

Supporting Information

for

A Dual Arylboronic acid-Aminothiourea Catalytic System for the Asymmetric Intramolecular Hetero-Michael Reaction of α,β -Unsaturated Carboxylic Acids

Takumi Azuma[†], Akihiro Murata[†], Yusuke Kobayashi[†], Tsubasa Inokuma,^{†,‡} and Yoshiji Takemoto^{*,†}

[†]*Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyo-ku,
Kyoto 606-8501, Japan*

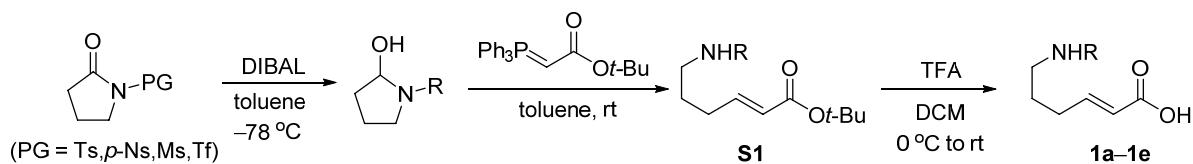
[‡]*Institute of Health Biosciences and Graduate School of Pharmaceutical Sciences, The
University of Tokushima, Shomachi, Tokushima 770-8505, Japan*

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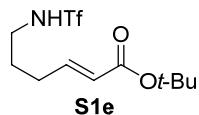
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1. General information: All non-aqueous reactions were carried out under a positive atmosphere of argon in dried glassware unless otherwise noted. Solvents and materials were obtained from commercial suppliers and used without further purification. Column chromatography was performed on Cica silica gel 60 (230–400 mesh) or Fuji Silysia silica gel (NH, 100–200 mesh), gel permeation chromatography was performed with LC-9201 and flash column chromatography was performed on Cica silica gel 60 (spherical/40–100 μ m). Reactions and chromatography fractions were analyzed employing pre-coated silica gel plate (Merck Silica Gel 60 F₂₅₄). All melting points were measured on BÜCHI M-565 melting point apparatus and are uncorrected. IR spectra were measured on JASCO FT/IR-4100. Unless otherwise noted, NMR spectra were obtained in CDCl_3 . ^1H NMR (500 MHz) spectra were recorded with JEOL ECP-500 spectrometers and chemical shifts are reported in δ (ppm) relative to TMS (in CDCl_3) as internal standard. Unless otherwise noted, ^{13}C NMR (126 MHz) spectra were also recorded using JEOL ECP-500 spectrometers and referenced to the residual CHCl_3 , $\text{CHD}_2\text{COCD}_3$, or CHD_2CN signals. ^1H NMR multiplicities are reported as follows: br = broad; m = multiplet; s = singlet; d = doublet; t = triplet; q = quartet; sep = septet. Low-resolution mass spectra were recorded on a JMS-HX/HX 110A or MS700 mass spectrometer. High-resolution mass spectra were obtained on a JMS-HX/MS700 (FAB) or a Shimazu LCMS-IT-TOF fitted with an ESI. Optical rotations were recorded on a JASCO P-2200 polarimeter with a path length of 1 cm; concentrations are quoted in grams per 100 mL. $[\alpha]_D$ values are measured in 10^{-1} deg cm^2g^{-1} . Enantiomeric excess was determined by high performance liquid chromatography (HPLC) analyses. Unless otherwise noted, all materials and solvent were purchased from Tokyo Kasei Co., Aldrich Inc., and other commercial suppliers and were used without purification. All non-commercially available substrates were prepared according to the literature procedure as indicated below.

2. Preparation of Substrates: α,β -Unsaturated carboxylic acids **1a–e** were generally prepared as indicated below.



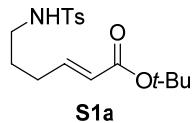
tert-Butyl (E)-6-(Trifluoromethylsulfonylamido)hex-2-enoate (S1e)



To a stirred solution of *N*-trifluoromethansulfonylpyrrolidone (850 mg, 3.9 mmol) in THF (20 mL) was added DIBAL (1.0 M solution in toluene, 4.0 mL) at -78°C . After being stirred at the same

temperature for 1 h, the reaction mixture was quenched with MeOH and a saturated potassium sodium tartrate solution, and the reaction mixture was warmed up to room temperature. The organic layer was separated and the aqueous layer was extracted with CHCl_3 twice. The combined organic extracts were washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. The crude hemiaminal (818 mg, ca. 3.73 mmol) was used for the next step without further purification. To a stirred solution of crude hemiaminal in toluene (25 mL) was added *tert*-butyl 2-(triphenylphosphoranylidene)acetate¹ (2.35 g, 6.24 mmol). After being stirred for 20 h, the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane : EtOAc = 7 : 1) to afford **S1e** (673 mg, 54% in 2 steps): colorless oil; ¹H NMR (CDCl_3) δ : 6.80 (dt, J = 15.5, 6.9 Hz, 1H), 5.79 (d, J = 15.5 Hz, 1H), 5.40–5.22 (br m, 1H), 3.36–3.29 (m, 2H), 2.31–2.23 (m, 2H), 1.82–1.76 (m, 2H), 1.48 (s, 9H) ppm; ¹³C NMR (CDCl_3) δ : 165.9, 145.3, 124.3, 119.7 (q, J_{C-F} = 323 Hz), 80.7, 43.8, 28.7, 28.6, 28.1 ppm; IR (ATR): 3205, 2981, 2940, 1691, 1372 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{11}\text{H}_{18}\text{NO}_4\text{F}_3\text{SNa}$ $[\text{M}+\text{Na}]^+$ 340.0801, found 340.0802.

***tert*-Butyl (E)-6-(4-Methylphenylsulfonamido)hex-2-enoate (S1a)**



A procedure similar to that described for the preparation of **S1e** afforded **S1a** (695 mg, 94% in 2 steps): colorless amorphous; ¹H NMR (CDCl_3) δ : 7.75 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 6.73 (dt, J = 15.5, 6.9 Hz, 1H), 5.68 (dt, J = 15.5, 1.6 Hz, 1H), 4.66 (t, J = 6.3 Hz, 1H), 2.98–2.92 (m, 2H), 2.43 (s, 3H), 2.20–2.13 (m, 2H), 1.65–1.58 (m, 2H), 1.47 (s, 9H) ppm; ¹³C NMR (CDCl_3) δ : 165.8, 145.9, 143.5, 136.8, 129.7, 127.1, 123.9, 80.3, 42.5, 28.9, 28.1, 28.1, 21.5 ppm; IR (ATR): 3253, 2980, 2933, 2874, 1704, 1323, 1144 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{17}\text{H}_{25}\text{NO}_4\text{SNa}$ $[\text{M}+\text{Na}]^+$ 362.1397, found 362.1408.

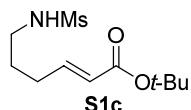
***tert*-Butyl (E)-6-[(Benzylxy)carbonyl]amino]hex-2-enoate (S1b)**



A procedure similar to that described for the preparation of **S1e** afforded **S1b** (313 mg, 78% in 2

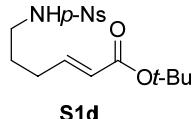
steps): colorless oil; ^1H NMR (CDCl_3) δ : 7.36–7.32 (5H, m), 6.82 (1H, dt, J = 15.8, 7.0 Hz), 5.75 (1H, d, J = 15.8 Hz), 5.10 (2H, s), 4.76 (1H, br s), 3.24–3.20 (2H, m), 2.23–2.19 (2H, m), 1.69–1.65 (2H, m), 1.48 (9H, s) ppm; ^{13}C NMR (CDCl_3) δ : ^{13}C -NMR (CDCl_3) δ : 165.8, 156.3, 146.4, 136.5, 128.5, 128.4, 128.1, 123.6, 80.1, 66.6, 40.4, 29.1, 28.4, 28.1; IR (ATR): 3342, 2977, 1705, 1699 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{18}\text{H}_{25}\text{NO}_4\text{Na}$ $[\text{M}+\text{Na}]^+$ 342.1676, found 343.1683.

tert-Butyl (E)-6-(Methylsulfonamido)hex-2-enoate (S1c)



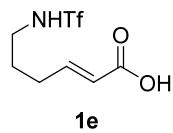
A procedure similar to that described for the preparation of **S1e** afforded **S1c** (454 mg, 24% in 2 steps): white solid; mp 42–44 °C (EtOAc : hexane); ^1H NMR (CDCl_3) δ : 6.84–6.79 (m, 1H), 5.78 (d, J = 15.5 Hz, 1H), 4.53–4.45 (br m, 1H), 3.19–3.12 (m, 2H), 2.96 (s, 3H), 2.30–2.23 (m, 2H), 1.77–1.72 (m, 2H), 1.48 (s, 9H) ppm; ^{13}C NMR (CDCl_3) δ : 165.8, 145.8, 124.1, 80.3, 42.6, 40.4, 28.9, 28.6, 28.1 ppm; IR (ATR): 3283, 2978, 1710 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{11}\text{H}_{21}\text{NO}_4\text{SNa}$ $[\text{M}+\text{Na}]^+$ 286.1084, found 286.1085.

tert-Butyl (E)-6-(4-nitrophenylsulfonamido)hex-2-enoate (S1d)



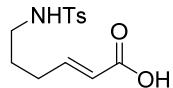
A procedure similar to that described for the preparation of **S1e** afforded **S1d** (540 mg, 46% in 2 steps): yellow solid; mp 103–104 °C (EtOAc : hexane); ^1H NMR (CDCl_3) δ : 8.38 (d, J = 8.6 Hz, 2H), 8.06 (d, J = 8.6 Hz, 2H), 6.74 (dt, J = 15.5, 6.9 Hz, 1H), 5.71 (dt, J = 15.6, 1.4 Hz, 1H), 4.88 (t, J = 5.7 Hz, 1H), 3.08–3.00 (m, 2H), 2.23–2.18 (m, 2H), 1.71–1.64 (m, 2H), 1.47 (s, 9H) ppm; ^{13}C NMR (CDCl_3) δ : 165.7, 150.1, 145.9, 145.4, 128.3, 124.5, 124.2, 80.5, 42.7, 28.7, 28.2, 28.1 ppm; IR (ATR): 3261, 2981, 2939, 1524, 1335 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{16}\text{H}_{22}\text{N}_2\text{O}_6\text{SNa}$ $[\text{M}+\text{Na}]^+$ 393.1091, found 393.1108.

(E)-6-(Trifluoromethylsulfonamido)hex-2-enoic Acid (1e)



To a stirred solution of **S1e** (339 mg, 1.06 mmol) in DCM (7 mL) was added TFA (1.6 mL) dropwise at 0 °C. After being stirred for 1 h, the reaction mixture was warmed up to room temperature. After 3 h, the reaction mixture was concentrated *in vacuo*. After the addition of hexane to the residue, the solvent was evaporated at 40 °C to remove the residual TFA. The same manipulation was conducted once again with hexane and twice with toluene. The residue was recrystallized (EtOAc : hexane) to give **1e** (234 mg, 84%): white solid; mp 96–97 °C (EtOAc : hexane); ¹H NMR (acetone-*d*6) δ: 6.94 (dt, *J* = 15.3, 7.0 Hz, 1H), 5.88 (d, *J* = 15.5 Hz, 1H), 3.38 (t, *J* = 7.2 Hz, 2H), 2.40–2.33 (m, 2H), 1.87–1.81 (m, 2H) ppm; ¹³C NMR (acetone-*d*6) δ: 167.2, 148.5, 123.0, 120.9 (q, *J*_{C-F} = 322 Hz), 44.3, 29.3 ppm (One carbon was overlapped with solvent signals); IR (ATR): 3299, 2957, 1686 cm⁻¹; HRMS (ESI): calcd. for C₇H₁₀NO₄F₃SnNa [M+Na]⁺ 284.0175, found 284.0175.

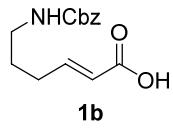
(E)-6-(4-Methylphenylsulfonamido)hex-2-enoic Acid (1a)



1a

A procedure similar to that described for the preparation of **1e** afforded **1a** (1.02 g, 91%): white solid; mp 136–137 °C (EtOAc : hexane); ¹H NMR (acetone-*d*6) δ: 7.73 (d, *J* = 8.3 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 6.86 (dt, *J* = 15.7, 7.0 Hz, 1H), 6.46–6.38 (br m, 1H), 5.78 (dt, *J* = 15.6, 1.6 Hz, 1H), 2.97–2.88 (m, 2H), 2.41 (s, 3H), 2.28–2.22 (m, 2H), 1.69–1.62 (m, 2H) ppm; ¹³C NMR (acetone-*d*6) δ: 167.2, 149.0, 143.7, 139.1, 130.4, 127.7, 122.7, 43.2, 29.6, 28.8, 21.3 ppm; IR (ATR): 3289, 3245, 2873, 2834, 1687, 1642 cm⁻¹; HRMS (ESI): calcd. for C₁₃H₁₇NO₄SnNa [M+Na]⁺ 306.0771, found 306.0772.

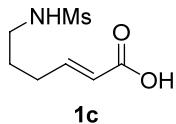
(E)-6-[(Benzoyloxy)carbonyl]amino]hex-2-enoic Acid (1b):



1b

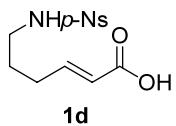
A procedure similar to that described for the preparation of **1e** afforded **1b** (102 mg, 94%): white solid; mp 77–78 °C; ¹H NMR (CDCl₃) δ 7.39–7.29 (m, 5H), 7.09–6.99 (m, 1H), 5.85 (d, *J* = 15.5 Hz, 1H), 5.10 (s, 2H), 4.83 (br s, 1H), 3.26–3.14 (m, 2H), 2.31–2.20 (m, 2H), 1.74–1.63 (m, 2H). ¹³C NMR (CDCl₃) δ 171.1, 156.4, 150.5, 136.4, 128.5, 128.2, 128.1, 121.4, 66.8, 40.4, 29.4, 28.3; IR (ATR): 3329, 2942, 1695, 1653 cm⁻¹; HRMS (ESI): calcd. for C₁₄H₁₆NO₄ [M-H]⁻ 262.1085, found 263.1083.

(E)-6-(Methylsulfonamido)hex-2-enoic Acid (1c)



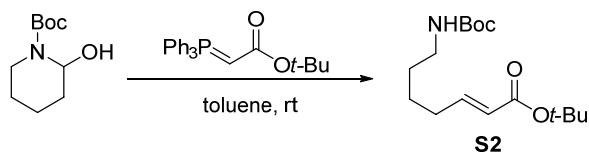
A procedure similar to that described for the preparation of **1e** afforded **1c** (227 mg, 99%): white solid; mp 95–96 °C (EtOAc : hexane); ¹H NMR (acetone-*d*6) δ: 10.51 (br s, 1H), 6.98–6.91 (m, 1H), 6.06–5.95 (br m, 1H), 5.86 (d, *J* = 15.7 Hz, 1H), 3.20–3.10 (m, 2H), 2.91 (s, 3H), 2.38–2.29 (m, 2H), 1.79–1.72 (m, 2H) ppm; ¹³C NMR (acetone-*d*6) δ: 167.4, 149.2, 122.7, 43.2, 39.9, 39.8, 29.3 ppm; IR (ATR): 3262, 2952, 1689, 1655 cm^{−1}; HRMS (ESI): calcd. for C₇H₁₃NO₄SnNa [M+Na]⁺ 230.0458, found 230.0458.

(E)-6-(4-Nitrophenylsulfonamido)hex-2-enoic Acid (1d)



A procedure similar to that described for the preparation of **1e** afforded **1d** (444 mg, 99%): white solid; mp 165–166 °C (EtOAc : hexane); ¹H NMR (acetone-*d*6) δ: 8.43 (d, *J* = 8.6 Hz, 2H), 8.13 (d, *J* = 8.9 Hz, 2H), 6.89 (t, *J* = 5.6 Hz, 1H), 6.84 (dt, *J* = 15.7, 6.9 Hz, 1H), 5.76 (dt, *J* = 15.7, 1.6 Hz, 1H), 3.08–3.02 (m, 2H), 2.30–2.23 (m, 2H), 1.72–1.66 (m, 2H) ppm; ¹³C NMR (acetone-*d*6) δ: 167.1, 150.9, 148.8, 147.6, 129.2, 125.2, 122.8, 81.7, 43.2, 28.8 ppm; IR (ATR): 3255, 3105, 3084, 2877, 2840, 1692, 1531 cm^{−1}; HRMS (ESI): calcd. for C₁₂H₁₄N₂O₆SnNa [M+Na]⁺ 337.0465, found 337.0469.

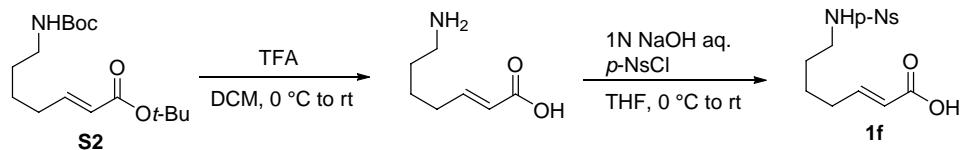
tert-Butyl (E)-7-[(tert-Butoxycarbonyl)amino]hept-2-enoate (S2)



To a stirred solution of *tert*-butyl 2-hydroxypiperidine-1-carboxylate² (275 mg, 1.37 mmol) in toluene (8 mL) was added *tert*-butyl 2-(triphenylphosphoranylidene)acetate (572 mg, 1.5 mmol) in toluene (5 mL) at room temperature. After being stirred at room temperature for 6 h, the reaction mixture was warmed up to 50 °C. After being stirred for 16 h at the same temperature, the reation mixture was concentrated *in vacuo*. The crude product was purified by column chlomatography on

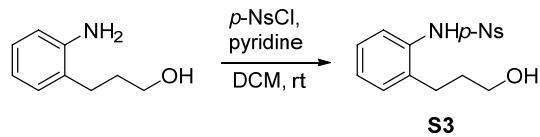
silica gel (hexane : EtOAc = 6 : 1) to afford **S2** (204 mg, 50%): colorless amorphous; ¹H NMR (CDCl₃) δ: 6.86–6.80 (m, 1H), 5.74 (d, *J* = 15.8 Hz, 1H), 4.51 (br s, 1H), 3.16–3.08 (m, 2H), 2.23–2.15 (m, 2H), 1.48 (s, 9H), 1.44 (s, 9H) ppm; ¹³C NMR (CDCl₃) δ: 166.0, 155.9, 147.3, 123.3, 80.0, 79.0, 40.2, 31.5, 29.6, 28.4, 28.1, 25.2 ppm; IR (ATR): 3372, 2978, 2936, 1703, 1171 cm⁻¹; HRMS (ESI): calcd. for C₁₆H₂₉NO₄Na [M+Na]⁺ 322.1989, found 322.1991.

tert-Butyl (E)-7-(4-nitrophenylsulfonamido)hept-2-enoate (1f)



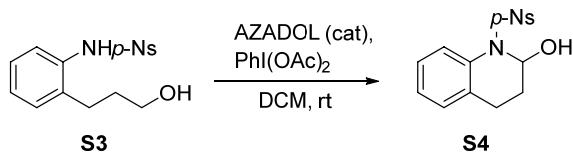
To a stirred solution of **S2** (0.683 mmol, 204 mg) in DCM (20 mL) was added TFA (2.5 mL) at 0 °C. After being stirred for 4 h at the same temperature, the reaction mixture was concentrated *in vacuo* to afford the crude product as colorless oil, which was used for the next step without further purification. To a stirred solution of the crude aminocarboxylic acid (98 mg, ca. 0.683 mmol) in THF (20 mL) were added 1N aqueous NaOH solution (2.0 mL) and *p*-NsCl (1.02 mmol, 227 mg) at 0 °C and the reaction mixture was stirred for 2 h. After the reaction mixture was warmed up to room temperature and stirred for 2 h, the mixture was acidified to pH 1.0 with 1N aqueous HCl solution and diluted with EtOAc. The organic layer was separated and the aqueous layer was extracted with EtOAc twice. The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel (hexane : EtOAc : CH₃COOH = 16 : 4 : 1) to afford **1f** (60 mg, 27% in 2 steps): yellow solid; mp 139–140 °C (EtOAc : hexane); ¹H NMR (acetone-*d*6) δ: 8.44 (d, *J* = 8.9 Hz, 2H), 8.13 (d, *J* = 8.9 Hz, 2H), 6.91–6.81 (m, 2H), 5.77 (d, *J* = 15.8 Hz, 1H), 3.07–3.00 (m, 2H), 2.23–2.15 (m, 2H), 1.58–1.45 (m, 4H) ppm; ¹³C NMR (acetone-*d*6) δ: 167.4, 150.9, 149.6, 147.7, 129.1, 125.2, 122.5, 43.6, 31.9, 29.7, 25.6 ppm; IR (ATR): 3268, 2942, 2868, 1688, 1641, 1529, 1167 cm⁻¹; HRMS (ESI): calcd. for C₁₃H₁₆N₂O₆Na [M+Na]⁺ 351.0621, found 351.0620.

N-[2-(3-Hydroxypropyl)phenyl]-4-nitrobenzenesulfonamide (S3)



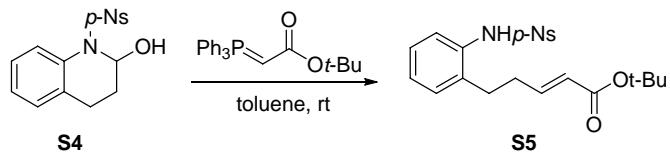
To a solution of 3-(2-aminophenyl)propan-1-ol³ (1.26 g, 8.33 mmol) in DCM (50 mL), was added *p*-NsCl (1.1 eq) in DCM (40 mL) at room temperature. After being stirred for 14 h, the reaction mixture was quenched with 1N HCl aq. and diluted with water and CHCl₃. The organic layer was separated and the aqueous layer was extracted with CHCl₃ twice. The combined organic extracts were washed with brine, dried over Na₂SO₄, and concentrated *in vacuo*. The crude product was recrystallized (EtOAc : hexane) to give **S3** (2.2 g, 78%): white solid; mp 132–133 °C (EtOAc : hexane); ¹H NMR (CDCl₃) δ: 8.79 (s, 1H), 8.26 (d, *J* = 9.2 Hz, 2H), 7.89 (d, *J* = 9.2 Hz, 2H), 7.52–7.48 (m, 1H), 7.25–7.20 (m, 1H), 7.18–7.13 (m, 1H), 7.10–7.05 (m, 1H), 3.51 (t, *J* = 5.4 Hz, 2H), 2.30 (t, *J* = 6.6 Hz, 2H), 2.07 (s, 1H), 1.75–1.70 (m, 2H) ppm; ¹³C NMR (CDCl₃) δ: 150.0, 145.8, 134.6, 134.3, 130.5, 128.2, 127.5, 126.8, 124.9, 124.1, 59.6, 31.9, 25.6 ppm; IR (ATR): 3549, 3106, 1523 cm^{−1}; HRMS (ESI): calcd. for C₁₅H₁₅N₂O₅S [M–H][−] 335.0707, found 335.0707.

1-(4-Nitrophenylsulfonyl)-1,2,3,4-tetrahydroquinolin-2-ol (**S4**)



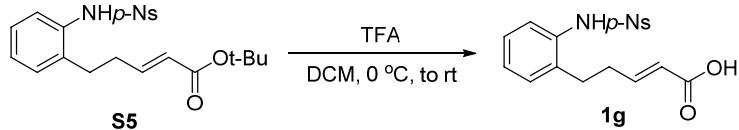
To a solution of **S3** (2.2 g, 6.54 mmol) in DCM (80 mL), were added AZADOL (50 mg, 0.33 mmol) and PhI(OAc)₂ (2.32 g, 7.19 mmol). After being stirred for 3 h, the mixture was quenched with saturated Na₂S₂O₃ aq. (30 mL) and NaHCO₃ aq. (30 mL). The organic layer was separated and the aqueous layer was extracted with CHCl₃ twice. The combined organic extracts were washed with brine, dried over Na₂SO₄, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel (hexane : EtOAc = 4 : 1 → 7 : 2) to afford **S4** (1.5 g, 69 %): yellow amorphous; ¹H NMR (CDCl₃) δ: 8.25 (d, *J* = 8.0 Hz, 2H), 7.77 (d, *J* = 7.4 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.28–7.22 (m, 2H), 7.13 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.05 (d, *J* = 7.4 Hz, 1H), 5.86–5.78 (br m, 1H), 3.44 (s, 1H), 2.55–2.45 (m, 1H), 2.23–2.13 (m, 1H), 1.86–1.74 (m, 2H) ppm; ¹³C NMR (CDCl₃) δ: 150.2, 144.4, 134.0, 132.7, 128.1, 128.0, 127.5, 126.0, 124.6, 124.3, 81.0, 30.9, 23.8 ppm; IR (ATR): 3519, 3106, 1529 cm^{−1}; HRMS (ESI): calcd. for C₁₅H₁₄N₂O₅SNa [M+Na]⁺ 357.0516, found 357.0514.

tert-Butyl (E)-5-[2-(4-Nitrophenylsulfonamido)phenyl]pent-2-enoate (**S5**)



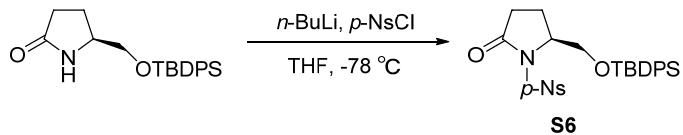
To a solution of **S4** (1.5 g, 4.49 mmol) in toluene (30 mL), was added *tert*-butyl 2-(triphenylphosphoranylidene)acetate (3.36 g, 8.88 mmol) at room temperature. After being stirred for 20 h, the mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane : EtOAc = 4 : 1) to afford **S5** (1.83 g, 94 %): white solid; mp 131–132 °C (EtOAc : hexane); ¹H NMR (CDCl₃) δ: 8.31 (d, *J* = 8.6 Hz, 2H), 7.92 (d, *J* = 8.9 Hz, 2H), 7.25–7.13 (m, 3H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.76 (dt, *J* = 15.7, 6.9 Hz, 1H), 6.43 (br s, 1H), 5.69 (d, *J* = 15.5 Hz, 1H), 2.63 (t, *J* = 7.9 Hz, 2H), 2.38–2.31 (m, 2H), 1.49 (s, 9H) ppm; ¹³C NMR (CDCl₃) δ: 165.8, 150.2, 145.6, 145.2, 136.6, 132.8, 130.1, 128.6, 128.0, 127.5, 126.2, 124.3, 124.1, 80.5, 32.2, 29.4, 28.1 ppm; IR (ATR): 3106, 2978, 1676, 1530 cm^{−1}; HRMS (ESI): calcd. for C₂₁H₂₄N₂O₆SNa [M+Na]⁺ 455.1247, found 455.1254.

(*E*)-5-[2-(4-Nitrophenylsulfonamido)phenyl]pent-2-enoic Acid (**1g**)



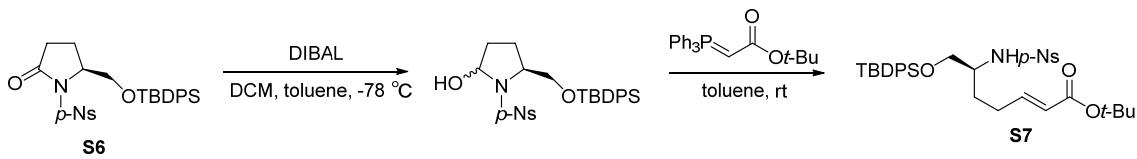
To a stirred solution of **S8** (1.62 g, 3.74 mmol) in DCM (15 mL) was added TFA (7 mL) dropwise at 0 °C. After being stirred for 4 h, the reaction mixture was warmed up to room temperature and concentrated *in vacuo*. After the addition of hexane to the residue, the solvent was evaporated at 40 °C to remove the residual TFA. The same manipulation was conducted once again with hexane and twice with toluene to give **1g** (1.37 g, 97%): white solid; mp 177–178 °C (EtOAc : hexane); ¹H NMR (acetone-*d*6) δ: 8.81 (s, 1H), 8.41 (dt, *J* = 9.2, 2.2 Hz, 2H), 8.00 (dt, *J* = 9.3, 2.2 Hz, 2H), 7.31 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.26–7.22 (m, 1H), 7.17–7.13 (m, 1H), 7.08 (dd, *J* = 8.0, 1.1 Hz, 1H), 6.87 (dt, *J* = 15.7, 6.7 Hz, 1H), 5.74 (dt, *J* = 15.6, 1.6 Hz, 1H), 2.77 (t, *J* = 8.0 Hz, 2H), 2.44–2.39 (m, 2H) ppm; ¹³C NMR (acetone-*d*6) δ: 167.2, 151.1, 148.9, 146.9, 138.8, 134.7, 130.9, 129.5, 128.3, 128.0, 127.8, 125.2, 122.5, 33.0 ppm (One carbon was overlapped with solvent signals.); IR (ATR): 3215, 3105, 1691, 1651, 1529 cm^{−1}; HRMS (ESI): calcd. for C₁₇H₁₆N₂O₆SNa [M+Na]⁺ 399.0621, found 399.0630.

(S)-5-(*tert*-Butyldiphenylsilyloxyethyl)-1-(4-nitrophenylsulfonyl)pyrrolidin-2-one (S6)



To a stirred mixture of *(S*)-5-(*tert*-butyldiphenylsilyloxyethyl)pyrrolidin-2-one⁴ (2.13 g, 6.01 mmol) in THF (40 mL) was added *n*-BuLi (2.6 M hexane solution, 2.6 mL) at -78 °C. After being stirred at the same temperature for 15 min, *p*-NsCl (2.14 g, 9.6 mmol) in THF (20 mL) was added dropwise at -78 °C. After being stirred at same temperature for 2 h, the mixture was warmed up to room temperature slowly and quenched with water. The mixture was extracted with Et₂O four times and the combined organic extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane : EtOAc = 20 : 1 → 1 : 1) to afford **S6** (3.14 g, 97%): white solid; mp 130–131 °C (EtOAc : hexane); [α]_D²⁵ -21.1 (c 0.50, CHCl₃); ¹H NMR (CDCl₃) δ: 8.19 (d, *J* = 8.9 Hz, 2H), 8.14 (d, *J* = 8.6 Hz, 2H), 7.56–7.52 (m, 2H), 7.52–7.43 (m, 4H), 7.43–7.35 (m, 4H), 4.51–4.47 (m, 1H), 4.01 (dd, *J* = 10.9, 3.7 Hz, 1H), 3.82 (dd, *J* = 11.2, 2.0 Hz, 1H), 2.79–2.70 (m, 1H), 2.44–2.37 (m, 1H), 2.32–2.22 (m, 1H), 2.11–2.04 (m, 1H), 0.98 (s, 9H) ppm; ¹³C NMR (CDCl₃) δ: 174.2, 150.5, 144.0, 135.5, 132.4, 132.1, 132.0, 130.2, 130.1, 129.6, 127.9, 127.9, 124.0, 65.7, 60.8, 31.5, 26.7, 22.7, 19.1 ppm; IR (ATR): 3104, 2949, 2932, 1733, 1526 cm⁻¹; HRMS (ESI): calcd. for C₂₇H₃₀N₂O₆SiSNa [M+Na]⁺ 561.1486, found 561.1482..

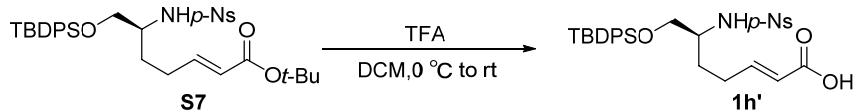
tert-Butyl (S,E)-7-[(*tert*-Butyldiphenylsilyl)oxy]-6-(4-nitrophenylsulfonamido)hept-2-enoate (S3)



To a stirred mixture of **S6** (3.13 g, 5.81 mmol) in DCM (50 mL) was added DIBAL (1.0 M toluene solution, 7.9 mL) at -78 °C. After being stirred for 6 h, the reaction mixture was added MeOH and a saturated potassium sodium tartrate solution. The mixture was warmed up to room temperature. The organic layer was separated and the aqueous layer was extracted with CHCl₃ twice. The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The

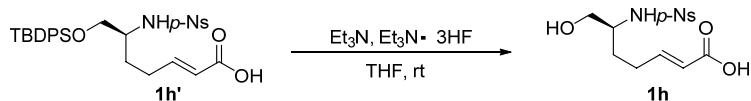
crude hemiaminal was used for the next step without further purification. To a stirred solution of crude hemiaminal (3.08 g, ca. 5.69 mmol) in toluene (60 mL) was added *tert*-butyl 2-(triphenylphosphoranylidene)acetate (4.51 g, 11.9 mmol). After being stirred for 16 h, the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane : EtOAc = 10 : 1 → 8 : 1) to afford **S7** (2.45 g, 66% in 2 steps): white solid; mp 112–113 °C (EtOAc : hexane); $[\alpha]^{22}_D +14.7$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃) δ: 8.19 (d, *J* = 9.2 Hz, 2H), 7.90 (d, *J* = 9.2 Hz, 2H), 7.51–7.42 (m, 6H), 7.39–7.34 (m, 4H), 6.73 (dt, *J* = 15.5, 6.9 Hz, 1H), 5.65 (d, *J* = 15.5 Hz, 1H), 4.92 (d, *J* = 8.6 Hz, 1H), 3.47 (dd, *J* = 10.6, 3.2 Hz, 1H), 3.35 (dd, *J* = 10.6, 4.3 Hz, 1H), 3.33–3.27 (m, 1H), 2.23–2.05 (m, 2H), 1.81–1.65 (m, 2H), 1.49 (s, 9H), 1.03 (s, 9H) ppm; ¹³C NMR (CDCl₃) δ: 165.8, 149.8, 146.7, 145.9, 135.4, 135.4, 132.3, 132.3, 130.2, 128.0, 127.9, 127.9, 124.3, 123.9, 80.3, 64.7, 54.9, 30.9, 28.1, 28.0, 26.8, 19.2 ppm (One carbon could not be observed.); IR (ATR): 3221, 2966, 1704, 1505 cm^{−1}; HRMS (ESI): calcd. for C₃₃H₄₂N₂O₇SiSNa [M+Na]⁺ 661.2374, found 661.2364.

(S,E)-7- (*tert*-Butyldiphenylsilyloxy)-6-(4-nitrophenylsulfonamido)hept-2-enoic Acid (1h')



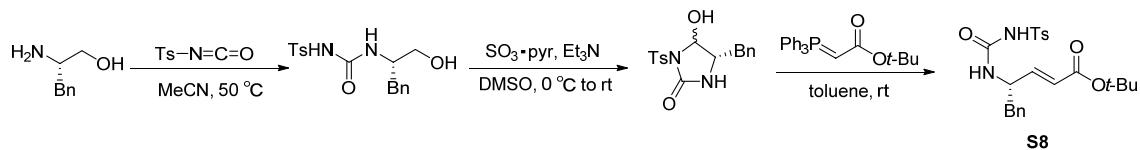
To a stirred solution of **S3** (324 mg, 0.508 mmol) in DCM (10 mL) was added TFA (4 mL) dropwise at 0 °C. After being stirred for 3 h, the reaction mixture was warmed up to room temperature and concentrated *in vacuo*. After the addition of hexane to the residue, the solvent was evaporated at 40 °C to remove the residual TFA. The same manipulation was conducted once again with hexane and twice with toluene to give **1h** (295 mg, 99%): white solid; mp 129–130 °C (EtOAc : hexane); $[\alpha]^{21}_D +20.2$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃) δ: 8.20 (d, *J* = 7.7 Hz, 2H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.51–7.43 (m, 6H), 7.40–7.33 (m, 4H), 6.99–6.92 (m, 1H), 5.76 (d, *J* = 15.5 Hz, 1H), 5.00 (d, *J* = 8.9 Hz, 1H), 3.49–3.43 (m, 1H), 3.36–3.28 (m, 2H), 2.33–2.15 (m, 2H), 1.86–1.67 (m, 2H), 1.03 (s, 9H) ppm; ¹³C NMR (CDCl₃) δ: 171.1, 150.2, 149.8, 146.6, 135.4, 135.4, 132.3, 132.2, 130.2, 128.0, 127.9, 127.9, 124.4, 121.4, 64.7, 54.8, 30.6, 28.3, 26.8, 19.2 ppm (One carbon could not be observed.); IR (ATR): 3384, 2960, 2928, 1684, 1641, 1525 cm^{−1}; HRMS (ESI): calcd. for C₂₉H₃₄N₂O₇SiSNa [M+Na]⁺ 605.1748, found 605.1744.

(S,E)-7-Hydroxy-6-(4-nitrophenylsulfonamido)hept-2-enoic Acid (1h)



To a stirred solution of Et_3N (0.222 mL, 1.59 mmol) and $\text{Et}_3\text{N} \cdot 3\text{HF}$ (0.549 g, 3.4 mmol) in THF (3 mL) was added a solution of **1h'** (0.37 g, 0.636 mmol) in THF (7 mL) dropwise at room temperature. After being stirred for 22 h, the reaction mixture was concentrated *in vacuo*, and the residue was purified by column chromatography on silica gel (hexane : EtOAc : AcOH = 20 : 20 : 1) to afford **1h** (219 mg, quant): white solid; mp 130–131 °C (EtOAc : hexane); $[\alpha]^{24}_D +20.0$ (c 1.0, acetone); ^1H NMR (acetone-*d*6) δ : 8.43 (d, J = 8.6 Hz, 2H), 8.17 (d, J = 8.6 Hz, 2H), 6.86–6.76 (m, 2H), 5.69 (d, J = 15.8 Hz, 1H), 3.88 (br s, 1H), 3.55–3.48 (m, 1H), 3.48–3.41 (m, 1H), 3.41–3.33 (m, 1H), 2.33–2.20 (m, 1H), 2.20–2.10 (m, 1H), 1.85–1.76 (m, 1H), 1.64–1.54 (m, 1H) ppm; ^{13}C NMR (acetone-*d*6) δ : 167.3, 150.8, 149.1, 148.7, 129.2, 125.1, 122.5, 64.8, 56.3, 30.8, 28.7 ppm; IR (ATR): 3370, 3239, 2950, 2929, 1644, 1528 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}_7\text{SNa}$ $[\text{M}+\text{Na}]^+$ 367.0570, found 367.0587.

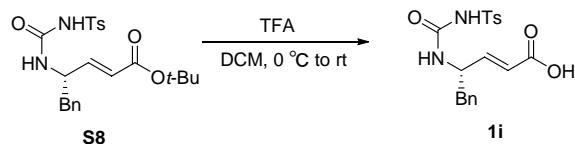
tert-Butyl (S,E)-5-Phenyl-4-(3-tosylureido)pent-2-enoate (S8)



To a stirred solution of (*S*)-2-amino-3-phenylpropan-1-ol (12 mmol) was added TsNCO (1.53 mL, 10 mmol) at 50 °C, and the reaction mixture was stirred for 13 h. After concentration *in vacuo* and dilution of obtained solid with 1M HCl aq, it was filtered, and washed with water and Et_2O . The resulting white solids were used for the next step without further purification. To a stirred solution of the crude urea (1.05 g, ca. 3 mmol) in DMSO (9 mL) were added Et_3N (1.26 mL, 9 mmol) and $\text{SO}_3 \cdot \text{pyr}$ (1.43 g, 9 mmol) in DMSO (3.3 mL), and the reaction mixture was stirred for 4 h. After the completion of the reaction, the mixture was quenched with ice water (15 mL). The aqueous layer was extracted with EtOAc three times and combined organic extracts were washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. The resulting brown solid was used for the next step without further purification. To a stirred solution of hemiaminal (311 mg, ca. 0.9 mmol) in toluene (9 mL) added *tert*-butyl 2-(triphenylphosphoranylidene)acetate (512 mg, 1.35 mmol) at

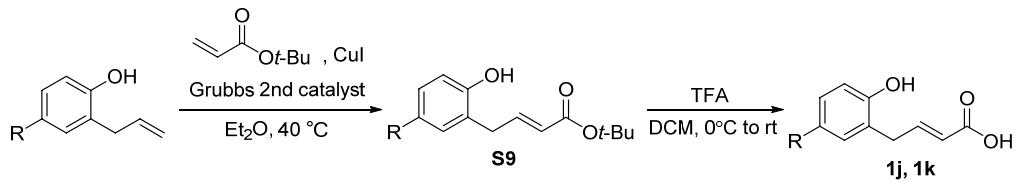
room temperature and the reaction mixture was stirred for 9 h. After concentration of reaction mixture *in vacuo*, the residue purified by column chromatography on silica gel (hexane : EtOAc = 2 : 1) to afford **S8** (220 mg, 35% in 3 steps): white solid; mp 156–157 °C (EtOAc : hexane); $[\alpha]^{21}_D$ = −3.7 (c 1.0, CHCl₃); ¹H NMR (CDCl₃) δ: 7.52 (d, *J* = 8.0 Hz, 2H), 7.34–7.24 (m, 3H), 7.24–7.20 (m, 2H), 7.20–7.15 (m, 2H), 6.77 (dd, *J* = 15.8, 5.4 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 5.69 (dd, *J* = 15.8, 1.4 Hz, 1H), 4.75–4.70 (m, 1H), 2.98 (dd, *J* = 14.3, 5.7 Hz, 1H), 2.83 (dd, *J* = 13.7, 8.0 Hz, 1H), 2.41 (s, 3H), 1.48 (s, 9H) ppm; ¹³C NMR (CDCl₃) δ: 165.2, 150.8, 145.0, 144.8, 136.4, 136.0, 130.0, 129.3, 128.7, 127.0, 126.7, 123.2, 80.7, 52.1, 40.4, 28.1, 21.6 ppm; IR (ATR): 3343, 3092, 2974, 2895, 1677, 1538 cm^{−1}; HRMS (ESI): calcd. for C₂₃H₂₈N₂O₅SNa [M+Na]⁺ 467.1611, found 467.1620.

(S,E)-5-Phenyl-4-(3-tosylureido)pent-2-enoic Acid (1i)

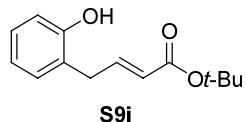


To a stirred solution of **S4** (116 mg, 0.26 mmol) in DCM (5 mL) was added TFA (5 mL) dropwise at 0 °C. After being stirred for 3 h, the reaction mixture was warmed up to room temperature and stirred at the same temperature for 4 h. After the completion of the reaction, the mixture was concentrated *in vacuo*. After the addition of hexane to the residue, the solvent was evaporated at 40 °C to remove the residual TFA. The same manipulation was conducted once again with hexane and twice with toluene to give **1i** (101 mg, quant): white solid; mp 143–144 °C (EtOAc : hexane); $[\alpha]^{21}_D$ = −10.3 (c 1.0, CHCl₃); ¹H NMR (acetone-*d*6) δ: 7.75 (d, *J* = 8.6 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.32–7.17 (m, 5H), 6.92 (dd, *J* = 16.0, 5.2 Hz, 1H), 6.57 (d, *J* = 8.0 Hz, 1H), 5.72 (dd, *J* = 15.5, 1.7 Hz, 1H), 4.72–4.62 (m, 1H), 3.05–2.91 (m, 2H), 2.42 (s, 3H) ppm; ¹³C NMR (acetone-*d*6) δ: 154.3, 145.2, 137.5, 137.1, 130.4, 130.3, 129.3, 128.7, 127.5, 58.6, 57.0, 56.9, 42.3, 39.9, 21.5 ppm; IR (ATR): 3335, 3106, 2906, 1652, 1538 cm^{−1}; HRMS (ESI): calcd. for C₁₉H₂₀N₂O₅SNa [M+Na]⁺ 411.0985, found 411.0994.

α,β -Unsaturated carboxylic acids **1j, k** were generally prepared as indicated below.

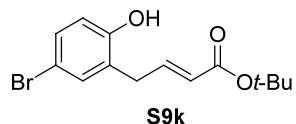


tert-Butyl (E)-4-(2-Hydroxyphenyl)but-2-enoate (S9j)



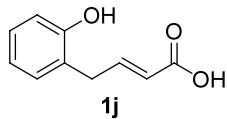
To a stirred solution of 2-allylphenol (0.26 mL, 2.0 mmol) in Et_2O (30 mL) were added *tert*-butyl acrylate (0.73 mL, 5.0 mmol), copper iodide (6.7 mg, 0.04 mmol), and Grubbs 2nd catalyst (34 mg, 0.04 mmol) at room temperature and the reaction mixture was warmed up to 40 °C. After being stirred for 19 h, the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane : EtOAc = 30 : 1 → 4 : 1) to give **S9j** (430 mg, 92%): white solid; mp 64–66 °C (EtOAc : hexane); ¹H NMR (CDCl_3) δ: 7.15–7.07 (m, 2H), 7.04 (dt, J = 15.7, 6.4 Hz, 1H), 6.88 (dd, J = 7.4, 7.4 Hz, 1H), 6.77 (d, J = 7.4 Hz, 1H), 5.73 (dt, J = 15.7, 1.6 Hz, 1H), 5.02 (s, 1H), 3.50 (dd, J = 6.6, 1.6 Hz, 2H), 1.46 (s, 9H) ppm; ¹³C NMR (CDCl_3) δ: 166.8, 154.0, 146.3, 130.6, 128.0, 124.3, 123.4, 120.6, 115.4, 80.6, 33.1, 28.1 ppm; IR (ATR): 3308, 2986, 1676, 1641 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{14}\text{H}_{18}\text{O}_3\text{Na}$ [$\text{M}+\text{Na}$]⁺ 257.1148, found 257.1143.

tert-Butyl (E)-4-(5-Bromo-2-hydroxyphenyl)but-2-enoate (S9k)



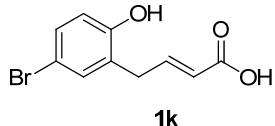
A procedure similar to that described for the preparation of **S9j** afforded **S9k** (327 mg, 45%): white solid; mp 124–125 °C (EtOAc : hexane); ¹H NMR (CDCl_3) δ: 7.17–7.16 (2H, m), 7.05 (1H, dt, J = 15.8, 6.9 Hz), 6.87 (1H, s), 6.64 (1H, d, J = 9.2 Hz), 5.76 (1H, d, J = 15.8 Hz), 3.44 (2H, d, J = 6.9 Hz), 1.49 (9H, s) ppm; ¹³C NMR (CDCl_3) δ: 167.2, 153.3, 145.8, 133.0, 130.7, 126.5, 123.4, 116.9, 112.1, 81.2, 33.2, 28.1 ppm; IR (ATR): 3360, 2979, 1685 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{14}\text{H}_{17}\text{BrO}_3\text{Na}$ [$\text{M}+\text{Na}$]⁺ 335.0253, found 335.0257.

(E)-4-(2-Hydroxyphenyl)but-2-enoic Acid (1j)



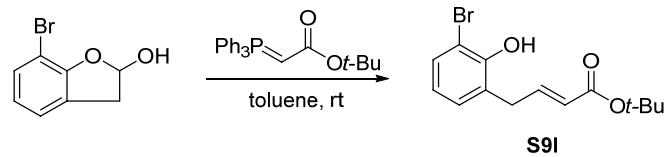
To a stirred solution of **S12j** (830 mg, 3.54 mmol) in DCM (5 mL) was added TFA (5 mL) dropwise at 0 °C. After being stirred for 1 h, the reaction mixture was warmed up to room temperature. After being stirred for another 4 h, the reaction mixture was concentrated *in vacuo*. After the addition of hexane to the residue, the solvent was evaporated at 40 °C to remove the residual TFA. The residue was purified by column chromatography on silica gel (hexane : AcOEt = 1 : 1) to give **1j** (612 mg, 97%): white solid; mp 107–108 °C (EtOAc : hexane); ¹H NMR (acetone-*d*6) δ: 7.15–7.04 (m, 3H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.83–6.75 (m, 1H), 5.80 (d, *J* = 14.3 Hz, 1H), 3.55 (d, *J* = 6.9 Hz, 2H) ppm; ¹³C NMR (acetone-*d*6) δ: 167.5, 155.9, 148.5, 131.1, 128.7, 125.4, 122.4, 120.6, 116.0, 33.4 ppm; IR (ATR): 3403, 2981, 2922, 1671, 1638 cm⁻¹; HRMS (ESI): calcd. for C₁₀H₉O₃ [M–H][−] 177.0557, found 177.0550.

(E)-4-(5-Bromo-2-hydroxyphenyl)but-2-enoic Acid (1k)



A procedure similar to that described for the preparation of **1j** afforded **1k** (231 mg, 94%): white solid ; mp 168–169 °C (EtOAc : hexane); ¹H NMR (acetone-*d*6) δ: 8.78 (1H, br s), 7.28 (1H, d, *J* = 2.3 Hz), 7.22 (1H, dd, *J* = 8.6, 2.3 Hz), 7.10 (1H, dt, *J* = 15.5, 6.9 Hz), 6.85 (1H, d, *J* = 8.6 Hz), 5.84 (1H, d, *J* = 15.5 Hz), 3.54 (2H, d, *J* = 6.9 Hz) ppm; ¹³C NMR (acetone-*d*6) δ: 167.8, 155.1, 147.7, 133.5, 131.4, 128.1, 122.8, 117.8, 111.8, 33.0 ppm; IR (ATR): 3399, 2921, 1681 cm⁻¹; HRMS (ESI): calcd. for C₁₀H₈BrO₃ [M–H][−] 254.9662, found 254.9665.

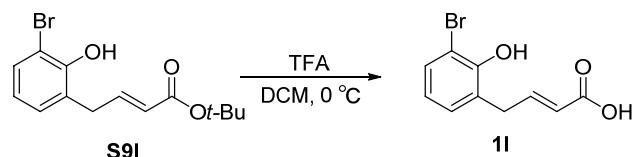
tert-Butyl (E)-4-(3-Bromo-2-hydroxyphenyl)but-2-enoate (S9l)



To a solution of 7-bromo-2,3-dihydrobenzofuran-2-ol (430 mg, 2.0 mmol) in toluene (10 mL), was added *tert*-butyl 2-(triphenylphosphoranylidene)acetate (748 mg, 2.0 mmol) at room temperature.

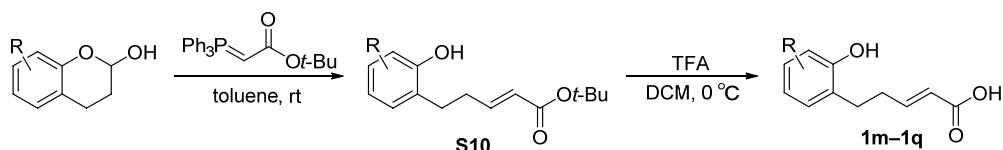
After being stirred for 12 h, the mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane : EtOAc = 10 : 1) to afford **S9I** (490 mg, 78 %): white solid; mp 102–103 °C (EtOAc : hexane); ¹H NMR (CDCl₃) δ: 7.35 (1H, d, *J* = 8.0 Hz), 7.04 (2H, d, *J* = 8.0 Hz), 6.99 (2H, dt, *J* = 15.8, 6.6 Hz), 6.76 (1H, dd, *J* = 8.0, 8.0 Hz), 5.72 (2H, d, *J* = 15.8 Hz), 3.53 (2H, d, *J* = 6.6 Hz), 1.47 (9H, s) ppm; ¹³C NMR (CDCl₃) δ: 165.9, 150.1, 144.7, 130.4, 129.9, 125.8, 124.0, 121.5, 110.6, 80.2, 76.8, 33.2, 28.1 ppm; IR (ATR): 3407, 2978, 1684 cm⁻¹; HRMS (ESI): calcd. for C₁₄H₁₇BrO₃Na [M+Na]⁺ 335.0253, found 335.0258.

(E)-4-(3-Bromo-2-hydroxyphenyl)but-2-enoic Acid (1I)

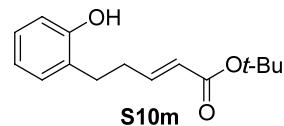


A procedure similar to that described for the preparation of **1j** afforded **1I** (357 mg, 89%): white solid; mp 145–146 °C (EtOAc : hexane); ¹H NMR (MeCN-*d*3) δ: 7.40 (1H, dd, *J* = 7.7, 1.4 Hz), 7.09 (1H, d, *J* = 7.7 Hz), 7.02 (1H, dt, *J* = 15.7, 6.7 Hz), 6.78 (1H, t, *J* = 7.7 Hz), 5.71 (1H, d, *J* = 15.7 Hz), 3.54 (2H, d, *J* = 6.7 Hz) ppm; ¹³C NMR (MeCN-*d*3) δ: 167.5, 151.7, 148.0, 131.9, 130.7, 127.5, 122.6, 122.4, 111.2, 33.7 ppm; IR (ATR): 3348, 1673, 1633 cm⁻¹; HRMS (ESI): calcd. for C₁₀H₈BrO₃ [M-H]⁻ 254.9662, found 254.9669.

α,β-Unsaturated carboxylic acids **1m–q** were generally prepared as indicated below.



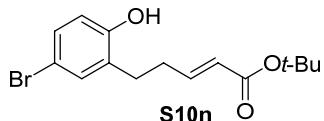
***tert*-Butyl (E)-5-(2-Hydroxyphenyl)pent-2-enoate (S10m)**



To a solution of chroman-2-ol (730 mg, 4.80 mmol) was added *tert*-butyl 2-(triphenylphosphoranylidene)acetate (2.89 g, 7.67 mmol) at room temperature and the reaction mixture was stirred at the same temperature for 5 h. To the mixture, was added a solution of another

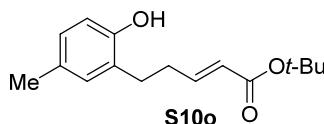
tert-butyl 2-(triphenylphosphoranylidene)acetate (367 mg, 0.96 mmol) in toluene (10 mL). After being stirred for 1 h, the mixture was concentrated in *vacuo*. The residue was purified by column chromatography on silica gel (hexane : EtOAc = 6 : 1) to afford **S13m** (918 mg, 76%): colorless oil; ¹H NMR (CDCl₃) δ: 7.14–7.06 (m, 2H), 6.94 (dt, *J* = 15.5, 6.9 Hz, 1H), 6.87 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 5.80 (d, *J* = 15.5 Hz, 1H), 4.98 (s, 1H), 2.76 (t, *J* = 7.7 Hz, 2H), 2.54–2.46 (m, 2H), 1.48 (s, 9H) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ: 166.3, 153.5, 147.4, 130.2, 127.4, 127.3, 123.3, 120.9, 115.2, 80.2, 32.2, 28.8, 28.2 ppm; IR (ATR): 3398, 3018, 2981, 1688 cm^{−1}; HRMS (ESI): calcd. for C₁₅H₂₀O₃Na [M+Na]⁺ 271.1305, found 271.1306.

***tert*-Butyl (E)-5-(5-Bromo-2-hydroxyphenyl)pent-2-enoate (S10n)**



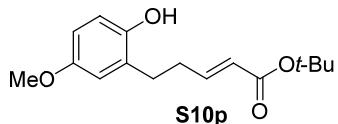
A procedure similar to that described for the preparation of **S10m** afforded **S10n** (1.38 g, 86%). white solid; mp 132–133 °C; ¹H NMR (CDCl₃) δ: 7.21 (1H, s), 7.17 (1H, d, *J* = 8.6 Hz), 6.92 (1H, dt, *J* = 16.6, 7.6 Hz), 6.64 (1H, d, *J* = 8.6 Hz), 5.79 (1H, d, *J* = 16.6 Hz), 5.61 (1H, br s), 2.72 (2H, t, *J* = 7.6 Hz), 2.47 (2H, q, *J* = 7.6 Hz), 1.49 (9H, s) ppm; ¹³C NMR (CDCl₃) δ: 166.9, 153.1, 147.5, 132.6, 130.0, 129.7, 123.2, 116.9, 112.2, 80.8, 32.0, 28.6, 28.1 ppm; IR (ATR): 3376, 2979, 1686 cm^{−1}; HRMS (ESI): calcd. for C₁₅H₁₈BrO₃ [M−H][−] 325.0445, found 325.0446.

***tert*-Butyl (E)-5-(2-Hydroxy-5-methylphenyl)pent-2-enoate (S10o)**



A procedure similar to that described for the preparation of **S10m** afforded **S10o** (1.48 g, 56%). white solid; mp 84–85 °C; ¹H NMR (CDCl₃) δ: 6.95 (1H, dd, *J* = 14.6, 7.7 Hz), 6.89 (1H, s), 6.86 (1H, d, *J* = 8.0 Hz), 6.65 (1H, d, *J* = 8.0 Hz), 5.82–5.76 (2H, m), 2.71 (2H, t, *J* = 7.8 Hz), 2.50–2.44 (2H, m), 2.24 (3H, s), 1.48 (9H, s) ppm; ¹³C NMR (CDCl₃) δ: 166.7, 151.5, 148.0, 130.7, 129.6, 127.7, 127.1, 122.9, 115.1, 80.4, 32.4, 28.8, 28.1, 20.4 ppm; IR (ATR): 3423, 2978, 1688 cm^{−1}; HRMS (ESI): calcd. for C₁₆H₂₂O₃Na [M+Na]⁺ 285.1461, found 285.1472.

tert-Butyl (E)-5-(2-Hydroxy-5-methoxyphenyl)pent-2-enoate (S10p)



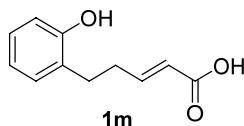
A procedure similar to that described for the preparation of **S10m** afforded **S10p**. Although a byproduct could not be removed, a mixture of the products was used in next step without further purification. A procedure for the next step is described below.

tert-Butyl (E)-5-(2-Hydroxy-4-methylphenyl)pent-2-enoate (S10q)



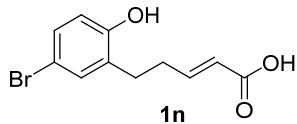
A procedure similar to that described for the preparation of **S10m** afforded **S10q** (1.85 g, 67%). white solid; mp 68–69 °C; ¹H NMR (CDCl₃) δ: 6.99 (1H, d, *J* = 8.3 Hz), 6.95 (1H, dt, *J* = 15.5, 7.9 Hz), 6.42 (1H, dd, *J* = 8.3, 2.6 Hz), 6.36 (1H, d, *J* = 2.6 Hz), 5.80 (1H, d, *J* = 15.5 Hz), 5.76 (1H, s), 3.76 (3H, s), 2.69 (2H, t, *J* = 7.7 Hz), 2.46 (2H, dt, *J* = 7.9, 7.7 Hz), 1.48 (9H, s) ppm; ¹³C NMR (CDCl₃) δ: 166.6, 159.0, 154.5, 147.9, 130.5, 123.0, 119.7, 105.5, 101.8, 80.3, 55.3, 32.6, 28.1 ppm; IR (ATR): 3401, 2978, 1709 cm⁻¹; HRMS (ESI): calcd. for C₁₆H₂₃O₄ [M+H]⁺ 279.1591, found 279.1596.

(E)-5-(2-Hydroxyphenyl)pent-2-enoic Acid (1m)



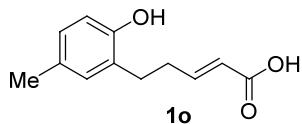
To a stirred solution of **S10m** (918 mg, 3.70 mmol) in DCM (10 mL) at 0 °C, was added TFA (3 mL) dropwise. After being stirred for 2.5 h, the reaction mixture was warmed up to room temperature and concentrated *in vacuo*. After the addition of hexane to the residue, the solvent was evaporated at 40 °C to remove the residual TFA to give **1m** (711 mg, quant.): white solid; mp 116–117 °C (EtOAc : hexane); ¹H NMR (acetone-*d*6) δ: 10.46 (br s, 1H), 8.22 (s, 1H), 7.12 (d, *J* = 7.4 Hz, 1H), 7.05–6.97 (m, 2H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.77 (dd, *J* = 7.4, 7.4 Hz, 1H), 5.83 (dt, *J* = 15.7, 1.4 Hz, 1H), 2.79 (t, *J* = 7.7 Hz, 2H), 2.57–2.52 (m, 2H) ppm; ¹³C NMR (acetone-*d*6) δ: 167.4, 155.9, 149.9, 130.9, 128.1, 122.3, 120.4, 115.9, 32.9, 29.6, 29.3 ppm; IR (ATR): 3331, 2945, 2861, 1667, 1626 cm⁻¹; HRMS (ESI): calcd. for C₁₁H₁₂O₃Na [M+Na]⁺ 215.0679, found 215.0671.

(E)-5-(2-Hydroxyphenyl)pent-2-enoic Acid (1n)



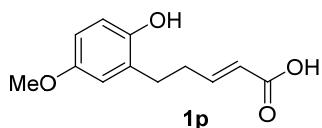
A procedure similar to that described for the preparation of **1m** afforded **1n** (910 mg, 88%): white solid; mp 137–138 °C (EtOAc : hexane); ¹H NMR (acetone-*d*6) δ: 10.54 (1H, br s), 8.64 (1H, br s), 7.28 (1H, d, *J* = 2.6 Hz), 7.17 (1H, dd, *J* = 8.6, 2.6 Hz), 6.98 (1H, dt, *J* = 15.6, 6.9 Hz), 6.80 (1H, d, *J* = 8.6 Hz), 5.83 (1H, d, *J* = 15.7 Hz), 2.77 (2H, t, *J* = 7.7 Hz), 2.56–2.51 (2H, m) ppm; ¹³C NMR (acetone-*d*6) δ: 167.3, 155.3, 149.4, 133.3, 131.1, 130.7, 122.4, 117.7, 115.9, 32.6 ppm (One carbon was overlapped with solvent signals); IR (ATR): 3328, 2945, 1669, 1623 cm^{−1}; HRMS (ESI): calcd. for C₁₁H₁₀BrO₃ [M–H][−] 268.9819, found 268.9818.

(E)-5-(2-Hydroxyphenyl)pent-2-enoic Acid (1o)



A procedure similar to that described for the preparation of **1m** afforded **1o** (752 mg, 95%): white solid; mp 109–110 °C (EtOAc : hexane); ¹H NMR (acetone-*d*6) δ: 10.56 (1H, br s), 8.04 (1H, br s), 7.00 (1H, dt, *J* = 15.5, 6.9 Hz), 6.92 (1H, s), 6.82 (1H, d, *J* = 8.0 Hz), 6.71 (1H, d, *J* = 8.0 Hz), 5.83 (1H, dt, *J* = 15.7, 1.5 Hz), 2.73 (2H, t, *J* = 7.7 Hz), 2.53–2.49 (2H, m), 2.18 (3H, s) ppm; ¹³C NMR (acetone-*d*6) δ: 167.5, 153.6, 150.0, 131.4, 129.0, 128.3, 127.8, 122.0, 115.7, 33.0, 29.6, 20.5 ppm; IR (ATR): 3355, 3011, 1684 cm^{−1}; HRMS (ESI): calcd. for C₁₂H₁₃O₃ [M–H][−] 205.0870, found 205.0877.

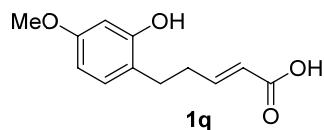
(E)-5-(2-Hydroxy-5-methoxyphenyl)pent-2-enoic Acid (1p)



A procedure similar to that described for the preparation of **1m** afforded **1p** (401 mg, 33% for 2 steps): white solid; mp 98–99 °C; ¹H NMR (acetone-*d*6) δ: 10.52 (1H, br s), 7.86 (1H, br s), 7.01 (1H, dt, *J* = 15.5, 6.9 Hz), 6.78–6.72 (2H, m), 6.61 (1H, dd, *J* = 8.6, 3.2 Hz), 5.84 (1H, dt, *J* = 15.5, 1.7 Hz), 3.70 (3H, d, *J* = 2.0 Hz), 2.77 (2H, t, *J* = 7.6 Hz), 2.56–2.52 (2H, m) ppm; ¹³C NMR

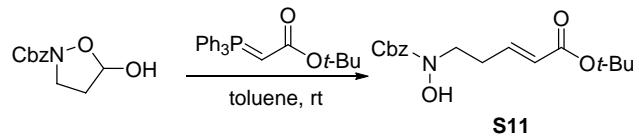
(acetone-*d*6) δ 167.3, 154.0, 149.8, 149.7, 129.1, 122.2, 116.5, 116.3, 112.8, 55.7, 32.9 ppm; IR (ATR): 3313, 2945, 1693 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{12}\text{H}_{13}\text{O}_4$ $[\text{M}-\text{H}]^-$ 221.0819, found 221.0821.

(*E*)-5-(2-Hydroxy-5-methoxyphenyl)pent-2-enoic Acid (1q)



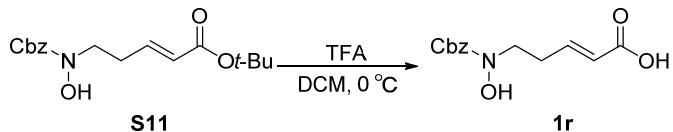
A procedure similar to that described for the preparation of **1m** afforded **1q** (935 mg, 87%): white solid; mp 165–166 $^\circ\text{C}$; ^1H NMR (acetone-*d*6) δ : 8.98 (1H, br s), 7.08–7.01 (2H, m), 6.49–6.48 (2H, m), 5.86 (1H, d, J = 15.8 Hz), 3.83 (3H, s), 2.76–2.73 (2H, m), 2.55–2.52 (2H, m) ppm; ^{13}C NMR (CDCl_3) δ 167.5, 160.2, 156.6, 150.1, 131.2, 122.1, 120.4, 105.3, 102.3, 55.3, 33.2, 28.9 ppm; IR (ATR): 3412, 2923, 2851, 1697 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{12}\text{H}_{13}\text{O}_4$ $[\text{M}-\text{H}]^-$ 221.0819, found 221.0820.

tert-Butyl (*E*)-5-[(Benzyl)carbonyl](hydroxy)amino]pent-2-enoate (S11)



To a solution of benzyl 5-hydroxyisoxazolidine-2-carboxylate⁵ (2.68 g, 12 mmol) in toluene (60 mL), was added *tert*-butyl 2-(triphenylphosphoranylidene)acetate (6.77 g, 18 mmol), and the mixture was stirred at room temperature for 24 h. The reaction mixture was then concentrated *in vacuo*, and the residue was purified by column chromatography on silica gel (hexane : EtOAc = 6 : 1) to afford **S11** (1.31 g, 34%): colorless oil; ^1H NMR (CDCl_3) δ : 7.45 (br, 1H), 7.33 (m, 5H), 6.82 (dt, J = 15.8 Hz, 6.9 Hz, 1H), 5.81 (d, J = 15.8 Hz, 1H), 5.15 (s, 2H), 3.65 (t, J = 7.2 Hz, 2H), 2.50 (q, J = 7.2 Hz, 2H), 1.46 (s, 9H) ppm; ^{13}C NMR (126 MHz, CDCl_3): 8165.7, 157.4, 143.6, 135.7, 128.6, 128.3, 128.1, 125.0, 80.4, 68.1, 48.9, 29.6, 28.1 ppm; IR (CHCl_3): 3345, 2978, 1715, 1699 cm^{-1} ; MS (FAB $^+$): 322 (MH^+ , 15), 91 (100); HRMS (ESI): calcd. for $\text{C}_{17}\text{H}_{23}\text{NO}_5\text{Na}$ $[\text{M}+\text{Na}]^+$ 344.1468, found 344.1462.

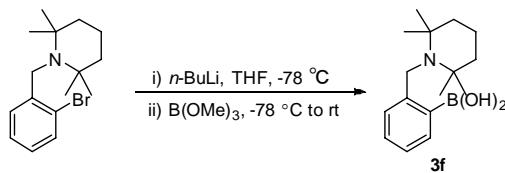
(E)-5-[(BenzylOxy)carbonyl](hydroxy)amino]pent-2-enoic Acid (1r)



To a stirred solution of **S12** (148 mg, 0.46 mmol) in DCM (10 mL) was added TFA (3 mL) dropwise at 0 °C. After the addition of hexane to the residue, the solvent was evaporated at 40 °C to remove the residual TFA. The same manipulation was conducted once again with hexane and twice with toluene to afford **1r** (128 mg, quant): colorless oil; ¹H NMR (CDCl₃) δ: 7.39–7.32 (m, 5H), 7.01 (dt, *J* = 15.7, 7.2 Hz, 1H), 5.89 (d, *J* = 15.8 Hz, 1H), 5.18 (s, 2H), 3.72 (t, *J* = 6.6 Hz, 2H), 2.59–2.55 (m, 2H) ppm; ¹³C NMR (CDCl₃) δ: 170.9, 157.6, 147.7, 135.5, 128.6, 128.4, 128.2, 122.8, 68.4, 48.7, 29.9 ppm; IR (ATR): 3223, 3018, 1703 cm⁻¹; HRMS (ESI): calcd. for C₁₃H₁₅NO₅Na [M+Na]⁺ 288.0842, found 288.0843.

3. Preparation of boronic acid catalysts

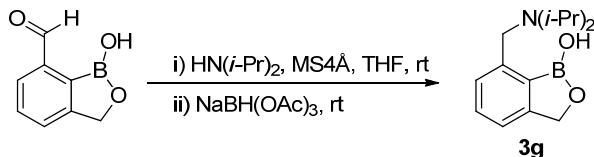
[2-[(2,2,6,6-Tetramethylpiperidin-1-yl)methyl]phenyl]boronic Acid (3f)



To a stirred solution of *N*-(2-bromobenzyl)-2,2,6,6-tetramethylpiperidine⁶ (0.4 g, 1.29 mmol) in THF (10 mL) was added *n*-BuLi (2.6 M hexane solution, 0.74 mL) at -78 °C. After being stirred at the same temperature for 1 h, B(OMe)₃ (0.22 mL, 2.0 mmol) was added dropwise at -78 °C and the reaction mixture was warmed up to room temperature. After being stirred at the same temperature for 1.5 h, the mixture was concentrated *in vacuo* and diluted with 1M HCl and CHCl₃. The organic layer was separated and the aqueous layer was washed with CHCl₃ once and then the aqueous layer was basified to pH 10 with Na₂CO₃ (solid). The aqueous layer was extracted with CHCl₃ five times. The organic extracts were dried over Na₂SO₄ and filtered. The filtrate was concentrated *in vacuo*. The residue was recylstallized (acetone : hexane) to afford **3f** (210 mg, 59%): white solid. mp 142–144 °C; ¹H NMR (CDCl₃) δ: 7.97 (d, *J* = 7.4 Hz, 1H), 7.32 (td, *J* = 7.4, 1.1 Hz, 1H), 7.25–7.19 (m, 2H), 4.07 (s, 2H), 1.80–1.64 (br m, 3H), 1.59–1.45 (br m, 3H), 1.21 (s, 6H), 1.07 (s, 6H) ppm; ¹³C NMR (CDCl₃) δ: 147.9, 137.2, 130.4, 128.2, 125.9, 57.3, 51.5, 40.5, 33.2, 21.1, 17.4 ppm (One carbon could not be observed.); IR (ATR): 3340, 3007, 2968, 2935, 1383, 1365 cm⁻¹; HRMS (ESI):

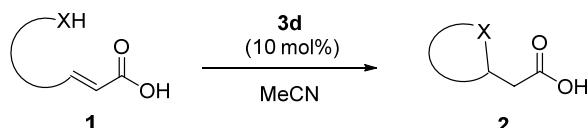
calcd. for $C_{16}H_{27}NO_2B$ $[M+H]^+$ 276.2127, found 276.2115;.

7-[(Diisopropylamino)methyl]benzo[c][1,2]oxaborol-1(3H)-ol (3g)



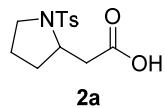
To a stirred solution of 1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborole-7-carbaldehyde⁷ (150 mg, 0.926 mmol) in THF (6 mL) were added activated $MS4\text{\AA}$ (670 mg) and diisopropylamine (0.13 mL, 0.926 mmol) at room temperature. After being stirred at the same temperature for 1 h, $NaBH(OAc)_3$ (393 mg, 1.85 mmol) was added, and the reaction mixture was stirred for 11 h. After the mixture was quenched with 1N aqueous HCl solution (4 mL), the resulting mixture was filtered through Celite and washed with $CHCl_3$ and water. The filtrate was washed with $CHCl_3$ twice and the aqueous layer was basified to pH10 with Na_2CO_3 (solid). It was extracted with $CHCl_3$ three times. and the combined organic extracts was dried over Na_2SO_4 , filtered and concentrated *in vacuo* to afford the benzoxaborole **3g** (52 mg, 23%): colorless oil; 1H NMR ($CDCl_3$) δ : 7.36 (dd, J = 7.5, 7.5 Hz, 1H), 7.20 (d, J = 7.4 Hz, 1H), 7.15 (d, J = 7.4 Hz, 1H), 5.13 (s, 2H), 3.93 (s, 2H), 3.27–3.19 (m, 2H), 1.14 (d, J = 6.9 Hz, 12H) ppm; ^{13}C NMR ($CDCl_3$) δ : 154.1, 144.3, 130.8, 125.7, 119.5, 71.8, 51.3, 49.0, 19.6 ppm (One carbon peak could not be observed.); IR (ATR): 2973, 2935, 1599, 1584, 1468, 1449, 1411, 1371 cm^{-1} ; HRMS (ESI): calcd. for $C_{14}H_{23}NO_2B$ $[M+H]^+$ 248.1814, found 248.1813.

4. General Procedure for Bifunctional Amino Boronic Acid-Catalyzed Intramolecular Michael Reactions of α,β -unsaturated carboxylic acids



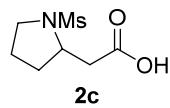
To a stirred solution of **1** (0.1 mmol) in $MeCN$ (1 mL) was added amino boronic acid catalyst **3d** (2.4 mg, 10 mol%) at room temperature. The reaction mixture was stirred at room temperature (or 50 °C, 80 °C, 110 °C) for 3–24 h. The reaction mixture was concentrated *in vacuo* and was purified by column chromatography on silica gel ($EtOAc$: hexane with 5% of $AcOH$) to afford **2**.

2-(1-Tosylpyrrolidin-2-yl)acetic Acid (2a)



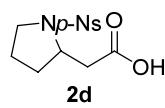
White solid; mp 146–147 °C (MeCN); $[\alpha]^{25}_D -62.6$ (*c* 0.21, CHCl₃, for 50% ee); ¹H NMR (CDCl₃) δ: 7.74 (d, *J* = 8.6 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 3.98–3.90 (m, 1H), 3.50–3.42 (m, 1H), 3.18–3.10 (m, 2H), 2.56 (dd, *J* = 16.3, 10.0 Hz, 1H), 2.44 (s, 3H), 1.87–1.74 (m, 2H), 1.74–1.63 (m, 1H), 1.59–1.49 (m, 1H) ppm; ¹³C NMR (CDCl₃) δ: 176.3, 143.6, 133.9, 129.8, 127.6, 56.3, 49.2, 41.1, 31.7, 23.7, 21.5 ppm; IR (ATR): 3060, 2988, 2952, 2881, 1701 cm^{−1}; HRMS (ESI): calcd. for C₁₃H₁₇NO₄SNa [M+Na]⁺ 306.0771, found 306.0771. HPLC (for methyl ester) [Chiraldak IC, hexane/2-propanol = 50/50, 1.0 mL/min, λ = 254 nm, retention times: (major) 15.3 min (minor) 22.6 min].

2-[1-(Methylsulfonyl)pyrrolidin-2-yl]acetic Acid (2c)



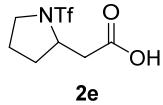
White solid; mp 108–109 °C (MeCN); ¹H NMR (acetone-*d*6) δ: 4.06–3.94 (m, 1H), 3.42–3.27 (m, 2H), 2.88 (s, 3H), 2.87–2.81 (m, 1H), 2.48 (dd, *J* = 16.0, 10.3 Hz, 1H), 2.22–2.12 (m, 1H), 2.00–1.86 (m, 2H), 1.86–1.77 (m, 1H) ppm; ¹³C NMR (acetone-*d*6) δ: 172.6, 57.5, 49.6, 41.4, 34.0, 32.3, 24.7 ppm; IR (ATR): 2965, 2929, 1411 cm^{−1}; HRMS (ESI): calcd. for C₇H₁₃NO₄SNa [M+Na]⁺ 230.0458, found 230.0458.

2-[1-[(4-Nitrophenyl)sulfonyl]pyrrolidin-2-yl]acetic Acid (2d)



White solid; mp 186–187 °C (MeCN); ¹H NMR (acetone-*d*6) δ: 8.36 (d, *J* = 9.2 Hz, 2H), 8.05 (d, *J* = 8.6 Hz, 2H), 3.91–3.81 (m, 1H), 3.44–3.33 (m, 1H), 3.20–3.10 (m, 1H), 2.83 (dd, *J* = 16.0, 3.4 Hz, 1H), 2.47 (dd, *J* = 16.0, 9.7 Hz, 1H), 1.85–1.58 (m, 3H), 1.51–1.40 (m, 1H) ppm; ¹³C NMR (acetone-*d*6) δ: 172.6, 151.2, 143.9, 129.8, 125.3, 57.9, 50.0, 41.3, 32.2, 24.3 ppm; IR (ATR): 3113, 2937, 2884, 1699, 1538 cm^{−1}; HRMS (ESI): calcd. for C₁₂H₁₄N₂O₆SNa [M+Na]⁺ 337.0465, found 337.0480.

2-[1-[(Trifluoromethyl)sulfonyl]pyrrolidin-2-yl]acetic Acid (2e)



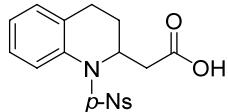
Colorless oil; ^1H NMR (acetone-*d*6) δ : 4.27–4.17 (br m, 1H), 3.49 (t, J = 6.6 Hz, 2H), 2.72 (dd, J = 16.0, 2.9 Hz, 1H), 2.55 (dd, J = 16.0, 10.3 Hz, 2H), 2.21–2.11 (m, 1H), 2.06–1.97 (m, 1H), 1.90–1.82 (m, 1H) ppm; ^{13}C NMR (acetone-*d*6) δ : 171.8, 121.4 (q, J_{C-F} = 325 Hz), 59.3, 50.6, 40.1, 32.3, 24.6 ppm; IR (ATR): 2985, 1714, 1388 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_7\text{H}_{10}\text{NO}_4\text{F}_3\text{SNa}$ $[\text{M}+\text{Na}]^+$ 284.0175, found 284.0166.

2-[1-[(4-Nitrophenyl)sulfonyl]piperidin-2-yl]acetic Acid (2f)



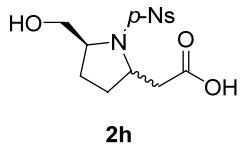
White solid; mp 173–174 °C (MeCN); ^1H NMR (acetone-*d*6) δ : 8.44 (d, J = 8.9 Hz, 2H), 8.15 (d, J = 8.9 Hz, 2H), 4.59–4.52 (m, 1H), 3.89–3.83 (m, 1H), 3.17–3.10 (m, 1H), 2.79–2.73 (m, 1H), 2.46 (dd, J = 15.3, 5.6 Hz, 1H), 1.68–1.52 (m, 5H), 1.39–1.27 (m, 1H) ppm; ^{13}C NMR (acetone-*d*6) δ : 172.1, 150.9, 148.2, 129.2, 125.4, 51.1, 42.0, 35.3, 28.6, 25.6, 18.8 ppm; IR (ATR): 3096, 2919, 1710, 1523 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}_6\text{SNa}$ $[\text{M}+\text{Na}]^+$ 351.0621, found 351.0620.

2-[1-[(4-Nitrophenyl)sulfonyl]-1,2,3,4-tetrahydroquinolin-2-yl]acetic Acid (2g)



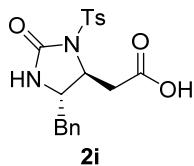
Yellow solid; mp 184–185 °C (MeCN); ^1H NMR (acetone-*d*6) δ : 8.35 (d, J = 9.2 Hz, 2H), 7.81 (d, J = 8.6 Hz, 2H), 7.65 (d, J = 8.0 Hz, 1H), 7.28 (dd, J = 7.7, 7.7 Hz, 1H), 7.19 (dd, J = 7.4, 7.4 Hz, 1H), 7.08 (d, J = 7.4 Hz, 1H), 4.78–4.70 (m, 1H), 2.75 (dd, J = 15.8, 5.4 Hz, 1H), 2.58–2.45 (m, 2H), 2.10–2.01 (m, 1H), 1.90–1.82 (m, 1H), 1.62–1.53 (m, 1H) ppm; ^{13}C NMR (acetone-*d*6) δ : 171.7, 151.3, 145.3, 135.3, 134.6, 129.4, 129.3, 128.0, 127.6, 127.3, 125.2, 54.5, 40.5, 28.6, 24.9 ppm; IR (ATR): 3105, 2956, 1703, 1527 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_6\text{SNa}$ $[\text{M}+\text{Na}]^+$ 399.0621, found 399.0636.

2-[(5*S*)-5-(Hydroxymethyl)-1-[(4-nitrophenyl)sulfonyl]pyrrolidin-2-yl]acetic Acid (2h)



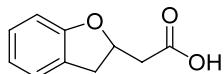
Colorless amorphous; ^1H NMR (acetone-*d*6) δ : 8.50 (d, J = 9.2 Hz, 1H), 8.43 (d, J = 8.6 Hz, 1H), 8.21 (d, J = 9.2 Hz, 2H), 4.33–4.26 (m, 0.5H), 4.03–3.95 (m, 1H), 3.80–3.67 (m, 2H), 3.53 (dd, J = 10.9, 6.9 Hz, 0.5H), 3.08 (dd, J = 15.8, 2.6 Hz, 0.5H), 2.98 (dd, J = 16.2, 4.3 Hz, 0.5H), 2.64 (dd, J = 16.0, 9.7 Hz, 0.5H), 2.45 (dd, J = 15.8, 10.6 Hz, 0.5H), 2.31–2.00 (m, 2H), 1.99–1.91 (m, 0.5H), 1.79–1.71 (m, 1.0H), 1.61–1.52 (m, 0.5H) ppm; ^{13}C NMR (acetone-*d*6) δ : 172.4, 172.4, 151.3, 150.8, 148.6, 143.8, 129.9, 129.1, 125.4, 125.2, 65.1, 64.0, 63.1, 63.0, 59.4, 58.8, 41.4, 39.4, 30.9, 30.1, 26.9, 26.7 ppm; IR (ATR): 3311, 3106, 2960, 2931, 1708, 1526 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}_7\text{SNa}$ $[\text{M}+\text{Na}]^+$ 367.0570, found 367.0585.

2-[(4*S,5S*)-5-Benzyl-2-oxo-3-tosylimidazolidin-4-yl]acetic Acid (2i)



White solid; mp. 143–144 $^{\circ}\text{C}$; $[\alpha]^{22}_{\text{D}} +17.7$ (*c* 0.65, acetone); ^1H NMR (acetone-*d*6) δ : 7.79 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.27–7.17 (m, 3H), 7.14 (d, J = 6.3 Hz, 2H), 6.71 (s, 1H), 4.40–4.30 (m, 1H), 3.85–3.75 (m, 1H), 2.99 (dd, J = 16.3, 3.2 Hz, 1H), 2.90 (dd, J = 13.7, 4.6 Hz, 1H), 2.81 (dd, J = 16.6, 9.7 Hz, 1H), 2.62 (dd, J = 13.5, 7.2 Hz, 1H), 2.44 (s, 3H) ppm; ^{13}C NMR (acetone-*d*6) δ : 154.3, 145.2, 137.5, 137.1, 130.4, 130.3, 129.3, 128.7, 127.5, 58.6, 57.0, 56.9, 42.3, 39.9, 21.5 ppm; IR (ATR): 3298, 2925, 1722 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_5\text{SNa}$ $[\text{M}+\text{Na}]^+$ 411.0985, found 411.0985.

