Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Addition of carbon nucleophiles to hemiaminals promoted by a Lewis acidic polyoxotungstate

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Content

1. General remarks

Reagents and chemicals were purchased from commercial sources and used as received. The Hf substituted polyoxotungstate (POM/Hf), *N*-Boc-2-hydroxypyrrolidine[1] and *N*-Boc-2-hydroxypiperidine[1] were prepared as described previously. Unless otherwise noted, reactions were carried out under argon atmosphere with magnetic stirring in redistilled solvents when necessary. Solvents were purified and dried by standard procedures. Merck 60F254 silica gel was used for thin-layer chromatography (TLC) and Merck Geduran SI 60 Å silica gel 60 (40-63 µM) was used for flash column chromatography.

Melting points were measured on a Stuart Scientific Melting Point SMP3 apparatus in open capillaries. IR spectra were recorded from a Bruker Tensor 27 ATR diamond PIKE spectrophotometer. NMR ^{1}H, ^{31}P, ^{13}C spectra were recorded at 400, 162, and 100 MHz, respectively, using a Bruker AVANCE 400 spectrometer equipped with a BBFO probe. Some ^{13}C NMR spectra were recorded at 50 MHz using a Bruker AVANCE 200. Chemical shifts are reported in ppm, using, for ^{1}H and ^{13}C, solvent residual peak as internal standard references and external H_3PO_4 for ^{31}P. Coupling constants (*J*) are given in Hertz (Hz), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet).

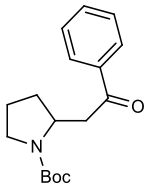
Mass spectrometry experiments have been carried out at the Institut Parisien de Chimie Moléculaire (FR2769) on an electrospray-ion trap instrument

2. General Procedures

General Procedure 1 (GP1). *POM/Hf catalyzed* a*ddition of Carbon Nucleophiles to hemiaminal **1***. To a solution of POM/Hf (1 mol%, 0.004 mmol) in CH_3CN (1 mL) were added *N*-Boc-2-hydroxypyrrolidine **1a** (0.4 mmol, 1 equiv.), the silyl enol ether **2** (ketene-acetals) (0.4 mmol, 1 equiv.), 1,3-dicarbonyl compounds **6** (0.4 mmol, 1 equiv.) allytrimethylsilane (2 mmol, 5 equiv.). After completion, 2 mL of a solution of acetone/ethanol (1/1) were added, followed by 20 mL of diethyl ether. The white precipitate (catalyst) was recovered by filtration or by centrifugation and the remaining organic solution was concentrated under reduced pressure. The residue was purified by flash column chromatography (EtOAc/Pentane) to afford the desired product.

3. Descriptions

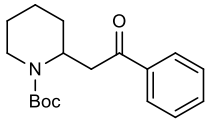
2-(2-Oxo-2-phenyl-ethyl)-pyrrolidine-l-carboxylic acid *tert-Butyl* ester (3a)



$C_{17}H_{23}NO_3$
M = 289.3694

Following **GP1**, from N-Boc-2-hydroxypyrrolidine **1a** (30 mg, 0.16 mmol), 1-phenylvinyl trimethylsilyl ether **2a** (34 μL, 0.16 mmol) and POM/Hf (1 mol%, 0.0016 mmol), to give the desired product **3a** as a clear oil (33 mg, 0.12 mmol, 72% yield). Spectral data correspond to those described in the literature. [2] [*Tetrahedron*, **1996**, *52*, 2629-2646]
IR υ max (neat) / cm^{-1} 1677, 1391; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (s, 9H, *t*-Bu), 1.64-1.72 (m, 1H, C*H*H), 1.73 –1.87 (m, 2H, CH_2), 1.99 (ddd, *J* = 16.7, 12.4, 7.6 Hz, 1H, CH*H*), 2.77 (dd, *J* = 15.4, 9.9 Hz, 1H, COC*H*H), 3.30 (t, *J* = 6.5 Hz, 2H, NCH_2), 3.57 (bs, 1H, COCH*H*), 4.26 (ddt, *J* = 10.8, 7.6, 3.2 Hz, 1H, N*CH*), 7.37 –7.41 (td, *J* = 7.0, 1.5 Hz, 2H, Harom), 7.47 – 7.50 (t, *J* = 7.4 Hz, 1H, Harom), 7.93 (d, *J* = 7.4 Hz, 2H, Harom); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.2 (CH_2), 28.5 (CH_3, *t*-Bu), 30.7 (CH_2), 43.4 (CH_2), 46.5 (CH_2), 54.3 (CH), 79.5 (*Ct*-Bu), 128.3 (CHarom), 128.6 (CHarom), 133.1 (CHarom), 136.9 (Carom), 154.4 (CO_2), 198.9 (CO).

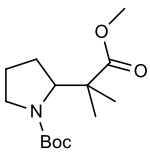
2-(2-oxo-2-phenylethyl) -piperidine-1-carboxylic acid *tert*-Butyl ester (3b)



$C_{18}H_{25}NO_3$
M = 303.40

Following **GP1** from *N*-Boc-2-hydroxypiperidine **1a** (40.8 mg, 0.20 mmol), 1-phenylvinyl trimethylsilyl ether **2a** (42 μL 0.20 mmol) and POM/Hf (1 mol %, 0.002 mmol), to give the desired product **3b** as a clear oil (10 mg, 0.03 mmol, 16% yield). Spectral data correspond to those described in the literature. [3][*Journal of the American Chemical Society*, **2008**, *130*, 13745-13754]
IR υ max (neat) / cm^{-1} 1684, 1669, 1409. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (s, 9H, *t*-Bu), 1.44 – 1.71 (m, 6H, $3CH_2$), 2.91 (td, *J* = 13.2, 2.7 Hz, 1H, NC*H*H), 3.11 (ddd, *J* = 20.5, 14.4, 7.3 Hz, 2H, CH_2Ph), 4.07 (d, *J* = 13.5 Hz, 1H, NCH*H*), 4.75 – 4.94 (m, 1H, NC*H*), 7.50 (t, *J* = 7.4 Hz, 2H, Harom), 7.59(t, *J* = 7.3 Hz, 2H, Harom), 8.02 (t, *J* = 7.2 Hz, 1H, Harom). ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.9 (CH_2), 25.3 (CH_2), 28.2 (CH_2), 28.3 (CH_3, *t*-Bu), 39.2 (CH_2), 39.4 (CH_2), 48.2 (CH), 79.6 (C*t*-Bu), 128.3 (CHarom), 128.6 (CHarom), 133.1 (CHarom), 136.9 (Carom), 154.7 (CO_2), 198.4 (CO).

2-(1-methoxy-2-methyl-1-oxopropan-2-yl)-pyrrolidine-1-carboxylic acid *tert*-Butyl ester (3c)

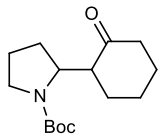


$C_{14}H_{25}NO_4$
M = 271.3526

Following **GP1** with *N*-Boc-2-hydroxypyrrolidine **1a** (34 mg, 0.18 mmol), 1-Methoxy-2-methyl-1-(trimethylsiloxy)propene **2b** (39 μL, 0.18 mmol), and POM/Hf (10 mol%, 0.018 mmol), to give the desired product **3c** as a clear oil (28 mg, 0.10 mmol, 58% yield). [4, 5][*Tetrahedron Lett.* **2006**, *47*, 7853-7856. *Tetrahedron Lett.* **2006**, *47*, 1669–1672.]

IR υ max (neat) / cm^{-1} 1692, 1377, 1365. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 1.39 (s, 9H, *t*-Bu), 1.59 – 1.79 (m, 3H, CH_2C*H*H), 1.80 – 1.96 (m, 1H, CH*H*), 3.11 (dt, *J* = 11.2, 6.9 Hz, 1H, NC*H*H), 3.47 – 3.67 (m, 4H, COOCH_3 + NCH*H*), 4.18 (dd, *J* = 8.6, 3.0 Hz, 1H, NC*H*). ^{13}C NMR (63 MHz, $CDCl_3$) δ 21.2 (CH_3). 24.1 (CH_2), 27.5 (CH_2), 28.4 (CH_3, *t*-Bu), 47.8 (CH_2), 51.9 (CO_2CH_3), 62.9 (CH), 79.5 (C*t*-Bu), 155.8 (CO_2), 177.3 (CO).

2-(2-oxocyclohexyl)-pyrrolidine-1-carboxylic acid *tert*-Butyl ester (3e)

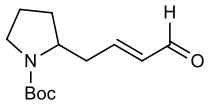


$C_{15}H_{25}NO_3$
M = 267.3639

Following **GP1** with *N*-Boc-2-hydroxypyrrolidine **1b** (30 mg, 0.16 mmol), 1-(trimethylsiloxy) cyclohexene **2c** (32 μL, 0.16 mmol), and POM/Hf (1 mol %, 0.0016 mmol), to give the desired product **3e** as a 30/70 mixture of diastereomers (27 mg, 0.10 mmol, 63% yield). With 10 mol% POM/Hf, (42 mg, 0.16 mmol, 98% yield).

IR υ max (neat) / cm^{-1} 1686, 1388. ^{1}H NMR (250 MHz, $CDCl_3$, mixture of diastereomers) δ [1.41] (s, 3.4 H, *t*-Bu, 1 *dia. mino*), 1.42 (s, 5.6 H, *t*-Bu, 1 *dia.*), 1.51 – 2.20 (m, 10H, 5CH_2), 2.20 – 2.45 (m, 2 H, CH_2), 3.15 – 3.28 (m, 2 H, C*H*H + CH), 3.43 (bs, 1H, CH*H*), [4.12] (bs, 0.3H, NCH, 1 *dia. mino*), 4.26 (bs, 0.69 H, NCH, 1 *dia.*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 24.4 (CH_2, 1 *dia.*), [24.9] (CH_2, 1 *dia.*), 26.7 (CH_2, 1 *dia.*), [27.1] (CH_2, 1 *dia.*), 27.6 (CH_2, 1 *dia.*), [28.0] (CH_2, 1 *dia.*), 28.5 (CH_3, *t*-Bu), 31.0 (CH_2), 42.0 (CH_2), 42.7 (CH_2), 45.9 (CH_2, 1 *dia.*), [47.2] (CH_2, 1 *dia.*), 52.1(CH, 1 *dia.*), [53.5] (CH, 1 *dia.*), 56.01 (NCH, 1 *dia.*), [56.7] (NCH, 1 *dia.*), 79.2 (*Ct*-Bu), 154.5 (CO_2, 1 *dia.*), [155.1] (CO_2, 1 *dia.*), 211.9 (CO). HRMS (ESI) m/z calcd for $C_{15}H_{25}NO_3$ $(M + Na)^+$ 290.1727, found 290.1730.

2-(1-oxobut-3-en-2-yl)-pyrrolidine-1-carboxylic acid *tert*-Butyl ester (3g)

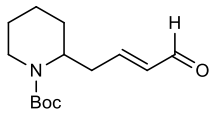


$C_{13}H_{21}NO_3$
M = 239.3107

Following **GP1** with *N*-Boc-2-hydroxypyrrolidine **1a** (96.4 mg, 0.51 mmol), 1-(trimethylsiloxy)-1,3-butadiene **2d** (98 μL, 0.55 mmol), and POM/Hf (1 mol%, 0.005 mmol), to give the desired product **3g** as a clear oil (83 mg, 0.35 mmol, 69% yield).

IR υ max (neat) / cm^{-1} 1683. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (s, 9H, *t*-Bu), 1.59 (bs, 1H, C*H*H), 1.71 – 1.84 (m, 2H, CH_2), 1.86 – 2.00 (m, 1H, CH*H*), 2.38 – 2.42 (m, 1H, C*H*HCH=CH), 2.68 (bs, 1H, CH*H*CH=CH), 3.24 – 3.33 (m, 2H, NCH_2), 3.91 (bs, 1H, NCH), 6.02 – 6.09(m, 1H, C*H*CHO), 6.75 (dt, *J* = 15.0, 7.0 Hz, 1H, C*H*=CHCHO), 9.44 (d, *J* = 7.0 Hz, 1H, CHO). ^{13}C NMR (100 MHz, $CDCl_3$, mixture of rotamers) δ 22.9 (CH_2), [23.6] (CH_2), 28.5 (CH_3, *t*-Bu), 30.0 (CH_2), [30.7] (CH_2), 37.7 (CH_2CH=CH), [38.1] (CH_2CH=CH), 46.4 (NCH_2), [46.6] (NCH_2), 56.0 (NCH), 79.4 (C*t*-Bu), [79.6] (C*t*-Bu), 134.5 (*CH*CHO), 154.5 (*CH*=CHCHO + CO_2), [155.0] (*CH*=CHCHO + CO_2), 193.6 (CHO), [193.8] (CHO). HRMS (ESI) m/z calcd for $C_{13}H_{21}NO_3$ $(M + Na)^+$ 262.1414, found 262.1416.

2-(1-oxobut-3-en-2-yl)-piperidine-1-carboxylic acid *tert*-Butyl ester (3h)

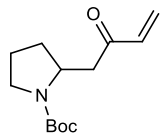


$C_{14}H_{23}NO_3$
M = 253.34

Following **GP1** with *N*-Boc-2-hydroxypiperidine **1b** (98.7 mg, 0.49 mmol), 1-(trimethylsiloxy)-1,3-butadiene **2d** (96 μL, 0.54 mmol) and POM/Hf (114 mg, 4 mol%, 0.02 mmol), to give the desired product **3h** as a clear oil (30 mg, 0.12 mmol, 24% yield).

IR υ max (neat) / cm^{-1} 1684. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 9H, *t*-Bu), 1.40 – 1.67 (m, 6H, $3CH_2$), 2.45 (dddd, *J* = 14.5, 7.3, 6.2, 1.4 Hz, 1H, C*H*HCH=CH), 2.69 – 2.84 (m, 2H, CH*H*CH=CH+NC*H*H), 4.00 (d, *J* = 13.1 Hz, 1H, NCH*H*), 4.49 (bs, 1H, NCH), 6.13 (dd, *J* = 15.5, 7.9 Hz, 1H, C*H*CHO), 6.81 (dt, *J* = 15.5, 7.4 Hz, 1H, C*H*=CHCHO), 9.49 (d, *J* = 7.9 Hz, 1H, CHO). ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.8 (CH_2), 25.3 (CH_2), 28.3 (CH_2), 28.4 (CH_3, *t*-Bu), 33.7 (*C*H_2CH=CH), 39.0 (NCH_2), 49.4 (NCH), 79.6 (C*t*-Bu), 134.3 (*CH*CHO), 154.9 (CO_2), 155.1 (*CH*=CHCHO), 193.7 (CHO). HRMS (ESI) m/z calcd for $C_{14}H_{23}NO_3$ $(M + Na)^+$ 276.1570, found 276.1574

2-(2-oxobut-3-en-1-yl)-pyrrolidine-1-carboxylic acid *tert*-Butyl ester (3i)

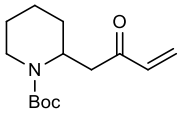


$C_{13}H_{21}NO_3$
M = 239.31

Following **GP1** with *N*-Boc-2-hydroxypyrrolidine **1a** (123.2 mg, 0.66 mmol), 2-trimethylsiloxy-1,3-butadiene **2e** (178 μL, 0.99 mmol), and POM/Hf (10 mol%, 0.066 mmol), to give the desired product **3i** as a clear oil (71 mg, 0.30 mmol, 45% yield).

IR υ max (neat) / cm^{-1} 1684, 1391. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 9H, *t*-Bu), 1.61 – 1.73 (m, 1H, C*H*H), 1.74 – 1.89 (m, 2H, CH_2), 1.94 – 2.10 (m, 1H, CH*H*), 2.52 (bs, 1H, C*H*HCO), 3.03 – 3.53 (m, 3H, NCH_2+CH*H*CO), 4.17 (ddt, *J* = 11.0, 7.6, 3.2 Hz, 1H, NCH), 5.82 – 5.91 (m, 1H, CH=CHH_{cis}), 6.31 (bs, 2H, C*H*=CHH_{trans}). ^{13}C NMR (100 MHz, $CDCl_3$, mixture of rotamers) δ 22.8 (CH_2), [23.5] (CH_2), 28.5 (CH_3, *t*-Bu), 30.3 (CH_2), [31.3] (CH_2), 43.7 (CH_2), [44.5] (CH_2), 46.2 (CH_2), [46.5] (CH_2), 53.8 (CH), [54.1] (CH), 79.2 (C, *t*-Bu), [79.6] (C*t*-Bu), 128.6 (CH_2), [128.9] (CH_2), 136.8 (CH), 154.3 (CO_2), 199.2 (CO), [199.7] (CO). HRMS (ESI) m/z calcd for $C_{13}H_{21}NO_3$ $(M + Na)^+$ 262.1414, found 262.1412.

2-(2-oxobut-3-en-1-yl)-piperidine-1-carboxylic acid *tert*-Butyl ester (3j)



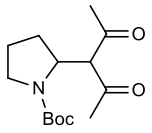
$C_{14}H_{23}NO_3$
M = 253.34

Following **GP1** with *N*-Boc-2-hydroxypiperidine **1b** (104.7 mg, 0.52 mmol), 2-(trimethylsiloxy)-1,3-butadiene **2e** (140 μL, 0.78 mmol), and POM/Hf (10 mol%, 0.052 mmol), to give the desired product **3j** as a clear oil (13 mg, 0.05 mmol, 10% yield).

IR υ max (neat) / cm^{-1} 1687. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (s, 9H, *t*-Bu), 1.53 – 1.69 (m, 6H, $3CH_2$), 2.74 – 2.87 (m, 3H, NC*H*H + CH_2CO), 3.99 (m, 1H, NCH*H*), 4.71 (dd, *J* = 12.2, 5.6 Hz, 1H, NCH), 5.85 (dd, *J* = 10.3, 1.2 Hz, 1H, CH=CHH_{cis}), 6.26 (dd, *J* = 13.0, 1.2 Hz, 1H, CH=CHH_{trans}), 6.38 (dd, *J* = 13.0, 10.3 Hz, 1H, COC*H*=CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.8 (CH_2), 25.3 (CH_2), 28.2 (CH_2), 28.4 (CH_3, *t*-Bu), 39.5 (N*C*H_2), 40.3 (*C*H_2CO), 47.8 (N*C*H), 79.7

(C*t*-Bu), 128.6 (CH=*CH*$_2$), 136.5 (*CH*=CH$_2$), 154.7 (CO_2), 198.9 (CO). HRMS (ESI) m/z calcd for $C_{14}H_{23}NO_3$ $(M + Na)^+$ 276.1570, found 276.1573.

