

A [3+2]-Annulation Approach to Tetrasubstituted Furans from MBH-Carbonates of Acetylenic Aldehydes *via* Sequential Substitution/Cycloisomerization

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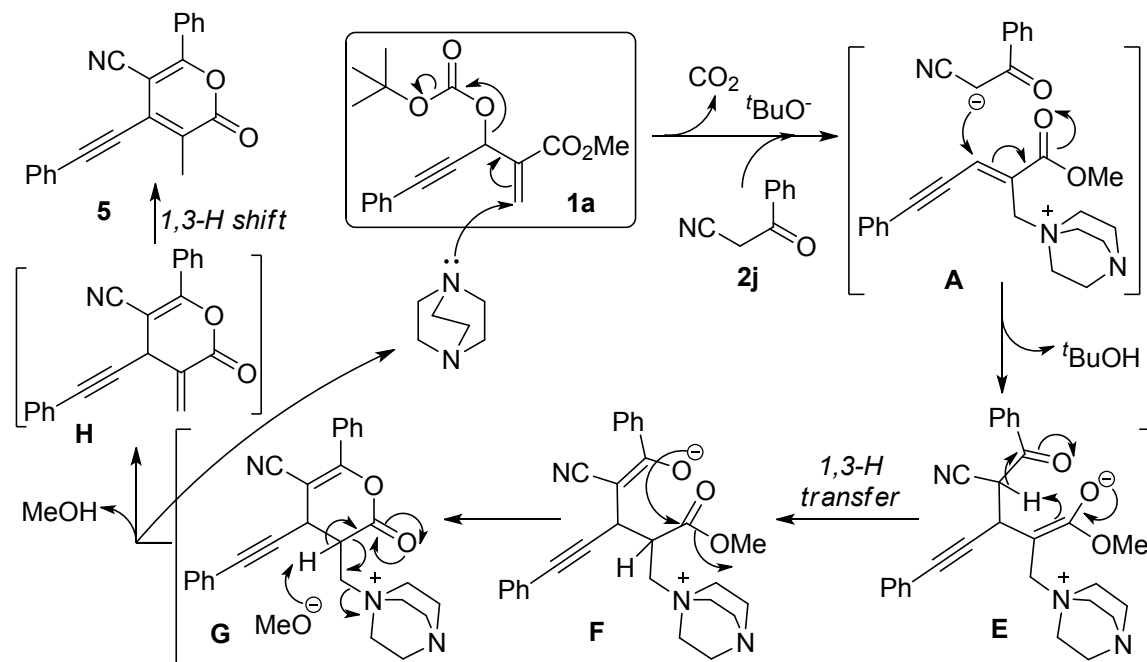
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In the reaction of MBH-carbonated with 1,3-dicarbonyls, formation of the furans was clearly the major pathway, whereas no lactonization of **4a** was observed. On the other hand, the latter pathway was dominant in the case of β -cyano ketone **2j** to produce α -pyrone **5**. Enolate **E** underwent 1,3-H transfer leading to the transesterification *via* enolate **F** to **G** and subsequent reverse polarization facilitated the regeneration of DABCO to provide the lactone **H**, which rapidly isomerized to pyran-2-one **5** (Scheme 1).¹ The formation of **5** from **1a** was accomplished using only catalytic amount of DABCO.



Scheme 1. Possible reaction pathway for the formation of **5**

1. Liua, W.; Zhao, G. *Org. Biomol. Chem.* **2014**, *12*, 832 – 835.

General procedure for the preparation of MBH-carbonates (1a to 1i): To a stirred solution of the corresponding MBH-alcohol (1 equiv.) in 10 mL of CH₂Cl₂ was added di-*tert*-butyl dicarbonate (1.2 equiv.) and DMAP (0.05 equiv.) at 0° C and stirred for given time. After completion of the reaction, the mixture was diluted with water (50 mL) and extracted with CH₂Cl₂ (3 x 30 mL). The combined organic layer was dried over anhydrous Na₂SO₄ and concentrated *in vacuo*. The crude was purified by flash column chromatography on silica gel (EtOAc:hexanes) to afford the corresponding MBH-carbonate. All these carbonates were fully characterized and spectral data is given below.

Methyl-3-((*tert*-butoxycarbonyl)oxy)-2-methylene-5-phenylpent-4-ynoate (1a): 1.02 g, 70%, White solid; R_f = 0.6 (petroleum ether : EtOAc = 9:1); M.P.: 37-39 °C; ¹H NMR (500 MHz, CDCl₃): δ 7.46 (dd, *J* = 7.4, 1.4 Hz, 2H), 7.33 (t, *J* = 7.8 Hz, 3H), 6.53 (s, 1H), 6.38 (s, 1H), 6.36 (s, 1H), 3.81 (s, 3H), 1.52 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ 164.9, 152.2, 136.5, 131.9, 129.4, 128.9, 128.3, 121.9, 87.7, 83.6, 83.2, 64.9, 52.3, 27.7; IR (KBr): ν_{max} = 2981, 2234, 1748, 1274, 1253, 1156, 1076, 849, 759 cm⁻¹; MS (ESI): *m/z* 339 (M+Na)⁺; HRMS (ESI): *m/z* calcd for C₁₈H₂₀O₅Na [M+Na]: 339.1203, found: 339.1224.

Methyl-3-((*tert*-butoxycarbonyl)oxy)-5-(4-chlorophenyl)-2-methylenepent-4-ynoate (1b): 1.0 g, 72%, Yellow solid; R_f = 0.4 (petroleum ether : EtOAc = 9:1); M.P.: 65-67 °C; ¹H NMR (500 MHz, CDCl₃): δ 7.41 – 7.37 (m, 2H), 7.31 – 7.28 (m, 2H), 6.52 (s, 1H), 6.36 (s, 1H), 6.32 (s, 1H), 3.82 (s, 3H), 1.52 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ 164.8, 152.1, 136.3, 135.0, 133.1, 129.3, 128.6, 120.4, 86.4, 84.6, 83.3, 64.7, 52.3, 27.4; IR (KBr): ν_{max} = 2979, 2240, 1745, 1720, 1491, 1252, 949, 844, 791 cm⁻¹; MS (ESI): *m/z* 373 (M+Na)⁺; HRMS (ESI): *m/z* calcd for C₁₈H₁₉ClO₅Na (M+Na)⁺: 373.0813, found: 373.0819.

Methyl-3-((*tert*-butoxycarbonyl)oxy)-2-methylene-5-(4-nitrophenyl)pent-4-ynoate (1c): 1.18 g, 86%, Yellow solid; R_f = 0.3 (petroleum ether : EtOAc = 9:1); M.P.: 59 - 61 °C; ¹H NMR (300 MHz, CDCl₃): δ 8.20 (d, *J* = 8.8 Hz, 2H), 7.61 (d, *J* = 8.8 Hz, 2H), 6.55 (s, 1H), 6.39 (s, 1H), 6.31 (s, 1H), 3.84 (s, 3H), 1.53 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 164.6, 152.0, 147.5, 135.9, 132.7, 129.4, 128.4, 123.5, 88.8, 85.3, 83.6, 64.5, 52.4, 27.7; IR (KBr): ν_{max} = 2982, 2292, 1745, 1522, 1346, 1274, 1157, 1081, 855, 771 cm⁻¹; MS (ESI): *m/z* 384 (M+Na)⁺; HRMS (ESI): *m/z* calcd for C₁₈H₁₉NO₇Na (M+Na)⁺: 384.1054, found: 384.1088.

Methyl-3-((*tert*-butoxycarbonyl)oxy)-5-(4-methoxyphenyl)-2-methylenepent-4-ynoate (1d): 1.29 g, 92%, Yellow solid; R_f = 0.4 (petroleum ether : EtOAc = 9:1); M.P.: 63 – 64 °C; ¹H NMR (500 MHz, CDCl₃): δ 7.40 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.51 (s, 1H), 6.36 (d, *J* = 7.6 Hz, 2H), 3.81 (s, 6H), 1.51 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 164.9, 160.0, 152.2, 136.6, 133.5, 129.3, 113.9, 87.8, 83.0, 82.2, 65.0, 55.3, 52.2, 27.7; IR (KBr): ν_{max} = 2934, 2230, 1746, 1681, 1271, 1159, 1075, 848, 760 cm⁻¹; MS (ESI): *m/z* 369 (M+Na)⁺; HRMS (ESI): *m/z* calcd for C₁₉H₂₂O₆Na (M+Na)⁺: 369.1308, found: 369.1315.

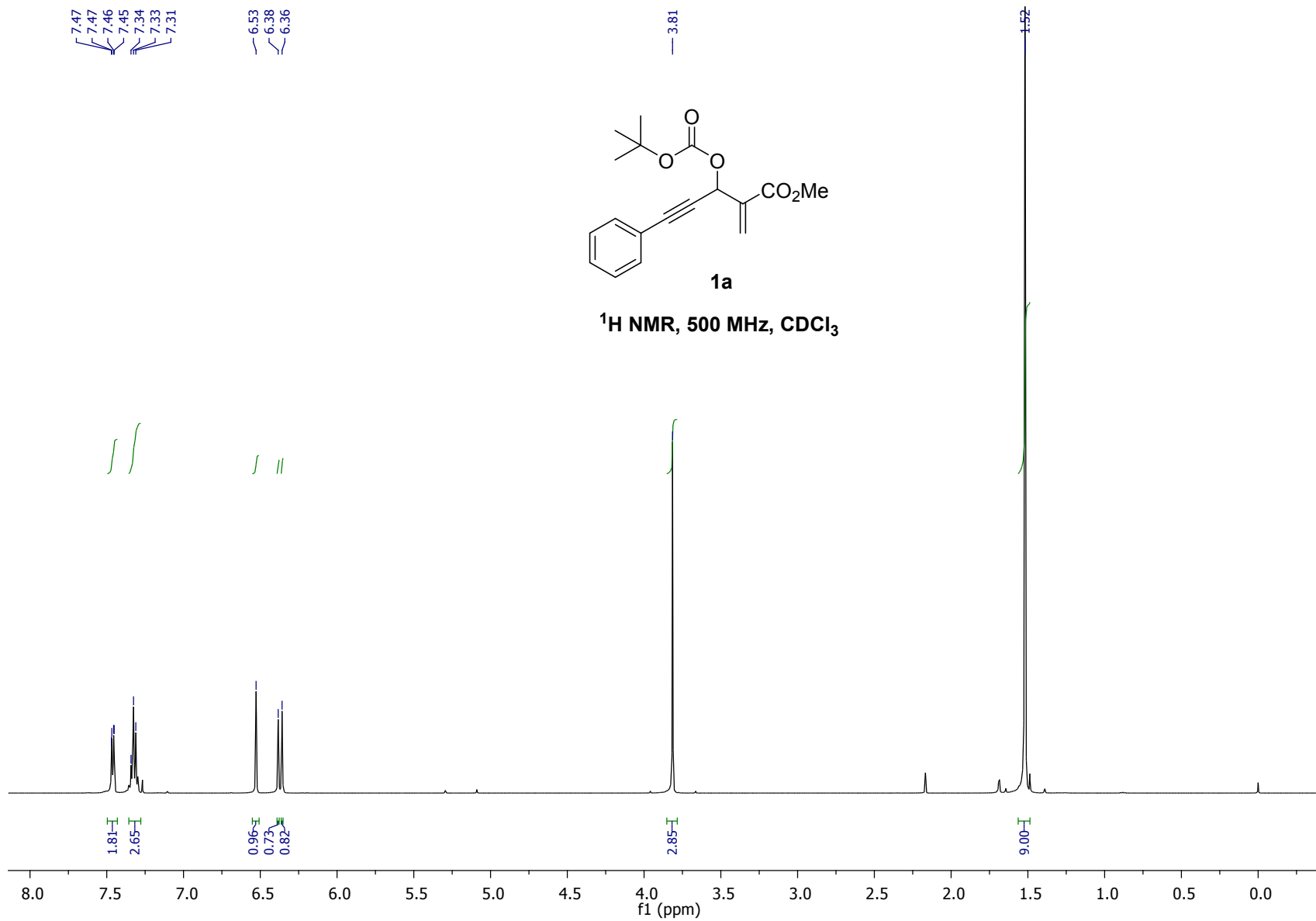
Methyl-3-((*tert*-butoxycarbonyl)oxy)-2-methylene-5-(thiophen-2-yl)pent-4-ynoate (1e): 1.23 g, 85%, Yellow solid; R_f = 0.5 (petroleum ether : EtOAc = 9:1); M.P.: 75-77 °C; ¹H NMR (500 MHz, CDCl₃): δ 7.29 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.27–7.25 (m, 1H), 6.98 (dd, *J* = 5.1, 3.7 Hz, 1H), 6.52 (s, 1H), 6.38 (s, 1H), 6.32 (s, 1H), 3.81 (s, 3H), 1.52 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ 164.8, 152.1, 136.2, 133.1, 129.4, 128.0, 126.9, 121.7, 87.4, 83.2, 81.0, 64.9, 52.3, 27.7; IR (KBr): ν_{max} = 2981, 2227, 1741, 1255, 1152, 1077, 956, 709 cm⁻¹; MS (ESI): *m/z* 345 (M+Na)⁺; HRMS (ESI): *m/z* calcd for C₁₆H₁₈O₅NaS (M+Na)⁺: 345.0767, Found: 345.0766.

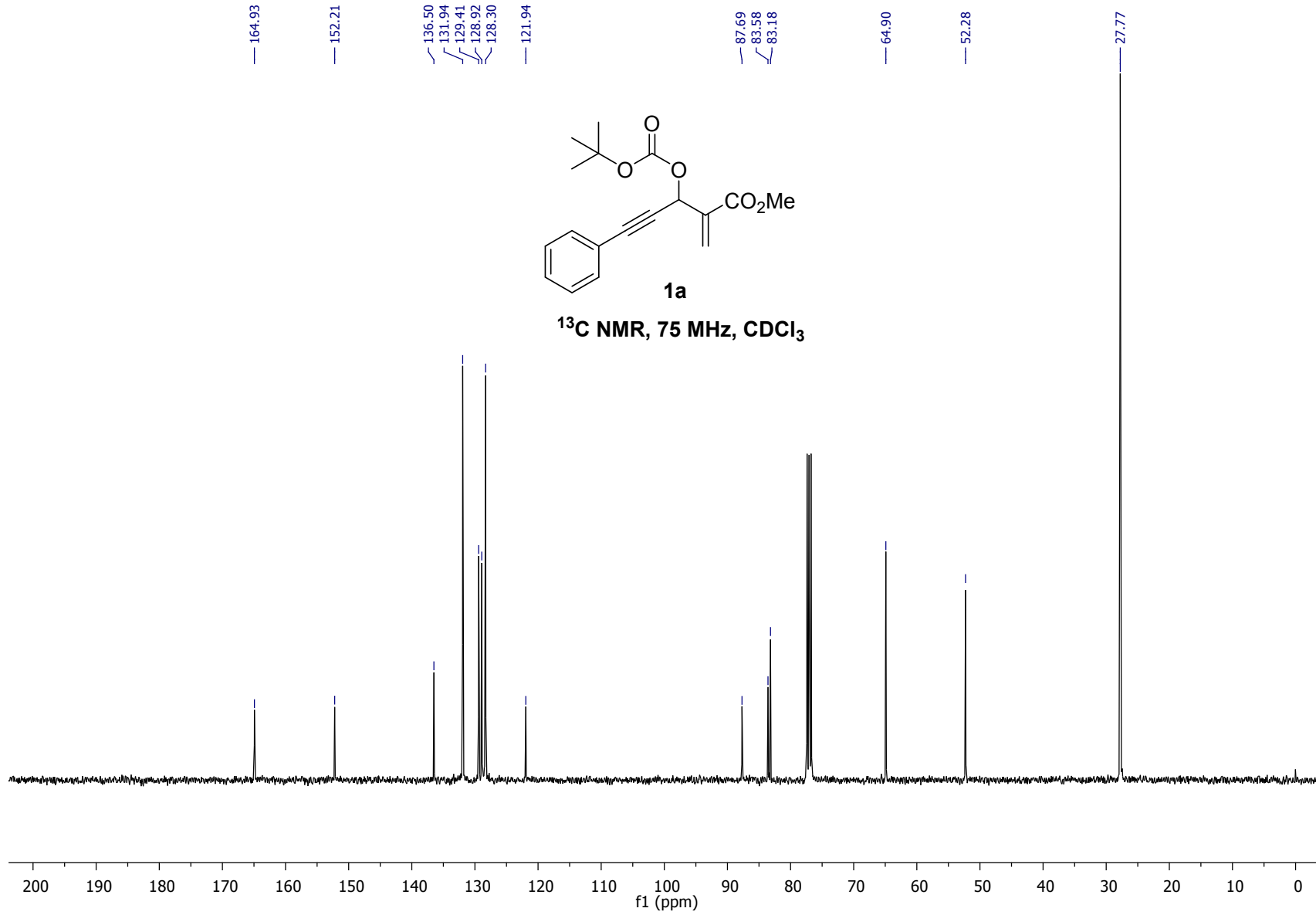
Methyl-3-((*tert*-butoxycarbonyl)oxy)-5-(2-iodophenyl)-2-methylenepent-4-ynoate (1f): 1.01 g, 78%, Yellow liquid; $R_f = 0.4$ (petroleum ether : EtOAc = 9:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.76 (dd, $J = 8.0, 1.0$ Hz, 1H), 7.39 (dd, $J = 7.7, 1.6$ Hz, 1H), 7.23 (td, $J = 7.6, 1.1$ Hz, 1H), 6.95 (td, $J = 7.8, 1.6$ Hz, 1H), 6.49 (s, 1H), 6.44 (s, 1H), 6.36 (s, 1H), 3.75 (s, 3H), 1.45 (s, 9H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 164.9, 152.1, 138.7, 136.0, 133.2, 130.0, 128.6, 127.7, 100.6, 89.3, 87.3, 83.2, 64.9, 52.3, 27.8; IR (KBr): $\nu_{\text{max}} = 2921, 2234, 1748, 1254, 1156, 1079, 954, 771$ cm^{-1} ; MS (ESI): m/z 465 ($\text{M}+\text{Na}$) $^+$; HRMS (ESI): m/z calcd for $\text{C}_{18}\text{H}_{19}\text{O}_5\text{INa}$ ($\text{M}+\text{Na}$) $^+$: 465.0169, found: 465.0169.

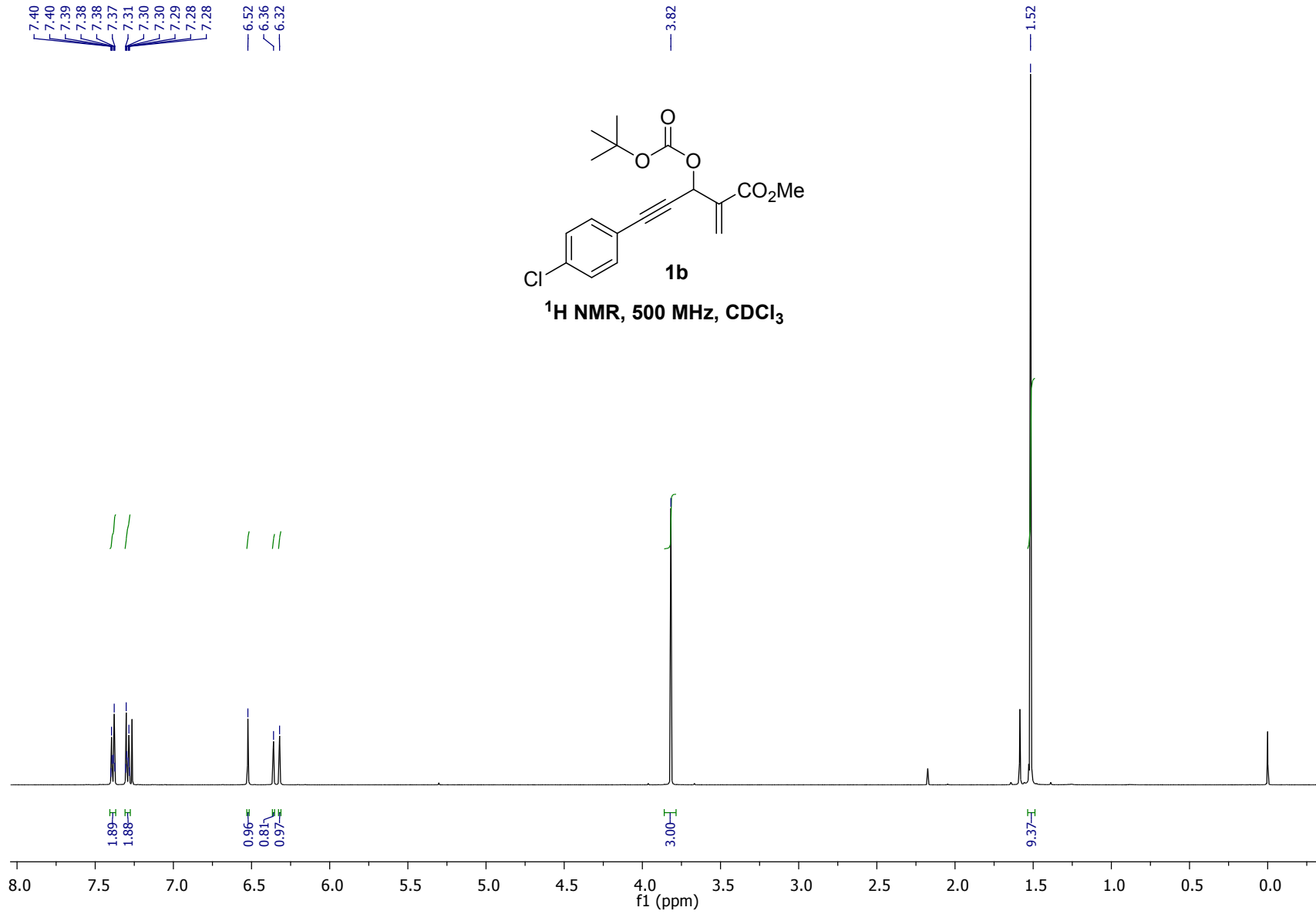
***tert*-Butyl-3-(3-((*tert*-butoxycarbonyl)oxy)-4-(methoxycarbonyl)pent-4-en-1-yn-1-yl)-1*H*-indole-1-carboxylate (1g):** 1.28 g, 82%, Pale yellow liquid; $R_f = 0.5$ (petroleum ether : EtOAc = 8:2); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 8.13 (d, $J = 8.2$ Hz, 1H), 7.80 (s, 1H), 7.64 (d, $J = 7.7$ Hz, 1H), 7.39 – 7.33 (m, 1H), 7.32 – 7.27 (m, 1H), 6.56 (s, 1H), 6.44 (s, 1H), 6.41 (s, 1H), 3.83 (s, 3H), 1.67 (s, 9H), 1.53 (s, 9H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 164.9, 152.2, 148.9, 136.5, 134.5, 130.3, 129.8, 129.3, 125.3, 123.3, 120.0, 115.3, 102.1, 87.2, 84.4, 83.1, 79.9, 65.1, 52.3, 28.1, 27.7; IR (KBr): $\nu_{\text{max}} = 2980, 2234, 1743, 1371, 1274, 1155, 852, 752$ cm^{-1} ; MS (ESI): m/z 478 ($\text{M}+\text{Na}$) $^+$; HRMS (ESI): m/z calcd for $\text{C}_{25}\text{H}_{29}\text{O}_7\text{NNa}$ ($\text{M}+\text{Na}$) $^+$: 478.1836, found: 478.1815.

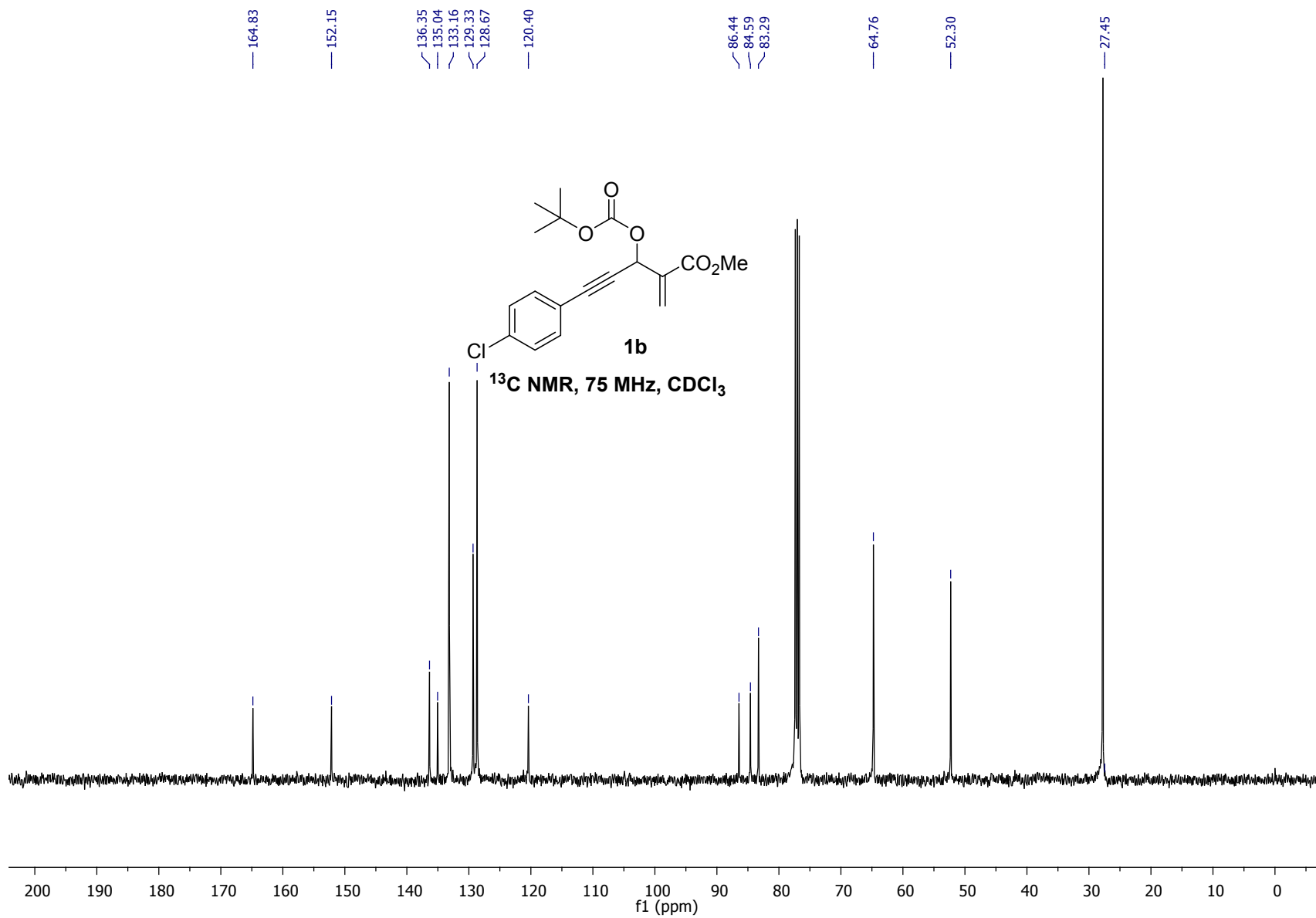
Methyl-3-((*tert*-butoxycarbonyl)oxy)-2-methyleneoct-4-ynoate (1h): 1.16 g, 75%, Pale yellow liquid. $R_f = 0.7$ (petroleum ether : EtOAc = 9:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 6.45 (s, 1H), 6.26 (s, 1H), 6.12 (s, 1H), 3.78 (s, 3H), 2.22 (td, $J = 7.0, 2.1$ Hz, 2H), 1.57 – 1.51 (m, 2H), 1.50 (s, 9H), 0.97 (t, $J = 7.4$ Hz, 3H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 165.0, 152.5, 136.9, 128.9, 88.9, 82.8, 74.9, 64.8, 52.1, 27.7, 21.7, 20.7, 13.4; IR (KBr): $\nu_{\text{max}} = 2966, 2935, 2238, 1748, 1273, 1254, 1154, 1078, 953$ cm^{-1} ; MS (ESI): m/z 305 ($\text{M}+\text{Na}$) $^+$; HRMS (ESI): m/z calcd for $\text{C}_{15}\text{H}_{22}\text{O}_5\text{Na}$ ($\text{M}+\text{Na}$) $^+$: 305.1359, found: 305.1357.

