Supplementary Information

Rhodium Catalyzed C–C bond Cleavage/Coupling of 2-(Azetidin-3-ylidene)acetates and Analogs

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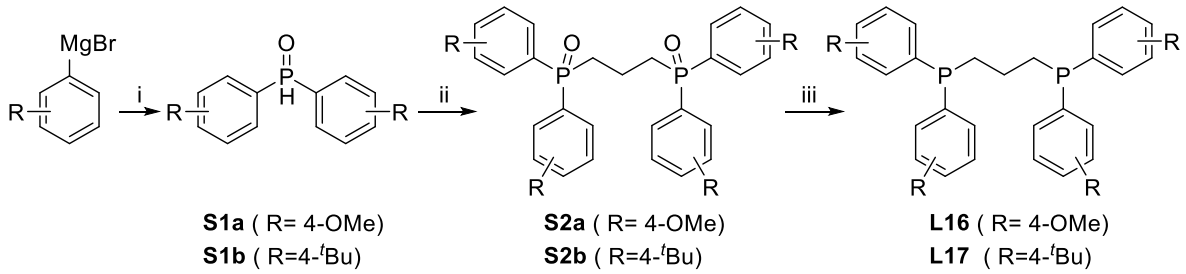
1. General Information

All air or moisture sensitive reactions were conducted in oven-dried glassware under argon atmosphere using dry solvents. Anhydrous solvents were treated as follow: tetrahydrofuran, toluene and *tert*-butyl methyl ether were distilled from sodium under argon atmosphere, dichloromethane was distilled from calcium hydride under argon atmosphere. Unless otherwise noted, other anhydrous solvents and reagents were obtained from commercial sources (Adamas-beta®, Energy Chemical® and 3A Chemicals®) and used without further purification. For product purification by flash column chromatography, silica gel (200~300 mesh). NMR data including ^{1}H NMR, ^{13}C NMR or ^{31}P NMR spectra were recorded on Bruker AVANCE III 500MHz. ^{1}H NMR Chemical shifts were reported in ppm relative to residual signals of the solvents ($CDCl_3$: 7.26 ppm). ^{13}C NMR chemical shifts were reported in ppm relative to the solvent ($CDCl_3$: 77.16 ppm). Chiral HPLC analyses were performed on Agilent 1100 Series using Phenomenex (Lux® 5 μm Amylose-1, 00G-4732-E0, 250 x 4.6 mm) column with hexane/^{i}PrOH as the eluent. High resolution mass spectra were obtained from Thermo Scientific LTQ Orbitrap XL.

2. Preparation of Ligands

Synthesis of ligands L16 and L17[1]



Bis(4-methoxyphenyl)phosphine oxide (S1a)

Into a dried 250 mL Schlenk flask containing Mg (1.32 g, 54.91 mmol) and THF (100 mL) was added a THF (20 mL) solution of *p*-bromoanisole (8.56 g, 45.76 mmol) dropwise at room temperature. The resulting mixture was refluxed for 2 hours with stirring. Then, diethylphosphite (1.48 mL, 11.44 mmol) was added via a syringe to the solution, and stirred at room temperature overnight. Aqueous ammonium chloride solution was introduced to the solution. The mixture was extracted with EtOAc. The organic phase was washed with sodium thiosulfate and sodium carbonate aqueous solutions and then brine. The organic extracts were dried with Na_2SO_4, filtrated and concentrated under vacuum. The residue was then purified by flash column chromatography (PE/EA = 1:10) to give **S1a** as a white powder (1.5 g, 50%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (d, *J* = 479.3 Hz, 1H, PH), 7.56 (dd, *J* = 12.9, 8.6 Hz, 4H, Ar-CH), 6.93 (d, *J* = 8.3 Hz, 4H, Ar-CH), 3.73 (s, 6H, OMe).

^{31}P NMR (202 MHz, $CDCl_3$): δ 20.76.

Bis(4-(*tert*-butyl)phenyl)phosphine oxide (S1b)

The procedure identical to the preparation of **S1a** was employed for the synthesis of **S1b** (1.84g, 74%).

^{1}H NMR (500 MHz, CDCl3): δ 8.09 (d, *J* = 477.4 Hz, 1H, PH), 7.68 (dd, *J* = 12.8, 8.0 Hz, 4H, Ar-CH), 7.56 (d, *J* = 6.8 Hz, 4H, Ar-CH), 1.37 (s, 18H, ^{t}Bu-CH_3).

^{31}P NMR (202 MHz, CDCl3): δ 21.22.

1,3-Bis(di(4-methoxyphenyl)phosphinyl)propane (S2a)

Into a solution of **1a** (1.2 g, 4.6 mmol) in THF (20 mL) was added NaH (0.18 g, 4.5 mmol). After stirred for 30 minutes, 1,3-dibromopropane (409 mg, 2.03 mmol) was

introduced and the mixture was stirred overnight at room temperature. The reaction mixture was quenched with water, extracted with EtOAc. The organic extracts were washed with brine and dried with Na_2SO_4, filtrated and concentrated under vacuum. The residue was then purified by flash column chromatography (MeOH/CH_2Cl_2 = 2:98) to give **S2a** as a white powder (0.6 g, 60%).

^{1}H NMR (500 MHz, CDCl3): δ 7.61–7.54 (m, 8H, Ar-CH), 6.92 (d, *J* = 7.5 Hz, 8H, Ar-CH), 3.82 (s, 12H, OMe), 2.39 (dd, *J* = 17.8, 8.2 Hz, 4H, P(=O)(CH_2)), 1.94 (m, 2H,CH_2).

^{31}P NMR (202 MHz, CDCl3): δ 32.32.

1,3-Bis(di(4-(*tert*-butyl)phenyl)phosphinyl)propane (S2b)

The procedure identical to the preparation of **S2a** was employed for the synthesis of **S2b** (836 mg, 50%).

^{1}H NMR (500 MHz, CDCl3): δ 7.69–7.64 (m, 8H, Ar-CH), 7.48 (d, *J* = 6.7 Hz, 8H, Ar-CH), 2.46 (dd, *J* = 17.9, 8.1 Hz, 4H, P(=O)(CH_2)), 2.05 (m, 2H, CH_2), 1.35 (s, 36H, ^{t}Bu-CH_3).

^{31}P NMR (202 MHz, CDCl3): δ 31.99.

^{13}C NMR (126 MHz, $CDCl_3$): δ 155.07, 155.05, 130.69, 130.61, 130.14, 129.34, 125.69, 125.59, 34.96, 31.23, 31.13, 30.92.

HRMS (ESI): m/z calcd for $C_{43}H_{59}O_2P_2^+$ $(M+H)^+$ 669.3984, found 669.3983.

1,3-Bis(di(4- methoxyphenyl)phosphino)propane (L16)

Into a refluxed solution of **S2a** (0.6 g, 1.2 mmol) and di(*p*-nitrophenyl) phosphoric acid (0.12 g, 0.35 mmol) in toluene (30 mL) was added diethoxymethylsilane (1.28 g, 9.53 mmol) dropwise. The resulting mixture was stirred for 48 hours, and then cooled to 0℃. Then, KOH in methanol (5.8 mL, 3 mol/L) was added slowly. After stirred for 3 hours, the mixture was poured into water, extracted with EtOAc. The organic extracts were washed with brine and dried with Na_2SO_4, filtrated and concentrated under vacuum. The residue was then purified by flash column chromatography (PE/EA = 5:1) to give **L16** as a white powder (321 mg, 51%).

^{1}H NMR (500 MHz, CDCl3): δ 7.33 (dd, *J* = 8.5, 7.1 Hz, 8H, Ar-CH), 6.89 (d, *J* = 8.4 Hz, 8H, Ar-CH), 3.84 (s, 12H, OMe), 2.18-2.12 (dd, 4H, P(=O)(CH_2)), 1.63-1.54 (m, 2H, CH_2).

^{31}P NMR (202 MHz, $CDCl_3$): δ -20.94.

1,3-Bis(di(4-(*tert*-butyl)phenyl)phosphino)propane (L17)[2]

To a mixture of **S2b**(0.56 g, 0.84 mmol) and diisopropylethylamine (5.3 mL, 34.4 mmol) in toluene (10 mL) was added Cl_3SiH (1.44 mL, 1.35 mmol) at 0℃. The reaction mixture was stirred at 110℃ for three days. After cooling to room temperature, the mixture was quenched with 12 N aqueous NaOH and diluted with EtOAc. The resulting suspension was filtered through celite and the solid was washed with EtOAc. The combined organic layer was dried with Na_2SO_4, filtrated and concentrated under vacuum. The residue was then purified by flash column chromatography (PE/EA = 10:1) to give **L17** as white powder (185 mg, 35%).

mp: 110-112℃

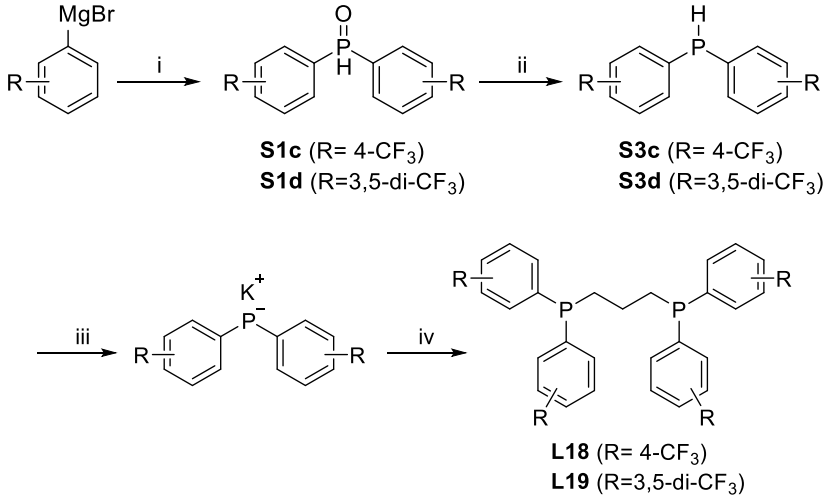
^{1}H NMR (500 MHz, CDCl3): δ 7.38 (dd, *J* = 10.7, 2.6 Hz, 16H, Ar-CH), 2.26–2.20 (m, 4H, P(=O)(CH_2)), 1.70 (m, 2H, CH_2), 1.37 (s, 36H, ^{t}Bu-CH_3).

^{31}P NMR (202 MHz, CDCl3): δ -20.07.

^{13}C NMR (126 MHz, $CDCl_3$): δ 151.49, 135.19, 135.10, 132.61, 132.46, 125.40, 125.35, 34.63, 31.63, 31.30, 30.10.

HRMS (ESI): m/z calcd for $C_{43}H_{59}P_2^+$ $(M+H)^+$ 637.4086, found 637.4083.

Synthesis of ligands L18 and L19



Bis(4-(trifluoromethyl)phenyl)phosphine oxide (S1c)

The procedure identical to the preparation of **S1a** was employed for the synthesis of **S1c** (1.56 g, 58%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (d, *J* = 492.0 Hz, 1H, PH), 7.88 (dd, *J* = 13.2, 8.2 Hz, 4H, Ar-CH), 7.82 (d, *J* = 6.2 Hz, 4H, Ar-CH).

^{31}P NMR (202 MHz, $CDCl_3$): δ 17.82.

Bis(3,5-bis(trifluoromethyl)phenyl)phosphine oxide (S1d)

The procedure identical to the preparation of **S1a** was employed for the synthesis of **S1d** (2.5 g, 56%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.31 (d, *J* = 505.1 Hz, 1H, PH), 8.20 (d, *J* = 13.5 Hz, 4H, Ar-CH), 8.16 (s, 2H, Ar-CH).

^{31}P NMR (202 MHz, $CDCl_3$): δ 14.37.

Bis(4-(trifluoromethyl)phenyl)phosphane (S3c)[3]

A 100 mL flask was equipped with a gas inlet, a bubble counter and an addition funnel. The addition funnel was charged with a solution of the bis (4-(trifluoromethyl) phenyl) phosphine oxide (**S1c**) (1.56 g, 4.61 mmol) in 11 mL THF. This solution was added over a period of 15 minutes to a 1M solution of DIBAL-H in hexane (14.29 ml) and stirred for 30 min at room temperature (caution: gas evolution). Subsequently 20 mL freshly degased MTBE was added via the addition funnel over ten minutes. After cooling the solution to 0℃, 11 mL 2N NaOH aq (freshly degassed) was added via the addition funnel over 15 minutes (caution: vigorous gas evolution), followed by 6 mL sat. aq. NaCl over 5 minutes. The solution was stirred for additional 5 minutes and warmed to room temperature. Stirring was subsequently stopped and the layers allowed separate. The organic layer was then transferred via cannula to a second 100 mL flask charged with Na_2SO_4. After stirring for 10 minutes the mixture was filtered and the solvent removed in vacuo get the phosphine（**S3c**） as a colorless oil (1.1 g, 74%).

Bis(3,5-bis(trifluoromethyl)phenyl)phosphane (S3d)

The procedure identical to the preparation of **S3c** was employed for the synthesis of **S3d** (2.04 g, 84%).

1,3-Bis(di(4-(trifluoromethyl)phenyl)phosphino)propane (L18)[4]

Bis(4-(trifluoromethyl)phenyl)phosphane (1.1 g, 3.4 mmol) was suspended in DMSO (11.7 mL). Addition of an aqueous solution of KOH (0.44 g, 7.9 mmol, H_2O, 0.29 mL,) gave a dark red solution. After stirring for 30 min 1,3-dibromopropane (0.29 g, 1.43 mmol) was added and stirred for a further 48 h at room temperature. The reaction mixture was poured into H_2O. The precipitate was separated, dissolved in MTBE, washed three times with water,

dried with Na_2SO_4, and evaporated. The residue was washed with *n*-pentane and evaporated in vacuo get the product (507 mg, 52%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8.0 Hz, 8H, Ar-CH), 7.50 (t, *J* = 7.4 Hz, 8H, Ar-CH), 2.34–2.29 (m, 4H, P(=O)(CH_2)), 1.65 (m, 2H, CH_2).

^{31}P NMR (202 MHz, $CDCl_3$): δ -17.15.

1,3-Bis{bis[3,5-bis(trifluoromethyl)phenyl]phosphino}-propane (L19)

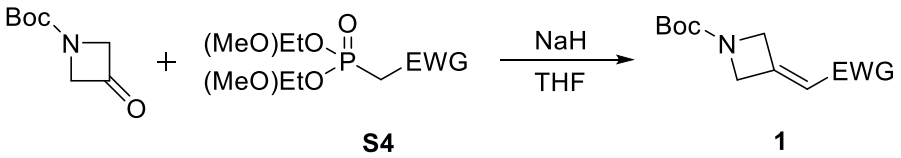
The procedure identical to the preparation of L18 was employed for the synthesis of **L19** (1.16 g, 57%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (s, 4H, Ar-CH), 7.83 (d, *J* = 6.0 Hz, 8H, Ar-CH), 2.44–2.38 (m, 4H, P(=O)(CH_2)), 1.66 (m, 2H, CH_2).

^{31}P NMR (202 MHz, $CDCl_3$): δ -15.45.

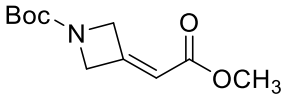
3. Preparation of Substrates

General Procedure A



S4 **1**

A suspension of NaH (60% dispersion in mineral oil, 269 mg, 6.72 mmol) in 25 mL of THF was cooled in a 100 mL flask in an ice bath. A solution of **S4** (1.1 mL, 6.72 mmol, 1.15 equiv.) in THF (20 mL) was added drop-wise. The reaction was warmed to room temperature for 1 h then cooled back to 0 ℃. Then a solution of *tert*-butyl 3-oxoazetidine-1- carboxylate (1.0 g, 5.84 mmol) in THF (10 mL) was added drop-wise over 30 min. The resulting reaction mixture was stirred overnight at room temperature, then quenched with water and concentrated to remove THF. The resulting aqueous solution was extracted with EtOAc. The combined organic layers were washed with brine and dried with Na_2SO_4, filtrated and concentrated under vacuum. The residue was then purified by flash column chromatography to give product[5].

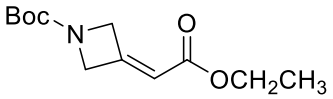


1a

***Tert*-butyl 3-(2-methoxy-2-oxoethylidene)azetidine-1-carboxylate (1a)**

This compound was prepared according to the general procedure A as a white solid (1.2 g, 91%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.84 (s, 1H, =CH), 4.86 (dd, *J* = 6.4, 2.8 Hz, 2H, NCH_2), 4.64 (dd, *J* = 5.4, 3.3 Hz, 2H, NCH_2), 3.77 (s, 3H, OMe), 1.50 (s, 9H, ^{t}Bu-CH_3).

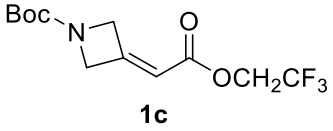


1b

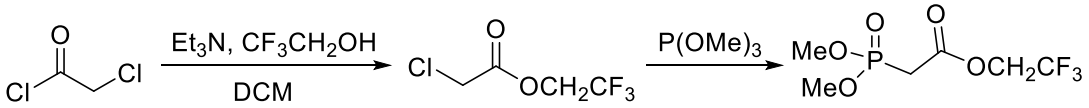
***Tert*-butyl 3-(2-ethoxy-2-oxoethylidene)azetidine-1-carboxylate (1b)**

This compound was prepared according to the general procedure A as colorless oil (2.8 g, 66%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.65 (s, 1H, =CH), 4.68 (dd, *J* = 6.2, 2.8 Hz, 2H, NCH_2), 4.46 (dd, *J* = 5.3, 2.9 Hz, 2H, NCH_2), 4.04 (q, *J* = 7.1 Hz, 2H, OCH_2), 1.32 (s, 9H, ^{t}Bu-CH_3), 1.14 (t, *J* = 7.2 Hz, 3H).



1c



S4a

2,2,2-Trifluoroethyl 2-(dimethoxyphosphoryl)acetate (S4a)[6]

To a solution of 2,2,2-trifluoroethanol (5.28 g, 52.8 mmol) in dichloromethane (14 mL) was added dropwise triethylamine (4.86 g, 48 mmol) during 15 min, and then chloroacetyl chloride (5.43 g, 48 mmol) in dichloromethane (14 mL) was added dropwise during 30 min. The solution was refluxed for 2 h and stirred overnight at room temperature. The formed triethylammonium salt was removed by filtration, and the filtrate was washed successively with 2 N HCl and saturated Na_2CO_3, dried with Na_2SO_4. The solvent was evaporated, the crude product was distilled and the fraction with boiling range of 120 ℃ was collected (3.3 g, 39%).

A mixture of 2,2,2-trifluoroethyl chloroacetate (3.3 g, 18.65 mmol) and trimethyl phosphite (2.55 g, 20.66 mmol) were added to a round bottom flask and stirred for 48h at 80℃. The volatile components were evaporated under reduced pressure and the residue was purified by column chromatography (EtOAc) to give 2,2,2-trifluoroethyl phosphonoacetate (**S4a**) as colorless oil (1.89 g, 41%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.51 (q, *J* = 8.4 Hz, 2H, P(=O)(CH_2)), 3.80 (d, *J* = 11.3 Hz, 6H, OMe), 3.07 (d, *J* = 21.7 Hz, 2H, OCH_2).

***Tert*-butyl 3-(2-oxo-2-(2,2,2-trifluoroethoxy)ethylidene)azetidine-1-carboxylate (1c)**

This compound was prepared according to the general procedure A as a white solid (376 mg, 73%).

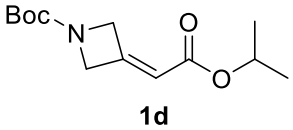
mp: 72-73℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.87 (s, 1H, =CH), 4.83 (s, 2H, NCH_2), 4.63 (s, 2H, NCH_2),

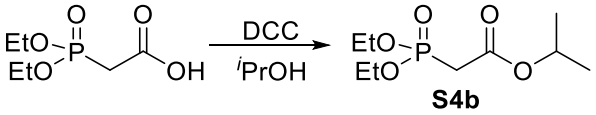
4.51 (q, J = 8.1 Hz, 2H, OCH_2), 1.46 (s, 9H, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 163.18, 156.40, 156.10, 126.24, 124.04, 121.83, 119.63, 111.98, 80.32, 60.64, 60.35, 60.05, 59.76, 28.30.

HRMS (ESI): m/z calcd for $C_{12}H_{17}F_3NO_4^+$ $(M+H)^+$ 296.1104, found 296.1109.



1d



S4b

Isopropyl 2-(diethoxyphosphoryl)acetate (S4b)[7]

To a solution of 2-(diethoxyphosphoryl) acetic acid (1 g, 5.1 mmol) in dichloromethane (5 mL) was added a solution of DCC (1.05 g, 5.1 mmol) in dichloromethane (5 mL). The reaction mixture was stirred for 1 h at room temperature, filtrated and concentrated under vacuum. The residue was purified by flash chromatography (PE/EA = 5:1) to give **S4b** (1.1 g, 91%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.83–4.72 (m, 1H, OCH), 3.97–3.87 (m, 4H, OCH_2), 2.68 (d, J = 21.6 Hz, 2H, P(=O)(CH_2)), 1.09 (dd, J = 9.4, 4.8 Hz, 6H, CH_3), 1.01 (d, J = 6.3 Hz, 6H, ^{i}Pr-CH_3).

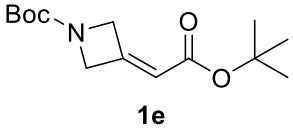
***Tert*-butyl 3-(2-isopropoxy-2-oxoethylidene)azetidine-1-carboxylate (1d)**

This compound was prepared according to the general procedure A as colorless oil (341 mg, 73%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.74 (s, 1H, =CH), 5.04 (m, 1H, OCH), 4.82 (dd, J = 6.2, 3.0 Hz, 2H, NCH_2), 4.59 (dd, J = 5.3, 3.3 Hz, 2H, NCH_2), 1.46 (s, 9H, ^{t}Bu-CH_3), 1.26 (d, J = 6.3 Hz, 6H, ^{i}Pr-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 164.77, 156.19, 152.17, 114.20, 80.02, 67.83, 28.32, 21.92.

HRMS (ESI): m/z calcd for $C_{13}H_{22}NO_4^+$ $(M+H)^+$ 256.1543, found 256.1540.

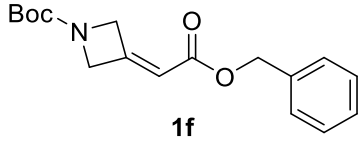


1e

***Tert*-butyl 3-(2-(*tert*-butoxy)-2-oxoethylidene)azetidine-1-carboxylate (1e)**

This compound was prepared according to the general procedure A as colorless oil (1.05 g, 67%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.71 (s, 1H, =CH), 4.83 (m, 2H, NCH_2), 4.60 (m, 2H, NCH_2), 1.50 (d, *J* = 8.0 Hz, 18H, ^{t}Bu-CH_3).

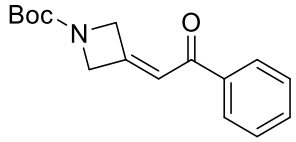


1f

***Tert*-butyl 3-(2-(benzyloxy)-2-oxoethylidene)azetidine-1-carboxylate (1f)**

This compound was prepared according to the general procedure A as colorless oil (624 mg, 61%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (s, 5H, Ar-CH), 5.82 (d, *J* = 12.1 Hz, 1H, =CH), 5.17 (s, 2H, OCH_2), 4.83 (m, 2H, NCH_2), 4.60 (m, 2H, NCH_2), 1.47 (s, 9H, ^{t}Bu-CH_3).



1g

***Tert*-butyl 3-(2-oxo-2-phenylethylidene)azetidine-1-carboxylate (1g)**

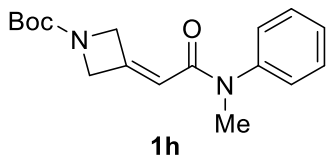
This compound was prepared according to the general procedure A as a white solid (416 mg, 75%).

mp: 122-124℃

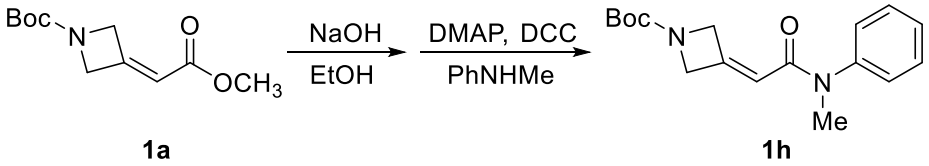
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (d, *J* = 7.4 Hz, 2H, Ar-CH), 7.58 (t, *J* = 7.4 Hz, 1H, Ar-CH), 7.49 (t, *J* = 7.6 Hz, 2H, Ar-CH), 6.98 (s, 1H, =CH), 5.03–4.96 (m, 2H, NCH_2), 4.71 (m, 2H, NCH_2), 1.49 (s, 9H, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 189.02, 156.26, 154.56, 137.70, 133.08, 128.74, 128.20, 115.90, 80.03, 30.89, 28.36.

HRMS (ESI): m/z calcd for $C_{16}H_{20}NO_3^+$ $(M+H)^+$ 274.1437, found 274.1439.



1h



1a **1h**

***Tert*-butyl 3-(2-(methyl(phenyl)amino)-2-oxoethylidene)azetidine-1-carboxylate (1h)**

To a solution of *tert*-butyl 3-(2-methoxy-2-oxoethylidene)azetidine-1-carboxylate (**1a**) (1.5 g, 8.76 mmol) in methanol (4 mL) was added 2 N NaOH (8.76 ml). The reaction mixture was stirred at room temperature until the starting material disappeared (monitored by TLC). Then the pH was adjusted to 1.0 with HCl (2 N), extracted with CH_2Cl_2, dried with Na_2SO_4, filtrated and concentrated under vacuum to give product[8].

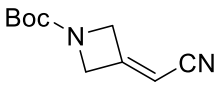
The above product (500 mg, 2.35 mmol), N-methylaniline (252 mg, 2.35 mmol), DMAP (57 mg, 0.47 mmol), and dichloromethane (15 ml) were added to a 100 ml three-neck round bottom flask. A solution of dicyclohexylcarbodiimide (581 mg, 2.82 mmol) in DCC (10 mL) was added drop-wise over 30 min at 0℃. The reaction mixture was stirred at room temperature overnight until the starting material disappeared (monitored by TLC). Filtrated and concentrated under vacuum, the residue was purified by column chromatography (EtOAc) to give product as white solid (437 mg, 62%) [9].

mp: 104-105℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 (t, *J* = 7.6 Hz, 2H, Ar-CH), 7.35 (t, *J* = 7.3 Hz, 1H, Ar-CH), 7.18 (d, *J* = 7.8 Hz, 2H, Ar-CH), 5.65 (s, 1H, =CH), 4.94 (m, 2H, NCH_2), 4.45 (s, 2H, NCH_2), 3.31 (s, 3H, NMe), 1.44 (s, 9H, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 164.99, 156.34, 149.53, 143.49, 129.73, 127.75, 127.27, 112.78, 79.77, 36.91, 33.99, 29.68, 28.35.

HRMS (ESI): m/z calcd for $C_{17}H_{23}N_2O_3^+$ $(M+H)^+$ 303.1703, found 303.1704.



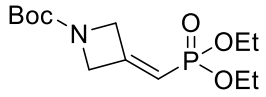
1i

***Tert*-butyl 3-(cyanomethylene)azetidine-1-carboxylate (1i)**

This compound was prepared according to the general procedure A as a white solid (1.22 g, 72% yield).

mp: 86-88℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.40 (s, 1H, =CH), 4.71 (dd, *J* = 6.0, 4.4 Hz, 2H, NCH_2), 4.62 (dd, *J* = 2.9, 1.5 Hz, 2H, NCH_2), 1.46 (s, 9H, ^{t}Bu-CH_3).

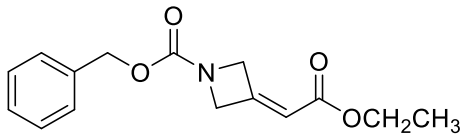


1j

***Tert*-butyl 3-((diethoxyphosphoryl) methylene)azetidine-1-carboxylate (1j)**

This compound was prepared according to the general procedure A as light yellow oil (346 mg, 64%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.64–5.55 (m, 1H, =CH), 4.76 (s, 2H, NCH_2), 4.60–4.55 (m, 2H, NCH_2), 4.13–4.05 (m, 4H, OCH_2), 1.45 (s, 9H, ^{t}Bu-CH_3), 1.34 (t, *J* = 7.1 Hz, 6H, CH_3).

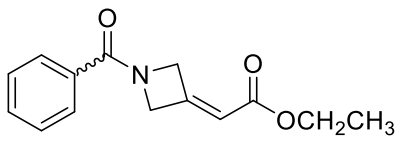


1k

Benzyl 3-(2-ethoxy-2-oxoethylidene)azetidine-1-carboxylate (1k)[10]

Tert-butyl 3-(2-ethoxy-2-oxoethylidene)azetidine-1-carboxylate (**1b**) (500 mg, 2.07 mmol) and trifluoroacetic acid(6.875 ml) were added to a round bottom flask and dissolved in dichloromethane (15 mL), the solution was stirred at room temperature for 30 min. The volatiles were removed in vacuo. The residue was dissolved in dichloromethane (15 ml), triethylamine (0.6 ml, 4.15 mmol) was added followed by benzyl chloroformate (389 mg, 2.28 mmol), and the mixture was stirred at room temperature until the starting material disappeared (monitored by TLC). The reaction mixture was directly purified by column chromatography (PE/EA = 3:1) to give product as light yellow oil (384 mg, 67%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 (d, *J* = 4.3 Hz, 5H, Ar-CH), 5.82 (s, 1H, =CH), 5.17 (s, 2H,CH_2O), 4.94 (m, 2H, NCH_2), 4.70 (m, 2H, NCH_2), 4.21 (q, *J* = 7.1 Hz, 2H, OCH_2), 1.31 (t, *J* = 7.1 Hz, 3H, CH_3).



1l

Ethyl 2-(1-benzoylazetidin-3-ylidene)acetate (1l)

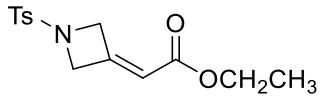
The procedure identical to the preparation of **1k** was employed for the synthesis of **1l** as orange red solid (472 mg, 77%).

mp: 74-76℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (s, 2H, Ar-CH), 7.47 (t, *J* = 7.3 Hz, 1H, Ar-CH), 7.41 (t, *J* = 7.4 Hz, 2H, Ar-CH), 5.82 (d, 1H; *rot-1*, 5.85; *rot-2*, 5.78, =CH), 5.10 (d, 2H; *rot-1*, 5.14; *rot-2*, 5.07, NCH_2), 4.87 (d, 2H; *rot-1*, 4.85; *rot-2*, 4.88, NCH_2), 4.15 (m, 2H, OCH_2), 1.27–1.22 (m, 3H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 170.61, 165.22, 151.80, 131.38, 128.48, 127.92, 114.04, 63.66, 60.49, 57.54, 14.24.

HRMS (ESI): m/z calcd for $C_{14}H_{16}NO_3^+$ $(M+H)^+$ 246.1124, found 246.1125.

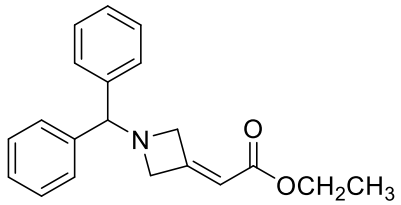


1m

Ethyl 2-(1-tosylazetidin-3-ylidene)acetate(1m)

Tert-butyl 3-(2-ethoxy-2-oxoethylidene)azetidine-1-carboxylate (**1b**) (1 g, 4.14 mmol) and trifluoroacetic acid (6.4 ml) were added to a round bottom flask and dissolved in dichloromethane (10 mL), the solution was stirred at room temperature for 30 min. The volatiles were removed in vacuo. The residue was dissolved in acetonitrile (20 ml), and DIPEA (3.6 ml, 20.7 mmol) was added slowly over 20 min, then paratoluensulfonyl chloride (941 mg, 4.44 mmol) was added slowly over 20 min. and the mixture was stirred at room temperature until the starting material disappeared (monitored by TLC). The reaction mixture was directly purified by column chromatography (PE/EA = 3:1) to give product as primrose yellow soild (704 mg, 58%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83 – 7.79 (m, 2H, Ar-CH), 7.42 (d, *J* = 8.0 Hz, 2H, Ar-CH), 5.72 (p, *J* = 2.4 Hz, 1H, =CH), 4.78 (q, *J* = 2.8 Hz, 2H, NCH_2), 4.57–4.53 (m, 2H, NCH_2), 4.18 (q, *J* = 7.1 Hz, 2H, OCH_2), 2.50 (s, 3H, Ar-CH_3), 1.29 (t, *J* = 7.1 Hz, 3H, CH_3).



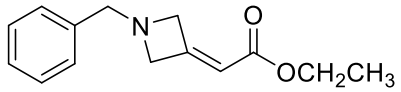
1n

Ethyl 2-(1-benzhydrylazetidin-3-ylidene)acetate (1n)

This compound was prepared from 1-benzhydrylazetidin-3-one according to the general procedure A as a white solid (0.67 g, 52%).

mp: 84-85℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 (d, *J* = 7.3 Hz, 4H, Ar-CH), 7.28 (t, *J* = 7.6 Hz, 4H, Ar-CH), 7.19 (t, *J* = 7.3 Hz, 2H, Ar-CH), 5.66 (s, 1H, =CH), 4.52 (s, 1H, NCH), 4.15 (m, 2H, NCH_2), 4.12 (q, *J* = 7.2 Hz, 2H, OCH_2), 3.89 (m, 2H, NCH_2), 1.22 (t, *J* = 7.1 Hz, 3H, CH_3).



1o

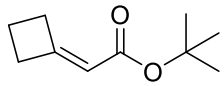
Ethyl 2-(1-benzylazetidin-3-ylidene)acetate (1o)[11]

Tert-butyl 3-(2-ethoxy-2-oxoethylidene)azetidine-1-carboxylate (**1b**) (500 mg, 2.07 mmol) and trifluoroacetic acid(6.875 ml) were added to a round bottom flask and dissolved in dichloromethane (15 mL), the solution was stirred at room temperature for 30 min. The volatiles were removed in vacuo. The residue, and triethylamine (0.6 ml, 4.15 mmol) were dissolved in dichloromethane (15 ml), Sodium triacetoxyborohydride (941 mg, 4.44 mmol) was added slowly over 20 min. and the resulting mixture was stirred at room temperature overnight. The reaction was quenched by the addition of sat. aq. K_2CO_3, diluted with water, extracted with CH_2Cl_2, dried with Na_2SO_4, filtrated and concentrated under vacuum, The residue was purified by column chromatography (PE/EA = 3:1) to give product as orange red oil (0.26 g, 54%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34–7.29 (m, 4H, Ar-CH), 7.27–7.23 (m, 1H, Ar-CH), 5.65 (s, 1H, =CH), 4.24 (m, 2H, NCH_2), 4.14 (q, *J* = 7.1 Hz, 2H, OCH_2), 3.96 (m, 2H, NCH_2), 3.75 (s, 2H, CH_2N), 1.24 (t, *J* = 7.1 Hz, 3H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 165.72, 156.84, 137.65, 128.46, 127.31, 112.40, 63.95, 63.11, 62.09, 60.02, 14.29.

HRMS (ESI): m/z calcd for $C_{14}H_{18}NO_2^+$ $(M+H)^+$ 232.1332, found 232.1331.

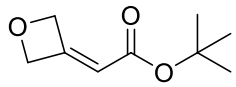


1p

***Tert*-butyl 2-cyclobutylideneacetate (1p)**

This compound was prepared from cyclobutanone according to the general procedure A as colorless oil (687 mg, 79%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.47–5.41 (m, 1H, =CH), 3.13–3.01 (m, 2H, CH_2), 2.84–2.72 (m, 2H, CH_2), 2.07–1.99 (m, 2H, CH_2), 1.42 (s, 9H, ^{t}Bu-CH_3).

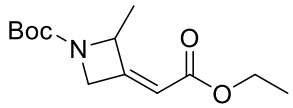


1q

***Tert*-butyl 2-(oxetan-3-ylidene)acetate (1q)**

This compound was prepared from oxetan-3-one according to the general procedure A as colorless oil (0.38 g, 81%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.44 (m, 1H, =CH), 5.39–5.36 (m, 2H, OCH_2), 5.17 (m, 2H, OCH_2), 1.37 (d, J = 2.0 Hz, 9H, ^{t}Bu-CH_3).



1r

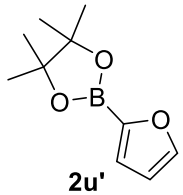
***Tert*-butyl (Z)-3-(2-ethoxy-2-oxoethylidene)-2-methylazetidine-1-carboxylate (1r)**

The N-(*tert*-Butoxycarbonyl)-L-alanine (3 g, 15.85 mmol) was dissolved in THF (20 mL) under argon atmosphere. DIPEA (3.48 g, 26.95 mmol) and Isobutyl chloroformate (3.25 g, 23.78 mmol, 1.0 equiv) were added at 0℃, after stirred for 4 h, $TMSCHN_2$(15.85ml, 31.7mmol) was added at 0℃. The mixture was stirred for 2 h, warm to room temperature stirred for an additional 6 h. After then, water was added, and extracted with AcOEt, washed with water and brine, dried over Na_2SO_4. Purification by flash chromatography on silca gel afforded the pure diazo ketone (1.83 g, 54 %). Under argon atmosphere, the diazo ketone was dissolved in CH_2Cl_2 (40 mL) and Et_3N (12 μL, 1.0 mol %) was added. After cooling to 0℃, $Rh_2(OAc)_4$ (17.7 mg, 0.04 mmol, 0.5 mol %) was added, and the mixture was stirred for 14 h. After then, water was added, extracted with CH_2Cl_2, washed with water and brine dried over

Na_2SO_4. Purification by flash chromatography on silca gel afforded pure ketone (684 mg, 43%)[12]. **1r** was prepared from the pure ketone according to the general procedure A as bright yellow oil [563mg, 60%, mixture of rotamers (3.3 : 1)].

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.75 (q, *J* = 2.6 Hz, 1H, =CH), 4.97 (br, 1H; *rot-1*, 5.11; *rot-2*, 4.86, NCH), 4.62 (br, 2H; *rot-1*, 4.53; *rot-2*, 4.74, NCH_2), 4.17 (q, *J* = 7.2 Hz, 2H, OCH_2), 1.46 (s, 12H, ^{t}Bu-CH_3, -CH_3), 1.28 (m, 3H, -CH_3,*rot-1*, 1.29; *rot-2*, 1,28).

^{13}C NMR (126 MHz, $CDCl_3$): δ 165.42, 164.74, 158.85, 157.60, 156.29, 113.75, 112.69, 79.86, 60.40, 60.35, 28.54, 28.52, 19.35, 17.97, 14.43.

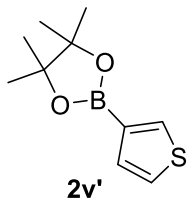


2u'

4,4,5,5-tetramethyl-2-(furan-2-yl)-1,3,2-dioxaborolane (2u')[13]

To the solution of furan-2-ylboronic acid (0.5 g, 4.47 mmol) in THF (9 mL) was added anhydrous pinacol (628 mg, 5.32 mmol) and anhydrous Na_2SO_4 (2.22g, 15.64 mmol). The reaction mixture was stirred for 24h at room temperature. The resulting solution was filtered. The filtrate was concentrated in vacuo, and then adds a small amount of acetone to dissolve, washed with petroleum ether, filtered. The filtrate was concentrated in vacuo to give product (**2u'**) as colorless oil (0.8 g, 92%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53–7.46 (m, 1H, Ar-CH), 6.97–6.90 (m, 1H, Ar-CH), 6.32–6.25 (m, 1H, Ar-CH), 1.19 (dd, *J* = 9.0, 2.9 Hz, 12H, CH_3).

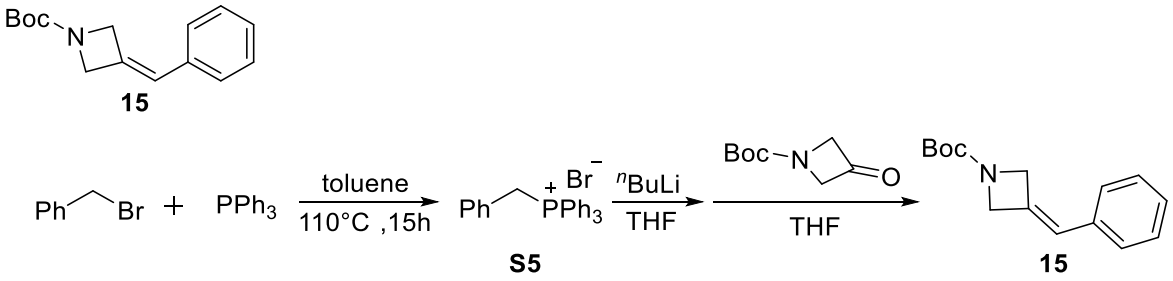


2v'

4,4,5,5-tetramethyl-2-(thiophen-3-yl)-1,3,2-dioxaborolane (2v')

The procedure identical to the preparation of **2u'** was employed for the synthesis of **2v**' as a white solid (0.71 g, 86%)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (d, *J* = 2.4 Hz, 1H, Ar-CH), 7.45 (d, *J* = 4.8 Hz, 1H, Ar-CH), 7.38 (dd, *J* = 4.7, 2.8 Hz, 1H, Ar-CH), 1.38 (s, 12H, CH_3).



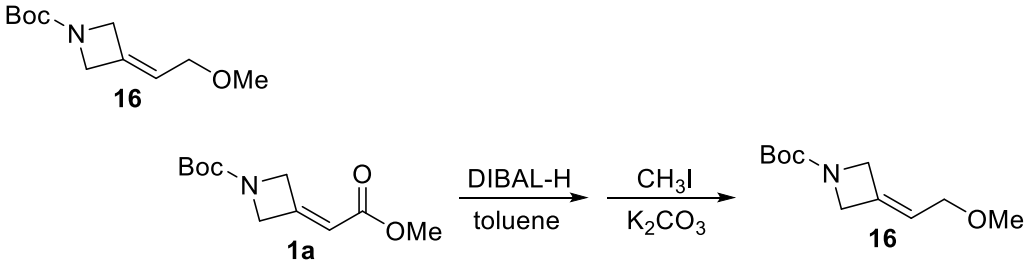
***Tert*-butyl 3-benzylideneazetidine-1-carboxylate (15)[14]**

Triphenylphosphine (3 g, 11.45 mmol) was added to a round bottom flask and dissolved in toluene (30 ml). To the mixture was then added benzyl bromide (1.38 mL, 11.45 mmol) via syringe, the flask was fitted with a condenser and the reaction mixture was stirred for 15h at room temperature. The mixture was then cooled to room temperature, filtered, washed with diethyl ether and dried in vacuo to give **S5** as a white solid (4.86 g, 98%).

S5 (4.42 g, 10.2 mmol) was added to an oven-dried 100 mL round-bottomed flask under argon atmosphere, anhydrous THF (20 mL) was then added via syringe and the solution was cooled to 0℃. A solution of butyl lithium (2.5 M in hexanes. 4.96 mL, 12.4 mmol) was added dropwise via syringe and the reaction was allowed to stir for 1 h. A solution of tert-butyl 3-oxoazetidine-1-carboxylate (1.92 g, 11.22 mmol) in dry THF (20 ml) was added dropwise via syringe over 30 min at 0℃ and the resulting solution was stirred at room temperature for 15 h. The reaction mixture was then poured into a saturated solution of NH_4Cl at 0℃ and extracted with CH_2Cl_2, dried with Na_2SO_4, filtrated and concentrated under vacuum. The residue was purified by column chromatography (PE/EA = 3:1) to give product **15** as a white solid (1.98 g, 71%).

mp: 62-64℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 (t, *J* = 7.6 Hz, 2H, Ar-CH), 7.27 (t, *J* = 7.2 Hz, 1H, Ar-CH), 7.15 (d, *J* = 7.6 Hz, 2H, Ar-CH), 6.30 (s, 1H, =CH), 4.87 (s, 2H, NCH_2), 4.69 (s, 2H, NCH_2), 1.53 (s, 9H, ^{t}Bu-CH_3).



***Tert*-butyl 3-(2-methoxyethylidene)azetidine-1-carboxylate (16)[15]**

The compound **1a** (0.2 g, 0.88 mmol) was added to an oven-dried Schlenk tube and dissolved in toluene (20 ml), Then the solution was added DIABL-H (2.64 ml, 2.64 mmol) at -20℃. The resulting mixture was stirred for 30 min, water (5 ml) was added, and stirring was continued for additional 2 h, filtrated and concentrated under vacuum to give product (75 mg, 43%).

The above product (75 mg, 0.38 mmol), iodomethane (328 mg, 2.26 mmol), and potassium carbonate (207 mg, 1.5 mmol) were added to a round bottom flask and dissolved in N,N-dimethylformamide (4 ml). The reaction mixture was stirred at room temperature until the starting material disappeared (monitored by TLC). The reaction mixture was poured to water, extracted with diethyl ether, dried with Na_2SO_4, filtrated and concentrated under vacuum. The residue was purified by column chromatography (PE/EA = 5:1) to give product as colorless oil (48 mg, 60%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.57–5.43 (m, 1H, =CH), 4.55 (s, 2H, NCH_2), 4.51 (d, *J* = 6.7 Hz, 2H, CH_2O), 4.46 (s, 2H, NCH_2), 3.77 (s, 3H, OMe), 1.43 (s, 9H, ^{t}Bu-CH_3).

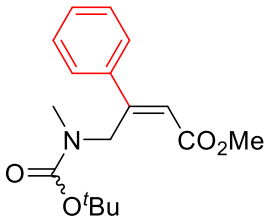
^{13}C NMR (126 MHz, $CDCl_3$): δ 156.22, 155.56, 135.62, 115.78, 79.80, 64.21, 54.84, 29.65, 28.31.

HRMS (ESI): m/z calcd for $C_{11}H_{20}NO_3^+$ $(M+H)^+$ 214.14377, found 214.14388.

4. Rhodium Catalyzed C–C bond Cleavage / Coupling

General Procedure B

The rhodium precursor (0.0055 mmol) and the ligand (0.0165 mmol) were added to an oven-dried Schlenk tube. The tube was then purged with vacuum and argon for three cycles, and finally filled with argon. Cyclopentyl methyl ether (1.6 mL) was added and the mixture was stirred for 30 min at 45 ℃. The resulting brick-red opaque mixture was transferred via syringe to another argon-filled Schlenk tube, which contained the aryl boronic acid (0.396 mmol), 2-(azetidin-3-ylidene) acetate esters (0.22 mmol), sodium *tert*-butoxide (0.044 mmol) and 2-methyl-2-butanol (0.021 ml). The reaction was stirred for 8 hours at 110 ℃. If necessary, the crude product was then evaporated and analyzed by ^{1}H NMR for the conversion and the CCP/CA ratio. The mixture was purified by column chromatography on silica gel to afford the desired product[16].



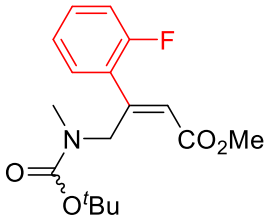
3aa

Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-phenylbut-2-enoate (3aa)

This compound was prepared according to the general procedure B as light yellow oil (88% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50 (s, 1H, Ar-CH), 7.36 (t, *J* = 8.5 Hz, 4H, Ar-CH), 6.15 (d, 1H; *rot-1*, 6.2; *rot-2*, 6.1, =CH), 5.05 (d, 2H; *rot-1*, 5.1; *rot-2*, 5.0, NCH_2), 3.77 (s, 3H, OMe), 2.62 (d, 3H; *rot-1*, 2.57; *rot-2*, 2.66, NMe), 1.39 (d, 9H; *rot-1*, 1.36; *rot-2*, 1.42, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.48, 166.37, 157.45, 156.96, 155.86, 155.21, 139.01, 138.34, 129.10, 128.30, 128.24, 127.26, 120.40, 120.18, 79.76, 79.34, 51.39, 46.43, 45.13, 32.97, 32.75, 28.28.



3ab

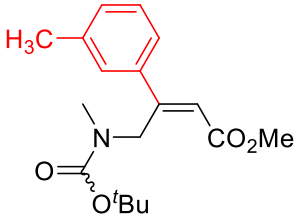
Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(2-fluorophenyl)but-2-enoate(3ab)

This compound was prepared according to the general procedure B as as light yellow oil (32% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (s, 1H, Ar-CH), 7.20 (d, *J* = 6.8 Hz, 1H, Ar-CH), 7.14 (t, *J* = 7.3 Hz, 1H, Ar-CH), 7.11–7.06 (m, 1H, Ar-CH), 6.06 (d, 1H; *rot-1*, 6.09; *rot-2*, 6.02, =CH), 4.93 (d, 2H; *rot-1*, 4.95; *rot-2*, 4.91, NCH_2), 3.80 (s, 3H, OMe), 2.73 (d, 3H; *rot-1*, 2.71; *rot-2*, 2.76, NMe), 1.31 (d, 9H; *rot-1*, 1.29; *rot-2*, 1.32, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 165.97, 160.60, 158.63, 155.33, 152.50, 130.24, 124.09, 123.72, 122.48, 115.72, 115.55, 79.62, 79.25, 51.49, 47.73, 47.36, 33.84, 28.09.

HRMS (ESI): m/z calcd for $C_{17}H_{22}FNO_4Na^+$ $(M+Na)^+$ 346.1425, found 346.1427.



3ac

Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(m-tolyl)but-2-enoate (3ac)

This compound was prepared according to the general procedure B as a white solid (84% yield).

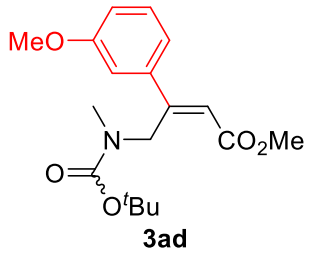
mp: 40-41℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34–7.26 (m, 1H, Ar-CH), 7.22 (t, *J* = 7.1 Hz, 1H, Ar-CH), 7.16 (t, *J* = 7.9 Hz, 2H, Ar-CH), 6.13 (d, 1H; *rot-1*, 6.19; *rot-2*, 6.08, =CH), 5.03 (d, 2H; *rot-1*, 5.08; *rot-2*, 4.98, NCH_2), 3.74 (s, 3H, OMe), 2.60 (d, 3H; *rot-1*, 2.55; *rot-2*, 2.65, NMe), 2.34 (s, 3H, CH_3), 1.39 (d, 9H; *rot-1*, 1.36; *rot-2*, 1.41, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.52, 166.40, 157.54, 157.13, 155.83, 155.25, 139.01, 138.19, 137.82, 129.94, 129.89, 128.15, 127.92, 127.81, 124.35, 120.23, 119.89, 116.17,

112.40, 79.68, 79.30, 51.34, 46.36, 45.04, 32.91, 32.71, 28.27, 21.41, 21.34.

HRMS (ESI): m/z calcd for $C_{18}H_{26}NO_4^+$ $(M+H)^+$ 320.1856, found 320.1857.



3ad

Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(3-methoxyphenyl)but-2-enoate (3ad)

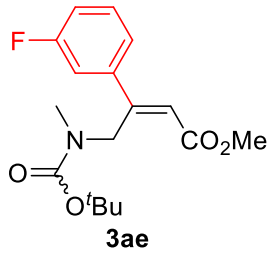
This compound was prepared according to the general procedure B as an off-white solid (73% yield).

mp: 42-43℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28–7.20 (m, 1H, Ar-CH), 7.07 (d, *J* = 8.3 Hz, 1H, Ar-CH), 6.96 (d, 1H, Ar-CH), 6.89 (d, *J* = 8.7 Hz, 1H, Ar-CH), 6.15 (d, 1H; *rot-1*, 6.21; *rot-2*, 6.10, =CH), 5.02 (d, 2H; *rot-1*, 5.07; *rot-2*, 4.96, NCH_2), 3.81 (s, 3H, CO_2Me), 3.76 (s, 3H, OMe), 2.62 (d, 3H; *rot-1*, 2.57; *rot-2*, 2.66, NMe), 1.38 (d, 9H; *rot-1*, 1.36; *rot-2*, 1.41, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.51, 166.38, 159.48, 157.13, 156.78, 155.88, 155.28, 140.39, 139.68, 129.33, 129.26, 120.41, 120.22, 119.59, 115.55, 113.86, 113.72, 112.16, 79.83, 79.39, 55.24, 51.43, 46.49, 45.01, 33.06, 32.80, 29.69, 28.28.

HRMS (ESI): m/z calcd for $C_{18}H_{26}NO_5^+$ $(M+H)^+$ 336.1805, found 336.1806.



3ae

Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(3-fluorophenyl)but-2-enoate(3ae)

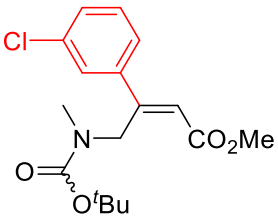
This compound was prepared according to the general procedure B as light yellow oil (87% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (s, 1H, Ar-CH), 7.24–7.09 (m, 2H, Ar-CH), 7.05 (s, 1H, Ar-CH), 6.15 (d, 1H; *rot-1*, 6.18; *rot-2*, 6.11, =CH), 5.01 (d, 2H; *rot-1*, 5.05; *rot-2*, 4.97,

NCH_2), 3.77 (s, 3H, OMe), 2.61 (d, 3H; *rot-1*, 2.57; *rot-2*, 2.65, NMe), 1.39 (d, 9H; *rot-1*, 1.36; *rot-2*, 1.43, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.27, 166.15, 163.52, 161.57, 156.09, 155.90, 155.40, 155.16, 141.07, 140.62, 129.98, 129.79, 123.00, 121.18, 120.95, 116.09, 115.92, 114.47, 114.29, 80.15, 79.66, 51.56, 46.26, 45.25, 32.89, 28.27.

HRMS (ESI): m/z calcd for $C_{17}H_{22}FNO_4Na^+$ $(M+Na)^+$ 346.1425, found 346.1428.



3af

Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(3-chlorophenyl)but-2-enoate(3af)

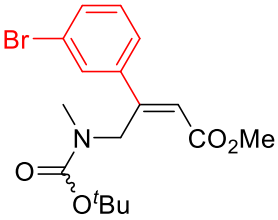
This compound was prepared according to the general procedure B as a white solid (82% yield).

mp: 48-49℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55–7.35 (m, 2H, Ar-CH), 7.32 (s, 1H, Ar-CH), 7.28 (d, *J* = 8.1 Hz, 1H, Ar-CH), 6.13 (d, 1H; *rot-1*, 6.17; *rot-2*, 6.09, =CH), 5.01 (d, 2H; *rot-1*, 5.05; *rot-2*, 4.97, NCH_2), 3.77 (s, 3H, OMe), 2.61 (d, 3H; *rot-1*, 2.57; *rot-2*, 2.66, NMe), 1.40 (d, 9H; *rot-1*, 1.36; *rot-2*, 1.44, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.19, 166.07, 156.04, 155.84, 155.35, 155.12, 140.77, 140.16, 134.26, 129.71, 129.48, 129.16, 127.35, 125.48, 121.32, 120.99, 116.00, 113.87, 80.13, 79.65, 51.55, 46.23, 45.22, 32.89, 28.27.

HRMS (ESI): m/z calcd for $C_{17}H_{23}ClNO_4^+$ $(M+H)^+$ 340.1310, found 340.1314.



3ag

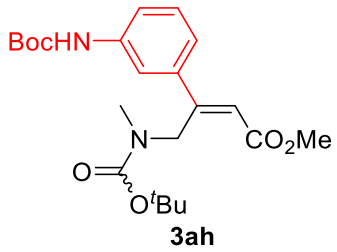
Methyl (*Z*)-3-(3-bromophenyl)-4-((*tert*-butoxycarbonyl)(methyl)amino)but-2-enoate (3ag)

This compound was prepared according to the general procedure B as light yellow oil (61% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68–7.27 (m, 4H, Ar-CH), 6.12 (d, 1H; *rot-1*, 6.16; *rot-2*, 6.08, =CH), 5.00 (d, *J* = 39.7 Hz, 2H; *rot-1*, 5.04; *rot-2*, 4.96, NCH_2), 3.77 (s, 3H, OMe), 2.61 (d, 3H; *rot-1*, 2.57; *rot-2*, 2.66, NMe), 1.40 (d, 9H; *rot-1*, 1.37; *rot-2*, 1.44, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.18, 166.06, 155.94, 155.30, 155.15, 141.07, 140.44, 132.10, 130.33, 130.17, 129.96, 129.75, 125.95, 122.41, 121.39, 121.04, 80.16, 79.69, 51.56, 51.50, 46.31, 45.25, 32.93, 28.32, 28.26.

HRMS (ESI): m/z calcd for $C_{17}H_{23}BrNO_4^+$ $(M+H)^+$ 384.0805, found 384.0807.



3ah

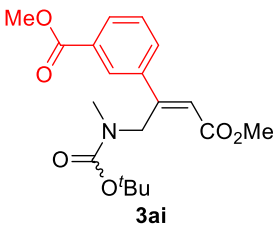
Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(3-((*tert*-butoxycarbonyl)amino) phenyl)but-2-enoate (3ah)

This compound was prepared according to the general procedure B as light yellow oil (82% yield).

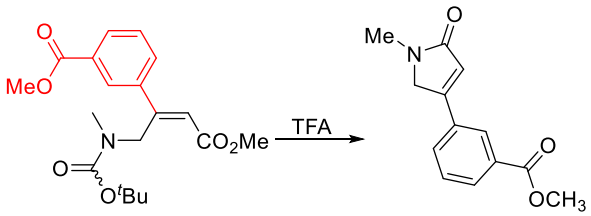
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (s, 1H, Ar-CH), 7.30 (d, *J* = 70.1 Hz, 2H, Ar-CH), 7.15 (d, *J* = 6.4 Hz, 1H, Ar-CH), 6.88–6.76 (m, 1H, NH), 6.14 (d, 1H; *rot-1*, 6.21; *rot-2*, 6.08, =CH), 5.00 (d, 2H; *rot-1*, 5.05; *rot-2*, 4.95, NCH_2), 3.75 (d, *J* = 2.6 Hz, 3H, OMe), 2.61 (d, 3H; *rot-1*, 2.55; *rot-2*, 2.66, NMe), 1.52–1.49 (m, 9H, ^{t}Bu-CH_3), 1.37 (d, 9H; *rot-1*, 1.35; *rot-2*, 1.39, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.51, 166.39, 156.91, 156.81, 155.95, 155.32, 152.82, 152.70, 140.03, 139.66, 138.84, 138.56, 128.94, 128.76, 121.85, 120.63, 120.35, 119.39, 119.14, 117.31, 110.17, 80.50, 80.36, 79.80, 79.50, 51.42, 46.51, 45.01, 33.08, 32.78, 29.68, 28.32.

HRMS (ESI): m/z calcd for $C_{22}H_{33}N_2O_6^+$ $(M+H)^+$ 421.2333, found 421.2337.



3ai



3ai 3ai'

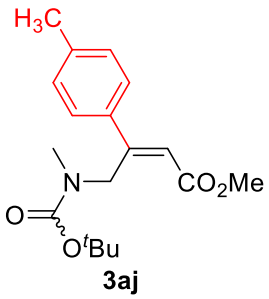
Methyl 3-(1-methyl-5-oxo-2,5-dihydro-1H-pyrrol-3-yl)benzoate (3ai')

This compound was prepared according to the general procedure B as a white solid (92% yield). **3ai** and trifluoroacetic acid were added to a round bottom flask and dissolved in dichloromethane. The reaction mixture was stirred at room temperature until the starting material disappeared (monitored by TLC). The solvent was removed in vacuo to get the product **3ai'** (for the reason of easy separation).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11 (d, *J* = 1.8 Hz, 1H, Ar-CH), 8.07 (d, *J* = 7.8 Hz, 1H, Ar-CH), 7.73–7.69 (m, 1H, Ar-CH), 7.51 (t, *J* = 7.8 Hz, 1H, Ar-CH), 6.50 (s, 1H, =CH), 4.39 (s, 2H, NCH_2), 3.95 (s, 3H, OMe), 3.12 (s, 3H, NMe).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.41, 152.82, 132.23, 131.07, 130.98, 130.04, 129.24, 126.66, 121.76, 54.38, 52.46, 29.16.

HRMS (ESI): m/z calcd for $C_{13}H_{14}NO_3^+$ $(M+H)^+$ 232.0968, found 232.0967.



3aj

Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(p-tolyl)but-2-enoate (3aj)

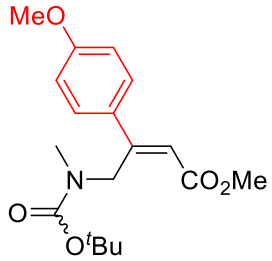
This compound was prepared according to the general procedure B as a white solid (81% yield).

mp: 75-76℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46–7.29 (m, 2H, Ar-CH), 7.17 (d, *J* = 7.9 Hz, 2H, Ar-CH), 6.17 (d, 1H; *rot-1*, 6.22; *rot-2*, 6.12, =CH), 5.06 (d, 2H; *rot-1*, 5.10; *rot-2*, 5.01, NCH_2), 3.78 (s, 3H, OMe), 2.62 (d, 3H; *rot-1*, 2.58; *rot-2*, 2.66, NMe), 2.37 (s, 3H, CH_3), 1.43 (d, 9H; *rot-1*, 1.39; *rot-2*, 1.46, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.64, 166.52, 157.17, 156.98, 155.92, 155.28, 139.29, 135.95, 135.31, 129.03, 127.16, 119.63, 119.43, 79.77, 79.35, 51.37, 46.22, 44.84, 32.85, 32.62, 28.38, 28.32, 21.22.

HRMS (ESI): m/z calcd for $C_{18}H_{25}NO_4Na^+$ $(M+Na)^+$ 342.1675, found 342.1677.



3ak

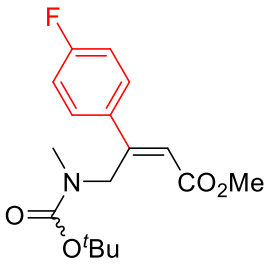
Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(4-methoxyphenyl)but-2-enoate (3ak)

This compound was prepared according to the general procedure B as light yellow oil (83% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.3 Hz, 1H, Ar-CH), 7.36 (d, *J* = 8.2 Hz, 1H, Ar-CH), 6.94–6.82 (m, 2H, Ar-CH), 6.13 (d, 1H; *rot-1*, 6.17; *rot-2*, 6.08, =CH), 5.04 (d, 2H; *rot-1*, 5.08; *rot-2*, 4.99, NCH_2), 3.80 (s, 3H, CO_2Me), 3.75 (s, 3H, OMe), 2.59 (d, 3H; *rot-1*, 2.56; *rot-2*, 2.63, NMe), 1.41 (d, 9H; *rot-1*, 1.38; *rot-2*, 1.45, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.67, 166.54, 160.63, 156.61, 156.36, 155.92, 155.24, 131.00, 130.38, 128.68, 128.57, 118.92, 118.54, 113.77, 113.70, 79.76, 79.35, 55.26, 51.30, 45.91, 44.51, 32.65, 32.47, 28.39, 28.30.