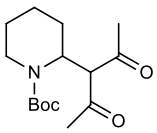
2-(2,4-dioxophentane-3-yl)-pyrrolidine-1-carboxylic acid *tert*-Butyl ester (7a)



$C_{14}H_{23}NO_4$
M = 269.3367

Following **GP1** with *N*-Boc-2-hydroxypyrrolidine **1a** (39mg, 0.21 mmol), 2,4-pentanedione **6a** (21.4 μL, 0.21 mmol), and POM/Hf (10 mol%, 0.021 mmol), to give the desired product **7a** as a clear oil (35 mg, 0.13 mmol, 63% yield). Spectral data correspond to those described in the literature. [6][*Journal of Organic Chemistry,* **1983**, *48*, 4058-4067.]
IR υ max (neat) / cm^{-1} 1686, 1389, 1364. ^{1}H NMR (400 MHz, C_6D_6) δ 1.12 – 1.23 (m, 1H, C*H*H), 1.24 – 1.33 (m, 1H, CH*H*), 1.42 (s, 9H, *t*-Bu), 1.70 (bs, 2H, CH_2), 1.84 (s, 3H, COCH_3), 1.88 (s, 3H, COCH_3), 2.94 – 3.25 (m, 2H, NCH_2), 4.41 – 4.45 (m, 2H, 2CH). ^{13}C NMR (101 MHz, C_6D_6) δ 22.3 (CH_2), 27.0 (CH_2 + CH_3, *t*-Bu), 27.8 (CH_3), 30.3 (CH_3), 45.5 (CH_2), 55.9 (NCH), 67.4 (CH), 77.9 (*Ct*-Bu), 153.1 (CO_2), 200.5 (CO), 203.3 (CO).

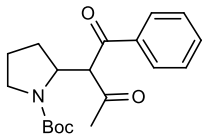
2-(2,4-dioxopentan-3-yl)-piperidine-1-carboxylic acid *tert*-Butyl ester (7b)



$C_{15}H_{25}NO_4$
M = 283.36

Following **GP1** with *N*-Boc-2-hydroxypiperidine (78 mg, 0.39 mmol), 2,4-pentanedione (40 μL, 0.39 mmol), and POM/Hf (10 mol%, 0.039 mmol), to give the desired product **7b** as a clear oil (63 mg, 0.22 mmol, 57% yield).
IR υ max (neat) / cm^{-1} 1686. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 – 1.64 (m, 15H, *t*-Bu + 3CH_2), 2.07 (s, 3H, $COCH_3$), 2.14 (s, 3H, $COCH_3$), 2.67 (bs, 1H, NC*H*H), 3.88 (bd, *J* = 51.8 Hz, 1H, NCH*H*), 4.23 (d, *J* = 10.8 Hz, 1H, CH), 5.06 (bd, *J* = 48.8 Hz, 1H, NCH). ^{13}C NMR (100 MHz, $CDCl_3$, mixture of rotamers) δ 19.2 (CH_2), 25.1 (CH_2), 26.9 (CO*CH$_3$* + *CH$_2$*), 28.3 (CH_3, *t*-Bu), 31.0 (CO*CH$_3$*), 39.0 (CH_2), [40.3] (CH_2), 49.8 (NCH), [51.1] (NCH), 68.9 (CH), 80.1 (*Ct*-Bu), 154.5 (CO_2), 202.2 (CO). HRMS (ESI) m/z calcd for $C_{15}H_{25}NO_4$ $(M + Na)^+$ 306.1676, found 306.1667.

2-(1,3-dioxo-1-phenylbutan-2-yl)-pyrrolidine-1-carboxylic acid *tert*-Butyl ester (7c)

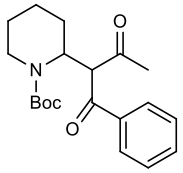


$C_{19}H_{25}NO_4$
M = 331.4061

Following **GP1** with *N*-Boc-2-hydroxypyrrolidine **1a** (39 mg, 0.21 mmol), 1-phenyl-1,3-butanedione **6b** (35 mg, 0.21 mmol), and POM/Hf (10 mol%, 0.021 mmol) , to give the desired product **7c** as a clear oil (44.5 mg, 0.13 mmol, 64% yield).

IR υ max (neat) / cm^{-1} 1681, 1389. ^1H NMR (400 MHz, $CDCl_3$, mixture of rotamers and diastereomers) δ 1.20 – 1.73 (m, 11H, CH_2 + *t*-Bu), 1.74 – 2.19(m, 5H, $COCH_3$ + CH_2), 2.70 – 3.53 (m, 2H, NCH_2), 4.24 – 4.69 (m, 1H, NCH), 4.77 – 5.54 (m, 1H, CH), 7.46 – 7.51 (m, 2H, Harom), 7.57 – 7.64 (m, 1H, Harom), 7.98 (d, *J* = 6.9 Hz, 2H, Harom). ^{13}C NMR (100 MHz, $CDCl_3$, mixture of rotamers and diastereomers) δ 22.7 (CH_2), [23.6] (CH_2), 28.2 (CH_2), 28.3 (CH_3, *t*-Bu), [28.4] (CH_3, *t*-Bu), 29.2 ($COCH_3$), [31.3] ($COCH_3$), 46.4 (CH_2), 57.6 (NCH), 63.0 (CH), [63.7] (CH), 79.6 (*Ct*-Bu), [80.3] (*Ct*-Bu), 128.7 (CHarom), [128.8] (CHarom), 133.5 (CHarom), [133.8] (CHarom), 136.7 (Carom), [137.4] (Carom), 154.7 (CO_2), 198.0 (CO), 202.9 (CO). HRMS (ESI) m/z calcd for $C_{19}H_{25}NO_4$ $(M + Na)^+$ 354.1676, found 354.1674.

2-(1,3-dioxo-1-phenylbutan-2-yl)-piperidine-1-carboxylic acid *tert*-Butyl ester (7d)

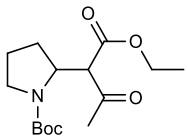


$C_{20}H_{27}NO_4$
M = 345.4327

Following **GP1** with *N*-Boc-2-hydroxypiperidine **1b** (75.6 mg, 0.38 mmol), and 1-phenyl-1,3-butanedione **6b** (61.5 mg, 0.38 mmol) and POM/Hf (10 mol%, 0.04 mmol), to give the desired product **7d** as a white solid, one diastereomer was separated in 8% (11 mg), the other one was obtained as a mixture with impurities (9.5 mg of product was expected from the ^1H NMR).

IR υ max (neat) / cm-1 1687, 1159. ^1H NMR (400 MHz, $CDCl_3$) δ 1.38 (s, 9H, *t*-Bu), 1.55 – 1.74 (m, 6H, $3CH_2$), 2.25 (s, 3H, $COCH_3$), 2.65 (bs, 1H, NC*H*H), 3.89 (bs, 1H, NCH*H*), 5.08 (d, *J* = 11.1 Hz, 1H, CH), 5.33 (d, *J* = 9.8 Hz, 1H, NCH), 7.48 (t, *J* = 7.6 Hz, 2H, Harom), 7.59 (t, *J* = 7.4 Hz, 1H, Harom), 7.97(d, *J* = 8.6 Hz, 2H, Harom). ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.3 (CH_2), 25.2 (CH_2), 27.2 (CH_2), 28.2 (CH_3, *t*-Bu), 28.5 ($COCH_3$), 39.2 (CH_2), 51.3 (NCH), 63.8 (CH), 79.8 (*Ct*-Bu), 128.6 (CHarom), 128.8 (CHarom), 133.5 (CHarom), 136.9 (Carom), 154.2 (CO_2), 193.9 (CO), 202.8 (CO). HRMS (ESI) m/z calcd for $C_{20}H_{27}NO_4$ $(M + Na)^+$ 368.1832, found 368.1831.

2-(1-ethoxy-1,3-dioxobutan-2-yl)-pyrrolidine-1-carboxylic acid *tert*-Butyl ester (7e)

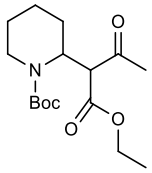


$C_{15}H_{25}NO_5$
M = 299.3627

Following **GP1** with *N*-Boc-2-hydroxypyrrolidine **1a** (51.4 mg, 0.28 mmol), ethyl acetoacetate **6c** (35 μL, 0.28 mmol), and POM/Hf (10 mol%, 0.028 mmol), to give the desired product **7e** as a 58/42 mixture of diastereomers (46 mg, 0.15 mmol, 55% yield).

IR υ max (neat) / cm^{-1} 1688, 1390, 1366, 1157. ^1H NMR (400 MHz, $CDCl_3$, mixture of diastereomers) δ 1.15 – 1.27 (m, 3H, CH_2CH_3), 1.39 (s, 5.2H, *t*-Bu, 1 *dia*.), [1.40] (s, 3.7H, *t*-Bu, 1 *dia. mino*), 1.64 – 1.81 (m, 2H, CH_2), 1.82 – 2.09 (m, 2H, CH_2), 2.16 (s, 3H, $COCH_3$), 3.12 – 3.23 (m, 2H, NC*H*H), 3.36 (bs, 1H, NCH*H*), 4.03 – 4.19 (m, 3H, CH + CH_2CH_3), 4.21 – 4.39 (m, 1H, NCH). ^{13}C NMR (100 MHz, $CDCl_3$, mixture of diastereomers) δ 14.0 (CH_3, 1 *dia*.), [14.1] (CH_3, 1 *dia*.), 23.6 (CH_2), 28.5 (CH_3, *t*-Bu), 29.2 (CH_2), 30.9 ($COCH_3$, 1 *dia*.), [31.8] ($COCH_3$, 1 *dia*.), 46.7 (CH_2, 1 *dia*.), [47.0] (CH_2, 1 *dia*.), 56.4 (NCH, 1 *dia*.), [57.0] (NCH, 1 *dia*.), 61.2 (CH_2), 61.5 (CH), 79.7 (*Ct*-Bu), 154.5 (CO_2), 168.5 (CO), [169.0] (CO, 1 *dia*.), 201.9 (CO , 1 *dia*.), [203.9] (CO, 1 *dia*.). HRMS (ESI) m/z calcd for $C_{15}H_{25}NO_5$ $(M + Na)^+$ 322.1625, found 322.1617.

2-(1-ethoxy-1,3-dioxobutan-2-yl)-piperidine-1-carboxylic acid *tert*-Butyl ester (7f)

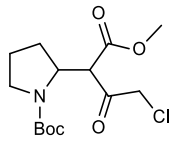


$C_{16}H_{27}NO_5$
M = 313.3893

Following **GP1** with *N*-Boc-2-hydroxypiperidine **1b** (77.5 mg, 0.39 mmol), ethyl acetoacetate **6c** (50 µL, 0.39 mmol), and POM/Hf (10 mol%, 0.039 mmol), to give the desired product **7f** as a colorless oil, only one diastereomer was successfully separated in 35% yield (42.4 mg).

IR υ max (neat) / cm^{-1} 1685, 1156. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (t, *J* = 7.1 Hz, 3H, CH_2CH_3), 1.38 – 1.54 (m, 12H, CH_2 + C*H*H + *t*-Bu), 1.59 – 1.69 (m, 3H, CH_2 + CH*H*), 2.28 (s, 3H, $COCH_3$), 2.85 (bs, 1H, NC*H*H), 3.83 – 4.28 (m, 4H, CH_2 + NCH*H* +CH), 5.02 (bs, 1H, NCH). ^{13}C NMR (100 MHz, $CDCl_3$, mixture of rotamers) δ 13.9 (CH_2CH_3), 19.0 (CH_2), 25.1 (CH_2), 27.1 (CH_2), 28.3 (CH_3, *t*-Bu), 28.9 ($COCH_3$), 38.9 (CH_2), [40.4] (CH_2), 49.5 (NCH), [50.3] (NCH), 59.5 (CH), 61.4 (CH_2), 79.7 (*Ct*-Bu), 154.4 (CO_2), 167.6 (CO), [168.4] (CO), 201.4 (CO). HRMS (ESI) m/z calcd for $C_{16}H_{27}NO_5$ $(M + Na)^+$ 336.1781, found 336.1788.

2-(4-chloro-1-methoxy-1,3-dioxobutan-2-yl)-pyrrolidine-1-carboxylic acid *tert*-Butyl ester (7g)

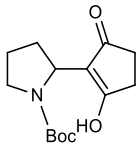


$C_{14}H_{22}ClNO_5$
M = 319.7812

Following **GP1** with Boc-2-hydroxypyrrolidine **1a** (37 mg, 0.20 mmol), Methyl 4-chloroacetoacetate **6d** (24 µL, 0.20 mmol), and POM/Hf (10 mol%, 0.02 mmol), to give the desired product **7g** as a 56/44 mixture of diastereomers (31 mg, 0.10 mmol, 49% yield).

IR υ max (neat) / cm^{-1} 1684, 1391, 1158. ^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereomers) δ 1.41 (s, 5H, *t*-Bu, 1 *dia.*), [1.42] (s, 4H, *t*-Bu, 1 *dia.*), 1.68 – 1.89 (m, 2.6H, CH_2 + C*H*H (1 *dia.*)), 1.96 – 2.06 (m, 0.6 H, CH*H*, 1 *dia.*), 2.06 – 2.16 (m, 1H, C*H*H, 2 *dias.*)3.18 – 3.28 (m, 1H, NC*H*H), 3.37 (bs, 1H, NCH*H*), 3.68 (s, 1.3H, $COOCH_3$, 1 *dia.*), [3.70] (s, 1.7 H, $COOCH_3$, 1 *dia.*), 4.06 – 4.63 (m, 4H, NCH + CH + CH_2Cl). ^{13}C NMR (100 MHz, $CDCl_3$, mixture of diastereomers) δ 23.5 (CH_2), 28.3 (CH_3, *t*-Bu), 28.5 (CH_2, 1 *dia.*), [29.21 *dia.*] (CH_2), 46.5 (CH_2, 1 *dia.*), [46.9] (CH_2, 1 *dia.*), 47.7 (CH_2, *1dia.*), [49.2] (CH_2, 1 *dia.*), 52.5 ($COOCH_3$, 1 *dia.*), [52.5] ($COOCH_3$, 1 *dia.*), 55.9 (NCH), 56.8 (CH, 1 *dia.*), [57.0] (CH, 1 *dia.*), 79.9 (*Ct*-Bu), 154.4 (CO_2), 167.9 (CO, 1 *dia.*), [168.5] (CO, 1 *dia.*), 195.7 ($COCH_2$, 1 *dia.*), [196.9] ($COCH_2$, 1 *dia.*). HRMS (ESI) m/z calcd for $C_{14}H_{22}ClNO_5$ $(M + Na)^+$ 342.1079, found 342.1082.

2-(2,5-dioxocyclopentyl)-pyrrolidine-1-carboxylic acid *tert*-Butyl ester (7i)

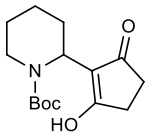


$C_{14}H_{21}NO_4$
M = 267.3208

Following **GP1** with *N*-Boc-2-hydroxypyrrolidine **1a** (39 mg, 0.21 mmol), 1,3-cyclopentanedione **6e** (21 mg, 0.21 mmol) and POM/Hf (12 mg, 1 mol%, 0.002 mmol), to give the desired product **7i** as a white solid (54 mg, 0.20 mmol, 95% yield), which is mainly in its enol form.

IR υ max (neat) / cm^{-1} 1625, 1388, 1160. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (s, 9H, *t*-Bu), 1.72 – 1.89 (m, 2H, 2C*H*H), 2.27 (bs, 1H, CH*H*), 2.34 (bs, 4H, $2CH_2$), 2.56 (bs, 1H, CH*H*), 3.19 – 3.38 (m, 2H, NCH_2), 4.46 – 4.56 (m, 1H, NCH).^{13}C NMR (100 MHz, C_6D_6) δ 25.7 (CH_2). 27.4 (CH_2), 28.2 (CH_3, *t*-Bu), 30.0 ($2CH_2$), 46.7 (CH_2), 52.3 (CH), 80.9 (*Ct*-Bu), 116.5 (C), 157.7 (CO_2), 195.9 (CO + *C*OH). HRMS (ESI) m/z calcd for $C_{14}H_{21}NO_4$ $(M + Na)^+$ 290.1363, found 290.1365.

2-(2,5-dioxocyclopentyl)-piperidine-1-carboxylic acid *tert*-Butyl ester (7j)

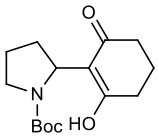


$C_{15}H_{23}NO_4$
M = 281.3474

Following **GP1** with *N*-Boc-2-hydroxypiperidine **1b** (58.4 mg, 0.29 mmol), 1,3-cyclopentanedione **6e** (29.2 mg, 0.29 mmol) and POM/Hf (1 mol%, 0.003 mmol), to give the desired product **7j** as a white solid (67.7 mg, 0.24 mmol, 83% yield), which is mainly in its enol form. [7][*Tetrahedron Letters*, 2004, *45*, 2821-2823]

IR υ max (neat) / cm^{-1} 1690, 1581, 1401, 1371. ^{1}H NMR (400 MHz, $CDCl_3$, mixture of rotamers) δ 1.36 – 1.58 (m, 10H, *t*-Bu + C*H*H), 1.58 – 1.77 (m, 3H, 2C*H*H + CH*H*), 2.23 – 2.37 (m, 2H, 2CH*H*), 2.49 (m, 4H, $2CH_2$), 2.75 (t, *J* = 11.9 Hz, 1H, NC*H*H), 3.87 (d, *J* = 12.3 Hz, 1H, NCH*H*), 4.88 (d, *J* = 6.4 Hz, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4 (CH_2). 24.7 (CH_2), 25.3 (CH_2), 28.4 (CH_3, *t*-Bu), 41.4 (CH_2), 46.2 (CH), 81.7 (*Ct*-Bu), 117.2 (C), 158.1 (CO_2). HRMS (ESI) m/z calcd for $C_{15}H_{23}NO_4$ $(M + Na)^+$ 304.1519, found 304.1518.