2-(2,3-Dihydrobenzofuran-2-yl)acetic Acid (2j)

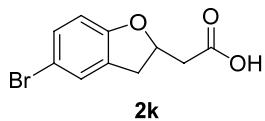


2j

White solid; mp 83–84 $^{\circ}\text{C}$ (MeCN); $[\alpha]^{26}_{\text{D}} +36.8$ (*c* 0.69, CHCl_3 , for 84% ee); ^1H NMR (acetone-*d*6)

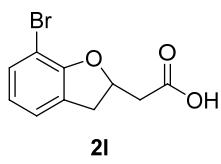
δ : 7.18 (d, J = 7.4 Hz, 1H), 7.08 (dd, J = 6.9, 6.9 Hz, 1H), 6.81 (dd, J = 7.4, 1.1 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 5.16–5.09 (m, 1H), 3.38–3.42 (m, 1H), 2.95–2.99 (m, 1H), 2.75–2.80 (m, 2H) ppm; ^{13}C NMR (acetone-*d*6) δ : 171.8, 160.1, 128.7, 127.6, 125.9, 121.2, 109.9, 80.0, 40.9, 35.8 ppm; IR (ATR): 3049, 2962, 2923, 2856, 1703 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{10}\text{H}_{10}\text{O}_3\text{Na} [\text{M}+\text{Na}]^+$ 201.0522, found 201.0520; HPLC (for methyl ester) [Chiralpak IB, hexane/2-propanol = 95/5, 1.0 mL/min, λ = 254 nm, retention times: (major) 6.2 min (minor) 6.8 min].

2-(5-Bromo-2,3-dihydrobenzofuran-2-yl)acetic Acid (2k)



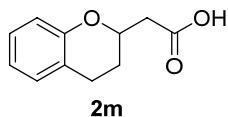
White solid; mp 132–133 °C (MeCN); $[\alpha]^{26}_D$ +43.5 (*c* 1.2, CHCl_3 , for 78% ee); ^1H NMR (CDCl_3) δ : 7.27 (1H, s), 7.22 (1H, d, J = 8.0 Hz), 6.67 (1H, d, J = 8.0 Hz), 5.22–5.16 (1H, m), 3.45–3.41 (1H, m), 2.95–2.92 (2H, m), 2.76–2.73 (1H, m) ppm; ^{13}C NMR (CDCl_3) δ : 175.7, 158.0, 131.0, 128.4, 127.9, 112.5, 111.1, 78.9, 40.2, 35.1 ppm; IR (ATR): 2922, 1704 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{10}\text{H}_8\text{BrO}_3 [\text{M}-\text{H}]^-$ 254.9662, found 254.9658; HPLC (for methyl ester) [Chiralpak IC, hexane/2-propanol = 98/2, 1.0 mL/min, λ = 254 nm, retention times: (major) 8.6 min (minor) 9.9 min].

2-(7-Bromo-2,3-dihydrobenzofuran-2-yl)acetic Acid (2l)



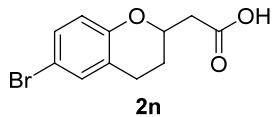
White solid; mp 102–103 °C (MeCN); $[\alpha]^{26}_D$ +43.5 (*c* 1.2, CHCl_3 , for 78% ee); ^1H NMR (CDCl_3) δ : 7.27 (1H, d, J = 7.5 Hz), 7.10 (1H, d, J = 7.5 Hz), 6.74 (1H, dd, J = 7.5, 7.5 Hz), 5.28–5.21 (1H, m), 3.57–3.54 (1H, m), 3.09–3.02 (2H, m), 2.80–2.77 (1H, m) ppm; ^{13}C NMR (CDCl_3) δ : 176.0, 156.2, 131.3, 127.4, 124.0, 122.1, 102.7, 78.8, 40.2, 36.2 ppm; IR (ATR): 2922, 1704 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{10}\text{H}_8\text{BrO}_3 [\text{M}-\text{H}]^-$ 254.9662, found 254.9662.

2-(Chroman-2-yl)acetic Acid (2m)



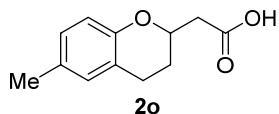
White solid; mp 89–90 °C (MeCN); $[\alpha]^{26}_D +74.0$ (*c* 1.56, CHCl₃, for 93% ee); ¹H NMR (acetone-*d*6) δ: 7.06–7.00 (m, 2H), 6.80 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.57 (dd, *J* = 7.2, 2.0 Hz, 1H), 4.33–4.25 (m, 1H), 2.81–2.68 (m, 1H), 2.67–2.49 (m, 1H), 2.03–1.95 (m, 1H), 1.70–1.56 (m, 1H) ppm; ¹³C NMR (acetone-*d*6) δ: 171.9, 155.5, 130.4, 127.9, 122.7, 120.9, 117.3, 73.5, 40.7, 27.7, 25.1 ppm; IR (ATR): 3040, 2927, 1696 cm^{−1}; HRMS (ESI): calcd. for C₁₁H₁₂O₃Na [M+Na]⁺ 215.0679, found 215.0675; HPLC (for methyl ester) [Chiraldak OJ-3, hexane/2-propanol = 98/2, 1.0 mL/min, λ = 254 nm, retention times: (major) 10.0 min (minor) 11.4 min].

2-(6-Bromochroman-2-yl)acetic Acid (2n)



White solid; mp 138–139 °C (MeCN); $[\alpha]^{26}_D +77.5$ (*c* 0.98, CHCl₃, for 94% ee); ¹H NMR (CDCl₃) δ: 7.18–7.16 (2H, m), 6.69 (1H, d, *J* = 9.2 Hz), 4.47–4.43 (1H, m), 2.89–2.83 (2H, m), 2.75 (1H, dd, *J* = 11.7, 8.3 Hz), 2.67 (1H, dd, *J* = 15.8, 5.7 Hz), 2.11–2.09 (1H, m), 1.83–1.76 (1H, m) ppm; ¹³C NMR (CDCl₃) δ: 176.3, 153.3, 132.0, 130.2, 123.6, 118.6, 112.4, 72.1 40.1, 26.2, 24.2 ppm; IR (ATR): 2924, 1711 cm^{−1}; HRMS (ESI): calcd. for C₁₁H₁₀BrO₃ [M-H][−] 268.9819, found 268.9814; HPLC (for methyl ester) [Chiraldak IA, hexane/2-propanol = 99/1, 0.2 mL/min, λ = 254 nm, retention times: (major) 43.2 min (minor) 47.1 min].

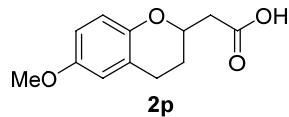
2-(6-Methylchroman-2-yl)acetic Acid (2o)



white solid; mp 120–121 °C (MeCN); $[\alpha]^{26}_D +58.9$ (*c* 0.58, CHCl₃, for 93% ee); ¹H NMR (CDCl₃) δ: 6.89 (1H, d, *J* = 8.3 Hz), 6.86 (1H, s), 6.71 (1H, d, *J* = 8.3 Hz), 4.45–4.42 (1H, m), 2.88–2.83 (2H, m), 2.74–2.71 (1H, m), 2.68–2.65 (1H, m), 2.24 (3H, s), 2.11–2.08 (1H, m), 1.82–1.80 (1H, m) ppm; ¹³C NMR (CDCl₃) δ: 176.5, 151.9, 129.8, 127.9, 121.1, 116.6, 71.9, 40.3, 27.2, 24.3, 20.5 ppm; IR (ATR): 2924, 1713 cm^{−1}; HRMS (ESI): calcd. for C₁₂H₁₃O₃ [M-H][−] 205.0870, found

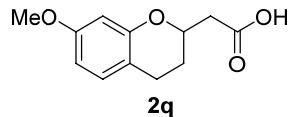
205.0870; HPLC (for methyl ester) [Chiralpak IC, hexane/2-propanol = 98/2, 1.0 mL/min, λ = 254 nm, retention times: (major) 10.6 min (minor) 11.8 min].

2-(6-Methoxylchroman-2-yl)acetic Acid (2p)



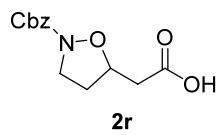
White solid; mp 108–109 °C (MeCN); $[\alpha]^{25}_D$ +76.1 (*c* 0.74, CHCl₃, for 93% ee); ¹H NMR (CDCl₃) δ : 6.74 (1H, d, *J* = 9.0 Hz), 6.67 (1H, dd, *J* = 9.0, 2.7 Hz), 6.59 (1H, d, *J* = 2.7 Hz), 4.44–4.40 (1H, m), 3.74 (3H, s), 2.89–2.81 (2H, m), 2.77–2.72 (1H, m), 2.69–2.64 (1H, m), 2.12–2.07 (1H, m), 1.83–1.77 (1H, m) ppm; ¹³C NMR (CDCl₃) δ : 176.5, 153.4, 148.3, 122.0, 117.4, 113.9, 113.3, 71.8, 55.7, 40.2, 27.1, 24.6 ppm; IR (ATR): 2933, 1713 cm^{−1}; HRMS (ESI): calcd. for C₁₂H₁₃O₄ [M–H][−] 221.0819, found 221.08221; HPLC (for methyl ester) [Chiralpak IC, hexane/2-propanol = 98/2, 1.0 mL/min, λ = 254 nm, retention times: (major) 10.6 min (minor) 11.8 min].

2-(7-Methoxylchroman-2-yl)acetic Acid (2q)



White solid; mp 62–64 °C; $[\alpha]^{25}_D$ +89.2 (*c* 0.89, CHCl₃, for 96% ee); ¹H NMR (CDCl₃) δ : 6.94 (1H, d, *J* = 8.3 Hz), 6.46 (1H, dd, *J* = 8.3, 2.6 Hz), 6.38 (1H, d, *J* = 2.6 Hz), 4.49–4.45 (1H, m), 3.76 (3H, s), 2.86–2.79 (2H, m), 2.73–2.65 (2H, m), 2.11–2.07 (1H, m), 1.82–1.78 (1H, m) ppm; ¹³C NMR (CDCl₃) δ : 176.3, 159.0, 154.9, 129.9, 113.5, 107.6, 101.4, 72.1, 55.3, 40.2, 27.2, 23.6 ppm; IR (ATR): 2932, 1711 cm^{−1}; HRMS (ESI): calcd. for C₁₂H₁₃O₄ [M–H][−] 221.0819, found 221.0815; HPLC (for methyl ester) [Chiralpak OJ-3, hexane/2-propanol = 98/2, 1.0 mL/min, λ = 254 nm, retention times: (major) 17.5 min (minor) 19.7 min].

2-[2-[(Benzyl)carbonyl]isoxazolidin-5-yl]acetic Acid (2r)

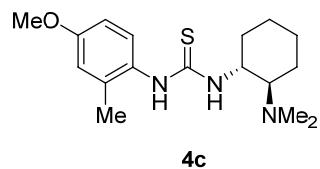


White solid; mp 82–83 °C (MeCN); ¹H NMR (CDCl₃) δ : 7.40–7.30 (m, 5H), 5.21 (s, 2H), 4.51–4.46 (m, 1H), 3.83–3.76 (m, 1H), 3.75–3.69 (m, 1H), 2.77 (dd, *J* = 16.0, 6.9 Hz, 1H), 2.57 (dd, *J* = 16.0,

6.6 Hz, 1H), 2.54–2.46 (m, 1H), 2.03–1.95 (m, 1H) ppm; ^{13}C NMR (CDCl_3) δ : 175.0, 158.1, 135.6, 128.5, 128.3, 128.2, 76.3, 68.2, 47.0, 38.0, 33.2 ppm; IR (ATR): 3151, 1686 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{13}\text{H}_{15}\text{NO}_5\text{Na} [\text{M}+\text{Na}]^+$ 288.0842, found 288.0847.

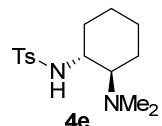
5. Preparation of new aminothiourea catalysts

1-[(1*R*,2*R*)-2-(Dimethylamino)cyclohexyl]-3-(4-methoxy-2-methylphenyl)thiourea (**4c**)



A procedure similar to that described for the preparation of **S4j** (see below) afforded **4c** (521 mg, 81%): white solid; mp 105–106 $^{\circ}\text{C}$ (CHCl_3 : hexane); $[\alpha]^{23}_{\text{D}} -55.2$ (c 0.70, CHCl_3); ^1H NMR (CDCl_3) δ : 7.48 (1H, br s), 7.12 (1H, d, J = 8.6 Hz), 6.80 (1H, s), 6.74 (1H, d, J = 8.6 Hz), 6.22 (1H, br s), 6.22 (1H, s), 3.90–3.84 (1H, m), 3.81 (3H, s), 2.73–2.67 (1H, m), 2.26 (3H, s), 2.23–2.17 (1H, m), 2.13 (6H, s), 1.81–1.75 (2H, m), 1.68–1.62 (1H, m), 1.36–0.92 (4H, m) ppm; ^{13}C NMR (CDCl_3) δ : 180.1, 137.9, 133.1, 128.5, 66.5, 55.8, 39.7, 32.6, 25.2, 24.4, 21.4, 18.0 ppm; IR (ATR): 3204, 2930, 1524 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{17}\text{H}_{28}\text{N}_3\text{OS} [\text{M}+\text{H}]^+$ 322.1948, found 323.1946.

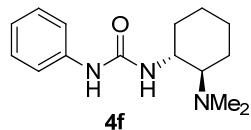
N-[(1*R*,2*R*)-2-(Dimethylamino)cyclohexyl]-4-methylbenzenesulfonamide (**4e**)



To a stirred solution of (1*R*,2*R*)- N^l,N^l -dimethylcyclohexane-1,2-diamine (284 mg, 2.0 mmol) and NEt_3 (303 mg, 3.0 mmol) in THF (5 mL), was added tosyl chloride (380 mg, 2.0 mmol) at room temperature. After being stirred for 3 h, the mixture was diluted with sat. NaHCO_3 aq. The mixture was extracted with EtOAc three times. The combined organic extracts were washed with brine. The organic phase were dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (CHCl_3 : MeOH : NEt_3 = 100 : 10 : 1) to afford **4e** (410 mg, 69%): colorless oil; $[\alpha]^{26}_{\text{D}} -83.4$ (c 1.12, CHCl_3); ^1H NMR (CDCl_3) δ : 7.77 (2H, d, J = 8.2 Hz), 7.30 (2H, d, J = 8.2 Hz), 2.63–2.61 (1H, m), 2.42 (3H, s), 2.38–2.35 (1H, m), 2.19–2.17 (1H, m), 1.95 (6H, s), 1.75–1.73 (2H, m), 1.66–1.64 (1H, m), 1.23–1.00 (4H, m) ppm; ^{13}C NMR (CDCl_3) δ : 143.1, 136.8, 129.5, 127.3, 66.2, 54.0, 39.6, 32.5, 25.0, 24.2, 21.5, 21.0 ppm; IR (ATR): 3205, 2935 cm^{-1} ;

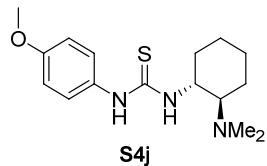
HRMS (ESI): calcd. for $C_{15}H_{25}N_2O_2S$ $[M+H]^+$ 297.1631, found 297.1620.

1-[(1*R*,2*R*)-2-(dimethylamino)cyclohexyl]-3-phenylurea (4f)



A procedure similar to that described for the preparation of **4j** (see below) afforded **4f** (810 mg, 62%). White solid; mp 120–121 °C ($CHCl_3$: hexane); $[\alpha]^{26}_D$ −63.7 (c 0.65, $CHCl_3$); 1H NMR ($CDCl_3$) δ : 7.32–7.24 (5H, m), 7.01 (1H, t, J = 7.2 Hz), 5.72 (1H, br s), 3.46–3.42 (1H, m), 2.47–2.42 (1H, m), 2.26–2.22 (1H, m), 2.23 (6H, s), 1.85–1.80 (2H, m), 1.69–1.63 (1H, m), 1.36–1.05 (4H, m) ppm; ^{13}C NMR ($CDCl_3$) δ : 156.6, 139.3, 129.0, 120.2, 66.8, 51.9, 40.0, 33.8, 25.2, 24.7, 21.4 ppm; IR (ATR): 3317, 2930, 1650 cm^{-1} ; HRMS (ESI): calcd. for $C_{15}H_{24}N_3O$ $[M+H]^+$ 262.1914 found 262.1914.

1-[(1*R*,2*R*)-2-(Dimethylamino)cyclohexyl]-3-(4-methoxyphenyl)thiourea (S4j)



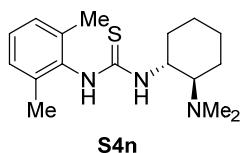
To a stirred solution of $(1R,2R)$ - N^I,N^I -dimethylcyclohexane-1,2-diamine (284 mg, 2.0 mmol) in THF (5 mL), was added 4-methoxyphenylisothiocyanate at room temperature. After being stirred at room temperature for 6 h, the mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel ($CHCl_3$: MeOH : NEt_3 = 100 : 10 : 1) to afford **4j** (587 mg, 96%): colorless amorphous; $[\alpha]^{26}_D$ −90.7 (c 0.95, $CHCl_3$); 1H NMR ($CDCl_3$) δ : 8.72 (1H, br s), 7.13 (2H, d, J = 8.9 Hz), 6.94 (1H, br s), 6.83 (2H, d, J = 8.9 Hz), 3.93–3.87 (1H, m), 3.69 (3H, s), 2.60–2.58 (1H, m), 2.31–2.23 (1H, m), 2.07 (6H, s), 1.79–1.72 (2H, m), 1.62–1.59 (1H, m), 1.31–0.82 (4H, m) ppm; ^{13}C NMR ($CDCl_3$) δ : 179.9, 157.8, 130.0, 126.9, 114.3, 66.4, 55.8, 55.3, 39.7, 32.7, 25.0, 24.4, 21.2 ppm; IR (ATR): 3256, 2932, 1508 cm^{-1} ; HRMS (ESI): calcd. for $C_{16}H_{26}N_3OS$ $[M+H]^+$ 308.1791, found 308.1778.

1-[(1*R*,2*R*)-2-(Dimethylamino)cyclohexyl]-3-(*o*-tolyl)thiourea (S4m)



A procedure similar to that described for the preparation of **4j** afforded **S4m** (414 mg, 71%): colorless amorphous; $[\alpha]^{26}_D -42.8$ (*c* 1.57, CHCl_3); ^1H NMR (CDCl_3) δ : 7.66 (1H, br s), 7.27–7.21 (4H, m), 6.44 (1H, br s), 3.92–3.86 (1H, m), 2.74–2.70 (1H, m), 2.31–2.29 (1H, m), 2.30 (3H, s), 2.14 (6H, s), 1.82–1.76 (2H, m), 1.70–1.64 (1H, m), 1.35–0.98 (4H, m) ppm; ^{13}C NMR (CDCl_3) δ : 180.4, 135.3, 135.1, 131.2, 127.7, 127.2, 126.9, 66.7, 56.1, 3, 32.6, 25.1, 24.5, 21.6, 17.7 ppm; IR (ATR): 3204, 2930, 1524 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{16}\text{H}_{26}\text{N}_3\text{S}$ $[\text{M}+\text{H}]^+$ 292.1842, found 292.1831.

1-[(1*R*,2*R*)-2-(Dimethylamino)cyclohexyl]-3-(2,6-dimethylphenyl)thiourea (S4n)



A procedure similar to that described for the preparation of **4j** afforded **S4n** (572 mg, 94%): white solid; mp 153–154 °C (CHCl_3 : hexane); $[\alpha]^{26}_D -37.6$ (*c* 0.52, CHCl_3); ^1H NMR (CDCl_3) δ : 7.39 (1H, br s), 7.20–7.07 (3H, m), 5.84 (1H, br s), 3.87–3.81 (1H, m), 2.76–2.70 (1H, m), 2.27 (6H, s), 2.09–2.07 (1H, m), 2.08 (6H, s), 1.76–1.60 (3H, m), 1.40–0.92 (4H, m) ppm; ^{13}C NMR (CDCl_3) δ : 180.1, 137.9, 133.1, 128.5, 66.5, 55.8, 39.7, 32.6, 25.2, 24.4, 21.4, 18.0 ppm; IR (ATR): 3154, 2931, 1521 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{17}\text{H}_{28}\text{N}_3\text{S}$ $[\text{M}+\text{H}]^+$ 306.1998, found 306.1983.

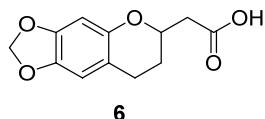
6. General procedure for the asymmetric reaction

To a stirred suspension of substrates (0.1 mmol) in solvent* (1 mL) and MS 4 Å (100 mg) at appropriate temperature were added chiral catalyst (0.02 mmol) and boronic acid (0.02 mmol). After being stirred at the same temperature for 24–120 h, the mixture was filtered through a pad of Celite and silica gel ($\text{EtOAc} : \text{AcOH} = 30 : 1$). (When the reaction temperature was 0 °C, to a stirred suspension of substrates (0.1 mmol) in solvent (1 mL) and MS 4 Å (100 mg) at –78 °C were added chiral catalyst (0.02 mmol) and boronic acid (0.02 mmol).) The filtrate was concentrated *in vacuo*. The residue was purified by PLC ($\text{CHCl}_3 : \text{AcOH} = 30 : 1$) to give the corresponding Michael adduct. Enantio excess of the product was estimated after the transformation of carboxylic acid into methyl

ester by the treatment with TMSCHN₂. The spectral data of the products except for **7** are shown above.

* The ratio of MTBE : CCl₄ as solvent was 1 : 1 (v/v) for **2j** and **2a**, and 1 : 2 (v/v) for all of the others.

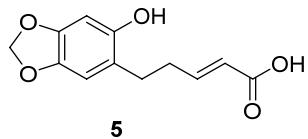
2-(7,8-Dihydro-6H-[1,3]dioxolo[4,5-g]chromen-6-yl)acetic Acid (6)



White solid; mp 122–124 °C (MeCN); $[\alpha]^{26}_D +59.0$ (*c* 0.40, CHCl₃, for 94% ee); ¹H NMR (CDCl₃) δ : 6.49 (1H, s), 6.36 (1H, s), 5.86 (2H, s), 4.43–4.37 (1H, m), 2.83–2.80 (2H, m), 2.67–2.63 (2H, m), 2.07–2.05 (1H, m), 1.80–1.75 (1H, m) ppm; ¹³C NMR (CDCl₃) δ : 176.4, 148.7, 146.4, 141.5, 112.8, 108.1, 100.8, 98.7, 71.9, 40.2, 27.1, 24.3 ppm; IR (ATR): 3251, 2925, 1715 cm^{−1}; HRMS (ESI): calcd. for C₁₂H₁₂O₅Na [M+Na]⁺ 259.0577, found 259.0567; HPLC (for methyl ester) [Chiralpak IC, hexane/2-propanol = 95/5, 1.0 mL/min, λ = 254 nm, retention times: (major) 10.9 min (minor) 12.7 min].

7. Asymmetric total synthesis of erythrococcamide B via one-pot reaction

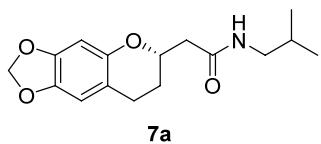
(E)-5-(6-Hydroxybenzo[d][1,3]dioxol-5-yl)pent-2-enoic Acid (5)



To a stirred mixture of 7,8-dihydro-6H-[1,3]dioxolochromen-6-ol⁵ (1.60 g, 8.24 mmol) in THF (20 mL), was added *tert*-butyl 2-(triphenylphosphoranylidene) acetate (4.65 g, 12.4 mmol) at room temperature. After being stirred for 12 h, the mixture was concentrated in *vacuo*. The residue was purified by silica gel chromatography (hexane : EtOAc = 1 : 1). Although a byproduct could not be removed, a mixture of the products was used for the next step without further purification. To a solution of the product mixture (2.1 g, ca. 7.19 mmol) in CH₂Cl₂ (15 mL), was added TFA (15 mL) at room temperature. After being stirred for 1 h, the mixture was concentrated in *vacuo*. The residue was purified by recrystallization (Et₂O : hexane) to afford **5** (802 mg, 47%). Additionally, the filtrate was purified by silica gel chromatography (hexane : EtOAc = 2 : 1 → 1 : 1) to afford **5** (562 mg, 33%): white solid; mp 153–154 °C (Et₂O : hexane); ¹H NMR (acetone-*d*6) δ : 10.52 (1H, br s), 8.01

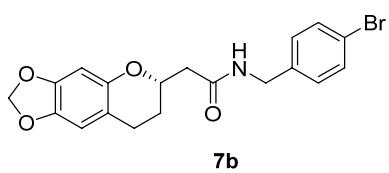
(1H, s), 6.98 (1H, dt, J = 15.8, 6.9 Hz), 6.65 (1H, s), 6.44 (1H, s), 5.83 (2H, s), 5.81 (3H, d, J = 15.8 Hz), 2.70 (2H, t, J = 7.6 Hz), 2.52–2.46 (2H, m) ppm; ^{13}C NMR (acetone-*d*6) δ : 167.5, 150.2, 149.9, 147.0, 141.3, 122.2, 119.8, 110.1, 101.5, 98.5, 33.2, 29.3 ppm; IR (ATR) 3361, 2928, 1653 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{12}\text{O}_5\text{Na} [\text{M}+\text{Na}]^+$ 259.0577, found 259.0569

(+)-Erythrococcamide B (7a)



To a stirred suspension of **5** (23.6 mg, 0.1 mmol) and MS4A (100 mg) in a mixture of CCl_4 and MTBE in a ratio of 1 : 2 (1 mL), were added **4c** (6.4 mg, 0.02 mmol) and **3b** (5.2 mg, 0.02 mmol) at room temperature. After being stirred for 24 h, isobutylamine (10 μL , 0.1 mmol) was added. After being stirred at 50 $^{\circ}\text{C}$ for 48 h, the mixture was filtered through a pad of Celite and silica gel (eluent was $\text{EtOAc} : \text{AcOH} = 30 : 1$). The residue was purified by PLC ($\text{EtOAc} : \text{hexane} = 1 : 1$) to give (+)-erythrococcamide B (18.1 mg, 62%, 94% ee). All spectral data were identical to that of the literature⁵. $[\alpha]^{25}_{\text{D}} +59.6$ (*c* 1.81, CHCl_3 , for 94% ee); ^1H NMR (500 MHz, CDCl_3): δ 6.51 (s, 1H), 6.32 (s, 1H), 6.13 (br, 1H), 5.87 (d, J = 5.5 Hz, 2H), 4.35–4.29 (m, 1H), 3.21–3.15 (m, 1H), 3.12–3.07 (m, 1H), 2.84–2.79 (m, 1H), 2.78–2.51 (m, 3H), 2.04–2.00 (m, 1H), 1.85–1.67 (m, 2H), 0.94 (d, J = 9.0 Hz, 6H) ppm; ^{13}C NMR (126 MHz, CDCl_3): δ 170.3, 148.4, 146.4, 141.7, 113.2, 108.2, 100.9, 98.3, 73.0, 46.9, 42.8, 28.4, 27.3, 24.5, 20.2 ppm

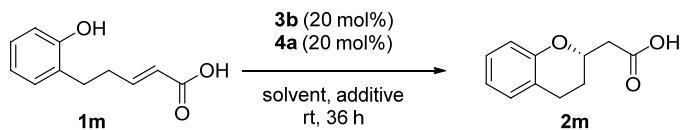
***N*-(4-Bromobenzyl)-2-(7,8-dihydro-6*H*-[1,3]dioxolo[4,5-g]chromen-6-yl)acetamide (7b)**



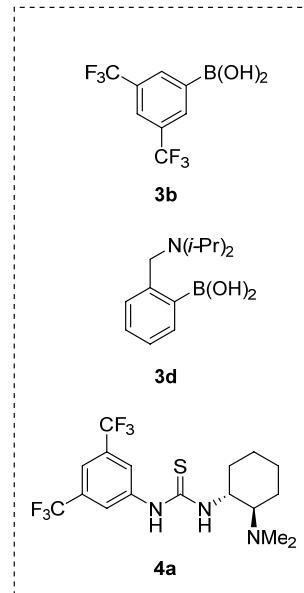
A procedure similar to that described for the preparation of **7a** afforded **7b** (81%). white solid; mp 110–111 $^{\circ}\text{C}$; $[\alpha]^{25}_{\text{D}} +46.3$ (*c* 0.47, CHCl_3 , for 91% ee); ^1H NMR (CDCl_3) δ : 7.45 (2H, d, J = 8.5 Hz), 7.17 (2H, t, J = 8.5 Hz), 6.50 (1H, s), 6.37 (1H, br s), 6.24 (1H, s), 5.87 (1H, d, J = 1.5 Hz), 5.86 (1H, d, J = 1.5 Hz), 4.49 (1H, dd, J = 15.1, 6.5 Hz), 4.41–4.33 (2H, m), 2.83–2.76 (1H, m), 2.64–2.57 (3H, m), 2.04–2.00 (1H, m), 1.79–1.71 (1H, m), 1.79 (1H, s) ppm; ^{13}C NMR (126 MHz, CDCl_3): δ 170.2, 148.3, 146.4, 141.7, 137.3, 131.8, 129.2, 121.3, 113.1, 108.3, 100.9, 98.3, 72.9, 42.8, 42.6, 27.3, 24.4 ppm; IR (ATR) 3293, 2920, 1646 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{18}\text{BrNO}_4\text{Na} [\text{M}+\text{Na}]^+$

426.0311, found 426.0303; HPLC [Chiralpak IC, hexane/2-propanol = 80/20, 1.0 mL/min, λ = 254 nm, retention times: (major) 13.3 min (minor) 17.2 min].

8. Optimization of solvents and additives for the asymmetric reaction



entryl	additive ^a	solvent	yield (%) ^b	ee(%) ^c
1	none	DCE	<1	-
2	MS4A	DCE	67	31
3 ^d	MS4A	DCE	>99	0
4	MS4A	MeCN	<1	-
5	MS4A	MTBE	28	51
6	MS4A	toluene	81	39
7	MS4A	CH ₂ Cl ₂	66	35
8	MS4A	CHCl ₃ ^e	77	43
9	MS4A	CHCl ₃ ^f	<1	-
10	MS4A	CCl ₄	70	47
11	MS4A	MTBE/CCl ₄ (1:1)	66	57
12	MS4A	MTBE/CCl ₄ (1:2)	79	59
13	Al ₂ O ₃	MTBE/CCl ₄ (1:1)	<1	-
14	SiO ₂	MTBE/CCl ₄ (1:1)	<1	-
15 ^g	MS4A	MTBE/CCl ₄ (1:1)	<1	-
16 ^h	MS4A	MTBE/CCl ₄ (1:1)	<1	-

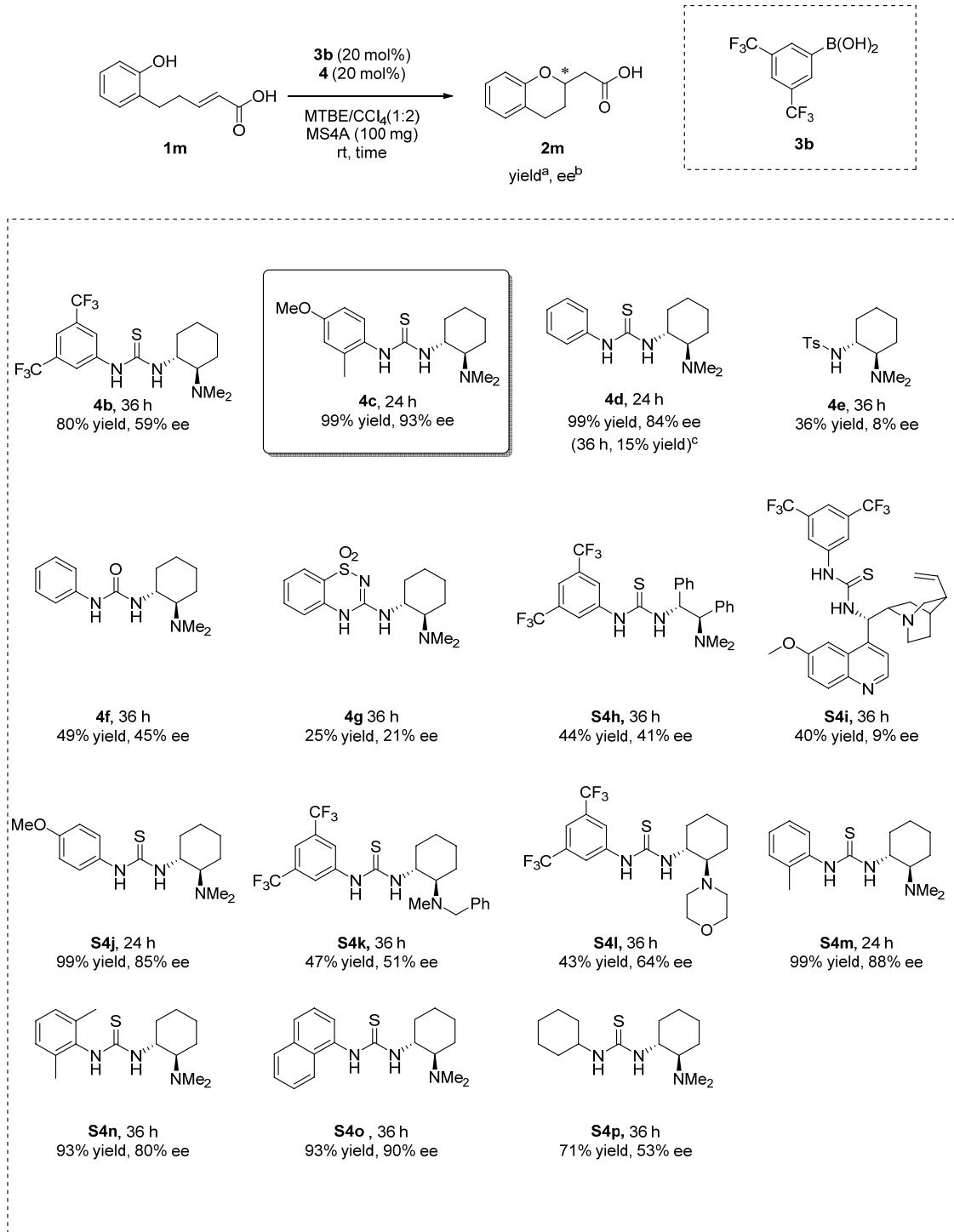


^a 30 mg of additive was used. ^b Determined by ¹H NMR. ^c Estimated after treatment with TMSCHN₂.

^d 3d was used instead of 3b. ^e Stabilized with amylene. ^f Stabilized with EtOH. ^g Without 3b.

^h Without 4a.

9. Optimization of catalysts for the asymmetric reaction

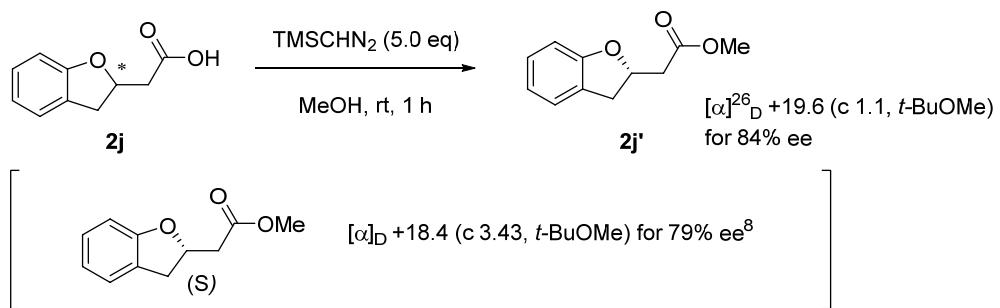


^a Determined by ¹H NMR. ^b Estimated after treatment with TMSCHN₂. ^c Phenylboronic acid was used instead of **3b**.

10. Determination of the absolute configuration

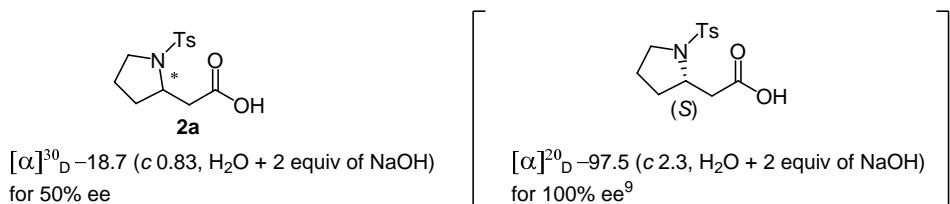
10-1. Determination of the absolute configuration of **2j**

The absolute configuration of **2j** was determined to be *S* by conversion into the corresponding methyl ester **2j'**⁸, followed by the comparison of its optical rotation value with the reported one (See below). The stereochemistry of **2k** was assigned in analogy to **2j**.



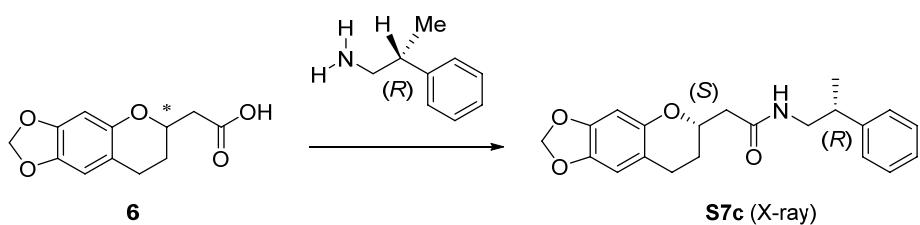
10-2. Determination of the absolute configuration of **2a**

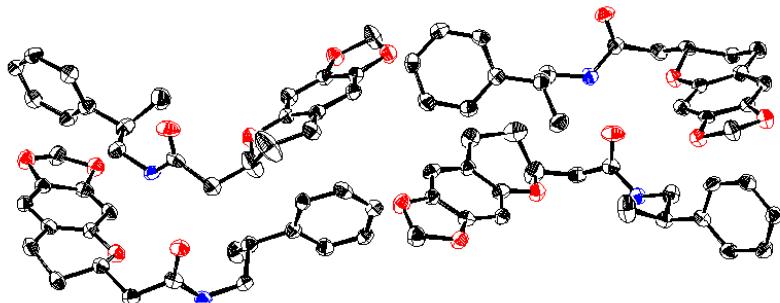
The absolute configuration of **2a** was determined as *S* by comparison of the optical rotation value with the reported one⁹ (See below).



10-3. Determination of the absolute configuration of **6**

The absolute configuration of **6** was determined as *S* by conversion into amide **S7c** (similar procedure to that described for the preparation of **7a**), followed by an X-ray crystallographic structure analysis (See below). The stereochemistry of the other chromane derivatives **2n–q** was assigned in analogy to **6**.





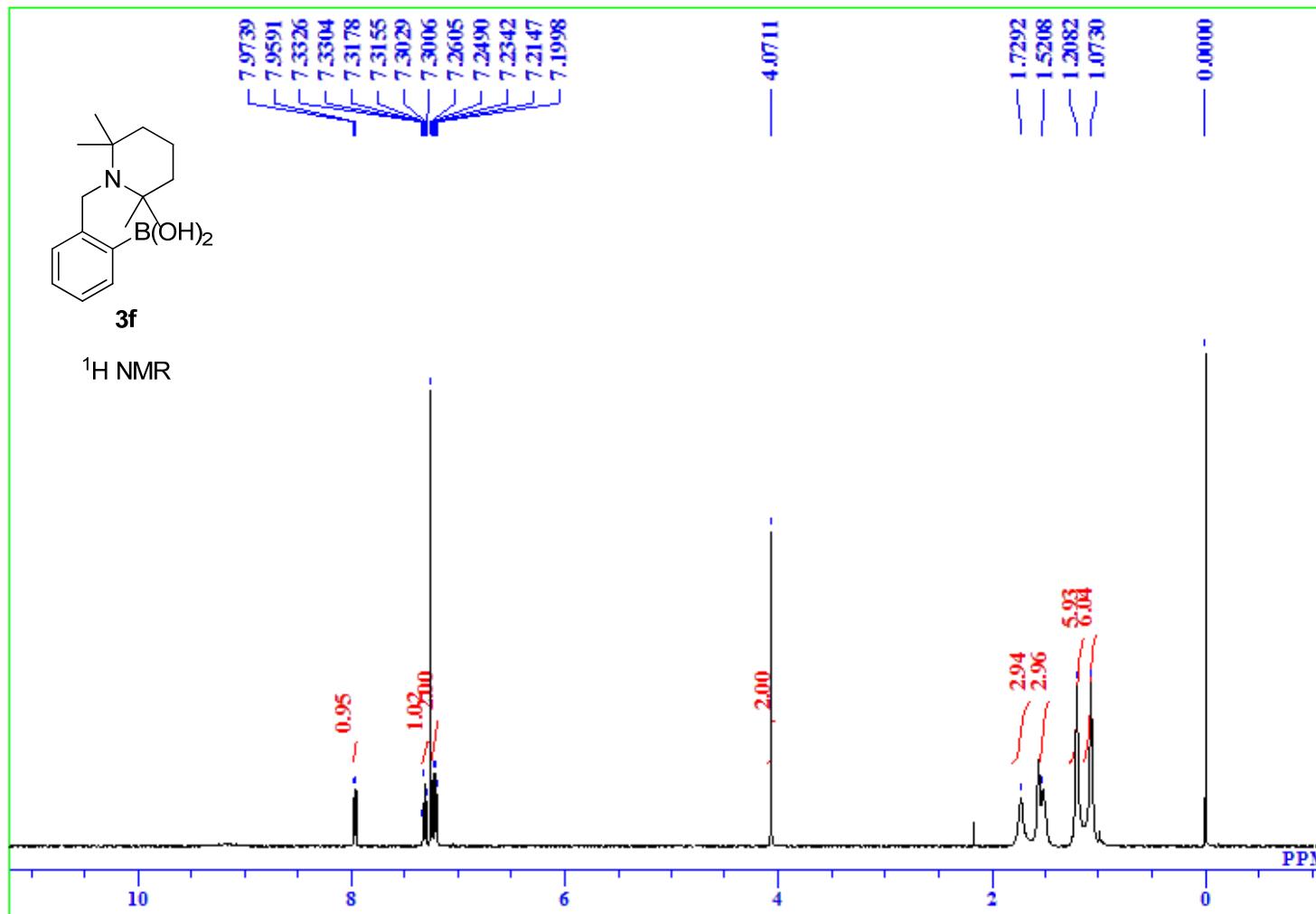
ORTEP diagram of **S7c**. Hydrogen atoms are omitted for clarity.

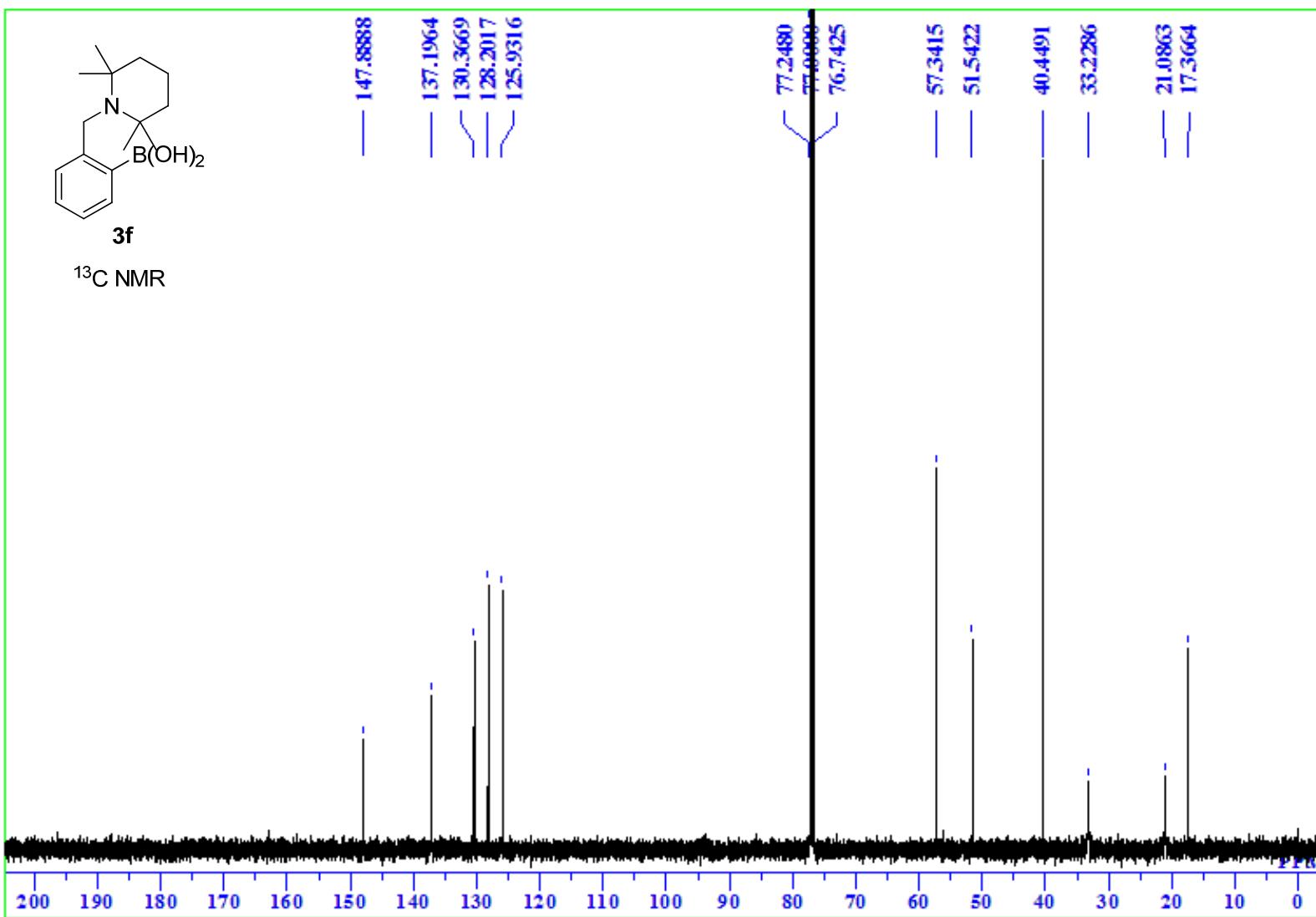
CCDC 1002990 (**S7c**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

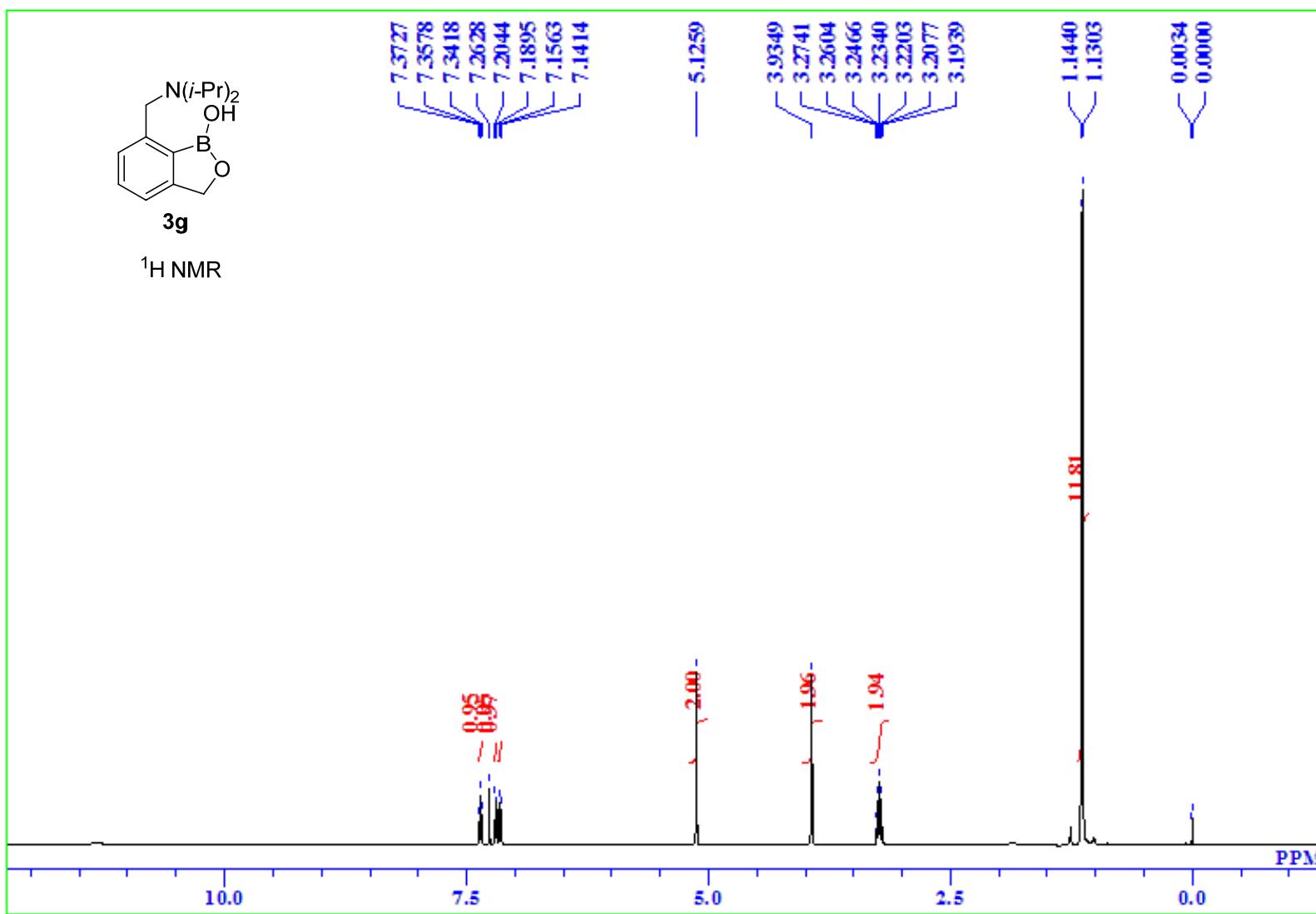
11. References

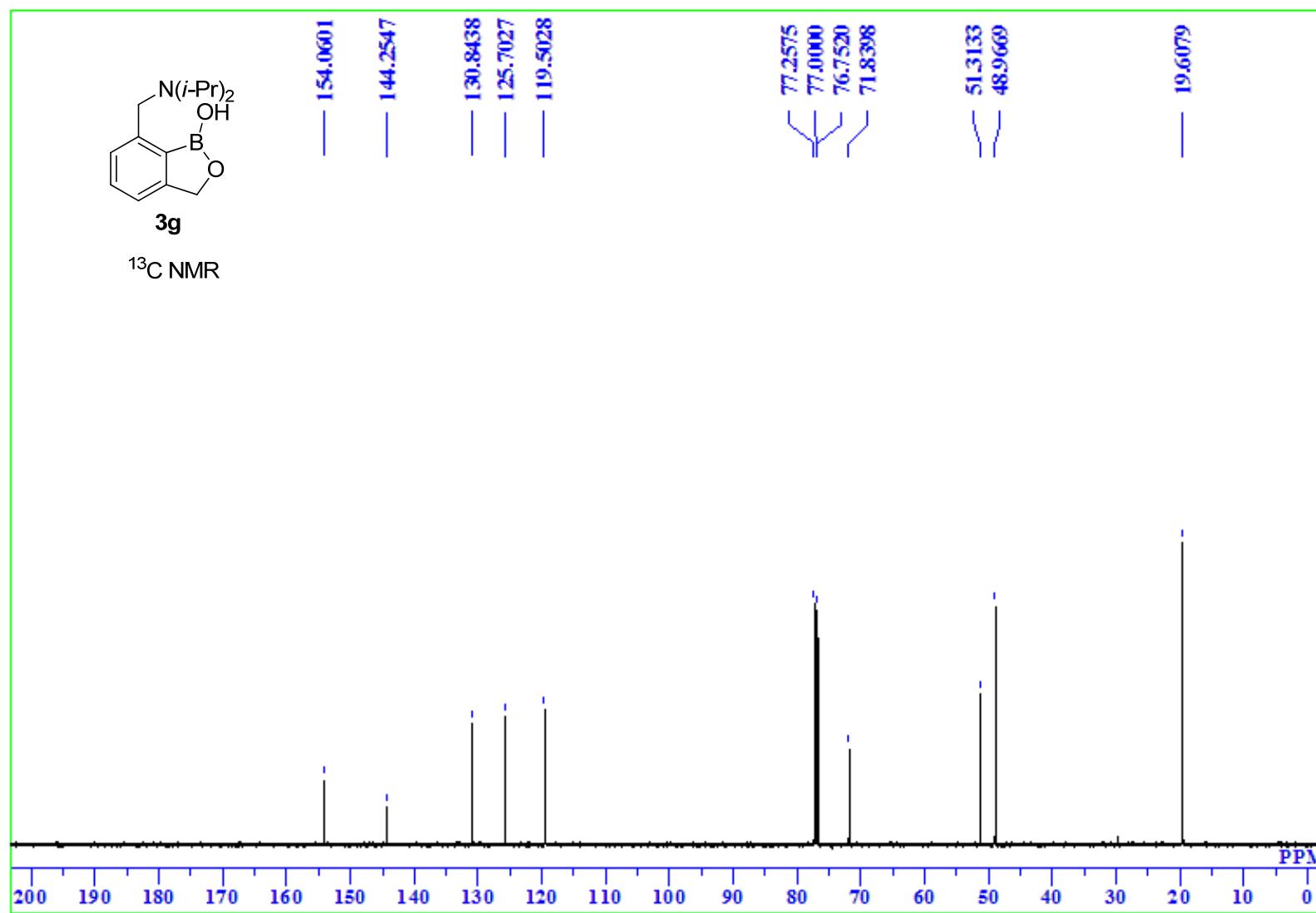
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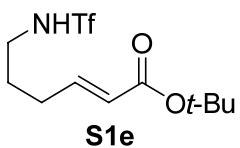
12. Copies of ^1H and ^{13}C NMR charts





