Supporting Information

Rh-Catalyzed three-component reaction for the diastereoselective synthesis of pyrazolone derivatives with contiguous quaternary stereocenters

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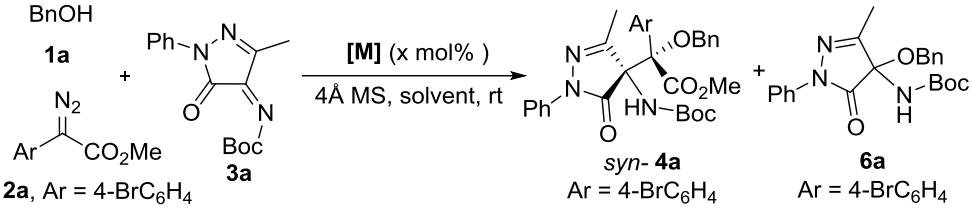
1. General information & materials

General: All ^{1}H NMR (400 MHz, 500MHz) and ^{13}C NMR (100 MHz, 125MHz) and ^{19}F NMR (376 MHz, 471MHz) spectra were recorded on 400 or 500 MHz spectrometers in D_6-DMSO or $CDCl_3$; chemical shifts were reported in ppm with the solvent signal as reference, and coupling constants (*J*) were given in Hertz. The peak information was described as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = composite signals. High-resolution mass spectrometry (HRMS) were recorded on a commercial apparatus (ESI or CI Source).

Materials: All reactions were carried out under nitrogen atmosphere in a well-dried glassware. Solvent CH_2Cl_2 was distilled over calcium hydride. Metal catalysts used in this reaction were purchased from commercial sources and used without further purification. Diazo compounds **2**[1], Ketimine **3**[2] were prepared according to literature procedures. 4 Å Molecular sieve was dried in a Muffle furnace at 250 ℃ over 5 h.

2. Experimental procedures

2.1 General procedure for optimization of conditions of the three-component reaction



entry	[M]	x mol%	solvent	yield (**4a**/**6a**)[b]	*dr*[b]
1	$Cu(CH_3CN)_4BF_4$	5	DCM	<10/ 90	-
2	$[PdCl(Allyl)]_2$	5	DCM	32/ 50	> 95: 5
3	$JohnphosAu(CH_3CN)SbF_6$	5	DCM	<10/ 40	-
4	$Rh_2(OAc)_4$	5	DCM	90[c]/ <10	> 95: 5
5	$Rh_2(OAc)_4$	1	DCM	90[c]/ <10	> 95: 5
6	$Rh_2(OAc)_4$	1	Toluene	89/ <10	> 95: 5
7	$Rh_2(OAc)_4$	1	THF	50/ <10	> 95: 5
8	$Rh_2(OAc)_4$	1	DCE	78/ <10	> 95: 5

To a 10-mL oven-dried vial containing a magnetic stirring bar, alcohol **1a** (0.24 mmol, 1.2 equiv), ketimine **3a** (0.2 mmol, 1.0 equiv), metal catalyst (x mol %), and activated 4Å molecular sieves (200 mg) in solvent (1 mL); **2** (0.24 mmol, 1.2 equiv) in solvent (1 mL) was added over 1 hour by syringe pump at room temperature. When the reaction was completed (monitored by TLC). Then filtrated and evaporated in *vacuo* to give the crude product. The residue was subjected to proton NMR analysis in $CDCl_3$ without any additional treatment. Recycled residue of **entry 4-5** were purified by flash column chromatography on silica gel without additional treatment (hexanes/ethyl acetate = 10:1 to 5:1) to afford the pure products.

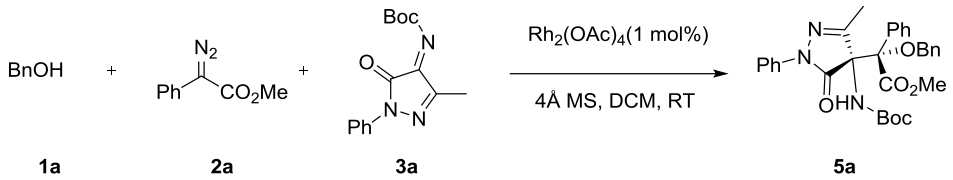
2.2 General procedure for the three-component reaction

To a 10-mL oven-dried vial containing a magnetic stirring bar, alcohol **1** (0.24 mmol, 1.2 equiv), ketimine **3** (0.2 mmol, 1.0 equiv), $Rh_2(OAc)_4$ (0.88 mg, 1 mol %), and activated 4Å molecular sieves (200 mg) in dry DCM (1 mL); **2** (0.24 mmol, 1.2 equiv) in dry DCM (1 mL) was added over 1 hour by syringe pump at room temperature. When the reaction was completed (monitored by TLC). Then the solvent was evaporated *in vacuo* and the residue was purified by flash column

chromatography on silica gel without additional treatment (hexanes/ethyl acetate = 10:1 to 5:1) to afford the pure products **4** or **5** in good to high yields.

3. General procedure for the scale up and product derivatizations

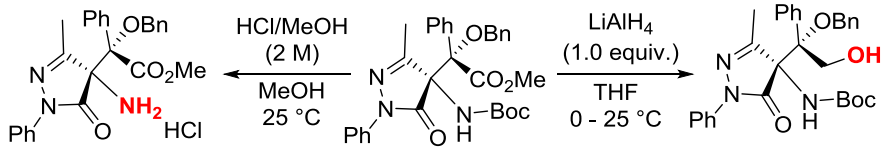
General procedure for the scale up



1a **2a** **3a** **5a**

***General procedure for the scale up*:** To a 25-mL oven-dried round-bottom flask containing a magnetic stirring bar, benzyl alcohol **1a** (3 mmol, 0.32 g, 1.2 equiv), ketimine **3a** (2.5 mmol, 0.72 g, 1.0 equiv), $Rh_2(OAc)_4$ (11 mg, 1 mol %), and activated 4Å molecular sieves (500 mg) in dry DCM (5 mL). Then **2a** (3 mmol, 0.53 g, 1.2 equiv) in dry DCM (5 mL) was added over 1 hour by syringe pump at room temperature. When the reaction was completed (monitored by TLC). Then the solvent was evaporated *in vacuo* and the residue was purified by flash column chromatography on silica gel without additional treatment (hexanes/ethyl acetate = 10:1 to 5:1) to afford 1.22 g pure **5a** as white solid (90% yield).

Product derivatization



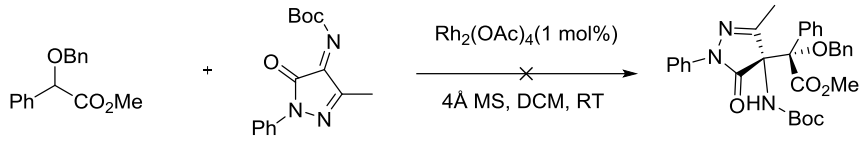
7a, 96%, > 95:5 *dr* **5a** **8a**, 90%, > 95:5 *dr*

***Synthesis of 7a*:** To a 10-mL oven-dried round-bottom flask with a magnetic stirring bar, **5a** (0.1 mmol, 54.3 mg, 1.0 equiv) in MeOH (1 mL). Then 2 M HCl in MeOH (0.06 mL, 1.2 equiv) was added into the flask. The mixture was stirred at room temperature about 24 hours. The mixture was evaporated *in vacuo* directly to give 46 mg pure product **7a** in 96% yields.

***Synthesis of 8a*:** To a 10-mL oven-dried round-bottom flask with a magnetic stirring bar, **5a** (0.1

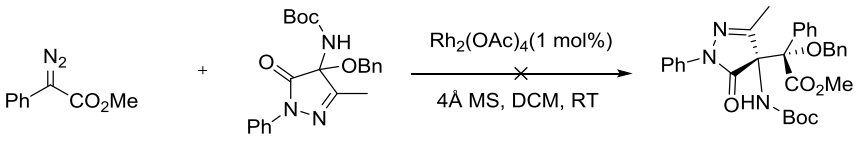
mmol, 54.3 mg, 1.0 equiv) in dry THF (1mL). The flask was sealed with a septum, evacuated and refilled with nitrogen (3 cycles). $LiAlH_4$ (2.5 mol/L in THF, 0.04 mL, 1.0 equiv) was dropped into the flask at 0 °C. The mixture was stirred at room temperature about 30 mins. MeOH (0.2 mL) was added slowly to quench the reaction. Then, water was added, and extracted with DCM. The organic extracts were combined and dried over Na_2SO_4. The solvent was evaporated *in vacuo* after filtration, and the residue was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 8:1- 4:1) to give 46.3 mg pure product **8a** in 90% yields.

4. Control experiments



9 **3a** **5a**

Control experiments starting from the O-H insertion product **9** and **3a** was conducted under the standard condition, in which no three-component product was observed. These results exclude the possibility that the product is generated from the O-H insertion product.



6a **5a**

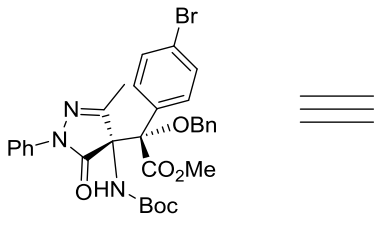
The by-product **6a** derived from **1a** and **3a**, could not convert to product **5a** under the reaction conditions, which indicate that **6a** is not the intermediate for this transformation.

5. References

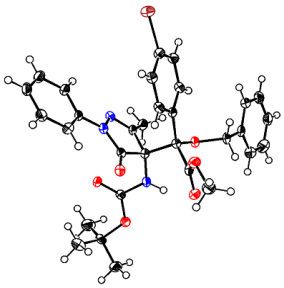
(1) Doyle, M. P.; Mckervey, M. A.; Ye, T. Modern Catalytic Methods for Organic Synthesis with Diazo Compounds; Wiley: New York, (1998)

(2) Kaya, U.; Chauhan, P.; Mahajan, S.; Deckers, K.; Valkonen, A.; Rissanen, K.; Enders, D. Squaramide‐Catalyzed Asymmetric aza‐Friedel–Crafts/N,O‐Acetalization Domino Reactions Between 2‐Naphthols and Pyrazolinone Ketimines. *Angew. Chem. Int. Ed*. **2017**, *56*, 15358-15362.

6. Single crystal X-ray diffraction data



syn-**4a**



CCDC: 1966115

Bond precision: C-C = 0.0061 A Wavelength=1.54184

Cell: a=8.3958(1) b=10.3211(2) c=33.5425(5)
alpha=90 beta=91.208(1) gamma=90
Temperature: 100 K

	Calculated	Reported
Volume	2905.94(8)	2905.94(8)
Space group	P 21/n	P 1 21/n 1
Hall group	-P 2yn	-P 2yn
Moiety formula	C31 H32 Br N3 O6	C31 H32 Br N3 O6
Sum formula	C31 H32 Br N3 O6	C31 H32 Br N3 O6
Mr	622.50	622.50
Dx,g cm-3	1.423	1.423
Z	4	4
Mu (mm-1)	2.333	2.333
F000	1288.0	1288.0
F000'	1288.90	
h,k,lmax	10,13,42	10,12,42
Nref	6135	5797
Tmin,Tmax	0.600,0.792	0.592,1.000
Tmin'	0.473	

Correction method= # Reported T Limits: Tmin=0.592 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.945 Theta(max)= 76.990

R(reflections)= 0.0647(5194) wR2(reflections)= 0.1546(5797)

S = 1.073 Npar= 375

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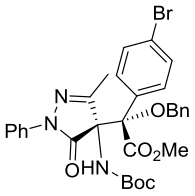
7. Analytical data of products



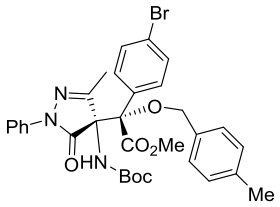
Methyl-(*S)-2-(benzyloxy)-2-(4-bromophenyl)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)acetate (4a).**

White solid, mp 143.9-144.6 °C. 111.8 mg, 90% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.51 (d, *J* = 7.0 Hz, 2H), 7.48 – 7.42 (comp, 5H), 7.42 – 7.39 (m, 2H), 7.39 – 7.36 (m, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.20 (t, *J* = 7.3 Hz, 2H), 4.41 (q, *J* = 11.1 Hz, 2H), 3.92 (s, 3H), 2.01 (s, 3H), *t*-Bu[1.36 (s, 6.5H)+1.13 (s, 2.5H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.2, 167.3, 157.8, 153.9, 137.4, 136.8, 130.9, 130.8, 130.5, 129.3, 129.1, 128.6, 127.9, 125.7, 123.2, 118.8, 85.8, 80.9, 71.5, 68.4, 53.9, 28.3, 15.6.

HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{32}N_3O_6BrNa^+$ [M + Na]$^+$: 644.1367, found 644.1367.



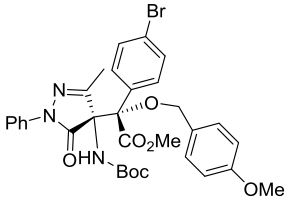
Methyl-(*S)-2-(4-bromophenyl)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-((4-methylbenzyl)oxy)acetate (4b).**

White solid, mp 155.5-156.3 °C. 80.0 mg, 63% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.49 – 7.36 (comp, 8H), 7.32 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.13 (s, 1H), 4.34 (q, *J* = 10.8 Hz, 2H), 3.92 (s, 3H), 2.34 (s, 3H), 1.98 (s, 3H), *t*-Bu[1.36 (s, 6H)+ 1.12 (s, 3H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.2, 167.3, 157.7, 153.8, 137.9, 137.4, 133.8, 130.9, 130.7, 130.6, 129.6, 129.3, 128.2, 125.7, 123.2, 118.8, 85.7, 80.9, 71.5, 68.4, 53.9, 28.3, 21.3, 15.6.

HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{34}N_3O_6BrNa^+$ [M + Na]$^+$: 658.1523, found 658.1526.

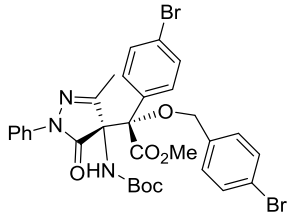


Methyl-(*S)-2-(4-bromophenyl)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-((4 methoxybenzyl)oxy)acetate (4c).**

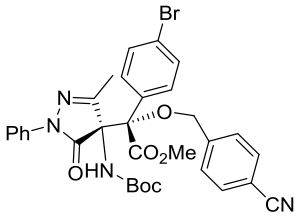
White solid, mp 163.8-164.1 °C. 102.1 mg, 78% yield.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.51 – 7.35 (comp, 8H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), NH[7.14 (s, 0.75H)+6.76 (s, 0.25H)], 7.01 (d, *J* = 8.6 Hz, 2H), 4.31 (q, *J* = 10.5 Hz, 2H), 3.92 (s, 3H), 3.79 (s, 3H), 1.97 (s, 3H), *t*-Bu[1.36 (s, 6H)+1.12 (s, 3H)].

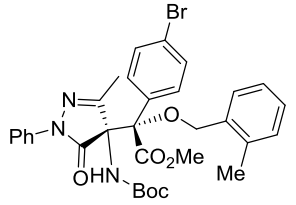
^{13}C NMR (125 MHz, DMSO-d_6) δ 169.2, 167.3, 159.7, 157.8, 153.8, 137.4, 130.9, 130.7, 130.6, 129.9, 129.3, 128.7, 125.6, 123.2, 118.8, 114.5, 85.7, 80.9, 71.4, 68.2, 55.6, 53.8, 28.3, 15.6.
HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{34}N_3O_7BrNa^+$ [M + Na]$^+$: 674.1472, found 674.1469.



Methyl-(*S)-2-((4-bromobenzyl)oxy)-2-(4-bromophenyl)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)acetate (4d).**
White solid, mp 160.5-161.2 ºC. 118.6 mg, 85% yield.
^{1}H NMR (500 MHz, DMSO-d_6) δ 7.66-7.63 (m, 2H), 7.52 – 7.44 (m, 4H), 7.43 – 7.36 (m, 4H), 7.30 (d, *J* = 8.3 Hz, 2H), NH[7.26 (s, 0.75H)+6.87(s, 0.25H)], 7.19 (t, *J* = 7.4 Hz, 1H), 4.39 (s, 2H), 3.91 (d, *J* = 2.0 Hz, 3H), 2.00 (s, 3H), *t*-Bu[1.36 (s, 6H)+1.13 (s, 3H)].
^{13}C NMR (125 MHz, DMSO-d_6) δ 169.2, 167.2, 157.7, 153.9, 137.4, 136.3, 132.0, 130.9, 130.76, 130.5, 130.2, 129.3, 125.6, 123.2, 121.7, 118.8, 85.8, 80.9, 71.4, 67.7, 53.9, 28.3, 15.6.
HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{31}N_3O_6Br_2Na^+$ [M + Na]$^+$: 722.0472, found 722.0471.



Methyl-(*S)-2-(4-bromophenyl)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-((4-cyanobenzyl)oxy)acetate (4e).**
White solid, mp 156.2-157.0 ºC. 106.3 mg, 82% yield.
^{1}H NMR (500 MHz, DMSO-d_6) δ 7.92 (d, *J* = 8.1 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 7.5 Hz, 2H), 7.40 (m, 4H), 7.29 (d, *J* = 8.8 Hz, 2H), 7.20 (t, *J* = 7.3 Hz, 1H), 4.51 (m, 2H), 3.90 (s, 3H), 2.03 (s, 3H), *t*-Bu[1.36 (s, 6H), 1.14 (s, 3H)].
^{13}C NMR (125 MHz, DMSO-d_6) δ 169.2, 167.1, 157.7, 154.0, 142.6, 137.4, 132.9, 130.8, 130.4, 129.3, 128.4, 125.6, 123.3, 119.2, 118.8, 111.1, 85.9, 80.9, 71.5, 67.6, 53.9, 28.3, 15.6.
HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{31}N_4O_6BrNa^+$ [M + Na]$^+$: 669.1319, found 669.1319.

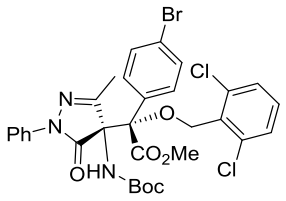


Methyl-(*S)-2-(4-bromophenyl)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-((2-methylbenzyl)oxy)acetate (4f).**
White solid, mp 147.9-148.5 ºC. 94.4 mg, 74% yield.

^{1}H NMR (400 MHz, DMSO- d_6) δ 7.47-7.44 (m, 5H), 7.42 – 7.35 (m, 2H), 7.35 – 7.24 (m, 5H), 7.20 (t, J = 7.2 Hz, 1H),NH [7.03 (s, 0.75H)+6.66(s, 0.25H)], 4.40 (s, 2H), 3.93 (s, 3H), 2.32 (s, 3H), 1.98 (s, 3H), *t*-Bu[1.35 (s, 6H), 1.13 (s, 3H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.1, 167.4, 157.7, 153.8, 137.3, 136.5, 134.8, 130.8, 130.8, 130.4, 129.4, 128.7, 128.5, 126.6, 125.7, 123.3, 118.9, 85.7, 81.0, 71.5, 66.7, 53.9, 28.3, 19.0, 15.6.

HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{34}N_3O_6BrNa^+$ [M + Na]$^+$: 658.1523, found 658.1519.



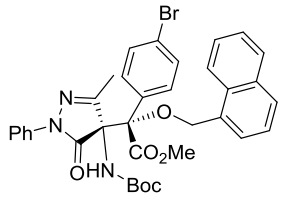
Methyl-(*S)-2-(4-bromophenyl)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-((2,6-dichlorobenzyl)oxy)acetate (4g).**

White solid, mp 157.9-158.7 °C. 115.7 mg, 84% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.63 (d, *J* = 8.1 Hz, 2H), 7.54 – 7.51 (m, 1H), 7.50 – 7.46 (m, 2H), 7.45 – 7.36 (m, 6H), 7.20 (t, *J* = 7.2 Hz, 1H), 6.90 (s, 1H), 4.75 (d, *J* = 10.1 Hz, 1H), 4.55 (d, *J* = 10.1 Hz, 1H), 3.94 (s, 3H), 1.88 (s, 3H), *t*-Bu[1.35 (s, 6H), 1.10 (s, 3H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.9, 166.7, 157.6, 153.5, 137.4, 136.3, 132.3, 131.7, 130.7, 130.1, 129.6, 129.3, 125.8, 123.5, 118.9, 85.7, 80.8, 71.4, 63.9, 53.9, 28.3, 15.4.

HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{30}N_3O_6Cl_2BrNa^+$ [M + Na]$^+$: 712.0587, found 712.0587.



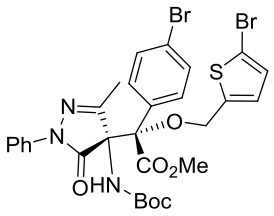
Methyl-(*S)-2-(4-bromophenyl)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-(naphthalen-1-ylmethoxy)acetate (4h).**

White solid, mp 153.8-154.6 °C. 122.2 mg, 91% yield.

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.17 (d, *J* = 8.0 Hz, 1H), 8.09 – 7.92 (m, 2H), 7.70 – 7.54 (m, 4H), 7.49 – 7.43 (m, 4H), 7.43 – 7.35 (m, 4H), 7.21 (t, *J* = 7.3 Hz, 1H), 7.01 (s, 1H), 4.91 (q, *J* = 11.4 Hz, 2H), 3.95 (s, 3H), 1.90 (s, 3H), *t*-Bu[1.34 (s, 6H)+1.13 (s, 3H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.0, 167.4, 157.7, 153.6, 137.3, 133.8, 132.4, 131.3, 130.9, 130.5, 129.4, 129.4, 129.2, 127.1, 126.7, 126.6, 126.0, 125.7, 124.0, 123.3, 118.9, 85.9, 80.8, 71.5, 67.0, 54.0, 28.3, 15.5.

HRMS (TOF MS ESI$^+$) calculated for $C_{35}H_{34}N_3O_6BrNa^+$ [M + Na]$^+$: 694.1523, found 694.1519.

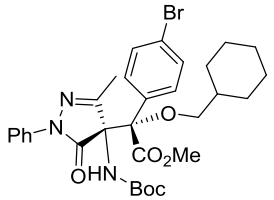


Methyl-(*S)-2-(4-bromophenyl)-2-((5-bromothiophen-2-yl)methoxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)acetate (4i).** White solid, mp 145.2-146.2 °C. 125.7 mg, 89% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.45 (comp, 4H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), NH[7.15 (s, 0.65H)+6.77(s, 0.27H)], 7.05 (s, 1H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.51 (d, *J* = 11.8 Hz, 1H), 3.91 (s, 3H), 1.99 (s, 3H), *t*-Bu[1.36 (s, 6.5H)+ 1.13 (s, 2.5H)].

^{13}C NMR (125 MHz, DMSO) δ 169.0, 166.9, 157.6, 153.7, 141.1, 137.3, 130.8, 130.7, 130.6, 130.4, 129.3, 128.7, 125.7, 123.4, 118.9, 112.6, 85.9, 80. 9, 71.3, 64.1, 54.1, 28.3, 15.6.

HRMS (TOF MS ESI$^+$) calculated for $C_{29}H_{29}N_3O_6Br_2SNa^+$ [M + Na]$^+$: 728.0036, found 728.0036.



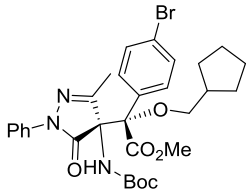
Methyl-(*S)-2-(4-bromophenyl)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-(cyclohexylmethoxy)acetate (4j).**

White solid, mp 158.7-159.6 °C. 120.1 mg, 96% yield.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.47 – 7.32 (m, 6H), 7.27 (d, *J* = 8.3 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 6.94 (s, 1H), 3.88 (s, 3H), 3.28 – 3.15 (m, 1H), 2.97 (t, *J* = 7.3 Hz, 1H), 2.04 (s, 3H), 1.93 – 1.57 (m, 6H), 1.36 (s, 5H), 1.31 – 1.23 (m, 3H), 1.22 – 0.96 (m, 6H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.2, 167.4, 157.8, 153.8, 137.3, 130.9, 130.6, 130.5, 129.3, 125.6, 123.0, 118.8, 85.2, 80.9, 71.5, 71.5, 53.7, 37.8, 29.8, 28.3, 26.5, 25.7, 15.6.

HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{38}N_3O_6BrNa^+$ [M + Na]$^+$: 650.1836, found 650.1835.



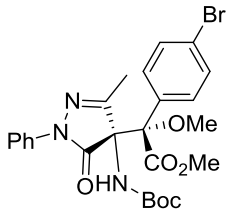
Methyl-(*S)-2-(4-bromophenyl)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-(cyclopentylmethoxy)acetate (4k).**

White solid, mp 142.1-142.7 °C. 118.2 mg, 96% yield.

^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 7.46 (s, 2H), 7.38 – 7.21 (comp, 6H), 7.15 (t, *J* = 7.0 Hz, 1H), 6.91 – 6.29 (m, 1H), 3.96 (s, 3H), 3.38 (t, *J* = 7.6 Hz, 1H), 3.19 – 2.98 (m, 1H), 2.46 – 2.27 (m, 1H), 2.12 (s, 3H), 1.88 (s, 2H), 1.64 (s, 4H), 1.51 – 1.11 (comp, 11H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.2, 167.4, 157.9, 153.8, 137.3, 130.9, 130.6, 129.3, 125.6, 123.0, 118.8, 85.2, 80.8, 71.5, 70.4, 53.7, 29.4, 28.3, 25.4, 25.2, 15.5.

HRMS (TOF MS ESI$^+$) calculated for $C_{30}H_{36}N_3O_6BrNa^+$ [M + Na]$^+$: 636.1680, found 636.1681.



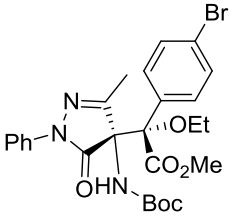
Methyl-(*S)-2-(4-bromophenyl)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-methoxyacetate (4l).**

White solid, 90 mg, 83 % yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.47 (d, *J* = 8.1 Hz, 2H), 7.44 – 7.36 (m, 4H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), NH[7.04 (s, 0.7H)+6.69 (s, 0.3H)], 3.89 (s, 3H), 3.28 (s, 3H), 2.01 (s, 3H), *t*-Bu[1.37 (s, 7H)+1.13 (s, 2H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.2, 167.2, 158.0, 153.8, 137.4, 130. 9, 130.6, 130.6, 129.3, 125.7, 123.1, 118.9, 86.1, 80.8, 71.3, 54.9, 53.7, 28.3, 15.6.

HRMS (TOF MS ESI$^+$) calculated for $C_{25}H_{28}N_3O_6BrNa^+$ [M + Na] $^+$: 568.1054, found 568.1023.



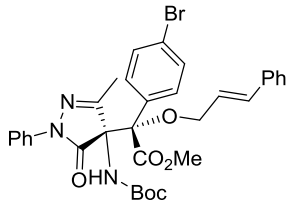
Methyl-(*S)-2-(4-bromophenyl)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-ethoxyacetate (4m).**

White solid, 97 mg, 87 % yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 – 7.42 (m, 2H), 7.32 (comp, 4H), 7.24 (d, *J* = 7.2 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), NH[6.78 (s, 0.6H)+ 6.44 (s, 0.4H)], 3.95 (s, 3H), 3.54 – 3.29 (m, 2H), 2.10 (s, 3H), Boc[1.41 (d, *J* = 21.9 Hz, 9H)], 1.24 (d, *J* = 21.6 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.3, 167.4, 158.0, 153.8, 137.4, 130.9, 130.8, 130.6, 129.3, 125.6, 123.0, 118.9, 85.4, 80.8, 71.3, 62.4, 53.7, 28.4, 15.6, 15.1.

HRMS (TOF MS ESI$^+$) calculated for $C_{26}H_{31}N_3O_6Br^+$ [M + H] $^+$: 560.1391, found 560.1345.



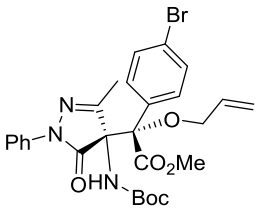
Methyl-(*S)-2-(4-bromophenyl)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-(cinnamyloxy)acetate (4n).**

White solid, mp 137.1-137.9 °C. 122.8 mg, 95% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.53 (d, *J* = 7.6 Hz, 2H), 7.47 (d, *J* = 8.1 Hz, 2H), 7.45 – 7.33 (comp, 8H), 7.31 (t, *J* = 7.3 Hz, 1H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.10 (s, 1H), 6.74 (d, *J* = 15.9 Hz, 1H), 6.61 (dt, *J* = 13.9, 7.8 Hz, 1H), 4.04 (d, *J* = 5.8 Hz, 2H), 3.90 (s, 3H), 2.06 (s, 3H), *t*-Bu[1.37 (s, 6H)+1.13 (s, 3H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.2, 167.3, 157.9, 153. 8, 137.4, 136.5, 133.3, 130.9, 130.7, 129.3, 129.1, 128.5, 127.1, 125.7, 124.8, 123.2, 118.8, 85.5, 80.9, 71.4, 67.7, 53.8, 28.3, 15.7.

HRMS (TOF MS ESI$^+$) calculated for $C_{33}H_{34}N_3O_6BrNa^+$ [M + Na]$^+$: 670.1523, found 670.1523.