HRMS (ESI): m/z calcd for $C_{18}H_{26}NO_5^+$ $(M+H)^+$ 336.1805, found 336.1807.



3al

Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(4-fluorophenyl)but-2-enoate (3al)

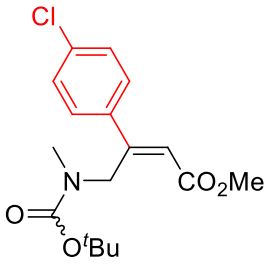
This compound was prepared according to the general procedure B as a white solid (87% yield).

mp: 57-58℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 (dd, *J* = 8.7, 5.2 Hz, 1H, Ar-CH), 7.38 (d, *J* = 7.1 Hz, 1H, Ar-CH), 7.02 (t, *J* = 8.0 Hz, 2H, Ar-CH), 6.11 (d, 1H; *rot-1*, 6.15; *rot-2*, 6.07, =CH), 5.02 (d, 2H; *rot-1*, 5.06; *rot-2*, 4.97, NCH_2), 3.76 (s, 3H, OMe), 2.60 (d, 3H; *rot-1*, 2.56; *rot-2*, 2.64, NMe), 1.39 (d, 9H; *rot-1*, 1.36; *rot-2*, 1.42, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.35, 166.22, 164.37, 162.39, 156.24, 155.88, 155.73, 155.14, 134.93, 134.27, 129.25, 129.18, 129.09, 120.14, 115.29, 115.13, 79.92, 79.52, 51.44, 46.37, 45.01, 32.90, 32.70, 28.33, 28.24.

HRMS (ESI): m/z calcd for $C_{17}H_{23}FNO_4^+$ $(M+H)^+$ 324.1605, found 324.1607.



3am

Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(4-chlorophenyl)but-2-enoate (3am)

This compound was prepared according to the general procedure B as a white solid (74% yield).

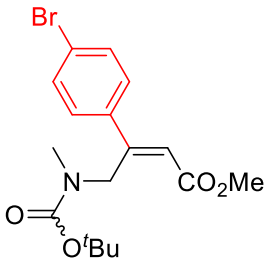
mp: 84-85℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.3 Hz, 1H, Ar-CH), 7.33 (d, *J* = 10.1 Hz, 3H, Ar-CH), 6.14 (d, 1H; *rot-1*, 6.16; *rot-2*, 6.09, =CH), 5.02 (d, 2H; *rot-1*, 5.07; *rot-2*, 4.98,

NCH_2), 3.78 (s, 3H, OMe), 2.61 (d, 3H; *rot-1*, 2.57; *rot-2*, 2.65, NMe), 1.41 (d, 9H; *rot-1*, 1.38; *rot-2*, 1.44, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.29, 166.17, 156.12, 155.89, 155.66, 155.13, 137.35, 136.72, 135.22, 128.68, 128.58, 128.48, 120.72, 120.50, 80.00, 79.60, 51.53, 46.35, 45.00, 32.98, 32.77, 28.36, 28.26.

HRMS (ESI): m/z calcd for $C_{17}H_{23}ClNO_4^+$ $(M+H)^+$ 340.1310, found 340.1312.



3an

Methyl (*Z*)-3-(4-bromophenyl)-4-((*tert*-butoxycarbonyl)(methyl)amino)but-2-enoate (3an)

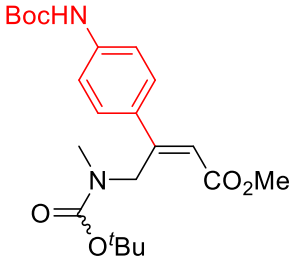
This compound was prepared according to the general procedure B as a white solid (27% yield).

mp: 81-82℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55–7.48 (m, 2H, Ar-CH), 7.39 (m, 1H, Ar-CH), 7.29 (d, *J* = 8.0 Hz, 1H, Ar-CH), 6.15 (d, 1H; *rot-1*, 6.20; *rot-2*, 6.11, =CH), 5.03 (d, 2H; *rot-1*, 5.08; *rot-2*, 4.99, NCH_2), 3.80 (s, 3H, OMe), 2.63 (d, 3H; *rot-1*, 2.59; *rot-2*, 2.67, NMe), 1.42 (d, 9H; *rot-1*, 1.39; *rot-2*, 1.45, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.27, 156.15, 155.91, 155.69, 155.17, 137.85, 137.24, 132.26, 131.46, 129.12, 128.94, 128.86, 123.50, 120.73, 120.55, 117.31, 80.05, 79.66, 51.54, 46.40, 45.06, 33.02, 32.82, 28.37, 28.29.

HRMS (ESI): m/z calcd for $C_{17}H_{23}BrNO_4^+$ $(M+H)^+$ 384.0805, found 384.0806.



3ao

Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(4-((*tert*-butoxycarbonyl)amino)phenyl)but-2-enoate (3ao)

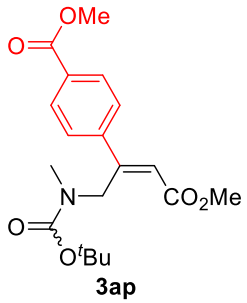
This compound was prepared according to the general procedure B as light yellow solid (66% yield).

mp: 122-124℃

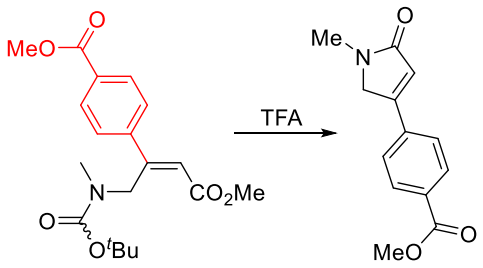
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 (dd, *J* = 42.5, 9.5 Hz, 4H, Ar-CH), 6.98 (s, 1H, NH), 6.15 (d, 1H; *rot-1*, 6.20; *rot-2*, 6.11, =CH), 5.05 (d, 2H; *rot-1*, 5.09; *rot-2*, 5.00, NCH_2), 3.77 (d, 3H, OMe), 2.60 (d, 3H; *rot-1*, 2.57; *rot-2*, 2.63, NMe), 1.53 (s, 9H, ^{t}Bu-H), 1.42 (d, 9H; *rot-1*, 1.39; *rot-2*, 1.46, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.66, 166.55, 156.46, 156.27, 155.94, 155.25, 152.64, 139.78, 132.95, 132.40, 128.04, 127.95, 127.14, 119.22, 118.98, 118.01, 80.69, 79.87, 79.44, 51.36, 45.94, 44.54, 32.74, 32.53, 28.43, 28.36, 28.31.

HRMS (ESI): m/z calcd for $C_{22}H_{33}N_2O_6^+$ $(M+H)^+$ 421.2333, found 421.2336.



3ap



3ap **3ap'**

Methyl 4-(1-methyl-5-oxo-2,5-dihydro-1H-pyrrol-3-yl)benzoate (3ap')

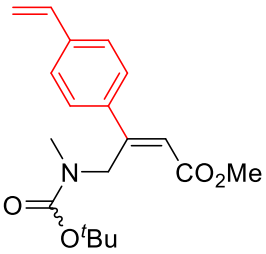
This compound was prepared according to the general procedure B as a white solid (76% yield). **3ap** and trifluoroacetic acid were added to a round bottom flask and dissolved in dichloromethane. The reaction mixture was stirred at room temperature until the starting material disappeared (monitored by TLC). The solvent was removed in vacuo to get the

product **3ap'** (for the reason of easy separation).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 (d, *J* = 8.5 Hz, 2H, Ar-CH), 7.54 (d, *J* = 8.5 Hz, 2H, Ar-CH), 6.54 (t, *J* = 1.5 Hz, 1H, =CH), 4.37 (d, *J* = 1.5 Hz, 2H, NCH_2), 3.94 (s, 3H, OMe), 3.12 (s, 3H, NMe).

^{13}C NMR (126 MHz, $CDCl_3$): δ 171.29, 166.33, 152.63, 135.89, 131.33, 130.29, 125.68, 122.82, 54.32, 52.38, 29.19.

HRMS (ESI): m/z calcd for $C_{13}H_{14}NO_3^+$ $(M+H)^+$ 232.0968, found 232.0966.



3aq

Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(4-vinylphenyl)but-2-enoate (3aq)

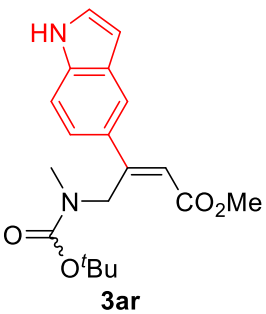
This compound was prepared according to the general procedure B as colorless solid (71% yield).

mp: 65-67℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56–7.38 (m, 4H, Ar-CH), 6.75 (dd, *J* = 17.7, 10.9 Hz, 1H, =CH), 6.20 (d, 1H; *rot-1*, 6.25; *rot-2*, 6.16, =CHCO), 5.82 (d, *J* = 17.7 Hz, 1H, $=CH_2$), 5.33 (d, *J* = 10.8 Hz, 1H, $=CH_2$), 5.07 (d, 2H; *rot-1*, 5.12; *rot-2*, 5.03, NCH_2), 3.81 (s, 3H, OMe), 2.64 (d, 3H; *rot-1*, 2.60; *rot-2*, 2.68, NMe), 1.44 (d, 9H; *rot-1*, 1.40; *rot-2*, 1.47, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.43, 156.79, 156.52, 155.92, 138.53, 136.25, 136.12, 127.51, 126.13, 120.05, 119.90, 114.89, 114.72, 79.88, 79.48, 51.46, 46.28, 44.91, 32.93, 32.70, 28.39, 28.32.

HRMS (ESI): m/z calcd for $C_{19}H_{26}NO_4^+$ $(M+H)^+$ 332.1856, found 332.1857.



3ar

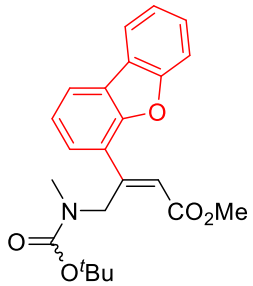
Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(1H-indol-5-yl)but-2-enoate (3ar)

This compound was prepared according to the general procedure B as light yellow oil (53% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.92 (d, 1H; *rot-1*, 8.80; *rot-2*, 8.93, Ar-CH), 7.83 (d, 1H, *rot-1*, 7.88; *rot-2*, 7.79, Ar-CH), 7.37–7.19 (m, 3H), 6.56 (s, 1H, NH), 6.28 (d, 1H; *rot-1*, 6.32; *rot-2*, 6.24, =CH), 5.21 (d, 2H; *rot-1*, 5.25; *rot-2*, 5.17, NCH_2), 3.82 (d, *J* = 2.2 Hz, 3H, OMe), 2.66 (d, 3H; *rot-1*, 2.61; *rot-2*, 2.70, NMe), 1.46 (d, 9H; *rot-1*, 1.41; *rot-2*, 1.51, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 167.01, 166.89, 158.45, 158.31, 156.18, 155.60, 136.64, 136.54, 130.25, 129.68, 127.87, 125.37, 125.11, 121.30, 120.02, 119.84, 118.99, 118.60, 111.08, 110.97, 103.03, 102.84, 79.92, 79.44, 51.34, 46.30, 44.95, 32.77, 32.57, 28.47, 28.38.

HRMS (ESI): m/z calcd for $C_{19}H_{25}N_2O_4^+$ $(M+H)^+$ 345.1808, found 345.1809.



3as

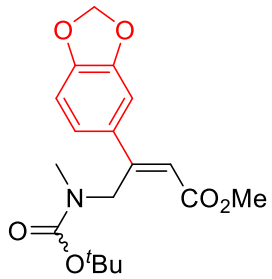
Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(dibenzo[b,d]furan-4-yl)but-2-enoate (3as)

This compound was prepared according to the general procedure B as light yellow oil (43% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (dd, *J* = 13.9, 7.4 Hz, 2H, Ar-CH), 7.62–7.56 (m, 1H, Ar-CH), 7.47 (t, *J* = 7.9 Hz, 1H, Ar-CH), 7.34 (m, 3H, Ar-CH), 6.49 (d, 1H; *rot-1*, 6.65; *rot-2*, 6.33, =CH), 5.15 (d, 2H; *rot-1*, 5.17; *rot-2*, 5.13, NCH_2), 3.81 (s, 3H, OMe), 2.66 (d, 3H; *rot-1*, 2.61; *rot-2*, 2.70, NMe), 1.22 (d, 9H; *rot-1*, 1.18; *rot-2*, 1.26, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.73, 166.38, 155.79, 155.43, 153.51, 153.18, 152.42, 151.82, 127.48, 127.36, 127.13, 126.81, 124.64, 124.11, 123.90, 123.57, 123.04, 122.83, 122.78, 122.61, 121.07, 120.76, 120.63, 113.67, 112.30, 111.82, 79.55, 79.35, 51.55, 47.24, 46.10, 33.78, 33.44, 29.72, 28.09.

HRMS (ESI): m/z calcd for $C_{23}H_{26}NO_5^+$ $(M+H)^+$ 396.1805, found 396.1808.



3at

Methyl (*Z*)-3-(benzo[d][1,3]dioxol-5-yl)-4-((*tert*-butoxycarbonyl)(methyl)amino)but-2-enoate (3at)

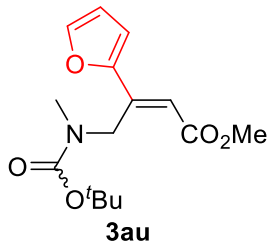
This compound was prepared according to the general procedure B as a white solid (77% yield).

mp: 81-83℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.09–6.99 (m, 1H, Ar-CH), 6.92 (d, *J* = 7.3 Hz, 1H, Ar-CH), 6.77 (d, *J* = 8.3 Hz, 1H, Ar-CH), 6.11 (d, 1H; *rot-1*, 6.14; *rot-2*, 6.07, =CH), 6.01–5.95 (m, 2H, OCH_2), 5.00 (d, 2H; *rot-1*, 5.04; *rot-2*, 4.96, NCH_2), 3.75 (s, 3H, OMe), 2.60 (d, 3H; *rot-1*, 2.56; *rot-2*, 2.63, NMe), 1.42 (d, 9H; *rot-1*, 1.38; *rot-2*, 1.46, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.59, 166.48, 156.73, 156.35, 155.97, 155.23, 148.62, 147.74, 132.74, 132.23, 121.62, 121.32, 119.43, 119.12, 108.22, 108.09, 107.67, 101.39, 101.32, 79.97, 79.50, 51.41, 46.03, 44.86, 32.66, 28.38, 28.34.

HRMS (ESI): m/z calcd for $C_{18}H_{24}NO_6^+$ $(M+H)^+$ 350.1598, found 350.1599.



3au

Methyl (E)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(furan-2-yl)but-2-enoate (3au)

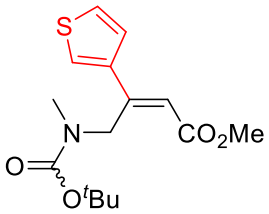
This compound was prepared according to the general procedure B, use 4,4,5,5-tetramethyl-2-(furan-2-yl)-1,3,2-dioxaborolane (**2u'**) (0.396 mmol), and potassium phosphate (0.022 mmol) get product as colorless oil (46% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47 (s, 1H, Ar-CH), 6.96 (d, *J* = 126.4 Hz, 1H, Ar-CH),

6.56 (d, 1H; *rot-1*, 6.58; *rot-2*, 6.54, =CH), 6.47 (s, 1H, Ar-CH), 4.94 (d, 2H; *rot-1*, 4.94; *rot-2*, 4.92, NCH_2), 3.79 (s, 3H, OMe), 2.79 (s, 3H, NMe), 1.52 (d, 9H; *rot-1*, 1.50; *rot-2*, 1.54, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.95, 156.05, 151.99, 144.03, 143.94, 142.04, 115.54, 113.16, 112.39, 79.77, 51.42, 42.14, 32.29, 28.46.

HRMS (ESI): m/z calcd for $C_{15}H_{22}NO_5^+$ $(M+H)^+$ 296.1492, found 296.1491.



3av

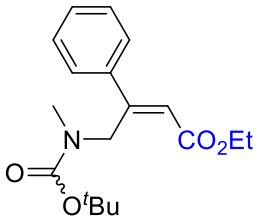
Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-(thiophen-3-yl)but-2-enoate (3av)

This compound was prepared according to the general procedure B, use 4,4,5,5-tetramethyl-2-(thiophen-3-yl)-1,3,2-dioxaborolane (**2v'**) (0.396 mmol), and potassium phosphate (0.022 mmol) get product as colorless oil (39% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 (d, *J* = 142.0 Hz, 1H, Ar-CH), 7.29 (s, 2H, Ar-CH), 6.31 (d, 1H; *rot-1*, 6.36; *rot-2*, 6.26, =CH), 4.98 (d, 2H; *rot-1*, 5.02; *rot-2*, 4.94, NCH_2), 3.76 (s, 3H, OMe), 2.68 (d, 3H; *rot-1*, 2.67; *rot-2*, 2.69, NMe), 1.46 (d, 9H; *rot-1*, 1.43; *rot-2*, 1.48, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.83, 156.12, 149.86, 139.25, 126.11, 125.87, 124.76, 118.88, 118.48, 80.09, 79.70, 51.42, 45.93, 44.20, 32.39, 28.43, 24.84.

HRMS (ESI): m/z calcd for $C_{15}H_{22}NO_4S^+$ $(M+H)^+$ 312.1264, found 312.1265.



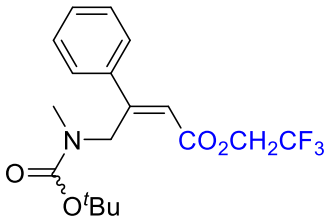
3ba

Ethyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-phenylbut-2-enoate (3ba)

This compound was prepared according to the general procedure B as light yellow oil (90% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 (d, *J* = 55.6 Hz, 2H, Ar-CH), 7.36–7.30 (m, 3H, Ar-CH), 6.13 (d, 1H; *rot-1*, 6.18; *rot-2*, 6.08, =CH), 5.03 (d, 2H; *rot-1*, 5.07; *rot-2*, 4.98, NCH_2), 4.22 (q, *J* = 7.1 Hz, 2H, OCH_2), 2.61 (d, 3H; *rot-1*, 2.56; *rot-2*, 2.65, NMe), 1.37 (d, 9H; *rot-1*, 1.34; *rot-2*, 1.40, ^{t}Bu-CH_3), 1.31 (t, *J* = 7.1 Hz, 3H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.11, 156.95, 156.53, 155.88, 155.25, 139.10, 138.42, 129.04, 128.28, 127.27, 120.95, 120.75, 79.76, 79.35, 60.28, 46.41, 45.12, 32.94, 32.74, 31.58, 30.04, 28.47, 28.32, 28.28.



3ca

2,2,2-trifluoroethyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-phenylbut-2-enoate (3ca)

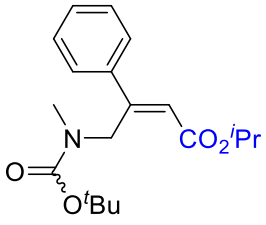
This compound was prepared according to the general procedure B as a white solid (83% yield).

mp: 54-55℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60–7.36 (m, 5H, Ar-CH), 6.23 (d, 1H; *rot-1*, 6.27; *rot-2*, 6.18, =CH), 5.06 (d, 2H; *rot-1*, 5.11; *rot-2*, 5.01, NCH_2), 4.58 (q, *J* = 8.4 Hz, 2H, OCH_2), 2.64 (d, 3H; *rot-1*, 2.59; *rot-2*, 2.69, NMe), 1.42 (d, 9H; *rot-1*, 1.39; *rot-2*, 1.45, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 164.04, 160.83, 160.36, 155.85, 138.55, 137.93, 129.57, 128.41, 128.35, 127.32, 124.19, 121.99, 118.36, 118.18, 79.99, 79.56, 60.58, 60.29, 60.00, 59.71, 46.72, 45.45, 33.19, 32.92, 28.27.

HRMS (ESI): m/z calcd for $C_{18}H_{23}F_3NO_4^+$ $(M+H)^+$ 374.1573, found 374.1575.



3da

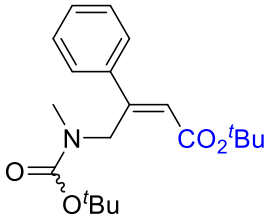
Isopropyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-phenylbut-2-enoate (3da)

This compound was prepared according to the general procedure B as colorless oil (95% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55–7.38 (m, 2H, Ar-CH), 7.38–7.33 (m, 3H, Ar-CH), 6.14 (d, 1H; *rot-1*, 6.19; *rot-2*, 6.09, =CH), 5.13 (q, *J* = 6.3 Hz, 1H, OCH), 5.05 (d, 2H; *rot-1*, 5.10; *rot-2*, 5.01, NCH_2), 2.64 (d, 3H; *rot-1*, 2.59; *rot-2*, 2.68, NMe), 1.40 (d, 9H; *rot-1*, 1.37; *rot-2*, 1.43, ^{t}Bu-CH_3), 1.32 (d, *J* = 6.3 Hz, 6H, ^{i}Pr-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 165.68, 165.56, 156.41, 156.07, 155.90, 155.27, 139.11, 138.42, 129.00, 128.28, 128.21, 127.27, 127.25, 121.52, 121.33, 79.75, 79.34, 67.71, 67.67, 46.33, 45.03, 32.91, 32.71, 28.35, 28.29, 21.94.

HRMS (ESI): m/z calcd for $C_{19}H_{28}NO_4^+$ $(M+H)^+$ 334.2012, found 334.2014.



3ea

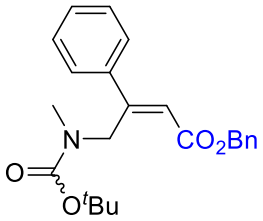
***Tert*-butyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-phenylbut-2-enoate (3ea)**

This compound was prepared according to the general procedure B as light yellow oil (89% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54–7.37 (m, 2H, Ar-CH), 7.37–7.32 (m, 3H, Ar-CH), 6.10 (d, 1H; *rot-1*, 6.15; *rot-2*, 6.01, =CH), 5.01 (d, 2H; *rot-1*, 5.05; *rot-2*, 4.98, NCH_2), 2.65 (d, 3H; *rot-1*, 2.60; *rot-2*, 2.69, NMe), 1.55 (s, 9H, ^{t}Bu-CH_3), 1.40 (d, 9H; *rot-1*, 1.37; *rot-2*, 1.44, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 165.63, 165.52, 155.91, 155.32, 154.90, 154.83, 139.23, 138.55, 128.84, 128.24, 128.19, 127.24, 122.91, 122.80, 80.78, 79.72, 79.31, 77.35, 77.10, 76.85, 46.18, 44.92, 32.82, 32.66, 28.37, 28.30, 28.25.

HRMS (ESI): m/z calcd for $C_{20}H_{30}NO_4^+$ $(M+H)^+$ 348.2169, found 348.2171.



3fa

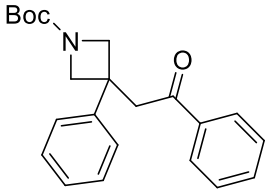
Benzyl (*Z*)-4-((*tert*-butoxycarbonyl) (methyl)amino)-3-phenylbut-2-enoate (3fa)

This compound was prepared according to the general procedure B as light yellow oil (98% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51–7.46 (m, 1H, Ar-CH), 7.41–7.35 (m, 5H, Ar-CH), 7.33 (m, 4H, Ar-CH), 6.19 (d, 1H; *rot-1*, 6.24; *rot-2*, 6.14, =CH), 5.20 (s, 2H, OCH_2), 5.05 (d, 2H; *rot-1*, 5.10; *rot-2*, 5.00, NCH_2), 2.59 (d, 3H; *rot-1*, 2.55; *rot-2*, 2.64, NMe), 1.37 (d, 9H; *rot-1*, 1.34; *rot-2*, 1.40, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 165.88, 165.76, 157.86, 157.44, 155.91, 155.27, 138.97, 138.31, 135.95, 129.21, 128.65, 128.61, 128.53, 128.34, 128.29, 127.32, 127.27, 120.51, 120.32, 79.85, 79.43, 66.23, 46.47, 45.15, 33.05, 32.83, 28.37, 28.33.

HRMS (ESI): m/z calcd for $C_{23}H_{28}NO_4^+$ $(M+H)^+$ 382.2012, found 382.2015.



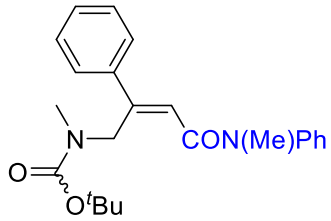
4ga

***Tert*-butyl 3-(2-oxo-2-phenylethyl)-3-phenylazetidine-1-carboxylate (4ga)**

This compound was prepared according to the general procedure B as pale yellow solid (75% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.82–7.78 (m, 2H, Ar-CH), 7.53–7.49 (m, 1H, Ar-CH), 7.38 (t, *J* = 7.8 Hz, 2H, Ar-CH), 7.30–7.27 (m, 4H, Ar-CH), 7.16 (m, 1H), 4.36 (d, *J* = 8.7 Hz, 2H, NCH_2), 4.22 (d, *J* = 8.7 Hz, 2H, NCH_2), 3.72 (s, 2H, CH_2), 1.44 (s, 9H, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, CDCl3): δ 197.15, 156.45, 144.55, 136.96, 133.20, 128.56, 128.34, 127.87, 126.53, 126.42, 79.60, 48.75, 39.70, 28.42.



3ha

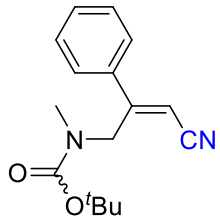
***Tert*-butyl (*Z*)-methyl(4-(methyl(phenyl)amino)-4-oxo-2-phenylbut-2-en-1-yl)carbamate (3ha)**

This compound was prepared according to the general procedure B as light yellow oil (70% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 (m, 4H, Ar-CH), 7.21 (s, 5H, Ar-CH), 7.10 (d, *J* = 6.7 Hz, 1H, Ar-CH), 5.95 (d, 1H; *rot-1*, 5.98; *rot-2*, 5.91, =CH), 4.94 (s, 2H, NCH_2), 3.38 (s, 3H, NMe), 2.64 (d, 3H; *rot-1*, 2.61; *rot-2*, 2.67, MeN), 1.37 (d, 9H; *rot-1*, 1.33; *rot-2*, 1.41, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.51, 166.21, 155.92, 155.39, 150.44, 150.19, 143.77, 139.58, 138.97, 134.07, 129.60, 128.34, 128.14, 128.08, 127.70, 127.66, 127.53, 127.12, 127.08, 126.95, 123.79, 79.66, 79.18, 46.76, 45.81, 37.09, 32.96, 32.74, 28.40, 28.33.

HRMS (ESI): m/z calcd for $C_{23}H_{29}N_2O_3^+$ $(M+H)^+$ 381.2172, found 381.2177.



3ia

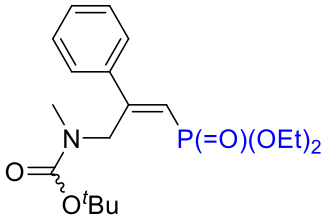
***Tert*-butyl (*Z*)-(3-cyano-2-phenylallyl)(methyl)carbamate (3ia)**

This compound was prepared according to the general procedure B as light yellow oil (68% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56–7.40 (m, 5H, Ar-CH), 5.69 (d, 1H; *rot-1*, 5.73; *rot-2*, 5.64, =CH), 4.74 (d, 2H; *rot-1*, 4.78; *rot-2*, 4.70, NCH_2), 2.75 (d, 3H; *rot-1*, 2.72; *rot-2*, 2.78, NMe), 1.47 (d, *J* = 28.8 Hz, 9H; *rot-1*, 1.44; *rot-2*, 1.50, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 161.31, 155.66, 154.82, 136.09, 135.58, 130.44, 128.78, 126.90, 116.38, 98.46, 97.92, 80.70, 80.58, 80.18, 50.39, 49.18, 33.43, 33.19, 29.70, 29.66,

28.34, 28.28.



3ja

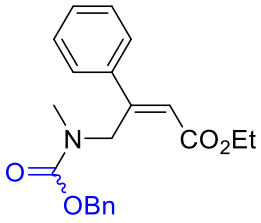
***Tert*-butyl (*Z*)-(3-(diethoxyphosphoryl)-2-phenylallyl)(methyl)carbamate (3ja)**

This compound was prepared according to the general procedure B as light yellow oil (30%, 54% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54–7.39 (m, 2H, Ar-CH), 7.38–7.33 (m, 3H, Ar-CH), 5.95 (dd, 1H; *rot-1*, 6.00 (d, *J* = 15.6 Hz, =CH); *rot-2*, 5.90 (d, *J* = 15.4 Hz)), 4.92 (dd, 2H; *rot-1*, 4.94 (d, *J* = 2.8 Hz); *rot-2*, 4.90 (d, *J* = 2.6 Hz) , NCH_2), 4.16 (m, 4H， OCH_2), 2.64 (d, 3H; *rot-1*, 2.60; *rot-2*, 2.68, NMe), 1.42 (d, *J* = 27.8 Hz, 6H, CH_3), 1.37 (d, 9H; *rot-1*, 1.36; *rot-2*, 1.38, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 159.96, 159.65, 155.83, 155.06, 138.42, 138.24, 129.30, 128.30, 127.09, 127.00, 118.85, 118.46, 117.36, 116.96, 79.92, 79.48, 61.79, 61.74, 47.85, 46.75, 46.69, 32.33, 32.10, 29.70, 28.40, 28.27, 16.45, 16.40.

HRMS (ESI): m/z calcd for $C_{19}H_{31}NO_5P^+$ $(M+H)^+$ 384.1934, found 384.1936.



3ka

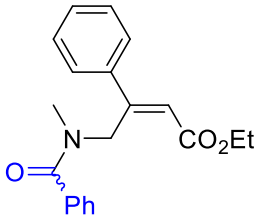
Ethyl (*Z*)-4-(((benzyloxy)carbonyl)(methyl)amino)-3-phenylbut-2-enoate (3ka)

This compound was prepared according to the general procedure B as colorless oil (76% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53 (d, *J* = 7.1 Hz, 1H, Ar-CH), 7.40 (m, 4H, Ar-CH), 7.33 (d, *J* = 7.1 Hz, 3H, Ar-CH), 7.25 (q, *J* = 7.0 Hz, 2H, Ar-CH), 6.20 (d, 1H; *rot-1*, 6.26; *rot-2*, 6.14, =CH), 5.16 (d, 4H; *rot-1*, 5.21; *rot-2*, 5.12, NCH_2), 4.28 (m, 2H, OCH_2), 2.74 (d, 3H; *rot-1*, 2.73; *rot-2*, 2.76, NMe), 1.37 (q, *J* = 6.9 Hz, 3H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.10, 165.97, 156.58, 155.98, 155.70, 138.66, 138.27, 136.99, 136.70, 129.28, 129.13, 128.55, 128.45, 128.41, 128.35, 128.13, 127.79, 127.48, 127.20, 127.12, 121.30, 121.23, 67.37, 66.99, 60.39, 46.05, 45.71, 33.43, 32.54, 14.29.

HRMS (ESI): m/z calcd for $C_{21}H_{24}NO_4^+$ $(M+H)^+$ 354.1699, found 354.1702.



3la

Ethyl (*Z*)-4-(N-methylbenzamido)-3-phenylbut-2-enoate (3la)

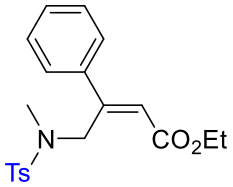
This compound was prepared according to the general procedure B as a yellow solid (72% yield).

mp: 83-84℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (m, 2H, Ar-CH), 7.41–7.37 (m, 3H, Ar-CH), 7.33–7.23 (m, 4H, Ar-CH), 6.94 (d, *J* = 7.4 Hz, 1H, Ar-CH), 6.18 (d, 1H; *rot-1*, 6.29; *rot-2*, 6.07, =CH), 5.26 (d, 2H; *rot-1*, 5.44; *rot-2*, 5.07, NCH_2), 4.25 (q, *J* = 7.1 Hz, 2H, OCH_2), 2.77 (d, 3H; *rot-1*, 2.64; *rot-2*, 2.90, NMe), 1.34 (t, *J* = 7.2 Hz, 3H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 171.49, 166.16, 156.02, 137.99, 136.10, 129.51, 129.40, 128.57, 128.28, 127.21, 126.54, 121.19, 60.45, 43.91, 36.35, 14.30.

HRMS (ESI): m/z calcd for $C_{20}H_{22}NO_3^+$ $(M+H)^+$ 324.1594, found 324.1597.



3ma

Ethyl (Z)-4-((N,4-dimethylphenyl)sulfonamido)-3-phenylbut-2-enoate (3ma)

This compound was prepared according to the general procedure B as a white solid (57% yield).

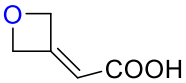
mp: 94-96℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66–7.62 (m, 2H, Ar-CH), 7.62–7.58 (m, 2H, Ar-CH), 7.40 (dd, J = 5.0, 1.9 Hz, 3H, Ar-CH), 7.31 (d, J = 8.0 Hz, 2H, Ar-CH), 6.24 (d, J = 1.2 Hz, 1H,

=CH), 4.77 (s, 2H, NCH_2), 4.14 (q, J = 7.1 Hz, 2H, OCH_2), 2.48 (s, 3H, NMe), 2.43 (s, 3H, Ar-CH_3), 1.24 (t, J = 7.1 Hz, 3H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 165.90, 153.25, 143.50, 137.86, 133.86, 129.75, 129.58, 128.58, 127.62, 127.46, 121.72, 60.41, 47.08, 33.99, 21.55, 14.16.

HRMS (ESI): m/z calcd for $C_{20}H_{24}NO_4S^+$ $(M+H)^+$ 374.1421, found 374.1425



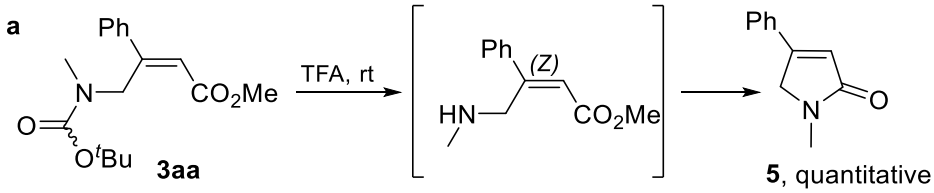
3qa'

2-(Oxetan-3-ylidene)acetic acid (3qa')

This compound was prepared according to the general procedure B as a white solid.

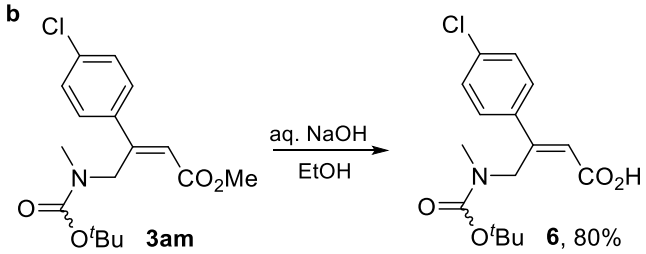
^{1}H NMR (500 MHz, $CDCl_3$): δ 6.03 (t, *J* = 1.8 Hz, 1H, =CH), 4.88 (s, 2H, OCH_2), 4.59 (s, 2H, OCH_2).

5. Transformations of the products and applications



Methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-phenylbut-2-enoate (**3aa**) (100 mg, 0.326 mmol)and trifluoroacetic acid (0.51 ml) were added to a round bottom flask and dissolved in dichloromethane (5 mL). The reaction mixture was stirred at room temperature until the starting material disappeared (monitored by TLC). The solvent was removed in vacuo to afford the product (NMR pure for the crude product).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53–7.49 (m, 2H, Ar-CH), 7.47–7.42 (m, 3H, Ar-CH), 6.46 (d, *J* = 1.5 Hz, 1H, =CH), 4.37 (d, *J* = 1.4 Hz, 2H, NCH_2), 3.13 (s, 3H, NMe).



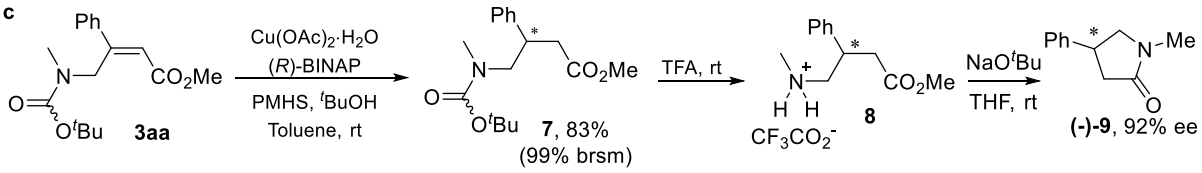
3am (100 mg, 0.294 mmol) was placed in a round bottom flask, then EtOH (2 mL) was added, the reaction mixture was stirred, and NaOH (10%, 1.6 mL) was added. The reaction mixture was stirred at room temperature until no starting material was detected by TLC. Then the pH was adjusted to 1.0 with HCl (1 N). The mixture was extracted with EtOAc. The combined organic layer was washed with saturated aqueous NaCl solution, dried with Na_2SO_4, The solvent was removed and purified by column chromatography on silica gel (EtOAc)to afford the desired product **6** as light brown solid (77 mg, 80%)[8].

mp: 118-120℃

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 (d, *J* = 8.4 Hz, 4H, Ar-CH), 6.17 (s, 1H, =CH), 4.99 (s, 2H, NCH_2), 2.62 (d, 3H; *rot-1*, 2.58; *rot-2*, 2.66, NMe), 1.42 (d, 9H; *rot-1*, 1.40; *rot-2*, 1.44, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 170.81, 156.12, 155.25, 137.03, 135.30, 133.14, 128.58, 121.61, 80.24, 46.01, 33.64, 33.00, 29.71, 28.31.

HRMS (ESI): m/z calcd for $C_{16}H_{20}ClNO_4Na^+$ $(M+Na)^+$ 348.0973, found 348.0974.



$Cu(OAc)_2·H_2O$ (1.64 mg, 0.082 mmol), (*R*)-BINAP (5.12 mg, 0.0082 mmol), and toluene (1.0 mL) were added into an oven-dried Schlenk tube. The resulting mixture was stirred at room temperature for 30 min. Then, PMHS (0.039 mL, 0.656 mmol) was added to the reaction mixture, which was stirred for 30 min. A solution of methyl (*Z*)-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-phenylbut-2-enoate (**3aa**) (26 mg, 0.085 mmol) in toluene (1.0 mL) was added, followed by *t*-BuOH (0.063 mL, 0.656 mmol). The reaction mixture was stirred for 24 h. Then quenched with saturated aqueous ammonium chloride solution, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtrated and concentrated under vacuum. The residue was purified by flash column chromatography (PE/EA = 5:1) to give product (**7**) (22 mg, 83%, brsm >99%)[17].

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (t, *J* = 7.5 Hz, 2H, Ar-CH), 7.29–7.21 (m, 3H, Ar-CH), 3.62 (d, *J* = 7.0 Hz, 3H, OMe), 3.52 (d, 2H; *rot-1*, 3.53; *rot-2*, 3.51, NCH_2), 3.43–3.23 (m, 1H, CH), 2.78 (d, 3H; *rot-1*, 2.77; *rot-2*, 2.79, NMe), 2.69 (m, 2H, CH_2), 1.45 (s, 9H, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 172.38, 155.95, 155.53, 141.53, 128.60, 127.67, 126.99, 79.60, 79.42, 54.75, 53.89, 51.61, 40.96, 40.65, 37.94, 34.69, 29.71, 28.35.

Methyl 4-((*tert*-butoxycarbonyl) (methyl)amino)-3-phenylbutanoate (**7**) (22 mg, 0.072 mmol) and trifluoroacetic acid (0.14 ml) were added to a round bottom flask and dissolved in dichloromethane (2 mL). The reaction mixture was stirred at room temperature until the starting material disappeared (monitored by TLC). The solvent was removed in vacuo to give product (**8**) (21 mg, 92%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.25 (d, *J* = 153.2 Hz, 2H, NH_2), 7.32 (t, *J* = 7.3 Hz, 2H, Ar-CH), 7.28 (s, 1H, Ar-CH), 7.21 (d, *J* = 7.5 Hz, 2H, Ar-CH), 3.60 (s, 3H, OMe), 3.26 (d, *J* = 52.4 Hz, 2H, NCH_2), 2.82 (dd, *J* = 16.5, 6.7 Hz, 1H, CH), 2.71 (dd, *J* = 16.3, 6.8 Hz, 2H, NCH_2), 2.57 (s, 3H, NMe).

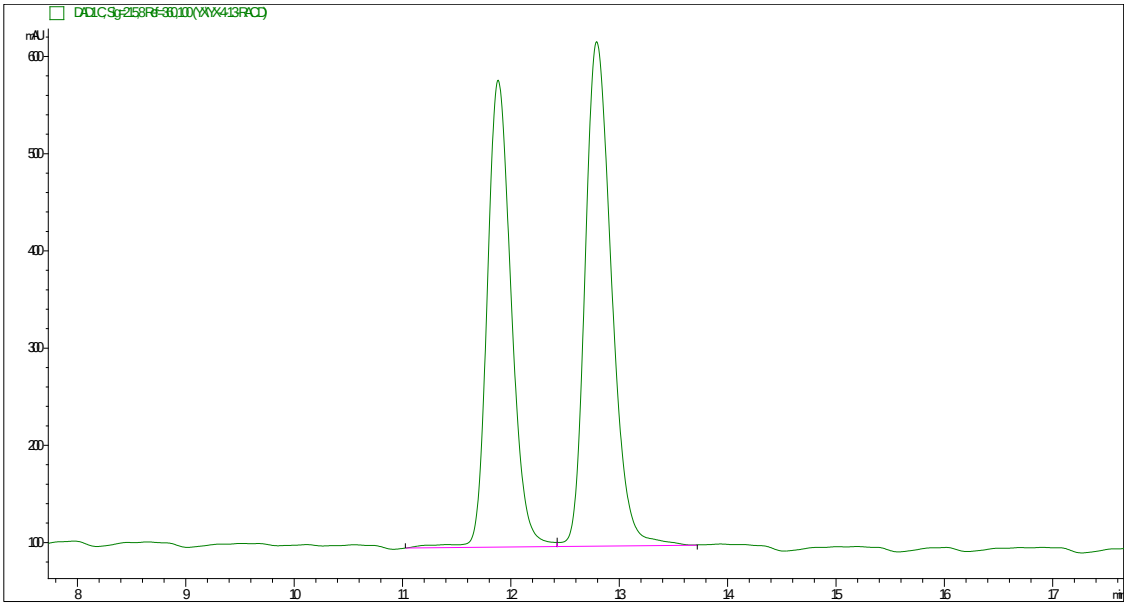
^{13}C NMR (126 MHz, $CDCl_3$): δ 171.87, 138.85, 129.28, 128.94, 128.16, 127.42, 126.74, 52.02, 39.07, 38.51, 33.61.

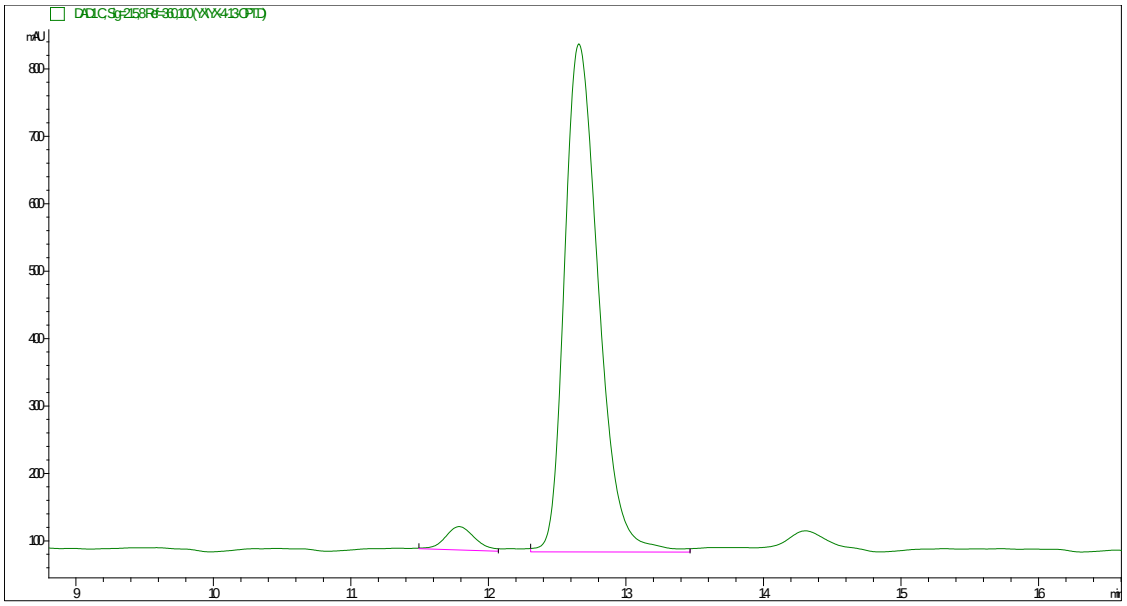
HRMS (ESI): m/z calcd for $C_{12}H_{18}NO_2^+$ $(M)^+$ 208.1332, found 208.1331.

4-Methoxy-N-methyl-4-oxo-2-phenyl-2λ_3-butan-1-aminium 2,2,2-trifluoroacetate (**8**) (21 mg, 0.066 mmol) and sodium *tert*-butoxide (12.5 mg, 0.13 mmol) were added to a round bottom flask and dissolved in THF (1 ml). The reaction mixture was stirred at room temperature until the starting material disappeared (monitored by TLC). The solvent was removed in vacuo, then purified by flash column chromatography (EtOAc) to give product (**9**) (11 mg, 73%, 92% ee), $[\alpha]_D^{20}$ = -4.42 (*c* 0.12, EtOAc) [18].

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (t, *J* = 7.5 Hz, 2H, Ar-CH), 7.28 (d, *J* = 1.3 Hz, 1H, Ar-CH), 7.24–7.20 (m, 2H, Ar-CH), 3.75 (dd, *J* = 9.7, 8.3 Hz, 1H, NCH_2), 3.58 (p, *J* = 8.3 Hz, 1H, CH), 3.41 (dd, *J* = 9.7, 7.0 Hz, 1H, NCH_2), 2.91 (s, 3H, NMe), 2.82 (dd, *J* = 16.9, 9.1 Hz, 1H, CH_2), 2.55 (dd, *J* = 16.9, 8.3 Hz, 1H, CH_2).

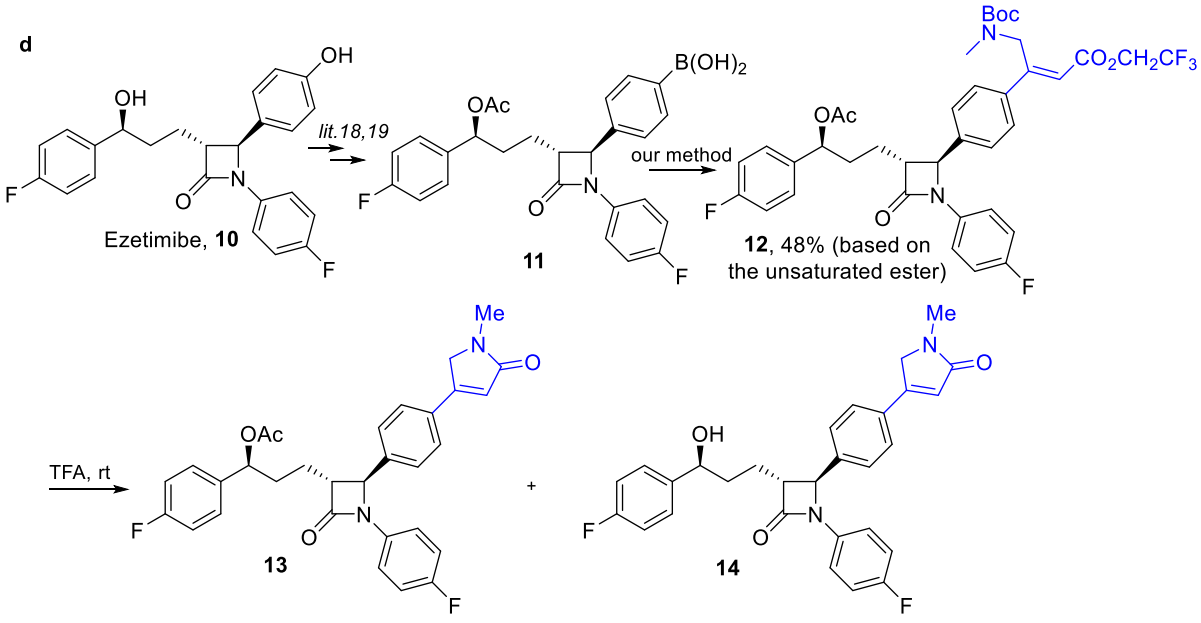
HPLC: Phenomenex column Lux® 5 μm Amylose-1, 00G-4732-E0, 250 x 4.6 mm; detected at 210 nm; *n*-hexane/*i*-propanol = 90/10; flow = 1.0 ml/min; Retention time: 11.8 min (minor), 12.7 min (major).





No.	Time	Peak Area	Peak Height	Peak Width	Symmetry Factor	Peak Area %
1	11.79	514.8	34.5	0.2485	0.858	3.828
2	12.658	12932.1	753.5	0.2682	0.683	96.172

Supplementary Figure 1. HPLC report of **(-)-9**



Ezetimibe (**10**) (2.11 g, 5.15 mmol) and 4-dimethylaminopyridine (126 mg, 1.03 mmol) were dissolved in methylene chloride (40 ml). Triethylamine (1.45 mL, 10.3 mmol) was added via syringe followed by *N*-Phenyltrifluoromethanesulfonimide (2.02 g, 5.67 mmol) added as a solid. The reaction was stirred for 3.5h at room temperature and then poured into water, extracted with EtOAc. The organic layer was washed with water and brine, then dried

over Na_2SO_4, filtrated and concentrated under vacuum. The residue was then purified by flash column chromatography (PE/EA = 9:1 to 1:9) to give product as a white solid (2.77 g, 99%) [19].

To a stirred solution of (trifluoromethanesulfonyl)ezetimibe (2.77 g, 5.12 mmol) in pyridine (10 mL) and dichloromethane (30 mL) was added acetyl chloride (534 mg, 6.8 mmol) at 0℃. The reaction was stirred at room temperature until the starting material disappeared (monitored by TLC) (additional acetyl chloride was added if starting material was not consumed). The mixture was extracted with CH_2Cl_2 and washed with diluted HCl and brine. The combined organic layer was dried over Na_2SO_4, filtrated and concentrated under vacuum. The residue was then purified by flash column chromatography (PE/EA = 3:1) to give ezetimibe derivative as a white solid (2.92 g, 98%) [20].

To a 250 mL of round-bottle flask were added ezetimibe derivative (2.92 g, 5 mmol), bis(pinacolato)diboron (1.53 g, 6 mmol), KOAc (981 mg, 10 mmol) and $Pd(dppf)Cl_2$ (366 mg, 0.5 mmol) under N_2, followed by dioxane (30 mL) with stirring. The reaction mixture was placed into a preheated oil bath at 90℃ for 12 h .The mixture was cooled to room temperature, extracted with EtOAc and washed with brine. The combined organic layer was dried over Na_2SO_4, filtrated and concentrated under vacuum. The residue was then purified by flash column chromatography (PE/EA = 6:1) to give a mixture of boronic ester and boraonic acid as a white solid, which was used directly for next step.

To a solution of the above mixture (1 g) in acetone (8 mL) and water (8 mL) were added NH_4OAc (0.83 g, 10.58 mmol) and $NaIO_4$ (2.26 g, 10.58 mmol). The resulting mixture was stirred at room temperature for 48 h, and then filtered through a pad of cellite. The filtrate was extracted with EtOAc, and the organic layer was dried over Na_2SO_4, filtrated and concentrated under vacuum. The residue was then purified by flash column chromatography (PE/EA = 1.5:1 to DCM/MeOH = 20:1) to give product **11** as a white solid (347 mg, 45%) [20]. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.21 (d, *J* = 7.7 Hz, 1H, OH), 7.83 (d, *J* = 7.7 Hz, 1H, OH), 7.45 (d, *J* = 7.7 Hz, 1H, Ar-CH), 7.33–7.19 (m, 6H, Ar-CH), 6.95 (m, 5H, Ar-CH), 5.71 (m, 1H, OCH), 4.65 (m, 1H, NCH), 3.09 (m, 1H, CHCO), 2.06 (s, 2H, CH_2), 2.04 (d, *J* = 2.5 Hz, 3H, OAc), 1.89 (m, 2H, CH_2).

The compound **12** was prepared according to the general procedure B as colorless oil (33

mg, 48%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (dd, *J* = 52.3, 7.8 Hz, 2H, Ar-CH), 7.33 (dd, *J* = 11.1, 5.5 Hz, 4H, Ar-CH), 7.24 (dd, *J* = 8.9, 4.6 Hz, 2H, Ar-CH), 7.06 (t, *J* = 8.5 Hz, 2H, Ar-CH), 6.97 (t, *J* = 8.5 Hz, 2H, Ar-CH), 6.22 (d, 1H; *rot-1*, 6.26; *rot-2*, 6.18, =CH), 5.76 (t, *J* = 6.8 Hz, 1H, OCH), 5.04 (d, 2H; *rot-1*, 5.01; *rot-2*, 5.07, NCH_2), 4.67–4.63 (m, 1H, NCH), 4.59 (q, *J* = 8.4 Hz, 2H, CH_2CF_3), 3.10 (s, 1H, CHCO), 2.67 (d, 3H; *rot-1*, 2.61; *rot-2*, 2.70, NMe), 2.10 (s, 3H, OAc), 2.07(m, 2H, CH_2), 2.01–1.86 (m, 2H, CH_2), 1.30 (d, 9H; *rot-1*, 1.30; *rot-2*, 1.31, ^{t}Bu-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ 170.18, 166.58, 163.85, 163.73, 163.46, 161.49, 160.06, 159.60, 159.12, 158.12, 155.75, 155.08, 139.08, 138.98, 135.68, 133.64, 128.37, 128.29, 128.22, 125.83, 119.03, 118.81, 118.35, 118.29, 116.02, 115.83, 115.65, 115.48, 80.14, 79.58, 74.87, 60.79, 60.38, 60.20, 60.09, 59.80, 46.44, 45.30, 33.70, 33.17, 32.99, 29.71, 29.67, 28.31, 28.18, 24.99, 21.19.

HRMS (ESI): m/z calcd for $C_{38}H_{39}F_5N_2O_7Na^+$ $(M+Na)^+$ 753.2569, found 753.2568.

2,2,2-trifluoroethyl(*Z*)-3-(4-((2S,3R)-3-((S)-3-acetoxy-3-(4-fluorophenyl)propyl)-1-(4-fluorophenyl)-4-oxoazetidin-2-yl)phenyl)-4-((*tert*-butoxycarbonyl)(methyl)amino)but-2-enoate (**12**) (25 mg, 0.034 mmol), and trifluoroacetic acid (0.066 ml) were added to a round bottom flask and dissolved in dichloromethane (2 mL). The reaction mixture was stirred at room temperature until the starting material disappeared (monitored by TLC). The solvent was removed in vacuo, and the residue was then purified by flash column chromatography (PE/EA = 6:1) to afford the product (**13**) (9.8 mg, 54%) and (**14**) (6.7 mg, 40%) as colorless oil.

Product (**13**)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 (d, *J* = 8.0 Hz, 2H, Ar-CH), 7.36 (d, *J* = 8.0 Hz, 2H, Ar-CH), 7.30–7.27 (m, 2H, Ar-CH), 7.20 (dd, *J* = 9.0, 4.4 Hz, 2H, Ar-CH), 7.02 (t, *J* = 8.6 Hz, 2H, Ar-CH), 6.94 (t, *J* = 8.6 Hz, 2H, Ar-CH), 6.45 (s, 1H, =CH), 5.70 (t, *J* = 6.8 Hz, 1H, OCH), 4.62 (d, *J* = 2.4 Hz, 1H, NCH), 4.32 (s, 2H, NCH_2), 3.10 (s, 3H, NMe), 3.07 (m, 1H, CHCO), 2.06 (s, 3H, OAc), 2.03(m, 2H, CH_2)1.88 (m, 2H, CH_2).

^{13}C NMR (126 MHz, $CDCl_3$): δ 171.49, 170.17, 166.48, 163.49, 161.53, 160.11, 158.17, 152.85, 139.58, 135.67, 135.64, 133.66, 133.64, 132.44, 128.30, 128.23, 126.70, 126.54,

121.49, 118.35, 118.29, 116.08, 115.90, 115.67, 115.50, 74.80, 60.81, 60.25, 54.28, 33.63, 29.14, 24.95, 21.18, 14.21.

HRMS (ESI): m/z calcd for $C_{31}H_{29}F_2N_2O_4^+$ $(M+H)^+$ 531.2089, found 531.2093.

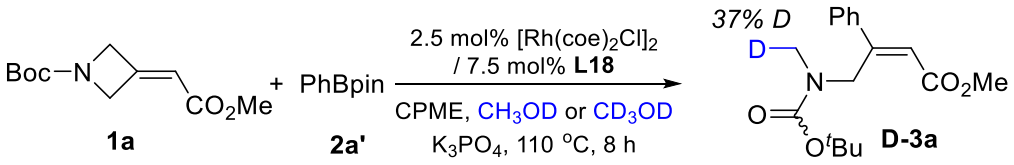
Product (**14**)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58–7.53 (m, 2H, Ar-CH), 7.43–7.34 (m, 4H, Ar-CH), 7.28–7.23 (m, 2H, Ar-CH), 7.12 (m, 2H, Ar-CH), 6.99 (t, *J* = 8.7 Hz, 2H, Ar-CH), 6.50 (d, *J* = 1.9 Hz, 1H, =CH), 5.92 (m, 1H, OCH), 4.66 (dd, *J* = 9.9, 2.4 Hz, 1H, NCH), 4.37 (s, 2H, NCH_2), 3.15 (s, 3H, NMe), 3.11 (dd, *J* = 7.8, 2.3 Hz, 1H, CHCO), 2.24 (q, *J* = 7.6 Hz, 1H, OH), 2.16–1.83 (m, 4H, CH_2CH_2).

^{13}C NMR (126 MHz, $CDCl_3$): δ 171.45, 166.09, 166.03, 164.03, 162.04, 160.16, 158.22, 156.86, 156.52, 152.77, 139.28, 139.25, 133.53, 133.16, 133.16, 133.13, 132.56, 128.50, 128.48, 128.43, 128.41, 126.74, 126.52, 121.56, 118.38, 118.32, 116.15, 116.11, 115.98, 115.93, 79.59, 79.38, 60.79, 60.72, 59.91, 59.89, 54.27, 33.26, 33.17, 29.71, 29.15, 24.89, 24.61, 24.57.

HRMS (ESI): m/z calcd for $C_{29}H_{27}F_2N_2O_3^+$ $(M+H)^+$ 489.1984, found 489.1988.

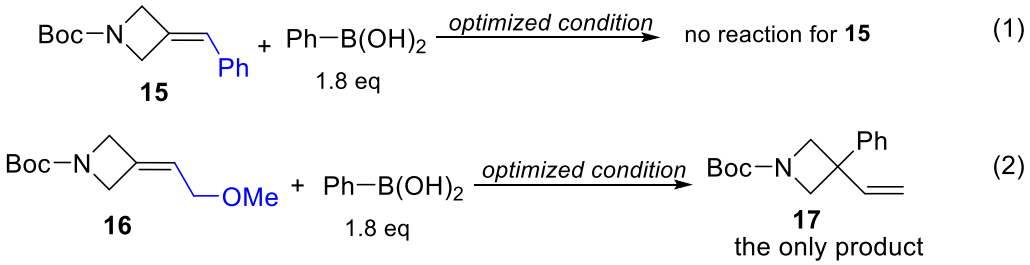
6. The Experiments for Mechanistic Study



The compound **D-3a** was prepared according to the general procedure B, using CH_3OD or CD_3OD to afford the deuterated product as colorless oil (55% yield).

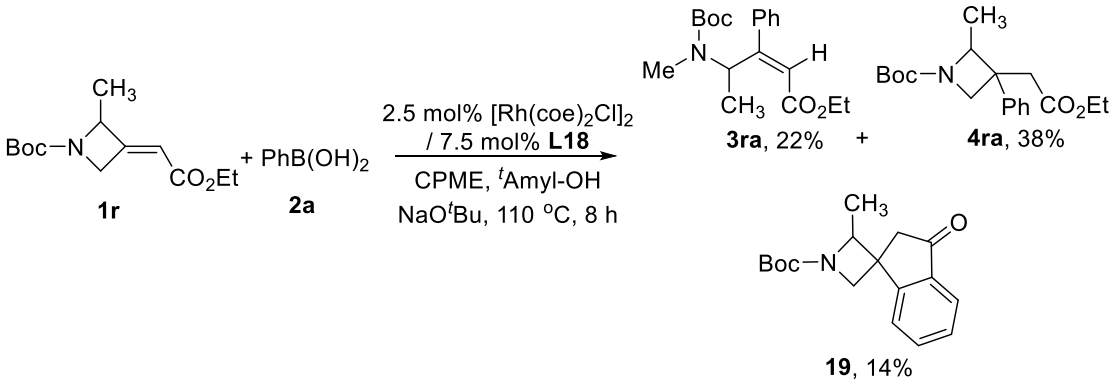
The deuterium experiment is performed with d-methanol or d^4-methanol as the protic agent, and the analysis of the product shows nearly the same result: 37% deuterium on the N-methyl group (existence of trace water resulted in the deuterium-free product), which demonstrated the existence of **IV** (Scheme 3). The proton source could be the protic agent, or the water that formed through the dehydration of phenylboronic acid, or the trace water introduced by the solvent.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53–7.43 (m, 1H, Ar-CH), 7.34 (dd, *J* = 5.6, 1.9 Hz, 4H, Ar-CH), 6.14 (d, 1H, *rot-1*, 6.18; *rot-2*, 6.09, =CH), 5.03 (d, 2H, *rot-1*, 5.08; *rot-2*, 4.98, NCH_2), 3.77 (s, 3H, OMe), 2.60 (d, 3H, *rot-1*, 2.55; *rot-2*, 2.64, NMe), 1.37 (d, 9H, *rot-1*, 1.34; *rot-2*, 1.41, ^{t}Bu-CH_3).



The reaction was operated according to the general procedure B. There was no reaction for (1) by monitoring with TLC and NMR. The reaction (2) gave **17** as the only product (colorless oil, 12 mg, 49% (82% brsm)).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.5 Hz, 2H, Ar-CH), 7.31 (s, 1H, Ar-CH), 7.22 (d, *J* = 7.0 Hz, 2H, Ar-CH), 6.32 (dd, *J* = 17.1, 10.4 Hz, 1H, CH=), 5.20 (d, *J* = 10.3 Hz, 1H, =CH), 4.89 (d, *J* = 17.1 Hz, 1H, =CH), 4.34 (d, *J* = 7.9 Hz, 2H, NCH_2), 4.22 (d, *J* = 8.1 Hz, 2H, NCH_2), 1.49 (s, 9H, ^{t}Bu-CH_3).



