Supporting Information

A Synthetic Route to Sodium α-Aminoalkanesulfinates and Their Application in the Generation of α-Aminoalkyl Radicals for Radical Addition Reactions

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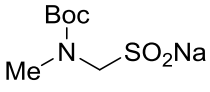
General Information

^{1}H NMR spectra were measured on JEOL JNM-ECA500 (500 MHz) spectrometer. Data were reported as follows: chemical shifts in ppm from tetramethylsilane as an internal standard in $CDCl_3$, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet-doublet, m = multiplet, br = broad), coupling constants (Hz), and assignment. ^{13}C NMR spectra were measured on JEOL JNM-ECA500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard. Infrared (IR) spectra were recorded on a Thermo Scientific Nicolet iS5 spectrometer. High-resolution mass spectra (HRMS) were performed on Brucker microTOF and Thermo Exactive plus. YMC syringe pump (model number: YSP-101) was used when slow addition of a solution was conducted. The products were purified by flash column chromatography (silica gel 60, Merck, 230-400 mesh) or preparative thin layer chromatography silica gel (PLC 60 F254. 0.5 mm). α-Imino ester **3a**,[1] α-keto imines **3c**,[2] **3e**[1] and **3f**,[1] 2-isocyanobiphenyls,[3] and electron-deficient olefins **6**,[4] DABSO[5] were prepared according to the literature procedure. Commercially available reagents were purchased from Wako, Aldrich, TCI and Alfa-aesar chemicals and used as received.

General Procedure for Synthesis of Sodium *α*-Aminoalkanesulfinates (1) (Scheme 2c)

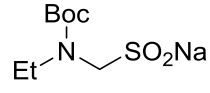
To a stirred solution of *N*-Boc-protected alkylamine (10 mmol) and N^1,N^1,N^2,N^2-tetramethyl-1,2-ethanediamine (1.8 mL, 12 mmol) in diethyl ether (20 mL) was added *sec*-butyllithium (1.0 M in cyclohexane and *n*-hexane, 12 mL, 12 mmol) slowly at –78 °C under argon atmosphere. After stirring for 1 h at the same temperature, to the mixture was added DABSO (2.4 g, 10 mmol) at –78 °C. After stirring for 3 h at room temperature, the reaction mixture was quenched with sat. Na_2CO_3 aq. and extracted with sat. Na_2CO_3 aq. three times. The combined aqueous layer was concentrated. To the residue was added methanol (30 mL) and stirred for 10 minutes. The mixture was then filtered, and the methanol was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (eluting with DCM/MeOH = 4/1) to provide the following compound. (Note: The silica for the silica plug was pre-washed with MeOH followed by hexane before use.)

Sodium ((*tert*-Butoxycarbonyl)(methyl)amino)methanesulfinate (1a)



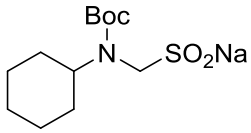
(white solid, 1.9 g, 81%); ^{1}H NMR (500 MHz, CD_3OD, 50 °C) δ 3.61 (s, 2H), 3.00 (s, 3H), 1.42 (s, 9H); ^{13}C NMR (125 MHz, CD_3OD, 50 °C) δ 164.6, 85.1, 81.3, 45.6, 28.7; HRMS calculated for $C_7H_{14}O_4NS$: *m/z* 208.0638 ($[M - Na]^-$), found: *m/z* 208.0631 ($[M - Na]^-$); IR (neat) 2466, 1675, 1392, 1121, 974 cm^{-1}.

Sodium ((*tert*-Butoxycarbonyl)(ethyl)amino)methanesulfinate (1b)



(white solid, 1.5 g, 62%); ^{1}H NMR (500 MHz, CD_3OD) δ 3.71 (app d, 2H), 3.47 (s, 2H), 1.47 (app d, J = 10.5 Hz, 9H), 1.13 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 163.0, 83.6, 81.5, 35.2, 27.0, 12.5; HRMS calculated for $C_8H_{16}O_4NS$: *m/z* 222.0784 ($[M - Na]^-$), found: *m/z* 222.0795 ($[M - Na]^-$); IR (neat) 2980, 2506, 1653, 1457, 1160 cm^{-1}.

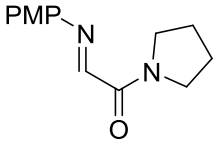
Sodium ((*tert*-Butoxycarbonyl)(cyclohexyl)amino)methanesulfinate (1c)



(white solid, 2.0 g, 66%); ^{1}H NMR (500 MHz, CD_3OD, 50 °C) δ 3.58 (brs, 2H), 3.16 (s, 1H), 1.75 (s, 4H), 1.59-1.53 (m, 2H), 1.43

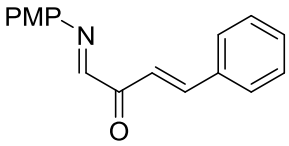
(s, 9H), 1.28 (d, J = 12.3 Hz, 3H), 1.13-1.07 (m, 1H); ^{13}C NMR (125 MHz, CD_3OD, 50 °C) δ 165.0, 81.5, 73.4, 32.6, 30.8, 28.7, 27.2, 26.7; HRMS calculated for $C_{12}H_{22}O_4NS$: *m/z* 276.1264 ([M – Na]$^-$), found: *m/z* 276.1254 ([M – Na]$^-$); IR (neat) 2932, 1692, 1152, 1087, 896 cm^{-1}.

(*E*)-2-((4-Methoxyphenyl)imino)-1-(pyrrolidin-1-yl)ethan-1-one (3b)



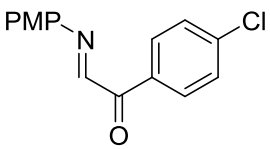
The title compound was prepared according to the literature procedure.[2] (brown liquid, 52 mg, 22%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.25 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 3.92 (t, J = 6.8 Hz, 2H), 3.83 (s, 3H), 3.63 (t, J = 6.8 Hz, 2H), 2.01-1.95 (m, 2H), 1.93-1.88 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.0, 159.6, 152.3, 142.1, 122.6, 114.3, 55.4, 47.8, 46.7, 26.3, 23.6; HRMS calculated for $C_{13}H_{16}O_2N_2Na$: *m/z* 255.1104 ([M + Na]$^+$), found: *m/z* 255.1090 ([M + Na]$^+$); IR (neat) 2972, 2237, 1608, 1504, 1441, 725 cm^{-1}.

(1*E*,3*E*)-1-((4-Methoxyphenyl)imino)-4-phenylbut-3-en-2-one (3d)



The title compound was prepared according to the literature procedure.[1] (brown solid, 0.21 g, 15%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.93 (d, J = 16.2 Hz, 1H), 7.87 (d, J = 16.2 Hz, 1H), 7.71-7.69 (m, 2H), 7.43-7.42 (m, 2H), 7.42-7.39 (m, 3H), 6.99-6.96 (m, 2H), 3.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.3, 160.8, 155.1, 144.6, 141.5, 135.1, 130.9, 129.1, 129.0, 124.0, 120.3, 114.8, 55.7; HRMS calculated for $C_{17}H_{15}O_2NNa$: *m/z* 288.0995 ([M + Na]$^+$), found: *m/z* 288.0998 ([M + Na]$^+$); IR (neat) 1660, 1608, 1574, 832, 724 cm^{-1}.

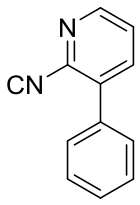
(*E*)-1-(4-Chlorophenyl)-2-((4-methoxyphenyl)imino)ethan-1-one (3g)



The title compound was prepared according to the literature procedure.[1] (yellow solid, 0.21 g, 77%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.29 (d, J = 8.8 Hz, 2H), 7.48 (d, J = 8.8 Hz, 2H), 7.40 (d, J = 9.1 Hz, 2H), 6.98 (d, J = 9.1 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.8, 160.9, 154.0, 141.5, 140.1, 133.9, 132.3, 128.8, 123.8, 114.9, 55.7;

HRMS calculated for $C_{15}H_{12}O_2NClNa$: m/z 296.0449 ($[M + Na]^+$), found: m/z 296.0457 ($[M + Na]^+$); IR (neat) 2953, 1647, 1584, 1328 cm^{-1}.

2-Isocyano-3-phenylpyridine



The title compound was prepared according to the literature procedure.[3] (yellow solid, 0.81 g, 45%); ^1H NMR (500 MHz, $CDCl_3$) δ 8.50 (dd, J = 4.8, 1.7 Hz, 1H), 7.83 (dd, J = 7.9, 1.7 Hz, 1H), 7.53-7.45 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 148.5, 139.5, 135.1, 134.4, 129.2, 129.0 (Three peaks were overlapped.), 125.0; HRMS calculated for $C_{12}H_8N_2Na$: *m/z* 203.0580 ($[M + Na]^+$), found: *m/z* 203.0581 ($[M + Na]^+$); IR (neat) 2955, 2122, 1406, 771 cm^{-1}.

General Procedure for 1,2-Addition of Sodium *α*-Aminoalkanesulfinates 1 to Imines 3 (Scheme 4)

Procedure A;

A test tube with a magnetic stir bar was charged with imine **3** (0.1 mmol), sodium α-aminoalkanesulfinate **1** (0.3 mmol), DIB (32 mg, 0.1 mmol) and DMSO (0.5 mL) under argon atmosphere. The mixture was stirred at room temperature for 2 h. The reaction was quenched with H_2O and extracted with ethyl acetate three times. The combined organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel to provide the following compound.

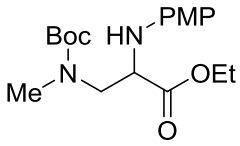
Procedure B;

To a stirred solution of *N*-Boc-protected alkylamine (10 mmol) and N^1,N^1,N^2,N^2-tetramethyl-1,2-ethanediamine (1.8 mL, 12 mmol) in diethyl ether (20 mL) was added *sec*-butyllithium (1.0 M in cyclohexane and *n*-hexane, 12 mL, 12 mmol) slowly at –78 °C under argon atmosphere. After stirring for 3 h at the same temperature, to the reaction mixture was added DABSO (2.4 g, 10 mmol) at –78 °C. After stirring for 3 h at room temperature, the reaction mixture was quenched with sat. Na_2CO_3 aq. and extracted with sat. Na_2CO_3 aq. three times. The combined aqueous layer was concentrated. To the residue was added methanol (30 mL) and stirred for 10 minutes. The mixture was then filtered,

and the methanol was evaporated in vacuo. The crude product was used directly for the next step without further purification.

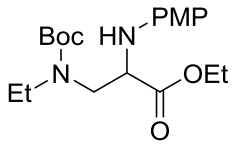
A test tube with a magnetic stir bar was charged with imine **3** (0.1 mmol), crude sodium α-aminoalkanesulfinate **1** (~0.3 mmol), DIB (32 mg, 0.1 mmol) and DMSO (0.5 mL) under argon atmosphere. The mixture was stirred at room temperature for 2 h. The reaction was quenched with H_2O and extracted with ethyl acetate three times. The combined organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel to provide the following compound.

Ethyl 3-((*tert*-Butoxycarbonyl)(methyl)amino)-2-((4-methoxyphenyl)amino) propanoate (4a)



Prepared by procedure A, The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/3) to afford the title compound (yellow liquid, 30 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 6.75 (d, J = 8.8 Hz, 2H), 6.57 (d, J = 8.8 Hz, 2H), 4.27 (br, 1H), 4.21-4.14 (m, 2H), 3.97 (br, 1H), 3.73 (s, 3H), 3.67 (br, 1H), 3.49 (s, 1H), 2.89 (s, 3H), 1.48 (s, 9H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 173.0, 156.6, 153.0, 141.2, 115.2, 115.0, 80.2, 61.4, 57.5, 55.9, 51.6, 35.7, 28.6, 14.3; HRMS calculated for $C_{18}H_{28}O_5N_2Na$: *m/z* 375.1890 ([M + Na]$^+$), found: *m/z* 375.1902 ([M + Na]$^+$) ; IR (neat) 3366, 2977, 1733, 1690, 1149 cm^{-1}.

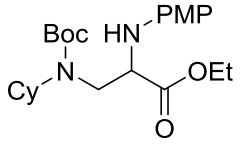
Ethyl 3-((*tert*-Butoxycarbonyl)(ethyl)amino)-2-((4-methoxyphenyl)amino) propanoate (4b)



Prepared by procedure A, The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/3) to afford the title compound (brown liquid, 26 mg, 72%). ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 6.75 (d, J = 8.8 Hz, 2H), 6.58 (d, J = 8.8 Hz, 2H), 4.22-4.14 (m, 3H), 3.73 (s, 3H), 3.67 (s, 1H), 3.44 (dd, J = 14.2, 6.0 Hz, 1H), 3.31 (s, 1H), 3.22-3.17 (m, 1H), 1.49 (s, 9H), 1.25 (t, J = 7.1 Hz, 3H), 1.09 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD, 50 °C) δ 174.7, 157.2, 154.3, 142.7, 116.2, 116.0, 81.4, 62.3, 58.7, 56.3,

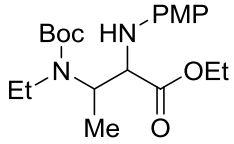
50.3, 44.4, 28.8, 14.4, 13.7; HRMS calculated for $C_{19}H_{30}O_5N_2Na$: *m/z* 389.2047 ([M + Na]$^+$), found: *m/z* 389.2061 ([M + Na]$^+$); IR (neat) 3360, 2975, 1733, 1688, 1513 cm^{-1}.

Ethyl 3-((*tert*-Butoxycarbonyl)(cyclohexyl)amino)-2-((4-methoxyphenyl)amino) propanoate (4c)



Prepared by procedure A, DMF (0.5 mL) was used as a solvent. The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/5) to afford the title compound (orange liquid, 42 mg, 99%). ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 6.74 (d, J = 8.8 Hz, 2H), 6.55 (br, 2H), 4.22-4.10 (m, 3H), 3.80 (br, 1H), 3.73 (s, 3H), 3.51 (br, 1H), 3.37 (dd, J = 14.3, 5.8 Hz, 1H), 1.79-1.70 (m, 5H), 1.62 (d, J = 12.8 Hz, 2H), 1.49 (s, 9H), 1.27-1.22 (m, 5H), 1.11-1.03 (m, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 174.8, 158.0, 154.1, 142.7, 116.1, 115.8, 81.5, 62.2, 59.5, 58.3, 56.1, 47.7, 32.3, 28.8, 27.3, 26.6, 14.5; HRMS calculated for $C_{23}H_{36}O_5N_2Na$: *m/z* 443.2516 ([M + Na]$^+$), found: *m/z* 443.2530 ([M + Na]$^+$) ; IR (neat) 3364, 2931, 1733, 1688, 1513 cm^{-1}.

Ethyl 3-((*tert*-Butoxycarbonyl)(ethyl)amino)-2-((4-methoxyphenyl)amino) butanoate (4d)



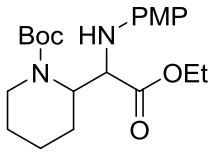
Prepared by procedure B, The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/6) to afford the title compound as a diastereomeric mixture (brown liquid, 34 mg, 89%).

Isomer a; ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 6.75 (d, J = 7.1 Hz, 2H), 6.60 (d, J = 9.1 Hz, 2H), 4.28 (d, J = 6.8 Hz, 1H), 4.18-4.08 (m, 2H), 4.02 (br, 1H), 3.73 (s, 3H), 3.16 (brs, 2H), 1.49 (s, 9H), 1.25-1.17 (m, 6H), 1.09 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.3, 155.6, 153.0, 141.4, 115.6, 115.0, 79.7, 61.8, 61.3, 55.9, 54.8, 40.3, 28.7, 16.4, 15.6, 14.3; HRMS calculated for $C_{20}H_{32}O_5N_2Na$: *m/z* 403.2203 ([M + Na]$^+$), found: *m/z* 403.2216 ([M + Na]$^+$); IR (neat) 3360, 2976, 1732, 1691, 1514, 1158, 821 cm^{-1}.

Isomer b; ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 6.73 (d, J = 9.1 Hz, 2H), 6.55 (d, J = 8.8 Hz, 2H), 4.50 (brs, 1H), 4.21-4.09 (m, 2H), 3.94 (d, J = 8.8 Hz, 1H), 3.72 (s, 3H), 3.14

(br, 2H), 1.49 (s, 9H), 1.27-1.21 (m, 6H), 1.09 (t, J = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$)δ 173.3, 157.0, 152.5, 141.4, 115.0, 114.5, 79.9, 62.7, 61.2, 55.9, 52.6, 38.2, 28.6, 16.1, 15.6, 14.3; HRMS calculated for $C_{20}H_{32}O_5N_2Na$: m/z 403.2203 ([M + Na]$^+$), found: m/z 403.2218 ([M + Na]$^+$); IR (neat) 3382, 2977, 1733, 1684, 1514, 1237, 820 cm^{-1}.

***tert*-Butyl 2-(2-Ethoxy-1-((4-methoxyphenyl)amino)-2-oxoethyl)piperidine-1-carboxylate (4e)**

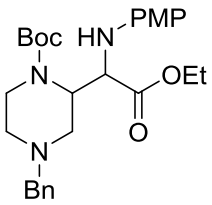


Prepared by procedure B, The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/3) to afford the title compound as a diastereomeric mixture (yellow liquid, 15 mg, 39%).

Isomer a; ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 6.74 (d, J = 9.1 Hz, 2H), 6.55 (d, J = 8.8 Hz, 2H), 4.61 (s, 1H), 4.30 (d, J = 10.5 Hz, 1H), 4.20-4.11 (m, 2H), 3.96 (s, 1H), 3.73 (s, 3H), 2.73-2.68 (m, 1H), 1.66 (s, 5H), 1.52 (s, 2H), 1.50 (s, 9H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 173.5, 156.7, 152.8, 141.6, 115.2, 114.6, 80.2, 61.1, 58.3, 56.0, 52.1, 39.9, 28.7, 26.1, 25.2, 19.6, 14.3; HRMS calculated for $C_{21}H_{32}O_5N_2Na$: *m/z* 415.2203 ([M + Na]$^+$), found: *m/z* 415.2219 ([M + Na]$^+$) ; IR (neat) 3390, 2936, 1733, 1680, 1515 cm^{-1}.

Isomer b; ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 6.76 (d, J = 8.8 Hz, 2H), 6.63 (d, J = 8.8 Hz, 2H), 4.37 (br, 1H), 4.30 (t, J = 9.8 Hz, 1H), 4.15-4.04 (m, 2H), 3.84 (d, J = 9.9 Hz, 1H), 3.74 (s, 3H), 3.01 (t, J = 13.3 Hz, 1H), 2.08 (d, J = 12.8 Hz, 1H), 1.64 (s, 2H), 1.58-1.52 (m, 3H), 1.46 (s, 9H), 1.19 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 173.1, 154.8, 153.5, 141.4, 116.1, 115.2, 79.9, 61.1, 58.2, 56.0, 53.8, 40.2, 28.6, 25.22, 25.16, 19.7, 14.2; HRMS calculated for $C_{21}H_{32}O_5N_2Na$: m/z 415.2203 ([M + Na]+), found: m/z 415.2216 ([M + Na]+) ; IR (neat) 3351, 2933, 1733, 1690, 1514 cm^{-1}.

***tert*-Butyl 4-Benzyl-2-(2-ethoxy-1-((4-methoxyphenyl)amino)-2-oxoethyl)piperazine -1-carboxylate (4f)**;



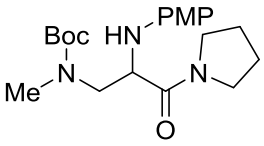
Prepared by procedure B, The crude product was purified by flash column chromatography on silica gel (eluting with ethyl

acetate/hexane = 1/5) to afford the title compound as a diastereomeric mixture (yellow liquid, 29 mg, 59%).

Isomer a; ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 7.25 (m, 3H), 7.18 (d, J = 7.7 Hz, 2H), 6.67 (d, J = 8.5 Hz, 2H), 6.53 (d, J = 8.5 Hz, 2H), 4.58 (brs, 1H), 4.43 (br, 1H), 3.99 (dt, J = 17.9, 7.2 Hz, 1H), 3.88 (dt, J = 17.6, 7.2 Hz, 1H), 3.68 (brs, 1H), 3.65 (s, 3H), 3.45 (d, J = 13.0 Hz, 1H), 3.38 (d, J = 13.0 Hz, 1H), 2.90 (brs, 1H), 2.74-2.69 (m, 2H), 2.13 (dd, J = 11.9, 3.4 Hz, 1H), 1.97 (t, J = 11.2 Hz, 1H), 1.40 (s, 9H), 1.02 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 173.4, 156.7, 152.5, 141.6, 137.9, 129.3, 128.4, 127.4, 115.2, 114.7, 80.4, 63.2, 60.9, 58.0, 56.0, 53.7, 52.8, 52.1, 40.8, 28.6, 14.3; HRMS calculated for $C_{27}H_{37}O_5N_3Na$: *m/z* 506.2625 ([M + Na]$^+$), found: *m/z* 506.2632 ([M + Na]$^+$); IR (neat) 3386, 1734, 1684, 1514, 1025 cm^{-1}.

Isomer b; ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 7.31 (m, 2H), 7.28-7.23 (m, 3H), 6.75 (d, J = 7.9 Hz, 2H), 6.65 (d, J = 8.5 Hz, 2H), 4.61 (brs, 1H), 4.40 (brs, 1H), 4.19 (brs, 1H), 4.09 (q, J = 6.5 Hz, 2H), 3.98 (brs, 1H), 3.74 (s, 3H), 3.59 (d, J = 13.2 Hz, 1H), 3.40 (d, J = 13.2 Hz, 1H), 3.33 (s, 1H), 3.23 (d, J = 11.6 Hz, 1H), 2.81 (d, J = 7.4 Hz, 1H), 2.17 (d, J = 11.6 Hz, 1H), 2.03 (t, J = 11.8 Hz, 1H), 1.45 (s, 9H), 1.20 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 173.1, 154.4, 153.2, 141.6, 138.0, 129.2, 128.5, 127.4, 115.7, 115.2, 80.2, 63.0, 61.2, 58.7, 56.0, 54.6, 53.5, 52.5, 41.3, 28.5, 14.2; HRMS calculated for $C_{27}H_{37}O_5N_3Na$: *m/z* 506.2625 ([M + Na]$^+$), found: *m/z* 506.2629 ([M + Na]$^+$); IR (neat) 3360, 2977, 1734, 1694, 1171 cm^{-1}.

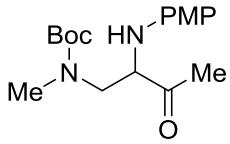
tert-Butyl (2-((4-Methoxyphenyl)amino)-3-oxo-3-(pyrrolidin-1-yl)propyl)(methyl) carbamate (4h)



Prepared by procedure A, DMF (0.5 mL) was used as a solvent. The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/3) to afford the title compound (brown liquid, 25 mg, 66%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.74 (d, J = 9.1 Hz, 2H), 6.62 (d, J = 8.8 Hz, 2H), 4.51 (brs, 1H), 4.37 (brs, 1H), 3.73 (s, 3H), 3.70 (s, 1H), 3.56-3.47 (m, 2H), 3.42 (brs, 2H), 2.87 (s, 3H), 1.93 (t, J = 6.2 Hz, 2H), 1.84 (s, 2H), 1.50 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 156.3, 152.8, 141.9, 115.3, 114.6, 79.8, 56.6, 56.0,

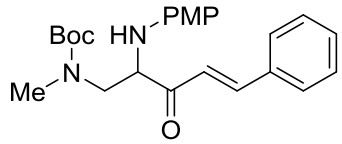
52.8, 46.7, 46.3, 37.3, 28.7, 26.3, 24.2; HRMS calculated for $C_{20}H_{31}O_4N_3Na$: *m/z* 400.2207 ([M + Na]$^+$), found: *m/z* 400.2219 ([M + Na]$^+$); IR (neat) 3331, 2973, 1636, 1626, 1511, 1149 cm^{-1}.

***tert*-Butyl (2-((4-Methoxyphenyl)amino)-3-oxobutyl)(methyl)carbamate (4i)**



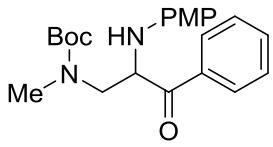
Prepared by procedure A, DMF (0.5 mL) was used as a solvent. The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/3) to afford the title compound (brown liquid, 16 mg, 51%). ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 6.76 (d, J = 8.8 Hz, 2H), 6.50 (d, J = 8.5 Hz, 2H), 4.07 (s, 1H), 3.76 (s, 1H), 3.74 (s, 3H), 3.37 (s, 1H), 2.87 (s, 3H), 2.22 (s, 3H), 1.49 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 211.0, 157.2, 152.8, 141.4, 115.4, 114.1, 80.5, 64.6, 56.0, 50.8, 35.7, 28.5, 27.0; HRMS calculated for $C_{17}H_{26}O_4N_2Na$: *m/z* 345.1785 ([M + Na]$^+$), found: *m/z* 345.1791 ([M + Na]$^+$); IR (neat) 3365, 2930, 1694, 1514, 1238, 1153, 820 cm^{-1}.

***tert*-Butyl (*E*)-(2-((4-Methoxyphenyl)amino)-3-oxo-5-phenylpent-4-en-1-yl)(methyl) carbamate (4j)**



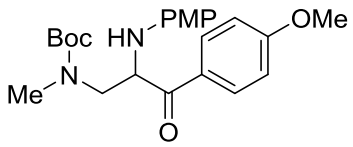
Prepared by procedure A, DMF (0.5 mL) was used as a solvent. The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/4) to afford the title compound (brown liquid, 19 mg, 47%). ^{1}H NMR (500 MHz, CD_3OD, 50 °C) δ 7.69 (d, J = 16.2 Hz, 1H), 7.61 (d, J = 4.0 Hz, 2H), 7.40-7.39 (m, 3H), 7.12 (d, J = 15.9 Hz, 1H), 6.74 (d, J = 8.5 Hz, 2H), 6.64 (d, J = 7.7 Hz, 2H), 4.59 (s, 1H), 3.73 (s, 1H), 3.69 (s, 3H), 3.52-3.56 (m, 1H), 2.90 (s, 3H), 1.41 (s, 9H); ^{13}C NMR (125 MHz, CD_3OD, 50 °C) δ 202.3, 157.3, 154.0, 145.0, 142.8, 136.0, 131.8, 130.0, 129.6, 124.4, 116.1, 115.8, 81.5, 62.6, 56.3, 52.1, 36.5, 28.7; HRMS calculated for $C_{17}H_{15}O_2NNa$: *m/z* 288.0995 ([M + Na]$^+$), found: *m/z* 288.0998 ([M + Na]$^+$); IR (neat) 1660, 1608, 1574, 1305, 1037 cm^{-1}.

***tert*-Butyl (2-((4-Methoxyphenyl)amino)-3-oxo-3-phenylpropyl)(methyl)carbamate (4k)**;



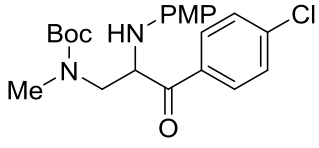
Prepared by procedure A, DMF (0.5 mL) was used as a solvent. The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/4) to afford the title compound (brown liquid, 35 mg, 92%). ^{1}H NMR (500 MHz, CD_3OD, 50 °C) δ 8.07 (dd, J = 13.7, 7.8 Hz, 2H), 7.62 (t, J = 6.9 Hz, 1H), 7.51 (t, J = 7.7 Hz, 2H), 6.73-6.69 (m, 4H), 5.43-5.31 (m, 1H), 3.68 (s, 3H), 3.65-3.42 (m, 2H), 2.81 (s, 3H), 1.38 (m, 9H); ^{13}C NMR (125 MHz, CD_3OD, 50 °C) δ 202.0, 157.6, 154.1, 142.6, 137.4, 134.8, 129.9, 129.5, 116.3, 116.1, 81.2, 59.2, 56.3, 53.5, 37.1, 28.7; HRMS calculated for $C_{22}H_{28}O_4N_2Na$: *m/z* 407.1941 ([M + Na]$^+$), found: *m/z* 407.1952 ([M + Na]$^+$); IR (neat) 3360, 2975, 1680, 1152, 1238 cm^{-1}.

***tert*-Butyl (3-(4-Methoxyphenyl)-2-((4-methoxyphenyl)amino)-3-oxopropyl) (methyl)carbamate (4l)**



Prepared by procedure A, DMF (0.5 mL) was used as a solvent. The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/3) to afford the title compound (orange liquid, 31 mg, 75%). ^{1}H NMR (500 MHz, CD_3OD, 50 °C) δ 8.06 (m, 2H), 7.02 (d, J = 8.8 Hz, 2H), 6.70 (m, 4H), 5.38-5.24 (m, 1H), 3.87 (s, 3H), 3.68 (s, 3H), 3.67-3.38 (m, 2H), 2.81 (s, 3H), 1.40 (app d, 9H); ^{13}C NMR (125 MHz, CD_3OD, 50 °C) δ 200.5, 165.9, 157.7, 154.2, 142.6, 132.0, 130.3, 116.3, 116.1, 115.2, 81.2, 58.7, 56.3, 56.2, 53.7, 37.1, 28.7; HRMS calculated for $C_{23}H_{30}O_5N_2Na$: *m/z* 437.2047 ([M + Na]$^+$), found: *m/z* 437.2058 ([M + Na]$^+$); IR ($CDCl_3$) 2975, 1673, 1239, 1171, 729 cm^{-1}.

***tert*-Butyl (3-(4-Chlorophenyl)-2-((4-methoxyphenyl)amino)-3-oxopropyl)(methyl) carbamate (4m)**



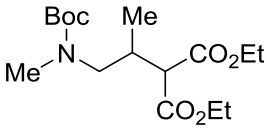
Prepared by procedure A, DMF (0.5 mL) was used as a solvent. The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/5) to afford the title compound (brown liquid, 36 mg, 86%). ^{1}H NMR (500 MHz, CD_3OD, 50 °C) δ 8.03 (d, J = 7.4 Hz, 2H), 7.50 (d, J = 7.9 Hz, 2H), 6.73 (d, J = 9.1 Hz, 2H), 6.69 (d, J = 8.8 Hz, 2H),

5.31 (br, 1H), 3.68 (s, 3H), 3.65 (m, 1H), 3.52 (m, 1H), 2.83 (s, 3H), 1.39 (s, 9H); ^{13}C NMR (125 MHz, CD_3OD, 50 °C) δ 200.8, 157.6, 154.1, 142.6, 141.1, 135.9, 131.2, 130.1, 116.2, 116.1, 81.2, 59.1, 56.3, 53.3, 37.1, 28.7; HRMS calculated for $C_{22}H_{27}O_4N_2ClNa$: *m/z* 441.1552 ([M + Na]$^+$), found: *m/z* 441.1559 ([M + Na]$^+$); IR ($CDCl_3$) 3361, 2930, 1683, 1513, 1240 cm^{-1}.

