Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

KI-Catalyzed Imidation of sp^3 C–H Bonds Adjacent to an Amide Nitrogen Atom

Supporting information

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(A) General Remarks

All the reagents were provided by commercial suppliers without further purification. The products were purified by column chromatography that was performed on silica gel (230-400 mesh, Merck). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AM-400 spectrometer in $CDCl_3$ solution. ^{1}H NMR chemical shifts (in ppm) were referenced to the hydrogen signal in tetramethylsilane (δ = 0 ppm) in the deuterated solvent. ^{13}C NMR spectra were referenced to the $CDCl_3$ triplet signal (δ = 77.0 ppm). The following abbreviations were used to describe splitting patterns: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. A Bruker APEX IV mass spectrometer was used to obtain the HR-ESI-MS.

(B) General Experimental Procedure

(a) Imidation of Amide

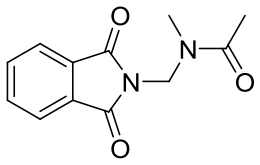
A reaction vessel was charged with imide (1 mmol), KI (0.2 mmol) and amide (1mL, about 9mmol). After the quick addition of TBHP (4 mmol, 70% aqueous solution), the mixture was stirred at 90 ℃ for proper time until imide was fully consumed. The reaction mixture was washed with saturated $NaSO_3$ solution (20 mL) until colorless. After extracting the water phase with CH_2Cl_2 (20 mL), combined organic phases were dried over $NaSO_4$. The crude mixture was purified by column chromatography (silica gel, petroleum ether: acetone= 3:1 to 6:1).

(b) Imidation of N,N-Dimethylaniline

A reaction vessel was charged with imide (1 mmol), KI (0.1 mmol) and N,N-dimethylaniline (1 mL, about 9 mmol). After the quick addition of TBHP (1.5 mmol, 70% aqueous solution), the mixture was stirred at 90 ℃ for proper time until imide was fully consumed. The reaction mixture was washed with saturated $NaSO_3$ solution (20 mL) until colorless. After extracting the water phase with CH_2Cl_2 (20 mL), combined organic phases were dried over $NaSO_4$. The crude mixture was purified by column chromatography (silica gel, petroleum ether: acetone= 3:1 to 6:1).

(C) Analytical Data for 3a-3q

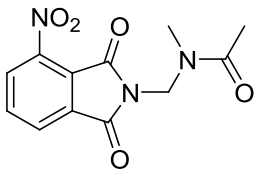
Note: The **rotamers**[1] lead to obvious **duplication (3a-3j, 3l, 3m, 3o, 3x) or triple copy (3k, 3n)** in spectra. Considering the difference between **3a** and **3p** in spectra (**3a** has **duplication** while **3p** doesn't have), it is plausible that *the nitrogen atom which originally belongs to amide* may be responsible for the **duplication**. In order to explain the ^{13}C NMR definitly, we discuss the **duplication of each peak** in detail.



3a

N-[(1,3-dihydro-1,3-dioxo-2*H*-isoindol-2-yl)methyl]-*N*-methyl-acetamide (**3a**)[2]

White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79-7.65 (m, 4H), 5.22, 5.14 (2×s, 2H), 3.02, 2.86 (2×s, 3H), 2.36, 1.99 (2×s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8 (1C), 167.5, 167.3 (2C), 134.3-123.2 (6C), 52.4, 49.1 (1C), 35.5, 32.2 (1C), 21.5, 21.1 (1C).

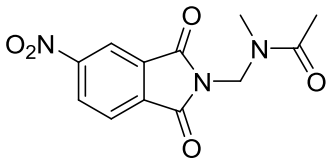


3b

N-[(4-nitro-1,3-dihydro-1,3-dioxo-2*H*-isoindol-2-yl)methyl]-*N*-methyl-acetamide (**3b**)

Slightly yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73-8.08 (m, 3H),

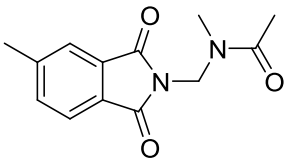
5.36, 5.31 (2×s, 2H), 3.20, 3.00 (s×2, 2H), 2.48, 2.11 (s×2, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 170.7 (1C), 165.2-162.3 (2C), 144.9-123.0 (6C), 53.1, 50.3 (1C), 36.2, 32.3 (1C), 21.5, 21.1 (1C). HRMS (ESI): calcd for $C_{12}H_{12}N_3O_5$ $[M+H]^+$ 278.07715, found 278.07702.



3c

N-[(5-nitro-1,3-dihydro-1,3-dioxo-2*H*-isoindol-2-yl)methyl]-*N*-methyl-acetamide (**3c**)

Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20-7.93 (m, 3H), 5.33, 5.29 (2×s, 2H), 3.19, 2.98 (2×s, 3H), 2.46, 2.10 (2×s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 170.9 (1C), 163.6-163.1 (2C), 139.5-120.6 (6C), 54.2, 51.6 (1C), 35.4, 31.4 (1C), 22.0, 21.4 (1C). HRMS (ESI): calcd for $C_{12}H_{12}N_3O_5$ $[M+H]^+$ 278.07715, found 278.07709.

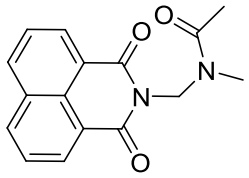


3d

N-[(5-methyl-1,3-dihydro-1,3-dioxo-2*H*-isoindol-2-yl)methyl]-*N*-methyl-acetamide (**3d**)

White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78-7.54 (m, 3H), 5.32, 5.21 (2×s, 2H), 3.10, 2.97 (2×s, 3H), 2.54, 2.52 (2×s, 3H), 2.47, 2.09 (2×s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.1, 170.9 (1C), 167.9, 167.8 (2C), 146.0-123.4 (6C), 52.5, 49.2 (1C), 35.6, 32.4 (1C), 21.9, 21.9 (1C), 21.8,

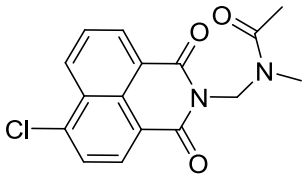
21.4 (1C). HRMS (ESI): calcd for $C_{13}H_{15}N_2O_3$ $[M+H]^+$ 247.10772, found 247.10757.



3e

N-[(1,8-naphthalimidol-N-yl)methyl]-*N*-methyl-acetamide (**3e**)

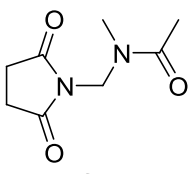
White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59-7.74 (m, 6H); 5.84, 5.75 (2×s, 2H), 3.07, 2.92 (2×s, 3H), 2.53, 2.08 (2×s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6 (1C), 164.2 (2C), 131.7-122.0 (10C), 54.2, 51.5 (1C), 31.4, 29.6 (1C), 22.0, 21.5 (1C). HRMS (ESI): calcd for $C_{16}H_{15}N_2O_3$ $[M+H]^+$ 283.10772, found 283.10778.



3f

N-[(4-chlorine-1,8-naphthalimidol-N-yl)methyl]-*N*-methyl-acetamide (**3f**)

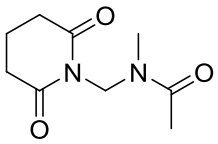
White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.67-7.85 (m, 5H), 5.85, 5.78 (2×s, 2H), 3.12, 2.94 (2×s, 3H), 2.55, 2.11 (2×s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 171.0 (1C), 165.5, 165.3 (2C), 152.0-118.9 (10C), 53.2, 50.6 (1C), 32.7, 29.6 (1C), 21.8, 21.4 (1C). HRMS (ESI): calcd for $C_{16}H_{14}ClN_2O_3$ $[M+H]^+$ 317.06875, found 317.06886.



3g

N-[(2,5-dioxo-1-pyrrolidinyl)methyl]-*N*-methyl-acetamide (**3g**)[3,4]

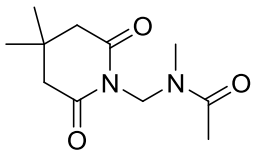
White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.06, 5.00 (2×s, 2H), 3.05, 2.87 (2×s, 3H), 2.74, 2.69 (2×s, 4H), 2.34, 2.03 (2×s, 3H), ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.7, 176.4 (1C), 171.2, 171.0 (2C); 53.1, 50.5 (1C); 36.3, 32.6 (1C), 28.0 (2C), 21.7, 21.3 (1C).



3h

N-[(2,6-dioxo-1-piperidinyl)methyl]-*N*-methyl-acetamide (**3h**)

White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.34, 5.33 (2×s, 2H), 2.98, 2.70 (2×s, 3H), 2.70-2.63 (m, 4H), 2.33, 2.02 (2×s, 3H), 1.98-1.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 172.2 (1C), 171.5 (2C), 53.2, 51.4 (1C), 32.8 (2C), 31.4 (1C), 22.0, 21.2 (1C), 16.9, 16.8 (1C). HRMS (ESI): calcd for $C_9H_{15}N_2O_3$ $[M+H]^+$ 199.10772, found 199.10752.

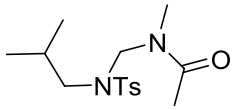


3i

N-[(3,3-dimethyl-2,6-dioxo-1-piperidinyl)methyl]-*N*-methyl-acetamide (**3i**)

White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.33, 5.32 (2×s, 2H), 2.99, 2.80 (2×s, 3H), 2.53, 2.50 (2×s, 4H), 2.34, 2.02 (2×s, 3H), 1.07, 1.05 (2×s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 171.6 (1C), 171.4 (2C); 53.2, 51.3 (1C), 46.3 (2C), 31.5 (1C), 29.5, 28.9 (1C), 27.6 (2C), 25.4, 21.2

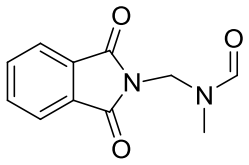
(1C). HRMS (ESI): calcd for $C_{11}H_{19}N_2O_3$ $[M+H]^+$ 227.13902, found 277.13893.



3j

N-[(N-tosyl-1-isobutylaminyl)methyl]-*N*-methyl-acetamide (**3j**)

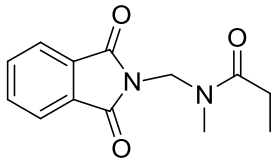
White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63, 7.61, 7.27, 7.25 (m, 4H), 4.81, 4.72 (2×s, 2H), 3.04, 2.72 (2×s, 3H), 2.91, 2.89, 2.87, 2.85 (2×d, 2H), 2.38 (s, 3H), 2.14, 2.03 (2×s, 3H), 1.92-1.83 (m, 1H), 0.85, 0.83, 0.76, 0.74 (2×d, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8 (1C), 143.4-126.8 (6C), 60.0 (1C), 56.1 (1C), 34.2 (1C), 27.2 (1C), 22.0 (1C), 20.0 (1C), 19.8 (2C). HRMS (ESI): calcd for $C_{15}H_{25}N_2O_3S$ $[M+H]^+$ 313.15804, found 313.15827.



3k

N-[(1,3-dihydro-1,3-dioxo-2*H*-isoindol-2-yl)methyl]-*N*-methyl-formamide (**3k)**

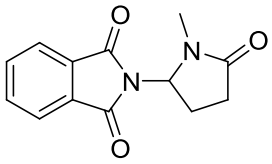
White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (s, 1H), 7.86-7.75 (m, 4H), 5.28, 5.28, 5.12 (3×s, 2H), 3.00, 2.90, 2.88 (3×s, 3H), ^{13}C NMR (100MHz, $CDCl_3$): δ 167.5 (1C), 163.6 (2C), 134.6-123.6 (6C), 51.4 (1C), 29.5 (1C). HRMS (ESI): calcd for $C_{11}H_{11}N_2O_3$ $[M+H]^+$ 219.07642, found 219.07625.



3l

N-[(1,3-dihydro-1,3-dioxo-2*H*-isoindol-2-yl)methyl]-*N*-methyl-propiona mide (**3l**)

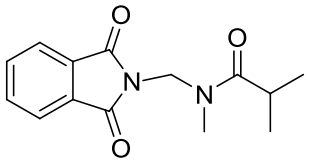
White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85-7.68 (m, 4H), 5.28, 5.20 (2×s, 2H), 3.08, 2.93 (2×s, 3H), 2.81-2.75, 2.31-2.26 (2×q, 2H), 1.18, 1.16, 1.14, 1.10, 1.08, 1.07 (2×t, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2 (1C), 167.8, 167.6 (2C), 134.5-123.4 (6C), 51.6, 50.0 (1C), 35.0, 32.7 (1C), 26.7, 25.9 (1C), 9.3, 8.7 (1C). HRMS (ESI): calcd for $C_{13}H_{15}N_2O_3$ $[M+H]^+$ 247.10772, found 247.10757.



3m

N-methyl-5-[(1,3-dihydro-1,3-dioxo-2*H*-isoindol-2-yl)methyl]-2-pyrrolid one (**3m**)

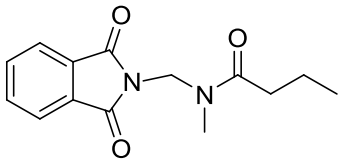
White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87-7.75 (m, 4H), 5.81-5.79 (m, 1H), 3.04-2.96 (m, 1H), 2.82, 2.72 (2×s, 3H), 2.60-2.40 (m, 2H), 2.31-2.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.3 (1C), 167.4 (2C), 134.5-131.4 (6C), 65.6 (1C), 29.6 (1C), 27.0 (1C), 23.2 (1C). HRMS (ESI): calcd for $C_{13}H_{12}N_2NaO_3$ $[M+Na]^+$ 267.07401, found 267.07389.



3n

N-[(1,3-dihydro-1,3-dioxo-2*H*-isoindol-2-yl)methyl]-*N*-methyl-isobutyramide (**3n**)

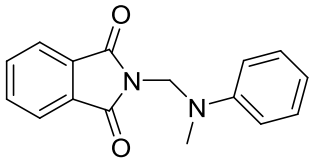
White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89-7.74 (m, 4H), 5.64-5.26 (m, 2H), 3.18-2.95 (m, 3H), 3.61-3.55, 2.84-2.74 (2×m, 1H), 1.26-1.11 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.7-177.3 (1C), 167.7-167.4 (2C), 138.0-123.2 (6C), 53.1-50.3 (1C), 36.2-33.0 (1C), 30.5-29.7 (1C), 19.7-18.8 (2C). HRMS (ESI): calcd for $C_{14}H_{17}N_2O_3$ $[M+H]^+$ 261.12337, found 261.12321.