2-(2-hydroxy-6-oxocyclohex-1-en-1-yl)-pyrrolidine-1-carboxylic acid *tert*-Butyl ester (7k)



$C_{15}H_{23}NO_4$
M = 281.3474

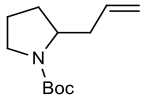
Following **GP1** with N-Boc-2-hydroxypyrrolidine **1a** (115 mg, 0.61 mmol), 1,3-Cyclohexanedione **6f** (71 µL, 0.61 mmol) and POM/Hf (34 mg, 1 mol%, 0.006 mmol), to give the desired product **7k** as a white solid (146 mg, 0.52 mmol, 85% yield), which is mainly in its enol form.

IR υ max (neat) / cm^{-1} 1633, 1383. ^{1}H NMR (400 MHz, C_6D_6) δ 1.20 – 1.49 (m, 12H, CH_2 + C*H*H+ *t*-Bu), 1.69 – 1.89 (m, 2H, 2C*H*H), 2.01 – 2.25 (m, 4H, CH_2 + 2CH*H*), 2.29 – 2.38 (m, 1H, CH*H*), 3.44 – 3.60 (m, 1H, NC*H*H), 3.60 – 3.67 (m, 1H, NCH*H*), 4.79 (dd, *J* = 9.3, 5.4 Hz, 1H, CH), 11.47 (s, 1H, OH). ^{13}C NMR (100 MHz, C_6D_6) δ 19.8 (CH_2), 25.5 (CH_2),

28.3 (CH_3, *t*-Bu), 29.4 (CH_2), 30.2 (CH_2), 37.6 (CH_2), 47.5 (NCH_2), 53.2 (CH), 80.4 (C*t*-Bu), 117.2 (C), 156.9 (CO_2), 175.9 (COH), 196.3 (CO). HRMS (ESI) m/z calcd for $C_{15}H_{23}NO_4$ $(M + Na)^+$ 304.1519, found 304.1527.

4. Allylation Reaction.

2-Allylpyrrolidine-1-carboxylic acid *tert*-butyl ester (8a)

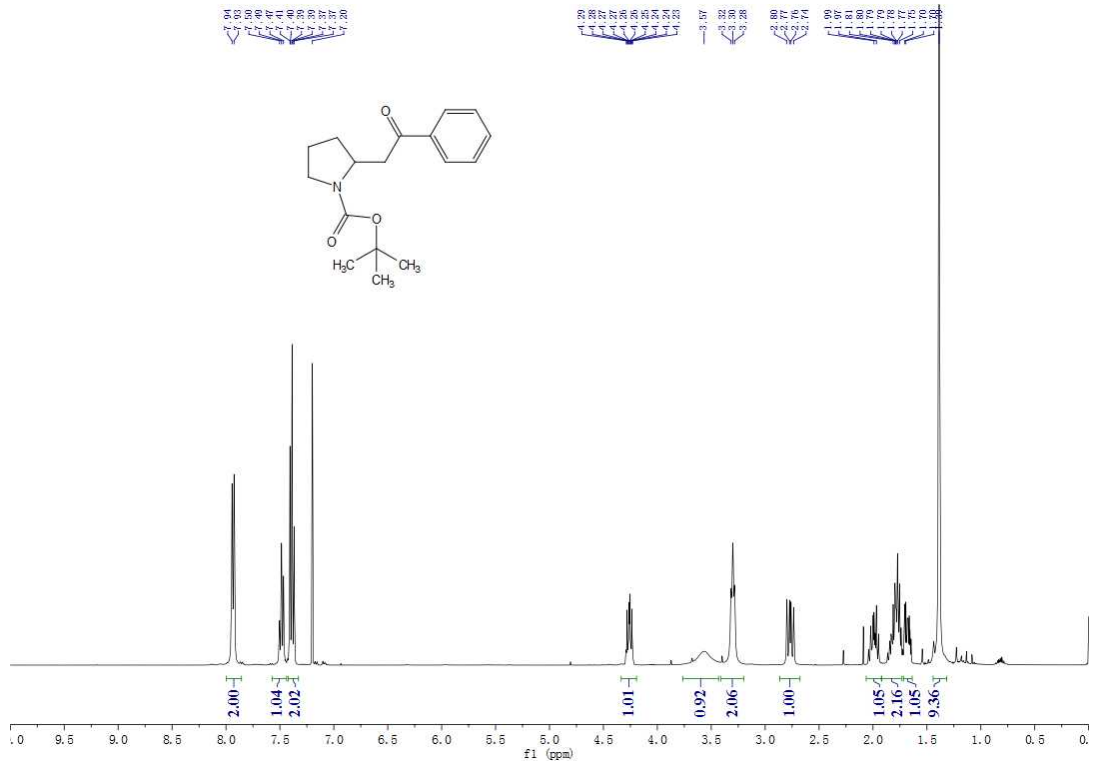


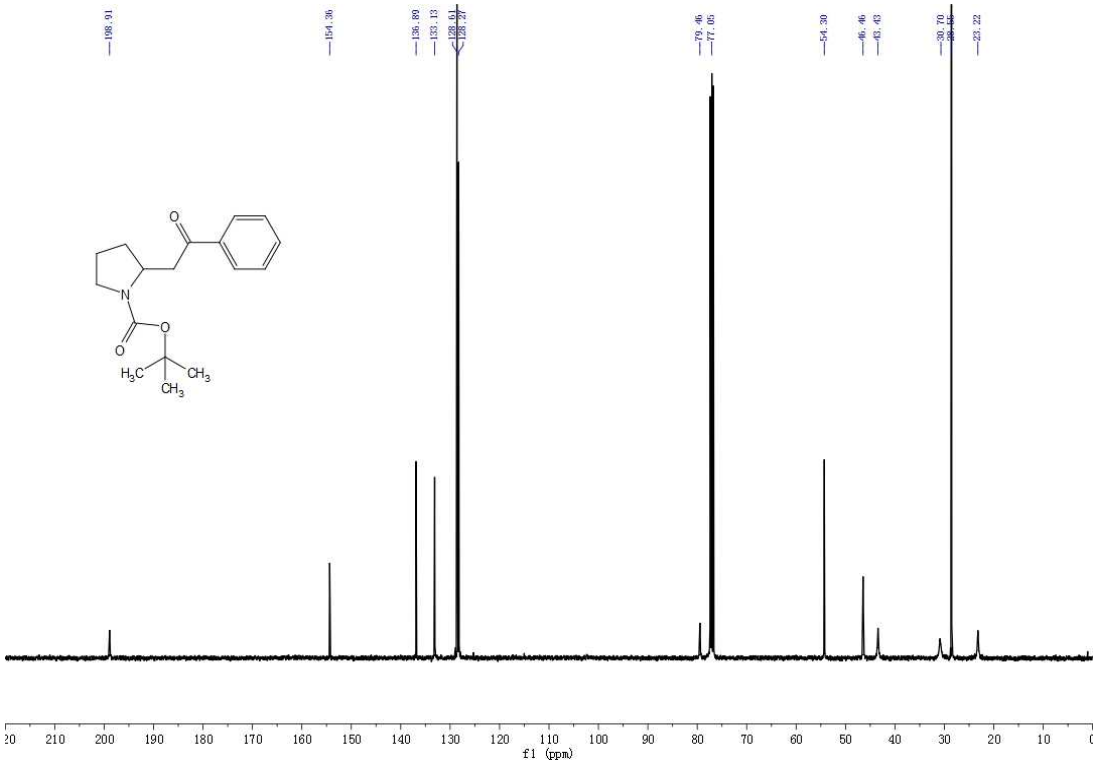
$C_{12}H_{21}NO_2$
M = 211.3006

Following **GP1** with *N*-Boc-2-hydroxypyrrolidine **1a** (116.2 mg, 0.62 mmol), allyltrimethylsilane (0.5 mL, 3.1 mmol) and POM/Hf (702 mg, 20 mol%, 0.12 mmol), to give the desired product **8a** as a clear oil (22.7 mg, 0.11 mmol, 17% yield). [8][*Org. Lett.*, 2010, *12*, 4176–4179]

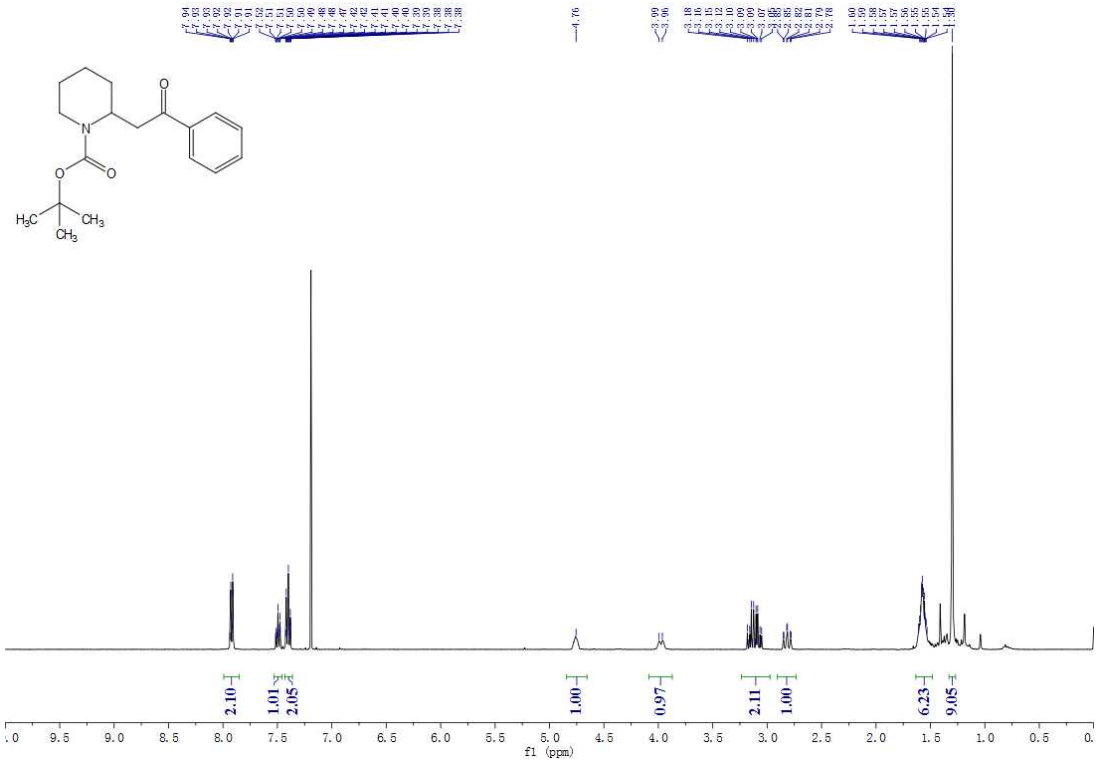
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49 (s, 9H, *t*-Bu), 1.63 – 1.99 (m, 4H, $2CH_2$), 2.06 – 2.23 (m, 1H, CH*H*CH=CH_2), 2.42 – 2.59 (m, 1H, C*H*HCH=CH_2), 3.25 – 3.47 (m, 2H, NCH_2), 3.76 – 3.90 (m, 1H, NCH), 5.00 – 5.14 (m, 2H, CH=CH_2), 5.67 – 5.87(m, 1H, C*H*=CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.2 (CH_2), 28.5 (CH_3, *t*-Bu), 29.7 (CH_2), 38.7 (CH_2), 46.5 (N*C*H_2), 56.8 (N*C*H), 79.0 (*Ct*-Bu), 116.9 (CH=*C*H_2), 135.3 (*C*H=CH_2), 154.5 (CO_2).

