Synthesis of Polysubstituted Cyclobutanes through Photoredox Strain-Release/[3,3]-Rearrangement Cascade

Fangqing Zhang[#], Chun Xu[#], Zichun Zhang, Zhuang Yang, Tao Peng, Wen Shao*, Xiaoming Feng*, Yangbin Liu*

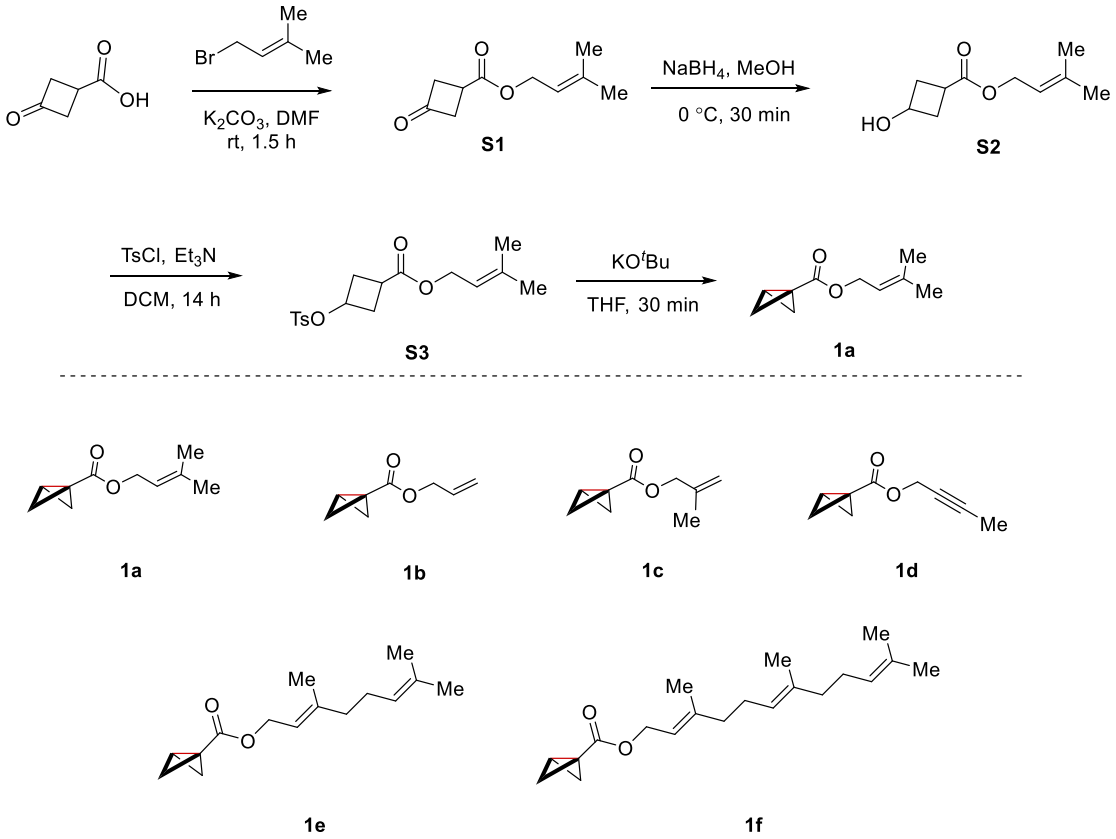
Contents

1. General information

All solvents were dried and distilled according to general practice prior to use. All reagents were purchased from commercial sources and used without further purification unless specified otherwise. Solvents for flash column chromatography were technical grade and distilled prior to use. Analytical thin-layer chromatography (TLC) was performed using Jiangyou silica gel plates with HSGF 254. Visualization of the developed chromatogram was performed by UV absorbance (254 nm) and appropriate stains. Flash column chromatography was performed using silica gel (300-400 mesh) from Leyan.com with the indicated solvent system according to standard techniques. $CDCl_3$ was bought from Leyan.com. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR were recorded on a Bruker NMR 400 (400 MHz). Multiplicities are described as: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet); and coupling constants (*J*) are reported in Hertz (Hz). ^{13}C NMR spectra were recorded with total proton decoupling. Melting points were recorded on a Shanghai Jingke SGWX-4B melting-point Meter and are uncorrected. XRD diffraction (Rigaku MicroMax-007 HF) and HRMS (ESI) analysis was performed by the Analytical Instrumentation Center at Peking University Shenzhen Graduate School and (HRMS) data were reported with ion mass/charge (m/z) ratios as values in atomic mass units.

2. Synthesis of substrates

2.1. Synthesis of bicyclo[1.1.0]butane-1-carboxylate 1



General procedures to synthesize bicyclo[1.1.0]butane-1-carboxylate **1a-1f**.

1) In a round-bottom flask, 3-oxocyclobutane-1-carboxylic acid (3.4 g, 30.0 mmol, 1.0 equiv.), K_2CO_3 (4.6 g, 33.0 mmol, 1.1 equiv.) were dissolved in DMF (30.0 mL). Then, corresponding allyl bromide (33.0 mmol, 1.1 equiv.) was added. The solution was stirred at rt for 1.5 h. Then the reaction was quenched with water (60.0 mL), and extracted with EtOAc (60.0 mL × 3). The combined organic layers were washed with brine three times and dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford intermediate **S1**.

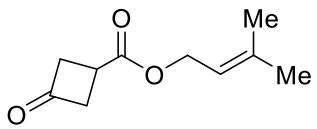
2) In a round-bottom flask, intermediate **S1** (25.0 mmol, 1.0 equiv.) was dissolved in MeOH (60.0 mL), and the mixture was cooled to 0 °C. $NaBH_4$ (2.3 g, 27.5 mmol, 1.1 equiv.) was added portionwise (attention: gas evolution) until full conversion (about 30 min, monitored by TLC) of the starting material. The reaction was quenched with

water, and the aq. layer was extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure to give the intermediate **S2**, which was used in the next step without further purification.

3) To an oven-dried round-bottom flask equipped with a magnetic stir bar was added the intermediate **S2** (22.0 mmol, 1.0 equiv.), Et_3N (4.0 mL, 28.8 mmol, 1.3 equiv.) and CH_2Cl_2 (30.0 mL). Then the solution was cooled to 0 °C, and TsCl (5.5 g, 28.8 mmol, 1.3 equiv.) was added slowly. Then the reaction was allowed to warm up to room temperature and stirred for 14 h. Afterwards, the reaction was quenched with water. The organic layer was separated, washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification by silica gel column chromatography gave the intermediate **S3.**

4) To an oven-dried round-bottom flask equipped with a magnetic stir bar was added the intermediate **S3** (12.0 mmol, 1.0 equiv.) and dry THF (40.0 mL). The flask was evacuated and backfilled with argon three times. Subsequently, the solution was cooled to 0 °C. KO^tBu (13.2 mL, 1.0 M in THF, 13.2 mmol, 1.1 equiv.) was added dropwise to the reaction flask at 0 °C. After stirring for 30 min, the reaction was quenched with sat. aq. NH_4Cl, and extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, and concentrated under reduced pressure. Purification by silica gel column chromatography gave the desired product **1a-1f**.

3-methylbut-2-en-1-yl 3-oxocyclobutane-1-carboxylate (S1)



Product **S1** was obtained as a colorless oil (4.5 g, 25.0 mmol, 83% yield).

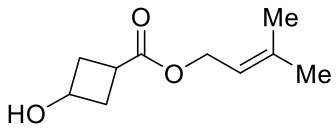
TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 3:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.32 (ddq, *J* = 8.7, 5.8, 1.4 Hz, 1H), 4.62 (d, *J* = 7.3 Hz, 2H), 3.44 – 3.33 (m, 2H), 3.31 – 3.15 (m, 3H), 1.74 (d, *J* = 1.4 Hz, 3H), 1.70 (d, *J* = 1.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 203.9, 174.1, 139.8, 118.1, 62.2, 51.6, 27.4, 25.8, 18.1.

HRMS: m/z $[M+Na]^+$ calcd for $C_{10}H_{14}NaO_3$: 205.0835; found: 205.0836.

3-methylbut-2-en-1-yl 3-hydroxycyclobutane-1-carboxylate (S2)



Product **S2** was obtained as a colorless oil (4.0 g, 22.0 mmol, 88% yield).

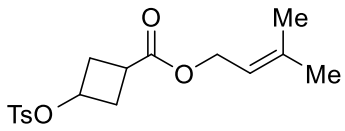
TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 2:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (dddd, *J* = 7.2, 5.8, 2.9, 1.5 Hz, 1H), 4.47 (d, *J* = 7.2 Hz, 2H), 4.12 – 4.00 (m, 1H), 3.88 – 3.49 (m, 1H), 2.46 (tdd, *J* = 8.5, 6.4, 3.9 Hz, 3H), 2.17 – 2.02 (m, 2H), 1.66 (d, *J* = 1.6 Hz, 3H), 1.61 (d, *J* = 1.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 139.1, 118.5, 62.9, 61.7, 36.9, 28.9, 25.7, 18.0.

HRMS: m/z $[M+Na]^+$ calcd for $C_{10}H_{16}NaO_3$: 207.0992; found: 207.0992.

3-methylbut-2-en-1-yl 3-(tosyloxy)cyclobutane-1-carboxylate (S3)



Product **S3** was obtained as a white solid (4.0 g, 12.0 mmol, 54% yield).

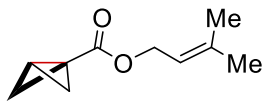
TLC: Rf = 0.5 (Petroleum ether/ethyl acetate 2:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.64 (m, 2H), 7.33 – 7.18 (m, 2H), 5.21 (ddq, *J* = 8.7, 5.8, 1.4 Hz, 1H), 4.70 – 4.60 (m, 1H), 4.46 (d, *J* = 7.3 Hz, 2H), 2.61 – 2.49 (m, 1H), 2.45 – 2.25 (m, 7H), 1.65 (d, *J* = 1.4 Hz, 3H), 1.60 (d, *J* = 1.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 145.0, 139.3, 133.8, 129.9, 127.8, 118.3, 69.7, 61.8, 34.1, 29.6, 25.7, 21.6, 18.0.

HRMS: m/z $[M+Na]^+$ calcd for $C_{17}H_{22}NaO_5S$: 361.1080; found: 361.1080.

3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (1a)



Following the general procedure, product **1a** was obtained as a colorless oil (1.7 g, 10.2 mmol, 85% yield).

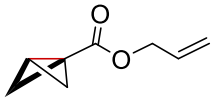
TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 20:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.48 – 5.26 (m, 1H), 4.64 (d, *J* = 7.1 Hz, 2H), 2.40 (d, *J* = 3.3 Hz, 2H), 2.10 (q, *J* = 3.2 Hz, 1H), 1.83 – 1.69 (m, 6H), 1.17 (d, *J* = 3.1 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 138.7, 118.8, 61.7, 35.6, 25.8, 18.1, 16.5, 9.2.

HRMS: m/z $[M+Na]^+$ calcd for $C_{10}H_{14}NaO_2$: 189.0886; found: 189.0884.

allyl bicyclo[1.1.0]butane-1-carboxylate (1b)



Following the general procedure, product **1b** was obtained as a colorless oil (0.47 g, 3.4 mmol, 11% yield for 4 steps).

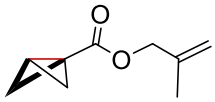
TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 20:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.94 (ddt, *J* = 17.2, 10.4, 5.6 Hz, 1H), 5.38 – 5.20 (m, 2H), 4.63 (dt, *J* = 5.6, 1.4 Hz, 2H), 2.41 (dt, *J* = 3.5, 1.1 Hz, 2H), 2.16 – 2.10 (m, 1H), 1.19 (dt, *J* = 2.9, 1.1 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 132.4, 117.9, 65.3, 35.6, 16.8, 9.1.

HRMS: m/z $[M+Na]^+$ calcd for $C_8H_{10}NaO_2$: 161.0573; found: 161.0570.

2-methylallyl bicyclo[1.1.0]butane-1-carboxylate (1c)



Following the general procedure, product **1c** was obtained as a colorless oil (1.5 g, 10.0 mmol, 33% yield for 4 steps).

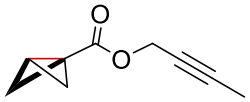
TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 20:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.95 (dp, *J* = 13.8, 1.3 Hz, 2H), 4.55 (s, 2H), 2.41 (dt, *J* = 3.5, 1.1 Hz, 2H), 2.13 (p, *J* = 3.2 Hz, 1H), 1.77 (t, *J* = 1.2 Hz, 3H), 1.20 (dt, *J* = 2.7, 1.0 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 140.2, 112.4, 67.7, 35.6, 19.5, 16.7, 9.1.

HRMS: m/z $[M+Na]^+$ calcd for $C_9H_{12}NaO_2$: 175.0730; found: 175.0731.

but-2-yn-1-yl bicyclo[1.1.0]butane-1-carboxylate (1d)



Following the general procedure, product **1d** was obtained as a colorless oil (0.75 g, 5.0 mmol, 17% yield for 4 steps).

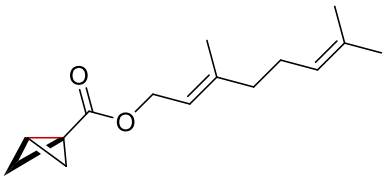
TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 20:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.66 (q, *J* = 2.4 Hz, 2H), 2.39 (dt, *J* = 3.5, 1.1 Hz, 2H), 2.14 (p, *J* = 3.2 Hz, 1H), 1.85 (t, *J* = 2.4 Hz, 3H), 1.17 (dt, *J* = 2.9, 1.1 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 83.0, 73.4, 53.0, 35.8, 17.1, 9.0, 3.7.

HRMS: m/z $[M+Na]^+$ calcd for $C_9H_{10}NaO_2$: 173.0573; found: 173.0575.

(*E*)-3,7-dimethylocta-2,6-dien-1-yl bicyclo[1.1.0]butane-1-carboxylate (1e)



Following the general procedure, product **1e** was obtained as a colorless oil (2.5 g, 10.7 mmol, 36% yield for 4 steps).

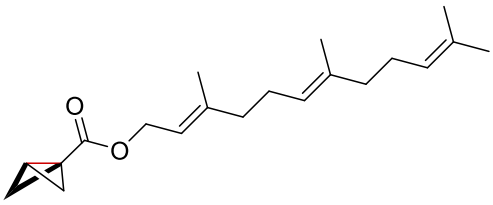
TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 20:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.30 (tq, *J* = 7.0, 1.3 Hz, 1H), 5.05 (ddp, *J* = 7.0, 5.9, 1.5 Hz, 1H), 4.59 (d, *J* = 7.0 Hz, 2H), 2.33 (dt, *J* = 3.5, 1.1 Hz, 2H), 2.11 – 2.04 (m, 2H), 2.04 – 1.98 (m, 3H), 1.66 (dd, *J* = 8.8, 1.5 Hz, 6H), 1.57 (d, *J* = 1.6 Hz, 3H), 1.13 – 1.08 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 141.8, 131.7, 123.8, 118.6, 61.6, 39.5, 35.5, 26.3, 25.7, 17.7, 16.5, 16.3, 9.1.

HRMS: m/z $[M+Na]^+$ calcd for $C_{15}H_{22}NaO_2$: 257.1512; found: 257.1512.

(2*E*,6*E*)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl bicyclo[1.1.0]butane-1-carboxylate (1f)



Following the general procedure, product **1f** was obtained as a colorless oil (2.7 g, 8.9 mmol, 30% yield for 4 steps).

TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 20:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.37 (td, *J* = 8.7, 7.2, 1.5 Hz, 1H), 5.16 – 5.07 (m, 2H), 4.62 (d, *J* = 7.2 Hz, 2H), 2.37 (d, *J* = 3.5 Hz, 2H), 2.15 – 2.11 (m, 3H), 2.08 (dt, *J* = 9.8, 3.5 Hz, 4H), 2.00 (dd, *J* = 9.2, 6.1 Hz, 2H), 1.78 (d, *J* = 1.4 Hz, 3H), 1.70 (d, *J* = 1.6 Hz, 3H), 1.62 (d, *J* = 1.5 Hz, 6H), 1.15 (d, *J* = 2.9 Hz, 2H).

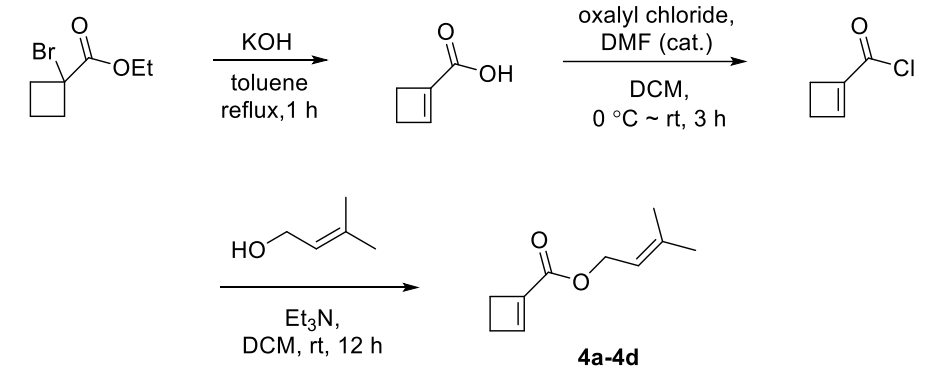
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 142.4, 135.8, 131.4, 124.3, 123.5, 119.4, 61.4, 39.8, 35.6, 32.2, 26.7, 26.7, 25.7, 23.6, 17.7, 16.4, 16.0, 9.2.

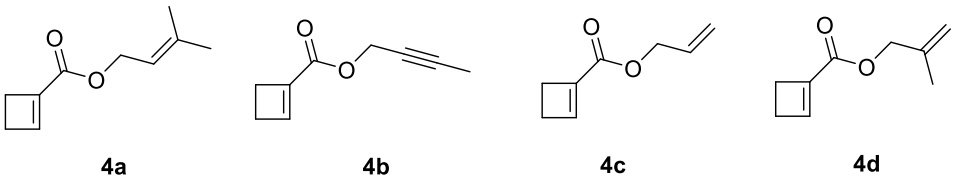
HRMS: m/z $[M+Na]^+$ calcd for $C_{20}H_{30}NaO_2$: 325.2138; found: 325.2139.

2.2. Synthesis of α-Silylamines

All the α-Silylamines were prepared according to the literature.[1]

2.3. Synthesis of cyclobut-1-ene-1-carboxylate 4





General procedures to synthesize cyclobut-1-ene-1-carboxylate **4a-4d**

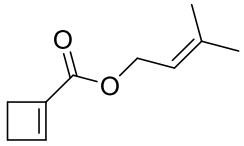
1) In a round-bottom flask, KOH (6.0 g, 100.0 mmol, 4.5 equiv.) and toluene (50.0 mL) were added. The solution was stirred at 120 °C for 30 min until most of KOH was dissolved. Then ethyl 1-bromocyclobutane-1-carboxylate (5.0 g, 24.0 mmol, 1.0 equiv.) was added, and the mixture was stirred at 120 °C for 1 h. The reaction was quenched with water (60.0 mL) and washed with petroleum ether (60.0 mL). The aqueous phase was then acidified to pH = 1 with an aqueous solution of HCl (2.0 M, 30.0 mL). The product was extracted from the aqueous layer with EtOAc (50.0 mL × 3), dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel to afford cyclobut-1-ene-1-carboxylic acid (2.0 g, 20.4 mmol, 85% yield).

2) In a round-bottom flask, cyclobut-1-ene-1-carboxylic acid (2.0 g, 20.4 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (10.0 mL), and the solution was cooled to 0 °C. DMF (5 drops) and oxalyl chloride (1.8 mL, 22.4 mmol, 1.1 equiv.) were then added dropwise (attention: gas evolution). The reaction was warmed to rt and stirred for 3 h to afford the cyclobut-1-ene-1-carbonyl chloride solution for next step.

3) To an oven-dried round-bottom flask equipped with a magnetic stir bar was added the corresponding allyl alcohol (22.4 mmol, 1.1 equiv.), Et_3N (6.1 mL, 44.9 mmol, 2.2 equiv.) and CH_2Cl_2 (15.0 mL). Then freshly prepared cyclobut-1-ene-1-carbonyl

chloride solution (20.4 mmol, 1.0 equiv.) was added dropwise at 0 °C. Then the reaction was warmed to rt and stirred for 12 h. Afterwards, the reaction was quenched with water. The organic layer was separated, washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification by silica gel column chromatography afforded the product **4a-4d.**

3-methylbut-2-en-1-yl cyclobut-1-ene-1-carboxylate (4a)



Following the general procedure, product **4a** was obtained as a colorless oil (2.1 g, 12.6 mmol, 53% yield for 3 steps).

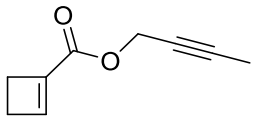
TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 20:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.72 (t, *J* = 1.3 Hz, 1H), 5.32 (ddt, *J* = 8.6, 5.8, 1.4 Hz, 1H), 4.59 (dt, *J* = 7.2, 0.9 Hz, 2H), 2.73 – 2.64 (m, 2H), 2.46 – 2.37 (m, 2H), 1.73 – 1.67 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 146.3, 138.9, 138.8, 118.7, 61.1, 29.2, 27.1, 25.8, 18.0.

HRMS: m/z $[M+Na]^+$ calcd for $C_{10}H_{14}NaO_2$: 189.0886; found: 189.0886.

but-2-yn-1-yl cyclobut-1-ene-1-carboxylate (4b)



Following the general procedure, product **4b** was obtained as a colorless oil (1.6 g, 10.7 mmol, 44% yield for 3 steps).

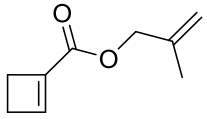
TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 20:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (t, *J* = 1.3 Hz, 1H), 4.69 (q, *J* = 2.4 Hz, 2H), 2.79 – 2.67 (m, 2H), 2.51 – 2.45 (m, 2H), 1.85 (t, *J* = 2.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 147.6, 138.0, 83.1, 73.2, 52.4, 29.2, 27.3, 3.7.

HRMS: m/z $[M+Na]^+$ calcd for $C_9H_{10}NaO_2$: 173.0573; found: 173.0573.

2-methylallyl cyclobut-1-ene-1-carboxylate (4d)



Following the general procedure, product **4d** was obtained as a colorless oil (1.3 g, 8.6 mmol, 36% yield for 3 steps).

TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 20:1)

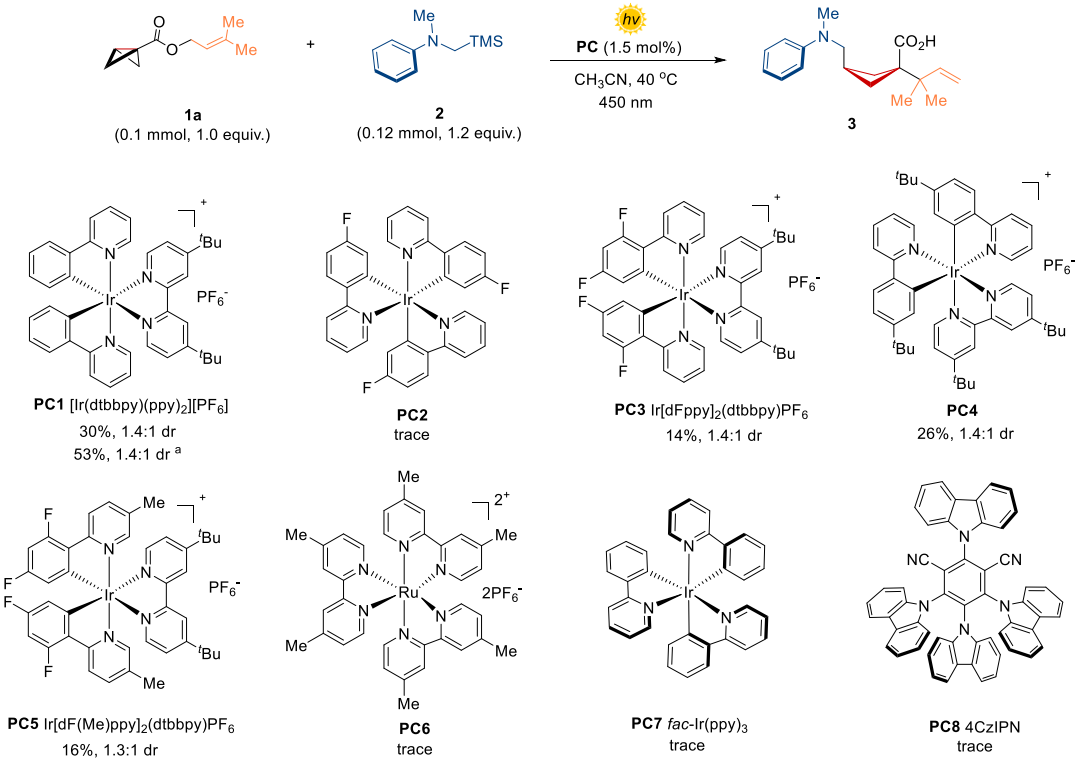
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (d, *J* = 1.3 Hz, 1H), 5.08 – 4.90 (m, 2H), 4.57 (s, 2H), 2.83 – 2.69 (m, 2H), 2.51 (td, *J* = 3.2, 1.5 Hz, 2H), 1.79 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 146.8, 140.0, 138.6, 112.8, 67.2, 29.2, 27.2, 19.5.

HRMS: m/z $[M+Na]^+$ calcd for $C_9H_{12}NaO_2$: 175.0730; found: 175.0731.

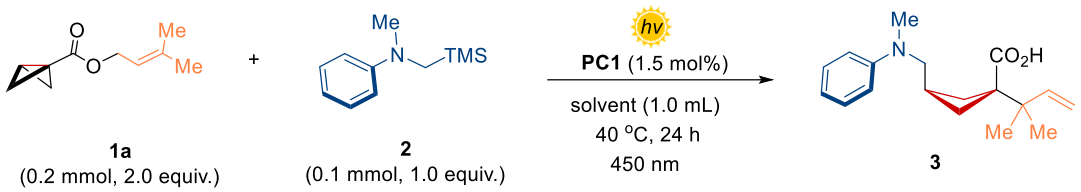
3. Reaction optimization

Table S1. Photocatalyst screening



Reaction conditions: unless otherwise noted, **1a** (0.1 mmol), **2** (0.12 mmol), **PC** (1.5 mol%) in CH_3CN (0.1 M), 24 h, 450 nm at 40 °C. The yields are determined by ^{1}H NMR analysis of the crude product mixtures by using 1,3,5-trimethoxybenzene as an internal standard. [a] **1a** (0.2 mmol, 2.0 equiv.) and **2** (0.1 mmol, 1.0 equiv.) were used.

Table S2. solvent screening



1a
(0.2 mmol, 2.0 equiv.)

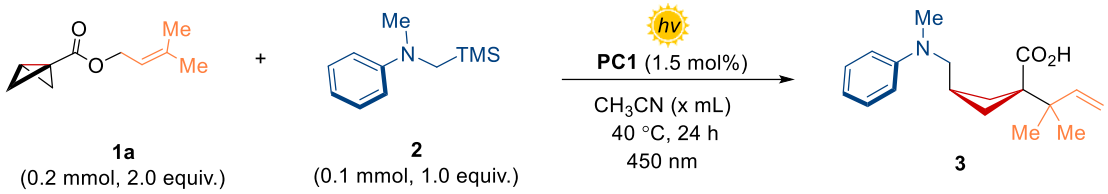
2
(0.1 mmol, 1.0 equiv.)

3

entry	solvent	yield (%)	dr
1	CH_3CN	53	1.4:1
2	EA	24	1.3:1
3	THF	22	1:1
4	DCM	33	1.3:1
5	DCE	46	1.3:1
6	toluene	24	1.3:1
7	DMF	45	1.1:1
8	DMSO	21	1.1:1
9	Dioxane	23	1.2:1

Reaction conditions: unless otherwise noted, **1a** (0.2 mmol), **2** (0.1 mmol), **PC1** (1.5 mol%) in solvent (0.1 M), 24 h, 450 nm at 40 °C. The yields are determined by ^{1}H NMR analysis of the crude product mixtures by using 1,3,5-trimethoxybenzene as an internal standard.

Table S3. concentration screening



1a
(0.2 mmol, 2.0 equiv.)

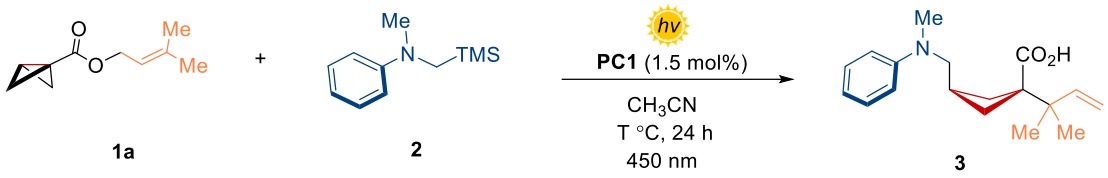
2
(0.1 mmol, 1.0 equiv.)

3

entry	x (mL)	yield (%)	dr
1	0.25	69	1.5:1
2	0.5	52	1.3:1
3	1	53	1.4:1
4	1.5	41	1.5:1
5	2	35	1.5:1
6[a]	0.25	86 (72)[b]	1.4:1

Reaction conditions: unless otherwise noted, **1a** (0.2 mmol), **2** (0.1 mmol), **PC1** (1.5 mol%) in CH_3CN (x mL), 24 h, 450 nm at 40 °C. The yields are determined by ^1H NMR analysis of the crude product mixtures by using 1,3,5-trimethoxybenzene as an internal standard. [a] **1a** (0.4 mmol) and **2** (0.2 mmol) were used. [b] For ease of separation, the carboxylic acid is converted to its methyl ester by $TMSCHN_2$. The isolated yield of two-step is reported.

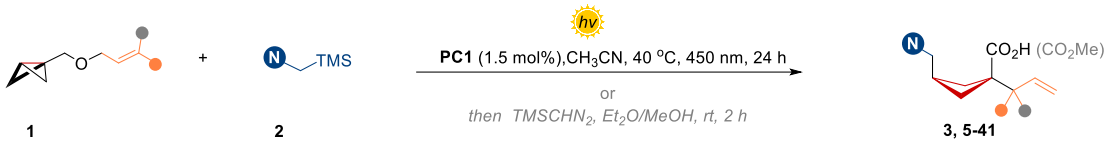
Table S4. temperature screening



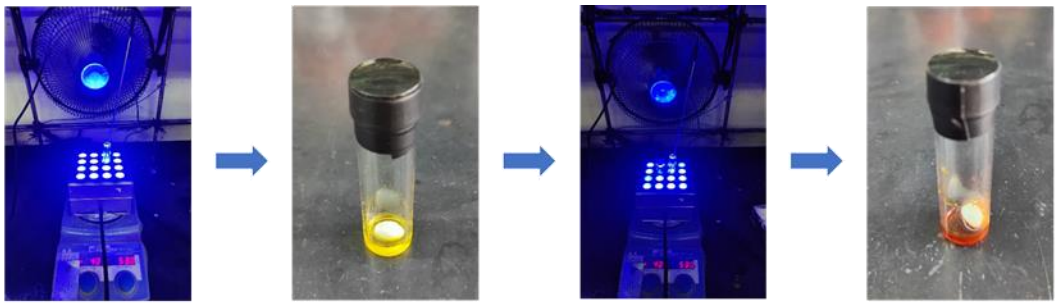
entry	T (°C)	yield (%)	dr
1	25	44	1.4:1
2	40	86	1.4:1
3	50	77	1.3:1

Reaction conditions: unless otherwise noted, **1a** (0.4 mmol), **2** (0.2 mmol), **PC1** (1.5 mol%) in CH_3CN (0.25 mL), 24 h, 450 nm at T °C. The yields are determined by ^1H NMR analysis of the crude product mixtures by using 1,3,5-trimethoxybenzene as an internal standard.

4. General procedures for the SRRC process of BCBs.

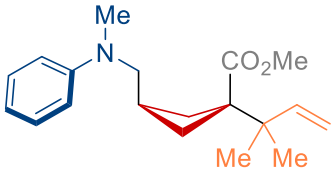


In the glovebox, bicyclo[1.1.0]butane-1-carboxylate **1** (0.4 mmol, 2.0 equiv.), α-silylamine **2** (0.2 mmol, 1.0 equiv.), Ir(dtbbpy)(ppy)$_2$][PF$_6$] (**PC1**) (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%) and dry CH_3CN (0.25 mL) were added respectively into a flame-dried reaction vial equipped with a stir bar. Then the vial was sealed and transferred out of the glove box. Afterwards, it was irradiated with a 1 W blue LED lamp (450 nm, SYNLED) for 24 h at 40 °C. When the reaction was completed (monitored by TLC), the crude mixture was concentrated by rotary evaporation. Then the residue was purified by silica gel flash chromatography or preparative thin layer chromatography to give the corresponding carboxylic acid. In some cases, for ease of separation, the carboxylic acid was converted to its methyl ester by treatment of $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in a mixture solution of Et_2O and MeOH (Et_2O/MeOH = 4:1, 2.0 mL) at room temperature for 2 h. Then the corresponding methyl ester products were purified by silica gel flash chromatography.



Preheat the photoreactor to 40 °C | Weighing completed | Reaction was lighted in 1 W (450 nm) LED for 24 h | The reaction was completed

methyl 3-((methyl(phenyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (3)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), *N*-methyl-*N*-((trimethylsilyl)methyl)aniline (38.6 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **3** was obtained as a colorless oil (44.5 mg, 74% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.6 (Petroleum ether/ethyl acetate 8:1)

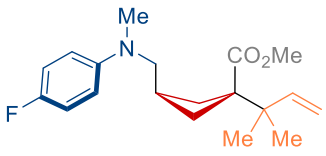
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.11 (m, 2H), 6.74 – 6.61 (m, 3H), 5.99 – 5.92 (m, 1H), 5.12 – 4.88 (m, 2H), 3.68 (s, 1.75H), 3.66 (s, 1.25H), 3.28 – 3.24 (m, 2H), 2.90 (s, 1.75H), 2.89 (s, 1.25H), 2.46 – 2.25 (m, 3H), 2.19 – 2.07 (m, 1.2H), 1.98 – 1.87 (m, 0.86H), 1.01 (s, 3.5H), 0.97 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.9, 149.5, 143.8, 129.2, 116.3, 112.7, 112.4, 58.9, 51.6, 51.4, 39.6, 38.9, 31.6, 26.5, 22.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.1, 149.5, 144.9, 129.2, 116.3, 112.4, 112.3, 57.5, 53.3, 50.8, 39.6, 38.8, 32.2, 27.8, 23.0.

HRMS: m/z $[M+Na]^+$ calcd for $C_{19}H_{27}NNaO_2$: 324.1934; found: 324.1933.

methyl 3-(((4-fluorophenyl)(methyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (5)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 4-fluoro-*N*-methyl-*N*-((trimethylsilyl)methyl)aniline (42.2 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was

treated with $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **5** was obtained as a colorless oil (31.9 mg, 50% yield for 2 steps, 1:1 dr).

TLC: Rf = 0.6 (Petroleum ether/ethyl acetate 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98 – 6.83 (m, 2H), 6.66 – 6.52 (m, 2H), 5.99 – 5.84 (m, 1H), 5.08 – 4.89 (m, 2H), 3.67 (s, 1.5H), 3.66 (s, 1.5H), 3.25 – 3.13 (m, 2H), 2.83 (s, 3H), 2.43 – 2.22 (m, 3H), 2.16 – 2.04 (m, 1H), 1.96 – 1.84 (m, 1H), 1.00 (s, 3H), 0.96 (s, 3H).

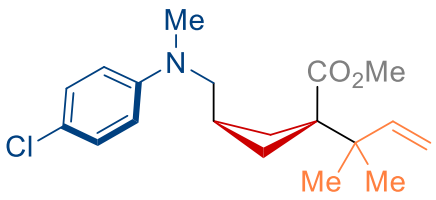
Diastereomer 1: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.8, 155.4 (d, *J* = 235.3 Hz), 146.5, 144.8, 115.5 (d, *J* = 22.2 Hz), 113.8 (d, *J* = 8.1 Hz), 112.3, 59.8, 51.6, 51.5, 39.6, 39.4, 31.7, 26.4, 22.3.

Diastereomer 2: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.2, 155.4 (d, *J* = 235.3 Hz), 146.5, 143.7, 115.5 (d, *J* = 22.2 Hz), 113.9 (d, *J* = 7.1 Hz), 112.7, 58.4, 53.3, 50.8, 39.6, 39.3, 32.2, 27.7, 22.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ −129.3, −129.4.

HRMS: m/z $[M+Na]^+$ calcd for $C_{19}H_{26}FNNaO_2$: 342.1840; found: 342.1840.

methyl 3-(((4-chlorophenyl)(methyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (6)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 4-chloro-*N*-methyl-*N*-((trimethylsilyl)methyl)aniline (45.4 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **6** was obtained as a colorless oil (43.7 mg, 65% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.6 (Petroleum ether/ethyl acetate 8:1)

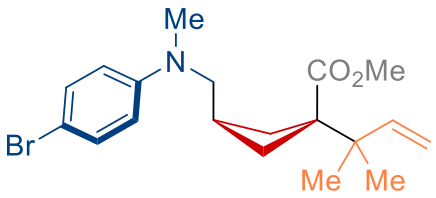
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 – 7.06 (m, 2H), 6.60 – 6.49 (m, 2H), 5.98 – 5.84 (m, 1H), 5.09 – 4.89 (m, 2H), 3.68 (s, 1.75H), 3.66 (s, 1.25H), 3.29 – 3.16 (m, 2H), 2.87 (s, 1.75H), 2.86 (s, 1.25H), 2.41 – 2.23 (m, 3H), 2.14 – 2.10 (m, 1.2H), 1.93 – 1.90 (m, 0.84H), 1.00 (s, 3.5H), 0.96 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.8, 148.1, 143.7, 128.9, 121.1, 113.5, 112.8, 58.8, 51.7, 51.5, 39.6, 39.1, 31.5, 26.4, 22.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.1, 148.1, 144.8, 128.9, 121.1, 113.4, 112.4, 57.5, 53.3, 50.8, 39.6, 39.0, 32.1, 27.7, 22.9.

HRMS: m/z $[M+Na]^+$ calcd for $C_{19}H_{26}ClNNaO_2$: 358.1544; found: 358.1545.

methyl 3-(((4-bromophenyl)(methyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (7)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 4-bromo-*N*-methyl-*N*-((trimethylsilyl)methyl)aniline (54.2 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **7** was obtained as a colorless oil (38.8 mg, 51% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.6 (Petroleum ether/ethyl acetate 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.15 (m, 2H), 6.56 – 6.44 (m, 2H), 5.98 – 5.84 (m, 1H), 5.10 – 4.88 (m, 2H), 3.68 (s, 1.75H), 3.66 (s, 1.25H), 3.30 – 3.14 (m, 2H), 2.87 (s, 1.75H), 2.86 (s, 1.25H), 2.41 – 2.21 (m, 3H), 2.16 – 2.05 (m, 1.22H), 1.92 – 1.89 (m, 0.86H), 1.00 (s, 3.5H), 0.96 (s, 2.5H).

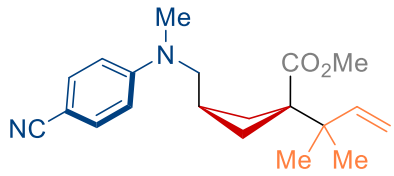
Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.8, 148.4, 143.7, 131.8, 113.9, 112.8, 108.1, 58.7, 51.7, 51.5, 39.6, 39.0, 31.5, 26.3, 22.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.0, 148.4, 144.8, 131.8, 113.9,

112.4, 108.1, 57.3, 53.3, 50.8, 39.6, 38.9, 32.1, 27.7, 22.9.

HRMS: m/z $[M+Na]^+$ calcd for $C_{19}H_{26}BrNNaO_2$: 402.1040, 404.1019; found: 402.1041, 404.1019.

methyl 3-(((4-cyanophenyl)(methyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (8)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 4-(methyl((trimethylsilyl)methyl)amino)benzonitrile (43.6 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **8** was obtained as a colorless oil (37.2 mg, 57% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.5 (Petroleum ether/ethyl acetate 8:1)

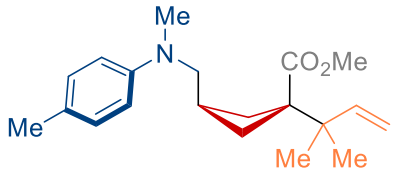
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.37 (m, 2H), 6.65 – 6.50 (m, 2H), 5.96 – 5.83 (m, 1H), 5.13 – 4.88 (m, 2H), 3.68 (s, 1.75H), 3.66 (s, 1.25H), 3.38 – 3.25 (m, 2H), 2.97 (s, 1.75H), 2.96 (s, 1.25H), 2.40 – 2.27 (m, 3H), 2.17 – 2.07 (m, 1.25H), 1.93 – 1.89 (m, 0.88H), 0.99 (s, 3.5H), 0.95 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.6, 151.6, 143.5, 133.5, 120.7, 113.0, 111.4, 97.4, 57.8, 51.7, 51.5, 39.5, 39.0, 31.3, 26.3, 22.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.8, 151.6, 144.7, 133.5, 120.7, 112.6, 111.4, 97.4, 56.6, 53.3, 50.8, 39.5, 38.9, 31.9, 27.8, 22.9.

HRMS: m/z $[M+Na]^+$ calcd for $C_{20}H_{26}N_2NaO_2$: 349.1886; found: 349.1886.

methyl 3-((methyl(p-tolyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (9)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), *N*,4-dimethyl-*N*-((trimethylsilyl)methyl)aniline (41.4 mg, 0.2 mmol, 1.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with TMSCH$_2$N$_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et$_2$O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **9** was obtained as a colorless oil (30.2 mg, 48% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.6 (Petroleum ether/ethyl acetate 8:1)

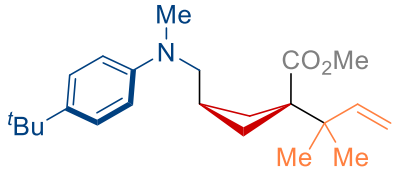
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.04 (d, *J* = 8.3 Hz, 2H), 6.61 (d, *J* = 8.2 Hz, 2H), 6.01 – 5.88 (m, 1H), 5.14 – 4.87 (m, 2H), 3.70 (s, 1.75H), 3.68 (s, 1.25H), 3.26 – 3.22 (m, 2H), 2.88 (s, 1.75H), 2.88 (s, 1.25H), 2.44 – 2.29 (m, 3H), 2.26 (s, 3H), 2.17 – 2.12 (m, 1.25H), 1.97 – 1.92 (m, 0.88H), 1.03 (s, 3.5H), 0.99 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, CDCl$_3$) δ 177.9, 147.6, 143.8, 129.7, 125.6, 112.8, 112.7, 59.3, 51.7, 51.5, 39.6, 39.1, 31.7, 26.4, 22.3, 20.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, CDCl$_3$) δ 177.2, 147.6, 144.9, 129.7, 125.6, 112.8, 112.3, 58.0, 53.3, 50.8, 39.6, 39.0, 32.2, 27.7, 23.0, 20.3.

HRMS: m/z [M+Na]$^+$ calcd for C$_{20}$H$_{29}$NNaO$_2$: 338.2090; found: 338.2090.

methyl 3-(((4-(*tert*-butyl)phenyl)(methyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (10)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 4-(*tert*-butyl)-*N*-methyl-*N*-((trimethylsilyl)methyl)aniline (50.0 mg, 0.2 mmol, 1.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with TMSCH$_2$N$_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et$_2$O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **10** was obtained as a white solid (34.4 mg,

48% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.6 (Petroleum ether/ethyl acetate 10:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.18 (m, 2H), 6.67 – 6.56 (m, 2H), 6.00 – 5.87 (m, 1H), 5.11 – 4.90 (m, 2H), 3.69 (s, 1.75H), 3.67 (s, 1.25H), 3.34 – 3.13 (m, 2H), 2.88 (s, 1.75H), 2.87 (s, 1.25H), 2.45 – 2.25 (m, 3H), 2.18 – 2.09 (m, 1.2H), 1.99 – 1.85 (m, 0.83H), 1.28 (s, 9H), 1.02 (s, 3.5H), 0.98 (s, 2.5H).

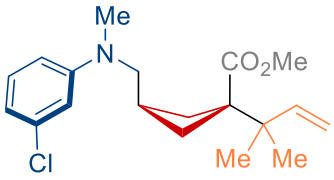
Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.9, 147.4, 143.8, 138.9, 125.9, 112.6, 112.1, 59.1, 51.6, 51.4, 39.6, 39.0, 33.8, 31.6, 31.6, 26.6, 22.4.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.2, 147.4, 144.9, 139.0, 125.9, 112.3, 112.2, 57.8, 53.3, 50.8, 39.6, 38.8, 33.8, 32.2, 31.6, 27.8, 23.0.

HRMS: m/z $[M+Na]^+$ calcd for $C_{23}H_{35}NNaO_2$: 380.2560; found: 380.2562.

m.p. 78–79 °C. (**10** was recrystallized from EA/PE = 1:10)

methyl 3-(((3-chlorophenyl)(methyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (11)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 3-chloro-*N*-methyl-*N*-((trimethylsilyl)methyl)aniline (45.4 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **11** was obtained as a colorless oil (41.0 mg, 61% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.6 (Petroleum ether/ethyl acetate 8:1)

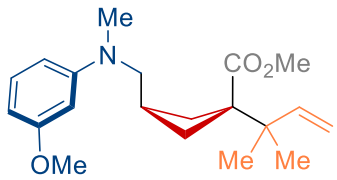
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 – 7.06 (m, 1H), 6.66 – 6.55 (m, 2H), 6.50 – 6.48 (m, 1H), 5.99 – 5.85 (m, 1H), 5.12 – 4.89 (m, 2H), 3.69 (s, 1.75H), 3.67 (s, 1.25H), 3.30 – 3.19 (m, 2H), 2.89 (s, 1.75H), 2.88 (s, 1.25H), 2.43 – 2.25 (m, 3H), 2.15 – 2.10 (m, 1.21H), 1.94 – 1.90 (m, 0.86H), 1.00 (s, 3.5H), 0.96 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.8, 150.5, 143.7, 135.1, 130.0, 115.9, 112.8, 112.0, 110.3, 58.4, 51.7, 51.5, 39.6, 38.9, 31.4, 26.4, 22.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.0, 150.5, 144.8, 135.1, 130.0, 115.9, 112.5, 112.0, 110.3, 57.1, 53.3, 50.8, 39.6, 38.8, 32.0, 27.7, 22.9.

HRMS: m/z $[M+Na]^+$ calcd for $C_{19}H_{26}ClNNaO_2$: 358.1544; found: 358.1545.

methyl 3-(((3-methoxyphenyl)(methyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (12)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 3-methoxy-*N*-methyl-*N*-((trimethylsilyl)methyl)aniline (44.6 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **12** was obtained as a colorless oil (31.1 mg, 47% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.5 (Petroleum ether/ethyl acetate 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (t, *J* = 8.2 Hz, 1H), 6.32 – 6.23 (m, 2H), 6.19 – 6.18 (m, 1H), 5.99 – 5.86 (m, 1H), 5.10 – 4.89 (m, 2H), 3.78 (s, 3H), 3.68 (s, 1.75H), 3.66 (s, 1.25H), 3.27 – 3.23 (m, 2H), 2.90 (s, 1.75H), 2.89 (s, 1.25H), 2.45 – 2.24 (m, 3H), 2.15 – 2.10 (m, 1.23H), 1.96 – 1.90 (m, 0.88H), 1.00 (s, 3.5H), 0.97 (s, 2.5H).

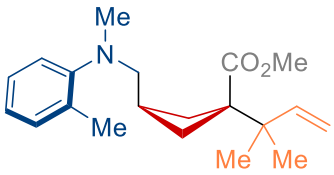
Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.9, 160.8, 150.8, 143.8, 129.8, 112.7, 105.5, 100.9, 99.0, 58.8, 55.2, 51.6, 51.4, 39.6, 39.0, 31.6, 26.5, 22.3.

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.1, 160.8, 150.9, 144.9, 129.8, 112.3, 105.5, 100.9, 99.0, 57.5, 55.2, 53.3, 50.8, 39.6, 38.9, 32.1, 27.8, 23.0.

HRMS: m/z $[M+Na]^+$ calcd for $C_{20}H_{29}NNaO_3$: 354.2040; found: 354.2040.

methyl 3-((methyl(o-tolyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-

carboxylate (13)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), *N*,2-dimethyl-*N*-((trimethylsilyl)methyl)aniline (41.4 mg, 0.2 mmol, 1.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with TMSCH$_2$N$_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et$_2$O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **13** was obtained as a colorless oil (28.4 mg, 45% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.6 (Petroleum ether/ethyl acetate 8:1)

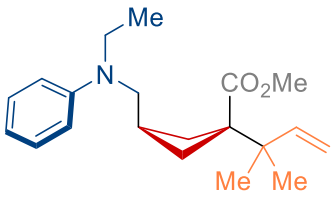
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.17 – 7.08 (m, 2H), 7.00 (d, *J* = 7.8 Hz, 1H), 6.97 – 6.93 (m, 1H), 6.01 – 5.83 (m, 1H), 5.07 – 4.87 (m, 2H), 3.68 (s, 1.25H), 3.63 (s, 1.75H), 2.85 – 2.81 (m, 2H), 2.59 (s, 1.25H), 2.57 (s, 1.75H), 2.39 – 2.33 (m, 1H), 2.31 – 2.13 (m, 5H), 2.09 – 2.01 (m, 1.2H), 1.87 – 1.82 (m, 0.84H), 1.01 (s, 3.5H), 0.95 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, CDCl$_3$) δ 177.9, 152.4, 143.9, 133.6, 131.0, 126.4, 123.2, 120.5, 112.5, 62.7, 51.6, 51.3, 42.4, 39.6, 31.9, 26.6, 22.3, 18.1.

Minor diastereomer: **^{13}C NMR** (101 MHz, CDCl$_3$) δ 177.4, 152.4, 144.9, 133.3, 131.0, 126.4, 123.1, 120.2, 112.1, 61.7, 53.3, 50.8, 42.3, 39.6, 32.4, 27.6, 23.0, 18.2.

HRMS: m/z [M+Na]$^+$ calcd for C$_{20}$H$_{29}$NNaO$_2$: 338.2090; found: 338.2090.

methyl 3-((ethyl(phenyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (14)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), *N*-ethyl-*N*-((trimethylsilyl)methyl)aniline (41.4 mg, 0.2 mmol, 1.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with TMSCH$_2$N$_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et$_2$O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **14** was

obtained as a colorless oil (31.5 mg, 50% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.6 (Petroleum ether/ethyl acetate 8:1)

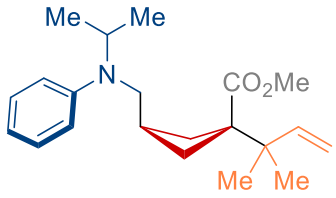
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.14 (m, 2H), 6.69 – 6.57 (m, 3H), 6.00 – 5.87 (m, 1H), 5.11 – 4.91 (m, 2H), 3.69 (s, 1.75H), 3.67 (s, 1.25H), 3.38 – 3.31 (m, 2H), 3.27 – 3.15 (m, 2H), 2.46 – 2.26 (m, 3H), 2.15 – 2.10 (m, 1.2H), 1.99 – 1.85 (m, 0.84H), 1.12 – 1.08 (m, 3H), 1.02 (s, 3.5H), 0.98 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.9, 148.1, 143.8, 129.2, 115.8, 112.7, 112.3, 56.9, 51.6, 51.4, 45.7, 39.6, 31.7, 26.6, 22.3, 12.2.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.2, 148.2, 144.9, 129.2, 115.8, 112.3, 112.3, 55.5, 53.1, 50.6, 45.5, 39.6, 32.2, 27.9, 23.0, 12.2.

HRMS: m/z $[M+Na]^+$ calcd for $C_{20}H_{29}NNaO_2$: 338.2090; found: 338.2090.

methyl 3-((isopropyl(phenyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (15)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), *N*-isopropyl-*N*-((trimethylsilyl)methyl)aniline (44.2 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **15** was obtained as a colorless oil (30.4 mg, 46% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.6 (Petroleum ether/ethyl acetate 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.17 (m, 2H), 6.78 – 6.63 (m, 3H), 5.97 – 5.88 (m, 1H), 5.09 – 4.91 (m, 2H), 3.98 – 3.89 (m, 1H), 3.69 (s, 1.75H), 3.64 (s, 1.25H), 3.04 (t, *J* = 6.2 Hz, 2H), 2.45 – 2.16 (m, 3H), 2.12 – 2.04 (m, 1.15H), 1.89 – 1.84 (m, 0.81H), 1.13 – 1.10 (m, 6H), 0.99 (s, 3.5H), 0.98 (s, 2.5H).

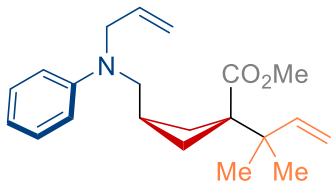
Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.0, 149.1, 143.9, 129.0, 117.3, 115.5, 112.5, 51.6, 50.5, 50.2, 49.8, 39.5, 31.8, 26.5, 22.4, 20.4.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.2, 149.0, 145.0, 129.0, 117.0,

115.0, 112.2, 52.4, 51.4, 50.2, 49.0, 39.7, 32.4, 27.9, 23.0, 20.4.

HRMS: m/z $[M+Na]^+$ calcd for $C_{21}H_{31}NNaO_2$: 352.2247; found: 352.2246.

methyl 3-((allyl(phenyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (16)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), *N*-allyl-*N*-((trimethylsilyl)methyl)aniline (43.9 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **16** was obtained as a colorless oil (32.7 mg, 50% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.6 (Petroleum ether/ethyl acetate 8:1)

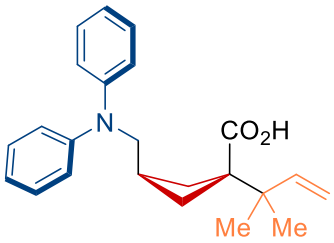
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 – 7.14 (m, 2H), 6.70 – 6.58 (m, 3H), 6.02 – 5.85 (m, 1H), 5.85 – 5.72 (m, 1H), 5.15 – 5.05 (m, 2H), 5.05 – 4.91 (m, 2H), 3.95 – 3.84 (m, 2H), 3.68 (s, 1.75H), 3.67 (s, 1.25H), 3.33 – 3.19 (m, 2H), 2.47 – 2.26 (m, 3H), 2.15 – 2.07 (m, 1.18H), 1.98 – 1.84 (m, 0.82H), 1.01 (s, 3.5H), 0.97 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.8, 148.5, 143.8, 134.3, 129.1, 116.2, 116.0, 112.7, 112.4, 57.1, 54.0, 51.6, 51.4, 39.6, 31.7, 26.6, 22.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.1, 148.5, 144.9, 134.4, 129.1, 116.2, 116.0, 112.5, 112.3, 55.8, 53.8, 53.1, 50.6, 39.6, 32.2, 27.8, 23.0.

HRMS: m/z $[M+Na]^+$ calcd for $C_{21}H_{29}NNaO_2$: 350.2090; found: 350.2092.

3-((diphenylamino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylic acid (17)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), *N*-phenyl-*N*-((trimethylsilyl)methyl)aniline (51.0 mg, 0.2 mmol, 1.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **17** was obtained as a colorless oil (46.8 mg, 67% yield, 1.4:1 dr).

TLC: Rf = 0.4 (Petroleum ether/ethyl acetate 3:1)

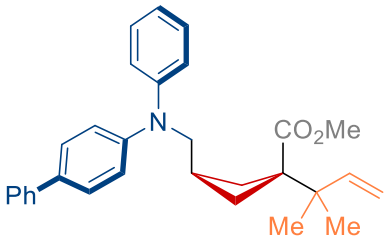
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.13 (m, 4H), 7.03 – 6.79 (m, 6H), 6.06 – 5.79 (m, 1H), 5.14 – 4.89 (m, 2H), 3.75 – 3.52 (m, 2H), 2.63 – 2.30 (m, 1.8H), 2.29 – 2.19 (m, 1.26H), 2.12 – 2.04 (m, 1.2H), 1.96 – 1.75 (m, 0.84H), 1.04 (s, 3.5H), 0.99 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.3, 148.4, 143.4, 129.3, 121.6, 121.3, 113.1, 58.1, 50.4, 39.4, 31.6, 26.7, 22.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.9, 148.4, 144.5, 129.3, 121.5, 121.2, 112.9, 57.0, 52.8, 39.4, 32.0, 27.8, 22.9.

HRMS: m/z [M+Na]$^+$ calcd for $C_{23}H_{27}NNaO_2$: 372.1934; found: 372.1934.

methyl 3-(([1,1'-biphenyl]-4-yl(phenyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (18)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), *N*-phenyl-*N*-((trimethylsilyl)methyl)-[1,1'-biphenyl]-4-amine (66.3 mg, 0.2 mmol, 1.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **18** was obtained as a white solid (37.8 mg, 43% yield for 2 steps, 1.8:1 dr).

TLC: Rf = 0.6 (Petroleum ether/ethyl acetate 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.53 (m, 2H), 7.53 – 7.45 (m, 2H), 7.46 – 7.37 (m,

2H), 7.36 – 7.26 (m, 3H), 7.07 – 6.98 (m, 3H), 6.98 – 6.88 (m, 2H), 6.00 – 5.81 (m, 1H), 5.07 – 4.88 (m, 2H), 3.74 – 3.60 (m, 5H), 2.57 – 2.22 (m, 3H), 2.12 – 2.03 (m, 1.3H), 1.90 – 1.81 (m, 0.72H), 1.00 (s, 3.85H), 0.94 (s, 2.15H).

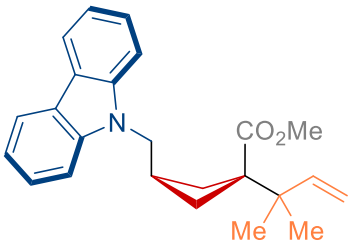
Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.8, 148.1, 147.9, 143.8, 140.9, 133.4, 129.5, 128.8, 127.9, 126.6, 122.8, 122.5, 120.0, 112.7, 58.1, 51.7, 51.4, 39.6, 31.5, 26.9, 22.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.2, 148.0, 147.8, 144.8, 140.9, 133.4, 129.5, 128.8, 127.9, 126.6, 122.6, 122.4, 119.9, 112.4, 57.1, 53.1, 50.7, 39.6, 32.1, 27.9, 23.0.

HRMS: m/z $[M+Na]^+$ calcd for $C_{30}H_{33}NNaO_2$: 462.2404; found: 462.2406.

m.p. 61–62 °C. (**18** was recrystallized from EA/PE = 1:10)

methyl 3-((9*H*-carbazol-9-yl)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (19)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 9-((trimethylsilyl)methyl)-9*H*-carbazole (50.6 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **19** was obtained as a white solid (18.0 mg, 25% yield for 2 steps, 2:1 dr).

TLC: Rf = 0.6 (Petroleum ether/ethyl acetate 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.02 (m, 2H), 7.51 – 7.33 (m, 4H), 7.27 – 7.18 (m, 2H), 5.90 (dd, *J* = 17.3, 10.8 Hz, 0.66H), 5.77 (dd, *J* = 17.4, 10.8 Hz, 0.33H), 5.05 – 4.84 (m, 2H), 4.28 (d, *J* = 7.5 Hz, 1.33H), 4.24 (d, *J* = 6.5 Hz, 0.66H), 3.75 (s, 2H), 3.62 (s, 1H), 2.77 – 2.59 (m, 1H), 2.39 – 2.27 (m, 3.33H), 2.10 – 2.03 (m, 0.67H), 0.98 (s, 4H), 0.89 (s, 2H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.7, 143.6, 140.6, 125.7, 122.9,

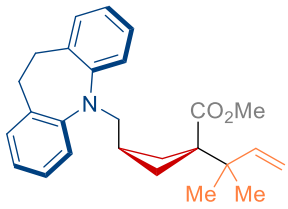
120.3, 118.9, 112.9, 108.8, 51.62, 51.58, 48.7, 39.6, 31.3, 27.8, 22.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.9, 144.6, 140.7, 125.7, 122.9, 120.4, 118.9, 112.6, 108.7, 52.7, 50.7, 47.1, 39.6, 31.7, 29.4, 22.8.

HRMS: m/z $[M+Na]^+$ calcd for $C_{24}H_{27}NNaO_2$: 384.1934; found: 384.1934.

m.p. 78–79 °C. (**19** was recrystallized from EA/PE = 1:10)

methyl 3-((10,11-dihydro-5*H*-dibenzo[b,f]azepin-5-yl)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (20)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 5-((trimethylsilyl)methyl)-10,11-dihydro-5*H*-dibenzo[b,f]azepine (56.2 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **20** was obtained as a white solid (36.1 mg, 46% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.6 (Petroleum ether/ethyl acetate 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 – 7.05 (m, 4H), 7.05 – 6.97 (m, 2H), 6.95 – 6.86 (m, 2H), 5.95 – 5.78 (m, 1H), 5.06 – 4.83 (m, 2H), 3.70 – 3.62 (m, 2H), 3.61 (s, 1.25H), 3.59 (s, 1.75H), 3.13 (s, 4H), 2.34 – 2.27 (m, 1H), 2.26 – 2.13 (m, 2H), 2.11 – 2.04 (m, 1.2H), 1.94 – 1.82 (m, 0.84H), 0.94 (s, 3.5H), 0.93 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.8, 148.4, 143.8, 134.3, 129.8, 126.3, 122.5, 120.1, 112.5, 57.4, 51.5, 51.4, 39.6, 32.2, 31.4, 25.9, 22.3.

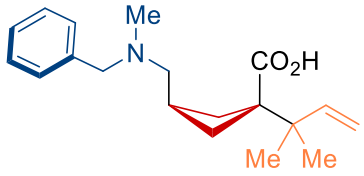
Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.2, 148.5, 144.8, 134.4, 129.8, 126.3, 122.5, 120.0, 112.2, 56.3, 52.9, 50.7, 39.6, 32.2, 31.8, 26.7, 23.0.

HRMS: m/z $[M+Na]^+$ calcd for $C_{26}H_{31}NNaO_2$: 412.2247; found: 412.2247.

m.p. 60–61 °C. (**20** was recrystallized from EA/PE = 1:10)

3-((benzyl(methyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-

carboxylic acid (21)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), *N*-benzyl-*N*-methyl-1-(trimethylsilyl)methanamine (41.4 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **21** was obtained as a yellow oil (44.5 mg, 74% yield, 1.4:1 dr).

TLC: Rf = 0.4 (Dichloromethane/methanol 8:1)

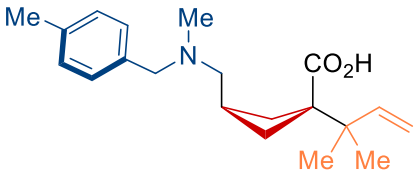
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.11 (m, 5H), 6.07 (dd, *J* = 17.2, 10.9 Hz, 0.59H), 5.92 (dd, *J* = 17.4, 10.8 Hz, 0.41H) 5.08 – 4.76 (m, 2H), 3.51 (s, 0.83H), 3.45 (s, 1.16H), 2.52 – 2.31 (m, 3H), 2.22 (t, *J* = 10.0 Hz, 1H), 2.14 (s, 1.66H), 2.08 (s, 2.33H), 2.04 – 1.97 (m, 1H), 1.77 – 1.63 (m, 1H), 1.01 (s, 3.5H), 0.94 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.1, 145.4, 137.7, 129.5, 128.3, 127.3, 111.7, 64.5, 61.9, 51.4, 41.6, 39.2, 33.2, 25.6, 22.6.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.6, 146.4, 137.0, 129.7, 128.3, 127.5, 111.2, 62.7, 62.2, 53.9, 41.4, 39.2, 33.4, 26.9, 23.3.

HRMS: m/z $[M+Na]^+$ calcd for $C_{19}H_{27}NNaO_2$: 324.1934; found: 324.1935.

3-((methyl(4-methylbenzyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylic acid (22)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), *N*-methyl-*N*-(4-methylbenzyl)-1-(trimethylsilyl)methanamine (44.2 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **22** was obtained as a colorless oil (36.6 mg, 58% yield, 1.4:1 dr).

TLC: Rf = 0.4 (Dichloromethane/methanol 8:1)

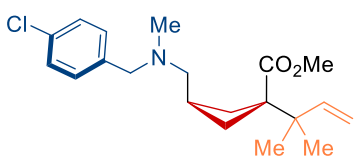
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 – 7.00 (m, 4H), 6.07 (dd, *J* = 17.8, 10.4 Hz, 0.58H), 5.94 (dd, *J* = 17.4, 10.8 Hz, 0.42H), 5.04 – 4.85 (m, 2H), 3.65 (s, 0.83H), 3.55 (s, 1.17H), 2.56 (d, *J* = 5.6 Hz, 1.75H), 2.47 – 2.40 (m, 1.25H), 2.31 (s, 1.25H), 2.29 (s, 1.75H), 2.27 – 2.02 (m, 6H), 1.78 – 1.66 (m, 1H), 1.03 (s, 3.5H), 0.98 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.0, 145.1, 137.3, 133.0, 129.9, 129.1, 111.4, 63.4, 60.9, 51.2, 40.7, 39.2, 33.1, 25.1, 22.6, 21.2.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.5, 146.2, 137.8, 131.5, 130.3, 129.2, 111.8, 62.0, 61.1, 54.2, 40.1, 39.1, 33.9, 27.0, 23.3, 21.2.

HRMS: m/z $[M+Na]^+$ calcd for $C_{20}H_{29}NNaO_2$: 338.2090; found: 338.2091.

3-(((4-chlorobenzyl)(methyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylic acid (23)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), *N*-(4-chlorobenzyl)-*N*-methyl-1-(trimethylsilyl)methanamine (48.4 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol,1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **23** was obtained as a colorless oil (33.6 mg, 48% yield, 1.8:1 dr).

TLC: Rf = 0.4 (Dichloromethane/methanol 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.10 (m, 4H), 5.97 (dd, *J* = 17.3, 10.8 Hz, 0.64H), 5.82 (dd, *J* = 17.4, 10.8 Hz, 0.36H), 5.12 – 4.83 (m, 2H), 3.68 (s, 1.08H), 3.60 (s, 1.92H), 3.36 (s, 2H), 2.43 – 2.33 (m, 1H), 2.32 – 2.26 (m, 3H), 2.25 – 2.12 (m, 1H), 2.10 (s, 1.08H), 2.09 (s, 1.92H), 2.03 – 1.96 (m, 1.28H), 1.85 – 1.75 (m, 0.72H), 1.00 (s, 3.85H), 0.93 (s, 2.15H).

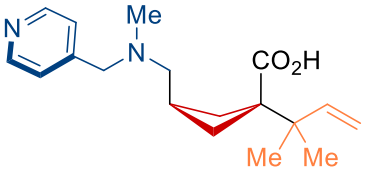
Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.8, 143.9, 137.9, 132.6, 130.2, 128.3, 112.6, 64.2, 62.0, 51.6, 51.3, 42.4, 39.5, 32.1, 26.4, 22.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.4, 144.8, 137.9, 132.6, 130.3,

128.3, 112.1, 62.9, 61.7, 53.3, 50.7, 42.5, 39.5, 32.5, 27.3, 22.9.

HRMS: m/z $[M+Na]^+$ calcd for $C_{19}H_{26}ClNNaO_2$: 372.1701; found: 372.1702.

3-((methyl(pyridin-4-ylmethyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylic acid (24)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), *N*-methyl-1-(pyridin-4-yl)-*N*-((trimethylsilyl)methyl)methanamine (41.6 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **24** was obtained as a white solid (28.4 mg, 47% yield, 1.4:1 dr).

TLC: Rf = 0.3 (Dichloromethane/methanol 8:1)

^{1}H NMR (400 MHz, CD_3OD) δ 8.58 – 8.31 (m, 2H), 7.50 – 7.30 (m, 2H), 6.12 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.94 (dd, *J* = 17.4, 10.8 Hz, 0.42H), 5.05 – 4.90 (m, 2H), 3.52 (s, 2H), 2.45 – 2.30 (m, 3H), 2.28 – 2.21 (m, 1H), 2.18 (s, 1.25H), 2.16 (s, 1.75H), 2.14 – 1.94 (m, 2H), 1.78 – 1.69 (m, 1H), 1.04 (s, 3.5H), 0.96 (s, 2.5H).

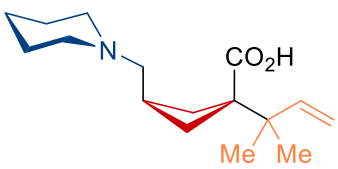
Major diastereomer: **^{13}C NMR** (101 MHz, CD_3OD) δ 183.5, 149.5, 148.6, 145.2, 124.4, 110.9, 64.6, 60.7, 51.6, 41.5, 38.7, 32.9, 25.3, 21.8.

Minor diastereomer: **^{13}C NMR** (101 MHz, CD_3OD) δ 182.1, 149.4, 148.6, 146.2, 124.6, 110.6, 62.8, 60.5, 53.7, 41.5, 38.8, 32.9, 26.5, 22.4.

HRMS: m/z $[M+Na]^+$ calcd for $C_{18}H_{26}N_2NaO_2$: 325.1886; found: 325.1887.

m.p. 180–181 °C. (**24** was recrystallized from DCM/PE = 1:5)

1-(2-methylbut-3-en-2-yl)-3-(piperidin-1-ylmethyl)cyclobutane-1-carboxylic acid (25)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 1-((trimethylsilyl)methyl)piperidine (34.2 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **25** was obtained

as a yellow oil (21.5 mg, 41% yield, 1.4:1 dr).

TLC: Rf = 0.3 (Dichloromethane/methanol 8:1)

Major diastereomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.17 – 6.00 (m, 1H), 5.04 – 4.87 (m, 2H), 2.86 – 2.33 (m, 6H), 2.31 – 1.98 (m, 5H), 1.63 (p, *J* = 5.5 Hz, 4H), 1.43 (s, 2H), 1.02 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 183.7, 145.7, 111.4, 64.8, 53.5, 51.3, 39.2, 32.9, 24.4, 23.8, 23.5, 22.7.

HRMS: m/z $[M+Na]^+$ calcd for $C_{16}H_{27}NNaO_2$: 288.1934; found: 288.1934.

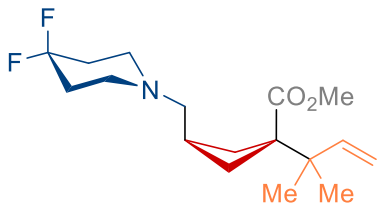
Minor diastereomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.06 – 4.82 (m, 2H), 2.60 (s, 3H), 2.44 (t, *J* = 9.0 Hz, 6H), 1.68 (d, *J* = 8.3 Hz, 6H), 1.56 – 1.38 (m, 2H), 1.02 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 182.6, 147.1, 110.7, 64.3, 54.6, 54.1, 38.9, 34.4, 27.2, 24.5, 23.6, 23.4.

HRMS: m/z $[M+Na]^+$ calcd for $C_{16}H_{27}NNaO_2$: 288.1934; found: 288.1934.

methyl 3-((4,4-difluoropiperidin-1-yl)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (26)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 4,4-difluoro-1-((trimethylsilyl)methyl)piperidine (41.4 mg, 0.2 mmol, 1.0 equiv.) and Ir(dtbbpy)$(ppy)_2$][PF_6] (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 4 h. Product **26** was obtained as a yellow oil (29.0 mg, 46% yield for 2 steps, 1.8:1 dr).

TLC: Rf = 0.6 (Dichloromethane/methanol 15:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96 (dd, *J* = 17.3, 10.9 Hz, 0.64H), 5.85 (dd, *J* = 17.4, 10.8 Hz, 0.36H), 5.06 – 4.88 (m, 2H), 3.67 (s, 1.08H), 3.63 (s, 1.92H), 2.44 (t, *J* = 5.7 Hz, 4H),

2.39 – 2.30 (m, 3H), 2.30 – 2.26 (m, 1H), 2.24 – 2.08 (m, 1H), 2.04 – 1.98 (m, 1H), 1.97 – 1.85 (m, 4H), 1.85 – 1.76 (m, 1H), 0.99 (s, 3.85H), 0.94 (s, 2.15H).

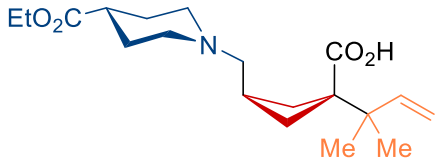
Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.8, 143.7, 122.0 (t, *J* = 242.4 Hz), 112.7, 64.4, 51.6, 51.3, 50.1 (t, *J* = 5.4 Hz), 39.5, 34.0 (t, *J* = 23.2 Hz), 32.4, 26.4, 22.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.3, 144.8, 122.0 (t, *J* = 242.4 Hz), 112.2, 63.3, 53.5, 50.7, 50.1 (t, *J* = 5.4 Hz), 39.5, 34.0 (t, *J* = 23.2 Hz), 32.8, 27.4, 23.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.1.

HRMS: m/z $[M+Na]^+$ calcd for $C_{17}H_{27}F_2NNaO_2$: 338.1902; found: 338.1903.

3-((4-(ethoxycarbonyl)piperidin-1-yl)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylic acid (27)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), ethyl 1-((trimethylsilyl)methyl)piperidine-4-carboxylate (48.6 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **27** was obtained as a yellow oil (44.5 mg, 66% yield, 1.4:1 dr).

TLC: Rf = 0.2 (Dichloromethane/methanol 8:1)

Major diastereomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.07 (dd, *J* = 17.2, 11.0 Hz, 1H), 5.03 – 4.87 (m, 2H), 4.09 (q, *J* = 7.2 Hz, 2H), 2.84 (d, *J* = 11.1 Hz, 2H), 2.40 (d, *J* = 6.5 Hz, 2H), 2.30 – 2.14 (m, 3H), 2.01 (dt, *J* = 19.5, 10.0 Hz, 5H), 1.85 (d, *J* = 10.6 Hz, 2H), 1.80 – 1.65 (m, 2H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.00 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 184.2, 174.9, 145.7, 111.5, 65.4, 60.4, 52.6, 51.5, 40.7, 39.1, 33.1, 27.6, 24.9, 22.7, 14.3.

HRMS: m/z $[M+Na]^+$ calcd for $C_{19}H_{31}NNaO_4$: 360.2145; found: 360.2145.

Minor diastereomer:

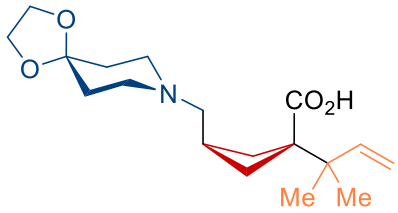
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96 (dd, *J* = 17.4, 10.8 Hz, 1H), 4.90 (dd, *J* = 26.1, 14.1 Hz,

2H), 4.10 (q, *J* = 7.1 Hz, 2H), 2.86 (d, *J* = 10.6 Hz, 2H), 2.45 – 2.19 (m, 6H), 2.10 (s, 2H), 1.91 – 1.61 (m, 6H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.95 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 182.6, 174.9, 146.8, 110.9, 64.2, 60.5, 54.3, 52.7, 40.4, 39.0, 34.0, 27.3, 23.3, 14.3.

HRMS: m/z $[M+Na]^+$ calcd for $C_{19}H_{31}NNaO_4$: 360.2145; found: 360.2144.

3-((1,4-dioxa-8-azaspiro[4.5]decan-8-yl)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylic acid (28)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 8-((trimethylsilyl)methyl)-1,4-dioxa-8-azaspiro[4.5]decane (45.8 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **28** was obtained as a white solid (42.6 mg, 66% yield, 1.4:1 dr).

TLC: Rf = 0.2 (Dichloromethane/methanol 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.15 – 5.94 (m, 1H), 5.12 – 4.78 (m, 2H), 3.93 (s, 4H), 2.67 (s, 4H), 2.58 (s, 1H), 2.48 – 2.35 (m, 2H), 2.28 – 2.17 (m, 1H), 2.17 – 2.02 (m, 2H), 1.87 – 1.61 (m, 5H), 1.03 (s, 3.5H), 0.98 (s, 2.5H).

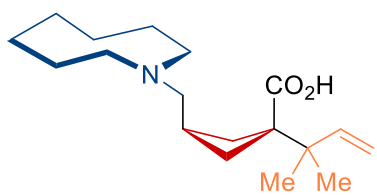
Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.8, 145.5, 111.7, 106.5, 64.3, 64.0, 51.2, 50.8, 39.2, 33.7, 32.5, 24.3, 22.6.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.2, 146.5, 111.3, 106.4, 64.3, 63.4, 54.2, 51.2, 39.0, 33.9, 33.7, 27.1, 23.3.

HRMS: m/z $[M+Na]^+$ calcd for $C_{18}H_{29}NNaO_4$: 346.1989; found: 346.1989.

m.p. 104–105 °C. (**28** was recrystallized from DCM/PE = 1:5)

3-(azocan-1-ylmethyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylic acid (29)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 1-((trimethylsilyl)methyl)azocane

(39.8 mg, 0.2 mmol, 1.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **29** was obtained as a yellow oil (41.0 mg, 70% yield, 1.4:1 dr).

TLC: Rf = 0.3 (Dichloromethane/methanol 8:1)

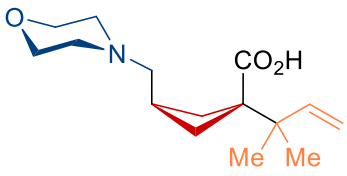
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.04 (dd, *J* = 17.4, 10.8 Hz, 0.58H), 5.94 (dd, *J* = 17.4, 10.8 Hz, 0.42H), 5.07 – 4.74 (m, 2H), 2.99 – 2.91 (m, 1H), 2.90 – 2.75 (m, 2H), 2.76 – 2.60 (m, 2H), 2.59 – 2.25 (m, 2H), 2.25 – 1.98 (m, 3H), 1.78 – 1.46 (m, 11H), 0.99 (s, 3.5H), 0.95 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.9, 145.4, 111.6, 62.1, 51.2, 50.5, 39.1, 32.6, 26.9, 25.5, 24.3, 22.6.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.4, 146.6, 111.2, 60.0, 54.4, 49.8, 38.9, 34.2, 26.8, 25.0, 24.3, 23.3.

HRMS: m/z [M+Na]$^+$ calcd for $C_{18}H_{31}NNaO_2$: 316.2247; found: 316.2247.

1-(2-methylbut-3-en-2-yl)-3-(morpholinomethyl)cyclobutane-1-carboxylic acid (30)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 4-((trimethylsilyl)methyl)morpholine (34.6 mg, 0.2 mmol, 1.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **30** was obtained as a colorless oil (34.2 mg, 64% yield, 1.4:1 dr).

TLC: Rf = 0.3 (Dichloromethane/methanol 8:1)

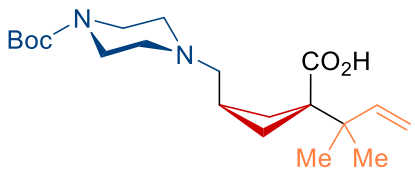
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.11 (dd, *J* = 17.4, 10.8 Hz, 0.58H), 6.01 (dd, *J* = 17.4, 10.8 Hz, 0.42H), 5.14 – 4.89 (m, 2H), 3.90 – 3.60 (m, 4H), 2.78 – 2.28 (m, 7H), 2.29 – 2.04 (m, 3H), 1.84 – 1.64 (m, 1H), 1.06 (s, 3.5H), 1.02 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 185.4, 145.2, 112.1, 66.4, 65.1, 53.6, 51.2, 39.3, 32.4, 26.6, 22.7.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 185.4, 146.3, 111.6, 66.2, 64.7, 53.6, 53.2, 39.2, 33.5, 29.8, 23.3.

HRMS: m/z [M+Na]$^+$ calcd for $C_{15}H_{25}NNaO_3$: 290.1727; found: 290.1727.

3-((4-(*tert*-butoxycarbonyl)piperazin-1-yl)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylic acid (31)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), *tert*-butyl 4-((trimethylsilyl)methyl)piperazine-1-carboxylate (54.4 mg, 0.2 mmol, 1.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **31** was obtained as a yellow solid (44.0 mg, 60% yield, 1.4:1 dr).

TLC: Rf = 0.4 (Dichloromethane/methanol 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.02 (dd, *J* = 17.2, 10.9 Hz, 0.58H), 5.89 (dd, *J* = 17.4, 10.8 Hz, 0.42H), 5.12 – 4.79 (m, 2H), 3.56 – 3.27 (m, 4H), 2.56 – 2.27 (m, 7H), 2.27 – 2.07 (m, 2H), 2.04 – 1.94 (m, 1H), 1.77 – 1.63 (m, 1H), 1.42 (s, 9H), 1.00 (s, 3.5H), 0.95 (s, 2.5H).

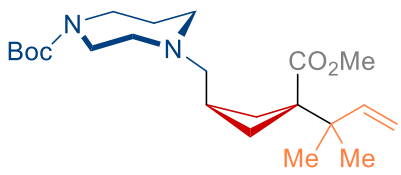
Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.1, 154.7, 144.7, 112.2, 79.8, 65.1, 52.6, 51.0, 42.5, 39.1, 32.9, 28.5, 24.9, 22.5.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.5, 154.6, 145.6, 111.8, 79.9, 63.9, 54.0, 52.8, 43.3, 39.1, 33.7, 28.5, 27.2, 23.2.

HRMS: m/z [M+Na]$^+$ calcd for $C_{20}H_{34}N_2NaO_4$: 389.2411; found: 389.2411.

m.p. 140–141 °C. (**31** was recrystallized from DCM/PE = 1:5)

***tert*-butyl 4-((3-(methoxycarbonyl)-3-(2-methylbut-3-en-2-yl)cyclobutyl)methyl)-1,4-diazepane-1-carboxylate (32)**



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), *tert*-butyl 4-((trimethylsilyl)methyl)-1,4-diazepane-1-carboxylate

(57.2 mg, 0.2 mmol, 1.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with TMSCH$_2$N$_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et$_2$O/MeOH solution (4:1, 2.0 mL) at rt for 4 h. Product **32** was obtained as a yellow oil (26.1 mg, 33% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.6 (Dichloromethane/methanol 15:1)

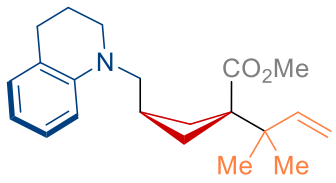
^{1}H NMR (400 MHz, CDCl$_3$) δ 5.99 (dd, *J* = 17.3, 10.8 Hz, 0.58H), 5.88 (dd, *J* = 17.4, 10.8 Hz, 0.42H), 5.10 – 4.90 (m, 2H), 3.70 (s, 1.25H), 3.66 (s, 1.75H), 3.52 – 3.32 (m, 4H), 2.66 – 2.51 (m, 4H), 2.50 – 2.43 (m, 2H), 2.42 – 2.35 (m, 1H), 2.35 – 2.10 (m, 3H), 2.07 – 2.00 (m, 1H), 1.85 – 1.75 (m, 2H), 1.45 (s, 9H), 1.02 (s, 3.5H), 0.97 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, CDCl$_3$) δ 177.9, 155.6, 143.8, 112.6, 79.3, 64.3, 56.1, 54.9, 51.6, 51.4, 46.6, 46.0, 39.5, 32.4, 28.6, 27.6, 26.7, 22.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, CDCl$_3$) δ 177.4, 155.7, 144.8, 112.1, 79.3, 63.2, 56.1, 54.9, 53.5, 50.7, 46.0, 45.2, 39.5, 32.8, 29.8, 28.6, 27.8, 23.0.

HRMS: m/z [M+Na]$^+$ calcd for $C_{22}H_{38}N_2NaO_4$: 417.2724; found: 417.2725.

methyl 3-((3,4-dihydroquinolin-1(2*H*)-yl)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (33)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 1-((trimethylsilyl)methyl)-1,2,3,4-tetrahydroquinoline (43.8 mg, 0.2 mmol, 1.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with TMSCH$_2$N$_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et$_2$O/MeOH solution (4:1, 2.0 mL) at rt for 2 h. Product **33** was obtained as a colorless oil (22.2 mg, 34% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.6 (Petroleum ether/ethyl acetate 8:1)

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.06 – 6.95 (m, 1H), 6.96 – 6.86 (m, 1H), 6.59 – 6.50 (m,

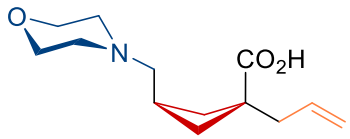
1H), 6.50 – 6.43 (m, 1H), 6.02 – 5.84 (m, 1H), 5.11 – 4.89 (m, 2H), 3.68 (s, 1.75H), 3.67 (s, 1.25H), 3.32 – 3.13 (m, 4H), 2.72 (t, *J* = 6.4 Hz, 2H), 2.48 – 2.28 (m, 3H), 2.17 – 2.10 (m, 1H), 1.98 – 1.83 (m, 3H), 1.01 (s, 3.5H), 0.98 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.9, 145.5, 143.8, 129.3, 127.0, 122.3, 115.6, 112.7, 110.6, 57.7, 51.6, 51.4, 50.4, 39.6, 32.3, 28.2, 26.2, 22.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.2, 145.5, 144.9, 129.3, 127.0, 122.3, 115.6, 112.3, 110.6, 56.3, 53.4, 50.7, 50.2, 39.6, 31.8, 28.2, 27.6, 23.0, 22.3.

HRMS: m/z $[M+H]^+$ calcd for $C_{21}H_{30}NO_2$: 328.2271; found: 328.2271.

1-allyl-3-(morpholinomethyl)cyclobutane-1-carboxylic acid (34)



Following the general procedure, allyl bicyclo[1.1.0]butane-1-carboxylate (55.2 mg, 0.4 mmol, 2.0 equiv.), 4-((trimethylsilyl)methyl)morpholine (34.6 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **34** was obtained as a yellow oil (23.4 mg, 49% yield, 1.4:1 dr).

TLC: Rf = 0.3 (Dichloromethane/methanol 8:1)

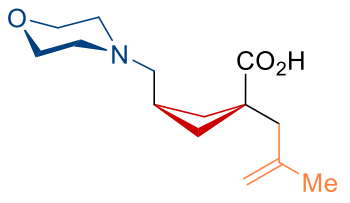
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.38 (s, 1H), 5.94 – 5.53 (m, 1H), 5.18 – 4.86 (m, 2H), 3.68 (t, *J* = 4.5 Hz, 4H), 2.68 – 2.22 (m, 10H), 2.20 – 1.77 (m, 2H), 1.68 – 1.50 (m, 1H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.5, 134.8, 117.4, 66.2, 64.6, 53.2, 44.2, 34.7, 25.1.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.5, 134.6, 117.1, 66.2, 65.3, 53.2, 41.8, 36.5, 27.1.

HRMS: m/z $[M+Na]^+$ calcd for $C_{13}H_{21}NNaO_3$: 262.1414; found: 262.1414.

1-(2-methylallyl)-3-(morpholinomethyl)cyclobutane-1-carboxylic acid (35)



Following the general procedure, 2-methylallyl bicyclo[1.1.0]butane-1-carboxylate (60.8 mg, 0.4 mmol, 2.0 equiv.), 4-((trimethylsilyl)methyl)morpholine (34.6 mg,

0.2 mmol, 1.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **35** was obtained as a yellow oil (21.3 mg, 42% yield, 1.4:1 dr).

TLC: Rf = 0.3 (Dichloromethane/methanol 8:1)

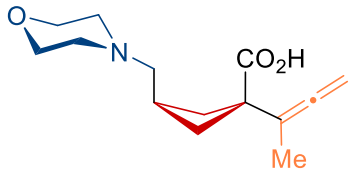
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 4.75 – 4.51 (m, 2H), 3.69 (t, *J* = 4.6 Hz, 4H), 2.76 – 2.23 (m, 10H), 2.21 – 2.00 (m, 2H), 1.71 – 1.56 (m, 4H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.1, 143.2, 111.9, 66.0, 64.2, 52.9, 48.1, 45.3, 35.4, 25.1, 23.6.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.6, 143.1, 111.7, 66.0, 65.1, 53.1, 45.9, 43.7, 38.2, 27.9, 23.5.