3o

N-[(1,3-dihydro-1,3-dioxo-2*H*-isoindol-2-yl)methyl]-*N*-methyl-n-butyramide (**3o**)

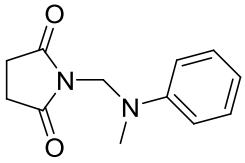
White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81-7.66 (m, 4H), 5.26, 5.18 (2×s, 2H), 3.06, 2.90 (2×s, 3H), 2.27, 2.71, 2.69, 2.24, 2.22, 2.20 (2×t, 2H), 1.68-1.56 (m, 2H), 0.96-0.85 (2×m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 173.3 (1C), 167.7, 167.5 (2C), 134.5-123.4 (6C), 51.7, 49.8 (1C), 35.3, 34.5 (1C), 32.5, 29.5 (1C), 18.6, 17.9 (1C), 13.8, 13.7 (1C). HRMS (ESI): calcd for $C_{14}H_{17}N_2NaO_3$ $[M+Na]^+$ 283.10517, found 283.10531.



3p

2-[(methylphenylamino)methyl]-1H-isoindole-1,3(2H)-dione (**3p**)[5]

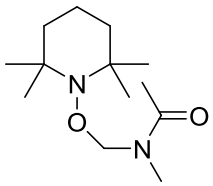
White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82-7.24 (m, 4H), 7.06-6.77 (m, 5H), 5.27 (s, 2H), 3.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.8 (2C), 147.3-113.6 (12C), 56.5 (1C), 39.1 (1C).



3q

1-[(methylphenylamino)methyl]-2,5-pyrrolidinedione (**3q**)[6]

White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-6.81 (m, 5H), 5.10 (s, 2H), 3.15 (s, 3H), 2.68 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.5 (2C), 147.1-113.2 (6C), 57.2 (1C), 39.4 (1C), 28.1 (2C).



3x

N-[(2,2,6,6-tetramethylpiperidinooxy-O-yl)methyl]-*N*-methyl-acetamide (**3x**)

Slight yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.96, 4.91 (2×s, 2H), 3.10, 3.04 (2×s, 3H), 2.22, 2.10 (2×s, 3H), 1.48-1.44 (m, 4H), 1.59-1.52, 1.36-1.31 (2×m, 2H), 1.25- 1.10 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6 (1C), 85.4, 81.4 (1C), 59.9, 59.7 (2C), 39.8 (4C), 34.0, 33.1 (1C),

22.0, 21.5 (1C), 20.0 (2C), 17.0, 16.9 (1C). HRMS (ESI): calcd for $C_{13}H_{27}N_2O_2$ $[M+H]^+$ 243.20670, found 243.20658.

(D) Reference

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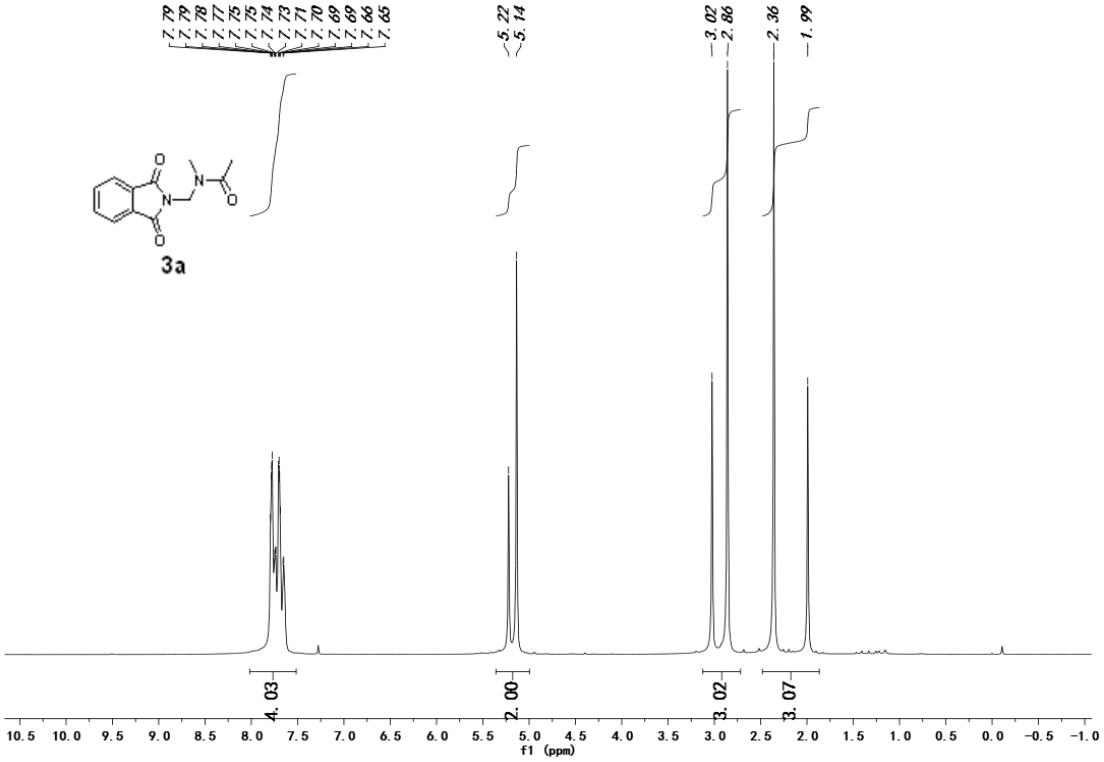
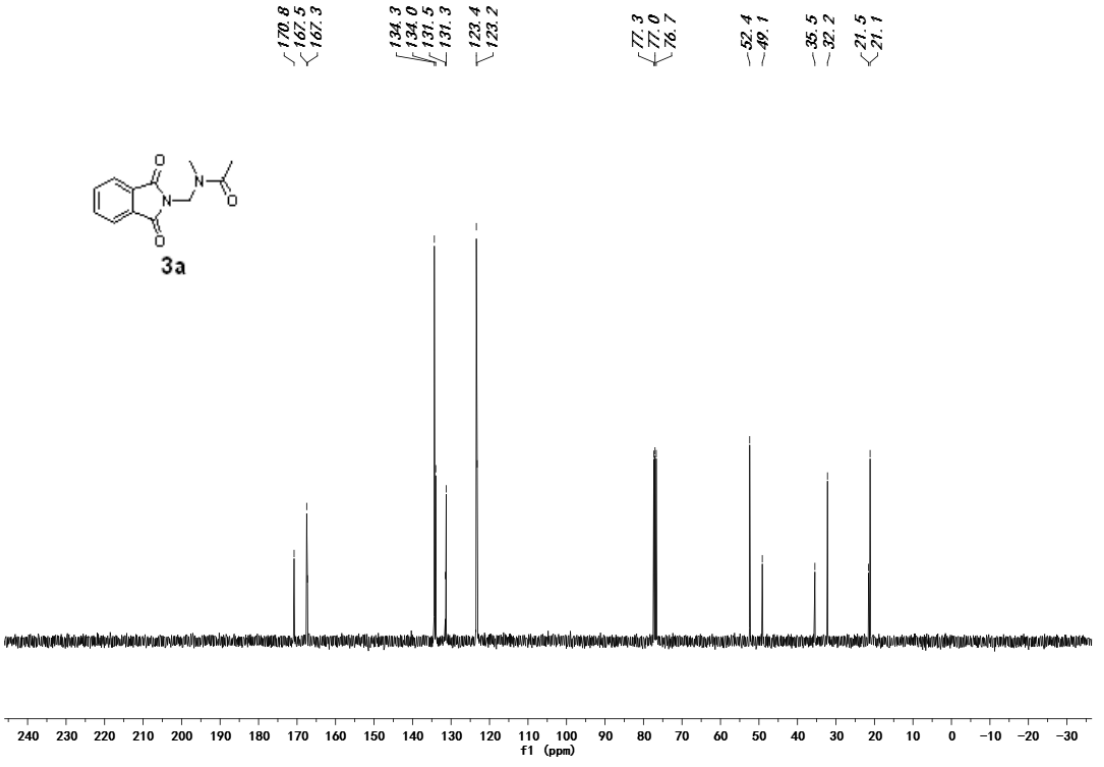
(E) ^{1}H NMR and ^{13}C NMR Spectra

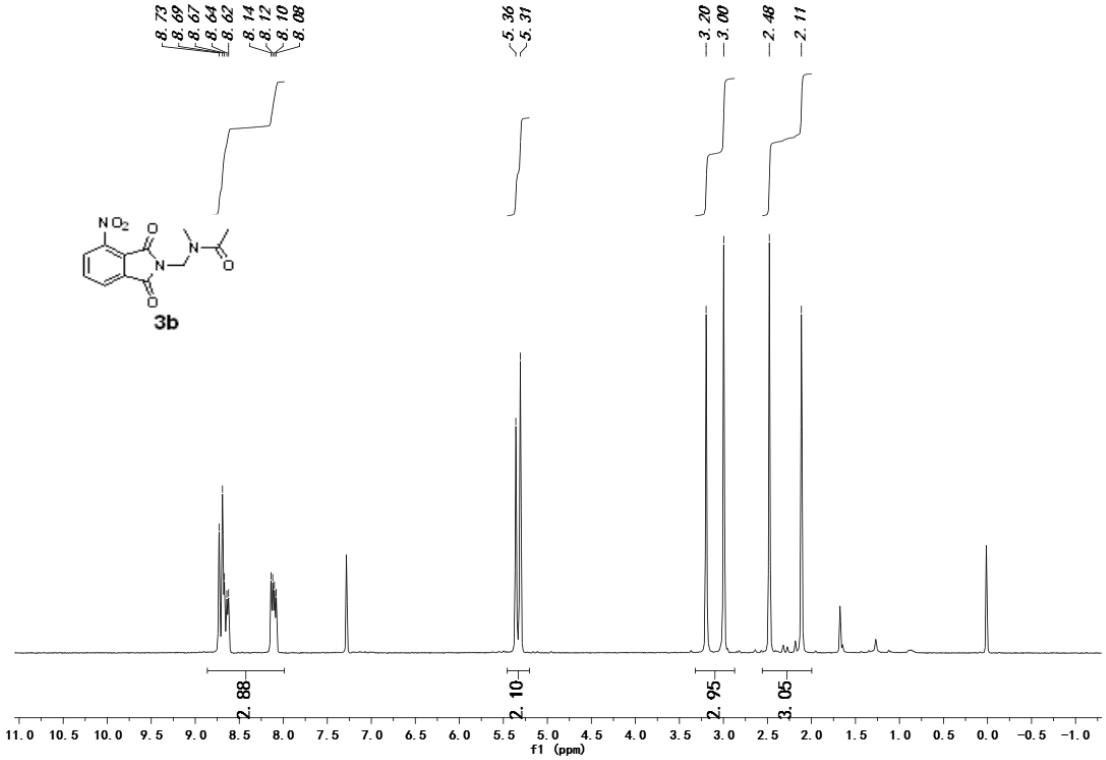
^{1}H NMR Spectra of Compound **3a** (400 MHz, $CDCl_3$)



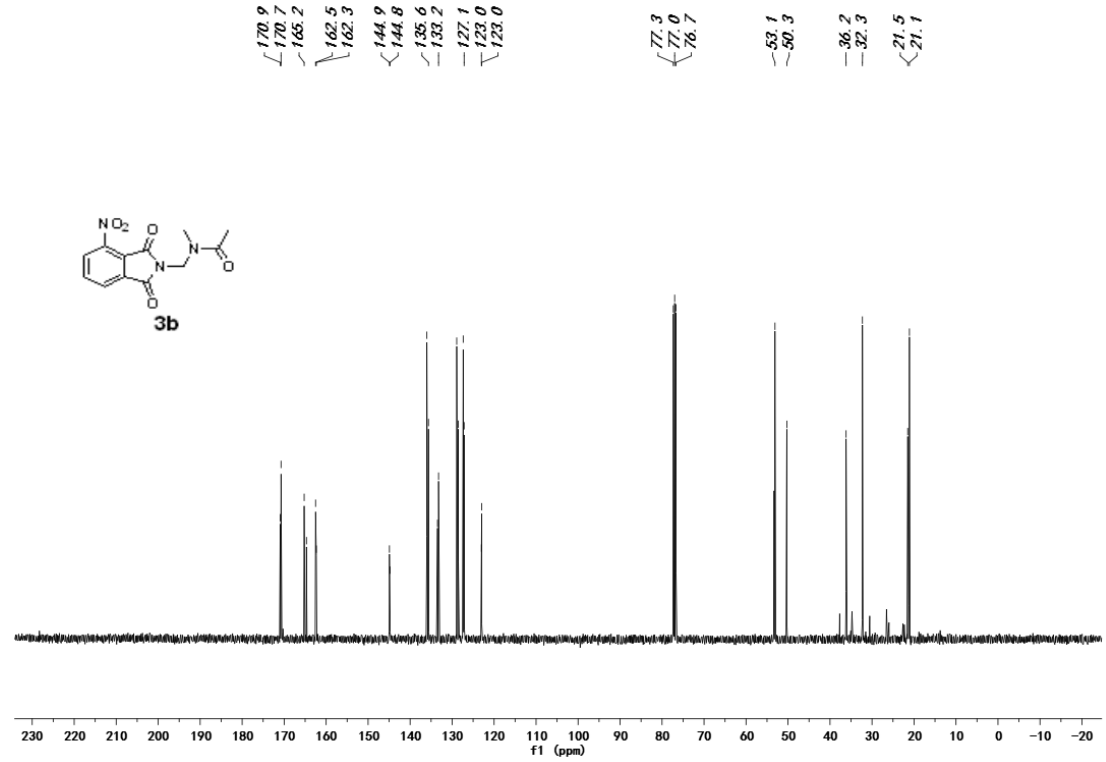
^{13}C NMR Spectra of Compound **3a** (100 MHz, $CDCl_3$)