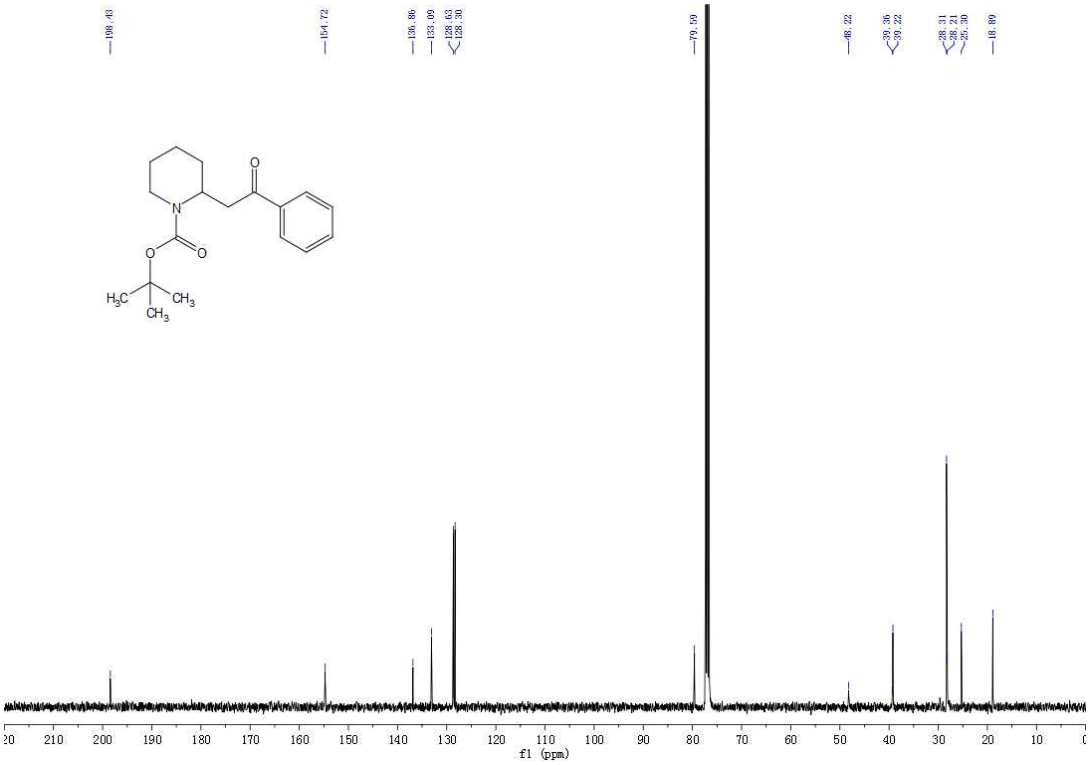
^{1}H and ^{13}C NMR Spectra of **3a**



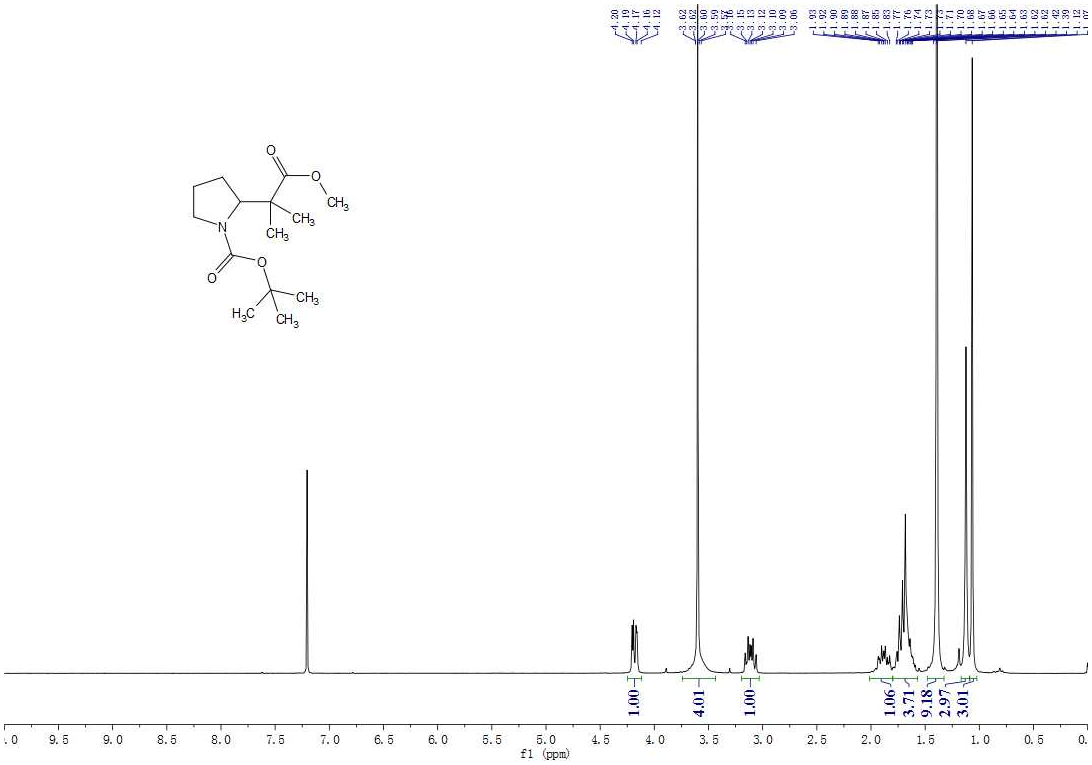


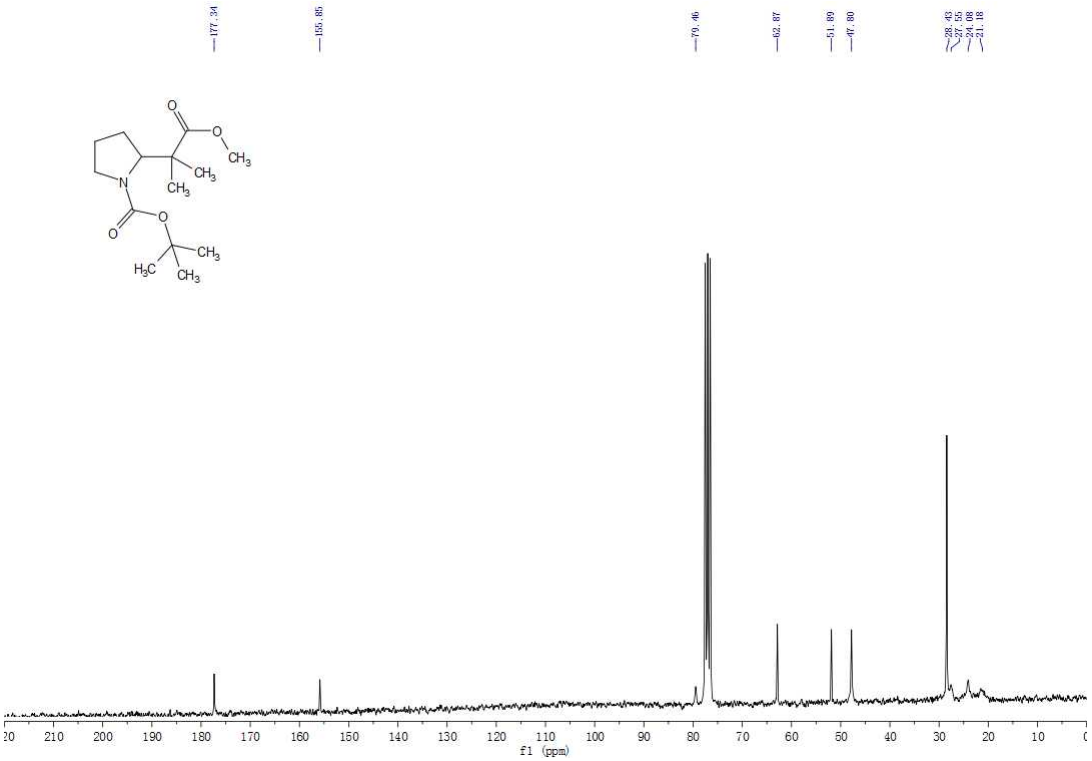
^{1}H and ^{13}C NMR Spectra of **3b**



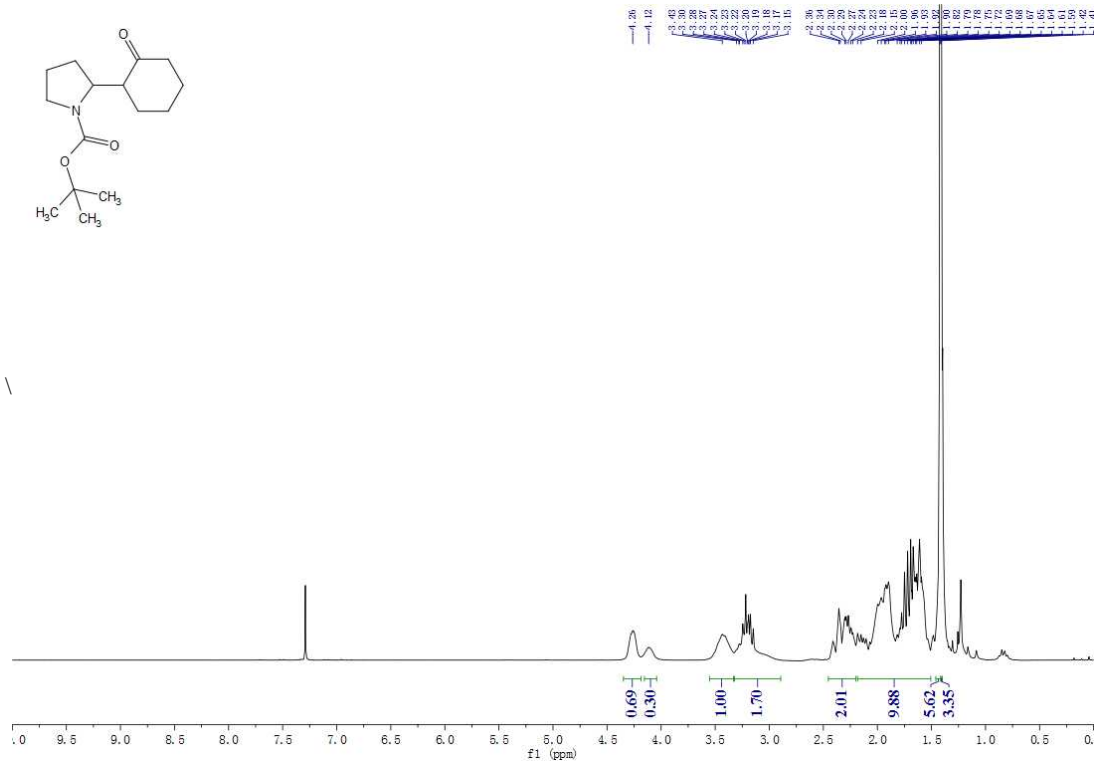


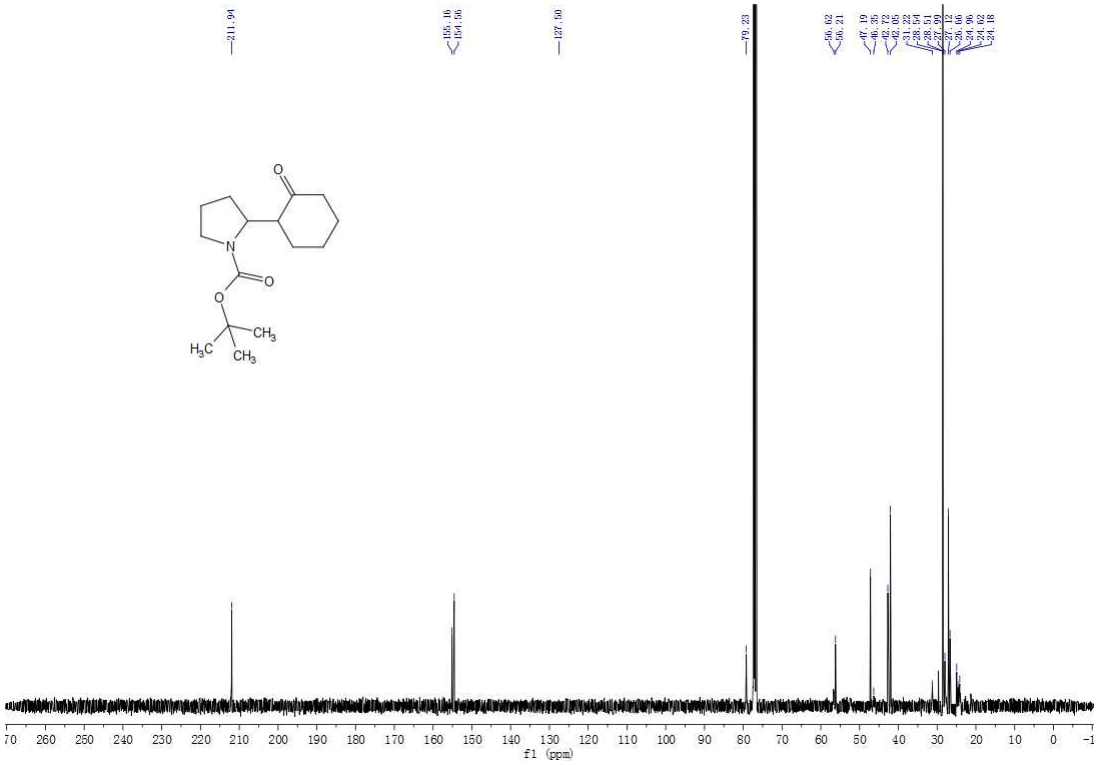
^{1}H and ^{13}C NMR Spectra of **3c**



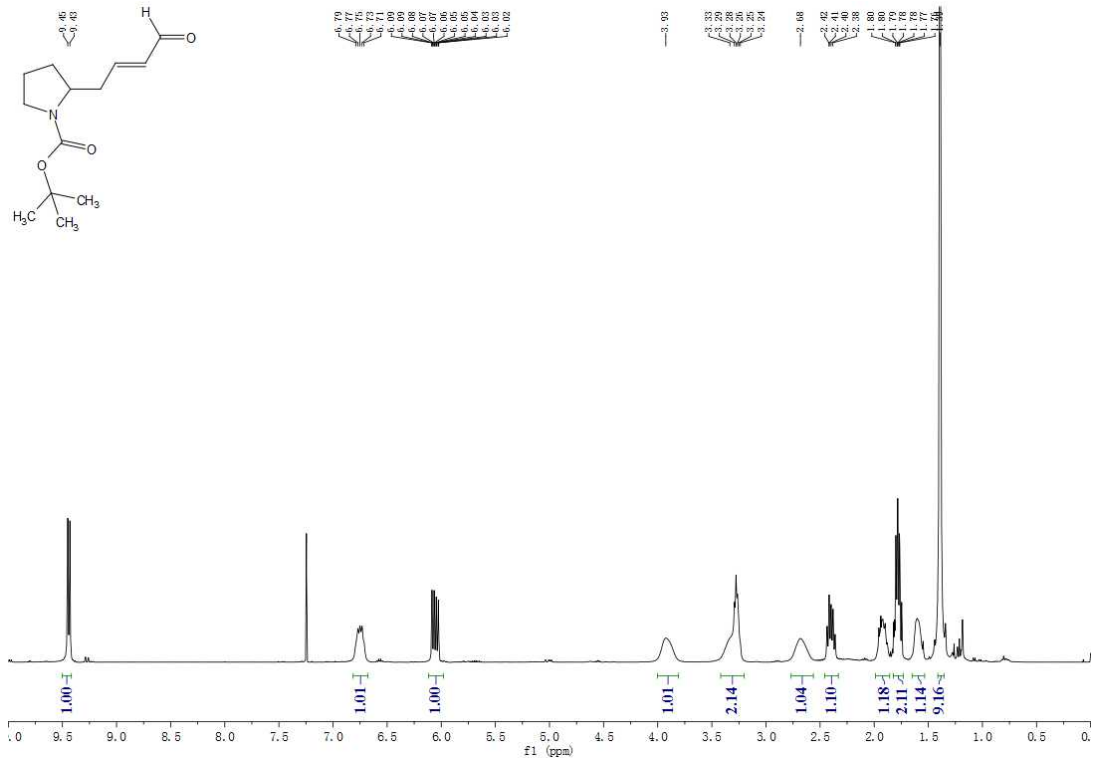


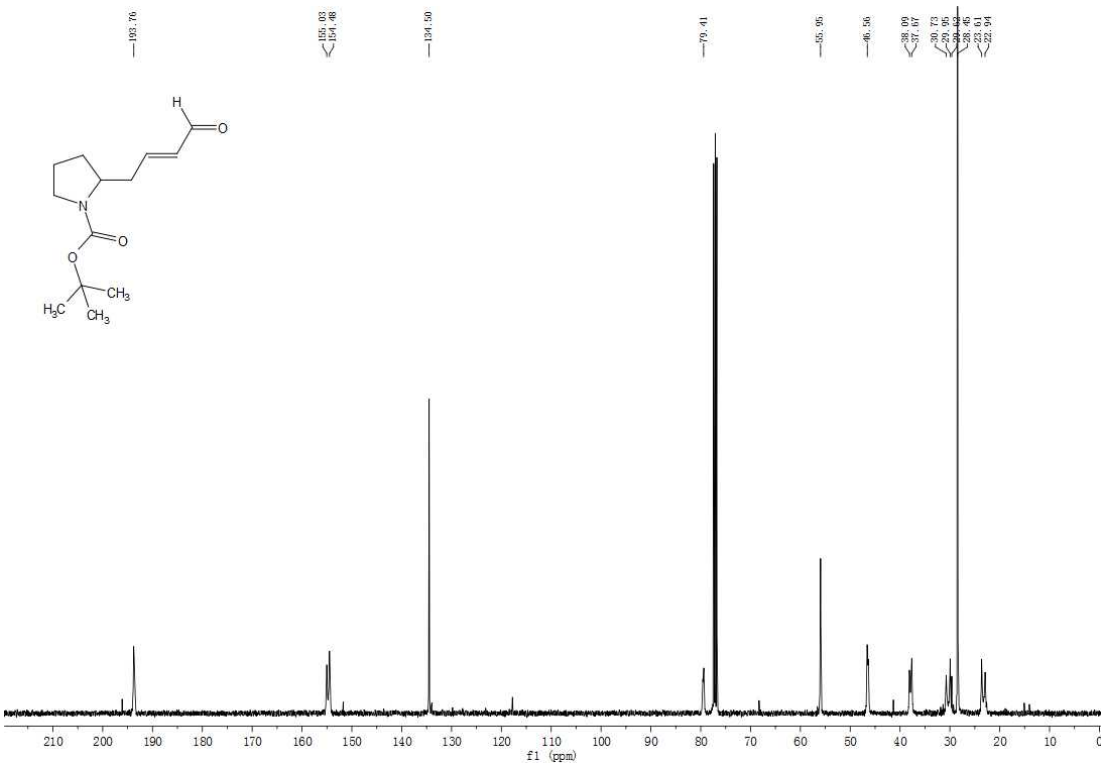
^{1}H and ^{13}C NMR Spectra of **3e**