The reaction was operated according to the general procedure B. **3ra** and **4ra** were obtained as a mixture and not separable.

As shown in above scheme, the β-C elimination occurred at the non-substituted side and it furnished **3ra** as the sole CCP product. Since the β-C elimination prefers the non-substituted side because of the steric hindrance between substituent group and Rh catalyst (four-member ring transition state was necessary), and the radical pathway prefers the substituted side (The methyl-substituted carbon has the higher electron density compared to the non-substituted carbon. Moreover, the steric effect is not the predominant effect in the radical pathway as the transition state includes the single electron which is much smaller than the Rh catalyst.), we could exclude the radical pathway.

Moreover, the selectivity between CCP product and "conjugate addition" CA product for **1r** was much lower than that for **1a**. It also matches the deduction that the steric effect makes the CCP more difficult.

Ethyl (Z)-4-((tert-butoxycarbonyl)(methyl)amino)-3-phenylpent-2-enoate (3ra)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.21 (t, *J* = 7.4 Hz, 3H, Ar-CH), 7.11 (m, 2H, Ar-CH), 6.04 (q, *J* = 7.4 Hz, 1H, NCH), 5.68 (s, 1H, =CH), 4.19 (d, *J* = 7.4 Hz, 2H, OCH_2), 2.29 (s, 3H, NMe), 1.47 (d, *J* = 7.4 Hz, 3H, $NCHCH_3$)1.44 (s, 9H, ^{t}Bu-CH_3), 1.29 (t, *J* = 7.2 Hz, 3H,OCH_2CH_3).

***Tert*-butyl 3-(2-ethoxy-2-oxo-1-phenylethyl)-2-methylazetidine-1-carboxylate (4ra)**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33–7.29 (m, 3H, Ar-CH), 7.15 (d, *J* = 7.2 Hz, 2H, Ar-CH), 4.44 (q, *J* = 6.5 Hz, 1H, NCH), 4.30 (d, *J* = 8.8 Hz, 1H, NCH_2), 4.17 (d, *J* = 7.2 Hz, 1H, NCH_2), 3.92 (q, *J* = 7.1 Hz, 2H, OCH_2), 3.04 (d, *J* = 14.8 Hz, 1H, CH_2), 2.76 (d, *J* = 14.8 Hz, 1H, CH_2), 1.52 (d, *J* = 6.5 Hz, 3H, $NCHCH_3$), 1.43 (s, 9H, ^{t}Bu-CH_3), 1.04 (t, *J* = 7.1 Hz, 3H,

OCH_2CH_3).

HRMS (ESI): m/z calcd for $C_{19}H_{28}NO_4^+$ $(M+H)^+$ 334.2013, found 334.2013.

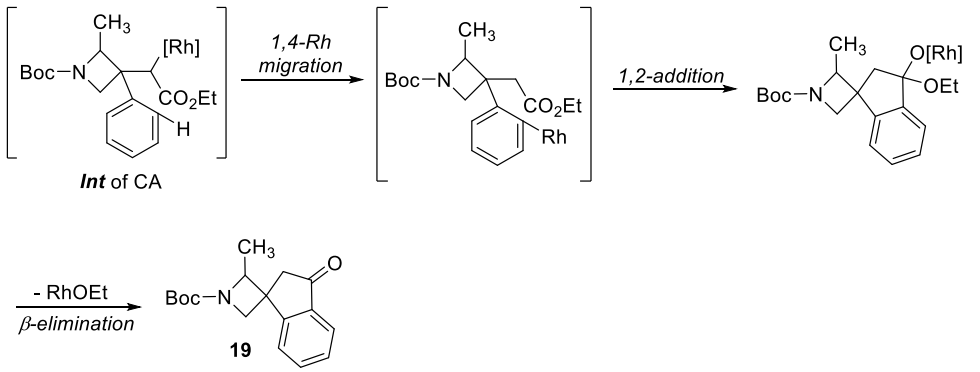
***Tert*-butyl 2-methyl-3'-oxo-2',3'-dihydrospiro[azetidine-3,1'-indene]-1-carboxylate (19)**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78–7.69 (m, 3H, Ar-CH), 7.48–7.43 (m, 1H, Ar-CH), 4.49 (q, *J* = 6.4 Hz, 1H, NCH), 4.13 (d, *J* = 8.7 Hz, 1H, NCH_2), 4.08 (d, *J* = 8.7 Hz, 1H, NCH_2), 3.09 (d, *J* = 19.3 Hz, 1H, CH_2), 2.68 (d, *J* = 19.3 Hz, 1H, CH_2), 1.50 (s, 9H, ^{t}Bu-CH_3), 1.41 (d, *J* = 6.5 Hz, 3H, $NCHCH_3$).

^{13}C NMR (126 MHz, $CDCl_3$): δ 204.43, 158.92, 156.69, 136.39, 136.29, 129.24, 124.38, 123.76, 80.57, 44.46, 43.32, 30.27, 29.08, 29.05, 18.04.

HRMS (ESI): m/z calcd for $C_{17}H_{22}NO_3^+$ $(M+H)^+$ 288.1594, found 288.1598.

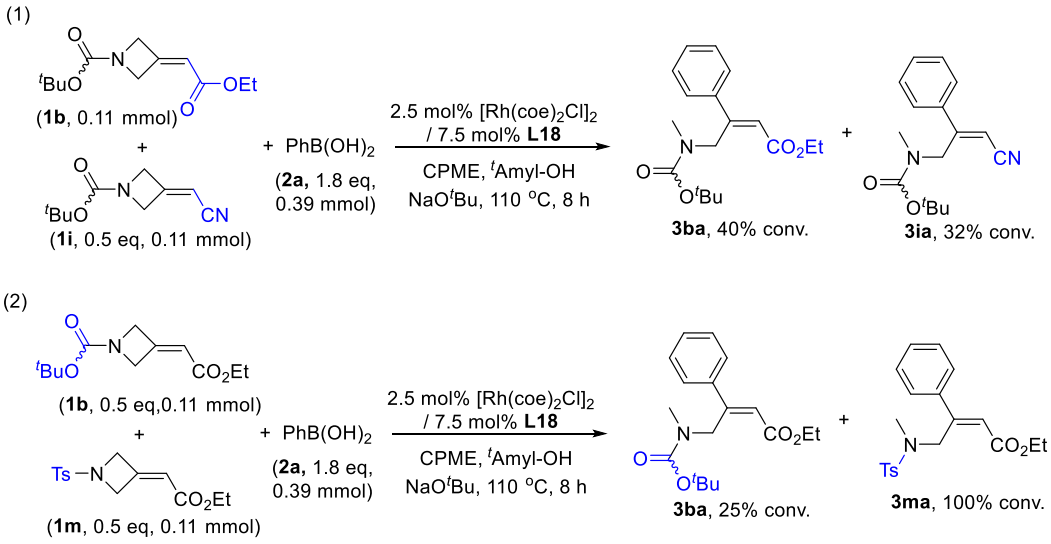
We deduced that the formation of spiro compound **19** was the result of the following procedures: conjugate addition -> 1,4-Rh migration -> 1,2-addition -> β-elimination.



It could be also taken as an evidence of the existence of **III-B** of our proposed catalytic cycle.

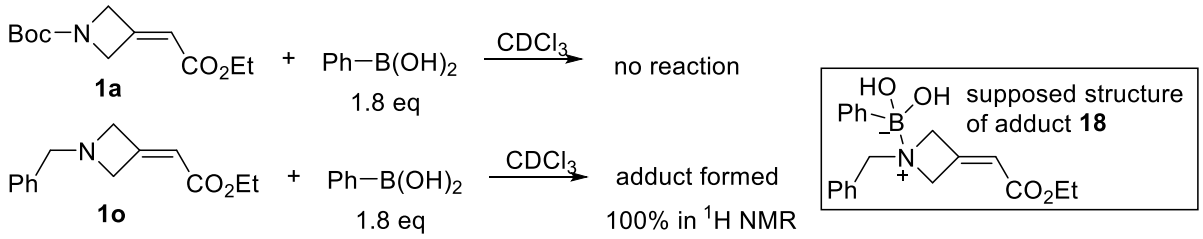
The Kinetic Studies:

Two reactions were conducted using the 1:1 mixture of different unsaturated substrates:



It shows that both the electro-withdrawing group and the substituent group on the nitrogen atom give influences on the reaction rate. It matches our deduction that the reaction starts with conjugate addition, in which step the HOMO and LUMO orbitals of the unsaturated compounds affect the efficiency of addition.

The NMR Studies:



The reason for the low reactivity and the void CCP selectivity of **1n** and **1o**, compared to their amide (**1g**) and carbamate (**1a**) analogs, is obscure. The possible explanations include electrical property, bond length, bond angle, coordination effect of amine with Rh, etc. One simple experiment might point out the main difference between these substrates: ^{1}H NMR spectra clearly showed that Lewis pair **18** formed in the mixture of **1o** and phenyl boronic acid **2a**, while there was no change for mixing **1a** and **2a**. It indicates that the problem of no CCP selectivity for **1n** and **1o** might come from the free electron pair on N atom, which could coordinate to the catalyst or the boronic acid.

7. References

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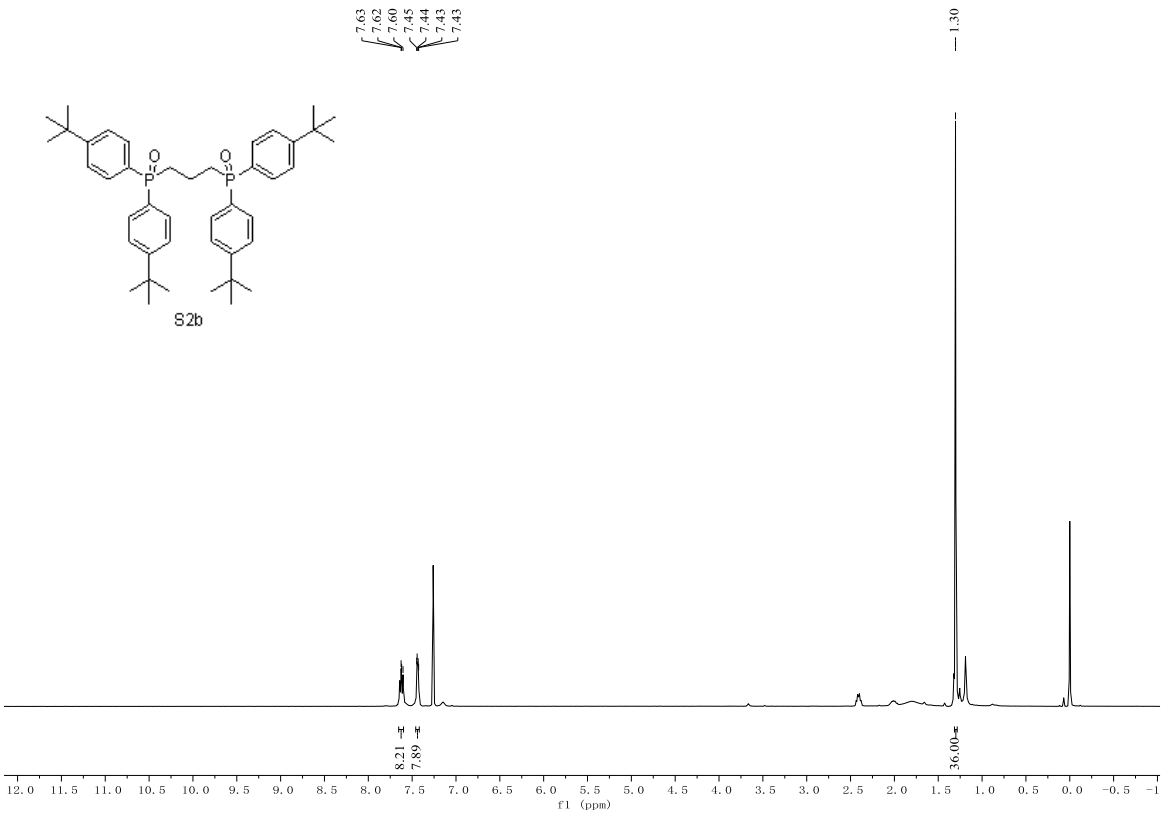
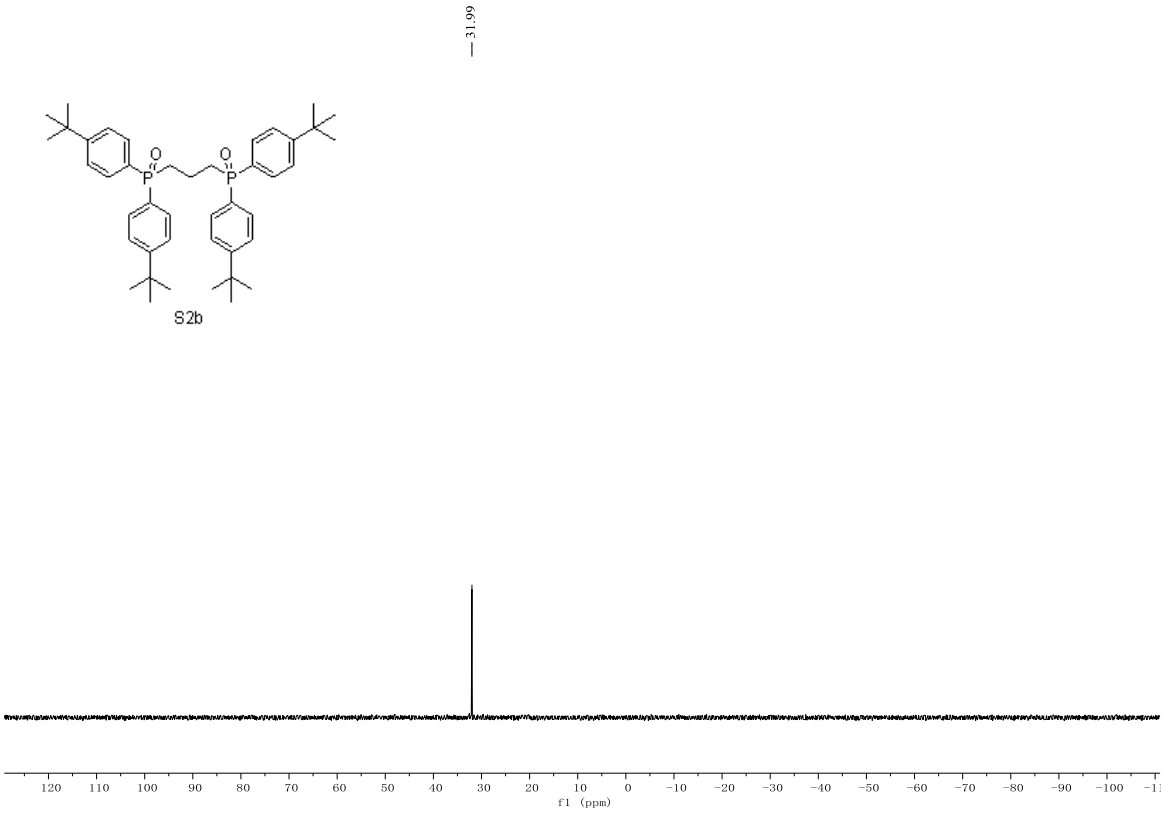
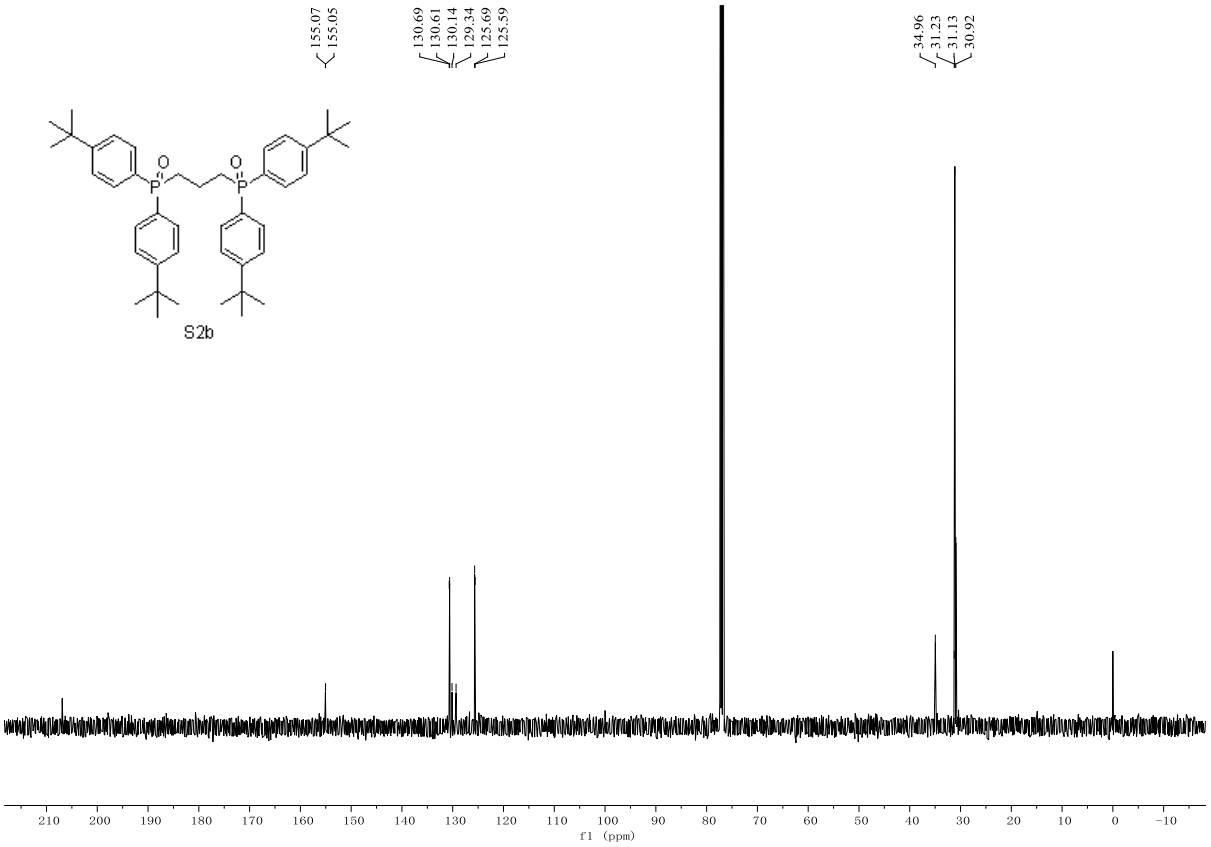
8. Spectra



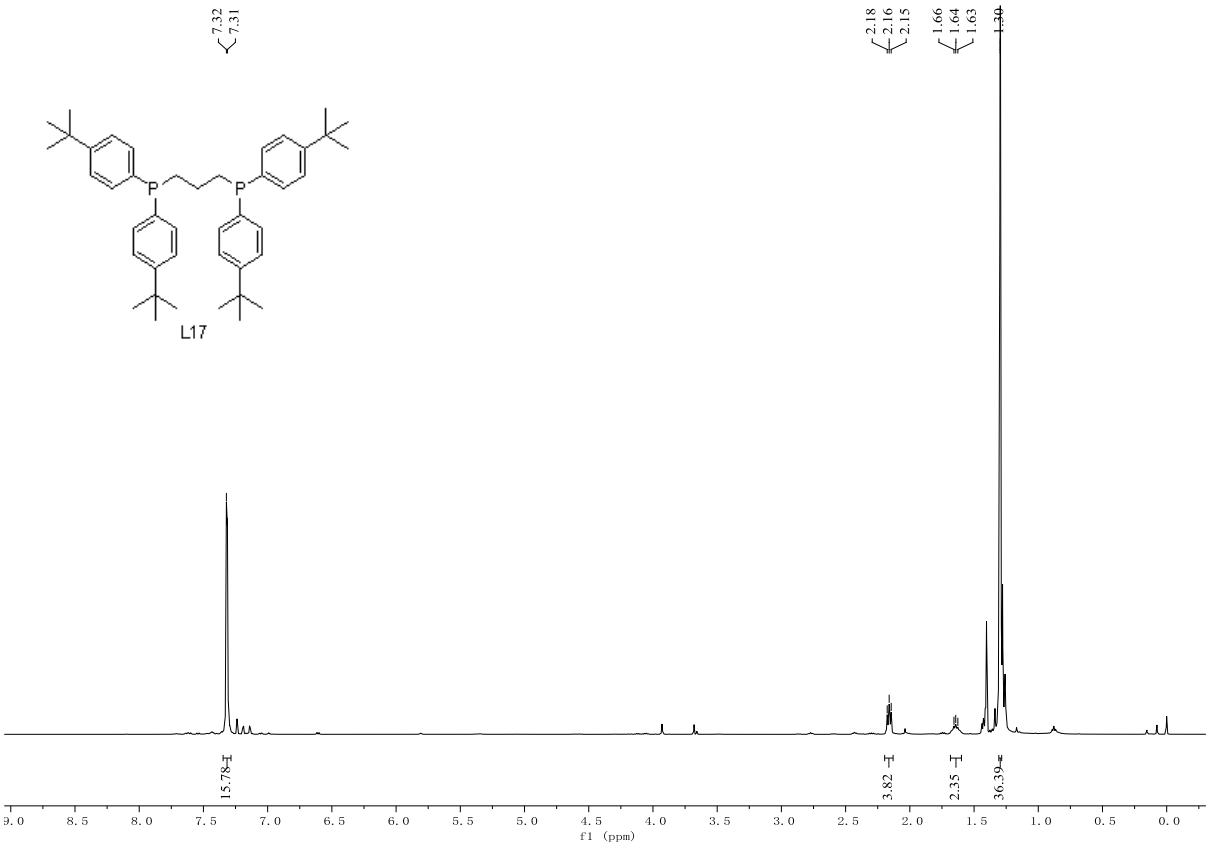
Supplementary Figure 2. ^{1}H NMR Spectra of **S2b**



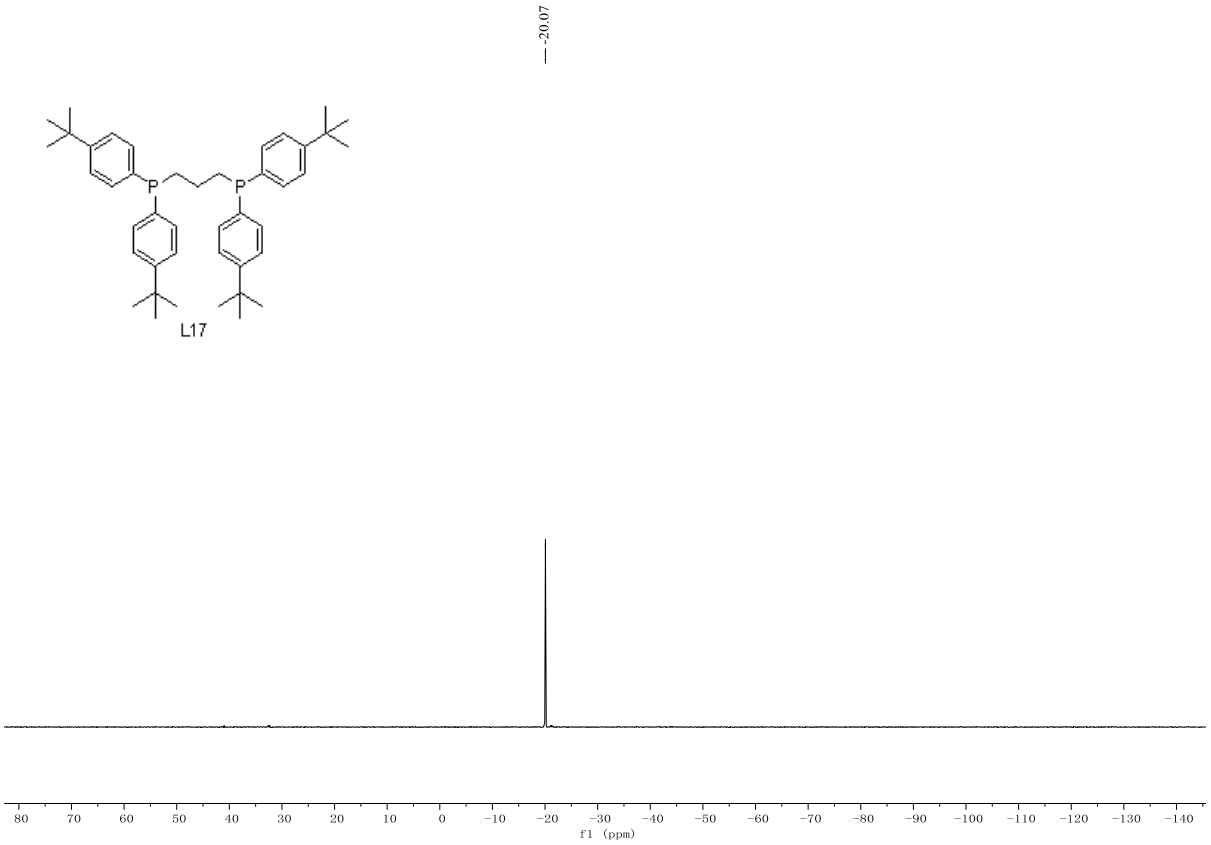
Supplementary Figure 3. ^{31}P NMR Spectra of **S2b**



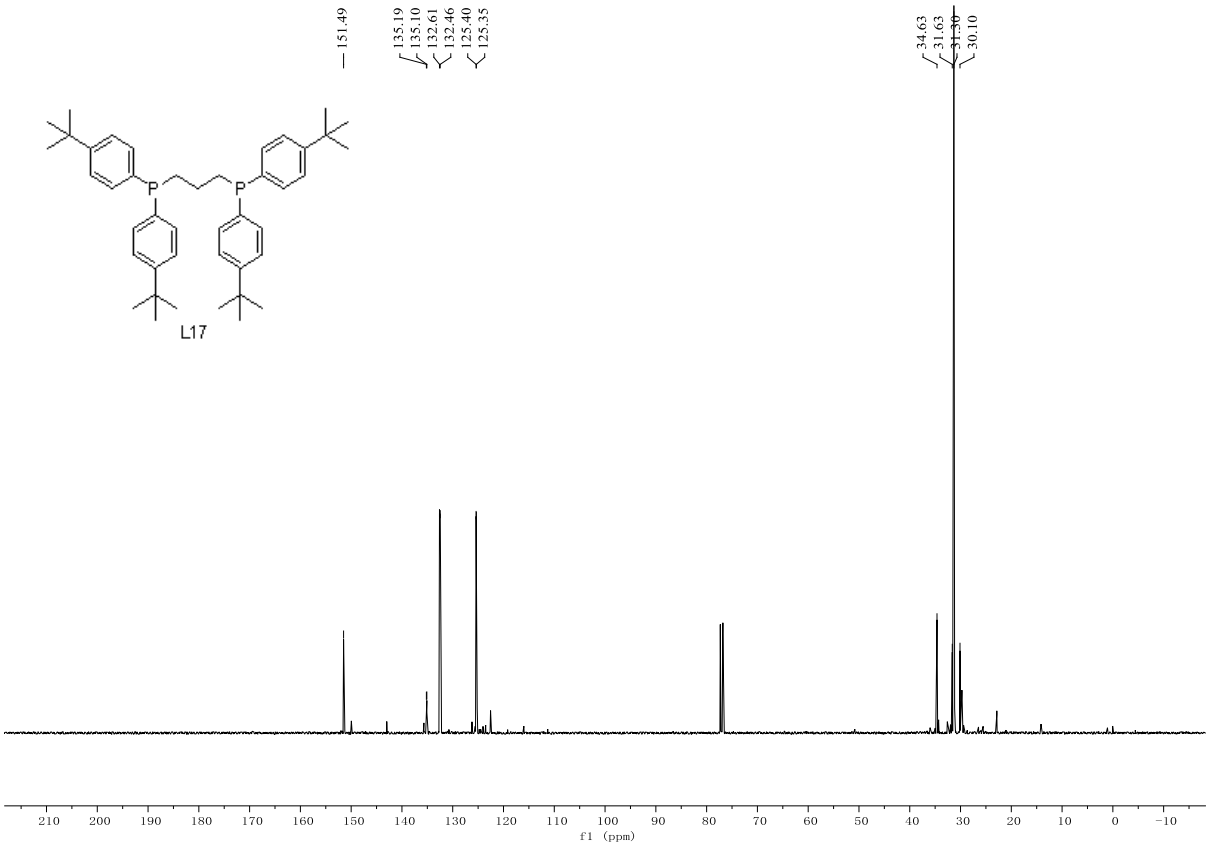
Supplementary Figure 4. ^{13}C NMR Spectra of **S2b**



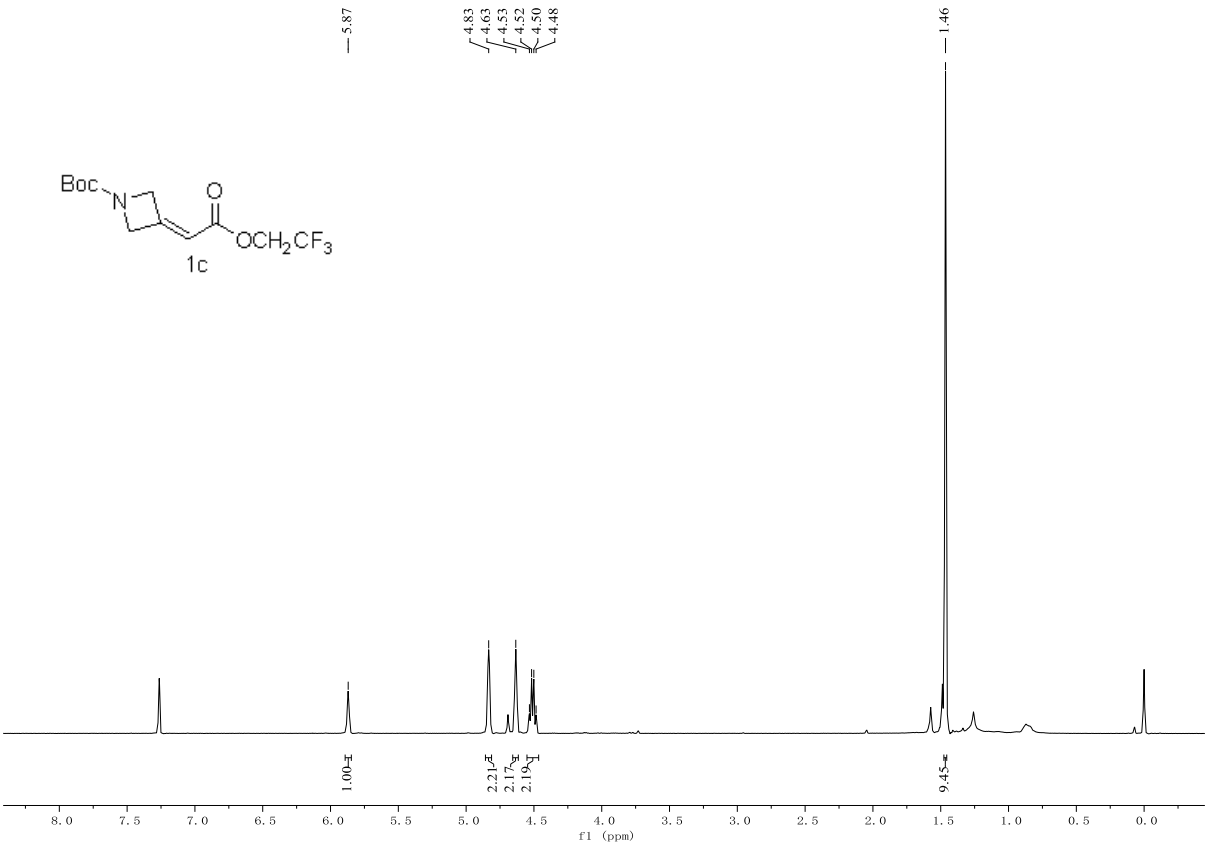
Supplementary Figure 5. ^{1}H NMR Spectra of **L17**



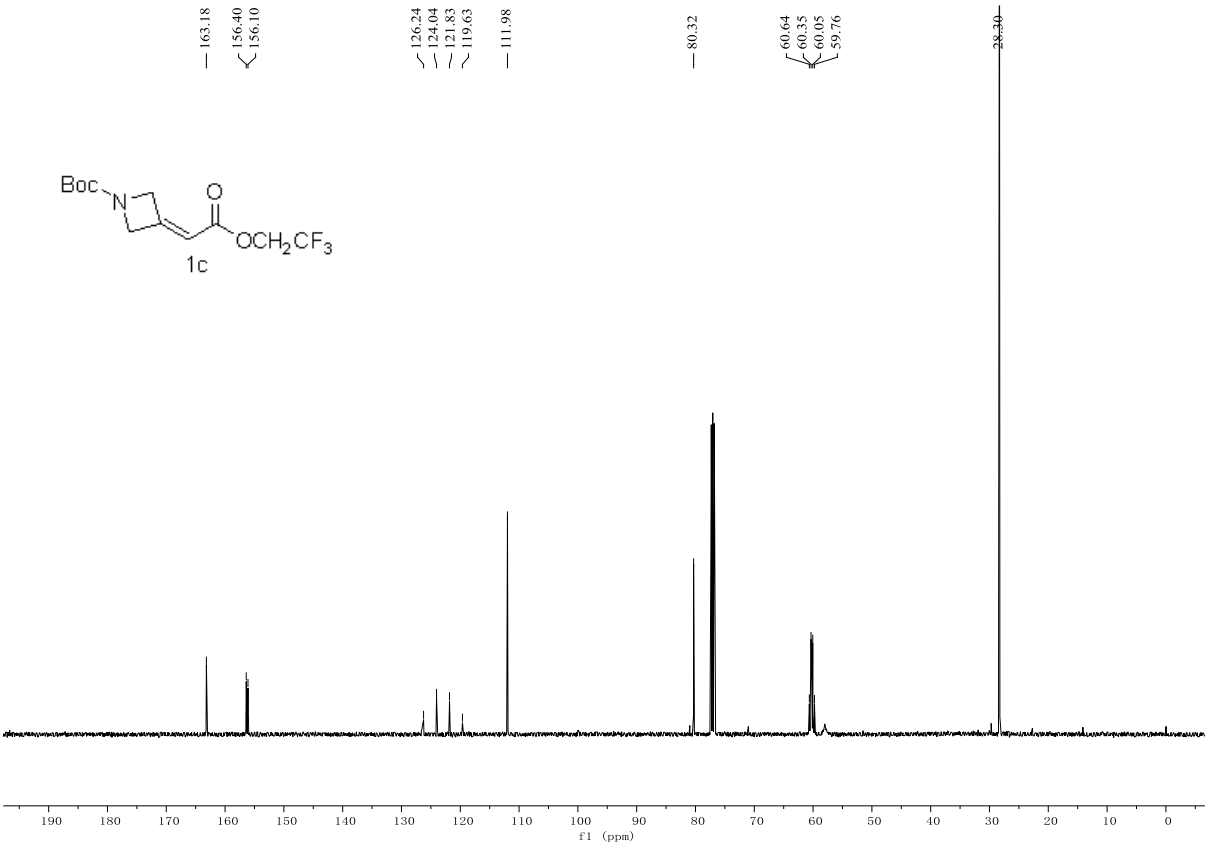
Supplementary Figure 6. ^{31}P NMR Spectra of **L17**



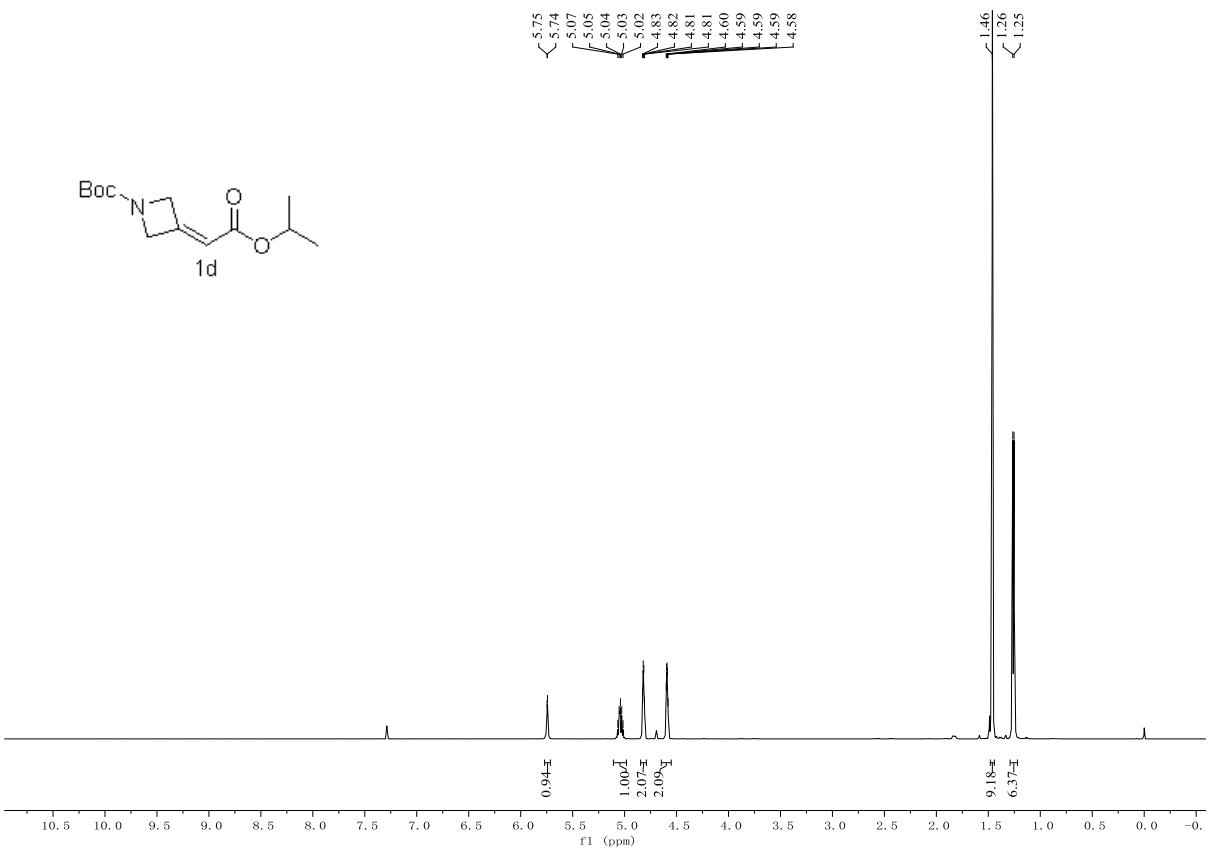
Supplementary Figure 7. ^{13}C NMR Spectra of **L17**



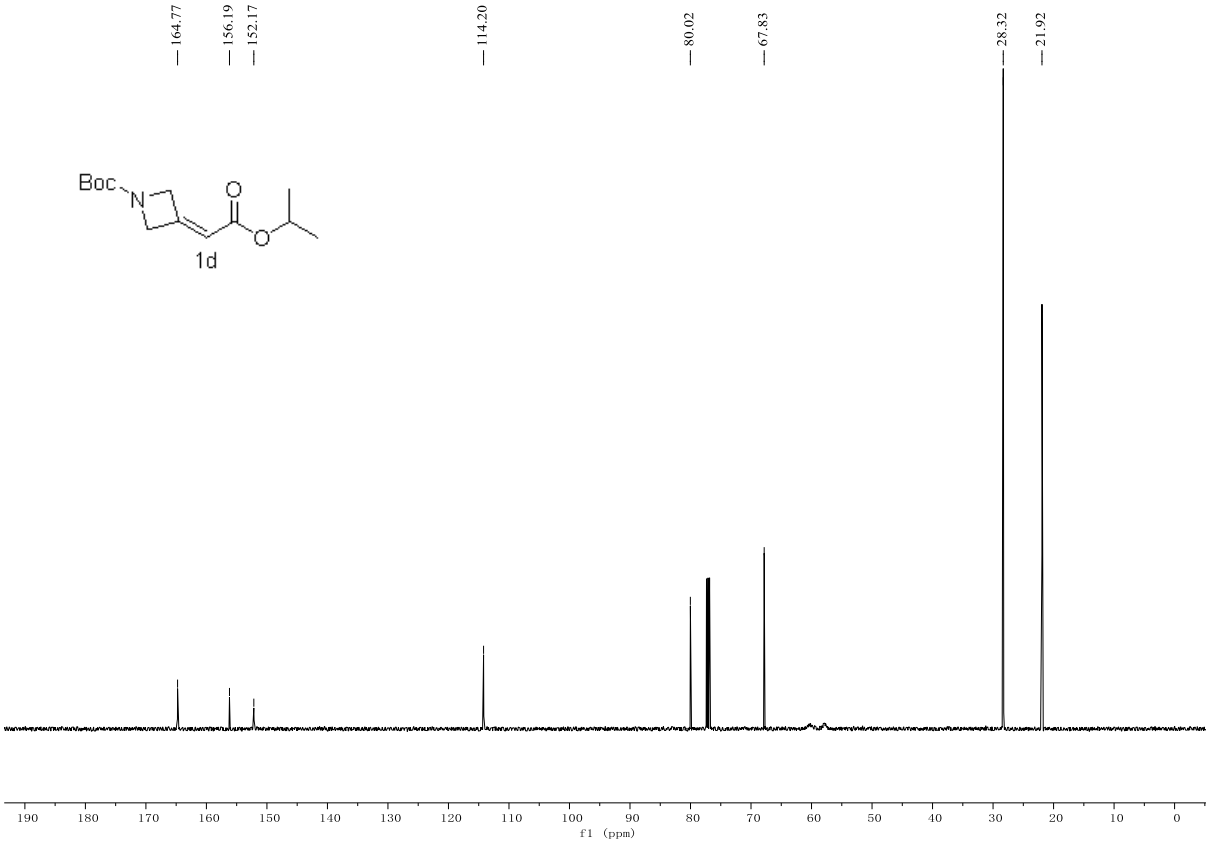
Supplementary Figure 8. ^{1}H NMR Spectra of **1c**



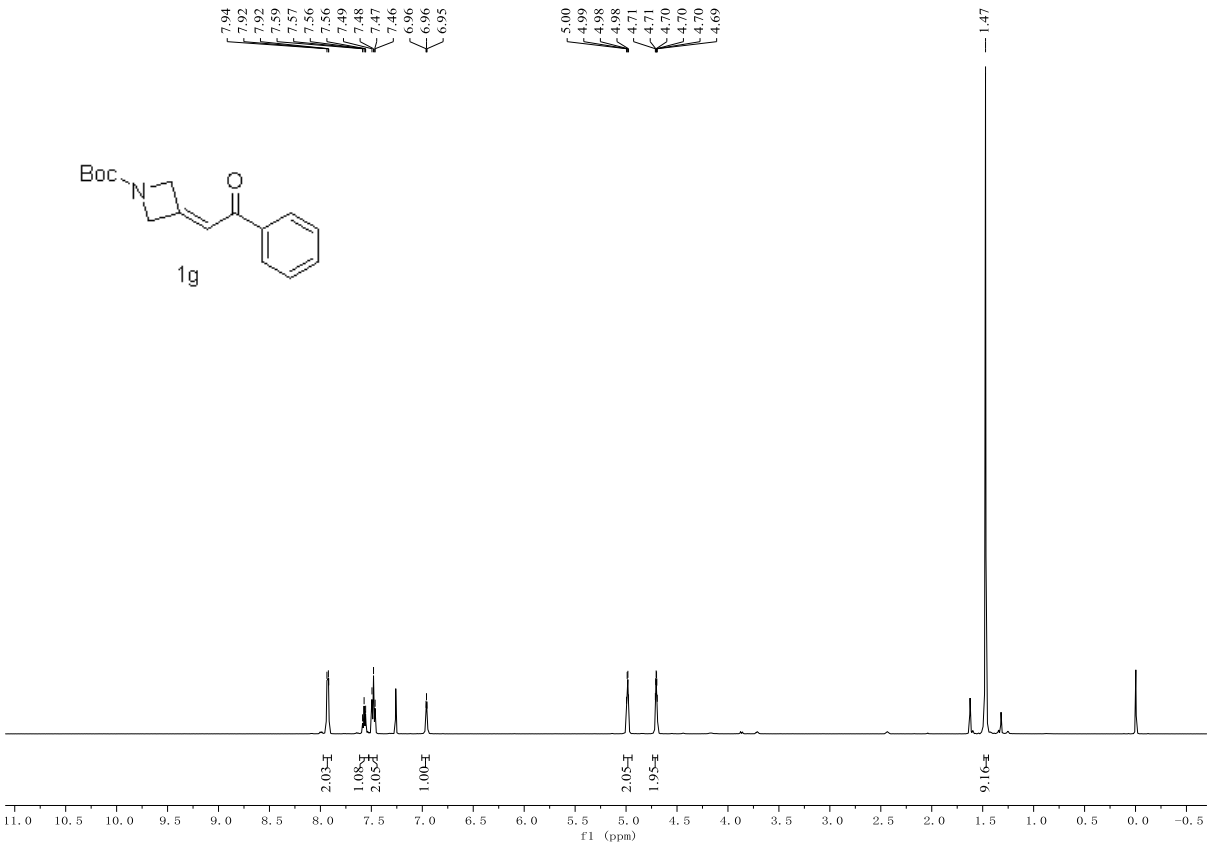
Supplementary Figure 9. ^{13}C NMR Spectra of **1c**



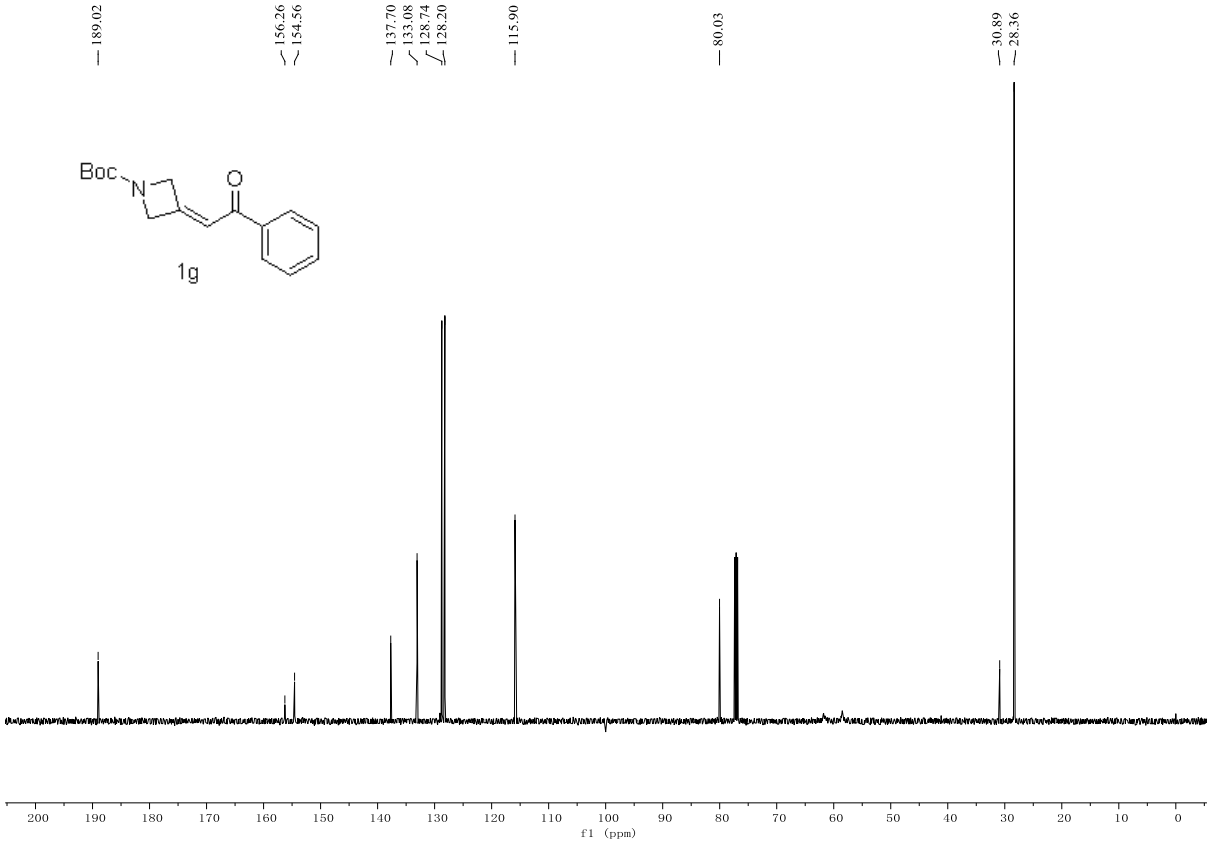
Supplementary Figure 10. ^{1}H NMR Spectra of **1d**



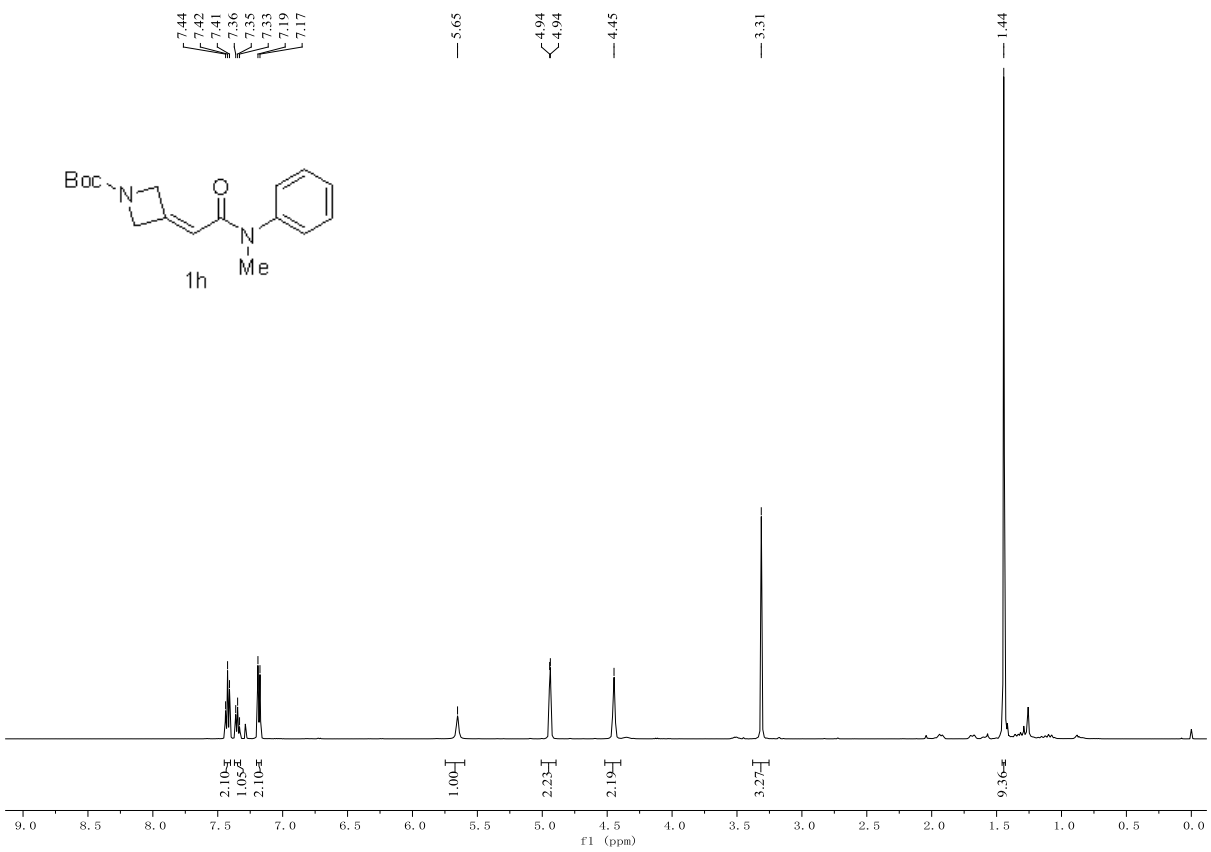
Supplementary Figure 11. ^{13}C NMR Spectra of **1d**



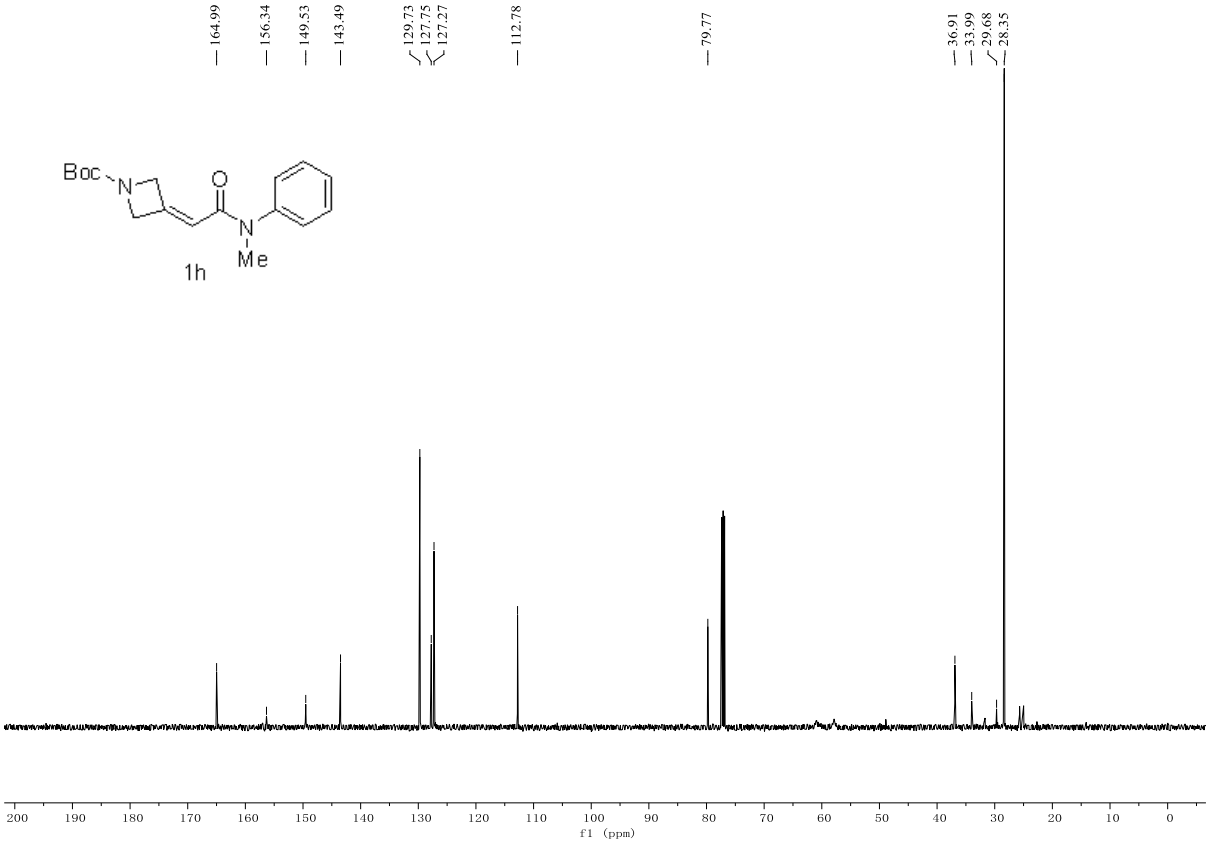
Supplementary Figure 12. ^{1}H NMR Spectra of **1g**



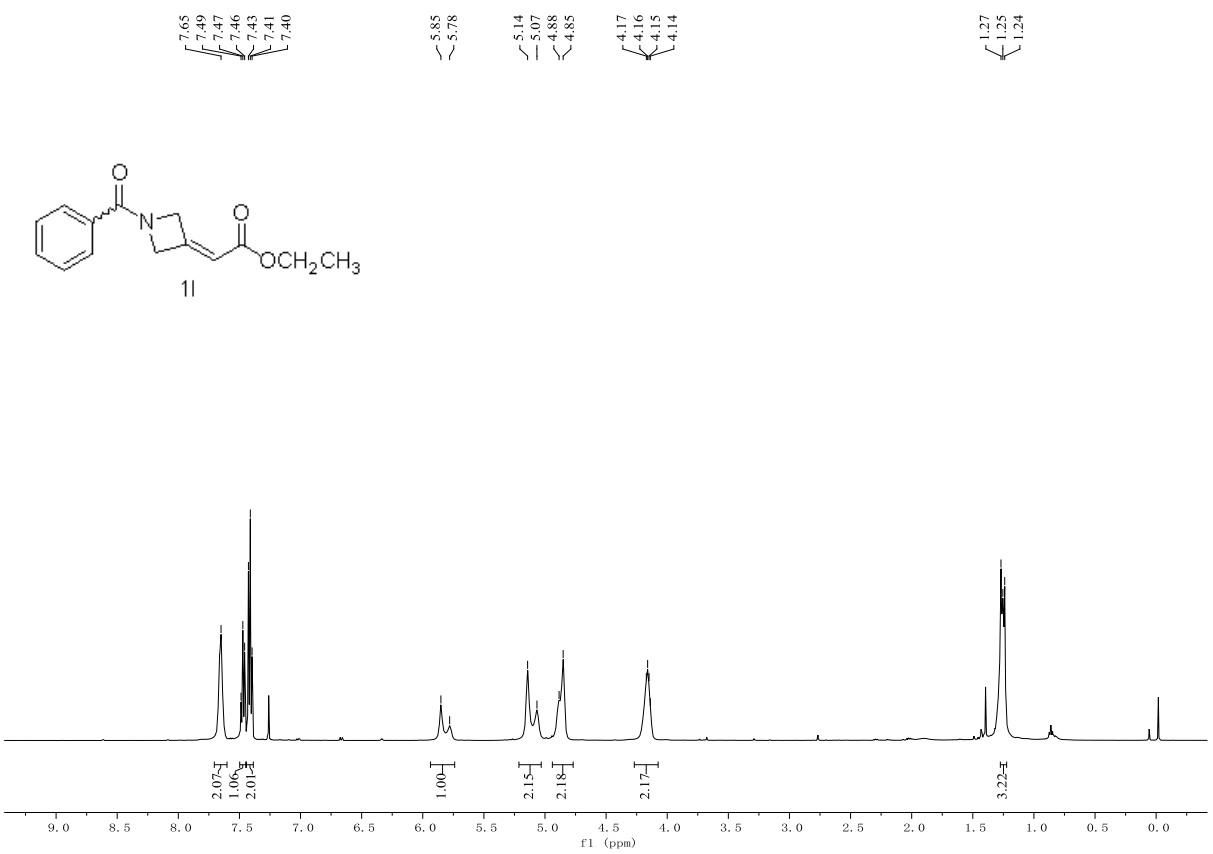
Supplementary Figure 13. ^{13}C NMR Spectra of **1g**



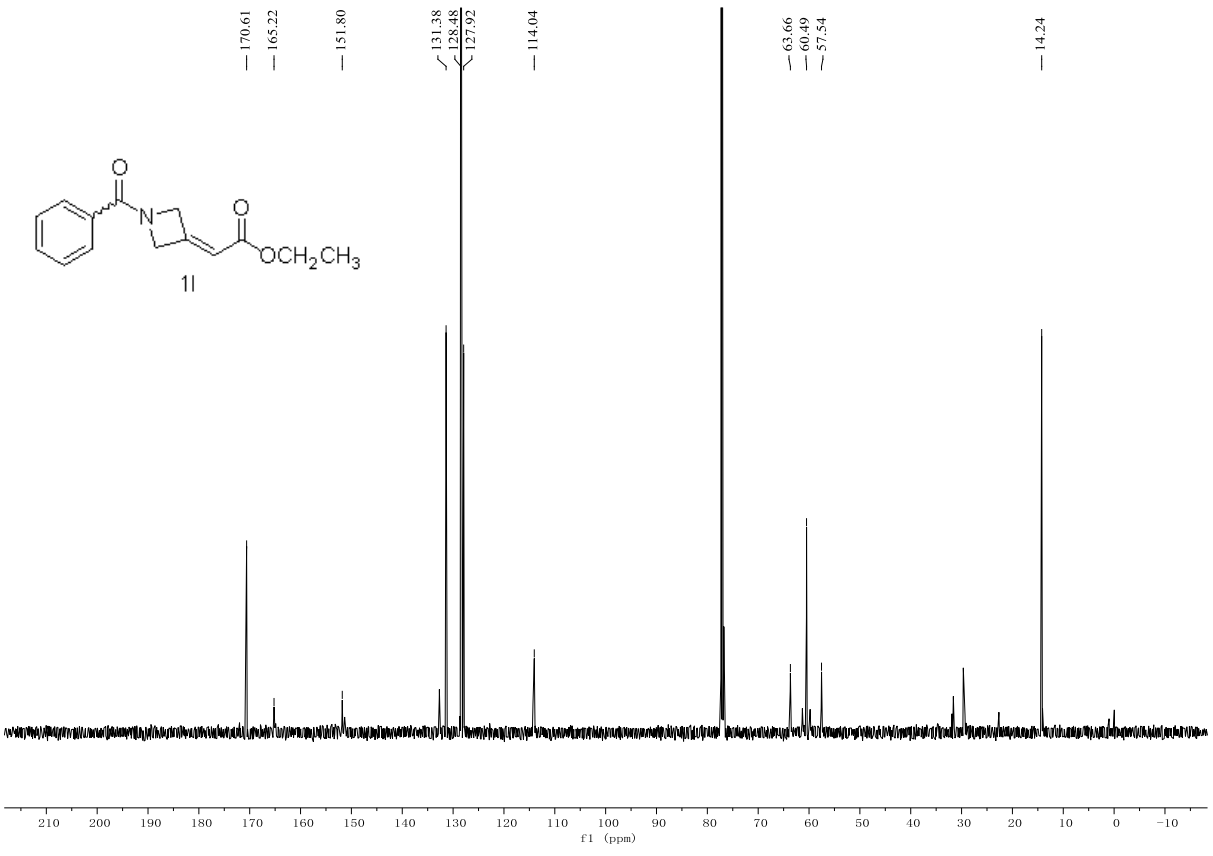
Supplementary Figure 14. ^{1}H NMR Spectra of **1h**