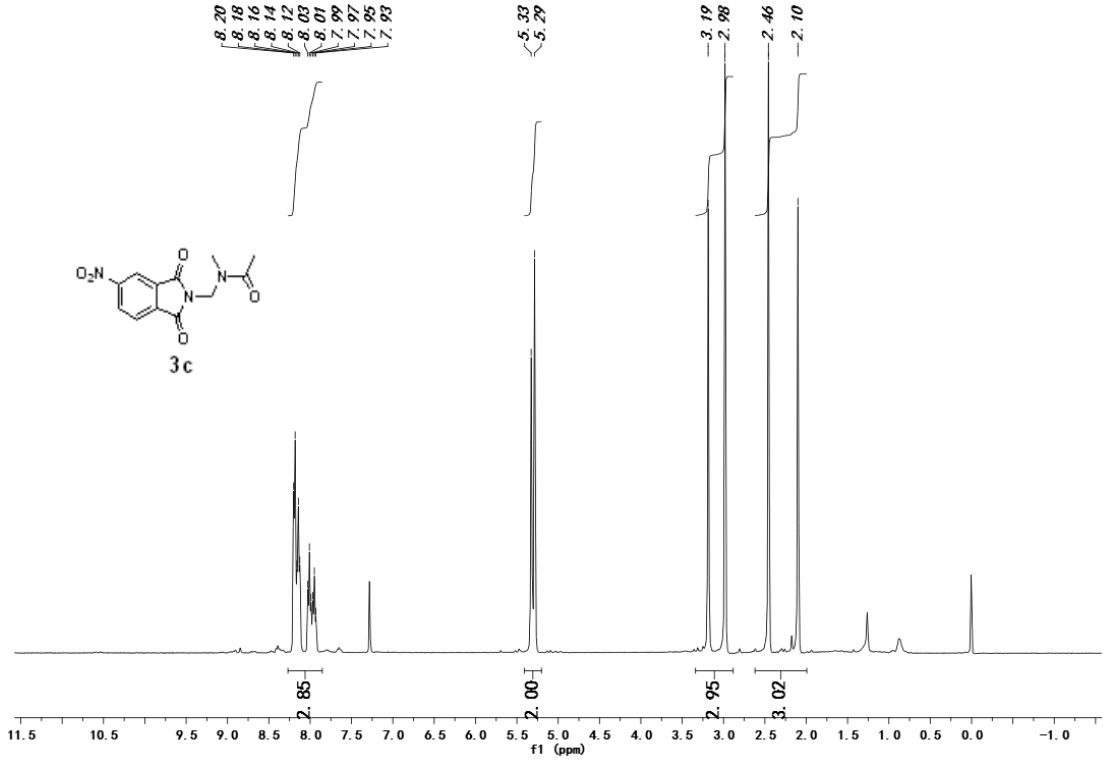
^{1}H NMR Spectra of Compound **3b** (400 MHz, $CDCl_3$)



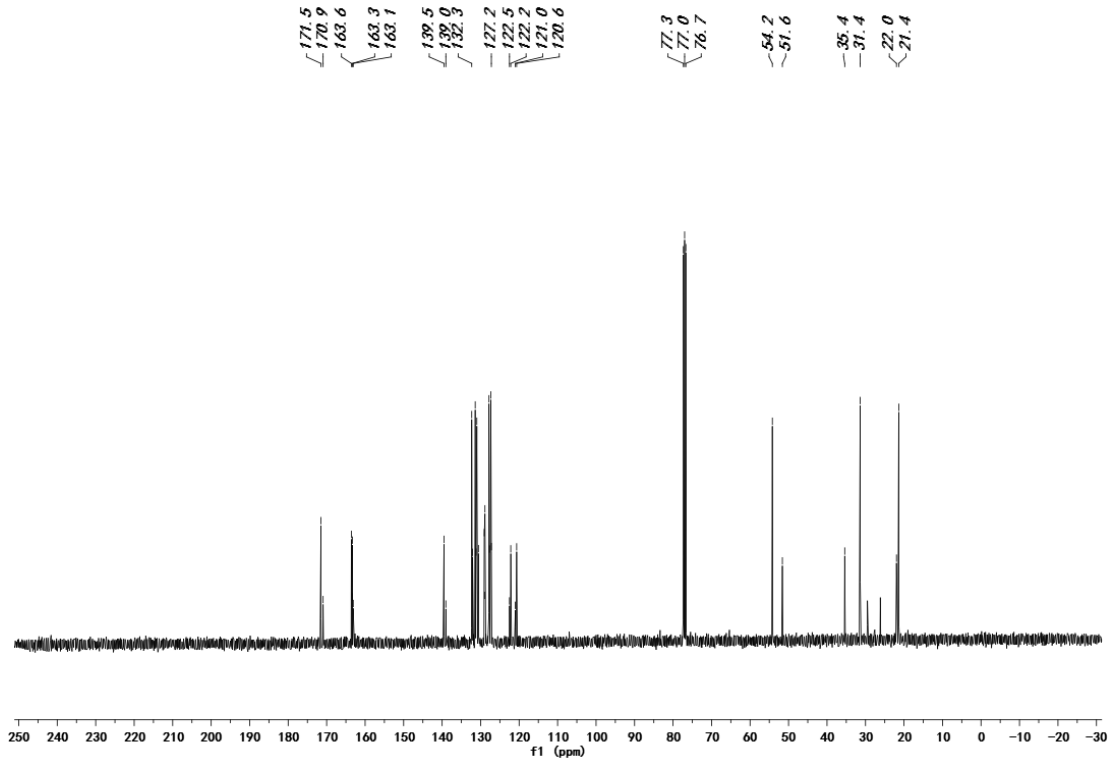
^{13}C NMR Spectra of Compound **3b** (100 MHz, $CDCl_3$)



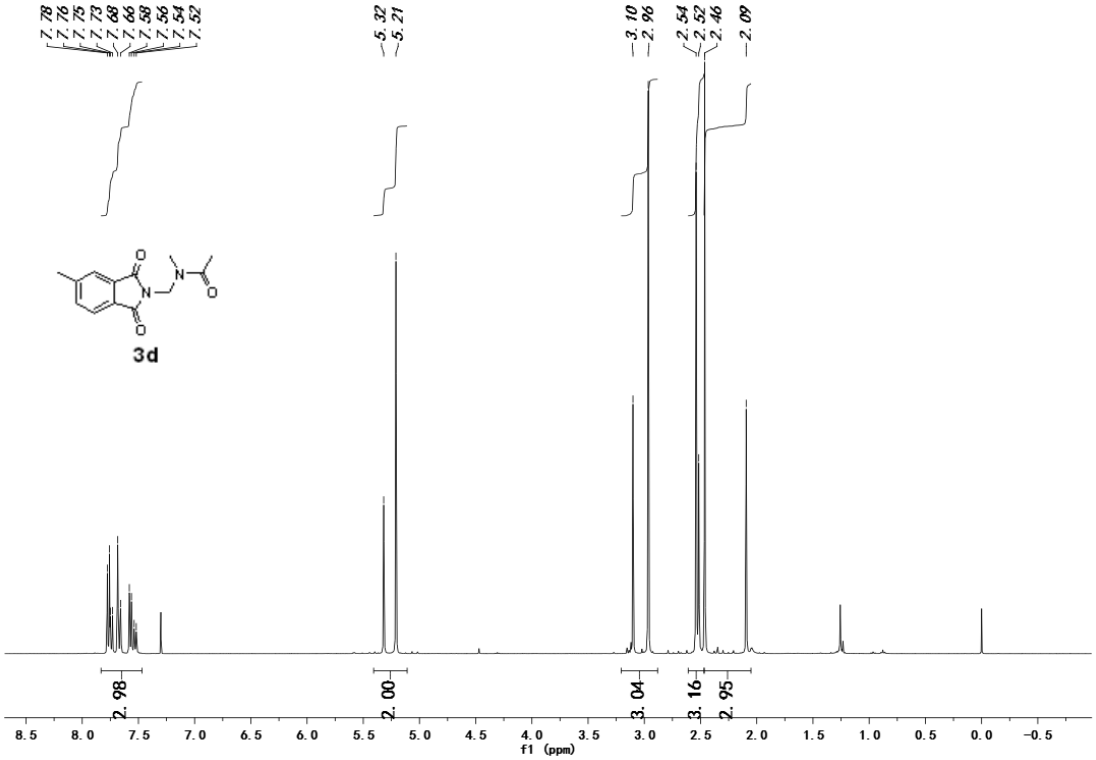
^{1}H NMR Spectra of Compound **3c** (400 MHz, $CDCl_3$)



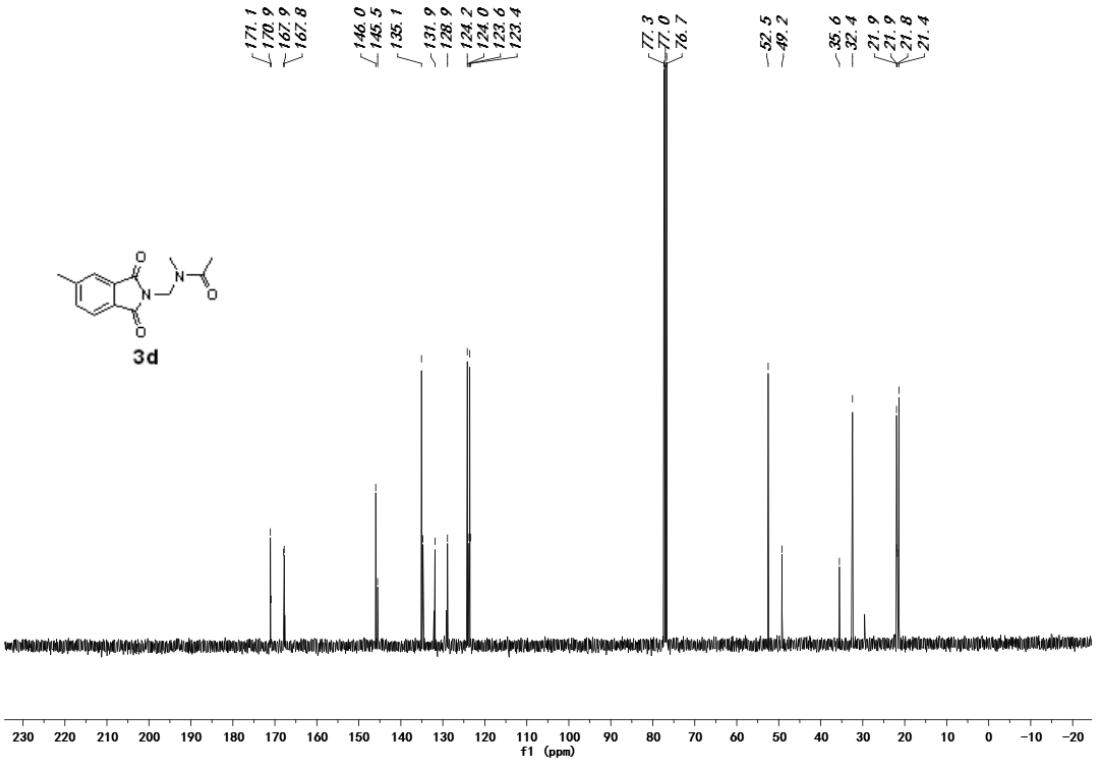
^{13}C NMR Spectra of Compound **3c** (100 MHz, $CDCl_3$)



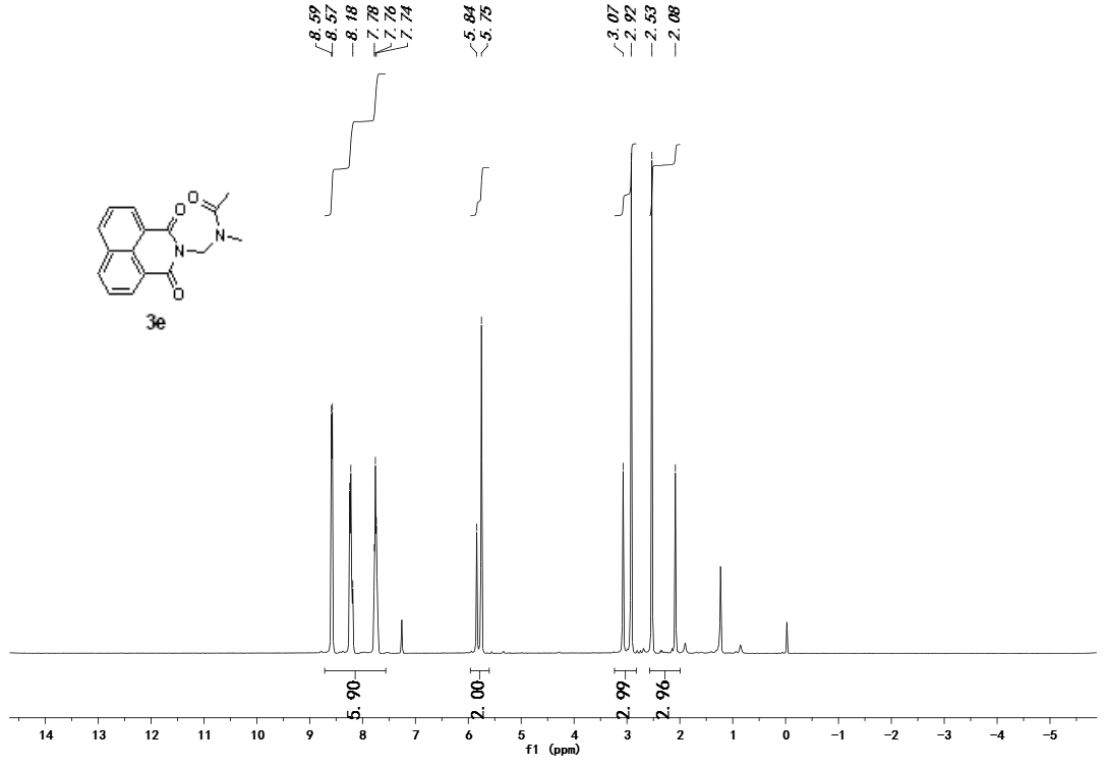
^{1}H NMR Spectra of Compound **3d** (400 MHz, $CDCl_3$)



