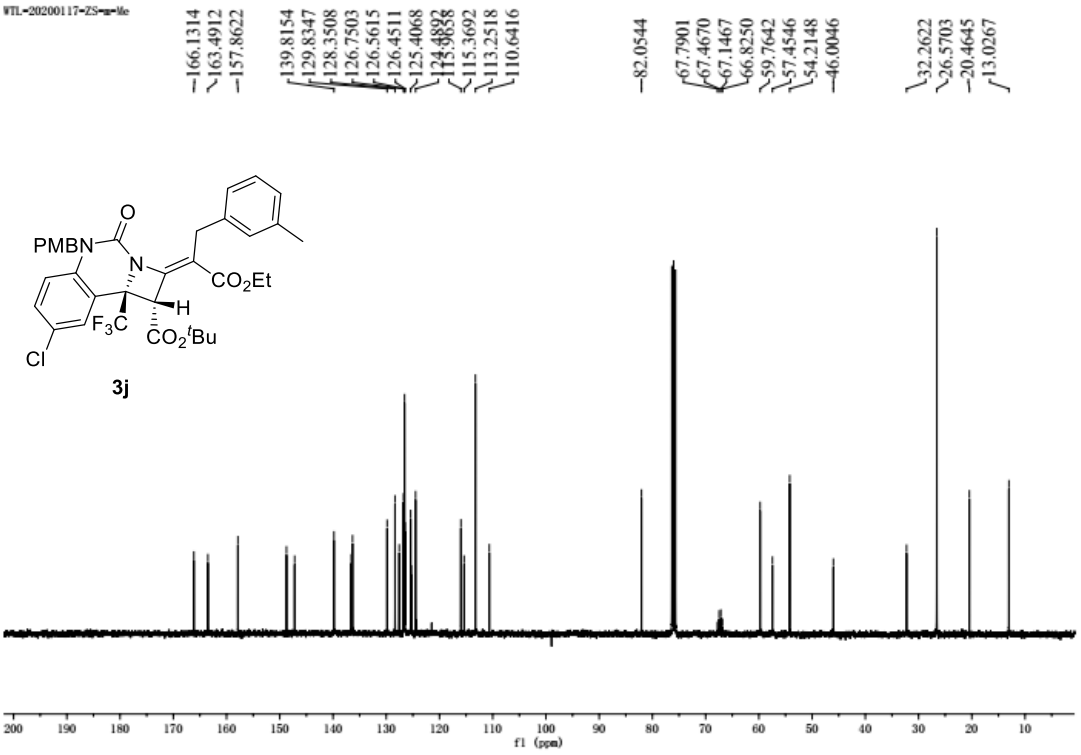


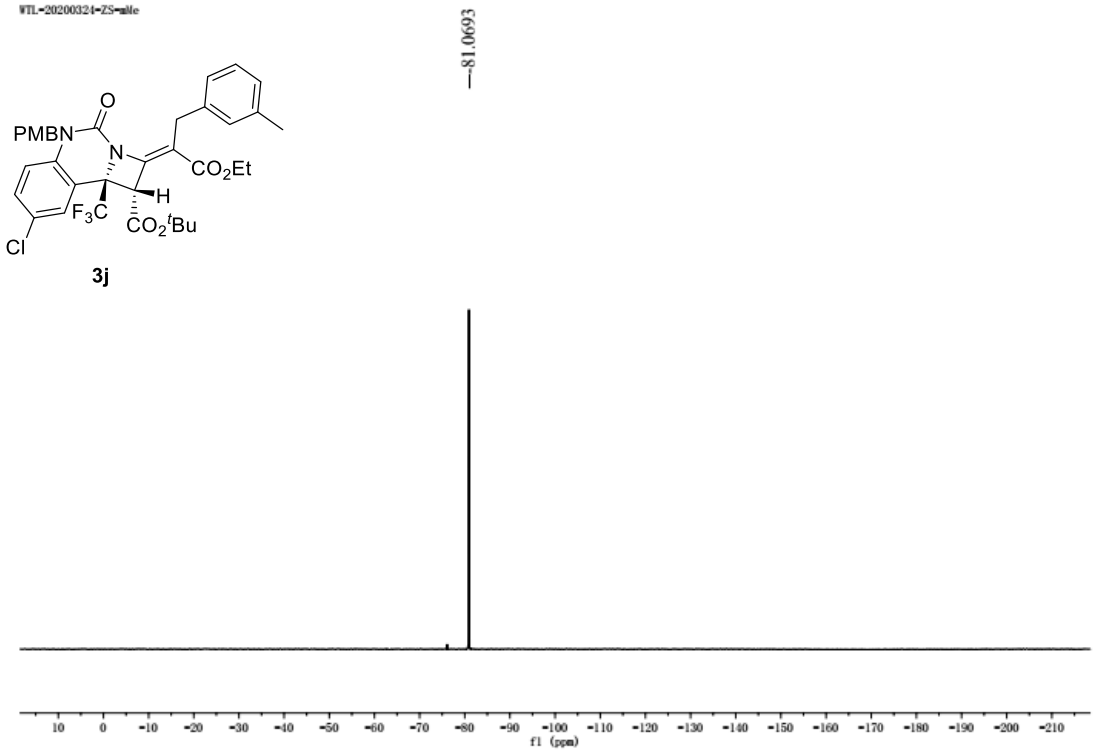

167.0056
164.4392
158.9263
151.3169
147.9662
140.8965
137.5937
132.4977
130.9319
128.8714
128.6517
127.6763
127.4488
127.0803
126.8133
126.3714
124.5541
117.0803
116.3646
114.2749
109.8573
83.3461
68.9459
68.6929
68.3699
60.8630
58.2653
55.2612
46.8944
34.0416
27.7317
14.0478
Br
O
PMBN
N
CO2Et
H
F3C
CO2tBu
Cl
3i
f1 (ppm)


80.9414
Br
O
PMBN
N
CO2Et
H
F3C
CO2tBu
Cl
3i
f1 (ppm)

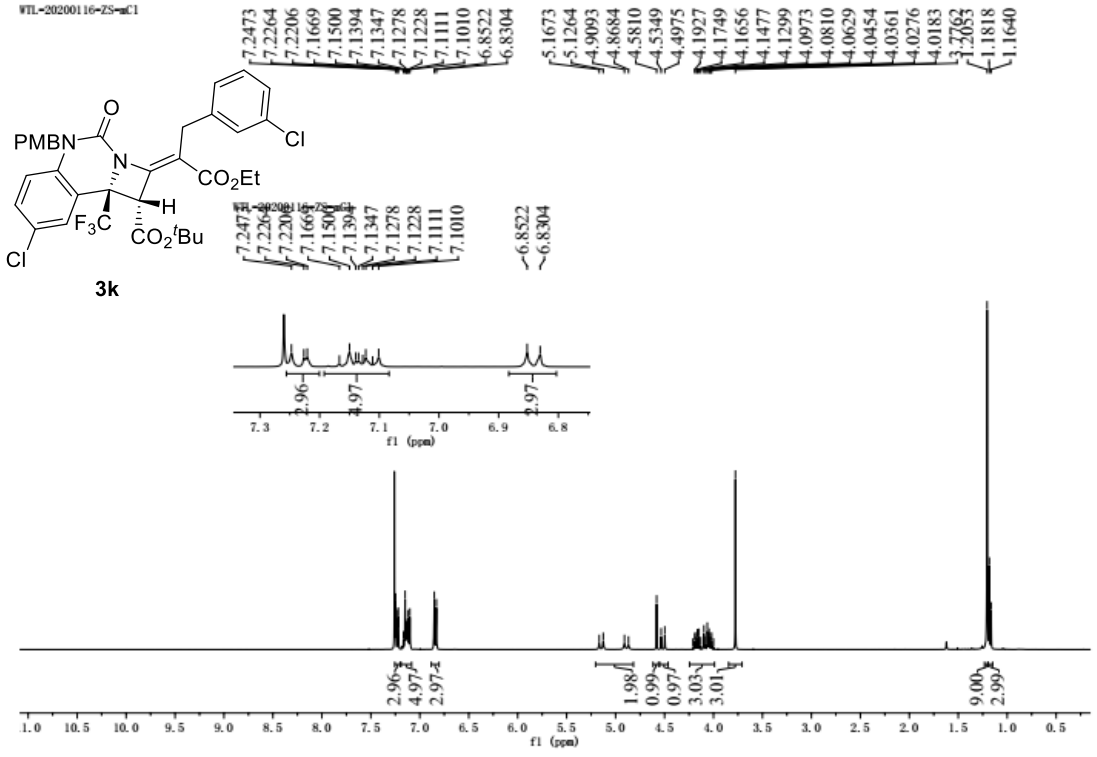
NMR of **3j** ($CDCl_3$)

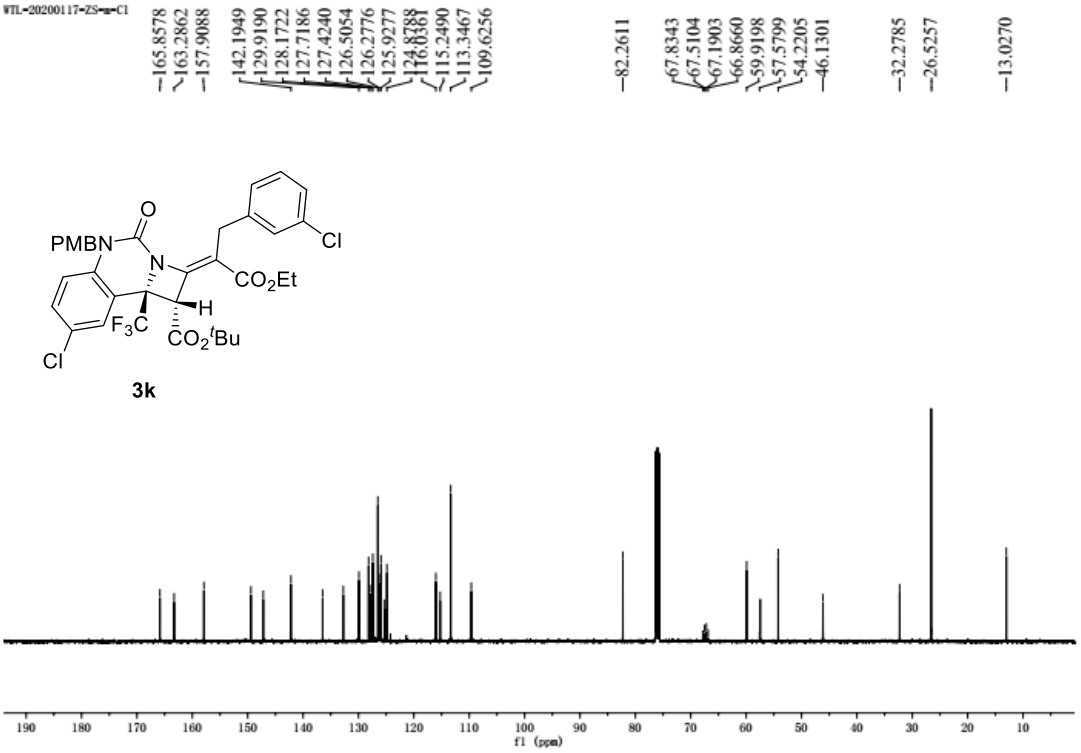






NMR of **3k** ($CDCl_3$)




WTL-20200117-ZS-m-C1
165.8578
163.2862
157.9088
142.1949
129.9190
128.1722
127.7186
127.4240
126.5054
126.2776
125.9277
124.8788
116.0381
115.2490
113.3467
109.6256
82.2611
67.8343
67.5104
67.1903
66.8660
59.9198
57.5799
54.2205
46.1301
32.2785
26.5257
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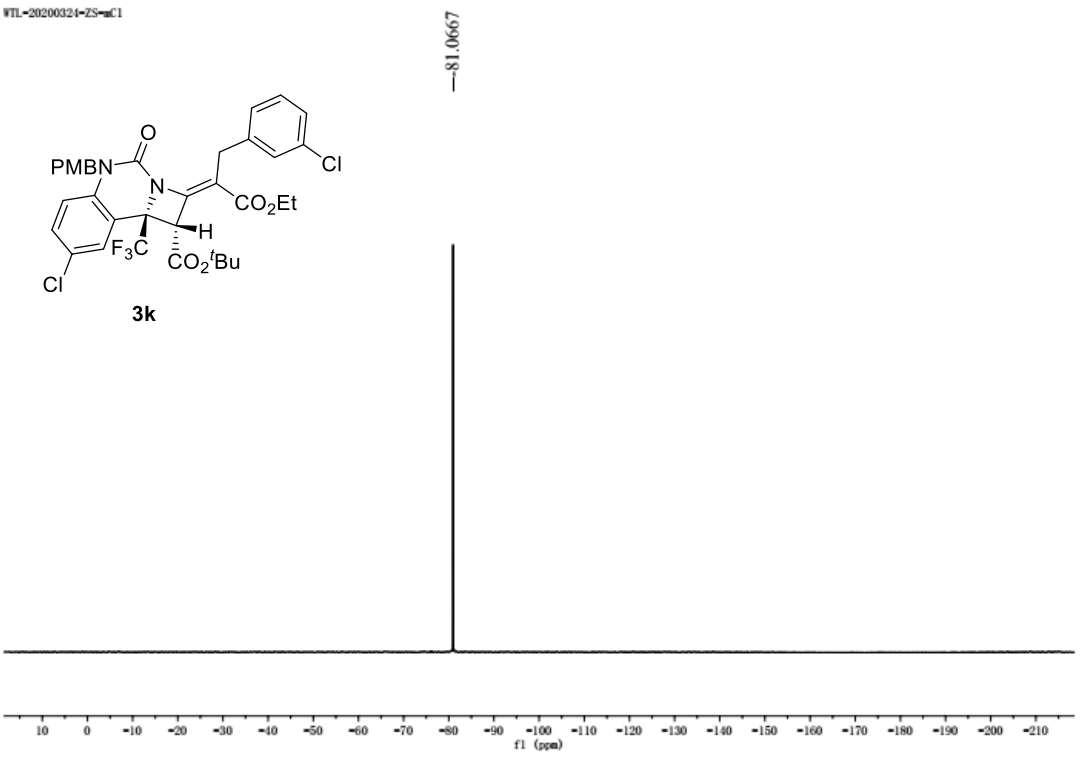
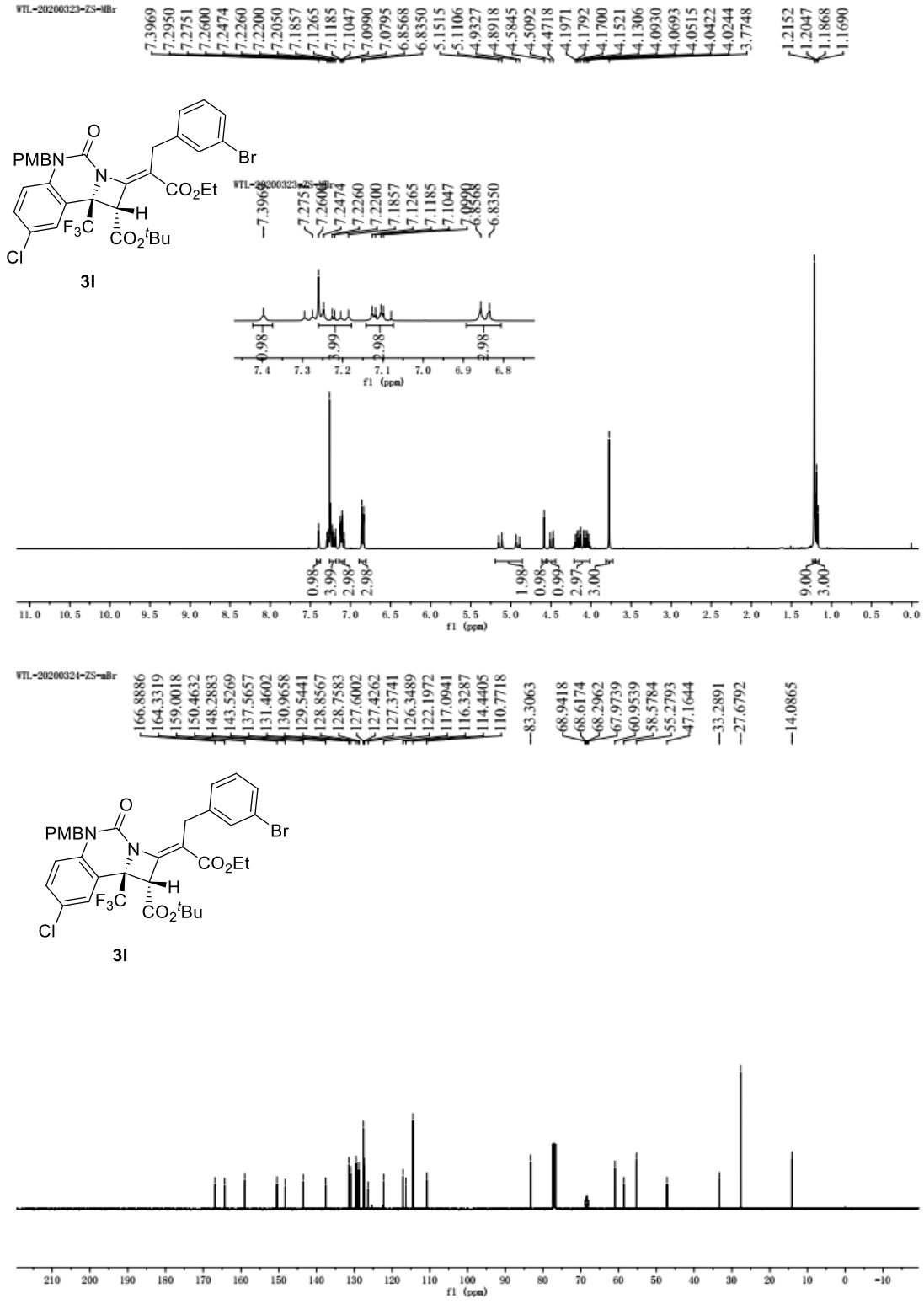
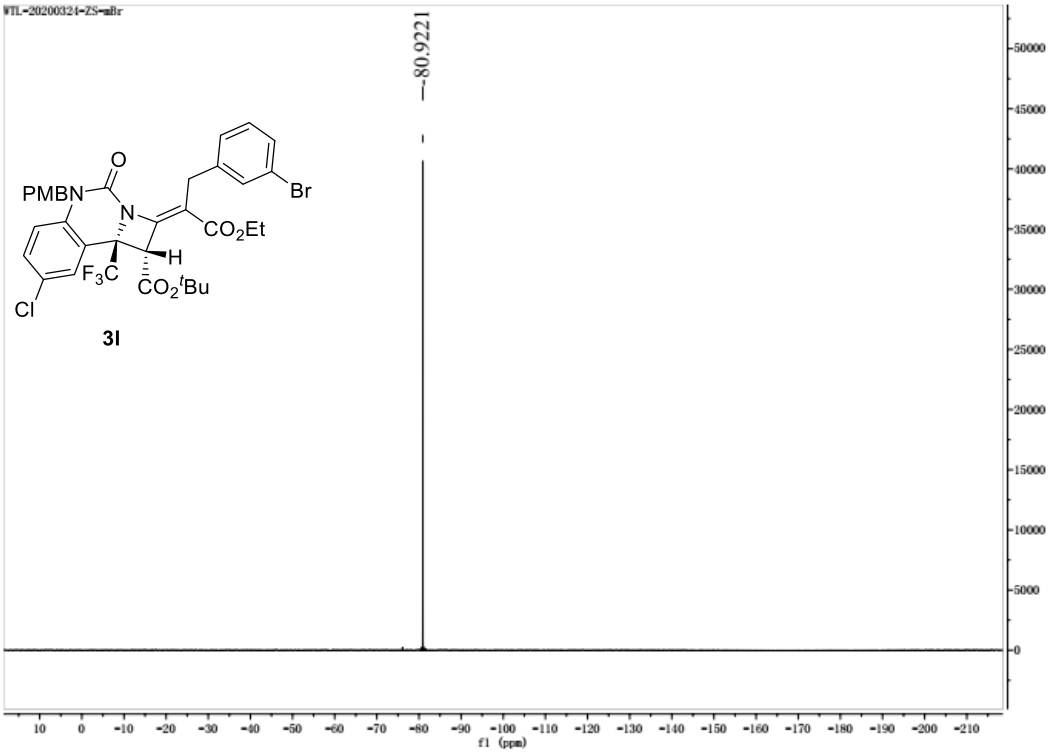
PMBN
O
N
Cl
CO2Et
H
F3C
CO2tBu
Cl
3k
f1 (ppm)

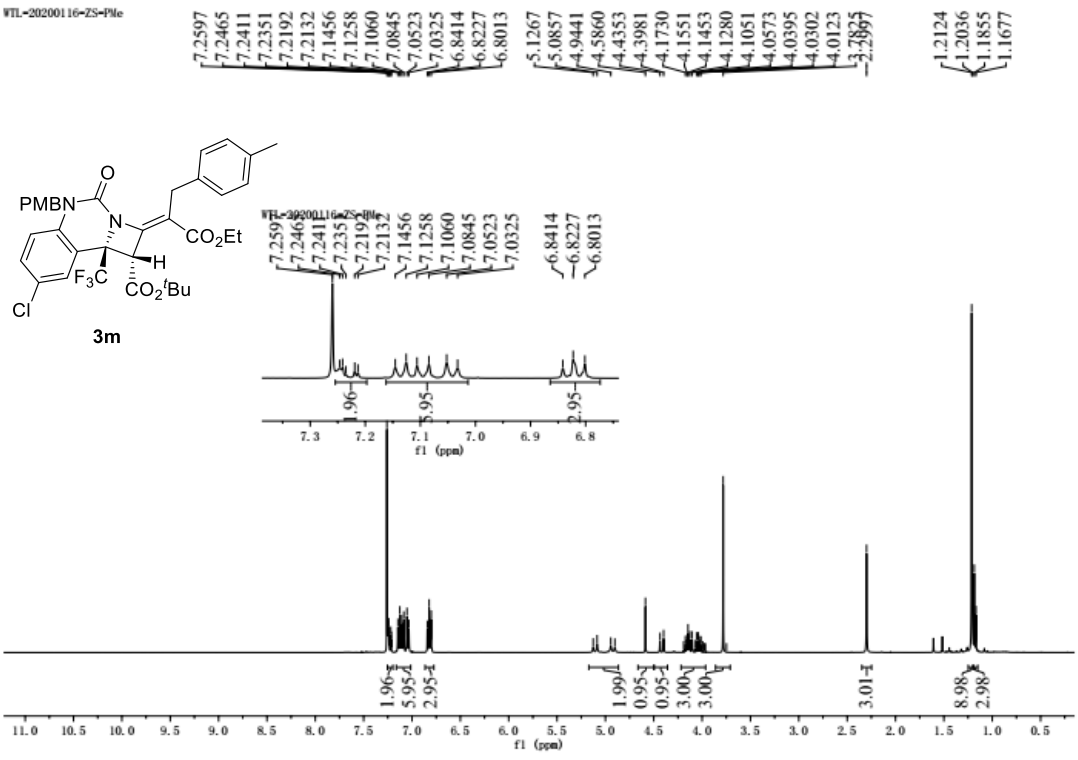

WTL-20200324-ZS-mC1
81.0667
PMBN
O
N
Cl
CO2Et
H
F3C
CO2tBu
Cl
3k
f1 (ppm)

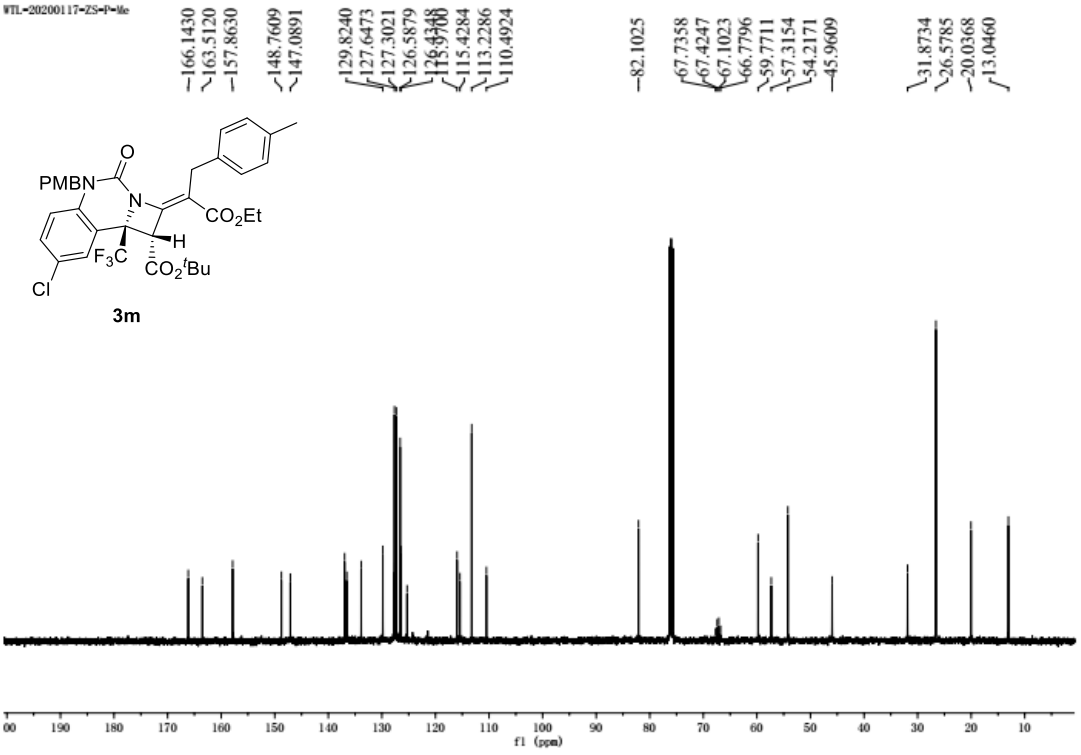
NMR of **3l** ($CDCl_3$)