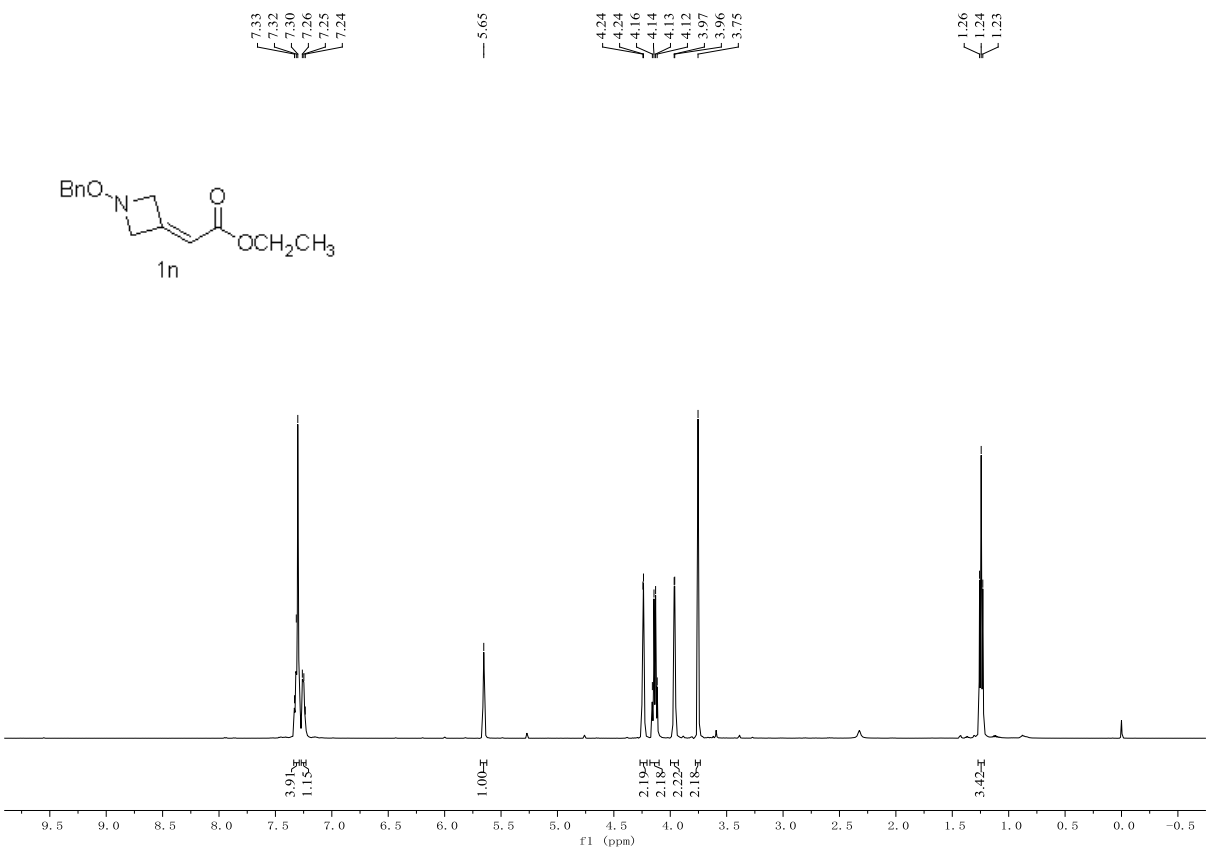
Supplementary Figure 15. ^{13}C NMR Spectra of **1h**



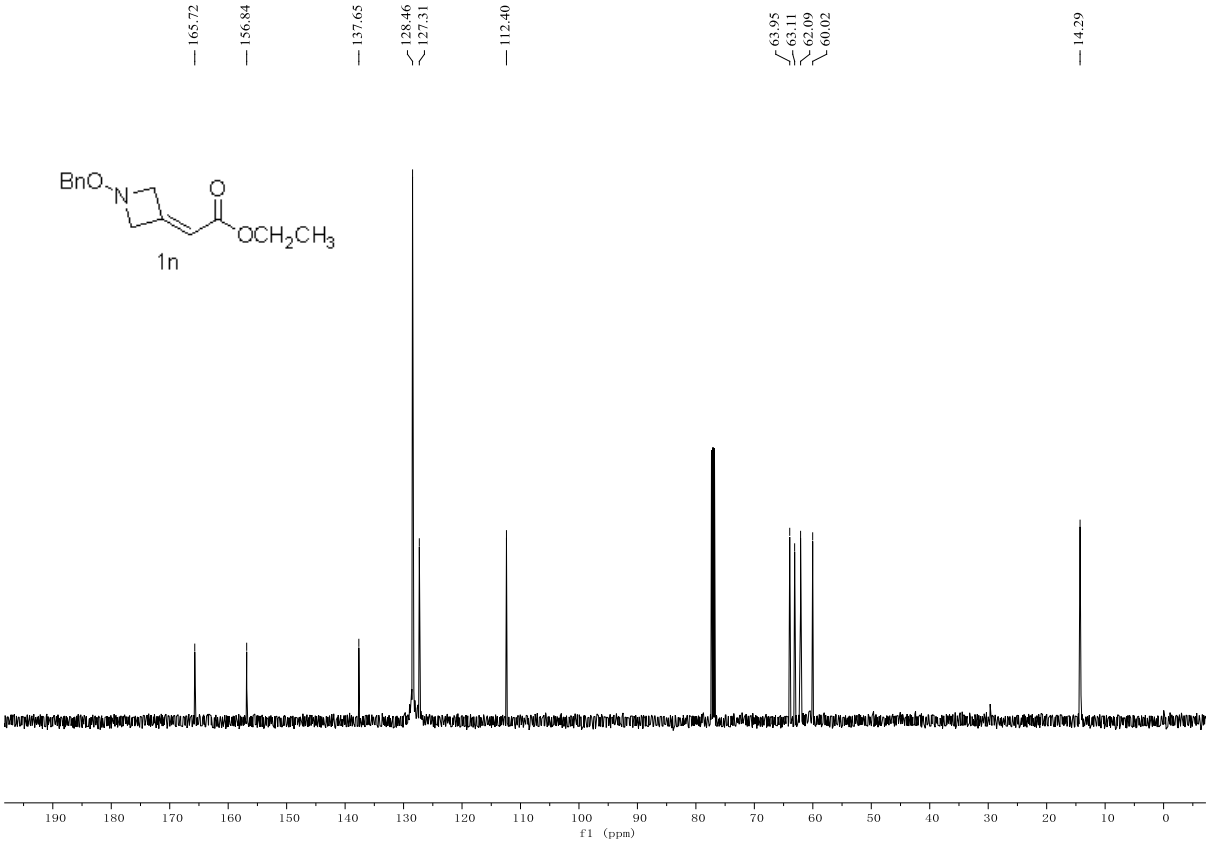
Supplementary Figure 16. ^{1}H NMR Spectra of **1l**



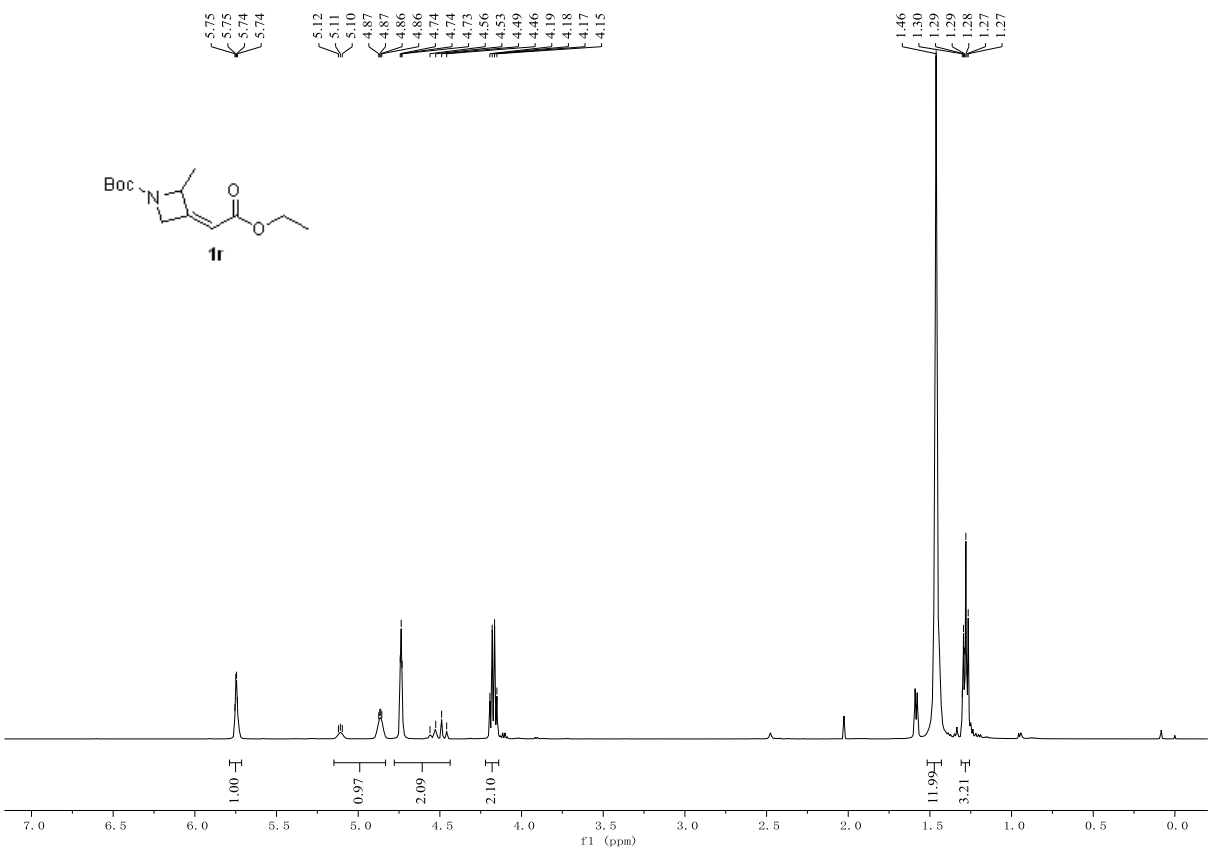
Supplementary Figure 17. ^{13}C NMR Spectra of **1l**



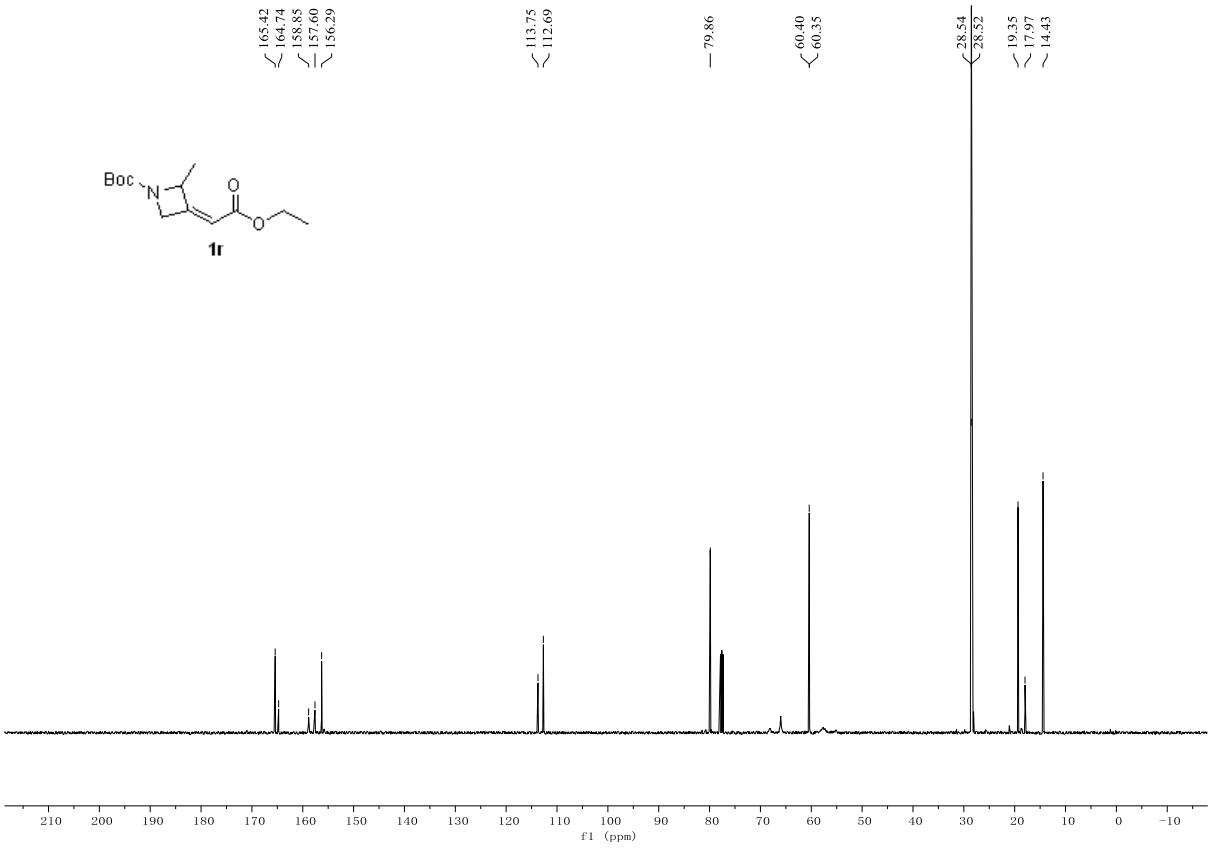
Supplementary Figure 18. ^{1}H NMR Spectra of **1n**



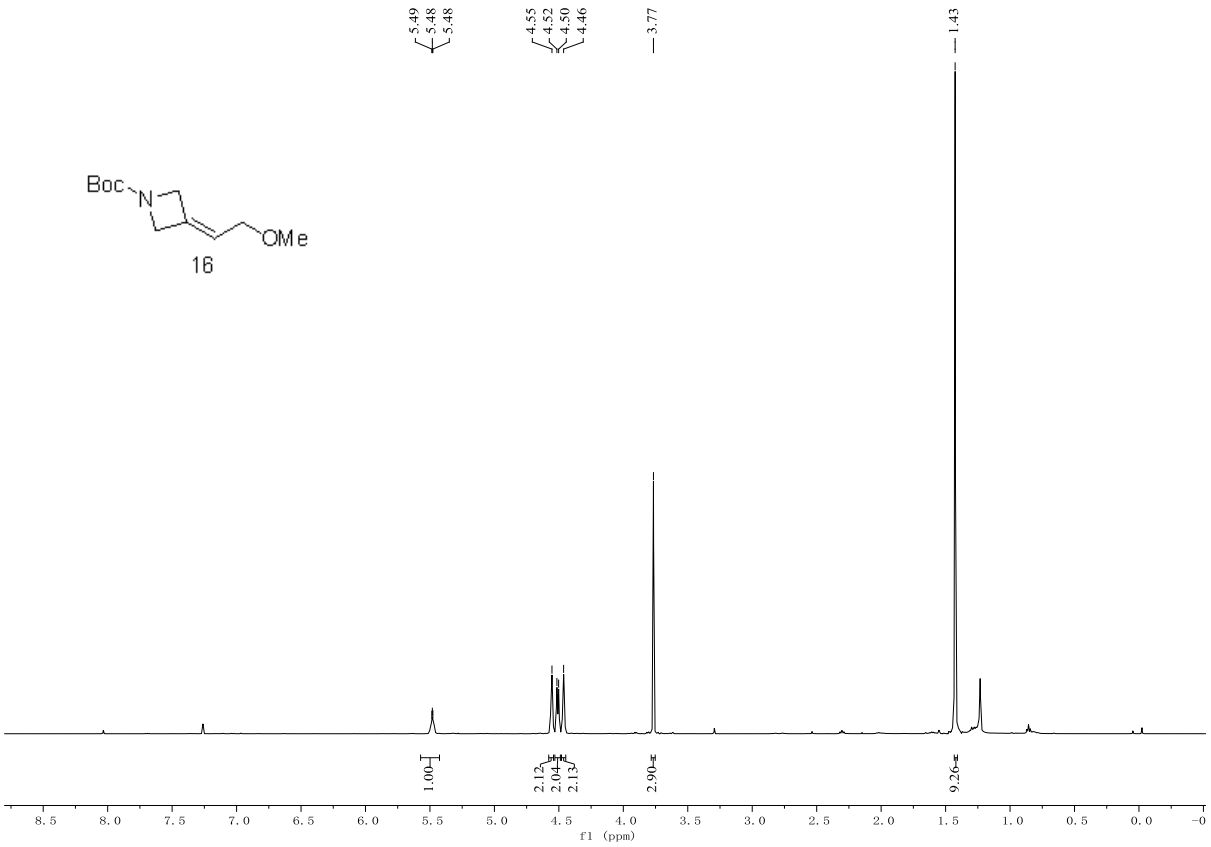
Supplementary Figure 19. ^{13}C NMR Spectra of **1n**



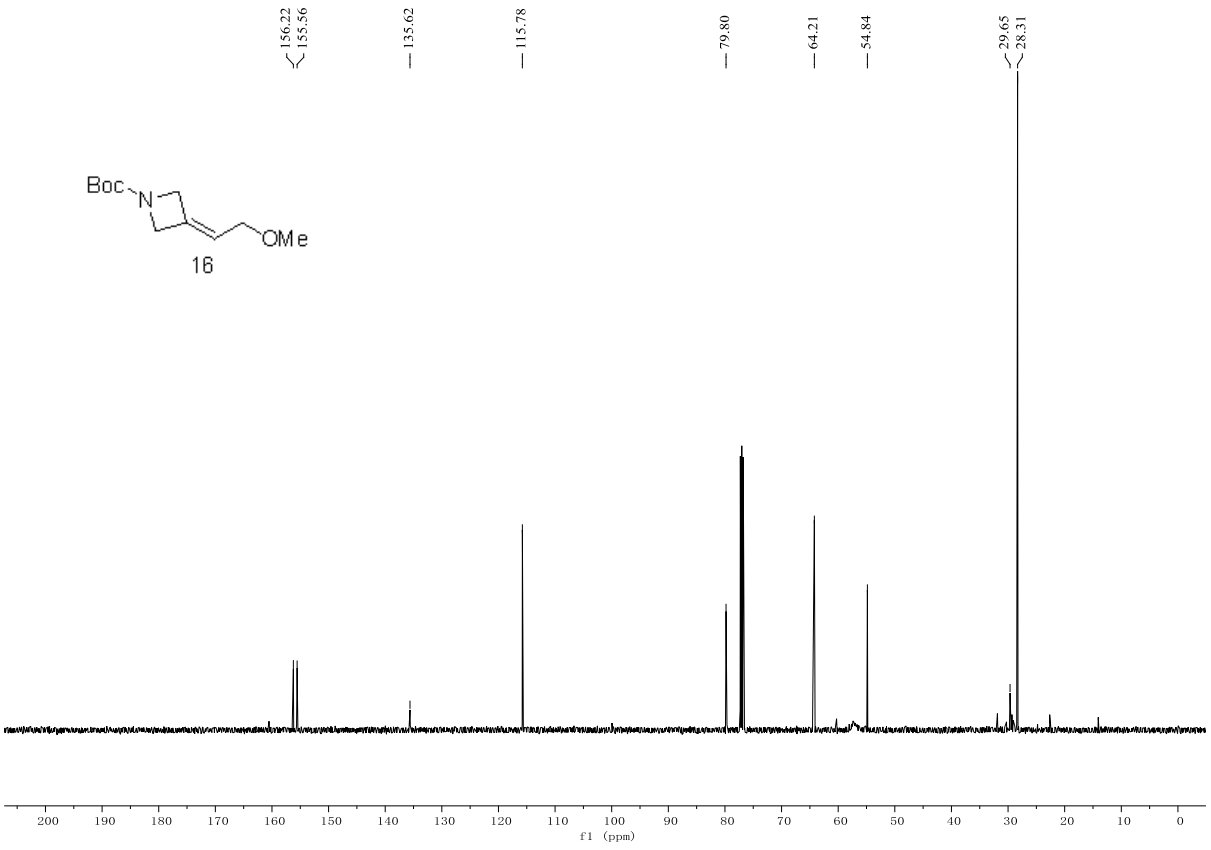
Supplementary Figure 20. ^{1}H NMR Spectra of **1r**



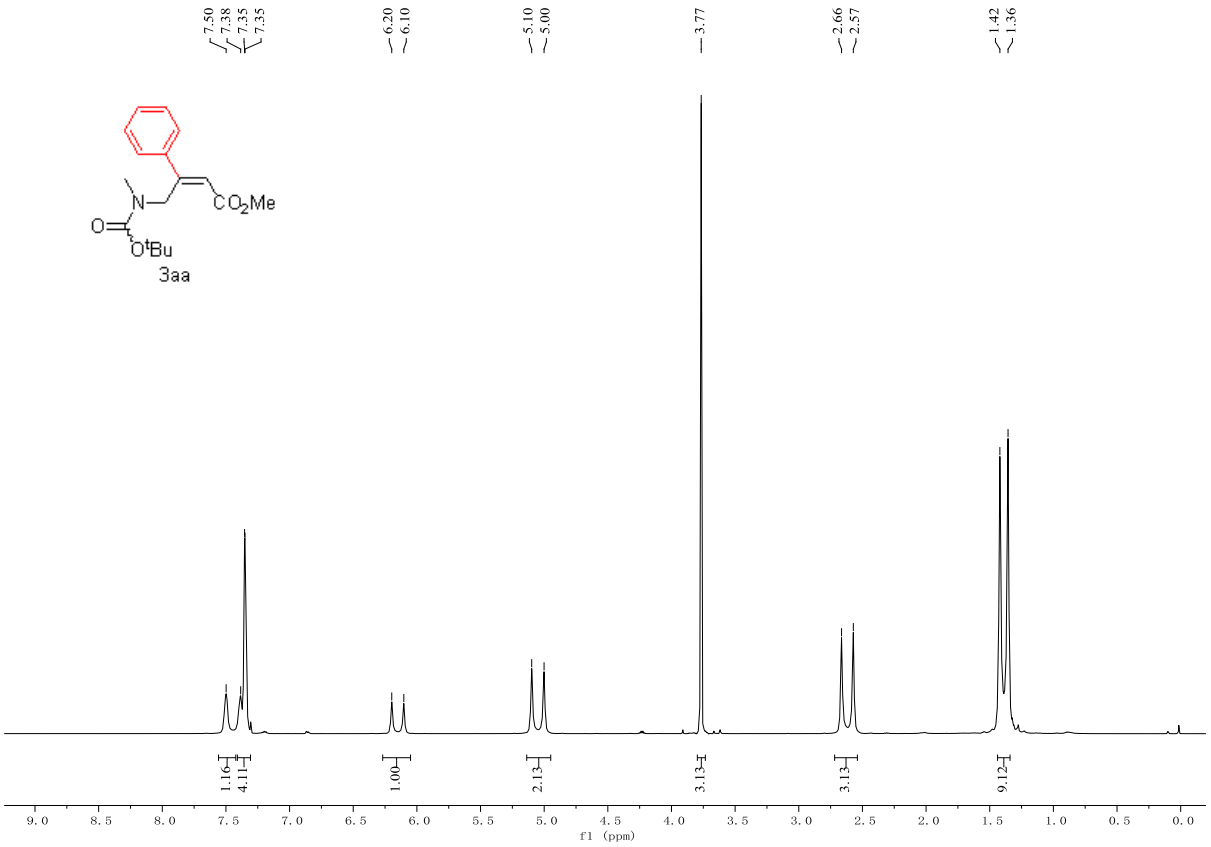
Supplementary Figure 21. ^{13}C NMR Spectra of **1r**



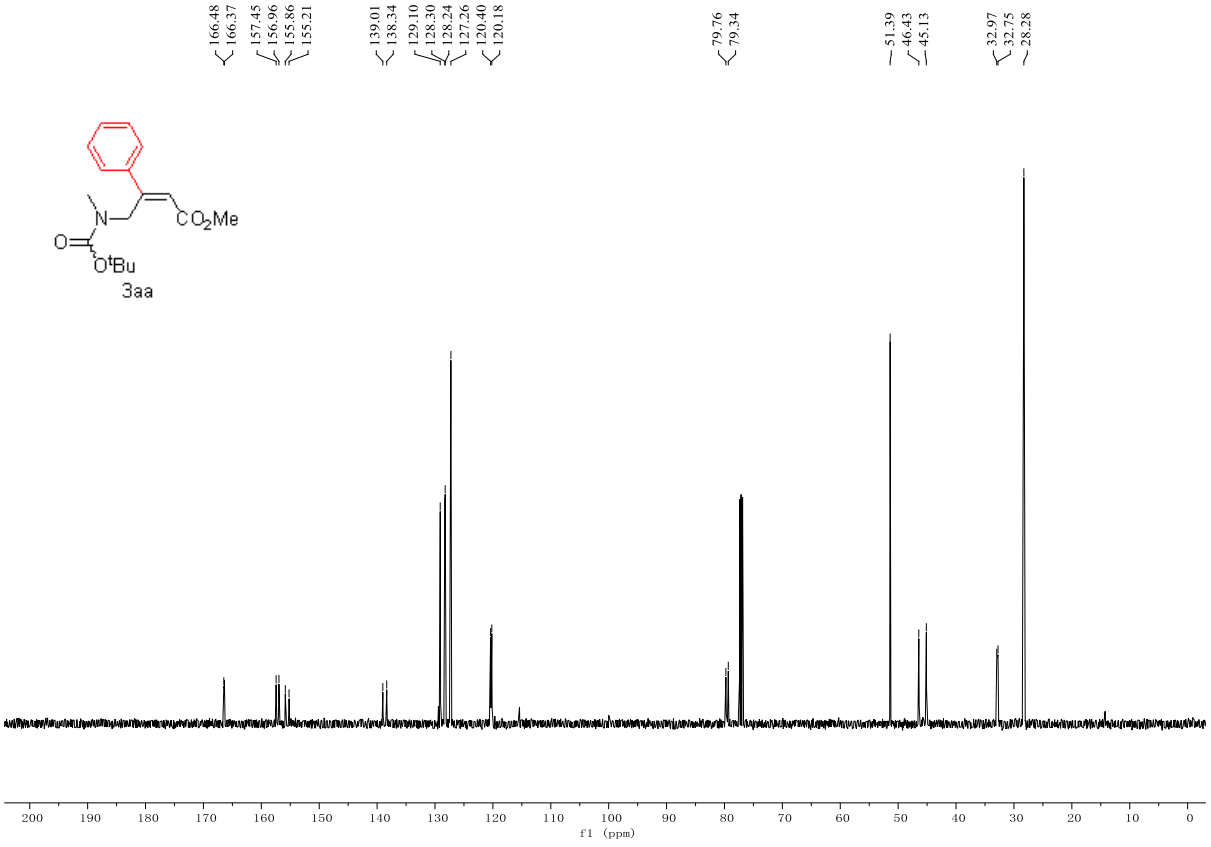
Supplementary Figure 22. ^{1}H NMR Spectra of **16**



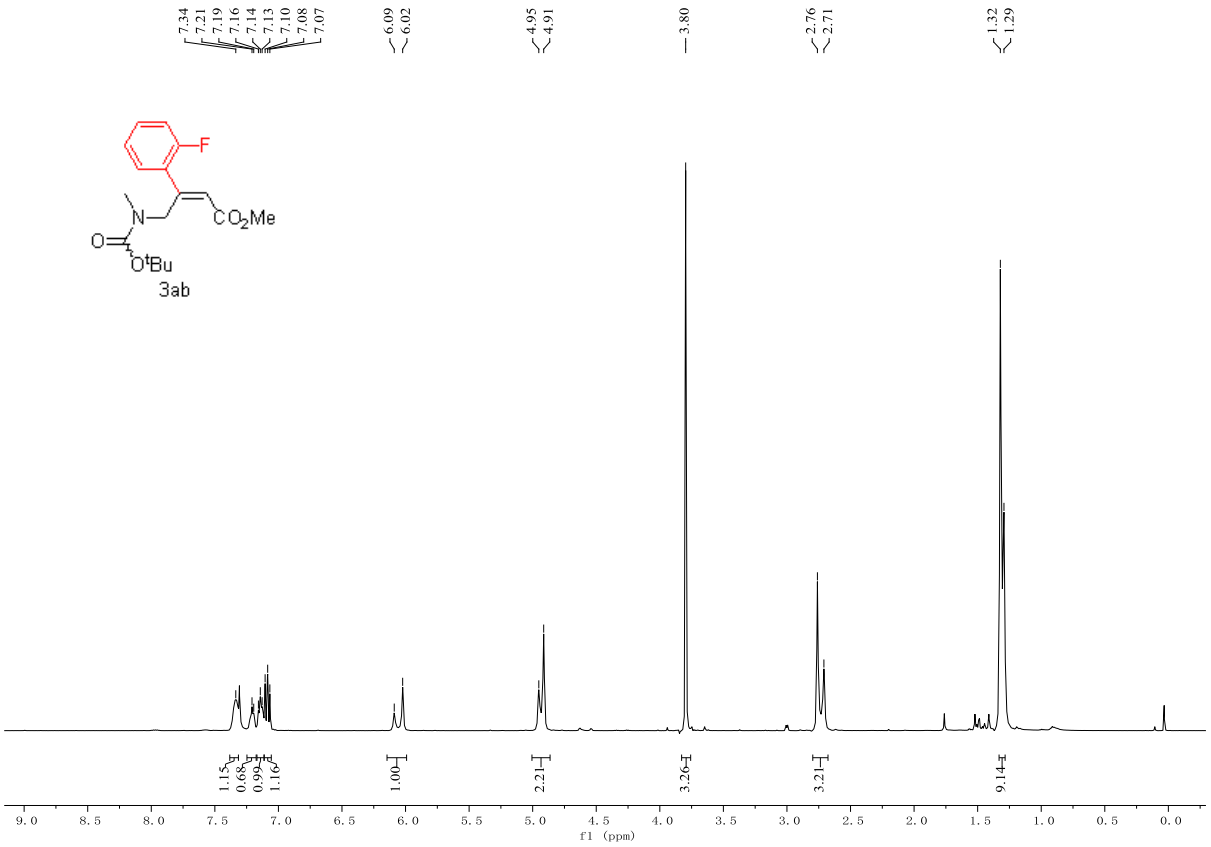
Supplementary Figure 23. ^{13}C NMR Spectra of **16**



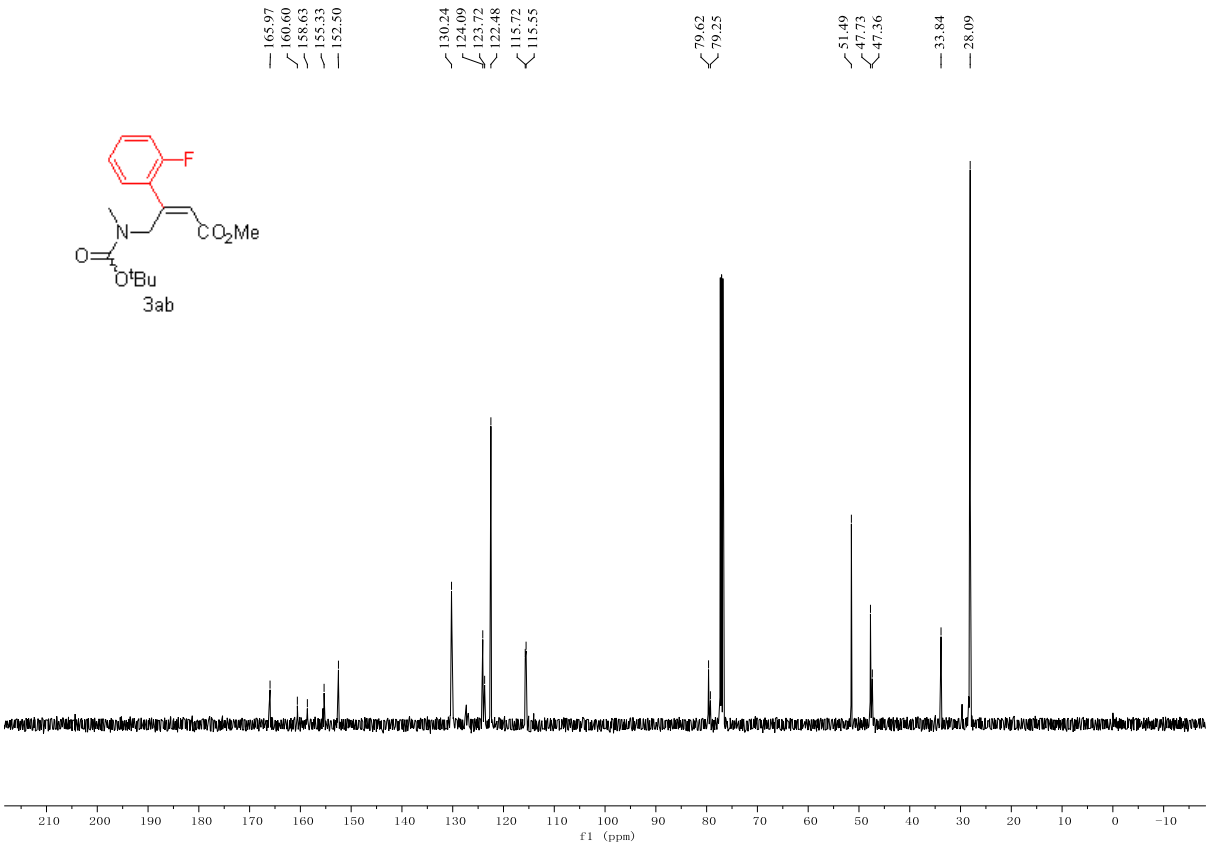
Supplementary Figure 24. ^{1}H NMR Spectra of **3aa**



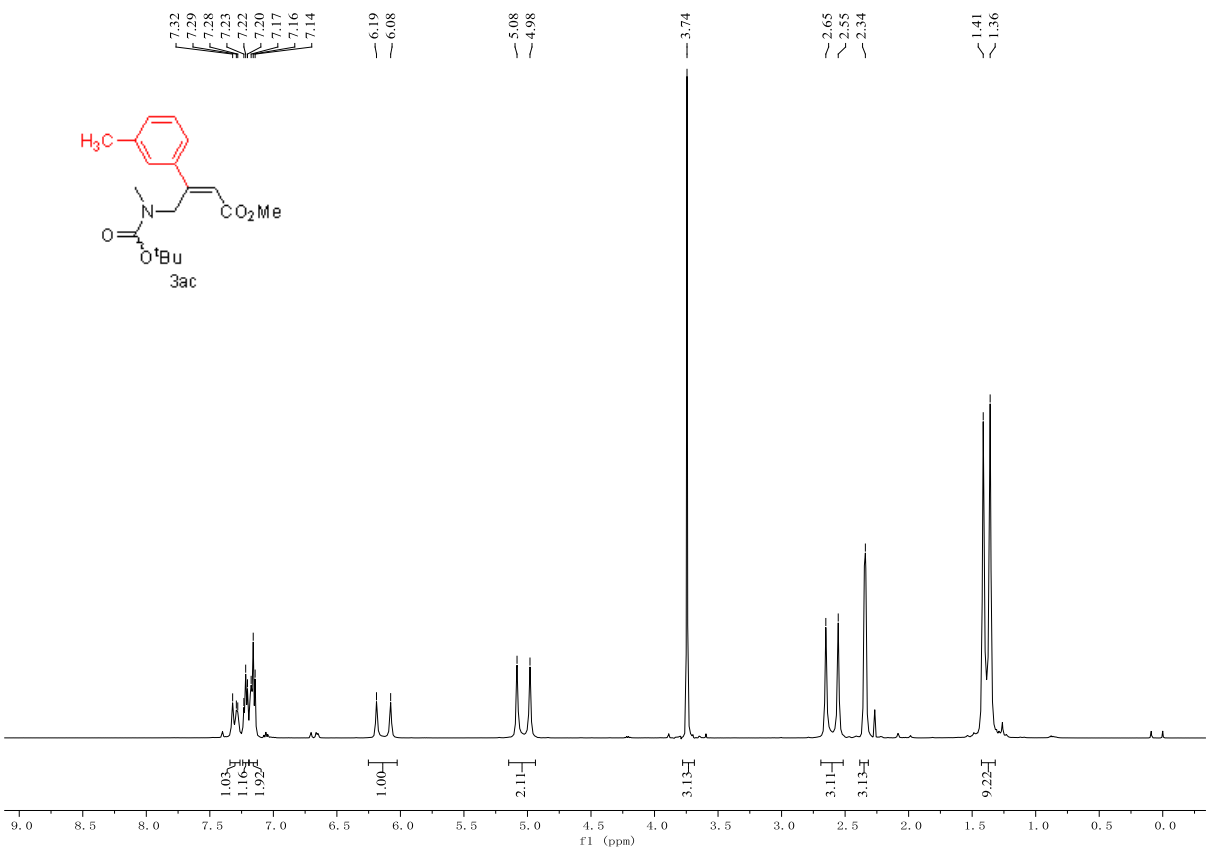
Supplementary Figure 25. ^{13}C NMR Spectra of **3aa**



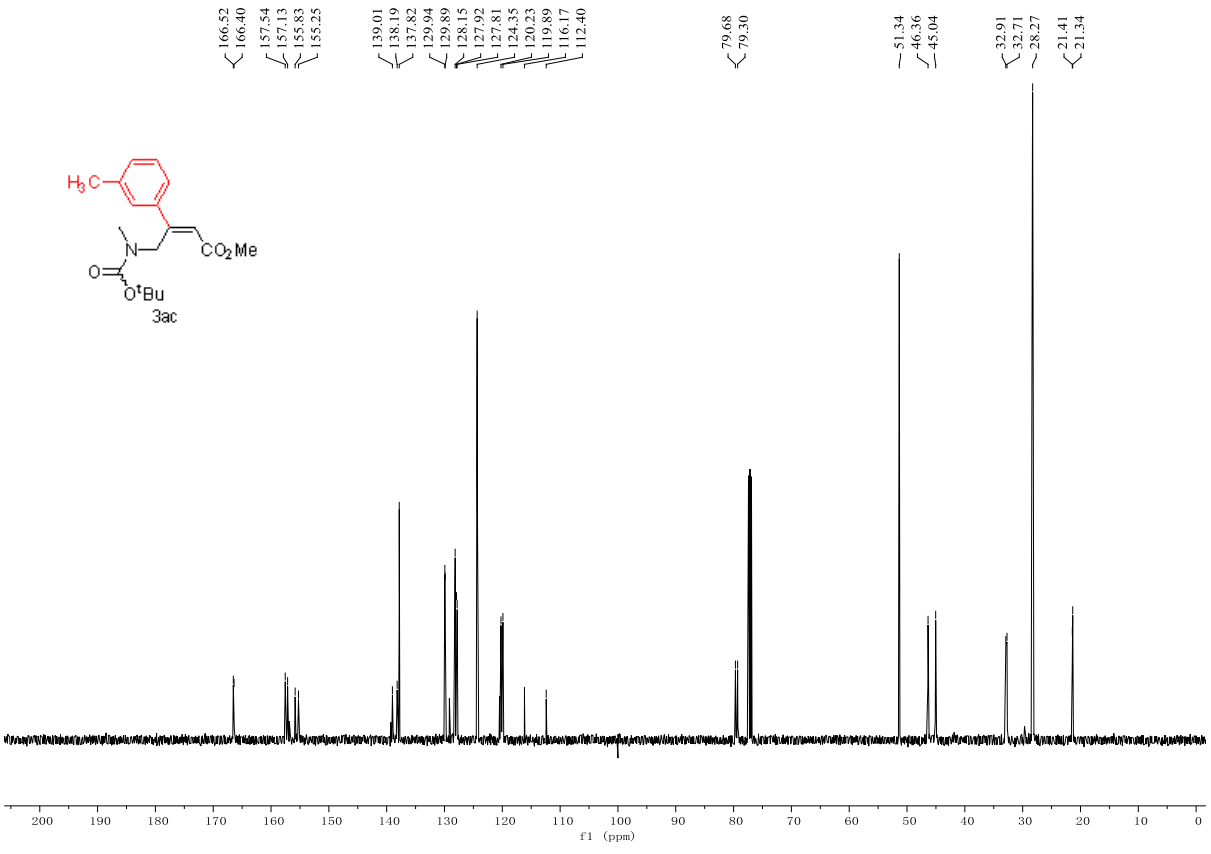
Supplementary Figure 26. ^{1}H NMR Spectra of **3ab**



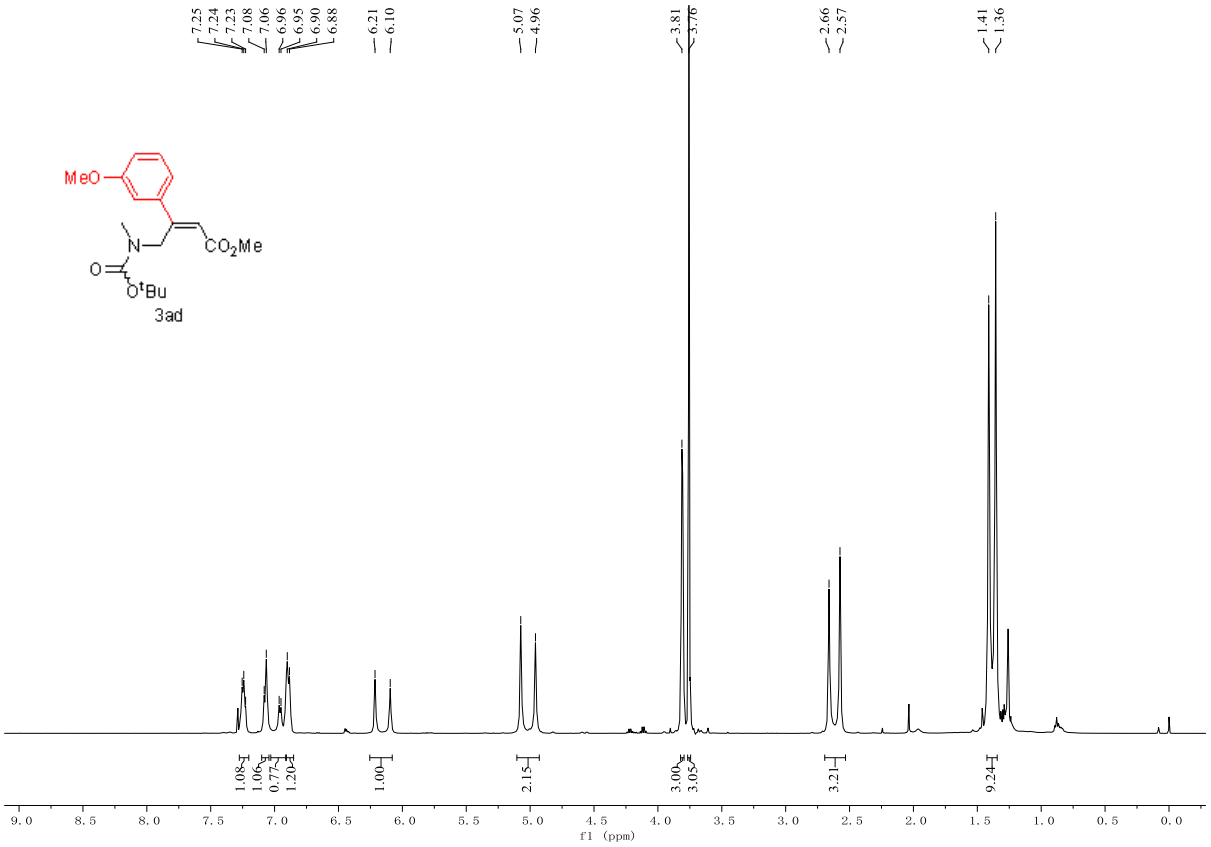
Supplementary Figure 27. ^{13}C NMR Spectra of **3ab**



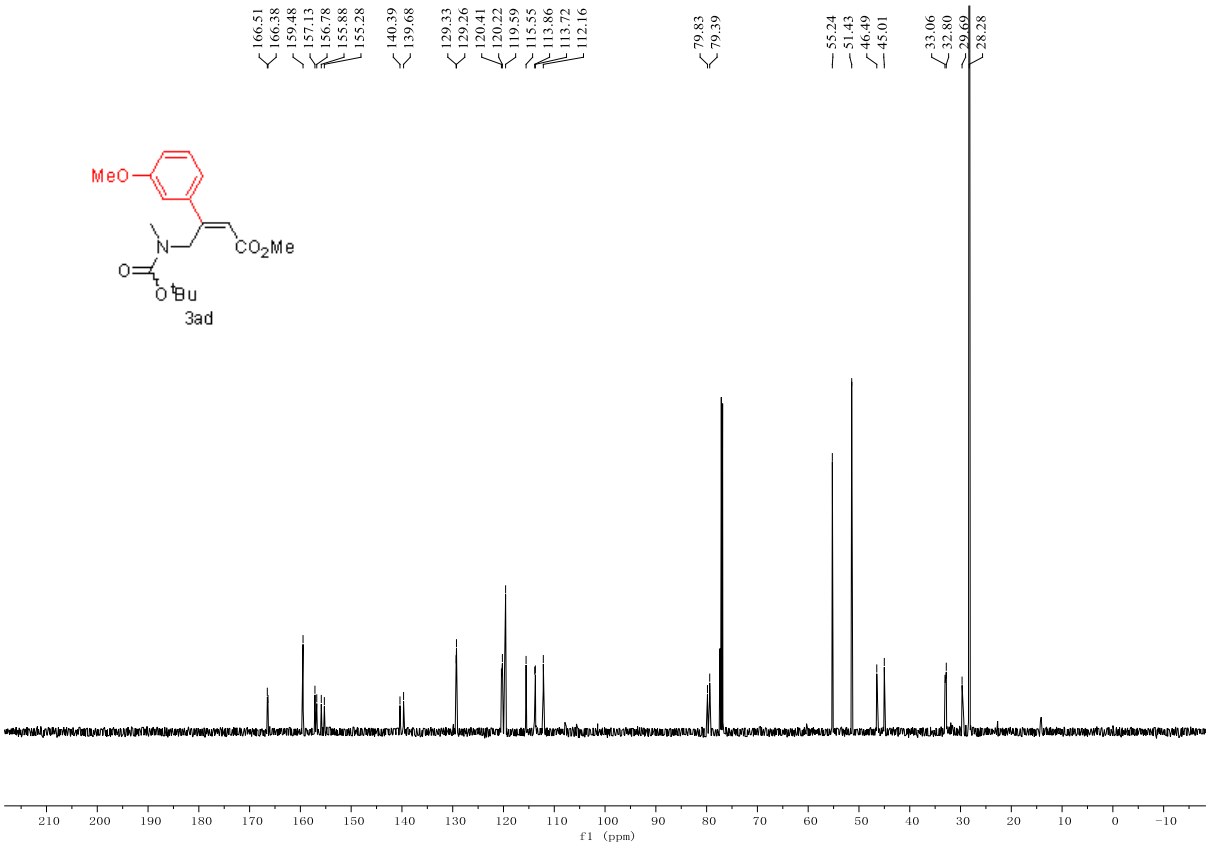
Supplementary Figure 28. ^{1}H NMR Spectra of **3ac**



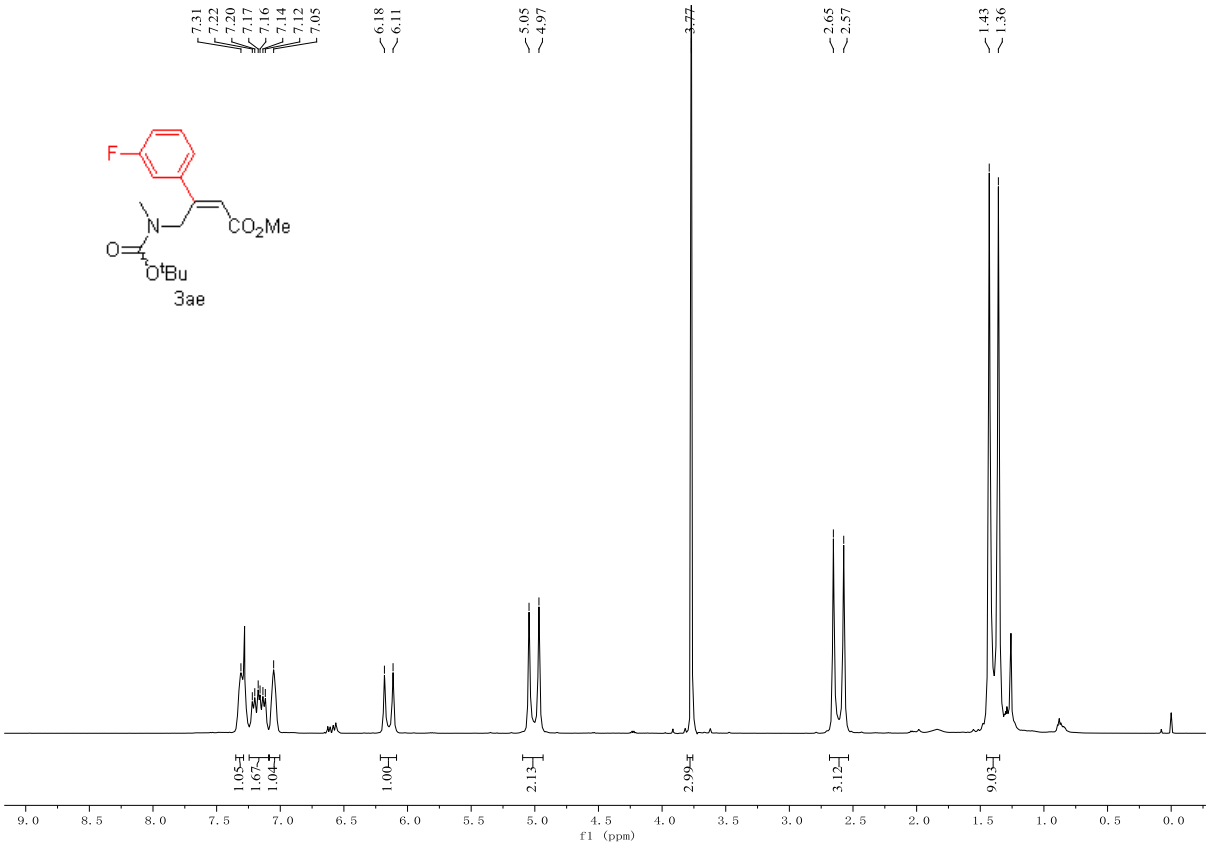
Supplementary Figure 29. ^{13}C NMR Spectra of **3ac**



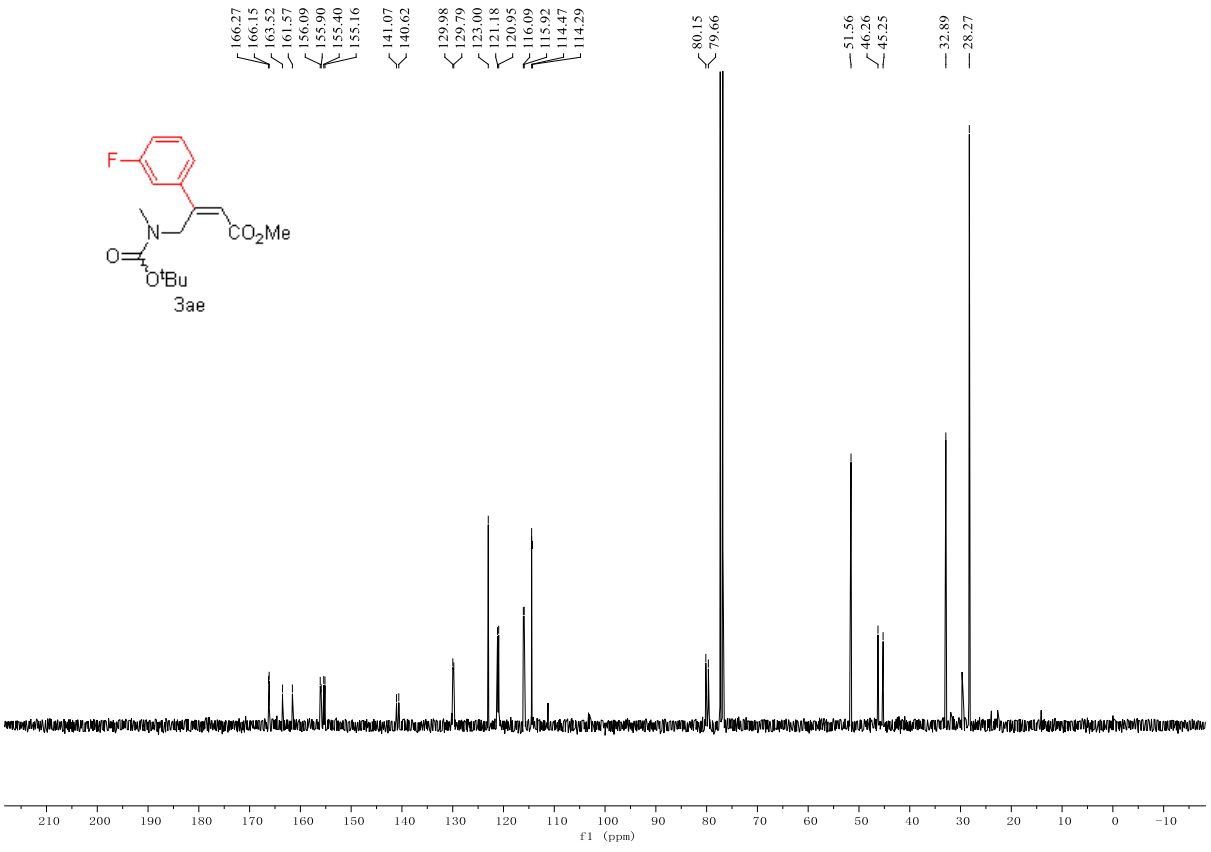
Supplementary Figure 30. ^{1}H NMR Spectra of **3ad**



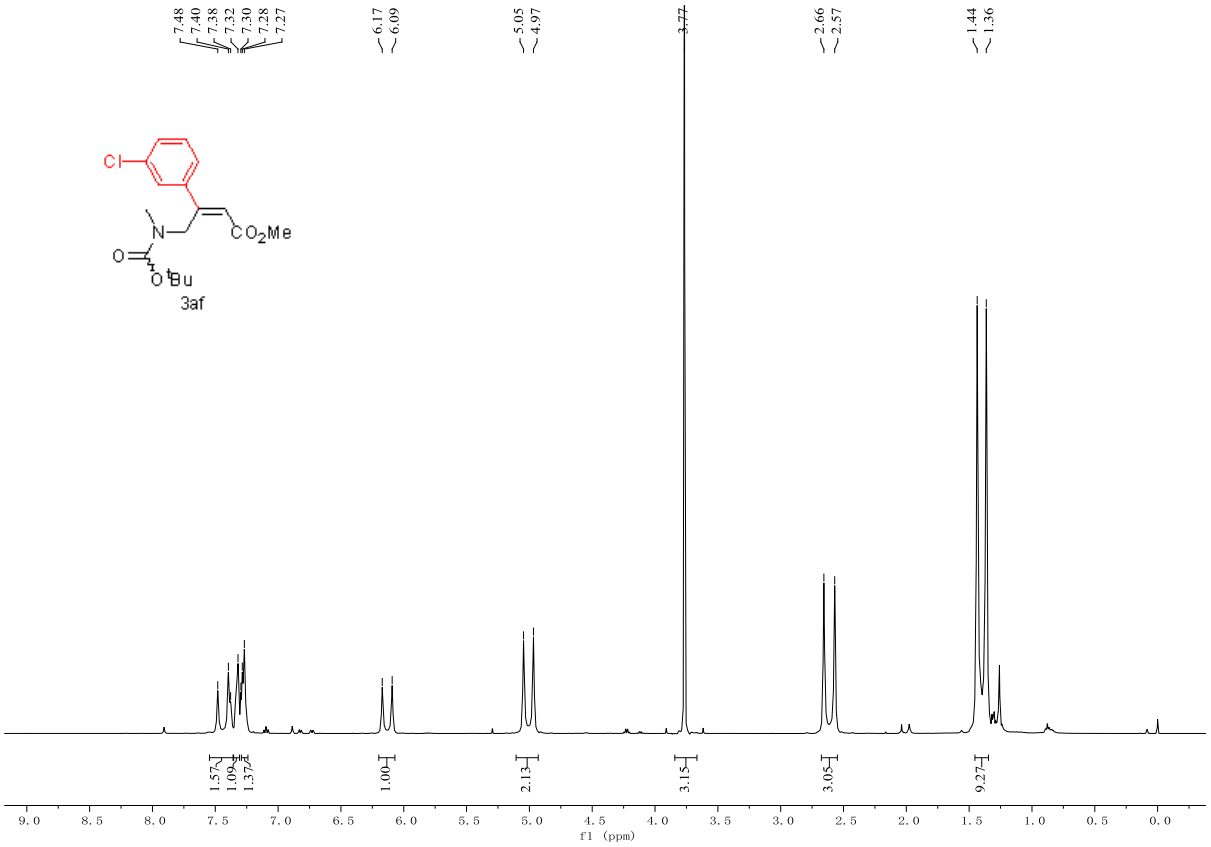
Supplementary Figure 31. ^{13}C NMR Spectra of **3ad**



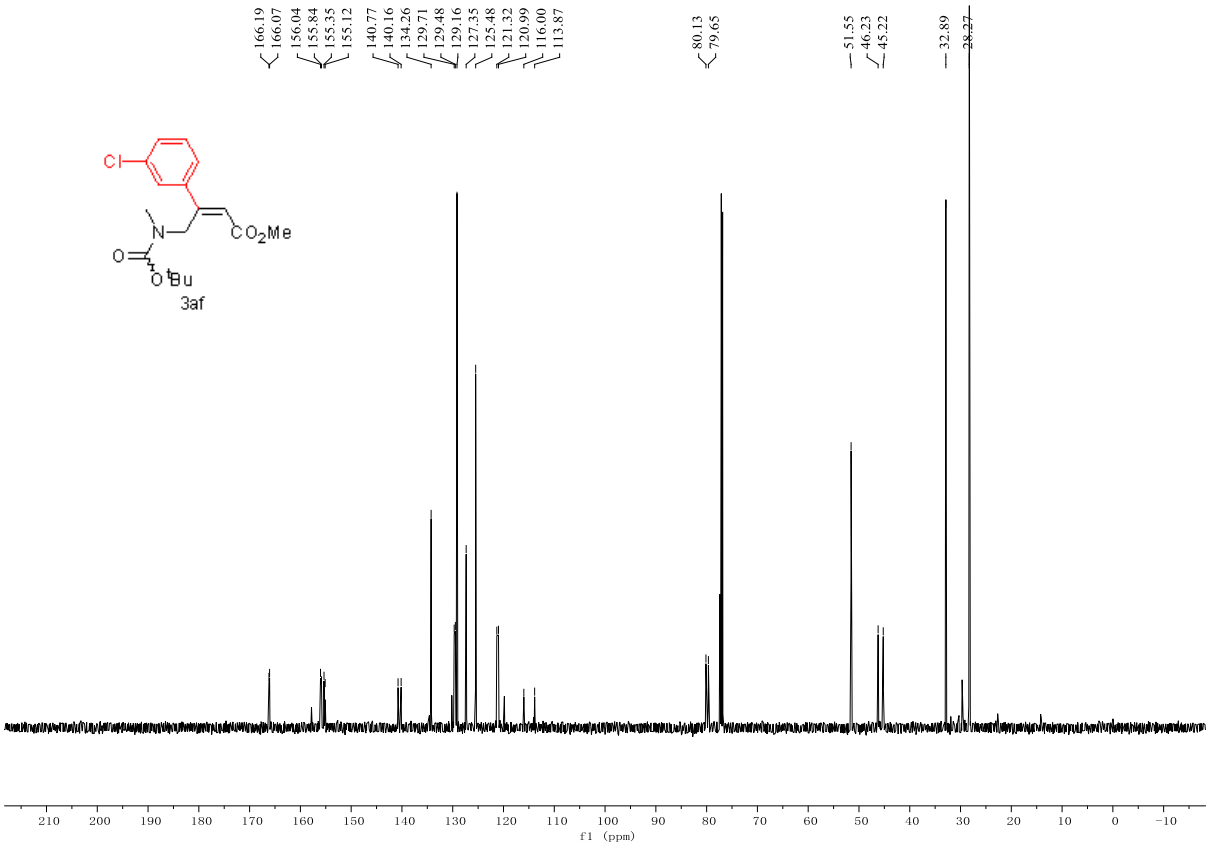
Supplementary Figure 32. ^{1}H NMR Spectra of **3ae**



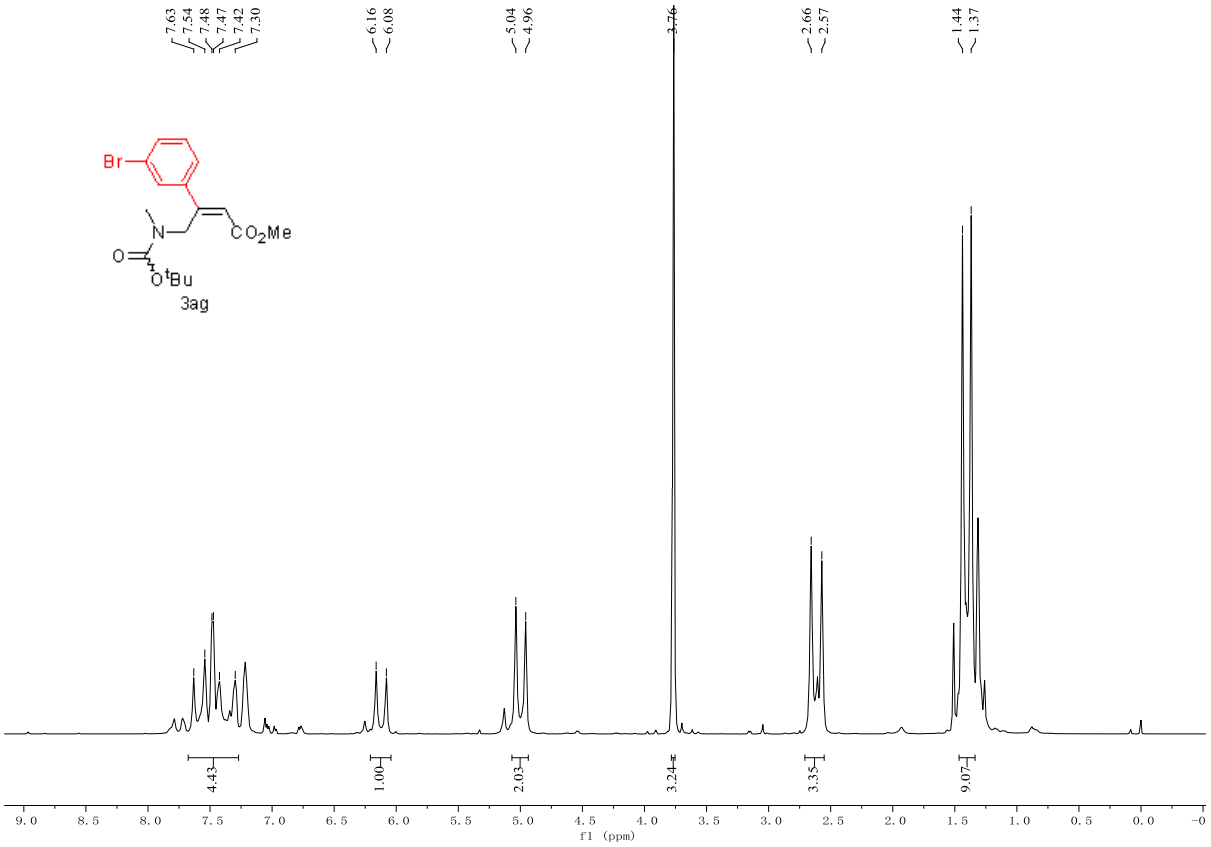
Supplementary Figure 33. ^{13}C NMR Spectra of **3ae**