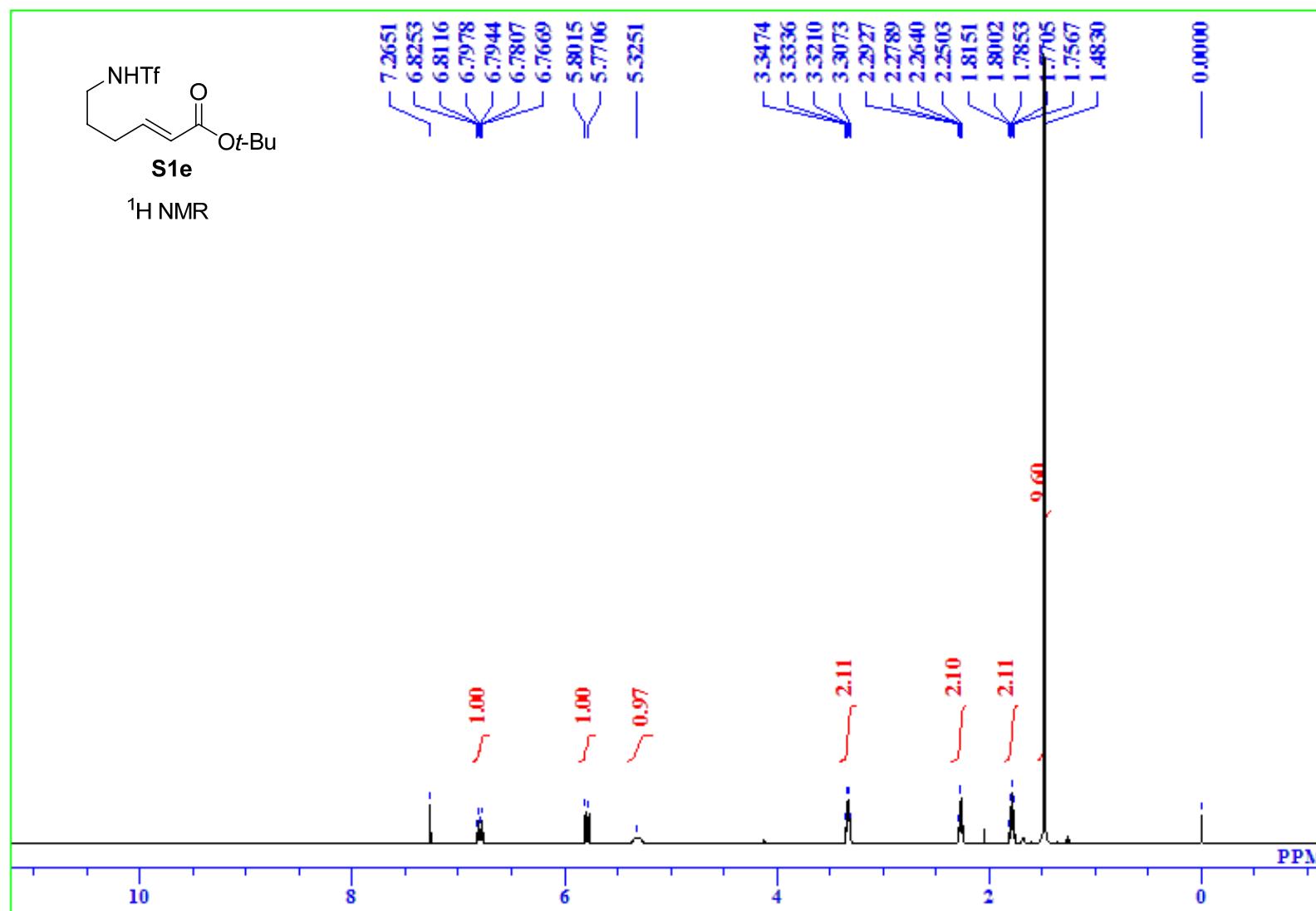


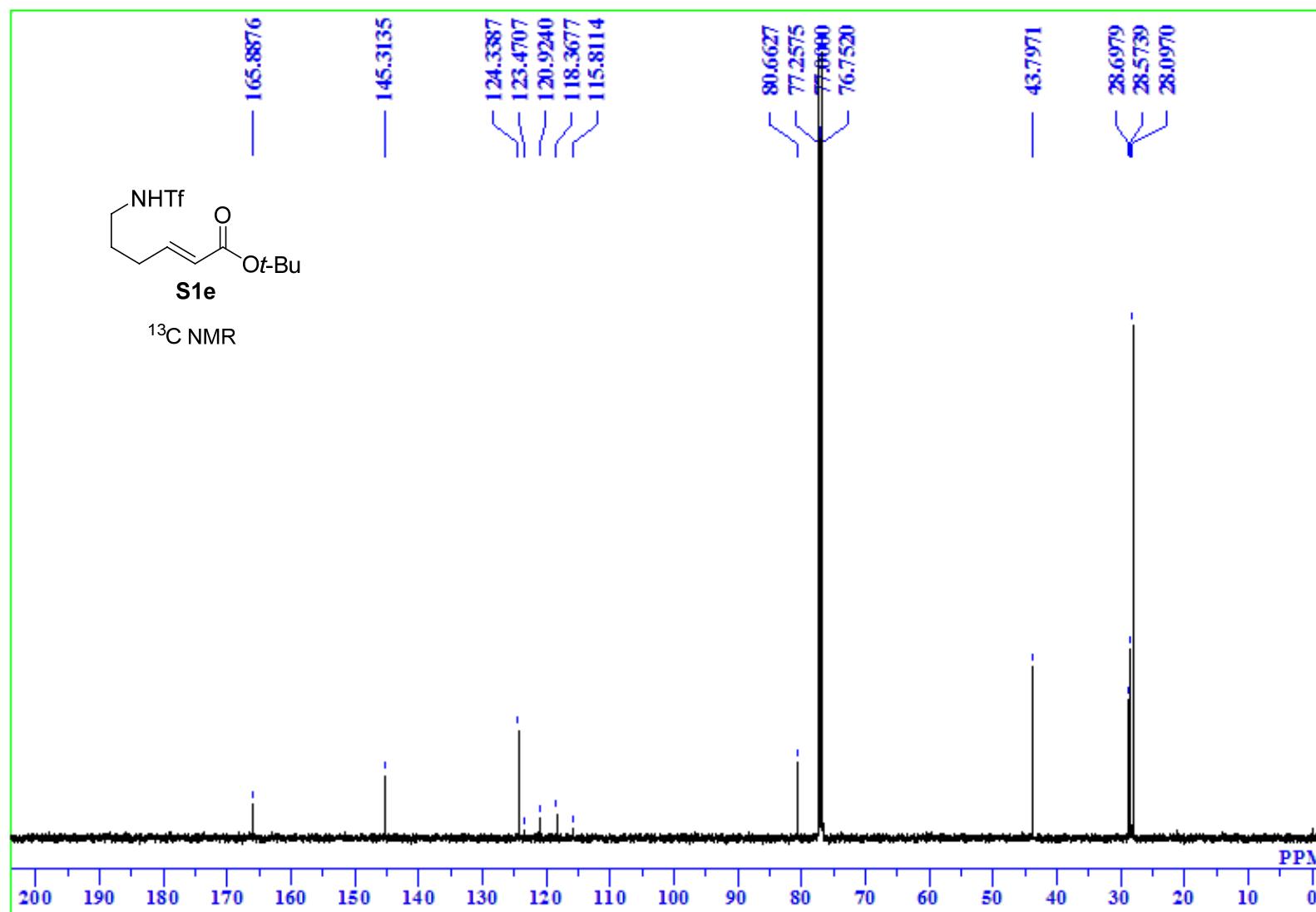


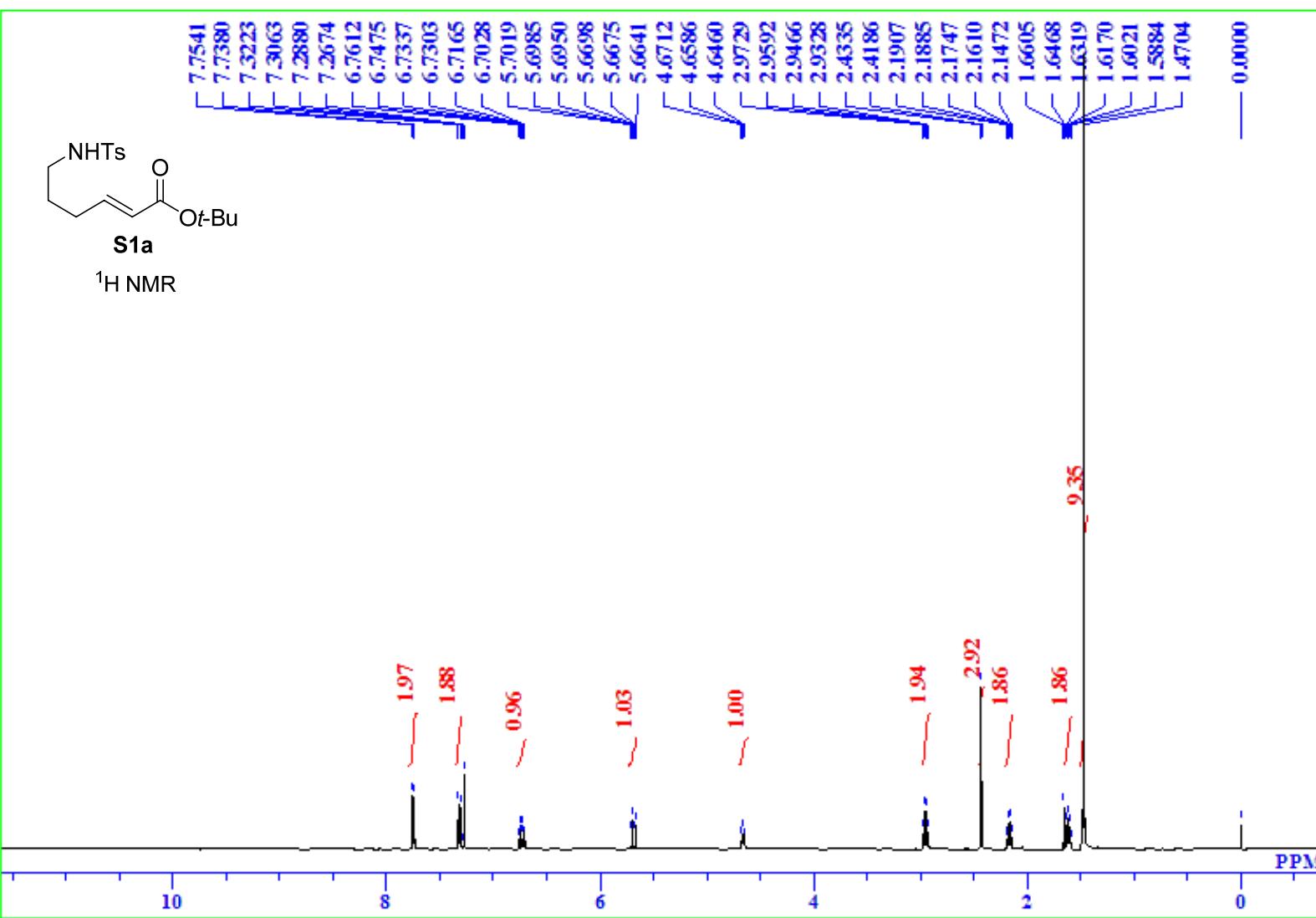


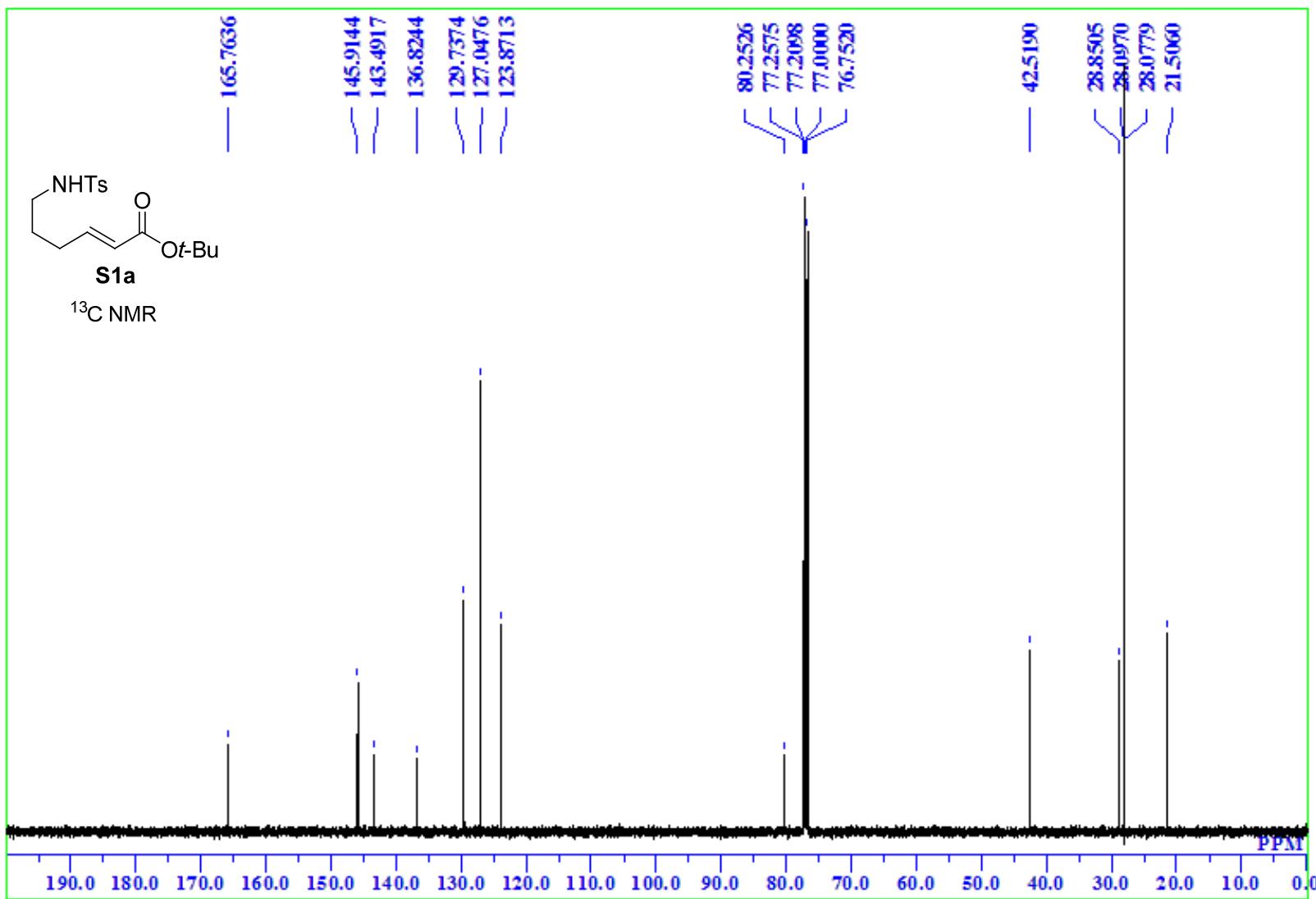
S1e

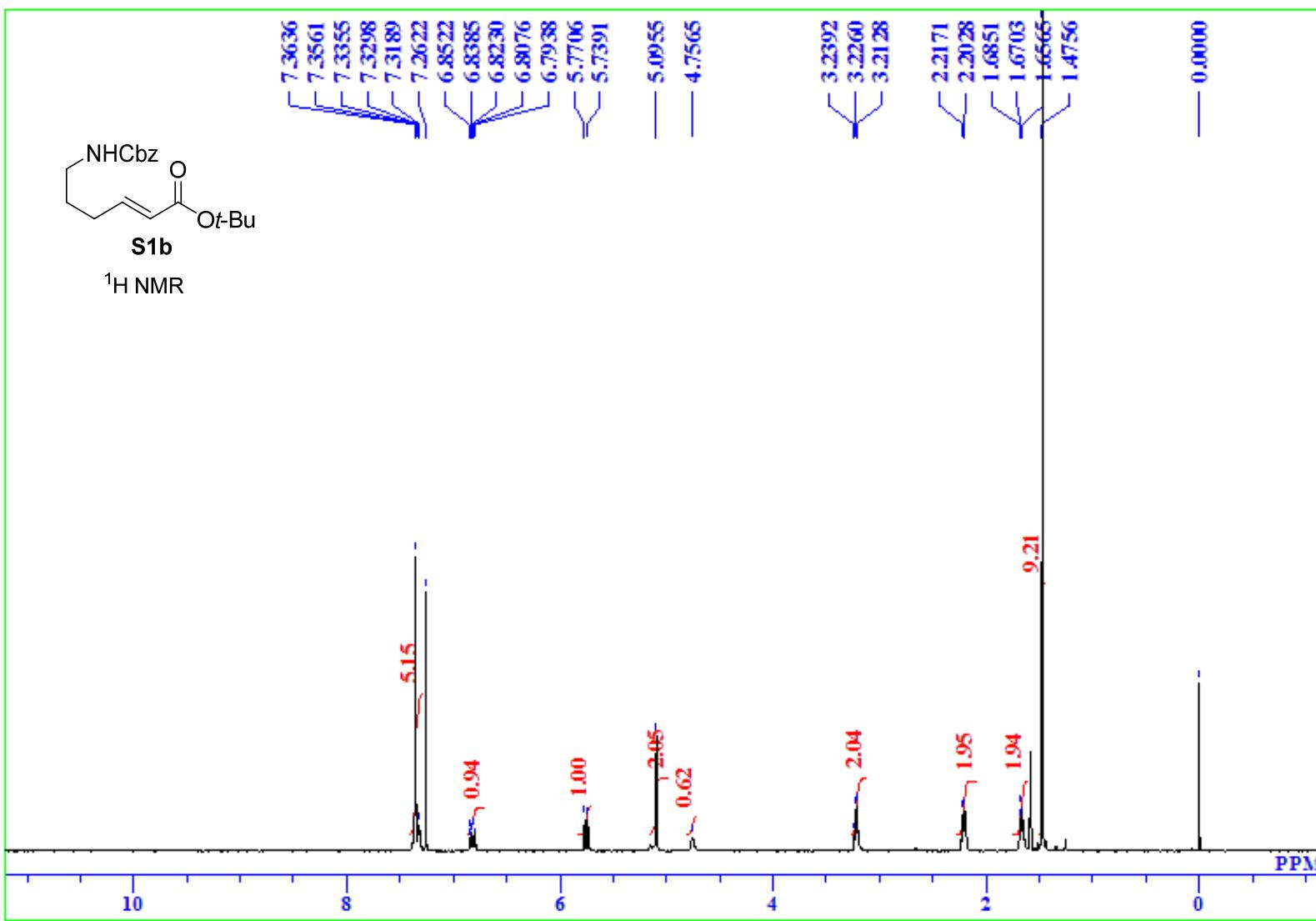
^1H NMR

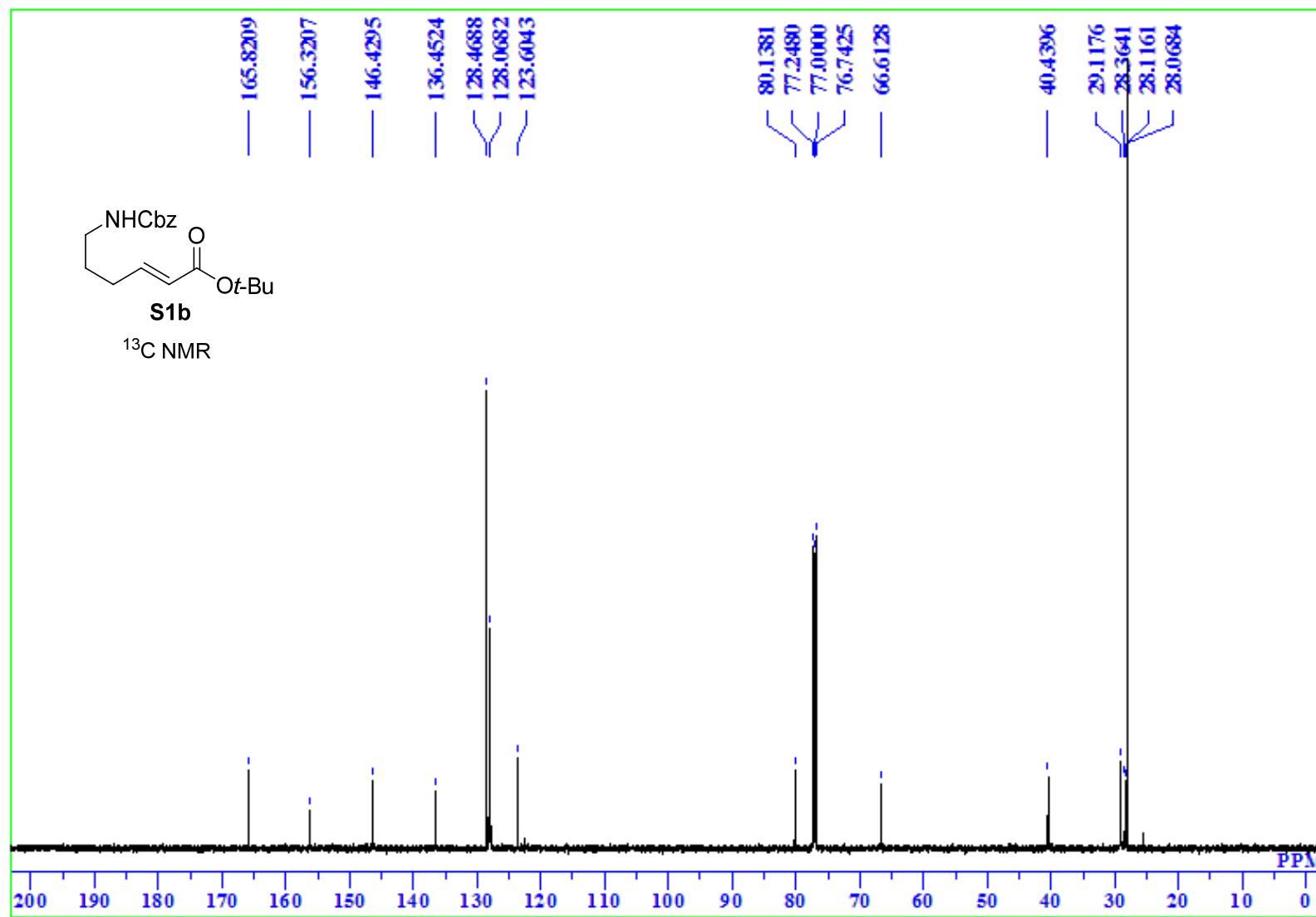


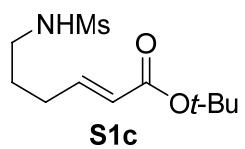




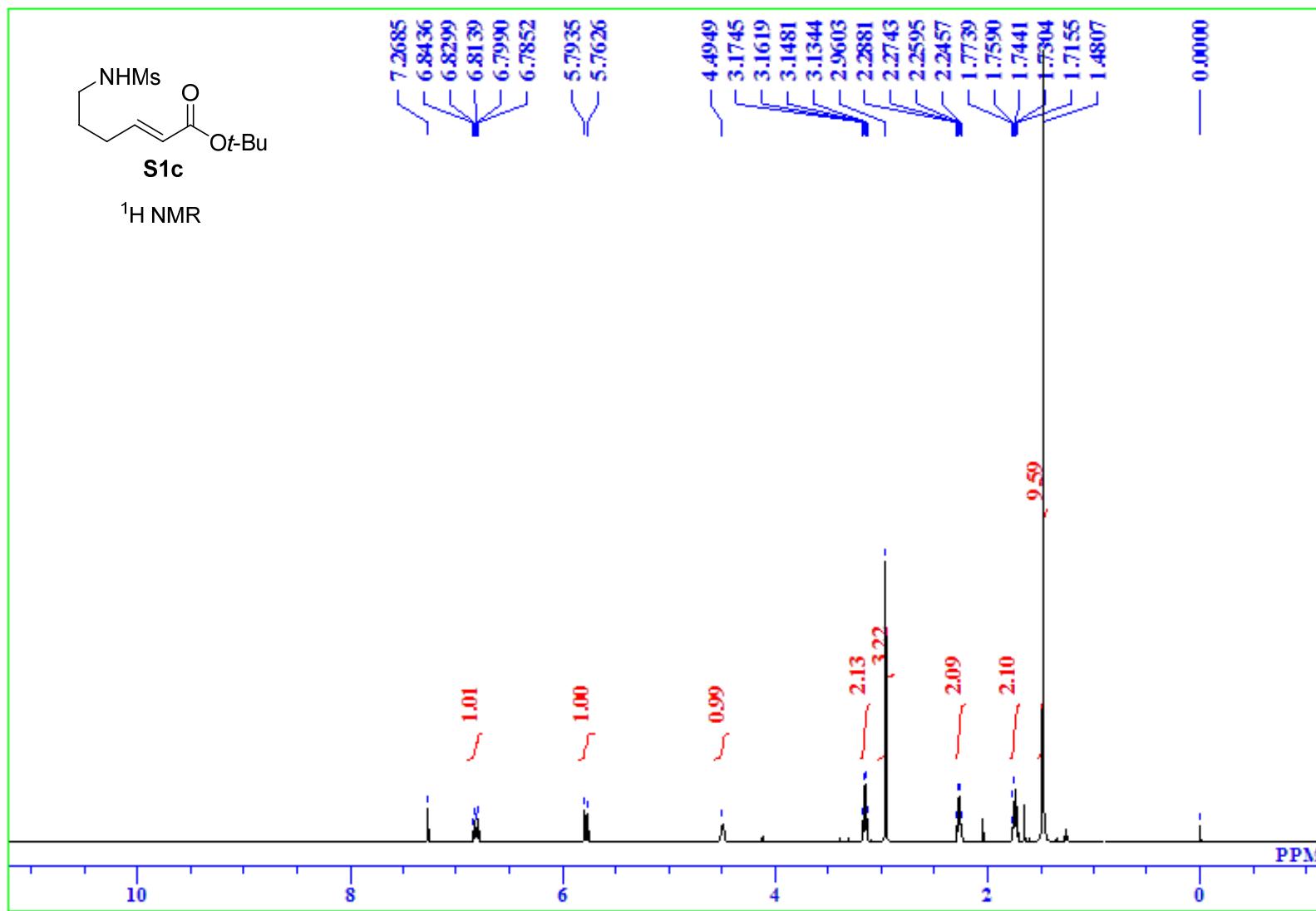


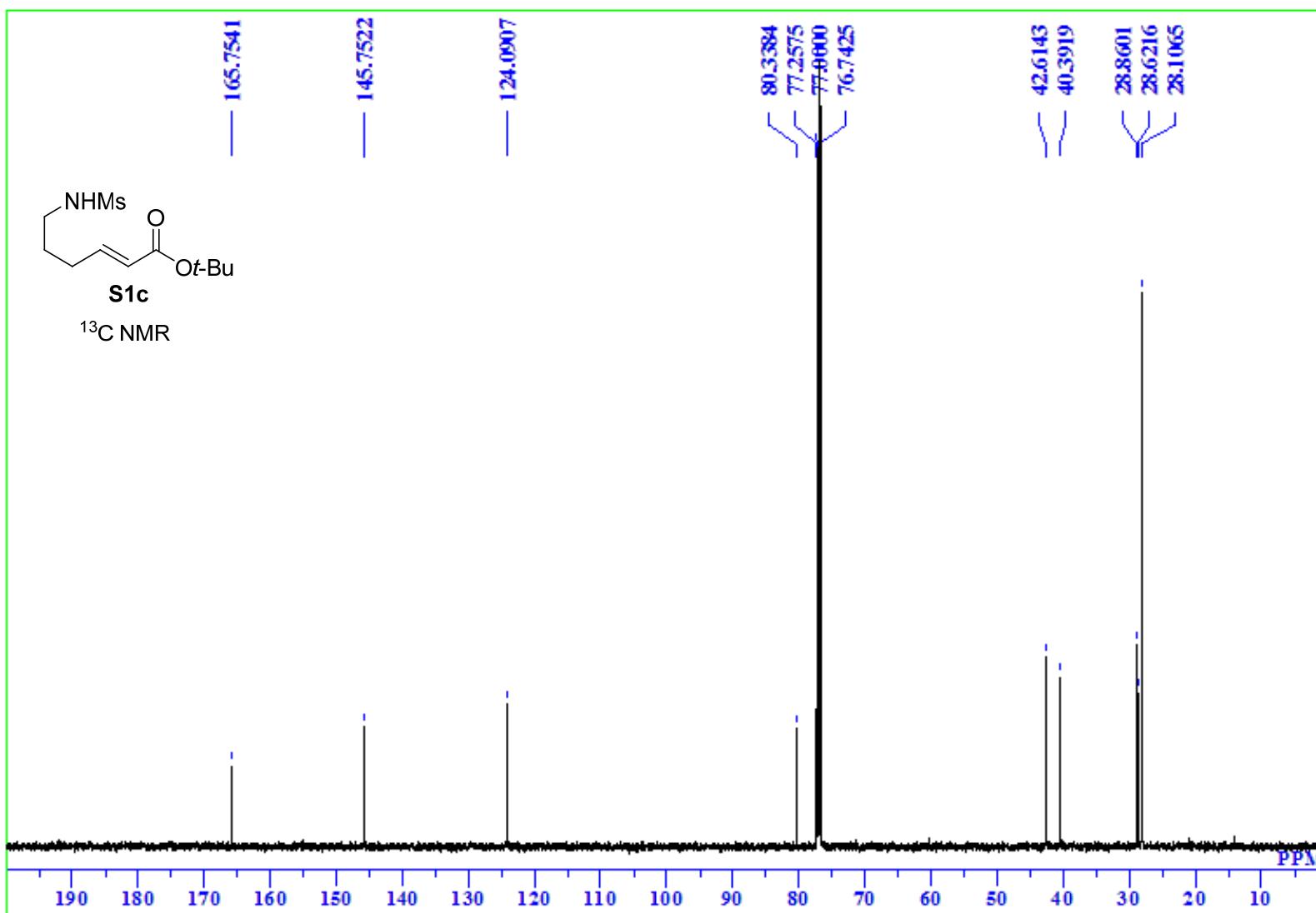




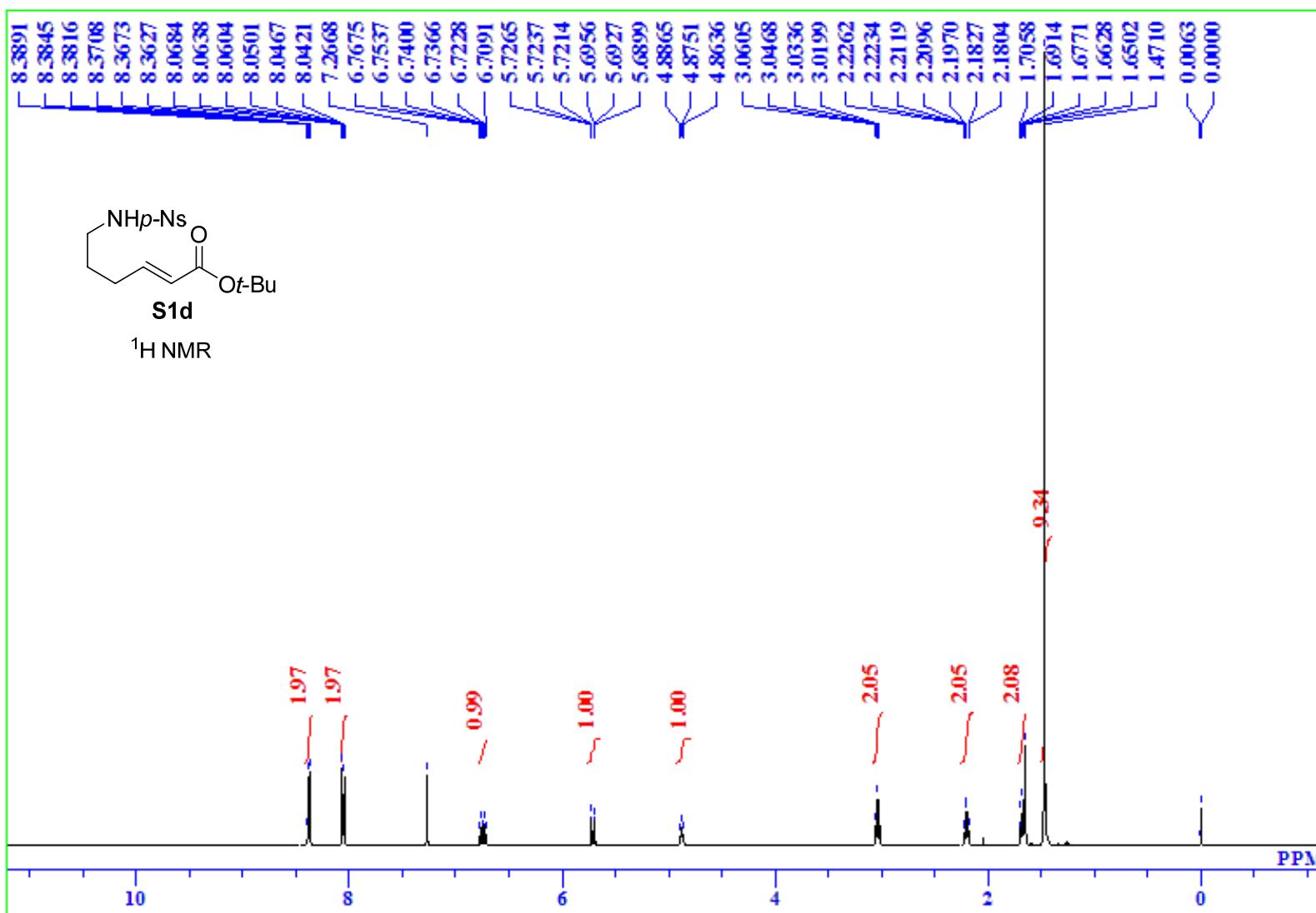


^1H NMR

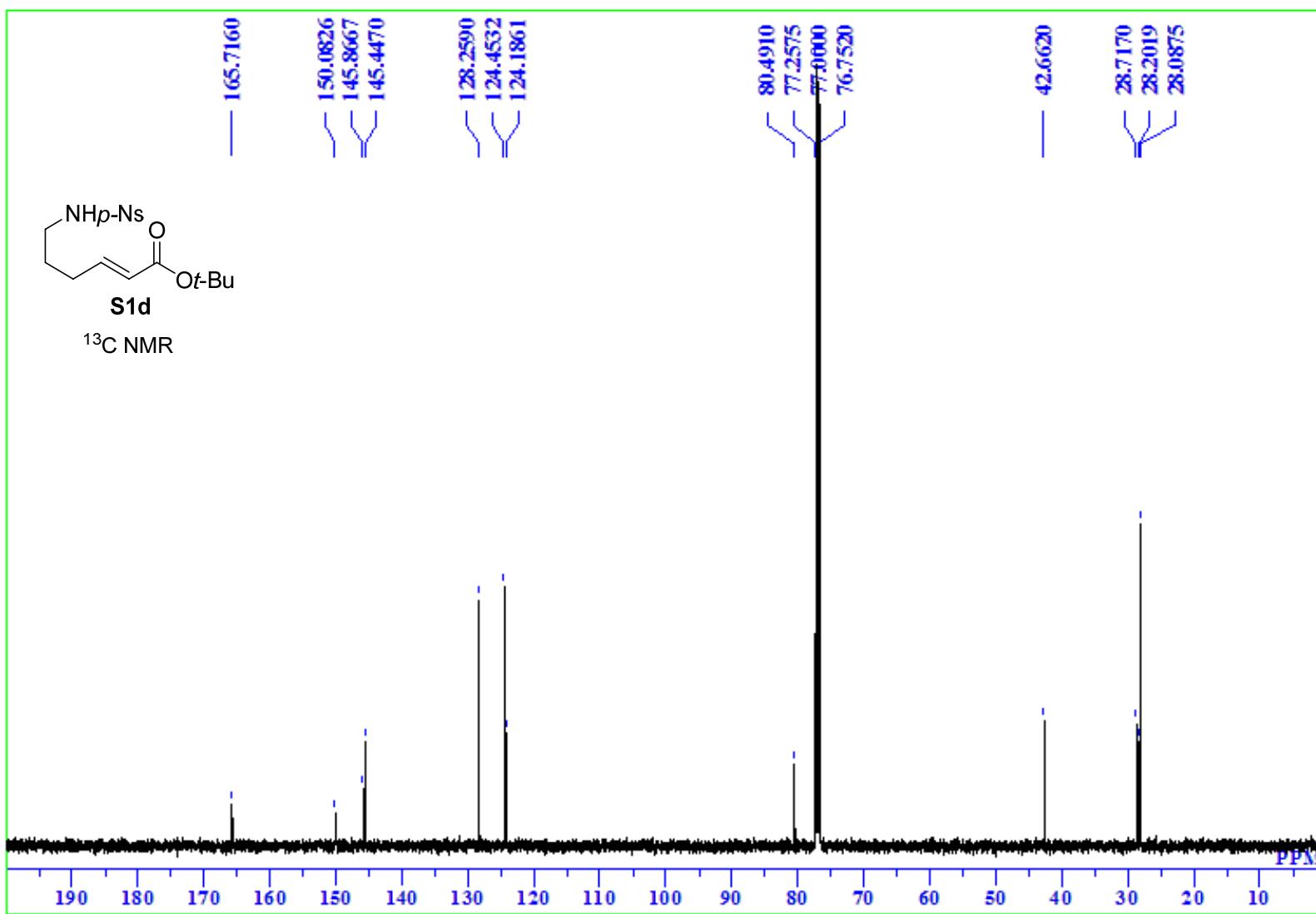


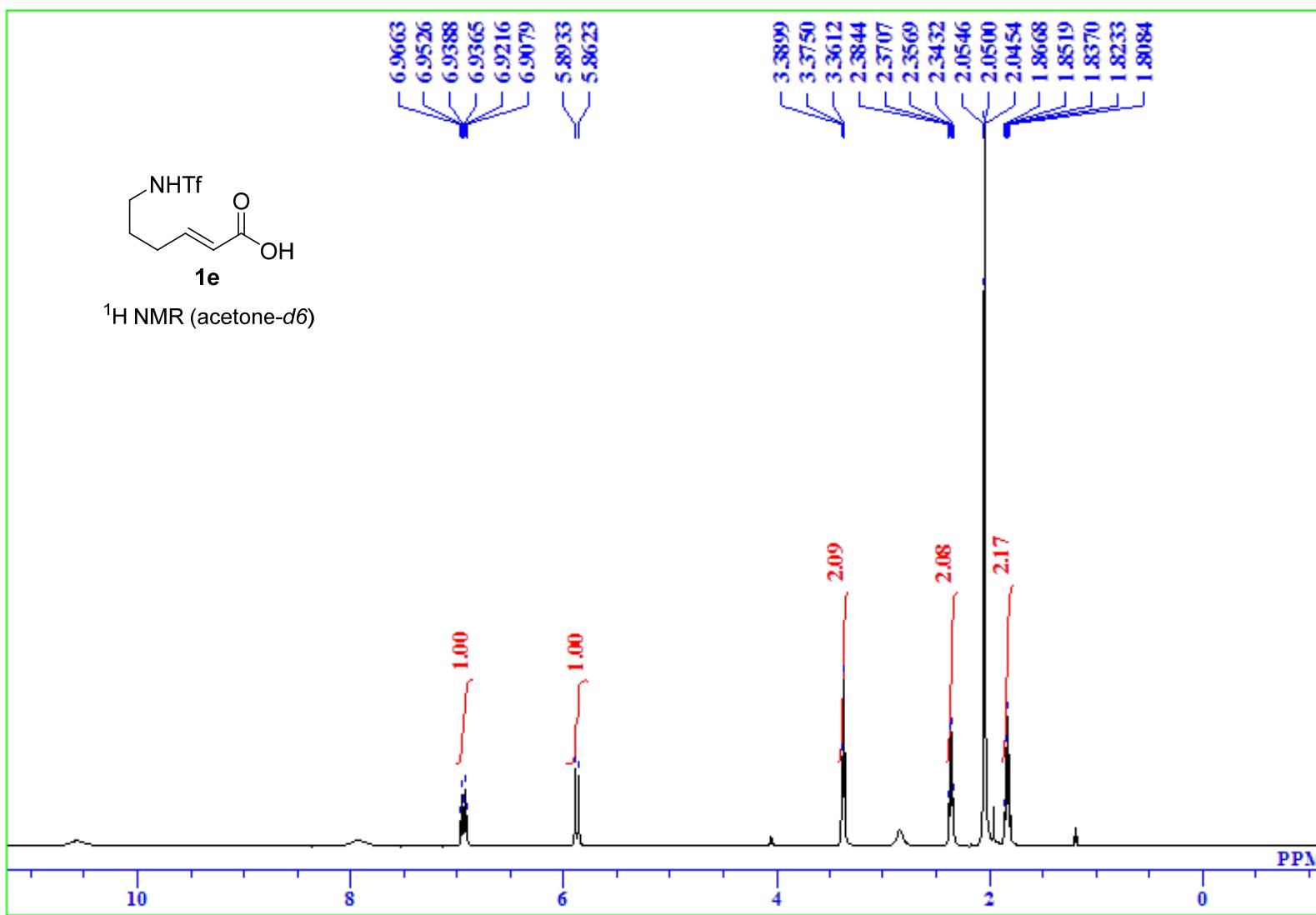


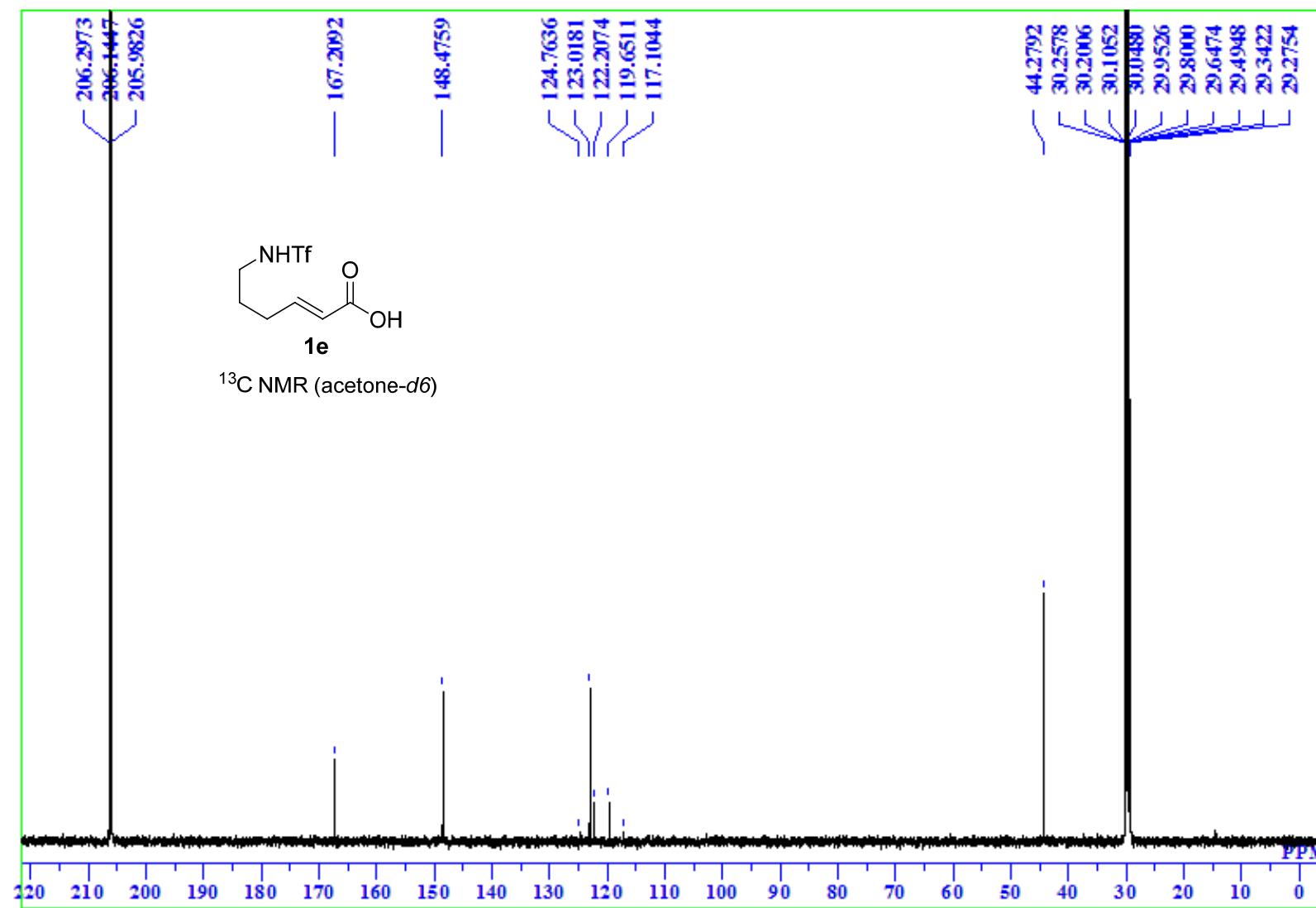
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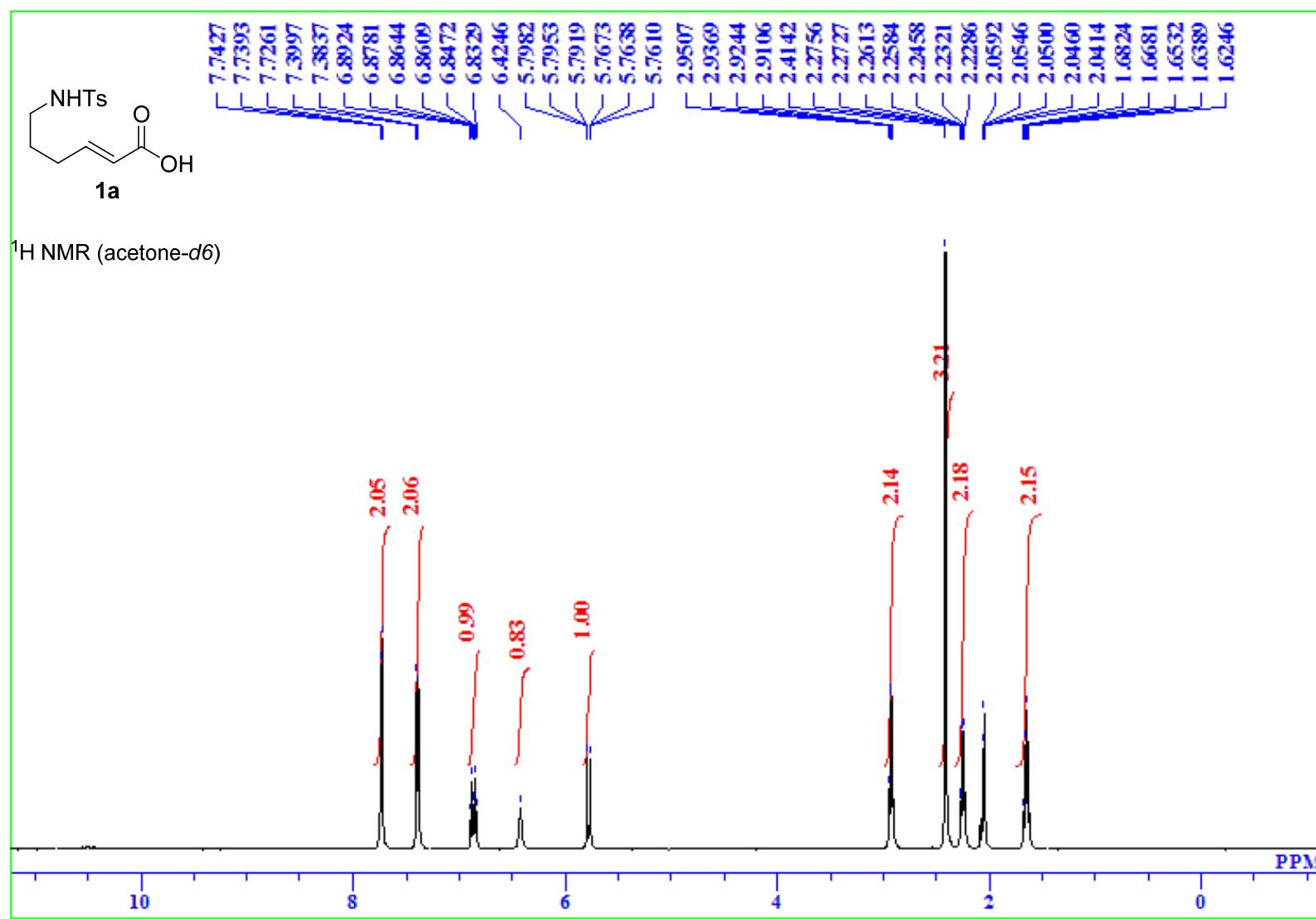


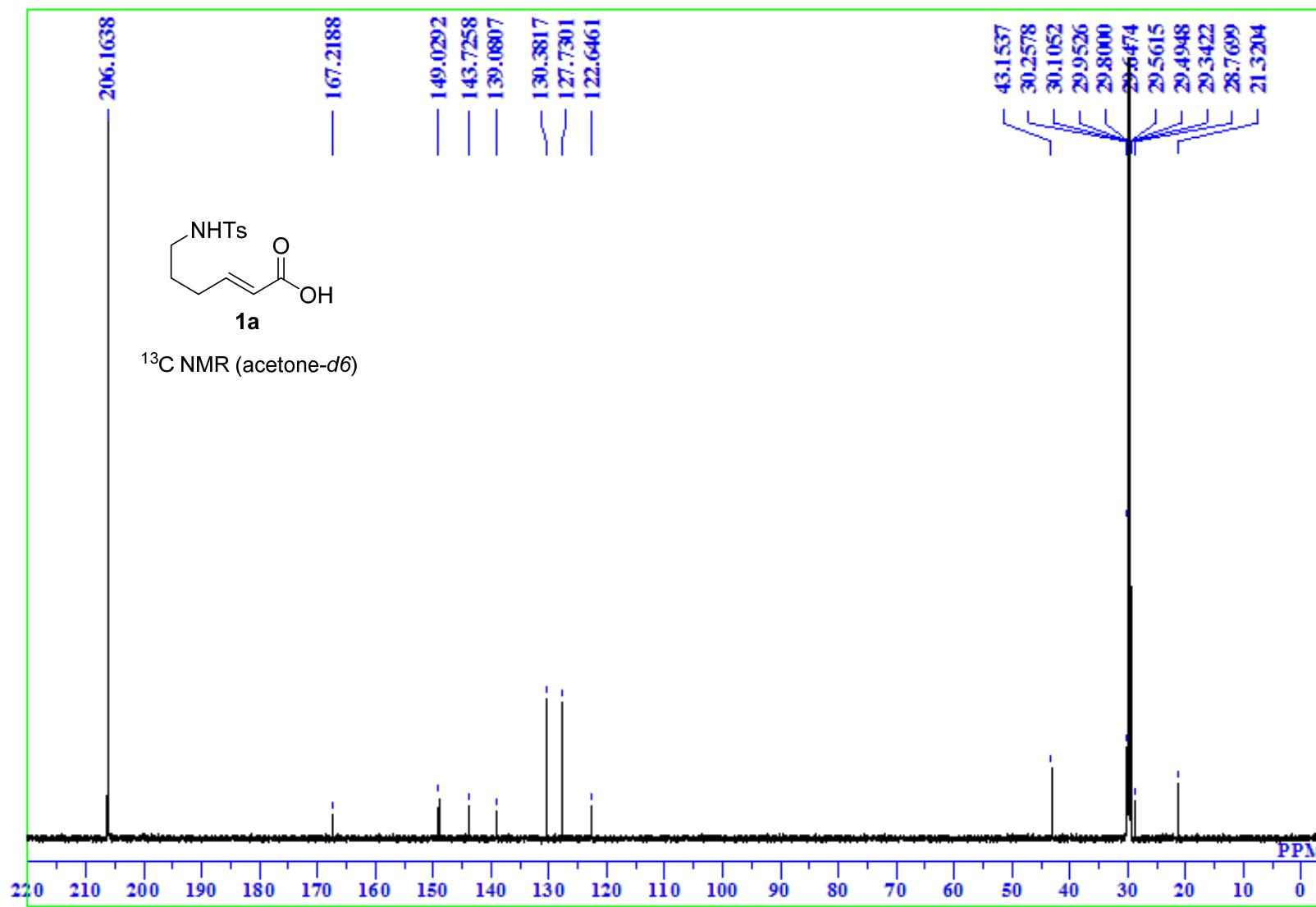
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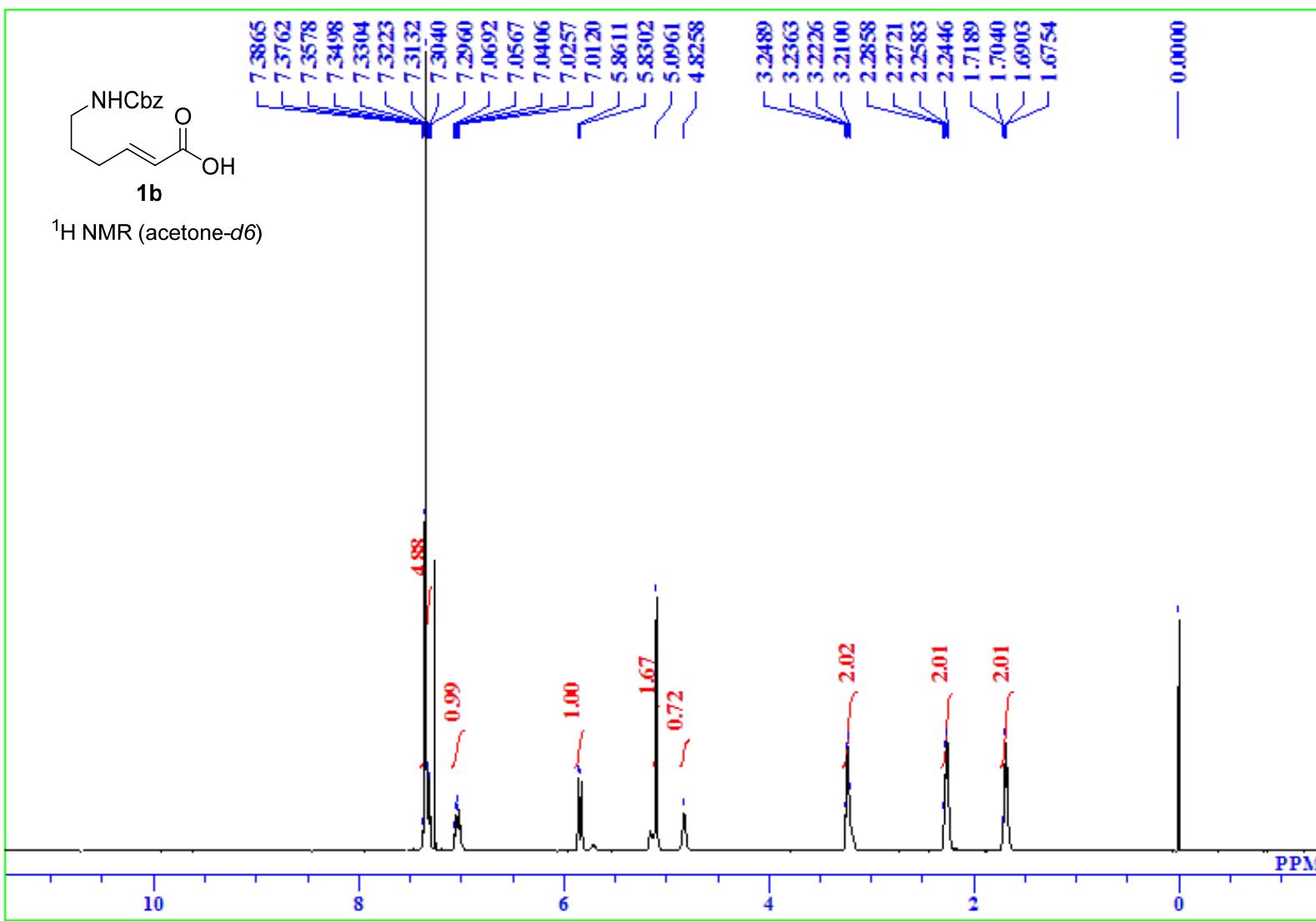