General Procedure for Radical 1,4-Addition of 1a to Electron-deficient Olefins 6 (Scheme 6)

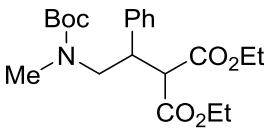
A test tube with a magnetic stir bar was charged with olefin **6** (0.1 mmol), **1a** (0.14 g, 0.6 mmol), 1,4-cyclohxadiene (9.4 μL, 0.1 mmol), DIB (96 mg, 0.3 mmol) and NMP (1 mL) under argon atmosphere. The mixture was stirred at room temperature for 4 h. The reaction was quenched with H_2O and extracted with ethyl acetate three times. The combined organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel to provide the following product.

Diethyl 2-(1-((*tert*-Butoxycarbonyl)(methyl)amino)propan-2-yl)malonate (7a)



The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/6) to afford the title compound (colorless liquid, 24 mg, 71%). ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 4.24-4.15 (m, 4H), 3.34 (brs, 1H), 3.26 (d, J = 7.5 Hz, 1H), 3.13 (s, 1H), 2.85 (s, 3H), 2.59-2.50 (m, 1H), 1.45 (s, 9H), 1.31-1.25 (m, 6H), 0.98 (d, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 168.5, 155.8, 79.5, 61.2, 55.0, 52.7, 34.6, 32.4, 28.4, 14.9, 14.1; HRMS calculated for $C_{16}H_{29}O_6NNa$: *m/z* 354.1887 ([M + Na]$^+$), found: *m/z* 354.1902 ([M + Na]$^+$); IR (neat) 2977, 1731, 1693, 1366, 1149, 1029 cm^{-1}.

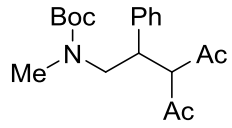
Diethyl 2-(2-((*tert*-Butoxycarbonyl)(methyl)amino)-1-phenylethyl)malonate (7b)



The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/5) to afford the title compound (colorless liquid, 29 mg, 74%). ^{1}H NMR (500 MHz, CD_3OD) δ 7.31-7.24 (m, 5H), 4.23 (m, 2H), 3.87-3.81 (m, 3H), 3.76-3.67 (m, 1H), 3.60-3.45(m, 2H), 2.64 (s, 3H), 1.33 (s, 9H), 1.28 (t, J = 7.1 Hz, 3H), 0.91 (t, J = 7.1 Hz,

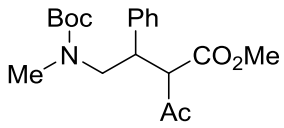
3H); ^{13}C NMR (125 MHz, CD_3OD) δ 169.5, 169.2, 157.2, 140.3, 130.1, 129.4, 128.4, 81.2, 62.9, 62.4, 56.7, 54.0, 45.5, 34.9, 28.5, 14.4, 14.0; HRMS calculated for $C_{21}H_{31}O_6NNa$: *m/z* 416.2045 ([M + Na]$^+$), found: *m/z* 416.2044 ([M + Na]$^+$); IR (neat) 2978, 1753, 1733, 1697, 1173, 1142 cm^{-1}.

***tert*-Butyl (3-Acetyl-4-oxo-2-phenylpentyl)(methyl)carbamate (7c)**



The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/3) to afford the title compound (colorless liquid, 30 mg, 91%). ^{1}H NMR (500 MHz, CD_3OD, 50 °C) δ 7.32-7.21 (m, 5H), 4.41 (d, J = 11.3 Hz, 1H), 3.83 (s, 1H), 3.42 (brs, 2H), 2.58 (s, 3H), 2.27 (s, 3H), 1.85 (s, 3H), 1.35 (s, 9H); ^{13}C NMR (125 MHz, CD_3OD, 50 °C) δ 204.4, 203.8, 157.4, 140.5, 130.0, 129.7, 128.4, 81.1, 73.3, 54.1, 45.6, 35.1, 30.4, 29.8, 28.6; HRMS calculated for $C_{19}H_{27}O_4NNa$: *m/z* 356.1832 ([M + Na]$^+$), found: *m/z* 356.1841 ([M + Na]$^+$); IR (neat) 2976, 1696, 1364 1155 cm^{-1}.

Methyl 2-Acetyl-4-((*tert*-butoxycarbonyl)(methyl)amino)-3-phenylbutanoate (7d)



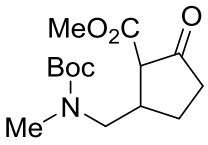
The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/4) to afford the title compound as a diastereomeric mixture (colorless liquid, 30 mg, 85%).

Isomer a; ^{1}H NMR (500 MHz, CD_3OD, 50 °C) δ 7.29-7.23 (m, 5H), 4.11 (d, J = 11.1 Hz, 1H), 3.76 (s, 1H), 3.51 (m, 2H), 3.38 (s, 3H), 2.59 (s, 3H), 2.28 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (125 MHz, CD_3OD, 50 °C) δ 202.9, 169.8, 157.4, 140.7, 129.9, 129.4, 128.3, 81.2, 64.6, 53.7, 52.7, 45.0, 35.0, 29.8, 28.6; HRMS calculated for $C_{19}H_{27}O_5NNa$: *m/z* 372.1781 ([M + Na]$^+$), found: *m/z* 371.1796 ([M + Na]$^+$); IR (neat) 2975, 1744, 1717, 1690, 1141, 879 cm^{-1}.

Isomer b; (orange liquid) ^{1}H NMR (500 MHz, CD_3OD) δ 7.32-7.24 (m, 5H), 4.15 (d, J = 11.1 Hz, 1H), 3.76 (s, 3H), 3.72 (s, 1H), 3.54-3.45 (m, 2H), 2.63 (s, 3H), 1.95 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (125 MHz, CD_3OD, 50 °C) δ 203.6, 170.2, 157.4, 140.3, 129.9, 129.7, 128.4, 81.2, 64.0, 53.1, 52.7, 45.5, 35.1, 30.0, 28.6; HRMS calculated for

$C_{19}H_{27}O_5NNa$: *m/z* 372.1781 ($[M + Na]^+$), found: *m/z* 372.1811 ($[M + Na]^+$); IR (neat) 2975, 1746, 1694, 1165, 1142, 702 cm^{-1}.

Methyl 2-(((*tert*-Butoxycarbonyl)(methyl)amino)methyl)-5-oxocyclopentane-1-carboxylate (7e)



The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/3) to afford the title compound as a diastereomeric mixture (colorless liquid, 20 mg, 70%); ^1H NMR (500 MHz, $CDCl_3$) δ 4.74 (s, 0.72H), 4.16 (d, J = 0.9 Hz, 0.29H), 3.85 (s, 0.87H), 3.74 (s, 2.21H), 3.47-3.44 (m, 1H), 3.27-3.21 (m, 1H), 2.95 (brs, 2H), 2.84 (s, 3H), 2.49-2.25 (m, 2H), 2.18-2.11 (m, 1H), 1.44 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 210.4, 169.4, 155.5, 80.0, 74.1, 59.7, 52.5, 40.4, 38.3, 34.9, 28.6, 25.2; HRMS calculated for $C_{14}H_{22}NO_5$: *m/z* 284.1385 ($[M - H]^-$), found: *m/z* 284.1503 ($[M - H]^-$); IR (neat) 2975, 1757, 1728, 1690, 1394, 1156, 732, 916 cm^{-1}.

General Procedure for Radical Addition/cyclization of 1a or 1e and 2-Isocyanobiphenyls (Scheme 7)

Procedure A

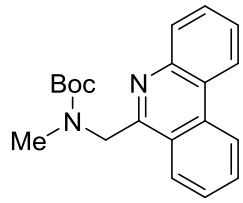
A test tube with a magnetic stir bar was charged with 2-isocyanobiphenyl (0.1 mmol), **1** (0.9 mmol), AcONa (24 mg, 0.3 mmol), 1,4-benzoquinone (2 mg, 0.02 mmol), DIB (97 mg, 0.3 mmol) and NMP (0.2 mL) under argon atmosphere. The mixture was stirred at room temperature for 4 h. The reaction was quenched with H_2O and extracted with ethyl acetate three times. The combined organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel to provide the following compound.

Procedure B

A test tube with a magnetic stir bar was charged with 2-isocyanobiphenyl (0.1 mmol), **1** (0.9 mmol), DIB (97 mg, 0.3 mmol) and NMP (0.2 mL) under argon atmosphere. The mixture was stirred at room temperature for 4 h. The reaction was quenched with H_2O and extracted with ethyl acetate three times. The combined organic layer was dried over

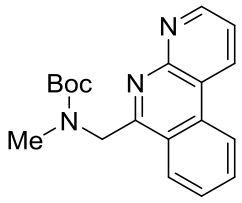
Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel to provide the following compound.

***tert*-Butyl Methyl(phenanthridin-6-ylmethyl)carbamate (8a)**



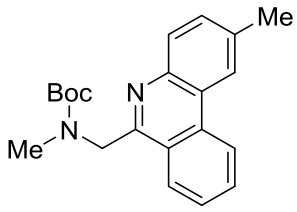
Prepared by procedure A, The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/6) to afford the title compound (white solid, 16 mg, 50%). ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 8.66 (d, J = 8.2 Hz, 1H), 8.56 (d, J = 7.9 Hz, 1H), 8.48 (br, 1H), 8.15 (d, J = 8.2 Hz, 1H), 7.85 (t, J = 7.4 Hz, 1H), 7.64-7.74 (m, 3H), 5.14 (s, 2H), 2.86 (s, 3H), 1.51 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 156.2, 143.8, 133.3, 130.7, 130.4, 128.7, 127.6, 127.1 (Two peaks were overlapped.), 125.1, 124.3, 122.6, 122.1 (Two peaks were overlapped.), 80.0, 53.3, 34.1, 28.7; HRMS calculated for $C_{20}H_{22}O_2N_2Na$: *m/z* 345.1573 ([M + Na]$^+$), found: *m/z* 345.1585 ([M + Na]$^+$); IR (neat) 2977, 1691, 1160, 1144, 765 cm^{-1}.

***tert*-Butyl (Benzo[c][1,8]naphthyridin-6-ylmethyl)(methyl)carbamate (8b)**



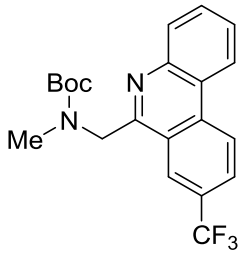
Prepared by procedure B, The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate) to afford the title compound (yellow solid, 26 mg, 79%). ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 9.08 (d, J = 4.3 Hz, 1H), 8.91 (dd, J = 8.1, 1.8 Hz, 1H), 8.63 (m, 2H), 7.90 (t, J = 7.7 Hz, 1H), 7.75 (t, J = 7.7 Hz, 1H), 7.61 (m, 1H), 5.23 (s, 2H), 2.91 (s, 3H), 1.53 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 161.7, 156.0, 153.2, 151.5, 133.5, 131.43, 131.38, 128.5, 127.1, 125.3, 122.6, 122.4, 119.2, 80.2, 53.1, 34.1, 28.7; HRMS calculated for $C_{19}H_{21}O_2N_3Na$: *m/z* 346.1526 ([M + Na]$^+$), found: *m/z* 346.1533 ([M + Na]$^+$); IR (neat) 2975, 1687, 1391, 1144 cm^{-1}.

***tert*-Butyl Methyl((2-methylphenanthridin-6-yl)methyl)carbamate (8c)**



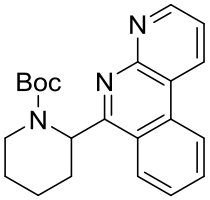
Prepared by procedure A, The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/6) to afford the title compound (orange liquid, 15 mg, 46%). ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 8.63 (d, J = 7.9 Hz, 1H), 8.46 (br, 1H), 8.34 (s, 1H), 8.04 (d, J = 8.5 Hz, 1H), 7.82 (t, J = 7.7 Hz, 1H), 7.66 (t, J = 7.5 Hz, 1H), 7.54 (d, J = 8.2 Hz, 1H), 5.11 (s, 2H), 2.85 (s, 3H), 2.63 (s, 3H), 1.51 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 156.1, 142.1, 137.0, 133.1, 130.4 (Two peaks were overlapped.), 130.1, 127.4, 126.7, 125.2, 124.1, 122.5, 121.8 (Two peaks were overlapped.), 79.9, 53.2, 34.3, 28.7, 22.1; HRMS calculated for $C_{21}H_{25}O_2N_2$: *m/z* 337.1911 ($[M + H]^+$), found: *m/z* 337.1920 ($[M + H]^+$); IR (neat) 2974, 1693, 1391, 1170, 1146, 825 cm^{-1}.

***tert*-Butyl Methyl((8-(trifluoromethyl)phenanthridin-6-yl)methyl)carbamate (8d)**



Procedure A, The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/8) to afford the title compound (white solid, 21 mg, 53%). ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ8.90 (brs, 1H), 8.76 (d, J = 8.2 Hz, 1H), 8.58 (d, J = 8.2 Hz, 1H), 8.20 (d, J = 8.2 Hz, 1H), 8.04 (d, J = 8.5 Hz, 1H), 7.80 (app t, J = 7.5 Hz, 1H), 7.72 (app t, J = 7.7 Hz, 1H), 5.17 (s, 2H), 2.86 (s, 3H), 1.51 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 156.0, 144.4, 135.5, 130.7, 130.0, 129.7 (d, J = 32.4 Hz), 127.7 (Two peaks were overlapped.), 126.6, 124.5, 124.1 (q, J = 274.1 Hz) 123.6, 123.5, 122.5 (Two peaks were overlapped.), 80.4, 53.3, 34.0, 28.6; HRMS calculated for $C_{21}H_{21}O_2N_2F_3Na$: *m/z* 413.1447 ($[M + Na]^+$), found: *m/z* 413.1456 ($[M + Na]^+$); IR (neat) 2974, 1691, 1171, 1145, 757 cm^{-1}.

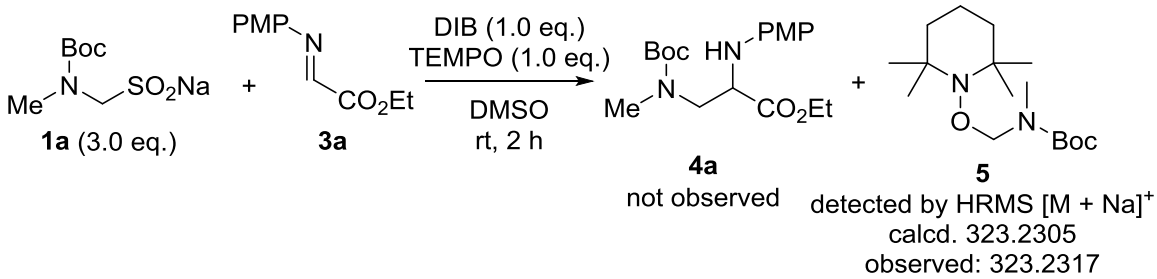
***tert*-Butyl 2-(Benzo[c][1,8]naphthyridin-6-yl)piperidine-1-carboxylate (8e)**



Procedure B, The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/3) to afford the title compound (white solid, 11 mg, 29%). ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 9.08 (app q, J = 2.0 Hz, 1H), 8.90 (dd, J = 8.1,

1.8 Hz, 1H), 8.62 (d, J = 8.2 Hz, 1H), 8.51 (d, J = 7.9 Hz, 1H), 7.88-7.85 (m, 1H), 7.73 (app t, J = 7.8 Hz, 1H), 7.58 (q, J = 4.2 Hz, 1H), 6.26 (s, 1H), 4.00 (d, J = 13.3 Hz, 1H), 3.63 (t, J = 13.0 Hz, 1H), 2.44 (d, J = 11.9 Hz, 1H), 2.21-2.11 (m, 2H), 1.79-1.61 (m, 3H), 1.40 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 165.8, 156.0, 152.9, 151.5, 133.5, 131.4, 130.9, 128.2, 126.5, 124.9, 122.7, 122.1, 118.7, 79.8, 42.7, 29.9, 28.6, 28.5, 25.6, 20.2; HRMS calculated for $C_{22}H_{25}O_2N_3Na$: *m/z* 386.1851 ($[M + Na]^+$), found: *m/z* 386.1839 ($[M + Na]^+$); IR (neat) 2929, 1683, 1365, 1272, 1161, 1047 cm^{-1}.

Radical Trap Experiment (Scheme 3c)



A test tube with a magnetic stir bar was charged with imine **3a** (0.1 mmol), sodium α-aminoalkanesulfinate **1a** (69 mg, 0.3 mmol), DIB (32 mg, 0.1 mmol), TEMPO (16 mg, 0.1 mmol) and DMSO (0.5 mL) under argon atmosphere. The mixture was stirred at room temperature for 2 h. The reaction was quenched with H_2O and extracted with ethyl acetate three times. The combined organic layer was dried over Na_2SO_4 and concentrated. The formation of **5** was detected by high resolution mass spectrometry.

General Procedure for 1,2-Addition of Sodium *α*-Aminoalkanesulfinate 1a to Imine 3a on Large Scale.

A test tube with a magnetic stir bar was charged with imine **3a** (207.2 mg, 1 mmol), sodium α-aminoalkanesulfinate **1a** (693.6 mg, 3 mmol), DIB (322.1 mg, 1 mmol) and DMSO (5 mL) under argon atmosphere. The mixture was stirred at room temperature for 2 h. The reaction was quenched with H_2O and extracted with ethyl acetate three times. The combined organic layer was dried over Na_2SO_4 and concentrated. The crude product was purified by flash column chromatography on silica gel (eluting with ethyl acetate/hexane = 1/3) to afford **4a** (brown liquid, 351 mg, 99% yield).

References

[1] Künzi, S. A.; Morandi, B.; Carreira, E. M. *Org*. *Lett*. **2012**, *14*, 1900.

[2] W. ZhiXin, and X. JiaXi *Sci*. *China*. *Chem*. **2011**, *54*, 1711.

[3] For 2-isocyanobiphenyls synthesis,

(a) Wang, Q.; Dong, X.; Xiao, T.; Zhou, L. *Org. Lett.* **2013**, *15*, 6286.

(b) Rong, J.; Deng, L.; Tan, P.; Ni, C.; Gu, Y.; Hu, J. *Angew. Chem., Int. Ed.* **2016**, *55*, 2743.

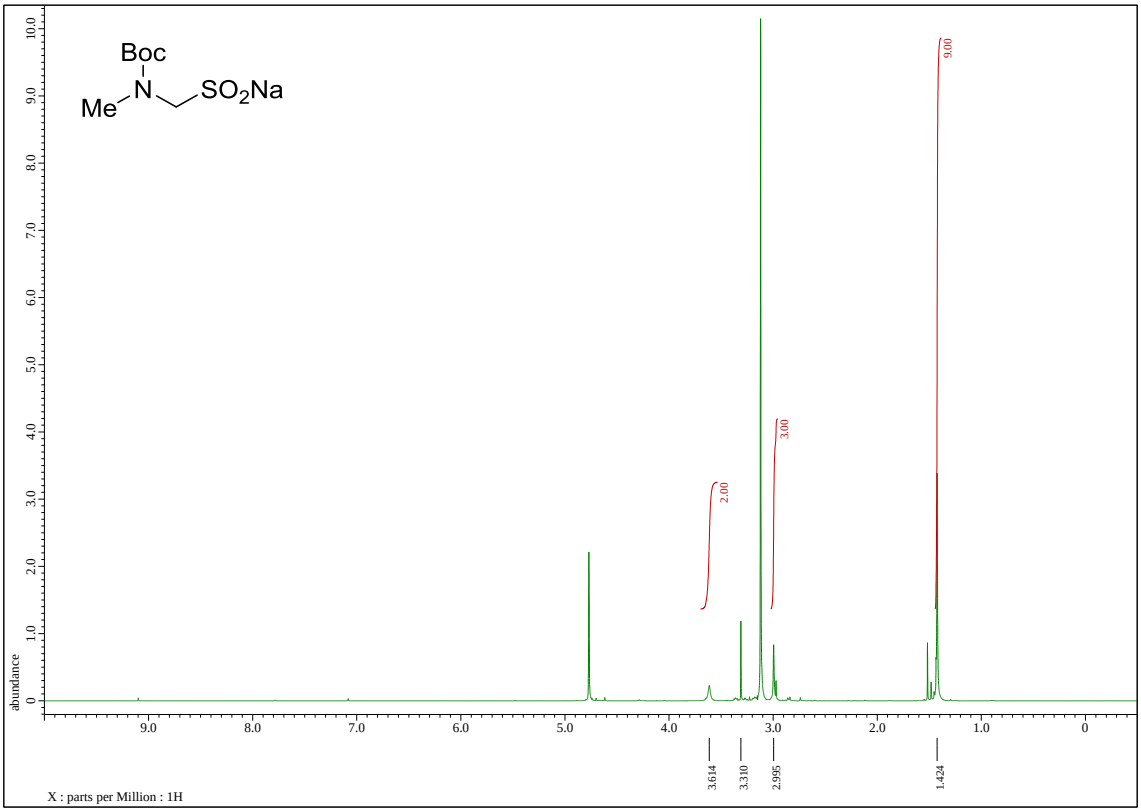
[4] For electron-deficient olefins synthesis,

(a) Clarke, P. A.; Martin, W. H. C.; Hargreaves, J. M.; Wilson C.; Blake, A. J. *Org. Biomol*. *Chem*. **2005**, *3*, 3551.

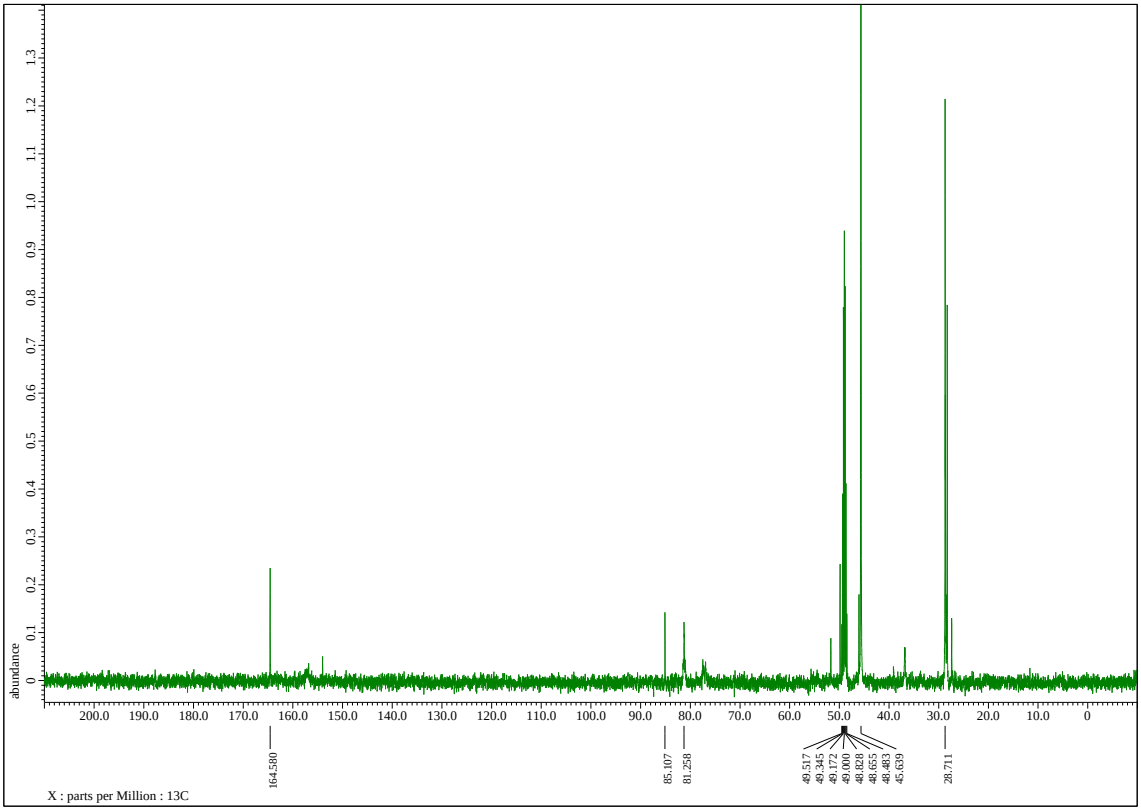
(b) Ohfusa, T.; Nishida, A. *Tetrahedron* **2011**, *67*, 1893

[5] Martial, L.; Bischoff, L. *Organic Synthesis*, **2013**, *90*, 301

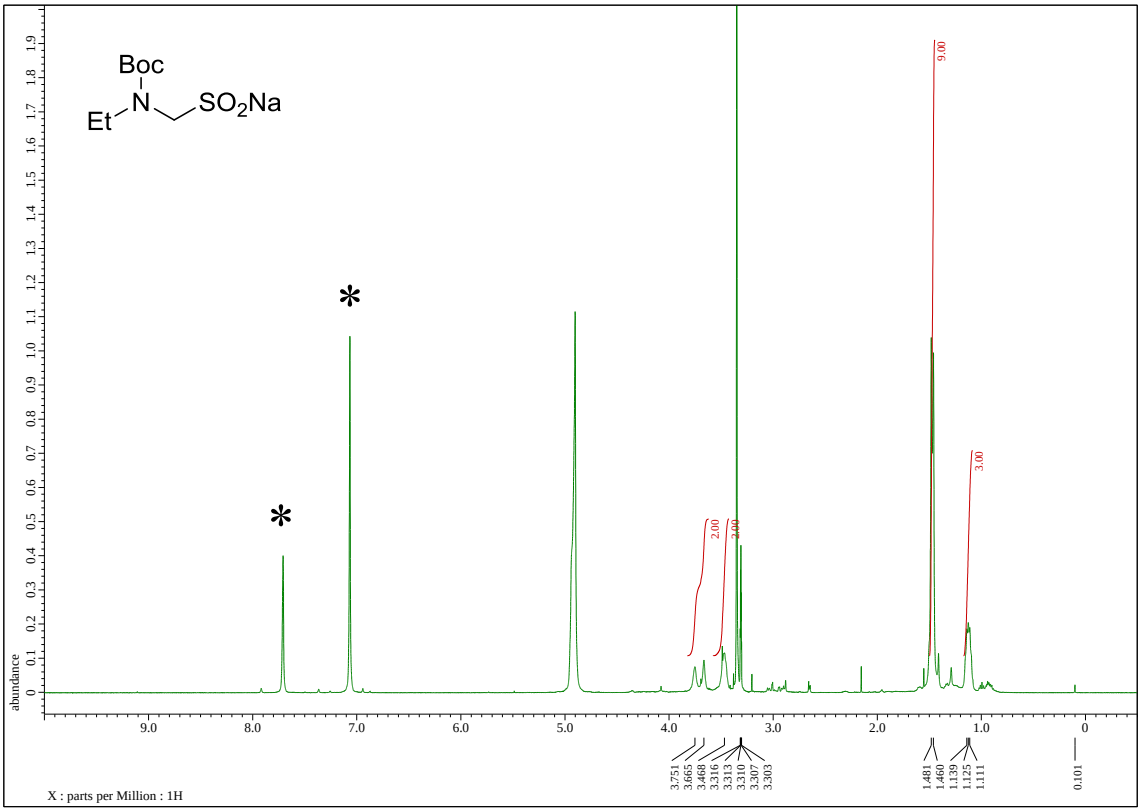
^{1}H NMR spectrum of **1a** (500 MHz, CD_3OD, 50 °C)



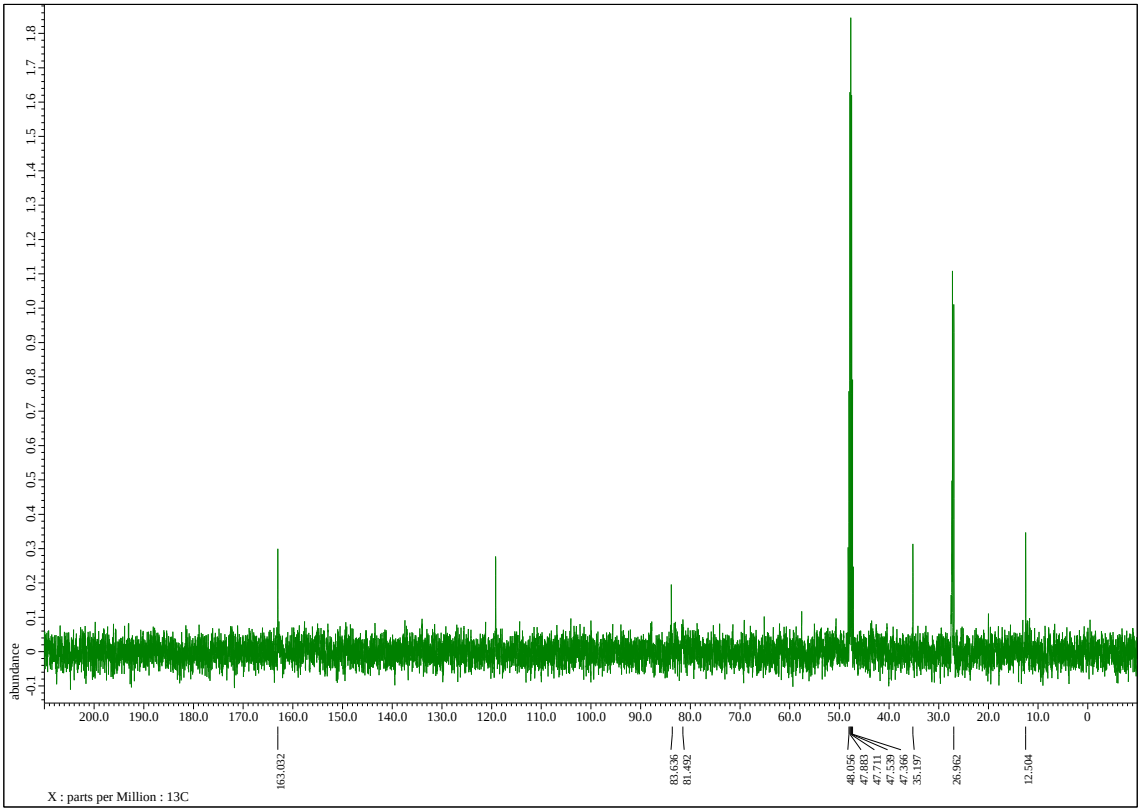
^{13}C NMR spectrum of **1a** (125 MHz, CD_3OD, 50 °C)