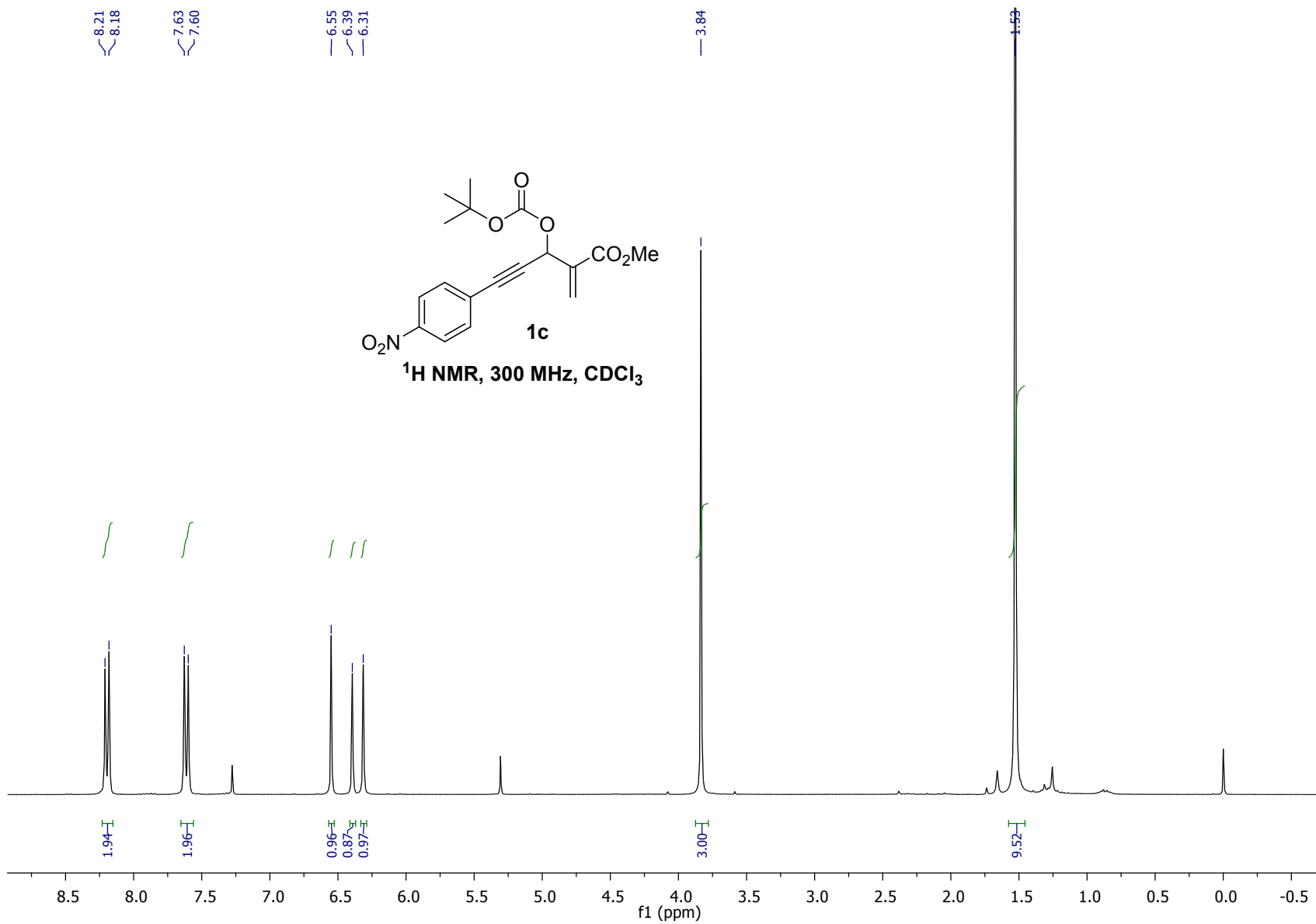
Dimethyl-5,5'-(1,3-phenylene)bis(3-((*tert*-butoxycarbonyl)-oxy)-2-methylenepent-4-ynoate) (1i): 1.21 g, 81%, Yellow liquid; $R_f = 0.4$ (petroleum ether : EtOAc = 9:1); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.57 (s, 1H), 7.47 – 7.41 (m, 2H), 7.30 (d, $J = 10.1$ Hz, 1H), 6.55 (s, 2H), 6.37 (s, 2H), 6.35 (s, 2H), 3.83 (s, 6H), 1.54 (s, 18H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 164.8, 152.1, 136.2, 135.2, 132.2, 129.5, 128.4, 122.2, 86.5, 84.3, 83.3, 64.7, 52.3, 27.7; IR (KBr): $\nu_{\text{max}} = 2982, 2239, 1746, 1273, 1255, 1157, 1079, 955, 772$ cm^{-1} ; MS (ESI): m/z 577 ($\text{M}+\text{Na}$) $^+$; HRMS (ESI): m/z calcd for $\text{C}_{30}\text{H}_{34}\text{O}_{10}\text{Na}$ ($\text{M}+\text{Na}$) $^+$: 577.2044, found: 577.2024.