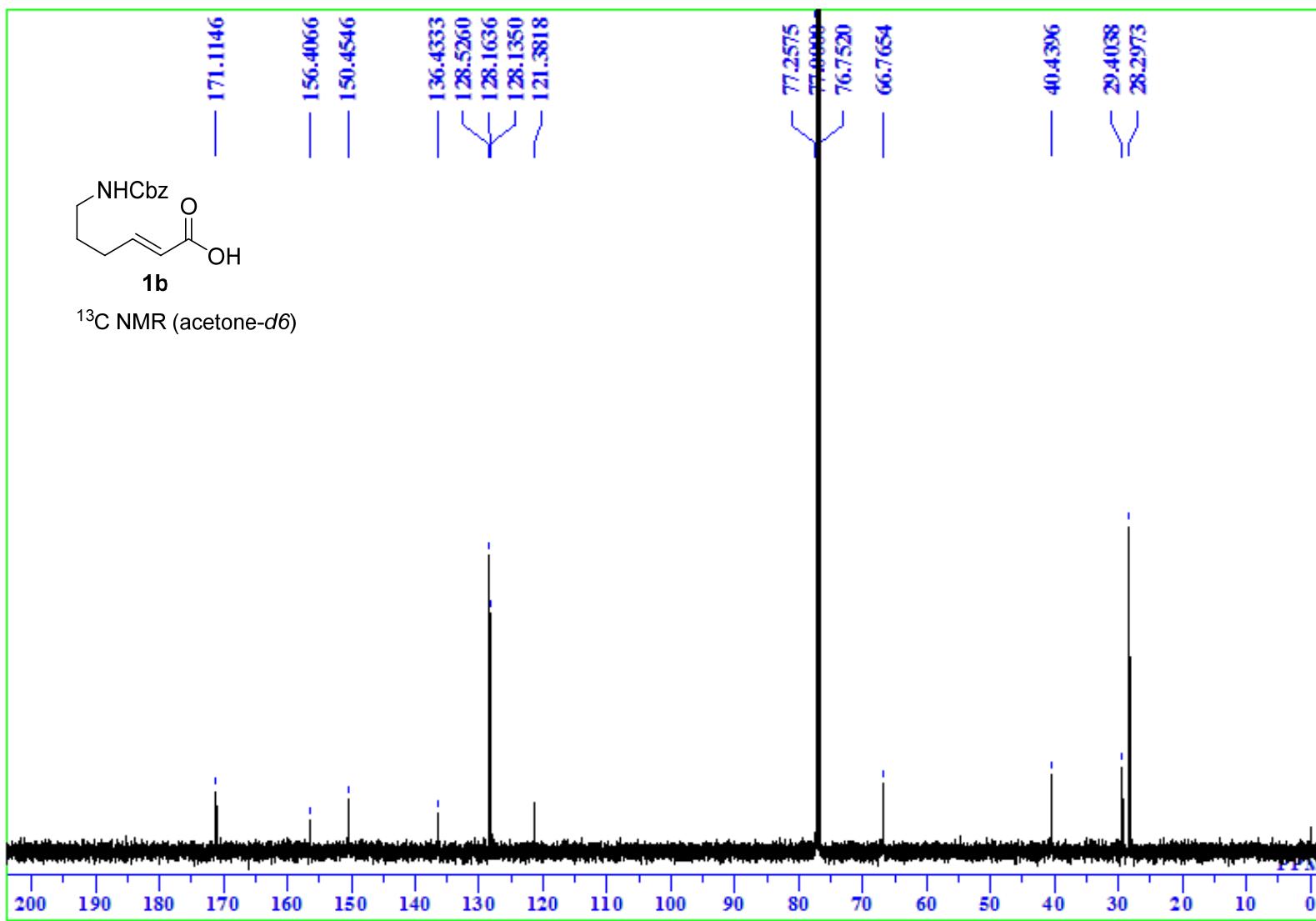


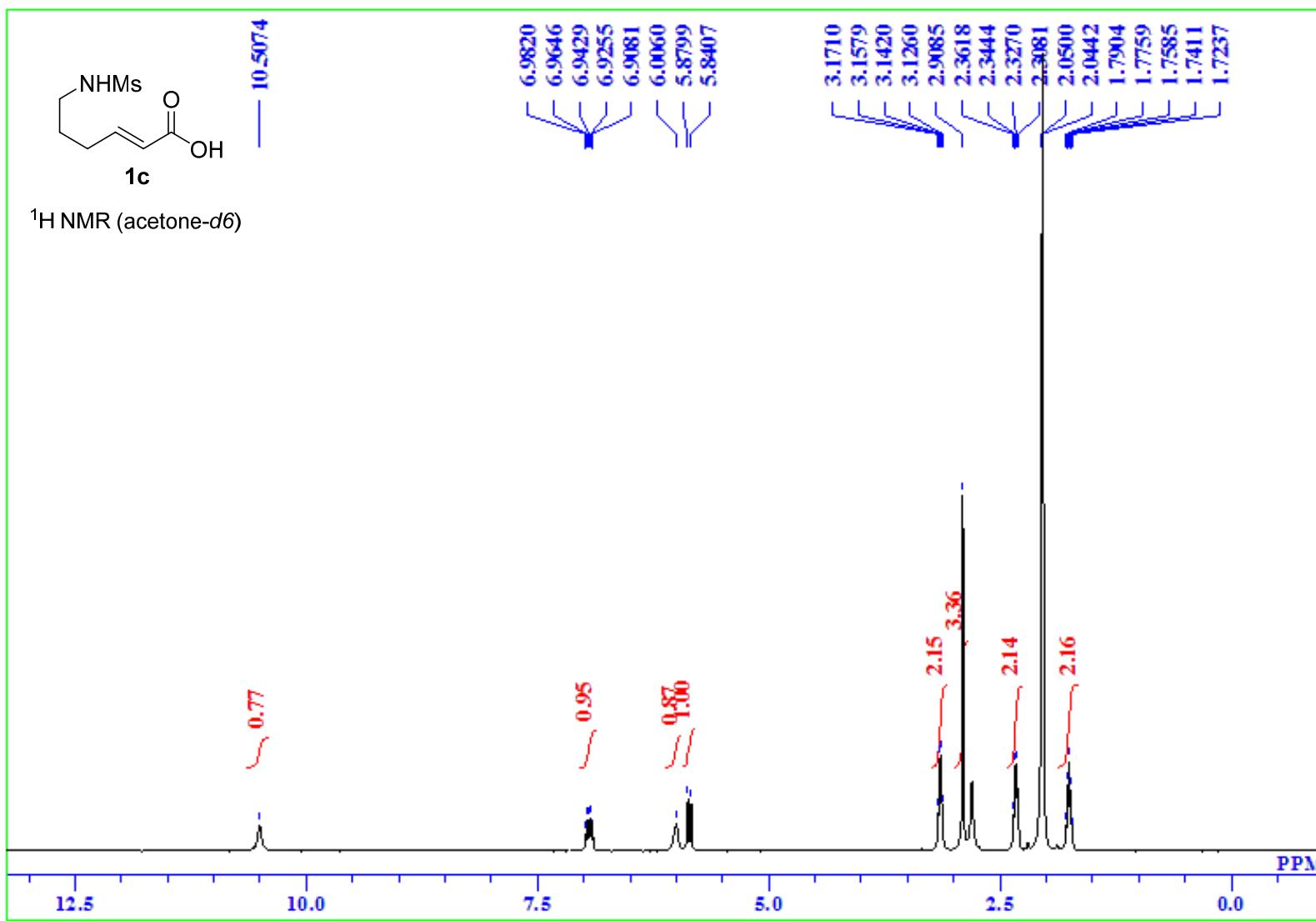


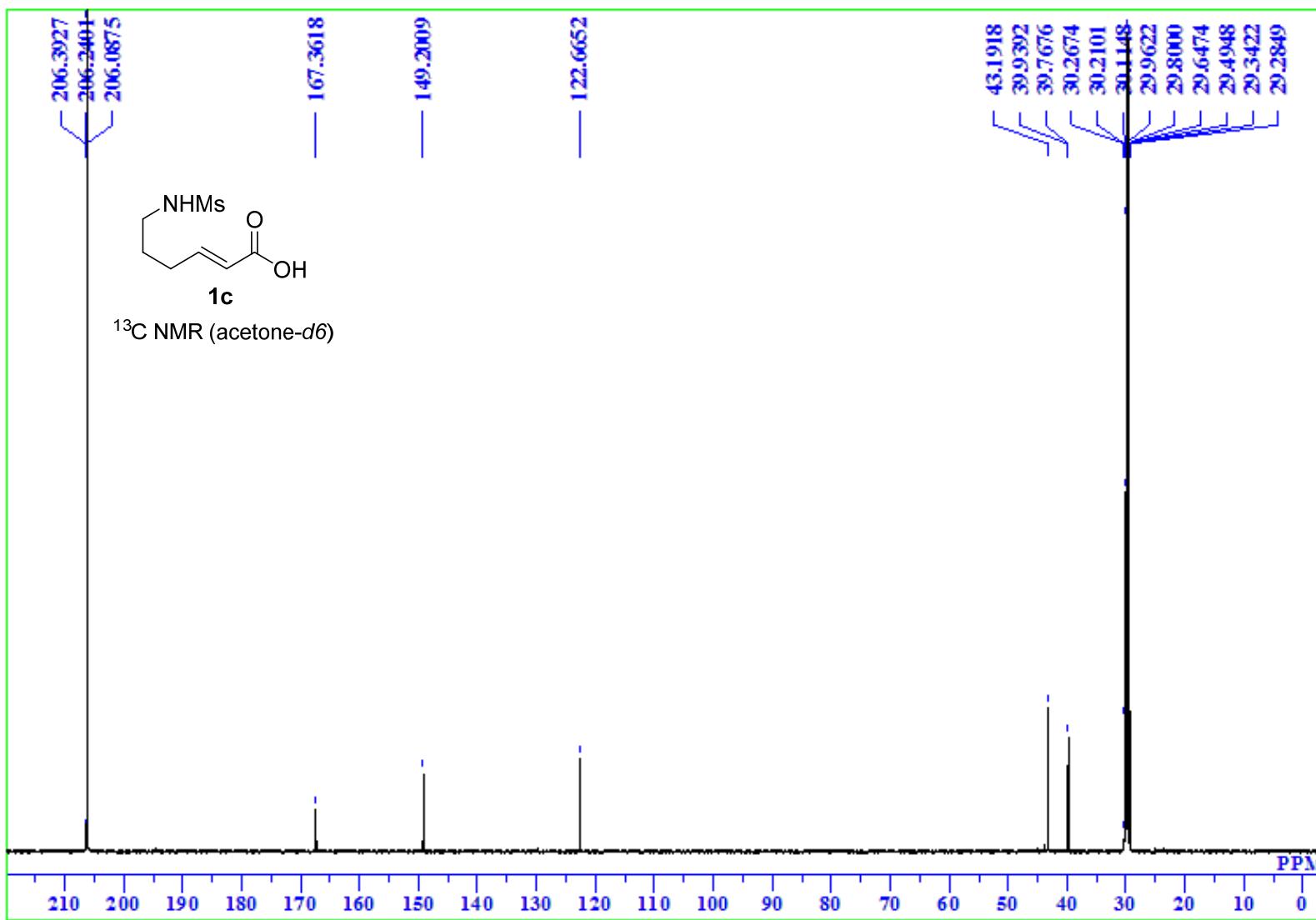


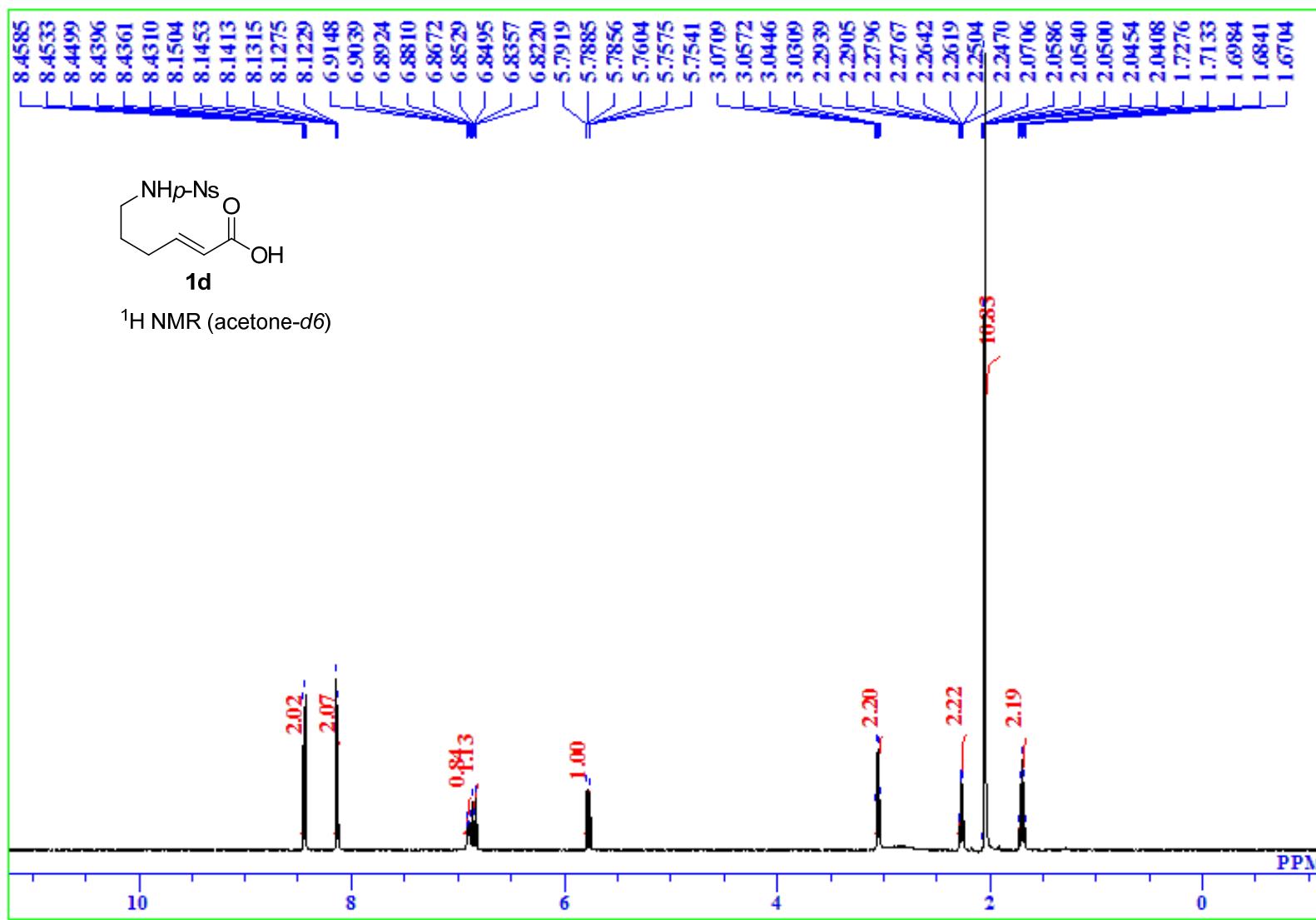


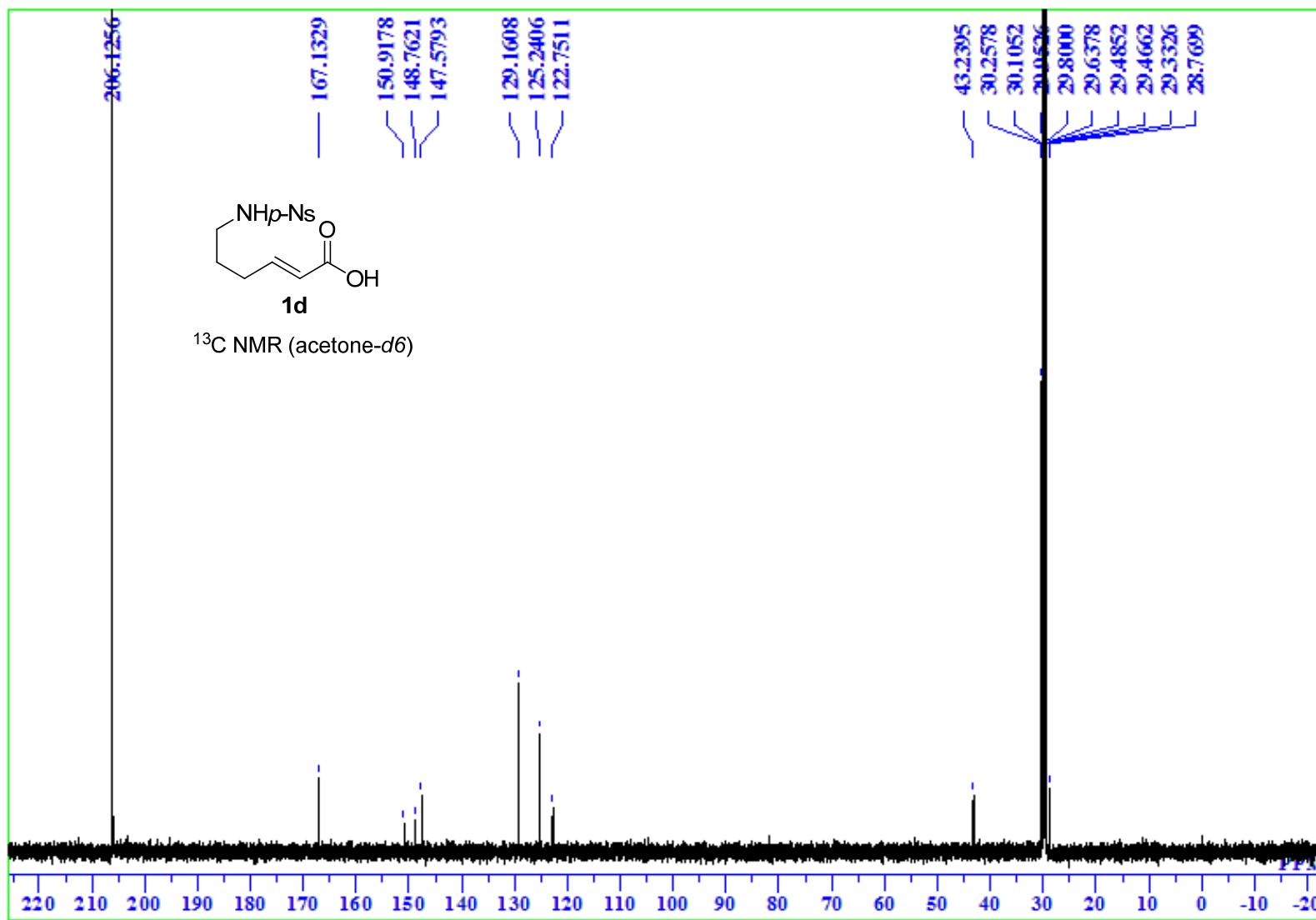


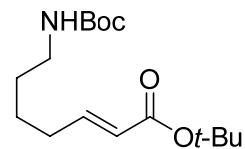






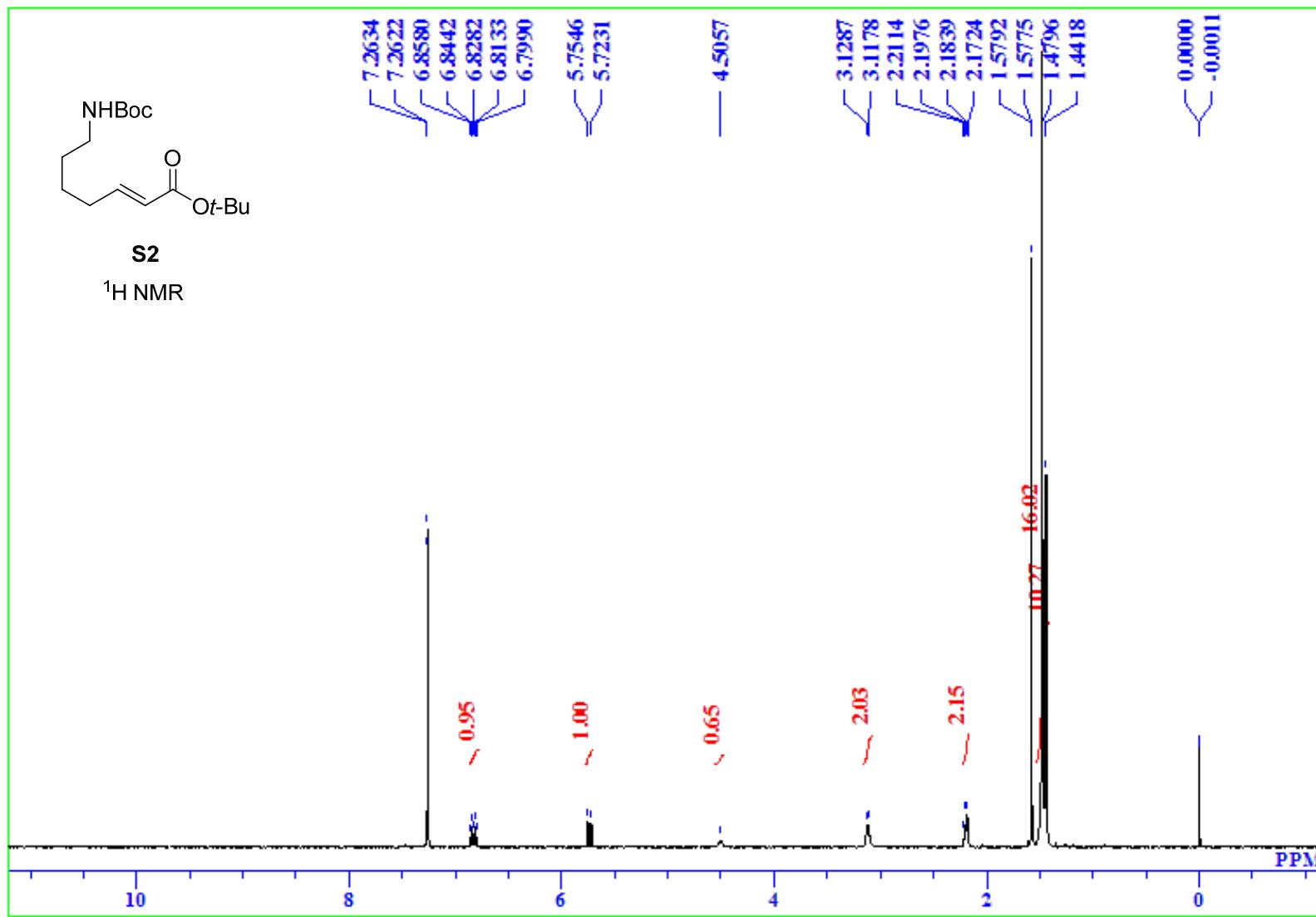


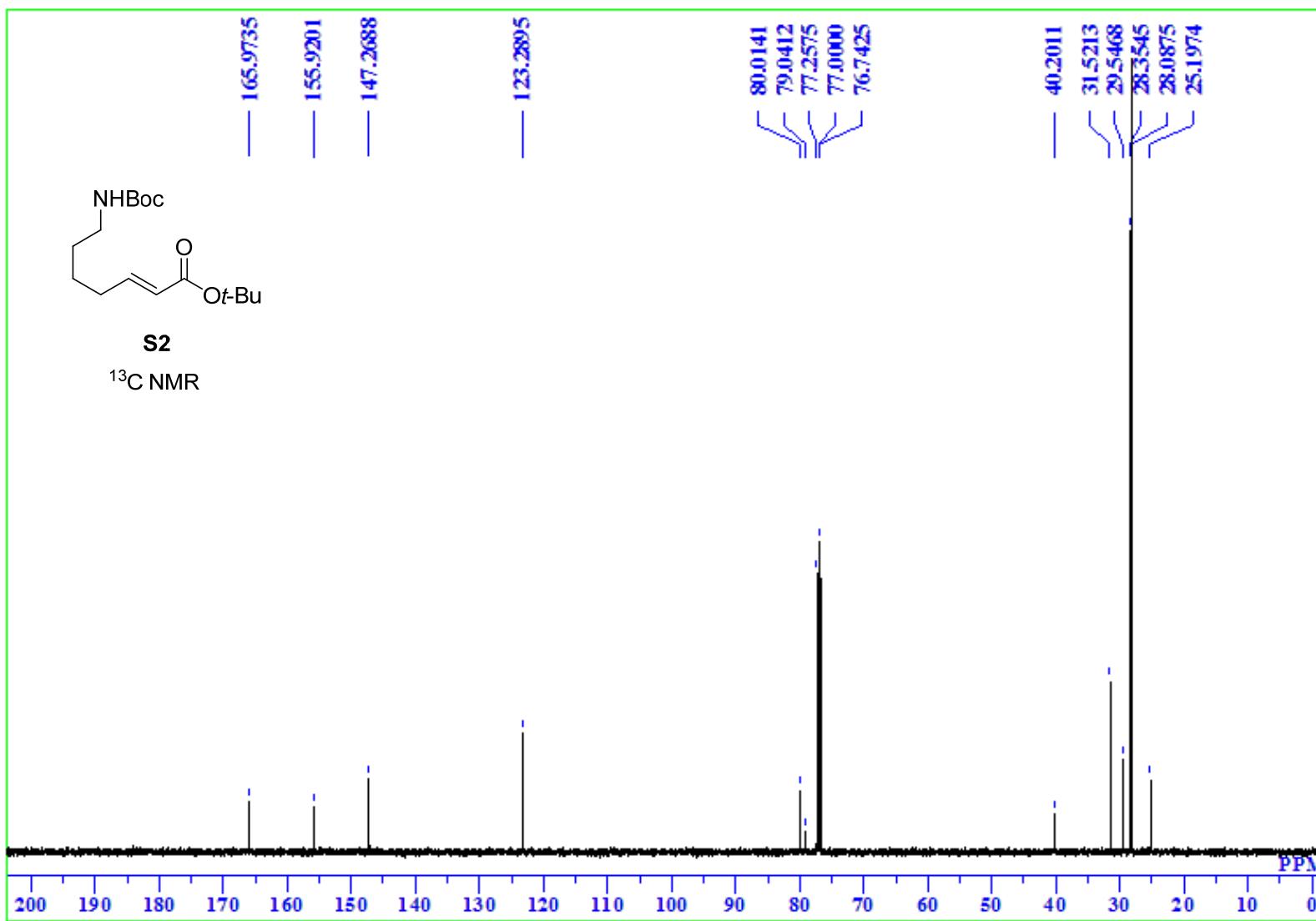


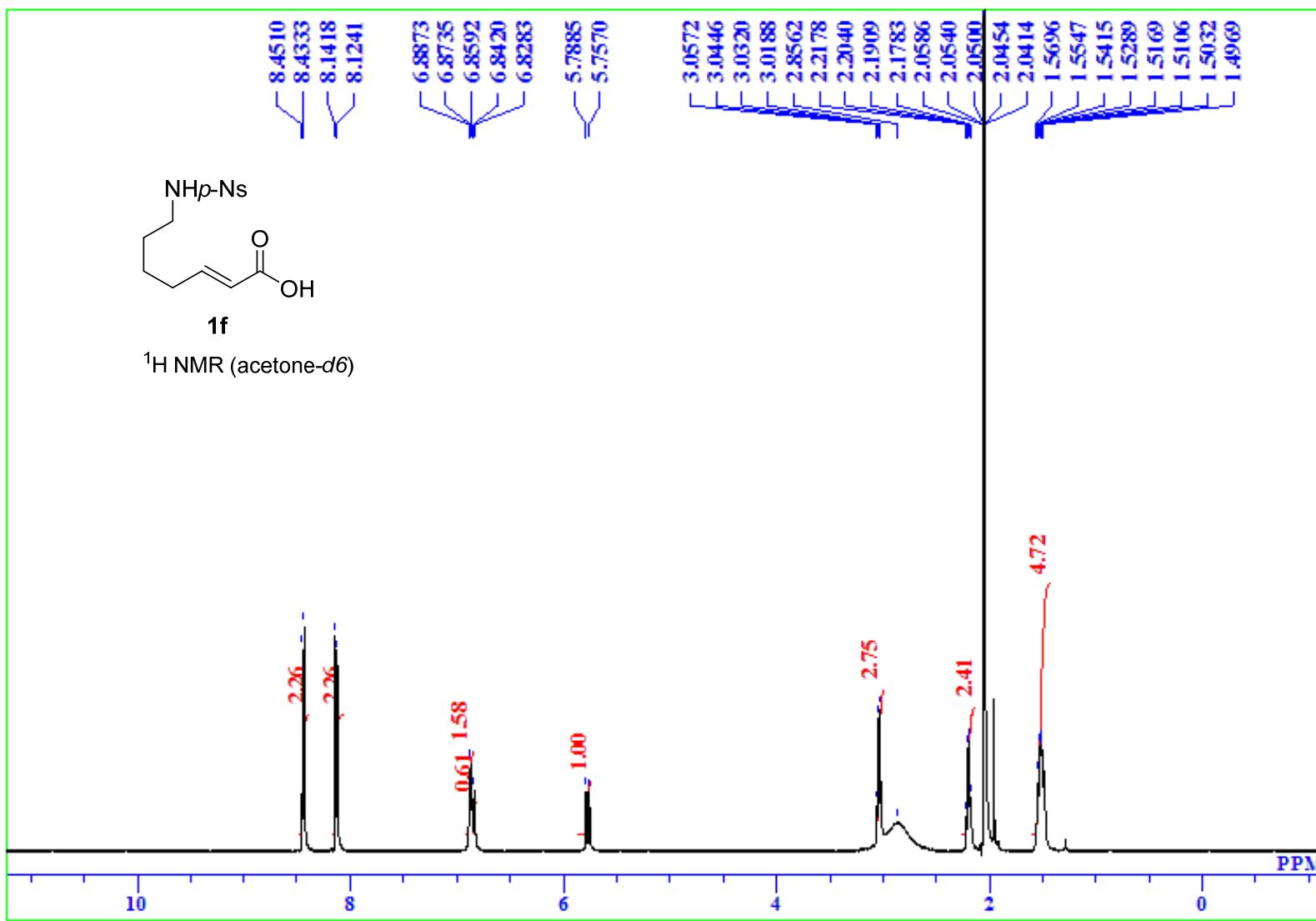


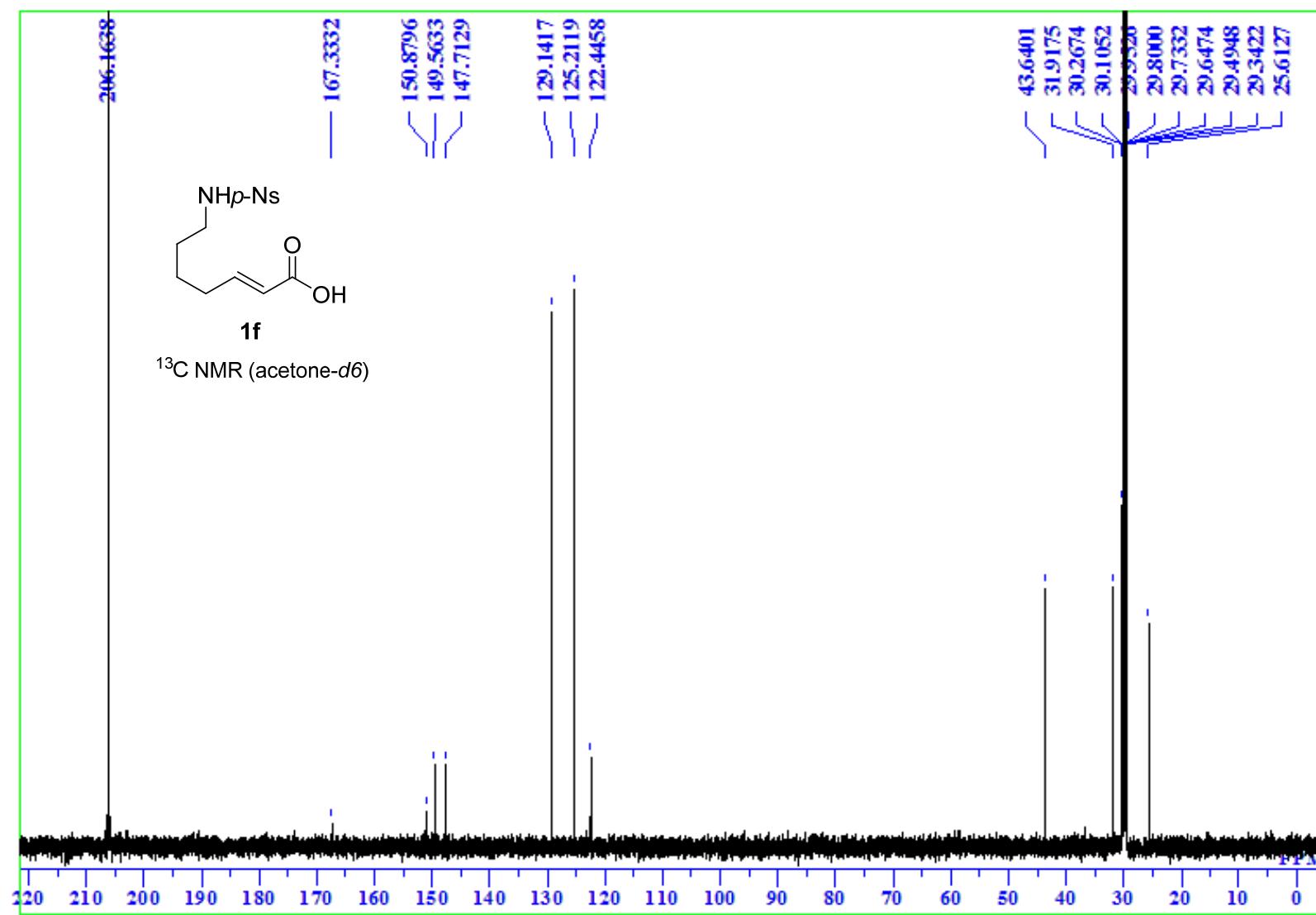
S2

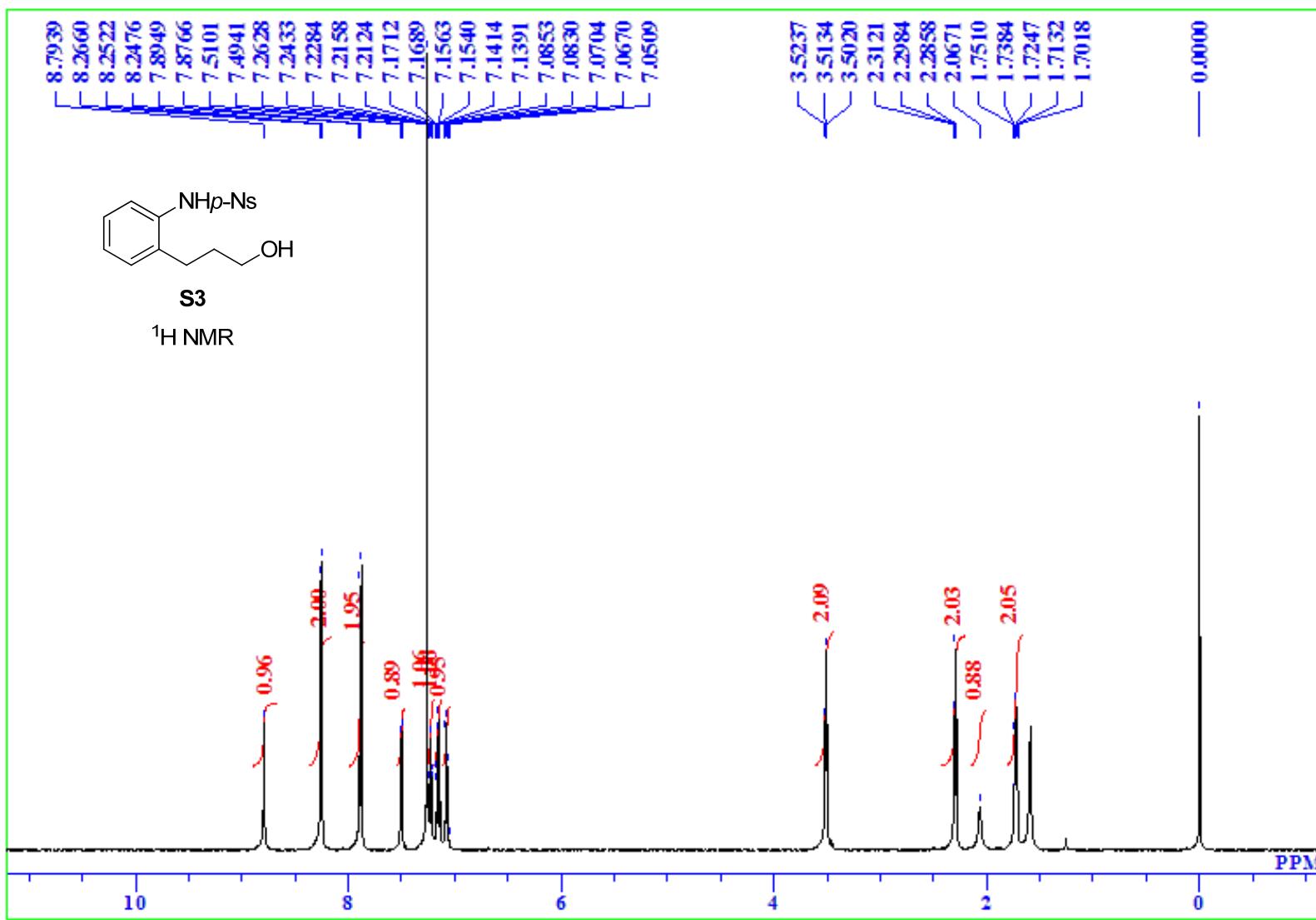
^1H NMR

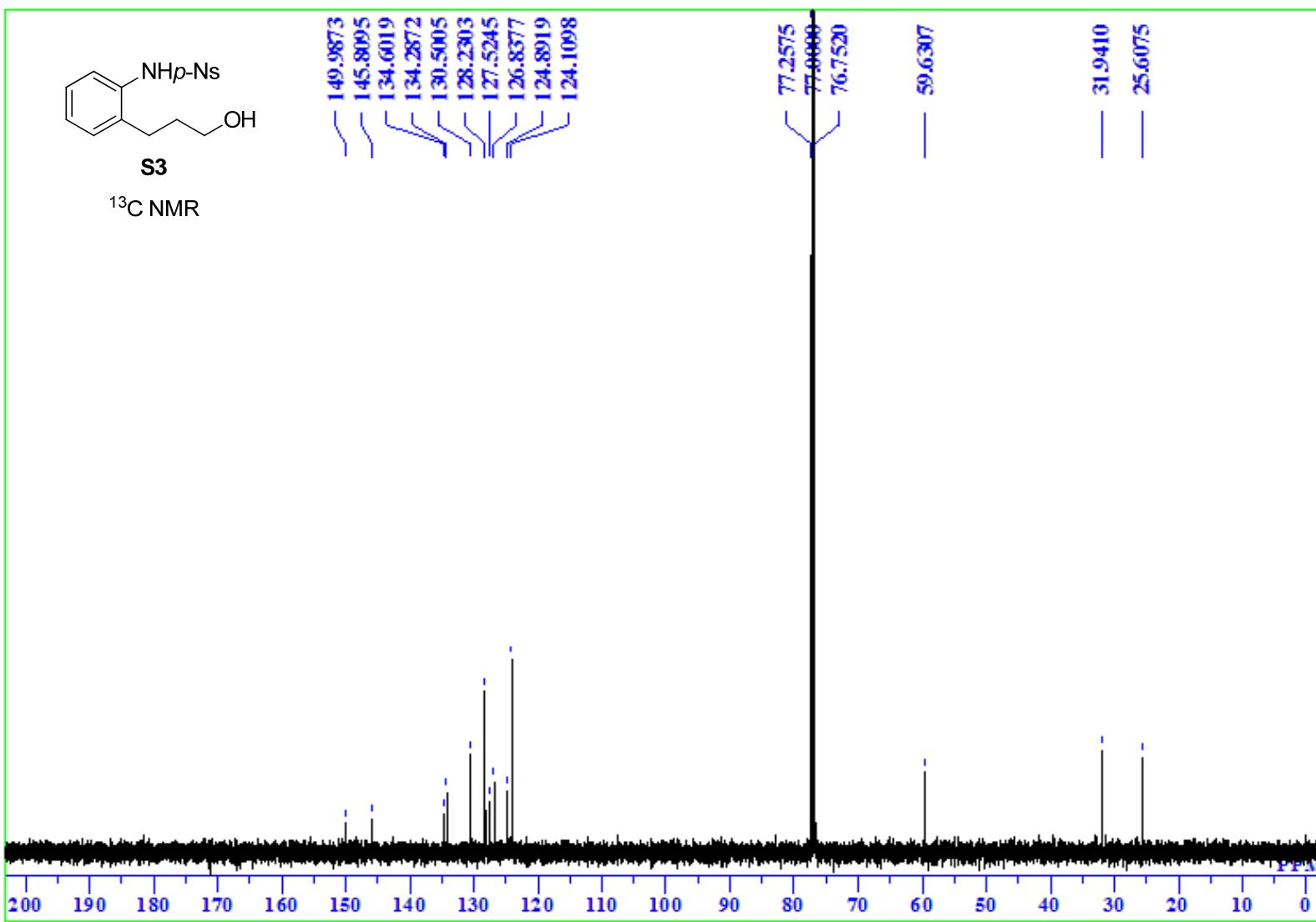


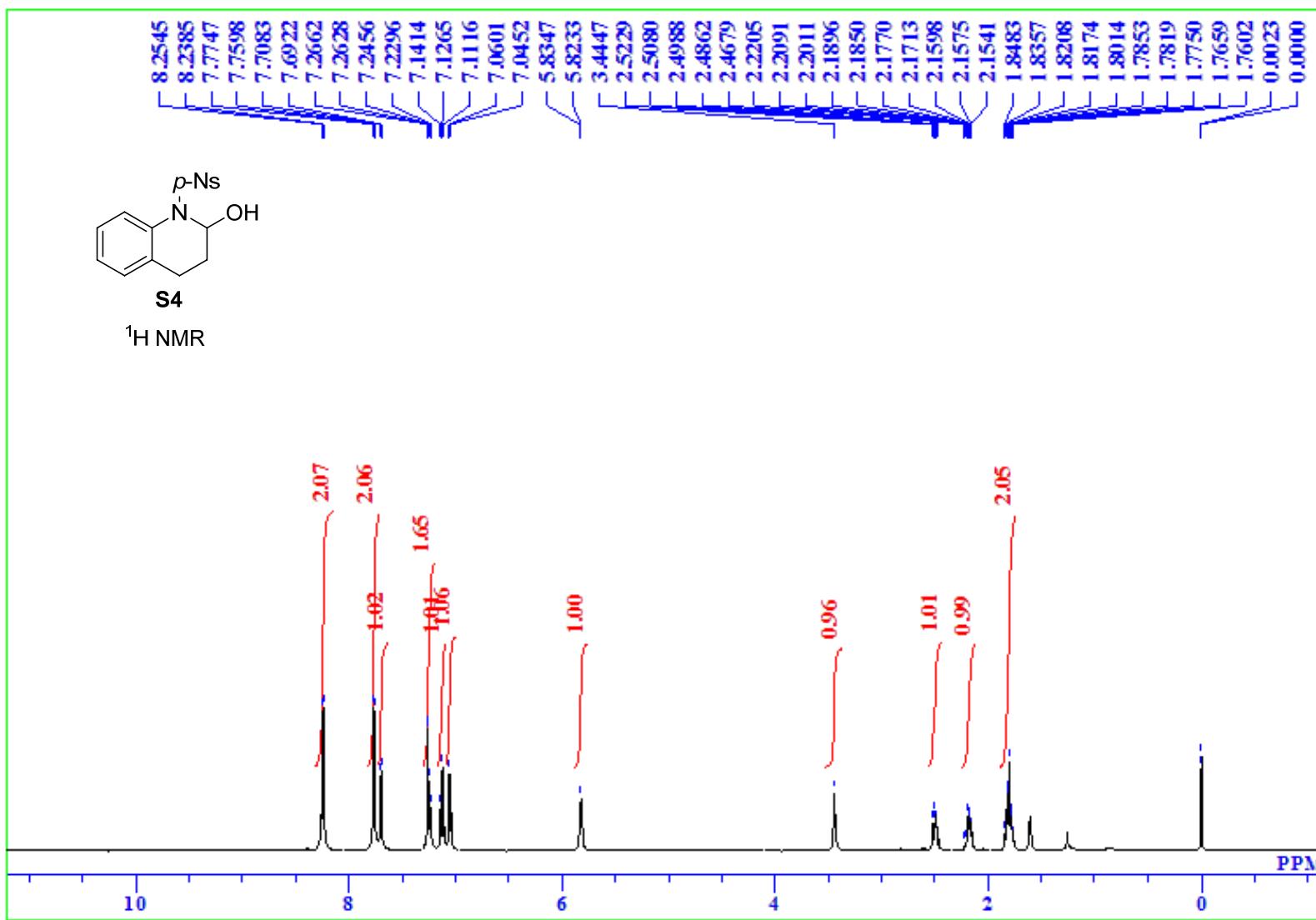


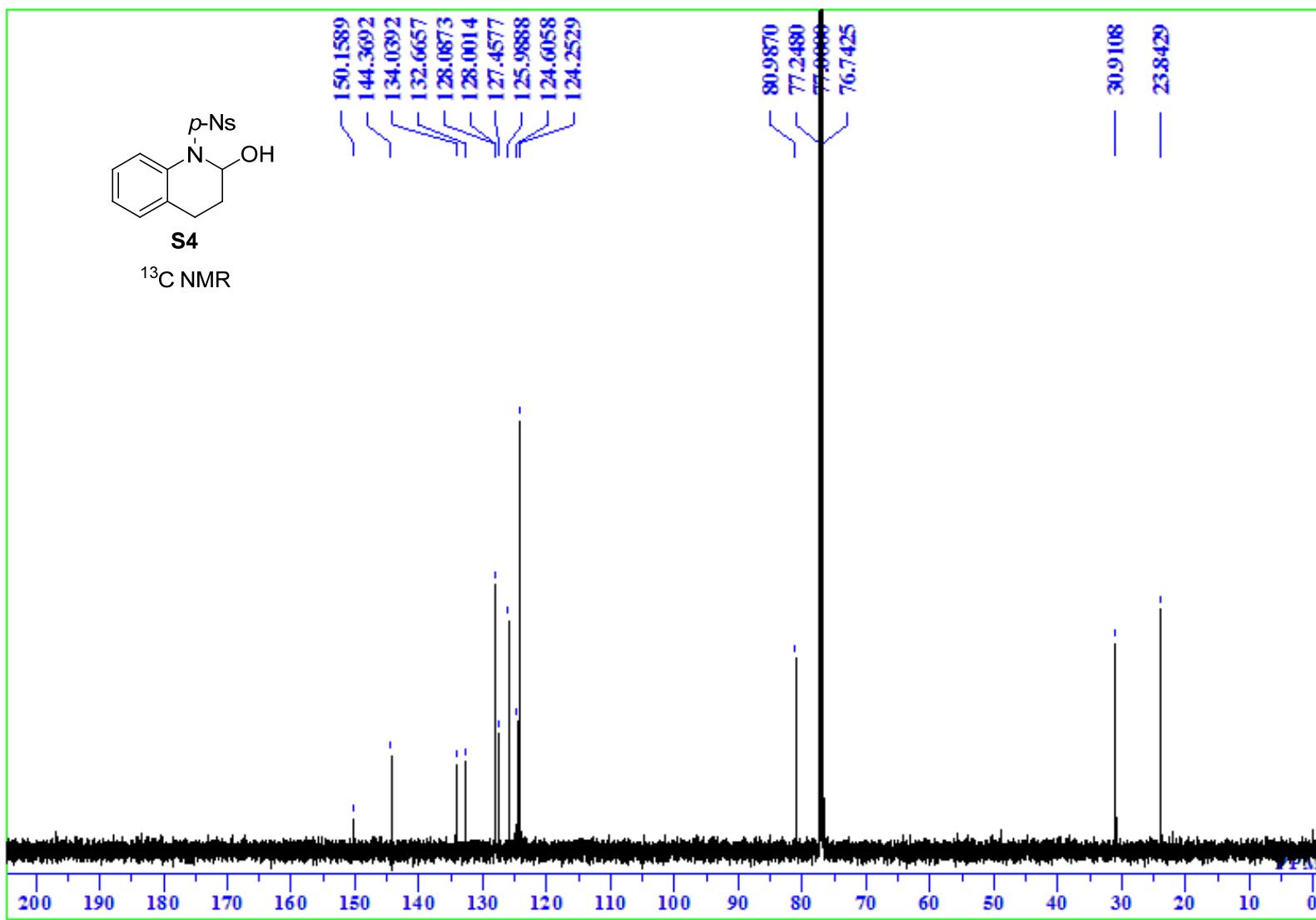




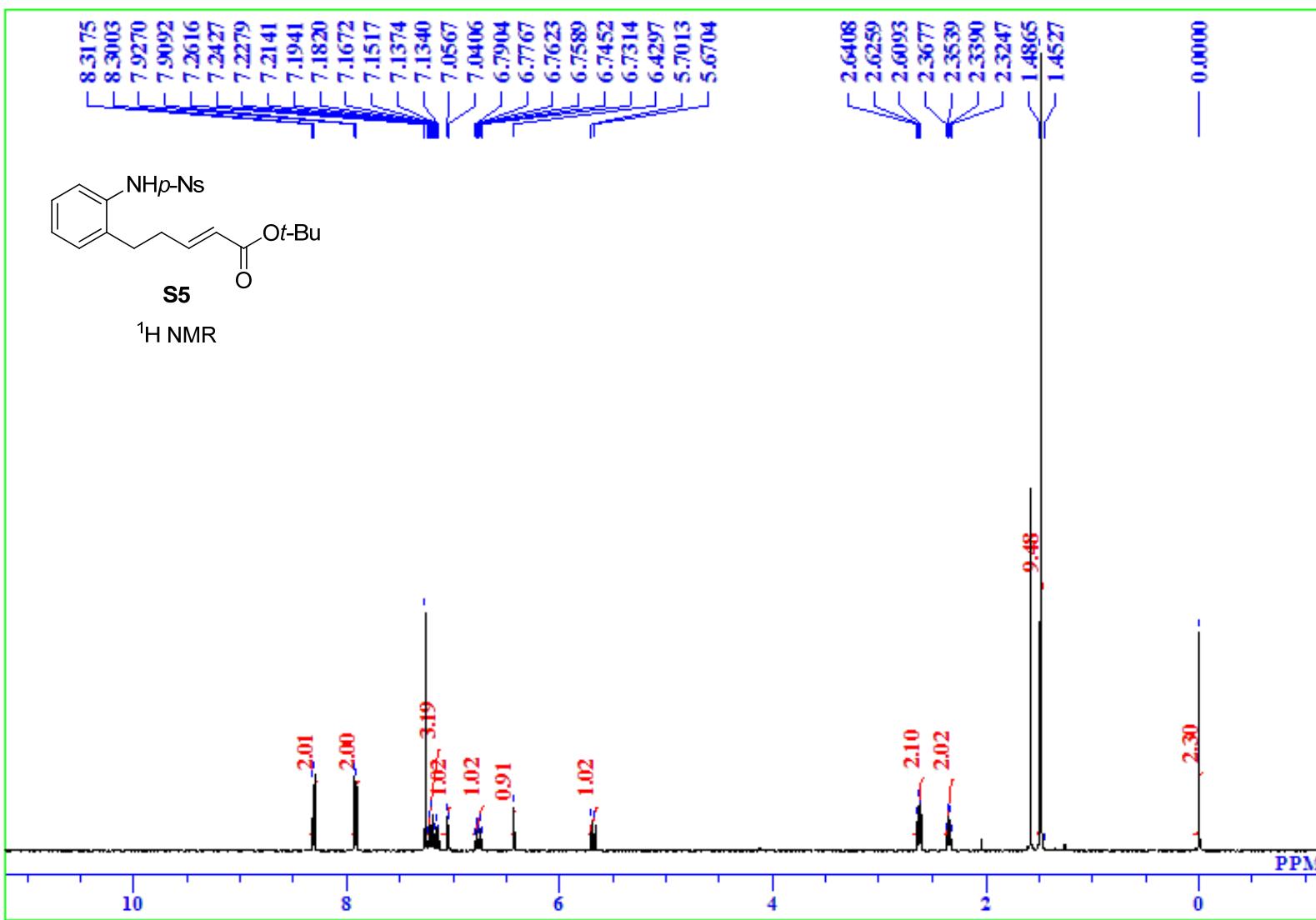


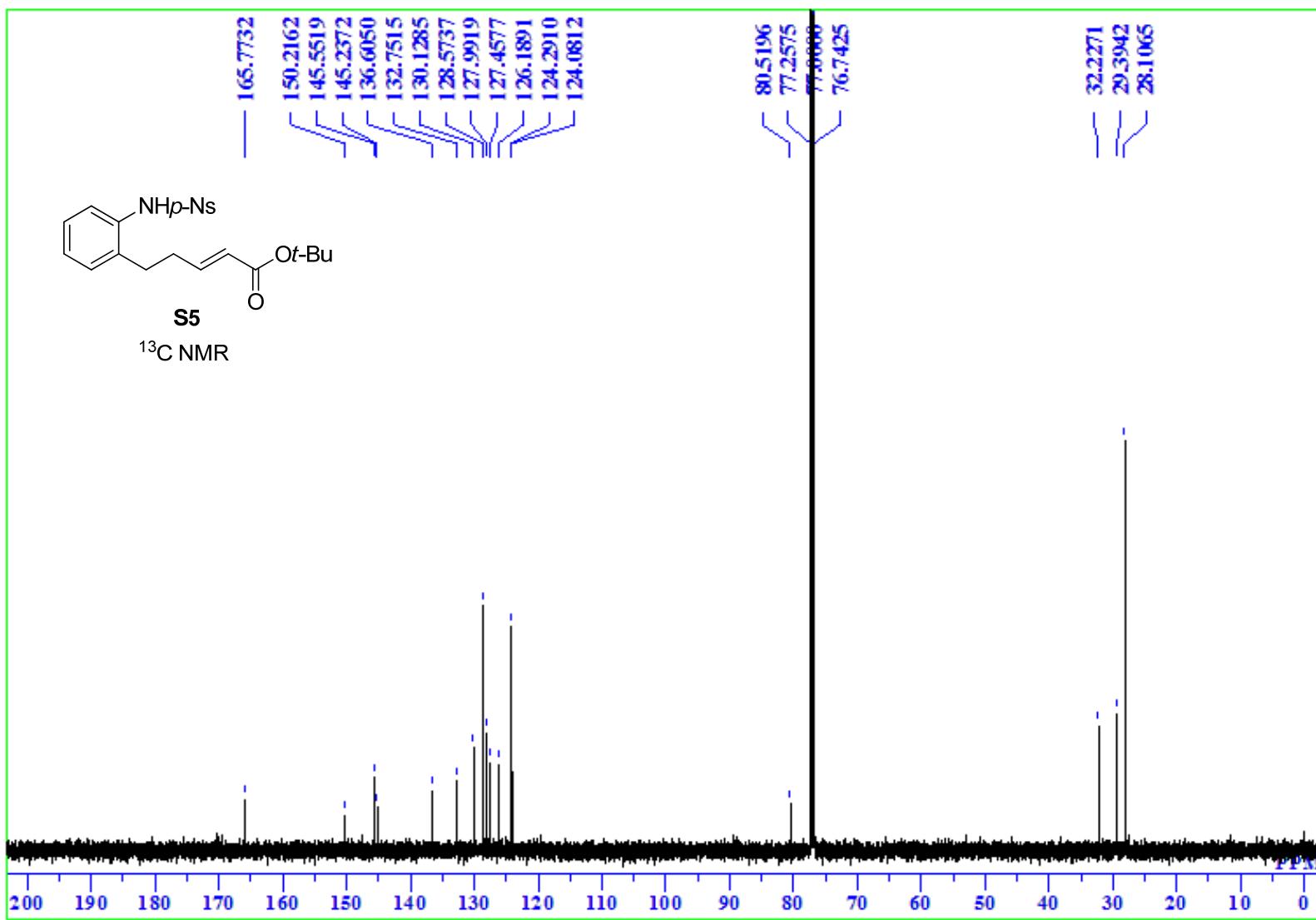


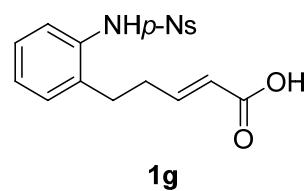




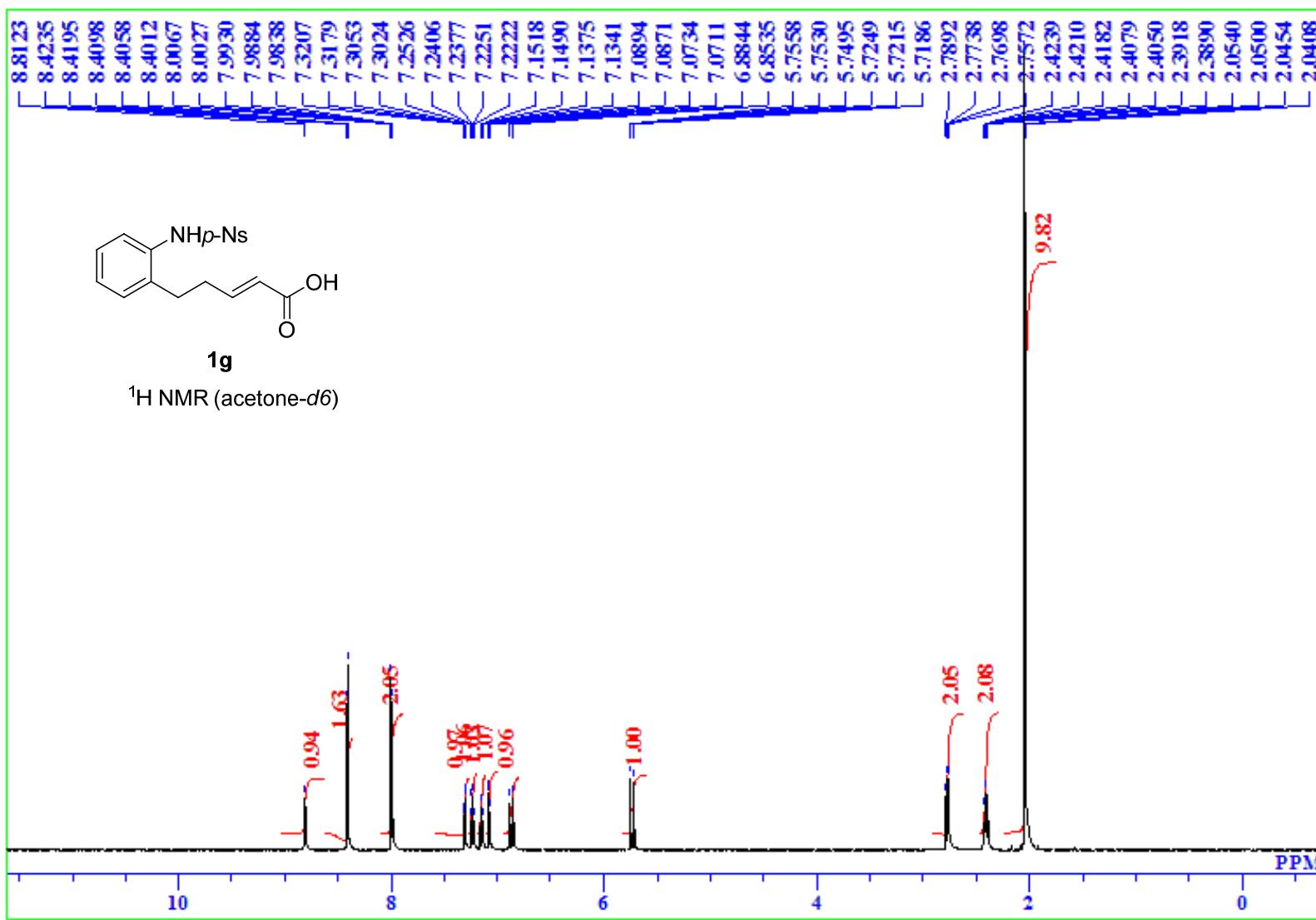
S70

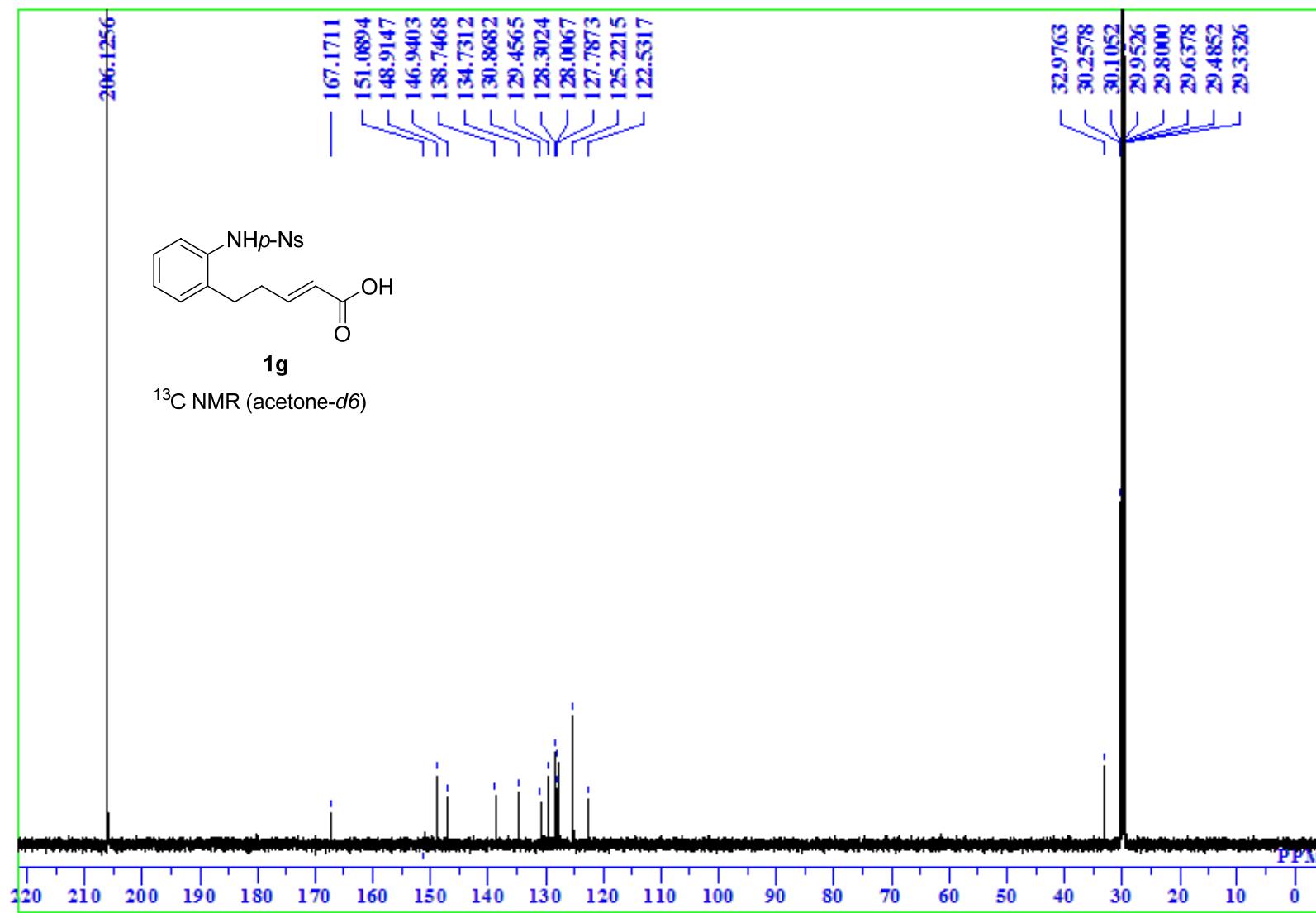


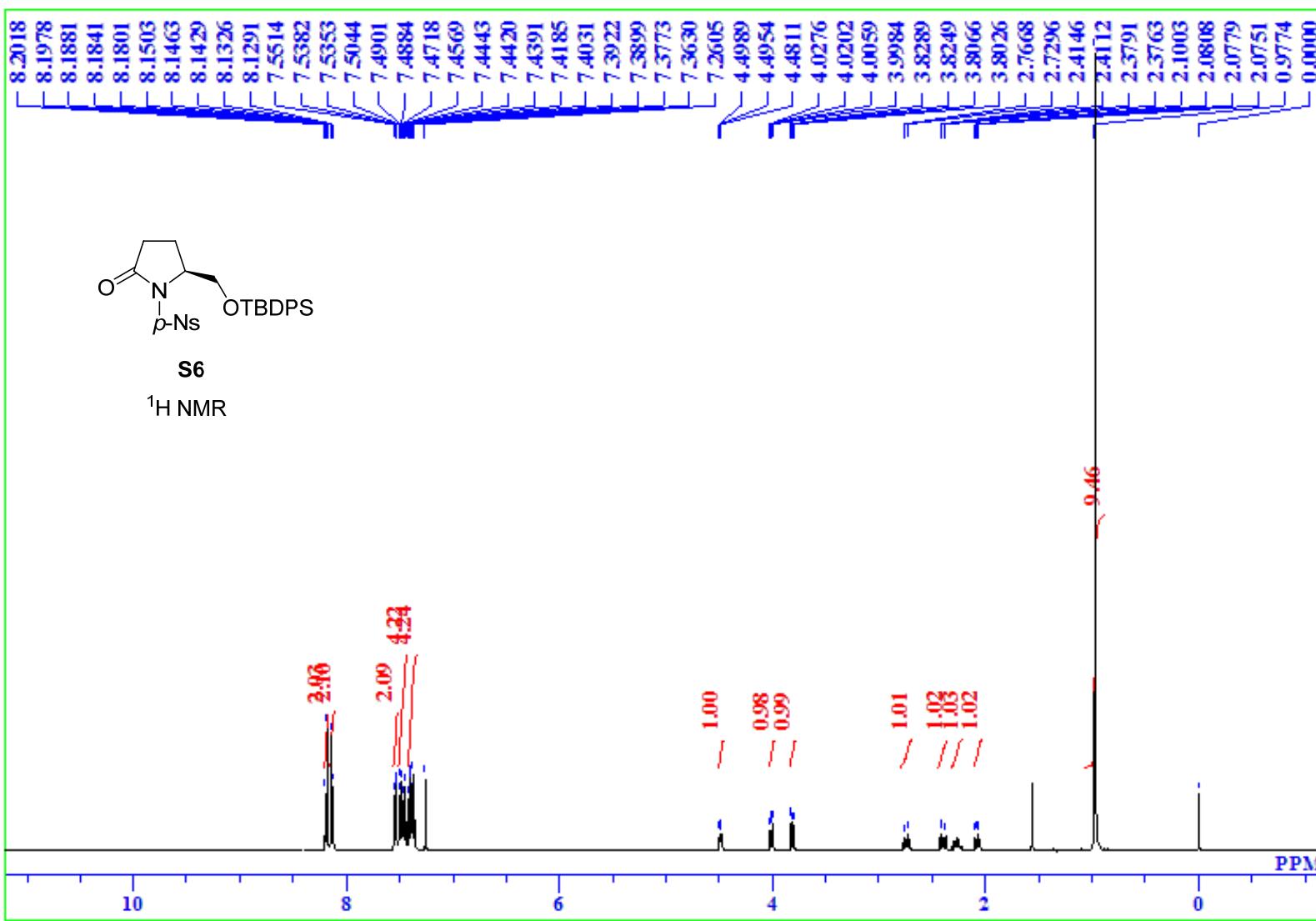


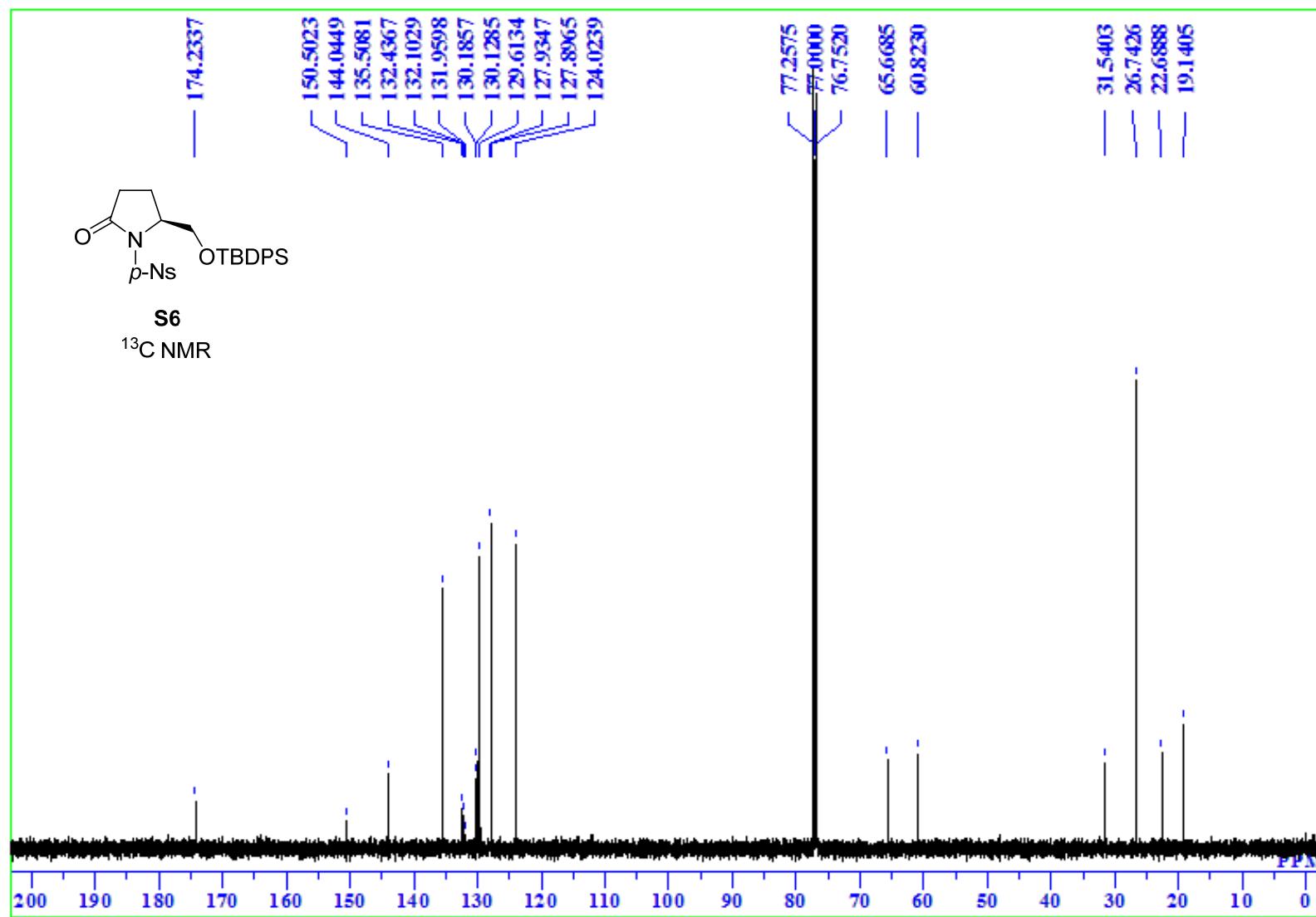


¹H NMR (acetone-d₆)

