

Supporting Information

for

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

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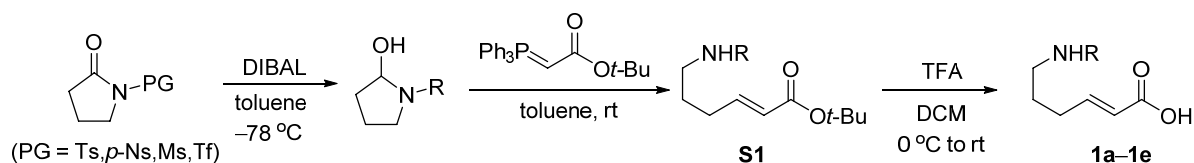
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CONTENTS

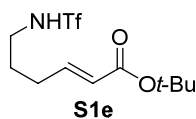
| | |
|---|------|
| 1. General information | S3 |
| 2. Preparation of substrates | S3 |
| 3. Preparation of boronic acid catalysts | S22 |
| 4. General procedure for bifunctional amino boronic acid-catalyzed intramolecular Michael reactions of α,β -unsaturated carboxylic acids | S23 |
| 5. Preparation of new aminothiurea catalysts | S30 |
| 6. General procedure for the asymmetric reaction | S32 |
| 7. Asymmetric total synthesis erythrococcamide B via one-pot reaction | S33 |
| 8. Optimization of solvents and additives for the asymmetric reaction | S35 |
| 9. Optimization of catalysts for the asymmetric reaction | S36 |
| 10. Determination of the absolute configuration | S37 |
| 11. References | S38 |
| 12. Copies of ^1H and ^{13}C NMR charts | S39 |
| 13. Copies of HPLC charts | S173 |

1. General informaiton: 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 μm). 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 $10^{-1} \text{ deg cm}^2\text{g}^{-1}$. 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.



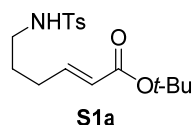
***tert*-Butyl (*E*)-6-(Trifluoromethylsulfonamido)hex-2-enoate (**S1e**)**



To a stirred solution of *N*-trifluoromethylsulfonylpyrrolidone (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

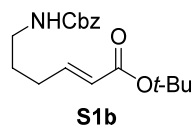
temperature for 1 h, the reaction mixture was quenched with MeOH and a saturated potassium sodium tartrate solution, and the reaction mixture was warmed up to room temperature. The organic layer was separated and the aqueous layer was extracted with CHCl₃ twice. The combined organic extracts were washed with brine, dried over Na₂SO₄, 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 (CDCl₃) 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 (CDCl₃) δ: 165.9, 145.3, 124.3, 119.7 (q, *J*_{C-F} = 323Hz), 80.7, 43.8, 28.7, 28.6, 28.1 ppm; IR (ATR): 3205, 2981, 2940, 1691, 1372 cm⁻¹; HRMS (ESI): calcd. for C₁₁H₁₈NO₄F₃SNa [M+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 (CDCl₃) 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 (CDCl₃) 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 C₁₇H₂₅NO₄SNa [M+Na]⁺ 362.1397, found 362.1408.

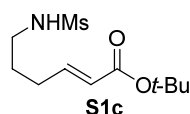
***tert*-Butyl (*E*)-6-[(Benzyloxy)carbonyl]amino]hex-2-enoate (**S1b**)**



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

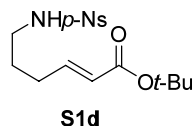
steps): colorless oil; ^1H NMR (CDCl_3) δ : 7.36–7.32 (5H, m), 6.82 (1H, dt, $J = 15.8, 7.0$ Hz), 5.75 (1H, d, $J = 15.8$ Hz), 5.10 (2H, s), 4.76 (1H, br s), 3.24–3.20 (2H, m), 2.23–2.19 (2H, m), 1.69–1.65 (2H, m), 1.48 (9H, s) ppm; ^{13}C NMR (CDCl_3) δ : ^{13}C -NMR (CDCl_3) δ : 165.8, 156.3, 146.4, 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**)**



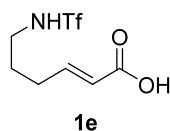
A procedure similar to that described for the preparation of **S1e** afforded **S1c** (454 mg, 24% in 2 steps): white solid; mp 42–44 °C (EtOAc : hexane); ^1H NMR (CDCl_3) δ : 6.84–6.79 (m, 1H), 5.78 (d, $J = 15.5$ Hz, 1H), 4.53–4.45 (br m, 1H), 3.19–3.12 (m, 2H), 2.96 (s, 3H), 2.30–2.23 (m, 2H), 1.77–1.72 (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**)**



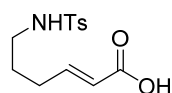
A procedure similar to that described for the preparation of **S1e** afforded **S1d** (540 mg, 46% in 2 steps): yellow solid; mp 103–104 °C (EtOAc : hexane); ^1H NMR (CDCl_3) δ : 8.38 (d, $J = 8.6$ Hz, 2H), 8.06 (d, $J = 8.6$ Hz, 2H), 6.74 (dt, $J = 15.5, 6.9$ Hz, 1H), 5.71 (dt, $J = 15.6, 1.4$ Hz, 1H), 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 C₇H₁₀NO₄F₃SNa [M+Na]⁺ 284.0175, found 284.0175.

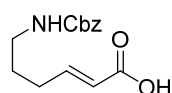
(*E*)-6-(4-Methylphenylsulfonamido)hex-2-enoic Acid (1a)



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 C₁₃H₁₇NO₄SNa [M+Na]⁺ 306.0771, found 306.0772.

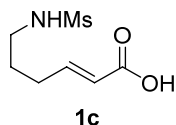
(*E*)-6-[[(Benzyloxy)carbonyl]amino]hex-2-enoic Acid (1b):



1b

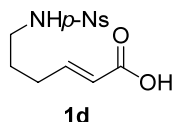
A procedure similar to that described for the preparation of **1e** afforded **1b** (102 mg, 94%): white solid; mp 77–78 °C; ¹H NMR (CDCl₃) δ 7.39–7.29 (m, 5H), 7.09–6.99 (m, 1H), 5.85 (d, *J* = 15.5 Hz, 1H), 5.10 (s, 2H), 4.83 (br s, 1H), 3.26–3.14 (m, 2H), 2.31–2.20 (m, 2H), 1.74–1.63 (m, 2H). ¹³C 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)



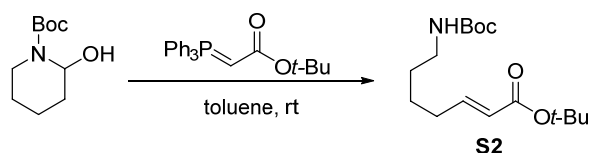
A procedure similar to that described for the preparation of **1e** afforded **1c** (227 mg, 99%): white solid; mp 95–96 °C (EtOAc : hexane); ¹H NMR (acetone-*d*₆) δ: 10.51 (br s, 1H), 6.98–6.91 (m, 1H), 6.06–5.95 (br m, 1H), 5.86 (d, *J* = 15.7 Hz, 1H), 3.20–3.10 (m, 2H), 2.91 (s, 3H), 2.38–2.29 (m, 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 C₇H₁₃NO₄SNa [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 C₁₂H₁₄N₂O₆SNa [M+Na]⁺ 337.0465, found 337.0469.

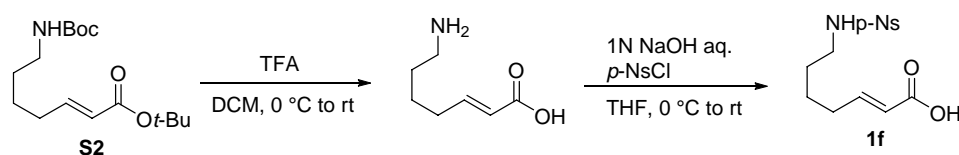
***tert*-Butyl (E)-7-[(*tert*-Butoxycarbonyl)amino]hept-2-enoate (S2)**



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 reaction mixture was concentrated *in vacuo*. The crude product was purified by column chromatography on

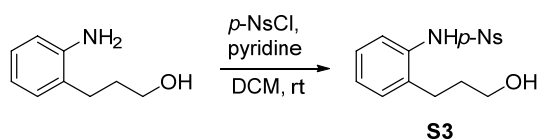
silica gel (hexane : EtOAc = 6 : 1) to afford **S2** (204 mg, 50%): colorless amorphous; ^1H NMR (CDCl_3) δ : 6.86–6.80 (m, 1H), 5.74 (d, J = 15.8 Hz, 1H), 4.51 (br s, 1H), 3.16–3.08 (m, 2H), 2.23–2.15 (m, 2H), 1.48 (s, 9H), 1.44 (s, 9H) ppm; ^{13}C NMR (CDCl_3) δ : 166.0, 155.9, 147.3, 123.3, 80.0, 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 $\text{C}_{16}\text{H}_{29}\text{NO}_4\text{Na}$ $[\text{M}+\text{Na}]^+$ 322.1989, found 322.1991.

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



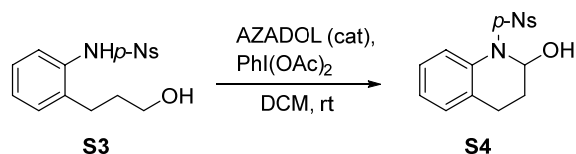
To a stirred solution of **S2** (0.683 mmol, 204 mg) in DCM (20 mL) was added TFA (2.5 mL) at 0 °C. After being stirred for 4 h at the same temperature, the reaction mixture was concentrated *in vacuo* to afford the crude product as colorless oil, which was used for the next step without further purification. 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 Na_2SO_4 , filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel (hexane : EtOAc : CH_3COOH = 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; ^{13}C 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 $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}_6\text{SNa}$ $[\text{M}+\text{Na}]^+$ 351.0621, found 351.0620.

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



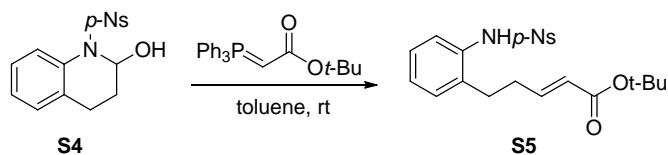
To a solution of 3-(2-aminophenyl)propan-1-ol³ (1.26 g, 8.33 mmol) in DCM (50 mL), was added *p*-NsCl (1.1 eq) in DCM (40 mL) at room temperature. After being stirred for 14 h, the reaction mixture was quenched with 1N HCl aq. and diluted with water and CHCl₃. The organic layer was separated and the 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**)



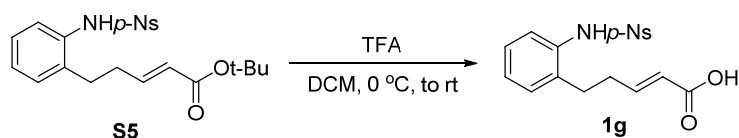
To a solution of **S3** (2.2 g, 6.54 mmol) in DCM (80 mL), were added AZADOL (50 mg, 0.33 mmol) and PhI(OAc)₂ (2.32 g, 7.19 mmol). After being stirred for 3 h, the mixture was quenched with saturated Na₂S₂O₃ aq. (30 mL) and NaHCO₃ aq. (30 mL). The organic layer was separated and the aqueous layer was 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**)



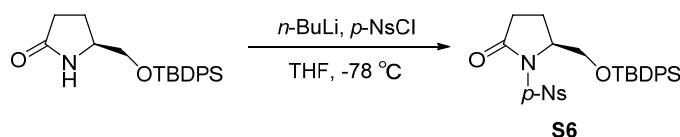
To a solution of **S4** (1.5 g, 4.49 mmol) in toluene (30 mL), was added *tert*-butyl 2-(triphenylphosphoranylidene)acetate (3.36 g, 8.88 mmol) at room temperature. After being stirred for 20 h, the mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane : EtOAc = 4 : 1) to afford **S5** (1.83 g, 94 %): white solid; mp 131–132 °C (EtOAc : hexane); ^1H NMR (CDCl_3) 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; ^{13}C NMR (CDCl_3) 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 $\text{C}_{21}\text{H}_{24}\text{N}_2\text{O}_6\text{SNa}$ $[\text{M}+\text{Na}]^+$ 455.1247, found 455.1254.

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



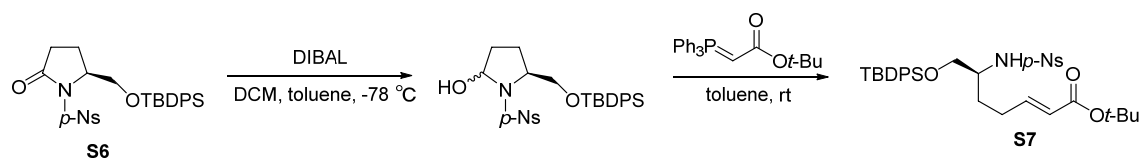
To a stirred solution of **S8** (1.62 g, 3.74 mmol) in DCM (15 mL) was added TFA (7 mL) dropwise at 0 °C. After being stirred for 4 h, the reaction mixture was warmed up to room temperature and concentrated *in vacuo*. After the addition of hexane to the residue, the solvent was evaporated at 40 °C to 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; ^{13}C 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 $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_6\text{SNa}$ $[\text{M}+\text{Na}]^+$ 399.0621, found 399.0630.

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



To a stirred mixture of (S)-5-(tert-butyldiphenylsilyloxymethyl)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 \rightarrow 1 : 1) to afford **S6** (3.14 g, 97%): white solid; mp 130–131 $^{\circ}\text{C}$ (EtOAc : hexane); $[\alpha]_{\text{D}}^{25} -21.1$ (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..

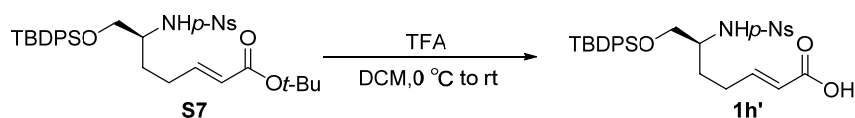
tert-Butyl (S,E)-7-[(tert-Butyldiphenylsilyl)oxy]-6-(4-nitrophenylsulfonamido)hept-2-enoate (S3)



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

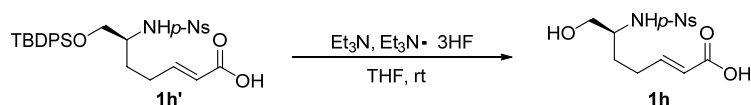
crude hemiaminal was used for the next step without further purification. To a stirred solution of crude hemiaminal (3.08 g, ca. 5.69 mmol) in toluene (60 mL) was added *tert*-butyl 2-(triphenylphosphoranylidene)acetate (4.51 g, 11.9 mmol). After being stirred for 16 h, the reaction mixture was concentrated *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); $[\alpha]_D^{22} +14.7$ (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 C₃₃H₄₂N₂O₇SiNa [M+Na]⁺ 661.2374, found 661.2364.

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



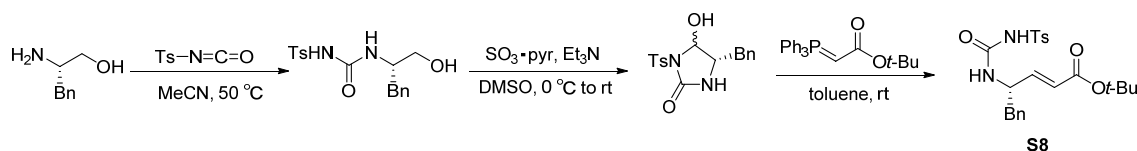
To a stirred solution of **S3** (324 mg, 0.508 mmol) in DCM (10 mL) was added TFA (4 mL) dropwise at 0 °C. After being stirred for 3 h, the reaction mixture was warmed up to room temperature and concentrated *in vacuo*. After the addition of hexane to the residue, the solvent was evaporated at 40 °C 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); $[\alpha]_D^{21} +20.2$ (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 C₂₉H₃₄N₂O₇SiNa [M+Na]⁺ 605.1748, found 605.1744.

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



To a stirred solution of Et₃N (0.222 mL, 1.59 mmol) and Et₃N · 3HF (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); [α]_D²⁴ +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; ¹³C 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 C₁₃H₁₆N₂O₇Na [M+Na]⁺ 367.0570, found 367.0587.

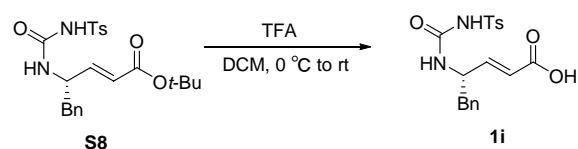
***tert*-Butyl (*S,E*)-5-Phenyl-4-(3-tosylureido)pent-2-enoate (**S8**)**



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 Et₂O. 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 Et₃N (1.26 mL, 9 mmol) and SO₃ · 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 Na₂SO₄, 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

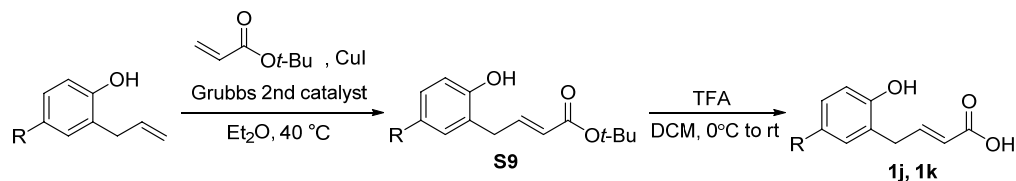
room temperature and the reaction mixture was stirred for 9 h. After concentration of reaction mixture *in vacuo*, the residue purified by column chromatography on silica gel (hexane : EtOAc = 2 : 1) to afford **S8** (220 mg, 35% in 3 steps): white solid; mp 156–157 °C (EtOAc : hexane); $[\alpha]_D^{21}$ –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**)**

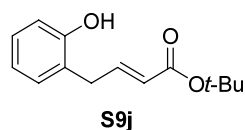


To a stirred solution of **S4** (116 mg, 0.26 mmol) in DCM (5 mL) was added TFA (5 mL) dropwise at 0 °C. After being stirred for 3 h, the reaction mixture was warmed up to room temperature and stirred at the same temperature for 4 h. After the completion of the reaction, the mixture was concentrated *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); $[\alpha]_D^{21}$ –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.

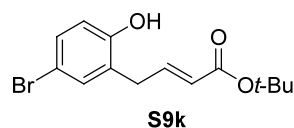


***tert*-Butyl (*E*)-4-(2-Hydroxyphenyl)but-2-enoate (**S9j**)**



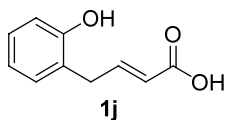
To a stirred solution of 2-allylphenol (0.26 mL, 2.0 mmol) in Et₂O (30 mL) were added *tert*-butyl acrylate (0.73 mL, 5.0 mmol), copper iodide (6.7 mg, 0.04 mmol), and Grubbs 2nd catalyst (34 mg, 0.04 mmol) at room temperature and the reaction mixture was warmed up to 40 °C. After being stirred for 19 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 (CDCl₃) 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 (CDCl₃) 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 C₁₄H₁₈O₃Na [M+Na]⁺ 257.1148, found 257.1143.

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



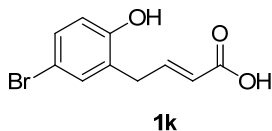
A procedure similar to that described for the preparation of **S9j** afforded **S9k** (327 mg, 45%): white solid; mp 124–125 °C (EtOAc : hexane); ¹H NMR (CDCl₃) δ : 7.17–7.16 (2H, m), 7.05 (1H, dt, *J* = 15.8, 6.9 Hz), 6.87 (1H, s), 6.64 (1H, d, *J* = 9.2 Hz), 5.76 (1H, d, *J* = 15.8 Hz), 3.44 (2H, d, *J* = 6.9 Hz), 1.49 (9H, s) ppm; ¹³C NMR (CDCl₃) 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 C₁₄H₁₇BrO₃Na [M+Na]⁺ 335.0253, found 335.0257.

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



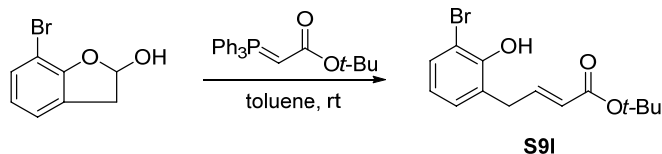
To a stirred solution of **S12j** (830 mg, 3.54 mmol) in DCM (5 mL) was added TFA (5 mL) dropwise at 0 °C. After being stirred for 1 h, the reaction mixture was warmed up to room temperature. After being stirred for another 4 h, the reaction mixture was concentrated *in vacuo*. After the addition of 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.

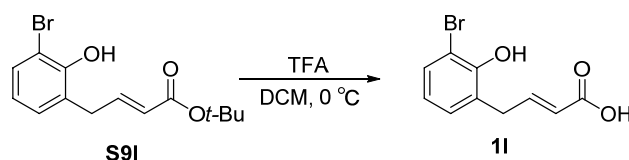
***tert*-Butyl (E)-4-(3-Bromo-2-hydroxyphenyl)but-2-enoate (S9l)**



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.

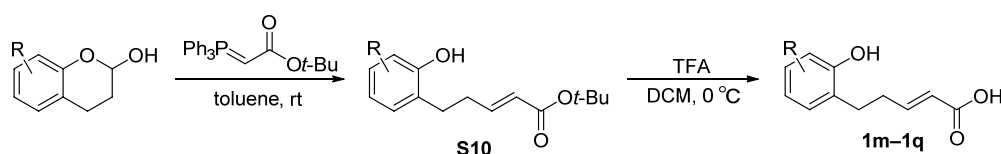
After being stirred for 12 h, the mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane : EtOAc = 10 : 1) to afford **S9I** (490 mg, 78 %): white solid; mp 102–103 °C (EtOAc : hexane); ^1H NMR (CDCl_3) δ : 7.35 (1H, d, J = 8.0 Hz), 7.04 (2H, d, J = 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; ^{13}C NMR (CDCl_3) 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 $\text{C}_{14}\text{H}_{17}\text{BrO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 335.0253, found 335.0258.

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

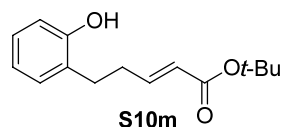


A procedure similar to that described for the preparation of **1j** afforded **1I** (357 mg, 89%): white solid; mp 145–146 °C (EtOAc : hexane); ^1H NMR ($\text{MeCN-}d_3$) δ : 7.40 (1H, dd, J = 7.7, 1.4 Hz), 7.09 (1H, d, J = 7.7 Hz), 7.02 (1H, dt, J = 15.7, 6.7 Hz), 6.78 (1H, t, J = 7.7 Hz), 5.71 (1H, d, J = 15.7 Hz), 3.54 (2H, d, J = 6.7 Hz) ppm; ^{13}C NMR ($\text{MeCN-}d_3$) 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 $\text{C}_{10}\text{H}_8\text{BrO}_3$ $[\text{M}-\text{H}]^-$ 254.9662, found 254.9669.

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



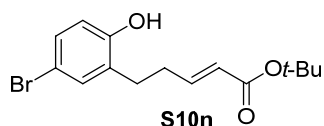
***tert*-Butyl (E)-5-(2-Hydroxyphenyl)pent-2-enoate (S10m)**



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

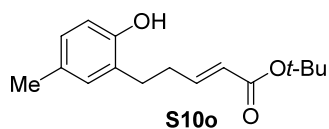
tert-butyl 2-(triphenylphosphoranylidene)acetate (367 mg, 0.96 mmol) in toluene (10 mL). After being stirred for 1 h, the mixture was concentrated in *vacuo*. The residue was purified by column chromatography on silica gel (hexane : EtOAc = 6 : 1) to afford **S13m** (918 mg, 76%): colorless oil; ^1H NMR (CDCl_3) 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; ^{13}C NMR (CDCl_3 , 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 $\text{C}_{15}\text{H}_{20}\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 271.1305, found 271.1306.

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



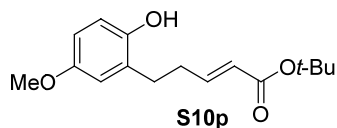
A procedure similar to that described for the preparation of **S10m** afforded **S10n** (1.38 g, 86%). white solid; mp 132–133 °C; ^1H NMR (CDCl_3) δ : 7.21 (1H, s), 7.17 (1H, d, J = 8.6 Hz), 6.92 (1H, dt, J = 16.6, 7.6 Hz), 6.64 (1H, d, J = 8.6 Hz), 5.79 (1H, d, J = 16.6 Hz), 5.61 (1H, br s), 2.72 (2H, t, J = 7.6 Hz), 2.47 (2H, q, J = 7.6 Hz), 1.49 (9H, s) ppm; ^{13}C NMR (CDCl_3) 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 $\text{C}_{15}\text{H}_{18}\text{BrO}_3$ $[\text{M}-\text{H}]^-$ 325.0445, found 325.0446.

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



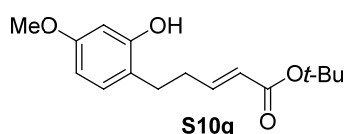
A procedure similar to that described for the preparation of **S10m** afforded **S10o** (1.48 g, 56%). white solid; mp 84–85 °C; ^1H NMR (CDCl_3) δ : 6.95 (1H, dd, J = 14.6, 7.7 Hz), 6.89 (1H, s), 6.86 (1H, d, J = 8.0 Hz), 6.65 (1H, d, J = 8.0 Hz), 5.82–5.76 (2H, m), 2.71 (2H, t, J = 7.8 Hz), 2.50–2.44 (2H, m), 2.24 (3H, s), 1.48 (9H, s) ppm; ^{13}C NMR (CDCl_3) 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 $\text{C}_{16}\text{H}_{22}\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 285.1461, found 285.1472.

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



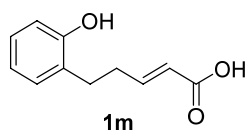
A procedure similar to that described for the preparation of **S10m** afforded **S10p**. Although a byproduct could not be removed, a mixture of the products was used in next step without further purification. A procedure for the next step is described below.

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



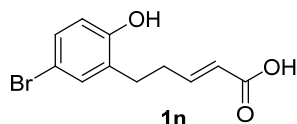
A procedure similar to that described for the preparation of **S10m** afforded **S10q** (1.85 g, 67%). white solid; mp 68–69 °C; ^1H NMR (CDCl_3) δ : 6.99 (1H, d, J = 8.3 Hz), 6.95 (1H, dt, J = 15.5, 7.9 Hz), 6.42 (1H, dd, J = 8.3, 2.6 Hz), 6.36 (1H, d, J = 2.6 Hz), 5.80 (1H, d, J = 15.5 Hz), 5.76 (1H, 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; ^{13}C NMR (CDCl_3) 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 $\text{C}_{16}\text{H}_{23}\text{O}_4$ $[\text{M}+\text{H}]^+$ 279.1591, found 279.1596.

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



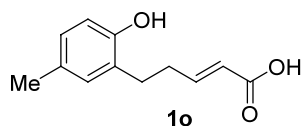
To a stirred solution of **S10m** (918 mg, 3.70 mmol) in DCM (10 mL) at 0 °C, was added TFA (3 mL) dropwise. After being stirred for 2.5 h, the reaction mixture was warmed up to room temperature and concentrated *in vacuo*. After the addition of hexane to the residue, the solvent was evaporated at 40 °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; ^{13}C 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 $\text{C}_{11}\text{H}_{12}\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 215.0679, found 215.0671.

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



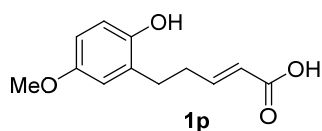
A procedure similar to that described for the preparation of **1m** afforded **1n** (910 mg, 88%): white solid; mp 137–138 °C (EtOAc : hexane); ¹H NMR (acetone-*d*₆) δ: 10.54 (1H, br s), 8.64 (1H, br s), 7.28 (1H, d, *J* = 2.6 Hz), 7.17 (1H, dd, *J* = 8.6, 2.6 Hz), 6.98 (1H, dt, *J* = 15.6, 6.9 Hz), 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.

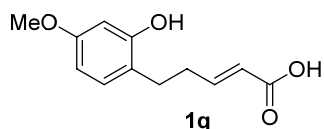
(E)-5-(2-Hydroxy-5-methoxyphenyl)pent-2-enoic Acid (1p)



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

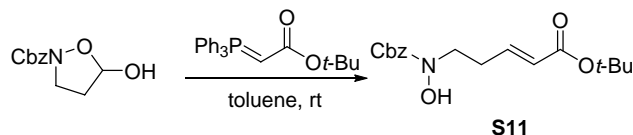
(acetone-*d*₆) δ 167.3, 154.0, 149.8, 149.7, 129.1, 122.2, 116.5, 116.3, 112.8 55.7, 32.9 ppm; IR (ATR): 3313, 2945, 1693 cm^{-1} ; HRMS (ESI): calcd. for $\text{C}_{12}\text{H}_{13}\text{O}_4$ $[\text{M}-\text{H}]^-$ 221.0819, found 221.0821.

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



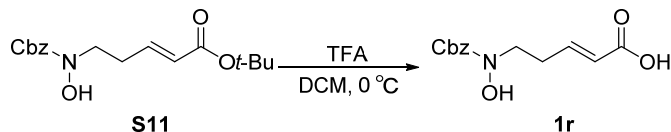
A procedure similar to that described for the preparation of **1m** afforded **1q** (935 mg, 87%): white solid; mp 165–166 °C; ^1H NMR (acetone-*d*₆) δ : 8.98 (1H, br s), 7.08–7.01 (2H, m), 6.49–6.48 (2H, m), 5.86 (1H, d, J = 15.8 Hz), 3.83 (3H, s), 2.76–2.73 (2H, m), 2.55–2.52 (2H, m) ppm; ^{13}C NMR (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-[[*(Benzyloxy)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): δ 165.7, 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.

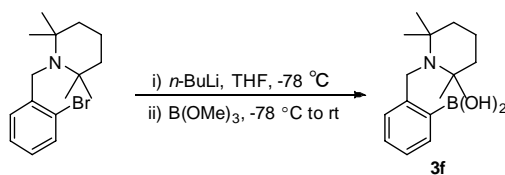
(E)-5-[[[(Benzyloxy)carbonyl](hydroxy)amino]pent-2-enoic Acid (1r)



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 (CDCl_3) 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; ^{13}C NMR (CDCl_3) 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 $\text{C}_{13}\text{H}_{15}\text{NO}_5\text{Na}$ $[\text{M}+\text{Na}]^+$ 288.0842, found 288.0843.

3. Preparation of boronic acid catalysts

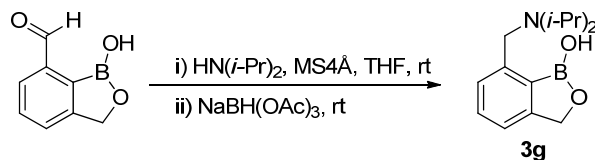
[2-[(2,2,6,6-Tetramethylpiperidin-1-yl)methyl]phenyl]boronic Acid (3f)



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, $\text{B}(\text{OMe})_3$ (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 CHCl_3 . The organic layer was separated and the aqueous layer was washed with CHCl_3 once and then the aqueous layer was basified to pH 10 with Na_2CO_3 (solid). The aqueous layer was extracted with CHCl_3 five times. The organic extracts were dried over Na_2SO_4 and filtered. The filtrate was concentrated *in vacuo*. The residue was recrystallized (acetone : hexane) to afford **3f** (210 mg, 59%): white solid. mp 142–144 °C ; ^1H NMR (CDCl_3) 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; ^{13}C NMR (CDCl_3) 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):

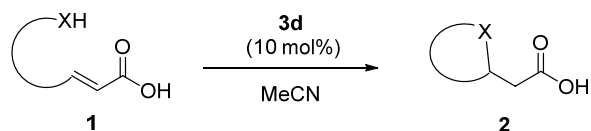
calcd. for $C_{16}H_{27}NO_2B$ $[M+H]^+$ 276.2127, found 276.2115;.

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



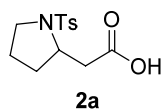
To a stirred solution of 1-hydroxy-1,3-dihydrobenzo[*c*][1,2]oxaborole-7-carbaldehyde⁷ (150 mg, 0.926 mmol) in THF (6 mL) were added activated MS4Å (670 mg) and diisopropylamine (0.13 mL, 0.926 mmol) at room temperature. After being stirred at the same temperature for 1 h, $NaBH(OAc)_3$ (393 mg, 1.85 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 were 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



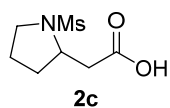
To a stirred solution of **1** (0.1 mmol) in MeCN (1 mL) was added amino boronic acid catalyst **3d** (2.4 mg, 10 mol%) at room temperature. The reaction mixture was stirred at room temperature (or 50 $^{\circ}C$, 80 $^{\circ}C$, 110 $^{\circ}C$) for 3–24 h. The reaction mixture was concentrated *in 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)



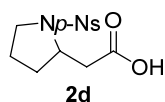
White solid; mp 146–147 °C (MeCN); $[\alpha]_D^{25} -62.6$ (*c* 0.21, CHCl₃, for 50% ee); ¹H NMR (CDCl₃) δ: 7.74 (d, *J* = 8.6 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 3.98–3.90 (m, 1H), 3.50–3.42 (m, 1H), 3.18–3.10 (m, 2H), 2.56 (dd, *J* = 16.3, 10.0 Hz, 1H), 2.44 (s, 3H), 1.87–1.74 (m, 2H), 1.74–1.63 (m, 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) [Chiralpak 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)

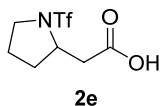


White solid; mp 108–109 °C (MeCN); ¹H NMR (acetone-*d*₆) δ: 4.06–3.94 (m, 1H), 3.42–3.27 (m, 2H), 2.88 (s, 3H), 2.87–2.81 (m, 1H), 2.48 (dd, *J* = 16.0, 10.3 Hz, 1H), 2.22–2.12 (m, 1H), 2.00–1.86 (m, 2H), 1.86–1.77 (m, 1H) ppm; ¹³C NMR (acetone-*d*₆) δ: 172.6, 57.5, 49.6, 41.4, 34.0, 32.3, 24.7 ppm; 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)



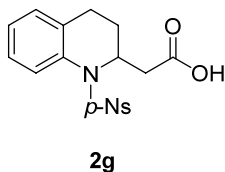
White solid; mp 186–187 °C (MeCN); ¹H NMR (acetone-*d*₆) δ: 8.36 (d, *J* = 9.2 Hz, 2H), 8.05 (d, *J* = 8.6 Hz, 2H), 3.91–3.81 (m, 1H), 3.44–3.33 (m, 1H), 3.20–3.10 (m, 1H), 2.83 (dd, *J* = 16.0, 3.4 Hz, 1H), 2.47 (dd, *J* = 16.0, 9.7 Hz, 1H), 1.85–1.58 (m, 3H), 1.51–1.40 (m, 1H) ppm; ¹³C NMR (acetone-*d*₆) 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, $J_{\text{C-F}}$ = 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.

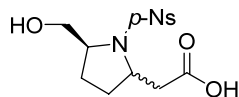
2-[1-[(4-Nitrophenyl)sulfonyl]piperidin-2-yl]acetic Acid (2f)

White solid; mp 173–174 $^{\circ}\text{C}$ (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 $^{\circ}\text{C}$ (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.

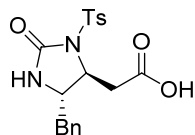
2-[(5*S*)-5-(Hydroxymethyl)-1-[(4-nitrophenyl)sulfonyl]pyrrolidin-2-yl]acetic Acid (2h)



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.

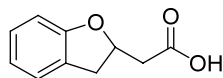
2-[(4*S*,5*S*)-5-Benzyl-2-oxo-3-tosylimidazolidin-4-yl]acetic Acid (2i)



2i

White solid; mp. 143–144 °C; $[\alpha]_{\text{D}}^{22} +17.7$ (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)

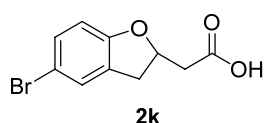


2j

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

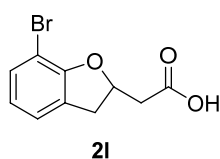
δ : 7.18 (d, J = 7.4 Hz, 1H), 7.08 (dd, J = 6.9, 6.9 Hz, 1H), 6.81 (dd, J = 7.4, 1.1 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 5.16–5.09 (m, 1H), 3.38–3.42 (m, 1H), 2.95–2.99 (m, 1H), 2.75–2.80 (m, 2H) ppm; ^{13}C NMR (acetone- d_6) δ : 171.8, 160.1, 128.7, 127.6, 125.9, 121.2, 109.9, 80.0, 40.9, 35.8 ppm; 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)



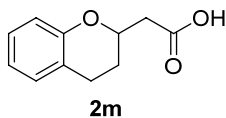
White solid; mp 132–133 °C (MeCN); $[\alpha]_D^{26} +43.5$ (c 1.2, CHCl_3 , for 78% ee); ^1H NMR (CDCl_3) δ : 7.27 (1H, s), 7.22 (1H, d, J = 8.0 Hz), 6.67 (1H, d, J = 8.0 Hz), 5.22–5.16 (1H, m), 3.45–3.41 (1H, m), 2.95–2.92 (2H, m), 2.76–2.73 (1H, m) ppm; ^{13}C NMR (CDCl_3) δ : 175.7, 158.0, 131.0, 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)



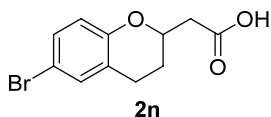
White solid; mp 102–103 °C (MeCN); $[\alpha]_D^{26} +43.5$ (c 1.2, CHCl_3 , for 78% ee); ^1H NMR (CDCl_3) δ : 7.27 (1H, d, J = 7.5 Hz), 7.10 (1H, d, J = 7.5 Hz), 6.74 (1H, dd, J = 7.5, 7.5 Hz), 5.28–5.21 (1H, m), 3.57–3.54 (1H, m), 3.09–3.02 (2H, m), 2.80–2.77 (1H, m) ppm; ^{13}C NMR (CDCl_3) δ : 176.0, 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)



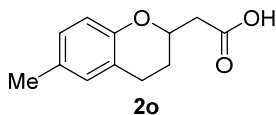
White solid; mp 89–90 °C (MeCN); $[\alpha]_D^{26} +74.0$ (*c* 1.56, CHCl₃, for 93% ee); ¹H NMR (acetone-*d*₆) δ: 7.06–7.00 (m, 2H), 6.80 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.57 (dd, *J* = 7.2, 2.0 Hz, 1H), 4.33–4.25 (m, 1H), 2.81–2.68 (m, 1H), 2.67–2.49 (m, 1H), 2.03–1.95 (m, 1H), 1.70–1.56 (m, 1H) ppm; ¹³C 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) [Chiralpak 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); $[\alpha]_D^{26} +77.5$ (*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) [Chiralpak IA, hexane/2-propanol = 99/1, 0.2 mL/min, λ = 254 nm, retention times: (major) 43.2 min (minor) 47.1 min].

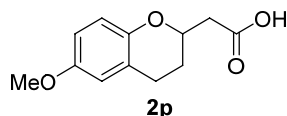
2-(6-Methylchroman-2-yl)acetic Acid (2o)



white solid; mp 120–121 °C (MeCN); $[\alpha]_D^{26} +58.9$ (*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

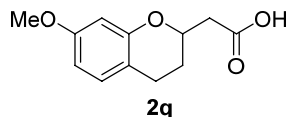
205.0870; HPLC (for methyl ester) [Chiralpak IC, hexane/2-propanol = 98/2, 1.0 mL/min, λ = 254 nm, retention times: (major) 10.6 min (minor) 11.8 min].

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



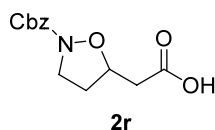
White solid; mp 108–109 °C (MeCN); $[\alpha]_D^{25} +76.1$ (*c* 0.74, CHCl₃, for 93% ee); ¹H NMR (CDCl₃) δ : 6.74 (1H, d, *J* = 9.0 Hz), 6.67 (1H, dd, *J* = 9.0, 2.7 Hz), 6.59 (1H, d, *J* = 2.7 Hz), 4.44–4.40 (1H, m), 3.74 (3H, s), 2.89–2.81 (2H, m), 2.77–2.72 (1H, m), 2.69–2.64 (1H, m), 2.12–2.07 (1H, 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; $[\alpha]_D^{25} +89.2$ (*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) 19.7min].

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

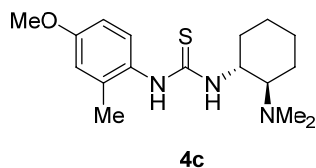


White solid; mp 82–83 °C (MeCN); ¹H NMR (CDCl₃) δ : 7.40–7.30 (m, 5H), 5.21 (s, 2H), 4.51–4.46 (m, 1H), 3.83–3.76 (m, 1H), 3.75–3.69 (m, 1H), 2.77 (dd, *J* = 16.0, 6.9 Hz, 1H), 2.57 (dd, *J* = 16.0,

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.

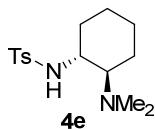
5. Preparation of new aminothiurea catalysts

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 °C (CHCl_3 : hexane); $[\alpha]_D^{23}$ –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.

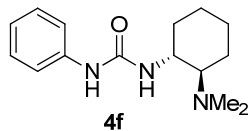
N-[(1*R*,2*R*)-2-(Dimethylamino)cyclohexyl]-4-methylbenzenesulfonamide (**4e**)



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; $[\alpha]_D^{26}$ –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} ;

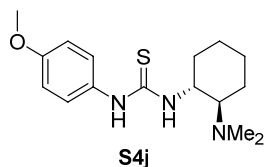
HRMS (ESI): calcd. for C₁₅H₂₅N₂O₂S [M+H]⁺ 297.1631, found 297.1620.

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



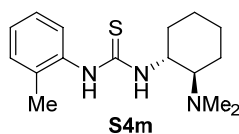
A procedure similar to that described for the preparation of **4j** (see below) afforded **4f** (810 mg, 62%). White solid; mp 120–121 °C (CHCl₃ : hexane); [α]_D²⁶ –63.7 (*c* 0.65, CHCl₃); ¹H NMR (CDCl₃) δ : 7.32–7.24 (5H, m), 7.01 (1H, t, *J* = 7.2 Hz), 5.72 (1H, br s), 3.46–3.42 (1H, m), 2.47–2.42 (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; ¹³C NMR (CDCl₃) 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 C₁₅H₂₄N₃O [M+H]⁺ 262.1914 found 262.1914.

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



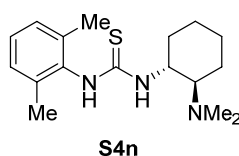
To a stirred solution of (1*R*,2*R*)-*N*^{*l*},*N*^{*l*}-dimethylcyclohexane-1,2-diamine (284 mg, 2.0 mmol) in THF (5 mL), was added 4-methoxyphenylisothiocyanate at room temperature. After being stirred at room temperature for 6 h, the mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (CHCl₃ : MeOH : NEt₃ = 100 : 10 : 1) to afford **4j** (587 mg, 96%): colorless amorphous; [α]_D²⁶ –90.7 (*c* 0.95, CHCl₃); ¹H NMR (CDCl₃) 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; ¹³C NMR (CDCl₃) 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 C₁₆H₂₆N₃OS [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; $[\alpha]_D^{26} -42.8$ (*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-[(1R,2R)-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); $[\alpha]_D^{26} -37.6$ (*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.

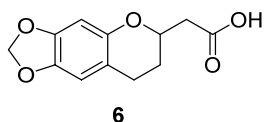
6. General procedure for the asymmetric reaction

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 (EtOAc : 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 (CHCl_3 : 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.

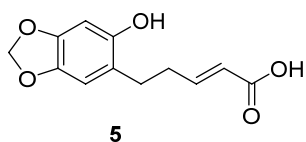
2-(7,8-Dihydro-6H-[1,3]dioxolo[4,5-g]chromen-6-yl)acetic Acid (6**)**



White solid; mp 122–124 °C (MeCN); $[\alpha]_D^{26} +59.0$ (*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

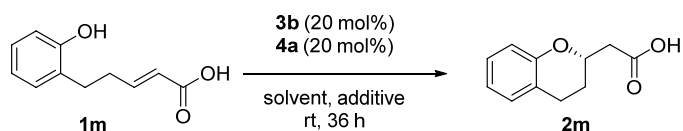
(E)-5-(6-Hydroxybenzo[d][1,3]dioxol-5-yl)pent-2-enoic Acid (5**)**



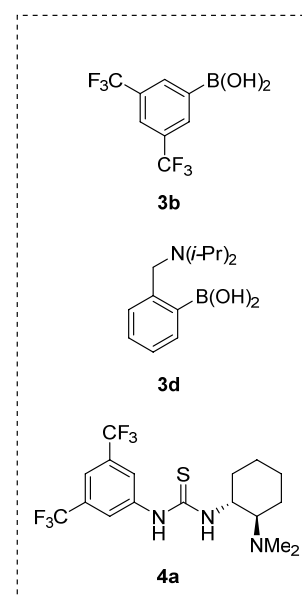
To a stirred mixture of 7,8-dihydro-6H-[1,3]dioxolochromen-6-ol⁵ (1.60 g, 8.24 mmol) in THF (20 mL), was added *tert*-butyl 2-(triphenylphosphoranylidene) acetate (4.65 g, 12.4 mmol) at room temperature. After being stirred for 12 h, the mixture was concentrated in *vacuo*. The residue was purified by 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

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



| entry ^l | 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 | - |

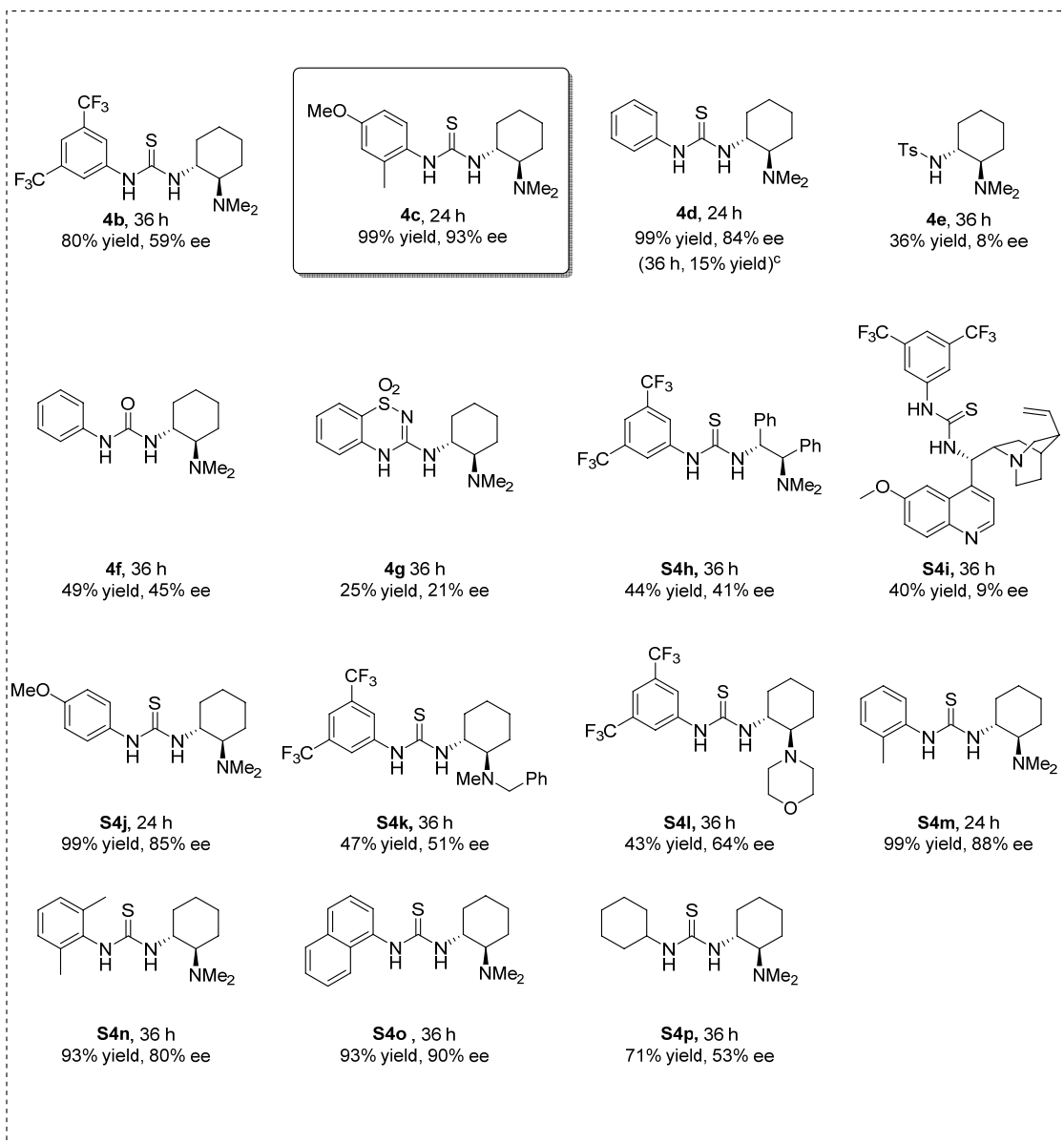
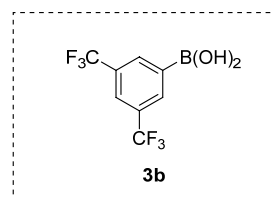
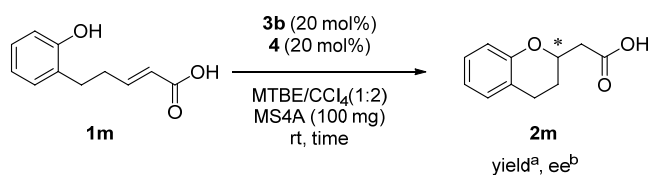


^a 30 mg of additive was used. ^b Determined by ¹H NMR. ^c Estimated after treatment with TMSCHN₂.

^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

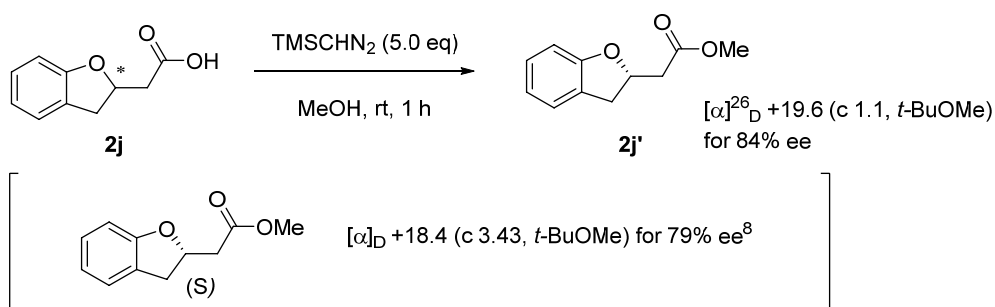


^a Determined by ¹H NMR. ^b Estimated after treatment with TMSCHN₂. ^c Phenylboronic acid was used instead of **3b**.

10. Determination of the absolute configuration

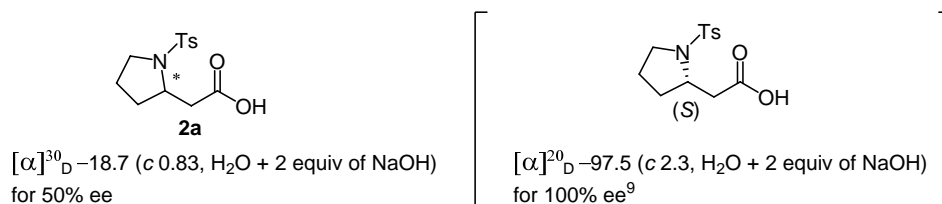
10-1. Determination of the absolute configuration of **2j**

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**.



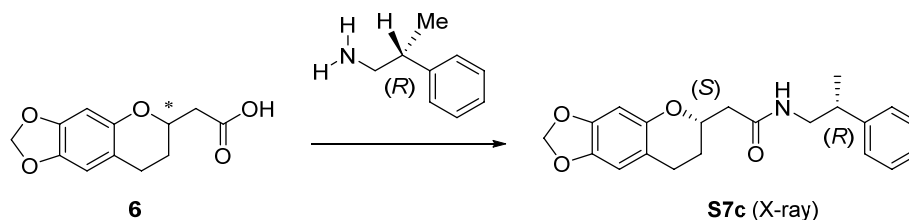
10-2. Determination of the absolute configuration of **2a**

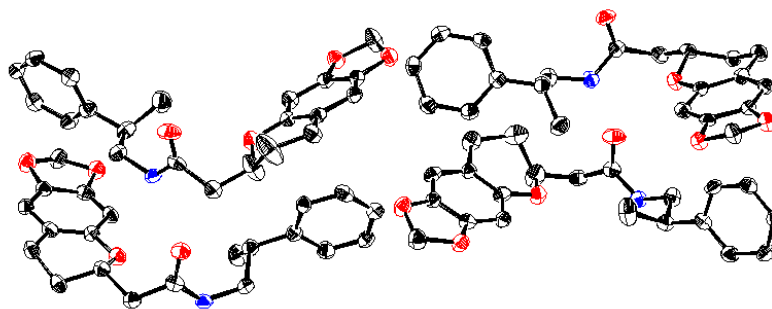
The absolute configuration of **2a** was determined as *S* by comparison of the optical rotation value with the reported one⁹ (See below).



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**.





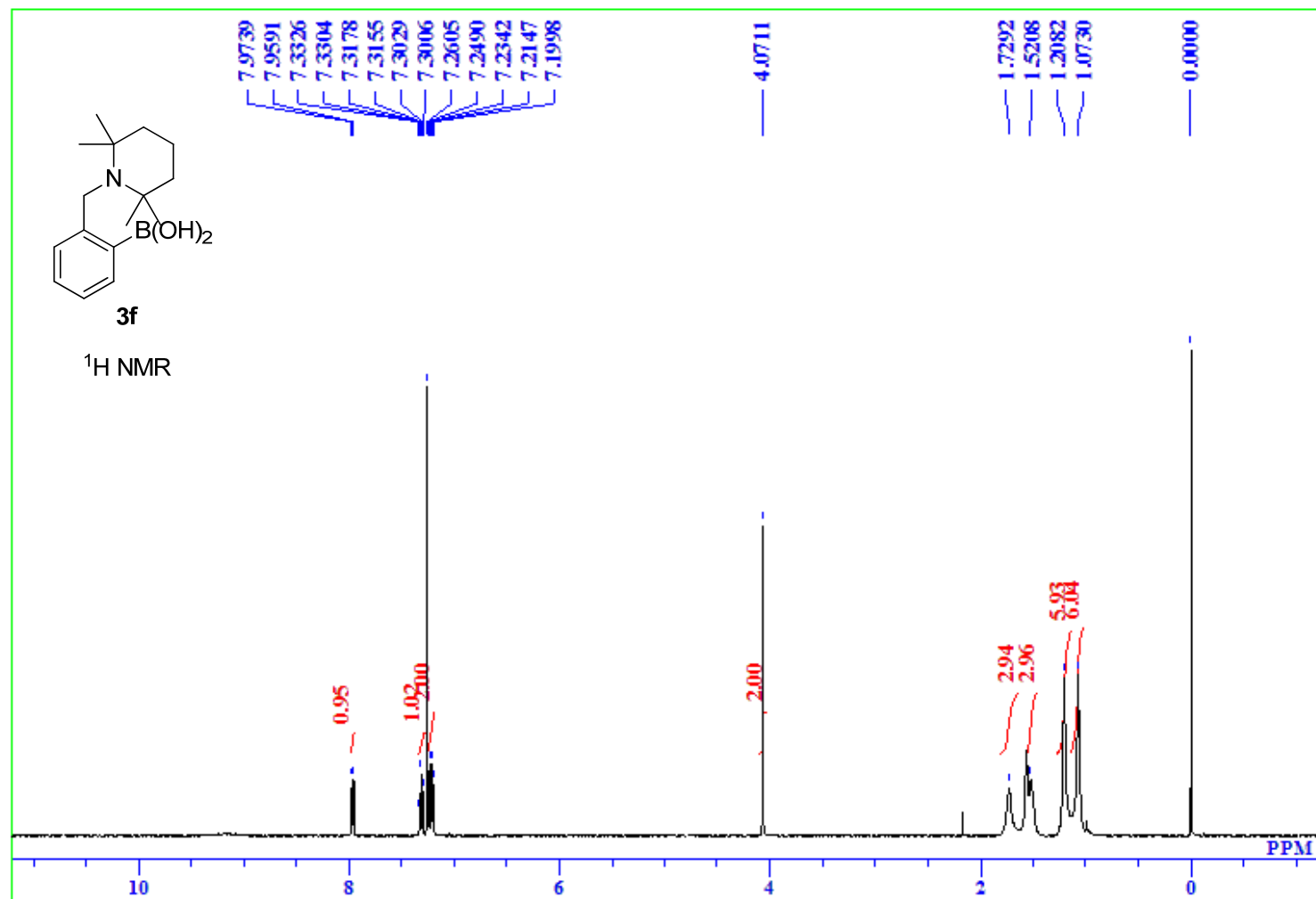
ORTEP diagram of **S7c**. Hydrogen atoms are omitted for clarity.

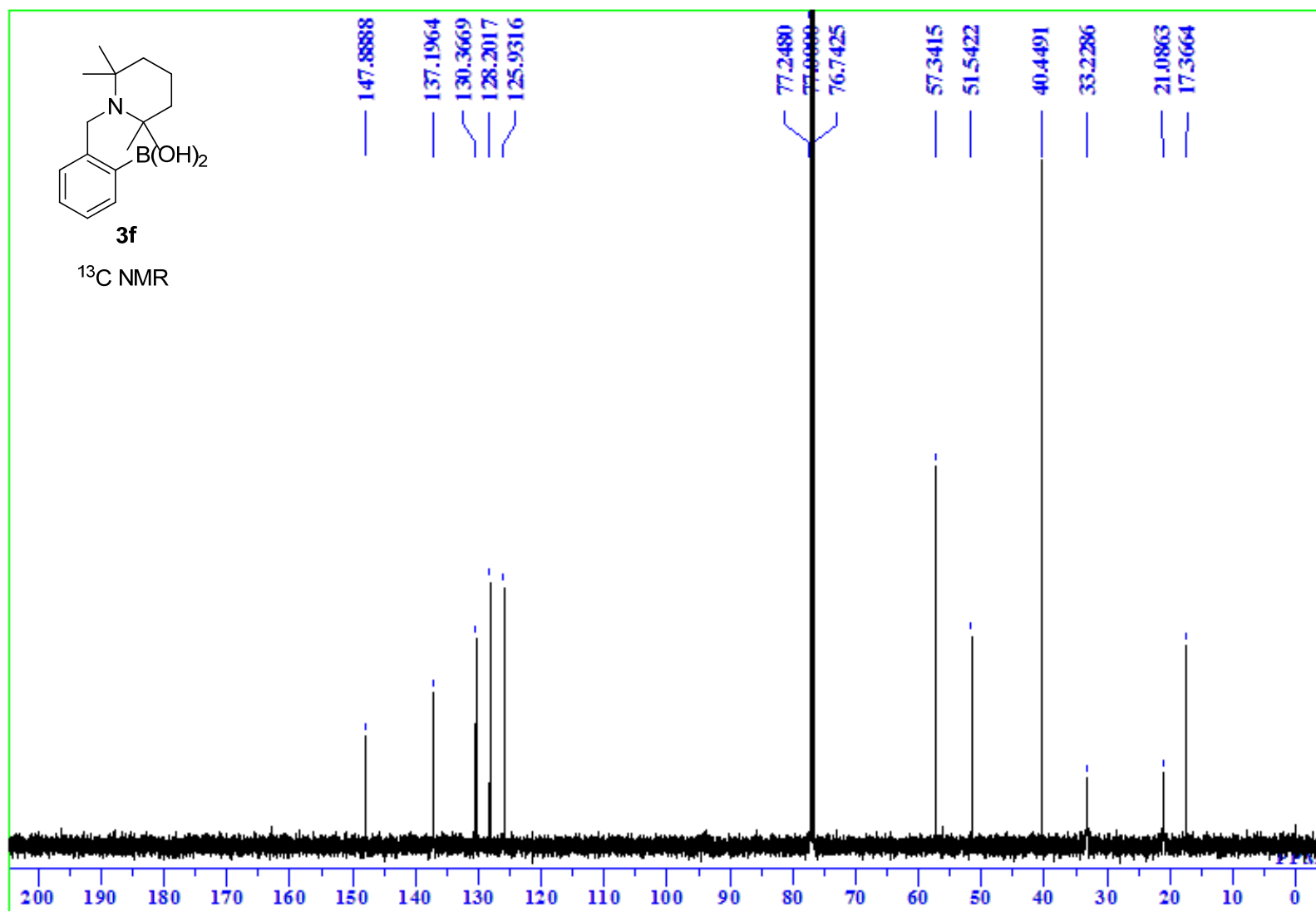
CCDC 1002990 (**S7c**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

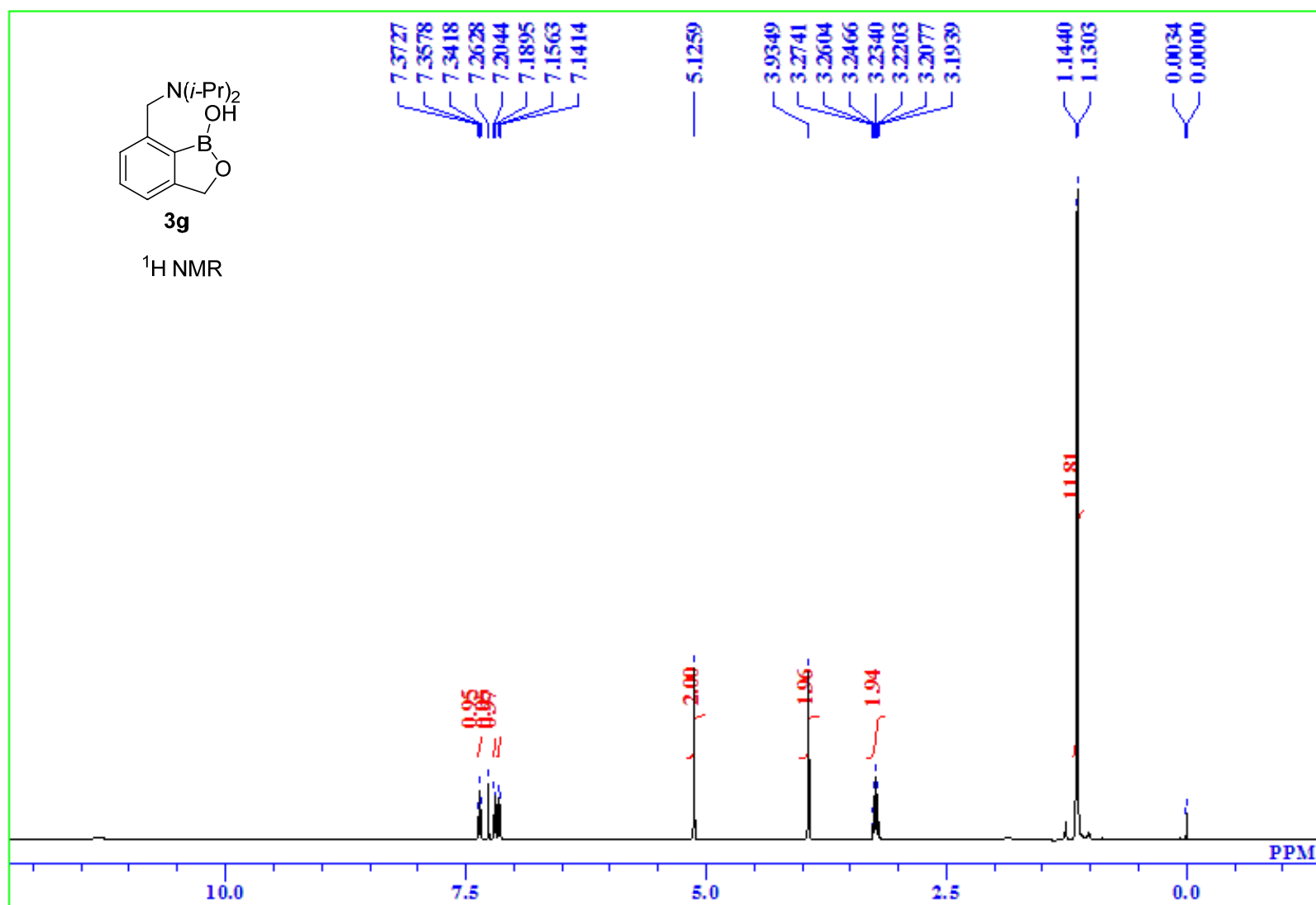
11. References

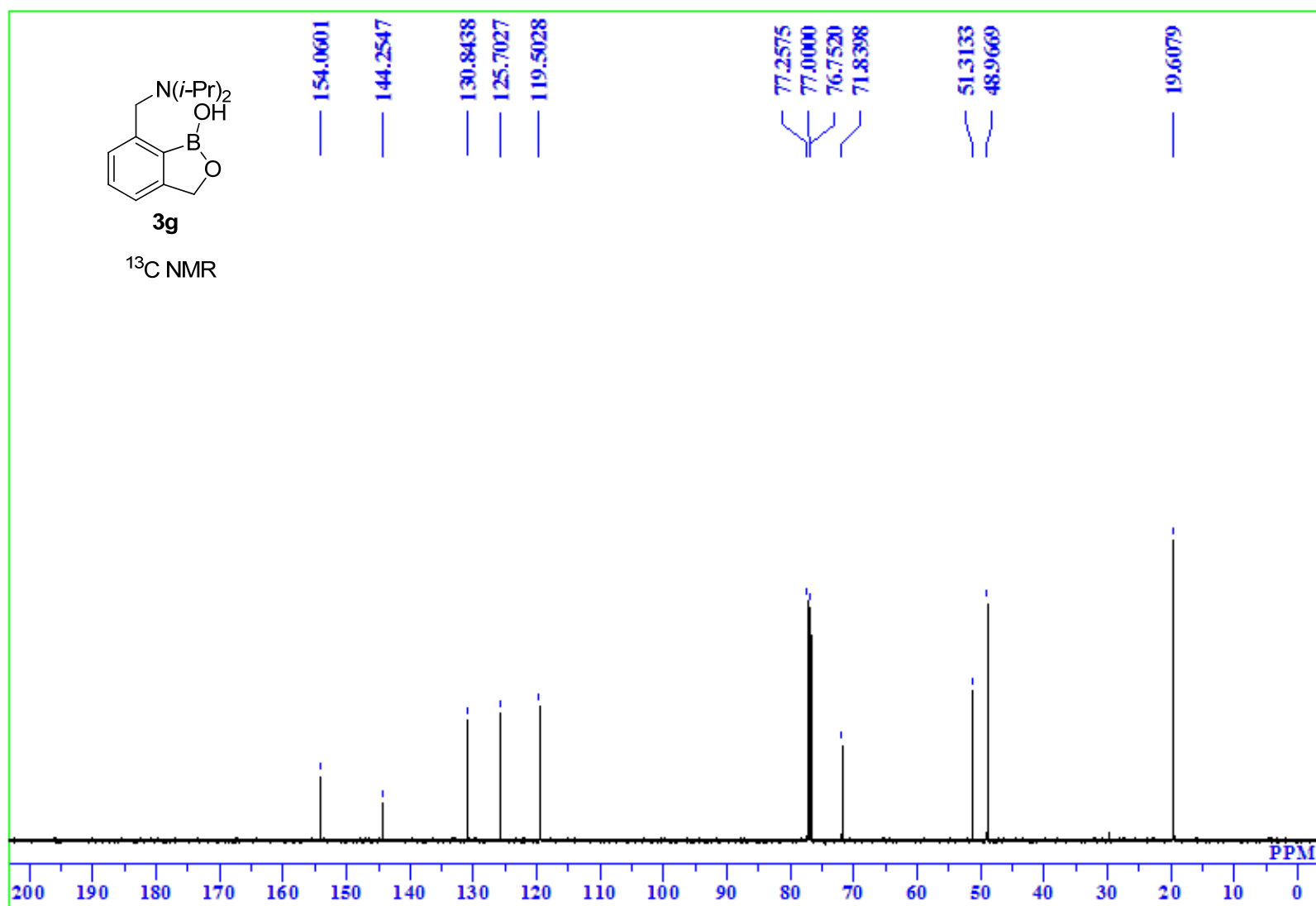
- 1) dos Santos, L. C.; Bahlaouan, Z.; Kassimi, K. E.; Troufflard, C.; Hendra, F.; Delarue-Cochin, S.; Zahouily, M.; Cavé, C.; Joseph, D. *Heterocycles*. **2007**, *73*, 751.
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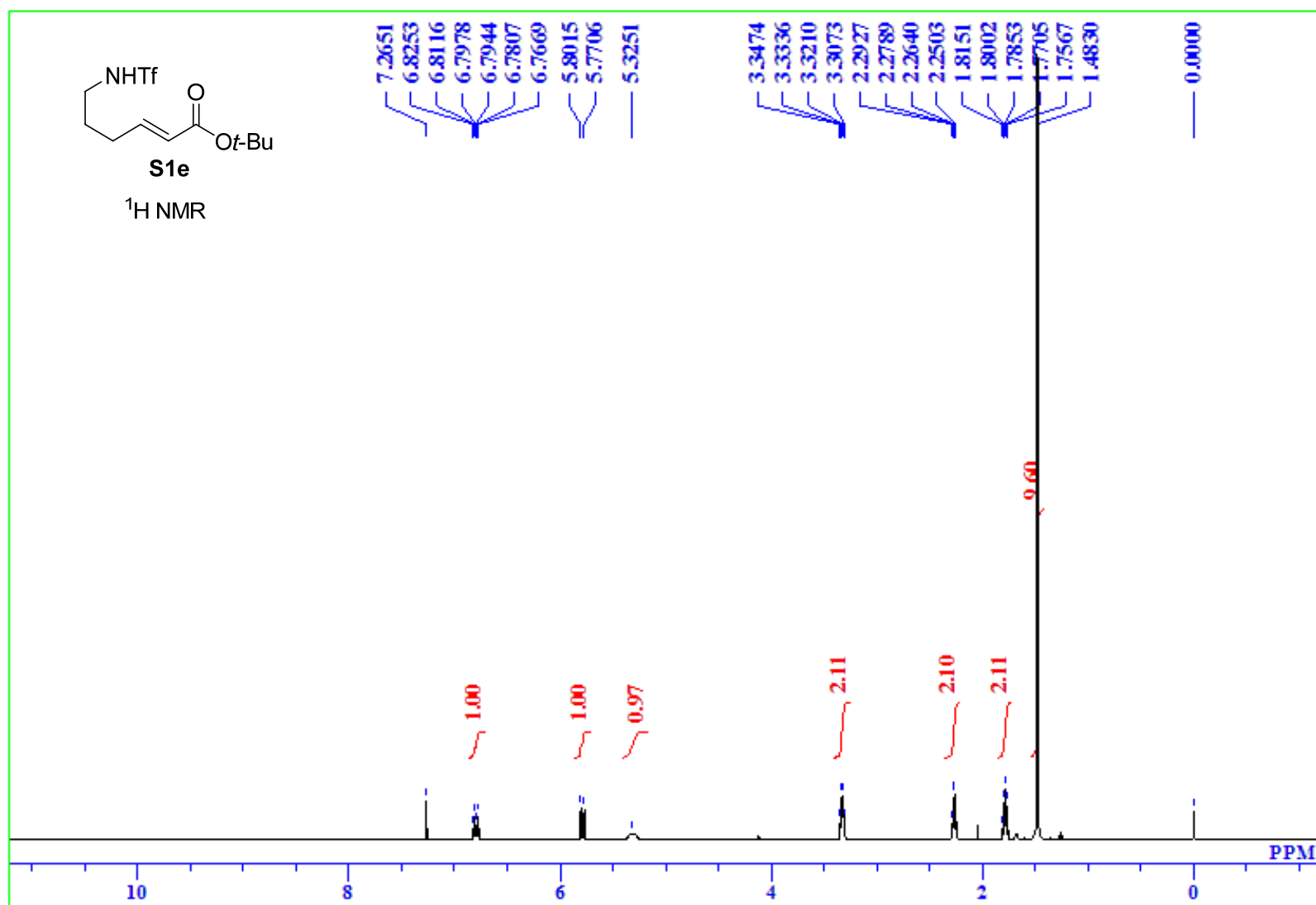
12. Copies of ^1H and ^{13}C NMR charts