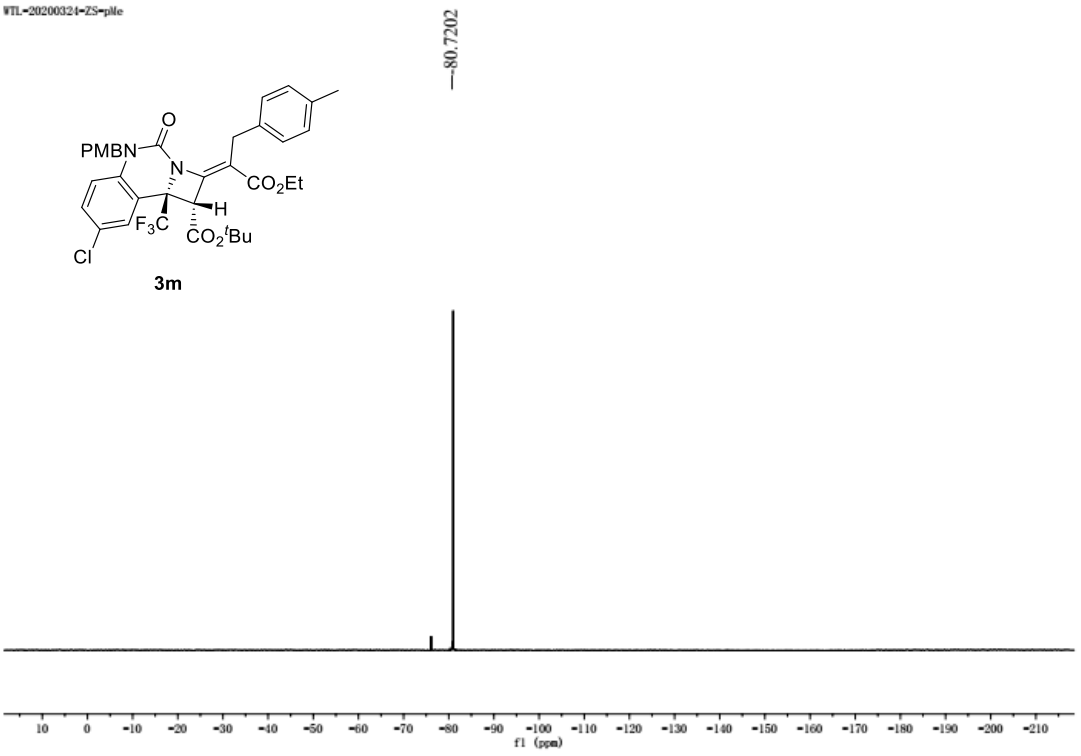




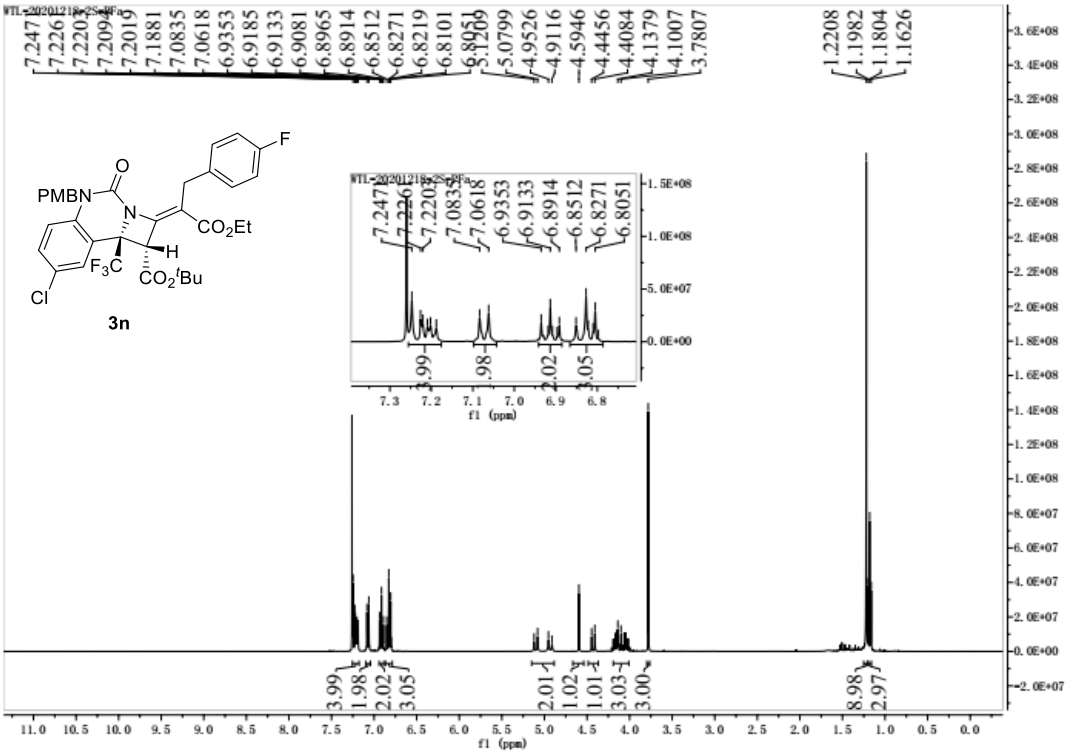
NMR of **3m** ($CDCl_3$)

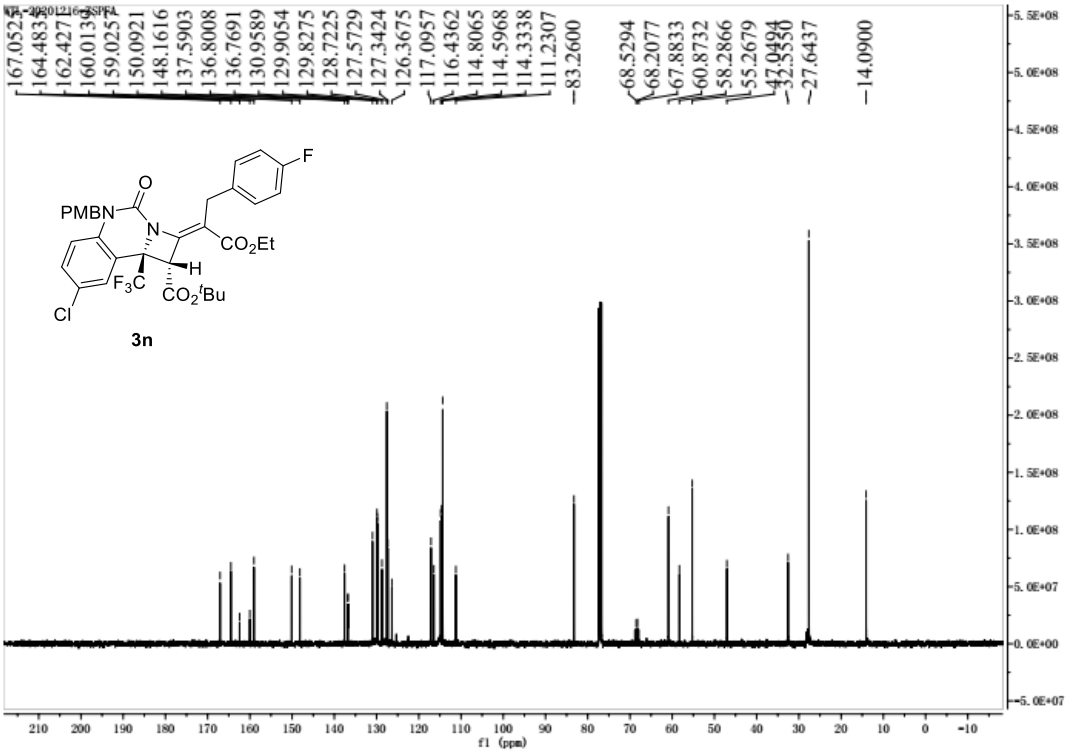


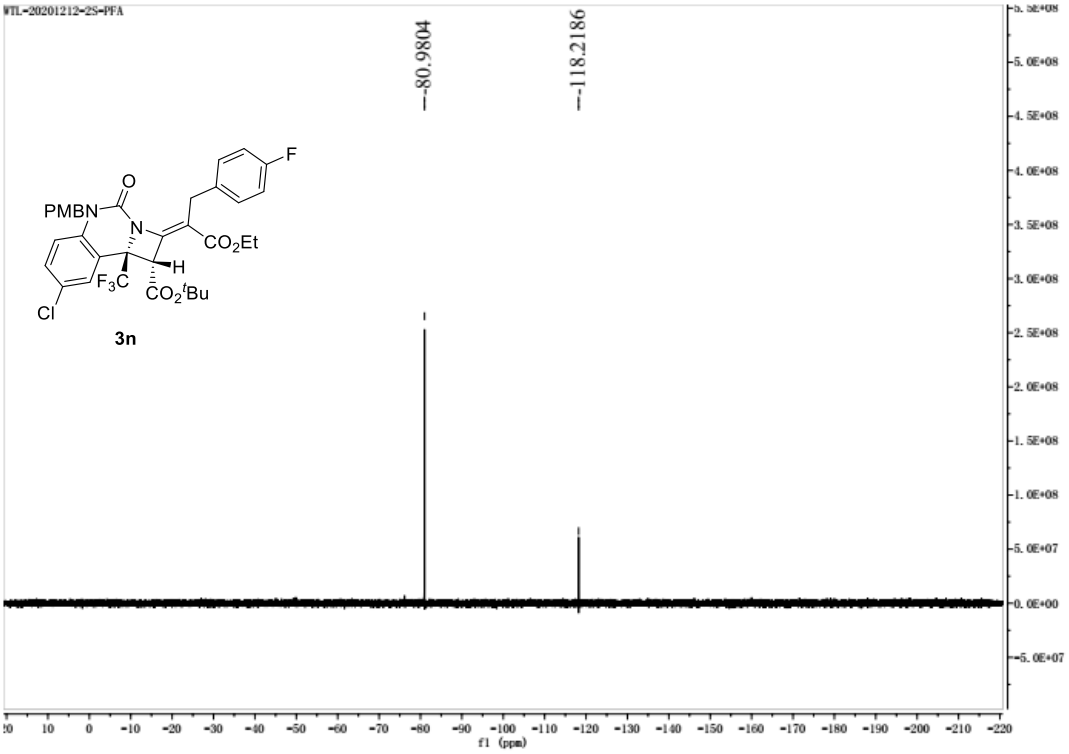

WTL-20200117-ZS-P-Me
166.1430
163.5120
157.8630
148.7609
147.0891
129.8240
127.6473
127.3021
126.5879
115.4284
113.2286
110.4924
82.1025
67.7358
67.4247
67.1023
66.7796
59.7711
57.3154
54.2171
45.9609
31.8734
26.5785
20.0368
13.0460
PMBN
O
N
CO2Et
H
F3C
CO2tBu
Cl
3m
f1 (ppm)


WTL-20200324-ZS-pMe
80.7202
PMBN
O
N
CO2Et
H
F3C
CO2tBu
Cl
3m
f1 (ppm)

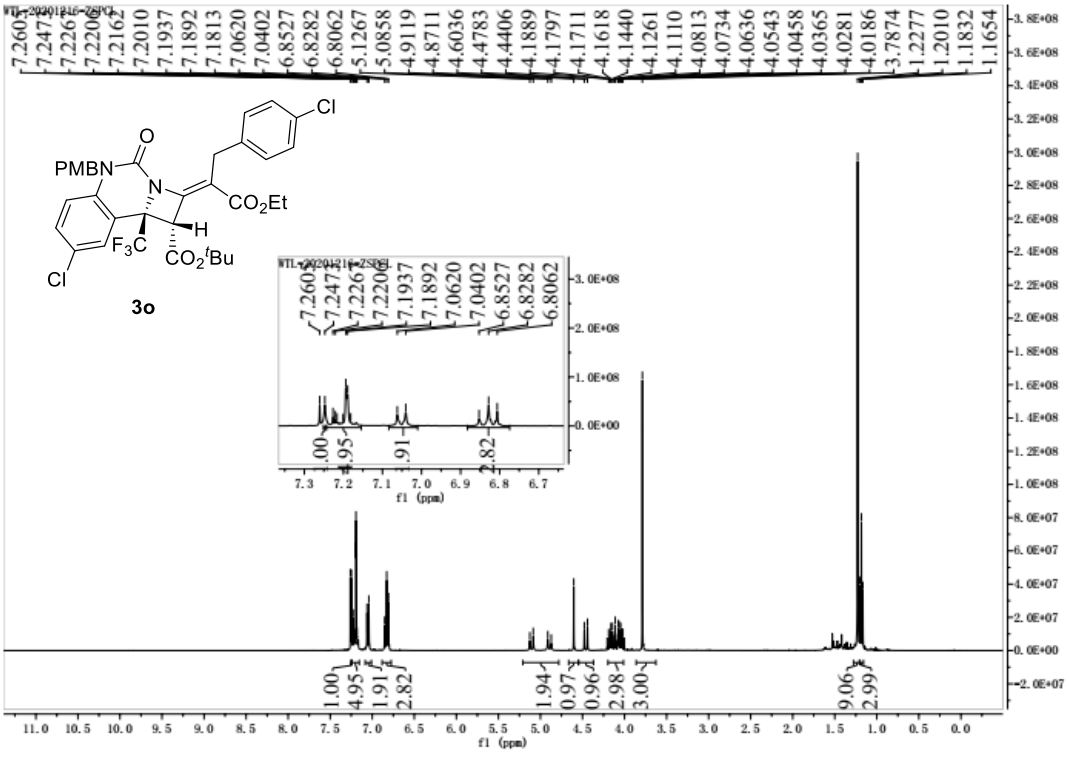
NMR of **3n** ($CDCl_3$)

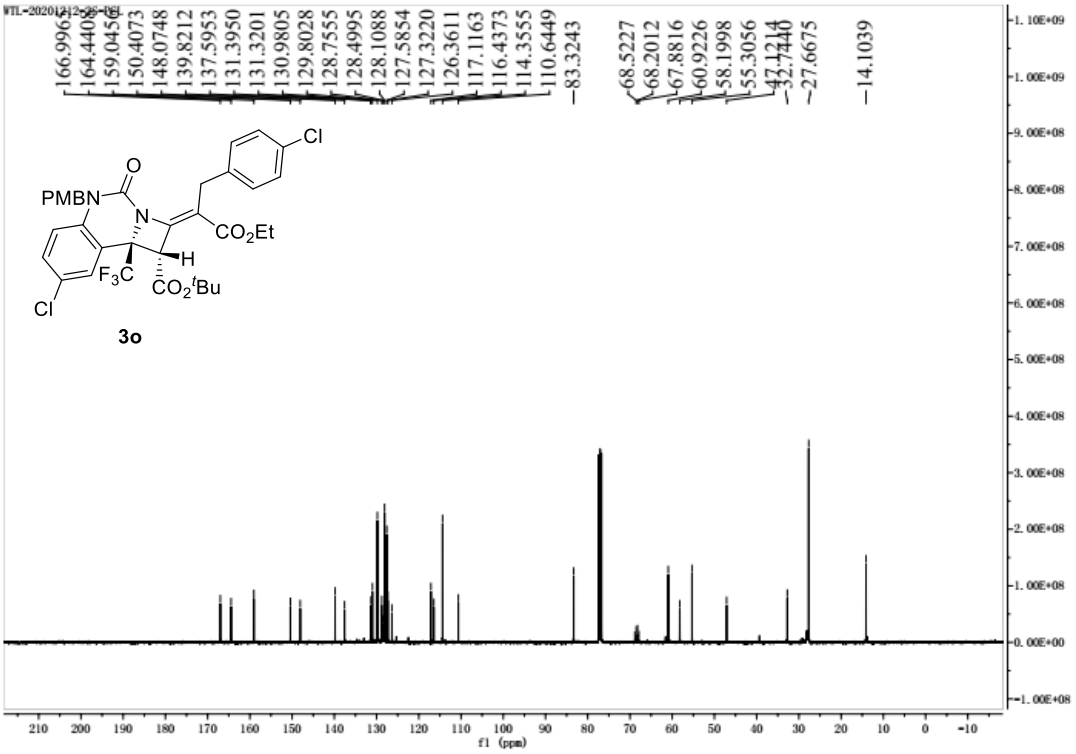


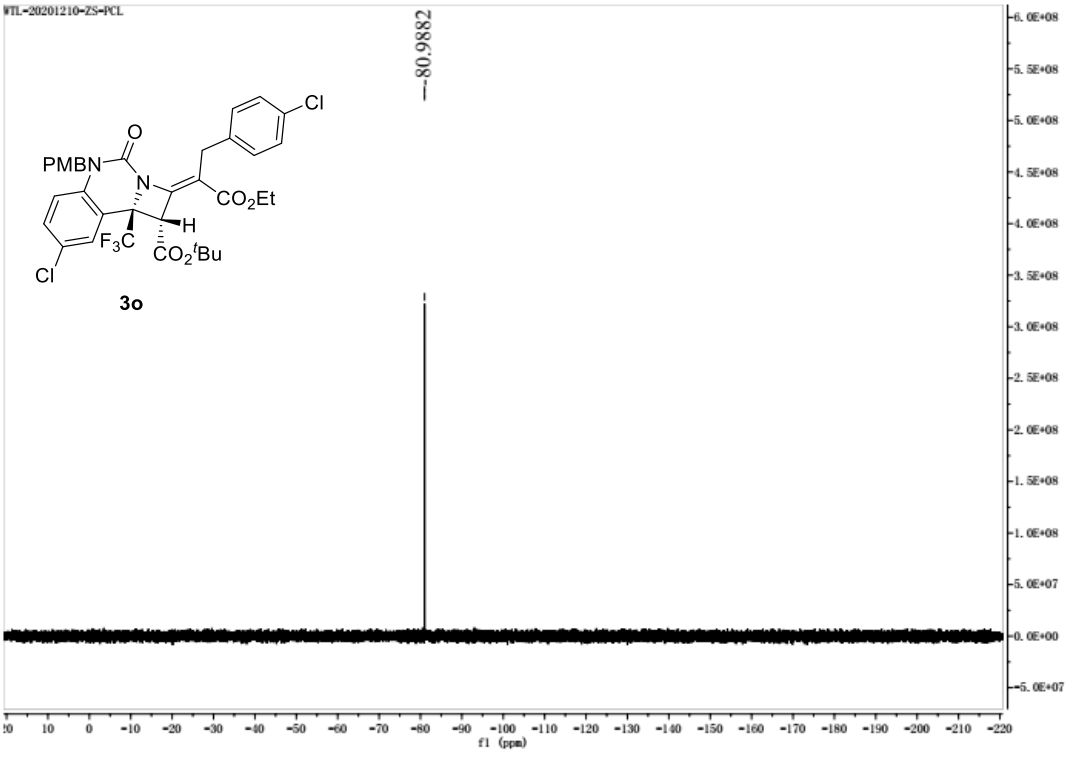




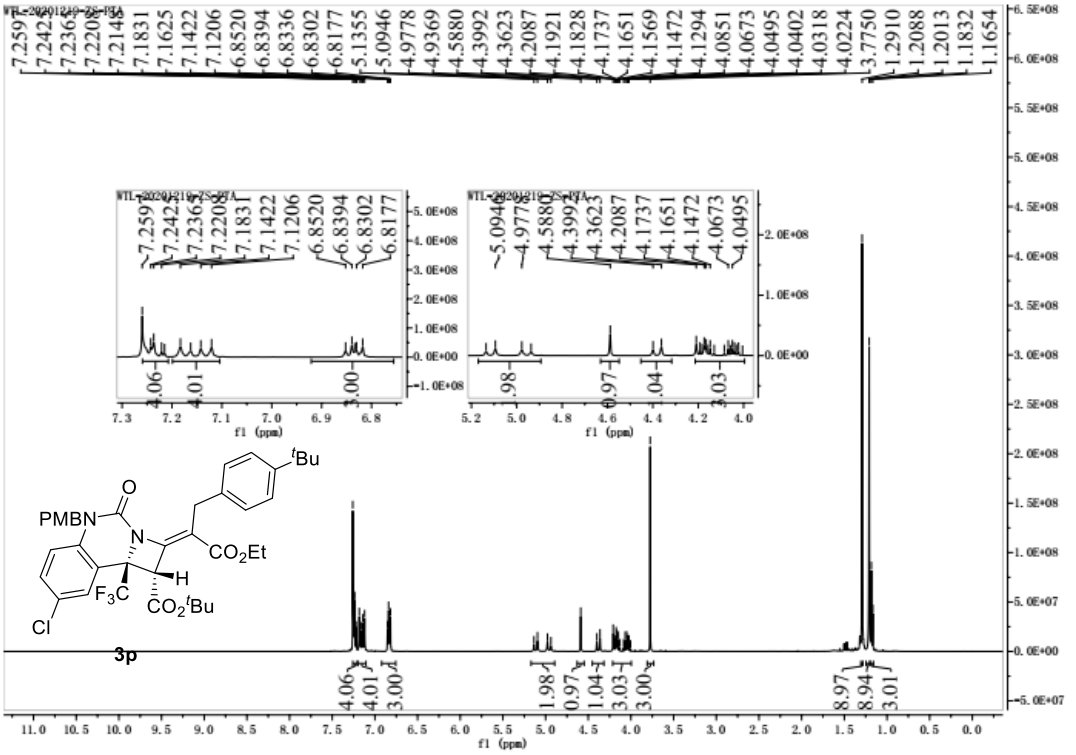
NMR of **3o** ($CDCl_3$)

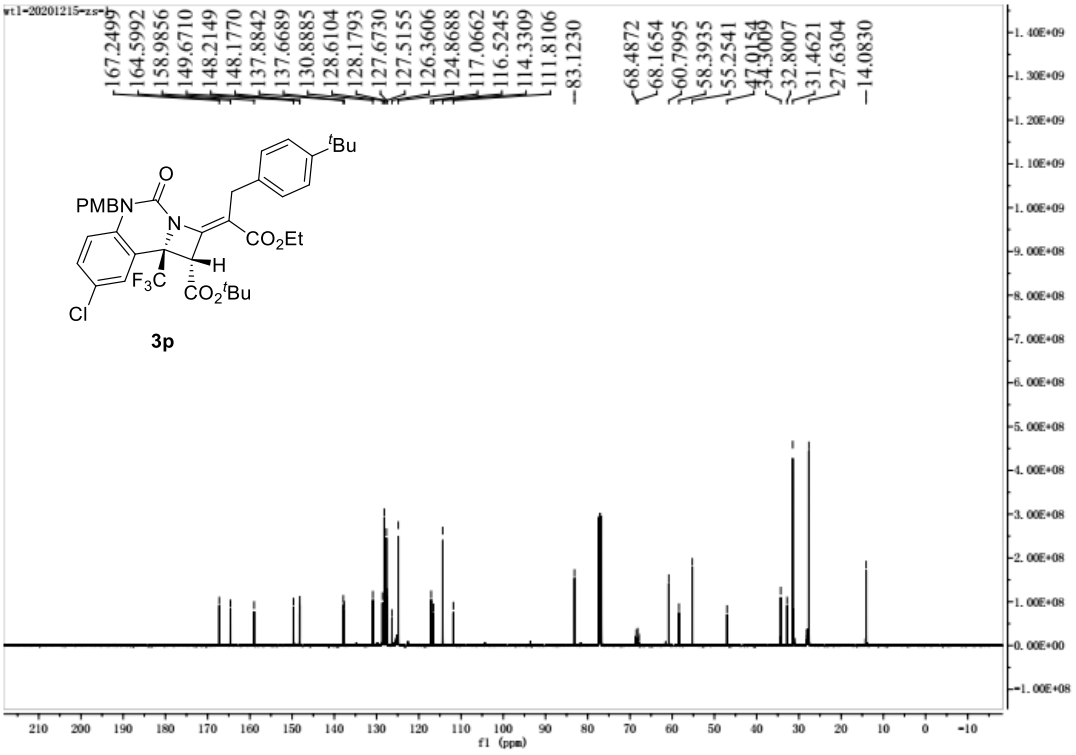


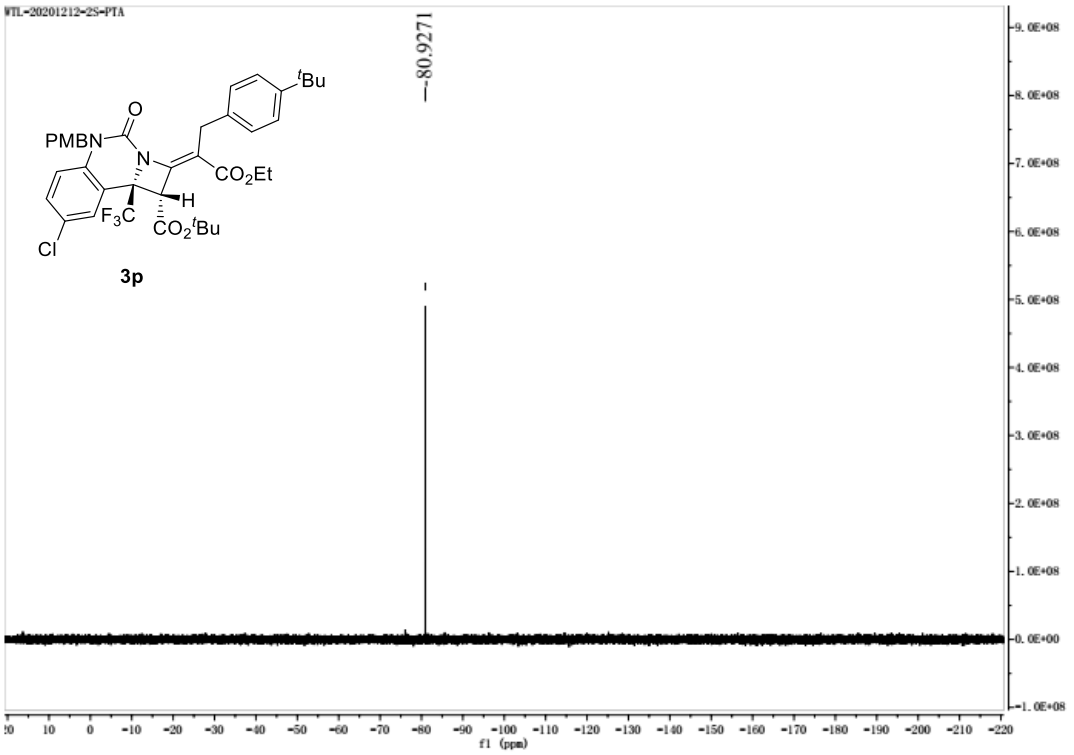

166.9962
164.4408
159.0456
150.4073
148.0748
139.8212
137.5953
131.3950
131.3201
130.9805
129.8028
128.7555
128.4995
128.1088
127.5854
127.3220
126.3611
117.1163
116.4373
114.3555
110.6449
83.3243
68.5227
68.2012
67.8816
60.9226
58.1998
55.3056
47.1214
32.7440
27.6675
14.1039
PMBN
O
N
Cl
CO2Et
F3C
H
CO2tBu
Cl
3o
f1 (ppm)