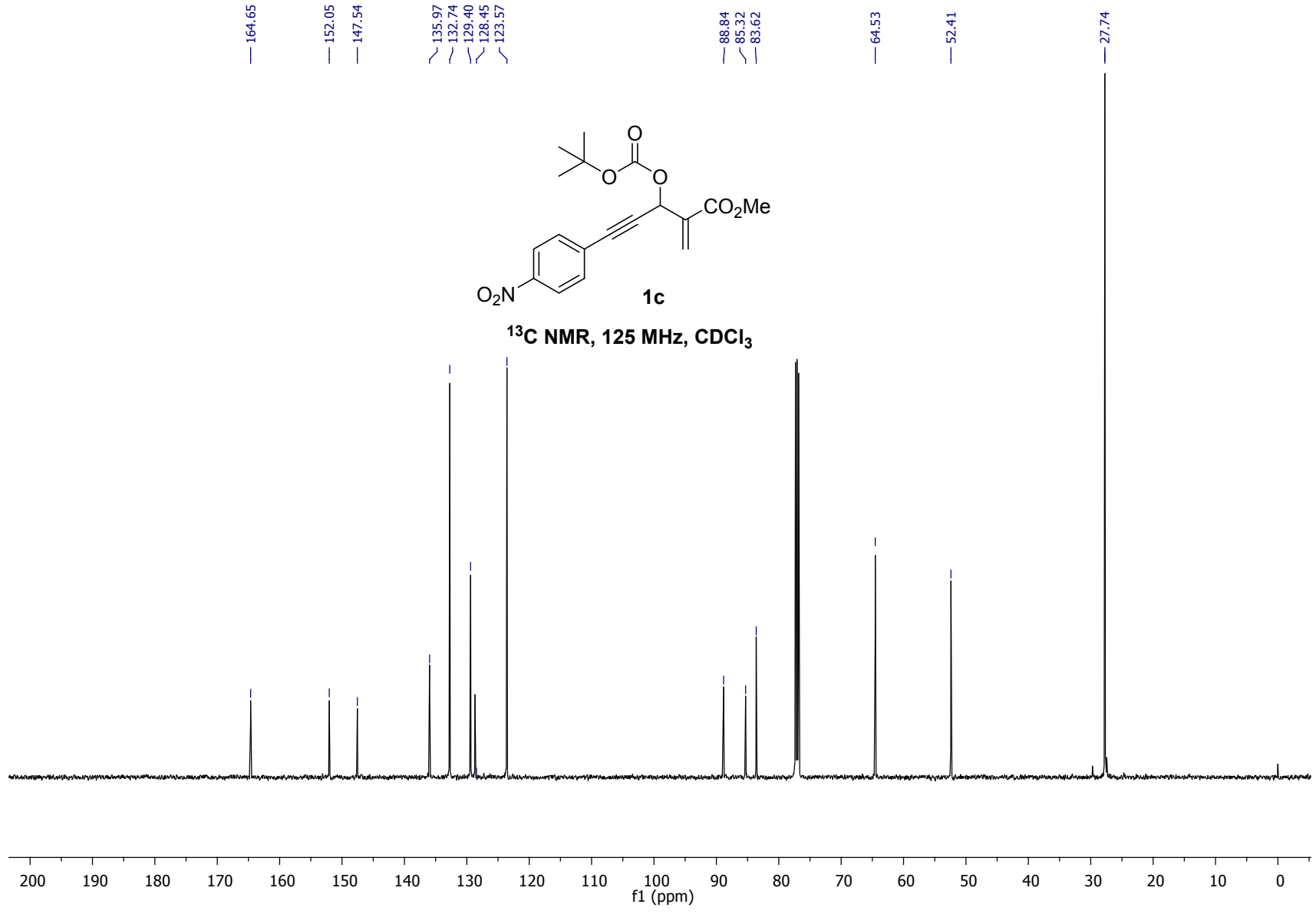


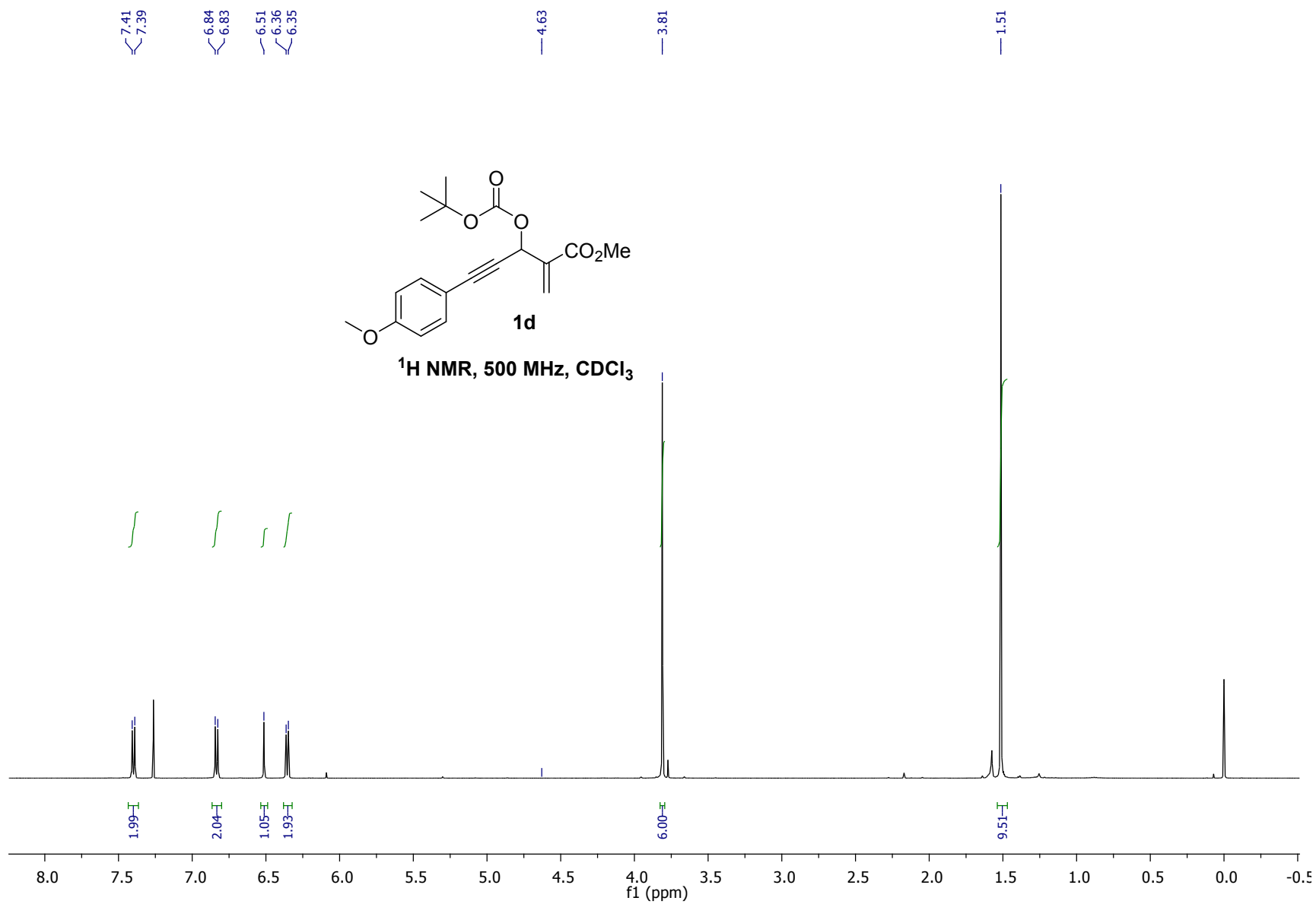


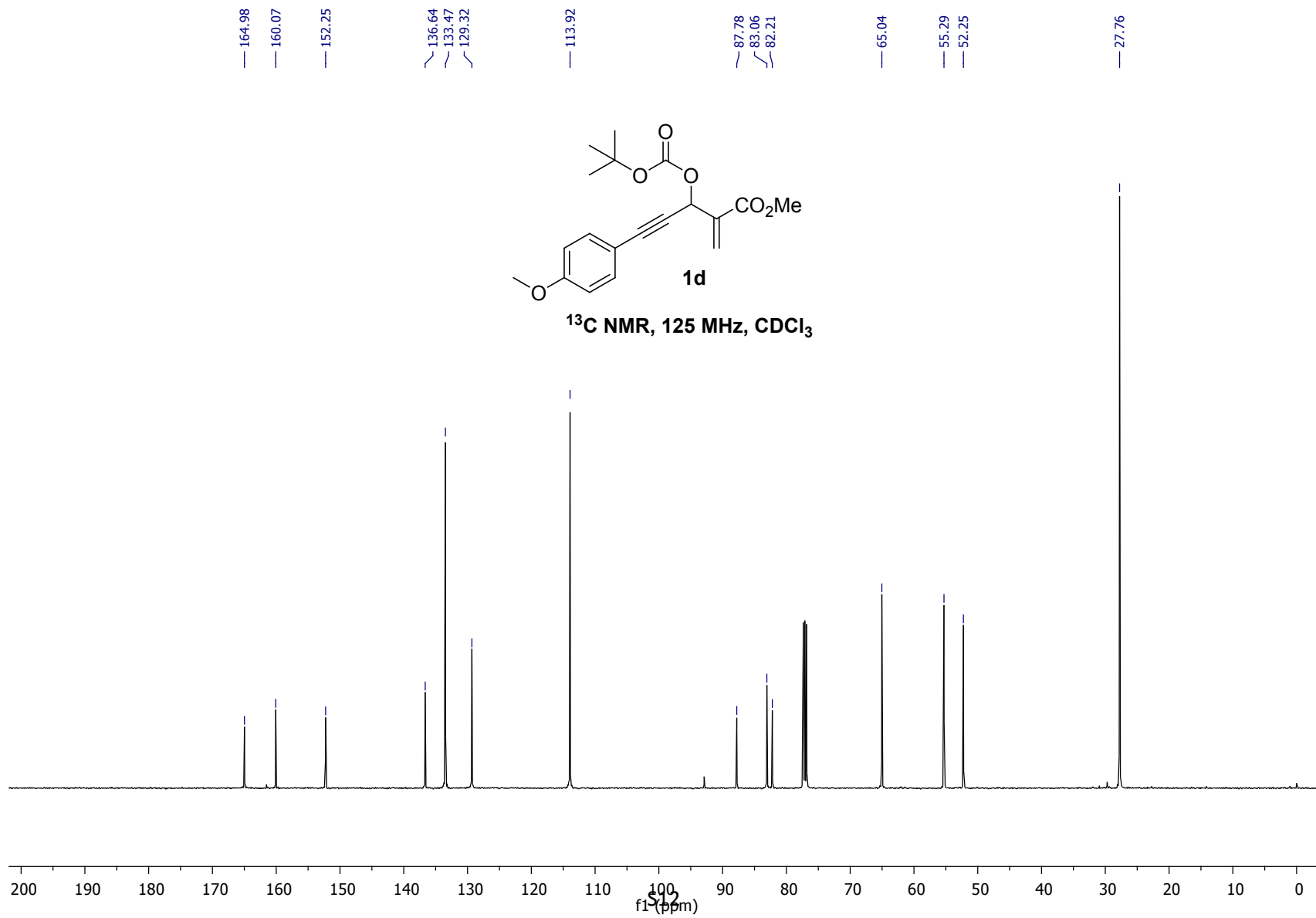


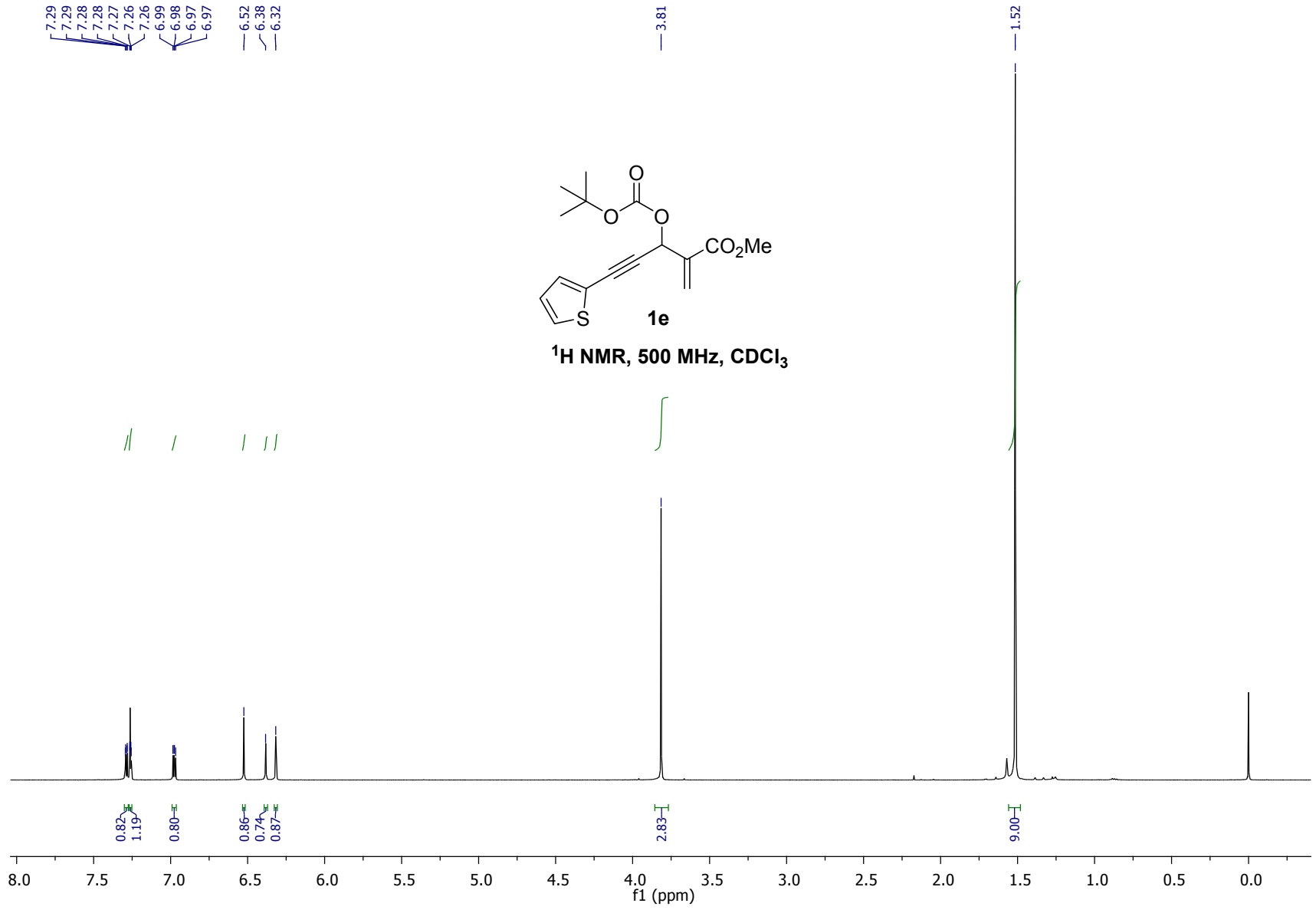


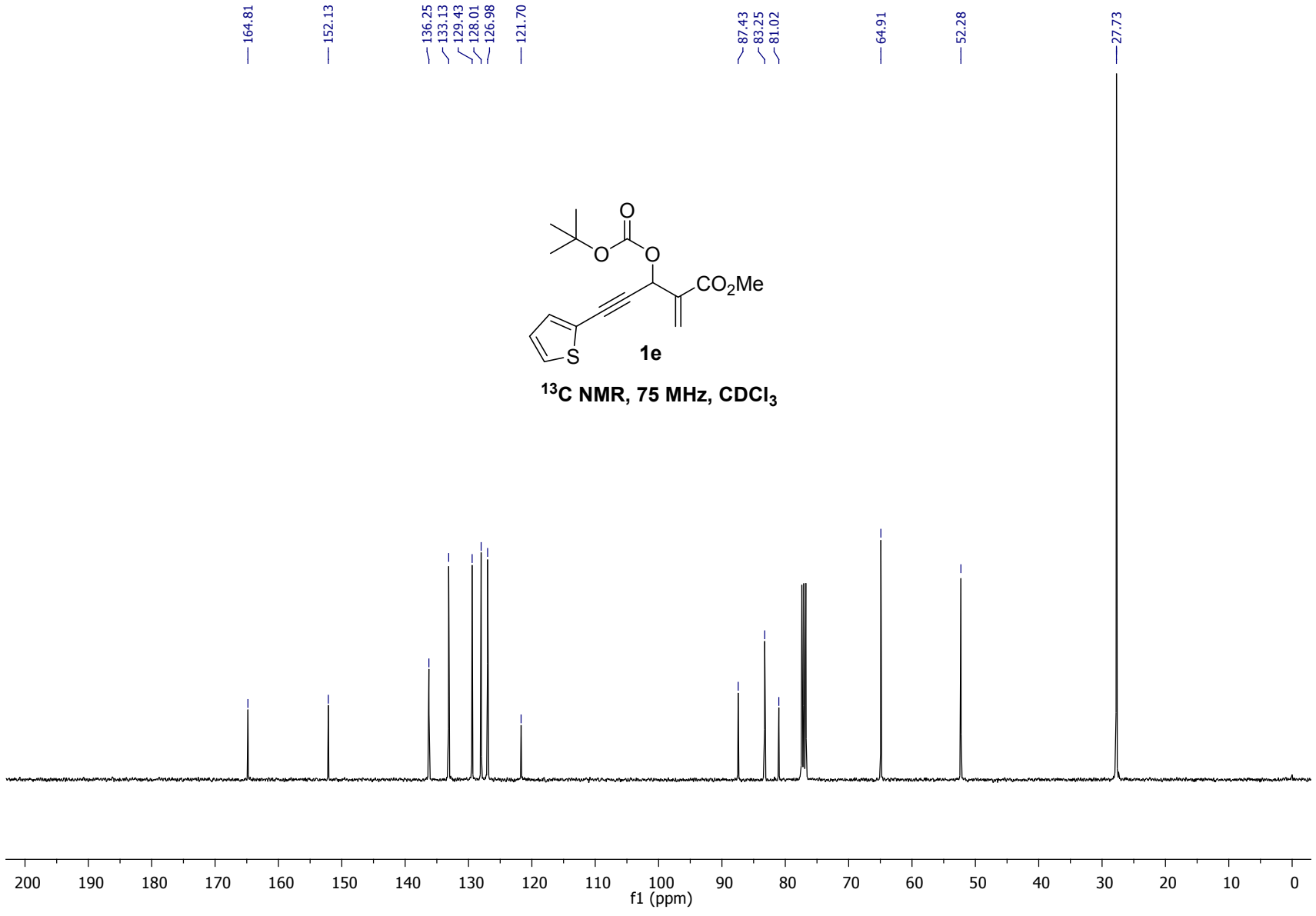


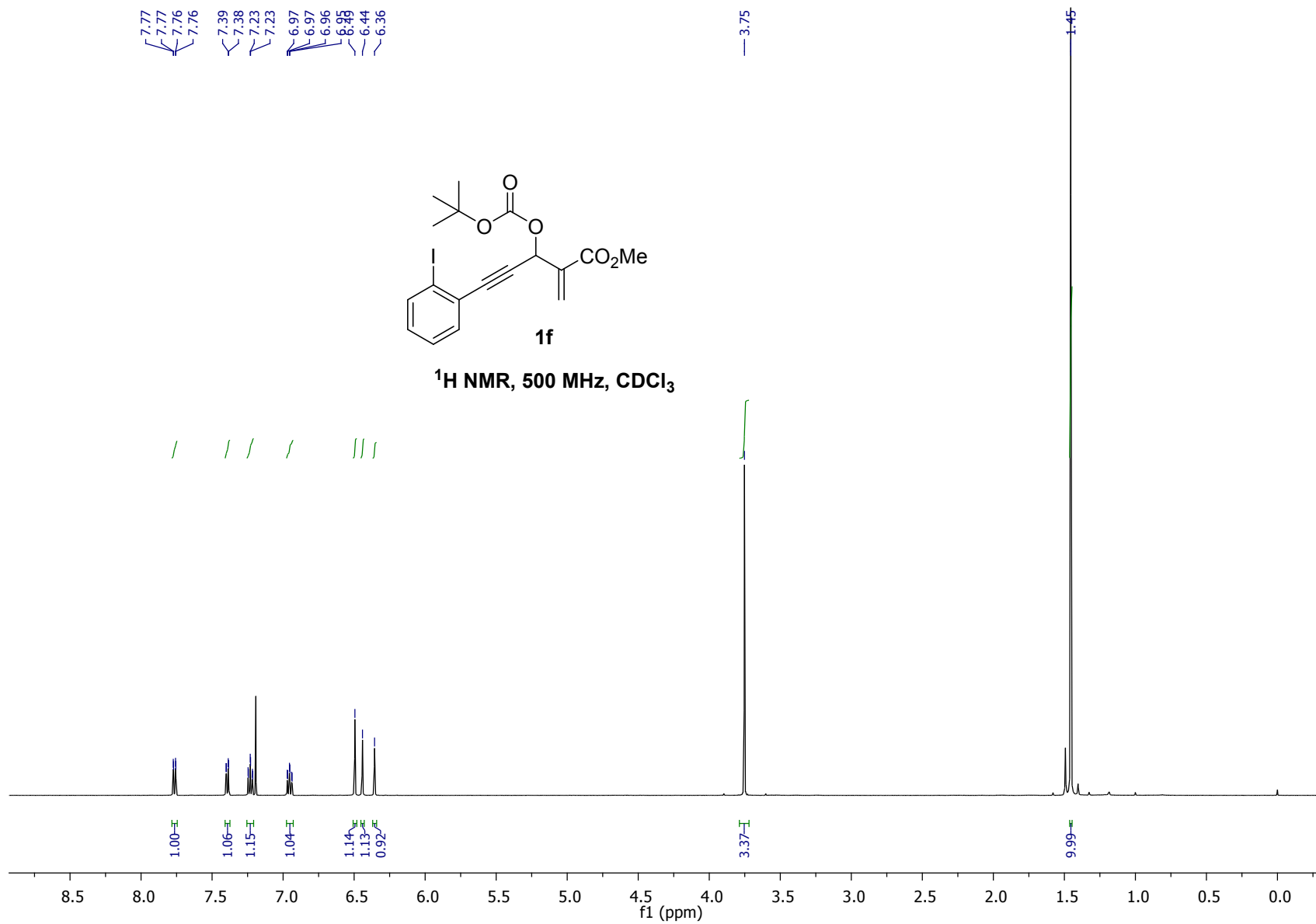


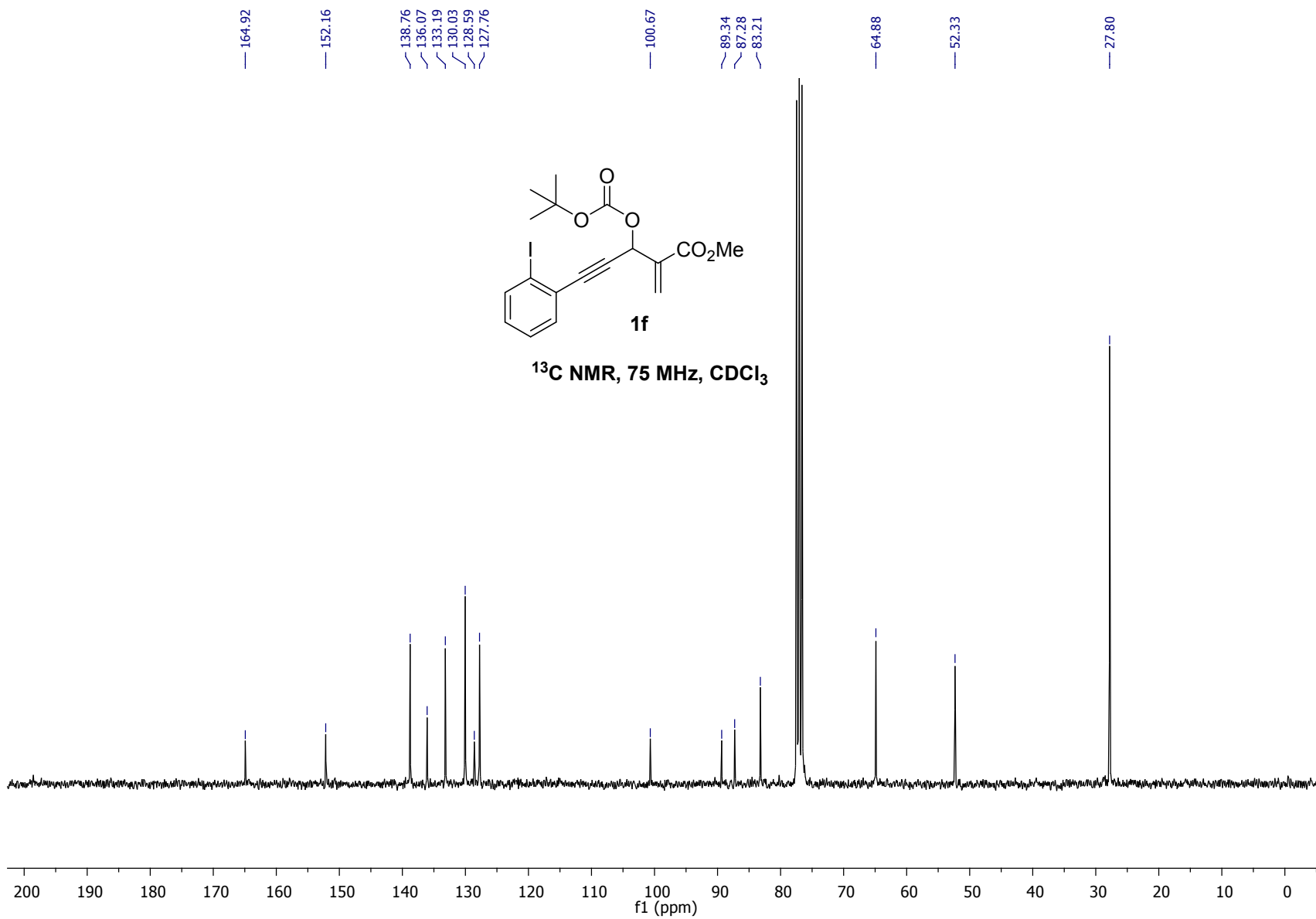


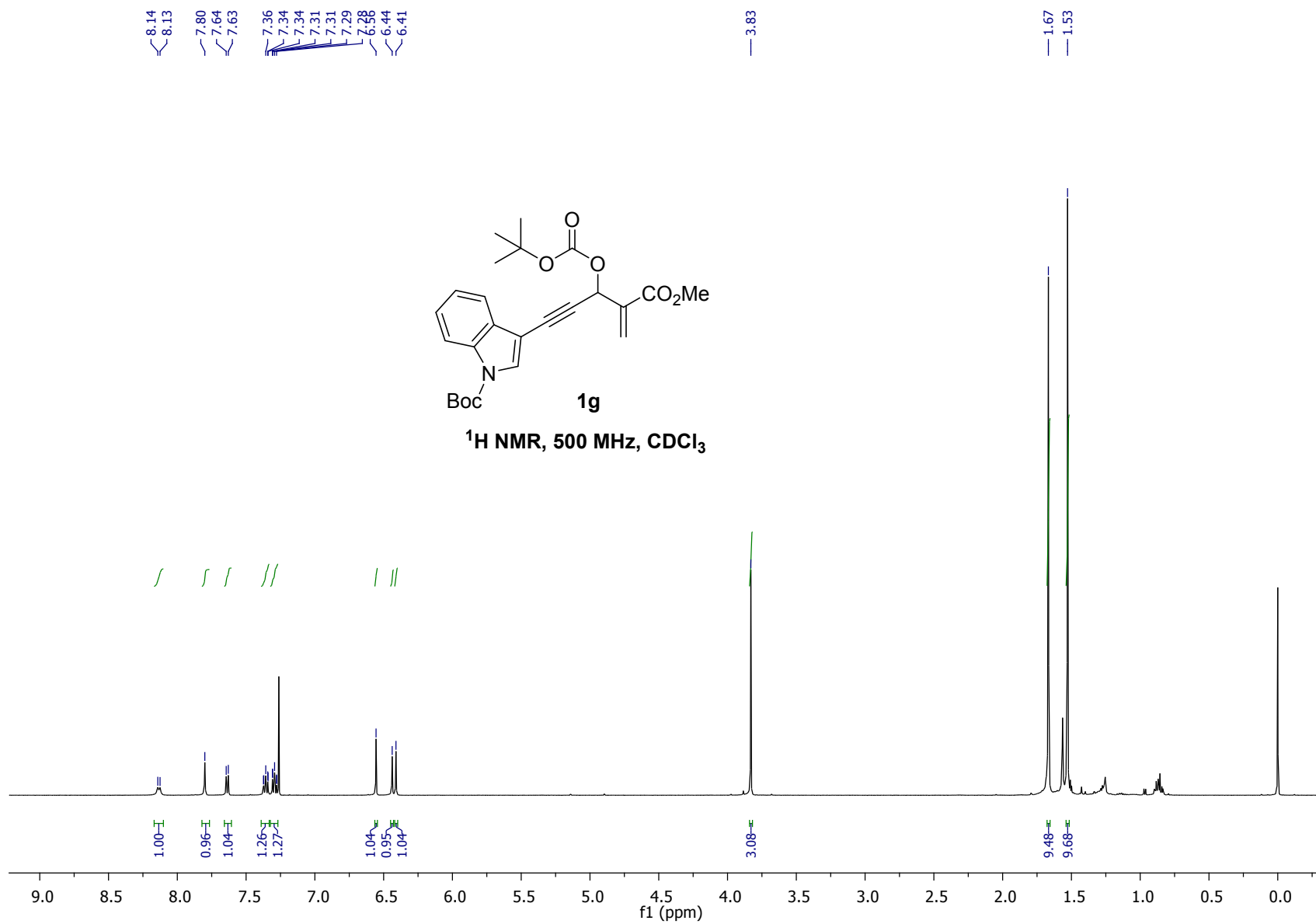


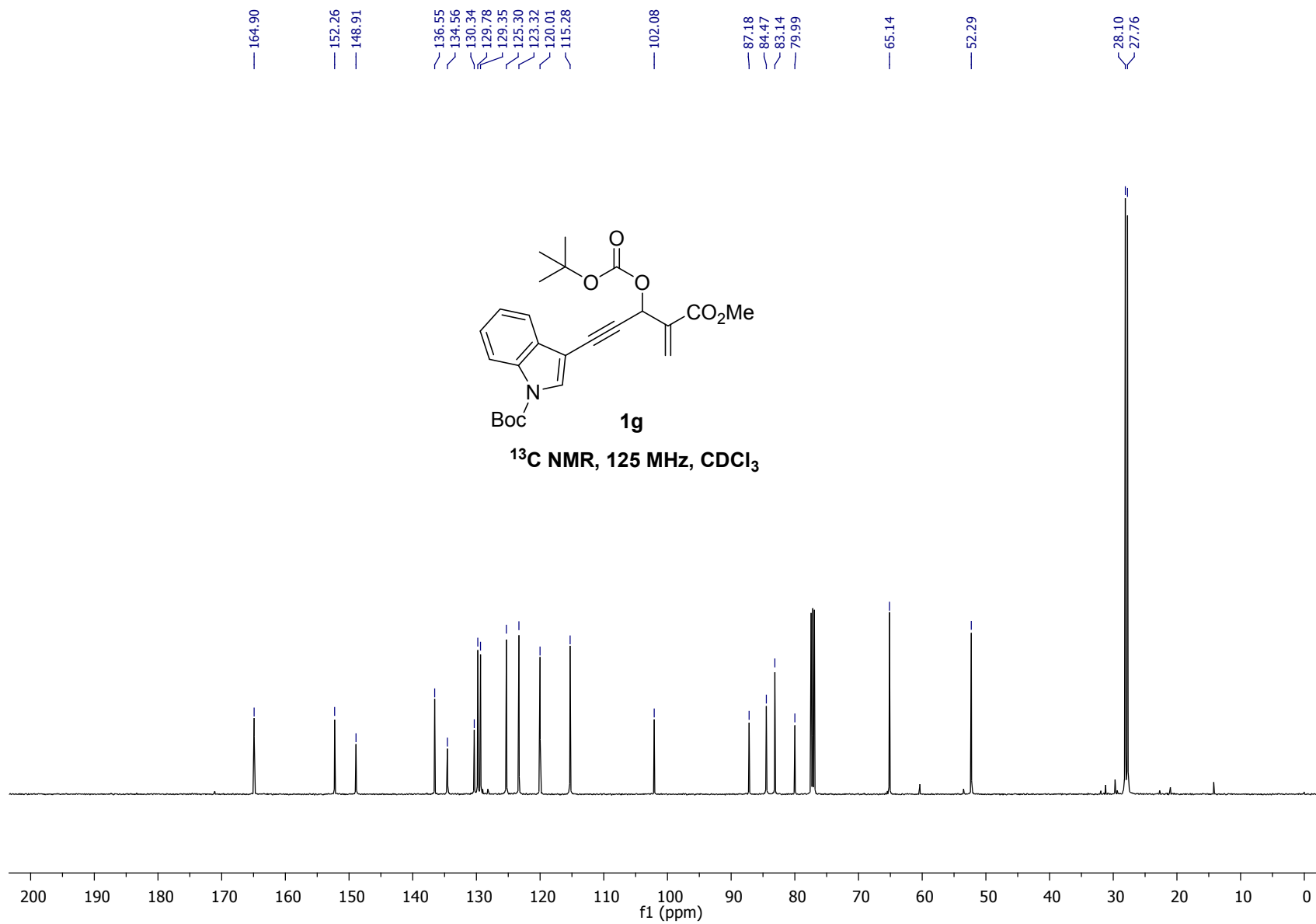