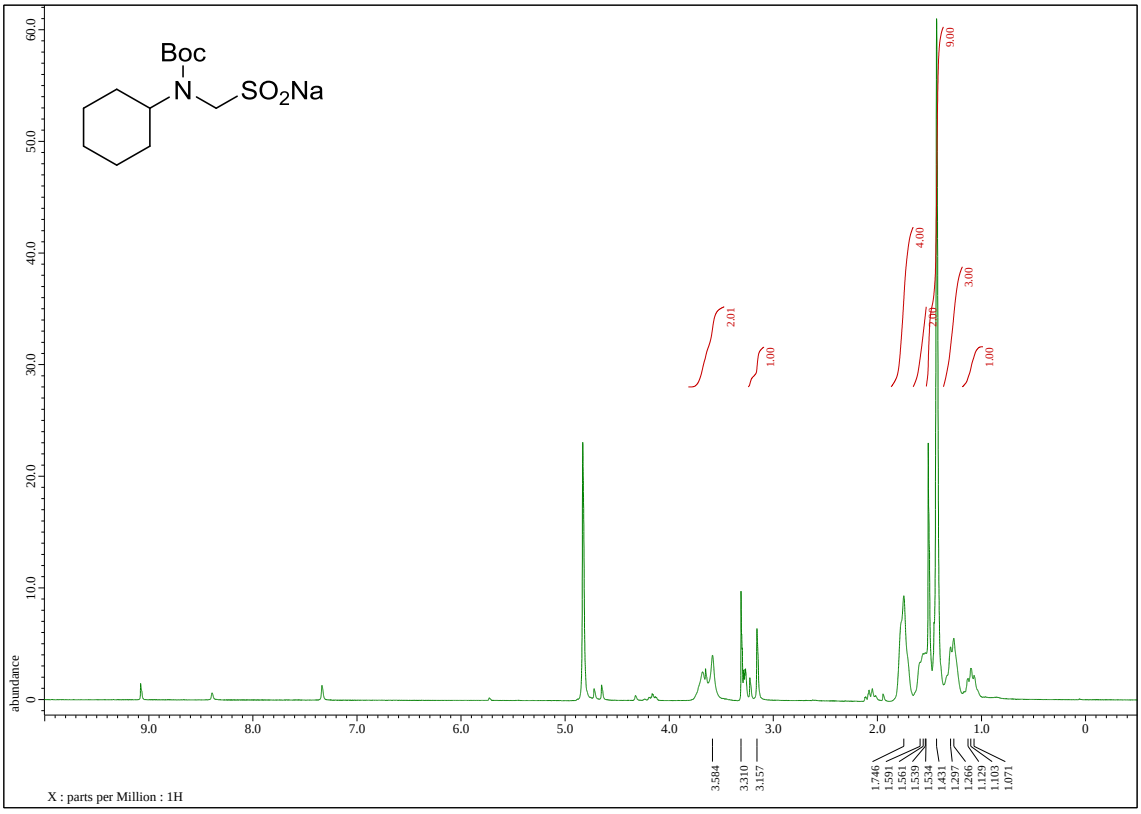
^{1}H NMR spectrum of **1b** (500 MHz, CD_3OD)



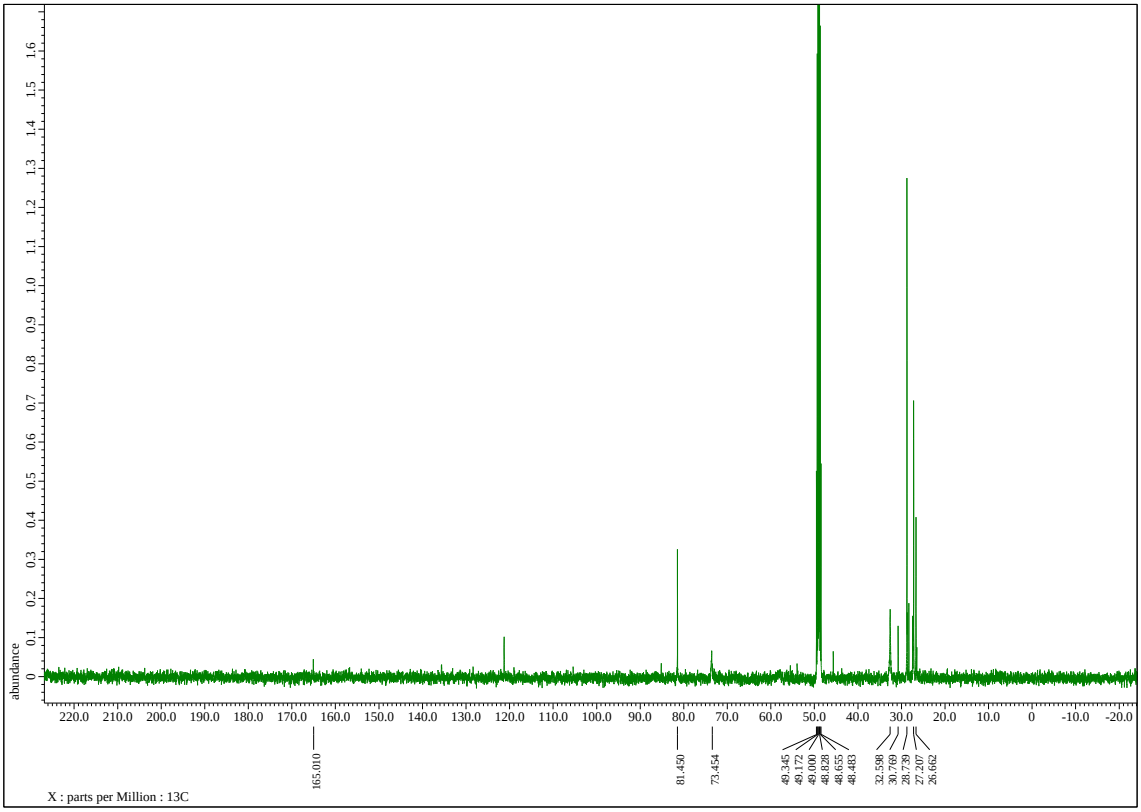
^{13}C NMR spectrum of **1b** (125 MHz, CD_3OD, 50 °C)



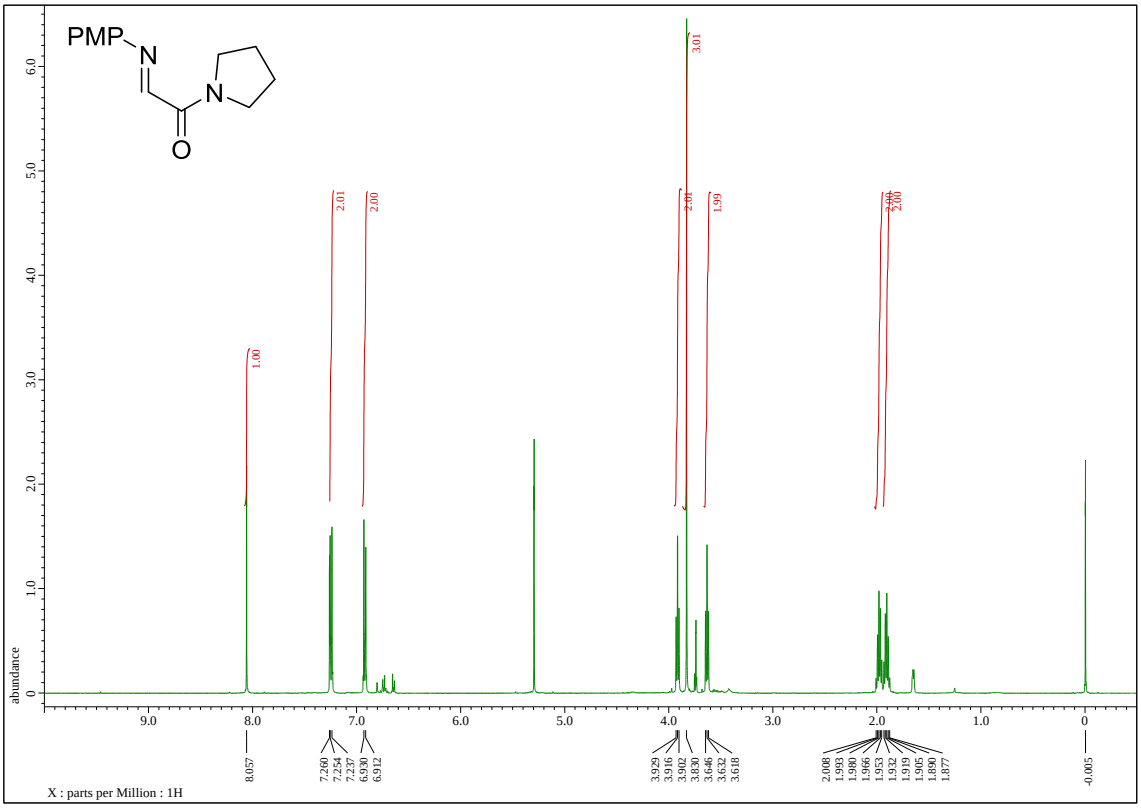
^{1}H NMR spectrum of **1c** (500 MHz, CD_3OD, 50 °C)



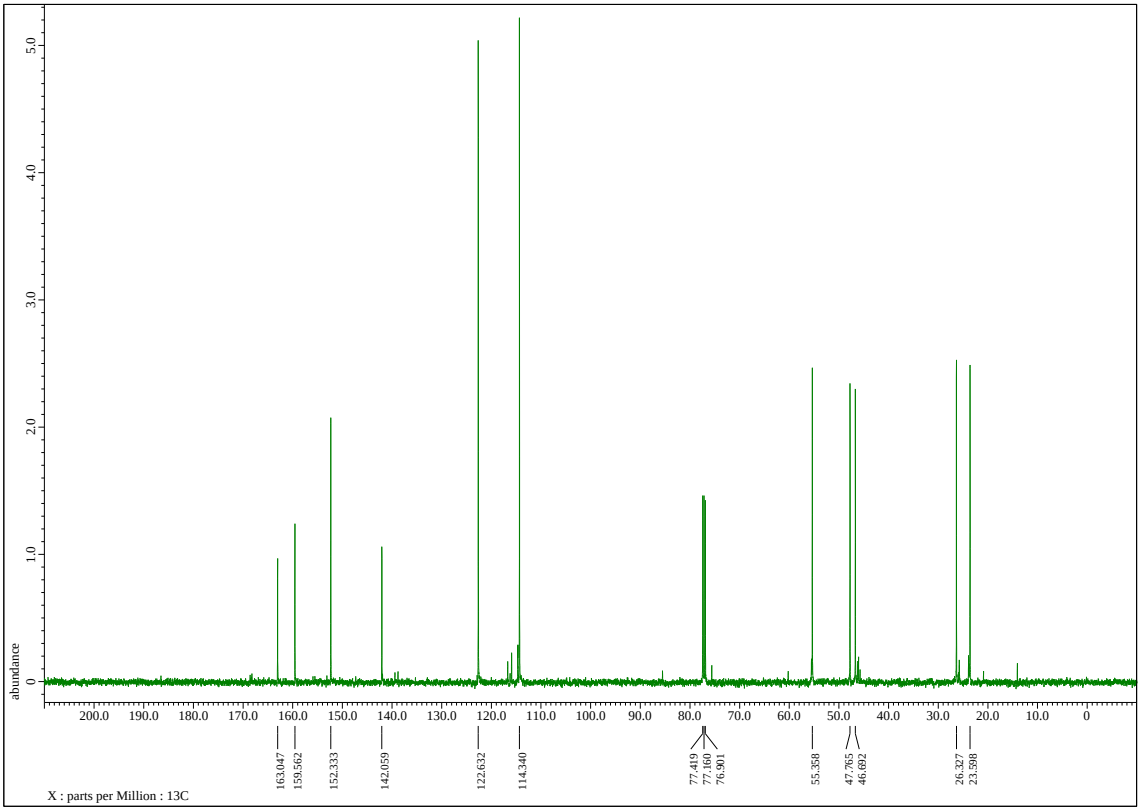
^{13}C NMR spectrum of **1c** (125 MHz, CD_3OD, 50 °C)



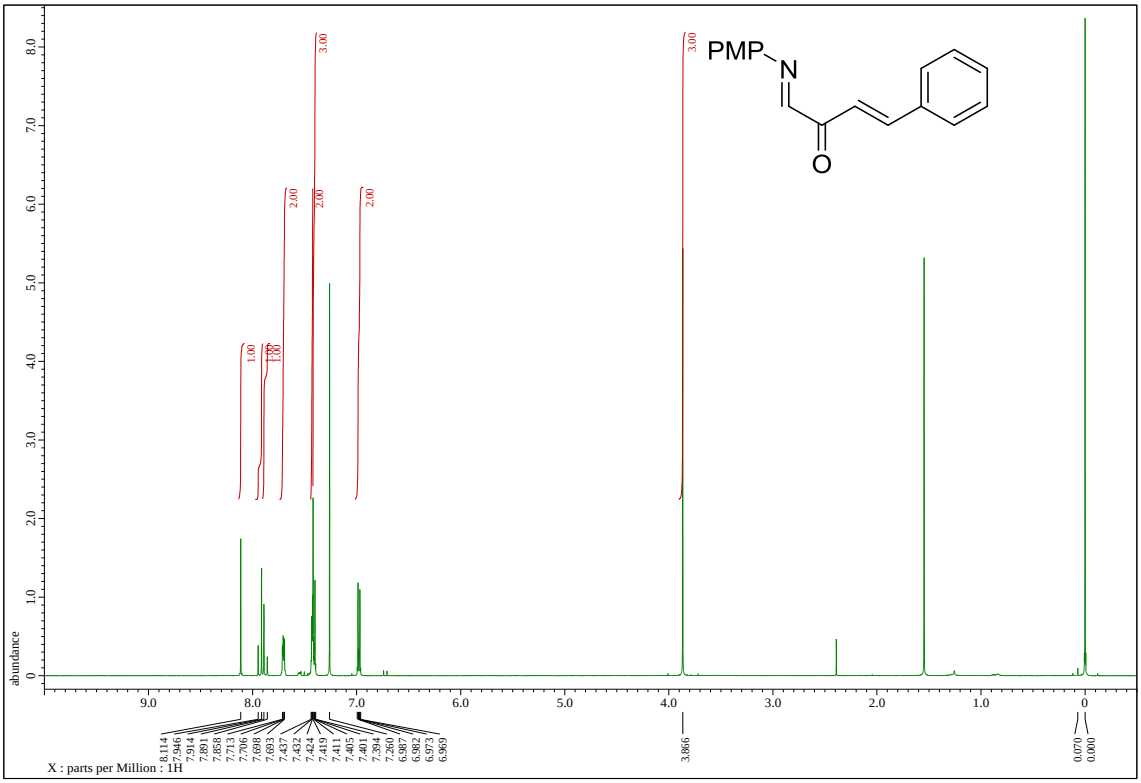
^{1}H NMR of spectrum of **3b** (500 MHz, $CDCl_3$)



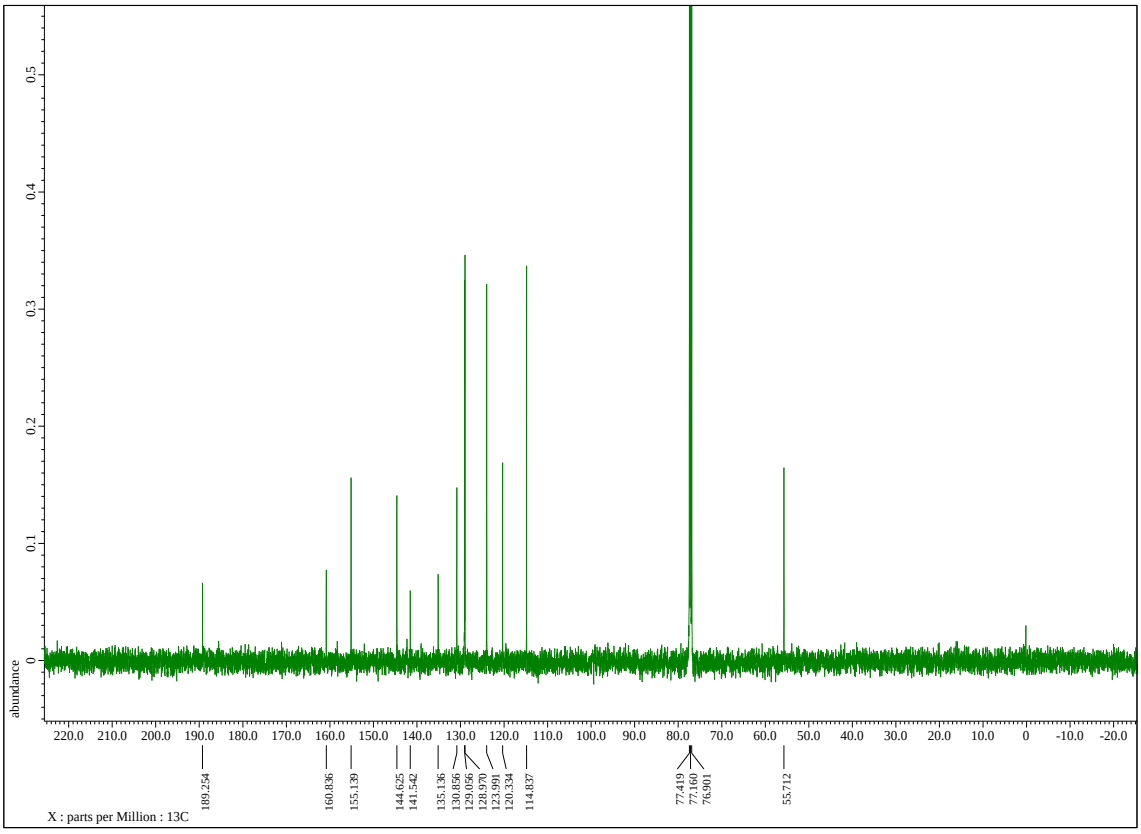
^{13}C NMR of spectrum of **3b** (125 MHz, $CDCl_3$)



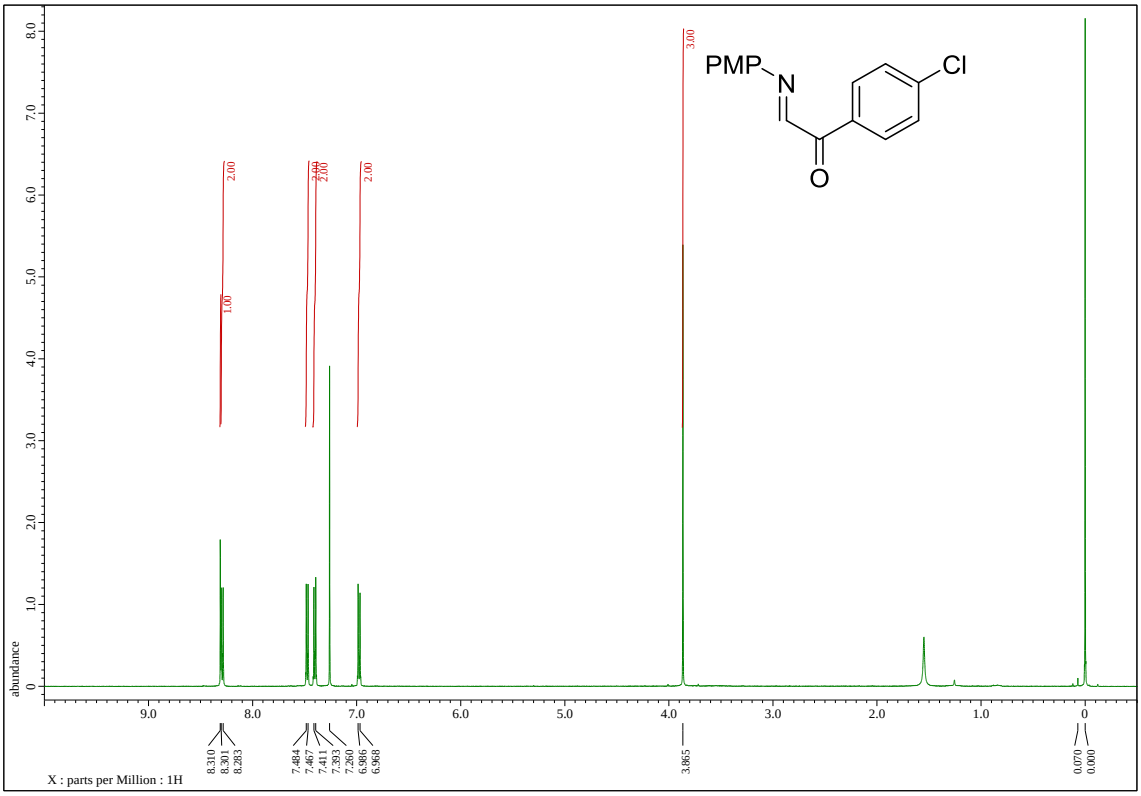
^{1}H NMR of spectrum of **3d** (500 MHz, $CDCl_3$)



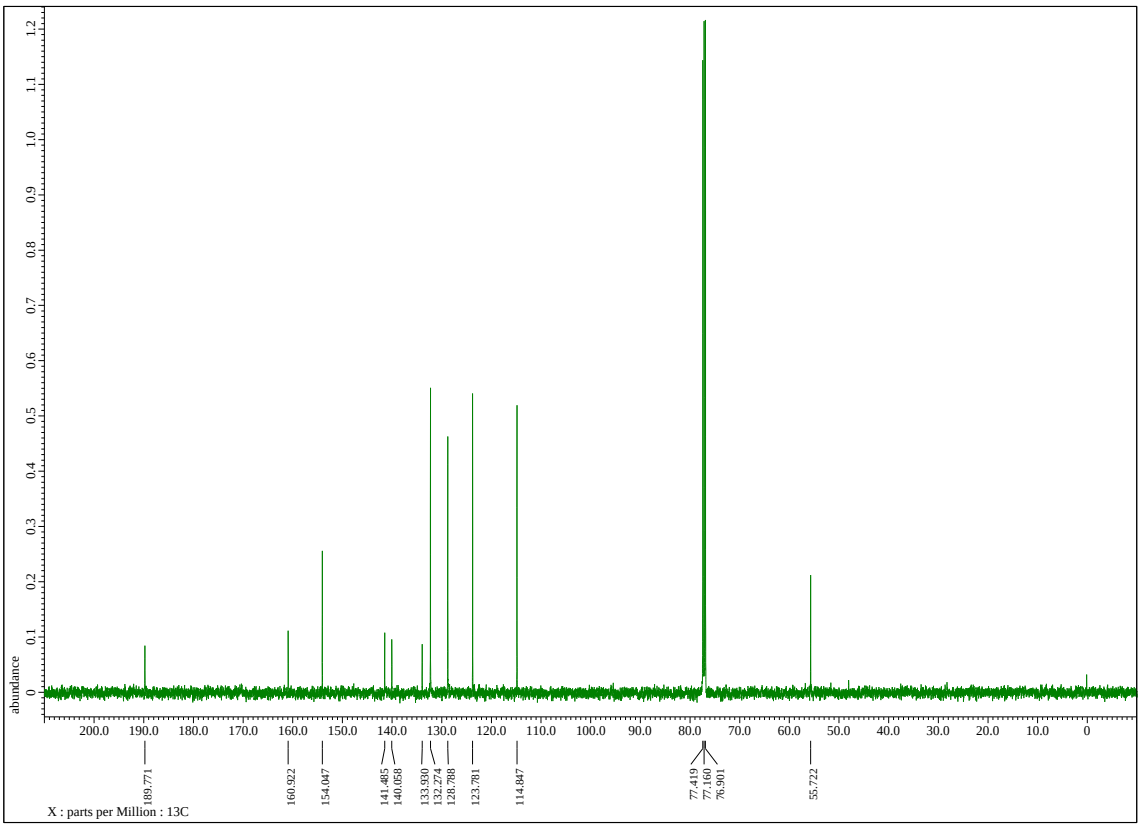
^{13}C NMR of spectrum of **3d**(125 MHz, $CDCl_3$)



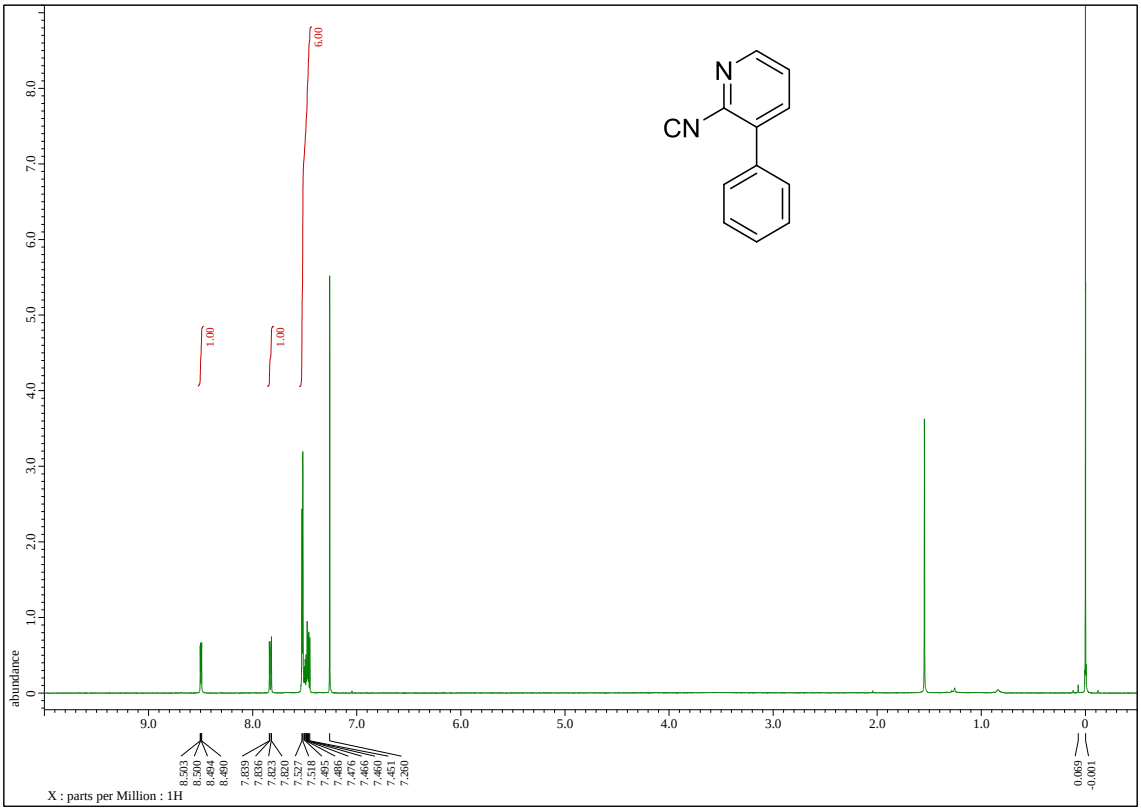
^{1}H NMR of spectrum of **3g** (500 MHz, $CDCl_3$)



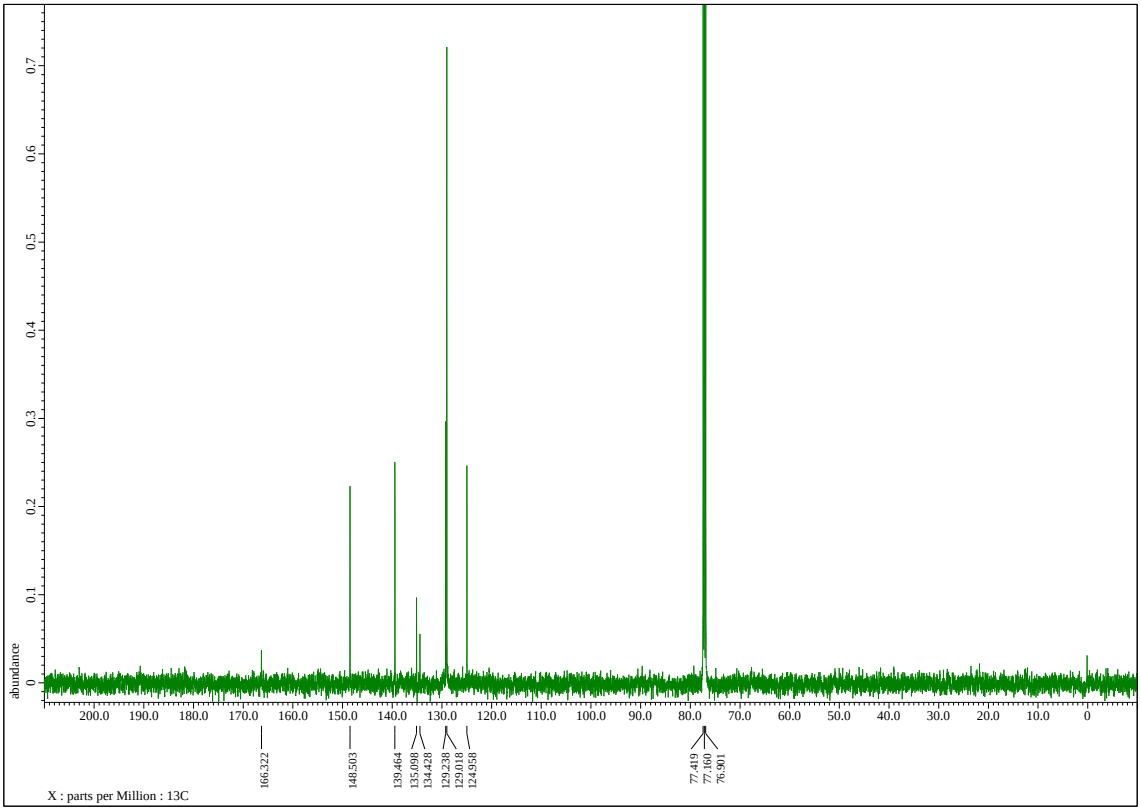
^{13}C NMR of spectrum of **3g** (125 MHz, $CDCl_3$)