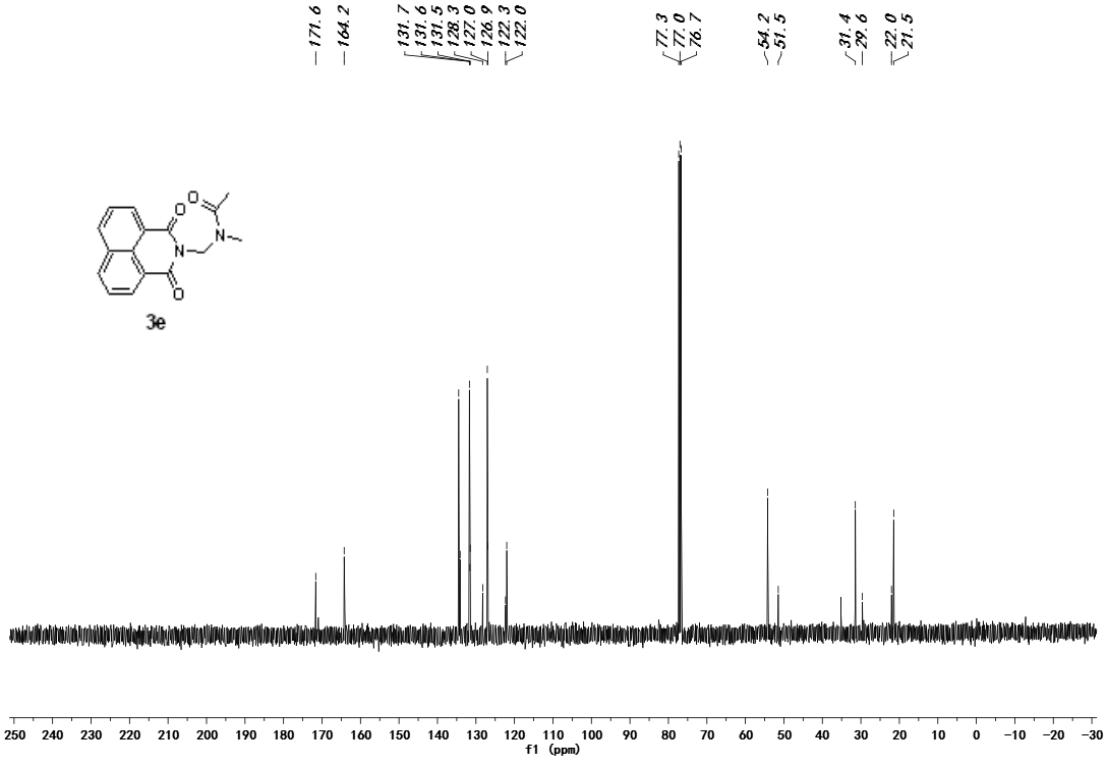
^{13}C NMR Spectra of Compound **3d** (100 MHz, $CDCl_3$)



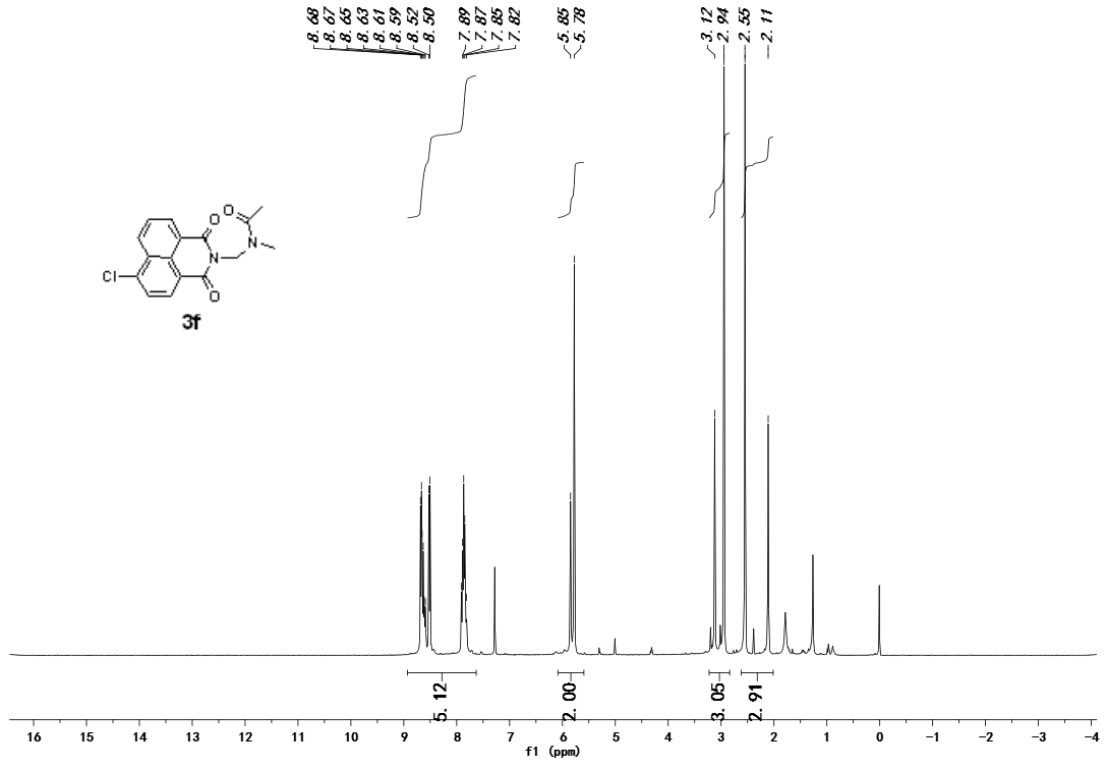
^{1}H NMR Spectra of Compound **3e** (400 MHz, $CDCl_3$)



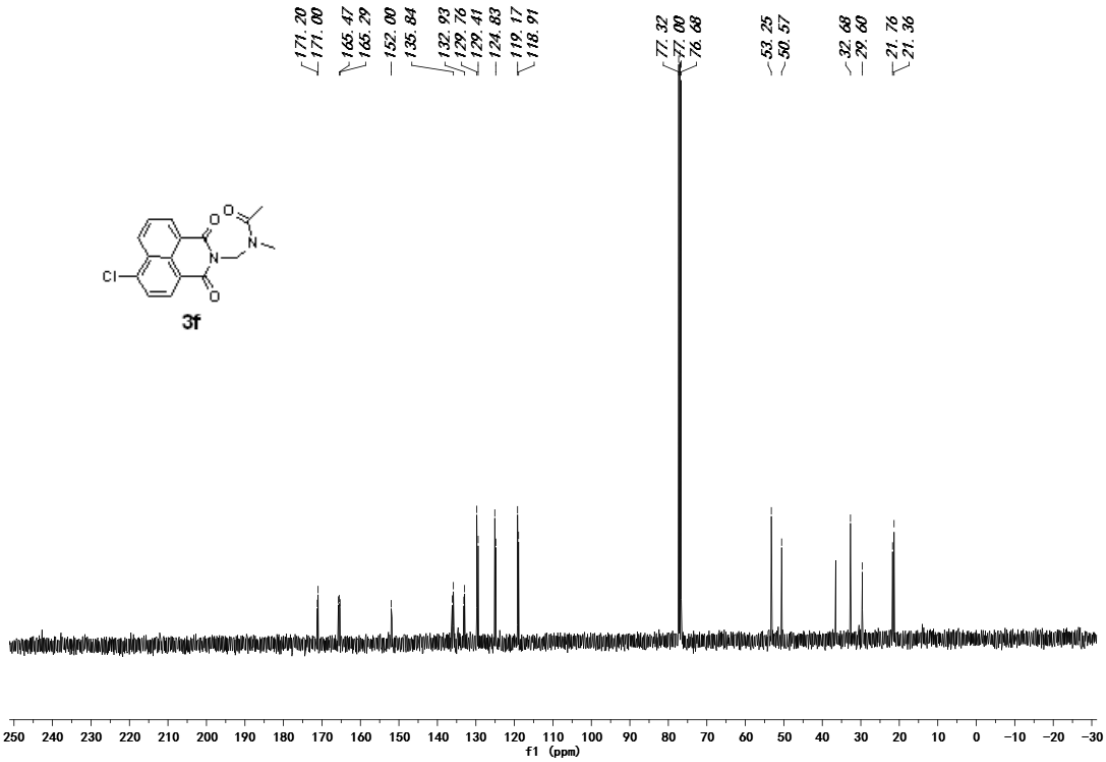
^{13}C NMR Spectra of Compound **3e** (100 MHz, $CDCl_3$)



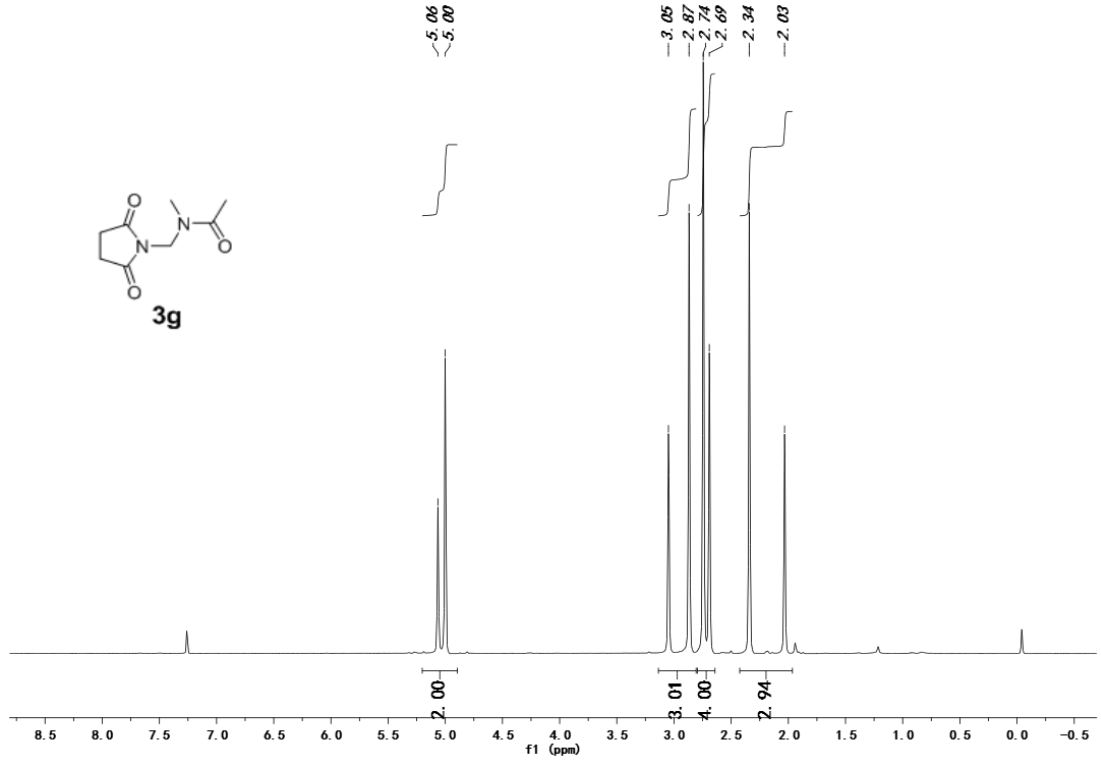
^{1}H NMR Spectra of Compound **3f** (400 MHz, $CDCl_3$)



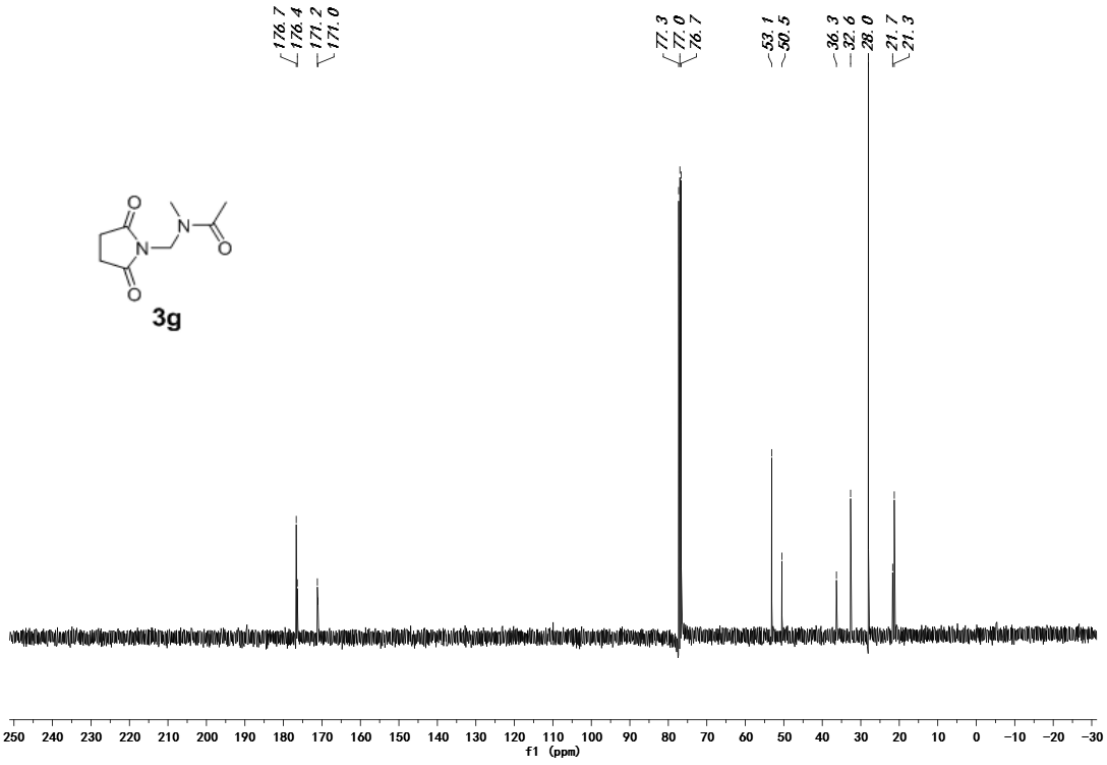
^{13}C NMR Spectra of Compound **3f** (100 MHz, $CDCl_3$)



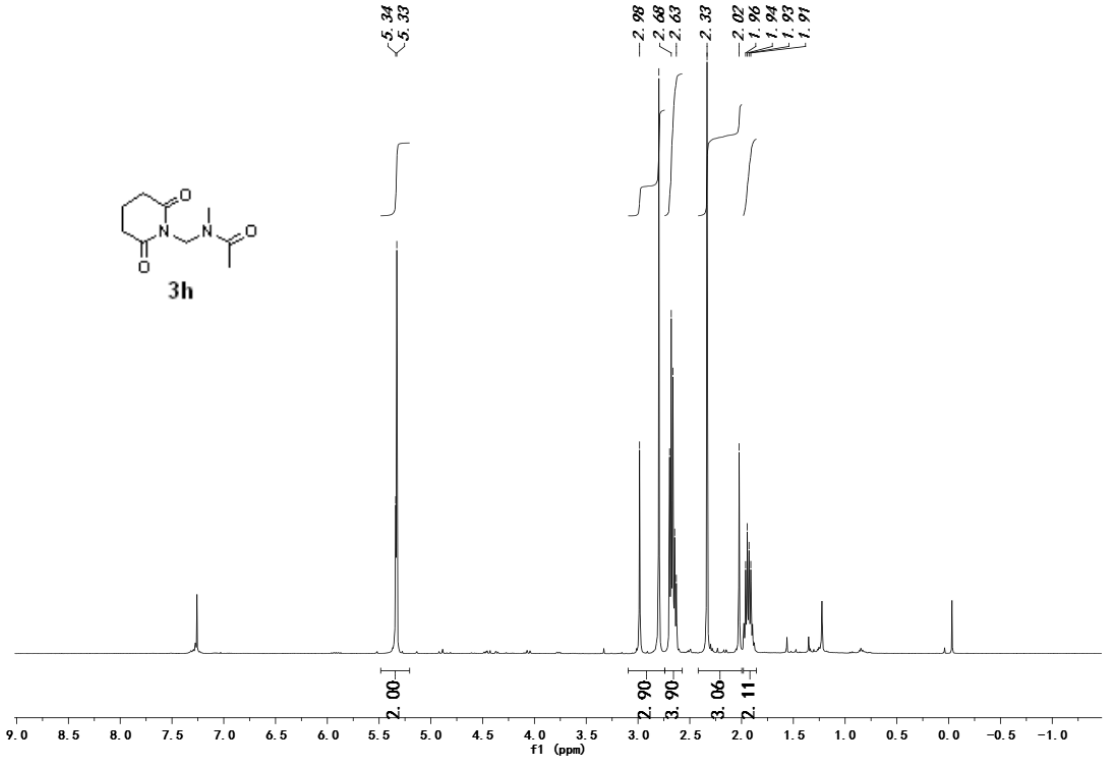
^{1}H NMR Spectra of Compound **3g** (400 MHz, $CDCl_3$)