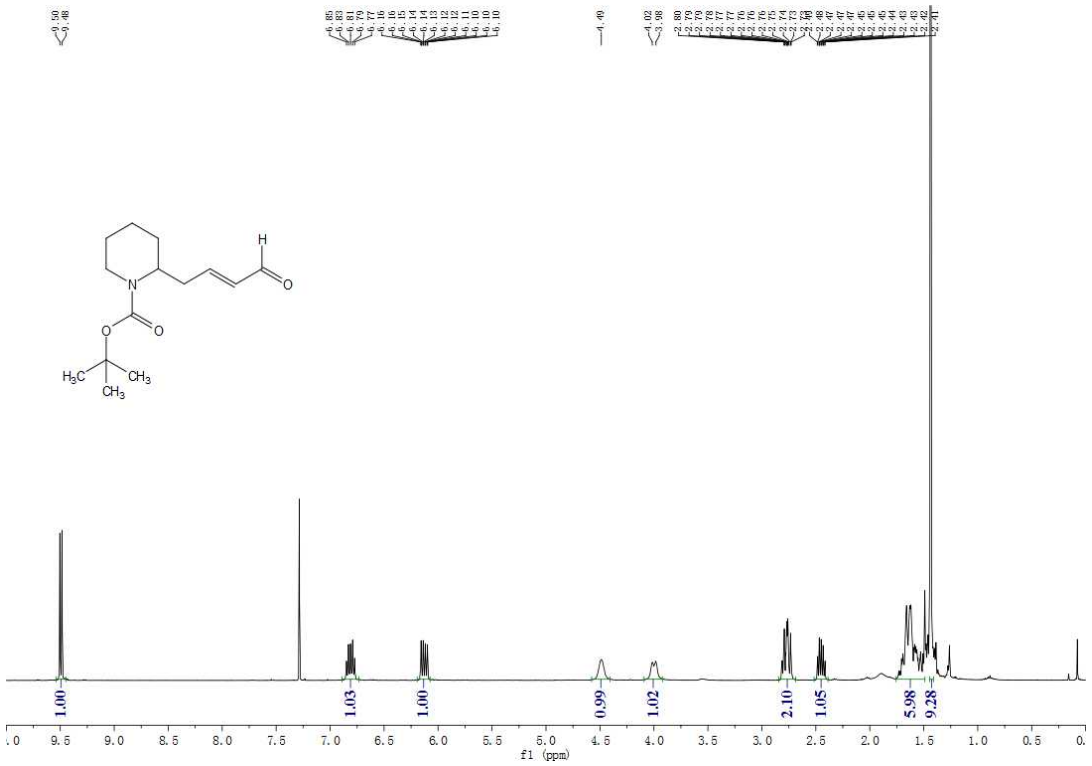


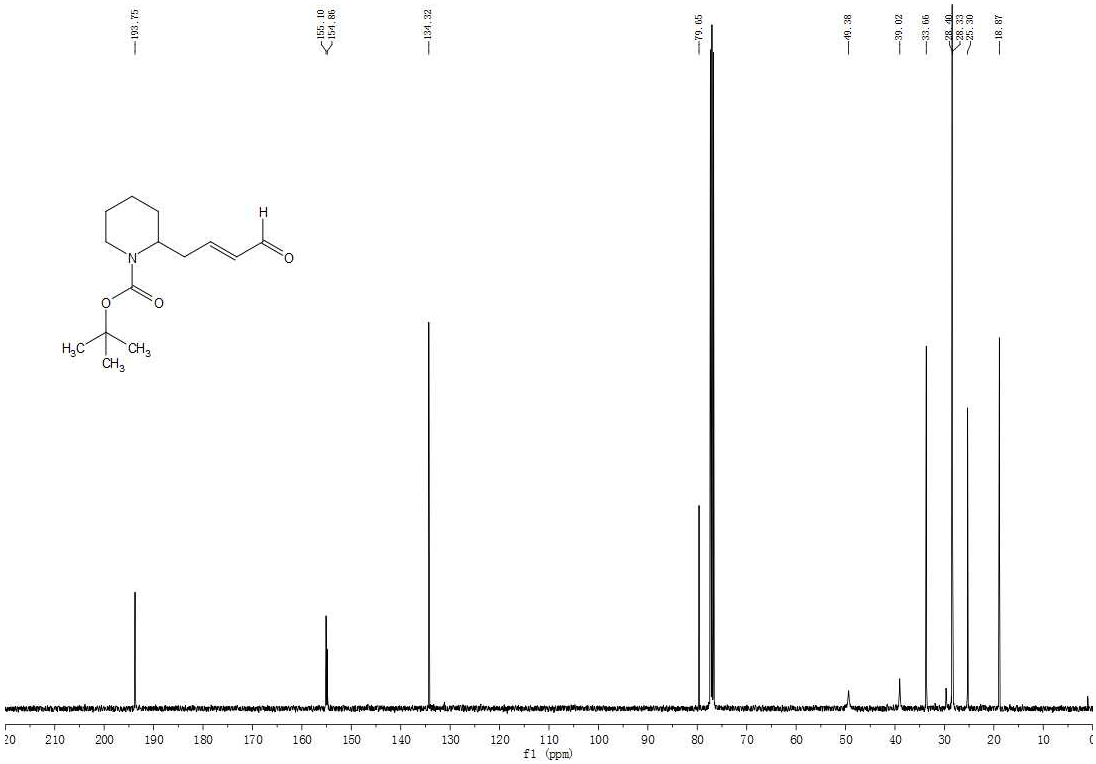
^{1}H and ^{13}C NMR Spectra of **3g**



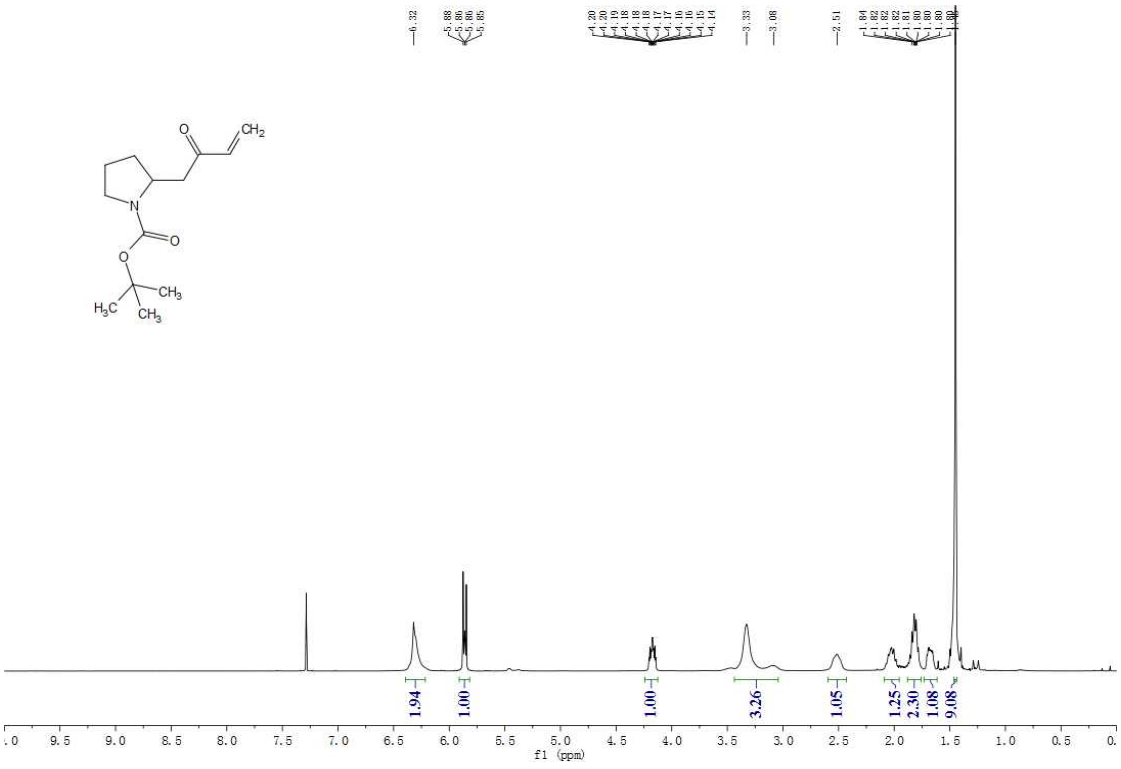


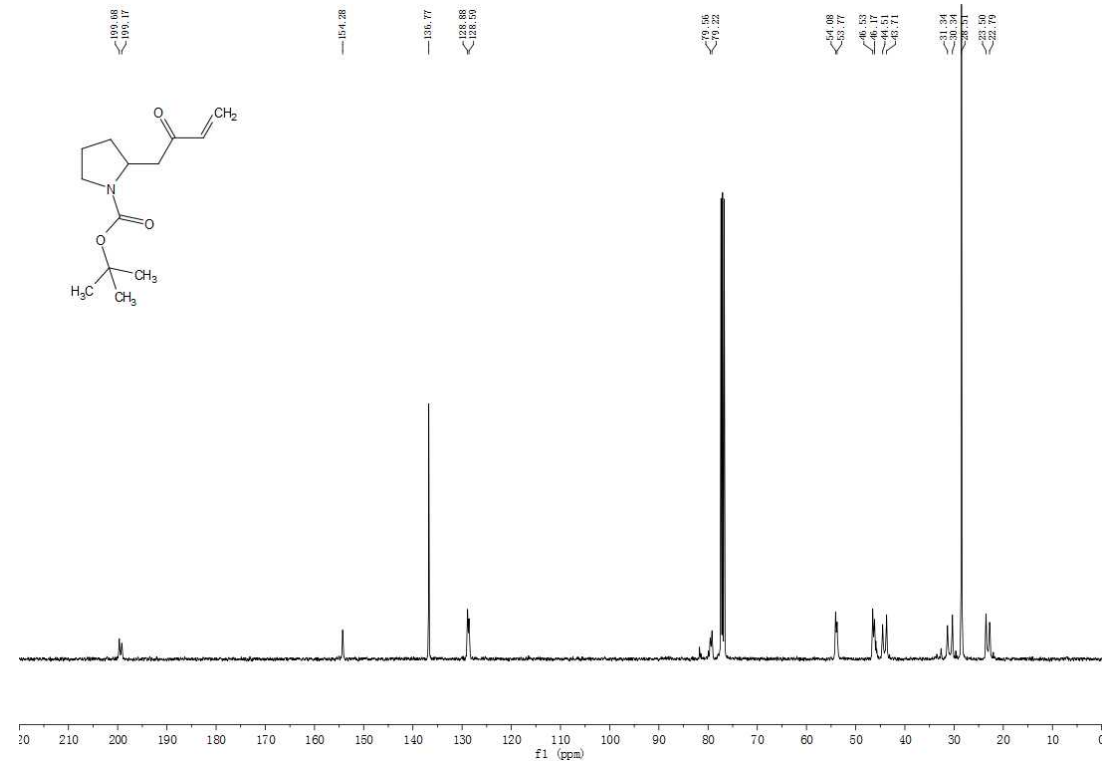
^{1}H and ^{13}C NMR Spectra of **3h**



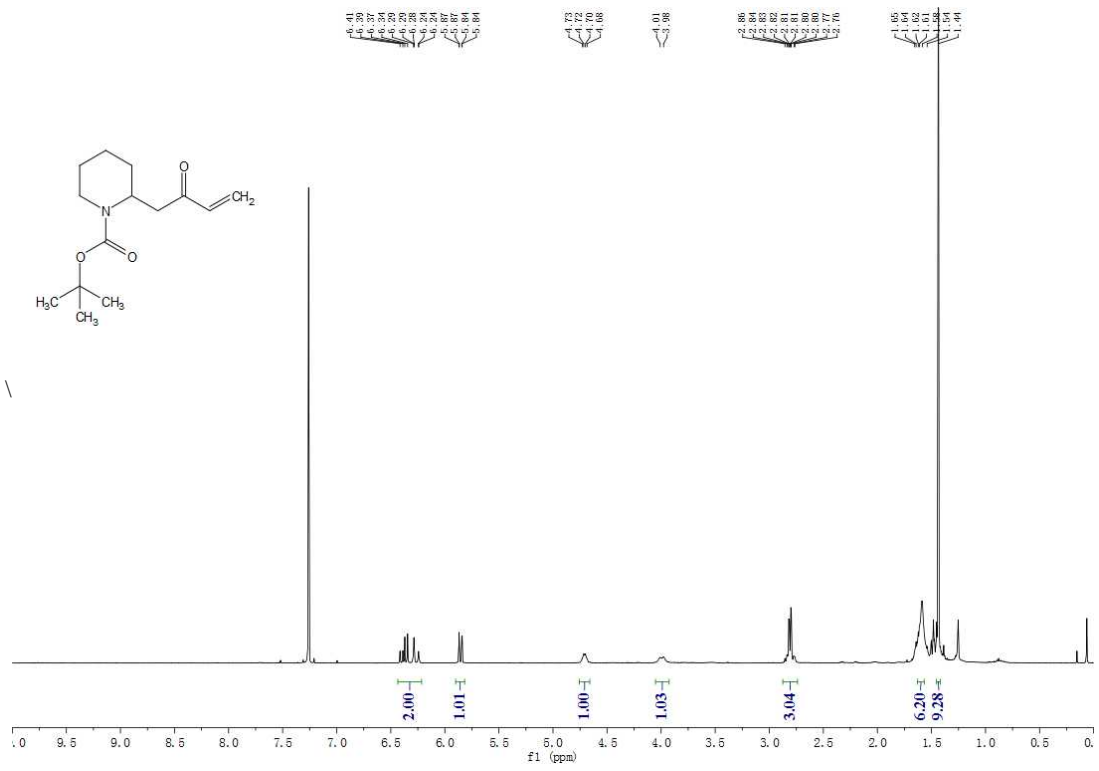


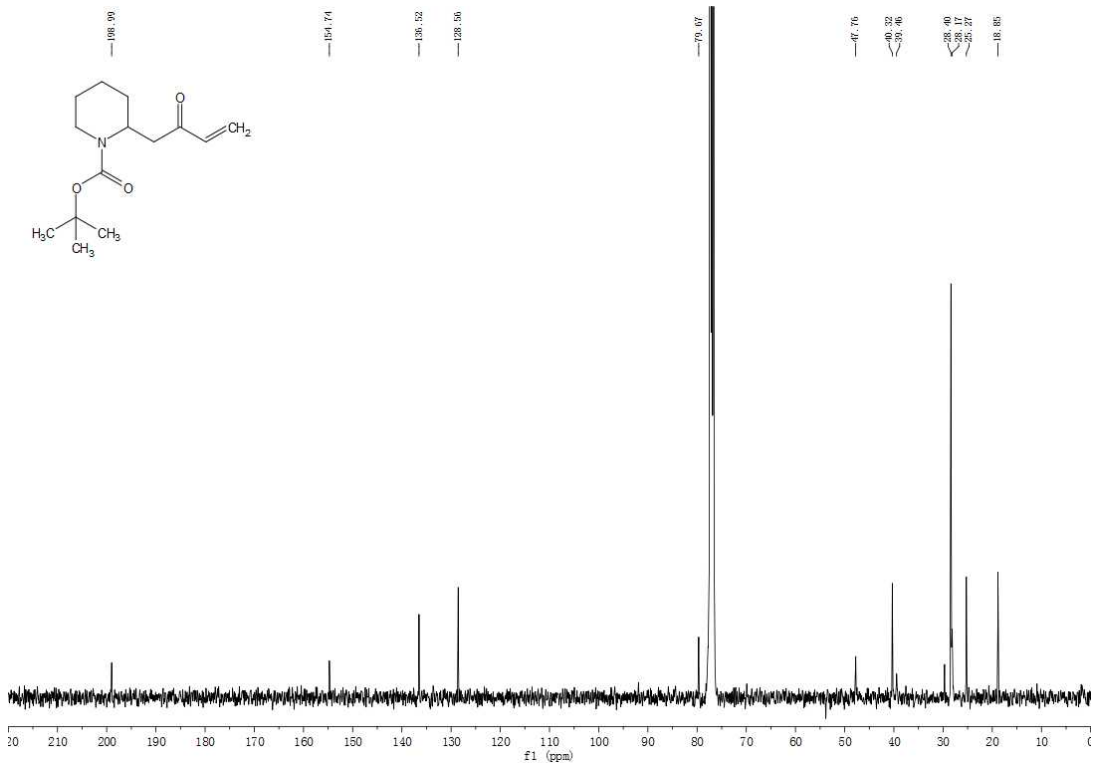
^{1}H and ^{13}C NMR Spectra of **3i**



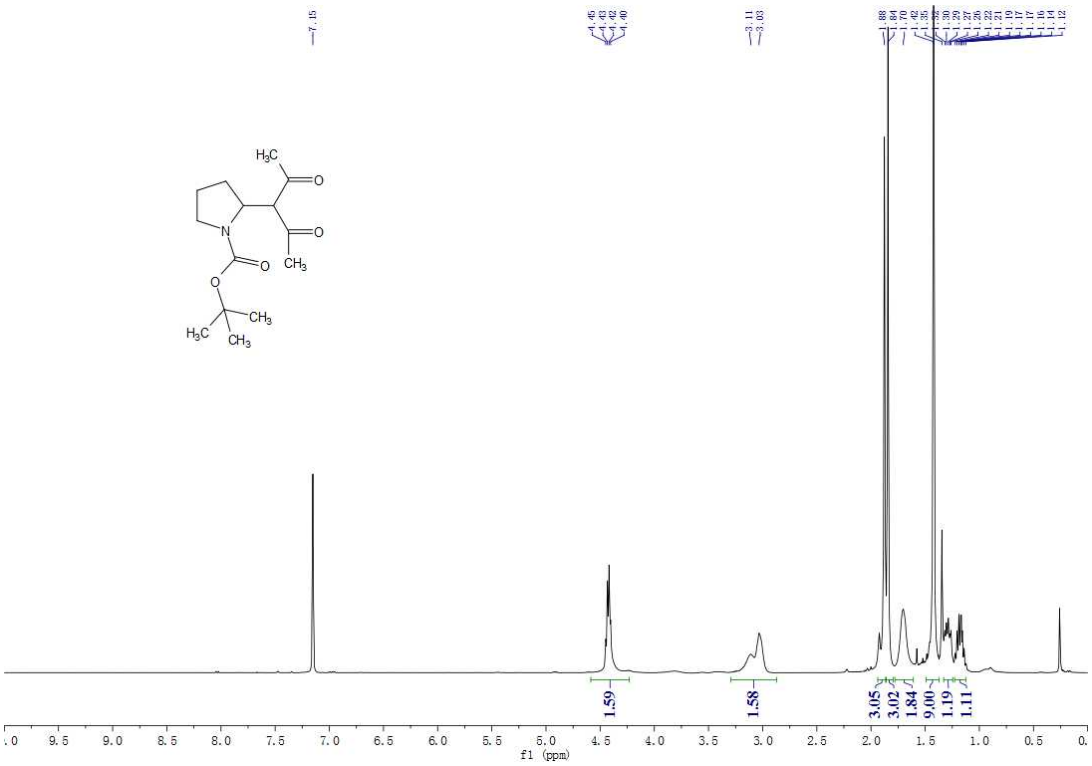


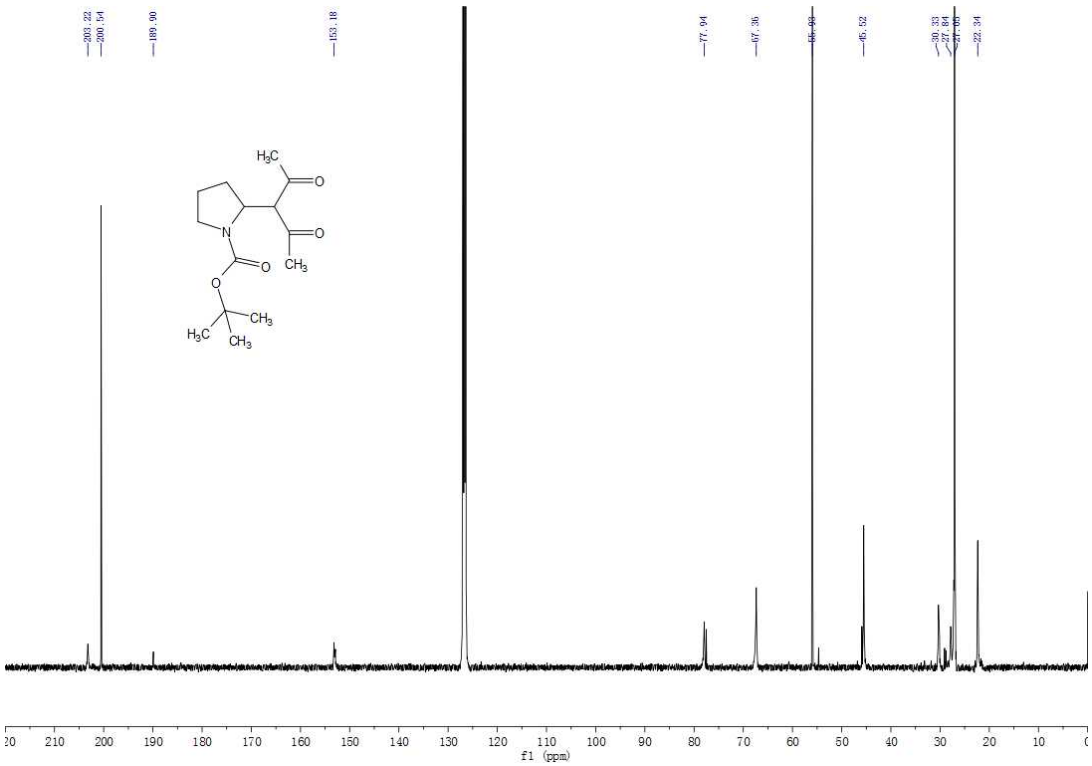