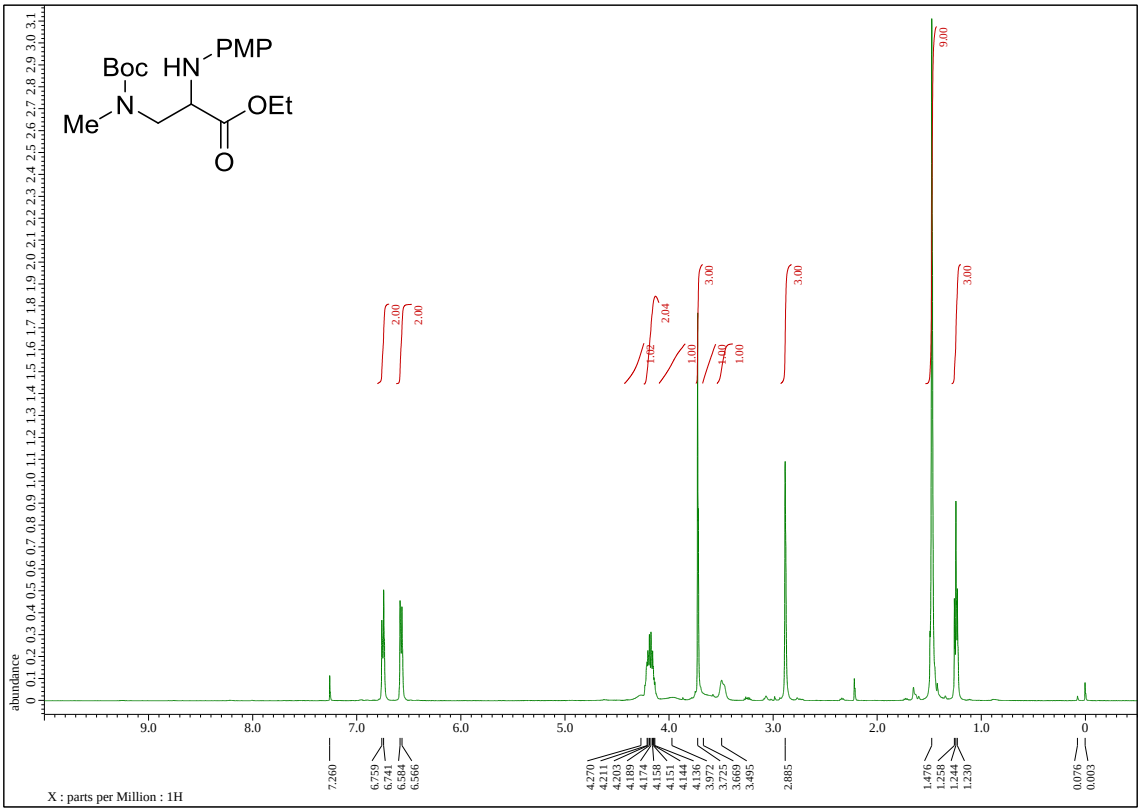
^{1}H NMR of spectrum of **2-Isocyano-3-phenylpyridine** (500 MHz, $CDCl_3$)



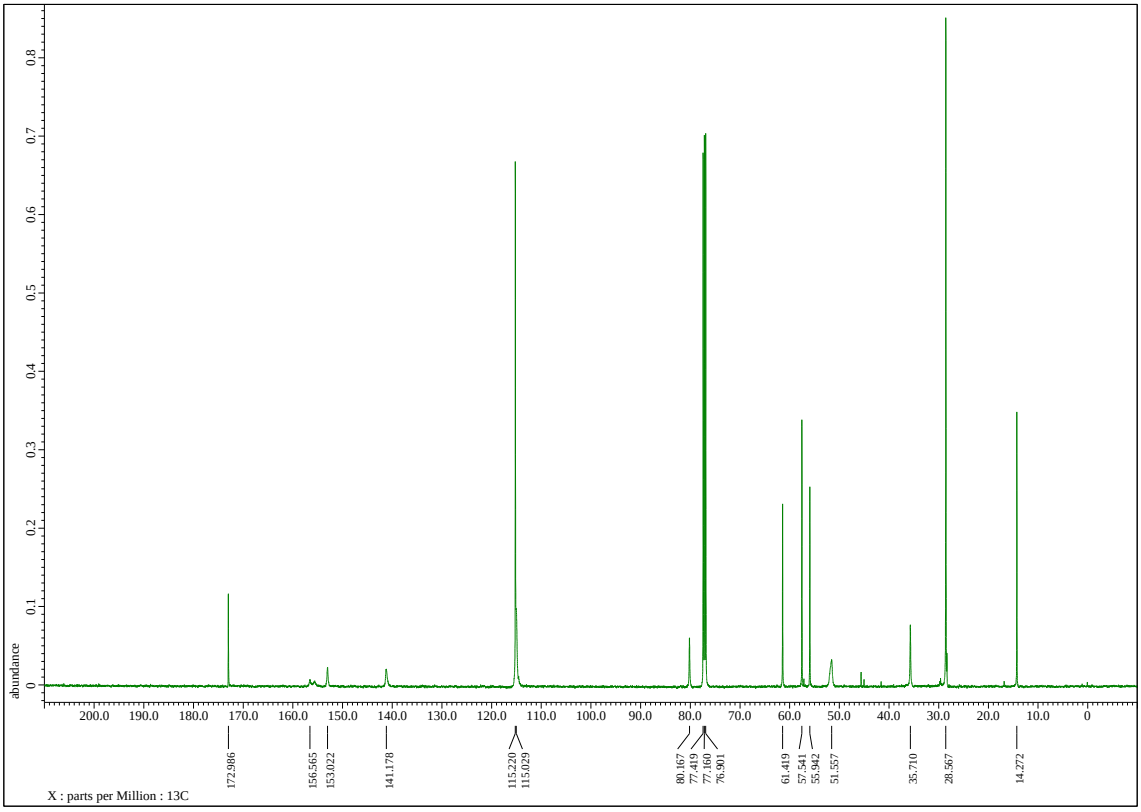
^{13}C NMR of spectrum of **2-Isocyano-3-phenylpyridine** (125 MHz, $CDCl_3$)



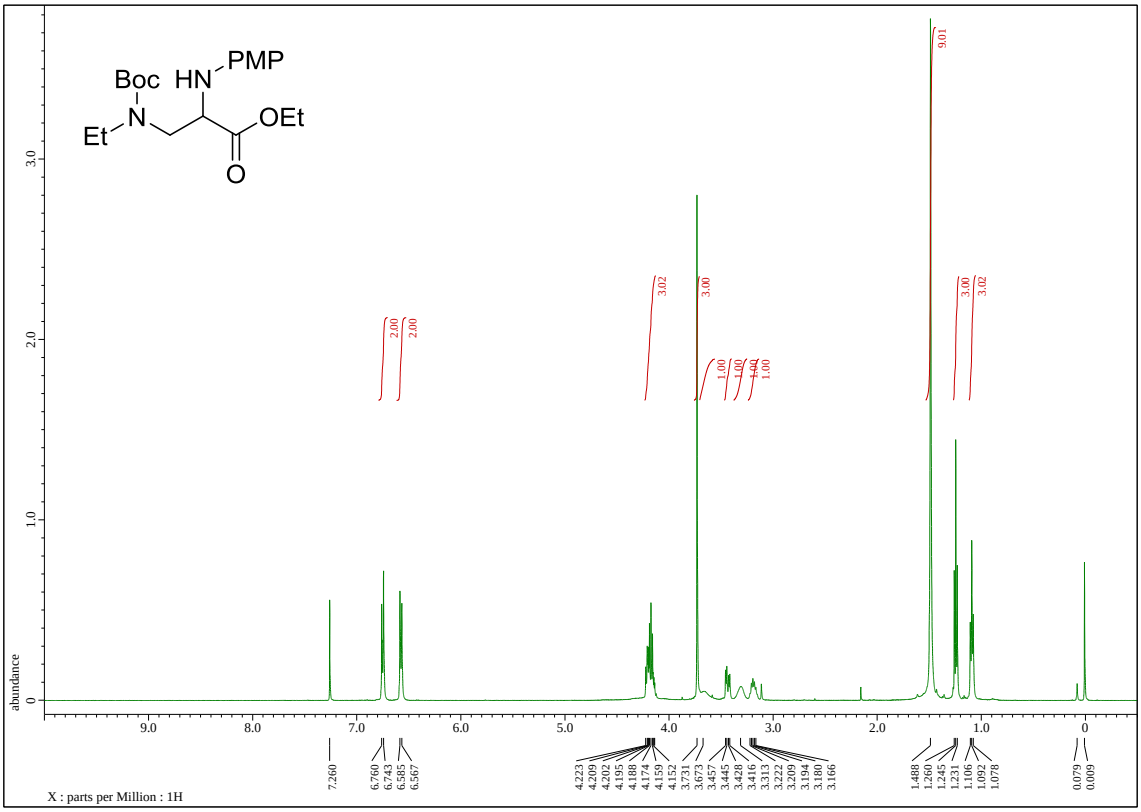
^{1}H NMR spectrum of **4a** (500 MHz, $CDCl_3$, 50 °C)



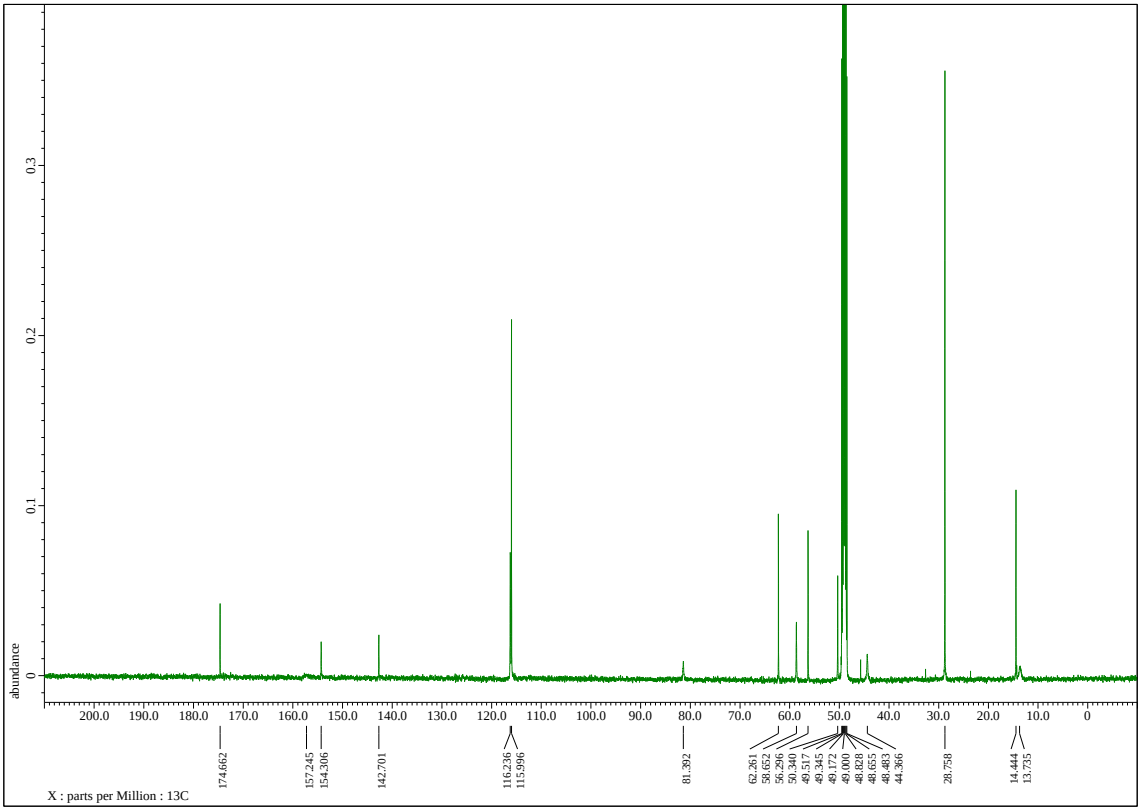
^{13}C NMR spectrum of **4a** (125 MHz, $CDCl_3$, 50 °C)



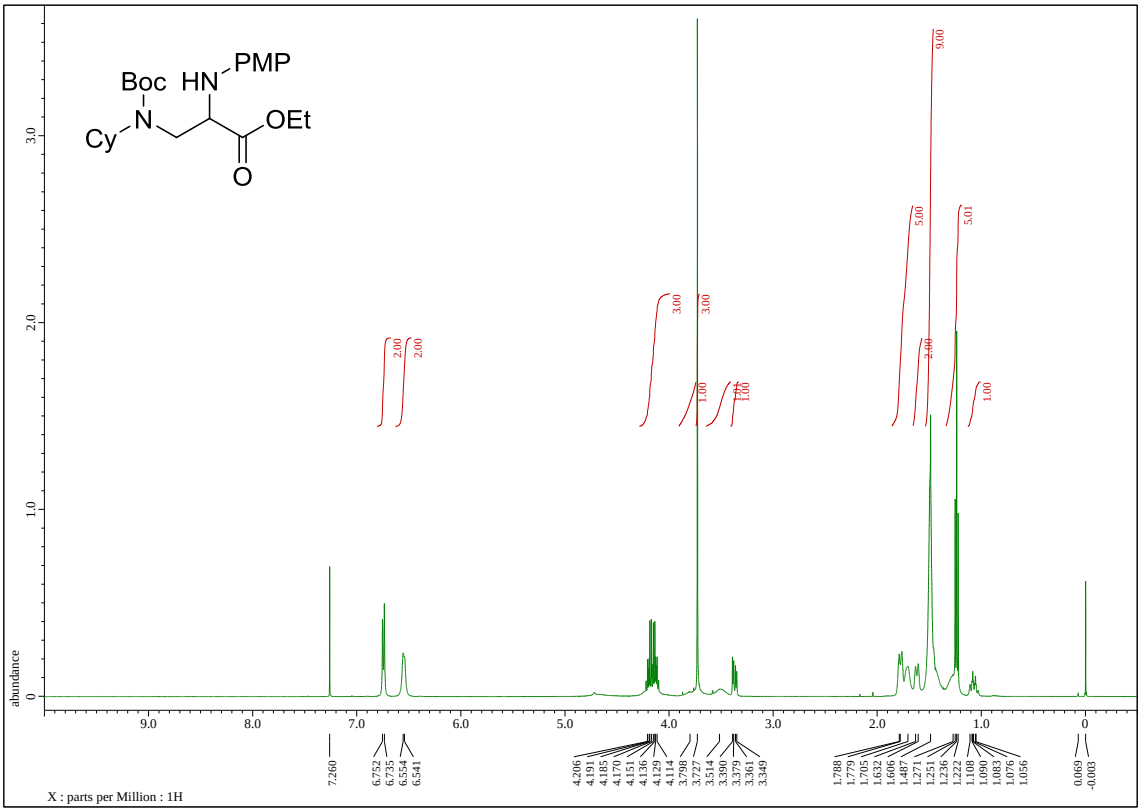
^{1}H NMR of spectrum of **4b** (500 MHz, $CDCl_3$, 50 °C)



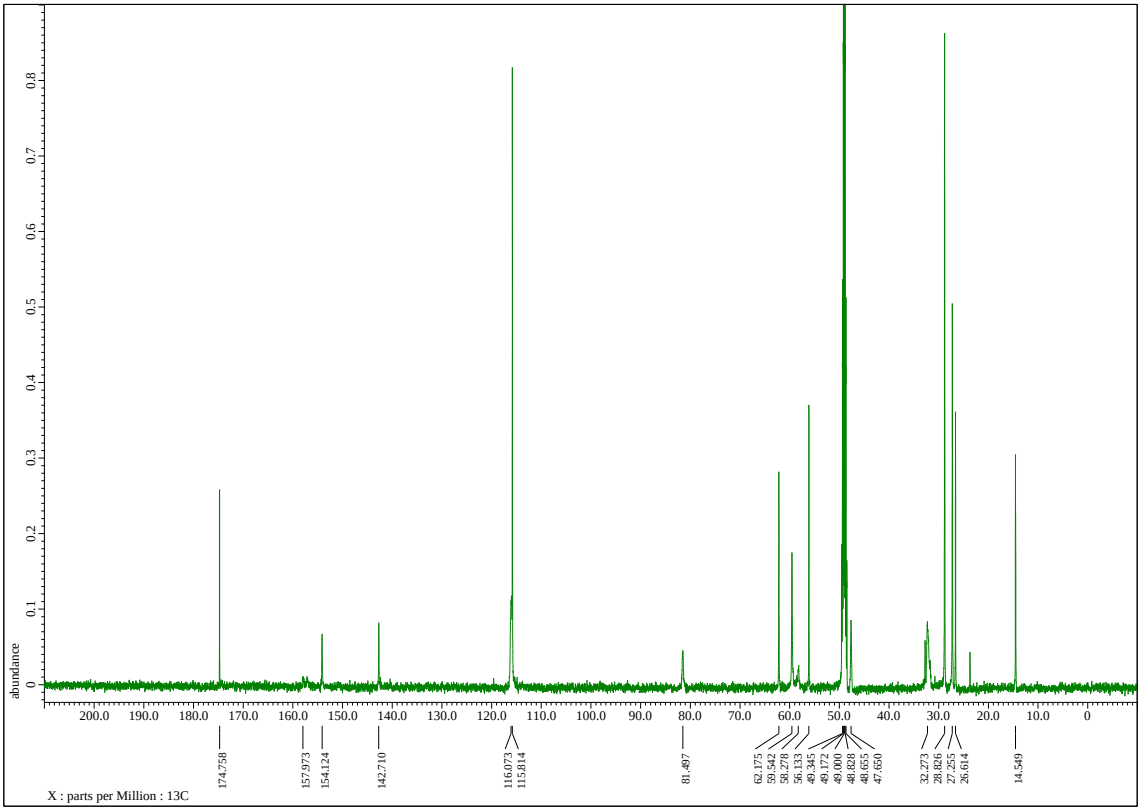
^{13}C NMR spectrum of **4b** (125 MHz, CD_3OD, 50 °C)



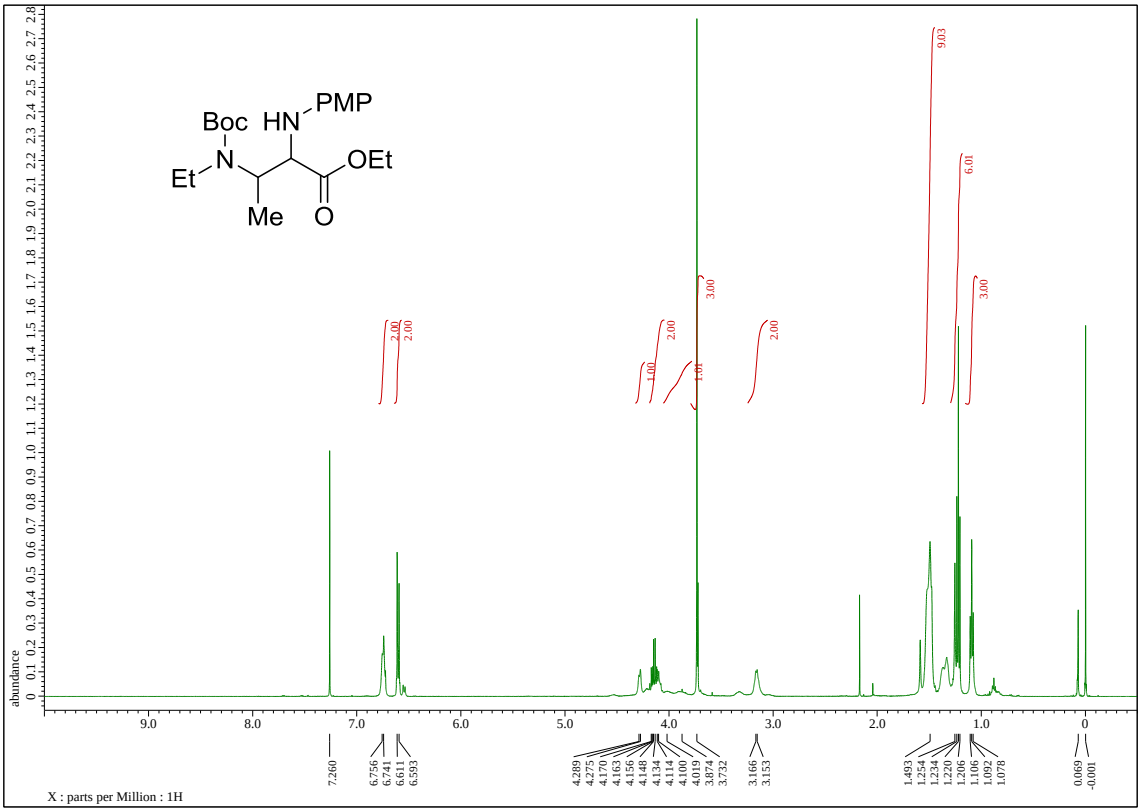
^{1}H NMR of spectrum of **4c** (500 MHz, $CDCl_3$, 50 °C)



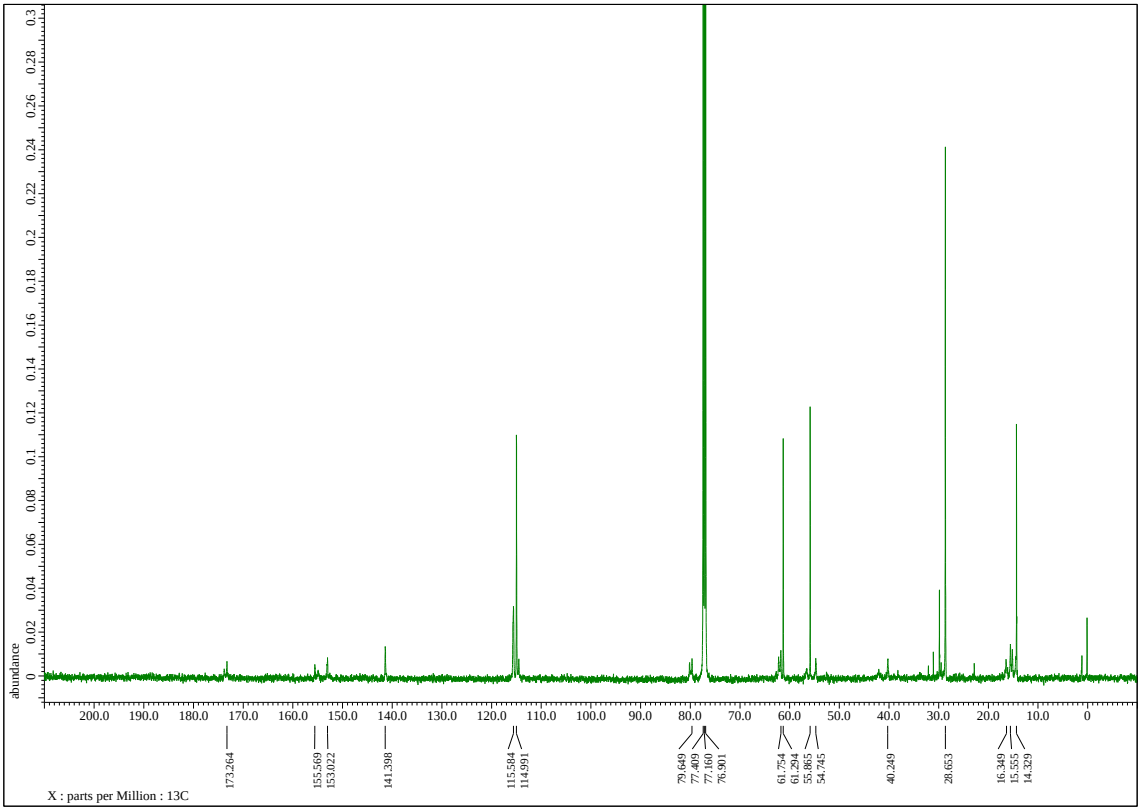
^{13}C NMR of spectrum of **4c** (125 MHz, CD_3OD)



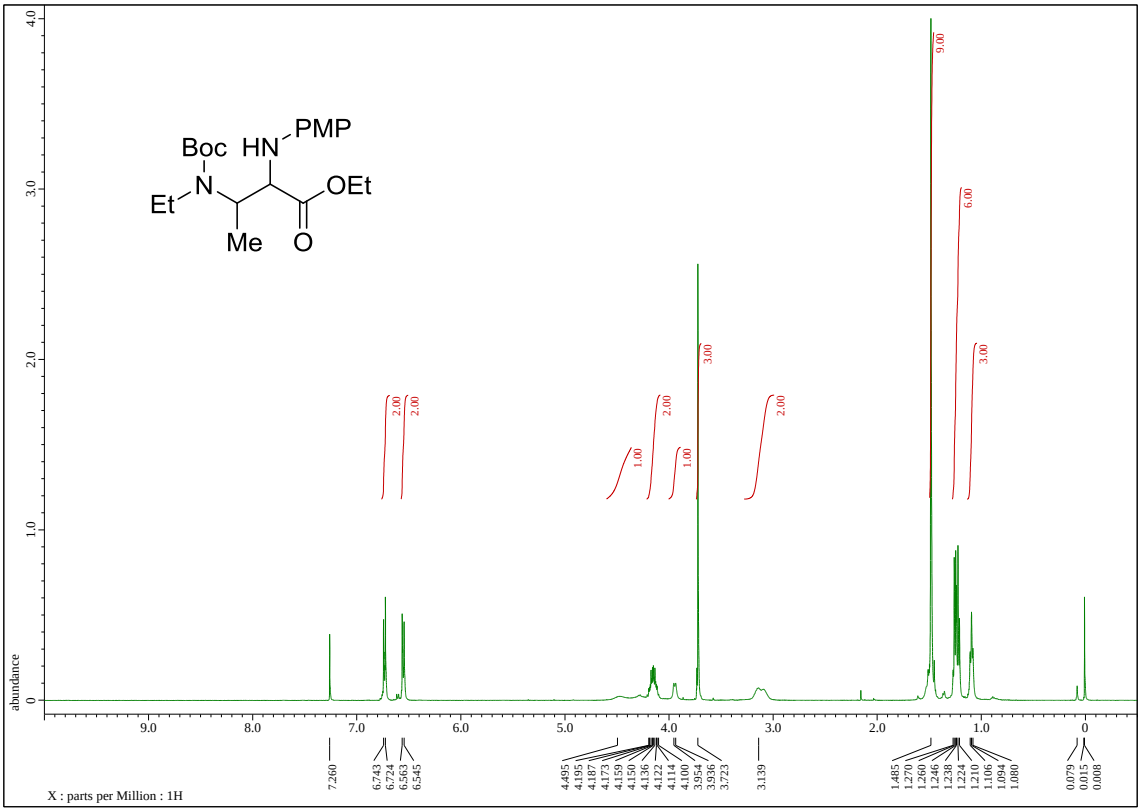
^{1}H NMR spectrum of **4d** (Isomer a) (500 MHz, $CDCl_3$, 50 °C)



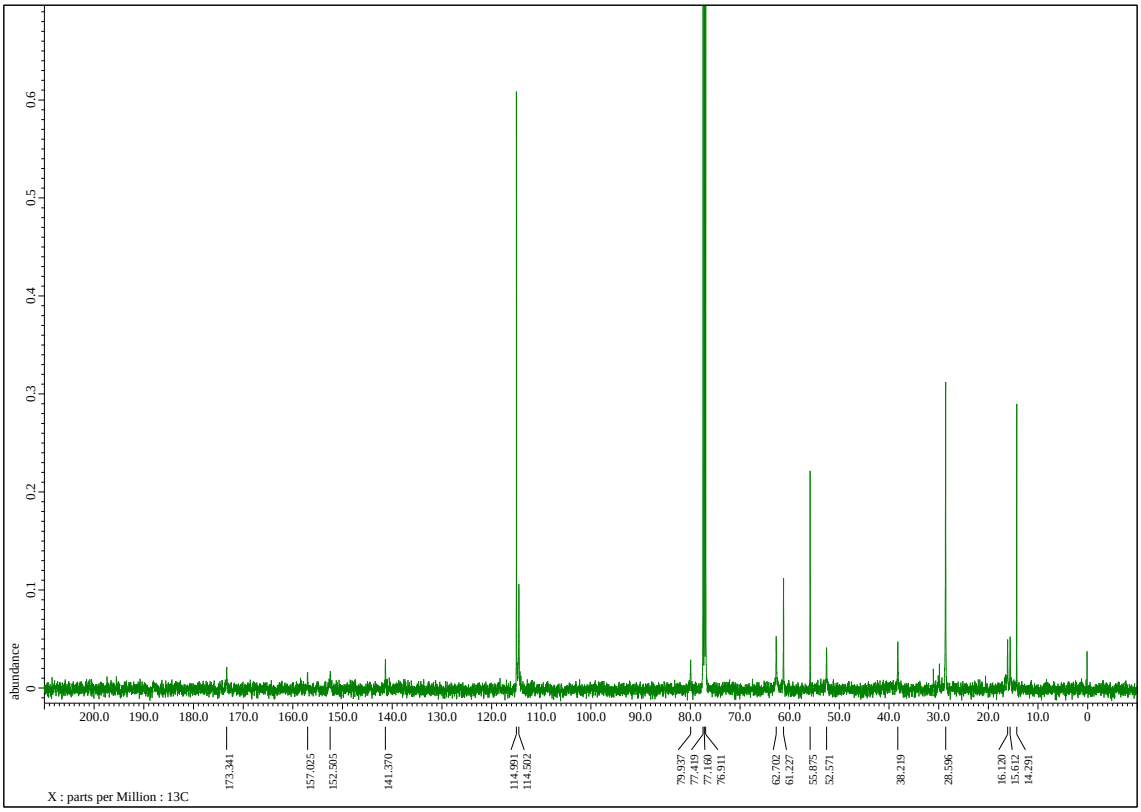
^{13}C NMR of spectrum of **4d** (Isomer a) (125 MHz, CD_3OD)