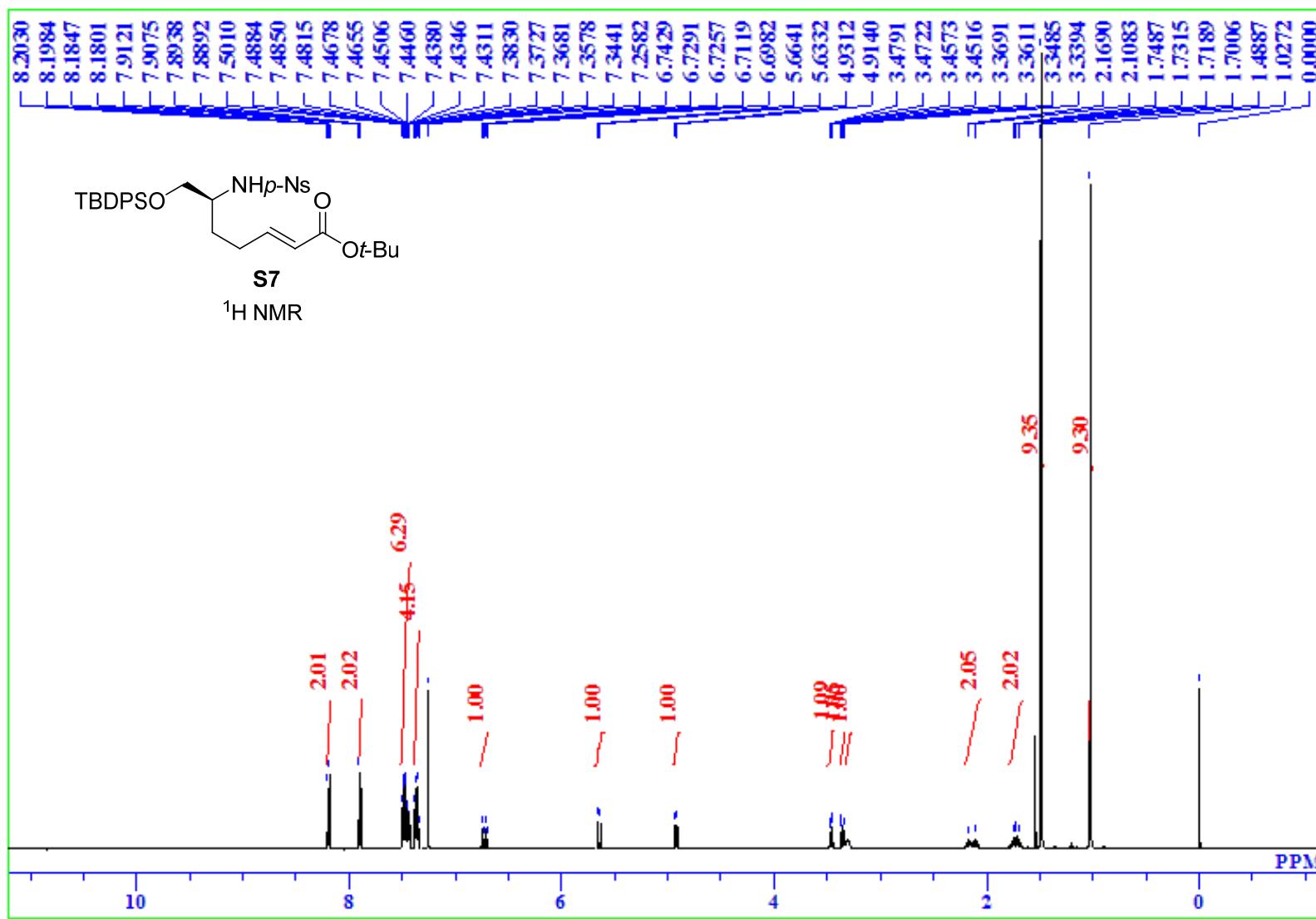




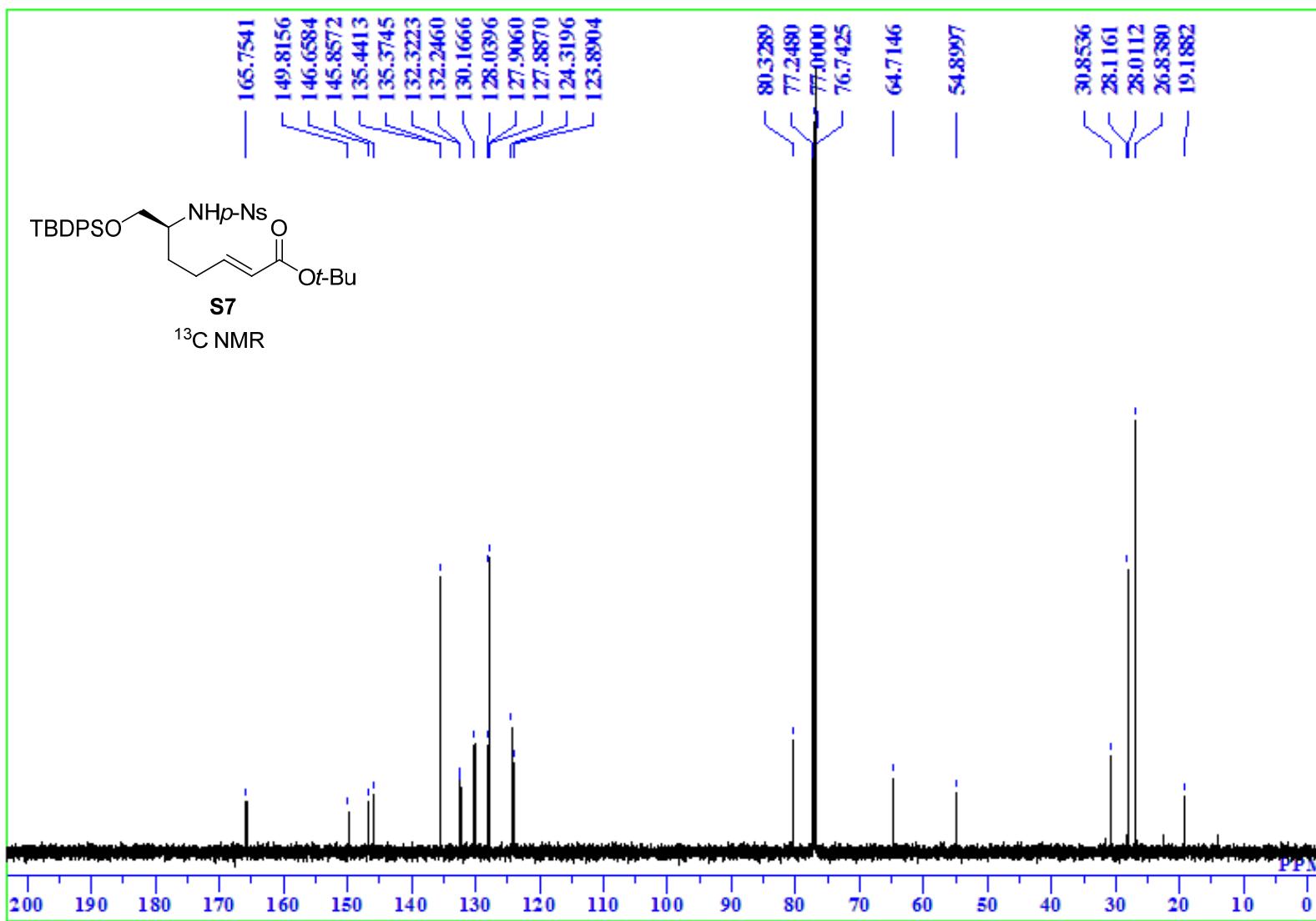




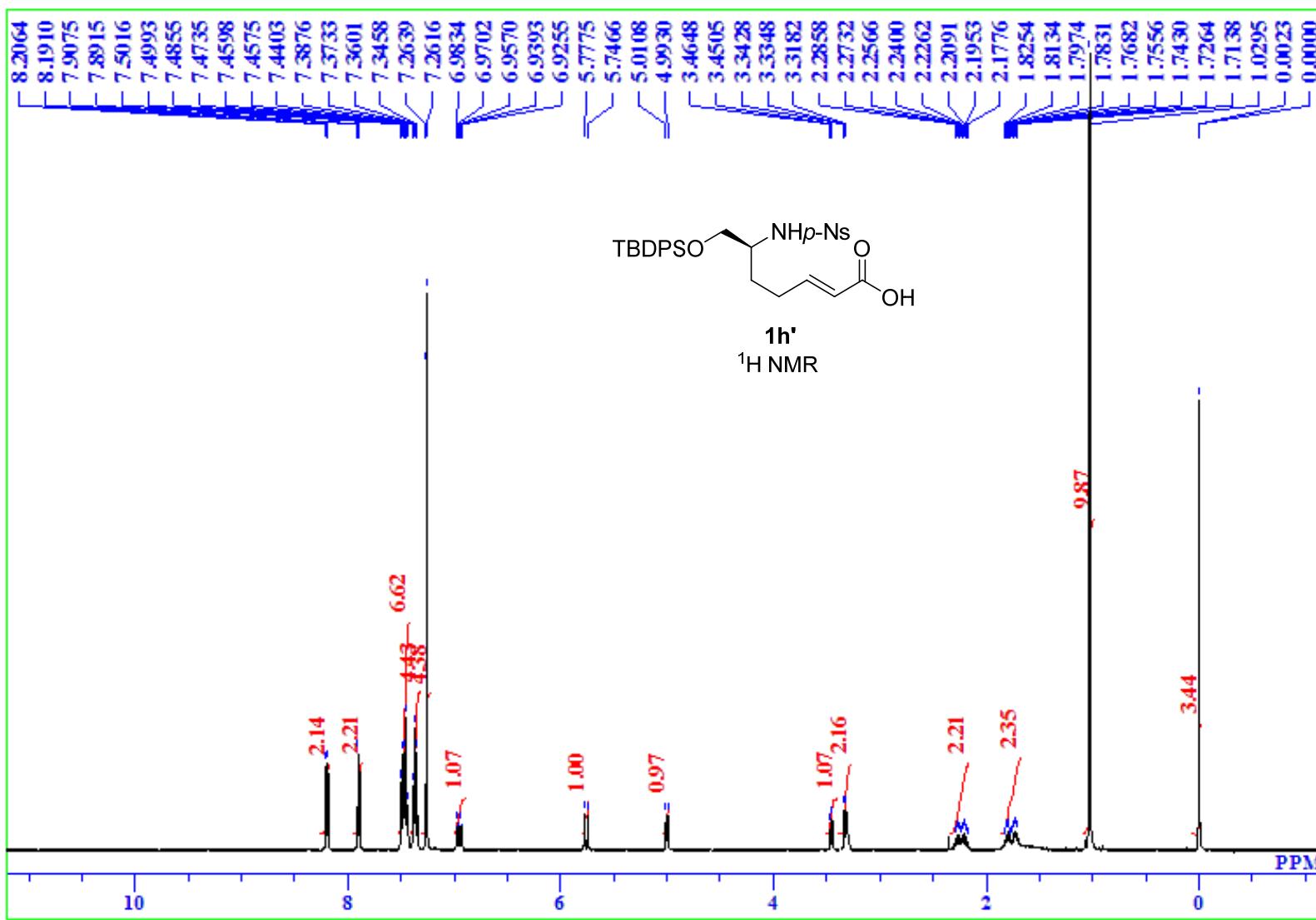
S76

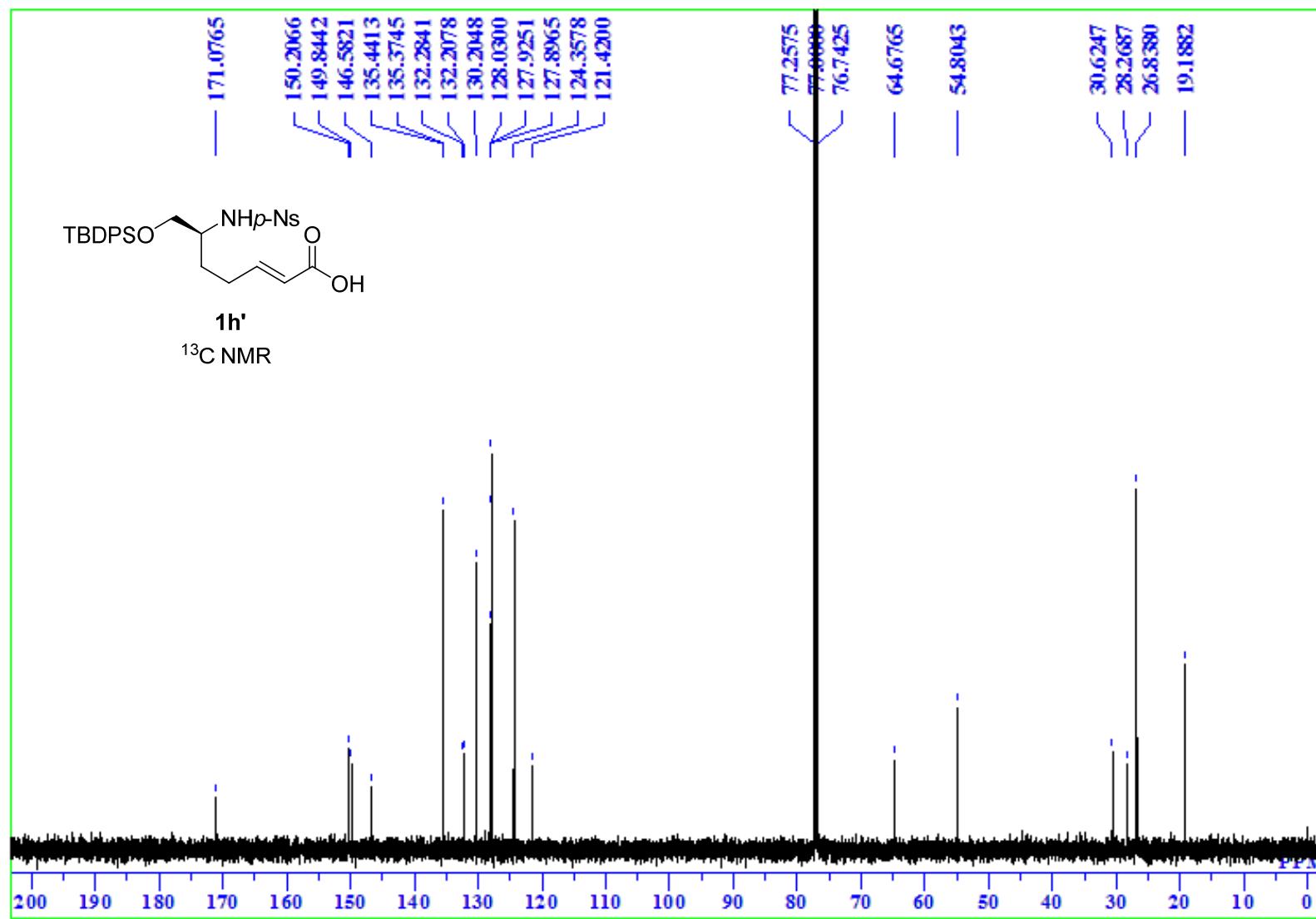


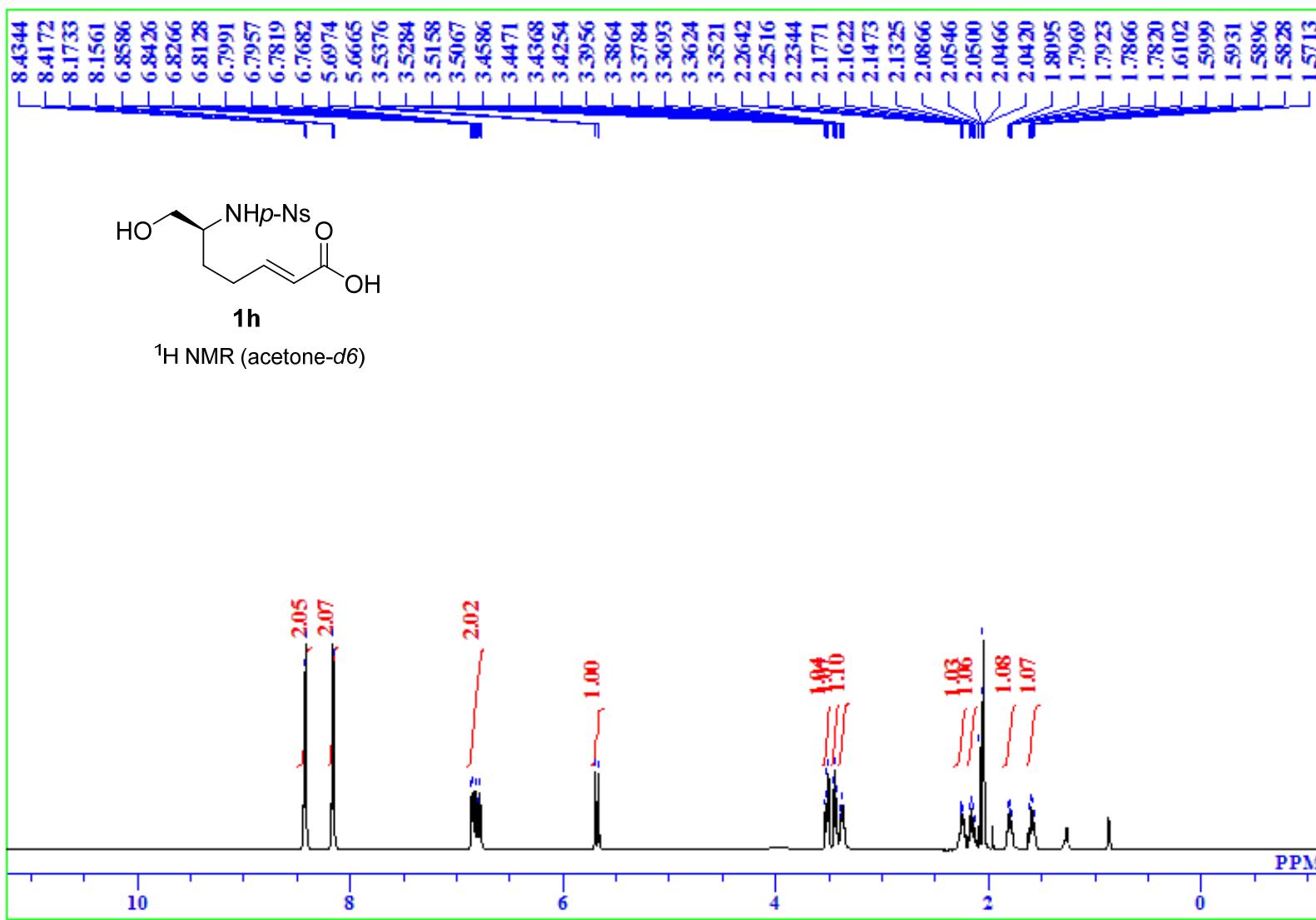
S77

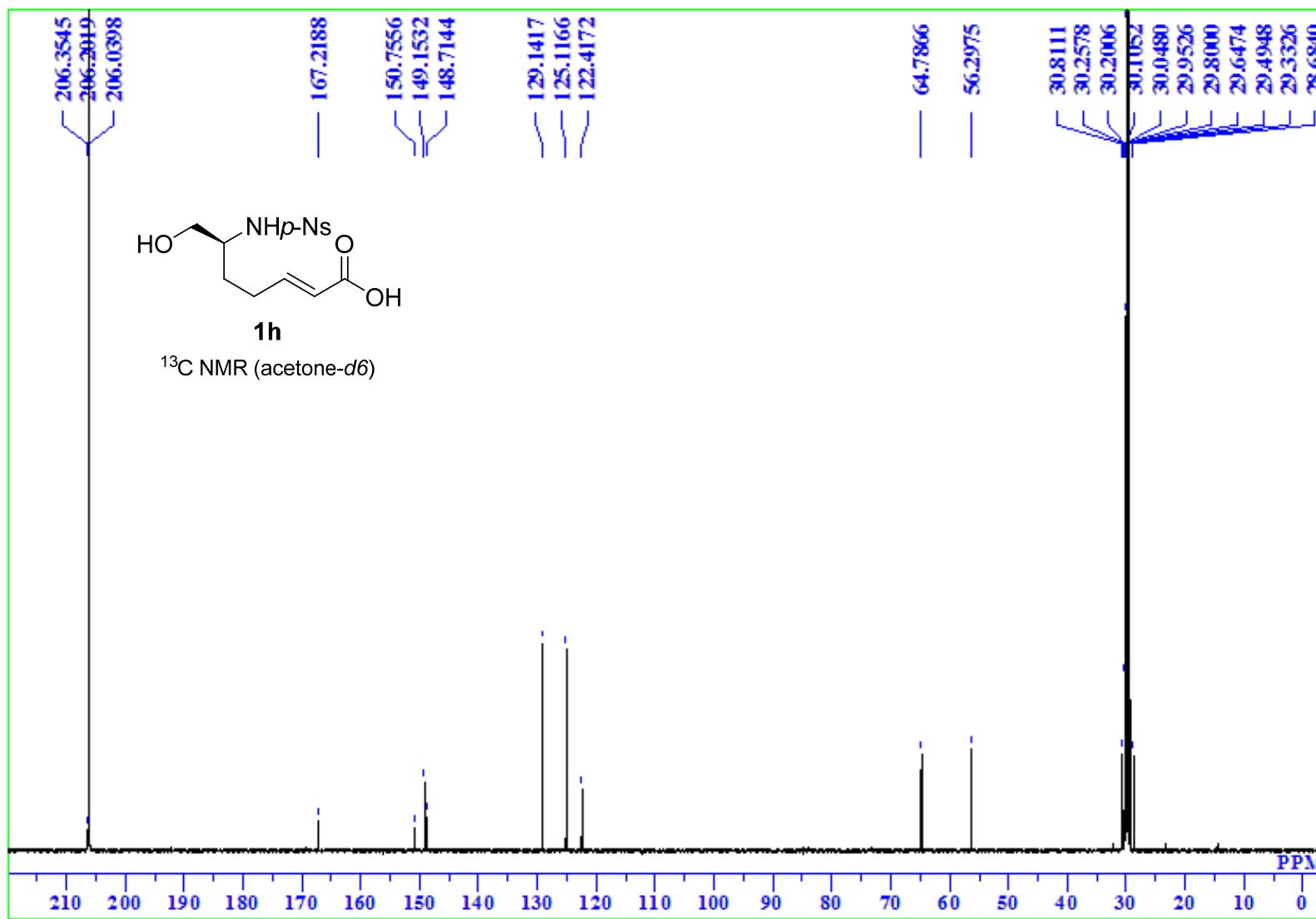


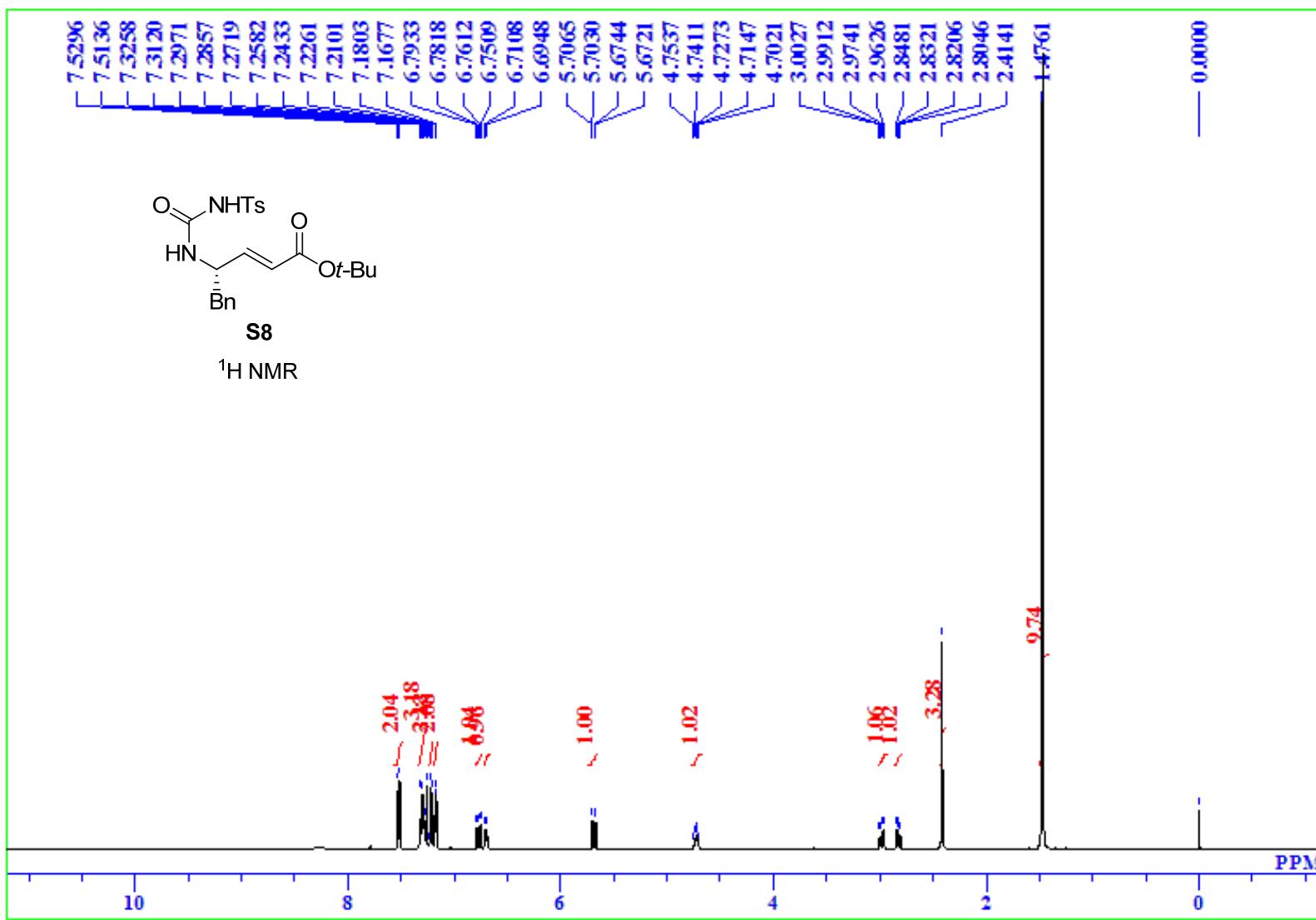
S78



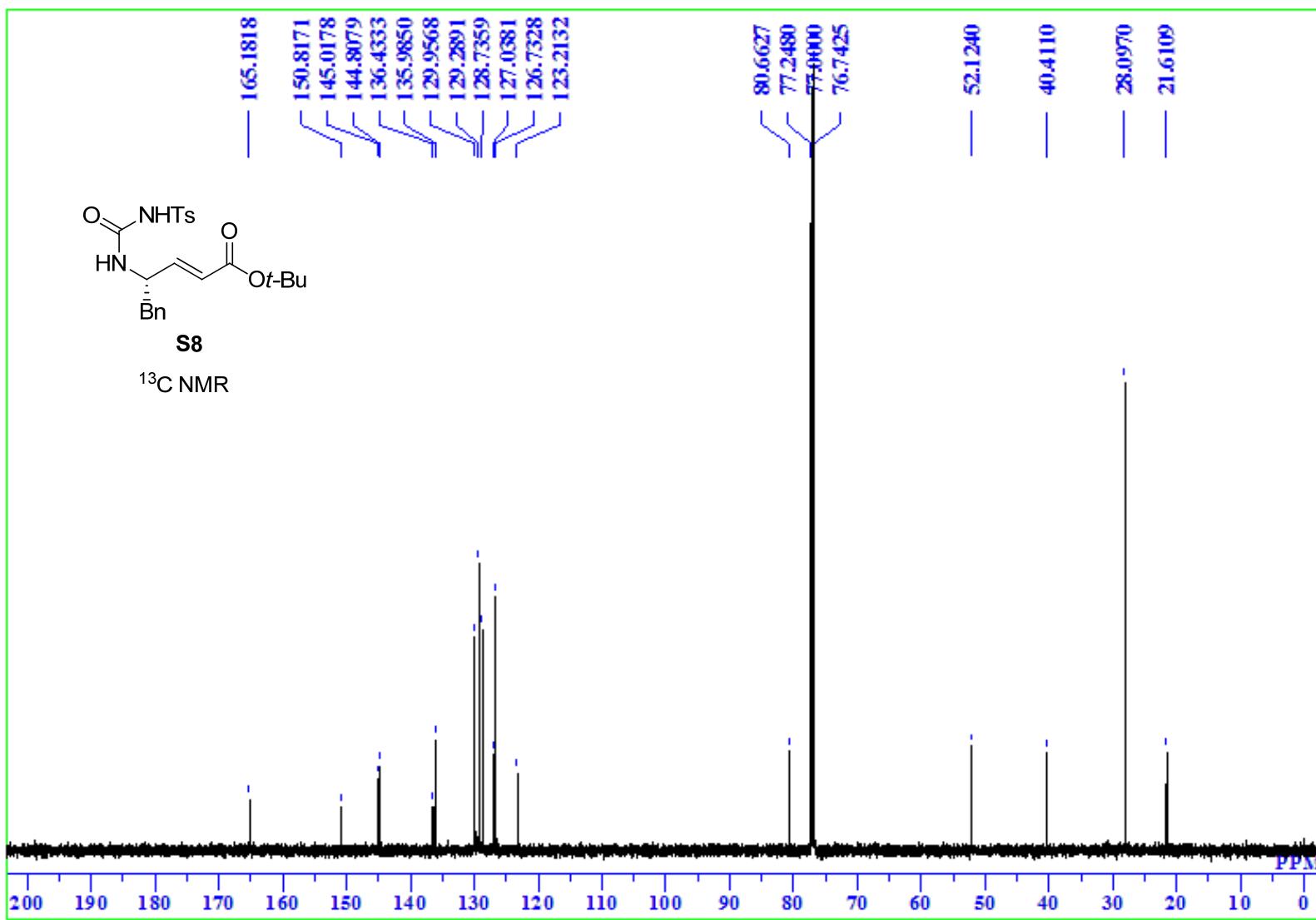


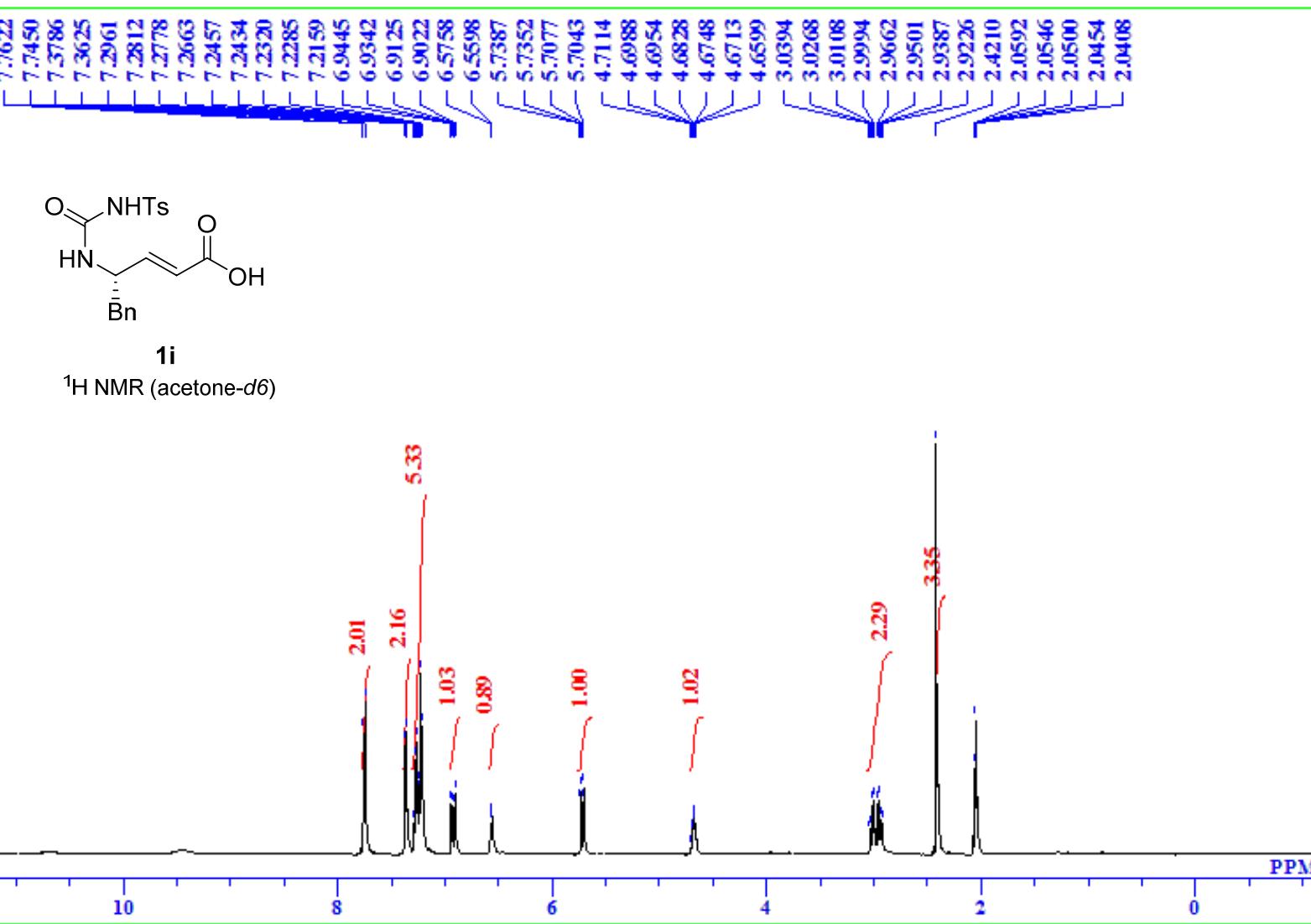


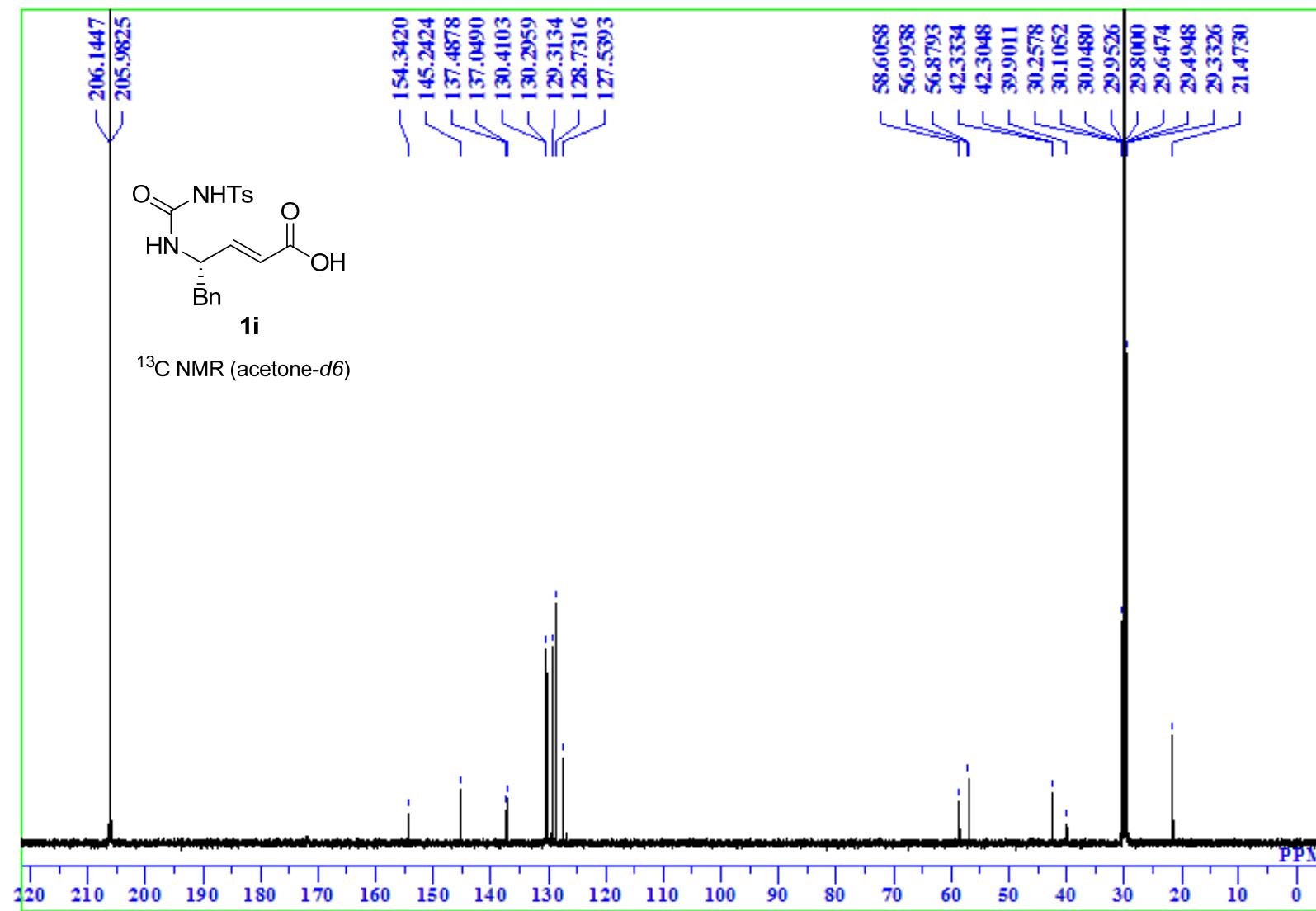


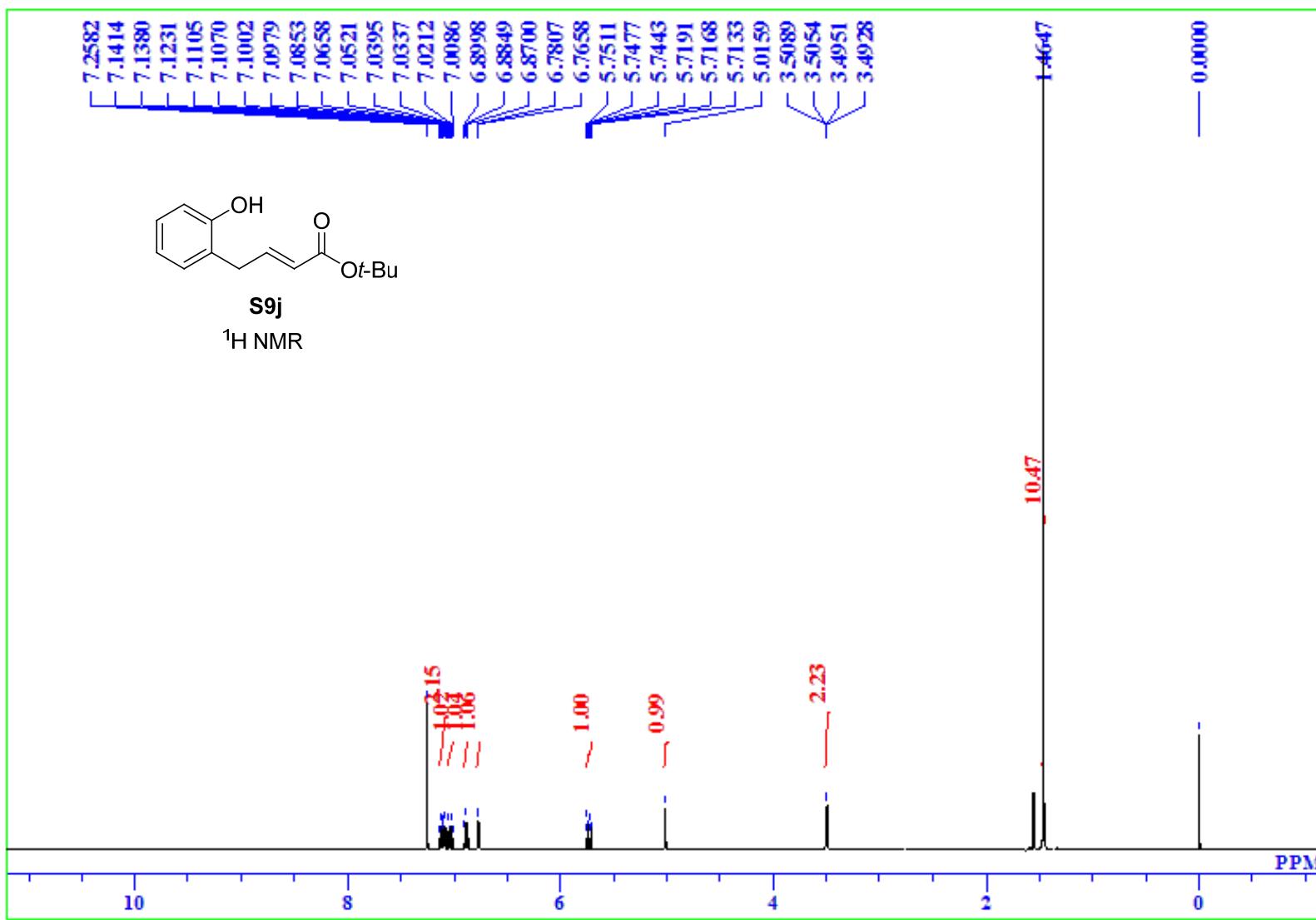


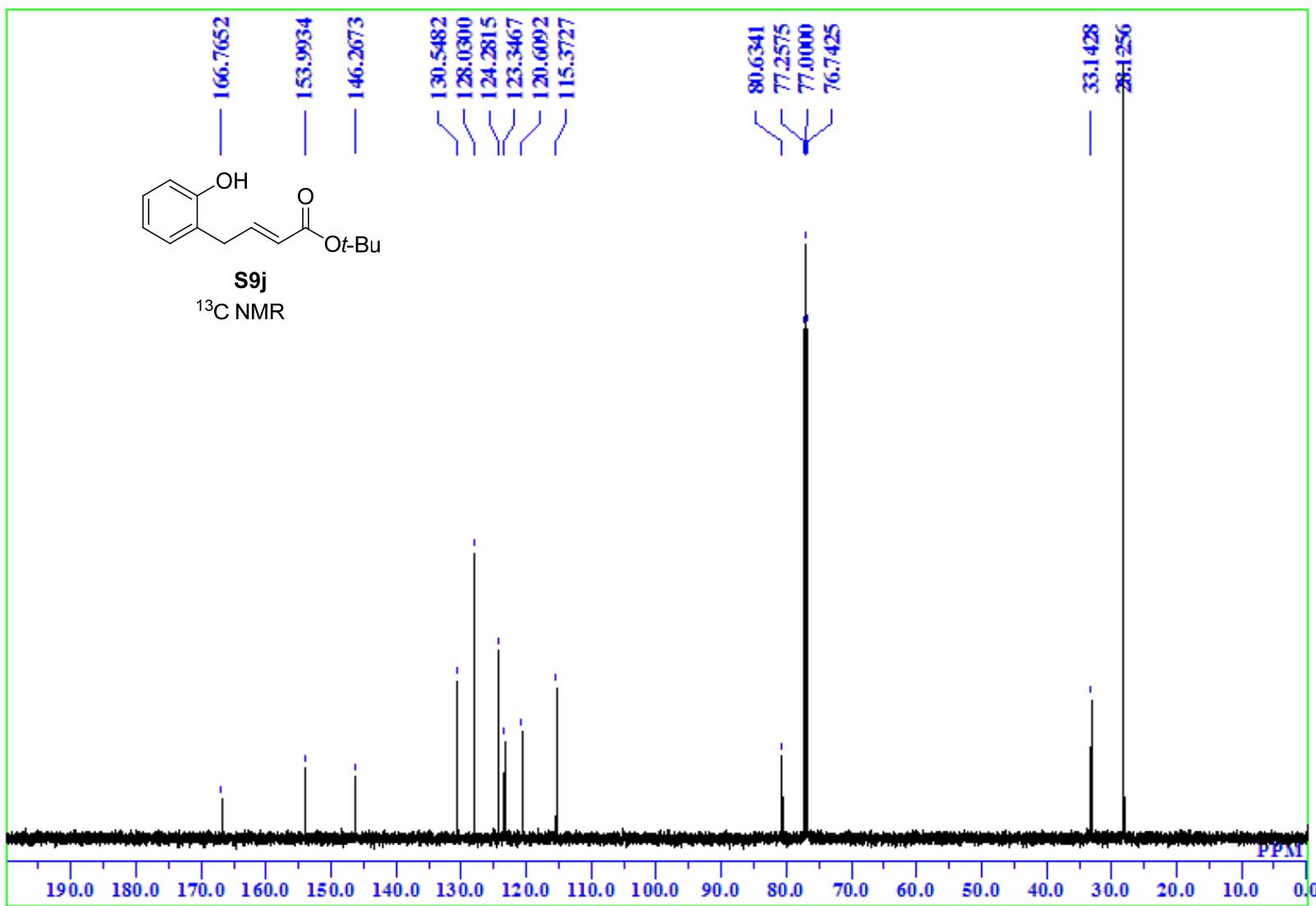
S83

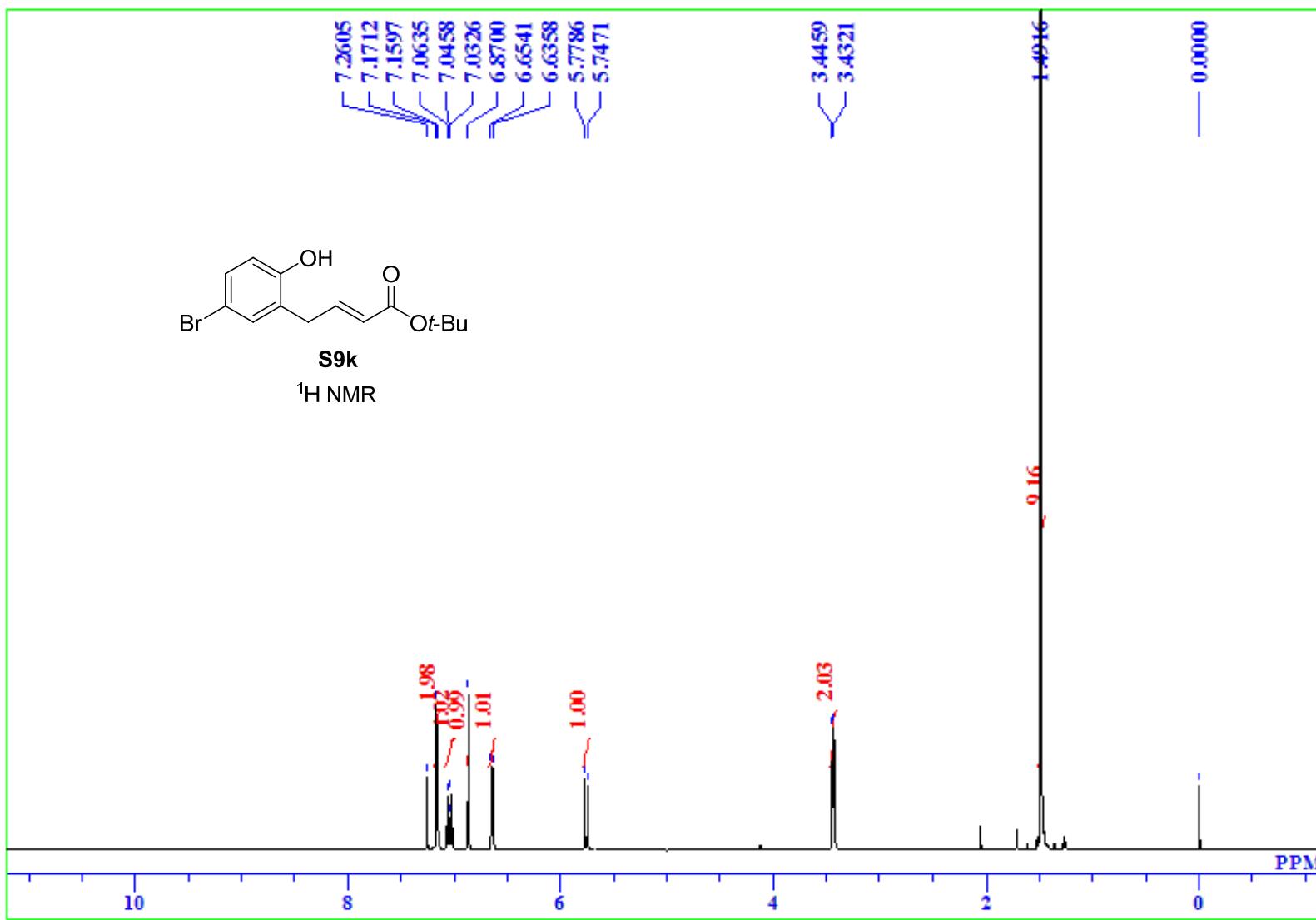


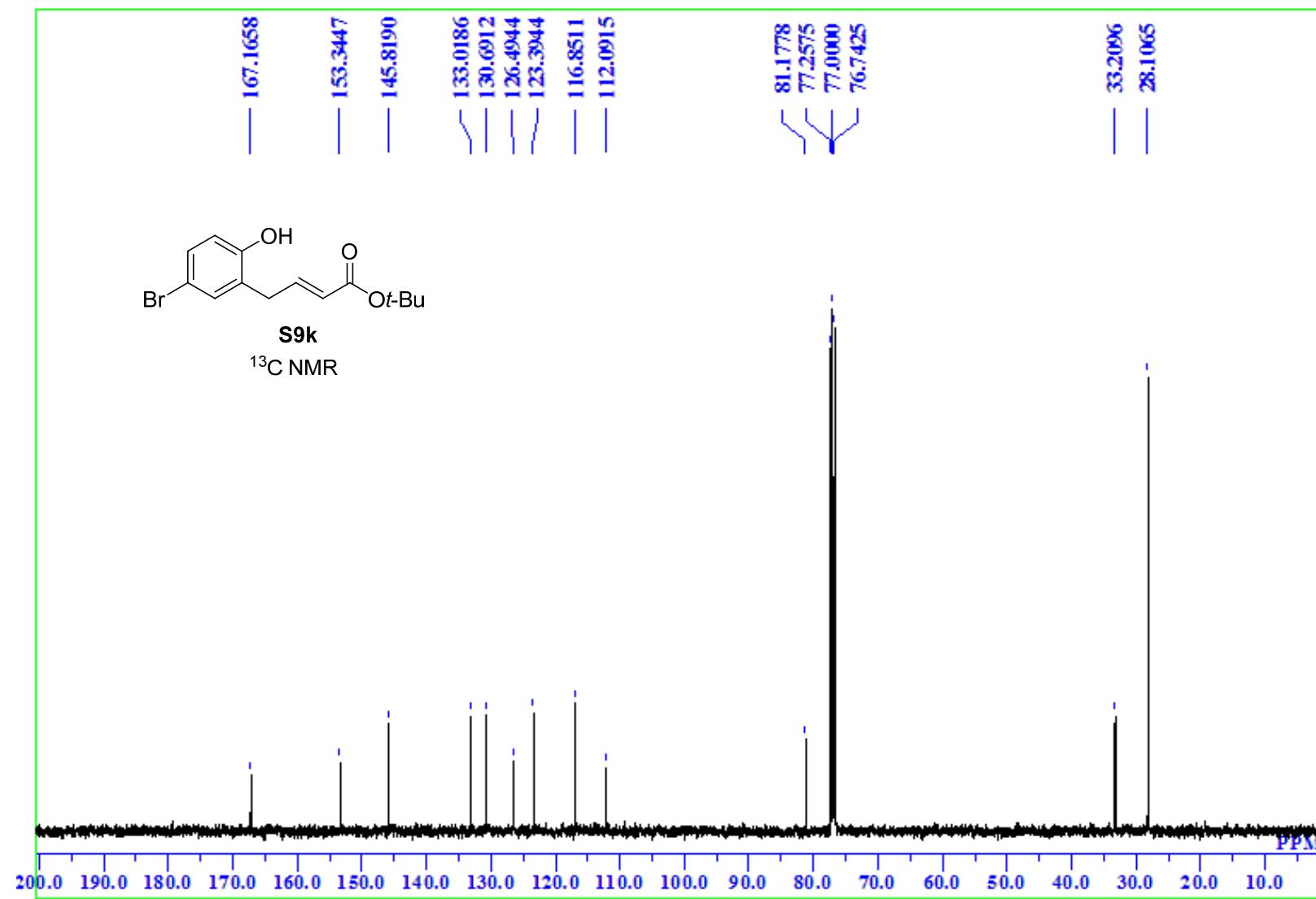




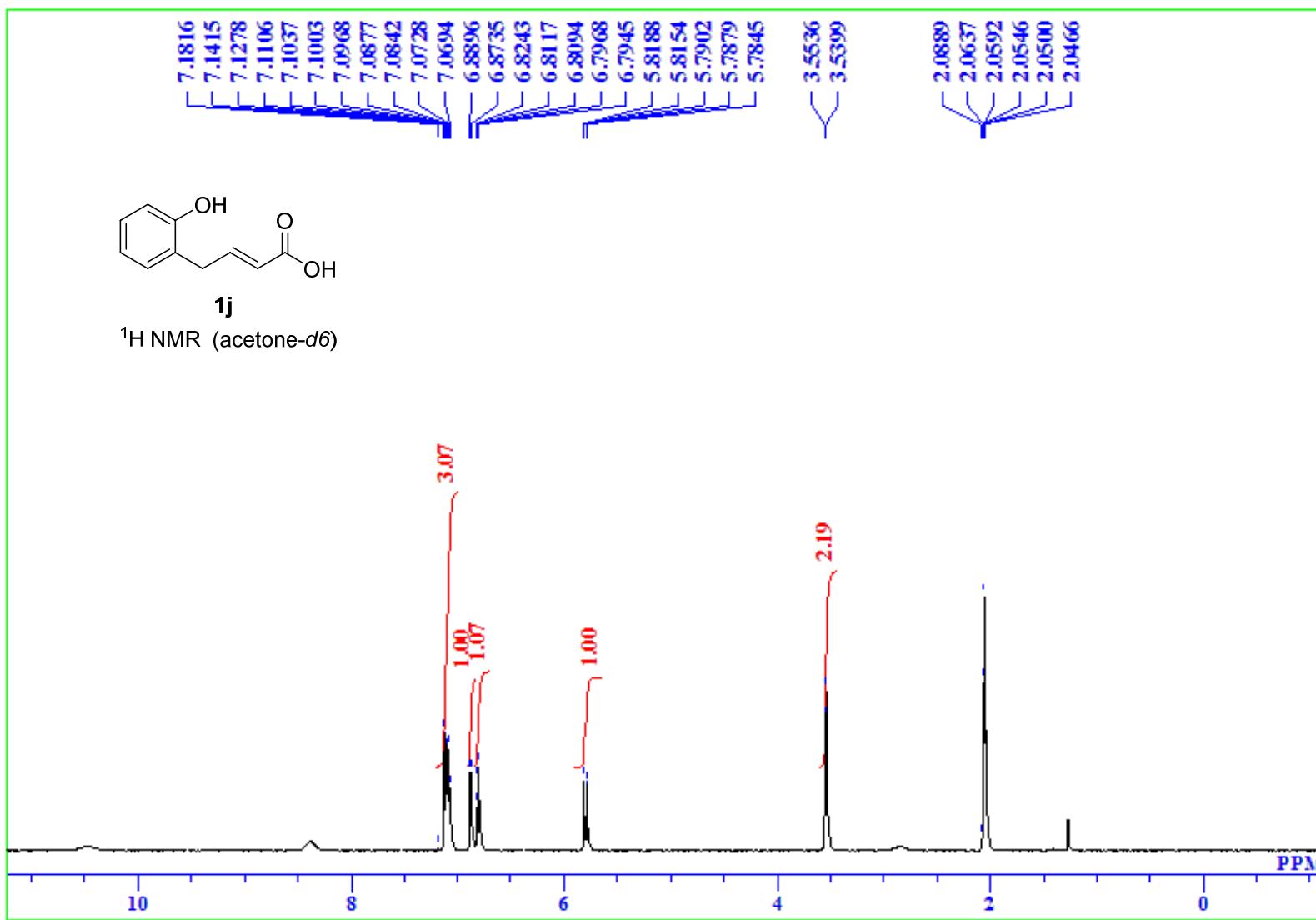


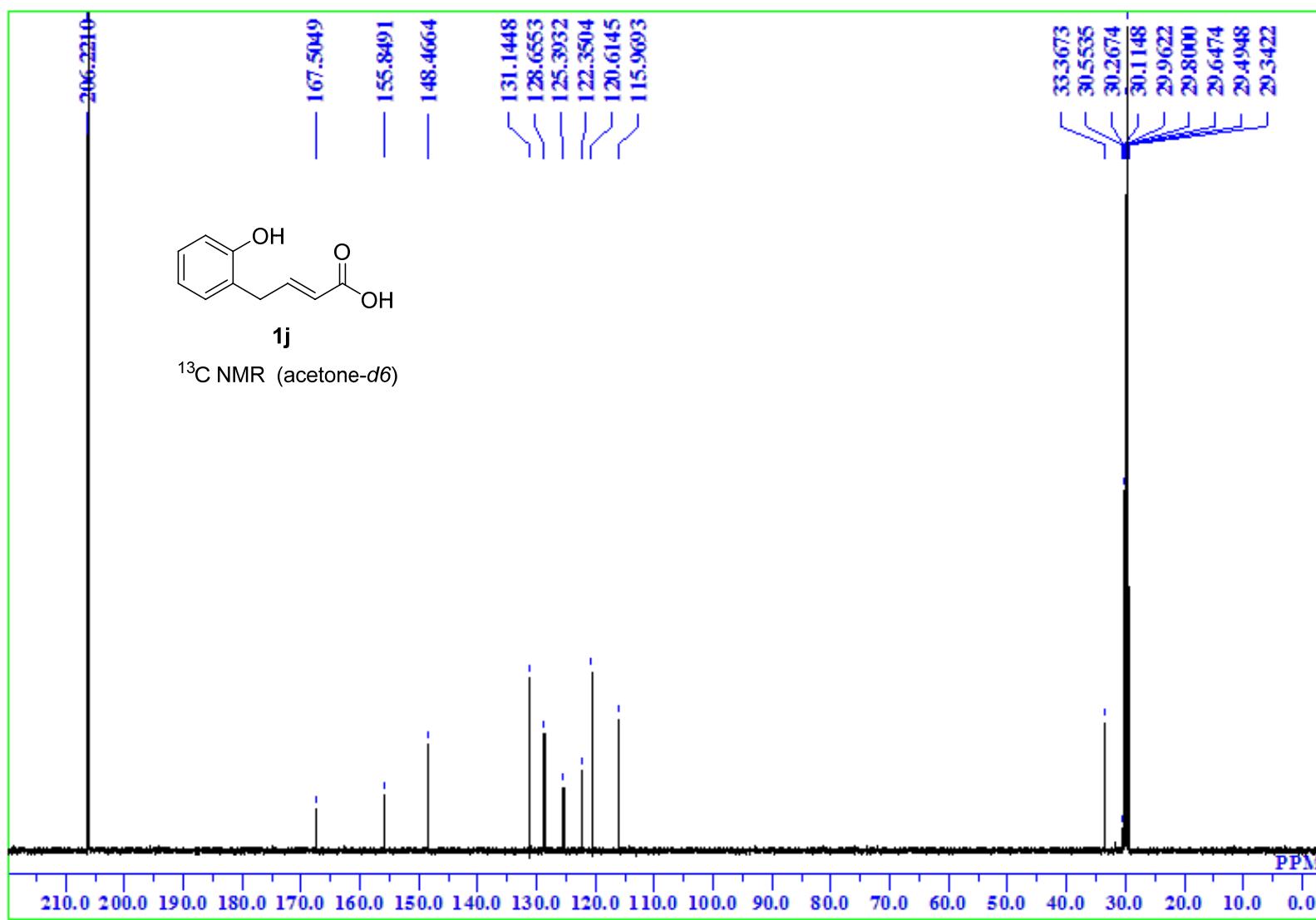


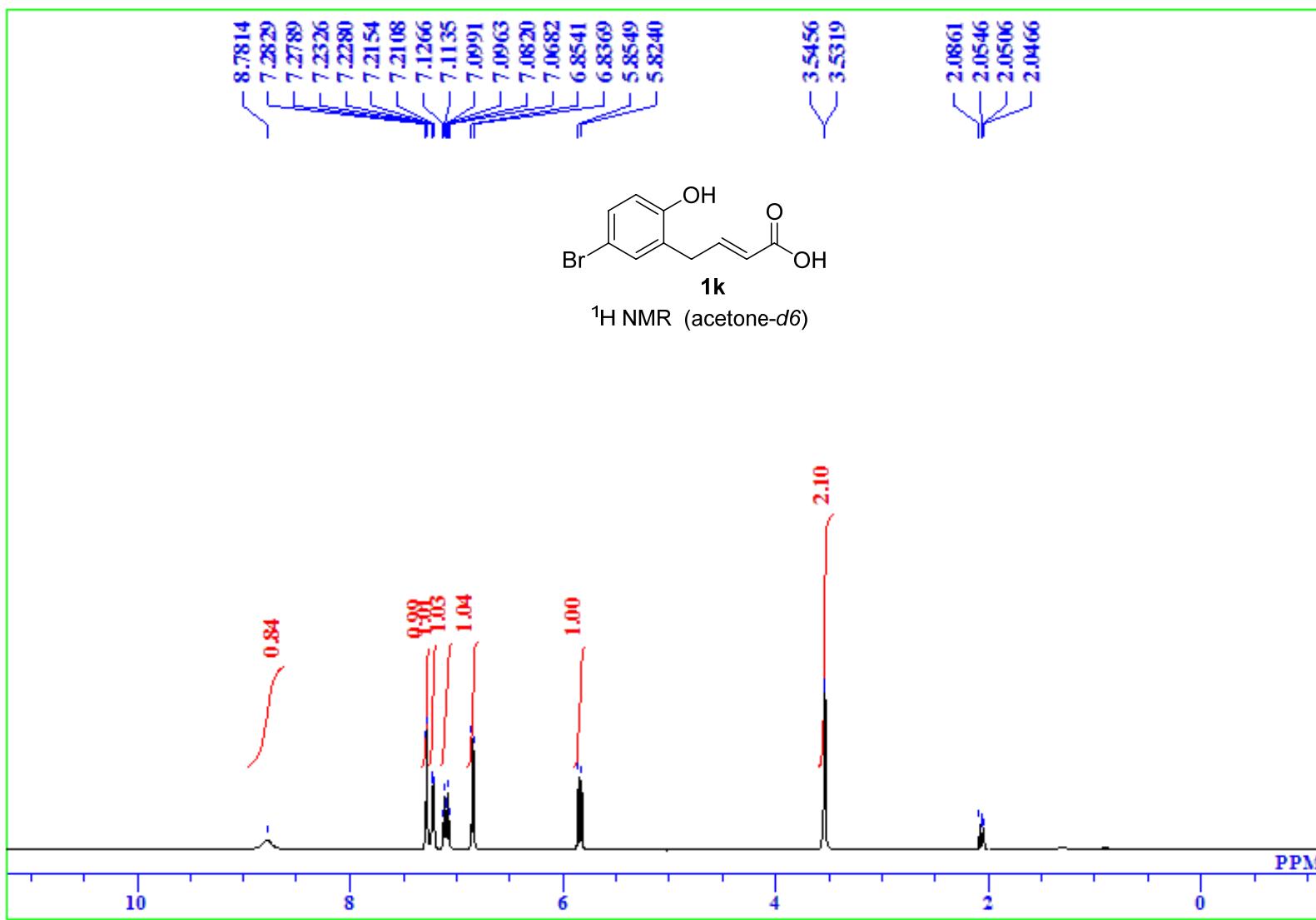


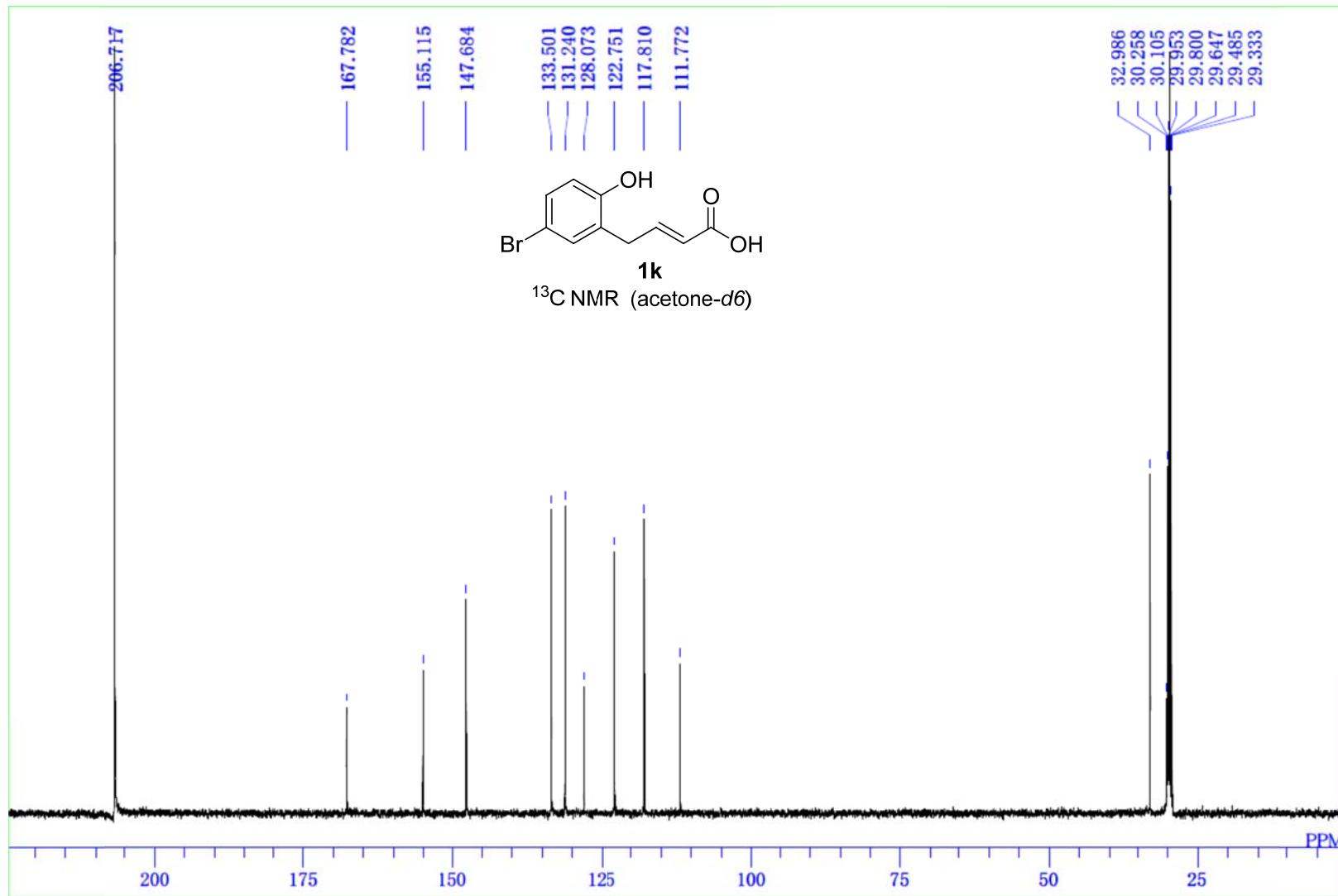


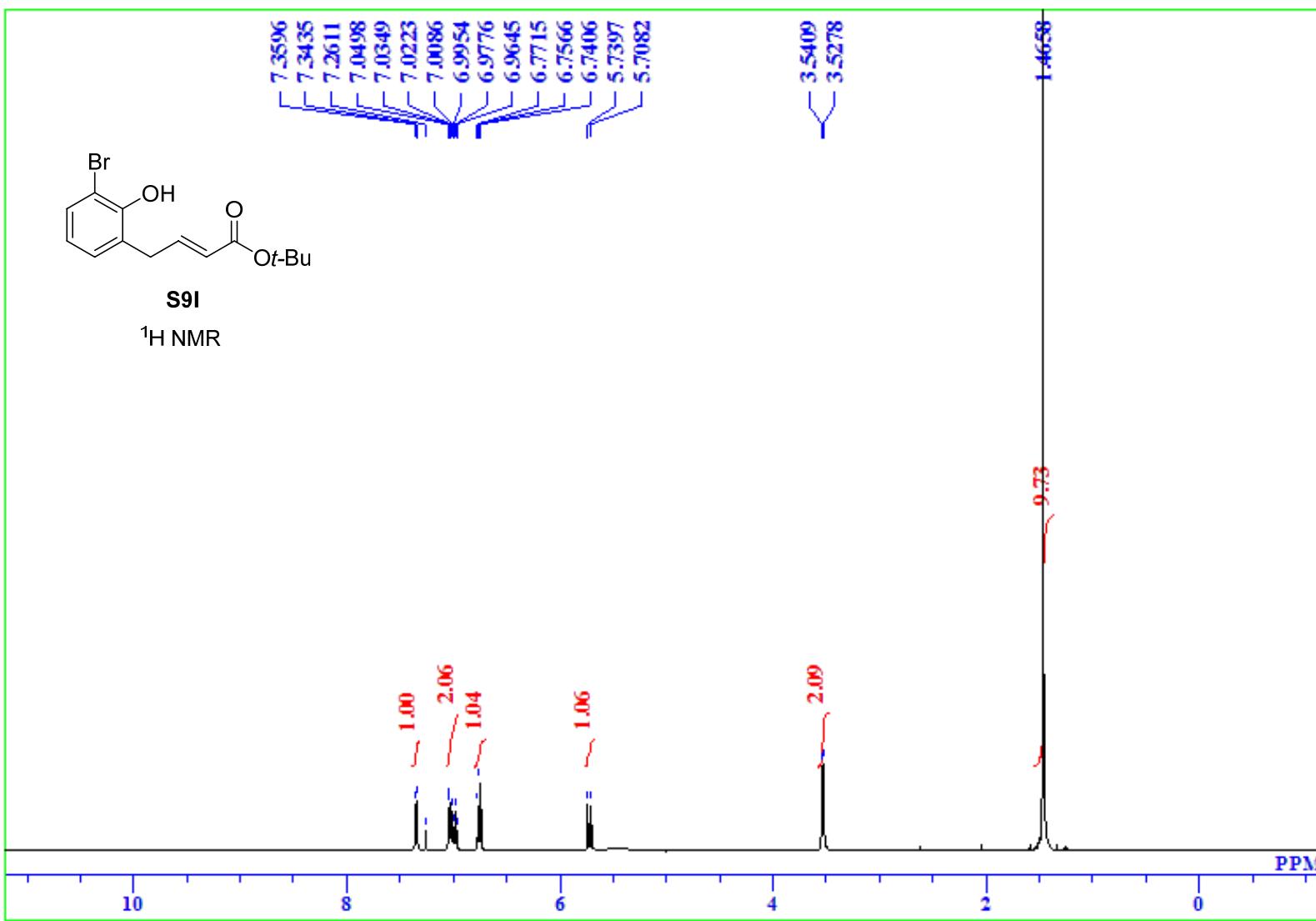
S90

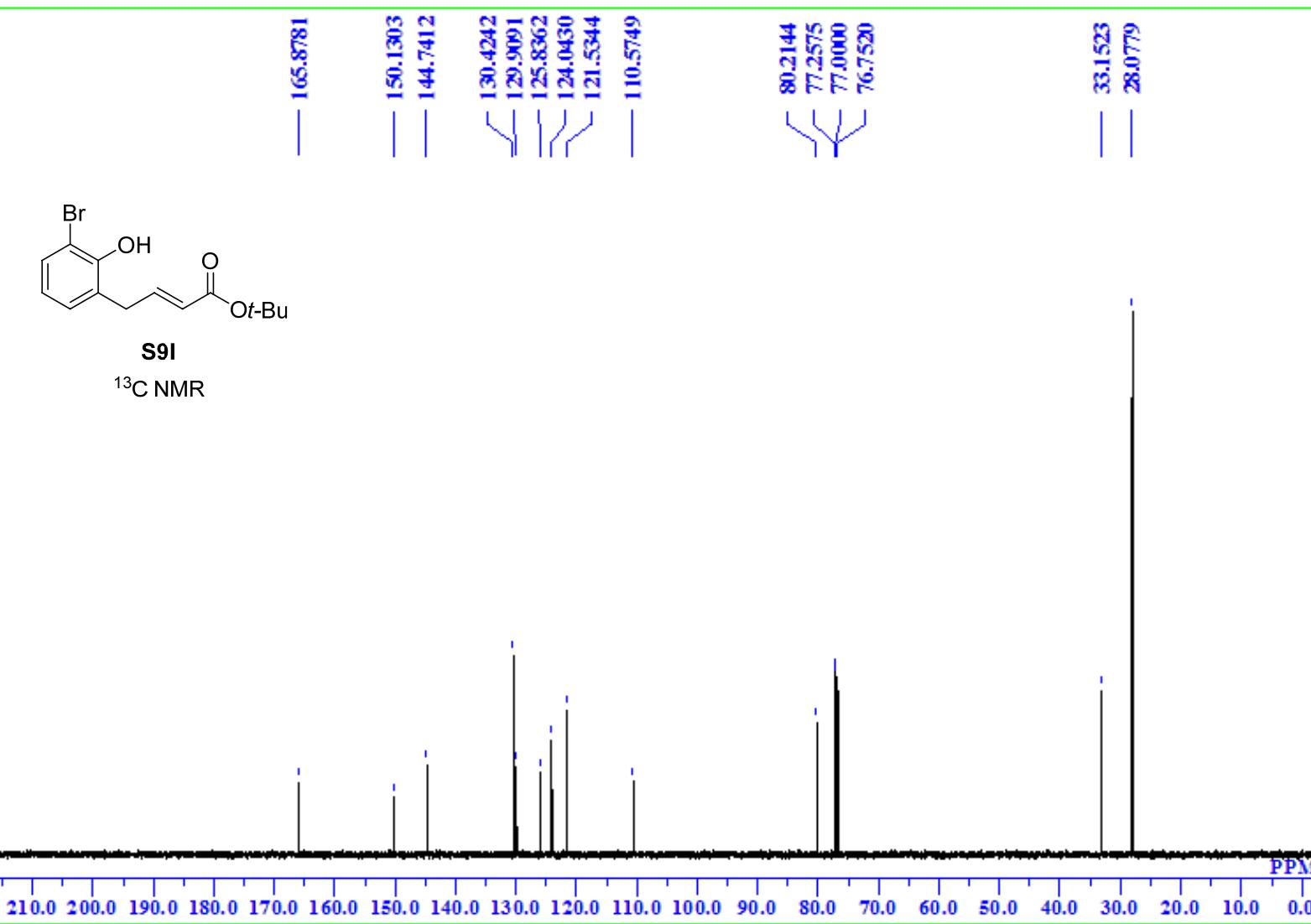


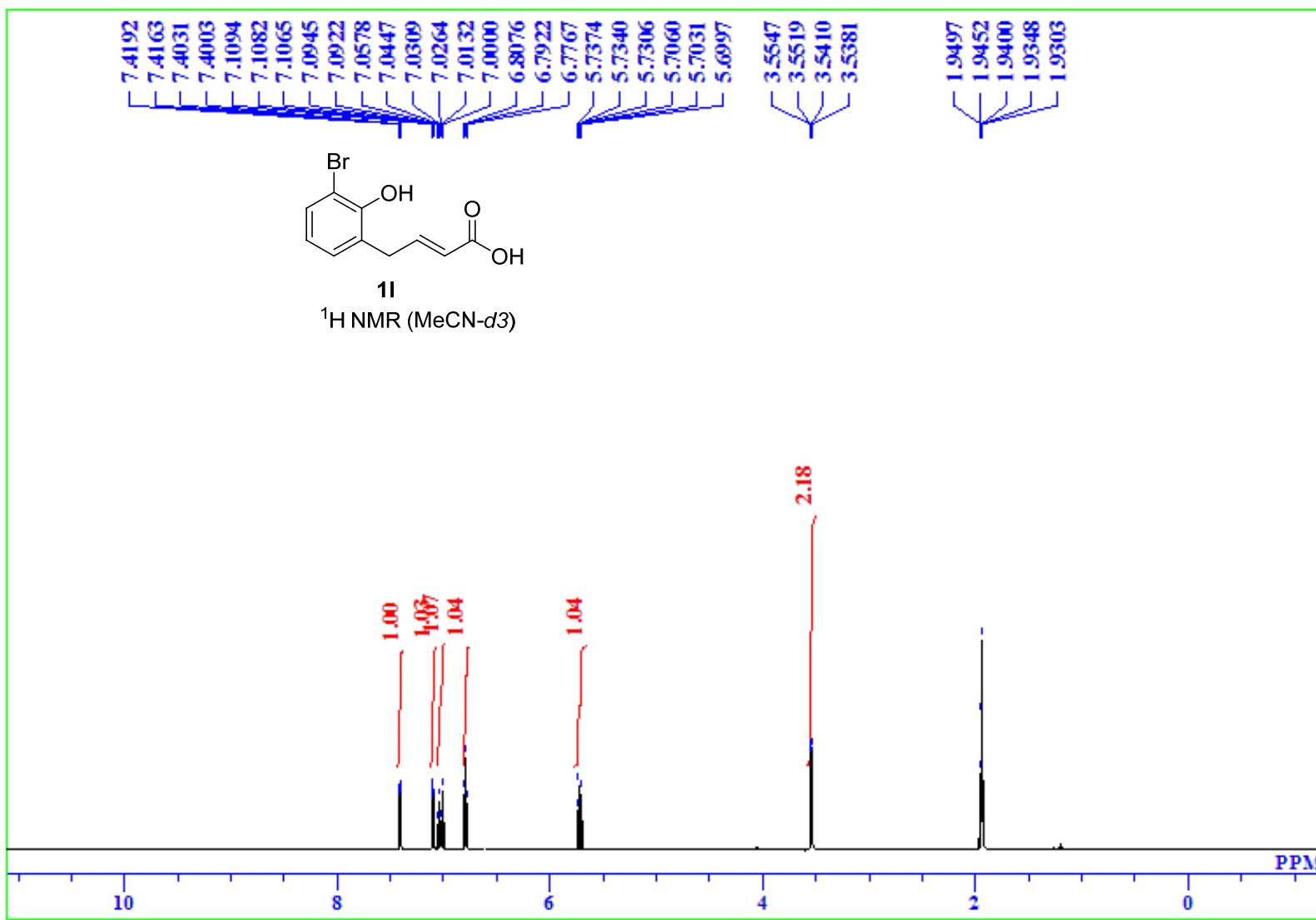


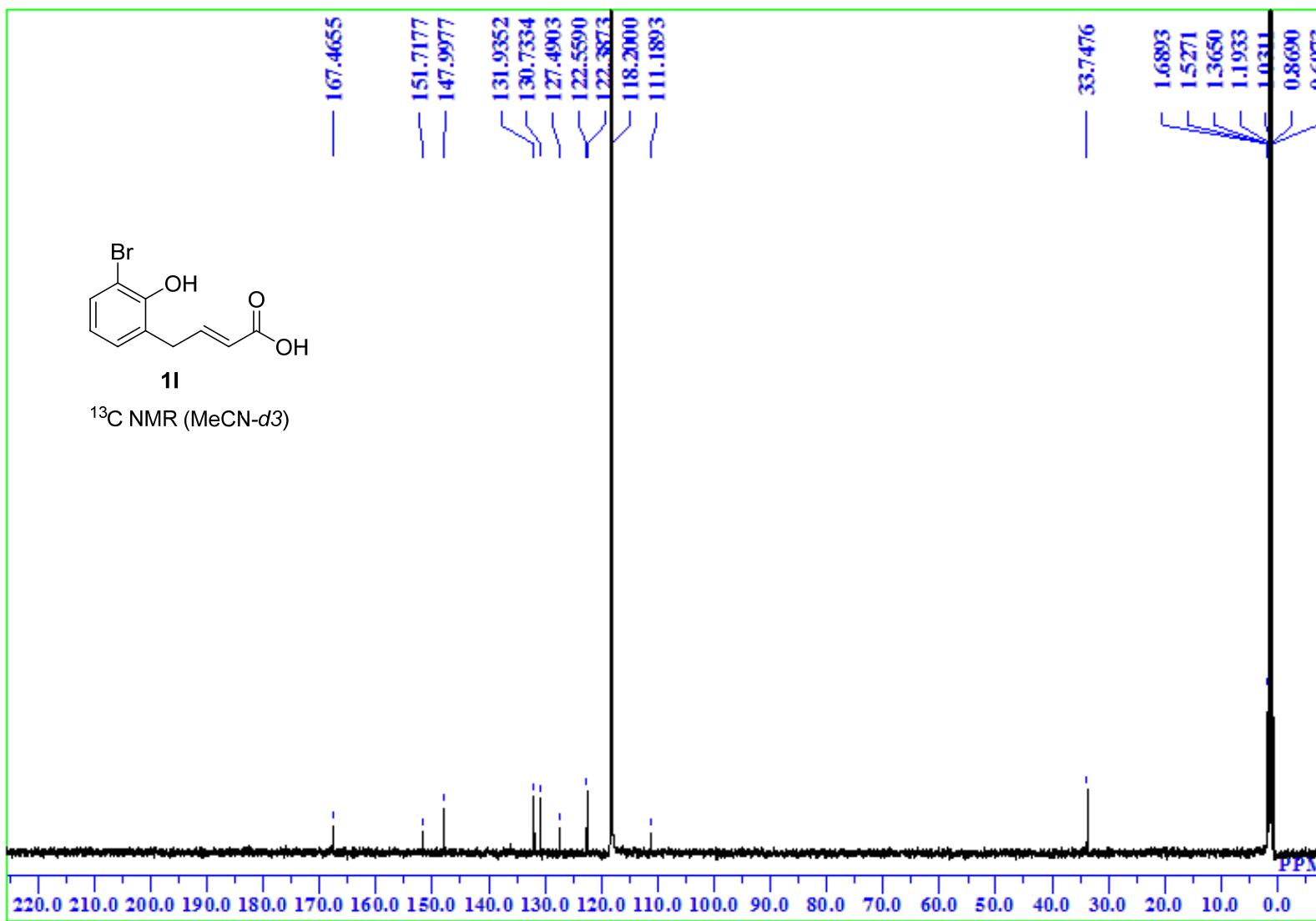


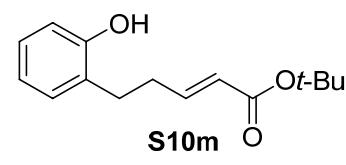






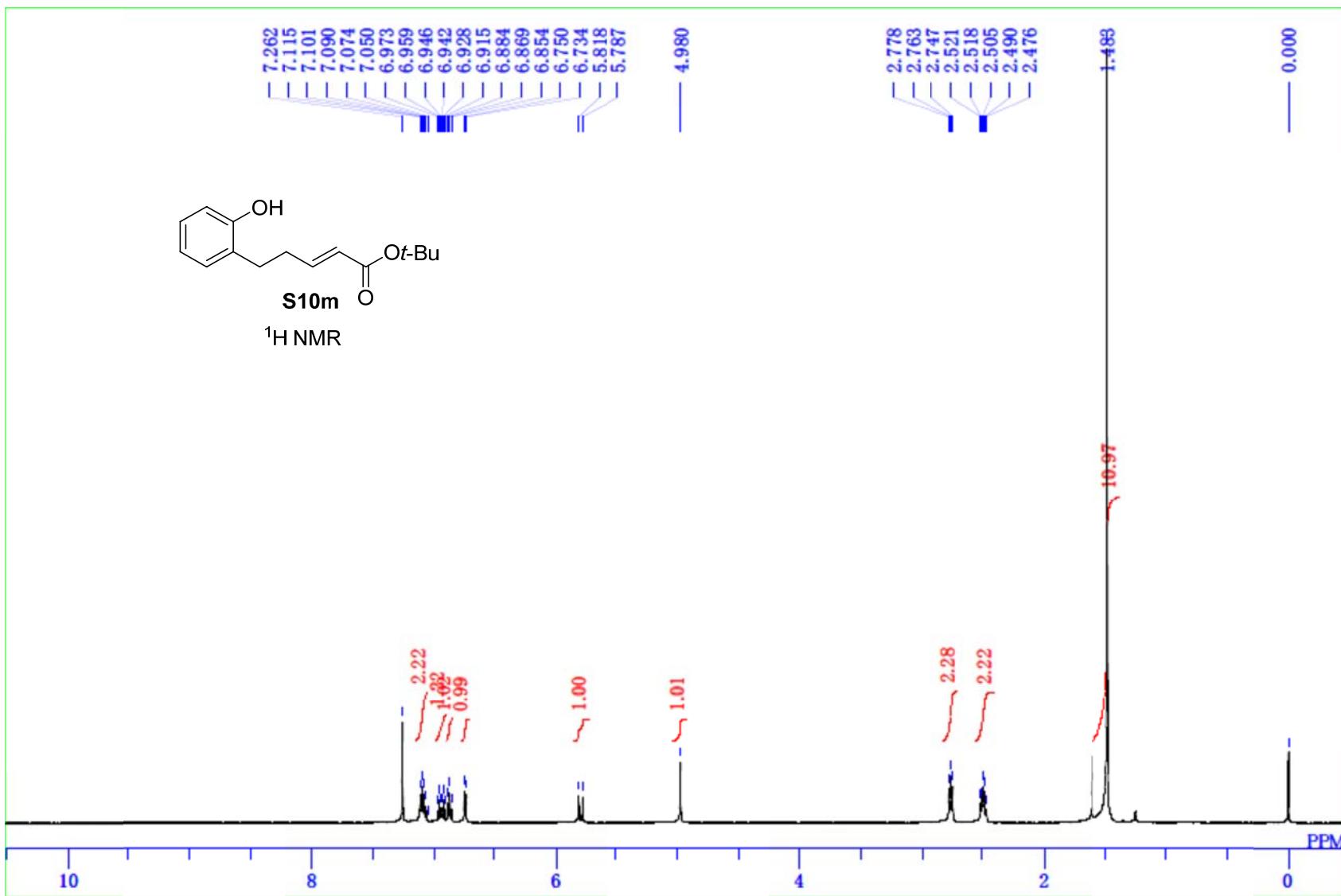


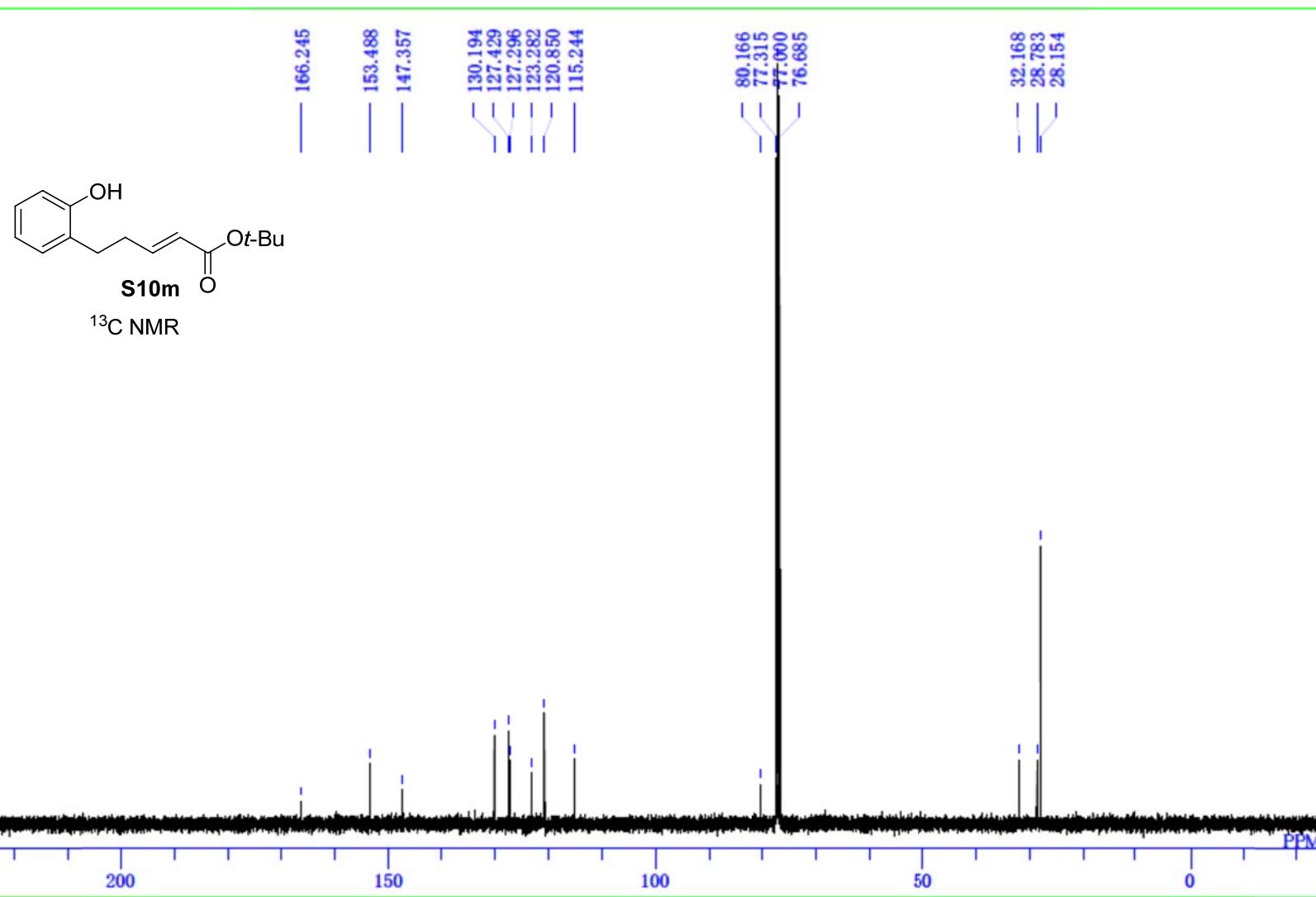




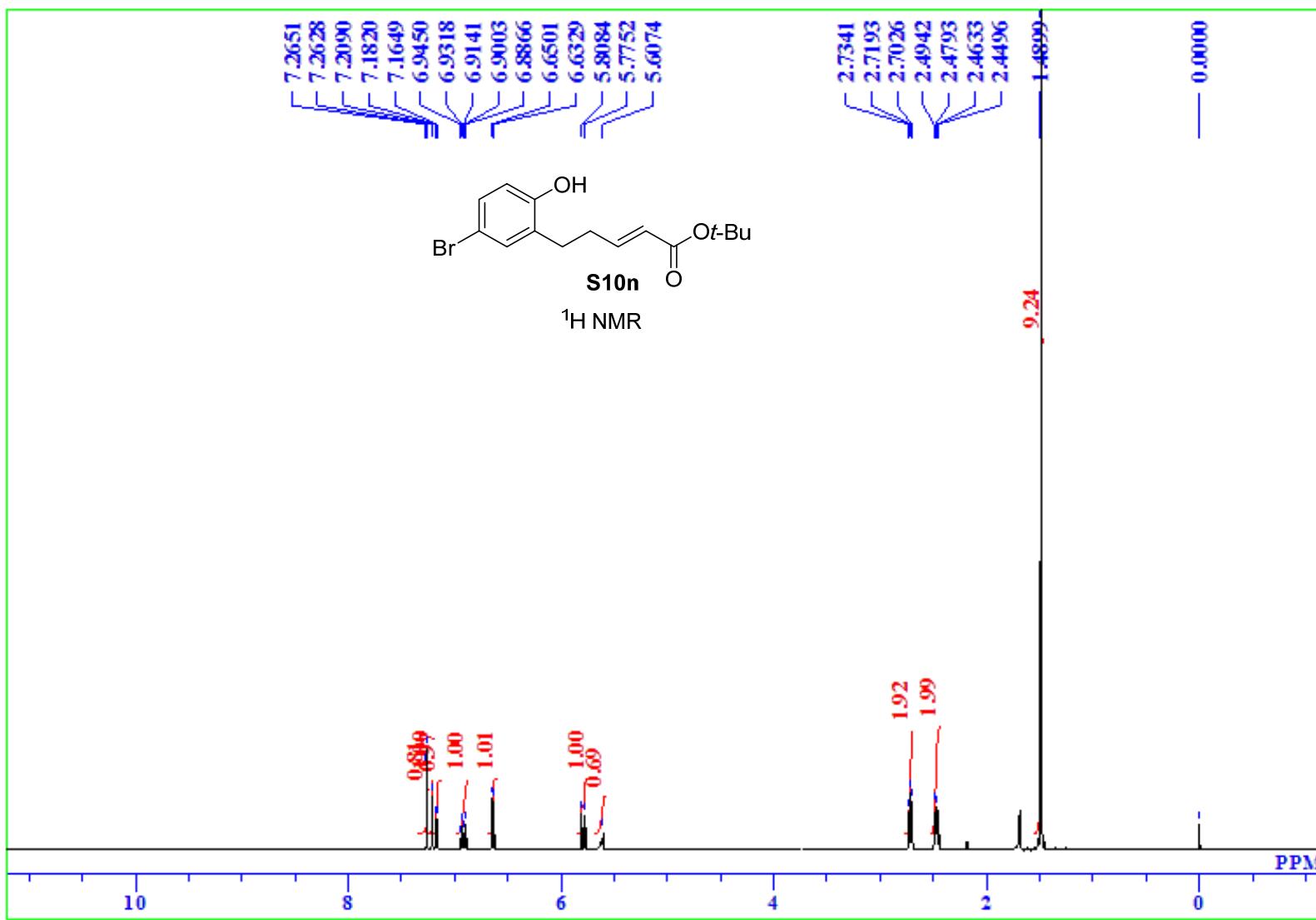
S10m

¹H NMR

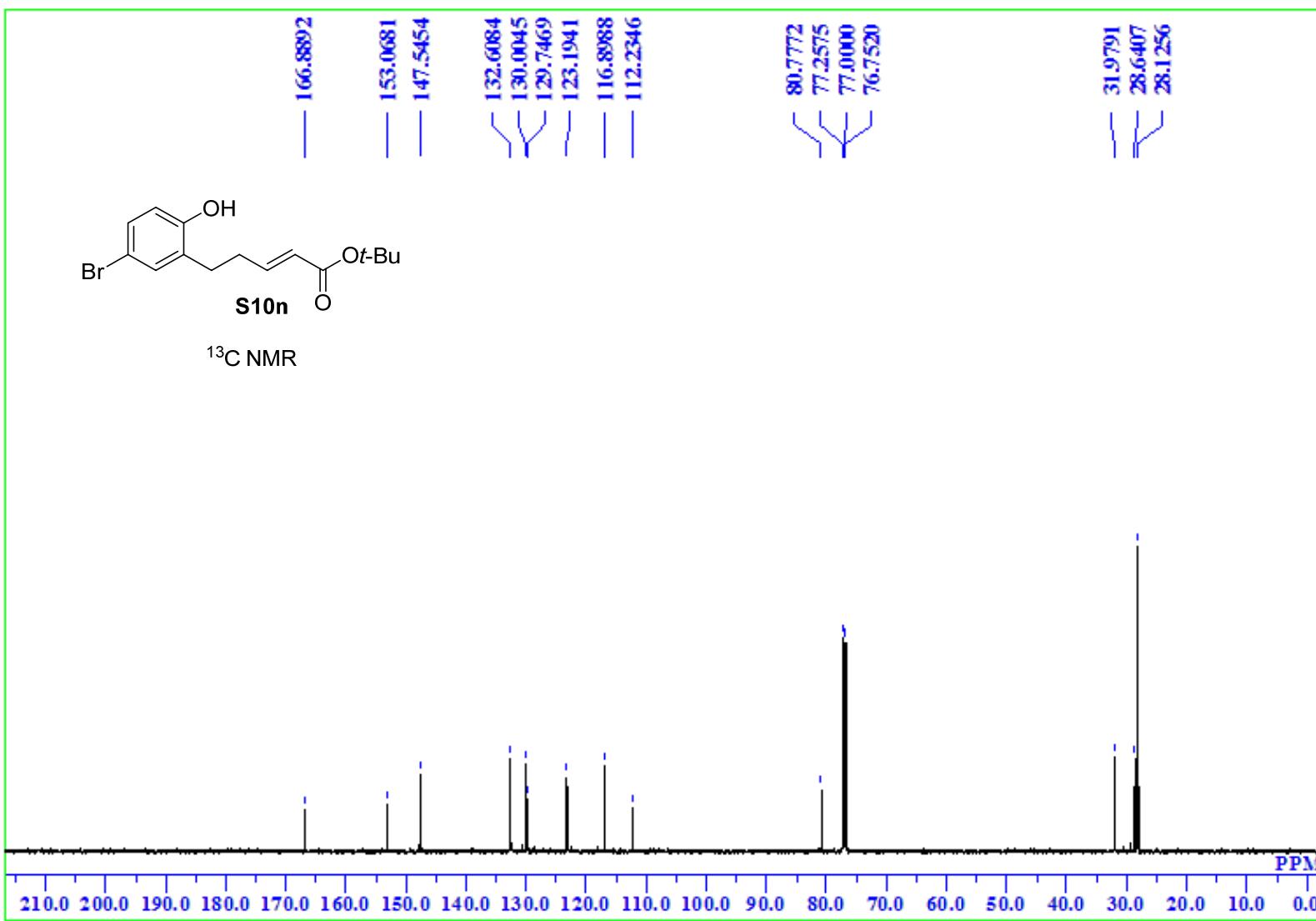




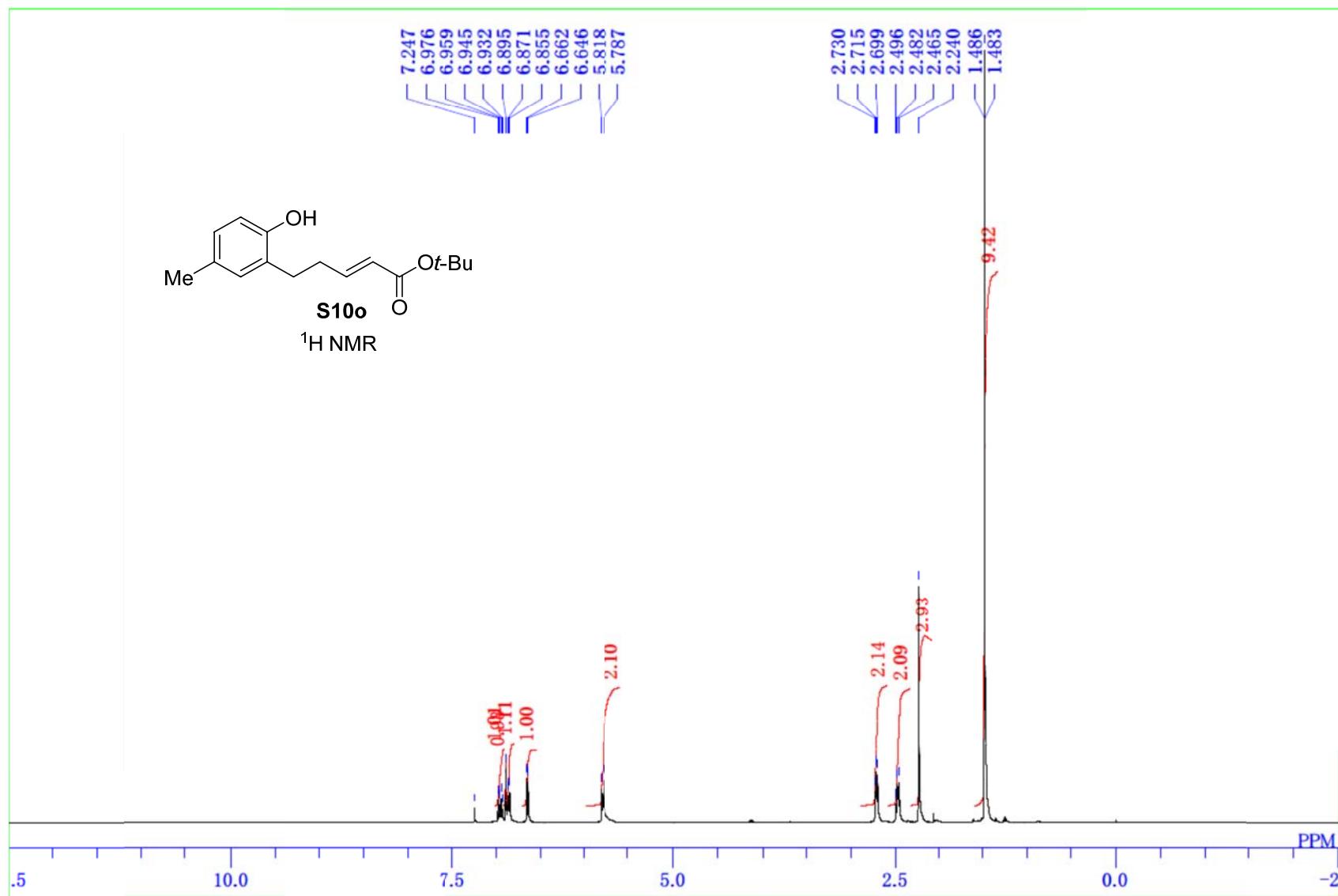
S100



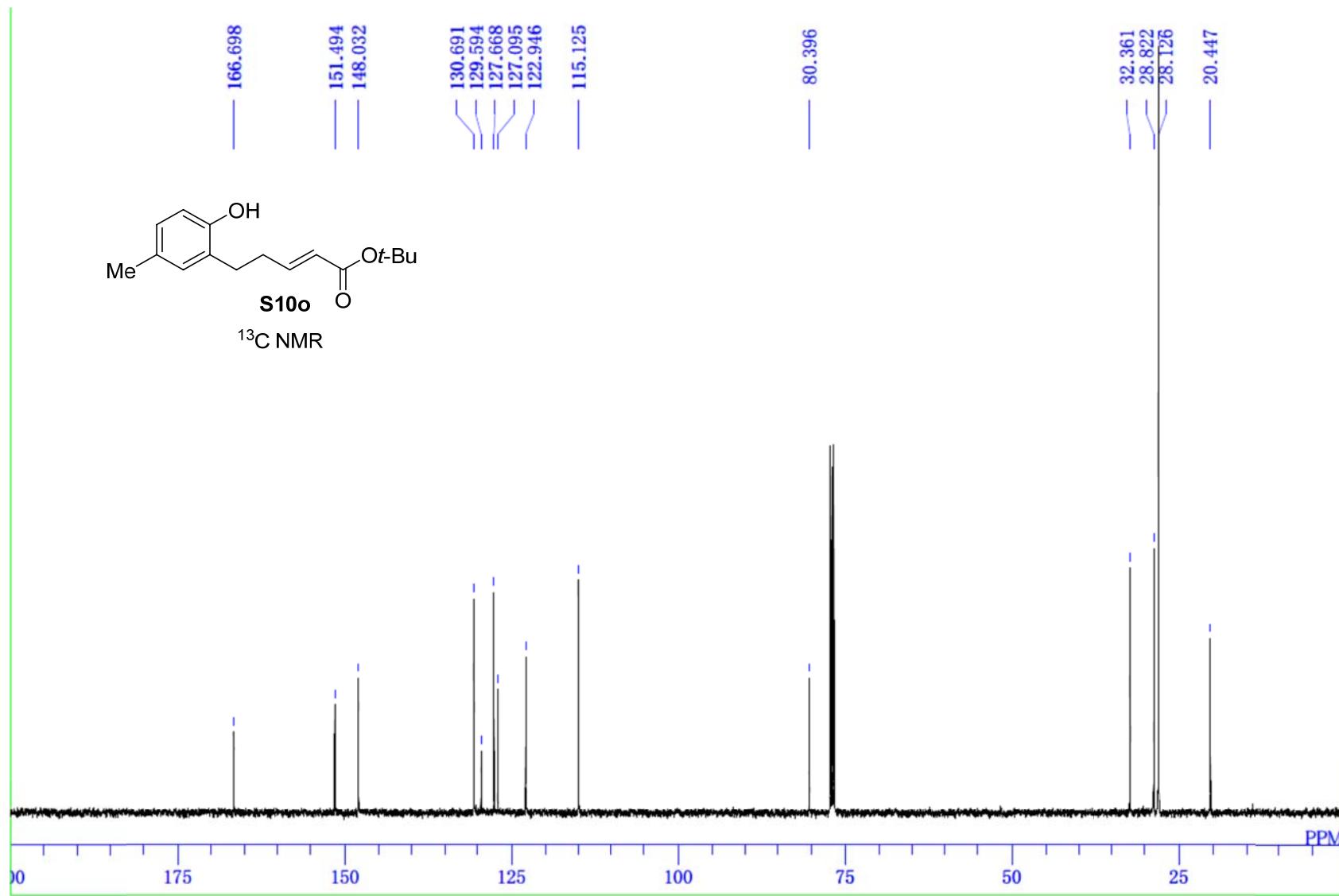
S101



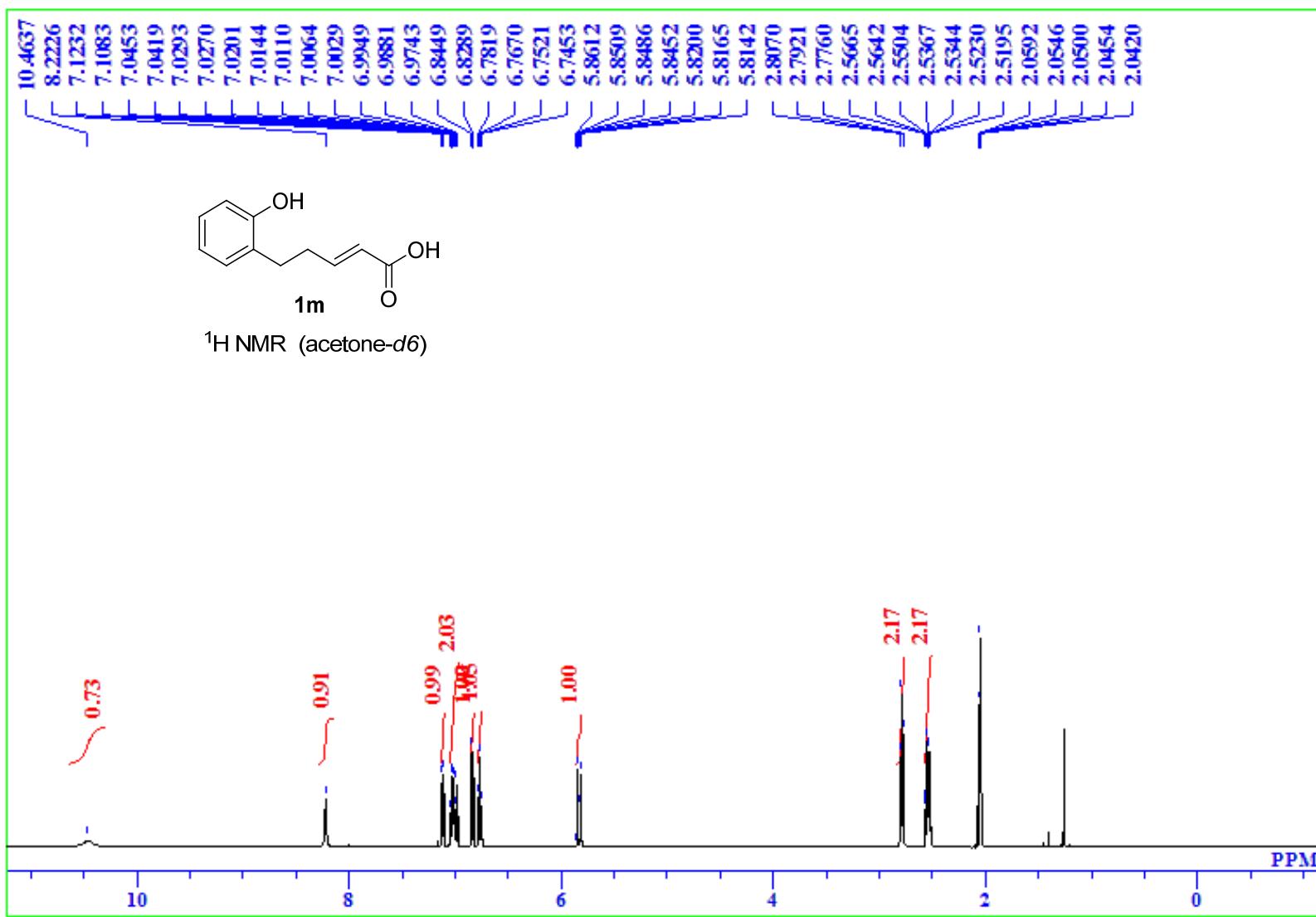
S102

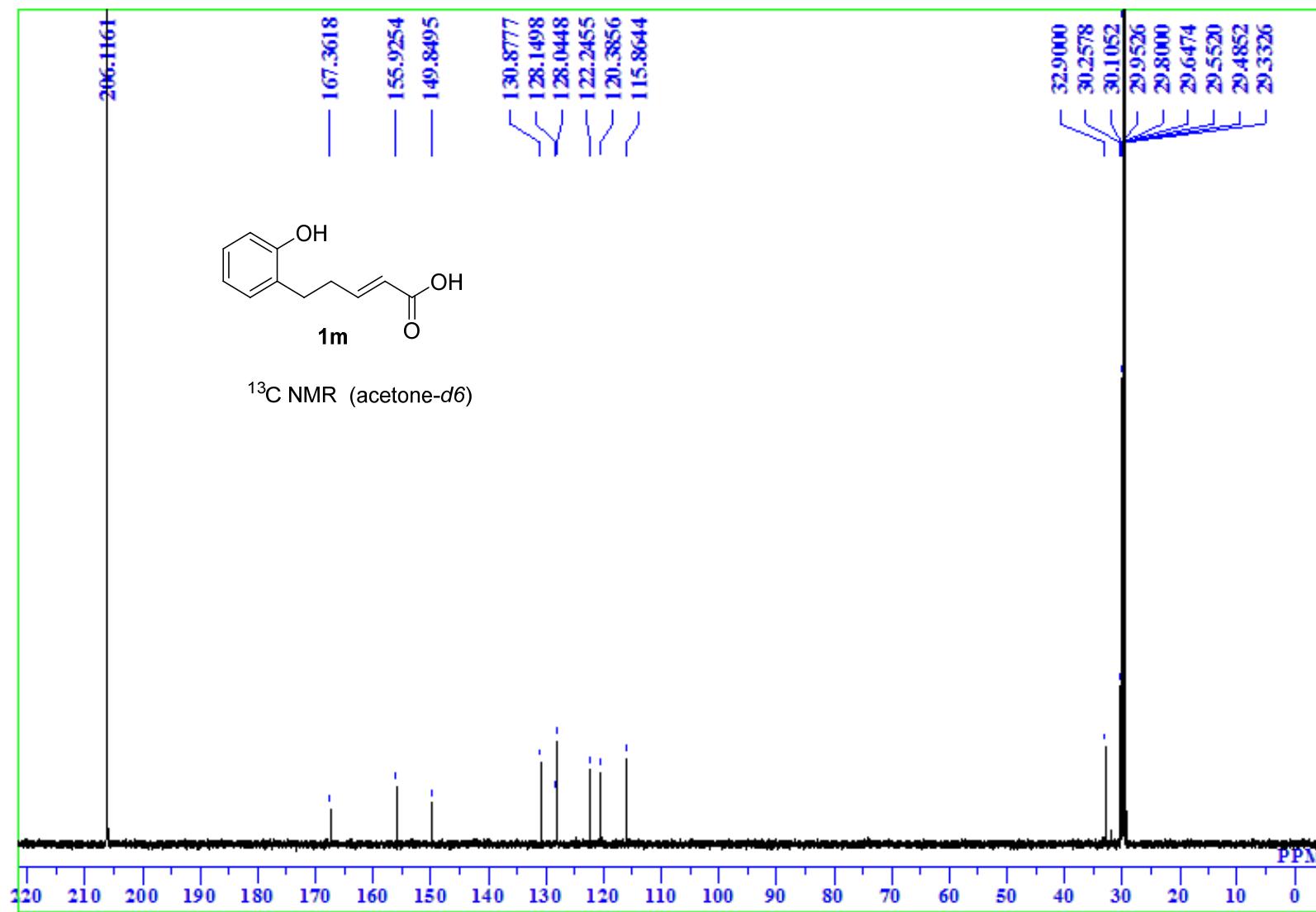


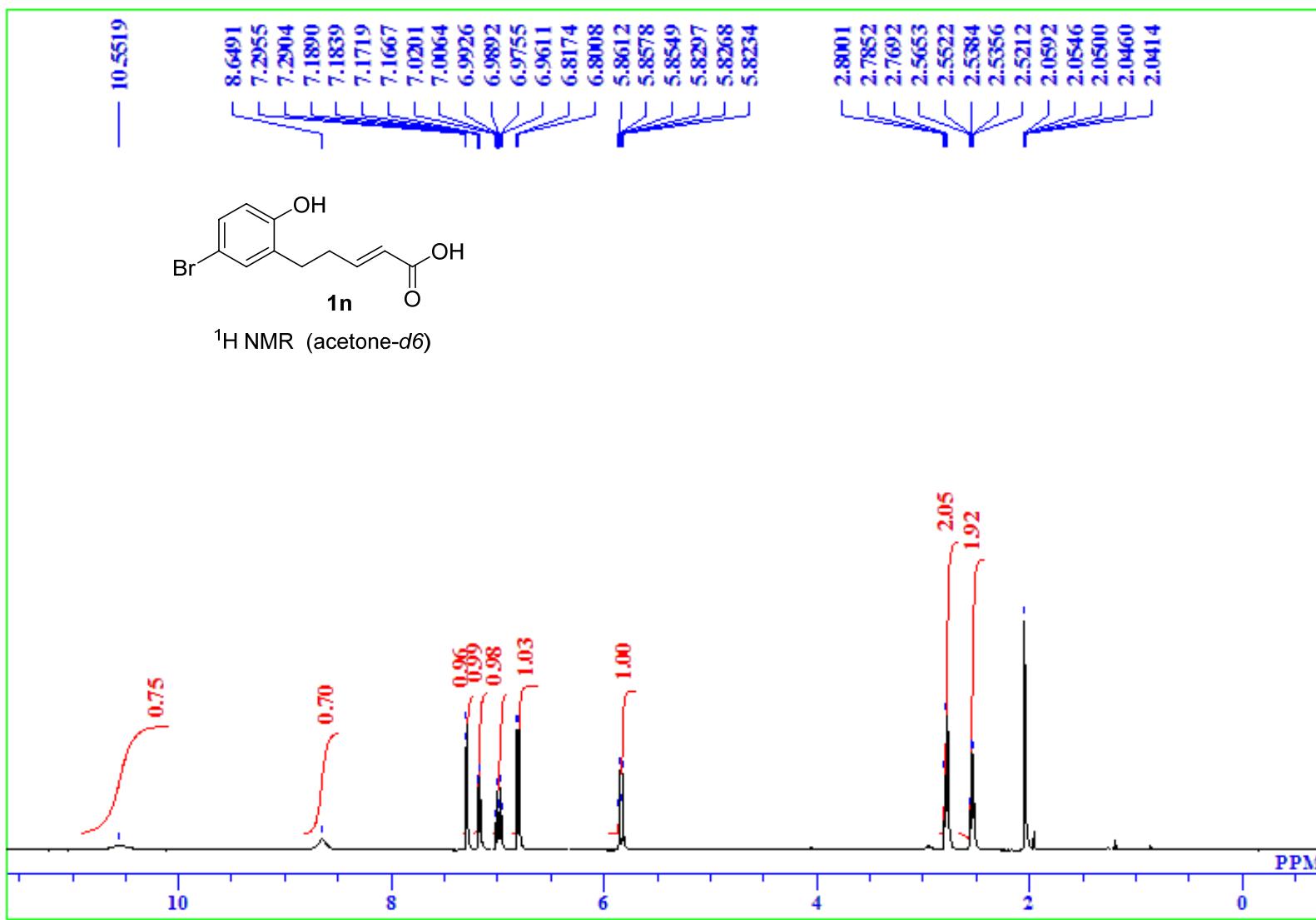
S103

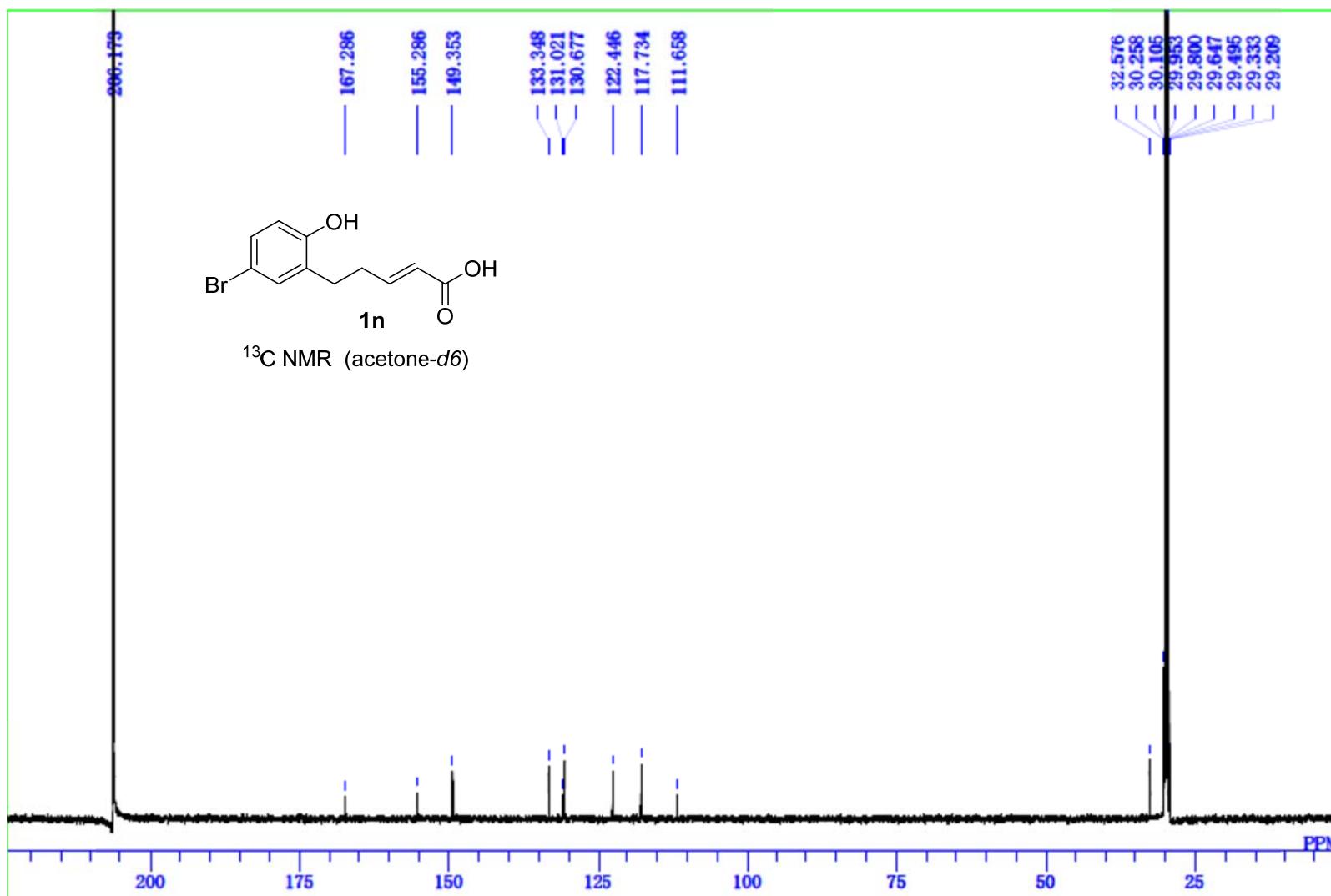


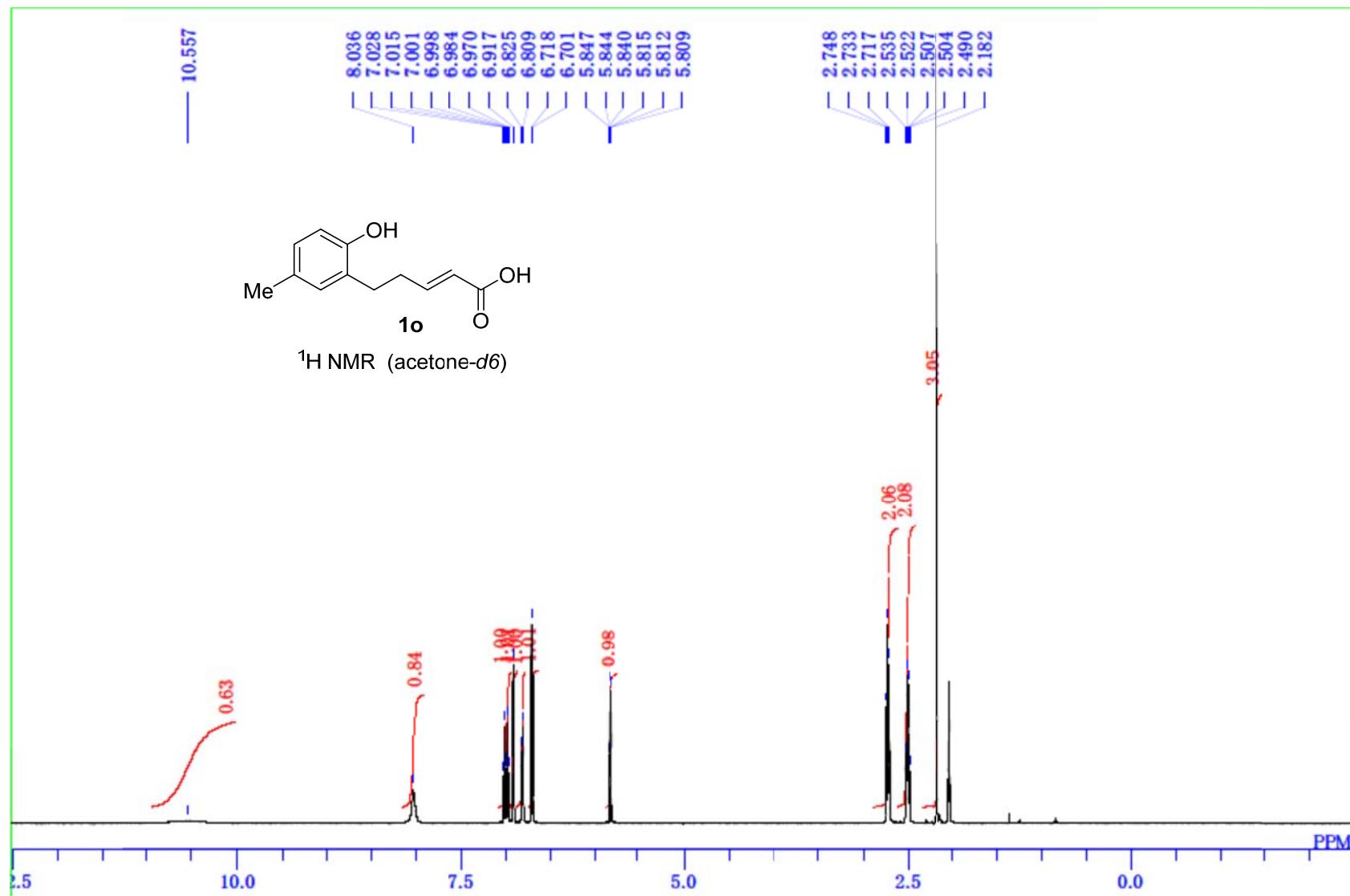
S104