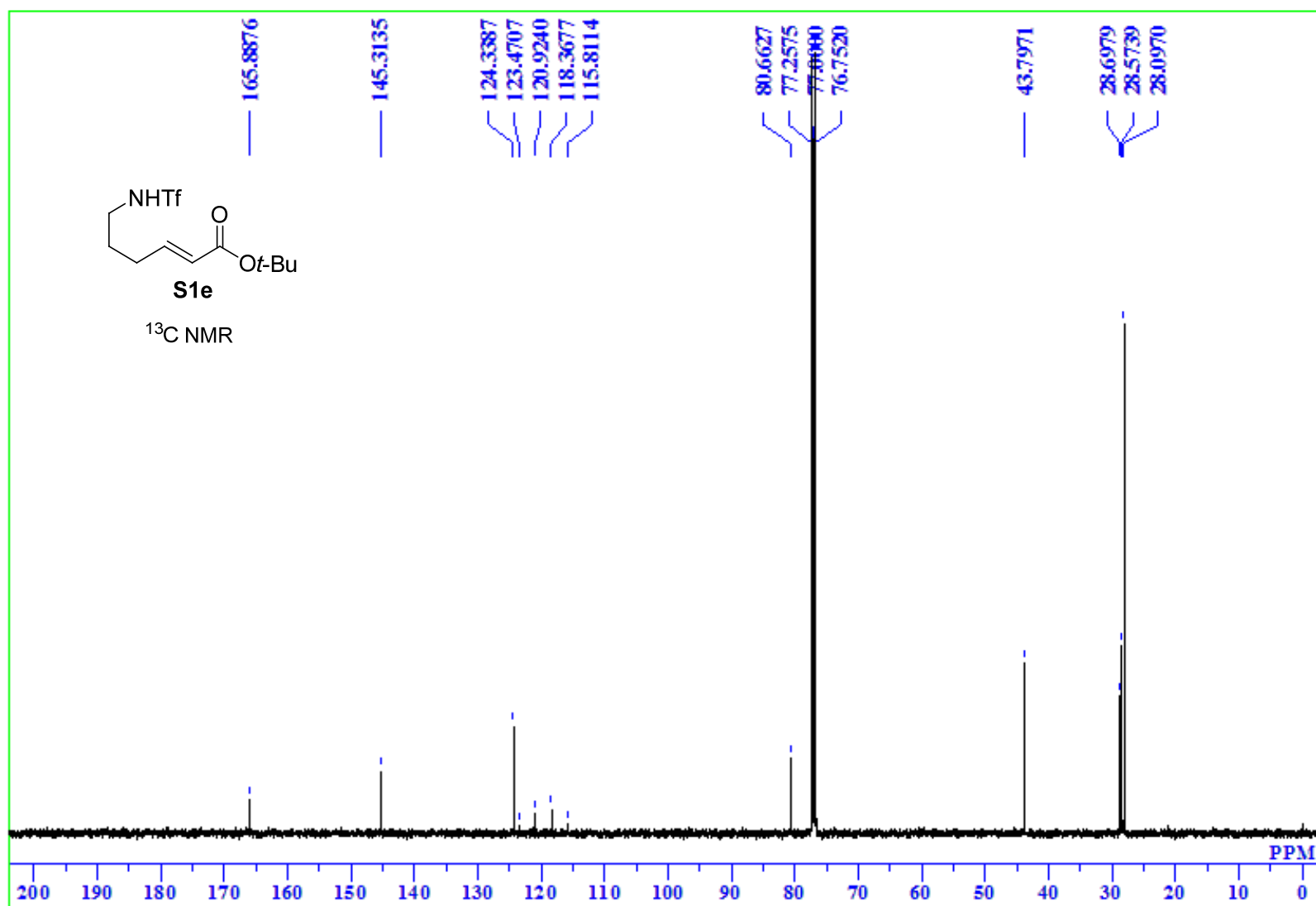


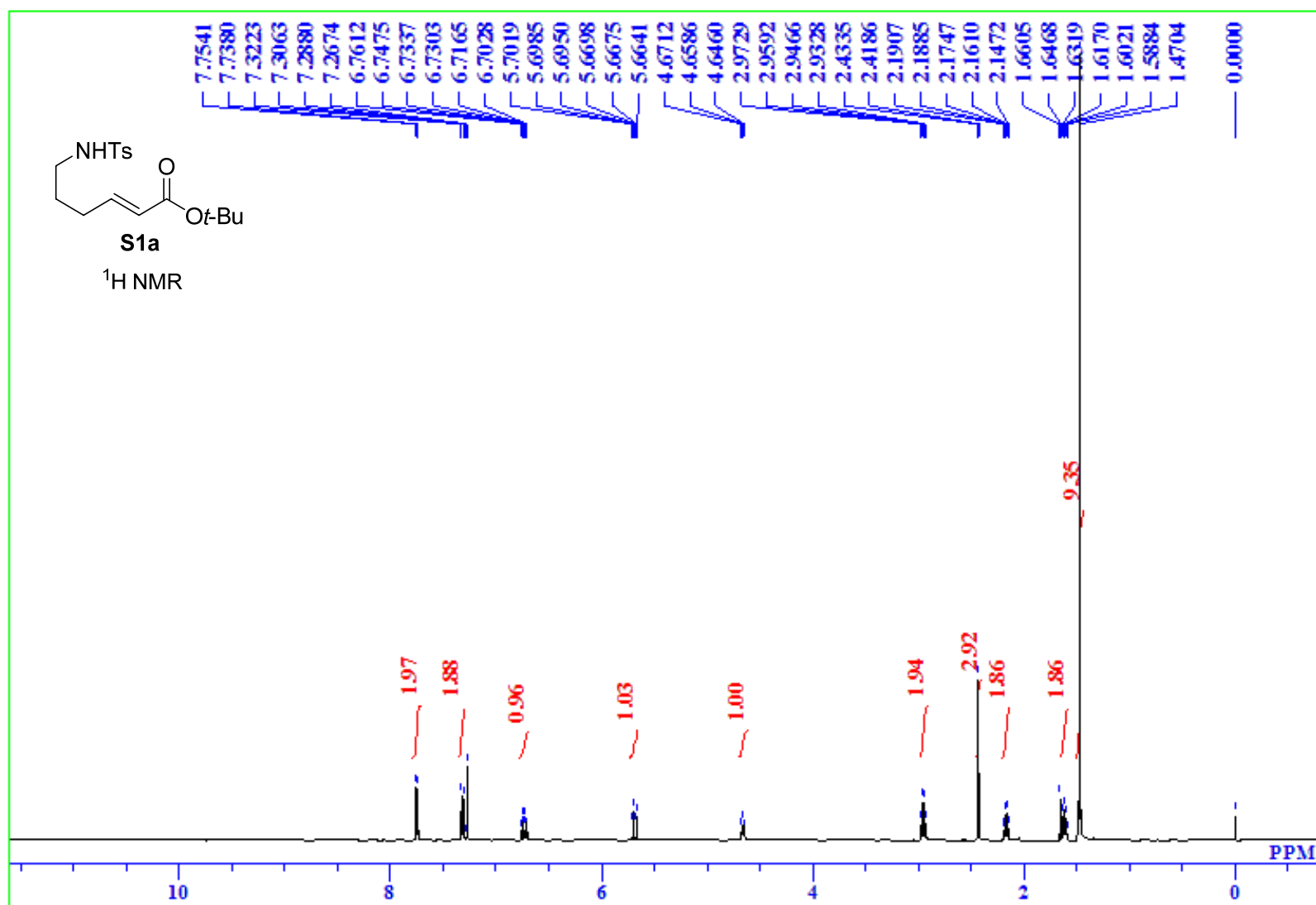


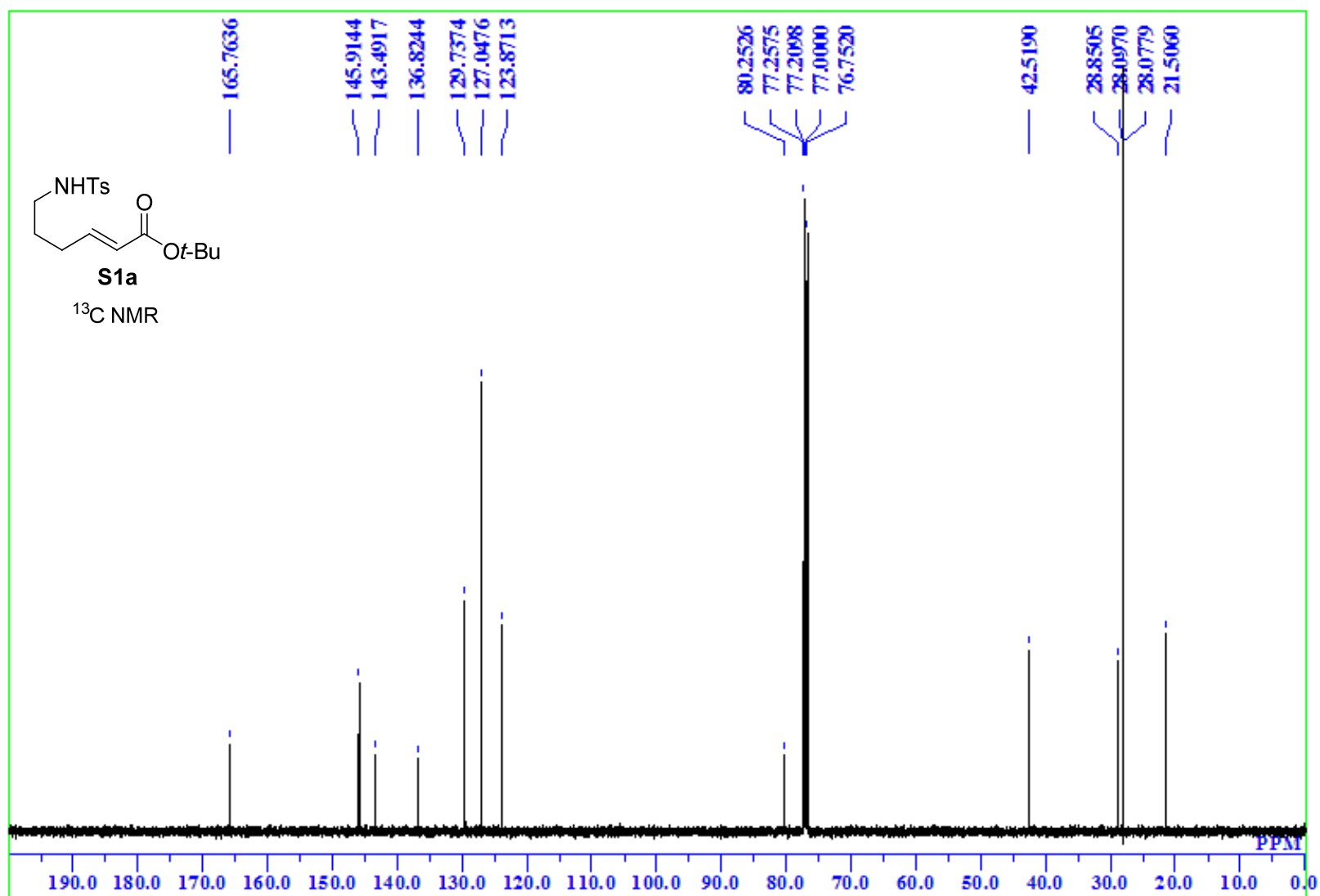


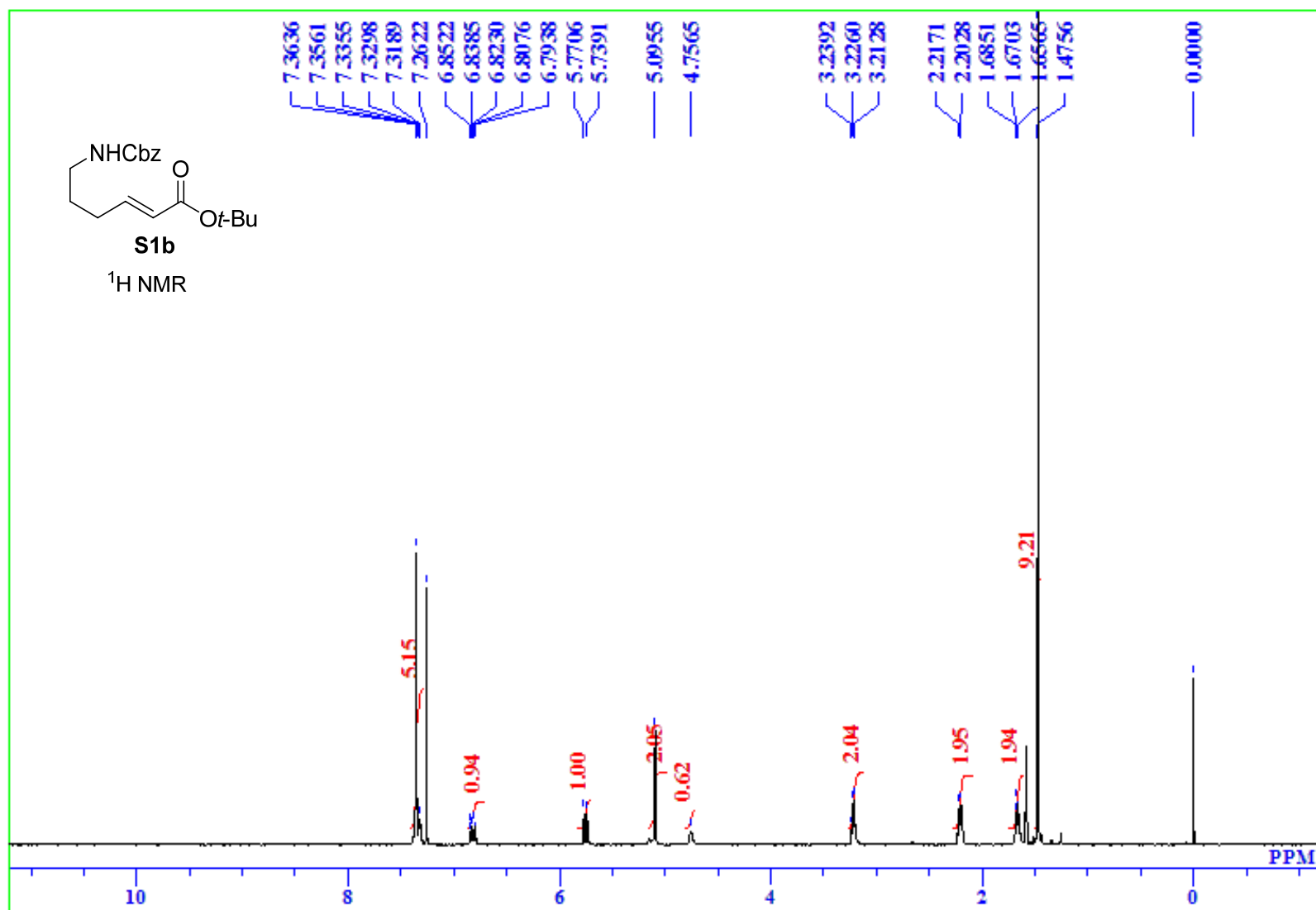


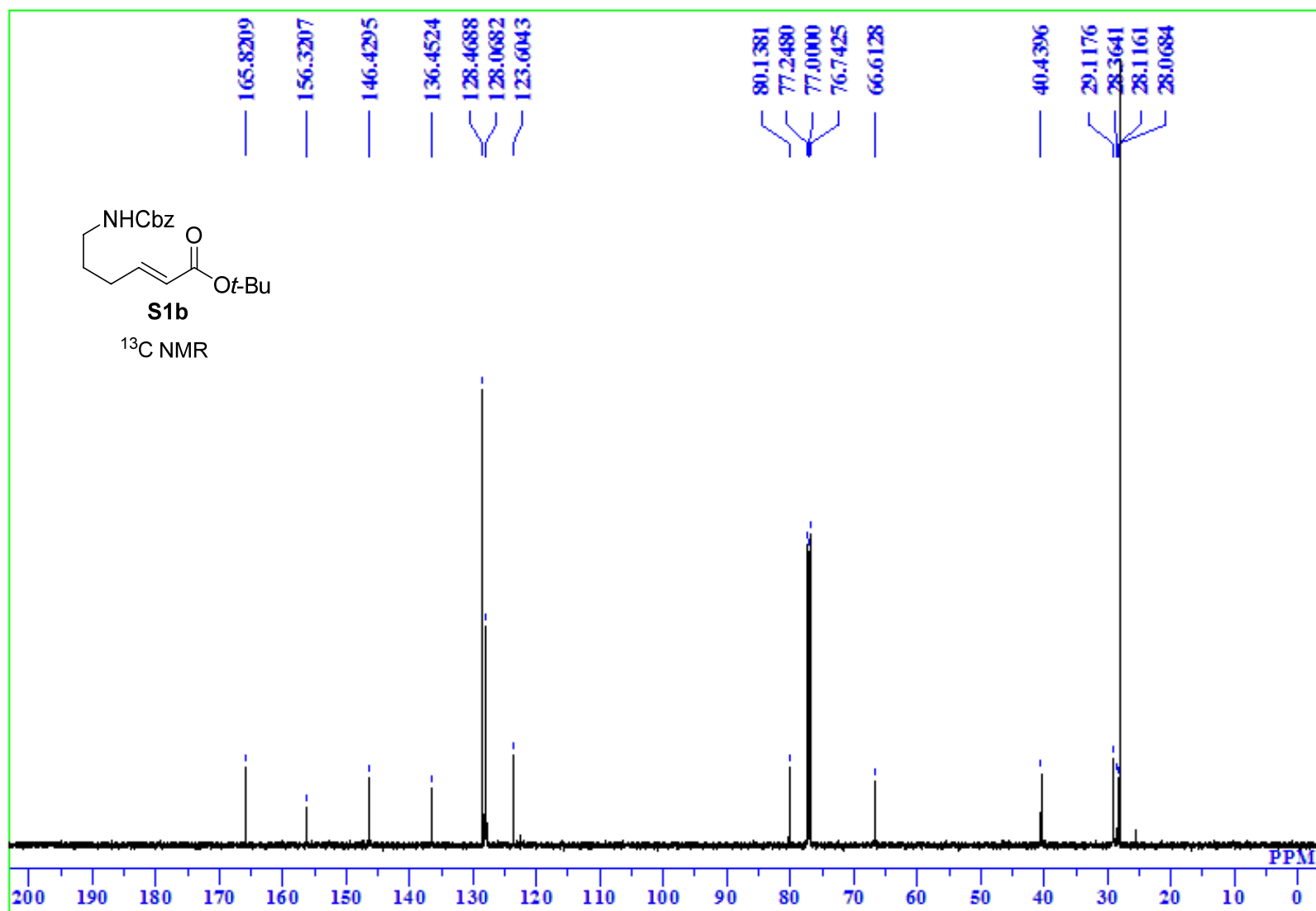


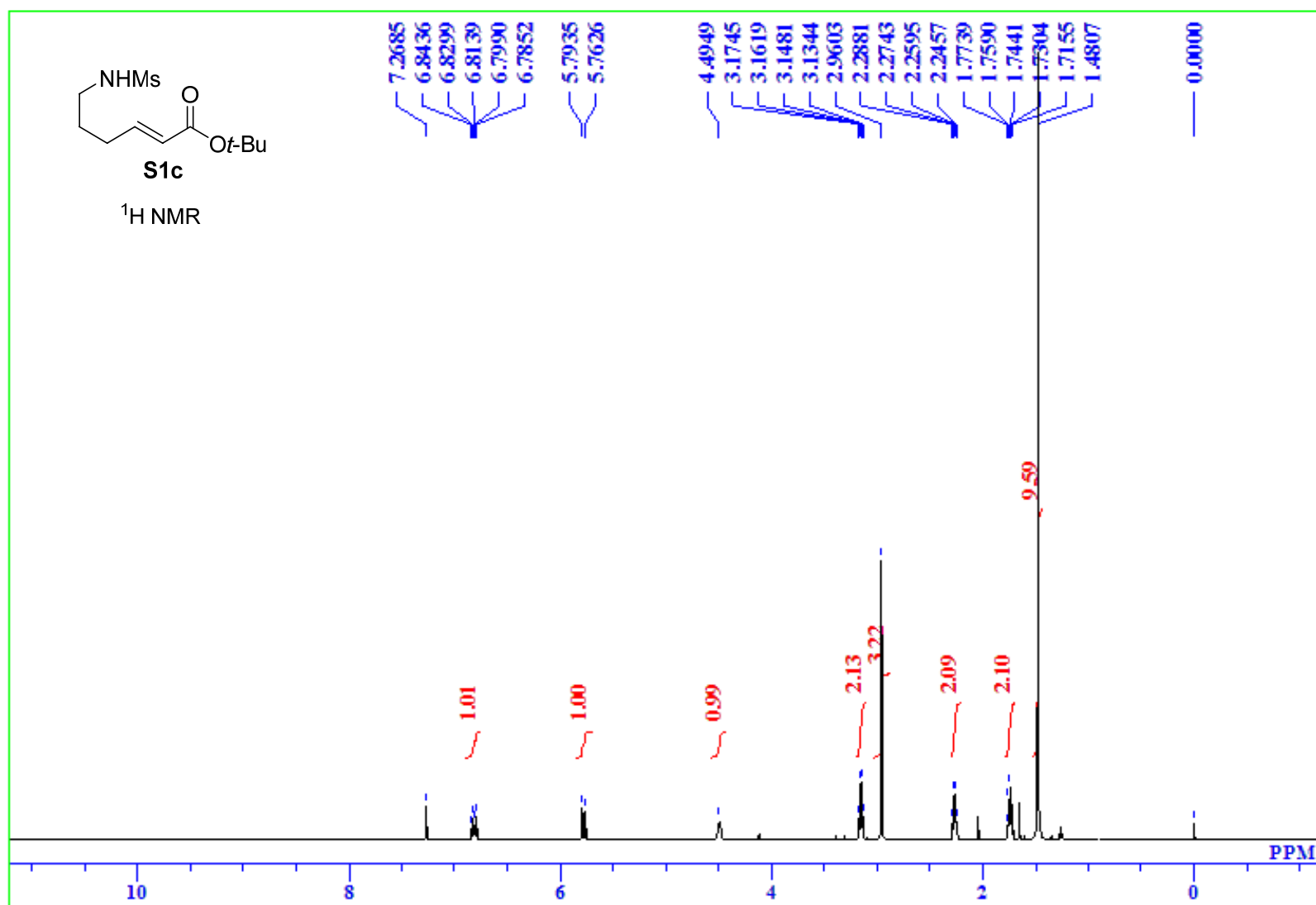


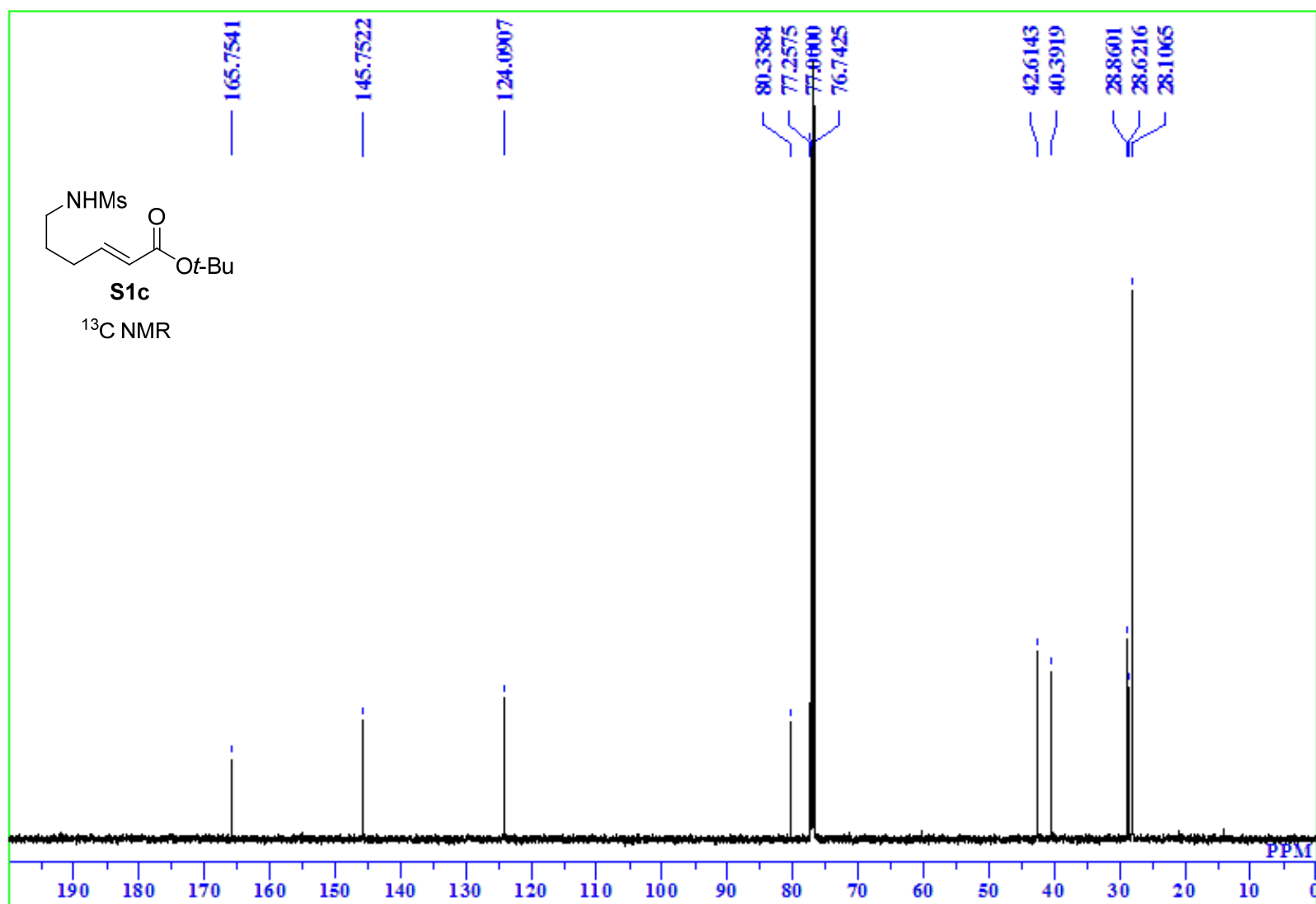


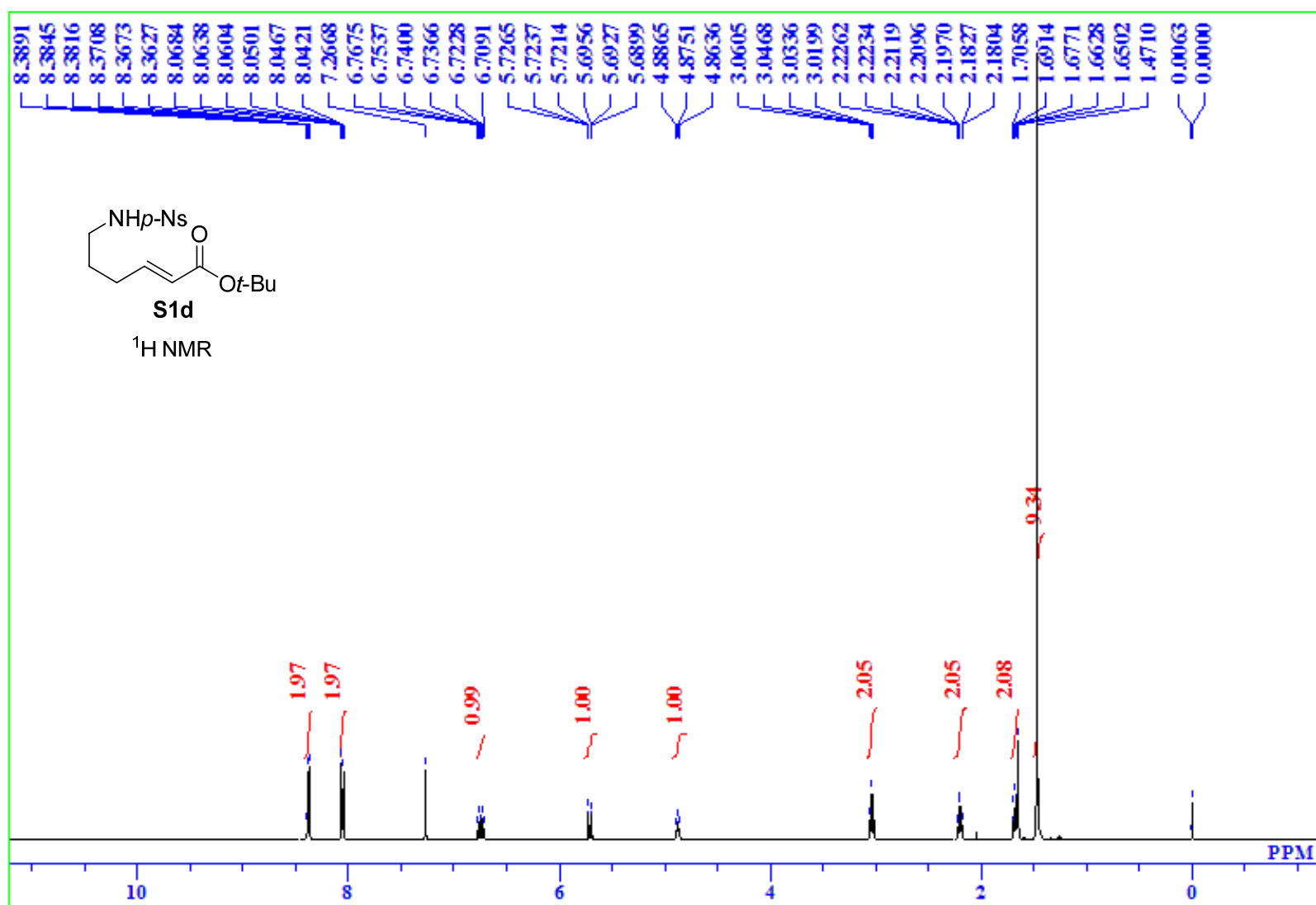


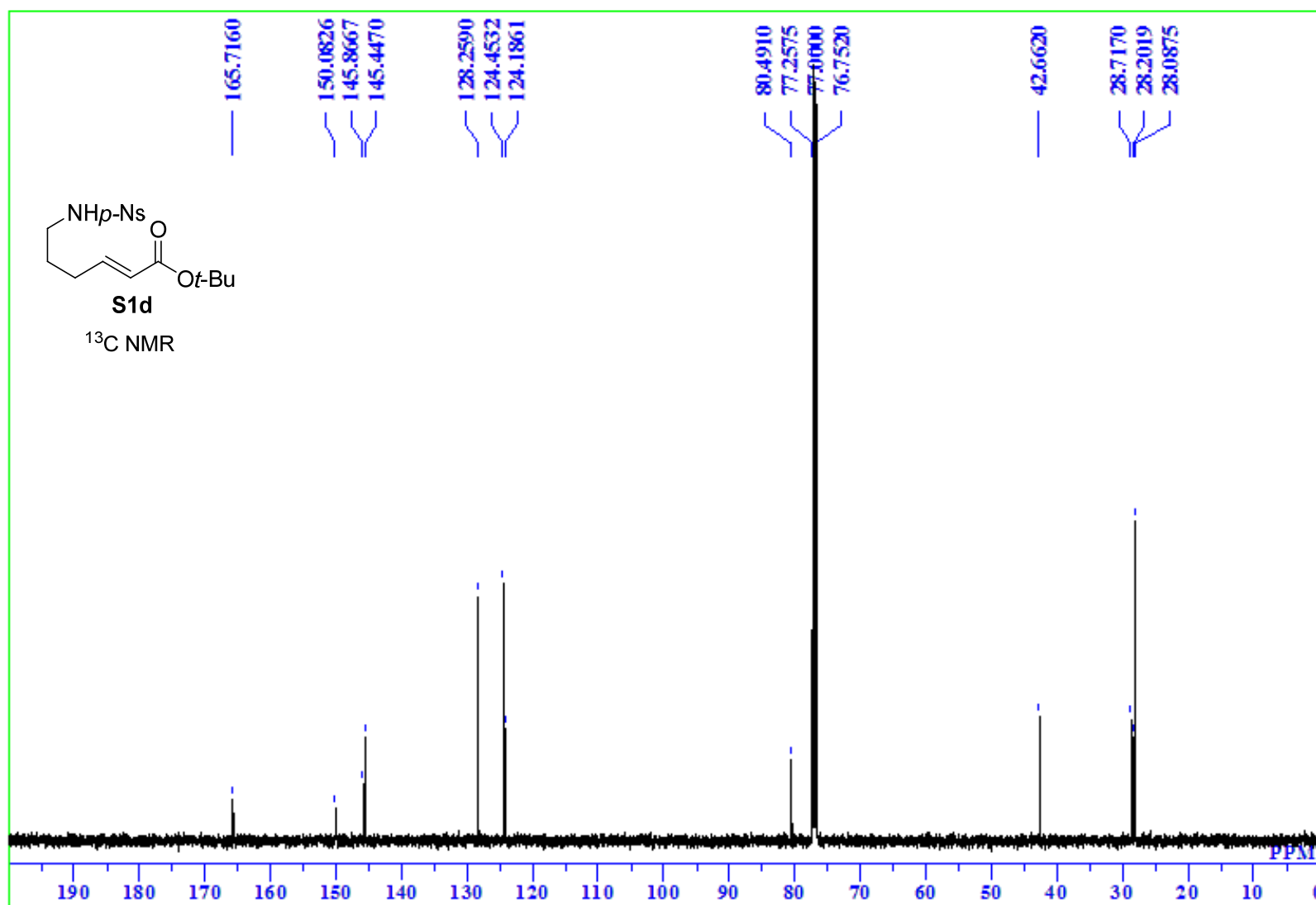


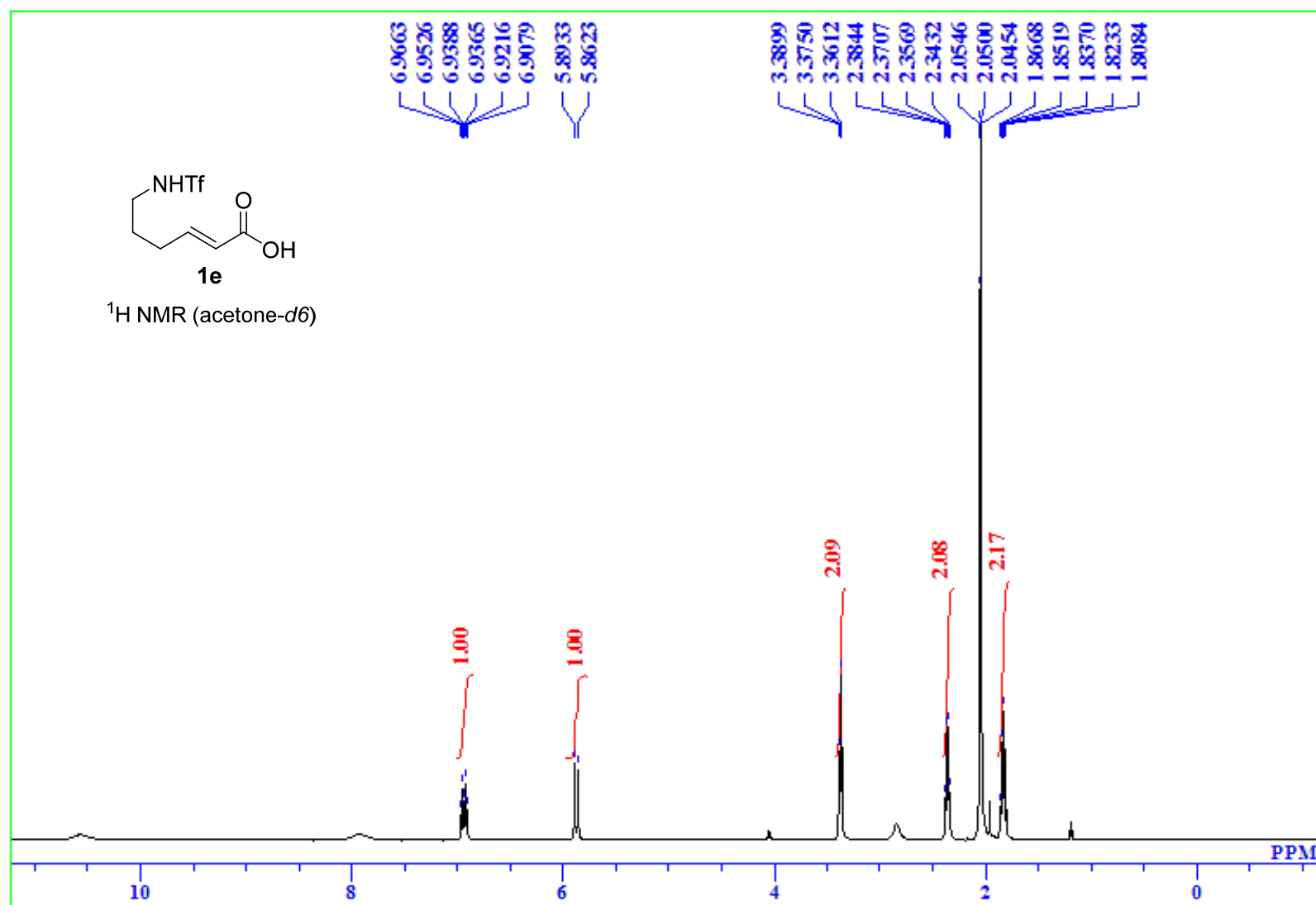


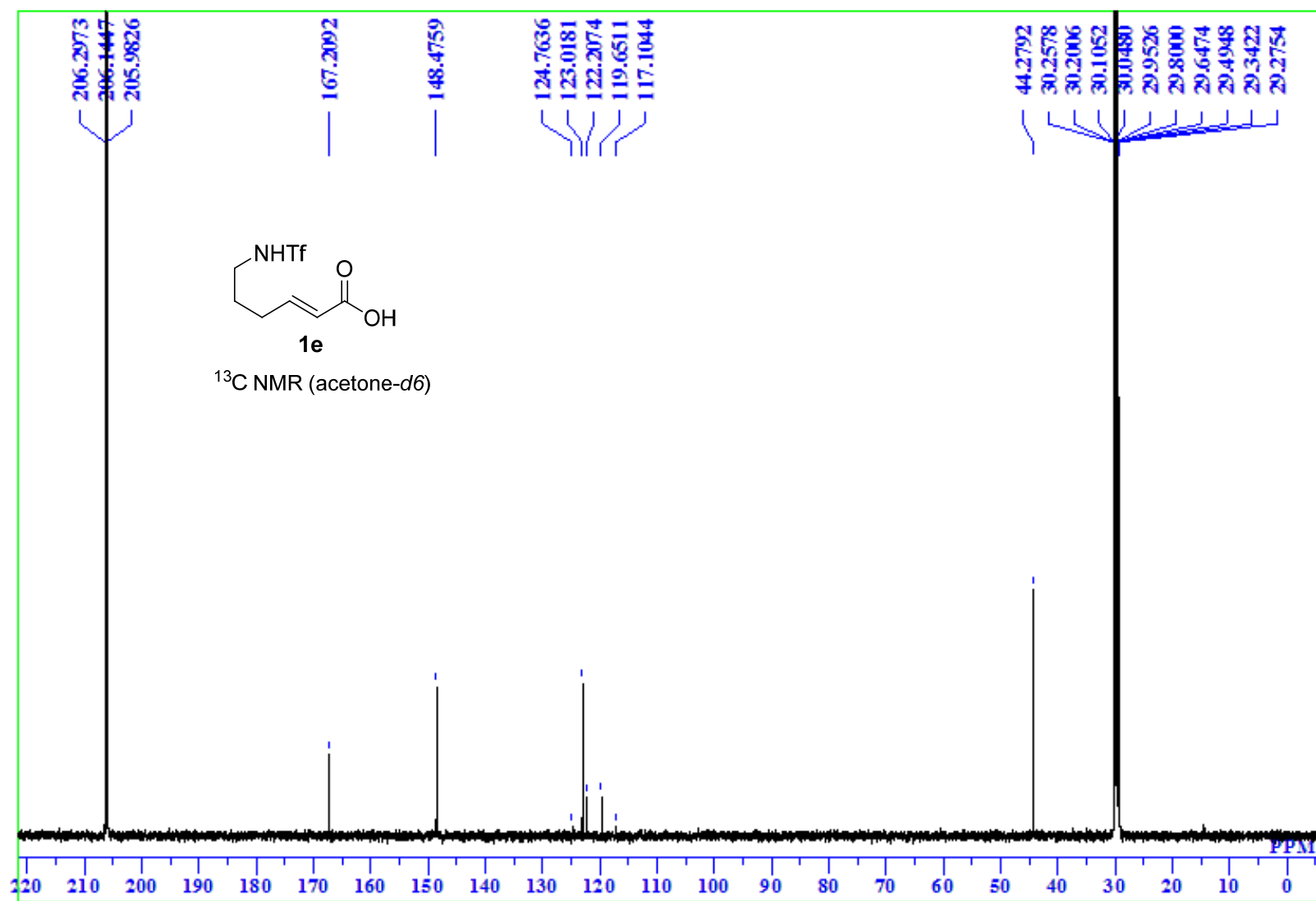


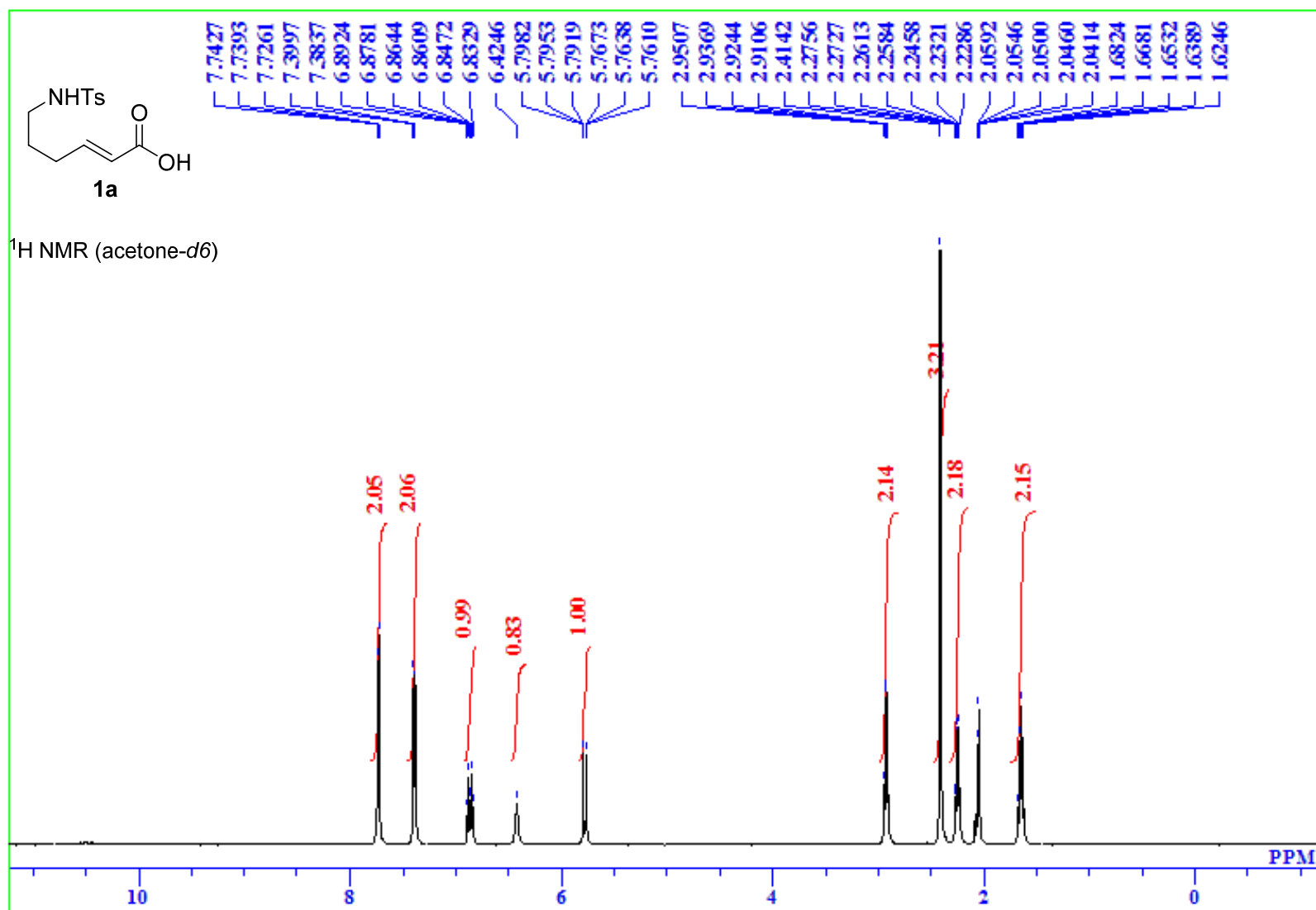


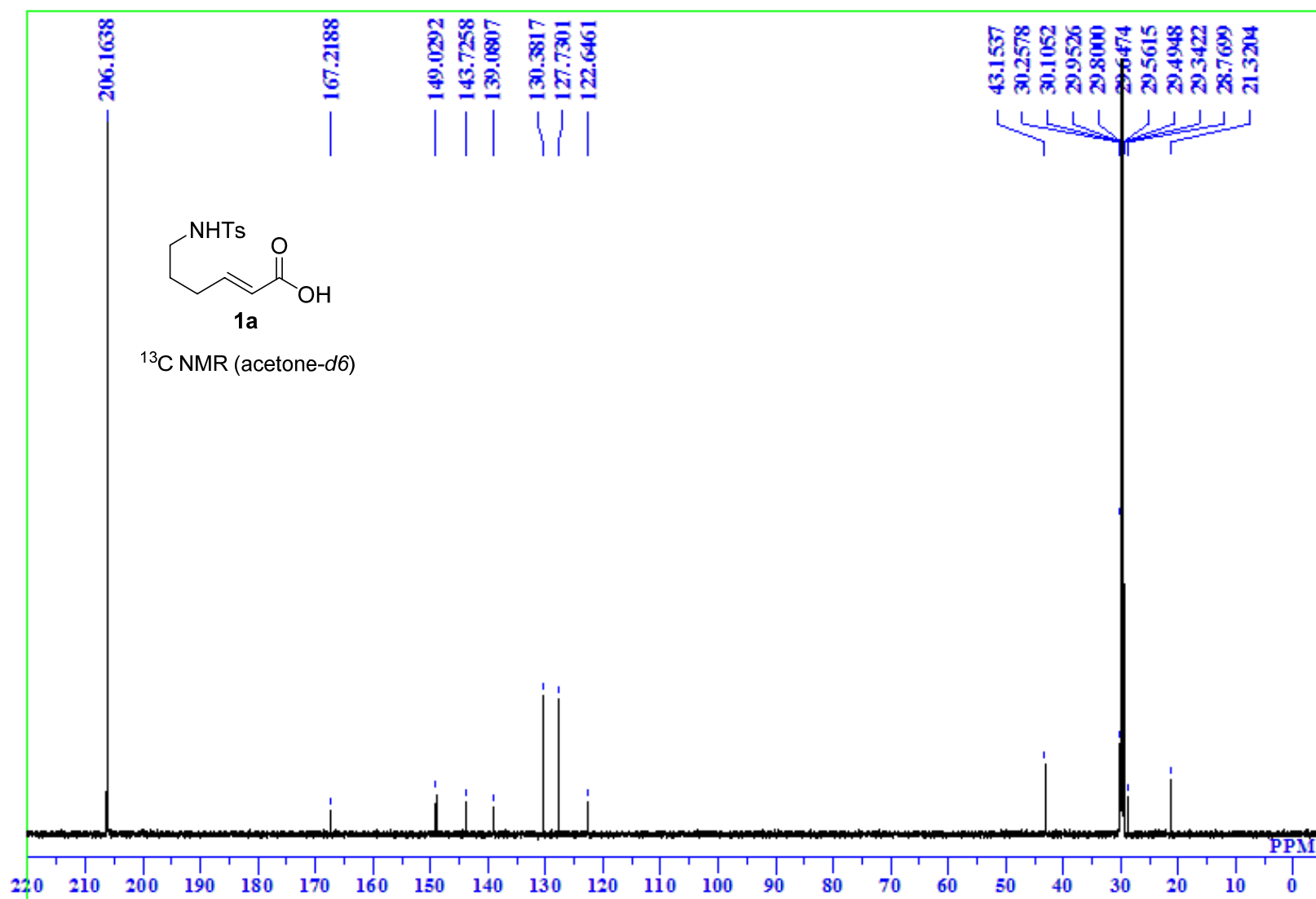


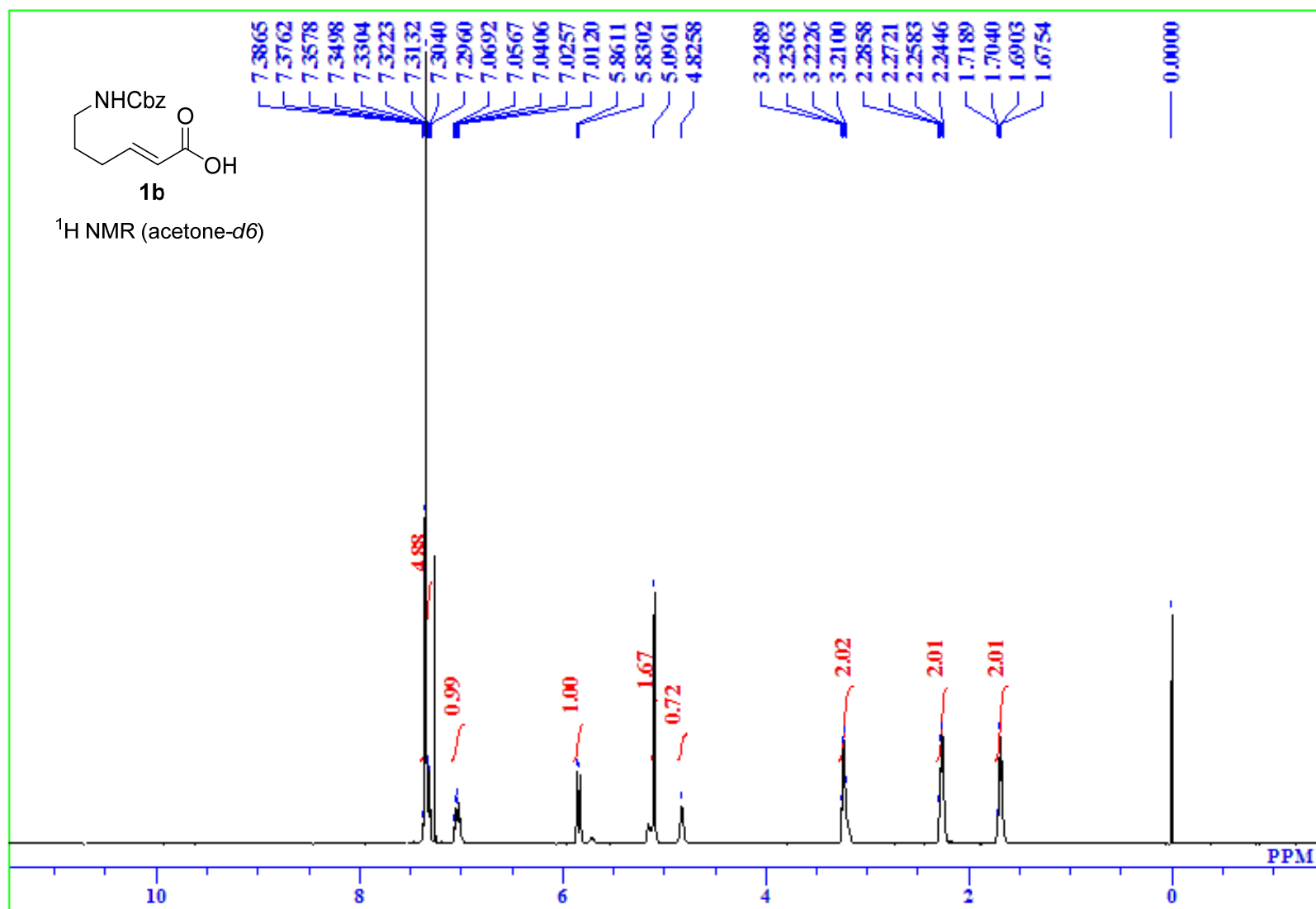


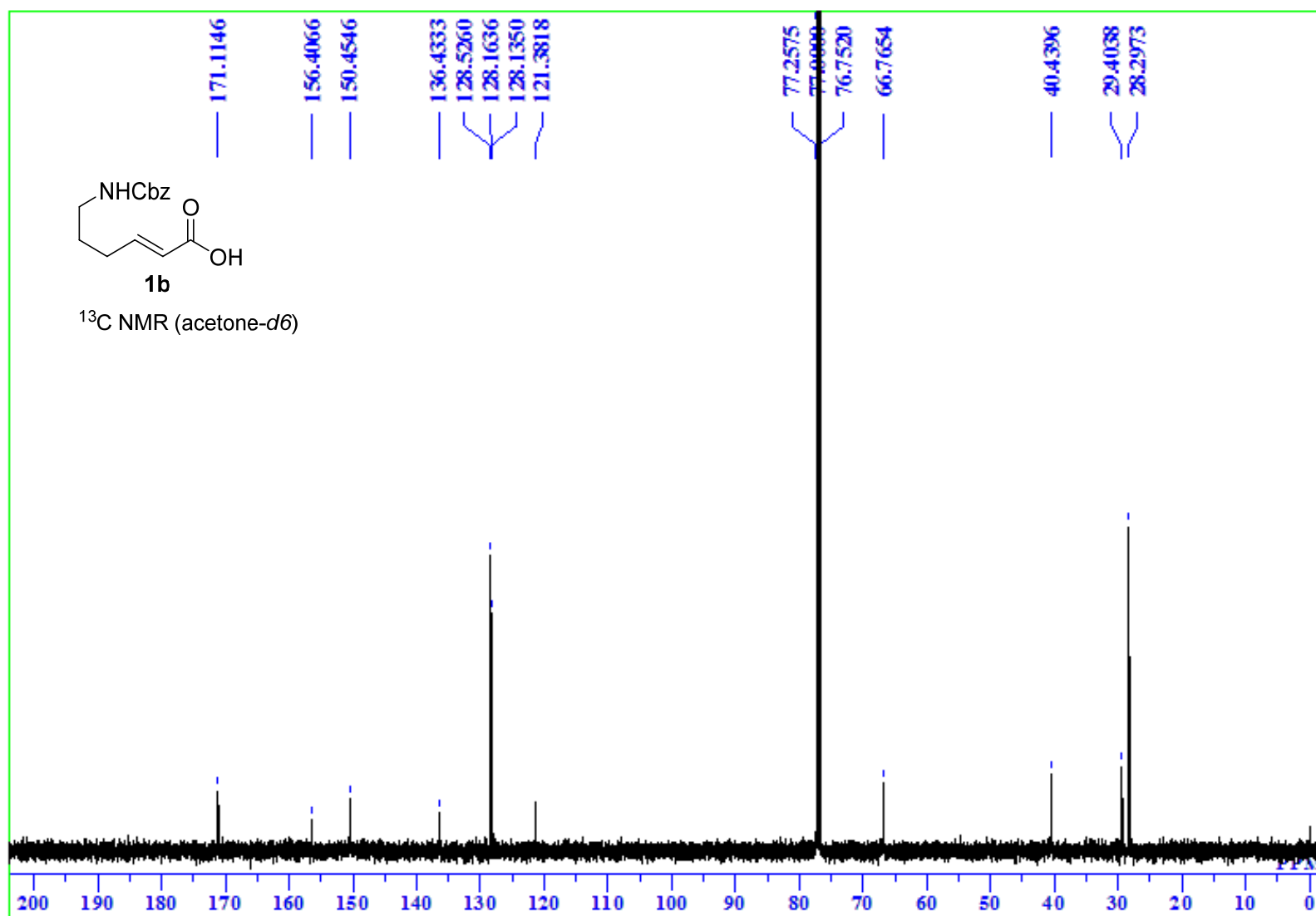


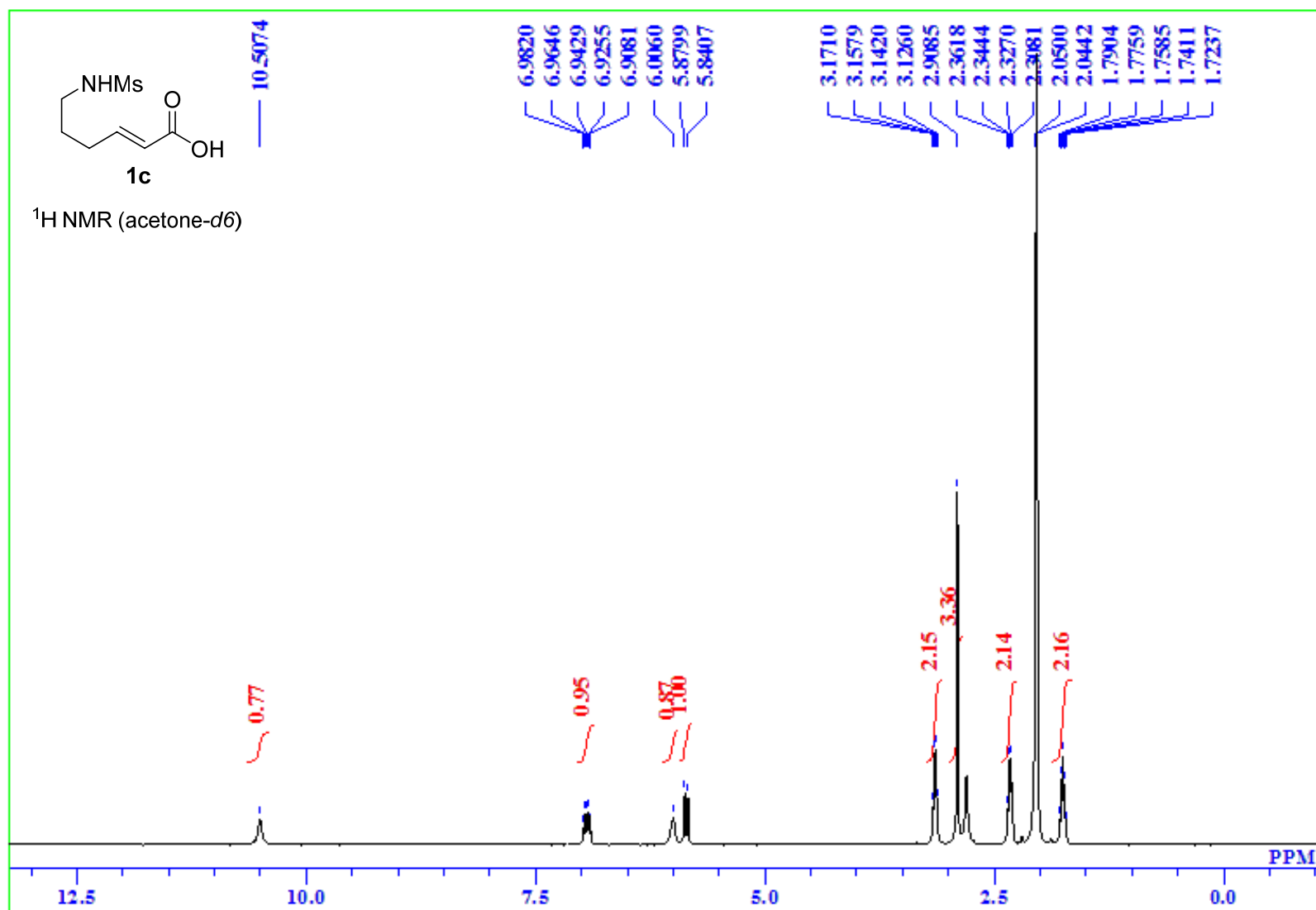


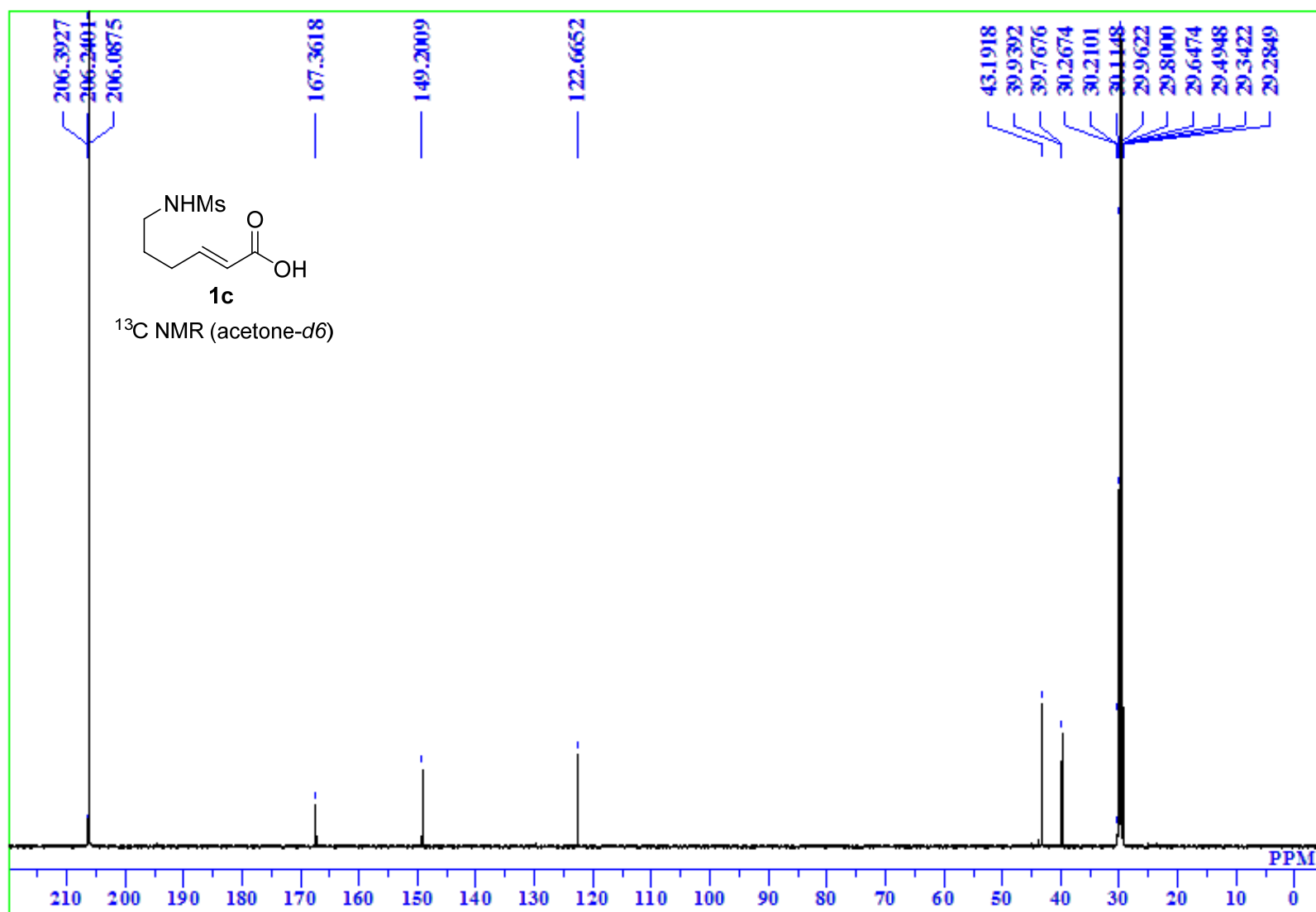


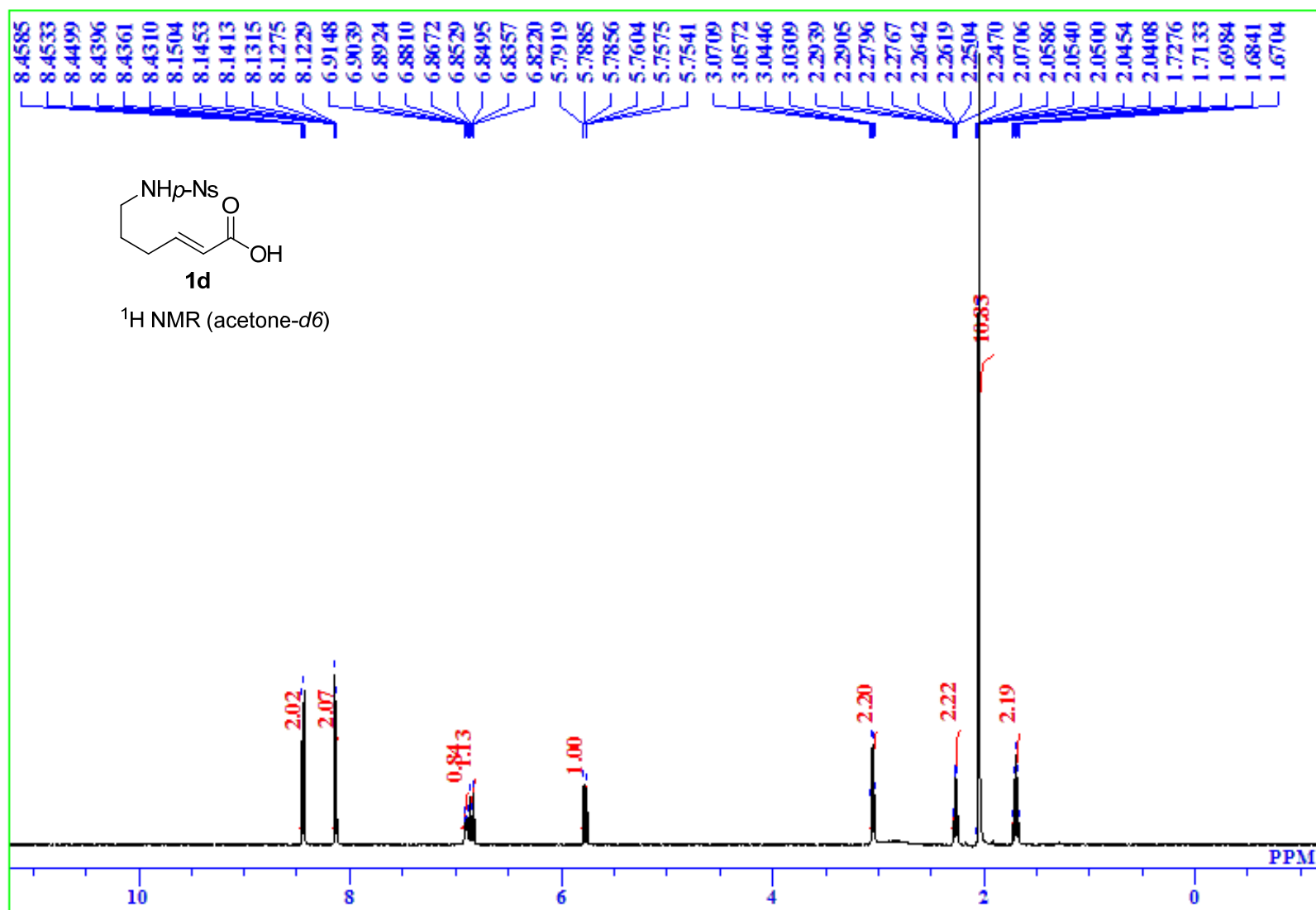


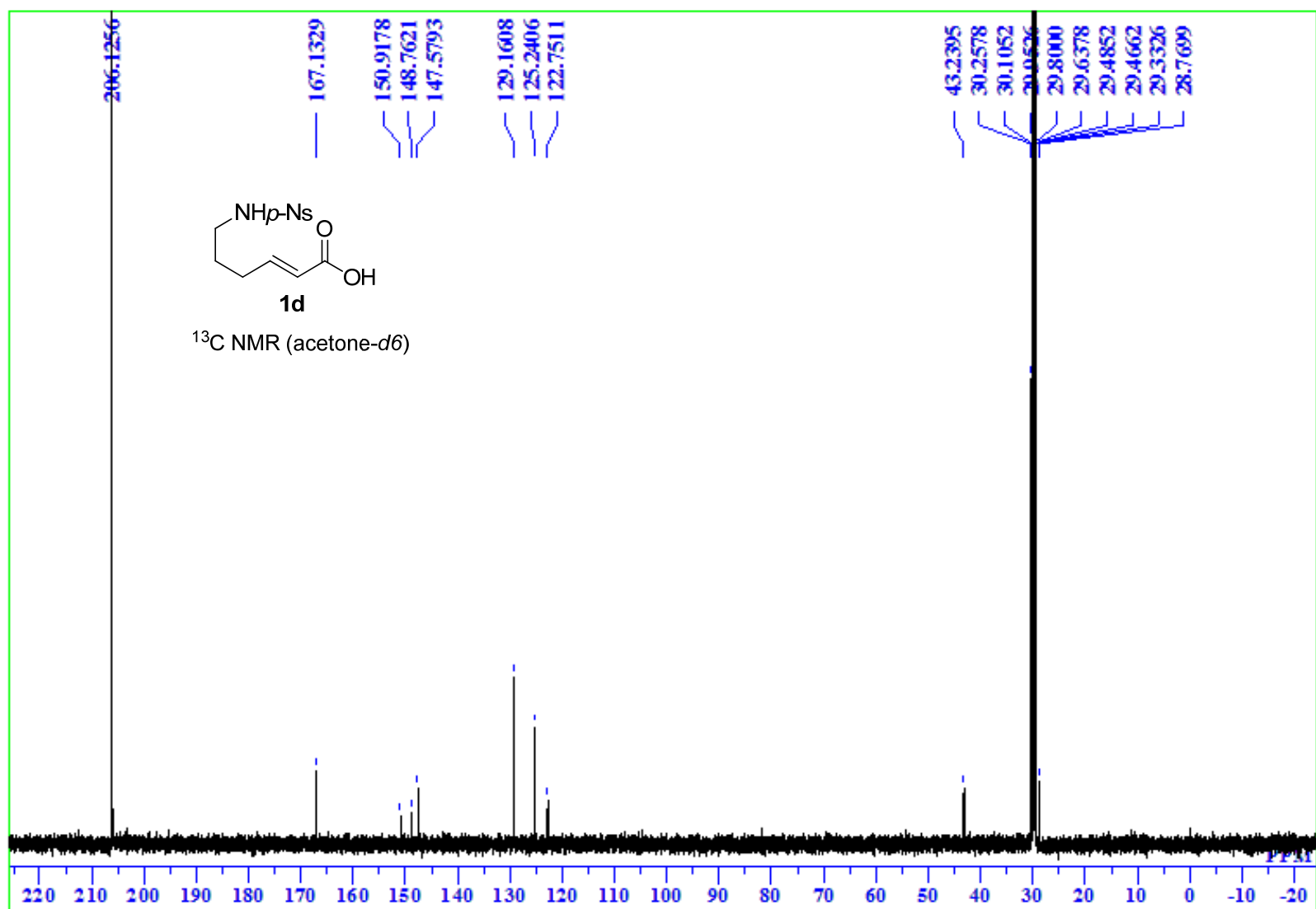


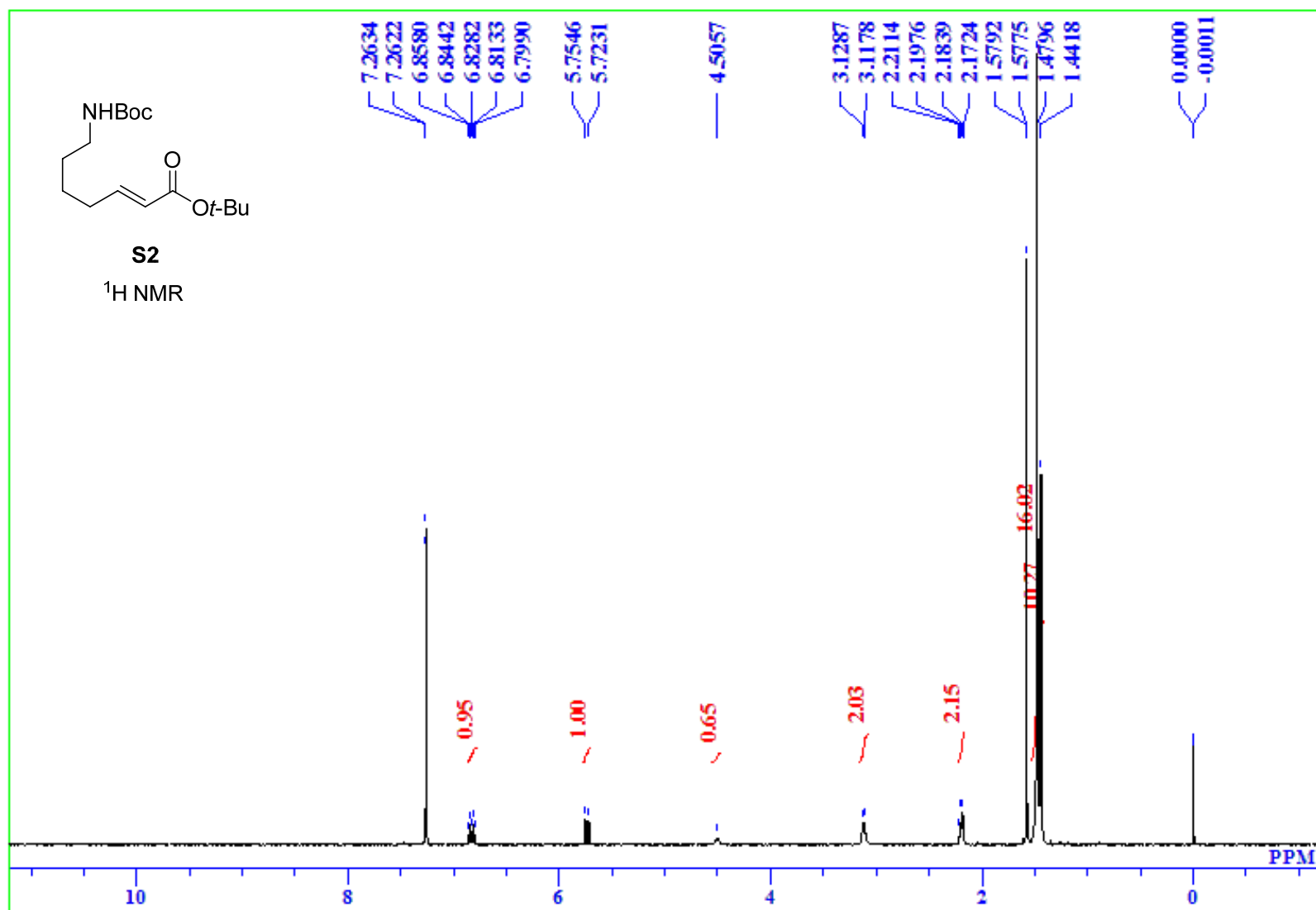


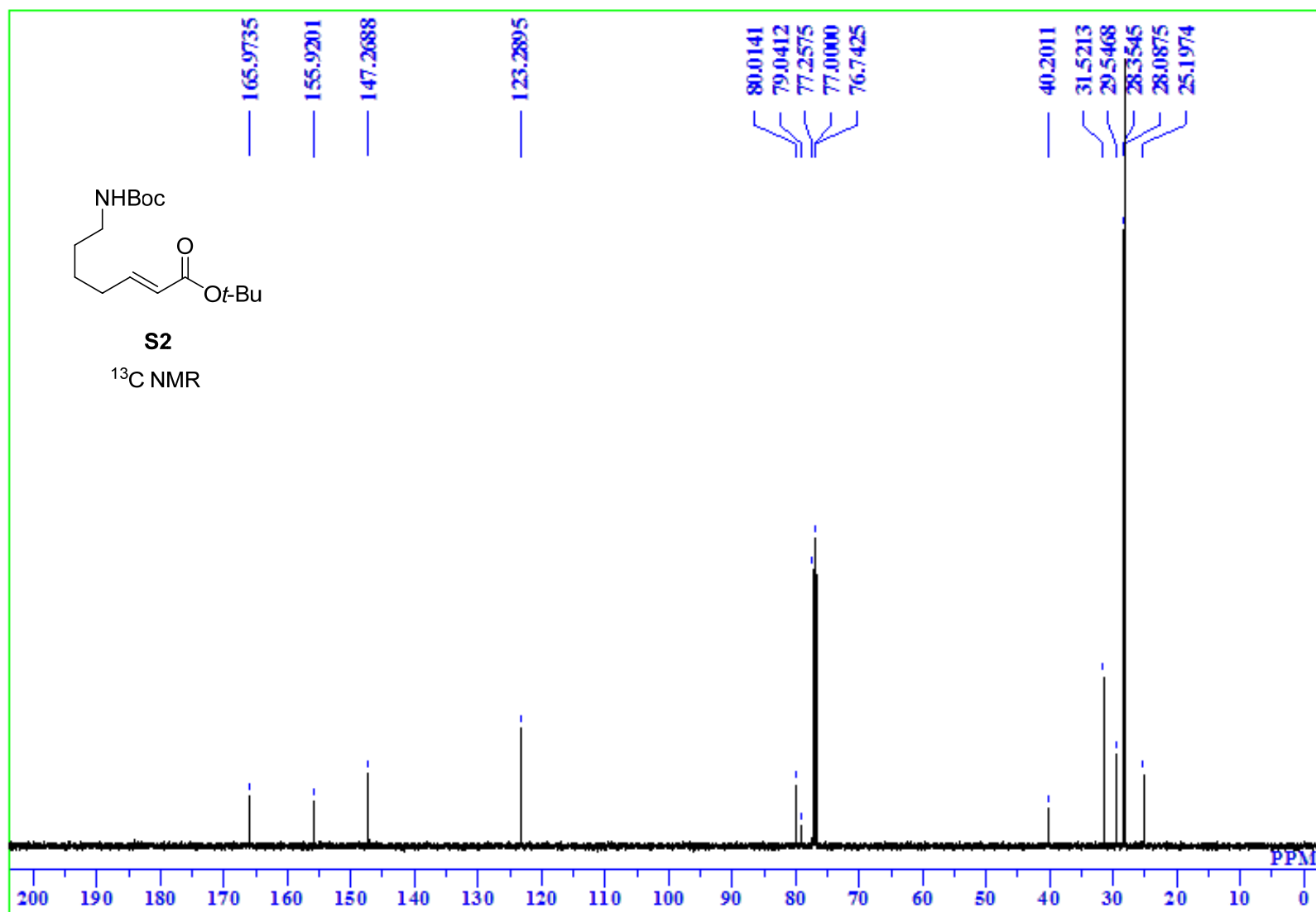