80.9882
PMBN
O
N
Cl
CO2Et
F3C
H
CO2tBu
Cl
3o
f1 (ppm)

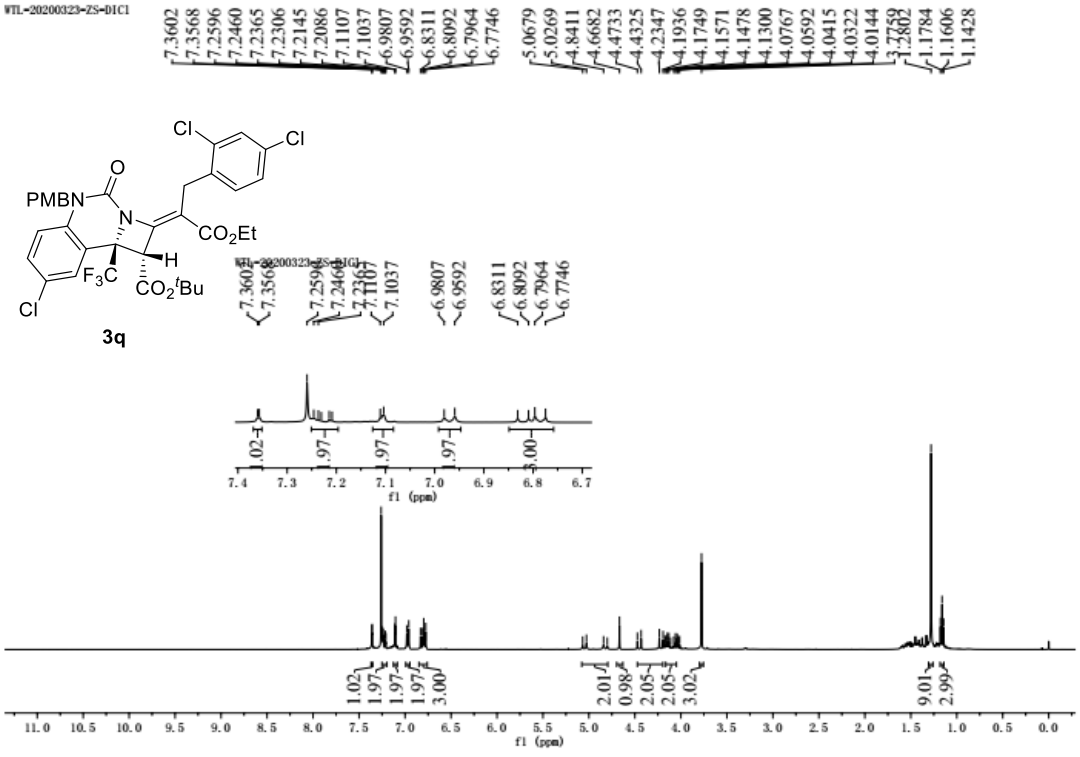
NMR of **3p** ($CDCl_3$)

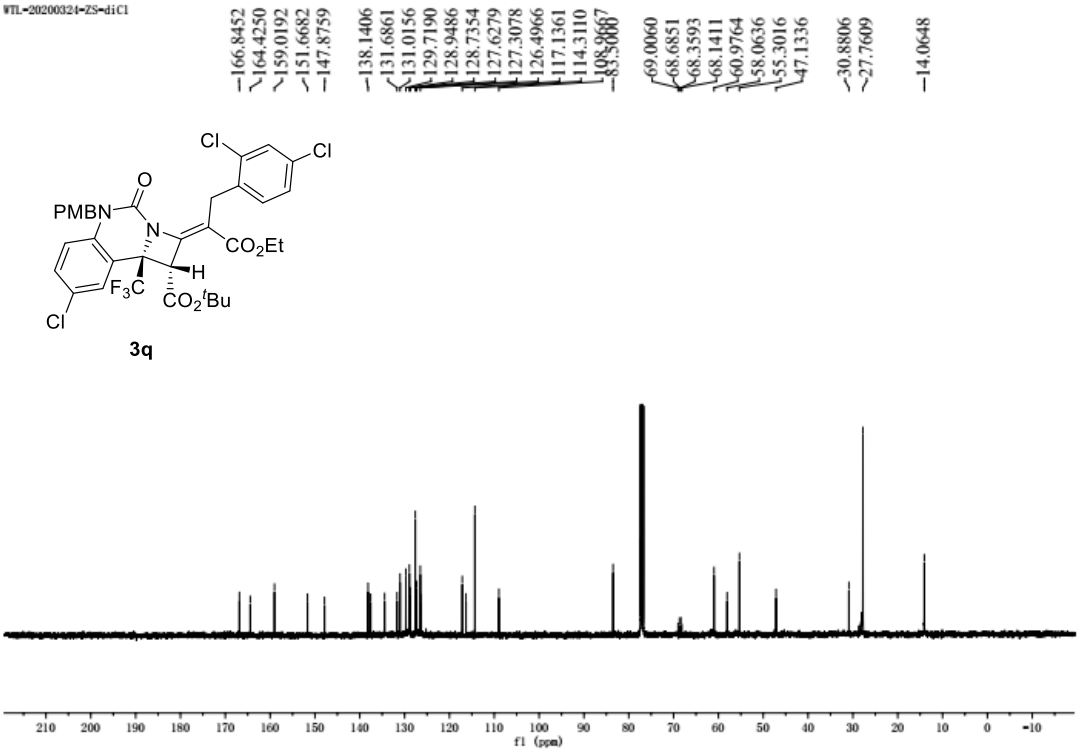


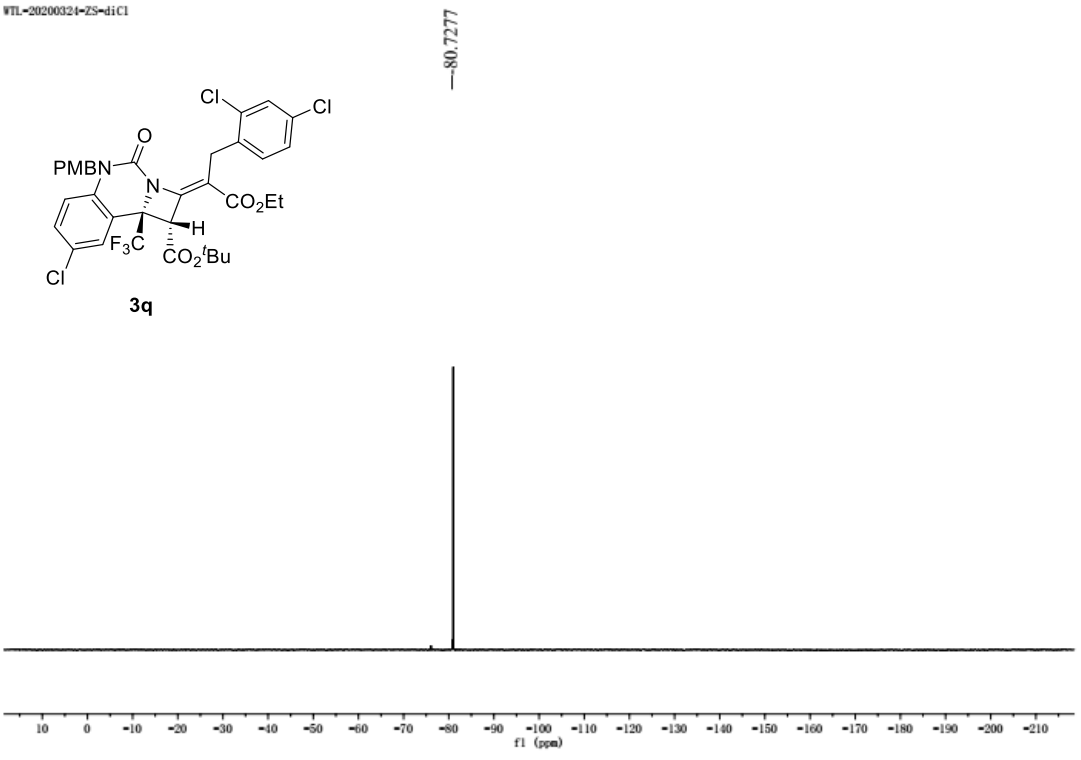




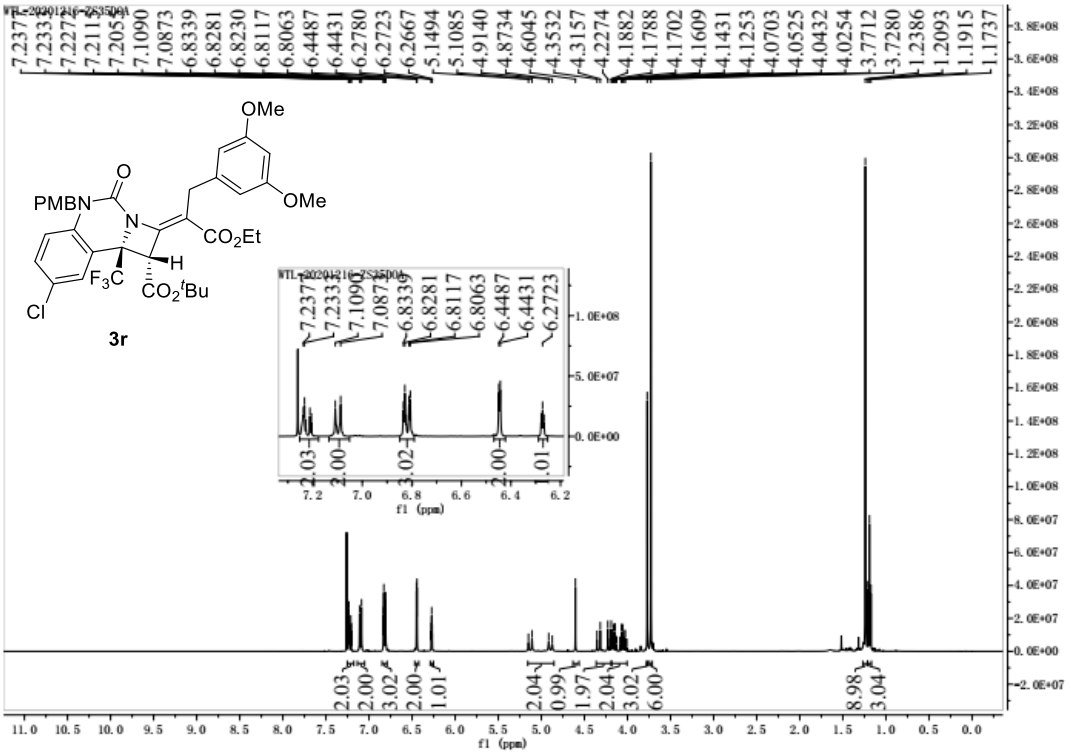
NMR of **3q** ($CDCl_3$)

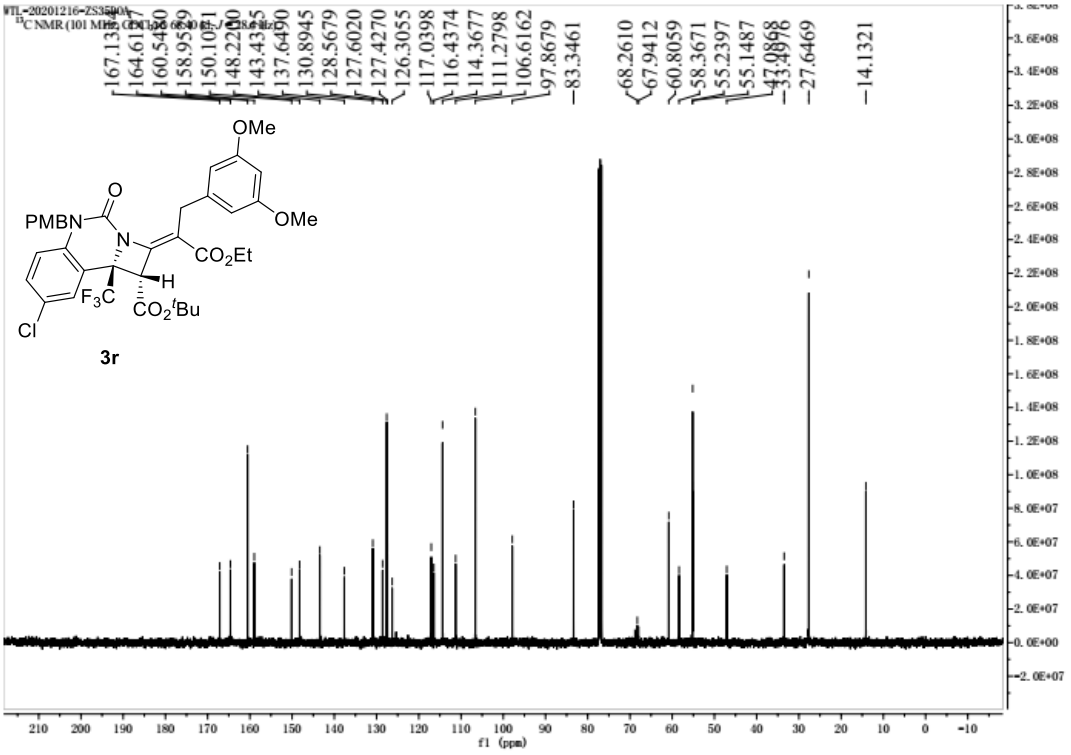


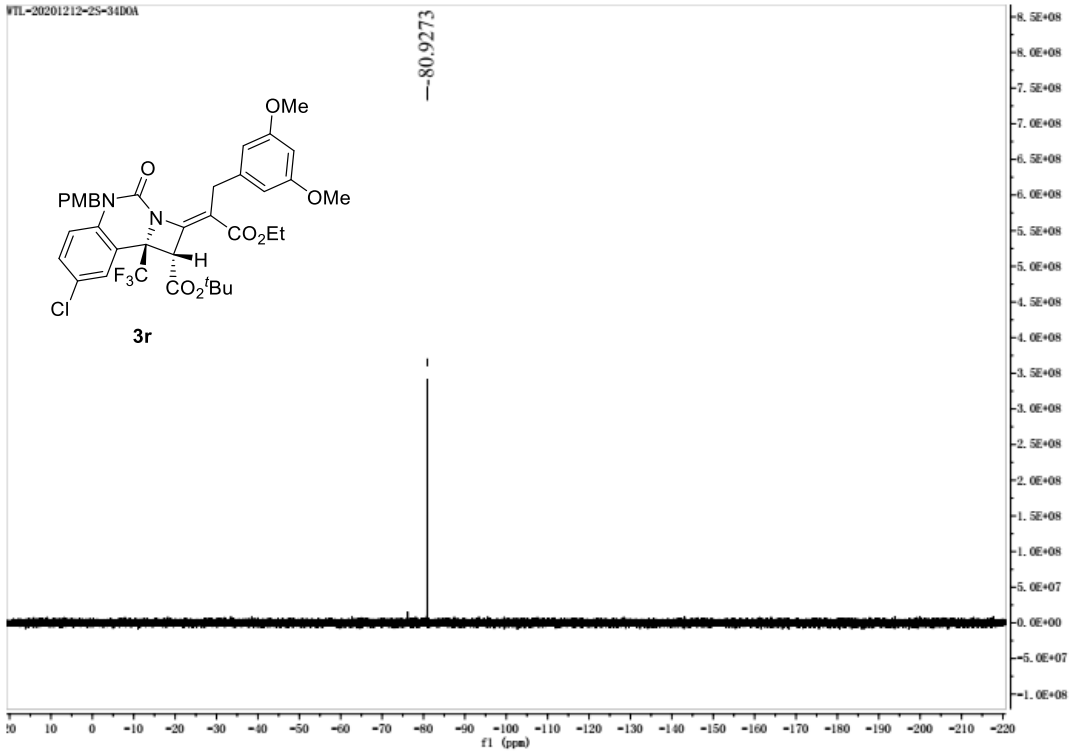

WTL-20200324-ZS-diCl
166.8452
164.4250
159.0192
151.6682
147.8759
138.1406
131.6861
131.0156
129.7190
128.9486
128.7354
127.6279
127.3078
126.4966
117.1361
114.3110
69.0060
68.6851
68.3593
68.1411
60.9764
58.0636
55.3016
47.1336
30.8806
27.7609
14.0648
Cl
Cl
O
PMBN
N
CO2Et
H
F3C
CO2tBu
Cl
3q
f1 (ppm)


WTL-20200324-ZS-diCl
80.7277
Cl
Cl
O
PMBN
N
CO2Et
H
F3C
CO2tBu
Cl
3q
f1 (ppm)

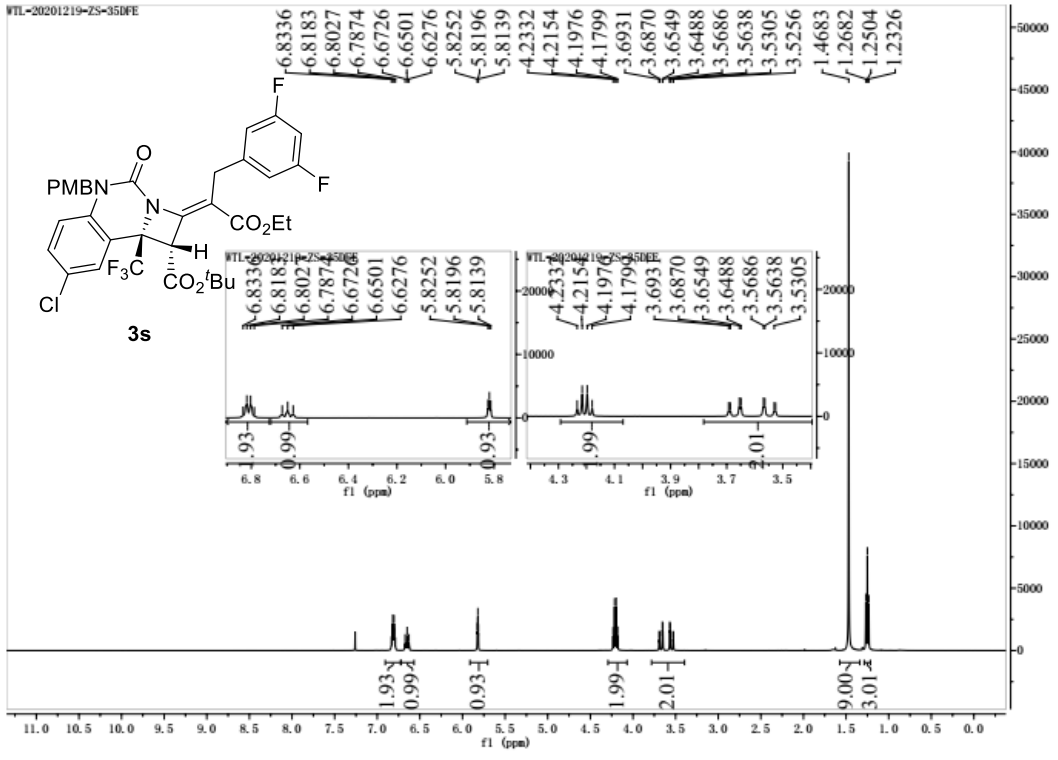
NMR of **3r** ($CDCl_3$)

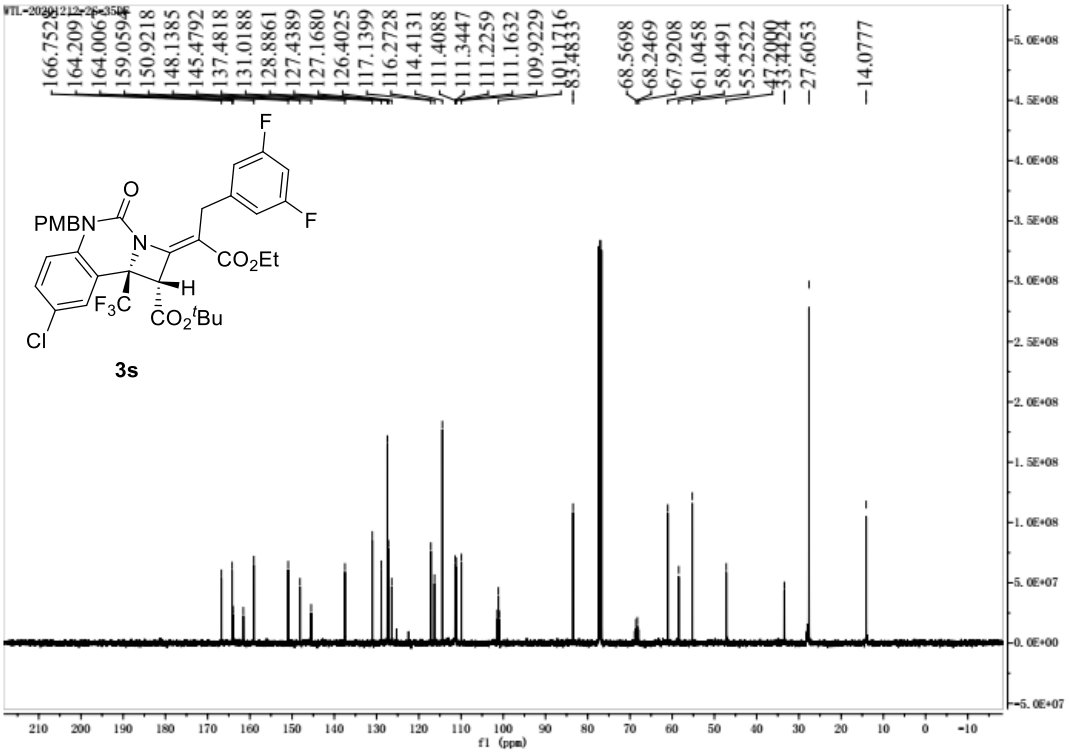


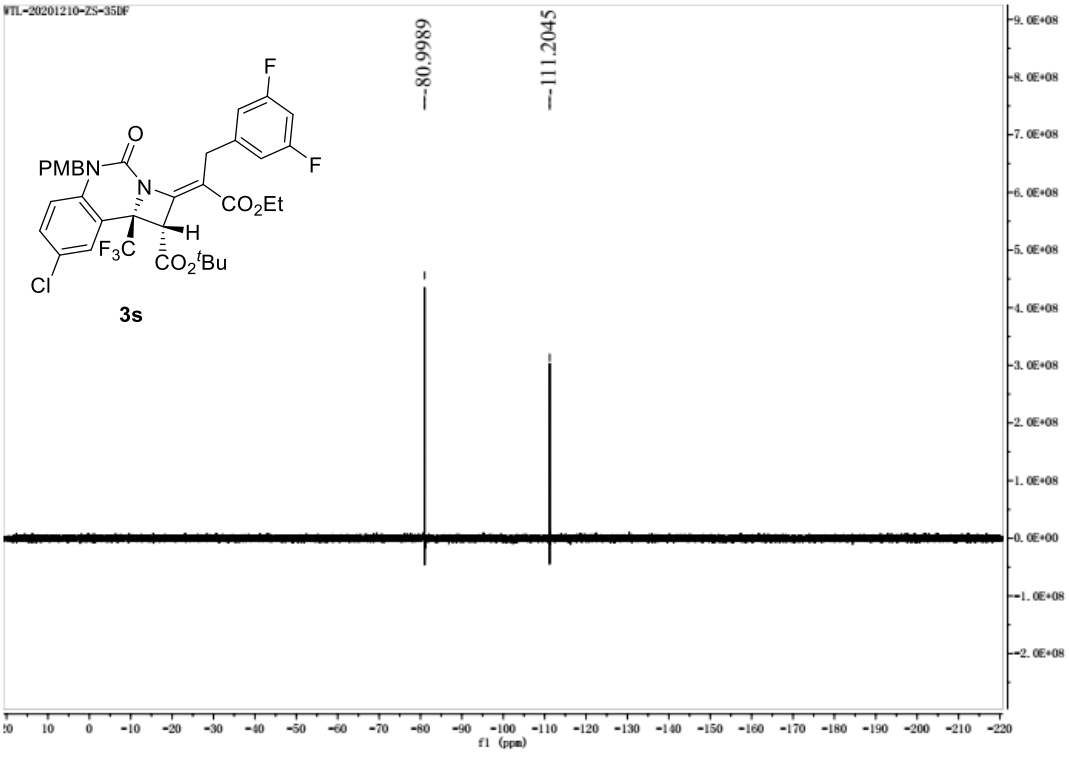




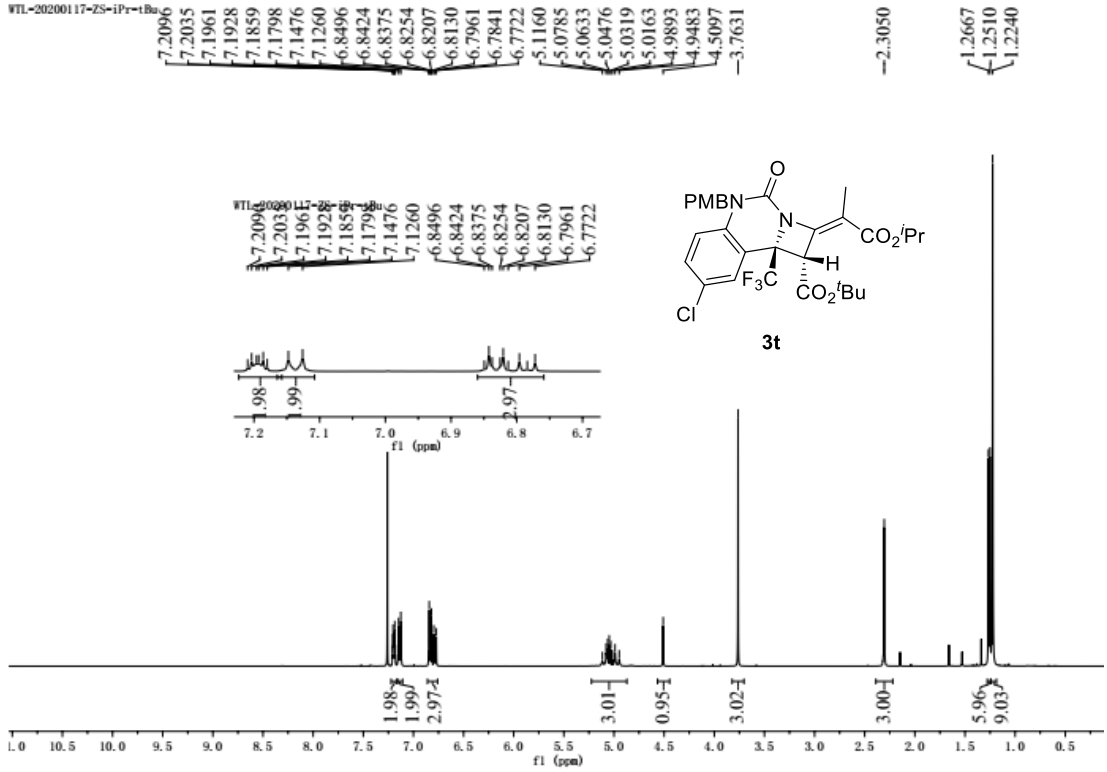
NMR of **3s** ($CDCl_3$)