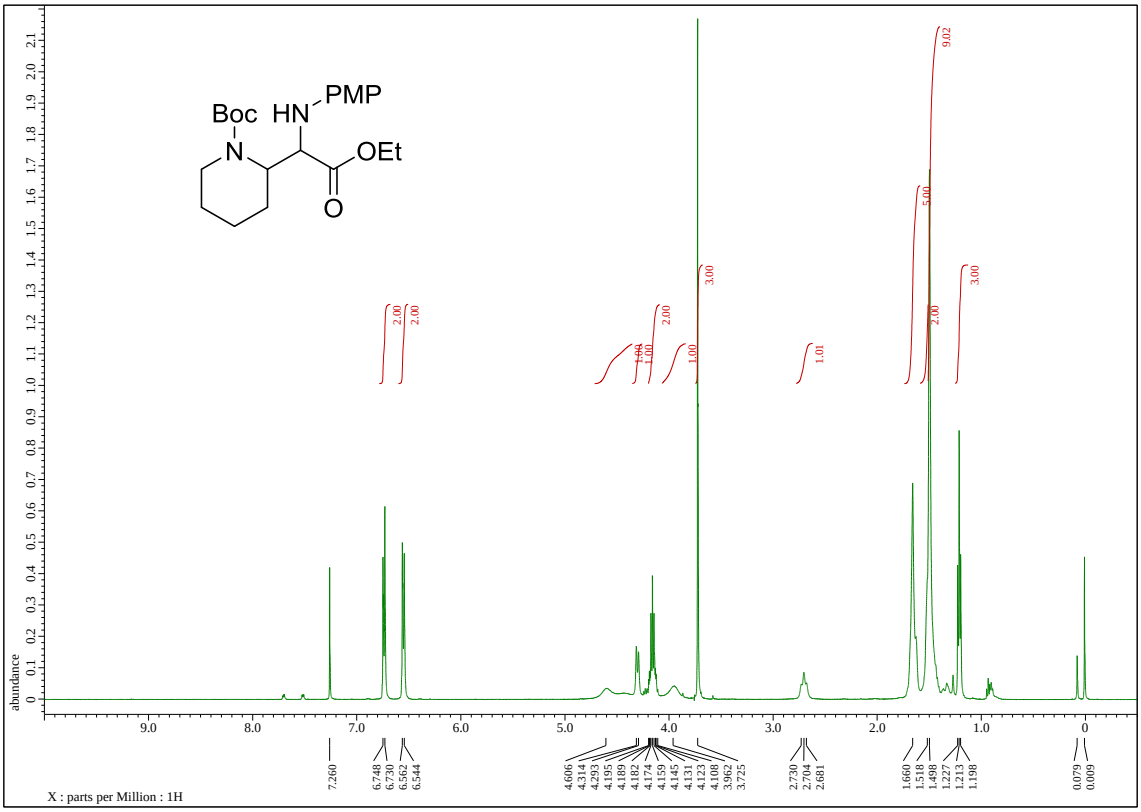
^{1}H NMR spectrum of **4d** (Isomer b) (500 MHz, $CDCl_3$, 50 °C)



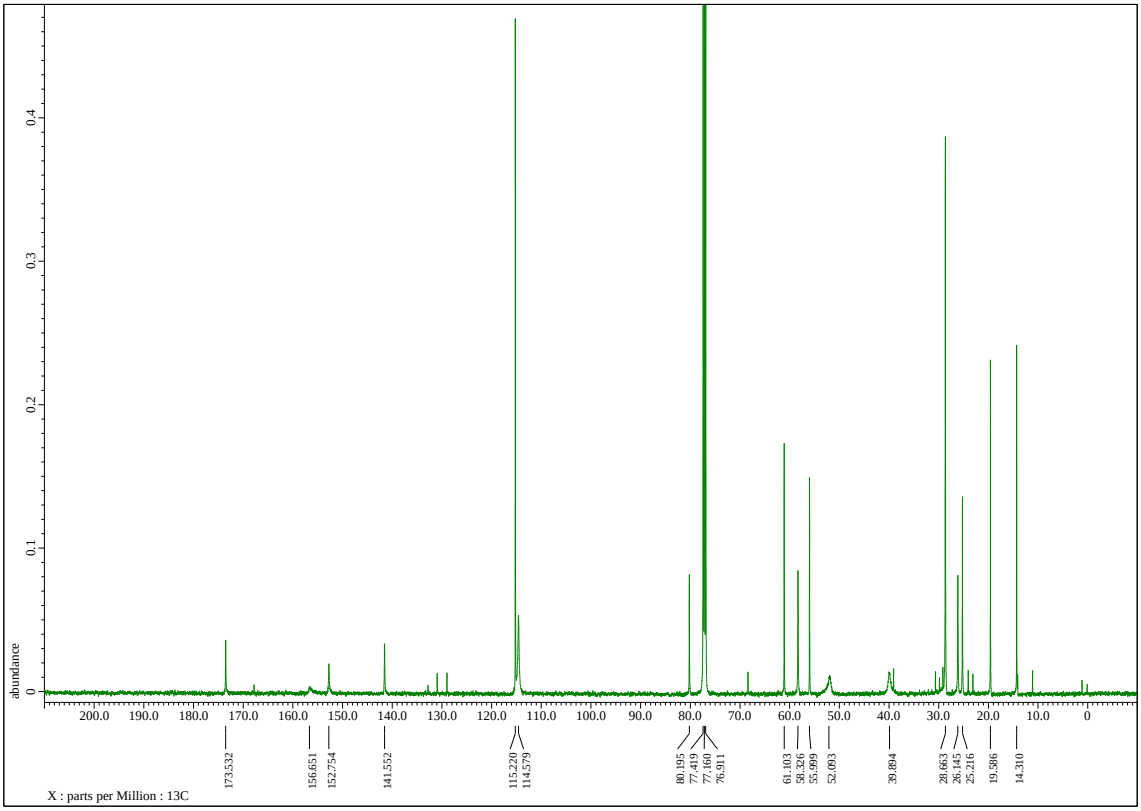
^{13}C NMR of spectrum of **4d** (Isomer b) (125 MHz, CD_3OD)



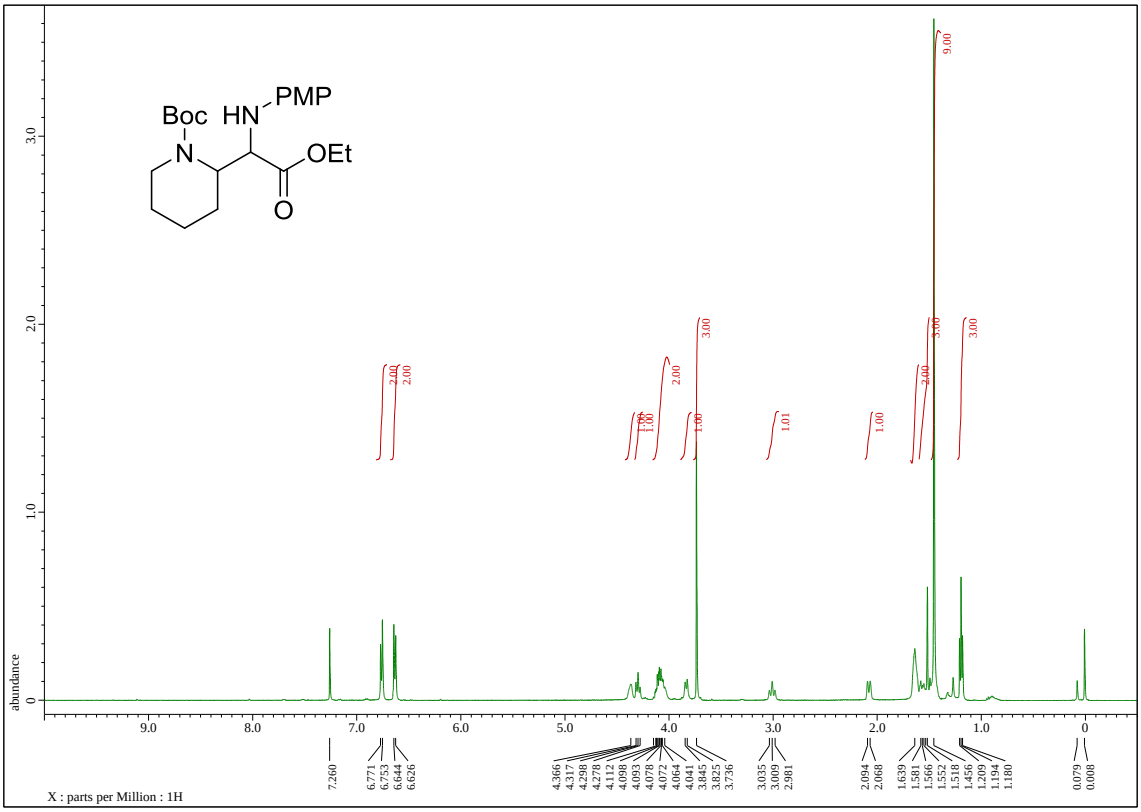
^{1}H NMR of spectrum of **4e** (Isomer a) (500 MHz, $CDCl_3$, 50 °C)



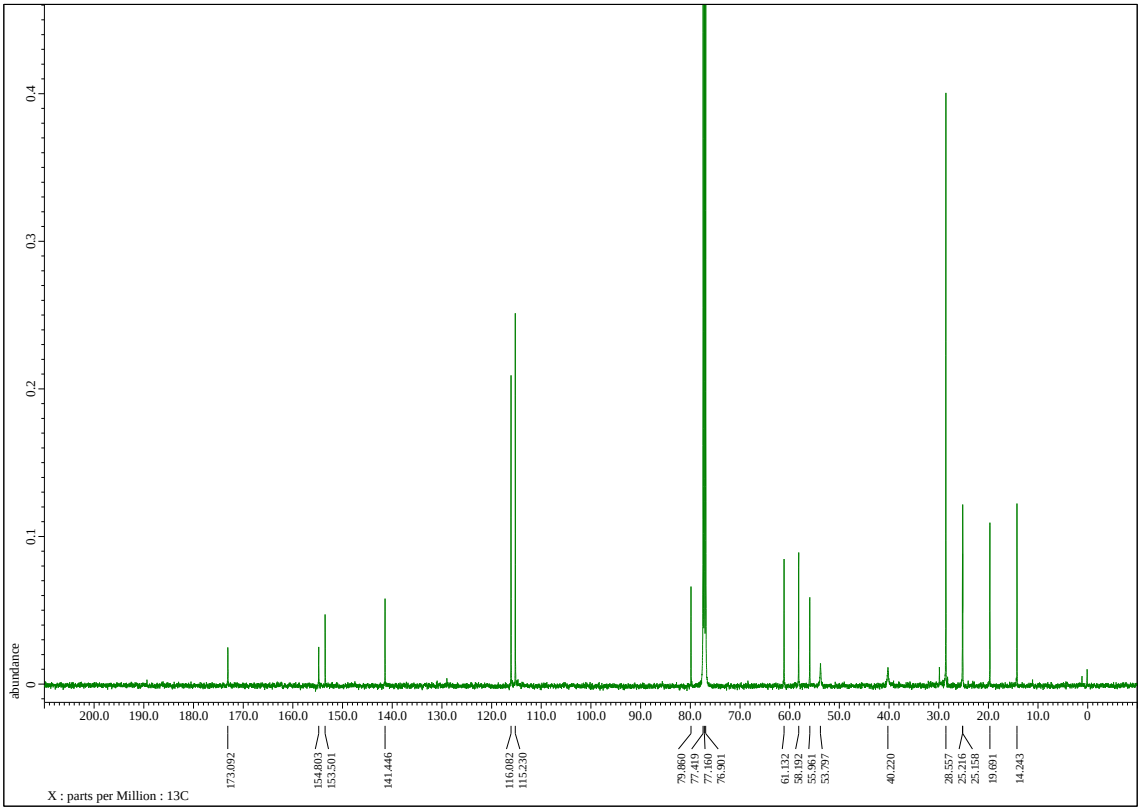
^{13}C NMR of spectrum of **4e** (Isomer a) (500 MHz, $CDCl_3$, 50 °C)



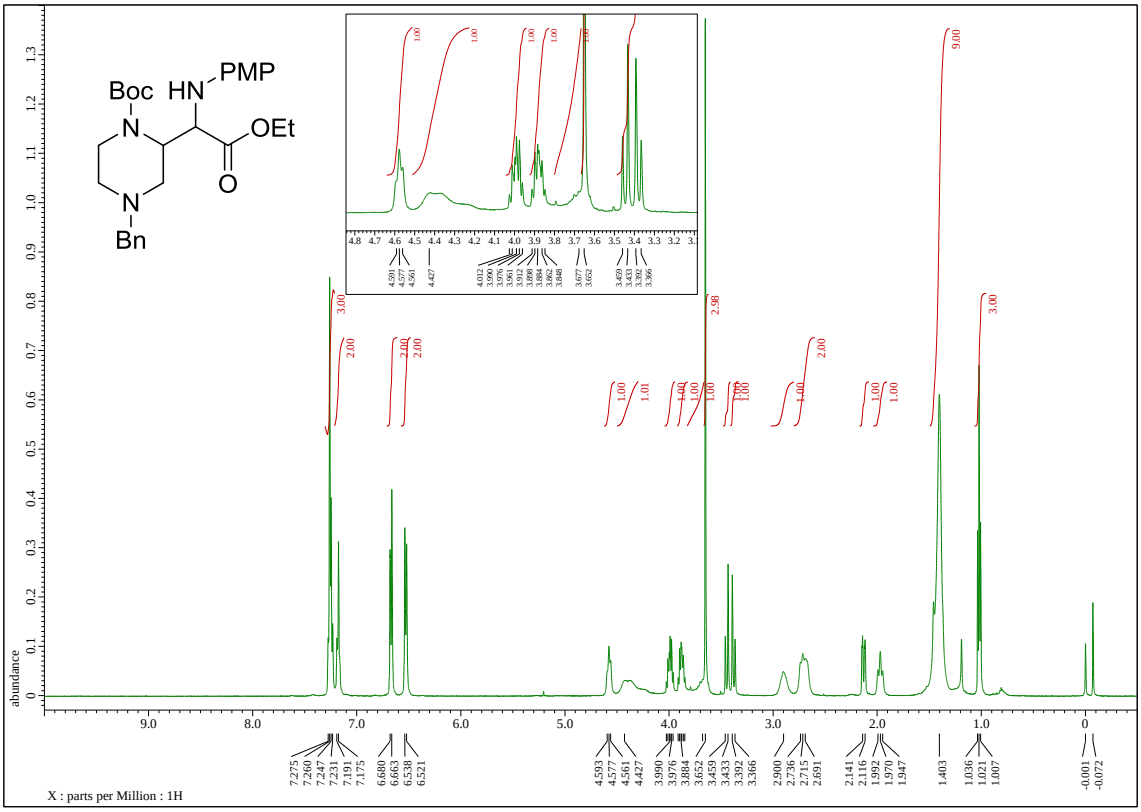
^{1}H NMR of spectrum of **4e** (Isomer b) (500 MHz, $CDCl_3$, 50 °C)



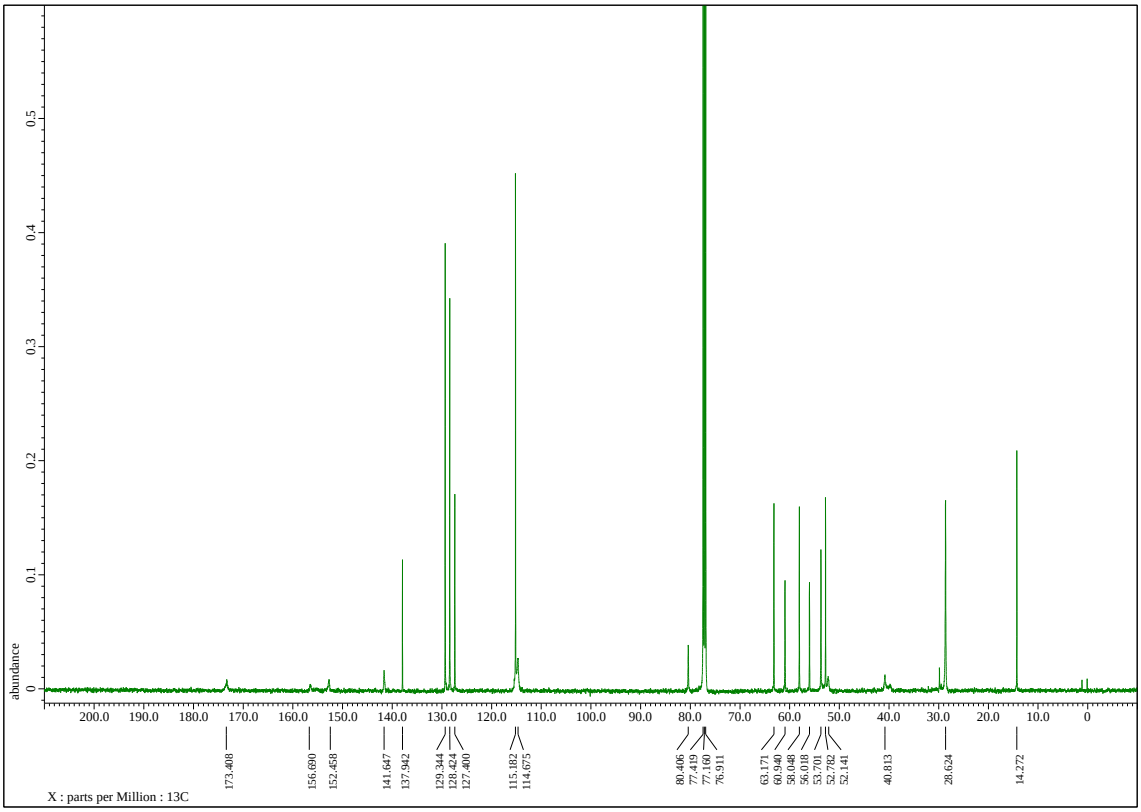
^{13}C NMR of spectrum of **4e** (Isomer b) (125 MHz, $CDCl_3$, 50 °C)



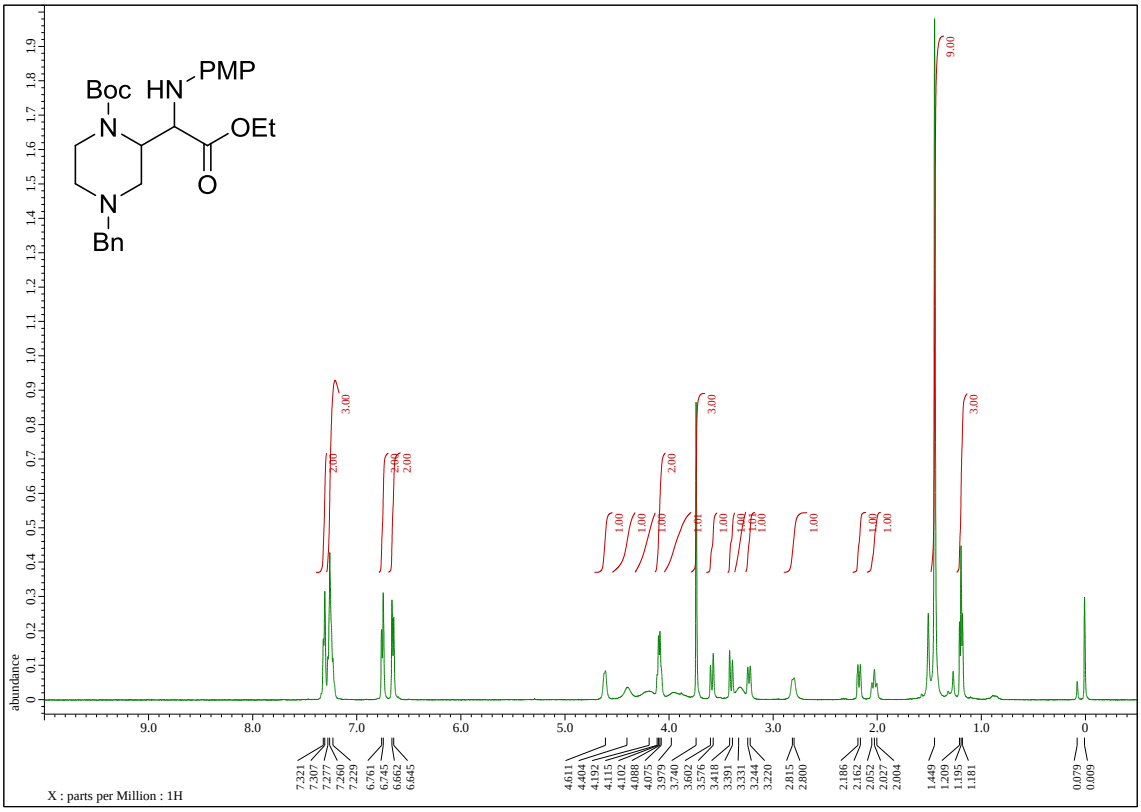
^{1}H NMR of spectrum of **4f** (Isomer a) (500 MHz, $CDCl_3$, 50 °C)



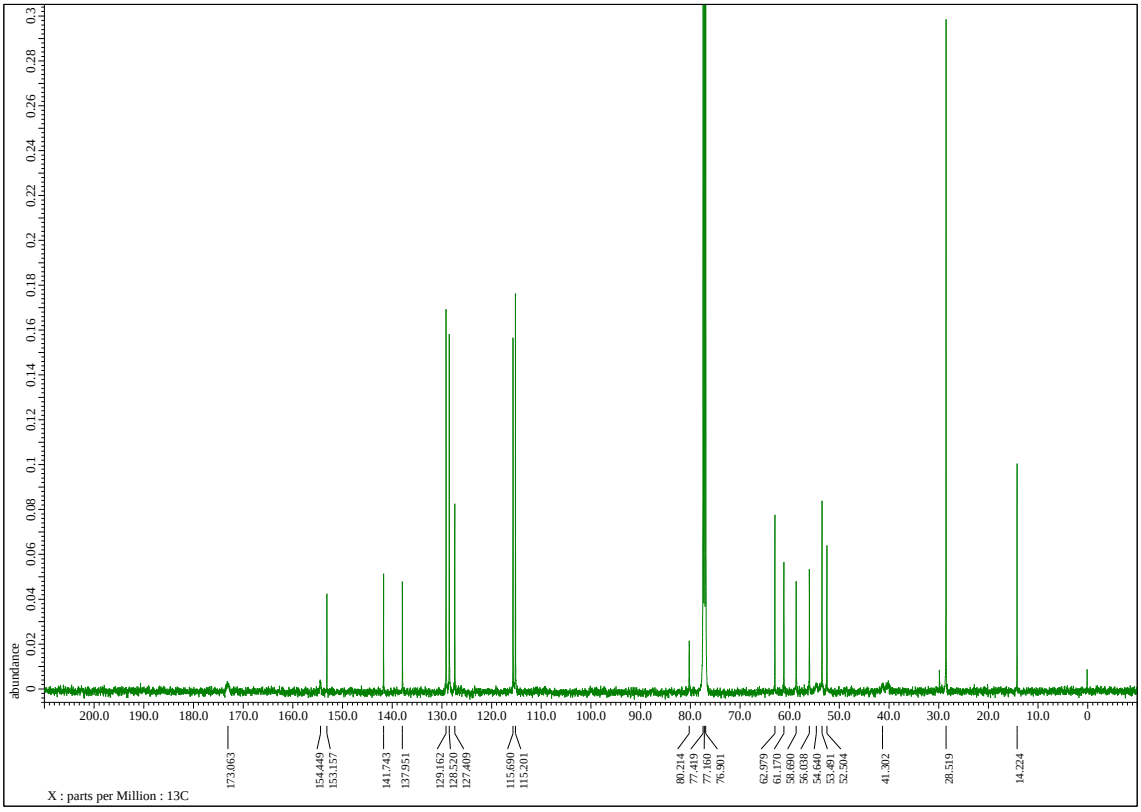
^{13}C NMR of spectrum of **4f** (Isomer a) (125 MHz, $CDCl_3$, 50 °C)



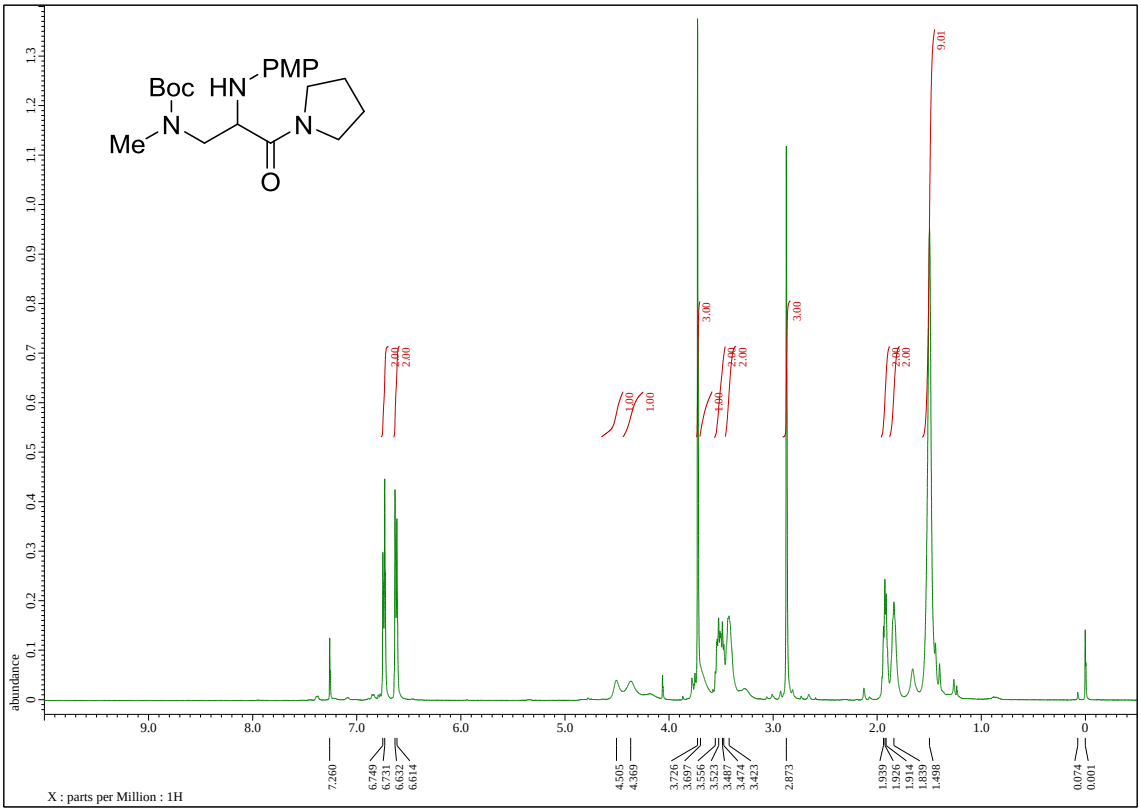
^{1}H NMR of spectrum of **4f** (Isomer b) (500 MHz, $CDCl_3$, 50 °C)



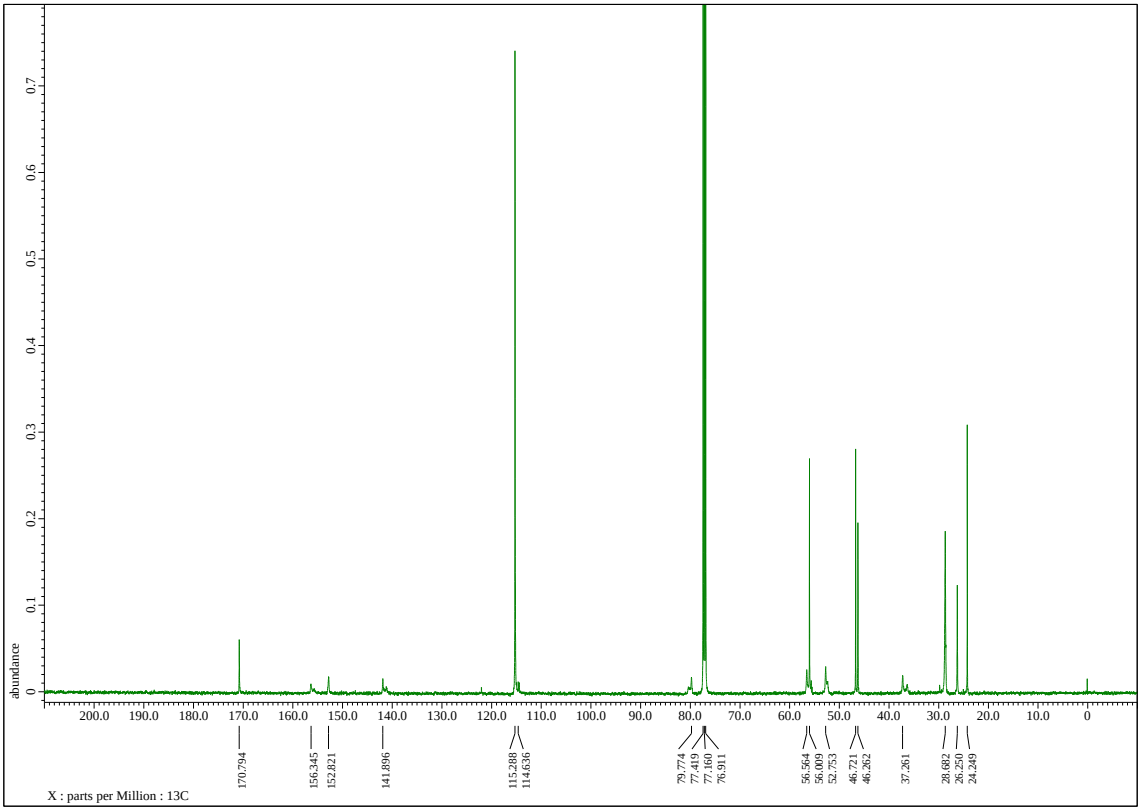
^{13}C NMR of spectrum of **4f** (Isomer b) (125 MHz, $CDCl_3$, 50 °C)