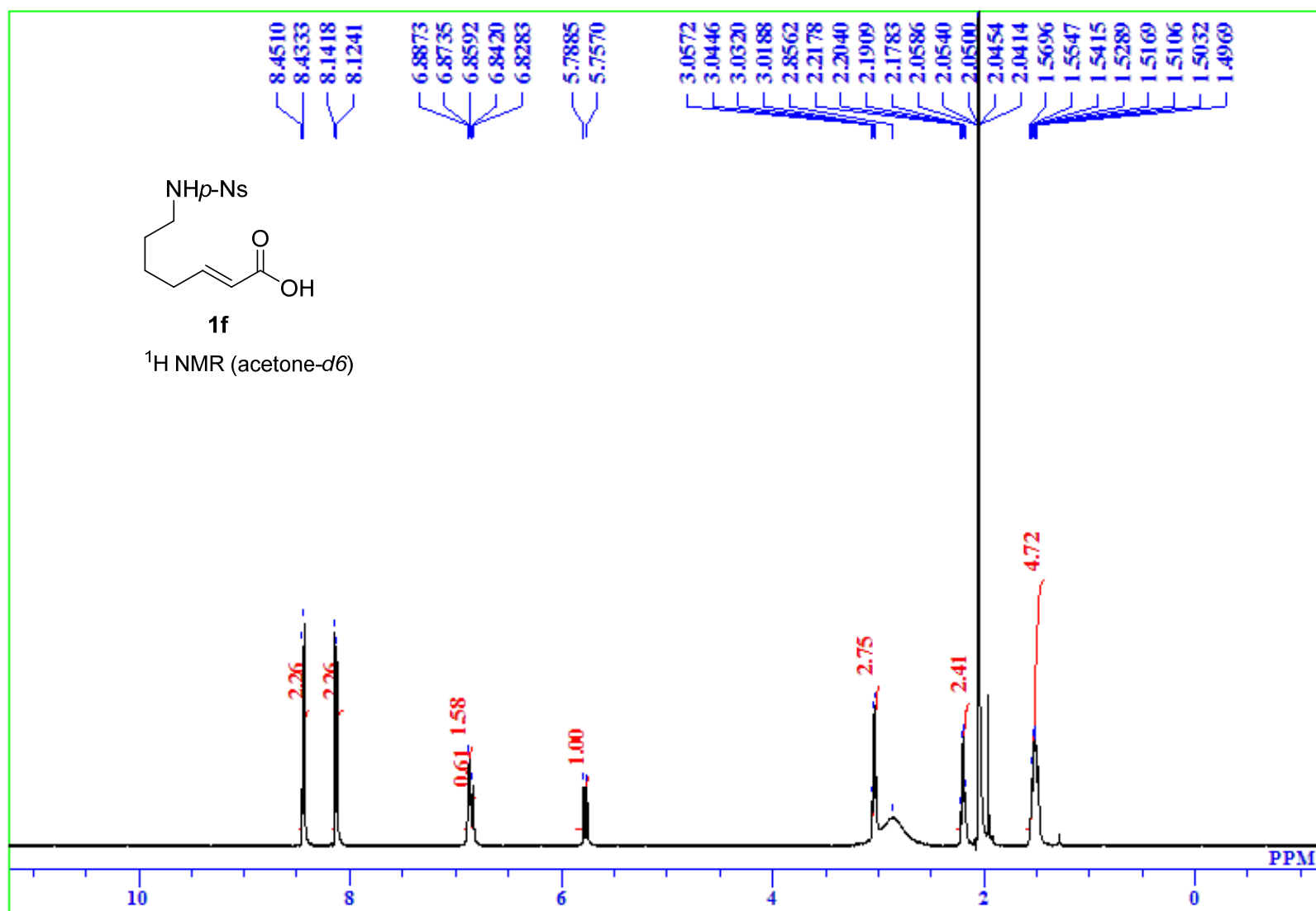


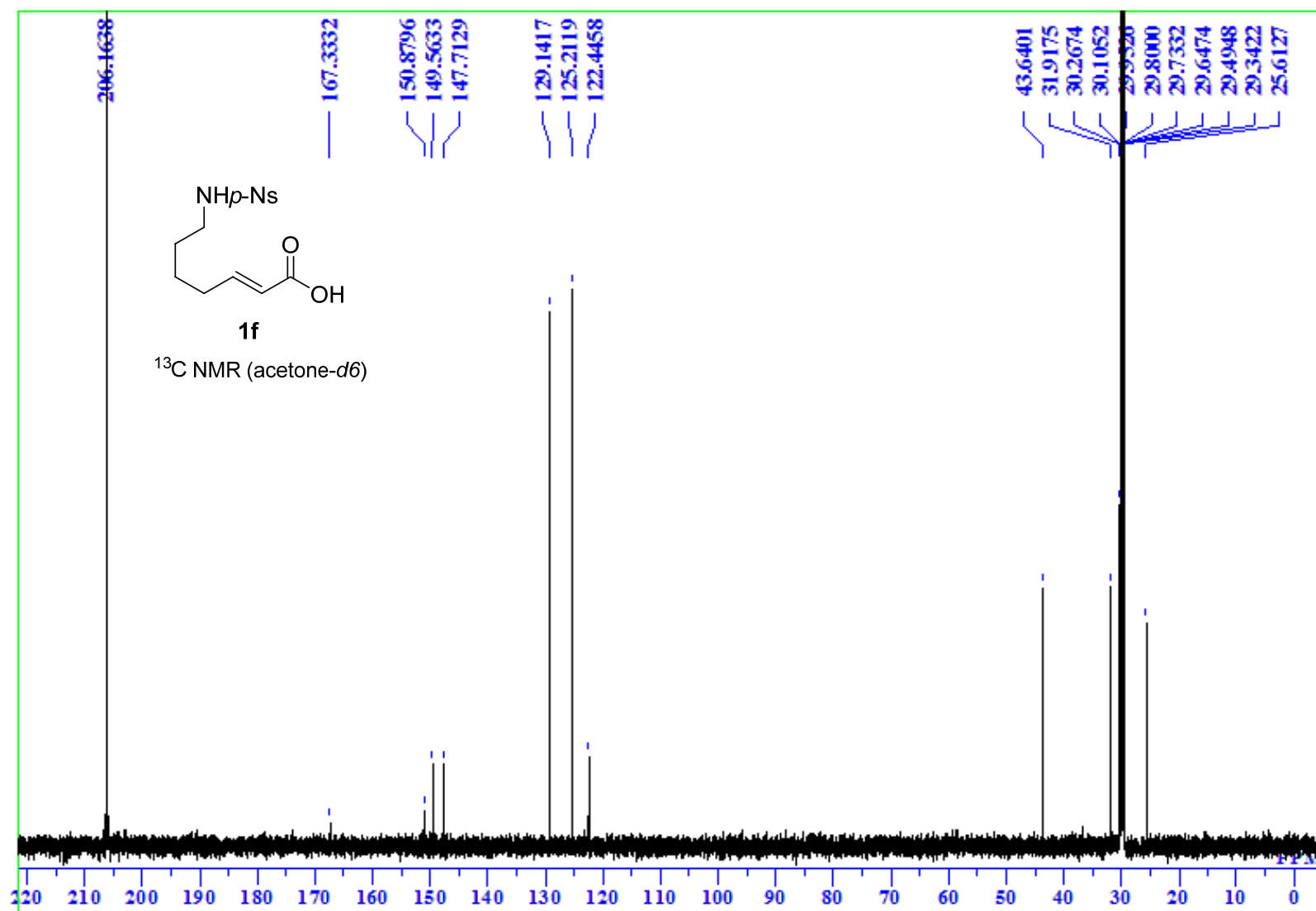


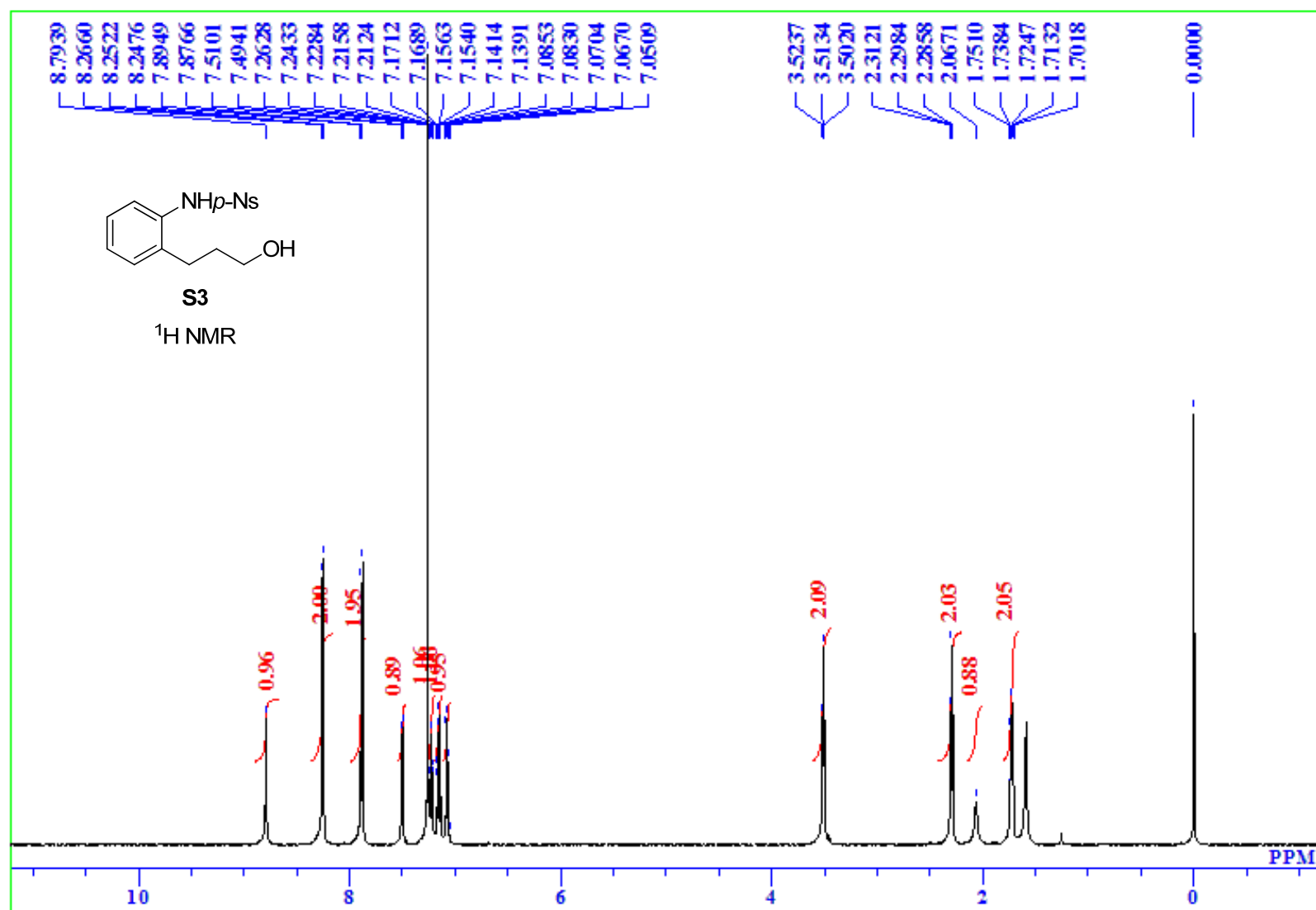


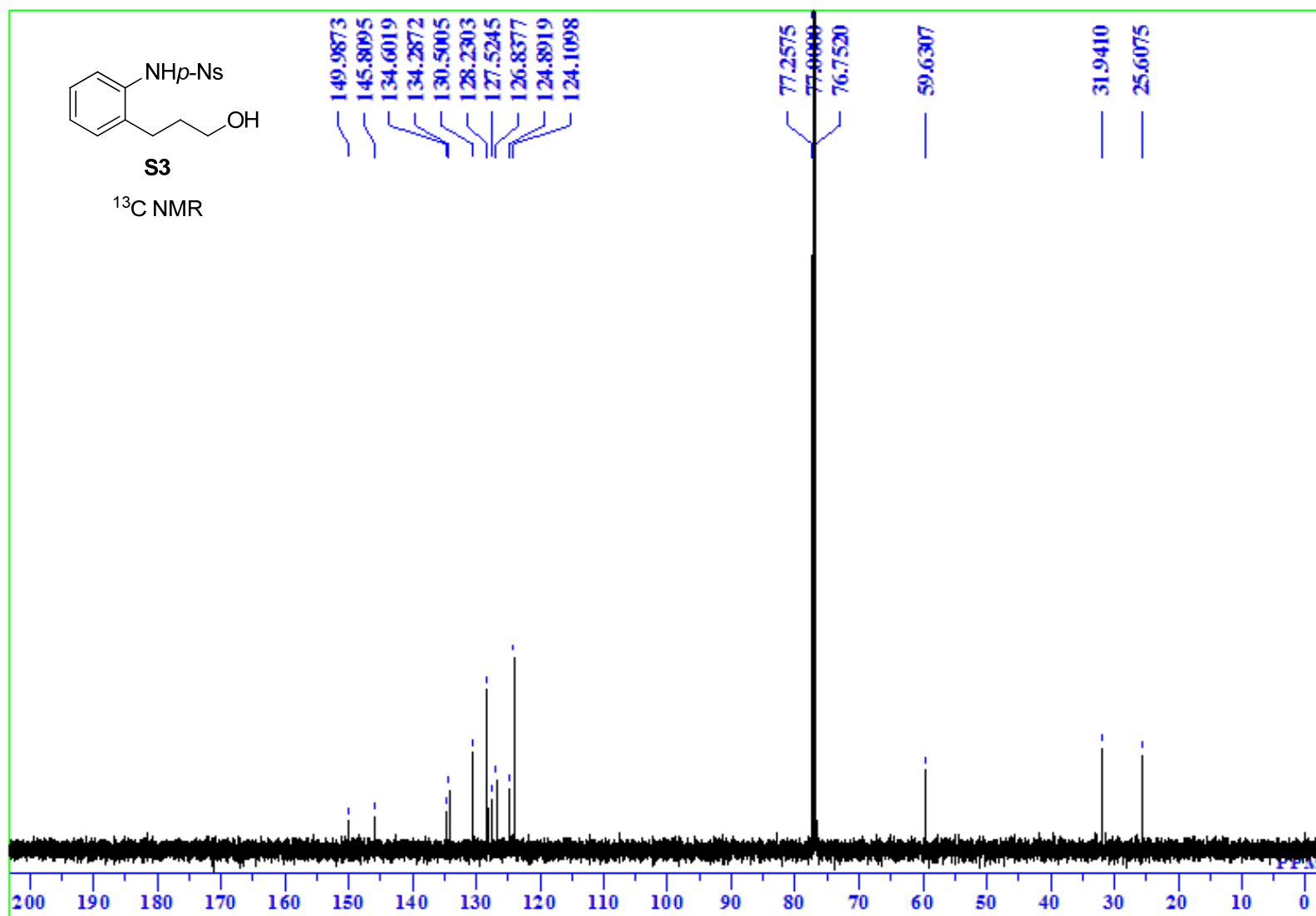


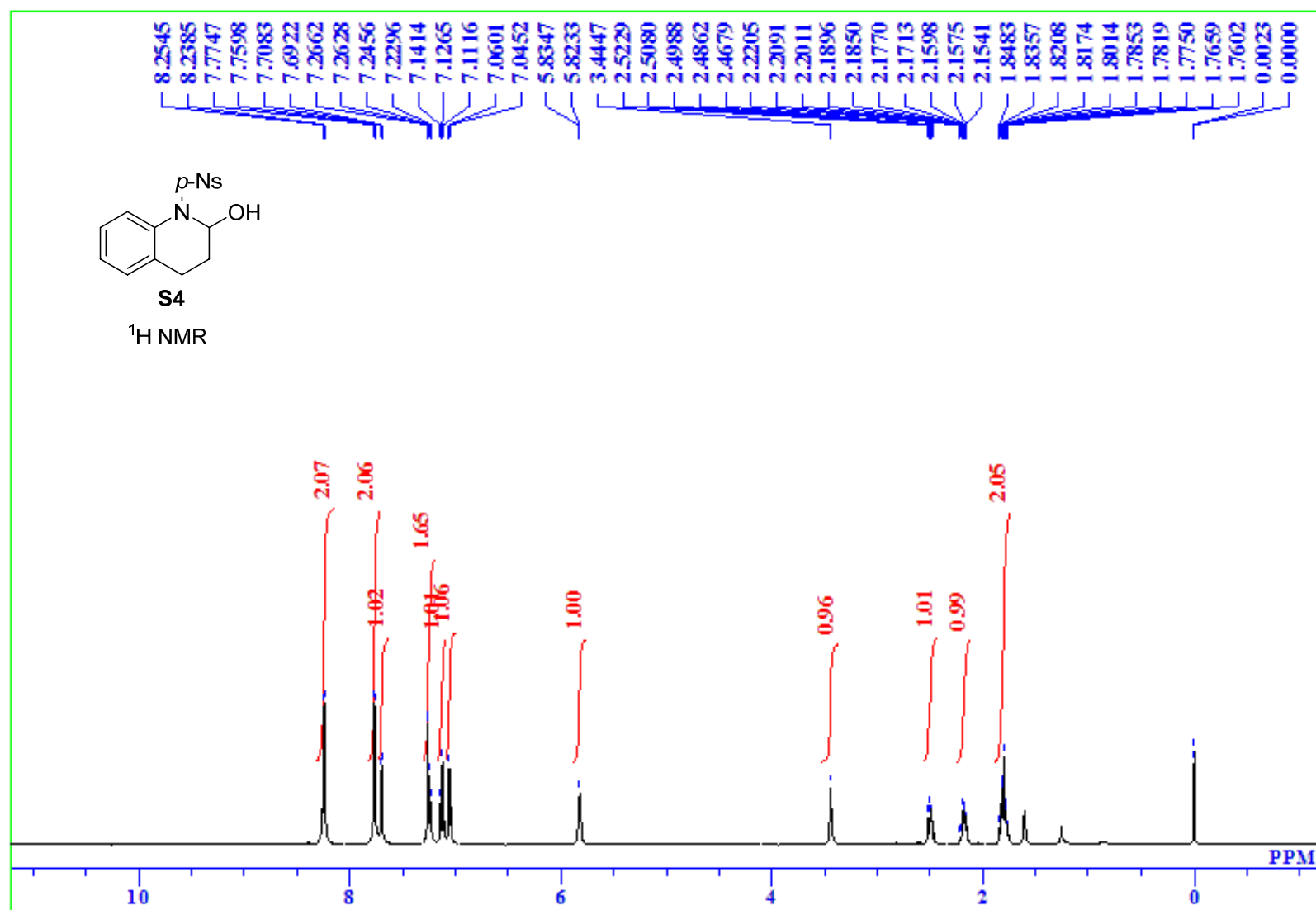


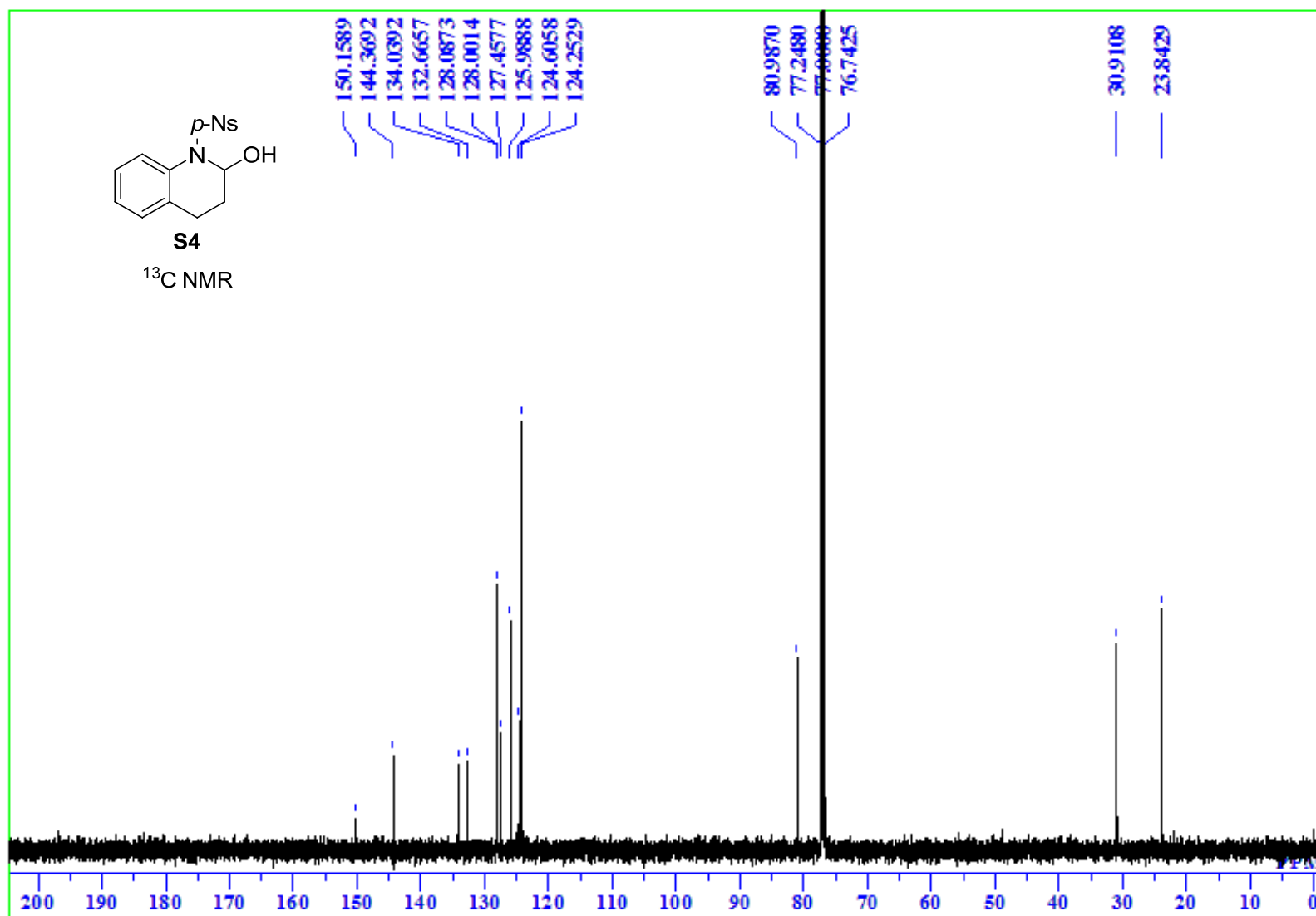


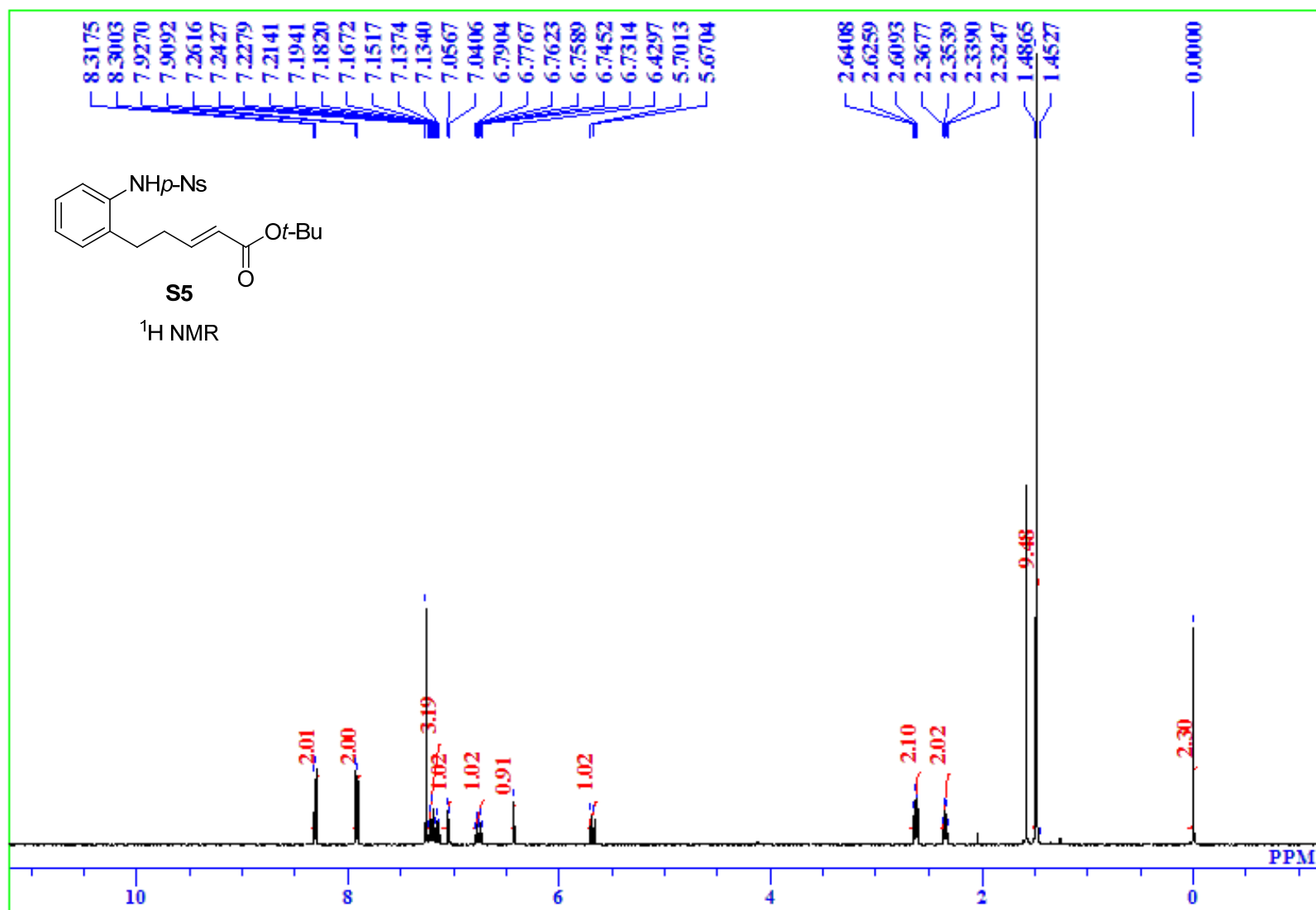


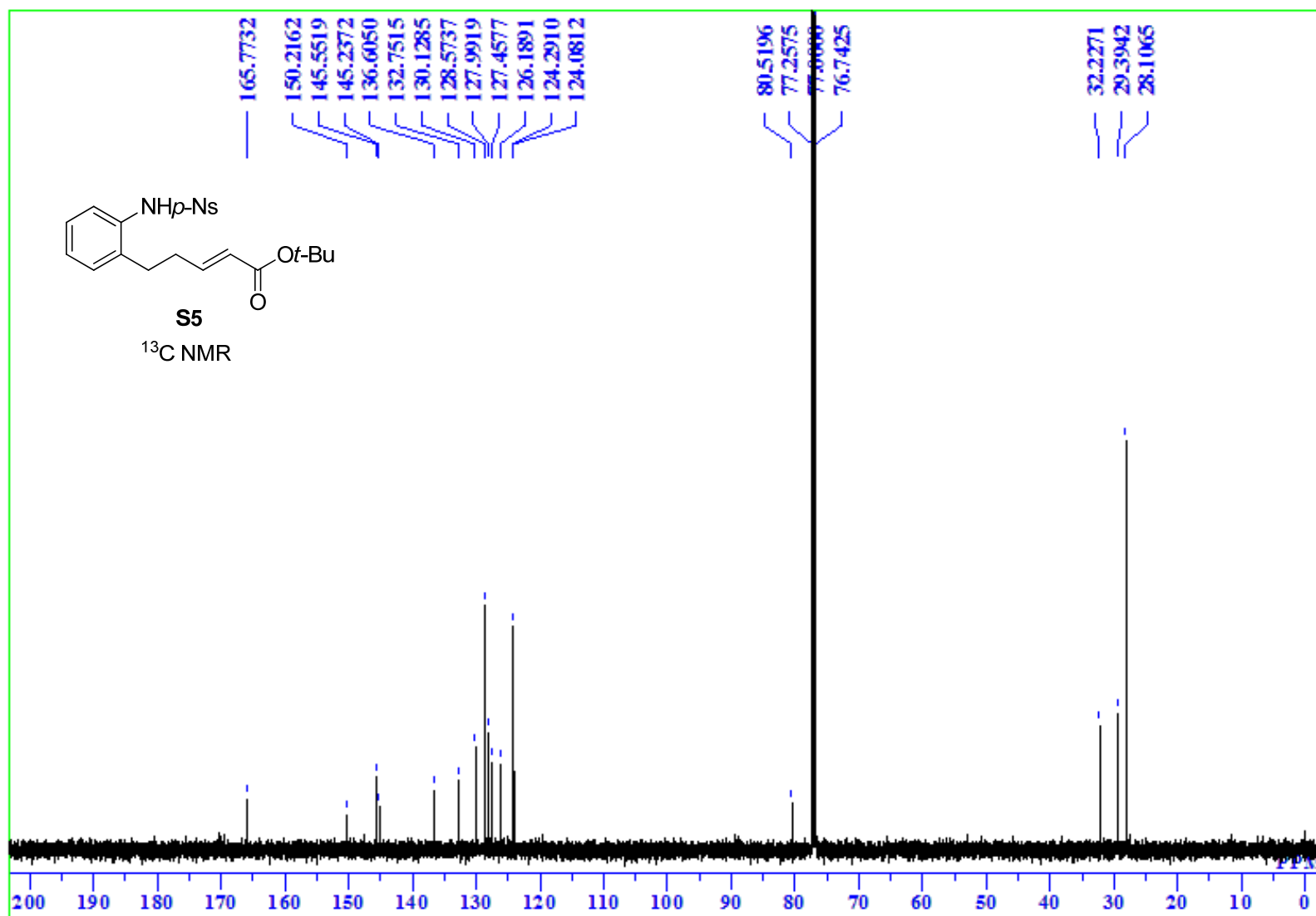


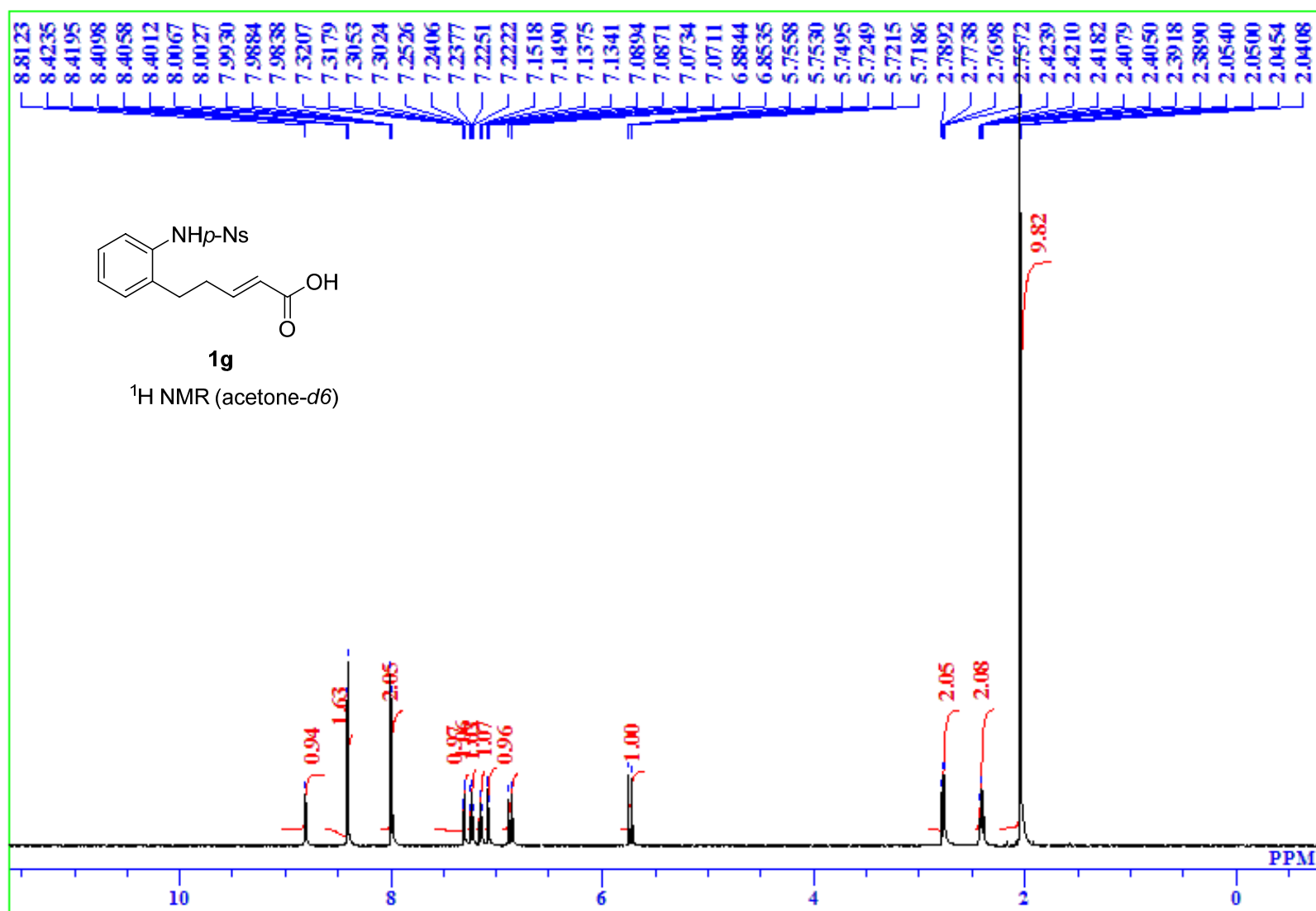


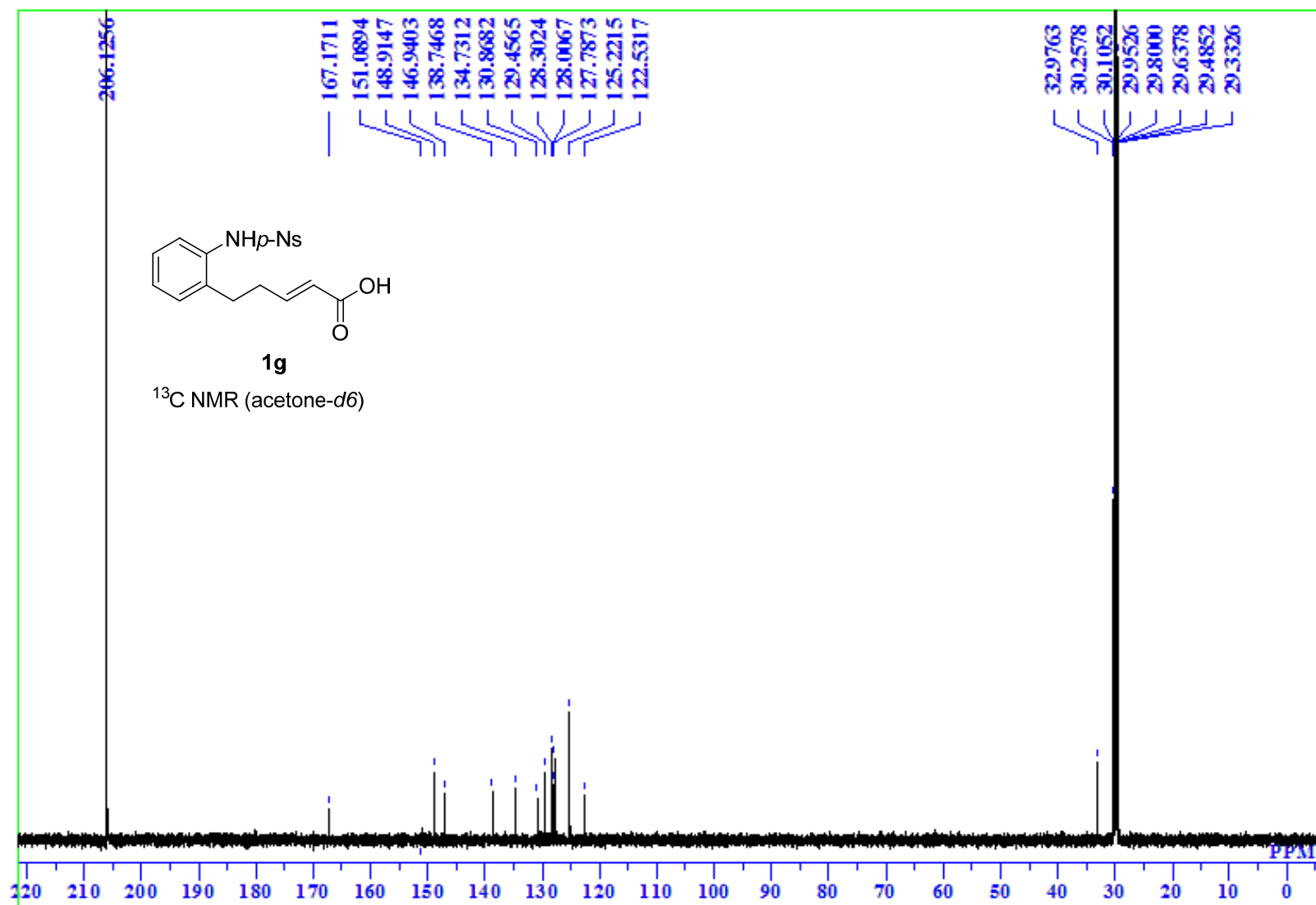


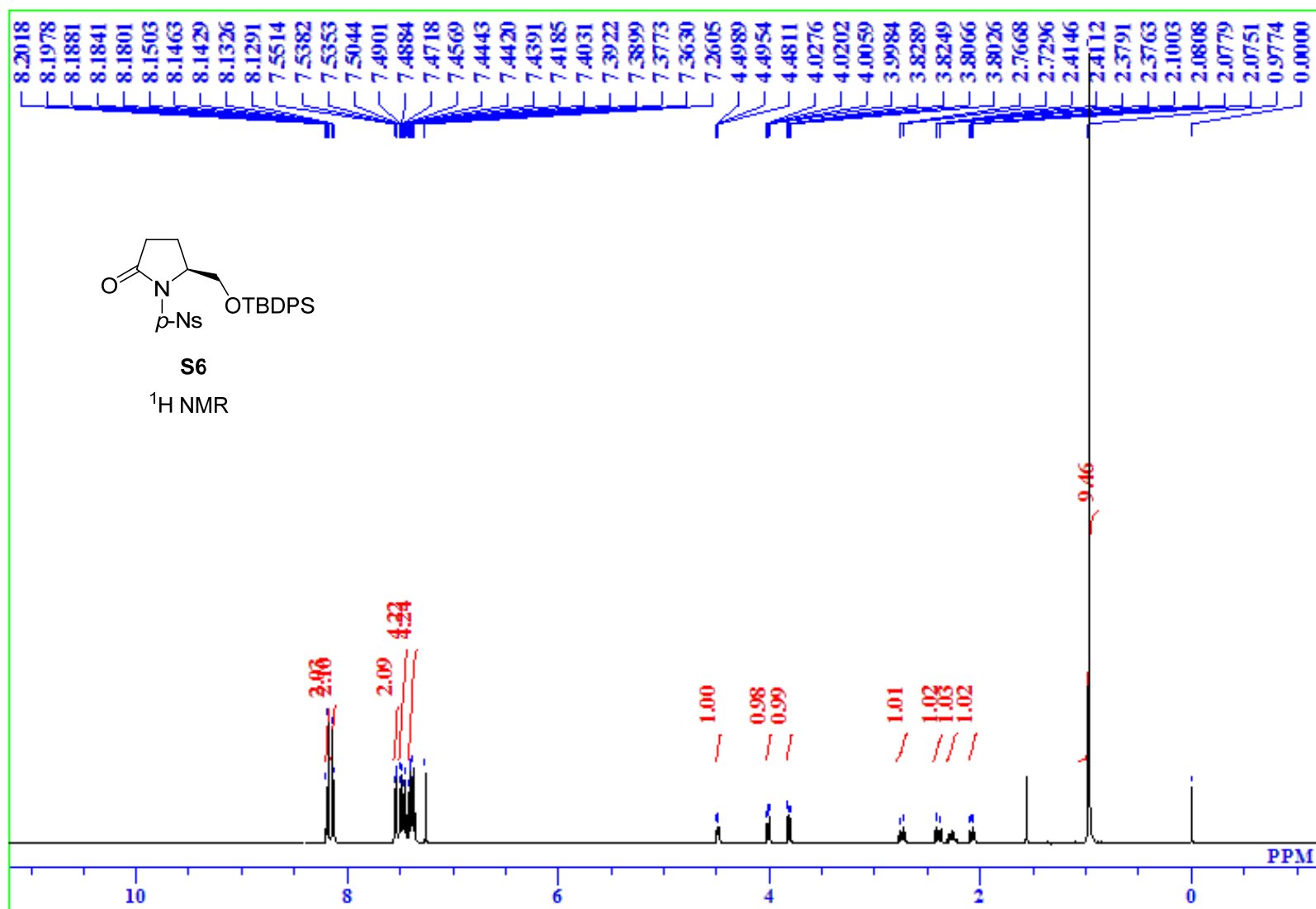


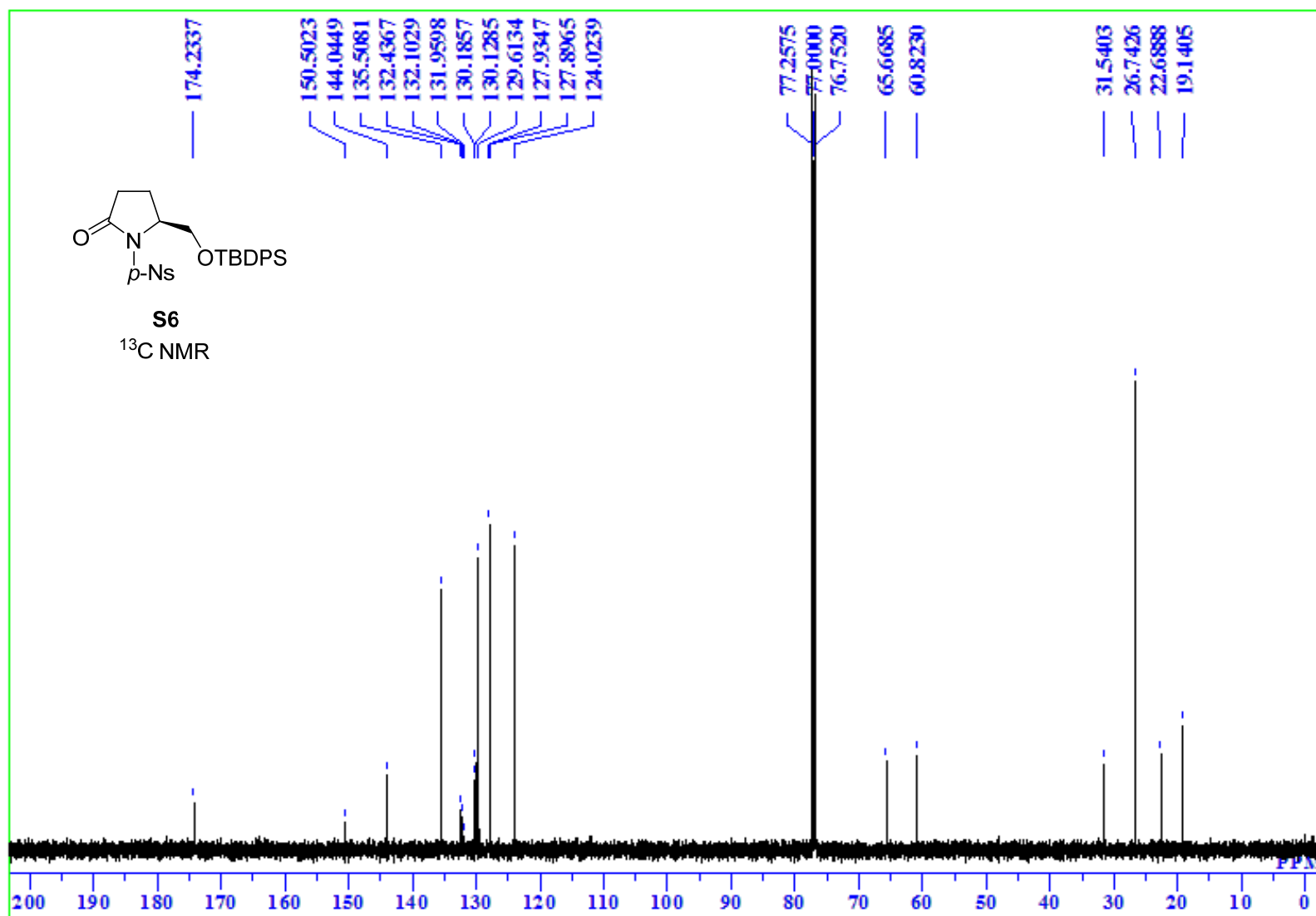


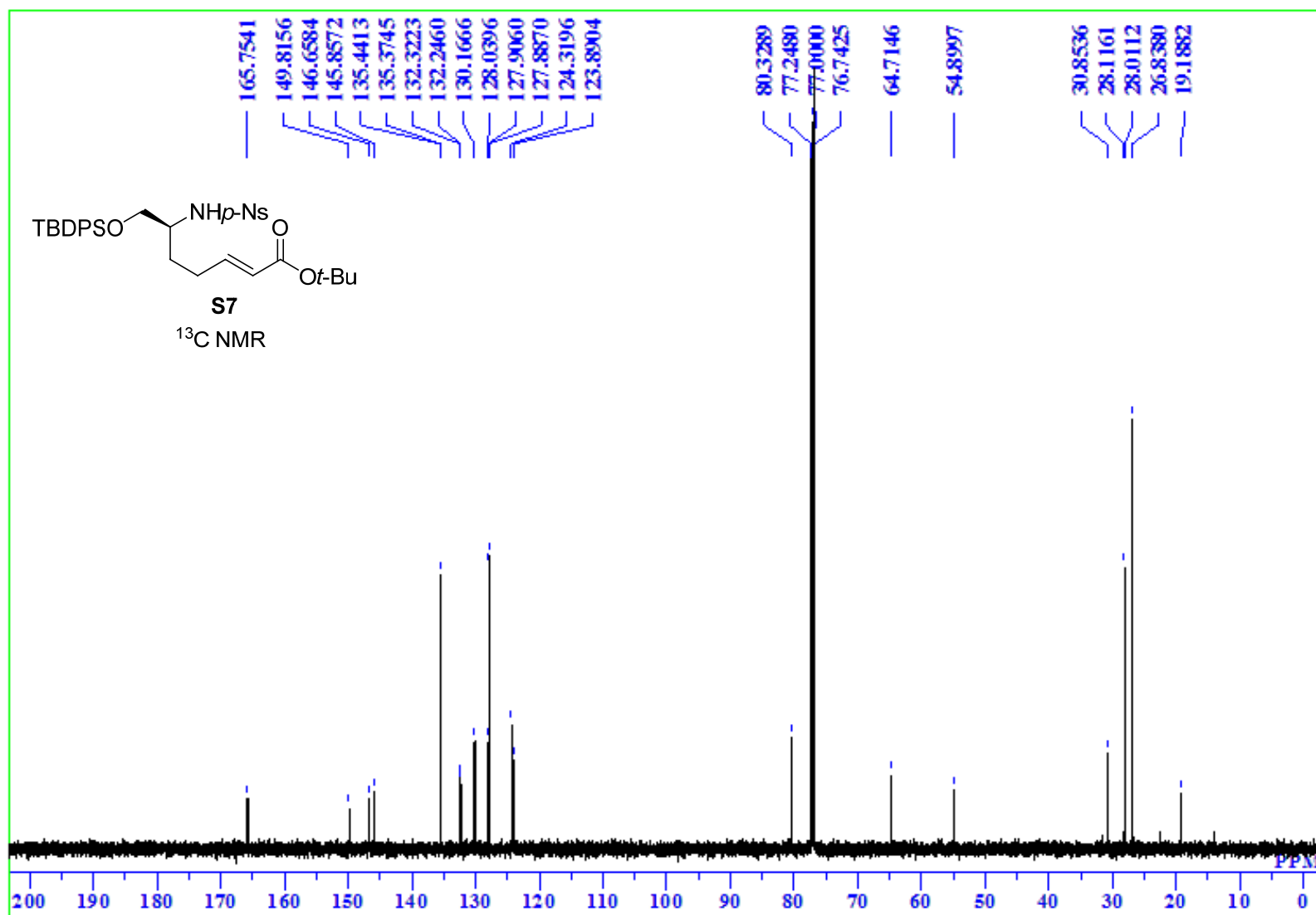


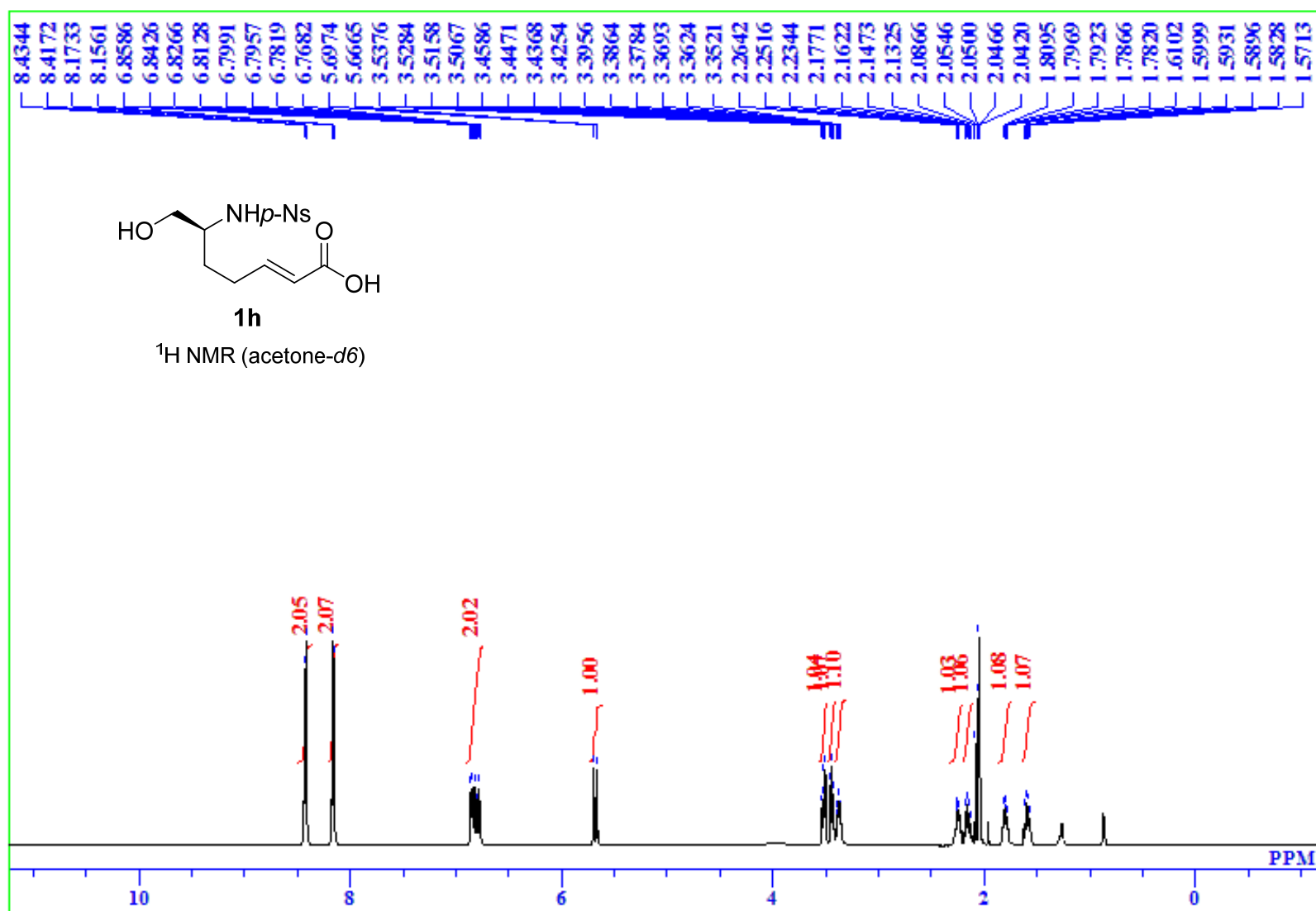


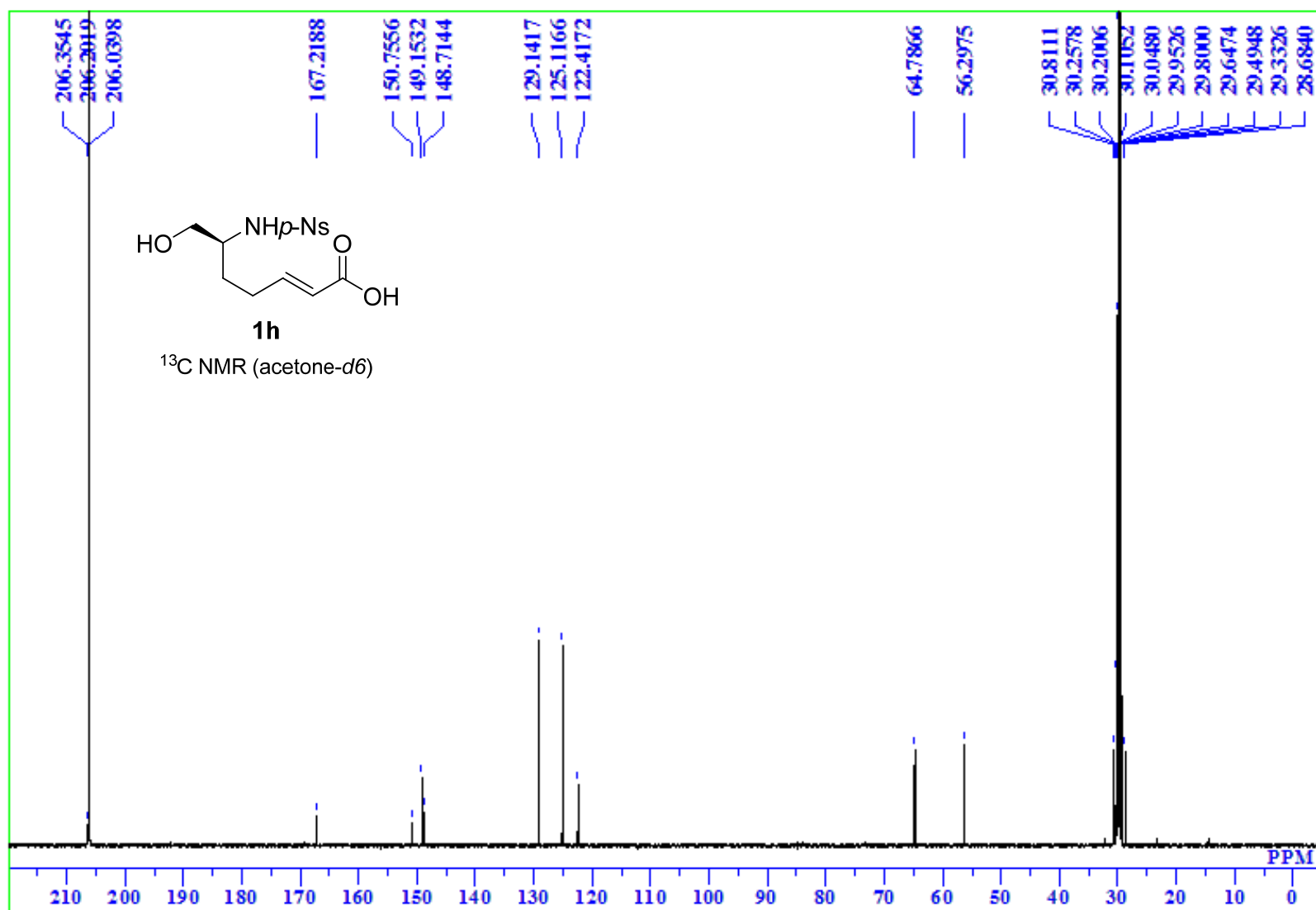


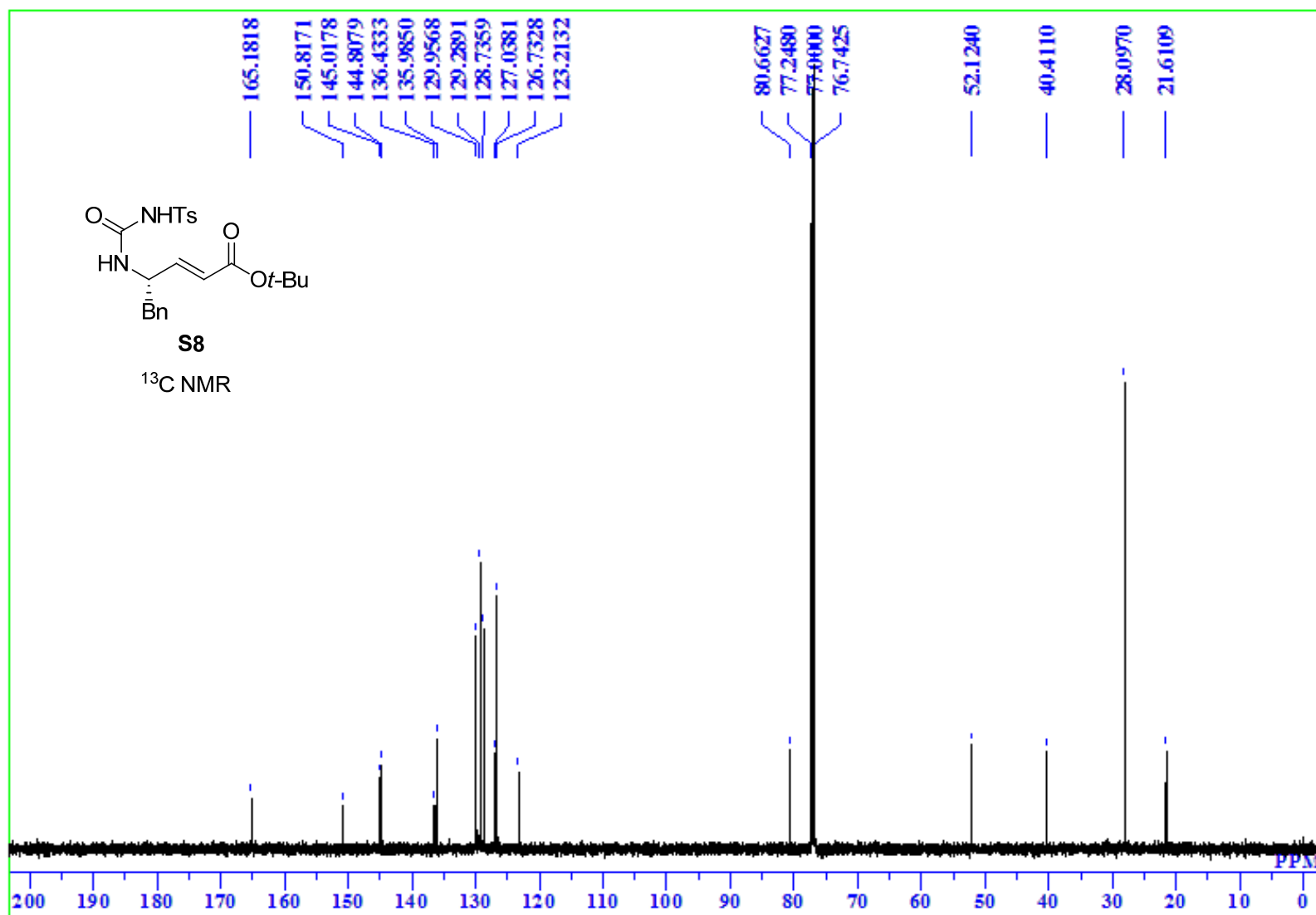


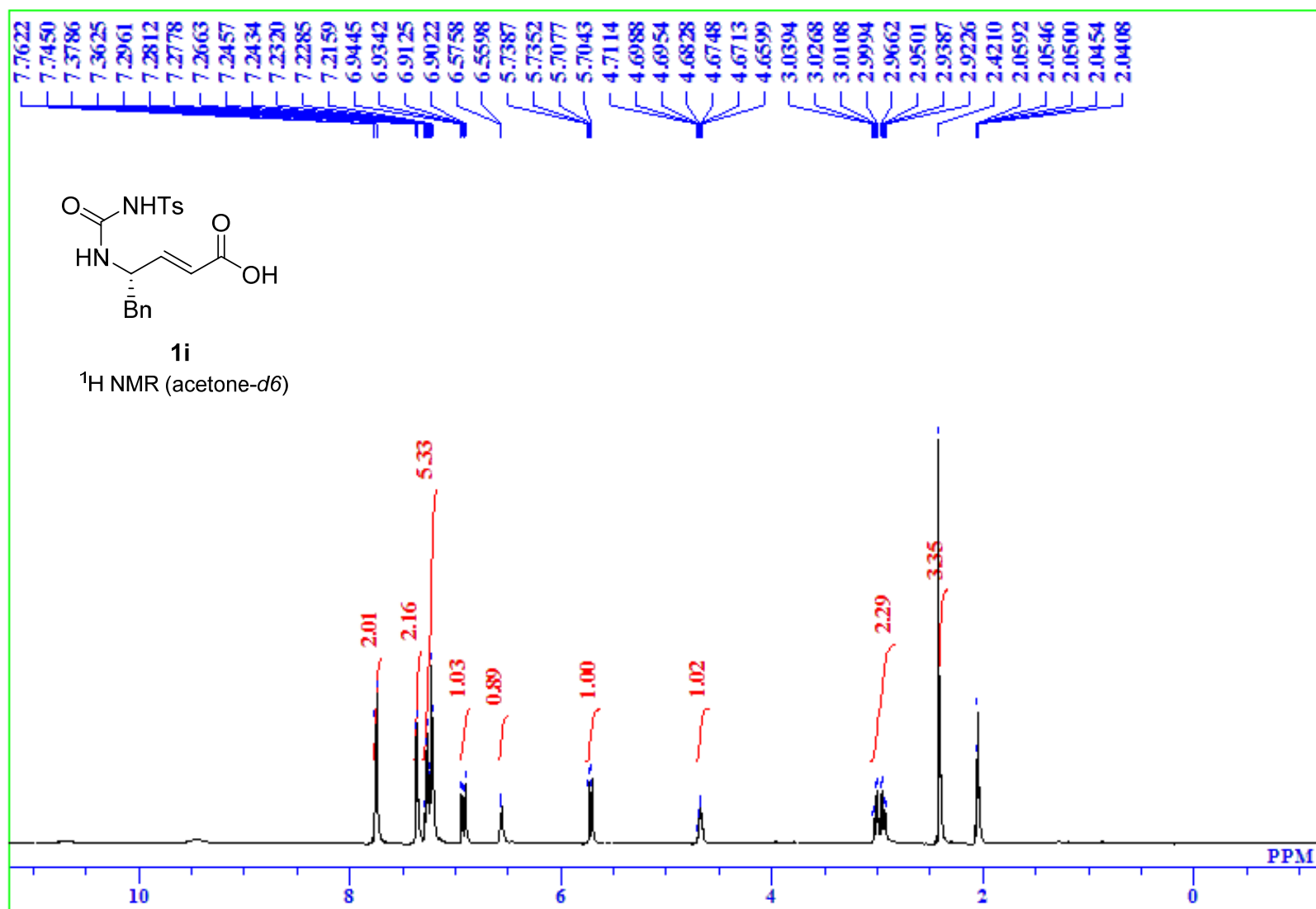


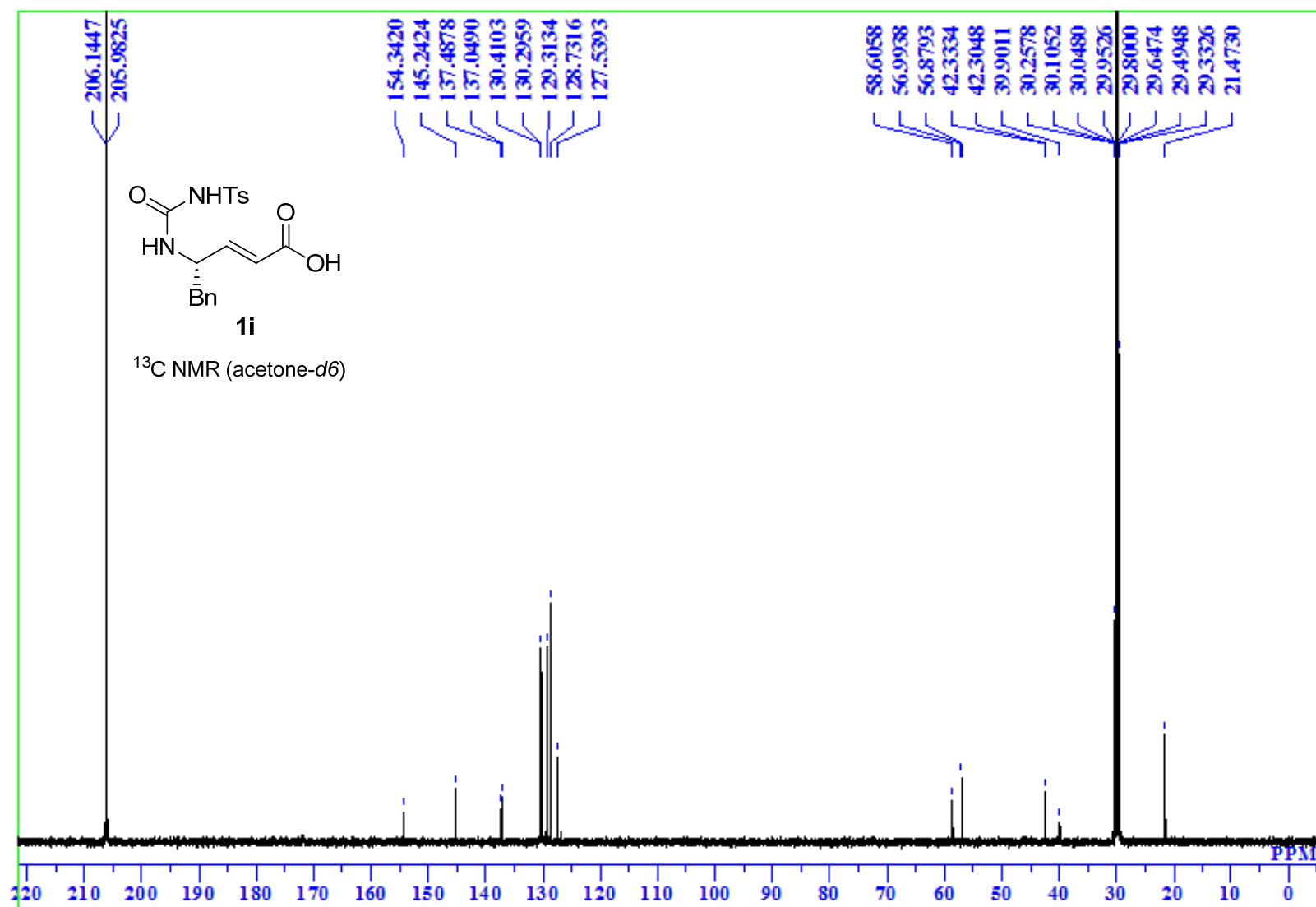


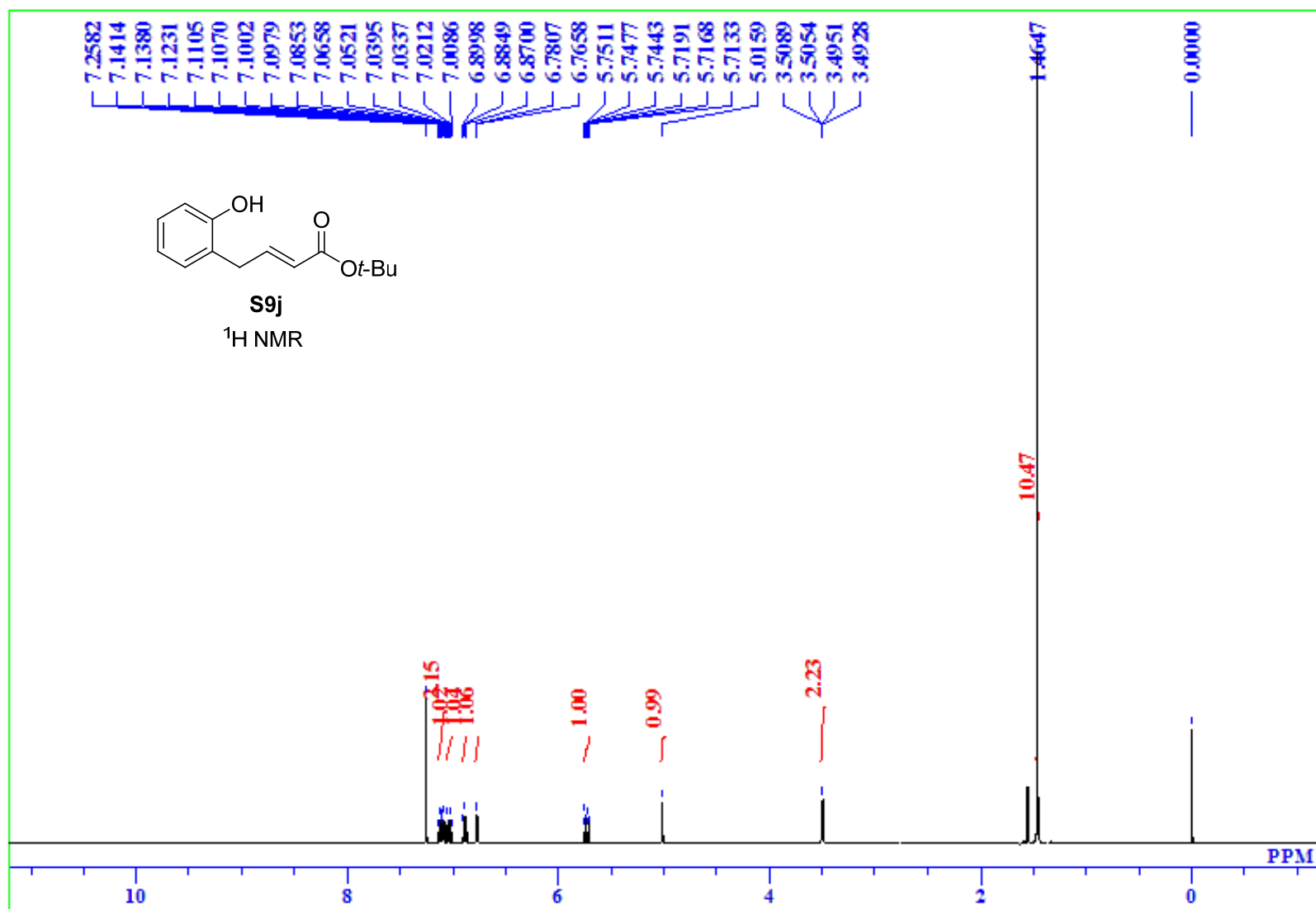


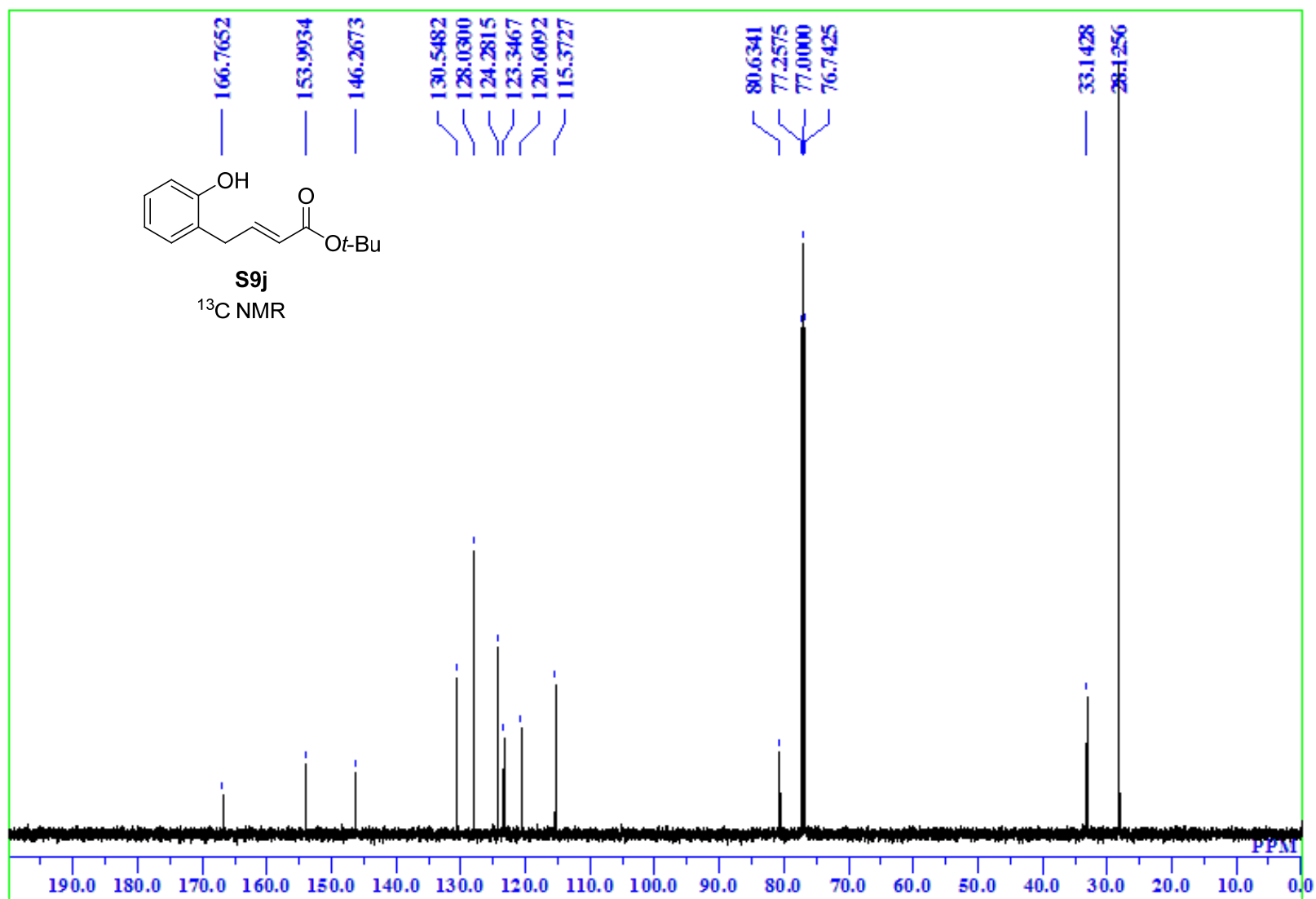


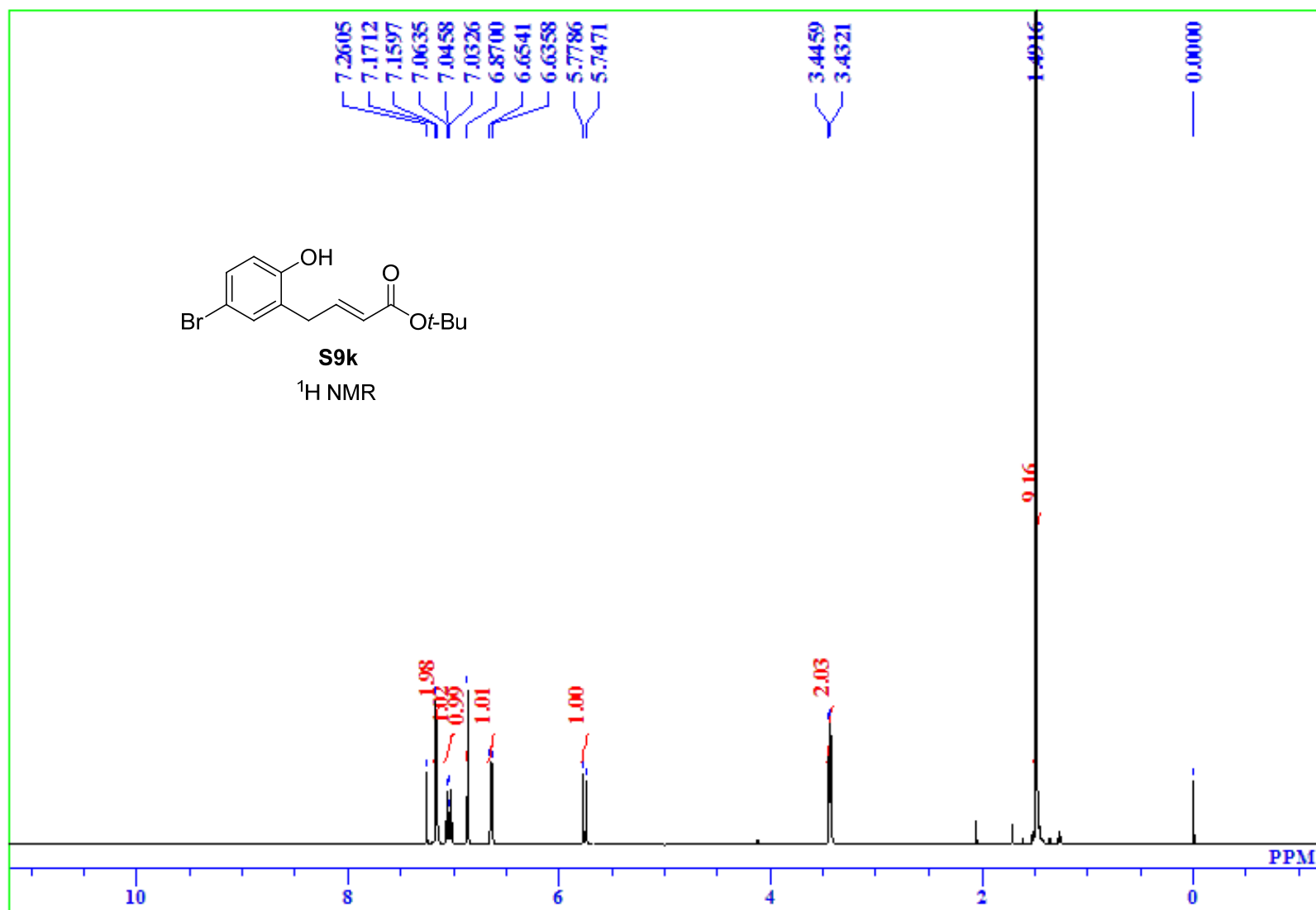