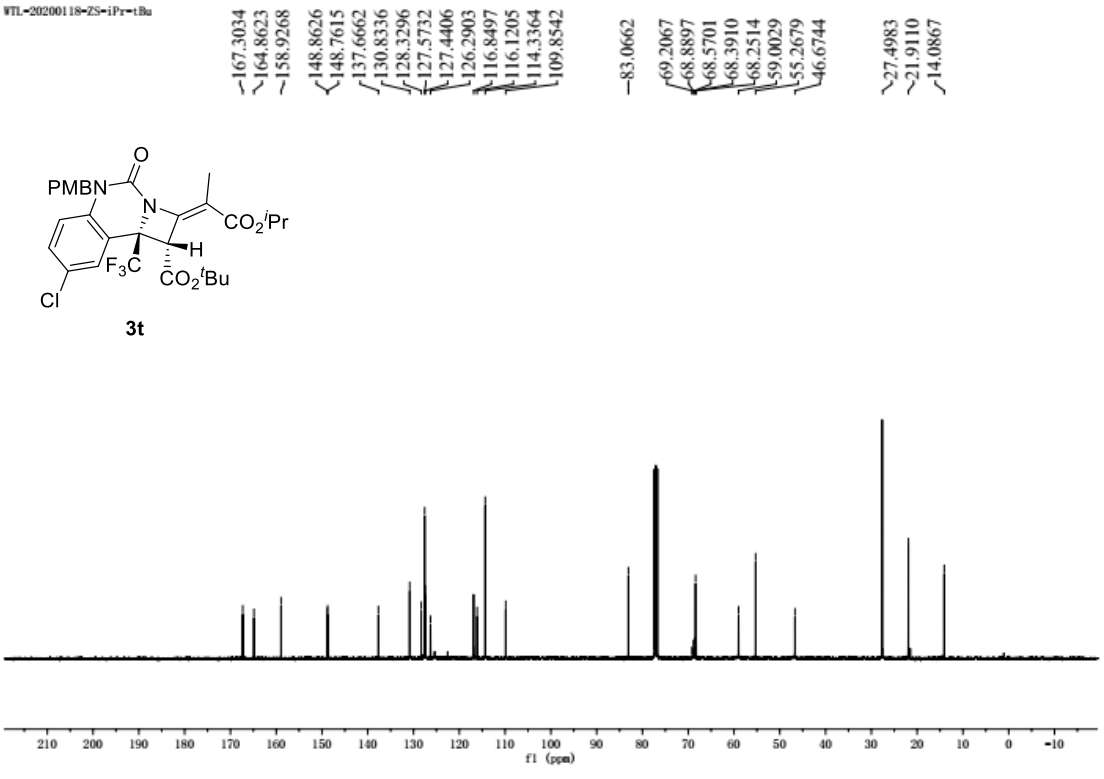


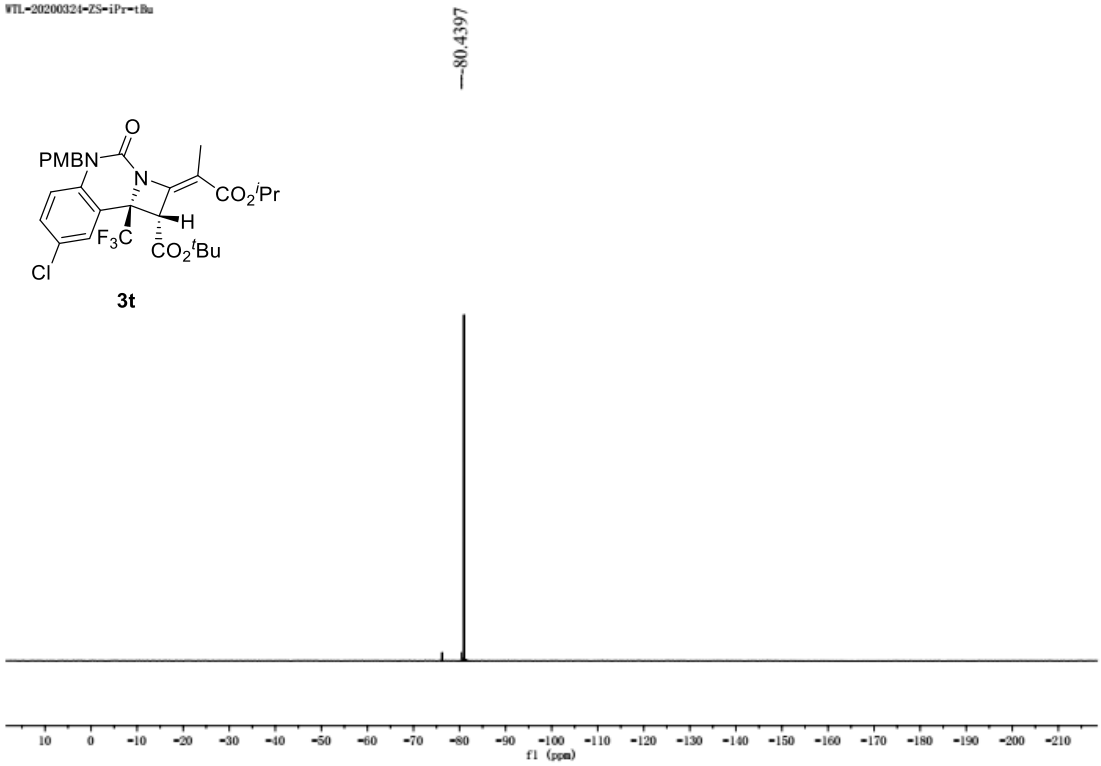

166.7521
164.2091
164.0067
159.0594
150.9218
148.1385
145.4792
137.4818
131.0188
128.8861
127.4389
127.1680
126.4025
117.1399
116.2728
114.4131
111.4088
111.3447
111.2259
111.1632
109.9229
101.1716
83.4833
68.5698
68.2469
67.9208
61.0458
58.4491
55.2522
47.2000
33.4424
27.6053
14.0777
F
F
O
PMBN
N
CO2Et
F3C
H
CO2tBu
Cl
3s
f1 (ppm)


WTL-20201210-ZS-35DF
-80.9989
-111.2045
F
F
O
PMBN
N
CO2Et
F3C
H
CO2tBu
Cl
3s
f1 (ppm)

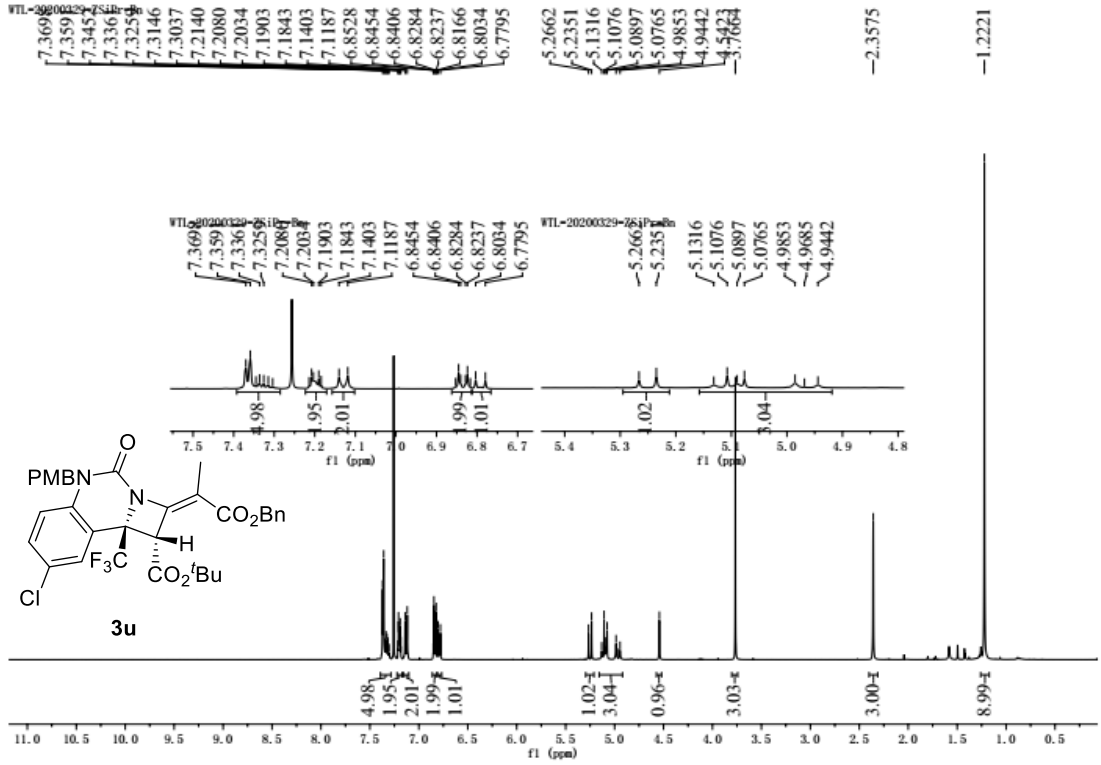
NMR of **3t** ($CDCl_3$)





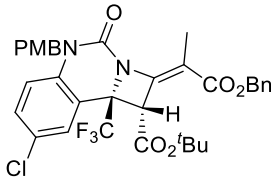


NMR of **3u** ($CDCl_3$)

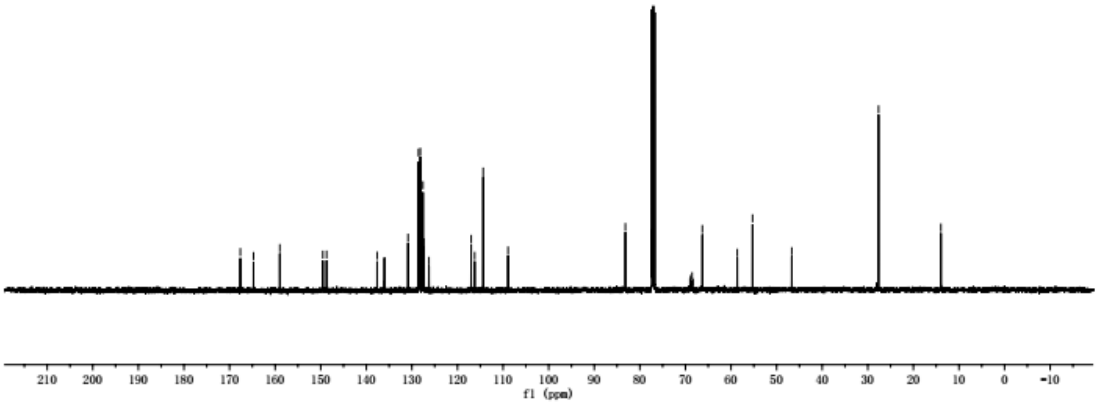


WTL-20200329-ZSiPr-Bn-C

167.6287
164.7409
158.9675
149.5276
148.7109
137.6247
130.8501
128.5541
128.3710
128.1879
128.1480
127.5699
127.3715
117.0021
116.2220
114.3711
108.9101
83.1686
68.9960
68.8631
68.5434
68.3173
66.2896
58.6369
55.2726
46.6668
27.6409
13.9564

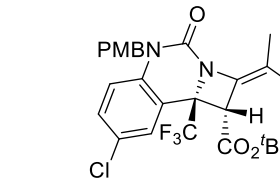


3u

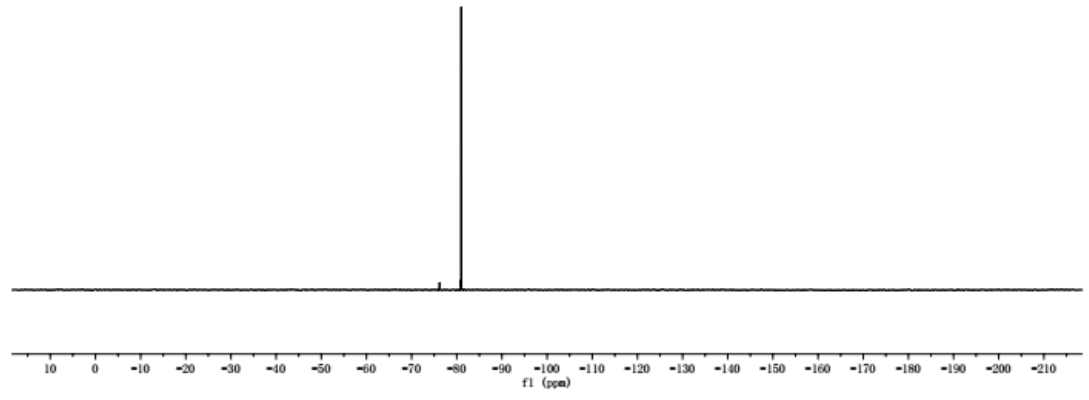


WTL-20200329-ZSiPr-Bn

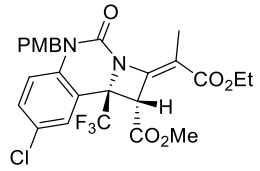
80.7212



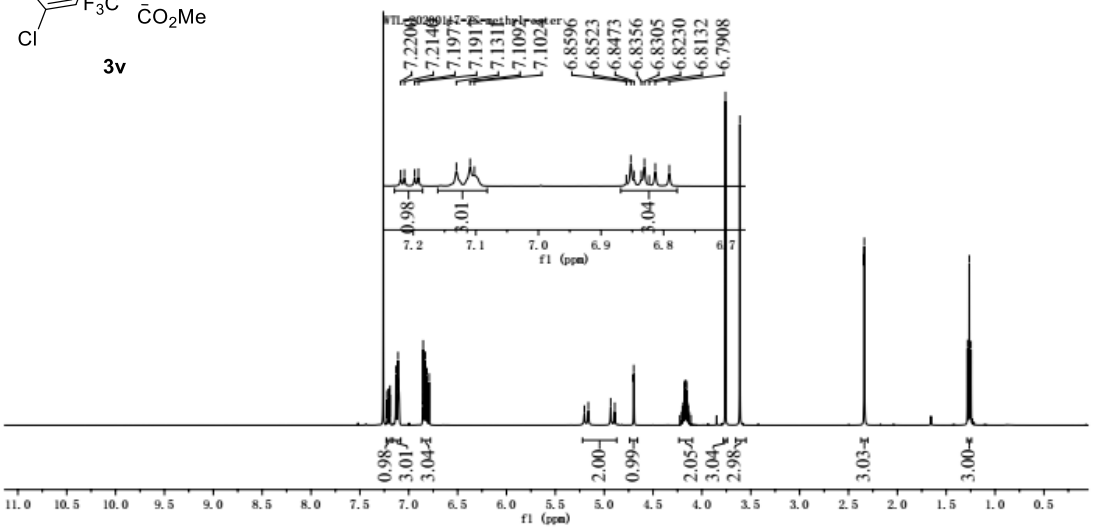
3u

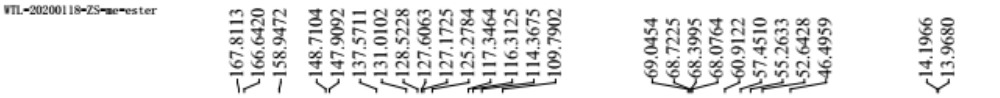


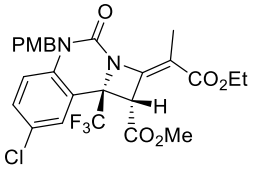
NMR of **3v** ($CDCl_3$)



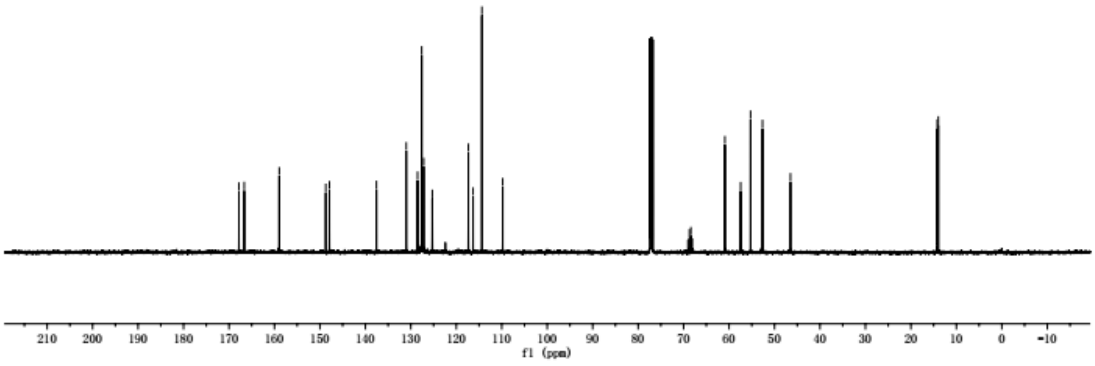
3v

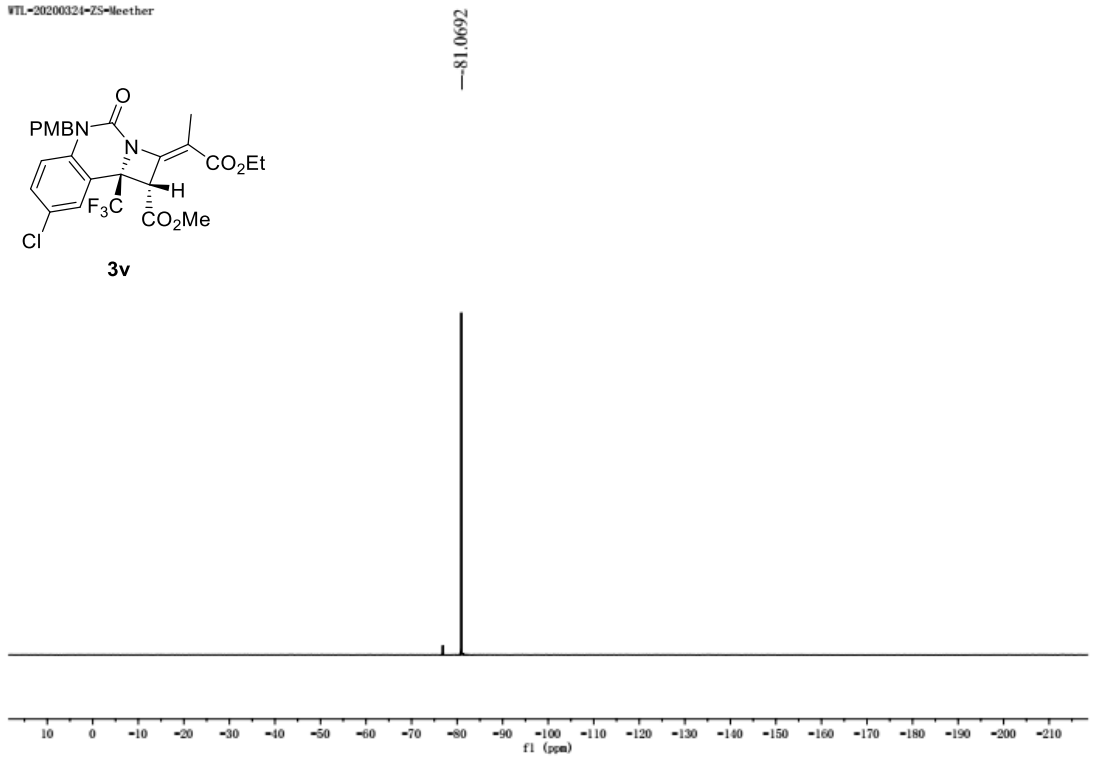




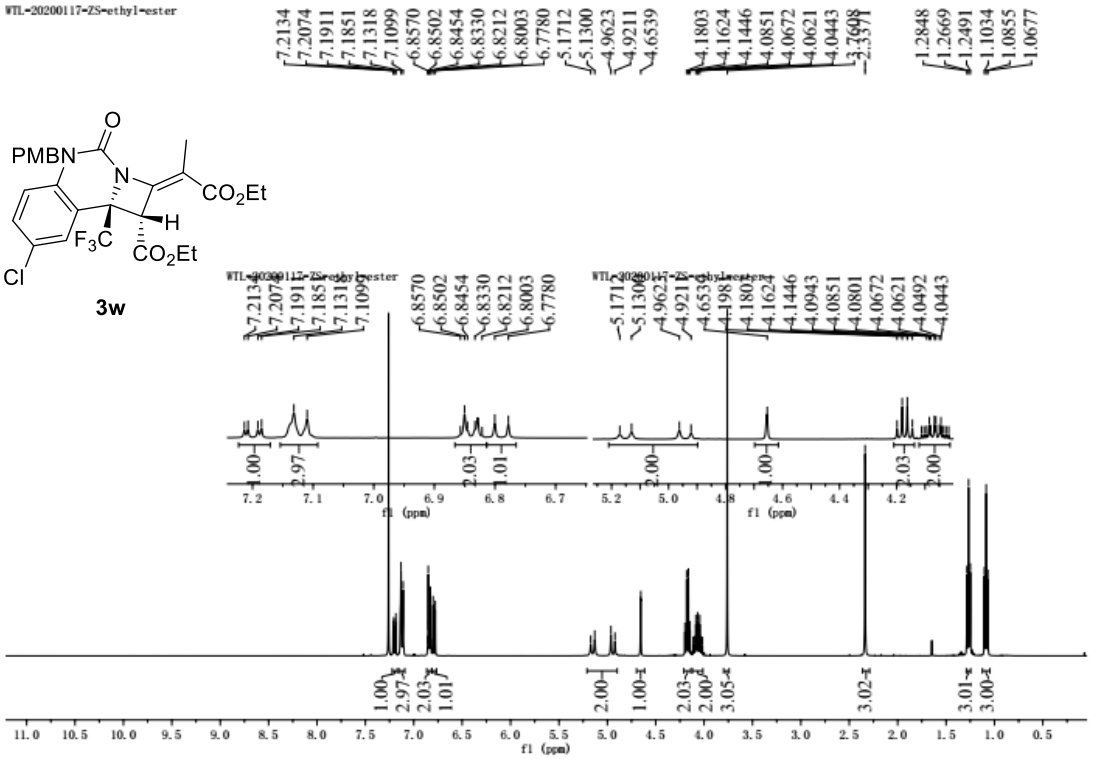


3v



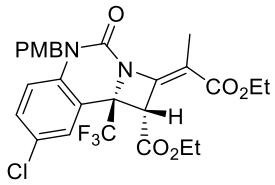


NMR of **3w** ($CDCl_3$)

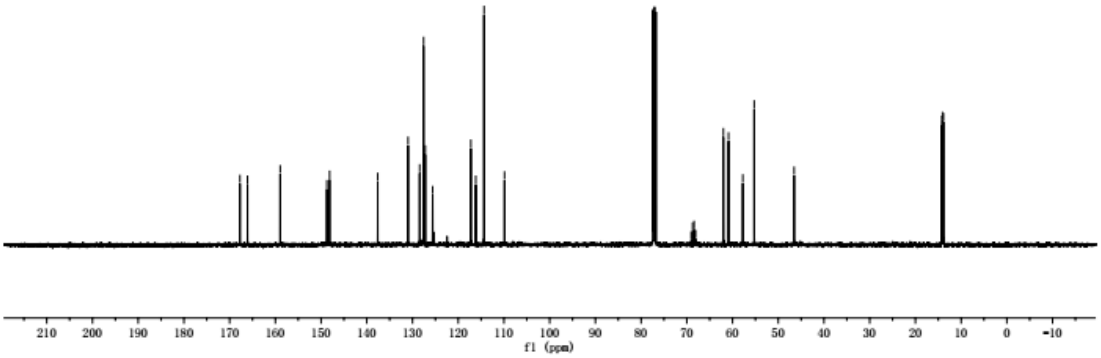


WTL-20200118-ZS-ethyl-ester

167.7442
166.0901
158.9408
148.7294
148.1342
137.6048
130.9669
128.4284
127.5707
127.2036
125.5895
117.2334
116.1682
114.3559
109.8741
69.0504
68.7295
68.4069
68.0867
62.0043
60.8732
57.7533
55.2680
46.5289
14.2166
14.0704
13.8748