HRMS: m/z [M+Na]$^+$ calcd for $C_{14}H_{23}NNaO_3$: 276.1570; found: 276.1571.

1-(buta-2,3-dien-2-yl)-3-(morpholinomethyl)cyclobutane-1-carboxylic acid (36)



Following the general procedure, but-2-yn-1-yl bicyclo[1.1.0]butane-1-carboxylate (60.0 mg, 0.4 mmol, 2.0 equiv.), 4-((trimethylsilyl)methyl)morpholine (34.6 mg, 0.2 mmol, 1.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **36** was obtained as a yellow oil (31.1 mg, 62% yield, 1.4:1 dr).

TLC: Rf = 0.3 (Dichloromethane/methanol 8:1)

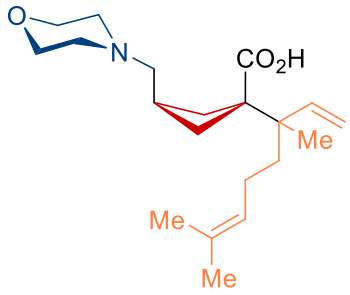
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (s, 1H), 4.94 – 4.59 (m, 2H), 3.85 – 3.53 (m, 4H), 2.69 – 2.36 (m, 7H), 2.38 – 2.26 (m, 1H), 2.26 – 2.16 (m, 1H), 2.14 – 2.03 (m, 1H), 1.87 – 1.71 (m, 1H), 1.61 (s, 1.75H), 1.56 (s, 1.25H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 205.7, 181.7, 101.7, 76.6, 66.3, 64.6, 53.2, 47.2, 35.5, 25.8, 15.1.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 205.8, 181.7, 103.9, 76.6, 66.3, 65.3, 53.4, 48.1, 36.6, 26.3, 14.8.

HRMS: m/z [M+Na]$^+$ calcd for $C_{14}H_{21}NNaO_3$: 274.1414; found: 274.1414.

1-(3,7-dimethylocta-1,6-dien-3-yl)-3-(morpholinomethyl)cyclobutane-1-carboxylic acid (37)



Following the general procedure, (*E*)-3,7-dimethylocta-2,6-dien-1-yl bicyclo[1.1.0]butane-1-carboxylate (93.6 mg, 0.4 mmol, 2.0 equiv.), 4-((trimethylsilyl)methyl)morpholine (34.6 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **37** was obtained as a yellow oil (28.8 mg, 43% yield, 1.4:1 dr).

TLC: Rf = 0.3 (Dichloromethane/methanol 8:1)

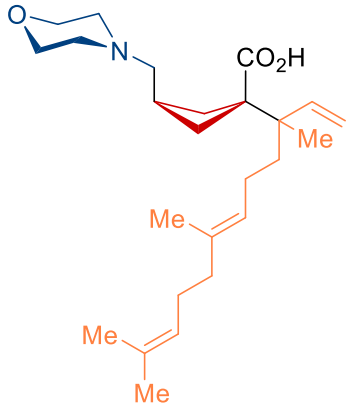
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 – 5.72 (m, 1H), 5.25 – 4.85 (m, 3H), 3.85 – 3.50 (m, 4H), 2.63 – 2.35 (m, 6H), 2.34 – 1.96 (m, 4H), 1.83 – 1.74 (m, 2H), 1.71 – 1.57 (m, 4H), 1.53 (s, 3H), 1.48 – 1.30 (m, 2H), 0.99 (s, 1.75H), 0.96 (s, 1.25H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.7, 142.7, 131.0, 125.2, 114.4, 66.1, 65.0, 53.0, 51.7, 42.6, 35.2, 32.7, 32.3, 25.8, 24.4, 23.4, 17.7, 17.0.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.0, 143.9, 131.0, 125.1, 113.9, 66.0, 64.1, 54.8, 53.3, 42.3, 36.6, 34.3, 34.0, 27.8, 25.8, 23.3, 18.1, 17.7.

HRMS: m/z $[M+Na]^+$ calcd for $C_{20}H_{33}NNaO_3$: 358.2353; found: 358.2352.

(*E*)-3-(morpholinomethyl)-1-(3,7,11-trimethyldodeca-1,6,10-trien-3-yl)cyclobutane-1-carboxylic acid (38)



Following the general procedure, (2*E*,6*E*)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl bicyclo[1.1.0]butane-1-carboxylate (120.8 mg, 0.4 mmol, 2.0 equiv.), 4-((trimethylsilyl)methyl)morpholine (34.6 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **38** was obtained as a

colorless oil (33.1 mg, 41% yield, 1.4:1 dr).

TLC: Rf = 0.3 (Dichloromethane/methanol 8:1)

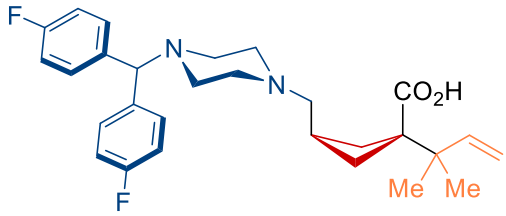
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 5.93 (dd, *J* = 17.4, 10.8 Hz, 0.58H), 5.84 (dd, *J* = 17.5, 10.8 Hz, 0.42H), 5.24 – 4.87 (m, 4H), 3.84 – 3.60 (m, 4H), 2.80 – 2.50 (m, 5H), 2.49 – 2.37 (m, 2H), 2.35 – 2.09 (m, 3H), 2.07 – 1.99 (m, 2H), 1.97 – 1.89 (m, 2H), 1.87 – 1.72 (m, 3H), 1.66 (s, 3H), 1.58 (s, 3H), 1.55 (s, 3H), 1.48 – 1.31 (m, 2H), 1.02 (s, 1.75H), 0.98 (s, 1.25H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.5, 142.4, 134.7, 131.3, 124.9, 124.4, 114.6, 65.9, 64.3, 52.6, 51.3, 42.6, 39.8, 35.3, 32.6, 32.2, 26.8, 25.7, 24.1, 23.3, 17.7, 17.0, 16.0.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 180.2, 143.8, 134.7, 131.3, 124.9, 124.4, 114.0, 65.7, 63.8, 54.8, 53.1, 42.3, 39.8, 36.6, 34.5, 34.1, 27.9, 26.8, 25.7, 23.1, 18.1, 17.7, 16.0.

HRMS: m/z $[M+Na]^+$ calcd for $C_{25}H_{41}NNaO_3$: 426.2979; found: 426.2977.

3-((4-(bis(4-fluorophenyl)methyl)piperazin-1-yl)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylic acid (39)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 1-(bis(4-fluorophenyl)methyl)-4-((trimethylsilyl)methyl)piperazine (75.0 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Product **39** was obtained as a yellow solid (46.9 mg, 50% yield, 1.4:1 dr).

TLC: Rf = 0.4 (Dichloromethane/methanol 8:1)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.19 (m, 4H), 6.90 – 6.82 (m, 4H), 5.94 (dd, *J* = 17.7, 10.4 Hz, 0.58H), 5.83 (dd, *J* = 17.4, 10.8 Hz, 0.42H), 4.97 – 4.81 (m, 2H), 4.12 (s, 1H), 2.81 – 2.50 (m, 4H), 2.51 – 2.23 (m, 6H), 2.22 – 1.92 (m, 4H), 1.69 – 1.56 (m, 1H), 0.93

(s, 3.5H), 0.89 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.2, 161.9 (d, *J* = 246.4 Hz), 144.6, 137.6 (d, *J* = 4.0 Hz), 129.3 (d, *J* = 6.1 Hz), 115.6 (d, *J* = 21.2 Hz), 112.2, 74.2, 63.0, 52.0, 50.6, 50.0, 39.2, 32.3, 23.8, 22.5.

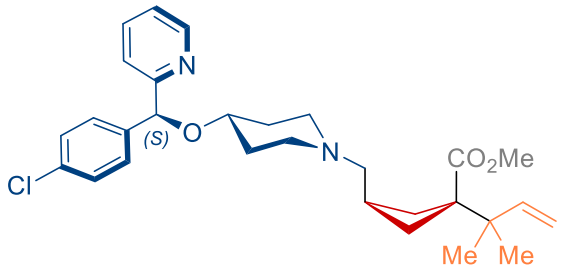
Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 180.1, 161.9 (d, *J* = 246.4 Hz), 145.8, 137.5 (d, *J* = 4.0 Hz), 129.2 (d, *J* = 6.1 Hz), 115.6 (d, *J* = 21.2 Hz), 111.7, 74.1, 62.9, 54.4, 52.7, 49.9, 38.9, 34.2, 27.3, 23.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -115.2, -115.3.

HRMS: m/z $[M+Na]^+$ calcd for $C_{28}H_{34}F_2N_2NaO_2$: 491.2481; found: 491.2484.

m.p. 103–104 °C. (**39** was recrystallized from DCM/PE = 1:5)

methyl 3-((4-((4-chlorophenyl)(pyridin-2-yl)methoxy)piperidin-1-yl)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (40)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), 2-((4-chlorophenyl)((1-((trimethylsilyl)methyl)piperidin-4-yl)oxy)methyl)pyridine (77.8 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with $TMSCH_2N_2$ (0.5 mL, 1.0 mmol, 5 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 4 h. Product **40** was obtained as a yellow oil (39.8 mg, 40% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.6 (Dichloromethane/methanol 15:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 – 8.43 (m, 1H), 7.68 – 7.61 (m, 1H), 7.54 – 7.47 (m, 1H), 7.37 – 7.30 (m, 2H), 7.27 – 7.21 (m, 2H), 7.16 – 7.08 (m, 1H), 5.96 (dd, *J* = 17.3, 10.9 Hz, 0.58H), 5.85 (dd, *J* = 17.4, 10.8 Hz, 0.42H), 5.56 (s, 1H), 5.07 – 4.86 (m, 2H), 3.66 (s, 1.25H), 3.62 (s, 1.75H), 3.46 – 3.36 (m, 1H), 2.69 – 2.58 (m, 2H), 2.41 – 2.26 (m, 4H), 2.24 – 2.14 (m, 1H), 2.13 – 2.04 (m, 2H), 2.03 – 1.97 (m, 1H), 1.90 – 1.76 (m, 3H),

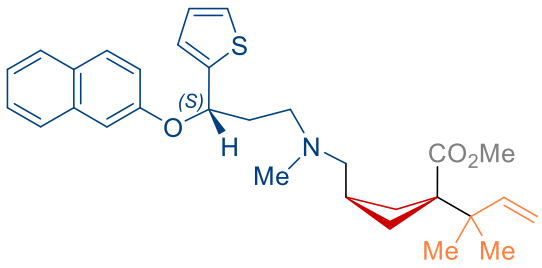
1.73 – 1.63 (m, 2H), 0.99 (s, 3.5H), 0.93 (s, 2.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.8, 162.2, 148.9, 143.8, 140.5, 136.9, 133.3, 128.5, 128.2, 122.5, 120.7, 112.6, 80.9, 73.1, 65.4, 51.6, 51.3, 51.0, 39.5, 32.7, 31.3, 26.5, 22.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.3, 162.2, 148.9, 144.8, 140.5, 136.9, 133.3, 128.5, 128.2, 122.5, 120.7, 112.1, 80.9, 73.1, 64.1, 53.5, 51.0, 50.6, 39.5, 33.0, 31.3, 27.4, 23.0.

HRMS: m/z $[M+Na]^+$ calcd for $C_{29}H_{37}ClN_2NaO_3$: 519.2385; found: 519.2385.

methyl (*R*)-3-((methyl(3-(naphthalen-2-yloxy)-3-(thiophen-2-yl)propyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylate (41)



Following the general procedure, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate (66.4 mg, 0.4 mmol, 2.0 equiv.), (*R*)-*N*-methyl-3-(naphthalen-2-yloxy)-3-(thiophen-2-yl)-*N*-((trimethylsilyl)methyl)propan-1-amine (76.6 mg, 0.2 mmol, 1.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 24 h. Then the isolated carboxylic acid product was treated with $TMSCH_2N_2$ (0.4 mL, 0.8 mmol, 4.0 equiv.) in Et_2O/MeOH solution (4:1, 2.0 mL) at rt for 4 h. Product **41** was obtained as a yellow oil (34.4 mg, 35% yield for 2 steps, 1.4:1 dr).

TLC: Rf = 0.6 (Dichloromethane/methanol 15:1)

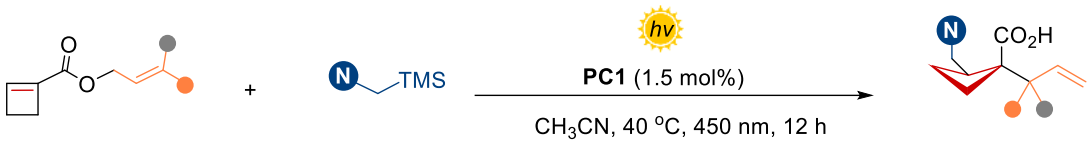
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 – 8.29 (m, 1H), 7.85 – 7.70 (m, 1H), 7.54 – 7.43 (m, 2H), 7.43 – 7.34 (m, 1H), 7.31 – 7.25 (m, 1H), 7.23 – 7.16 (m, 1H), 7.10 – 7.02 (m, 1H), 6.98 – 6.90 (m, 1H), 6.90 – 6.81 (m, 1H), 5.87 – 5.69 (m, 2H), 5.00 – 4.83 (m, 2H), 3.66 (s, 1.25H), 3.61 (s, 1.75H), 2.64 – 2.49 (m, 1H), 2.44 – 2.33 (m, 2H), 2.30 (t, *J* = 6.5 Hz, 2H), 2.26 – 2.10 (m, 6H), 2.08 – 1.92 (m, 2H), 1.82 – 1.67 (m, 1H), 0.92 (s, 2.5H), 0.90 (s, 3.5H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.9, 153.5, 145.5, 143.9, 134.7, 127.6, 126.6, 126.3, 126.2, 125.8, 125.2, 124.7, 124.6, 122.2, 120.5, 112.4, 107.0, 74.2, 65.0, 53.4, 51.6, 51.3, 42.8, 39.4, 37.0, 32.2, 26.5, 22.2, 22.1.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.4, 153.6, 145.6, 144.9, 134.7, 127.5, 126.6, 126.3, 126.2, 125.8, 125.2, 124.7, 124.6, 122.2, 120.6, 112.1, 107.1, 74.5, 63.6, 54.0, 53.3, 50.7, 42.4, 39.5, 36.8, 32.6, 27.3, 23.0, 22.9.

HRMS: m/z $[M+Na]^+$ calcd for $C_{30}H_{37}NNaO_3S$: 514.2386; found: 514.2386.

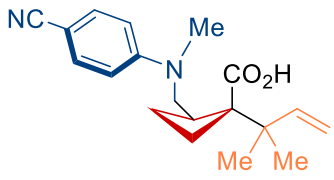
5. General procedures for the SRRC process of cyclobutenes



4 **2** **42-53**

In the glovebox, cyclobut-1-ene-1-carboxylate **4** (0.2 mmol, 1.0 equiv.), α-silylamine **2** (0.4 mmol, 2.0 equiv.), Ir(dtbbpy)(ppy)$_2$][PF$_6$] (**PC1**, 3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%) and dry CH_3CN (0.25 mL) were added respectively into a flame-dried reaction vial equipped with a stir bar. Then the vial was sealed and transferred out of the glove box. Afterwards, it was irradiated with a 1 W blue LED lamp (450 nm, SYNLED) for 12 h at 40 °C. When the reaction was completed (monitored by TLC), the crude mixture was concentrated by rotary evaporation. Then the residue was purified by silica gel flash chromatography or preparative thin layer chromatography to give the corresponding carboxylic acid product.

2-(((4-cyanophenyl)(methyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylic acid (42)



Following the general procedure, 3-methylbut-2-en-1-yl cyclobut-1-ene-1-carboxylate (33.2 mg, 0.2 mmol, 1.0 equiv.), 4-(methyl((trimethylsilyl)methyl)amino) benzonitrile (87.2 mg, 0.4 mmol, 2.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 12 h. Product **42** was obtained as a white solid (41.2 mg, 66% yield, >20:1 dr).

TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 3:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 9.0 Hz, 2H), 6.59 (d, *J* = 9.1 Hz, 2H), 6.02 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.17 – 4.98 (m, 2H), 3.83 (dd, *J* = 15.0, 3.8 Hz, 1H), 3.26 (dd, *J* = 15.0, 10.8 Hz, 1H), 2.97 (s, 3H), 2.80 – 2.61 (m, 1H), 2.42 (ddd, *J* = 12.6, 9.7, 4.0 Hz, 1H), 2.12 – 1.95 (m, 1H), 1.93 – 1.80 (m, 1H), 1.79 – 1.63 (m, 1H), 1.12 (s, 3H), 1.10 (s, 3H).

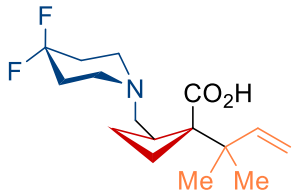
^{13}C NMR (101 MHz, $CDCl_3$) δ 180.4, 151.5, 144.3, 133.5, 120.7, 113.2, 111.5, 97.2, 58.7,

55.7, 40.3, 39.4, 37.0, 24.1, 23.6, 22.8, 22.8.

HRMS: m/z $[M+Na]^+$ calcd for $C_{19}H_{24}N_2NaO_2$: 335.1730; found: 335.1730.

m.p. 150–151 °C. (**42** was recrystallized from EA/PE = 1:10)

2-((4,4-difluoropiperidin-1-yl)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylic acid (43)



Following the general procedure, 3-methylbut-2-en-1-yl cyclobut-1-ene-1-carboxylate (33.2 mg, 0.2 mmol, 1.0 equiv.), 4,4-difluoro-1-((trimethylsilyl)methyl)piperidine (82.8 mg, 0.4 mmol, 2.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 12 h. Product **43** was obtained as a yellow solid (36.1 mg, 60% yield, >20:1 dr).

TLC: Rf = 0.3 (Dichloromethane/methanol 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.04 (dd, *J* = 17.0, 11.2 Hz, 1H), 5.15 – 5.02 (m, 2H), 3.07 – 2.72 (m, 3H), 2.70 – 2.51 (m, 3H), 2.51 – 2.42 (m, 2H), 2.17 – 1.93 (m, 5H), 1.86 (dtd, *J* = 12.3, 10.0, 8.1 Hz, 1H), 1.28 (ddt, *J* = 12.3, 11.2, 5.0 Hz, 1H), 1.10 (s, 3H), 1.03 (s, 3H).

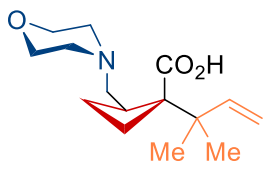
^{13}C NMR (101 MHz, $CDCl_3$) δ 177.3, 144.1, 120.7 (t, *J* = 242.4 Hz), 113.4, 60.2, 58.9, 49.5, 40.1, 33.6, 33.0 (t, *J* = 24.2 Hz), 24.8, 23.0, 21.9, 18.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ –96.5, –102.1.

HRMS: m/z $[M+Na]^+$ calcd for $C_{16}H_{25}F_2NNaO_2$: 324.1746; found: 324.1746.

m.p. 140–141 °C. (**43** was recrystallized from DCM/PE = 1:5)

1-(2-methylbut-3-en-2-yl)-2-(morpholinomethyl)cyclobutane-1-carboxylic acid (44)



Following the general procedure, 3-methylbut-2-en-1-yl cyclobut-1-ene-1-carboxylate (33.2 mg, 0.2 mmol, 1.0 equiv.), 4-((trimethylsilyl)methyl)morpholine (69.2 mg, 0.4 mmol, 2.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 12 h. Product **44** was obtained as a yellow solid

(28.3 mg, 53% yield, >20:1 dr).

TLC: Rf = 0.3 (Dichloromethane/methanol 8:1)

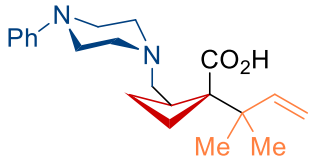
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.06 (dd, *J* = 17.7, 10.5 Hz, 1H), 5.15 – 4.97 (m, 2H), 3.71 (d, *J* = 26.9 Hz, 4H), 2.84 – 2.68 (m, 2H), 2.69 – 2.56 (m, 2H), 2.56 – 2.33 (m, 4H), 2.10 (dddd, *J* = 13.4, 10.2, 4.9, 1.4 Hz, 1H), 1.85 (dtd, *J* = 12.3, 10.0, 8.3 Hz, 1H), 1.31 – 1.22 (m, 1H), 1.10 (s, 3H), 1.04 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 177.5, 144.3, 113.4, 65.8, 61.4, 58.9, 40.2, 32.7, 24.9, 23.1, 21.9, 18.7.

HRMS: m/z $[M+Na]^+$ calcd for $C_{15}H_{25}NNaO_3$: 290.1727; found: 290.1727.

m.p. 143–144 °C. (**44** was recrystallized from DCM/PE = 1:5)

1-(2-methylbut-3-en-2-yl)-2-((4-phenylpiperazin-1-yl)methyl)cyclobutane-1-carboxylic acid (45)



Following the general procedure, 3-methylbut-2-en-1-yl cyclobut-1-ene-1-carboxylate (33.2 mg, 0.2 mmol, 1.0 equiv.), 1-phenyl-4-((trimethylsilyl)methyl)piperazine (99.2 mg, 0.4 mmol, 2.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 12 h. Product **45** was obtained as a yellow solid (31.5 mg, 46% yield, >20:1 dr).

TLC: Rf = 0.4 (Dichloromethane/methanol 8:1)

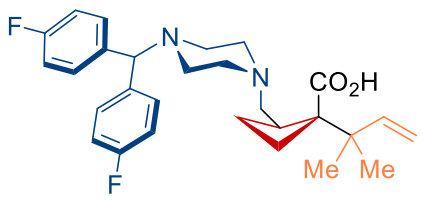
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.20 (m, 2H), 6.95 – 6.86 (m, 3H), 6.09 (dd, *J* = 17.6, 10.5 Hz, 1H), 5.16 – 5.04 (m, 2H), 3.55 – 2.88 (m, 6H), 2.87 – 2.79 (m, 1H), 2.78 – 2.58 (m, 3H), 2.57 – 2.43 (m, 2H), 2.12 (dddd, *J* = 13.4, 10.2, 4.9, 1.4 Hz, 1H), 1.88 (dtd, *J* = 12.3, 10.0, 8.3 Hz, 1H), 1.30 (ddt, *J* = 12.3, 11.2, 4.9 Hz, 1H), 1.12 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 177.7, 150.6, 144.4, 129.3, 120.8, 116.6, 113.3, 60.8, 58.9, 48.4, 40.2, 33.0, 24.9, 23.1, 22.0, 18.7.

HRMS: m/z $[M+Na]^+$ calcd for $C_{21}H_{30}N_2NaO_2$: 365.2199; found: 365.2199.

m.p. 134–135 °C. (**45** was recrystallized from DCM/PE = 1:5)

2-((4-(bis(4-fluorophenyl)methyl)piperazin-1-yl)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylic acid (46)



Following the general procedure, 3-methylbut-2-en-1-yl cyclobut-1-ene-1-carboxylate (33.2 mg, 0.2 mmol, 1.0 equiv.), 1-(bis(4-fluorophenyl)methyl)-4-((trimethylsilyl)methyl)piperazine (150.0 mg, 0.4 mmol, 2.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 12 h. Product **46** was obtained as a white solid (47.8 mg, 51% yield, >20:1 dr).

TLC: Rf = 0.4 (Dichloromethane/methanol 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 4H), 7.02 – 6.86 (m, 4H), 6.06 (dd, *J* = 17.8, 10.4 Hz, 1H), 5.10 – 4.92 (m, 2H), 4.20 (s, 1H), 3.11 – 2.63 (m, 4H), 2.63 – 2.37 (m, 5H), 2.37 – 2.14 (m, 2H), 2.13 – 1.92 (m, 2H), 1.84 (dtd, *J* = 12.3, 9.9, 8.4 Hz, 1H), 1.29 – 1.19 (m, 1H), 1.08 (s, 3H), 1.01 (s, 3H).

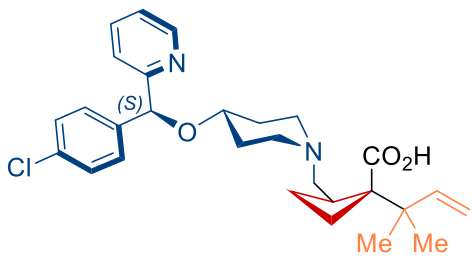
^{13}C NMR (101 MHz, $CDCl_3$) δ 178.2, 162.0 (d, *J* = 247.5 Hz), 144.6, 137.8 (d, *J* = 3.0 Hz), 137.6 (d, *J* = 3.0 Hz), 129.12 (d, *J* = 8.1 Hz), 129.09 (d, *J* = 8.1 Hz), 115.73 (d, *J* = 22.2 Hz), 115.71 (d, *J* = 22.2 Hz), 113.1, 74.2, 60.4, 58.7, 50.4, 40.1, 32.8, 25.0, 23.1, 21.9, 18.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -115.0, -115.1.

HRMS: m/z $[M+Na]^+$ calcd for $C_{28}H_{34}F_2N_2NaO_2$: 491.2481; found: 491.2480.

m.p. 200–201 °C. (**46** was recrystallized from DCM/PE = 1:5)

2-((4-((4-chlorophenyl)(pyridin-2-yl)methoxy)piperidin-1-yl)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carboxylic acid (47)



Following the general procedure, 3-methylbut-2-en-1-yl cyclobut-1-ene-1-carboxylate (33.2 mg, 0.2 mmol, 1.0 equiv.), 2-((4-chlorophenyl)((1-((trimethylsilyl)methyl) piperidin-4-yl)oxy)methyl)pyridine (155.6 mg, 0.4 mmol, 2.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%),

lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 12 h. Product **47** was obtained as a colorless oil (40.6 mg, 42% yield, >20:1 dr).

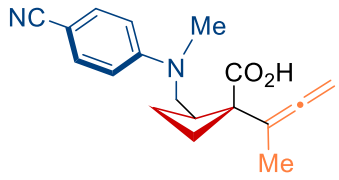
TLC: Rf = 0.3 (Dichloromethane/methanol 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 – 8.48 (m, 1H), 7.75 – 7.67 (m, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.38 – 7.34 (m, 2H), 7.33 – 7.29 (m, 2H), 7.23 – 7.15 (m, 1H), 6.16 (dd, *J* = 17.6, 10.5 Hz, 1H), 5.58 (s, 1H), 5.15 – 5.04 (m, 2H), 3.89 – 3.18 (m, 1H), 2.89 (s, 3H), 2.75 – 2.40 (m, 4H), 2.26 – 1.66 (m, 7H), 1.33 – 1.24 (m, 1H), 1.15 (s, 3H), 1.08 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.3, 161.4, 149.1, 144.9, 139.7, 137.1, 137.1, 133.6, 128.7, 128.1, 120.6, 120.6, 112.8, 81.4, 60.4, 58.8, 40.0, 32.8, 24.9, 23.2, 21.7, 18.6.

HRMS: m/z $[M+Na]^+$ calcd for $C_{28}H_{35}ClN_2NaO_3$: 505.2228; found: 505.2229.

1-(buta-2,3-dien-2-yl)-2-(((4-cyanophenyl)(methyl)amino)methyl)cyclobutane-1-carboxylic acid (48)



Following the general procedure, but-2-yn-1-yl cyclobut-1-ene-1-carboxylate (30.0 mg, 0.2 mmol, 1.0 equiv.), 4-(methyl((trimethylsilyl)methyl)amino)benzonitrile (87.2 mg, 0.4 mmol, 2.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 12 h. Product **48** was obtained as a yellow solid (36.1 mg, 61% yield, >20:1 dr).

TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 3:1)

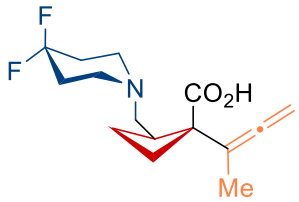
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.36 (m, 2H), 6.66 – 6.58 (m, 2H), 4.84 (q, *J* = 3.0 Hz, 2H), 3.69 (dd, *J* = 15.0, 4.6 Hz, 1H), 3.31 (dd, *J* = 15.0, 10.1 Hz, 1H), 3.04 – 2.85 (m, 4H), 2.65 – 2.50 (m, 1H), 2.05 – 1.89 (m, 3H), 1.66 (t, *J* = 3.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 205.8, 179.5, 151.5, 133.6, 133.4, 120.6, 111.7, 111.6, 102.0, 97.3, 54.1, 53.5, 40.6, 39.1, 28.3, 22.6, 15.0.

HRMS: m/z $[M+Na]^+$ calcd for $C_{18}H_{20}N_2NaO_2$: 319.1417; found: 319.1417.

m.p. 123–124 °C. (**48** was recrystallized from EA/PE = 1:10)

1-(buta-2,3-dien-2-yl)-2-((4,4-difluoropiperidin-1-yl)methyl)cyclobutane-1-carboxylic acid (49)



Following the general procedure, but-2-yn-1-yl cyclobut-1-ene-1-carboxylate (30.0 mg, 0.2 mmol, 1.0 equiv.), 4,4-difluoro-1-((trimethylsilyl)methyl)piperidine (82.8 mg, 0.4 mmol, 2.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 12 h. Product **49** was obtained as a white solid (28.5 mg, 50% yield, >20:1 dr).

TLC: Rf = 0.3 (Dichloromethane/methanol 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.89 (dq, *J* = 9.5, 3.1 Hz, 1H), 4.76 (dq, *J* = 9.6, 3.0 Hz, 1H), 3.21 – 2.83 (m, 3H), 2.78 – 2.65 (m, 2H), 2.65 – 2.47 (m, 3H), 2.14 – 1.94 (m, 6H), 1.65 (t, *J* = 3.1 Hz, 3H), 1.56 – 1.45 (m, 1H).

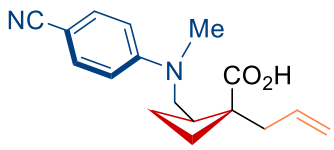
^{13}C NMR (101 MHz, $CDCl_3$) δ 205.6, 175.7, 120.7 (t, *J* = 243.4 Hz), 103.8, 60.1, 54.7, 49.6, 37.2, 33.0 (t, *J* = 24.2 Hz), 28.3, 20.0, 14.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -99.2.

HRMS: m/z $[M+Na]^+$ calcd for $C_{15}H_{21}F_2NNaO_2$: 308.1433; found: 308.1433.

m.p. 147–148 °C. (**49** was recrystallized from DCM/PE = 1:5)

1-allyl-2-(((4-cyanophenyl)(methyl)amino)methyl)cyclobutane-1-carboxylic acid (50)



Following the general procedure, allyl cyclobut-1-ene-1-carboxylate (27.6 mg, 0.2 mmol, 1.0 equiv.), 4-(methyl((trimethylsilyl)methyl)amino)benzonitrile (87.2 mg, 0.4 mmol, 2.0 equiv.) and Ir(dtbbpy)(ppy)$_2$][PF$_6$] (3.0 mg, 3.0 × 10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 12 h. Product **50** was obtained as a yellow oil (34.1 mg, 60% yield, 2.5:1 dr).

TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 3:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.36 (m, 2H), 6.73 – 6.53 (m, 2H), 5.91 – 5.68 (m, 1H), 5.28 – 5.04 (m, 2H), 3.80 (dd, *J* = 14.9, 4.3 Hz, 0.29H), 3.70 (dd, *J* = 14.9, 4.9 Hz, 0.71H), 3.49 – 3.33 (m, 0.85H), 3.03 (s, 2.15H), 3.00 (s, 2H), 2.75 – 2.55 (m, 2H), 2.54 –

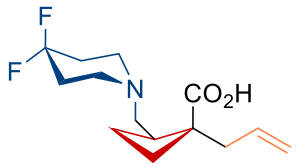
2.34 (m, 2H), 2.13 – 1.87 (m, 3H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.1, 151.5, 133.5, 133.3, 120.7, 118.5, 111.6, 97.3, 53.6, 50.5, 42.6, 41.3, 39.1, 26.6, 22.4.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.0, 151.4, 133.6, 132.9, 120.7, 118.7, 111.6, 97.3, 52.5, 49.4, 39.4, 39.1, 35.2, 25.6, 22.4.

HRMS: m/z $[M+Na]^+$ calcd for $C_{17}H_{20}N_2NaO_2$: 307.1417; found: 307.1417.

1-allyl-2-((4,4-difluoropiperidin-1-yl)methyl)cyclobutane-1-carboxylic acid (51)



Following the general procedure, allyl cyclobut-1-ene-1-carboxylate (27.6 mg, 0.2 mmol, 1.0 equiv.), 4,4-difluoro-1-((trimethylsilyl)methyl)piperidine (82.8 mg, 0.4 mmol, 2.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 12 h. Product **51** was obtained as a yellow oil (27.3 mg, 50% yield, 2.5:1 dr).

TLC: Rf = 0.3 (Dichloromethane/methanol 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 – 5.62 (m, 1H), 5.26 – 5.00 (m, 2H), 2.97 – 2.71 (m, 3H), 2.68 – 2.44 (m, 5H), 2.42 – 2.21 (m, 1H), 2.20 – 1.92 (m, 5H), 1.94 – 1.54 (m, 2H), 1.52 – 1.40 (m, 1H).

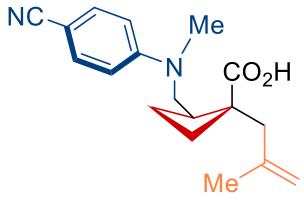
Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.1, 133.5, 120.6 (t, *J* = 243.4 Hz), 118.5, 59.3, 52.0, 49.1, 45.4, 37.5, 32.9 (t, *J* = 24.2 Hz), 28.1, 19.7.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.2, 132.5, 120.8 (t, *J* = 243.4 Hz), 118.7, 56.4, 50.5, 50.3, 38.4, 35.3, 33.3 (t, *J* = 24.2 Hz), 25.1, 20.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ -99.0.

HRMS: m/z $[M+Na]^+$ calcd for $C_{14}H_{21}F_2NNaO_2$: 296.1433; found: 296.1433.

2-(((4-cyanophenyl)(methyl)amino)methyl)-1-(2-methylallyl)cyclobutane-1-carboxylic acid (52)



Following the general procedure, 2-methylallyl cyclobut-1-ene-1-carboxylate (30.4 mg, 0.2 mmol, 1.0 equiv.), 4-(methyl((trimethylsilyl)methyl)amino)benzonitrile (87.2 mg, 0.4 mmol, 2.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 12 h. Product **52** was obtained as a yellow oil (42.9 mg, 72% yield, 2:1 dr).

TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 3:1)

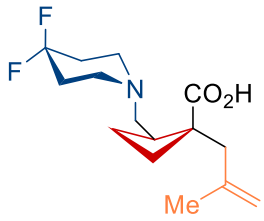
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.32 (m, 2H), 6.69 – 6.41 (m, 2H), 4.87 – 4.49 (m, 2H), 3.77 (dd, *J* = 14.9, 4.2 Hz, 0.33H), 3.67 (dd, *J* = 14.9, 4.5 Hz, 0.66H), 3.41 – 3.23 (m, 1H), 2.98 (s, 1H), 2.95 (s, 2H), 2.83 – 2.69 (m, 1H), 2.67 – 2.45 (m, 2.33H), 2.35 (d, *J* = 15.0 Hz, 0.67H), 2.10 – 1.98 (m, 1H), 1.97 – 1.82 (m, 2H), 1.71 (s, 1H), 1.68 (s, 2H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.0, 151.5, 141.8, 133.6, 120.6, 112.5, 111.5, 97.5, 53.6, 50.9, 46.3, 42.7, 39.0, 27.2, 23.6, 23.1.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.4, 151.4, 141.5, 133.5, 120.6, 113.1, 111.6, 97.4, 52.4, 49.0, 40.5, 39.0, 38.0, 25.6, 23.6, 22.7.

HRMS: m/z $[M+Na]^+$ calcd for $C_{18}H_{22}N_2NaO_2$: 321.1573; found: 321.1574.

2-((4,4-difluoropiperidin-1-yl)methyl)-1-(2-methylallyl)cyclobutane-1-carboxylic acid (53)



Following the general procedure, 2-methylallyl cyclobut-1-ene-1-carboxylate (30.4 mg, 0.2 mmol, 1.0 equiv.), 4,4-difluoro-1-((trimethylsilyl)methyl)piperidine (82.8 mg, 0.4 mmol, 2.0 equiv.) and $Ir(dtbbpy)(ppy)_2][PF_6]$ (3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%), lighted in 1 W blue LED (450 nm, SYNLED) at 40 °C for 12 h. Product **53** was obtained as a white solid (39.6 mg, 69% yield, 2.5:1 dr).

TLC: Rf = 0.3 (Dichloromethane/methanol 8:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.86 – 4.66 (m, 2H), 2.92 – 2.79 (m, 2H), 2.79 – 2.72 (m, 1H), 2.68 – 2.60 (m, 2H), 2.60 – 2.53 (m, 2H), 2.53 – 2.41 (m, 2H), 2.41 – 2.29 (m, 1H), 2.15 – 1.93 (m, 5H), 1.93 – 1.85 (m, 1H), 1.71 (s, 3H), 1.64 – 1.42 (m, 1H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.6, 142.2, 120.6 (t, *J* = 243.4 Hz), 114.0, 59.3, 52.4, 49.3, 49.2, 38.7, 33.0 (t, *J* = 24.2 Hz), 29.3, 23.1, 20.8.

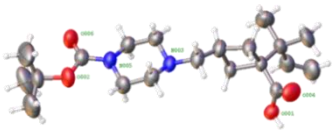
Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.6, 141.1, 120.8 (t, *J* = 243.4 Hz), 114.4, 56.5, 50.3, 50.1, 39.4, 38.3, 33.2 (t, *J* = 24.2 Hz), 24.9, 23.3, 20.8.

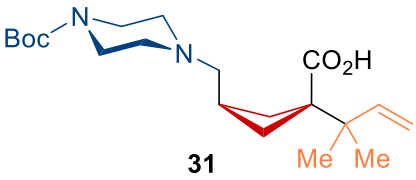
^{19}F NMR (376 MHz, $CDCl_3$) δ -99.2.

HRMS: m/z $[M+Na]^+$ calcd for $C_{15}H_{23}F_2NNaO_2$: 310.1589; found: 310.1590.

m.p. 144–145 °C. (**53** was recrystallized from DCM/PE = 1:5)

6. X-ray Crystallographic Data





31

CCDC 2403838

Compound	**31**
Formula	$C_{20}H_{34}N_2O_4$
Dcalc./ g cm-3	1.135
m/mm-1	0.631
Formula Weight	366.504
T/K	300.69(10)
Crystal System	monoclinic
Space Group	C2/c
a/Å	26.4619(3)
b/Å	6.3388(1)
c/Å	26.1419(3)
a/°	90
b/°	101.877(1)
g/°	90
V/Å3	4291.08(10)
Z	8
Z'	1
Wavelength/Å	1.54184
Radiation type	Cu Ka
Qmin/°	3.41
Qmax/°	77.06
Measured Refl.	22227
Independent Refl.	4373
Reflections with I≥s(I)	3782
Rint	0.0200
Parameters	241
Restraints	1
Largest Peak	0.6843
Deepest Hole	-0.2815
GooF	1.0297
wR2 (all data)	0.2379
wR2	0.2300
R1 (all data)	0.0780
R1	0.0721

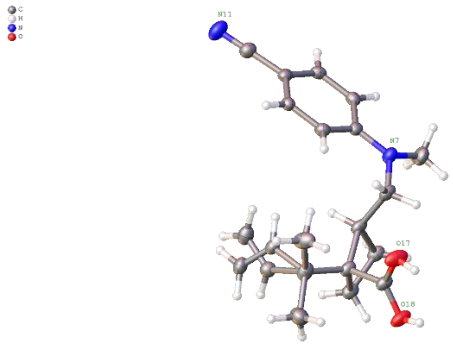
Table S4. Bond Lengths in Å for 31.

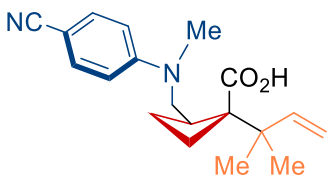
Atom	Atom	Length/Å
O001	C007	1.308(2)
O002	C00E	1.327(3)
O002	C00K	1.466(3)
N003	C00B	1.459(3)
N003	C00F	1.473(3)
N003	C00J	1.486(3)
O004	C007	1.214(2)
N005	C00C	1.454(3)
N005	C00E	1.361(3)
N005	C00G	1.463(3)
O006	C00E	1.211(3)
C007	C008	1.513(3)
C008	C009	1.556(2)
C008	C00D	1.568(3)
C008	C00I	1.552(3)
C009	C00H	1.554(3)
C00A	C00D	1.506(3)
C00A	C00N	1.295(4)
C00B	C00C	1.497(3)
C00D	C00L	1.536(3)
C00D	C00M	1.549(4)
C00F	C00G	1.520(3)
C00H	C00I	1.545(3)
C00H	C00J	1.486(3)
C00K	C00O	1.535(4)
C00K	C00P	1.490(5)

Table S5. Bond Angles in ° for 31.

Atom	Atom	Atom	Angle/°
C00K	O002	C00E	121.3(2)
C00F	N003	C00B	108.19(15)
C00J	N003	C00B	113.43(17)
C00J	N003	C00F	108.20(16)
C00E	N005	C00C	118.01(18)
C00G	N005	C00C	114.07(16)
C00G	N005	C00E	122.99(18)
O004	C007	O001	122.11(19)
C008	C007	O001	114.12(16)
C008	C007	O004	123.77(19)
C009	C008	C007	113.16(15)
C00D	C008	C007	109.19(14)
C00D	C008	C009	116.98(16)
C00I	C008	C007	112.06(17)
C00I	C008	C009	88.92(13)
C00I	C008	C00D	115.40(17)
C00H	C009	C008	89.94(14)
C00N	C00A	C00D	127.5(2)
C00C	C00B	N003	111.20(17)
C00B	C00C	N005	110.71(18)
C00A	C00D	C008	109.58(16)
C00L	C00D	C008	109.4(2)
C00L	C00D	C00A	112.2(2)
C00M	C00D	C008	110.46(18)
C00M	C00D	C00A	106.6(2)
C00M	C00D	C00L	108.6(2)
N005	C00E	O002	111.31(19)

Atom	Atom	Atom	Angle/°
O006	C00E	O002	125.1(2)
O006	C00E	N005	123.6(2)
C00G	C00F	N003	111.09(17)
C00F	C00G	N005	110.53(18)
C00I	C00H	C009	89.25(15)
C00J	C00H	C009	118.41(19)
C00J	C00H	C00I	114.4(2)
C00H	C00I	C008	90.37(15)
C00H	C00J	N003	115.36(19)
C00O	C00K	O002	102.2(2)
C00P	C00K	O002	109.9(2)
C00P	C00K	C00O	108.8(3)
C00Q	C00K	O002	109.2(2)





42

CCDC 2403839

Compound	**42**
Empirical formula	$C_{19}H_{24}N_2O_2$
Formula weight	312.40
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	9.7265(2)
b/Å	14.7461(2)
c/Å	12.5014(2)
α/°	90
β/°	108.624(2)
γ/°	90
Volume/Å^3	1699.16(5)
Z	4
ρ_{calc}g/cm^3	1.221
μ/mm^{-1}	0.630
F(000)	672.0
Crystal size/mm^3	0.2 × 0.2 × 0.2
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	9.576 to 153.82
Index ranges	-10 ≤ h ≤ 12, -18 ≤ k ≤ 15, -15 ≤ l ≤ 13
Reflections collected	10262
Independent reflections	3388 [R_{int} = 0.0212, R_{sigma} = 0.0206]
Data/restraints/parameters	3388/52/233
Goodness-of-fit on F^2	1.037
Final R indexes [I>=2σ (I)]	R_1 = 0.0376, wR_2 = 0.0956
Final R indexes [all data]	R_1 = 0.0408, wR_2 = 0.0979
Largest diff. peak/hole / e Å^{-3}	0.21/-0.23

Table S6. Bond Lengths in Å for 42.

Atom	Atom	Length/Å
C1	C2	1.4135(15)
C1	C6	1.4127(15)
C1	N7	1.3768(14)
C2	C3	1.3803(16)
C3	C4	1.3966(16)
C4	C5	1.3990(15)
C4	C10	1.4336(16)
C5	C6	1.3759(15)
C8	N7	1.4567(16)
C9	C12	1.5230(17)
C9	N7	1.4658(15)
C10	N11	1.1485(17)
C12	C13	1.5762(15)
C12	C15	1.5481(15)
C13	C14	1.5549(15)
C13	C16	1.5226(15)
C13	C19	1.5713(16)
C14	C15	1.5390(17)
C16	O17	1.2684(14)
C16	O18	1.2597(14)
C19	C23	1.551(2)
C19	C20	1.5327(18)
C19	C21	1.5227(18)
C19	C23A	1.542(3)
C22	C23	1.319(3)
C22A	C23A	1.310(5)

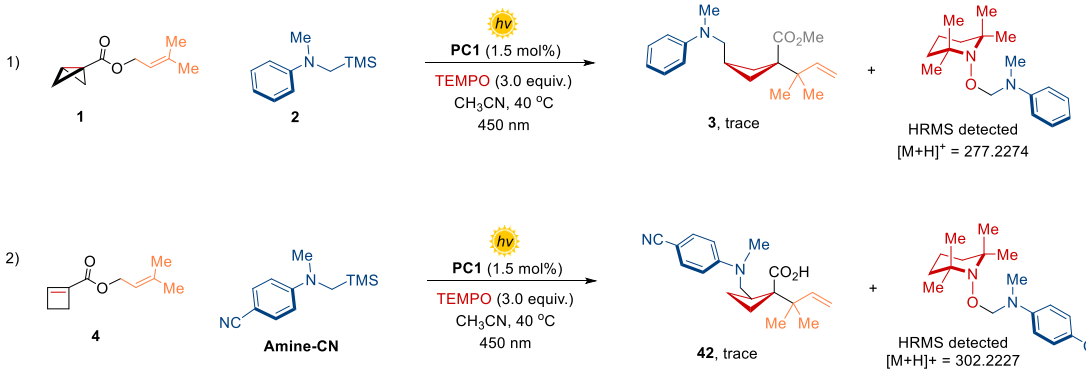
Table S7. Bond Angles in ° for 42.

Atom	Atom	Atom	Angle/°
C6	C1	C2	117.44(10)
N7	C1	C2	121.05(10)
N7	C1	C6	121.51(10)
C3	C2	C1	120.65(10)
C2	C3	C4	121.15(10)
C3	C4	C5	118.71(10)
C3	C4	C10	121.21(10)
C5	C4	C10	120.04(10)
C6	C5	C4	120.54(10)
C5	C6	C1	121.44(10)
N7	C9	C12	112.04(9)
N11	C10	C4	179.36(13)
C9	C12	C13	123.12(9)
C9	C12	C15	118.86(10)
C15	C12	C13	87.96(8)
C14	C13	C12	87.37(8)
C14	C13	C19	117.89(10)
C16	C13	C12	110.88(9)
C16	C13	C14	110.43(9)
C16	C13	C19	110.02(9)
C19	C13	C12	118.47(9)
C15	C14	C13	89.06(8)
C14	C15	C12	88.94(9)
O17	C16	C13	118.04(10)
O18	C16	C13	119.24(10)
O18	C16	O17	122.70(10)
C23	C19	C13	109.45(10)

Atom	Atom	Atom	Angle/°
C20	C19	C13	109.58(10)
C20	C19	C23	99.72(14)
C20	C19	C23A	124.8(2)
C21	C19	C13	111.65(10)
C21	C19	C23	116.41(13)
C21	C19	C20	109.31(10)
C21	C19	C23A	93.44(18)
C23A	C19	C13	107.00(15)
C22	C23	C19	124.3(2)
C1	N7	C8	119.23(10)
C1	N7	C9	119.99(9)
C8	N7	C9	116.89(9)
C22A	C23A	C19	121.4(4)

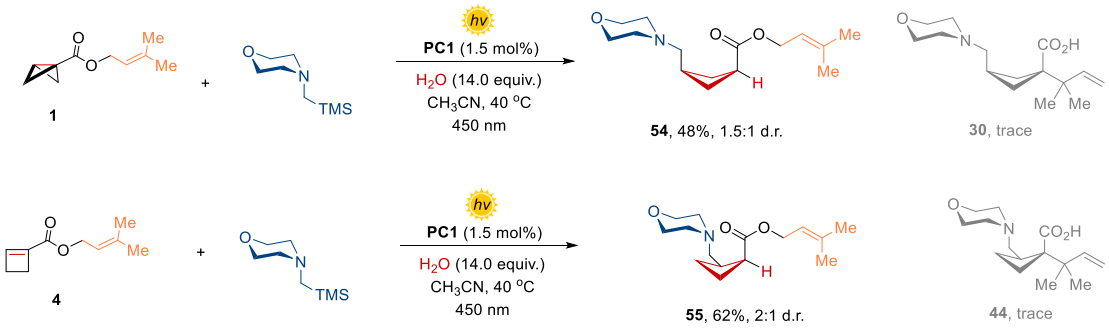
7. Mechanistic study

7.1 Radical trapping experiment with TEMPO



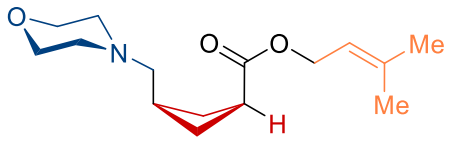
Results: The crude residue was detected by ^{1}H NMR and HRMS analysis. Only trace of targeted product was found and the expected TEMPO-aminoalkyl adduct was detected by HRMS. It suggests a possible radical reaction pathway and the involvement of aminoalkyl radical species in the catalytic process.

7.2 Intermediate confirmation experiment



Results: In the presence of external water, the desired radical addition/rearrangement cascade reaction was completely inhibited. However, the aminoalkylation-protonation products **54** and **55** were detected in good yields. It supports the possible generation of α-ester anion species, which are quite sensitive to the moisture.

3-methylbut-2-en-1-yl 3-(morpholinomethyl)cyclobutane-1-carboxylate (54)



product **54** was obtained as a colorless oil (25.6 mg, 48% yield, 1.5:1 dr).

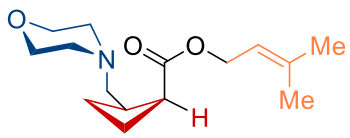
TLC: Rf = 0.3 (Dichloromethane/methanol 30:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.41 – 5.26 (m, 1H), 4.59 (d, *J* = 7.2 Hz, 2H), 3.71 – 3.66 (m, 4H), 3.12 – 3.00 (m, 1H), 2.72 – 2.58 (m, 1H), 2.46 – 2.33 (m, 8H), 2.03 – 1.92 (m, 2H), 1.76 (s, 3H), 1.71 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.2, 139.1, 118.7, 67.0, 64.9, 61.5, 53.8, 35.3, 29.6, 29.6, 25.8, 18.1.

HRMS: m/z $[M+Na]^+$ calcd for $C_{15}H_{25}NNaO_3$: 290.1727; found: 290.1725.

3-methylbut-2-en-1-yl 2-(morpholinomethyl)cyclobutane-1-carboxylate (55)



product **55** was obtained as a colorless oil (33.1 mg, 62% yield, 2:1 dr).

TLC: Rf = 0.3 (Dichloromethane/methanol 30:1)

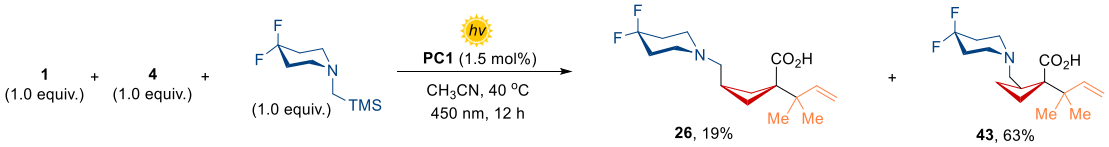
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.43 – 5.27 (m, 1H), 4.66 – 4.50 (m, 2H), 3.74 – 3.60 (m, 4H), 3.26 – 2.73 (m, 2H), 2.67 – 2.27 (m, 6H), 2.26 – 1.98 (m, 3H), 1.80 – 1.71 (m, 6H), 1.71 – 1.60 (m, 1H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.7, 138.9, 118.8, 66.9, 64.4, 61.3, 53.8, 42.9, 36.6, 25.8, 24.5, 22.2, 18.1.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.2, 138.7, 118.9, 67.0, 61.2, 60.0, 53.7, 40.1, 34.8, 25.8, 23.8, 21.1, 18.1.

HRMS: m/z $[M+Na]^+$ calcd for $C_{15}H_{25}NNaO_3$: 290.1727; found: 290.1727.

7.3 Competition experiments



Procedure: In the glovebox, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate **1** (33.2 mg, 0.2 mmol, 1.0 equiv.), 3-methylbut-2-en-1-yl cyclobut-1-ene-1-carboxylate **4** (33.2 mg, 0.2 mmol, 1.0 equiv.), 4,4-difluoro-1-((trimethylsilyl)methyl)piperidine (41.4 mg, 0.2 mmol, 1.0 equiv.), Ir(dtbbpy)(ppy)$_2$][PF$_6$] (**PC1**, 3.0 mg, 3.0×10^{-3} mmol, 1.5 mol%) and dry CH_3CN (0.25 mL) were added respectively into a flame-dried reaction vial equipped with a stir bar. Then the vial was sealed and transferred out of the glove box. Afterwards, it was irradiated with a 1 W blue LED lamp (450 nm, SYNLED) for 12 h at 40 °C. The crude mixture was concentrated by rotary evaporation. Then the residue was purified by flash column chromatography on silica gel to afford **26** (11.4 mg, 19% yield, 1.4:1 dr) and **43** (37.9 mg, 63%, >20:1 dr).

Results: In the competition experiment, the cyclobutenes proved to be higher reaction rates as compared to BCBs for such radical addition reactions.

7.4 UV-Vis absorption spectroscopy

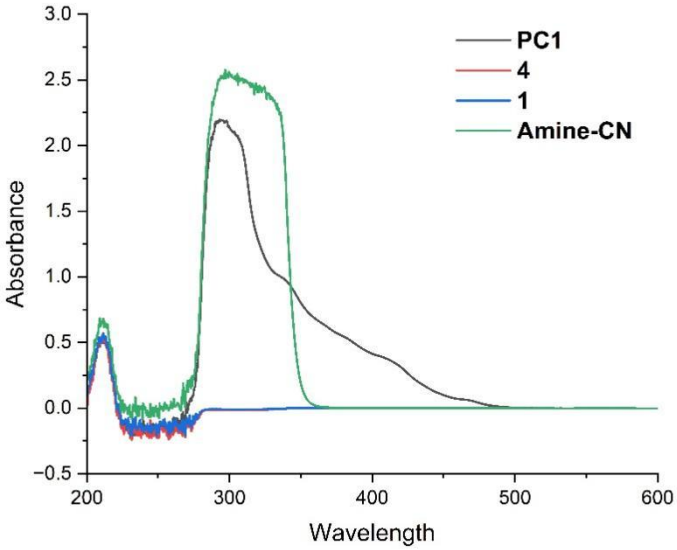


Fig S1. Absorption spectra of **PC1** (0.1 mM in MeCN, black line), **4** (0.5 mM in MeCN, red line), **1** (0.5 mM in MeCN, blue line), Amine-CN (0.5 mM in MeCN, green line). Absorbance is measured in arbitrary units (a.u.).

7.5 Stern–Volmer luminescence quenching analysis

Stern–Volmer luminescence quenching analysis was carried out to identify quenchers of the excited photoredox catalyst through measuring the luminescence of the excited photocatalyst (**PC1***) in the presence of varying concentrations of potential quencher (**1**, **4**, **Amine-CN**).

Stock solution of **PC1** ($Ir(dtbbpy)(ppy)_2][PF_6]$, 2.0 mM in CH_3CN; solution **a**) and **Amine-CN** (20.0 mM in CH_3CN; solution **b**) were prepared in a 5.0 mL volumetric flask. Then 250.0 μL of solution **a** was diluted to 5.0 mL with CH_3CN (0.1 mM; solution **c**). Then the solution **c** was transferred to a 10 x 10 mm light path quartz fluorescence cuvette equipped with a PTFE lid. The emission spectra were recorded using a Spectrophotometer. Subsequently, a series of PC solution containing different concentrations of **Amine-CN** were prepared (as following table, solution **c**-**h**, diluted to 5.0 mL with CH_3CN), and the emission spectrum of the title solution was recorded. The excitation wavelength was fixed at 350 nm while the emission light was acquired from 370 nm to 700 nm. Emission intensity at λ = 571 nm was used for quenching data.

Solution	Volume of solution **a** [μL]	Volume of solution **b** [μL]	Concentration of **Amine-CN** [mM]
c	250.0	0	0
d	250.0	125.0	0.5
e	250.0	250.0	1.0
f	250.0	500.0	2.0
g	250.0	750.0	3.0
h	250.0	1000.0	4.0

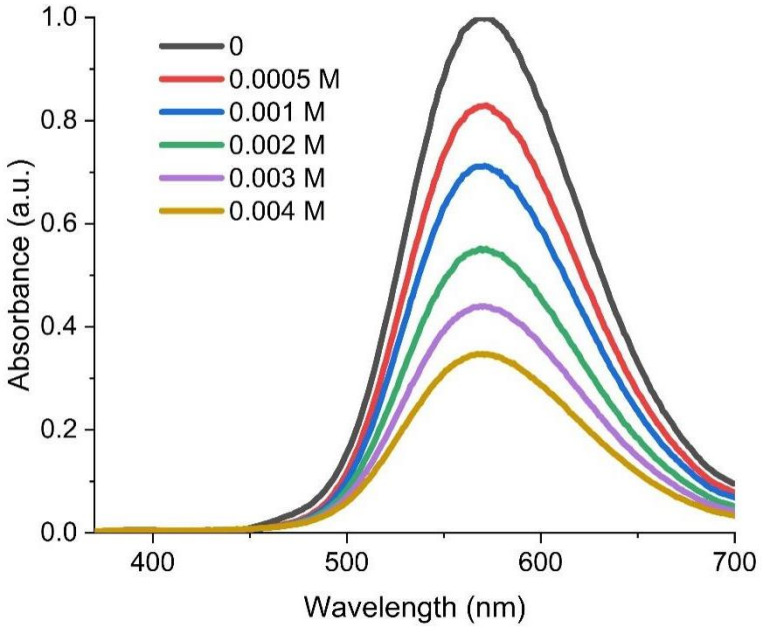


Fig. S2. Quenching of the **PC1** emission (0.1 mM in CH_3CN) in the presence of **Amine-CN.**

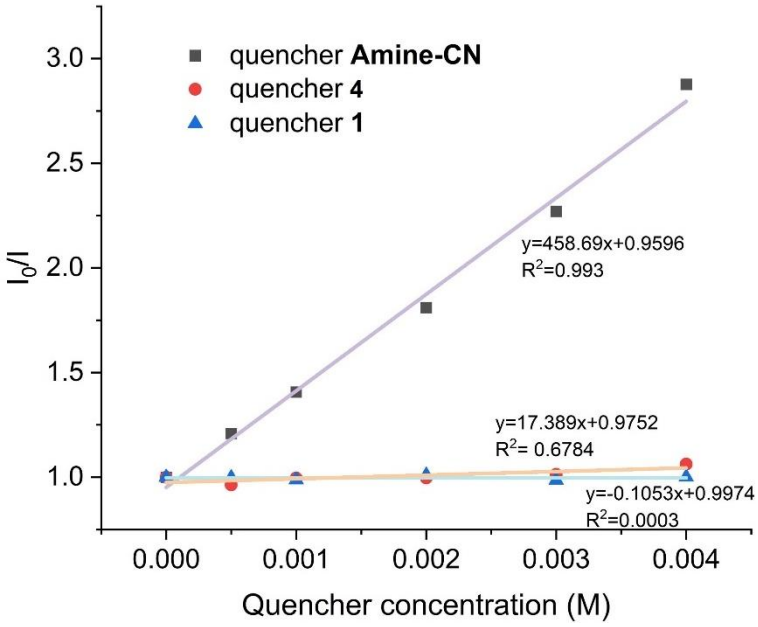
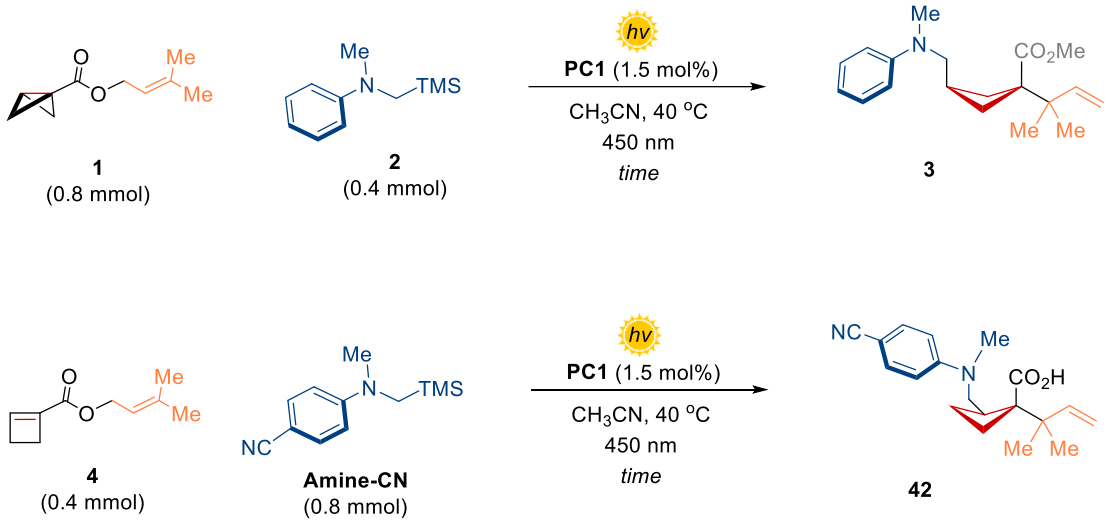


Fig. S3. Stern-Volmer plot for the quenching studies. Emission wavelength fixed at 571 nm. The Stern-Volmer constant (KSV) for the quenching by **Amine-CN** being 458.7 mM^{-1}.

7.6 Light on/off experiment



1) In the glovebox, 3-methylbut-2-en-1-yl bicyclo[1.1.0]butane-1-carboxylate **1** (132.8 mg, 0.8 mmol, 2.0 equiv.), *N*-methyl-*N*-((trimethylsilyl)methyl)aniline **2** (77.2 mg, 0.4 mmol, 1.0 equiv.), Ir(dtbbpy)(ppy)$_2$][PF$_6$] **PC1** (6.0 mg, 6.0 × 10^{-3} mmol, 1.5 mol%) and dry CH_3CN (0.5 mL) were added respectively into a flame-dried reaction vial equipped with a stir bar. Then the vial was sealed and transferred out of the glove box. Afterwards, it was irradiated with a 1 W blue LED lamp (450 nm, SYNLED) at 40 °C. As the time period indicated, at the end of each period, a small portion (50.0 μL) of the reacting solution was taken by a syringe. Then, the mixture was detected by ^{1}H NMR (1,3,5-trimethoxybenzene as the internal standard).

2) In the glovebox, 3-methylbut-2-en-1-yl cyclobut-1-ene-1-carboxylate **4** (66.4 mg, 0.4 mmol, 1.0 equiv.), **Amine-CN** (174.4 mg, 0.8 mmol, 2.0 equiv.), Ir(dtbbpy)(ppy)$_2$][PF$_6$] **PC1** (6.0 mg, 6.0 × 10^{-3} mmol, 1.5 mol%) and dry CH_3CN (0.5 mL) were added respectively into a flame-dried reaction vial equipped with a stir bar. Then the vial was sealed and transferred out of the glove box. Afterwards, it was irradiated with a 1 W blue LED lamp (450 nm, SYNLED) at 40 °C. As the time period indicated, at the end of each period, a small portion (50.0 μL) of the reacting solution was taken by a syringe. Then, the mixture was detected by ^{1}H NMR (1,3,5-trimethoxybenzene as the internal standard).

Time (h)	Light	NMR yield of **3** (%)	NMR yield of **42** (%)
6	On	15	19
7	Off	15	19
13	On	30	36
14	Off	30	36
21	On	43	46
22	Off	43	46
29	On	52	55

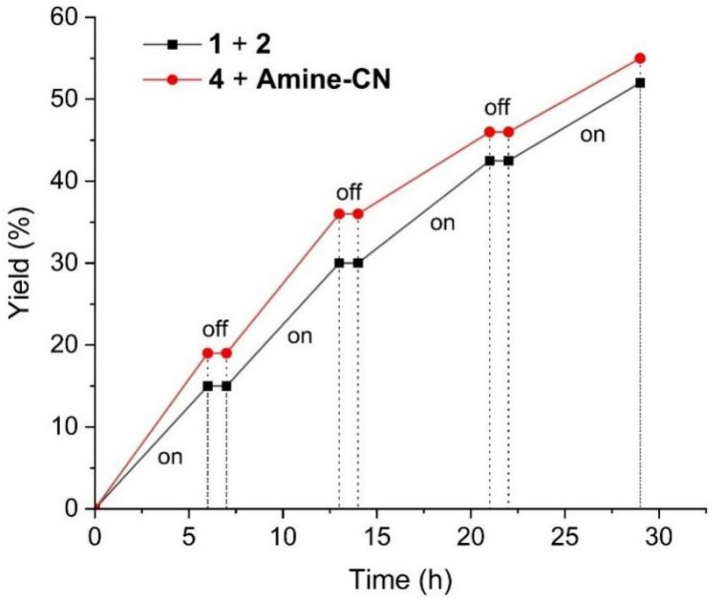
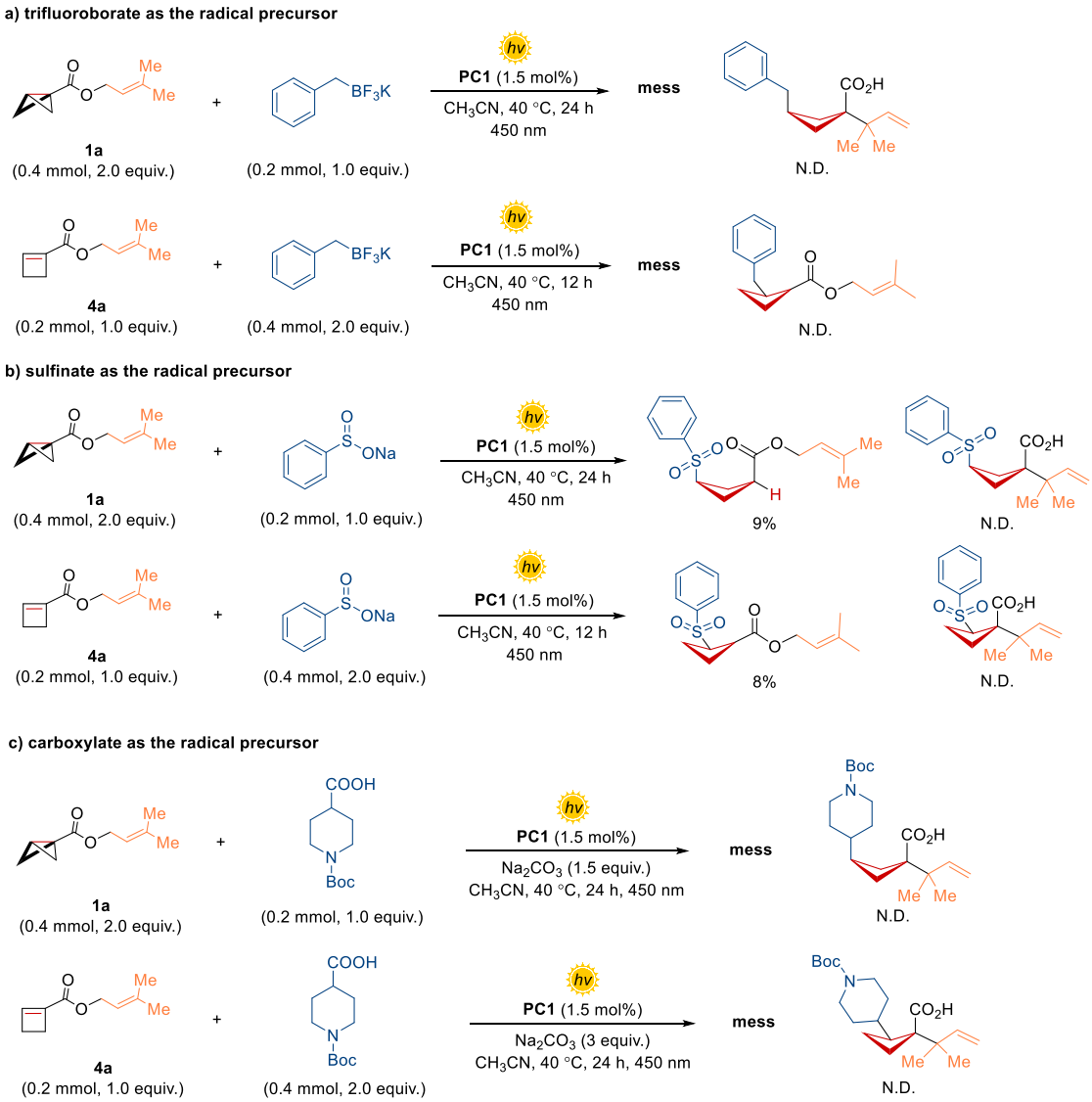


Fig. S4. The light on/off experiment.

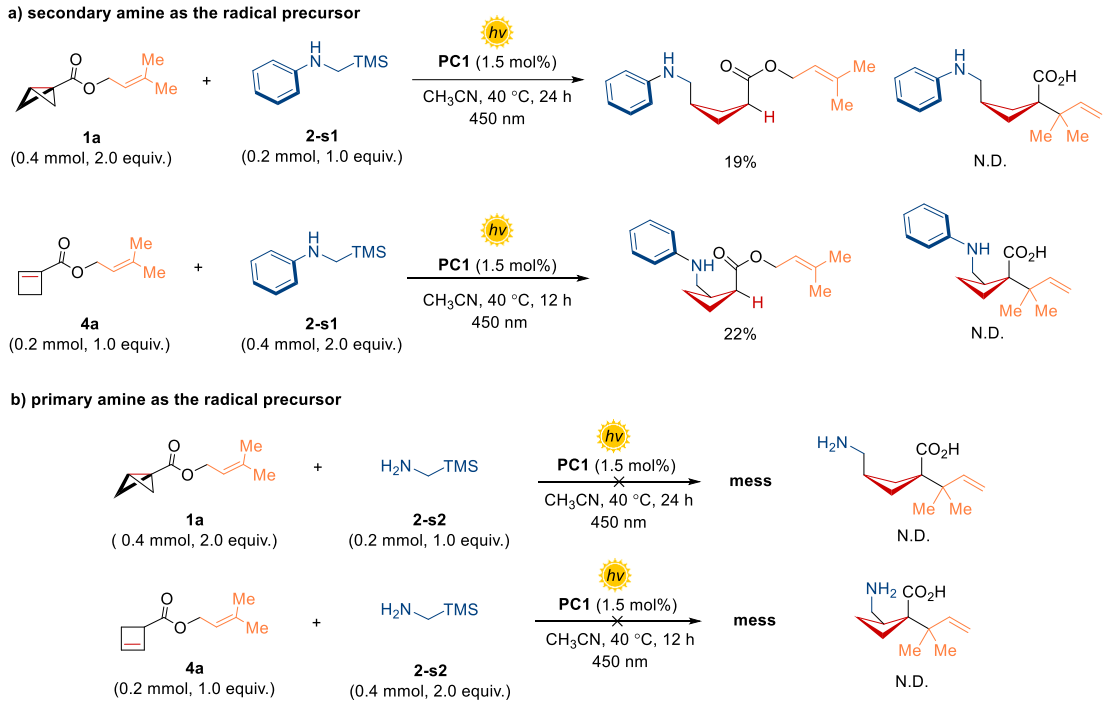
8. Supplementary discussions

8.1 Exploration of other radical precursors

Other radical precursors (such as boronate, sulfinate, and carboxylate) have been investigated in this SRRC process as below. When employing the benzyl trifluoroborate as the radical precursor, the SRRC products were not detected under the standard conditions. Then we evaluated the performance of sodium benzenesulfinate as the radical precursor, it was showed that the SRRC products were not obtained, but the sulfonylation-protonation products were observed. When using the acid derivative as the radical precursor, the SRRC products were not detected either.

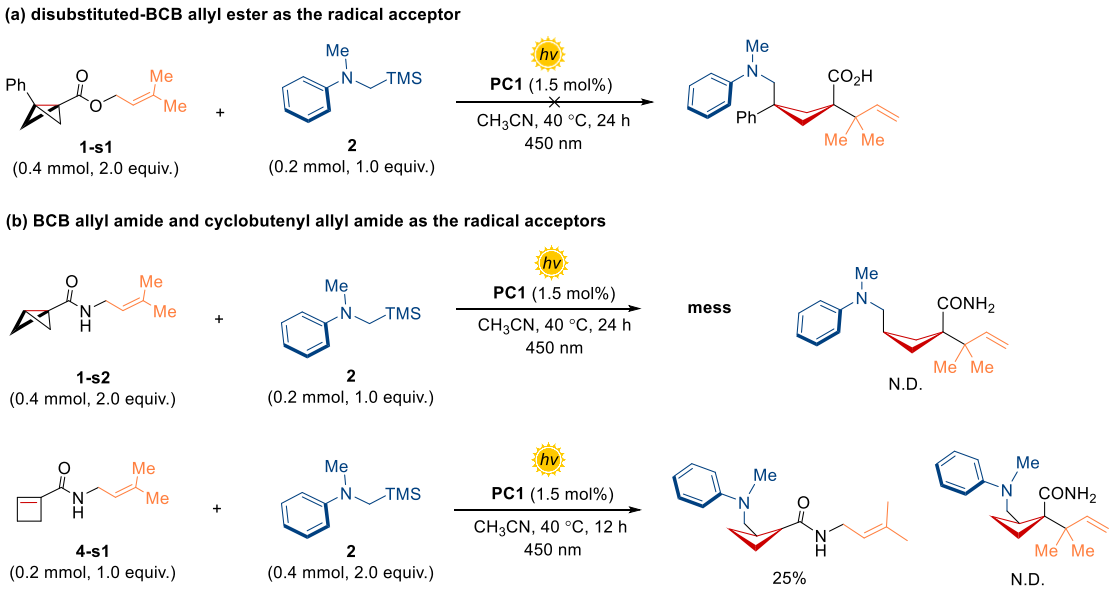


Secondary amine **2-s1** and primary amine **2-s2** as radical precursors were also tested under the standard conditions. However, neither **2-s1** nor **2-s2** gave the desired products.

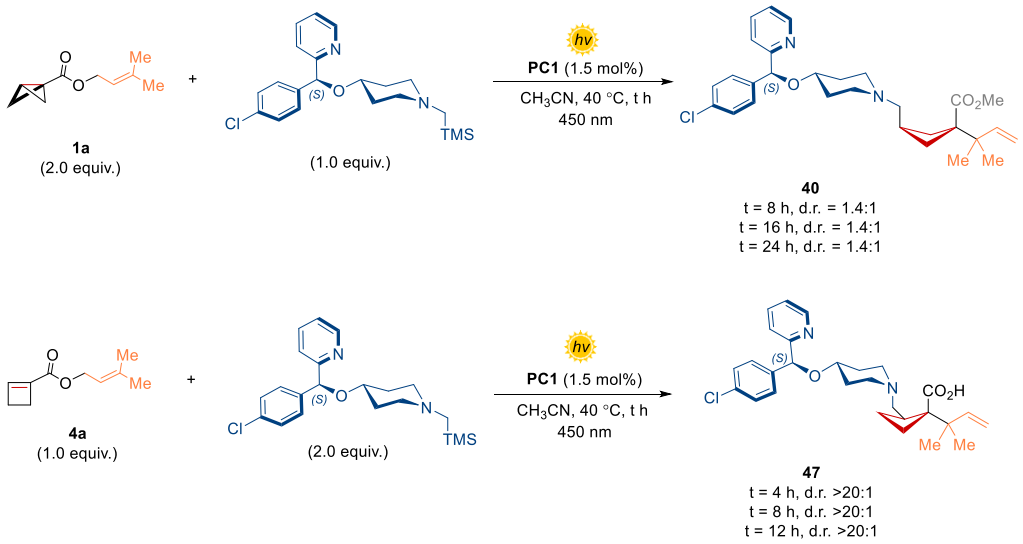


8.2 Exploration of other radical acceptors

The disubstituted bicyclobutane **1-s1**, BCB allyl amide **1-s2** and cyclobutenyl allyl amide **4-s1** as radical acceptors were evaluated. Unfortunately, there were no desired products observed under the standard conditions.



8.3 Determining whether chiral substrates undergo racemization

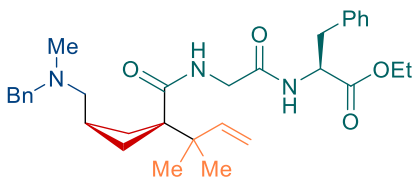


To determine whether chiral substrates undergo racemization, The dr values of the chiral products **40** and **47** were monitored under the standard conditions at different reaction times. And the results showed that the dr values of **40** and **47** remained consistent across different time points, indicating that the stereochemistry of the benzylic position was well retained throughout the reaction process.

9. Post-functionalization of products

An oven-dried vial was charged with **21** (60.2 mg, 0.2 mmol, 1.0 equiv., 1.4:1 dr) in anhydrous DMF (2.0 mL). Then ethyl glycyl-*L*-phenylalaninate (75.0 mg, 0.3 mmol, 1.5 equiv.), HATU (114.0 mg, 0.3 mmol, 1.5 equiv.) and DIPEA (103.4 mg, 0.8 mmol, 4.0 equiv.) were added under argon atmosphere. The resulting reaction mixture was stirred for 12 h at 60 °C. After this time, a saturated aqueous NH_4Cl solution was added, and the aqueous phase was extracted with EtOAc twice. The combined organic layers were washed with brine, dried (anhydrous Na_2SO_4), filtered, and the solvent was evaporated under reduced pressure. After purification by chromatography on silica gel (dichloromethane/methanol 30:1), the product **56** was obtained as a colorless oil (50.2 mg, 47% yield, 2:1 dr).

ethyl (3-((benzyl(methyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carbonyl)glycyl-L-phenylalaninate (56)



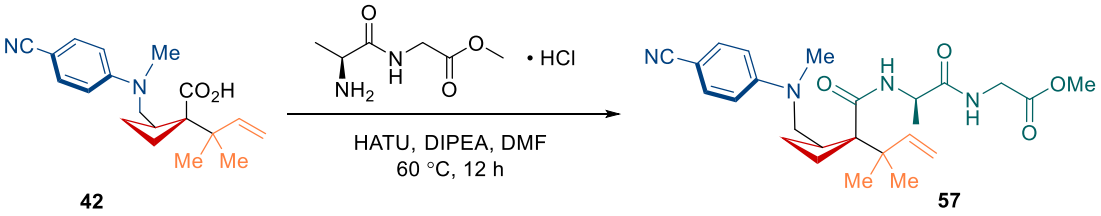
TLC: Rf = 0.3 (Dichloromethane/methanol 30:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.24 (m, 8H), 7.19 – 7.12 (m, 2H), 6.79 – 6.68 (m, 1H), 6.43 (t, *J* = 5.1 Hz, 0.3H), 6.11 – 5.97 (m, 1.3H), 5.89 (dd, *J* = 17.5, 10.8 Hz, 0.32H), 5.14 – 4.94 (m, 2H), 4.90 – 4.80 (m, 1H), 4.22 – 4.11 (m, 2H), 4.08 – 3.81 (m, 2H), 3.44 (s, 2H), 3.22 – 3.05 (m, 2H), 2.41 – 2.33 (m, 4H), 2.32 – 2.18 (m, 1H), 2.17 – 2.13 (m, 3H), 2.05 – 1.97 (m, 1.34H), 1.89 (s, 0.66H), 1.27 – 1.21 (m, 3H), 1.08 (s, 4H), 0.98 (s, 2H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.0, 171.3, 168.8, 143.9, 139.0, 135.8, 129.4, 129.1, 128.7, 128.2, 127.2, 127.0, 113.4, 64.5, 62.6, 61.6, 53.4, 51.0, 43.2, 42.4, 39.4, 38.0, 32.4, 26.5, 22.3, 14.2.

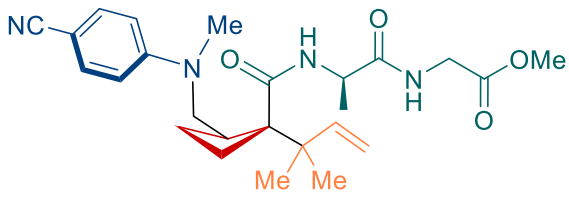
Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.8, 171.3, 168.8, 144.8, 139.1, 135.8, 129.4, 129.1, 128.6, 128.2, 127.2, 127.0, 113.2, 62.7, 62.4, 61.6, 53.5, 53.4, 43.5, 42.6, 39.5, 38.0, 32.4, 26.8, 23.2, 14.2.

HRMS: m/z $[M+Na]^+$ calcd for $C_{32}H_{43}N_3NaO_4$: 556.3146; found: 556.3144.



An oven-dried vial was charged with **42** (62.4 mg, 0.2 mmol, 1.0 equiv., >20:1 dr) in anhydrous DMF (2.0 mL). Then methyl *L*-alanylglycinate hydrochloride (59.1 mg, 0.3 mmol, 1.5 equiv.), HATU (114.0 mg, 0.3 mmol, 1.5 equiv.) and DIPEA (103.4 mg, 0.8 mmol, 4.0 equiv.) were added under argon atmosphere. The resulting reaction mixture was stirred for 12 h at 60 °C. After this time, a saturated aqueous NH_4Cl solution was added, and the aqueous phase was extracted with EtOAc twice. The combined organic layers were washed with brine, dried (anhydrous Na_2SO_4), filtered, and the solvent was evaporated under reduced pressure. After purification by chromatography on silica gel (petroleum ether/ethyl acetate 5:1), the product **57** was obtained as a colorless oil (54.6 mg, 60% yield, 1.2:1 dr).

methyl (2-(((4-cyanophenyl)(methyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutane-1-carbonyl)-D-alanylglycinate (57)



TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 5:1)

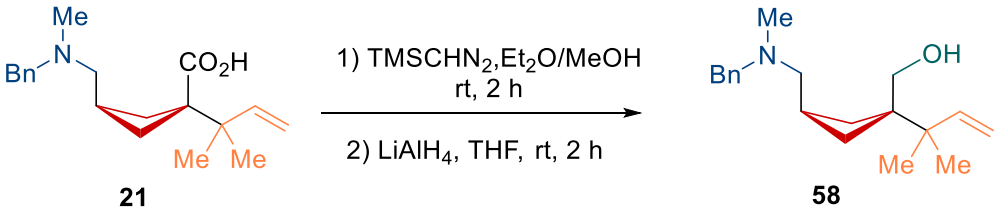
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.32 (m, 2H), 6.91 (t, *J* = 5.5 Hz, 0.5H), 6.85 (t, *J* = 5.4 Hz, 0.5H), 6.65 – 6.55 (m, 2H), 6.50 (d, *J* = 7.0 Hz, 0.5H), 6.41 (d, *J* = 7.2 Hz, 0.5H),, 6.09 – 5.92 (m, 1H), 5.18 – 5.01 (m, 2H), 4.64 – 4.50 (m, 1H), 4.16 – 3.93 (m, 2H), 3.93 – 3.76 (m, 1H), 3.78 – 3.64 (m, 3H), 3.34 – 3.18 (m, 1H), 3.04 – 2.88 (m, 3H), 2.76 –

2.58 (m, 1H), 2.32 – 2.00 (m, 2H), 1.94 – 1.83 (m, 1H), 1.76 – 1.54 (m, 1H), 1.45 – 1.35 (m, 3H), 1.14 – 0.96 (m, 6H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.3, 172.4, 170.0, 151.6, 144.7, 133.5, 120.8, 113.8, 111.5, 97.1, 58.4, 55.3, 52.4, 48.9, 41.2, 40.6, 39.4, 36.7, 24.0, 23.9, 22.5, 22.4, 18.3.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.4, 172.6, 170.1, 151.6, 144.4, 133.5, 120.9, 113.5, 111.4, 96.9, 58.3, 55.2, 52.4, 48.8, 41.2, 39.3, 38.7, 36.9, 24.4, 23.4, 23.0, 22.3, 18.0.

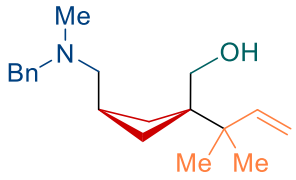
HRMS: m/z $[M+Na]^+$ calcd for $C_{25}H_{34}N_4NaO_4$: 477.2472; found: 477.2473.



21 **58**

An oven-dried vial was charged with **21** (60.2 mg, 0.2 mmol, 1.0 equiv., 1.4:1 dr) in MeOH (1.0 mL) and Et_2O (4.0 mL). Then $TMSCHN_2$ (2.0 M in hexanes, 0.5 mL, 1.0 mmol, 5.0 equiv.) was added slowly at room temperature. After stirring for 2 h, all volatiles were removed under reduced pressure and the compound was subsequently used without further purification. The above mixture was dissolved in dry THF (1.0 mL), which was added into the stirred suspension of $LiAlH_4$ (23.5 mg, 0.6 mmol, 3.0 equiv.) in THF (1.0 mL) at 0 °C under the argon atmosphere. The reaction mixture was stirred at room temperature for 2 h. Then it was quenched by water and 2.0 M HCl and extracted by ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (dichloromethane/methanol 30:1) to afford product **58** (24.7 mg, 43% yield for 2 steps, 2:1 dr).

(3-((benzyl(methyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutyl)methanol (58)



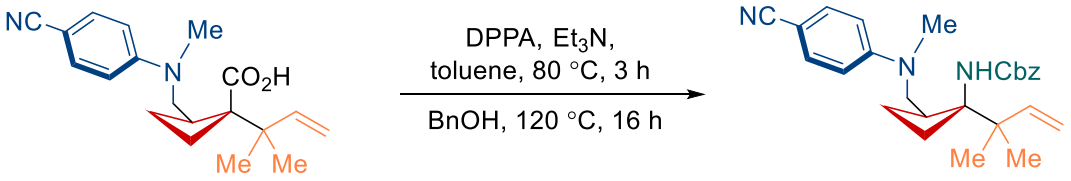
TLC: Rf = 0.4 (Dichloromethane/methanol 30:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.26 (m, 5H), 6.12 – 5.88 (m, 1H), 5.08 – 4.95 (m, 2H), 3.71 (s, 0.67H), 3.53 (s, 1.33H), 3.50 (s, 0.67H), 3.45 (s, 1.33H), 2.54 – 2.50 (m, 1H), 2.49 – 2.37 (m, 2H), 2.37 – 2.25 (m, 1H), 2.23 (s, 2H), 2.21 (s, 1H), 2.15 – 2.07 (m, 1.34H), 1.90 – 1.78 (m, 0.66H), 1.76 – 1.68 (m, 0.66H), 1.68 – 1.61 (m, 1.34H), 1.04 (s, 4H), 0.96 (s, 2H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.8, 138.5, 129.4, 128.3, 127.2, 111.8, 68.0, 63.5, 62.6, 44.9, 42.5, 39.5, 28.5, 25.9, 22.0.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 146.8, 138.9, 129.2, 128.3, 127.0, 111.4, 68.0, 63.2, 62.5, 45.3, 42.6, 39.7, 29.2, 28.5, 22.5.