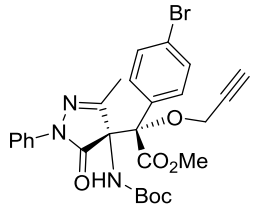
Methyl-(*S)-2-(allyloxy)-2-(4-bromophenyl)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)acetate (4o).**

White solid, mp 125.5-126.1 °C. 108.0 mg, 95% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.46 (d, *J* = 8.0 Hz, 2H), 7.40 (comp, 4H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.20 (t, *J* = 7.3 Hz, 1H), NH[7.05 (s, 0.7H)+ 6.69 (s, 0.3H)], 6.15 – 6.00 (m, 1H), 5.43 (d, *J* = 17.3 Hz, 1H), 5.31 (d, *J* = 11.8 Hz, 1H), 3.88 (comp, 5H), 2.03 (s, 3H), *t*-Bu[1.36 (s, 6.5H)+1.13 (s, 2.5H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.1, 167.2, 157.8, 153.8, 137.3, 133.7, 130.7, 130.7, 129.3, 125.7, 123.2, 118.9, 118.1, 85.5, 80.9, 71.3, 67.6, 53.8, 28.3, 15.6.

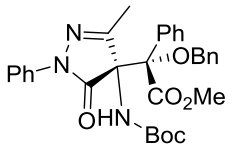
HRMS (TOF MS ESI$^+$) calculated for $C_{27}H_{30}N_3O_6BrNa^+$ [M + Na]$^+$: 594.1210, found 594.1215.



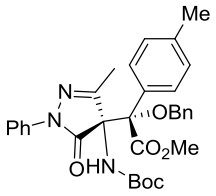
Methyl-(*S)-2-(4-bromophenyl)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-(prop-2-yn-1-yloxy)acetate (4p).**

White solid, mp 143.7-144.6 °C. 101.0 mg, 89% yield.

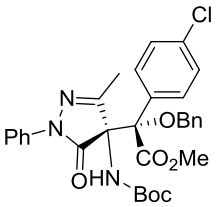
^{1}H NMR (500 MHz, DMSO-d_6) δ 7.44 (comp, 4H), 7.42 – 7.36 (m, 2H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.08 (s, 1H), 4.18 (d, *J* = 15.1 Hz, 1H), 4.08 (d, *J* = 15.2 Hz, 1H), 3.87 (d, *J* = 2.0 Hz, 3H), 3.73 (d, *J* = 2.5 Hz, 1H), 2.03 (s, 3H), *t*-Bu[1.37 (s, 7H)+1.14 (s, 2H)].
^{13}C NMR (125 MHz, DMSO-d_6) δ 168.9, 166.6, 157.6, 153.8, 137.3, 130.8, 130.6, 130.4, 129.3, 125.7, 123.4, 118.9, 85.8, 80.9, 79.2, 79.0, 71.2, 55.8, 53.9, 28.3, 15.6.
HRMS (TOF MS ESI$^+$) calculated for $C_{27}H_{28}N_3O_6BrNa^+$ [M + Na]$^+$: 592.1054, found 592.1051.



Methyl-(*S)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-phenylacetate (5a).**
White solid, mp 120.8-121.5 °C. 105.6 mg, 97% yield.
^{1}H NMR (400 MHz, DMSO-d_6) δ 7.51 (d, *J* = 7.1 Hz, 2H), 7.49 – 7.42 (comp, 4H), 7.42 – 7.33 (comp, 5H), 7.29 (t, *J* = 7.1 Hz, 1H), 7.24 – 6.76 (comp, 4H), 4.48 (d, *J* = 11.1 Hz, 1H), 4.39 (d, *J* = 11.1 Hz, 1H), 3.91 (s, 3H), 2.00 (s, 3H), *t*-Bu[1.36 (s, 6H)+1.12 (s, 3H)].
^{13}C NMR (125 MHz, DMSO-d_6) δ 169.3, 167.7, 157.6, 153.8, 137.5, 137.0, 131.0, 129.5, 129.3, 129.1, 128.5, 128.5, 127.8, 127.8, 125.5, 118.7, 86.0, 80.8, 71.6, 68.3, 53.7, 28.3, 15.6.
HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{33}N_3O_6Na^+$ [M + Na]$^+$: 566.2262, found 566.2258.



Methyl-(*S)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-(p-tolyl)acetate (5b).**
White solid, mp 134.6-135.4 °C. 108.1 mg, 97% yield.
^{1}H NMR (400 MHz, DMSO-d_6) δ 7.52 – 7.42 (comp, 6H), 7.38 (m, 3H), 7.26 (d, *J* = 8.1 Hz, 2H), 7.18 (t, *J* = 7.3 Hz, 1H), NH[7.11 (s, 0.7H)+6.75(s, 0.3H)], 7.01 (d, *J* = 8.0 Hz, 2H), 4.46 (d, *J* = 11.2 Hz, 1H), 4.38 (d, *J* = 11.2 Hz, 1H), 3.90 (s, 3H), 2.21 (s, 3H), 2.00 (s, 3H), *t*-Bu[1.36 (s, 6H)+1.14 (s, 3H)].
^{13}C NMR (125 MHz, DMSO-d_6) δ 169.4, 167.8, 157.6, 153.8, 138.9, 137.5, 137.1, 129.2, 129.1, 128.5, 128. 3, 128.0, 127.8, 125.5, 118.8, 86.0, 80.8, 71.6, 68.2, 53.6, 28.3, 21.0, 15.6.
HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{35}N_3O_6Na^+$ [M + Na]$^+$: 580.2418, found 580.2416.



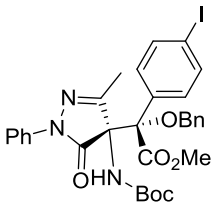
Methyl-(*S)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-(4-chlorophenyl)acetate (5c).**

White solid, mp 122.8-123.8 °C. 109.6 mg, 95% yield.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.51 (d, *J* = 7.2 Hz, 2H), 7.48 – 7.43 (comp, 4H), 7.39 (comp, 5H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.20 (t, *J* = 7.2 Hz, 2H), 4.42 (q, *J* = 11.1 Hz, 2H), 3.93 (s, 3H), 2.02 (s, 3H), *t*-Bu[1.36 (s, 6H)+1.15 (s, 3H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.2, 167.3, 157.7, 153.9, 137.4, 136.8, 134.5, 130.6, 130.1, 129.3, 129.1, 128.6, 127.9, 127.8, 125.6, 118.8, 85.7, 80.9, 71.6, 68.4, 53.9, 28.3, 15.6.

HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{32}N_3O_6ClNa^+$ [M + Na]$^+$: 600.1872, found 600.1868.



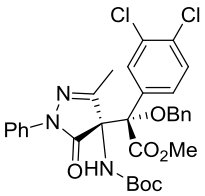
Methyl-(*S)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-(4-iodophenyl)acetate (5d).**

White solid, mp 153.6-154.5 °C. 122.1 mg, 91% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.58 (d, *J* = 7.6 Hz, 2H), 7.50 (d, *J* = 7.1 Hz, 2H), 7.48 – 7.42 (comp, 4H), 7.39 (t, *J* = 7.0 Hz, 3H), 7.23 – 7.13 (m, 4H), 4.43 (d, *J* = 10.9 Hz, 1H), 4.37 (d, *J* = 11.0 Hz, 1H), 3.91 (s, 3H), 2.00 (s, 3H), *t*-Bu[1.36 (s, 7H)+1.13 (s, 2H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.2, 167.3, 157.7, 153.8, 137.4, 136.9, 136.6, 130.9, 130.8, 129.3, 129.1, 128.6, 127.9, 125.7, 118.9, 96.7, 85.8, 80.9, 71.5, 68.4, 53.9, 28.3, 15.6.

HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{32}N_3O_6INa^+$ [M + Na]$^+$: 692.1228, found 692.1231.



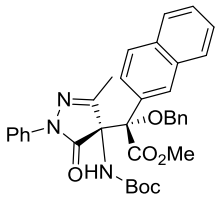
Methyl-(*S)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-(3,4-dichlorophenyl)acetate (5e).**

White solid, mp 141.5-141.8 °C. 102.6 mg, 84% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.56 (d, *J* = 8.7 Hz, 1H), 7.51 (d, *J* = 7.5 Hz, 2H), 7.49 – 7.44 (m, 5H), 7.40 (d, *J* = 8.5 Hz, 4H), 7.27 (s, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 4.46 (d, *J* = 11.3 Hz, 1H), 4.40 (d, *J* = 11.3 Hz, 1H), 3.94 (d, *J* = 2.4 Hz, 3H), 2.00 (s, 3H), *t*-Bu[1.37 (s, 7H)+1.13 (s, 2H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.1, 166.8, 157.9, 154.0, 137.2, 136.7, 132.6, 132.3, 131.2, 130.8, 130.1, 129.4, 129.1, 128.7, 128.0, 125.7, 118.7, 85.5, 81.0, 71. 6, 68.7, 54.1, 28.3, 15.5.

HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{31}N_3O_6Cl_2Na^+$ [M + Na]$^+$: 634.1482, found 634.1476.



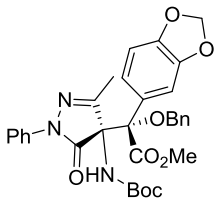
Methyl-(*S)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-(naphthalen-2-yl)acetate (5f).**

White solid, mp 130.5-131.2 °C. 112.8 mg, 95% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.95 (s, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.71 (d, *J* = 8.7 Hz, 1H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.57 (d, *J* = 7.3 Hz, 2H), 7.49 (t, *J* = 7.5 Hz, 3H), 7.47 – 7.40 (m, 3H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.30 (t, *J* = 7.9 Hz, 2H), NH[7.21 (s, 0.65H)+6.83(s, 0.25H)], 7.14 (t, *J* = 7.3 Hz, 1H), 4.58 (d, *J* = 11.1 Hz, 1H), 4.46 (s, 1H), 3.95 (s, 3H), 2.02 (s, 3H), *t*-Bu[1.37 (s, 6.5H)+1.12 (s, 2.5H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.4, 167.7, 157.8, 153.9, 137.4, 137.1, 133.1, 132.2, 129.2, 129.1, 128.8, 128.8, 128.6, 128.6, 128.0, 127.6, 127.6, 126.8, 126.7, 125.7, 125.5, 118.7, 86.3, 80.8, 71.7, 68.6, 53.8, 28.3, 15.6.

HRMS (TOF MS ESI$^+$) calculated for $C_{35}H_{35}N_3O_6Na^+$ [M + Na]$^+$: 616.2418, found 616.2420.

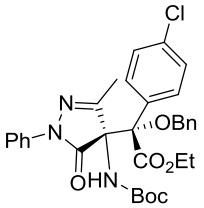


Methyl-(*S)-2-(benzo[d][1,3]dioxol-5-yl)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)acetate (5g).** White solid, mp 135.0-136.3 °C. 110.3 mg, 94% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.51 – 7.42 (comp, 6H), 7.39 (m, 3H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.11 (s, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 6.83 – 6.75 (m, 2H), 5.98 (s, 1H), 5.82 (s, 1H), 4.47 (d, *J* = 11.3 Hz, 1H), 4.39 (d, *J* = 11.2 Hz, 1H), 3.90 (s, 3H), 2.00 (s, 3H), *t*-Bu[1.36 (s, 6.5H)+1.14(s, 2.5H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.4, 167.7, 157.9, 153.8, 148.1, 147.1, 137.5, 137.1, 129.3, 129.1, 128.5, 127.7, 125.5, 124.4, 122.5, 118.8, 109.2, 107.6, 101.8, 86.0, 80.8, 71.7, 68.3, 53.7, 28.3, 15.6.

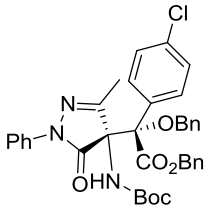
HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{33}N_3O_8Na^+$ [M + Na]$^+$: 610.2160, found 610.2163.



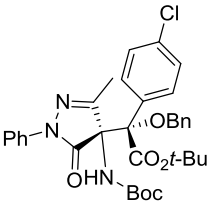
Ethyl-(*S)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-(4-chlorophenyl)acetate (5h).**

White solid, mp 101.5-102.2 °C. 111.0 mg, 94% yield.

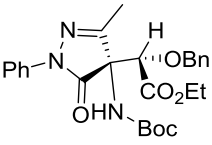
^{1}H NMR (500 MHz, DMSO-d_6) δ 7.50 (d, *J* = 7.1 Hz, 2H), 7.46 (m, 4H), 7.43 (s, 1H), 7.42 – 7.35 (m, 4H), 7.30 (d, *J* = 8.3 Hz, 2H), 7.19 (t, *J* = 7.3 Hz, 1H), 7.11 (s, 1H), 4.55 – 4.29 (comp, 4H), 2.03 (s, 3H), 1.43 – 1.29 (comp, 9H), 1.12 (s, 3H).
^{13}C NMR (125 MHz, DMSO-*d*) δ 169.2, 166.5, 157.7, 153.8, 137.4, 136.9, 134.4, 130.7, 130.1, 129.3, 129.1, 128.5, 127.9, 127.8, 125.6, 118.9, 85.6, 80.7, 71.4, 68.3, 63.2, 28.3, 15.6, 14.2.
HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{34}N_3O_6ClNa^+$ [M + Na]$^+$: 614.2028, found 614.2028.



Benzyl-(*S)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-(4-chlorophenyl)acetate (5i).**
White solid, mp 107.2-108.0 °C. 117.7 mg, 90% yield.
^{1}H NMR (400 MHz, DMSO-d_6) δ 7.52 (d, *J* = 5.4 Hz, 2H), 7.42 (comp, 14H), 7.29 (d, *J* = 7.8 Hz, 2H), 7.20 (t, *J* = 7.3 Hz, 1H), 7.00 (s, 1H), 5.49 (d, *J* = 12.2 Hz, 1H), 5.35 (s, 1H), 4.46 (d, *J* = 11.0 Hz, 1H), 4.36 (d, *J* = 10.5 Hz, 1H), 2.01 (s, 3H), *t*-Bu[1.30 (s, 7H)+1.13 (s, 2H)].
^{13}C NMR (125 MHz, DMSO-d_6) δ 169.2, 166.5, 157.7, 153.6, 137.4, 136.7, 135.2, 134.5, 130.6, 130.0, 129.3, 129.1, 129.0, 129.0, 128.9, 128.6, 128.0, 127.8, 125.7, 118.9, 85.8, 80.7, 71.4, 68.8, 68.4, 28.2, 15.6.
HRMS (TOF MS ESI$^+$) calculated for $C_{37}H_{36}N_3O_6ClNa^+$ [M + Na]$^+$: 676.2185, found 676.2180.



***t*-Butyl-(*S**)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-(4-chlorophenyl)acetate (5j).**
White solid, mp 119.6-120.5 °C. 81.6 mg, 66% yield.
^{1}H NMR (400 MHz, DMSO-d_6) δ 7.53 – 7.51 (m, 2H), 7.49 – 7.45 (comp, 3H), 7.43 (s, 2H), 7.42 – 7.35 (comp, 4H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.04 (s, 1H), 4.53 (d, *J* = 11.2 Hz, 1H), 4.37 (d, *J* = 11.2 Hz, 1H), 2.04 (s, 3H), 1.58 (s, 9H), *t*-Bu[1.36 (s, 7H)+1.13 (s, 2H)].
^{13}C NMR (125 MHz, DMSO-d_6) δ 169.3, 165.0, 157.7, 153.7, 137.4, 137.1, 134.3, 130.8, 130.2, 129.3, 129.1, 128.5, 127.7, 127.7, 125.6, 118.9, 85.9, 85.6, 80.6, 71.3, 68.1, 28.3, 28.0, 15.7.
HRMS (TOF MS ESI$^+$) calculated for $C_{34}H_{38}N_3O_6ClNa^+$ [M + Na]$^+$: 642.2341, found 642.2344.



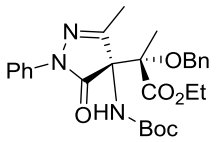
Ethyl-(*S)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4, 5-dihydro-1H-pyrazol-4-yl)acetate (5k).**

White solid, mp 157.1-157.9 °C. 91.4 mg, 95% yield.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.93 (s, 1H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.49 – 7.34 (comp, 6H), 7.34 – 7.26 (m, 1H), 7.18 (t, *J* = 7.3 Hz, 1H), 4.62 (d, *J* = 10.7 Hz, 1H), 4.47 (d, *J* = 10.8 Hz, 1H), 4.35 (s, 1H), 4.04 – 3.95 (m, 1H), 3.95 – 3.86 (m, 1H), 2.04 (s, 3H), *t*-Bu[1.35 (s, 6.5H)+1.15 (s, 2.5H)], 0.94 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.9, 167.7, 159.4, 154.4, 138.3, 137.6, 129.4, 128.8, 128.7, 128.2, 128.2, 125.1, 118.1, 80.3, 79.4, 72.7, 68.0, 62.0, 28.4, 15.2, 14.0.

HRMS (TOF MS ESI$^+$) calculated for $C_{26}H_{31}N_3O_6Na^+$ [M + Na]$^+$: 504.2105, found 504.2106.



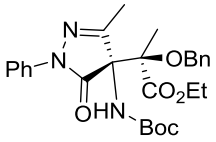
Ethyl-(*S)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4, 5-dihydro-1H-pyrazol-4-yl)propanoate (*syn*-5l).**

White solid, mp 100.6-101.5 °C. 43.6 mg, 44% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.77 (d, *J* = 6.6 Hz, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.38 – 7.27 (comp, 5H), 7.21 (t, *J* = 7.3 Hz, 1H), 6.62 (s, 1H), 4.58 (d, *J* = 10.9 Hz, 1H), 4.28 (comp, 3H), 2.03 (s, 3H), 1.51 (s, 3H), *t*-Bu[1.33 (s, 6H) +1.13 (s, 3H)], 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.5, 158.4, 153.8, 138.1, 137.7, 129.5, 128.8, 128.2, 128.1, 125.4, 118.5, 80.8, 80.5, 70.4, 67.0, 62.5, 28.3, 15.6, 15.2, 14.3.

HRMS (TOF MS ESI$^+$) calculated for $C_{27}H_{33}N_3O_6Na^+$ [M + Na]$^+$:518.2262, found 518.2264.



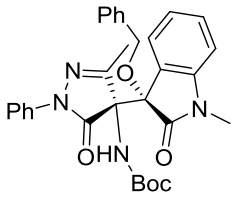
Ethyl-(*R)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4 ,5-dihydro-1H-pyrazol-4-yl)propanoate (*anti*-5l).**

White solid, mp 133.8-134.6 °C. 45.5 mg, 46% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.84 – 7.72 (m, 3H), 7.48 (d, *J* = 7.3 Hz, 2H), 7.45 – 7.34 (comp, 4H), 7.32 (t, *J* = 7.0 Hz, 1H), 7.17 (t, *J* = 6.8 Hz, 1H), 4.57 (d, *J* = 10.0 Hz, 1H), 4.35 (d, *J* = 9.9 Hz, 1H), 4.13 – 3.93 (m, 1H), 3.92 – 3.71 (m, 1H), 2.01 (s, 3H), 1.80 (s, 3H), *t*-Bu [1.34 (s, 6H)+1.12 (s, 3H)], 1.04 – 0.83 (m, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 170.0, 169.5, 160.3, 154.7, 138.4, 138.3, 129.3, 128.6, 128.5, 128.1, 124.9, 118.2, 83.7, 80.2, 69.8, 67.1, 62.3, 28.5, 16.2, 13.9, 13.8.

HRMS (TOF MS ESI$^+$) calculated for $C_{27}H_{33}N_3O_6Na^+$ [M + Na]$^+$:518.2262, found 518.2264.



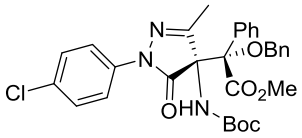
tert-Butyl-((*R)-4-((*S**)-3-(benzyloxy)-1-methyl-2-oxoindolin-3-yl)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)carbamate (5m).**

White solid, mp 194.9-195.9 °C. 80.0 mg, 74% yield.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.40 – 7.31 (comp, 5H), 7.31 – 7.19 (comp, 7H), 7.15 – 7.07 (m, 2H), 7.02 (t, *J* = 7.5 Hz, 1H), 4.09 (d, *J* = 10.6 Hz, 1H), 4.00 (d, *J* = 10.6 Hz, 1H), 3.20 (s, 3H), 2.28 (s, 3H), *t*-Bu[1.35 (s, 6.5H)+ 1.14 (s, 2.5H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 171.5, 168.7, 156.9, 154.1, 144.6, 137.2, 136.8, 132.4, 129.1, 128.9, 128.5, 128.5, 128.3, 125.6, 125.2, 123.3, 119.9, 119.0, 110.2, 81.0, 80.2, 71.1, 68.0, 28.3, 26.8, 16.3.

HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{32}N_4O_5Na^+$ [M + Na]$^+$: 563.2265, found 563.2260.



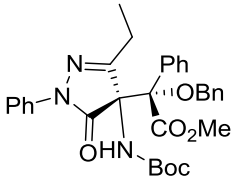
Methyl-(*S)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-1-(4-chlorophenyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-2-phenylacetate (5n).**

White solid, mp 152.9-153.6 °C. 102.6 mg, 89% yield.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.54 – 7.43 (m, 7H), 7.43 – 7.34 (m, 4H), 7.29 (t, *J* = 7.3 Hz, 1H), 7.21 (comp, 3H), 4.48 (d, *J* = 11.1 Hz, 1H), 4.40 (d, *J* = 11.1 Hz, 1H), 3.91 (s, 3H), 2.00 (s, 3H), *t*-Bu[1.35 (s, 6H)+1.13 (s, 3H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.4, 167.6, 158.1, 153.9, 137.0, 136.3, 131.0, 129.6, 129.3, 129.3, 129.1, 128.5, 127.8, 127.8, 120.1, 86.0, 80.9, 71.7, 68.3, 53.7, 28.3, 15.6.

HRMS (TOF MS ESI$^+$) calculated for $C_{31}H_{32}N_3O_6ClNa^+$ [M + Na]$^+$: 600.1872, found 600.1868.



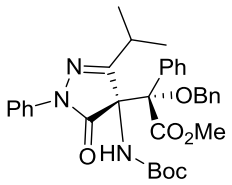
Methyl-(*S)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-ethyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-phenylacetate (5o).**

White solid, mp 121.4-122.2 °C. 96.1 mg, 86% yield.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.53 – 7.44 (comp, 6H), 7.43 – 7.34 (comp, 5H), 7.30 (t, *J* = 7.3 Hz, 1H), 7.19 (q, *J* = 7.3 Hz, 3H), NH[7.12 (s, 0.75H)+6.76(s, 0.25H)], 4.49 (d, *J* = 11.1 Hz, 1H), 4.39 (d, *J* = 11.1 Hz, 1H), 3.91 (s, 3H), 2.60 – 2.52 (m, 1H), 2.44 – 2.29 (m, 1H), 1.36 (s, 6H), 1.13 (s, 3H), 0.97 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.5, 167.7, 161.2, 153.8, 137.6, 137.0, 131.0, 129.5, 129.2, 129.1, 128.6, 128.5, 127.8, 127.7, 125.5, 118.8, 86.1, 80.7, 71.7, 68.3, 53.7, 28.3, 22.7, 9.7.

HRMS (TOF MS ESI$^+$) calculated for $C_{32}H_{35}N_3O_6Na^+$ [M + Na]$^+$: 580.2418, found 580.2418.



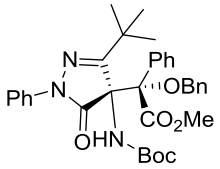
Methyl-(*S)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-isopropyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-phenylacetate (5p).**

White solid, mp 118.0-118.8 ºC. 95.8 mg, 84% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.55 – 7.44 (comp, 6H), 7.39 (m, 3H), 7.31 (m, 3H), 7.24 – 7.13 (comp, 4H), 4.57 – 4.31 (m, 2H), 3.89 (s, 3H), 3.04 (m, 1H), 1.35 (s, 6H), 1.19 – 1.00 (m, 6H), 0.88 (m, 6.8 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.3, 167.6, 163.2, 153.7, 137.7, 137.2, 131.1, 129.5, 129.3, 129.2, 128.6, 127.7, 127.5, 125.5, 118.9, 86.4, 80.5, 71.8, 68.3, 53.6, 30.1, 28.4, 21.9, 19.5.

HRMS (TOF MS ESI$^+$) calculated for $C_{33}H_{37}N_3O_6Na^+$ [M + Na]$^+$: 594.2575, found 594.2580.



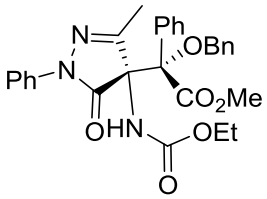
Methyl-(*S)-2-(benzyloxy)-2-((*R**)-4-((tert-butoxycarbonyl)amino)-3-(tert-butyl)-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-phenylacetate (5q).**

White solid, mp 125.5-126.5 ºC. 75.1 mg, 64% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ7.54 – 7.53 (m, 3H), 7.50 – 7.45 (m, 2H), 7.45 – 7.34 (comp, 6H), 7.28 (t, *J* = 7.0 Hz, 1H), 7.16 – 6.79 (comp, 4H), 4.51 – 4.30 (m, 2H), 3.88 (s, 3H), 1.38 (s, 6H), 1.12 (s, 6H), 1.09 (s, 6H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.7, 168.1, 165.6, 153.7, 137.6, 136.6, 131.4, 129.5, 129.4, 129.3, 129.0, 128.9, 128.7, 127.2, 125.5, 118.8, 87.8, 80.5, 74.3, 69.2, 53.4, 36.4, 30.7, 28.5.

HRMS (TOF MS ESI$^+$) calculated for $C_{34}H_{39}N_3O_6Na^+$ [M + Na]$^+$: 608.2731, found 608.2735.



Methyl-(*S)-2-(benzyloxy)-2-((*R**)-4-((ethoxycarbonyl)amino)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-phenylacetate (5r)**

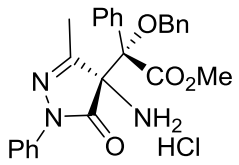
White solid, 88 mg, 86 % yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.2 Hz, 2H), 7.48 – 7.41 (comp, 6H), 7.41 – 7.36 (m, 1H), 7.30 (comp, *J* = 7.1 Hz, 3H), 7.20 (t, *J* = 7.6 Hz, 2H), 7.14 (d, *J* = 7.4 Hz, 1H), 7.04 (s, 1H), 4.56 (d, *J* = 11.1 Hz, 1H), 4.45 (d, *J* = 11.0 Hz, 1H), 4.10 (t, *J* = 7.1 Hz, 2H), 3.98 (s, 3H), 2.09 (s,

3H), 1.26 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 169.1, 167.7, 157.3, 154.6, 137.3, 136.4, 130.5, 129.6, 128.8, 128.6, 128.3, 128.3, 127.6, 127.1, 125.4, 119.7, 86.2, 71.7, 68.2, 61. 8, 53.3, 15.5, 14.5.

HRMS (TOF MS ESI$^+$) calculated for $C_{29}H_{29}N_3O_6Na^+$ [M + Na] $^+$: 538.1949, found 538.1913.



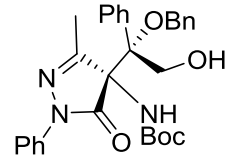
Methyl-(*S)-2-((*R**)-4-amino-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)-2-(benzyloxy)-2-phenylacetate (7a)**

White solid. mp 110.5-112.1 ºC, 46 mg, 96% yield

^{1}H NMR (500 MHz, $CDCl_3$-d) δ 10.15 (s, 2H), 7.64 (s, 2H), 7.43 (s, 2H), 7.26 (comp, 6H), 7.21 – 7.14 (comp, 4H), 7.11 (s, 1H), 4.57 (d, J = 10.5 Hz, 1H), 4.38 (d, J = 10.3 Hz, 1H), 3.98 (s, 3H), 2.22 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$-d) δ 166.6, 165.6, 155.0, 136.4, 135.6, 130.2, 129.6, 128.6, 128.5, 128.1, 128.0, 127.9, 126.1, 120.3, 85.2, 69.0, 68.2, 54.4, 16.7.

HRMS (TOF MS ESI+) calculated for $C_{26}H_{25}N_3O_4Na^+$ [M + Na]$^+$: 466.1737, found 466.1732.



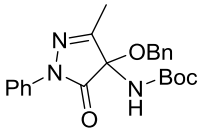
***tert*-Butyl-((*R**)-4-((*S**)-1-(benzyloxy)-2-hydroxy-1-phenylethyl)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)carbamate (8a)**

White solid, mp 125.5-126.3 ºC, 46.3 mg, 90% yield

^{1}H NMR (500 MHz, DMSO-d_6) δ NH8.25 (s, 1H), 7.47 (d, *J* = 7.0 Hz, 2H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.34 (t, *J* = 7.3 Hz, 1H), 7.31 – 7.12 (m, 9H), 7.07 (t, *J* = 7.0 Hz, 1H), 6.21 (t, *J* = 3.8 Hz, 1H), 5.13 (dd, *J* = 12.1, 4.8 Hz, 1H), 4.74 (t, *J* = 11.1 Hz, 1H), 4.22 (d, *J* = 10.7 Hz, 1H), 4.14 (dd, *J* = 12.2, 3.4 Hz, 1H), 2.14 (s, 3H), *t*-Bu[1.35 (s, 6.5H)+1.12 (s, 2.5H)].

^{13}C NMR (125 MHz, DMSO-d_6) δ 171.0, 159.3, 154.4, 138.4, 137.5, 134.8, 128.9, 128.9, 128.2, 128.1, 128.1, 127.0, 125.1, 118.8, 81.9, 80.1, 73.3, 65.2, 59.1, 28.4, 16.9.

HRMS (TOF MS ESI$^+$) calculated for $C_{30}H_{33}N_3O_5Na^+$ [M + Na]$^+$: 538.2312, found 538.2311.