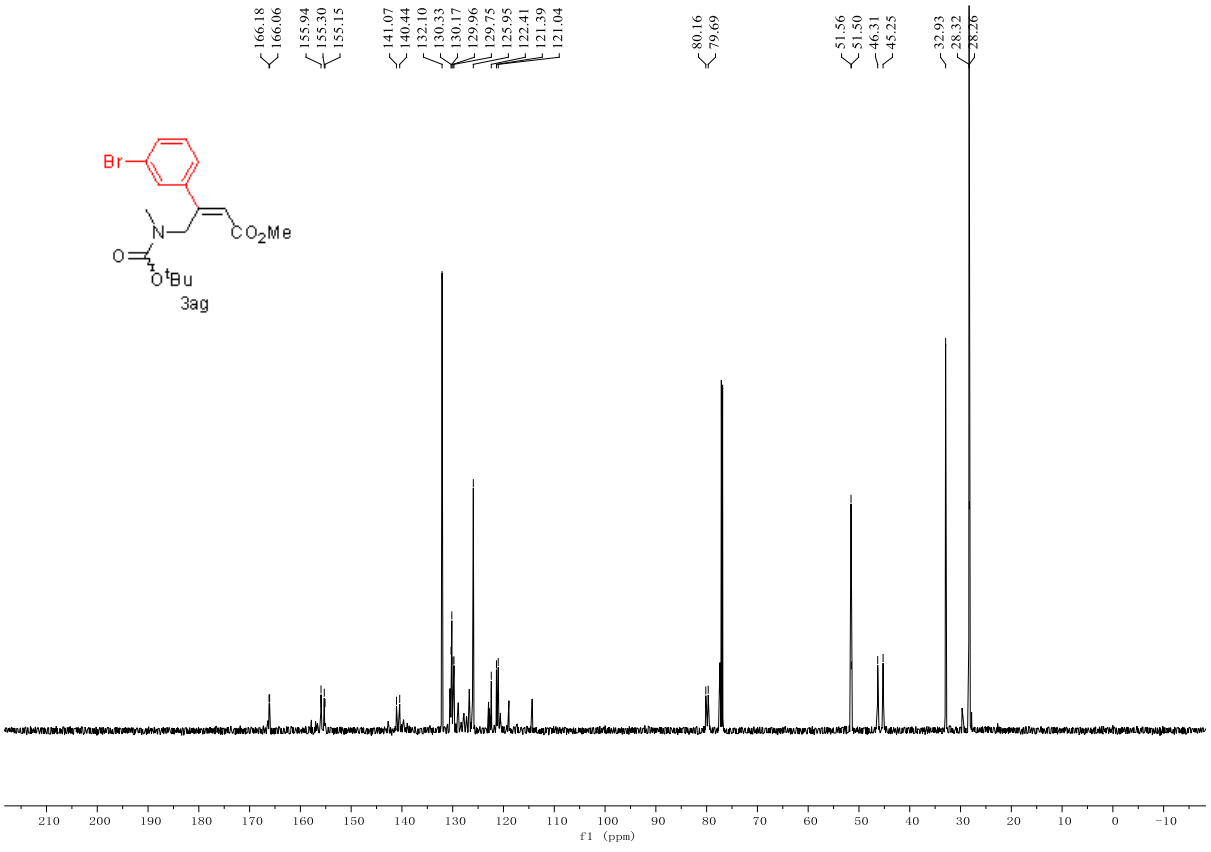
Supplementary Figure 34. ^{1}H NMR Spectra of **3af**



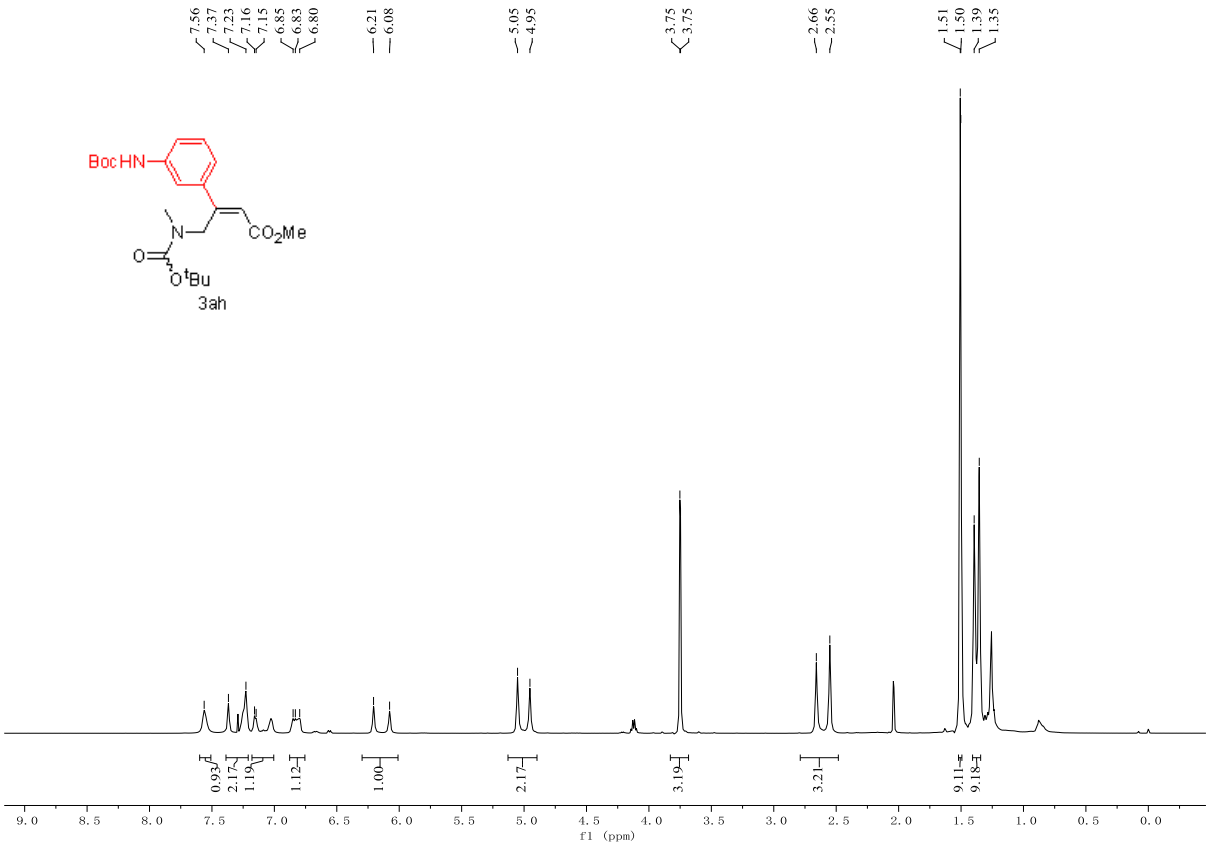
Supplementary Figure 35. ^{13}C NMR Spectra of **3af**



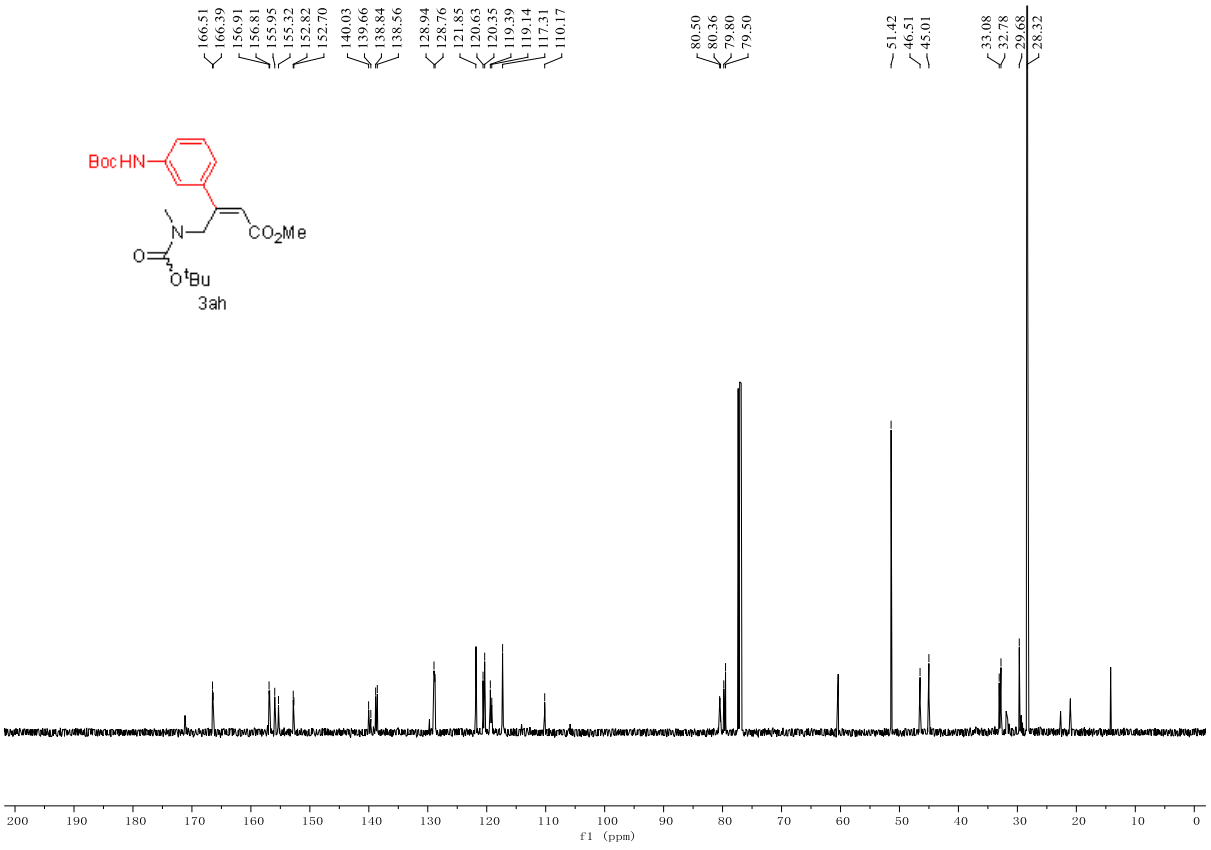
Supplementary Figure 36. ^{1}H NMR Spectra of **3ag**



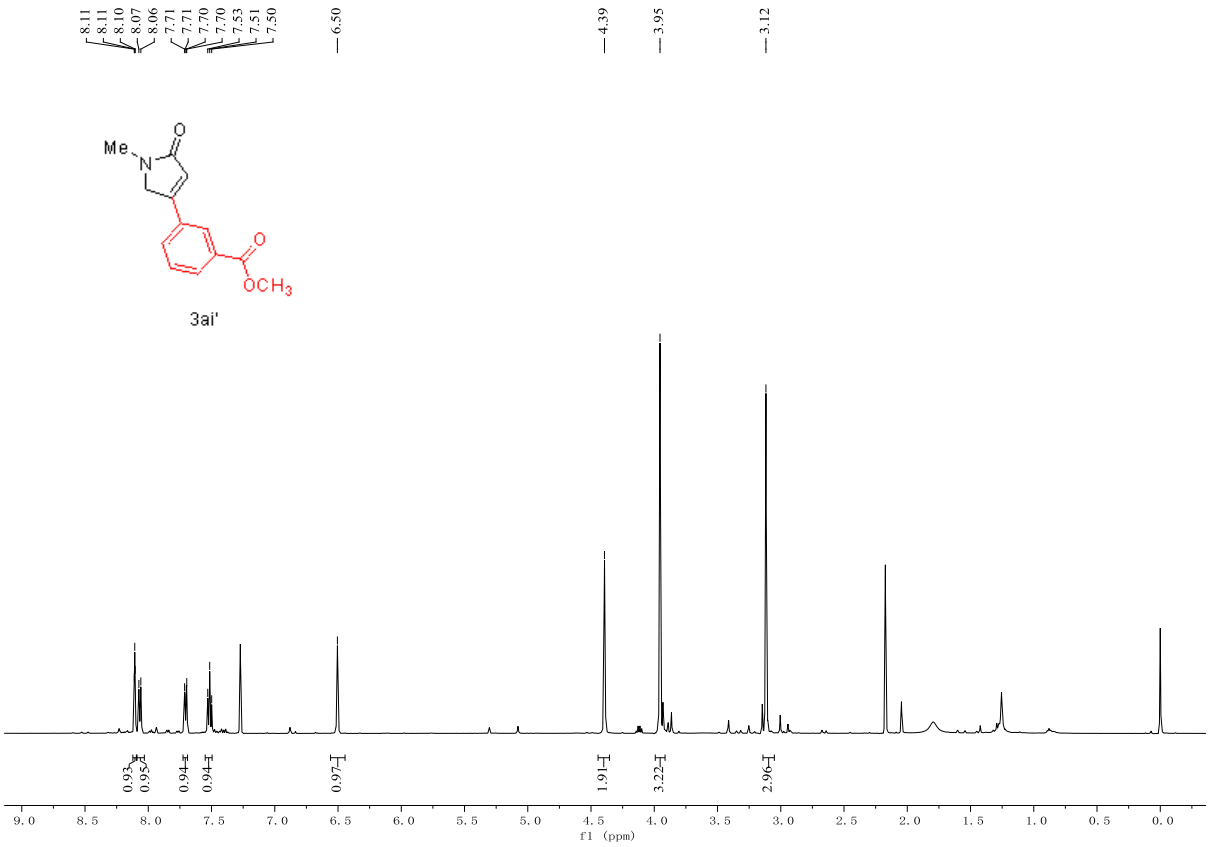
Supplementary Figure 37. ^{13}C NMR Spectra of **3ag**



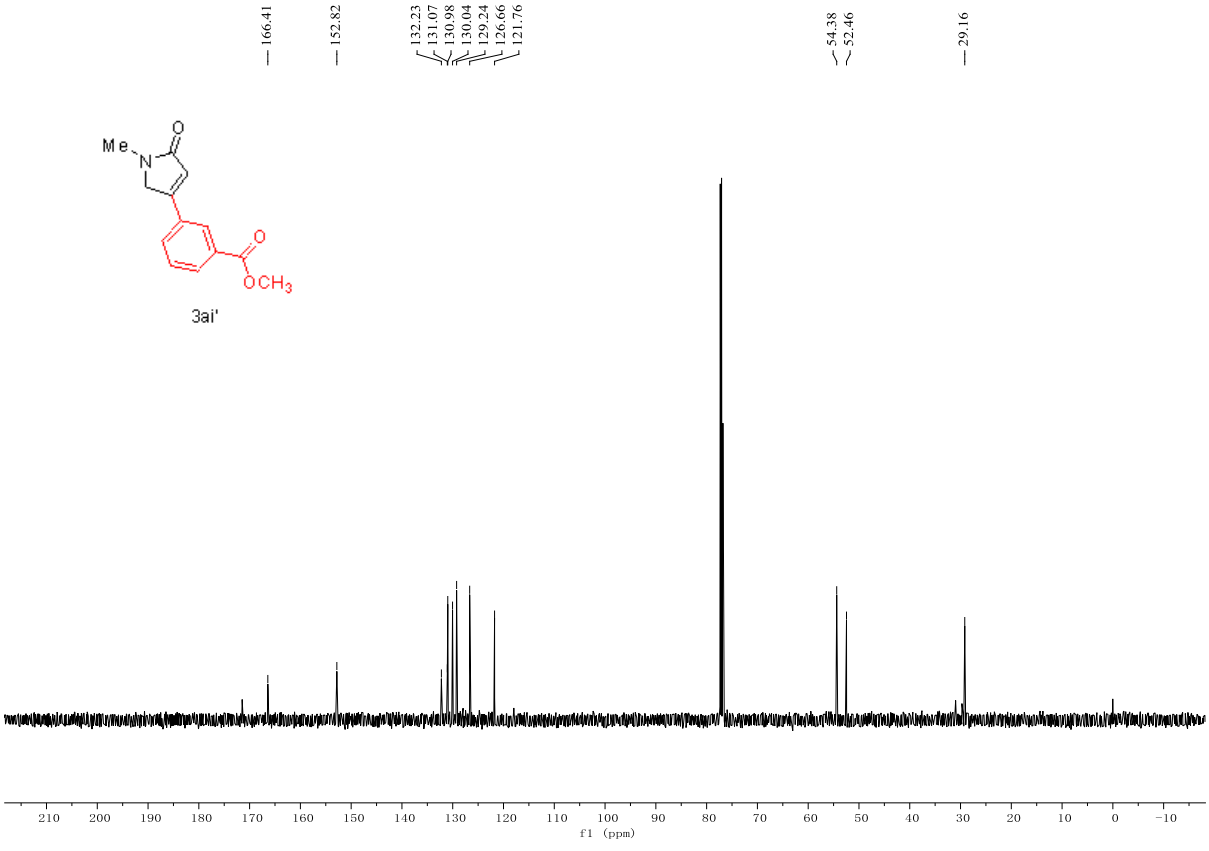
Supplementary Figure 38. ^{1}H NMR Spectra of **3ah**



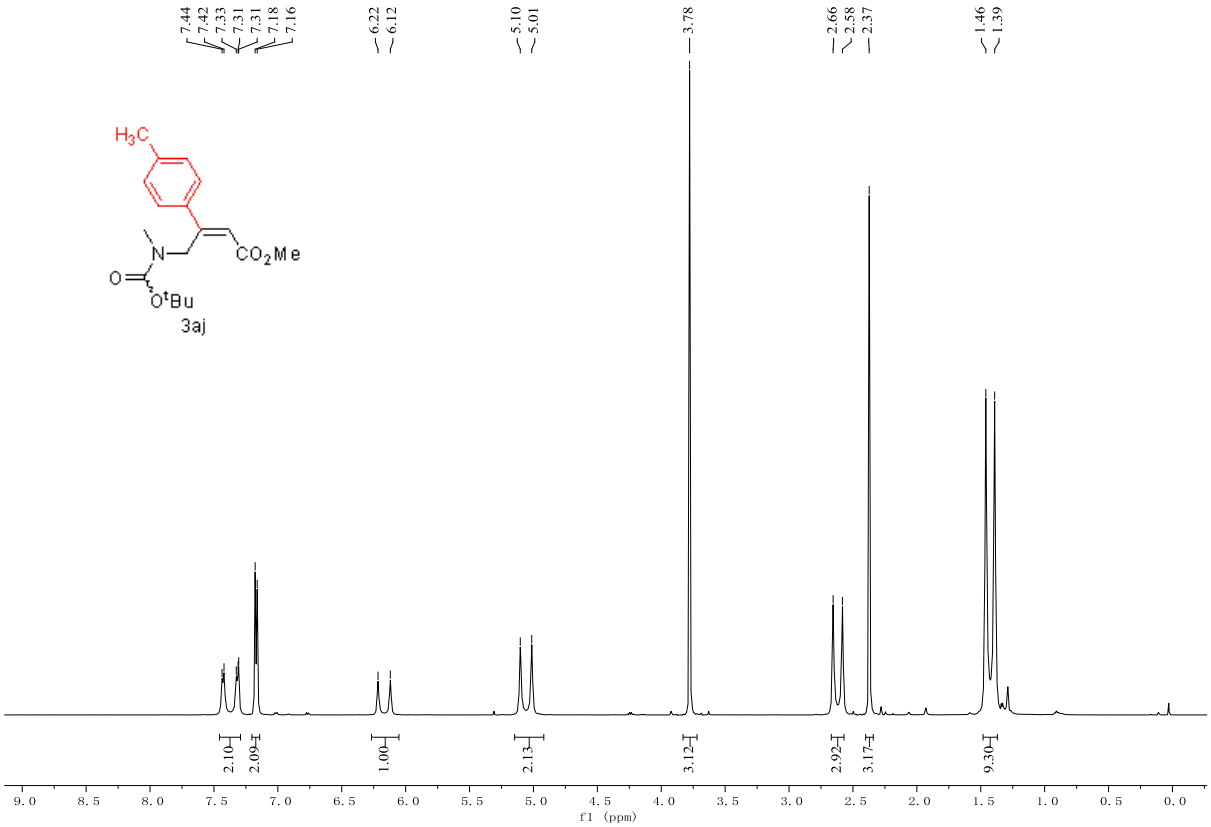
Supplementary Figure 39. ^{13}C NMR Spectra of **3ah**



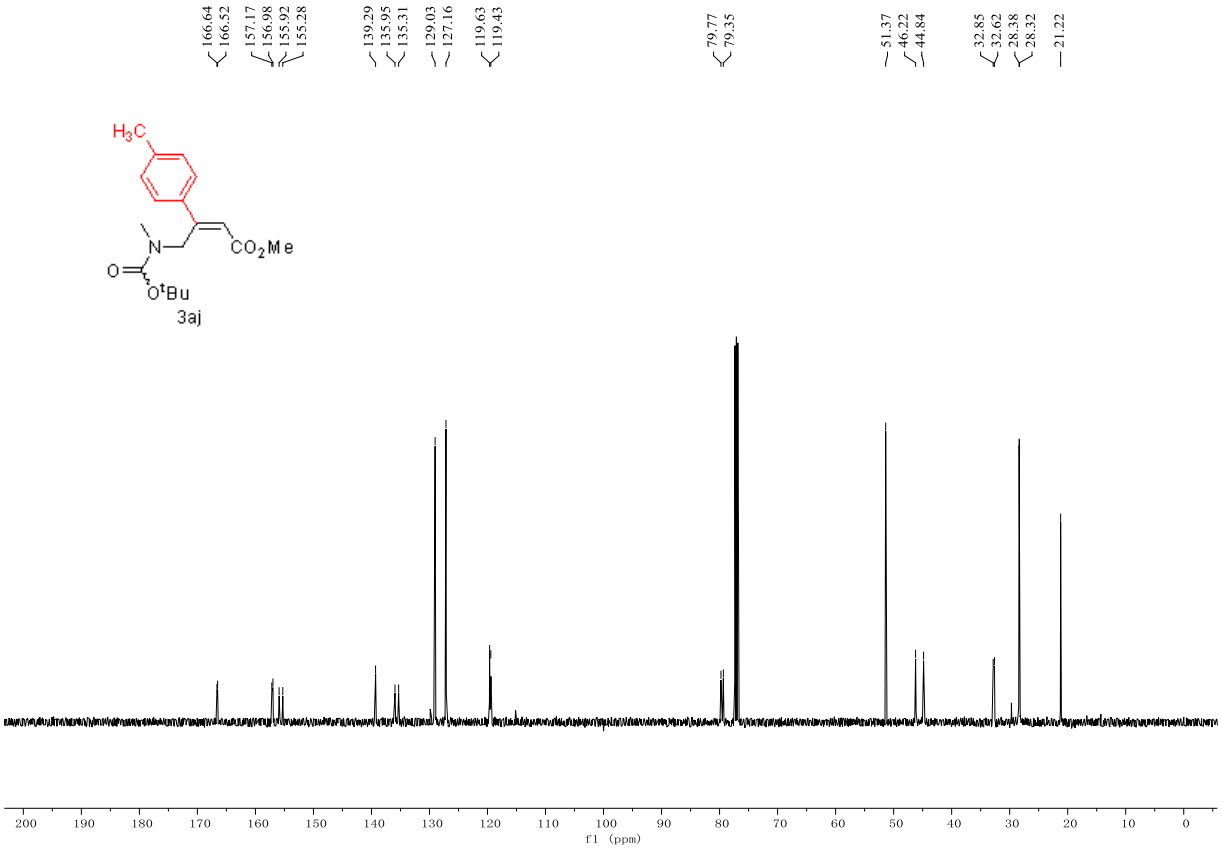
Supplementary Figure 40. ^{1}H NMR Spectra of **3ai'**



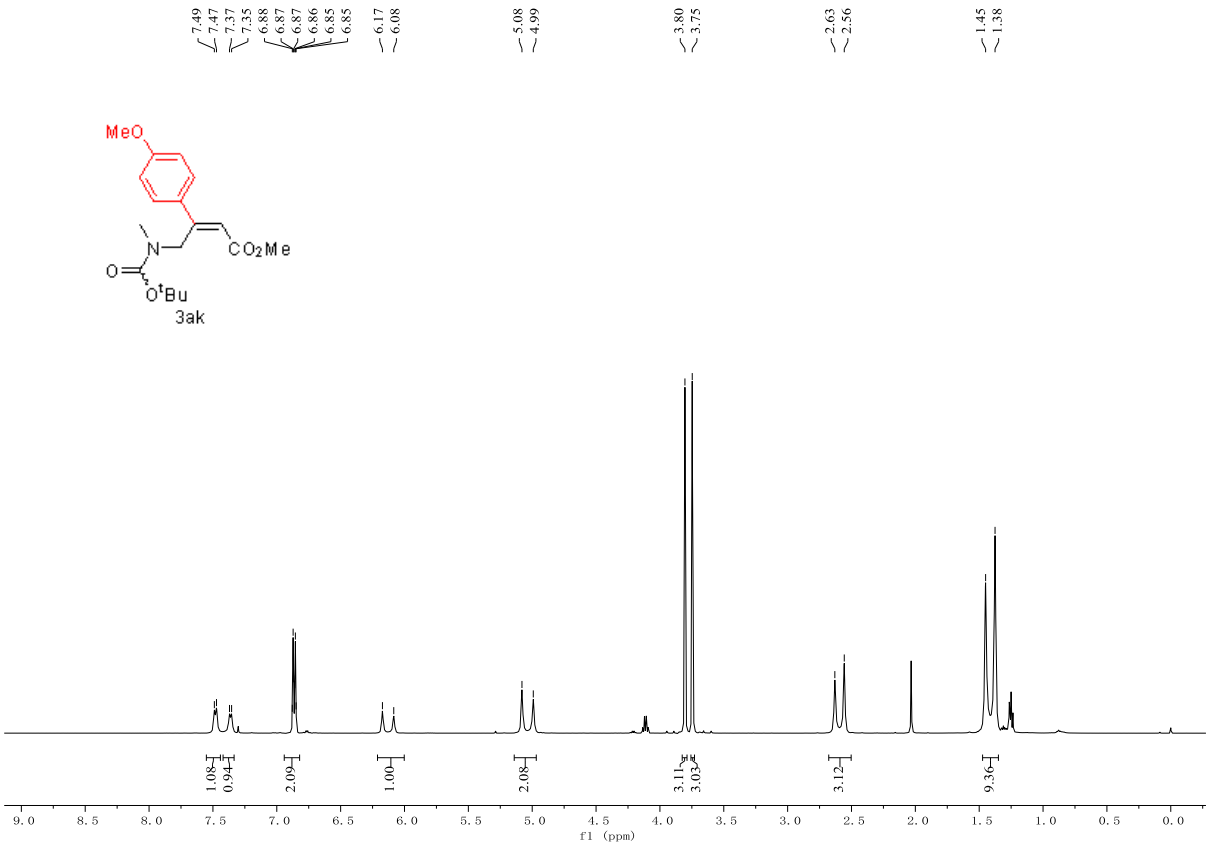
Supplementary Figure 41. ^{13}C NMR Spectra of **3ai'**



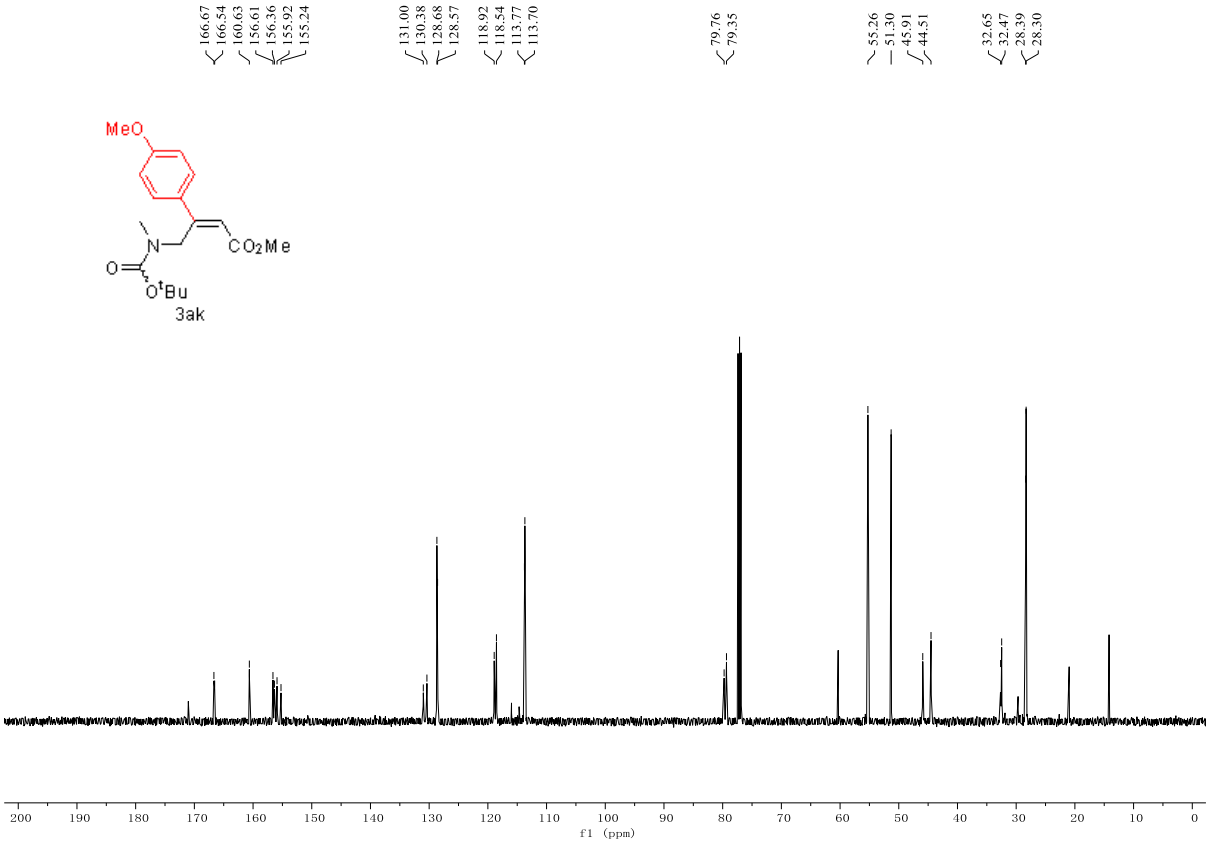
Supplementary Figure 42. ^{1}H NMR Spectra of **3aj**



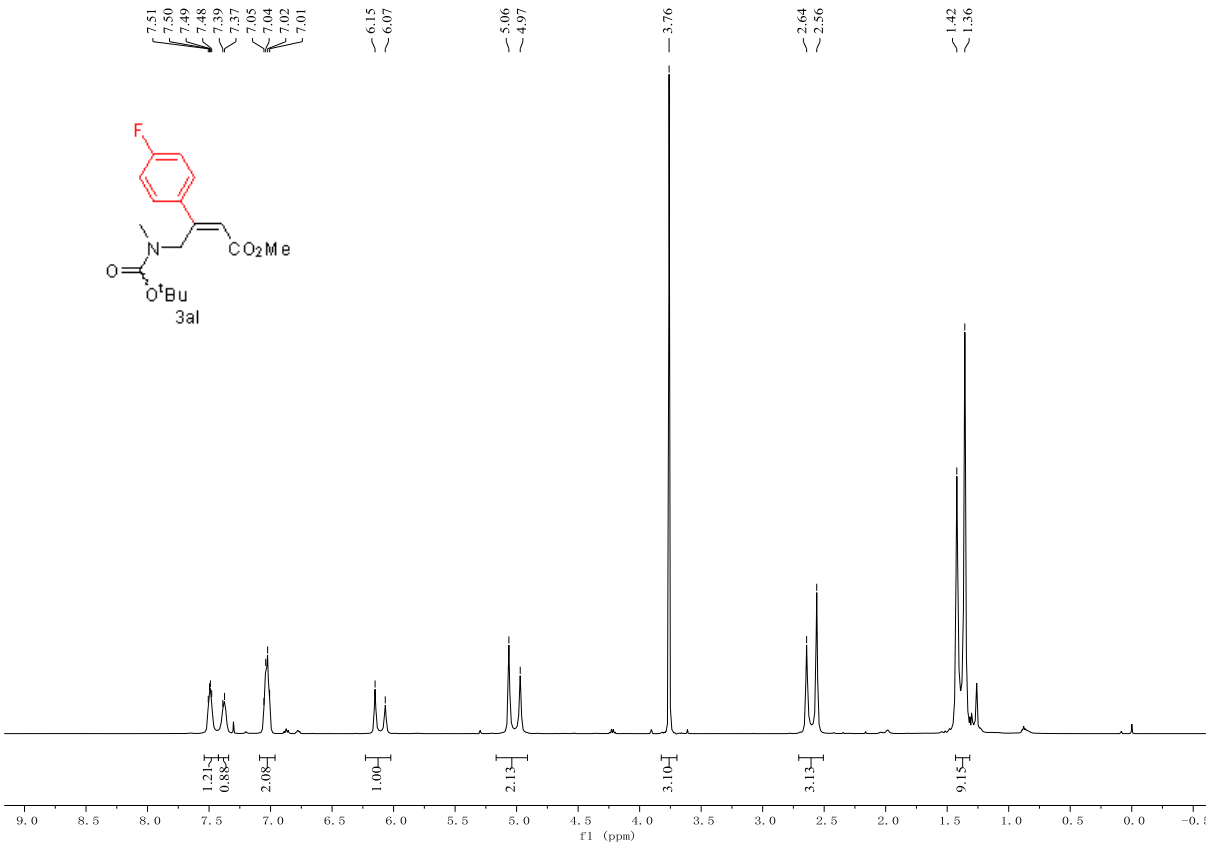
Supplementary Figure 43. ^{13}C NMR Spectra of **3aj**



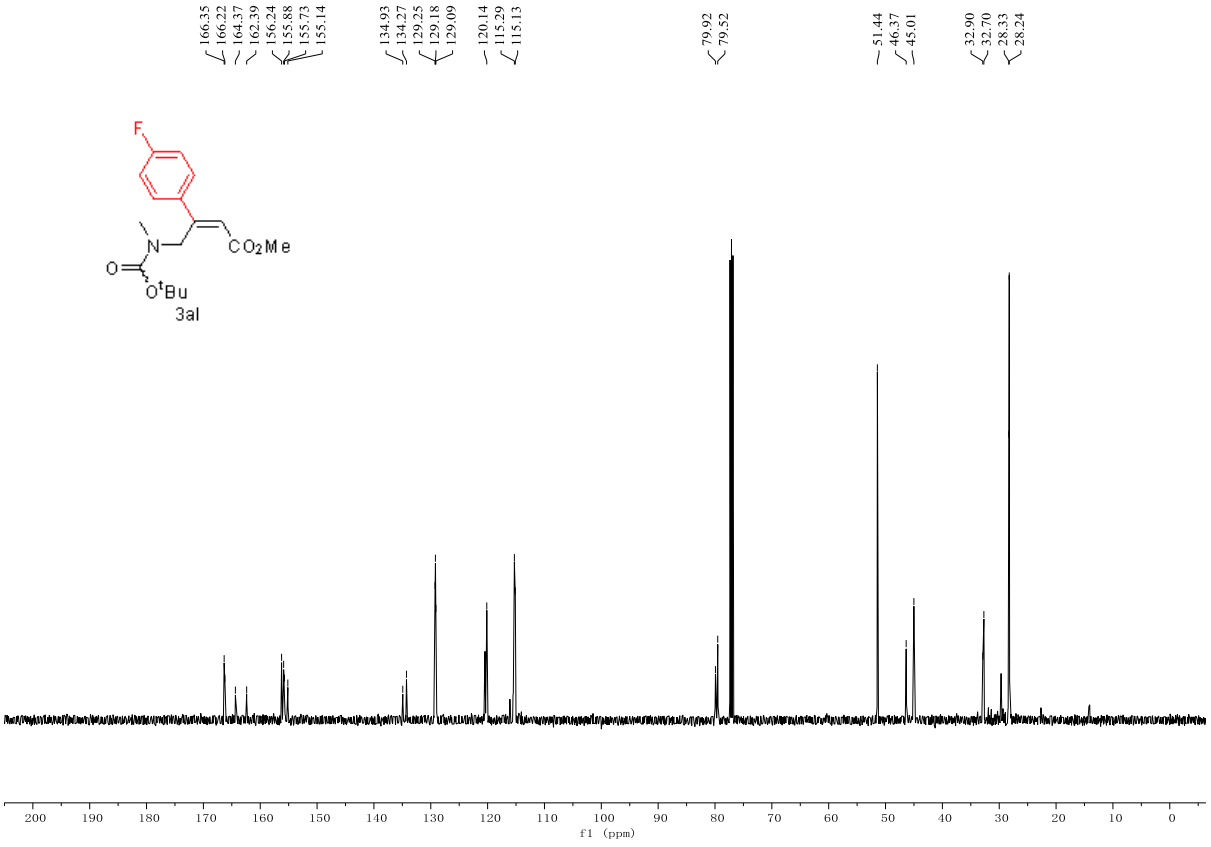
Supplementary Figure 44. ^{1}H NMR Spectra of **3ak**



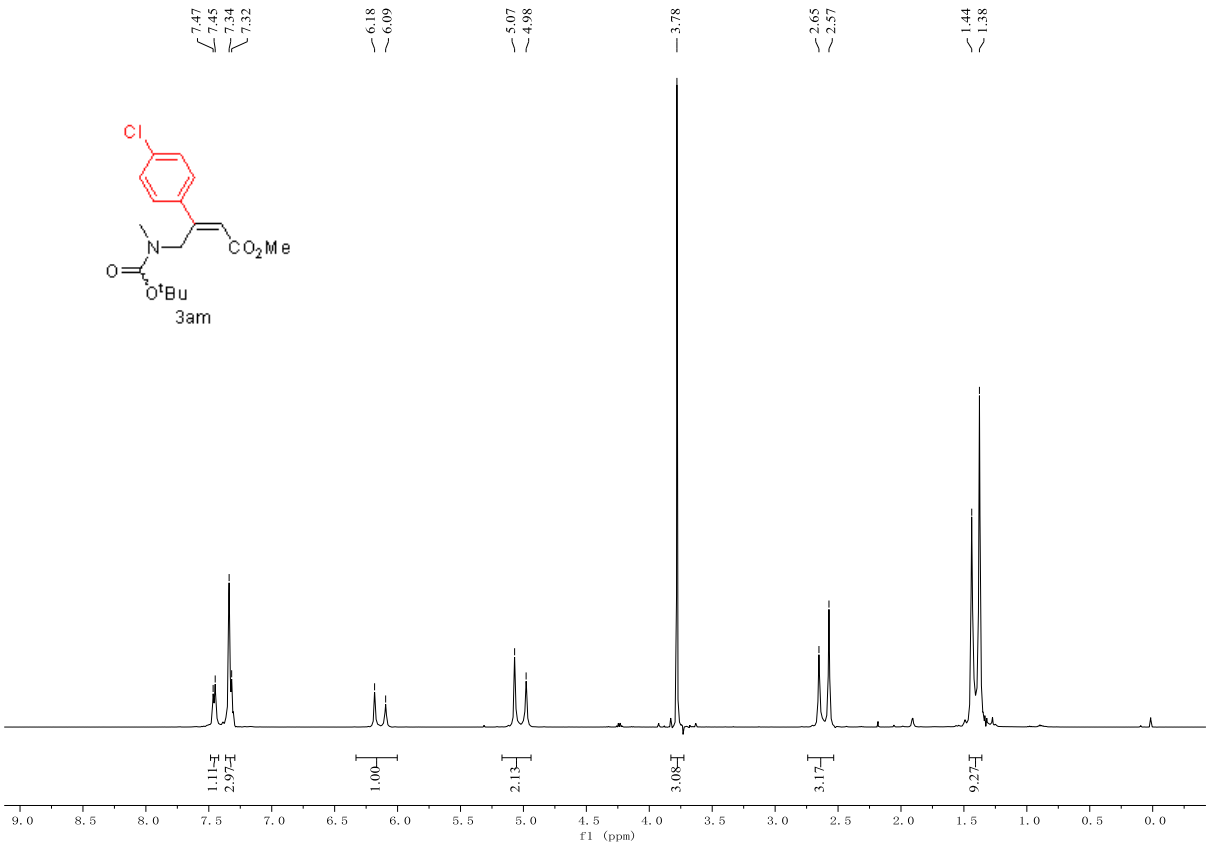
Supplementary Figure 45. ^{13}C NMR Spectra of **3ak**



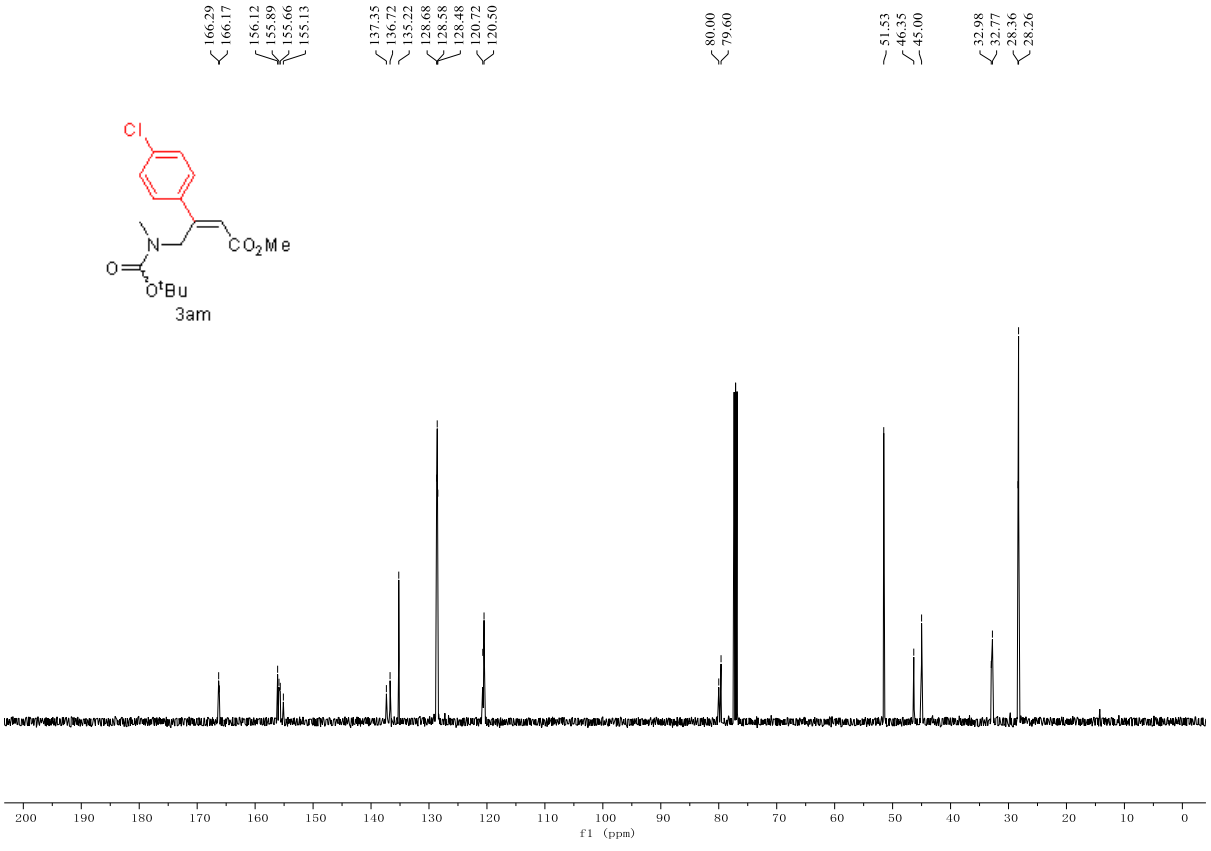
Supplementary Figure 46. ^{1}H NMR Spectra of **3al**



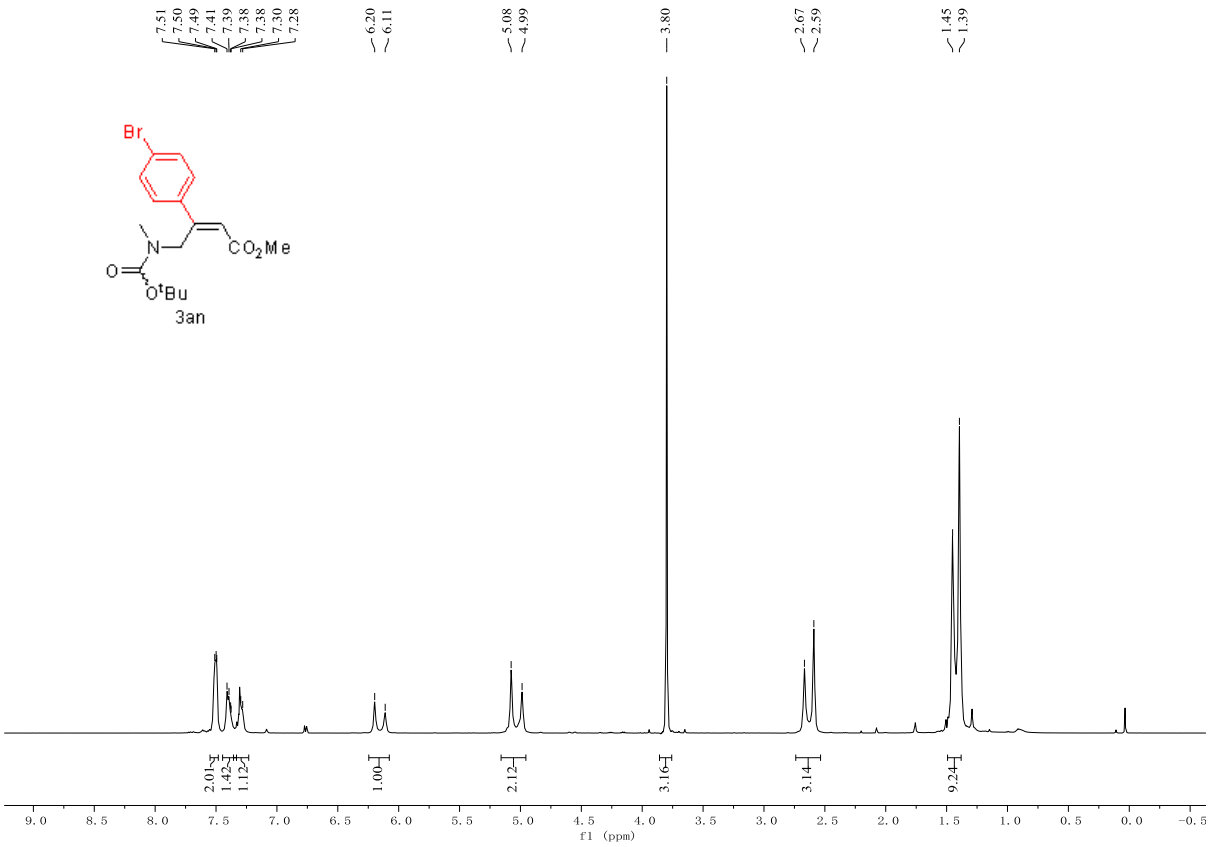
Supplementary Figure 47. ^{13}C NMR Spectra of **3al**



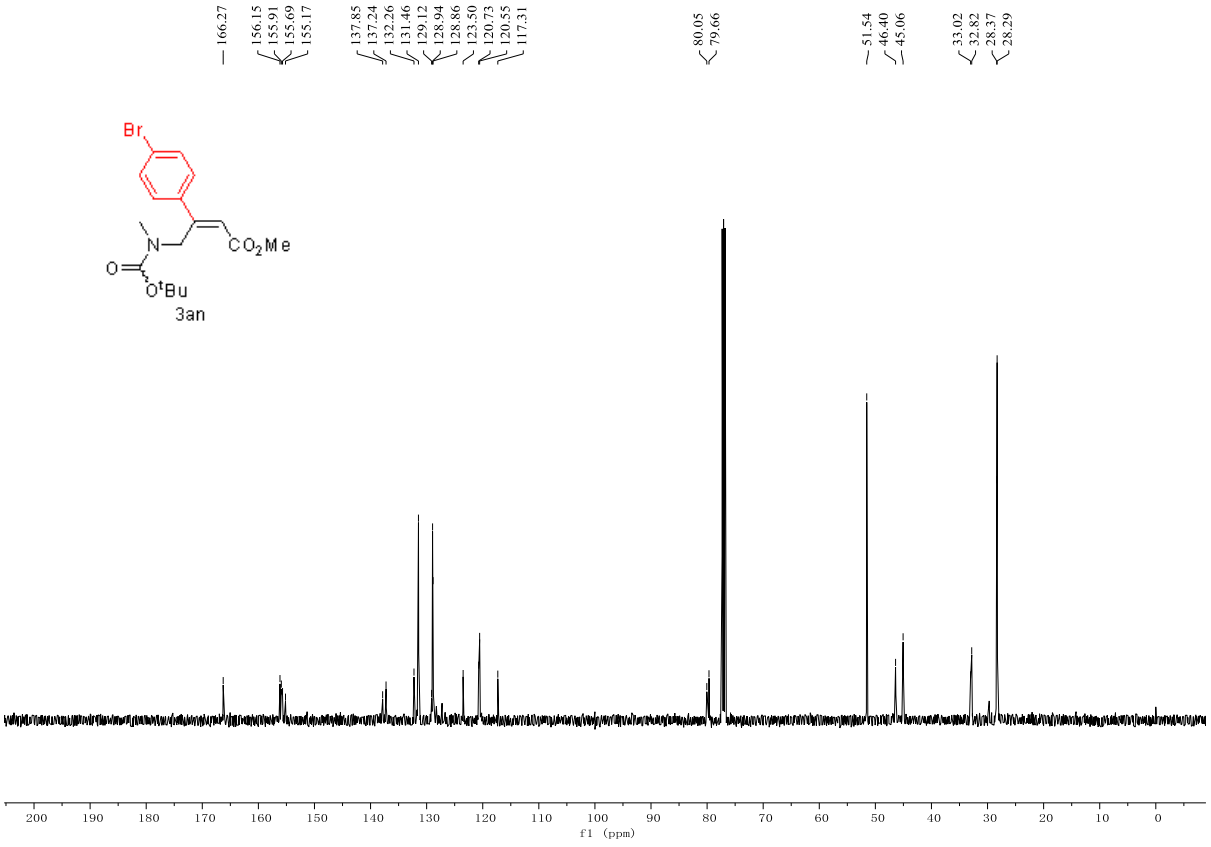
Supplementary Figure 48. ^{1}H NMR Spectra of **3am**



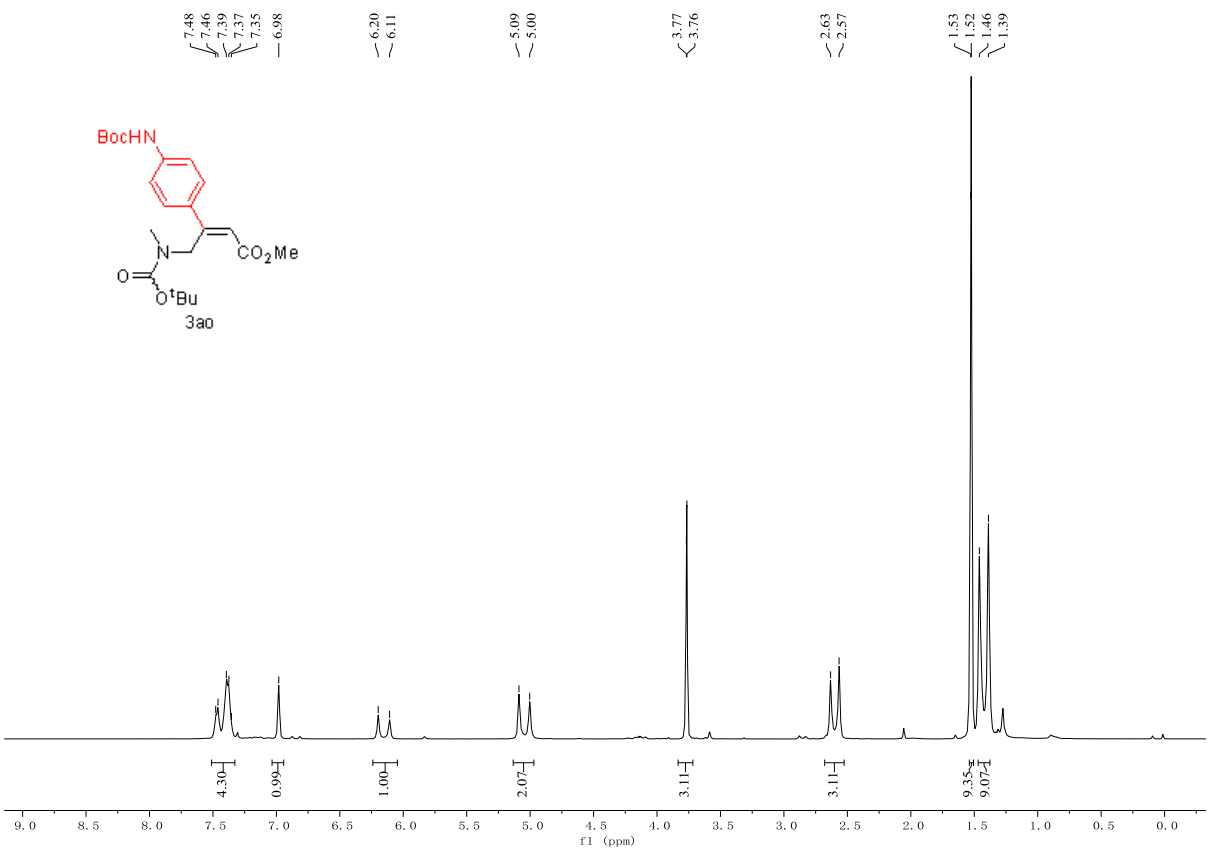
Supplementary Figure 49. ^{13}C NMR Spectra of **3am**



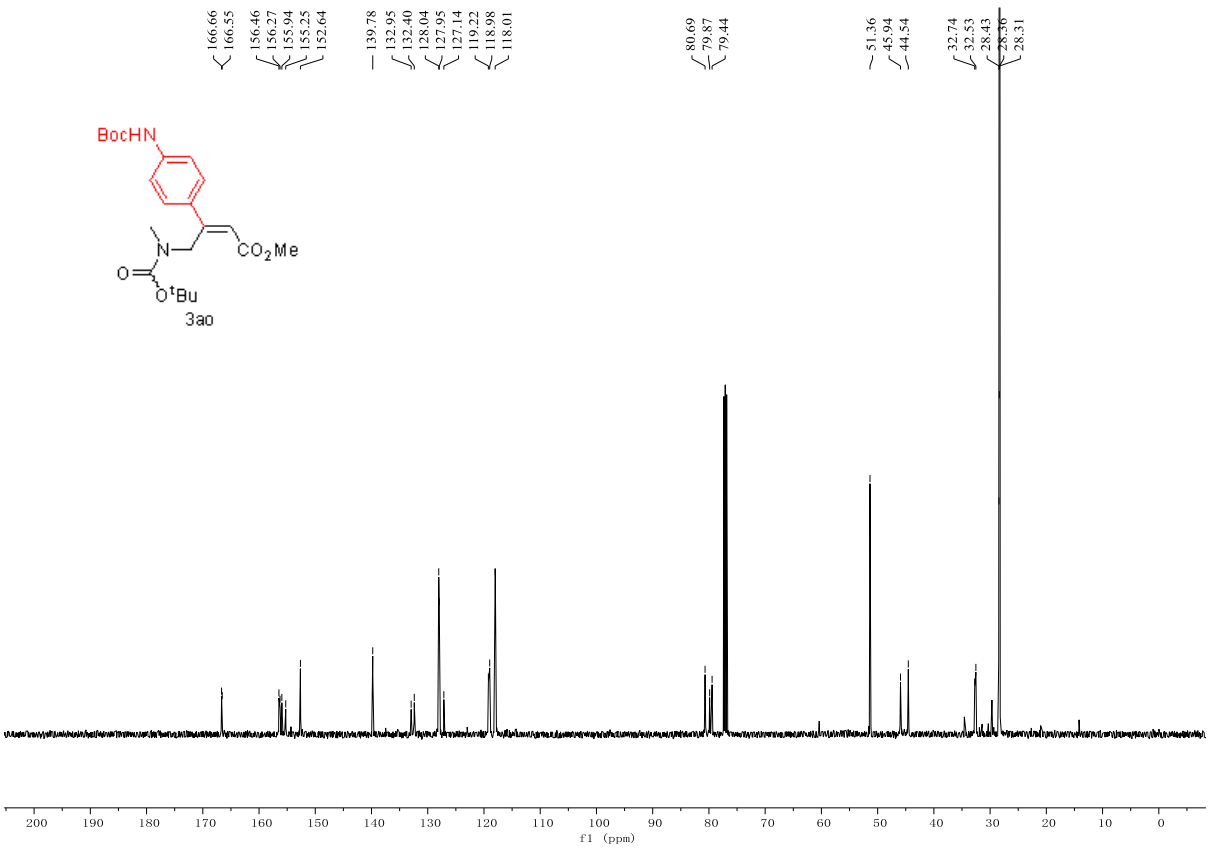
Supplementary Figure 50. ^{1}H NMR Spectra of **3an**



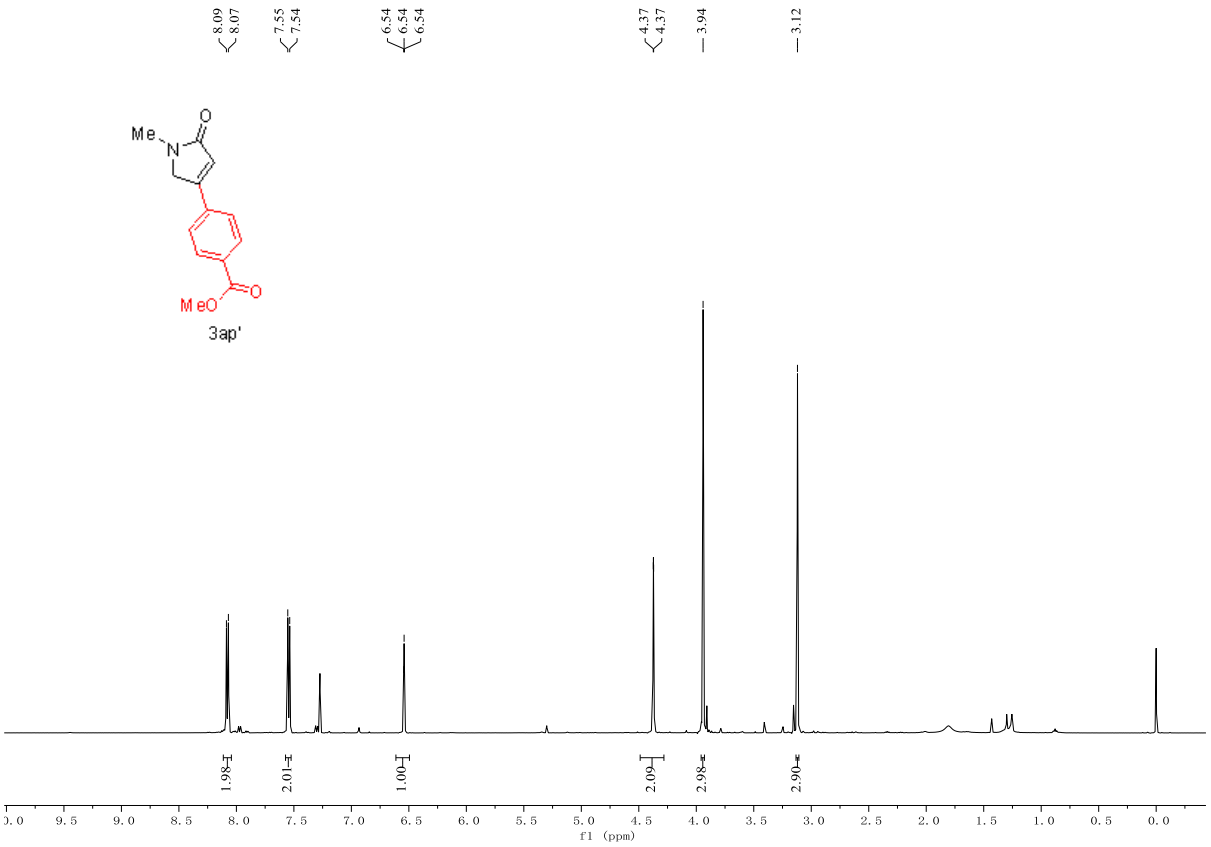
Supplementary Figure 51. ^{13}C NMR Spectra of **3an**



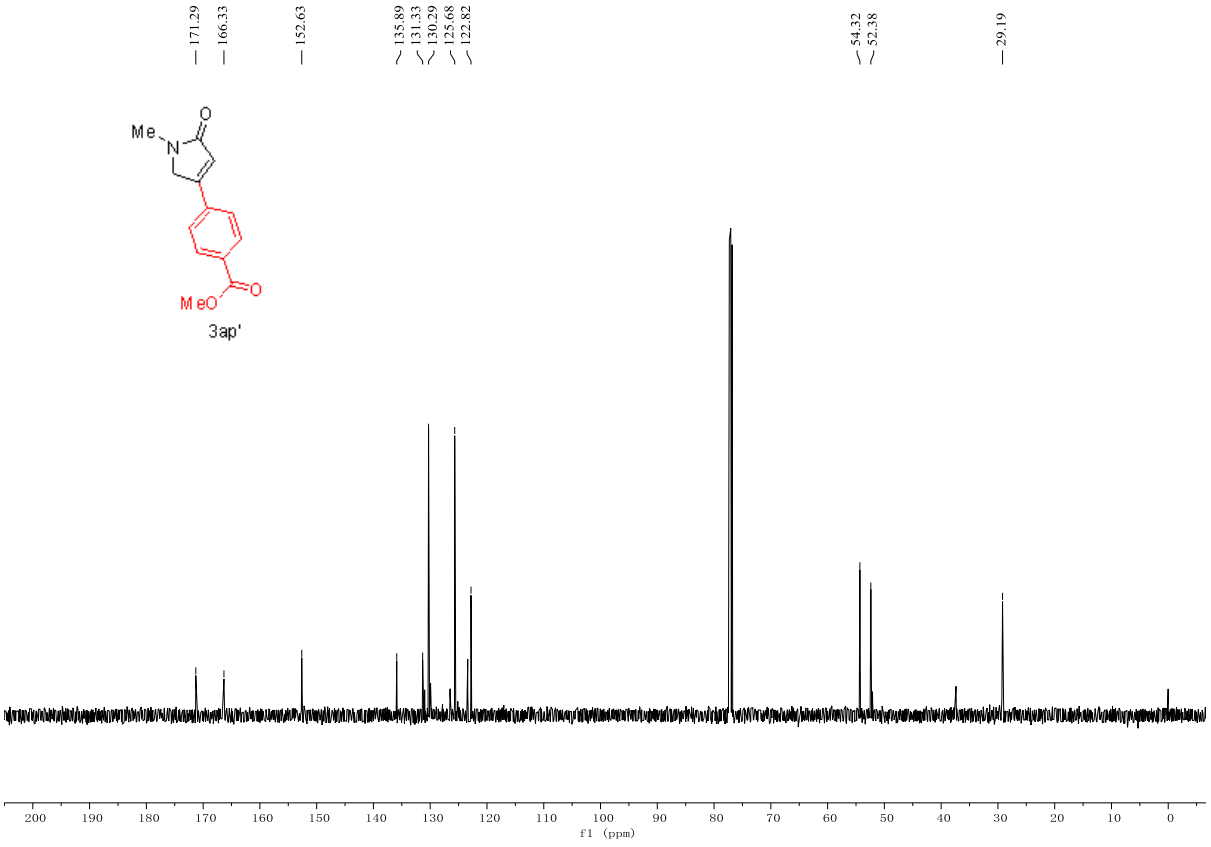
Supplementary Figure 52. ^{1}H NMR Spectra of **3ao**