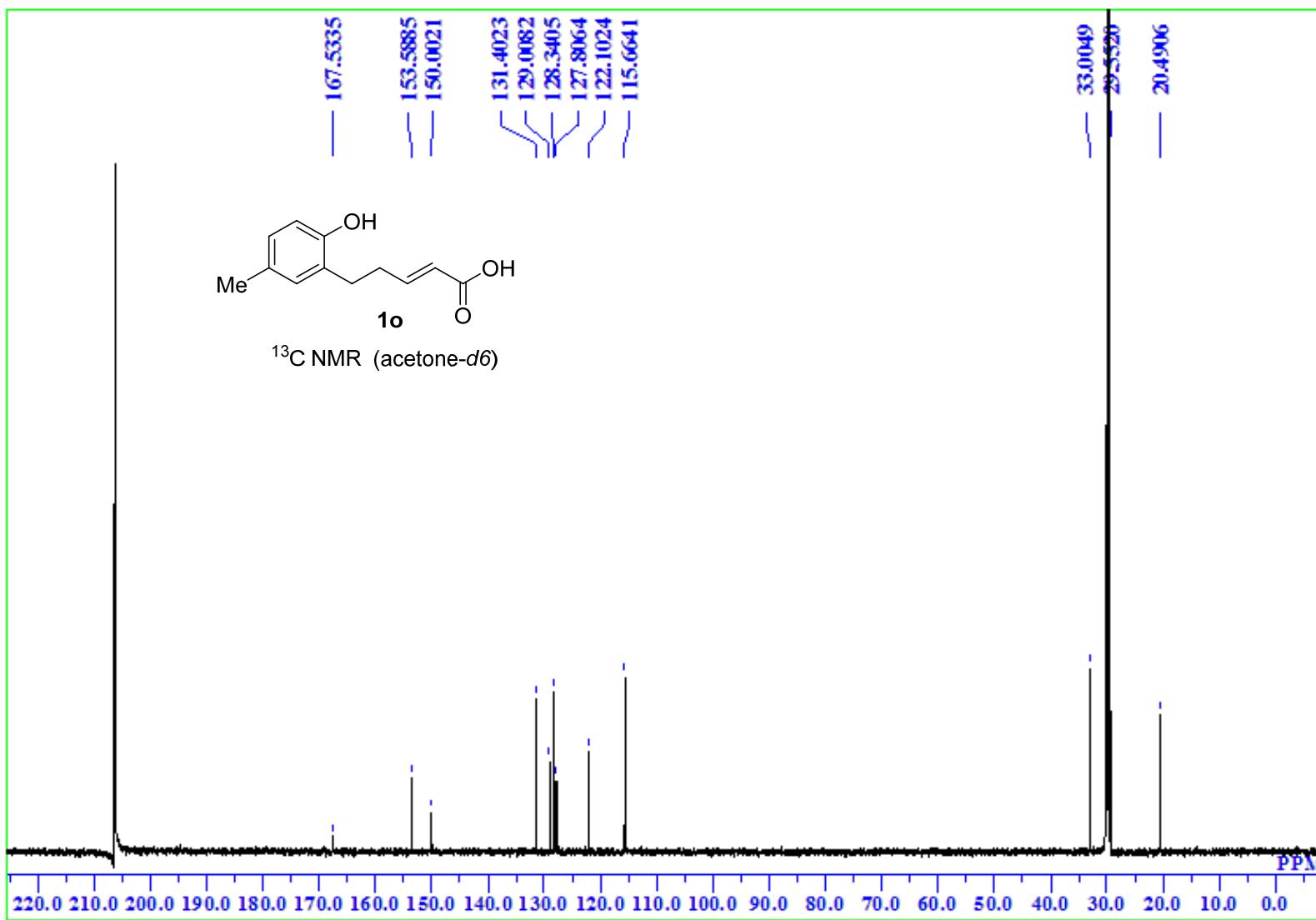


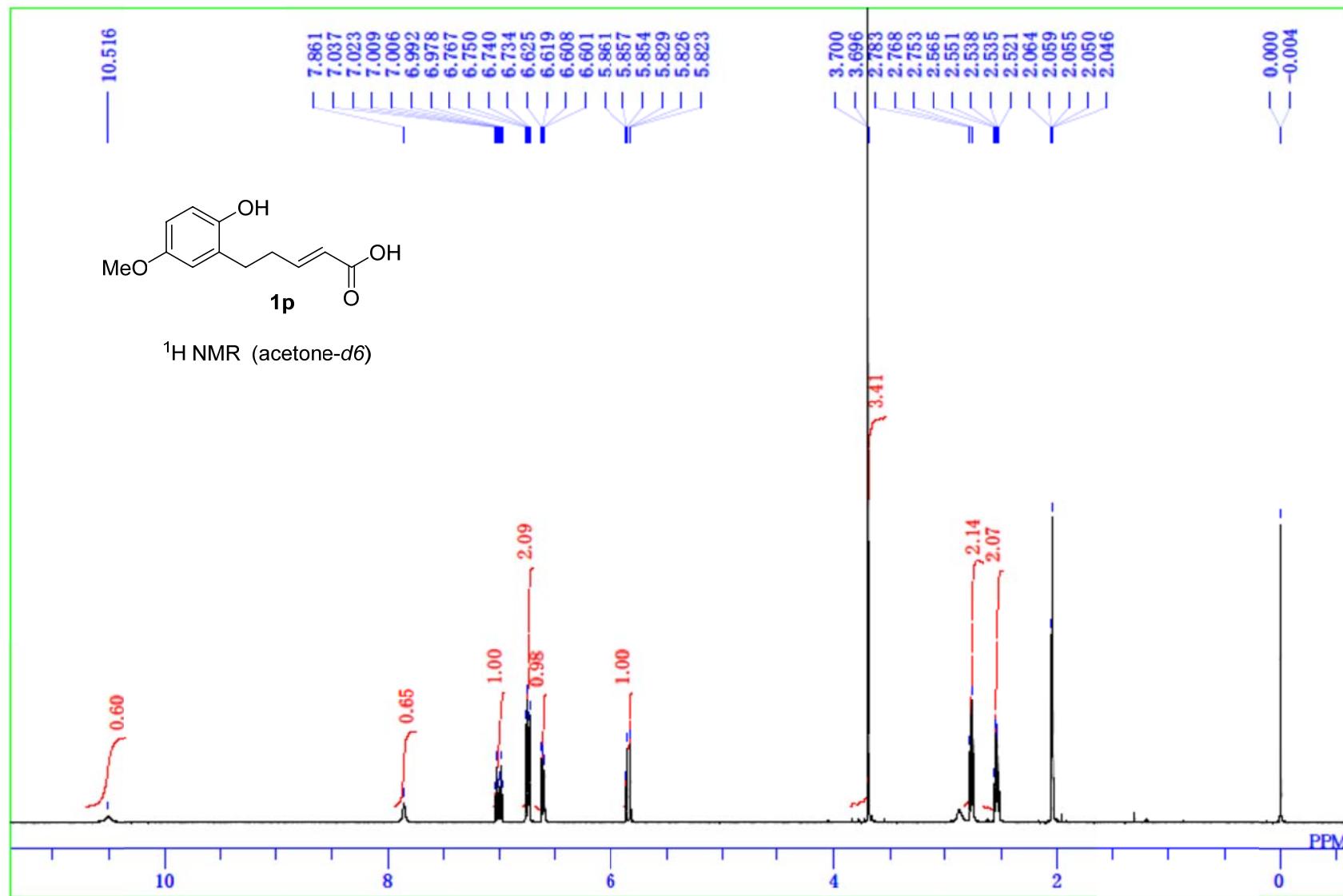


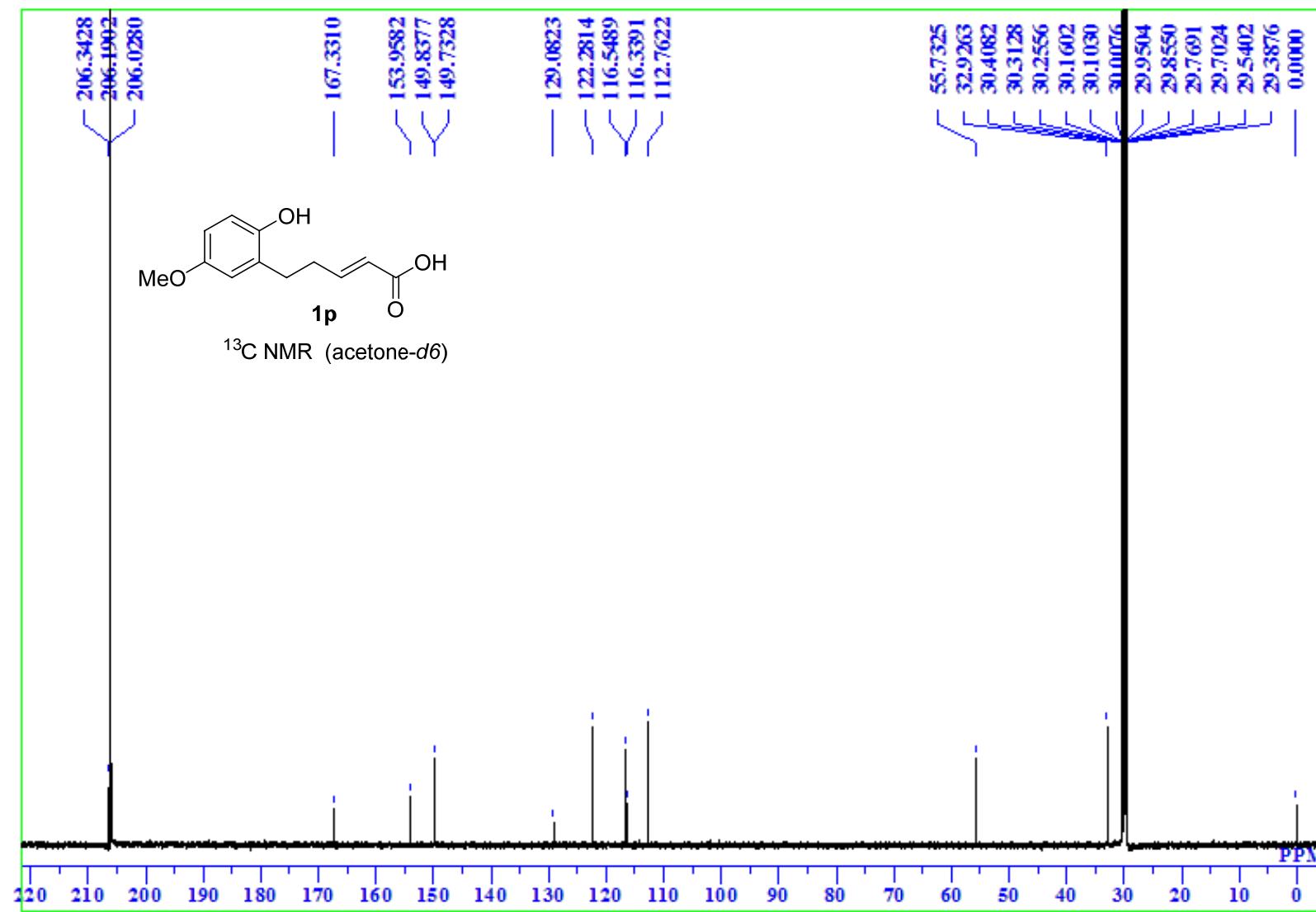


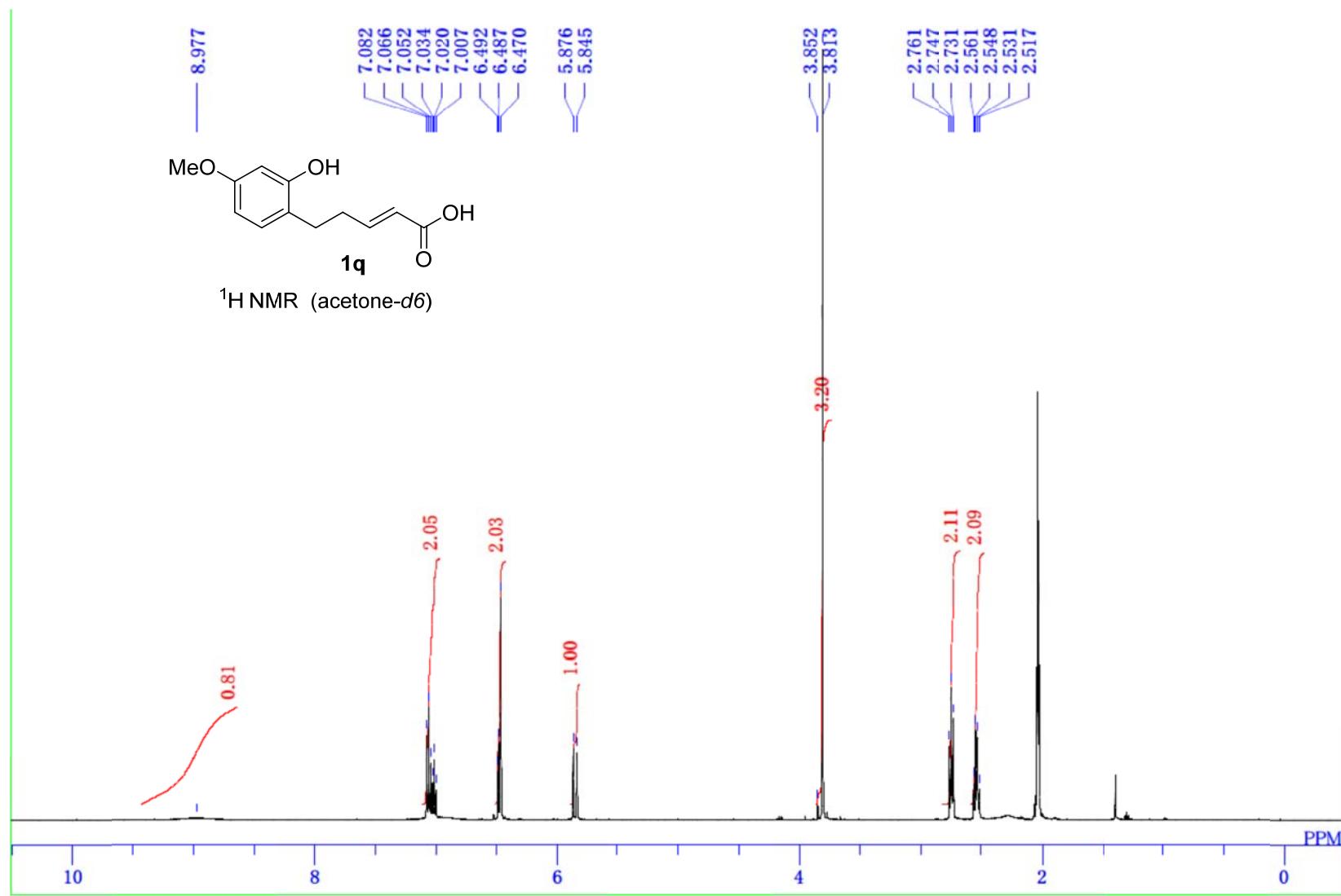


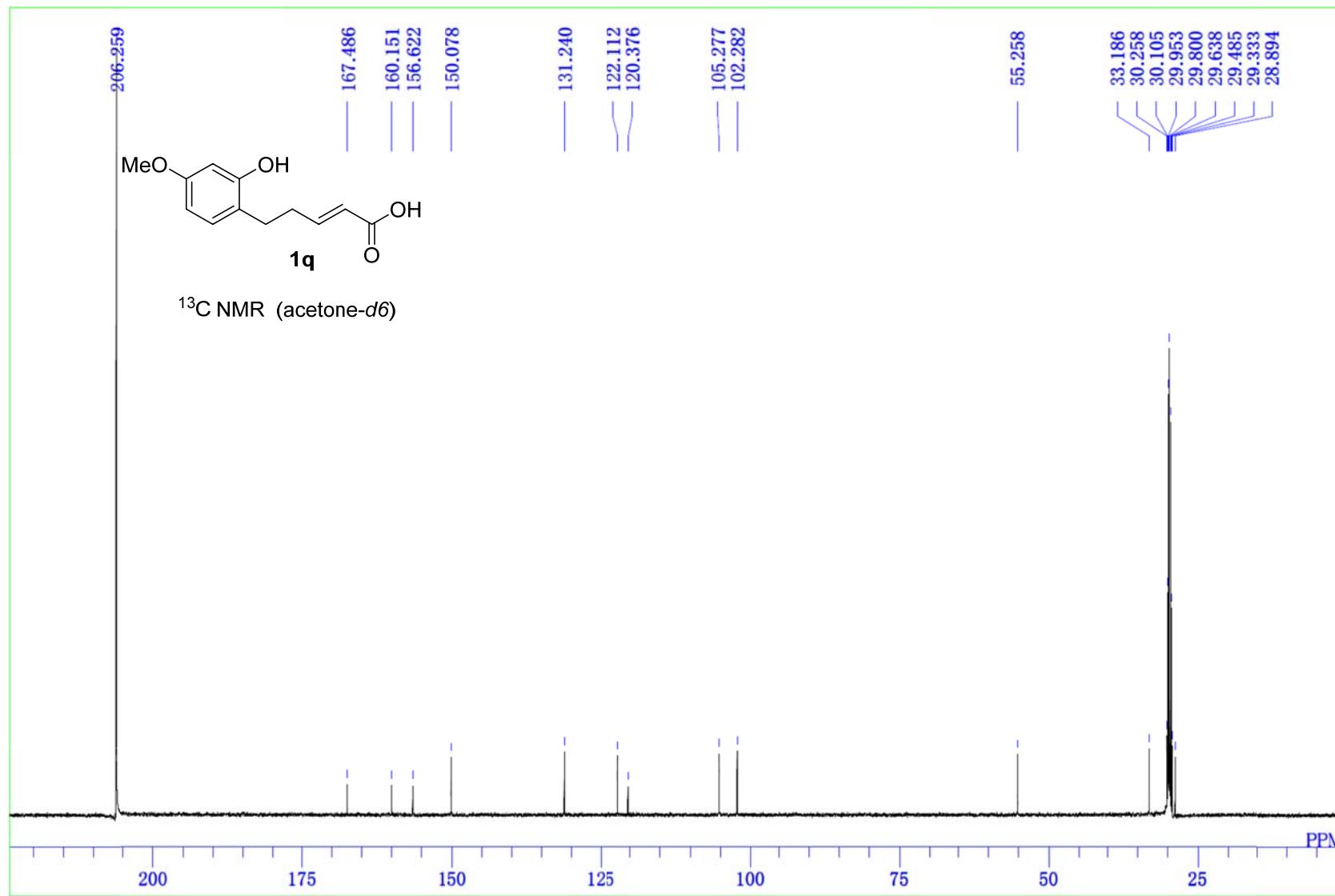


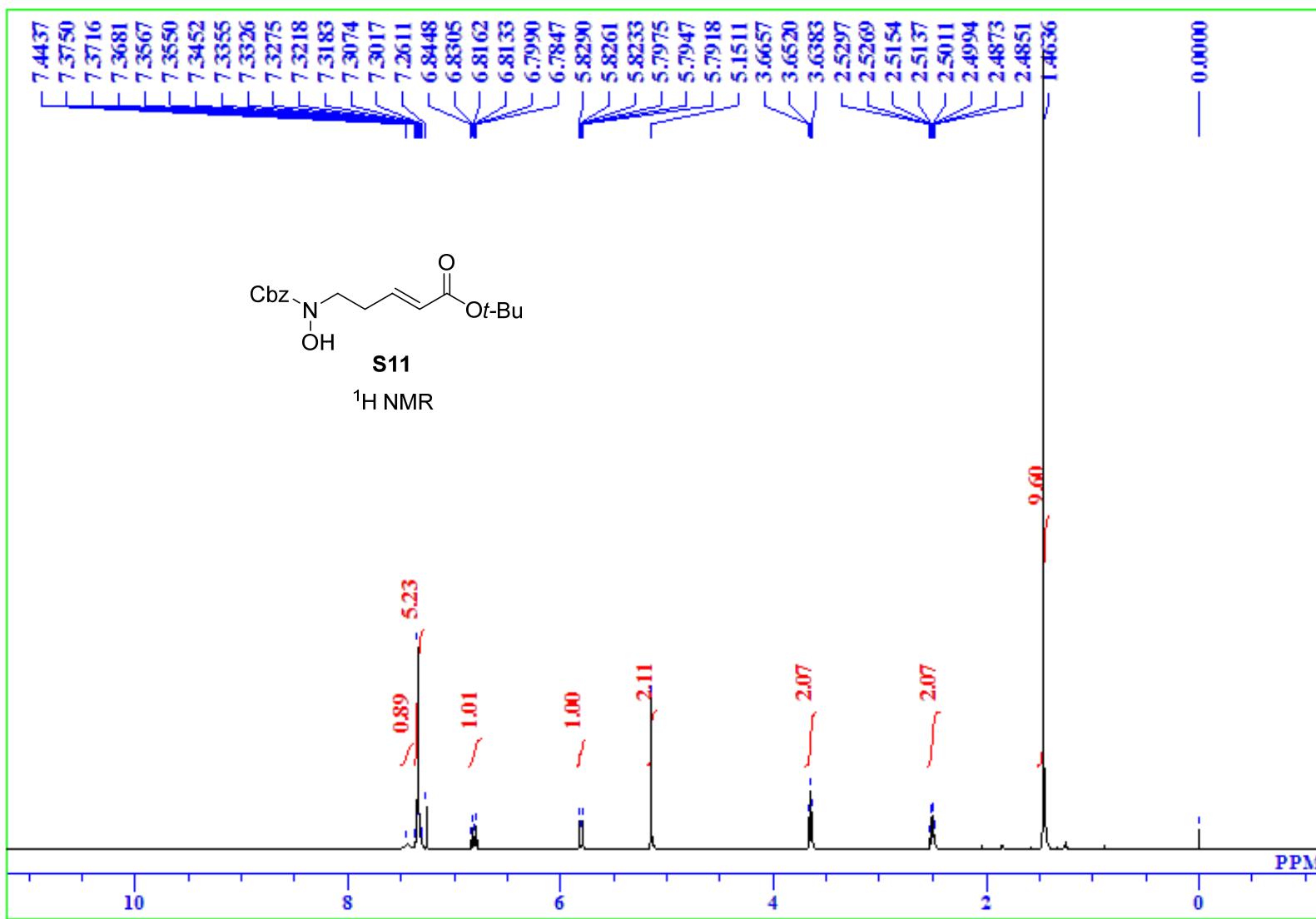




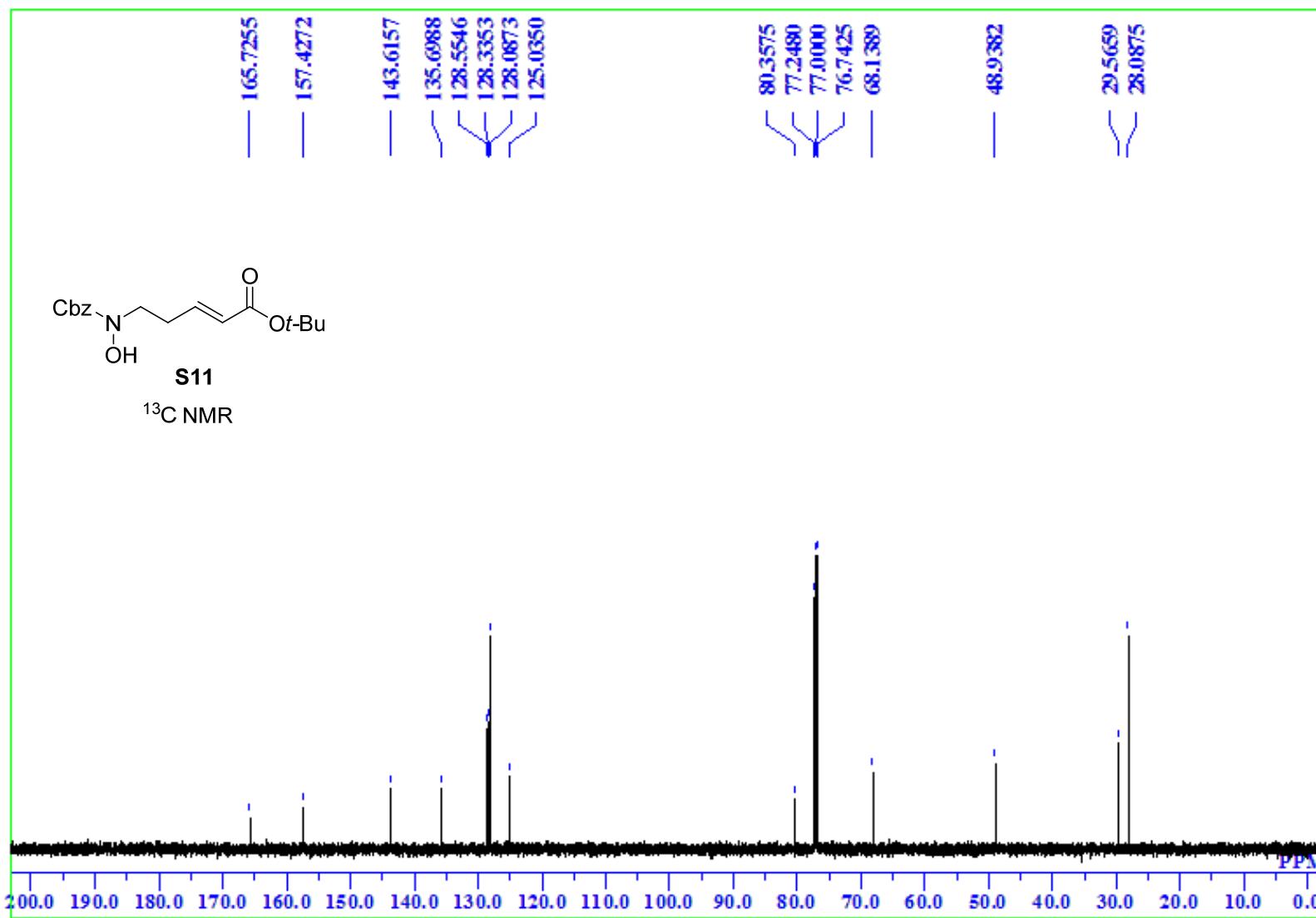




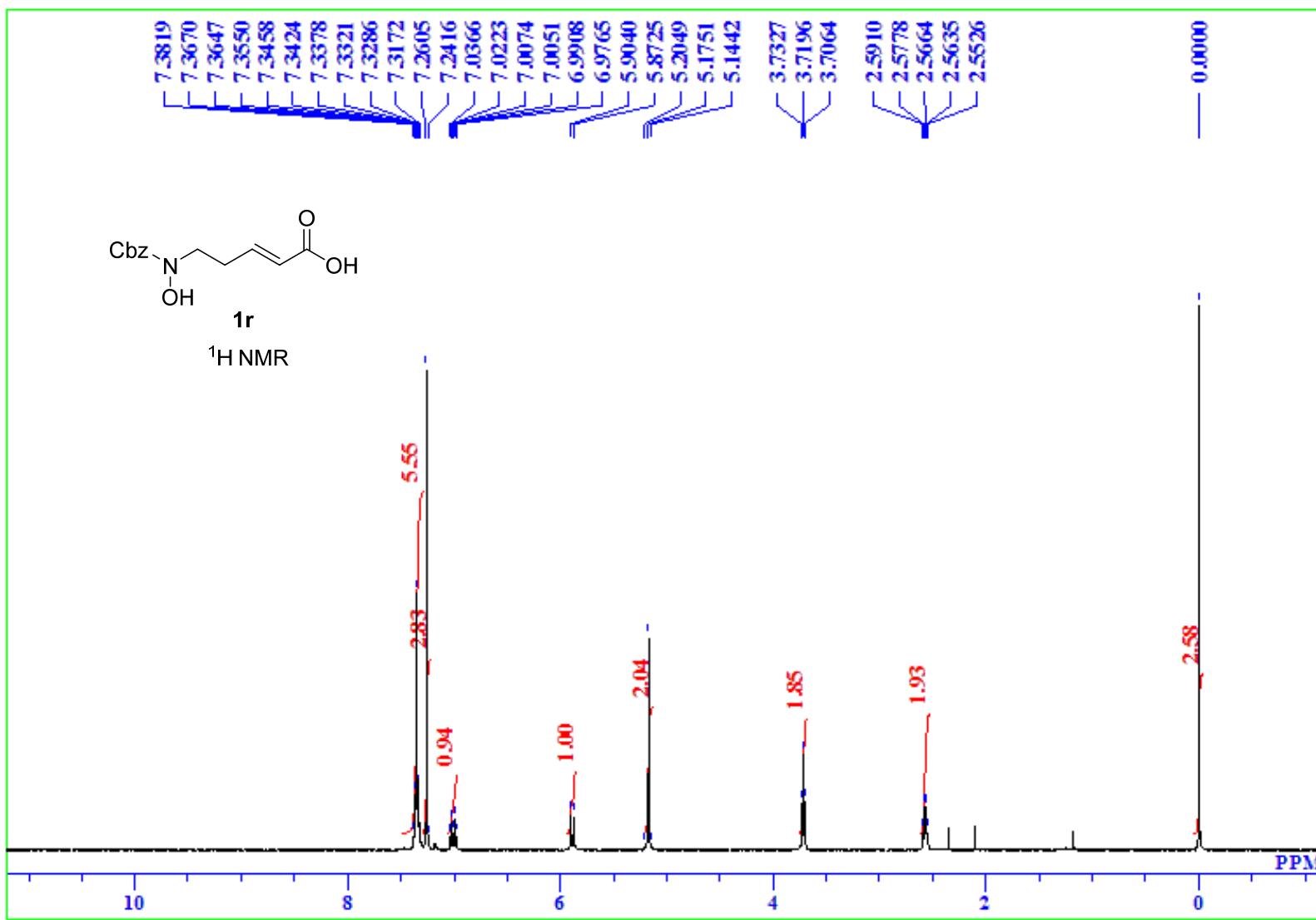


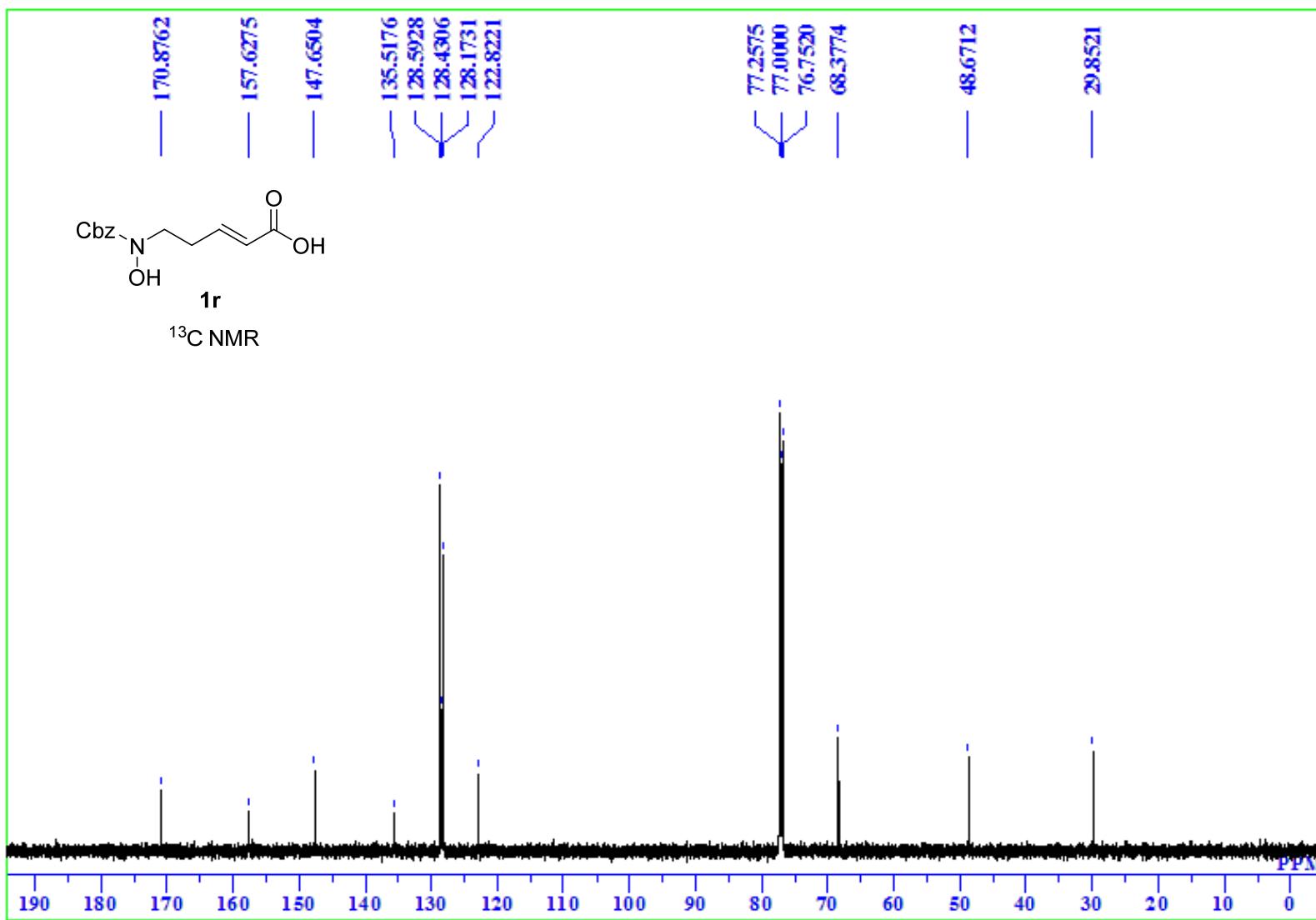


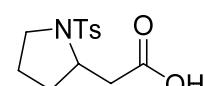
S115



S116

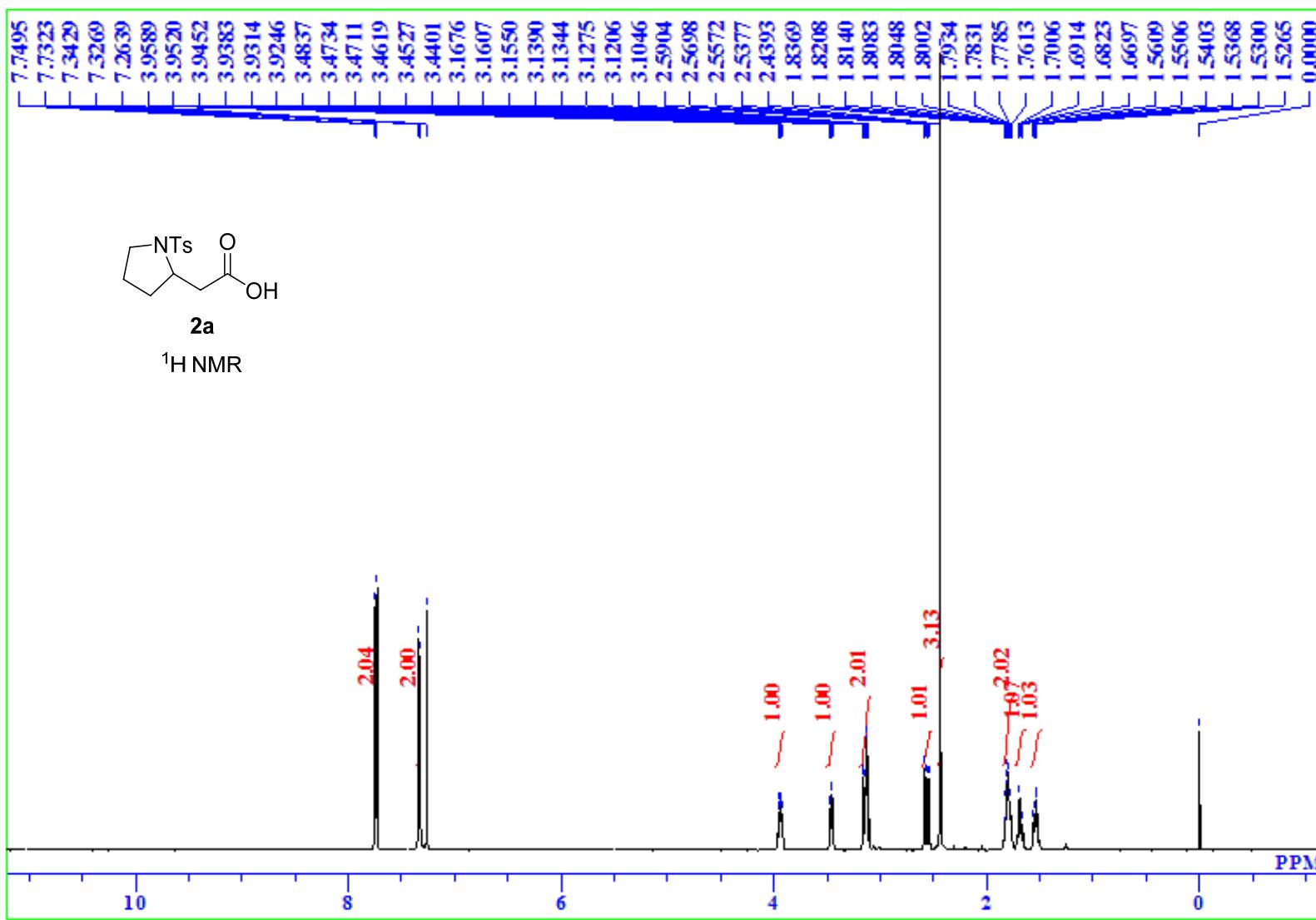


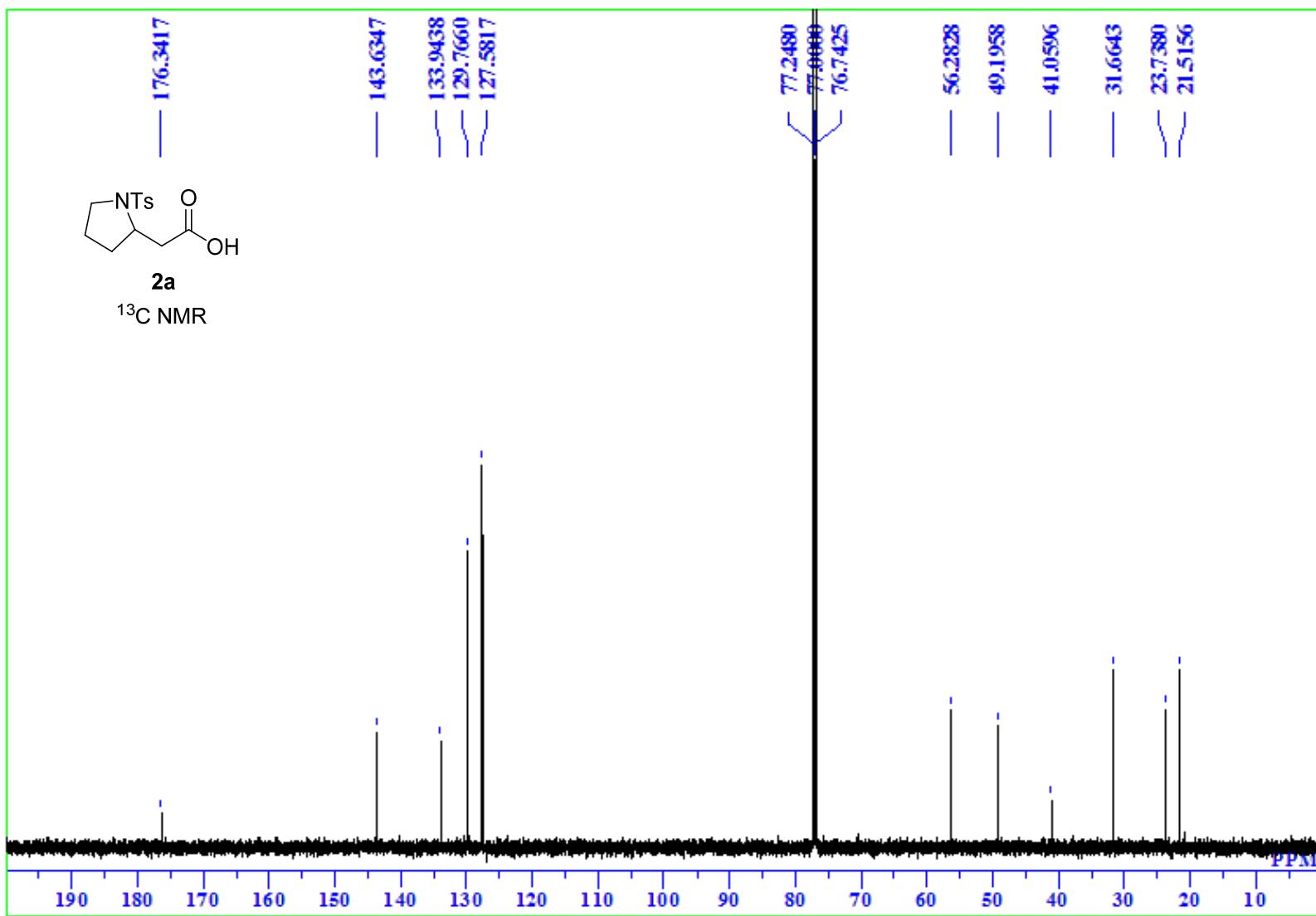




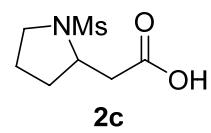
2a

¹H NMR

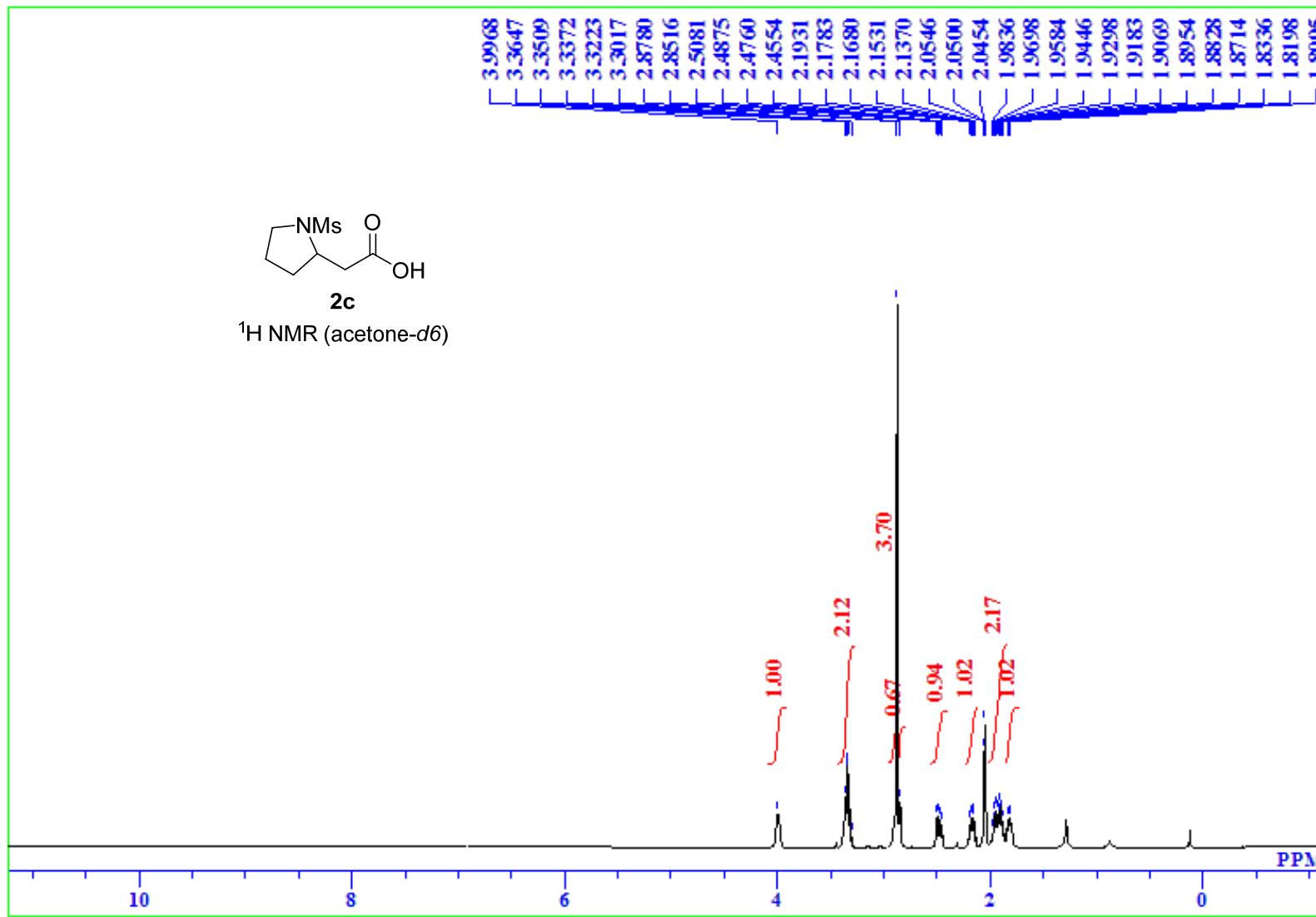


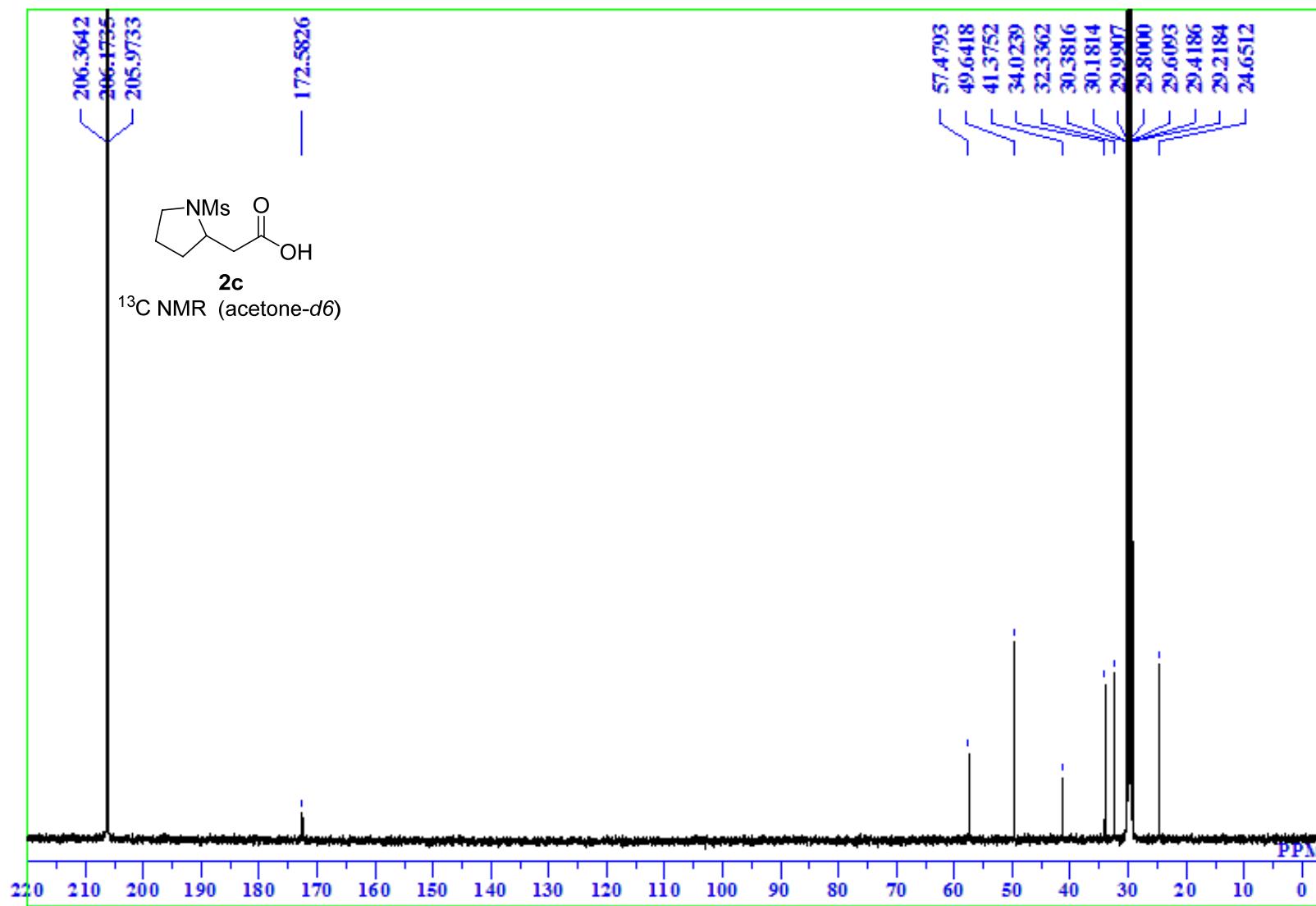


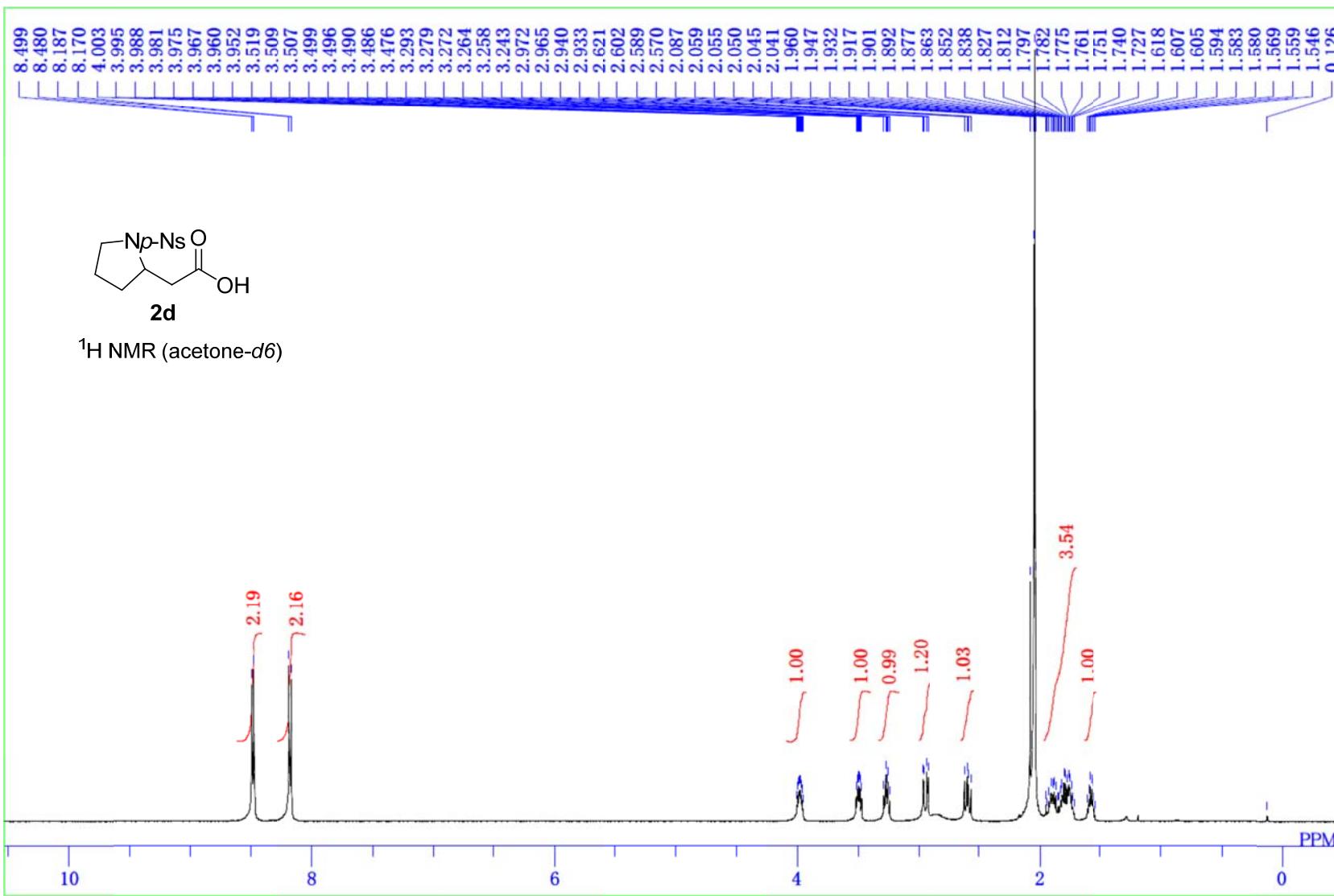
S120

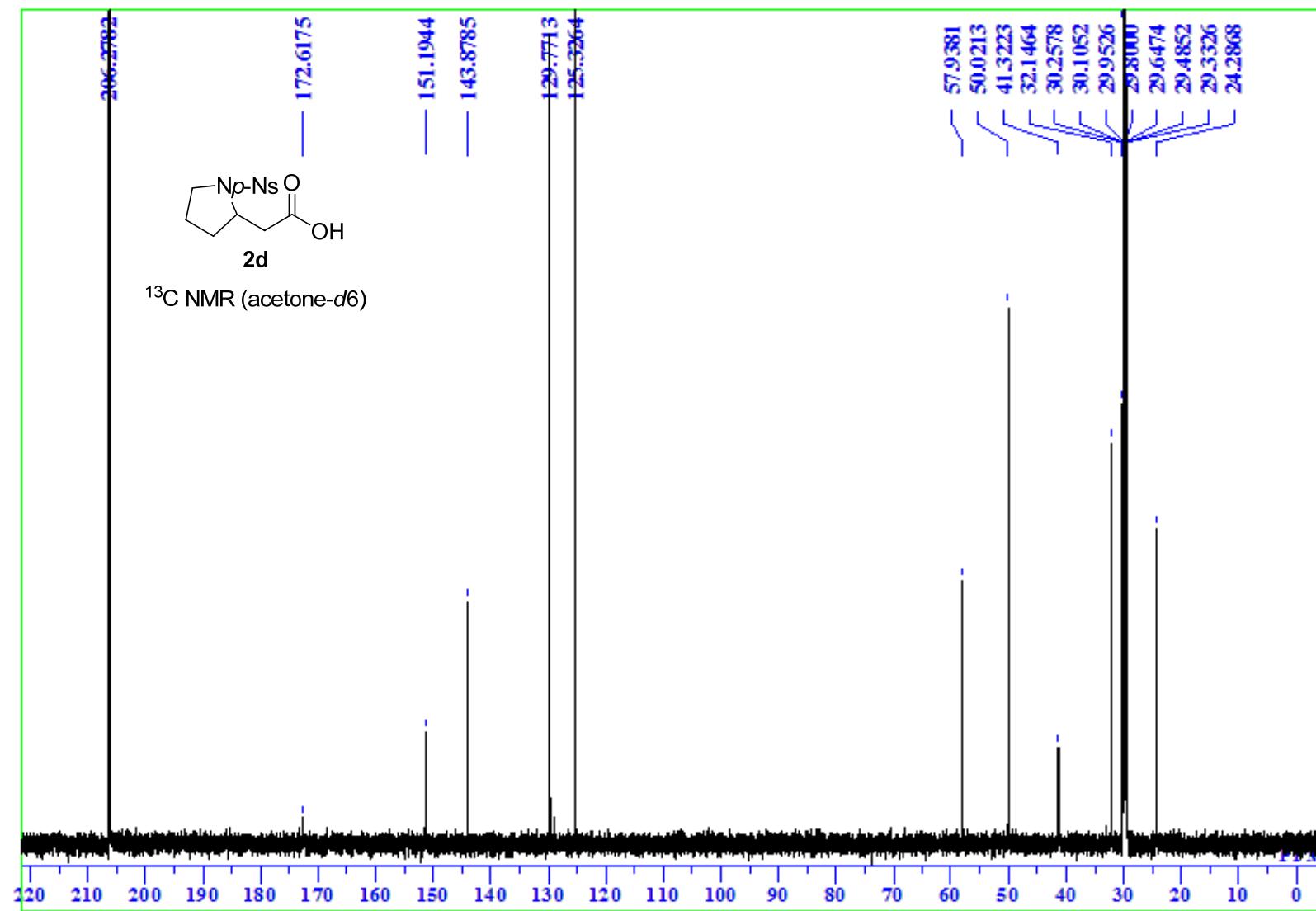


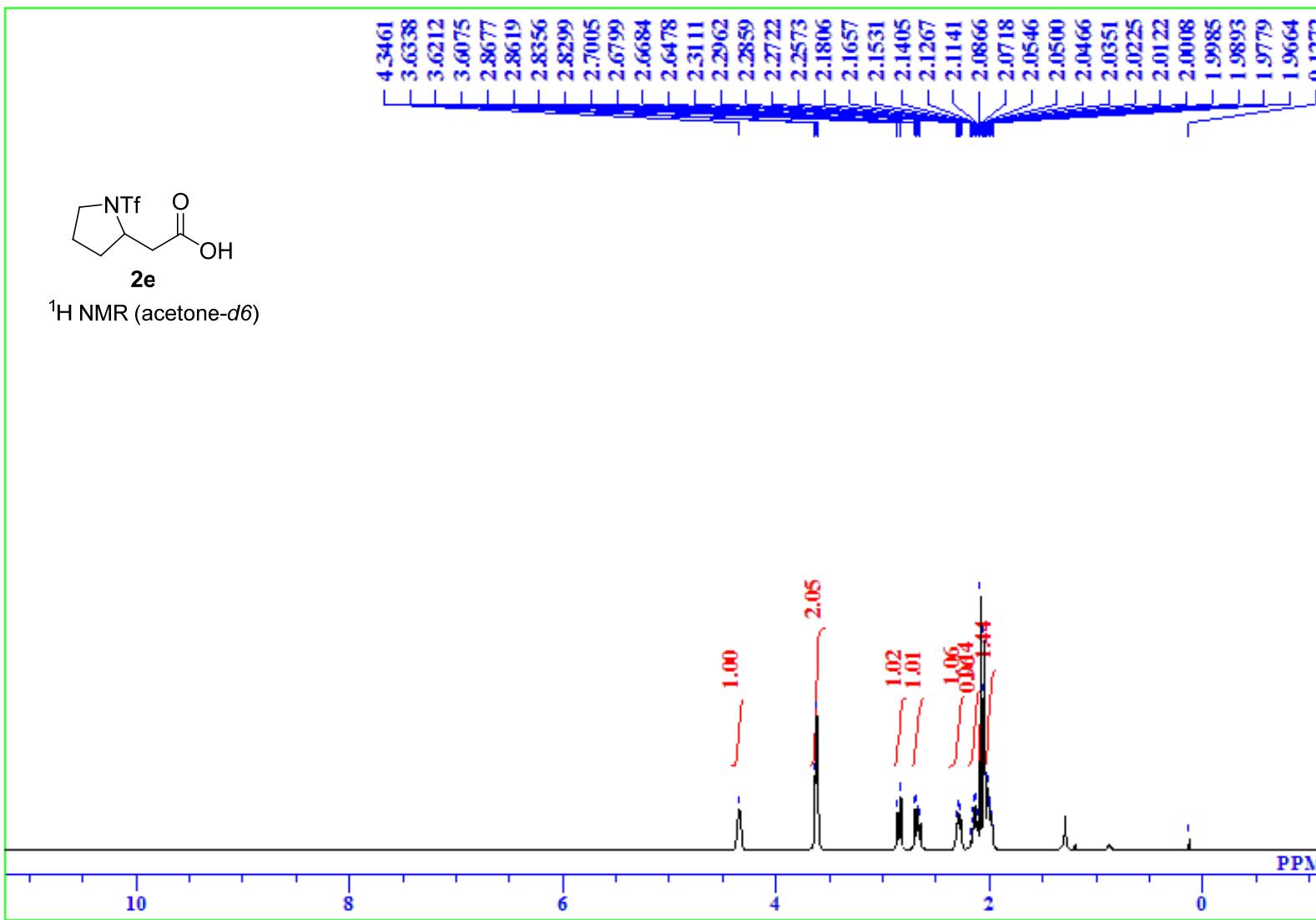
2c
 ^1H NMR (acetone-*d*6)

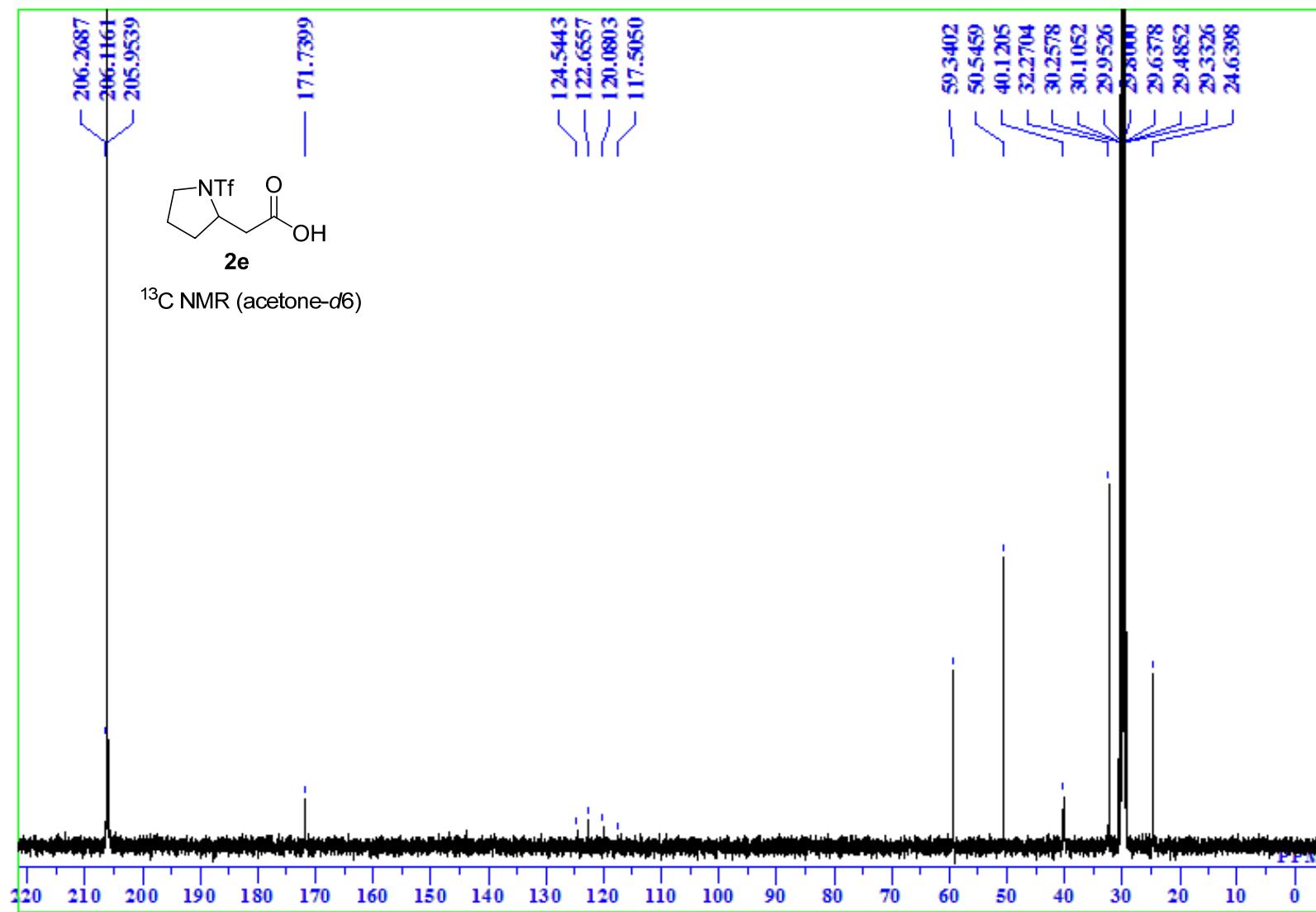


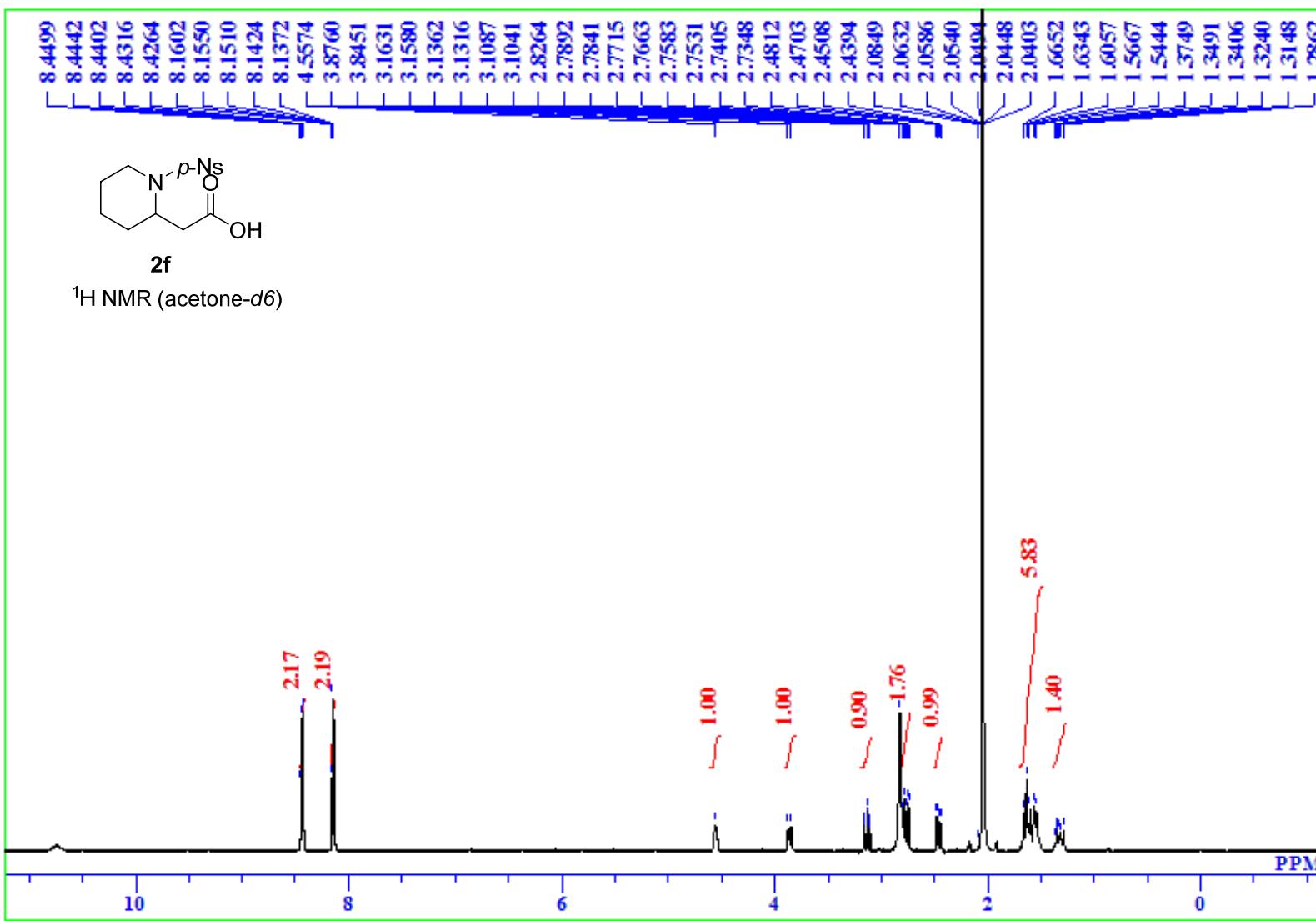


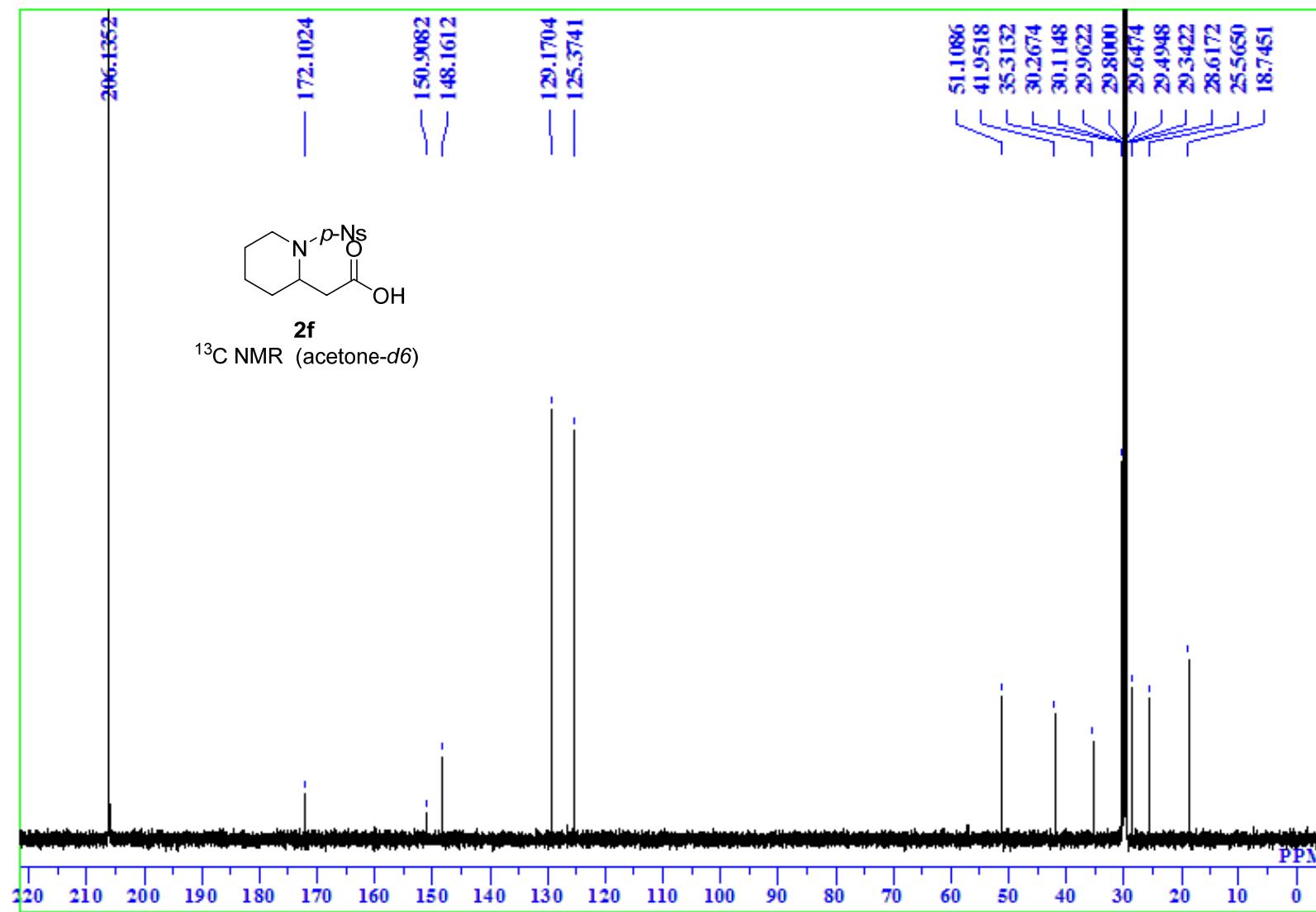


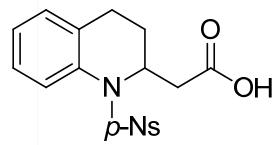




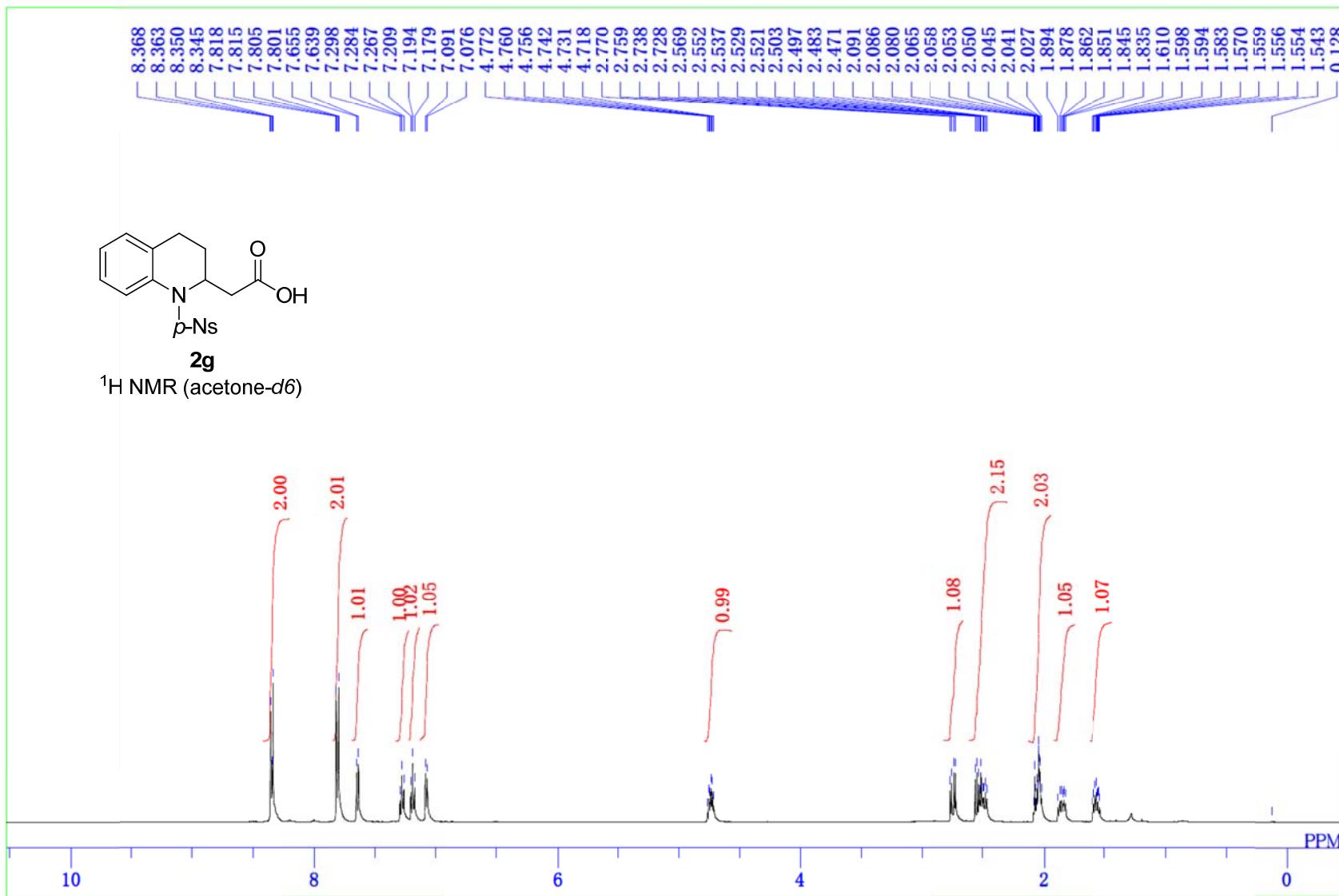


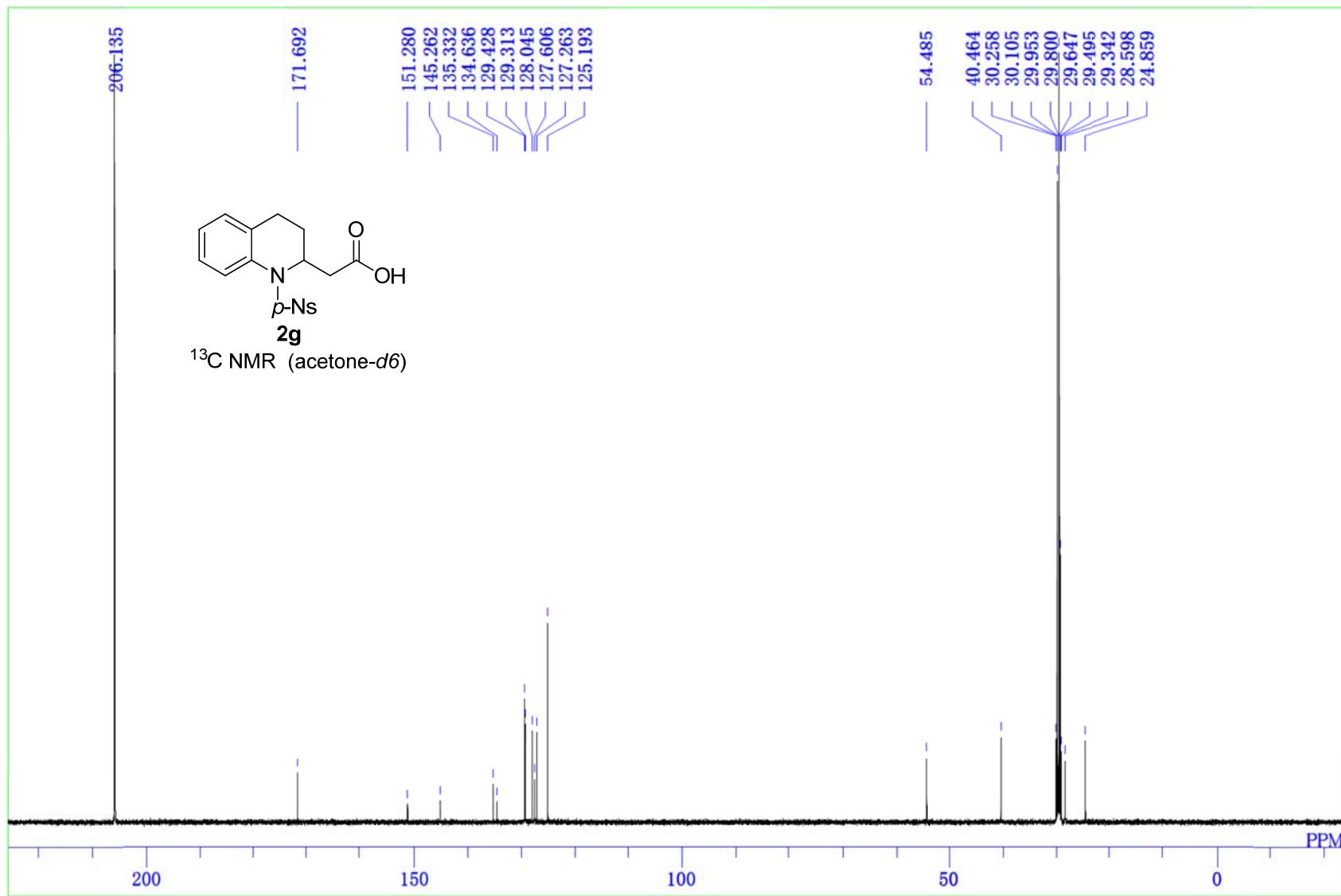




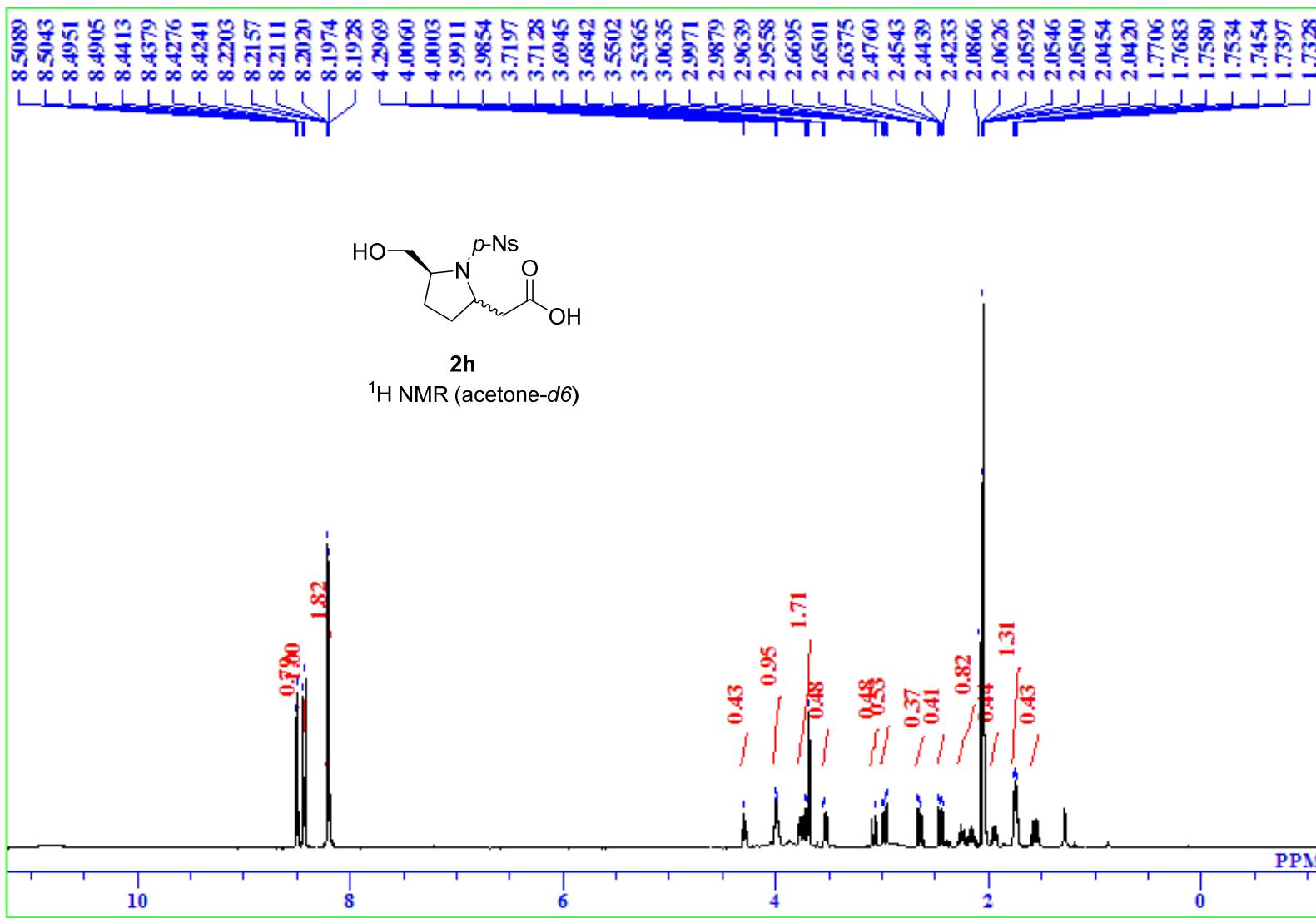


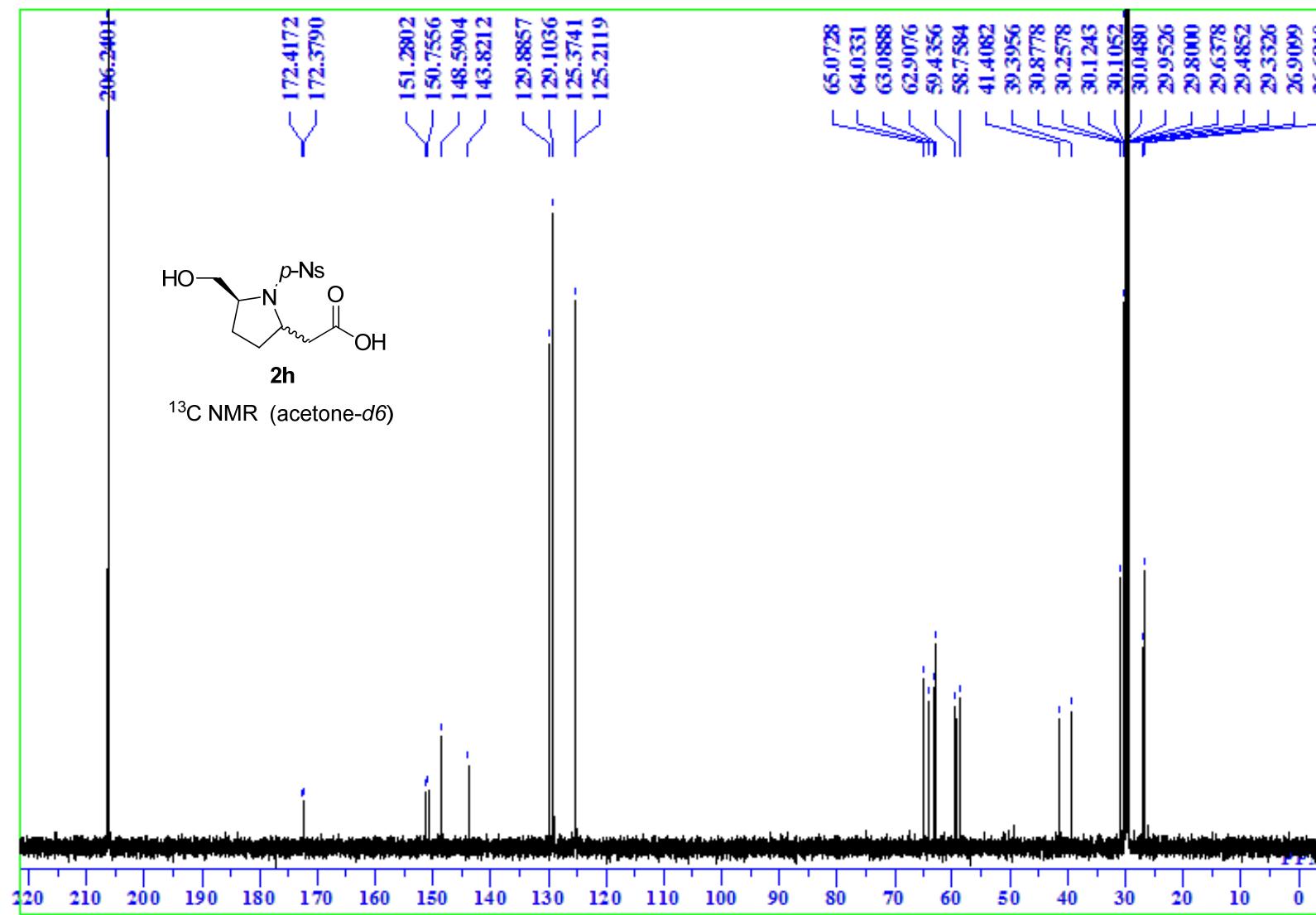
2g ¹H NMR (acetone-*d*6)

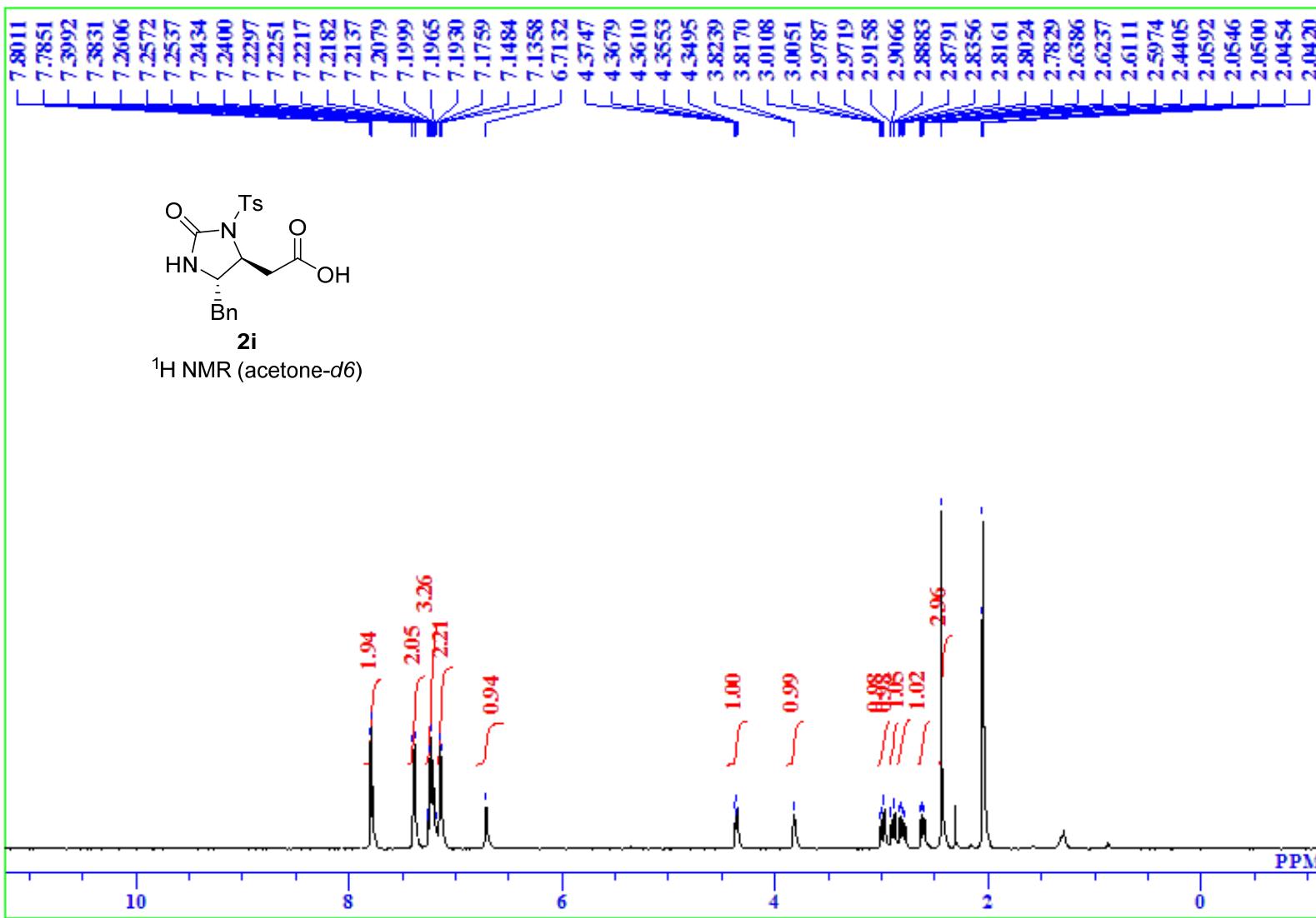


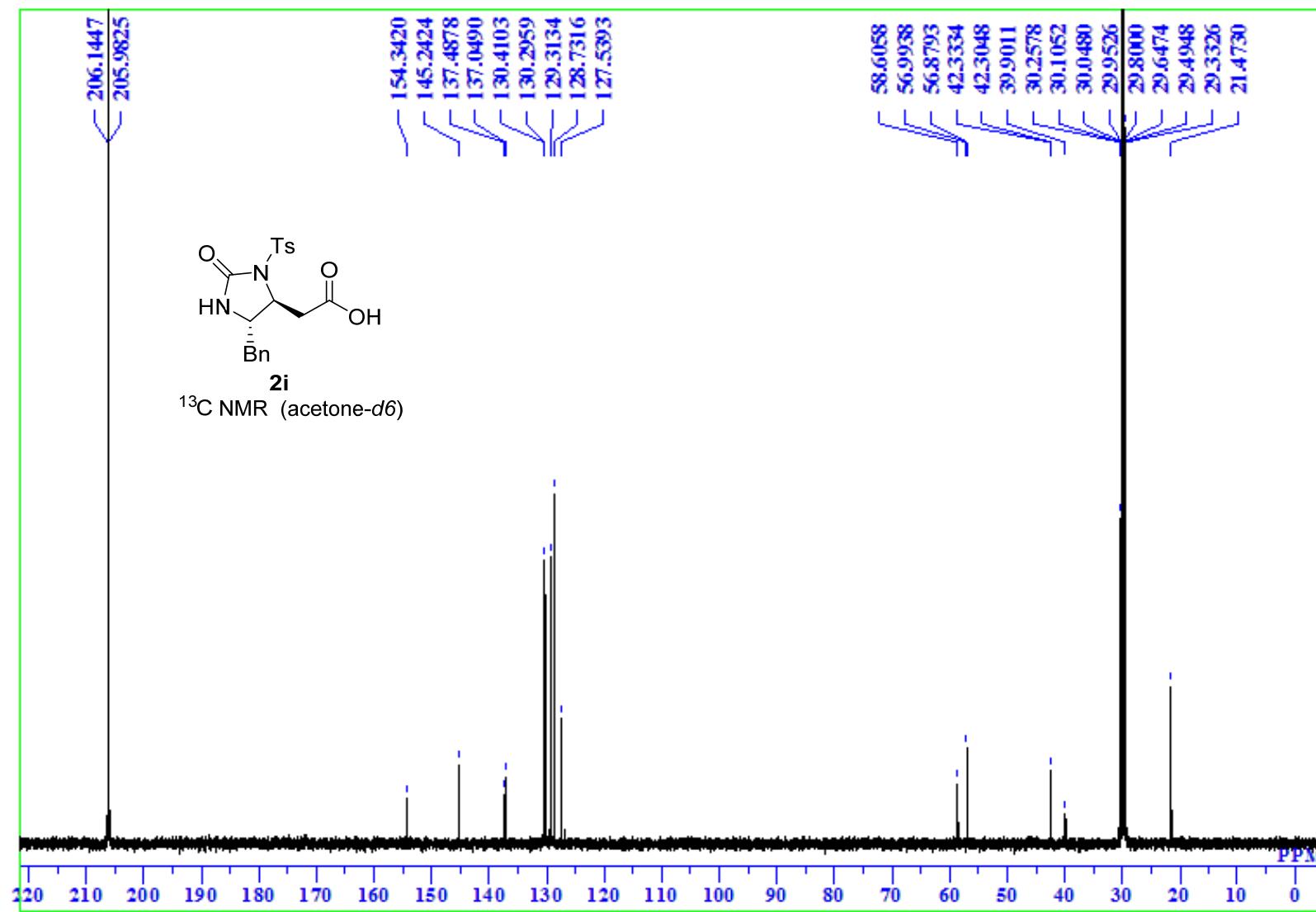


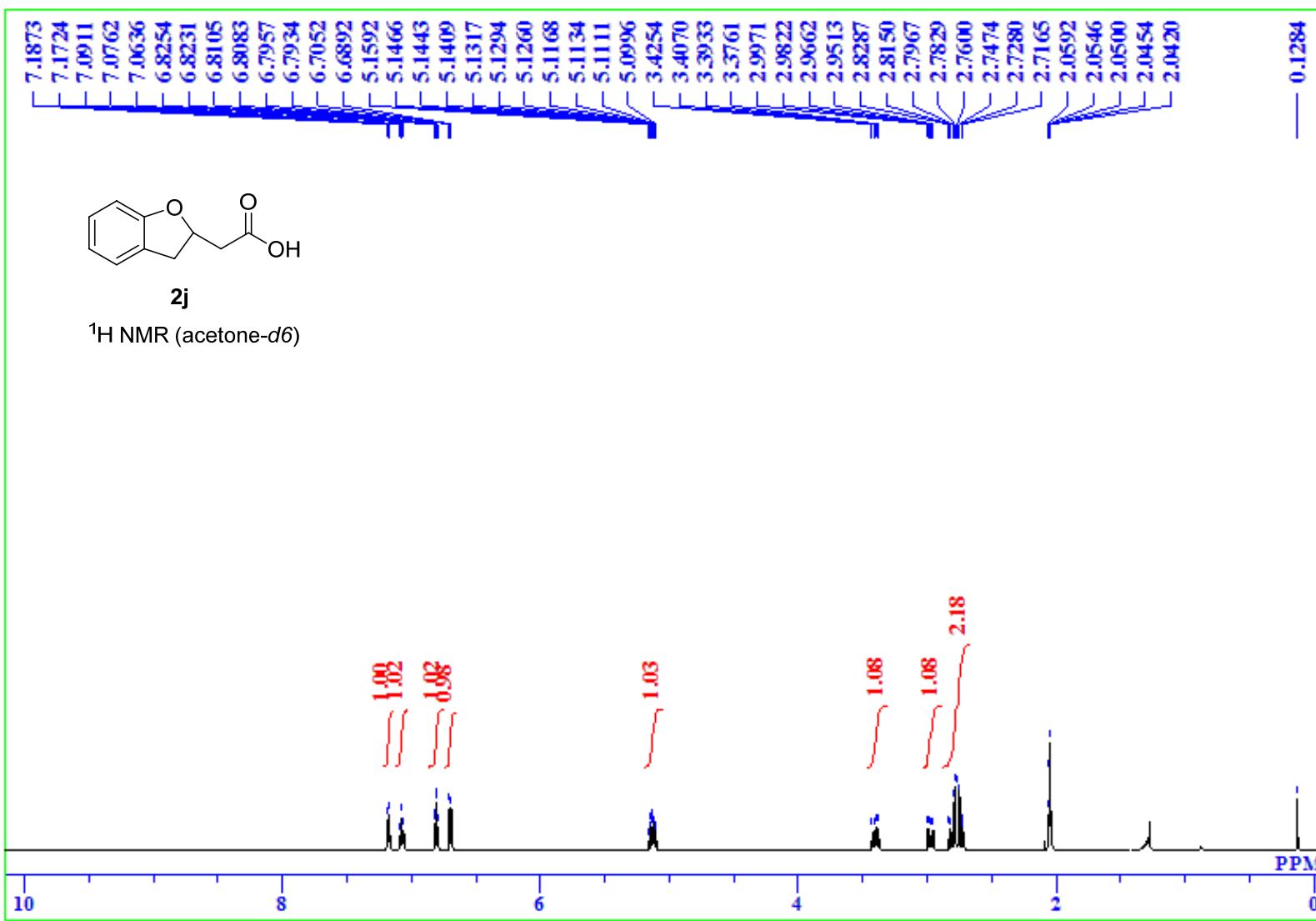
S130

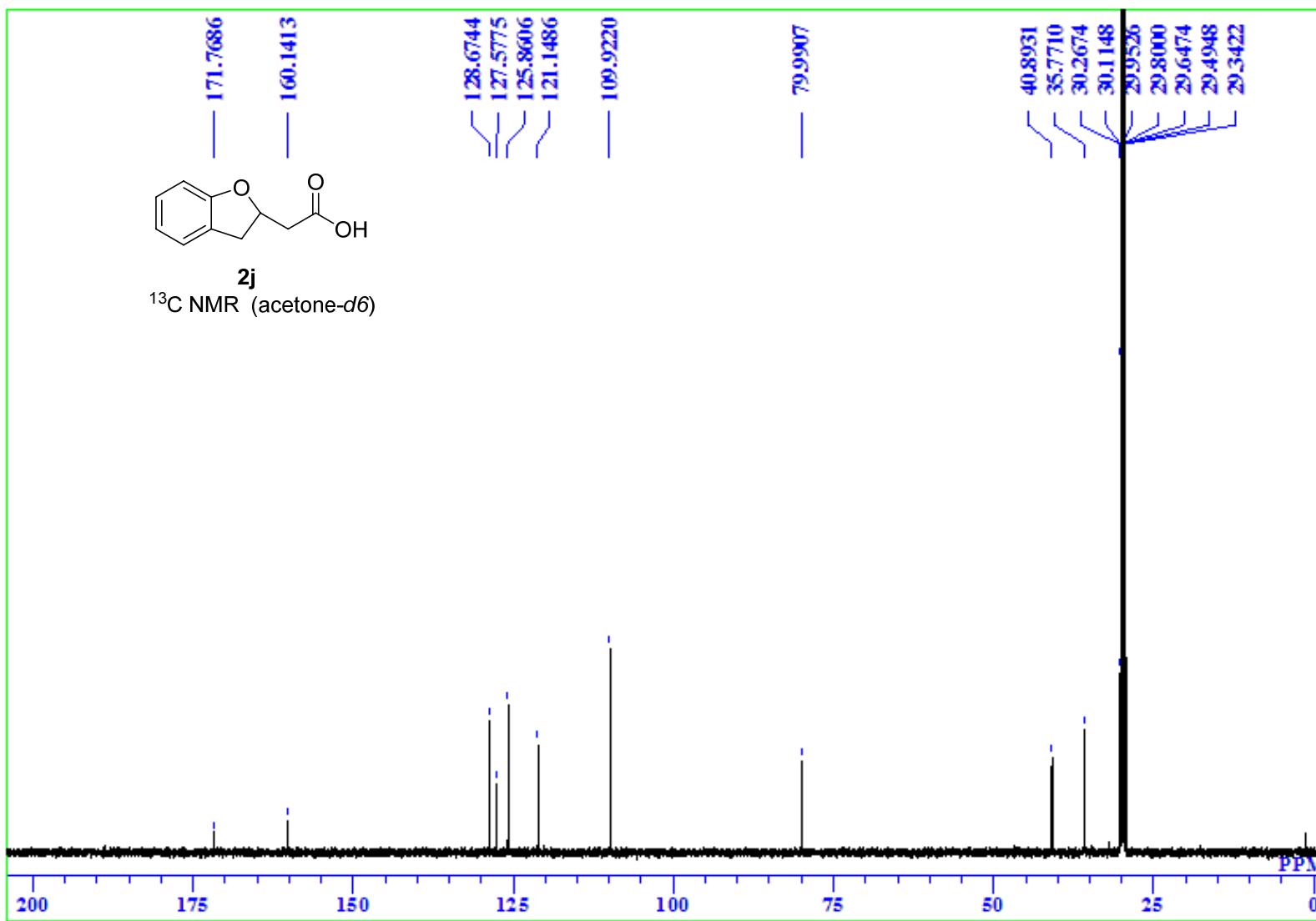


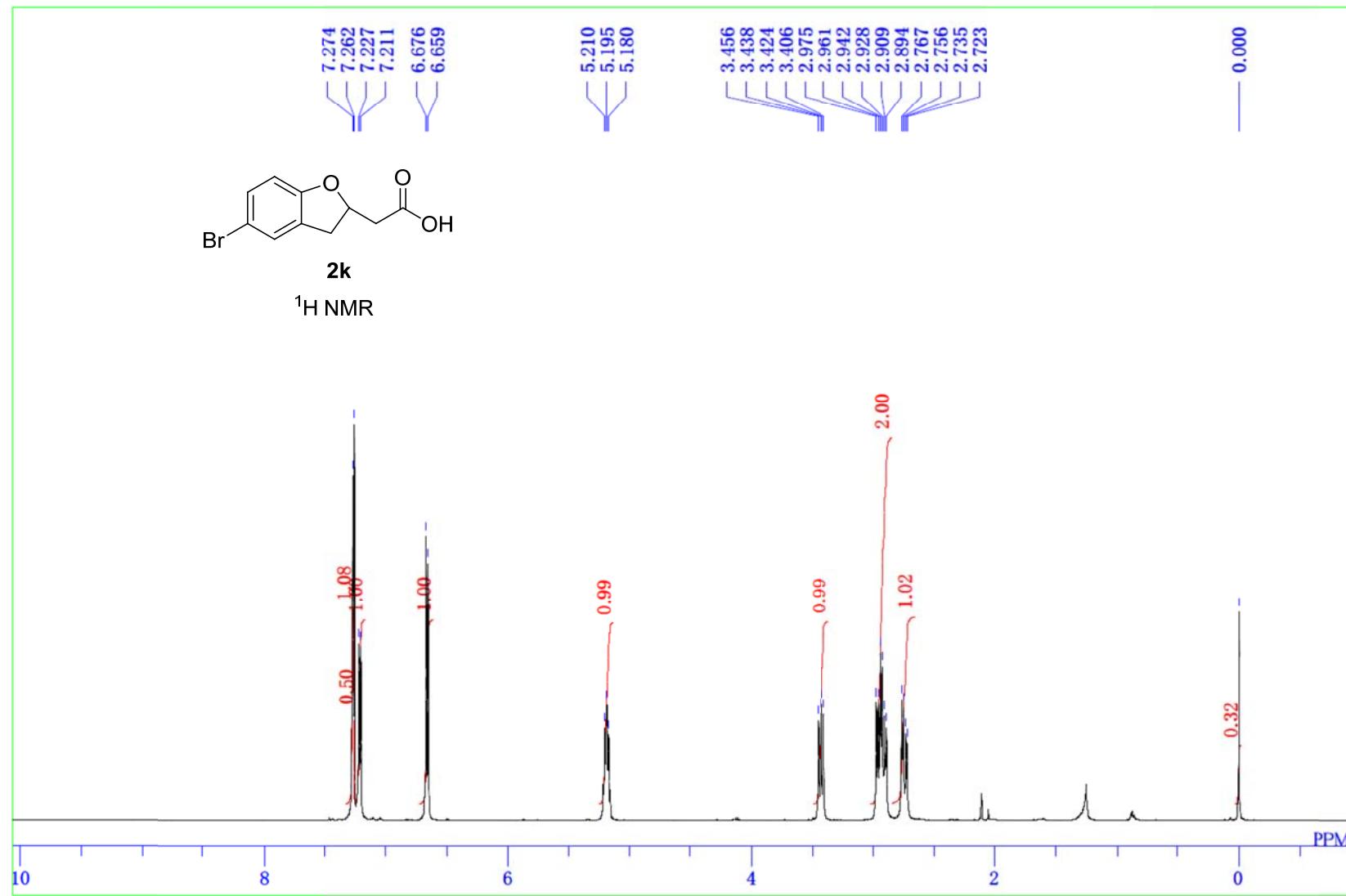


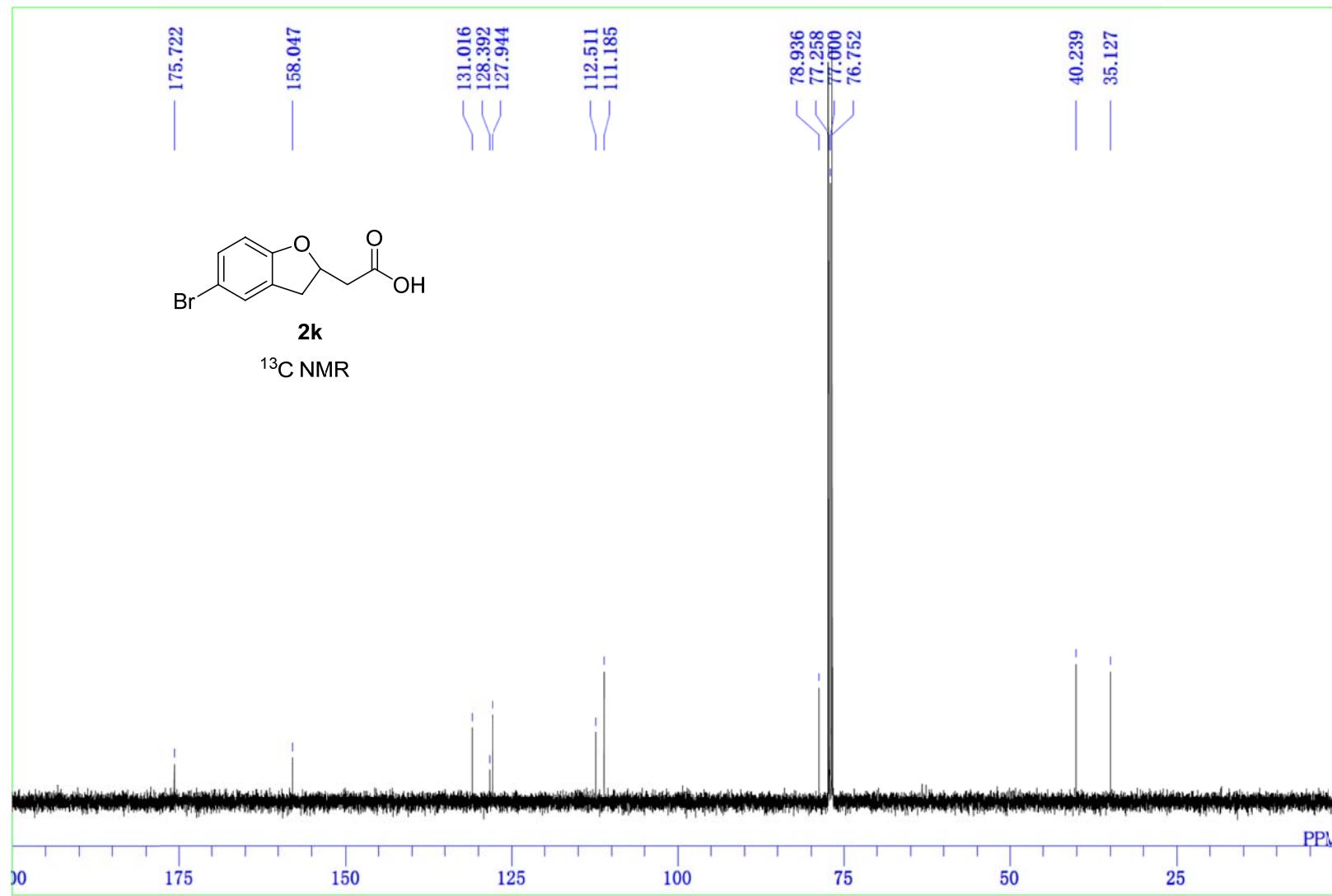


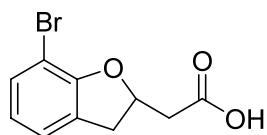
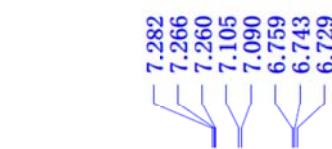