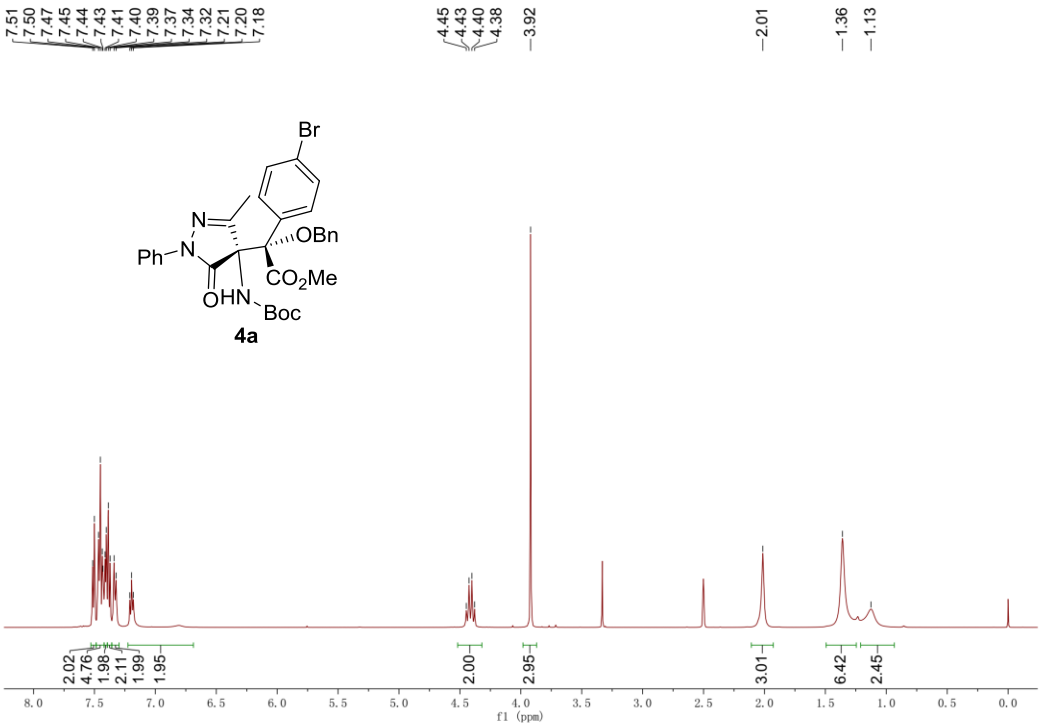
***tert*-Butyl-(4-(benzyloxy)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)carbamate(6a).**

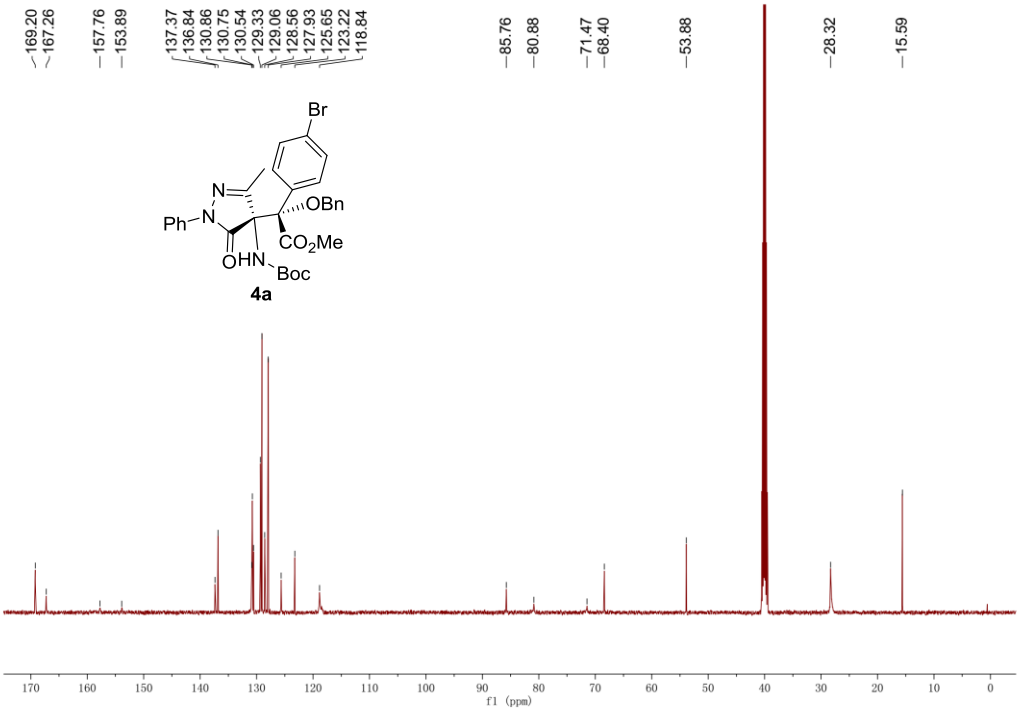
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 8.0 Hz, 2H), 7.41 (t, J = 7.9 Hz, 2H), 7.36 – 7.27 (m, 5H), 7.20 (t, J = 7.6 Hz, 1H), 5.35 (s, 1H), 4.66 (d, J = 10.9 Hz, 1H), 4.55 (d, J = 10.9 Hz, 1H), 2.19 (s, 3H), 1.36 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 157.3, 152.5, 137.6, 136.0, 128.9, 128.5, 128.3, 128.0, 125.3, 118.6, 85.7, 66.4, 28.1, 13.0.

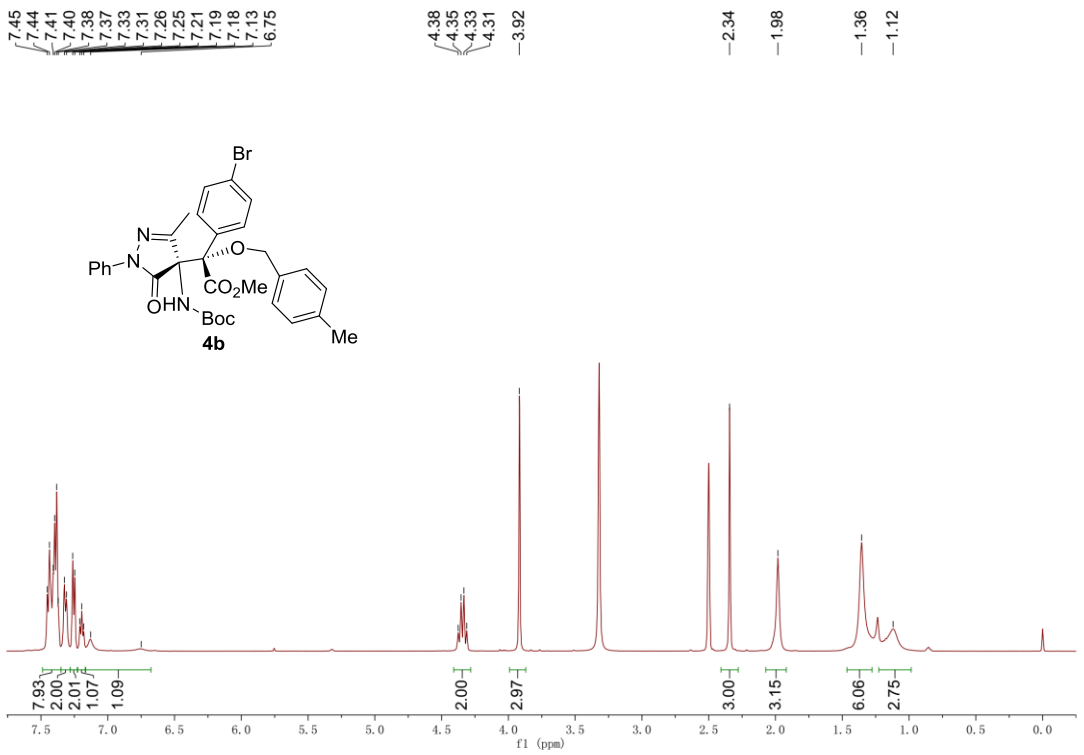
8. NMR spectra of products

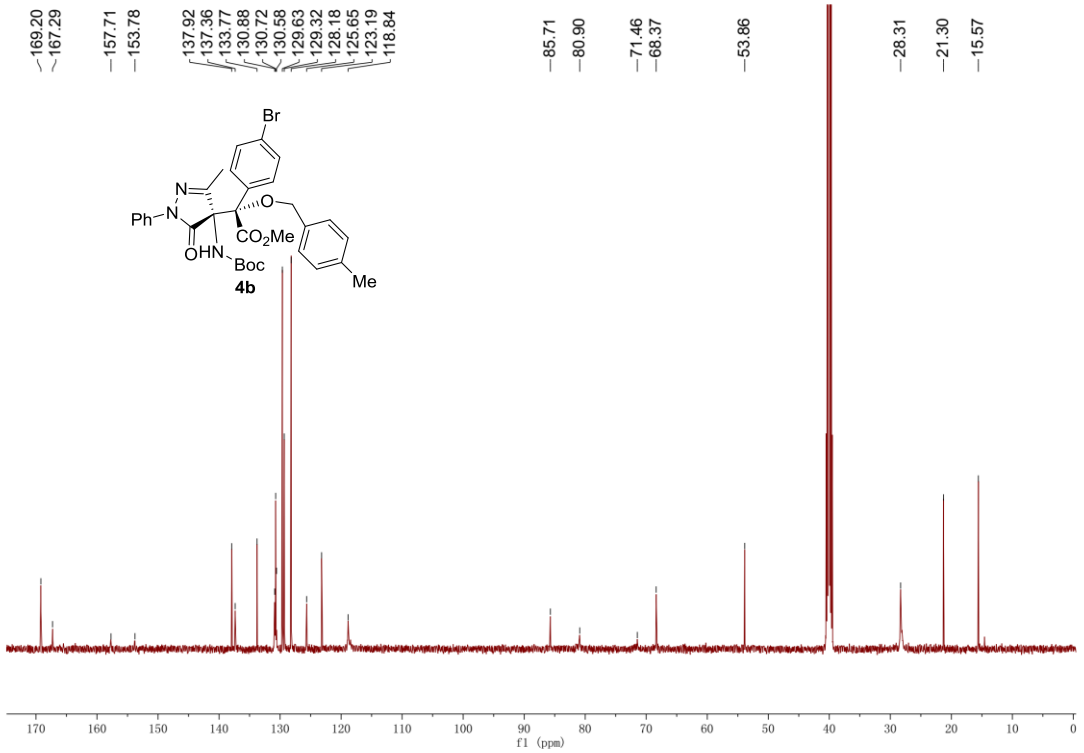
^{1}H NMR and ^{13}C NMR spectrum for **4a**



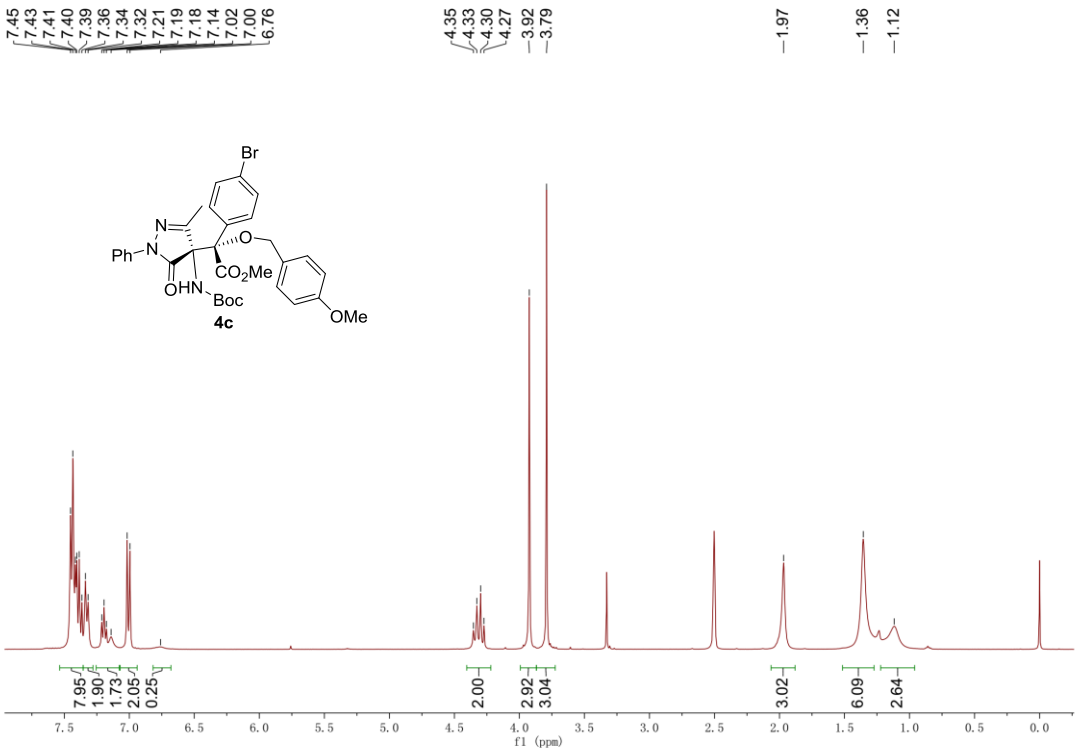


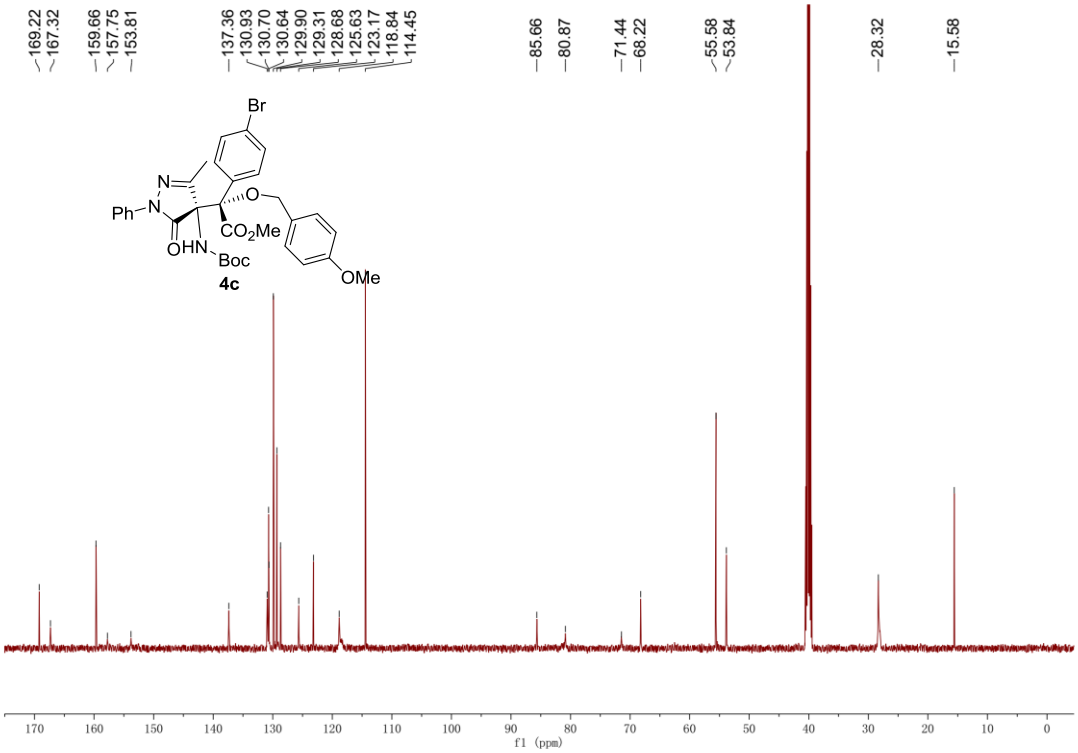
^{1}H NMR and ^{13}C NMR spectrum for **4b**



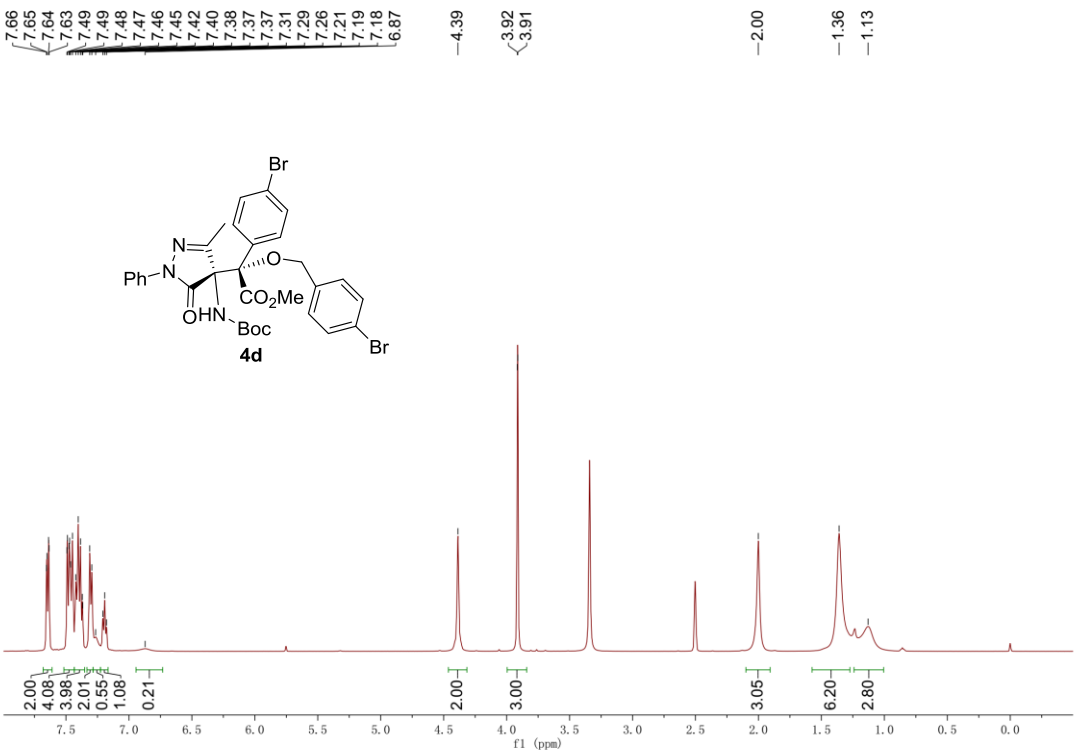


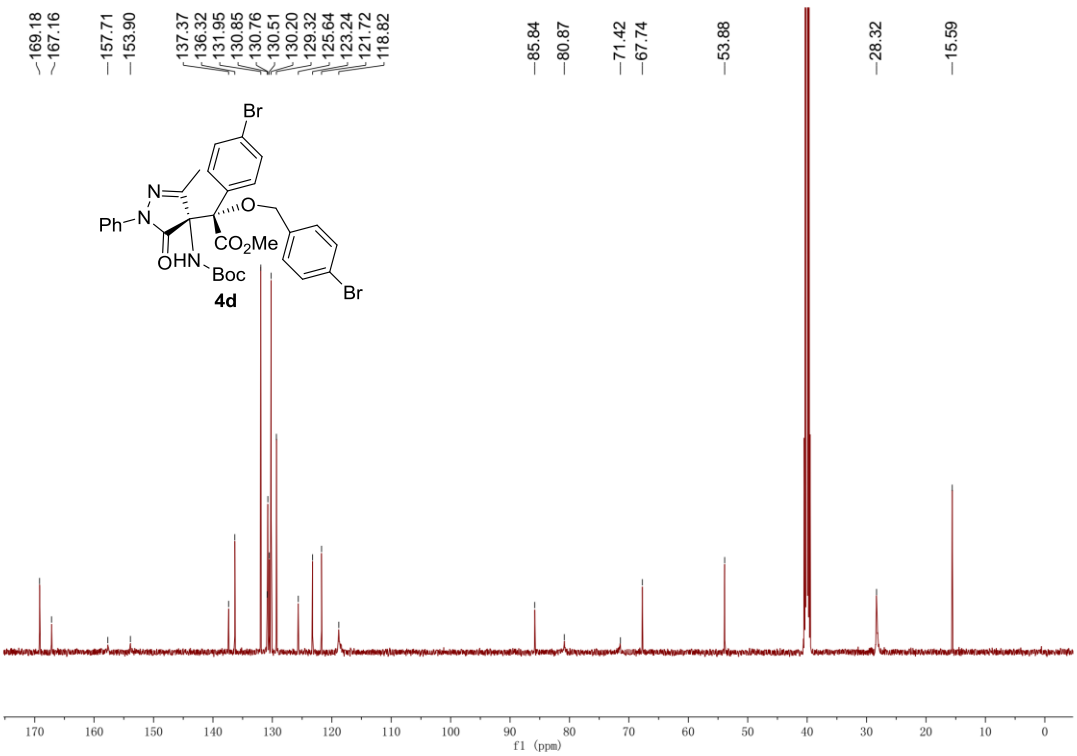
^{1}H NMR and ^{13}C NMR spectrum for **4c**



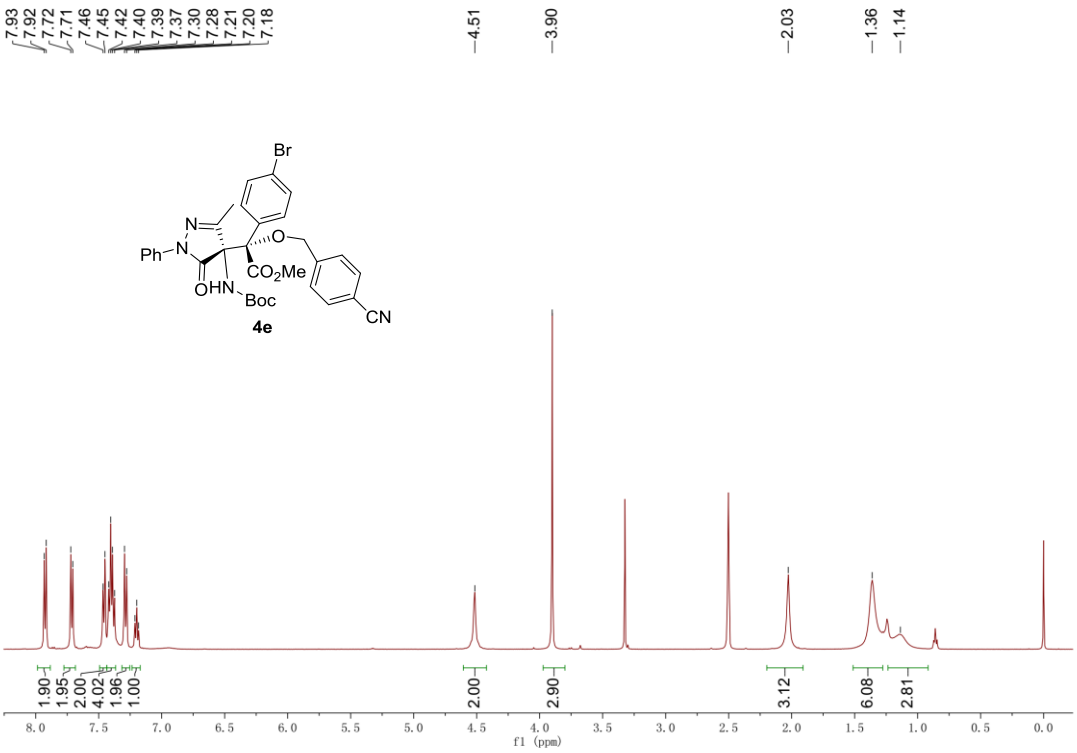


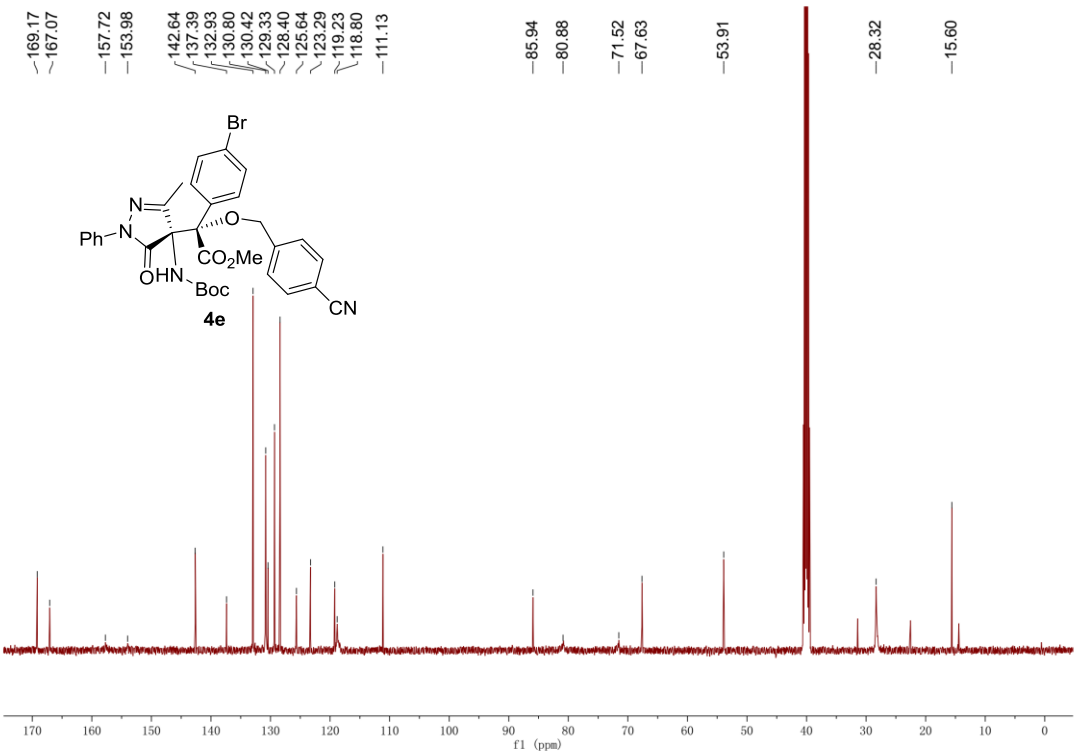
^{1}H NMR and ^{13}C NMR spectrum for **4d**



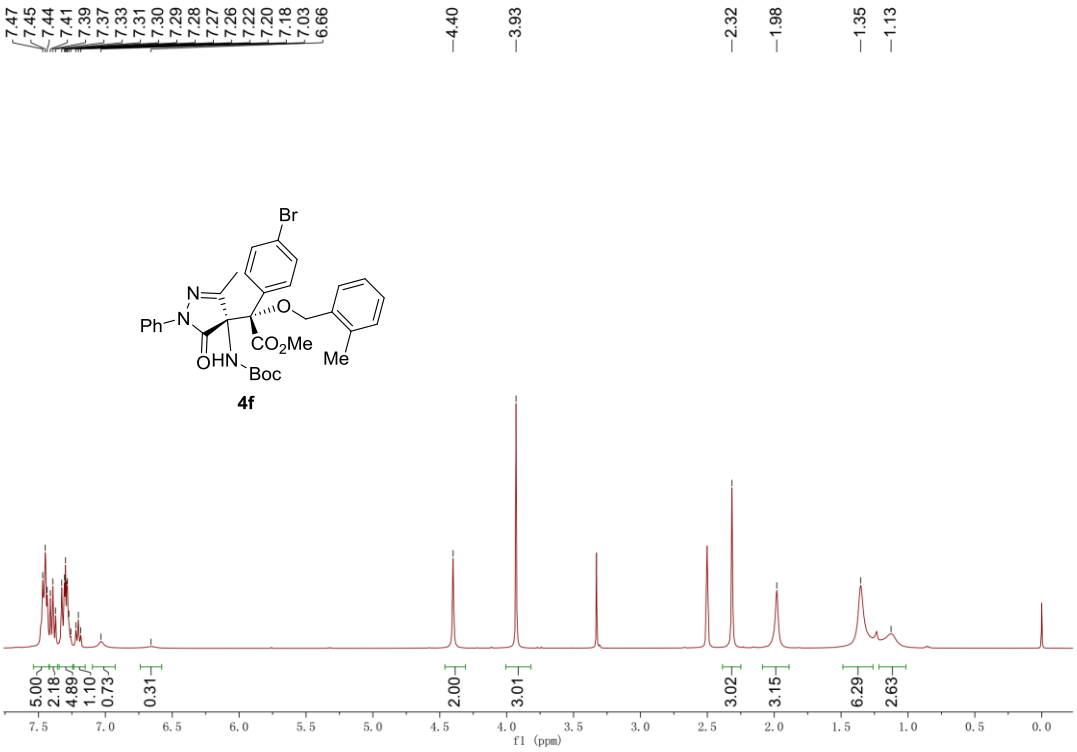


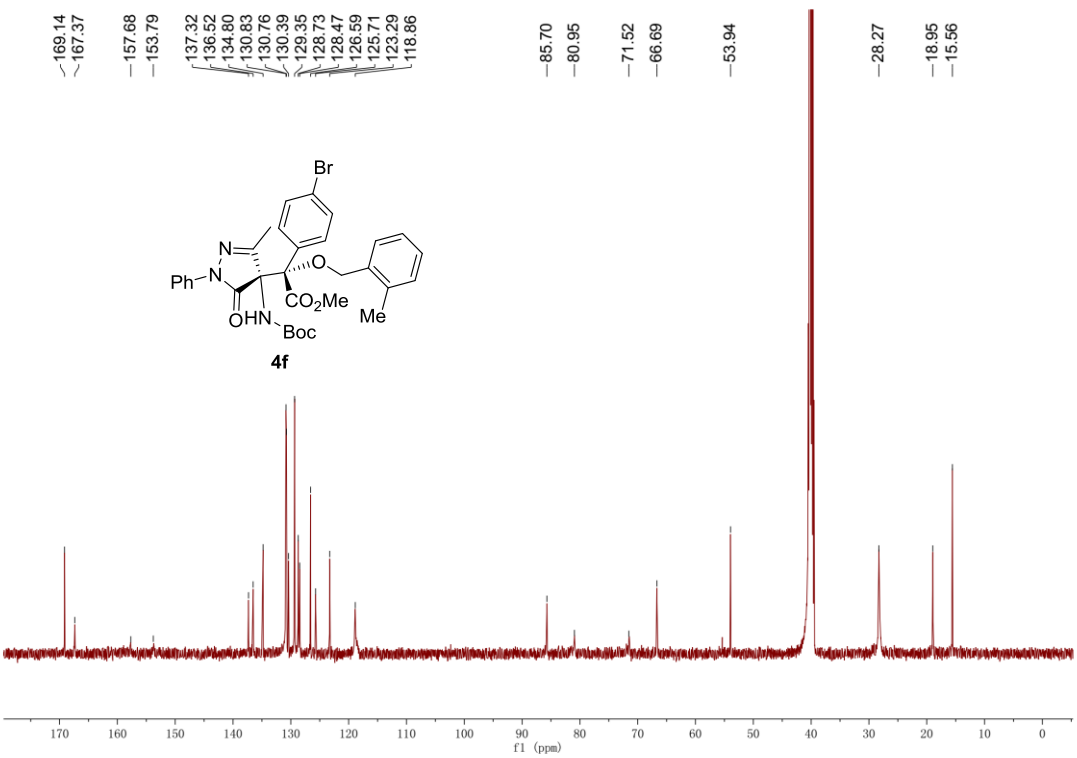
^{1}H NMR and ^{13}C NMR spectrum for **4e**