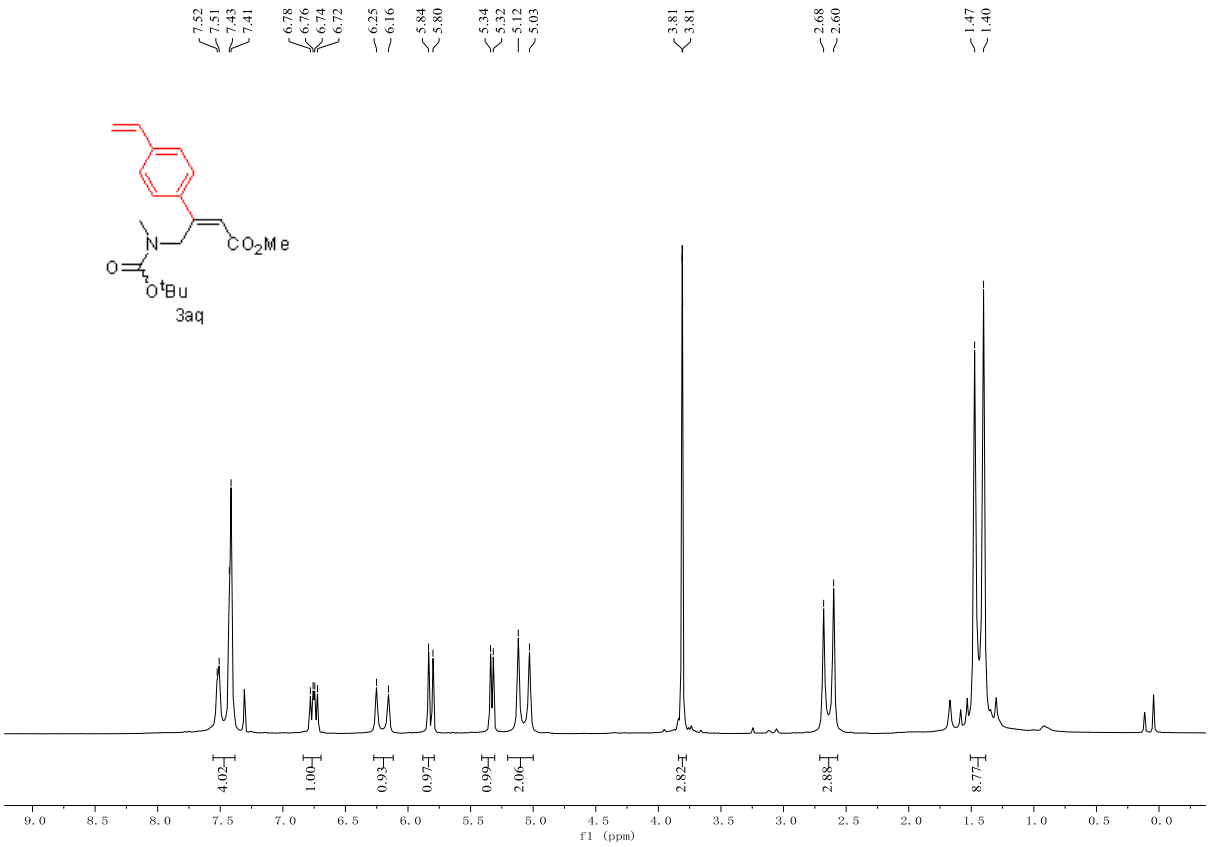
Supplementary Figure 53. ^{13}C NMR Spectra of **3ao**



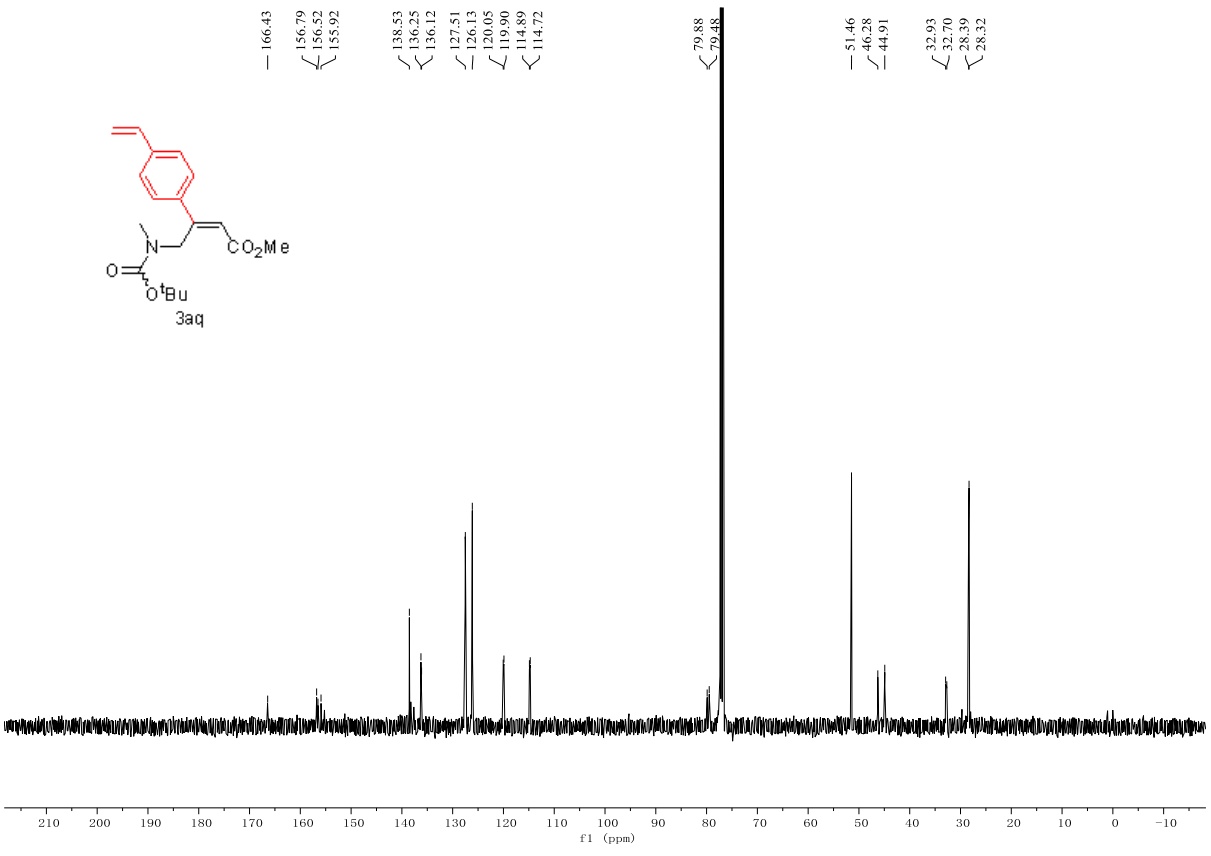
Supplementary Figure 54. ^{1}H NMR Spectra of **3ap'**



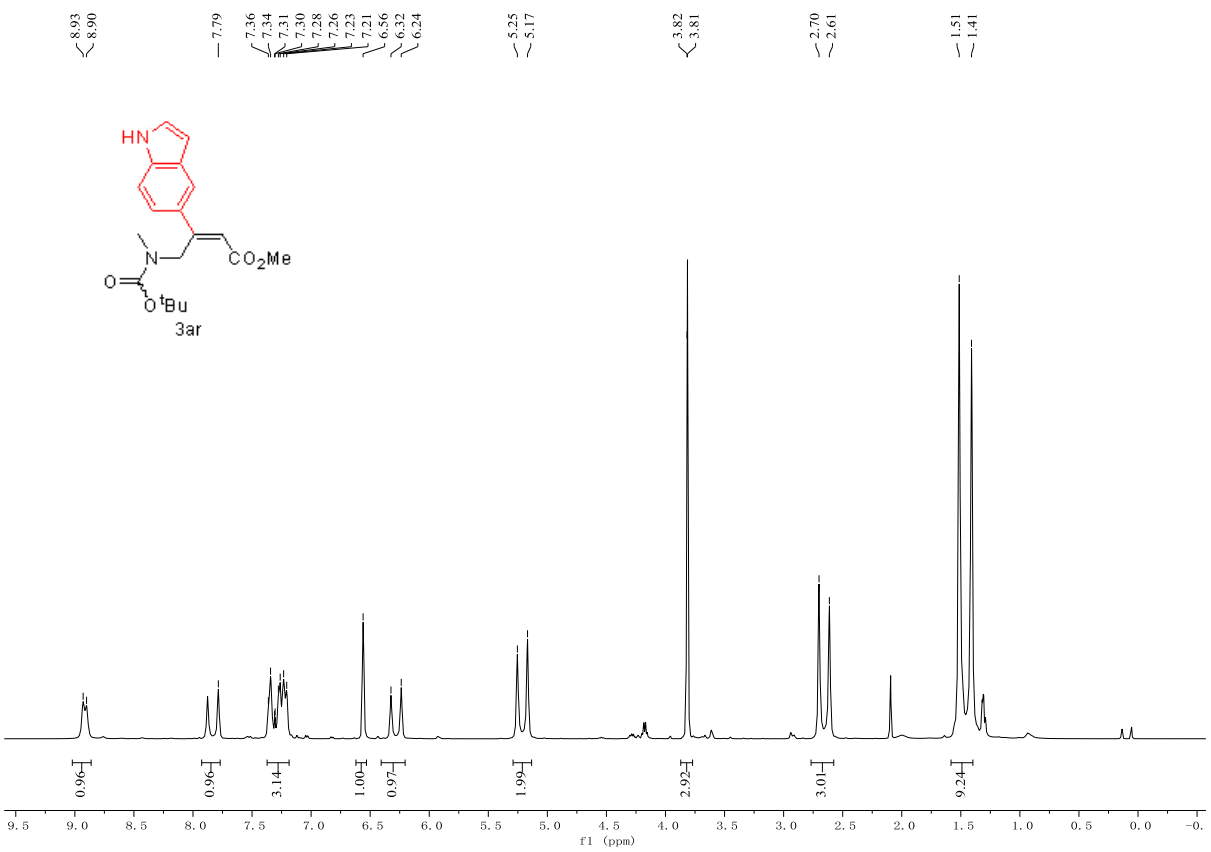
Supplementary Figure 55. ^{13}C NMR Spectra of **3ap'**



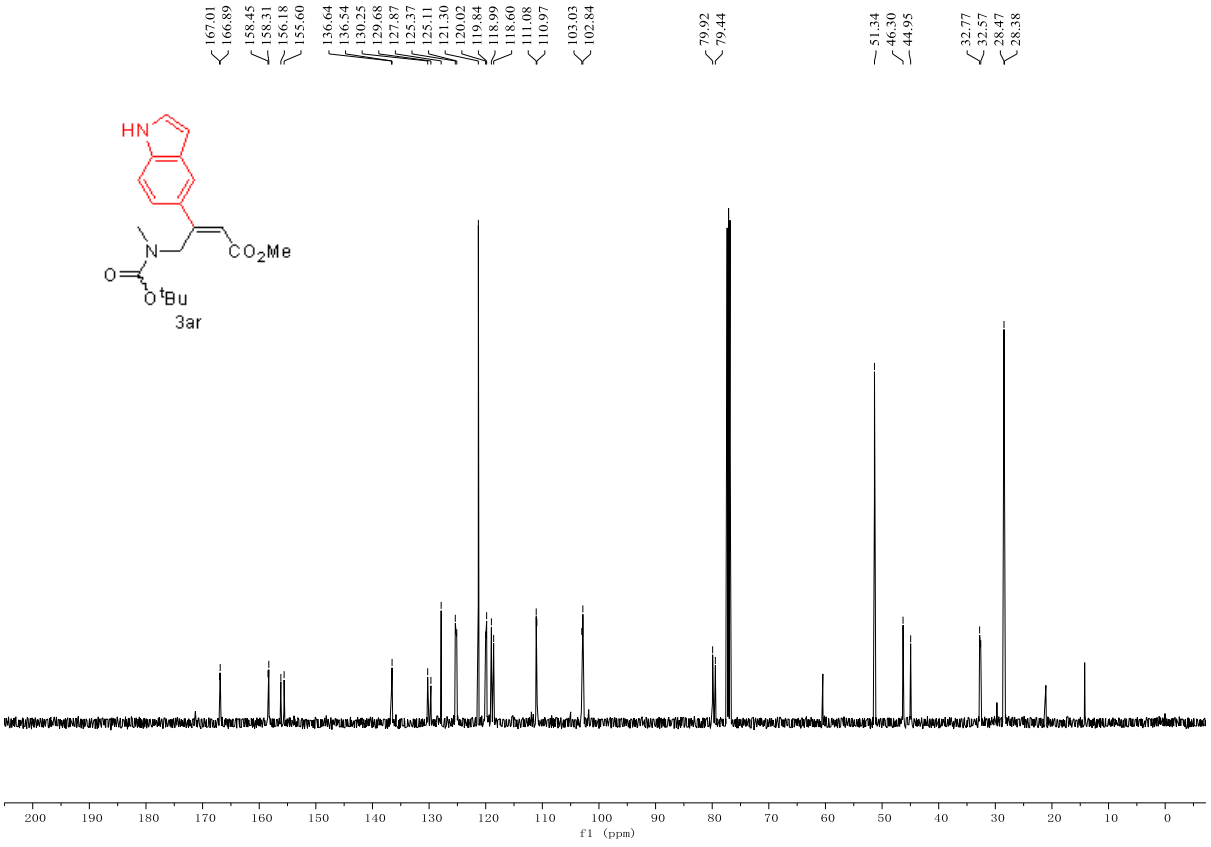
Supplementary Figure 56. ^{1}H NMR Spectra of **3aq**



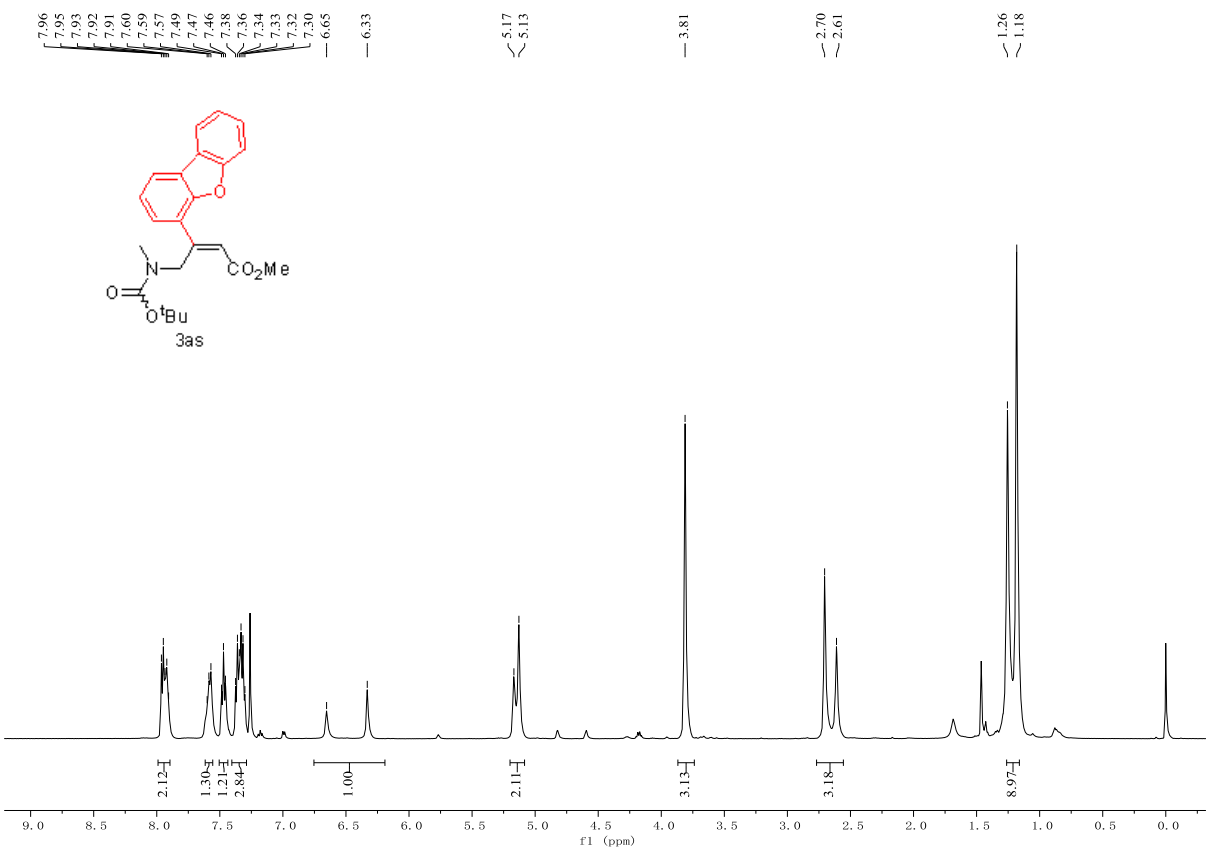
Supplementary Figure 57. ^{13}C NMR Spectra of **3aq**



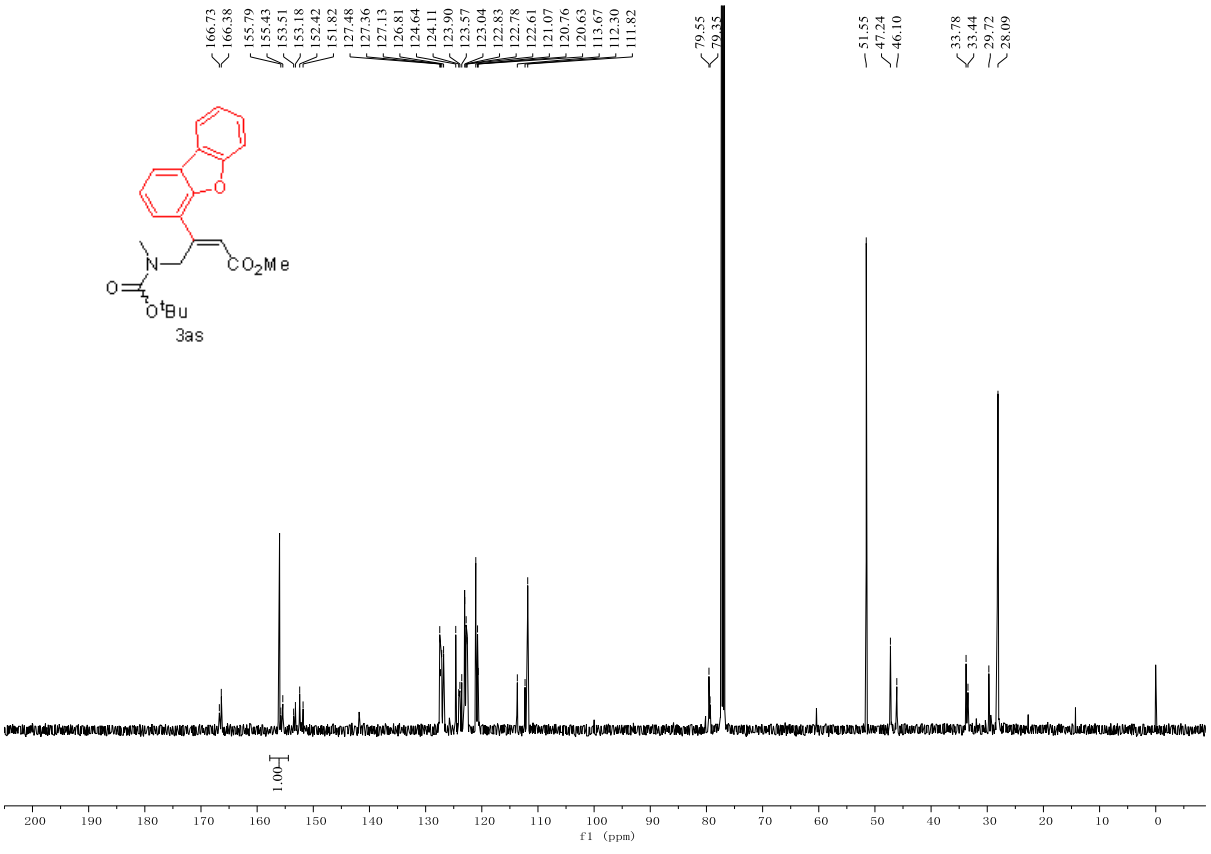
Supplementary Figure 58. ^{1}H NMR Spectra of **3ar**



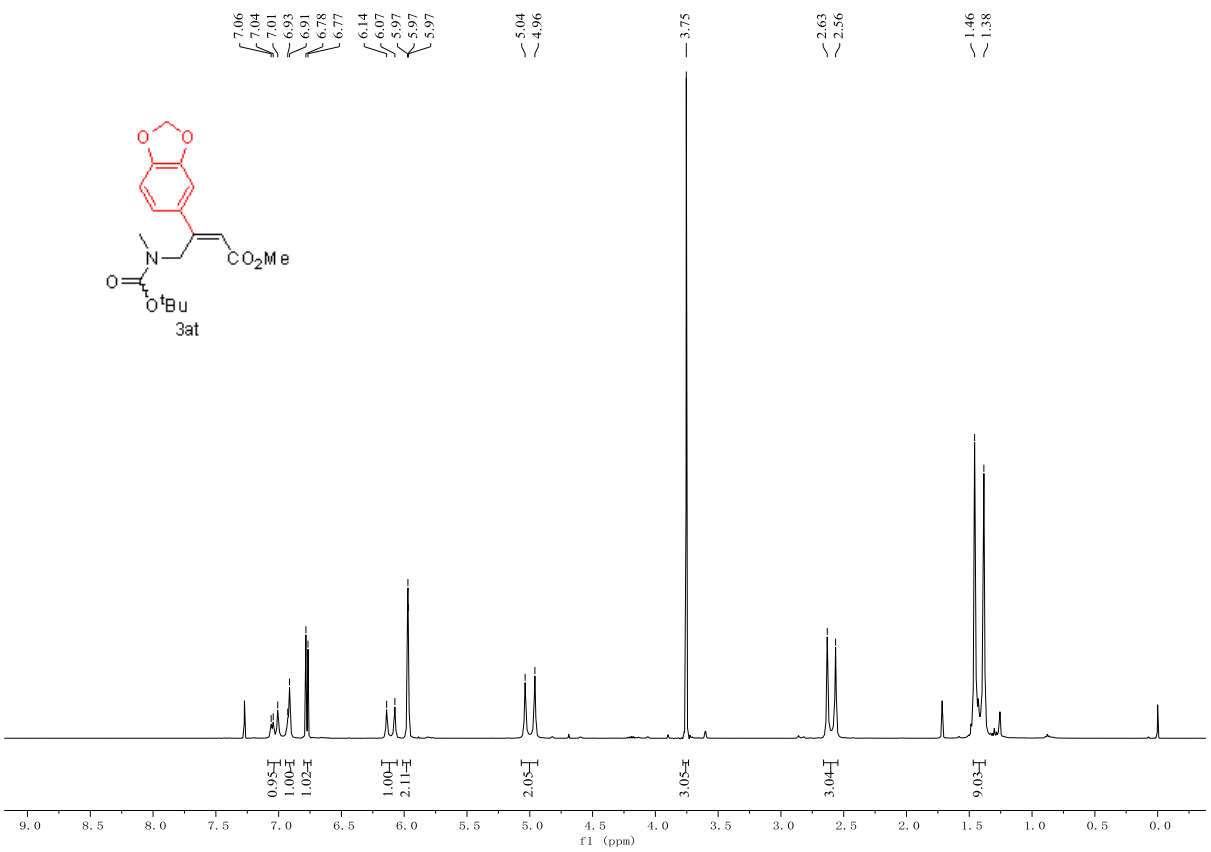
Supplementary Figure 59. ^{13}C NMR Spectra of **3ar**



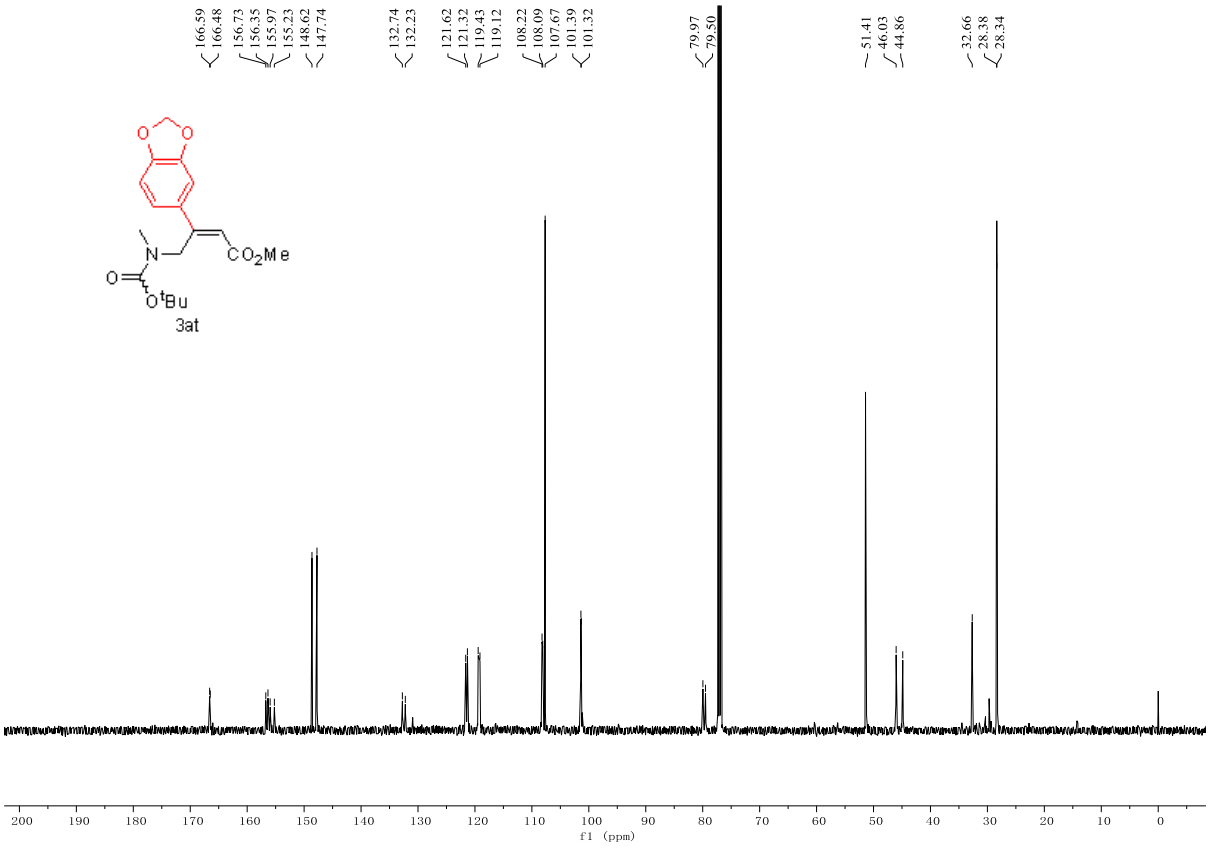
Supplementary Figure 60. ^{1}H NMR Spectra of **3as**



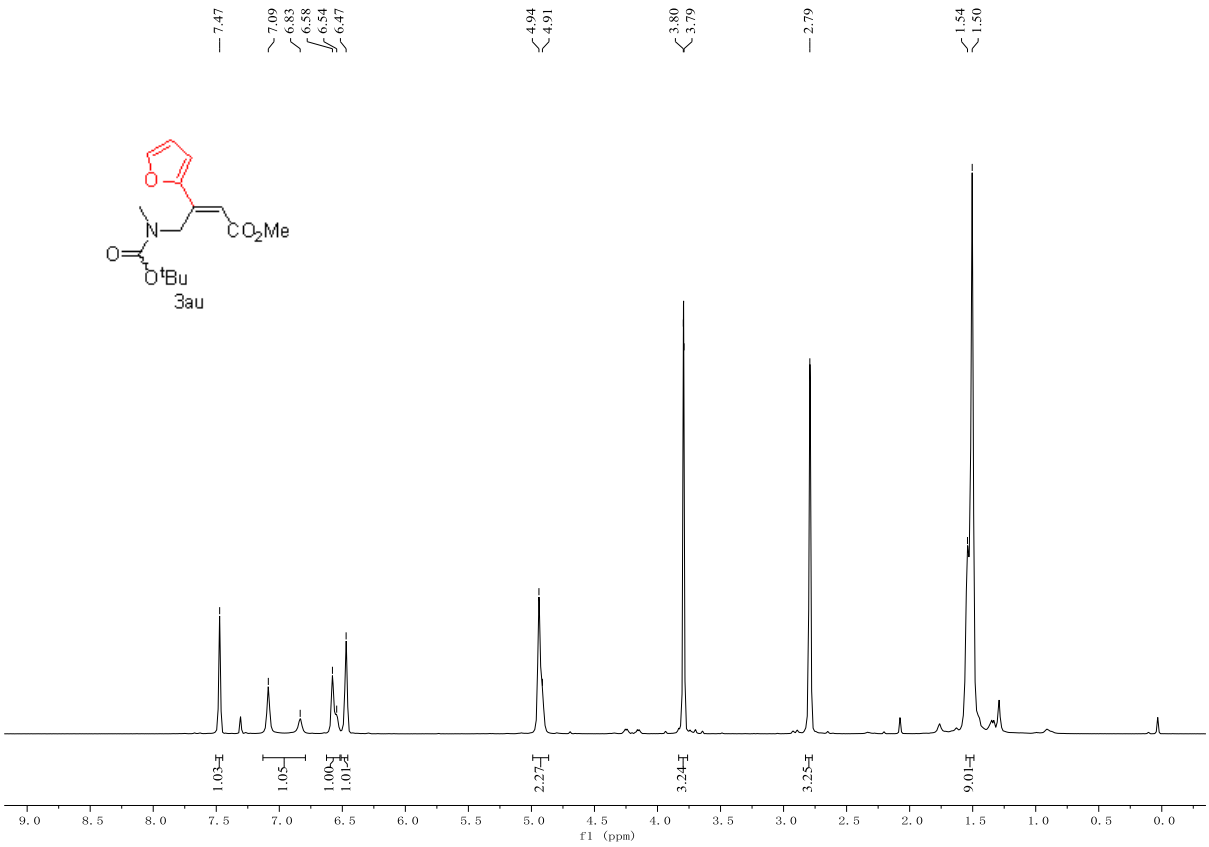
Supplementary Figure 61. ^{13}C NMR Spectra of **3as**



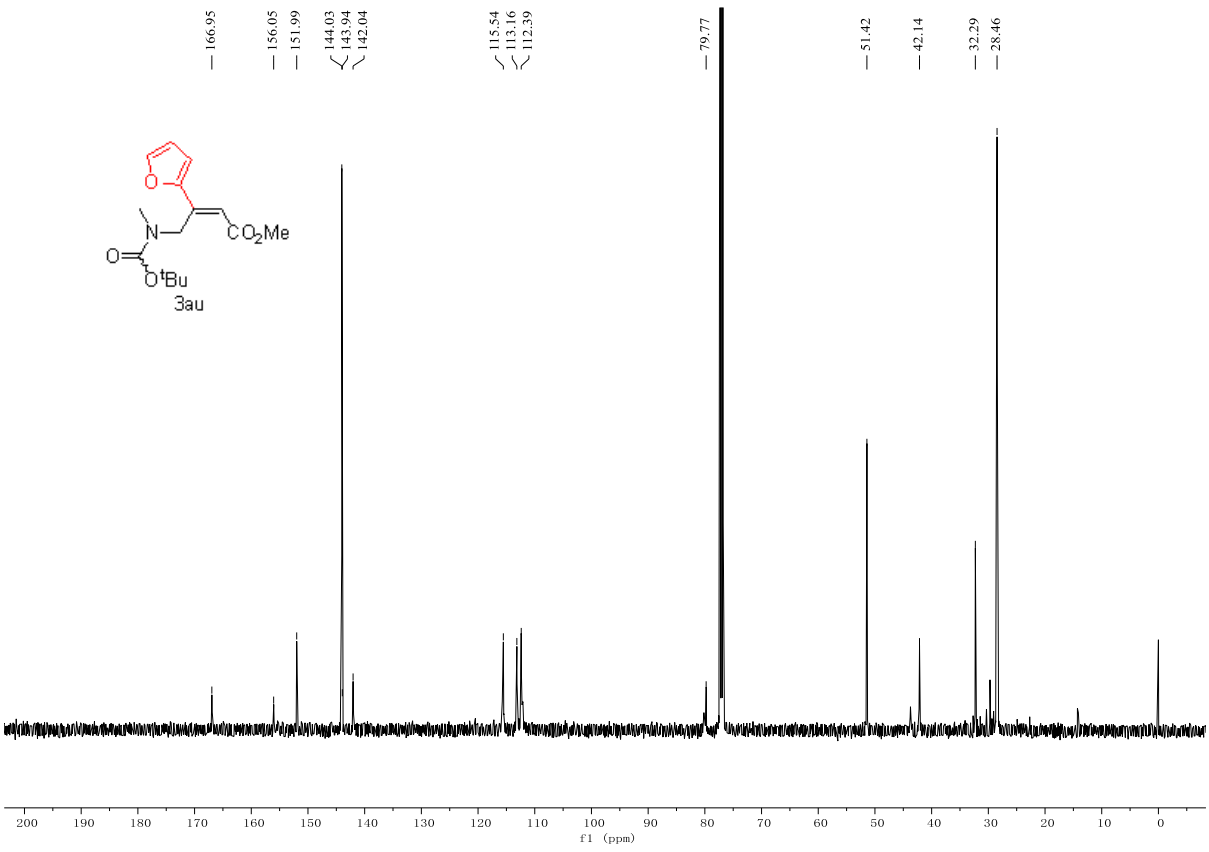
Supplementary Figure 62. ^{1}H NMR Spectra of **3at**



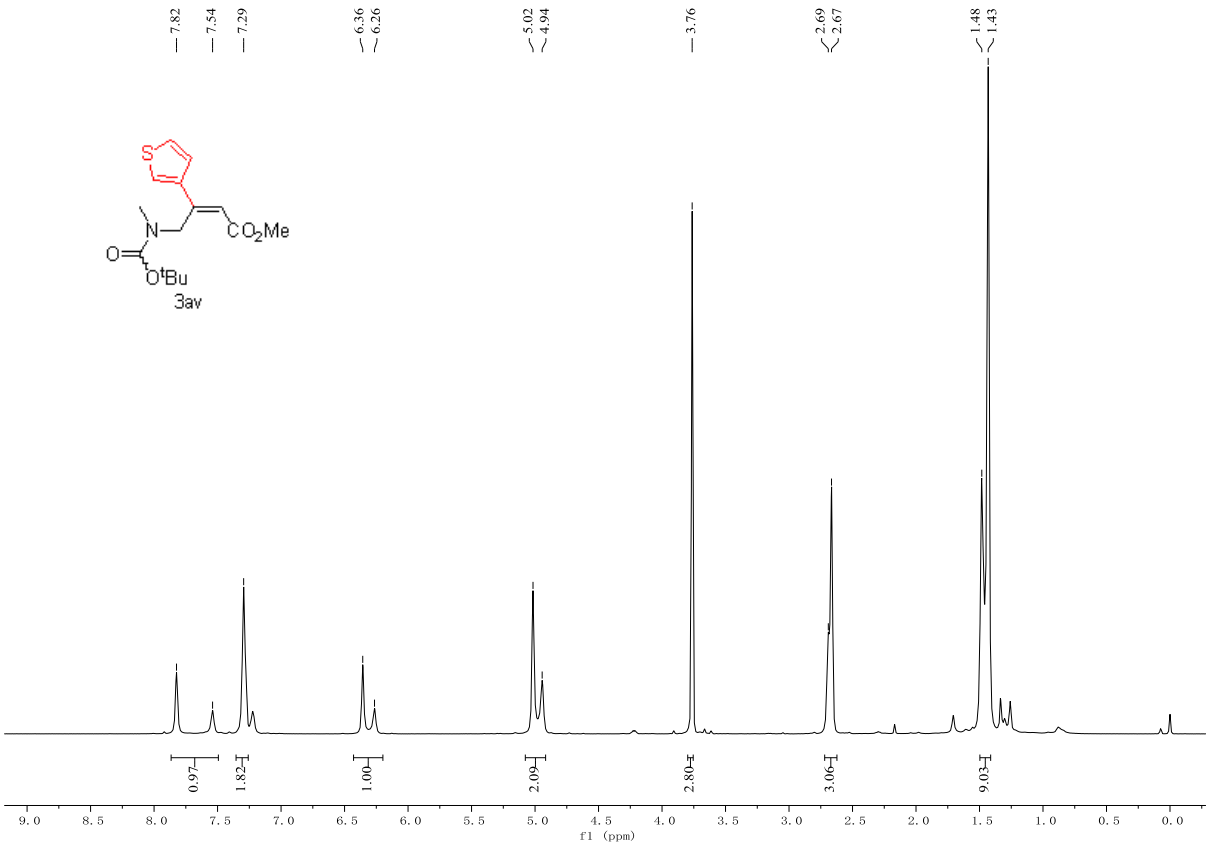
Supplementary Figure 63. ^{13}C NMR Spectra of **3at**



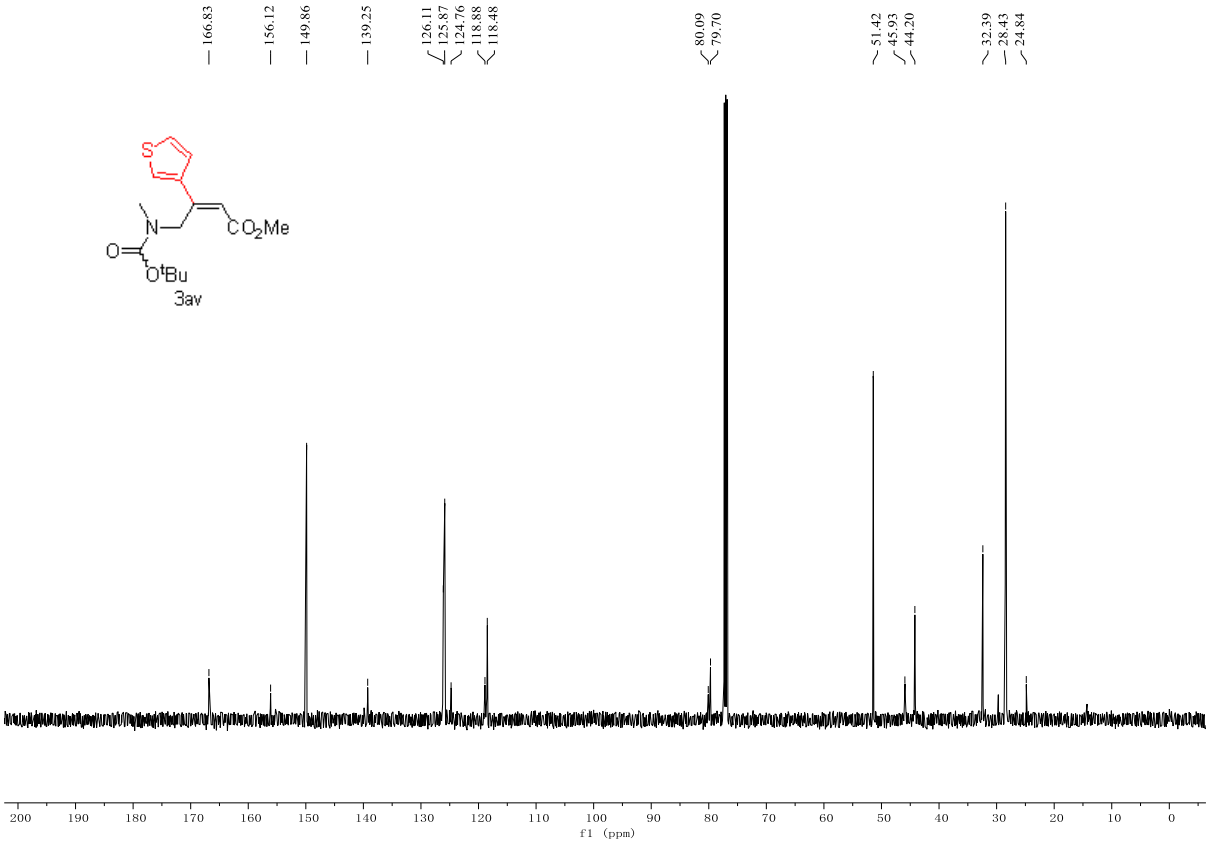
Supplementary Figure 64. ^{1}H NMR Spectra of **3au**



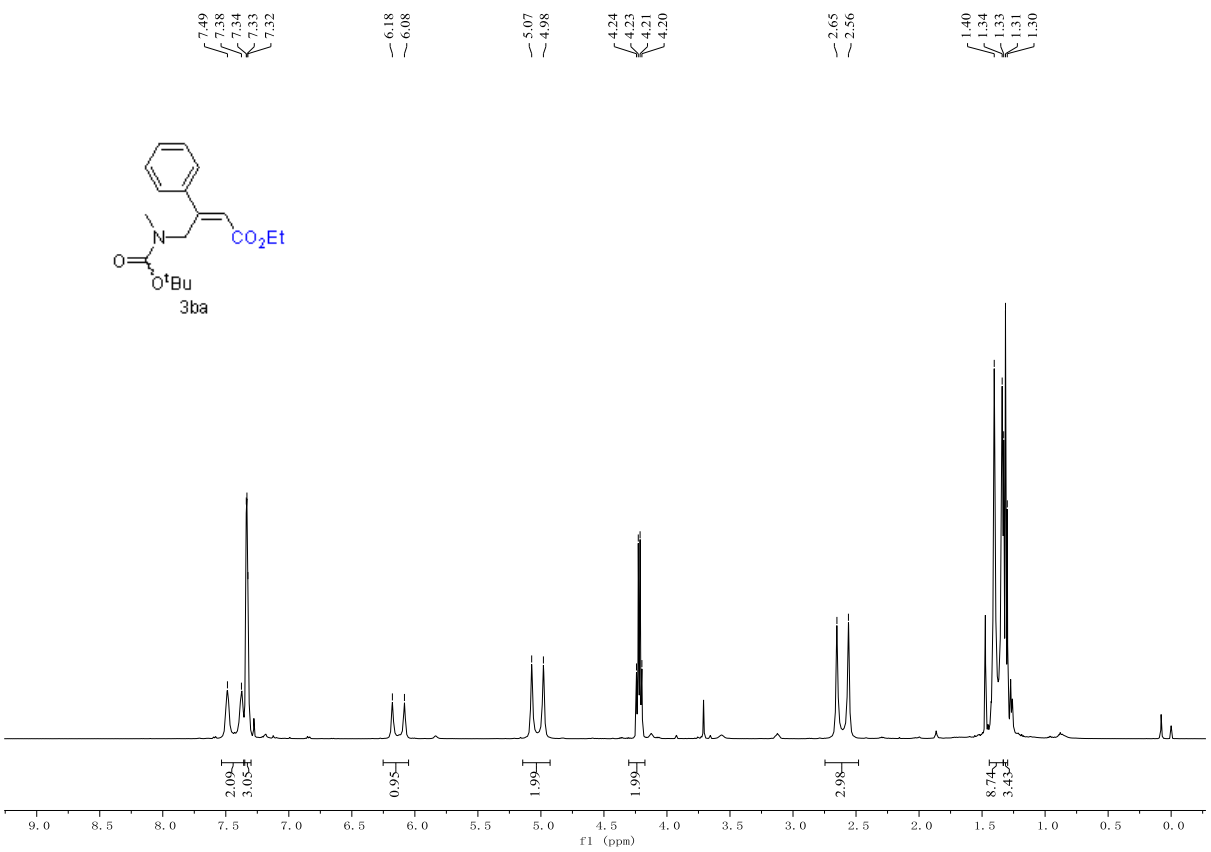
Supplementary Figure 65. ^{13}C NMR Spectra of **3au**



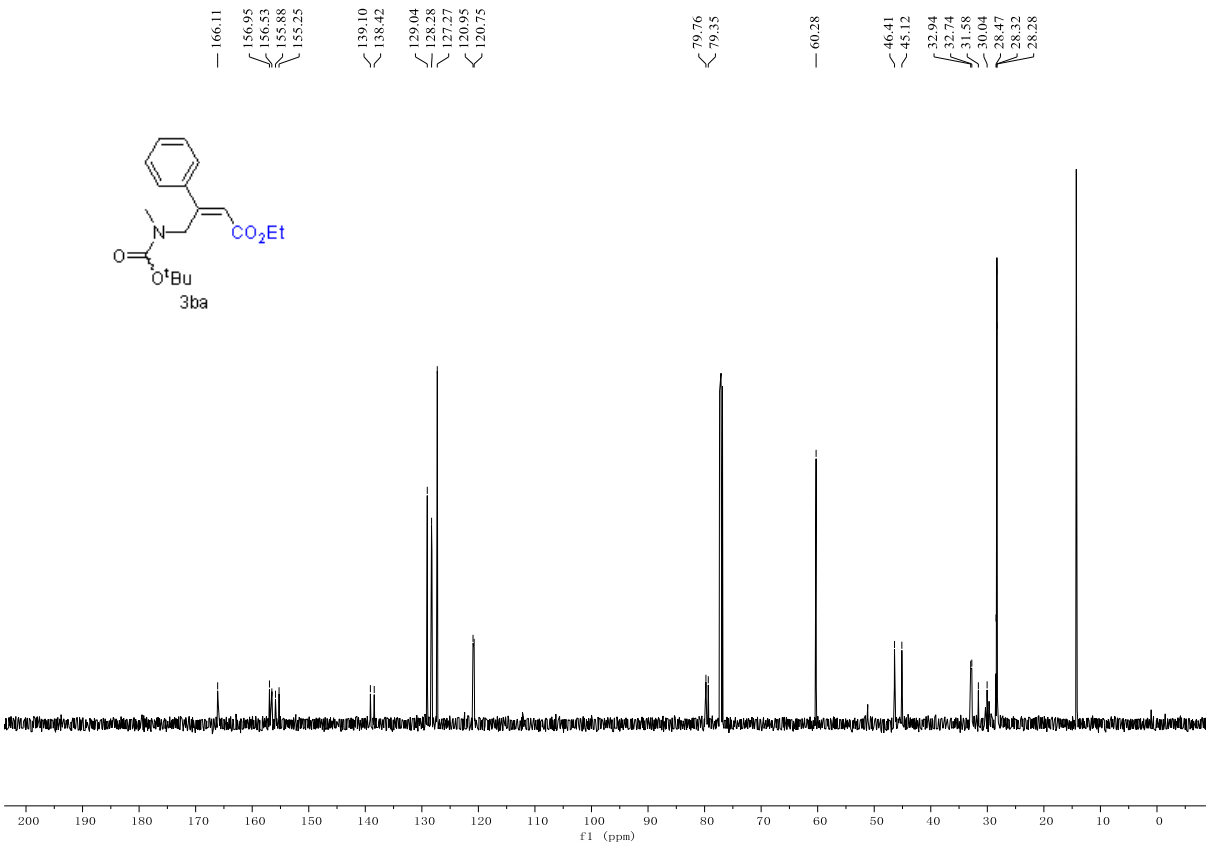
Supplementary Figure 66. ^{1}H NMR Spectra of **3av**



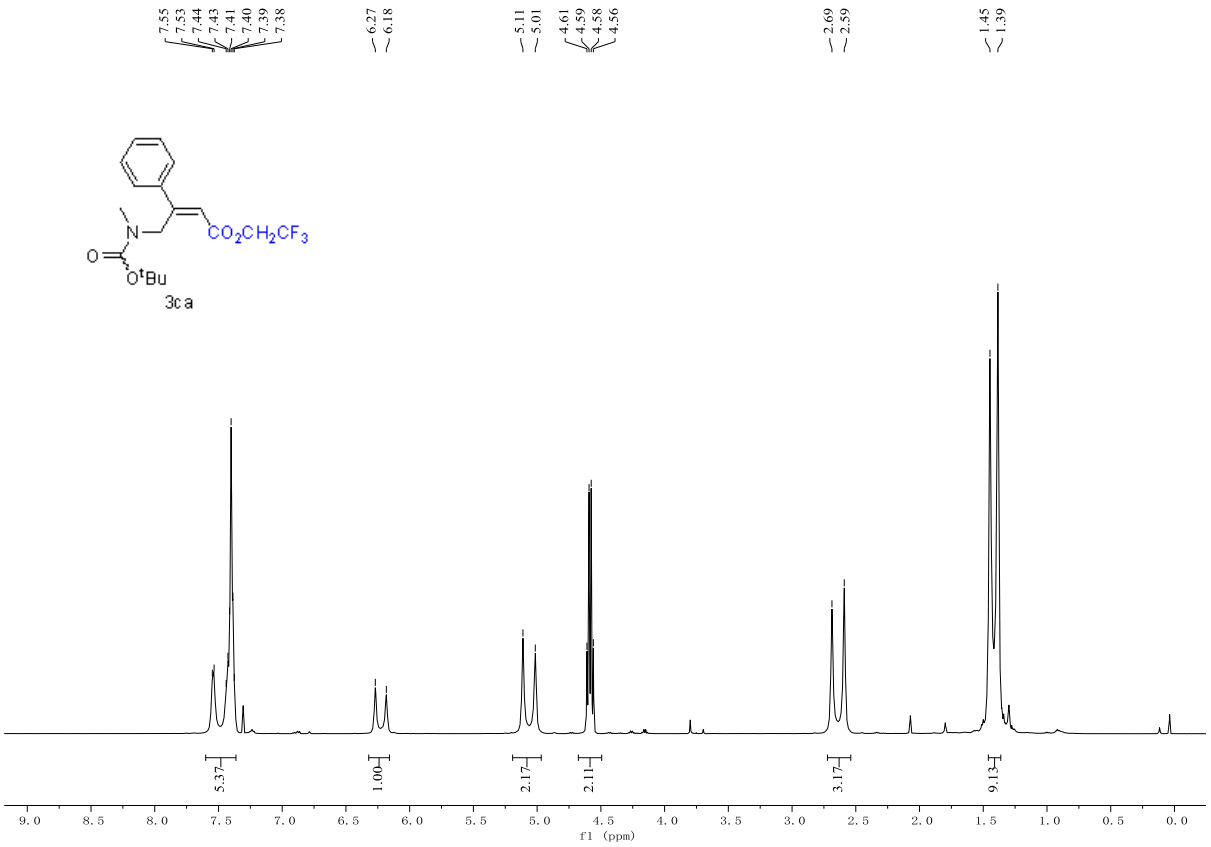
Supplementary Figure 67. ^{13}C NMR Spectra of **3av**



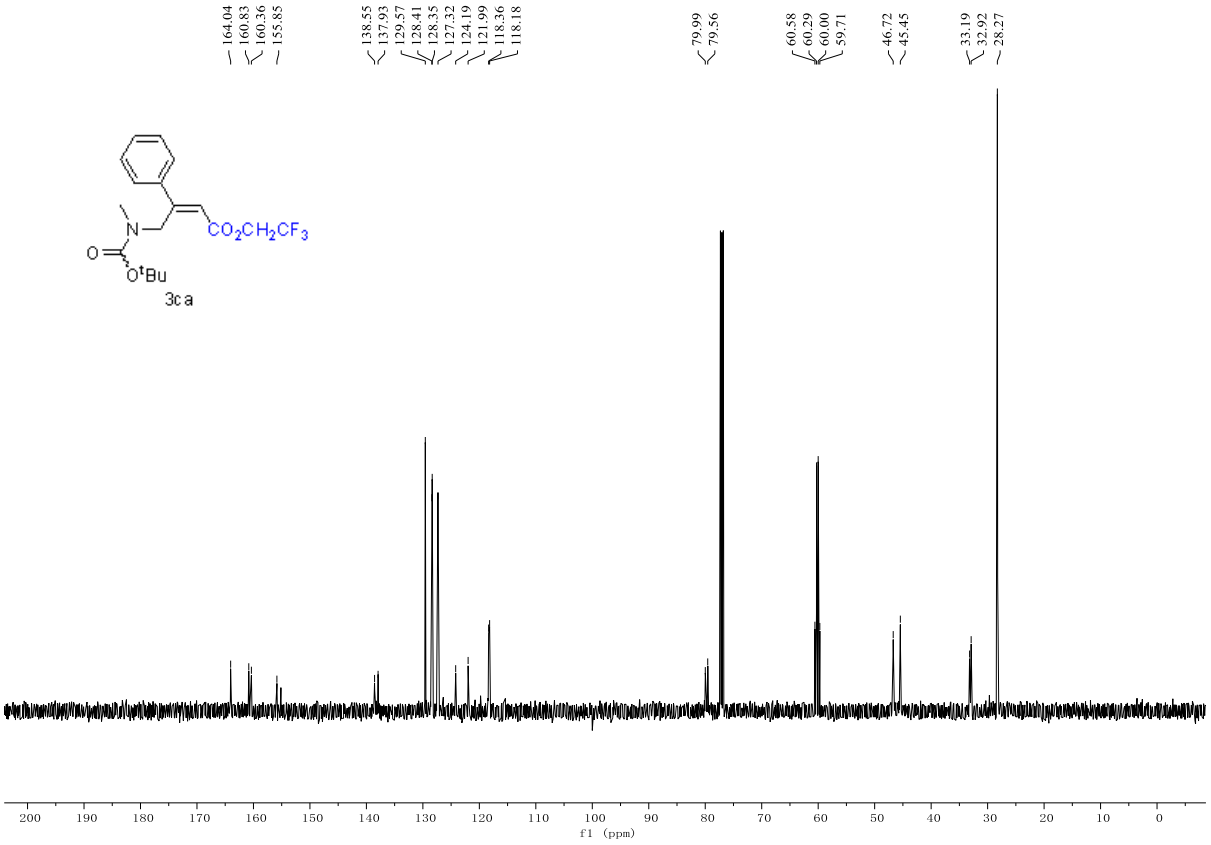
Supplementary Figure 68. ^{1}H NMR Spectra of **3ba**



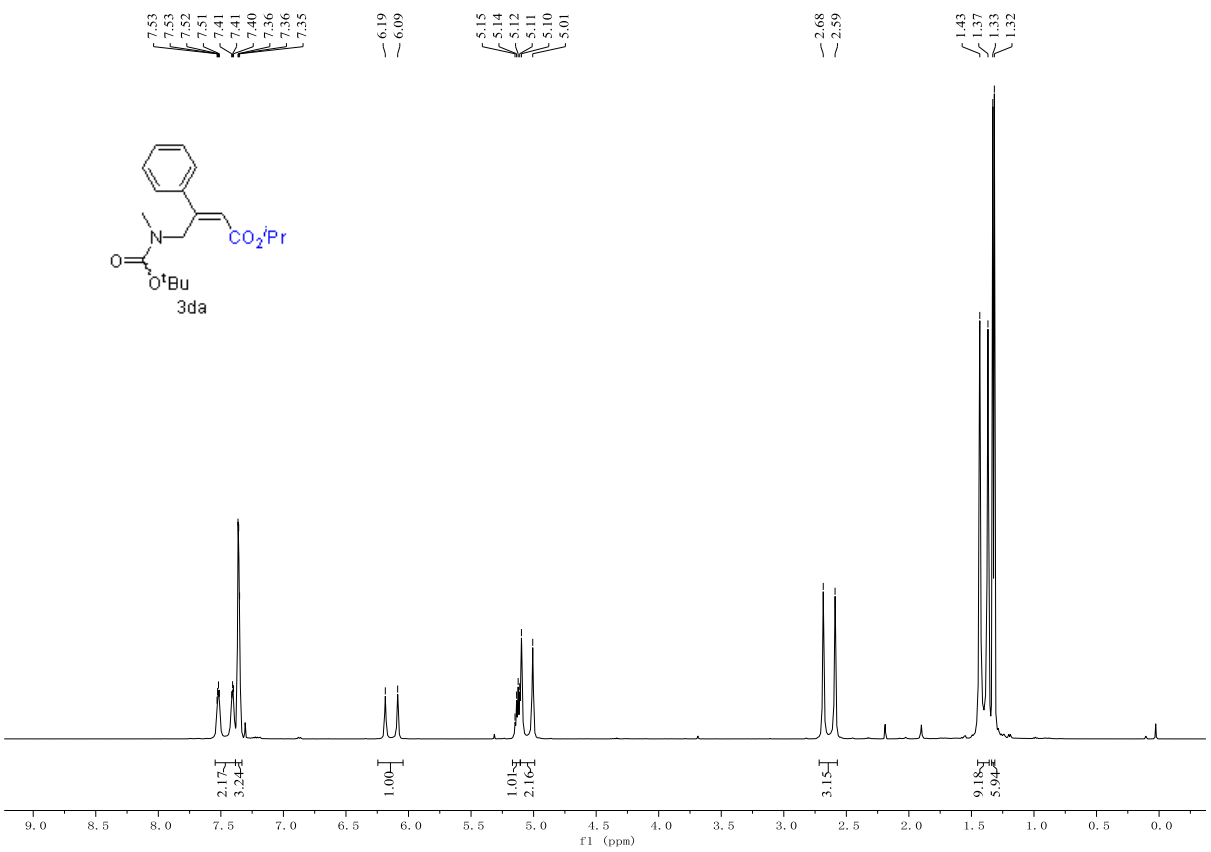
Supplementary Figure 69. ^{13}C NMR Spectra of **3ba**



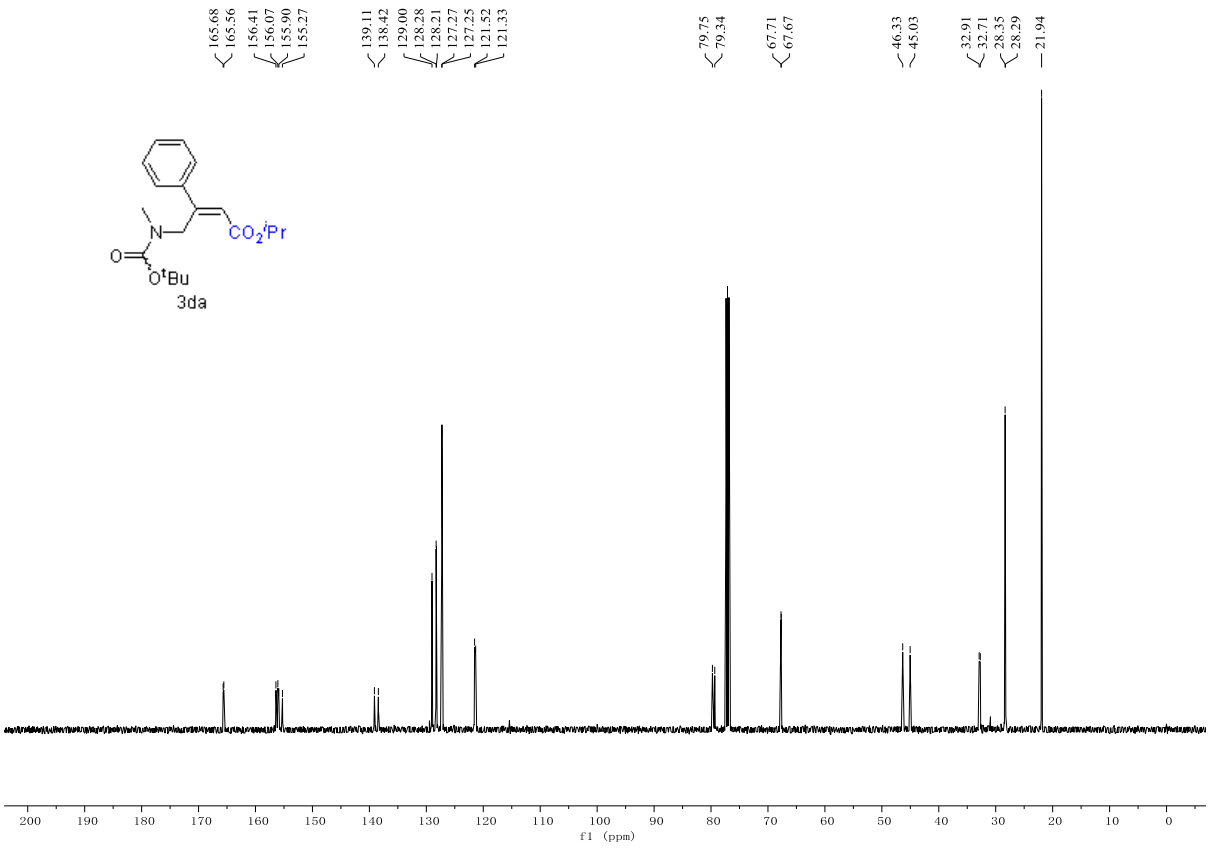
Supplementary Figure 70. ^{1}H NMR Spectra of **3ca**



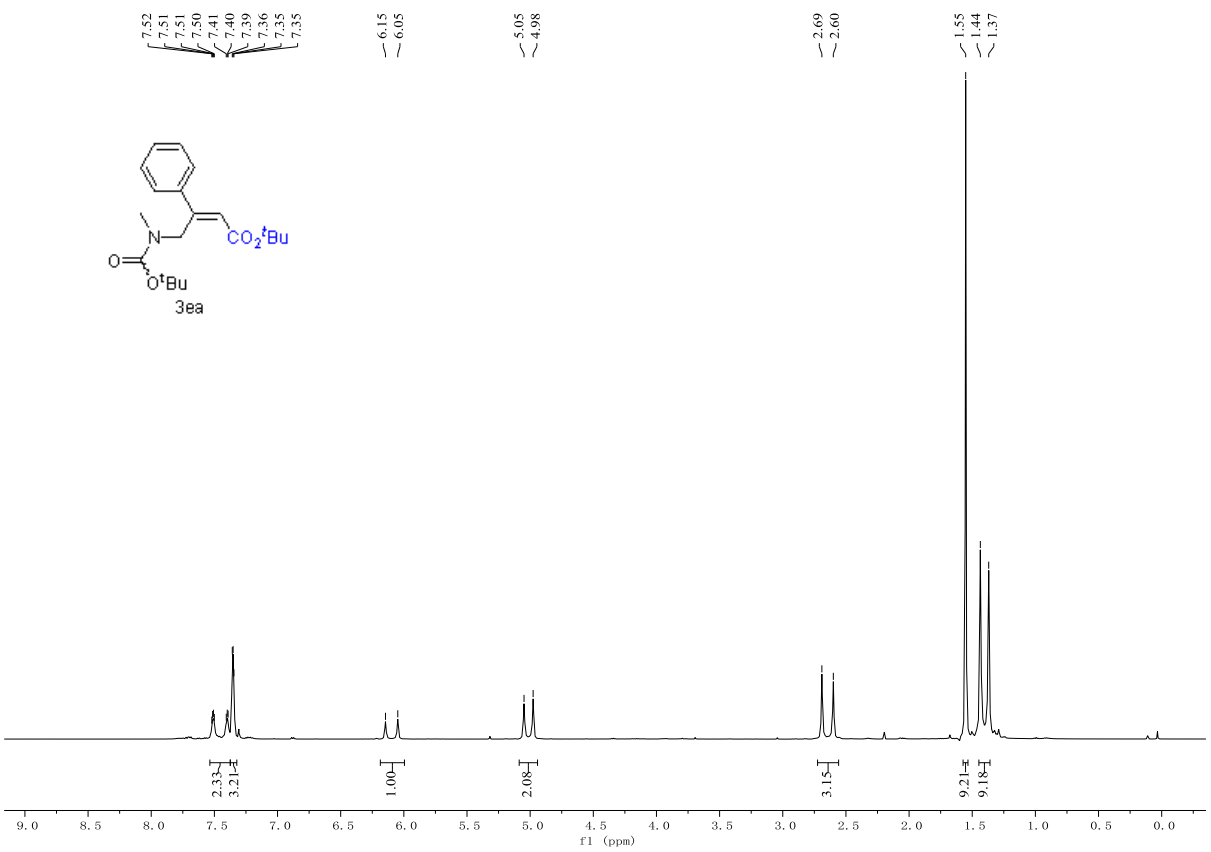
Supplementary Figure 71. ^{13}C NMR Spectra of **3ca**