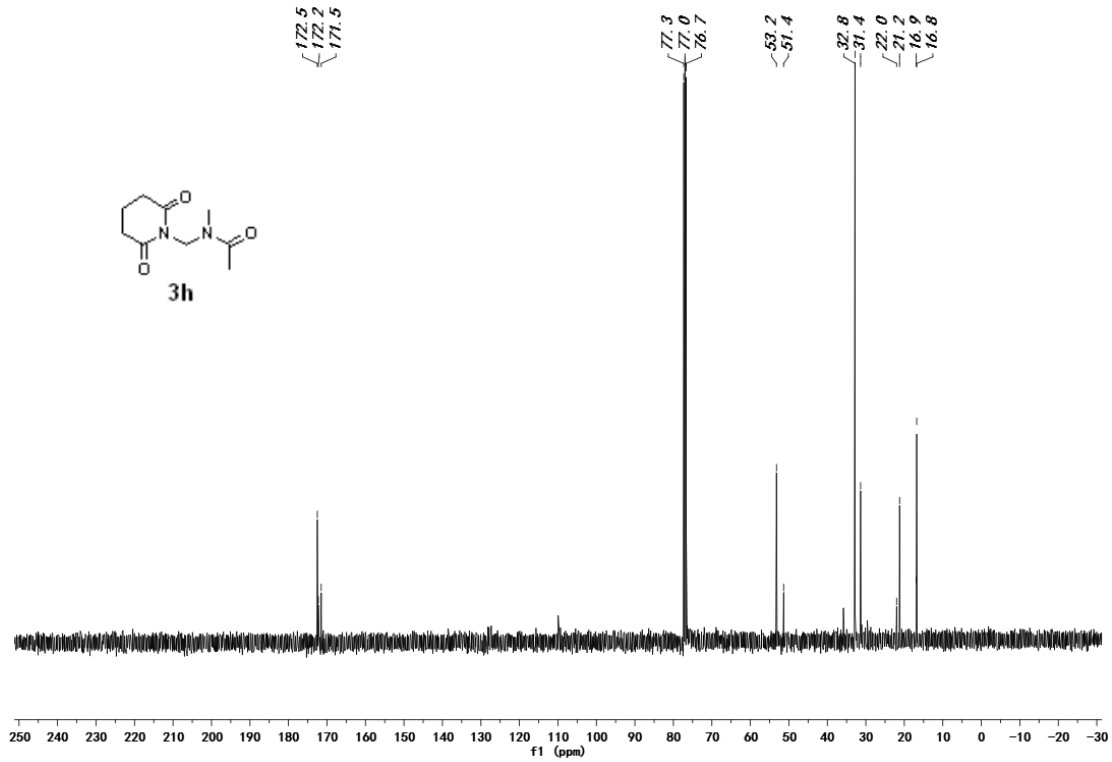
^{13}C NMR Spectra of Compound **3g** (100 MHz, $CDCl_3$)



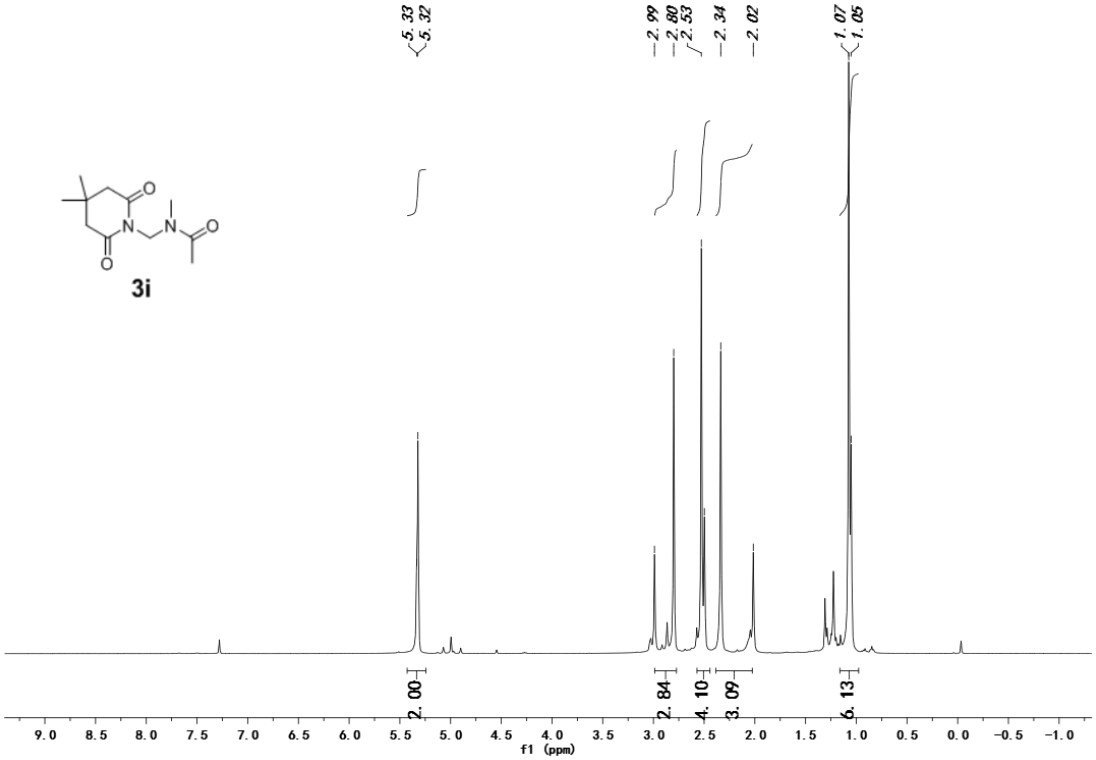
^{1}H NMR Spectra of Compound **3h** (400 MHz, $CDCl_3$)



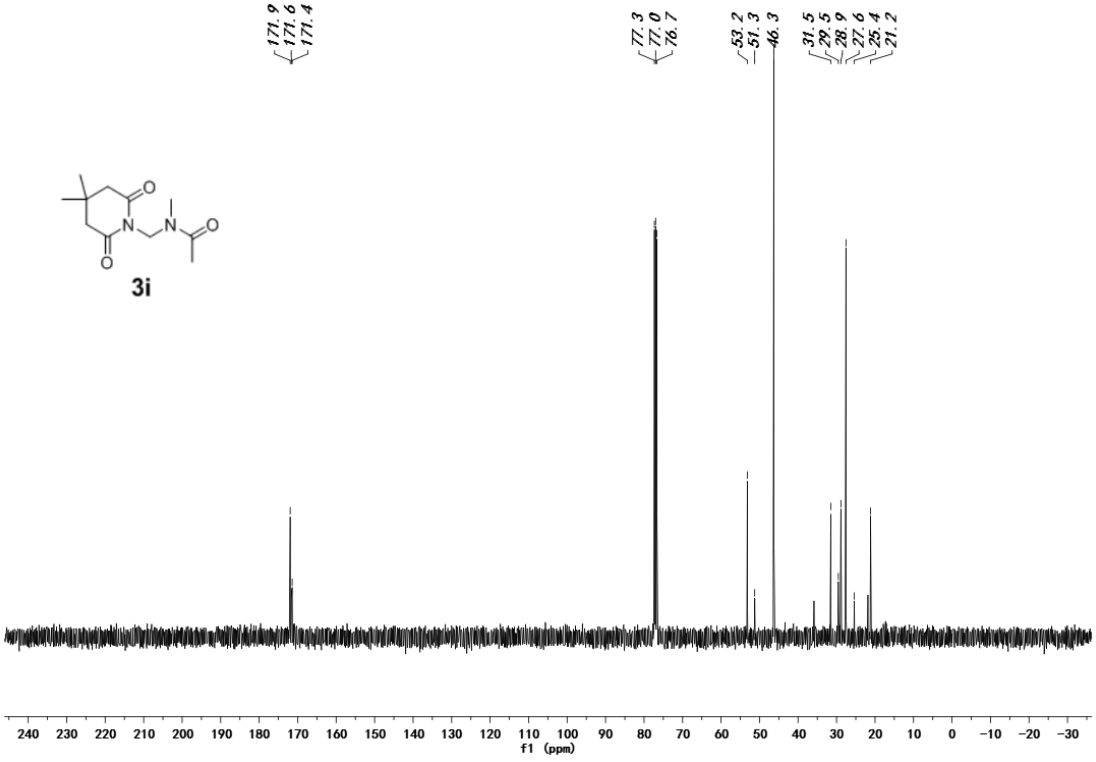
^{13}C NMR Spectra of Compound **3h** (100 MHz, $CDCl_3$)



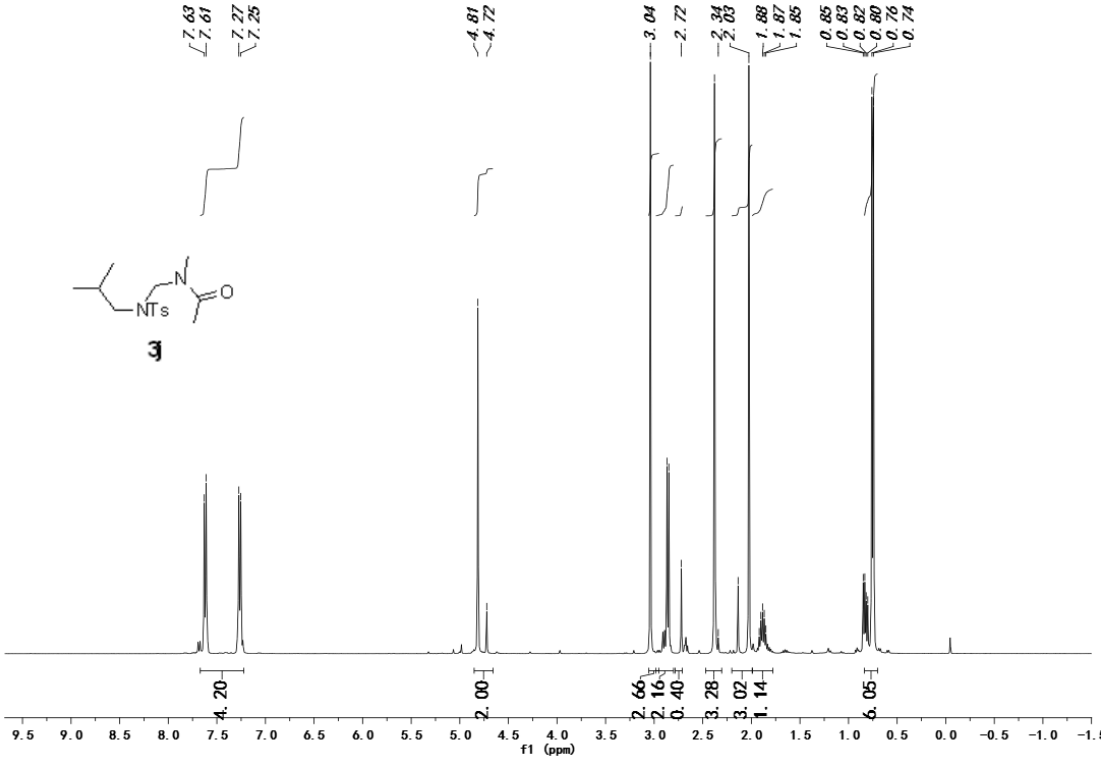
^{1}H NMR Spectra of Compound **3i** (400 MHz, $CDCl_3$)



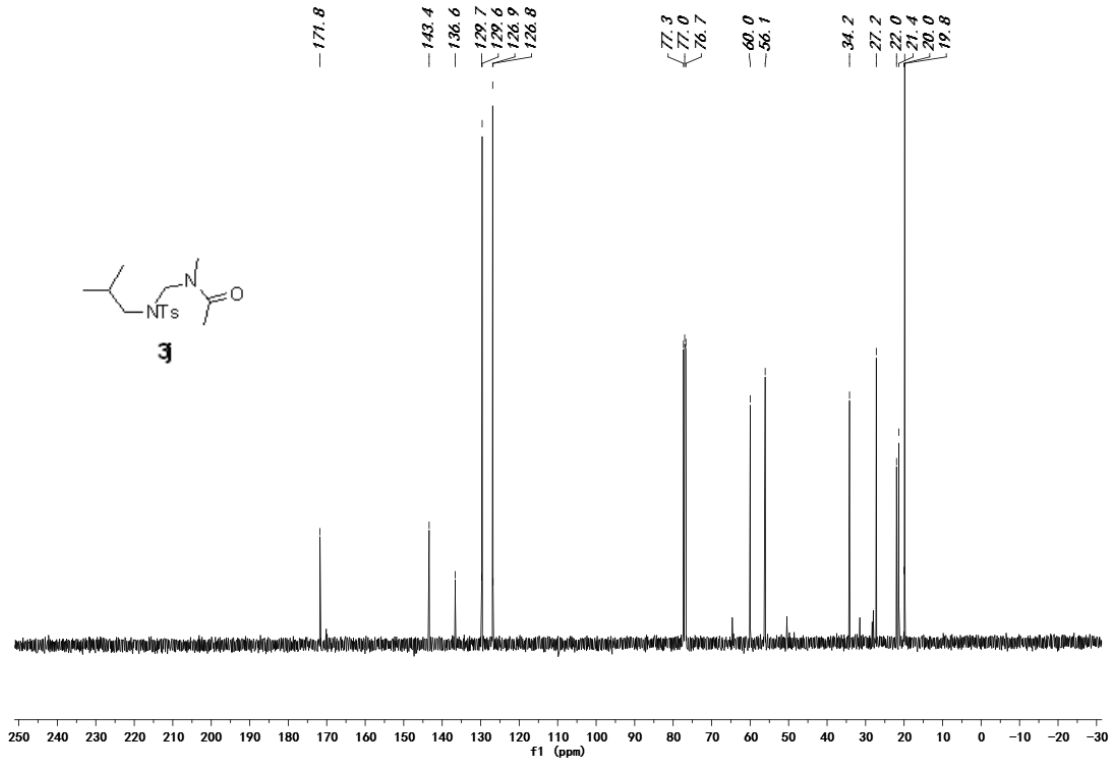
^{13}C NMR Spectra of Compound **3i** (100 MHz, $CDCl_3$)