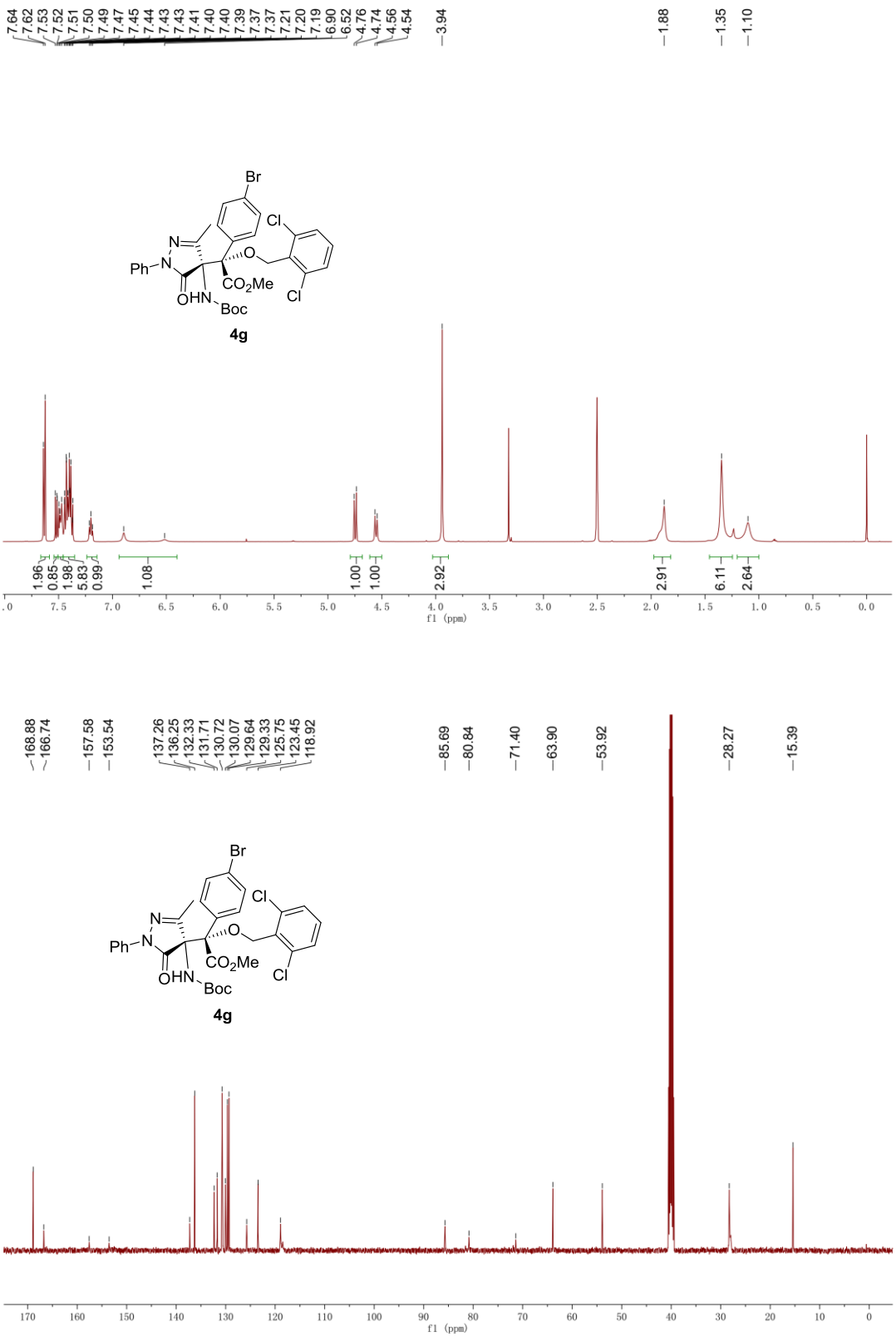


^{1}H NMR and ^{13}C NMR spectrum for **4f**

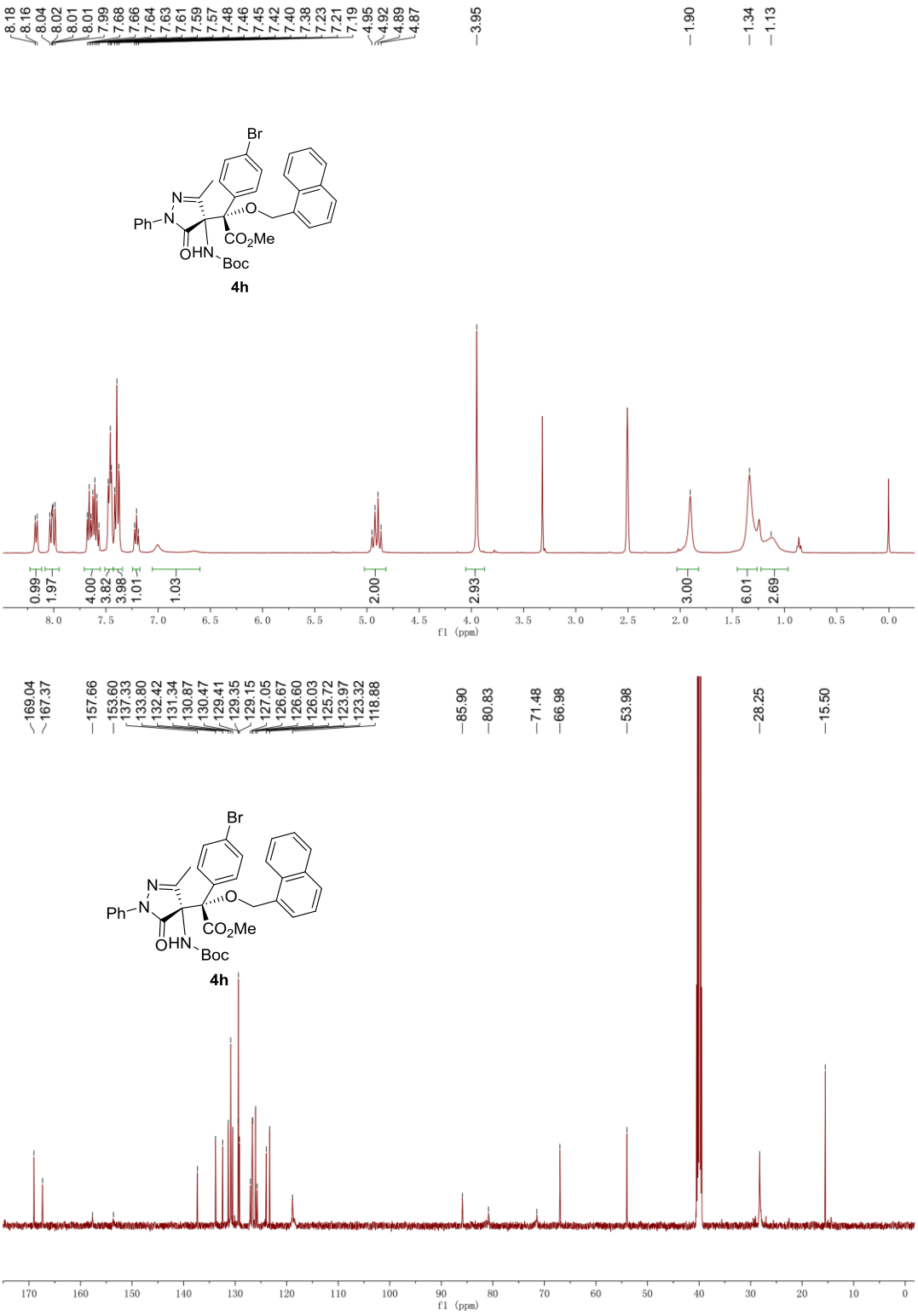




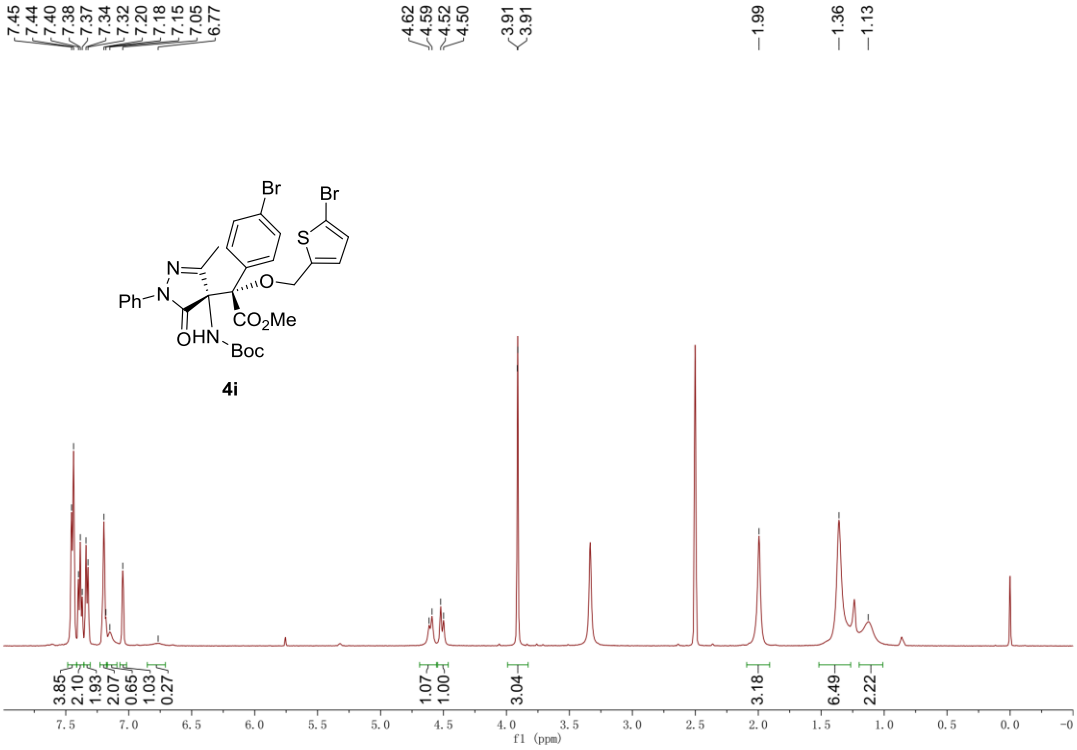
^{1}H NMR and ^{13}C NMR spectrum for **4g**

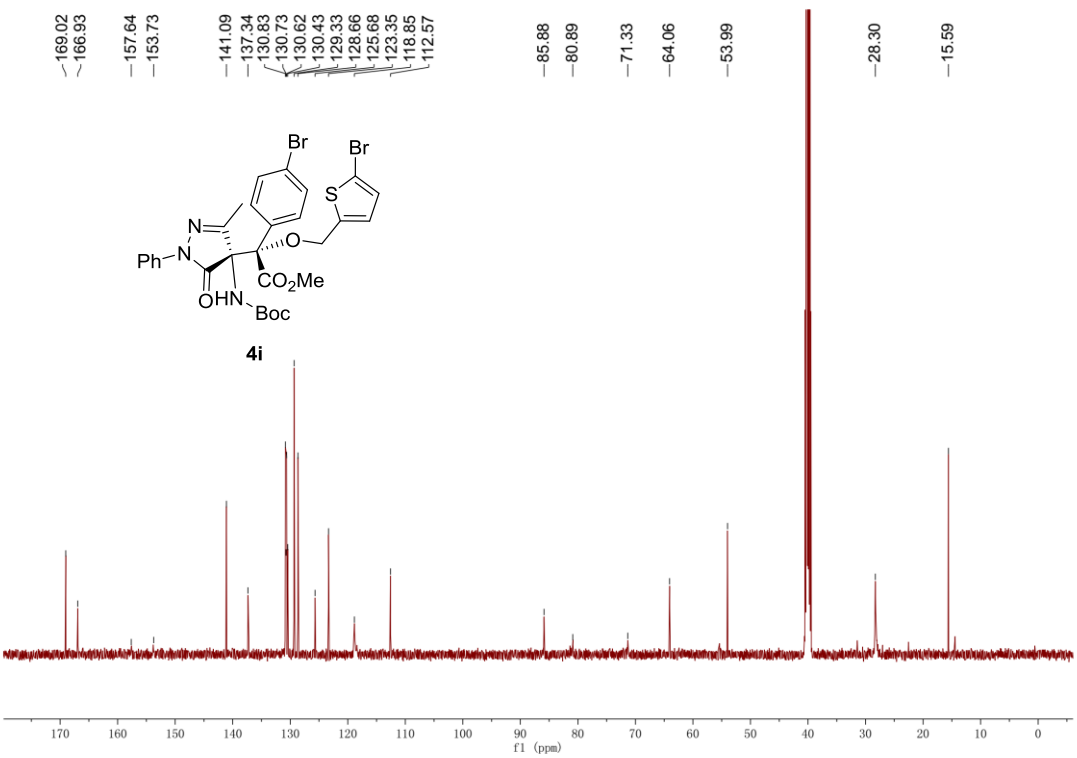


^{1}H NMR and ^{13}C NMR spectrum for **4h**

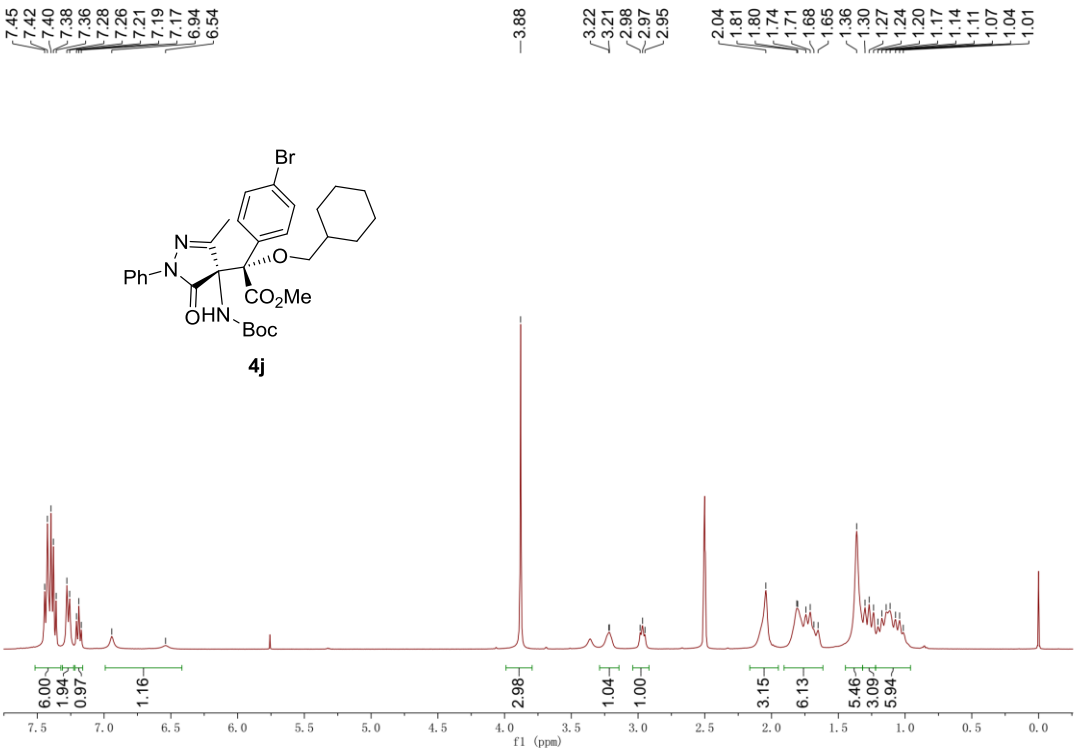


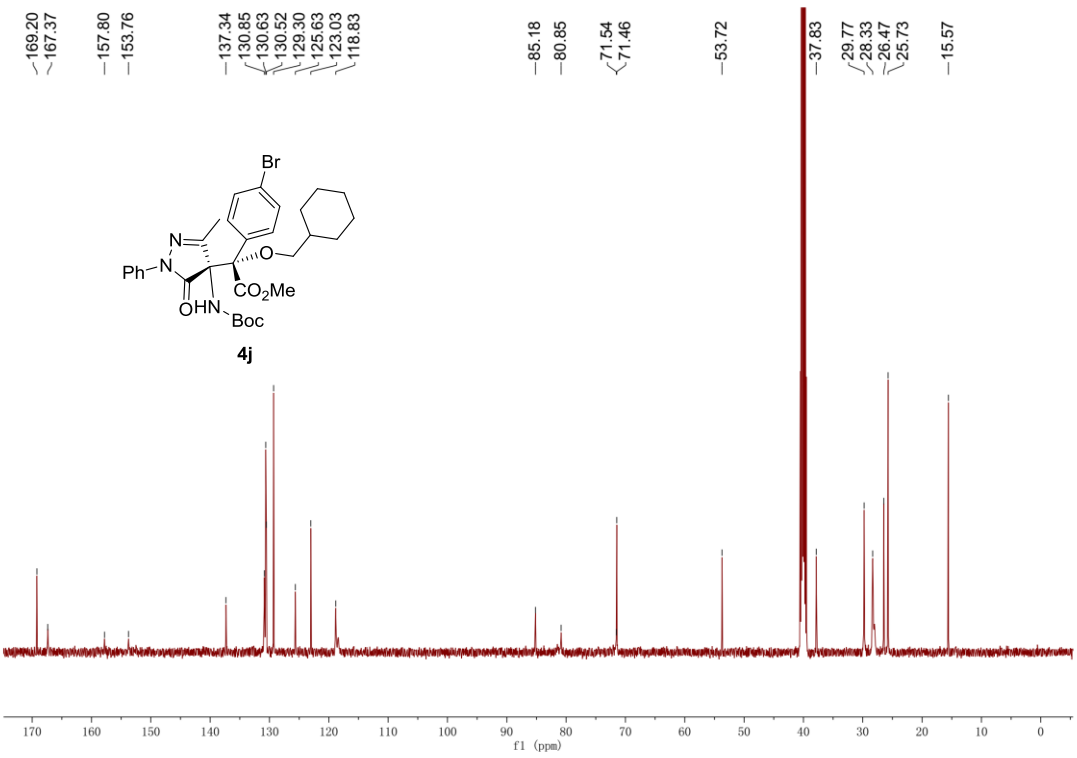
^{1}H NMR and ^{13}C NMR spectrum for **4i**



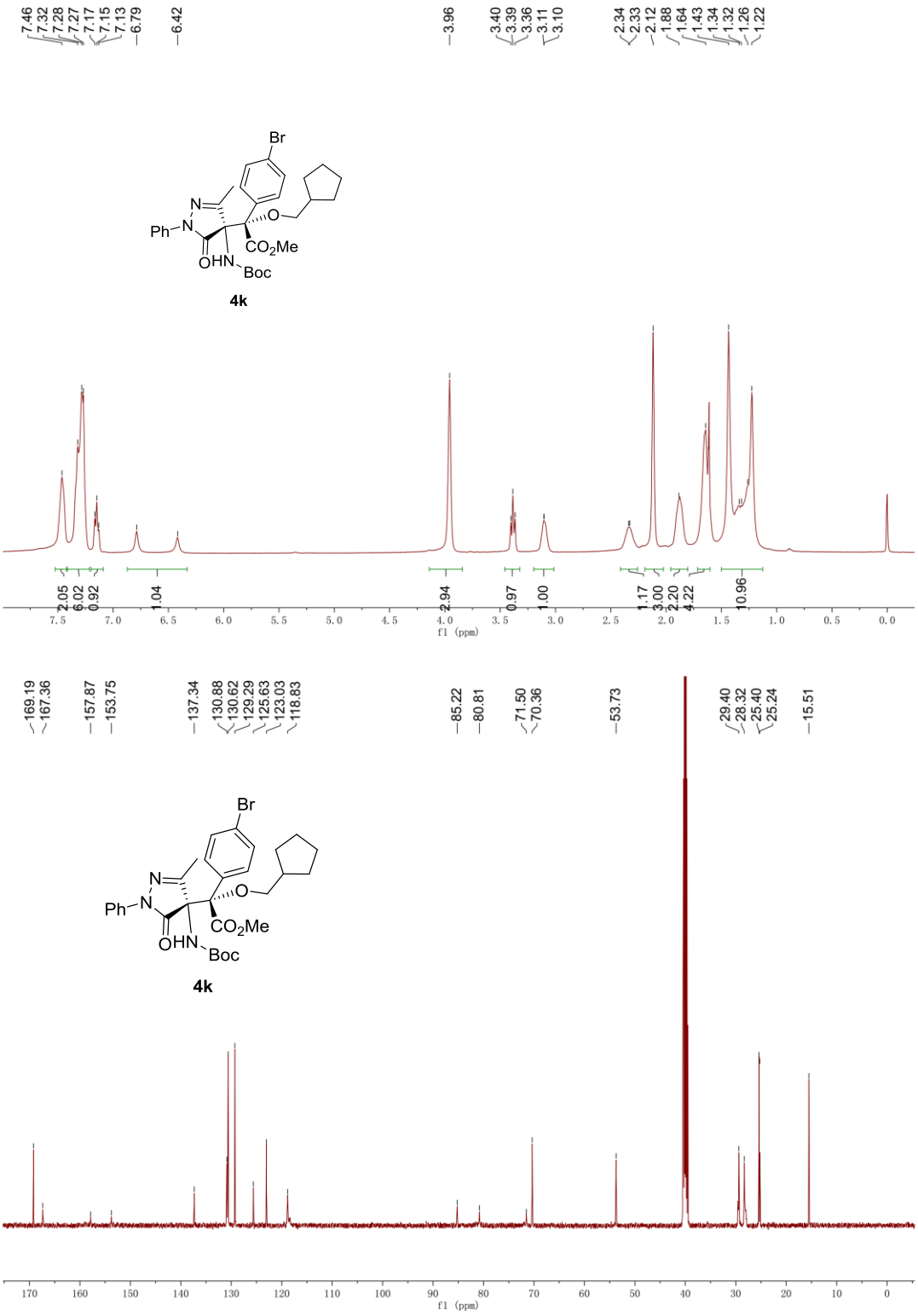


^{1}H NMR and ^{13}C NMR spectrum for **4j**

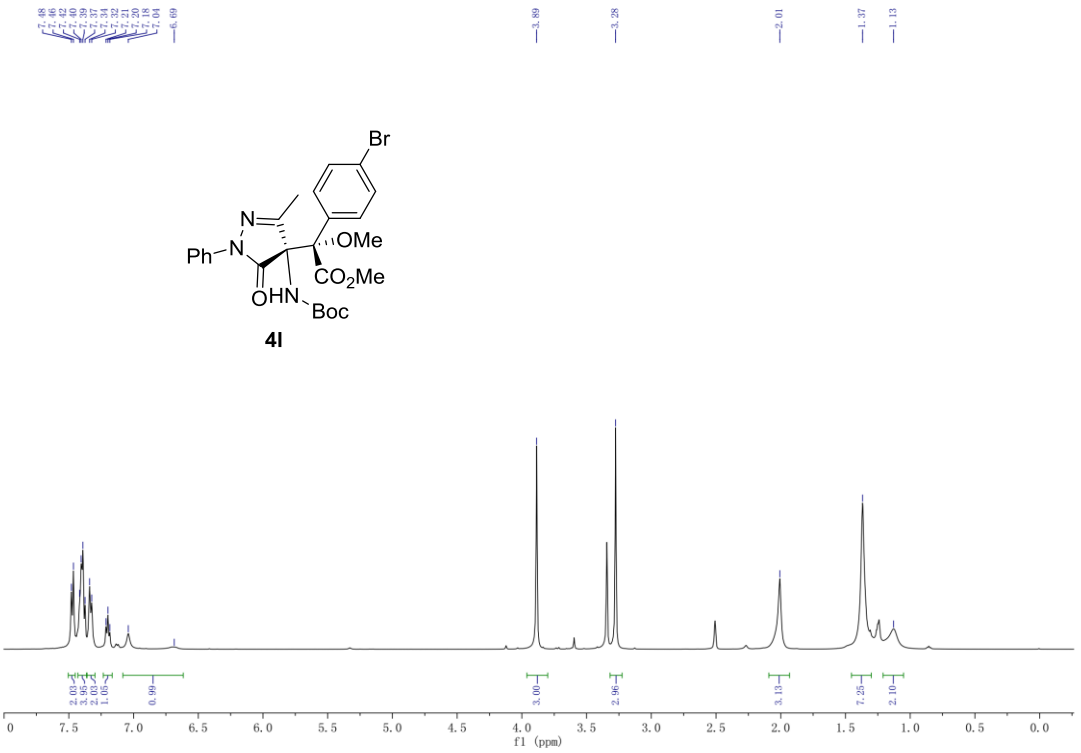


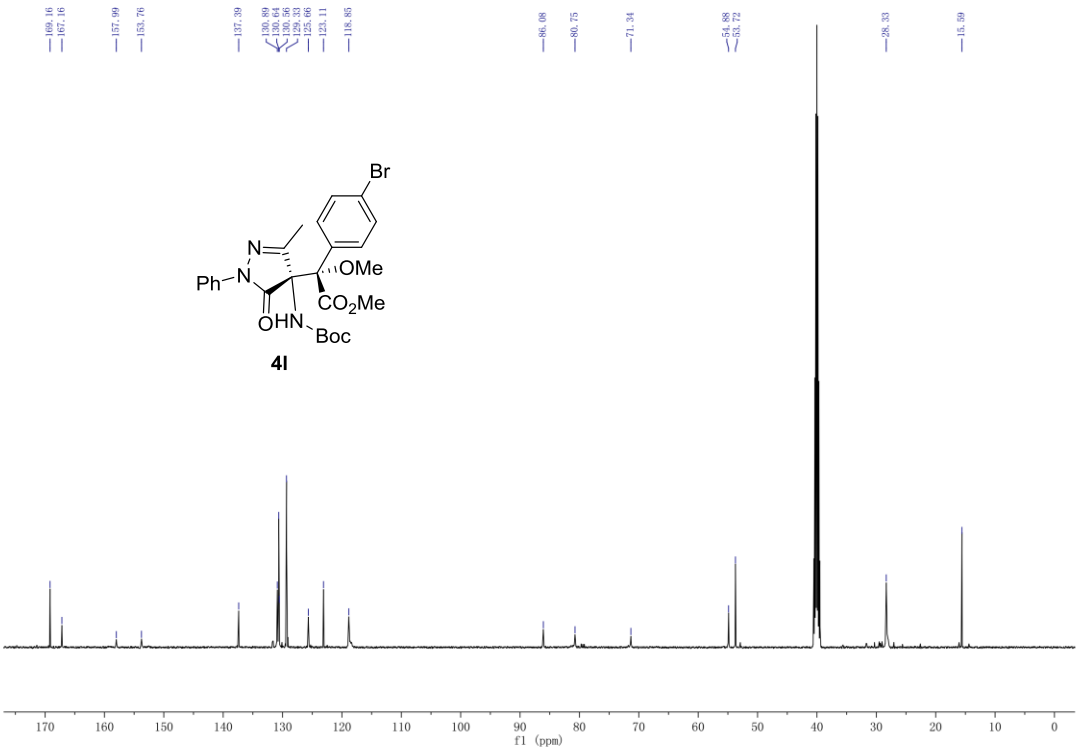


^{1}H NMR and ^{13}C NMR spectrum for **4k**

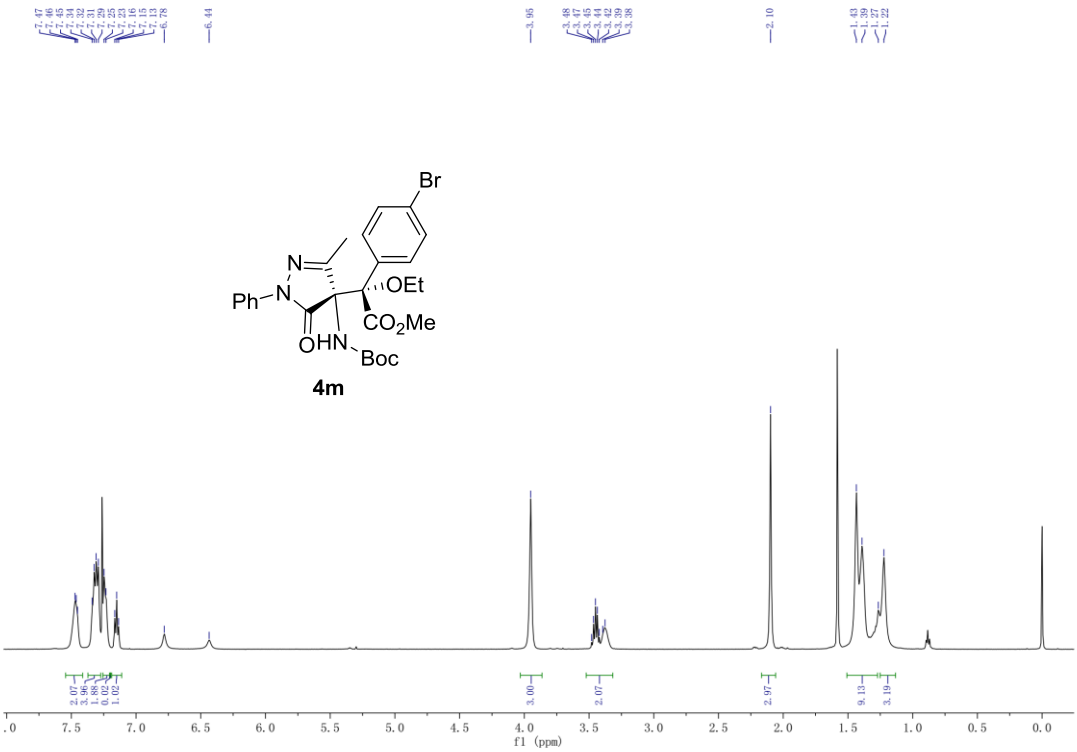


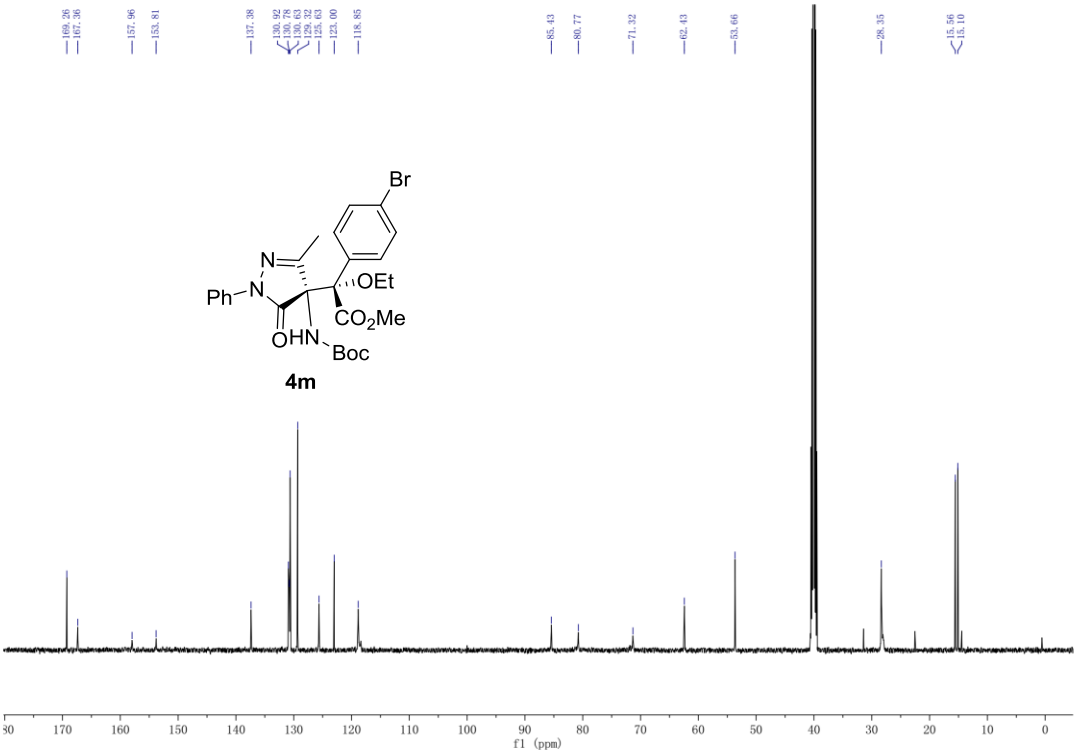
^{1}H NMR and ^{13}C NMR spectrum for **4l**