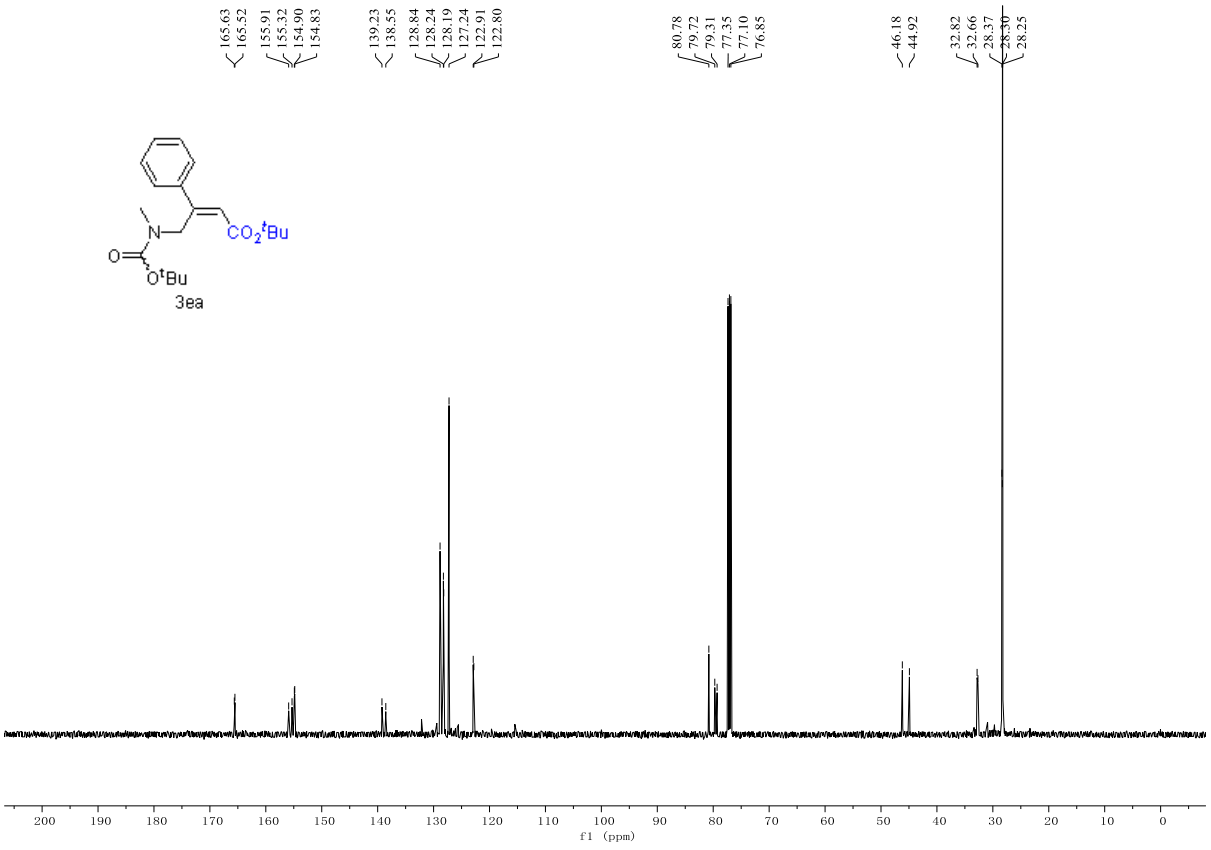
Supplementary Figure 72. ^{1}H NMR Spectra of **3da**



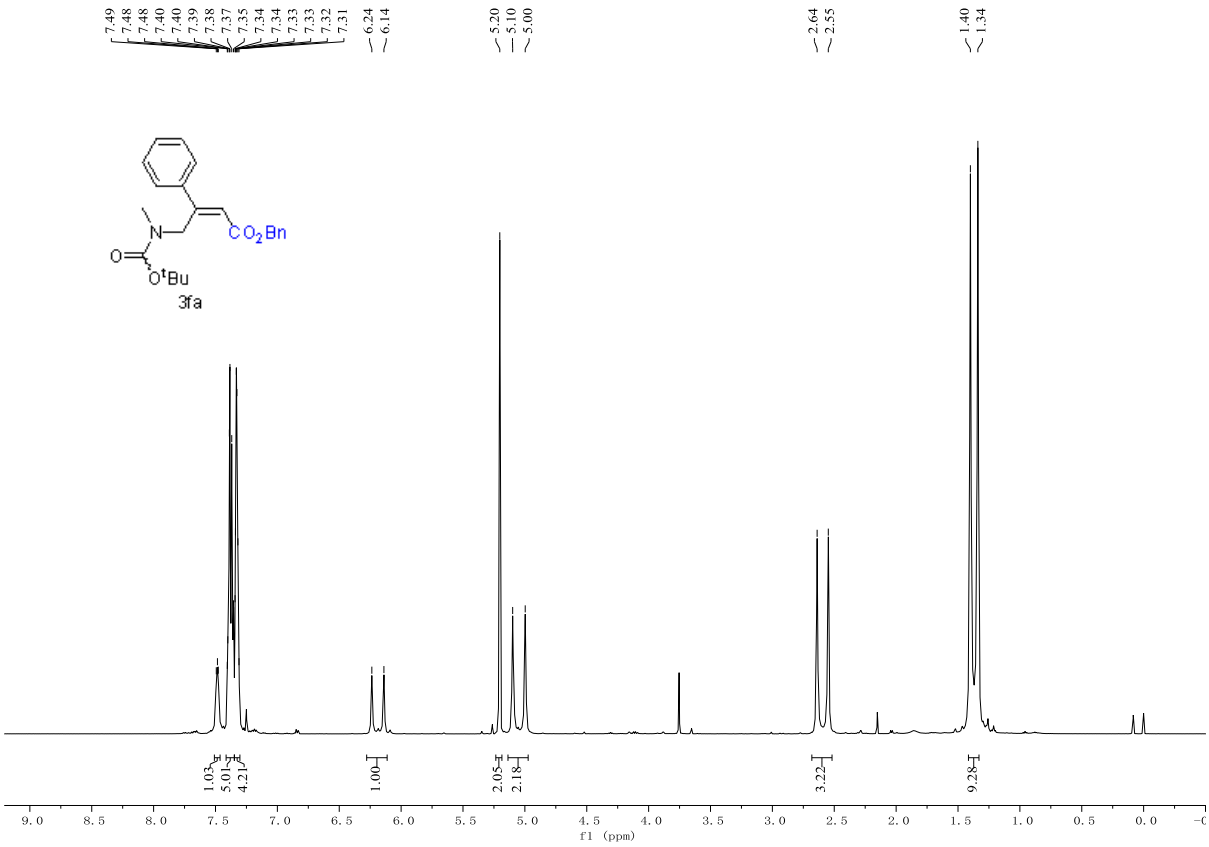
Supplementary Figure 73. ^{13}C NMR Spectra of **3da**



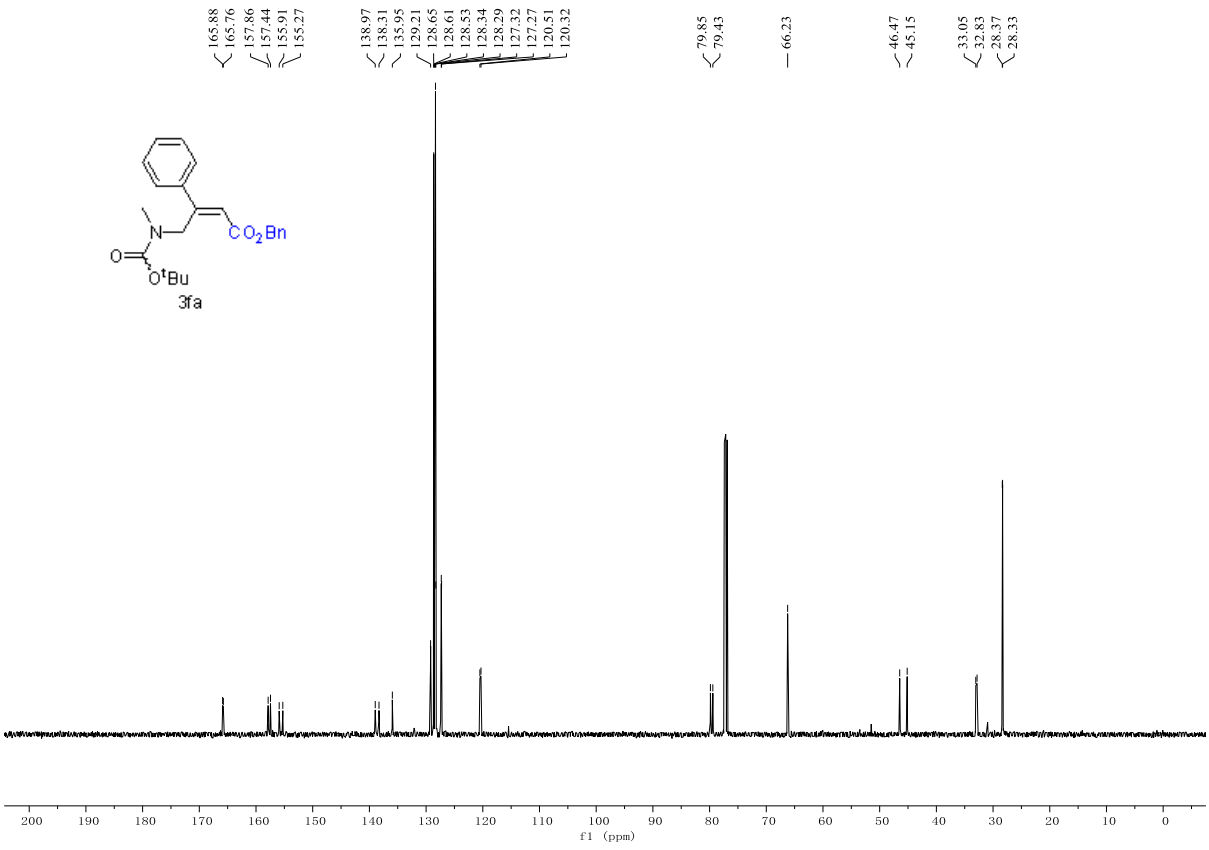
Supplementary Figure 74. ^{1}H NMR Spectra of **3ea**



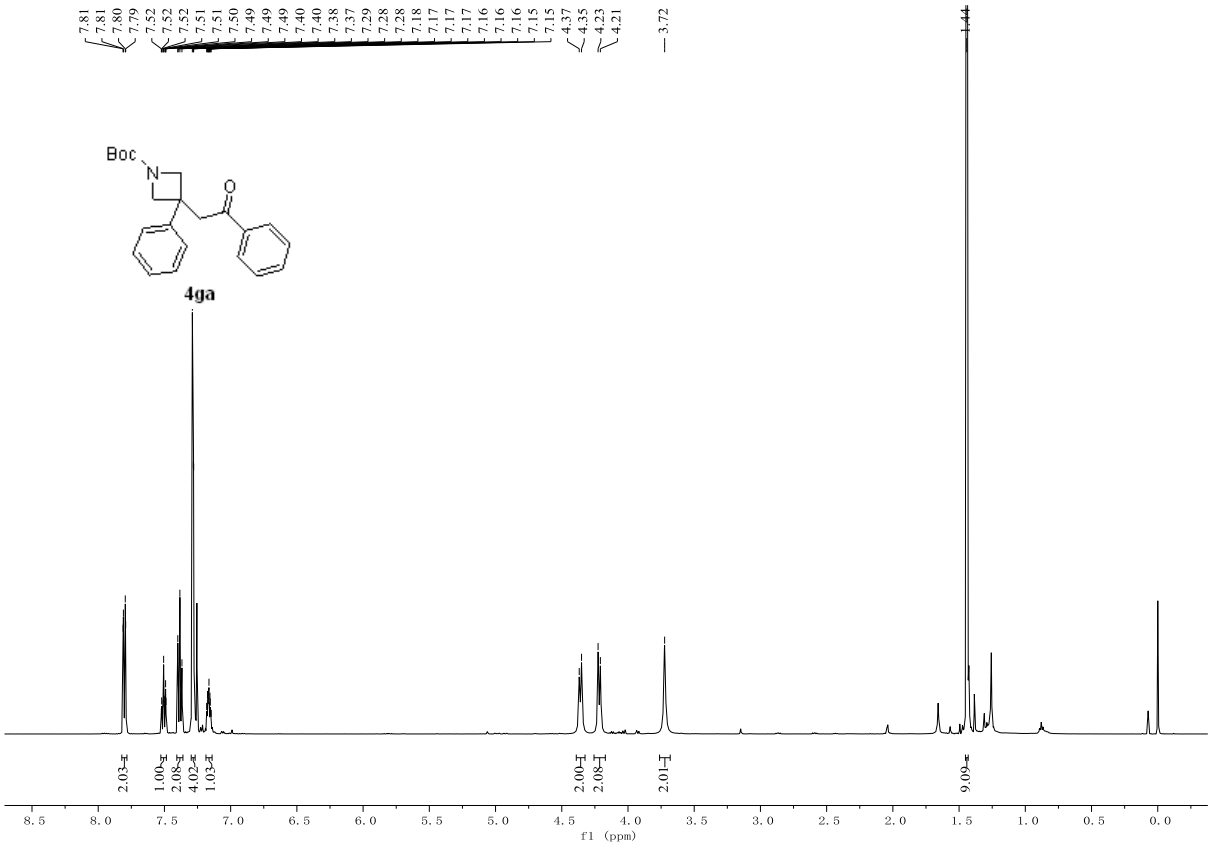
Supplementary Figure 75. ^{13}C NMR Spectra of **3ea**



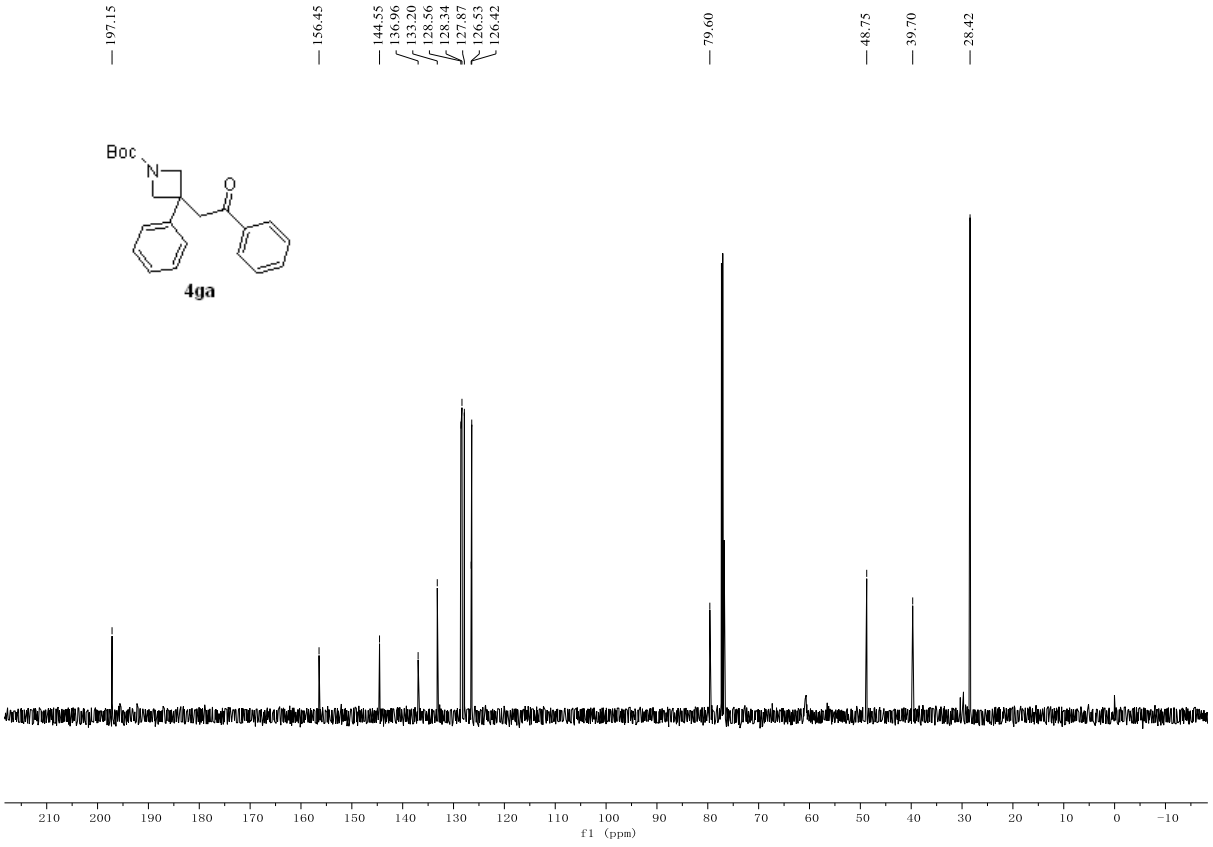
Supplementary Figure 76. ^{1}H NMR Spectra of **3fa**



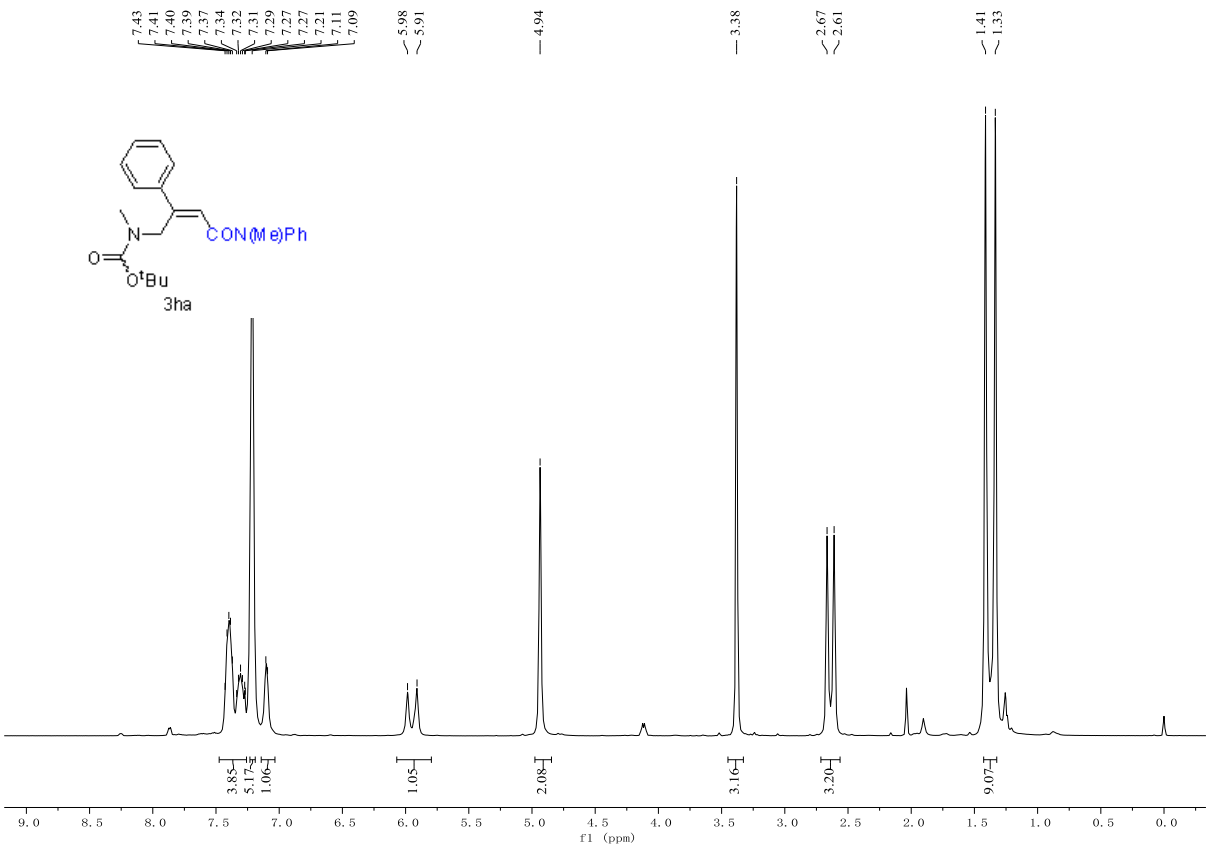
Supplementary Figure 77. ^{13}C NMR Spectra of **3fa**



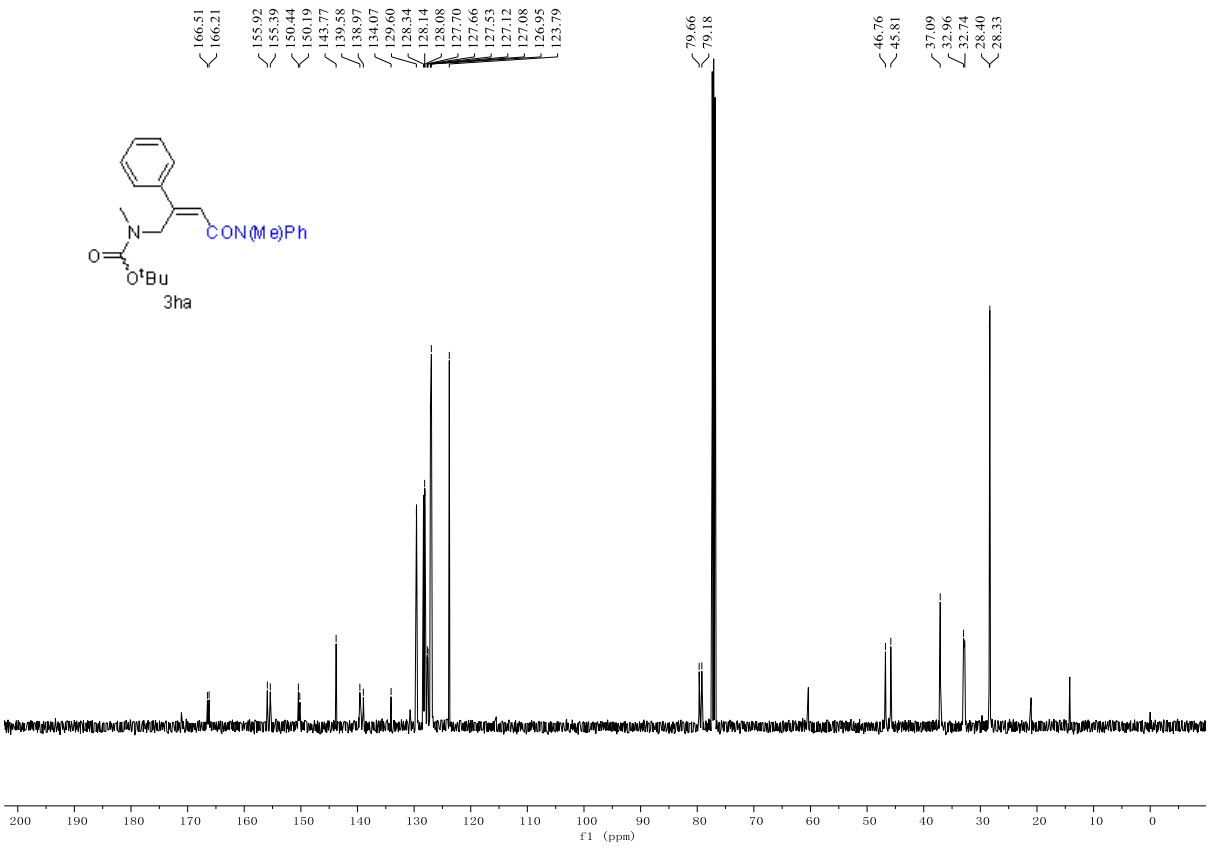
Supplementary Figure 78. ^{1}H NMR Spectra of **4ga**



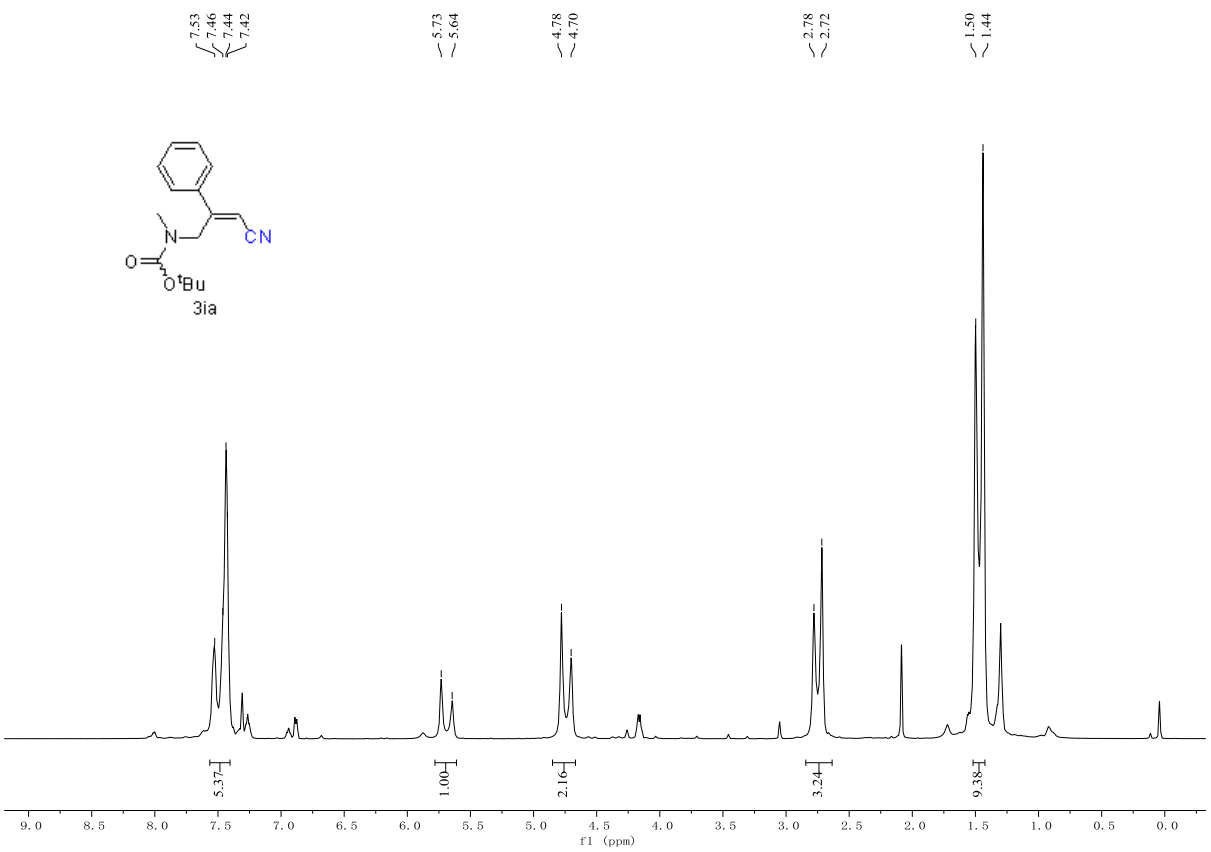
Supplementary Figure 79. ^{13}C NMR Spectra of **4ga**



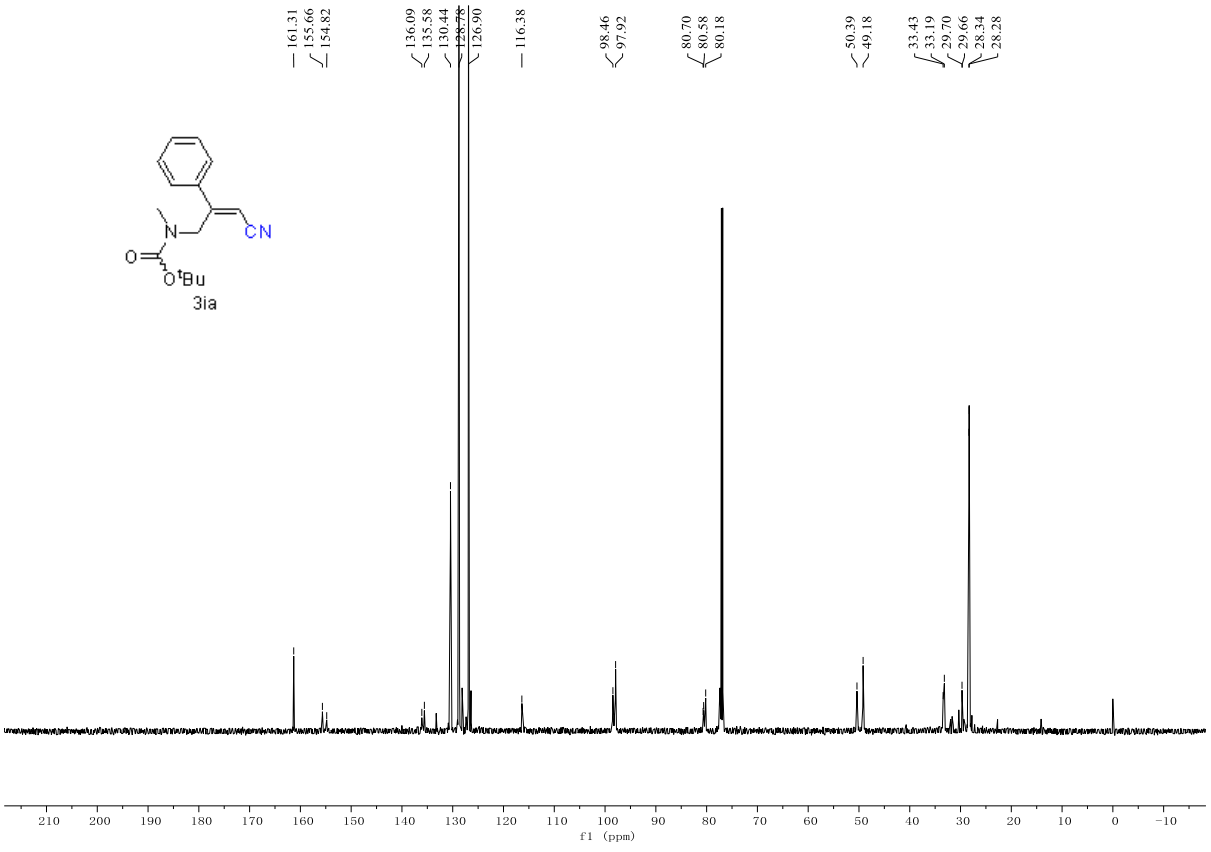
Supplementary Figure 80. ^{1}H NMR Spectra of **3ha**



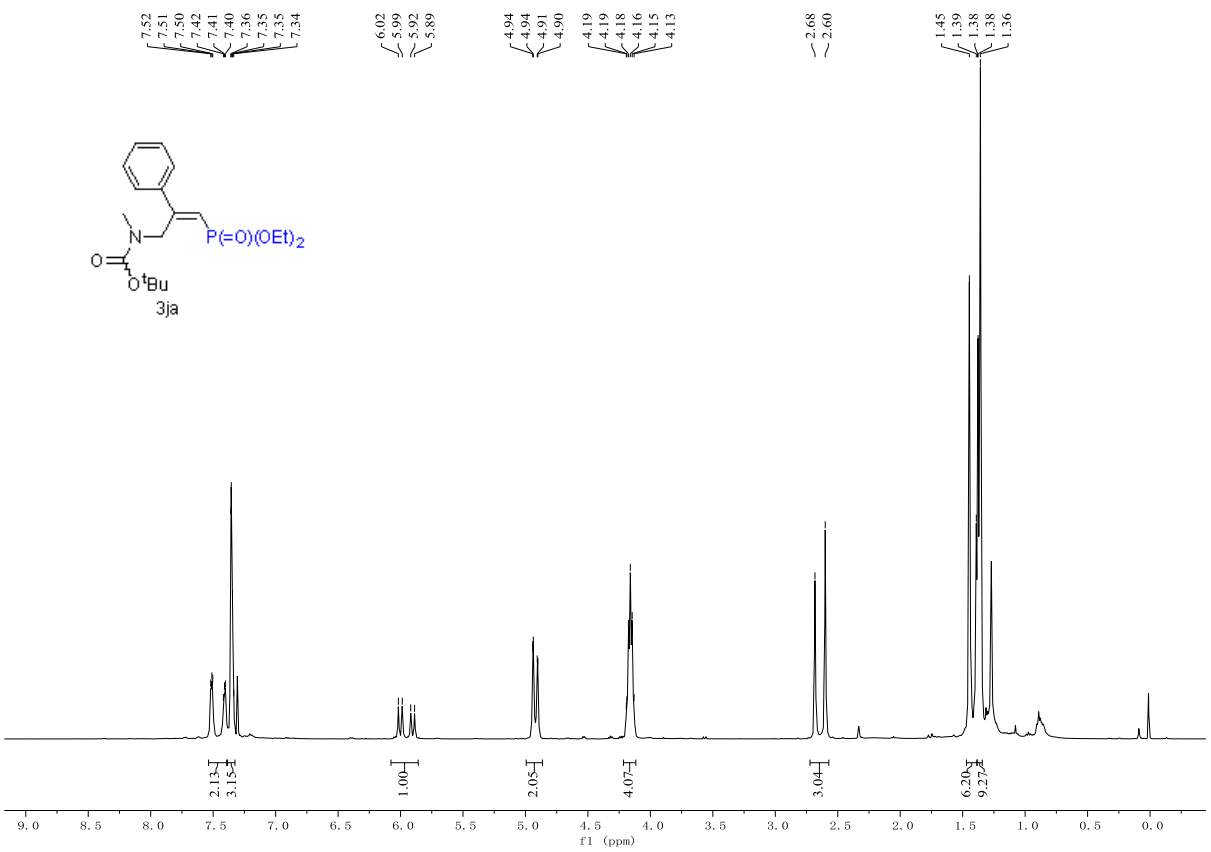
Supplementary Figure 81. ^{13}C NMR Spectra of **3ha**



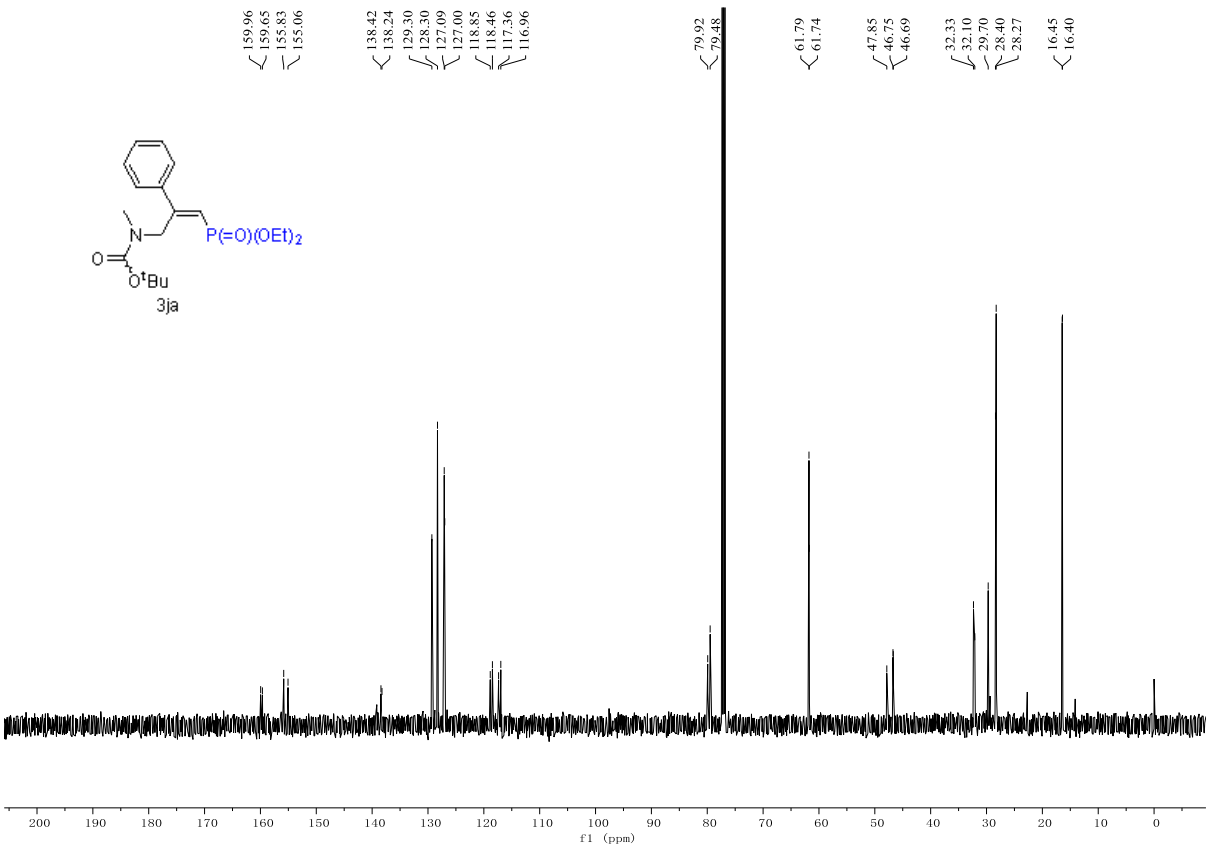
Supplementary Figure 82. ^{1}H NMR Spectra of **3ia**



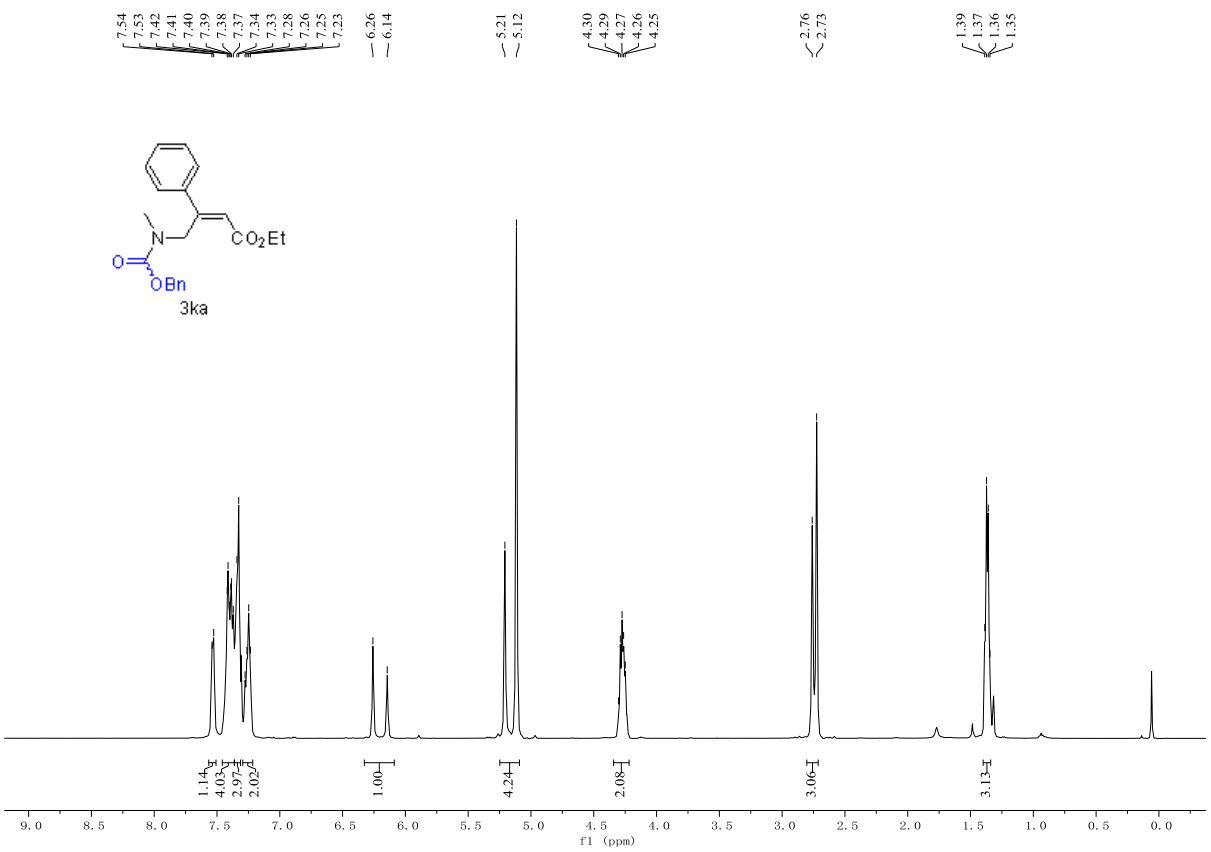
Supplementary Figure 83. ^{13}C NMR Spectra of **3ia**



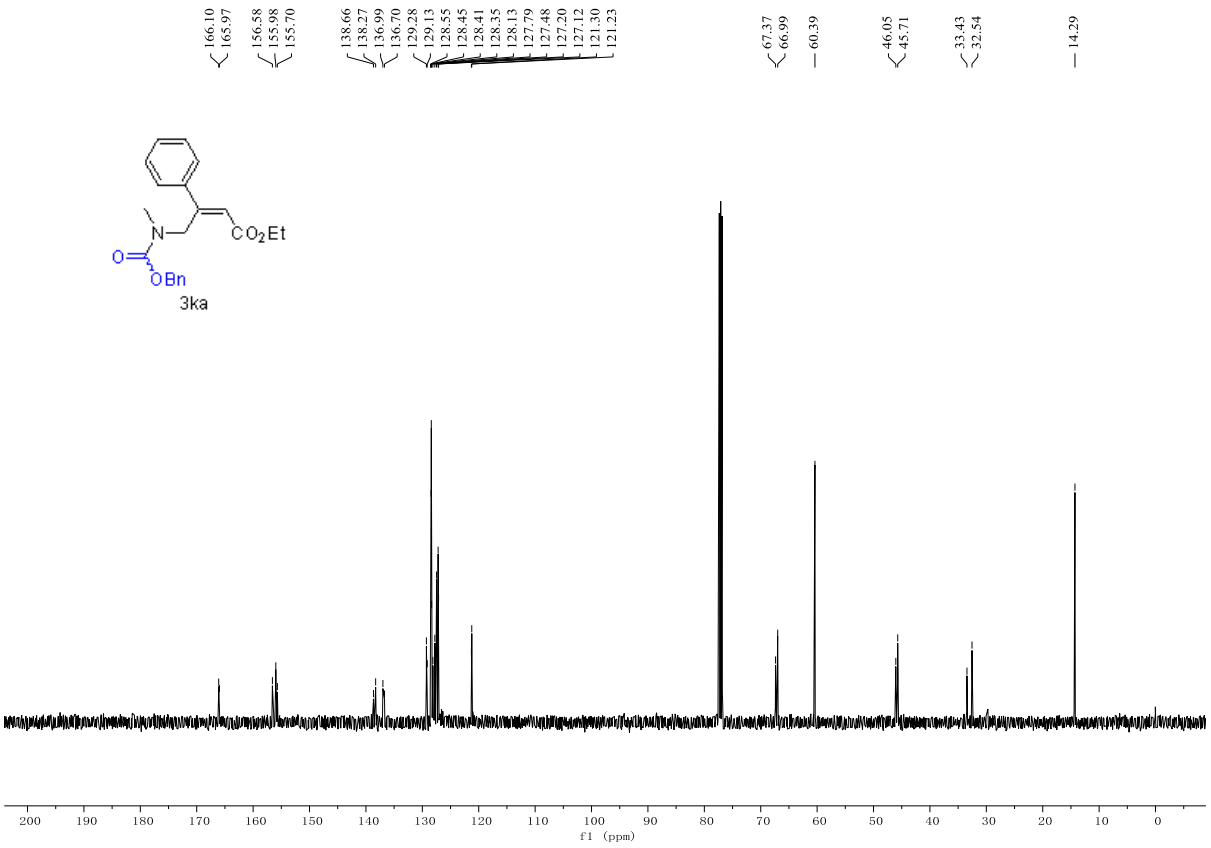
Supplementary Figure 84. ^{1}H NMR Spectra of **3ja**



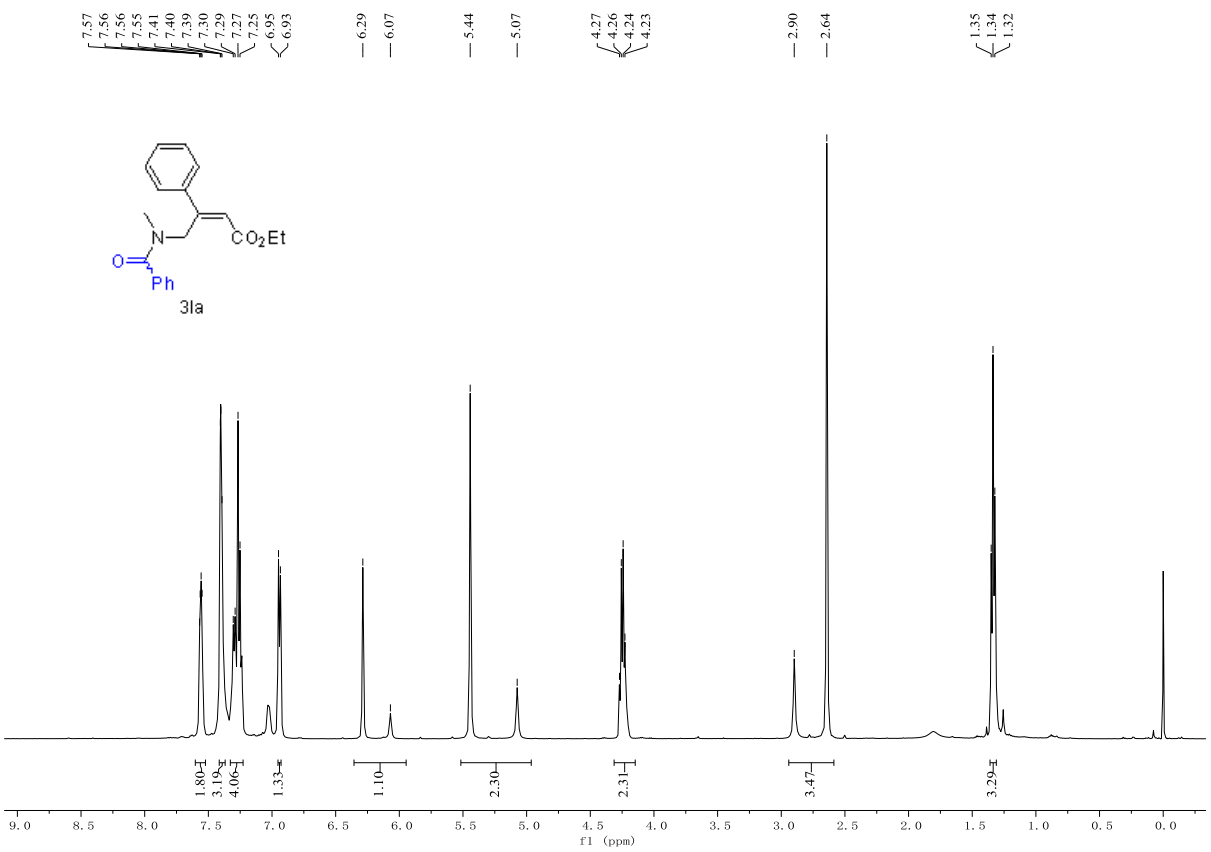
Supplementary Figure 85. ^{13}C NMR Spectra of **3ja**



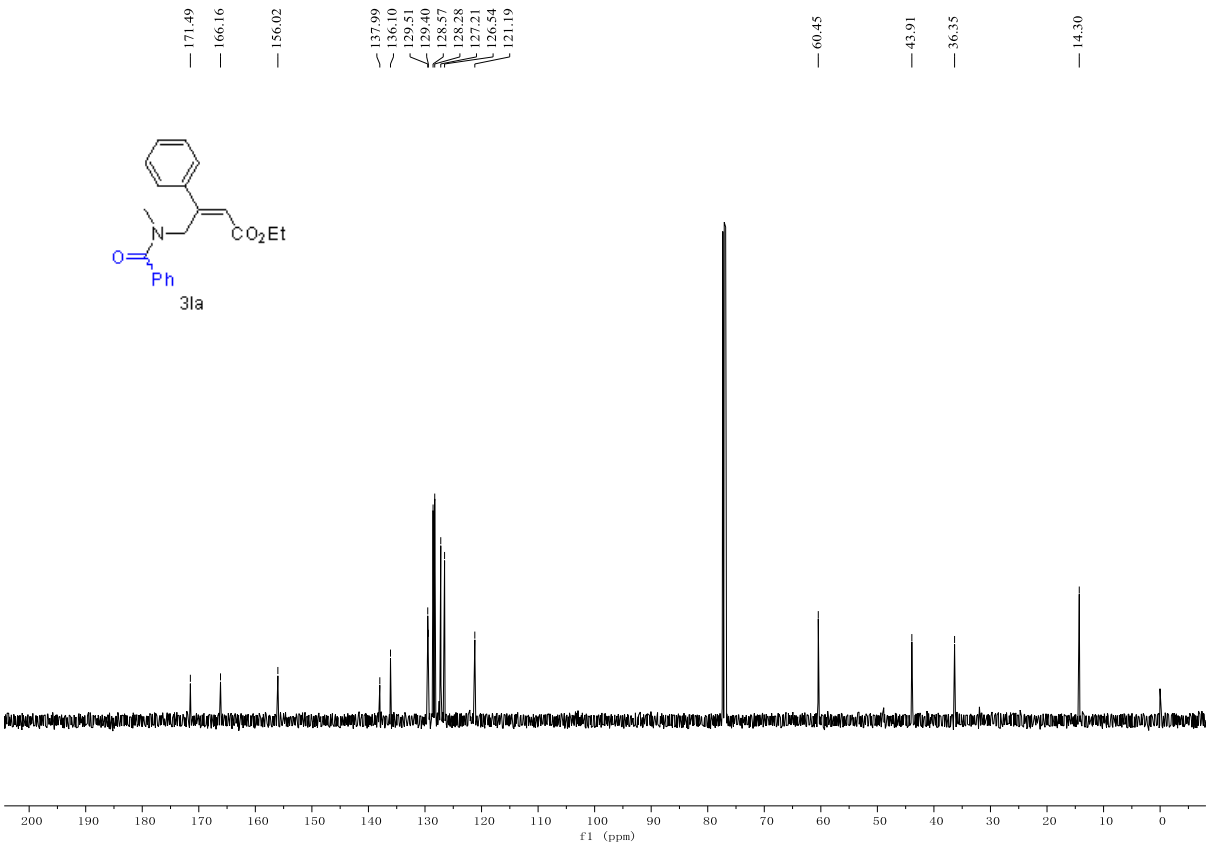
Supplementary Figure 86. ^{1}H NMR Spectra of **3ka**



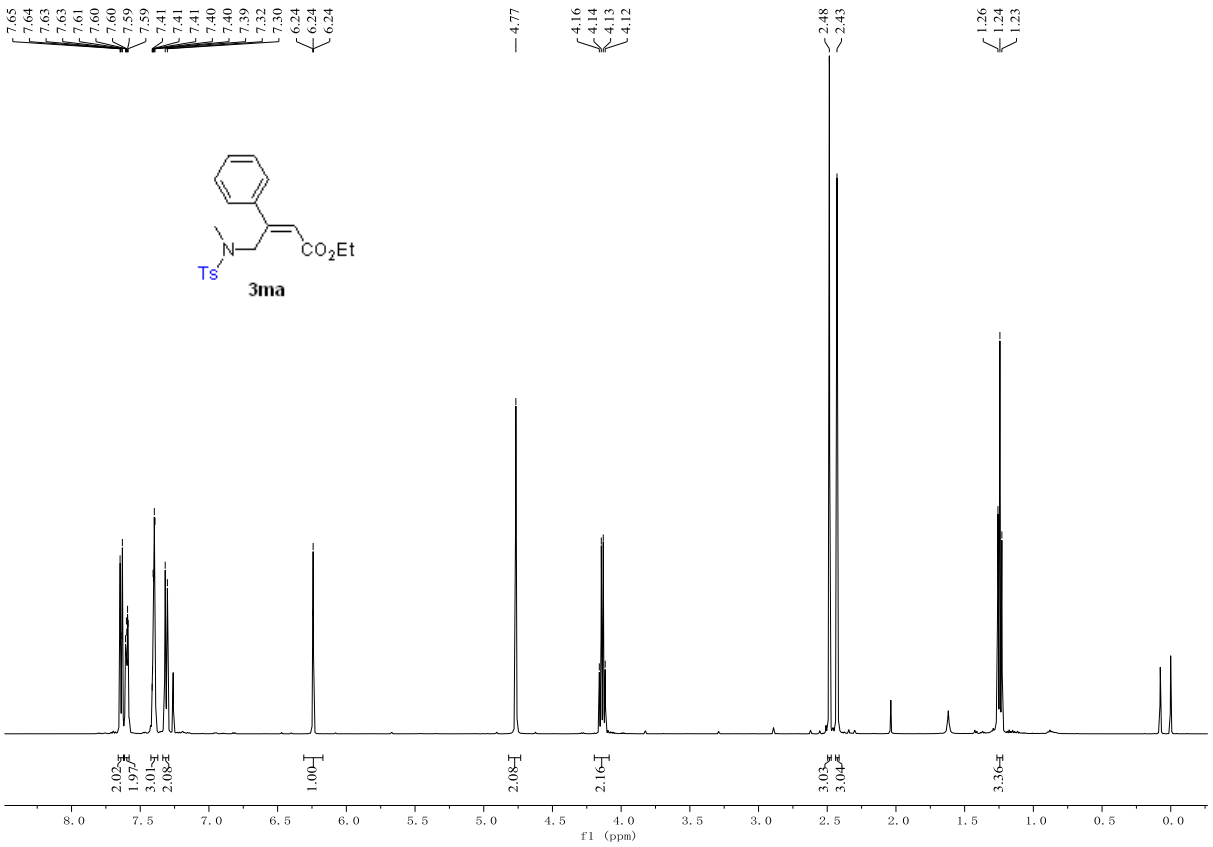
Supplementary Figure 87. ^{13}C NMR Spectra of **3ka**



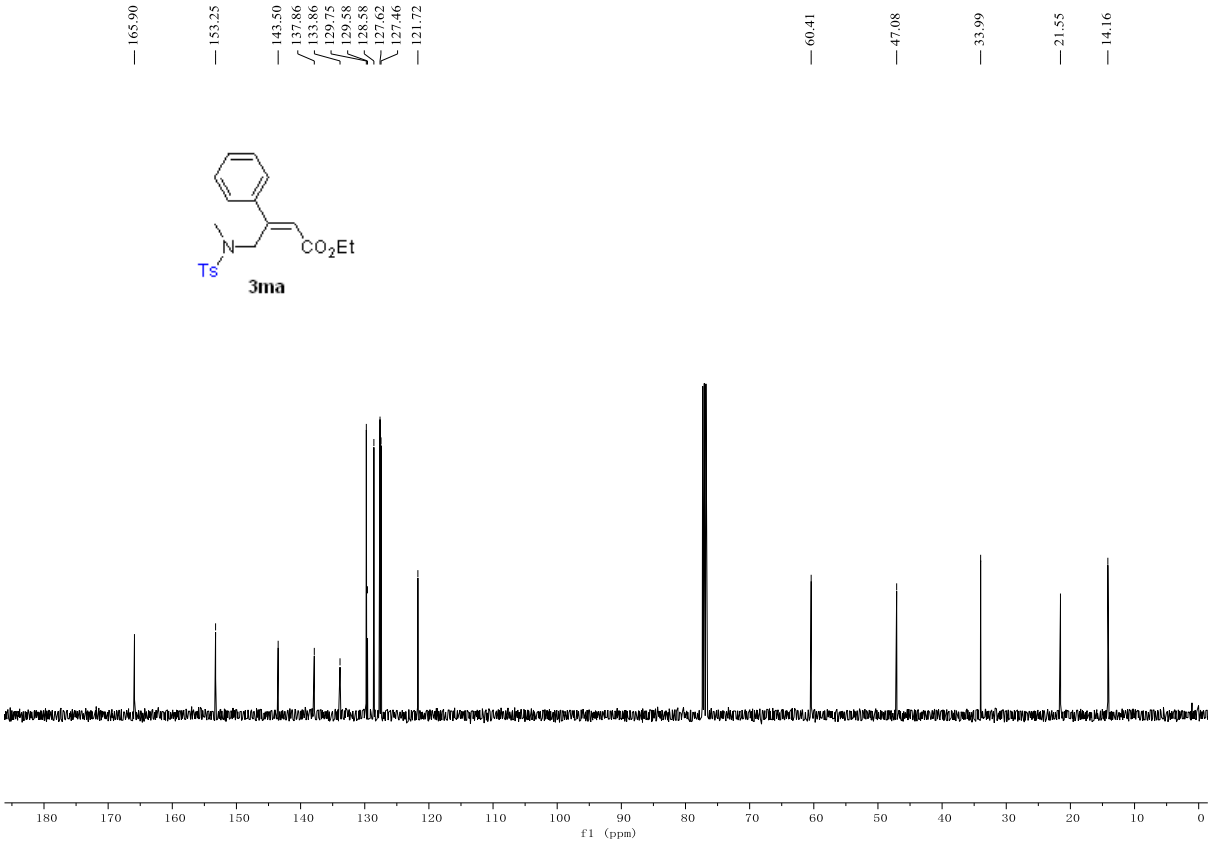
Supplementary Figure 88. ^{1}H NMR Spectra of **3la**



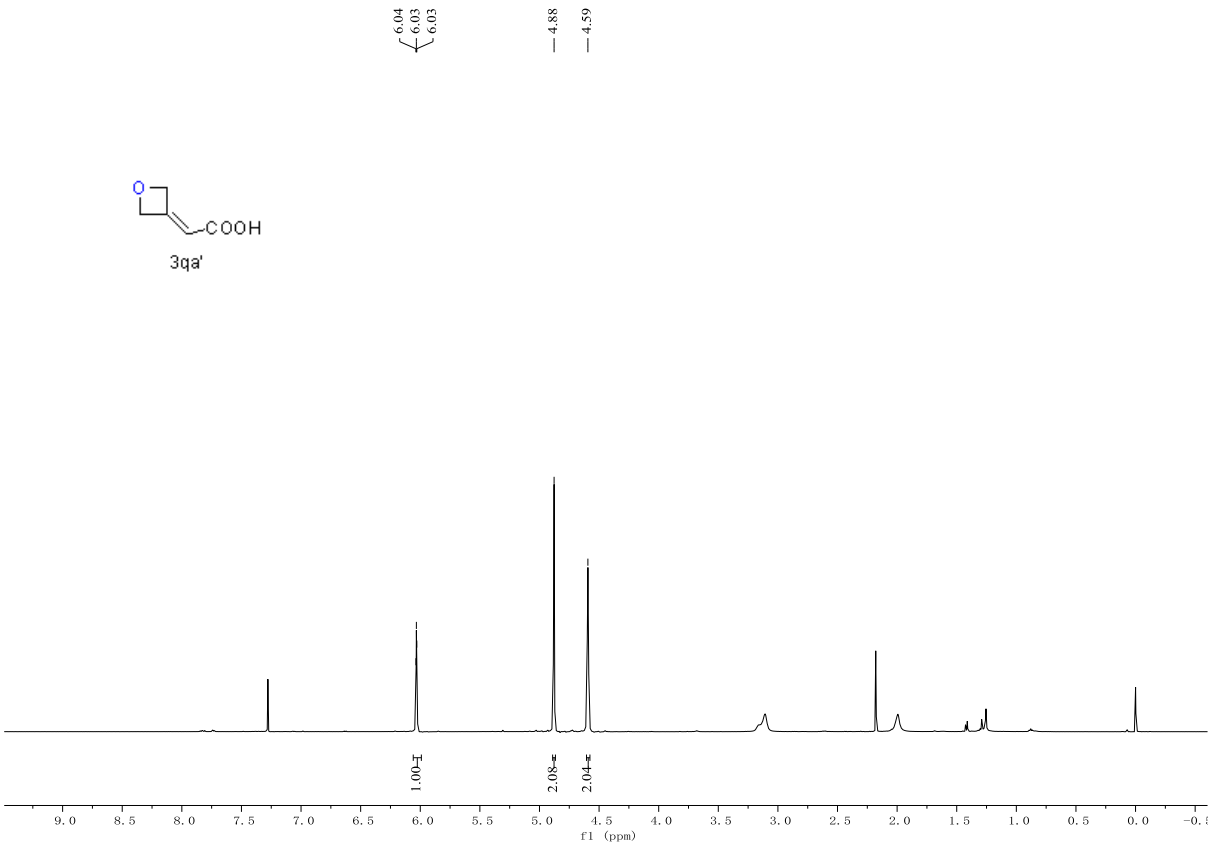
Supplementary Figure 89. ^{13}C NMR Spectra of **3la**