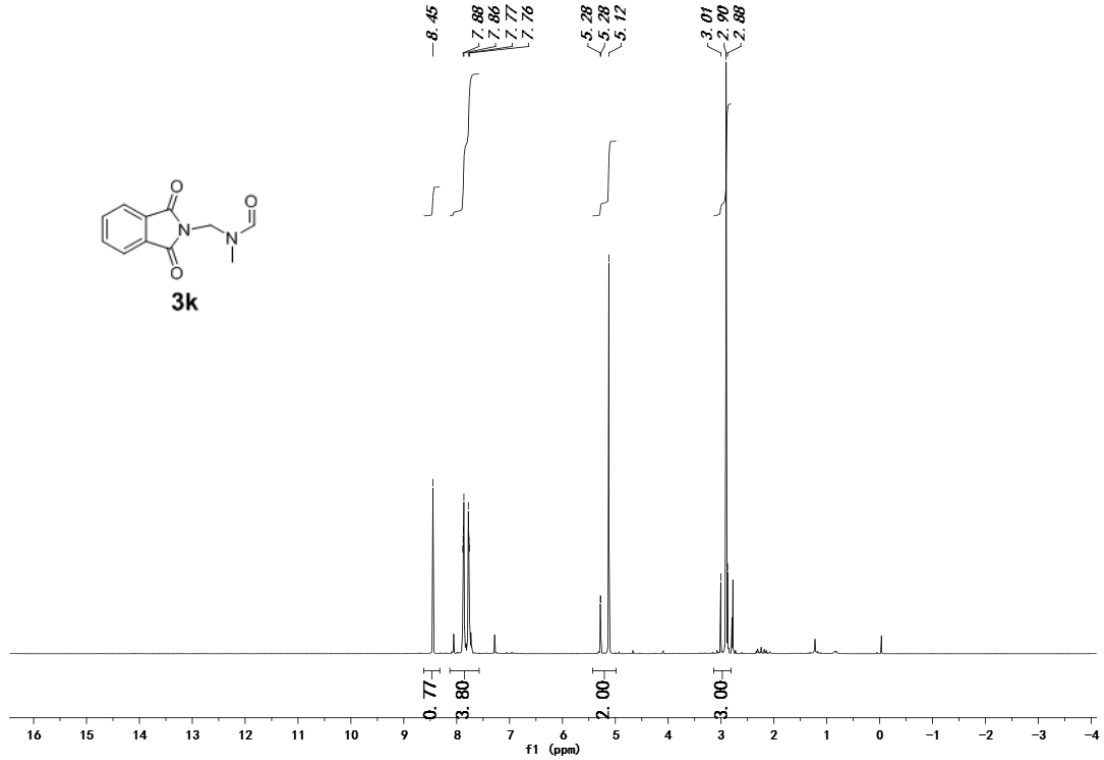
^{1}H NMR Spectra of Compound **3j** (400 MHz, $CDCl_3$)



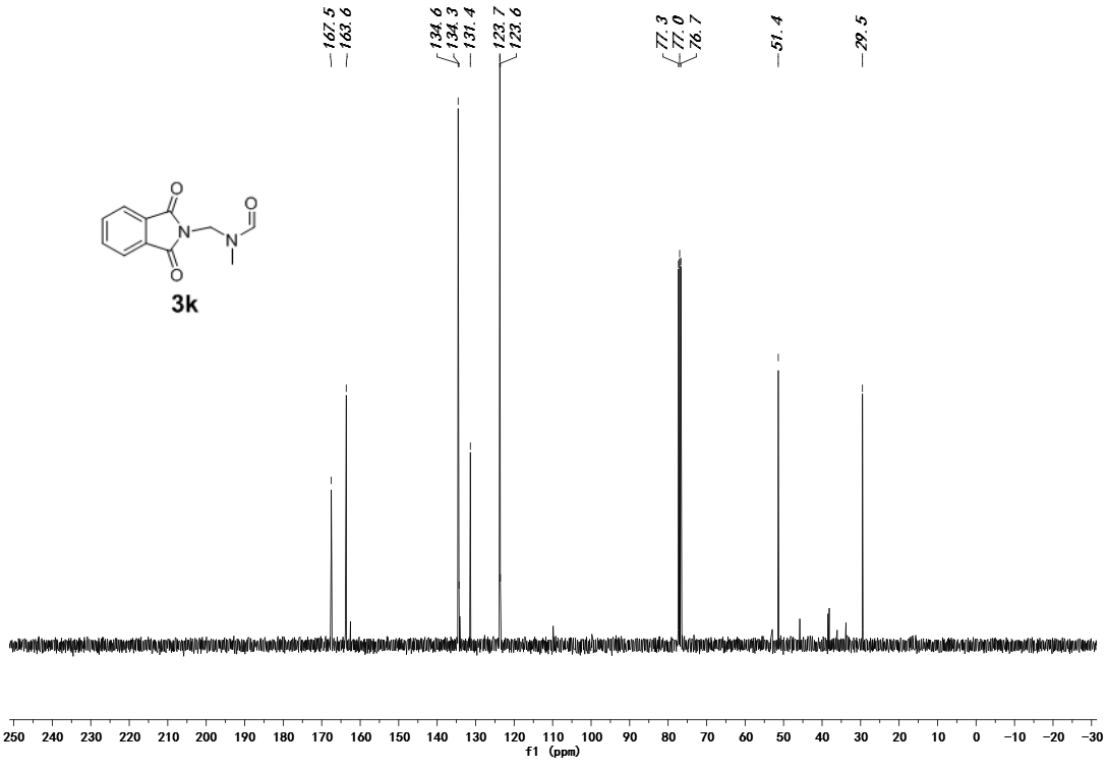
^{13}C NMR Spectra of Compound **3j** (100 MHz, $CDCl_3$)



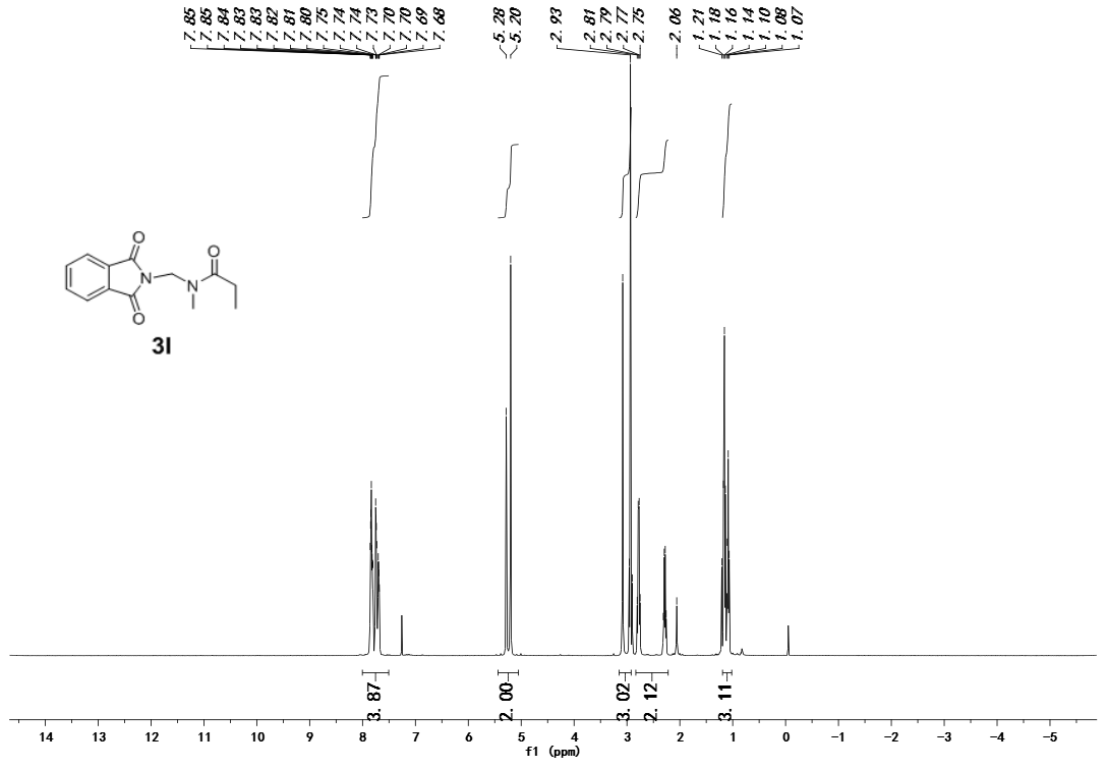
^{1}H NMR Spectra of Compound **3k** (400 MHz, $CDCl_3$)



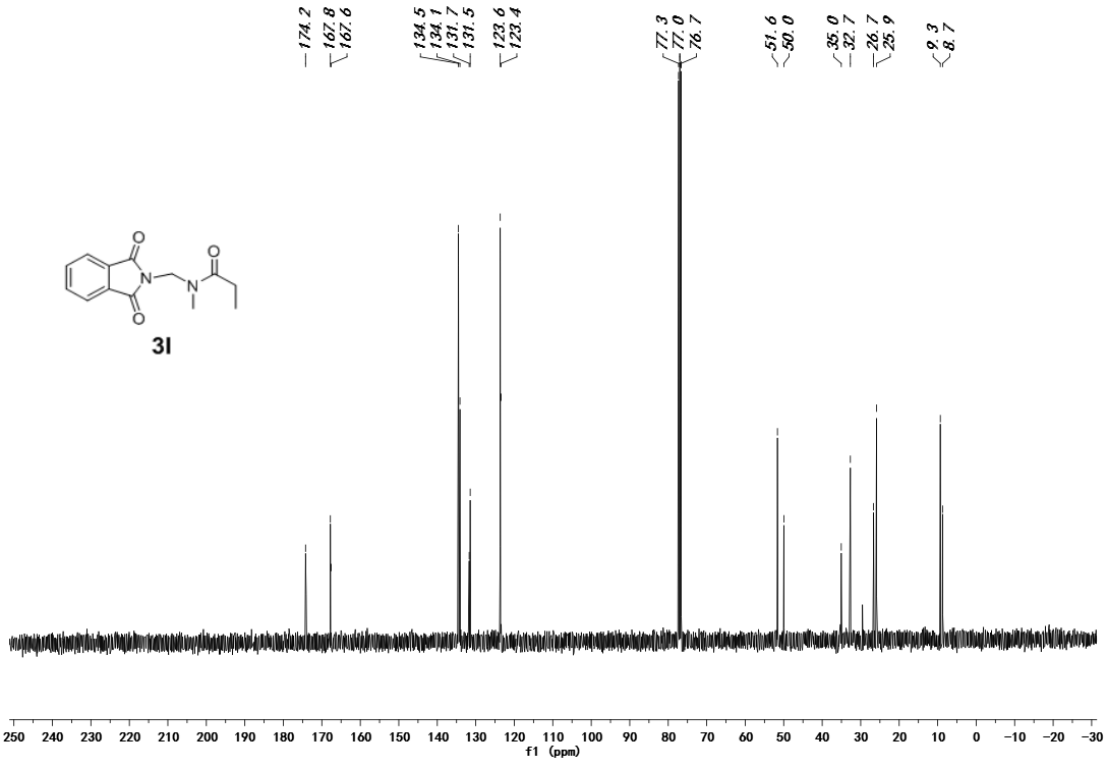
^{13}C NMR Spectra of Compound **3k** (100 MHz, $CDCl_3$)



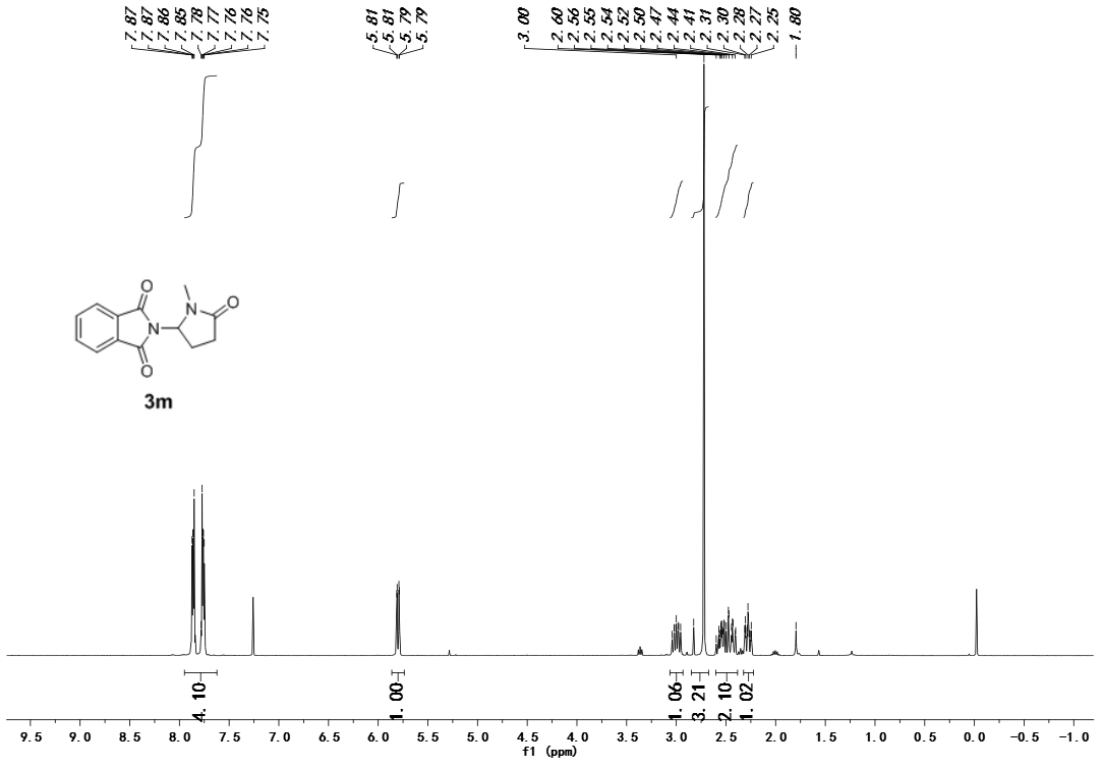
^{1}H NMR Spectra of Compound **3l** (400 MHz, $CDCl_3$)