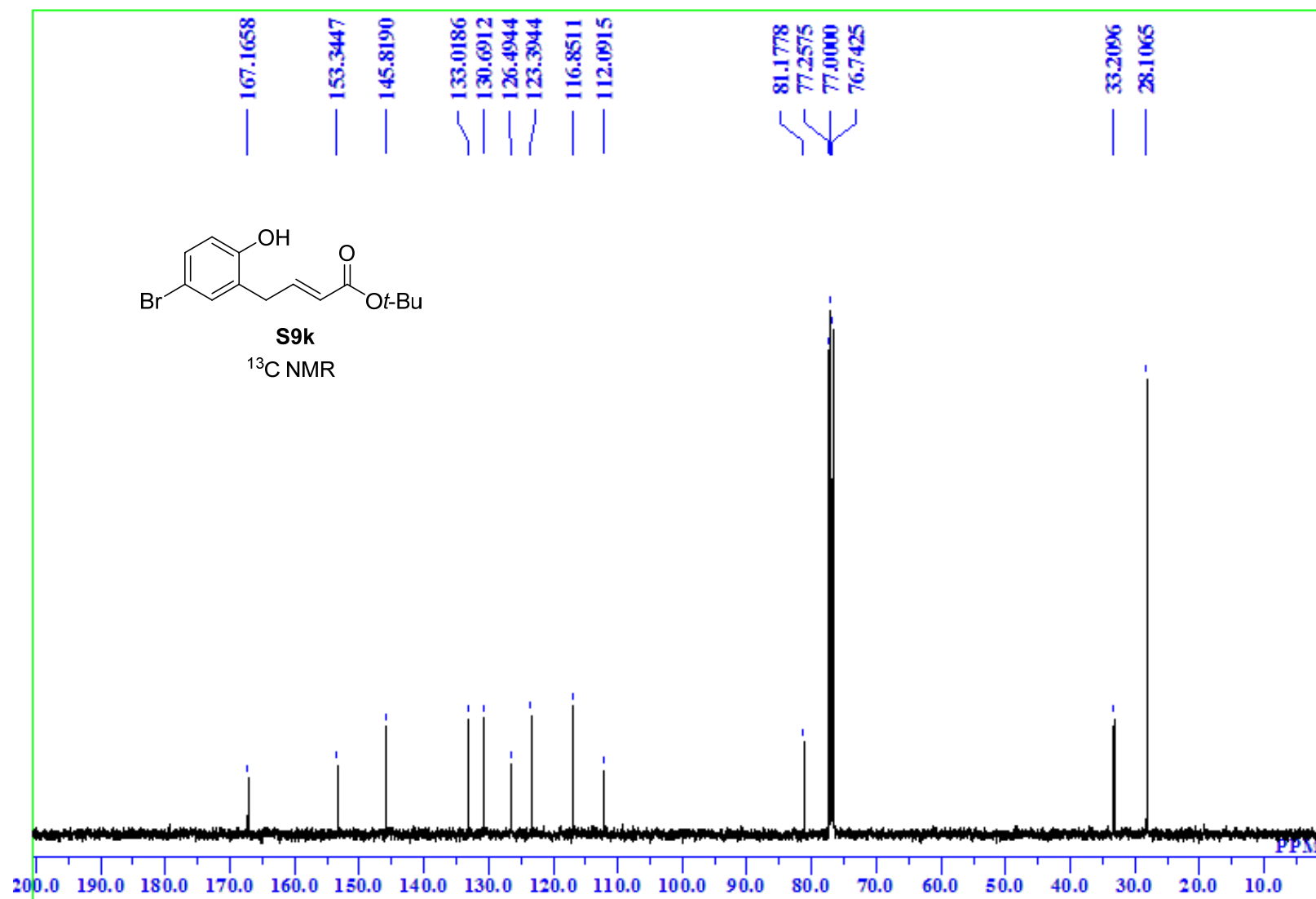


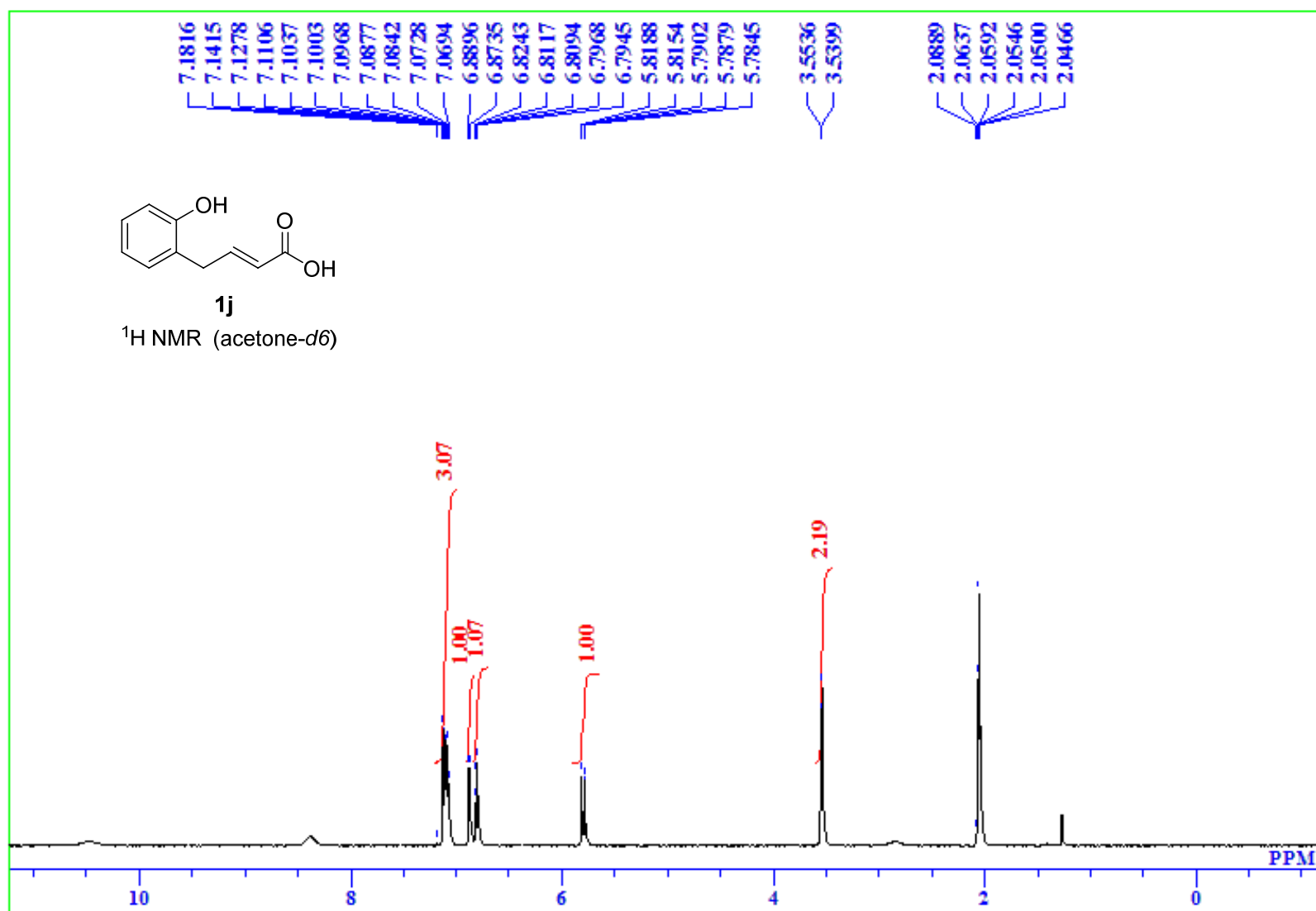


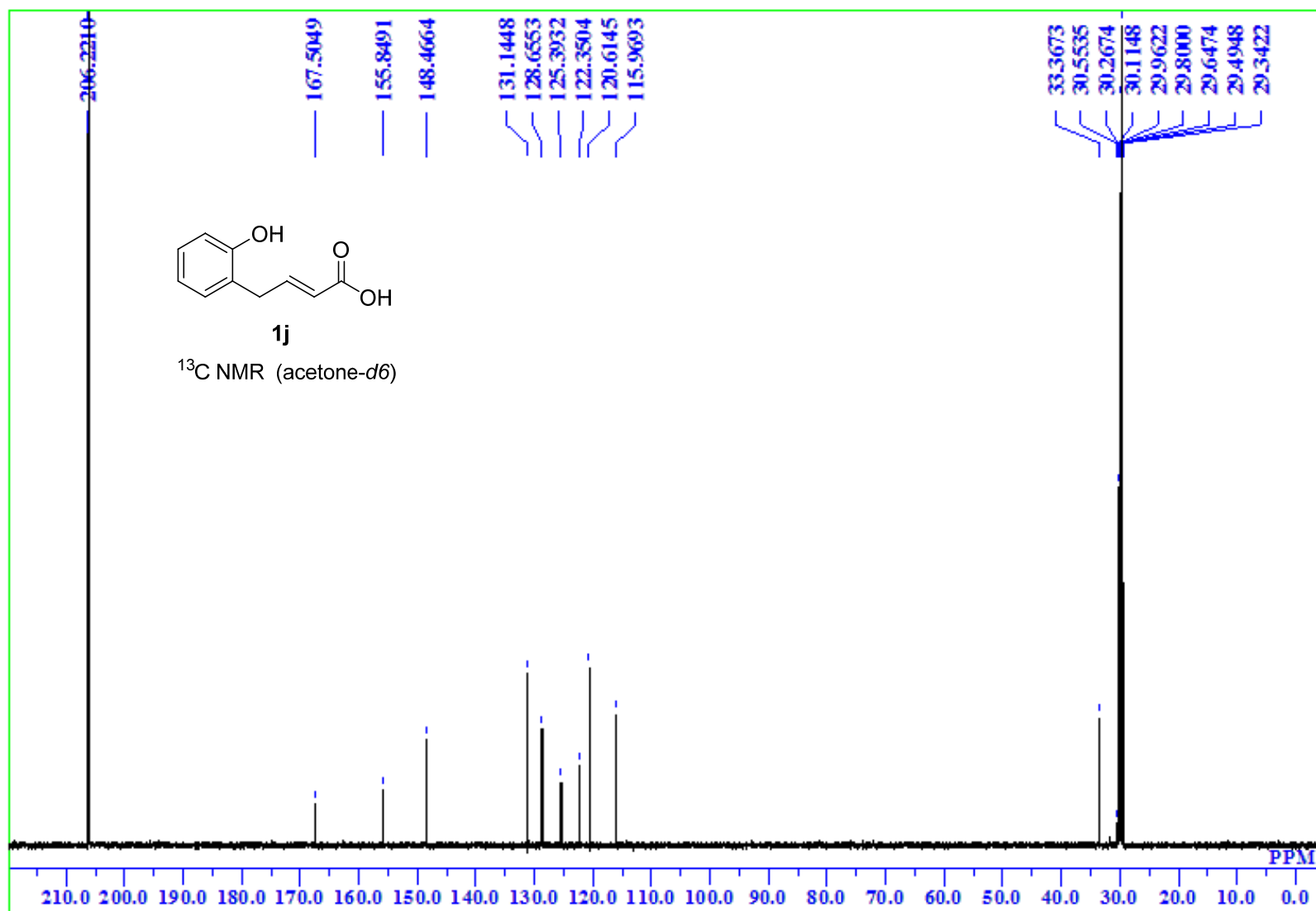


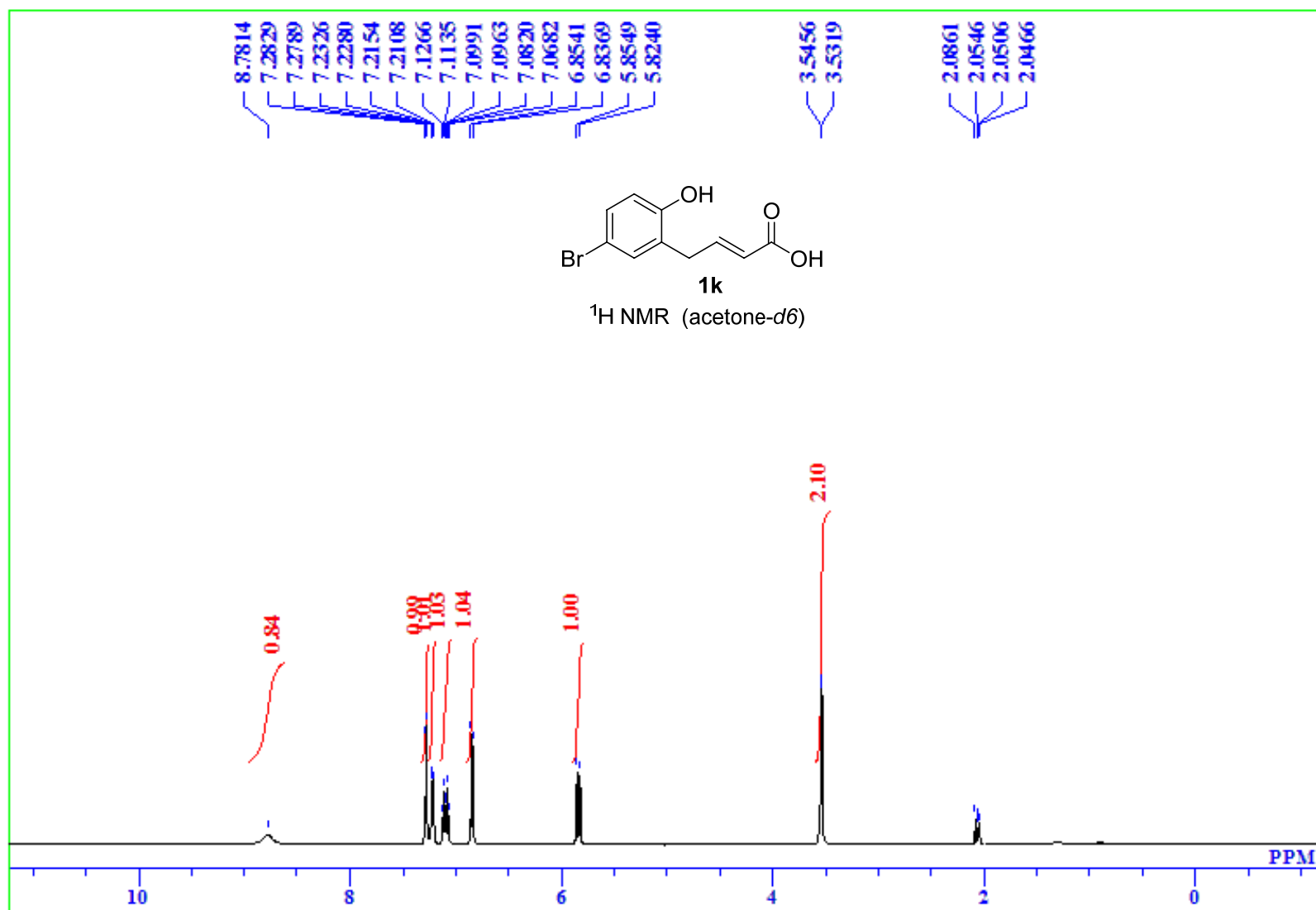


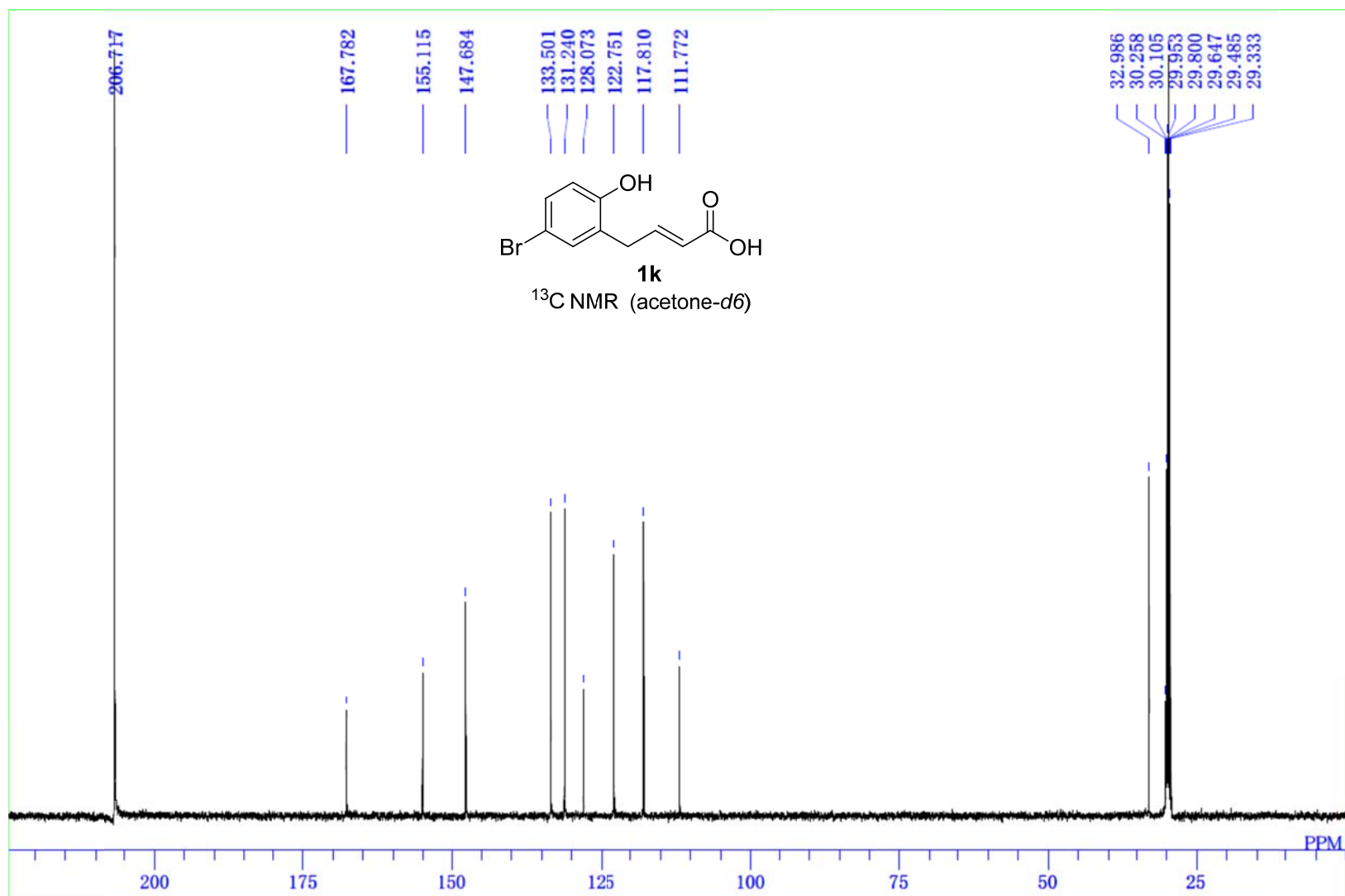


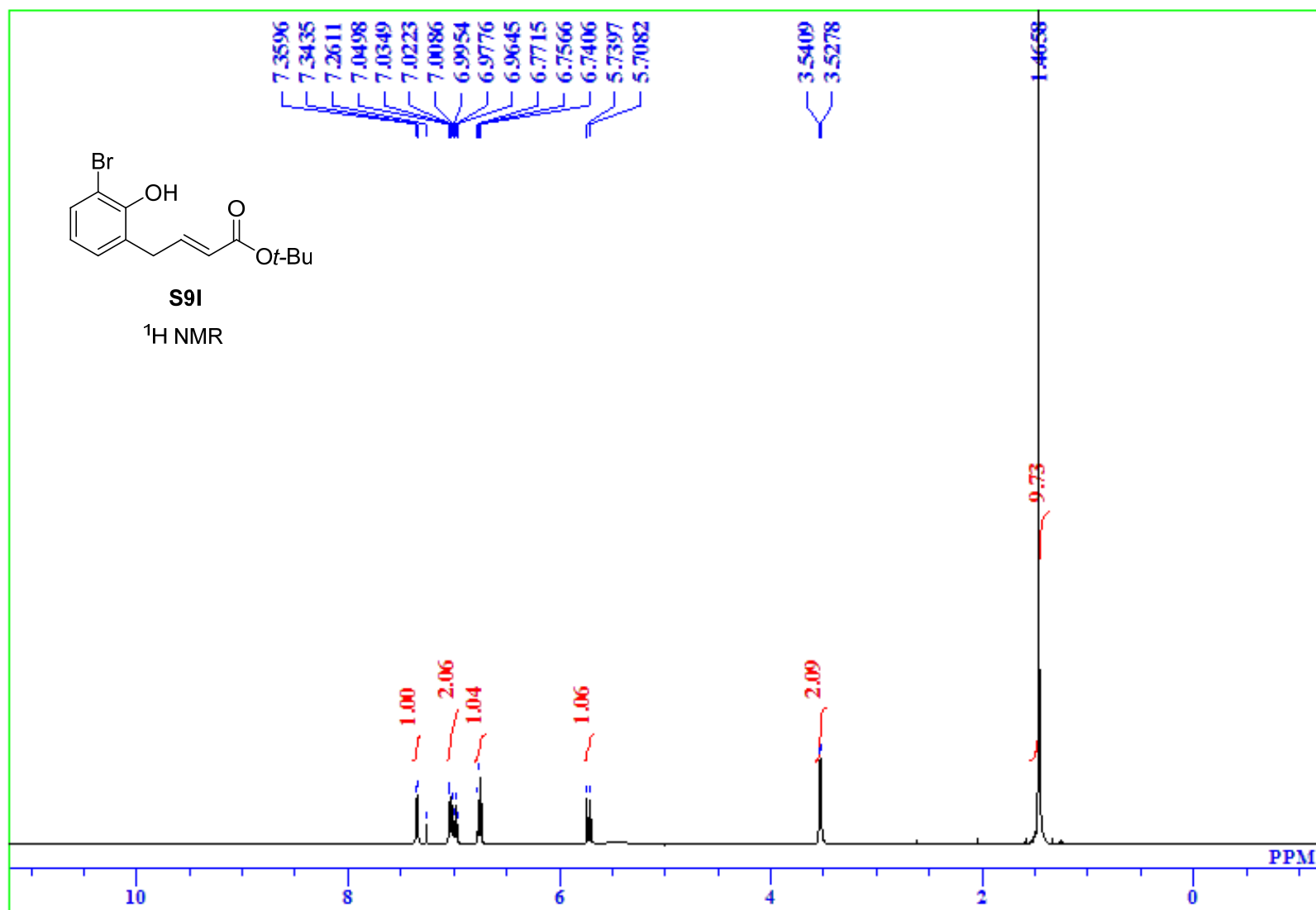




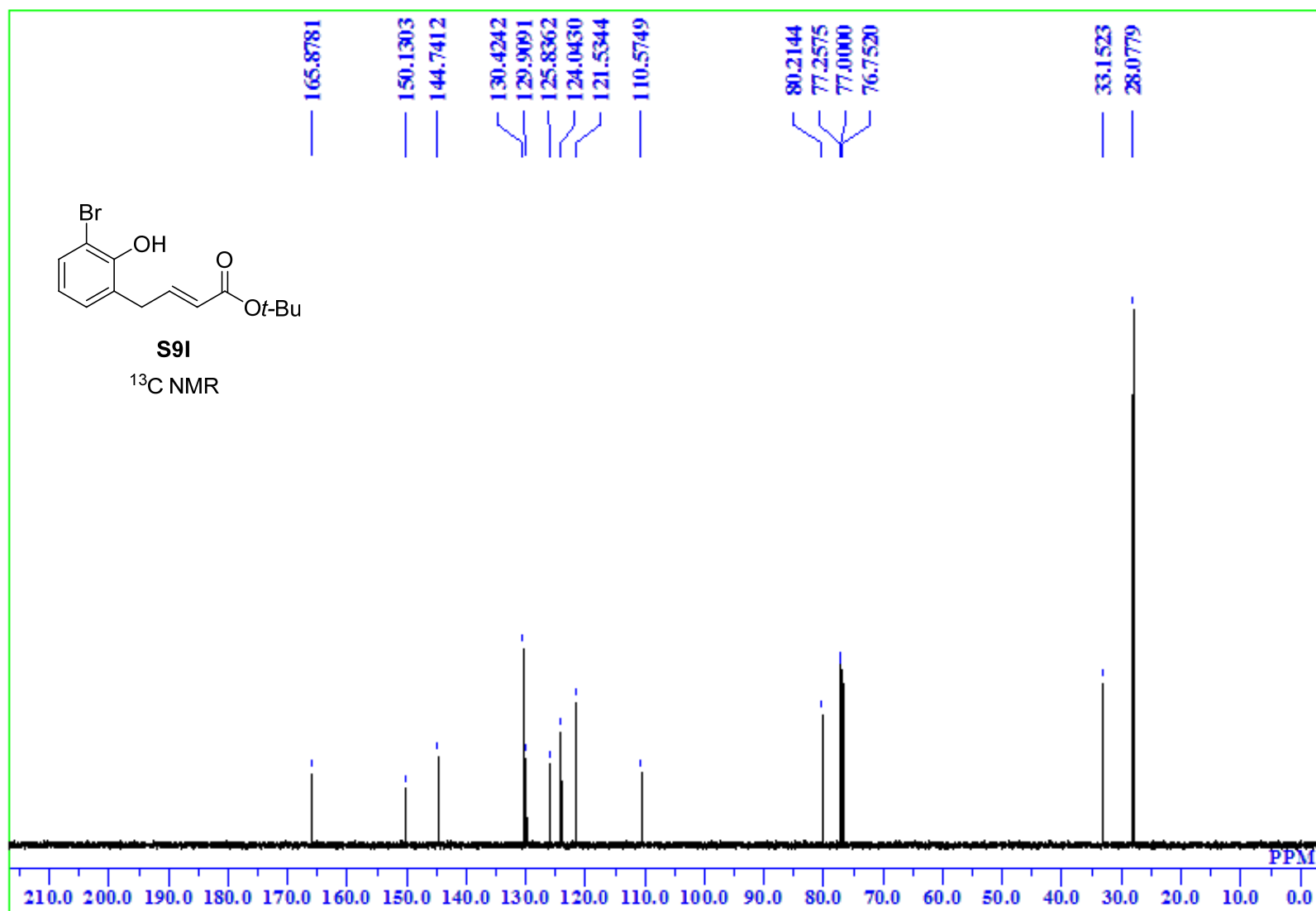


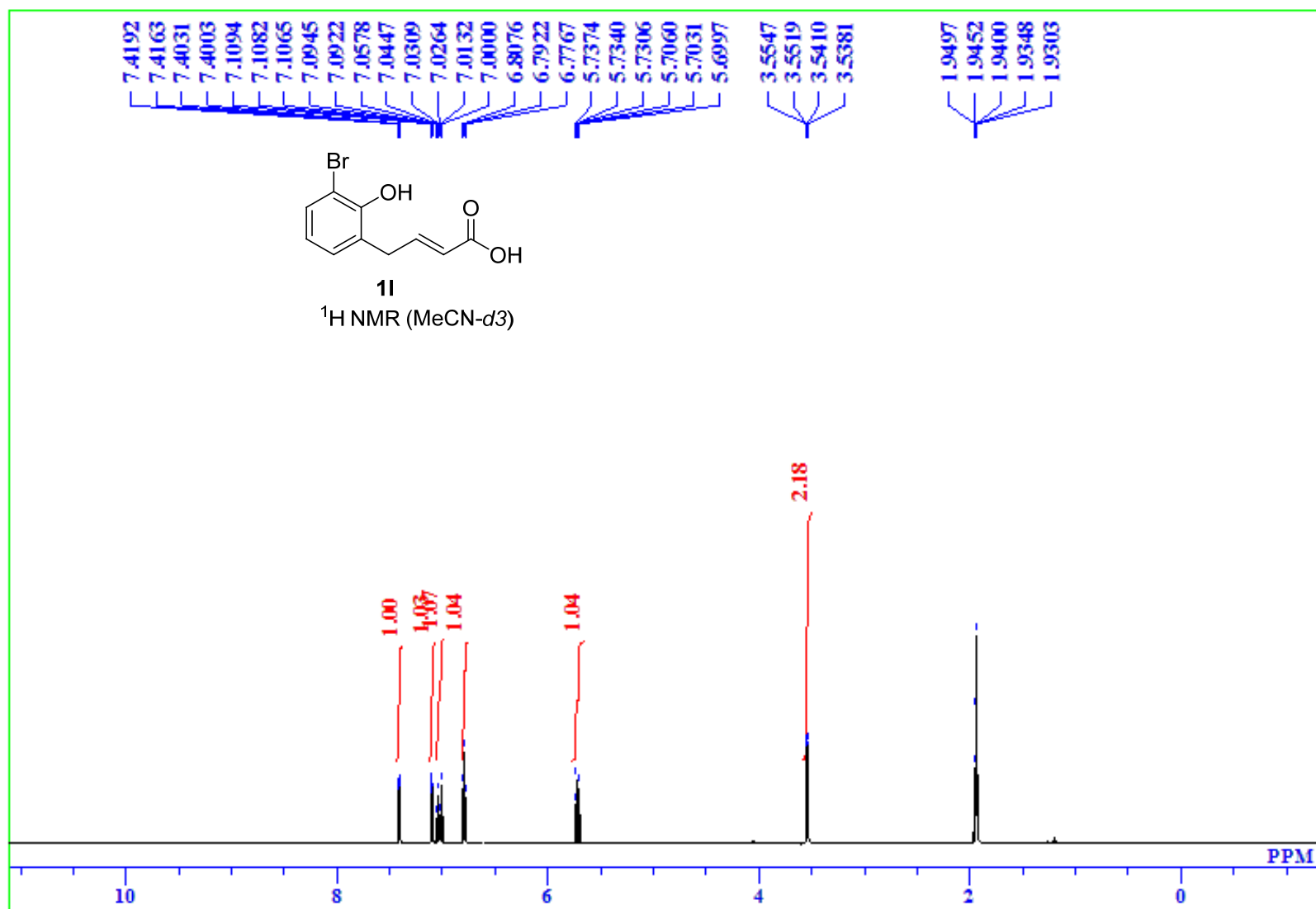


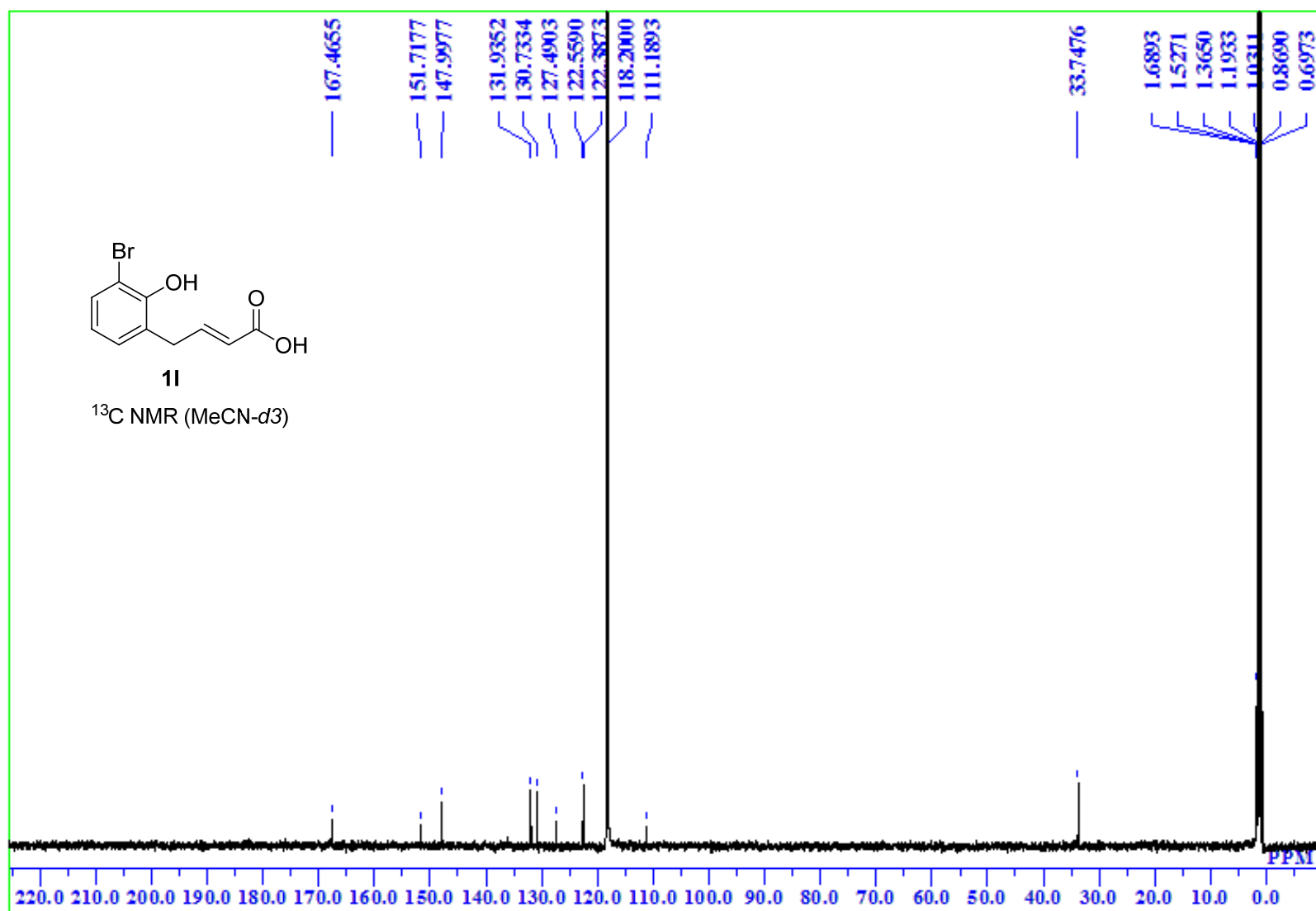


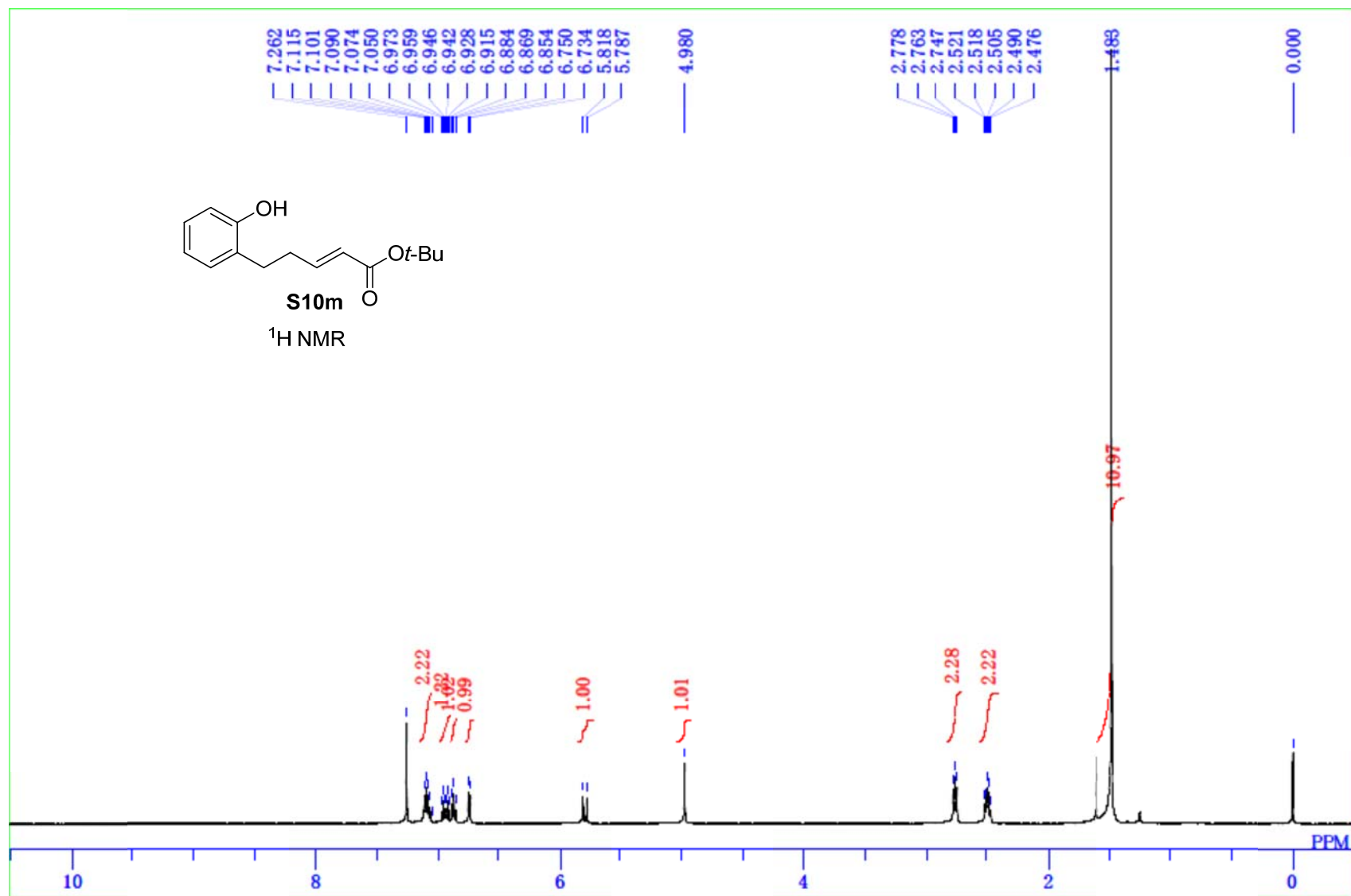


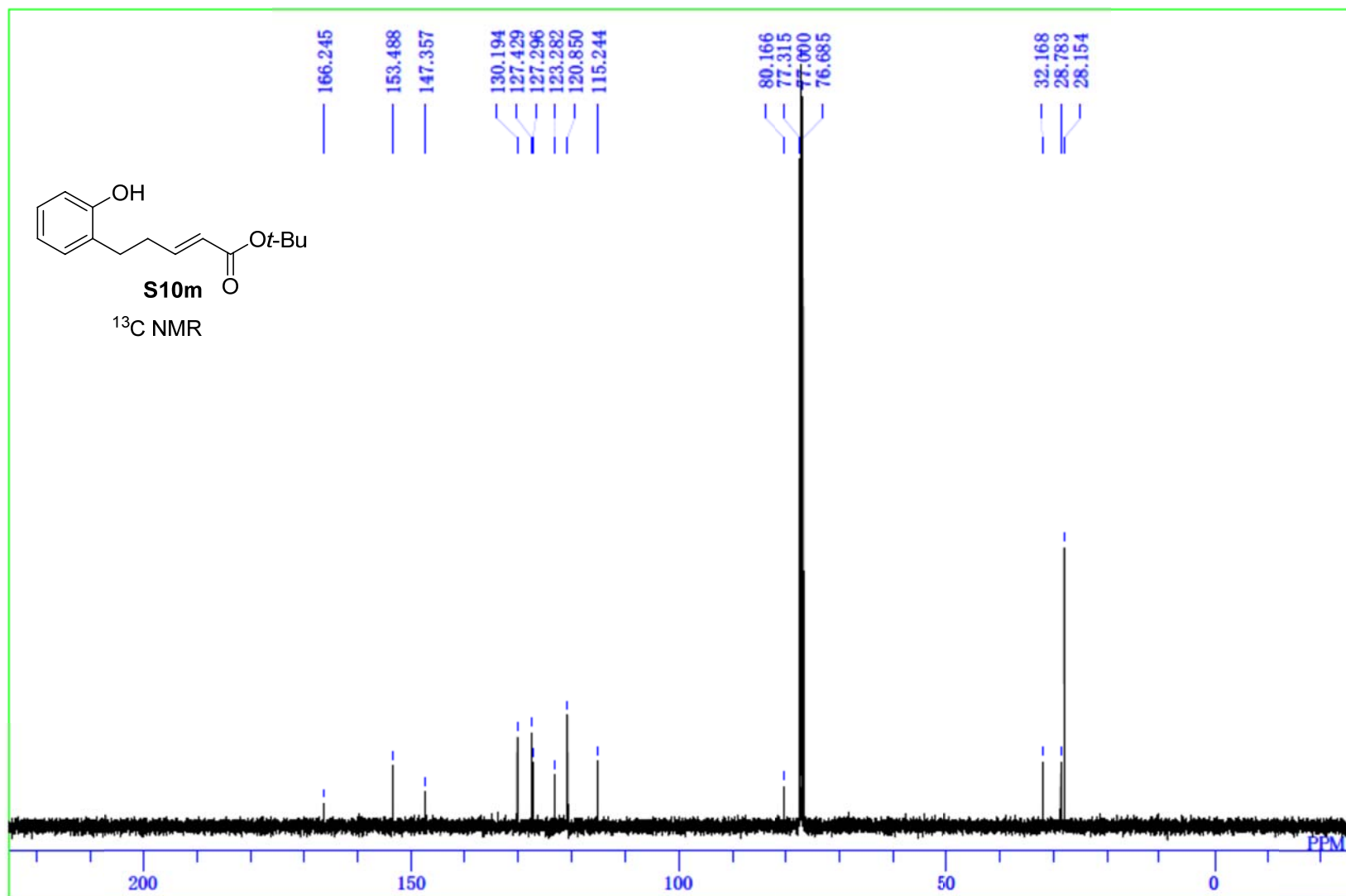
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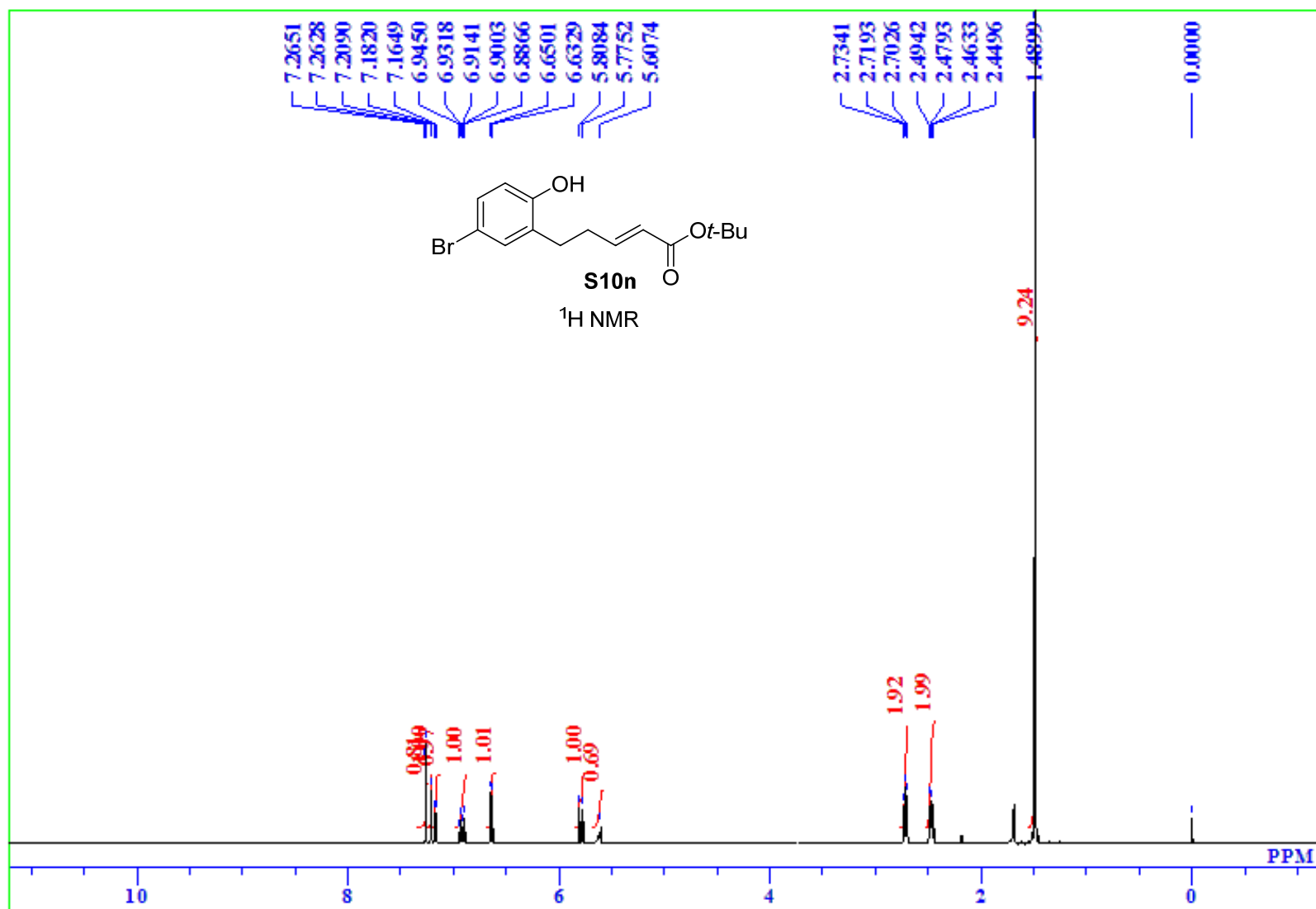




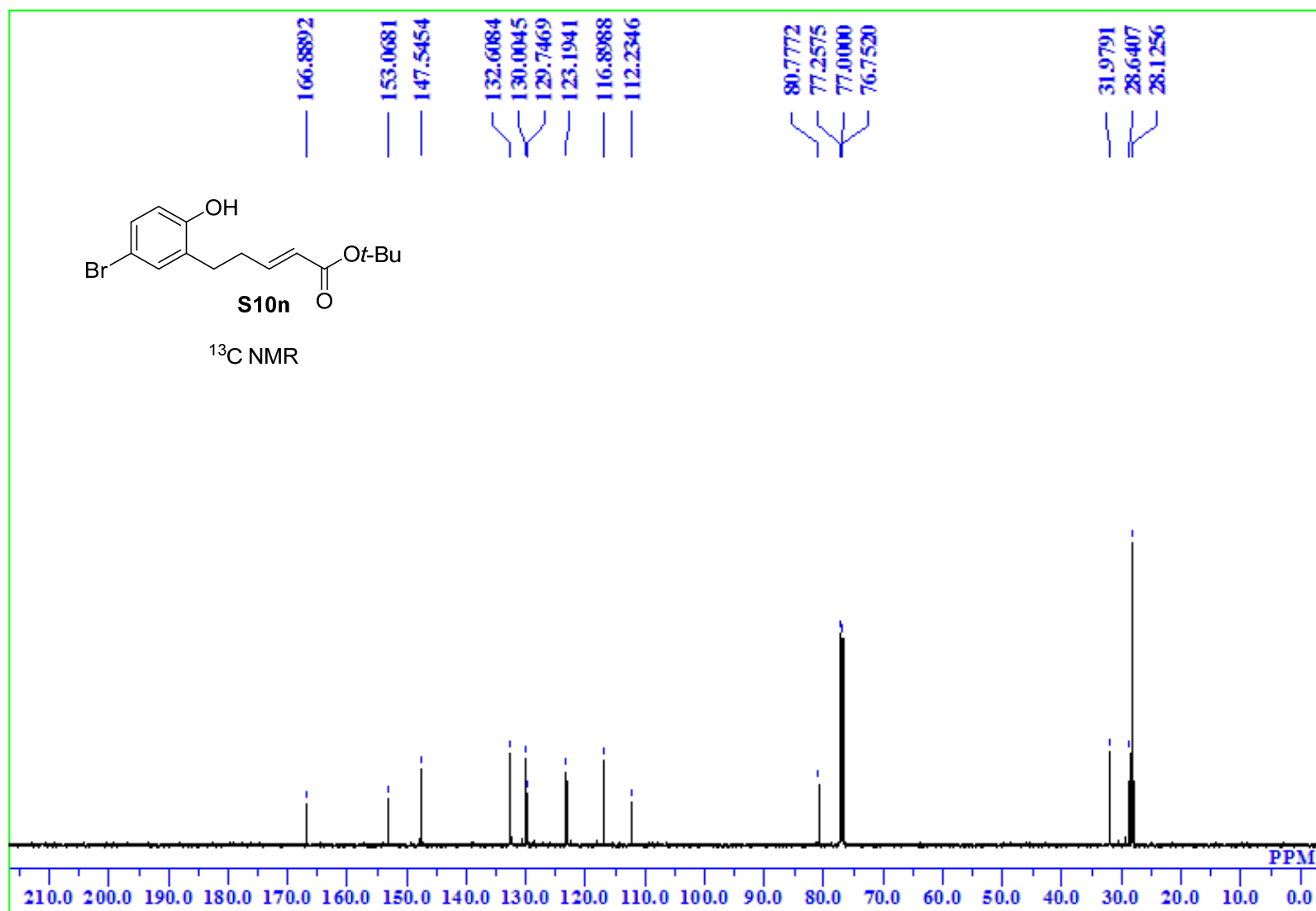


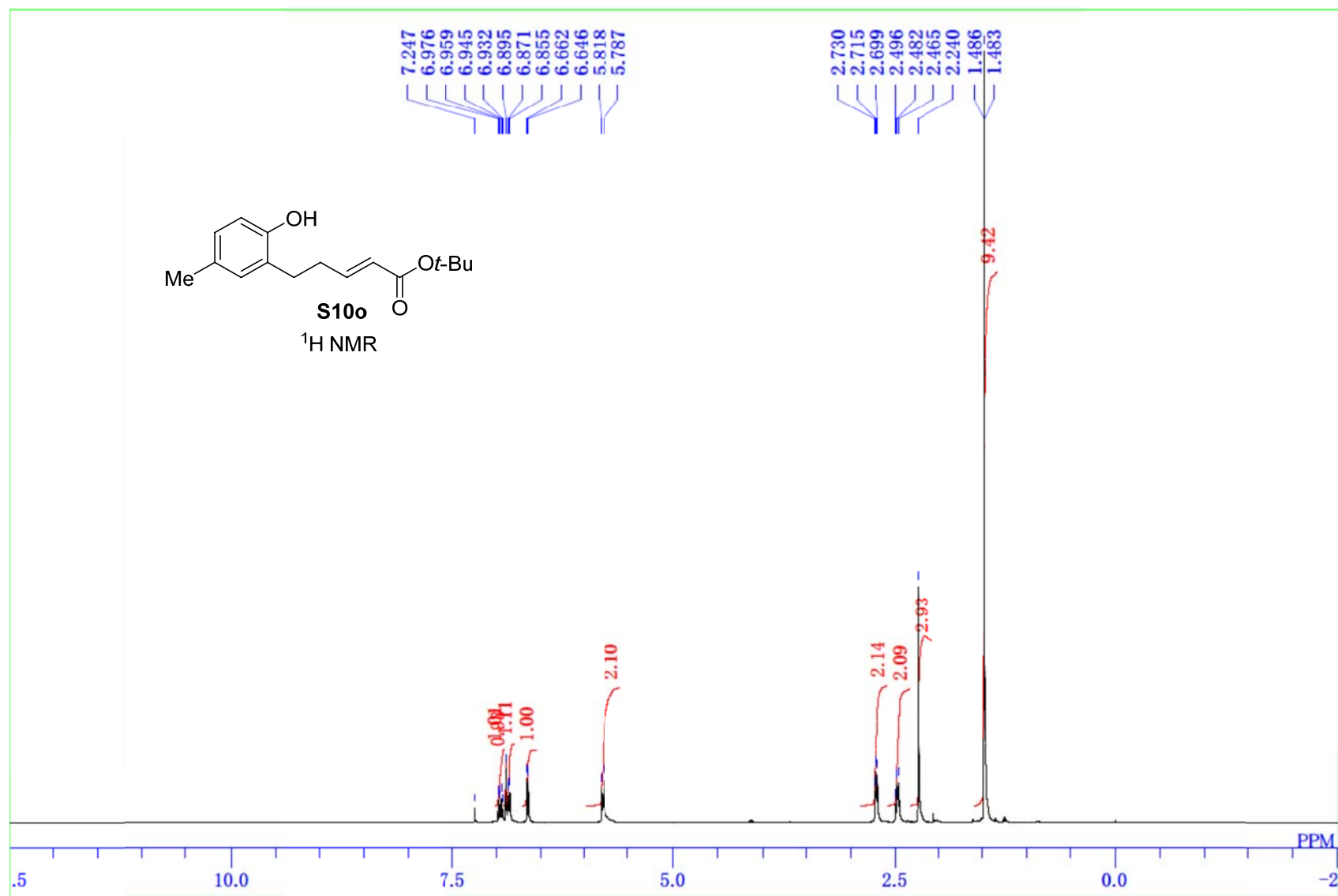


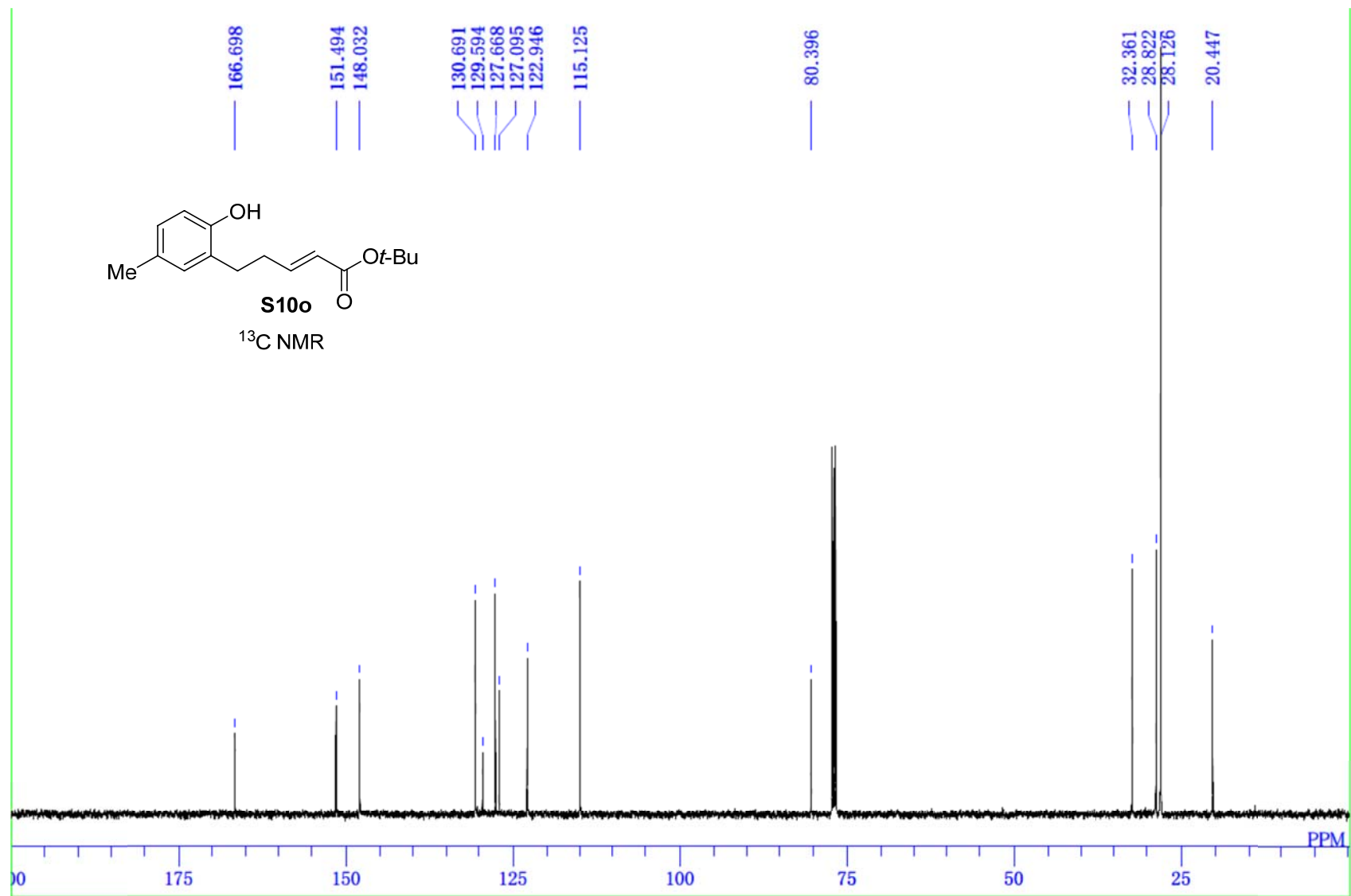
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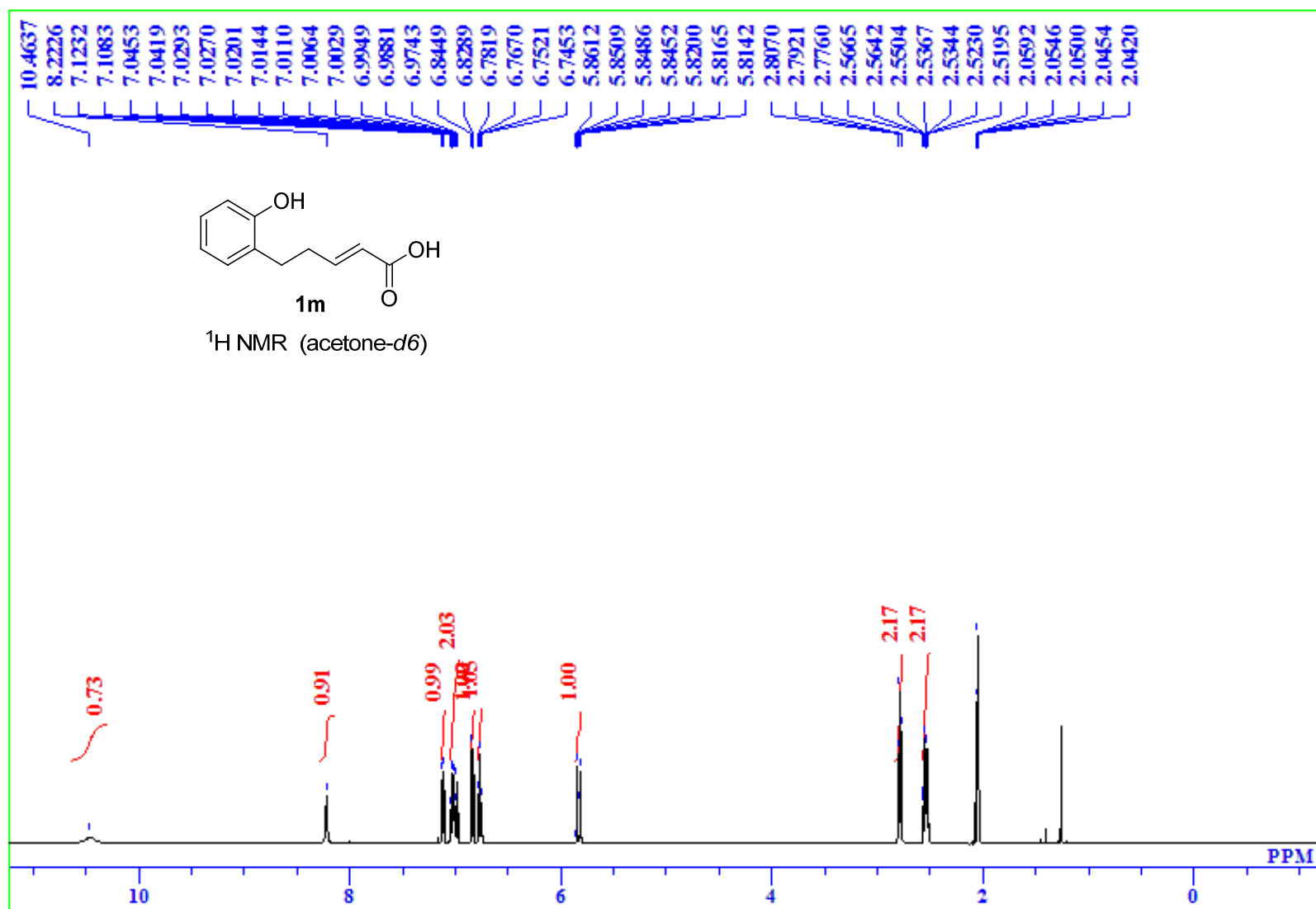
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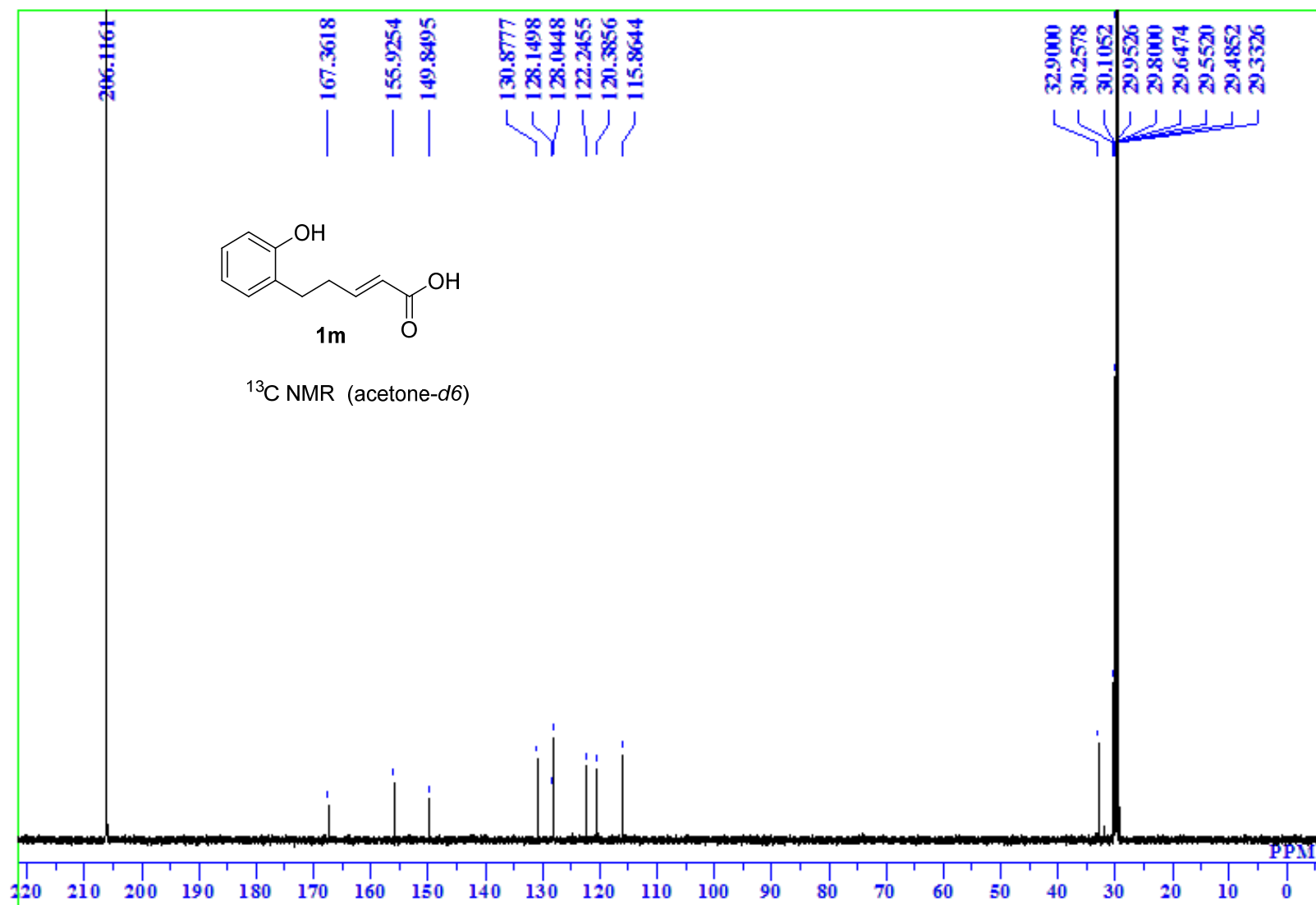