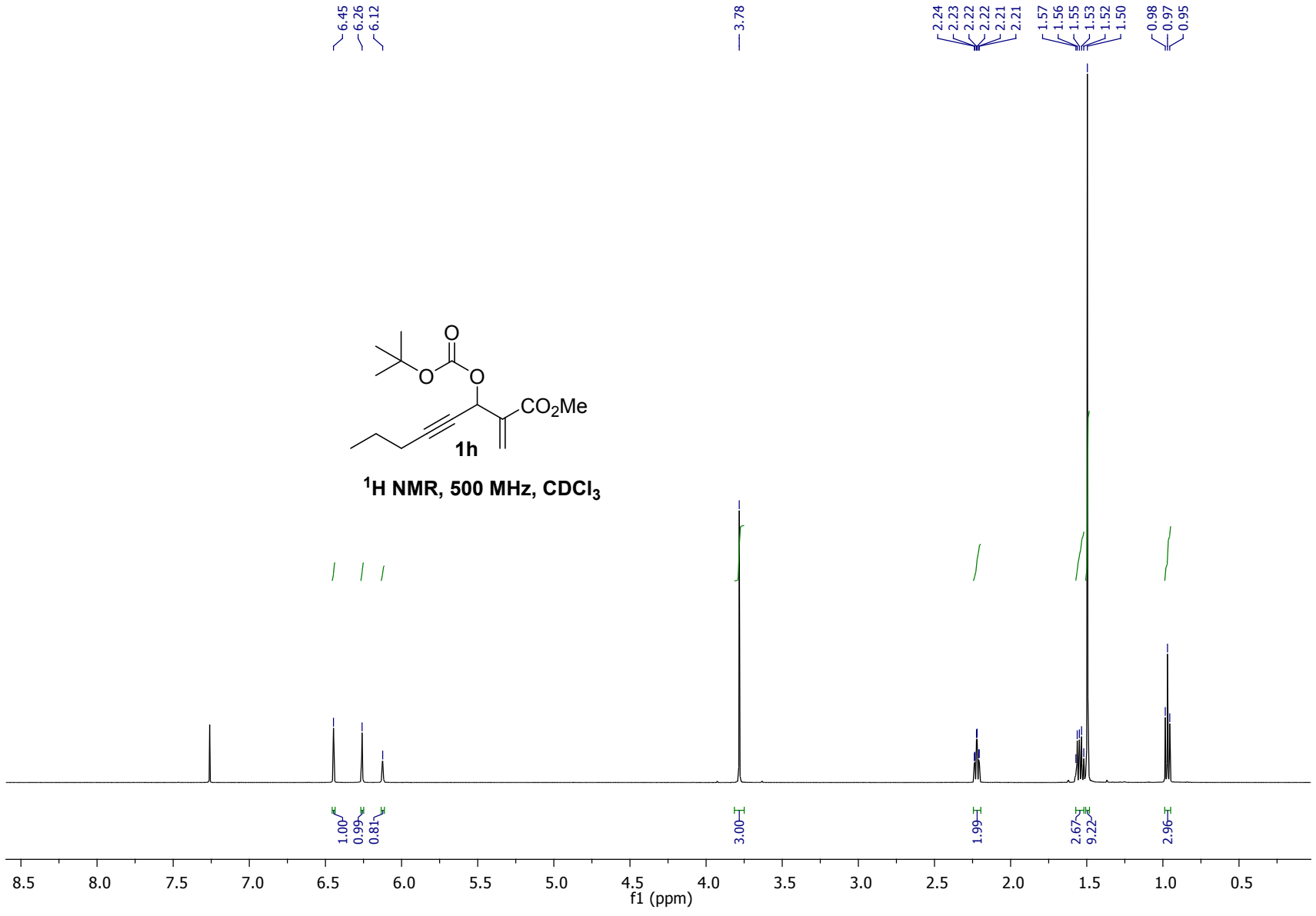


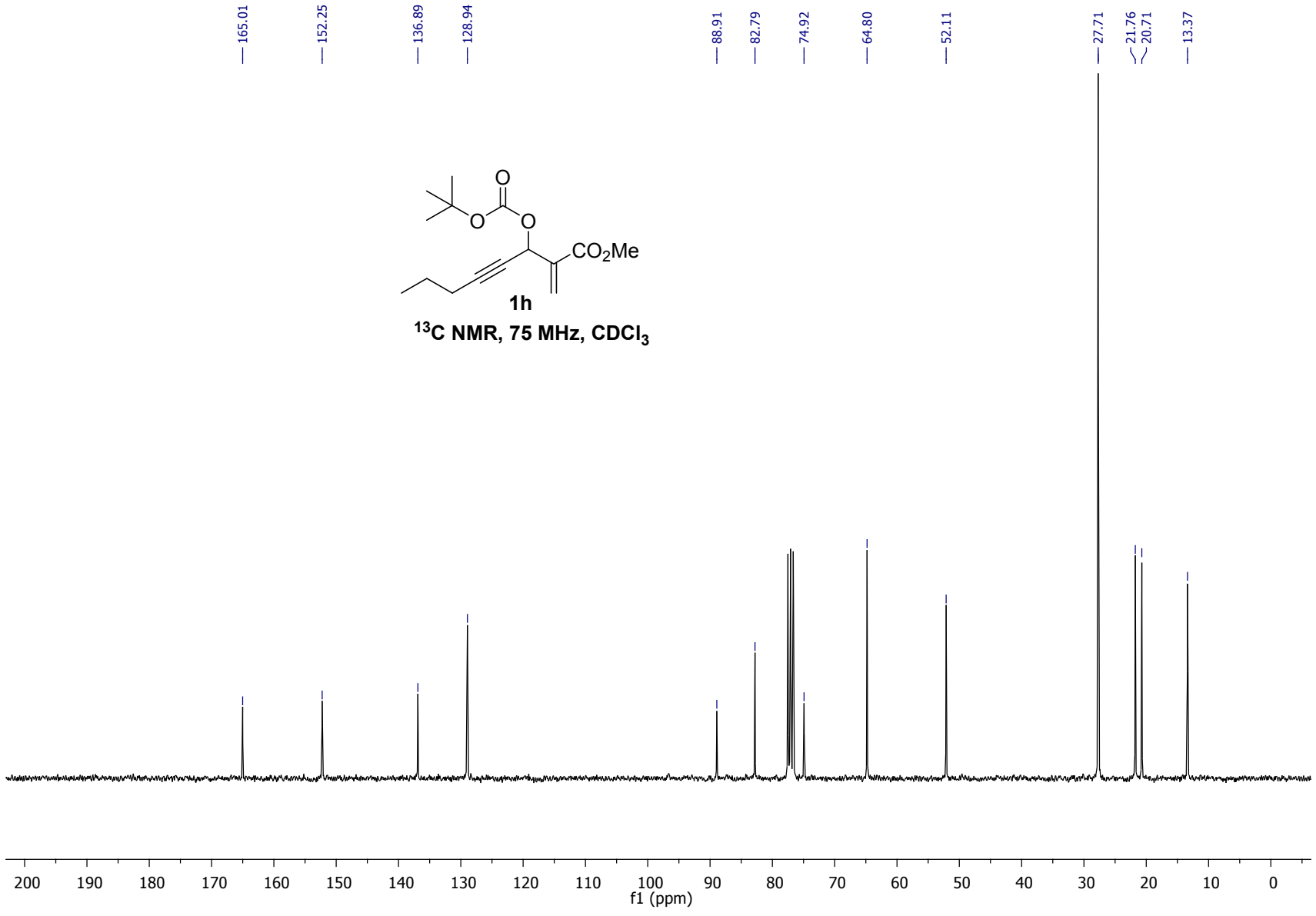


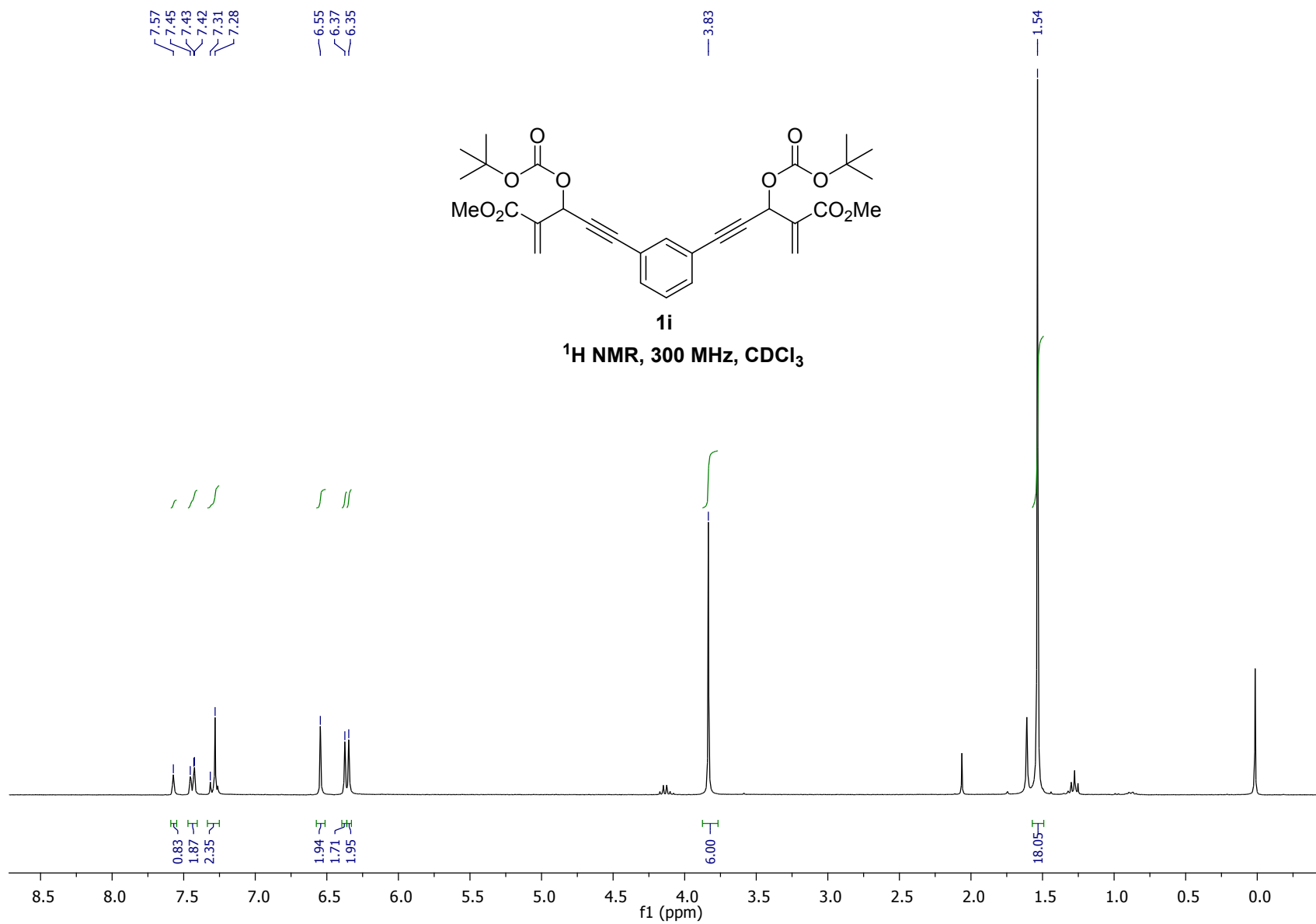


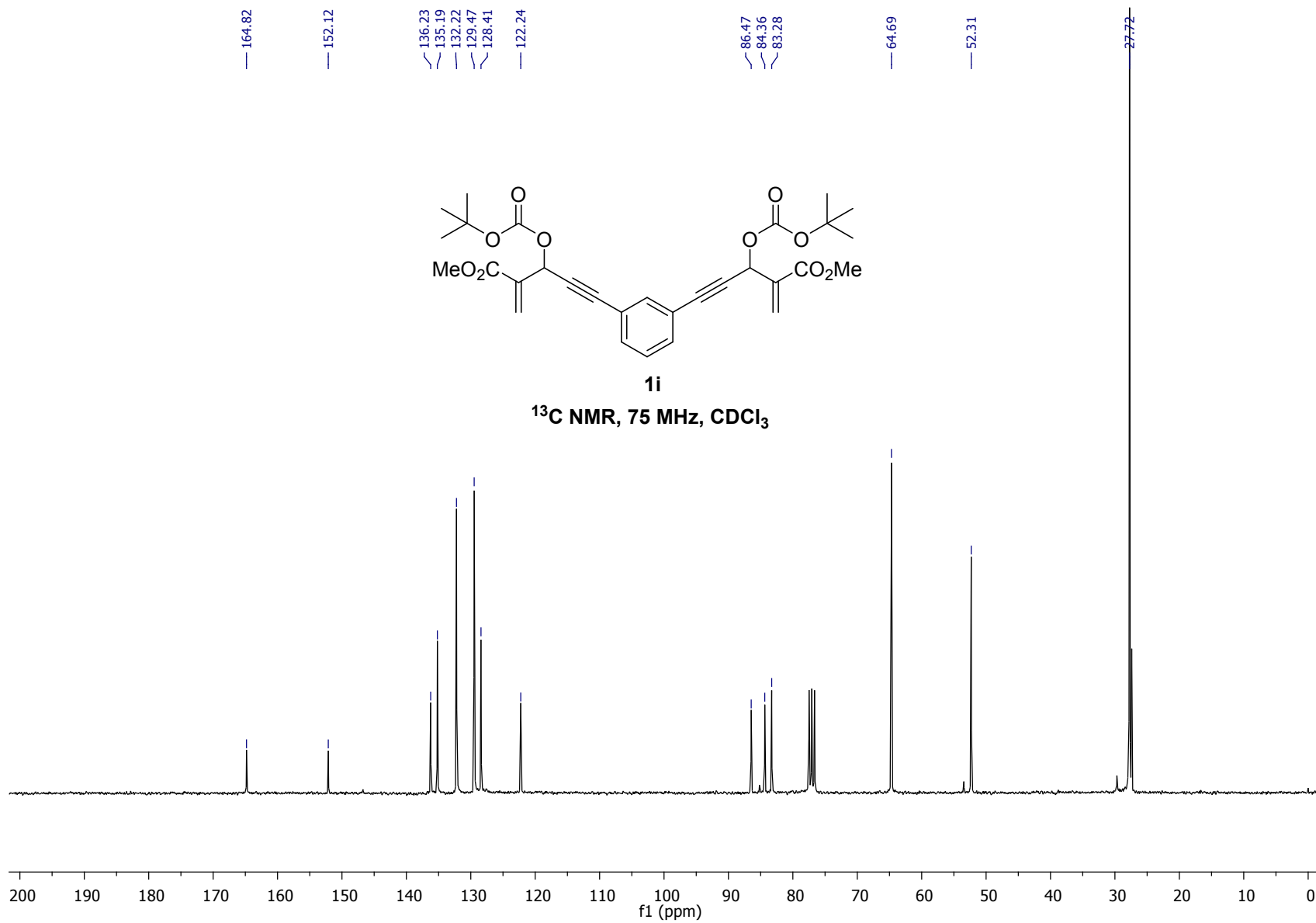


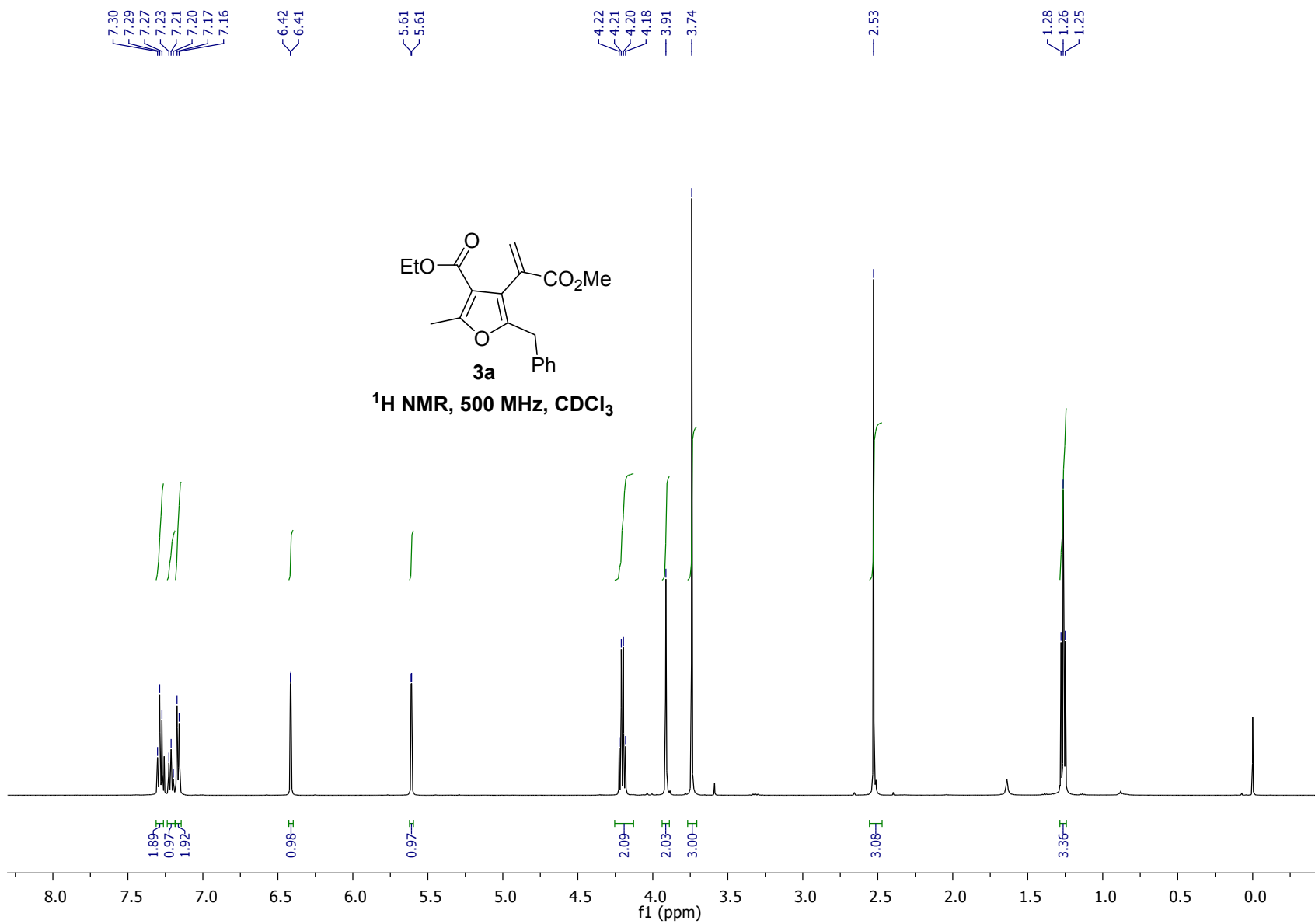


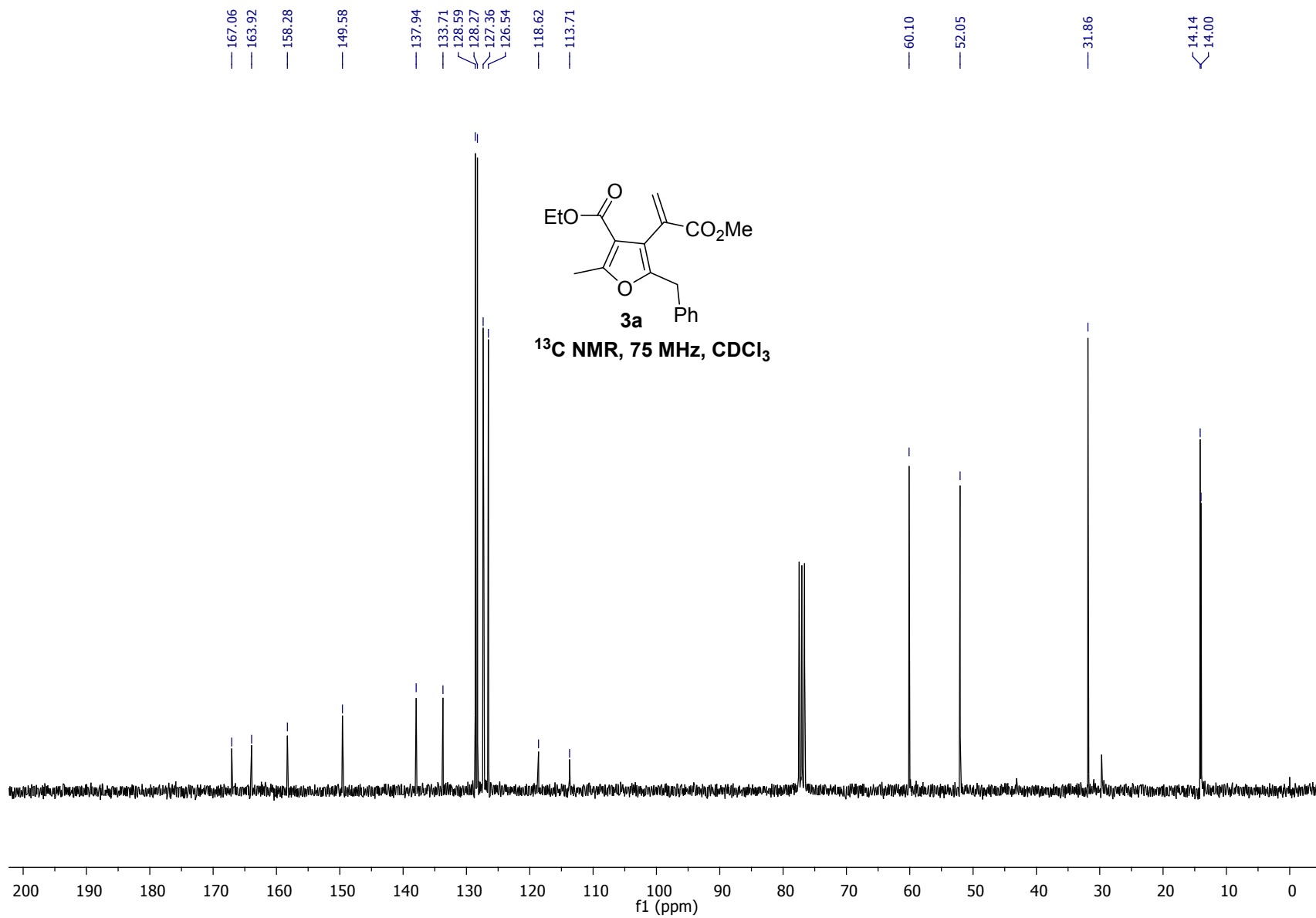


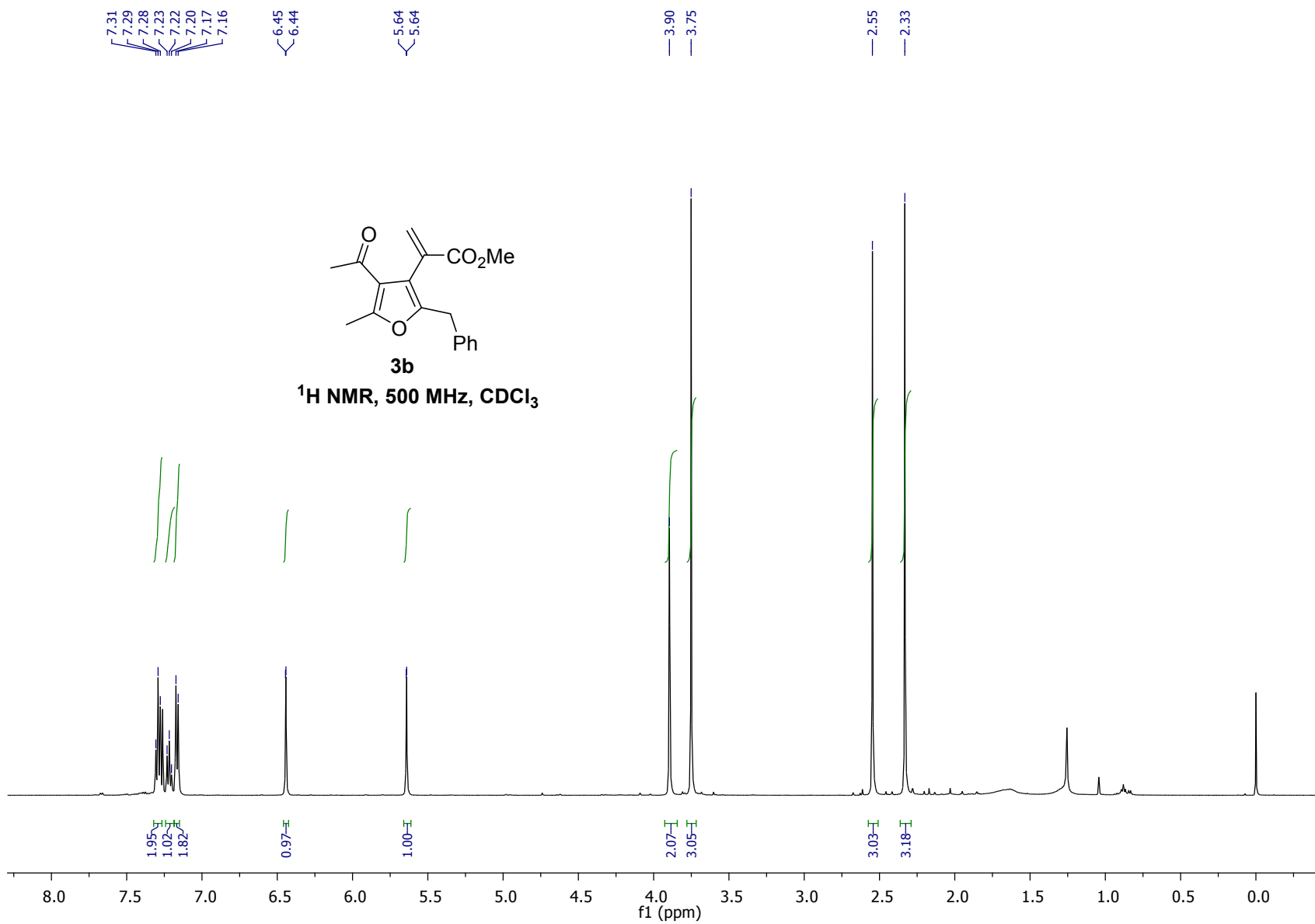


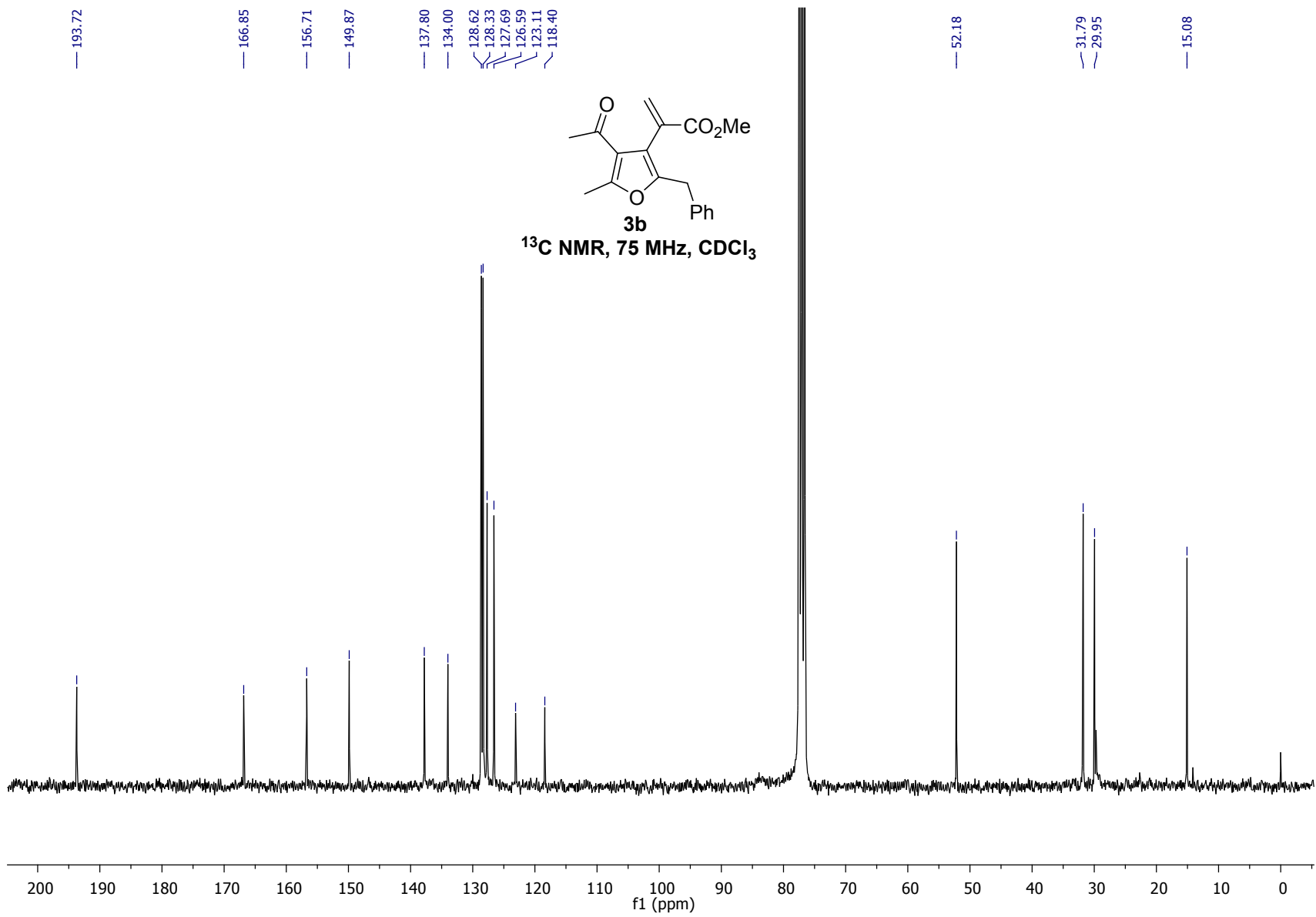


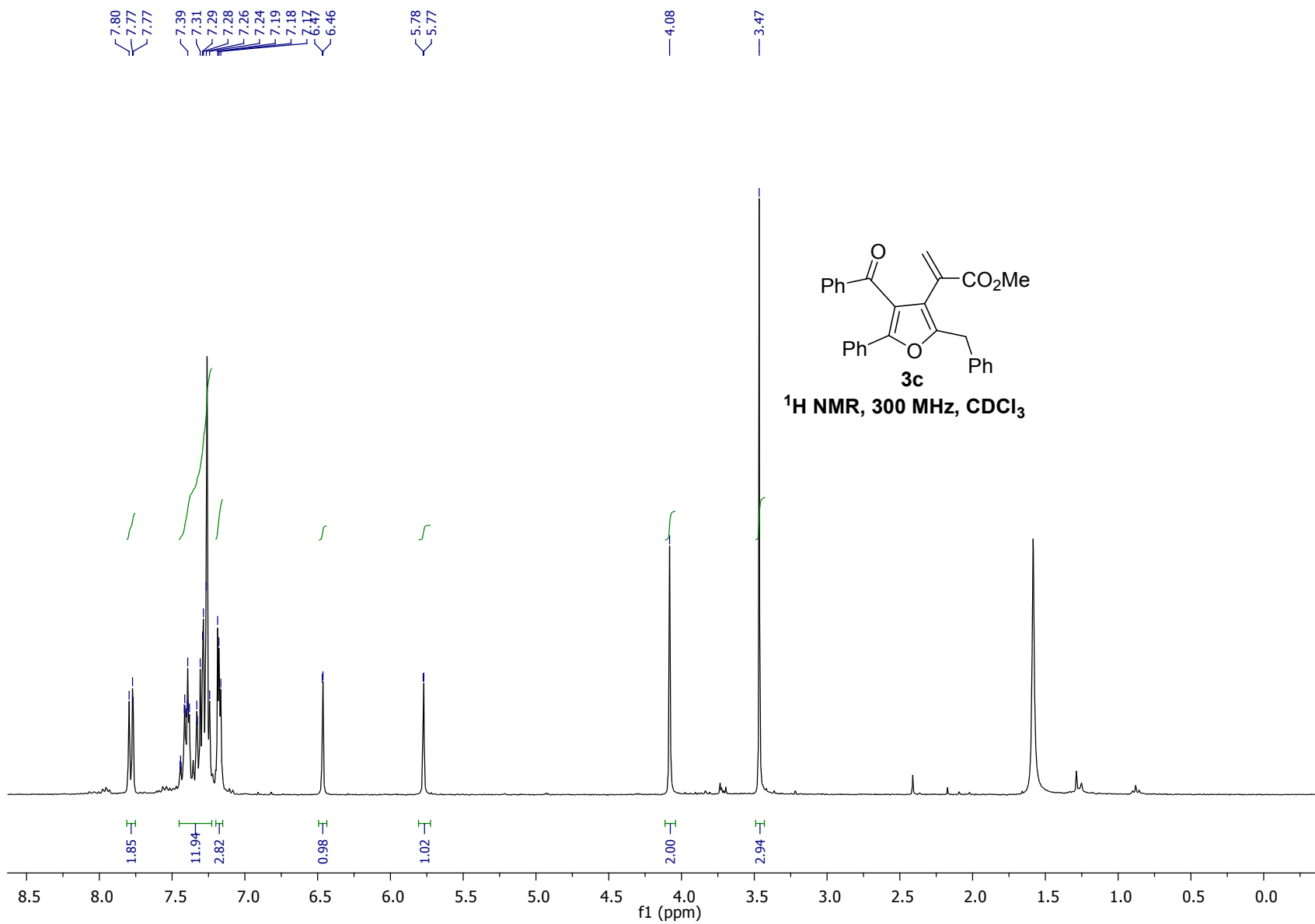


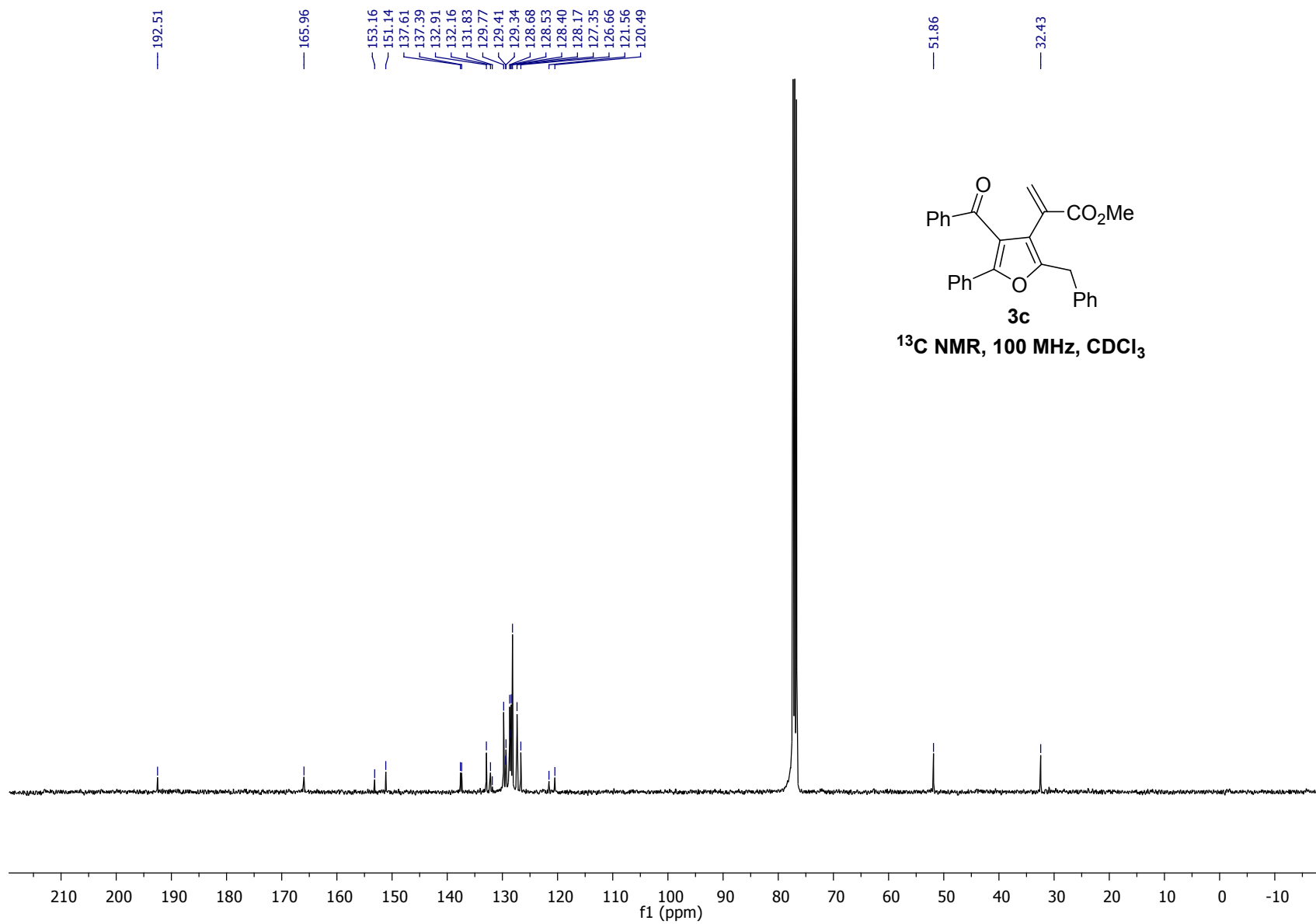