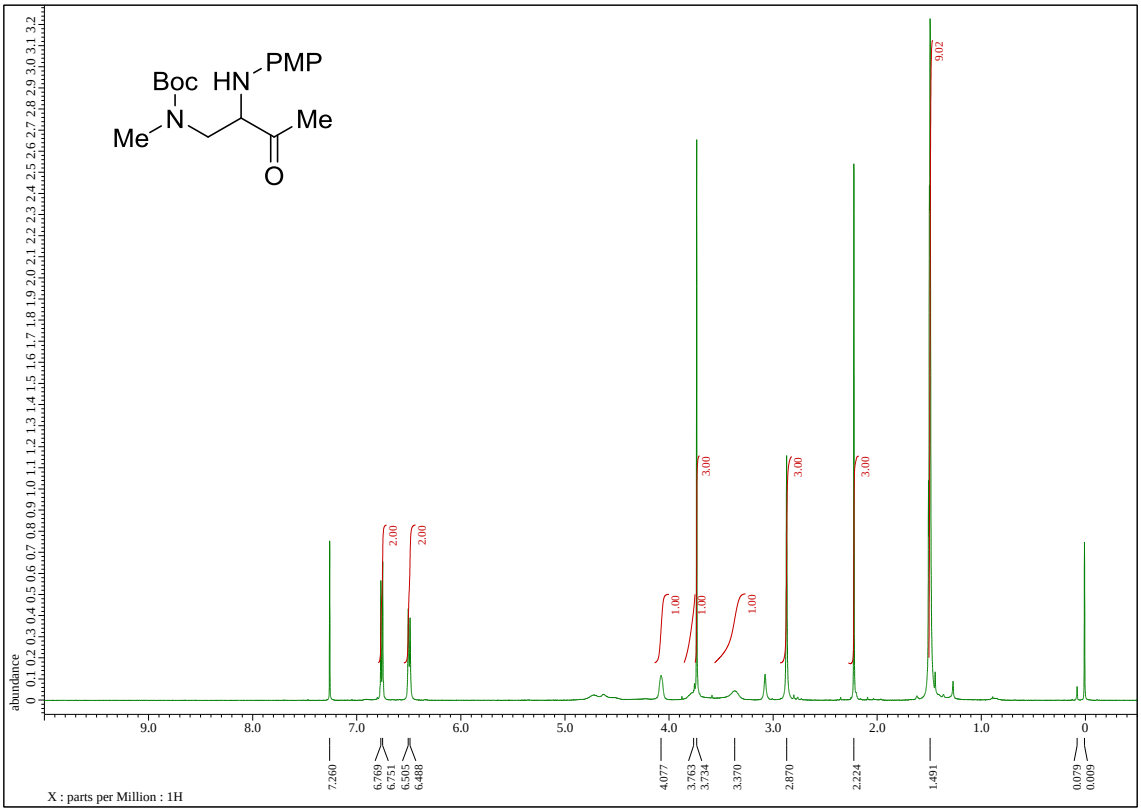
^{1}H NMR of spectrum of **4h** (500 MHz, $CDCl_3$, 50 °C)



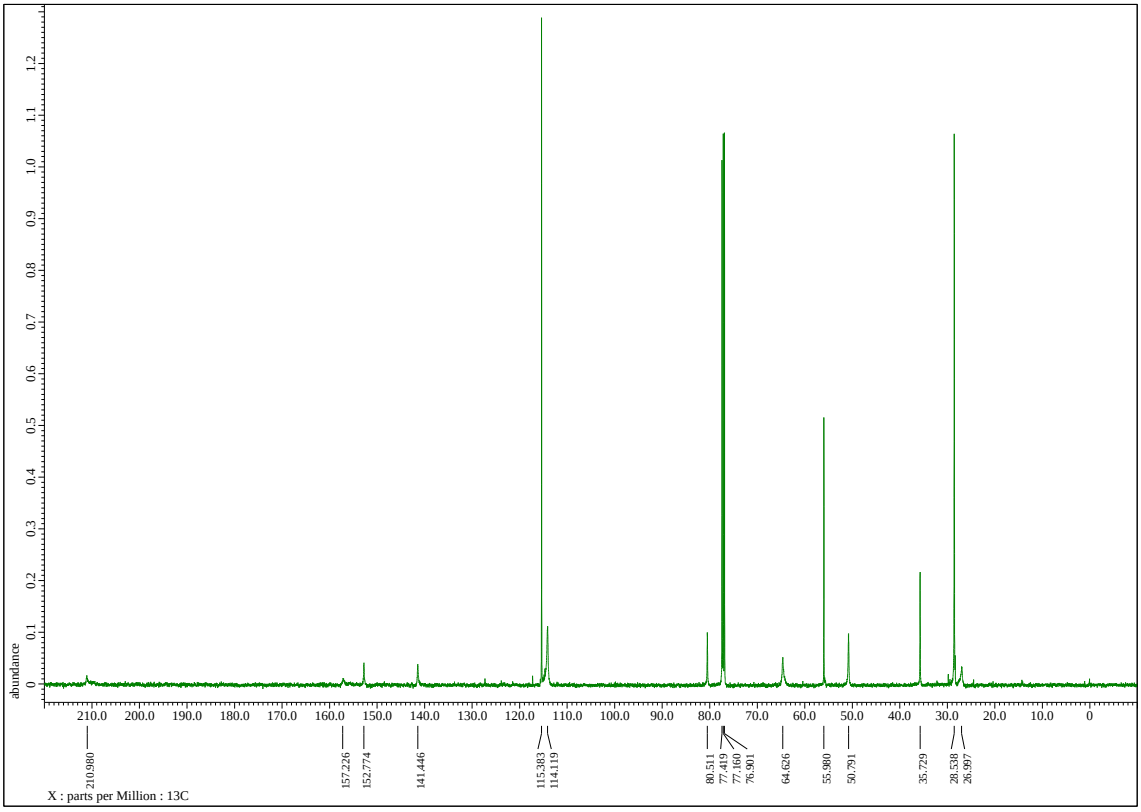
^{13}C NMR of spectrum of **4h** (125 MHz, $CDCl_3$, 50 °C)



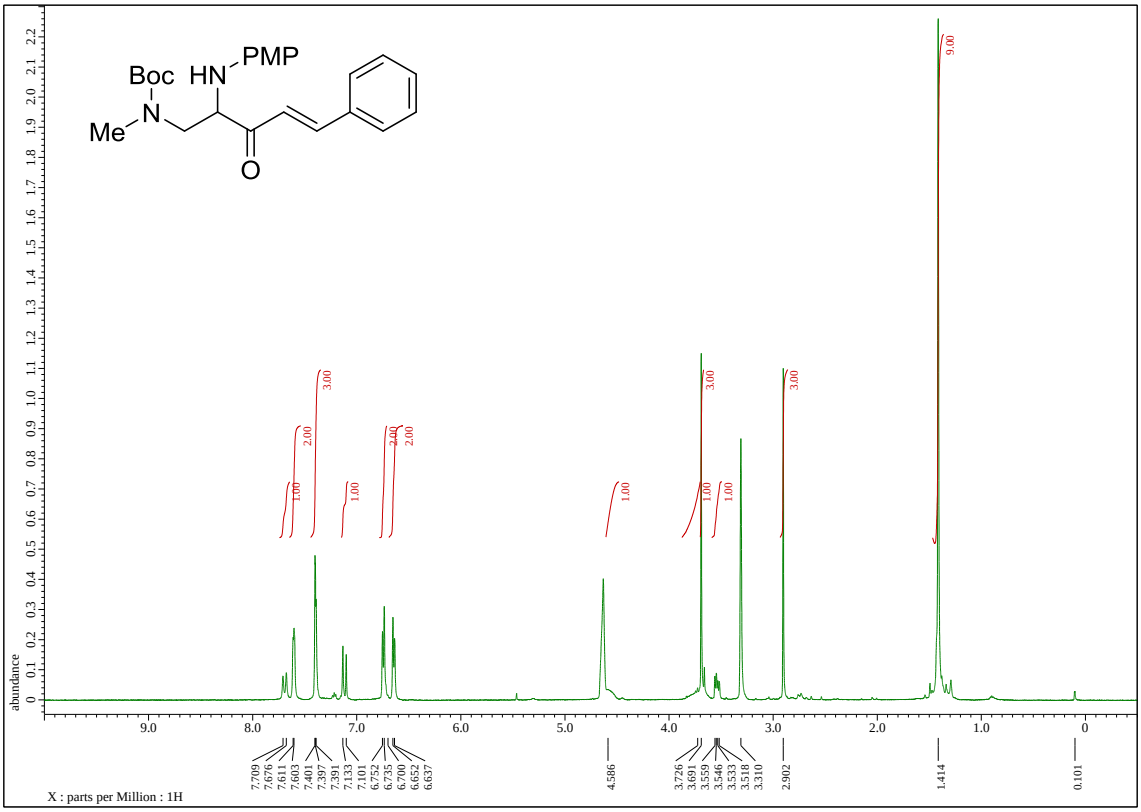
^{1}H NMR of spectrum of **4i** (500 MHz, $CDCl_3$, 50 °C)



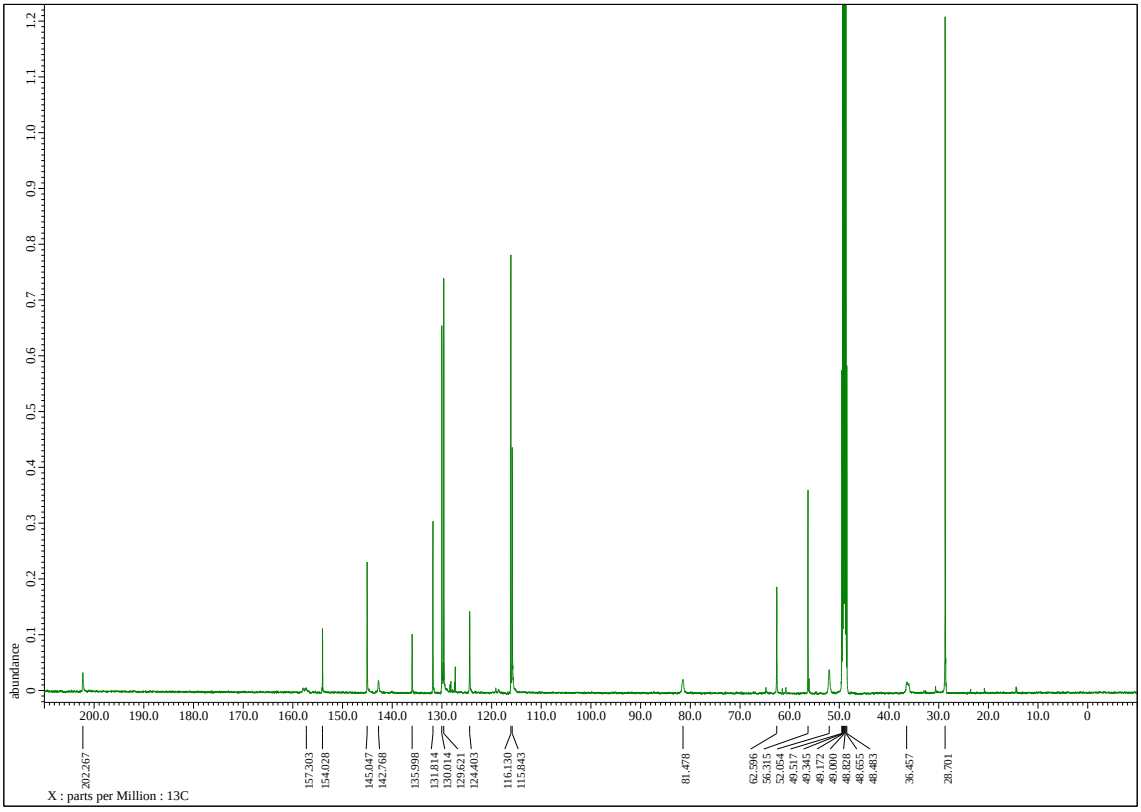
^{13}C NMR of spectrum of **4i** (125 MHz, $CDCl_3$, 50 °C)



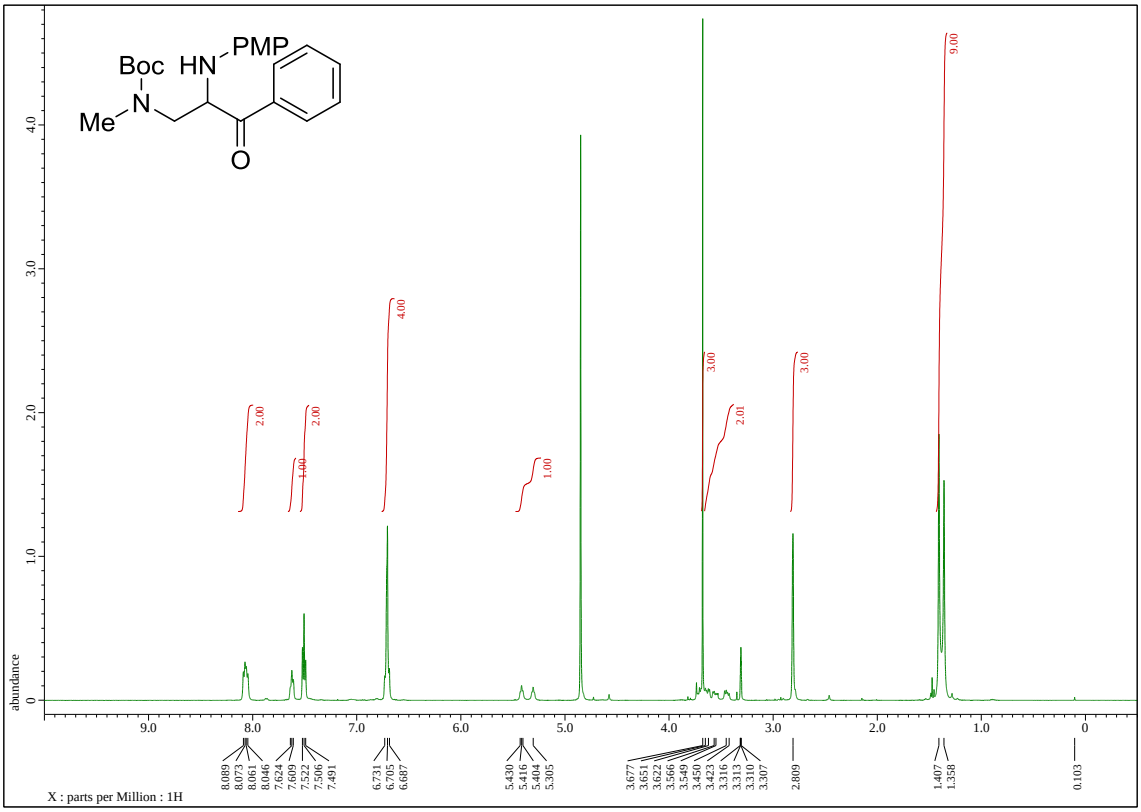
^{1}H NMR of spectrum of **4j** (500 MHz, CD_3OD, 50 °C)



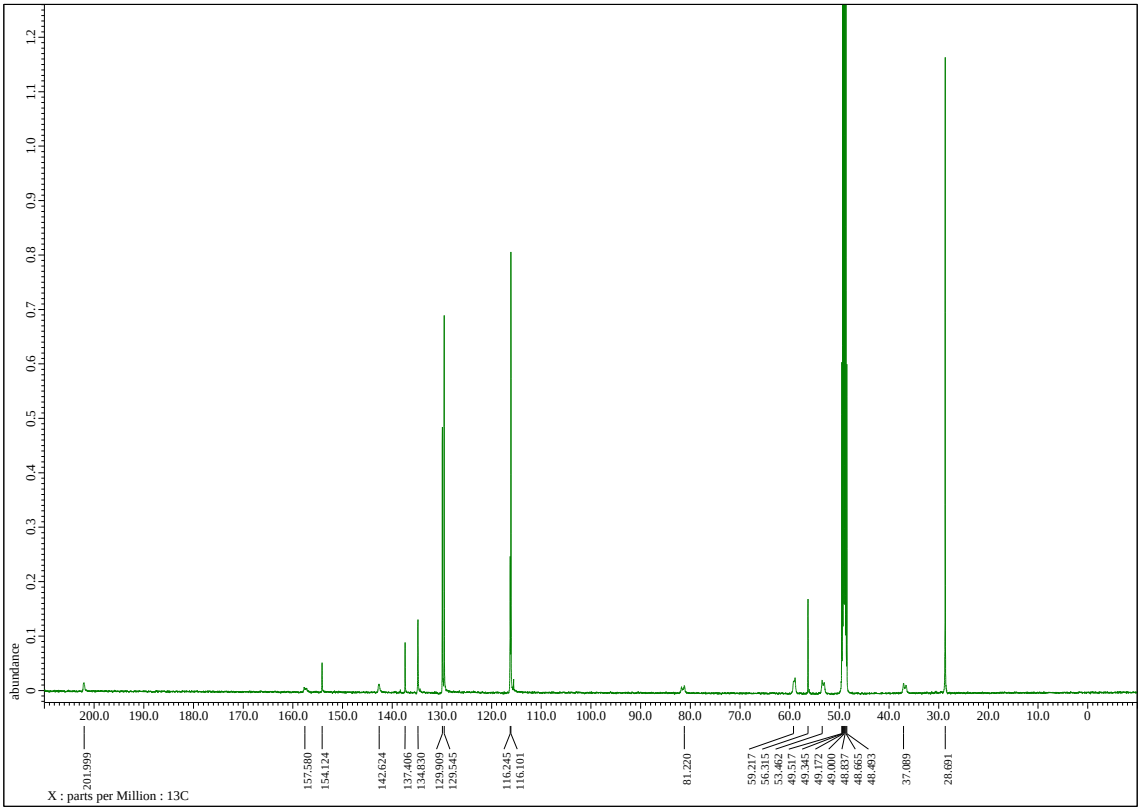
^{13}C NMR of spectrum of **4j** (125 MHz, CD_3OD, 50 °C)



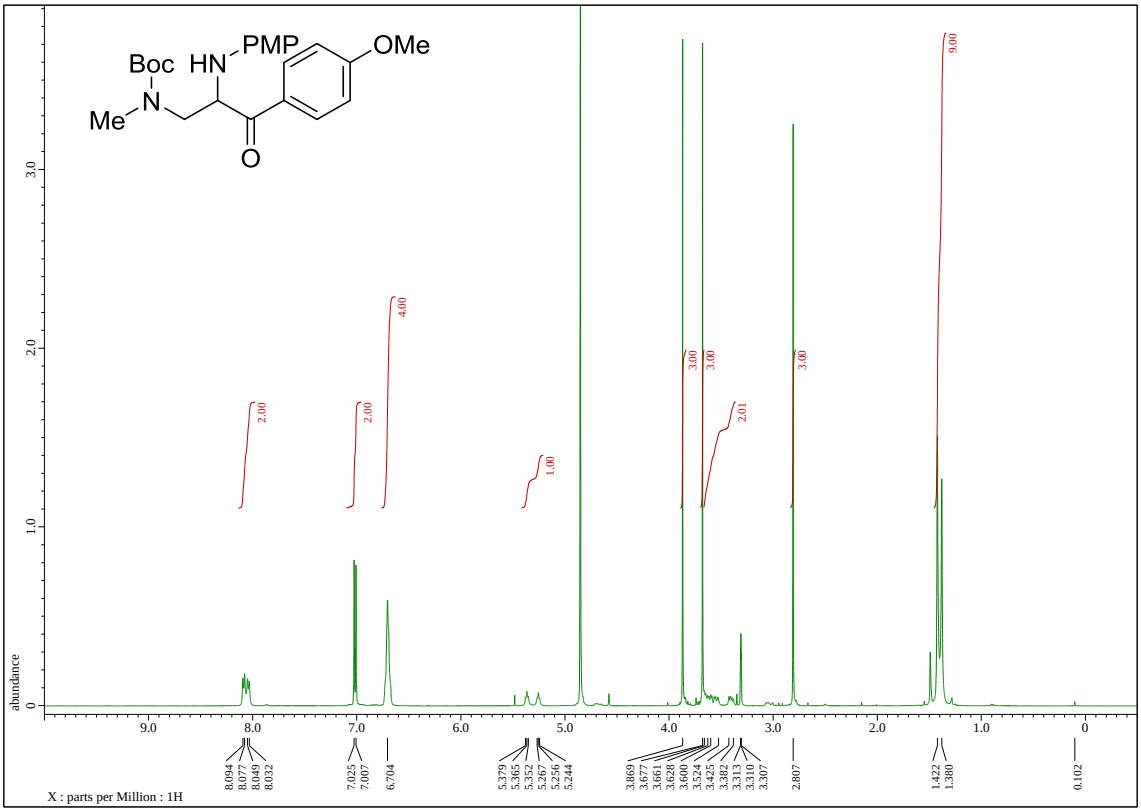
^{1}H NMR of spectrum of **4k** (500 MHz, CD_3OD, 50 °C)



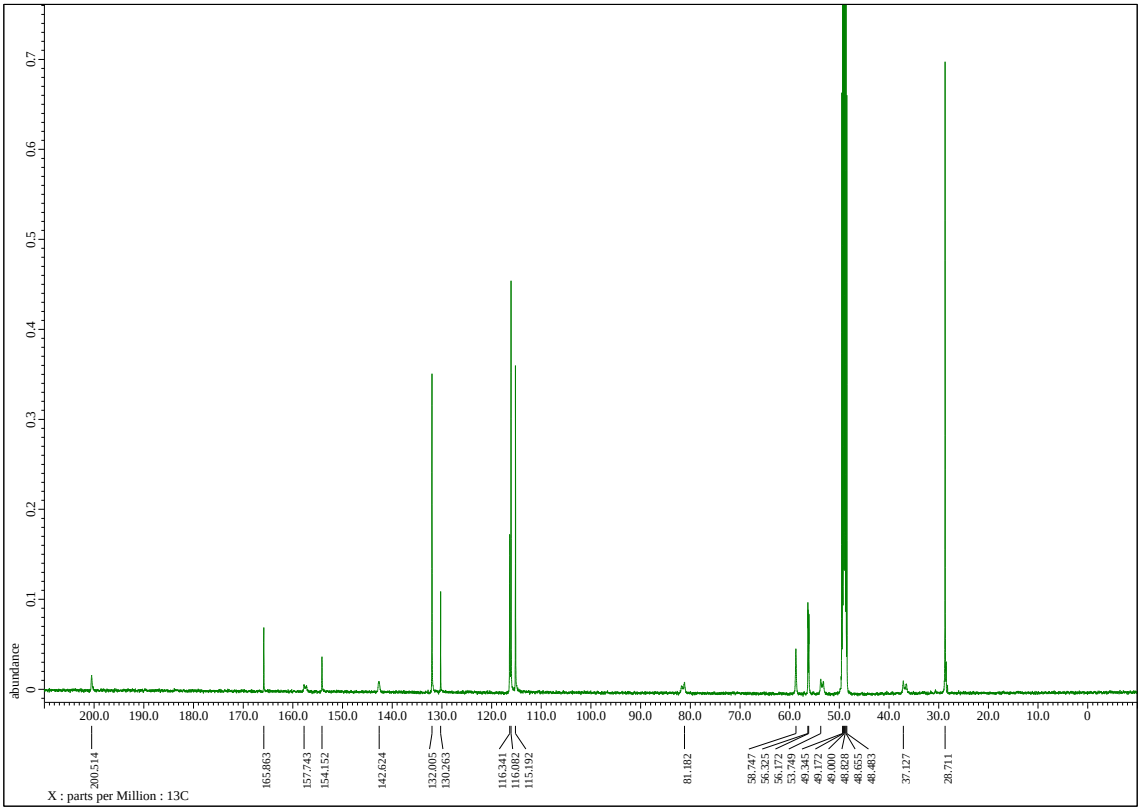
^{13}C NMR of spectrum of **4k** (125 MHz, CD_3OD, 50 °C)



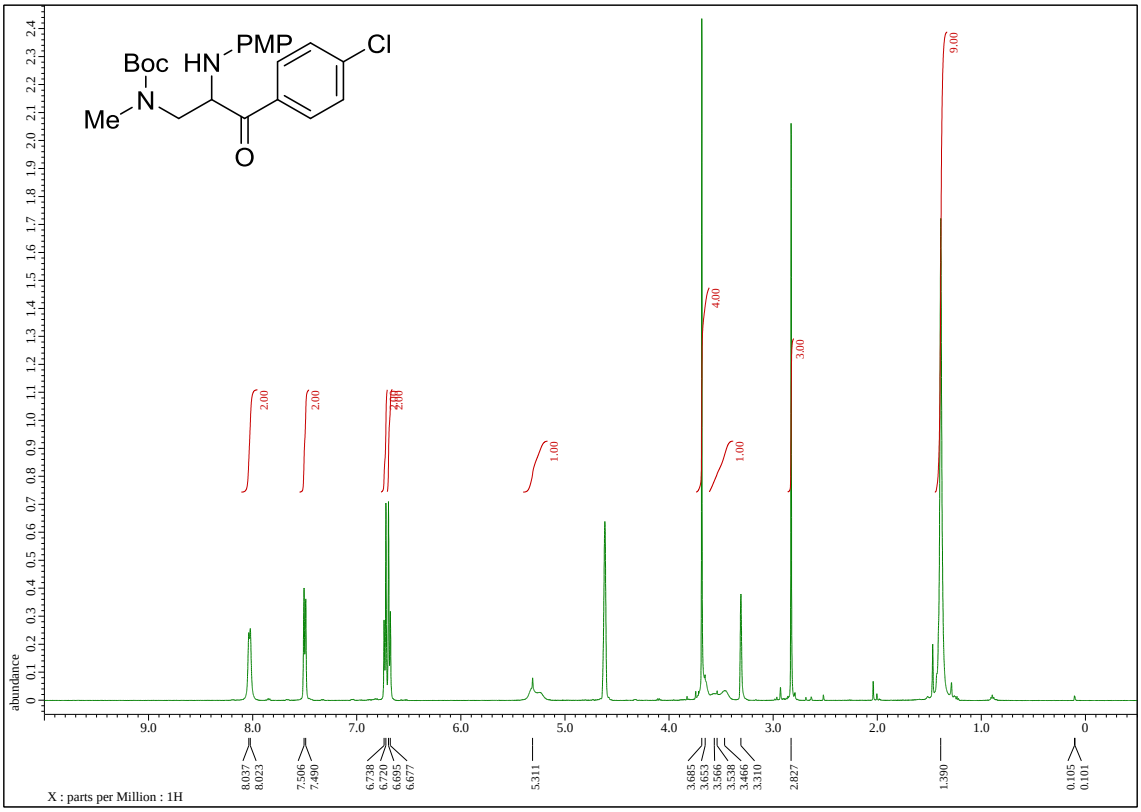
^{1}H NMR of spectrum of **4l** (500 MHz, CD_3OD, 50 °C)



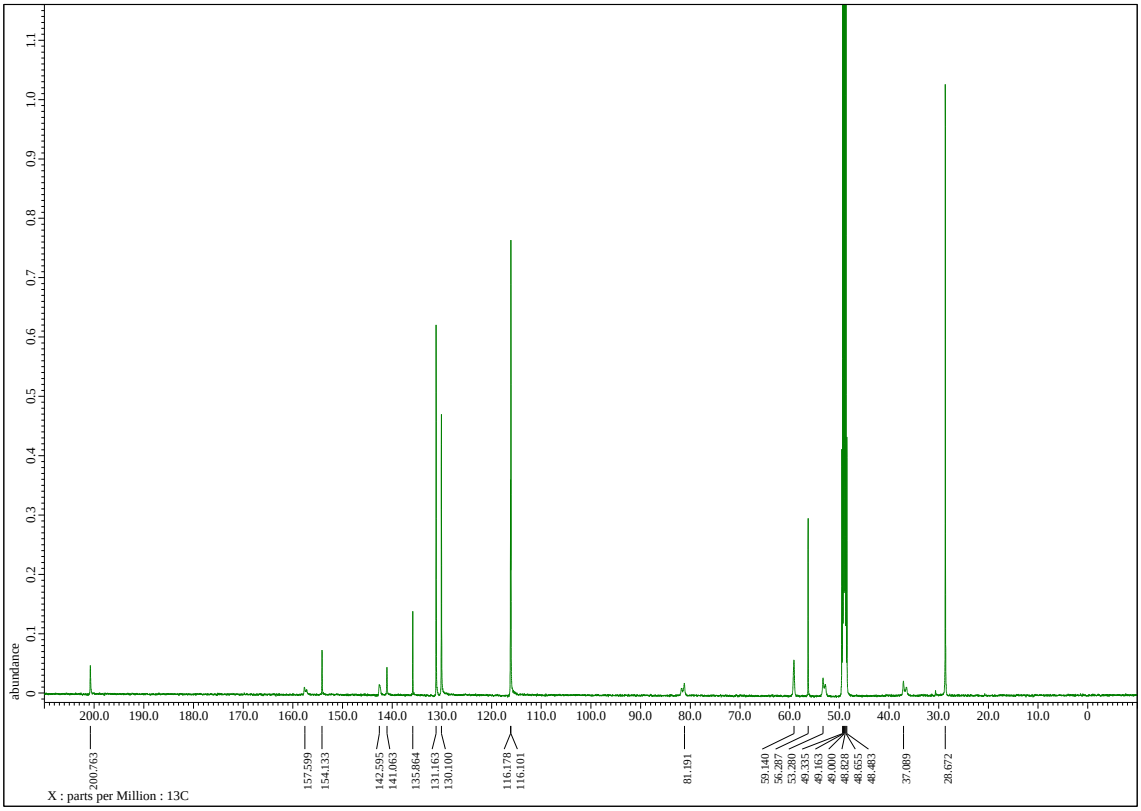
^{13}C NMR of spectrum of **4l** (125 MHz, CD_3OD, 50 °C)



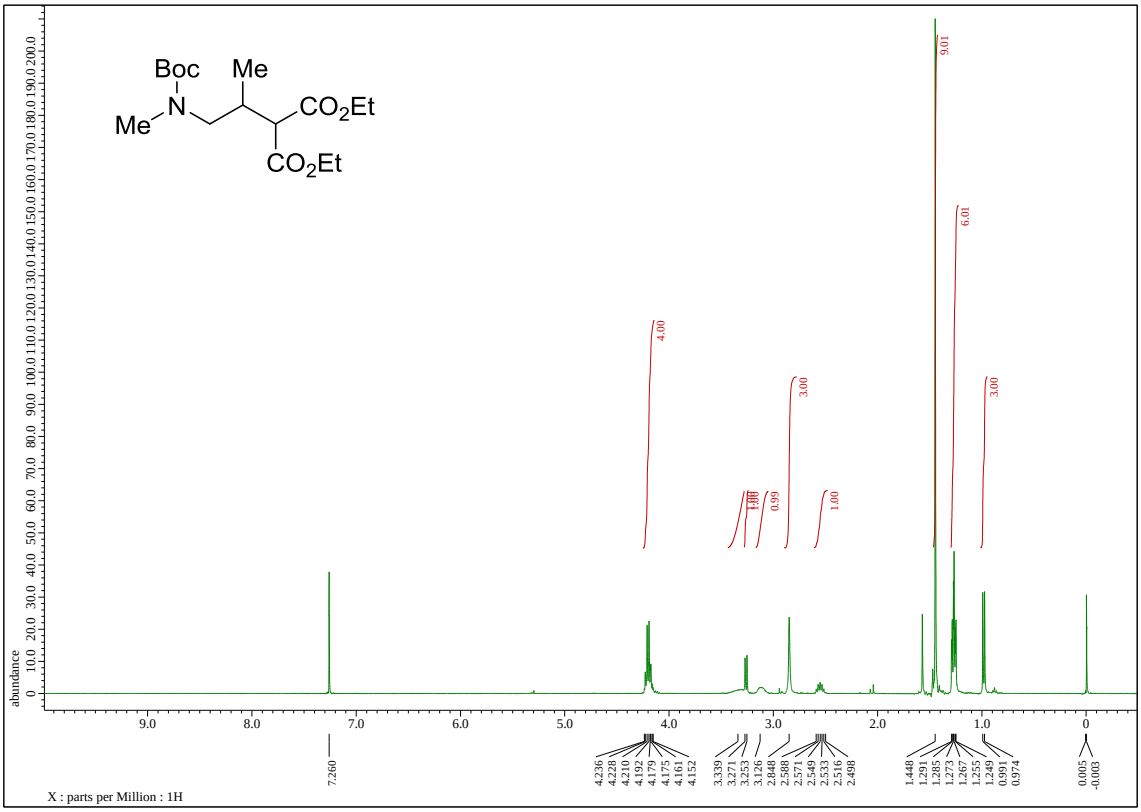
^{1}H NMR of spectrum of **4m** (500 MHz, CD_3OD, 50 °C)