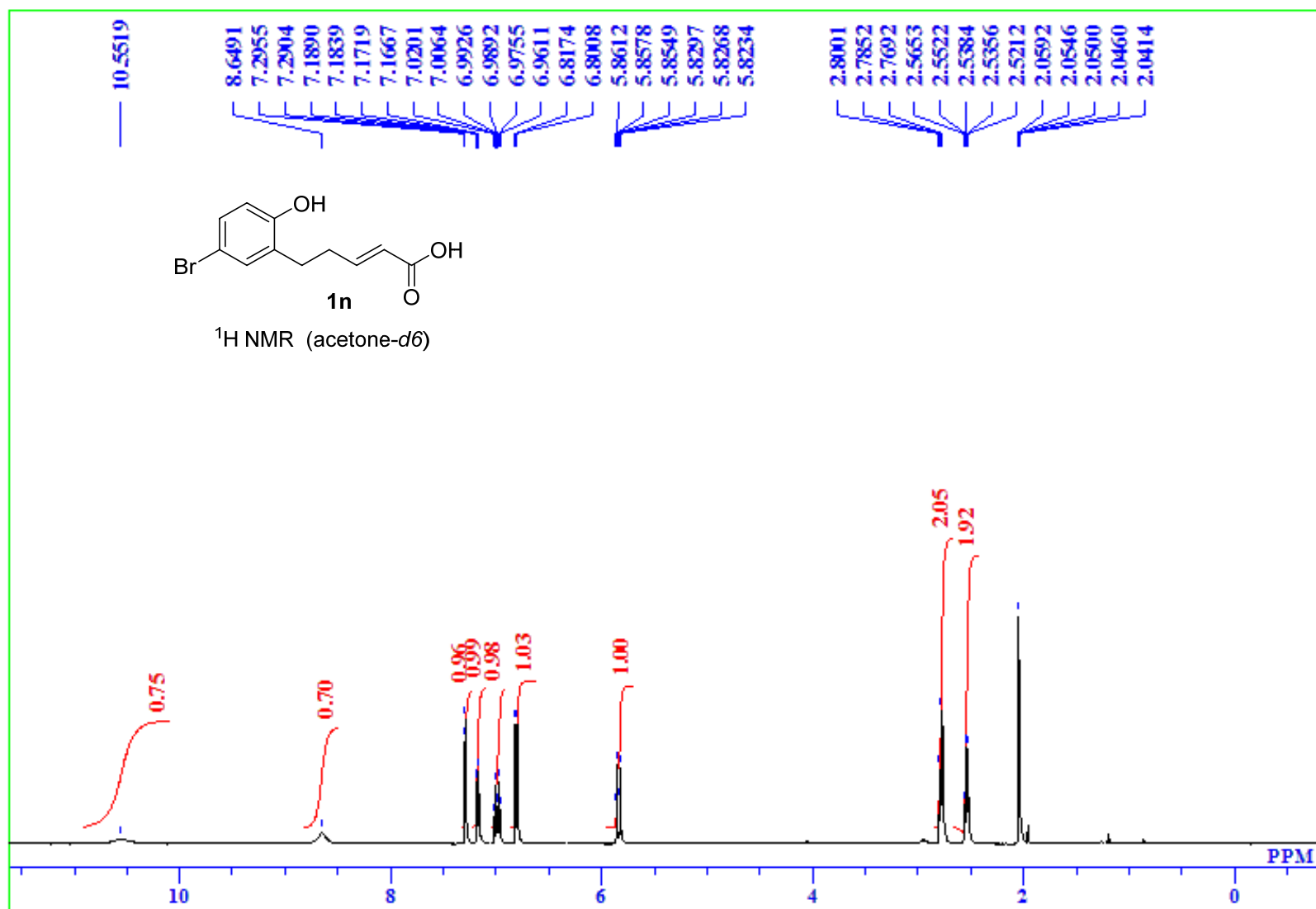


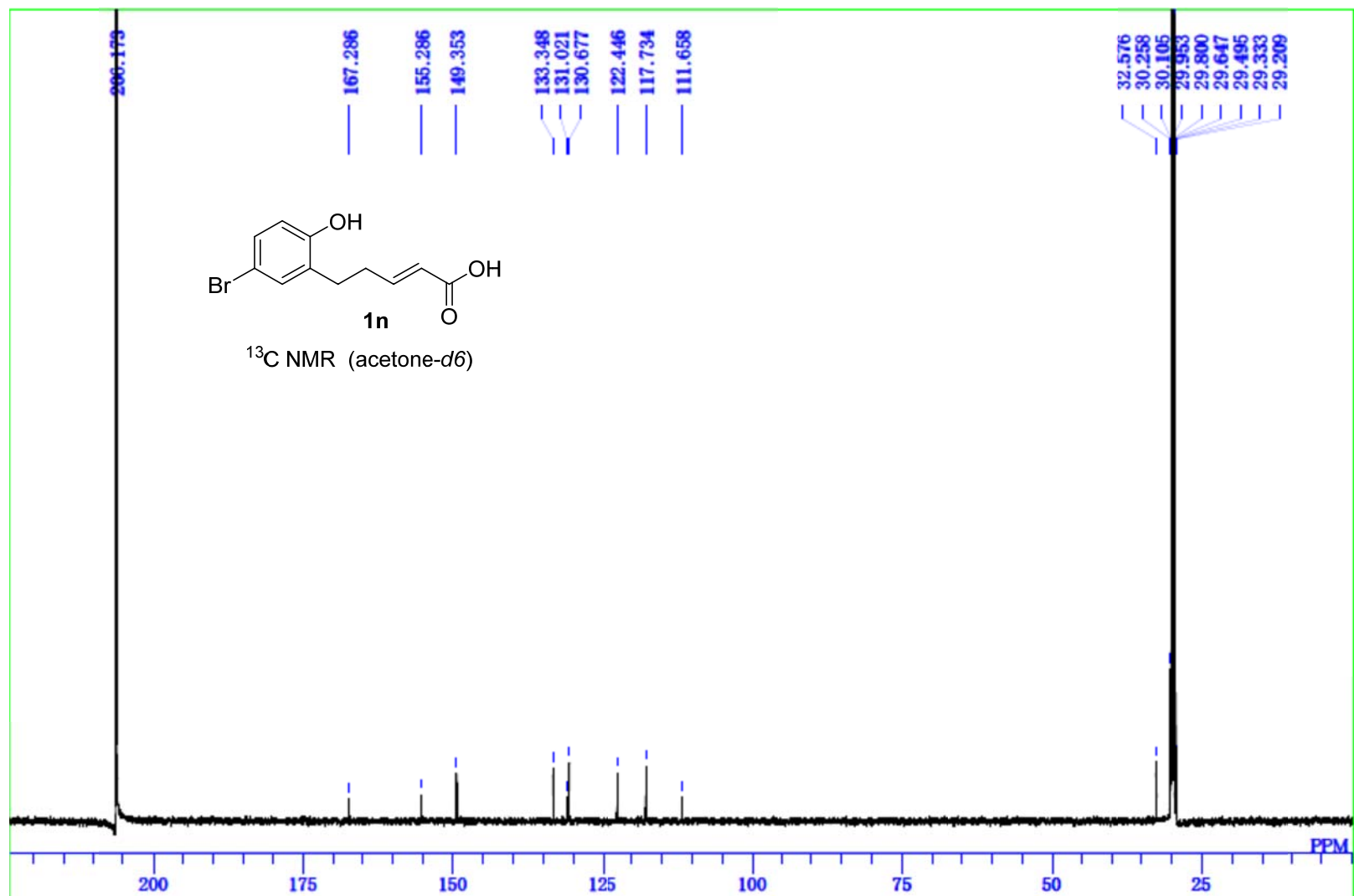


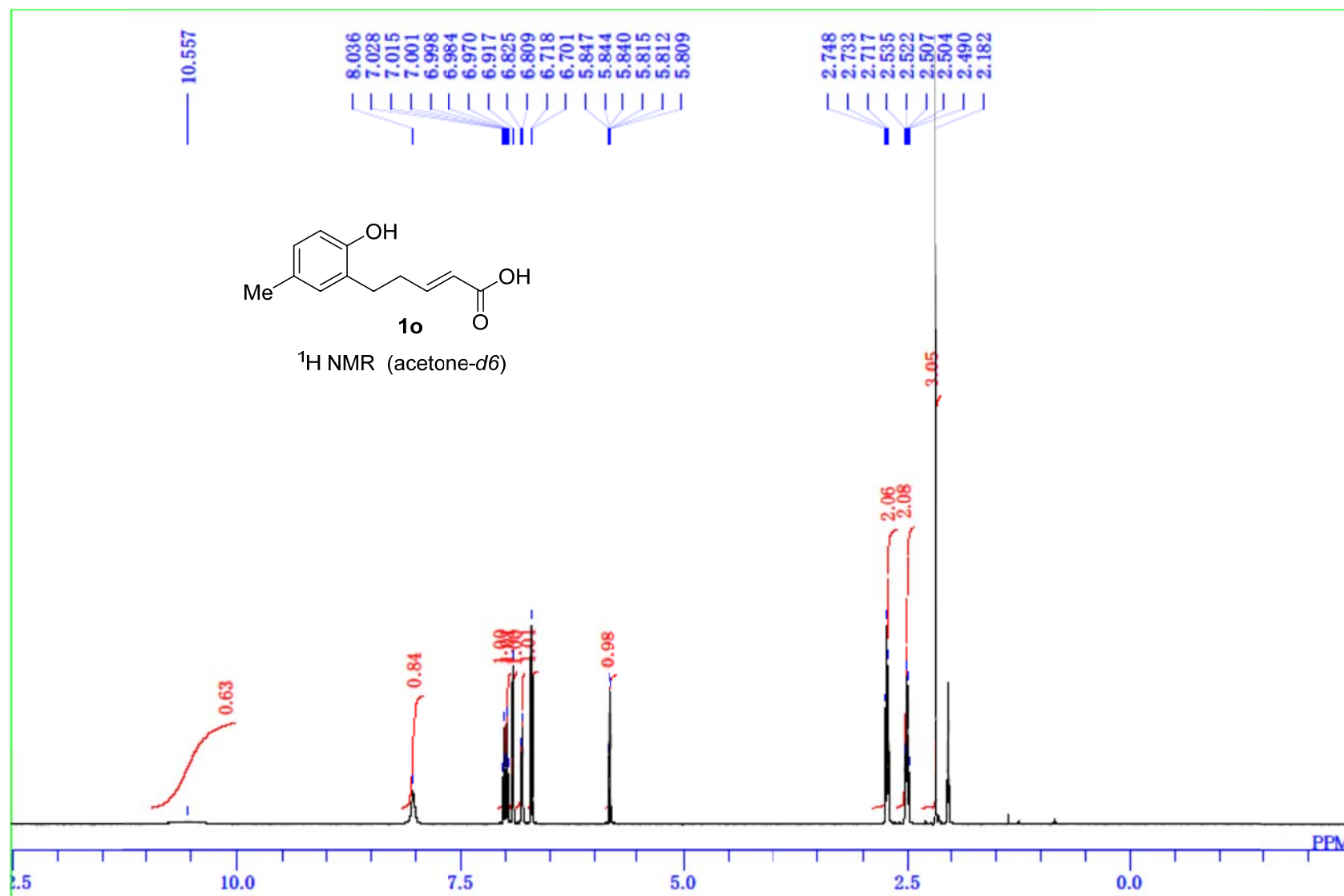
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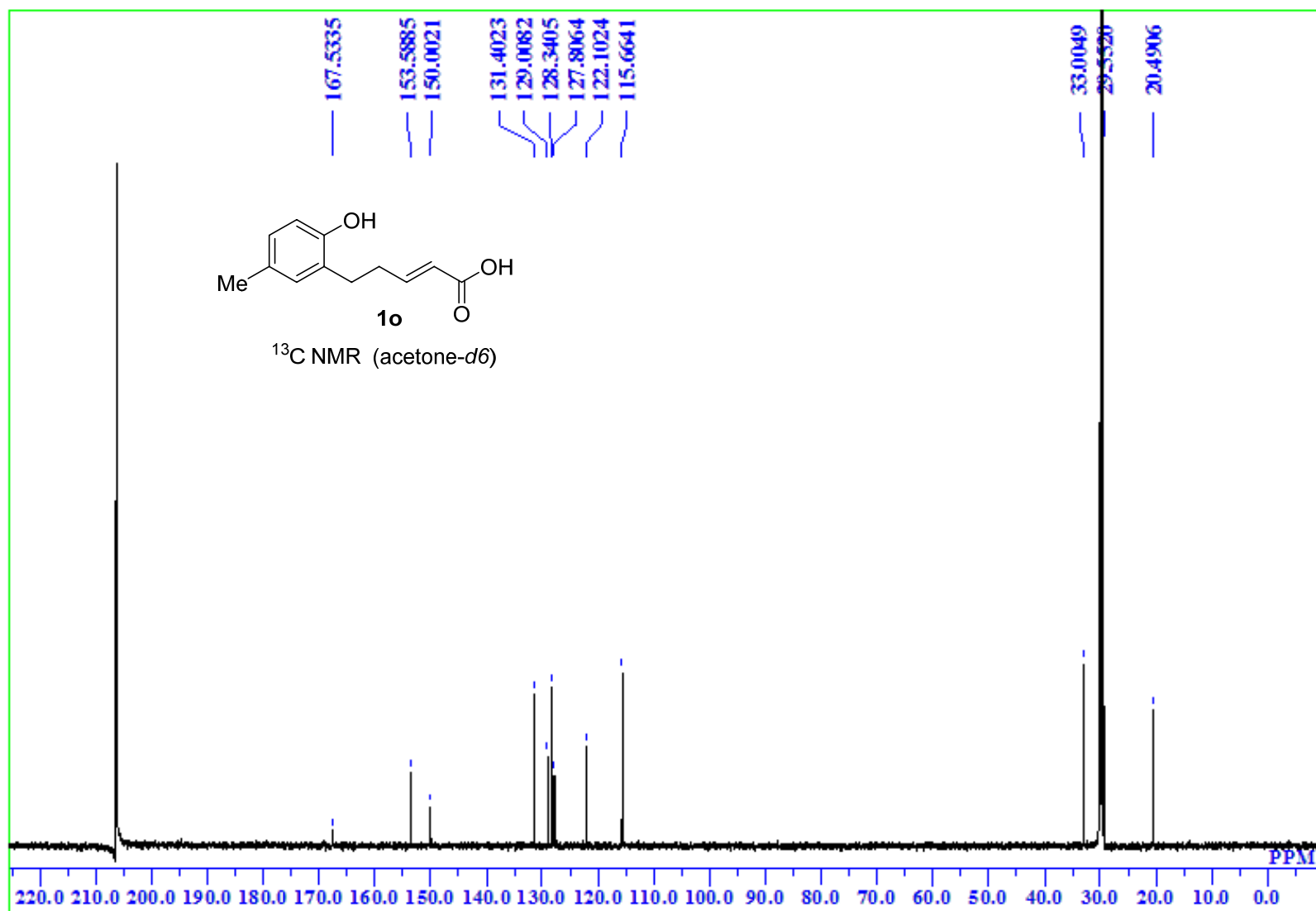