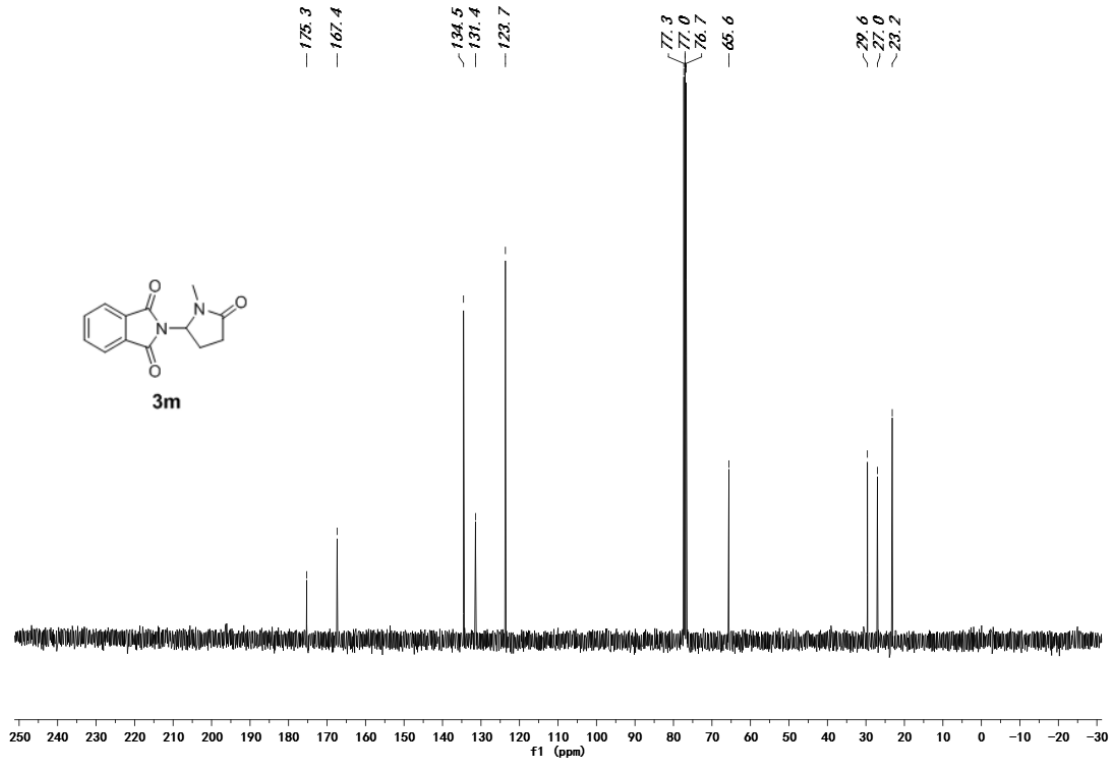
^{13}C NMR Spectra of Compound **3l** (100 MHz, $CDCl_3$)



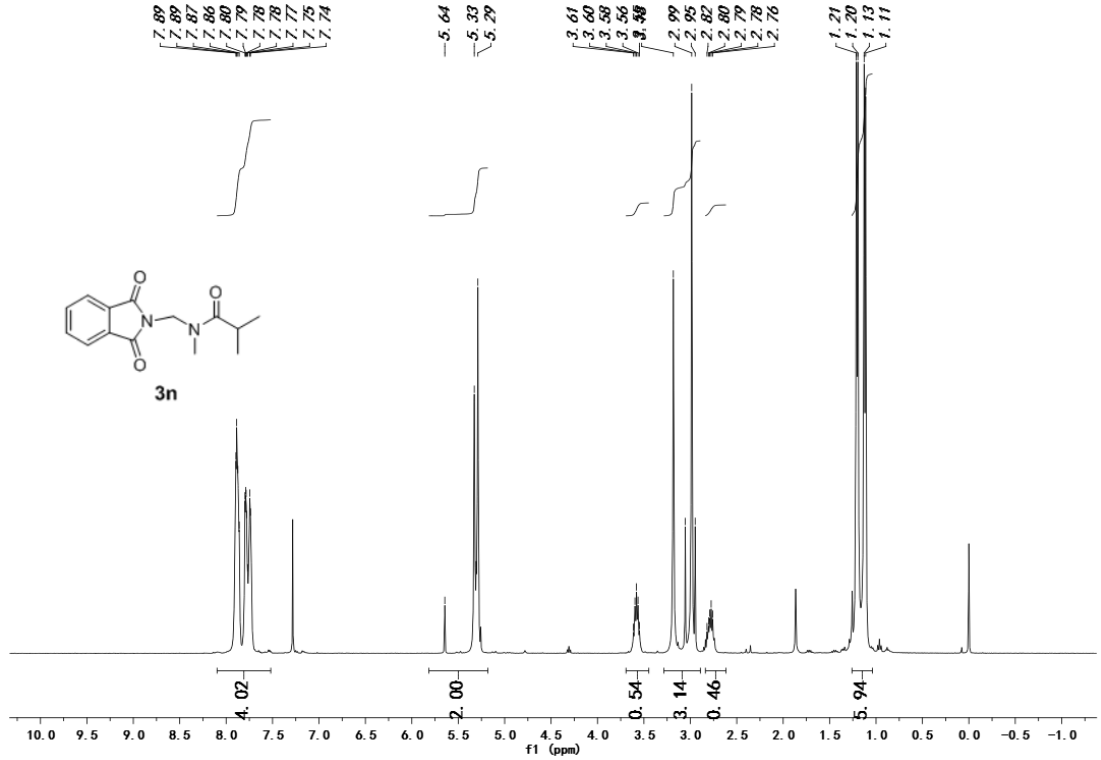
^{1}H NMR Spectra of Compound **3m** (400 MHz, $CDCl_3$)



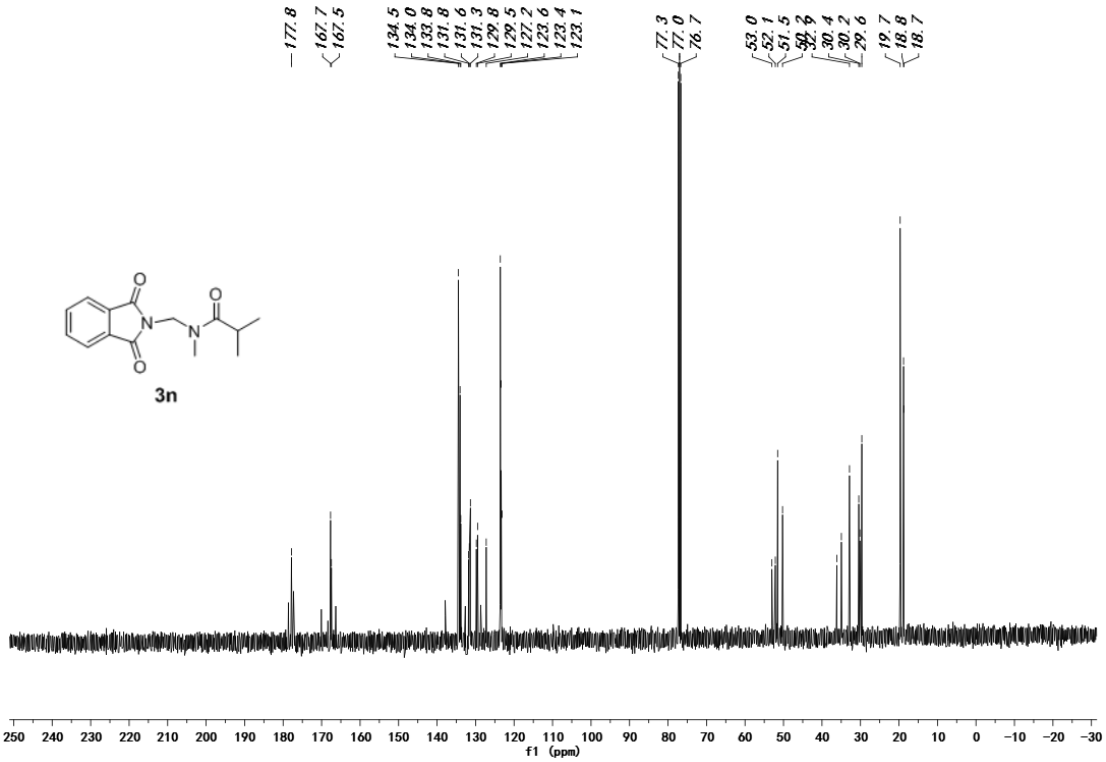
^{13}C NMR Spectra of Compound **3m** (100 MHz, $CDCl_3$)



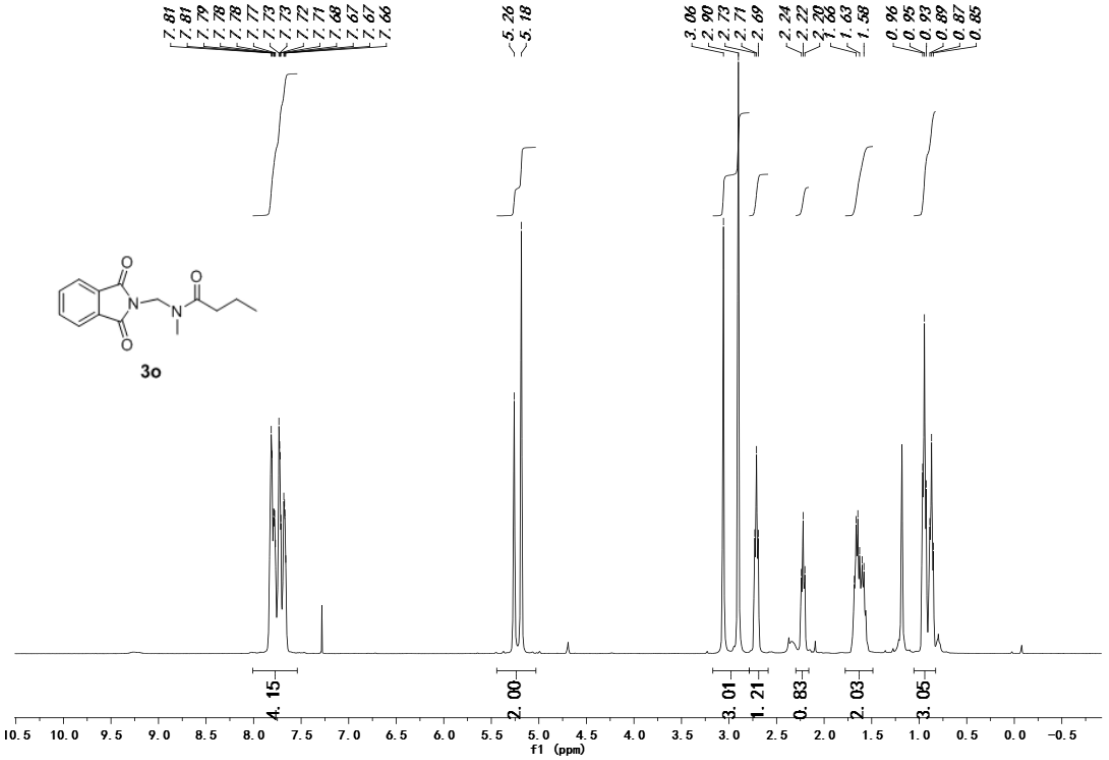
^{1}H NMR Spectra of Compound **3n** (400 MHz, $CDCl_3$)



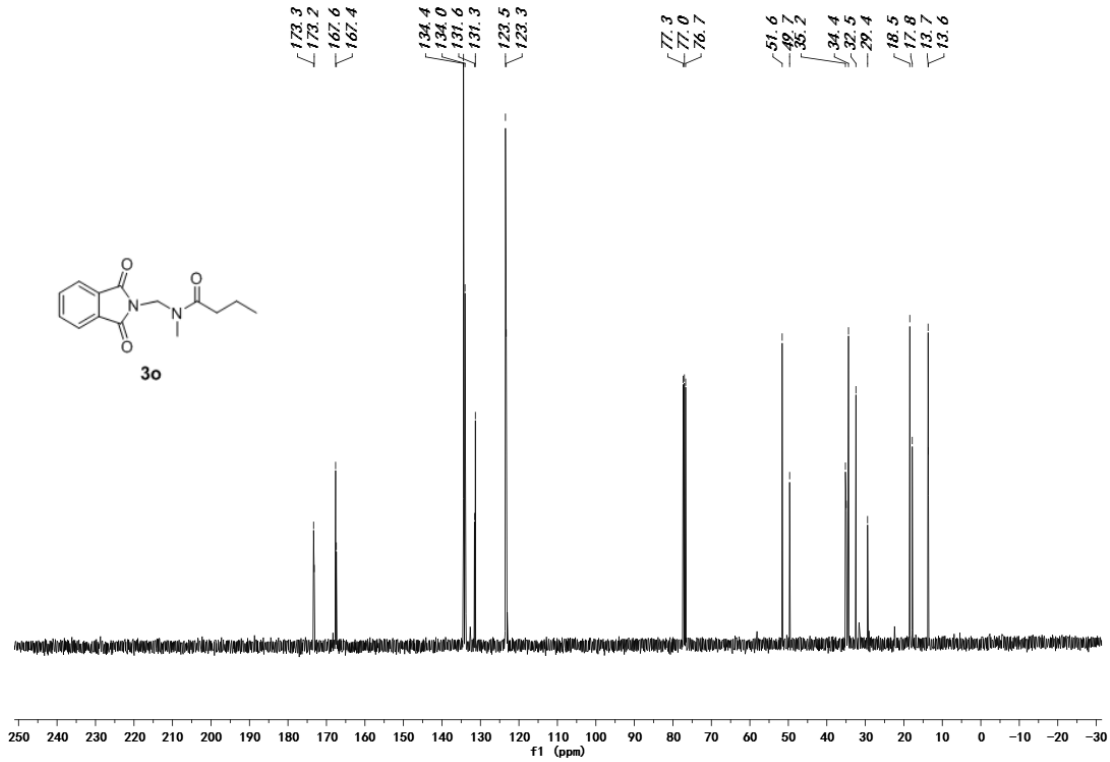
^{13}C NMR Spectra of Compound **3n** (100 MHz, $CDCl_3$)