^{1}H and ^{13}C NMR Spectra of **3j**



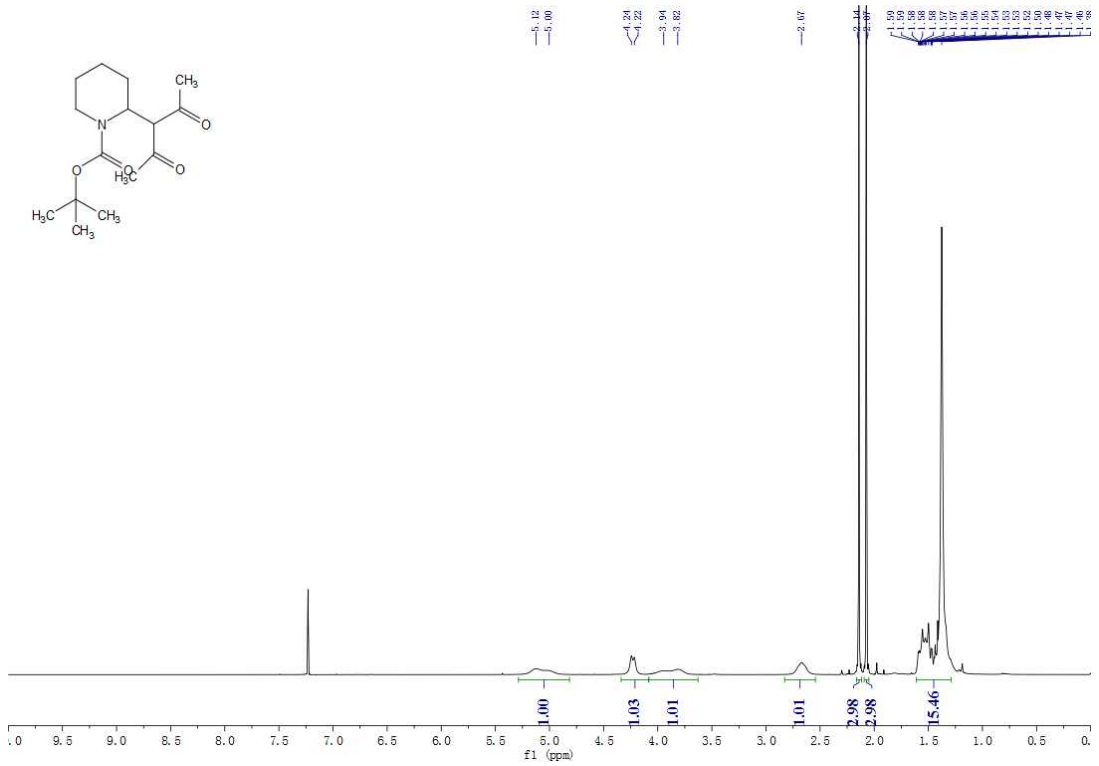


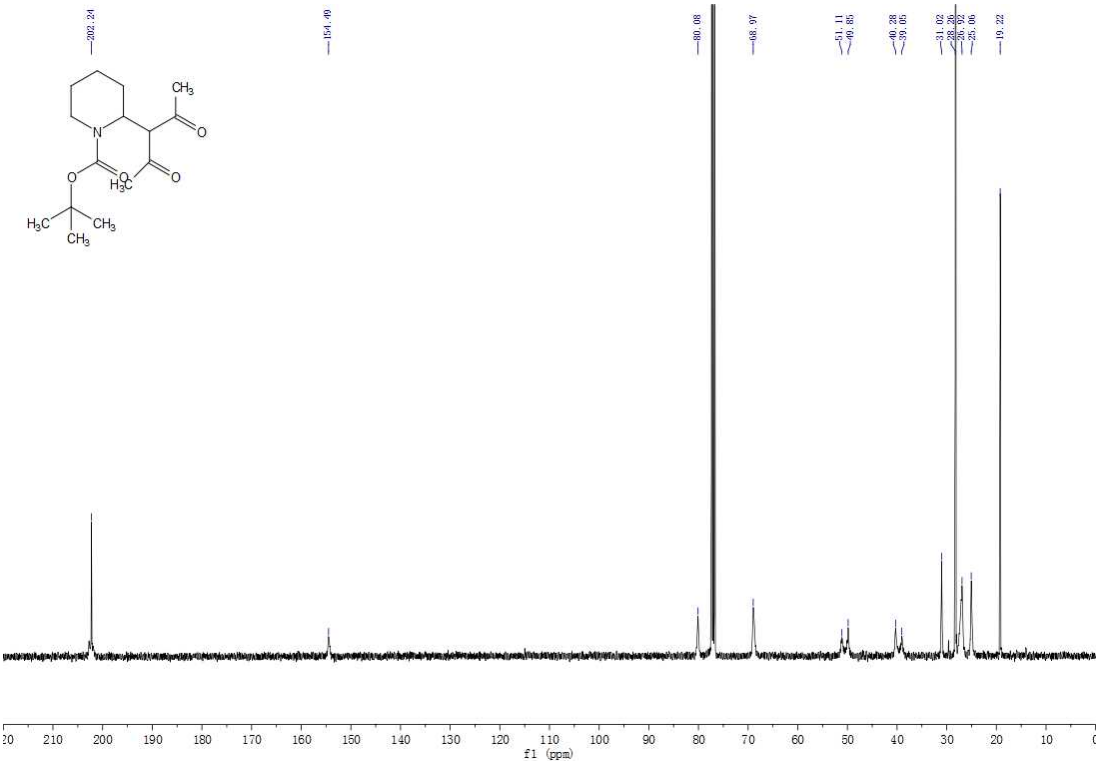
^{1}H and ^{13}C NMR Spectra of **7a**



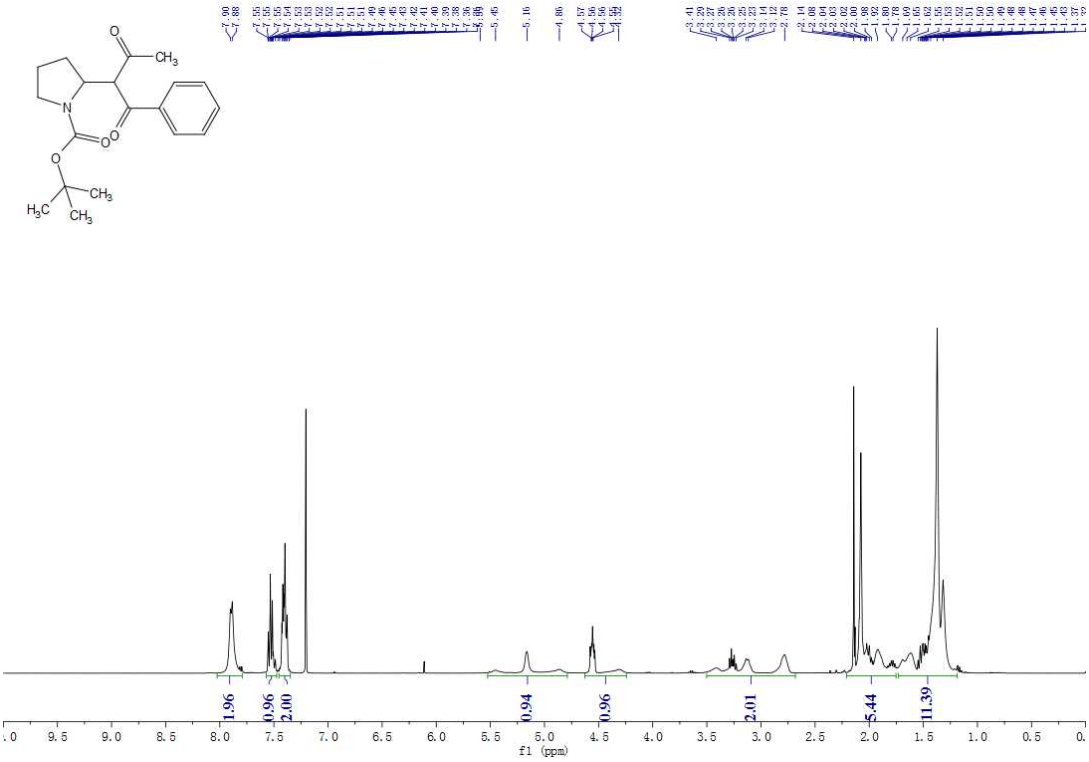


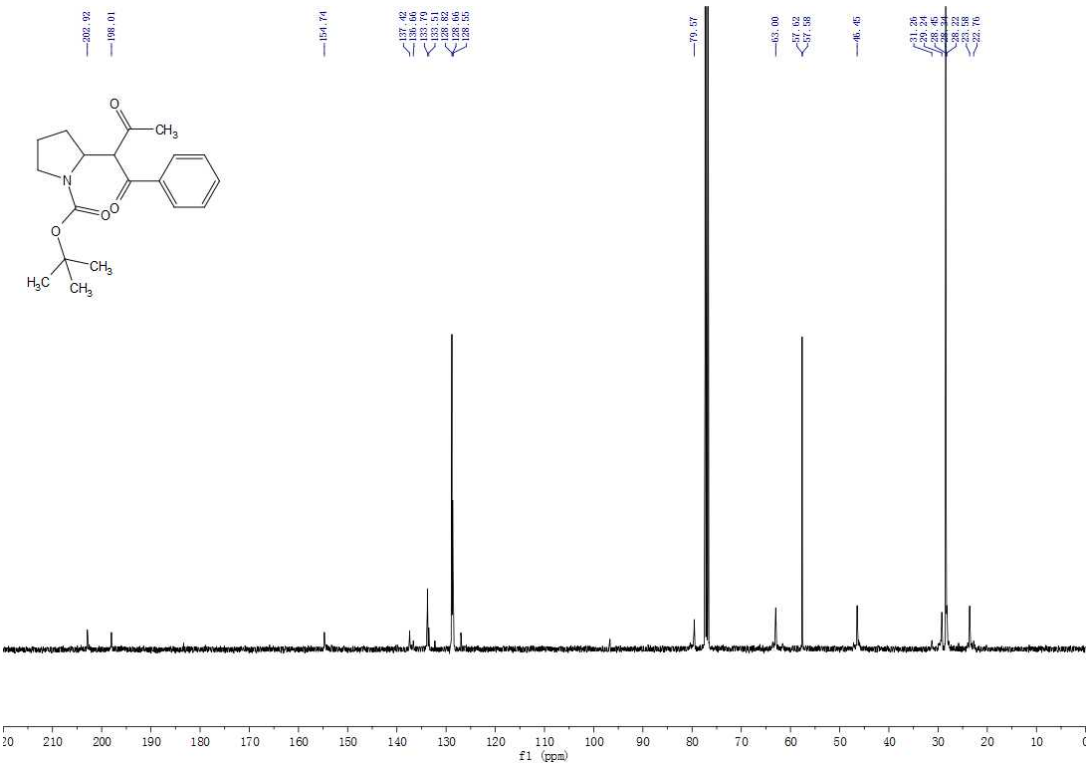
^{1}H and ^{13}C NMR Spectra of **7b**



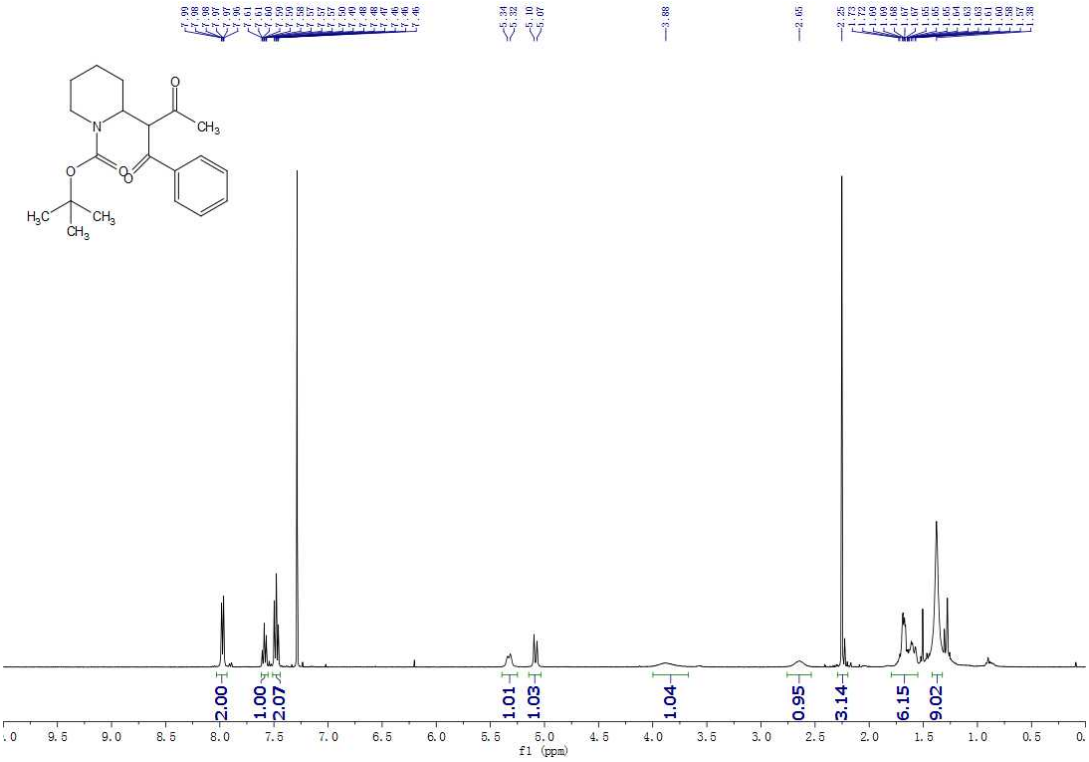


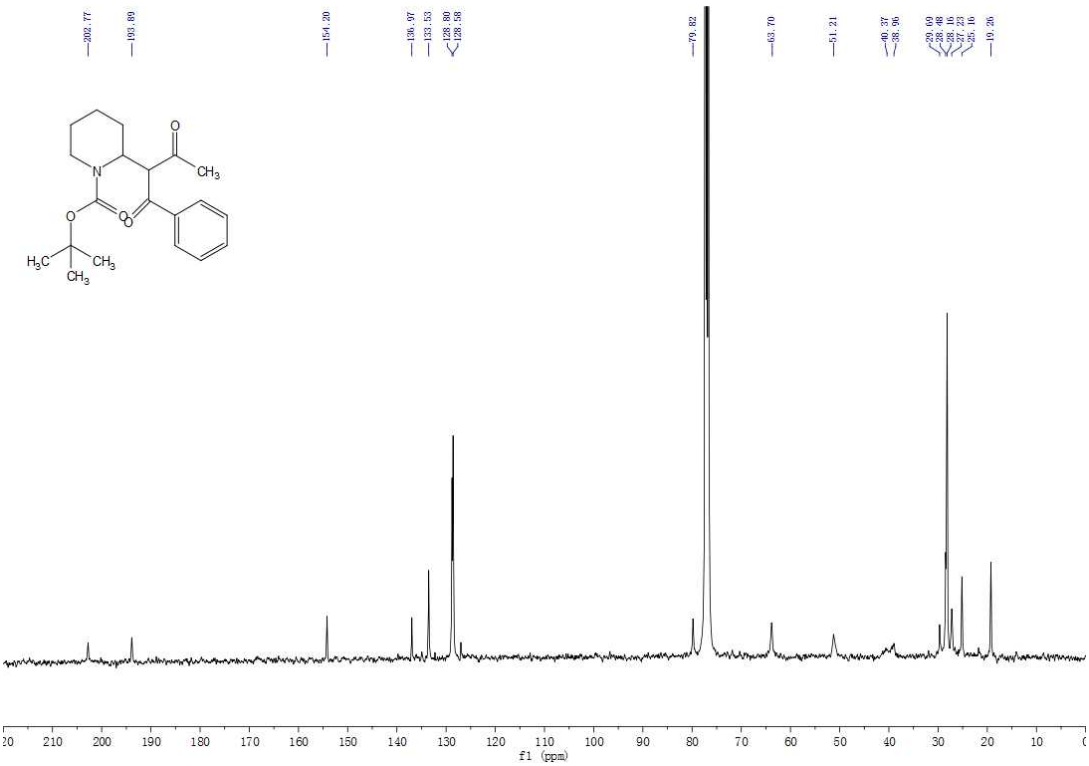
^{1}H and ^{13}C NMR Spectra of **7c**



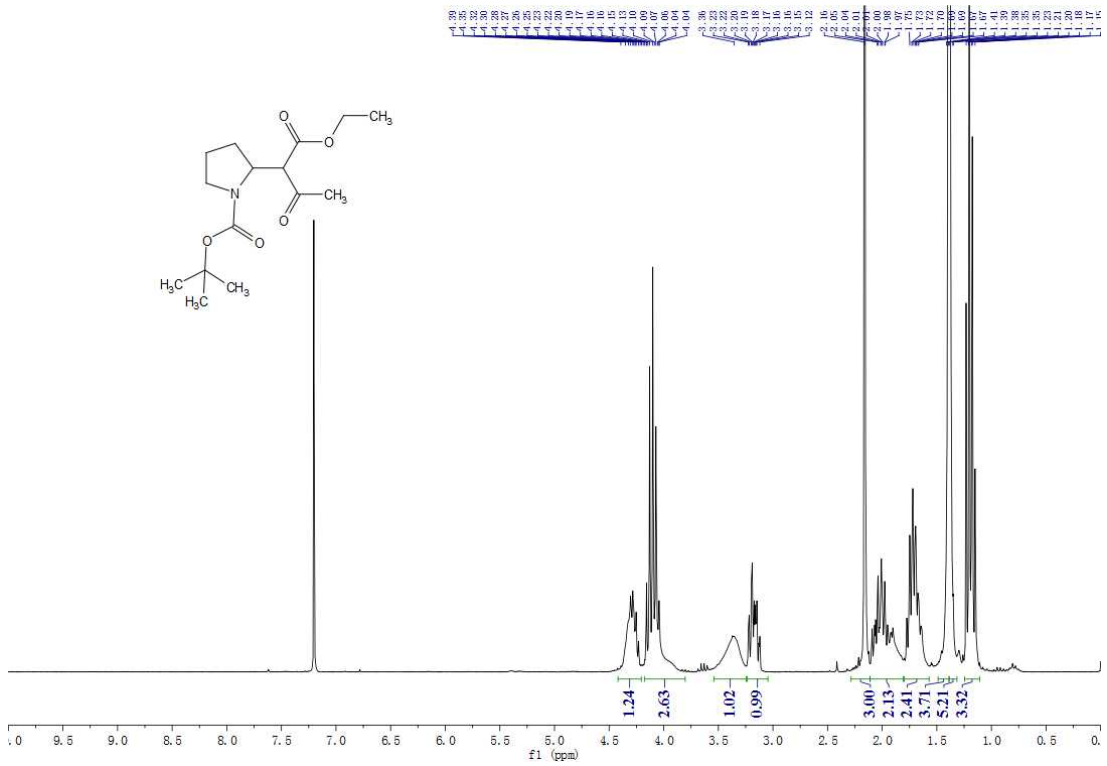