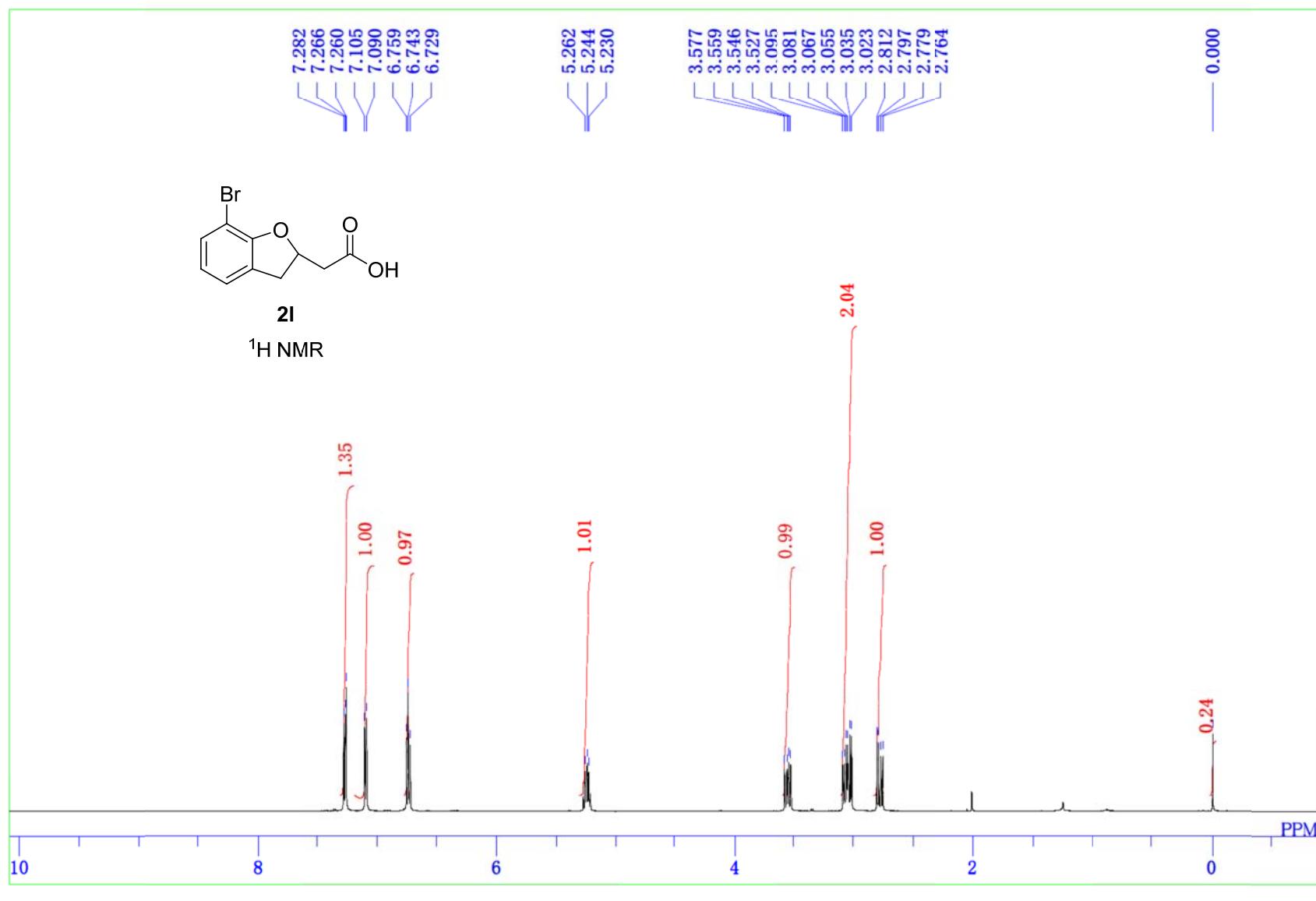




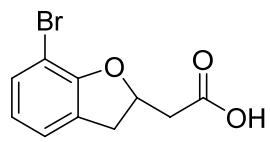


2l

^1H NMR

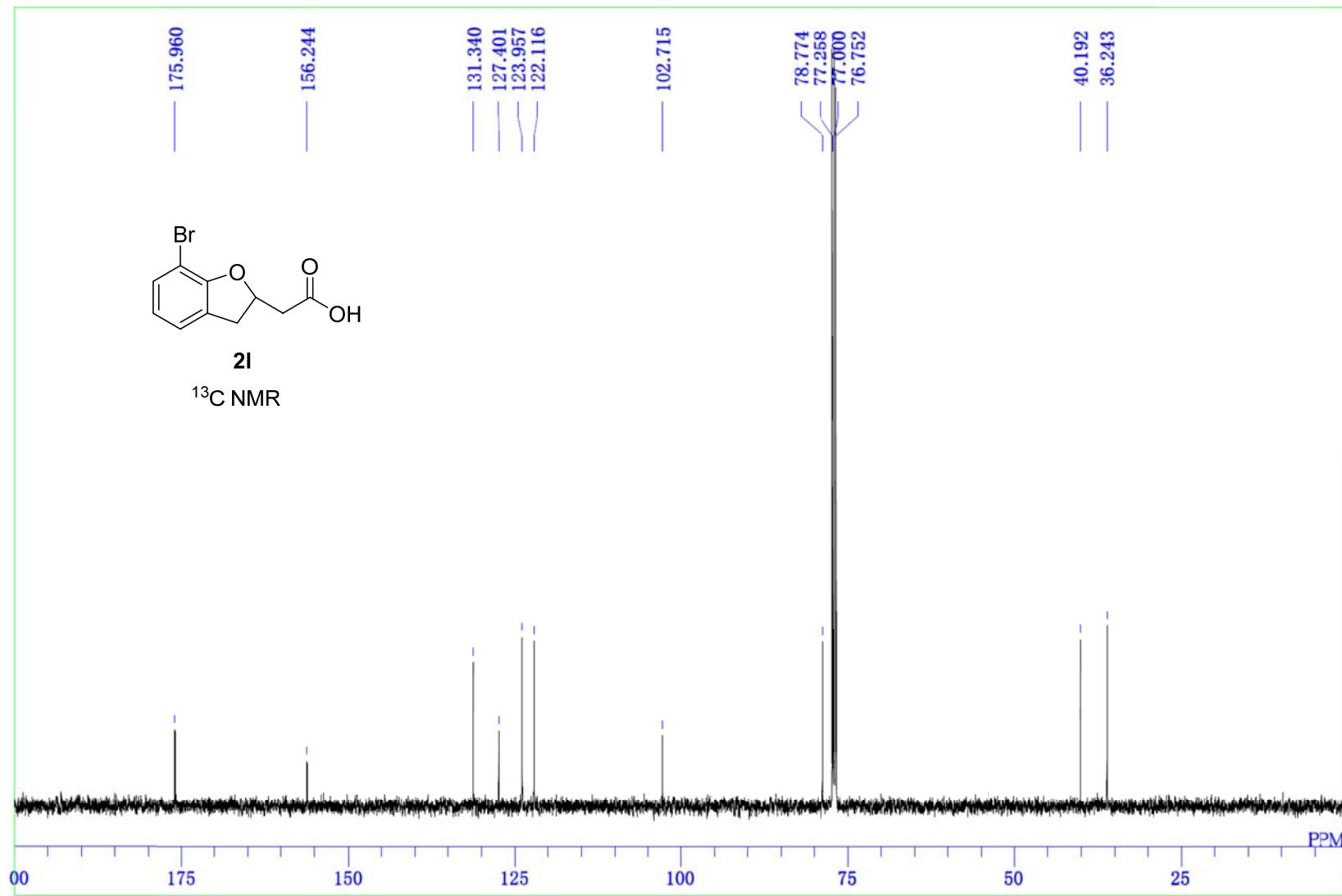


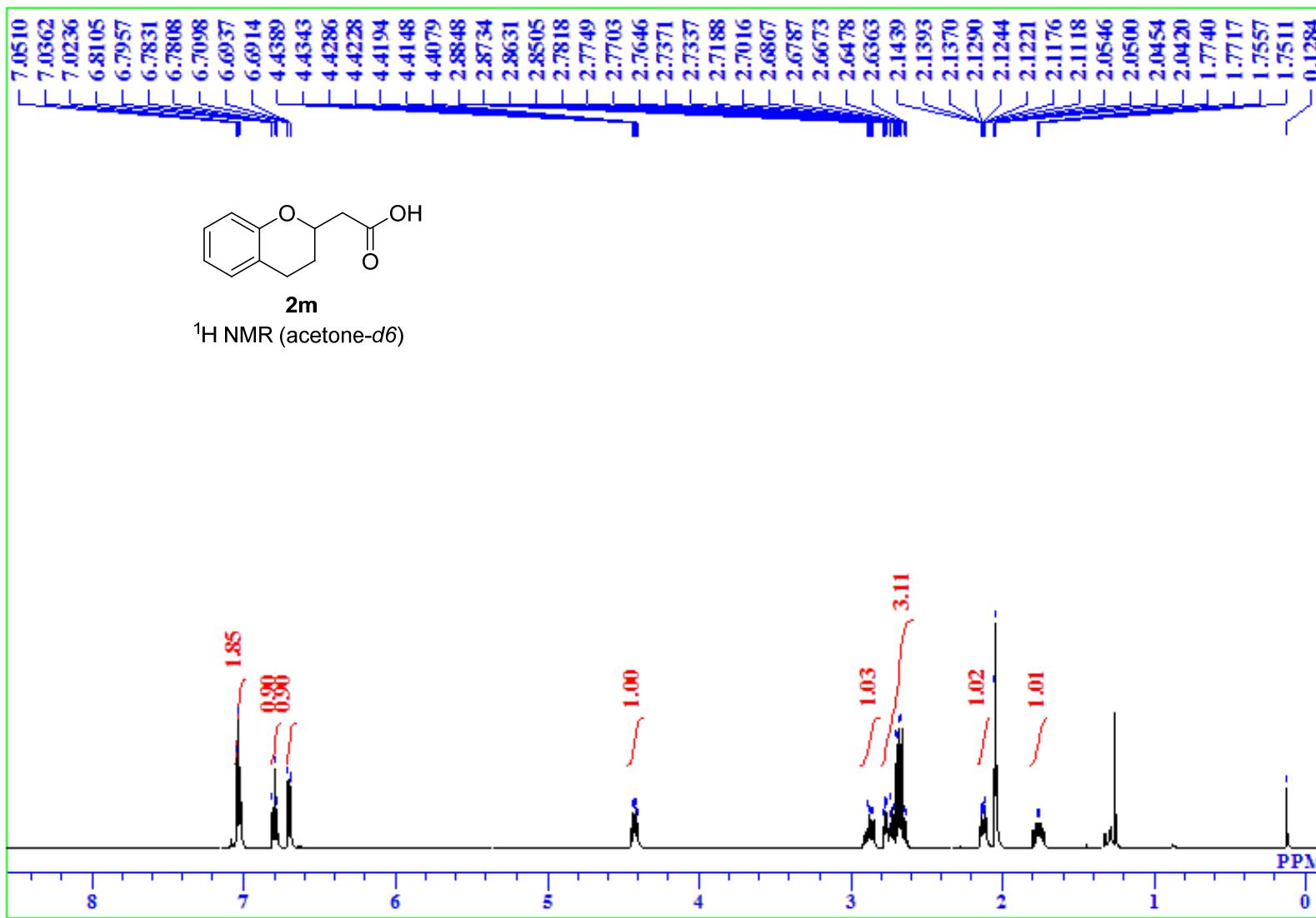
S139

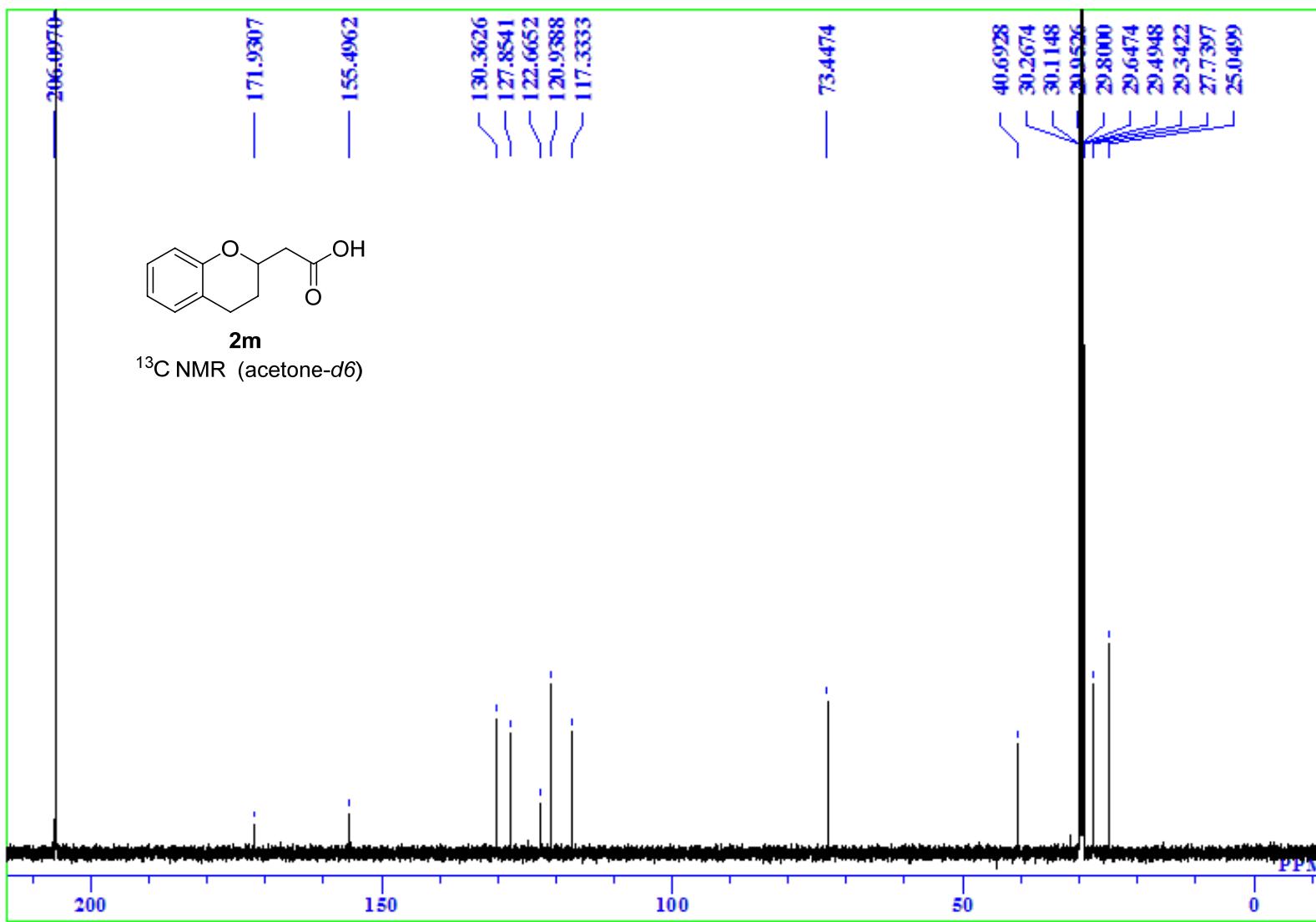


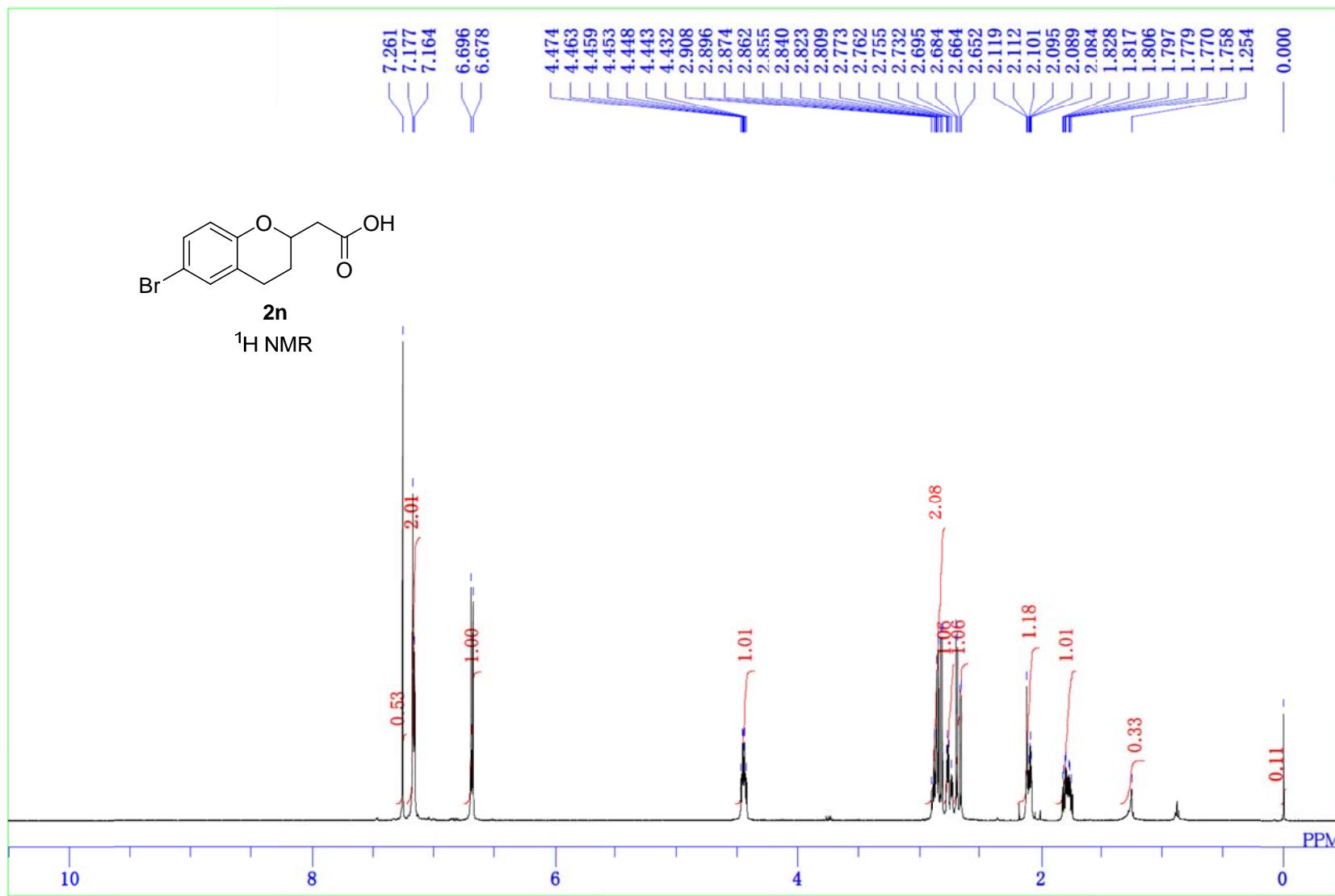
2l

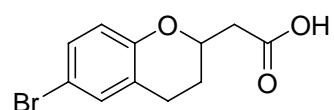
^{13}C NMR



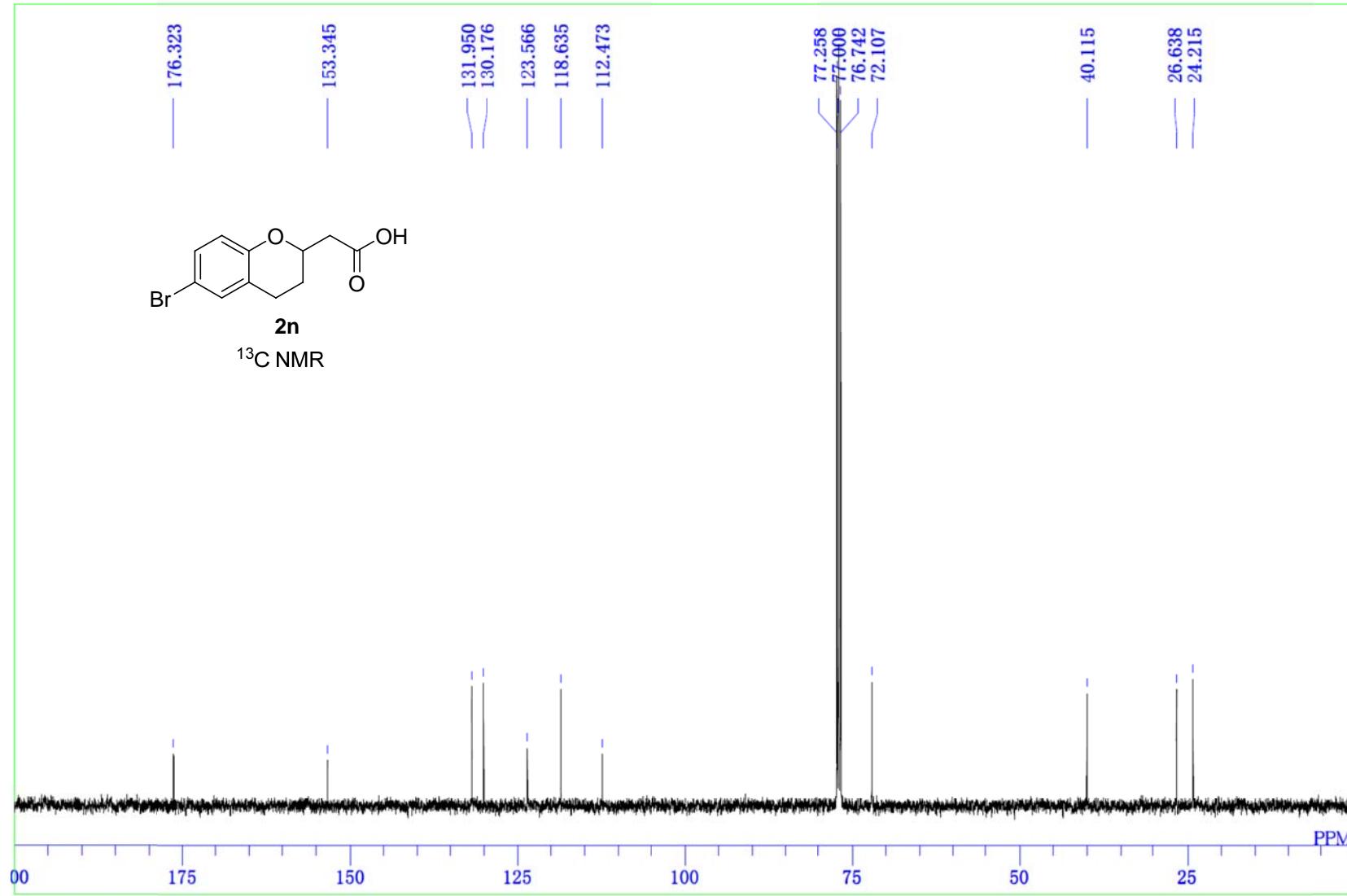


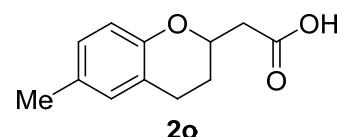




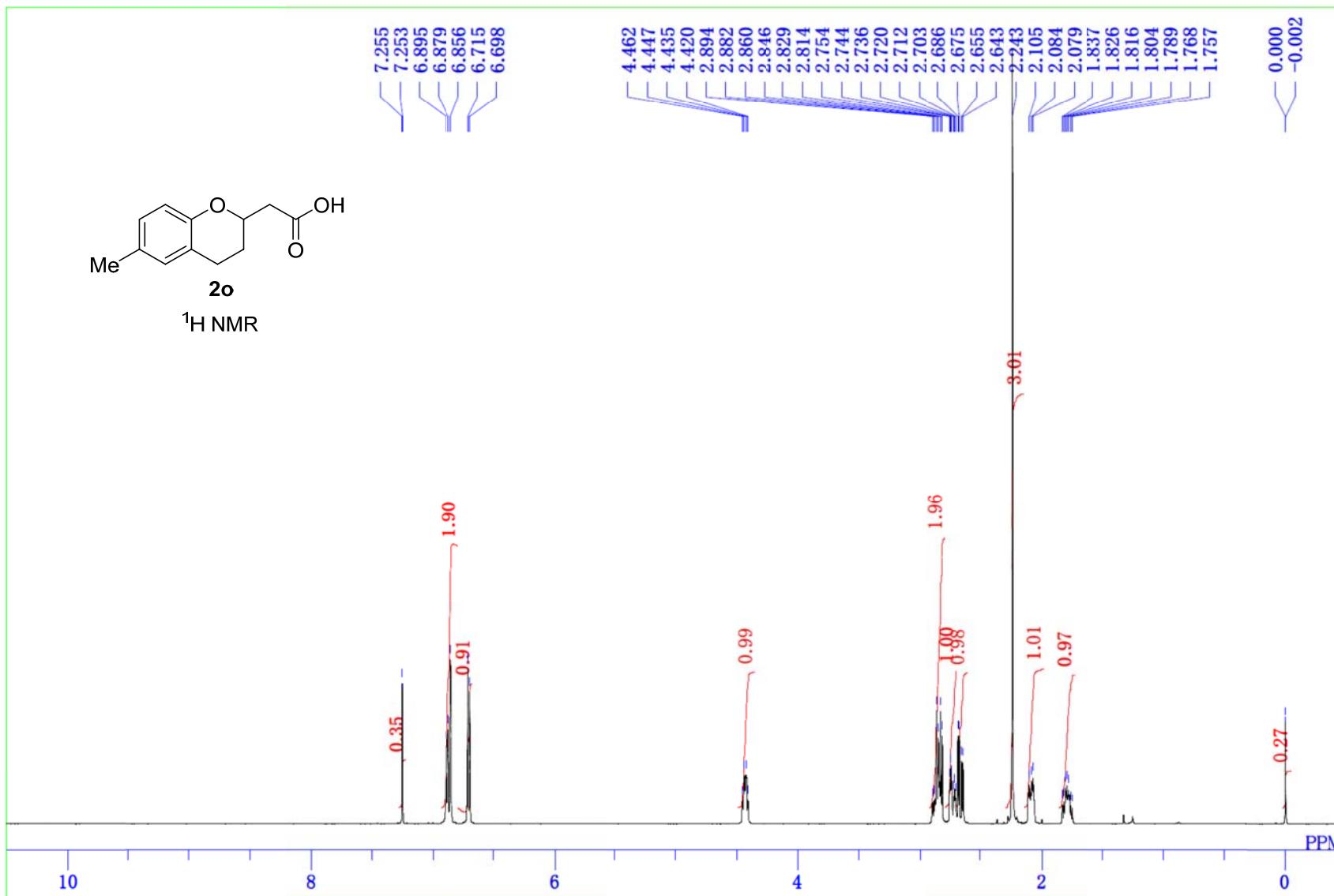


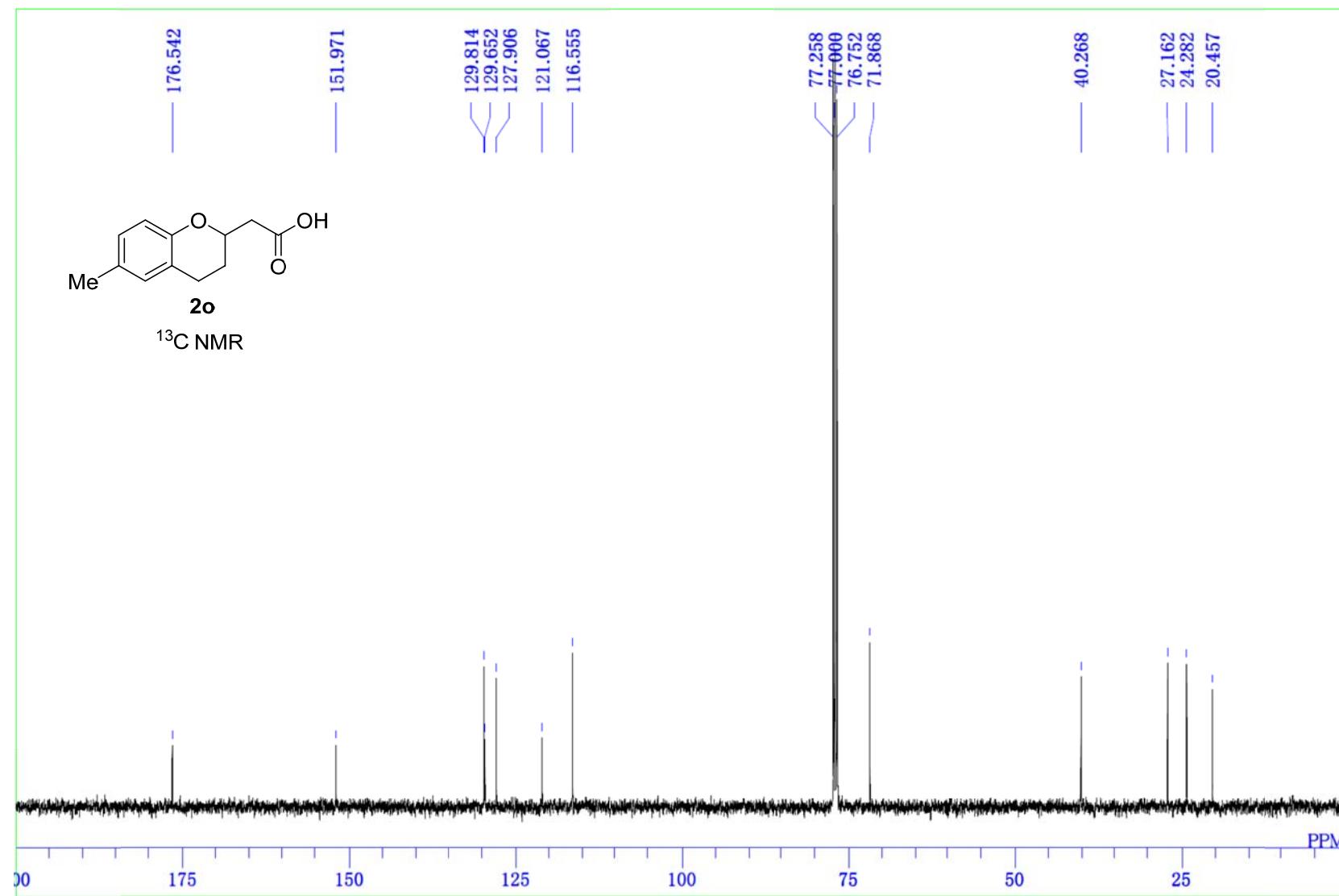
2n
¹³C NMR

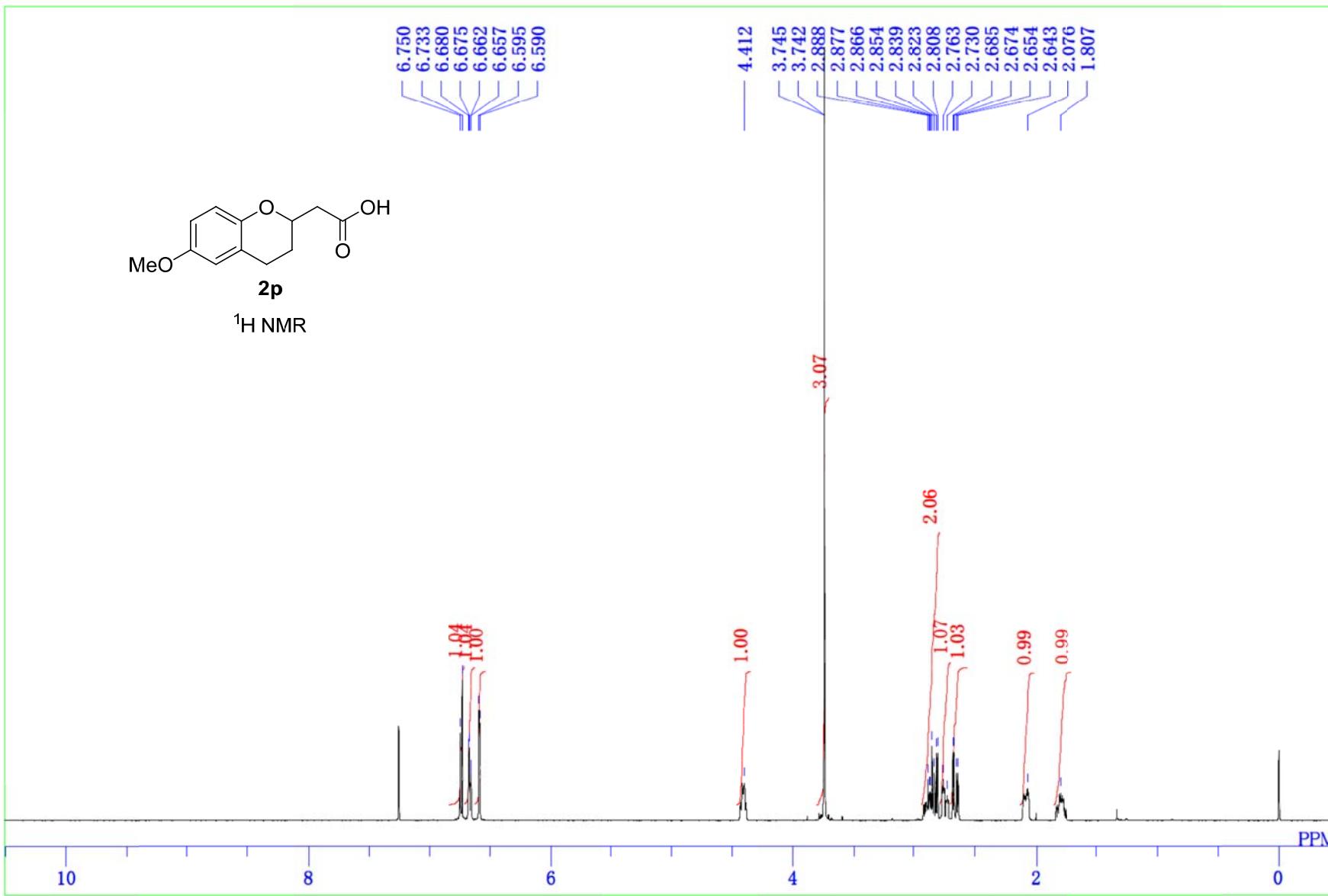
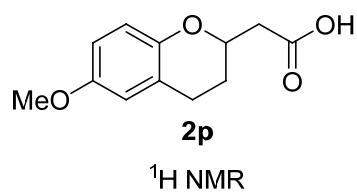