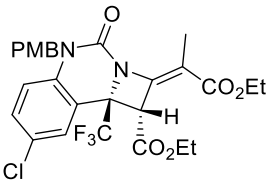


3w

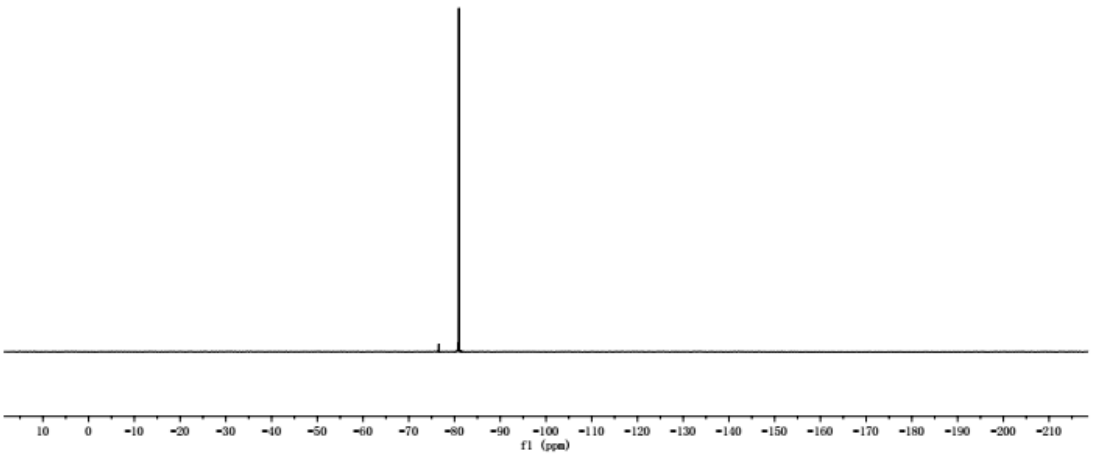


WTL-20200324-ZS-ethylether

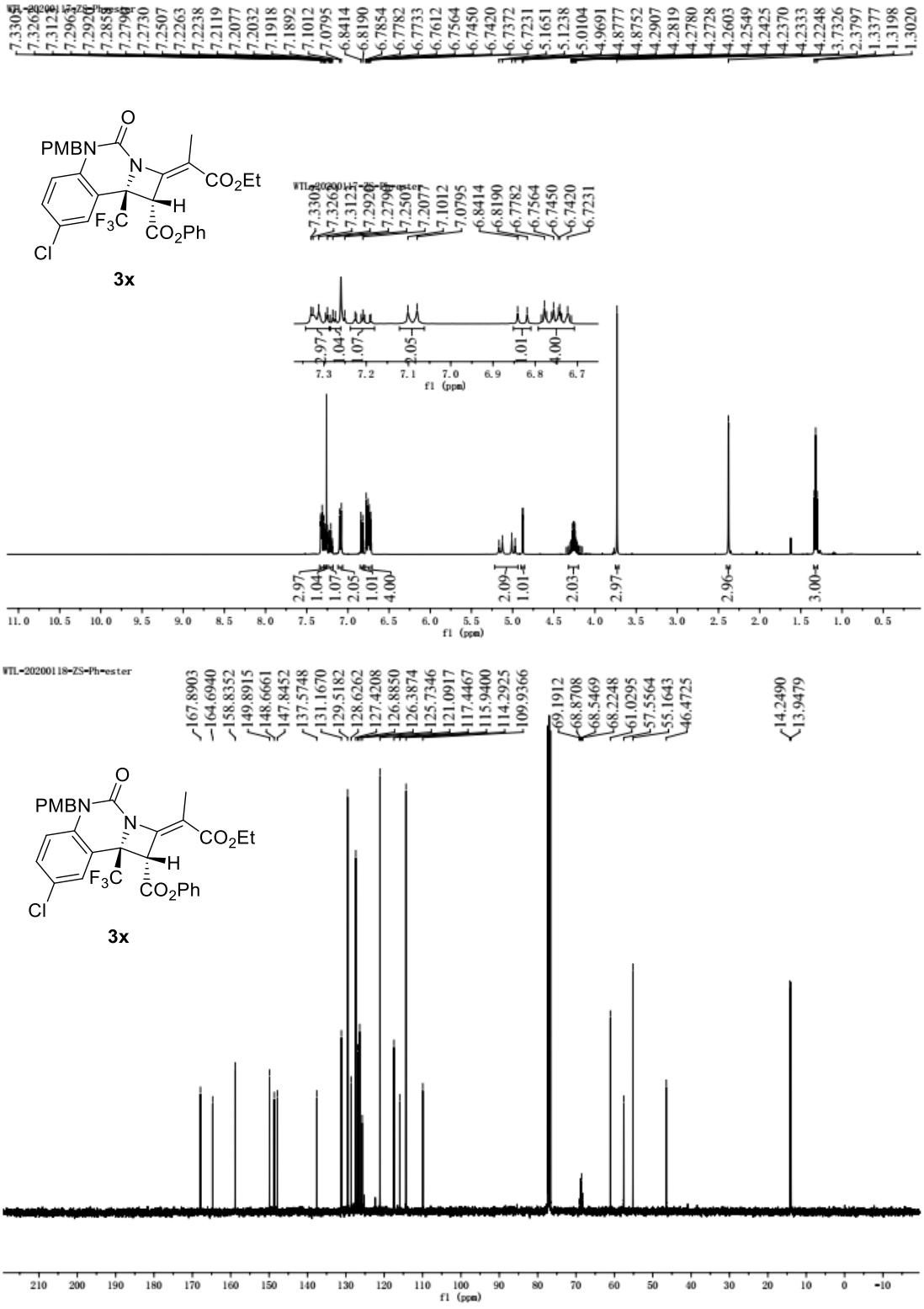
80.7184

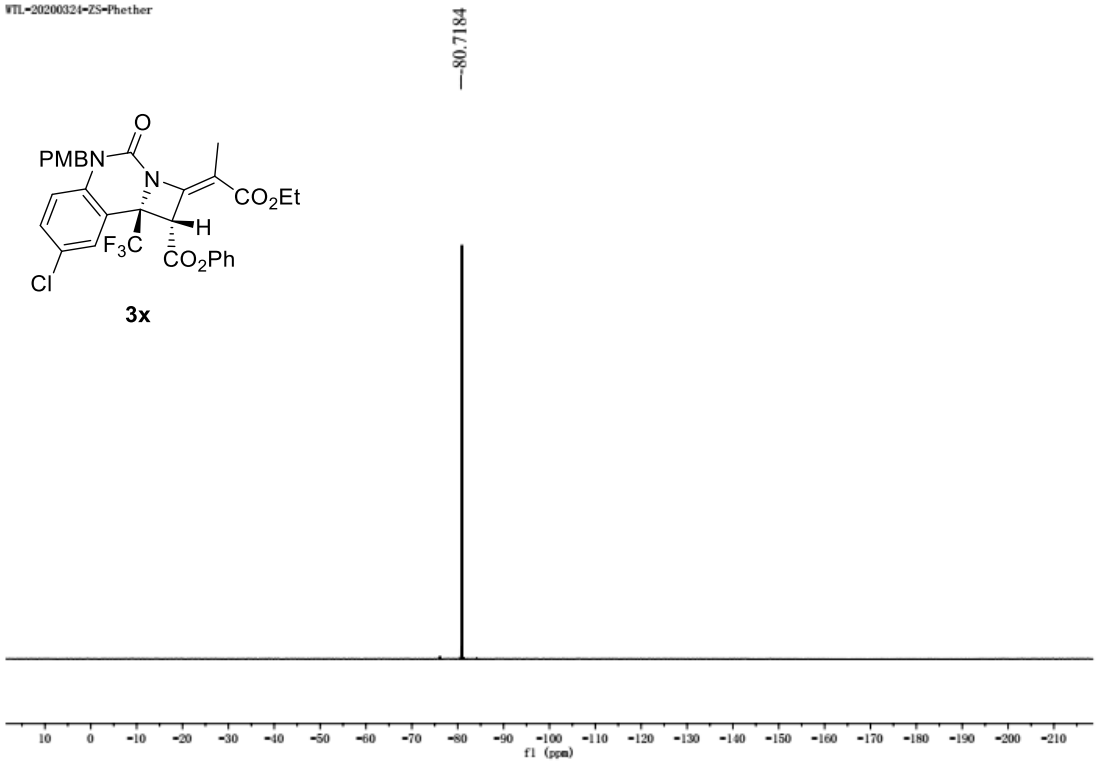


3w

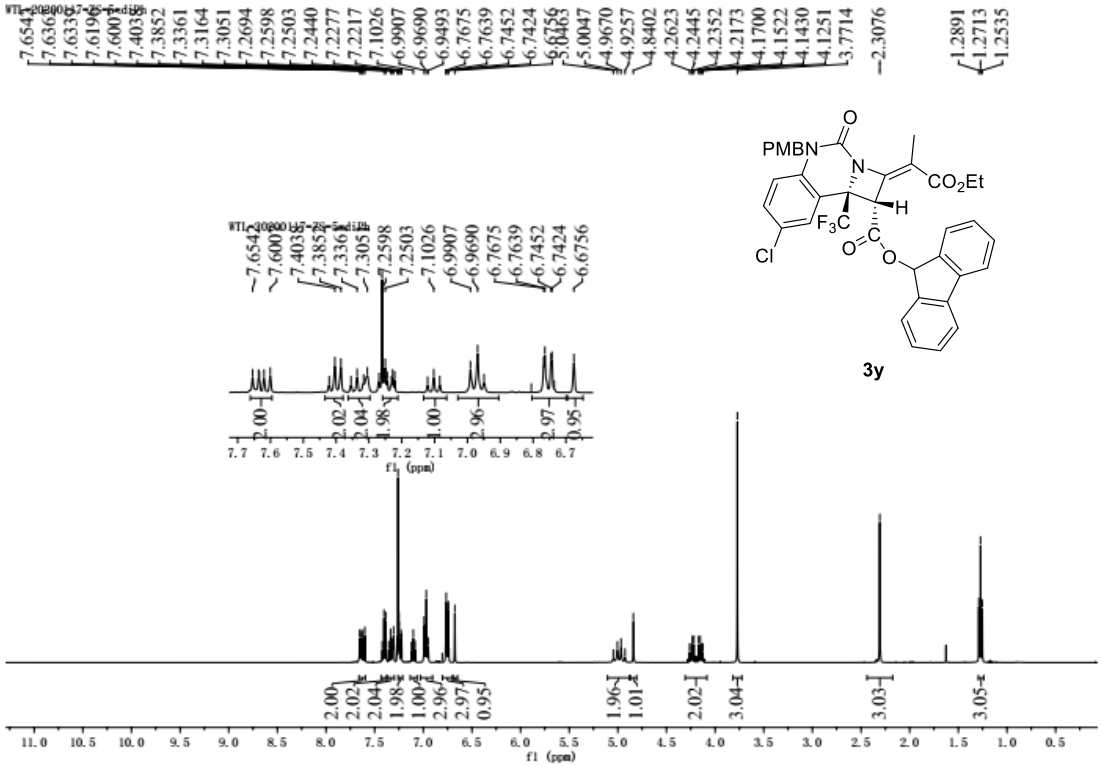


NMR of **3x** ($CDCl_3$)

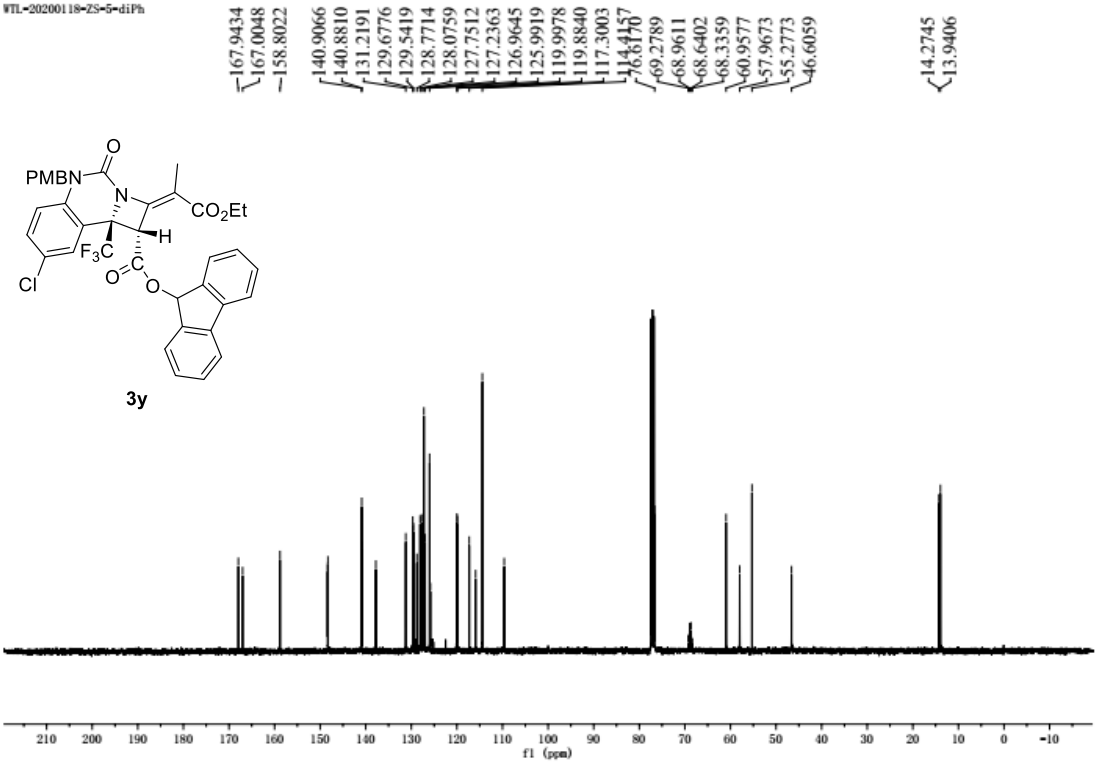




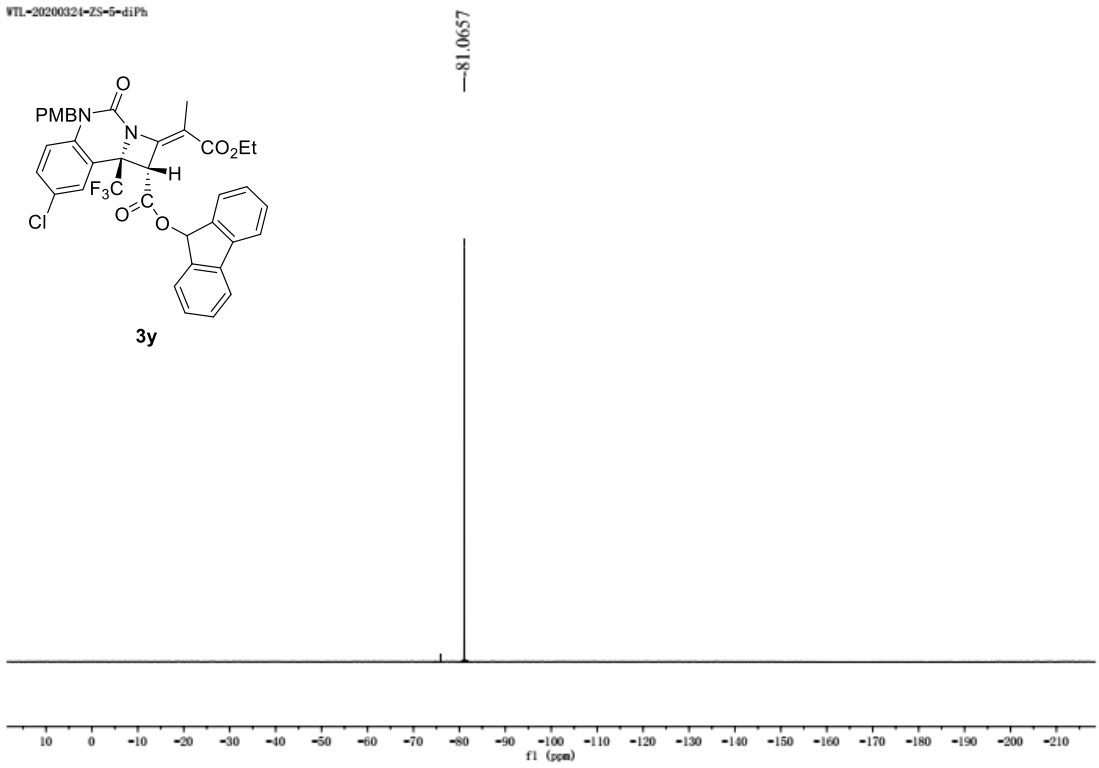
NMR of **3y** ($CDCl_3$)



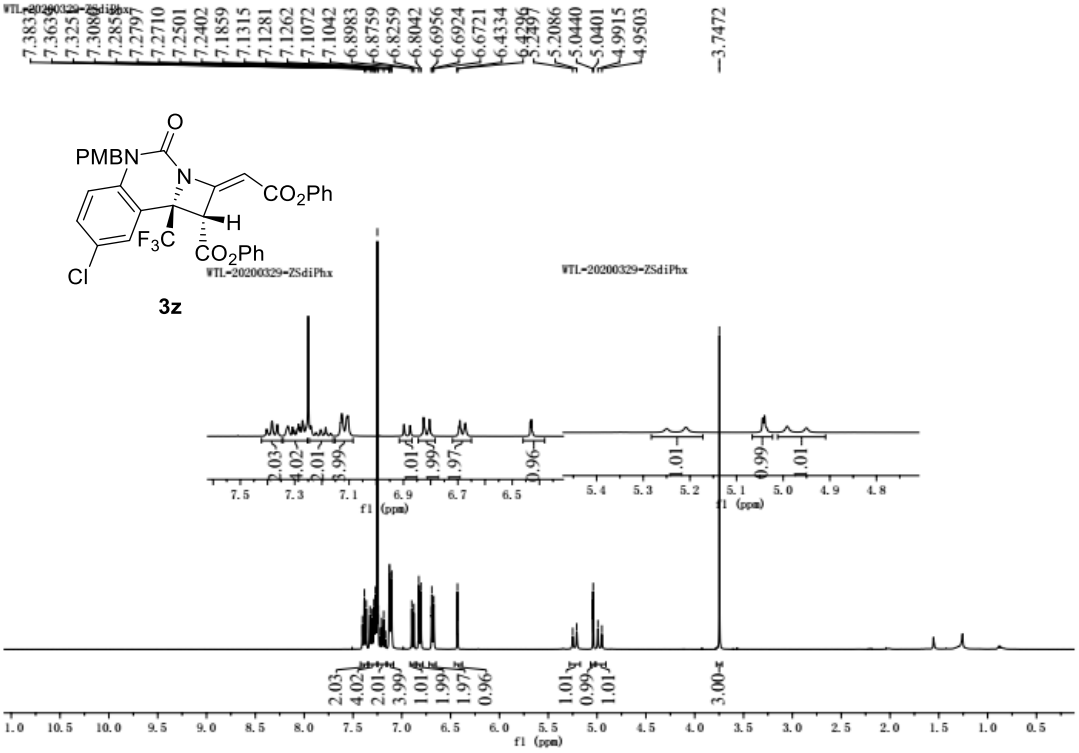
WTL-20200118-ZS-5-diPh

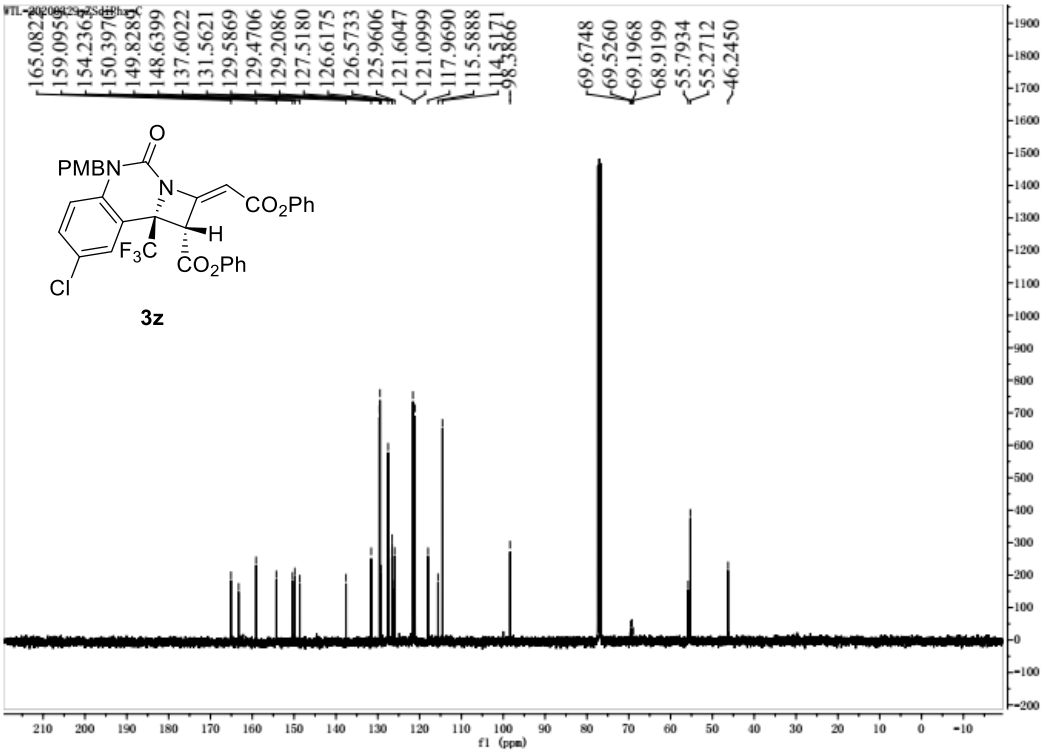


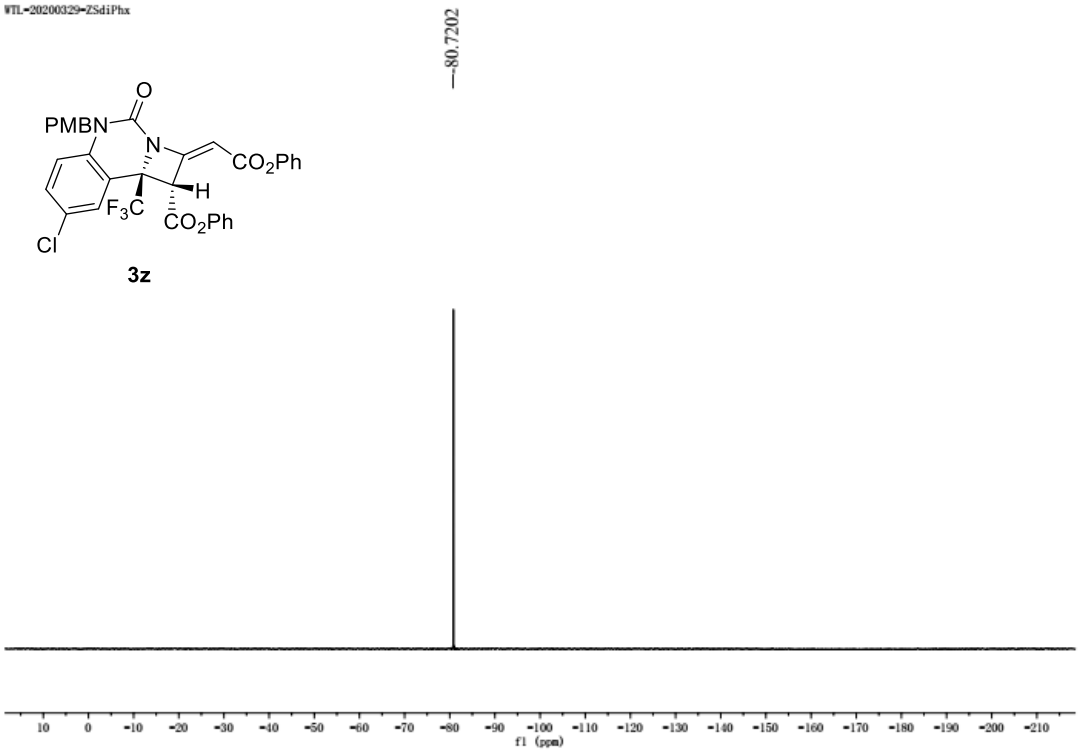
WTL-20200324-ZS-5-diPh



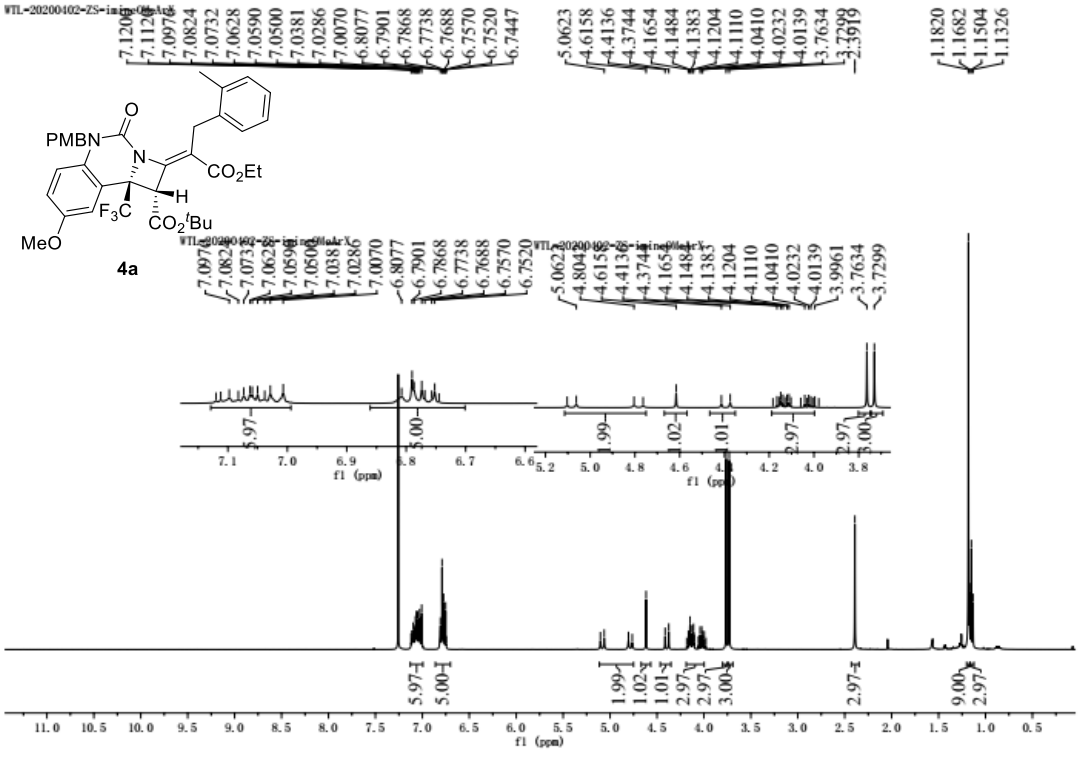
NMR of **3z** ($CDCl_3$)