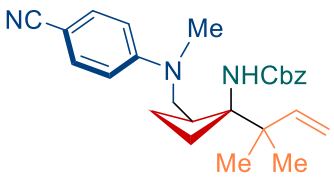
HRMS: m/z $[M+Na]^+$ calcd for $C_{19}H_{29}NNaO$: 310.2141; found: 310.2139.



42 **59**

An oven-dried vial was charged with **42** (62.4 mg, 0.2 mmol, 1.0 equiv., >20:1 dr), DPPA (70.0 μL, 0.3 mmol, 1.5 equiv.), Et_3N (54.0 μL, 0.4 mmol, 2.0 equiv.) and dry toluene (4.0 mL). Then the reaction mixture was stirred at 80 °C for 3 h. Afterwards, BnOH (0.2 mL, 2.0 mmol, 10.0 equiv.) was added. Then the mixture was stirred at 120 °C for 16 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography directly on silica gel (petroleum ether/ethyl acetate 20:1) to obtain product **59** as a colorless oil (54.3 mg, 65% yield, >20:1 dr).

benzyl (2-(((4-cyanophenyl)(methyl)amino)methyl)-1-(2-methylbut-3-en-2-yl)cyclobutyl)carbamate (59)

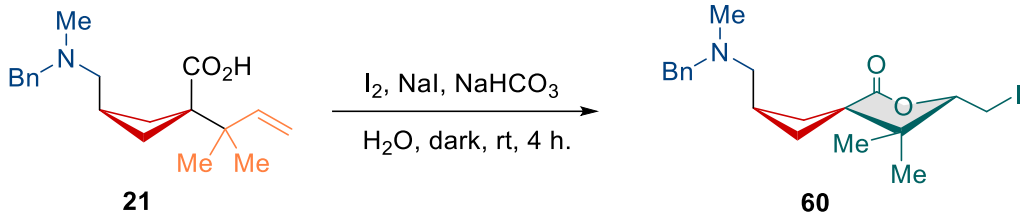


TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 20:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.30 (m, 7H), 6.60 (d, *J* = 9.1 Hz, 2H), 5.72 (dd, *J* = 17.4, 10.9 Hz, 1H), 5.16 – 4.95 (m, 4H), 4.82 (s, 1H), 3.56 – 3.37 (m, 2H), 3.03 – 2.92 (m, 1H), 2.91 (s, 3H), 2.80 (p, *J* = 7.8 Hz, 1H), 2.29 – 2.12 (m, 1H), 1.93 – 1.73 (m, 2H), 1.02 (s, 3H), 0.94 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.7, 151.7, 143.0, 136.7, 133.5, 128.6, 128.3, 128.3, 120.5, 114.6, 112.0, 97.9, 66.4, 64.0, 54.0, 43.6, 39.2, 36.9, 23.3, 22.1, 20.5, 19.9.

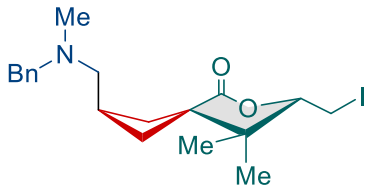
HRMS: m/z $[M+Na]^+$ calcd for $C_{26}H_{31}N_3NaO_2$: 440.2308; found: 440.2308.



21 **60**

To a suspension of **21** (60.2 mg, 0.2 mmol, 1.0 equiv., 1.4:1 dr) and $NaHCO_3$ (50.4 mg, 0.6 mmol, 3.0 equiv.) in H_2O (1.0 mL) was added NaI (90.0 mg, 1.2 mmol, 6.0 equiv.), followed by I_2 (50.8 mg, 0.2 mmol, 1.0 equiv.) under the argon atmosphere. The flask was covered with aluminum foil. Then the reaction mixture was stirred in dark for 4 h before being uncovered to reveal a brown precipitate. The reaction was extracted with CH_2Cl_2, washed with 10% $Na_2S_2O_3$ (aq.), 10% $NaHCO_3$ (aq.), and brine respectively. The organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel (dichloromethane/methanol 40:1) to afford the product of **60** (42.7 mg, 50% yield, 1.1:1 dr)**.**

2-((benzyl(methyl)amino)methyl)-7-(iodomethyl)-8,8-dimethyl-6-oxaspiro[3.4]octan-5-one (60)



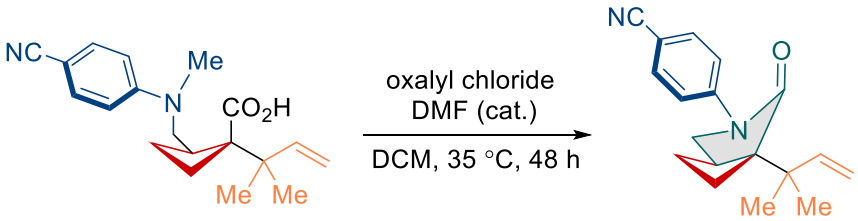
TLC: Rf = 0.4 (Dichloromethane/methanol 40:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.23 (m, 5H), 4.37 – 4.18 (m, 1H), 3.59 – 3.43 (m, 2H), 3.33 – 3.22 (m, 1H), 3.21 – 3.12 (m, 1H), 2.95 – 2.85 (m, 0.47H), 2.62 (s, 0.47H), 2.60 (s, 0.53H), 2.50 – 2.40 (m, 1H), 2.39 (s, 0.53H), 2.37 (s, 0.47H), 2.34 – 2.27 (m, 0.6H), 2.25 – 2.14 (m, 4.6H), 1.96 – 1.87 (m, 0.47H), 1.87 – 1.80 (m, 0.5H), 1.66 – 1.56 (m, 0.55H), 1.26 (s, 1.45H), 1.07 (s, 1.55H), 0.90 (s, 1.45H), 0.81 (s, 1.55H).

Major diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.9, 138.9, 129.1, 128.3, 127.1, 85.7, 63.3, 62.3, 50.5, 43.4, 42.6, 31.5, 29.7, 27.7, 21.0, 16.4, -0.4.

Minor diastereomer: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.0, 138.8, 129.1, 128.3, 127.1, 85.3, 63.3, 62.7, 49.9, 43.7, 42.5, 30.8, 27.7, 26.1, 20.0, 16.6, -0.6.

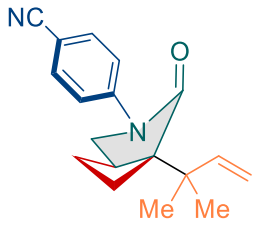
HRMS: m/z $[M+Na]^+$ calcd for $C_{19}H_{26}INNaO_2$: 450.0900; found: 450.0889.



42 **61**

The compound **42** (21.7 mg, 0.1 mmol, 1.0 equiv., >20:1 dr) was dissolved in dry DCM (5.0 mL), and oxalyl chloride (42.0 μL, 0.5 mmol, 5.0 equiv.) was added dropwise at 0 °C under the argon atmosphere. Then dry DMF (0.2 mL) was added, and the reaction mixture was stirred for 12 h at 35 °C. Afterwards, another portion of oxalyl chloride (42.0 μL, 0.5 mmol, 5.0 equiv.) was added at 0 °C, and the reaction mixture was stirred for another 36 h at 35 °C. Then it was concentrated under reduced pressure. The residue was purified by column chromatography (petroleum ether/ethyl acetate 3:1) to afford product **61** as a colorless oil (14.0 mg, 50% yield, >20:1 dr).

4-(1-(2-methylbut-3-en-2-yl)-2-oxo-3-azabicyclo[3.2.0]heptan-3-yl)benzonitrile (61)

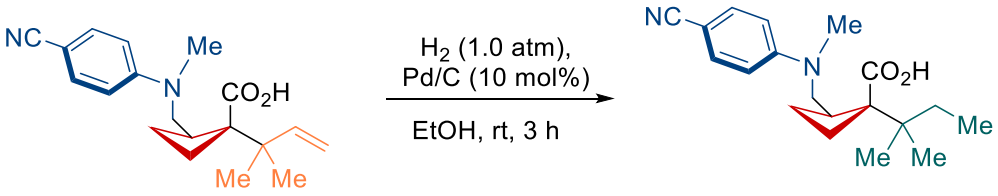


TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 3:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.79 (m, 2H), 7.75 – 7.59 (m, 2H), 6.04 – 5.85 (m, 1H), 5.16 – 4.95 (m, 2H), 3.83 (dd, *J* = 9.9, 6.8 Hz, 1H), 3.53 (d, *J* = 9.8 Hz, 1H), 2.92 (dt, *J* = 8.9, 6.8 Hz, 1H), 2.36 – 2.26 (m, 1H), 2.22 – 2.13 (m, 1H), 2.13 – 2.03 (m, 1H), 1.81 – 1.69 (m, 1H), 1.14 (s, 3H), 1.07 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 178.8, 143.7, 143.7, 133.0, 119.6, 119.0, 113.3, 107.1, 57.8, 53.2, 39.5, 31.5, 24.9, 22.1, 21.9, 21.9.

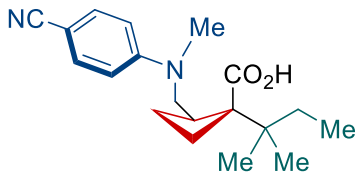
HRMS: m/z $[M+Na]^+$ calcd for $C_{18}H_{20}N_2NaO$: 303.1468; found: 303.1468.



42 **62**

To an oven-dried 25.0 mL round-bottom flask was added **42** (62.4 mg, 0.2 mmol, 1.0 equiv., >20:1 dr), Pd/C (11.0 mg, 2.0×10^{-2} mmol, 0.1 equiv.) and EtOH (5.0 mL). Then the mixture was stirred at rt for 3 h under H_2 atmosphere. The solvent was removed under reduced pressure and the residue was purified by flash chromatography directly on silica gel (petroleum ether/ethyl acetate 3:1) to obtain product **62** as a colorless oil (47.1 mg, 75% yield, >20:1 dr).

2-(((4-cyanophenyl)(methyl)amino)methyl)-1-(tert-pentyl)cyclobutane-1-carboxylic acid (62)

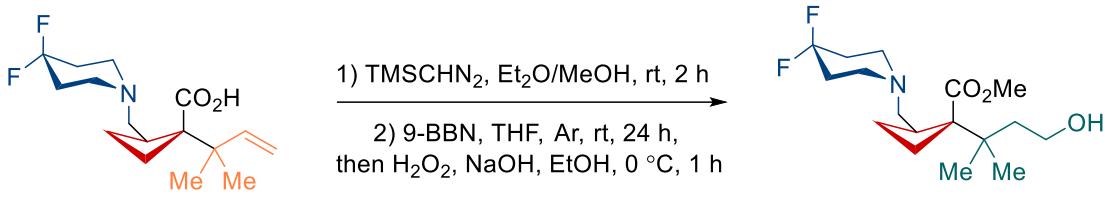


TLC: Rf = 0.3 (Petroleum ether/ethyl acetate 3:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 9.0 Hz, 2H), 6.60 (d, *J* = 9.0 Hz, 2H), 3.85 (dd, *J* = 15.1, 3.8 Hz, 1H), 3.28 (dd, *J* = 15.1, 10.8 Hz, 1H), 2.98 (s, 3H), 2.84 – 2.66 (m, 1H), 2.42 (ddd, *J* = 12.8, 9.6, 3.8 Hz, 1H), 2.15 – 1.99 (m, 1H), 1.96 – 1.79 (m, 1H), 1.72 (dq, *J* = 11.1, 9.2 Hz, 1H), 1.53 – 1.38 (m, 1H), 1.32 – 1.24 (m, 1H), 1.02 (s, 3H), 0.97 (s, 3H), 0.86 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 181.1, 151.5, 133.6, 120.7, 111.4, 97.2, 60.1, 55.9, 39.4, 37.5, 36.9, 30.7, 24.3, 23.3, 22.8, 22.4, 8.8.

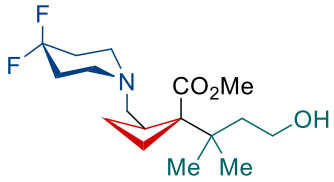
HRMS: m/z $[M+Na]^+$ calcd for $C_{19}H_{26}N_2NaO_2$: 337.1886; found: 337.1887.



43 **63**

To a solution of **43** (60.2 mg, 0.2 mmol, 1.0 equiv., >20:1 dr) in MeOH (1.0 mL) and Et_2O (4.0 mL) was added $TMSCHN_2$ (2.0 M in hexane, 0.5 mL, 1.0 mmol, 5.0 equiv.) slowly at room temperature. After stirring for 2 h, the reaction mixture was concentrated under reduced pressure. The residue was used for next step without purification. The above residue was dissolved in 9-BBN (0.5 M in tetrahydrofuran, 1.8 mL, 0.9 mmol, 4.5 equiv.) under an argon atmosphere, and the resulting solution was stirred 24 h at room temperature. The reaction was diluted with ethanol (6.0 mL) and treated with 4.0 M sodium hydroxide (1.0 mL). Then 30% hydrogen peroxide (1.2 mL) was added dropwise at 0 °C. The reaction was stirred at 0 °C for 1 h, which was then quenched by addition of saturated NH_4Cl. The mixture was extracted with diethyl ether. The combine organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (dichloromethane/methanol 30:1) to afford product **63** (29.3 mg, 44% yield for 2 steps, >20:1 dr).

methyl 2-((4,4-difluoropiperidin-1-yl)methyl)-1-(4-hydroxy-2-methylbutan-2-yl)cyclobutane-1-carboxylate (63)



TLC: Rf = 0.3 (Dichloromethane/methanol 30:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.69 (s, 3H), 3.65 (t, *J* = 7.6 Hz, 2H), 2.70 (dd, *J* = 12.7, 3.7 Hz, 1H), 2.66 – 2.56 (m, 1H), 2.56 – 2.44 (m, 3H), 2.44 – 2.36 (m, 1H), 2.17 (dd, *J* = 12.7, 10.4 Hz, 1H), 2.05 – 1.84

(m, 6H), 1.72 – 1.51 (m, 4H), 1.51 – 1.42 (m, 1H), 1.03 (s, 3H), 0.98 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.0, 122.0, 61.4, 59.7, 59.5, 51.2, 50.4 (t, *J* = 5.1 Hz), 41.3, 36.9, 36.8, 34.2, 34.0 (t, *J* = 23.2 Hz), 33.8, 23.8, 23.7, 23.6, 23.6.

HRMS: m/z $[M+Na]^+$ calcd for $C_{17}H_{29}F_2NNaO_3$: 356.2008; found: 356.2008.

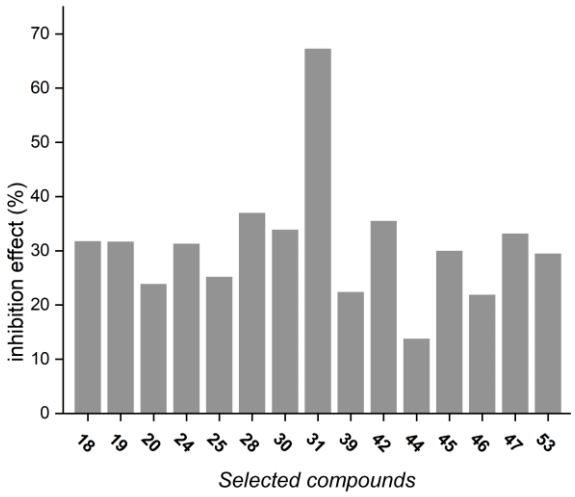
10.Anticancer activity study

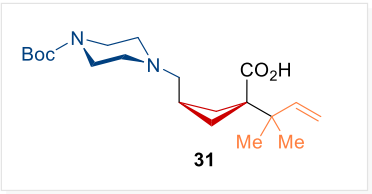
Cell culture

TMD-8, KPC or HCT-116 cells were cultured in IMEM (Gibco, Milano, Italy). The above media contained 10% fetal bovine serum (FBS) (Invitrogen, Milano, Italy), 100.0 units/mL penicillin (Gibco, Milano, Italy), and 100.0 μg/mL streptomycin (Gibco, Milano, Italy). Cells were incubated at 37 °C in a humidified atmosphere of 5% CO_2. The source of the tumor cell lines was from American Type Culture Collection (ATCC). Tumor cells were subcultured and seeded in vitro by State Key Laboratory of Biotherapy and Cancer Center, National Clinical Research Center for Geriatrics, West China Hospital of Sichuan University, China.

Cell viability assay

Cells in logarithmic phase were seeded into 96-well culture plates at densities of 3000-5000 cells per well and subsequently treated with various concentrations of compounds for 72 h in final volumes of 200.0 μL. Upon end point, 20.0 μL of MTT (5.0 mg/mL) was added to each well, and the cells were incubated for an additional 1-3 h. After carefully removal of the medium, the precipitates were dissolved in 150.0 μL of DMSO via mechanically shaking, and then absorbance values at a wavelength of 570 nm were taken on a spectrophotometer (Molecular Devices, Sunnyvale, USA). IC_{50} values were calculated using percentage of growth versus untreated control.





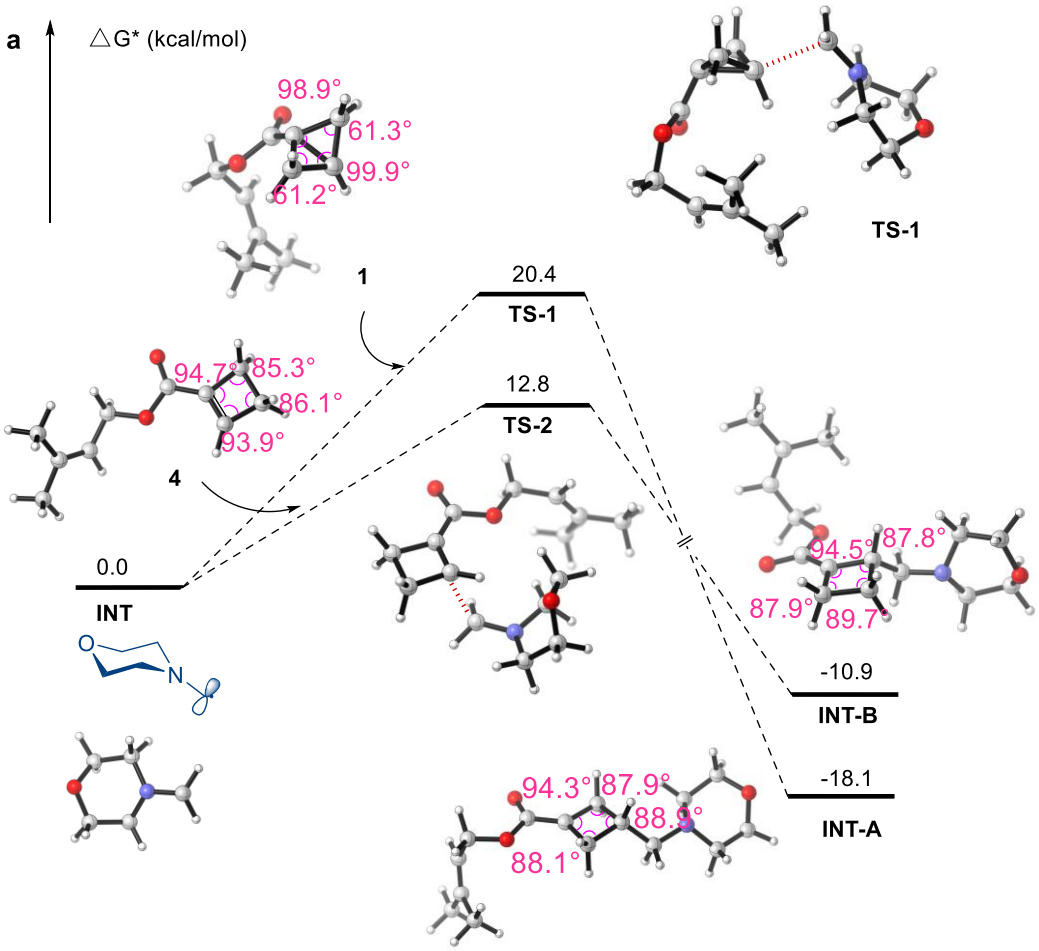
31

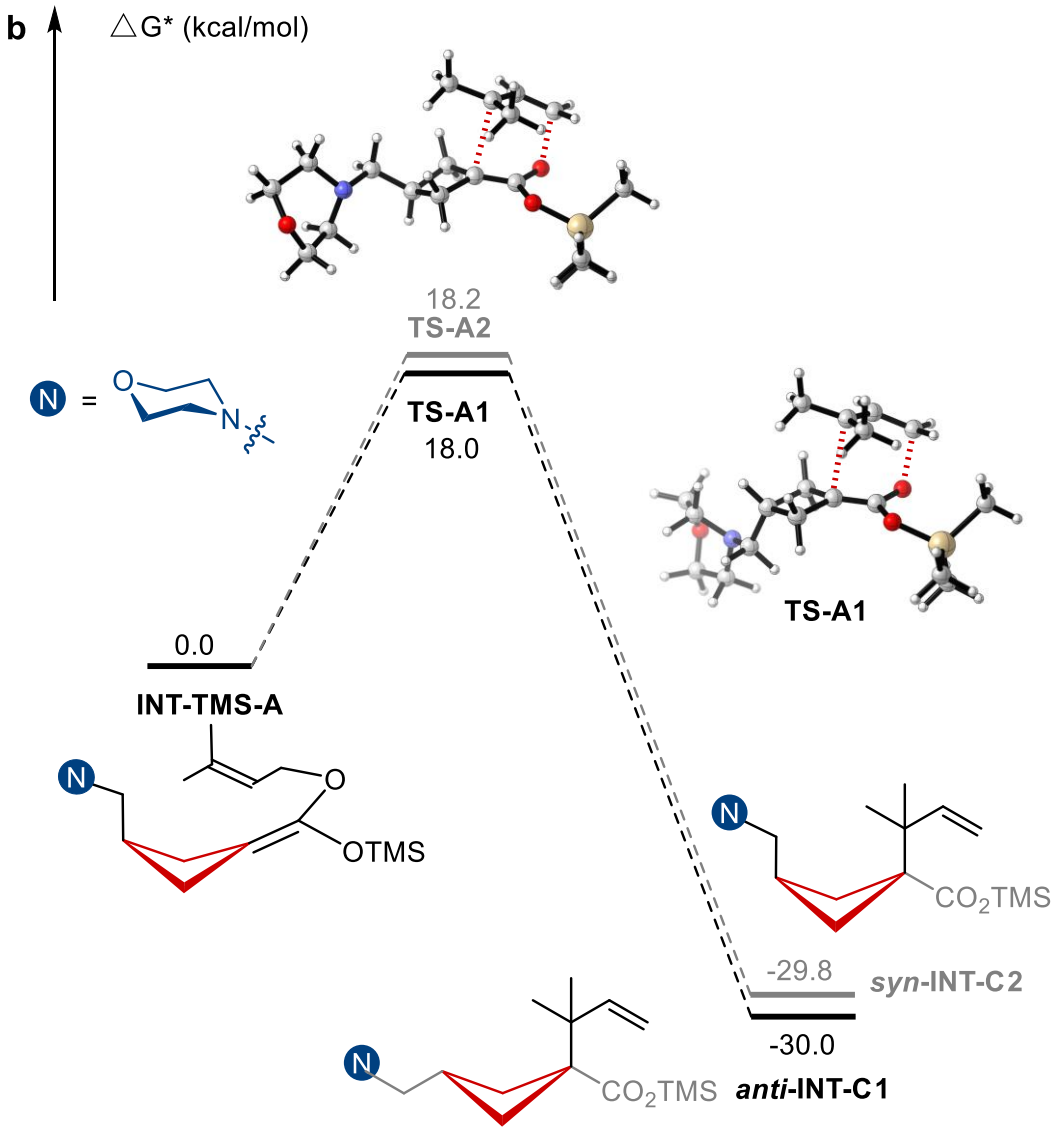
Cell lines	IC_{50} (μM)
TMD-8	5.7±0.2
KPC	8.0±0.6
HCT-116	8.2±0.7

Fig. S5. Anticancer activity study. TMD-8 inhibition induced by selected compounds at 10.0 μM for 72 h, and IC_{50} values of compound **31** in different cancer cell lines, including TMD-8, KPC and HCT-116. IC_{50} values were evaluated using the MTT assay.

11. DFT calculation

All calculations were performed by using the Gaussian 09 program.[2] B3LYP functional and the 6-31G(d,p) basis set, combined with Grimme's D3(BJ) dispersion correction and the IEFPCM solvation model were utilized for the initial geometry optimizations and frequency calculations. For single-point energy calculations of intermediates and transition states, we operated them at the M06/def2-TZVP/SMD (acetonitrile) level.[3] And the Intrinsic Reaction Coordinate (IRC) method was employed to verify the accuracy of the transition states, ensuring that the transition states connected two energy minima. To further confirm the reliability of our conclusions, the single-point energies were recalculated via the range-separated meta-GGA hybrid functional ωB97M-V[4–6] and the def2-TZVPP basis set using ORCA software.[7] And the consistent results were obtained. Furthermore, Multiwfn 3.8 (dev)[8] was utilized to analyze non-covalent interactions between fragments based on the Independent Gradient Model (IGMH) with Hirshfeld partitioning; and the structures were visualized by using VMD (version 1.9.3)[9] with an isovalue of 0.007; and the high-quality three-dimensional (3D) images were generated by CYLview.[10] All energies were discussed in terms of Gibbs free energies in solution (kcal/mol). The choice of functionals and basis sets was based on the recent benchmark studies, ensuring the accuracy of the computational methods and the credibility of the results.


a
△G* (kcal/mol)
98.9°
61.3°
99.9°
61.2°
1
20.4
TS-1
TS-1
12.8
TS-2
94.7°
85.3°
86.1°
93.9°
4
0.0
INT
O
N
94.5°
87.8°
87.9°
89.7°
-10.9
INT-B
-18.1
INT-A
94.3°
87.9°
88.9°
88.1°


b
△G* (kcal/mol)
N = O N
18.2
TS-A2
TS-A1
18.0
TS-A1
0.0
INT-TMS-A
N
O
OTMS
N
CO2TMS
-29.8
syn-INT-C2
-30.0
N
CO2TMS
anti-INT-C1

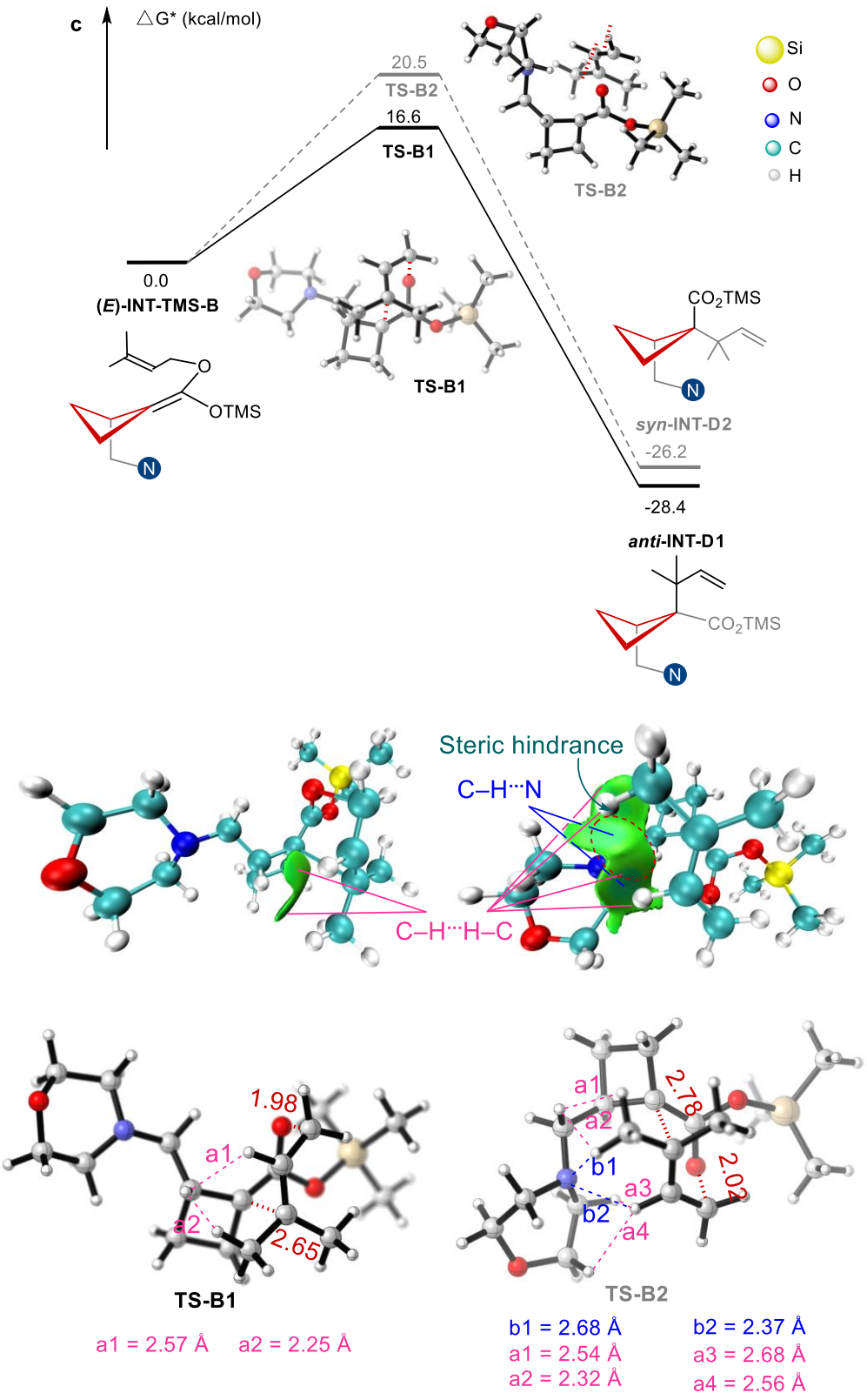


Fig. S6. Insights from DFT calculations. a, aminoalkyl radical addition to BCB **1** and cyclobutene **4**. **b**, relative energies for [3,3]-rearrangement of BCB-TMS intermediate. **c**, relative energies for [3,3]-rearrangement of (*E*)-cyclobutene-TMS intermediate. Calculations were performed at the B3LYP/6-31G(d,p)/SMD (acetonitrile) level of theory.

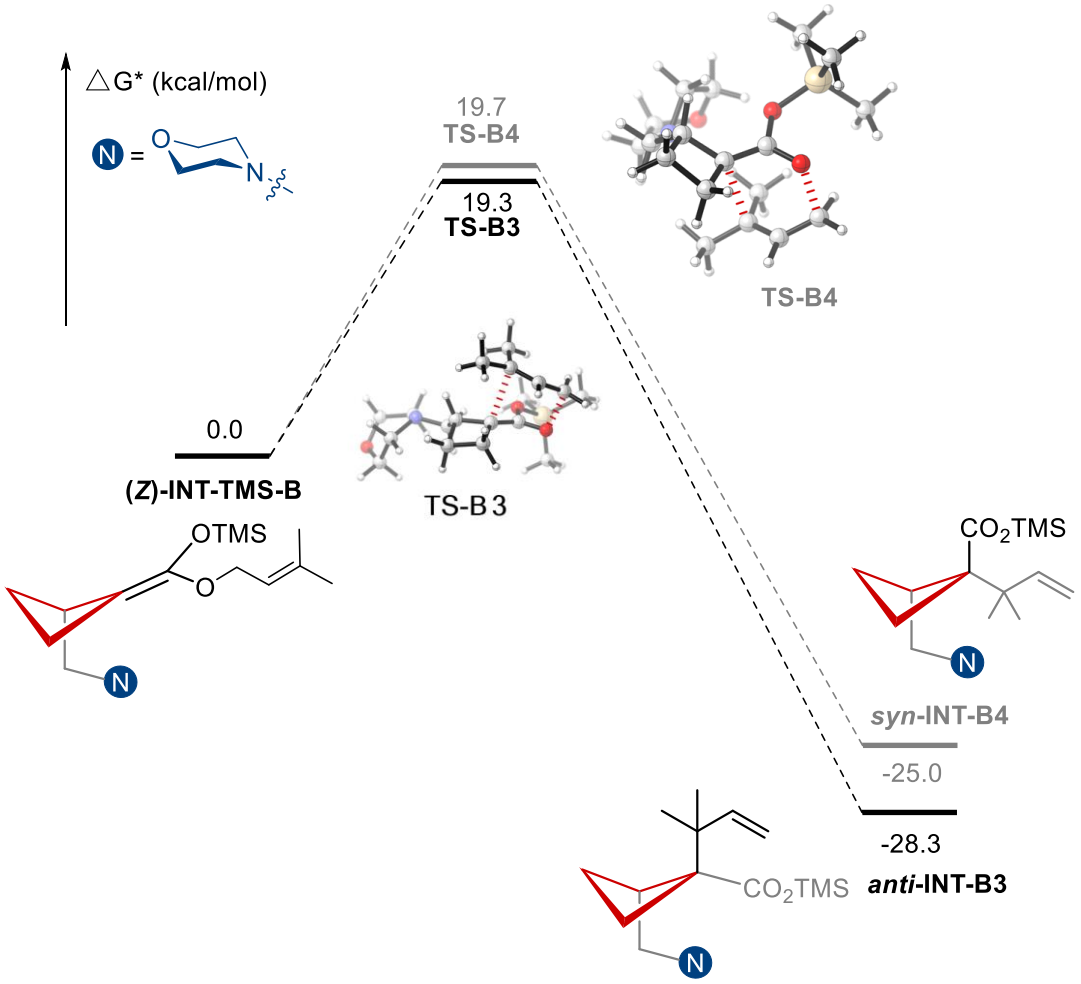


Fig. S7. Relative energies for [3,3]-rearrangement of (*Z*)-cyclobutene-TMS intermediate.

Cartesian Coordinates (Å) for the Optimized Structures

1

C	-2.22793300	-1.34492400	0.56657700
C	-3.18534500	-0.27289600	0.96598600
C	-2.34563400	-1.25745300	-0.91743000
H	-1.41160000	-1.75446400	1.14413300
H	-3.00907100	0.21784200	1.91941300
H	-4.23548900	-0.37106300	0.68753700
H	-1.48692300	-1.57546100	-1.50174900
H	-3.31314100	-1.45179300	-1.38275600
C	-1.05036300	0.92153800	-0.03581000
O	-0.88949100	1.74677700	0.84997000
O	-0.18424000	0.72772400	-1.05270300
C	1.07967000	1.44960200	-0.95138100
H	1.51441700	1.32936800	-1.94539400
H	0.86338600	2.50566000	-0.78389300
C	1.96766800	0.90763900	0.13360300
H	2.18231300	1.58092400	0.95924300
C	2.47104400	-0.33536500	0.16349200
C	3.33202700	-0.79937400	1.30855800
H	2.88216200	-1.66739500	1.80681800
H	4.31584500	-1.12461200	0.94761600
H	3.47939800	-0.01353500	2.05354700
C	2.21249200	-1.36704700	-0.90332200
H	1.63663700	-2.20374100	-0.48789900
H	1.65577900	-0.97299300	-1.75415600
H	3.15771900	-1.78910700	-1.26511100
C	-2.19389100	0.01400600	-0.12618800

TS-1

C	-0.20228100	-1.61815200	-0.39401000

C	-0.48341600	-2.67143600	0.62897400
C	-1.18876700	-2.03005500	-1.43411800
H	-0.03947900	-0.58321700	-0.12714000
H	-0.33575300	-2.41033000	1.67437900
H	-0.17881000	-3.69120700	0.38287200
H	-1.60780800	-1.25404100	-2.06867300
H	-0.98723600	-2.96638500	-1.95972400
C	-2.60448700	-1.19814900	0.61597600
O	-2.70367400	-1.03651000	1.82965300
O	-3.31430600	-0.46093100	-0.28806400
C	-3.89399900	0.75930900	0.24184600
H	-4.50880700	1.12947200	-0.58208800
H	-4.54468800	0.51193400	1.08248100
C	-2.84213300	1.75227300	0.66331300
H	-2.85194300	2.04522400	1.71008500
C	-1.88707100	2.25149700	-0.13566800
C	-0.84473800	3.20050300	0.39548900
H	0.16268900	2.78588500	0.26224500
H	-0.86292500	4.14967000	-0.15460700
H	-0.98815900	3.41269100	1.45787900
C	-1.75595500	1.91021500	-1.59753000
H	-0.82641200	1.35553500	-1.78039800
H	-2.58074000	1.30138900	-1.96807300
H	-1.69254800	2.82519900	-2.19852500
C	-1.72868700	-2.14836300	-0.03154100
N	2.78492700	-0.72716800	-0.55621900
C	2.62144200	0.62598900	-1.09375400
H	1.56461200	0.84463900	-1.31361900
H	3.17452100	0.69573100	-2.03769900

C	2.99272200	-0.79290300	0.88319400
H	2.10615900	-0.43487200	1.42889100
H	3.14147500	-1.83630600	1.17159500
C	3.15456900	1.64938800	-0.08894300
H	2.41673100	1.83808100	0.70451700
H	3.35162800	2.59956500	-0.58994500
C	4.23558400	0.02527300	1.26107500
H	5.14074100	-0.56730100	1.09828600
H	4.18440300	0.29364200	2.32602000
O	4.38608700	1.20423800	0.46086300
C	2.10642200	-1.75276900	-1.17977800
H	2.30114100	-2.75210400	-0.80581700
H	1.94662800	-1.63279700	-2.24617500

4

C	3.89462200	0.27141700	0.20466800
C	2.62368500	-1.40985700	0.11630600
H	4.37454900	0.75027400	-0.65404700
H	4.13762300	0.83626800	1.10961200
H	1.95750300	-2.26480200	0.06912400
C	1.25586000	0.77770200	-0.17411000
O	1.30435600	1.99748000	-0.22696500
O	0.11872200	0.06431300	-0.28955300
C	-1.09798300	0.84058700	-0.50018300
H	-1.24447300	1.49738500	0.35859600
H	-0.94065300	1.47454300	-1.37917000
C	-2.21593200	-0.12358800	-0.71227600
H	-2.11056500	-0.75385800	-1.59387500
C	-3.31111000	-0.27069900	0.04880300
C	-4.37120700	-1.27529600	-0.32435900

H	-4.51914100	-2.00019300	0.48575700
H	-5.33834200	-0.78060300	-0.47864200
H	-4.11499300	-1.82181200	-1.23526100
C	-3.60964400	0.51510900	1.29882900
H	-3.80096000	-0.16826600	2.13481800
H	-2.80779300	1.19339700	1.59265800
H	-4.52339200	1.10750100	1.16691200
C	2.42927300	-0.07993600	0.02503500
C	4.12072600	-1.28186100	0.31094200
H	4.49990400	-1.62969900	1.27753300
H	4.73636700	-1.71594800	-0.48379400

TS-2

C	-3.43762200	-2.08730500	0.15470700
C	-2.36541700	-0.34788000	-0.44823500
H	-3.89640000	-2.85065900	-0.48391000
H	-3.59323400	-2.37323200	1.20185000
H	-1.87548400	0.45661800	-0.98277300
C	-0.79270400	-2.40152400	-0.19461300
O	-0.67002000	-3.60162900	0.05395100
O	0.28346800	-1.59684600	-0.46041700
C	1.58431200	-2.23386300	-0.40244300
H	1.72900300	-2.65280400	0.59563200
H	1.59724200	-3.06771500	-1.11174900
C	2.60510900	-1.20193700	-0.76030600
H	2.66057200	-0.95476100	-1.81905000
C	3.41130600	-0.54195900	0.08582400
C	4.37357200	0.49874500	-0.42610200
H	4.16193900	1.47473300	0.02872600
H	5.40576700	0.24614400	-0.15321000

H	4.31939000	0.60624800	-1.51219400
C	3.44220400	-0.74239300	1.57843900
H	3.24853100	0.20930700	2.08829600
H	2.71224500	-1.46980100	1.93560200
H	4.43835600	-1.06916800	1.90066300
C	-2.02752200	-1.66848800	-0.21706600
C	-1.53499900	0.88220000	1.49128600
H	-1.03099500	0.01236300	1.89322400
H	-2.51465100	1.13163700	1.88211100
N	-0.73839300	1.92966400	1.13172700
C	-1.34589200	3.17742100	0.66011500
H	-1.22878500	3.97511700	1.40645600
H	-2.41444200	3.00176100	0.51508400
C	0.61079000	1.68852100	0.63737200
H	1.26839000	2.47559900	1.02238200
H	0.96915500	0.73299400	1.01851300
C	-0.69982500	3.59930900	-0.67068400
H	0.22564600	4.16697700	-0.49752100
H	-1.38256900	4.23690200	-1.23642200
C	0.63072300	1.66798000	-0.90862300
H	0.48473700	0.65113500	-1.27080800
H	1.60039000	2.04084300	-1.26943300
O	-0.43614900	2.44805600	-1.46088400
C	-3.84502100	-0.60918800	-0.19288000
H	-4.30407100	-0.04242400	0.62301200
H	-4.48446700	-0.51994700	-1.07851700

INT

C	-2.37021000	-0.09395600	-0.25625200
H	-2.85676100	-1.03029500	-0.01600600

H	-2.92898100	0.83362900	-0.21996600
N	-1.00017800	-0.02461600	-0.09523900
C	-0.35826100	1.28318500	-0.01266100
H	-0.84014900	1.91836600	0.74881100
H	-0.46020500	1.79332700	-0.97898200
C	-0.25215100	-1.13187900	0.47137400
H	-0.16339200	-1.03691500	1.56603000
H	-0.79222400	-2.06176000	0.27737900
C	1.12214800	1.10946700	0.33085400
H	1.25264300	0.90239600	1.40281300
H	1.67015500	2.02626000	0.10195600
C	1.13687700	-1.21260700	-0.17875700
H	1.07197100	-1.73091900	-1.14061400
H	1.81268800	-1.78255800	0.47531100
O	1.69563600	0.07694000	-0.45967500

INT-A

C	-0.17208200	3.00204400	-0.99785800
C	0.60621300	0.97490100	-0.62123200
H	-0.76321000	3.26991600	-1.88312700
H	-0.10439500	3.89778400	-0.36816200
H	0.40381500	0.16834400	-1.33929600
C	-1.84595100	1.46487600	0.41433400
O	-2.78658400	2.24659800	0.54820900
O	-1.83300200	0.20846700	0.93492600
C	-3.05545900	-0.21249100	1.60400900
H	-2.74423400	-1.09611000	2.16412200
H	-3.35300800	0.56701400	2.30747900
C	-4.17015300	-0.51130400	0.64051900
H	-5.02296800	0.16183600	0.66804800

C	-4.16528700	-1.51473400	-0.24977400
C	-5.32338800	-1.72946100	-1.18818100
H	-4.99569000	-1.66122200	-2.23322400
H	-5.74540300	-2.73431600	-1.06069800
H	-6.11924500	-0.99765700	-1.02884000
C	-3.02383400	-2.48475200	-0.40814500
H	-2.59469600	-2.40045900	-1.41449700
H	-2.21906900	-2.32029500	0.30905500
H	-3.38049100	-3.51711000	-0.30825900
C	-0.63510900	1.75980700	-0.30017800
C	1.39315700	0.41907700	0.57159900
H	0.80652100	-0.38044600	1.05771600
H	1.50908200	1.22055800	1.31055100
N	2.72902400	-0.02001300	0.19277000
C	3.60282400	-0.15037400	1.36747000
H	3.07565600	-0.60726600	2.22517600
H	3.91735700	0.85345300	1.67521100
C	2.76125100	-1.24476000	-0.59823400
H	2.48679000	-2.13199300	0.00234300
H	2.03651700	-1.18402900	-1.41348000
C	4.82208900	-1.02688300	1.02870500
H	4.61301300	-2.08219800	1.25787800
H	5.68775400	-0.72601000	1.62344300
C	4.16730900	-1.39619100	-1.20082800
H	4.24490700	-0.82018100	-2.12758800
H	4.36127600	-2.45458100	-1.43253400
O	5.18464400	-0.88177700	-0.33699300
C	1.17436900	2.26497100	-1.29504400
H	2.03356900	2.67539000	-0.76096700

H	1.42683100	2.16501600	-2.35184700

INT-B

C	-0.93397700	-1.08110800	-0.81255100
H	-1.60328300	-1.07934100	-1.67618600
H	-0.53344400	-0.07393600	-0.68785700
C	1.43219000	-1.94179700	-0.30445500
O	2.41194400	-2.65591300	-0.51387700
O	1.42196400	-0.95322500	0.63080000
C	2.69164500	-0.66700600	1.27741100
H	2.40226000	-0.11406800	2.17331300
H	3.15481000	-1.60875200	1.57504000
C	3.61236600	0.12551500	0.39132800
H	4.52712900	-0.37076100	0.07732200
C	3.36299300	1.36684600	-0.05222400
C	4.33053000	2.08030800	-0.95912500
H	3.85103100	2.34241600	-1.91071300
H	4.66145200	3.02442600	-0.50839600
H	5.21258100	1.47214300	-1.17454700
C	2.11363900	2.13867400	0.28558400
H	1.52330500	2.31564900	-0.62259500
H	1.47229700	1.62351000	1.00160900
H	2.36899600	3.12646900	0.68745600
C	0.17523200	-2.03843500	-1.00994000
H	0.07431800	-2.89241000	-1.67088900
C	-1.77090500	-1.42598600	0.47837900
H	-1.07543600	-1.46479100	1.32139700
H	-2.18961600	-2.42968100	0.35003400
N	-2.84821400	-0.52512800	0.82787900
C	-3.97571500	-0.45106400	-0.10836500

H	-4.92393000	-0.65482200	0.41202300
H	-3.85181400	-1.22929400	-0.86618600
C	-2.48046000	0.78068700	1.35675500
H	-3.31935600	1.14467300	1.96308900
H	-1.62618300	0.66962900	2.03032300
C	-4.06355800	0.93104900	-0.78880900
H	-4.66702300	1.62533700	-0.18444700
H	-4.53395200	0.85140200	-1.77199900
C	-2.15808800	1.82338700	0.25382300
H	-1.08425300	1.88586900	0.05990000
H	-2.50477700	2.82005300	0.56977900
O	-2.76052800	1.46485600	-0.99061000

INT-TMS-A

C	-1.33815600	2.10000100	-0.45947500
C	-0.87523500	1.27659700	-1.70012100
C	0.54344300	1.41872500	-1.18499300
C	0.14889900	2.51063500	-0.20624200
H	-2.01856400	2.93036300	-0.66570500
H	-1.05714700	1.79706000	-2.64849600
H	-1.28857500	0.26645000	-1.77266000
H	0.37728700	3.52041600	-0.56866600
H	0.49434000	2.43631300	0.82885500
C	1.63941600	0.69877600	-1.42759300
O	1.64457600	-0.20041400	-2.46090100
O	2.84111300	0.80383800	-0.80015200
C	-1.86052400	1.20897400	0.66297500
H	-1.99976900	1.81081900	1.58304300
H	-1.08488300	0.46752100	0.89140200
N	-3.06425100	0.46637000	0.31264800

C	-3.30229600	-0.63718900	1.25107500
H	-3.10905800	-0.33818900	2.29846600
H	-2.60466600	-1.44800400	1.01222900
C	-4.26485000	1.28137200	0.17721700
H	-4.62168300	1.65976700	1.15384200
H	-4.05272100	2.15767600	-0.43943400
C	-4.76061100	-1.11888800	1.14872900
H	-5.39514200	-0.58048500	1.86820200
H	-4.83089300	-2.18425300	1.38084200
C	-5.34662200	0.43778500	-0.51687500
H	-5.21999000	0.48114500	-1.60267600
H	-6.34423900	0.83084400	-0.26791100
O	-5.25820400	-0.94750800	-0.17081700
C	0.91926600	-2.15205500	-1.21334100
H	-0.09596300	-1.94561700	-1.54888900
C	1.08744400	-2.88462100	-0.10249800
C	2.42293000	-3.27643200	0.47400500
H	3.26908100	-2.86362800	-0.07629700
H	2.49898500	-2.95027200	1.51803400
H	2.52842200	-4.36816900	0.47844700
C	-0.10359000	-3.39256600	0.66972600
H	-1.04652700	-3.10762300	0.19630300
H	-0.07875800	-4.48554700	0.76043700
H	-0.09635100	-2.99406000	1.69234600
Si	3.21702700	0.88335700	0.85791600
C	1.84474400	0.10887900	1.88231700
H	2.27273500	-0.36249500	2.77335900
H	1.10471100	0.84158500	2.21350900
H	1.32591200	-0.65996300	1.30397300

C	4.81016900	-0.09332900	1.01073600
H	4.65497900	-1.15173800	0.78236100
H	5.57500900	0.29354800	0.32975900
H	5.20277300	-0.02404900	2.03110900
C	3.52623000	2.67610400	1.31972500
H	4.35264500	3.09060900	0.73321800
H	2.64483700	3.30174400	1.15446200
H	3.79773400	2.75015700	2.37886000
C	1.98031200	-1.56040000	-2.09125800
H	2.97079800	-1.58119800	-1.63056000
H	2.04034500	-2.08386900	-3.05081900

TS-A1

C	1.62199900	0.41986500	-0.97953200
C	0.95895900	0.61380400	0.42082700
C	-0.38220300	0.32678700	-0.22531900
C	0.21365600	0.14468500	-1.60259500
H	2.07805500	1.33455900	-1.36772000
H	1.08989600	1.60441900	0.86636800
H	1.27945100	-0.12601200	1.16335700
H	-0.10743600	0.87614500	-2.35591600
H	0.08789100	-0.85280100	-2.04235100
C	-1.55879600	-0.11469400	0.32310500
O	-1.85678500	0.01444200	1.56900300
O	-2.51651600	-0.59282700	-0.54538200
C	2.58406600	-0.75463200	-1.07272300
H	2.86908600	-0.92449400	-2.13023400
H	2.05223400	-1.65798600	-0.74702900
N	3.75275600	-0.61406700	-0.21122400
C	4.45032400	-1.89564000	-0.04208900

H	4.50853100	-2.46212100	-0.99031500
H	3.88014800	-2.50699600	0.66702300
C	4.69411500	0.41750000	-0.63021000
H	5.23776400	0.13365500	-1.55108900
H	4.15929700	1.34268600	-0.85571000
C	5.88415400	-1.66055800	0.46638400
H	6.58231500	-1.56986800	-0.37886500
H	6.21726500	-2.50151400	1.07925700
C	5.66974700	0.68226200	0.52768100
H	5.23110500	1.39166500	1.23569100
H	6.60396800	1.11429000	0.13740000
O	5.94716000	-0.50019100	1.28364500
C	-1.60055800	2.63687300	1.22942500
H	-0.76722200	2.97422500	1.84127100
C	-1.46700500	2.75926900	-0.14098000
C	-2.57242900	2.48163200	-1.12135900
H	-3.35346300	1.83437600	-0.72775500
H	-3.02737100	3.43421700	-1.42421200
H	-2.17682500	2.01605900	-2.02862200
C	-0.30920100	3.52905400	-0.71135700
H	0.49757900	3.66058300	0.01270700
H	0.09141200	3.03794500	-1.60409800
H	-0.64574200	4.52452200	-1.03033700
Si	-3.80127600	-1.59189300	-0.04941500
C	-4.52514000	-2.18144700	-1.67775200
H	-3.78347700	-2.73262400	-2.26469900
H	-5.37836400	-2.84564400	-1.50256200
H	-4.87627000	-1.33813800	-2.28157400
C	-3.12691400	-3.03002600	0.95204400

H	-2.39782900	-3.60357200	0.37016400
H	-2.63413700	-2.67223100	1.86004900
H	-3.93464500	-3.70985200	1.24432000
C	-5.10272000	-0.64120400	0.91584100
H	-4.73057400	-0.33954100	1.89796700
H	-5.42048800	0.25710300	0.37565100
H	-5.98943300	-1.26805200	1.06402800
C	-2.56420500	1.83245500	1.84924100
H	-2.58140000	1.76275500	2.93009600
H	-3.51071700	1.62992100	1.36619900

***anti*-INT-C1**

C	-1.16454800	-1.43066500	-1.20670000
C	-0.59223500	-1.86825600	0.16653300
C	0.81486100	-1.37382300	-0.28780100
C	0.28592300	-1.34589200	-1.75477200
H	-1.79683500	-2.17270800	-1.70210000
H	-0.63677400	-2.94856600	0.30374900
H	-1.01165500	-1.37408500	1.04250300
H	0.57264400	-2.24149800	-2.30854500
H	0.54656200	-0.46783800	-2.34971800
C	1.05170100	0.02839600	0.26425700
O	0.67359000	0.39403200	1.36557400
O	1.72935700	0.83356600	-0.56727700
C	-1.85345200	-0.06567300	-1.18430900
H	-2.14449200	0.21175200	-2.21682800
H	-1.13404700	0.69531900	-0.86250000
N	-2.97739000	0.00845200	-0.26163300
C	-3.34974800	1.40084700	0.01799400
H	-3.32489600	2.02734600	-0.89327200

H	-2.61598600	1.81722500	0.71812700
C	-4.14673600	-0.76241300	-0.66349300
H	-4.66023400	-0.31438600	-1.53511900
H	-3.84348900	-1.76864200	-0.96185300
C	-4.77031200	1.46315900	0.60626200
H	-5.51366800	1.58362800	-0.19567500
H	-4.87072700	2.31808100	1.27914100
C	-5.09480900	-0.86830200	0.54206700
H	-4.79406100	-1.69969600	1.18640800
H	-6.12254800	-1.05331200	0.19394900
O	-5.05316200	0.29842100	1.36901000
C	2.40373000	-2.14989000	1.49285000
H	1.58777500	-2.45145300	2.14968200
C	2.08477500	-2.25881200	0.01500200
C	3.25722000	-1.81382100	-0.87382600
H	3.54951700	-0.78035700	-0.68413800
H	4.12591300	-2.45587400	-0.70193300
H	2.98445400	-1.89698200	-1.92947700
C	1.79590200	-3.74771000	-0.28038900
H	1.05108200	-4.16541700	0.40085000
H	1.44570700	-3.89798100	-1.30554500
H	2.71755600	-4.32267000	-0.15339500
Si	2.14350200	2.46029500	-0.12920700
C	3.03001000	3.06182900	-1.66466300
H	2.37264500	3.02511900	-2.53912800
H	3.36052100	4.09780200	-1.53471000
H	3.91284700	2.44995000	-1.87524300
C	0.56473800	3.42242600	0.17546100
H	-0.10658200	3.34552300	-0.68632000

H	0.03950300	3.04192400	1.05444000
H	0.78740800	4.48317200	0.33345400
C	3.28640200	2.40638900	1.35363100
H	2.77888600	1.97630300	2.22005500
H	4.16972200	1.79704400	1.13644600
H	3.62667400	3.41466600	1.61285000
C	3.54824400	-1.74035200	2.03939200
H	3.67374300	-1.70796700	3.11747300
H	4.39727500	-1.42147500	1.44326900

TS-A2

C	-1.55141200	0.01565500	-1.25662000
C	-0.70337800	-0.39244900	-0.01094800
C	0.46637500	0.33805700	-0.62831300
C	-0.37671600	0.92906600	-1.74269700
H	-1.68664100	-0.83070600	-1.93552400
H	-0.57014100	-1.46353200	0.17139400
H	-1.08587400	0.05579300	0.91672800
H	-0.00964400	0.75307200	-2.75853700
H	-0.59837200	1.99831700	-1.64821900
C	1.81044300	0.06482700	-0.61341900
O	2.26673300	-0.80327900	0.35561900
O	2.66749600	0.66623200	-1.36282100
C	-2.87348600	0.71386300	-0.98009800
H	-3.32748400	1.04979200	-1.93390900
H	-2.67146700	1.62227600	-0.39979900
N	-3.79678500	-0.09522400	-0.19275400
C	-4.89223300	0.71870400	0.34996400
H	-5.26697100	1.45180500	-0.38868600
H	-4.50781700	1.28705400	1.20507900

C	-4.33105200	-1.25962800	-0.88839500
H	-5.04597100	-0.97653900	-1.68392700
H	-3.52154200	-1.80732800	-1.37568000
C	-6.06697300	-0.18107700	0.77340800
H	-6.77533300	-0.30626400	-0.05885200
H	-6.61398800	0.26738200	1.60613500
C	-4.99421300	-2.18065800	0.14810700
H	-4.24280200	-2.82307900	0.61675200
H	-5.74012200	-2.82226000	-0.34550100
O	-5.59968500	-1.44722900	1.21693300
C	3.13575000	2.38415100	-0.51493900
H	3.73784500	1.93186200	0.26163400
H	3.69509700	2.76149500	-1.36238900
C	1.88251600	2.93368600	-0.22088100
H	1.41910700	3.55410200	-0.98451300
C	1.07363600	2.49434700	0.81051300
C	1.57621600	1.75010300	2.01667500
H	1.67459200	2.45316000	2.85462300
H	0.85690600	0.98563100	2.32410000
H	2.53559000	1.26134200	1.86016300
C	-0.31121000	3.05535400	0.96260700
H	-0.66318200	3.54515000	0.05217800
H	-1.02487400	2.27467700	1.24550800
H	-0.32531100	3.79548600	1.77370700
Si	3.76226100	-1.60651000	0.24955000
C	3.65978400	-2.86775800	1.63586000
H	2.81794700	-3.55171600	1.48784500
H	4.57651200	-3.46554300	1.68157100
H	3.53134800	-2.37770400	2.60662500

C	3.90657900	-2.45000500	-1.42206700
H	3.08214900	-3.15384600	-1.57715500
H	3.88452000	-1.71428800	-2.23048800
H	4.84543900	-3.01005100	-1.49241800
C	5.20793300	-0.44572700	0.55287500
H	5.33208900	0.26016700	-0.27200100
H	5.07136100	0.12440900	1.47812700
H	6.13516400	-1.02125700	0.65336900

***syn*-INT-C2**

C	-1.35407100	0.50961600	-0.94968000
C	-0.65386600	0.50883800	0.42988700
C	0.61159700	1.11632200	-0.24866900
C	-0.28656700	1.51406700	-1.45833900
H	-1.21938300	-0.45612400	-1.44785600
H	-0.52876800	-0.44147500	0.95108700
H	-1.12720800	1.22219200	1.10991200
H	0.14224100	1.34882800	-2.44662500
H	-0.64763400	2.54079200	-1.38639000
C	1.57074200	0.00987900	-0.68195900
O	1.97431100	-0.77109300	0.33003500
O	1.94777200	-0.16036200	-1.83021200
C	-2.80799500	0.94800100	-0.99276100
H	-3.15568500	1.01009900	-2.04338900
H	-2.87190800	1.96463500	-0.58427100
N	-3.68040300	0.10681200	-0.17936200
C	-4.98432600	0.74584300	0.04162700
H	-5.36287600	1.23795700	-0.87378000
H	-4.86099700	1.52559700	0.80226100
C	-3.86532400	-1.24680700	-0.68920400

H	-4.47942500	-1.26314800	-1.60932100
H	-2.89901100	-1.68362800	-0.95008000
C	-6.02169000	-0.29903300	0.49100600
H	-6.54972600	-0.71607500	-0.37925400
H	-6.77057000	0.15798100	1.14220900
C	-4.50663700	-2.09797500	0.41847600
H	-3.73616500	-2.47799000	1.09586100
H	-5.03107400	-2.95704800	-0.02725800
O	-5.40227000	-1.33850600	1.23542200
C	3.91823800	2.47093000	0.13733700
H	4.18665500	2.12788200	1.13135500
H	4.73883100	2.73633000	-0.52228500
C	2.65162100	2.56597000	-0.26727800
H	2.45056200	2.91387000	-1.28096500
C	1.40830200	2.23110200	0.53279200
C	1.73430500	1.75970100	1.95923800
H	2.25645000	2.55125000	2.50477000
H	0.81192300	1.53508400	2.50186400
H	2.35511100	0.86445700	1.96642500
C	0.56568000	3.52138900	0.64227800
H	0.42020500	4.00174000	-0.32814600
H	-0.41840300	3.32402100	1.07834100
H	1.08323300	4.23511700	1.28957800
Si	3.17795600	-2.00377000	0.13588900
C	3.39644400	-2.60341800	1.89628800
H	2.45459400	-2.98447800	2.30353300
H	4.13386000	-3.41199000	1.93820500
H	3.74589700	-1.79433000	2.54563100
C	2.49263200	-3.34852100	-0.97325300

H	1.55604900	-3.74609300	-0.56906500
H	2.29879200	-2.96384300	-1.97747200
H	3.20409400	-4.17773900	-1.05117700
C	4.74933300	-1.23007100	-0.52694100
H	4.60616500	-0.86555000	-1.54658400
H	5.05446400	-0.38418300	0.09684400
H	5.56212700	-1.96435000	-0.52789200

(*E*)-INT-TMS-B

C	-1.66776000	-3.37531000	-0.92785800
C	-1.02745900	-2.04589000	-0.58789000
H	-2.59880900	-3.62458200	-0.40878000
H	-1.82351400	-3.52790600	-2.00340800
C	-1.56135700	-0.87361400	-0.24329400
O	-2.90524900	-0.66321500	-0.28981800
O	-0.84862200	0.19903100	0.22998100
C	1.22123700	-2.29161600	0.76530600
H	1.73427400	-3.19594800	1.14518000
H	0.56706000	-1.94144400	1.56880500
N	2.18663300	-1.23493500	0.46796900
C	2.51458900	-0.42236100	1.64804400
H	2.55352300	-1.03003200	2.56959600
H	1.72294000	0.32396100	1.77367700
C	3.39476300	-1.73005600	-0.17828300
H	4.01248400	-2.33649900	0.51089400
H	3.12272100	-2.38720500	-1.00918400
C	3.88317600	0.25572000	1.47501800
H	4.68529700	-0.39956700	1.84545300
H	3.92288000	1.18287600	2.05159500
C	4.19035800	-0.54201900	-0.73174000

H	3.77366600	-0.22555500	-1.69243200
H	5.23888100	-0.83731600	-0.88783300
O	4.12361000	0.60654300	0.11929400
C	0.00946400	0.84955600	-0.73687700
H	0.85457200	0.18766600	-0.94635900
H	-0.56613100	1.01270800	-1.65840600
C	0.46184800	2.14007700	-0.11706800
H	-0.10137800	2.44514300	0.76286900
C	1.46837100	2.90716400	-0.55379600
C	2.30393000	2.56895900	-1.76032600
H	3.34090500	2.39348900	-1.45458100
H	1.95313100	1.67607100	-2.28187800
H	2.30427100	3.40069800	-2.47551100
C	1.85095400	4.17706100	0.15955700
H	1.21782600	4.36213500	1.03135900
H	2.89488800	4.13052600	0.49582700
H	1.77877900	5.04397900	-0.50957400
Si	-3.70463800	0.74206800	0.25813800
C	-5.50730500	0.30666700	-0.02691200
H	-5.79362800	-0.58729000	0.53630100
H	-6.15437400	1.12930300	0.29619900
H	-5.70787600	0.11898700	-1.08671000
C	-3.37037300	1.01804100	2.08399900
H	-3.94869700	1.87243600	2.45297800
H	-3.65950000	0.13956400	2.67046100
H	-2.31027900	1.21539800	2.26100500
C	-3.23926700	2.23889700	-0.77653700
H	-2.23198900	2.60087900	-0.55717300
H	-3.29466900	2.00584200	-1.84516800

H	-3.94288000	3.05551000	-0.57850000
C	-0.36187700	-4.05518600	-0.41343600
H	-0.47552800	-4.42358400	0.61062100
H	0.07296200	-4.84515500	-1.03112500
C	0.35516100	-2.66779200	-0.43852800
H	0.94806500	-2.56814700	-1.35784100

TS-B1

C	0.34222300	1.02882000	2.24067600
C	0.35679400	0.58441400	0.79747000
H	0.84850400	0.36574500	2.95032600
H	0.72725900	2.04407200	2.40860900
C	1.29581500	-0.12274600	0.08761200
O	2.54903100	-0.23119200	0.64955600
O	1.11247600	-0.57030400	-1.10607800
C	-1.80537300	-0.67892300	0.17205600
H	-1.63041400	-1.48432900	0.91413400
H	-1.28291800	-0.97959700	-0.74138100
N	-3.21948300	-0.54271600	-0.15870400
C	-3.70928500	-1.73647700	-0.86070500
H	-3.29964400	-2.66714500	-0.42512200
H	-3.36777400	-1.68937900	-1.90161700
C	-4.08718400	-0.22605400	0.96917600
H	-4.17985500	-1.07267100	1.67611200
H	-3.66981000	0.60894500	1.53426900
C	-5.24417900	-1.80976500	-0.79118200
H	-5.56274900	-2.37665900	0.09620400
H	-5.64524800	-2.32136800	-1.66947300
C	-5.46317500	0.19213700	0.42506400
H	-5.45572300	1.25314100	0.15792600

H	-6.23260300	0.03495000	1.19653400
O	-5.81194800	-0.50761200	-0.77294600
C	1.42001600	0.91290200	-2.38534000
H	2.49500400	0.89672400	-2.26652700
H	1.04758400	0.37072100	-3.24587000
C	0.65281300	1.94720800	-1.84088800
H	-0.38343400	2.02129500	-2.16234000
C	1.01719400	2.66509200	-0.71624200
C	2.42981300	2.78415000	-0.21606100
H	3.08433100	1.98576500	-0.55986900
H	2.84593300	3.74474000	-0.54771300
H	2.45216100	2.78820100	0.87747600
C	0.06299000	3.66629400	-0.13034600
H	-0.95579700	3.53351000	-0.50004100
H	0.05355300	3.61225400	0.96348700
H	0.38879500	4.68296500	-0.38688500
Si	3.68003800	-1.40814200	0.16619400
C	5.00157800	-1.28684400	1.49334300
H	4.58863500	-1.50049800	2.48439000
H	5.80706300	-2.00391700	1.30148000
H	5.44424600	-0.28564100	1.51931700
C	2.86671000	-3.10043600	0.17314200
H	3.58980900	-3.87810600	-0.09587400
H	2.46929300	-3.33863200	1.16533800
H	2.04159700	-3.13551900	-0.54312500
C	4.42695600	-1.01402300	-1.51180800
H	3.69736500	-1.14588000	-2.31452300
H	4.79803600	0.01595300	-1.54772900
H	5.27622000	-1.67799400	-1.70905100

C	-1.21431300	0.94267300	2.20247700
H	-1.61073900	0.11593500	2.79768800
H	-1.74577200	1.85946900	2.47011100
C	-1.16112900	0.61392900	0.66995600
H	-1.54311600	1.43471100	0.05329800

***anti*-INT-D1**

C	0.60689000	0.79809800	2.23951500
C	0.50140800	0.99028600	0.69786900
H	1.51861800	0.33237900	2.61026700
H	0.44074300	1.73278500	2.77504400
C	1.33278500	-0.02754700	-0.07833500
O	2.35721400	-0.55234600	0.61031000
O	1.11581100	-0.32027400	-1.24364000
C	-1.63118200	-0.33373200	-0.28586300
H	-1.21276100	-1.35709500	-0.23865300
H	-1.34429000	0.06136500	-1.26366100
N	-3.09034200	-0.34635100	-0.23327600
C	-3.65058100	-0.91055900	-1.46965000
H	-3.07408300	-1.78676900	-1.82035500
H	-3.58974700	-0.14735600	-2.25427000
C	-3.65035400	-1.03256400	0.92603100
H	-3.48781700	-2.12610100	0.87823400
H	-3.16210900	-0.68333600	1.83677600
C	-5.10781100	-1.35236200	-1.24620700
H	-5.14714900	-2.40686200	-0.93530300
H	-5.68364100	-1.26036100	-2.17022200
C	-5.14867400	-0.69978200	1.01302700
H	-5.29429500	0.25095200	1.53445400
H	-5.67383000	-1.48720500	1.57517800

O	-5.74275800	-0.53018600	-0.27699000
C	0.85829800	2.88098400	-2.40647400
H	1.92388900	3.08580800	-2.43140300
H	0.32584600	2.97120000	-3.34852400
C	0.22303400	2.52716700	-1.29014000
H	-0.84968500	2.34322400	-1.33809700
C	0.81166100	2.41785600	0.10179800
C	2.33033300	2.65623400	0.12216500
H	2.86240400	1.97737500	-0.54945600
H	2.56346600	3.67974200	-0.18463000
H	2.72202400	2.50987500	1.13281500
C	0.14224000	3.53036300	0.94234500
H	-0.93755200	3.38799500	1.03629800
H	0.57009400	3.59223100	1.94579900
H	0.30685000	4.49291100	0.45039200
Si	3.48715500	-1.64984100	-0.11885200
C	4.65189400	-2.00939300	1.30215200
H	4.12063400	-2.46749900	2.14243300
H	5.43957300	-2.70083200	0.98441200
H	5.13221100	-1.09334500	1.66028000
C	2.57642700	-3.19104100	-0.66858800
H	3.28446200	-3.93516600	-1.04909300
H	2.03525500	-3.64074800	0.17028300
H	1.85746900	-2.95859400	-1.45734100
C	4.36209000	-0.76322800	-1.51792300
H	3.65574800	-0.47430400	-2.29964000
H	4.86075800	0.14017500	-1.15185500
H	5.12552400	-1.41150600	-1.96140400
C	-0.67539100	-0.06070900	2.19513600

H	-0.44953100	-1.12984900	2.12051500
H	-1.40352800	0.08972800	2.99607200
C	-1.00559800	0.53612700	0.80147900
H	-1.63027500	1.42667100	0.91405400

TS-B2

C	0.70170500	2.47960200	-1.12657300
C	0.34445500	1.08319700	-0.67144100
H	0.45594100	3.25761600	-0.39006500
H	1.73344000	2.63878000	-1.45348500
C	1.19244600	0.04717400	-0.36656100
O	2.50760200	0.37443500	-0.09275700
O	0.82762300	-1.17476700	-0.20377200
N	-2.80109600	0.11078600	-0.16664100
C	-4.16940300	0.32163900	0.33968600
H	-4.45008300	1.37187200	0.21391600
H	-4.20727800	0.10742000	1.41687200
C	-2.63440000	-1.20547500	-0.79226800
H	-2.91732600	-1.19998400	-1.86179800
H	-1.58152500	-1.49852300	-0.73072800
C	-5.18901100	-0.56238300	-0.36968000
H	-5.21325700	-0.31520900	-1.44180800
H	-6.19305100	-0.39654300	0.03361400
C	-3.49479900	-2.22976300	-0.07198400
H	-3.20953000	-2.26458900	0.99063700
H	-3.33108700	-3.22561000	-0.49472300
O	-4.89582200	-1.95176200	-0.19106000
C	0.39954700	-1.36246900	1.75770700
H	0.01123800	-2.36925500	1.66265500
Si	3.79019400	-0.71188400	-0.33901000

C	3.62297400	-1.49947600	-2.03606300
H	4.46444900	-2.17147900	-2.23661400
H	2.69779700	-2.07837700	-2.10310900
H	3.60609100	-0.73634000	-2.82124800
C	5.30509600	0.39350400	-0.24985400
H	5.37084100	0.89296000	0.72248000
H	6.22031200	-0.19242800	-0.38742200
H	5.27835400	1.16555200	-1.02552300
C	3.88550200	-2.02015100	1.00633200
H	3.90473900	-1.56526500	2.00254400
H	3.03610400	-2.70587700	0.95741100
H	4.80515400	-2.60541000	0.89274500
H	1.43676700	-1.29598100	2.05669000
C	-0.48566300	-0.30208100	1.96278000
H	-1.53456100	-0.47816900	1.75321300
C	-0.10275900	1.02078500	2.07817700
C	-1.15048400	2.09434400	2.15628000
H	-1.19975300	2.49145600	3.17946500
H	-0.89284600	2.94080900	1.51017200
H	-2.13405600	1.71836700	1.87675300
C	1.27662800	1.47543400	2.46178800
H	2.04215000	0.71470300	2.32838800
H	1.56878600	2.35295200	1.87738400
H	1.26523200	1.78425700	3.51593100
C	-0.38748700	2.34209100	-2.23286100
H	-1.11581200	3.15600800	-2.30001700
H	0.03786600	2.16235500	-3.22257200
C	-2.32020700	1.20906200	-0.99435500
H	-2.97779200	1.37434400	-1.87326800

H	-2.36096200	2.12615100	-0.39777500
C	-0.90828300	1.02983700	-1.55398400
H	-0.90175600	0.16182400	-2.22013100

***syn*-INT-D2**

C	0.88265600	1.90534800	-1.88511600
C	0.37967900	1.12502900	-0.62828500
H	1.35237500	2.87347500	-1.70253800
H	1.56874400	1.30317400	-2.48308000
C	1.14582500	-0.15405700	-0.33923400
O	2.46907800	-0.05026400	-0.53796900
O	0.62402900	-1.18852000	0.04674300
N	-2.75750100	-0.14912500	0.03834500
C	-4.09096900	0.06800200	0.63369900
H	-4.37837100	1.11620800	0.51325700
H	-4.04900600	-0.12944100	1.71269200
C	-2.61764400	-1.50971700	-0.50344200
H	-2.94609400	-1.56023600	-1.55847900
H	-1.56625400	-1.80442600	-0.46800300
C	-5.15671500	-0.82923000	0.01446800
H	-5.24633000	-0.61460400	-1.06126200
H	-6.13329100	-0.64454000	0.47370100
C	-3.45319800	-2.48624500	0.30723000
H	-3.13049700	-2.45758000	1.35889900
H	-3.30347500	-3.50550500	-0.06070200
O	-4.85667500	-2.21501700	0.21464000
C	0.11052100	0.97386200	3.02676200
H	-0.47125400	0.39660000	3.74010400
Si	3.57311900	-1.29554100	-0.04845900
C	3.22366200	-2.86566100	-1.00743400

H	3.98493800	-3.62148700	-0.78553600
H	2.24300300	-3.27142900	-0.74951000
H	3.24525200	-2.67458100	-2.08534100
C	5.22862400	-0.55921500	-0.52002000
H	5.39718400	0.39188100	-0.00526000
H	6.04154400	-1.24005700	-0.24598200
H	5.28890400	-0.37977700	-1.59815400
C	3.41240100	-1.50628200	1.80696700
H	3.69536500	-0.58567600	2.32754700
H	2.38463000	-1.75356900	2.08359700
H	4.06940600	-2.30807800	2.16053500
H	1.06195300	1.35697700	3.38248000
C	-0.34258000	1.18220200	1.78960700
H	-1.29374800	0.74341400	1.49216800
C	0.34848100	1.98309800	0.70031900
C	-0.43151800	3.30638000	0.50763700
H	-0.36373300	3.88988100	1.43000500
H	-0.00710400	3.90920400	-0.29981600
H	-1.48915500	3.15000900	0.29915900
C	1.78376600	2.37124900	1.10706000
H	2.38282700	1.50630300	1.39246500
H	2.29746500	2.88187700	0.28913700
H	1.75350200	3.05732400	1.95799200
C	-0.55278900	1.91934200	-2.45350700
H	-1.06718700	2.86390700	-2.25439700
H	-0.67288600	1.67387900	-3.51165300
C	-2.39086600	0.87702300	-0.93254900
H	-3.02449400	0.81797300	-1.84218500
H	-2.59852600	1.84935200	-0.48306900

C	-0.95226300	0.82165900	-1.43906700
H	-0.80075100	-0.15533500	-1.90665700

(*Z*)-INT-TMS-B

C	-0.01803900	-2.78299100	-1.13460300
C	-0.01558100	-1.26262400	-1.12271700
H	-0.62324000	-3.29437300	-0.37927800
H	-0.26438600	-3.22117500	-2.10954900
C	-0.92481900	-0.28508000	-1.20574900
O	-0.55330100	1.01589800	-1.31372700
O	-2.28543300	-0.41128400	-1.21444000
C	2.00159500	-0.31814700	0.17043400
H	1.66601100	-0.77002000	1.12612000
H	1.51417600	0.65908400	0.09976600
N	3.43933800	-0.07328400	0.16007200
C	3.79634400	0.97514700	1.12564400
H	3.22224900	0.88104300	2.06647700
H	3.54249000	1.94826700	0.68798700
C	4.26313500	-1.25797500	0.36802200
H	4.17903200	-1.64914600	1.39997900
H	3.93469900	-2.05791300	-0.29757700
C	5.29397500	0.90383300	1.46855200
H	5.45941700	0.24585400	2.33458100
H	5.67650000	1.89348100	1.72972500
C	5.72087200	-0.90681200	0.02798000
H	5.89023200	-1.00276200	-1.04867100
H	6.40158200	-1.59800800	0.54825800
O	6.04620500	0.44786900	0.35310700
C	-2.85376000	-1.51051600	-0.46345400
H	-2.80422500	-2.41977500	-1.07517700

H	-2.24827700	-1.67155700	0.43069800
C	-4.26908900	-1.15195300	-0.14897000
H	-4.89068900	-0.95519000	-1.02118100
C	-4.82620400	-1.05085300	1.06772100
C	-4.11115300	-1.29398600	2.37161000
H	-3.04763000	-1.50553000	2.25586800
H	-4.21411200	-0.42003000	3.02581200
H	-4.56810600	-2.13732400	2.90372500
C	-6.28062300	-0.68243700	1.21441200
H	-6.75942300	-0.51350400	0.24679500
H	-6.83194400	-1.47232000	1.73975500
H	-6.38912800	0.22674300	1.81878100
Si	-1.30115600	2.26438900	-0.41060500
C	0.04073800	3.57052400	-0.30993500
H	0.38540500	3.85885300	-1.30828100
H	-0.33197400	4.47093400	0.18994300
H	0.90514100	3.20471200	0.25385100
C	-2.80218100	2.90827500	-1.33069700
H	-3.25062200	3.75130600	-0.79335200
H	-2.53059400	3.25521300	-2.33306000
H	-3.55604000	2.12282100	-1.43100300
C	-1.75222100	1.60427500	1.28769200
H	-2.64685300	0.97861900	1.23978700
H	-0.93534900	1.00371800	1.70179500
H	-1.94760600	2.43022400	1.97972800
C	1.51235500	-2.73288800	-0.84067900
H	1.75772400	-3.05315900	0.17562600
H	2.14953400	-3.27424400	-1.54409000
C	1.49787000	-1.17375700	-0.99135100

H	1.99777800	-0.83538100	-1.90885900

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C	-0.56657100	-2.27621600	1.71870300
C	-0.67639800	-1.16761100	0.68999700
H	-0.88453700	-2.01315900	2.73240800
H	-1.06137200	-3.21336400	1.44562900
C	-1.54600500	-0.10375600	0.66793400
O	-2.67168700	-0.10020200	1.28675900
O	-1.26091300	0.94047200	-0.18591800
C	1.61716300	-0.05268900	0.12325500
H	1.71248000	0.42126300	1.12075800
H	1.06357100	0.65514100	-0.49797700
N	2.91298900	-0.26497200	-0.51917600
C	3.89167900	-1.02075300	0.28833000
H	4.42862700	-1.73220400	-0.35240200
H	3.37078500	-1.60989200	1.04370200
C	3.47192200	1.01431000	-0.98074500
H	2.97684100	1.31688800	-1.91159500
H	3.30237900	1.82631300	-0.24984800
C	4.91089900	-0.11217000	0.96745300
H	5.62237100	-0.69985800	1.55665300
H	4.39672400	0.57728700	1.65416100
C	4.96968000	0.88891600	-1.20781400
H	5.37151100	1.82091000	-1.61593600
H	5.16534700	0.08893100	-1.93777700
O	5.67595100	0.63156200	0.01077500
C	-3.99345300	-0.99439500	0.09115400
H	-4.79373200	-0.99852300	0.82100800
H	-4.02154200	-0.17452000	-0.61443500

C	-3.33842500	-2.18886200	-0.21878800
H	-3.50272700	-3.03233300	0.44782800
C	-2.27812900	-2.28384100	-1.10411300
C	-2.00327800	-1.29144400	-2.19977200
H	-2.42882000	-0.30741800	-2.01482800
H	-0.92614000	-1.16863800	-2.34593500
H	-2.41190700	-1.67961500	-3.14237700
C	-1.55606400	-3.59220400	-1.25610400
H	-1.77147800	-4.28251100	-0.43786000
H	-1.85496100	-4.07444200	-2.19620600
H	-0.47272300	-3.44251400	-1.31772600
Si	-1.82881200	2.52355200	0.06411300
C	-0.75812100	3.53217500	-1.10160600
H	-1.01793500	4.59498800	-1.05224500
H	0.30137500	3.42966800	-0.84490600
H	-0.88748600	3.20279500	-2.13786400
C	-3.63948200	2.68313600	-0.40736700
H	-3.81413200	2.31538400	-1.42423500
H	-4.27495500	2.11506100	0.27688600
H	-3.95194700	3.73293200	-0.37525900
C	-1.53594100	3.01385900	1.85277300
H	-2.10608400	2.37128400	2.52909300
H	-0.47531800	2.92560600	2.11086800
H	-1.84042900	4.05174400	2.02538900
C	0.97026600	-2.28698100	1.45886500
H	1.42175600	-3.25714700	1.23658600
H	1.52587600	-1.81168700	2.27200700
C	0.76944600	-1.31788700	0.24311300
H	0.84910100	-1.85947100	-0.71144800

***anti*-INT-B3**

C	0.74076000	-2.32616800	-1.77492400
C	0.90947900	-1.46741000	-0.48658500
H	1.37769300	-2.05011700	-2.61488000
H	0.84196600	-3.39150000	-1.57382000
C	1.38690000	-0.06981300	-0.88046600
O	1.77662700	0.23580800	-1.99645600
O	1.32040200	0.81706900	0.11981700
C	-1.40709600	-0.26771600	0.17879900
H	-1.29540000	0.57310000	-0.53142900
H	-0.93304300	0.05816000	1.10807000
N	-2.81085100	-0.54146600	0.48232100
C	-3.67327200	-0.69107900	-0.70947600
H	-4.35159000	-1.54284400	-0.57184400
H	-3.06026700	-0.91350600	-1.58395700
C	-3.34720100	0.46493800	1.41052700
H	-2.99558700	0.24846100	2.42636000
H	-3.00119000	1.48497800	1.16196400
C	-4.50311500	0.55807500	-0.98582900
H	-5.13405700	0.41444600	-1.86873800
H	-3.83653200	1.41057500	-1.18665200
C	-4.86666400	0.45622200	1.37797700
H	-5.26667100	1.15220800	2.12117500
H	-5.23236100	-0.55140200	1.62690900
O	-5.37821200	0.86639300	0.10494400
C	4.07905700	-0.99712200	1.08262200
H	5.10517300	-0.85734000	0.75607100
H	3.78771900	-0.49377800	1.99887100
C	3.23043000	-1.75095100	0.38358900

H	3.58426100	-2.22518500	-0.53279900
C	1.77538700	-2.03405200	0.70578100
C	1.33824200	-1.43595700	2.05356200
H	1.42380600	-0.35101200	2.07339100
H	0.29867900	-1.70280600	2.26359000
H	1.95260200	-1.85009400	2.85868300
C	1.61960100	-3.56783500	0.81351800
H	2.05866500	-4.08996300	-0.03968700
H	2.13328200	-3.91790200	1.71348400
H	0.56820900	-3.86139200	0.89251200
Si	1.80747800	2.46930100	-0.03931700
C	1.55363900	3.10168200	1.70478900
H	1.80660500	4.16484200	1.77365200
H	0.51121500	2.98107500	2.01653700
H	2.18582600	2.55721700	2.41354100
C	3.60882700	2.53845300	-0.54583100
H	4.21525100	1.91786300	0.12142100
H	3.74289000	2.17260000	-1.56636100
H	3.98264700	3.56643100	-0.49003700
C	0.65755400	3.30941300	-1.25662600
H	0.74633700	2.85968600	-2.24873100
H	-0.38345600	3.21813600	-0.92960800
H	0.89388300	4.37586800	-1.33706000
C	-0.74314600	-1.90237100	-1.83403800
H	-1.47620100	-2.66516000	-2.10736500
H	-0.88352400	-1.02693300	-2.47615200
C	-0.66168000	-1.49404900	-0.33956700
H	-0.93231200	-2.34439000	0.29371400

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C	-0.19189800	2.88340900	1.48774500
C	-0.22223000	1.48016500	0.91400200
H	0.36979700	3.61172300	0.89221200
H	-1.16721900	3.32055700	1.72194400
C	-1.33241900	0.81753300	0.43051800
O	-2.38401400	1.39833400	-0.00821100
O	-1.24430800	-0.55751000	0.35235800
C	2.22790100	0.66804300	1.50627700
H	2.81383600	0.44676500	2.42232600
H	2.66525700	1.57804500	1.07973200
N	2.37241600	-0.38600100	0.51215500
C	3.76469000	-0.51187900	0.07247500
H	4.47204400	-0.46301600	0.92211700
H	3.99657200	0.33048200	-0.59033000
C	1.83446900	-1.68665900	0.89264400
H	2.44297200	-2.17389400	1.67804100
H	0.82429400	-1.56449400	1.28134800
C	3.97250200	-1.85152300	-0.65678700
H	4.29896200	-2.62760300	0.05143800
H	4.74615800	-1.75733700	-1.42264900
C	1.75083500	-2.56139600	-0.36856400
H	0.80813100	-2.36960300	-0.88556400
H	1.79062700	-3.62598600	-0.09135700
O	2.78150000	-2.25825400	-1.31462000
C	-0.80623300	2.63462400	-1.79158800
H	-0.76818400	3.68935700	-1.52852000
C	0.37231200	1.90977500	-1.69142000
C	0.51271100	0.48526300	-2.14325000
H	1.22393900	-0.03496800	-1.49906100

H	-0.42631200	-0.06615400	-2.13793400
H	0.91095500	0.47829600	-3.16813600
C	1.67023700	2.64407900	-1.50815300
H	1.54189900	3.58522000	-0.96781000
H	2.40286800	2.02523600	-0.98981700
H	2.09226900	2.88409000	-2.49427400
Si	-2.60462300	-1.56207500	0.17943700
C	-3.87358700	-1.14998300	1.50163100
H	-4.22944900	-0.12277500	1.38848900
H	-4.73472000	-1.82394300	1.43583100
H	-3.44069500	-1.25432800	2.50221700
C	-3.34406500	-1.44483100	-1.54350400
H	-3.82994400	-0.47898400	-1.70149200
H	-2.57355200	-1.57357900	-2.31129200
H	-4.09152600	-2.23296300	-1.68883900
C	-1.89733500	-3.28027100	0.45346300
H	-1.18228100	-3.54827200	-0.33044900
H	-1.38186800	-3.34492900	1.41715300
H	-2.69593200	-4.03008100	0.44723600
C	-2.05941400	2.04740800	-1.91901300
H	-2.94679100	2.66783400	-1.94384200
H	-2.17551500	1.05617500	-2.33447300
C	0.63812800	2.32025100	2.68315900
H	0.05674600	2.23271800	3.60353200
H	1.57530500	2.84074600	2.90287900
C	0.79000100	0.95528100	1.93176900
H	0.40413000	0.10042200	2.49751000