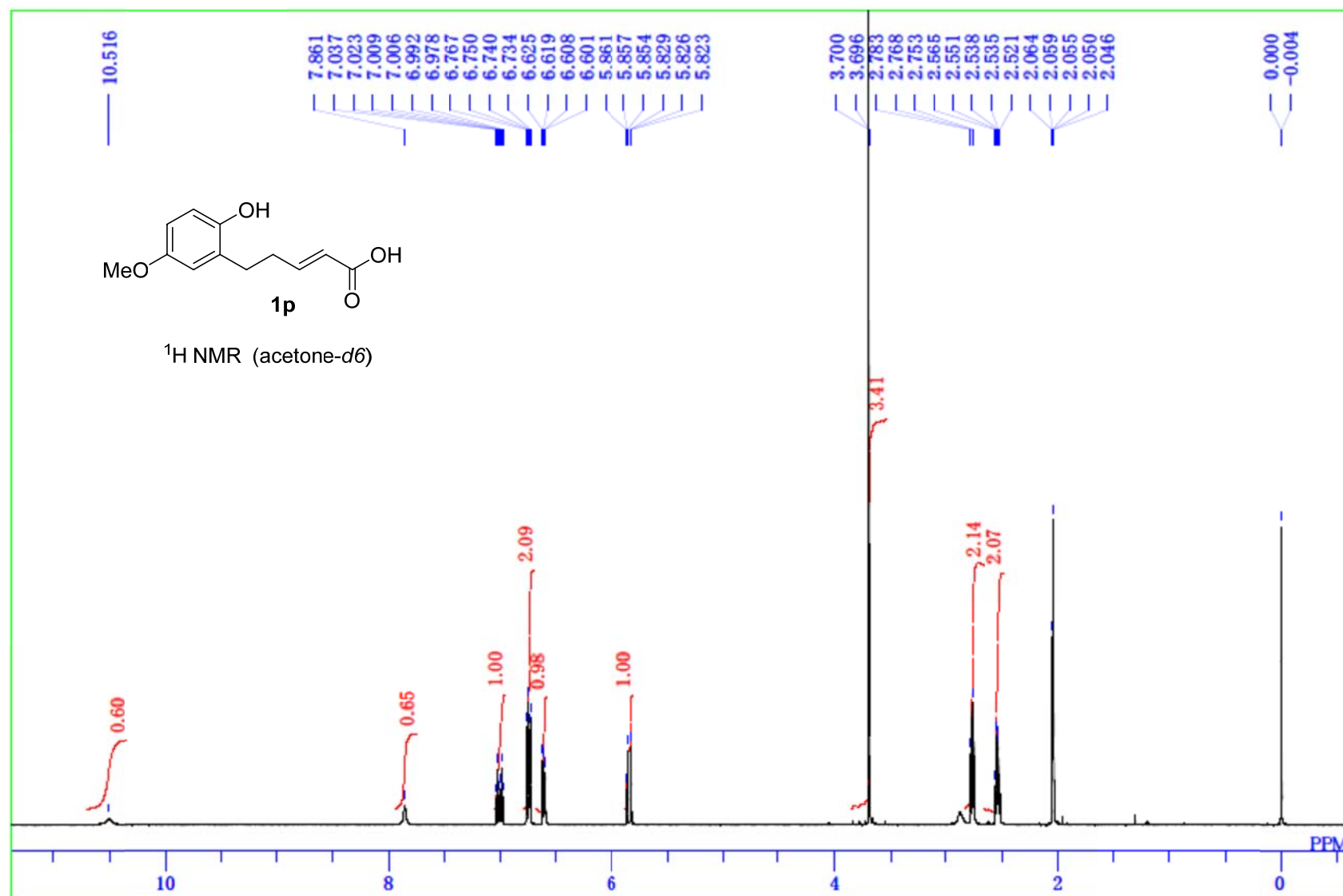


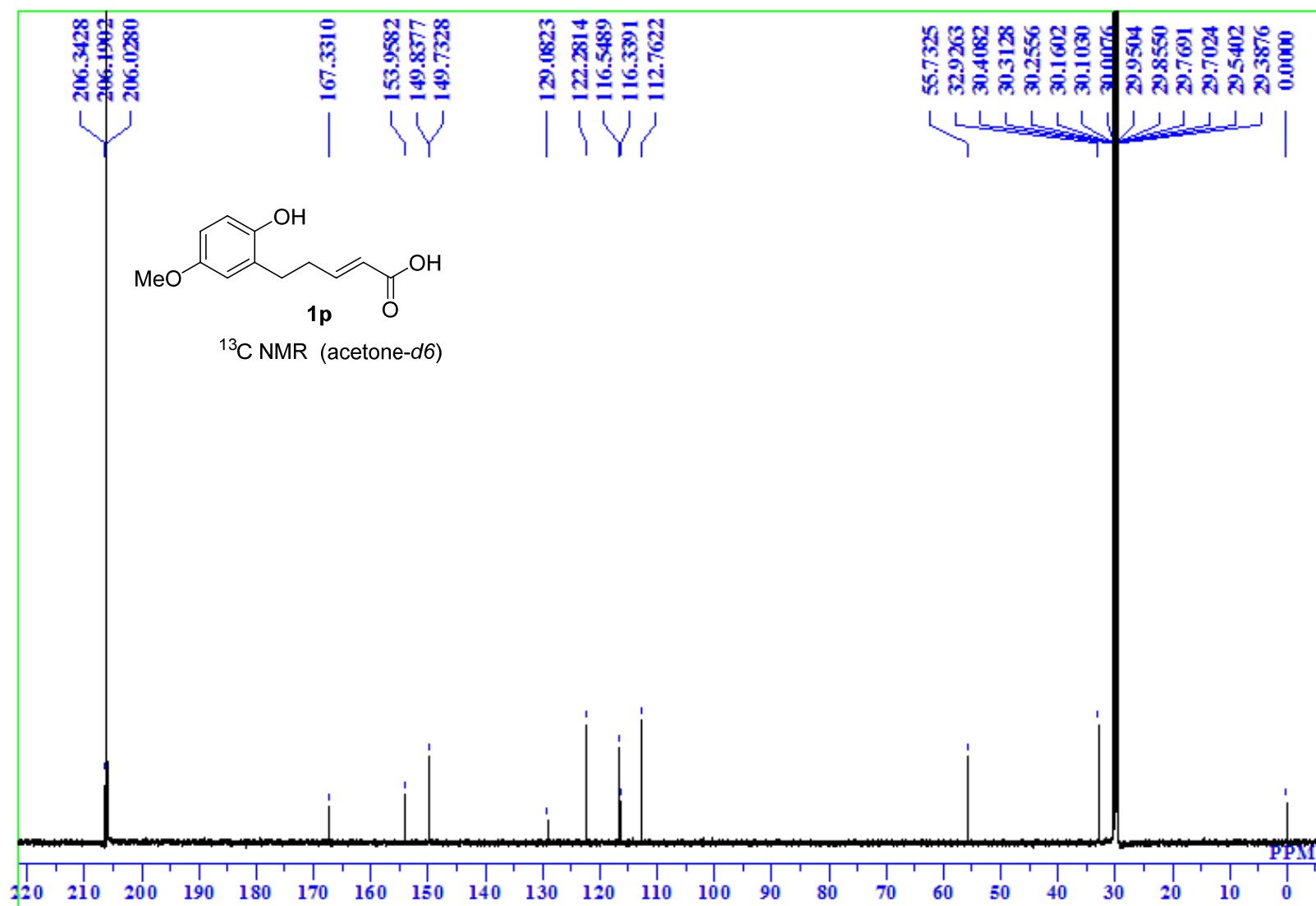


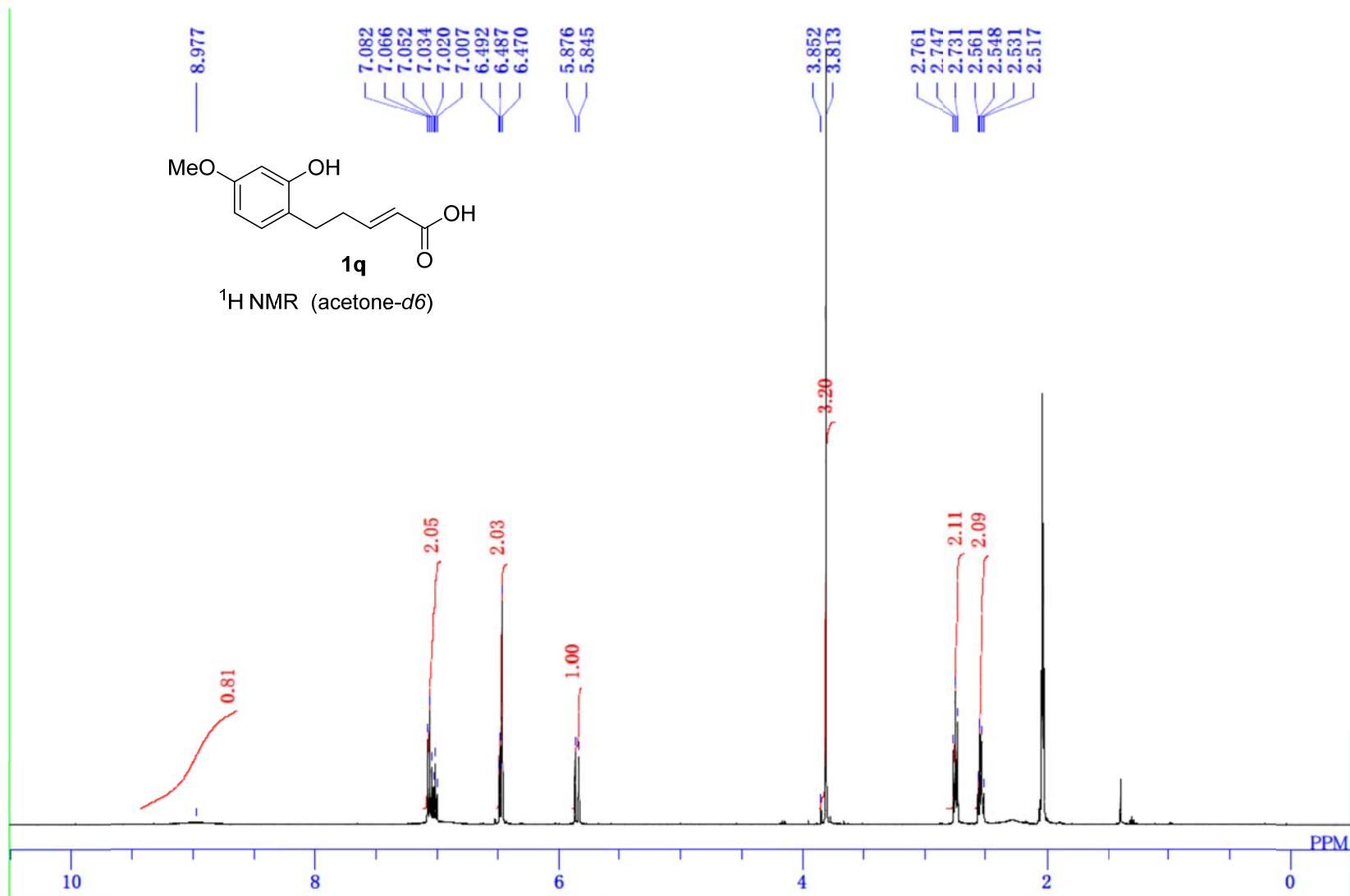


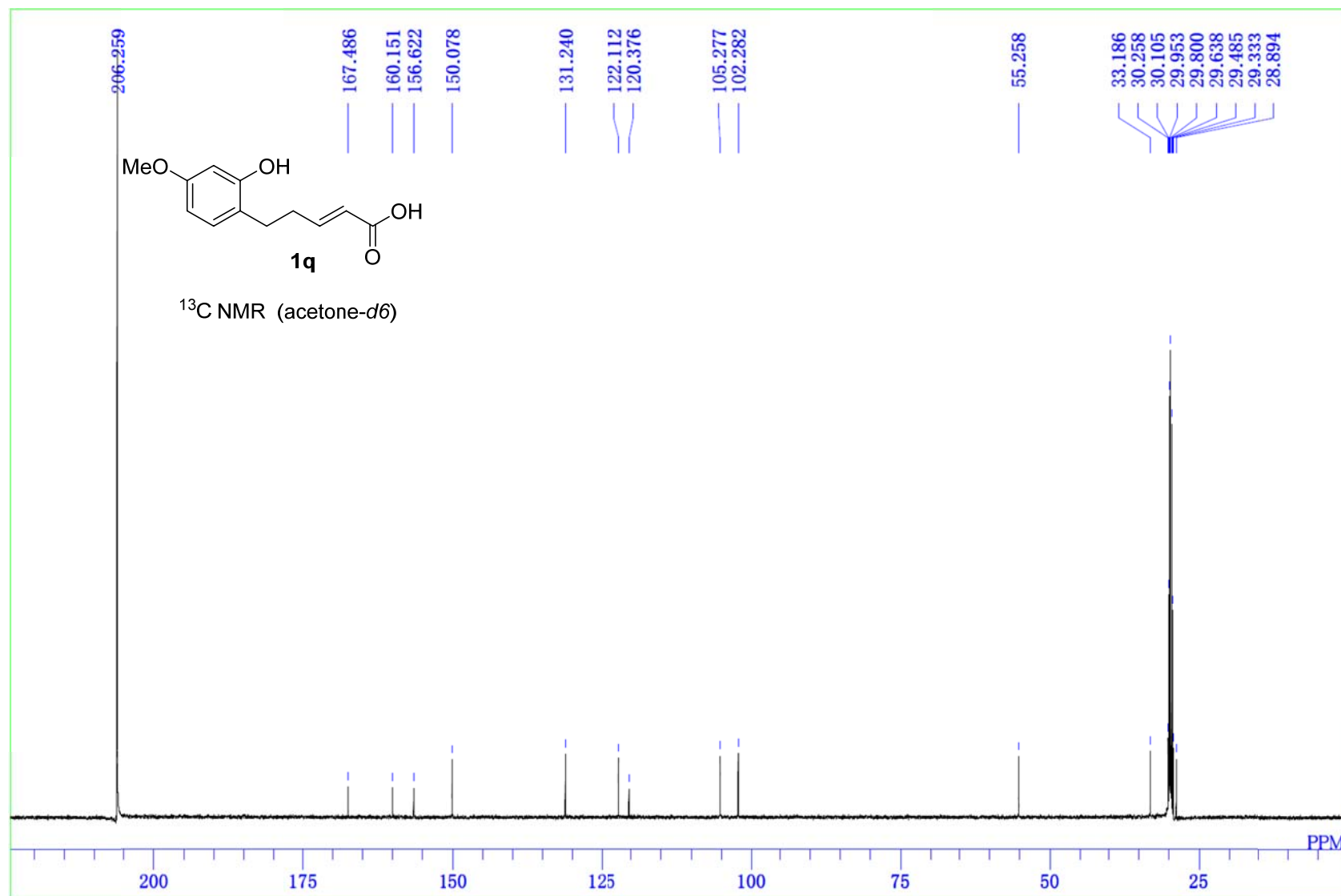


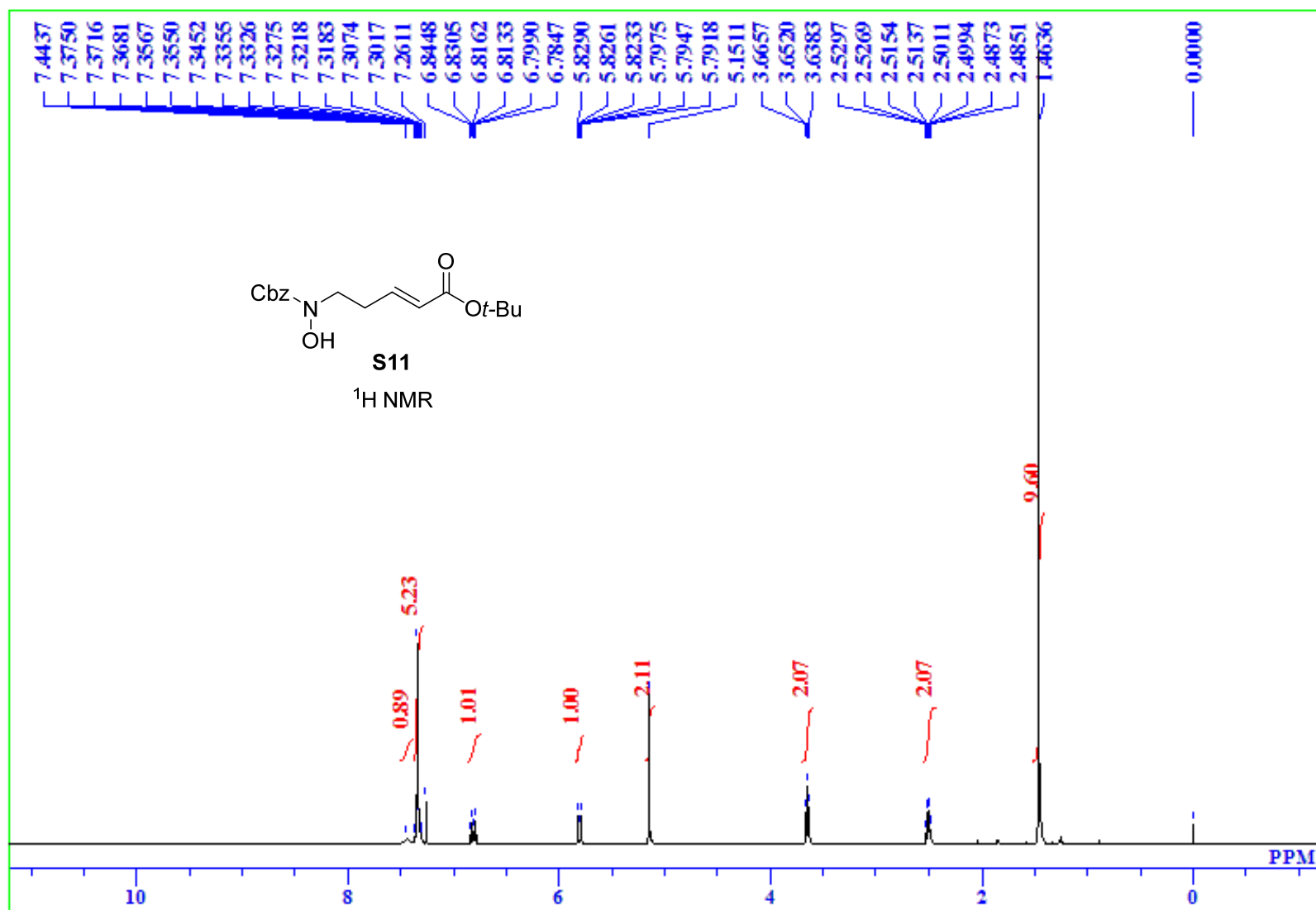


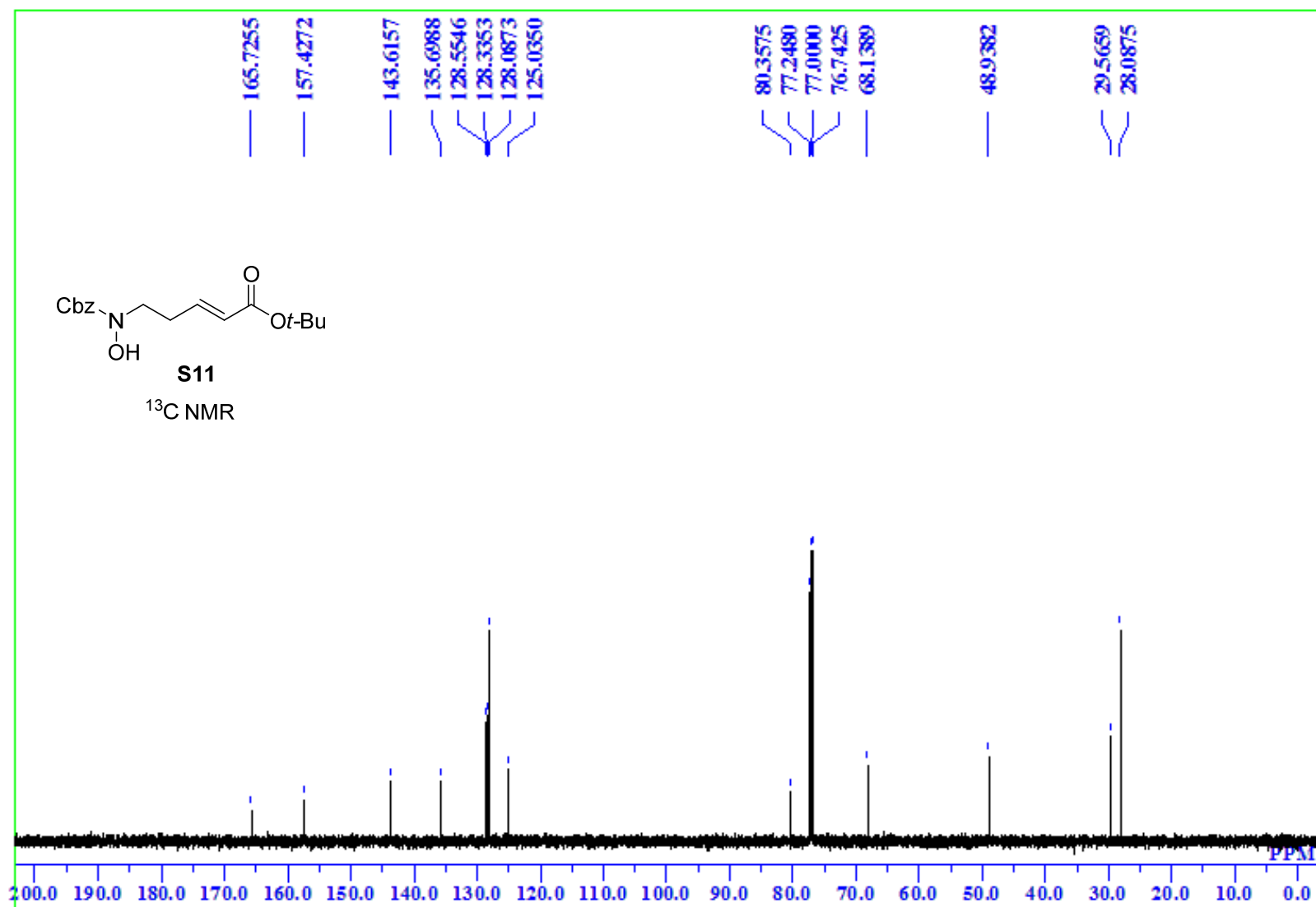


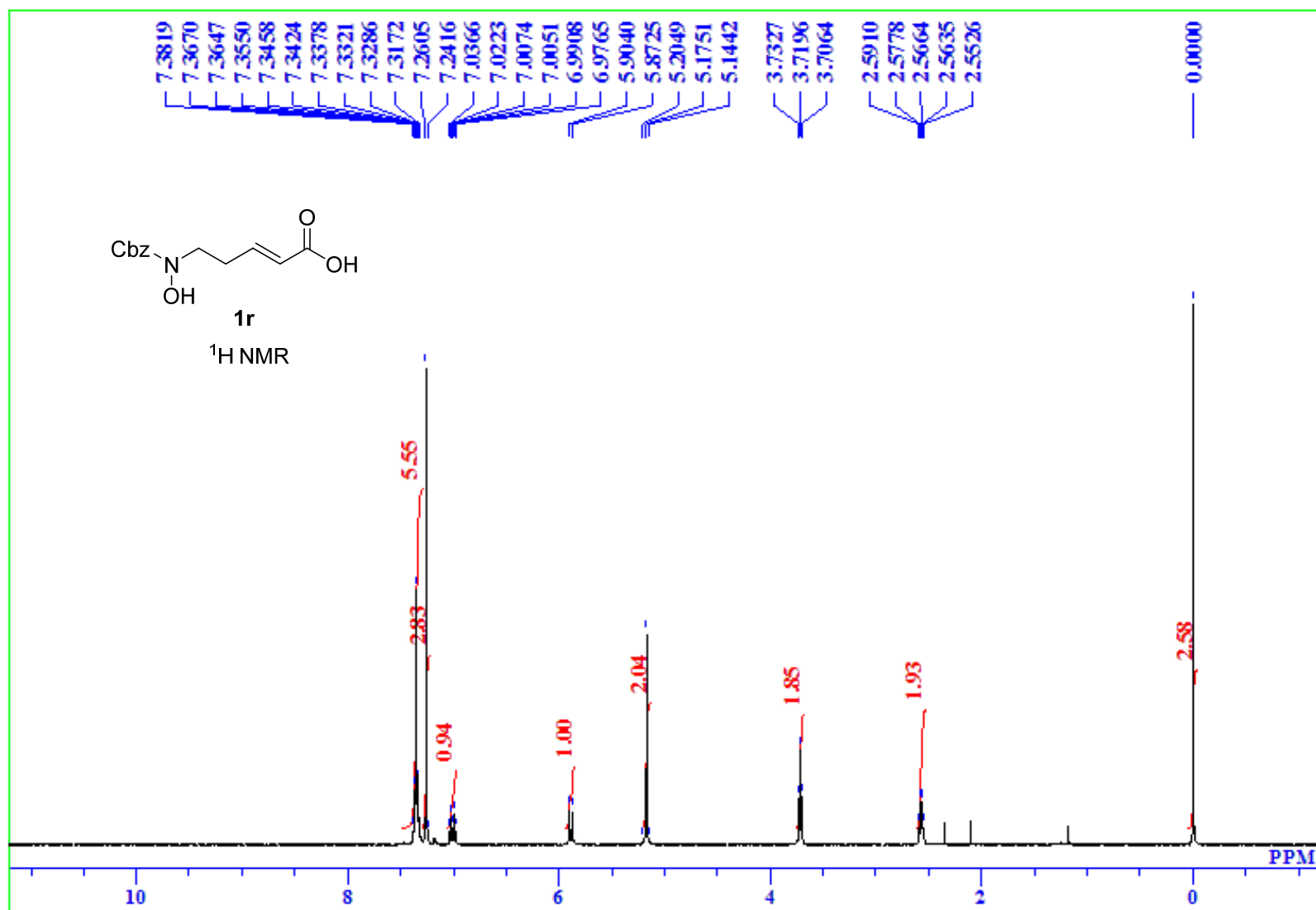


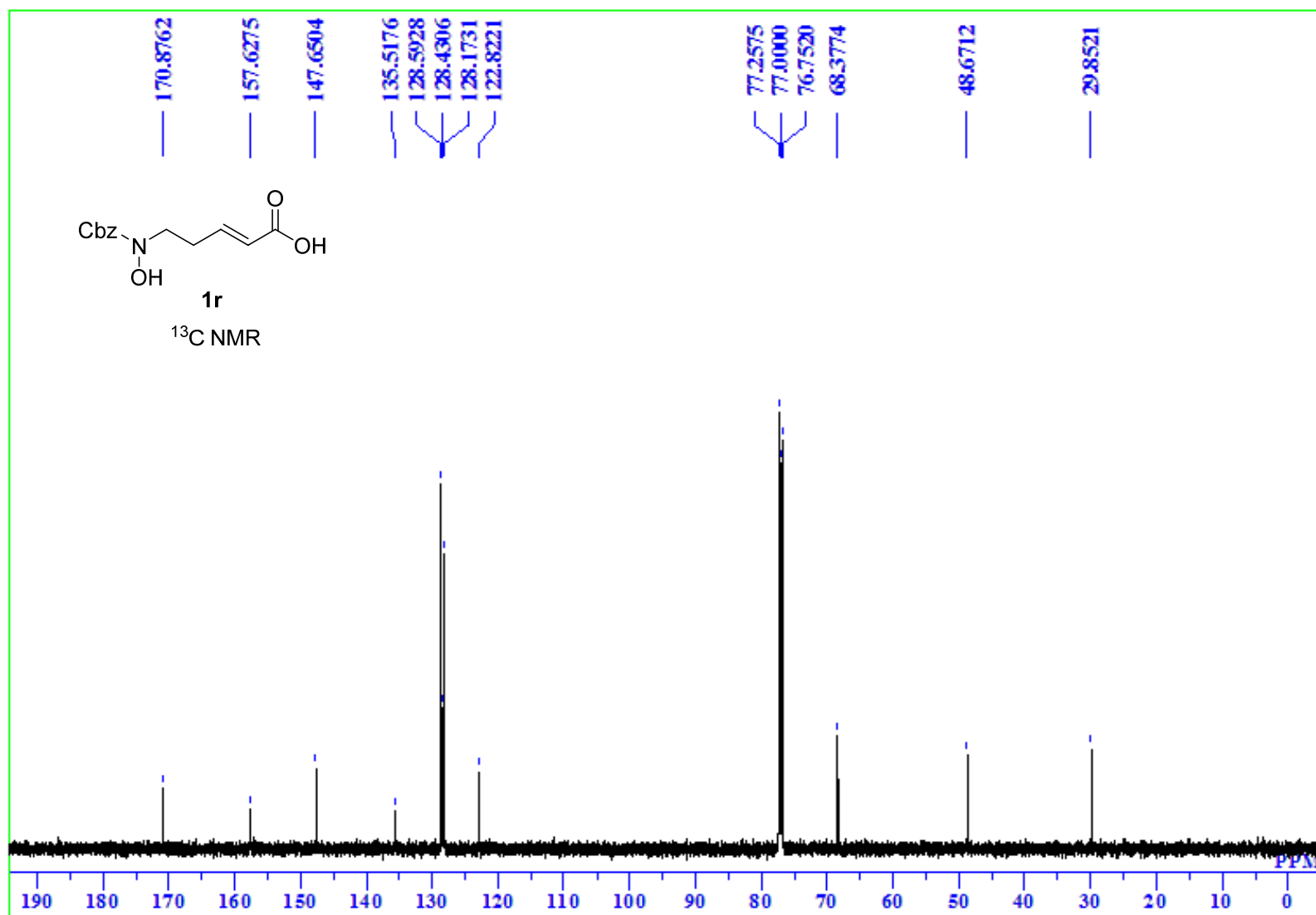


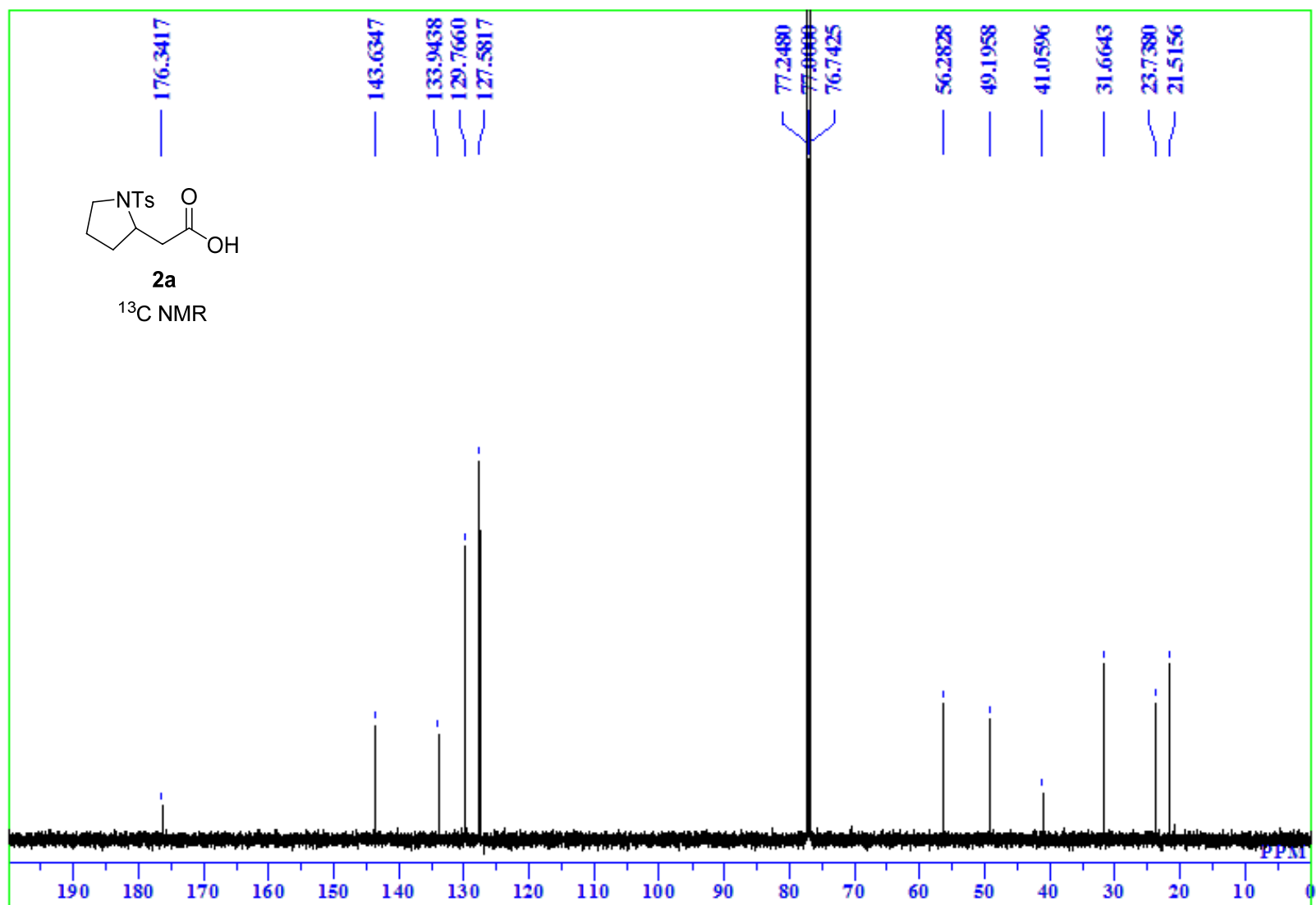


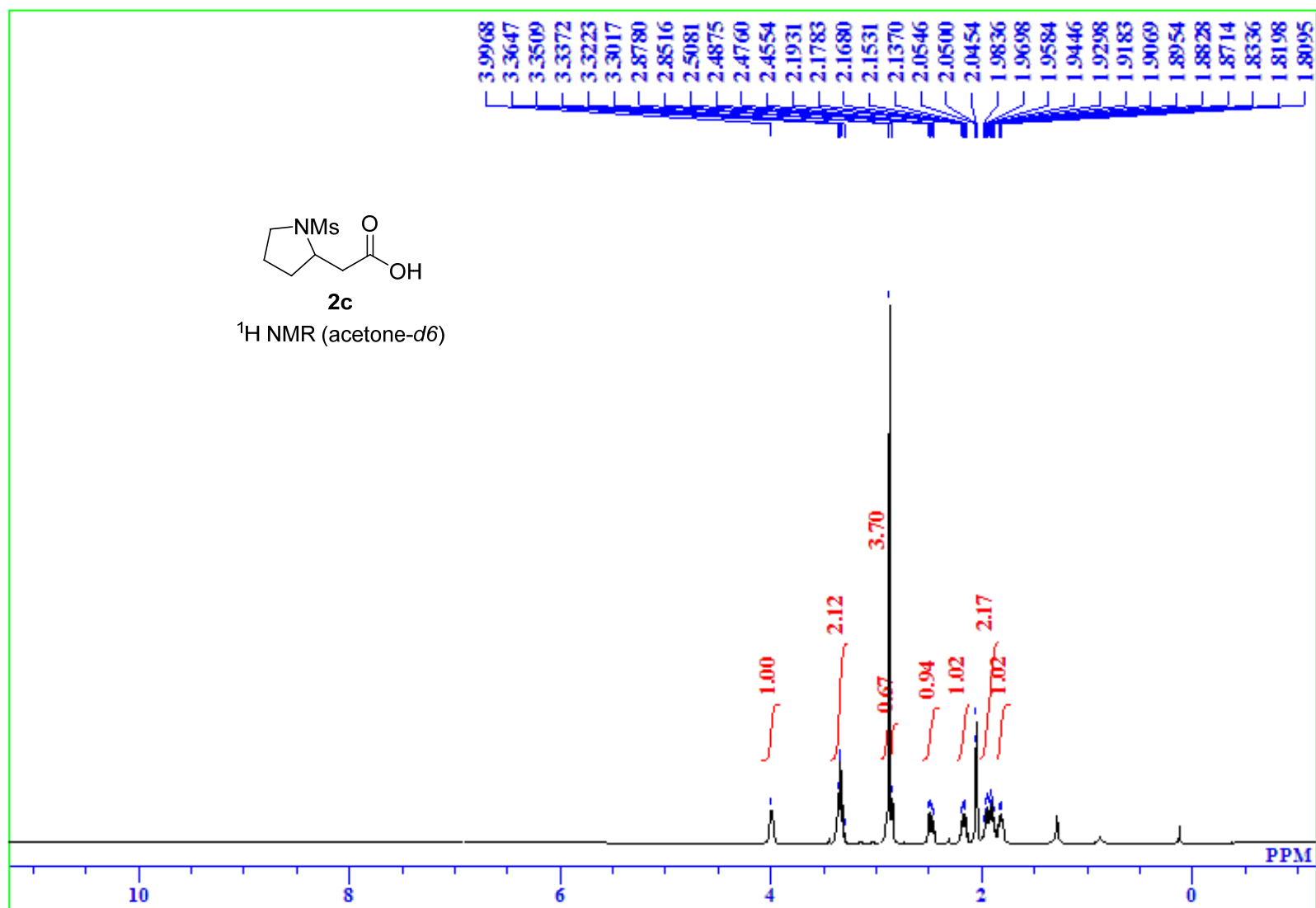


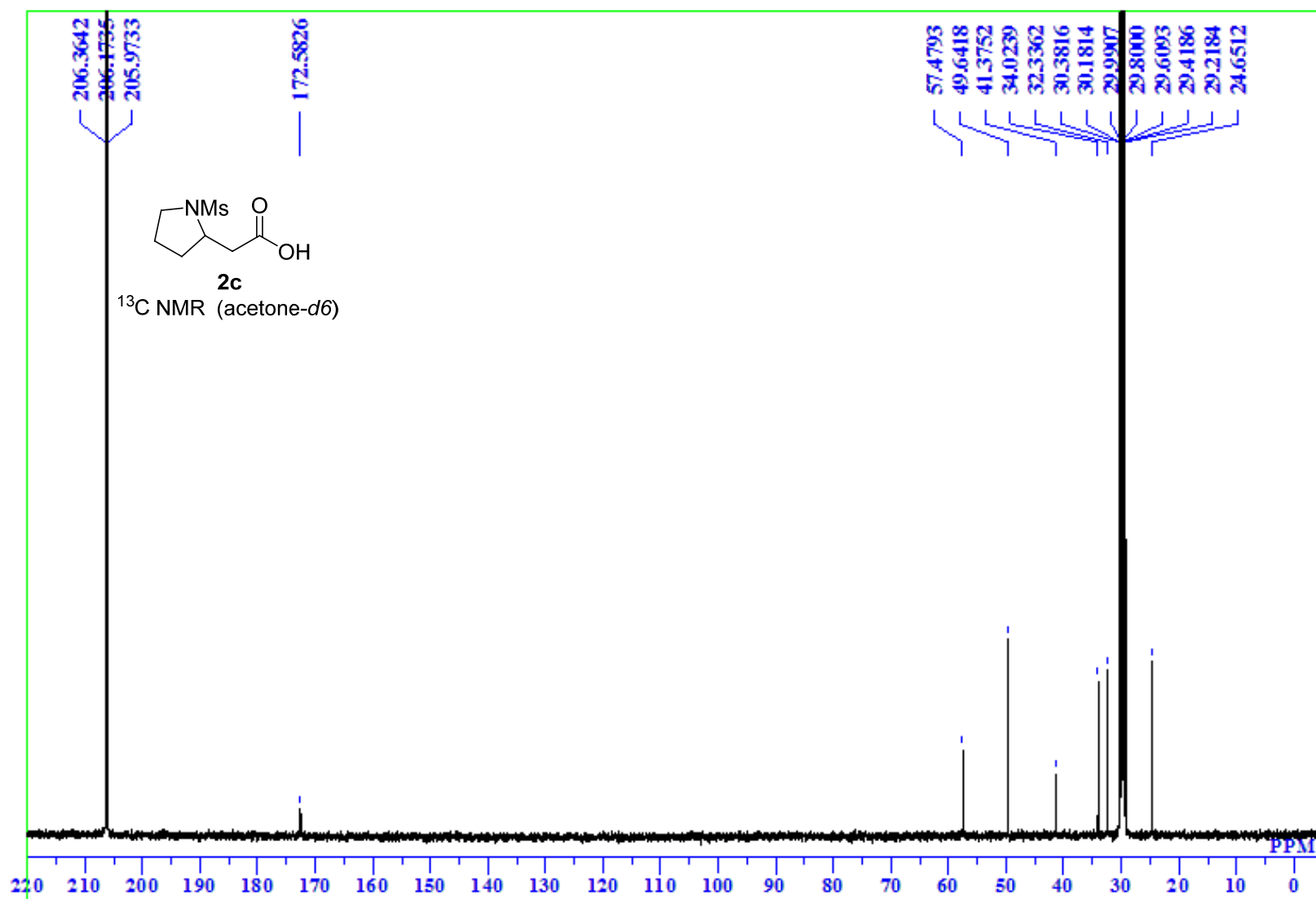


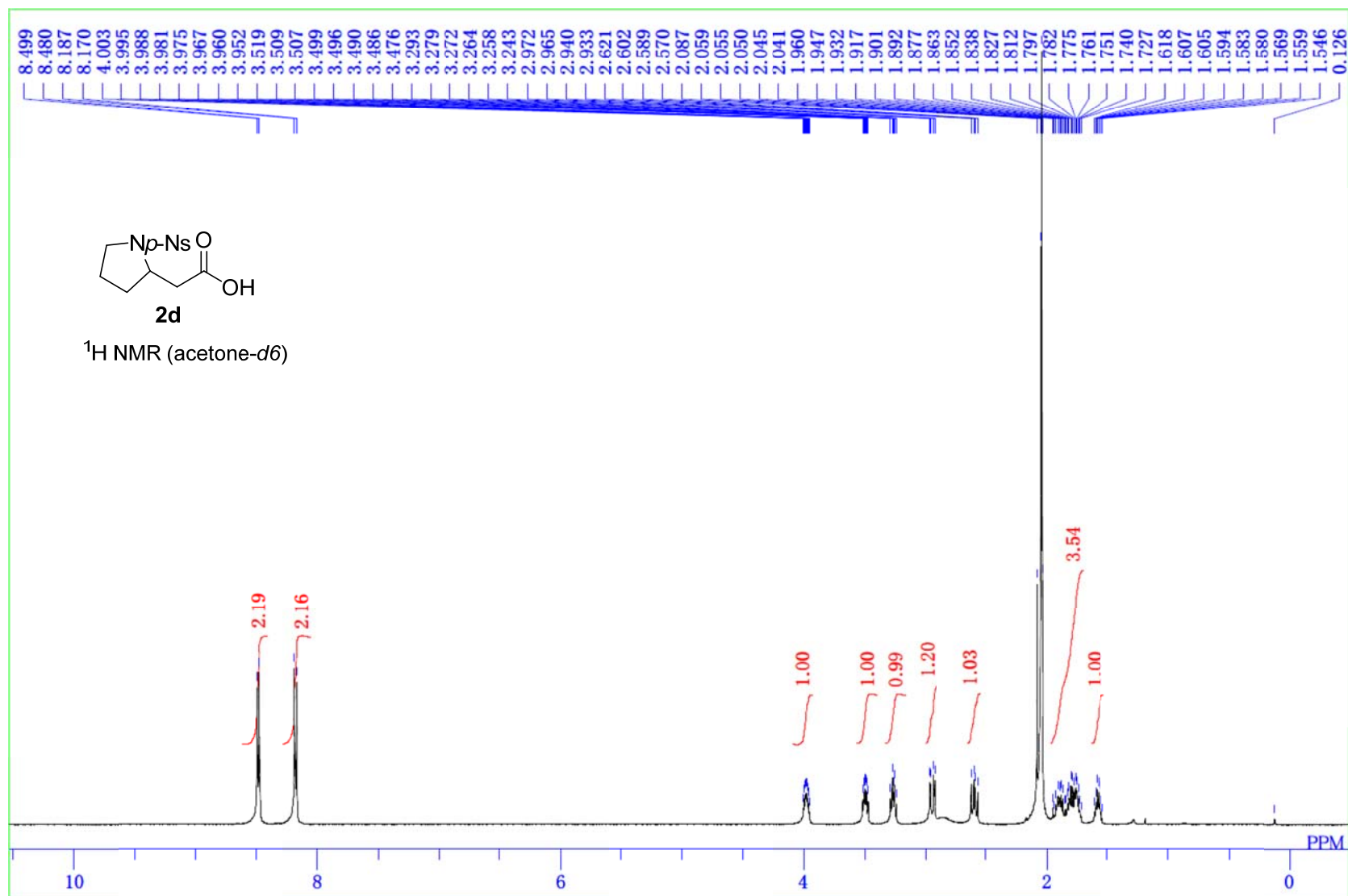


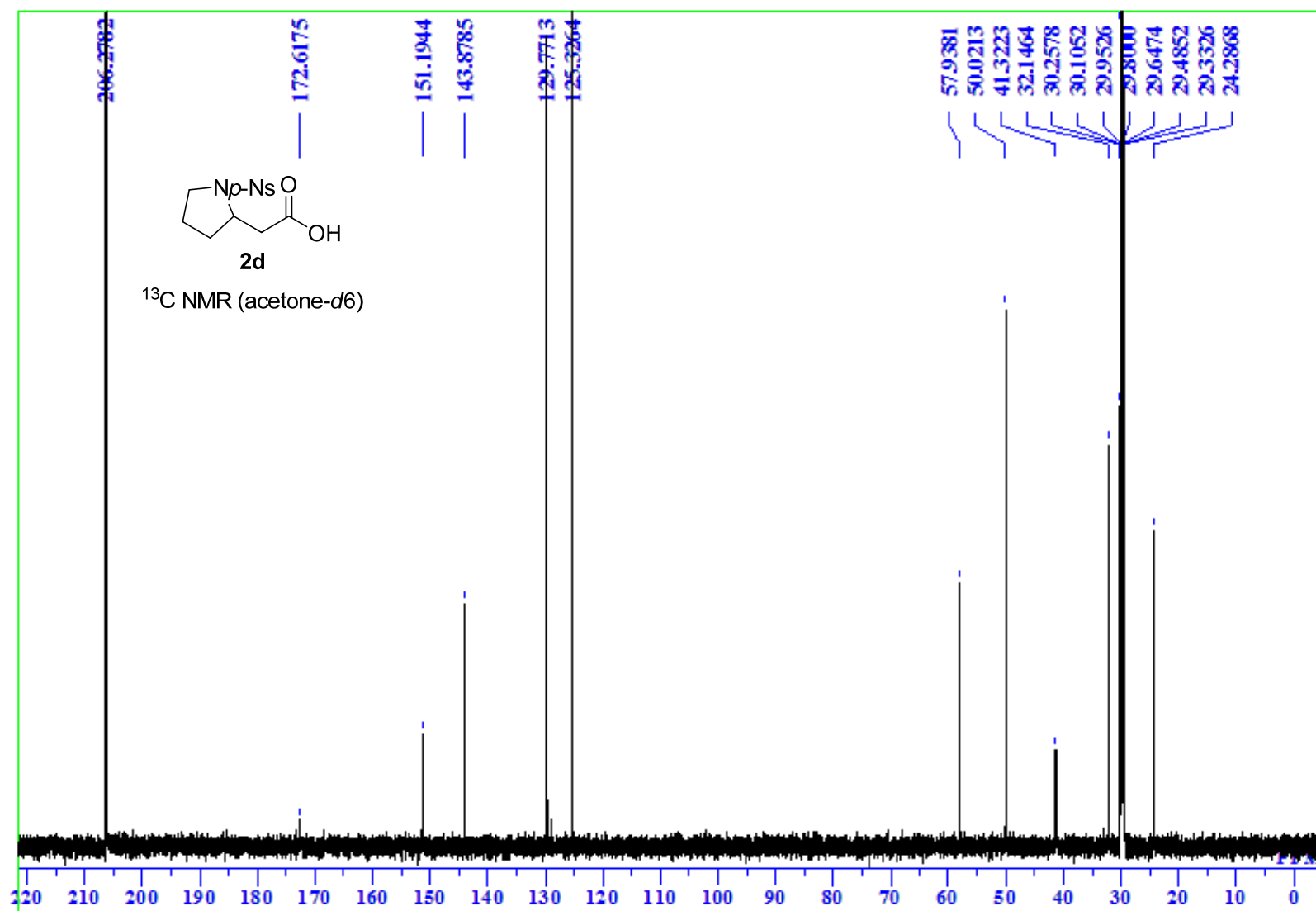


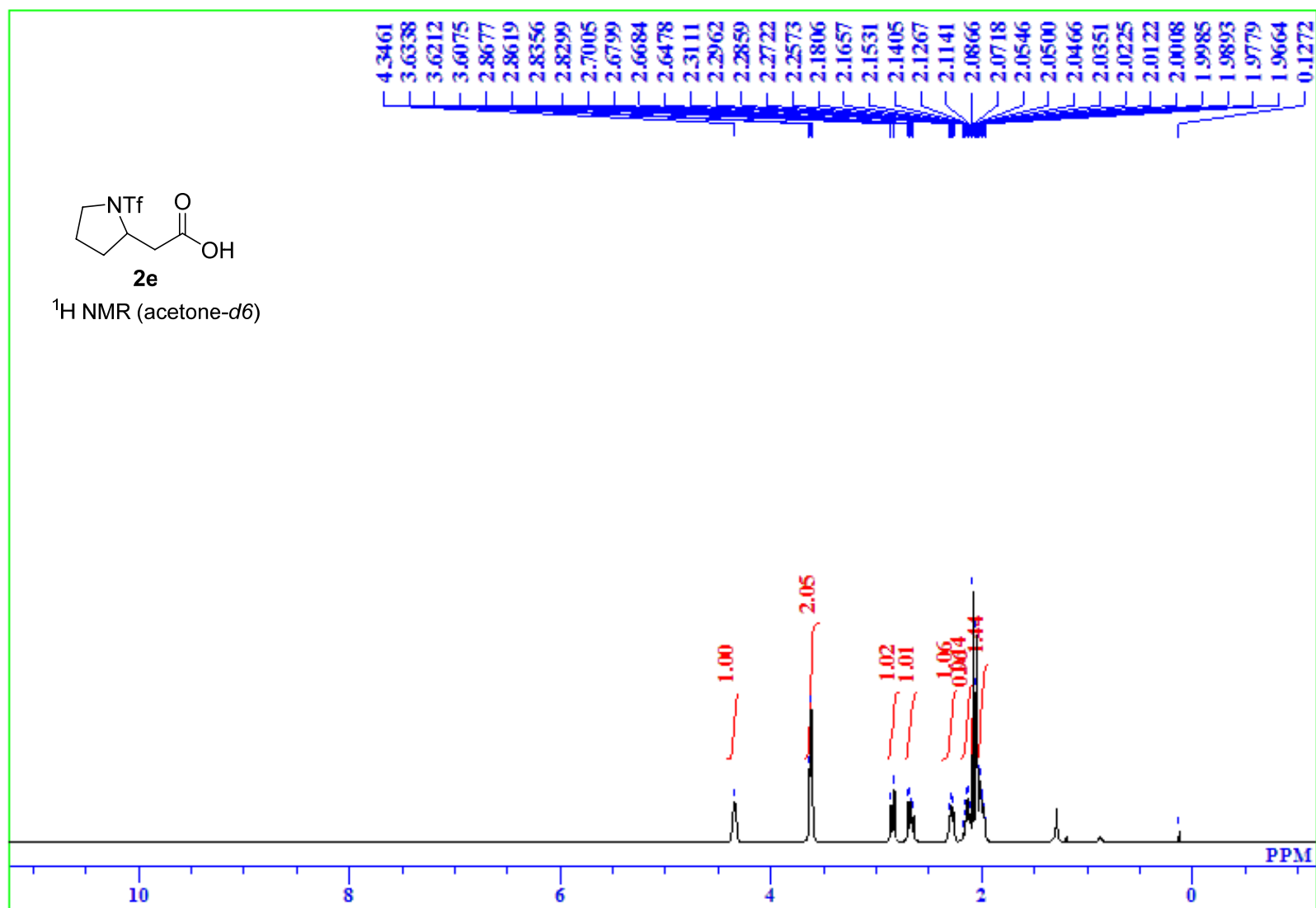


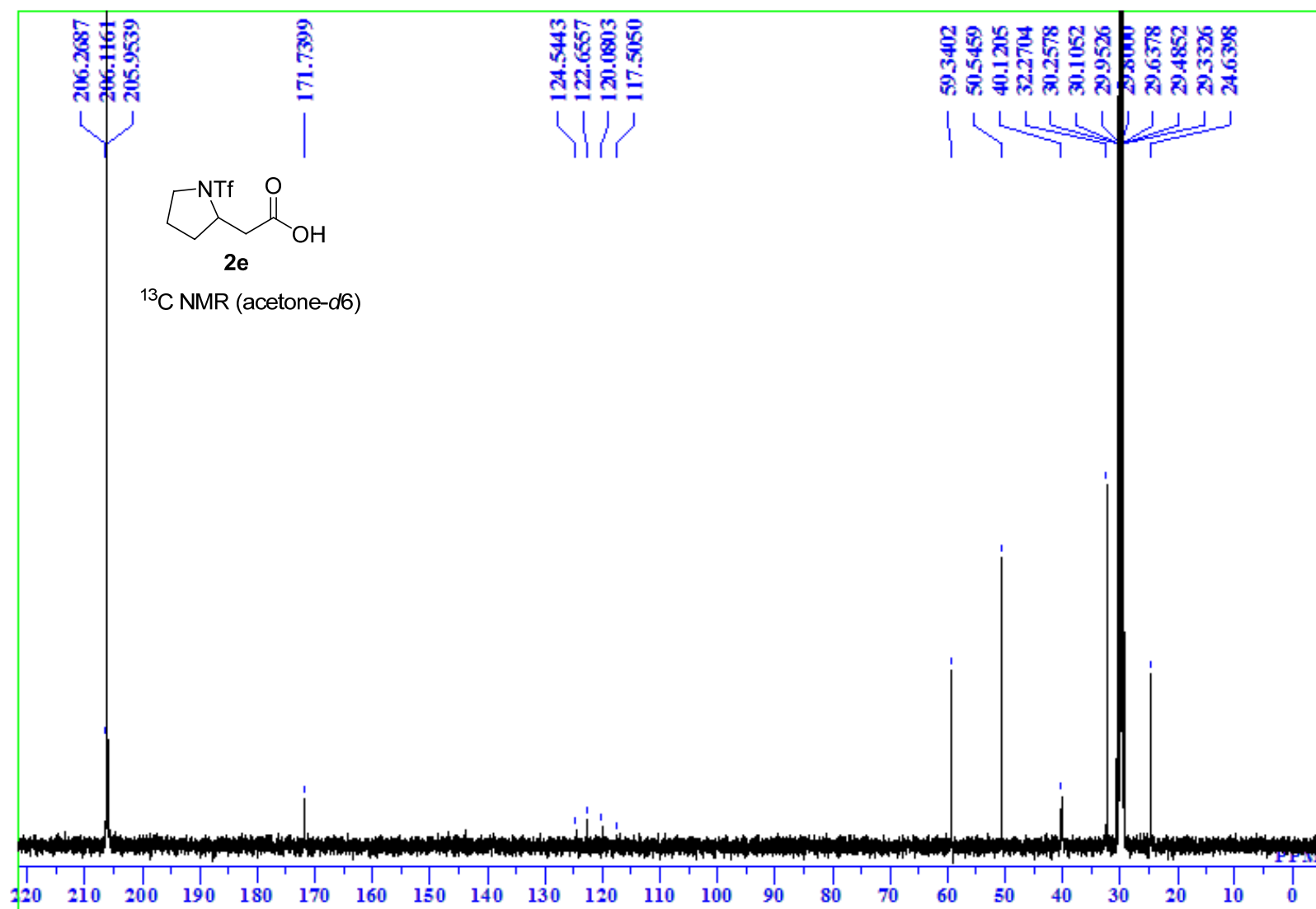


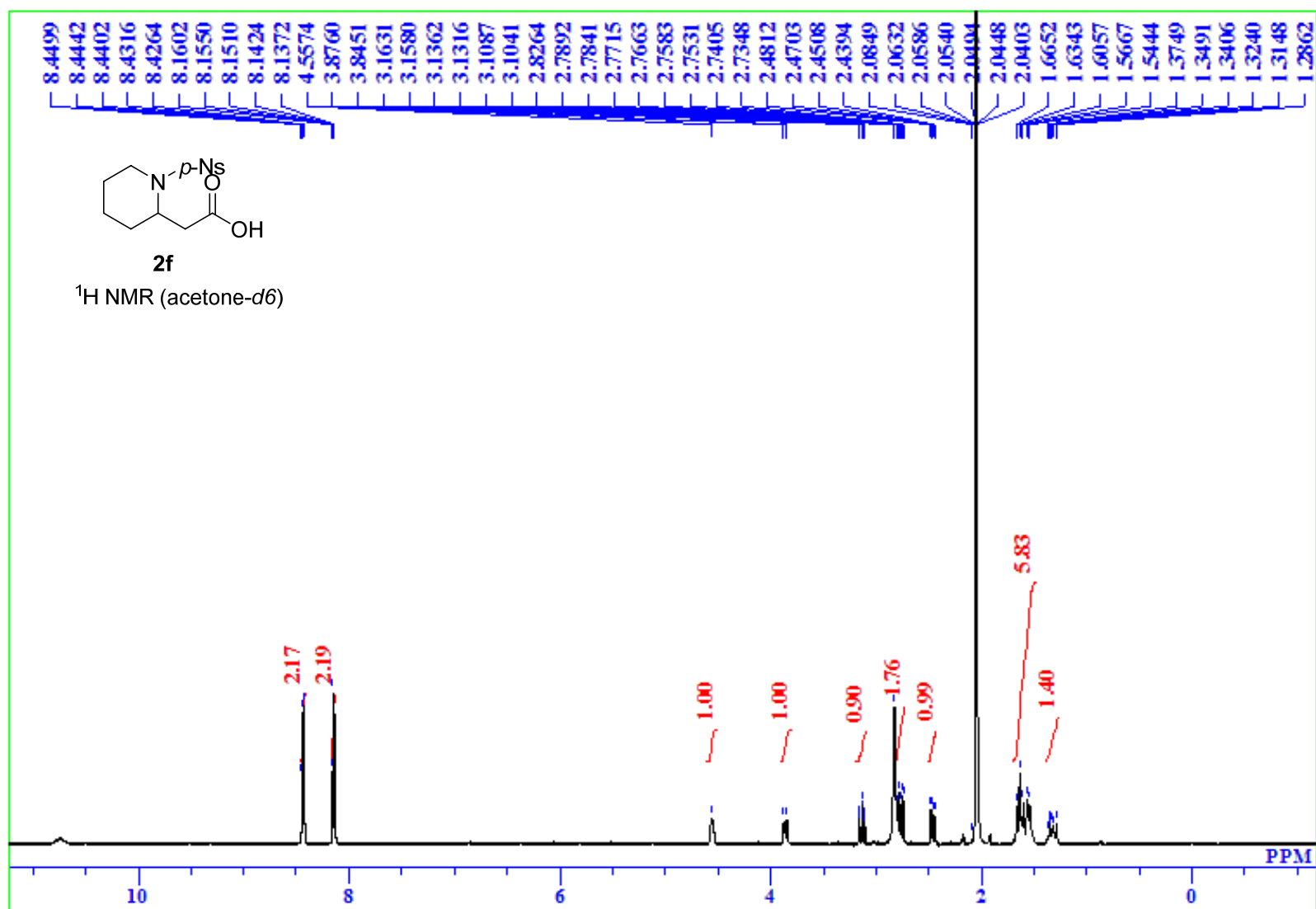


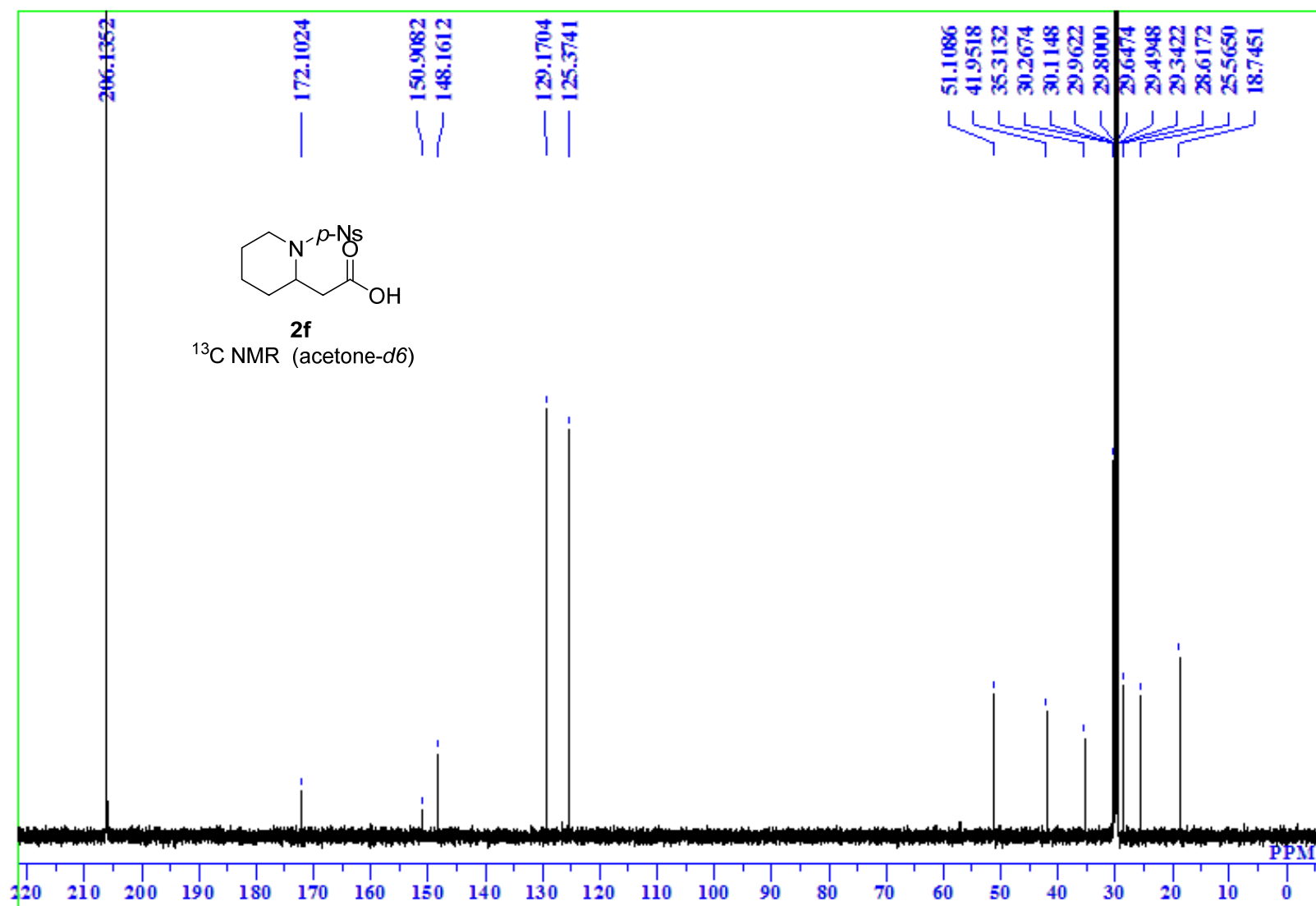


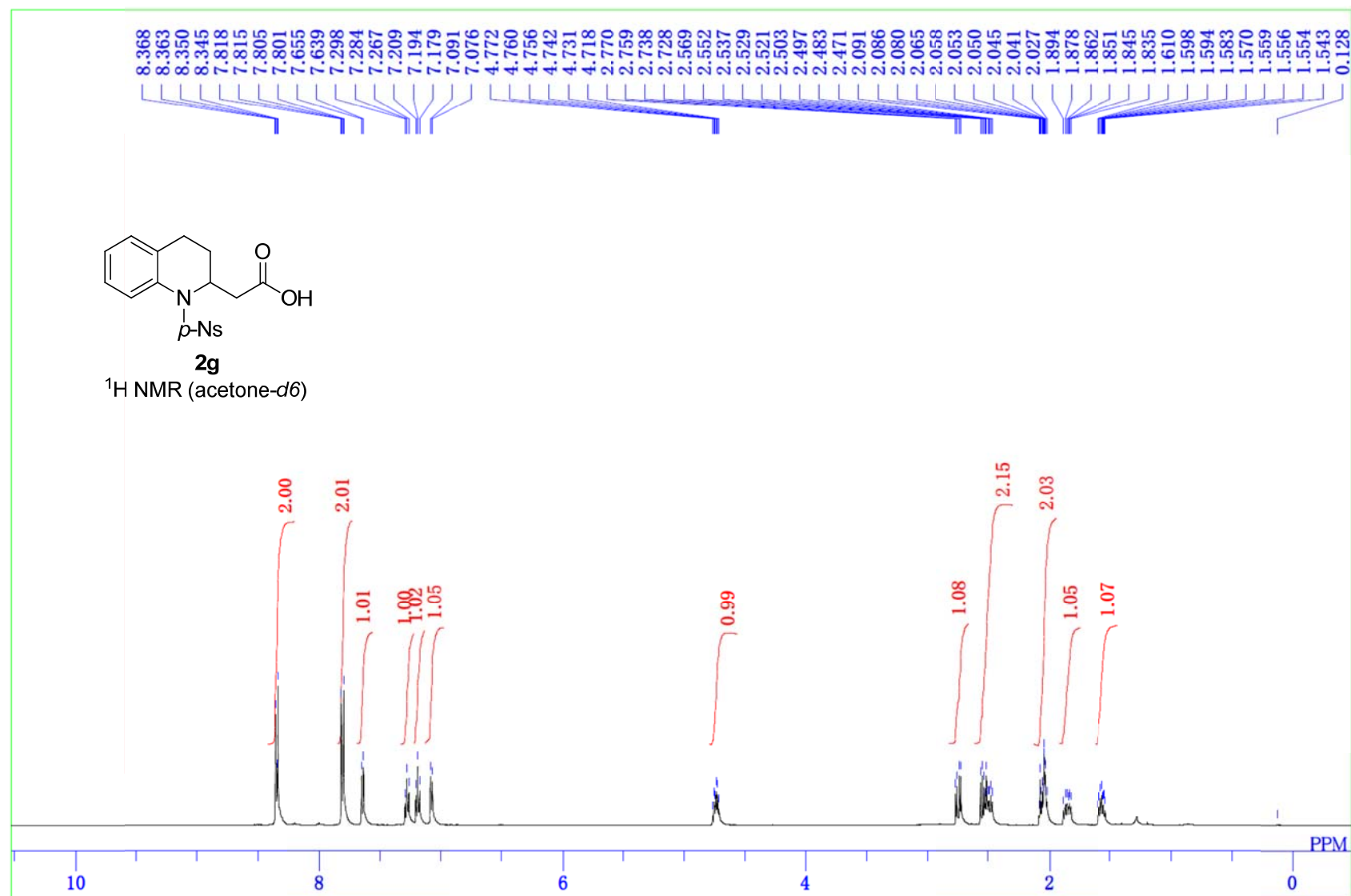


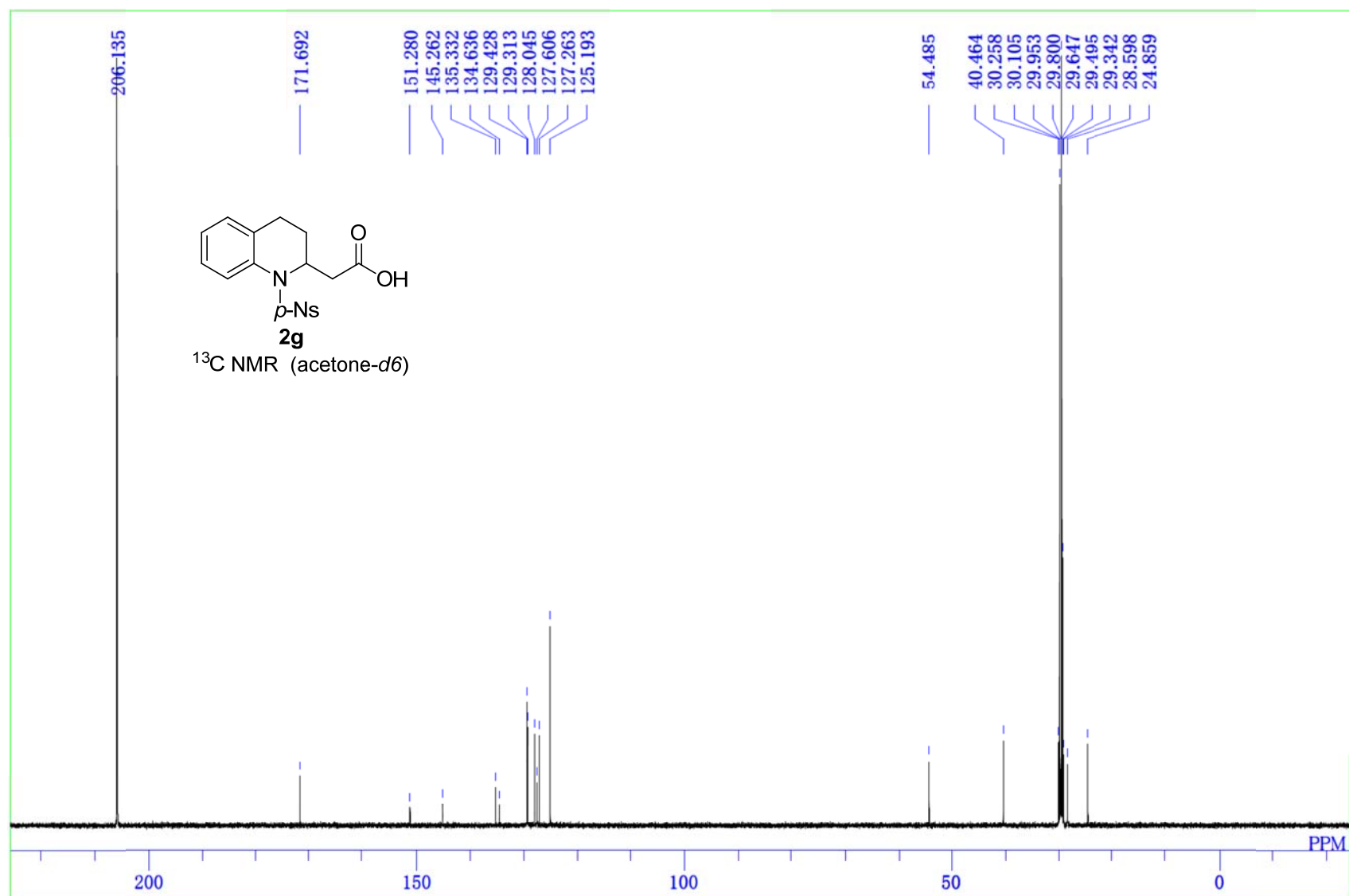


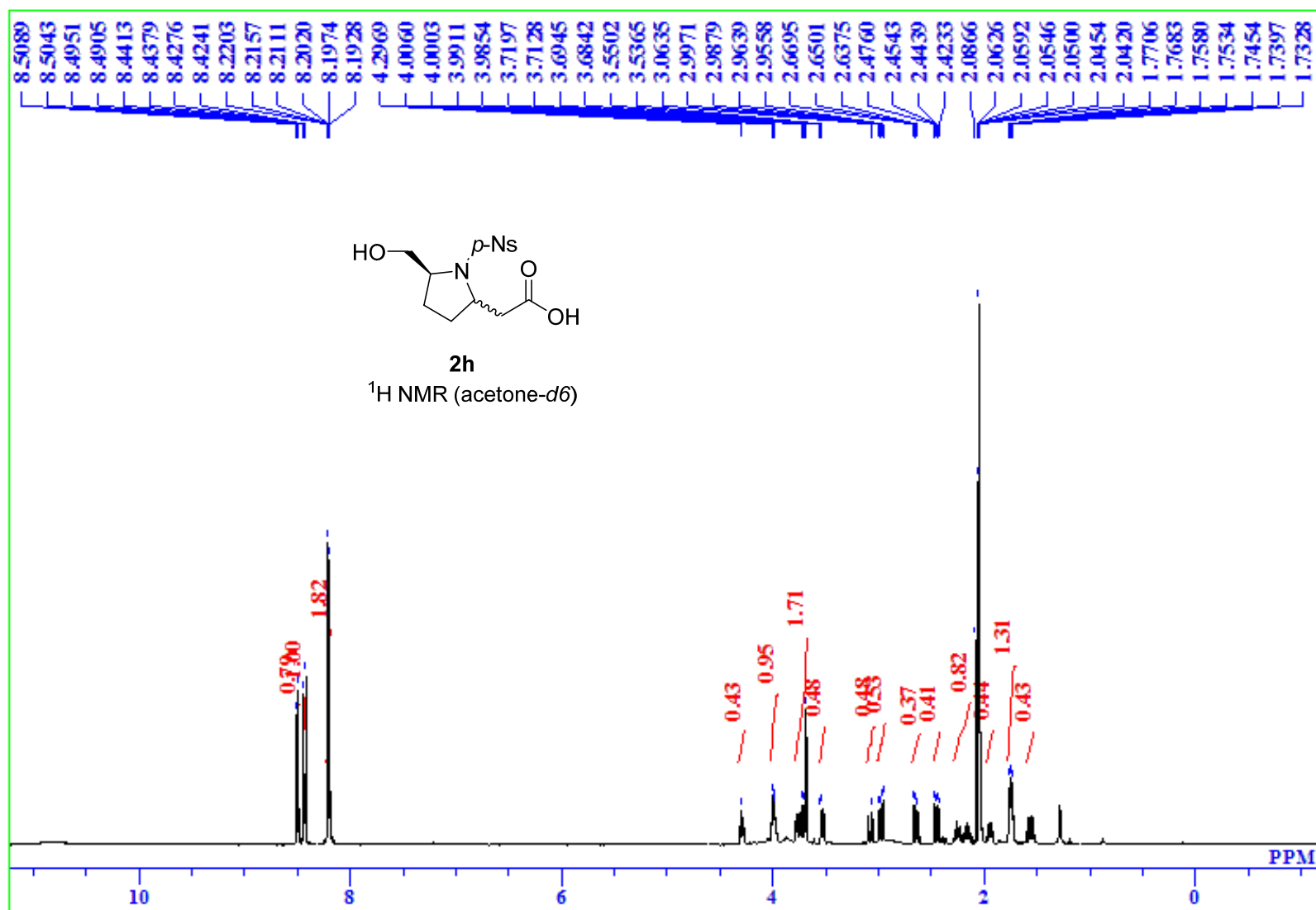


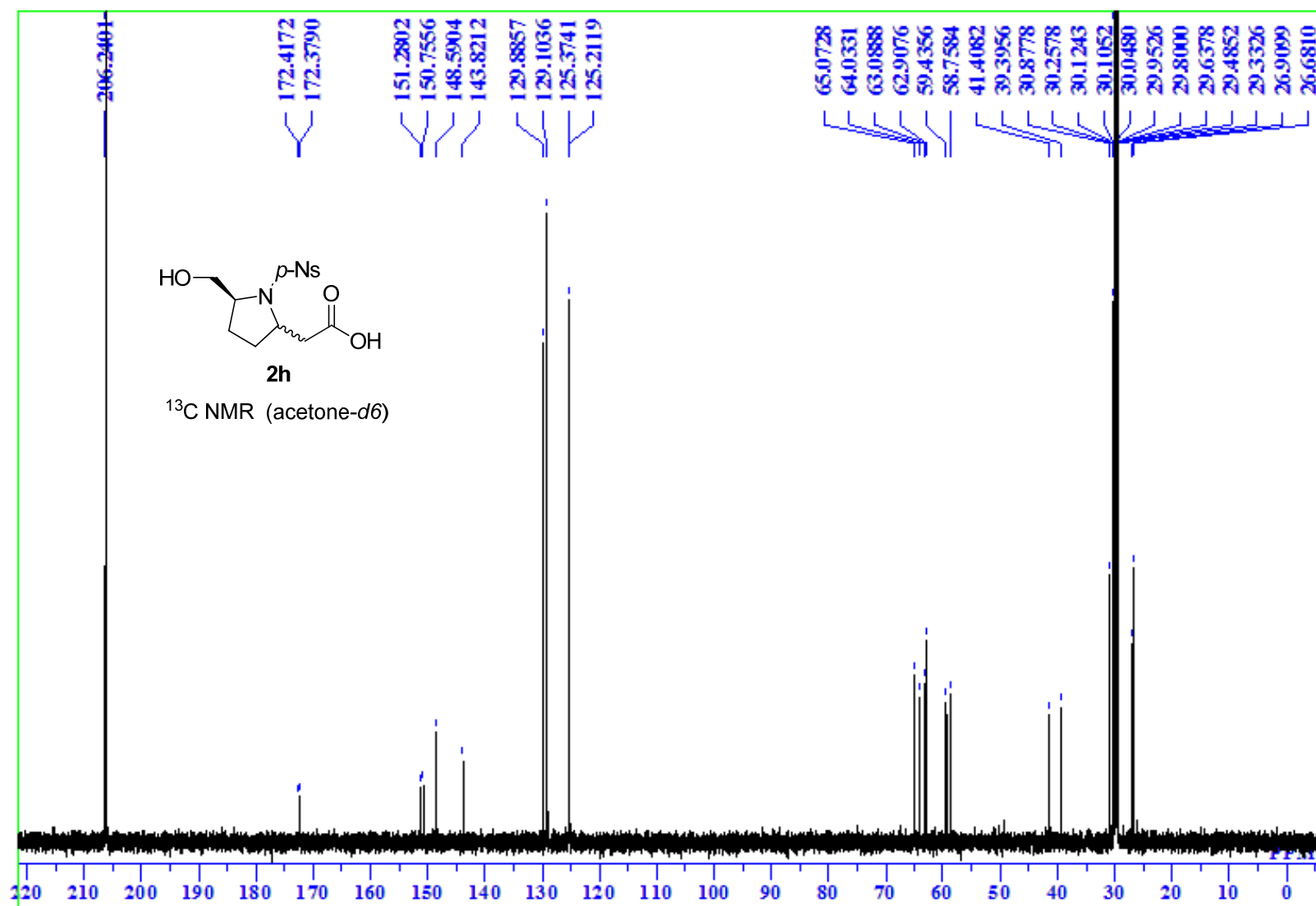


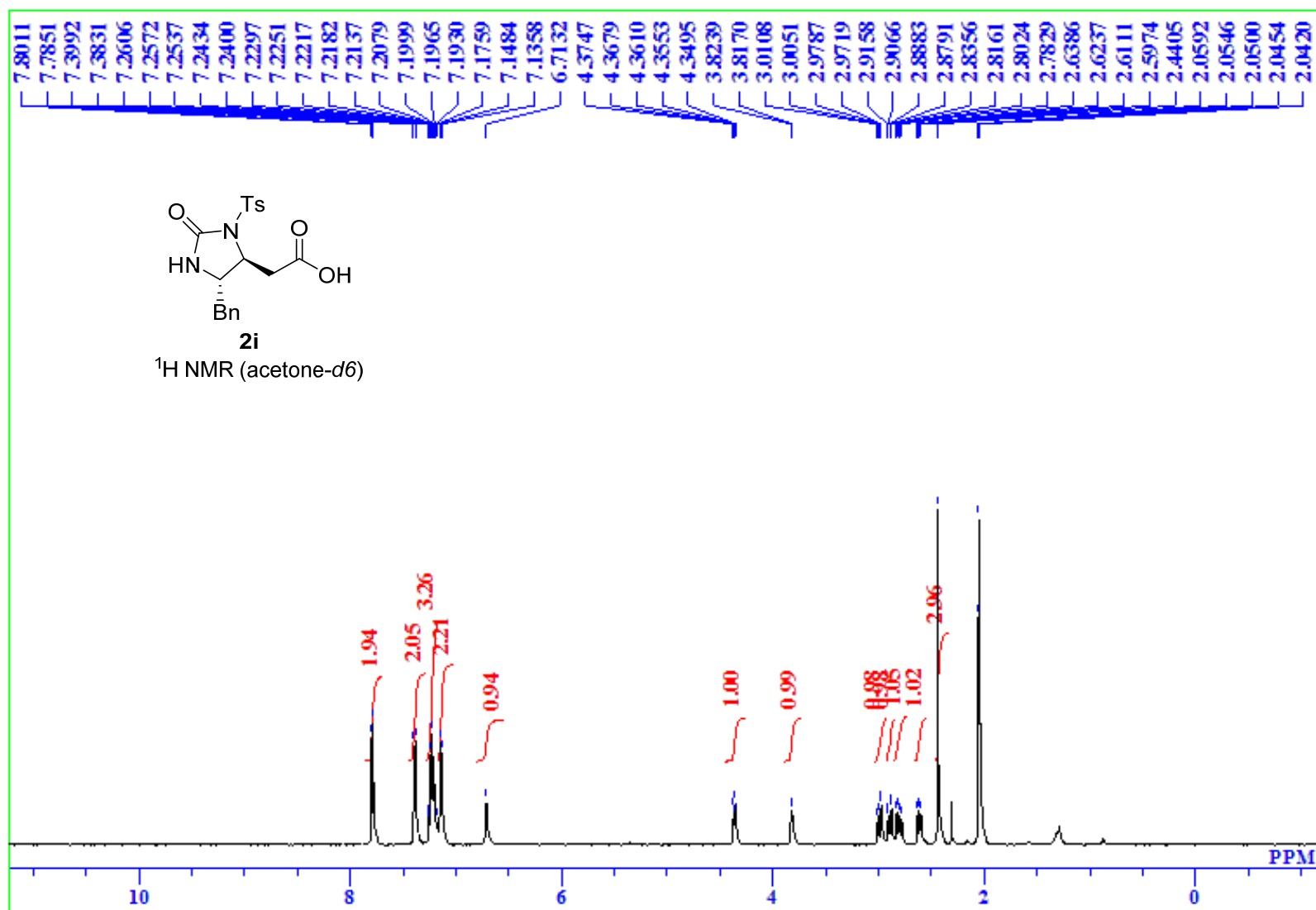