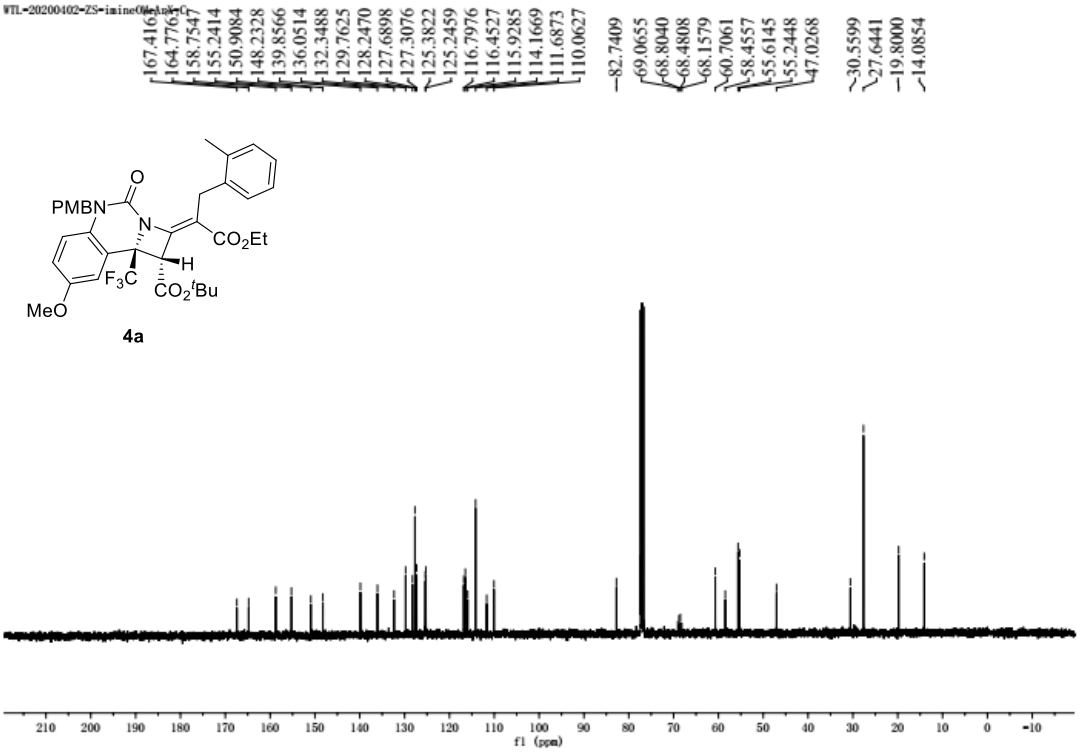


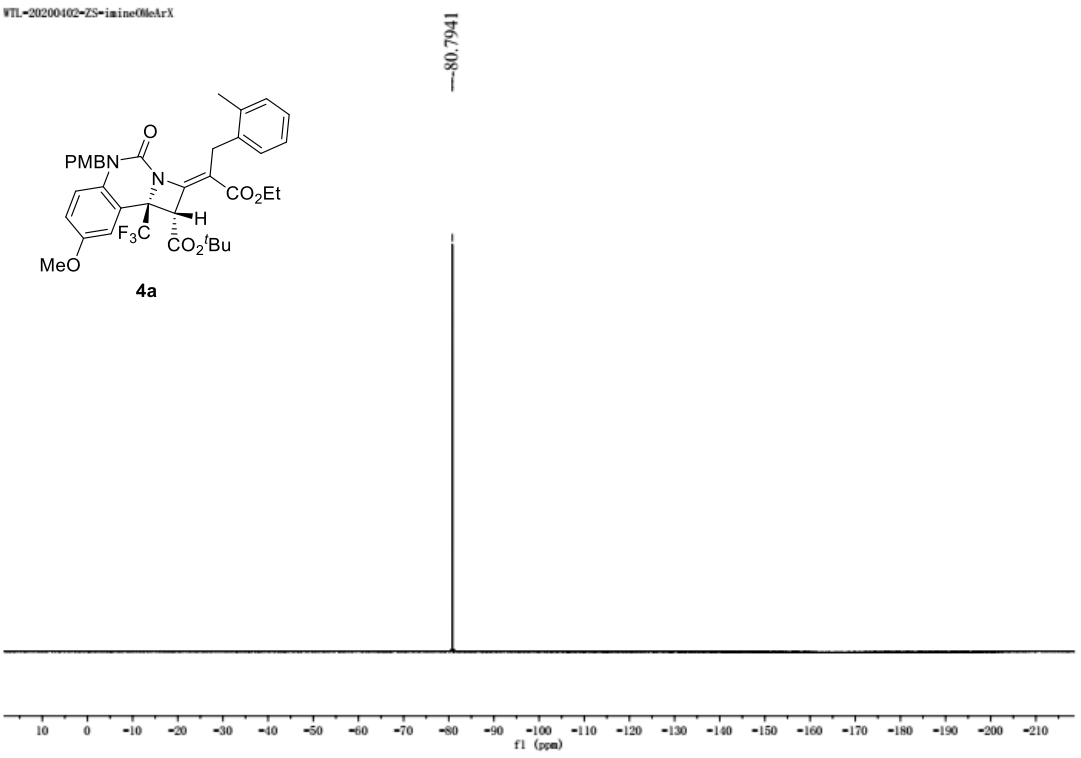




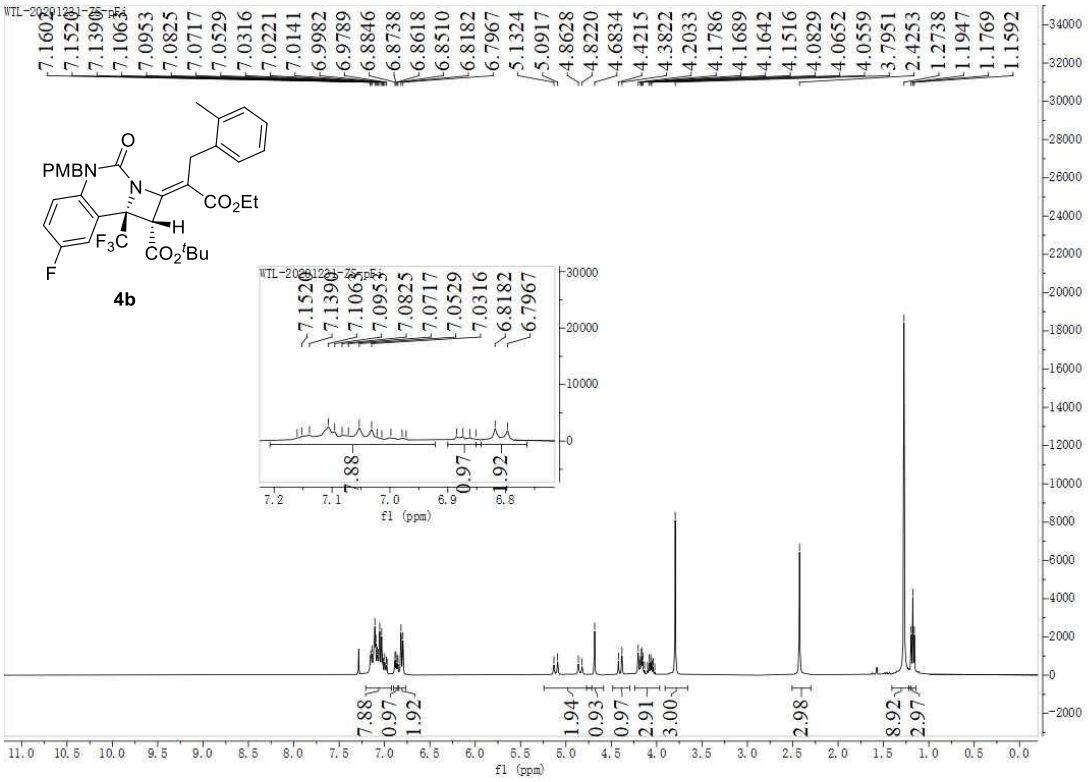
NMR of **4a** ($CDCl_3$)

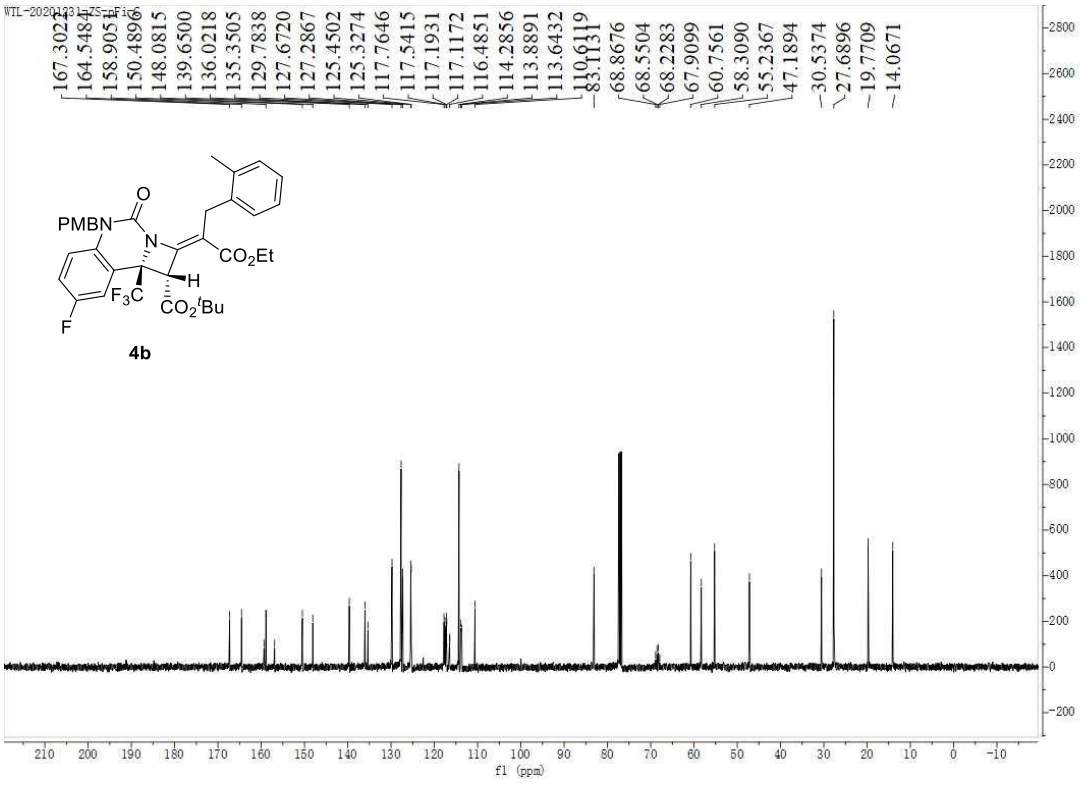


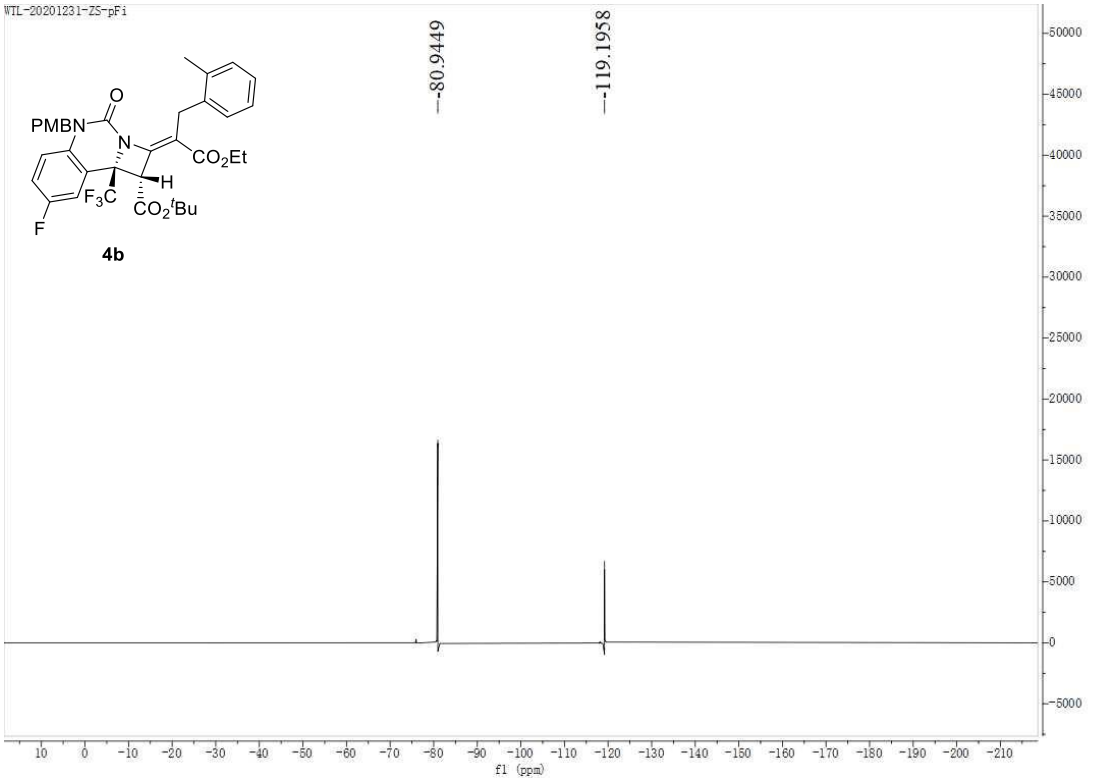

WTL-20200402-ZS-imineOMeArX-C
167.4162
164.7763
158.7547
155.2414
150.9084
148.2328
139.8566
136.0514
132.3488
129.7625
128.2470
127.6898
127.3076
125.3822
125.2459
116.7976
116.4527
115.9285
114.1669
111.6873
110.0627
82.7409
69.0655
68.8040
68.4808
68.1579
60.7061
58.4557
55.6145
55.2448
47.0268
30.5599
27.6441
19.8000
14.0854
PMBN
O
N
CO2Et
H
F3C
CO2tBu
MeO
4a
f1 (ppm)


WTL-20200402-ZS-imineOMeArX
80.7941
PMBN
O
N
CO2Et
H
F3C
CO2tBu
MeO
4a
f1 (ppm)

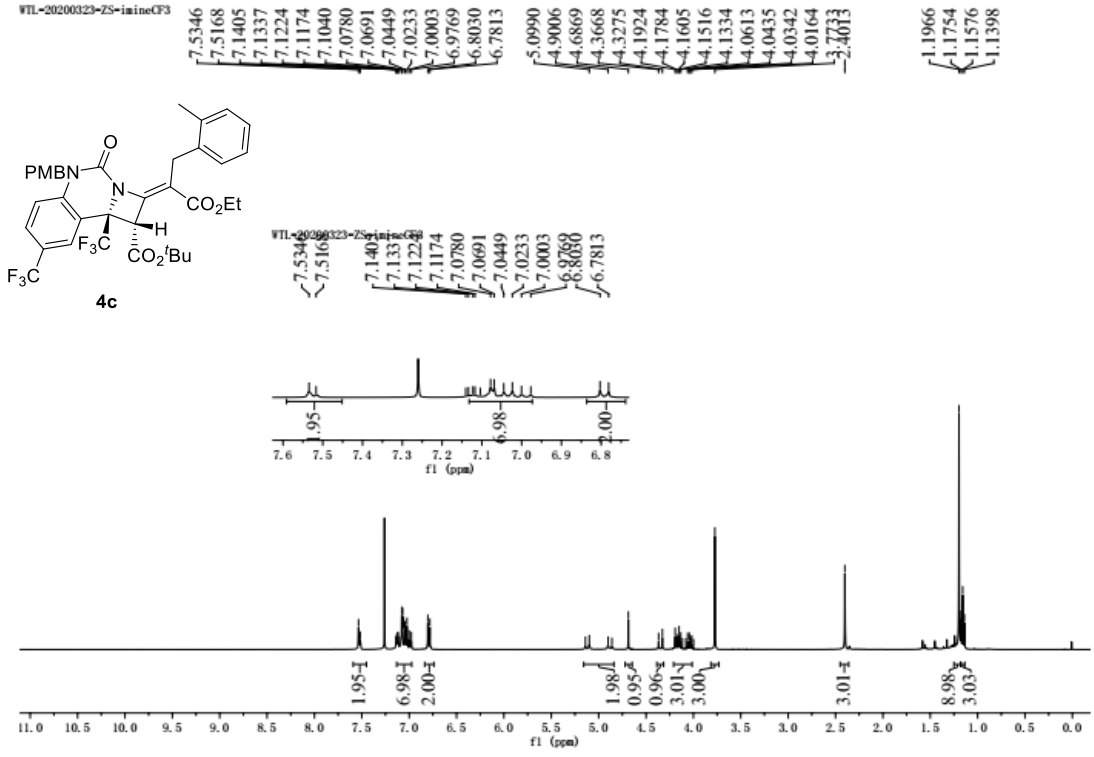
NMR of **4b** ($CDCl_3$)

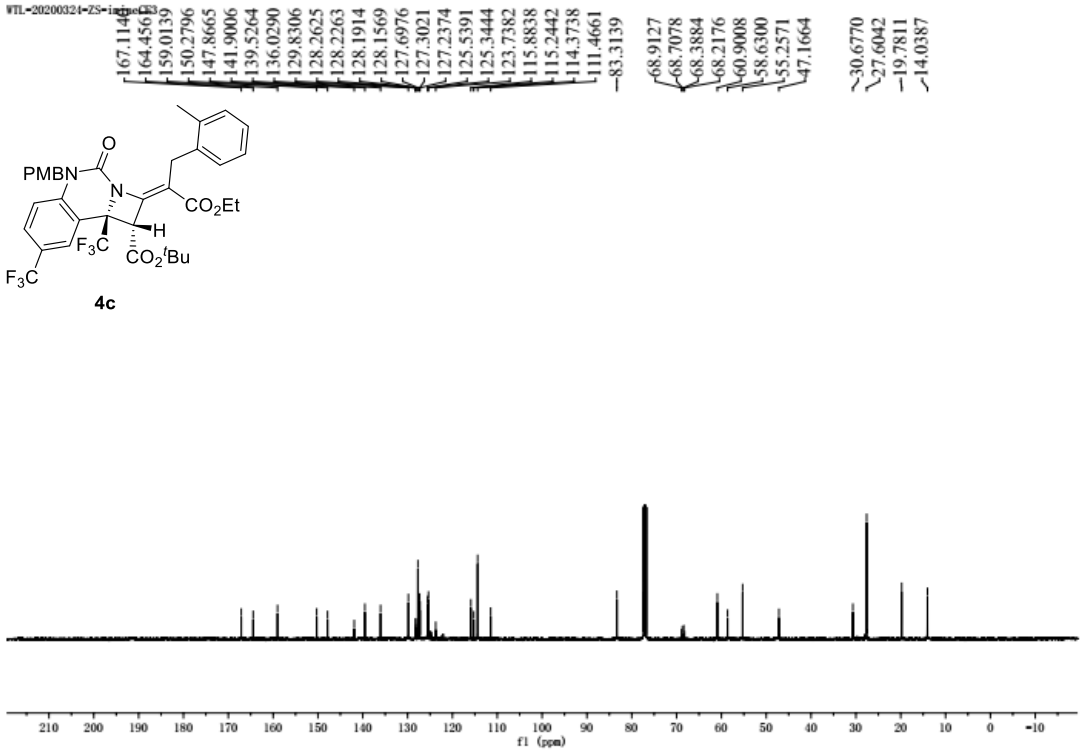


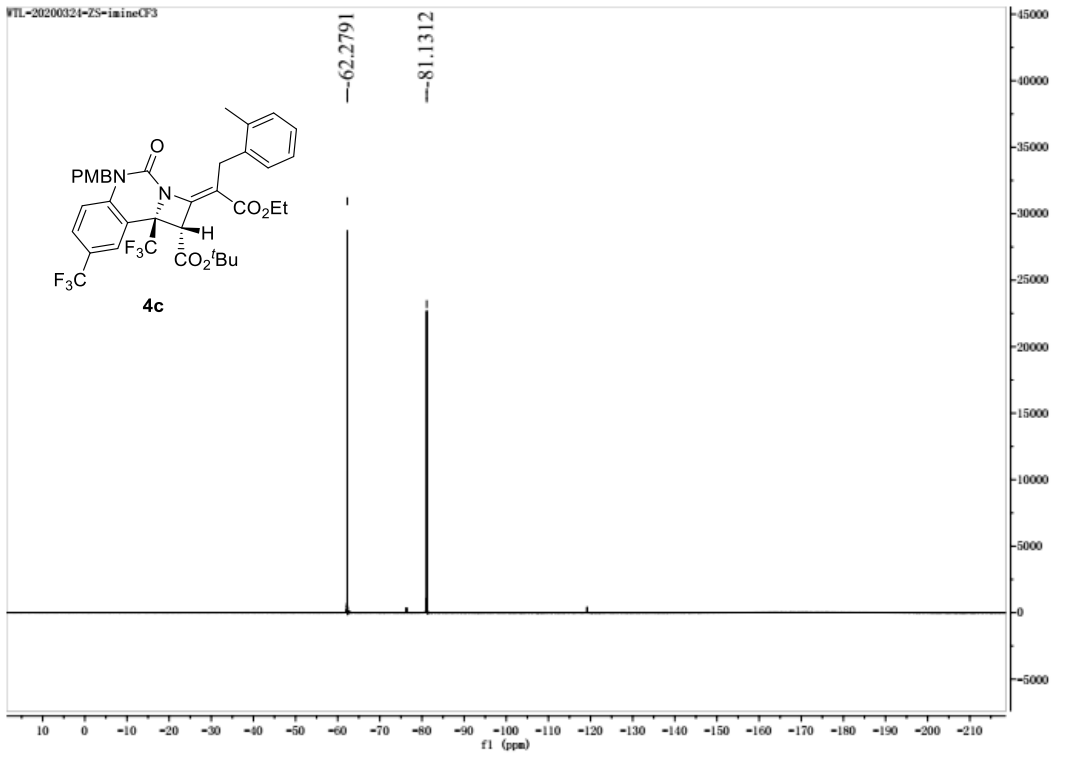




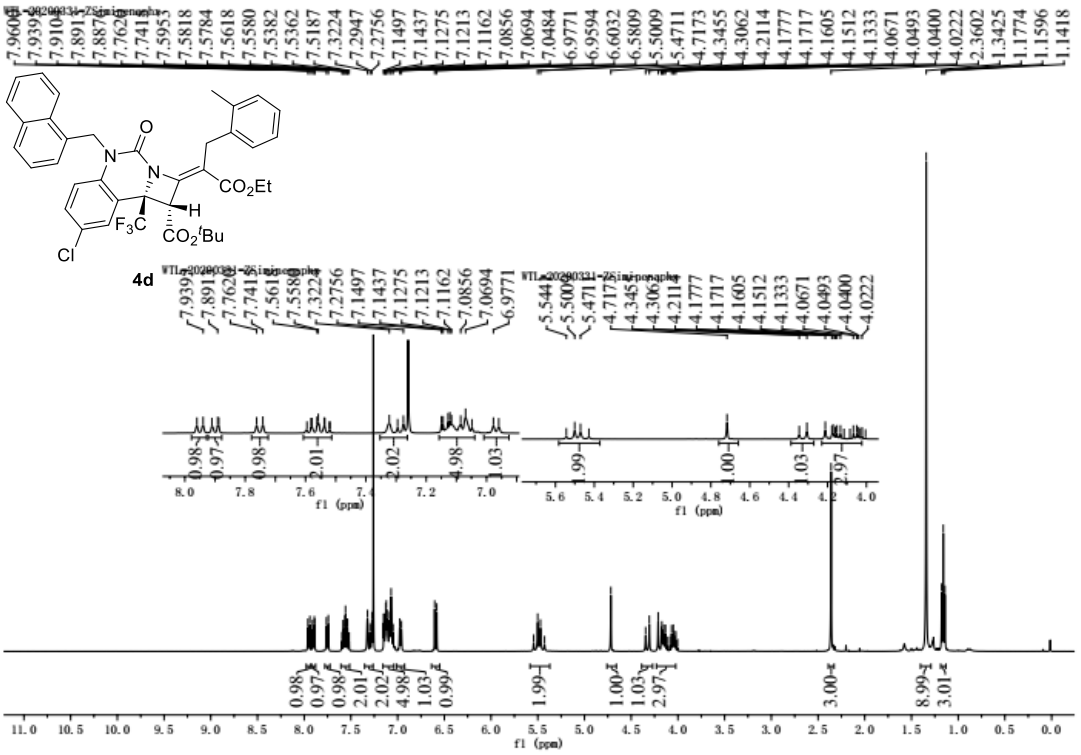
NMR of **4c** ($CDCl_3$)