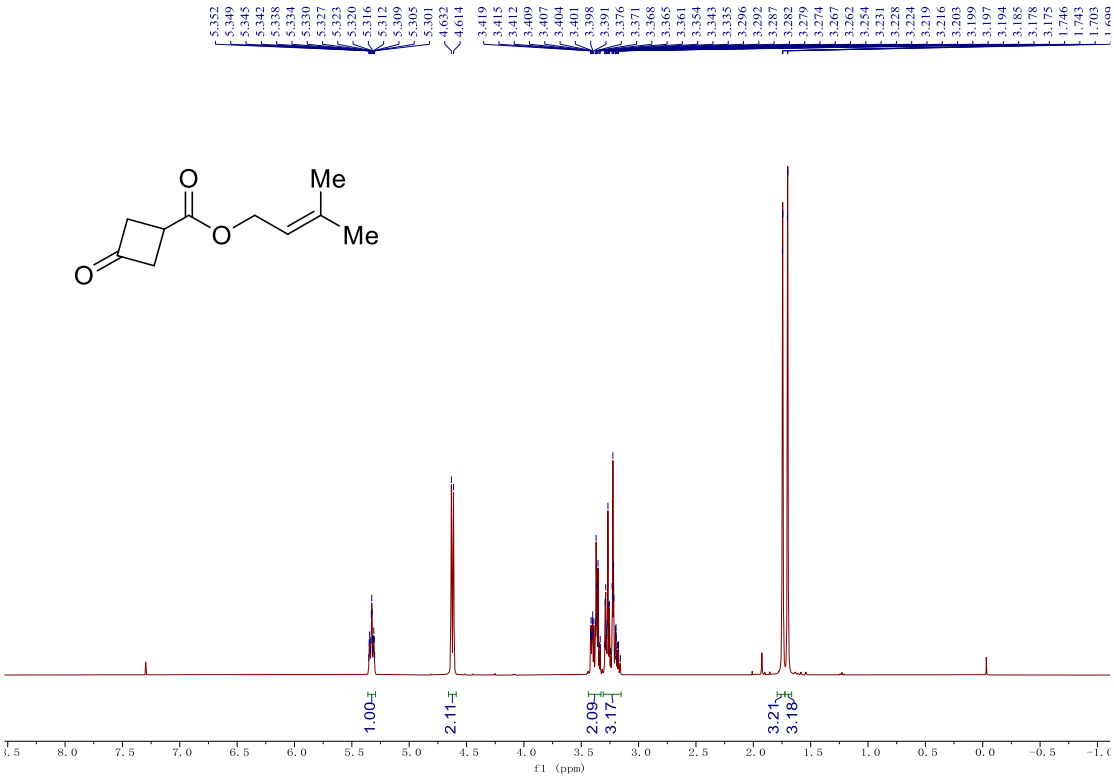
***syn*-INT-B4**

C	-0.45353900	-2.71002200	-1.48708700

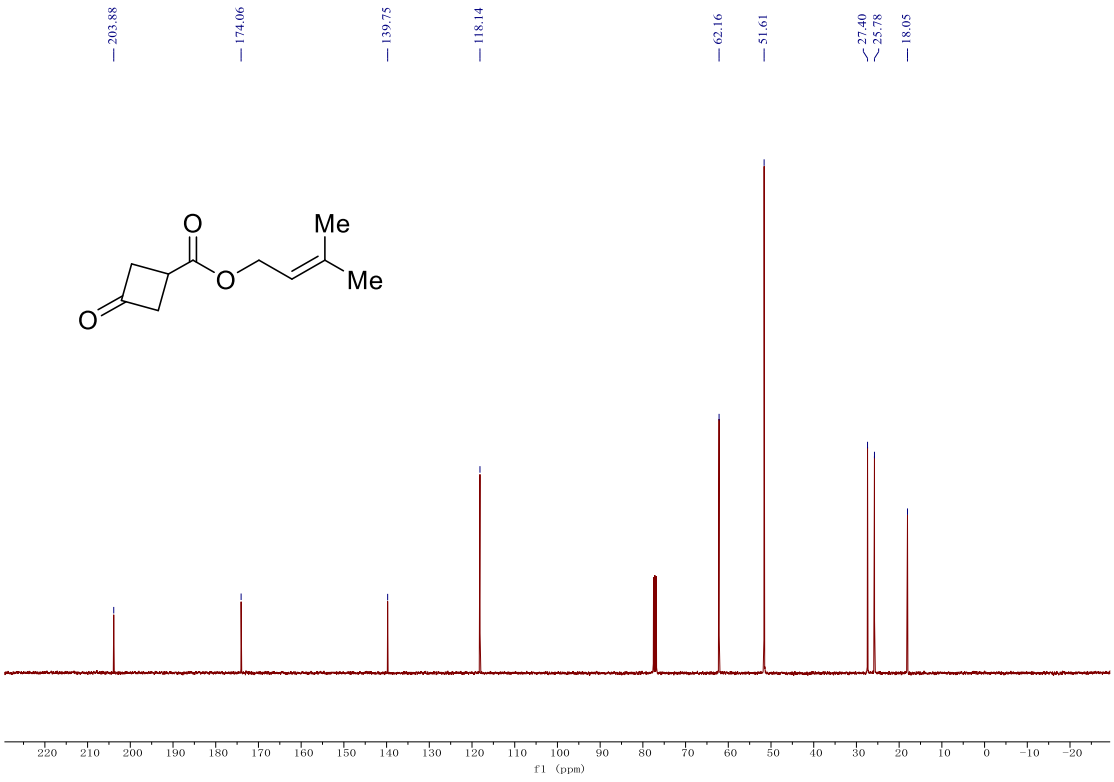
C	-0.29646600	-1.47199100	-0.55707800
H	0.17261300	-3.54842200	-1.17891000
H	-1.47723400	-3.06456200	-1.61169000
C	-1.61698500	-0.70390800	-0.50253700
O	-2.72098900	-1.21338600	-0.59554300
O	-1.44411200	0.61601500	-0.32587800
C	2.12118300	-0.67530000	-1.54634200
H	2.49391300	-0.37946300	-2.54884400
H	2.56637700	-1.65071200	-1.32900400
N	2.55111400	0.26344800	-0.52231000
C	3.98962000	0.28025400	-0.30327500
H	4.53423200	0.77581300	-1.12855100
H	4.36144600	-0.74773900	-0.25508100
C	2.04100500	1.62428700	-0.72929100
H	2.10810300	1.93033100	-1.79070300
H	0.98549600	1.64923300	-0.44541200
C	4.26502500	0.98021500	1.03892500
H	5.28172000	1.40191800	1.04141000
H	4.18467100	0.26438700	1.86188200
C	2.84799400	2.61936400	0.12309500
H	2.22113900	3.46384900	0.41926700
H	3.69953100	3.02054100	-0.44620500
O	3.30413800	2.00201900	1.31929900
C	-0.91382700	-2.70337300	1.50545400
H	-1.02803400	-3.64170300	0.96340600
C	0.14357400	-1.77005900	0.93720700
C	0.30112400	-0.50308800	1.79370100
H	1.05955700	0.14563500	1.35652100
H	-0.62940500	0.05512100	1.89650800

H	0.63252100	-0.78796400	2.79775600
C	1.48927400	-2.53076000	1.00558100
H	1.52349100	-3.39830700	0.34222400
H	2.31485100	-1.86214400	0.76504700
H	1.63508200	-2.89378200	2.02748600
Si	-2.73356600	1.72193100	-0.00406800
C	-3.88708900	1.78036800	-1.47809000
H	-4.37256800	0.81334600	-1.62975700
H	-4.66205500	2.53941900	-1.32612200
H	-3.33856500	2.03748800	-2.39010300
C	-3.58480800	1.18096300	1.57534700
H	-3.97012200	0.16293300	1.47811000
H	-2.88866900	1.20479500	2.41990000
H	-4.42158600	1.84764100	1.80941700
C	-1.80186000	3.33099200	0.21810100
H	-1.08041700	3.25196500	1.03766100
H	-1.25392300	3.59469500	-0.69222400
H	-2.48925200	4.15144000	0.44923100
C	-1.67042200	-2.50042000	2.58376100
H	-2.38450300	-3.24905100	2.91417600
H	-1.61386700	-1.59187100	3.17436500
C	0.16838500	-1.91438800	-2.65691100
H	-0.56797400	-1.57368100	-3.38928300
H	0.98270400	-2.41159100	-3.19196900
C	0.60836300	-0.79391400	-1.67453400
H	0.21727300	0.18677200	-1.94657600

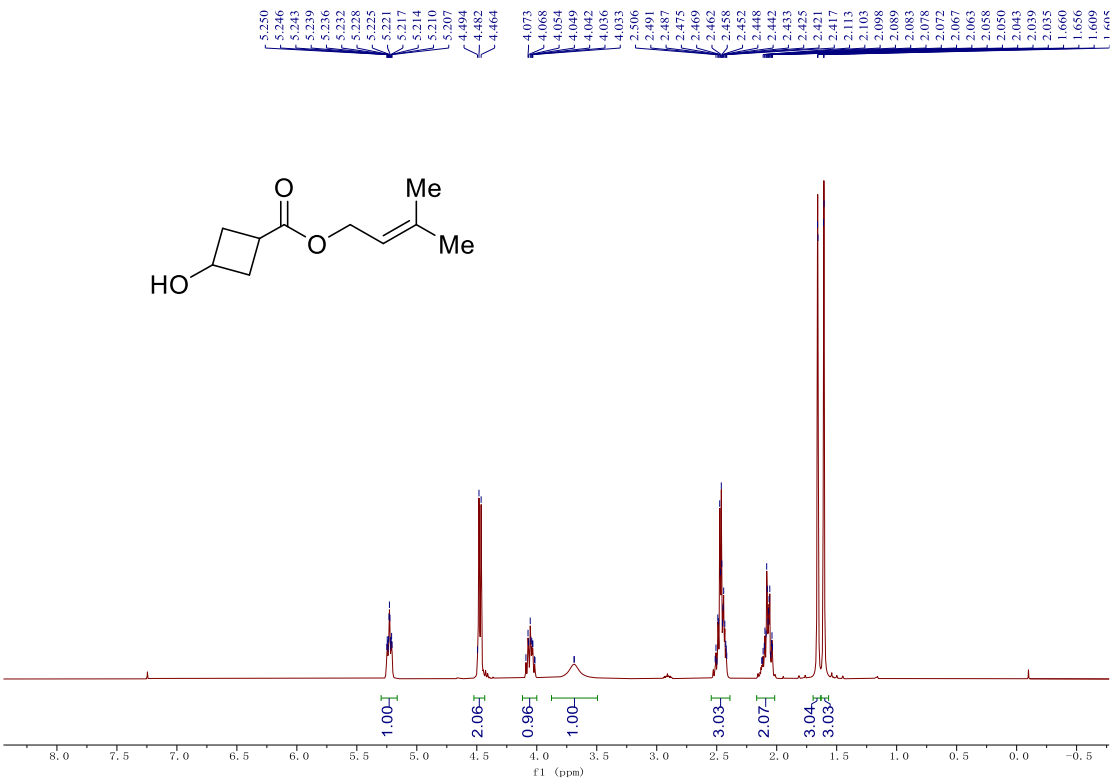
12. NMR spectrum



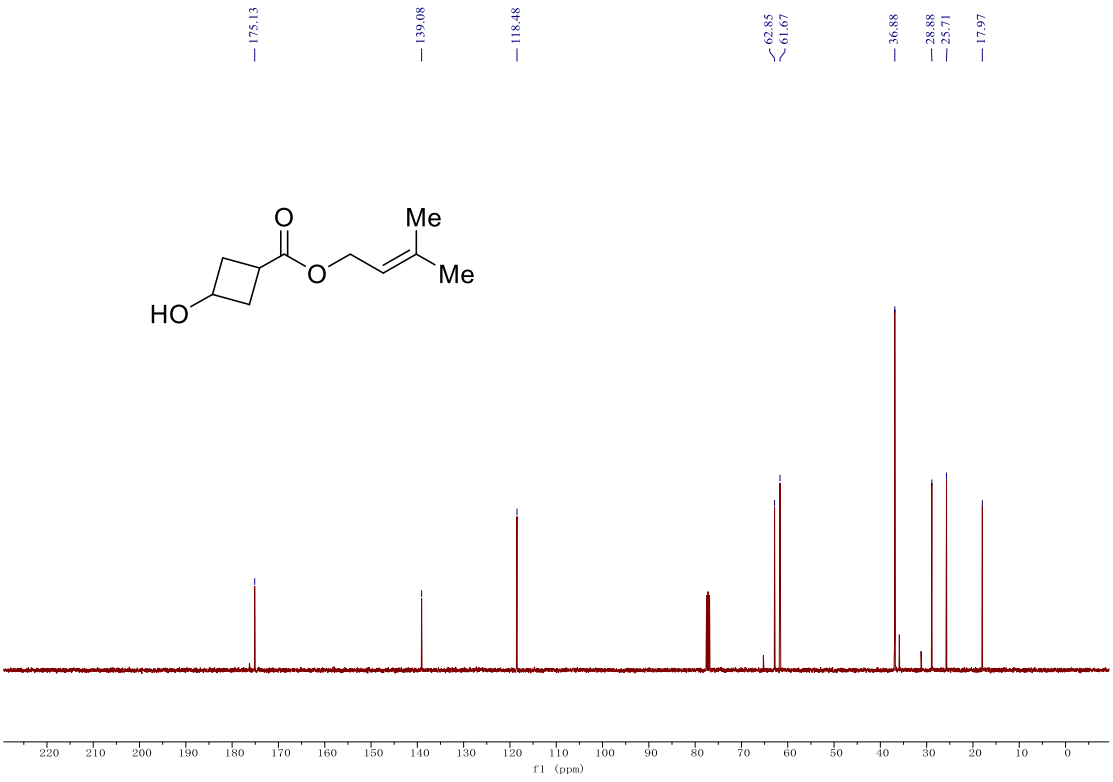
^{1}H NMR of compound **S1** (400 MHz, $CDCl_3$)



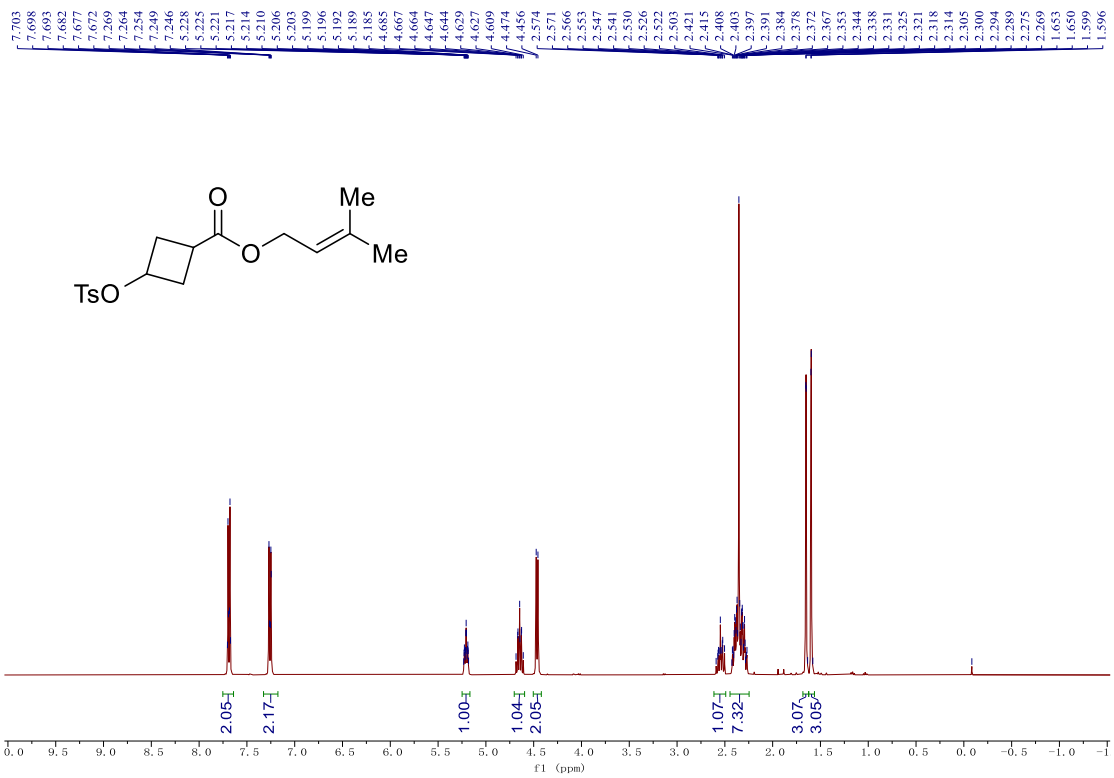
^{13}C NMR of compound **S1** (101 MHz, $CDCl_3$)



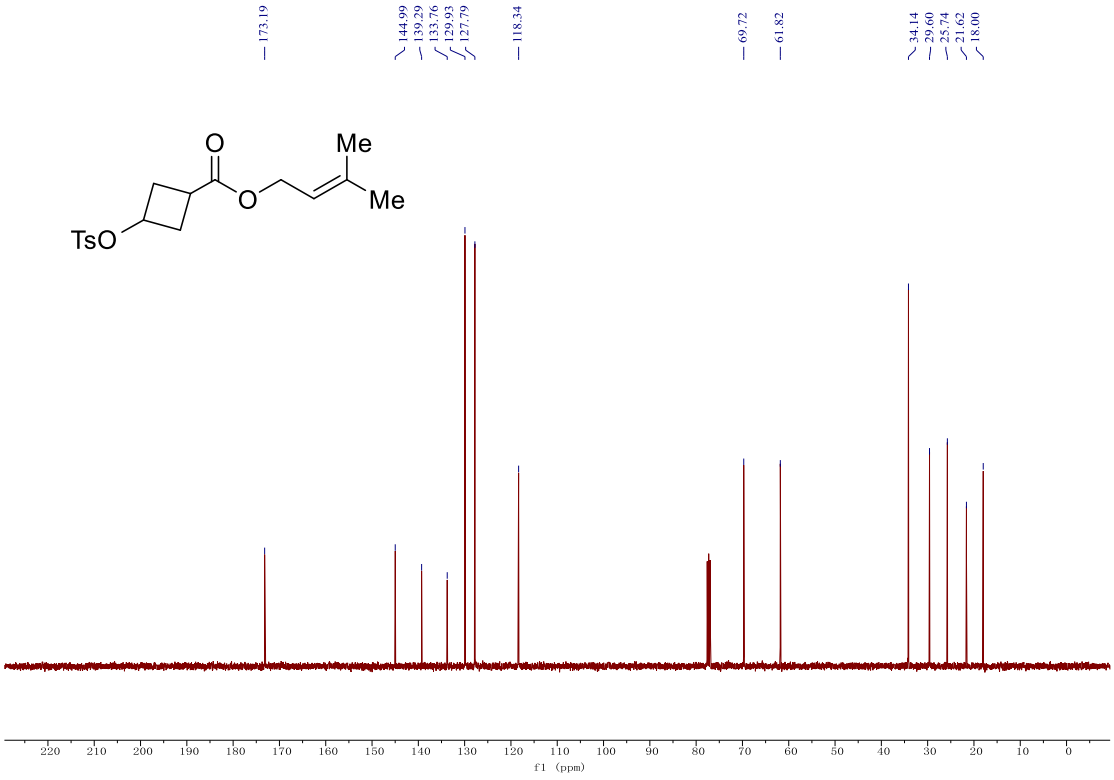
^{1}H NMR of compound **S2** (400 MHz, $CDCl_3$)



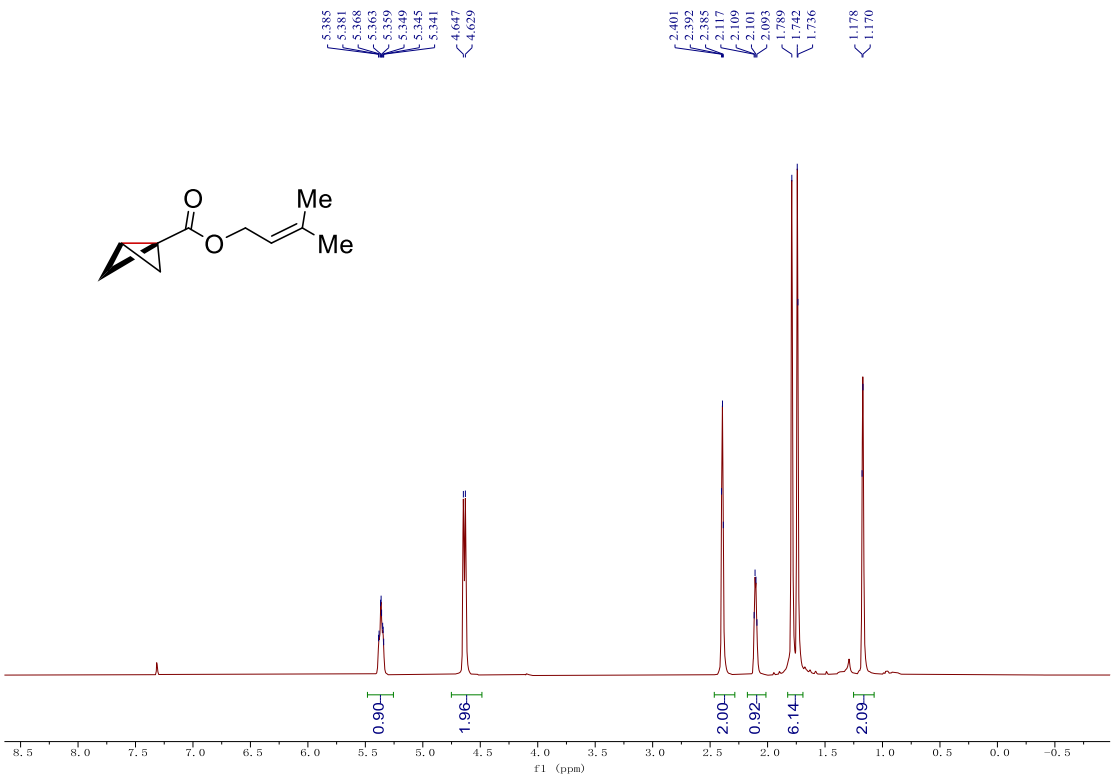
^{13}C NMR of compound **S2** (101 MHz, $CDCl_3$)



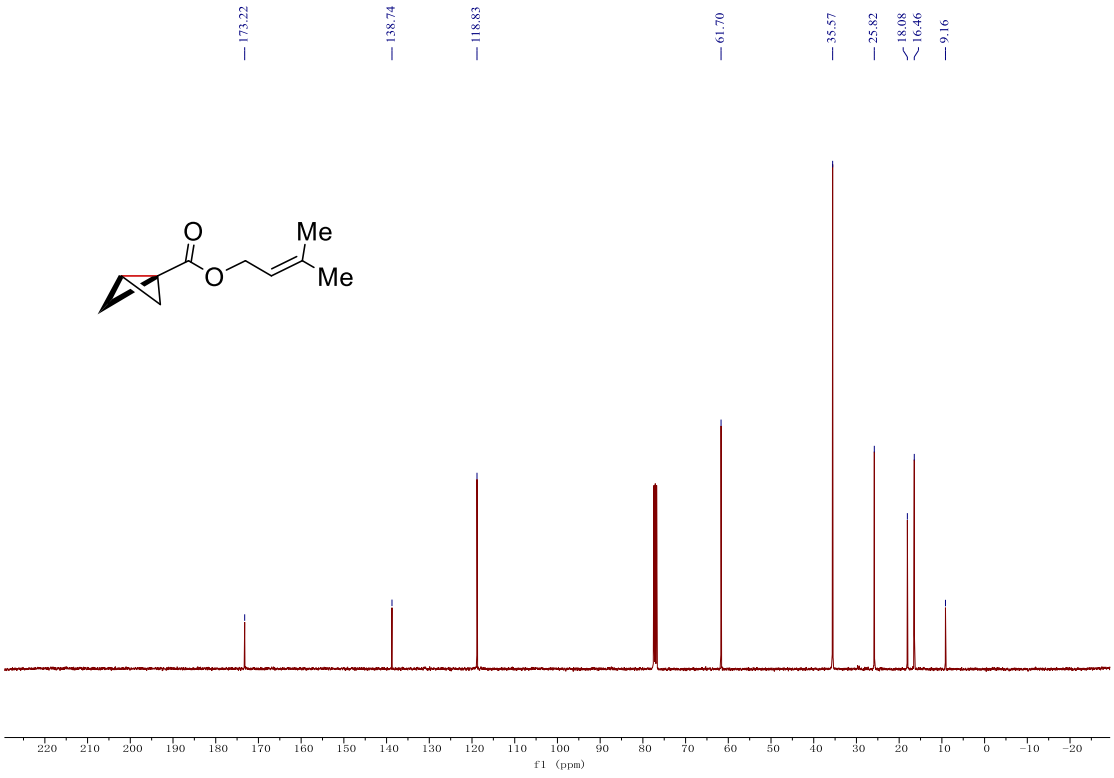
^{1}H NMR of compound **S3** (400 MHz, $CDCl_3$)



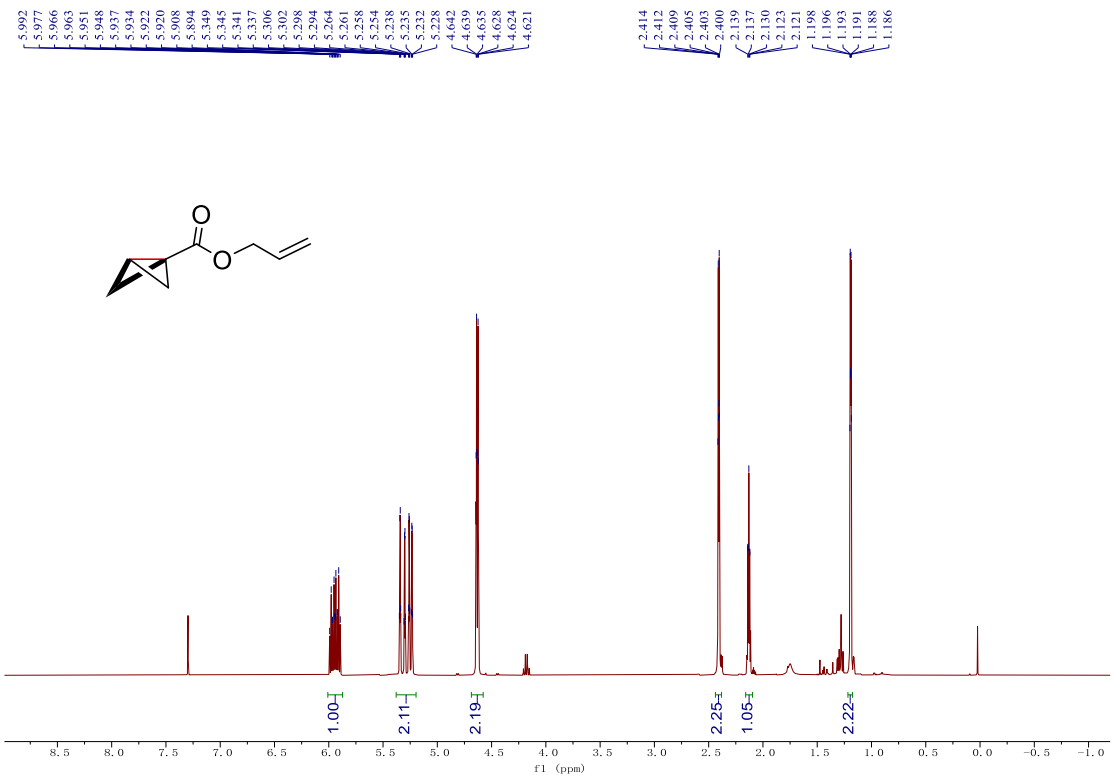
^{13}C NMR of compound **S3** (101 MHz, $CDCl_3$)



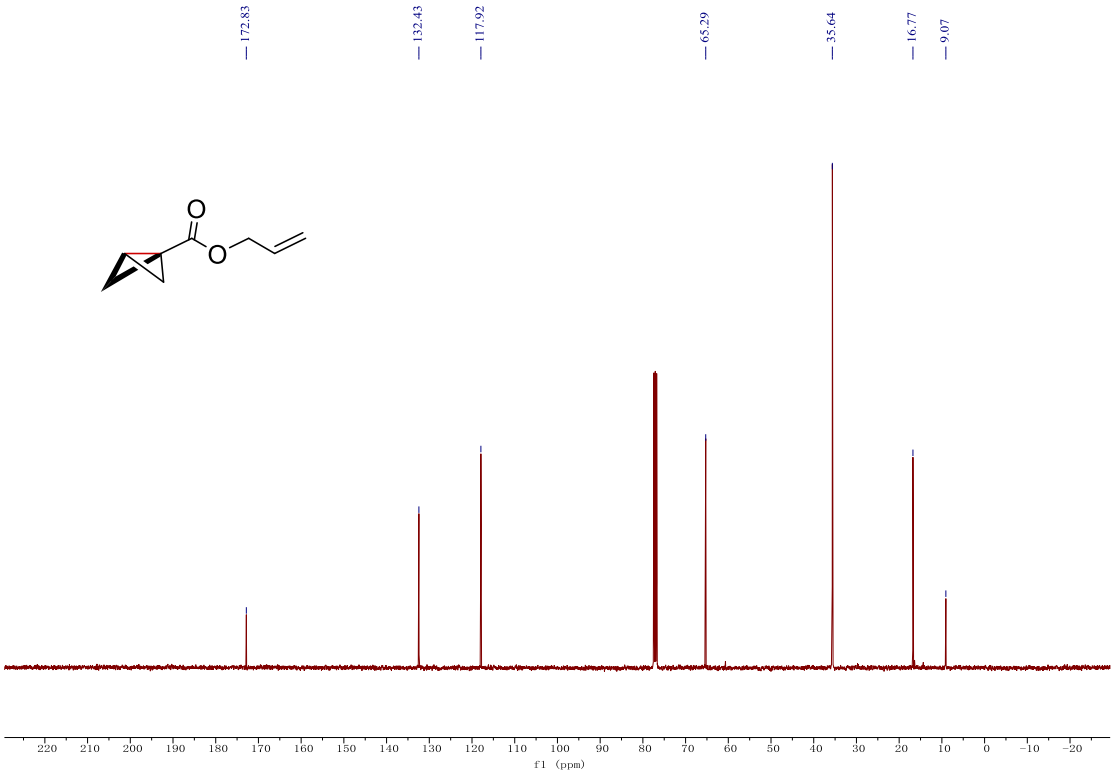
^{1}H NMR of compound **1a** (400 MHz, $CDCl_3$)



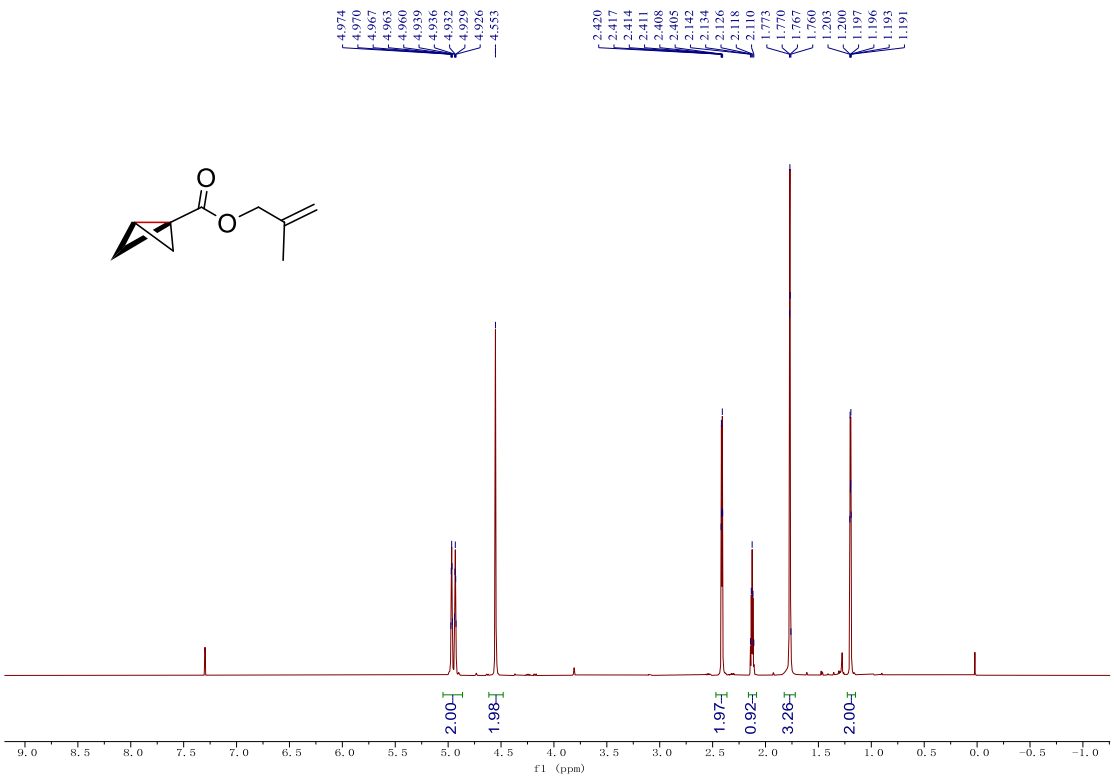
^{13}C NMR of compound **1a** (101 MHz, $CDCl_3$)



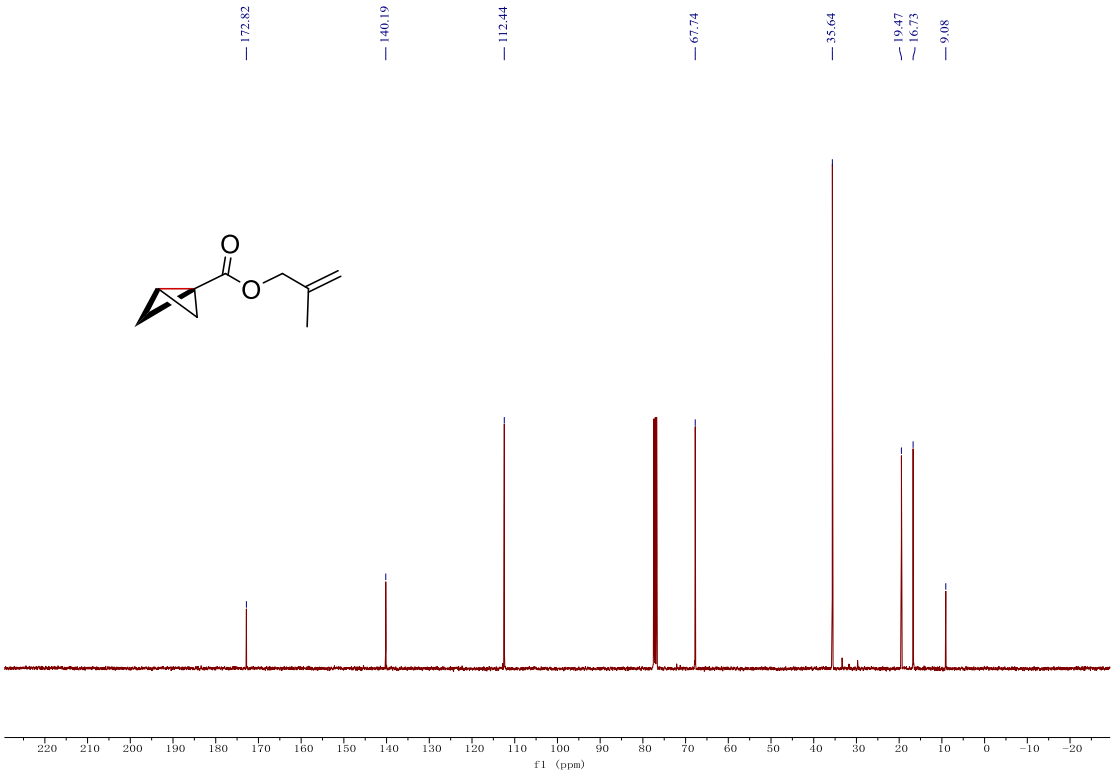
^{1}H NMR of compound **1b** (400 MHz, $CDCl_3$)



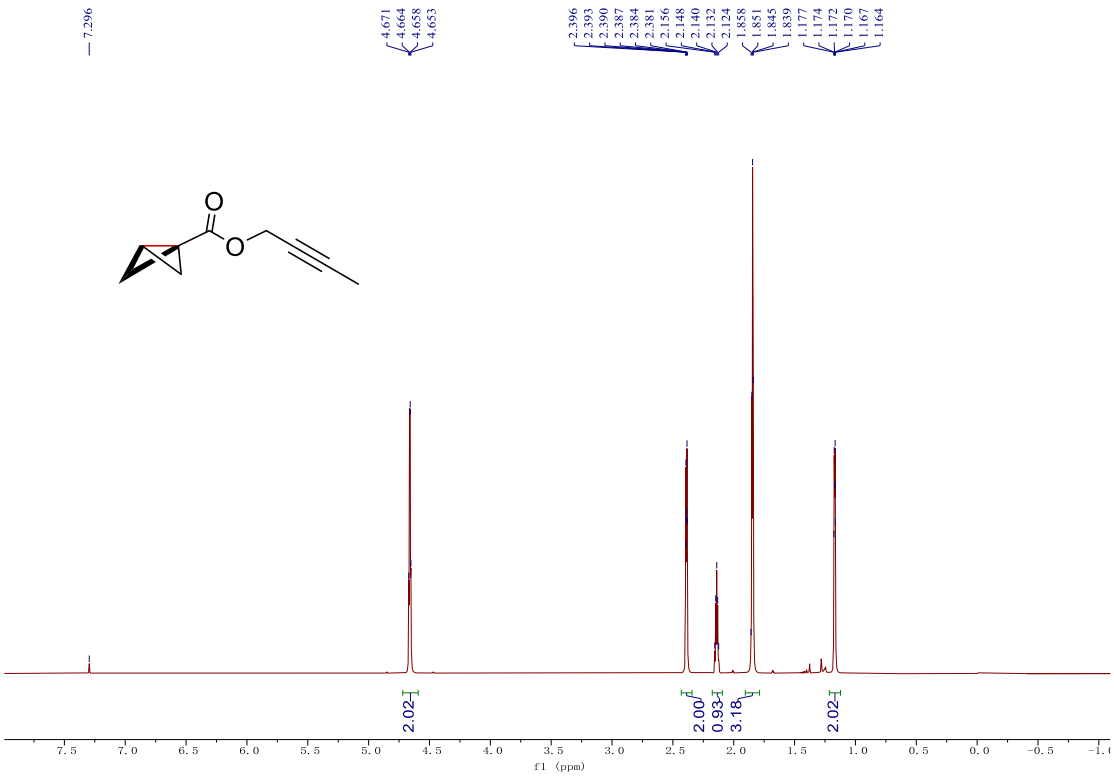
^{13}C NMR of compound **1b** (101 MHz, $CDCl_3$)



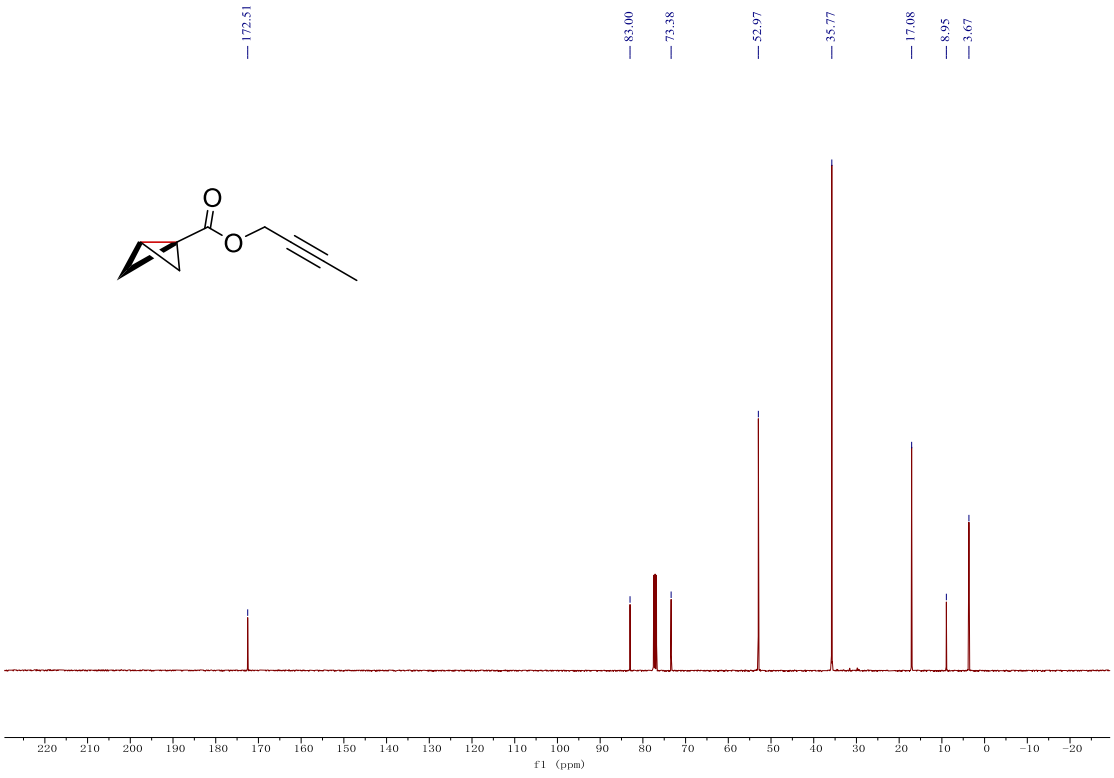
^{1}H NMR of compound **1c** (400 MHz, $CDCl_3$)



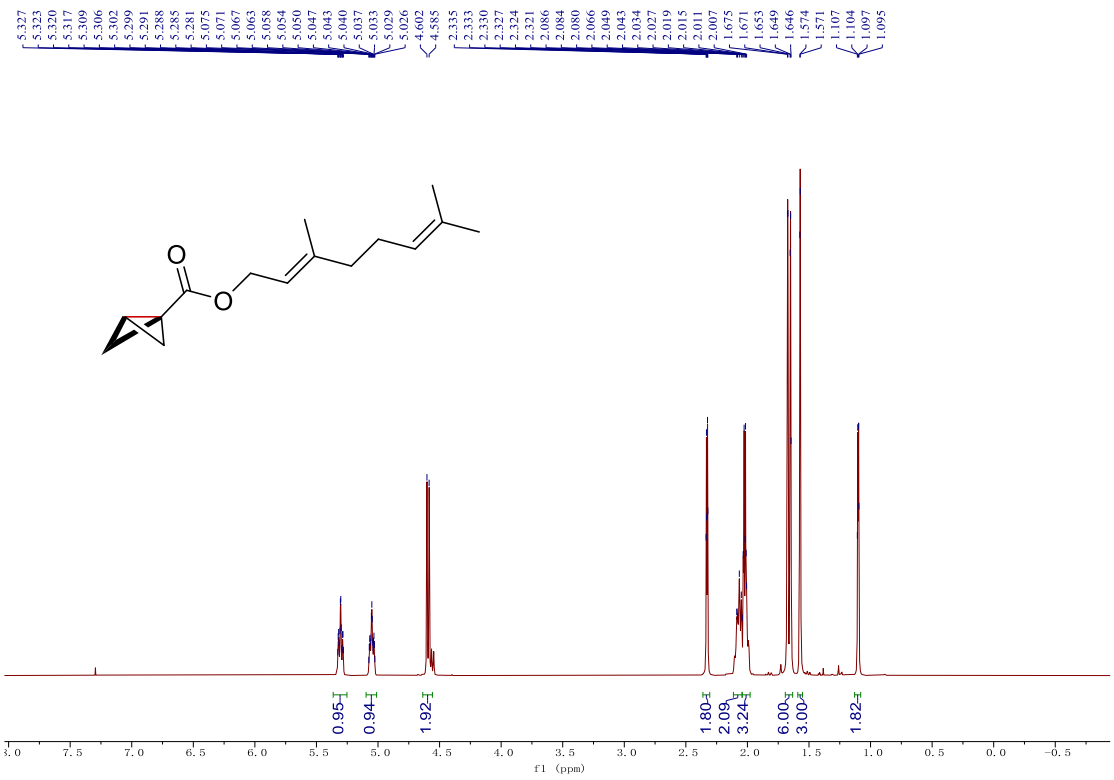
^{13}C NMR of compound **1c** (101 MHz, $CDCl_3$)



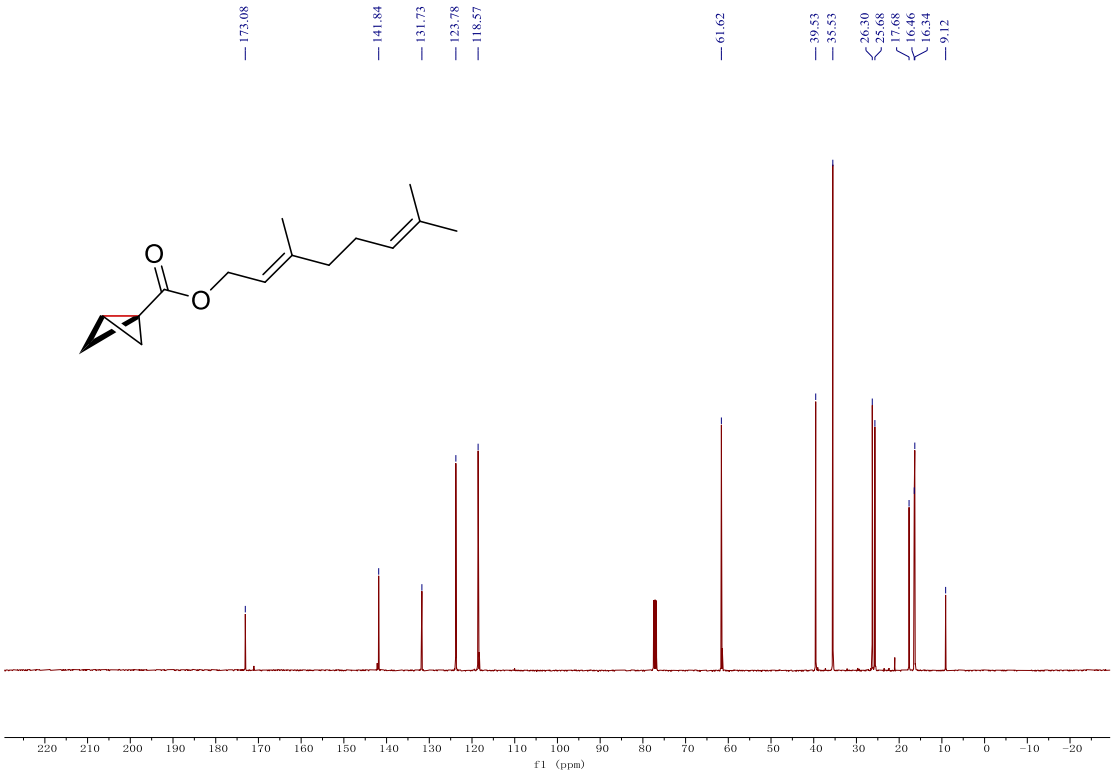
^{1}H NMR of compound **1d** (400 MHz, $CDCl_3$)



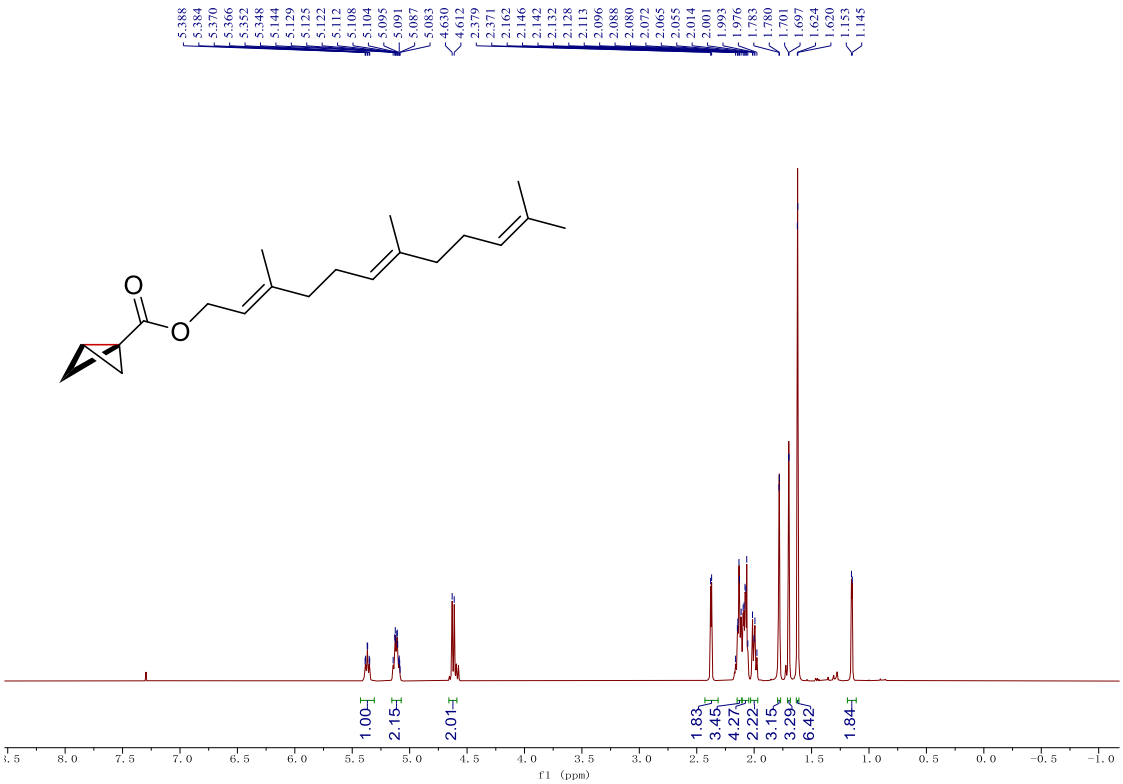
^{13}C NMR of compound **1d** (101 MHz, $CDCl_3$)



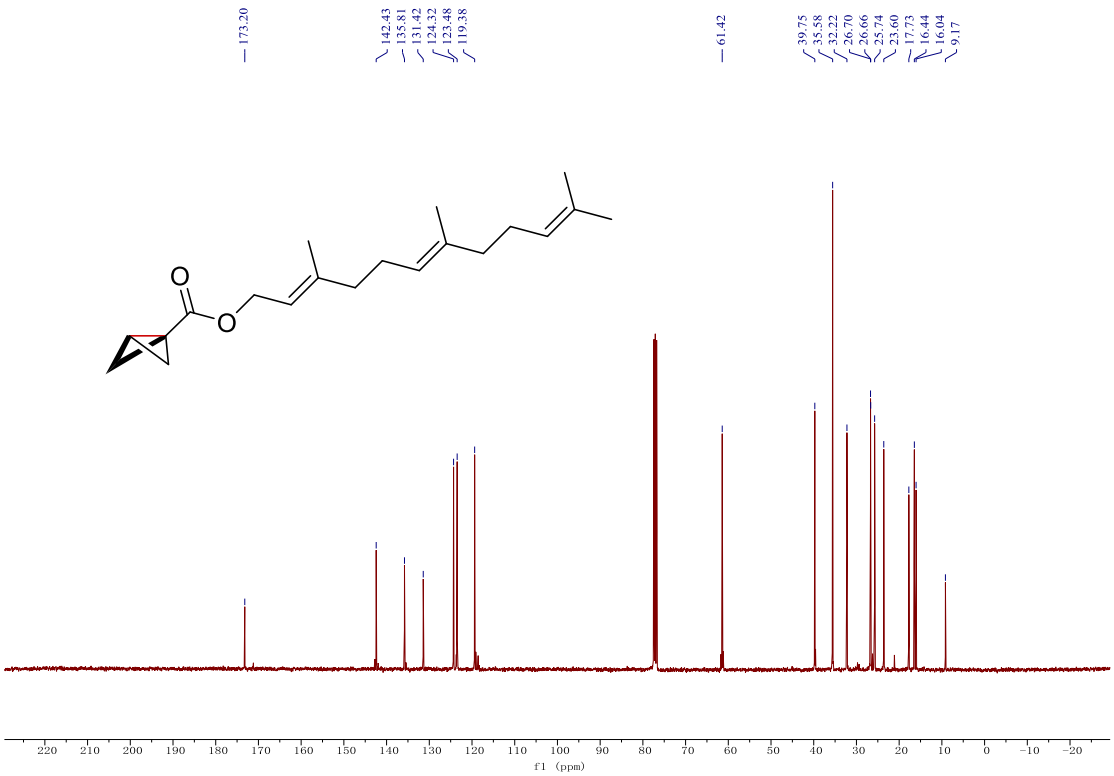
^{1}H NMR of compound **1e** (400 MHz, $CDCl_3$)



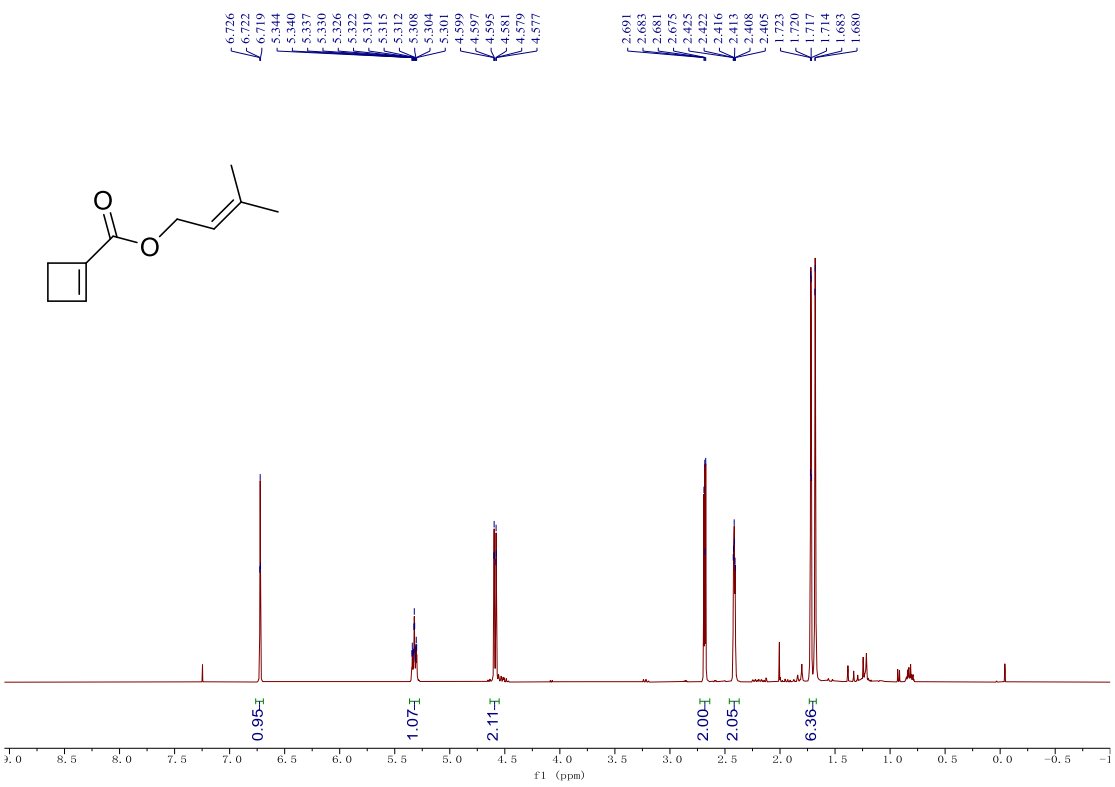
^{13}C NMR of compound **1e** (101 MHz, $CDCl_3$)



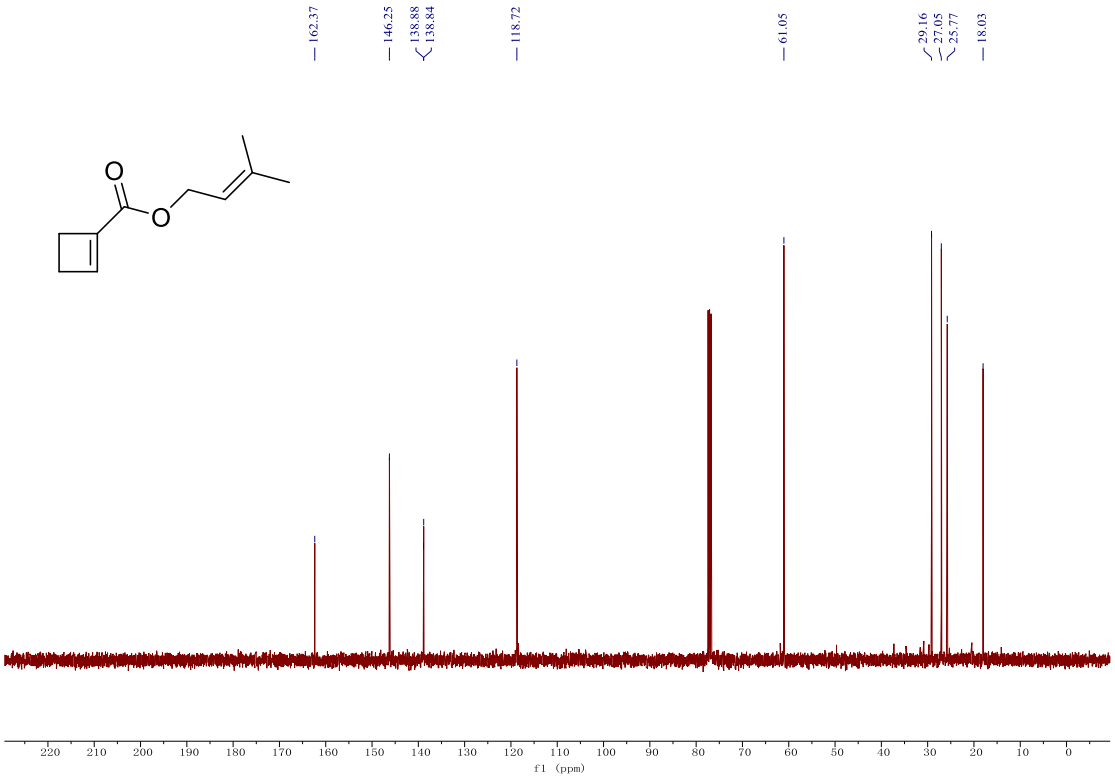
^{1}H NMR of compound **1f** (400 MHz, $CDCl_3$)



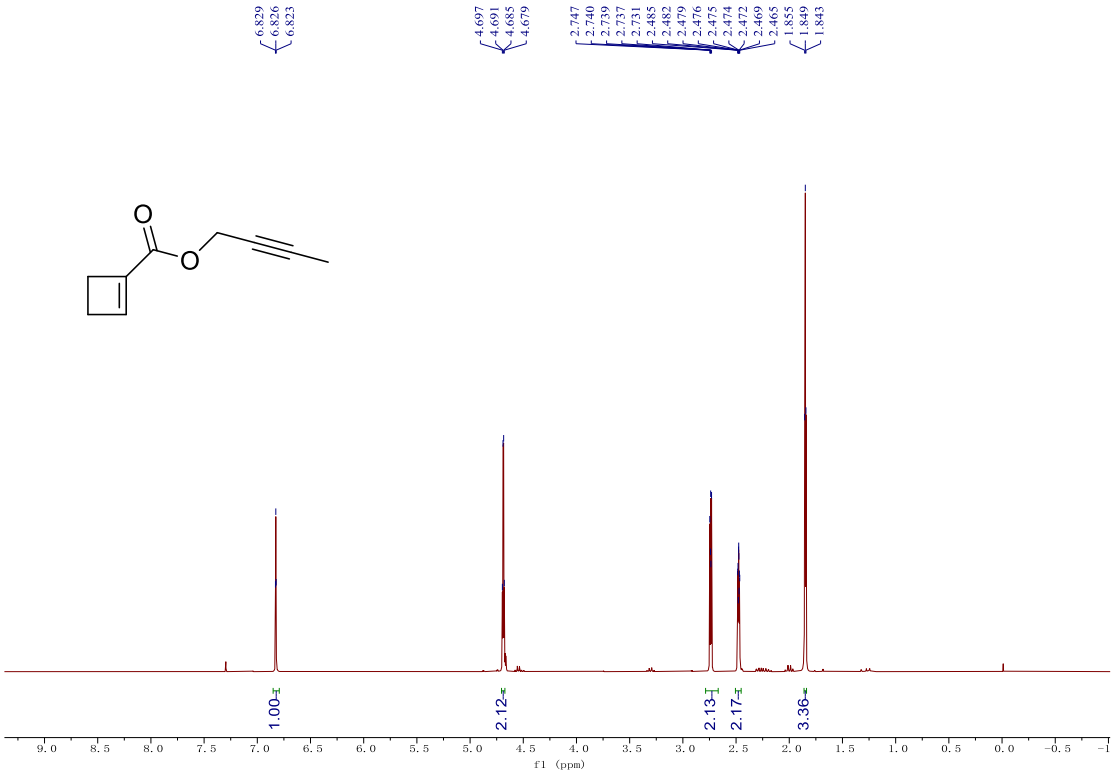
^{13}C NMR of compound **1f** (101 MHz, $CDCl_3$)



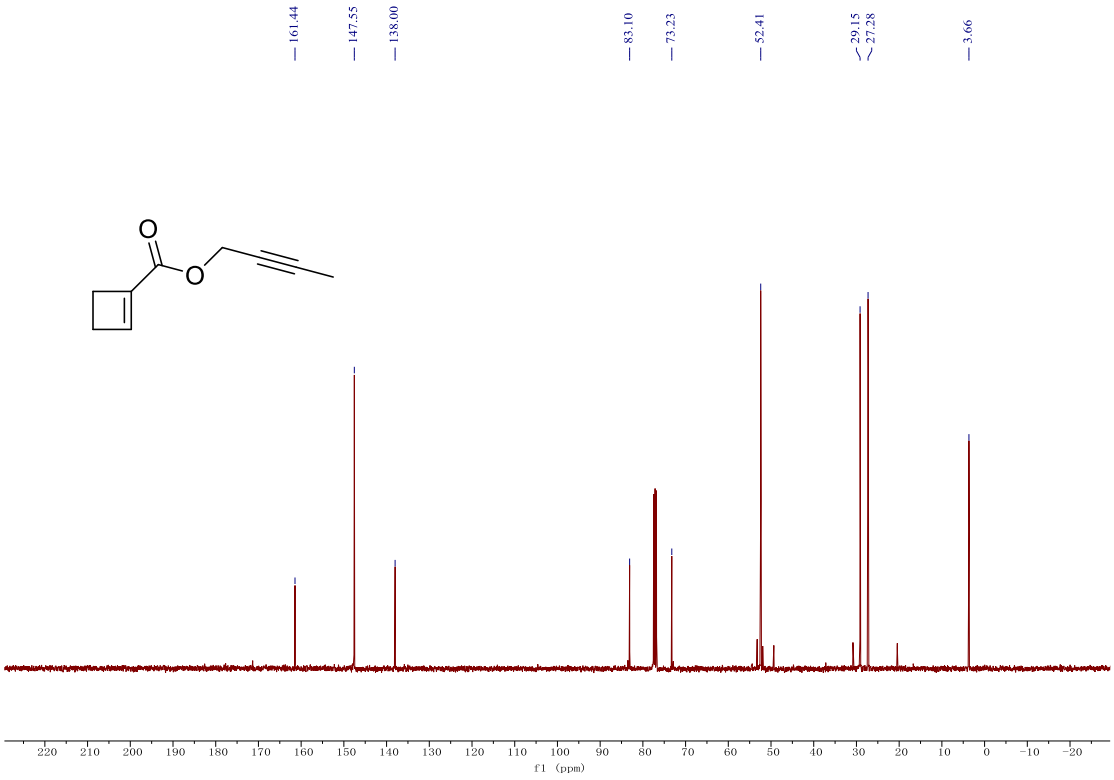
^{1}H NMR of compound **4a** (400 MHz, $CDCl_3$)



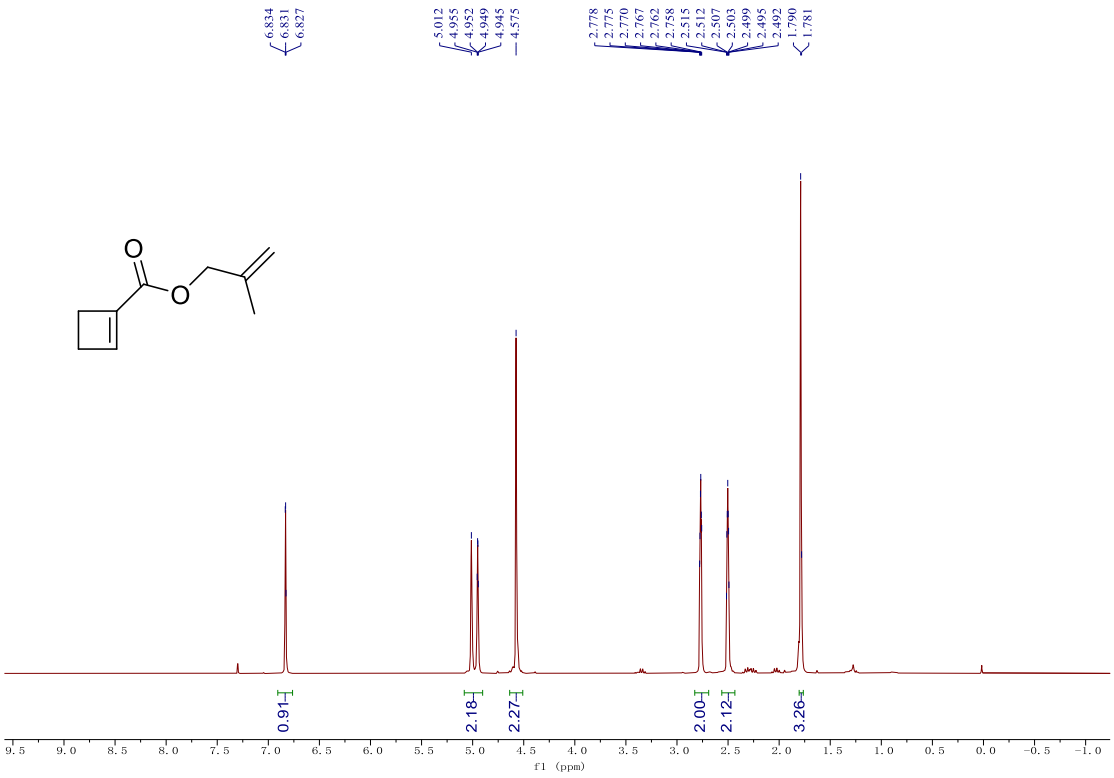
^{13}C NMR of compound **4a** (101 MHz, $CDCl_3$)



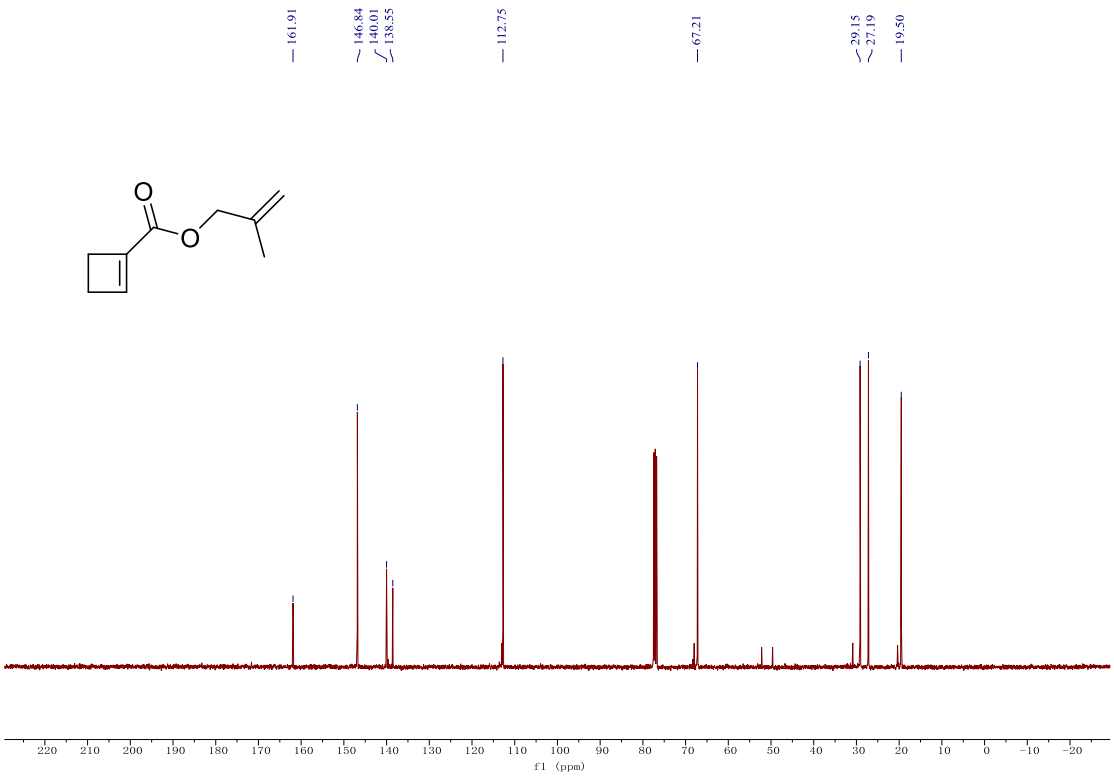
^{1}H NMR of compound **4b** (400 MHz, $CDCl_3$)



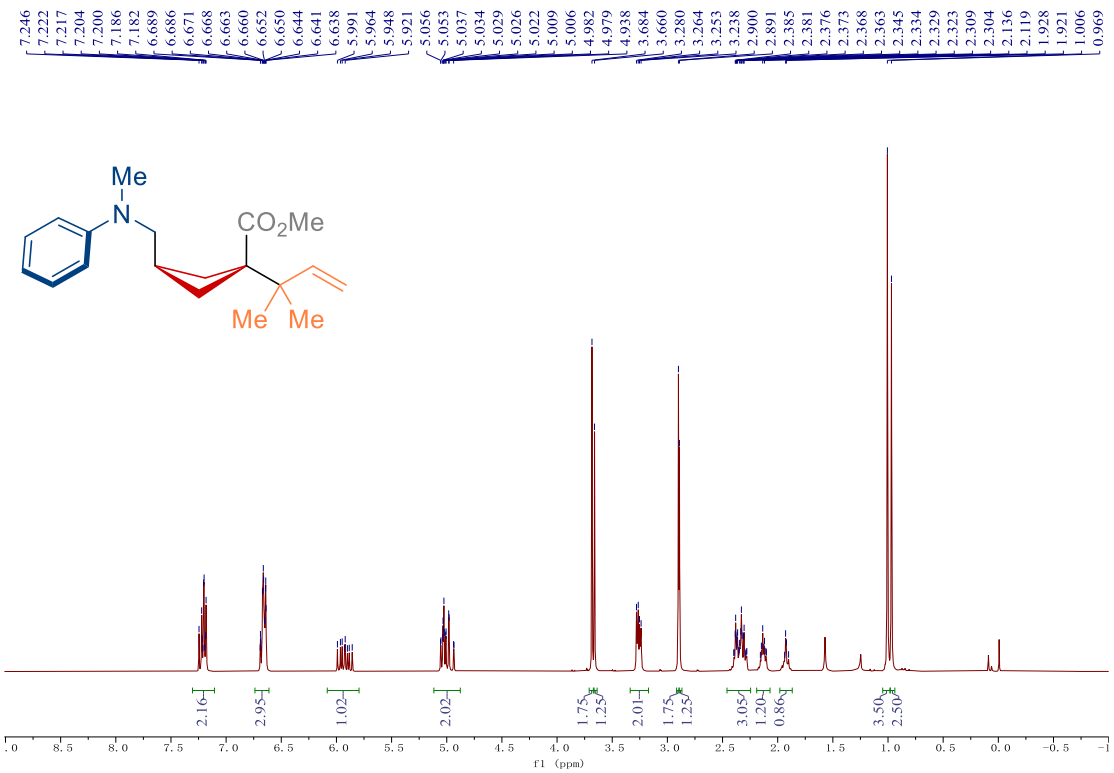
^{13}C NMR of compound **4b** (101 MHz, $CDCl_3$)



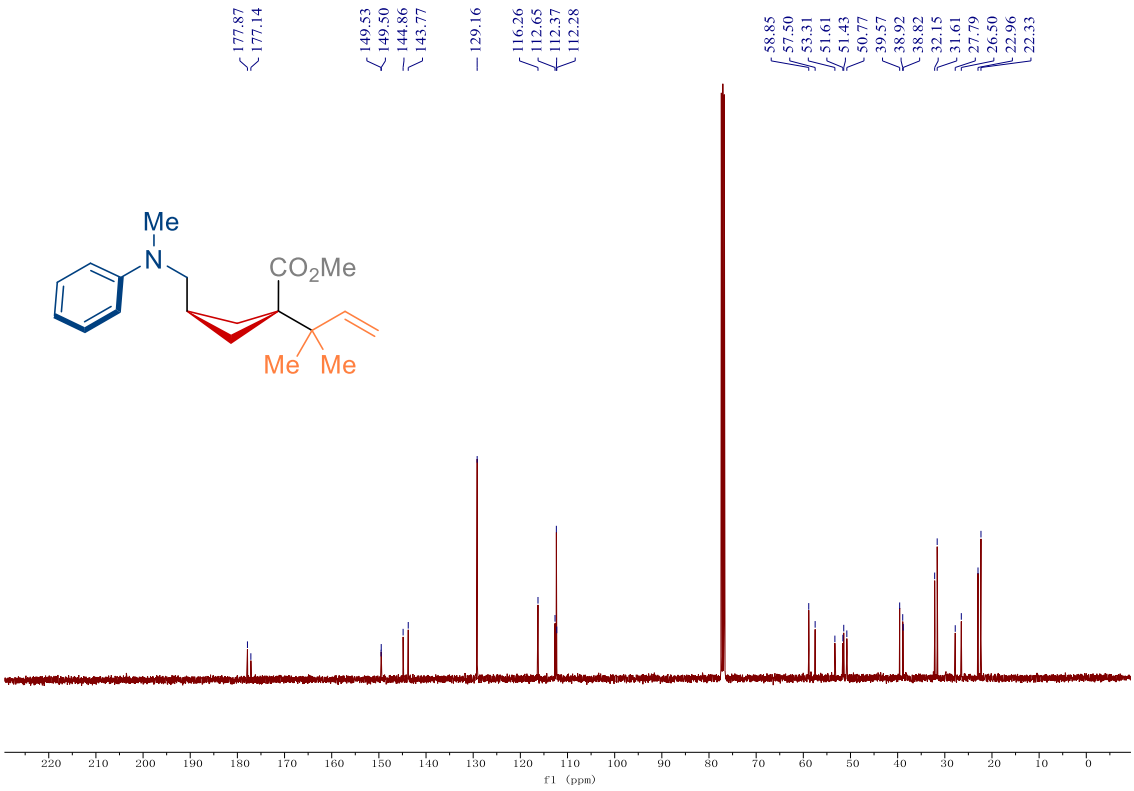
^{1}H NMR of compound **4d** (400 MHz, $CDCl_3$)



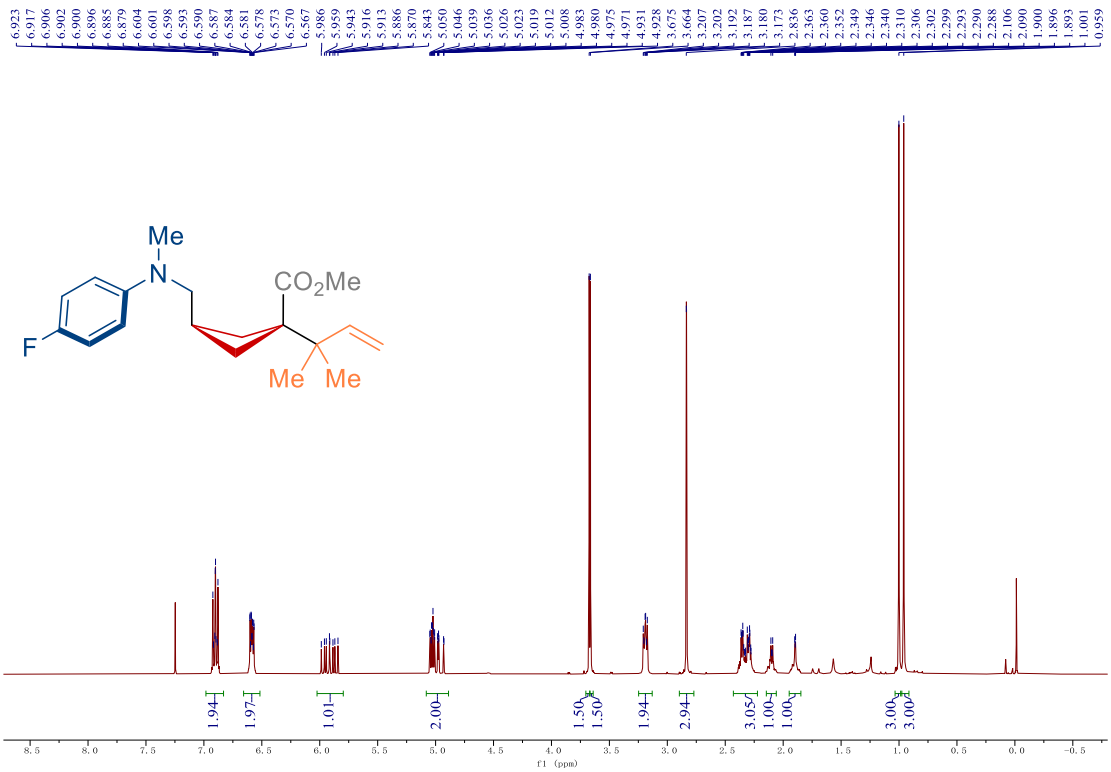
^{13}C NMR of compound **4d** (101 MHz, $CDCl_3$)



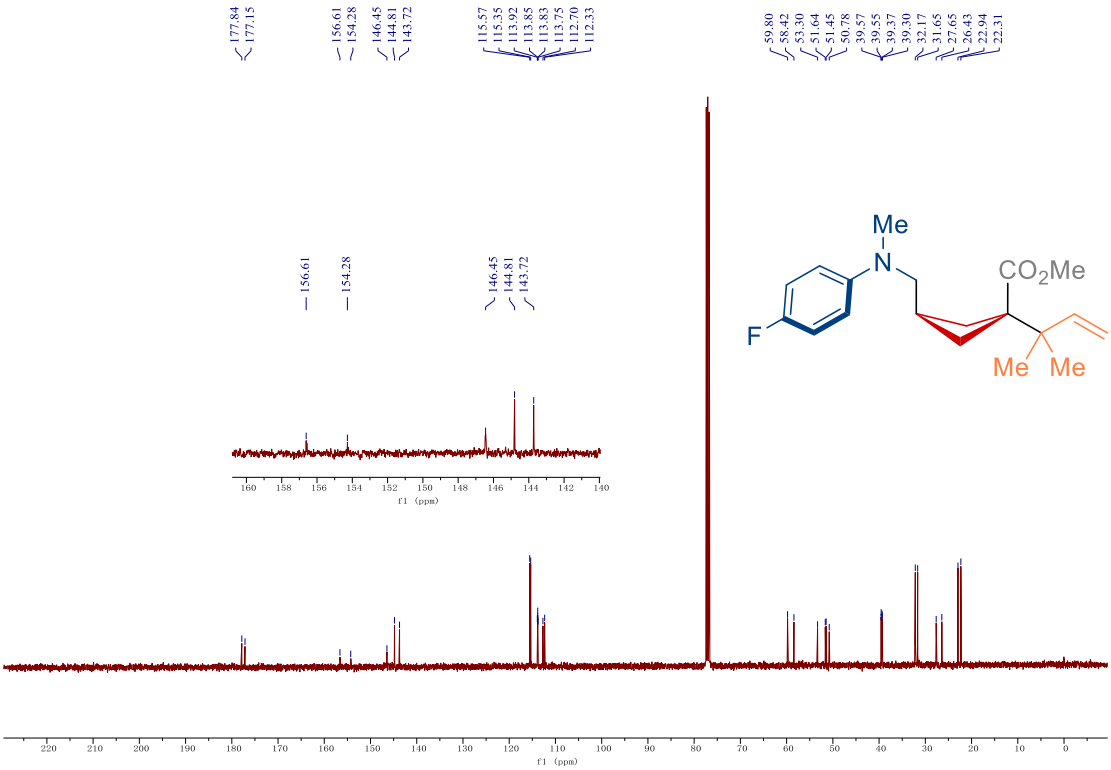
^{1}H NMR of compound **3** (400 MHz, $CDCl_3$)



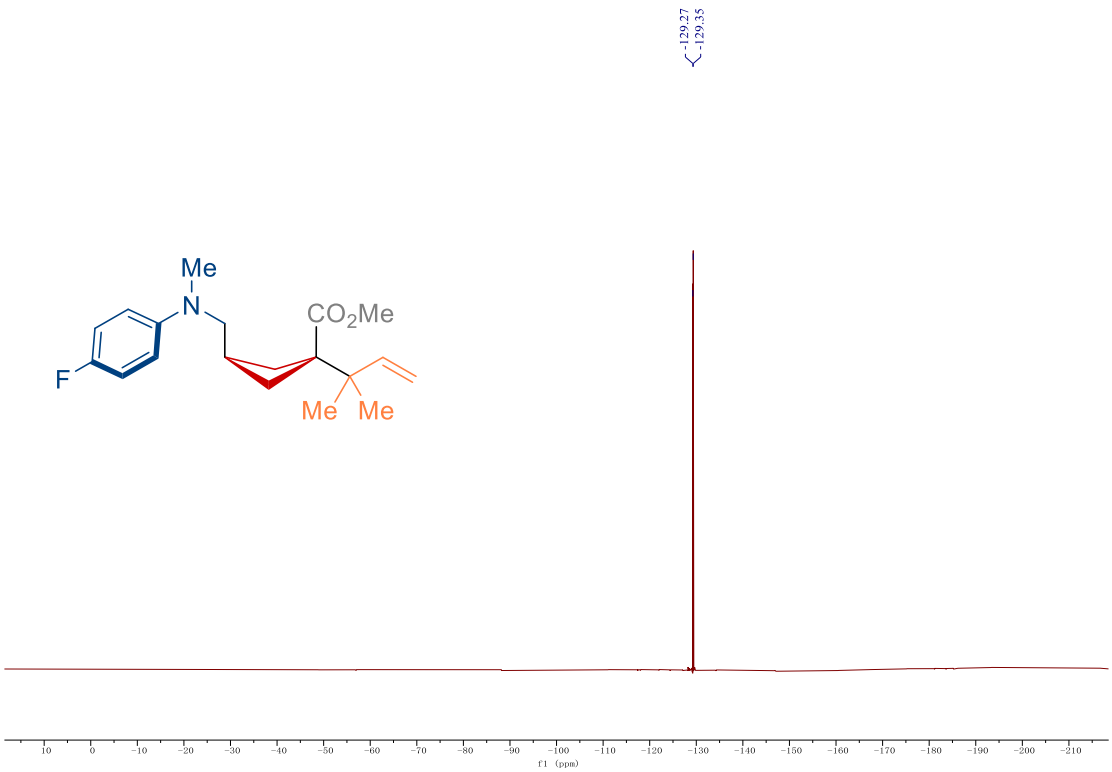
^{13}C NMR of compound **3** (101 MHz, $CDCl_3$)



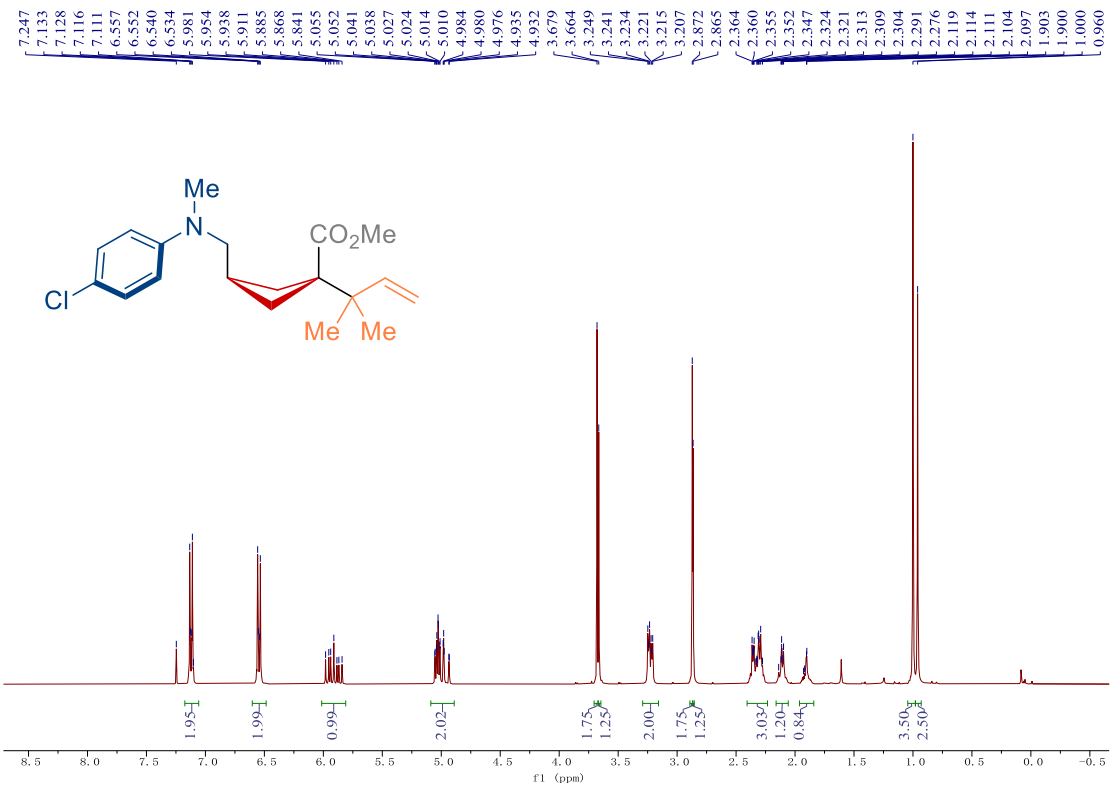
^{1}H NMR of compound **5** (400 MHz, $CDCl_3$)



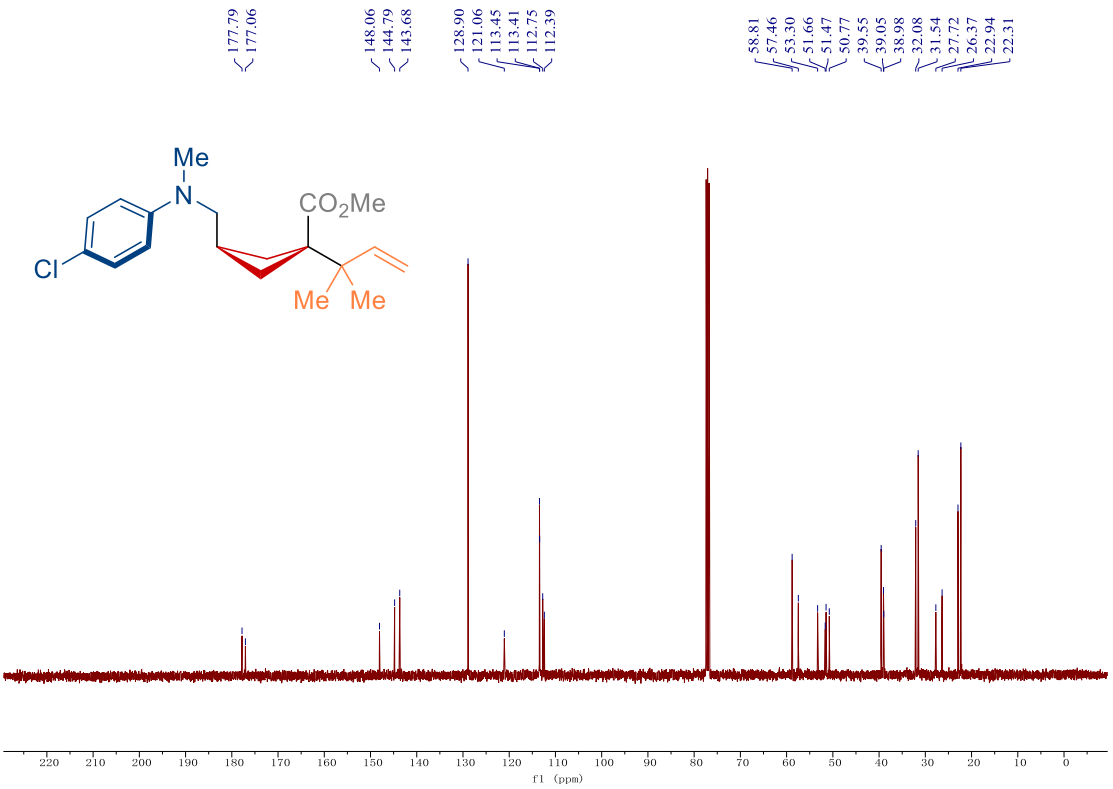
^{13}C NMR of compound **5** (101 MHz, $CDCl_3$)