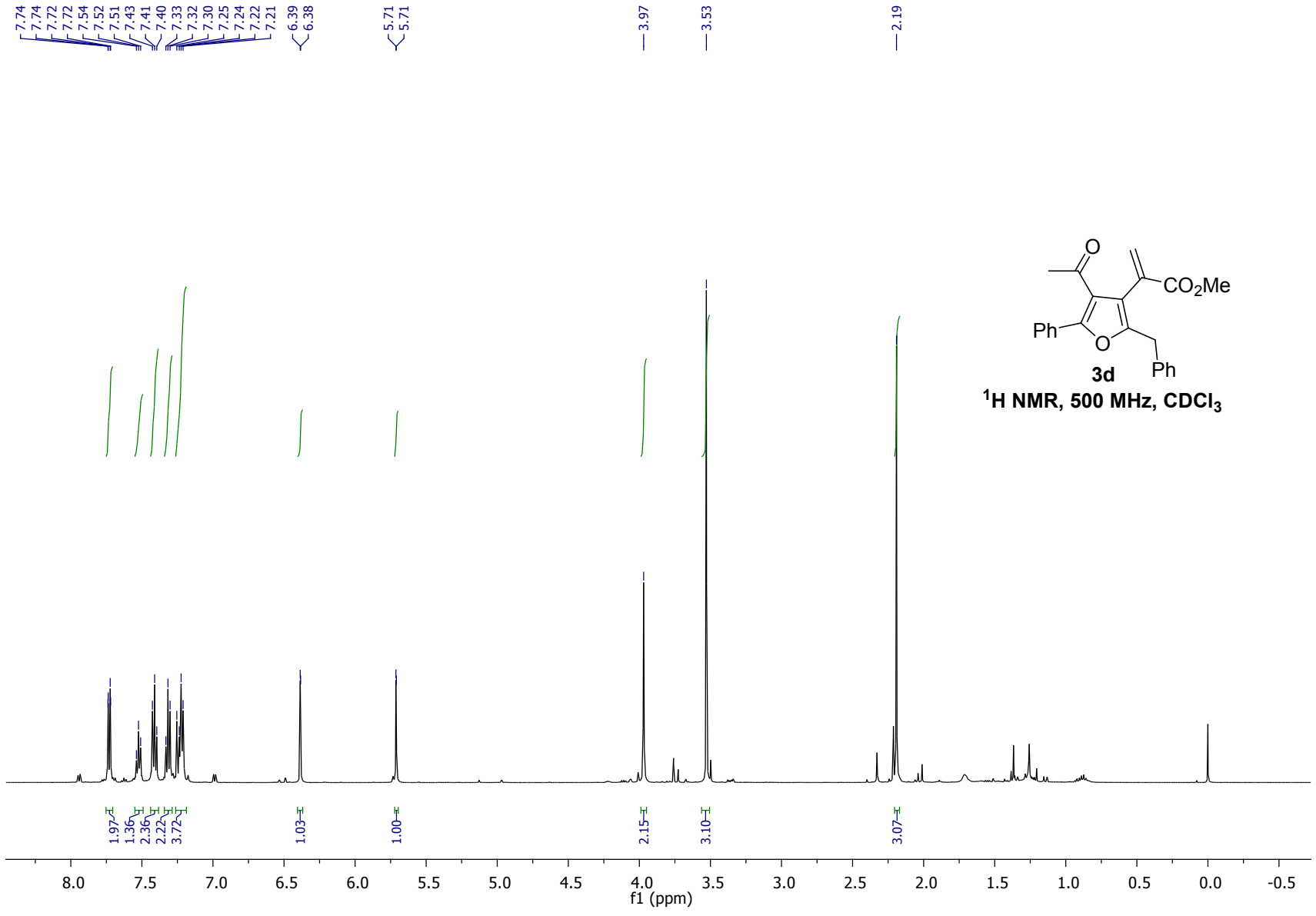


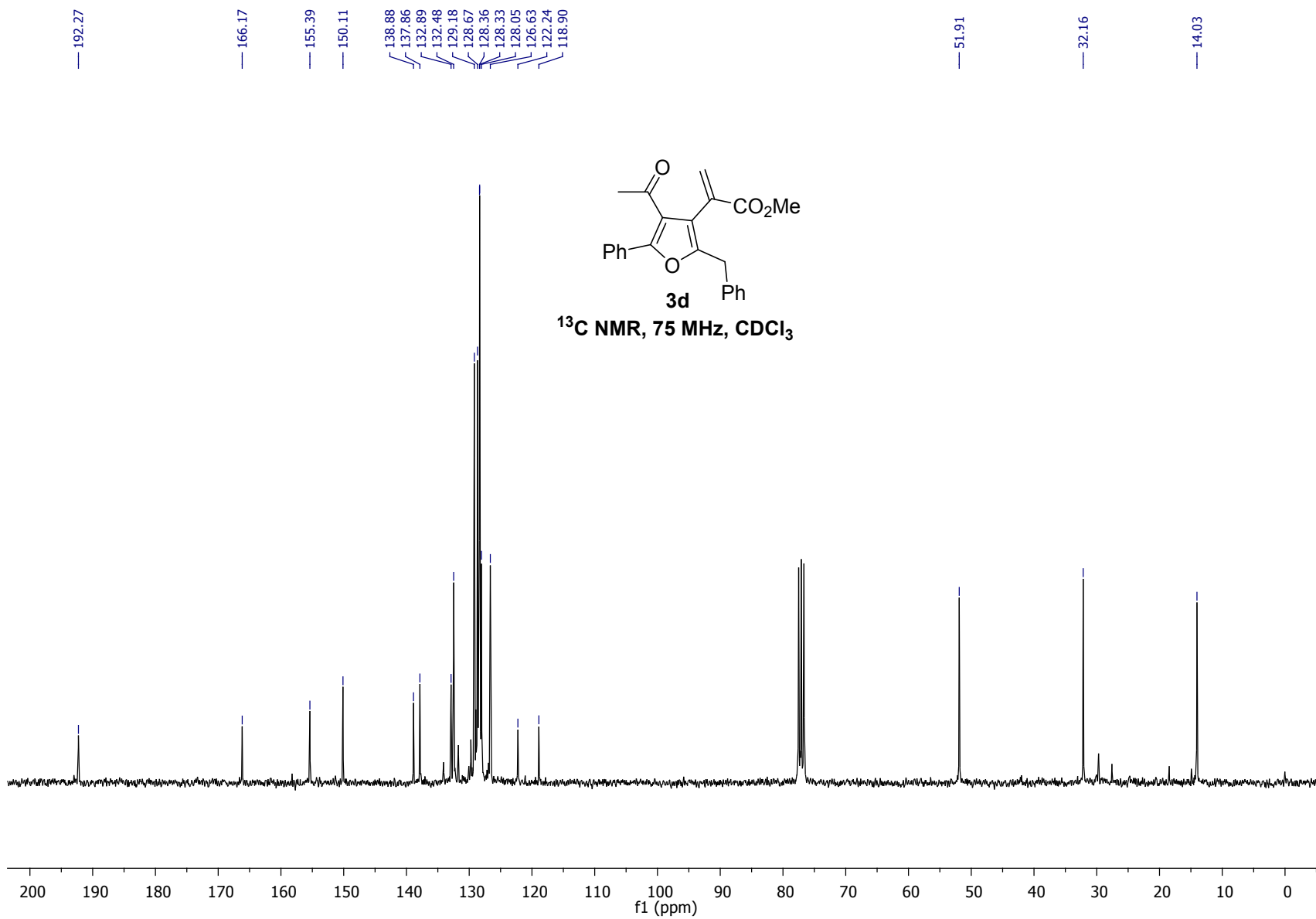


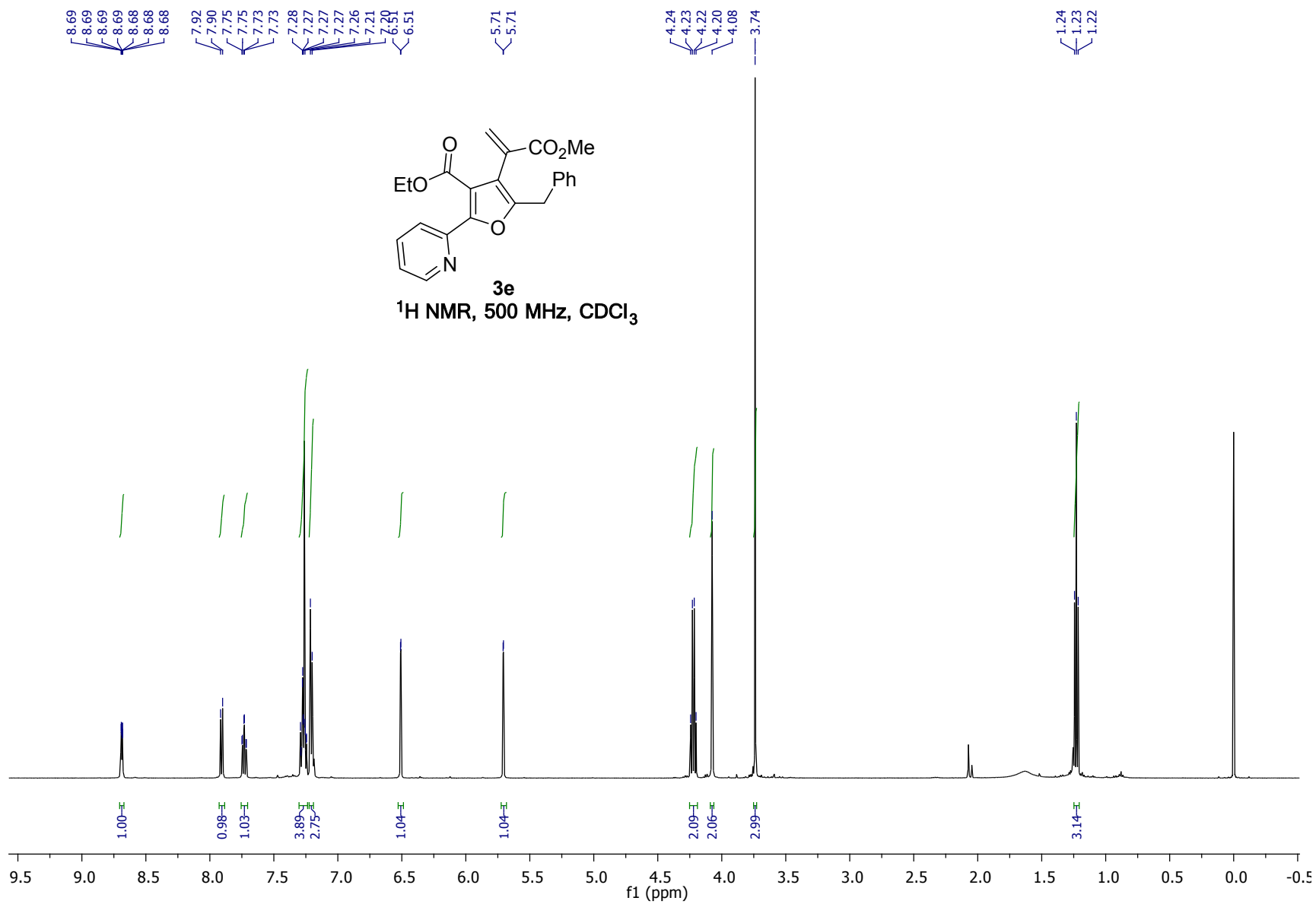


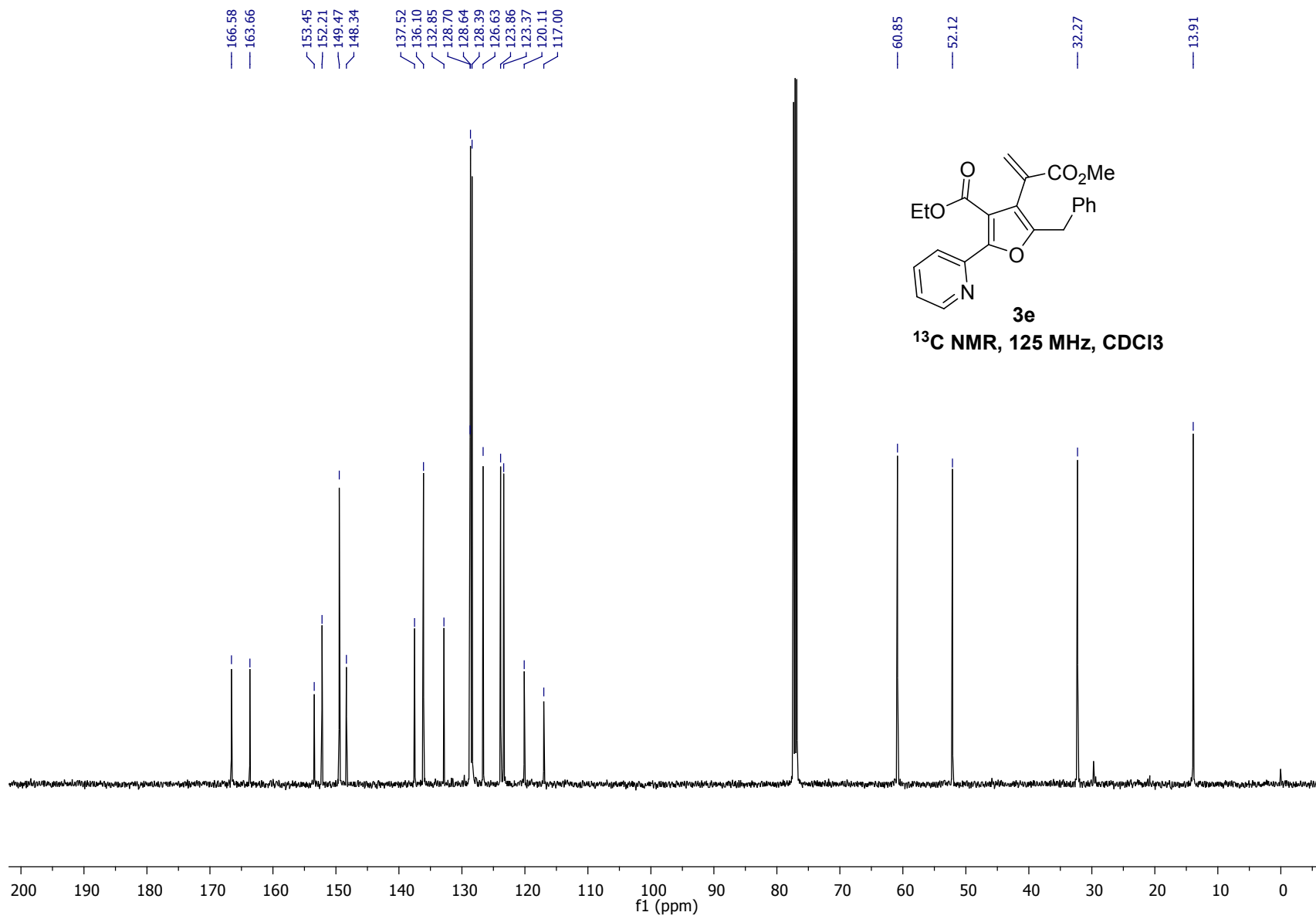


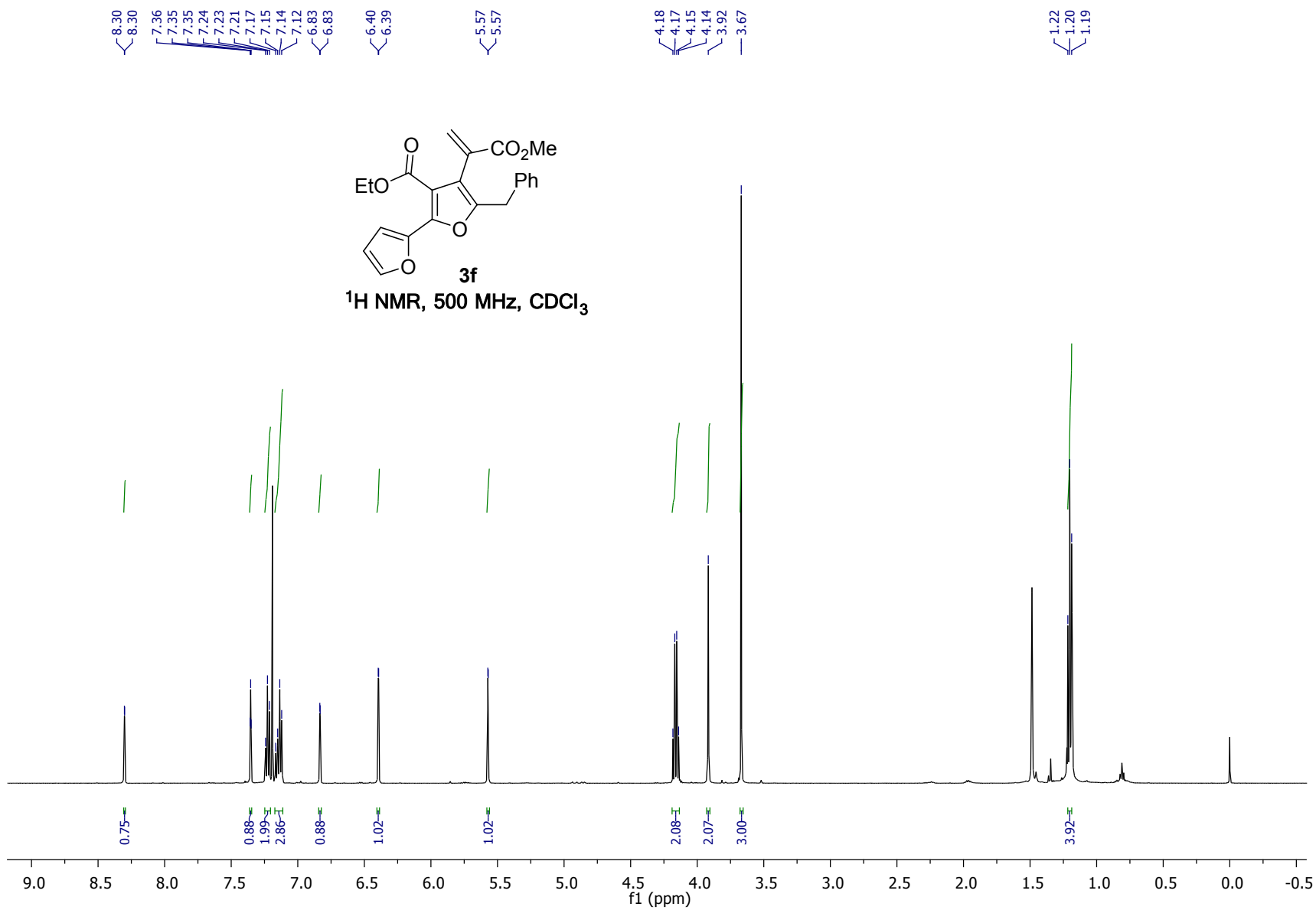


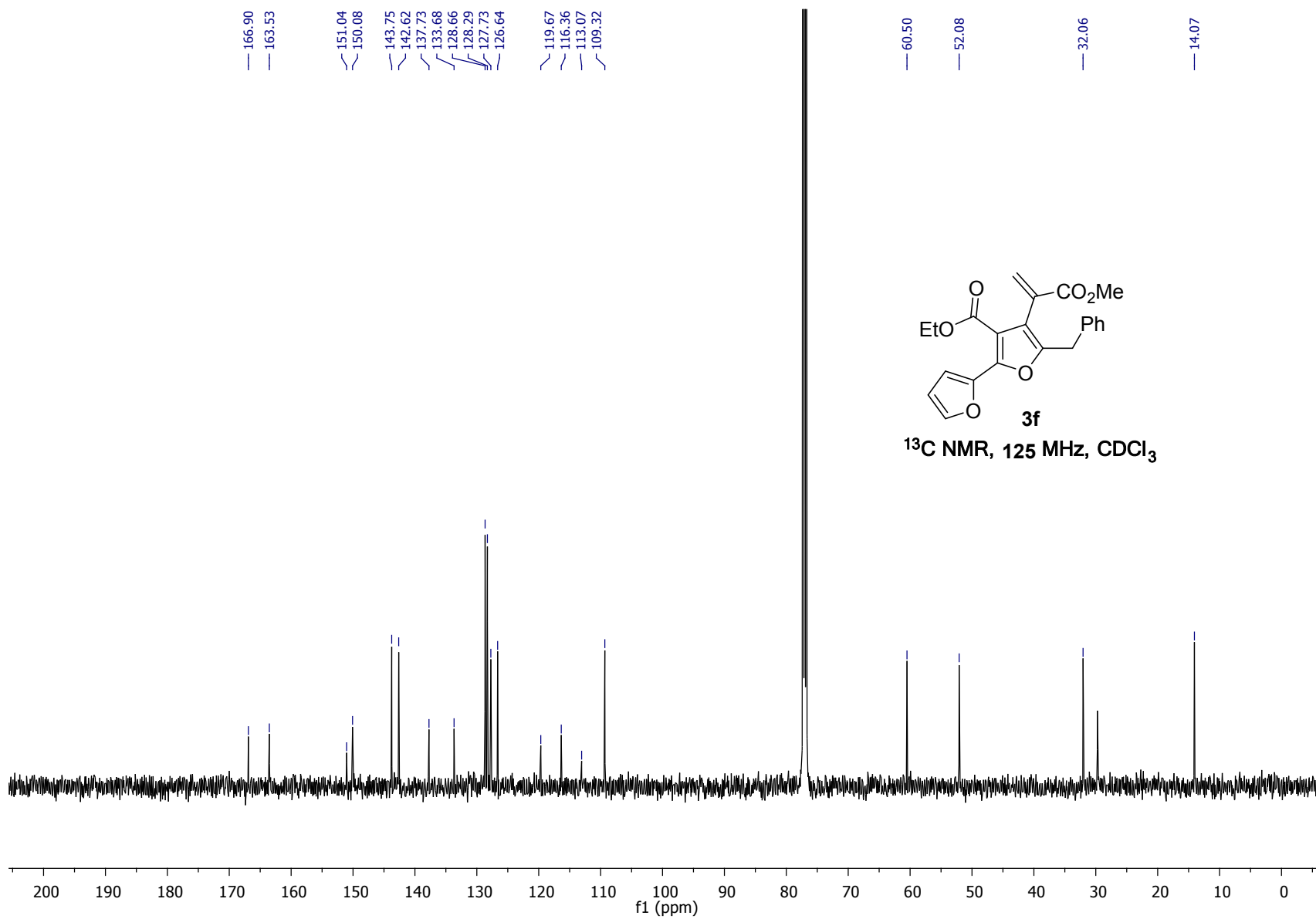


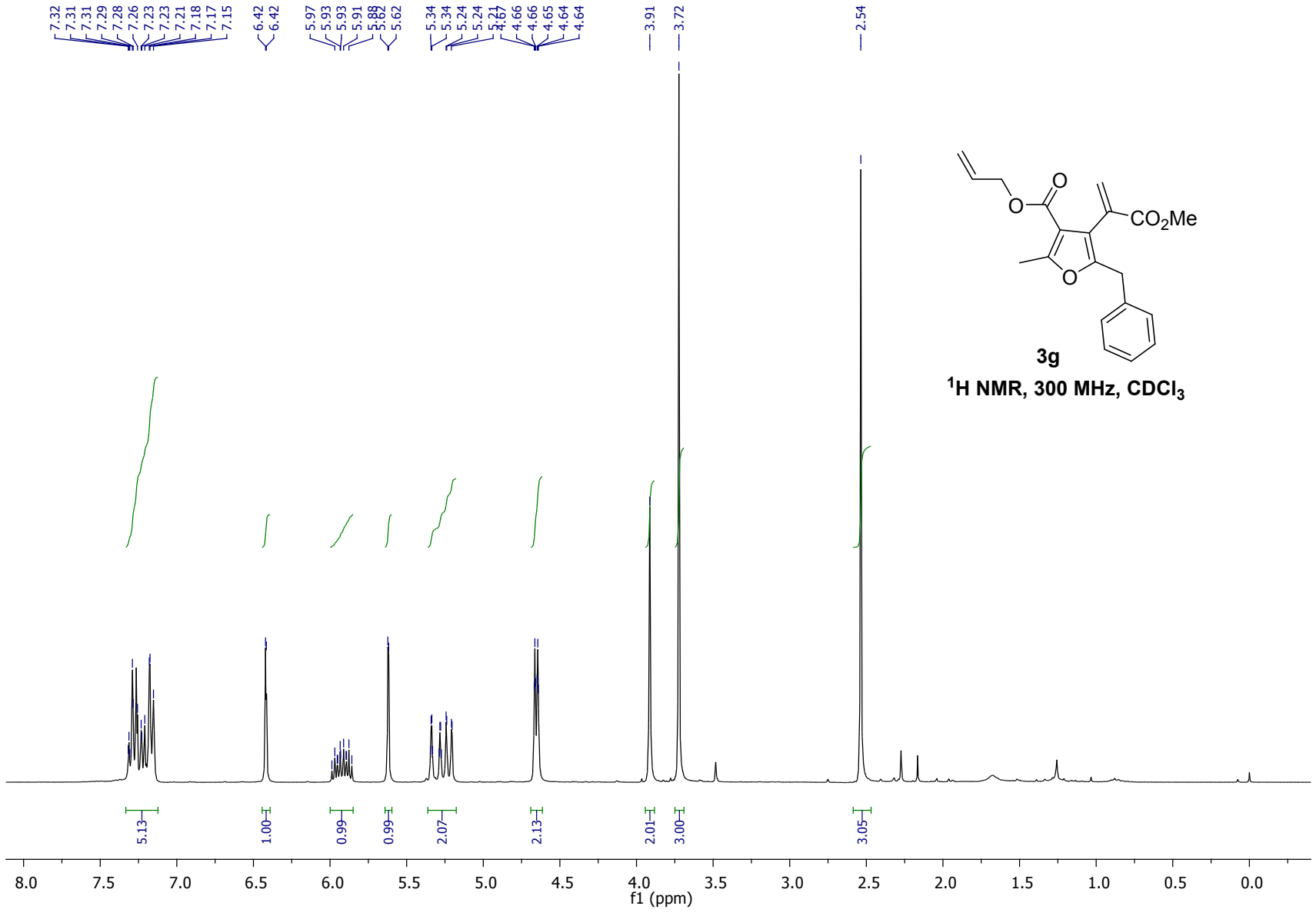


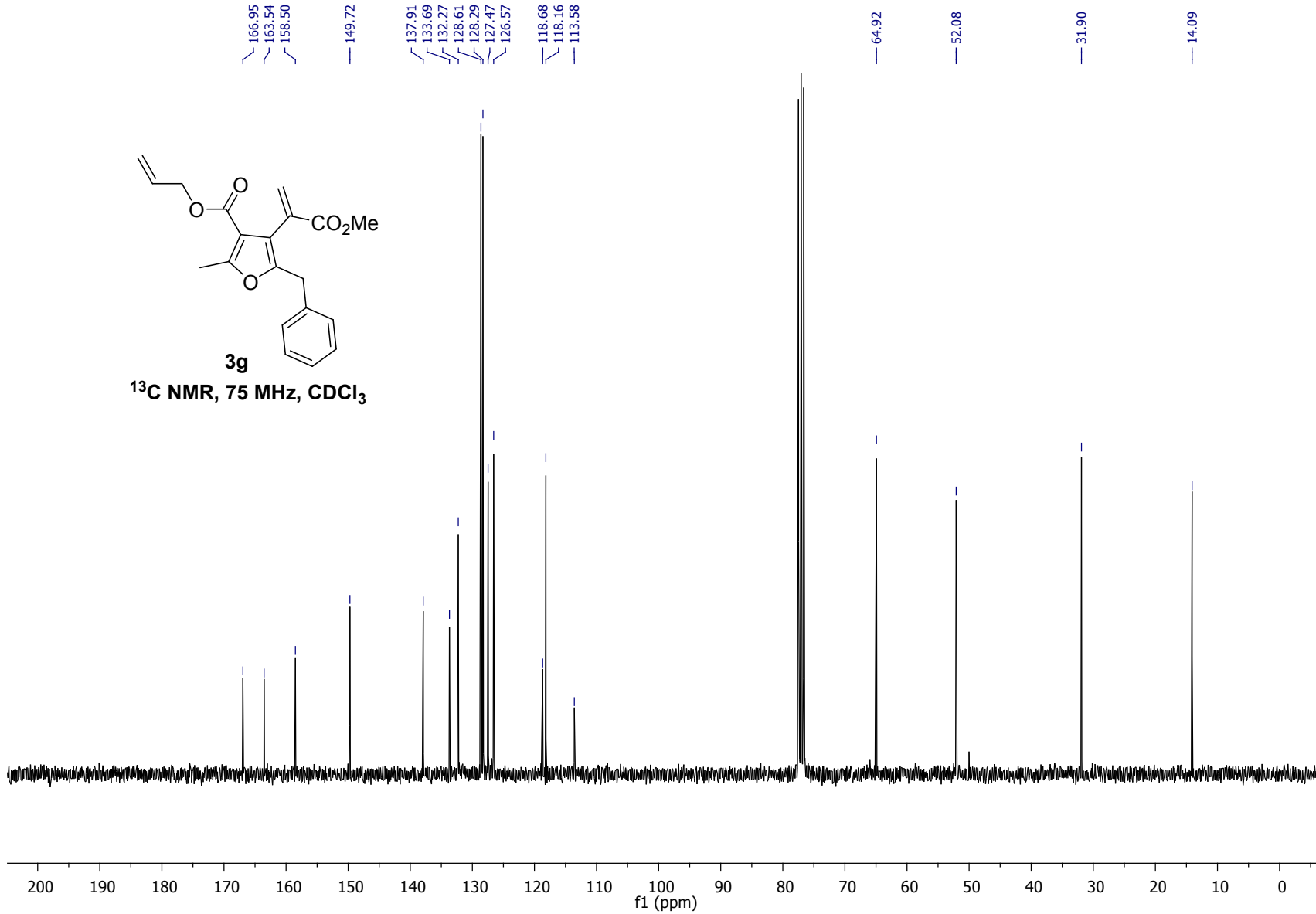
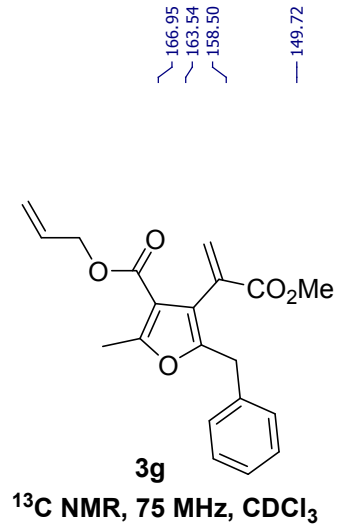