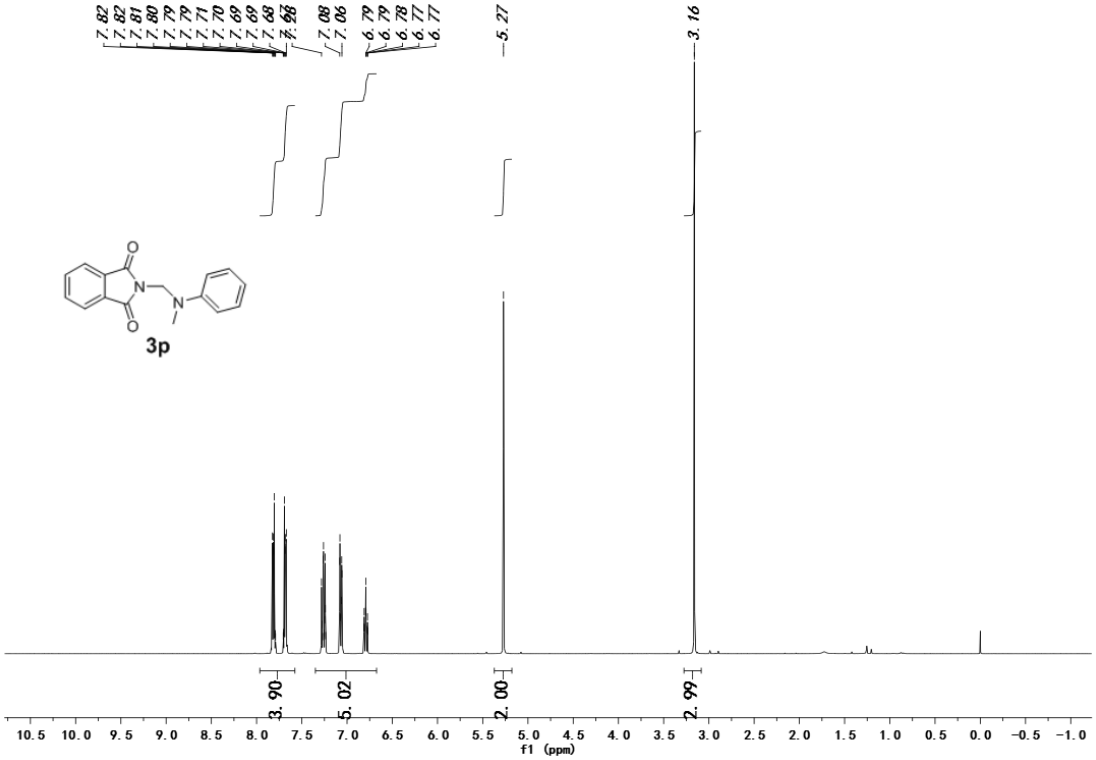
^{1}H NMR Spectra of Compound **3o** (400 MHz, $CDCl_3$)



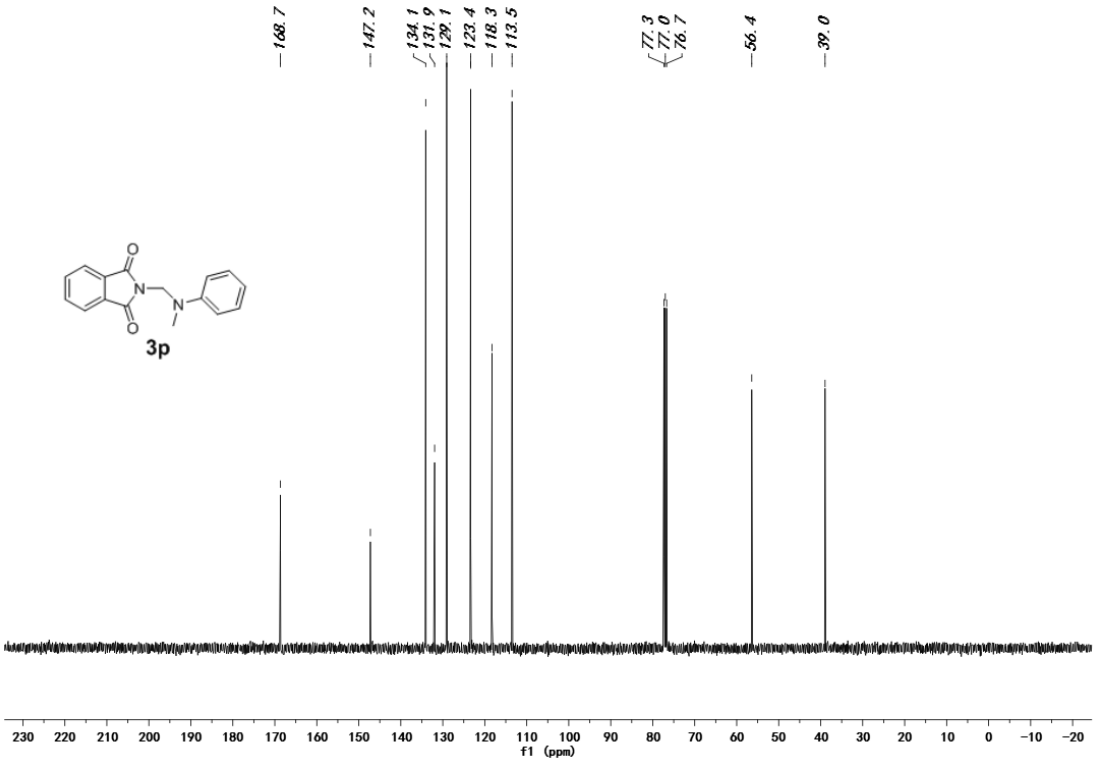
^{13}C NMR Spectra of Compound **3o** (100 MHz, $CDCl_3$)



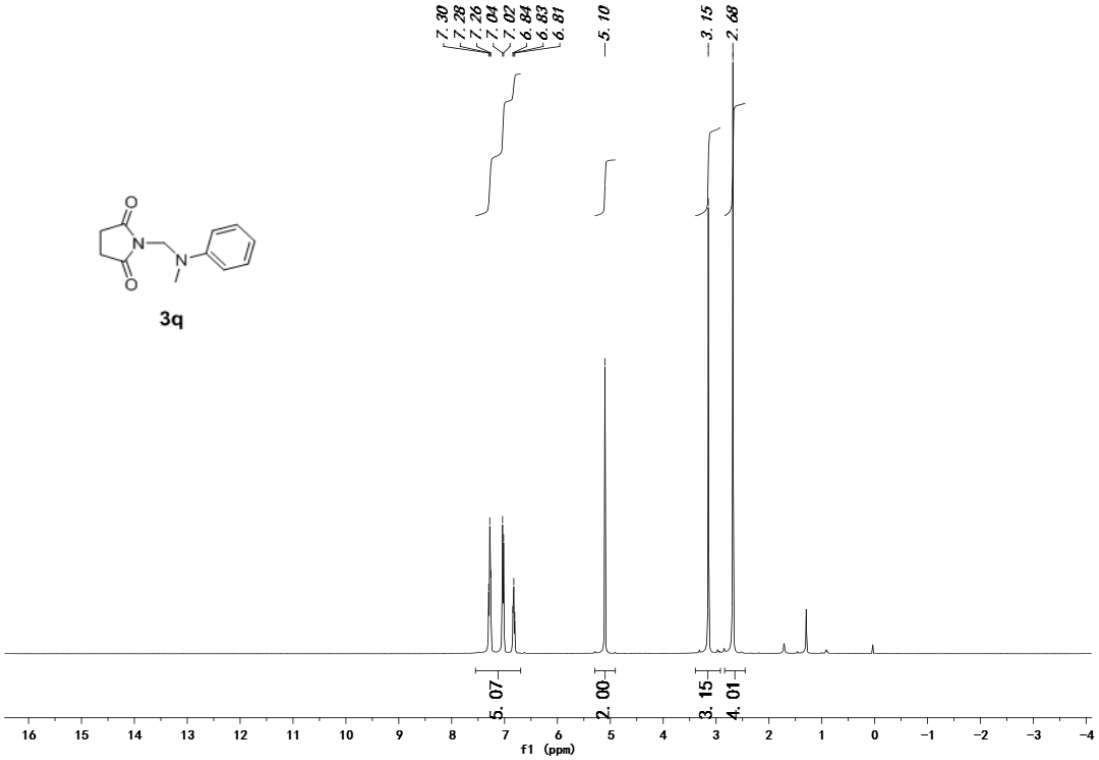
^{1}H NMR Spectra of Compound **3p** (400 MHz, $CDCl_3$)



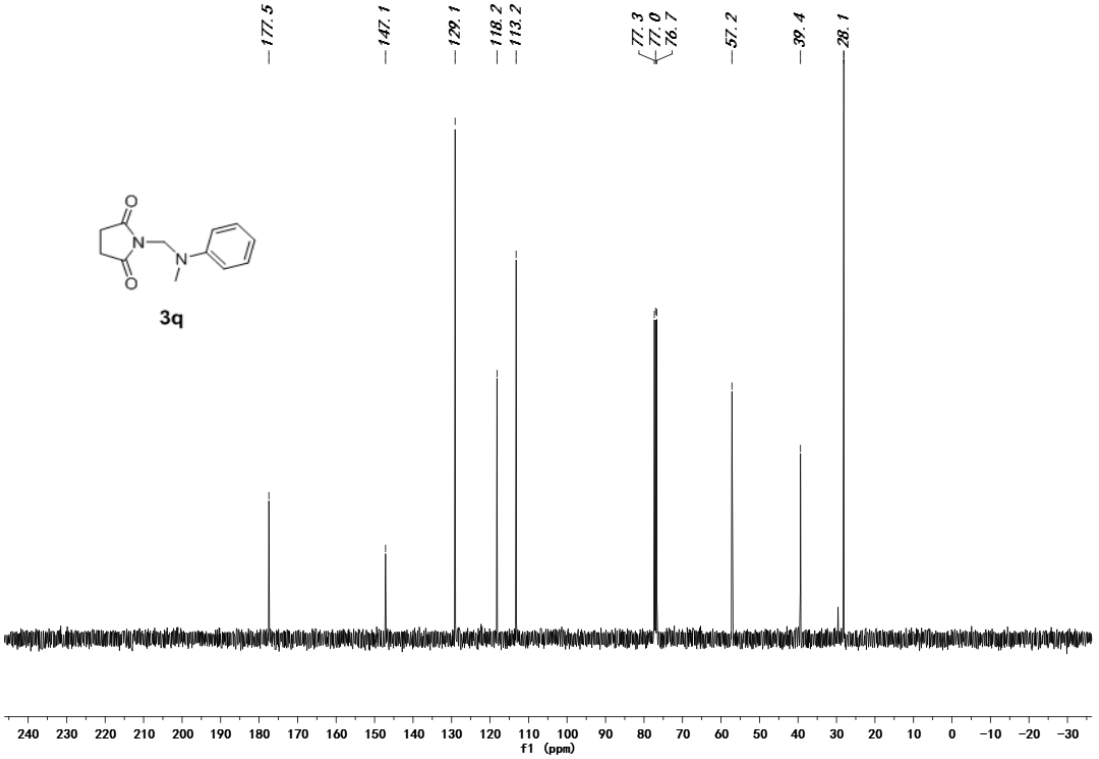
^{13}C NMR Spectra of Compound **3p** (100 MHz, $CDCl_3$)



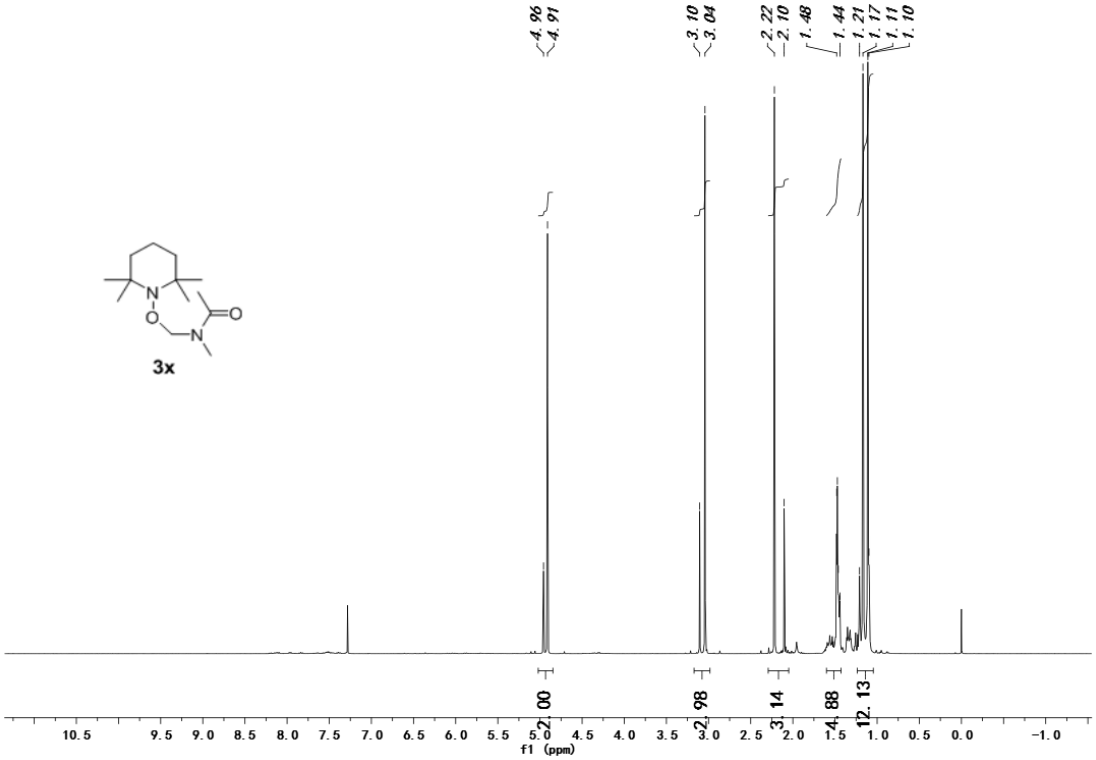
^{1}H NMR Spectra of Compound **3q** (400 MHz, $CDCl_3$)



^{13}C NMR Spectra of Compound **3q** (100 MHz, $CDCl_3$)



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



^{13}C NMR Spectra of Compound **3x** (100 MHz, $CDCl_3$)