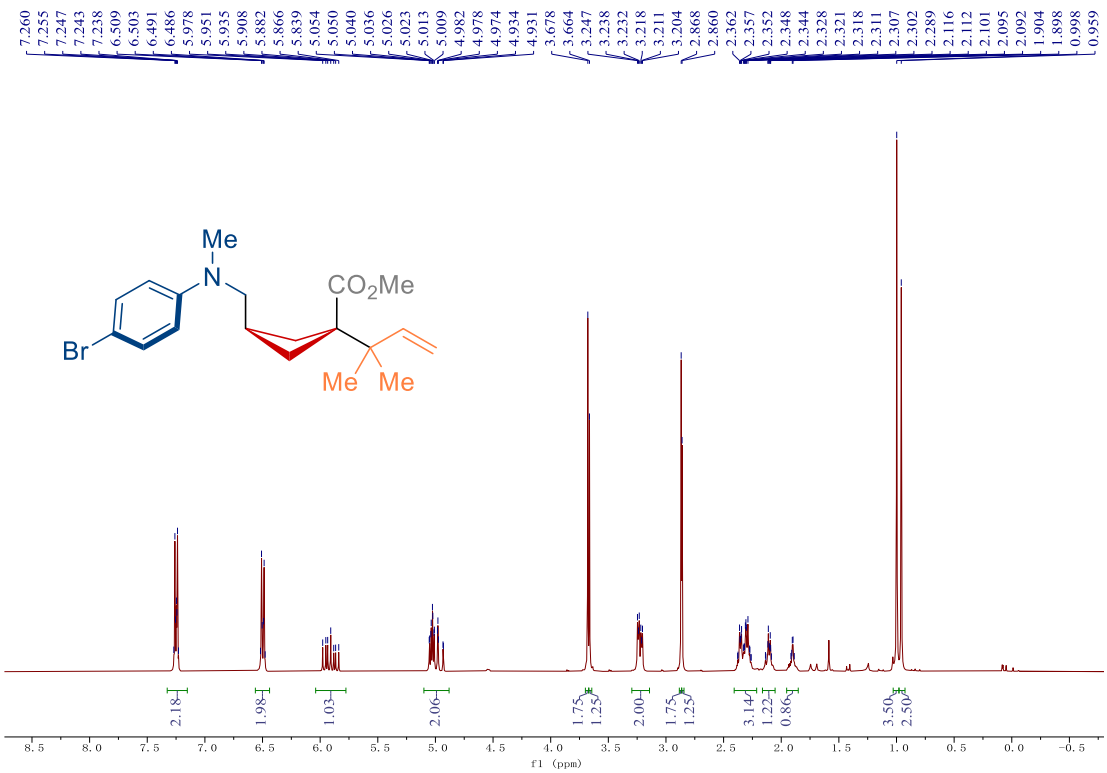
^{19}F NMR of compound **5** (376 MHz, $CDCl_3$)



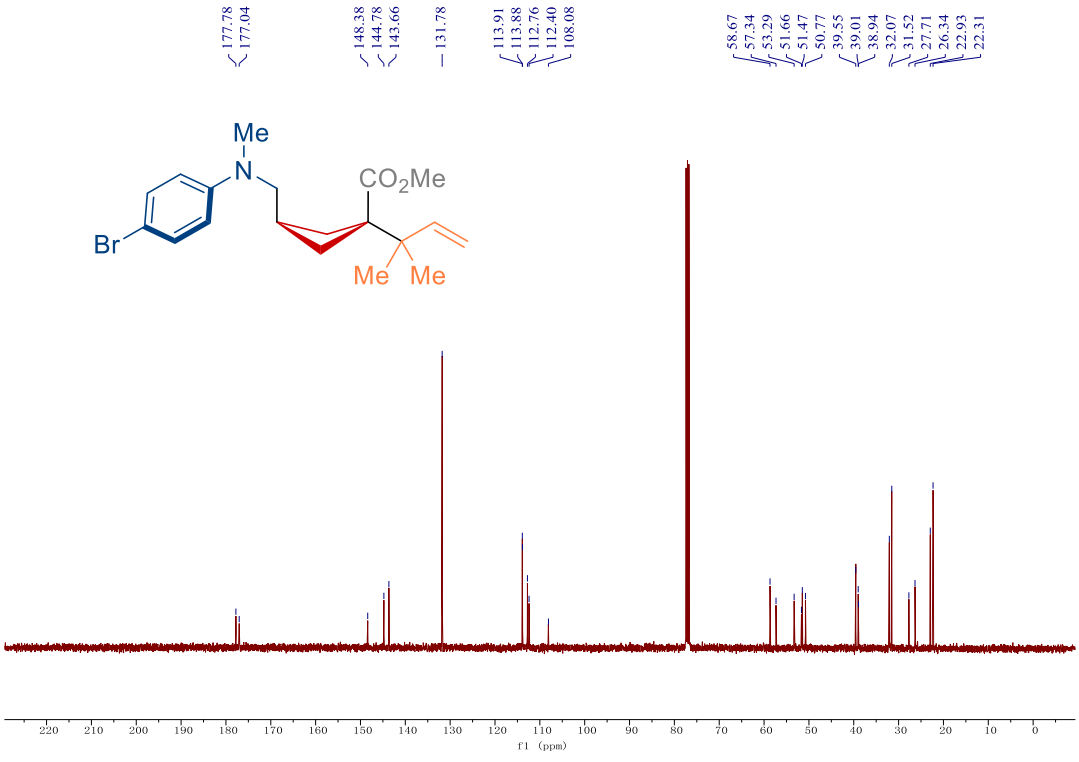
^{1}H NMR of compound **6** (400 MHz, $CDCl_3$)



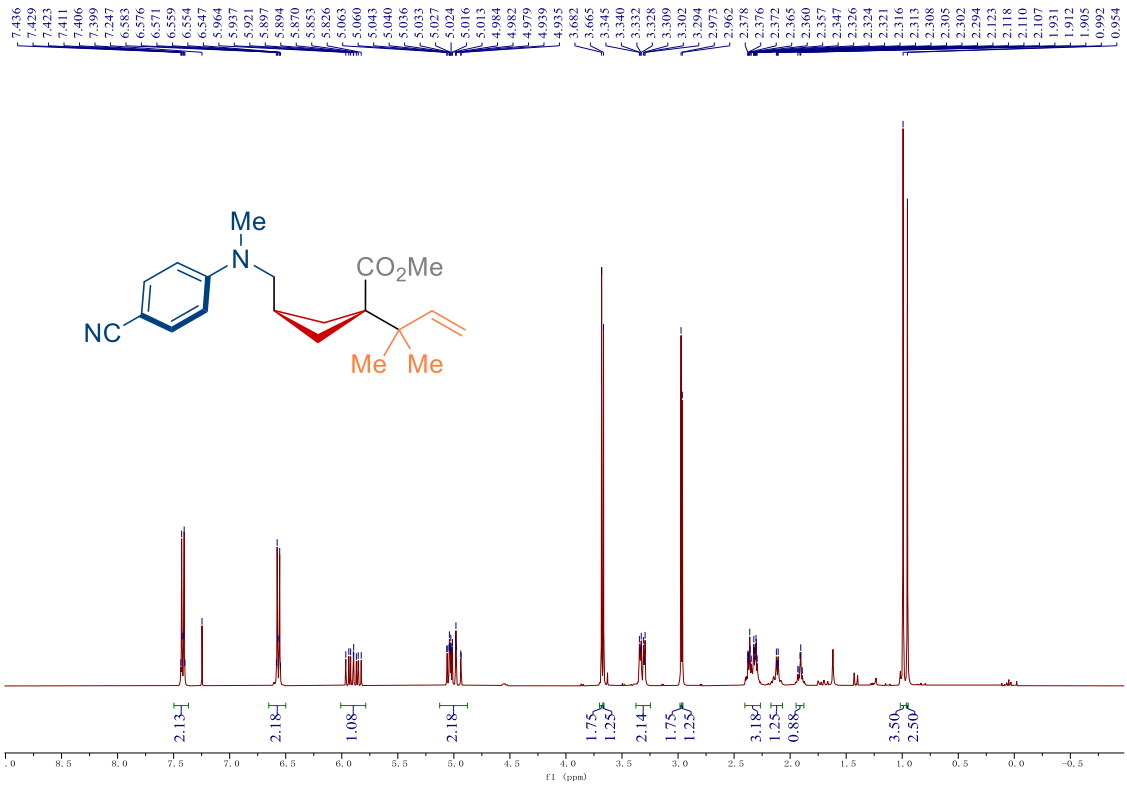
^{13}C NMR of compound **6** (101 MHz, $CDCl_3$)



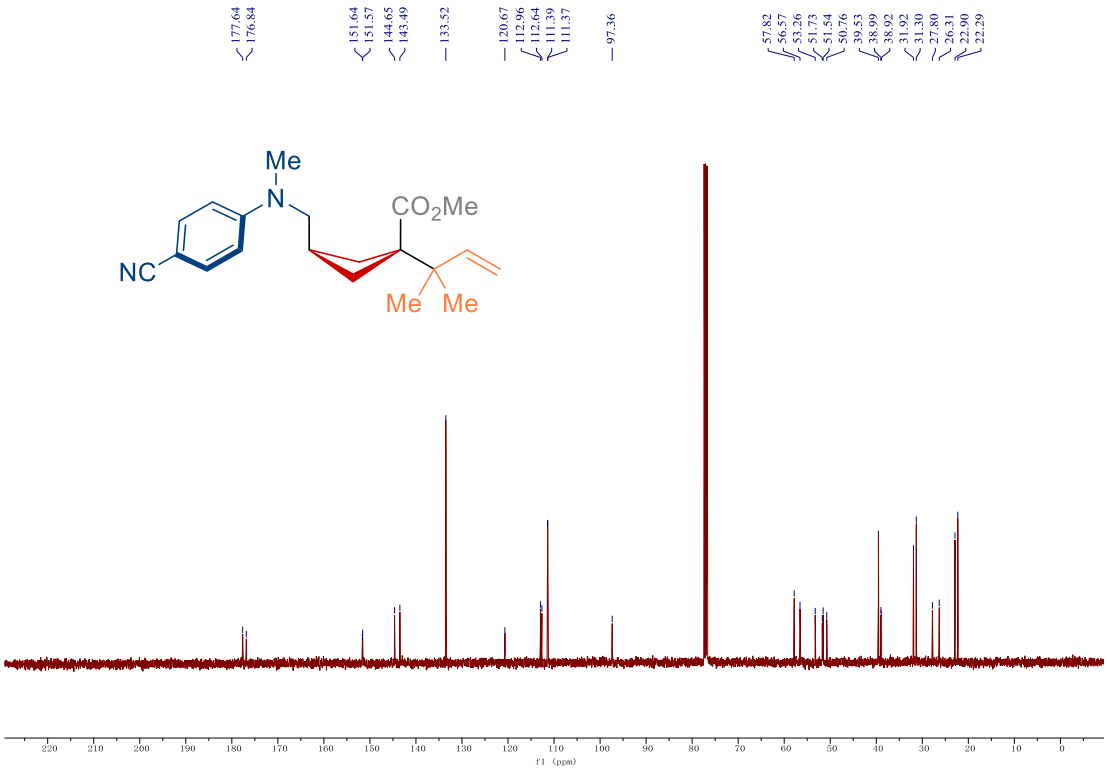
^{1}H NMR of compound **7** (400 MHz, $CDCl_3$)



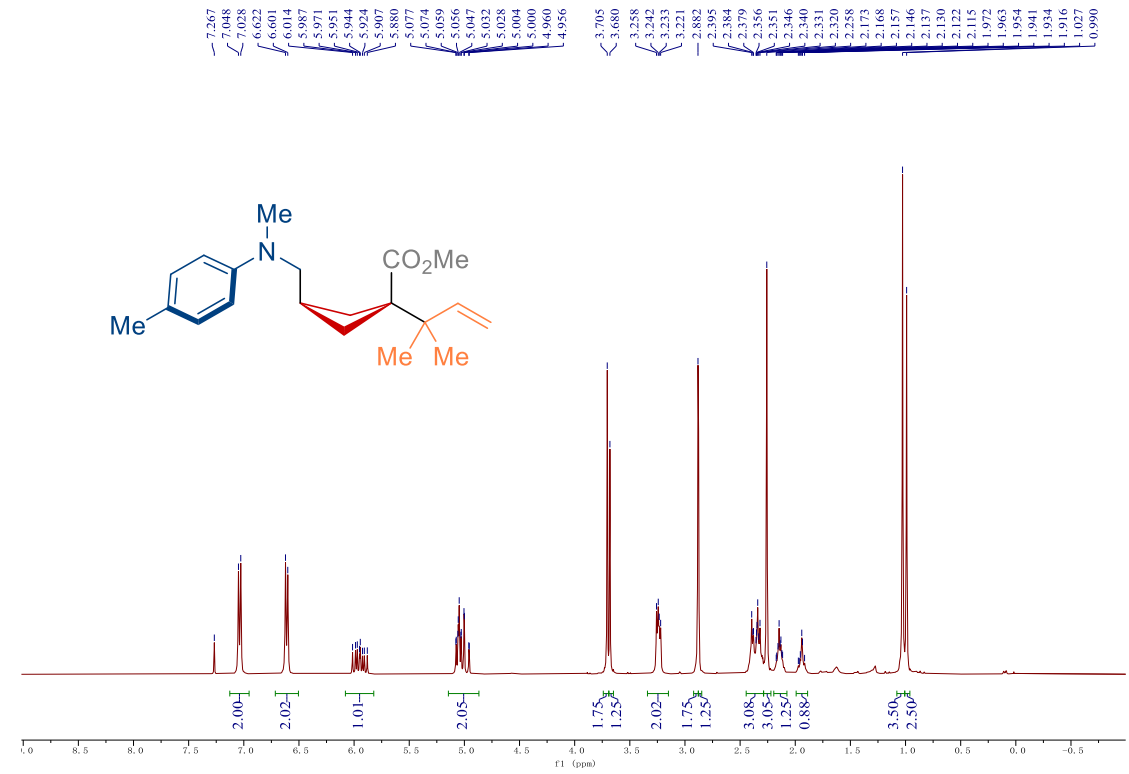
^{13}C NMR of compound **7** (101 MHz, $CDCl_3$)



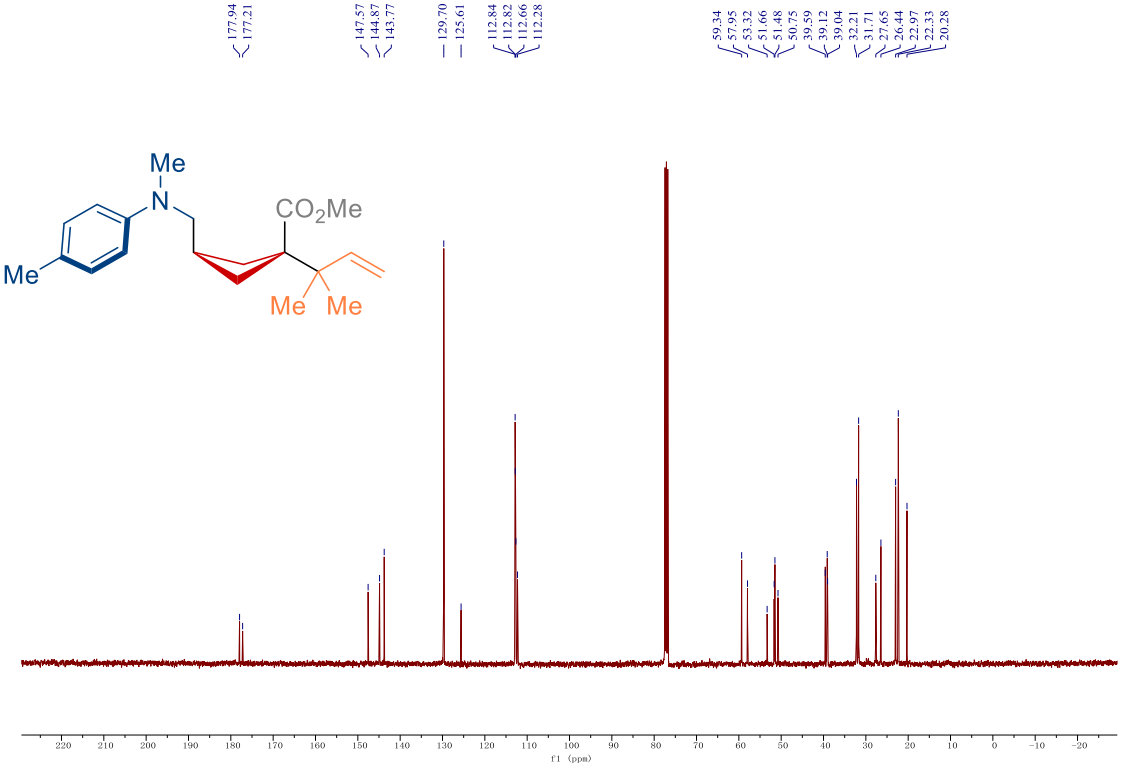
^{1}H NMR of compound **8** (400 MHz, $CDCl_3$)



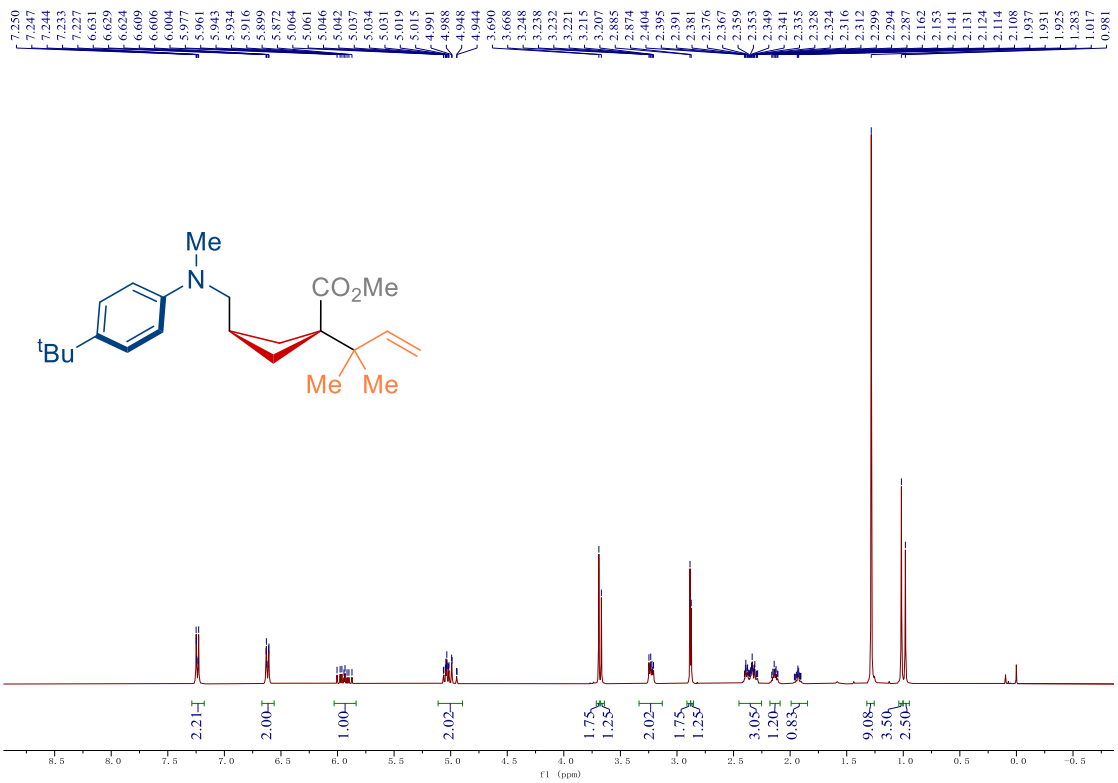
^{13}C NMR of compound **8** (101 MHz, $CDCl_3$)



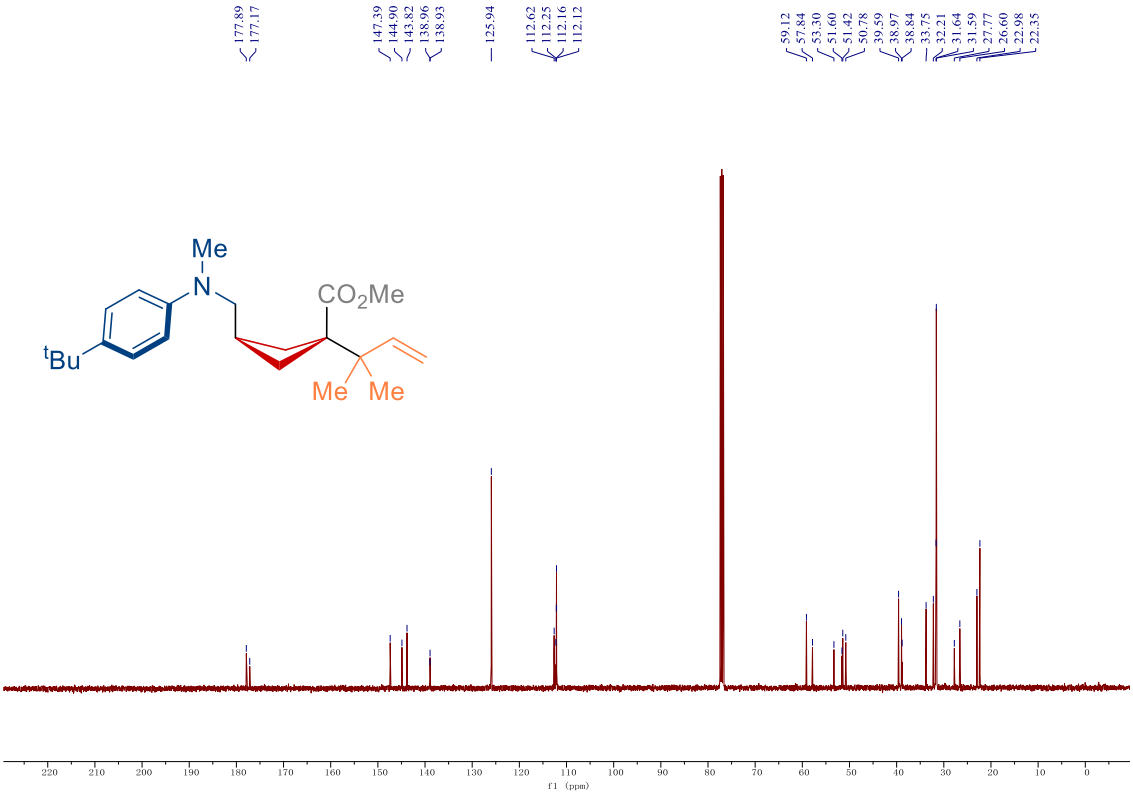
^{1}H NMR of compound **9** (400 MHz, $CDCl_3$)



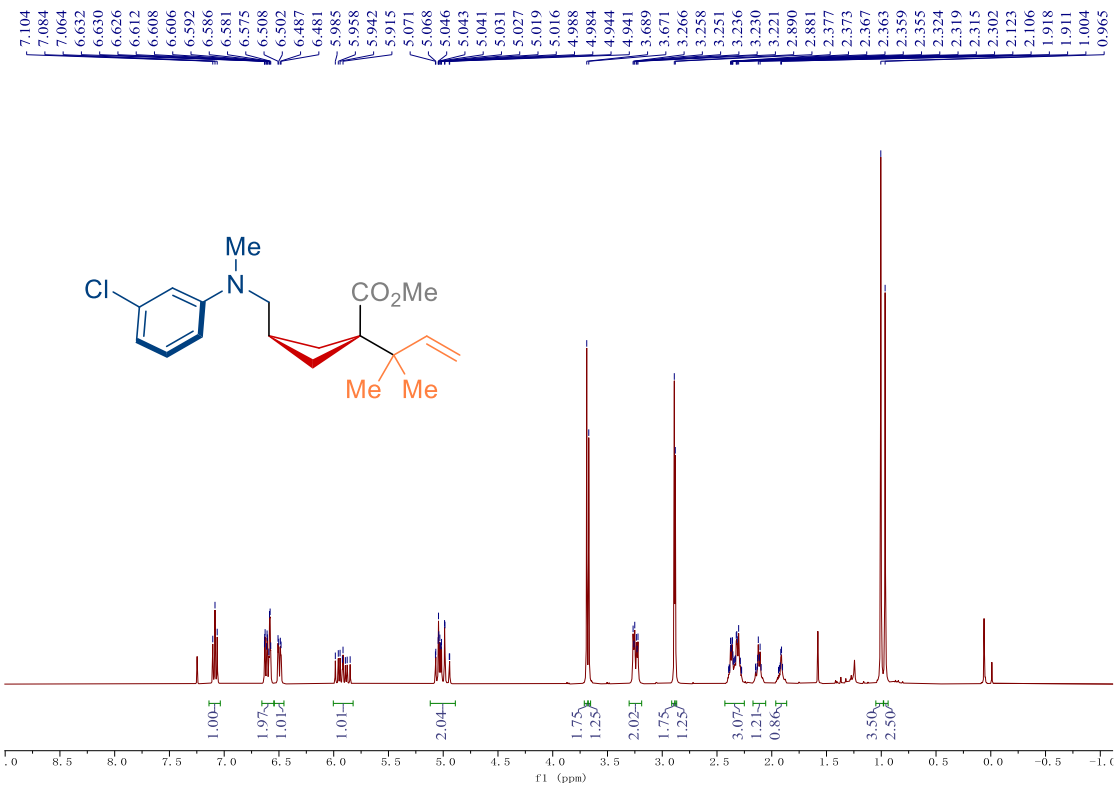
^{13}C NMR of compound **9** (101 MHz, $CDCl_3$)



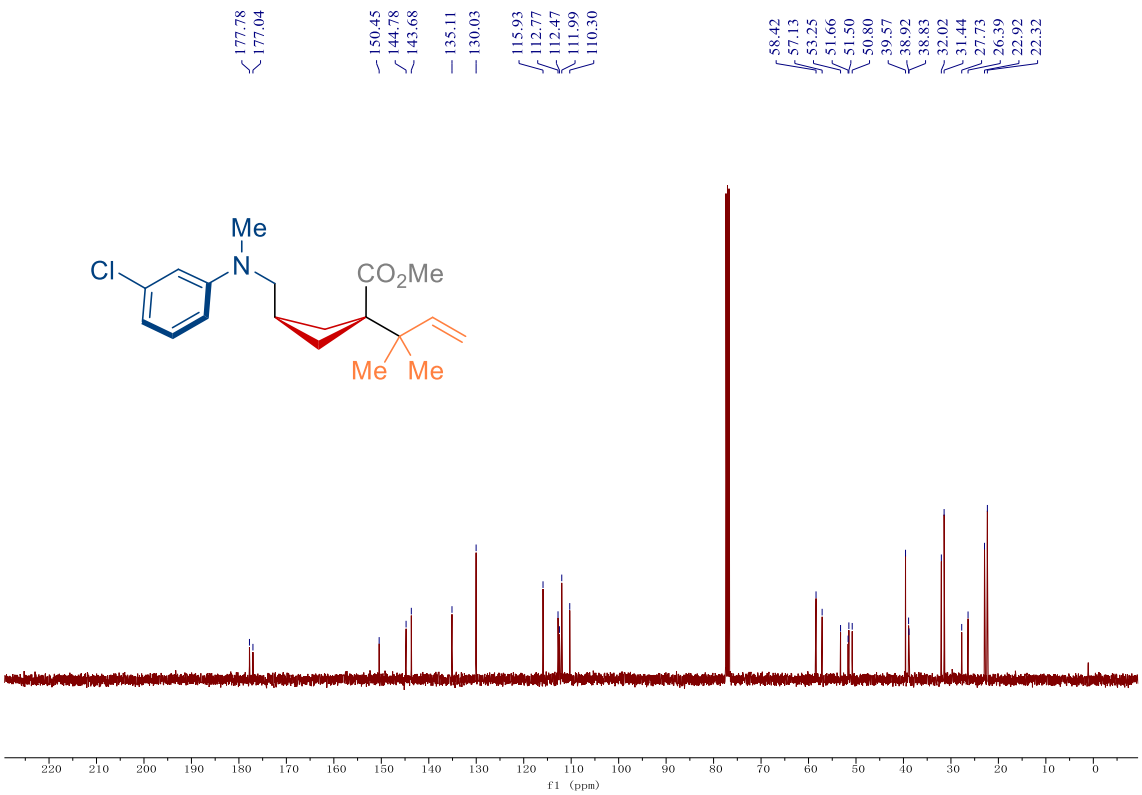
^{1}H NMR of compound **10** (400 MHz, $CDCl_3$)



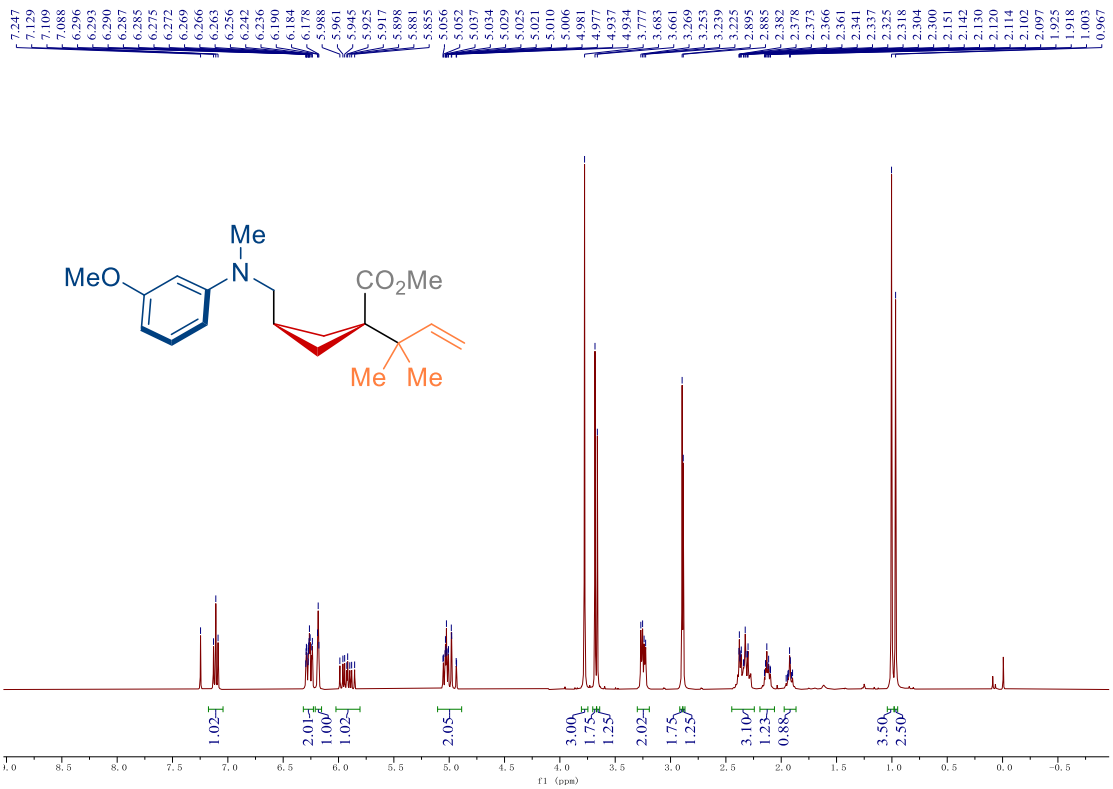
^{13}C NMR of compound **10** (101 MHz, $CDCl_3$)



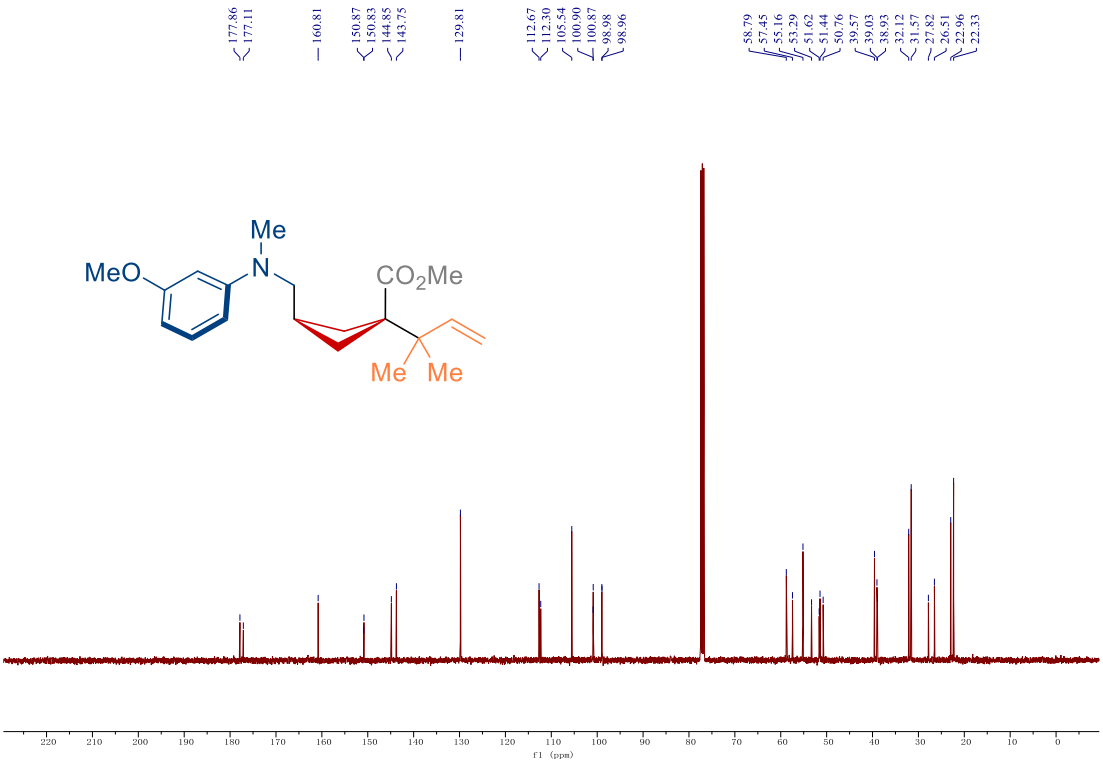
^{1}H NMR of compound **11** (400 MHz, $CDCl_3$)



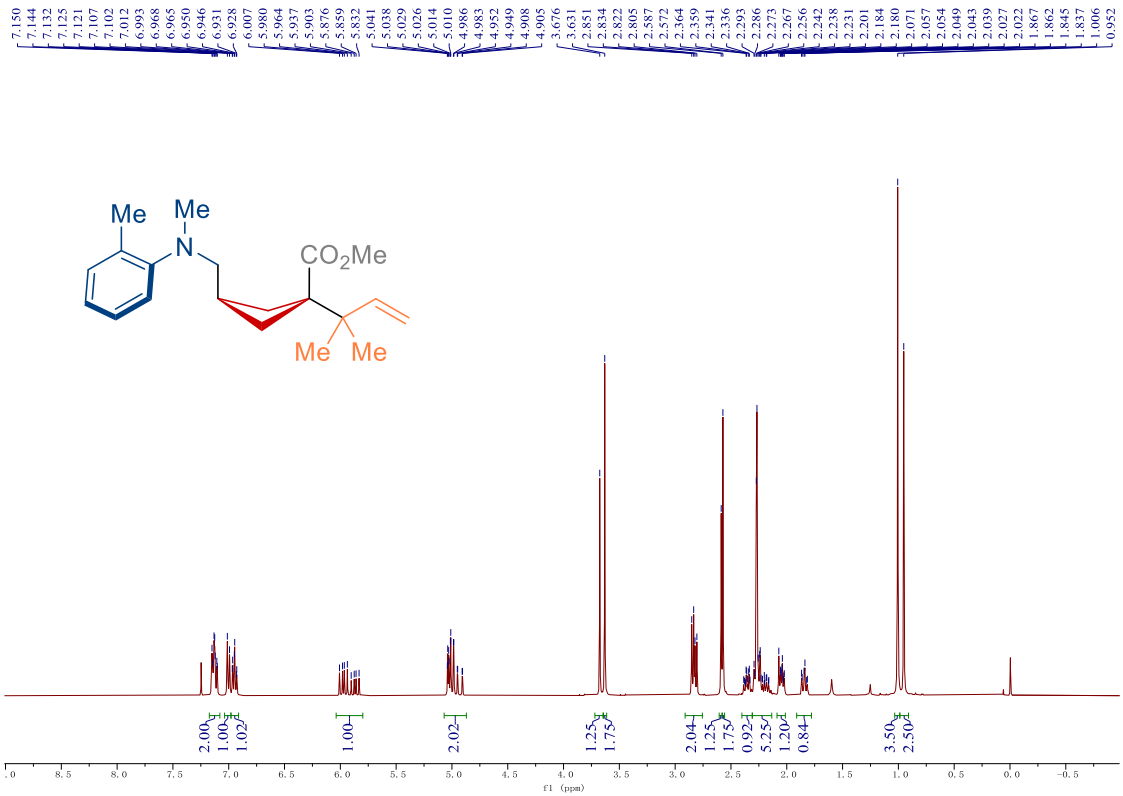
^{13}C NMR of compound **11** (101 MHz, $CDCl_3$)



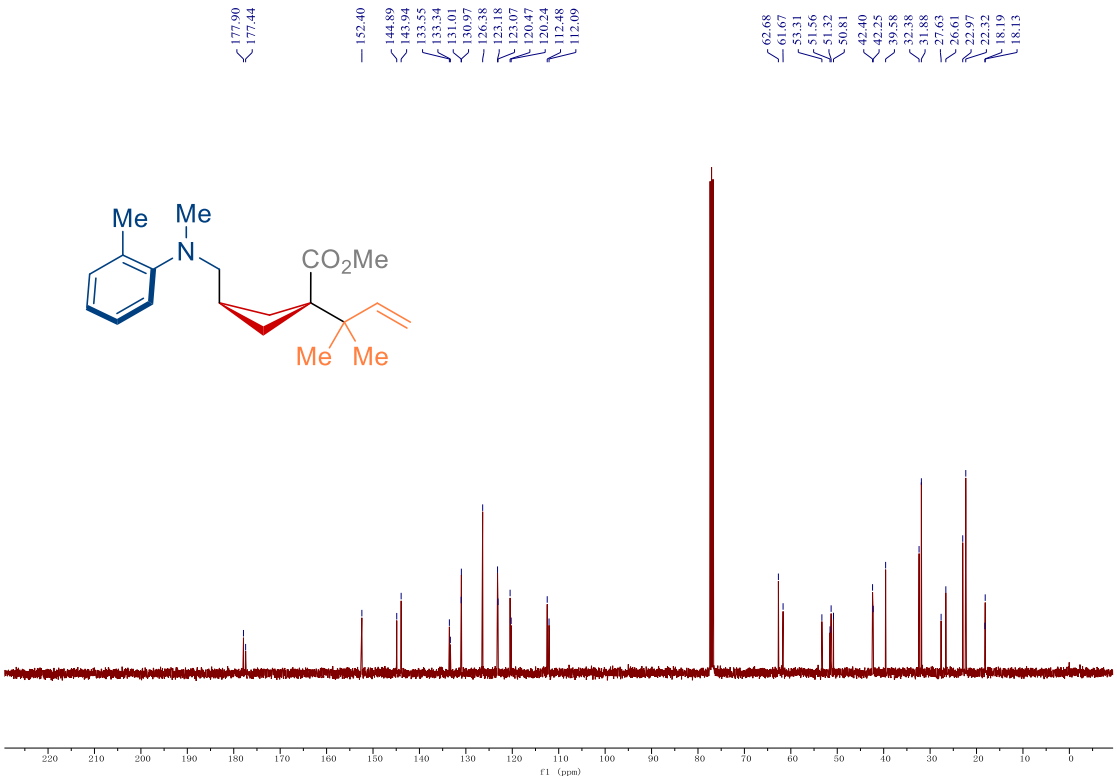
^{1}H NMR of compound **12** (400 MHz, $CDCl_3$)



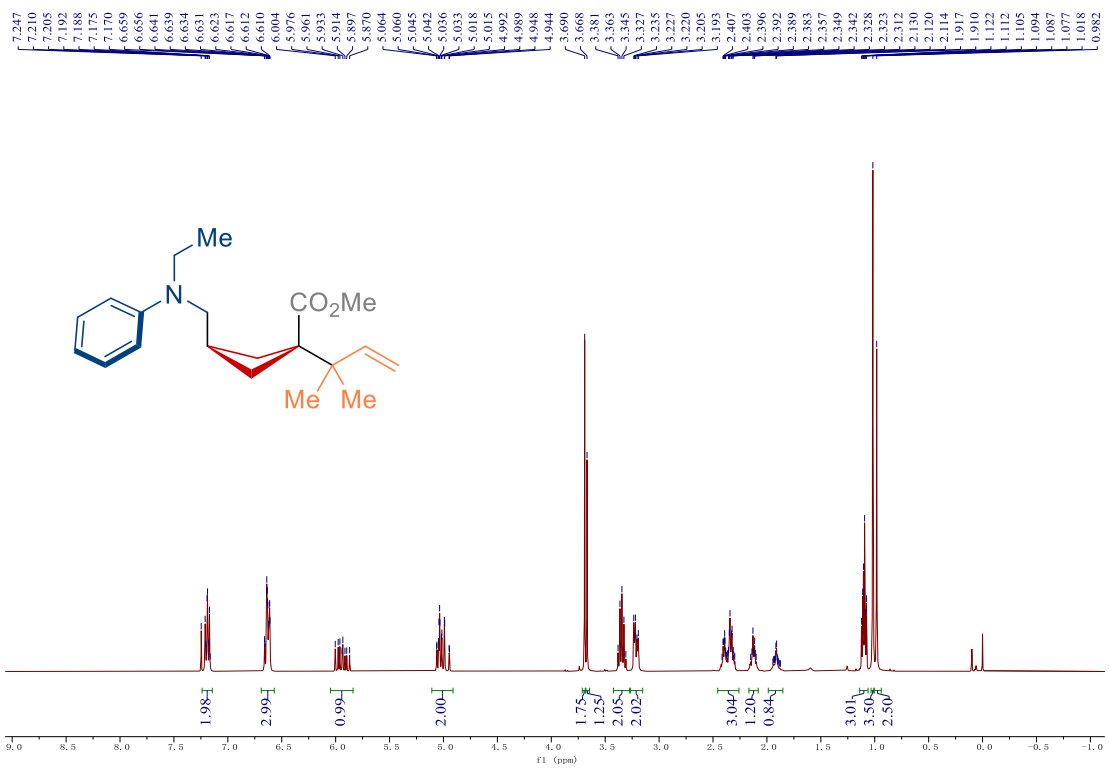
^{13}C NMR of compound **12** (101 MHz, $CDCl_3$)



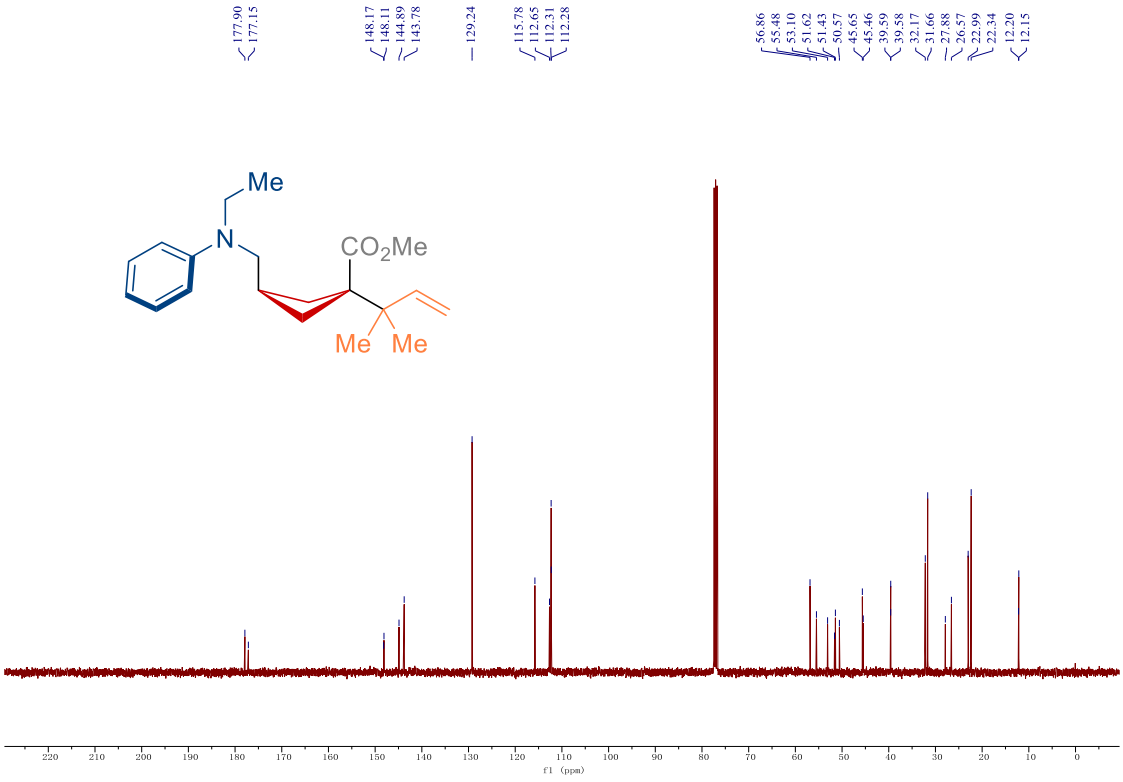
^{1}H NMR of compound **13** (400 MHz, $CDCl_3$)



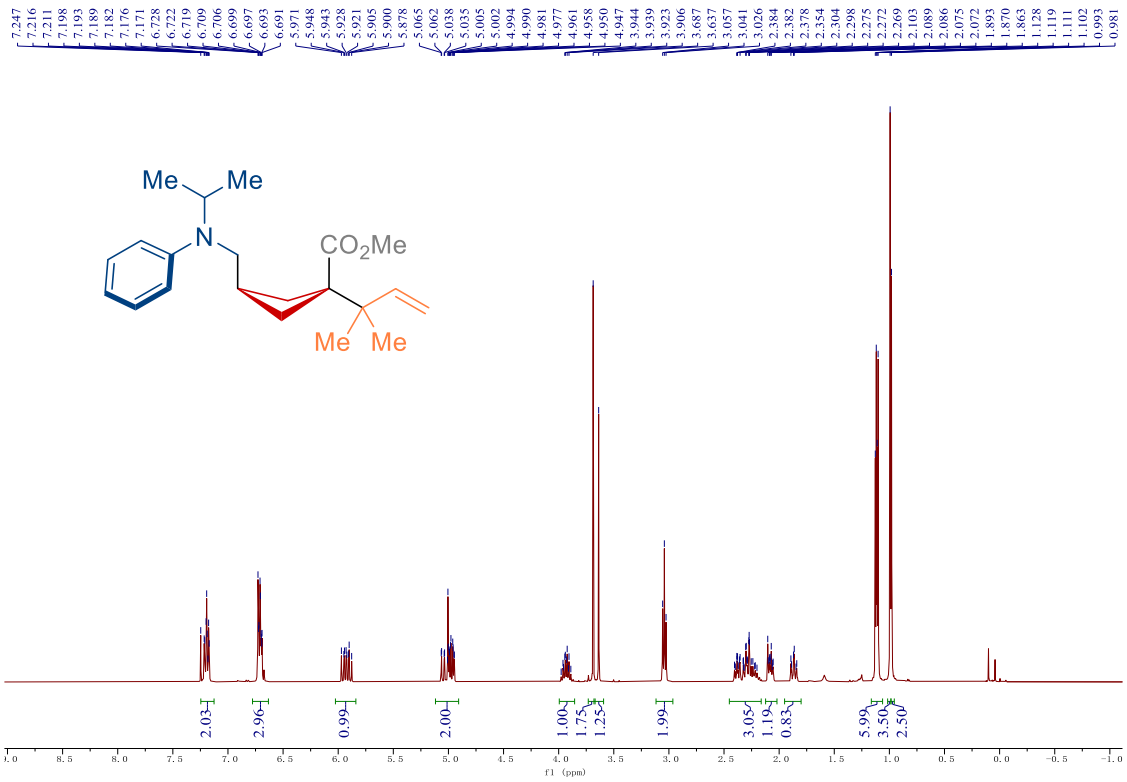
^{13}C NMR of compound **13** (101 MHz, $CDCl_3$)



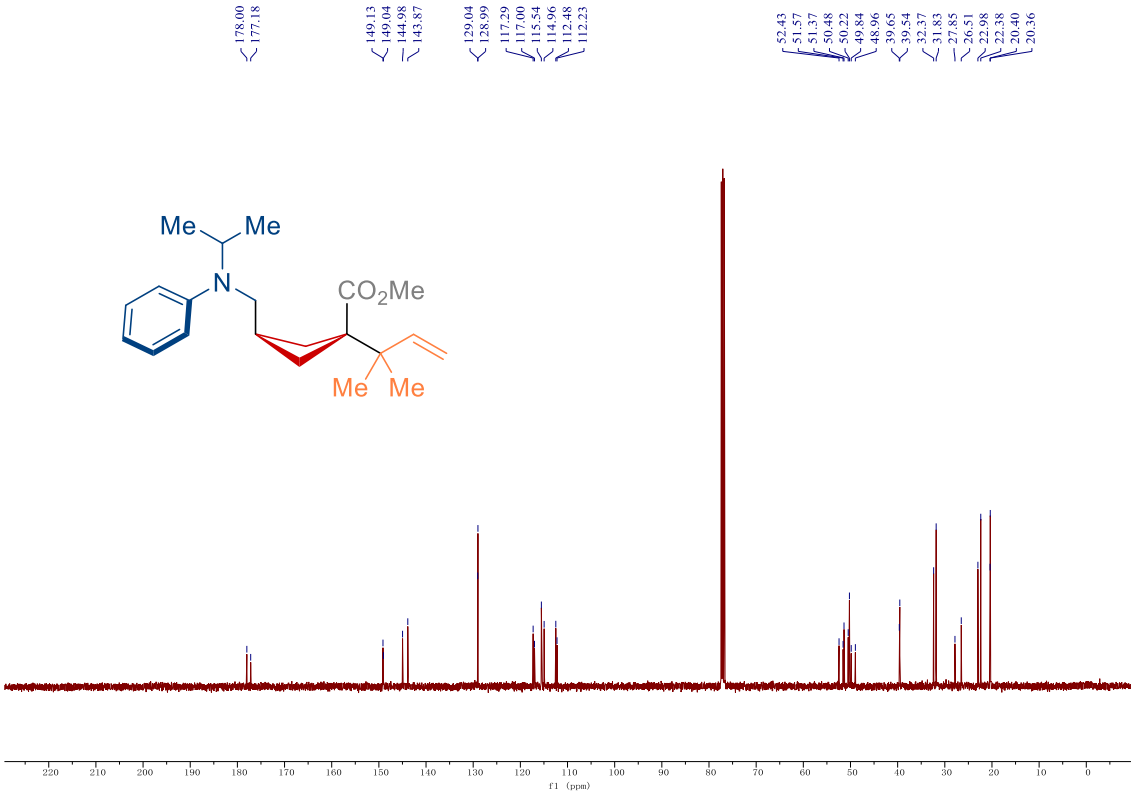
^{1}H NMR of compound **14** (400 MHz, $CDCl_3$)



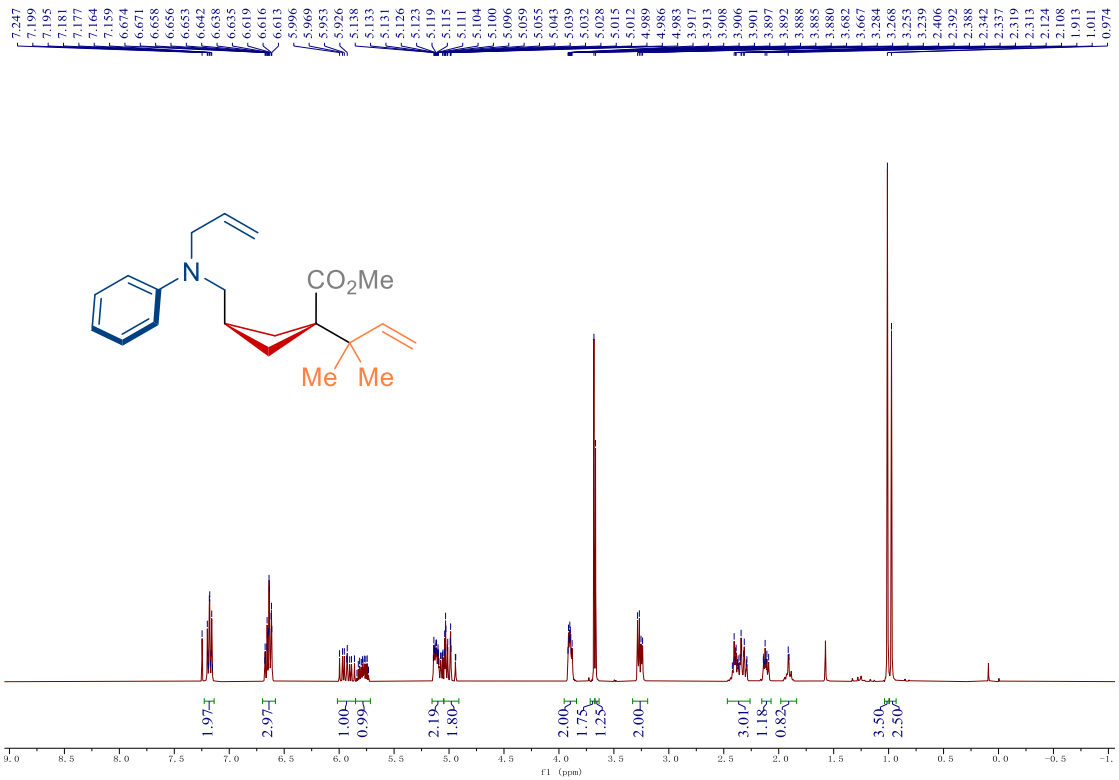
^{13}C NMR of compound **14** (101 MHz, $CDCl_3$)



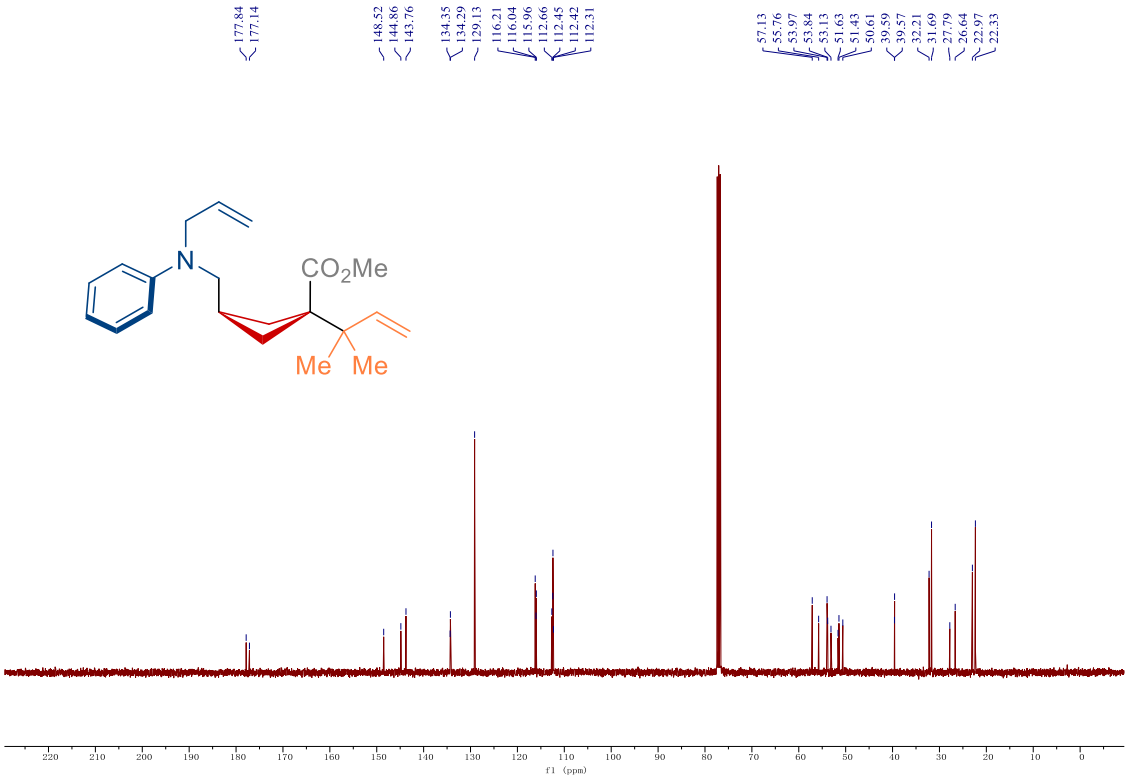
^{1}H NMR of compound **15** (400 MHz, $CDCl_3$)



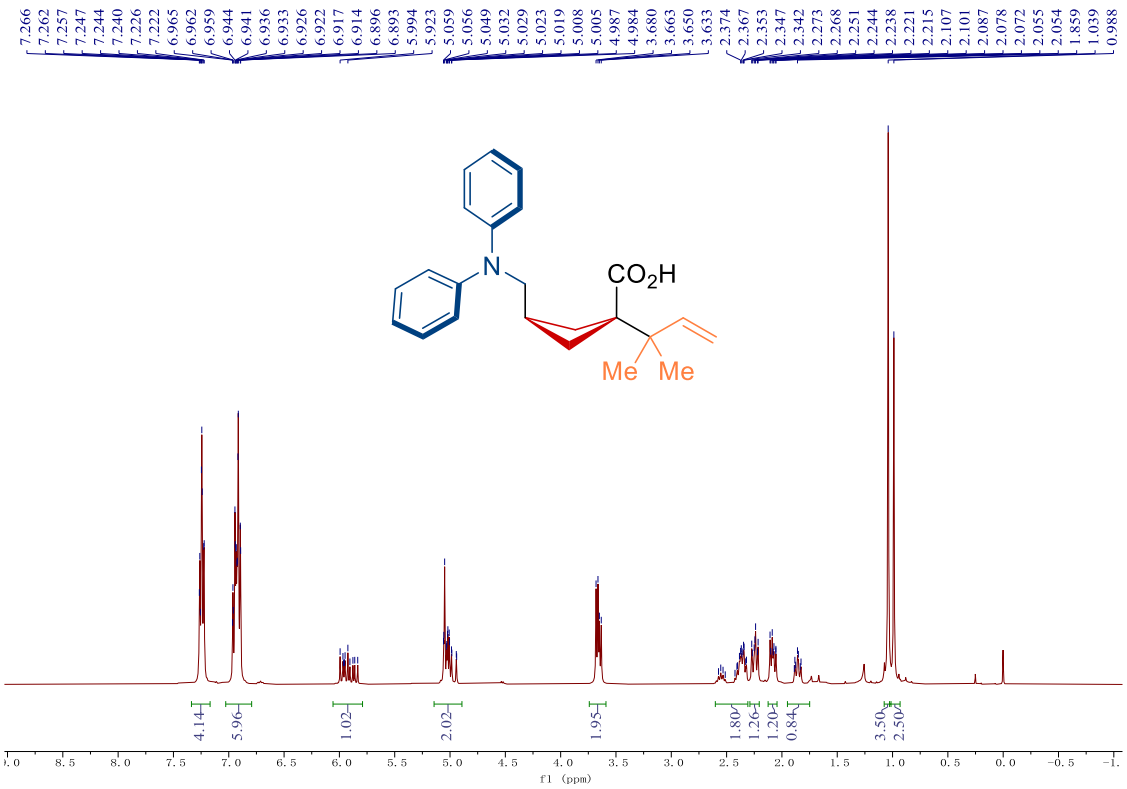
^{13}C NMR of compound **15** (101 MHz, $CDCl_3$)



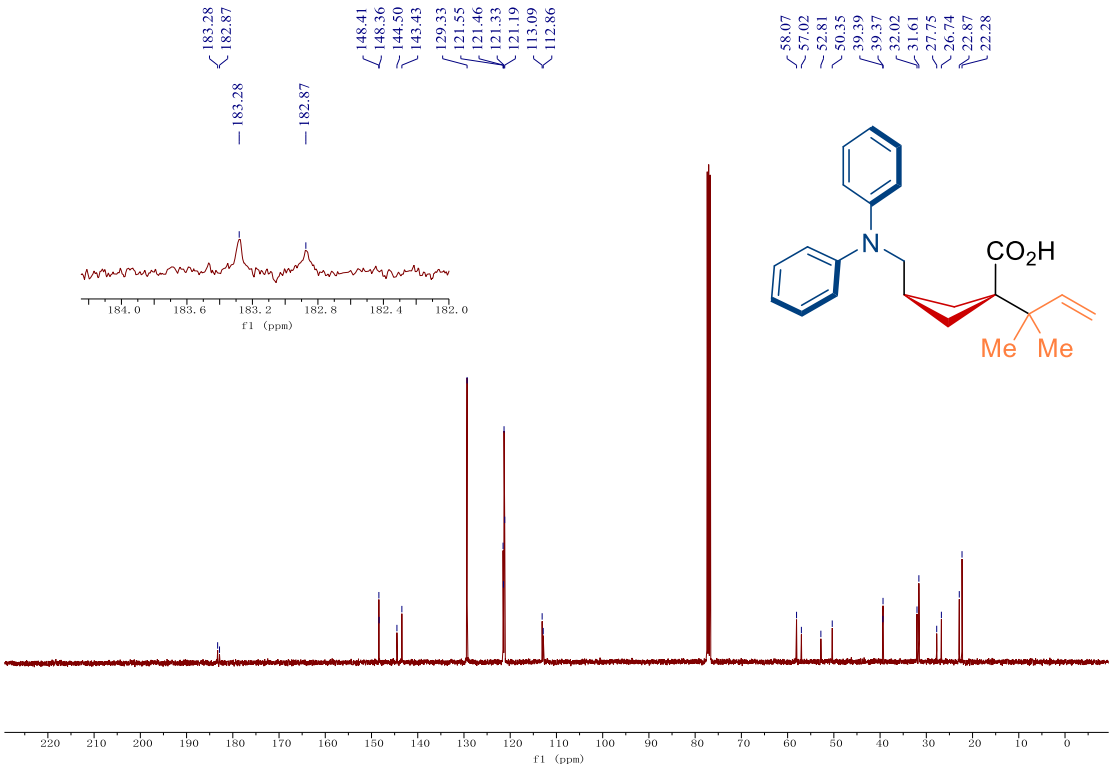
^{1}H NMR of compound **16** (400 MHz, $CDCl_3$)



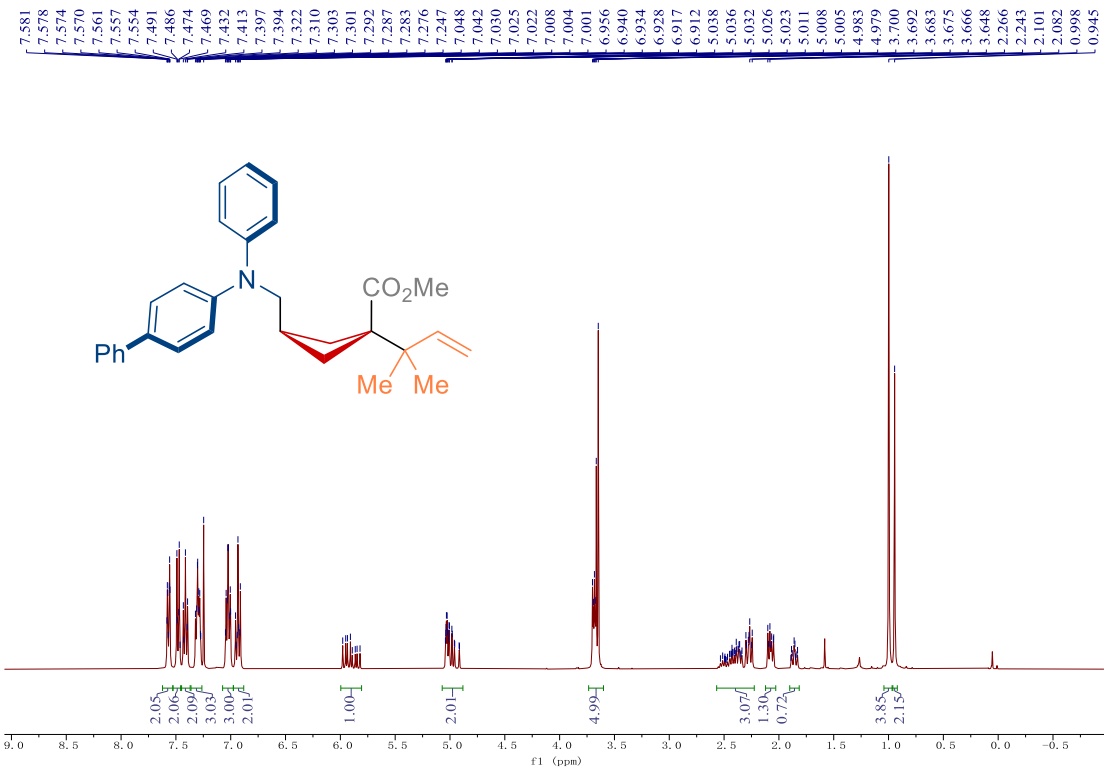
^{13}C NMR of compound **16** (101 MHz, $CDCl_3$)



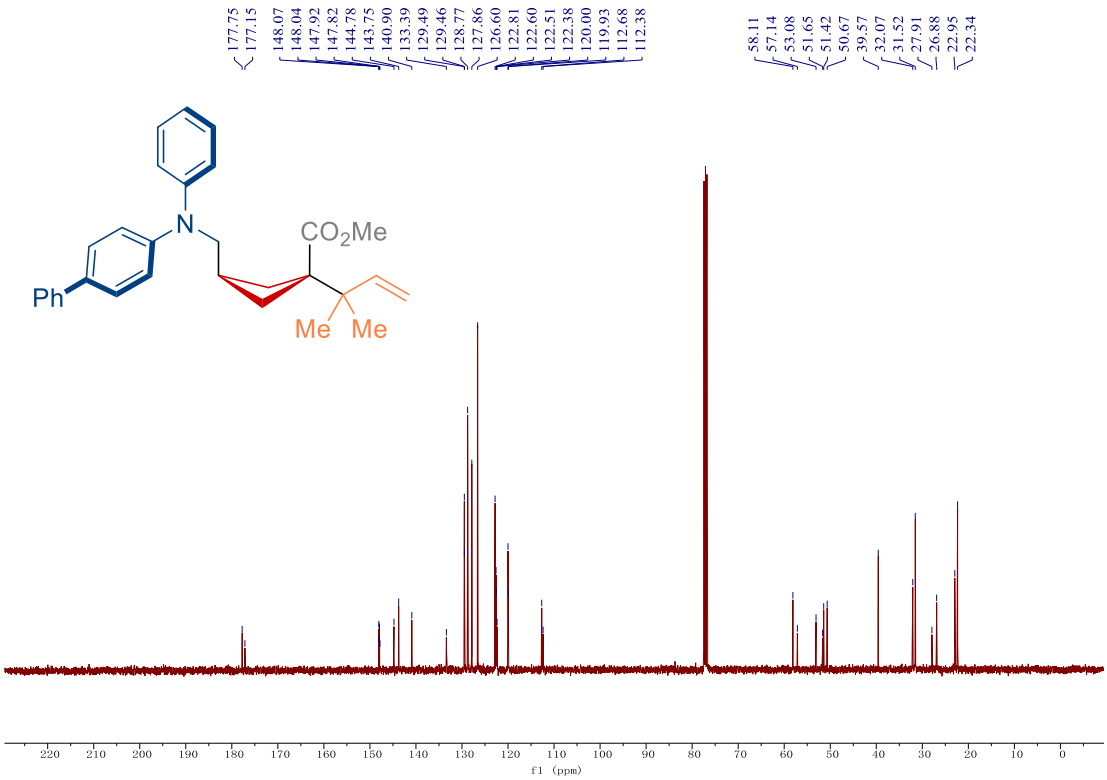
^{1}H NMR of compound **17** (400 MHz, $CDCl_3$)



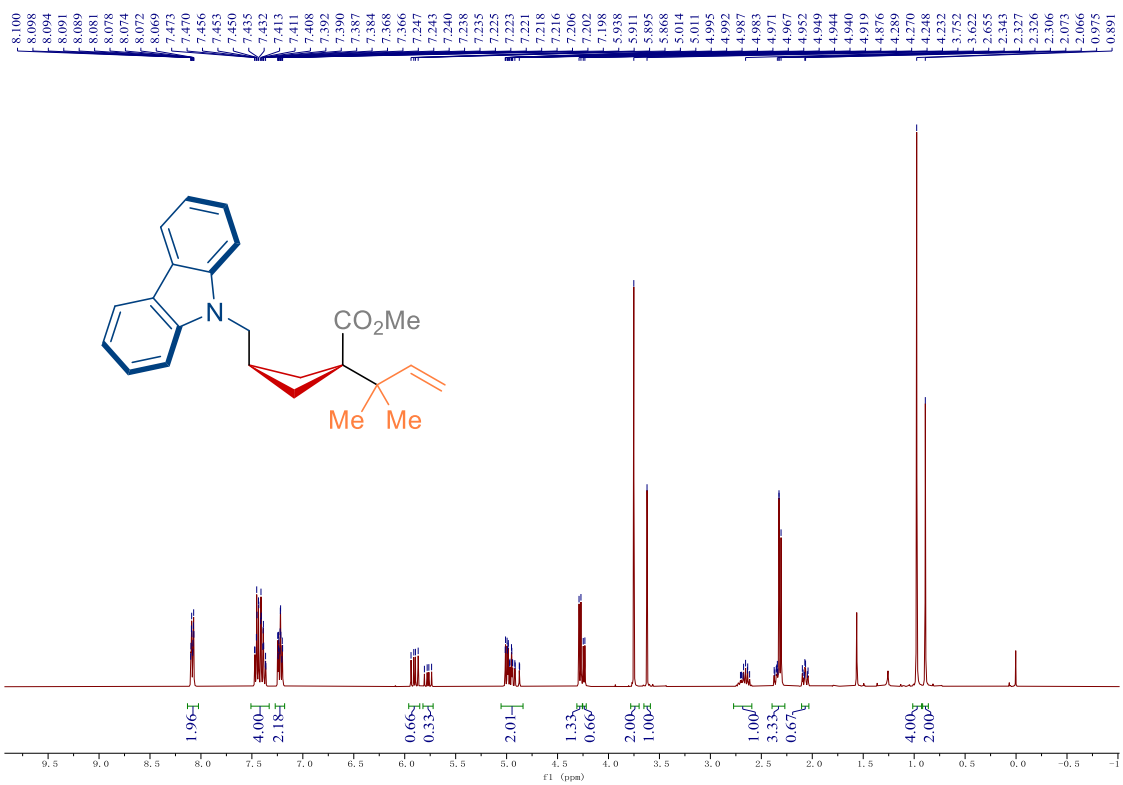
^{13}C NMR of compound **17** (101 MHz, $CDCl_3$)



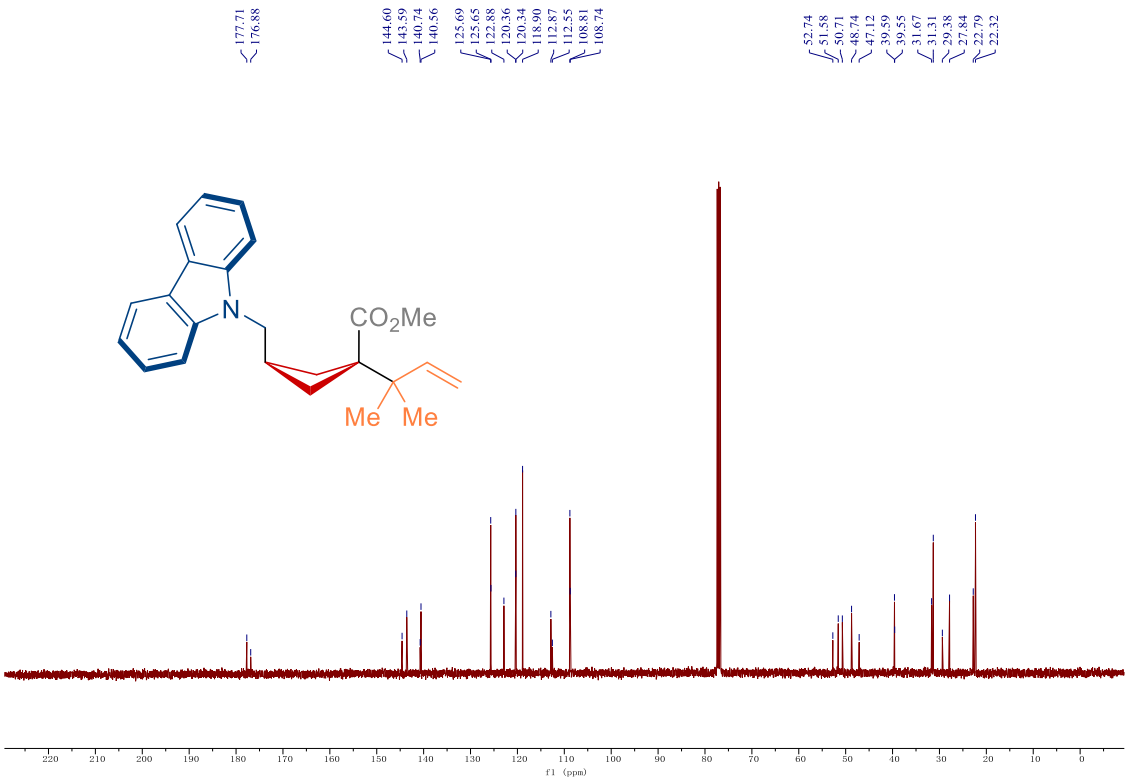
^{1}H NMR of compound **18** (400 MHz, $CDCl_3$)



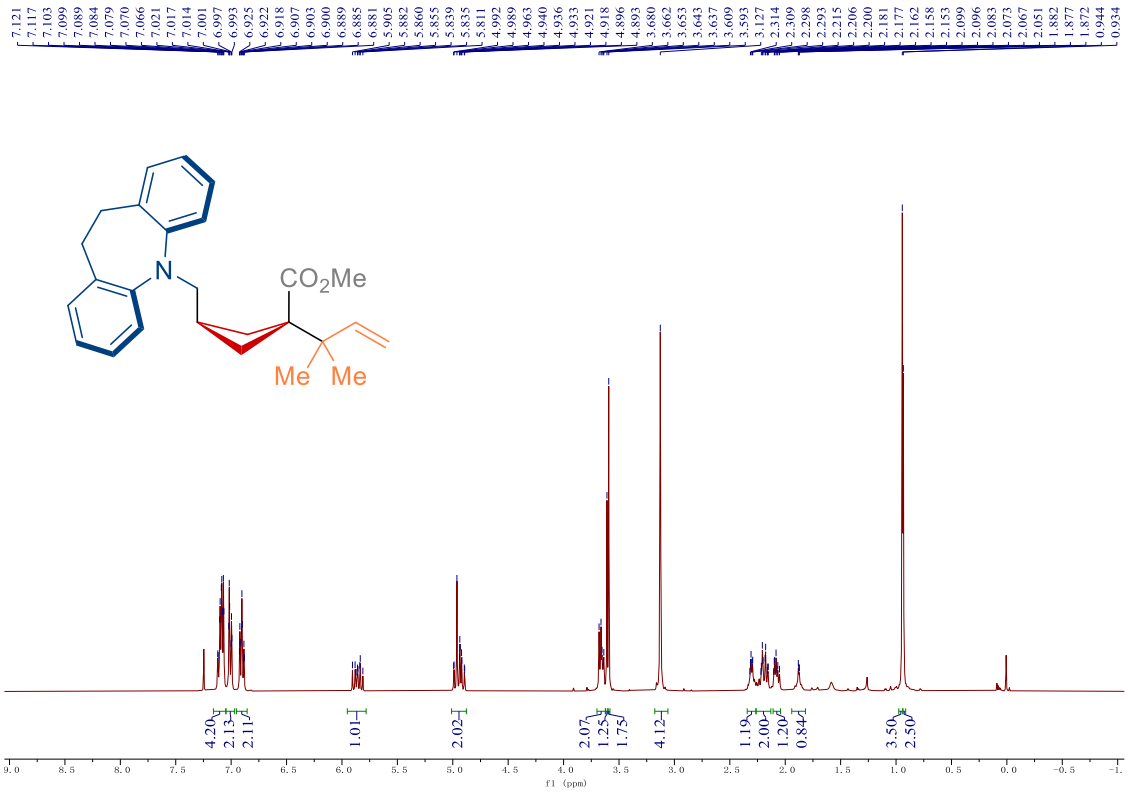
^{13}C NMR of compound **18** (101 MHz, $CDCl_3$)



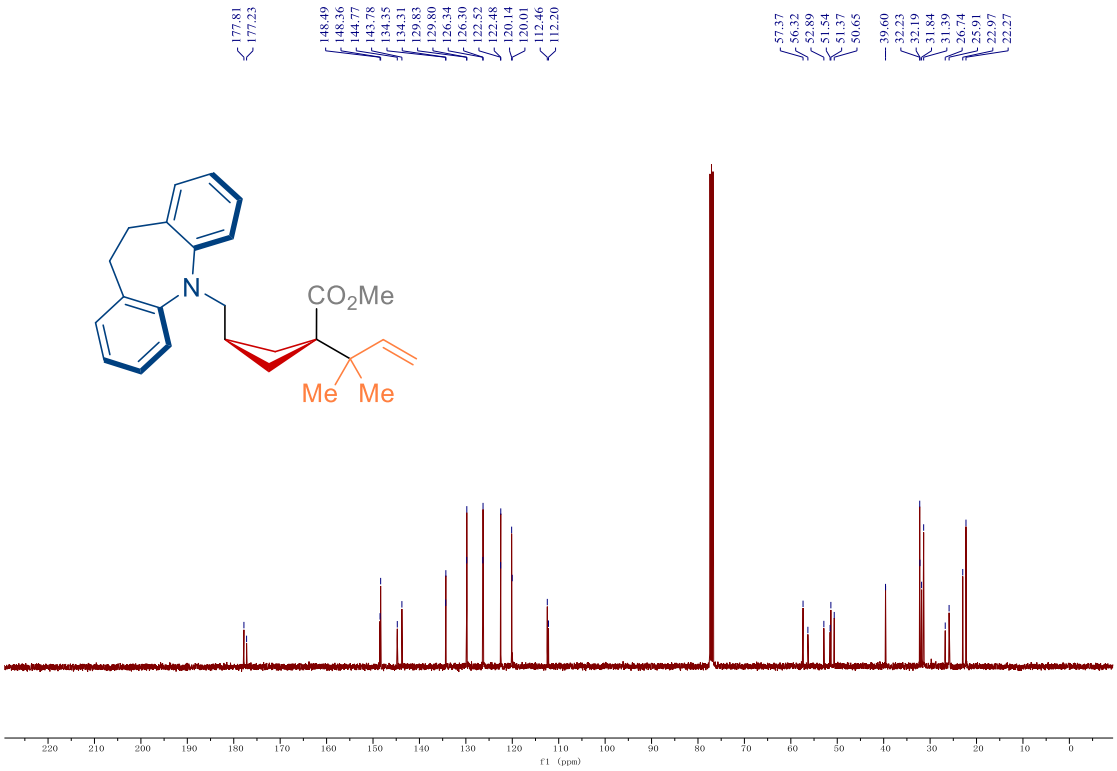
^{1}H NMR of compound **19** (400 MHz, $CDCl_3$)



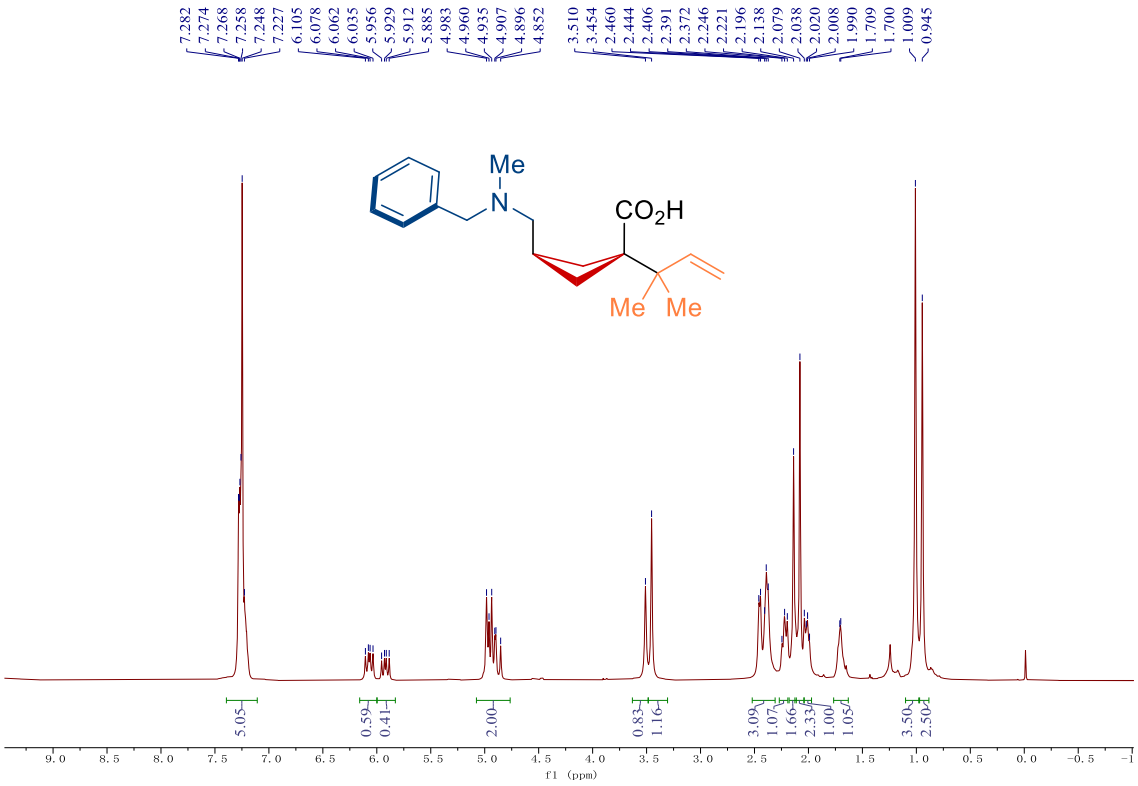
^{13}C NMR of compound **19** (101 MHz, $CDCl_3$)



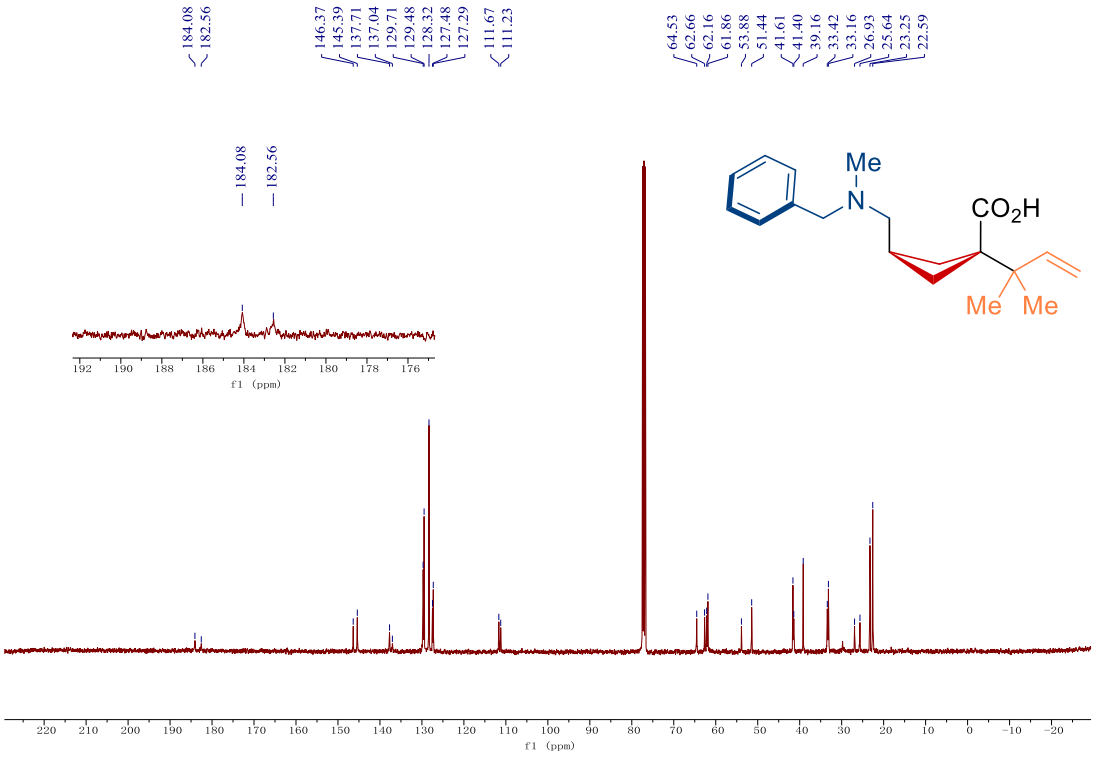
^{1}H NMR of compound **20** (400 MHz, $CDCl_3$)



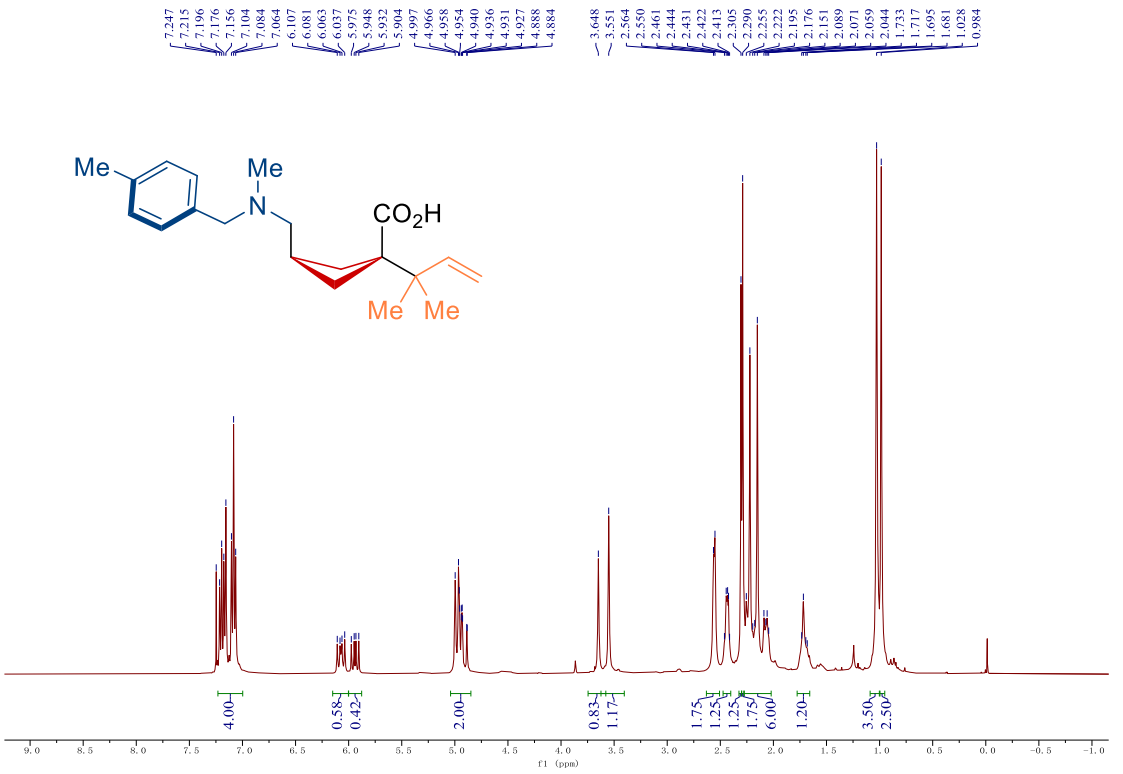
^{13}C NMR of compound **20** (101 MHz, $CDCl_3$)