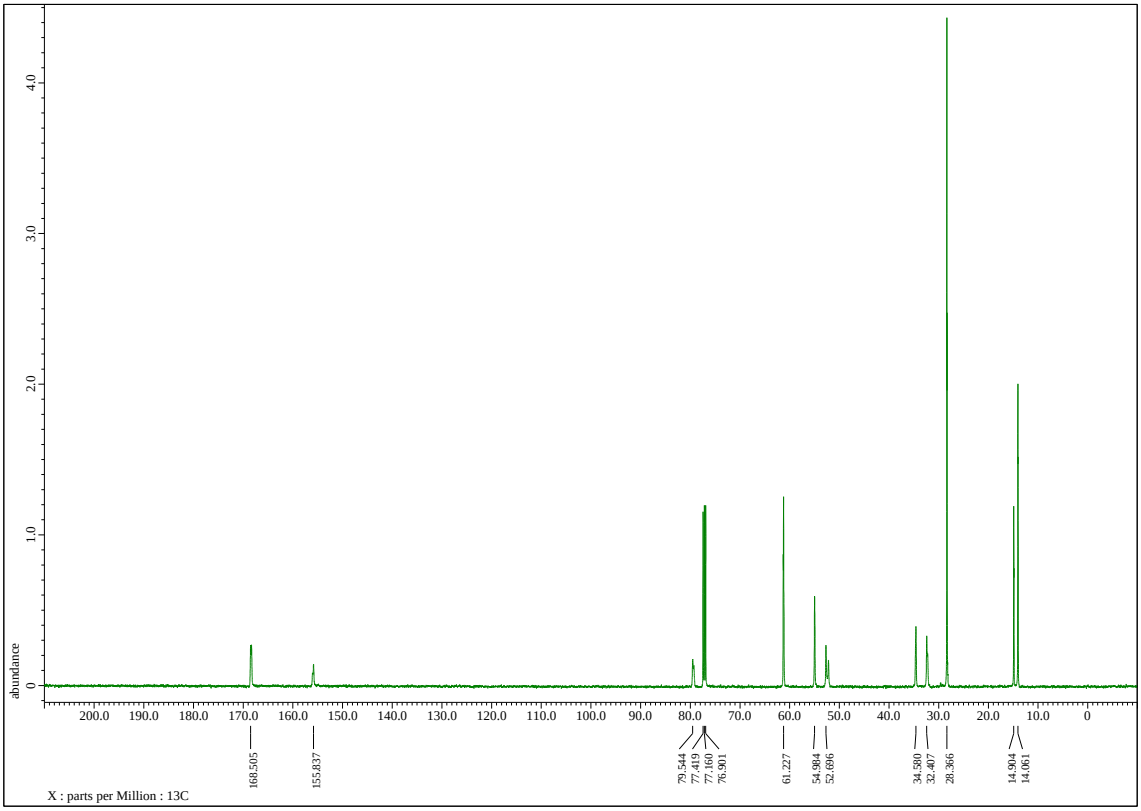
^{13}C NMR of spectrum of **4m** (125 MHz, CD_3OD, 50 °C)



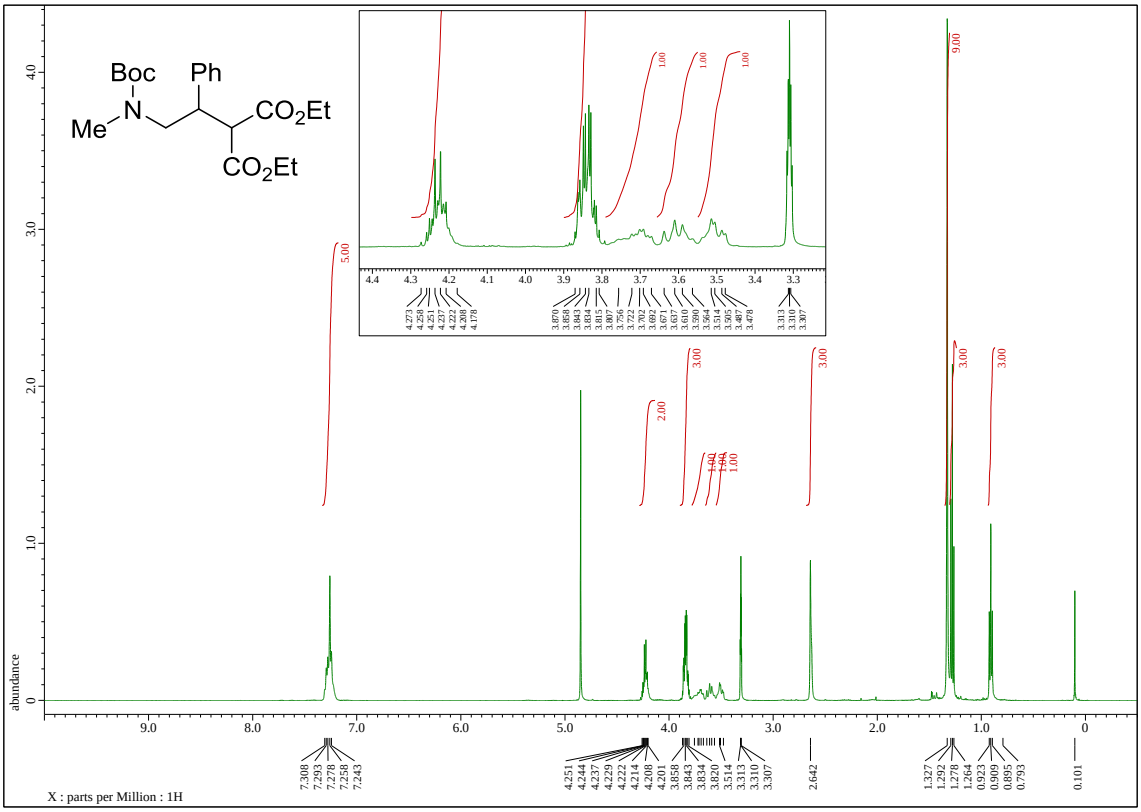
^{1}H NMR of spectrum of **7a** (500 MHz, $CDCl_3$, 50 °C)



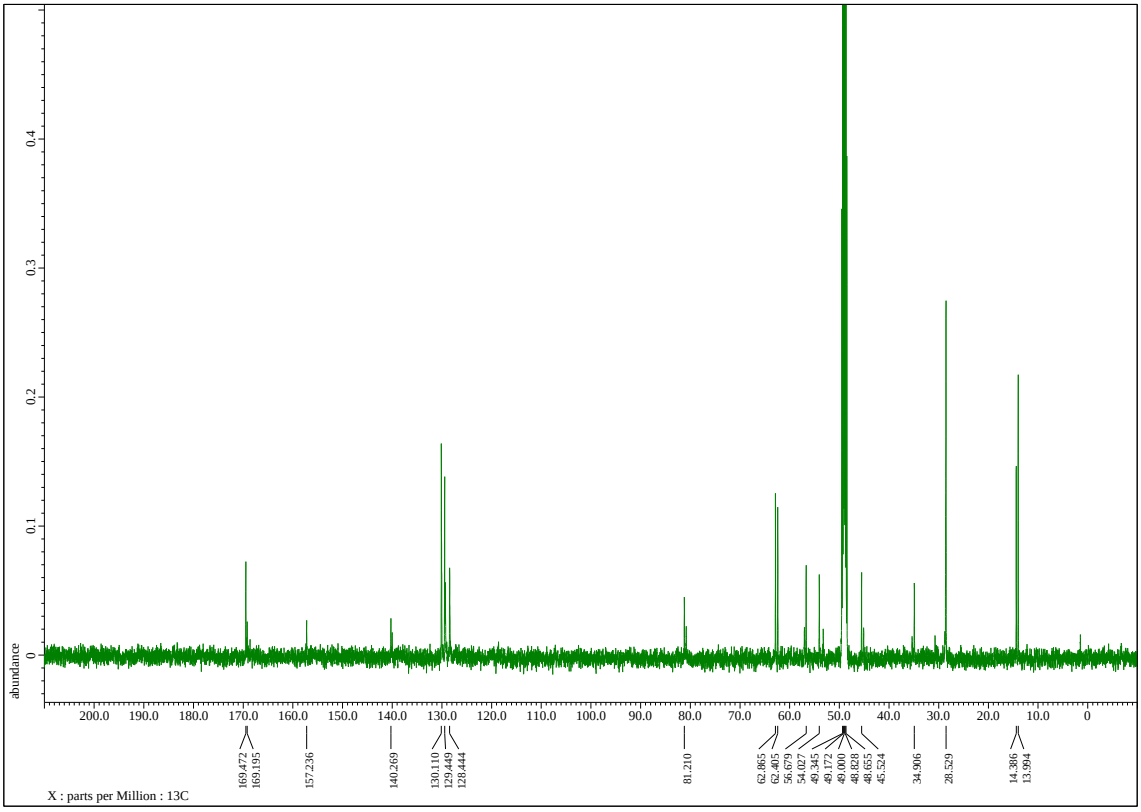
^{13}C NMR of spectrum of **7a** (125 MHz, $CDCl_3$, 50 °C)



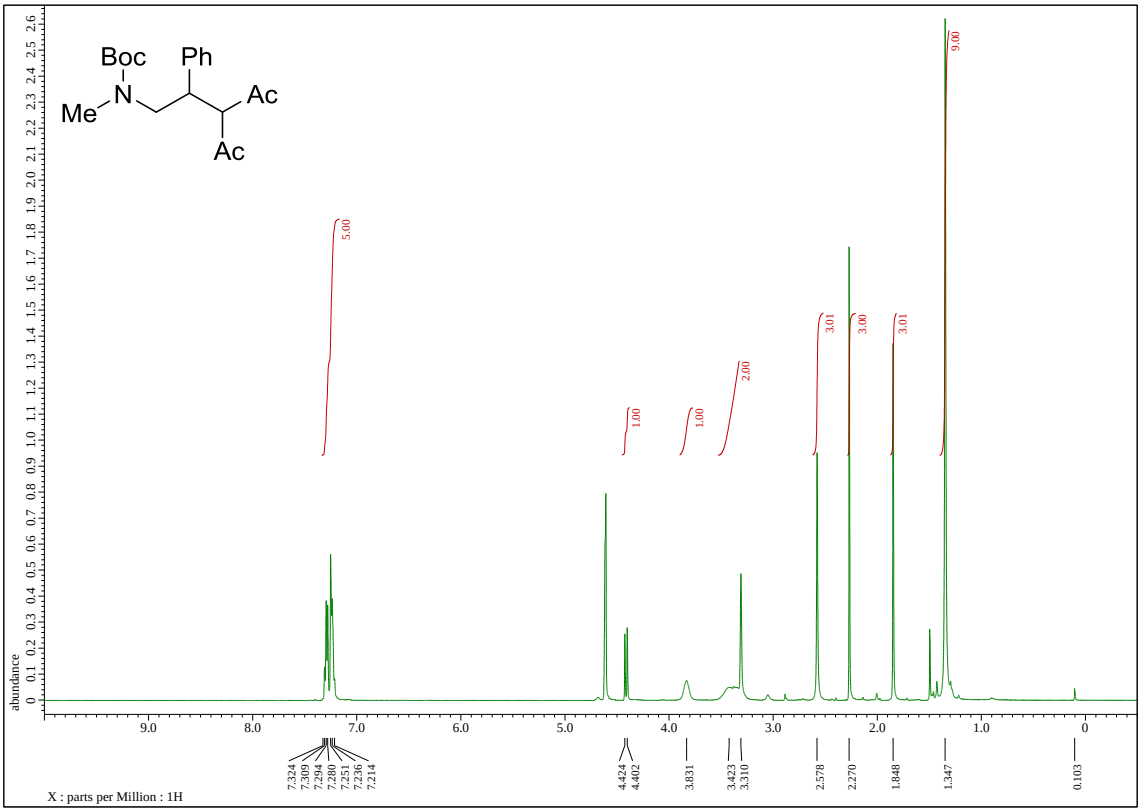
^{1}H NMR of spectrum of **7b** (500 MHz, $CDCl_3$, 50 °C)



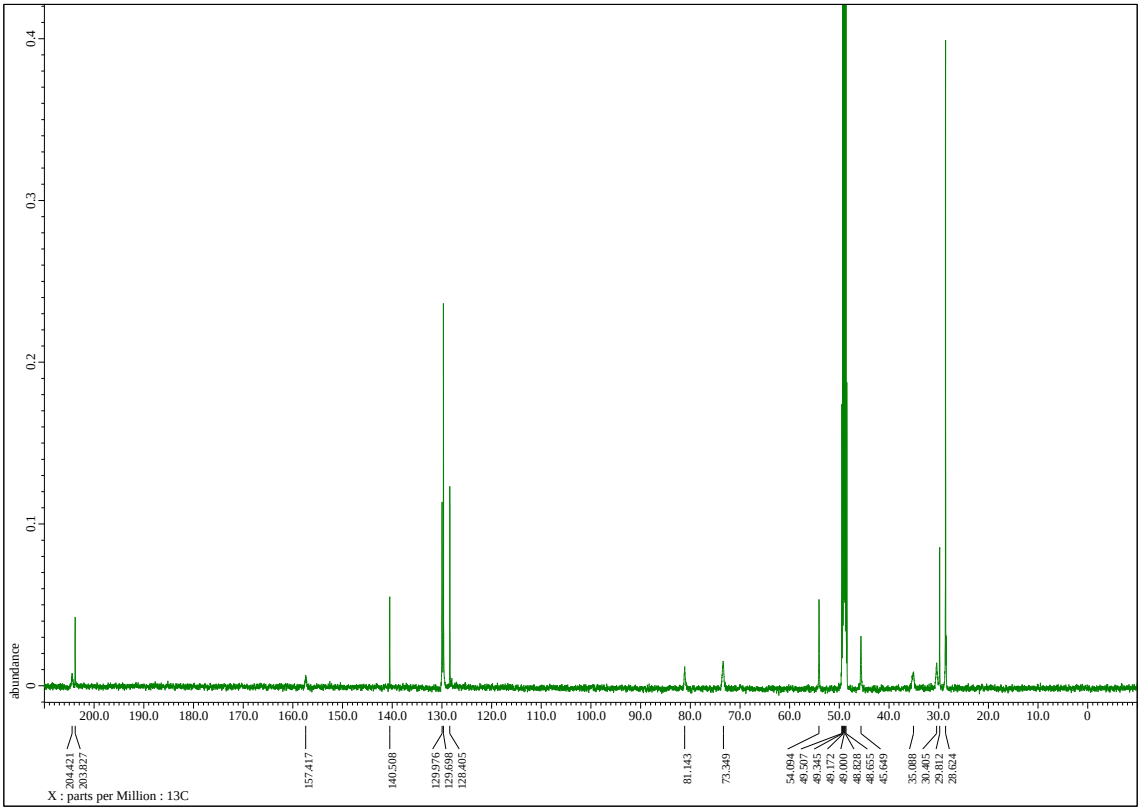
^{13}C NMR of spectrum of **7b** (125 MHz, $CDCl_3$, 50 °C)



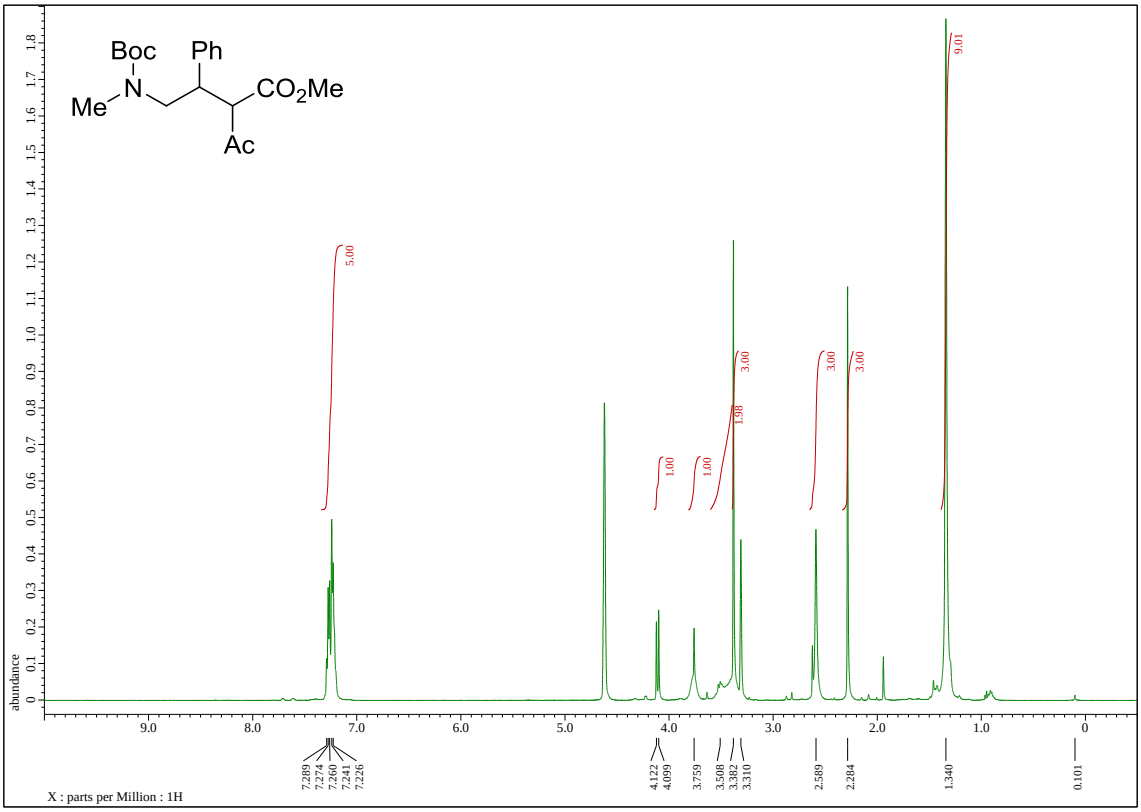
^{1}H NMR of spectrum of **7c** (500 MHz, CD_3OD, 50 °C)



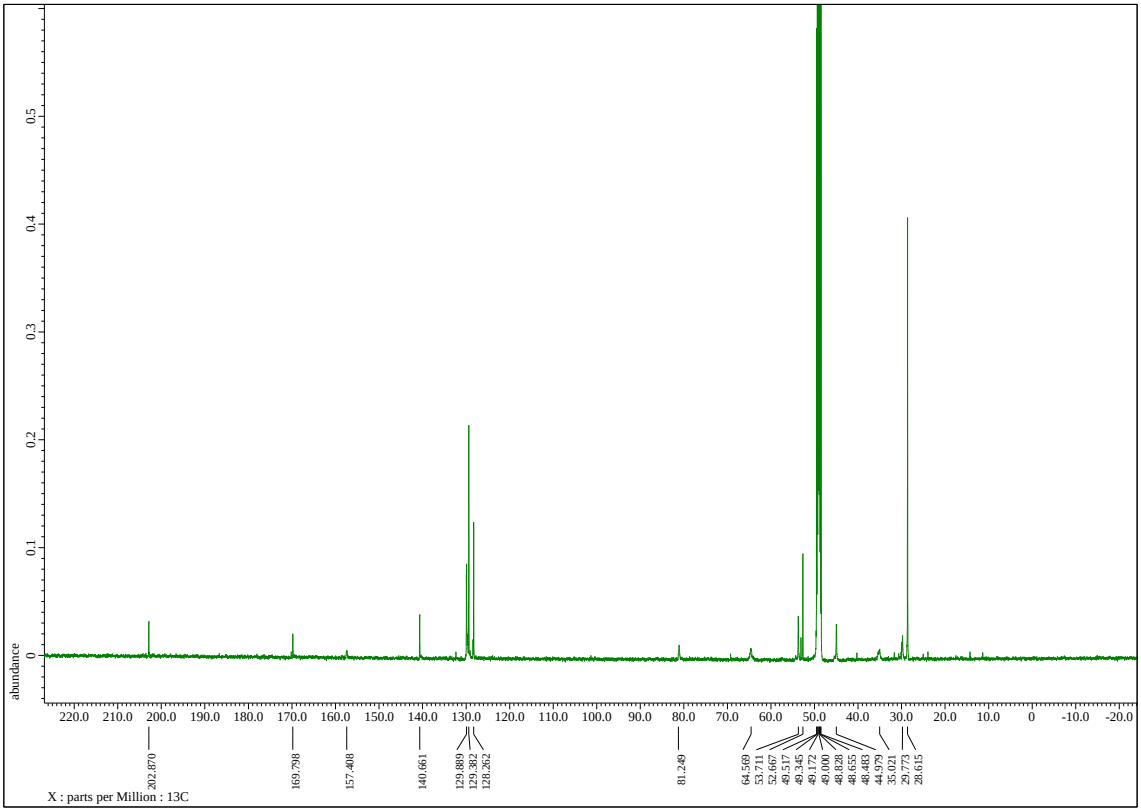
^{13}C NMR of spectrum of **7c** (125 MHz, CD_3OD, 50 °C)



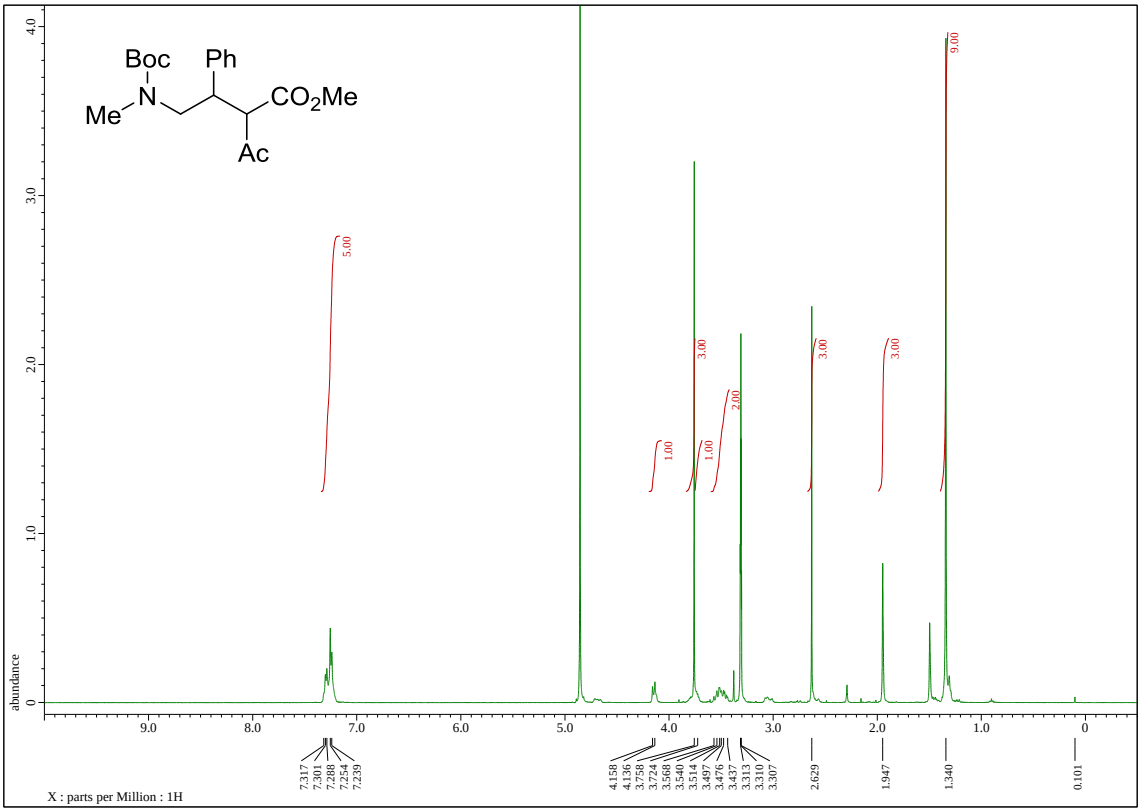
^{1}H NMR of spectrum of **7d** (Isomer a) (500 MHz, CD_3OD, 50 °C)



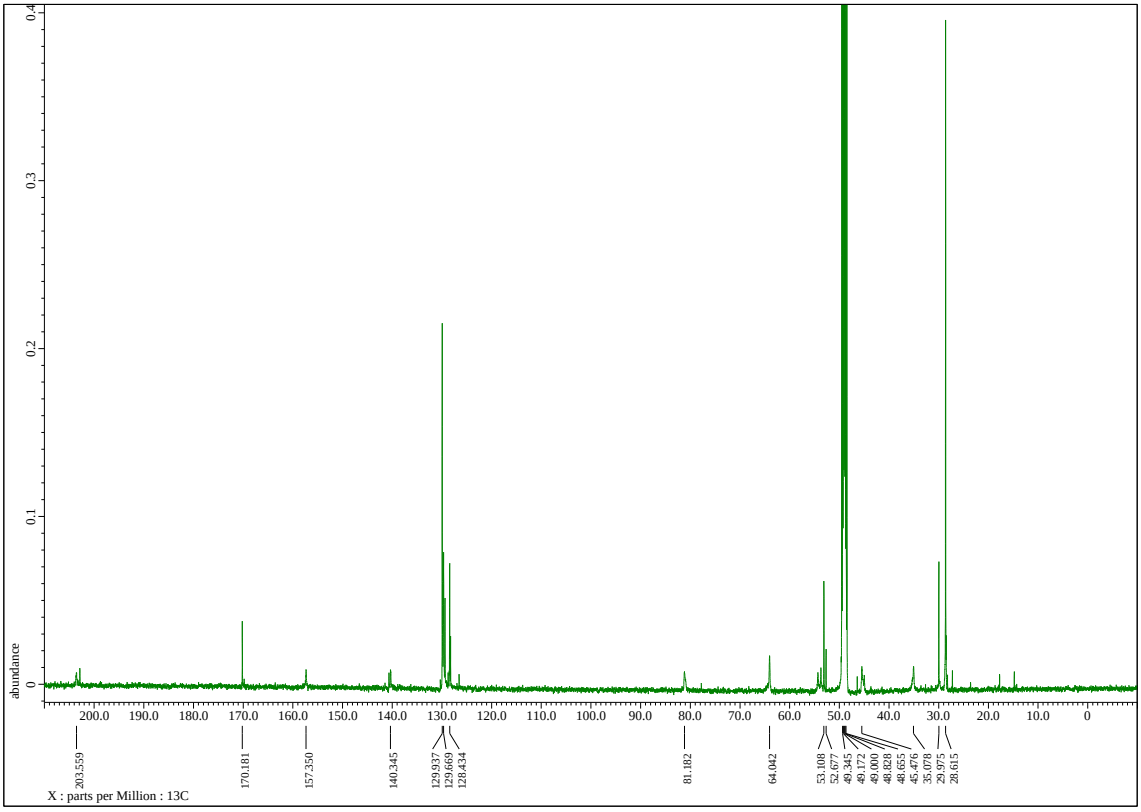
^{13}C NMR of spectrum of **7d** (Isomer a) (125 MHz, CD_3OD, 50 °C)



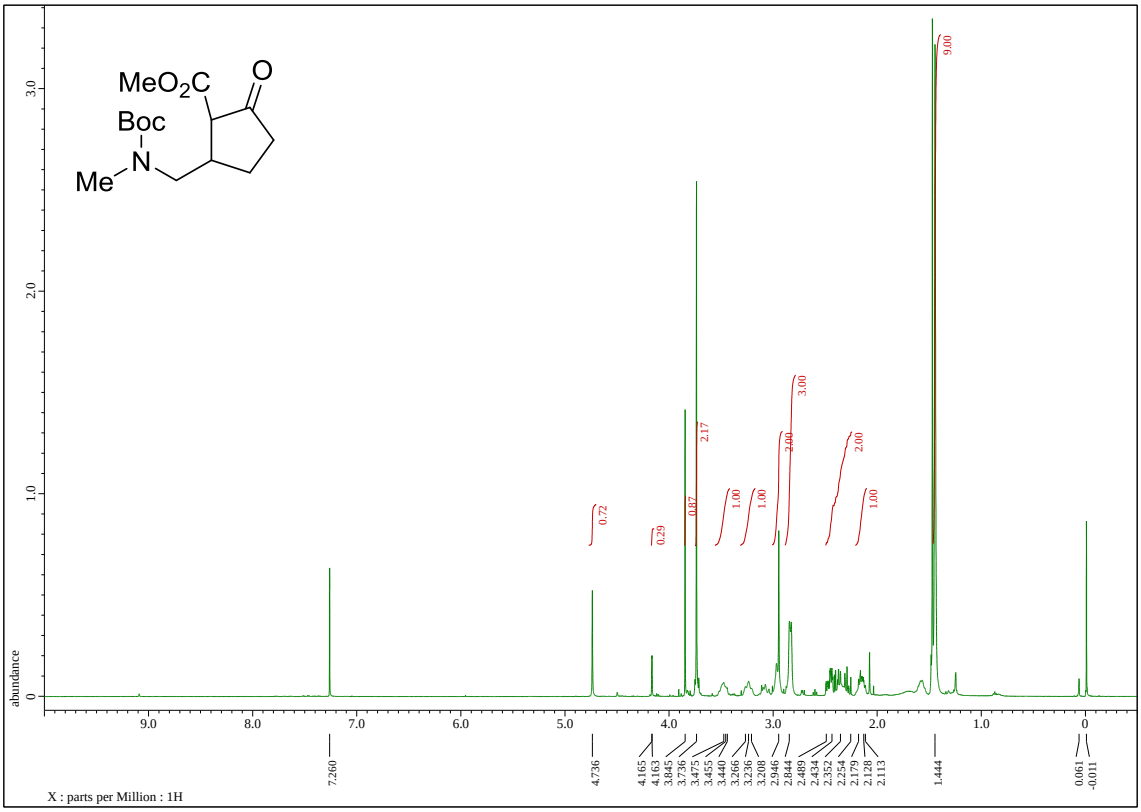
^{1}H NMR of spectrum of **7d** (Isomer b) (500 MHz, CD_3OD, 50 °C)