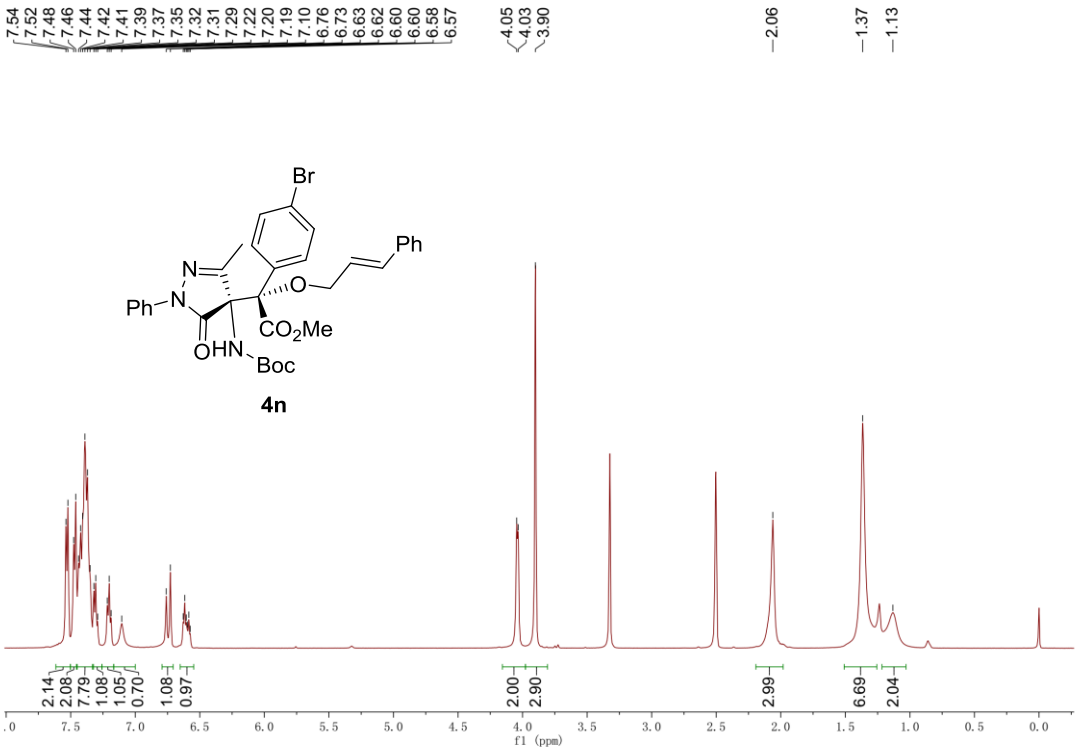


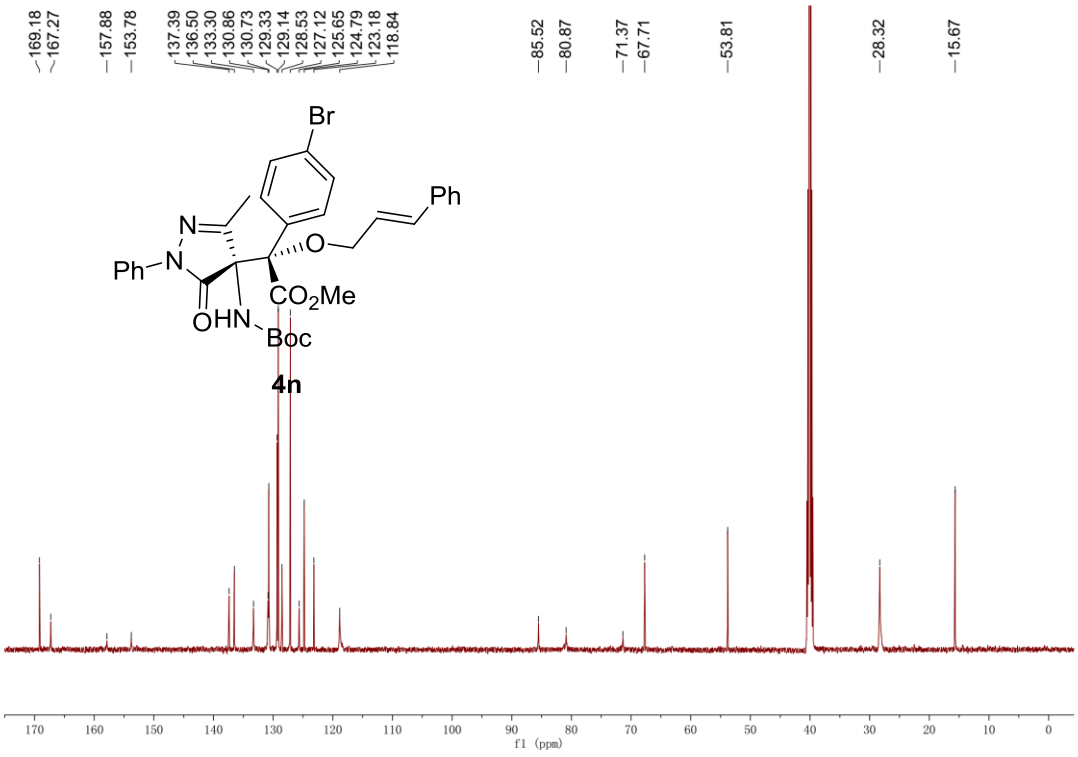
^{1}H NMR and ^{13}C NMR spectrum for **4m**



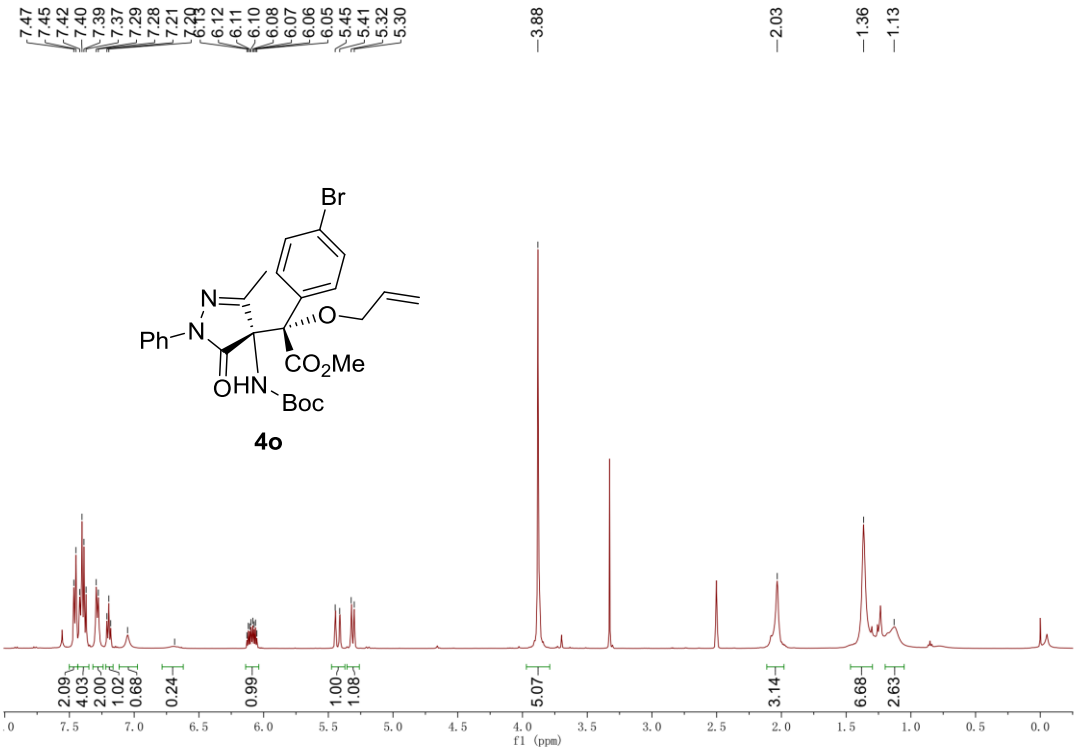


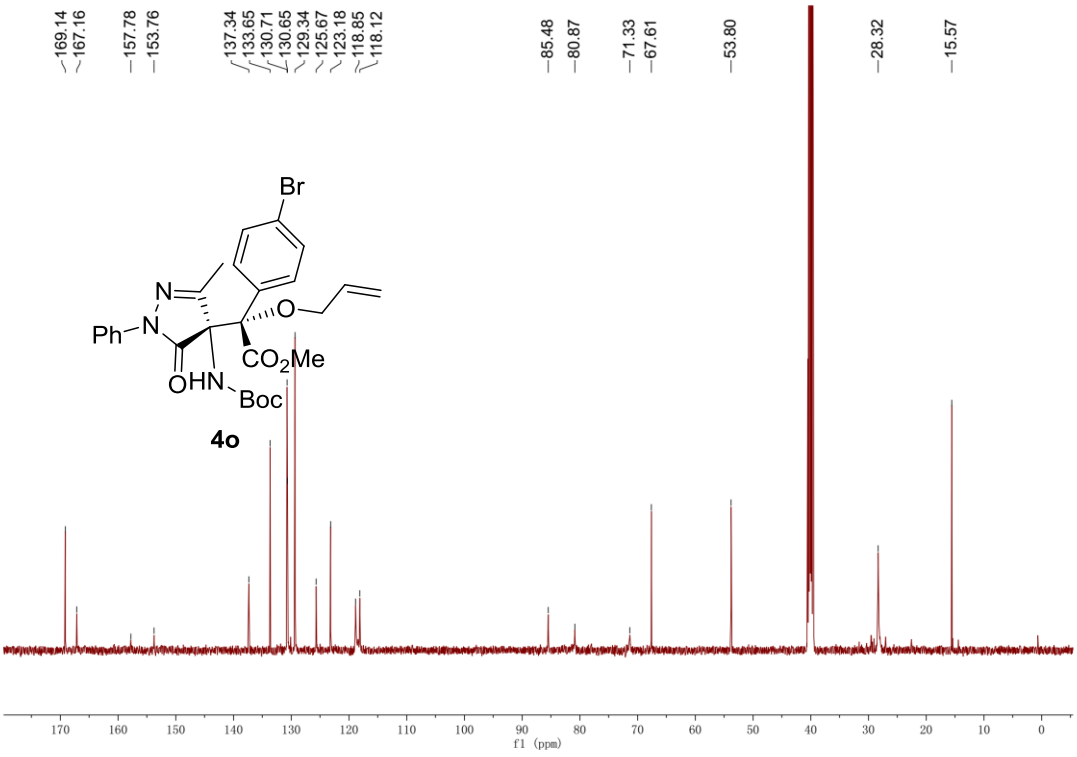
^{1}H NMR and ^{13}C NMR spectrum for **4n**



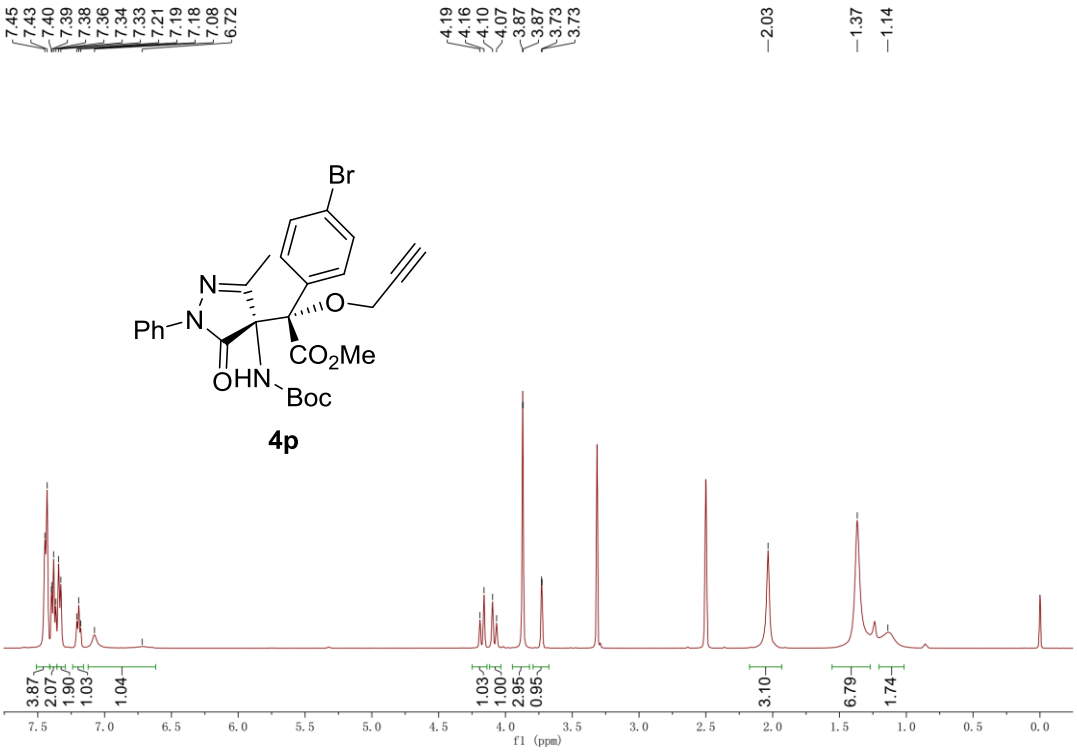


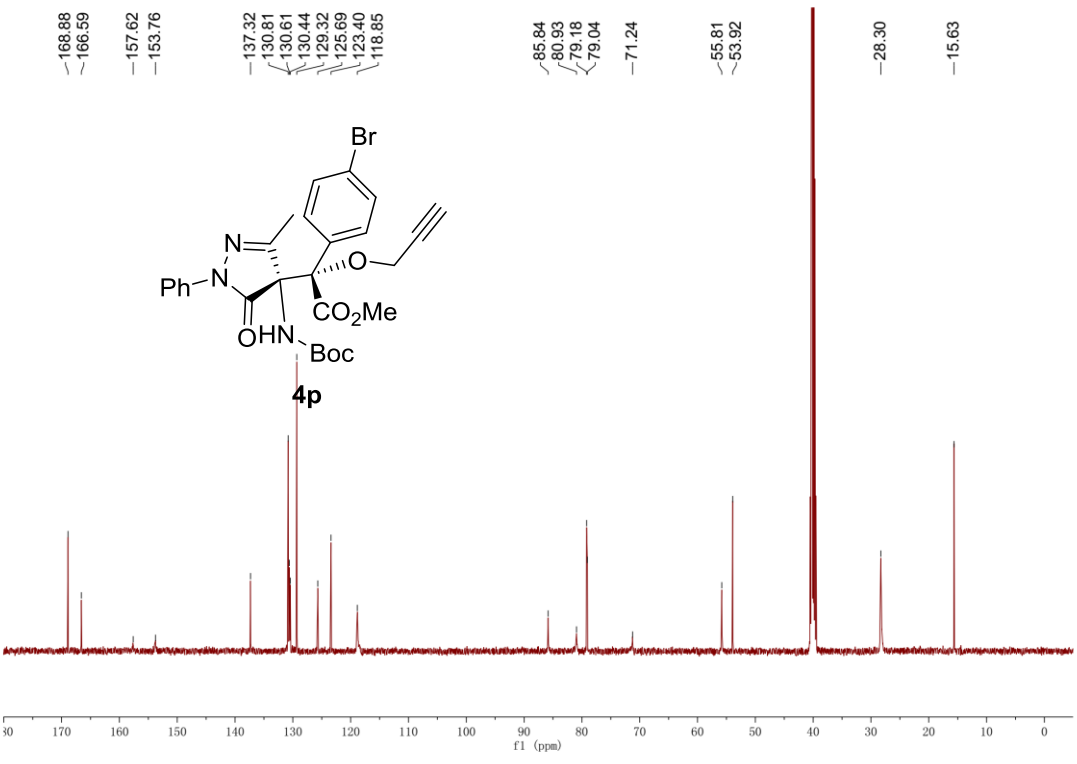
^{1}H NMR and ^{13}C NMR spectrum for **4o**



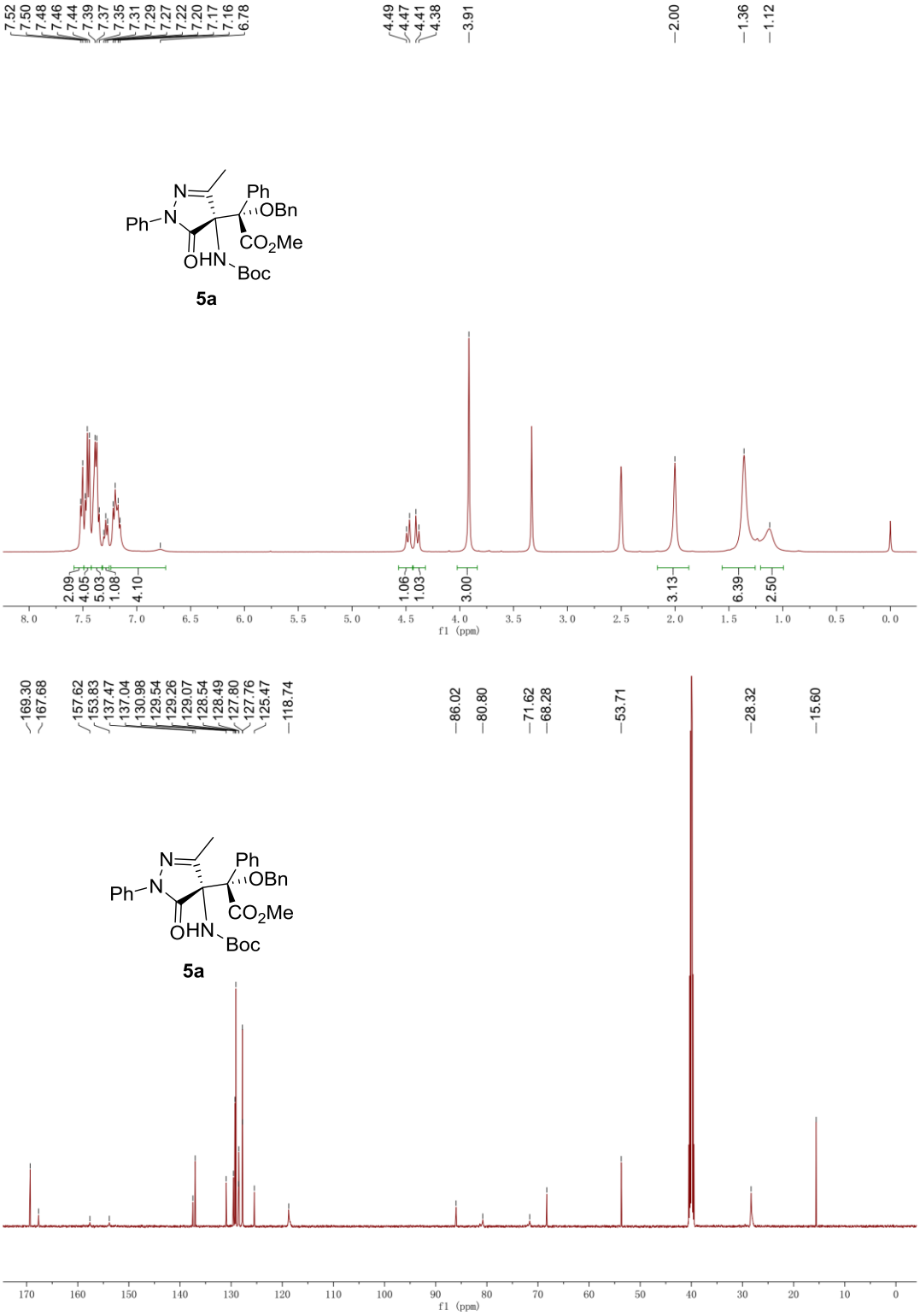


^{1}H NMR and ^{13}C NMR spectrum for **4p**

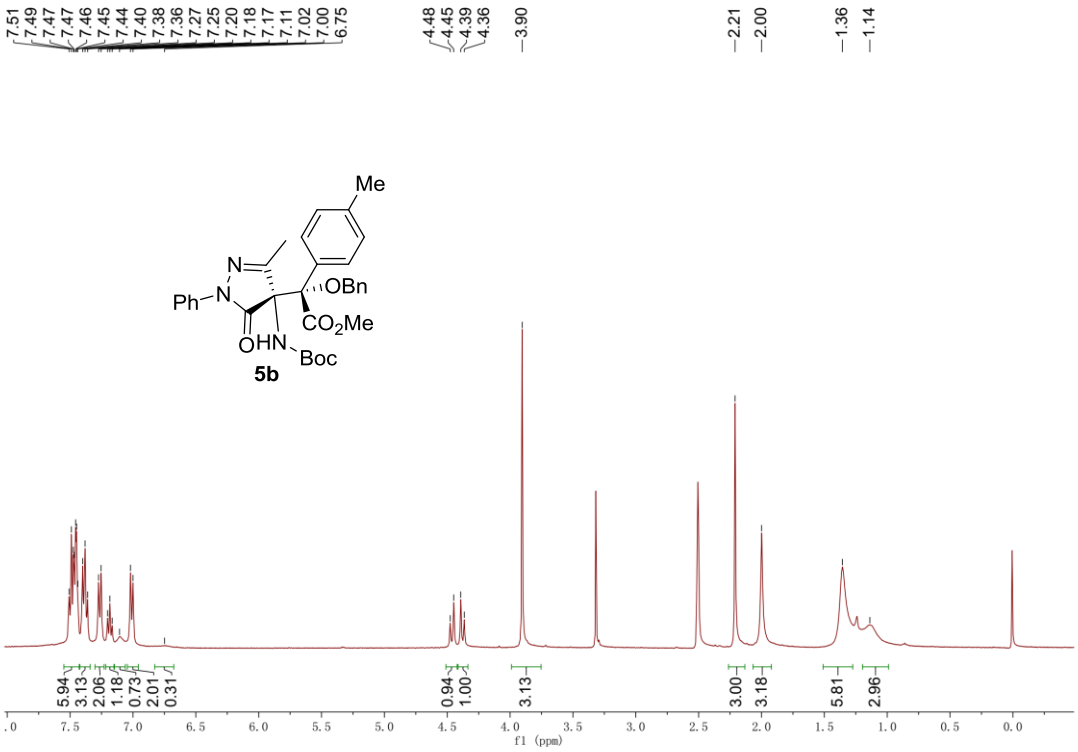


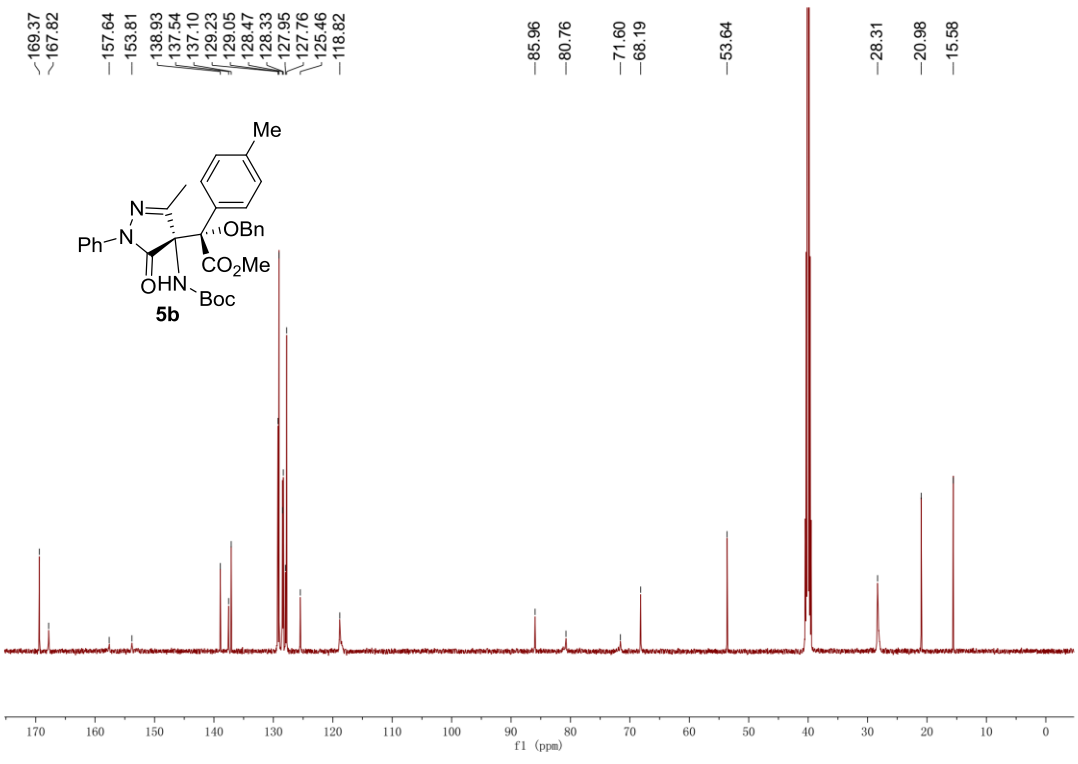


^{1}H NMR and ^{13}C NMR spectrum for **5a**

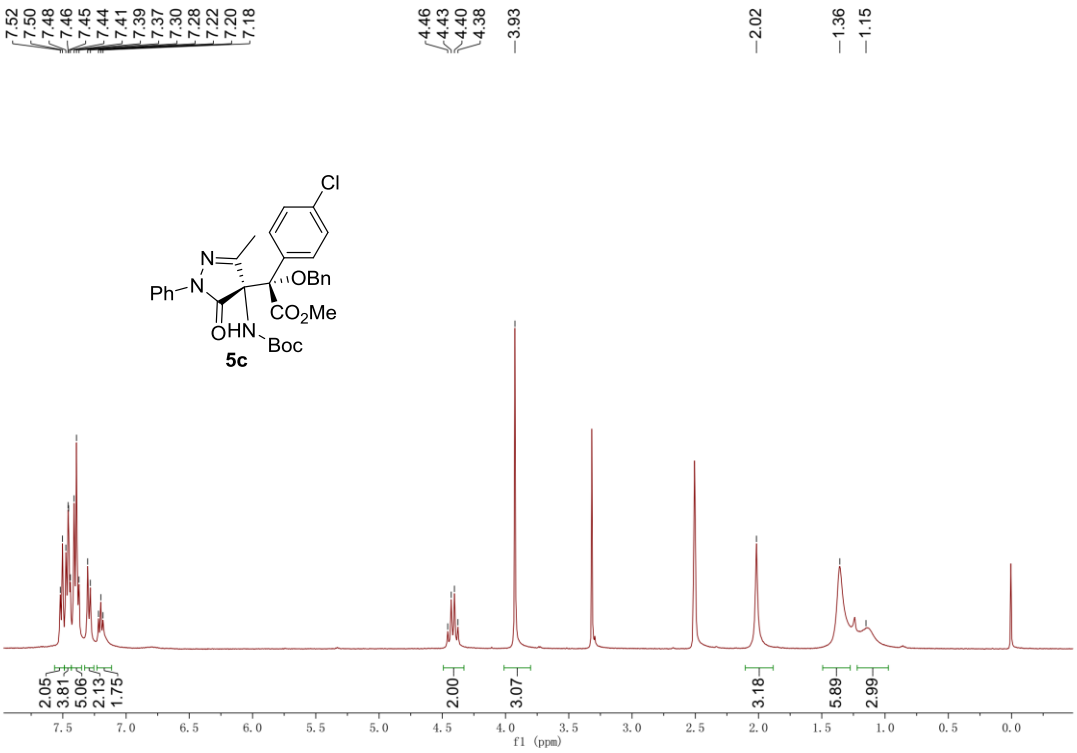


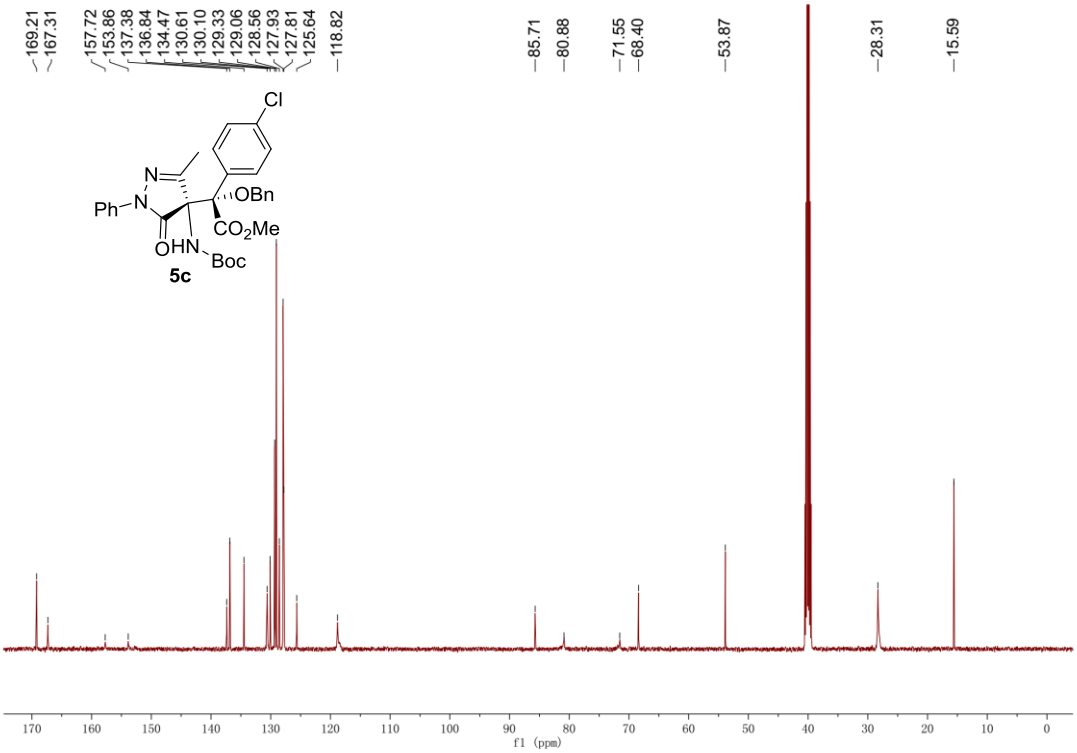
^{1}H NMR and ^{13}C NMR spectrum for **5b**