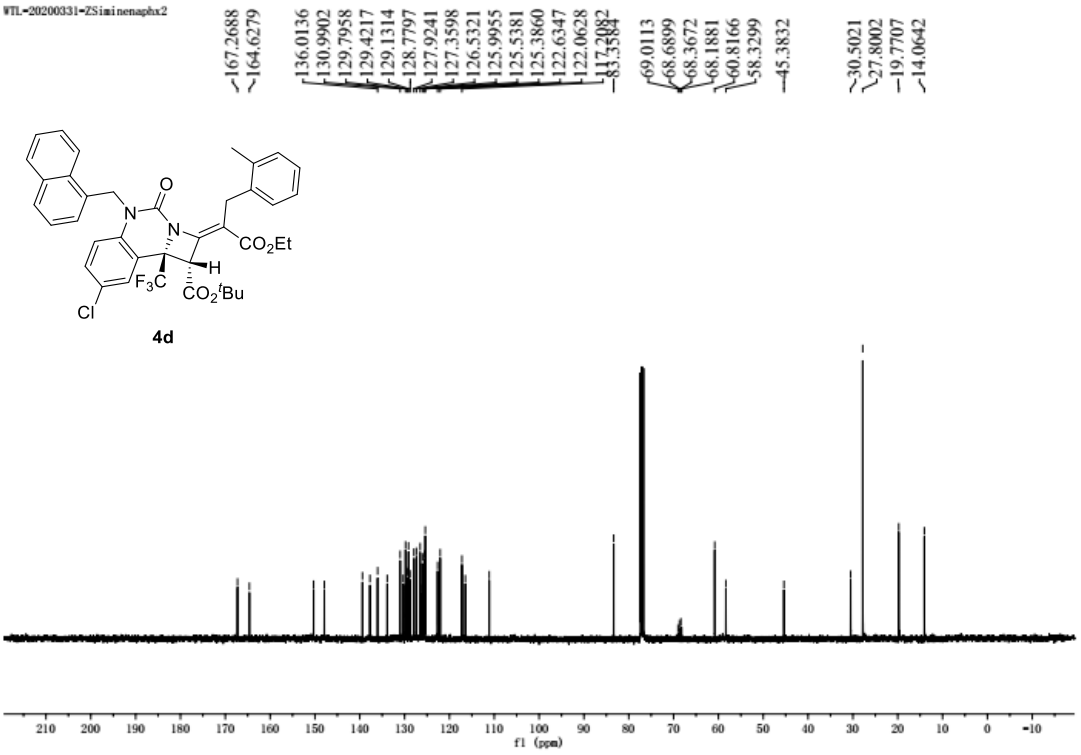


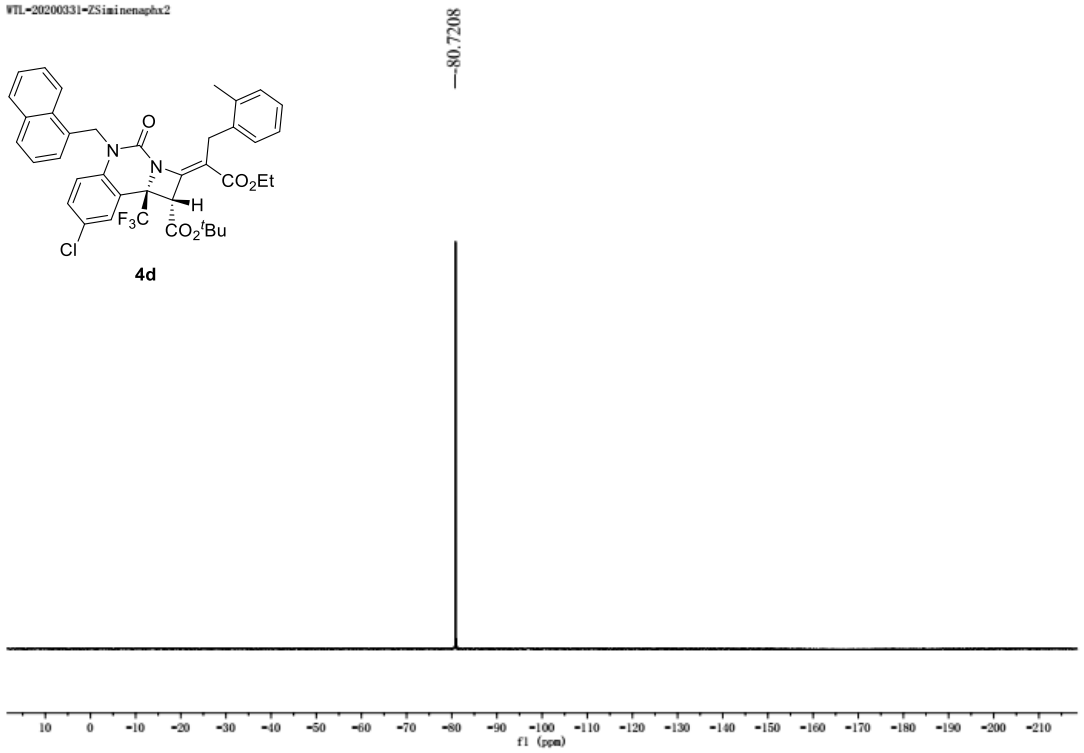

WTL-20200324-ZS-imineCF3
167.1140
164.4567
159.0139
150.2796
147.8665
141.9006
139.5264
136.0290
129.8306
128.2625
128.2263
128.1914
128.1569
127.6976
127.3021
127.2374
125.5391
125.3444
123.7382
115.8838
115.2442
114.3738
111.4661
83.3139
68.9127
68.7078
68.3884
68.2176
60.9008
58.6300
55.2571
47.1664
30.6770
27.6042
19.7811
14.0387
PMBN
O
N
CO2Et
F3C
H
CO2tBu
F3C
4c
f1 (ppm)


WTL-20200324-ZS-imineCF3
-62.2791
-81.1312
PMBN
O
N
CO2Et
F3C
H
CO2tBu
F3C
4c
f1 (ppm)

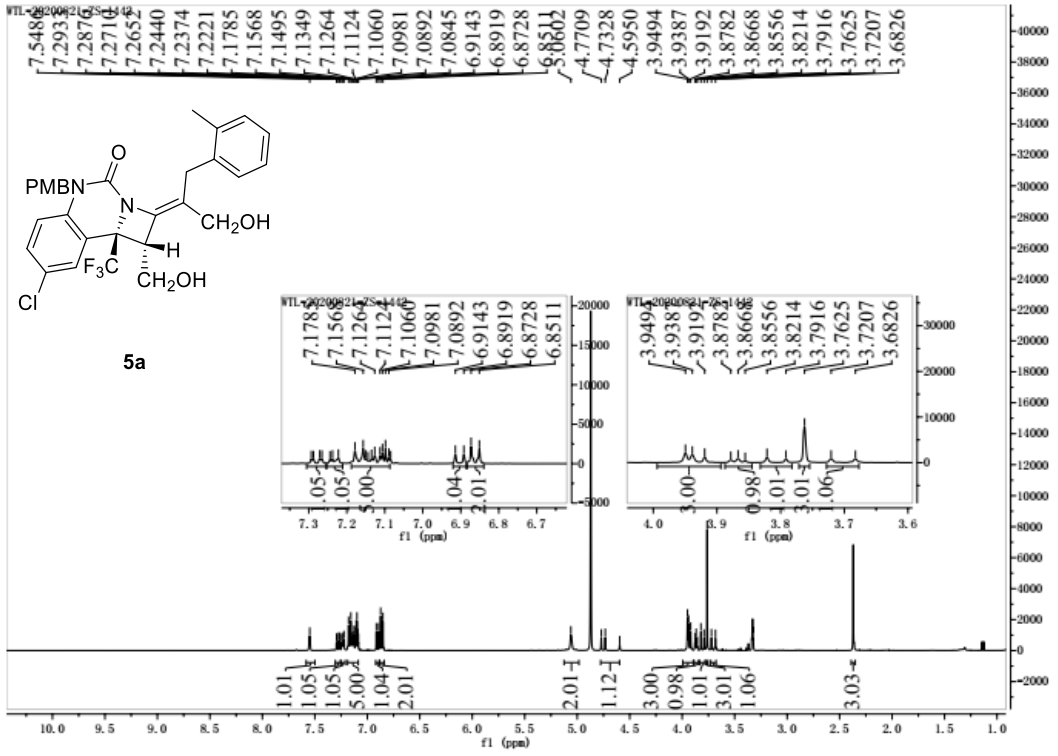
NMR of **4d** ($CDCl_3$)

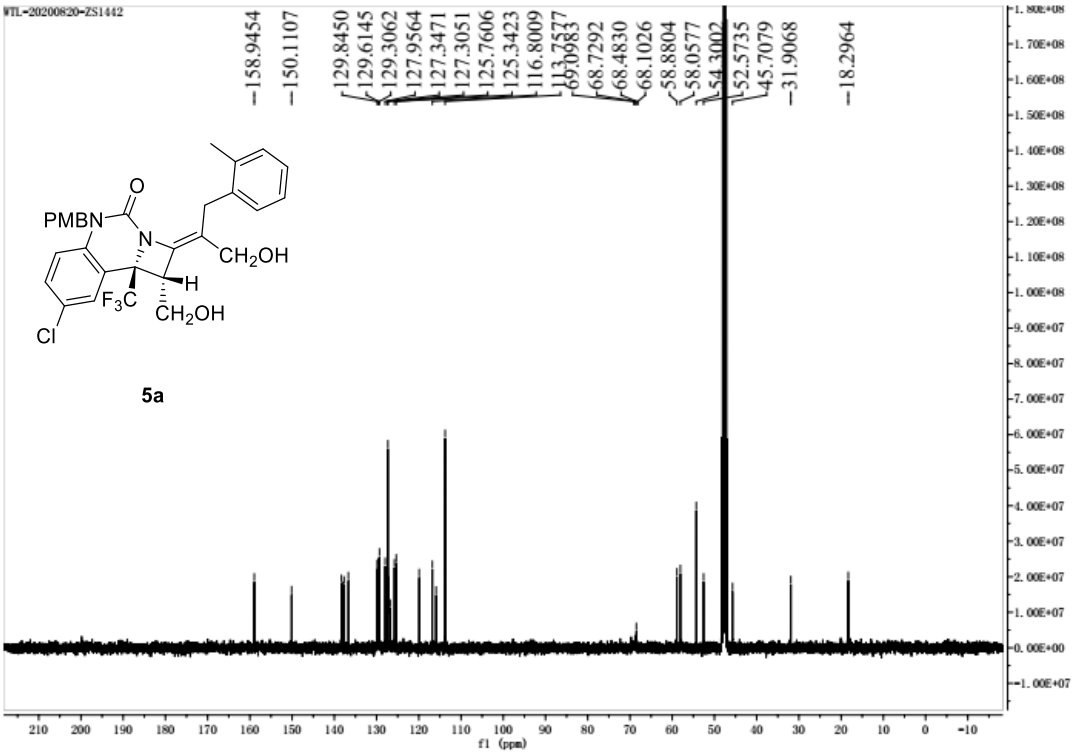


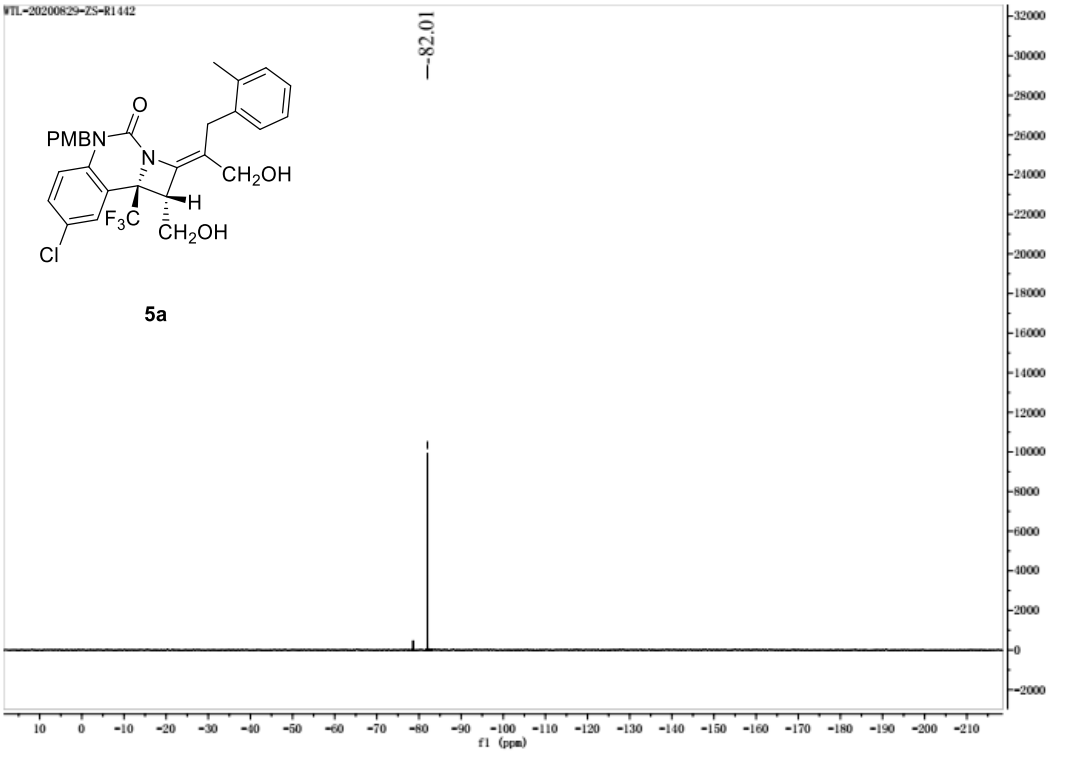




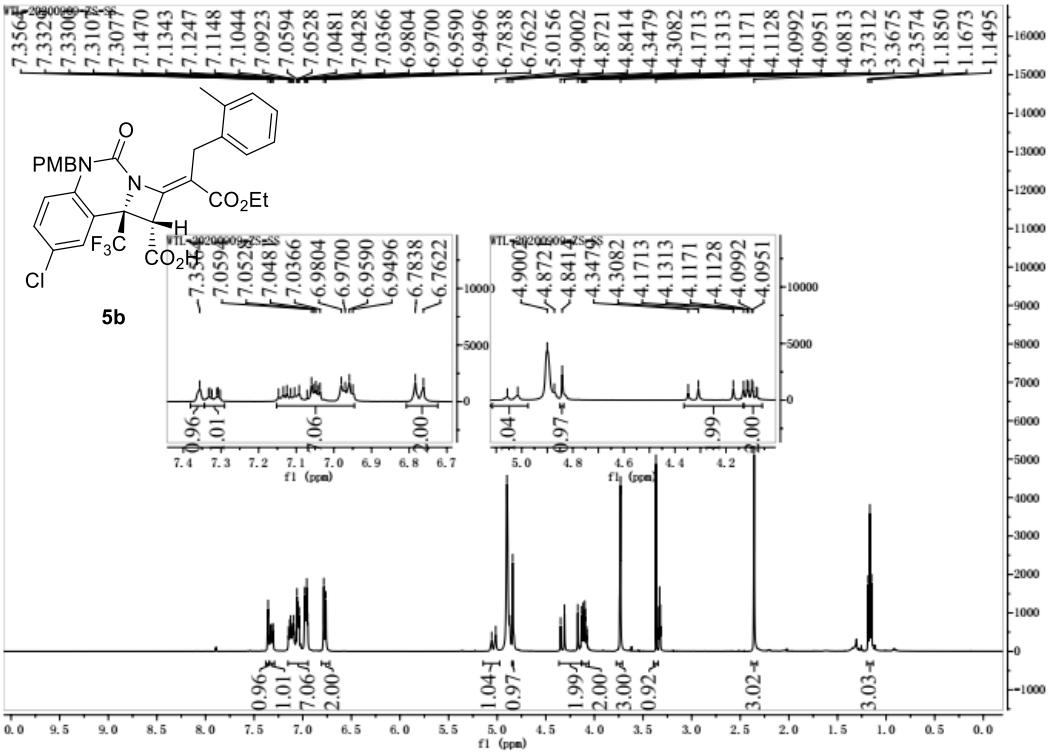
NMR of **5a**(CD_3OD)

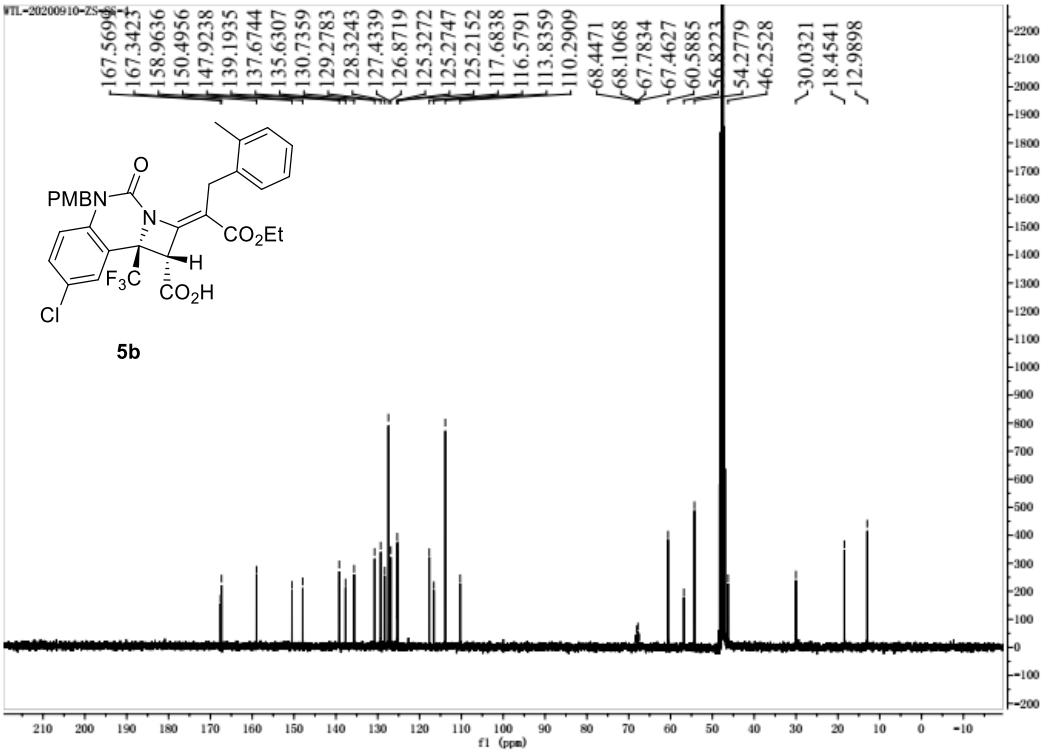


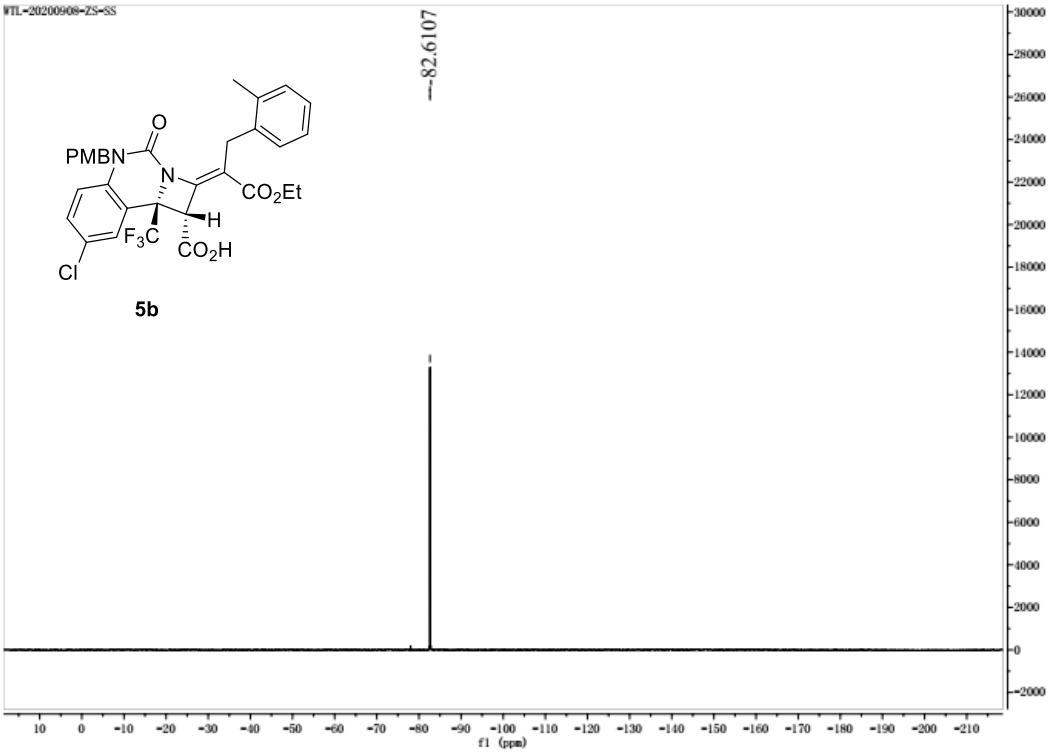

WTL-20200820-ZS1442
158.9454
150.1107
129.8450
129.6145
129.3062
127.9564
127.3471
127.3051
125.7606
125.3423
116.8009
113.7577
69.0983
68.7292
68.4830
68.1026
58.8804
58.0577
54.3002
52.5735
45.7079
31.9068
18.2964
PMBN
O
N
CH2OH
H
F3C
CH2OH
Cl
5a
f1 (ppm)


WTL-20200829-ZS-R1442
82.01
PMBN
O
N
CH2OH
H
F3C
CH2OH
Cl
5a
f1 (ppm)

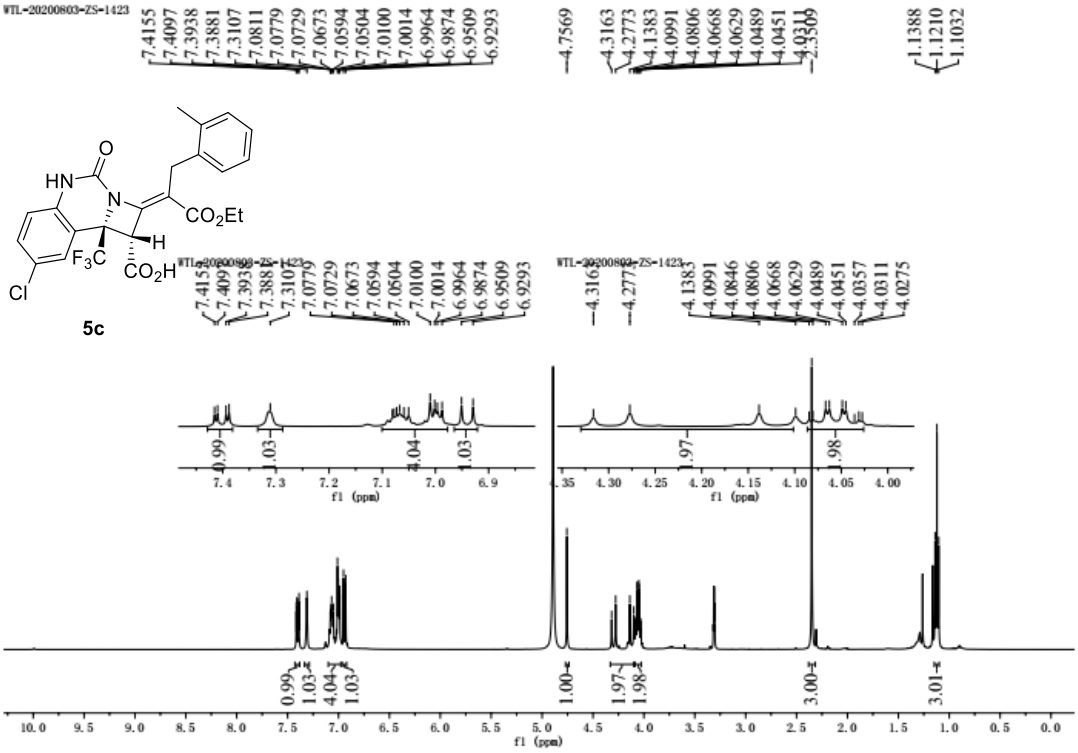
NMR of **5b** (CD_3OD)

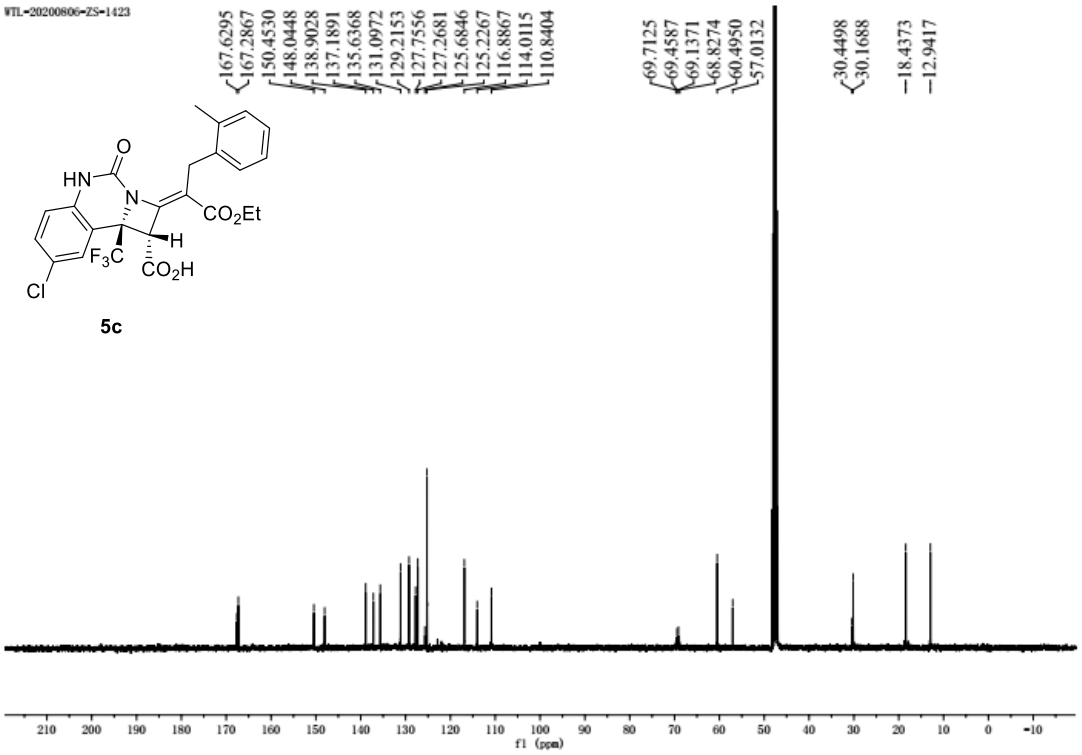




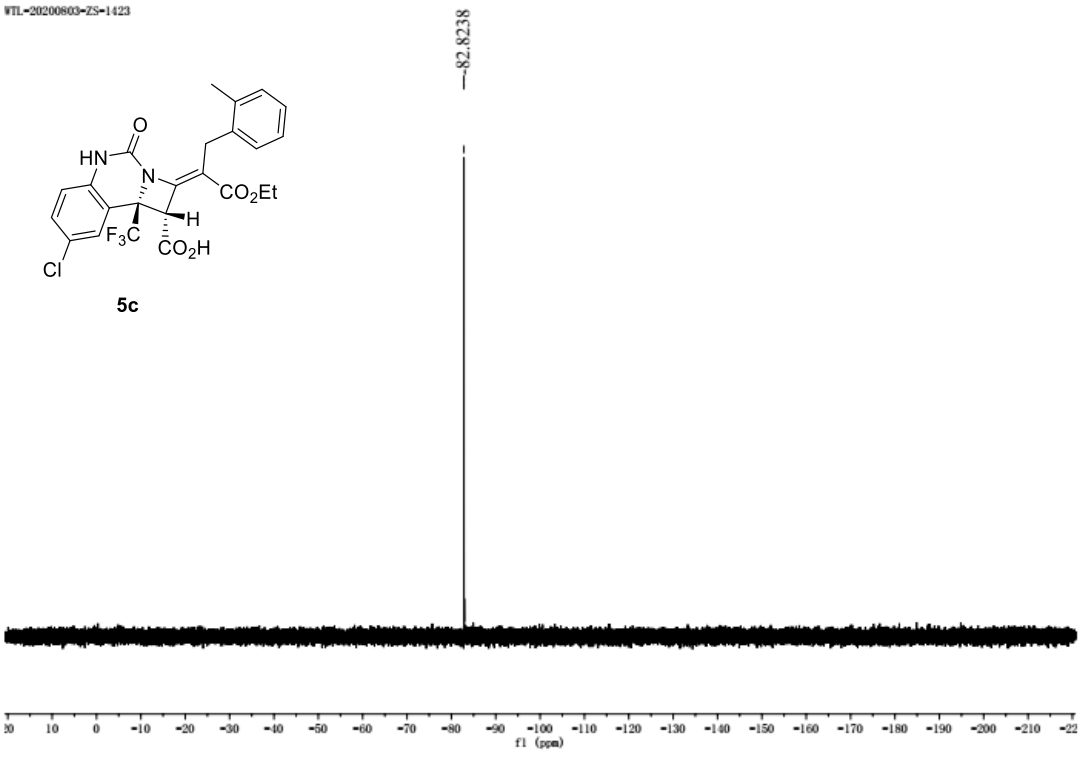


NMR of **5c** (CD_3OD)