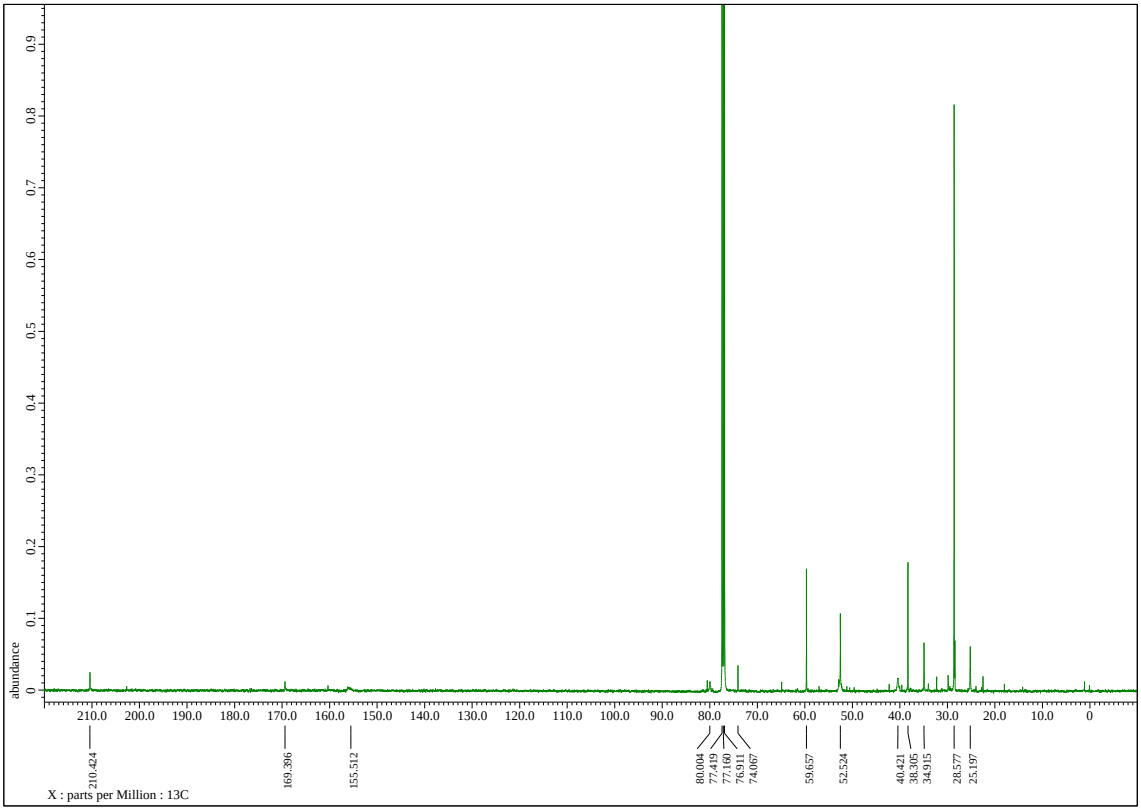
^{13}C NMR of spectrum of **7d** (Isomer b) (125 MHz, CD_3OD, 50 °C)



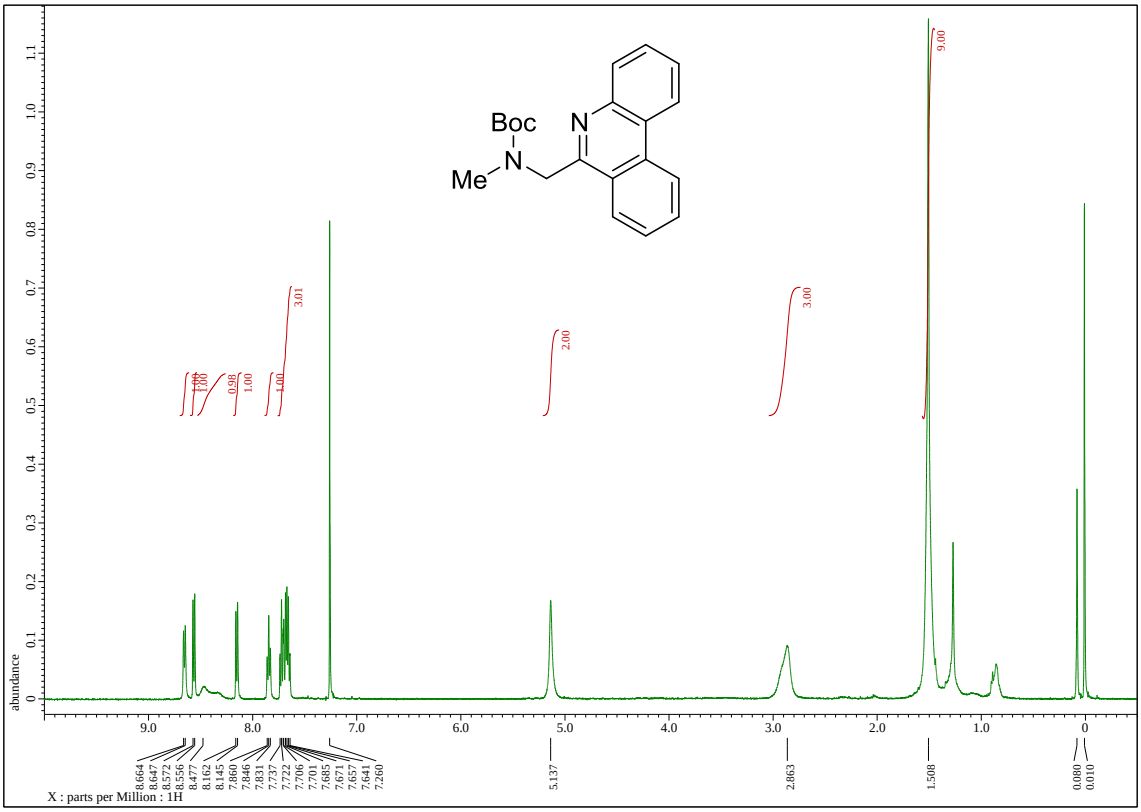
^{1}H NMR of spectrum of **7e** (500 MHz, $CDCl_3$, 50 °C)



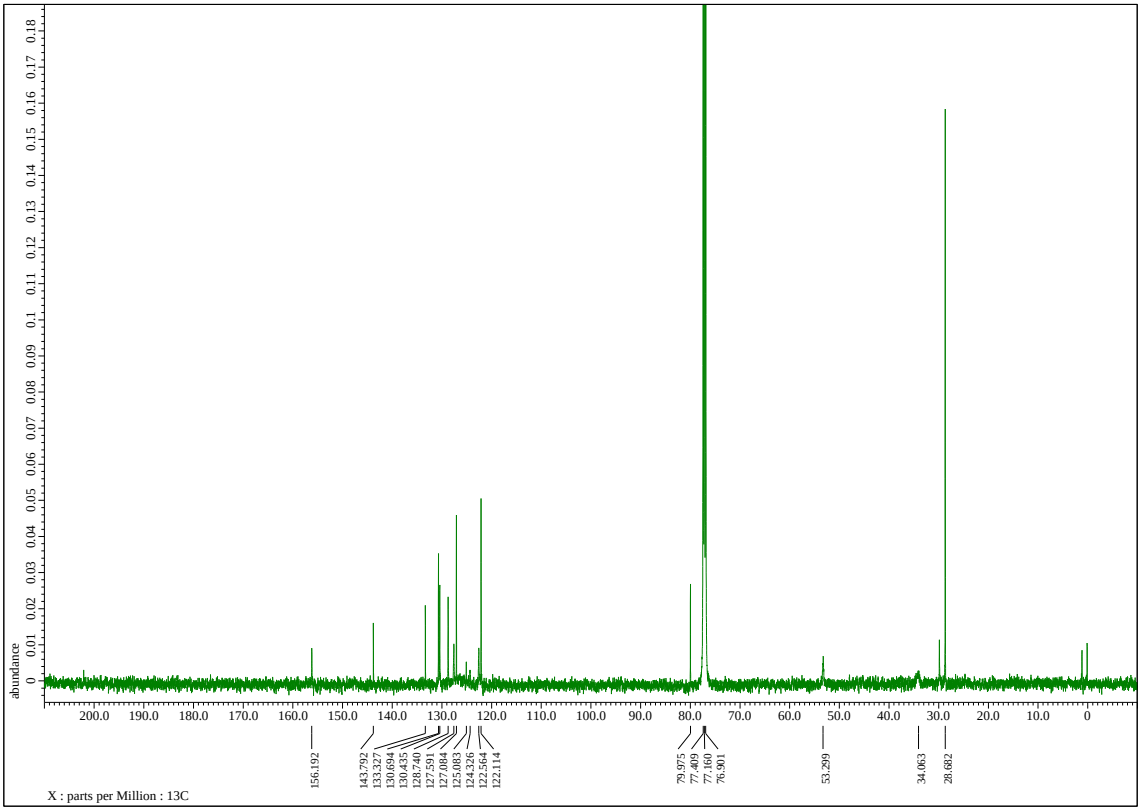
^{13}C NMR of spectrum of **7e** (125 MHz, $CDCl_3$, 50 °C)



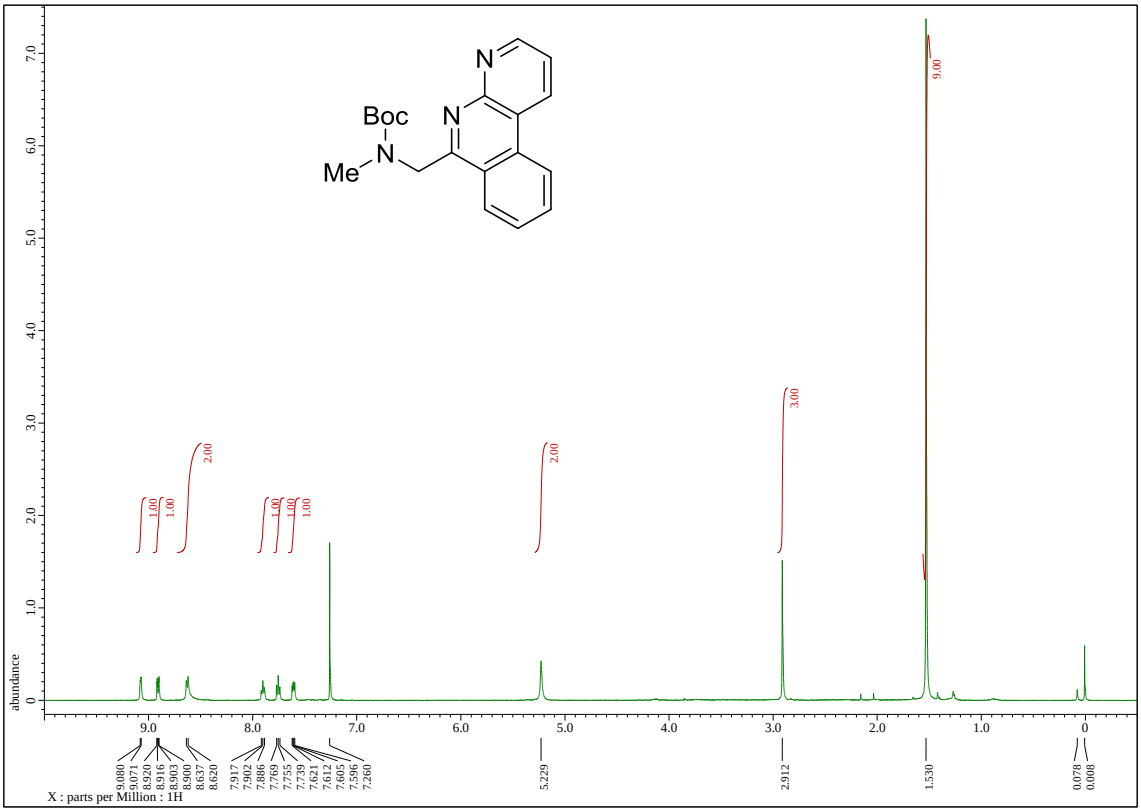
^{1}H NMR of spectrum of **8a** (500 MHz, $CDCl_3$, 50 °C)



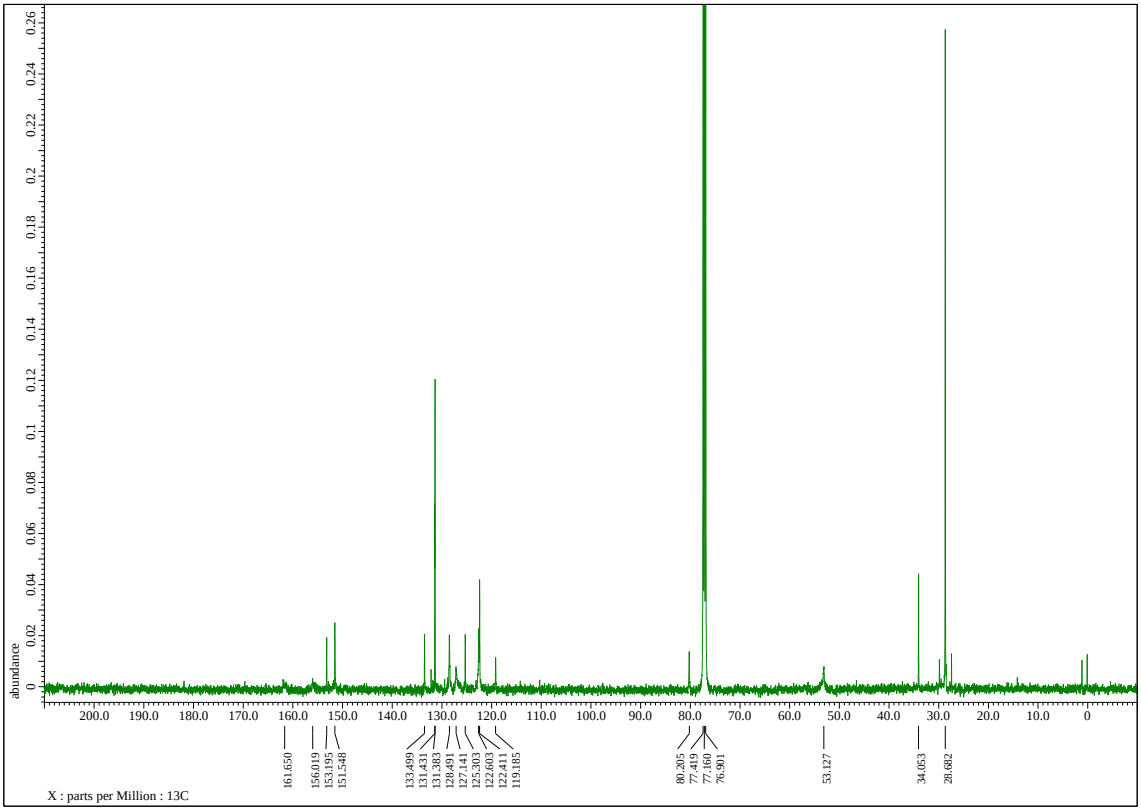
^{13}C NMR of spectrum of **8a** (125 MHz, $CDCl_3$, 50 °C)



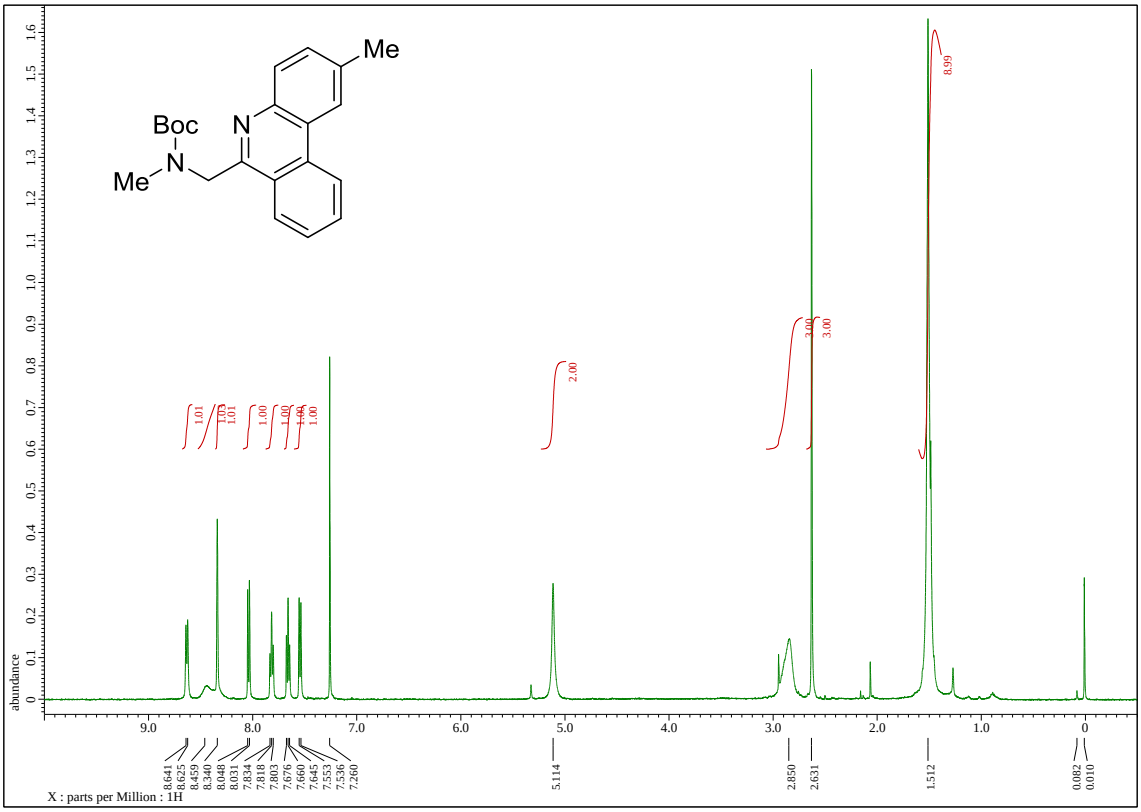
^{1}H NMR of spectrum of **8b** (500 MHz, $CDCl_3$, 50 °C)



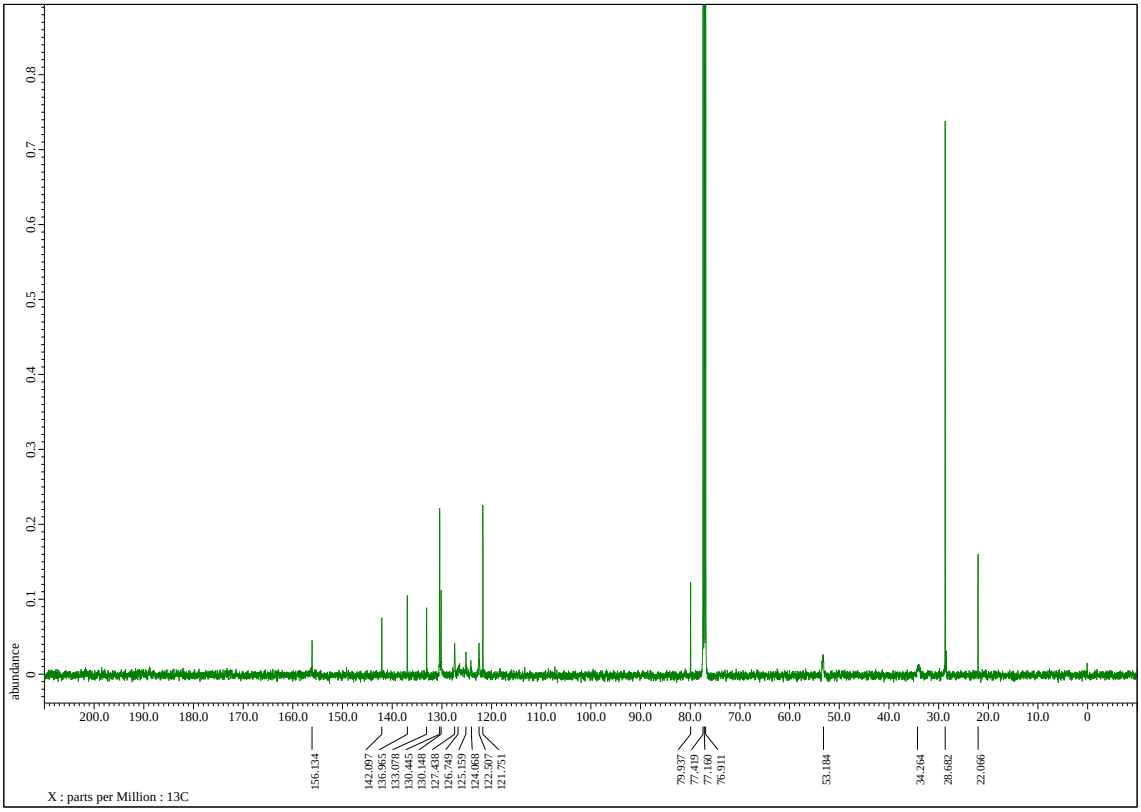
^{13}C NMR of spectrum of **8b** (125 MHz, $CDCl_3$, 50 °C)



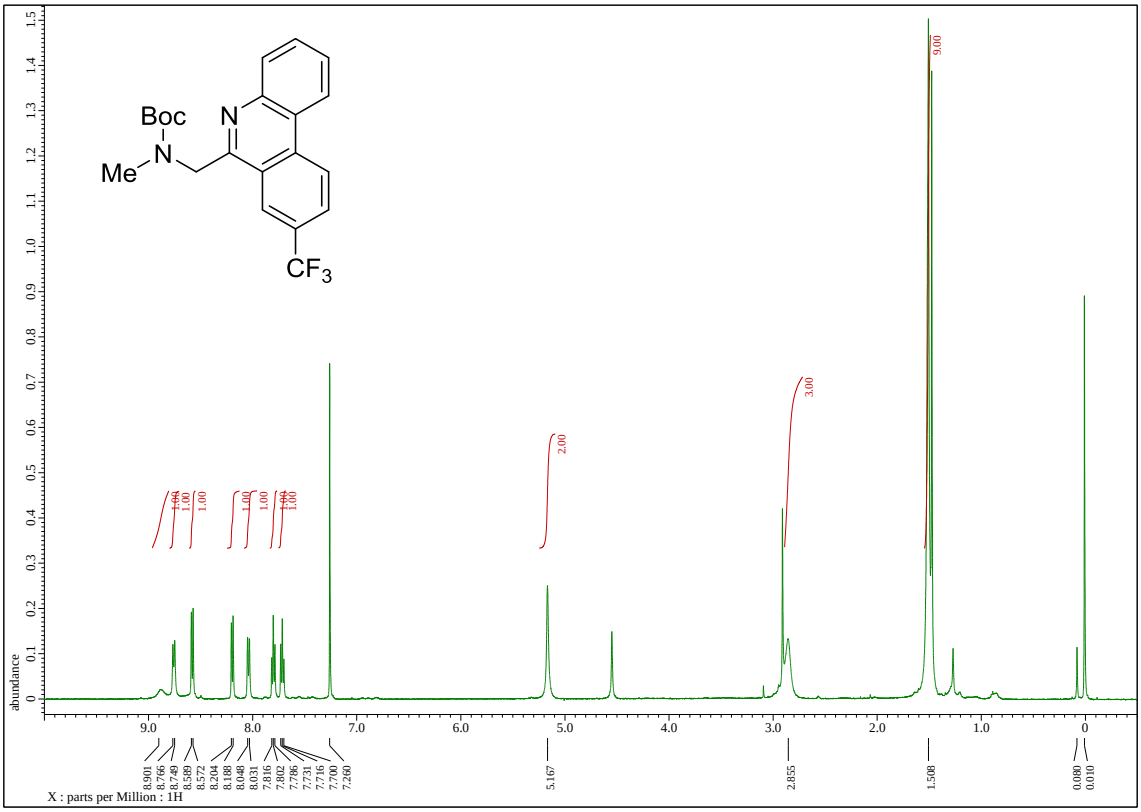
^{1}H NMR of spectrum of **8c** (500 MHz, $CDCl_3$, 50 °C)



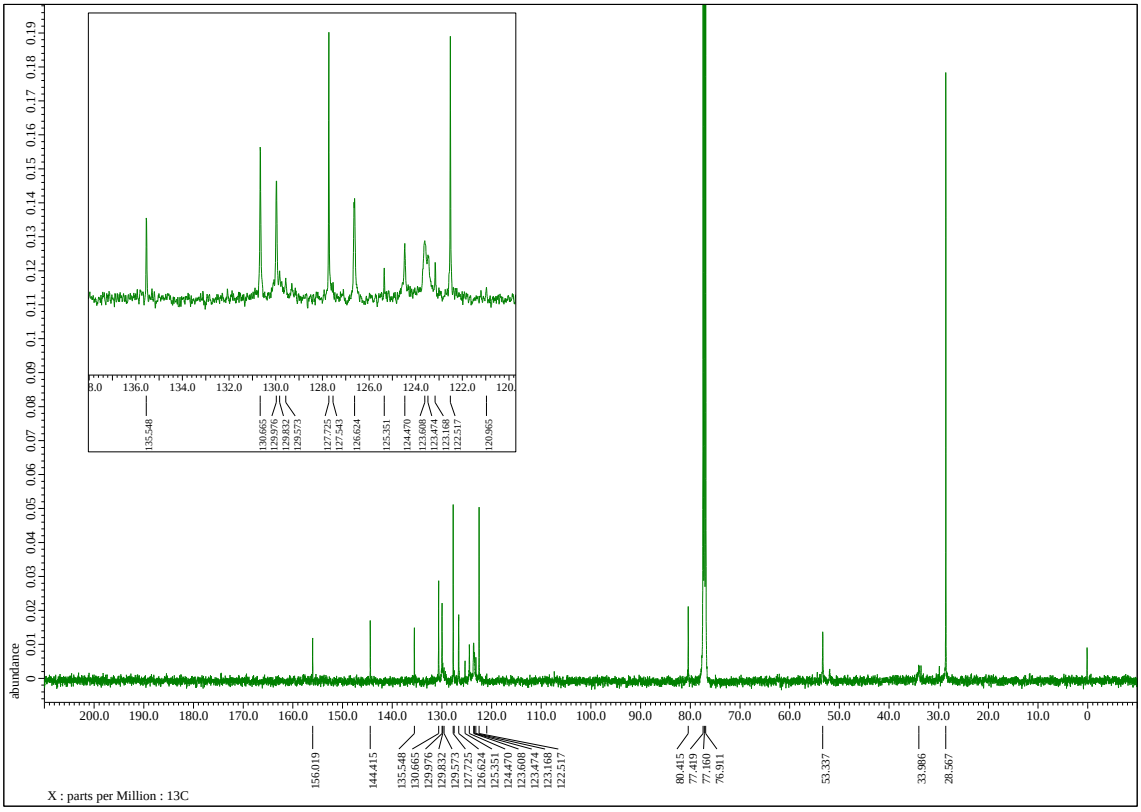
^{13}C NMR of spectrum of **8c** (125 MHz, $CDCl_3$, 50 °C)



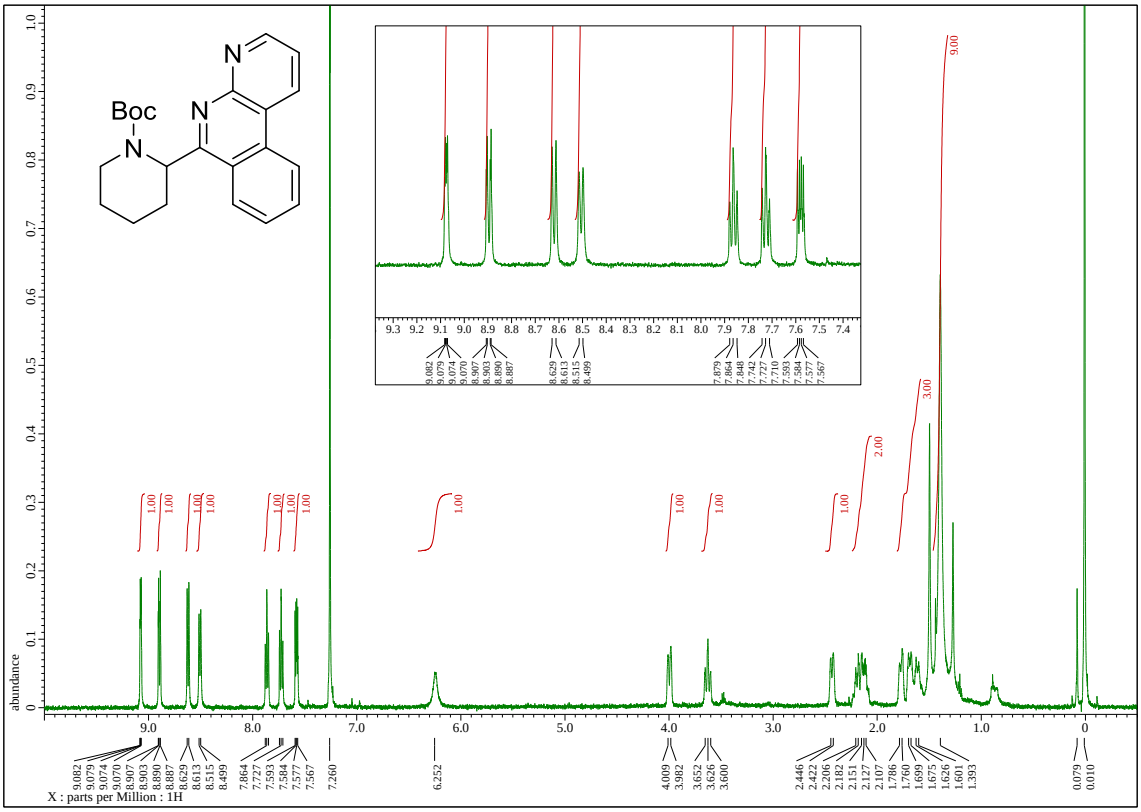
^{1}H NMR of spectrum of **8d** (500 MHz, $CDCl_3$, 50 °C)



^{13}C NMR of spectrum of **8d (**125 MHz, $CDCl_3$, 50 °C)



^{1}H NMR of spectrum of **8e** (500 MHz, $CDCl_3$, 50 °C)



^{13}C NMR of spectrum of **8e** (125 MHz, $CDCl_3$, 50 °C)