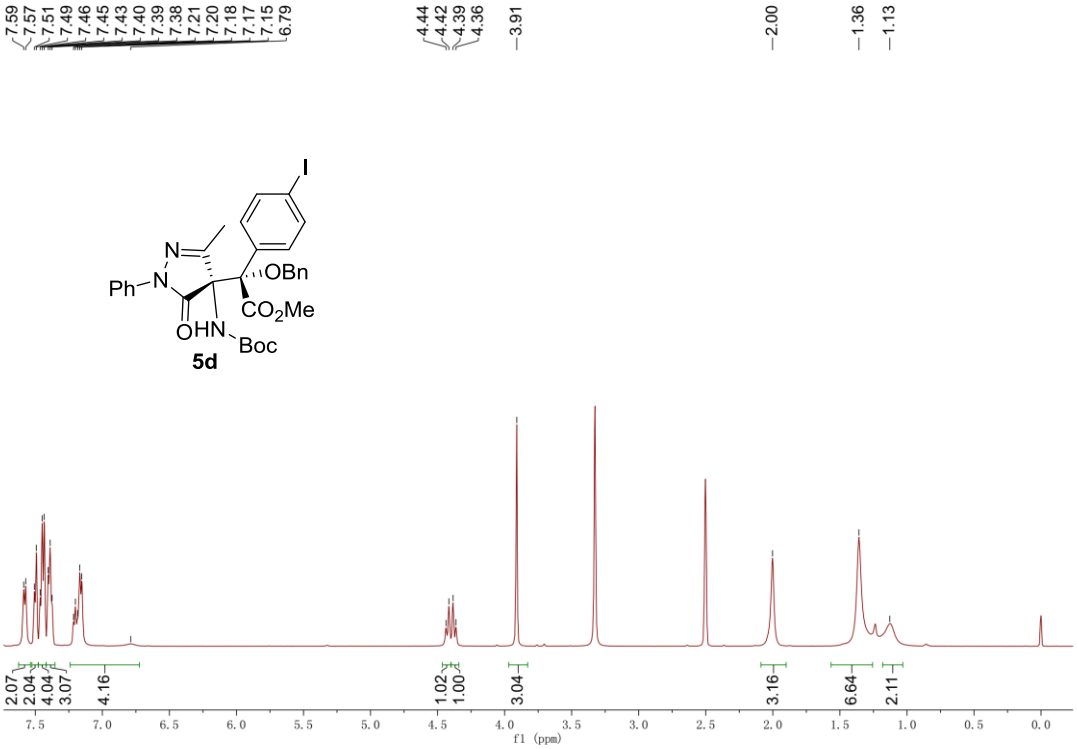


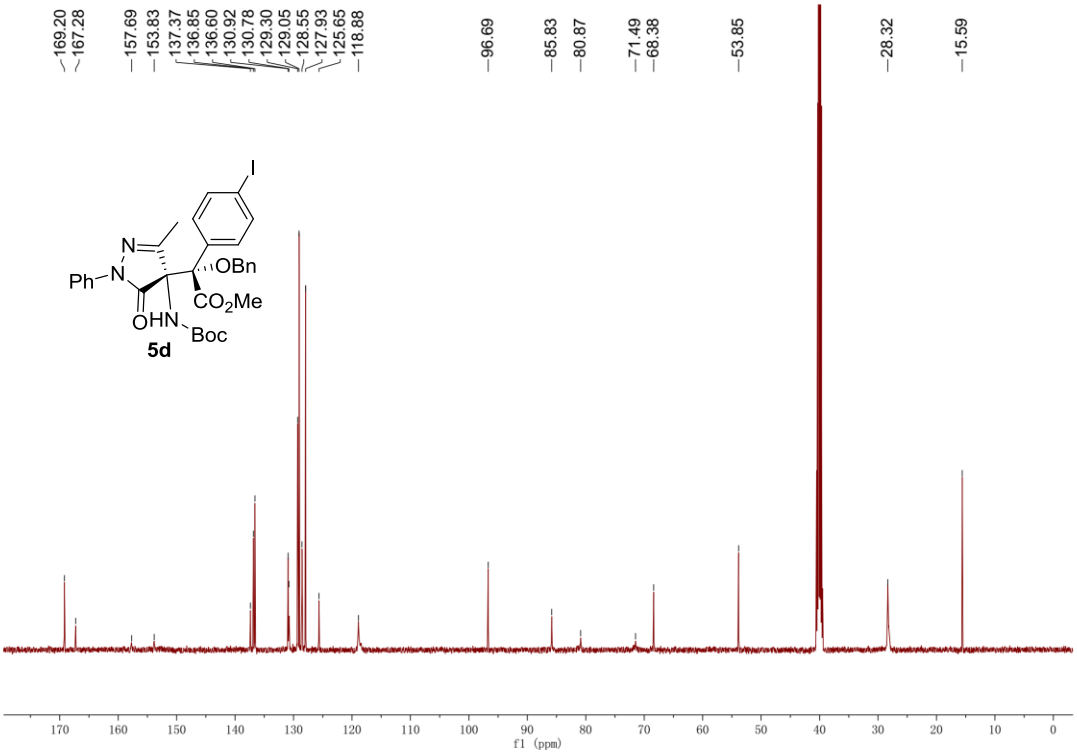
^{1}H NMR and ^{13}C NMR spectrum for **5c**



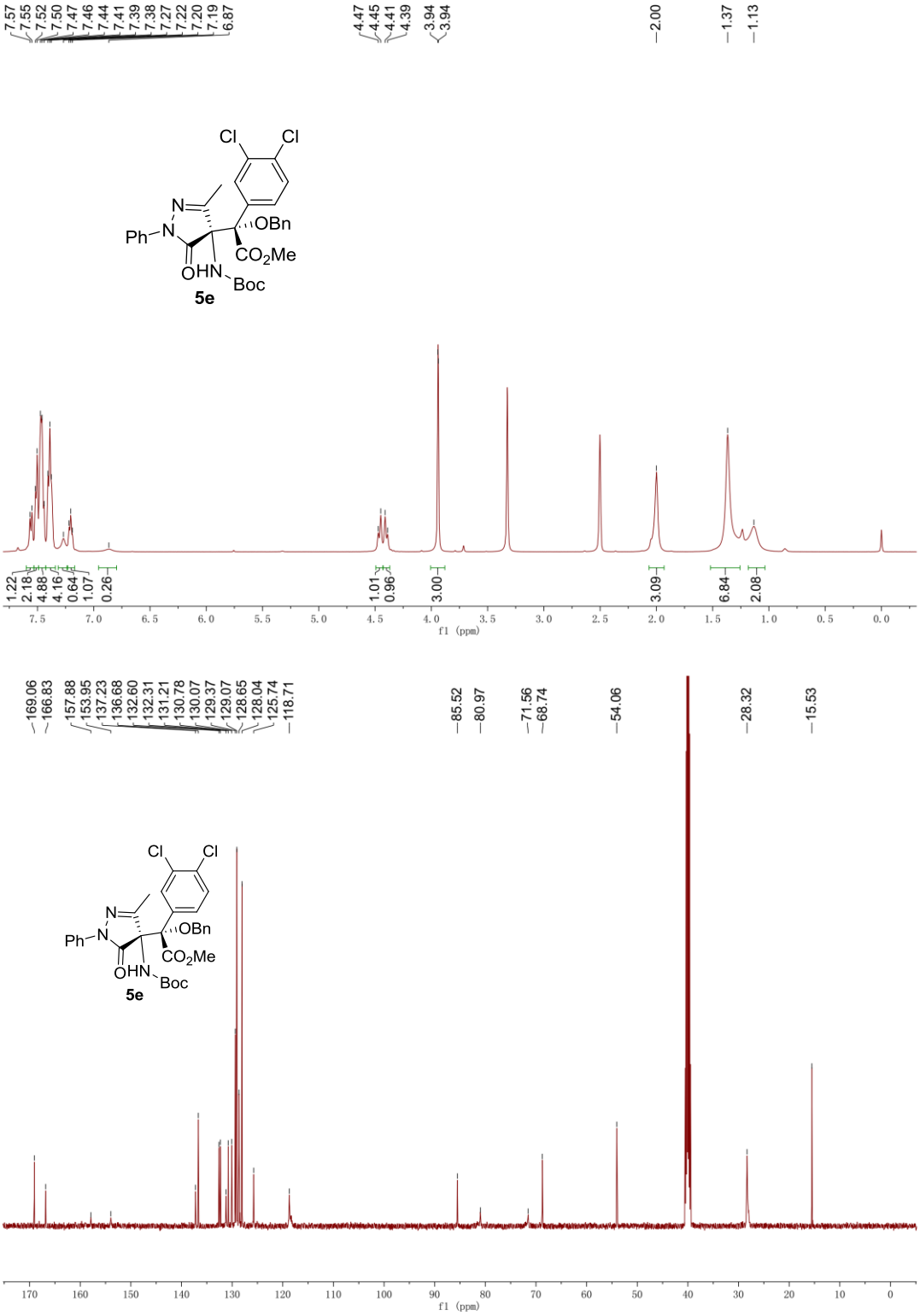


^{1}H NMR and ^{13}C NMR spectrum for **5d**

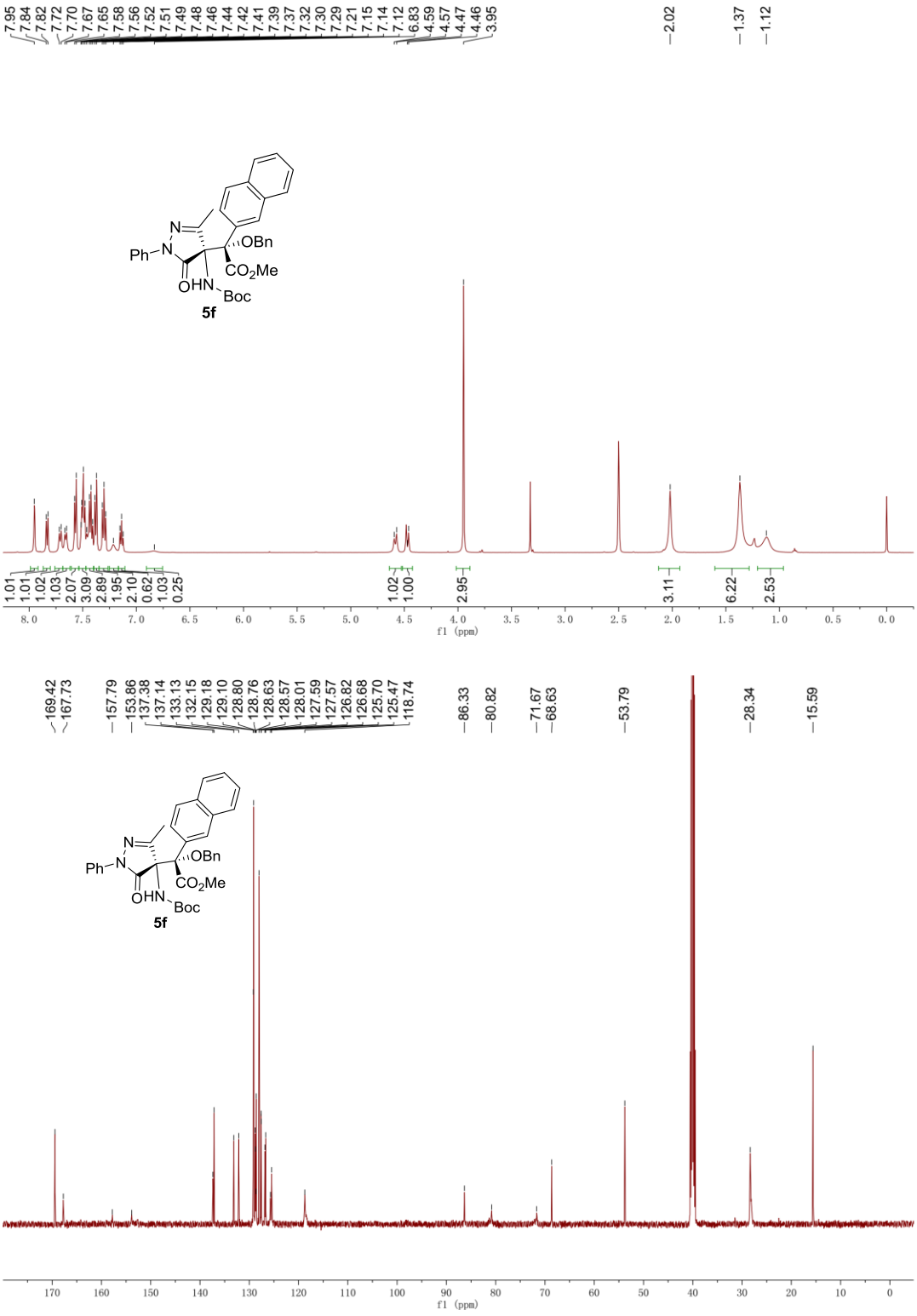




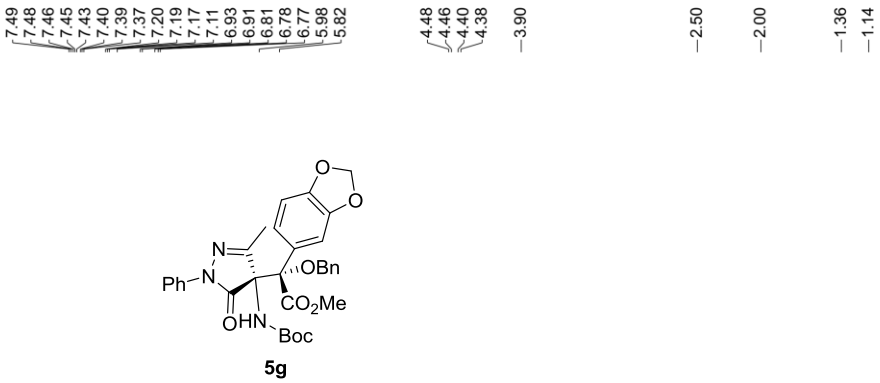
^{1}H NMR and ^{13}C NMR spectrum for **5e**

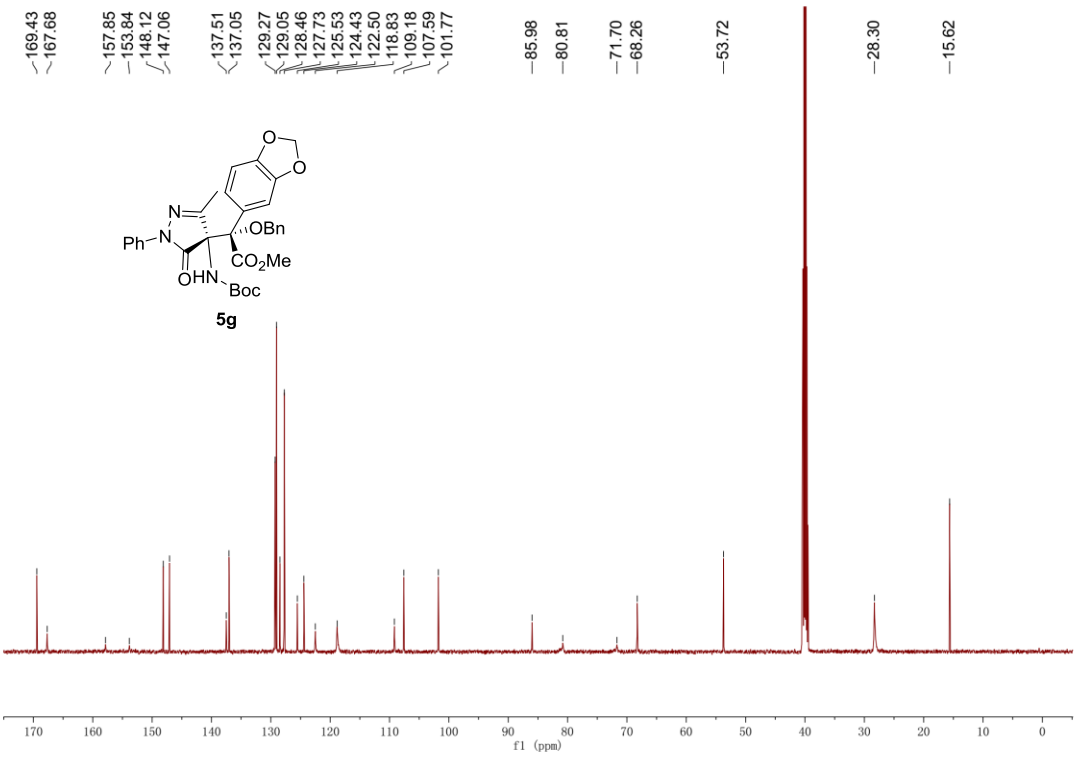


^{1}H NMR and ^{13}C NMR spectrum for **5f**

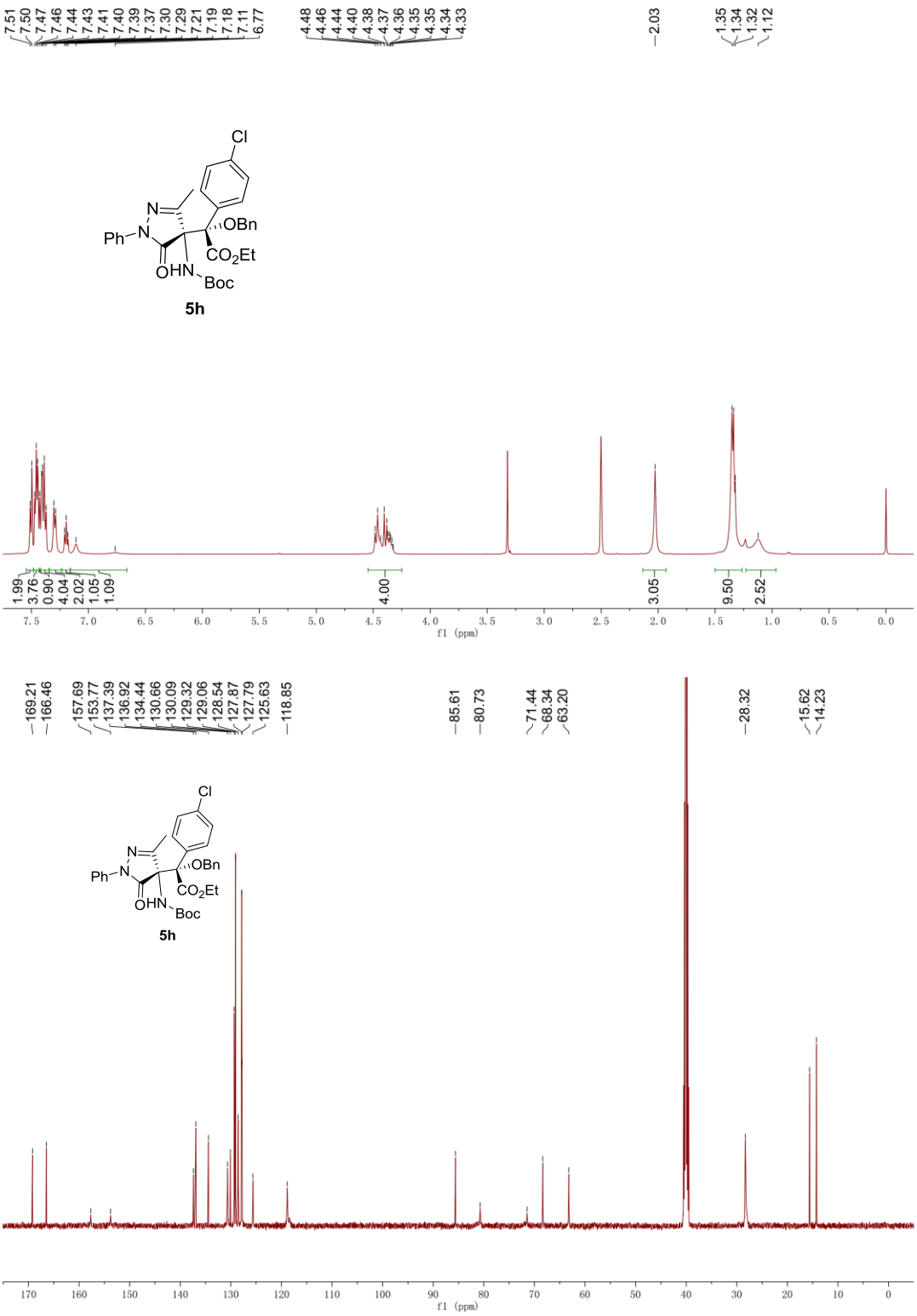


^{1}H NMR and ^{13}C NMR spectrum for **5g**

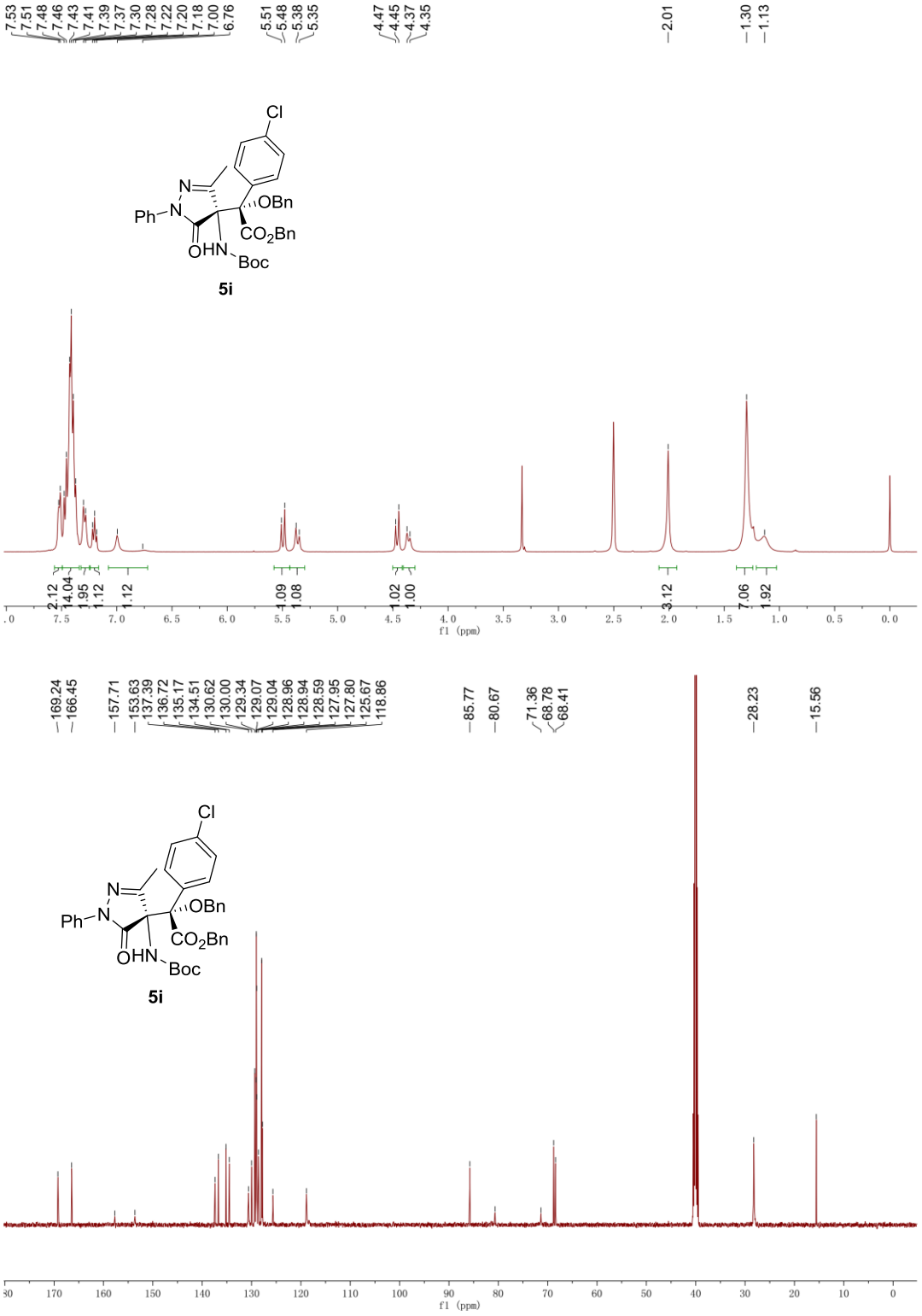




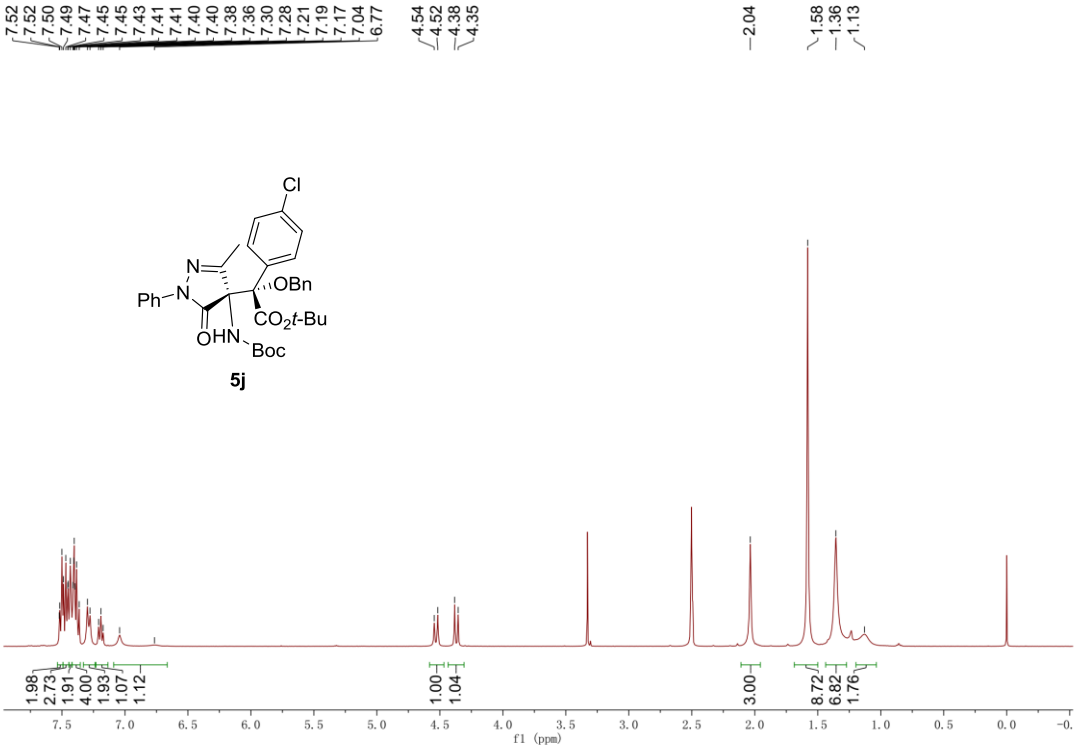
^{1}H NMR and ^{13}C NMR spectrum for **5h**