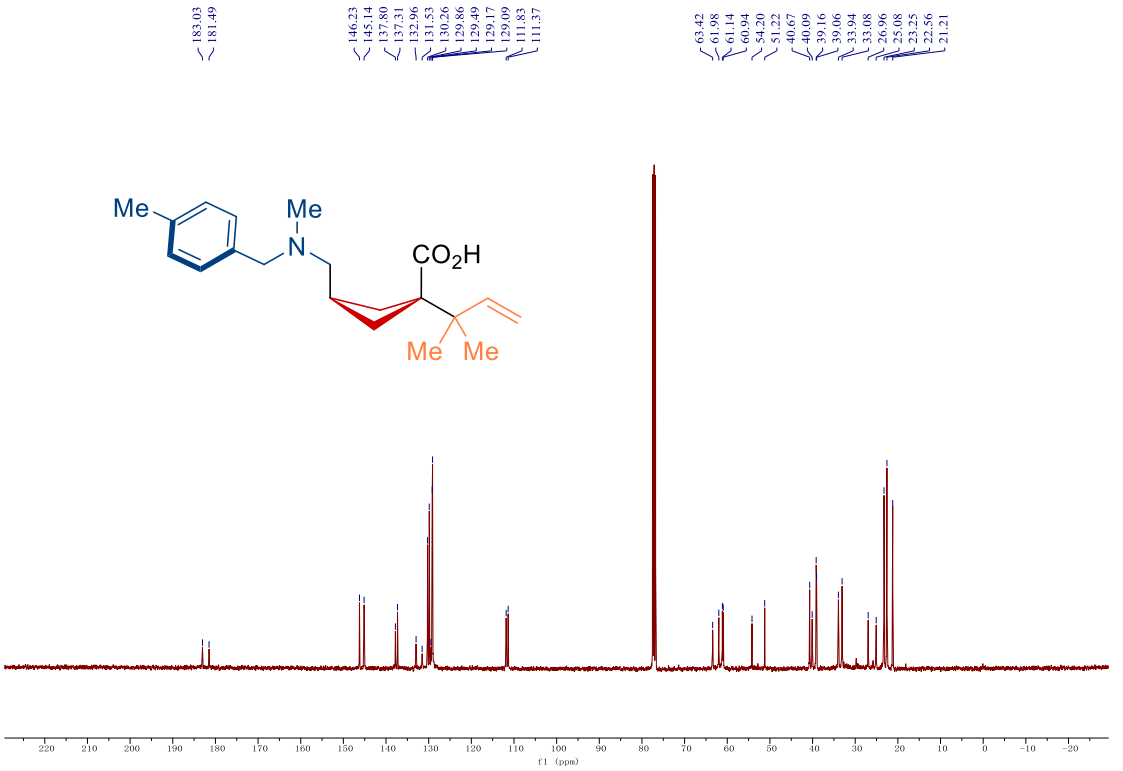
^{1}H NMR of compound **21** (400 MHz, $CDCl_3$)



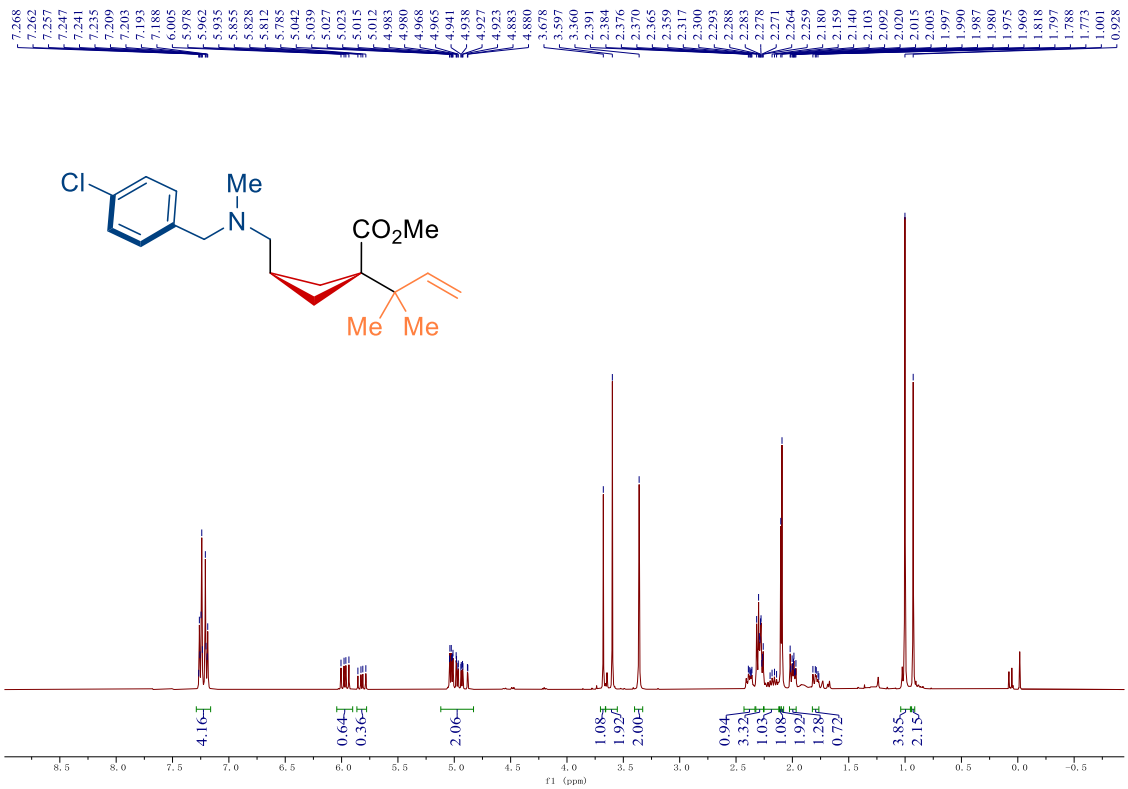
^{13}C NMR of compound **21** (101 MHz, $CDCl_3$)



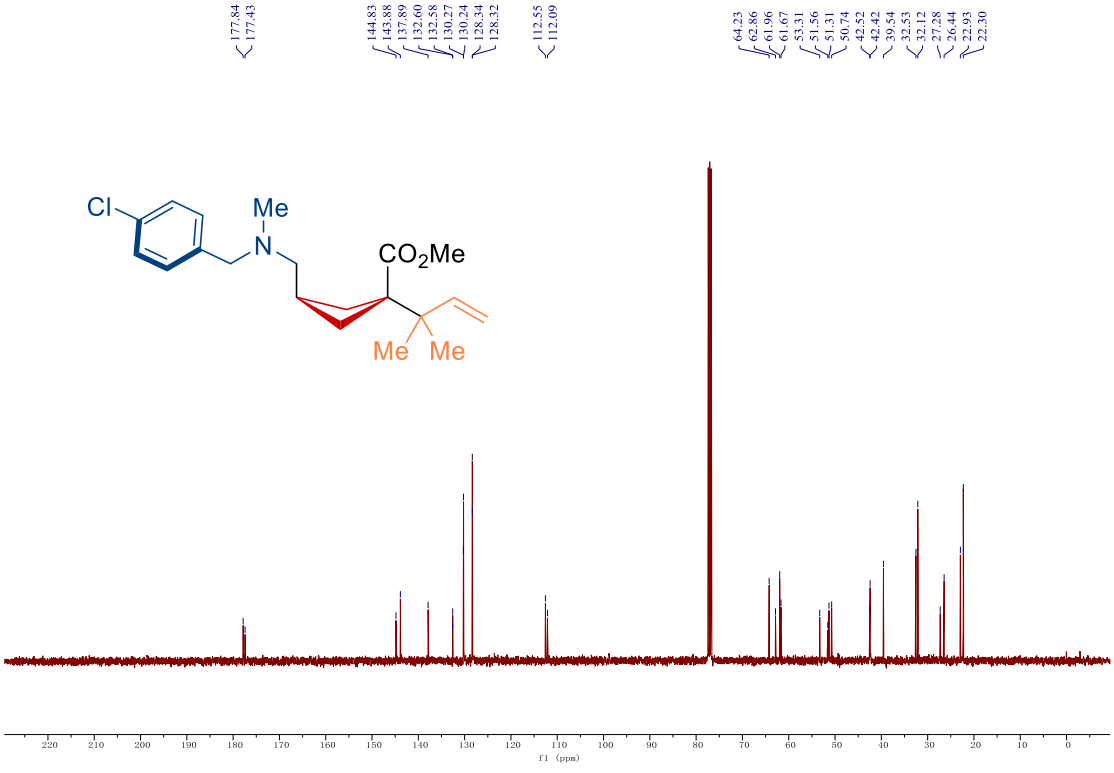
^{1}H NMR of compound **22** (400 MHz, $CDCl_3$)



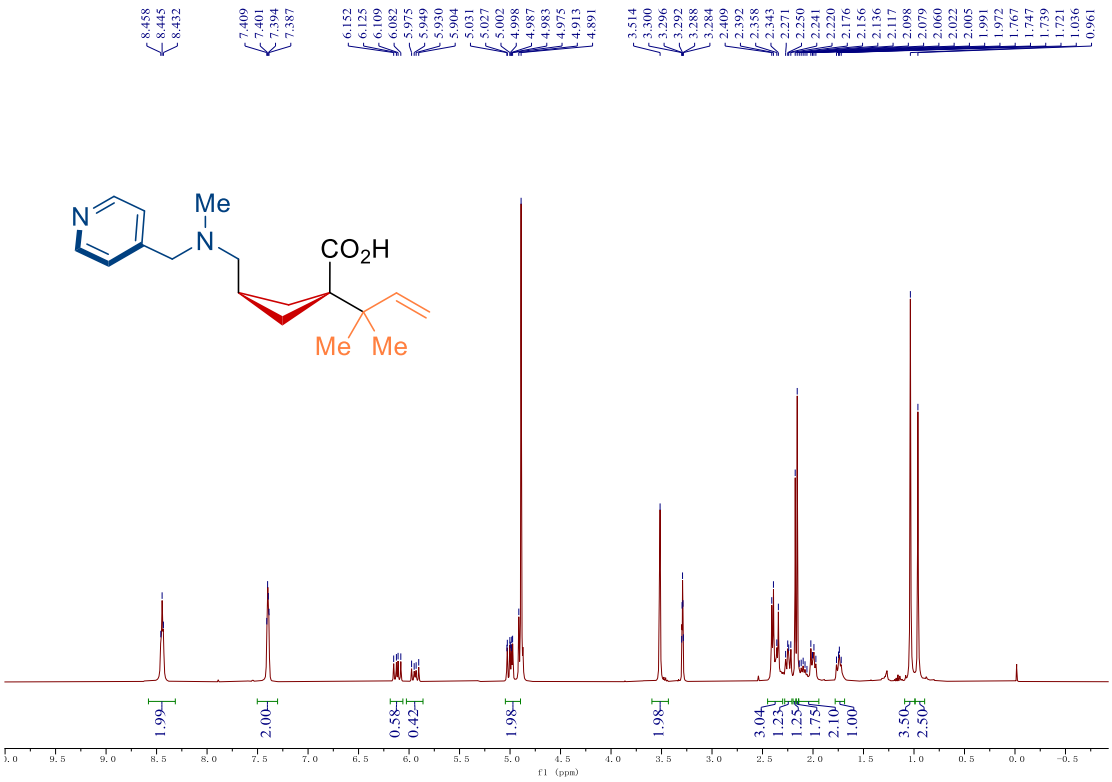
^{13}C NMR of compound **22** (101 MHz, $CDCl_3$)



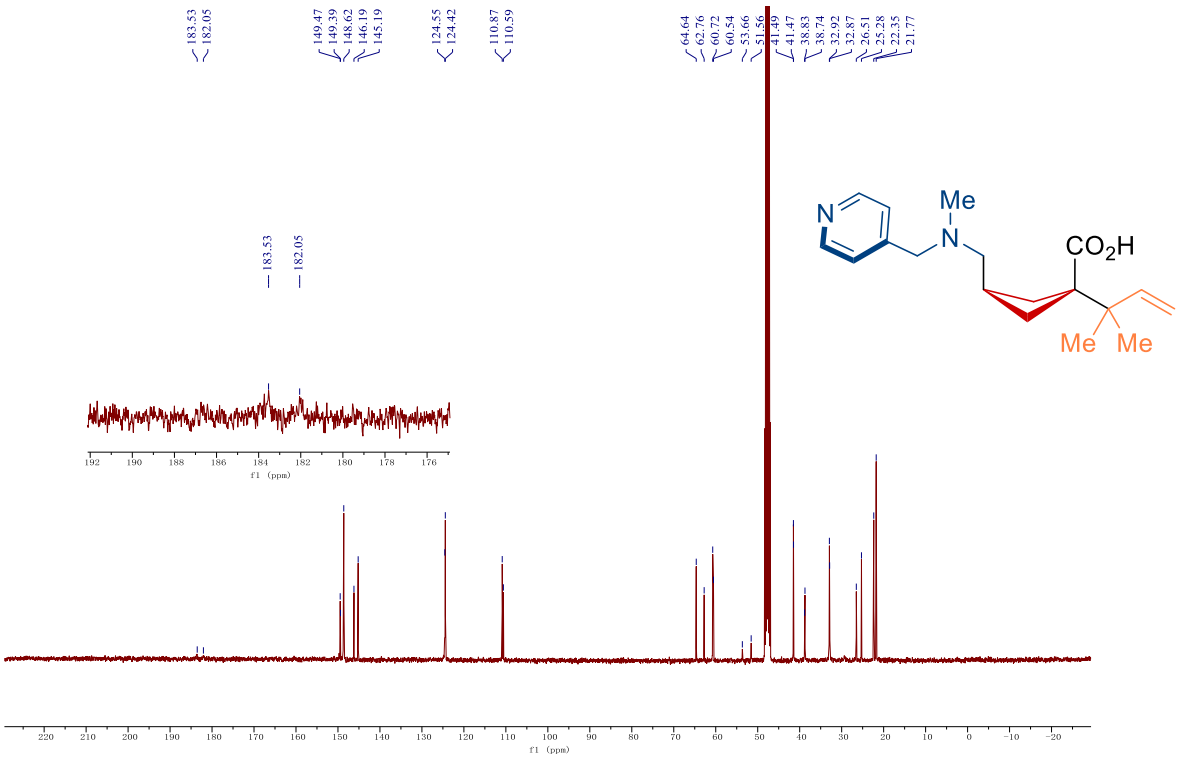
^{1}H NMR of compound **23** (400 MHz, $CDCl_3$)



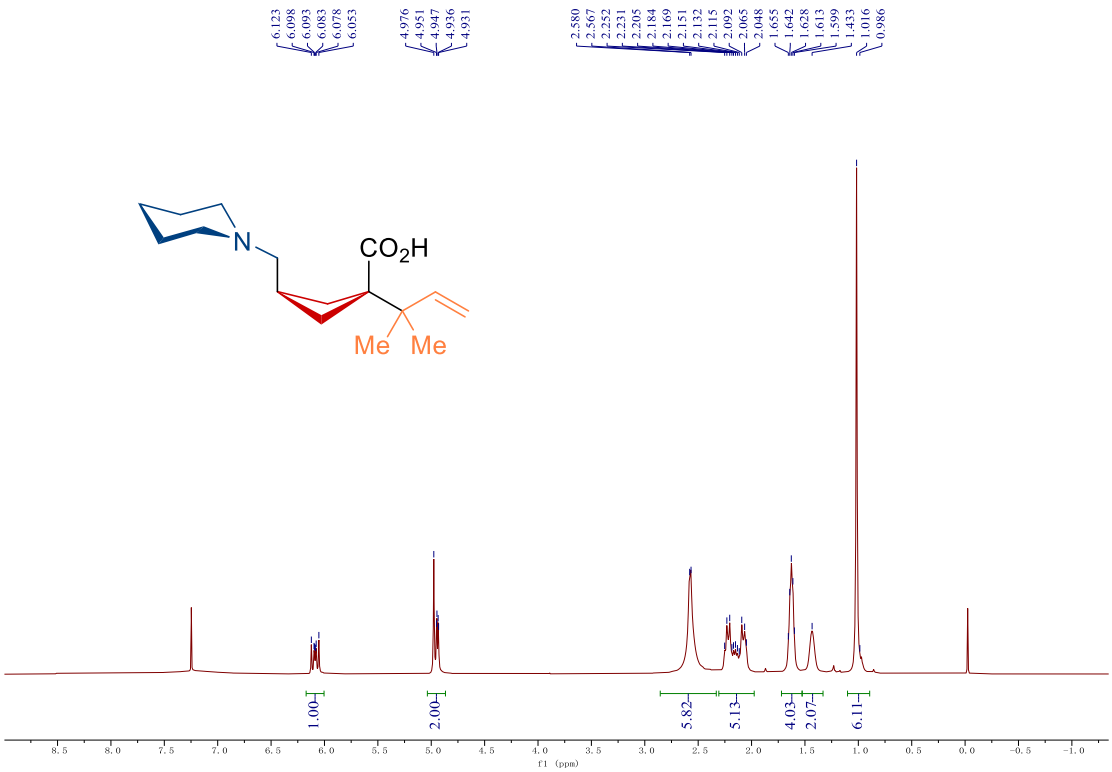
^{13}C NMR of compound **23** (101 MHz, $CDCl_3$)



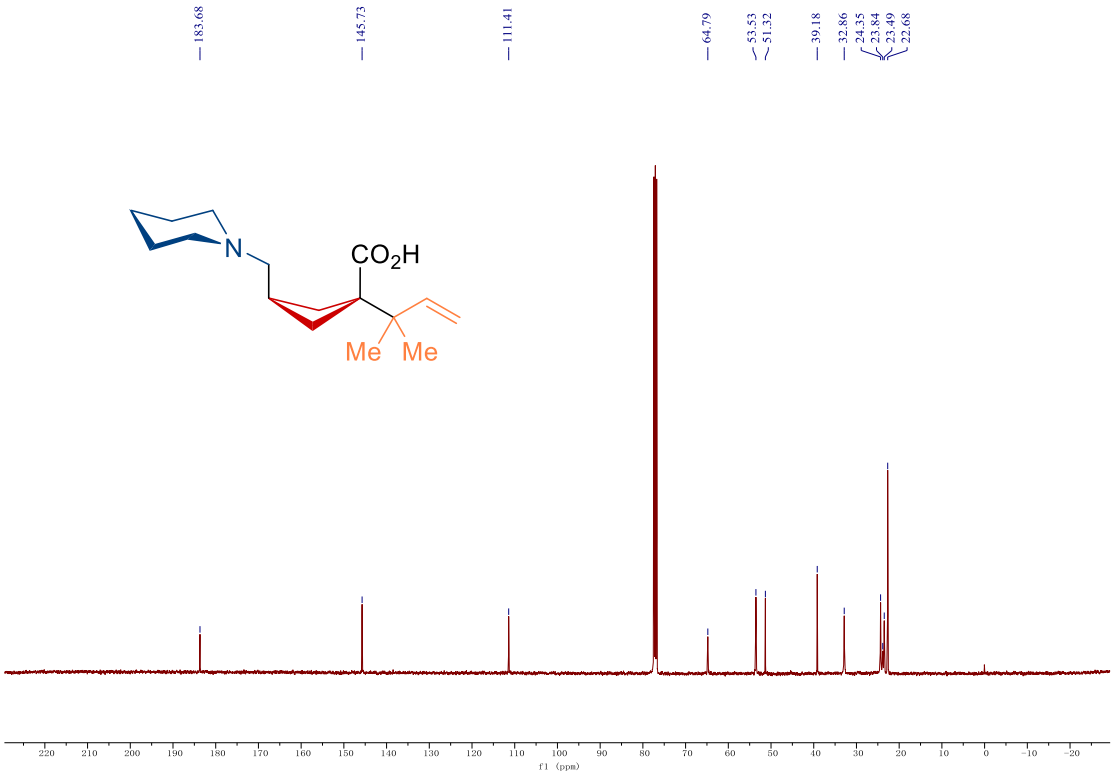
^{1}H NMR of compound **24** (400 MHz, CD_3OD)



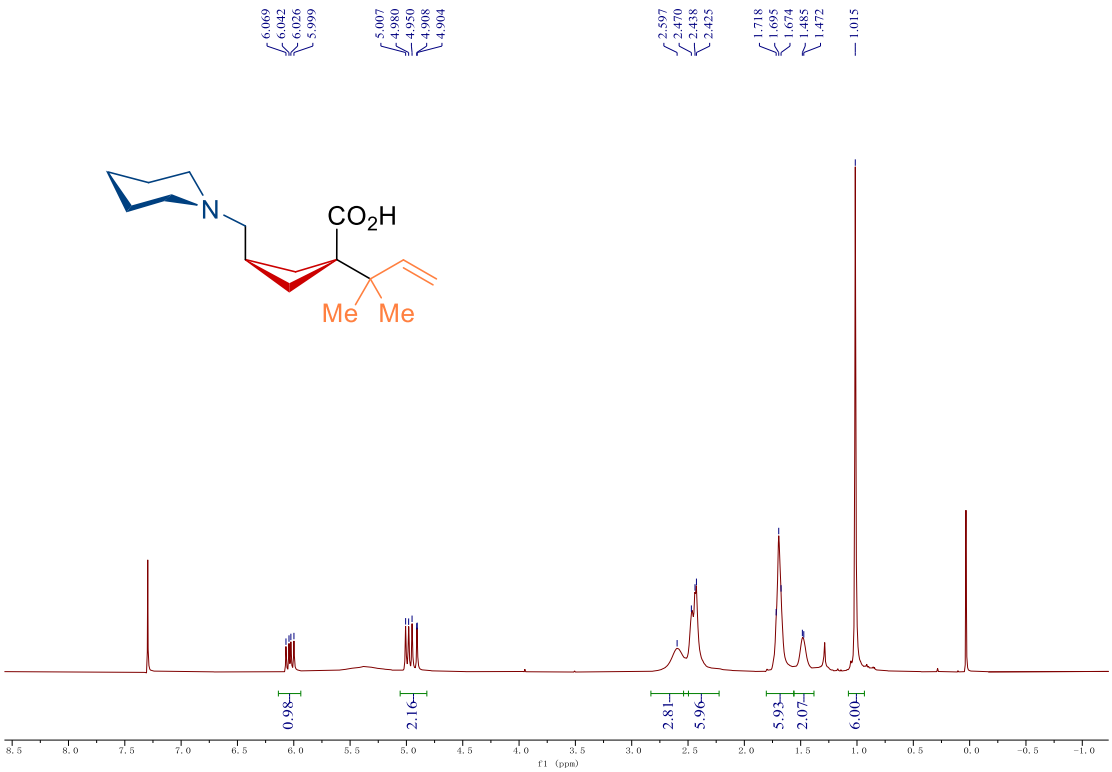
^{13}C NMR of compound **24** (101 MHz, CD_3OD)



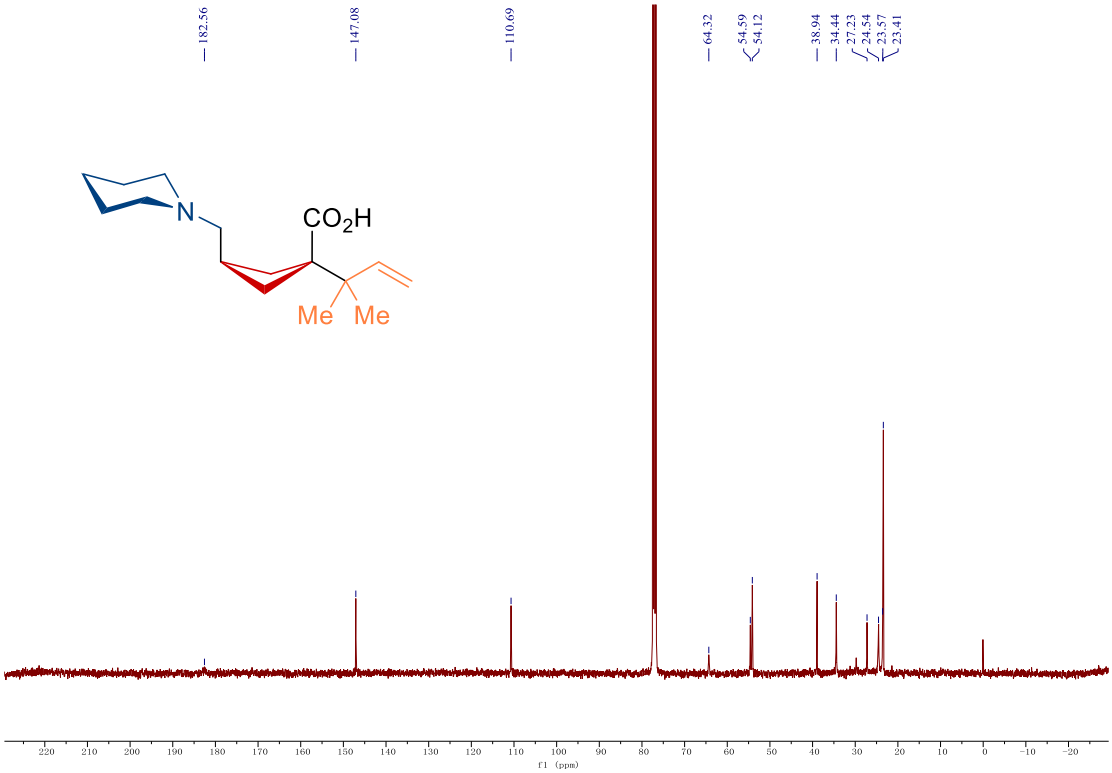
^{1}H NMR of compound **25** (major diastereomer, 400 MHz, $CDCl_3$)



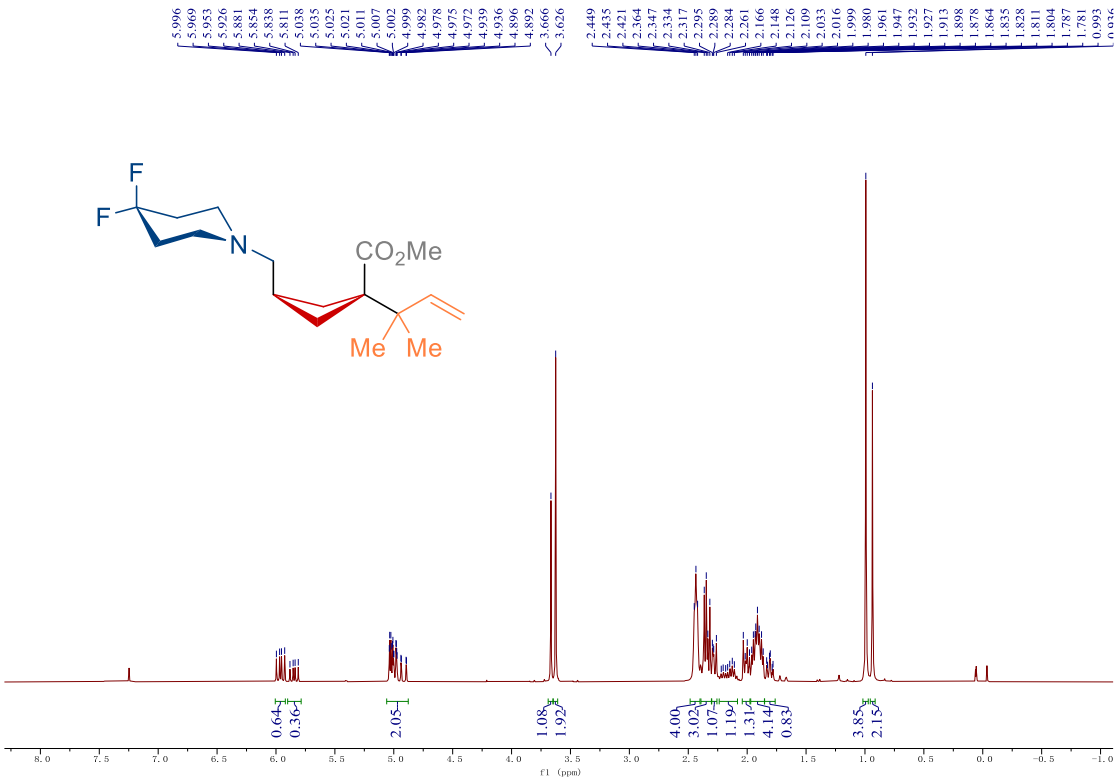
^{13}C NMR of compound **25** (major diastereomer, 101 MHz, $CDCl_3$)



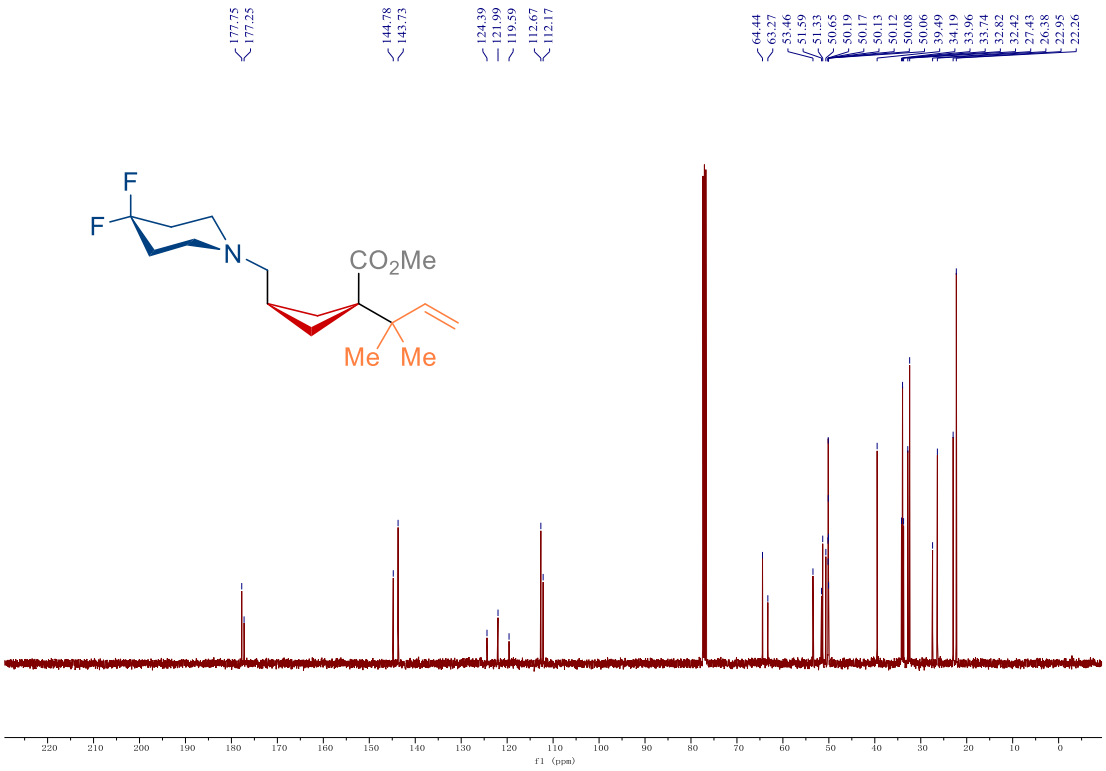
^{1}H NMR of compound **25** (minor diastereomer, 400 MHz, $CDCl_3$)



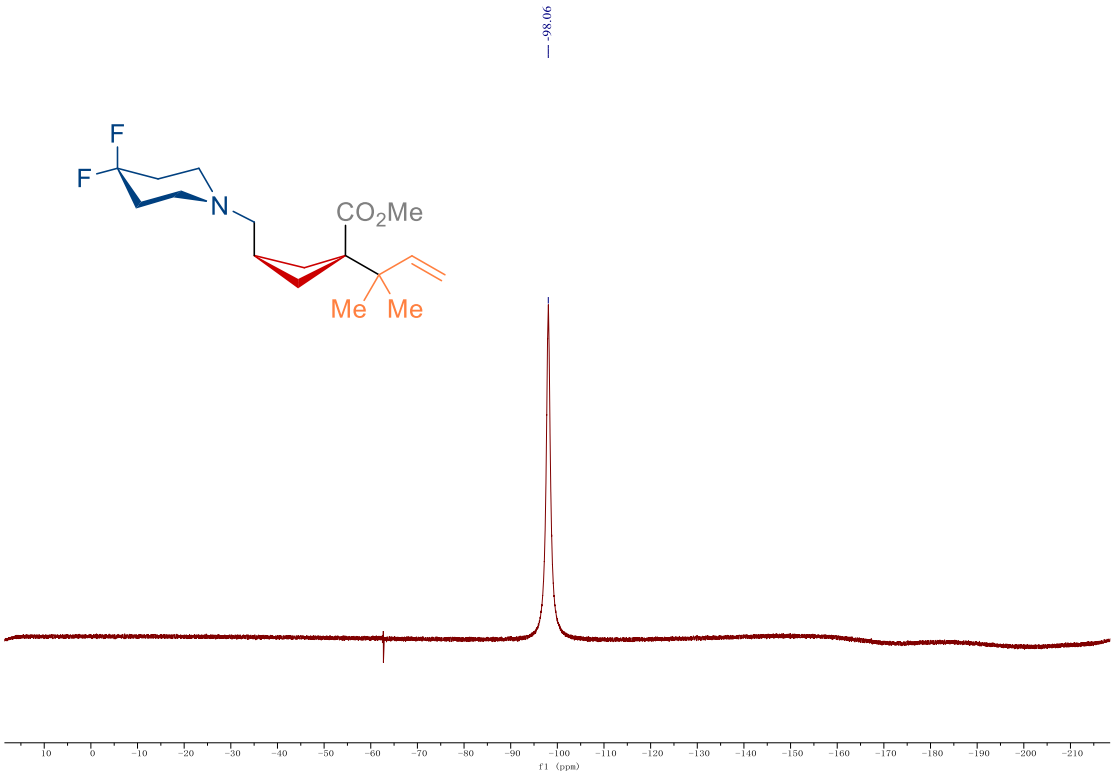
^{13}C NMR of compound **25** (minor diastereomer, 101 MHz, $CDCl_3$)



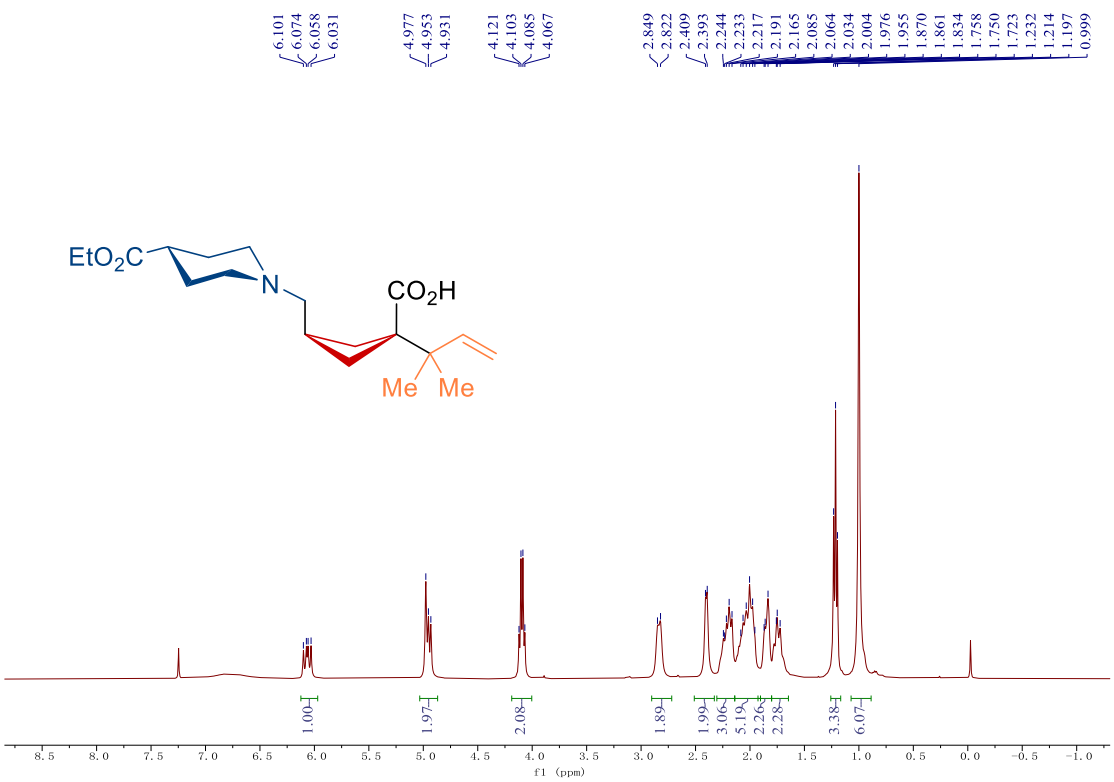
^{1}H NMR of compound **26** (400 MHz, $CDCl_3$)



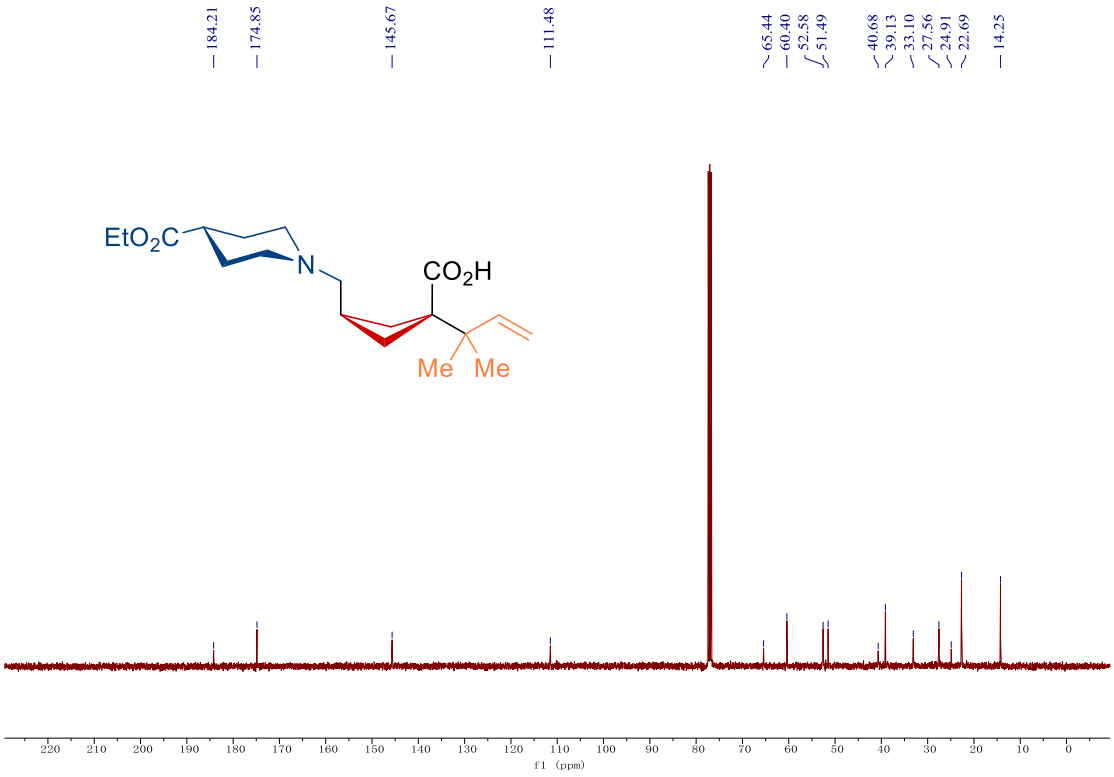
^{13}C NMR of compound **26** (101 MHz, $CDCl_3$)



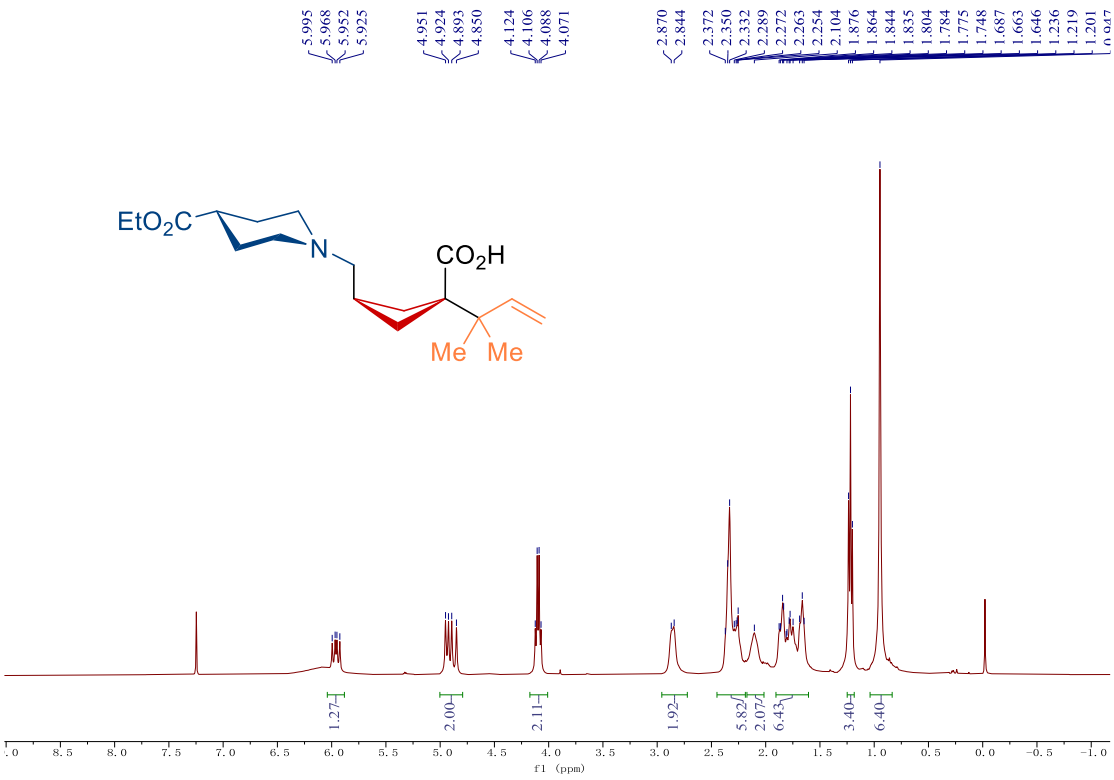
^{19}F NMR of compound **26** (376 MHz, $CDCl_3$)



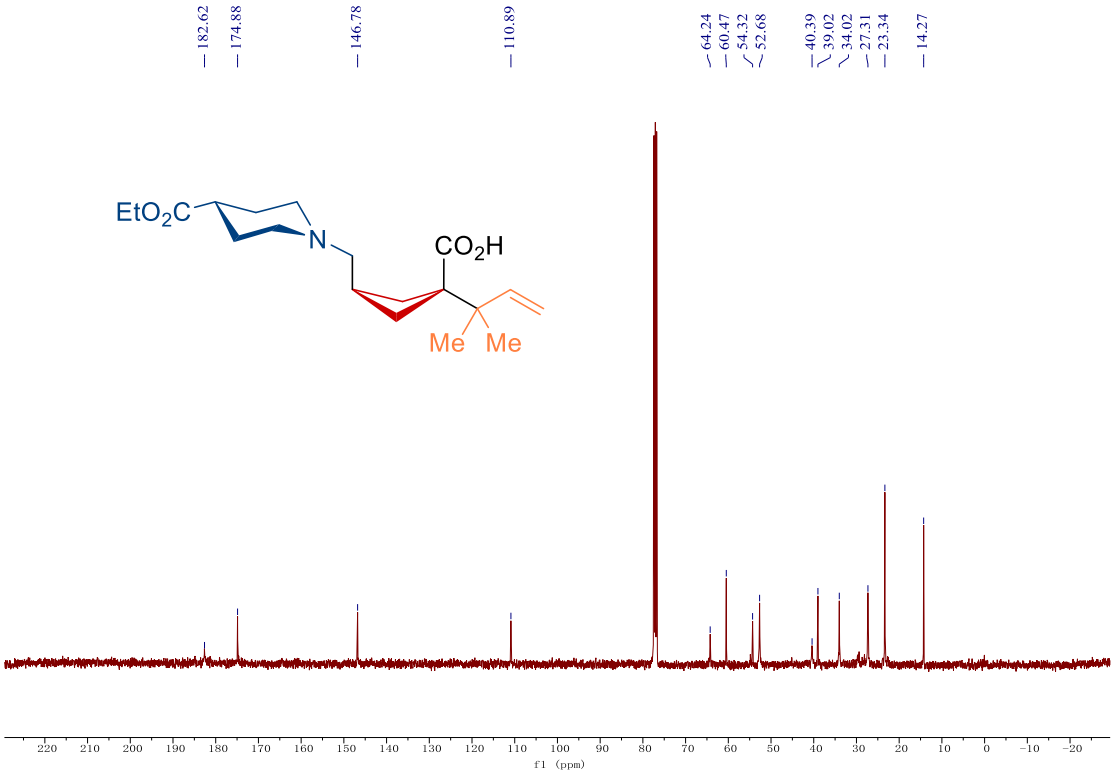
^{1}H NMR of compound **27** (major diastereomer, 400 MHz, $CDCl_3$)



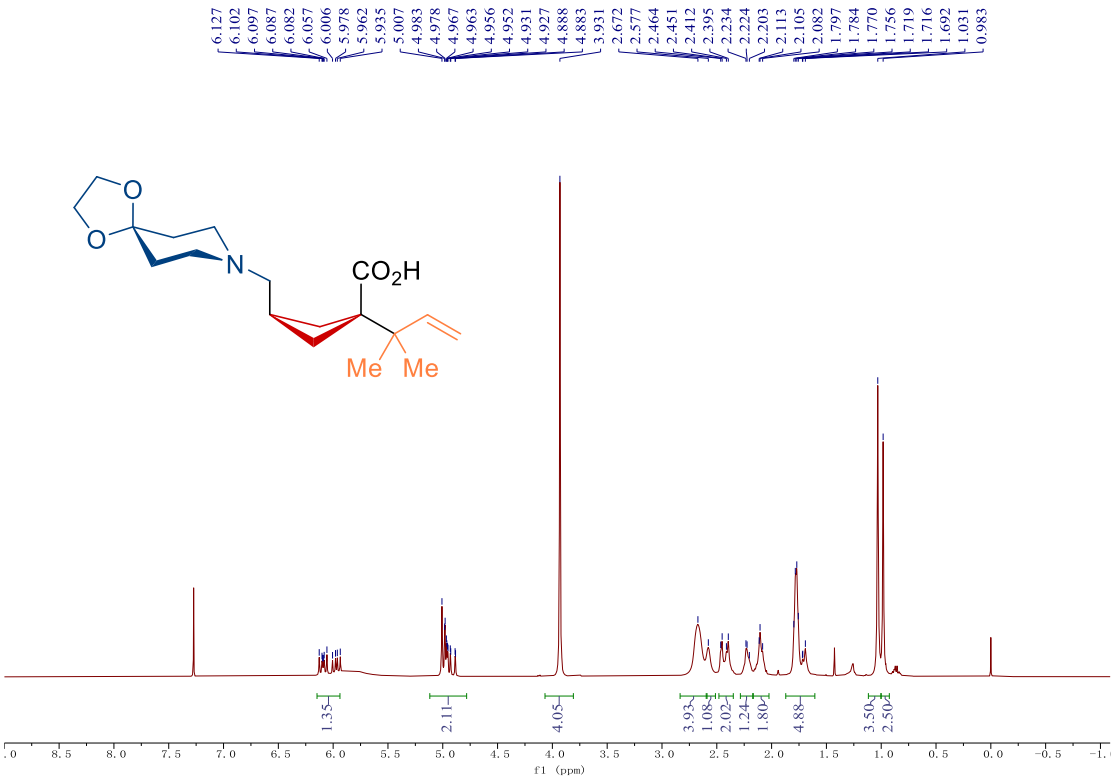
^{13}C NMR of compound **27** (major diastereomer, 101 MHz, $CDCl_3$)



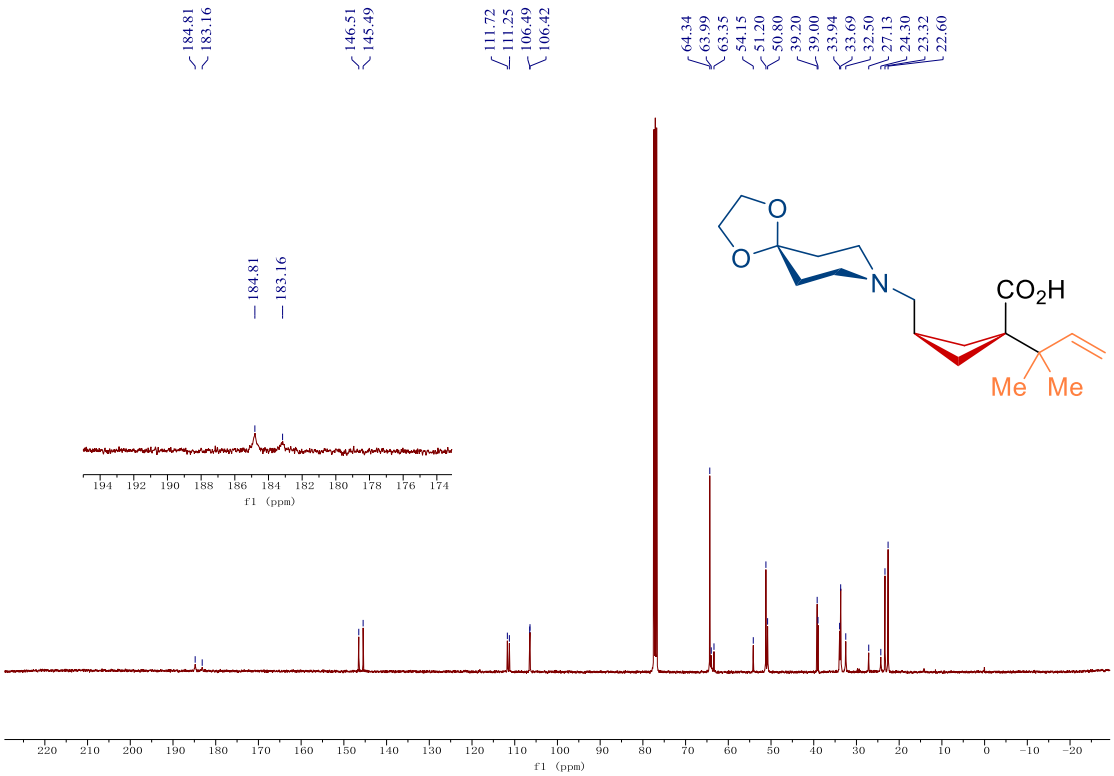
^{1}H NMR of compound **27** (minor diastereomer, 400 MHz, $CDCl_3$)



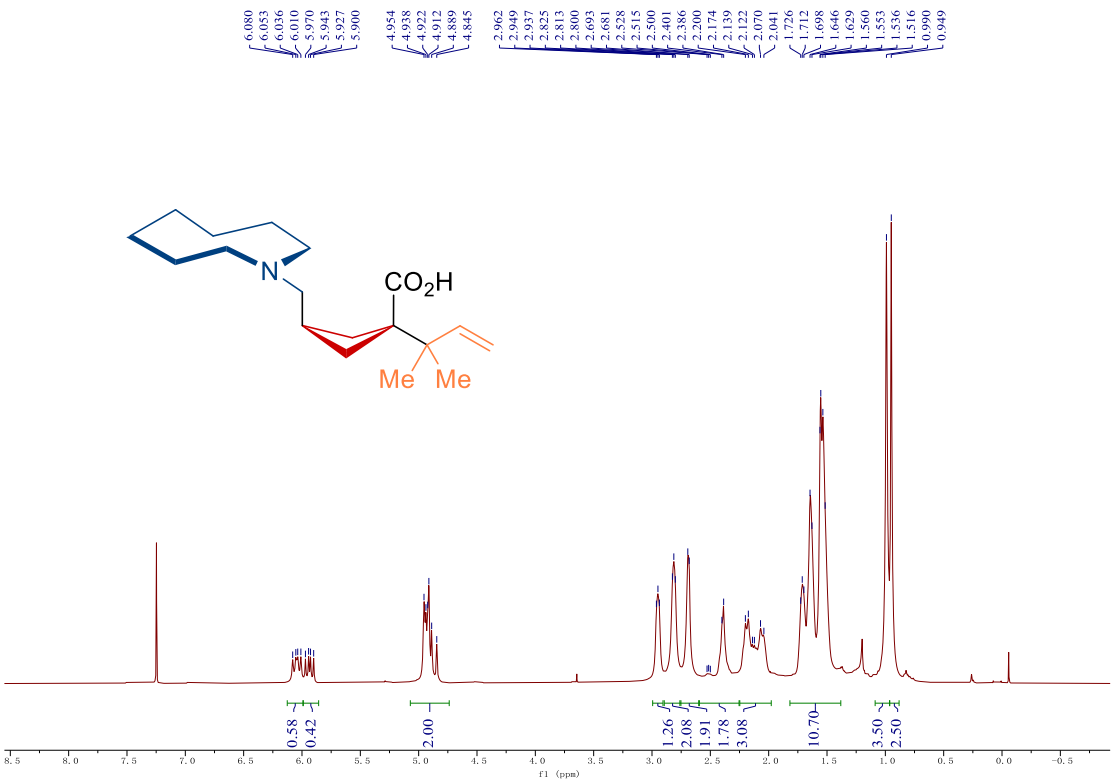
^{13}C NMR of compound **27** (minor diastereomer, 101 MHz, $CDCl_3$)



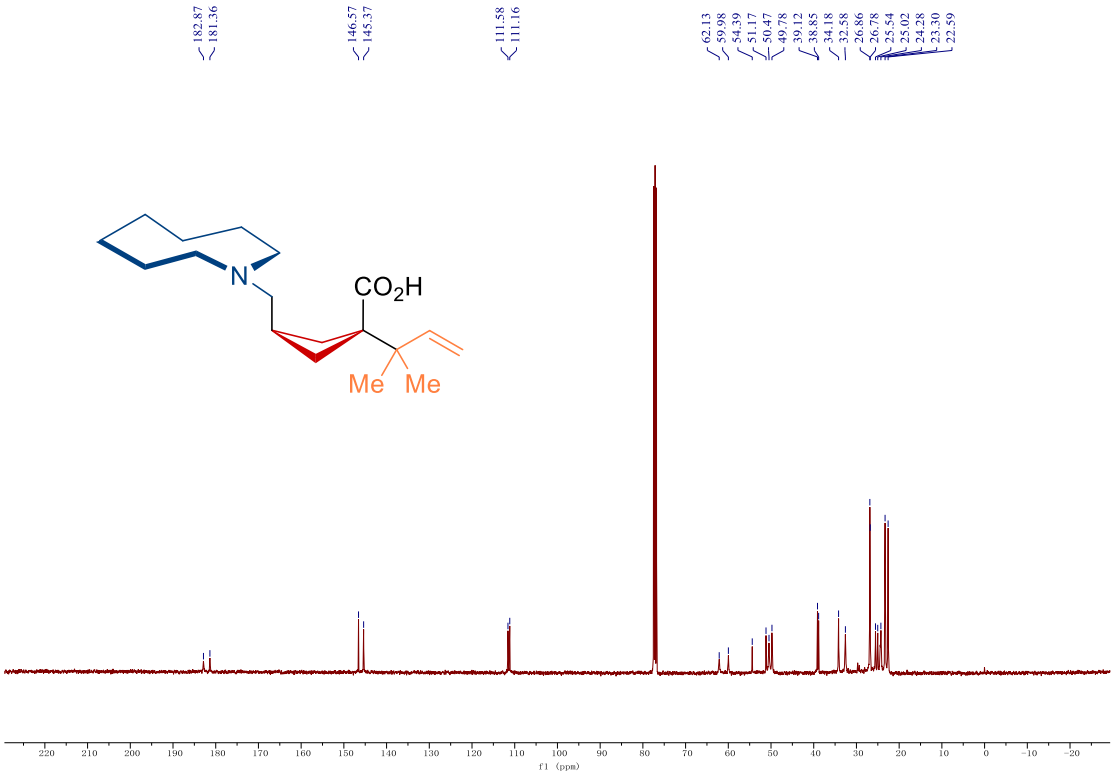
^{1}H NMR of compound **28** (400 MHz, $CDCl_3$)



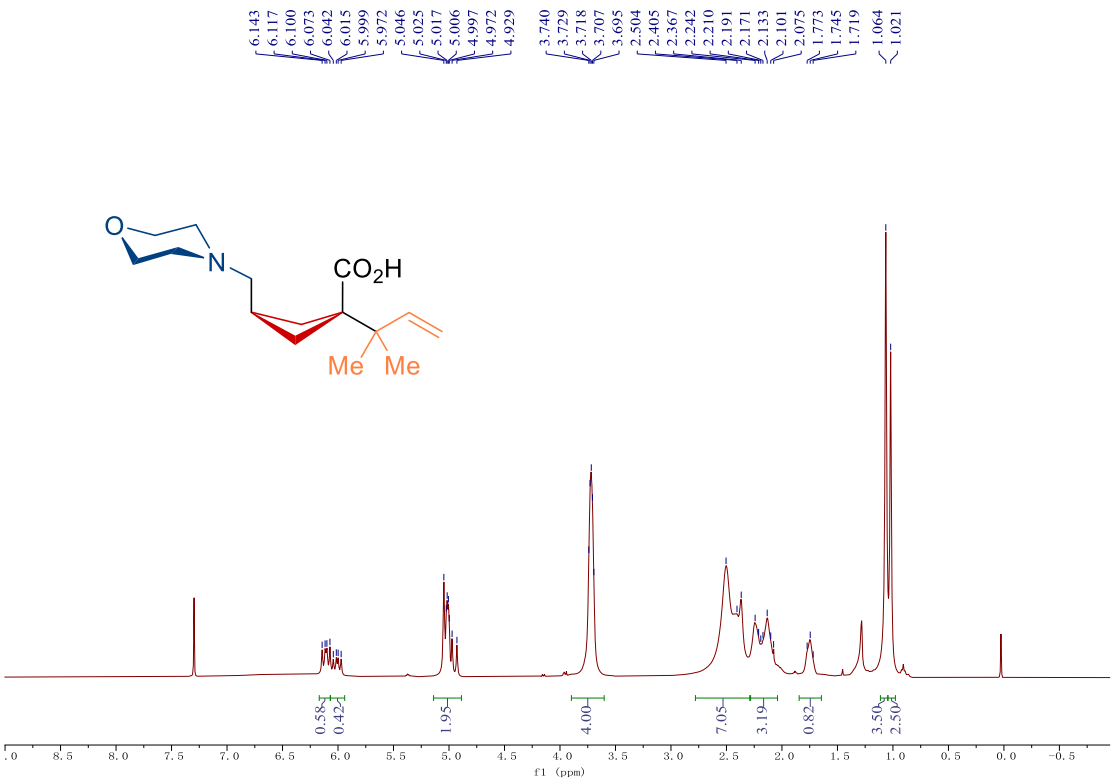
^{13}C NMR of compound **28** (101 MHz, $CDCl_3$)



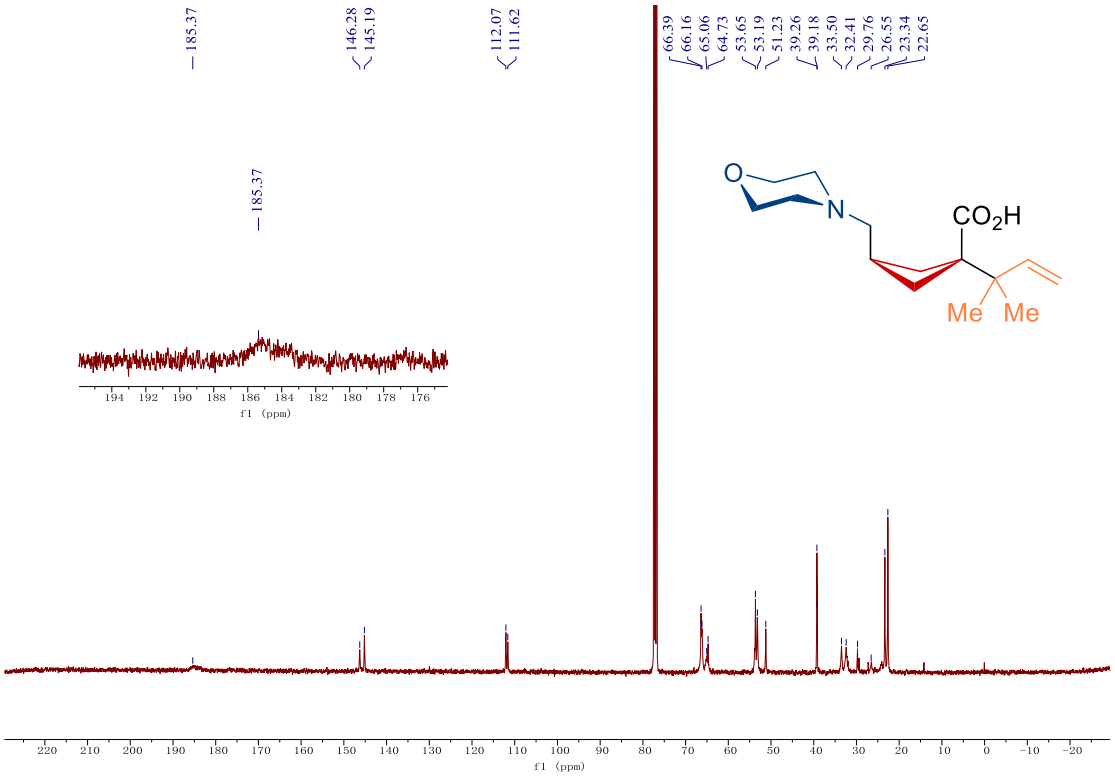
^{1}H NMR of compound **29** (400 MHz, $CDCl_3$)



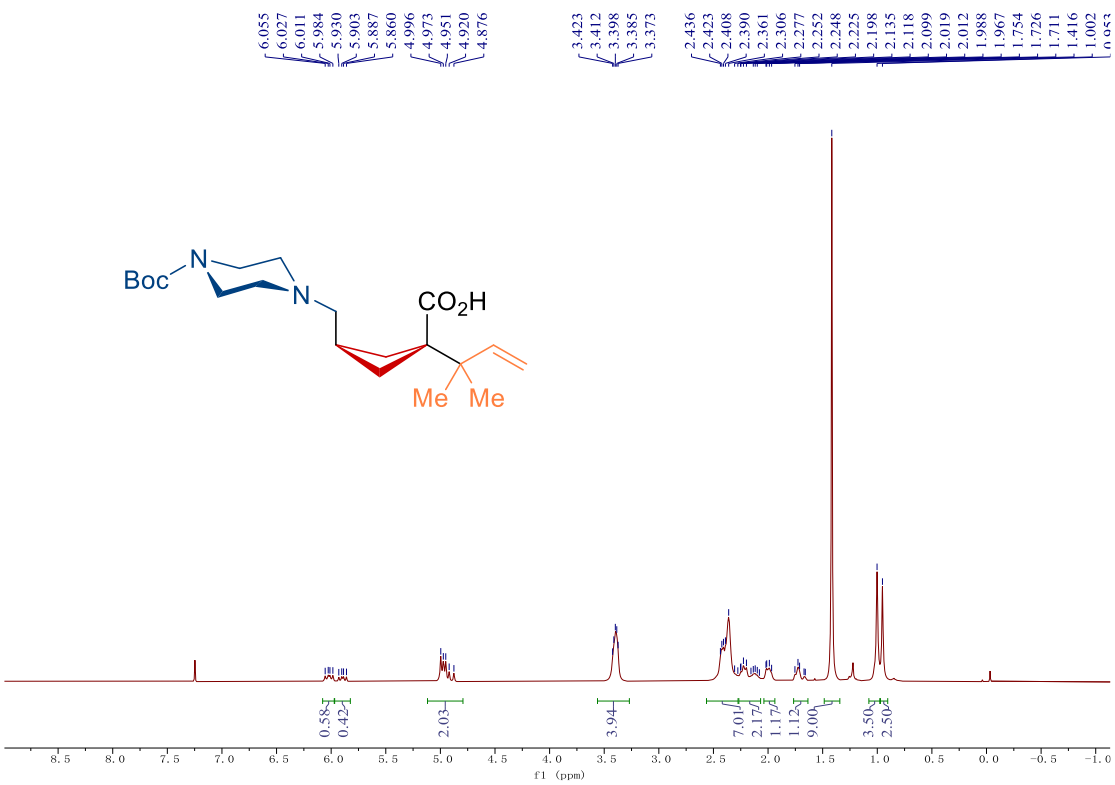
^{13}C NMR of compound **29** (101 MHz, $CDCl_3$)



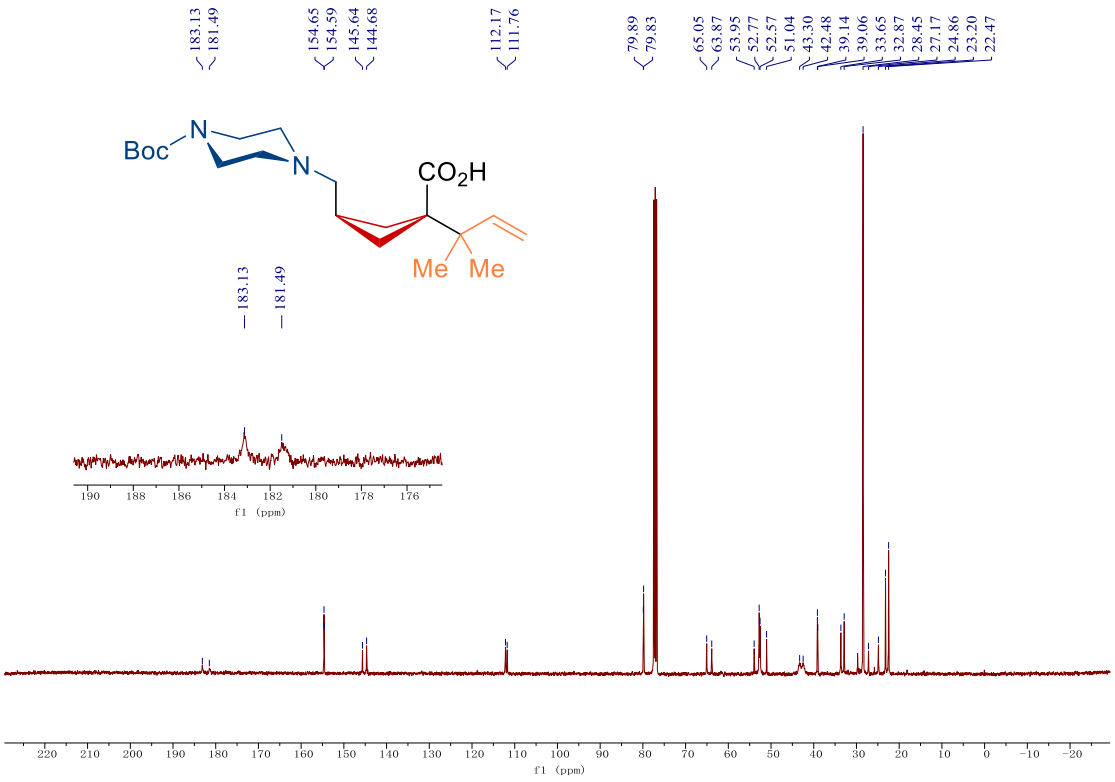
^{1}H NMR of compound **30** (400 MHz, $CDCl_3$)



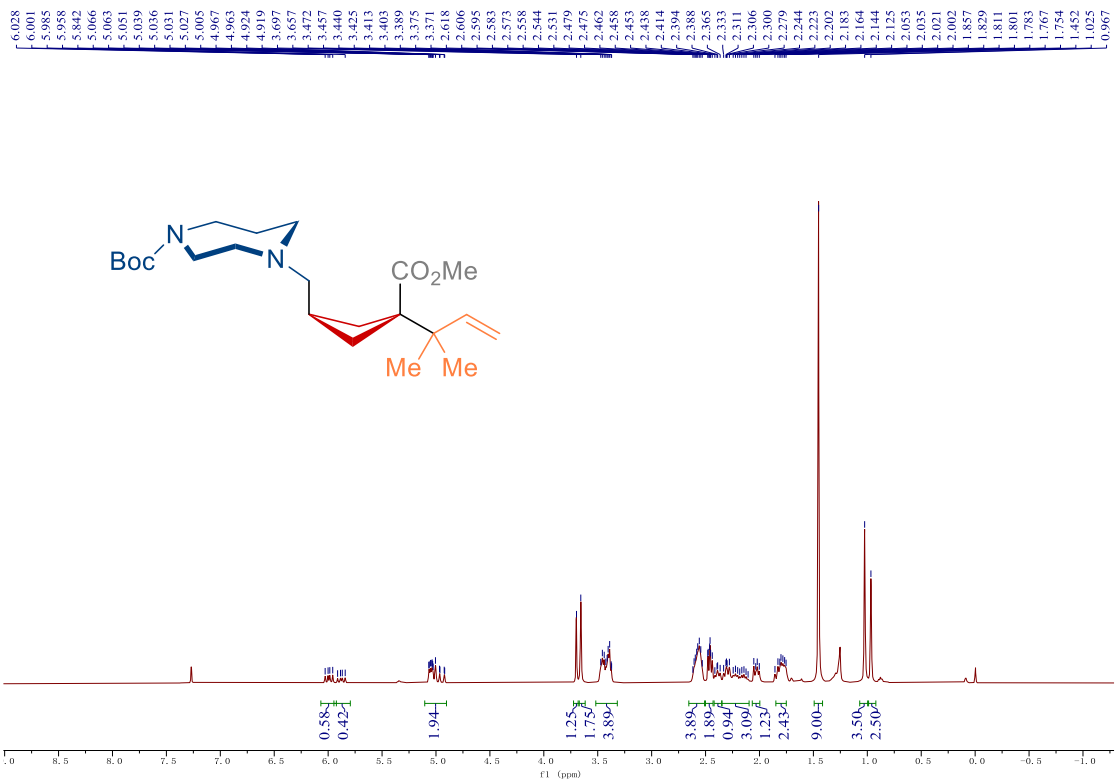
^{13}C NMR of compound **30** (101 MHz, $CDCl_3$)



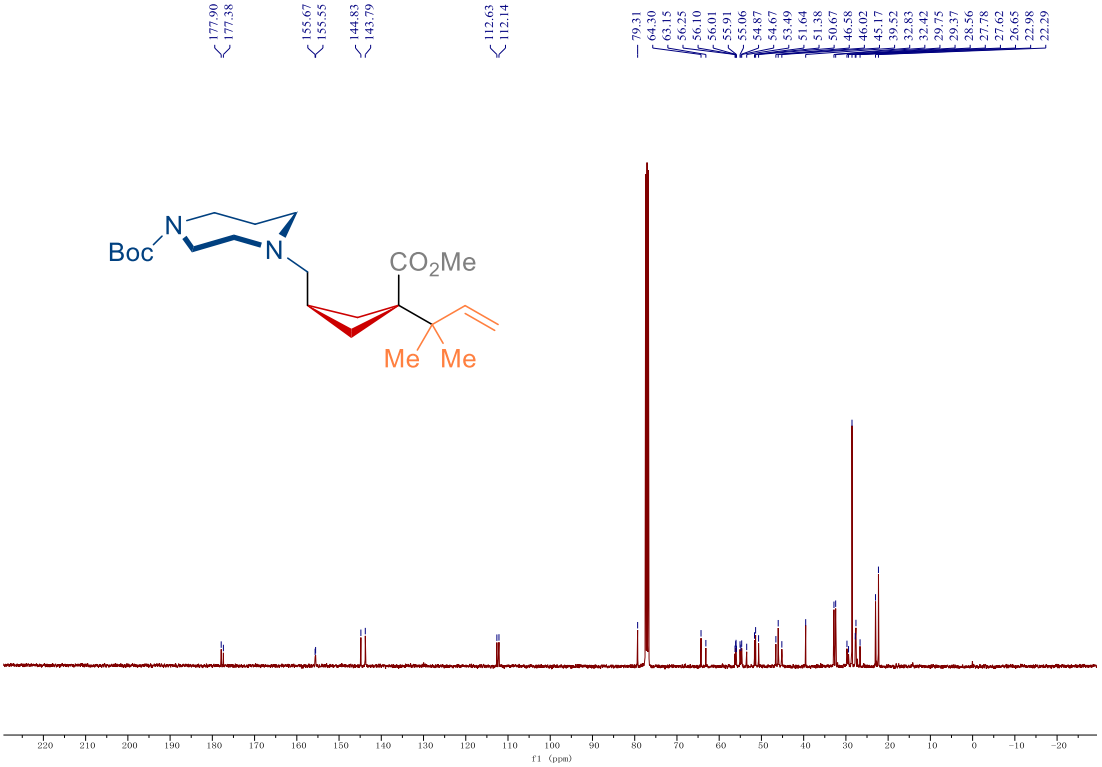
^{1}H NMR of compound **31** (400 MHz, $CDCl_3$)



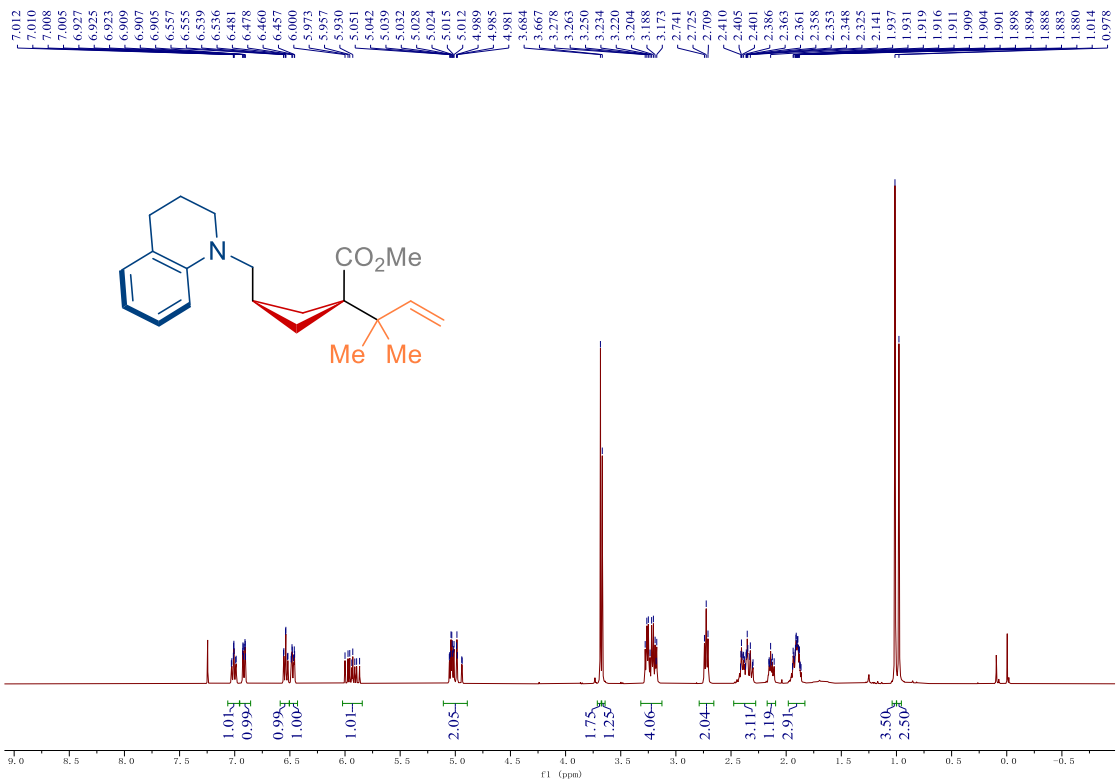
^{13}C NMR of compound **31** (101 MHz, $CDCl_3$)



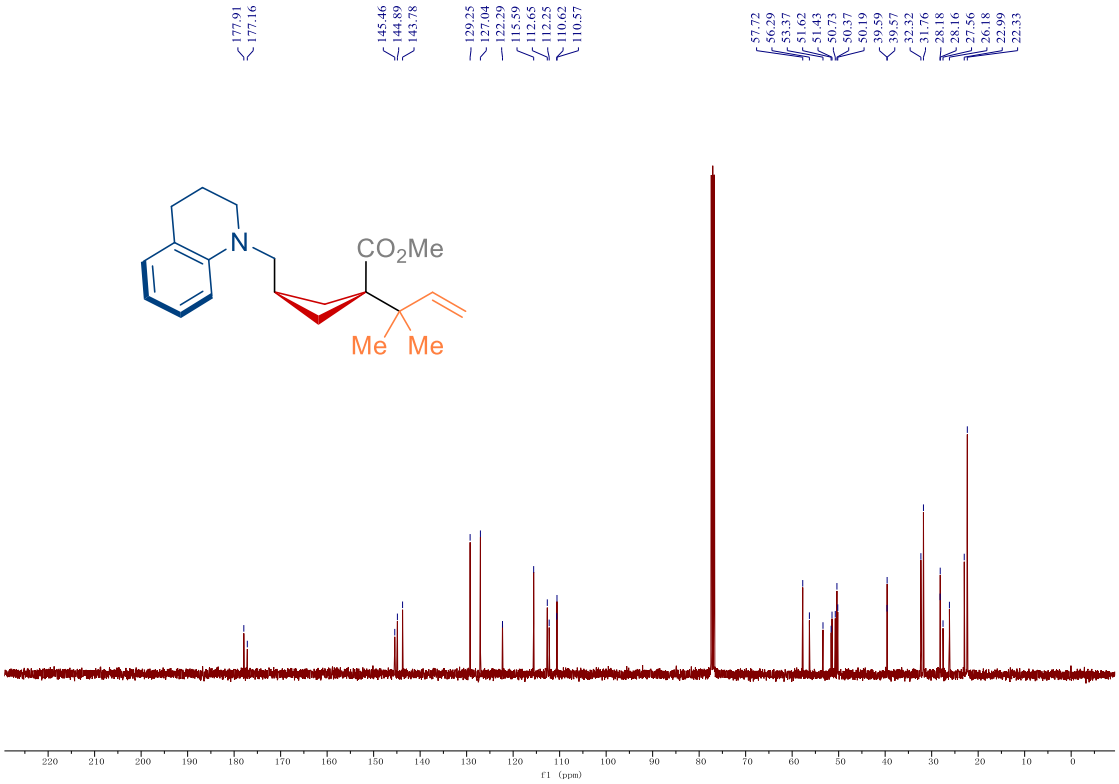
^{1}H NMR of compound **32** (400 MHz, $CDCl_3$)



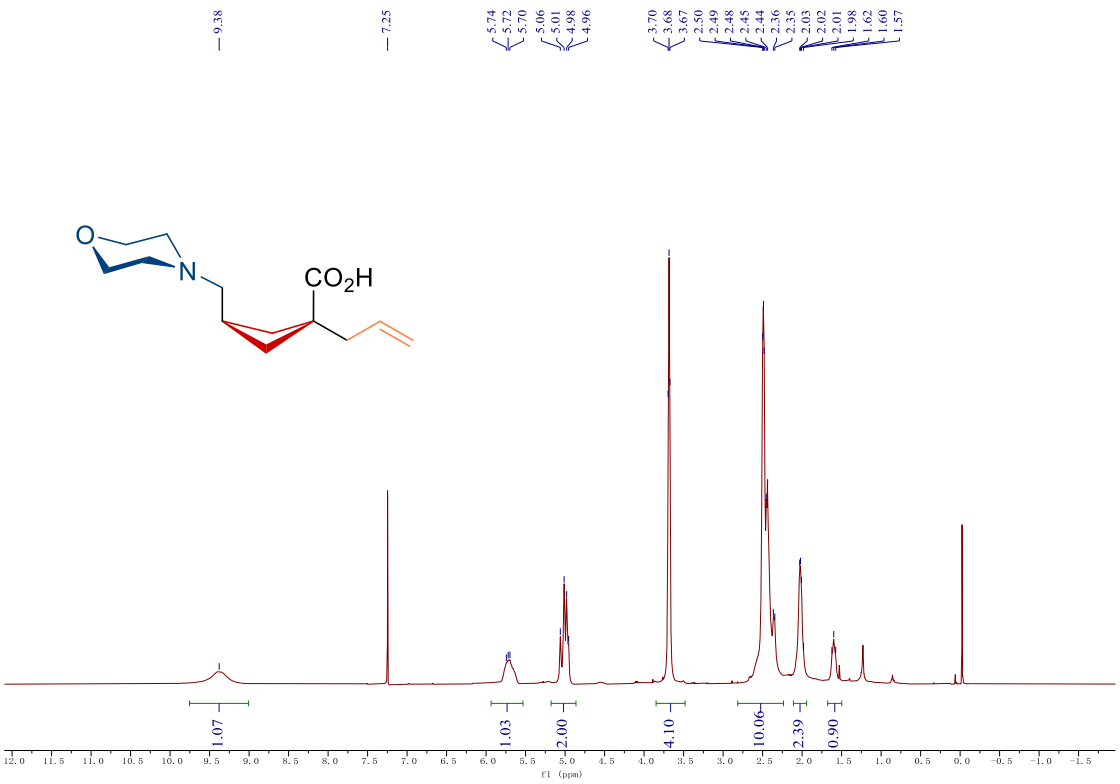
^{13}C NMR of compound **32** (101 MHz, $CDCl_3$)



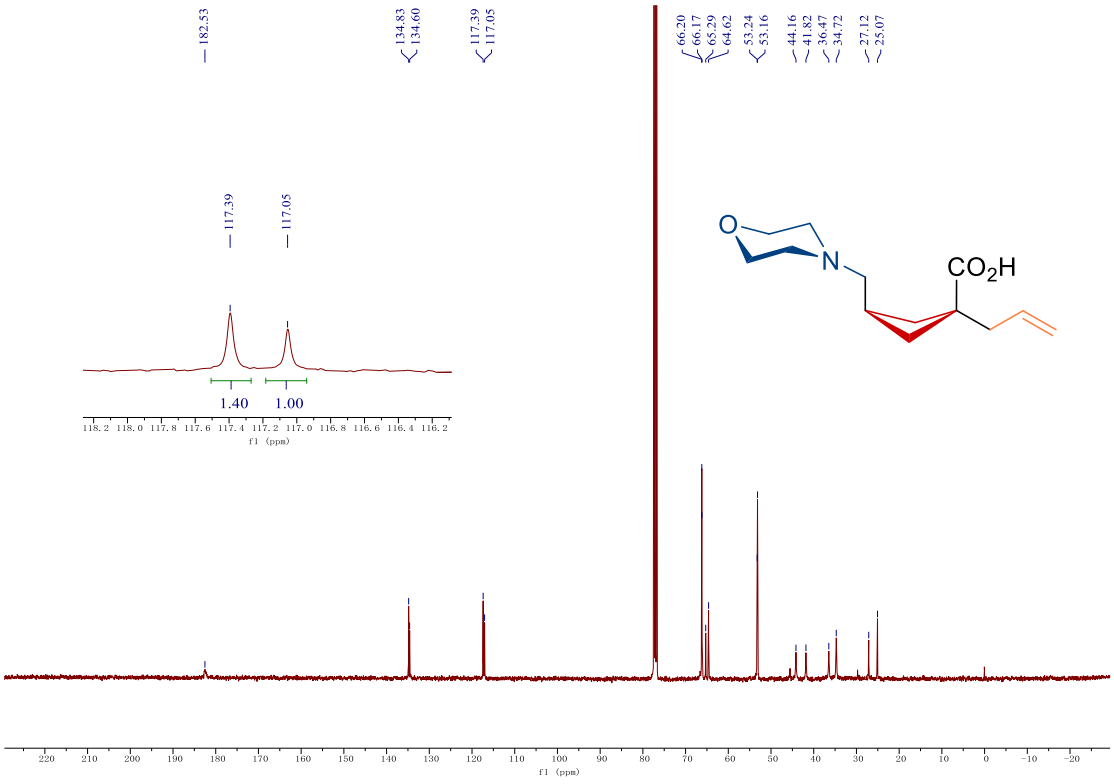
^{1}H NMR of compound **33** (400 MHz, $CDCl_3$)



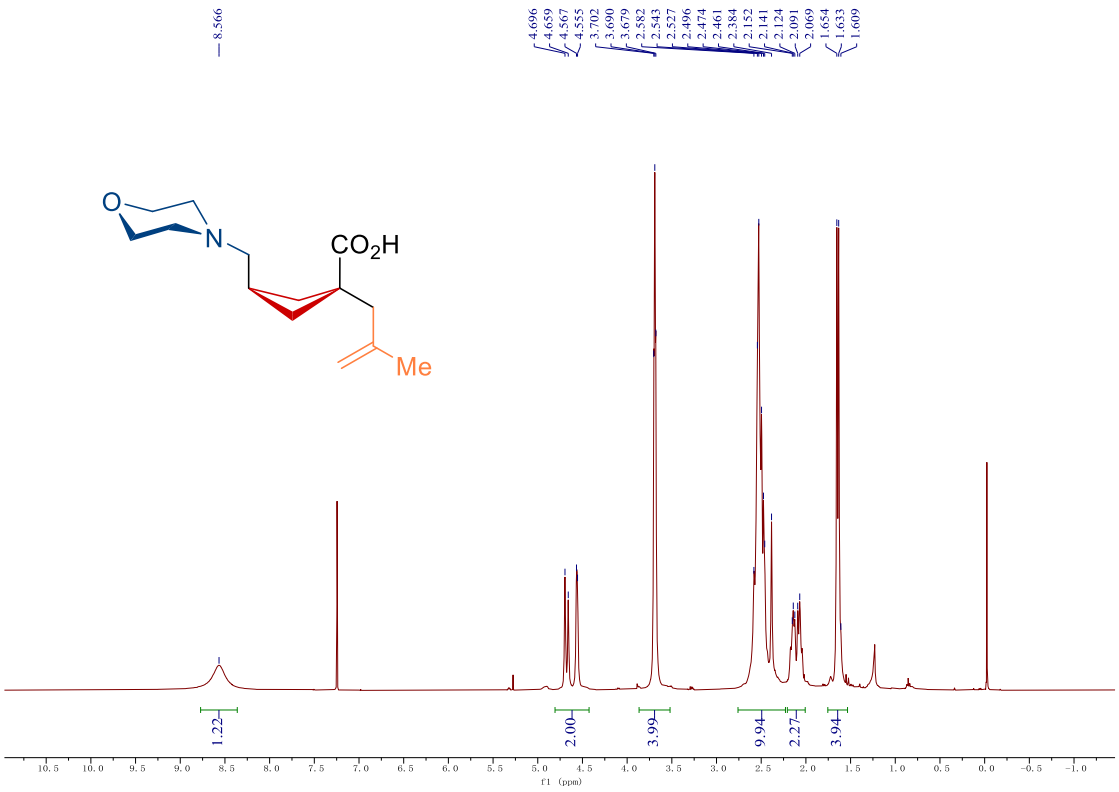
^{13}C NMR of compound **33** (101 MHz, $CDCl_3$)