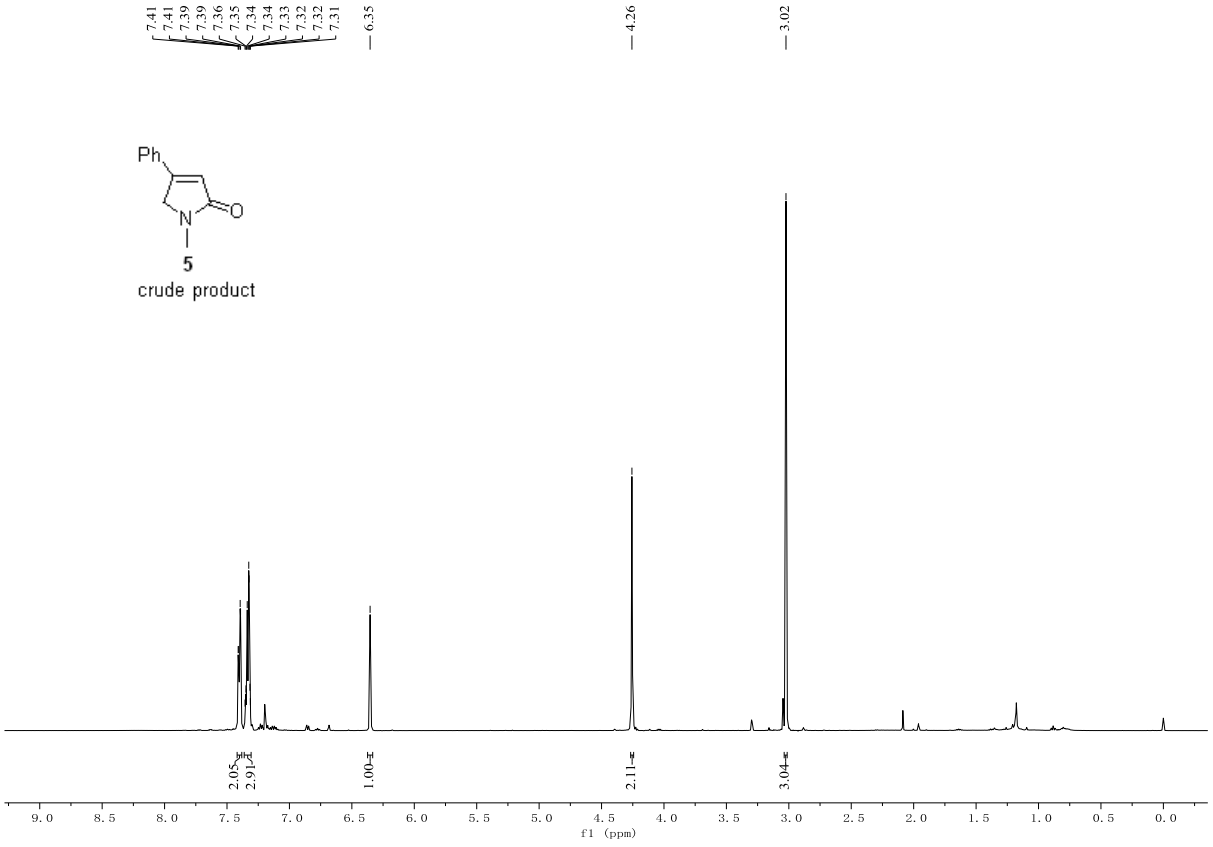
Supplementary Figure 90. ^{13}C NMR Spectra of **3ma**



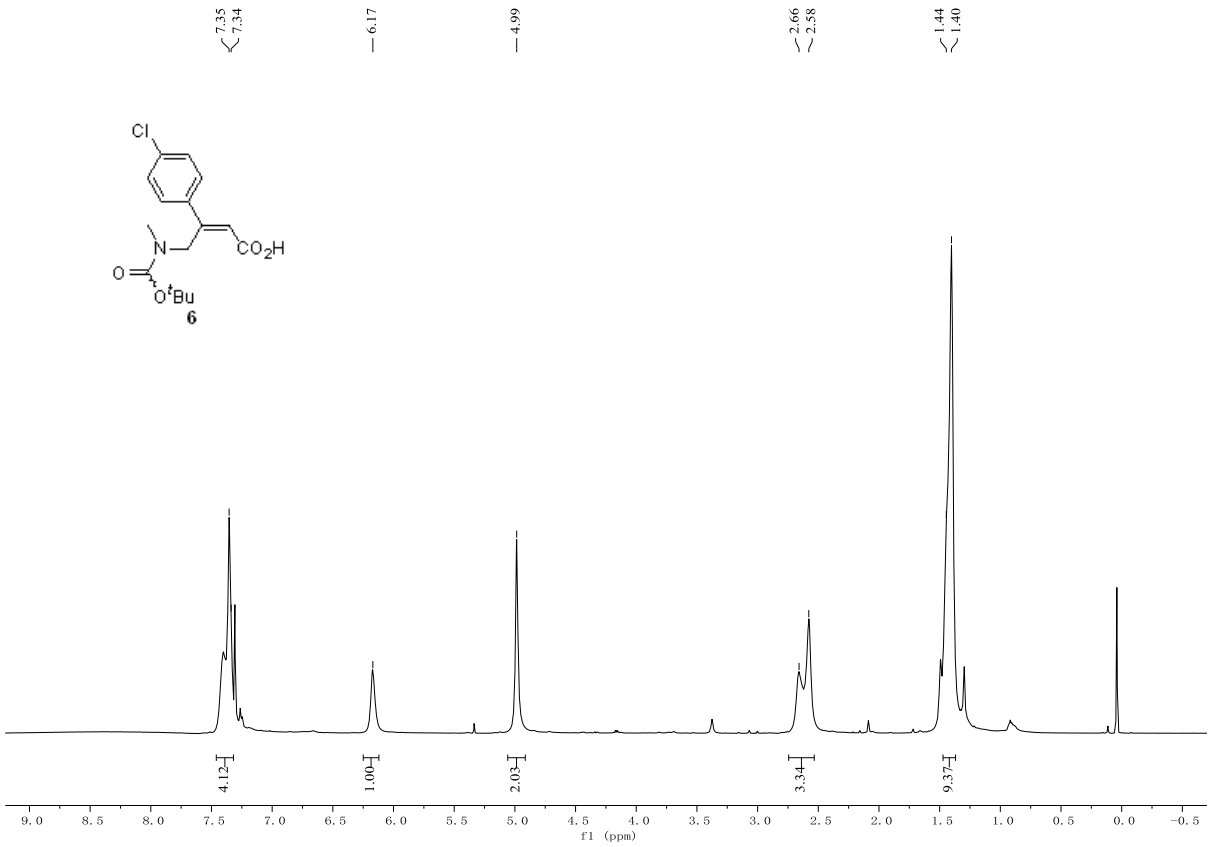
Supplementary Figure 91. ^{13}C NMR Spectra of **3ma**



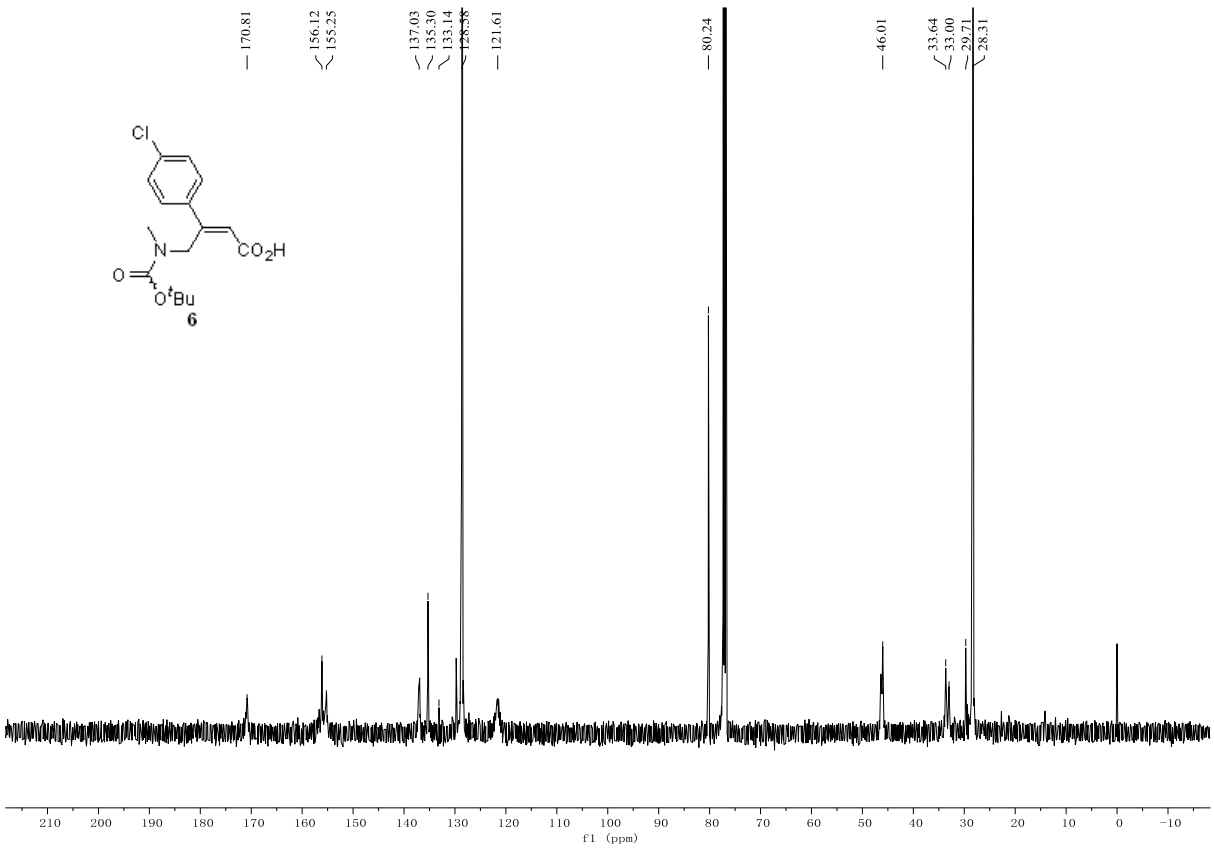
Supplementary Figure 92. ^{1}H NMR Spectra of **3qa'**



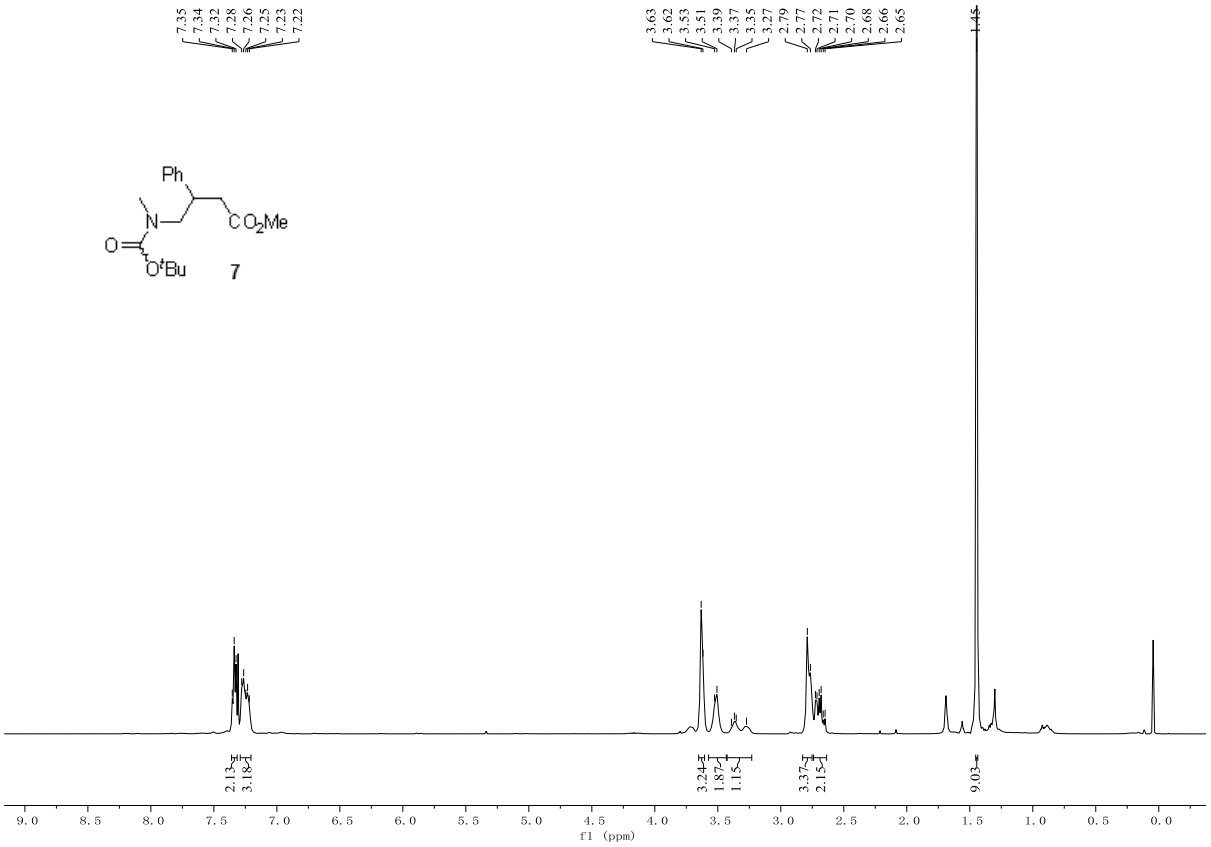
Supplementary Figure 93. ^{1}H NMR Spectra of **5**



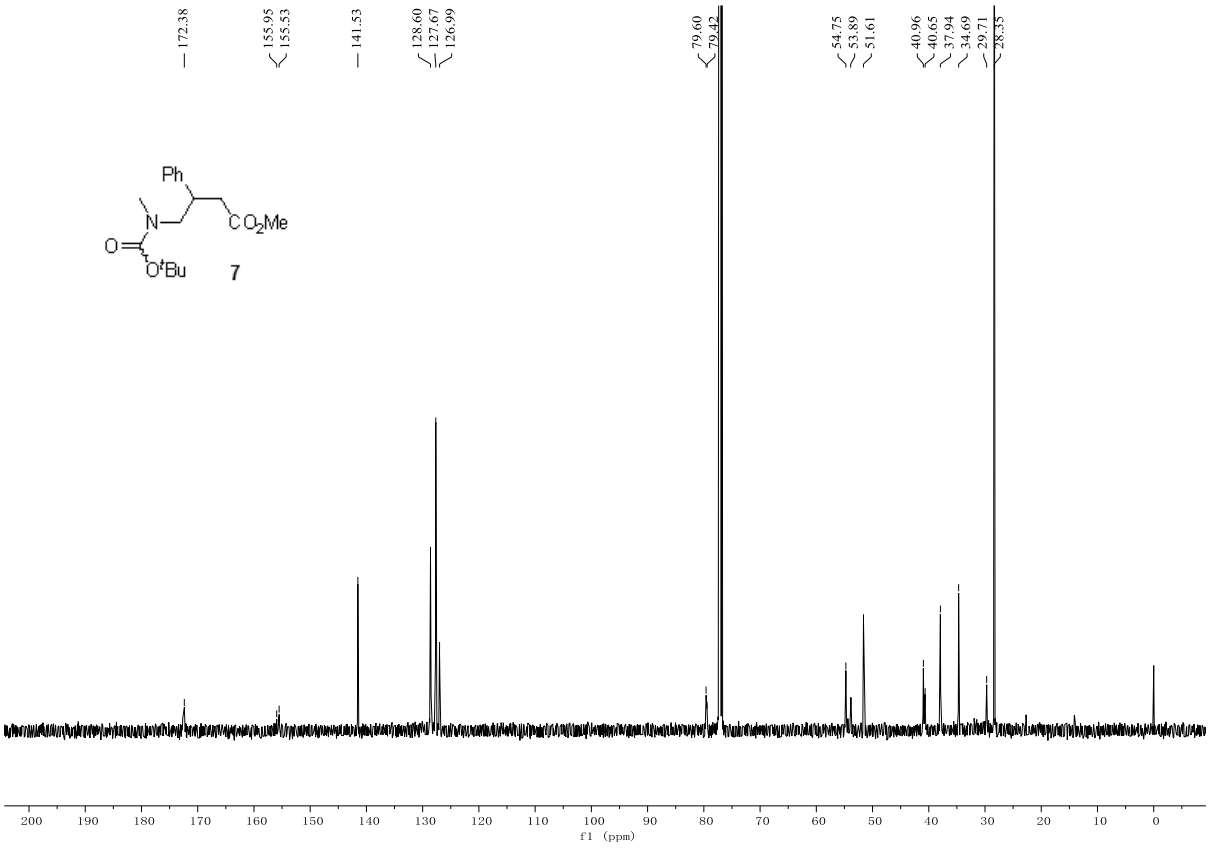
Supplementary Figure 94. ^{1}H NMR Spectra of **6**



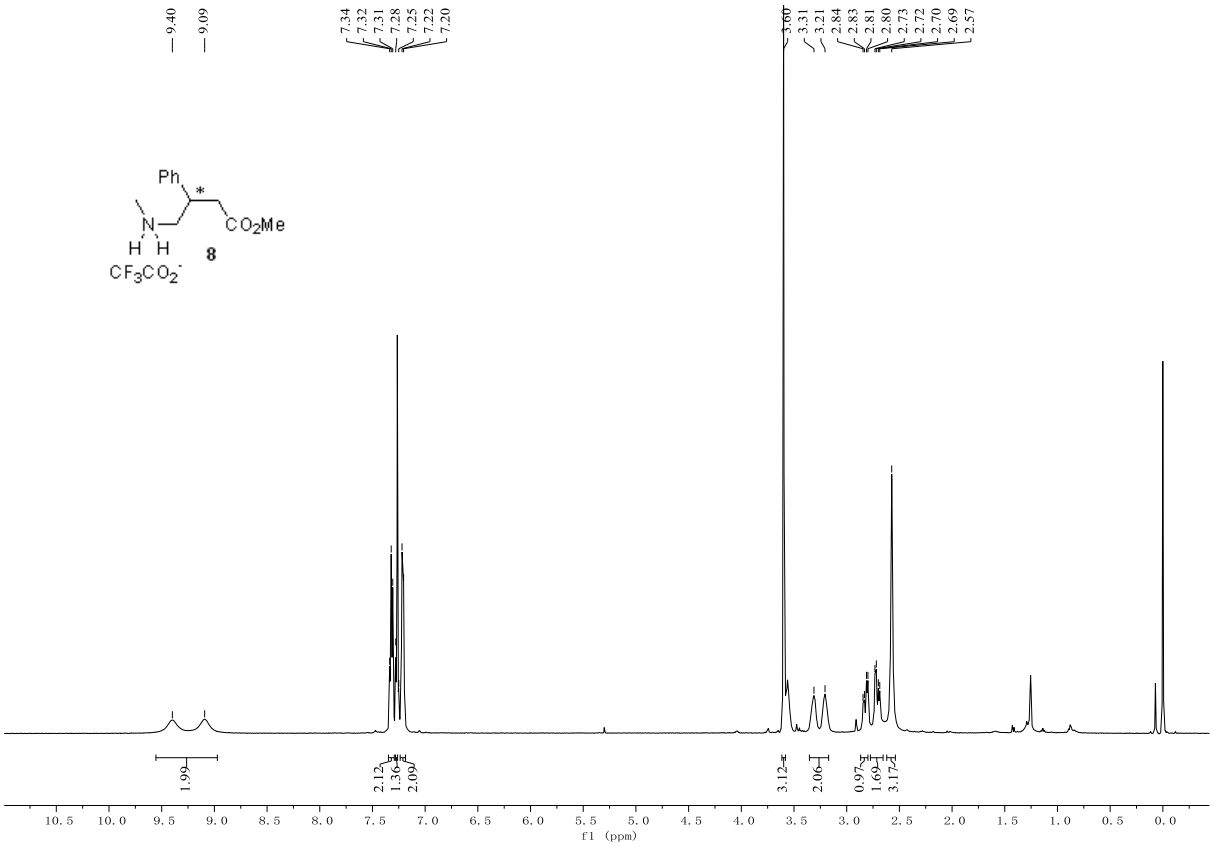
Supplementary Figure 95. ^{13}C NMR Spectra of **6**



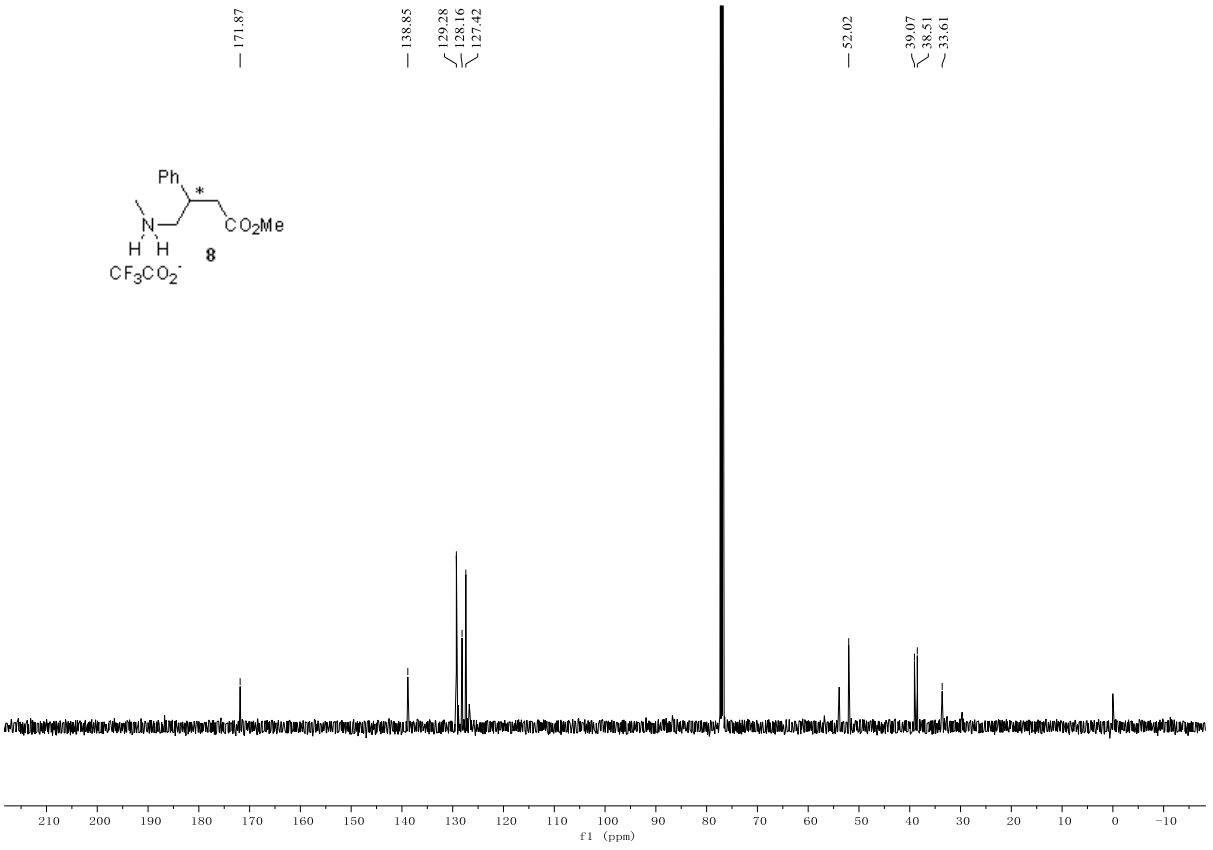
Supplementary Figure 96. ^{1}H NMR Spectra of **7**



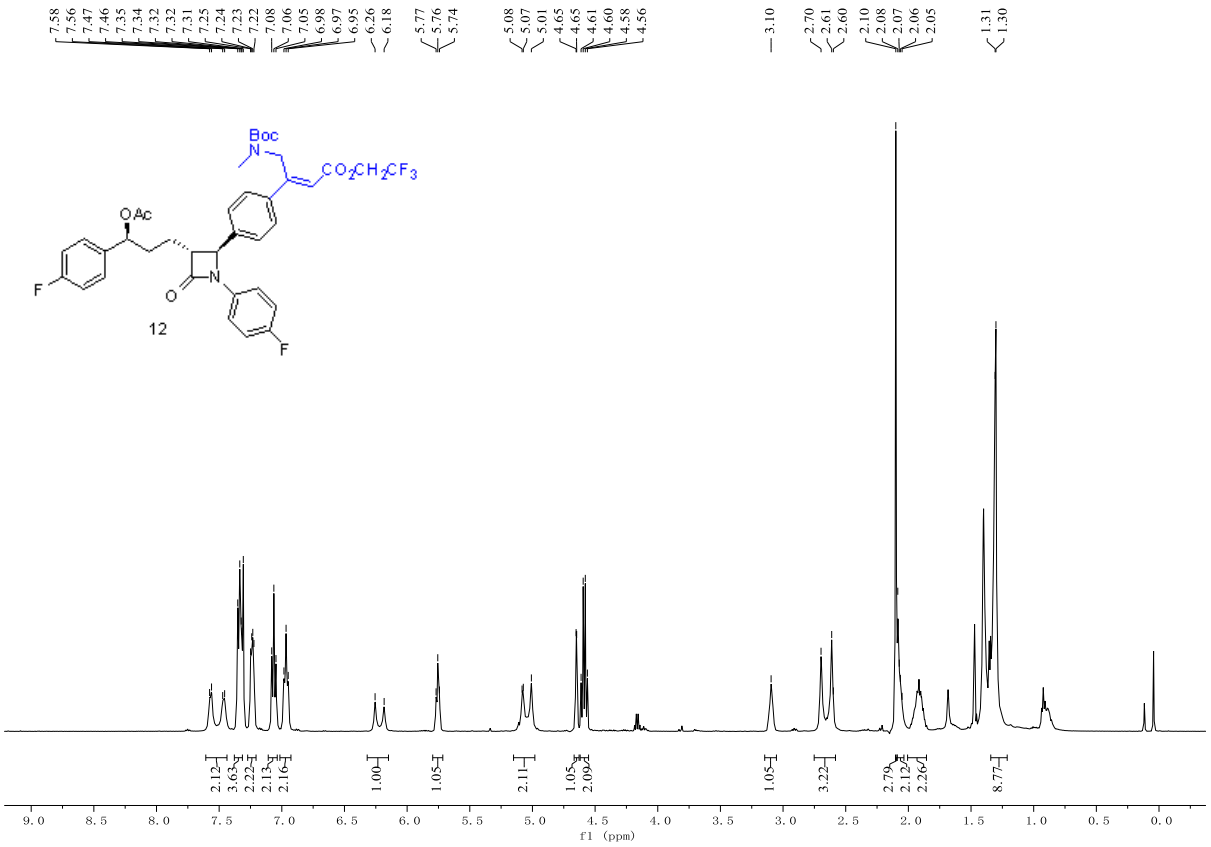
Supplementary Figure 97. ^{13}C NMR Spectra of **7**



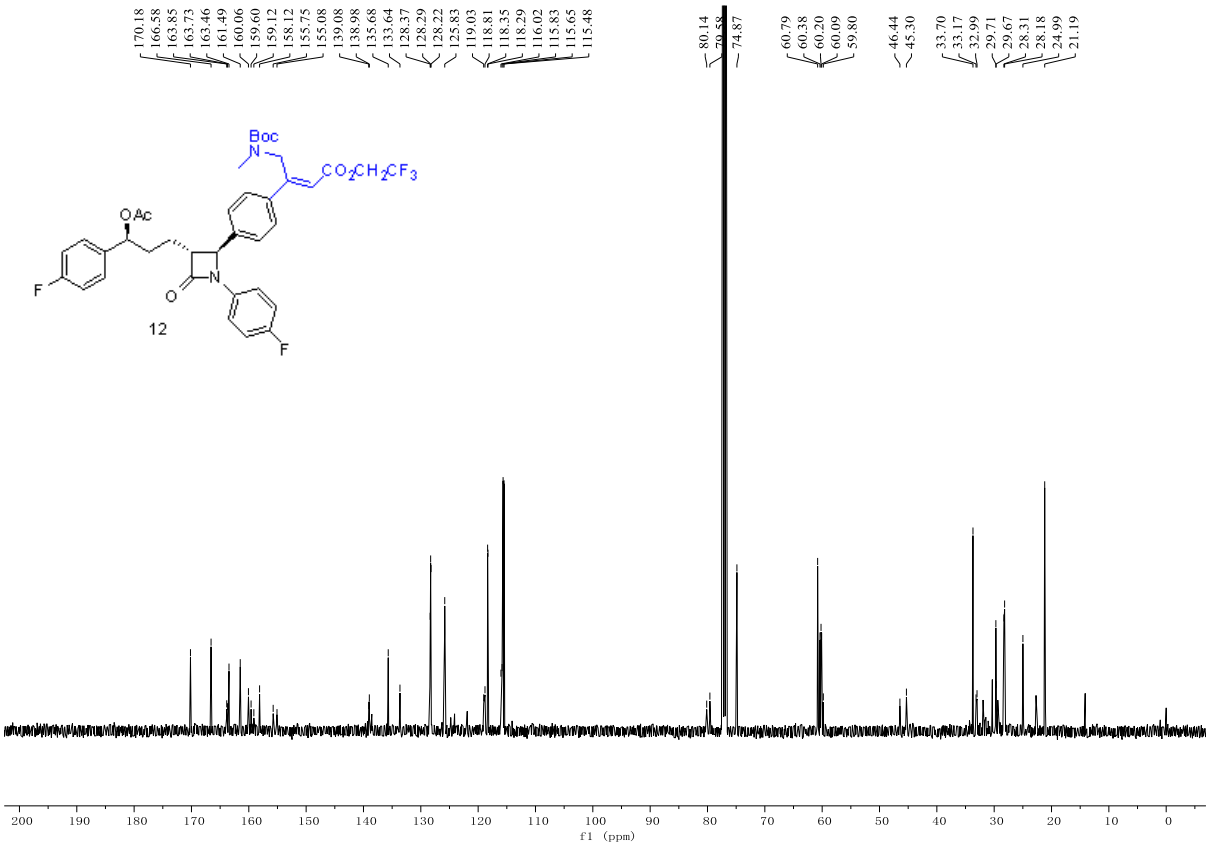
Supplementary Figure 98. ^{1}H NMR Spectra of **8**



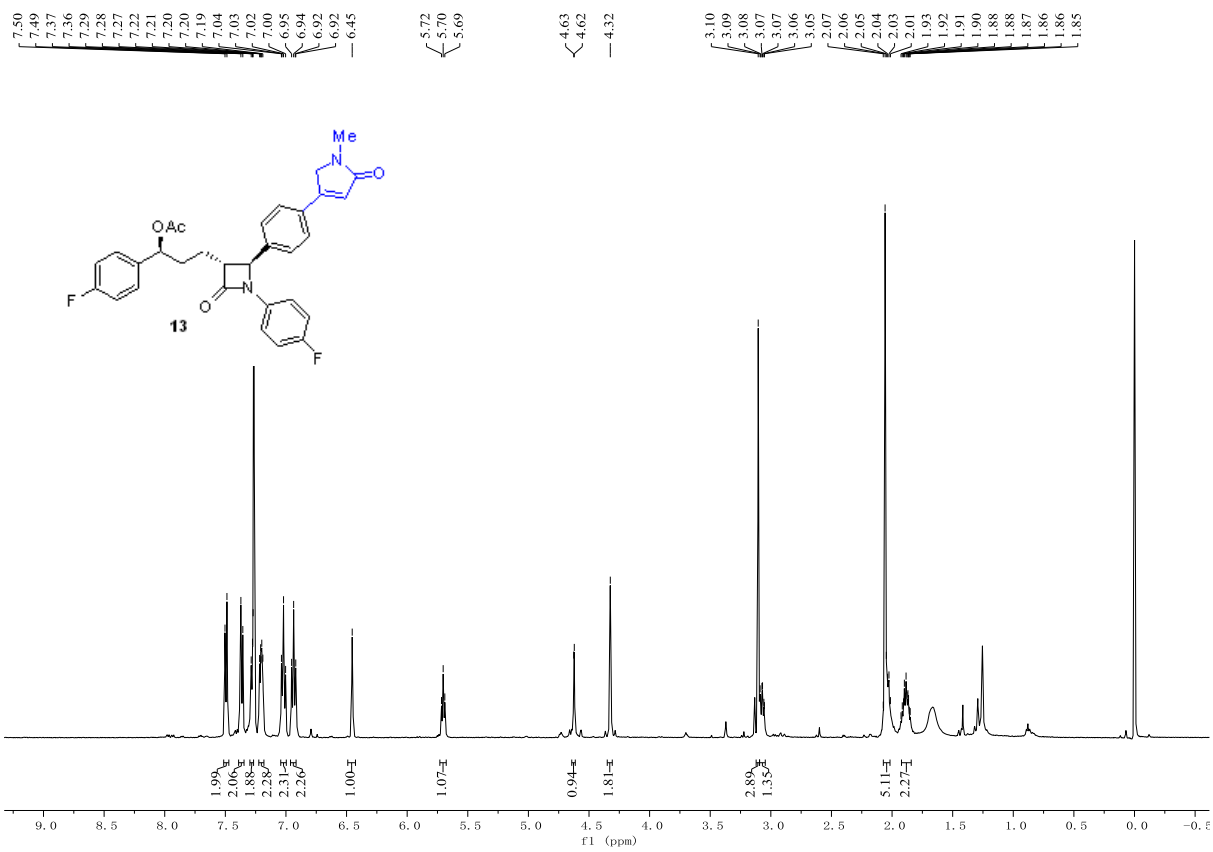
Supplementary Figure 99. ^{13}C NMR Spectra of **8**



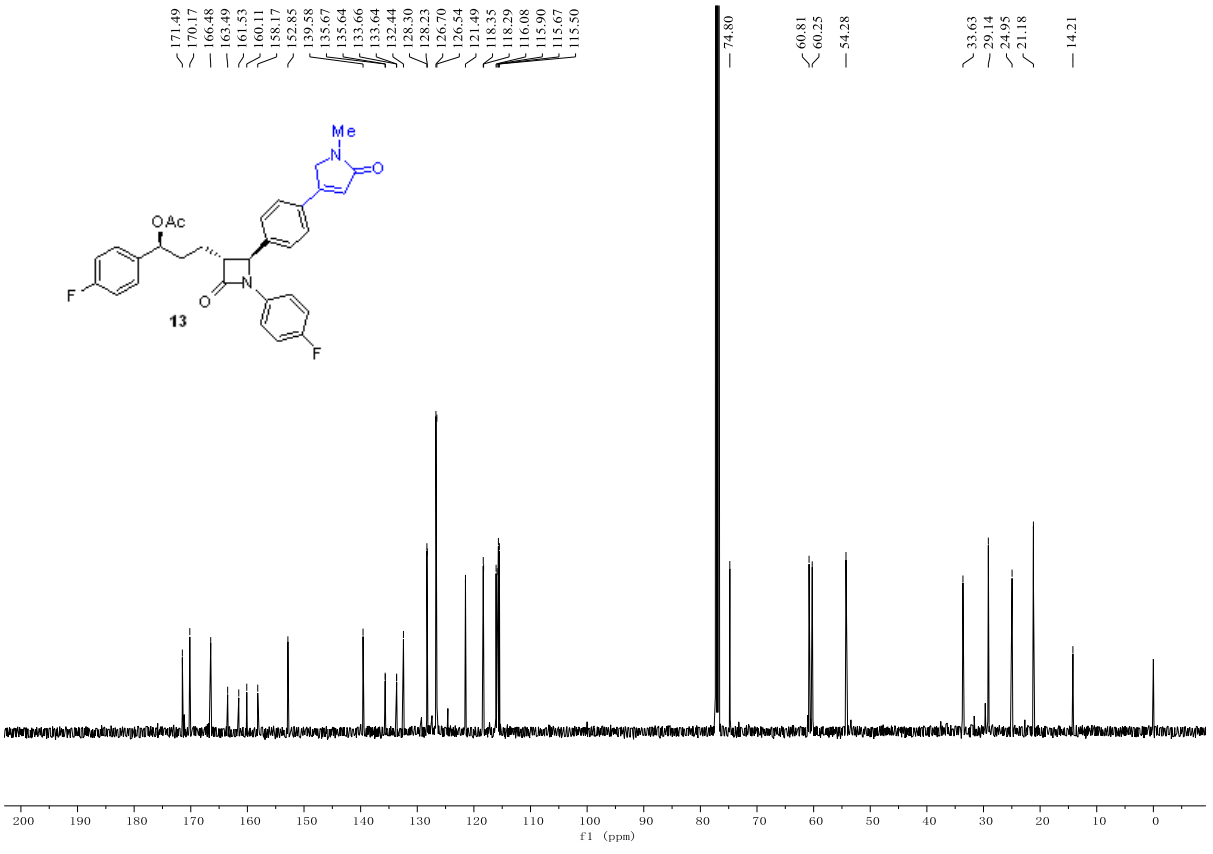
Supplementary Figure 100. ^{1}H NMR Spectra of **12**



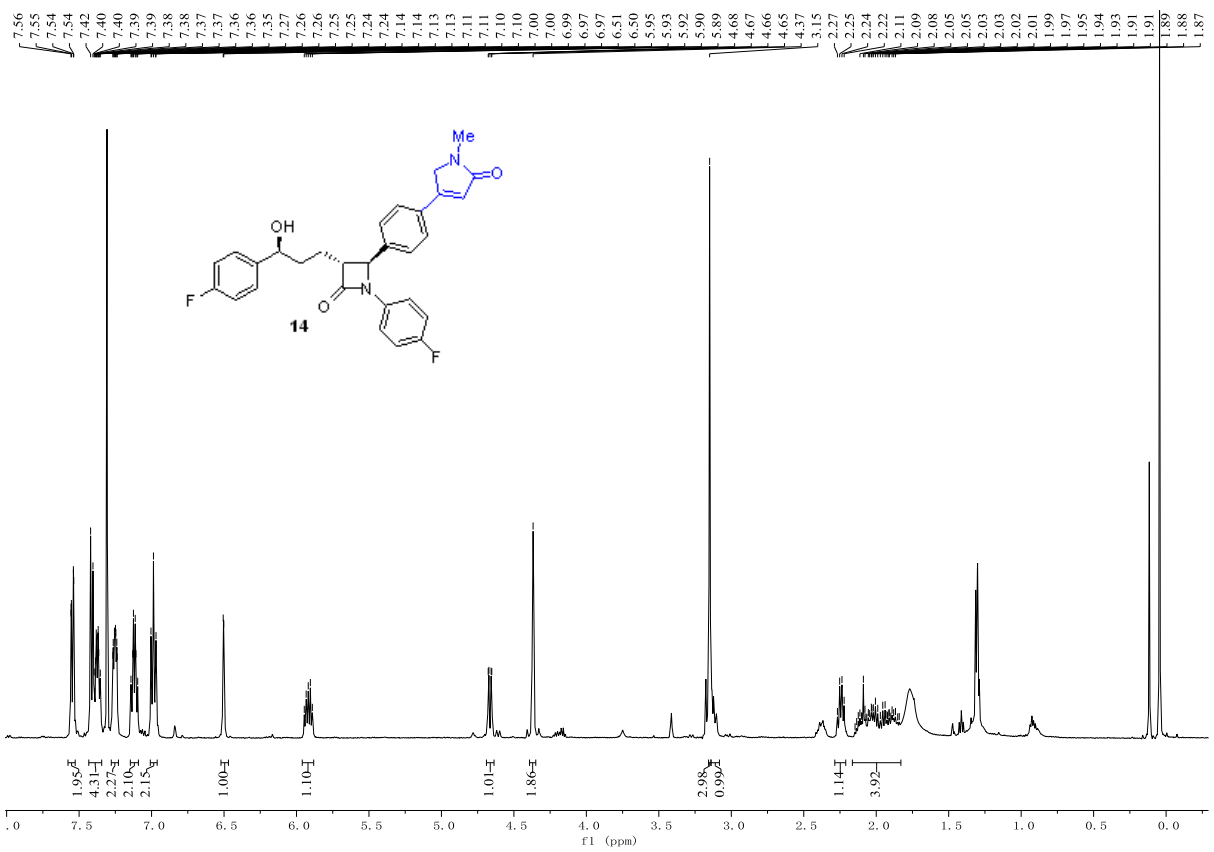
Supplementary Figure 101. ^{13}C NMR Spectra of **12**



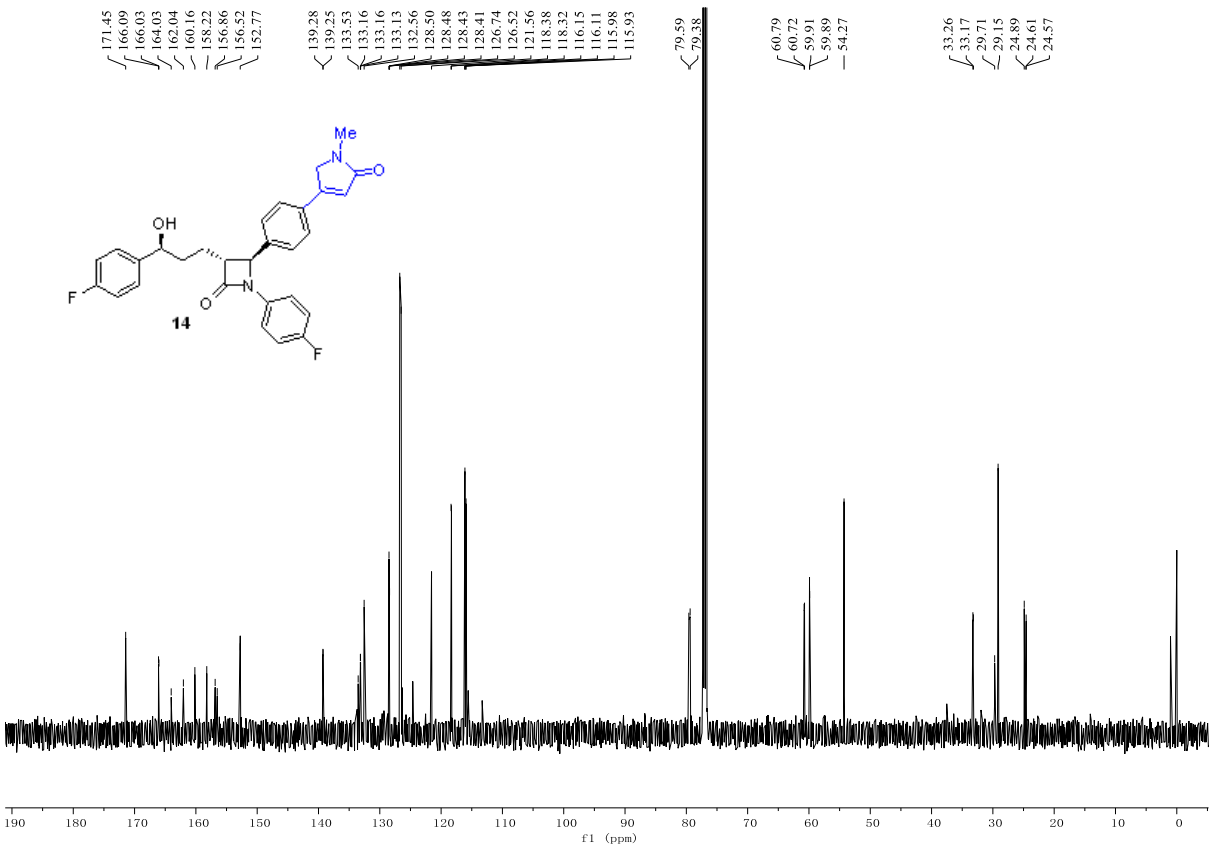
Supplementary Figure 102. ^{1}H NMR Spectra of **13**



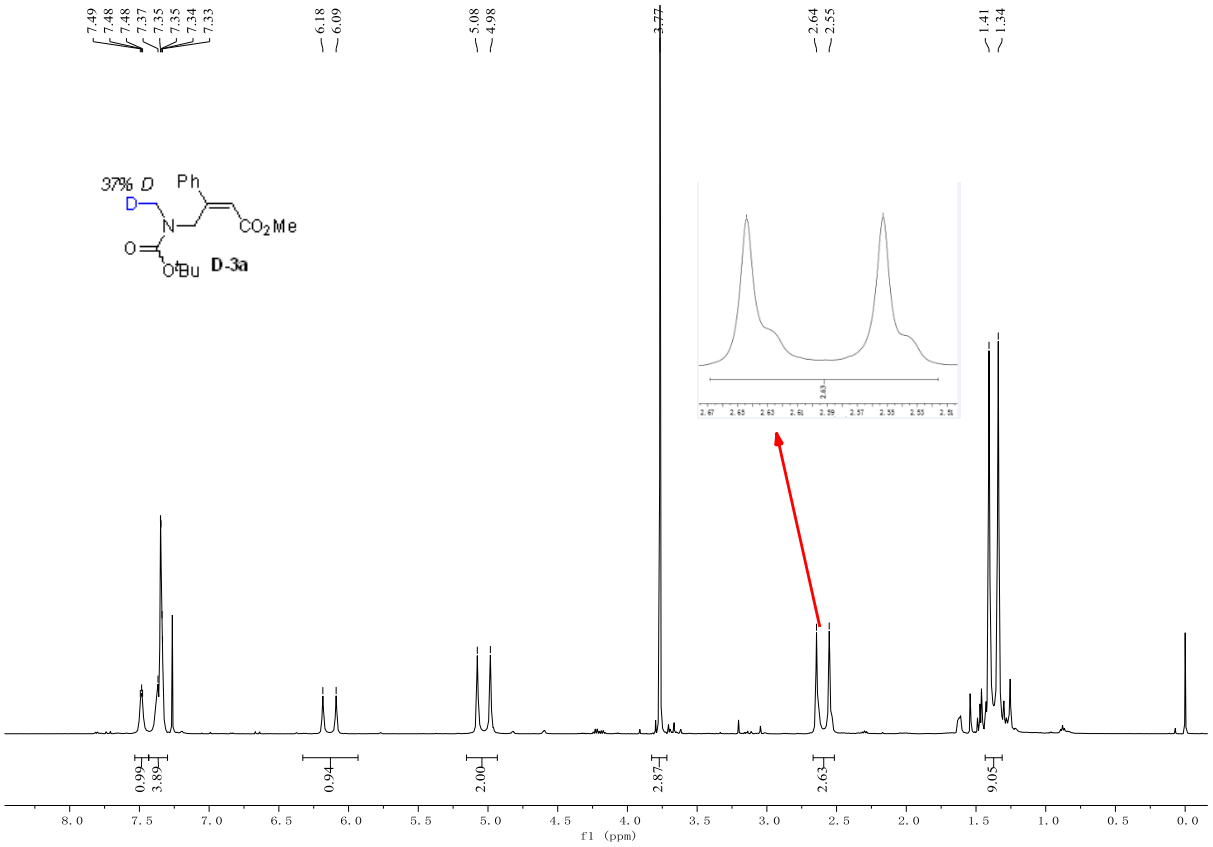
Supplementary Figure 103. ^{13}C NMR Spectra of **13**



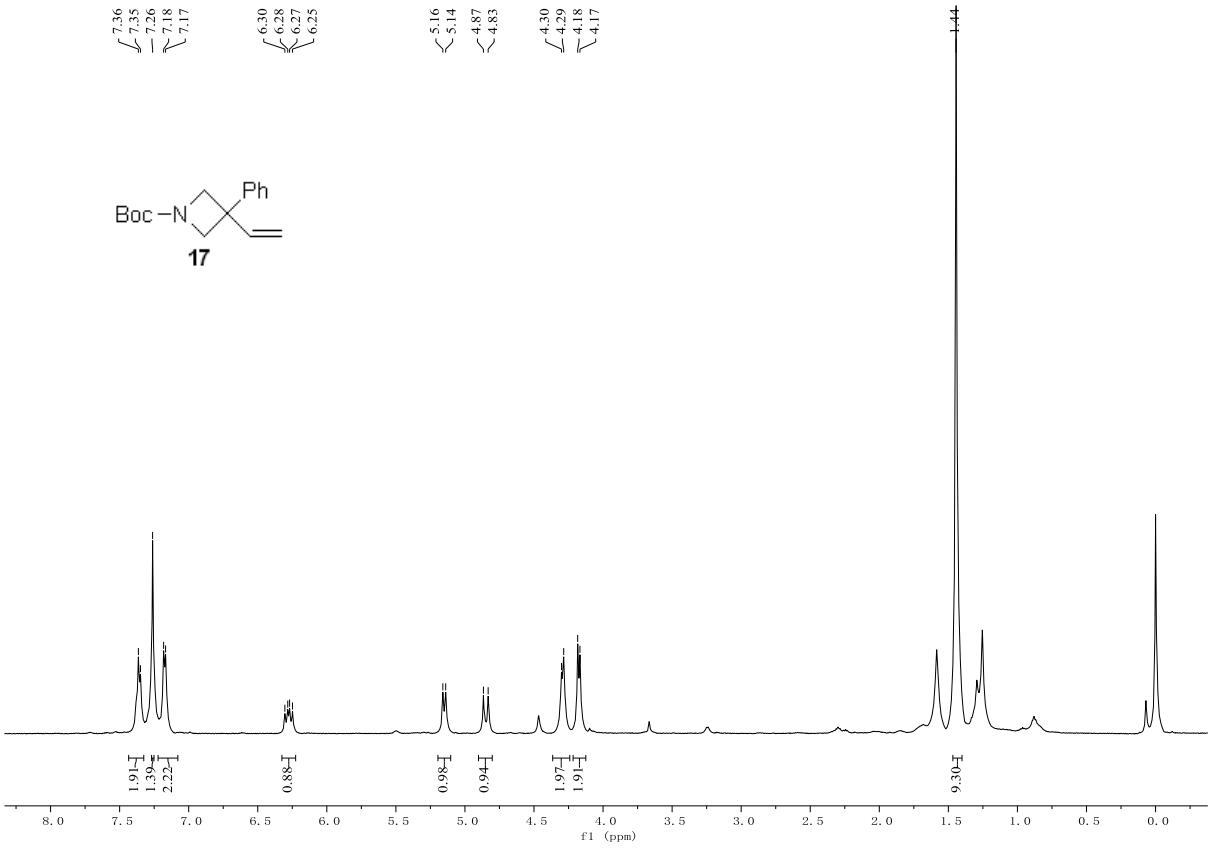
Supplementary Figure 104. ^{1}H NMR Spectra of **14**



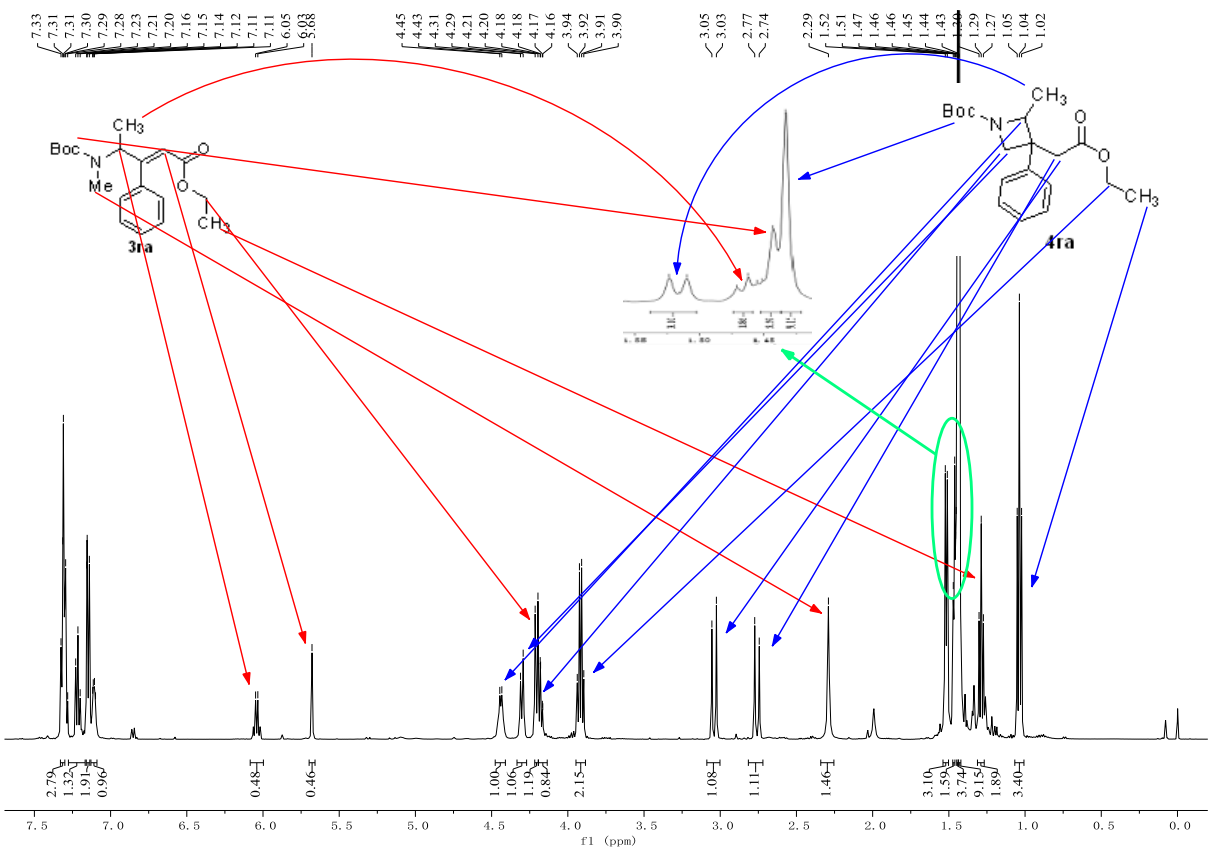
Supplementary Figure 105 ^{13}C NMR Spectra of **14**



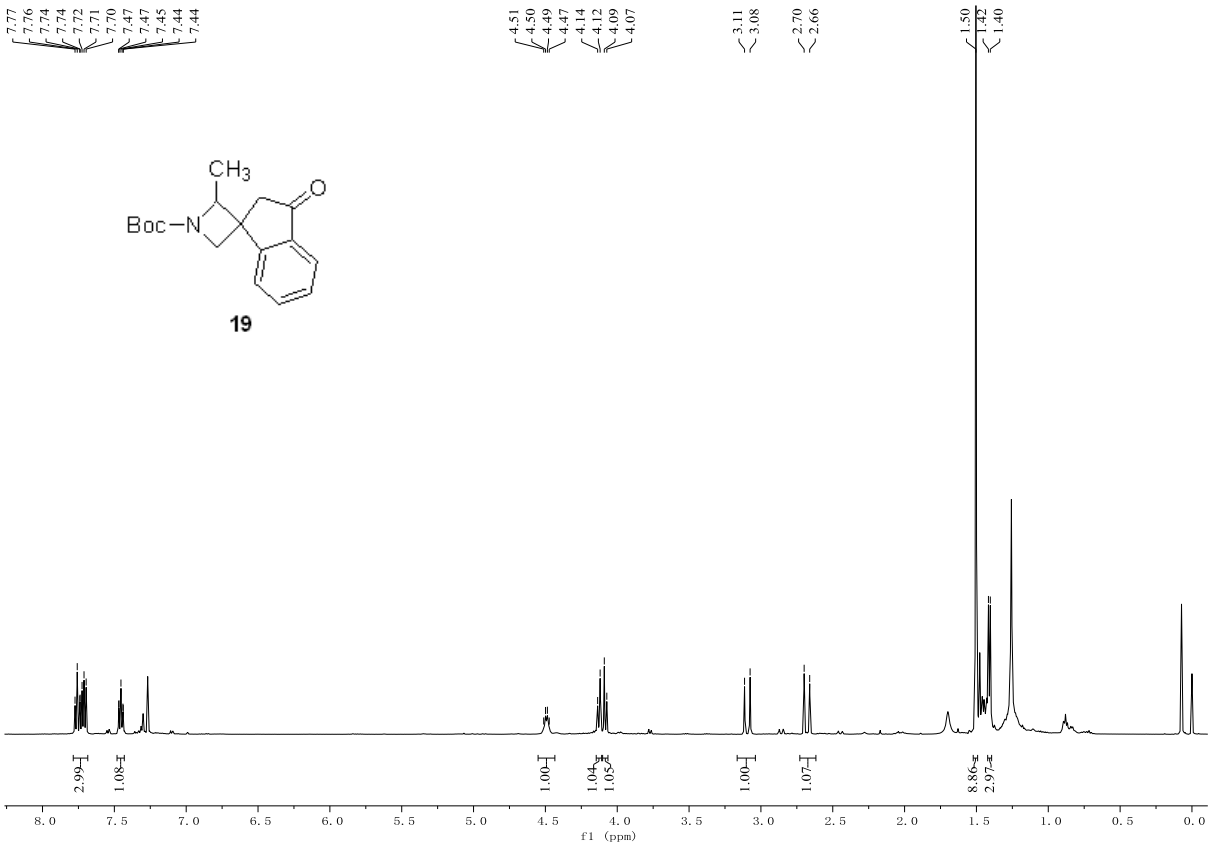
Supplementary Figure 106. ^{1}H NMR Spectra of **D-3a**



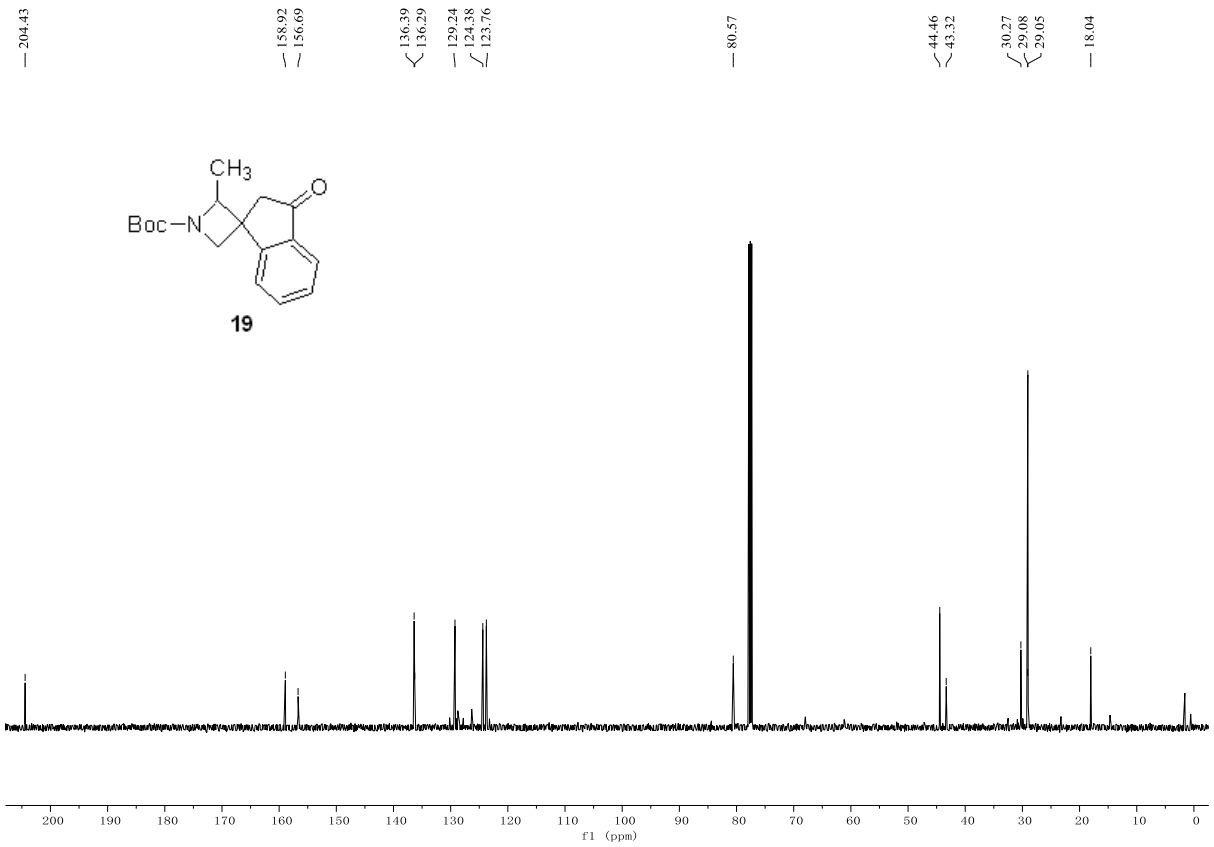
Supplementary Figure 107. ^{1}H NMR Spectra of **17**



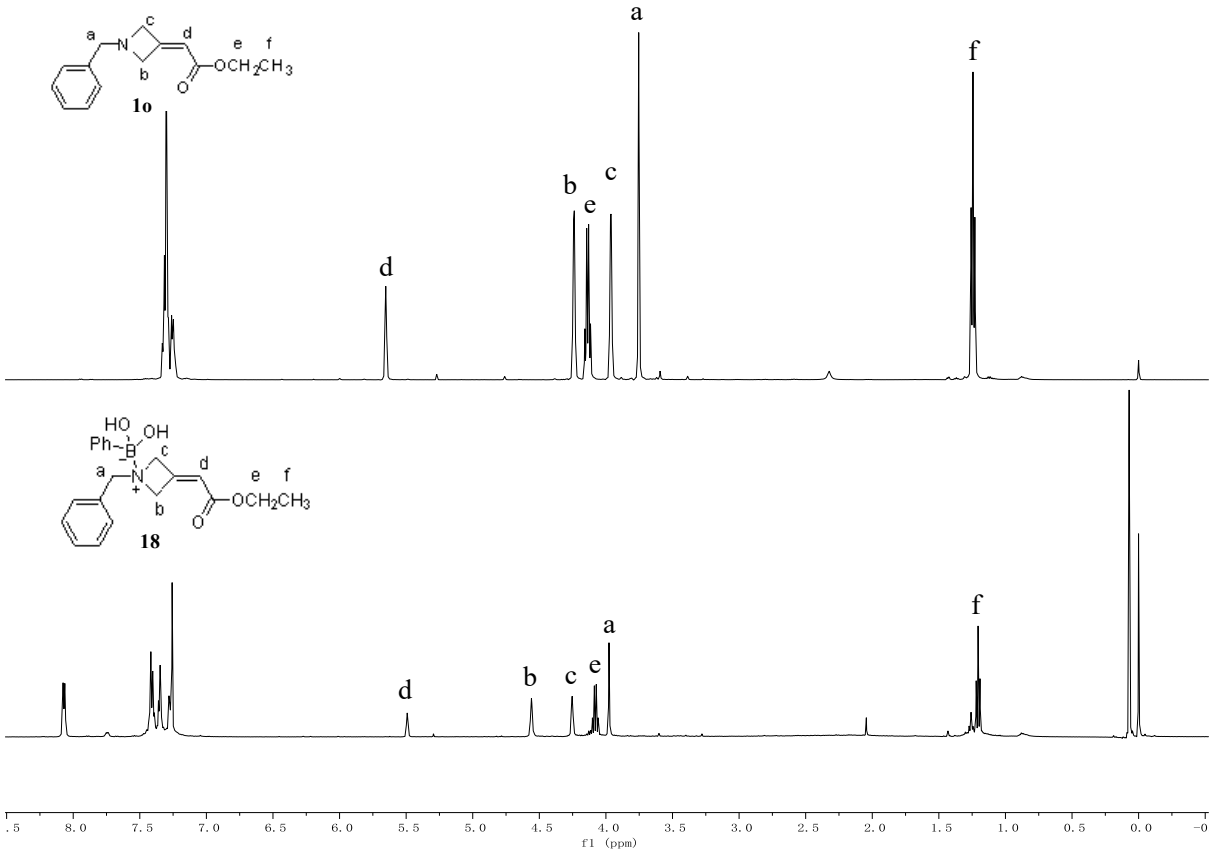
Supplementary Figure 108. ^{1}H NMR Spectra of **3ra** and **4ra**



Supplementary Figure 109. ^{1}H NMR Spectra of **19**



Supplementary Figure 110. ^{13}C NMR Spectra of **19**



Supplementary Figure 111. ^{1}H NMR Spectra of **18**