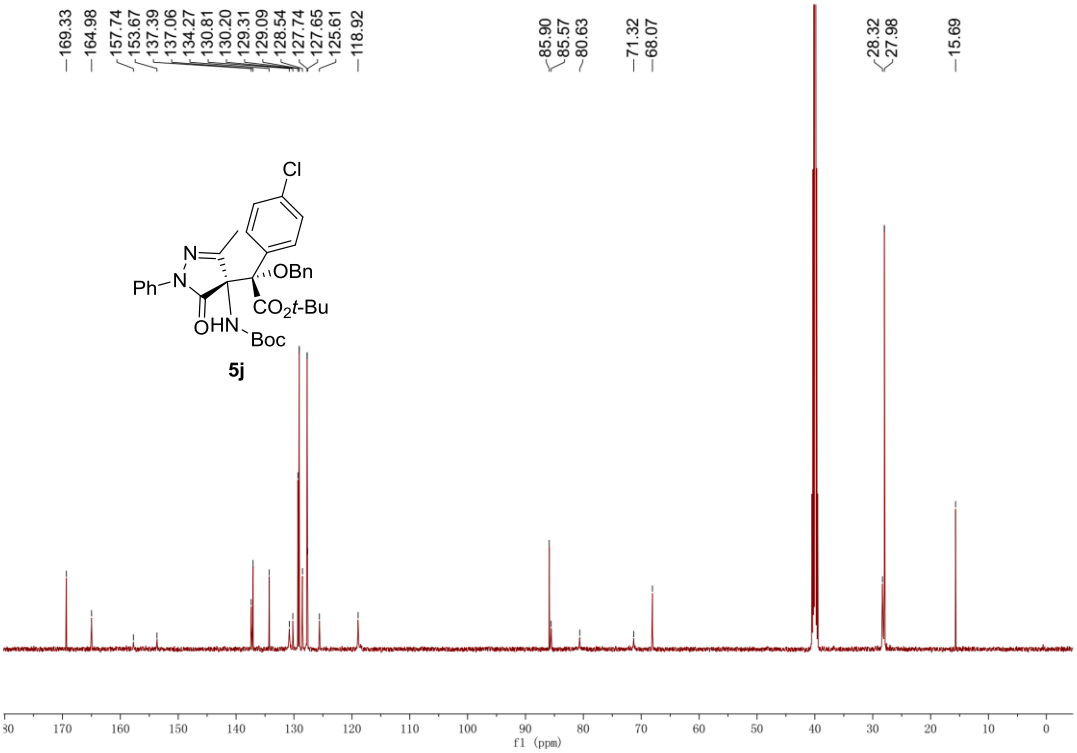


^{1}H NMR and ^{13}C NMR spectrum for **5i**

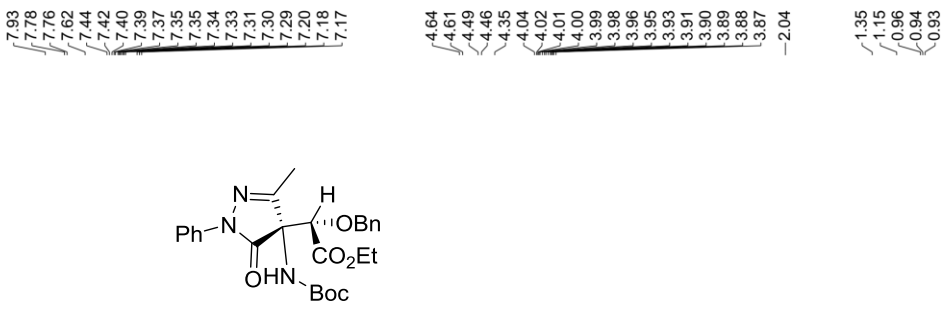


^{1}H NMR and ^{13}C NMR spectrum for **5j**

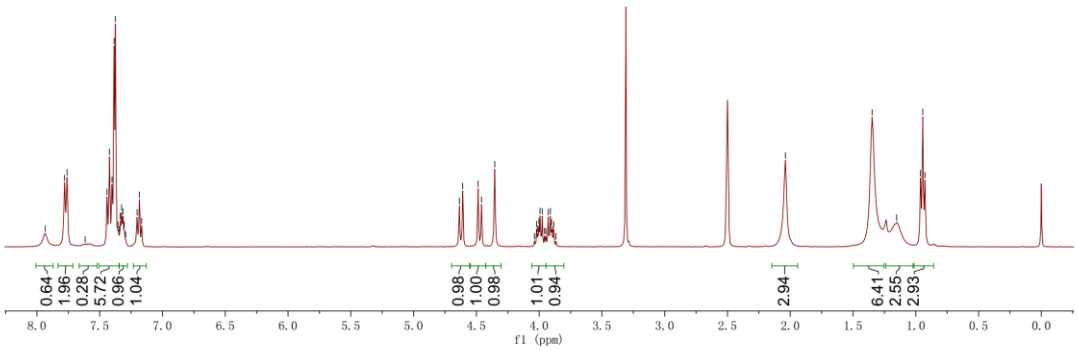


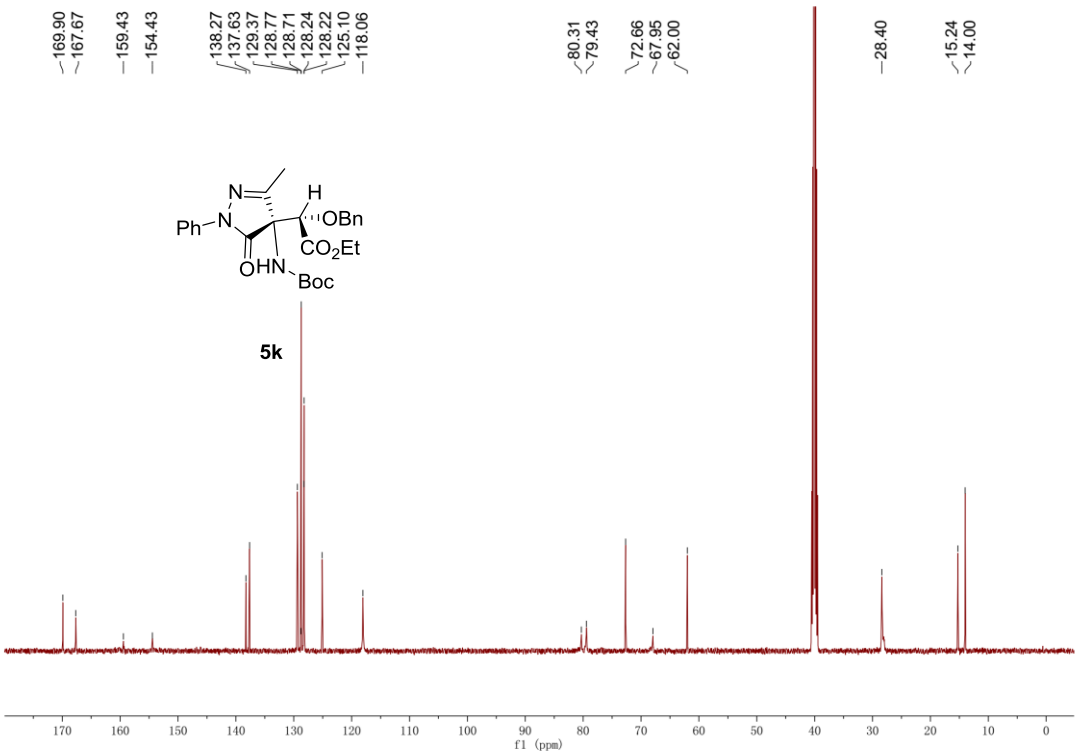


^{1}H NMR and ^{13}C NMR spectrum for **5k**



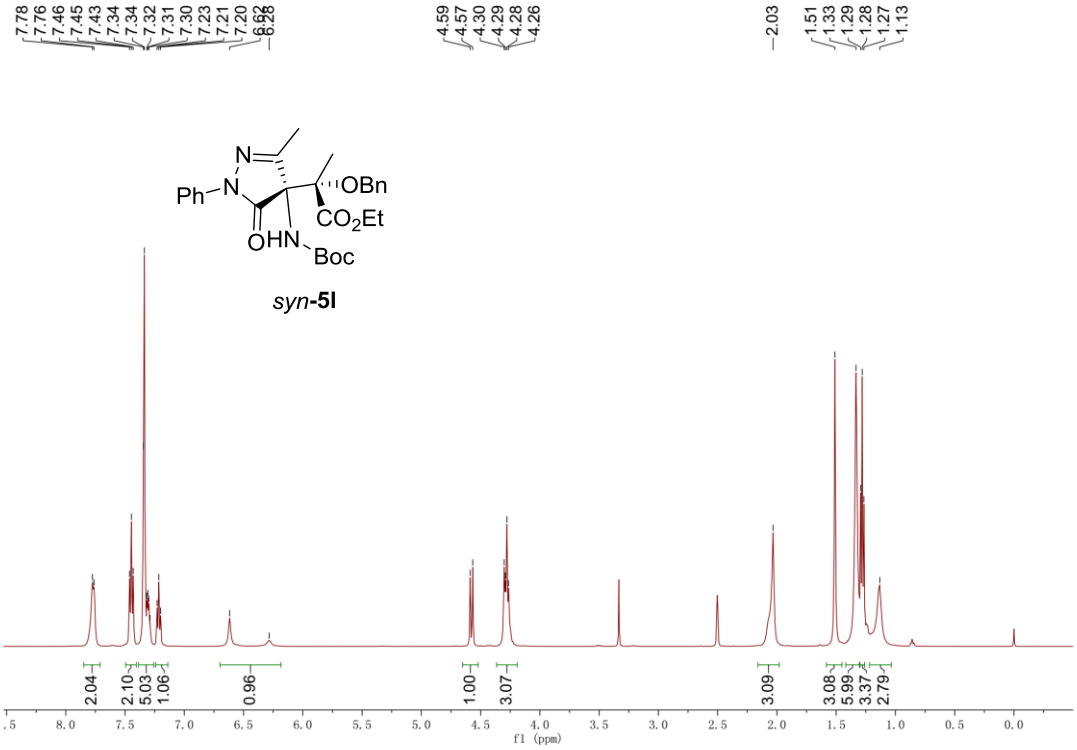
5k



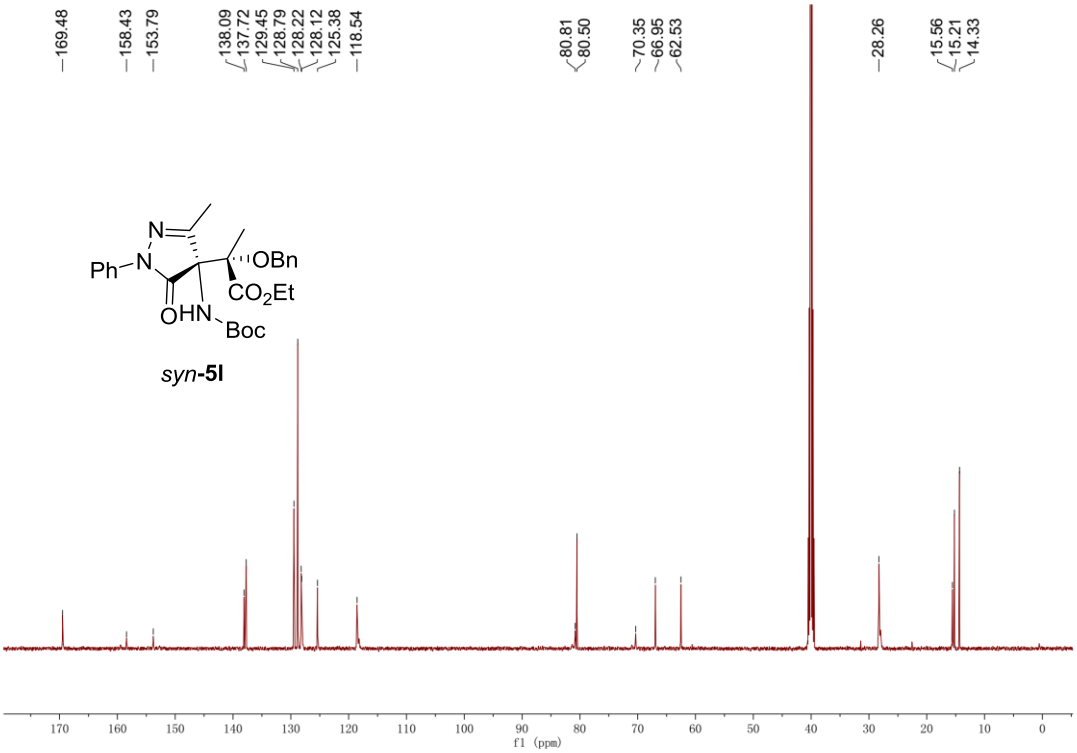


5k

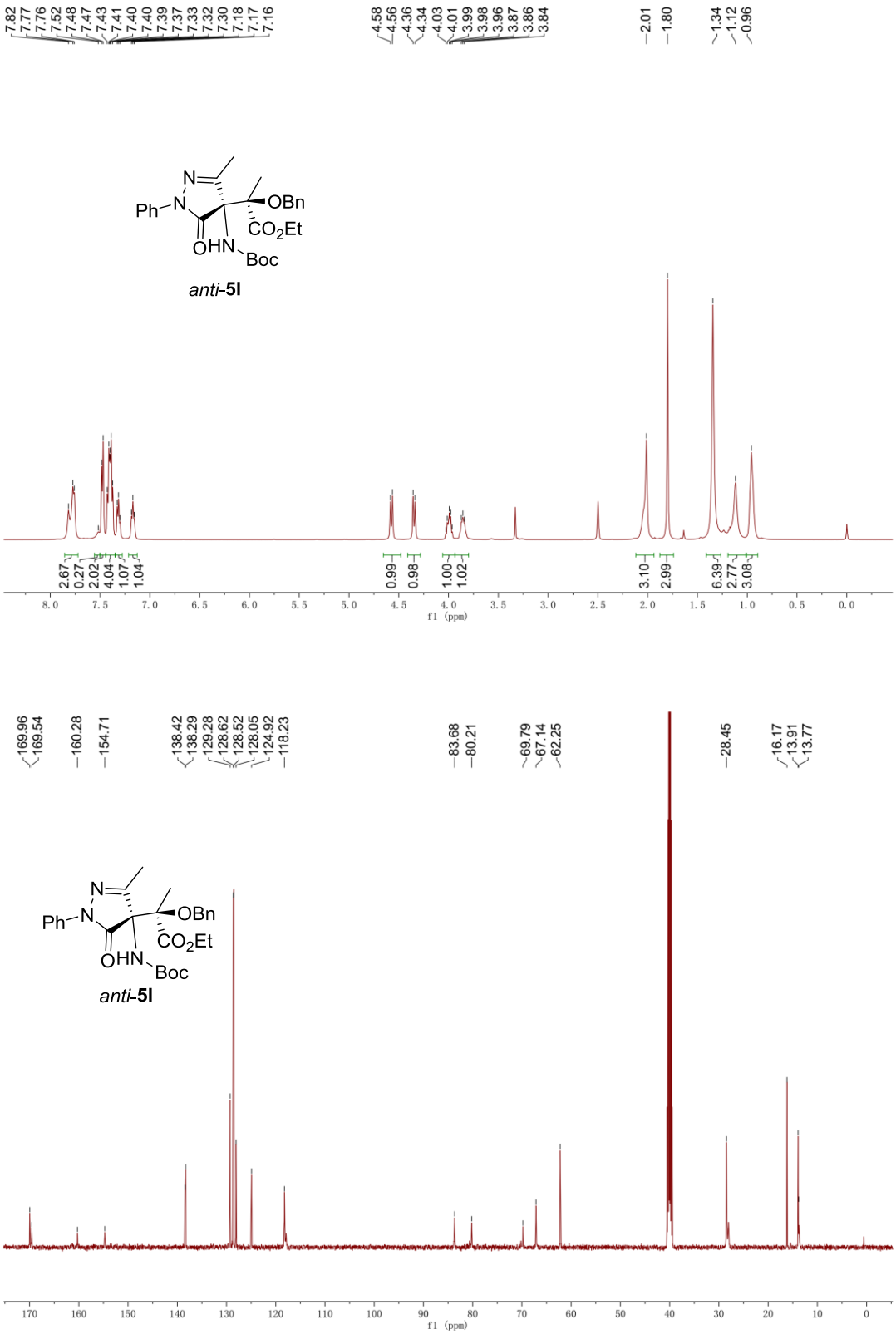
^{1}H NMR and ^{13}C NMR spectrum for *syn*-**5l**



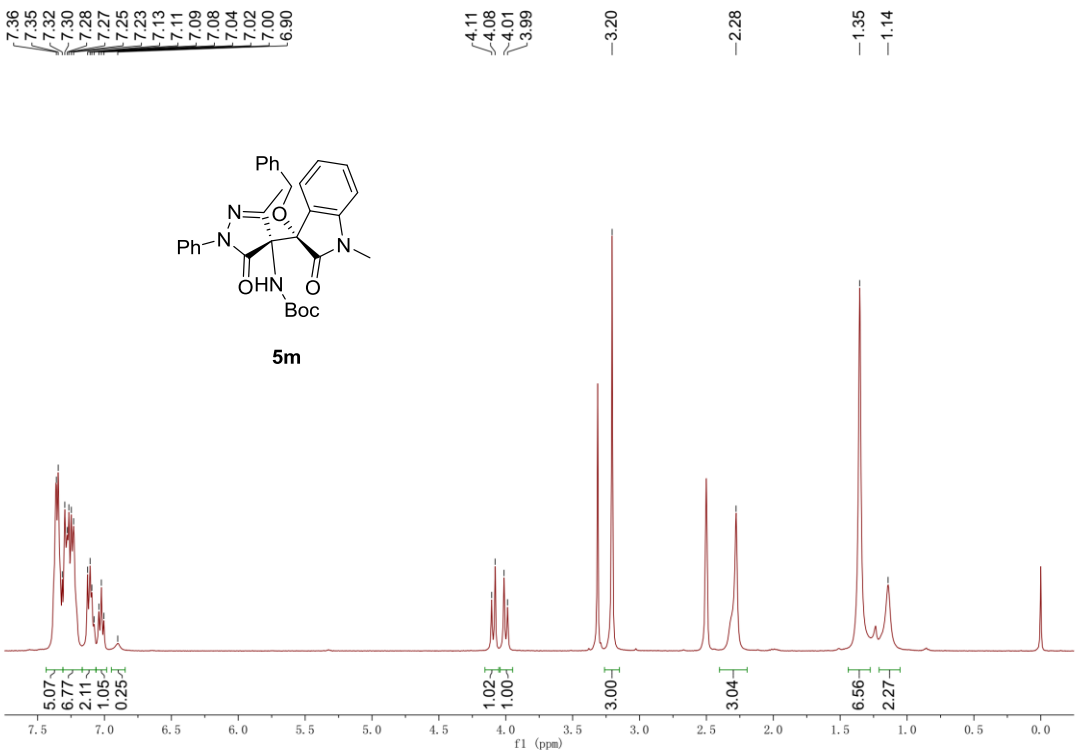
^{13}C NMR spectrum for *syn*-**5l**

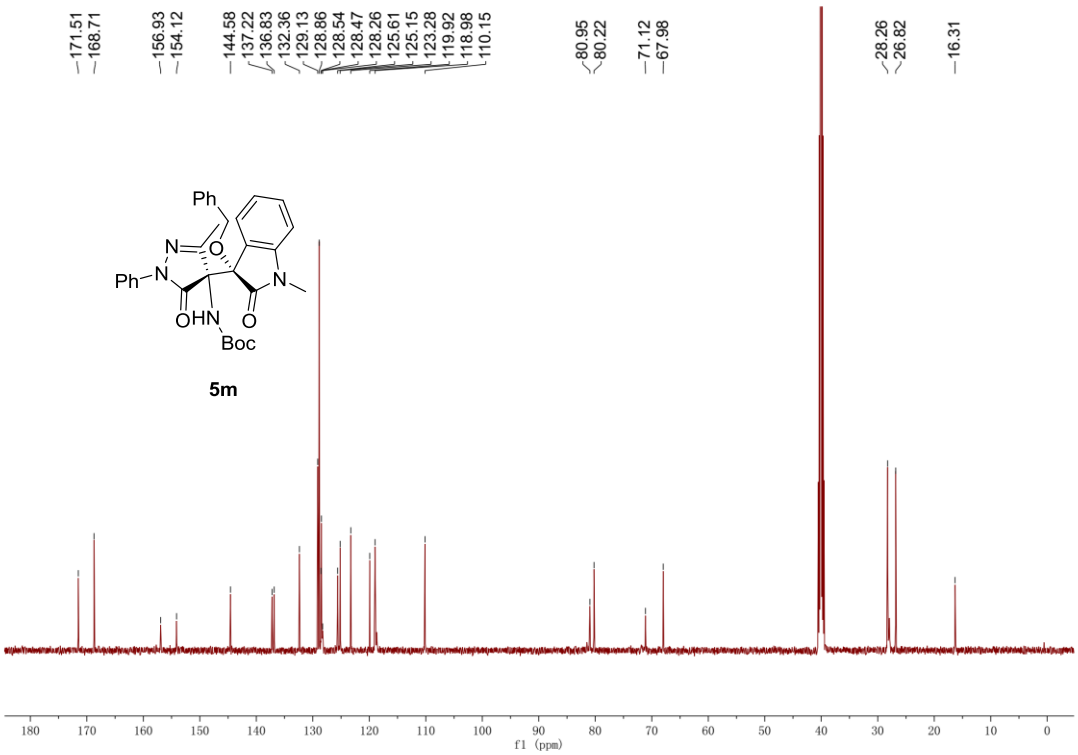


^{1}H NMR and ^{13}C NMR spectrum for *anti*-**5l**

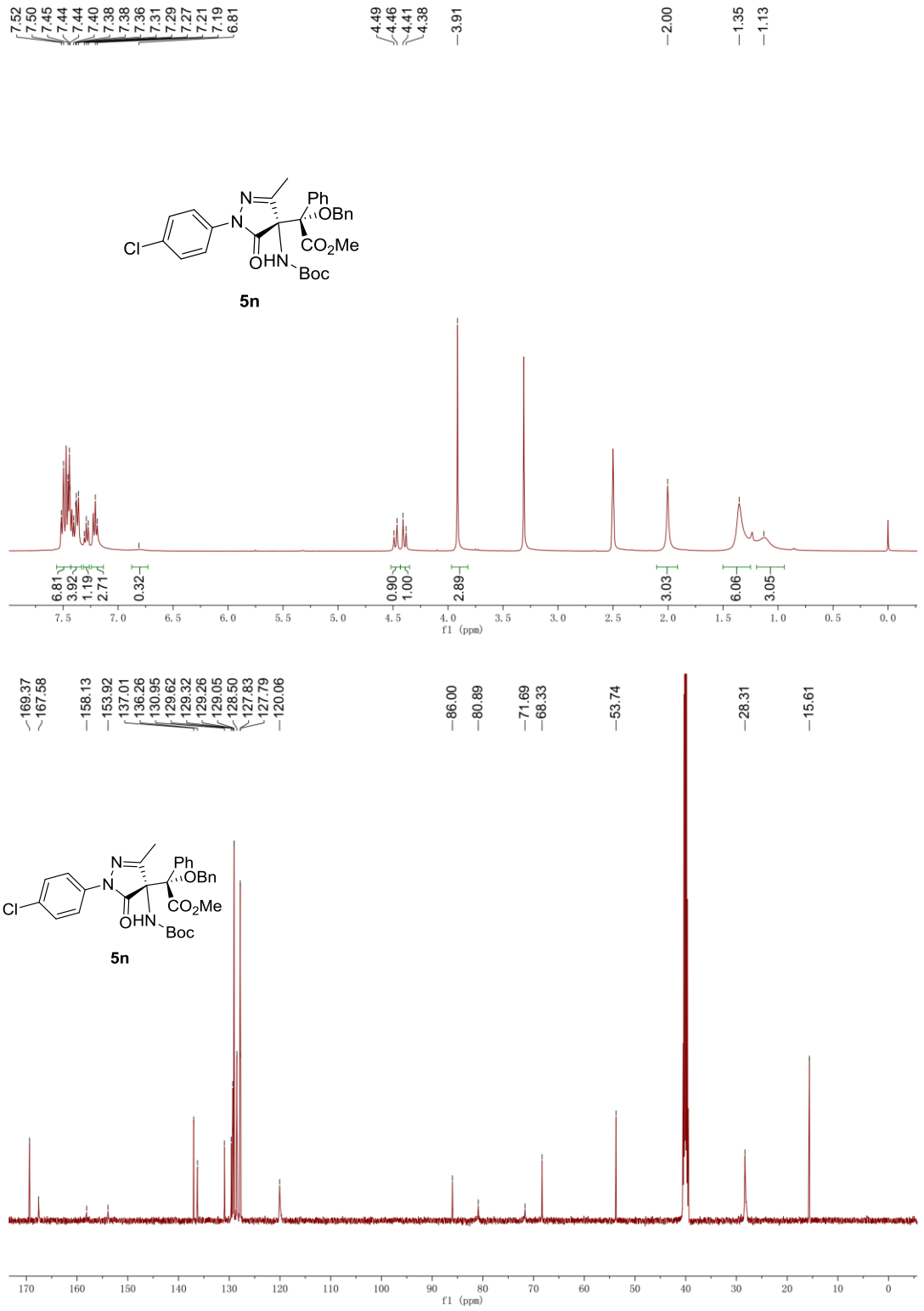


^{1}H NMR and ^{13}C NMR spectrum for **5m**

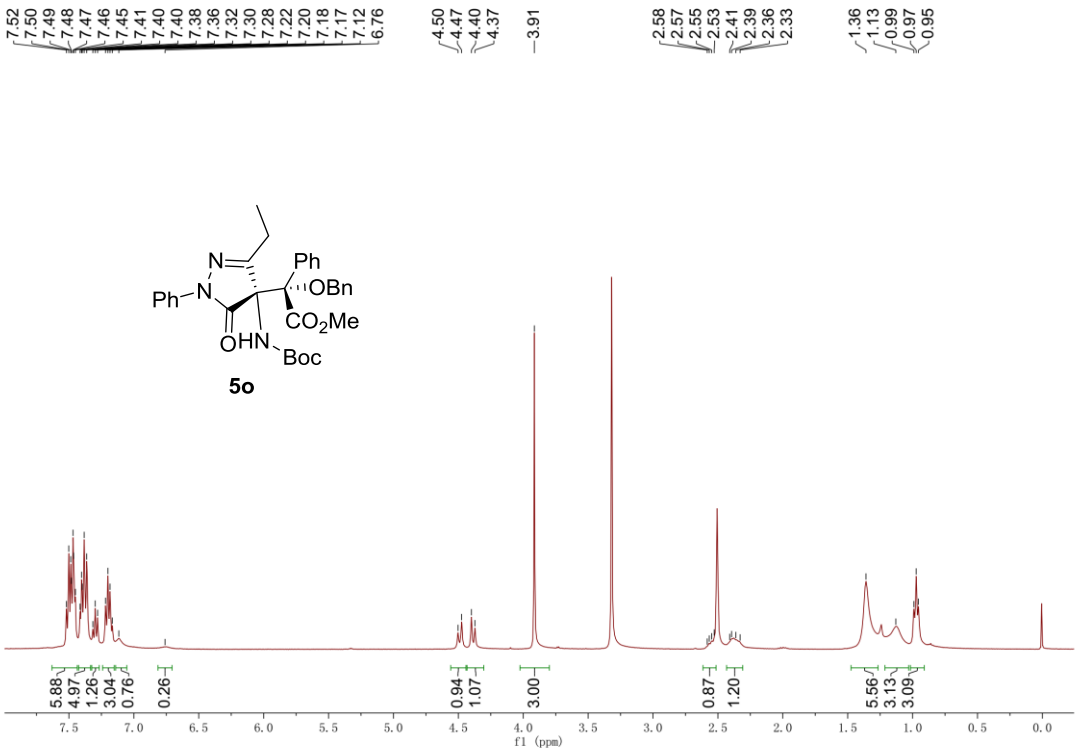




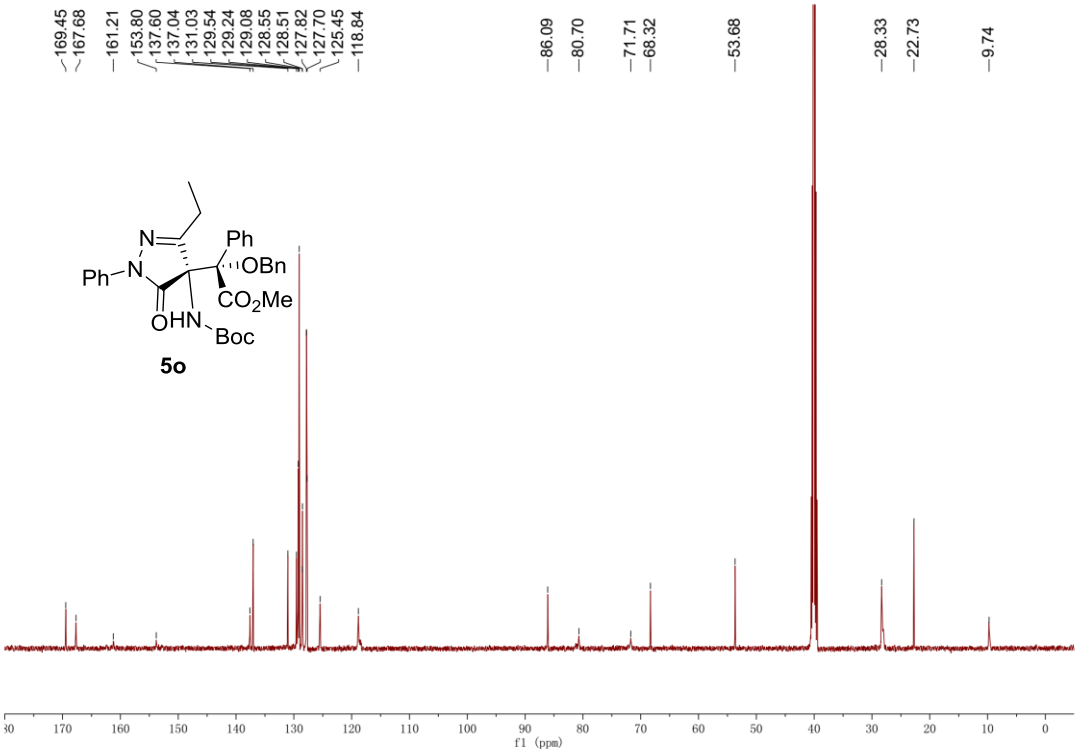
^{1}H NMR and ^{13}C NMR spectrum for **5n**