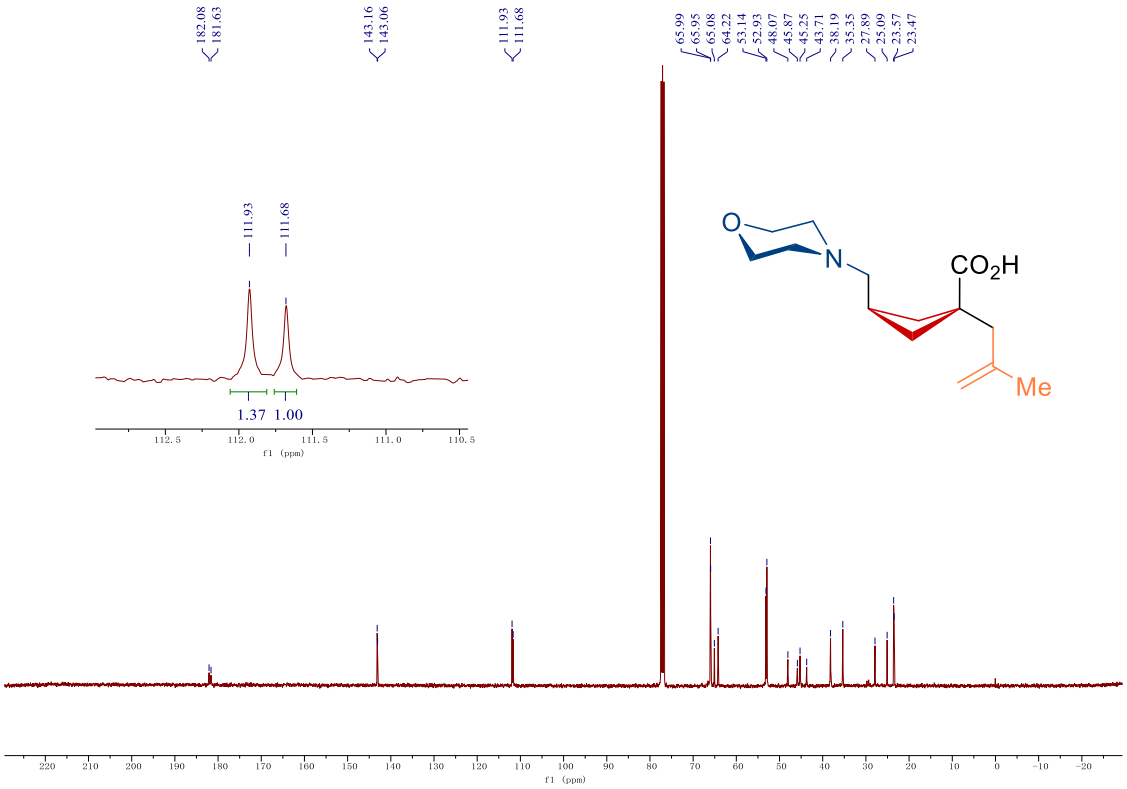
^{1}H NMR of compound **34** (400 MHz, $CDCl_3$)



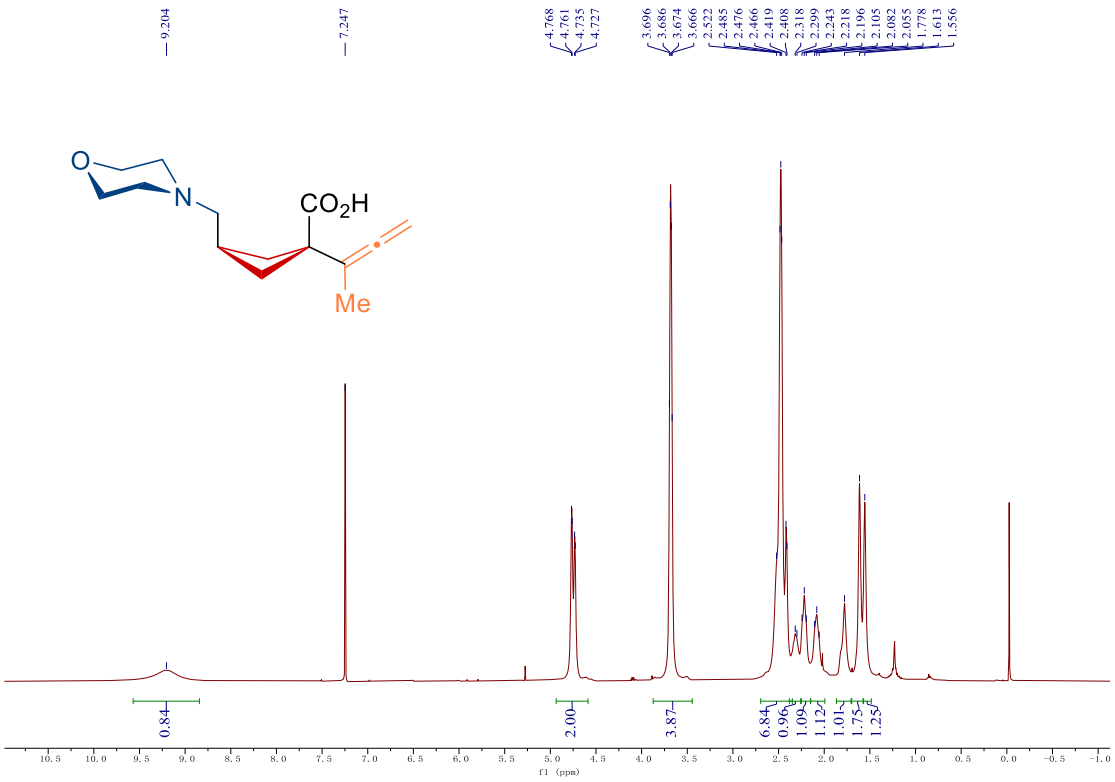
^{13}C NMR of compound **34** (101 MHz, $CDCl_3$)



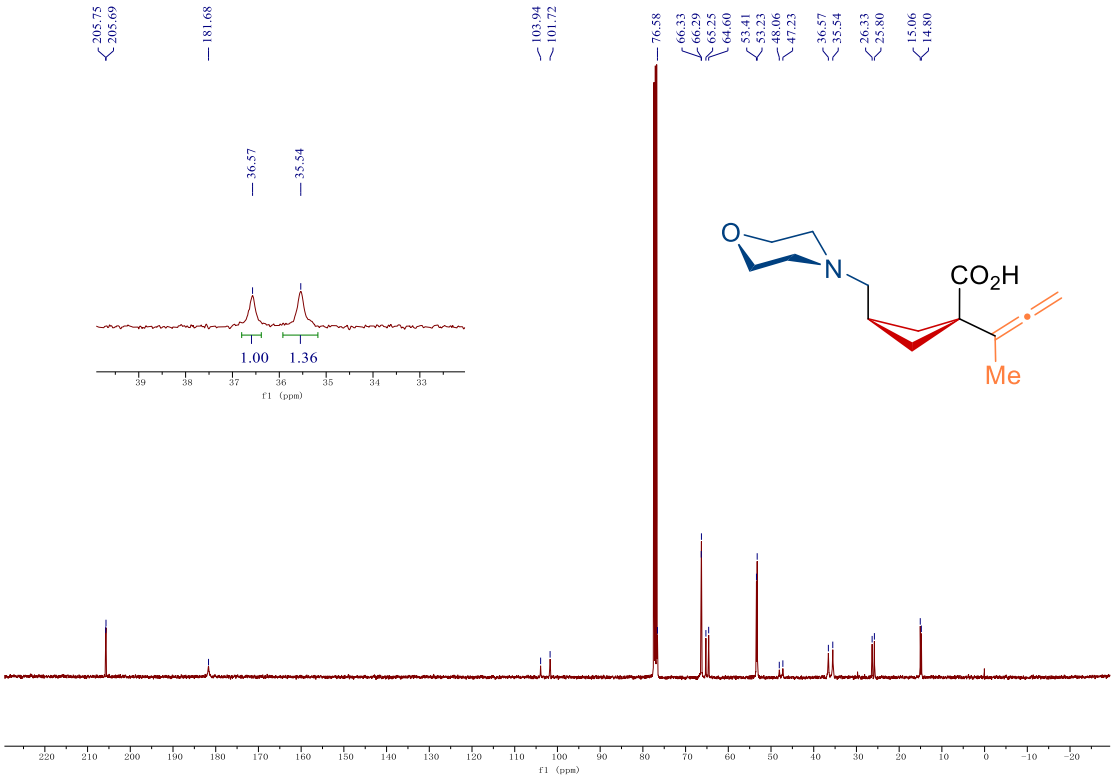
^{1}H NMR of compound **35** (400 MHz, $CDCl_3$)



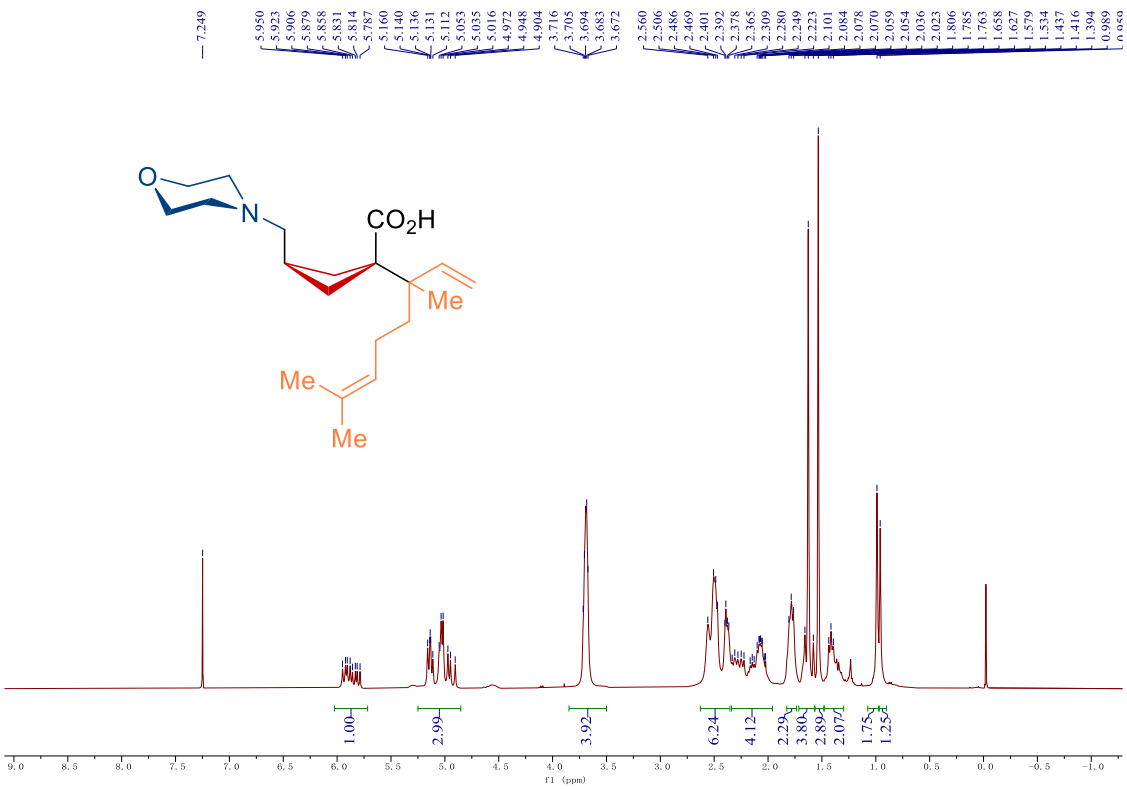
^{13}C NMR of compound **35** (101 MHz, $CDCl_3$)



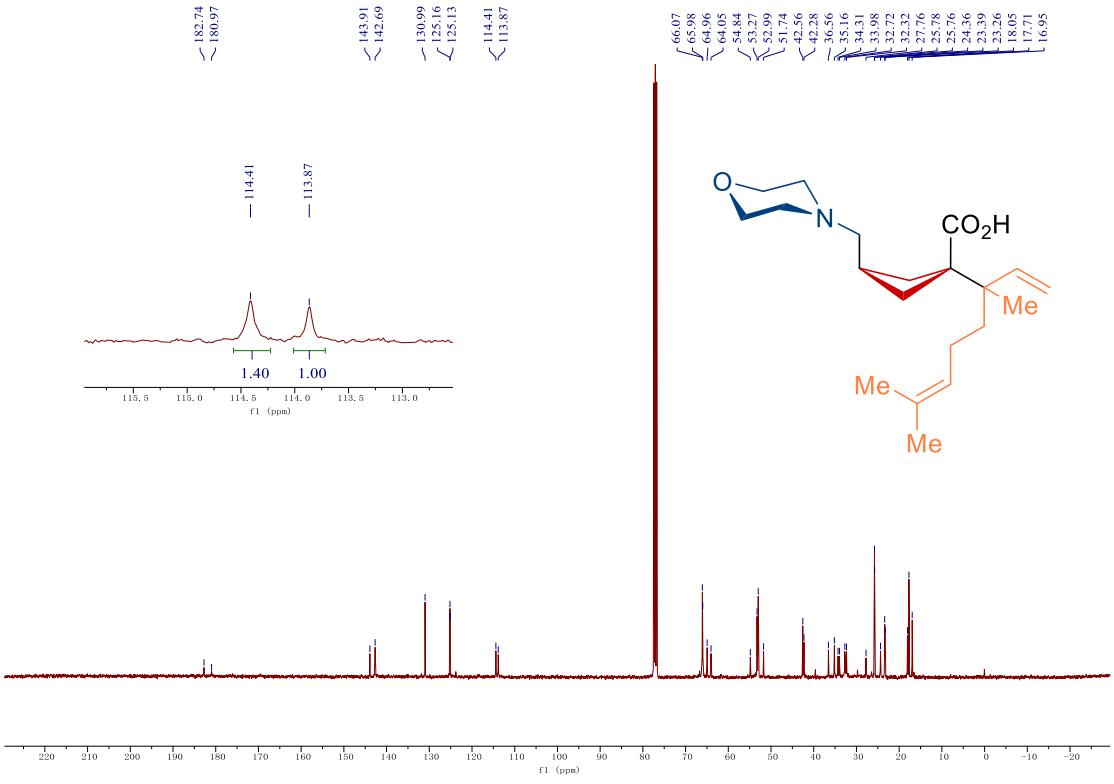
^{1}H NMR of compound **36** (400 MHz, $CDCl_3$)



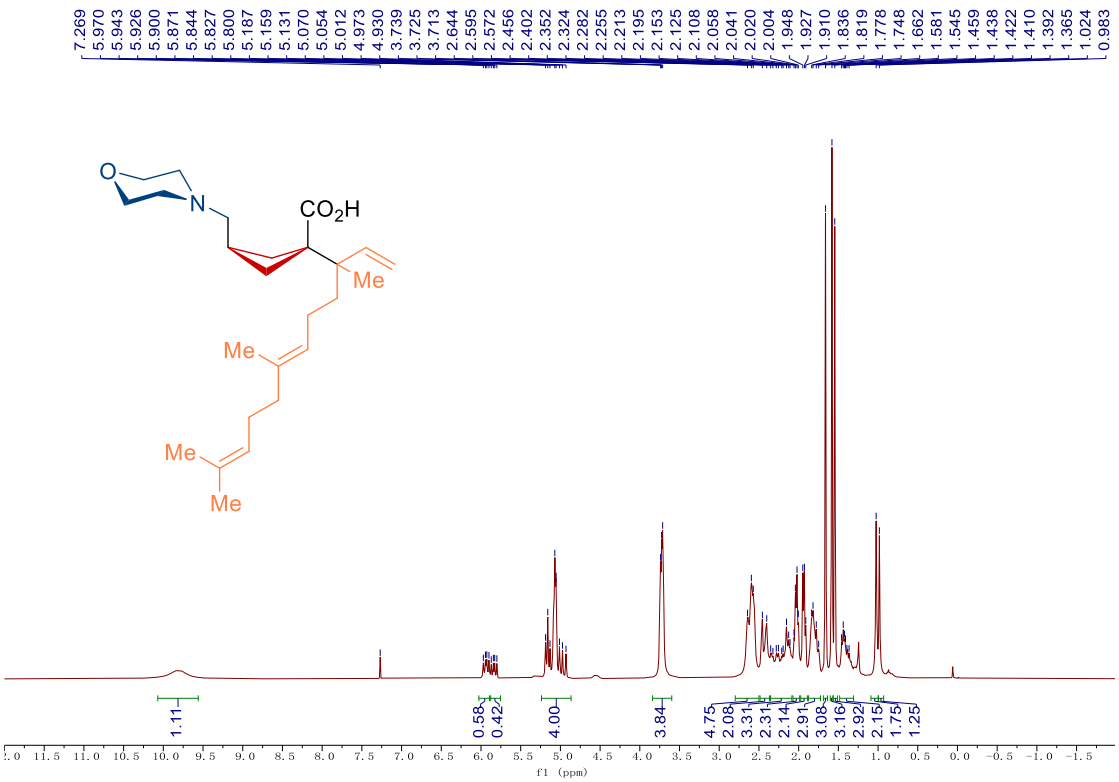
^{13}C NMR of compound **36** (101 MHz, $CDCl_3$)



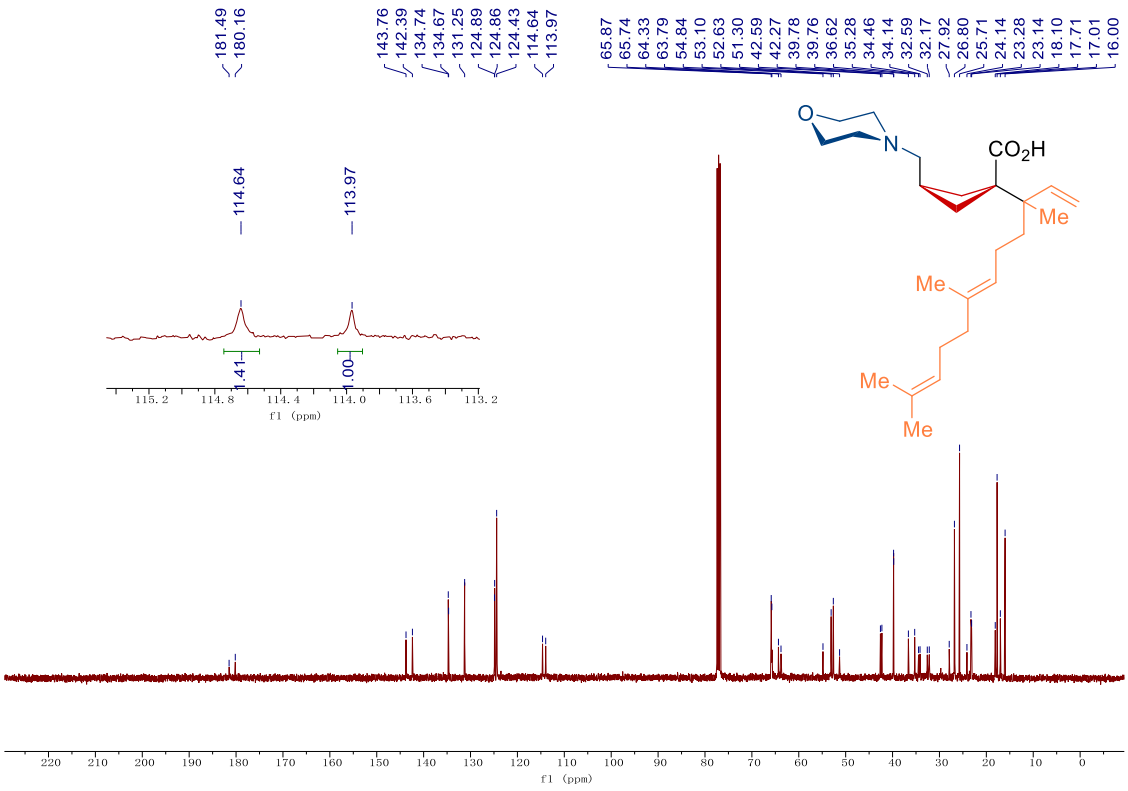
^{1}H NMR of compound **37** (400 MHz, $CDCl_3$)



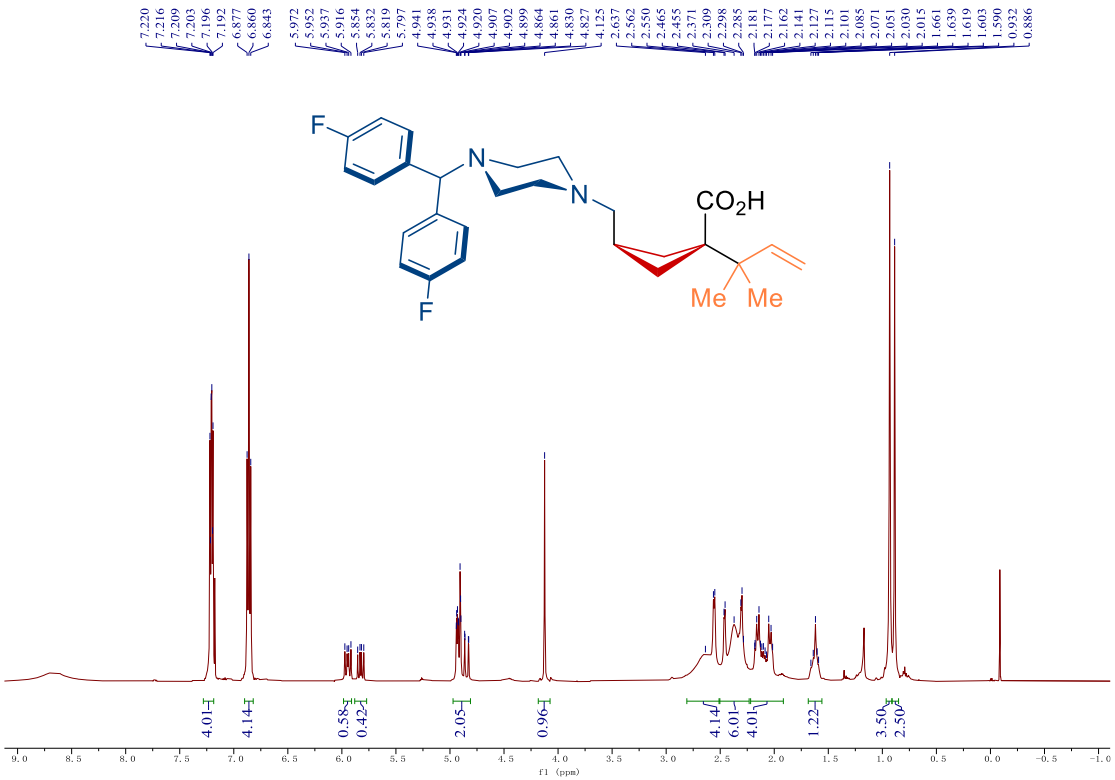
^{13}C NMR of compound **37** (101 MHz, $CDCl_3$)



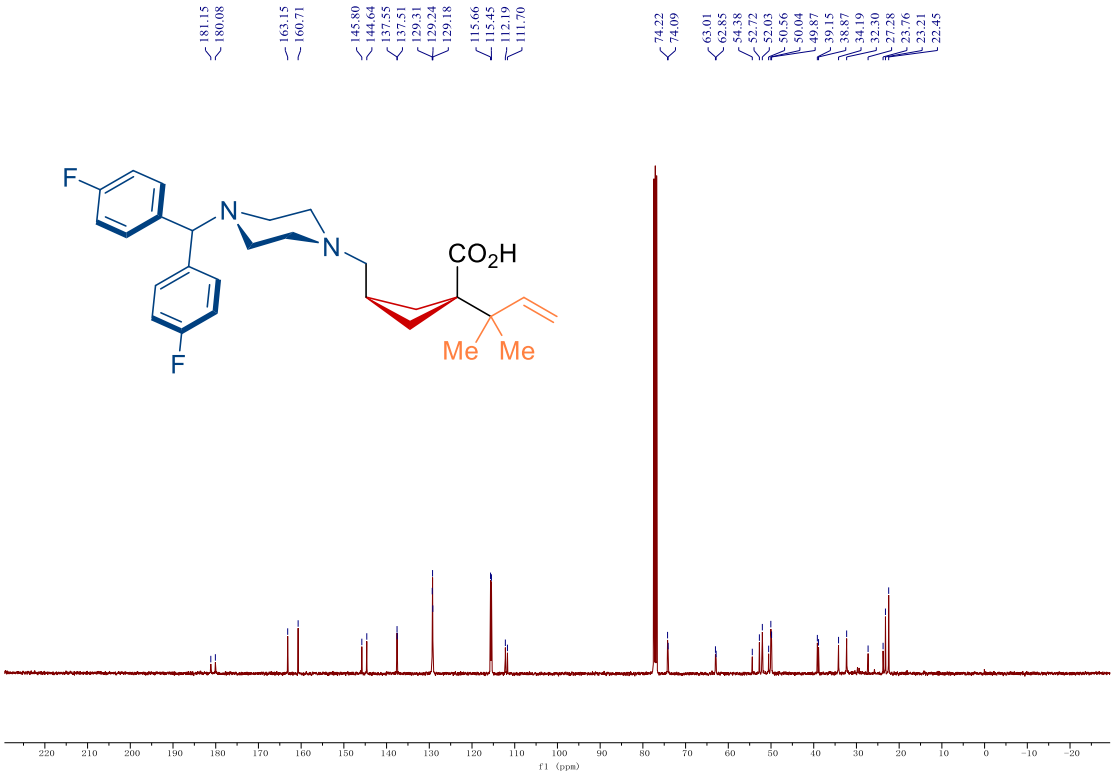
^{1}H NMR of compound **38** (400 MHz, $CDCl_3$)



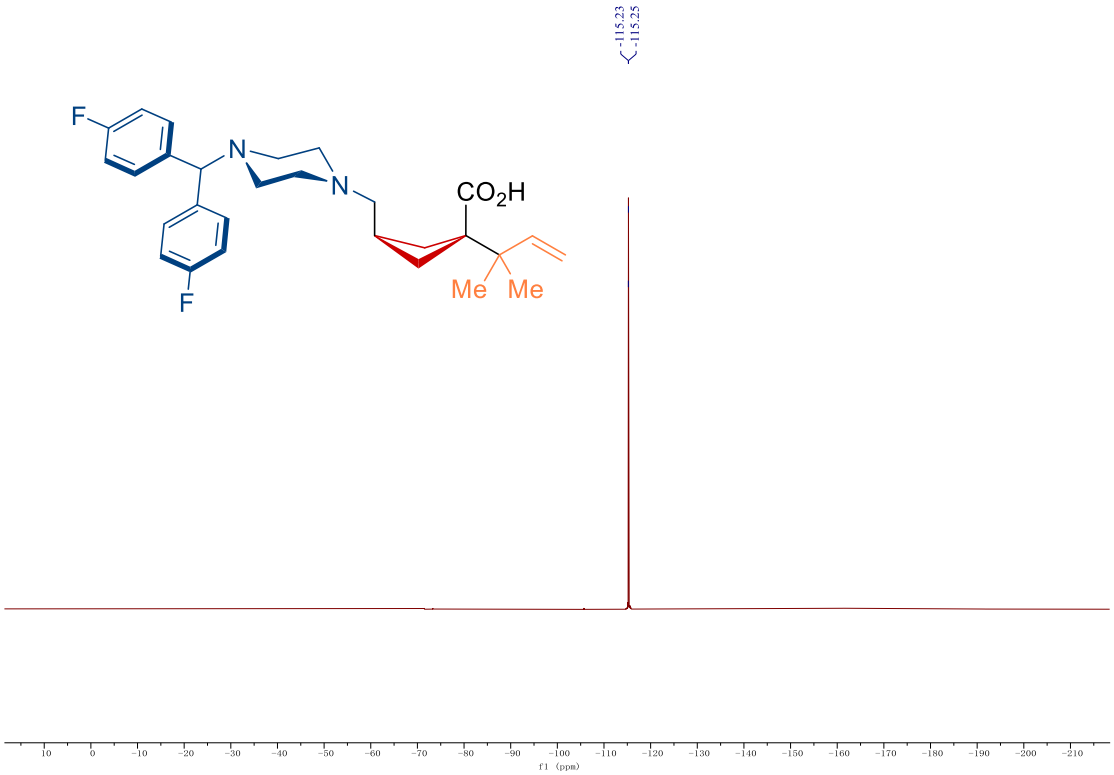
^{13}C NMR of compound **38** (101 MHz, $CDCl_3$)



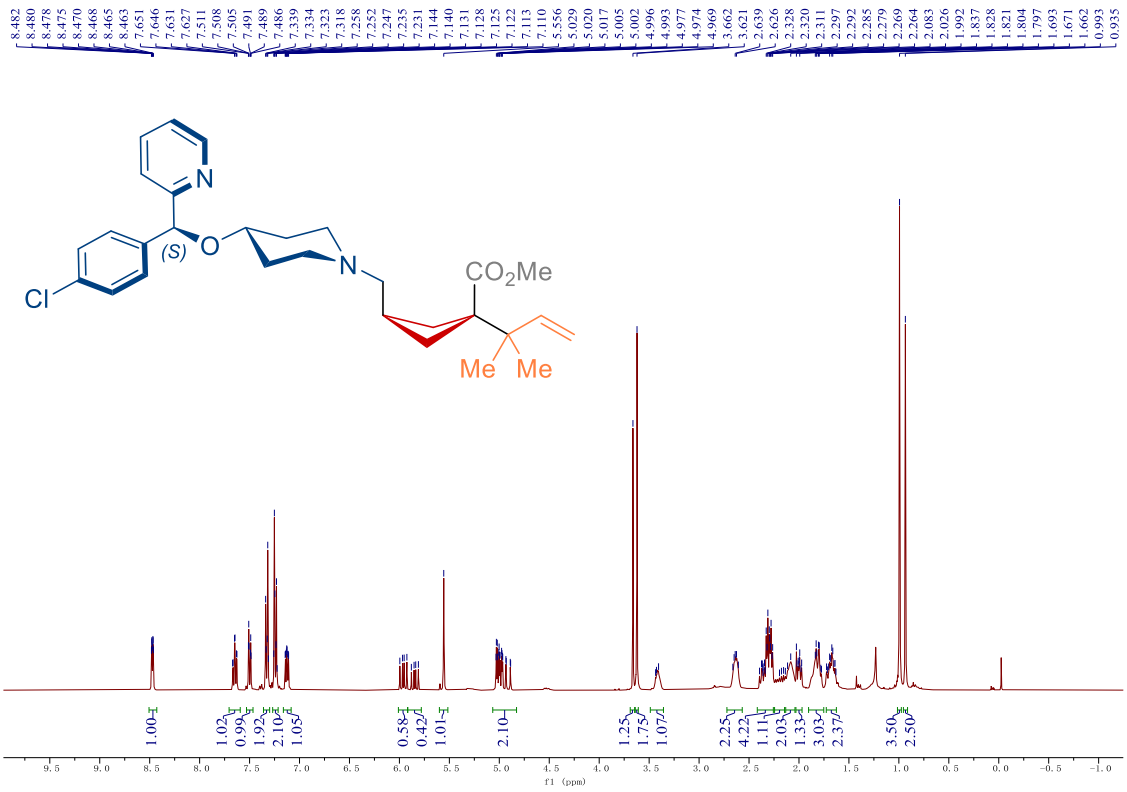
^{1}H NMR of compound **39** (400 MHz, $CDCl_3$)



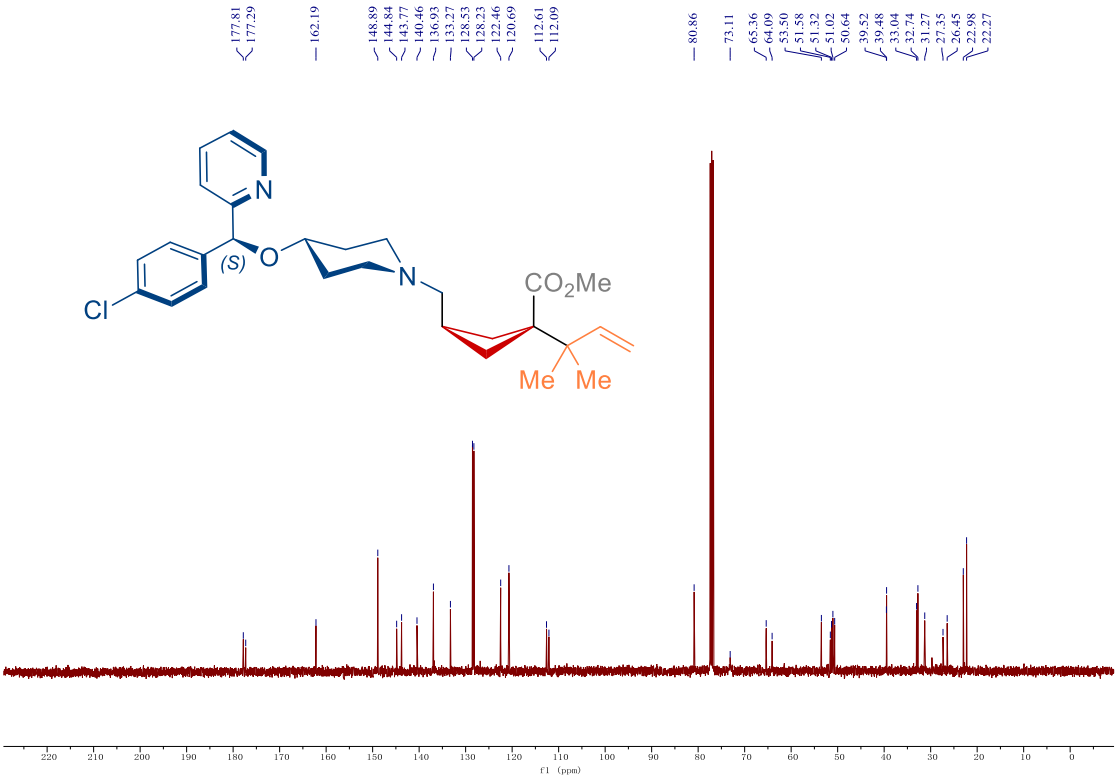
^{13}C NMR of compound **39** (101 MHz, $CDCl_3$)



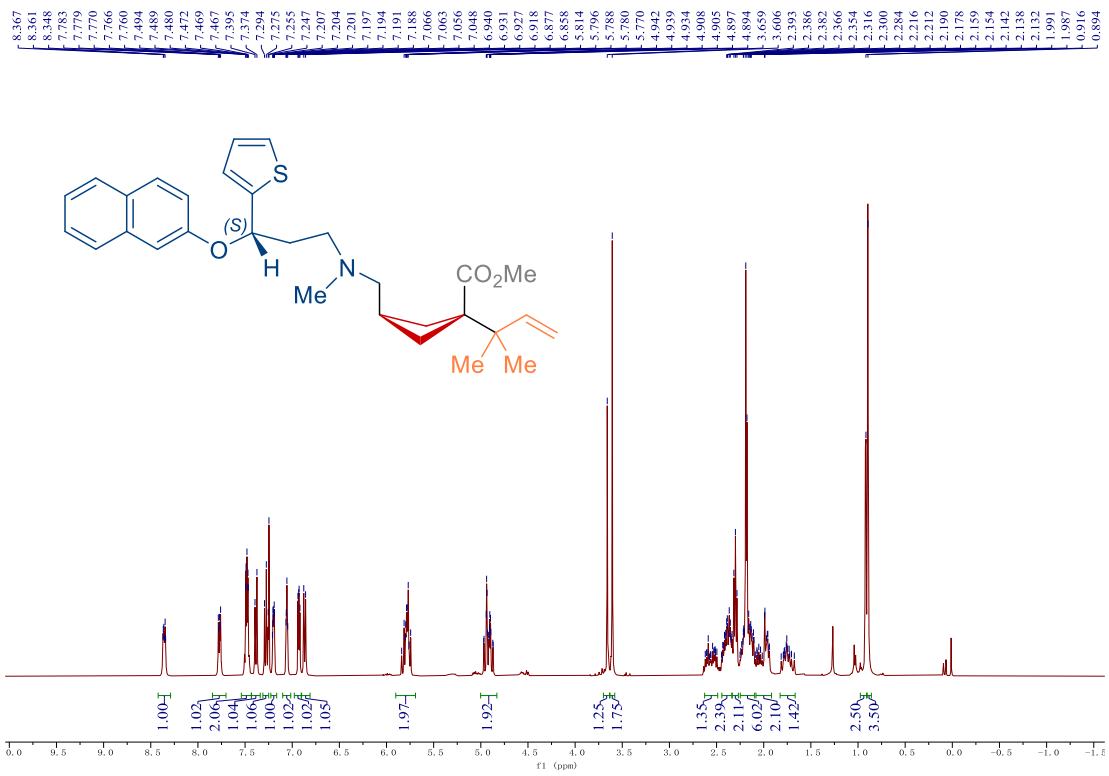
^{19}F NMR of compound **39** (376 MHz, $CDCl_3$)



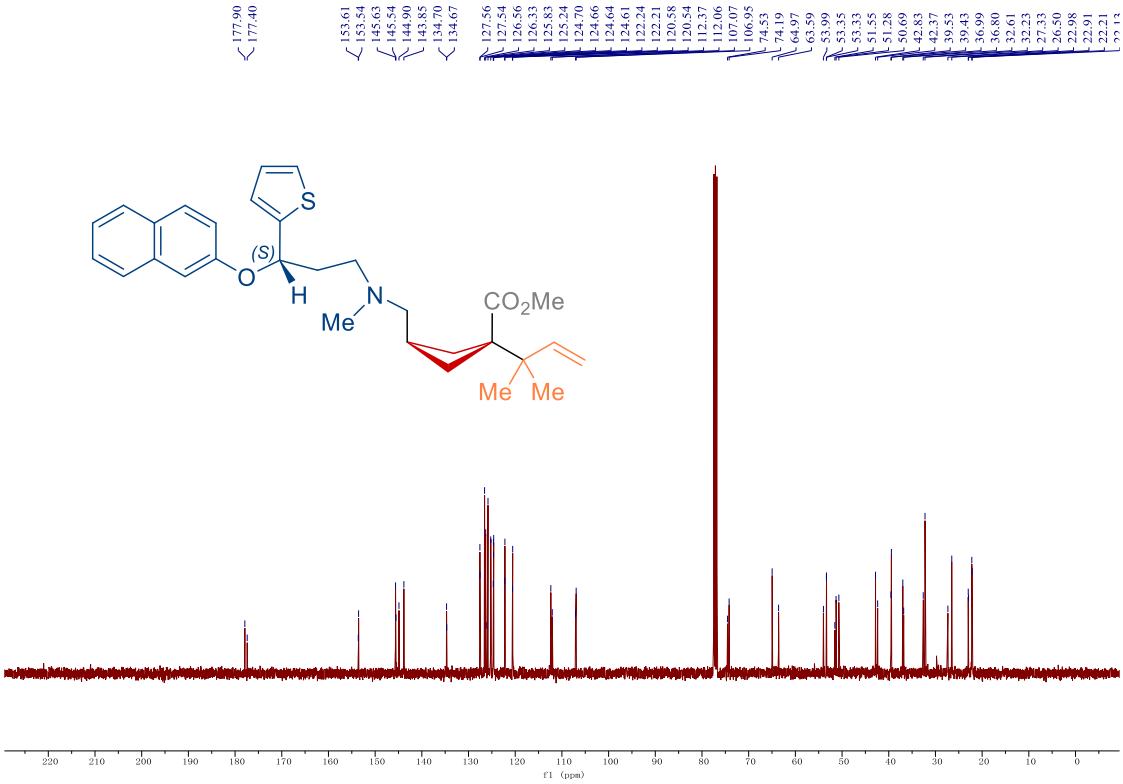
^{1}H NMR of compound **40** (400 MHz, $CDCl_3$)



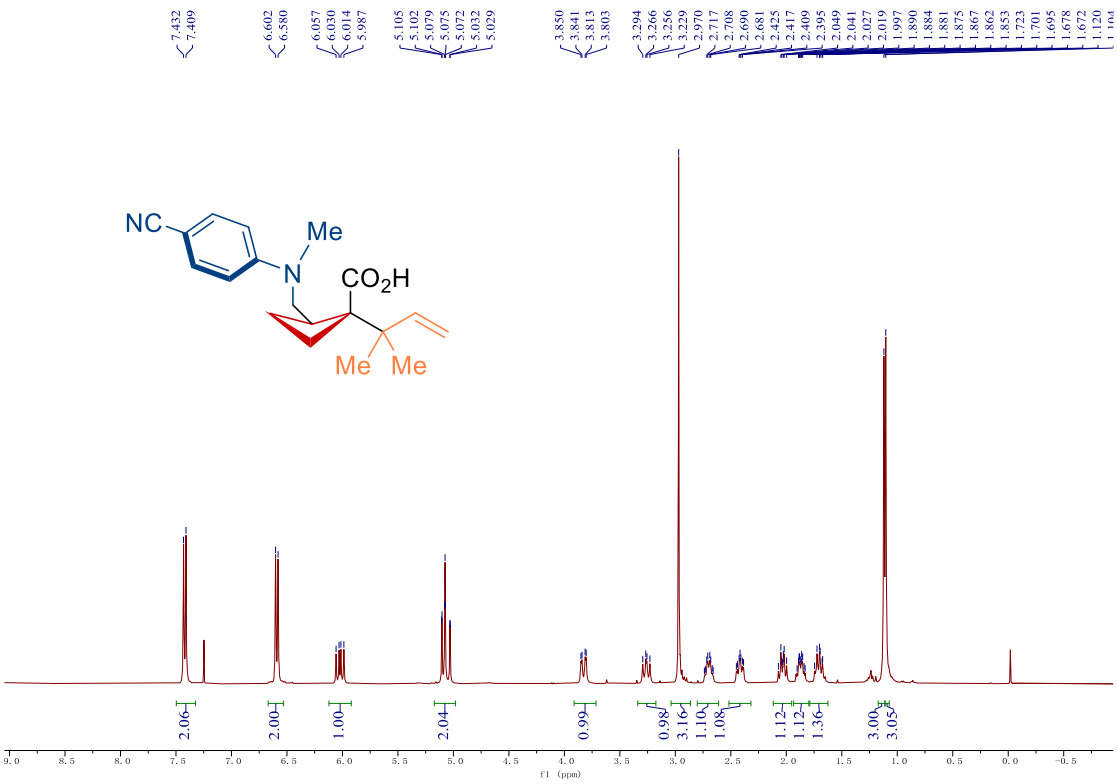
^{13}C NMR of compound **40** (101 MHz, $CDCl_3$)



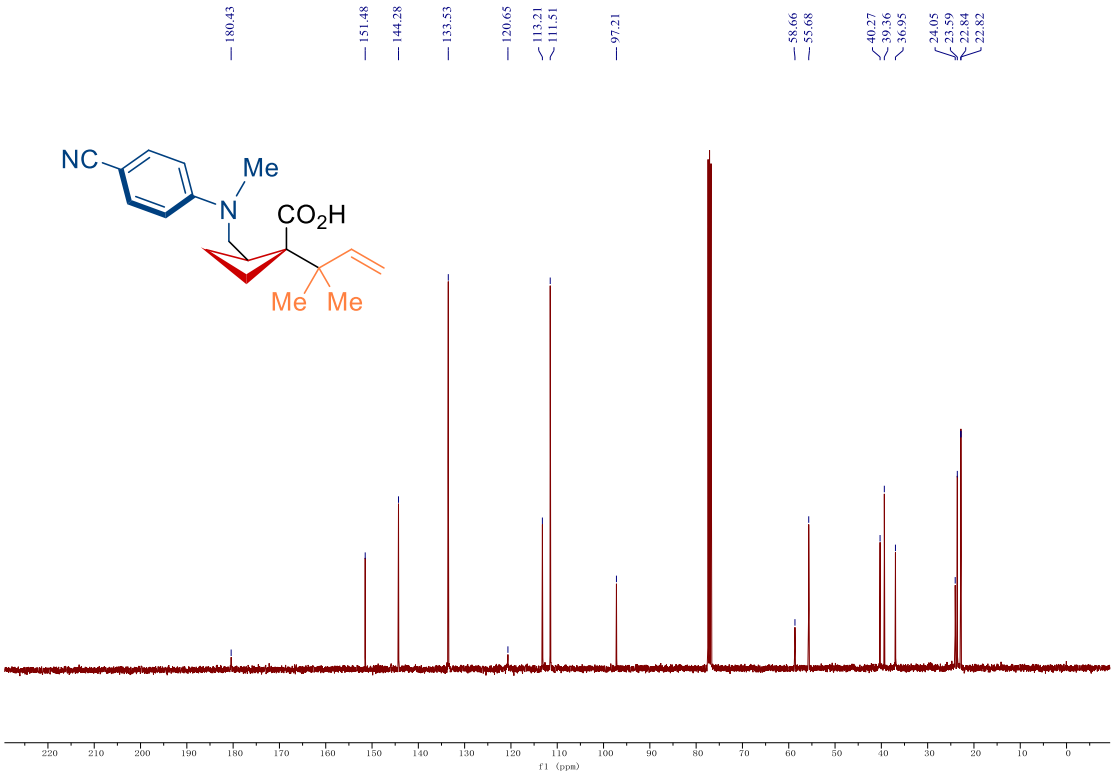
^{1}H NMR of compound **41** (400 MHz, $CDCl_3$)



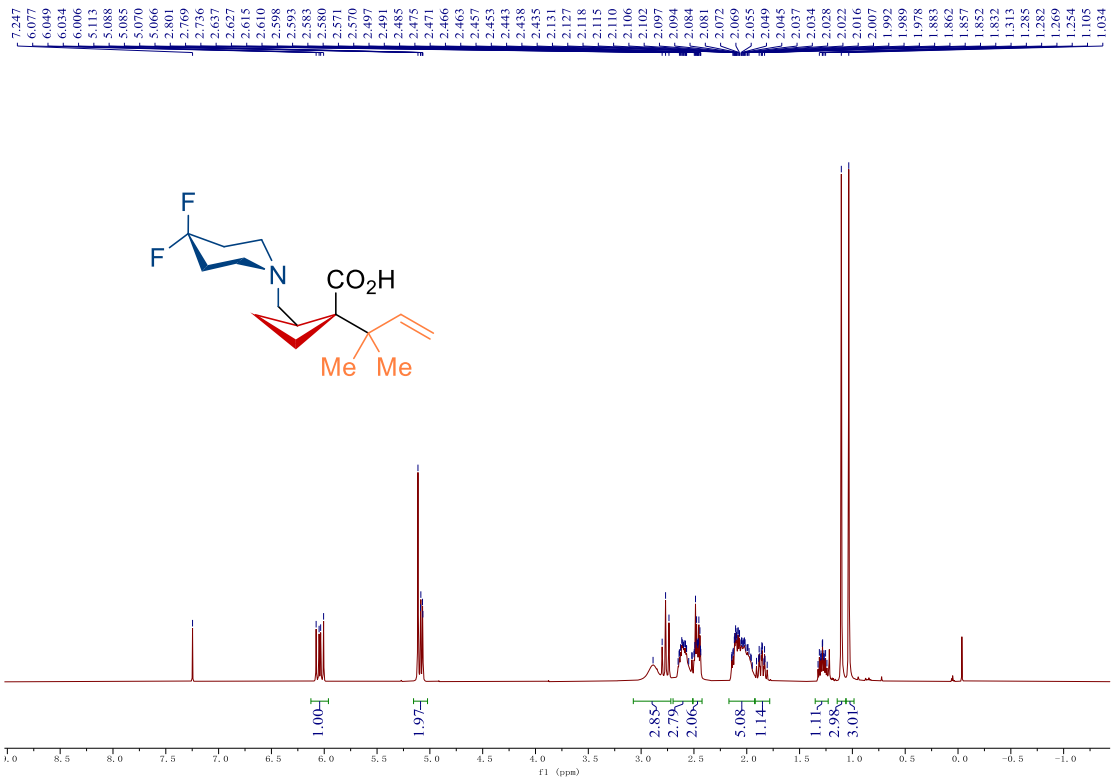
^{13}C NMR of compound **41** (101 MHz, $CDCl_3$)



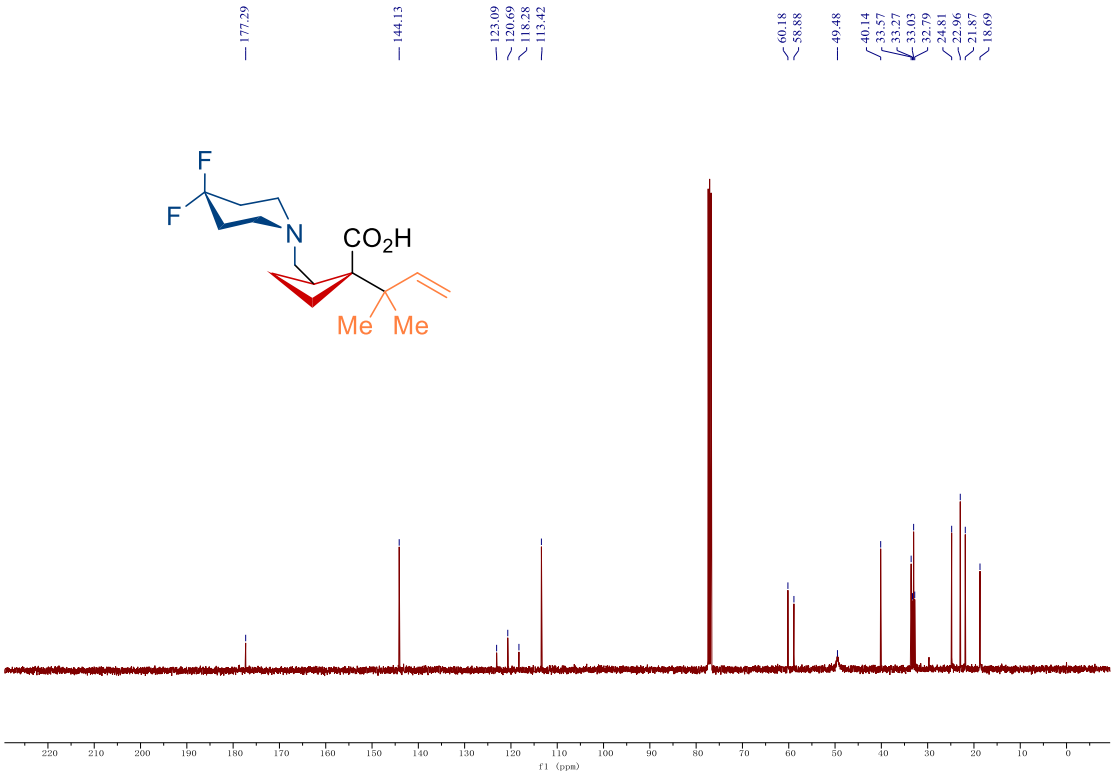
^{1}H NMR of compound **42** (400 MHz, $CDCl_3$)



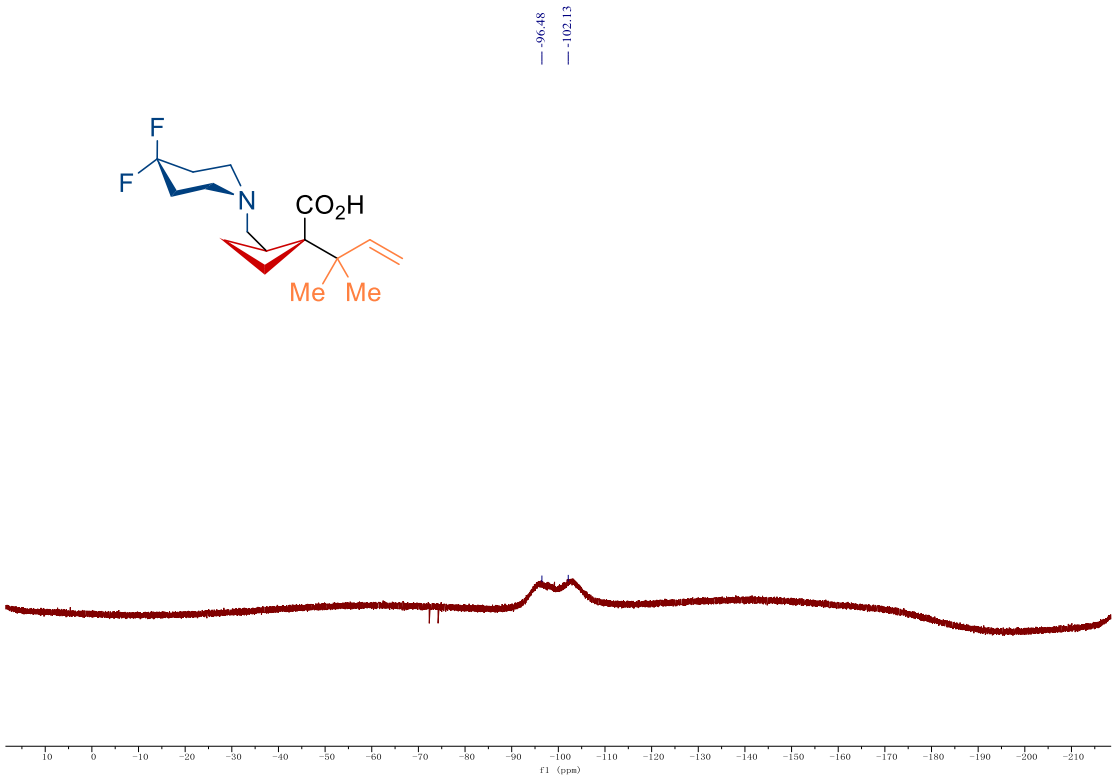
^{13}C NMR of compound **42** (101 MHz, $CDCl_3$)



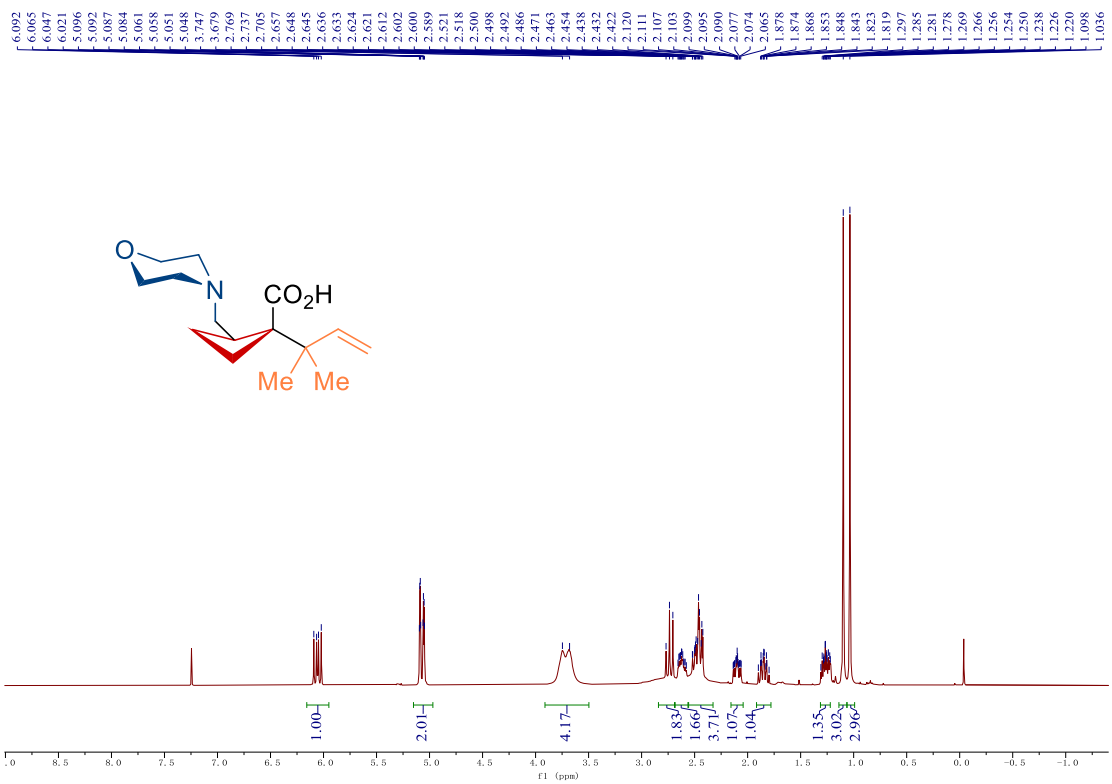
^{1}H NMR of compound **43** (400 MHz, $CDCl_3$)



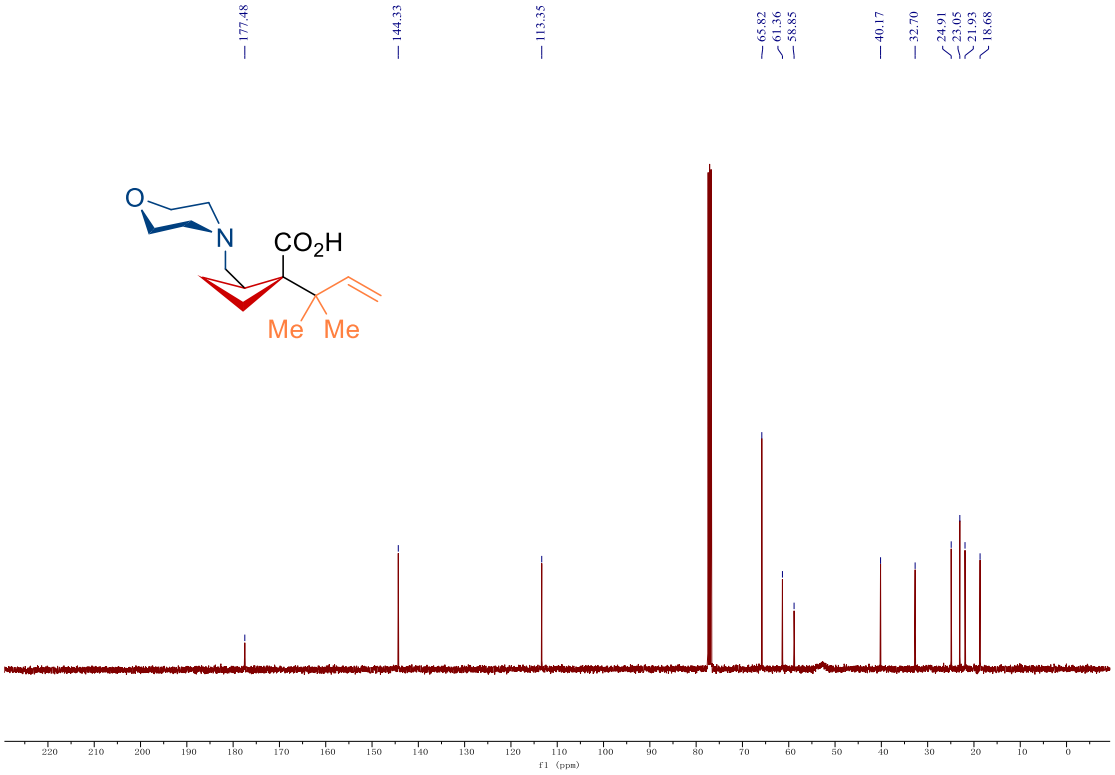
^{13}C NMR of compound **43** (101 MHz, $CDCl_3$)



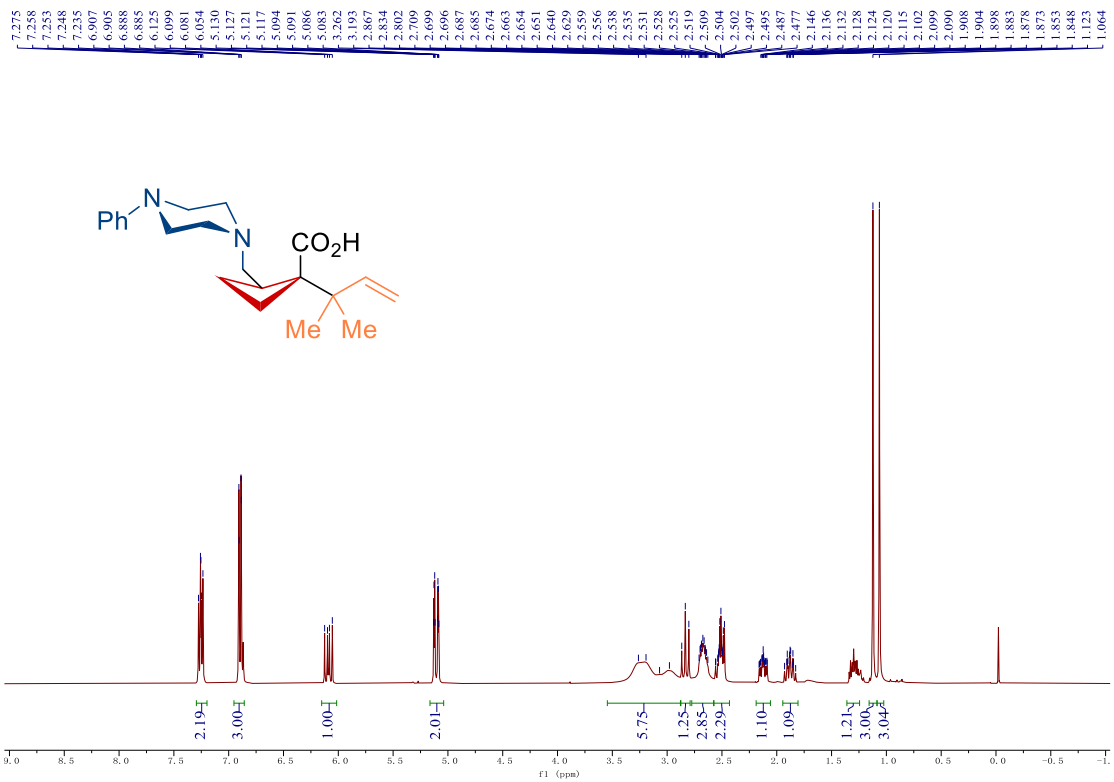
^{19}F NMR of compound **43** (376 MHz, $CDCl_3$)



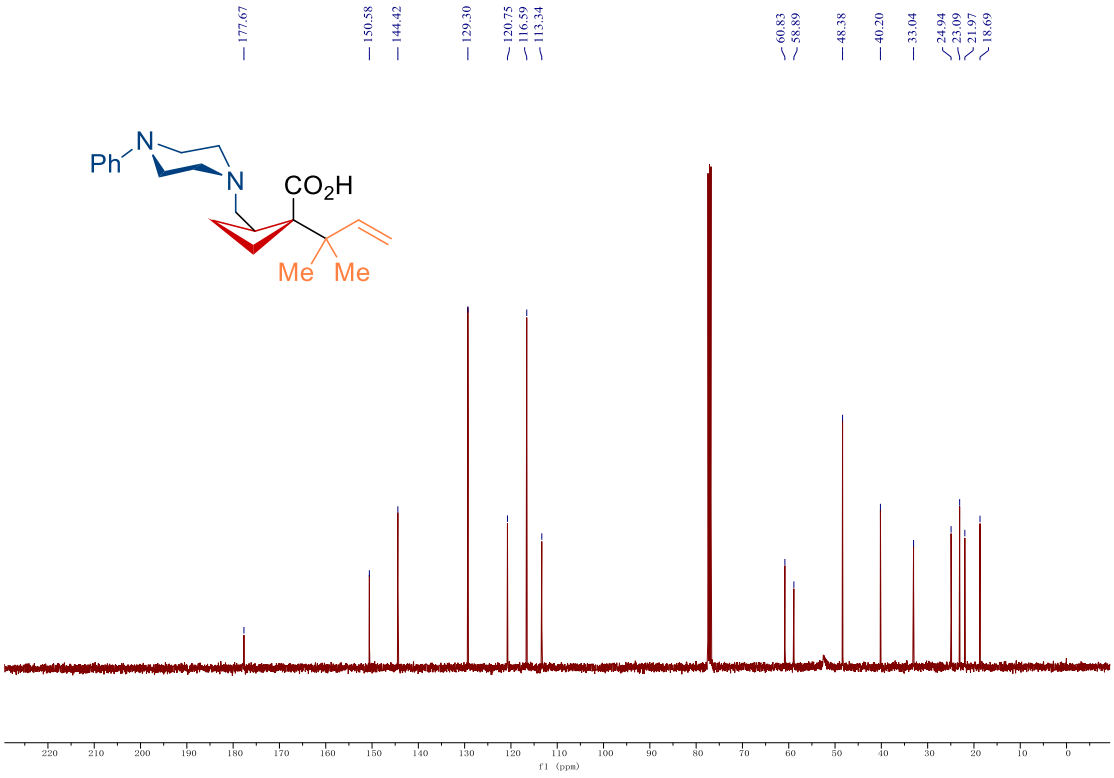
^{1}H NMR of compound **44** (400 MHz, $CDCl_3$)



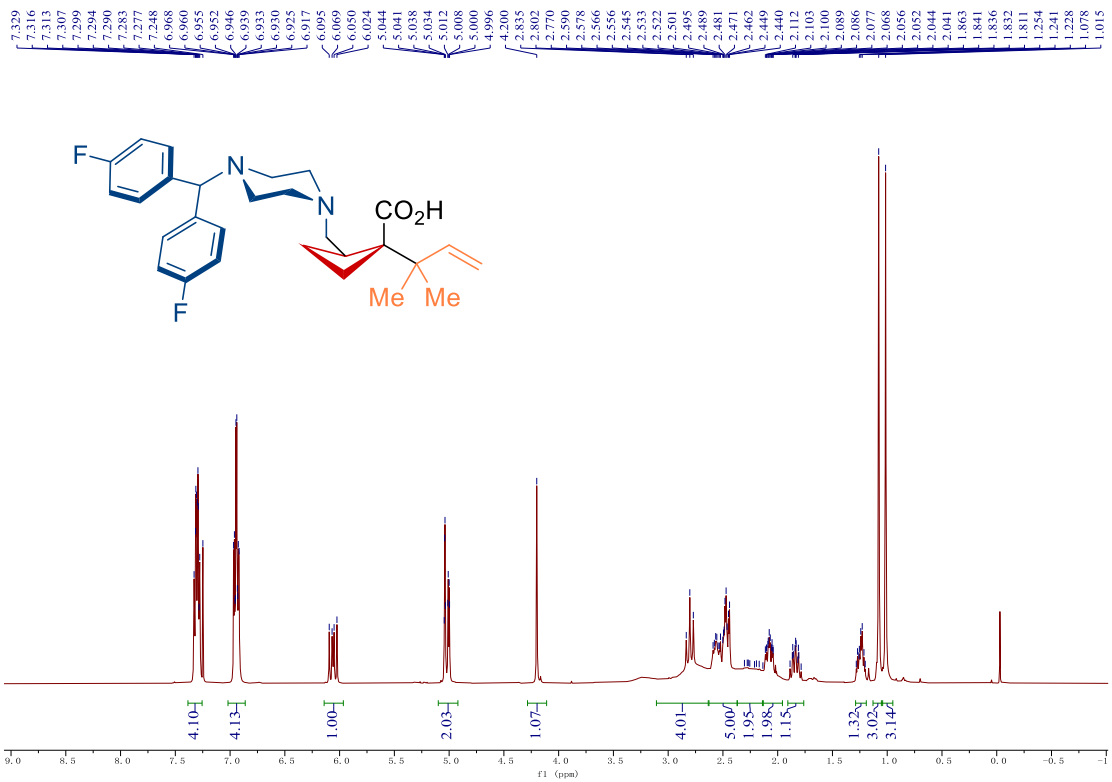
^{13}C NMR of compound **44** (101 MHz, $CDCl_3$)



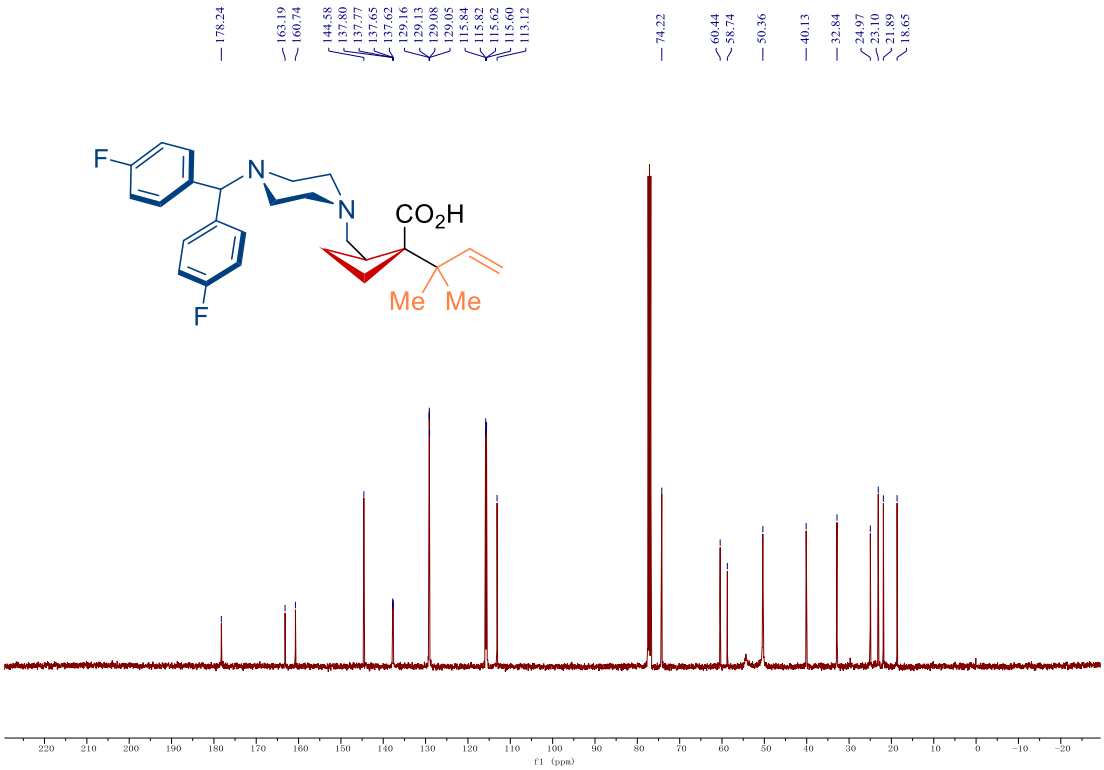
^{1}H NMR of compound **45** (400 MHz, $CDCl_3$)



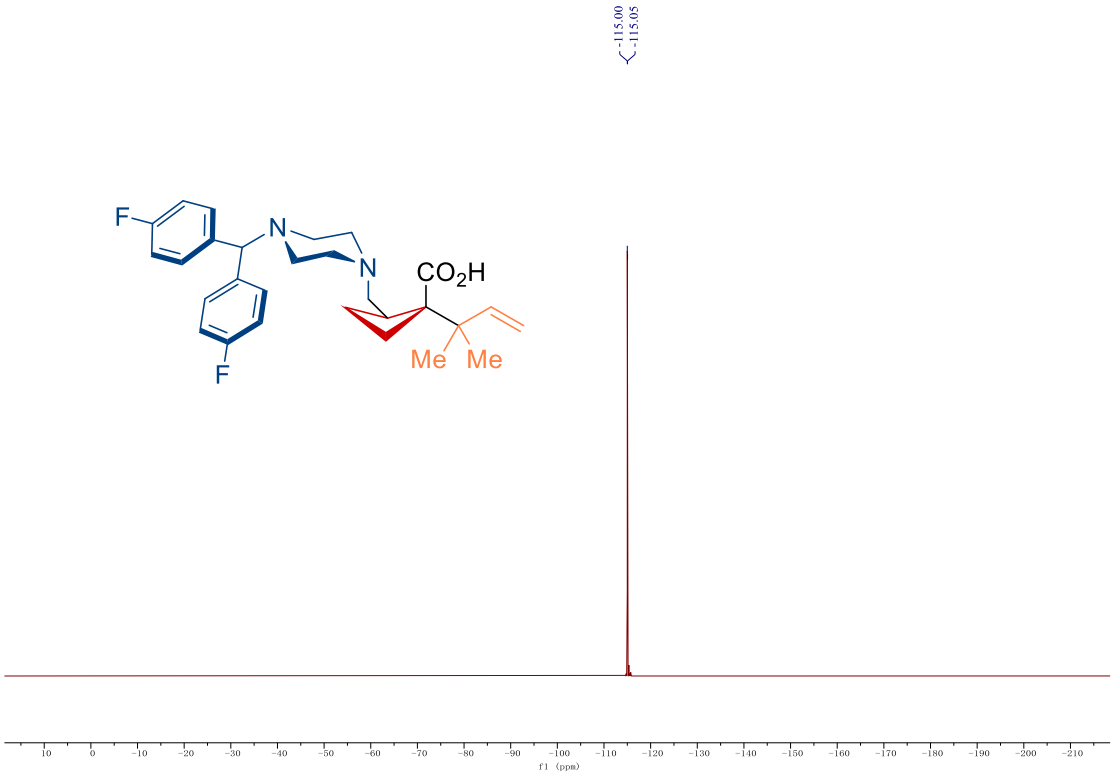
^{13}C NMR of compound **45** (101 MHz, $CDCl_3$)



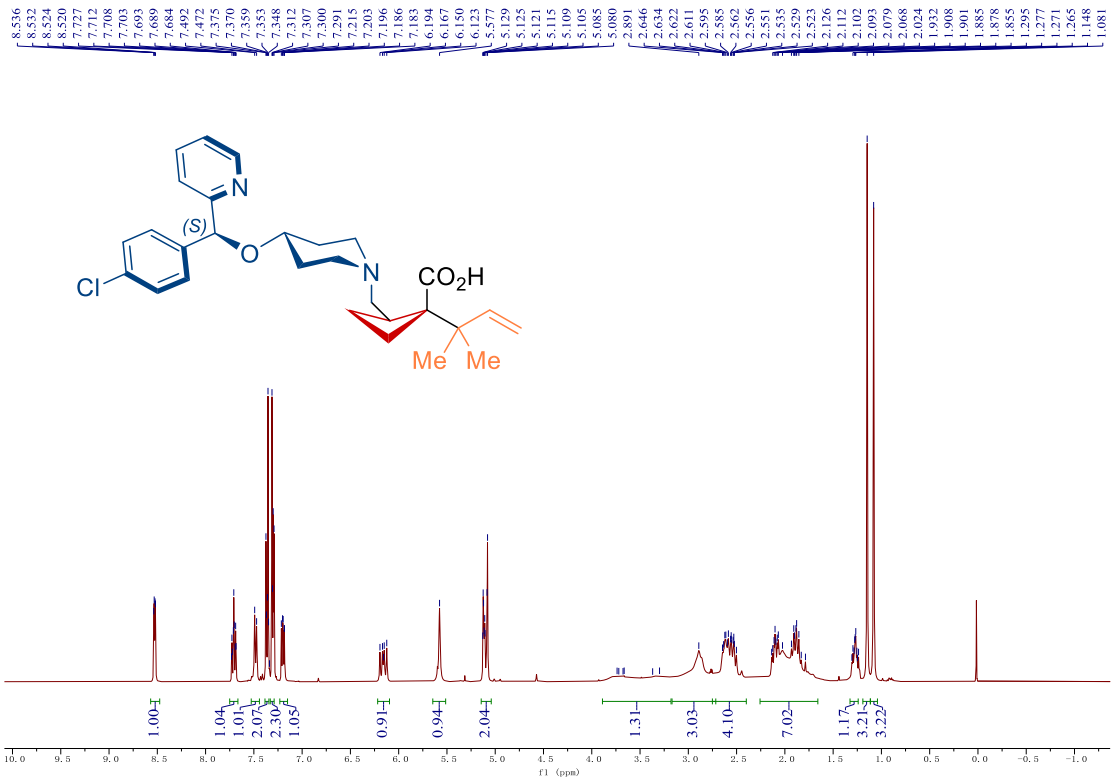
^{1}H NMR of compound **46** (400 MHz, $CDCl_3$)



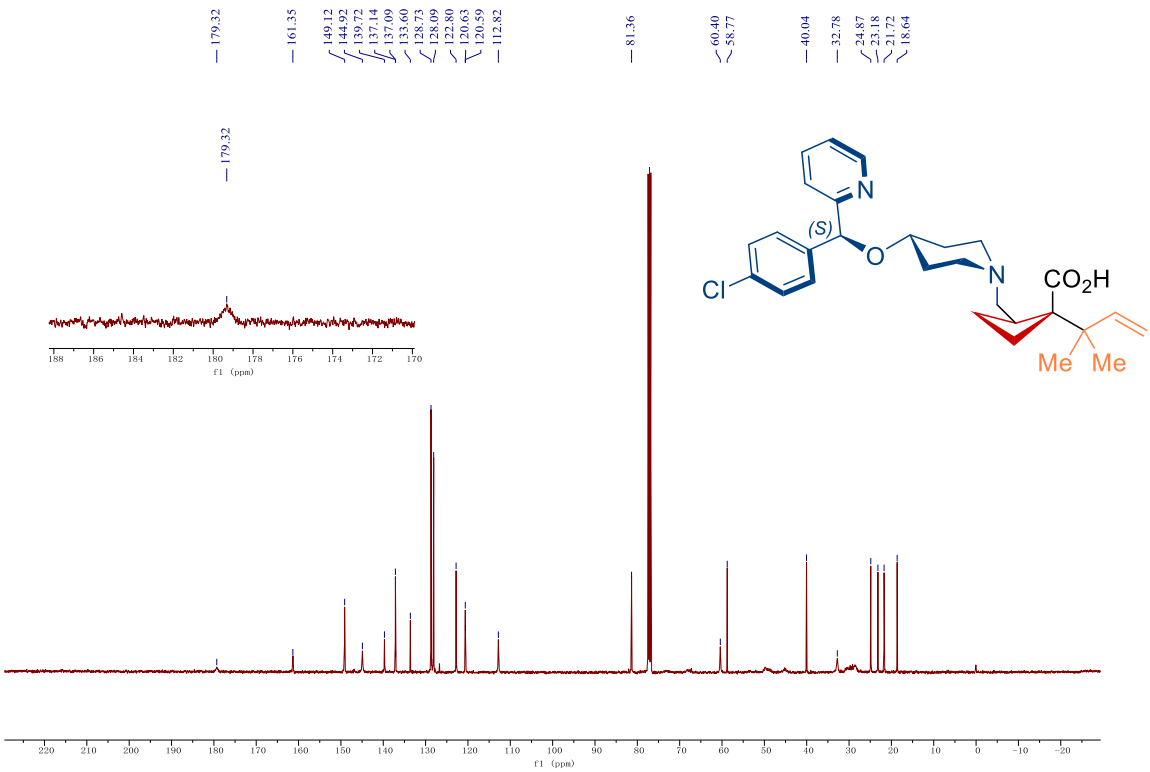
^{13}C NMR of compound **46** (101 MHz, $CDCl_3$)



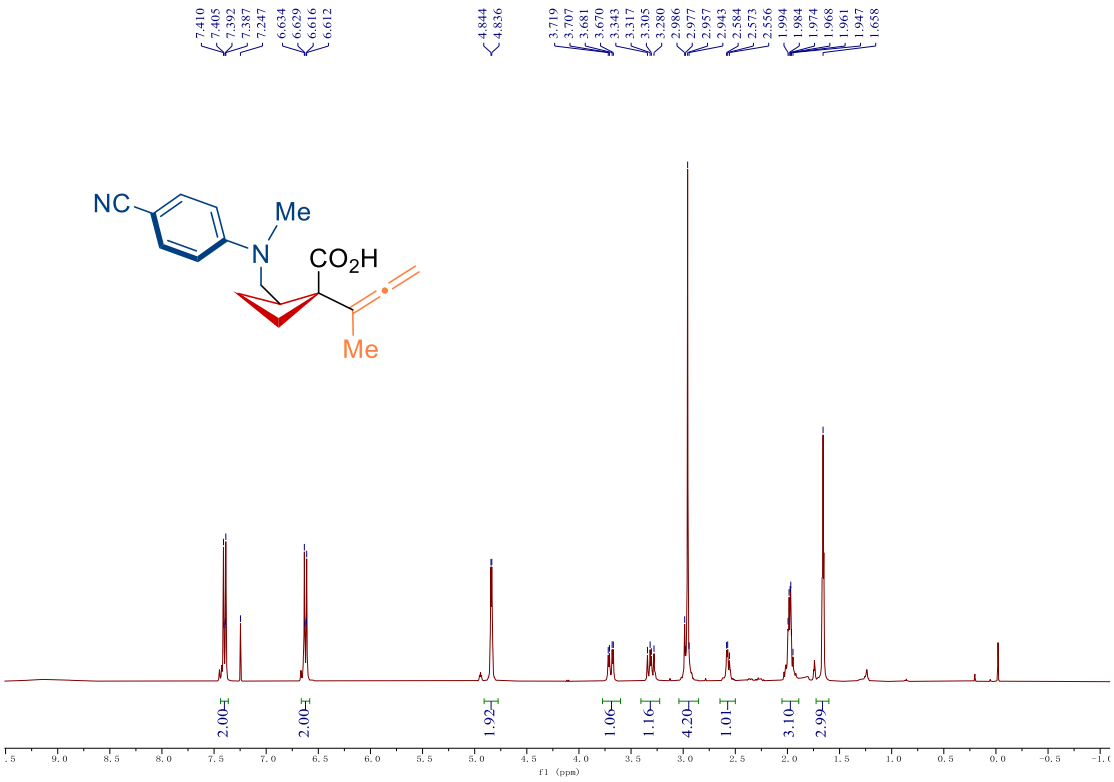
^{19}F NMR of compound **46** (376 MHz, $CDCl_3$)



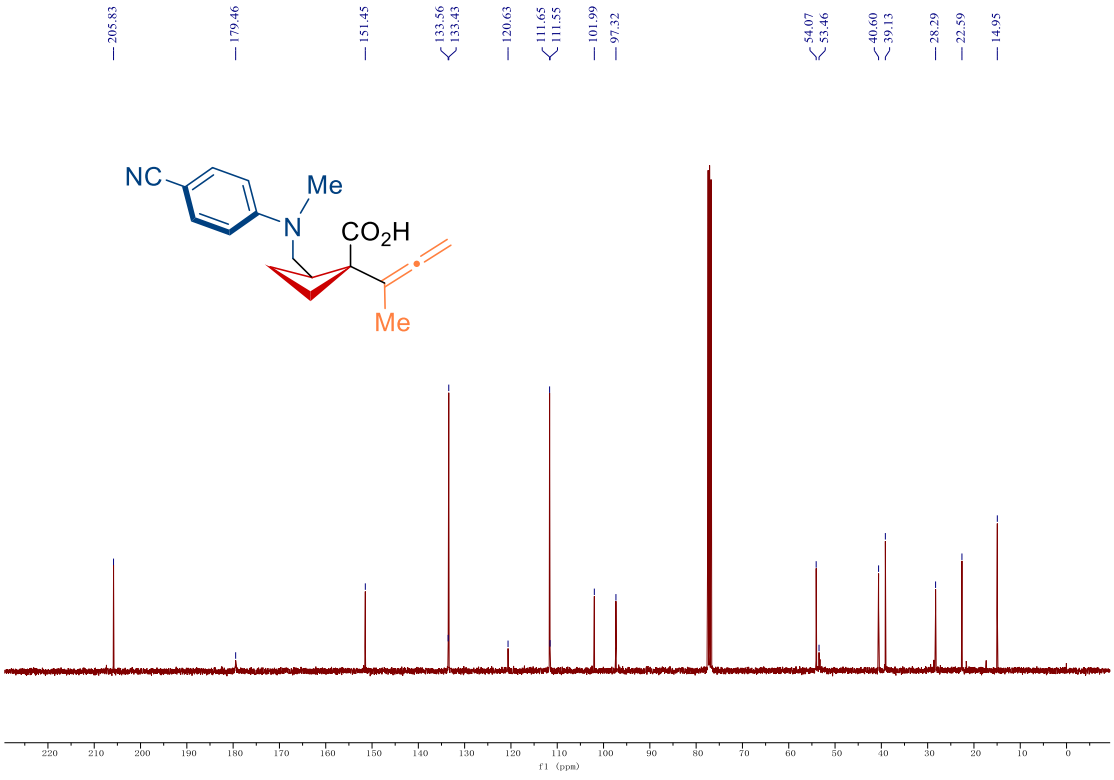
^{1}H NMR of compound **47** (400 MHz, $CDCl_3$)



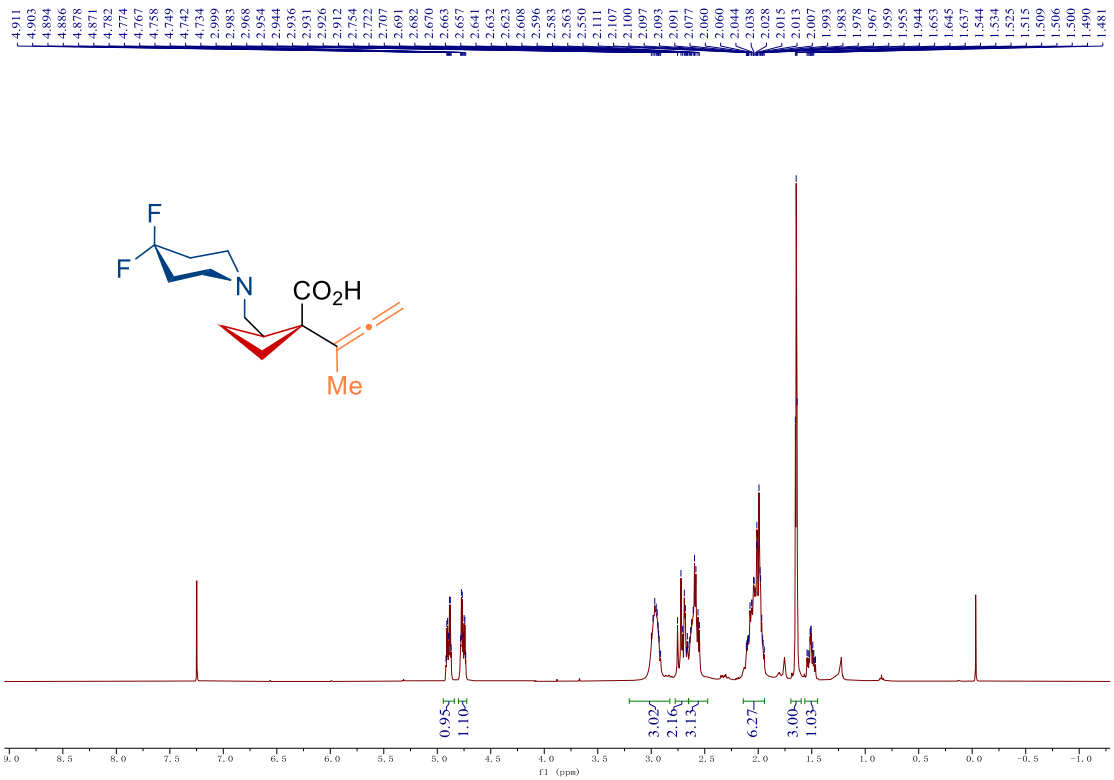
^{13}C NMR of compound **47** (101 MHz, $CDCl_3$)