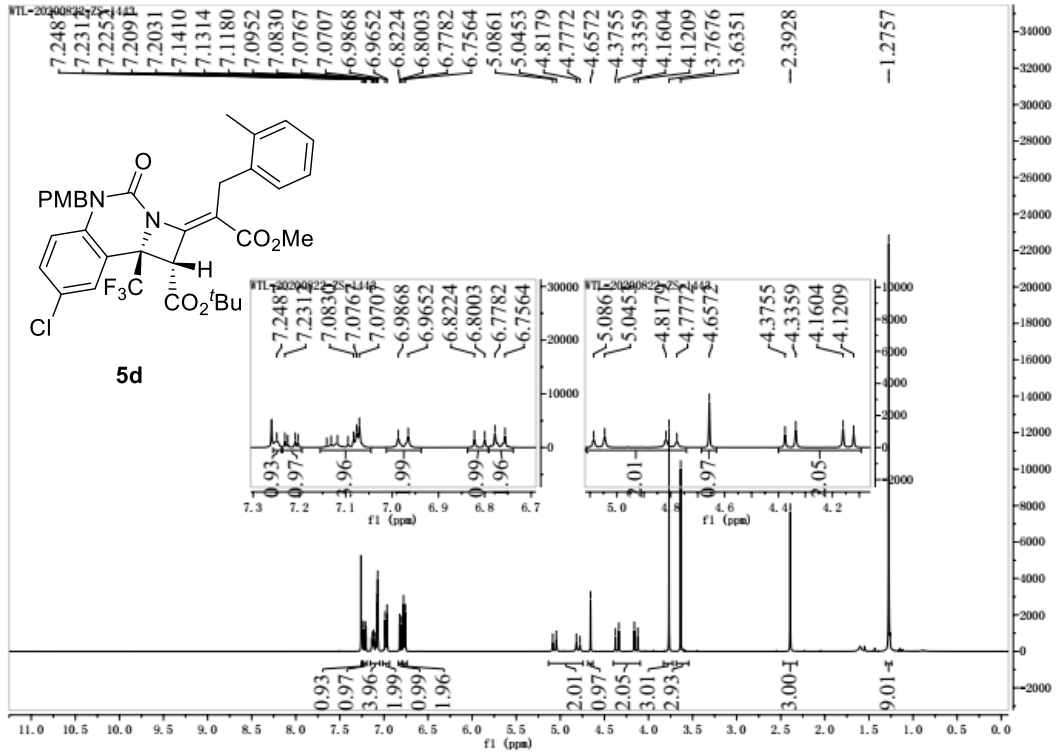

WTL-20200806-ZS-1423
167.6295
167.2867
150.4530
148.0448
138.9028
137.1891
135.6368
131.0972
129.2153
127.7556
127.2681
125.6846
125.2267
116.8867
114.0115
110.8404
69.7125
69.4587
69.1371
68.8274
60.4950
57.0132
30.4498
30.1688
18.4373
12.9417
HN
O
N
CO2Et
H
F3C
CO2H
Cl
f1 (ppm)

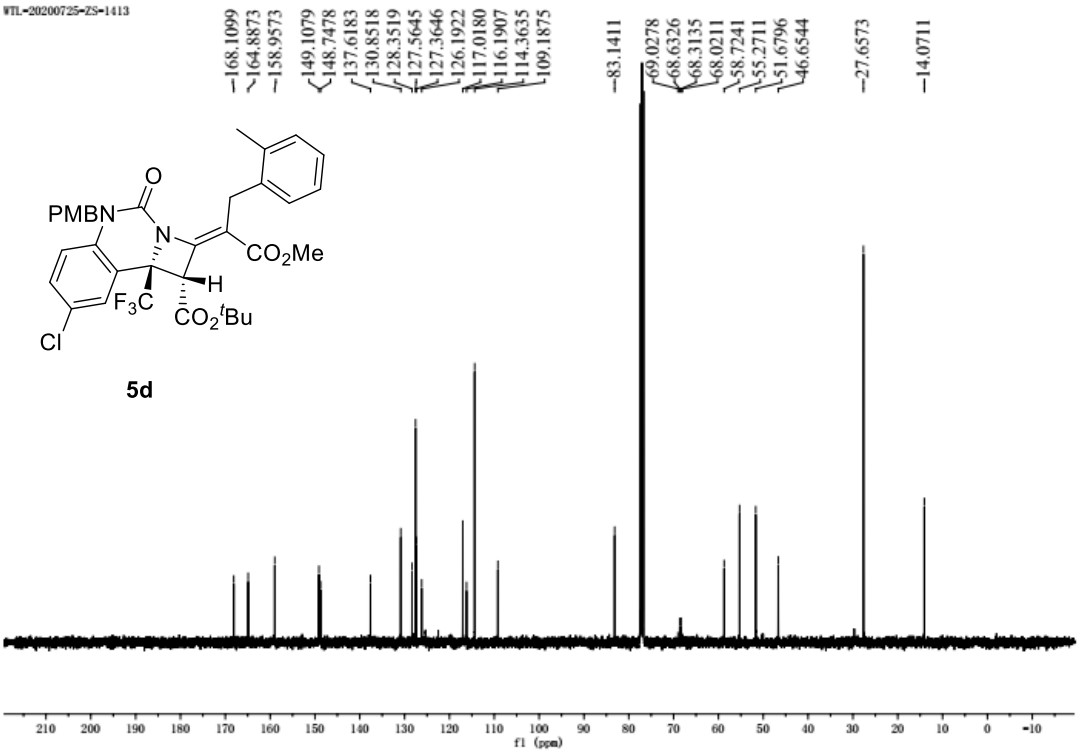
5c

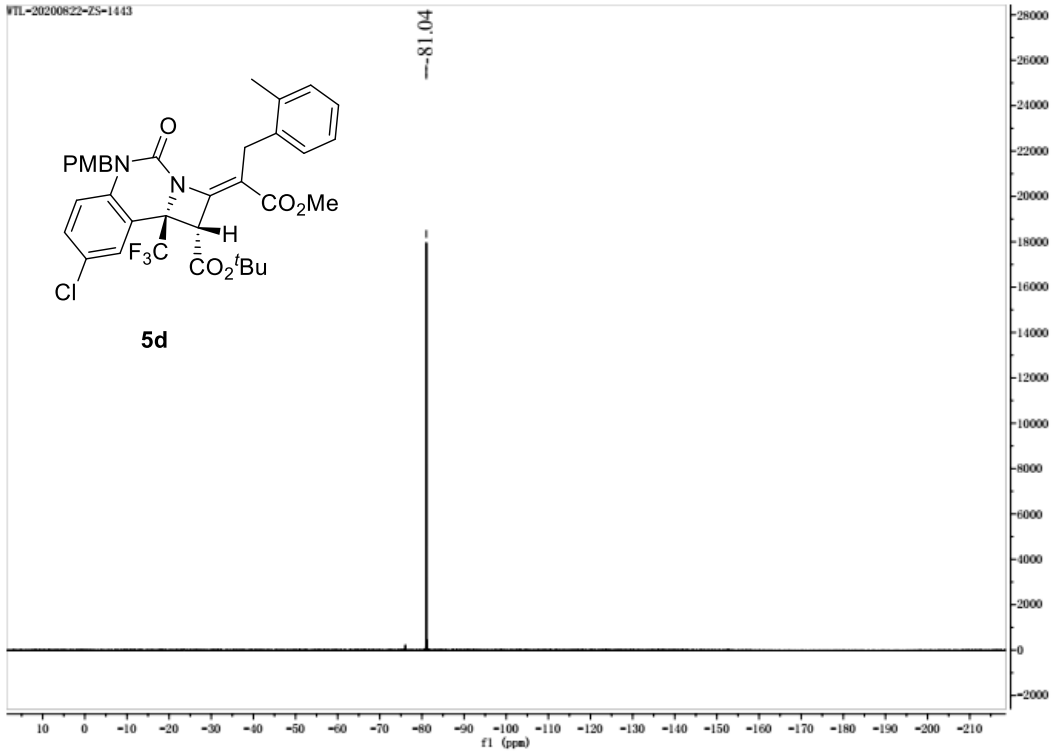

WTL-20200803-ZS-1423
-82.8238
HN
O
N
CO2Et
H
F3C
CO2H
Cl
f1 (ppm)

5c

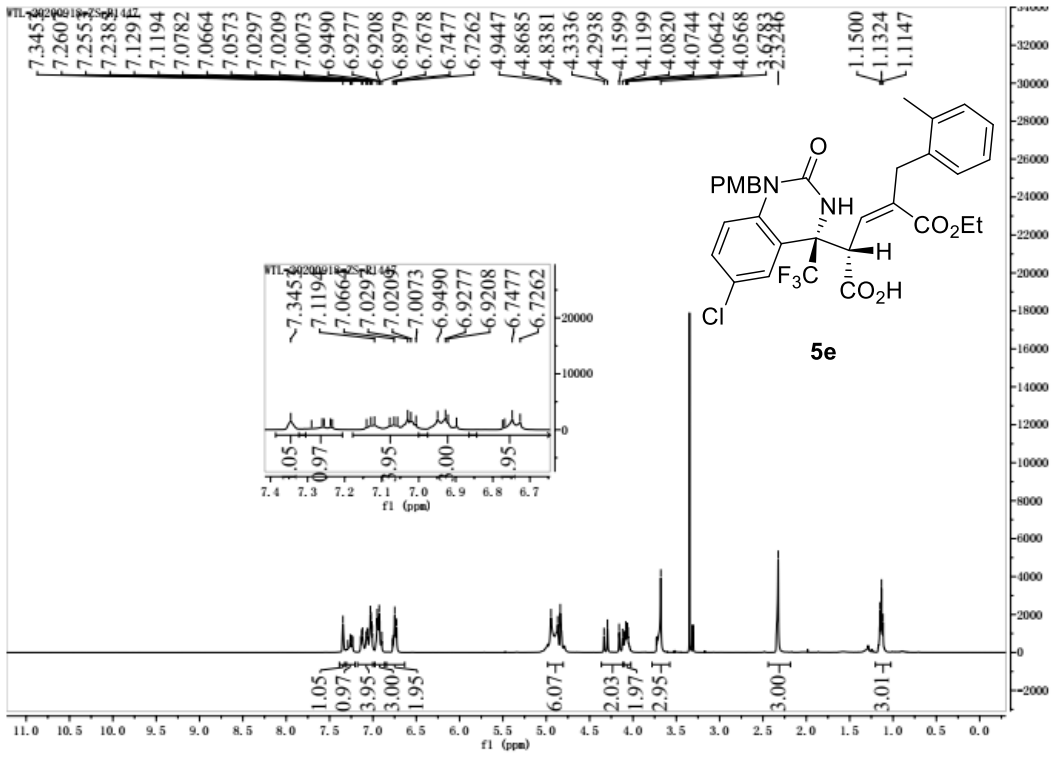
NMR of **5d** ($CDCl_3$)

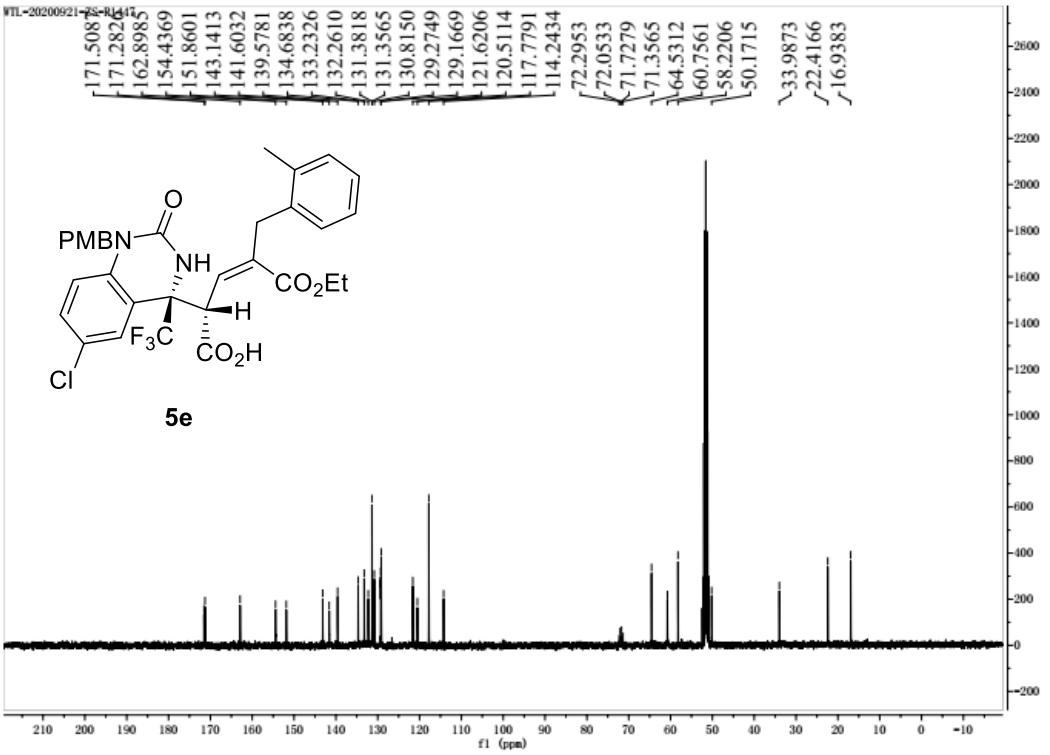


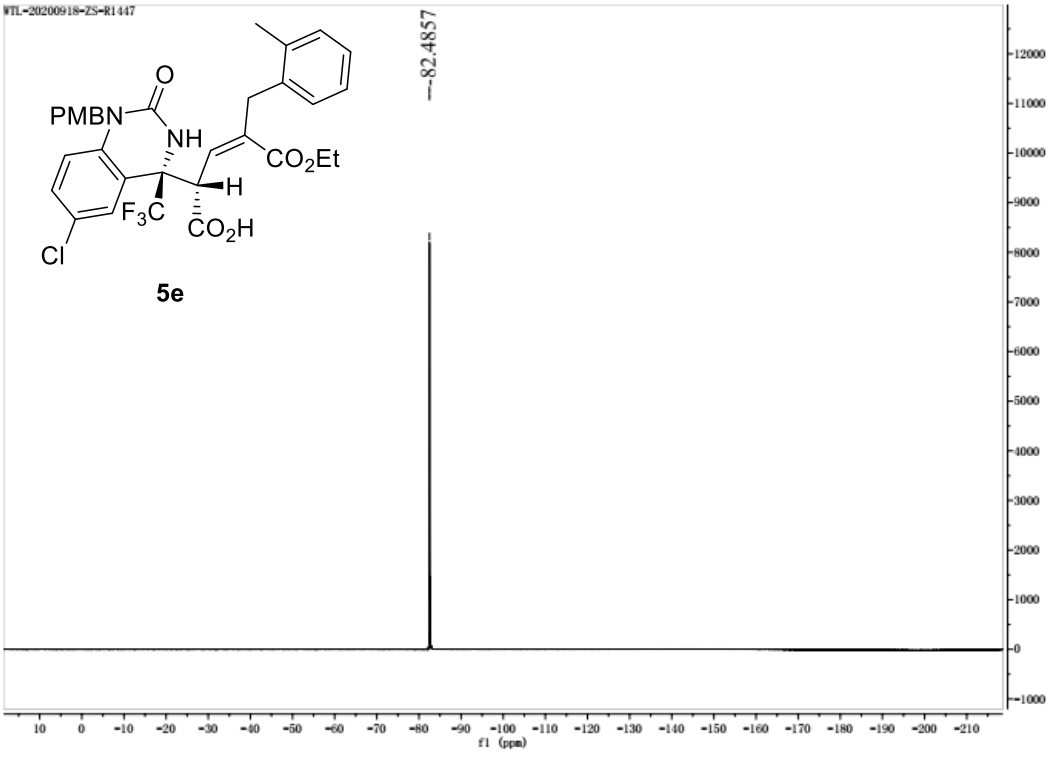




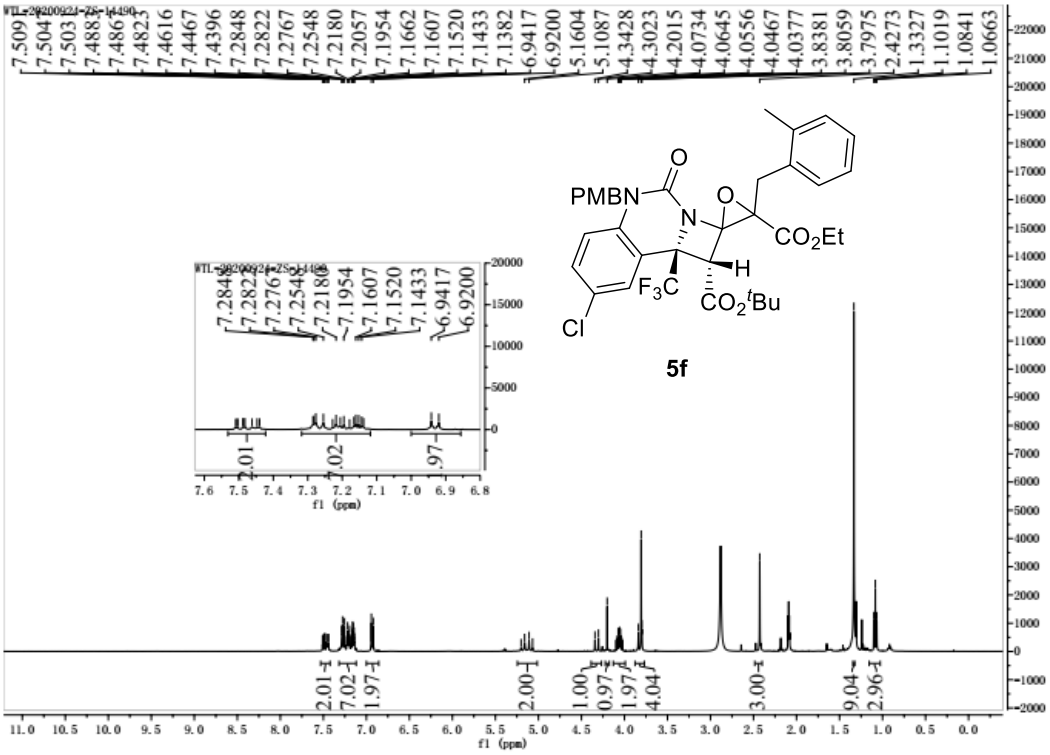
NMR of **5e** (CD_3OD)

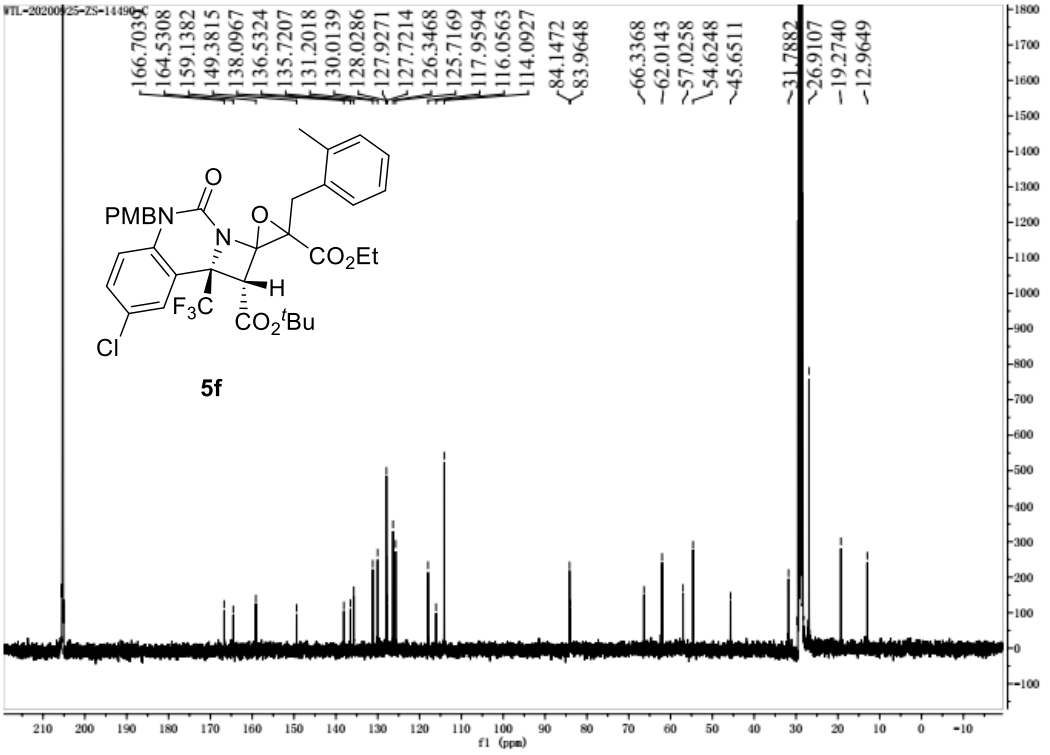


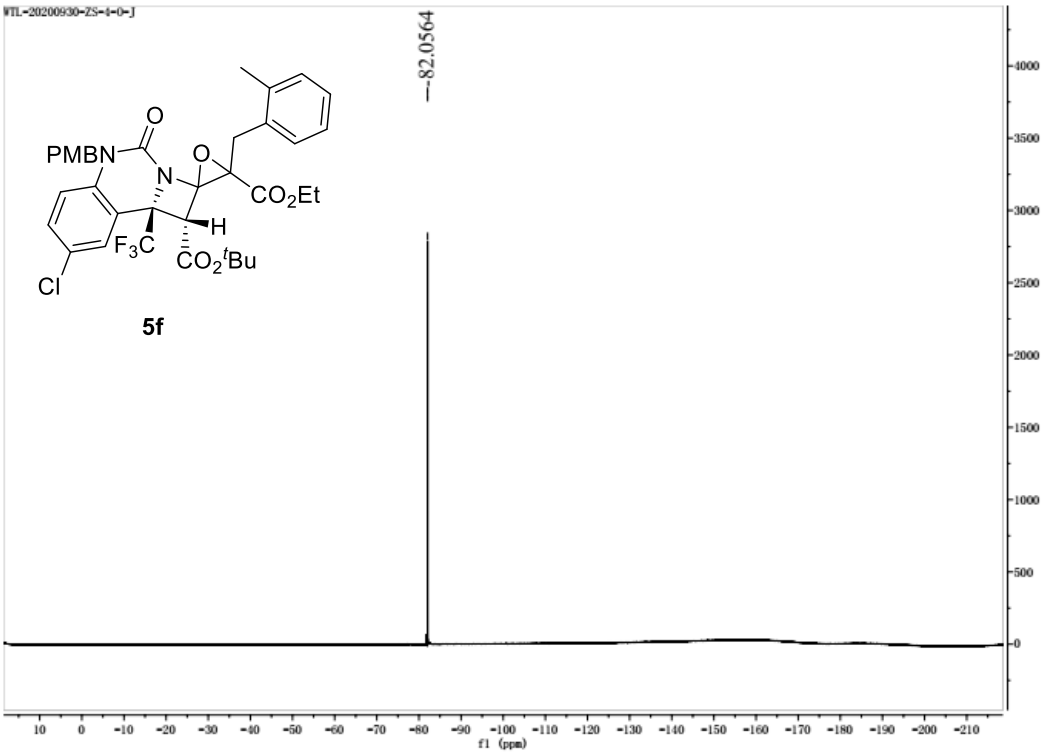

171.5087
171.2826
162.8985
154.4369
151.8601
143.1413
141.6032
139.5781
134.6838
133.2326
132.2610
131.3818
131.3565
130.8150
129.2749
129.1669
121.6206
120.5114
117.7791
114.2434
72.2953
72.0533
71.7279
71.3565
64.5312
60.7561
58.2206
50.1715
33.9873
22.4166
16.9383
PMBN
O
NH
CO2Et
H
F3C
CO2H
Cl
5e
f1 (ppm)


-82.4857
PMBN
O
NH
CO2Et
H
F3C
CO2H
Cl
5e
f1 (ppm)

NMR of **5f** (Acetone-d6)






WTL-20200930-ZS-4-0-J
-82.0564
PMBN
O
N
O
CO2Et
F3C
H
CO2tBu
Cl
4000
3500
3000
2500
2000
1500
1000
500
0
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

5f