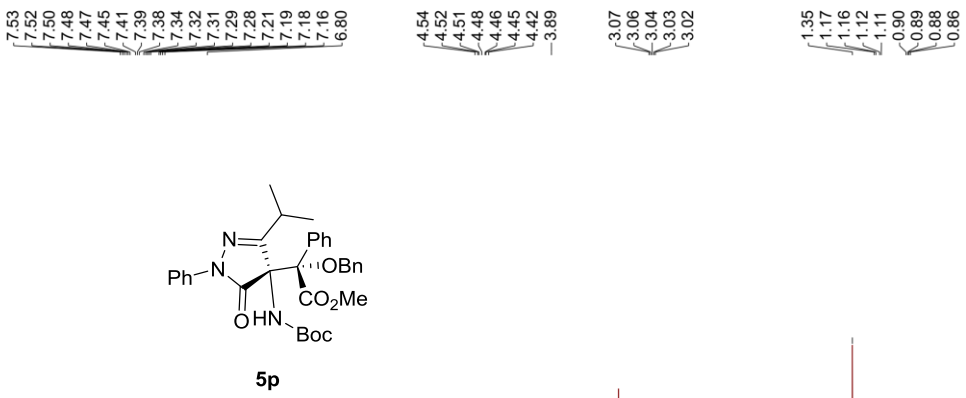
^{1}H NMR and ^{13}C NMR spectrum for **5o**

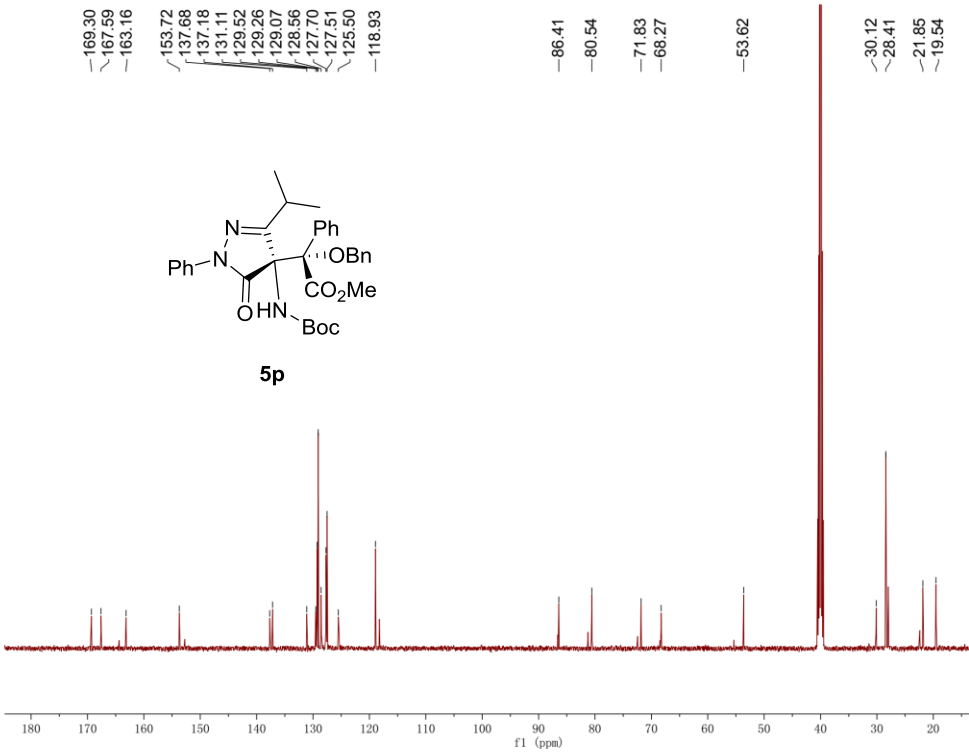


^{13}C NMR spectrum for **5o**

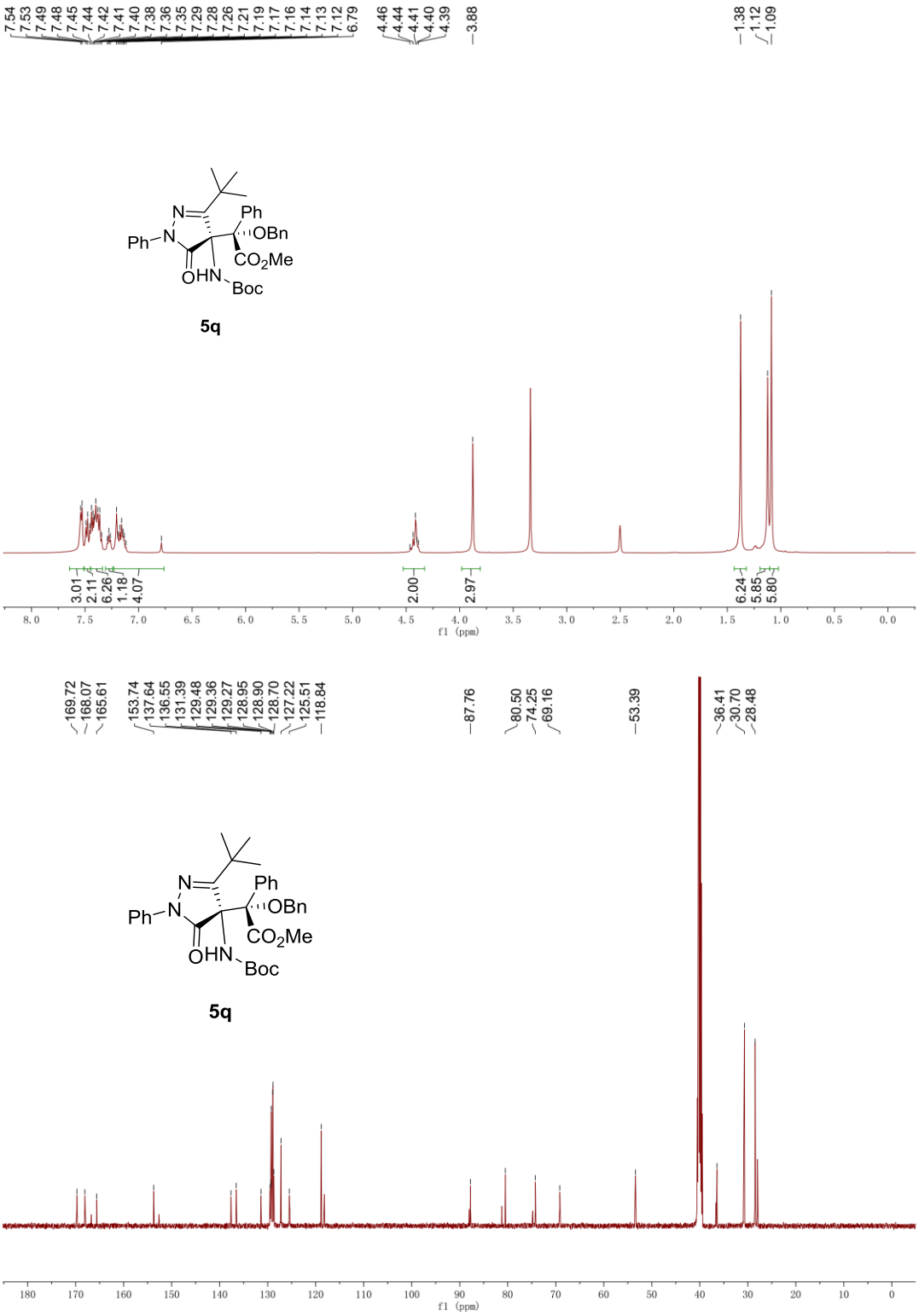


^{1}H NMR and ^{13}C NMR spectrum for **5p**

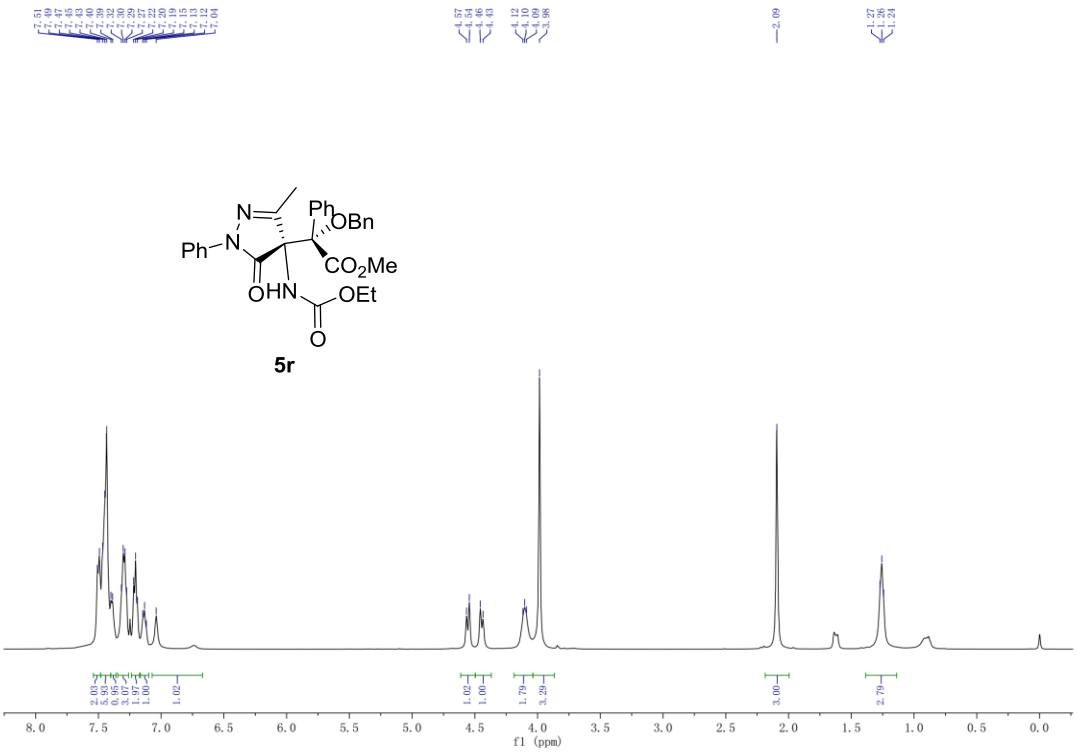


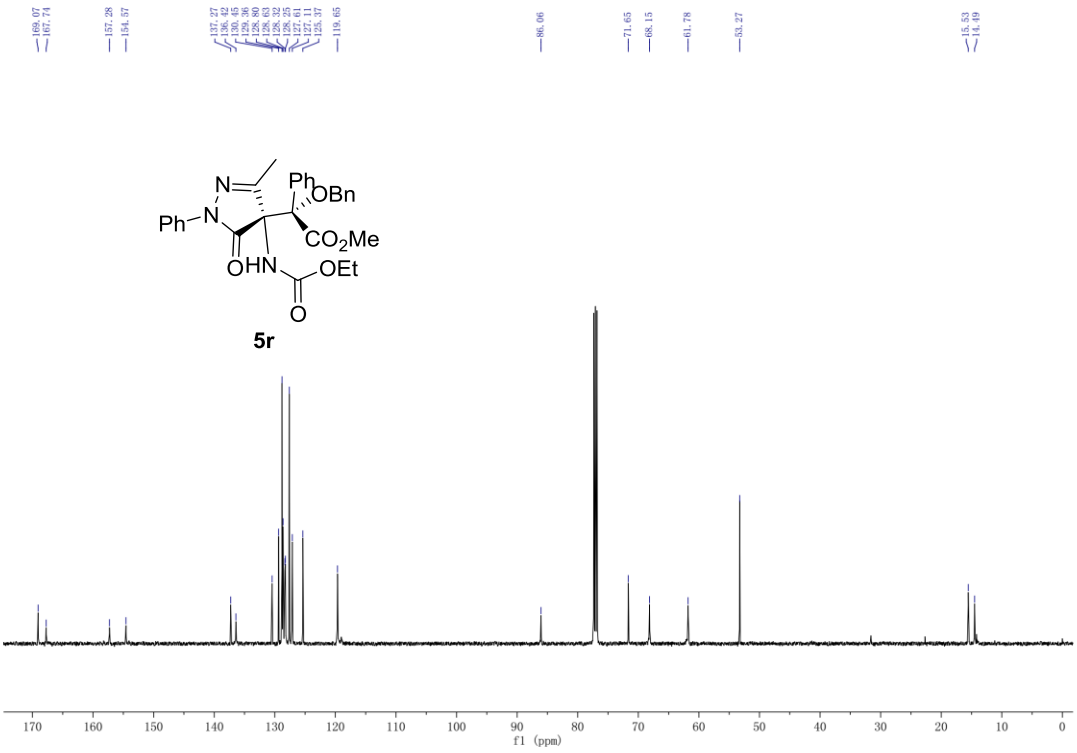


^{1}H NMR and ^{13}C NMR spectrum for **5q**

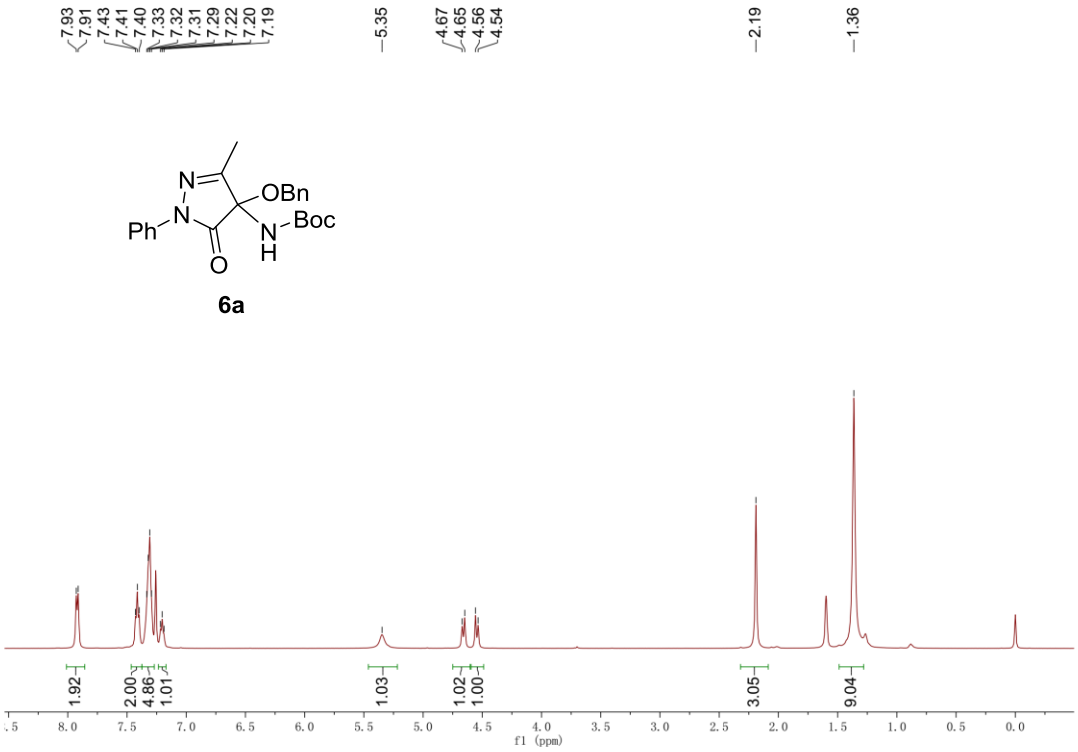


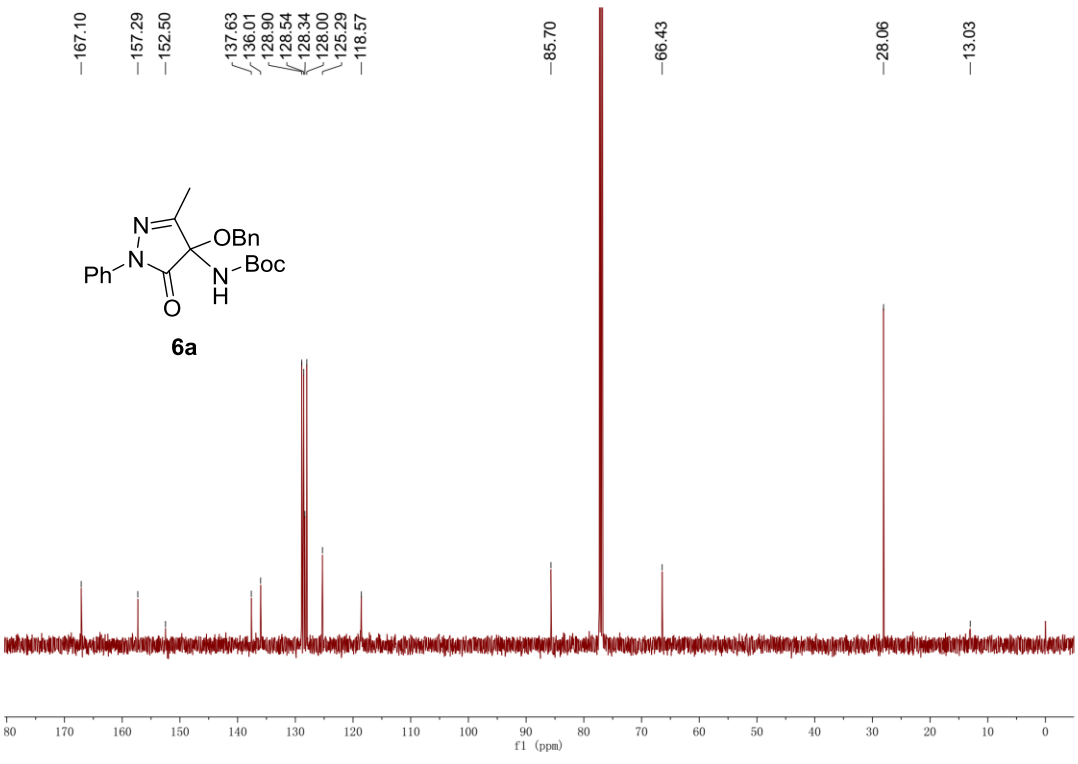
^{1}H NMR and ^{13}C NMR spectrum for **5r**



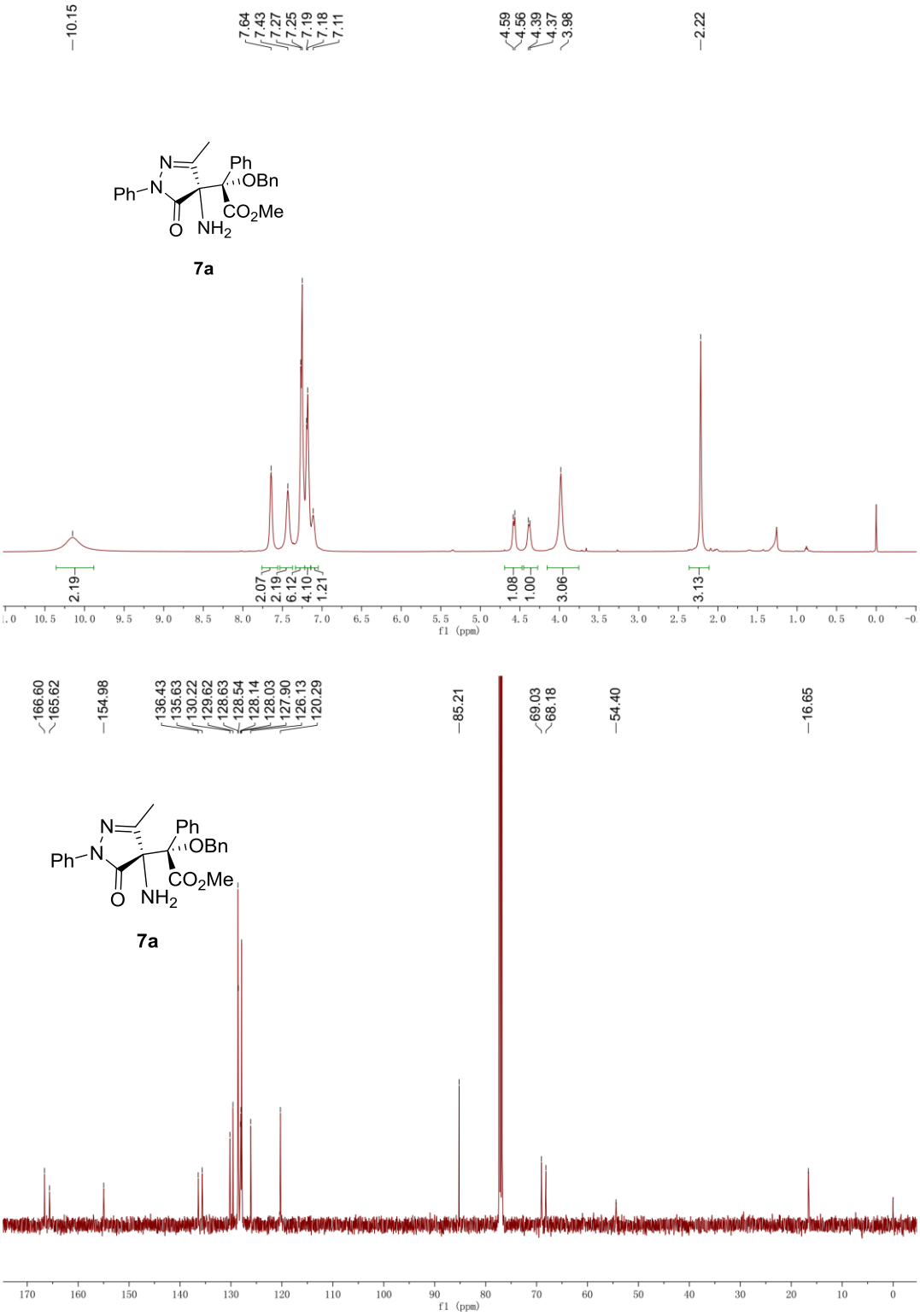


^{1}H NMR and ^{13}C NMR spectrum for **6a**

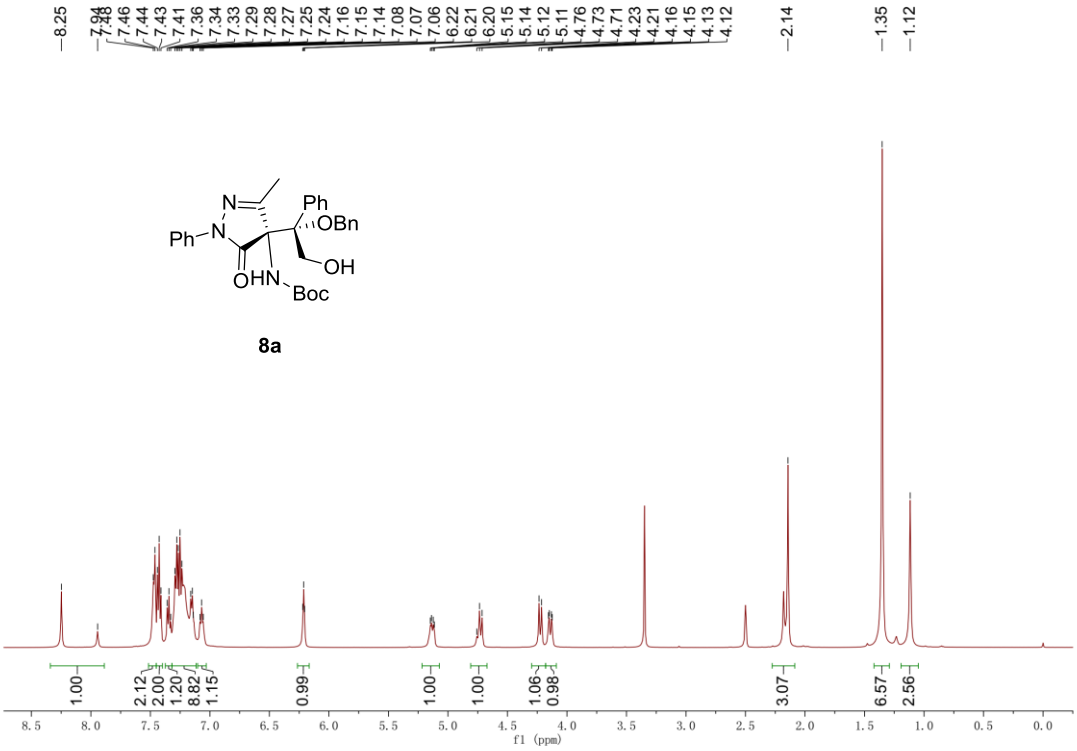




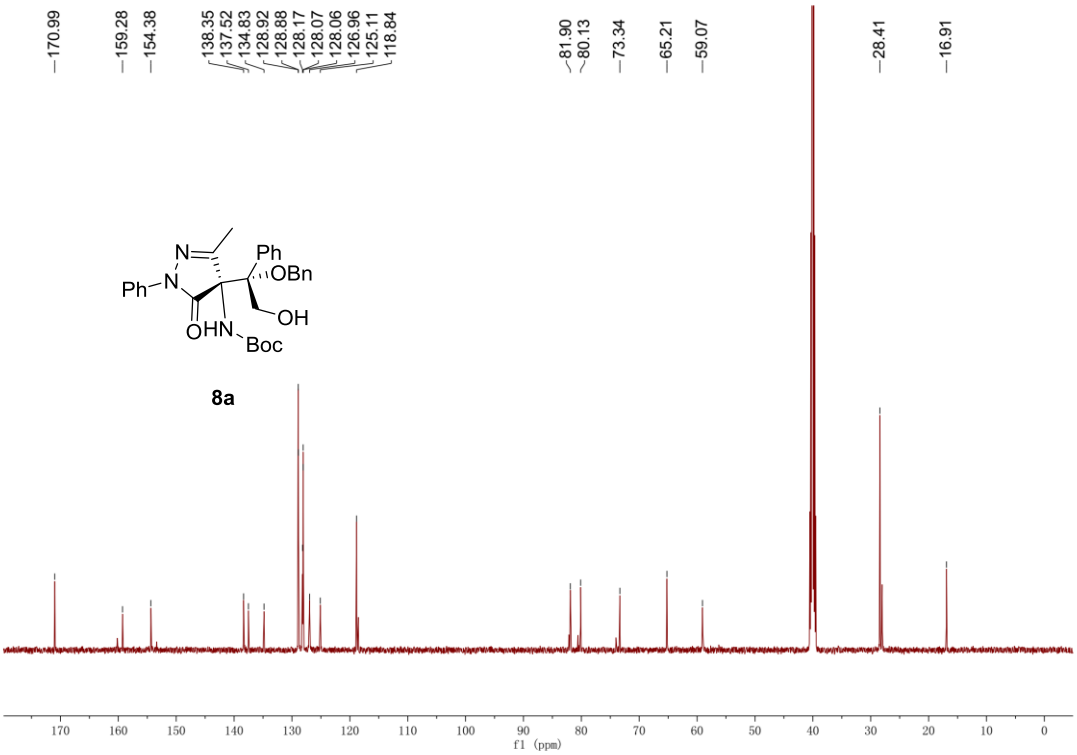
^{1}H NMR and ^{13}C NMR spectrum for **7a**



^{1}H NMR and ^{13}C NMR spectrum for **8a**


8.25
7.94
7.46
7.44
7.43
7.41
7.36
7.34
7.33
7.29
7.28
7.27
7.25
7.24
7.16
7.15
7.14
7.08
7.07
7.06
6.22
6.21
6.20
5.15
5.14
5.12
5.11
4.76
4.73
4.71
4.23
4.21
4.16
4.15
4.13
4.12
2.14
1.35
1.12
Ph
N
Ph
OBn
OH
OHN
Boc
1.00
2.12
2.00
1.20
8.82
1.15
0.99
1.00
1.00
1.06
0.98
3.07
6.57
2.56
f1 (ppm)

8a


170.99
159.28
154.38
138.35
137.52
134.83
128.92
128.88
128.17
128.07
128.06
126.96
125.11
118.84
81.90
80.13
73.34
65.21
59.07
28.41
16.91
Ph
N
Ph
OBn
OH
OHN
Boc
f1 (ppm)

8a