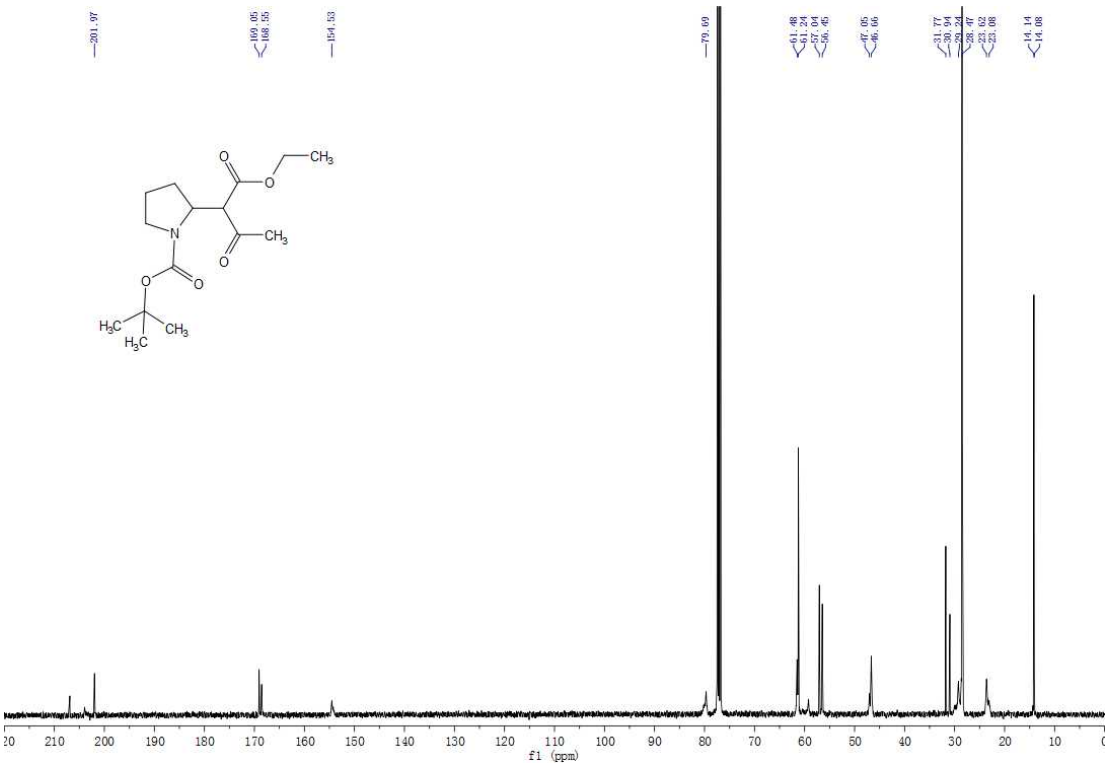
^{1}H and ^{13}C NMR Spectra of **7d**



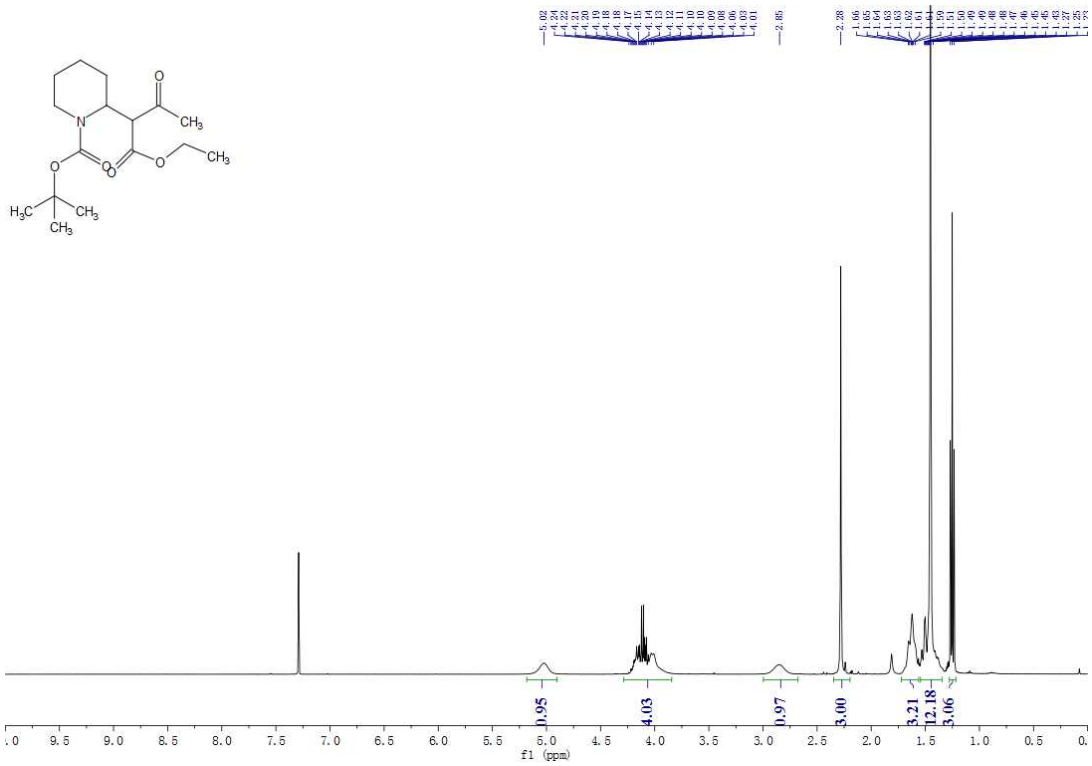


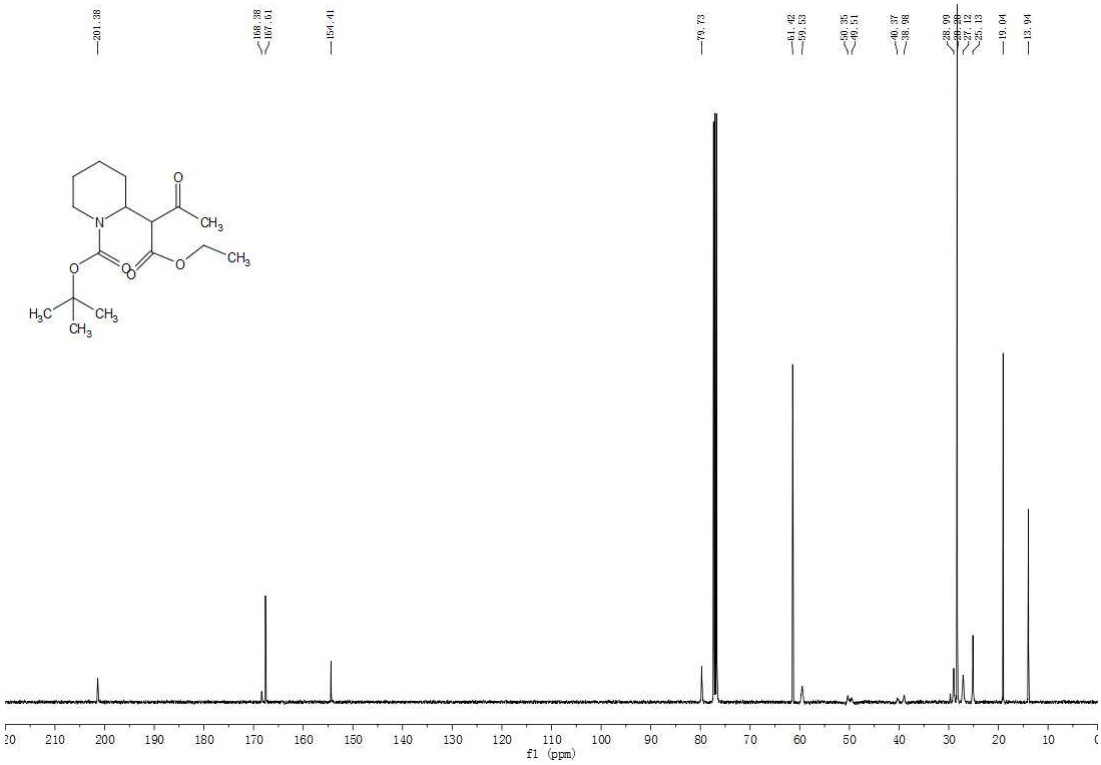
^{1}H and ^{13}C NMR Spectra of **7e**



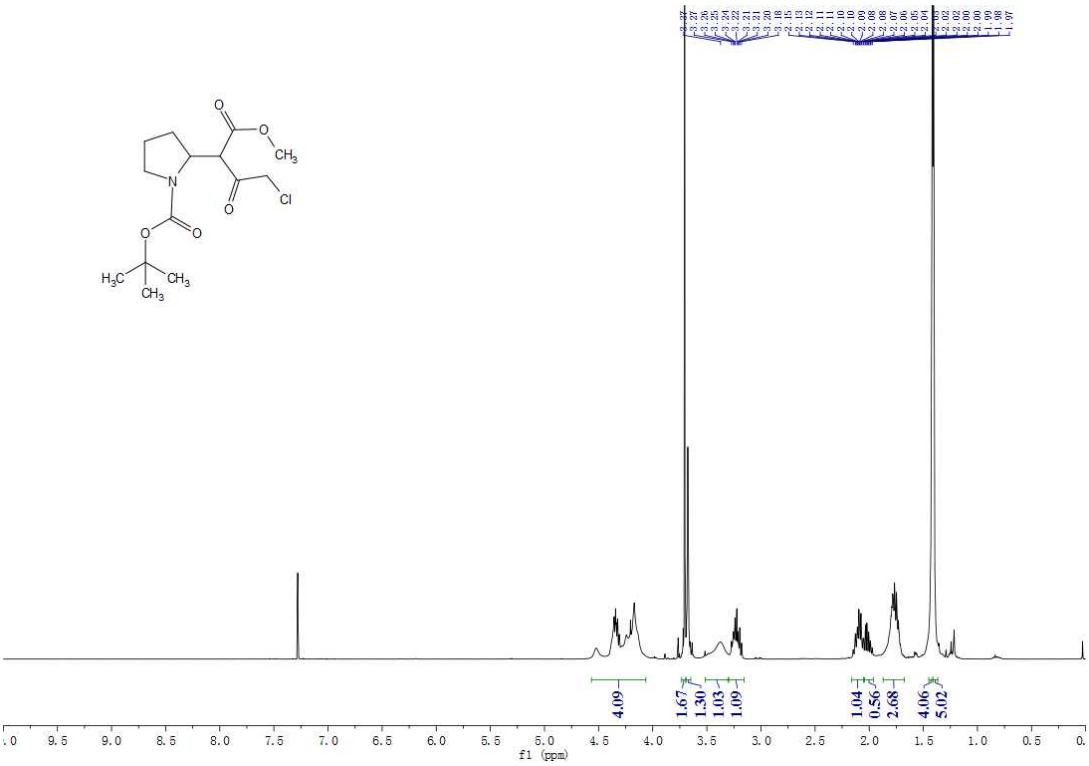


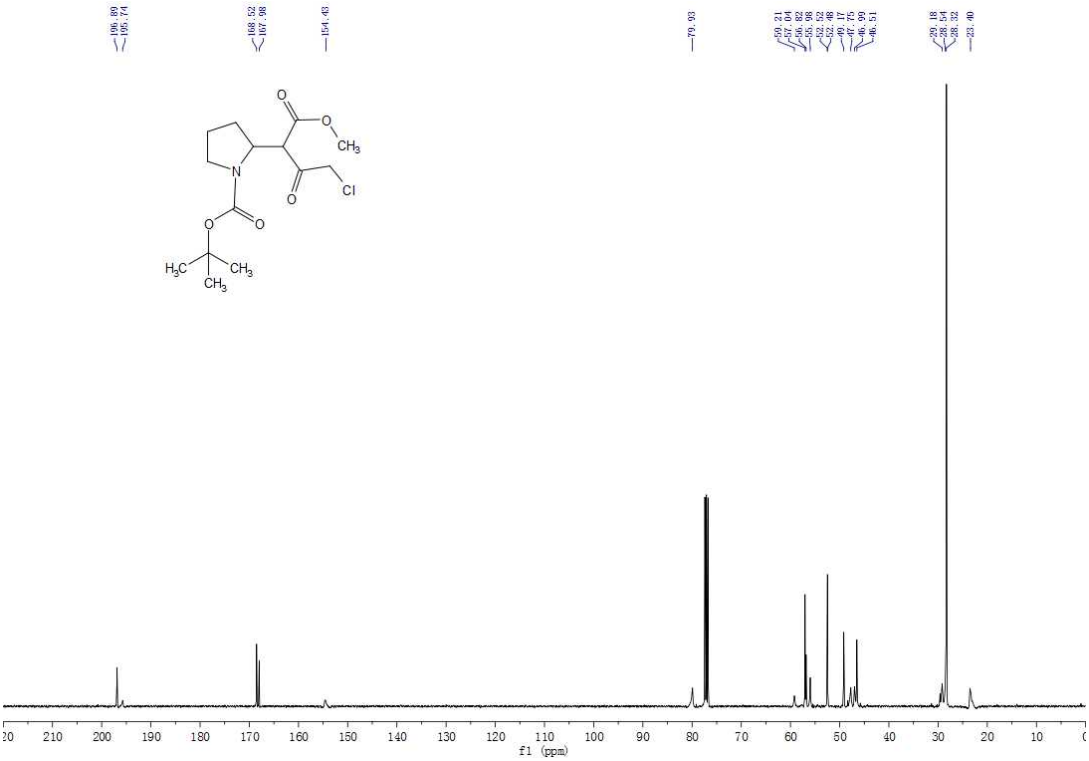
^{1}H and ^{13}C NMR Spectra of **7f**



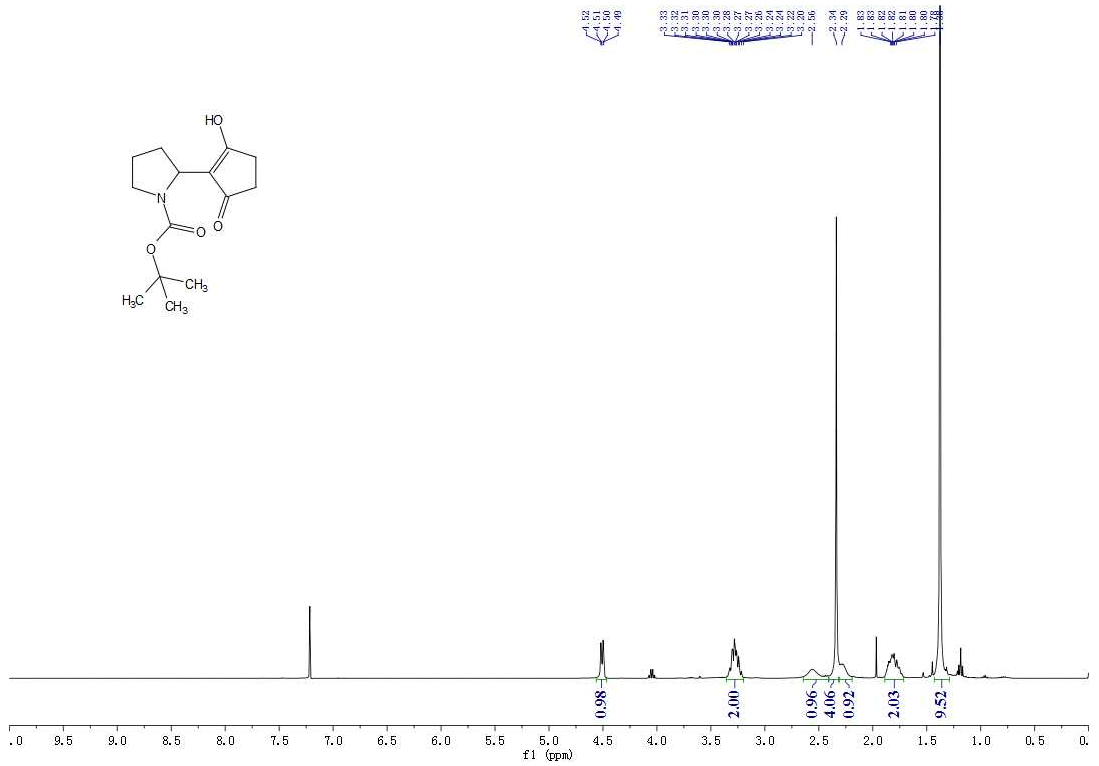


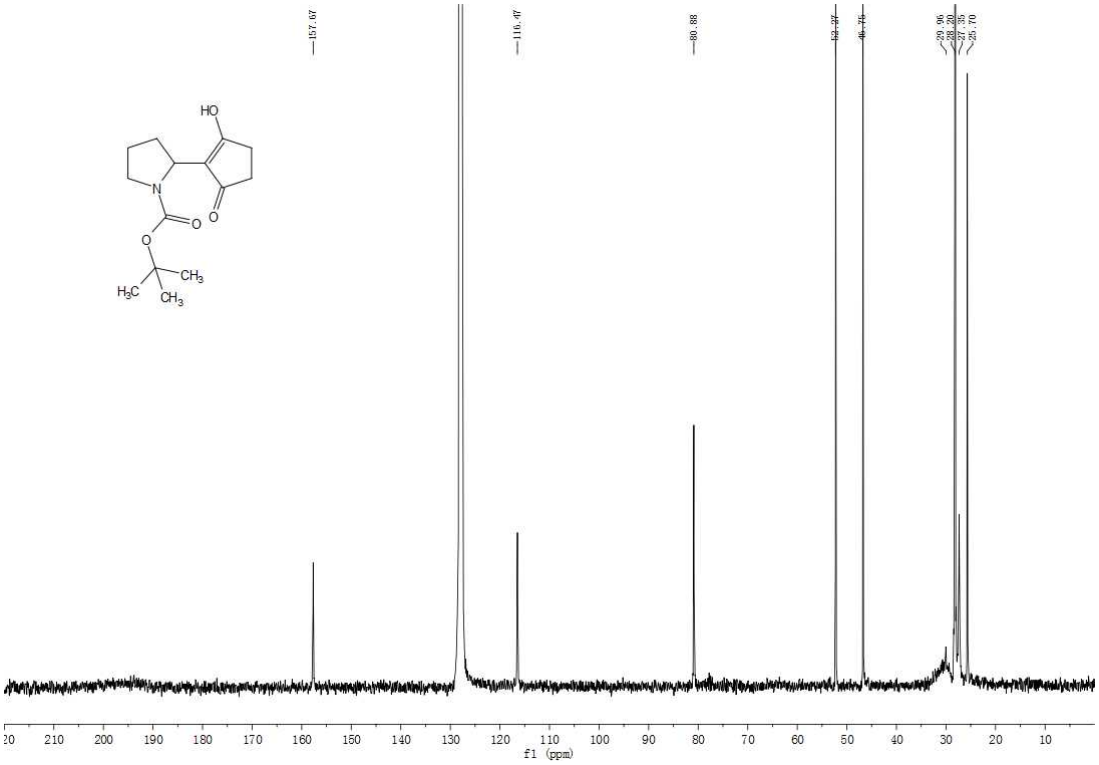
^{1}H and ^{13}C NMR Spectra of **7g**