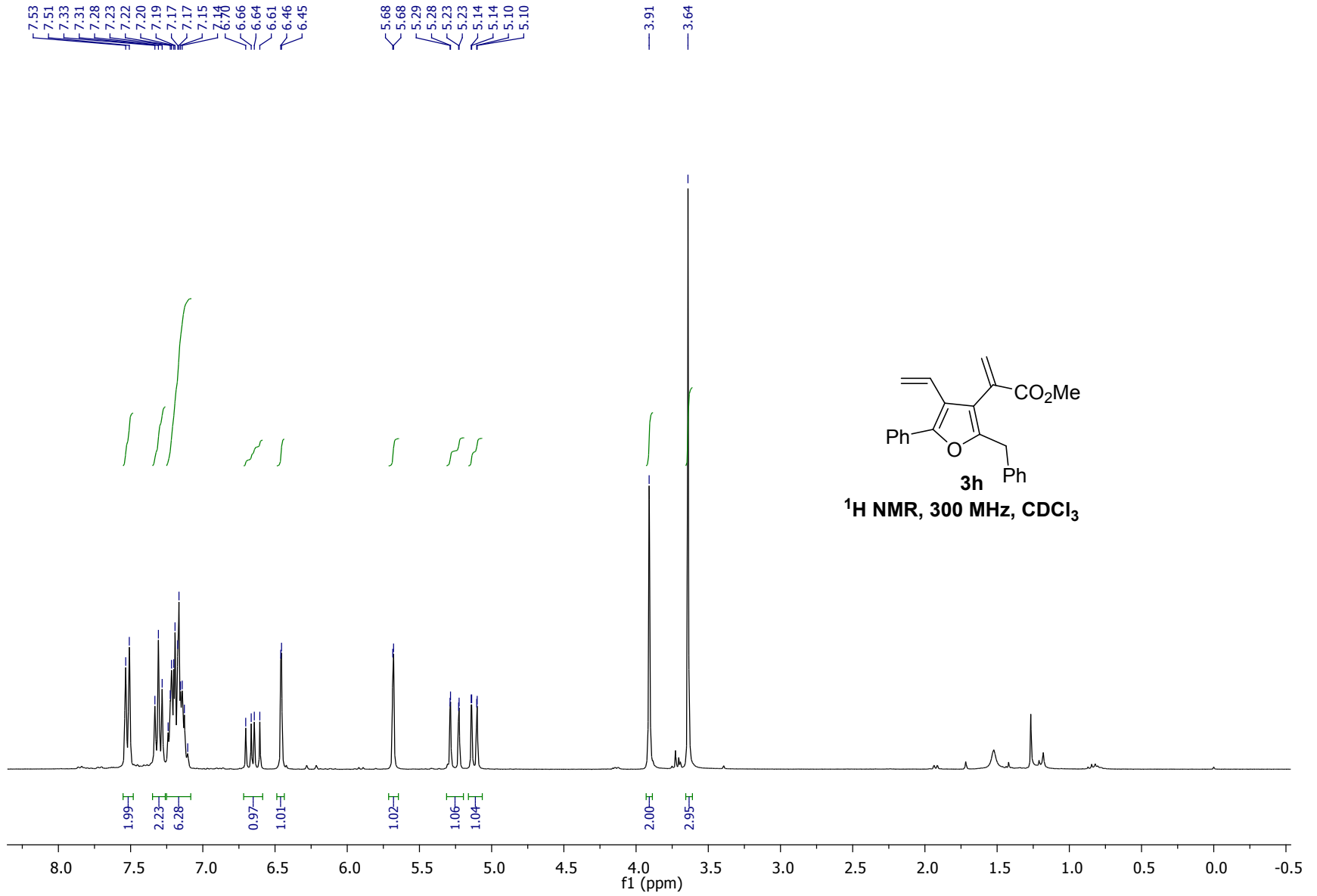


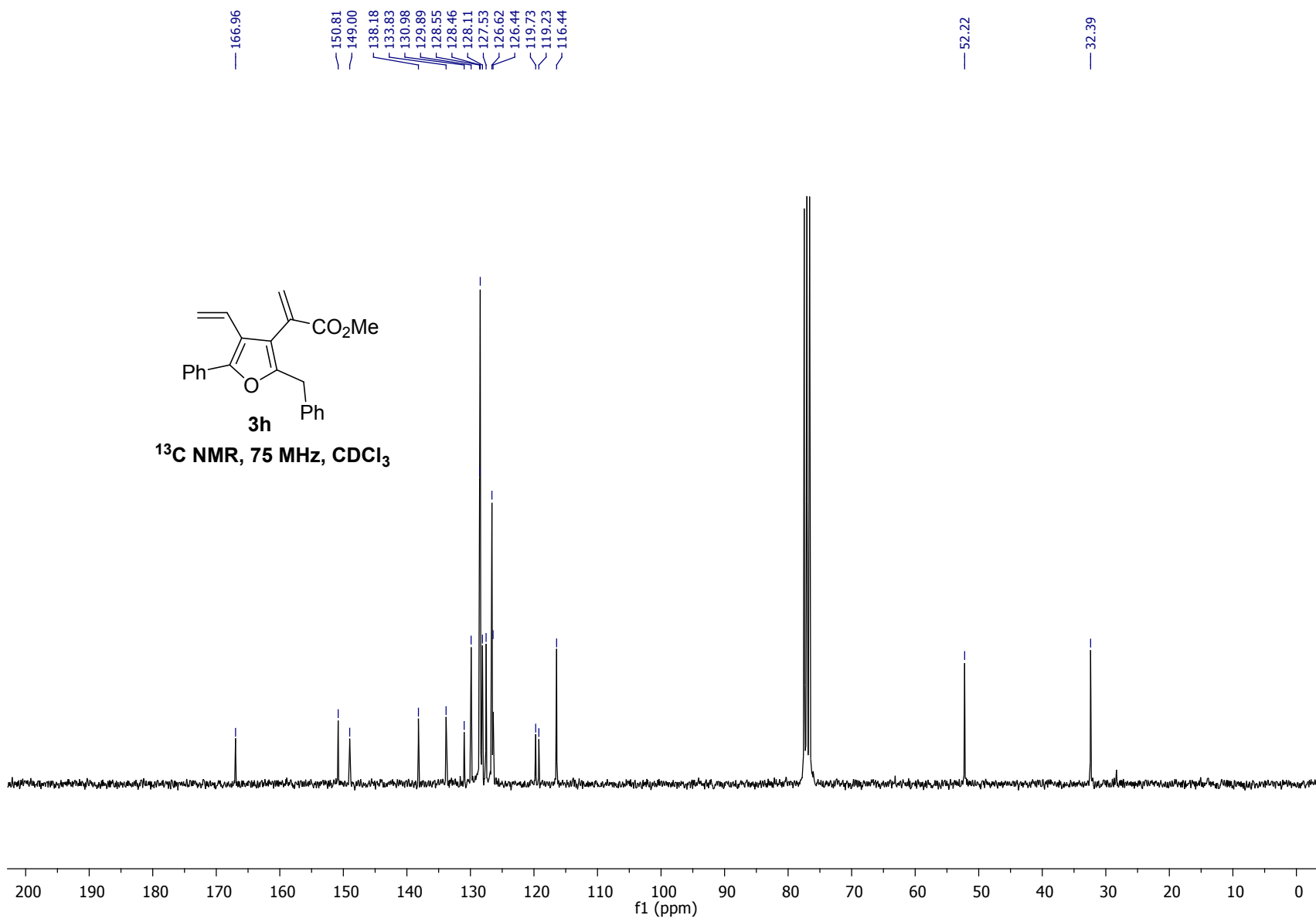


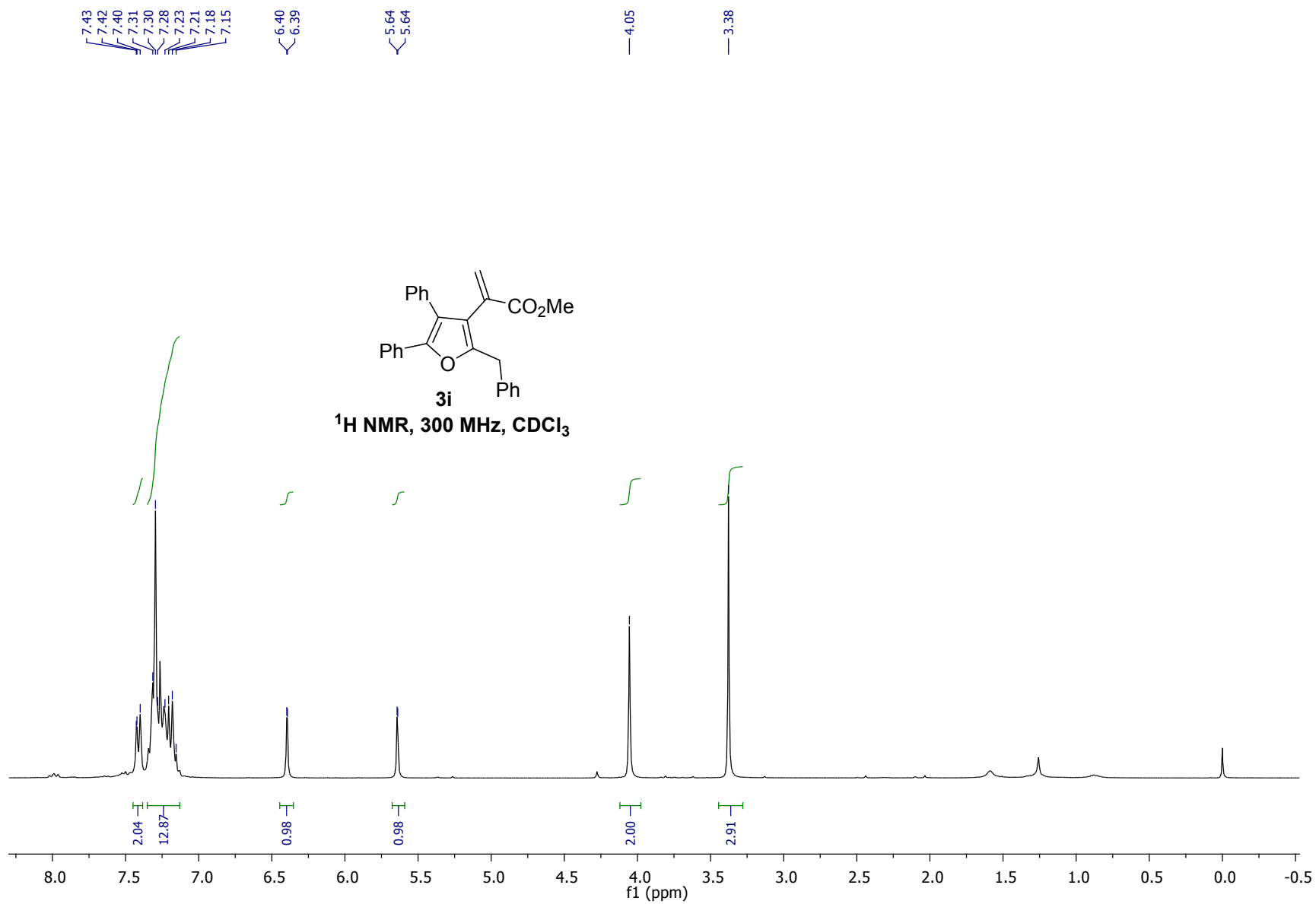


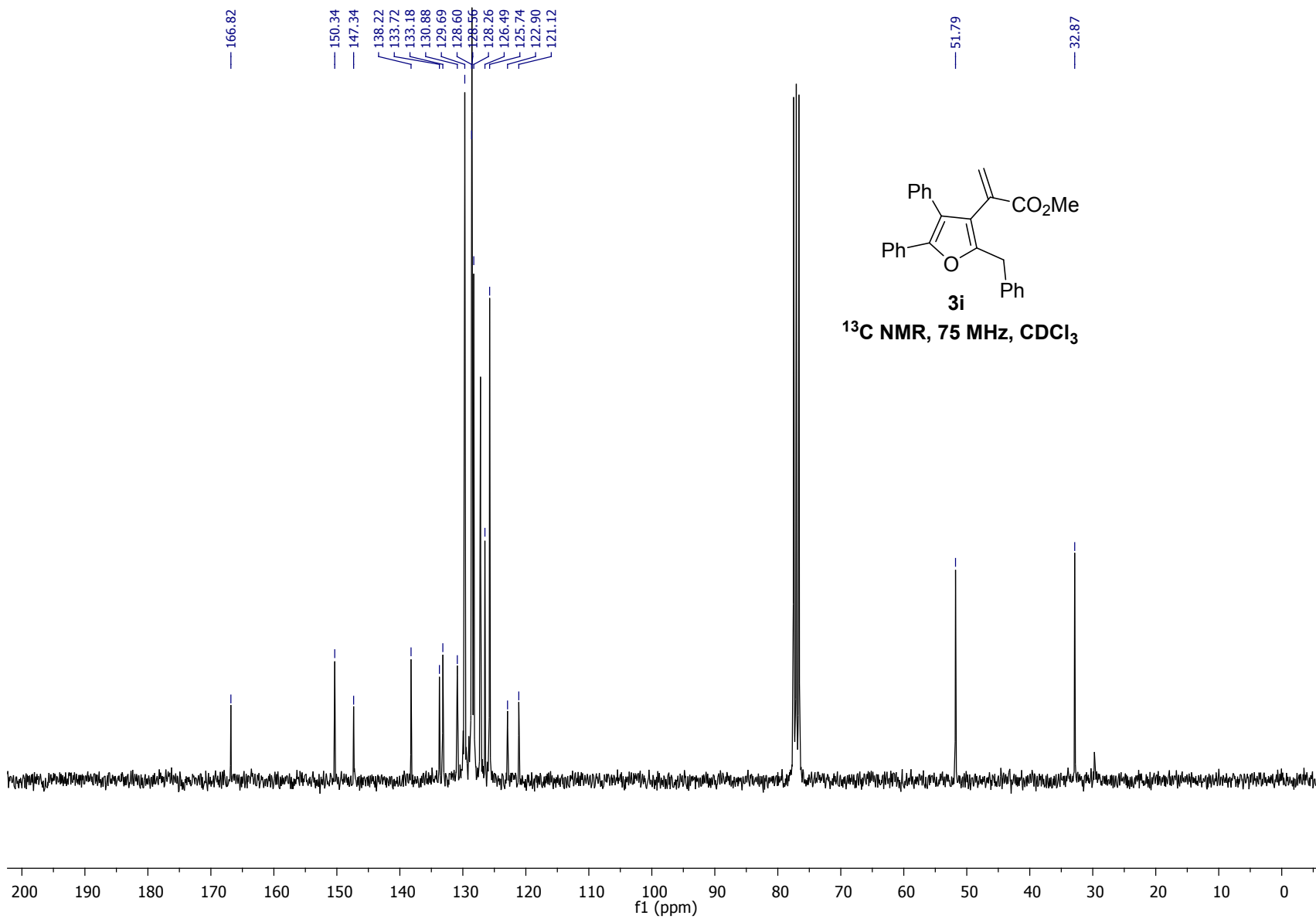


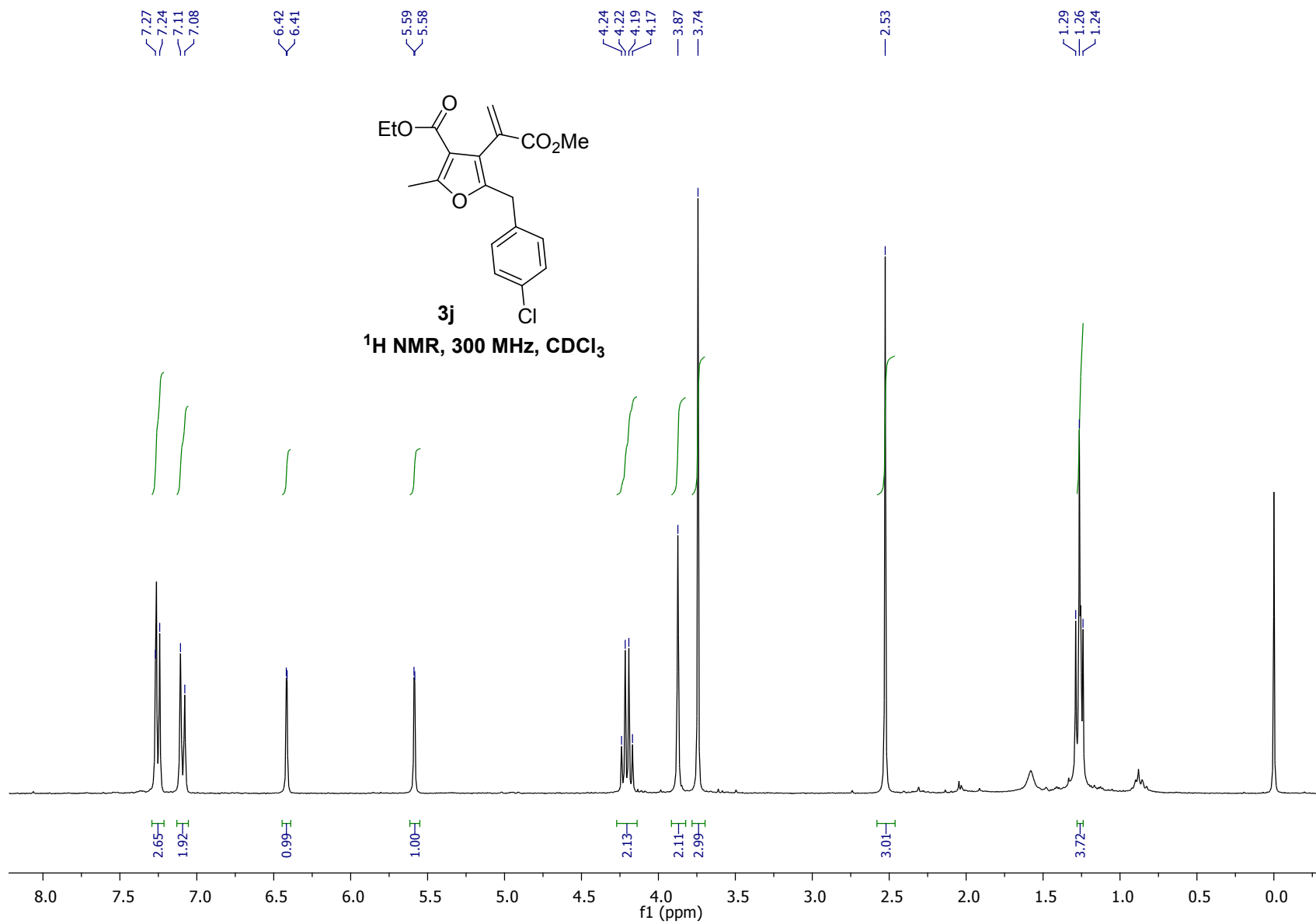


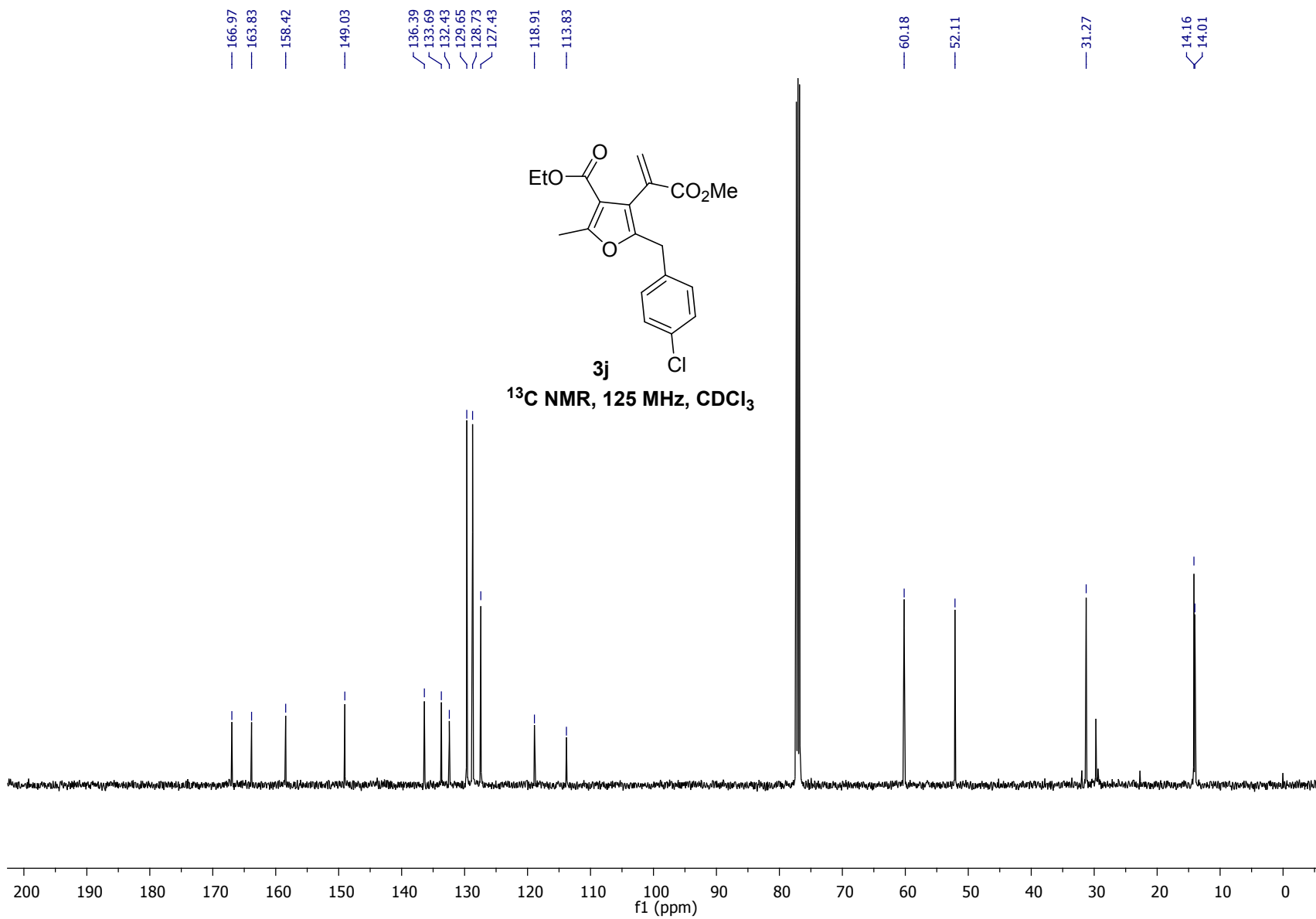


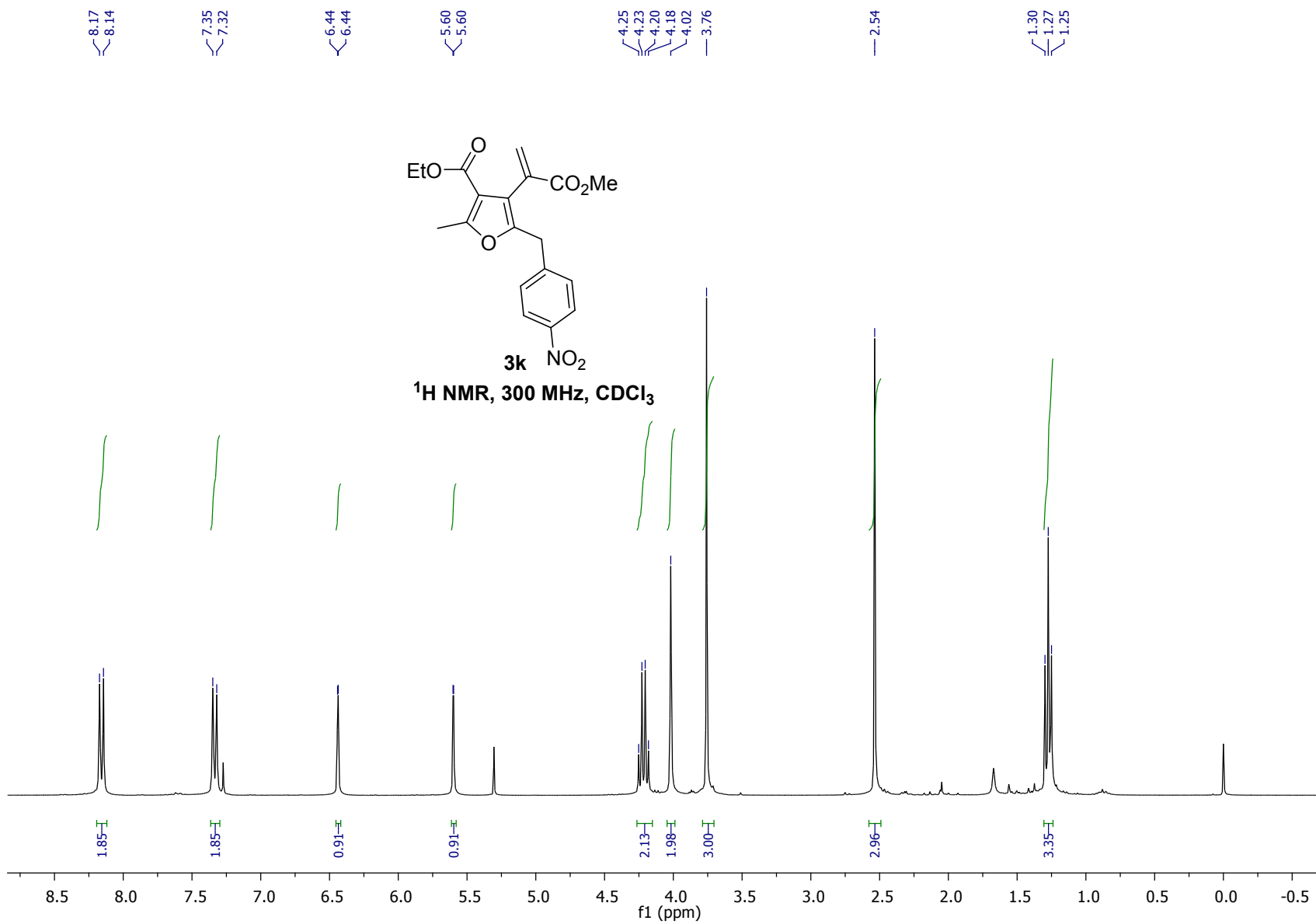


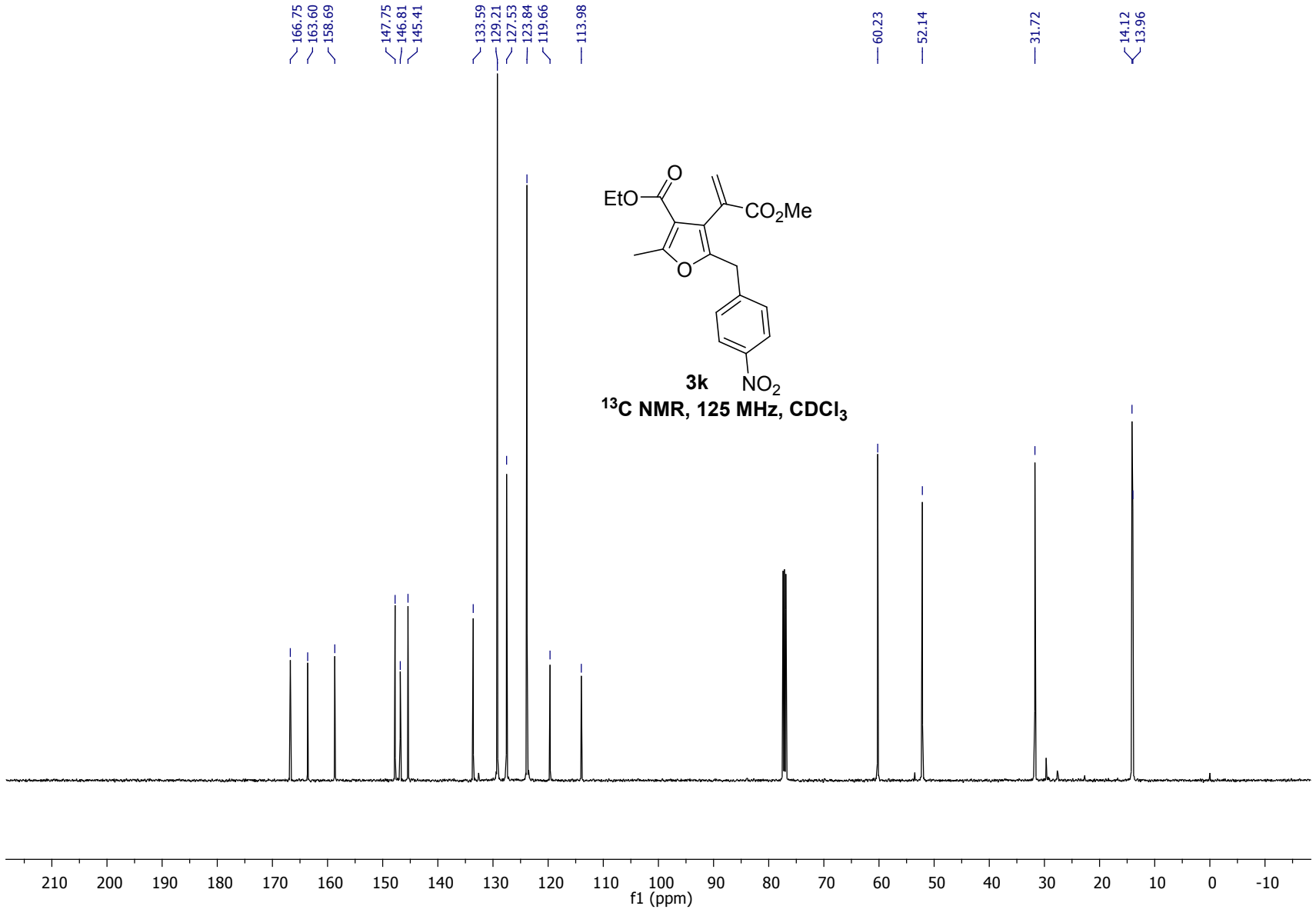


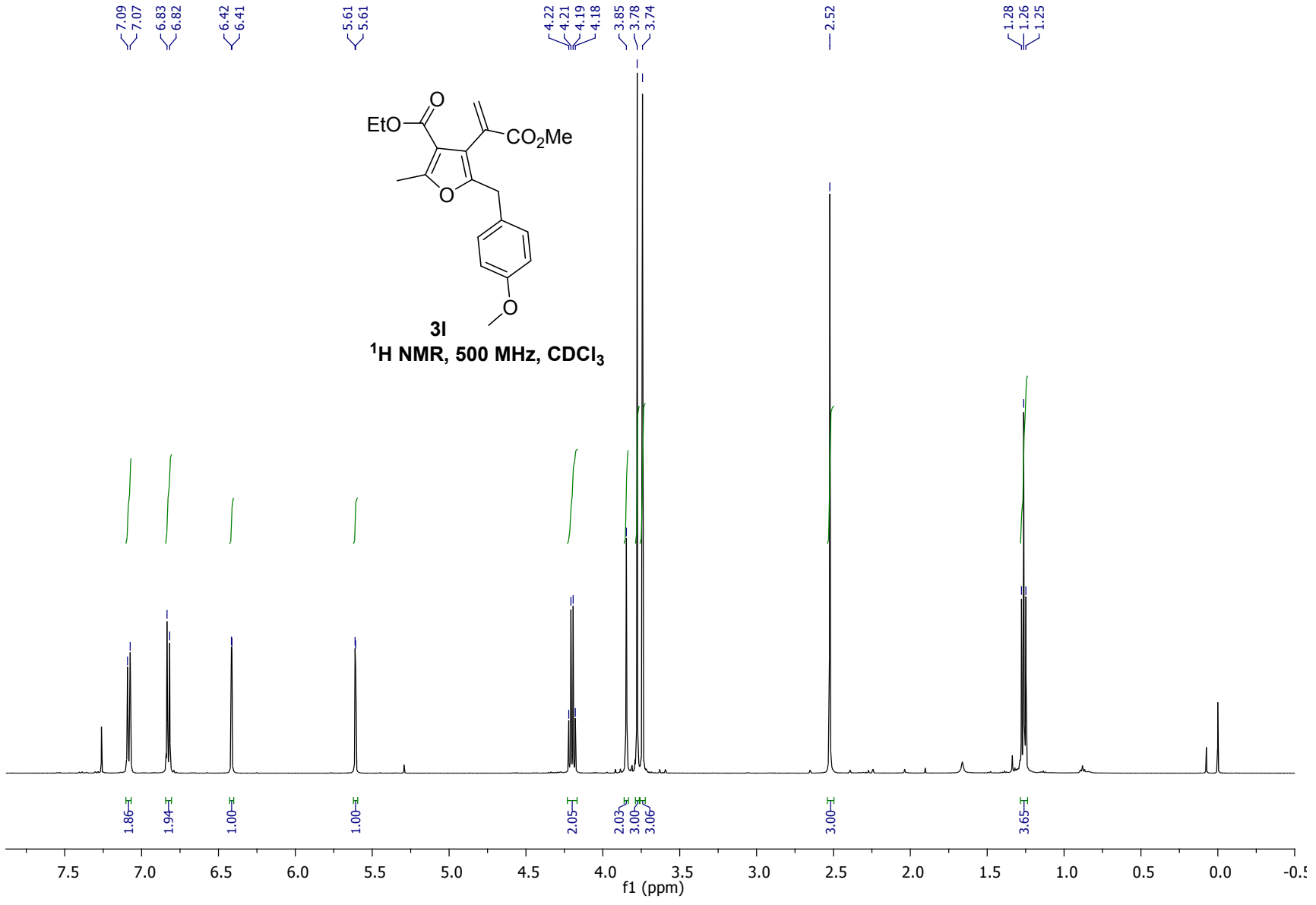


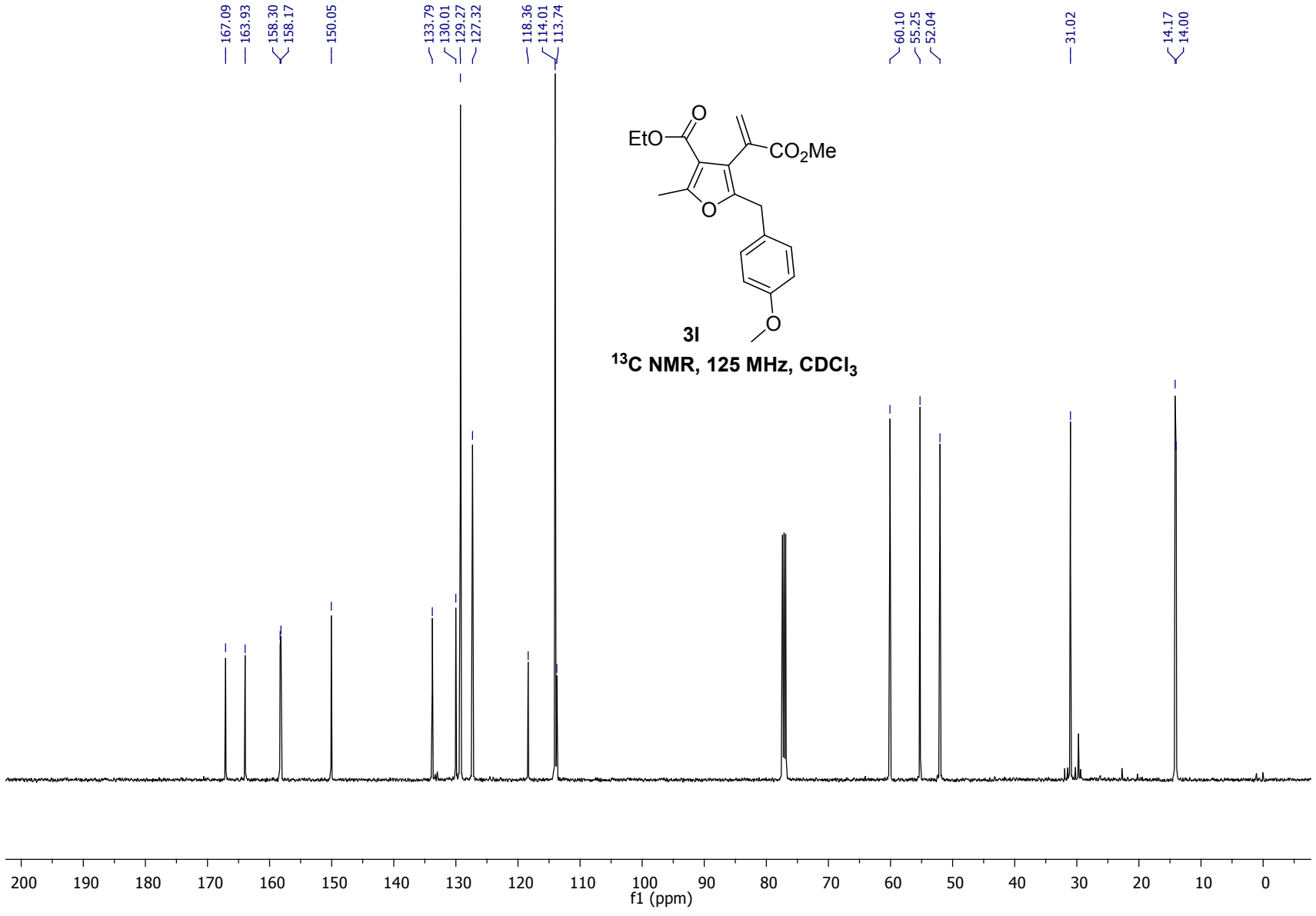