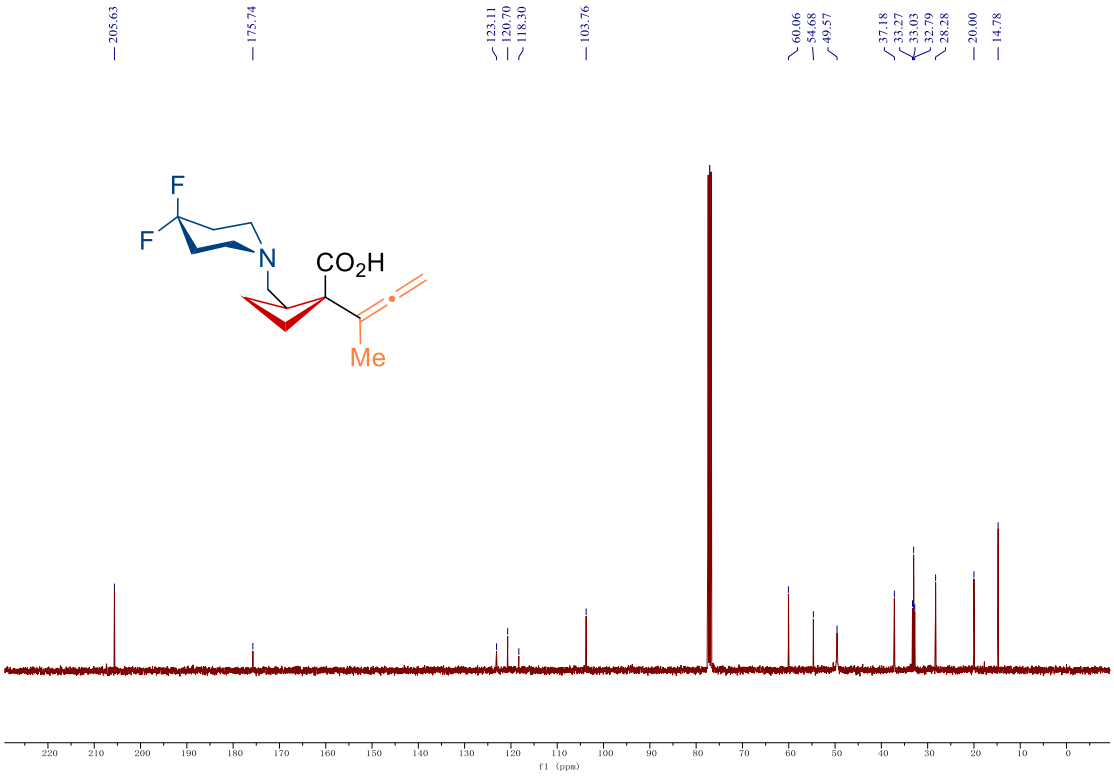
^{1}H NMR of compound **48** (400 MHz, $CDCl_3$)



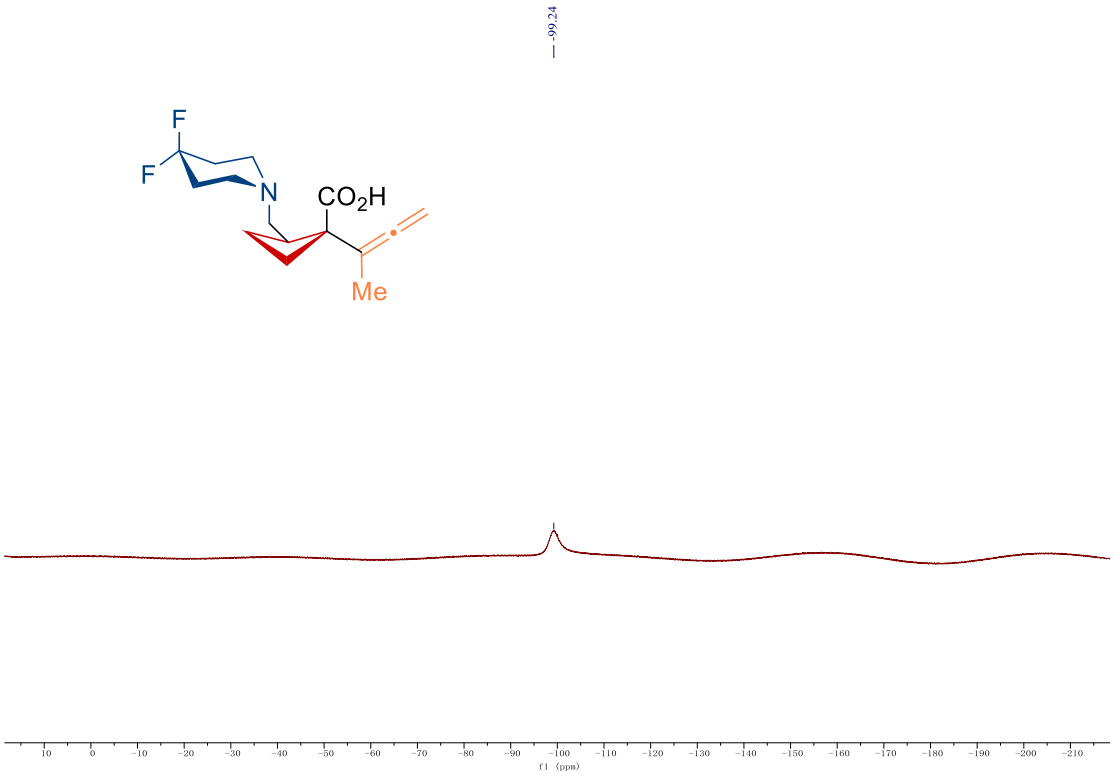
^{13}C NMR of compound **48** (101 MHz, $CDCl_3$)



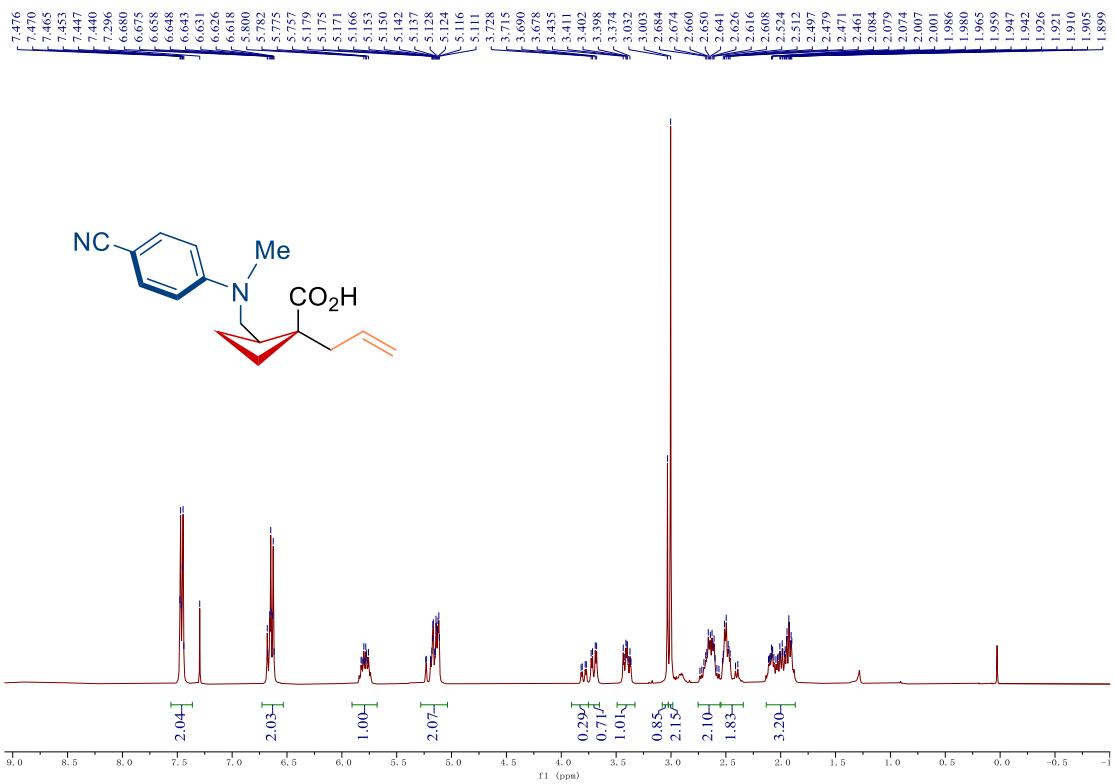
^{1}H NMR of compound **49** (400 MHz, $CDCl_3$)



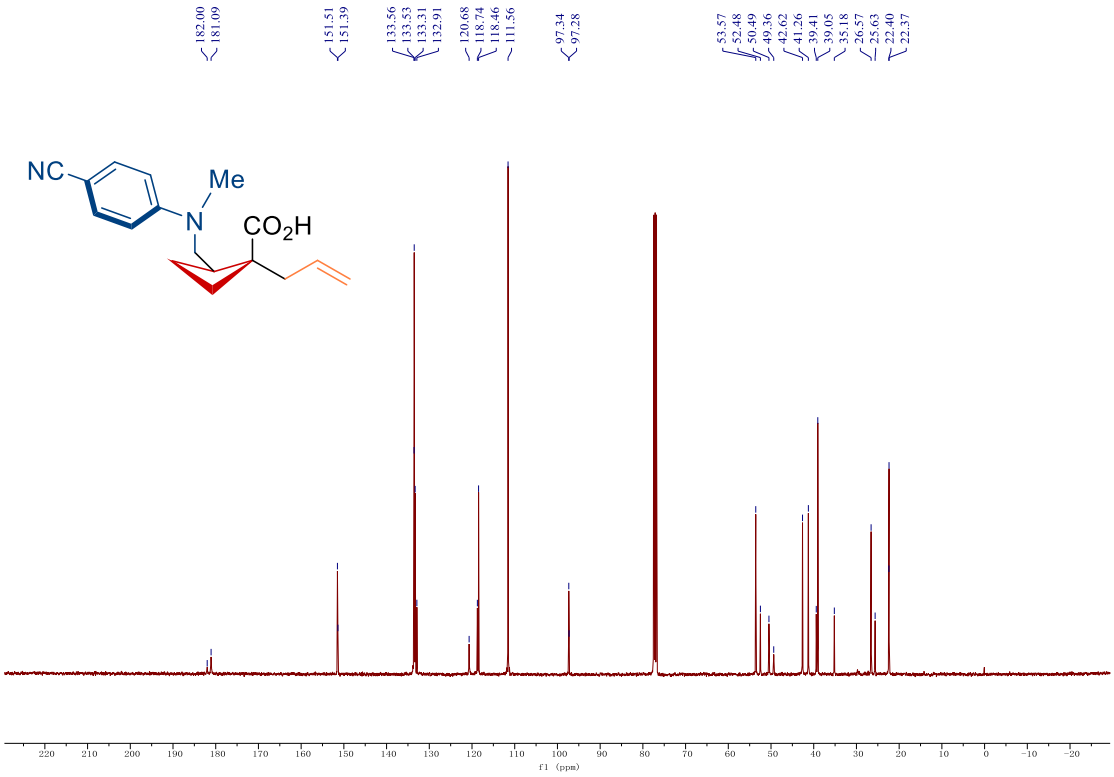
^{13}C NMR of compound **49** (101 MHz, $CDCl_3$)



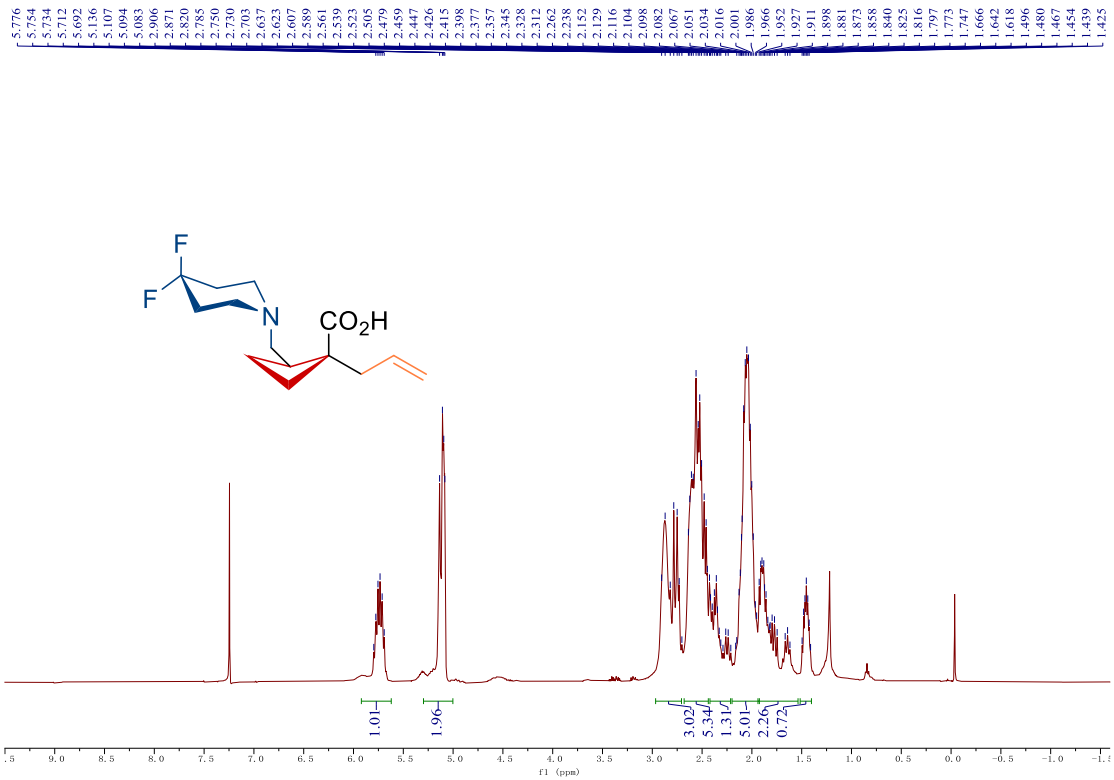
^{19}F NMR of compound **49** (376 MHz, $CDCl_3$)



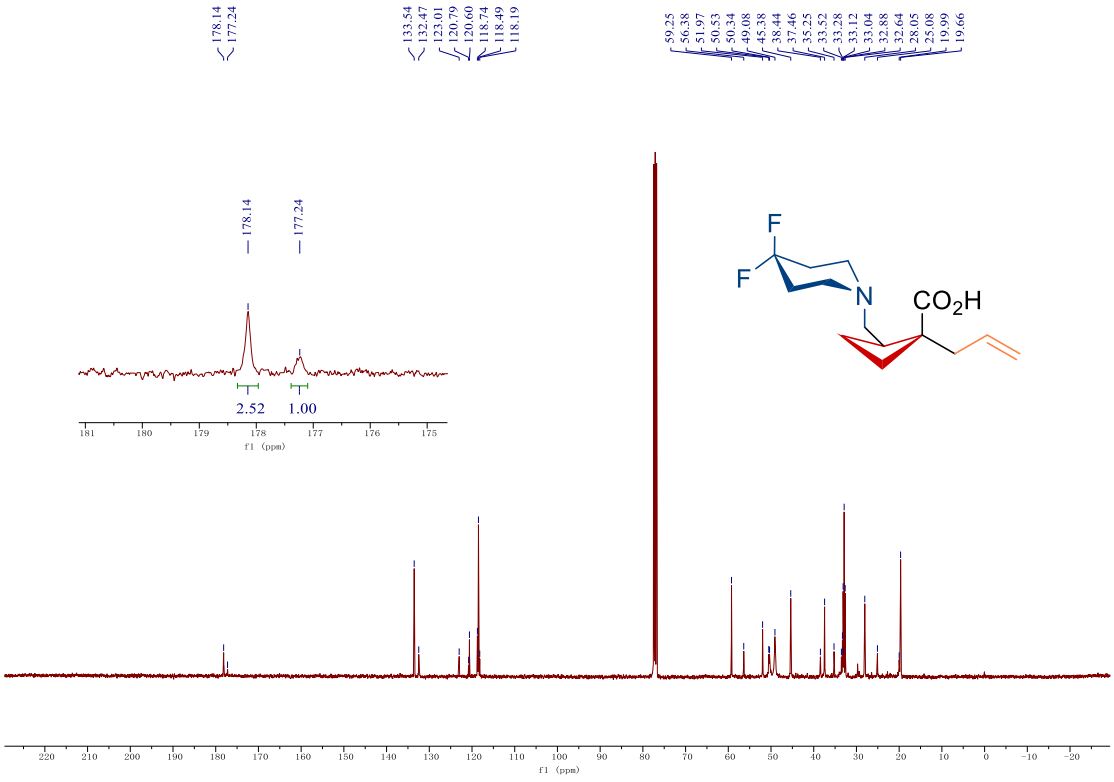
^{1}H NMR of compound **50** (400 MHz, $CDCl_3$)



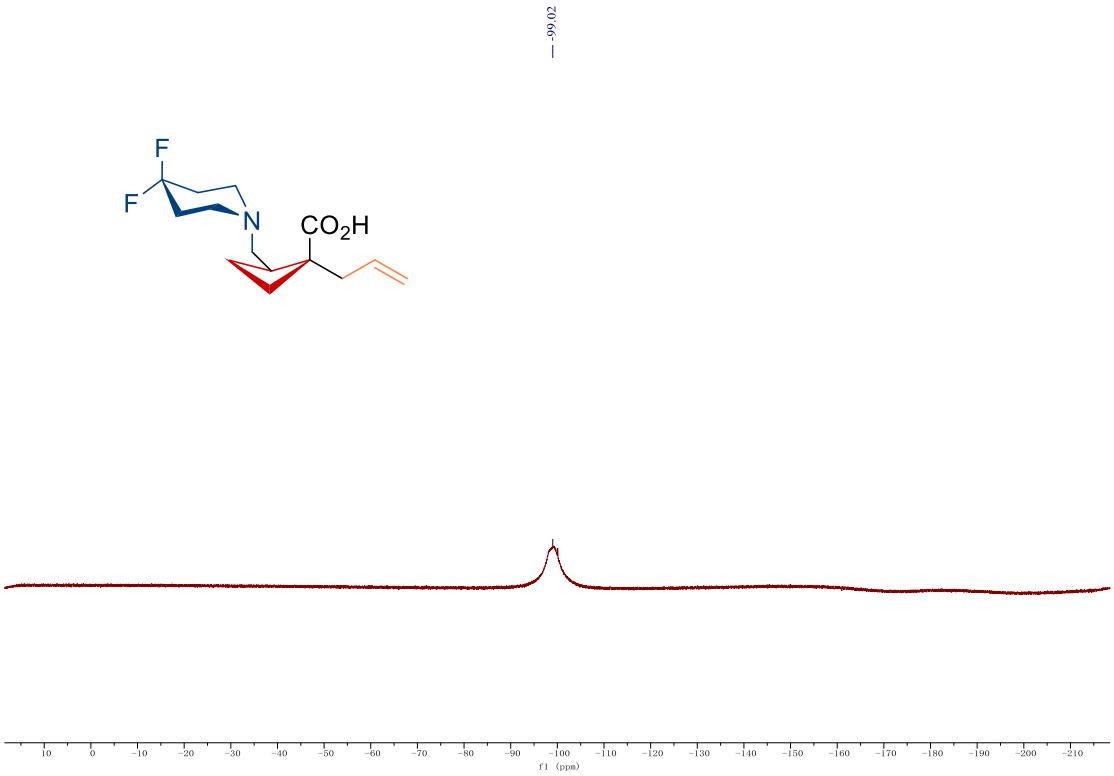
^{13}C NMR of compound **50** (101 MHz, $CDCl_3$)



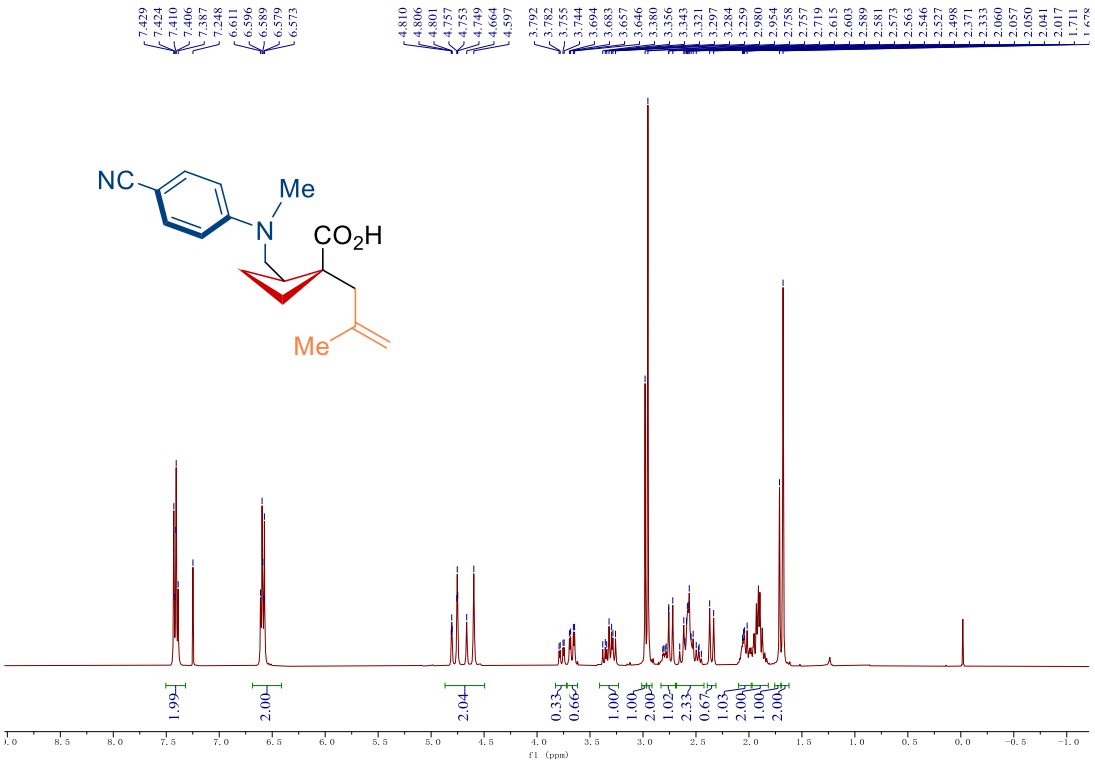
^{1}H NMR of compound **51** (400 MHz, $CDCl_3$)



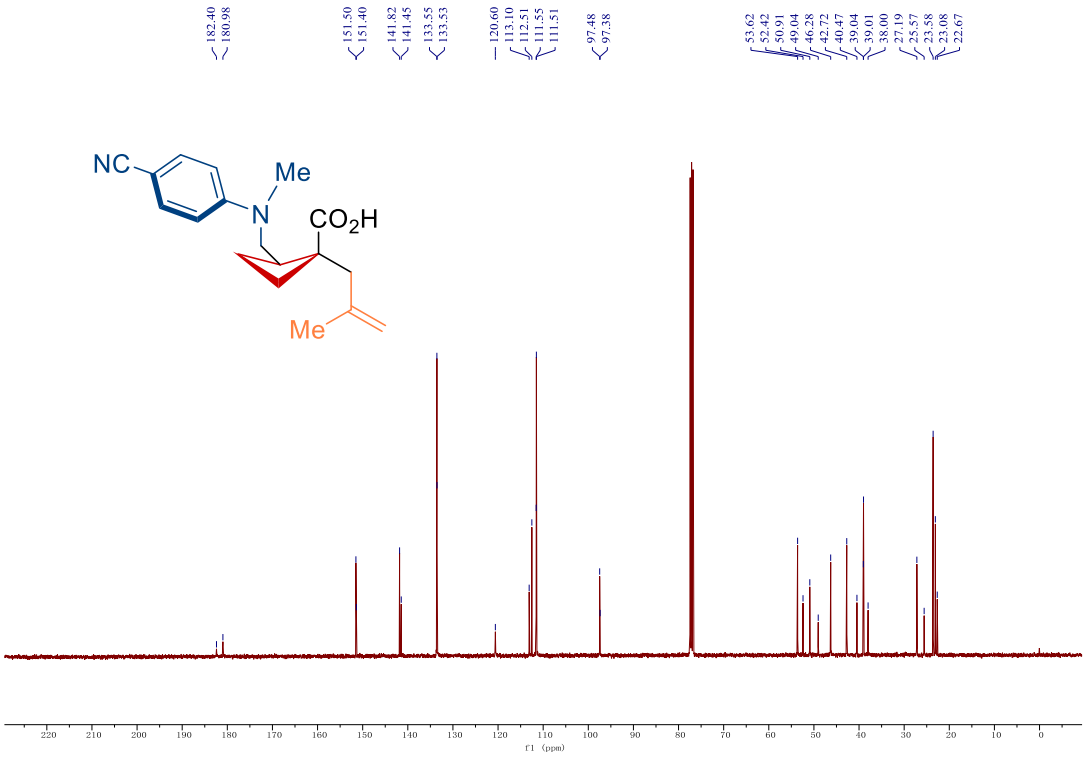
^{13}C NMR of compound **51** (101 MHz, $CDCl_3$)



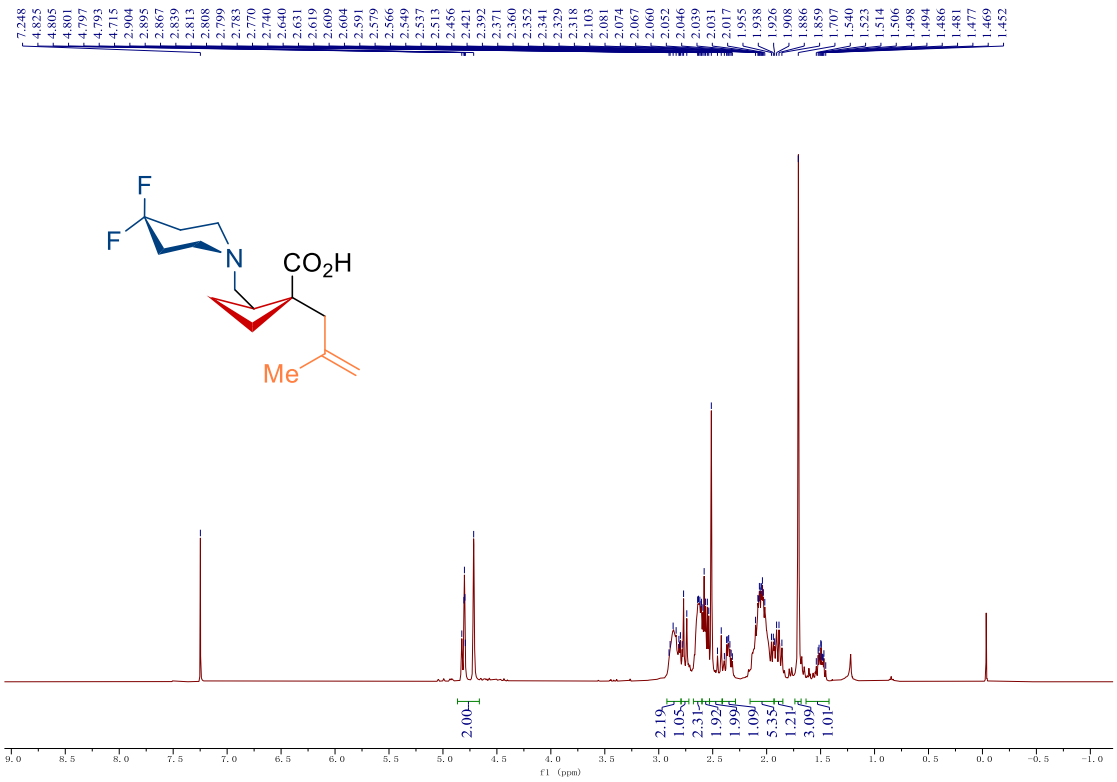
^{19}F NMR of compound **51** (376 MHz, $CDCl_3$)



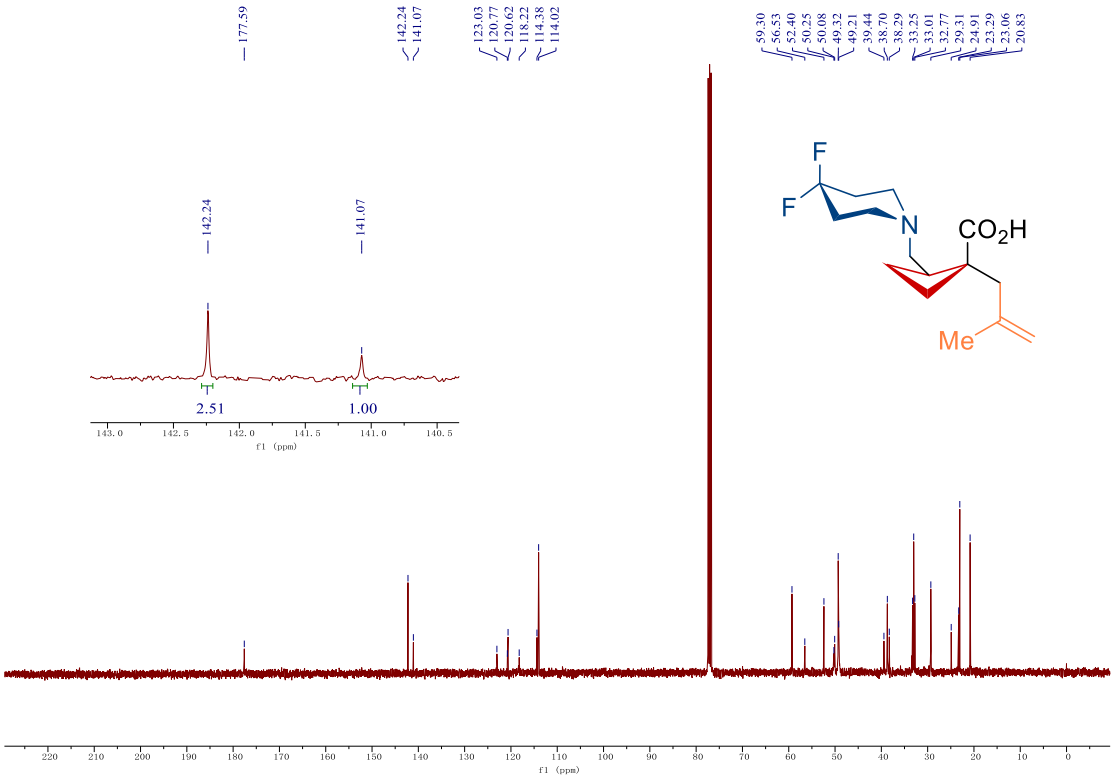
^{1}H NMR of compound **52** (400 MHz, $CDCl_3$)



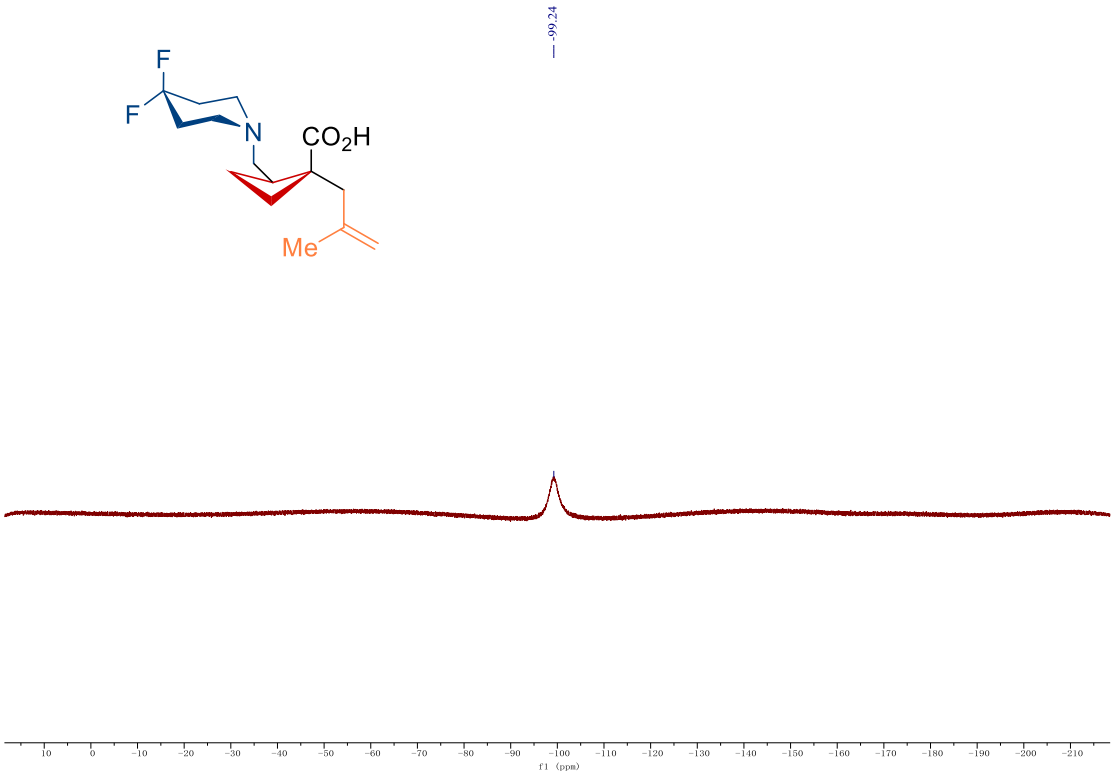
^{13}C NMR of compound **52** (101 MHz, $CDCl_3$)



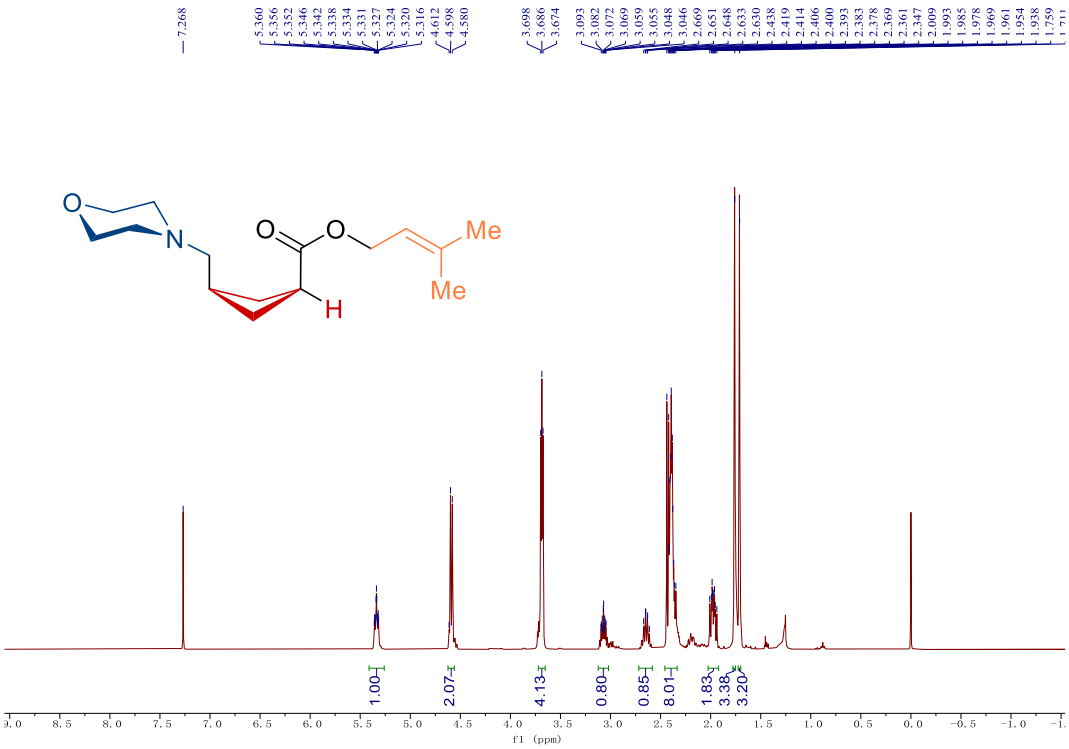
^{1}H NMR of compound **53** (400 MHz, $CDCl_3$)



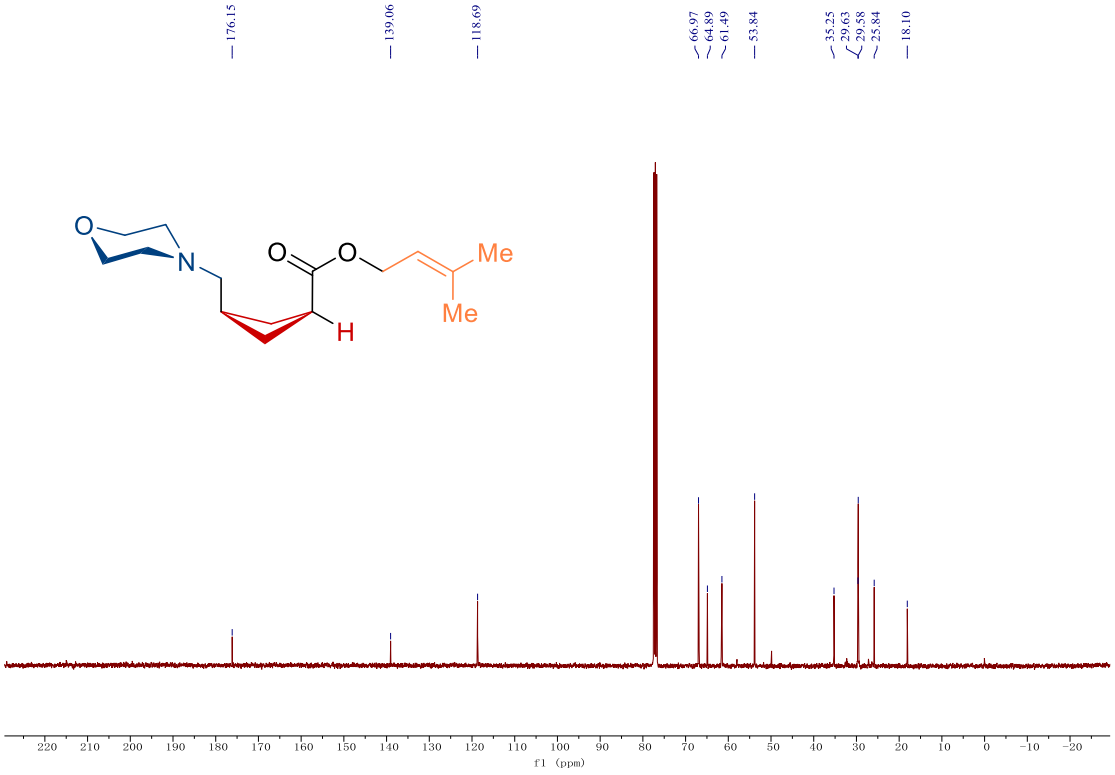
^{13}C NMR of compound **53** (101 MHz, $CDCl_3$)



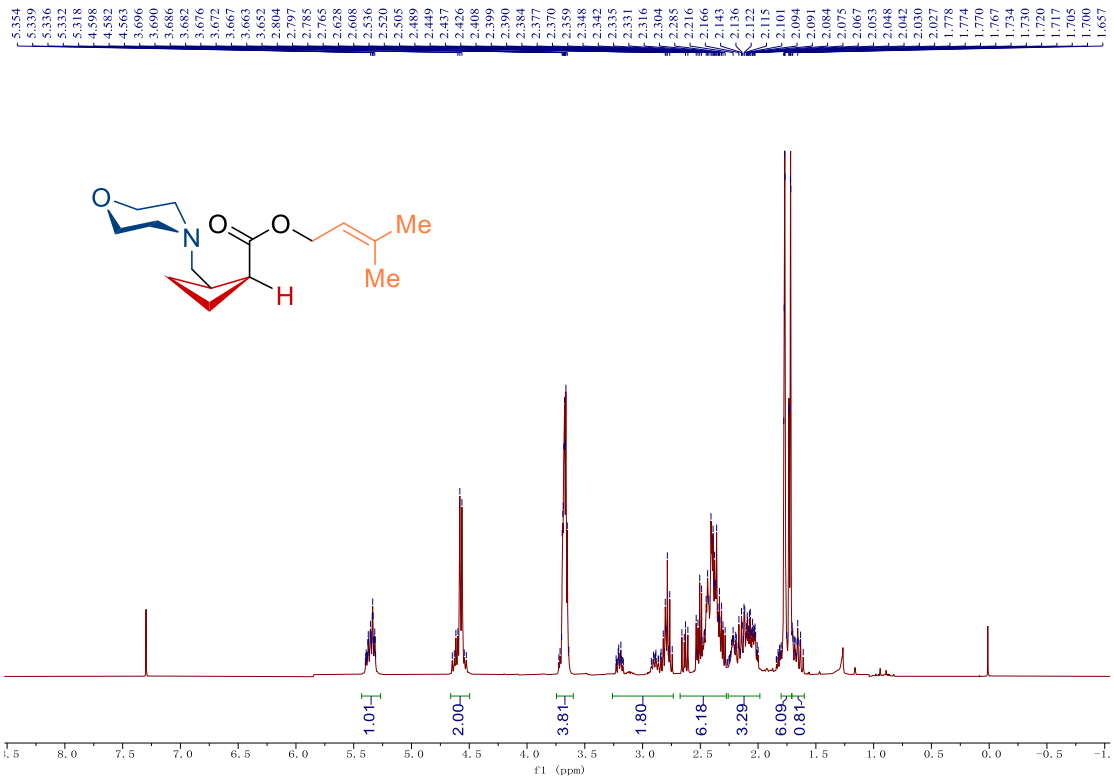
^{19}F NMR of compound **53** (376 MHz, $CDCl_3$)



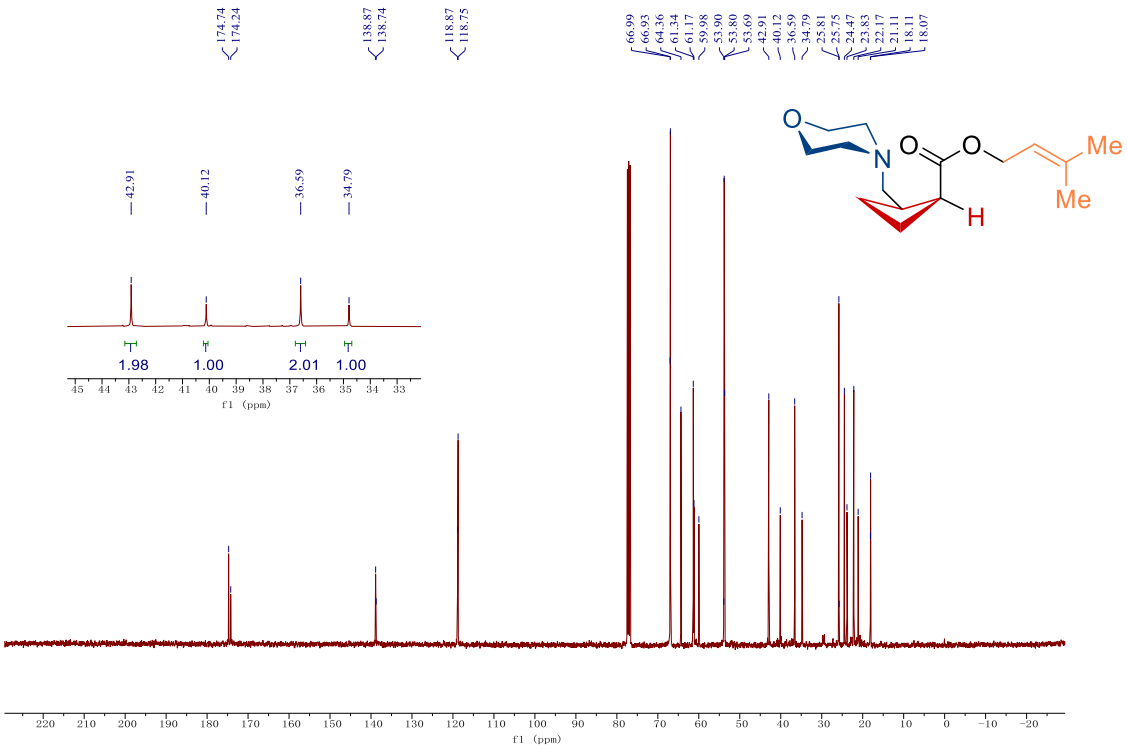
^{1}H NMR of compound **54** (400 MHz, $CDCl_3$)



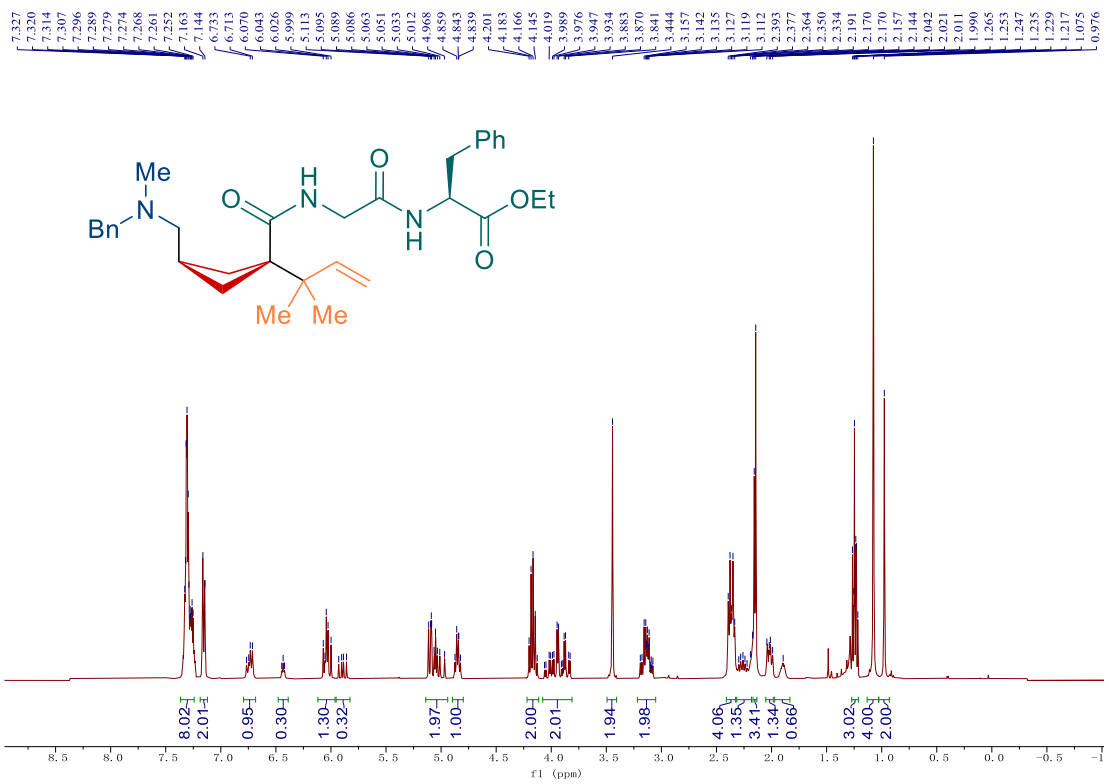
^{13}C NMR of compound **54** (101 MHz, $CDCl_3$)



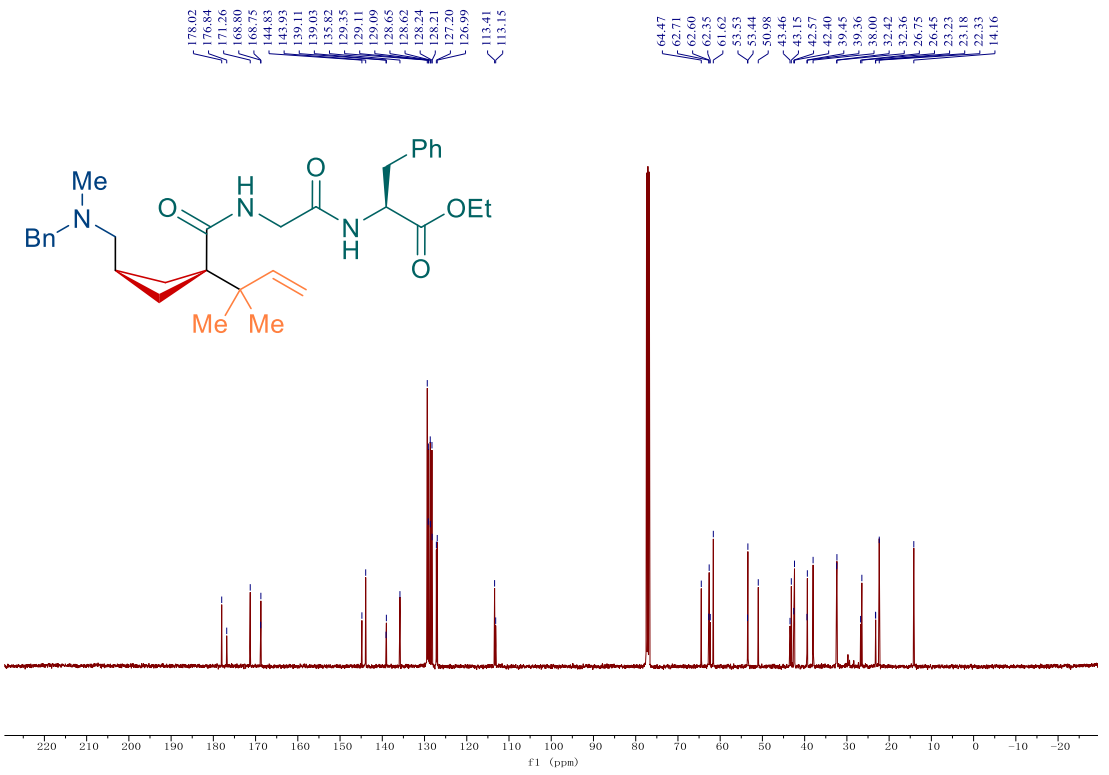
^{1}H NMR of compound **55** (400 MHz, $CDCl_3$)



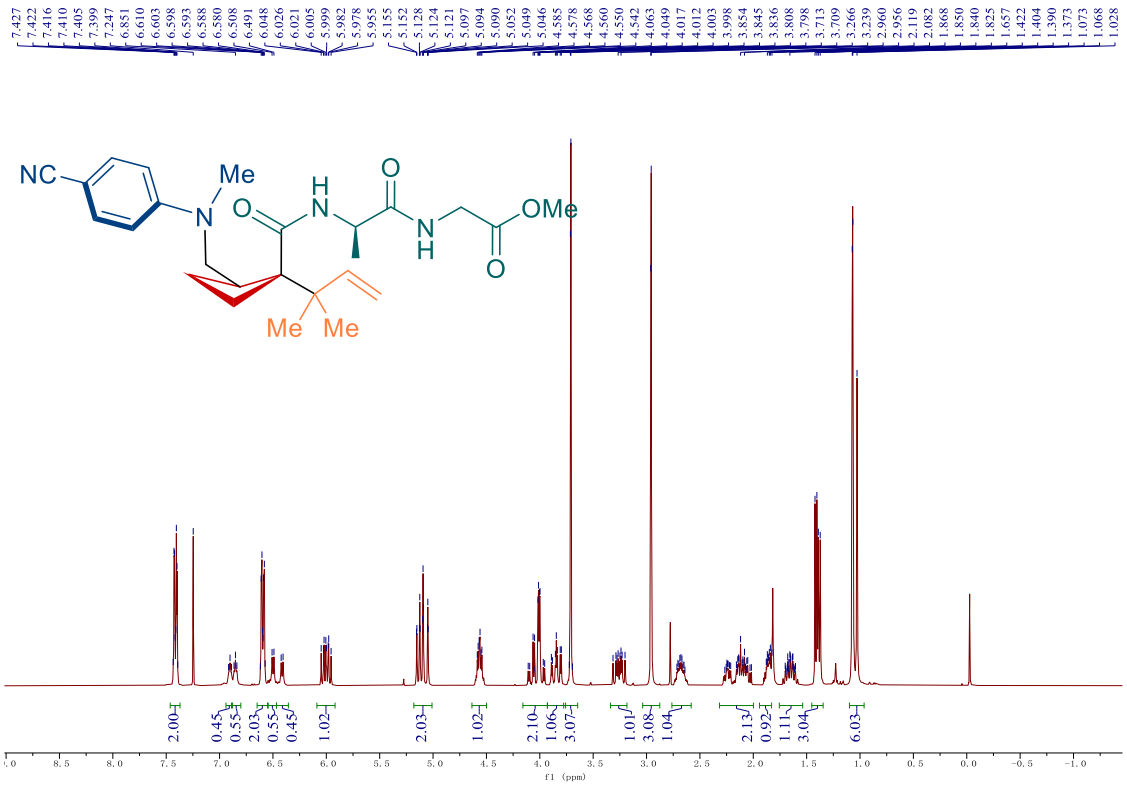
^{13}C NMR of compound **55** (101 MHz, $CDCl_3$)



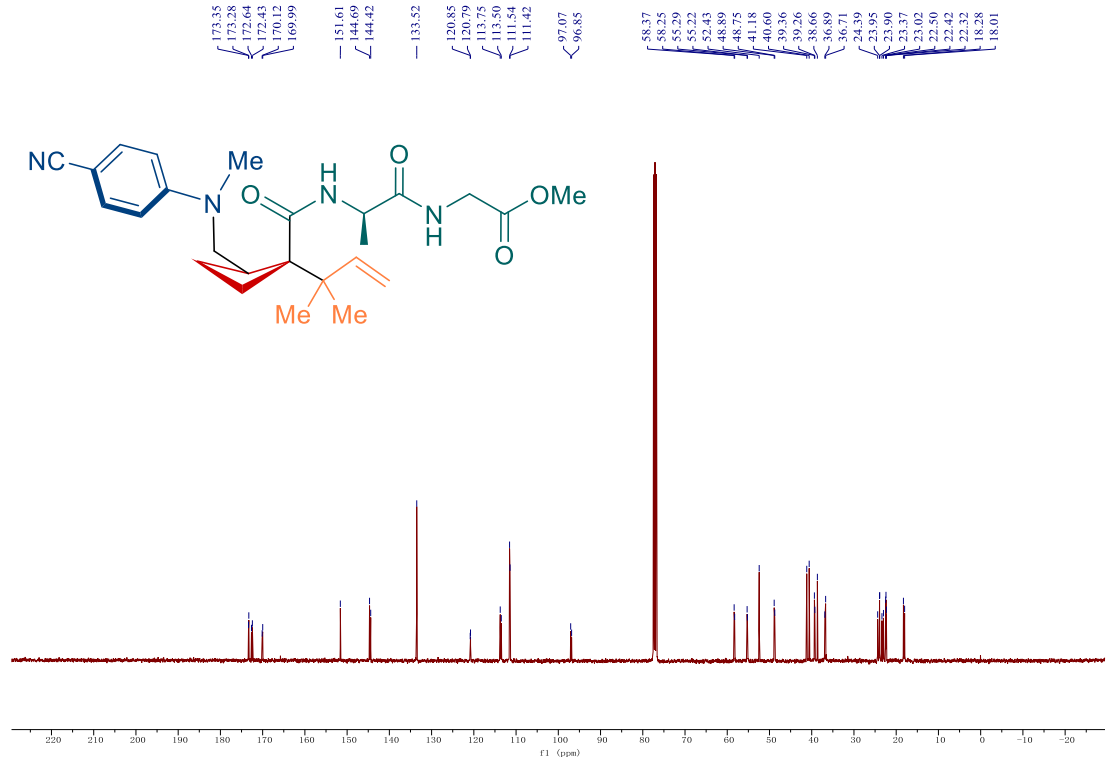
^{1}H NMR of compound **56** (400 MHz, $CDCl_3$)



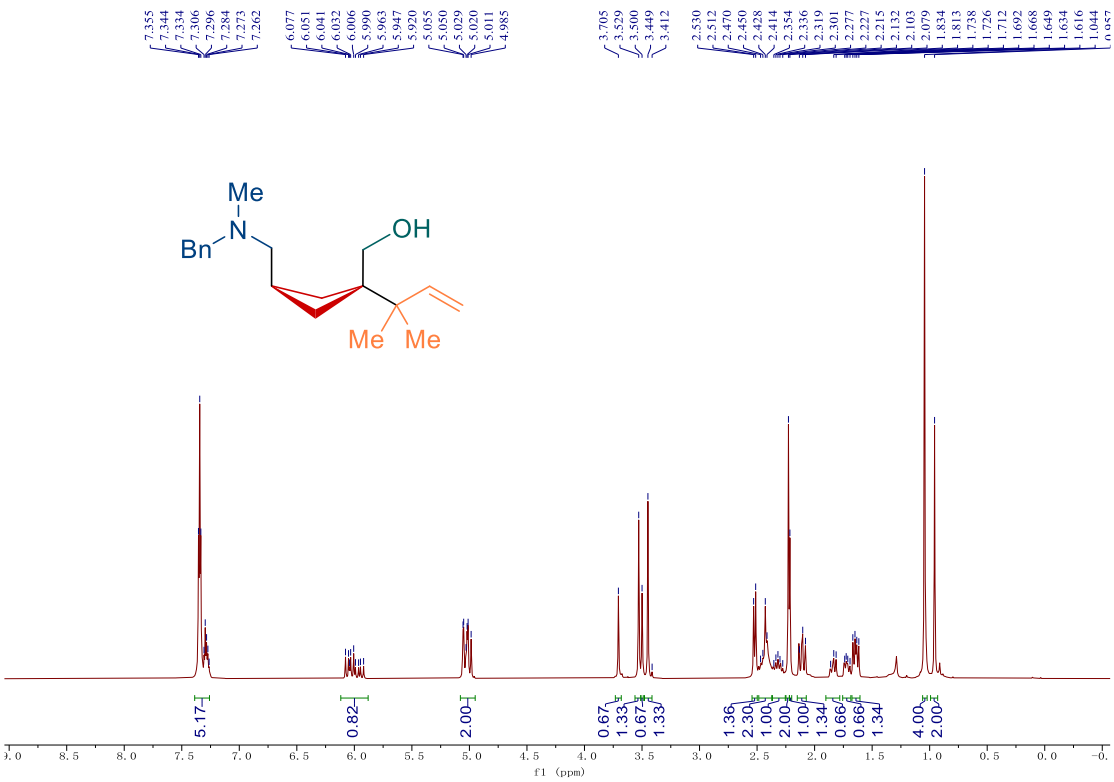
^{13}C NMR of compound **56** (101 MHz, $CDCl_3$)



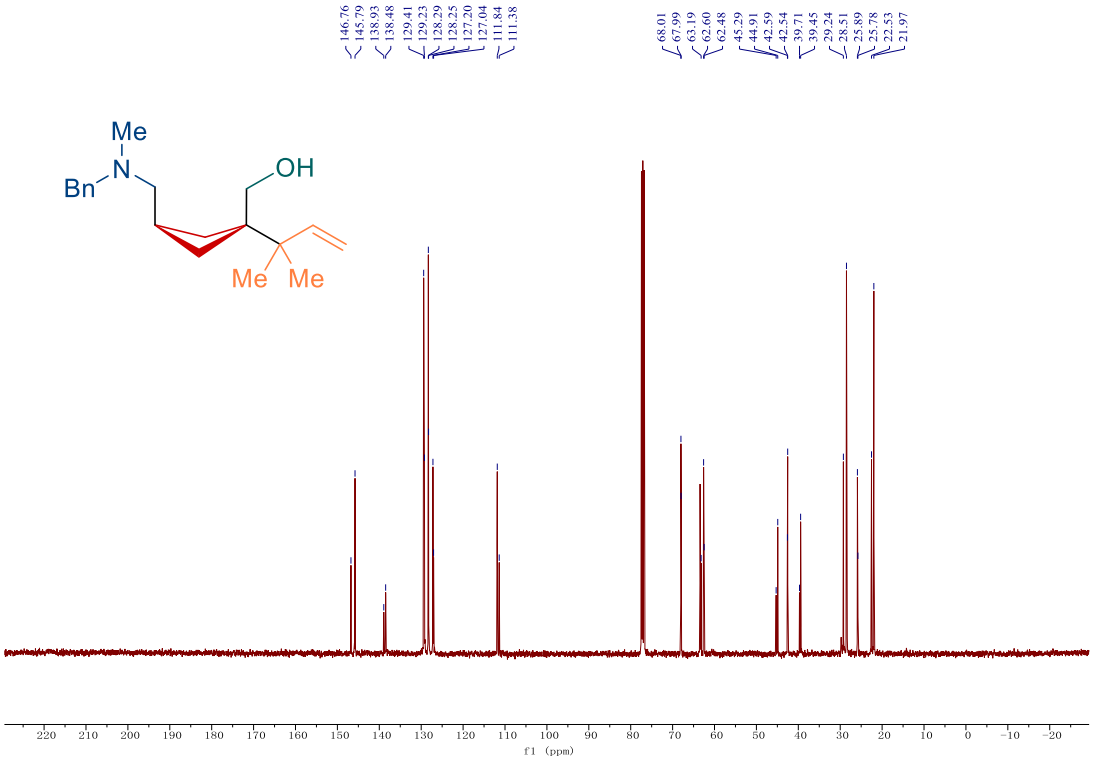
^{1}H NMR of compound **57** (400 MHz, $CDCl_3$)



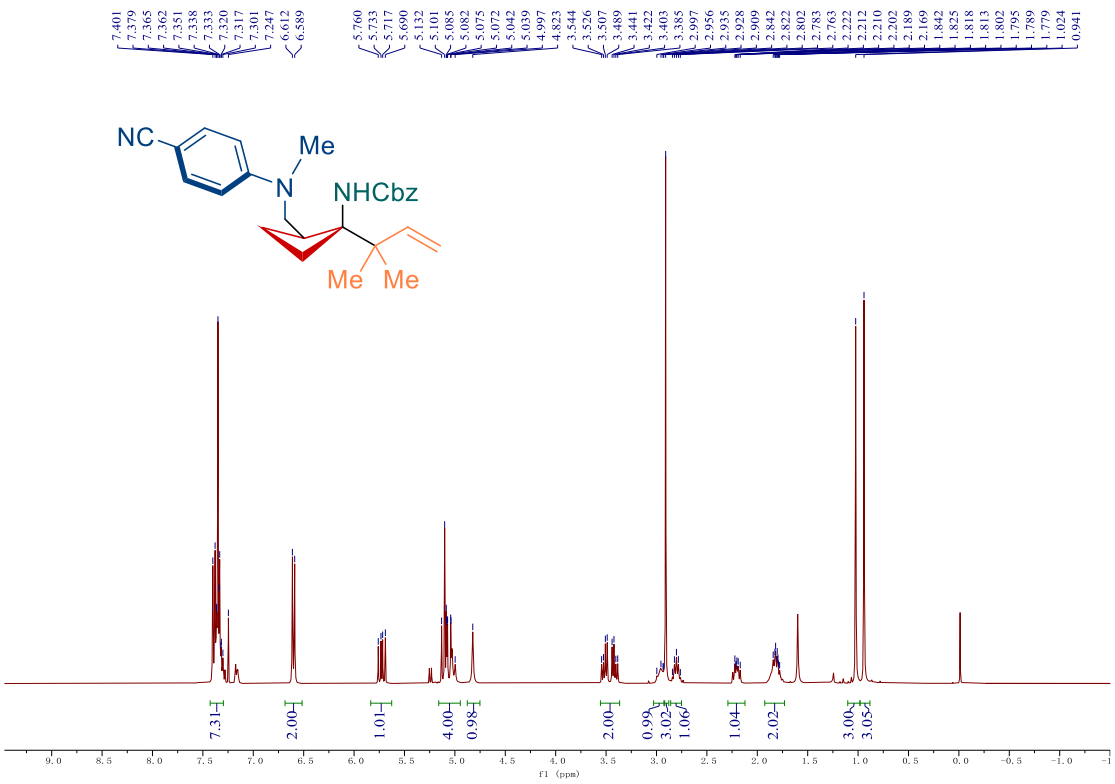
^{13}C NMR of compound **57** (101 MHz, $CDCl_3$)



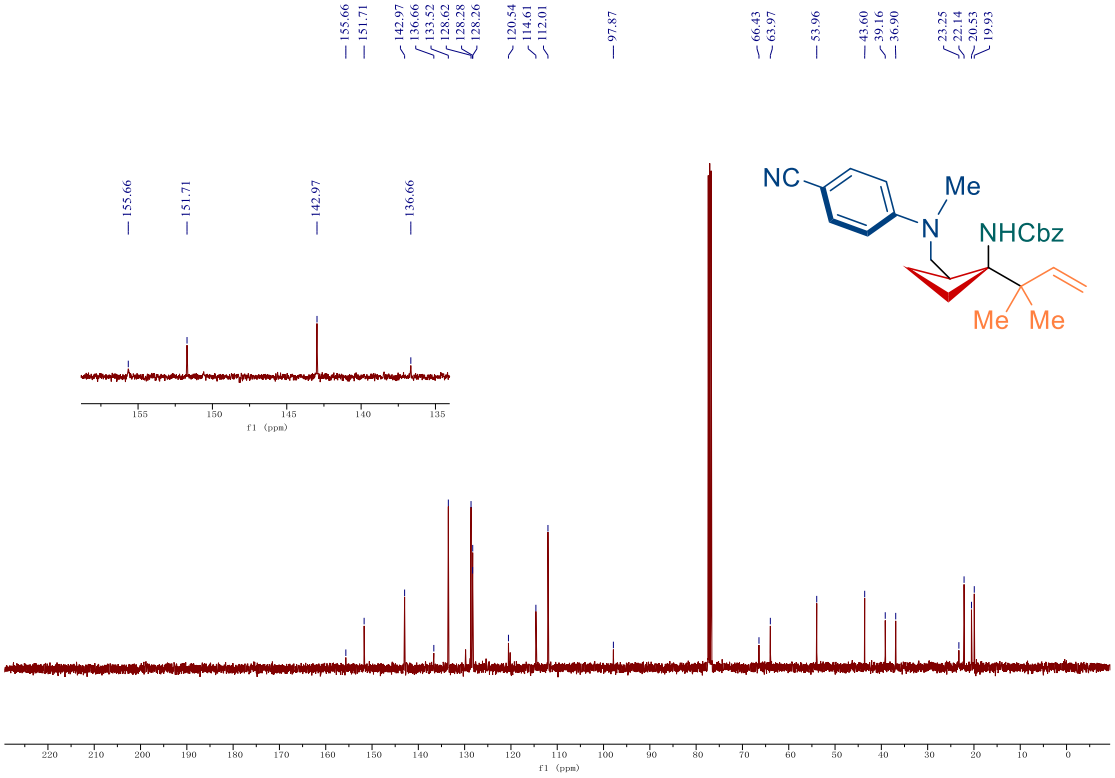
^{1}H NMR of compound **58** (400 MHz, $CDCl_3$)



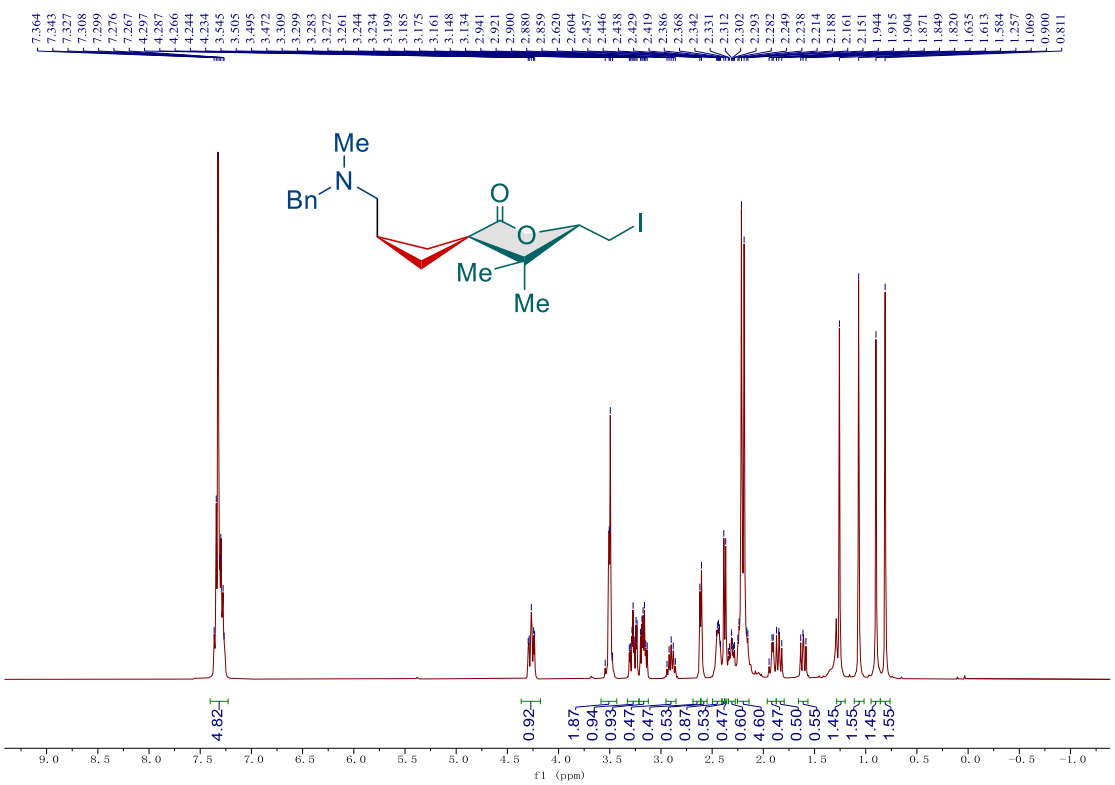
^{13}C NMR of compound **58** (101 MHz, $CDCl_3$)



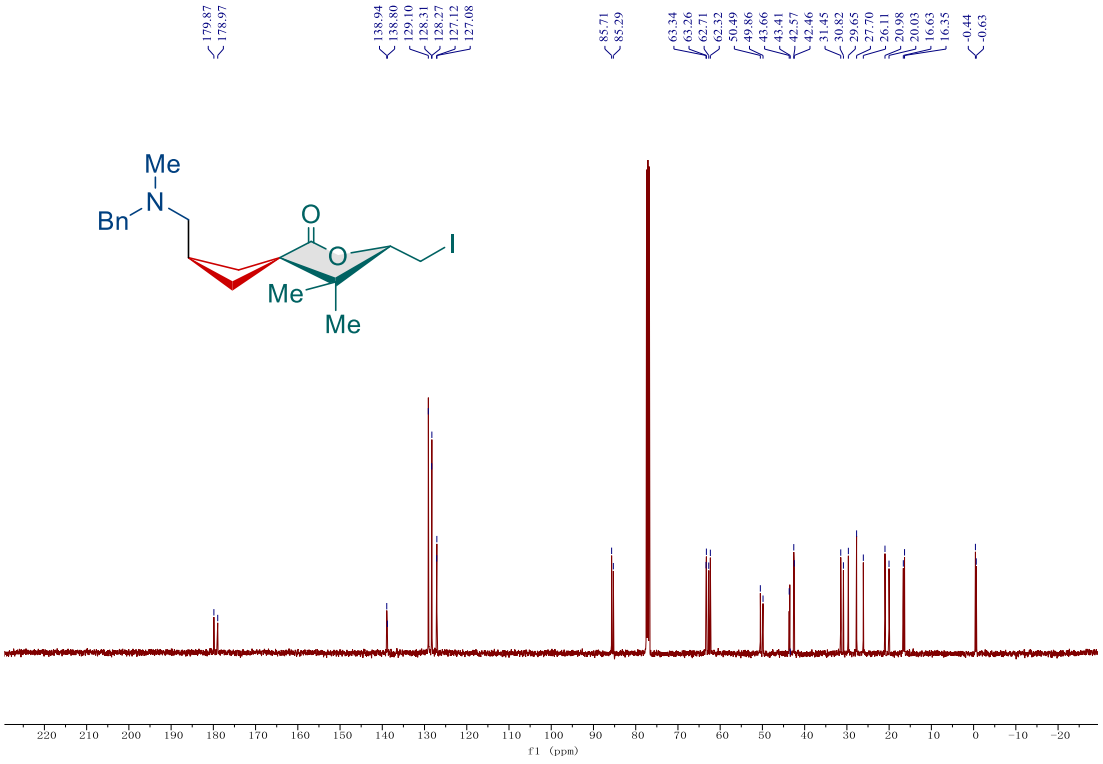
^{1}H NMR of compound **59** (400 MHz, $CDCl_3$)



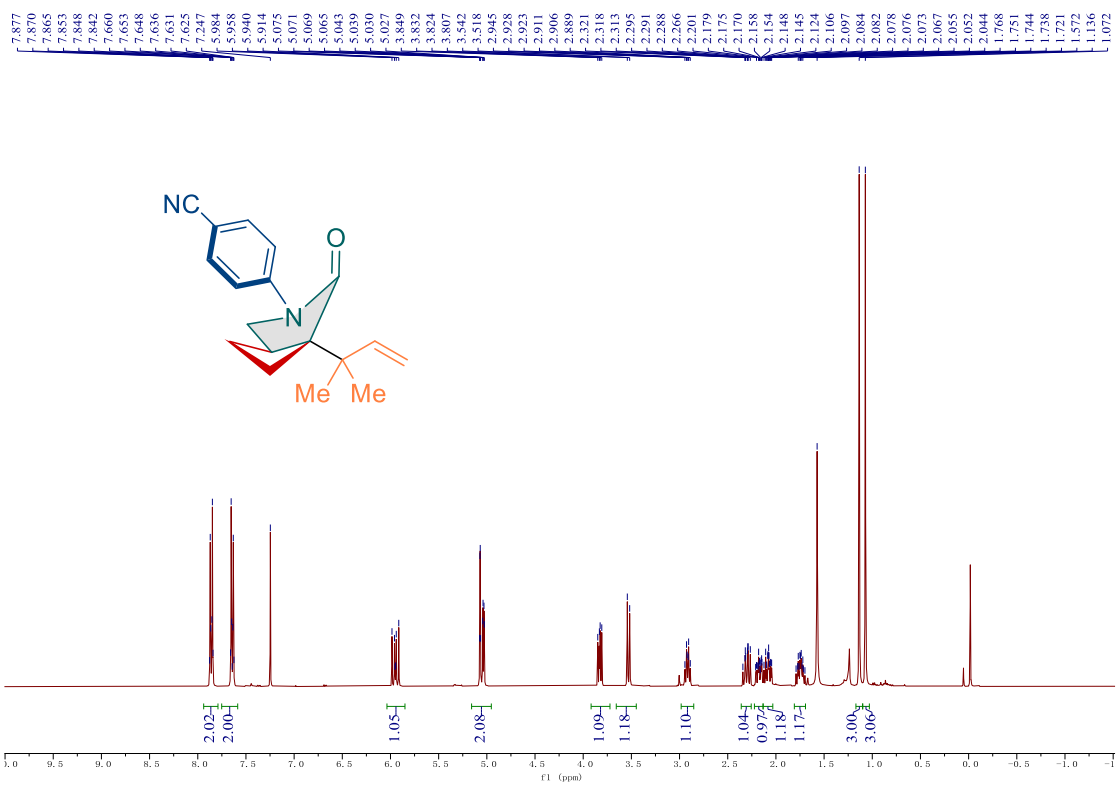
^{13}C NMR of compound **59** (101 MHz, $CDCl_3$)



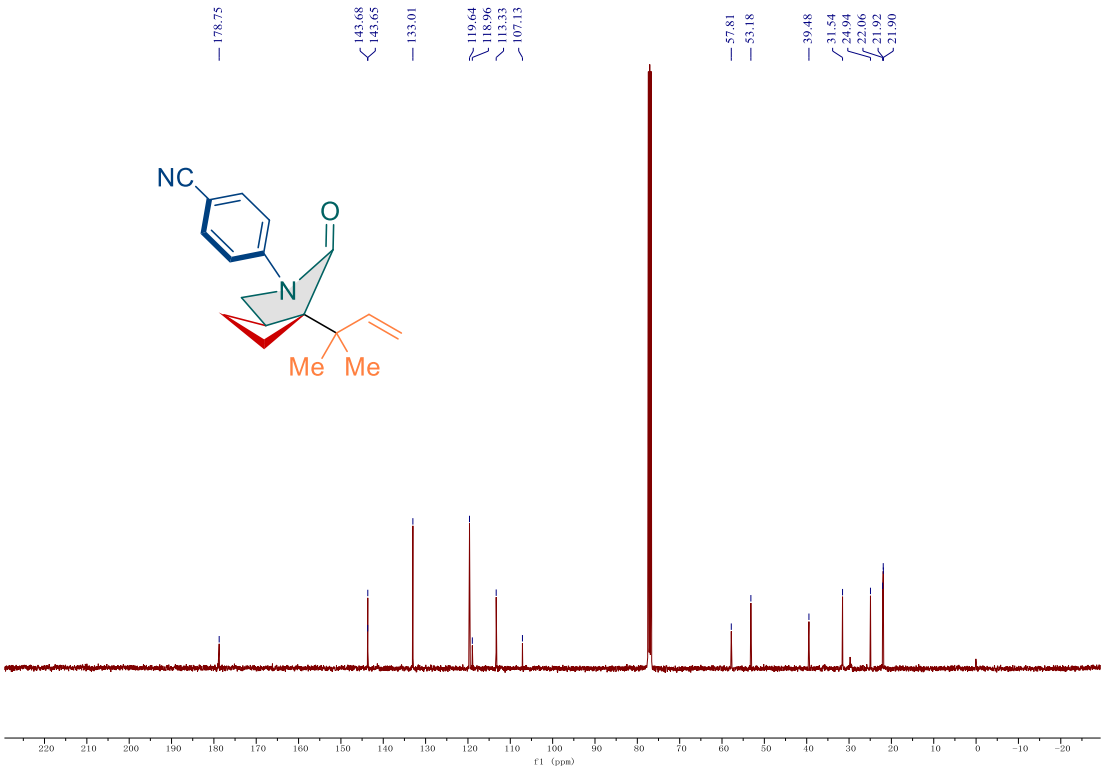
^{1}H NMR of compound **60** (400 MHz, $CDCl_3$)



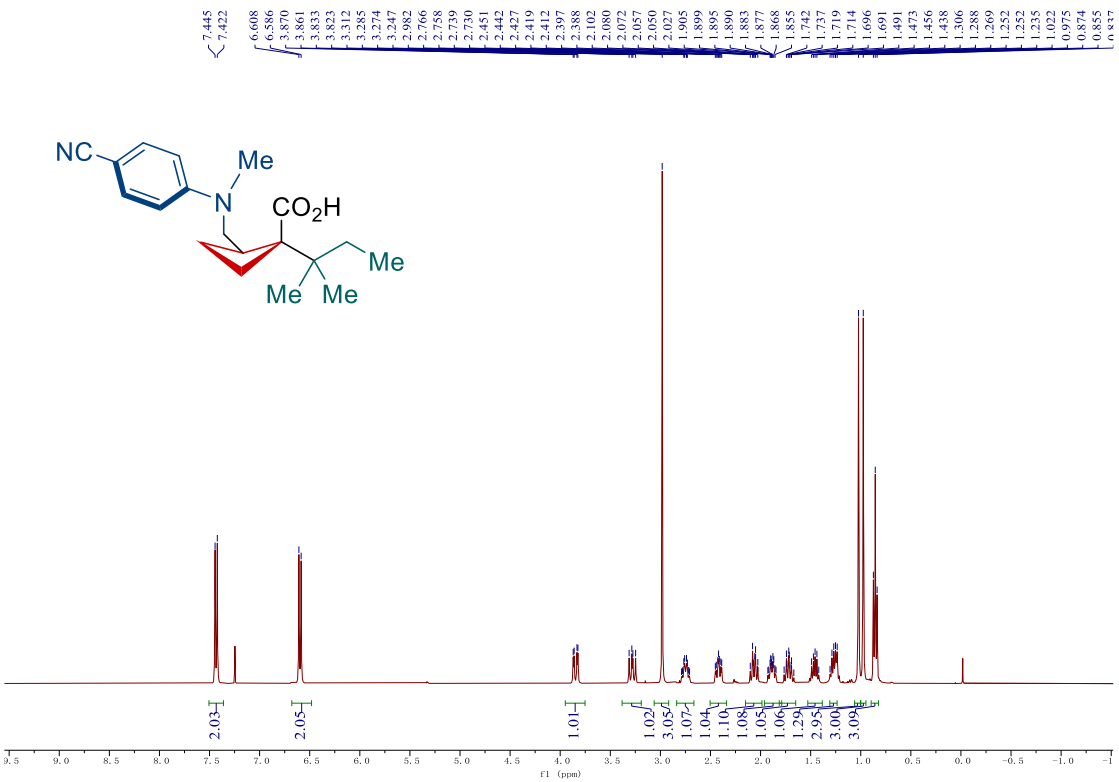
^{13}C NMR of compound **60** (101 MHz, $CDCl_3$)



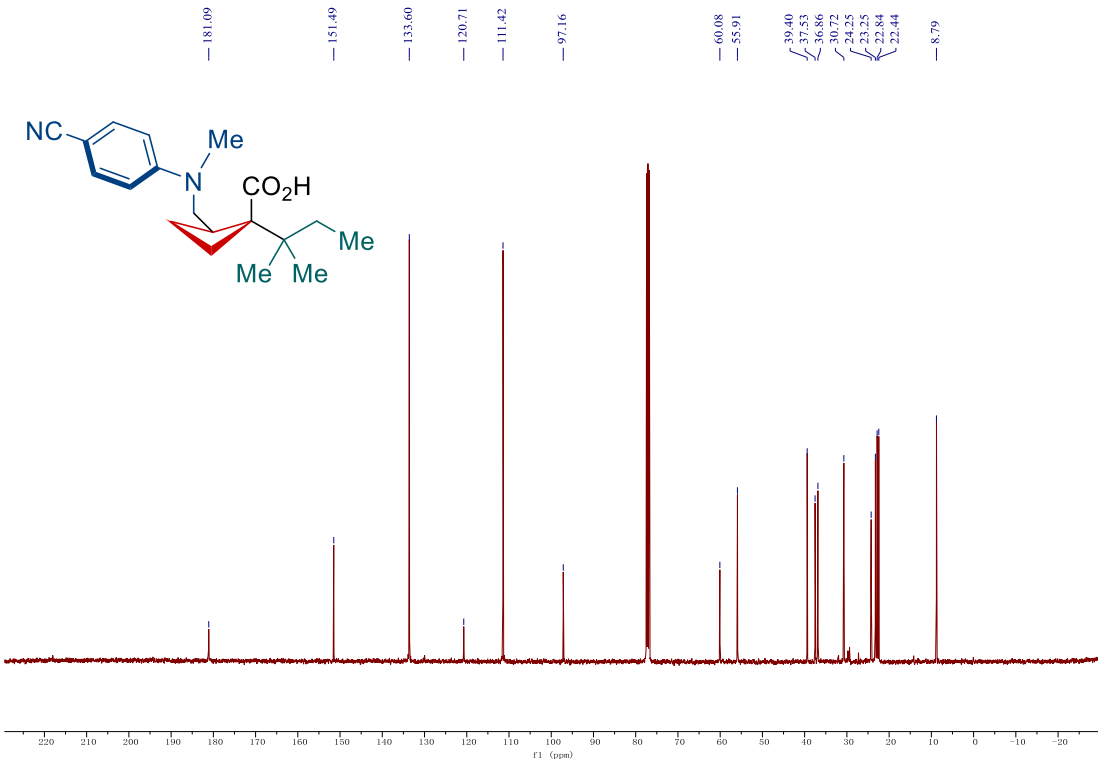
^{1}H NMR of compound **61** (400 MHz, $CDCl_3$)



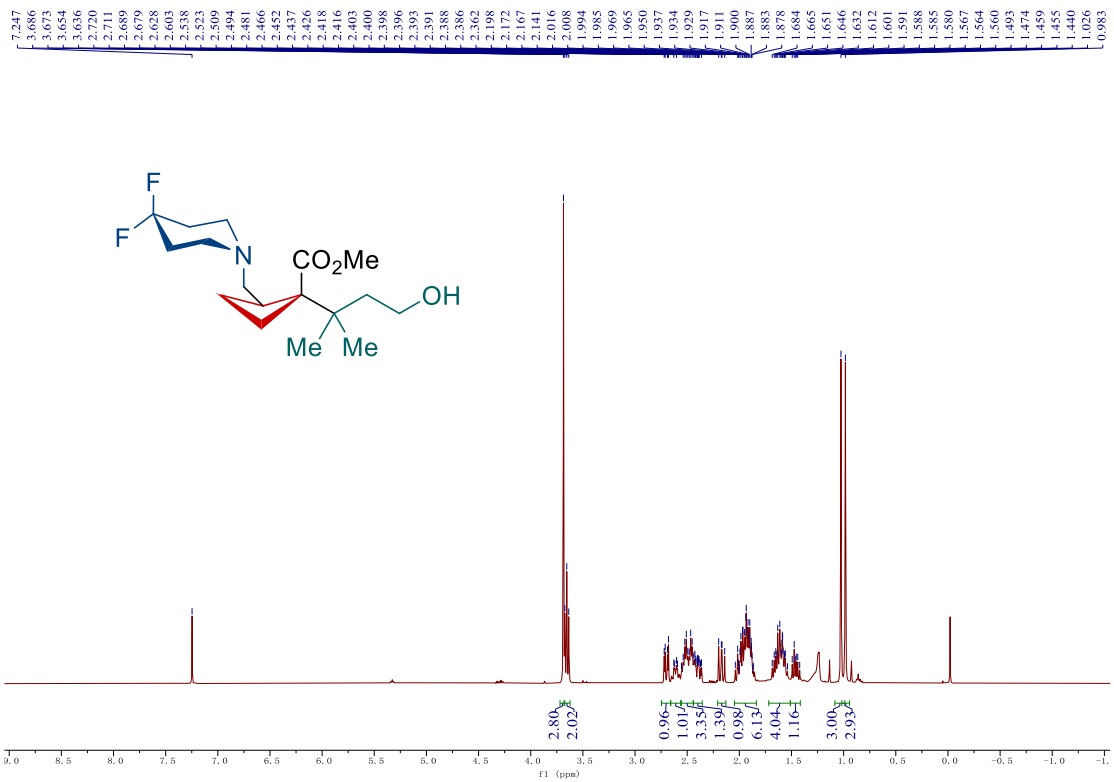
^{13}C NMR of compound **61** (101 MHz, $CDCl_3$)



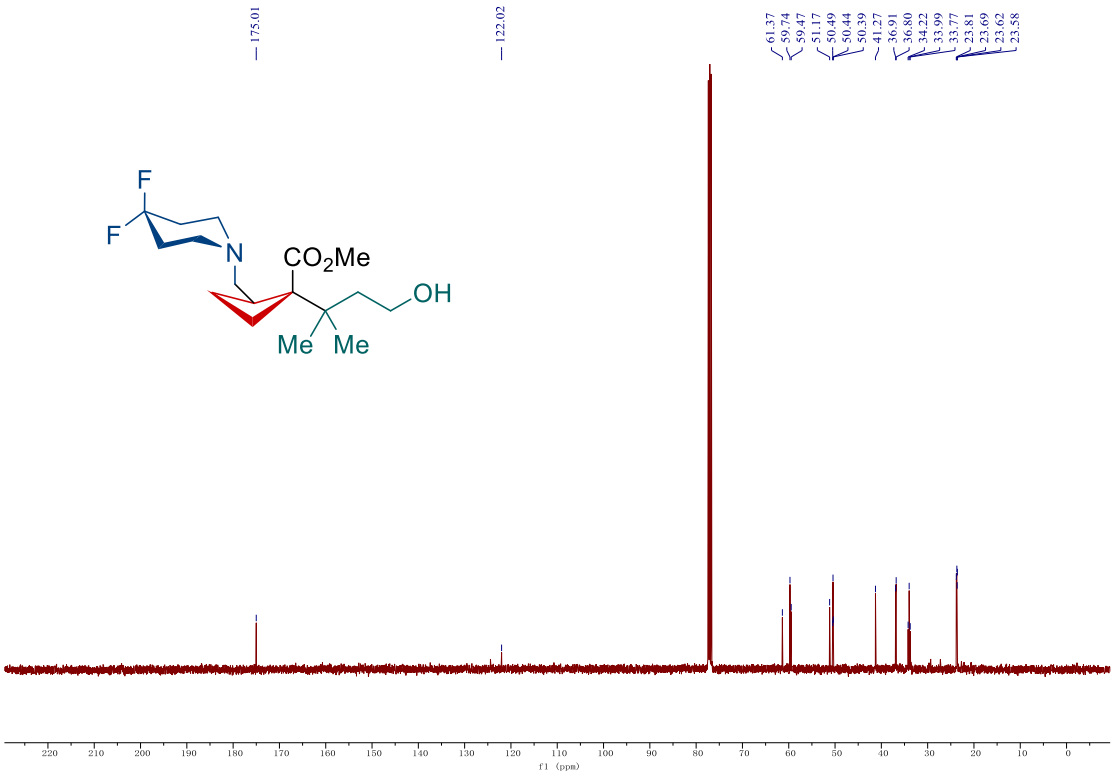
^{1}H NMR of compound **62** (400 MHz, $CDCl_3$)



^{13}C NMR of compound **62** (101 MHz, $CDCl_3$)



^{1}H NMR of compound **63** (400 MHz, $CDCl_3$)



^{13}C NMR of compound **63** (101 MHz, $CDCl_3$)

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