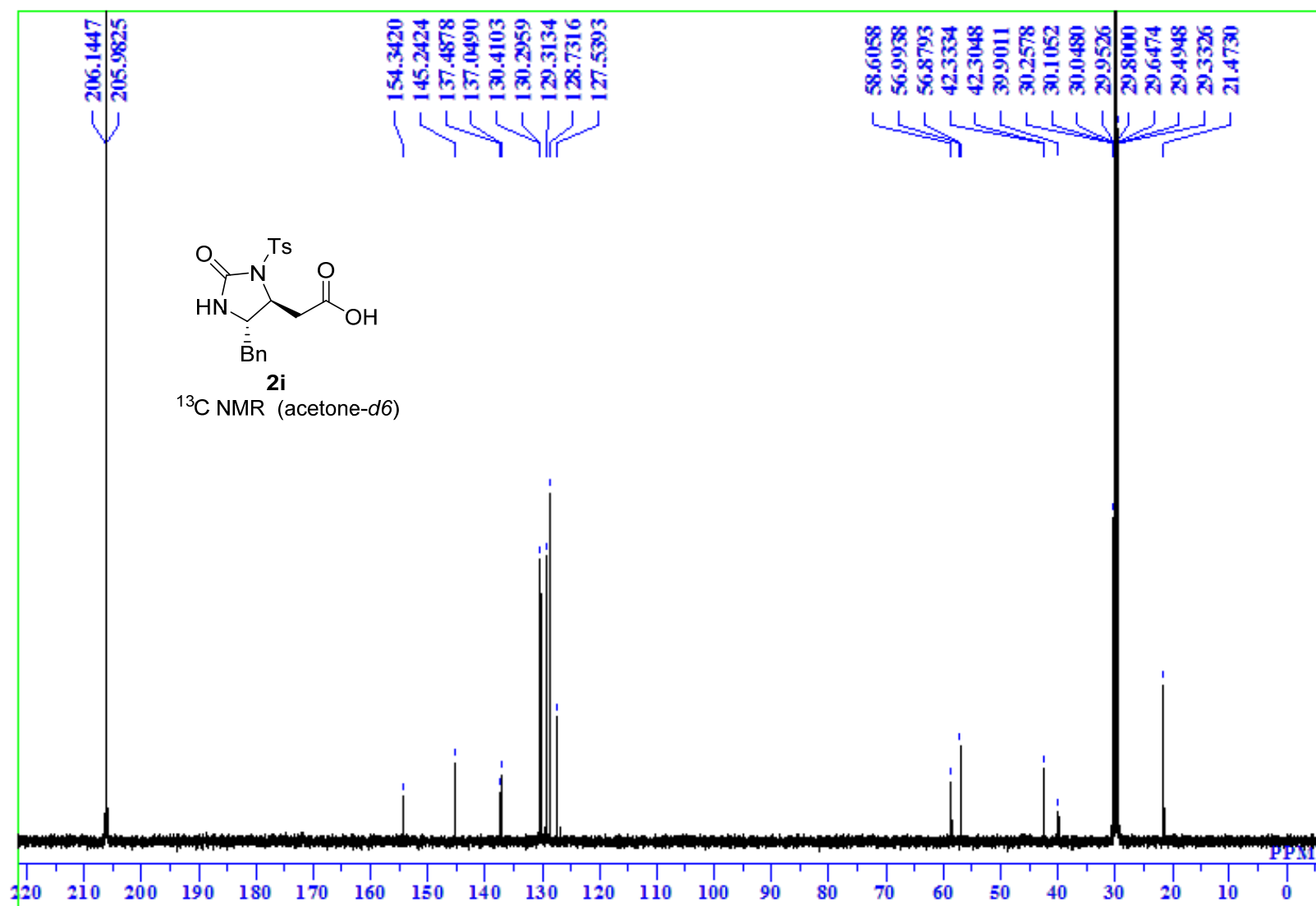


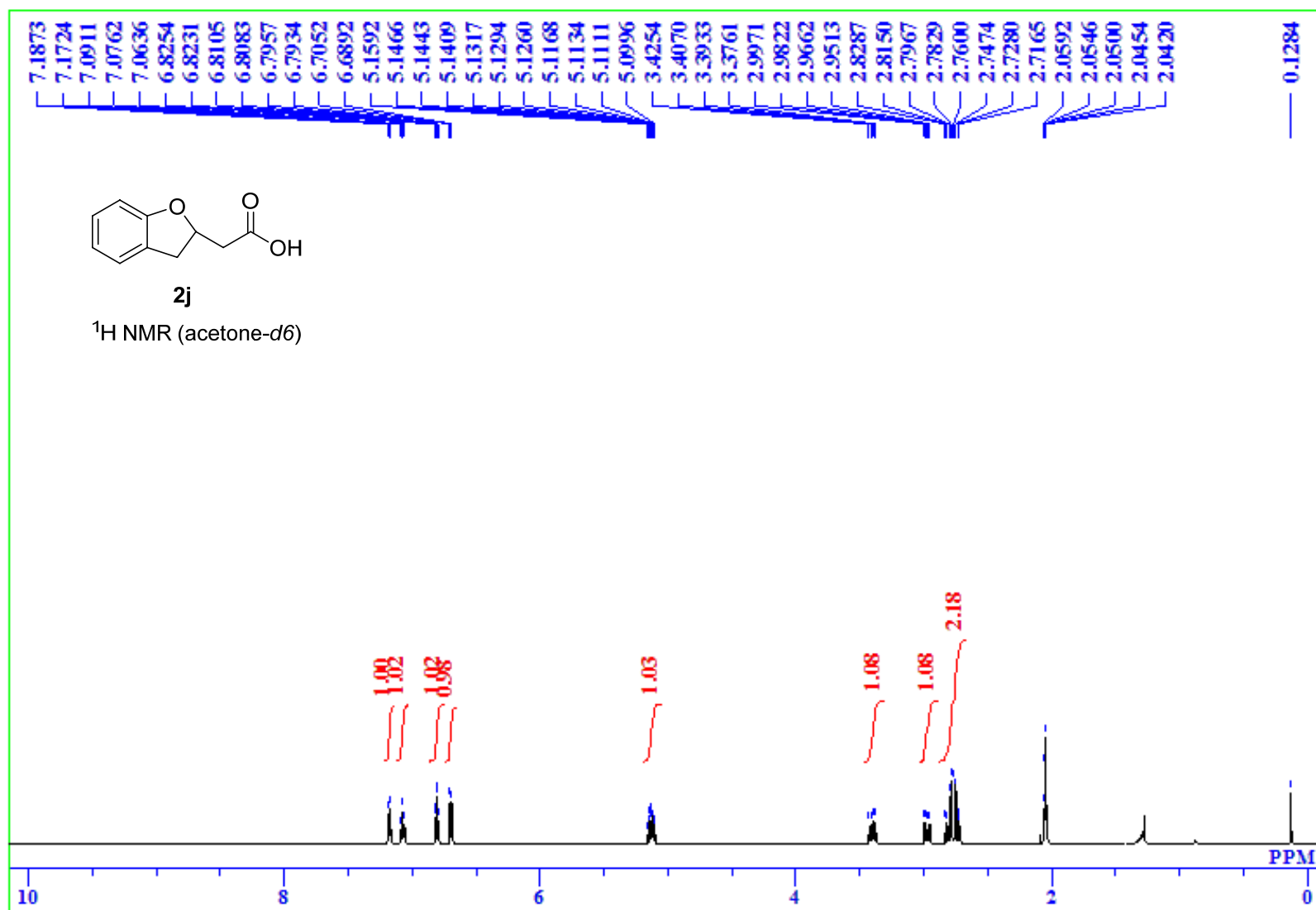


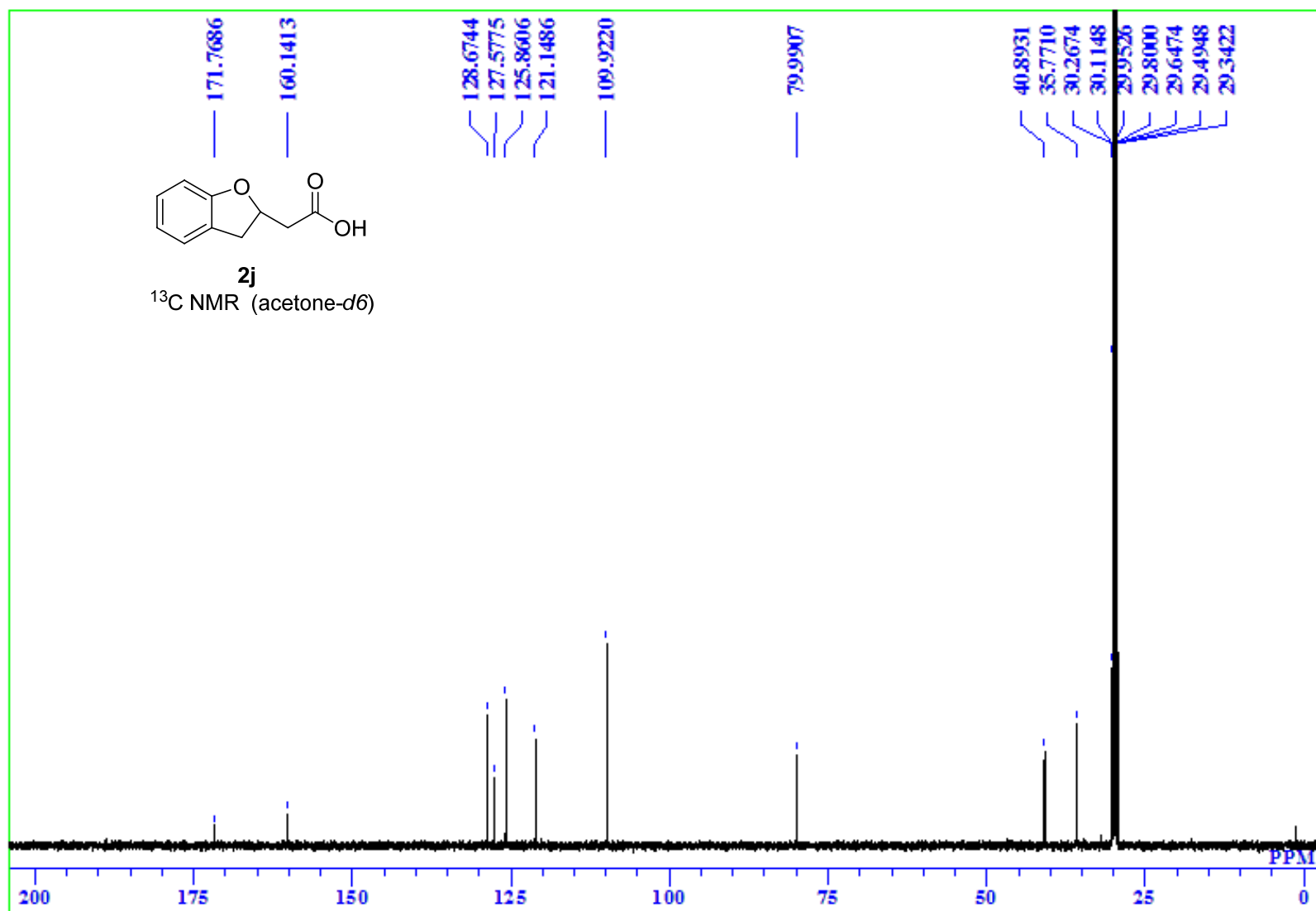


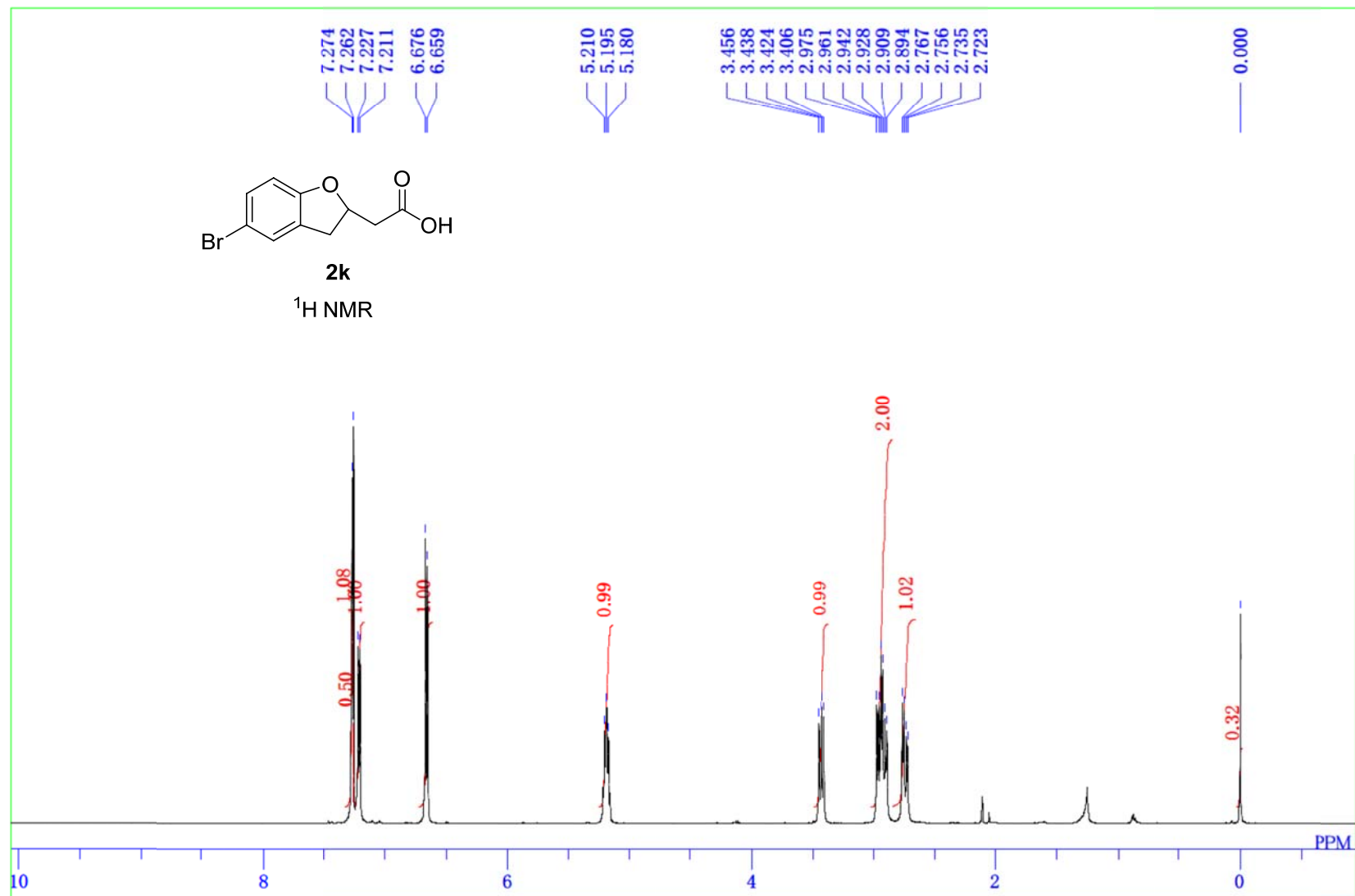


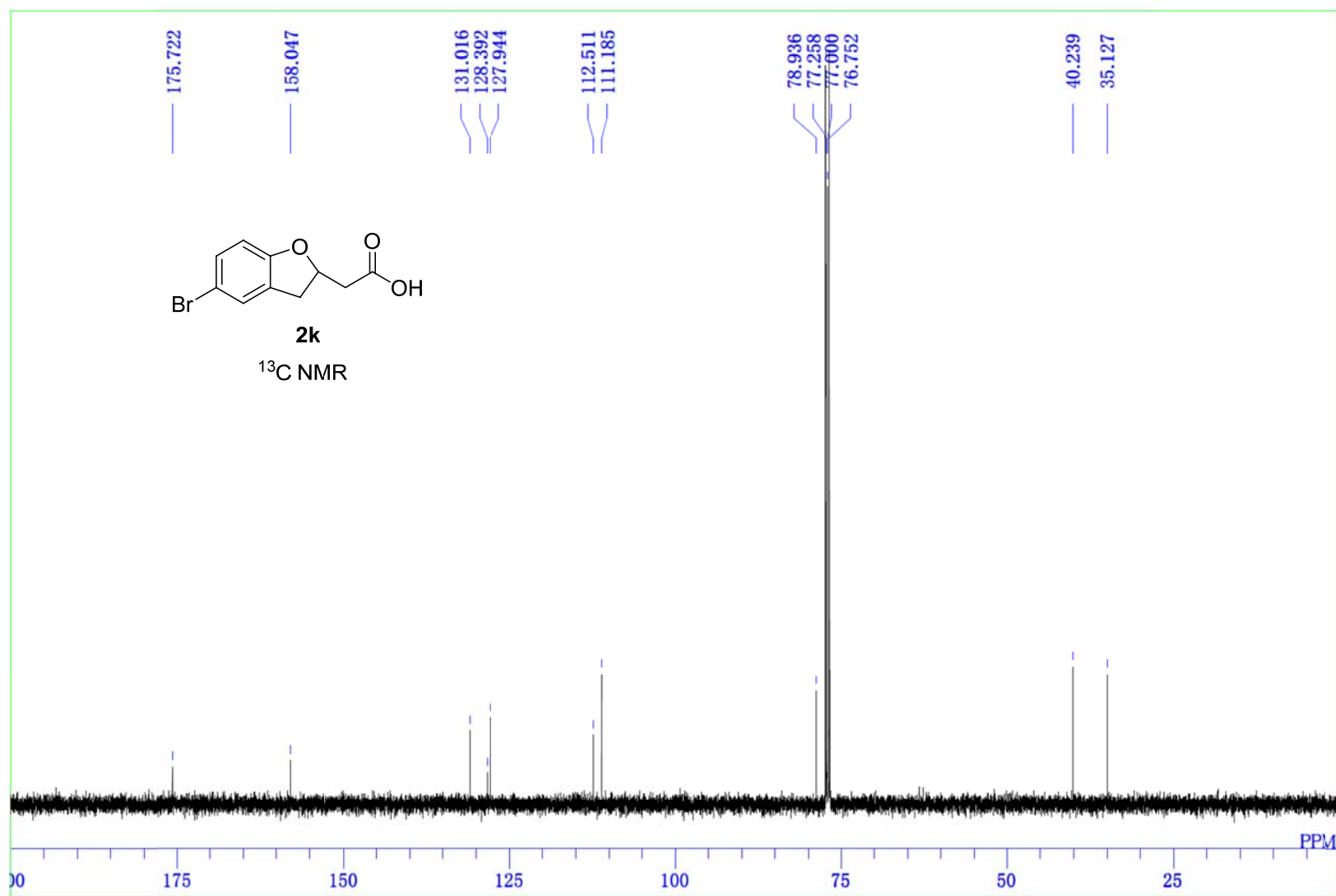


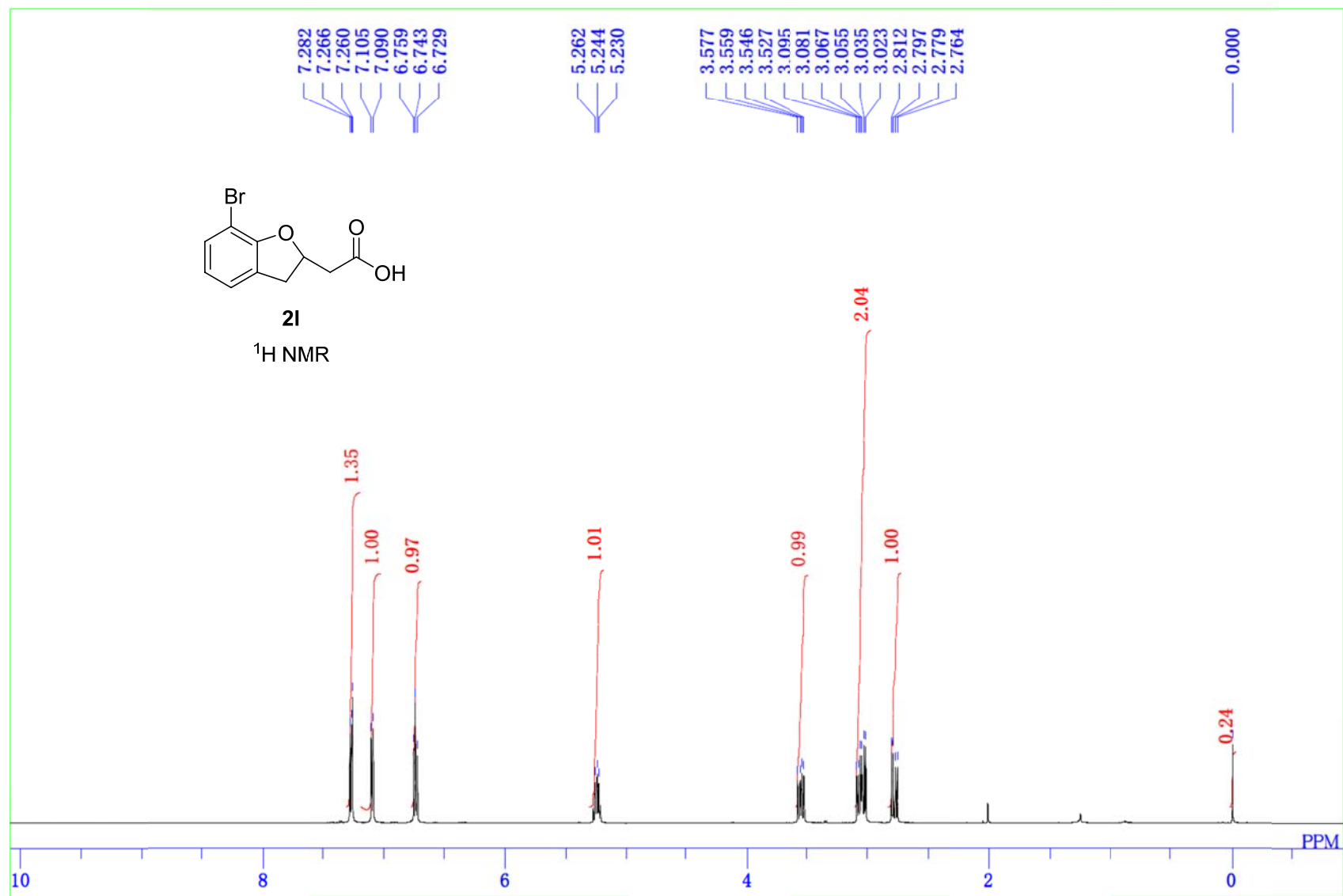


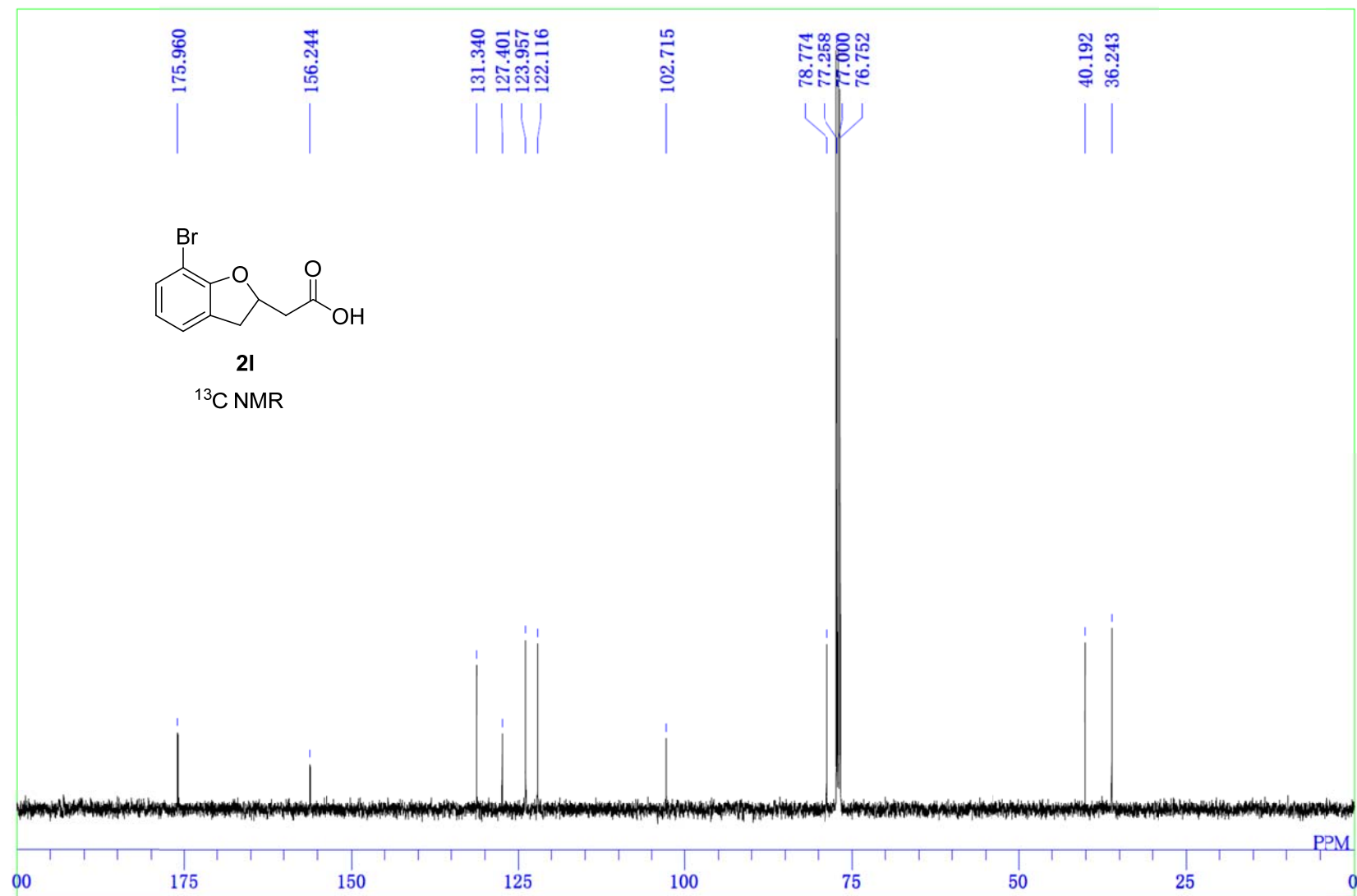


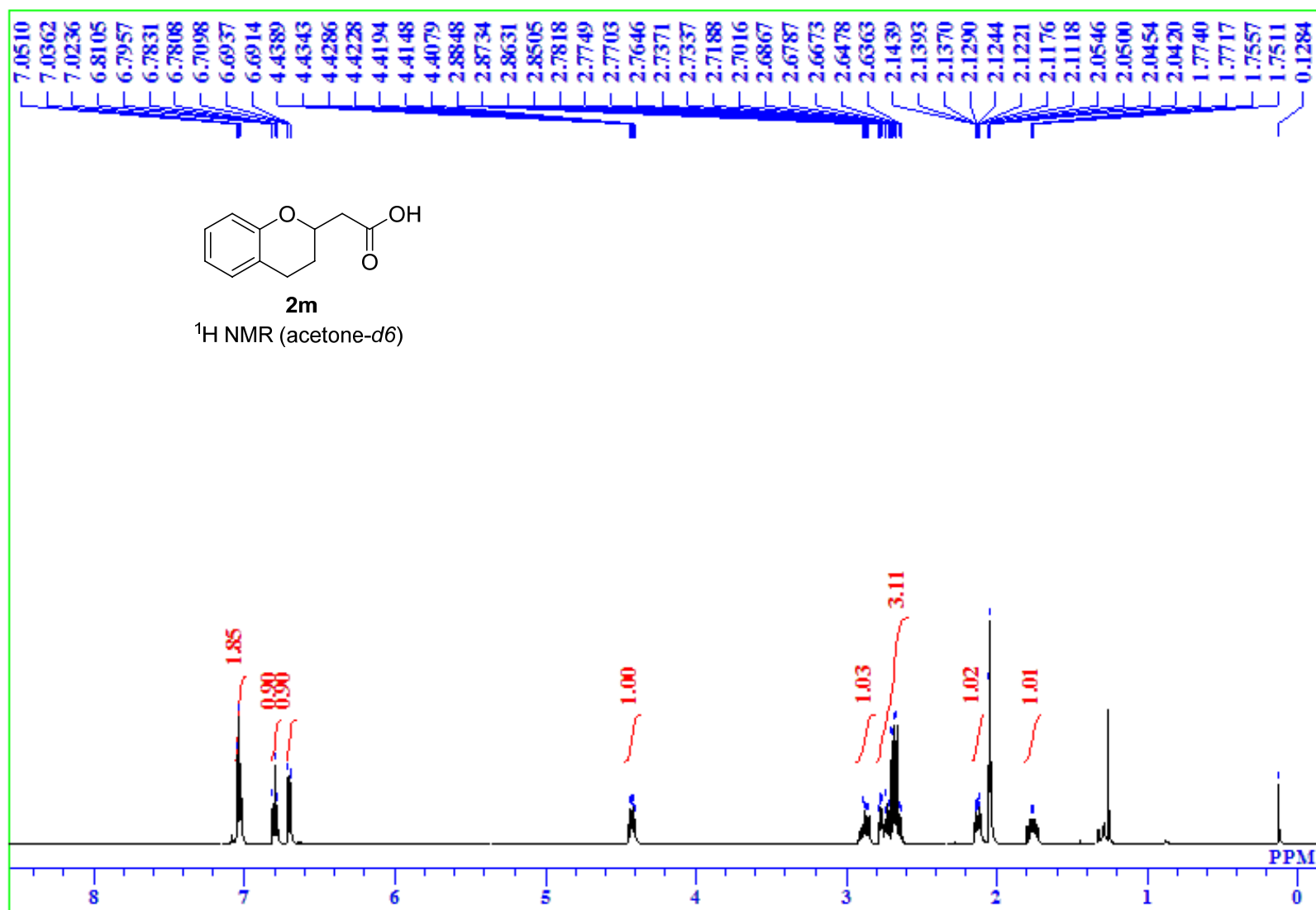


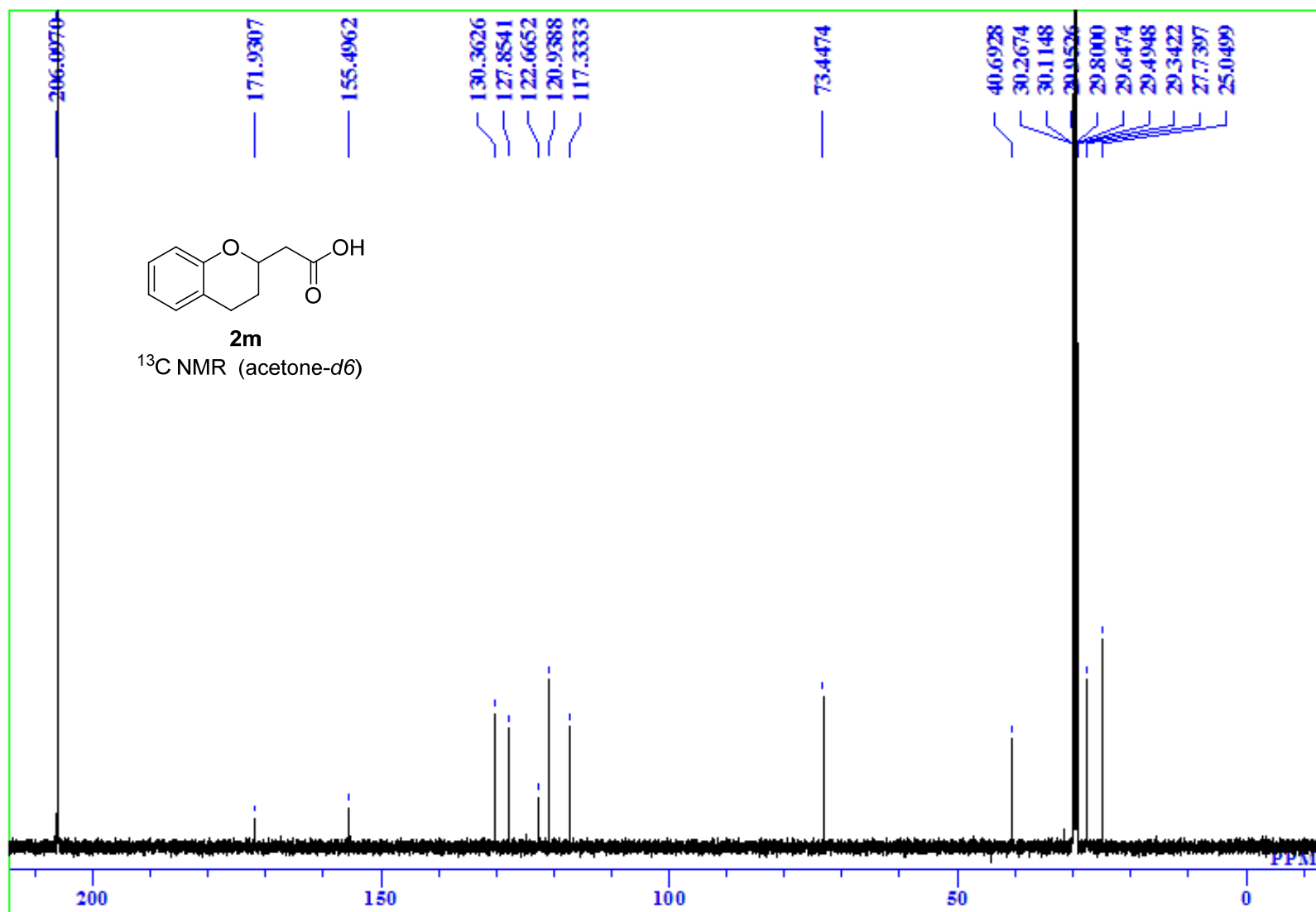


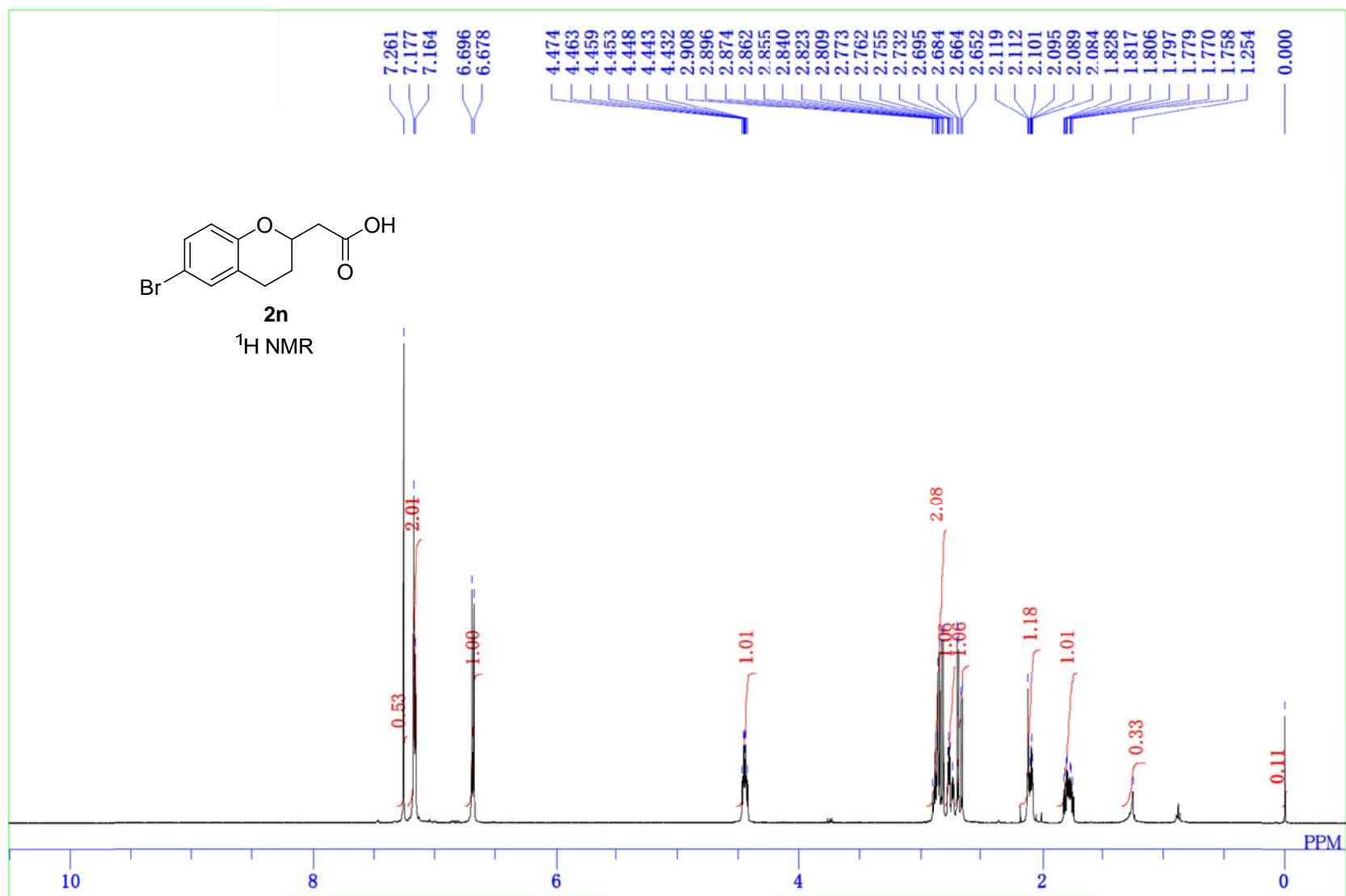


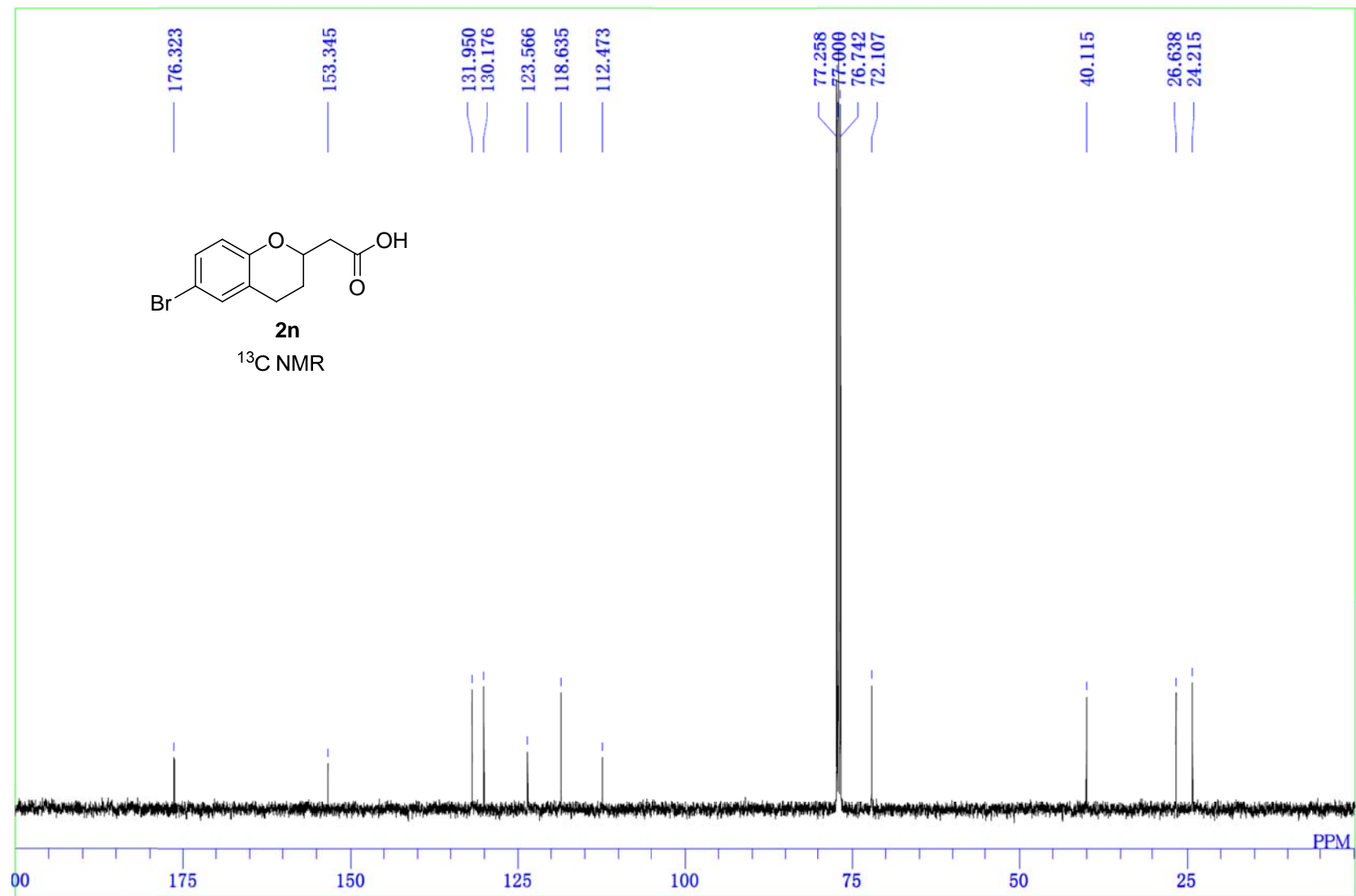


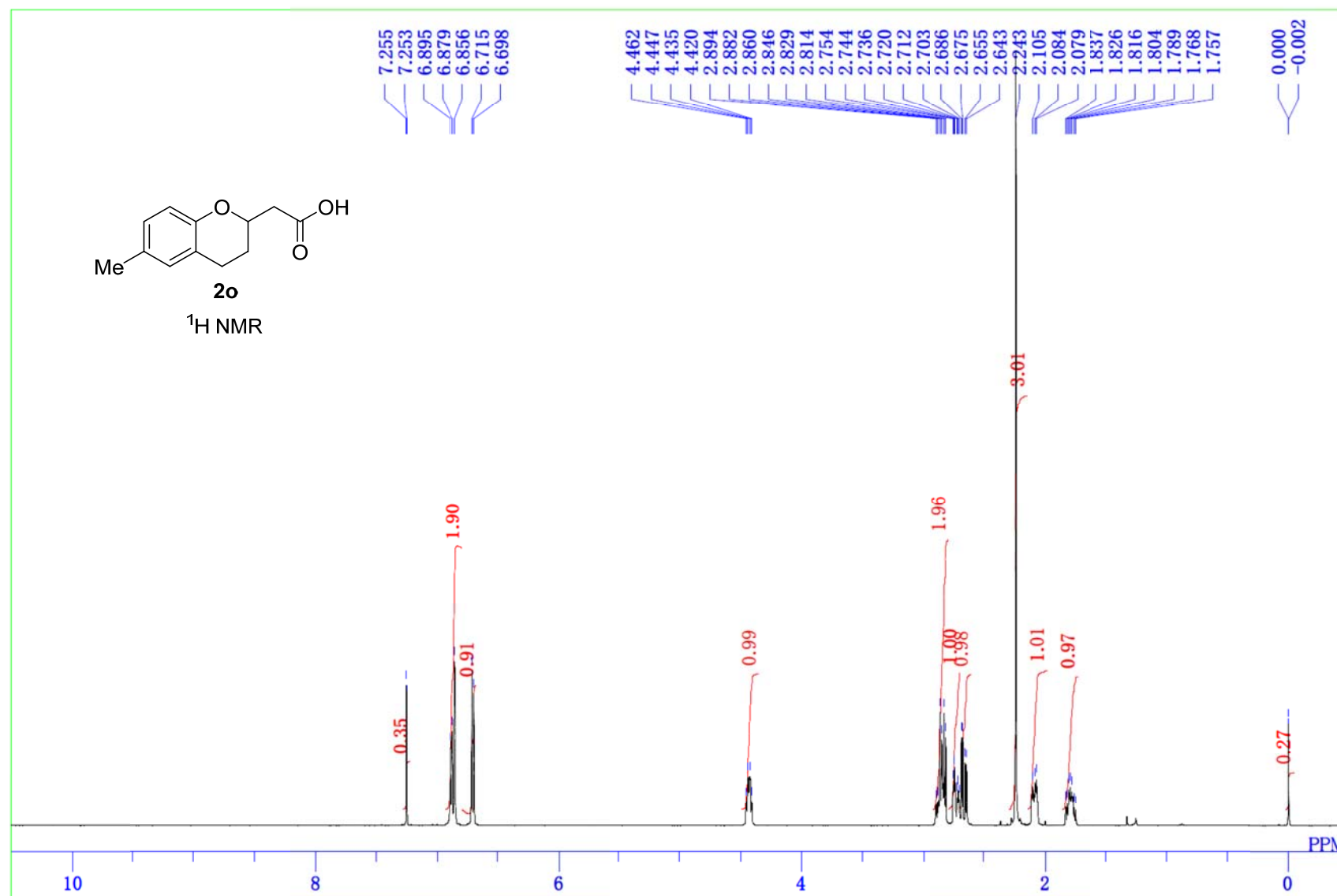


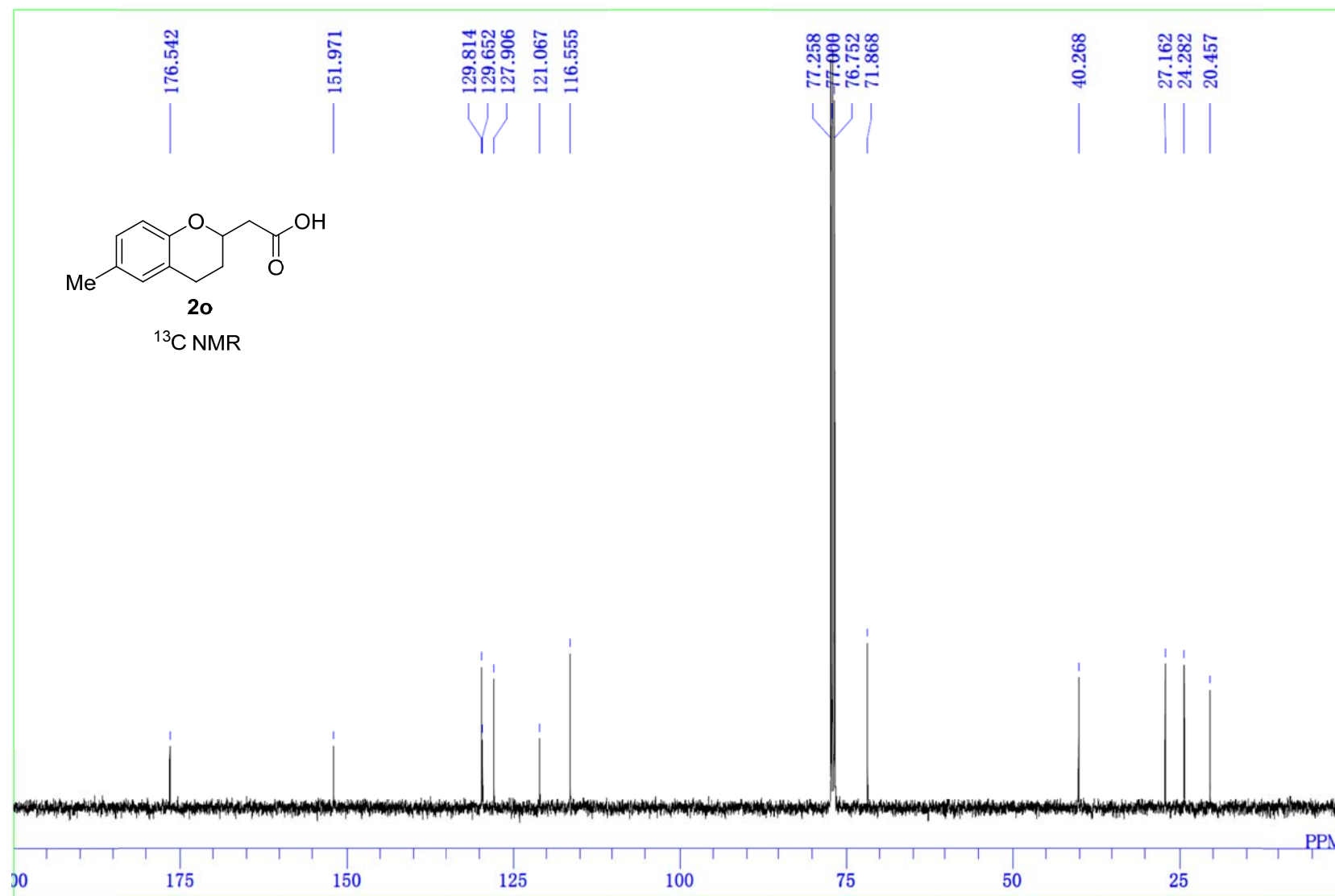


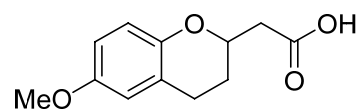




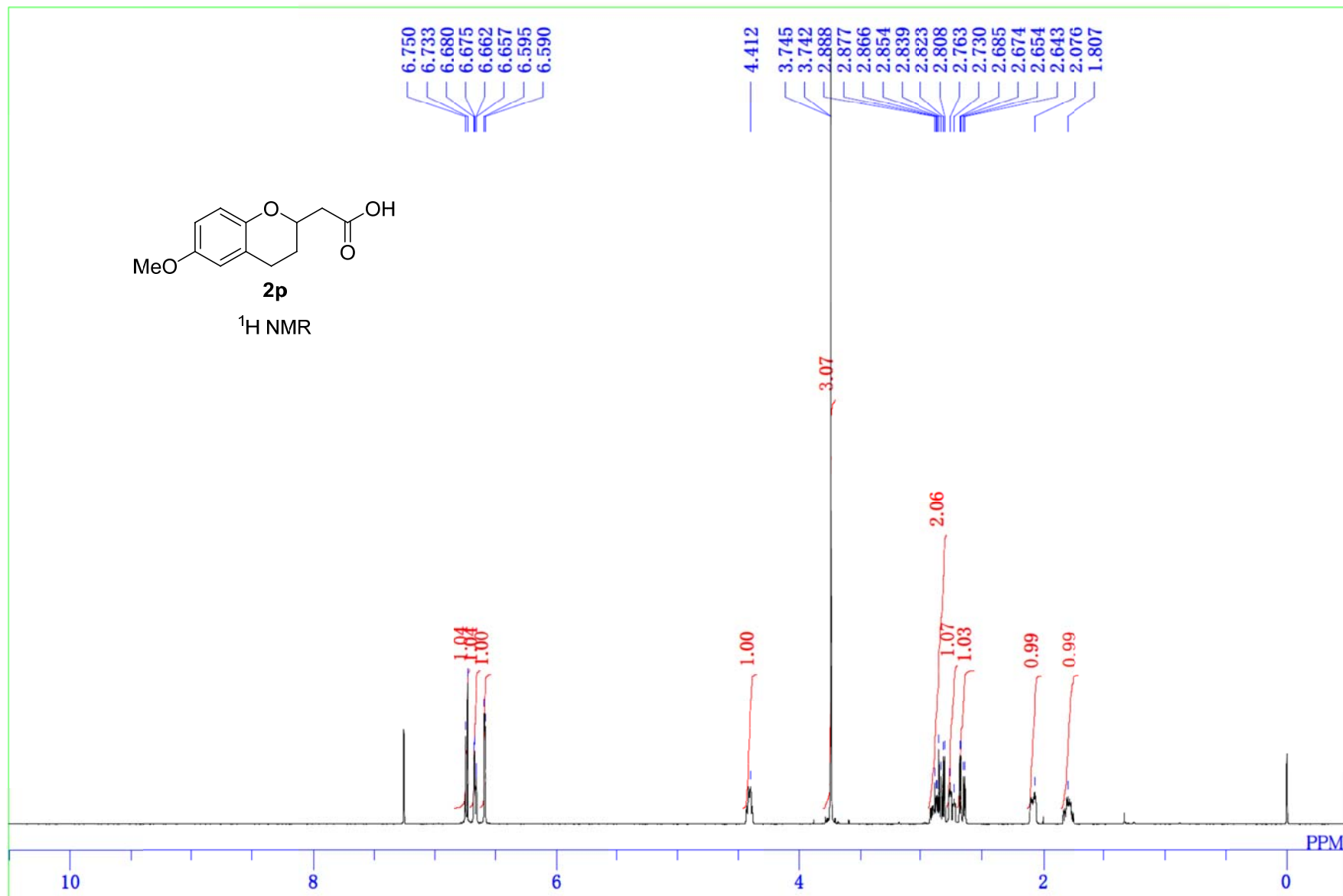


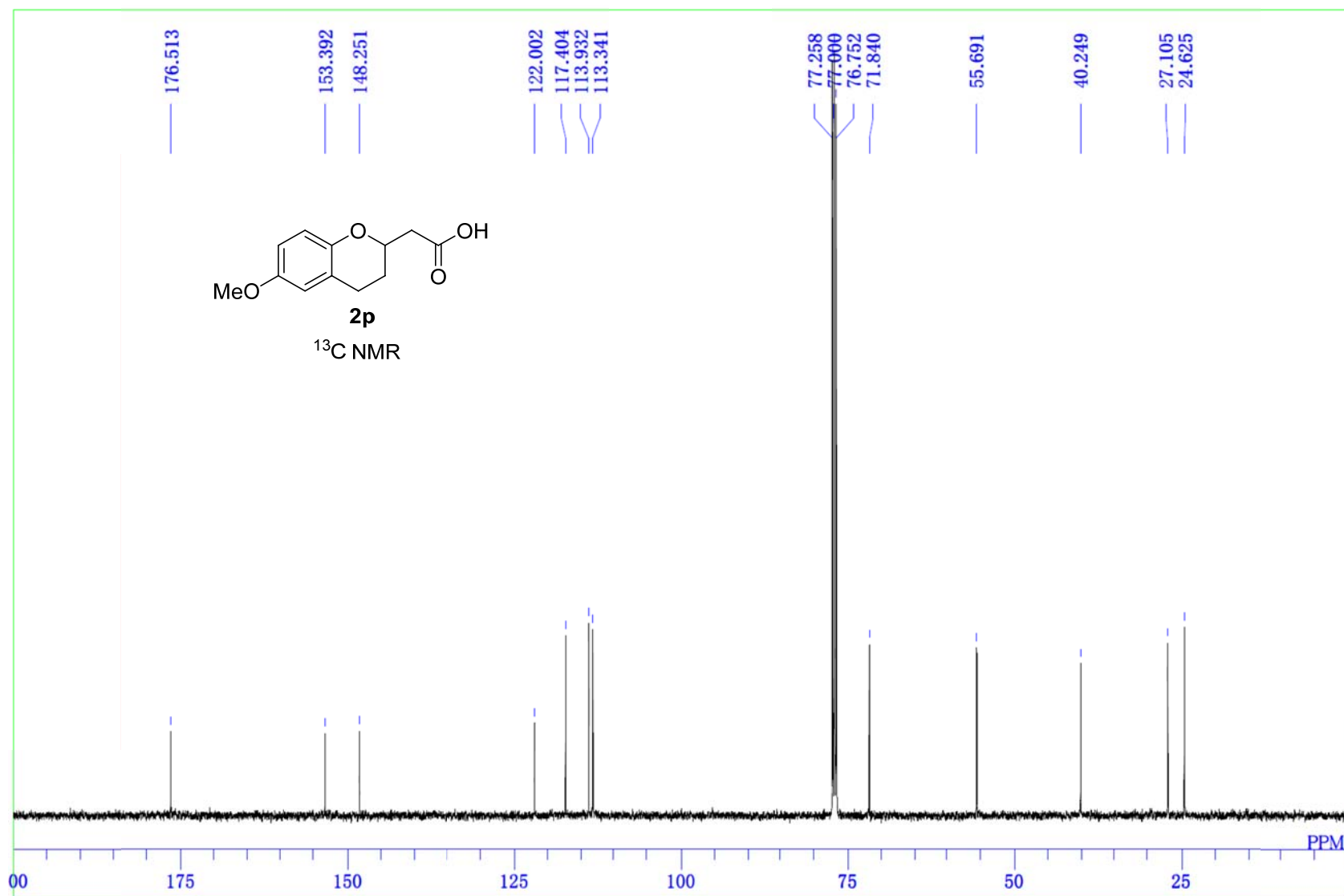


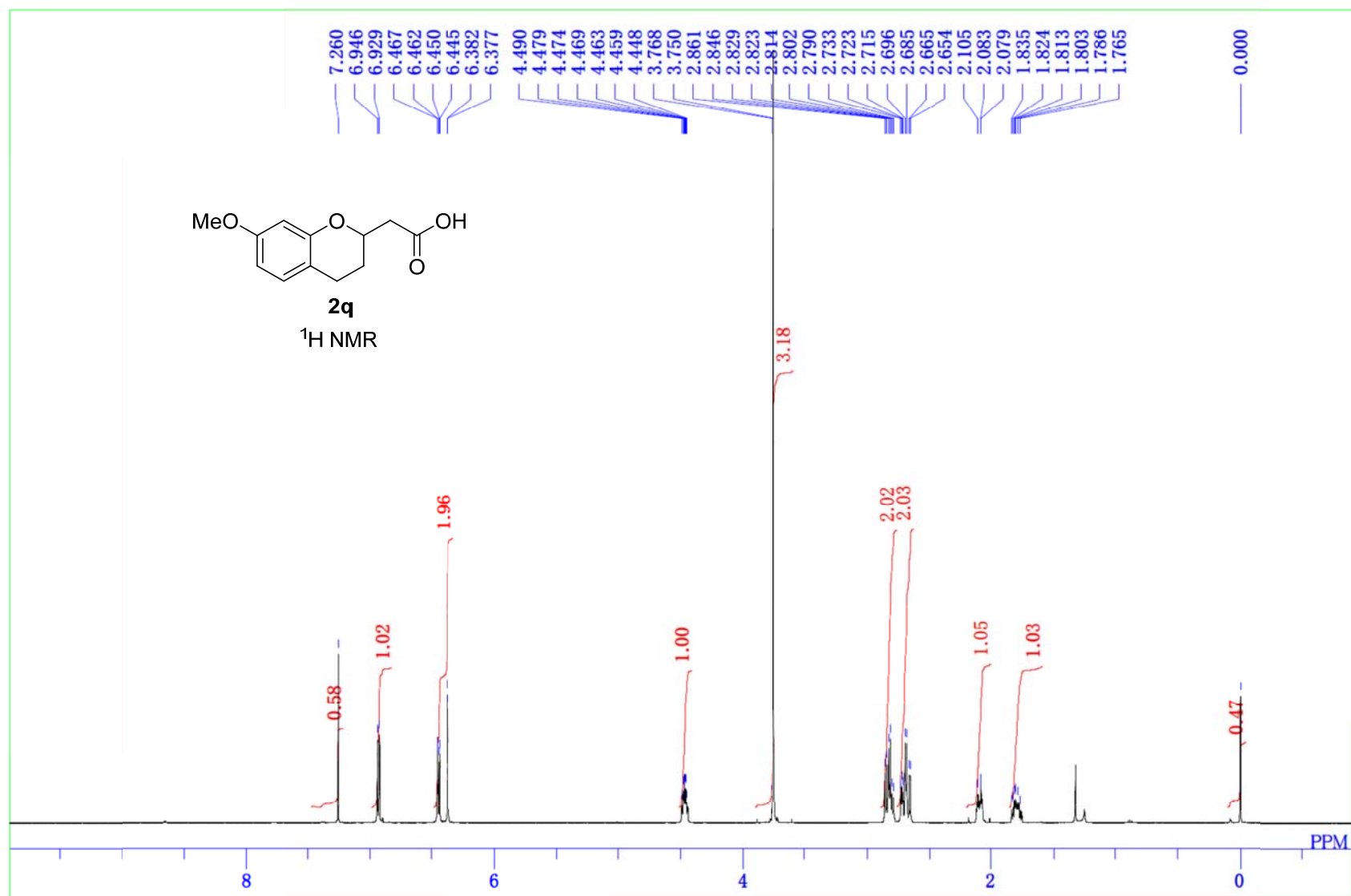


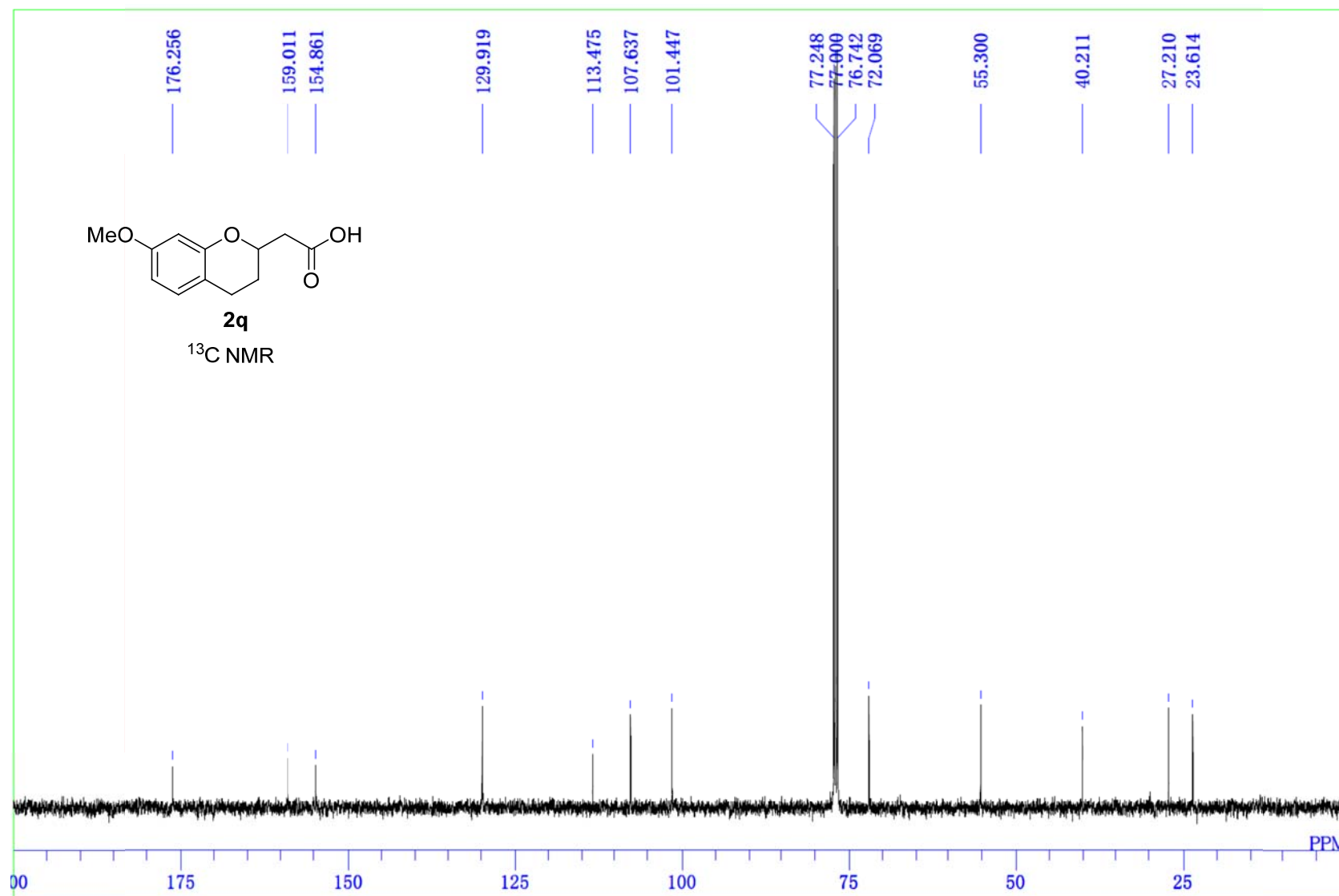


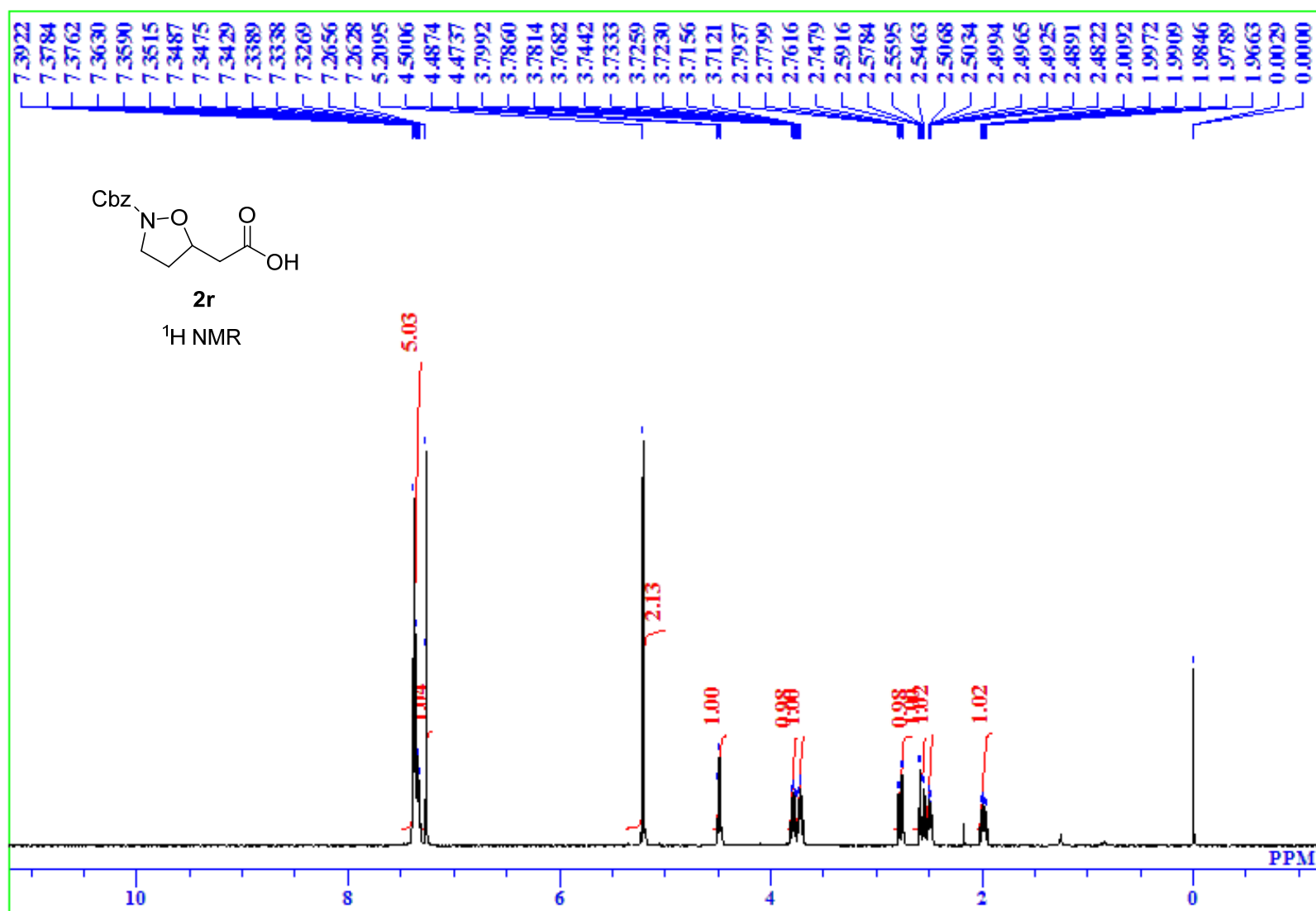
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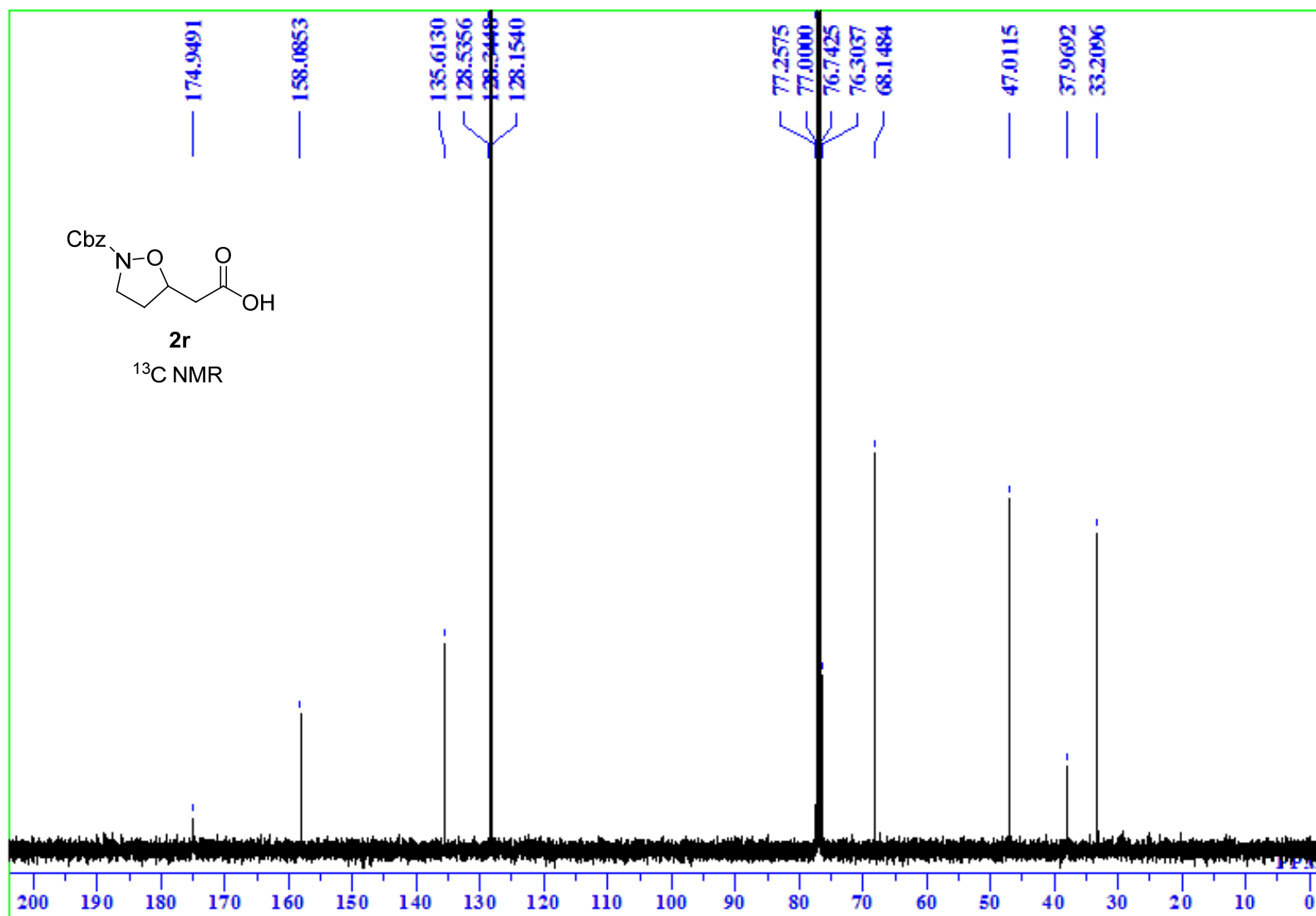