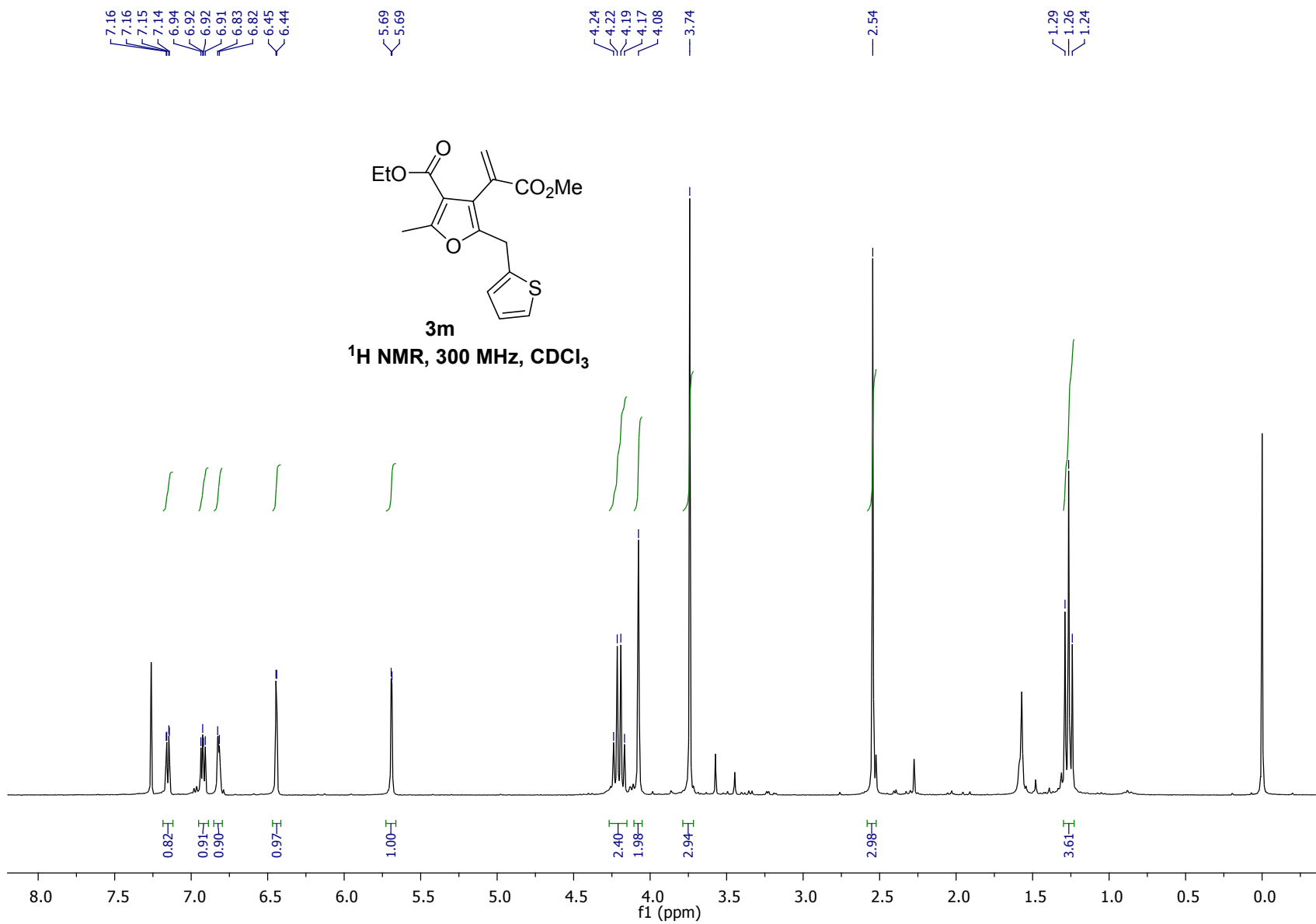


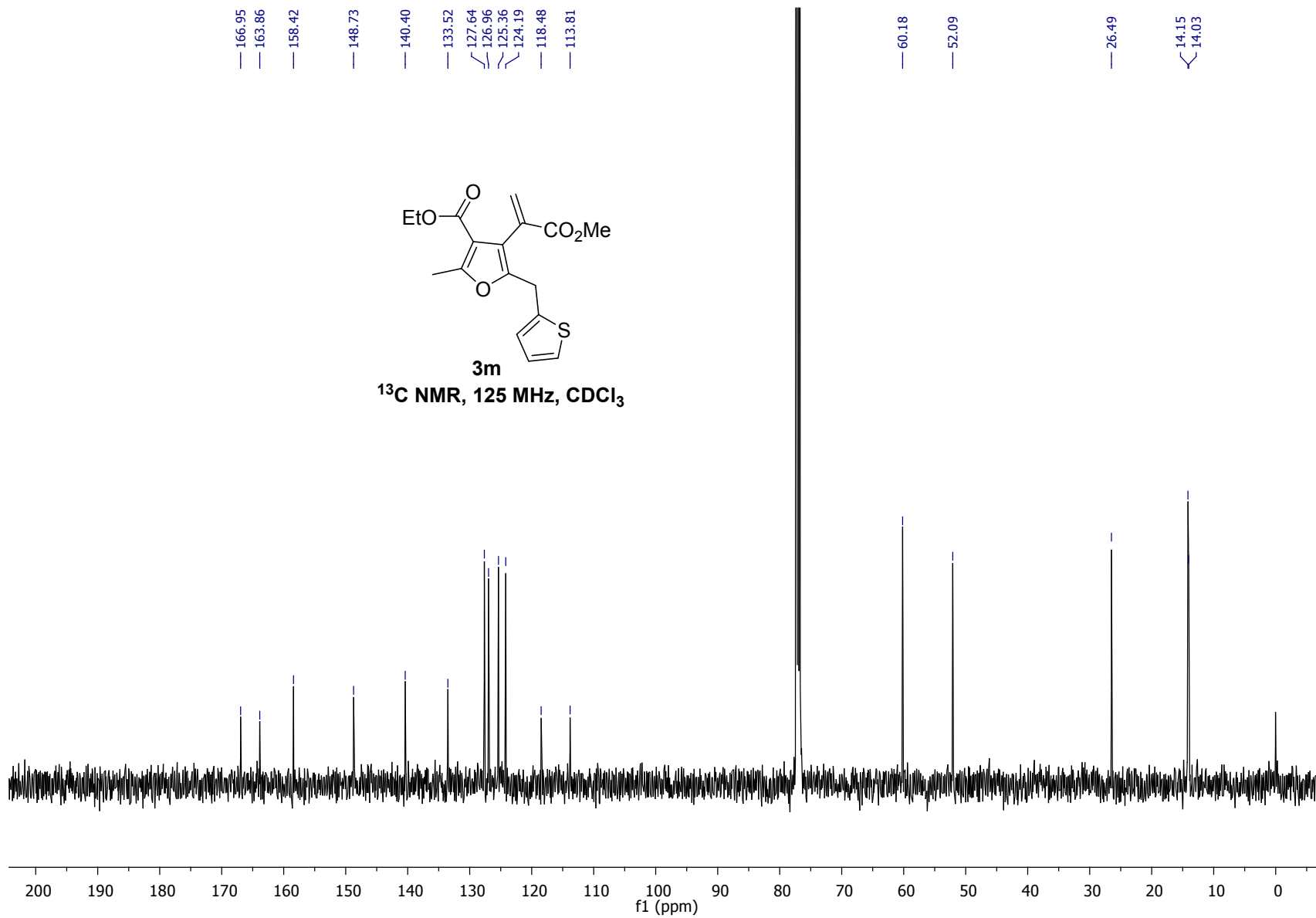


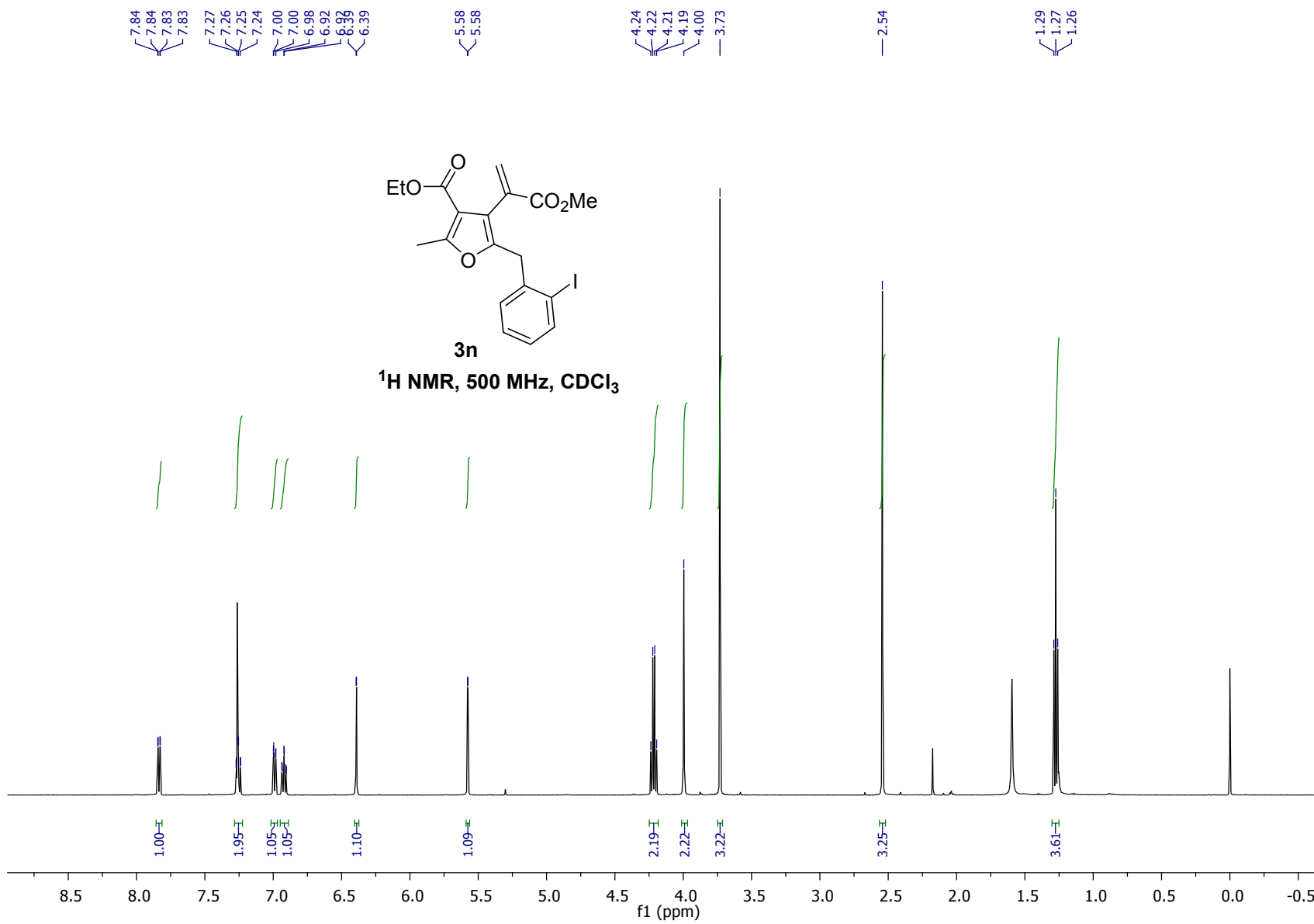


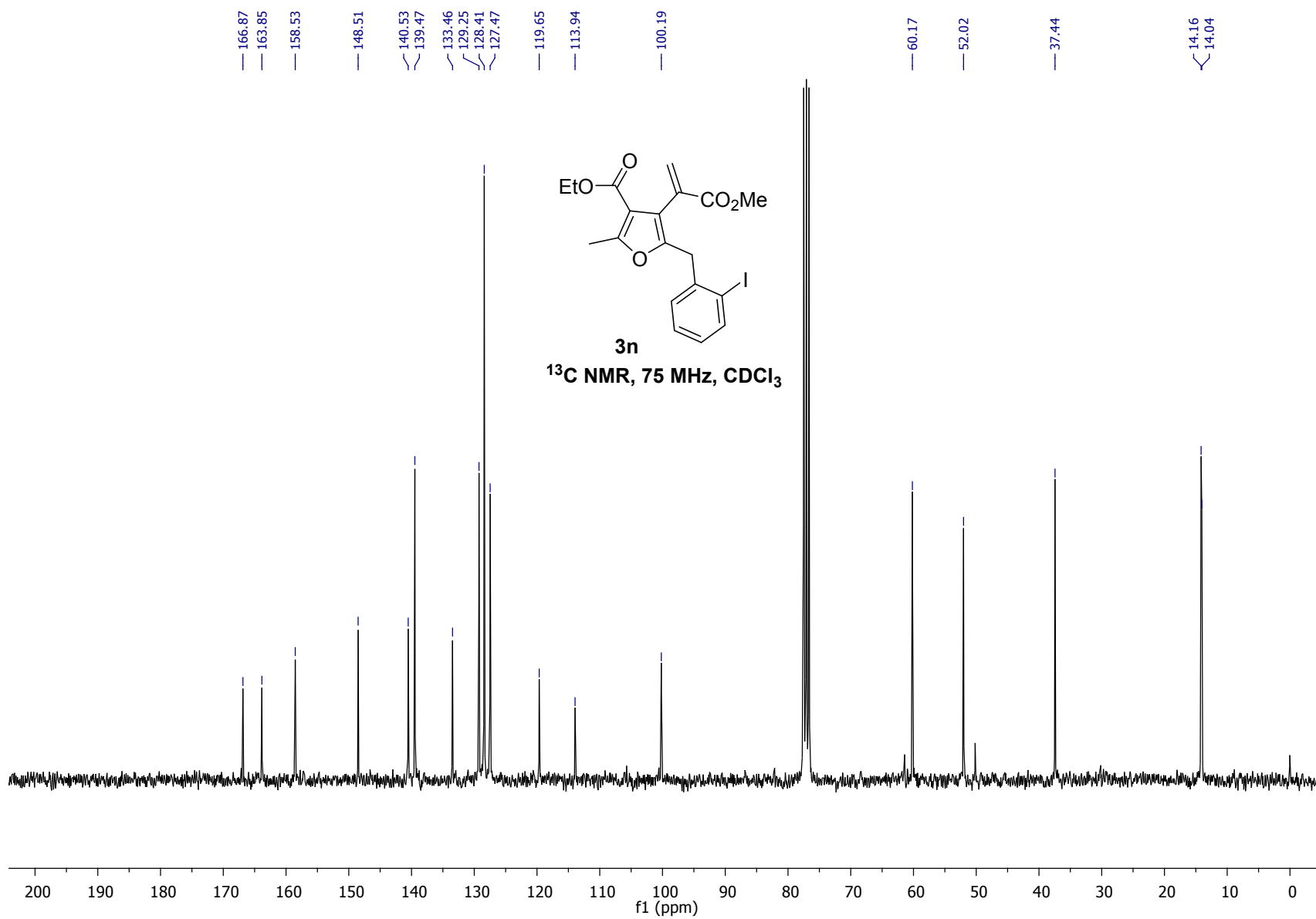


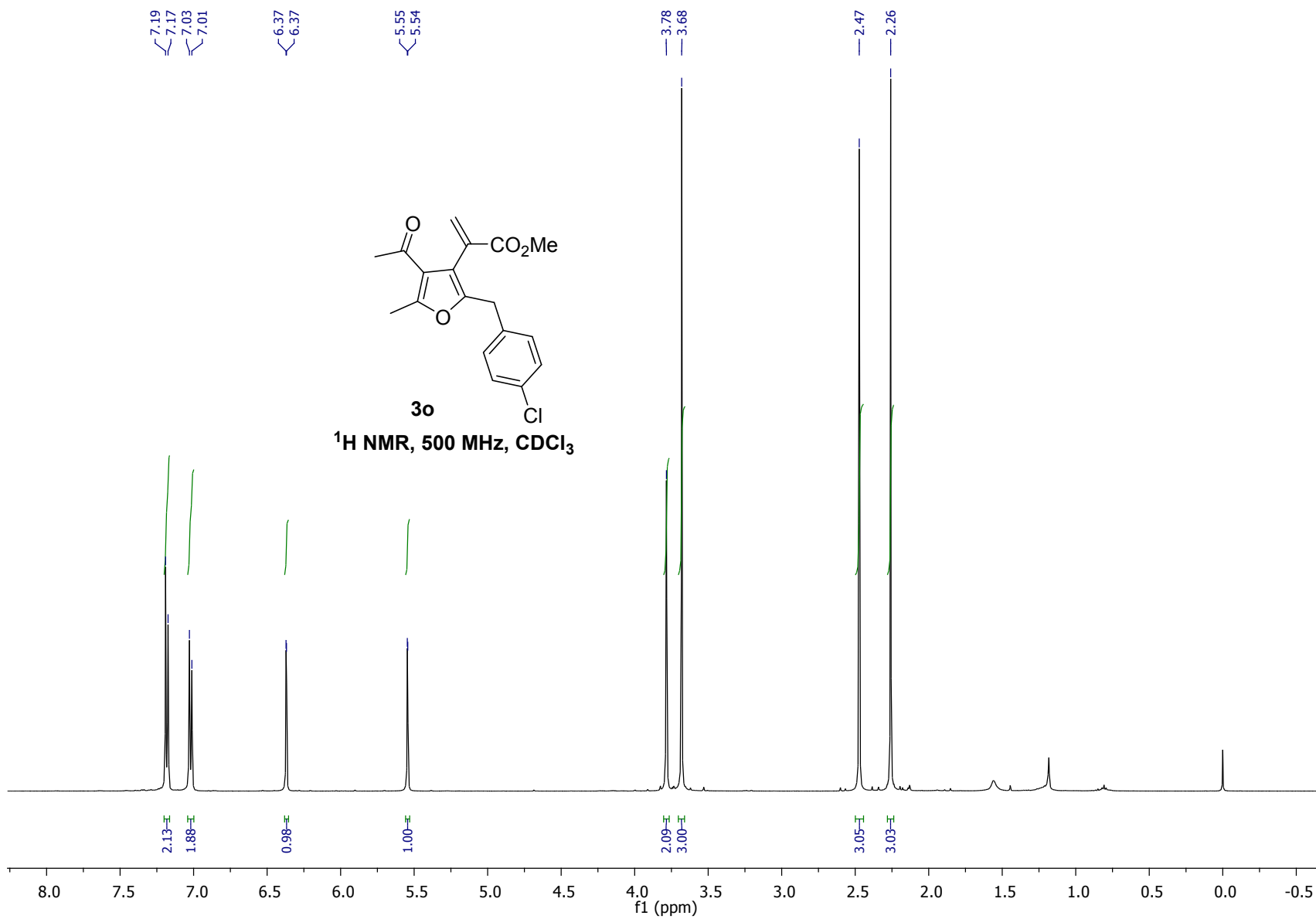


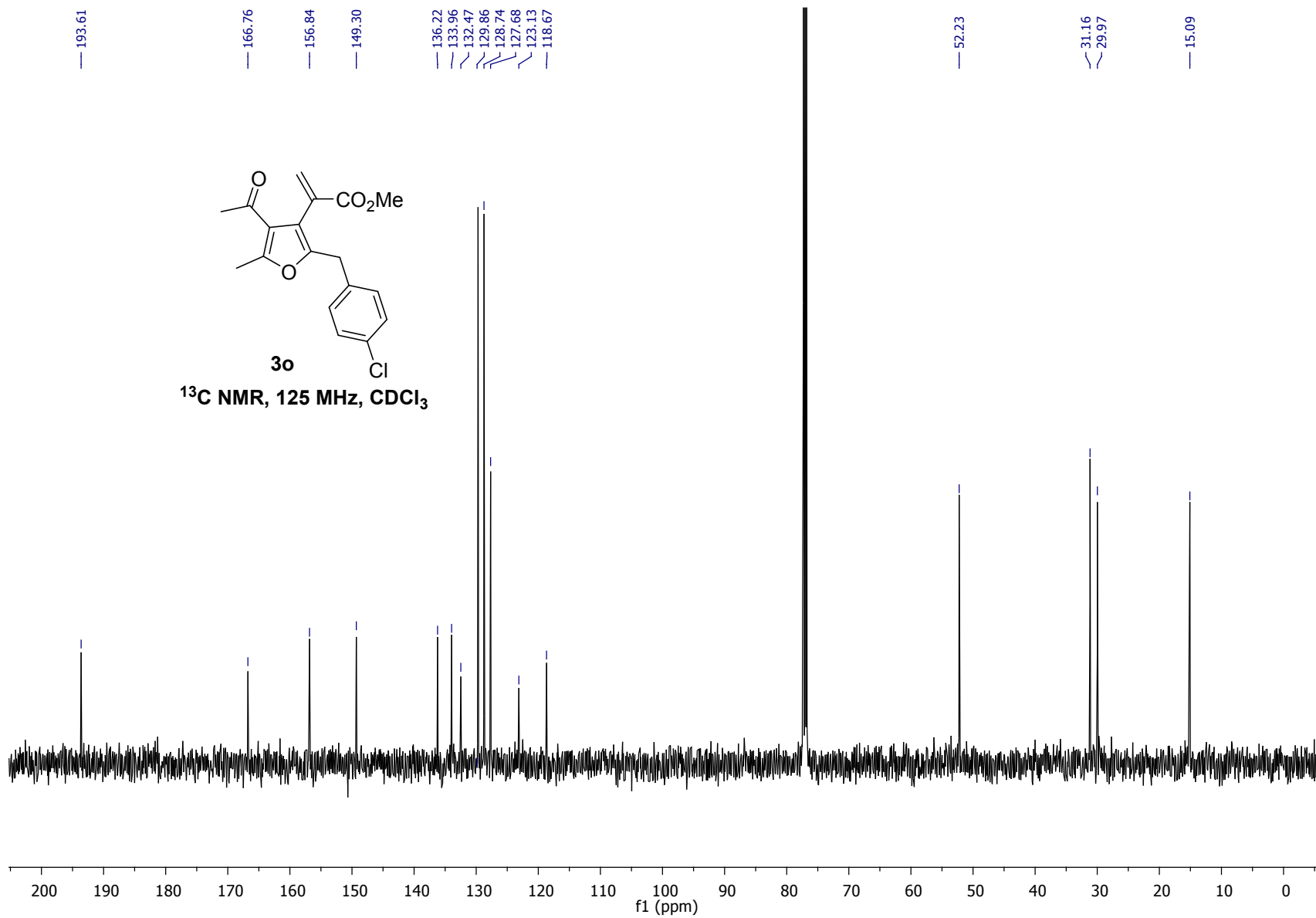


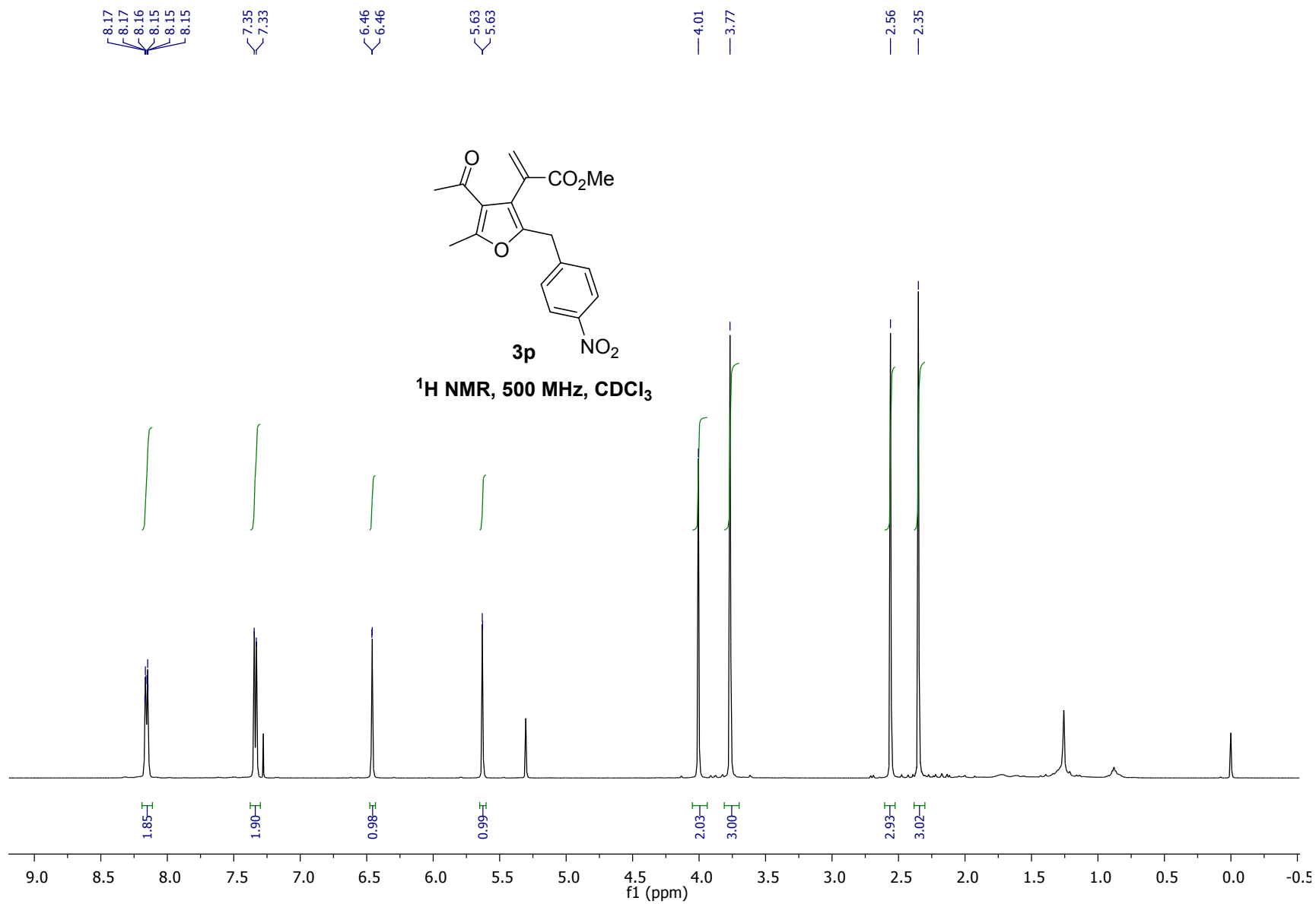


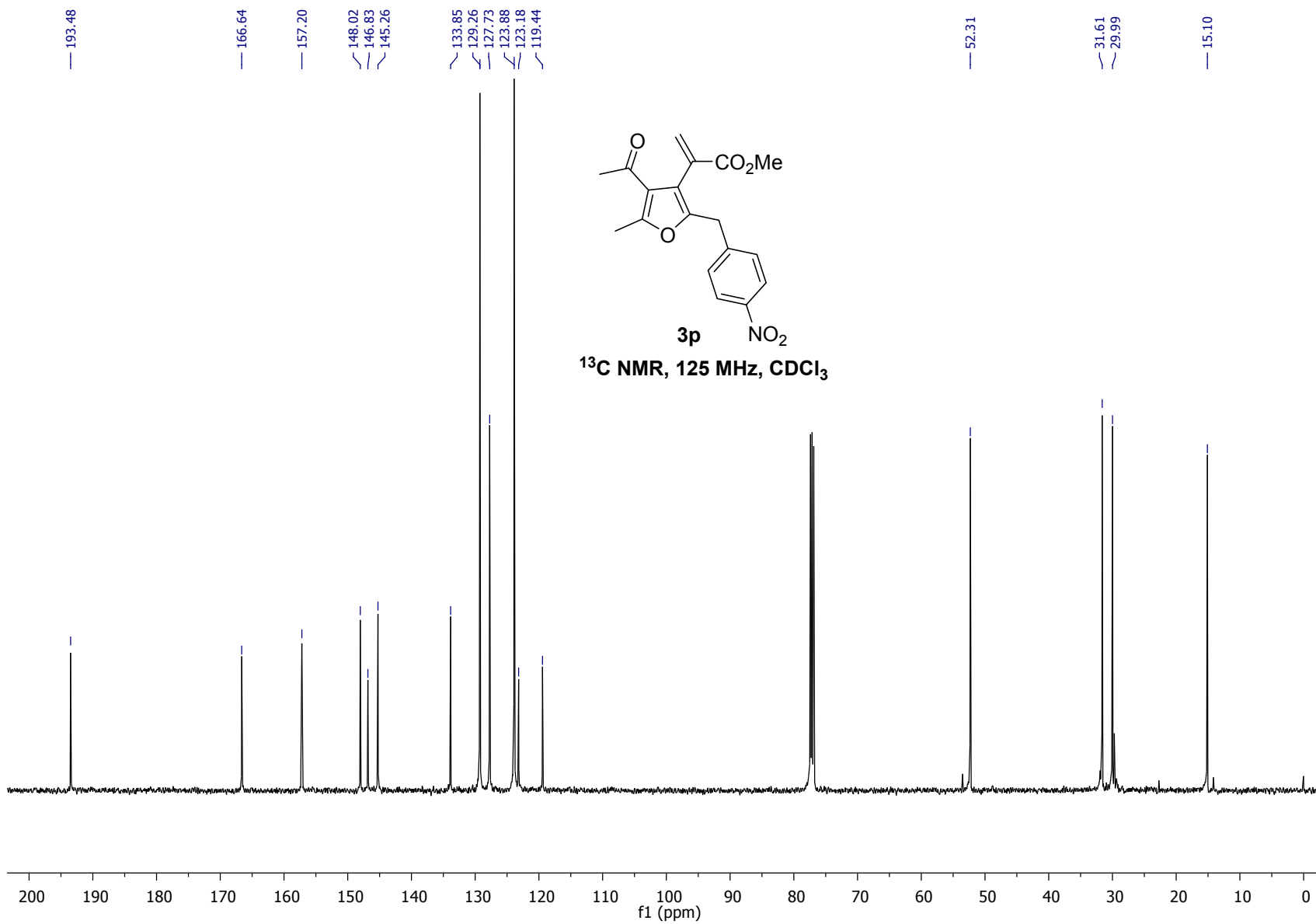


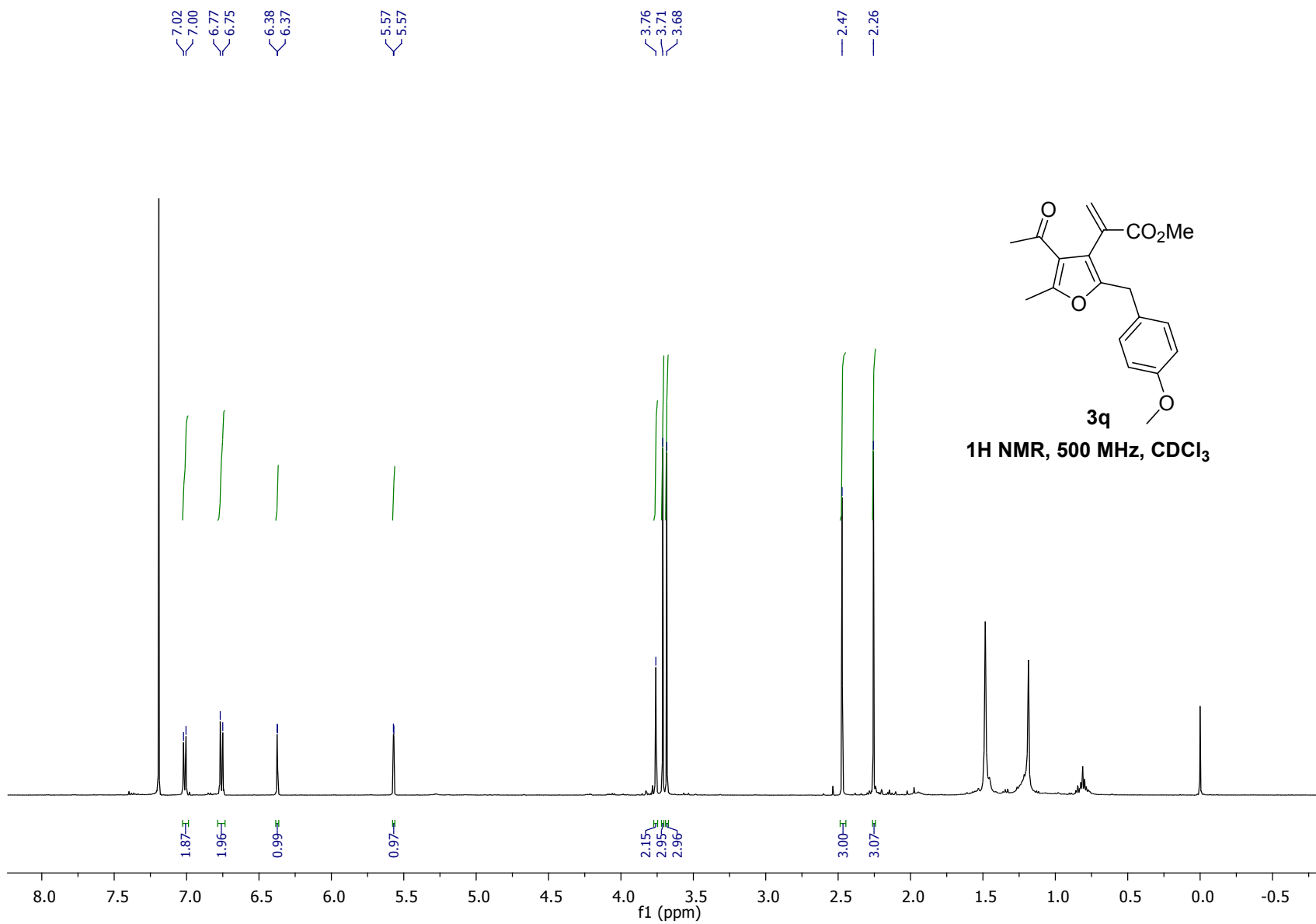


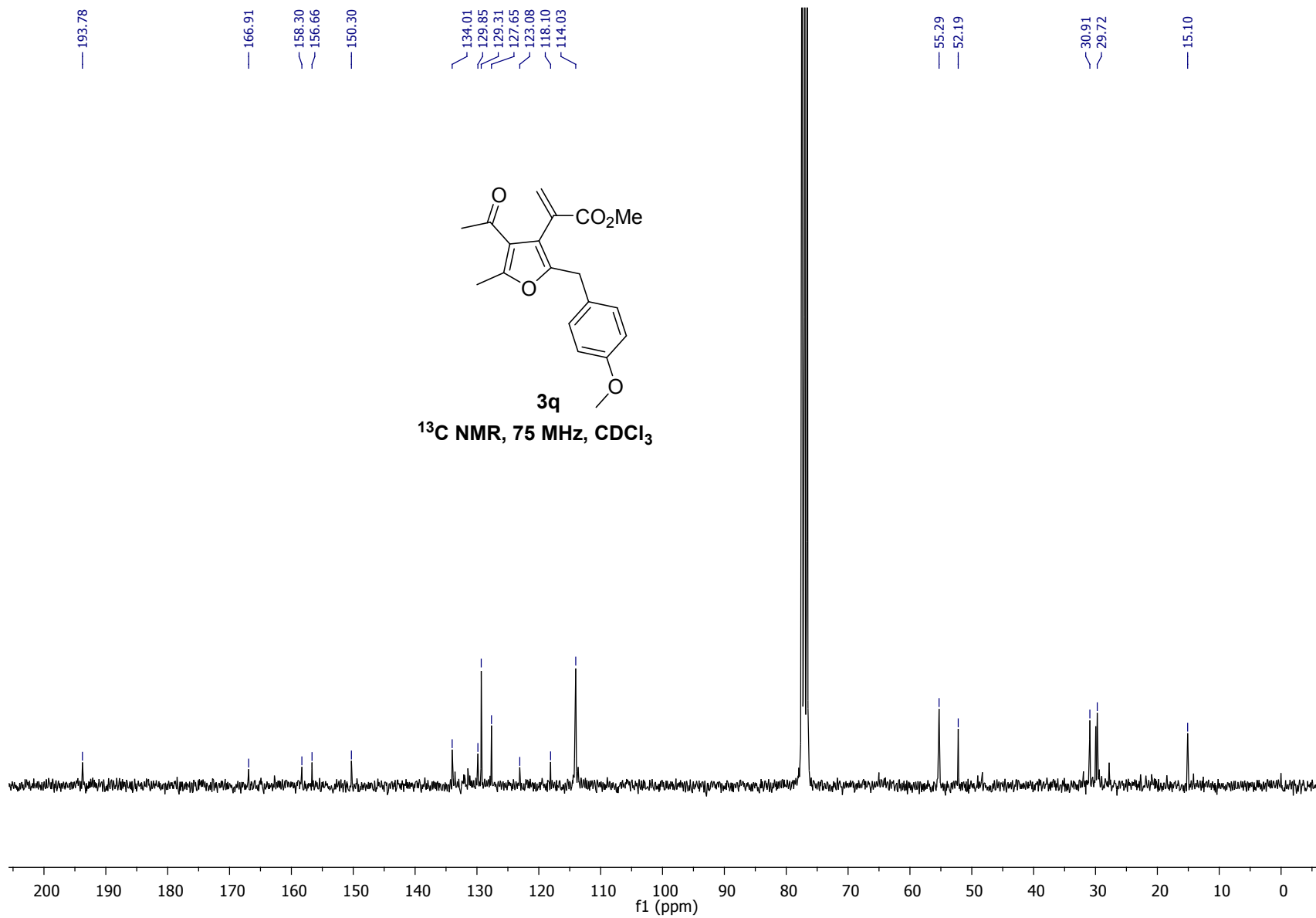


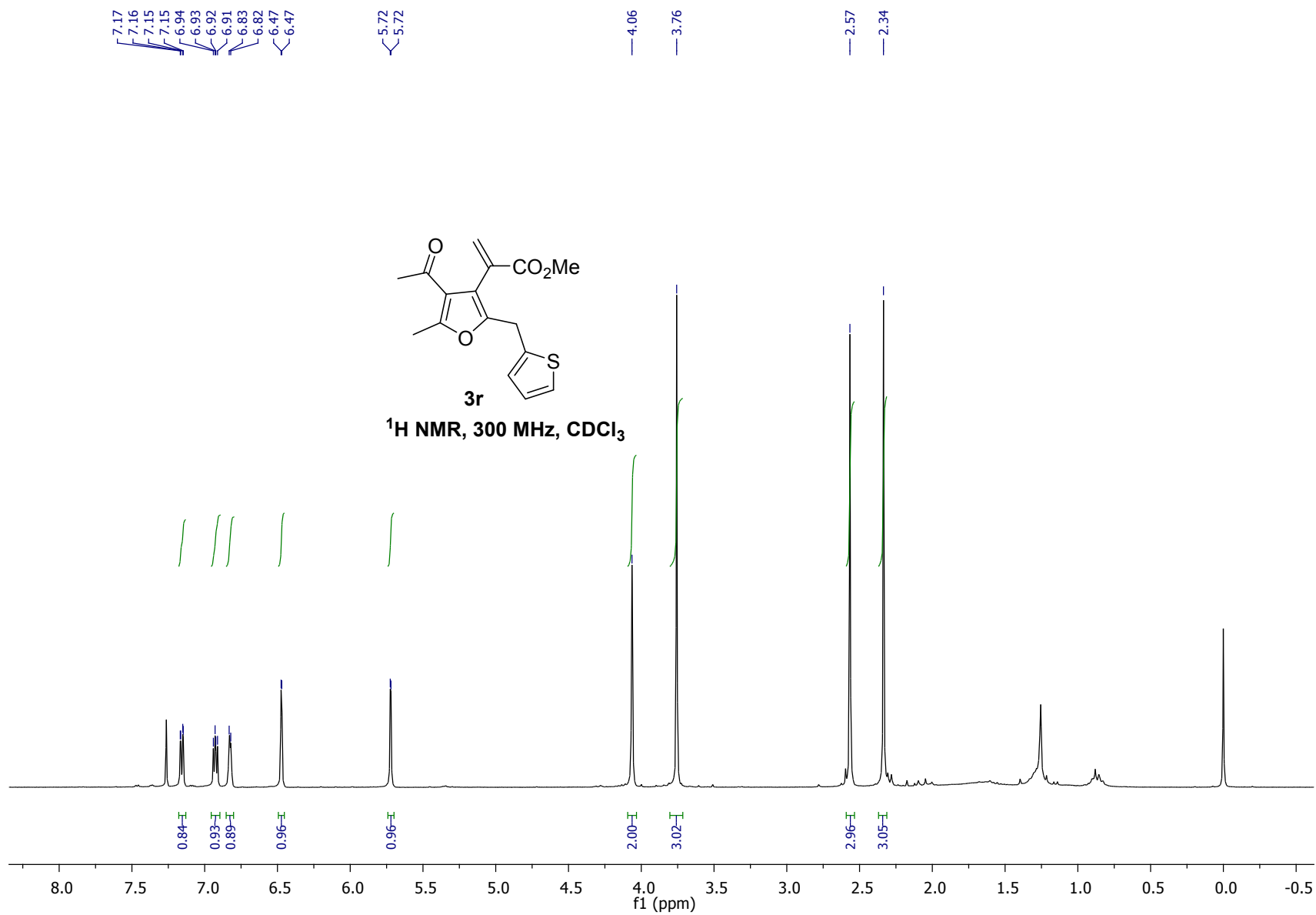