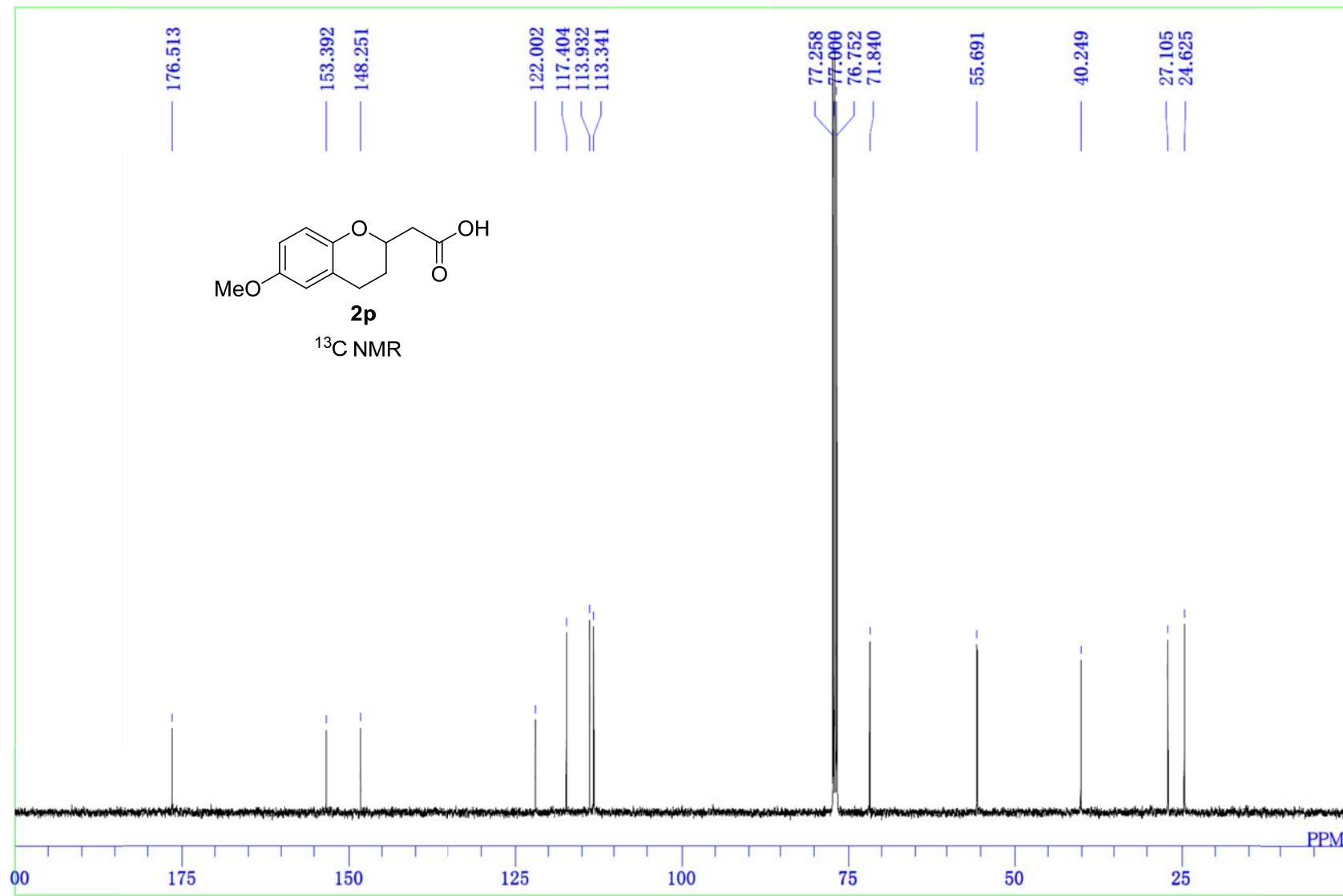


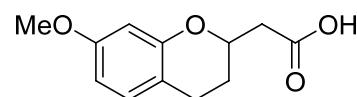
^1H NMR





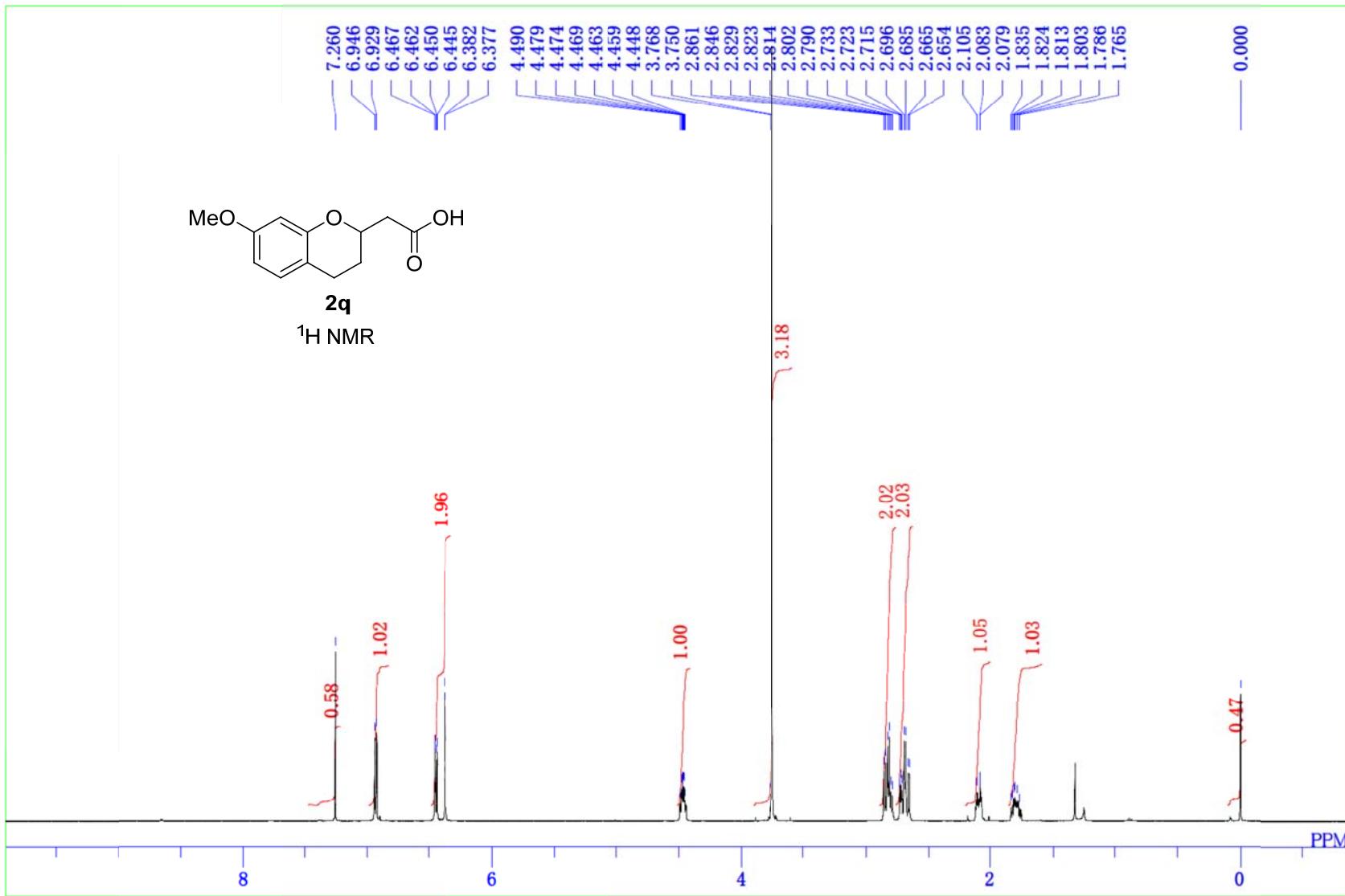


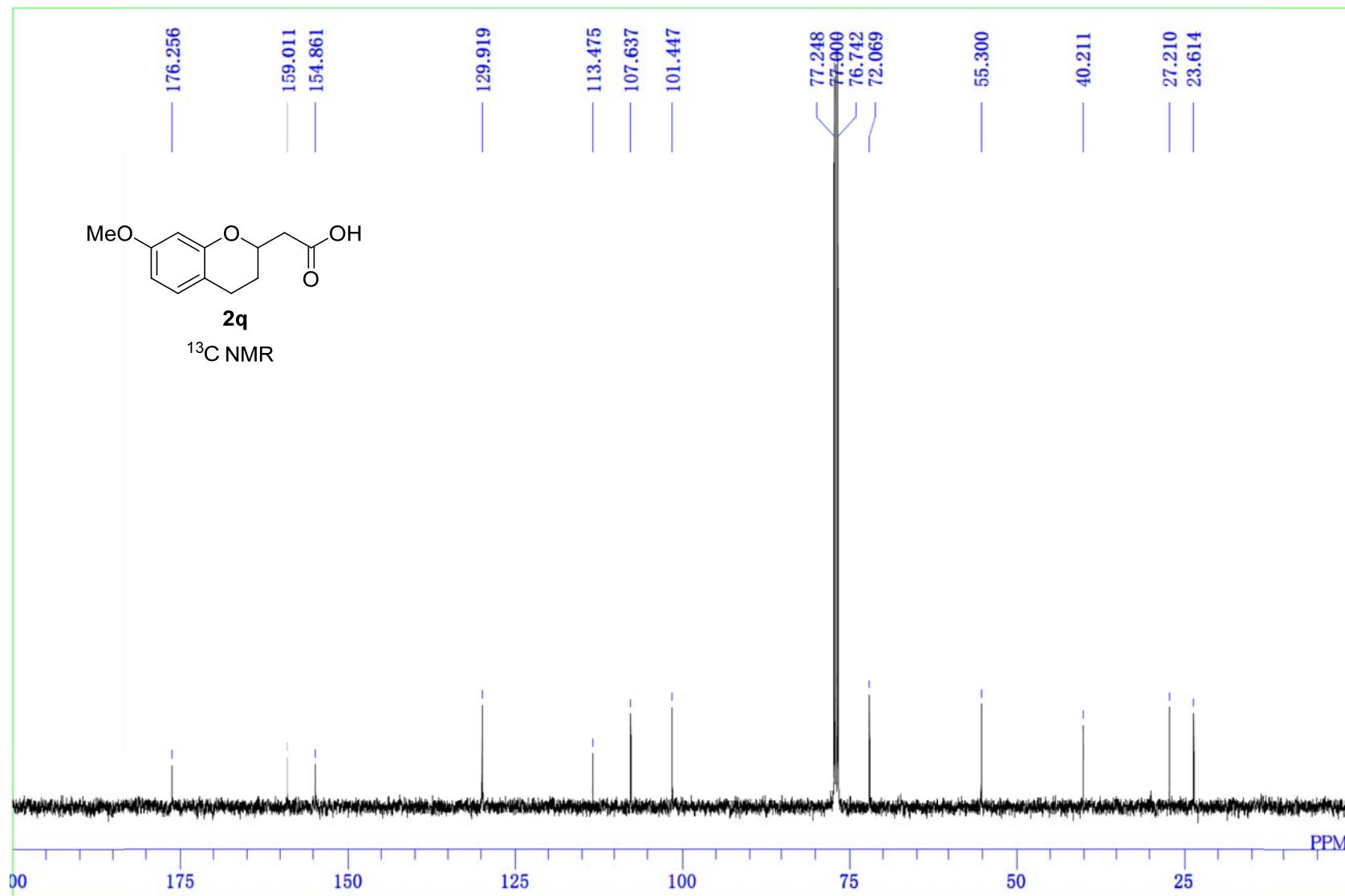




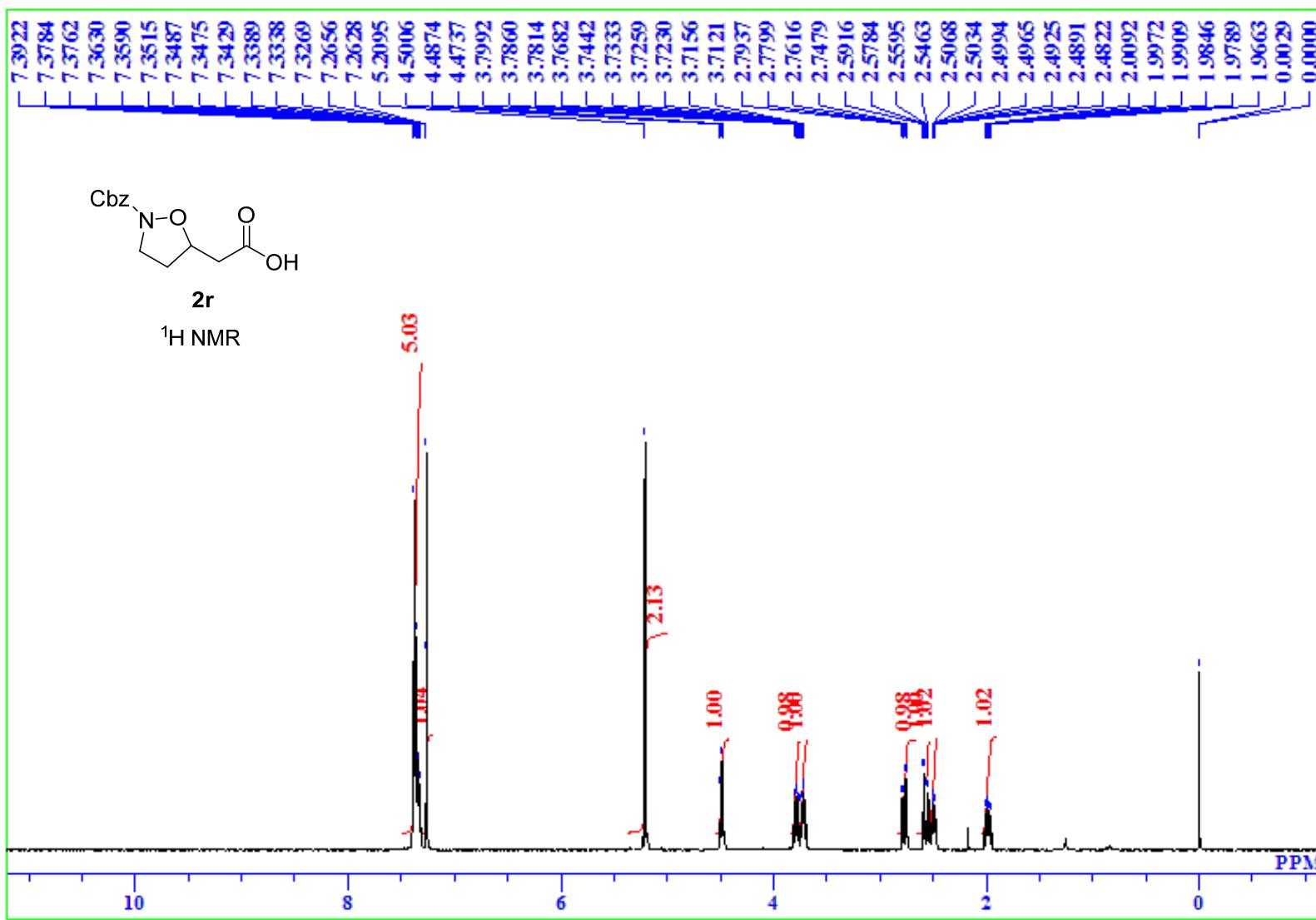
2q

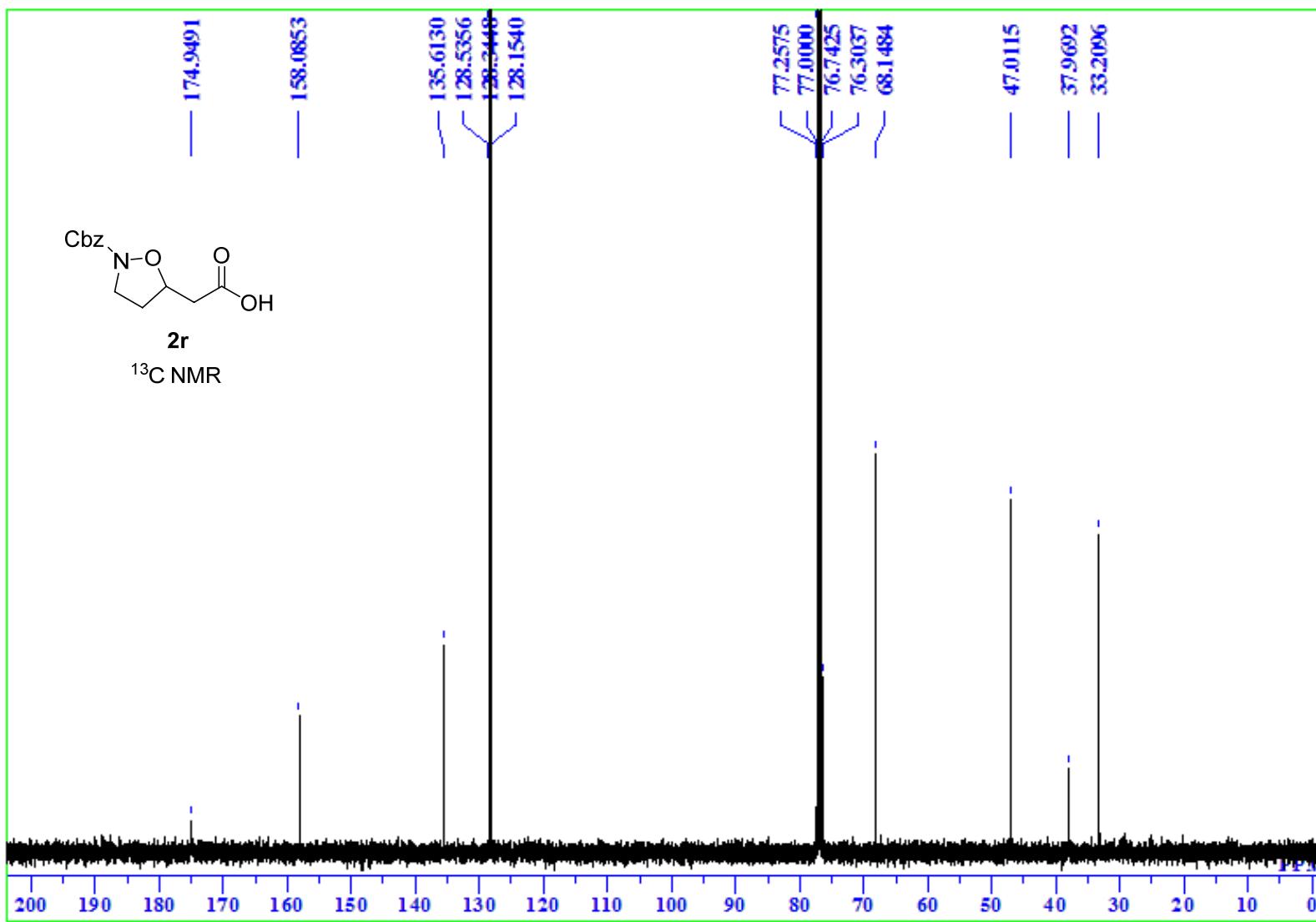
^1H NMR

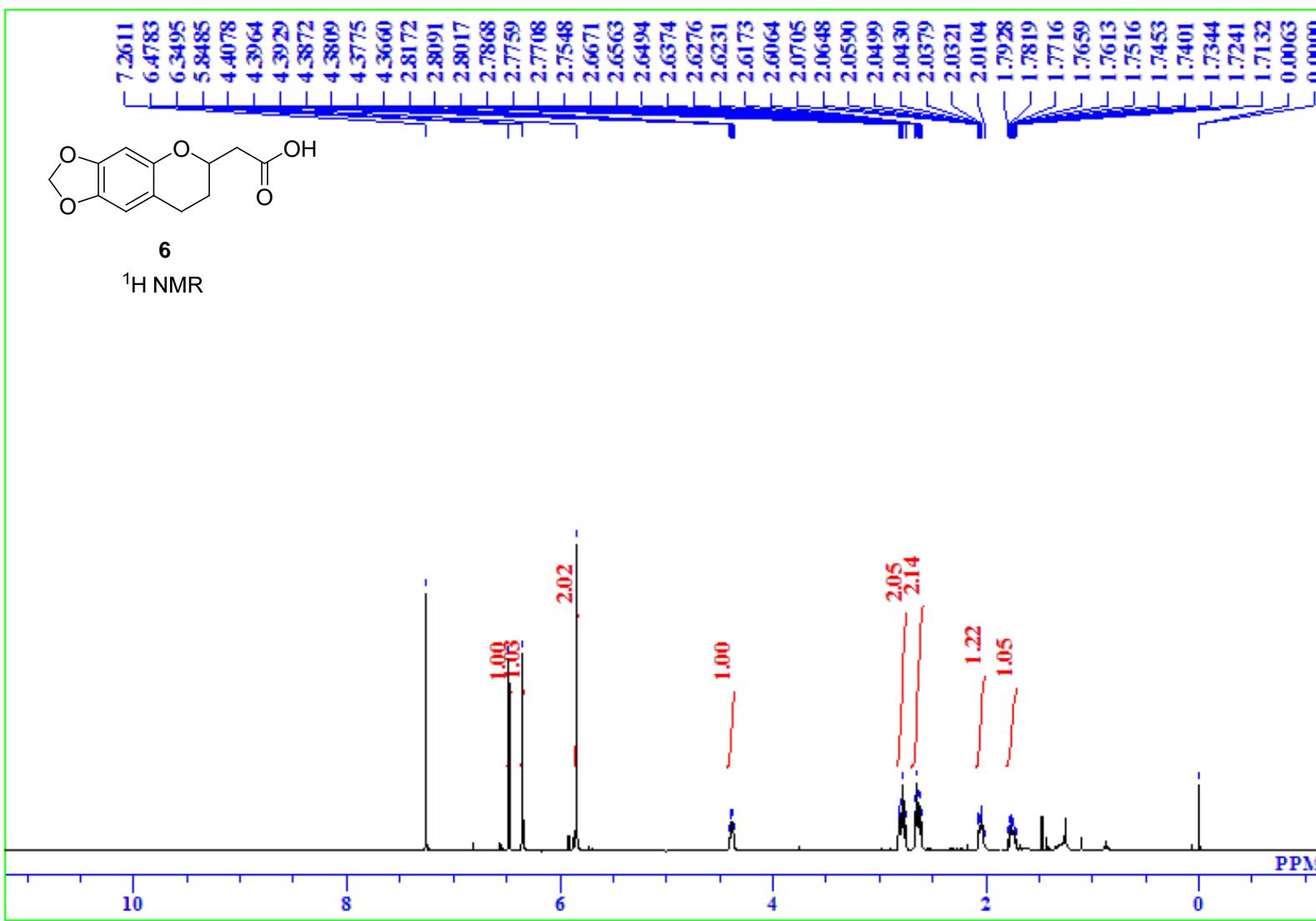


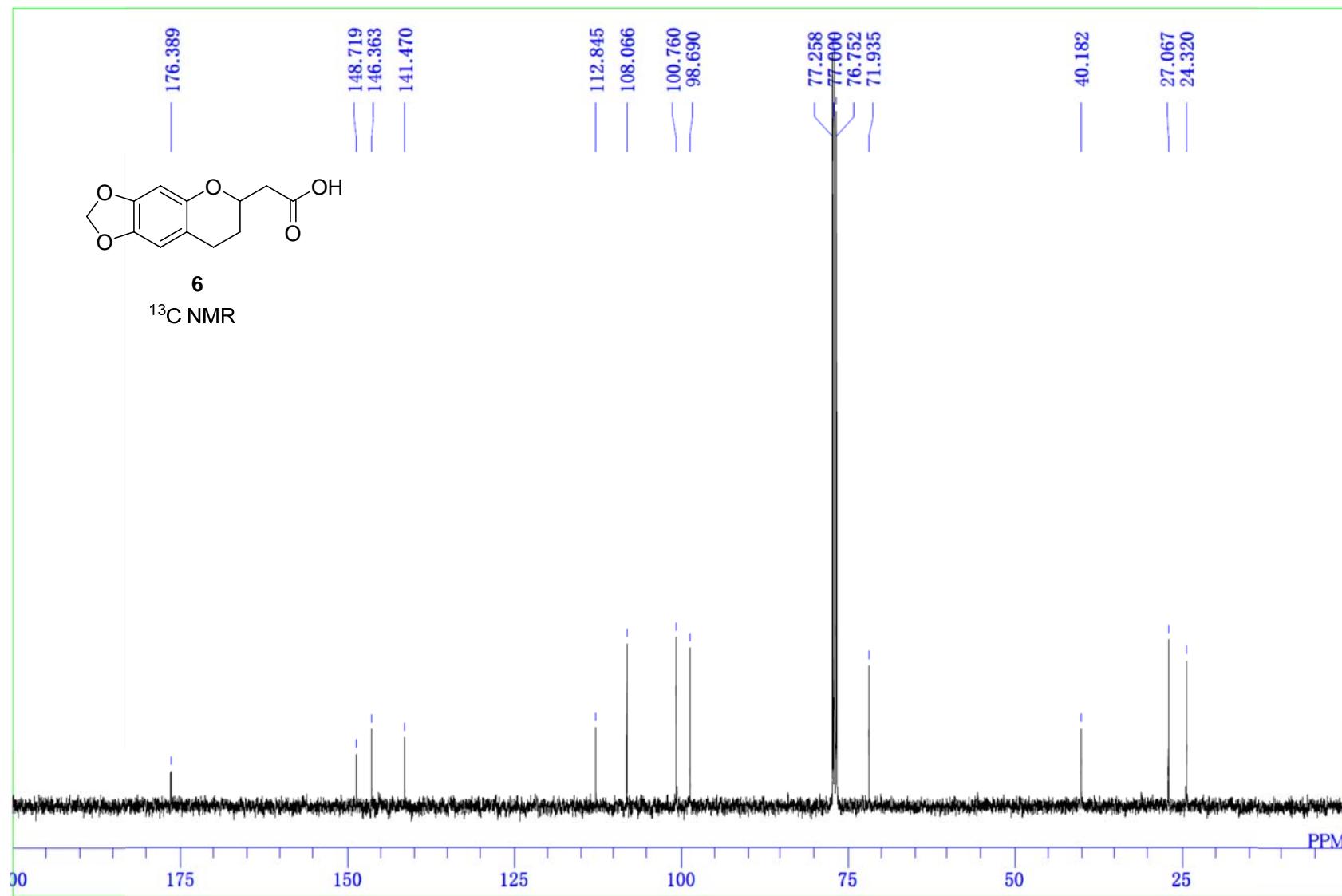


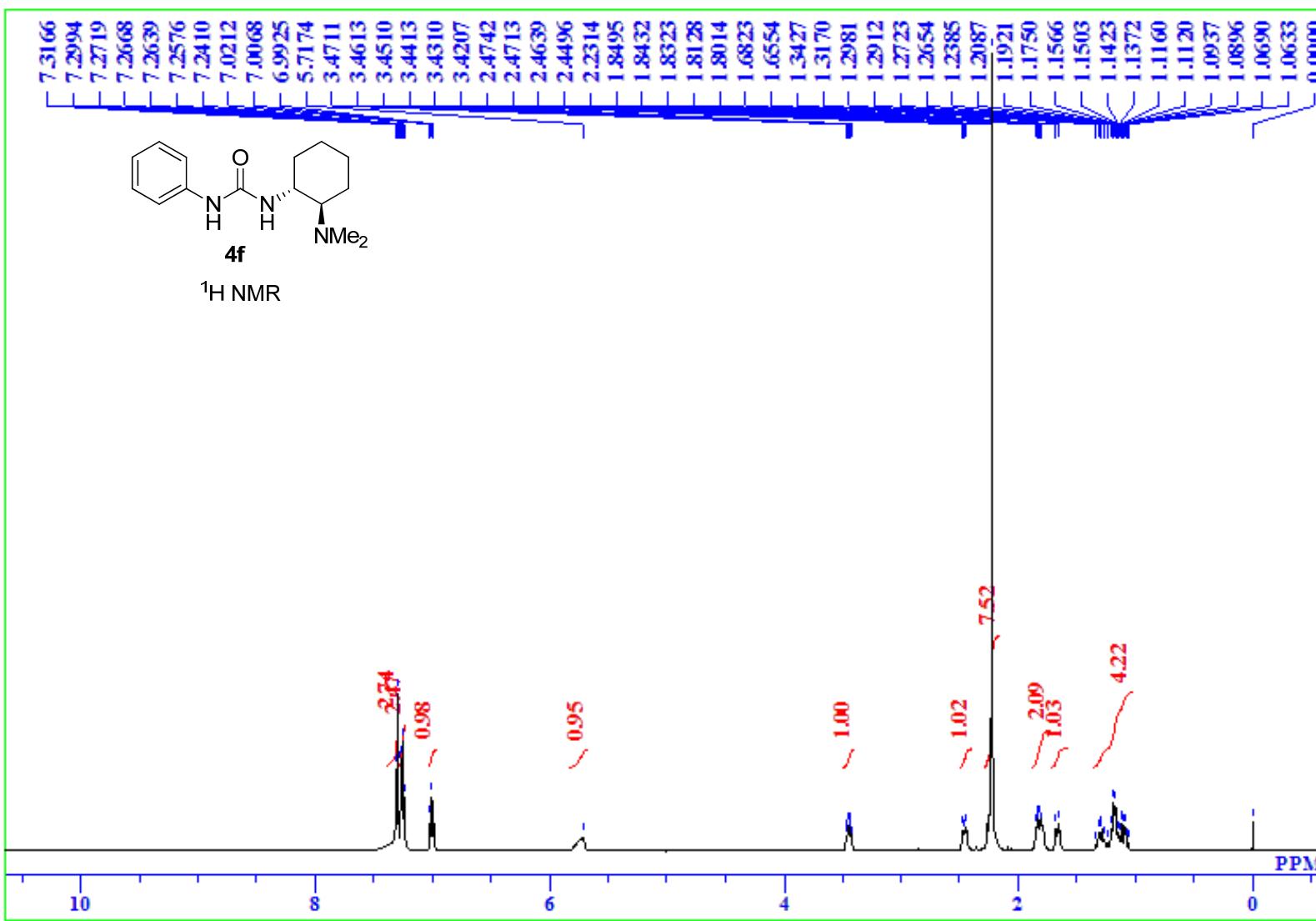
S150

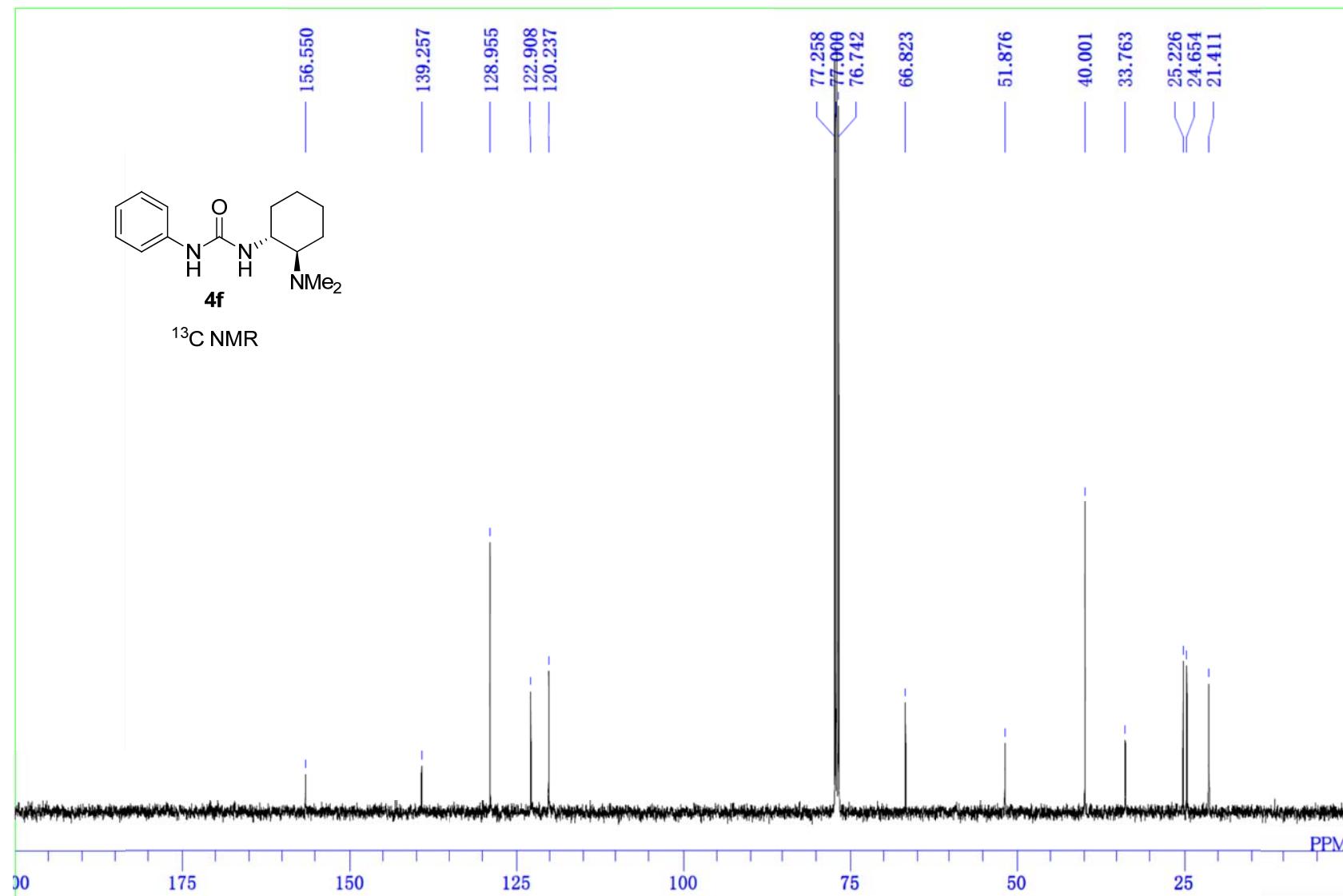


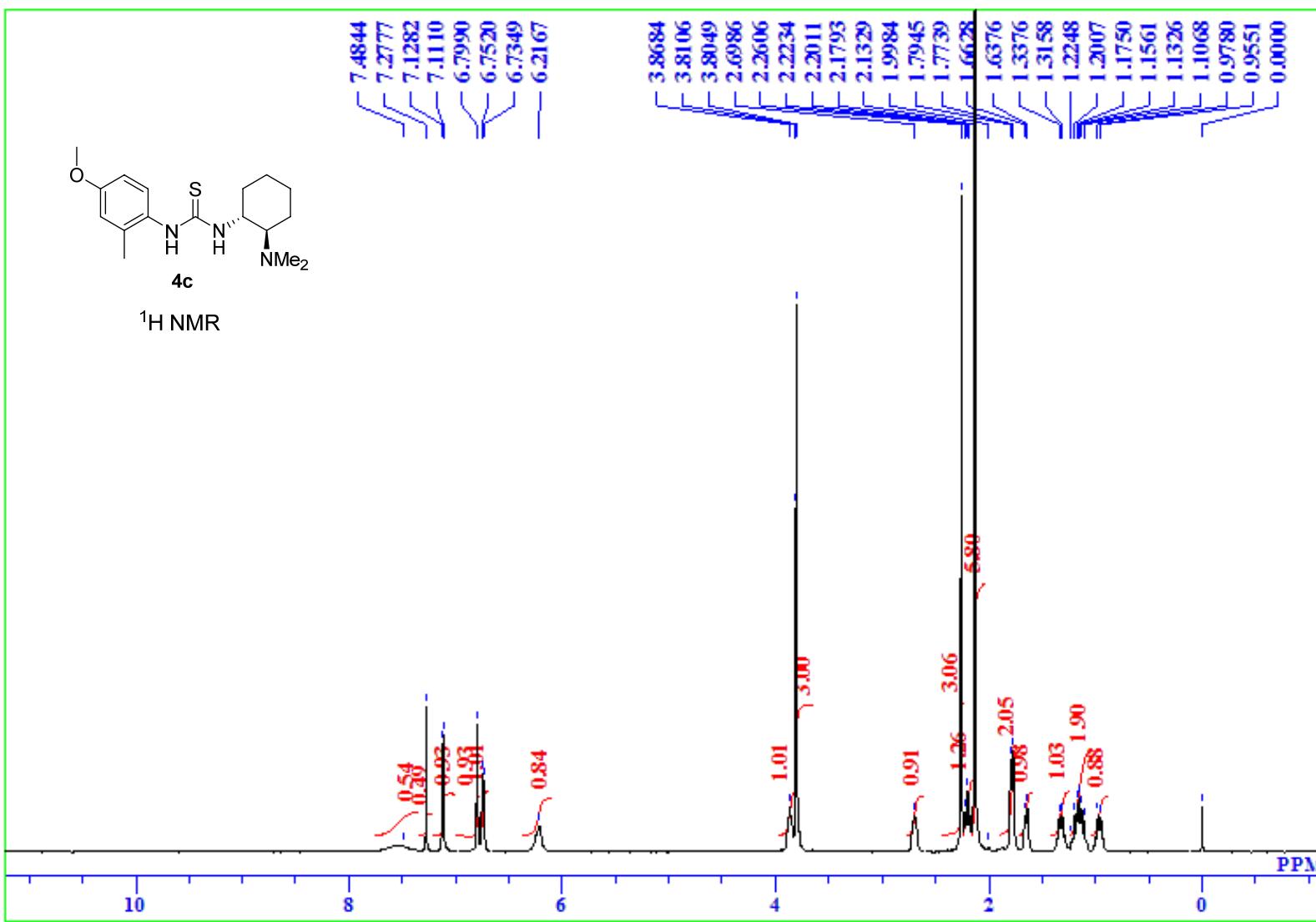


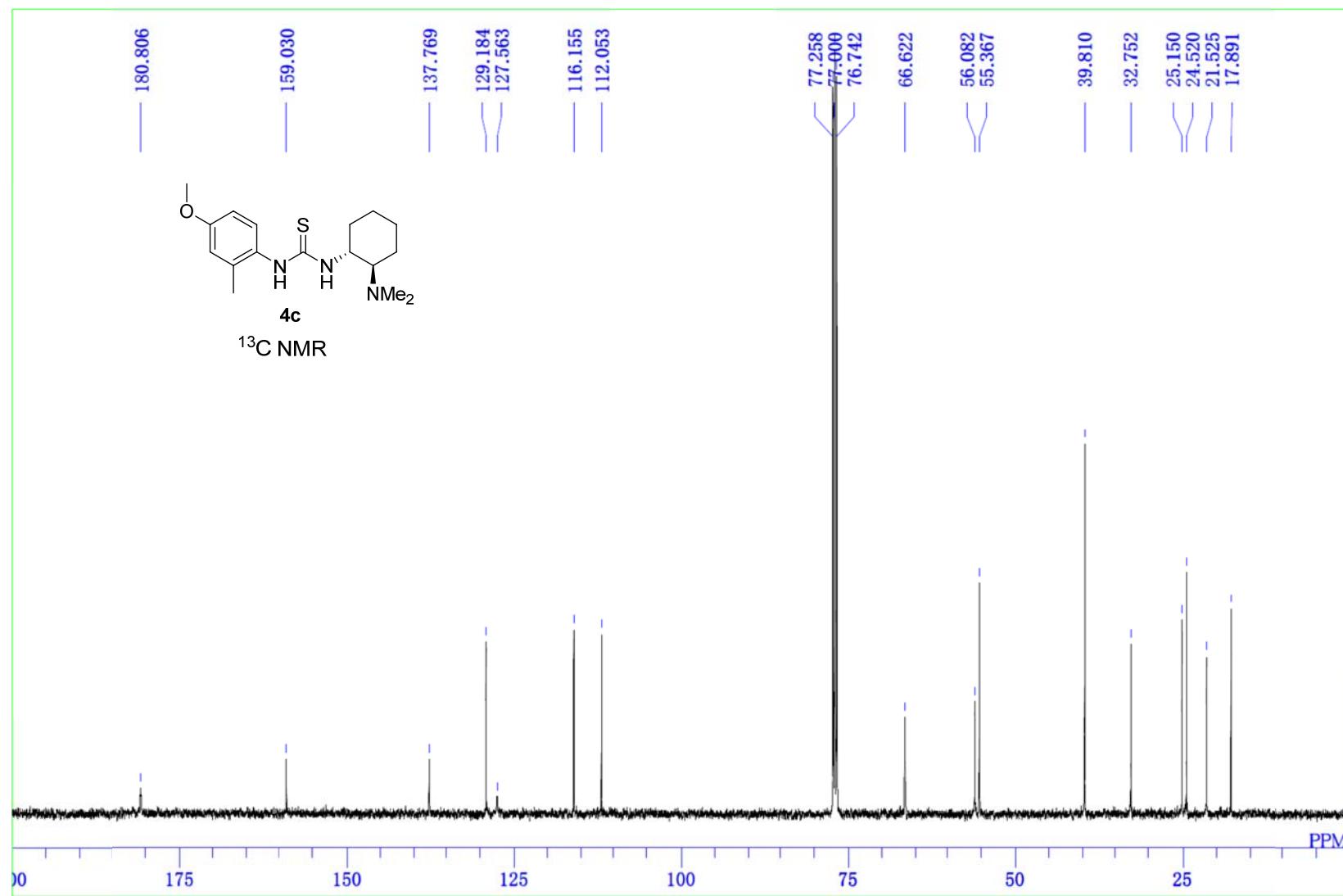


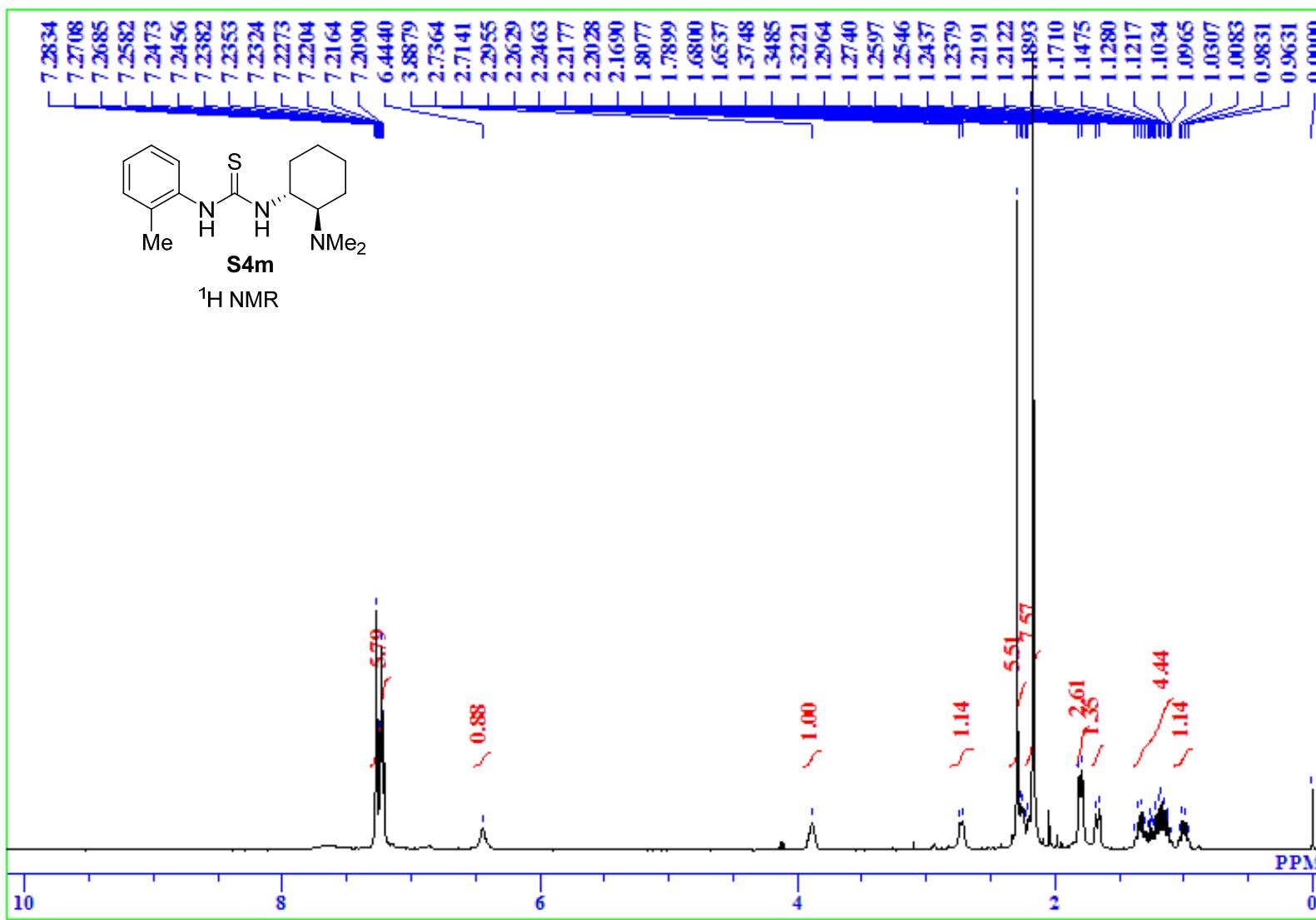


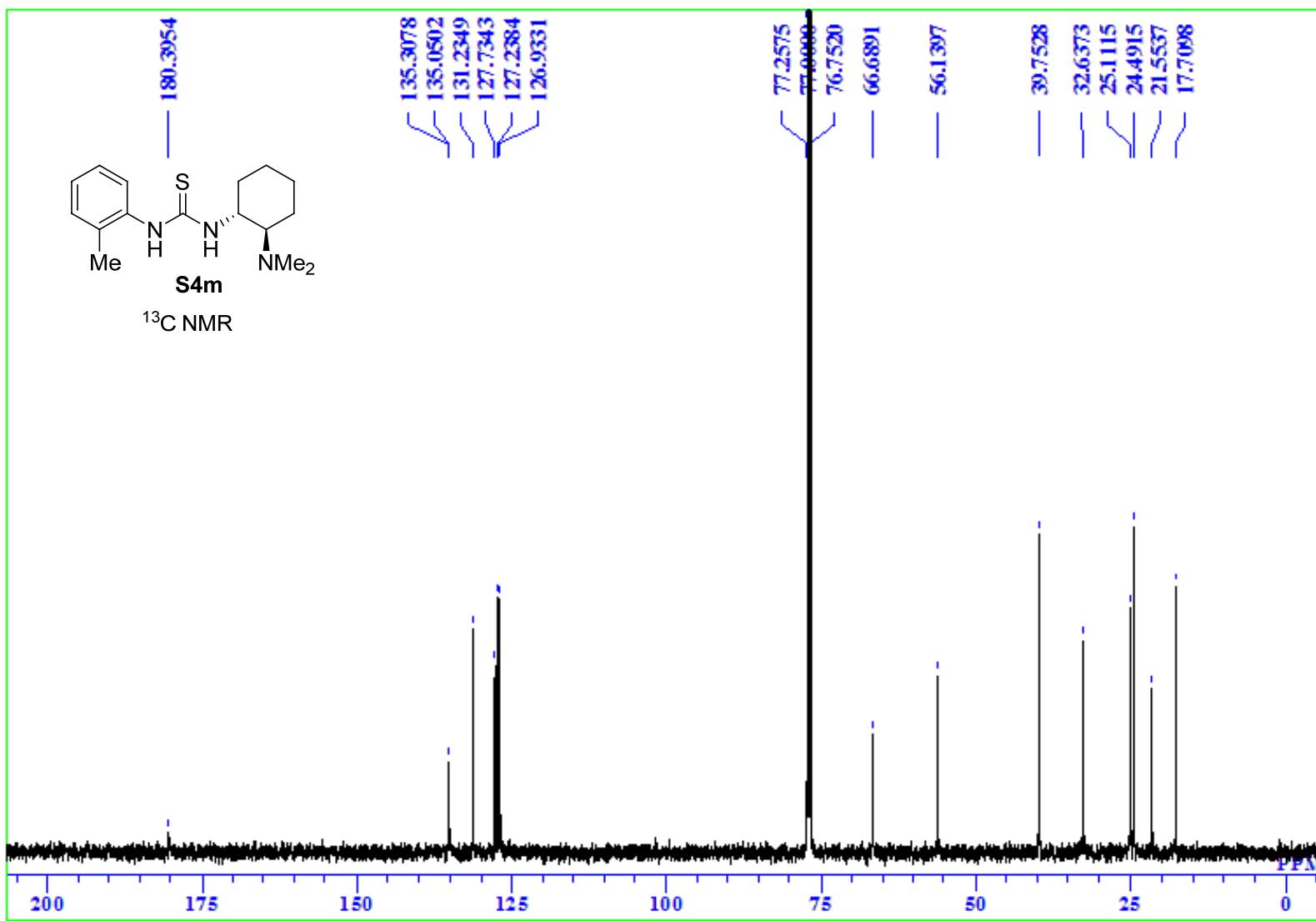




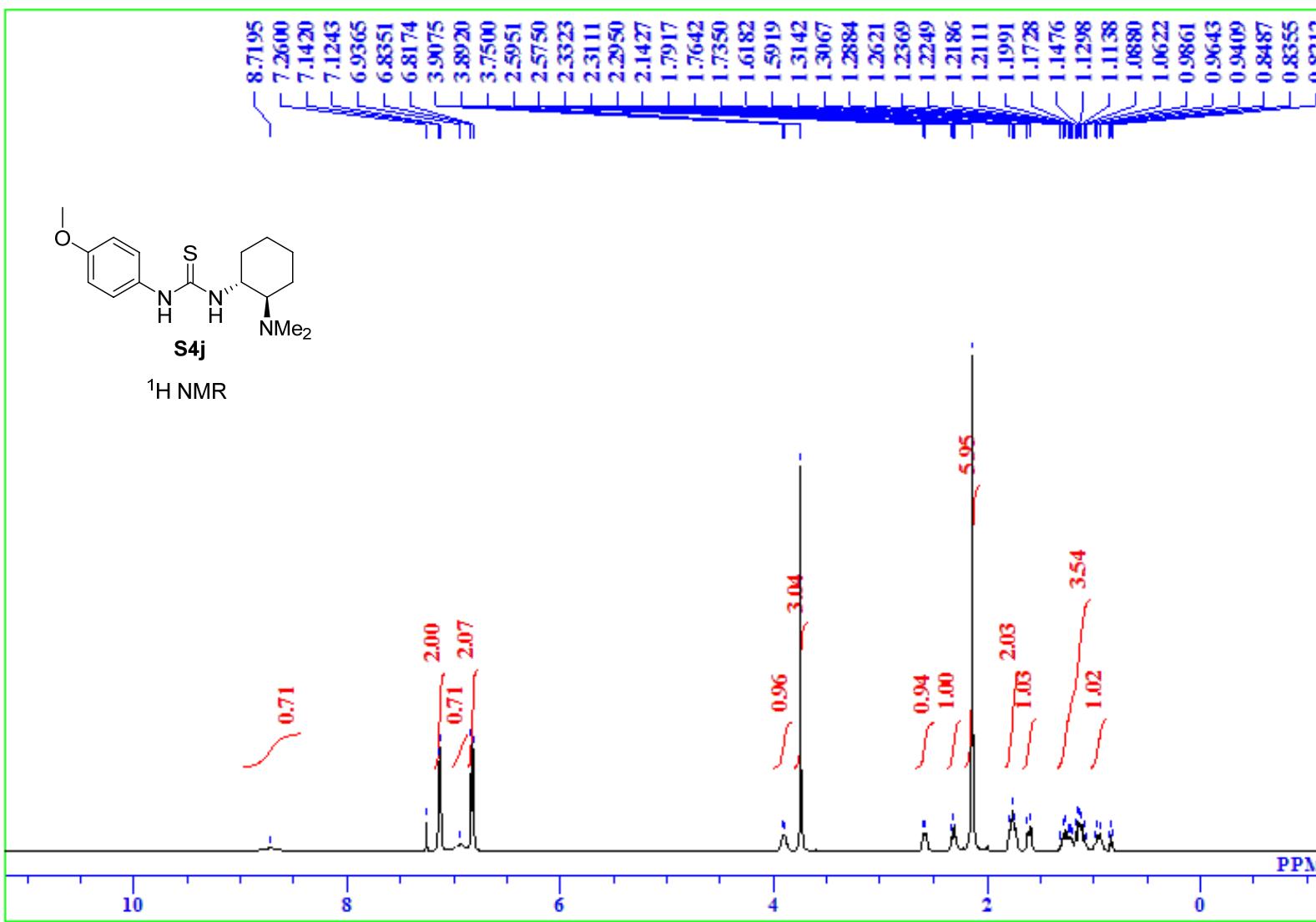


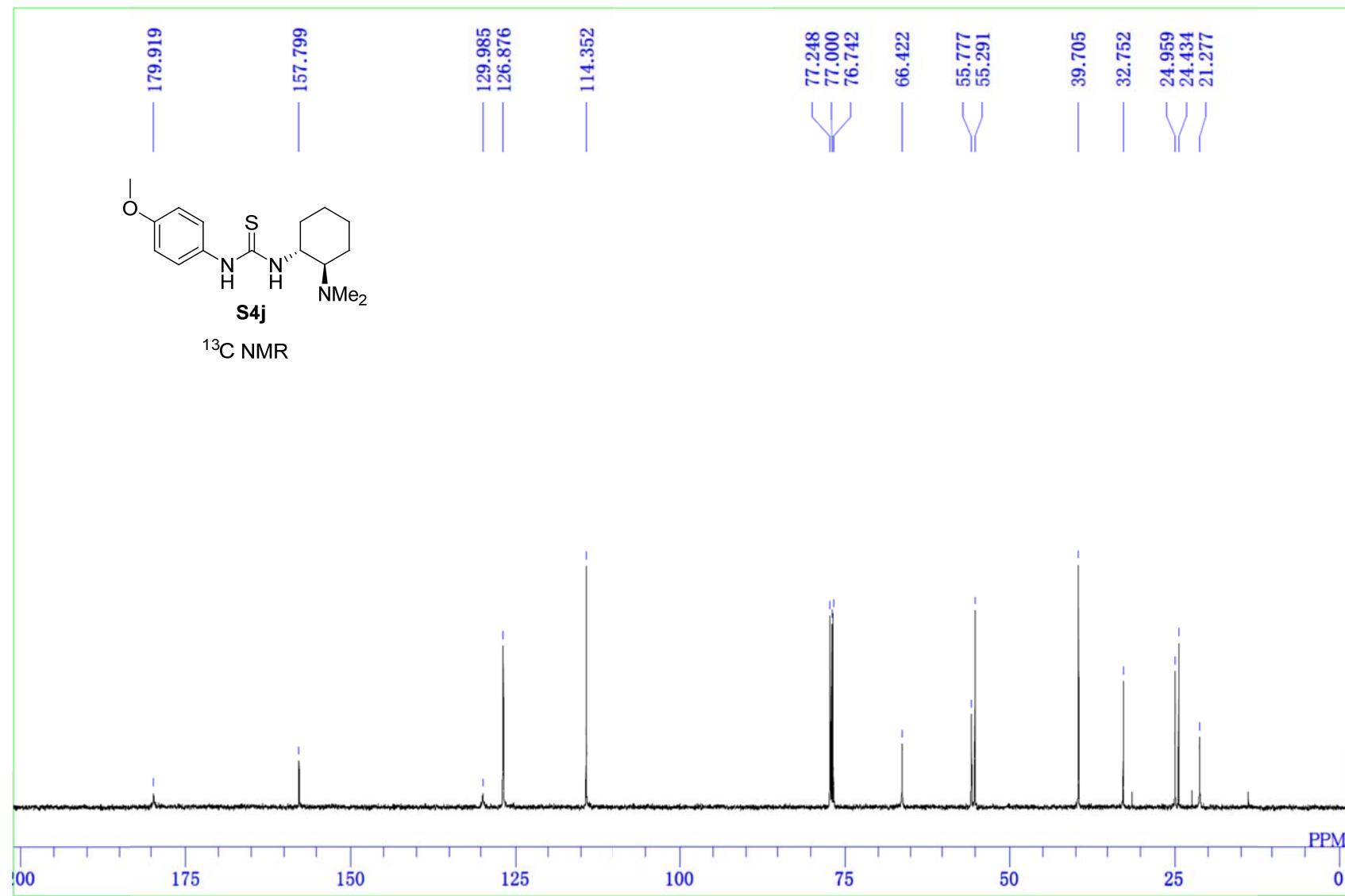


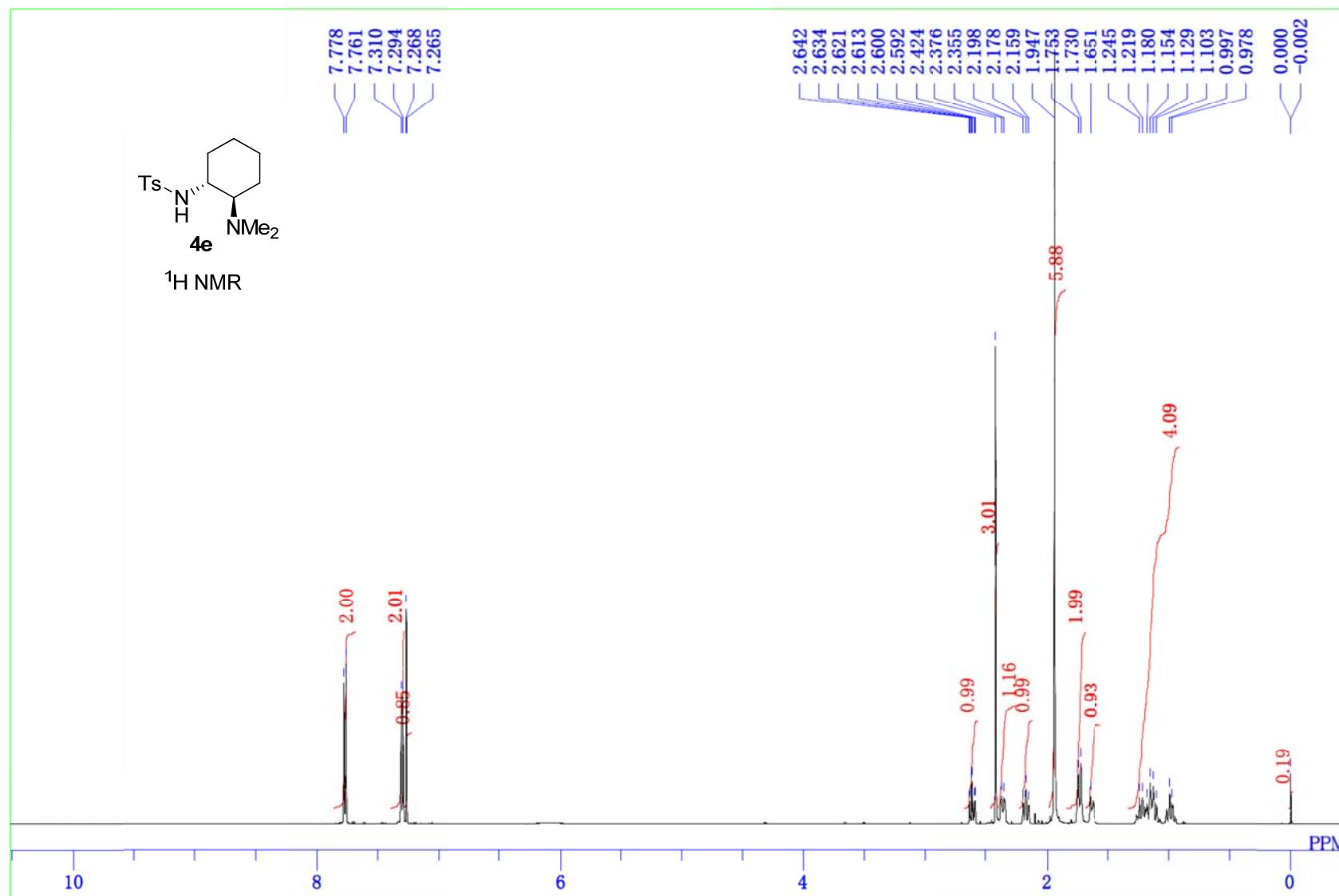


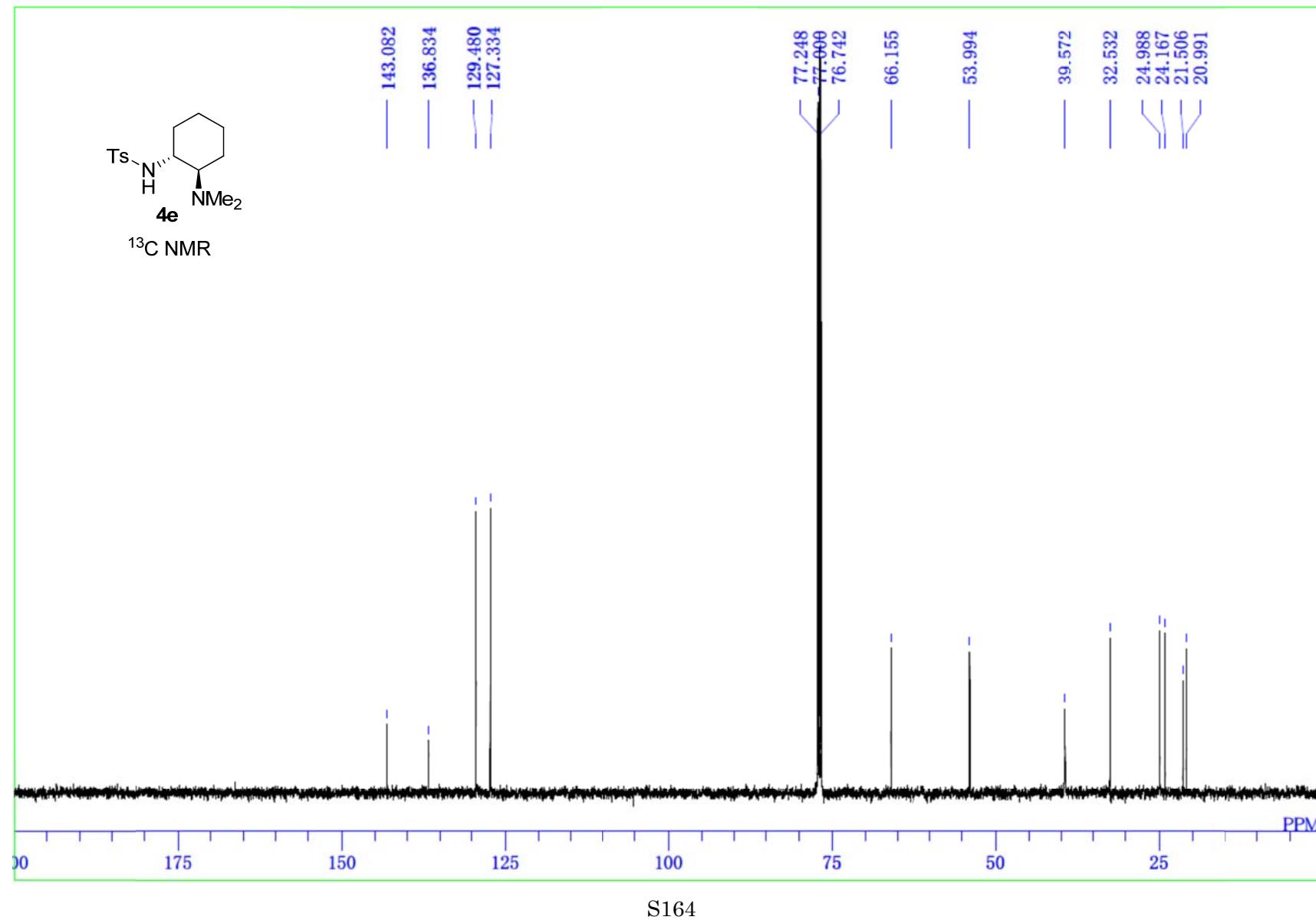


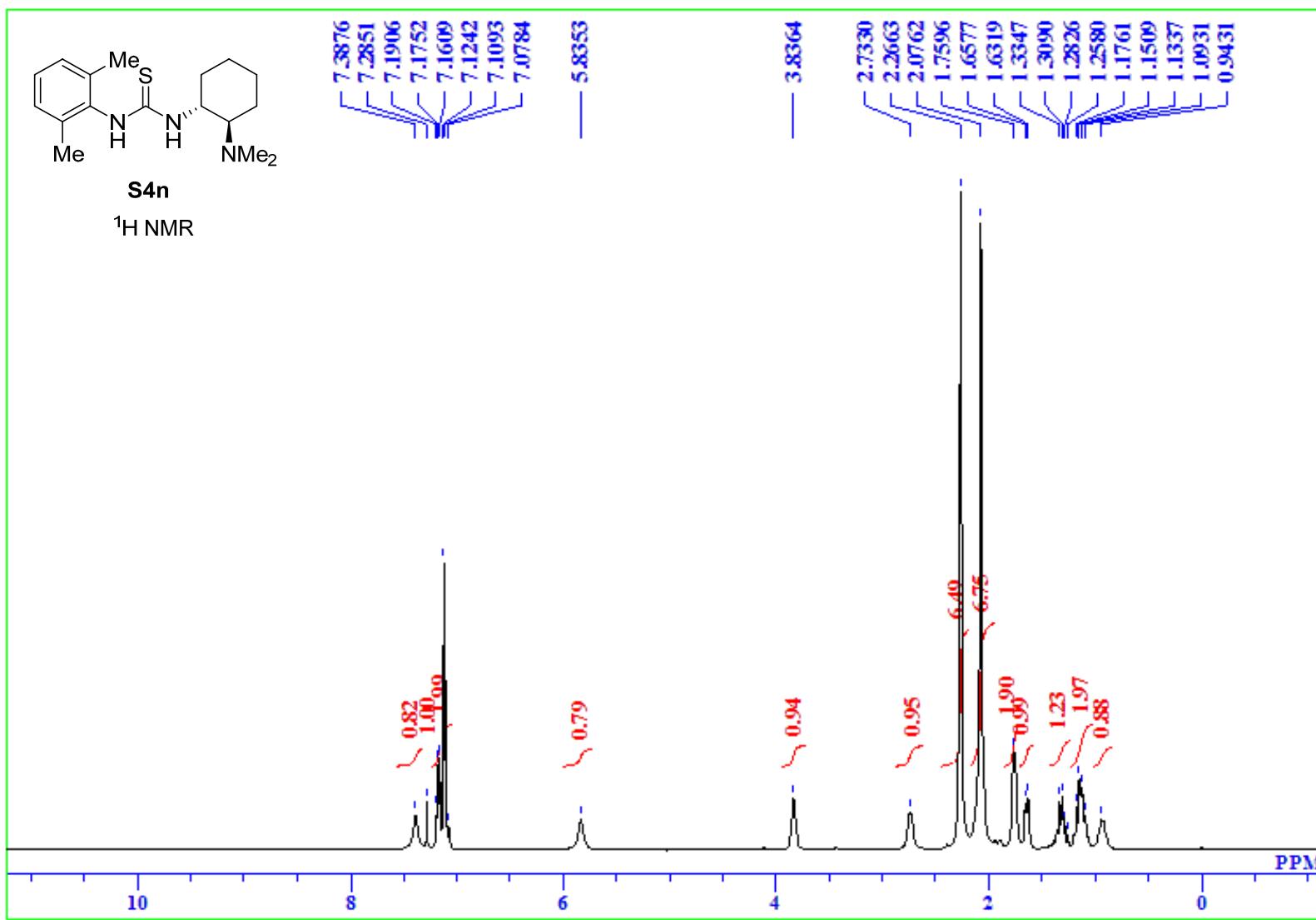
S160

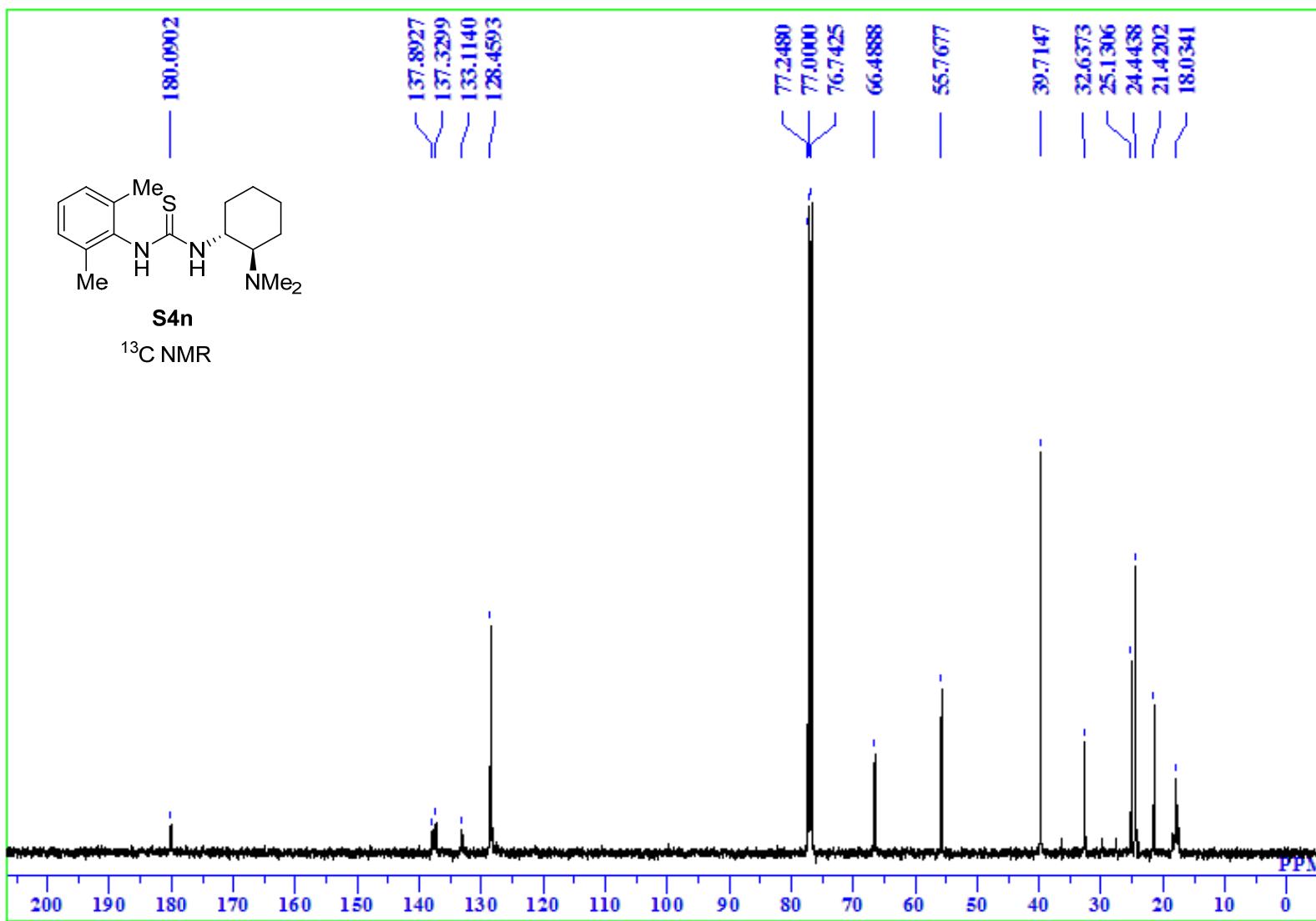


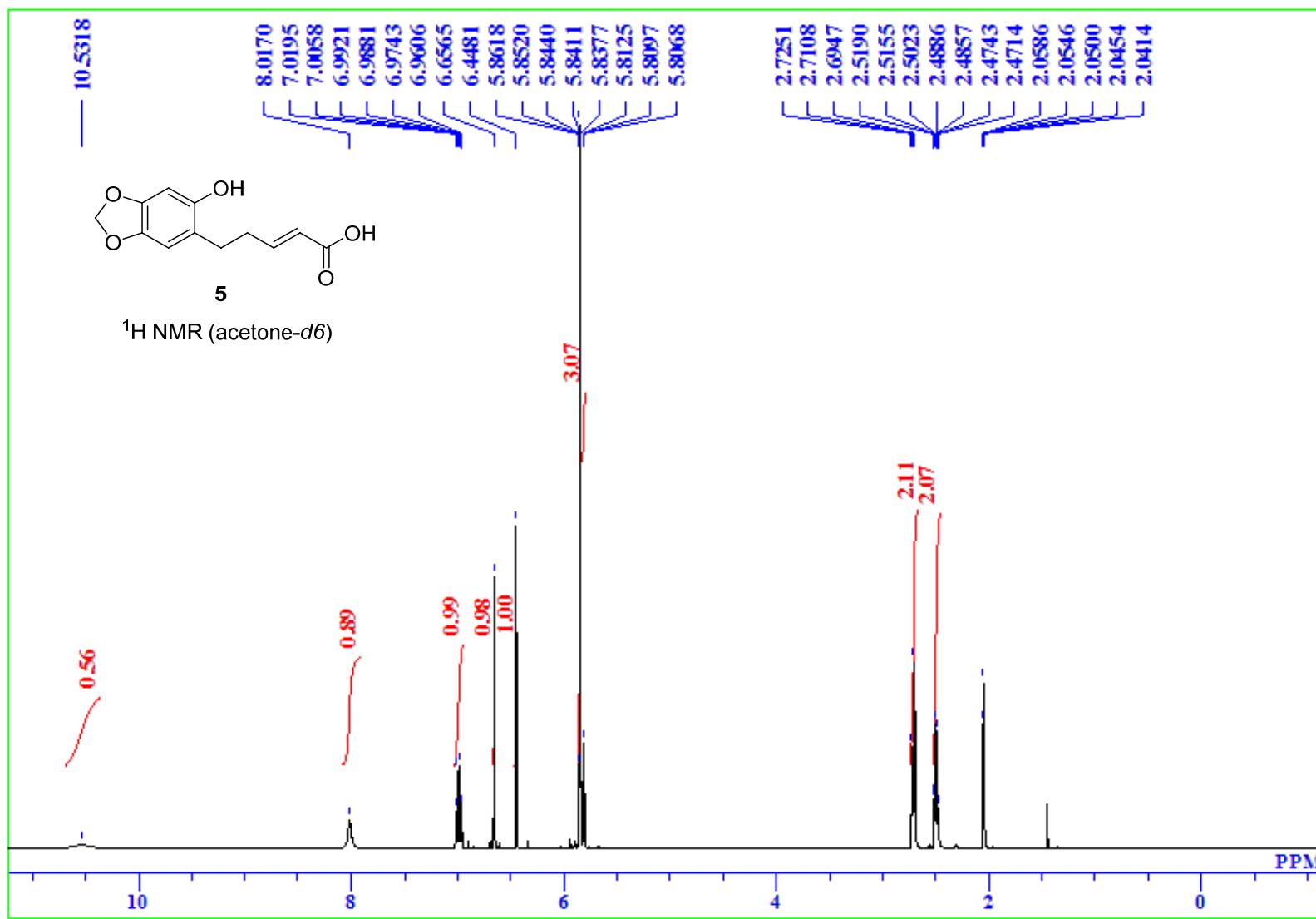


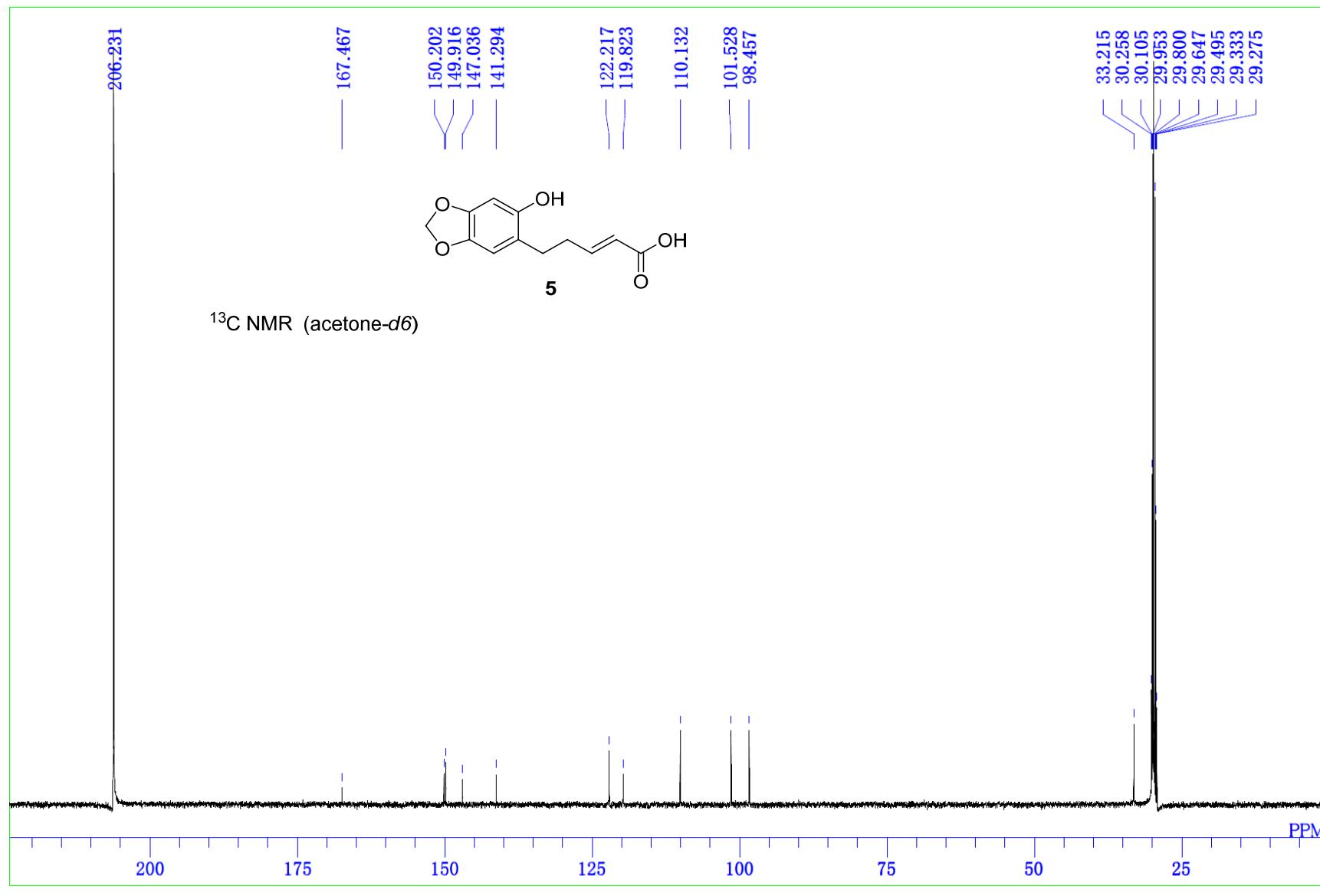


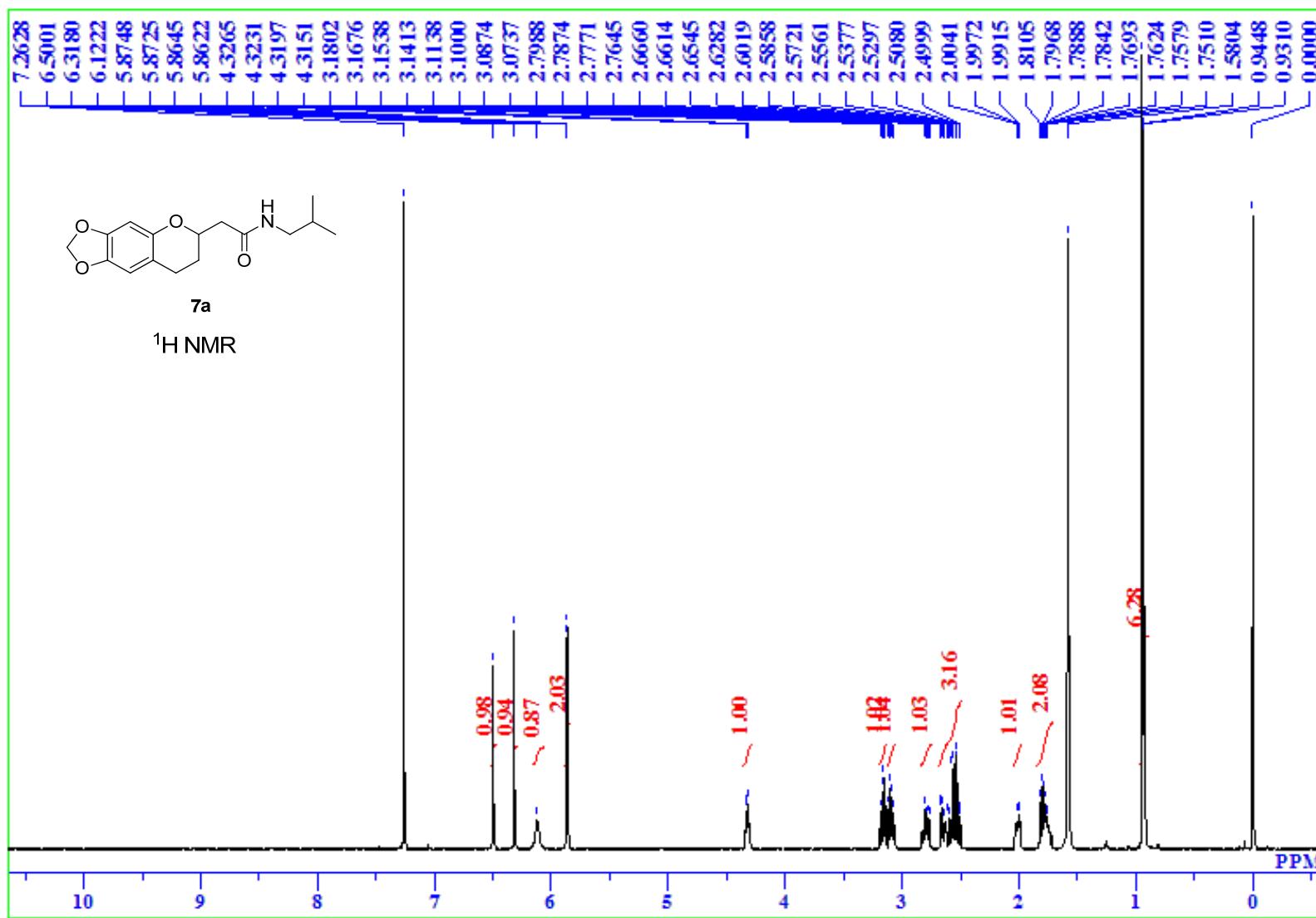


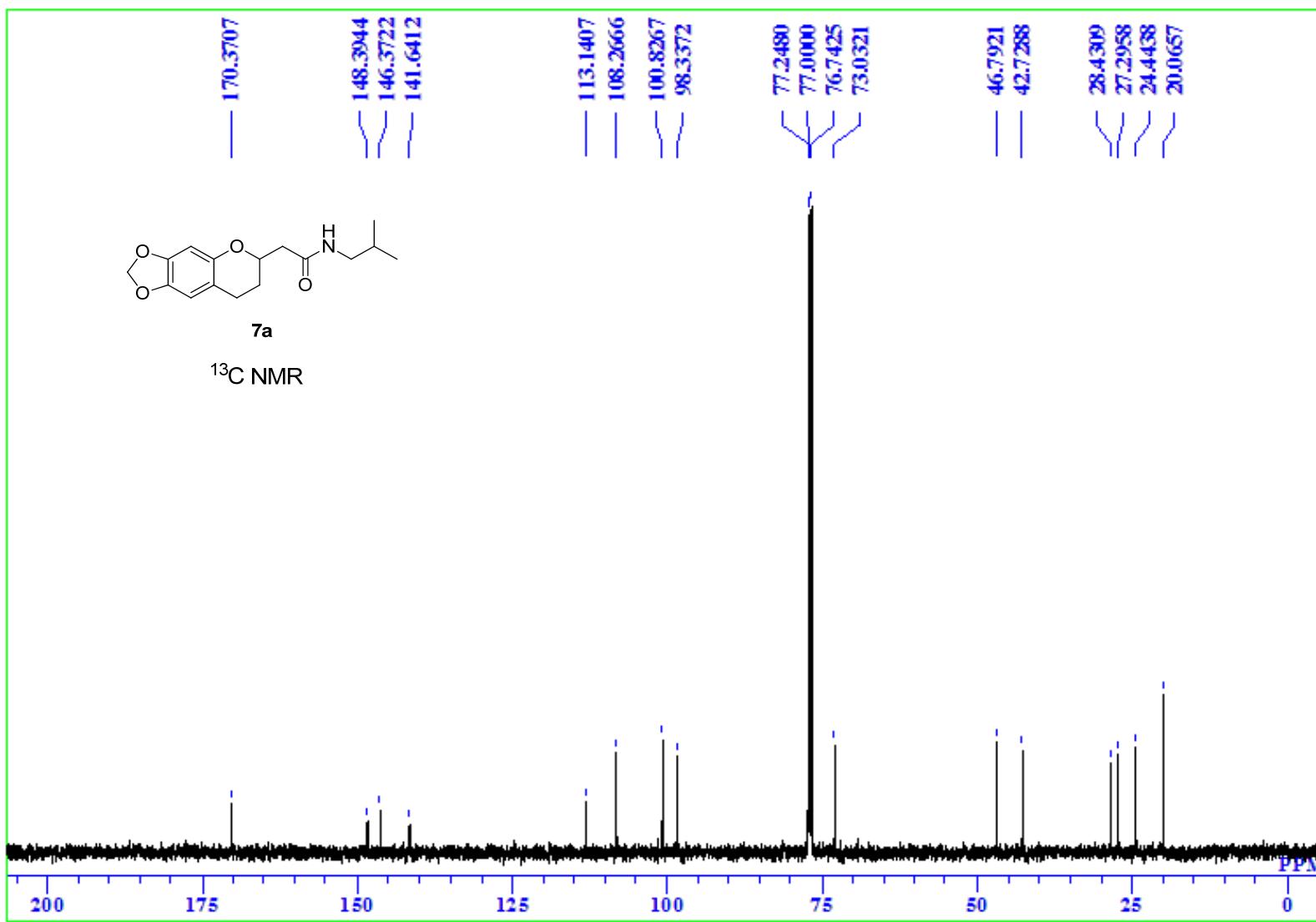




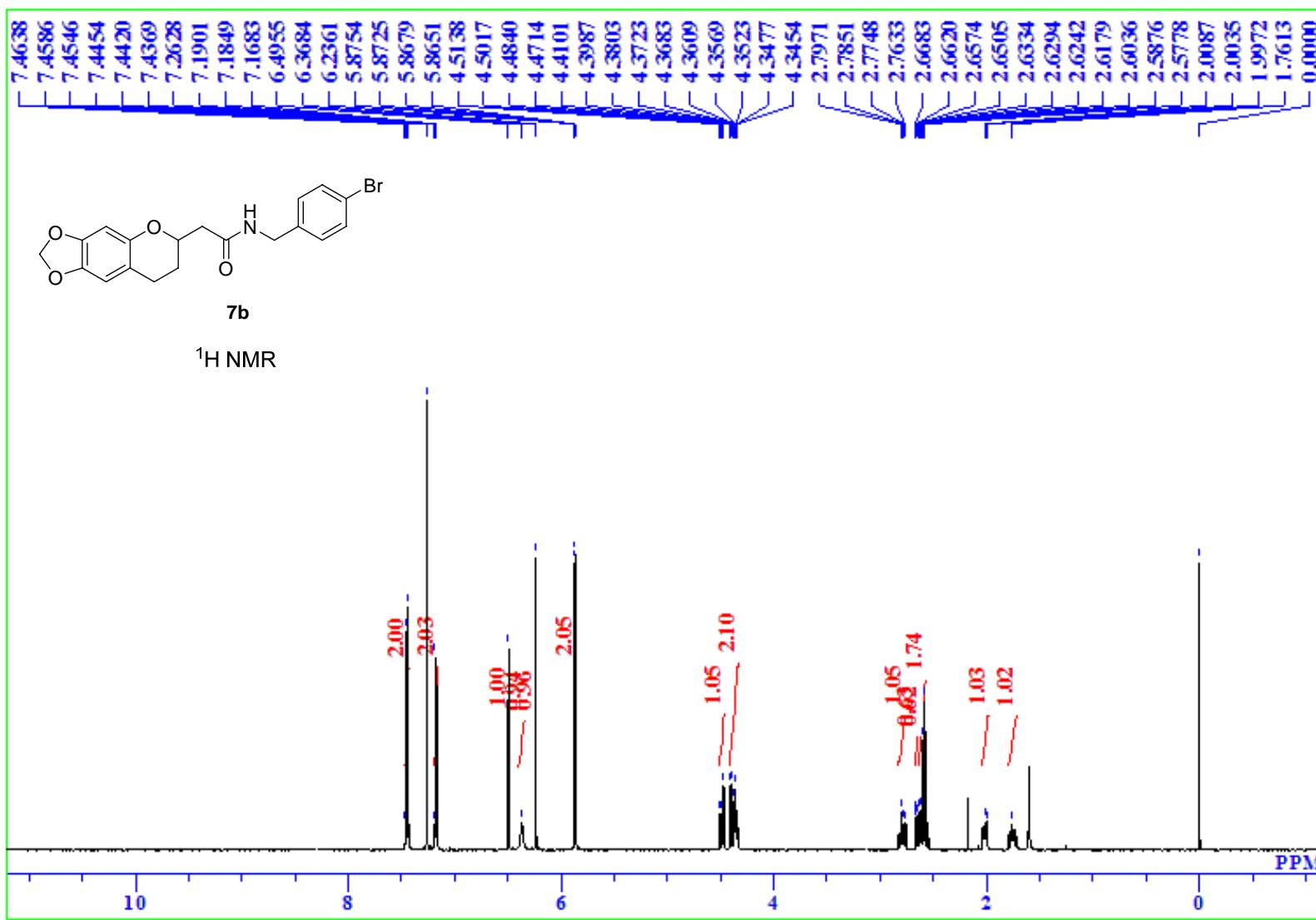


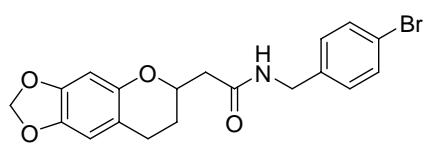






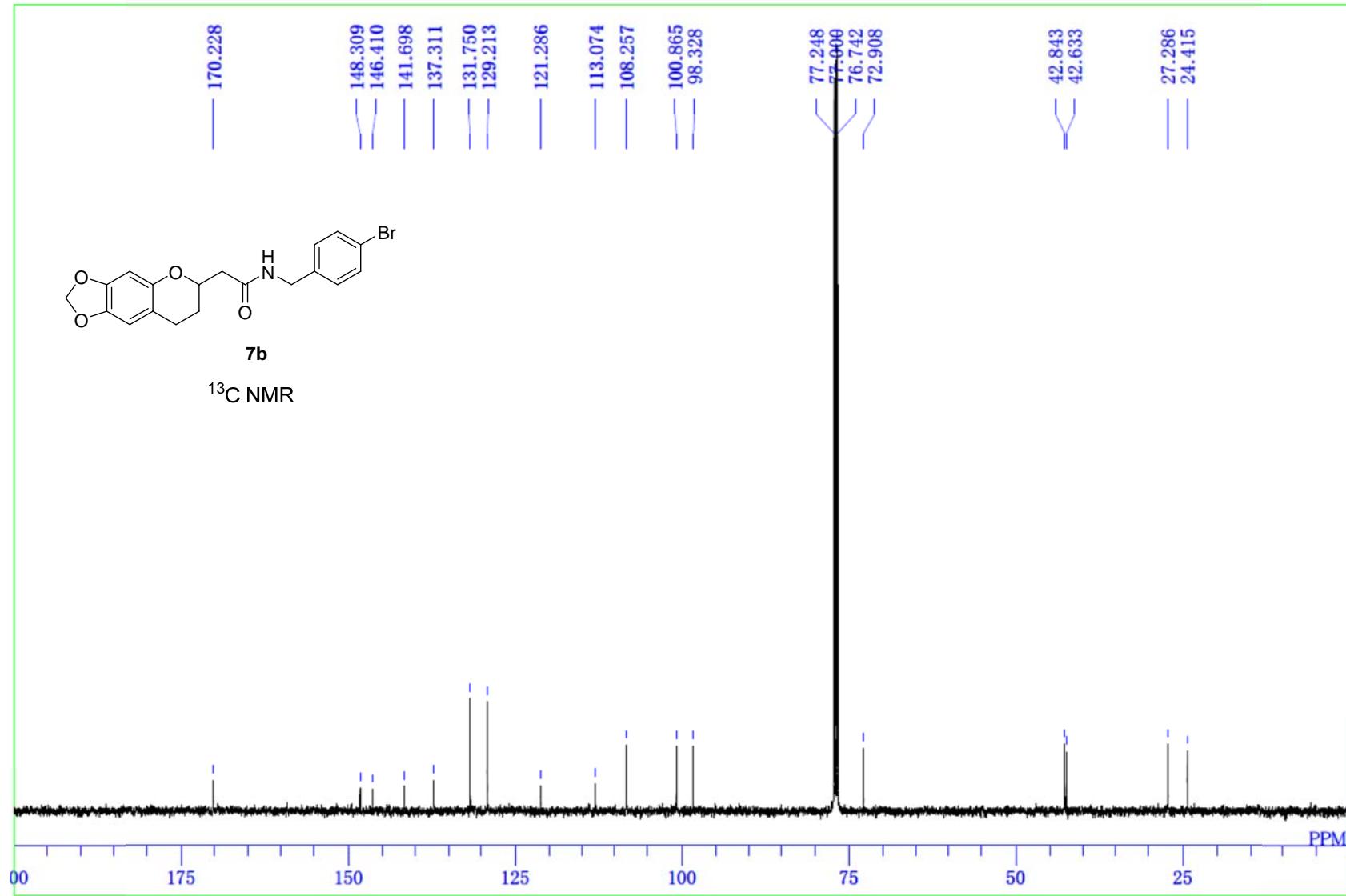
S170



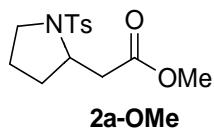


7b

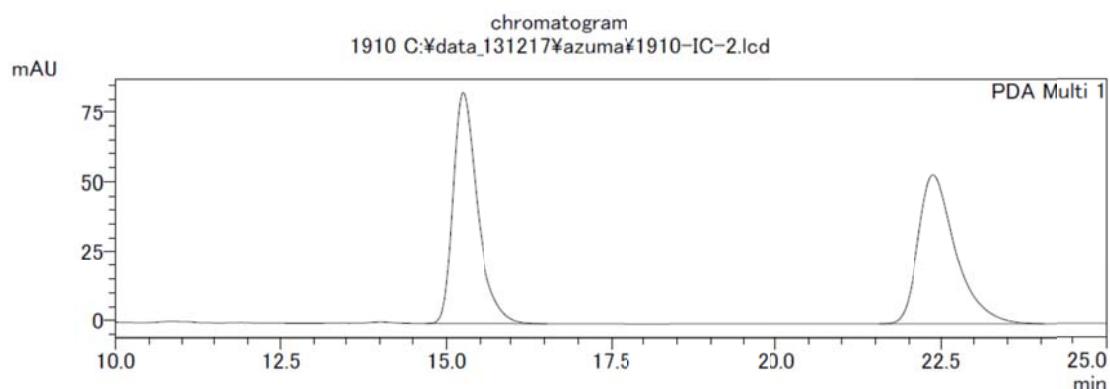
¹³C NMR



13. Copies of HPLC charts



⟨Chromatogram⟩



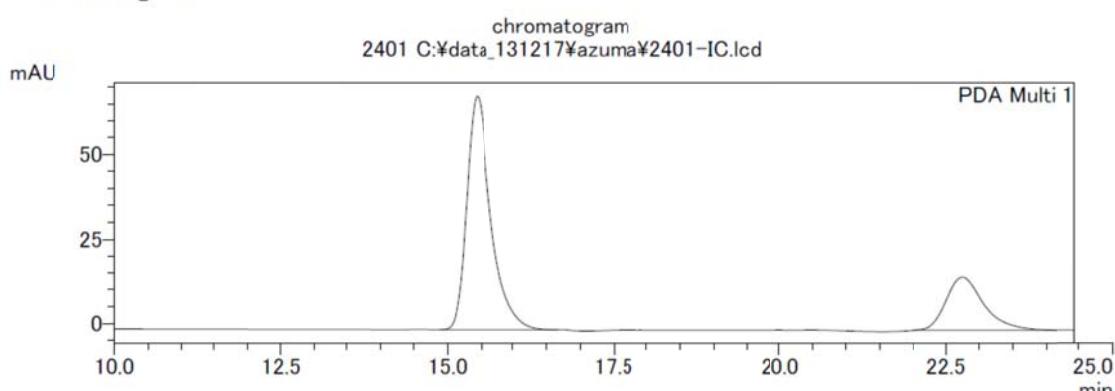
⟨Peak Report⟩

peak table C:\data_131217\azuma\1910-IC-2.cd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	15.244	2171264	50.437
2	22.376	2133625	49.563

⟨Chromatogram⟩

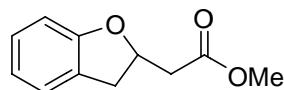


⟨Peak Report⟩

peak table C:\data_131217\azuma\2401-IC.lcd

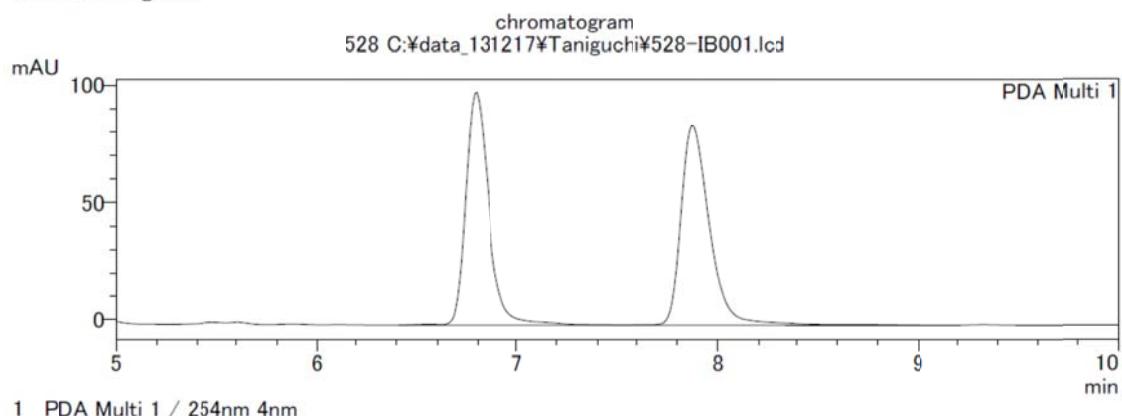
PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	15.436	1828659	74.853
2	22.742	614330	25.147



2j-OMe

<Chromatogram>



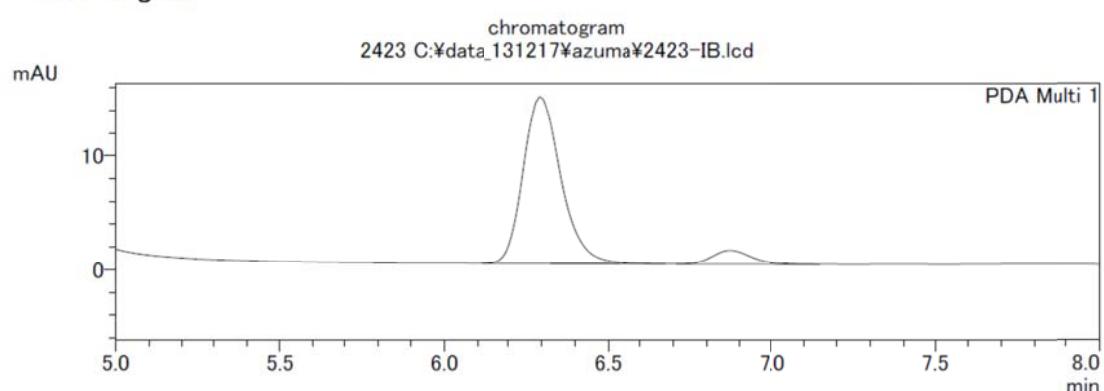
<Peak Report>

peak table C:\data_131217\Taniguchi\528-IB001.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	6.786	821404	49.552
2	7.870	836248	50.448

<Chromatogram>

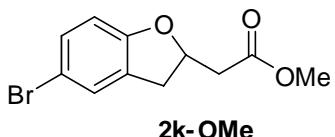


<Peak Report>

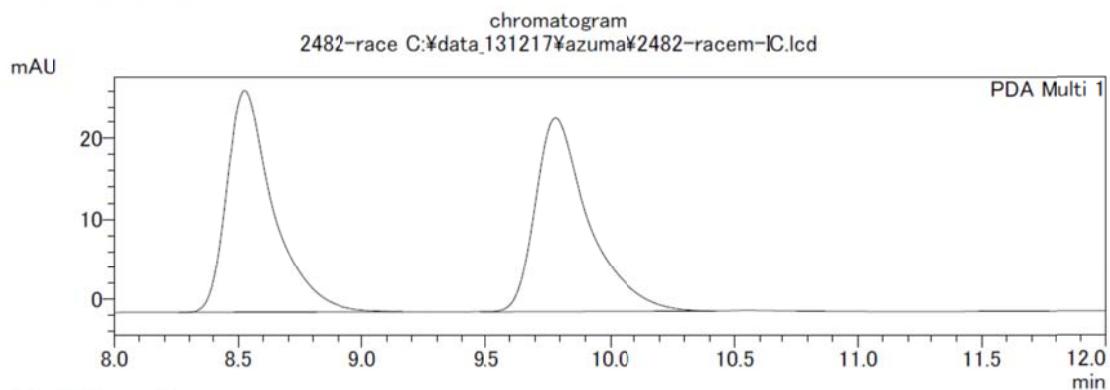
peak table C:\data_131217\azuma\2423-IB.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	6.290	115830	91.958
2	6.867	10129	8.042



<Chromatogram>



<Peak Report>

peak table C:\data_131217\azuma\2482-racem-IC.lcd

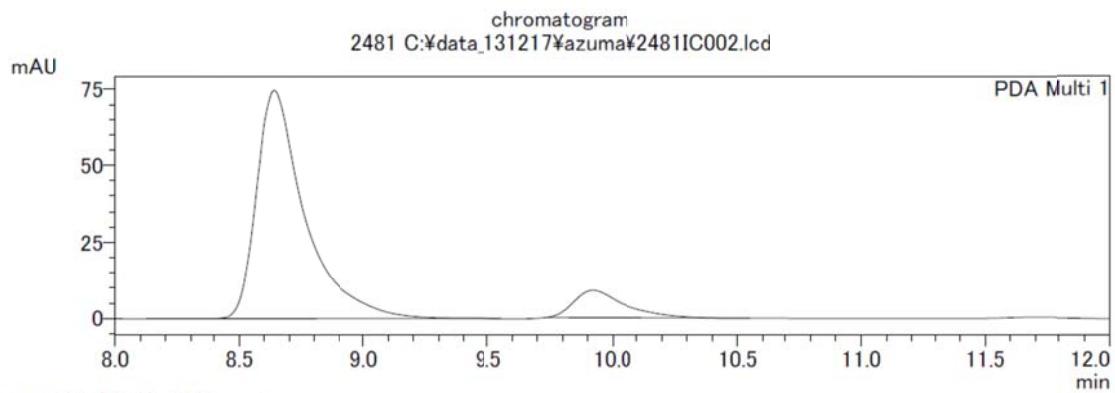
PDA Ch1 254nm 4nm

peak #	retention time (min)	area	area (%)
1	8.521	358363	50.101
2	9.777	356916	49.899

C:\data_131217\azuma\2481IC002.lcd

sample ID : 2481
 method name : 1.0-02-1.lcm
 acquisition date : 2014/03/20 7:35:02
 modified date : 2014/03/20 7:58:06

<Chromatogram>



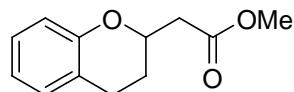
1 PDA Multi 1 / 254nm 4nm

<Peak Report>

peak table C:\data_131217\azuma\2481IC002.lcd

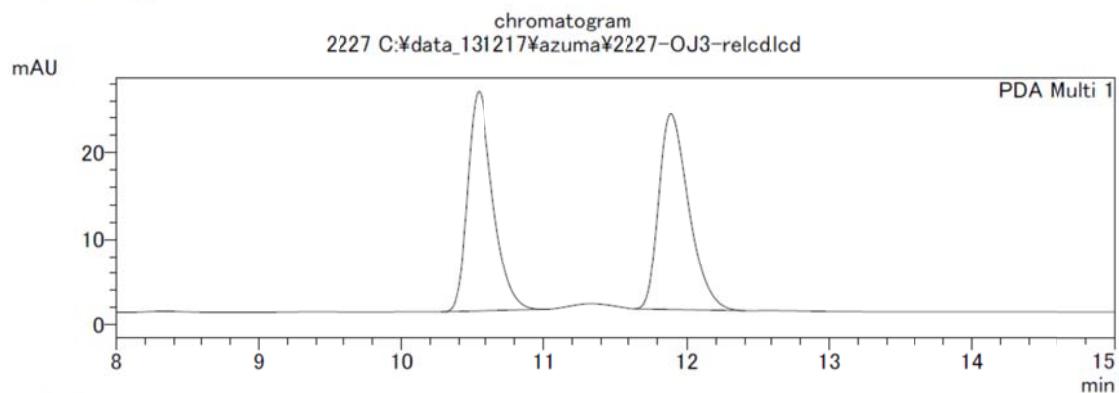
PDA Ch1 254nm 4nm

peak #	retention time (min)	area	area (%)
1	8.634	1004990	88.751
2	9.917	127375	11.249



2m-OMe

<Chromatogram>



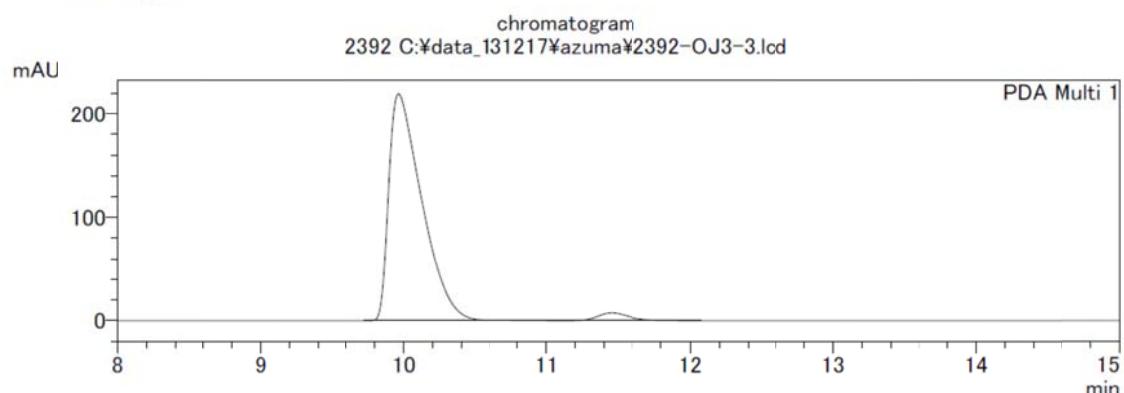
<Peak Report>

peak table C:\data_131217\azuma\2227-OJ3-reclcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	10.530	331181	50.230
2	11.885	328146	49.770

<Chromatogram>

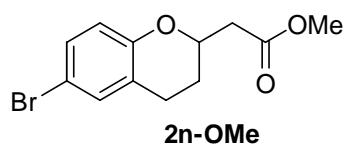


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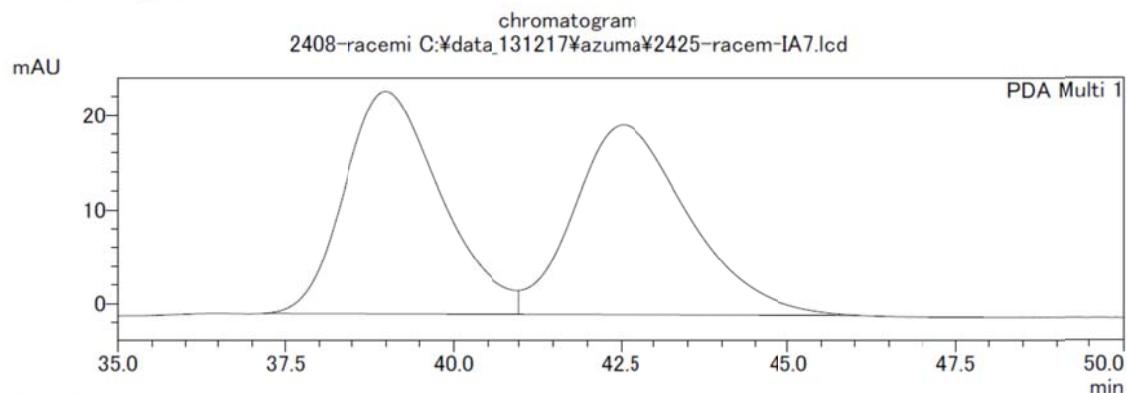
peak table C:\data_131217\azuma\2392-OJ3-3.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	9.958	3463896	96.747
2	11.444	116455	3.253



<Chromatogram>



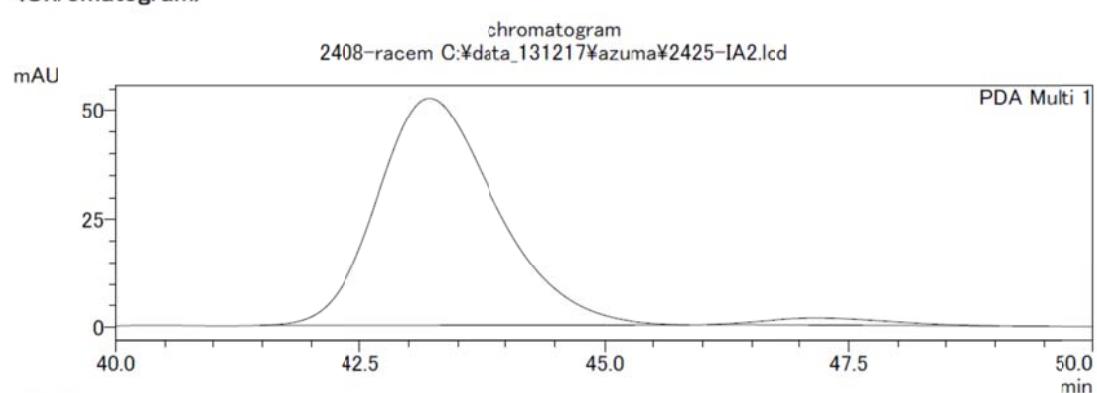
<Peak Report>

peak table C:\data_131217\azuma\2425-racem-IA7.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	38.986	2372928	49.722
2	42.521	2399432	50.278

<Chromatogram>



<Peak Report>

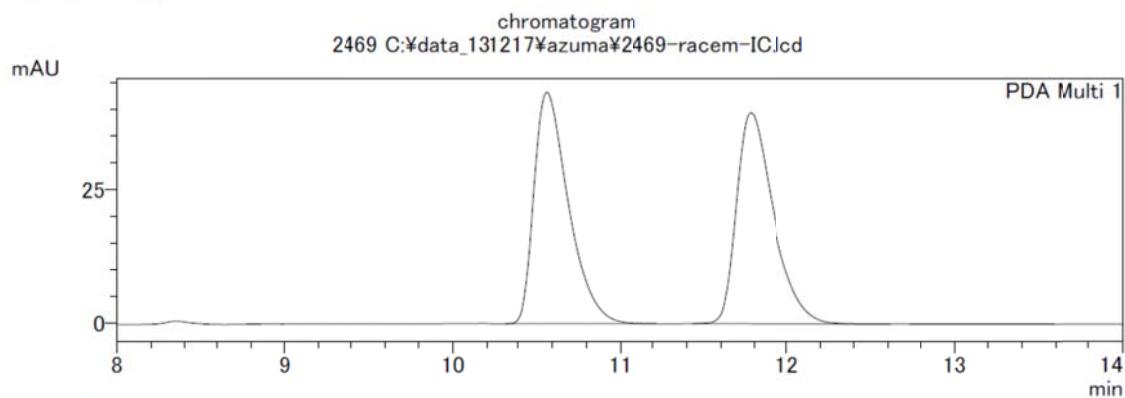
peak table C:\data_131217\azuma\2425-IA2.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	43.202	4449093	96.940
2	47.186	140446	3.060



<Chromatogram>



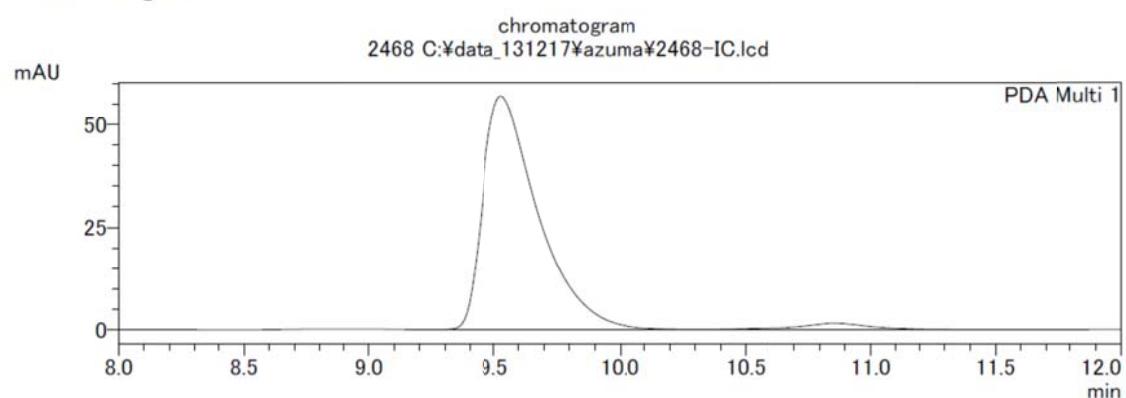
<Peak Report>

peak table C:\data_131217\azuma\2469-racem-IC.lcd

PDA Ch1 254nm 4nm

peak #	retention time (min)	area	area (%)
1	10.563	607904	49.977
2	11.773	608463	50.023

<Chromatogram>

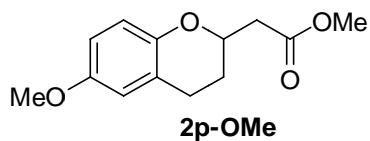


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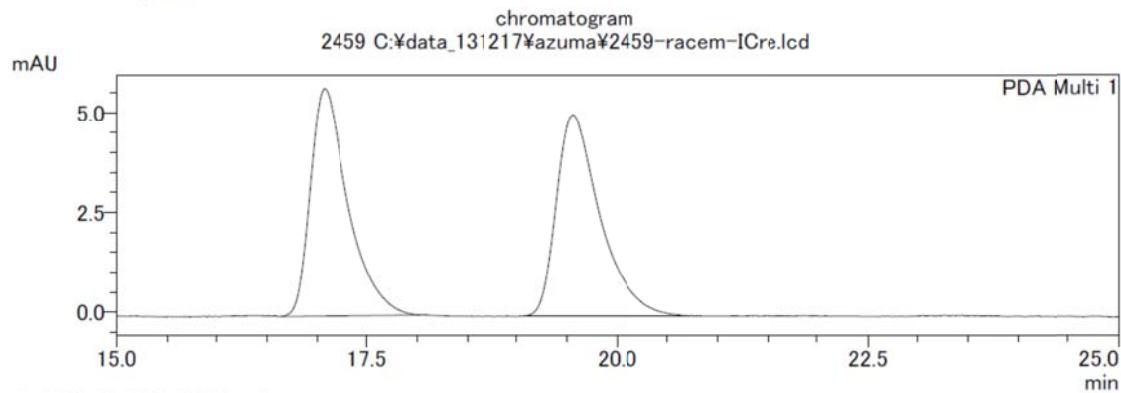
peak table C:\data_131217\azuma\2468-IC.cd

PDA Ch1 254nm 4nm

peak #	retention time (min)	area	area (%)
1	9.524	885847	96.670
2	10.847	30519	3.330



<Chromatogram>



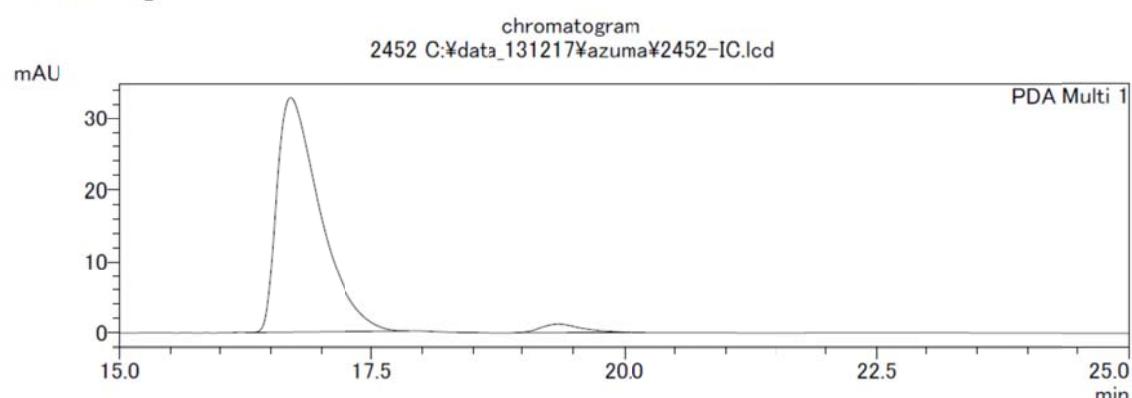
<Peak Report>

peak table C:\data_131217\azuma\2459-racem-ICre.lcd

PDA Ch1 254nm 4nm

peak #	retention time (min)	area	area (%)
1	17.070	151230	49.970
2	19.555	151414	50.030

<Chromatogram>

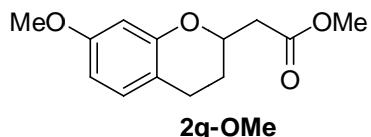


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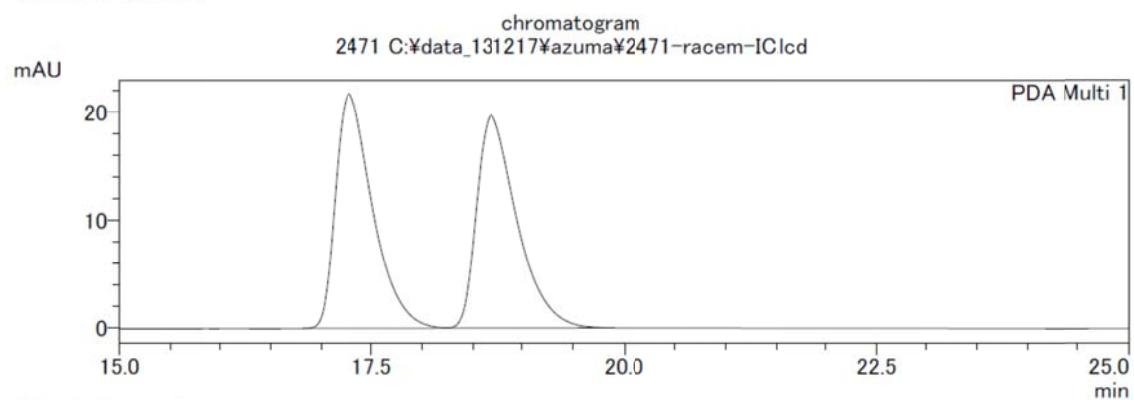
peak table C:\data_131217\azuma\2452-IC.cd

PDA Ch1 254nm 4nm

peak #	retention time (min)	area	area (%)
1	16.688	975394	96.694
2	19.334	33349	3.306



<Chromatogram>



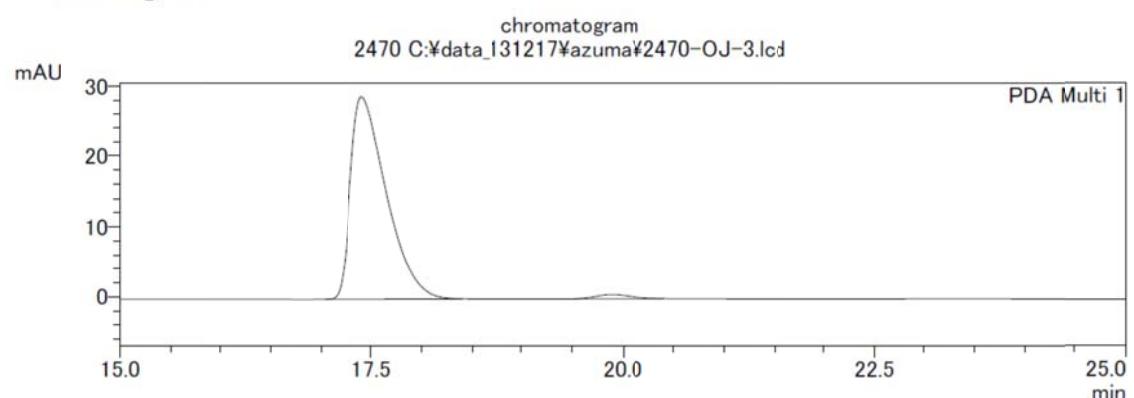
<Peak Report>

peak table C:\data_131217\azuma\2471-racem-IC.lcd

PDA Ch1 254nm 4nm

peak #	retention time (min)	area	area (%)
1	17.272	569163	49.980
2	18.679	569610	50.020

<Chromatogram>

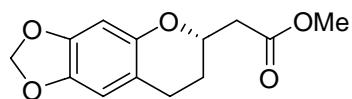


<Peak Report>

peak table C:\data_131217\azuma\2470-OJ-3.lcd

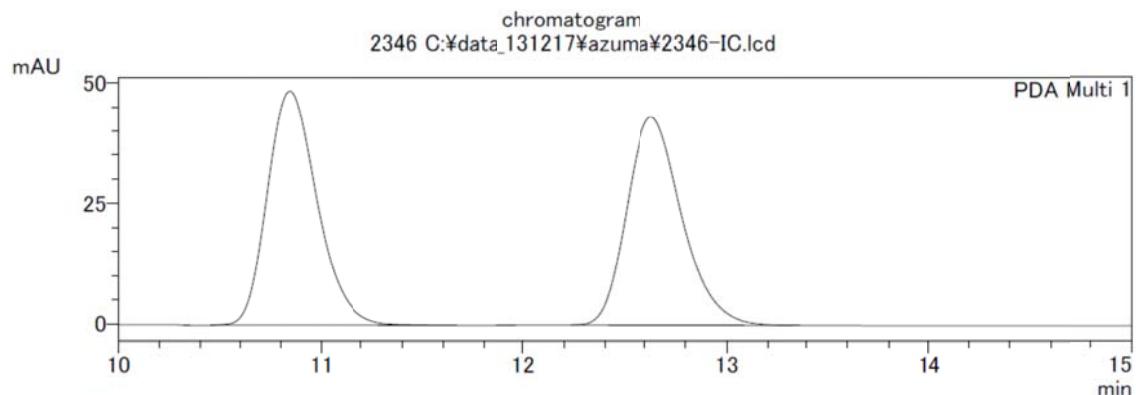
PDA Ch1 254nm 4nm

peak #	retention time (min)	area	area (%)
1	17.404	711973	97.976
2	19.909	14706	2.024



6-OMe

<Chromatogram>



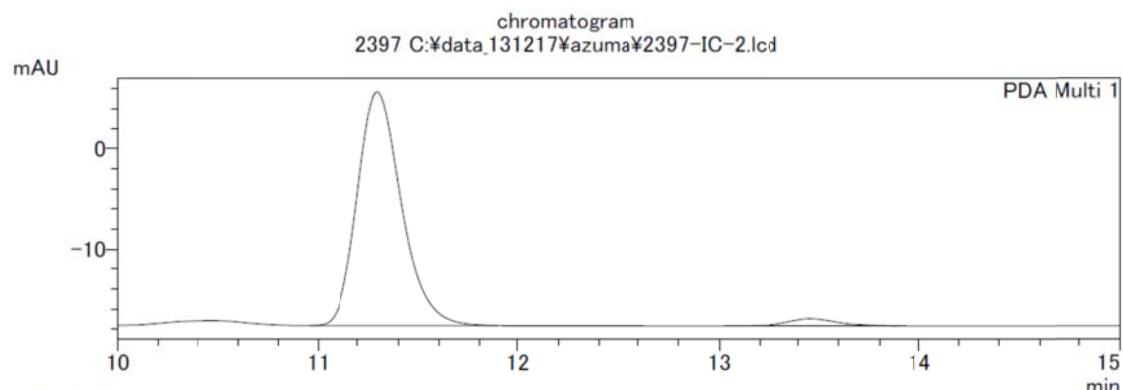
<Peak Report>

peak table C:\data_131217\azuma\2346-IC.lcd

PDA Ch1 254nm 4nm

peak #	retention time (min)	area	area (%)
1	10.839	821801	50.092
2	12.625	818780	49.908

<Chromatogram>

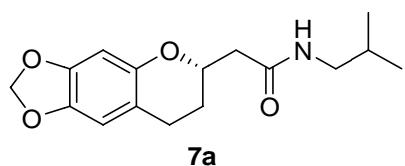


<Peak Report>

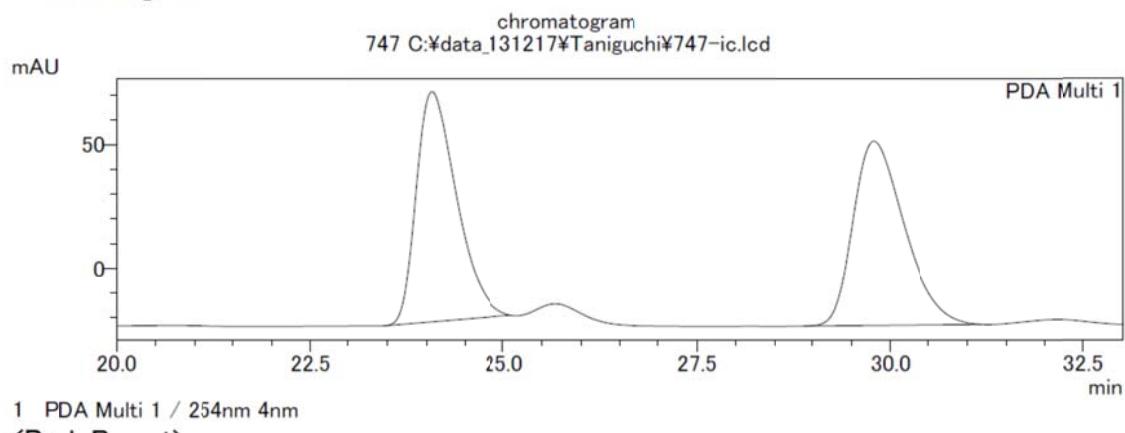
peak table C:\data_131217\azuma\2397-IC-2.lcd

PDA Ch1 254nm 4nm

peak #	retention time (min)	area	area (%)
1	11.291	353694	96.850
2	13.448	11504	3.150



<Chromatogram>



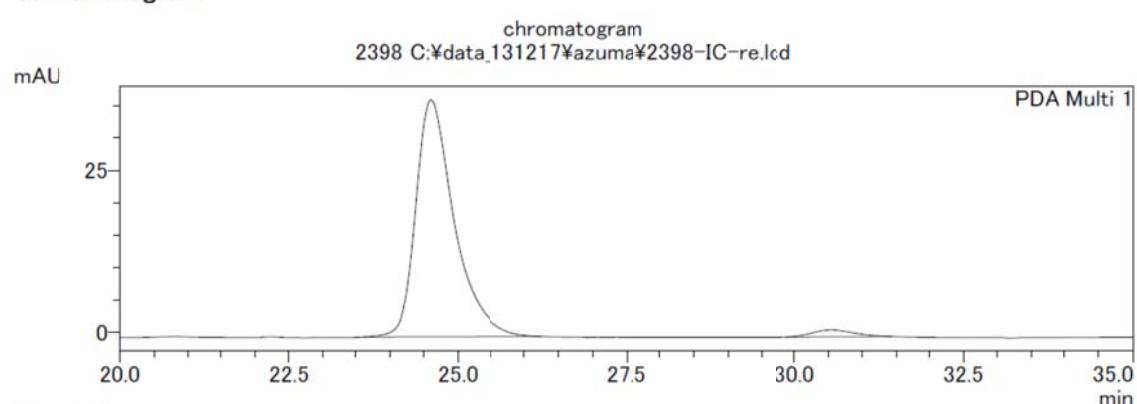
<Peak Report>

peak table C:\data_131217\Taniguchi\747-ic.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	24.066	3329480	49.492
2	29.781	3397790	50.508

<Chromatogram>

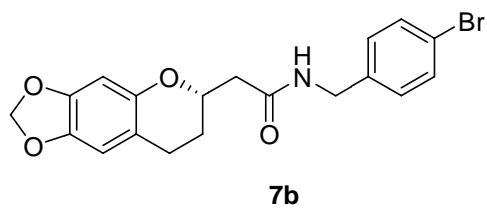


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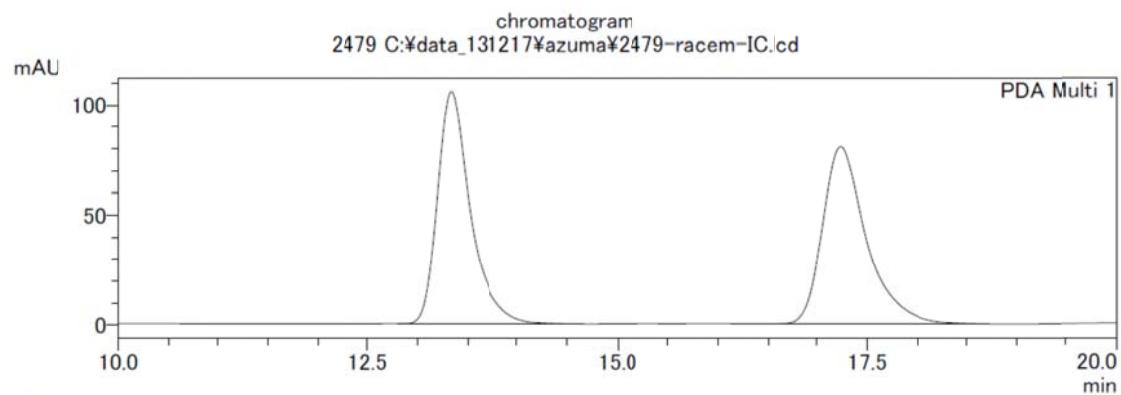
peak table C:\data_131217\azuma\2398-IC-re.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	24.598	1434491	96.916
2	30.503	45640	3.084



〈Chromatogram〉



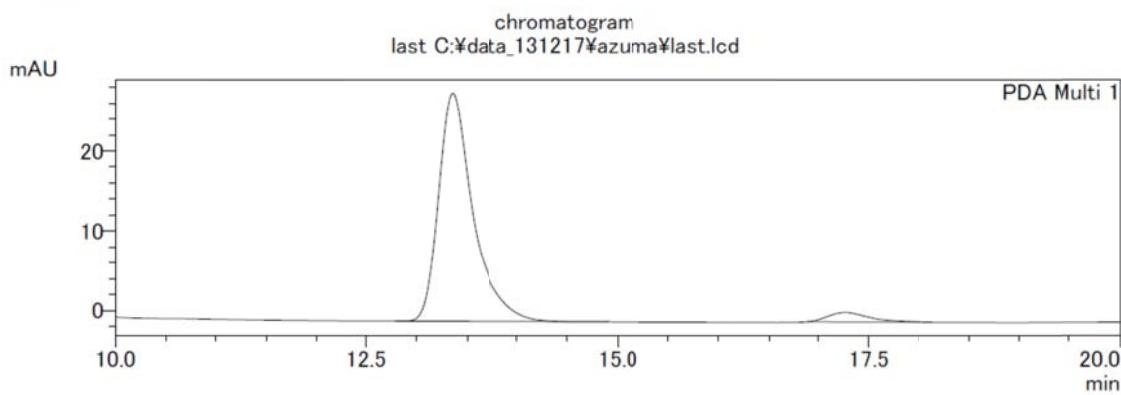
〈Peak Report〉

peak table C:\data_131217\azuma\2479-racem-IC.lcd

PDA Ch1 254nm 4nm

peak #	retention time (min)	area	area (%)
1	13.326	2401275	49.892
2	17.236	2411644	50.108

〈Chromatogram〉



〈Peak Report〉

peak table C:\data_131217\azuma\last.lcd

PDA Ch1 254nm 4nm

peak #	retention time (min)	area	area (%)
1	13.347	681001	95.476
2	17.273	32270	4.524