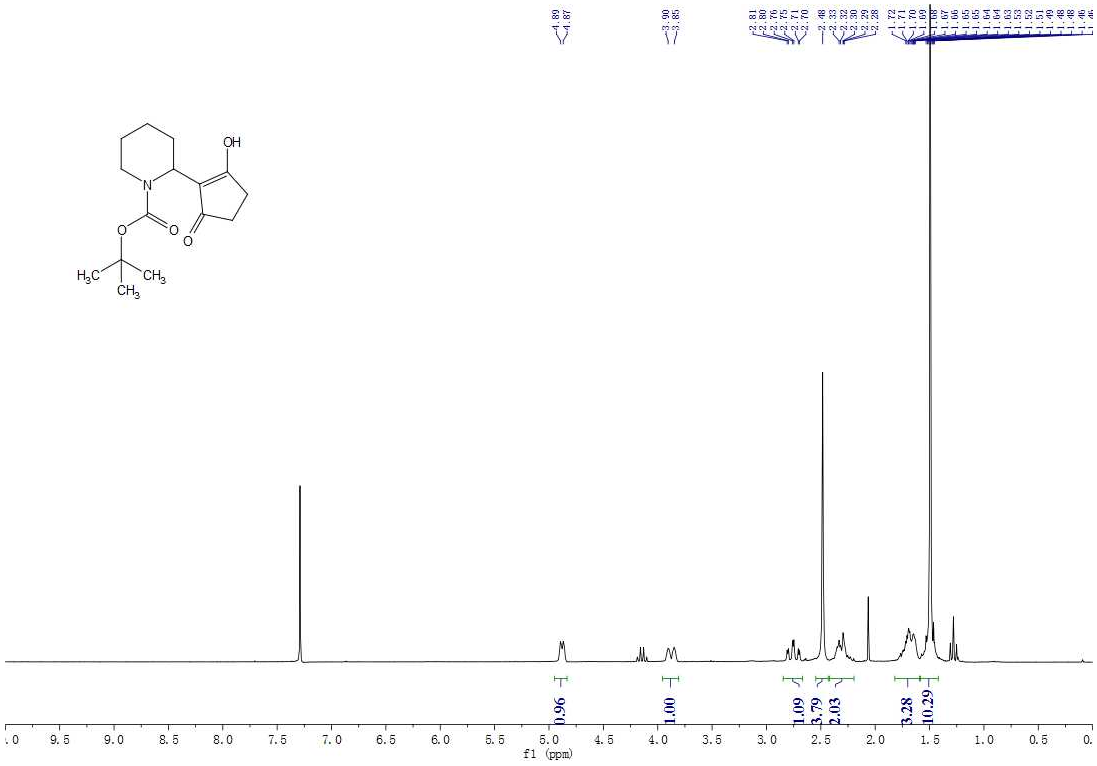


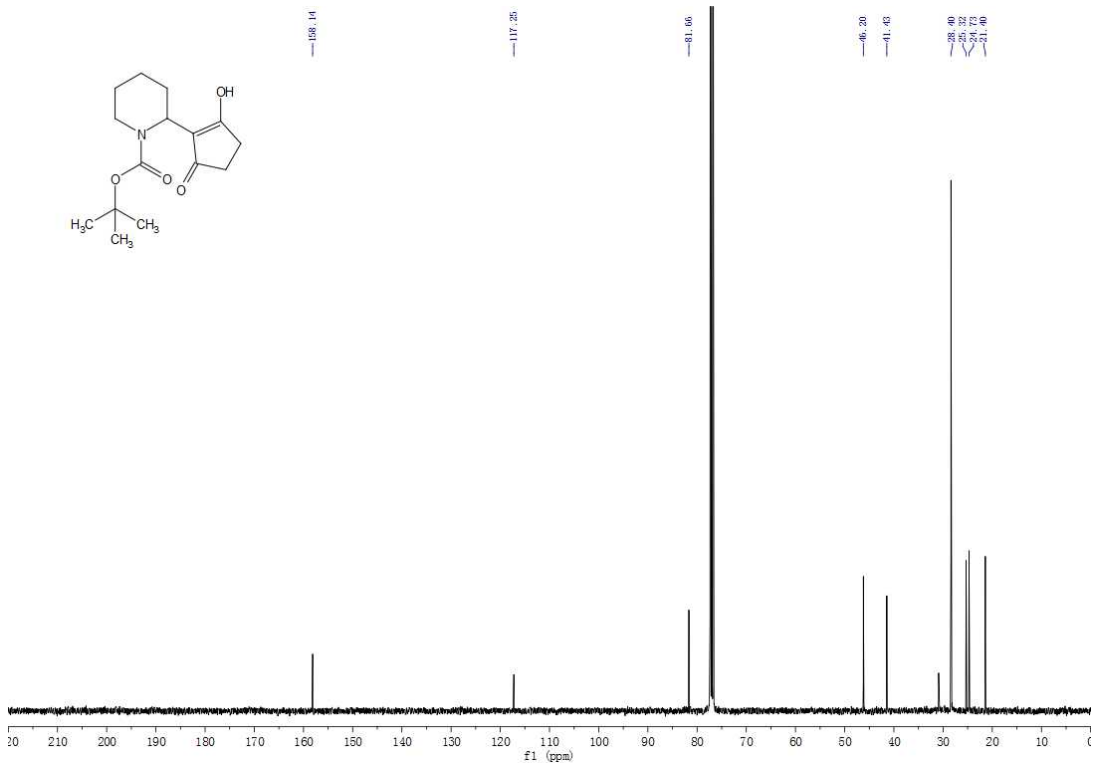
^{1}H and ^{13}C NMR Spectra of **7i**



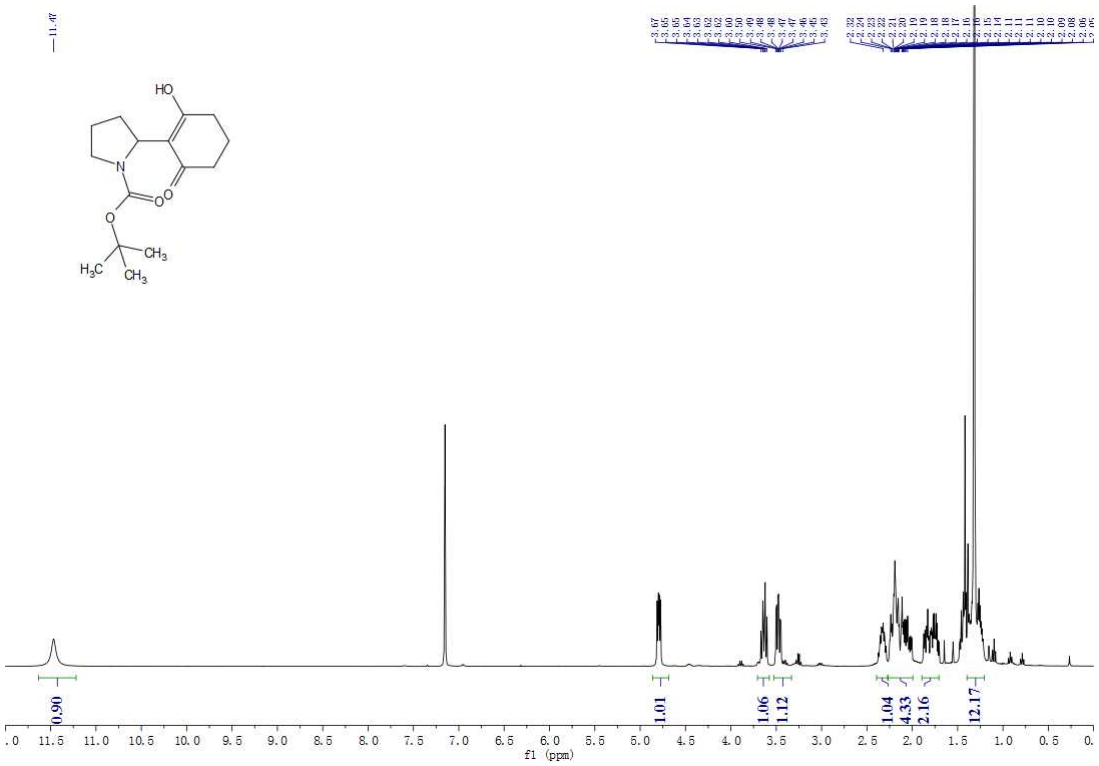


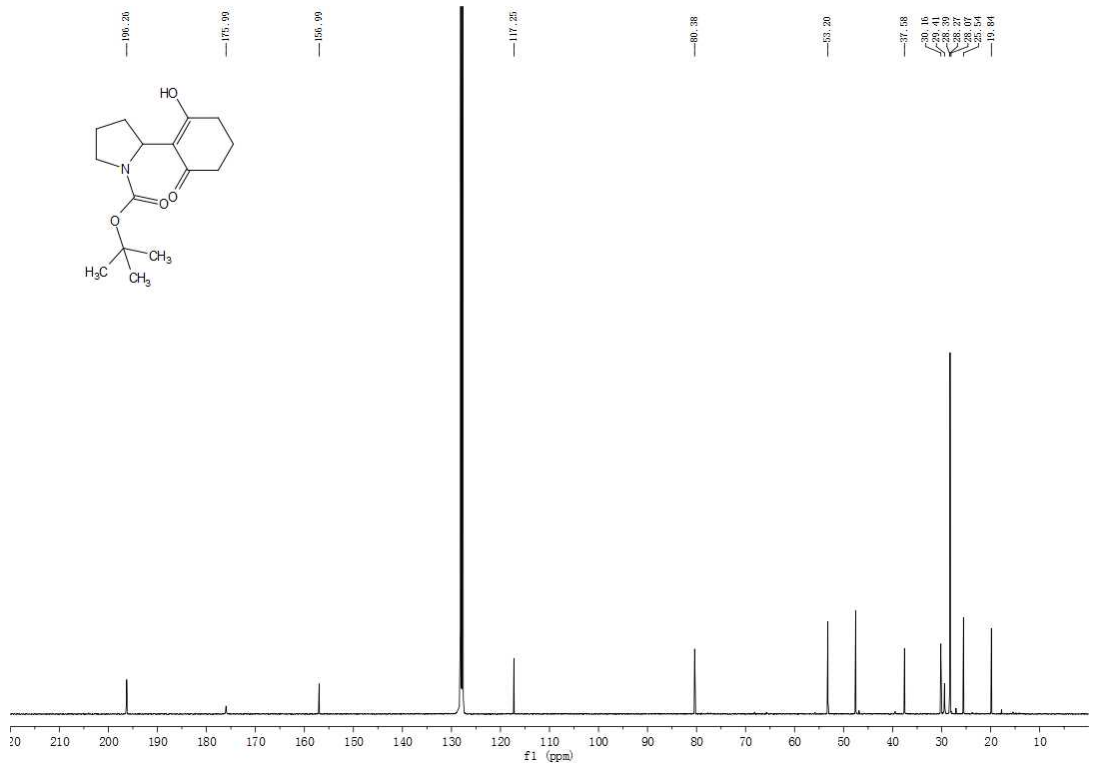
^{1}H and ^{13}C NMR Spectra of **7j**



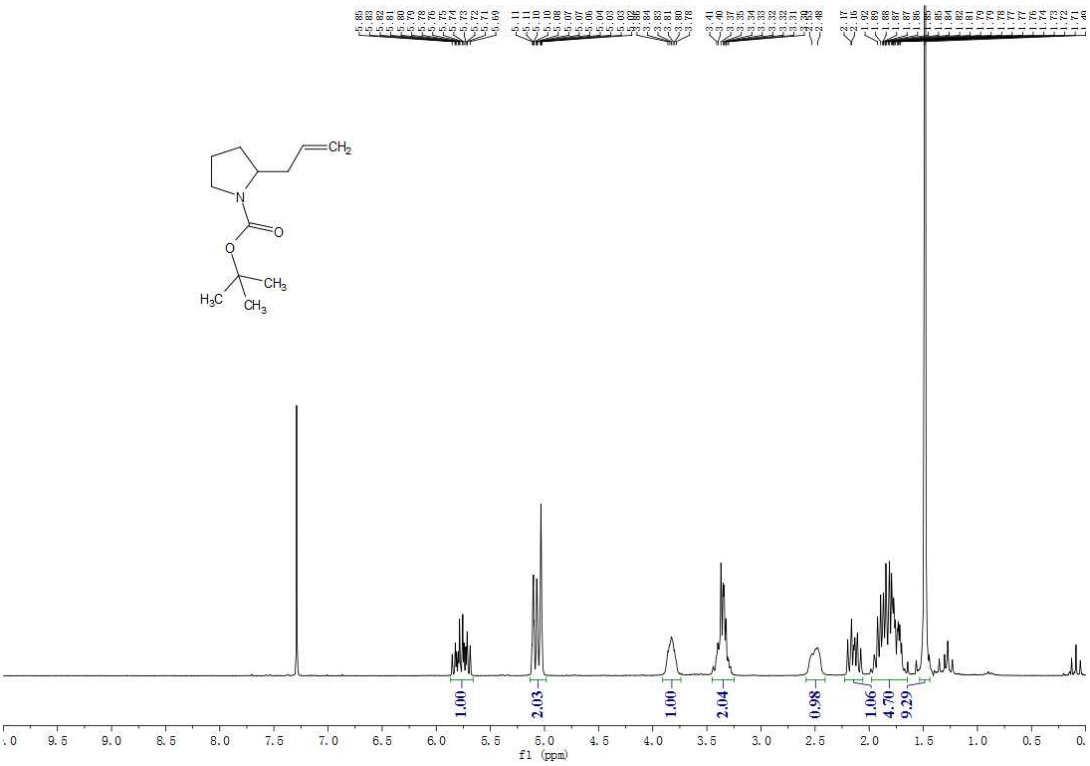


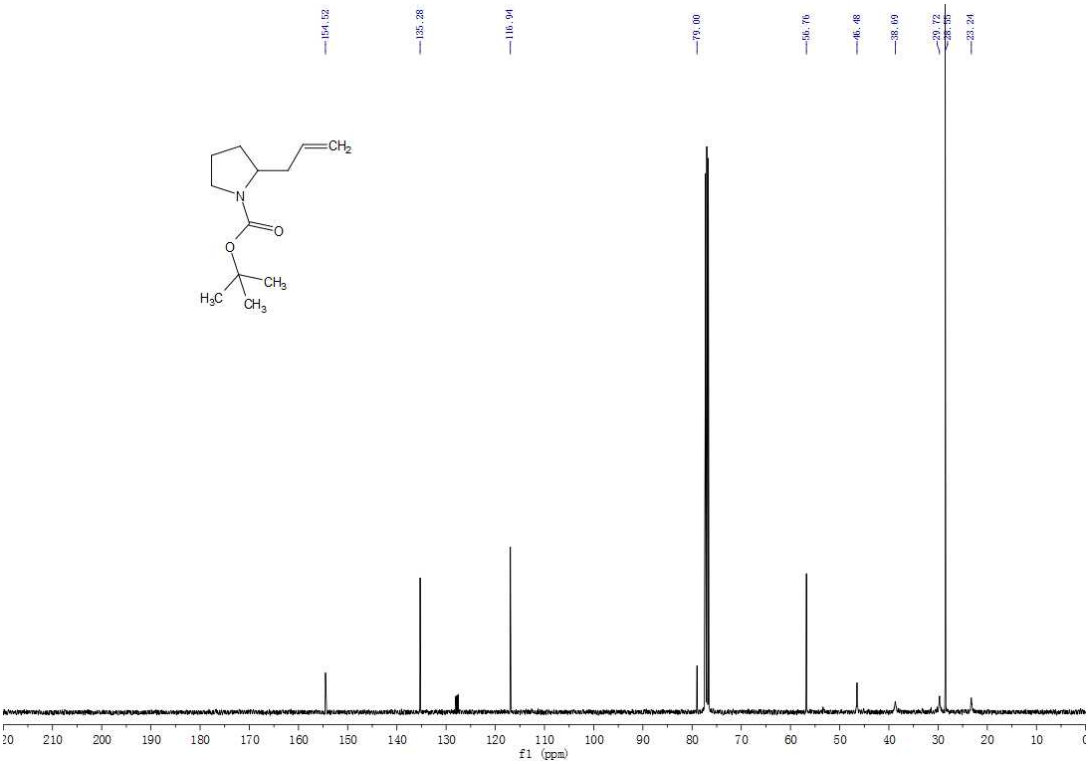
^{1}H and ^{13}C NMR Spectra of **7k**





^{1}H and ^{13}C NMR Spectra of **8a**





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