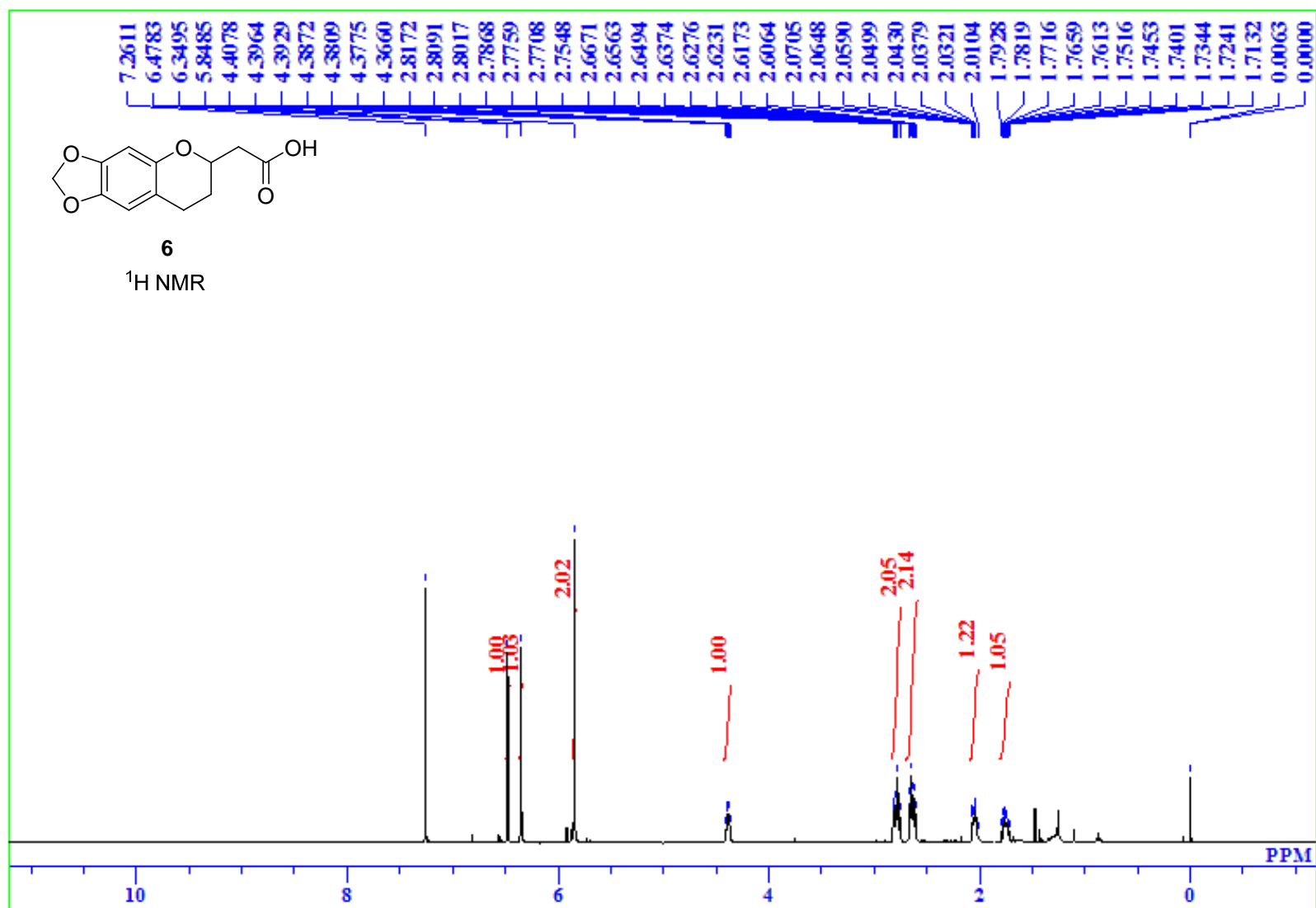


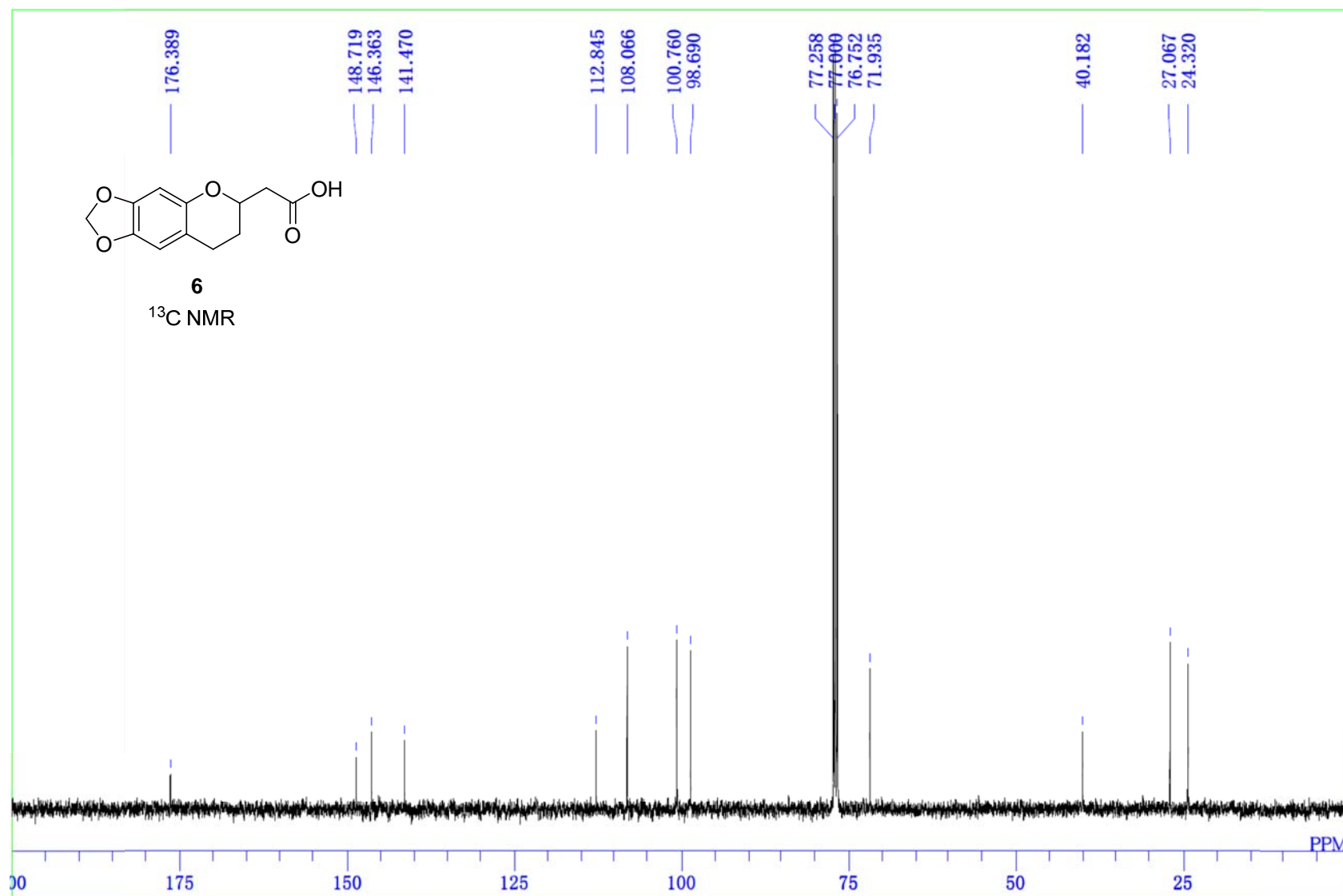


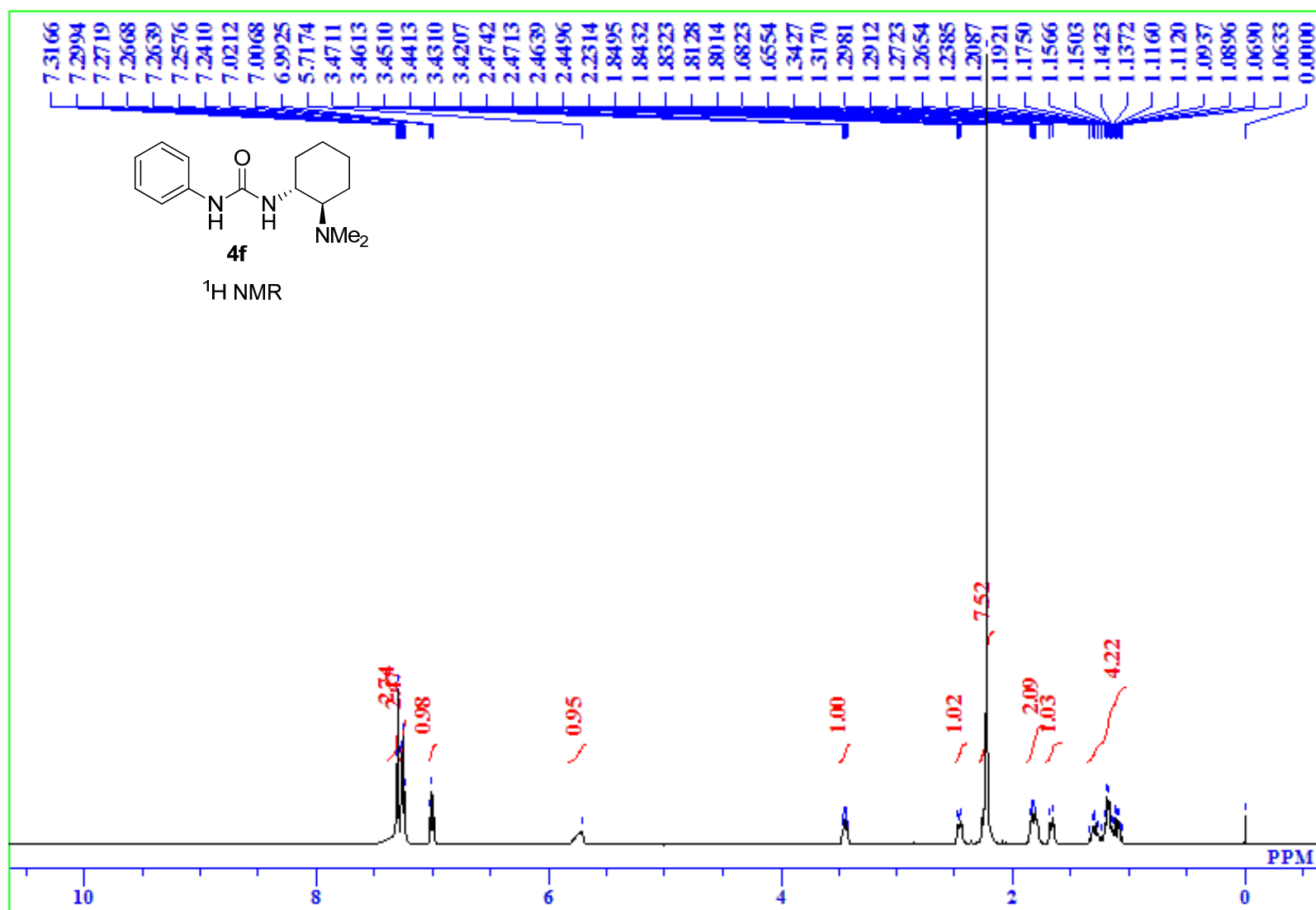


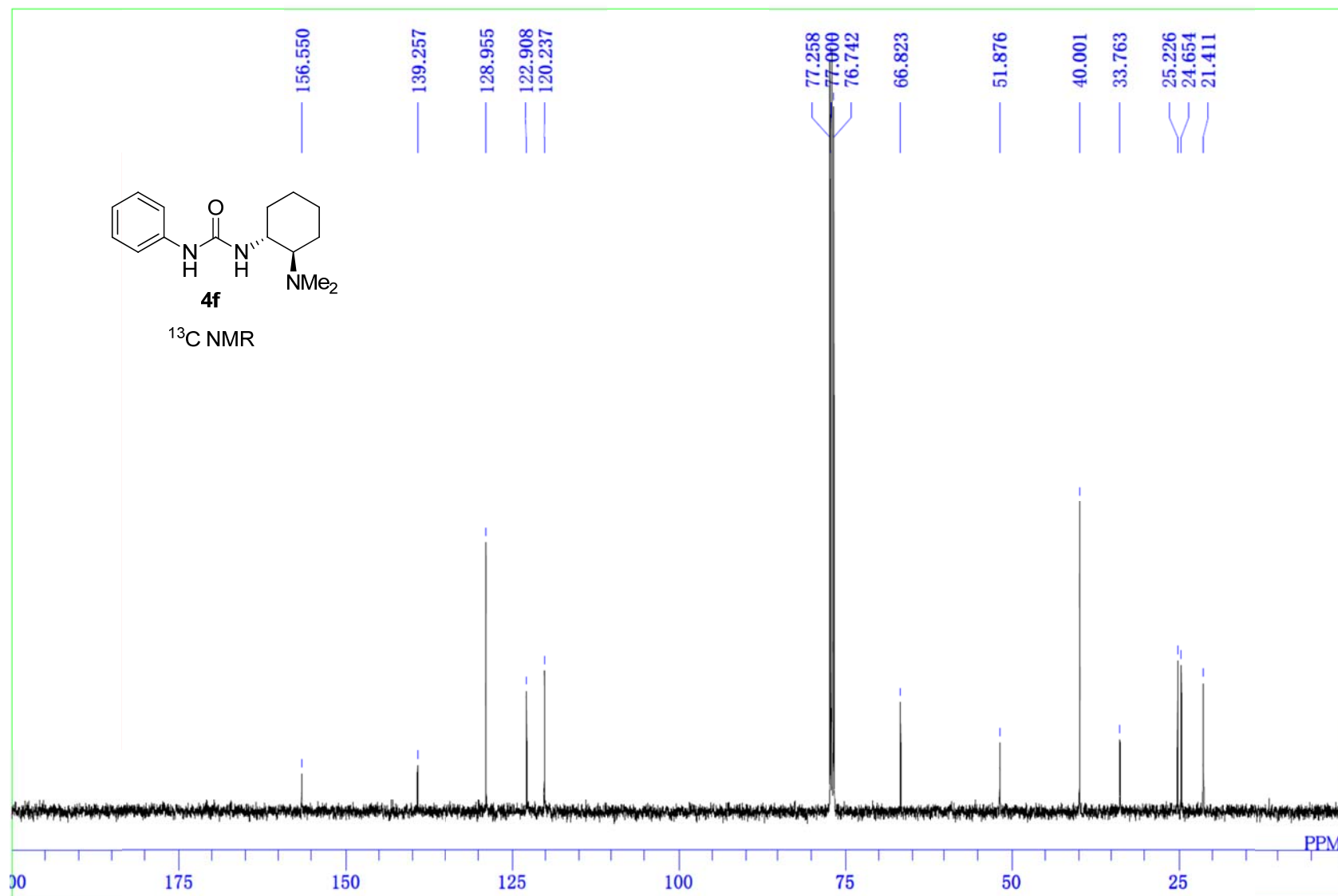


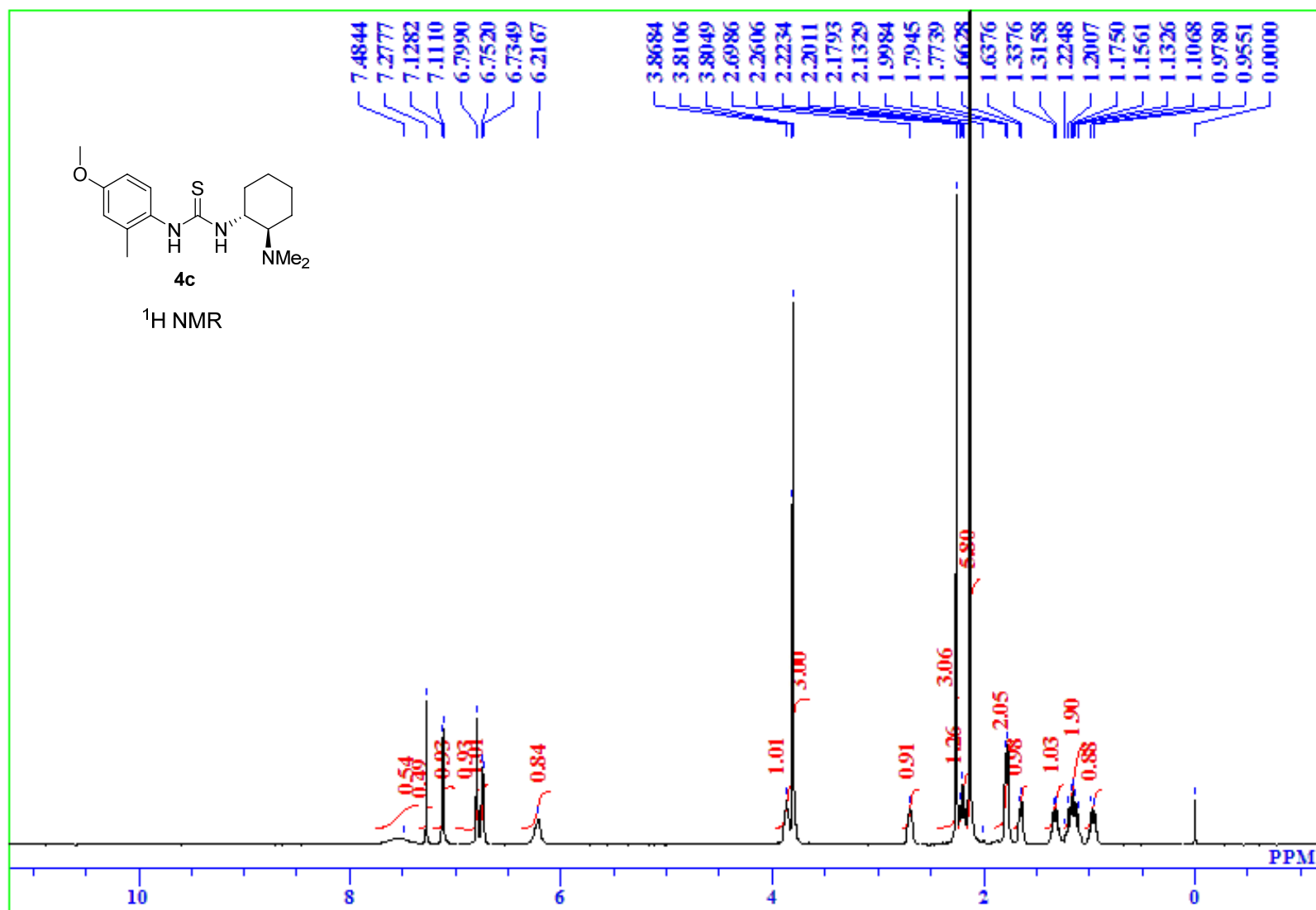


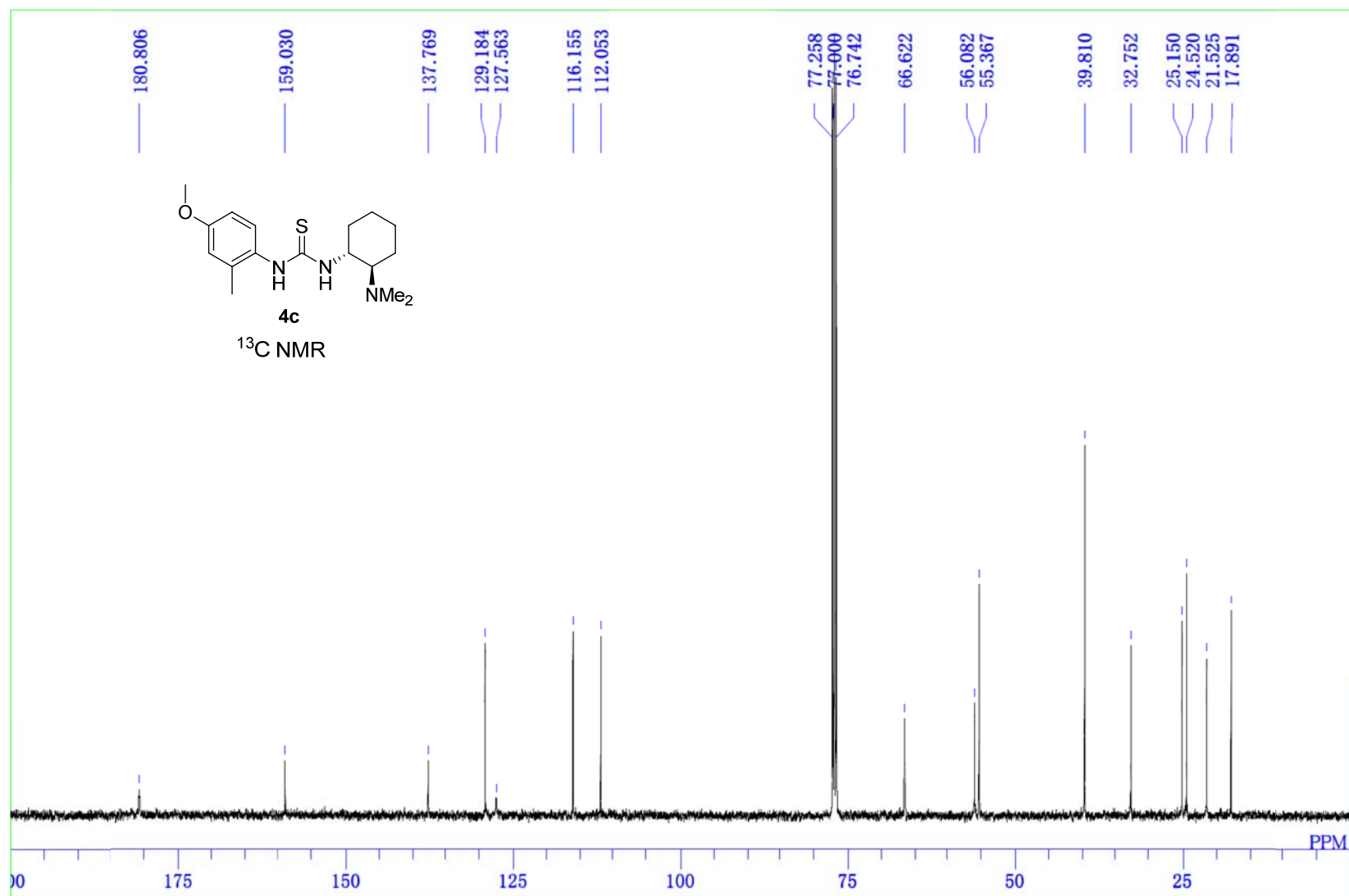


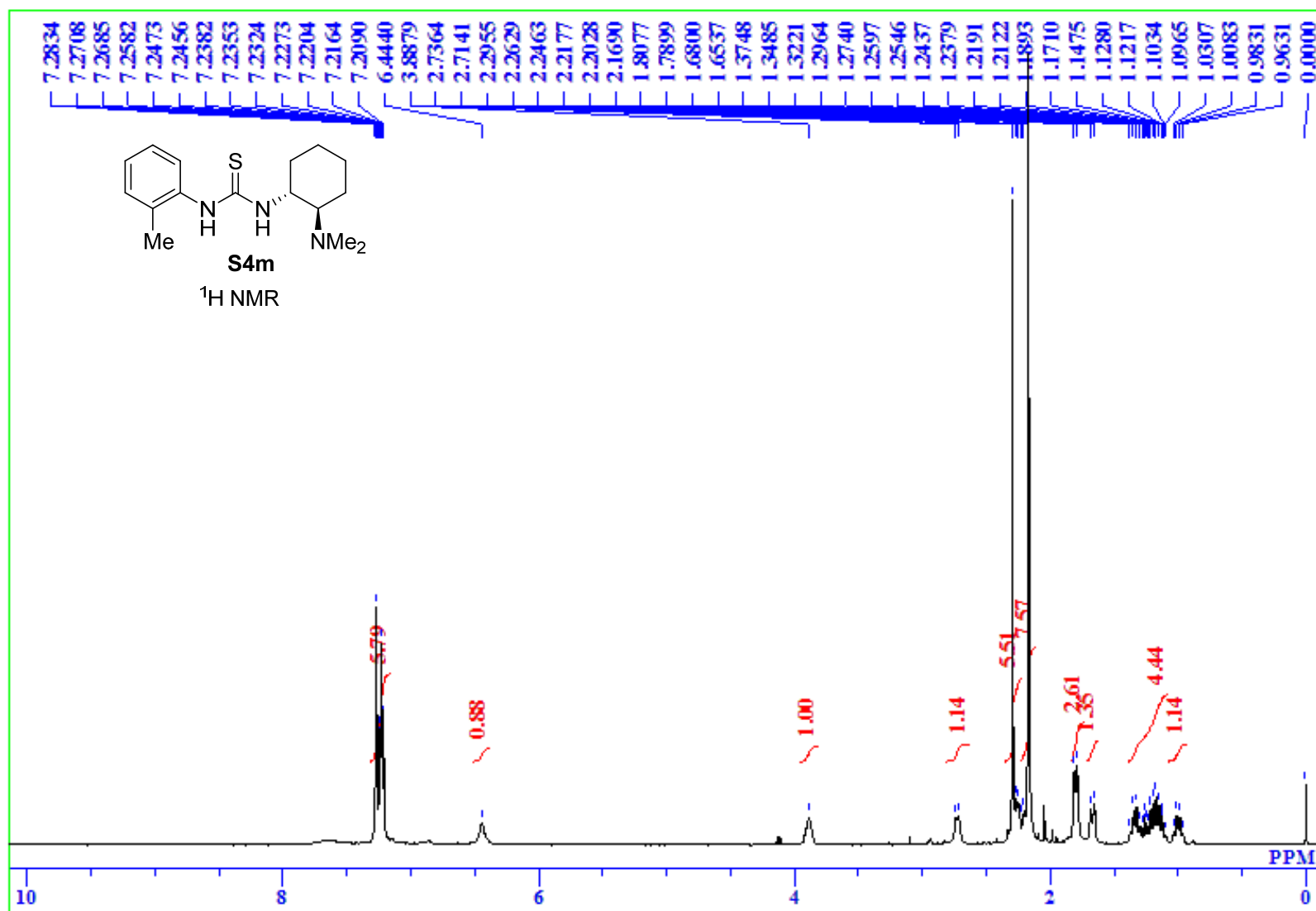


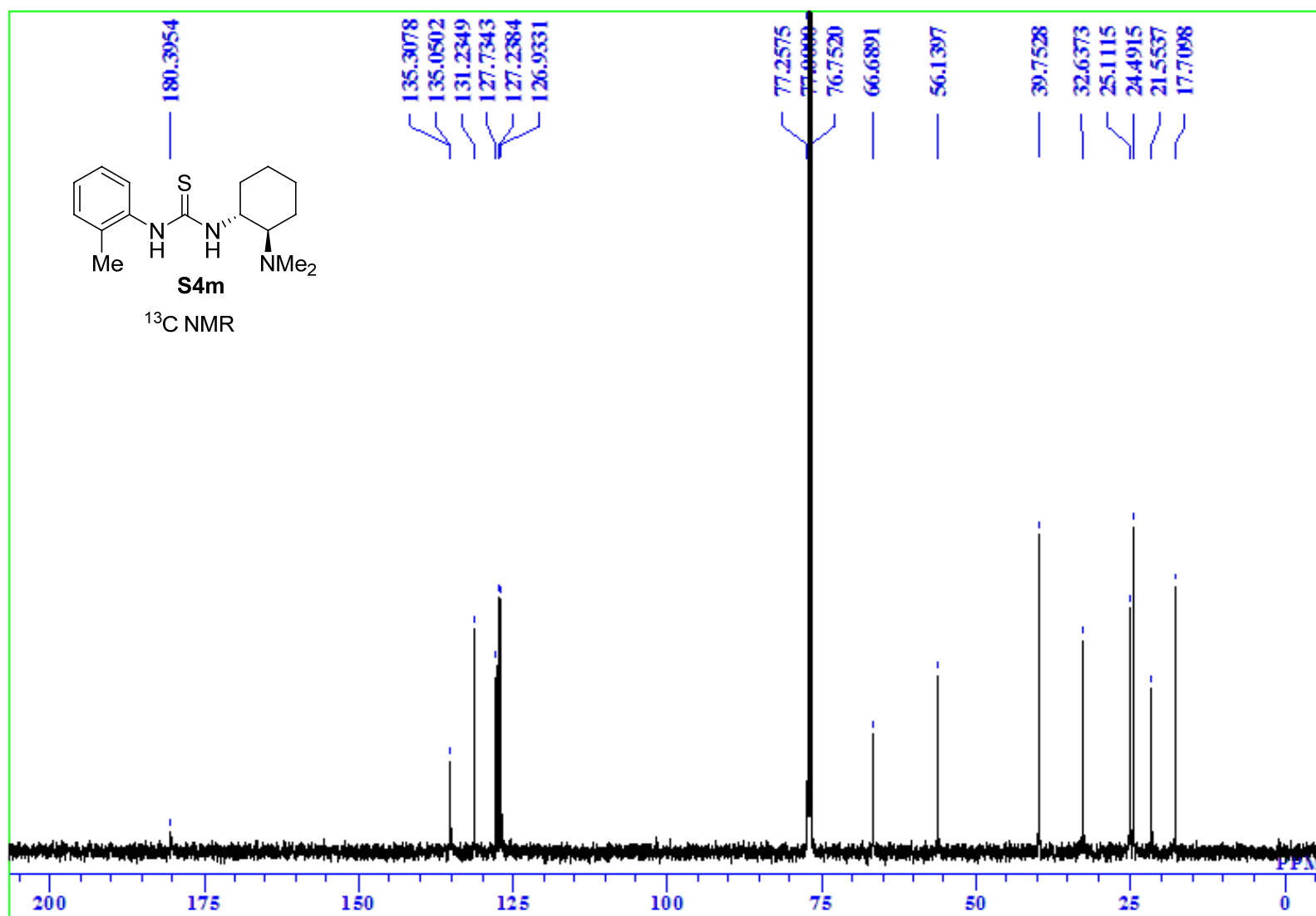


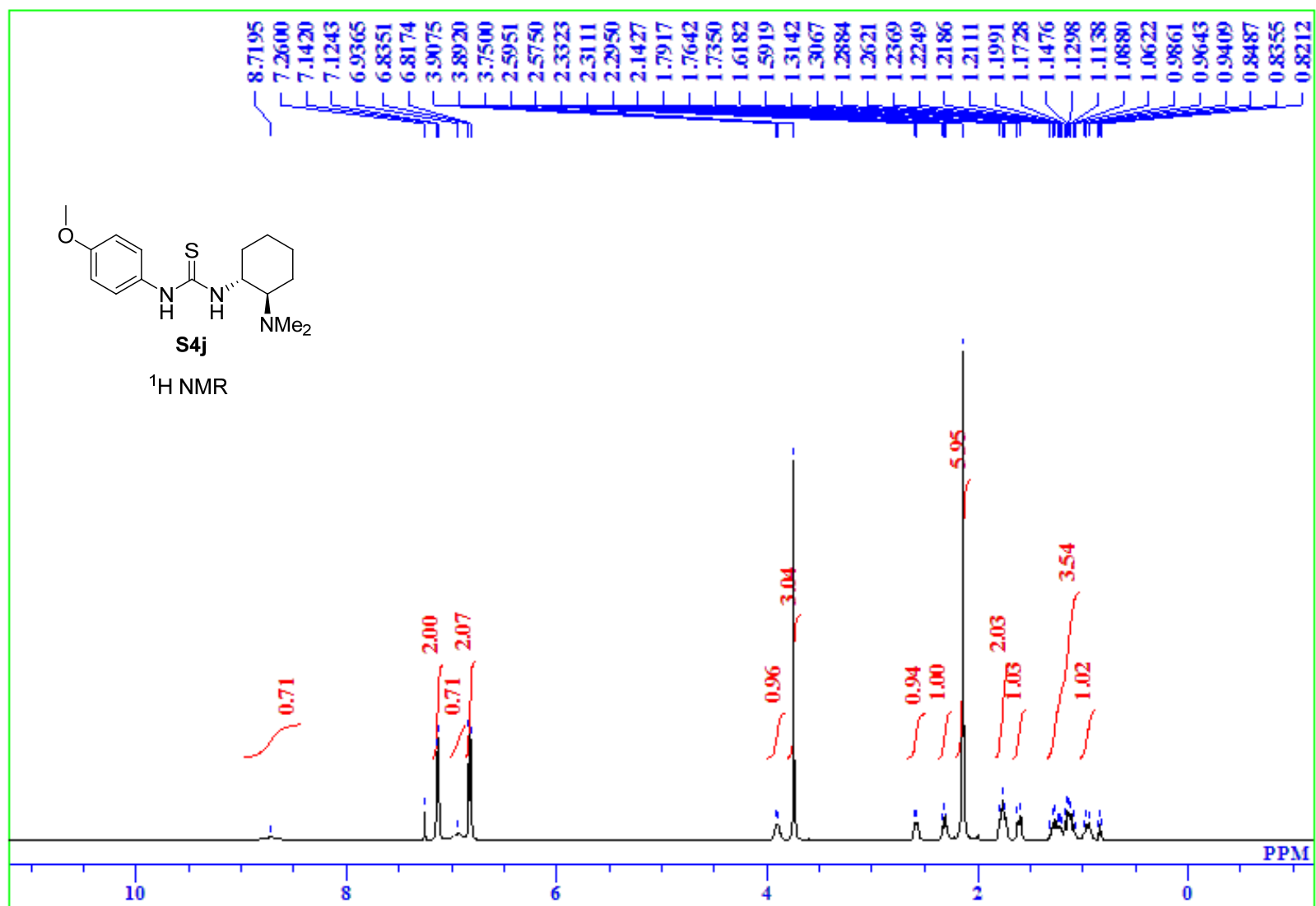


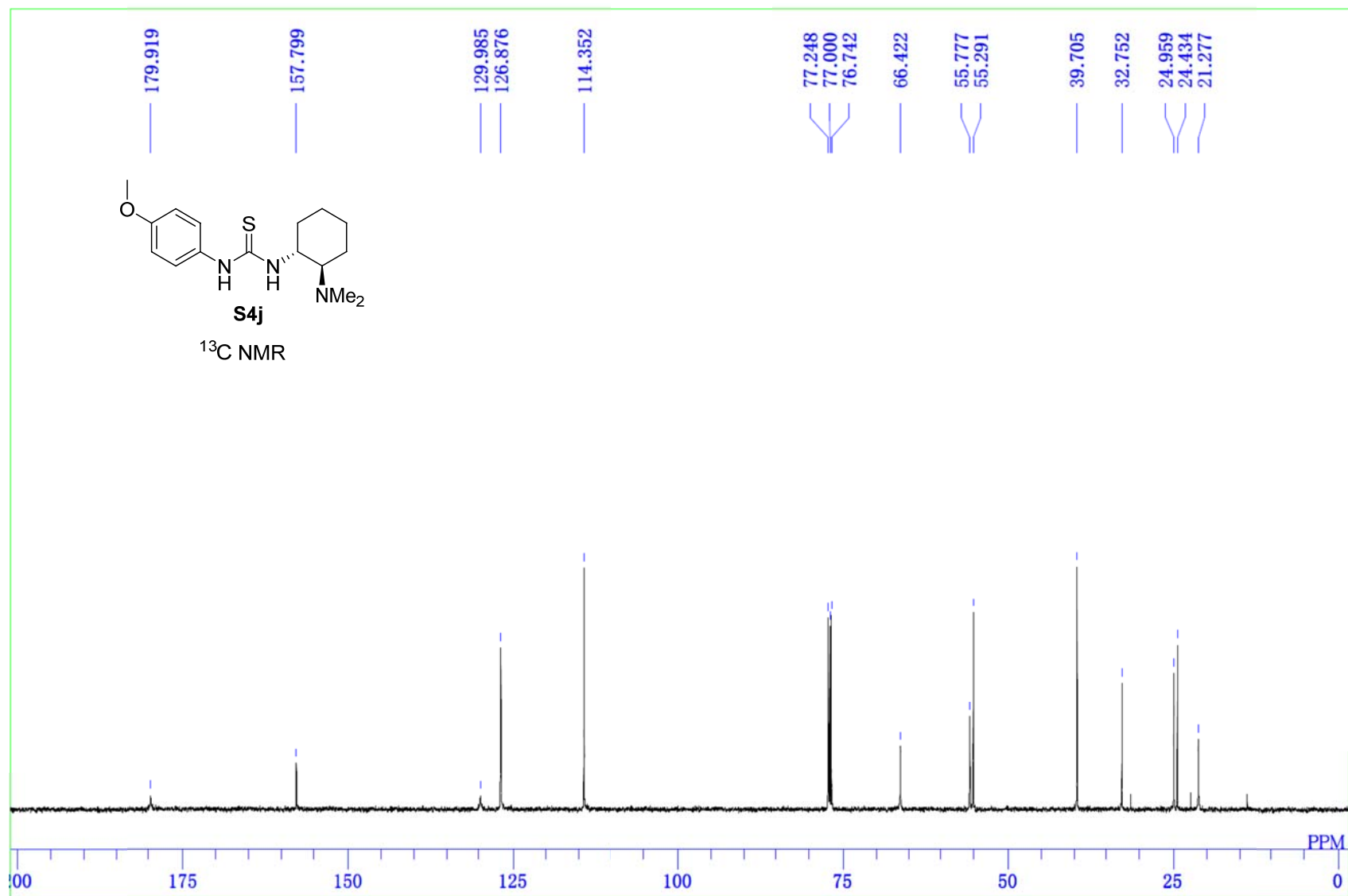


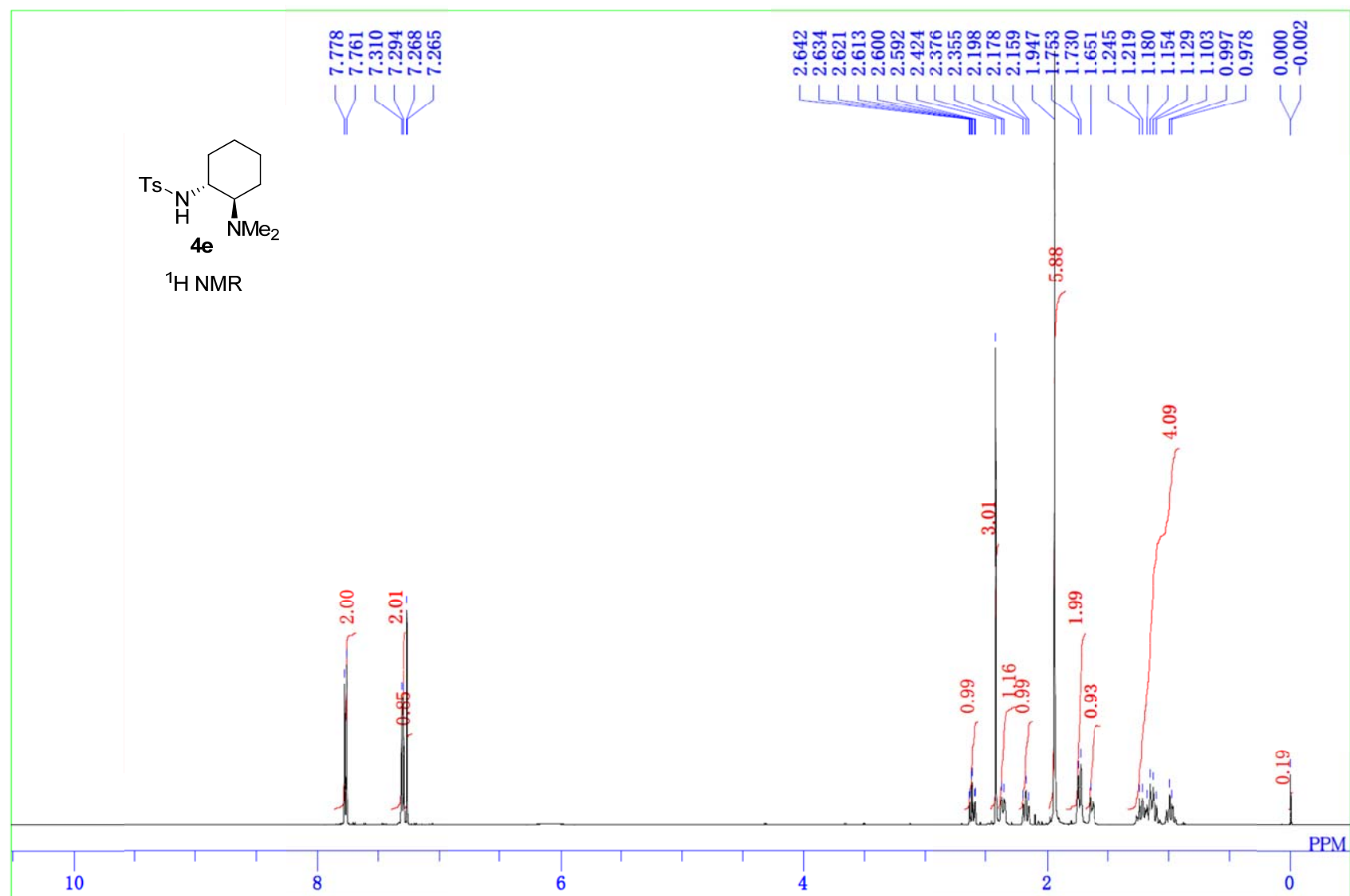


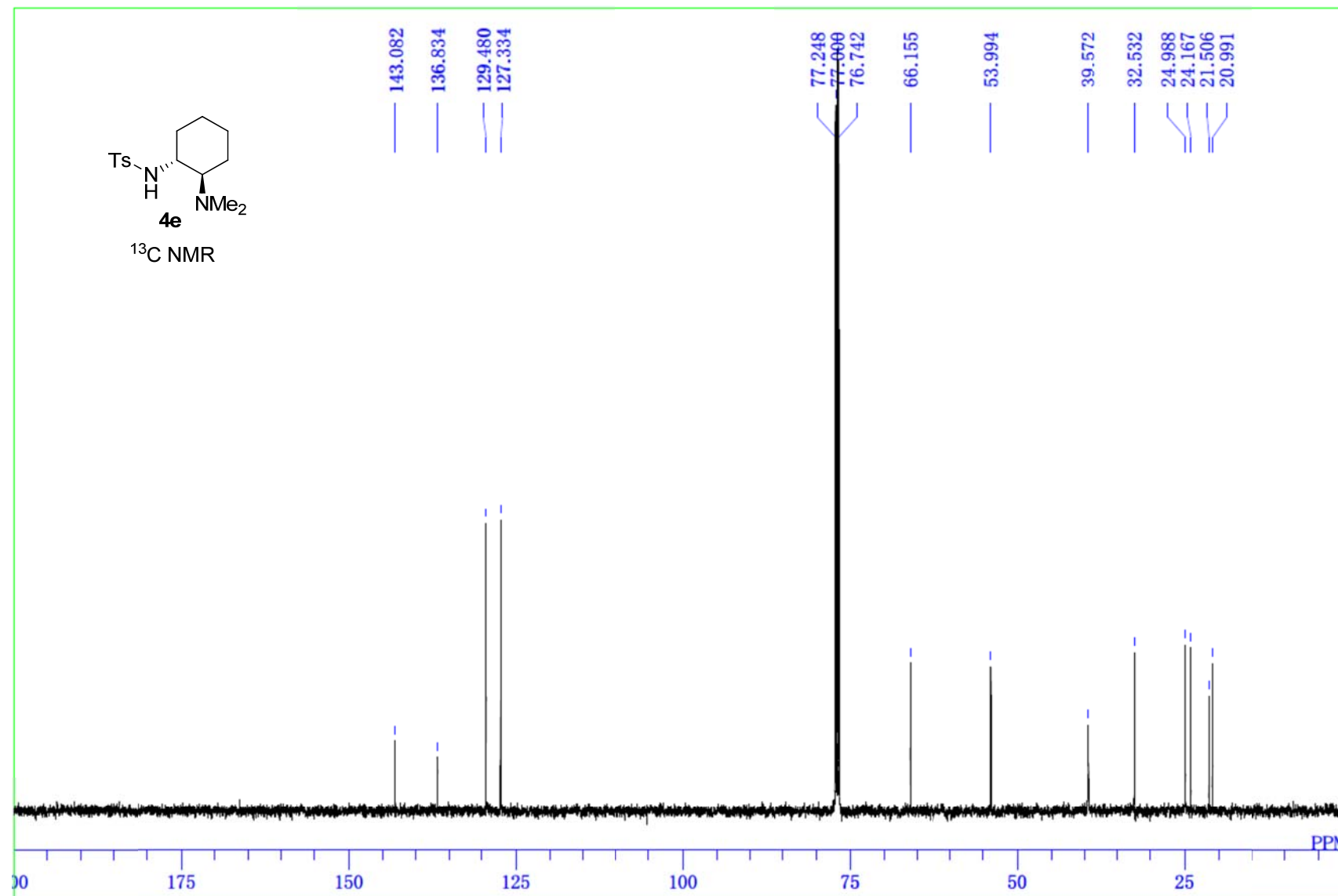


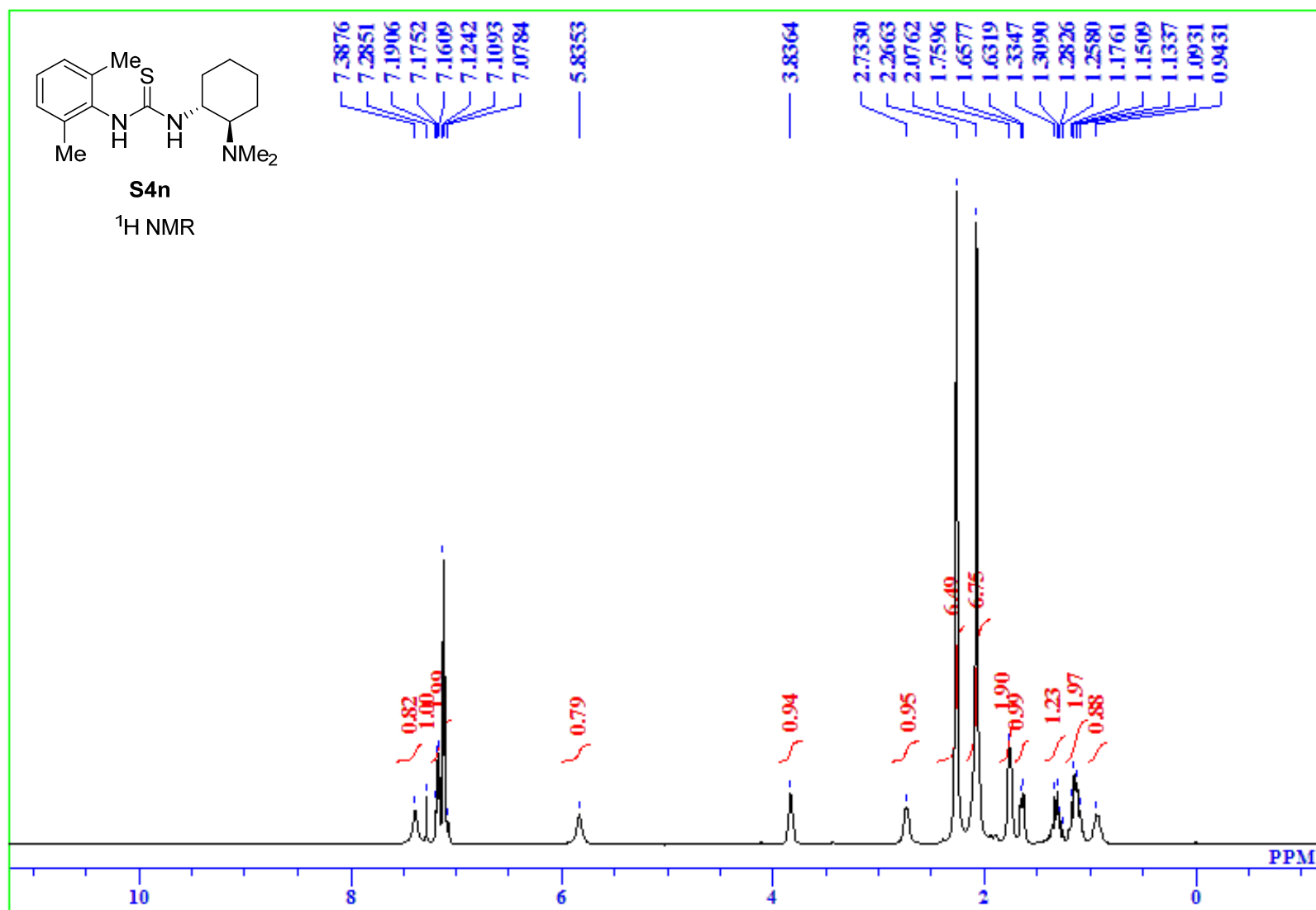


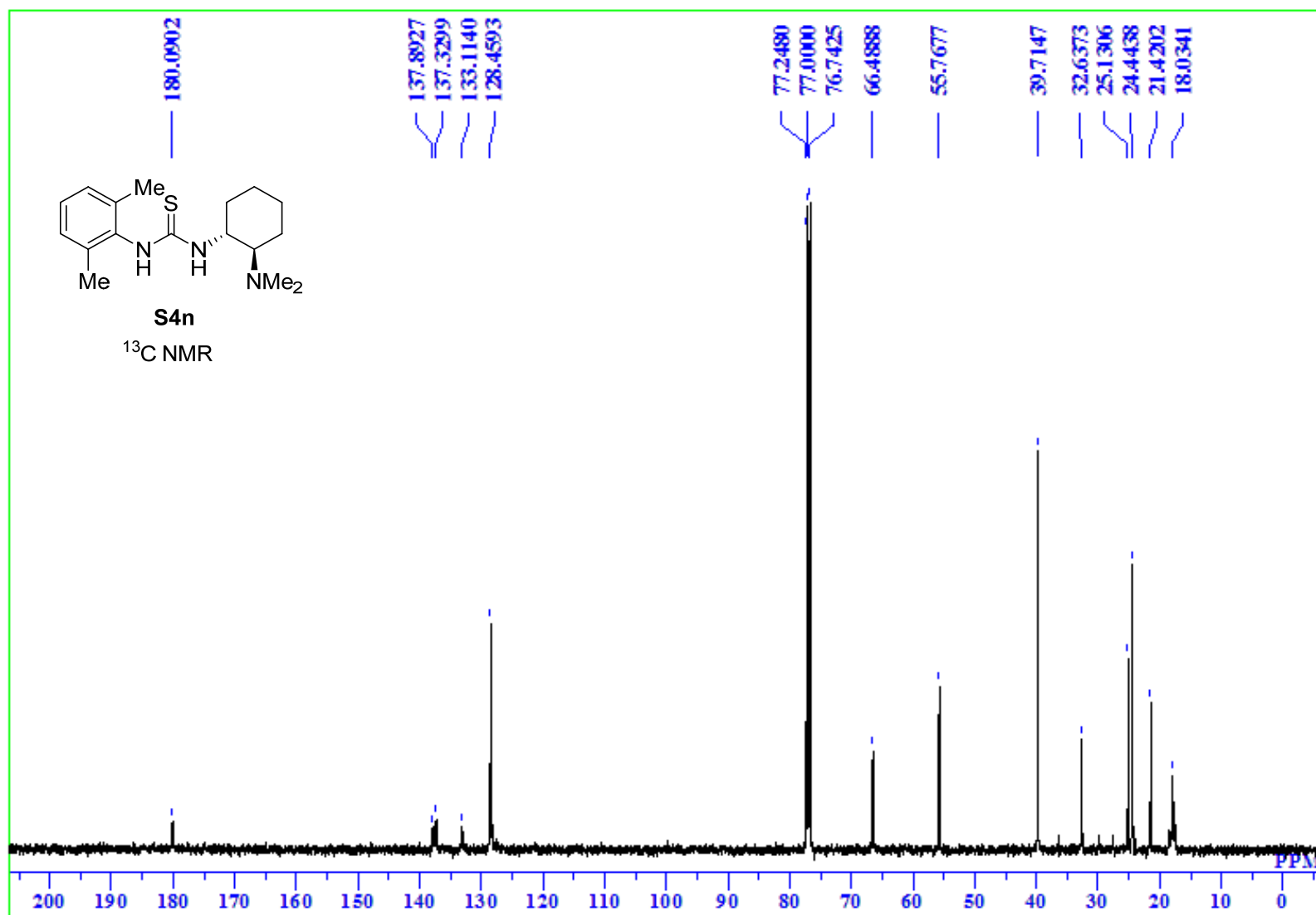


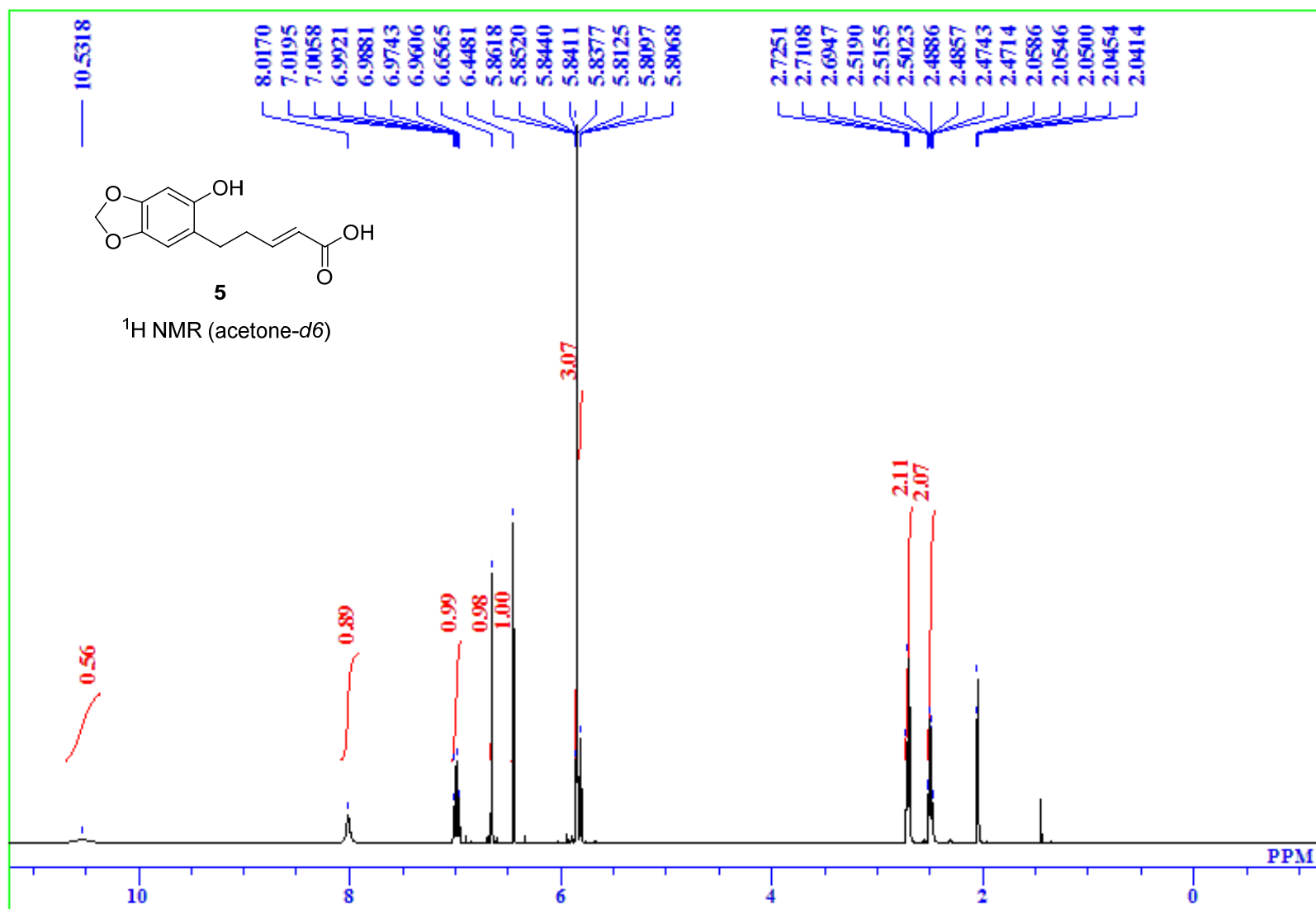


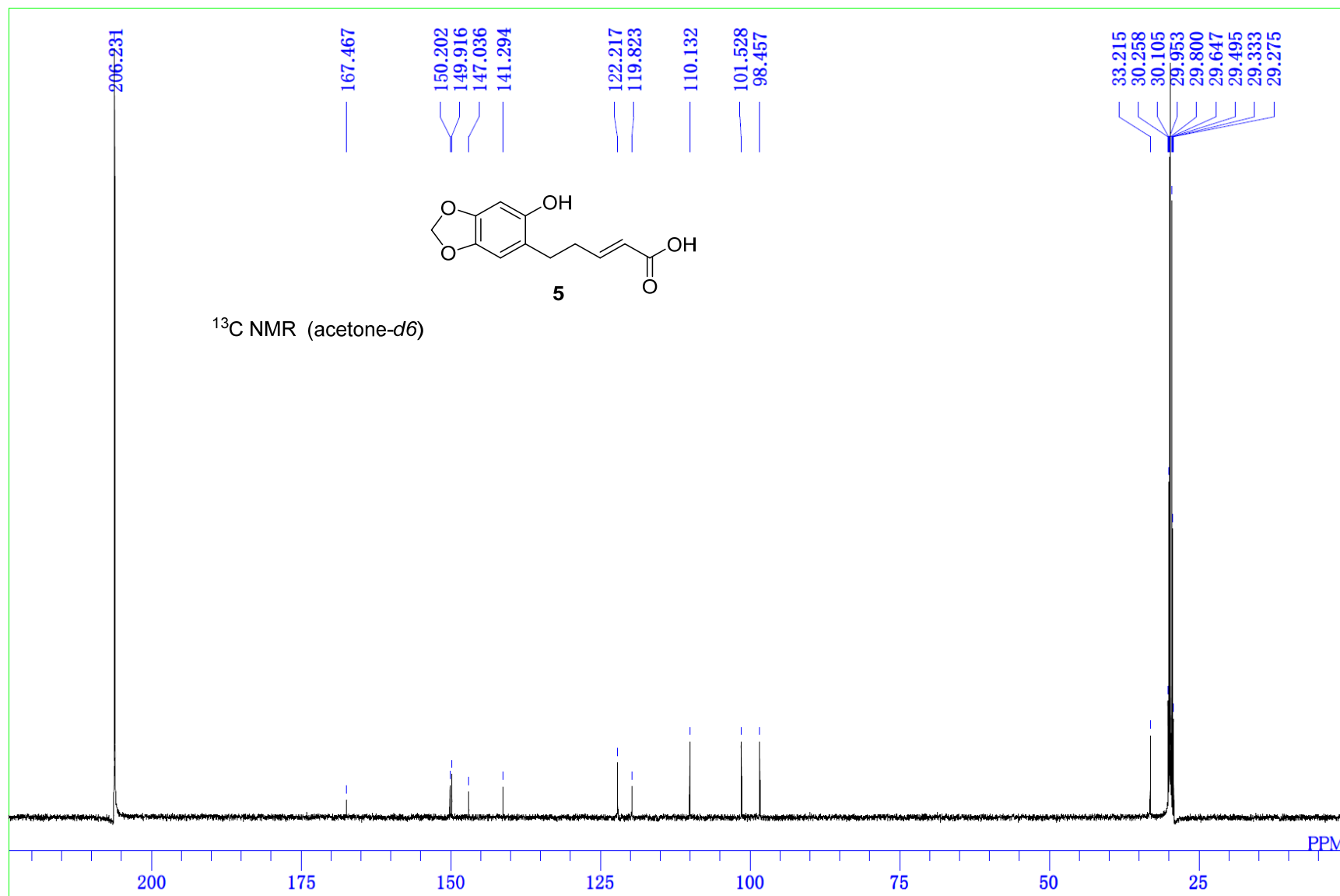


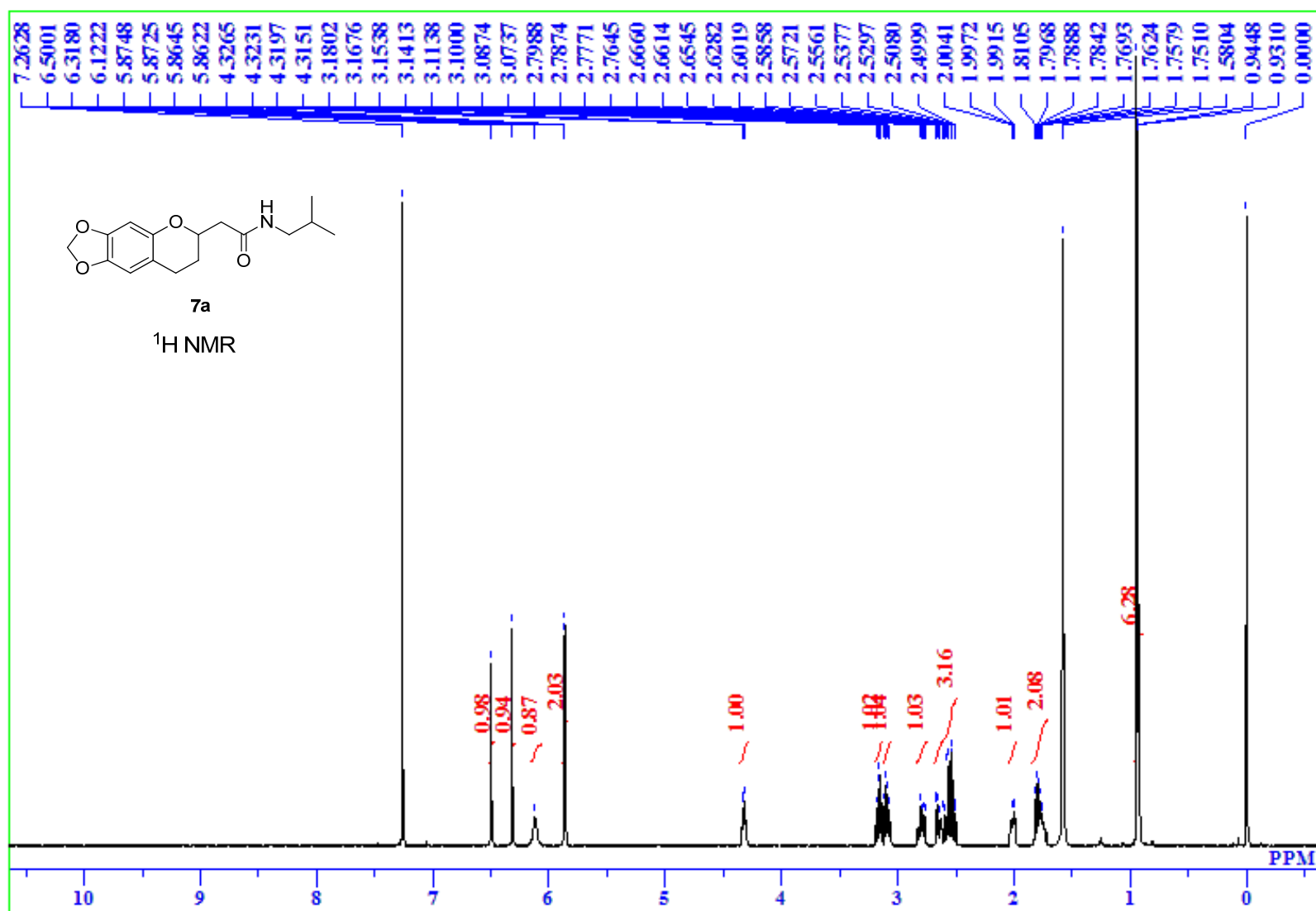


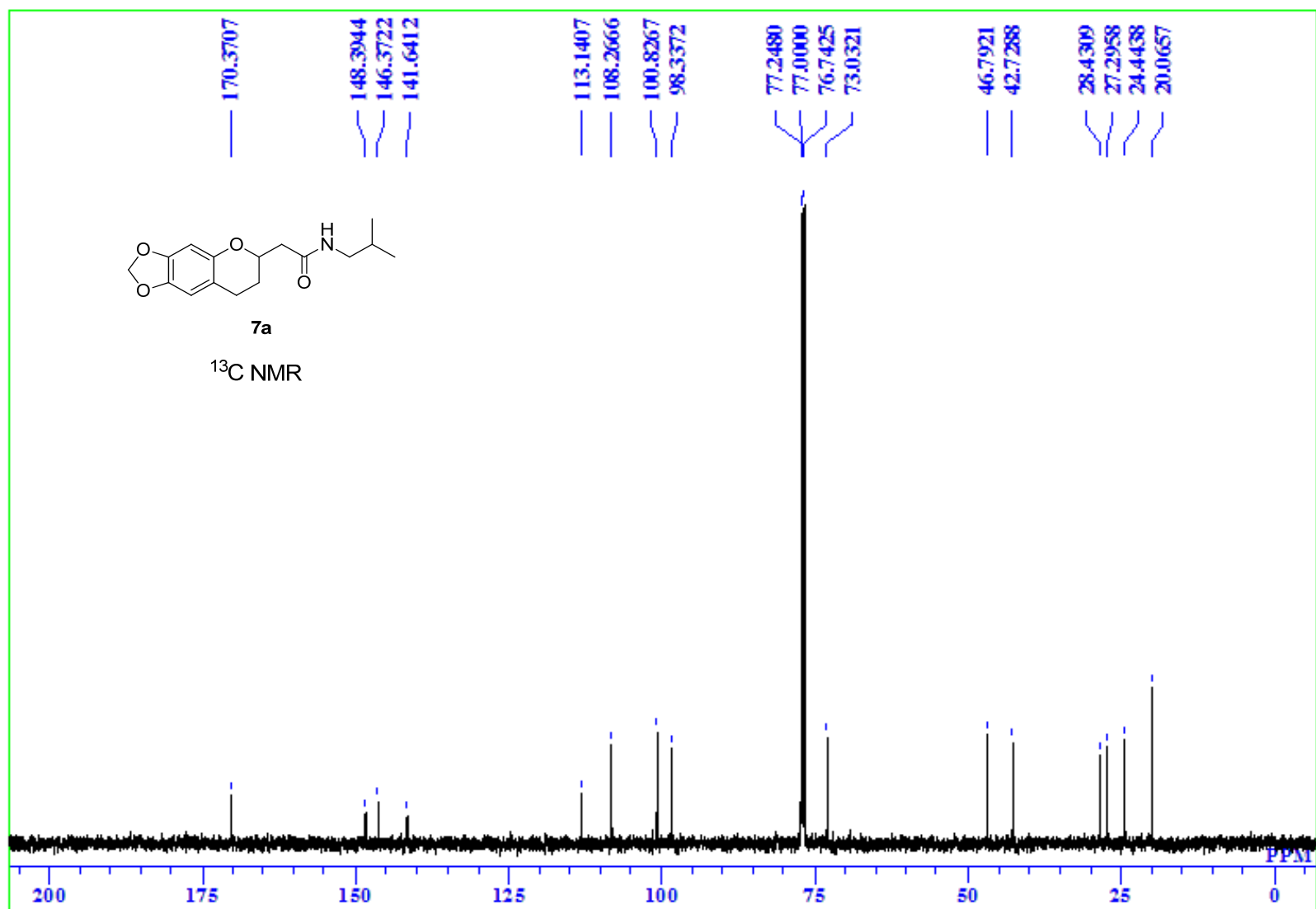


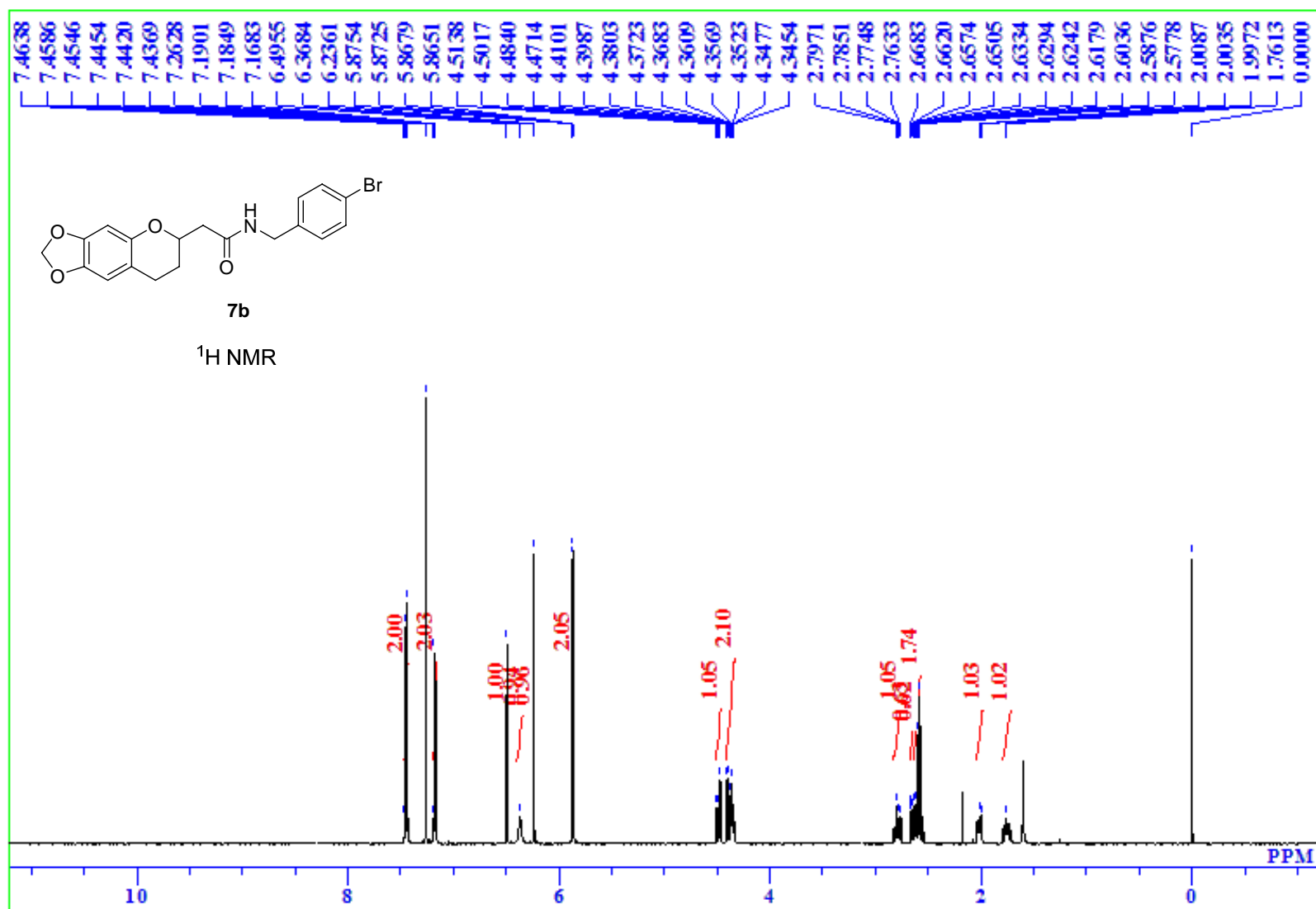


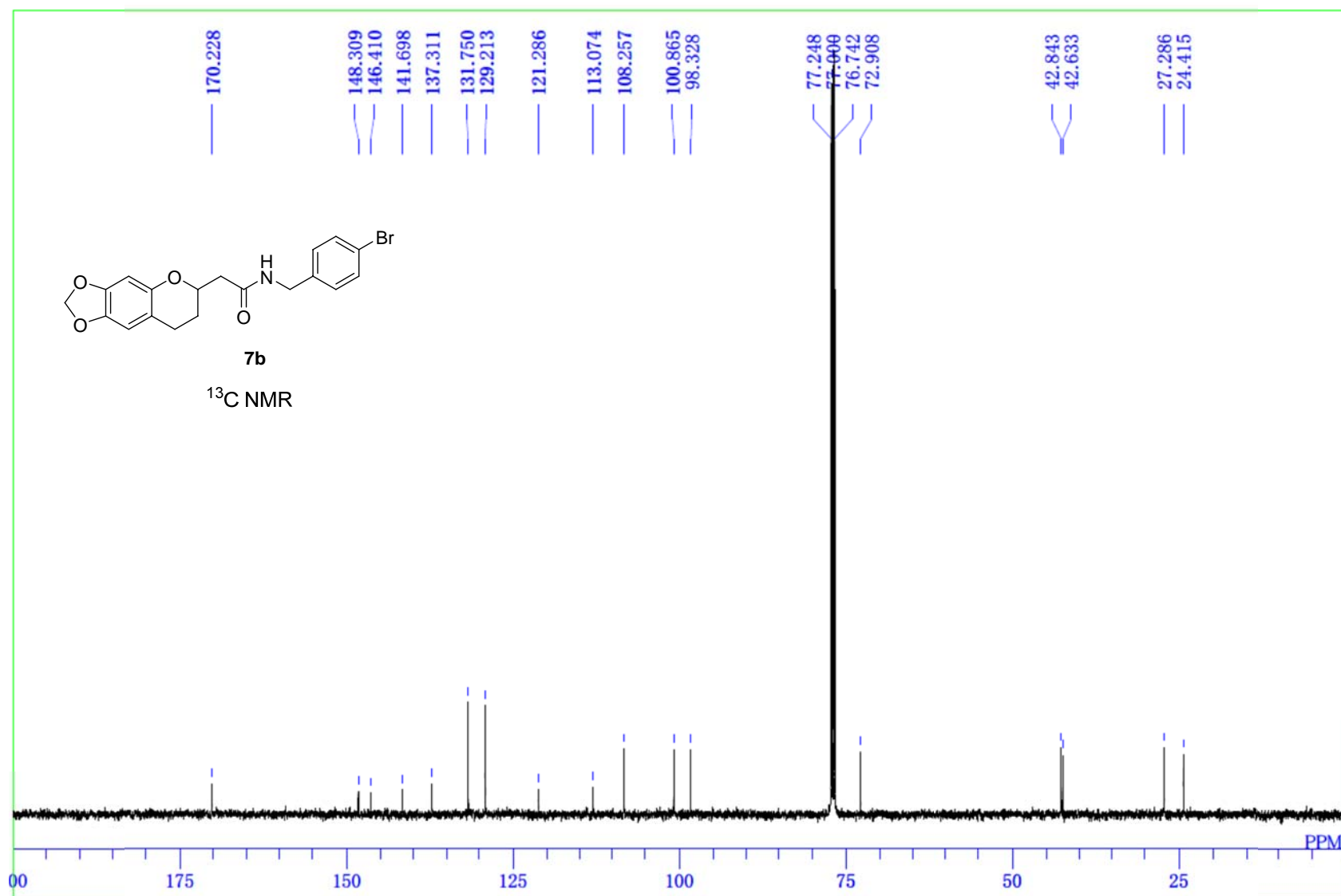




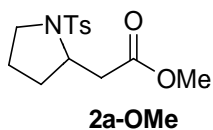




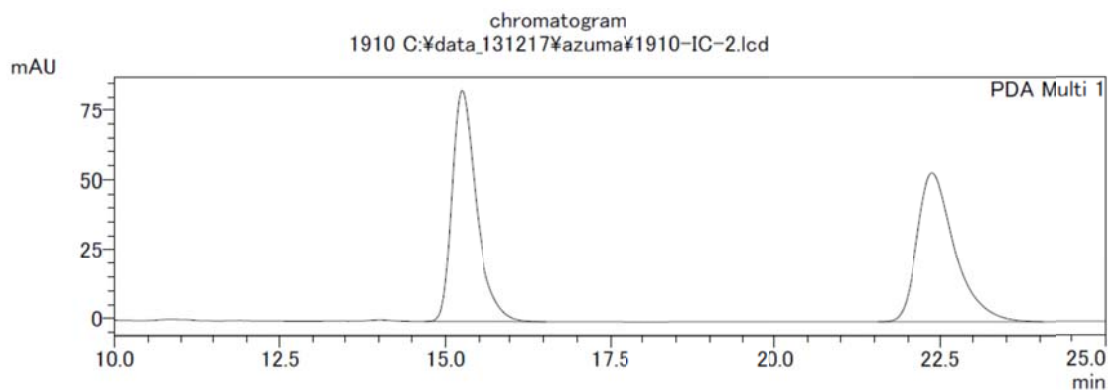




13. Copies of HPLC charts



<Chromatogram>



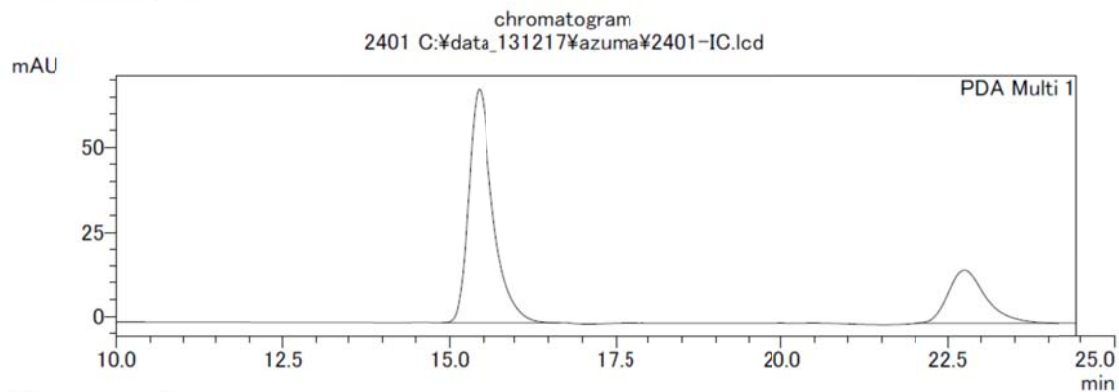
<Peak Report>

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

PDA Ch1 254nm 4nm

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

<Chromatogram>

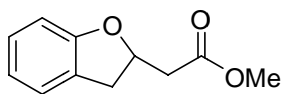


<Peak Report>

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

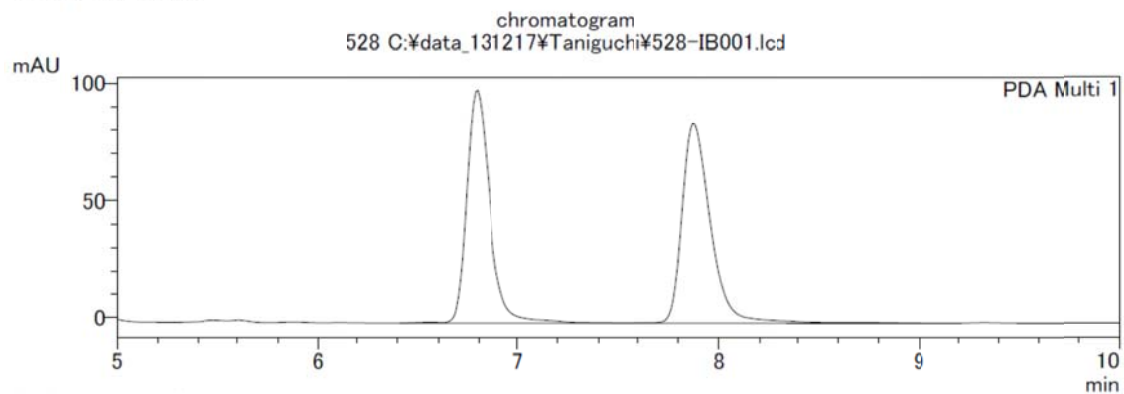
PDA Ch1 254nm 4nm

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



2j-OMe

<Chromatogram>



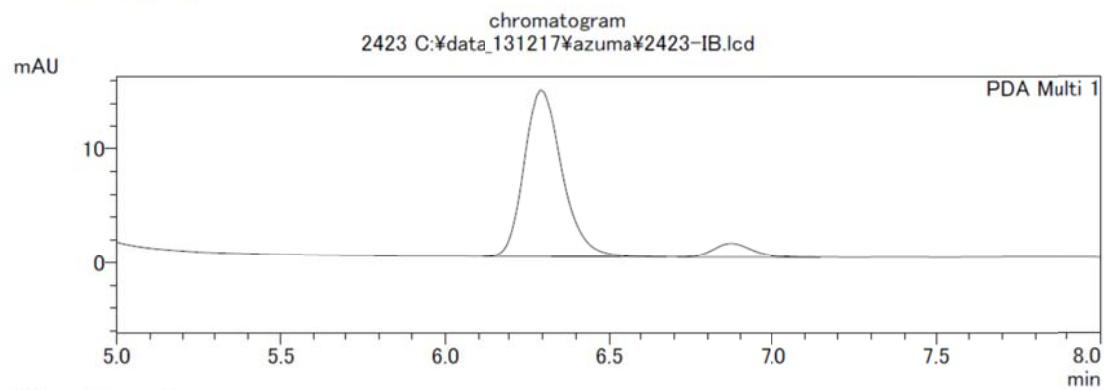
<Peak Report>

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>

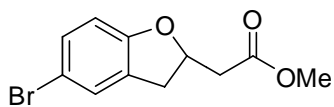


<Peak Report>

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

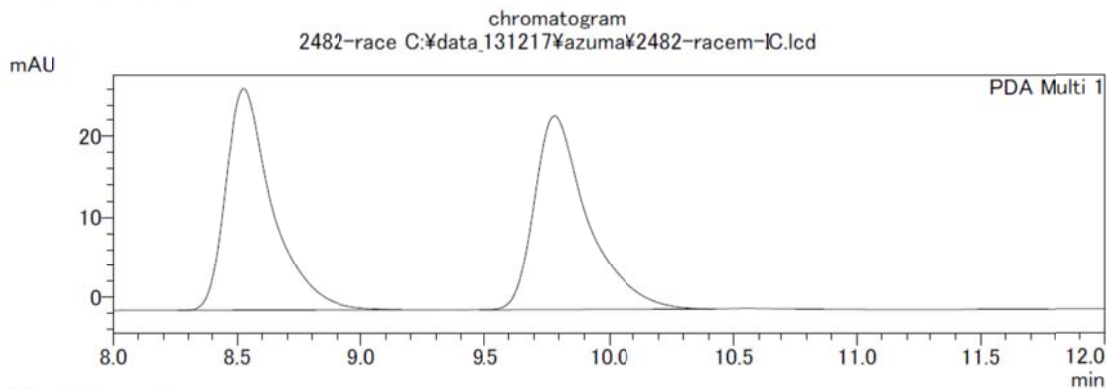
PDA Ch1 254nm 4nm

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



2k-OMe

<Chromatogram>



<Peak Report>

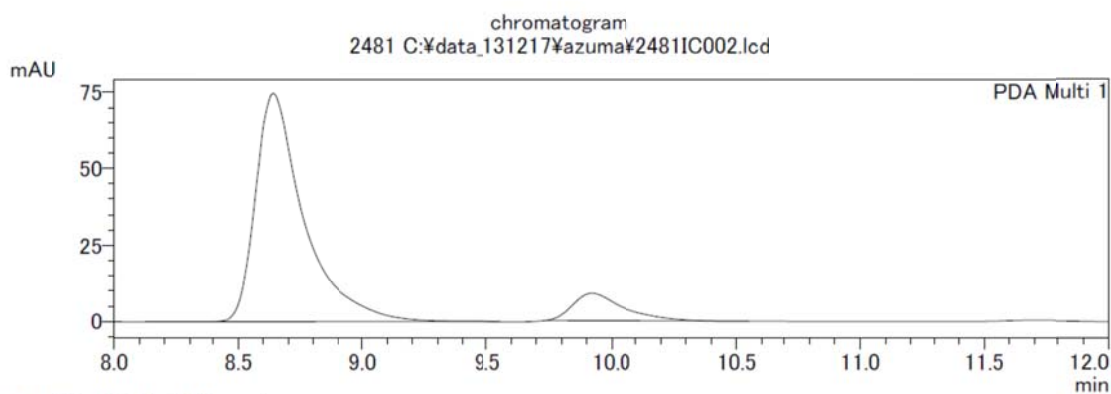
peak table C:\data_131217\azuma\2482-racem-IC.lcd

| 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>

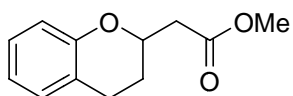


1 PDA Multi 1 / 254nm 4nm

<Peak Report>

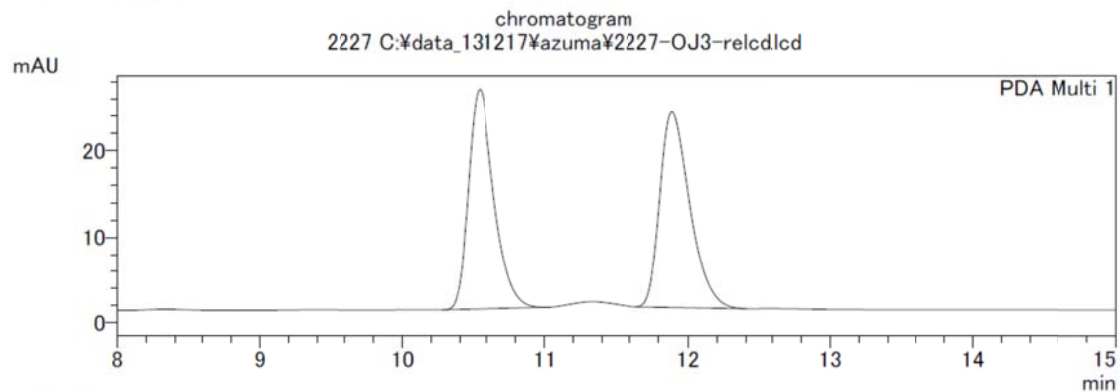
peak table C:\data_131217\azuma\2481IC002.lcd

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



2m-OMe

<Chromatogram>

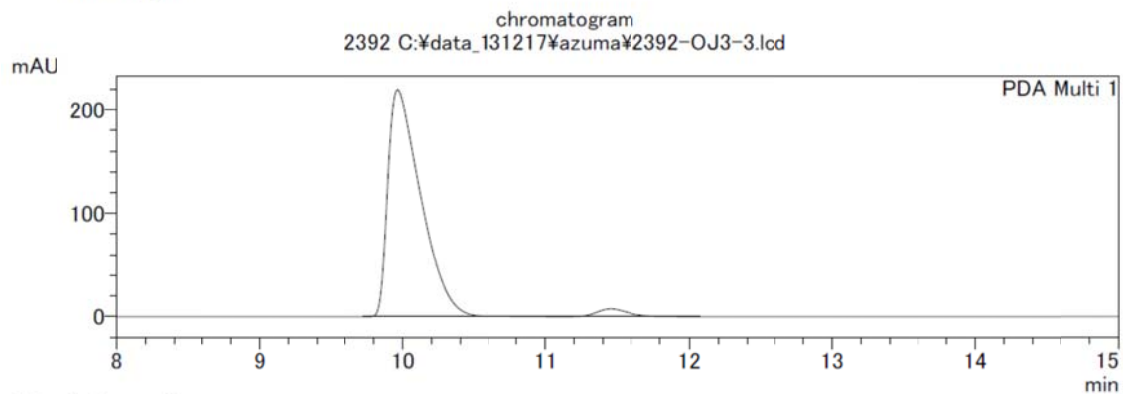


<Peak Report>

peak table C:\data_131217\azuma\2227-OJ3-re cd.lcd

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

<Chromatogram>



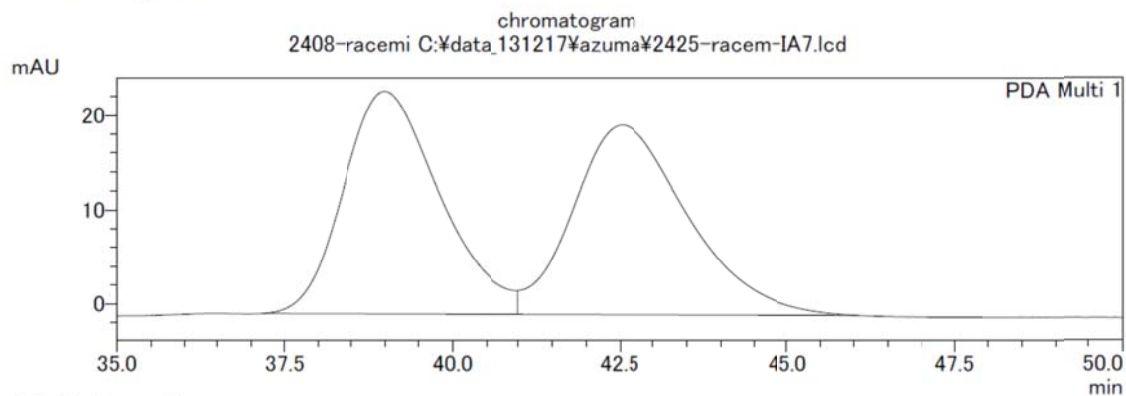
<Peak Report>

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

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



<Chromatogram>

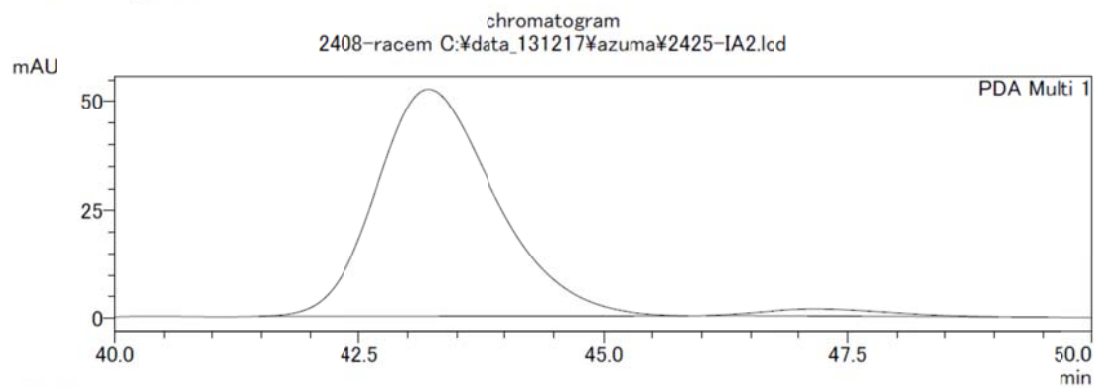


<Peak Report>

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

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

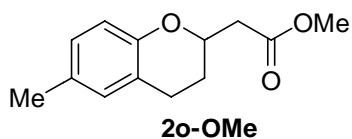
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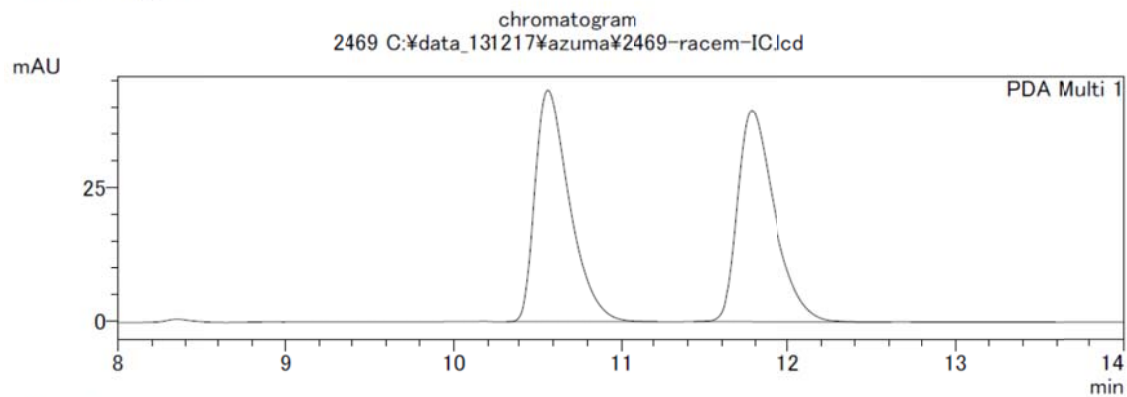
<Peak Report>

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

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



<Chromatogram>

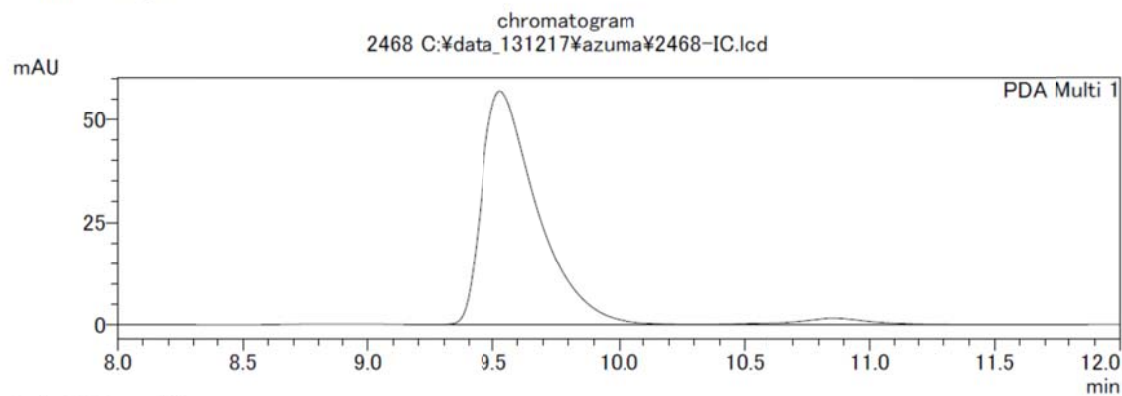


<Peak Report>

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

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

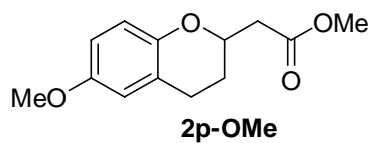
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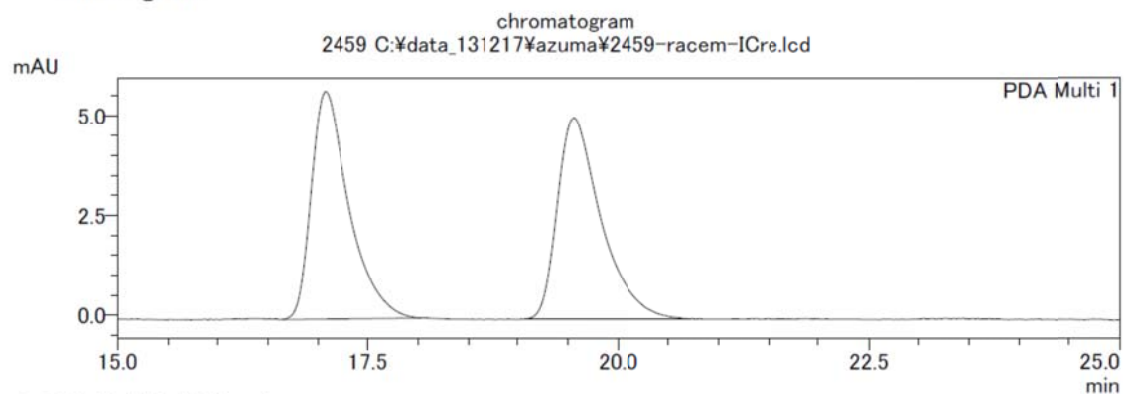
<Peak Report>

peak table C:\data_131217\azuma¥2468-IC.lcd

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



<Chromatogram>

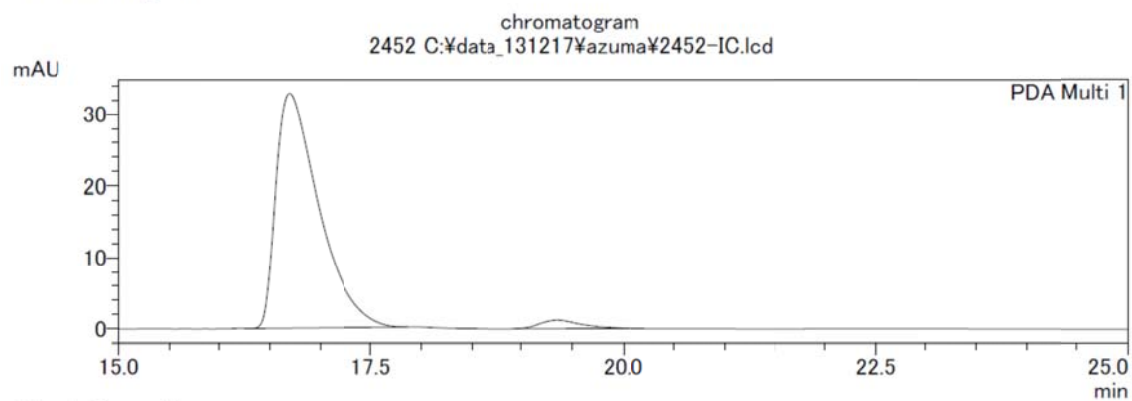


<Peak Report>

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

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

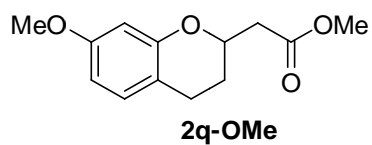
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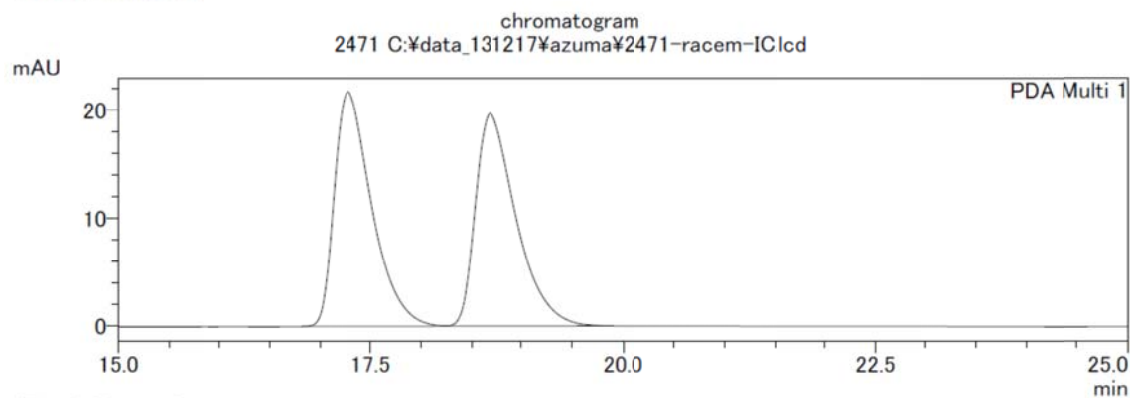
<Peak Report>

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

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



<Chromatogram>

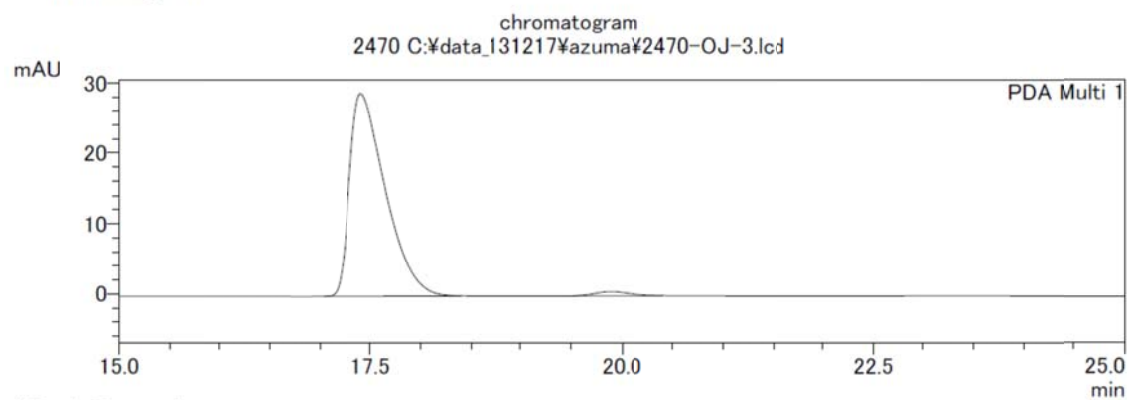


<Peak Report>

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

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

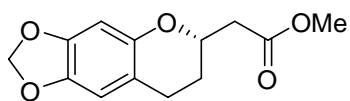
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<Peak Report>

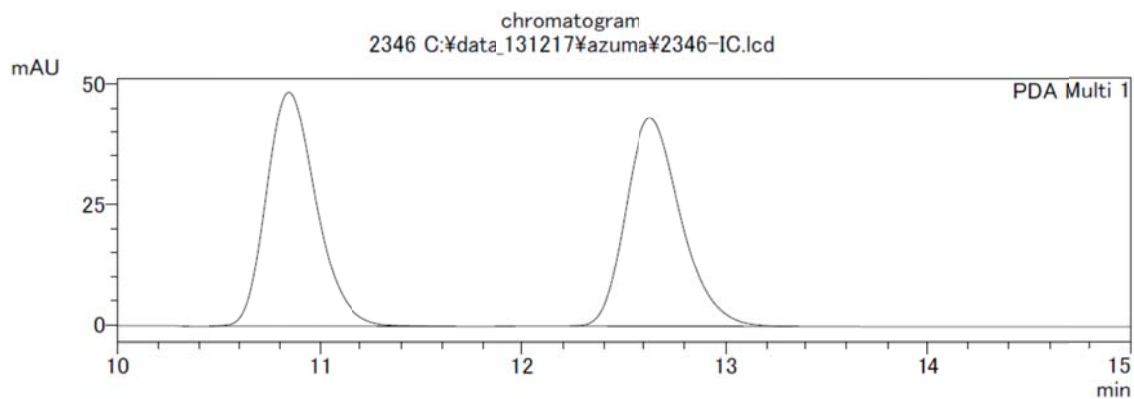
peak table C:\data_131217\azuma\2470-OJ-3.lcd

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



6-OMe

<Chromatogram>



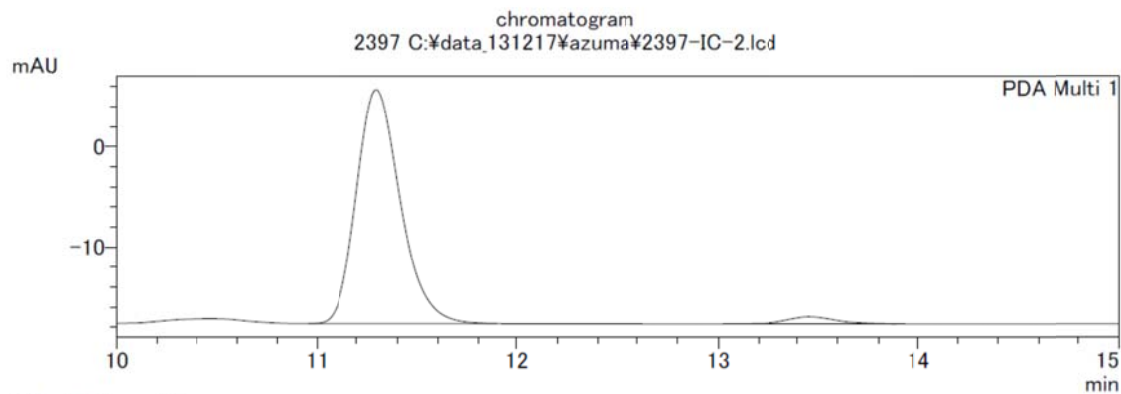
<Peak Report>

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>

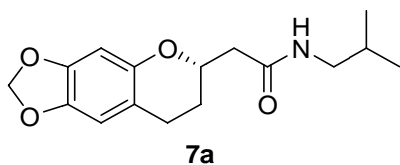


<Peak Report>

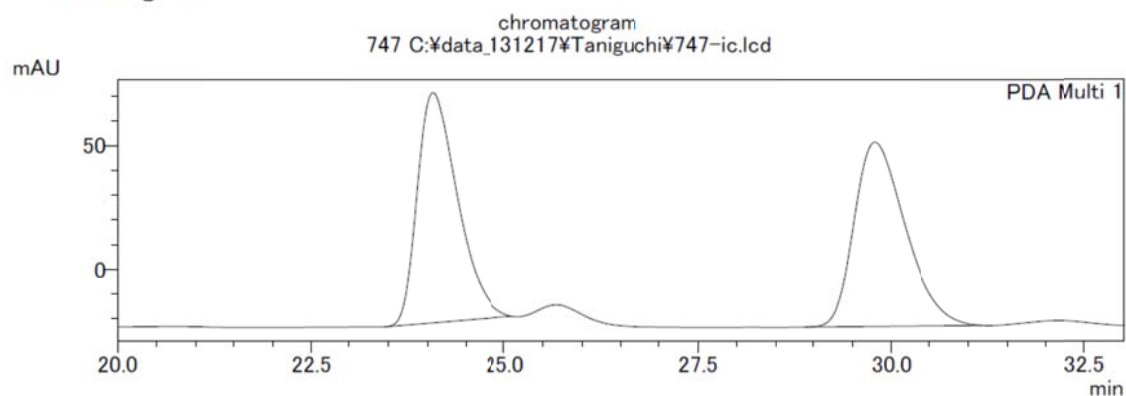
peak table C:\data_131217\azuma\2397-IC-2.lcd

PDA Ch1 254nm 4nm

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



<Chromatogram>

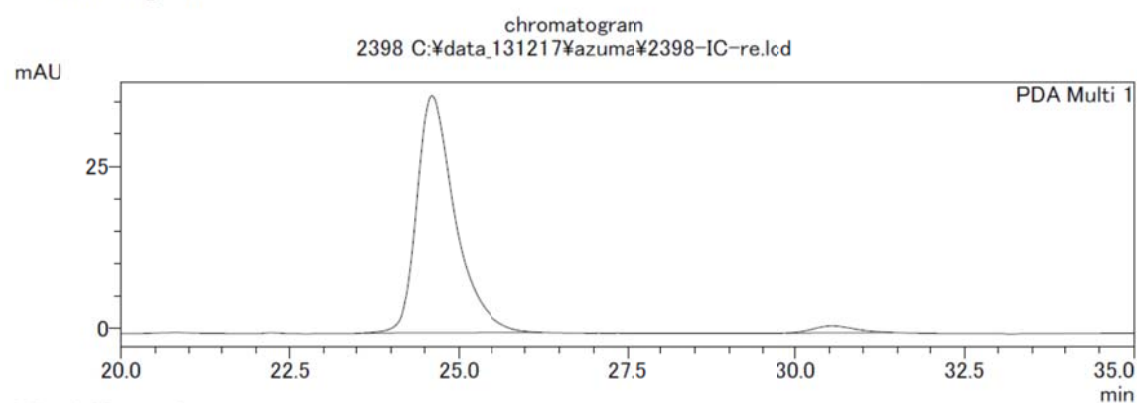


<Peak Report>

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

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

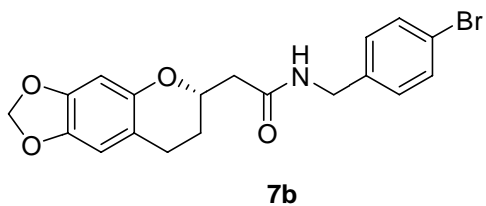
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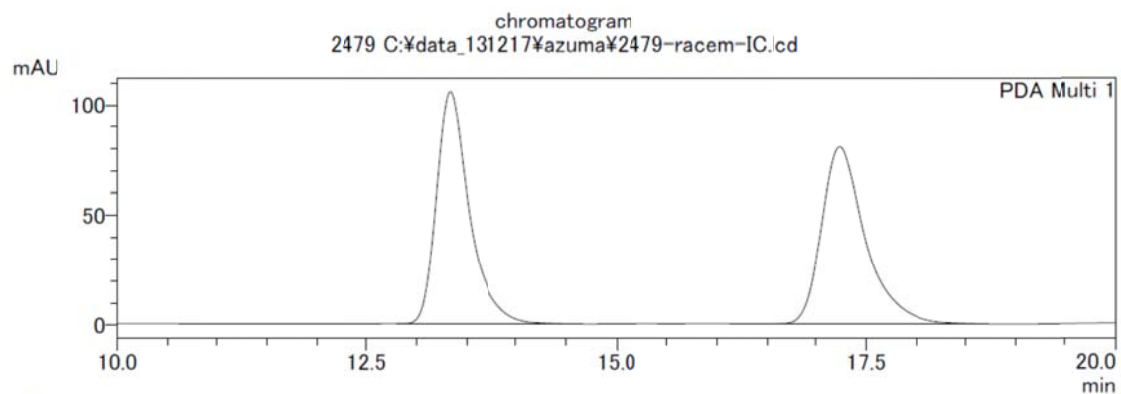
<Peak Report>

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

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



<Chromatogram>



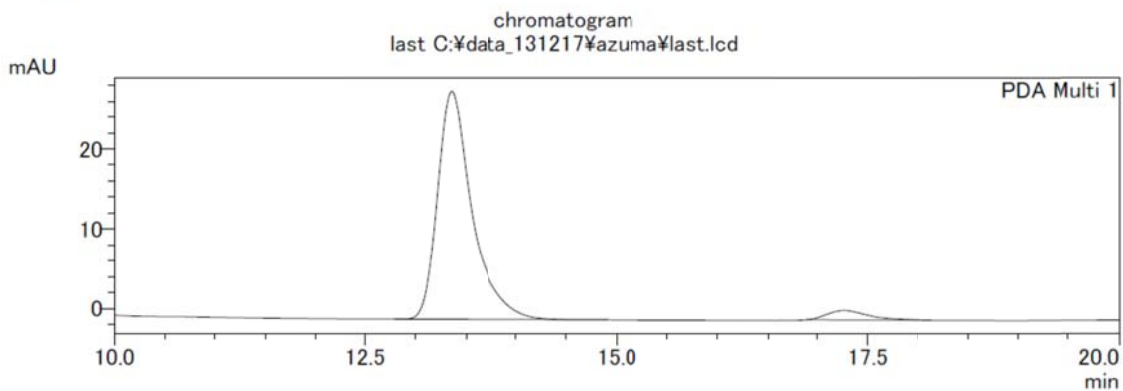
<Peak Report>

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 |