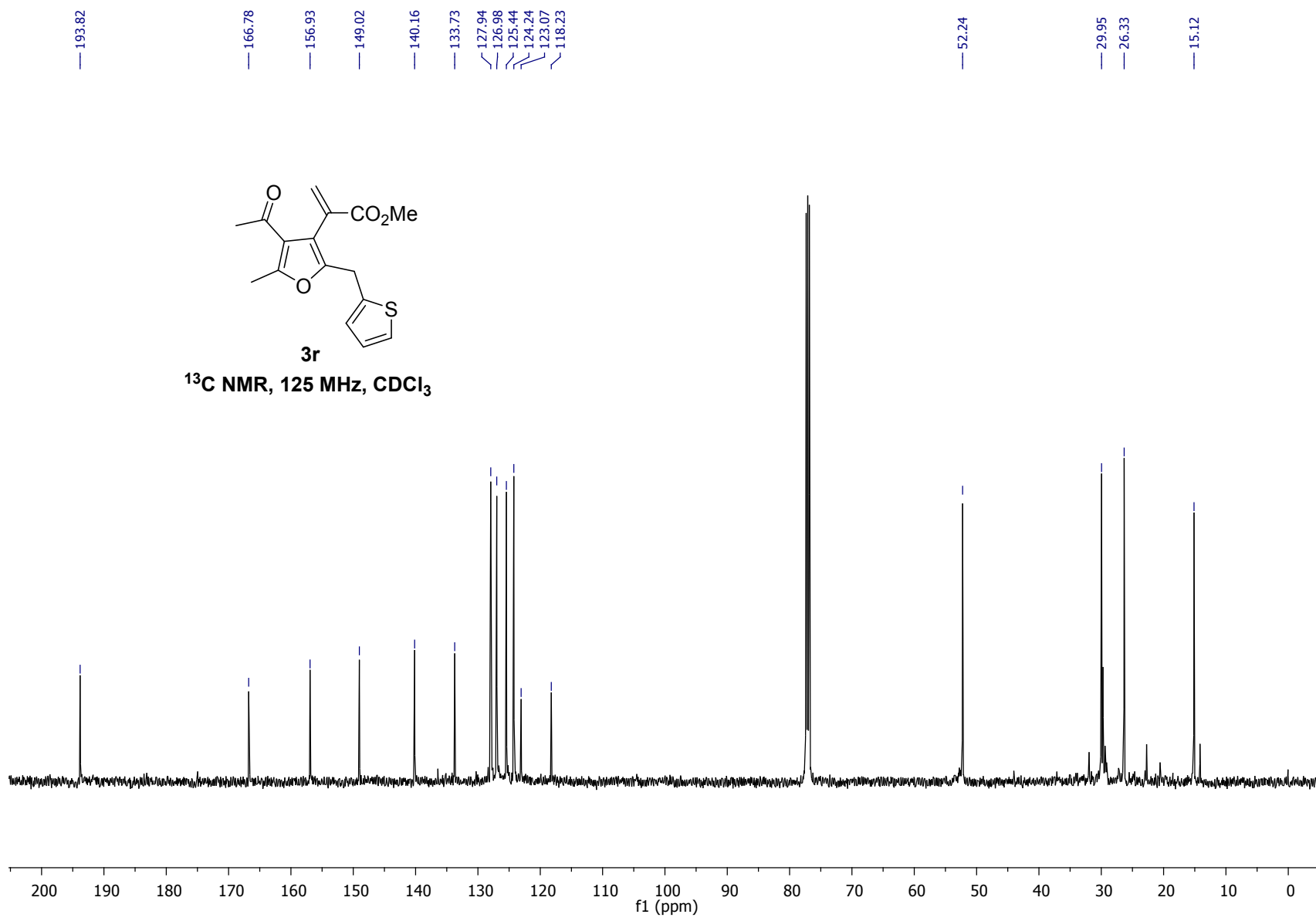


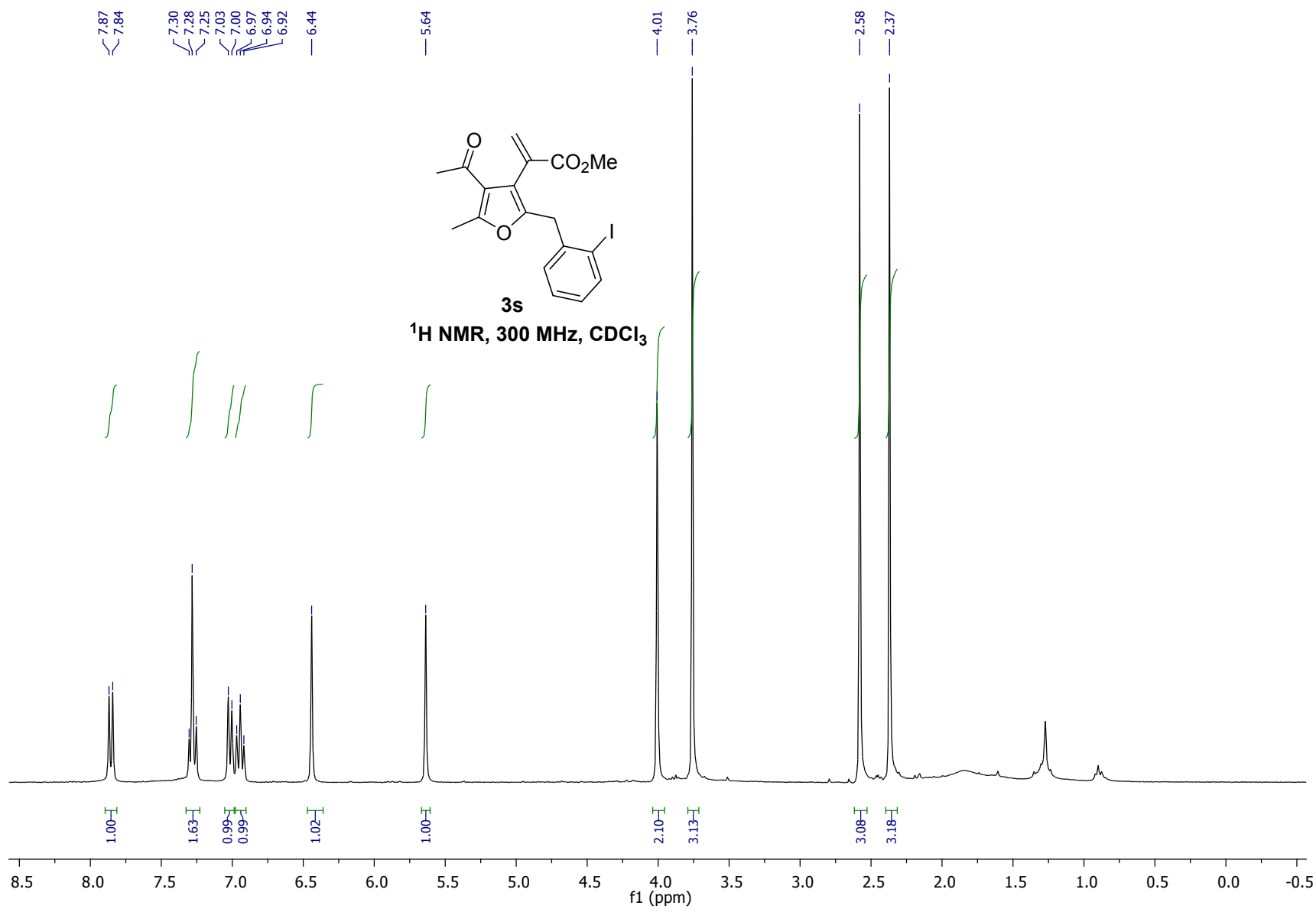


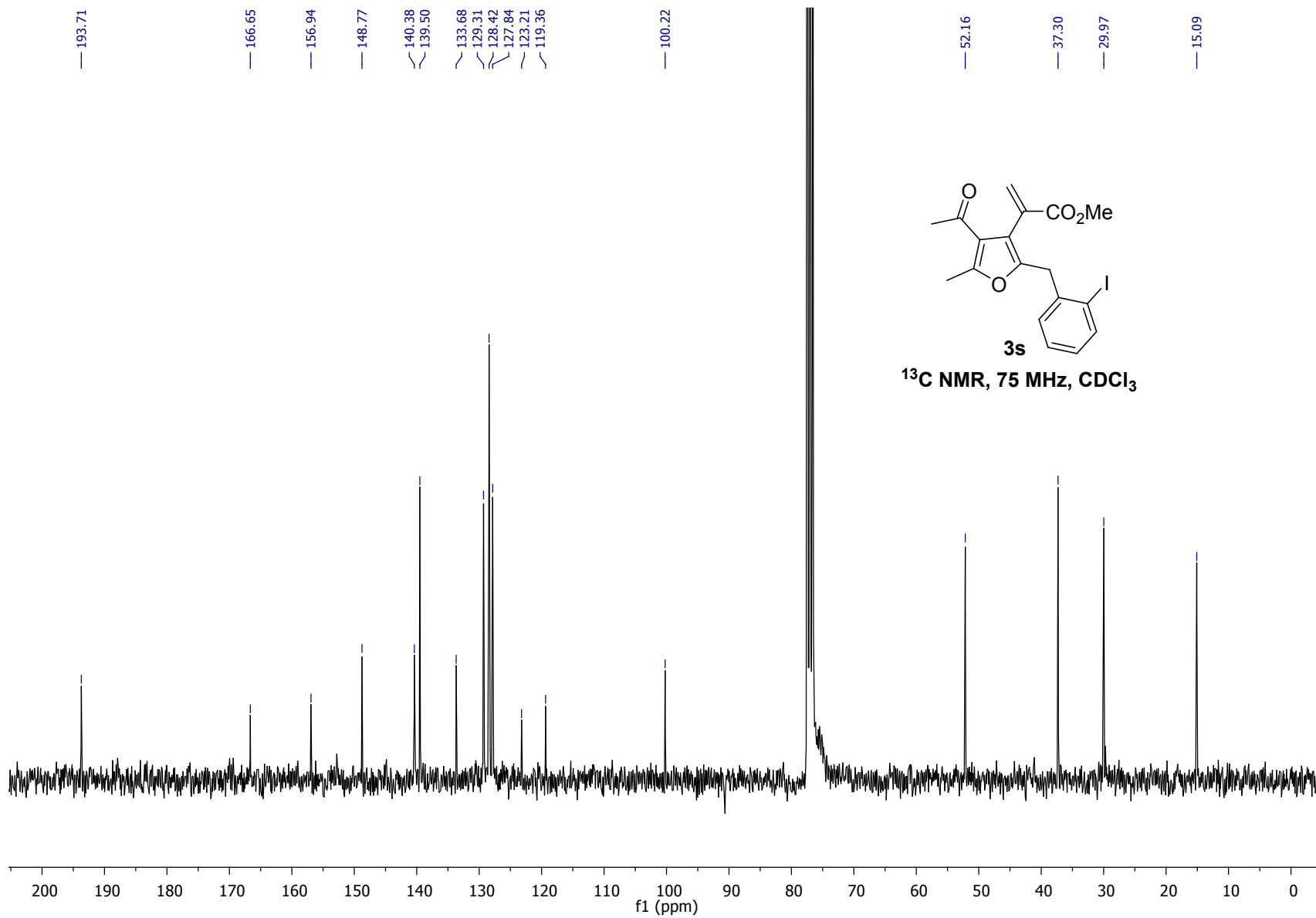










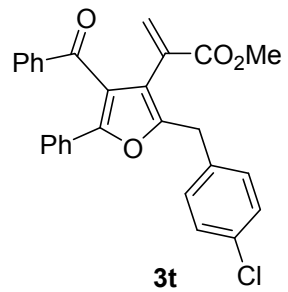


7.79
7.77
7.55
7.53
7.44
7.42
7.40
7.39
7.38
7.37
7.31
7.29
7.28
7.27
7.26
7.22
7.19
6.47
6.47

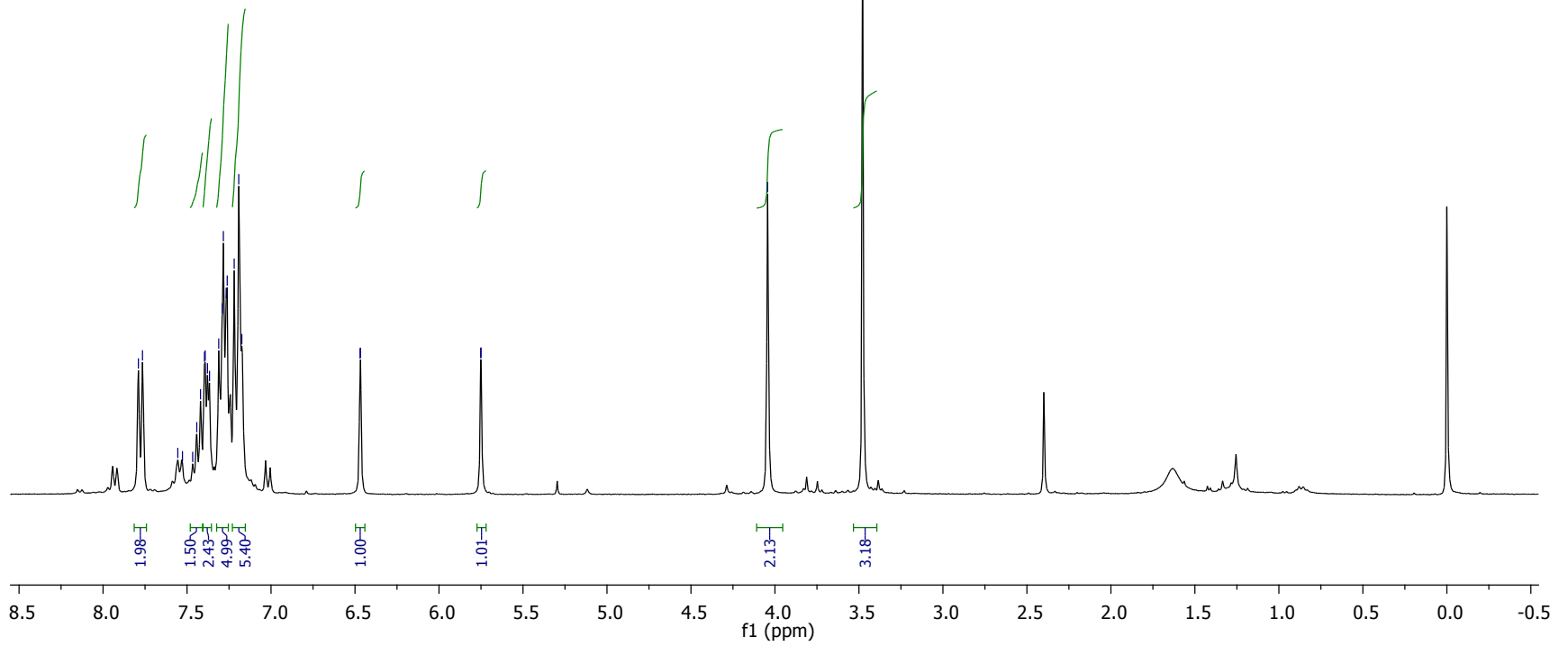
5.75
5.75

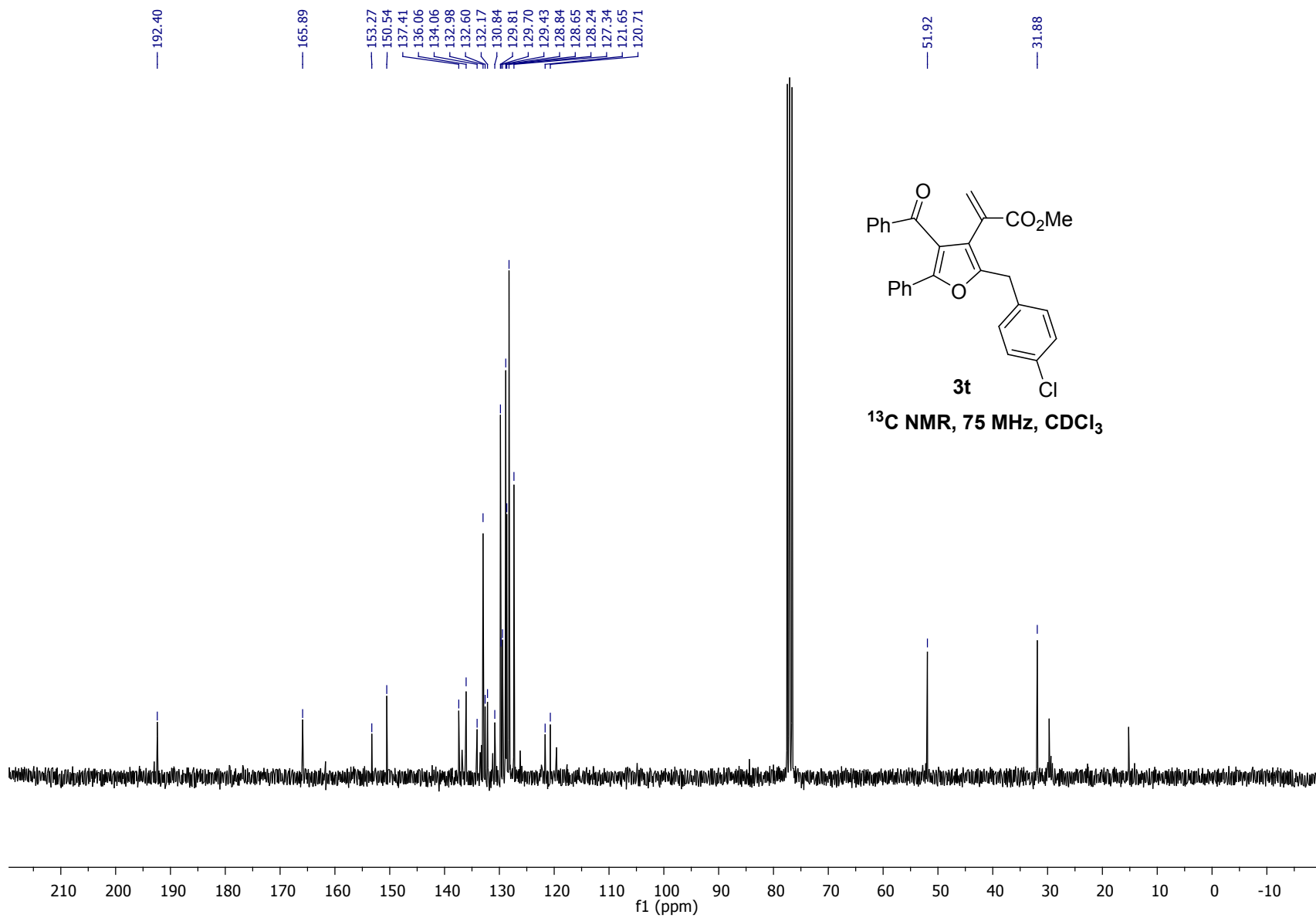
4.04

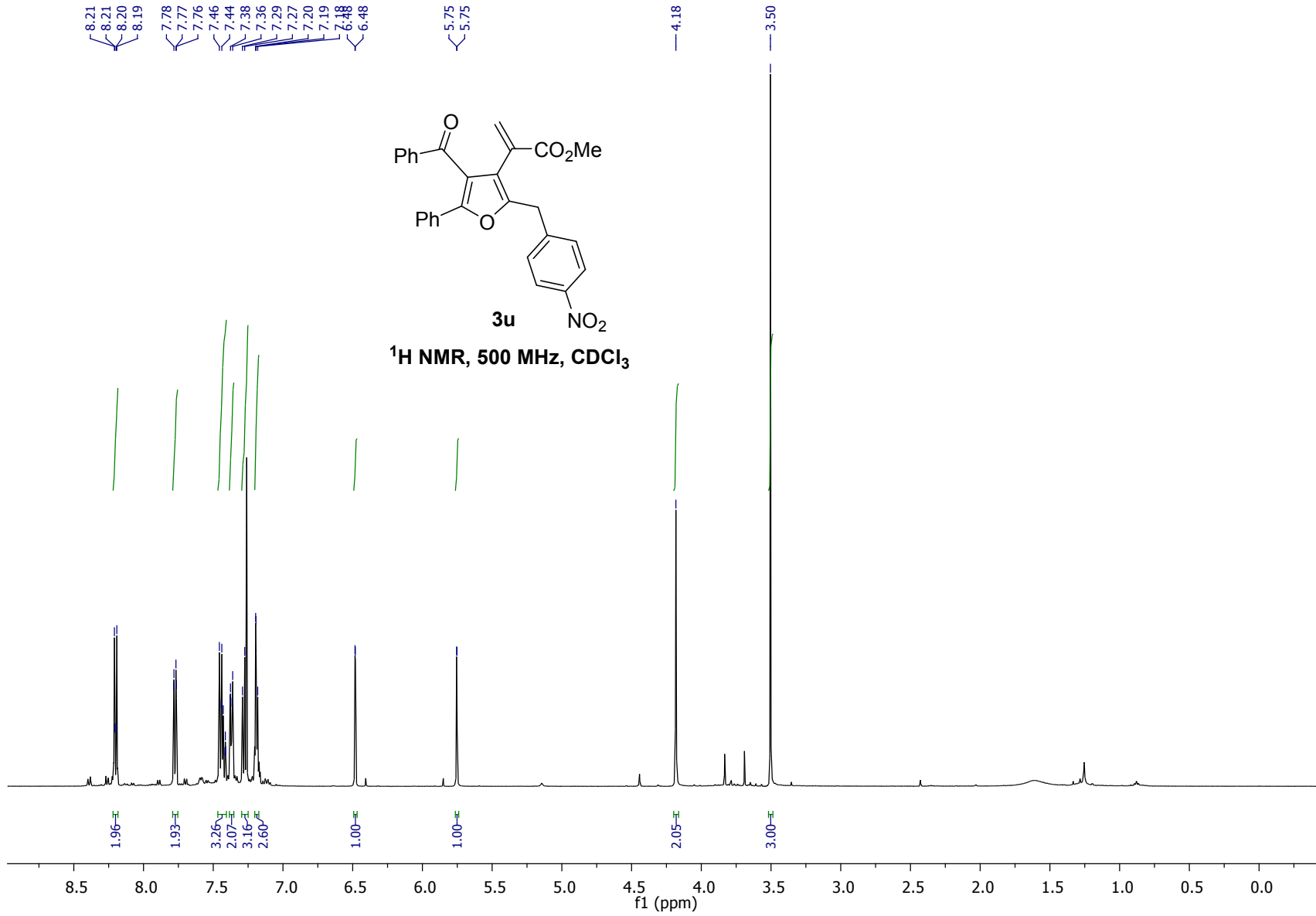
3.48

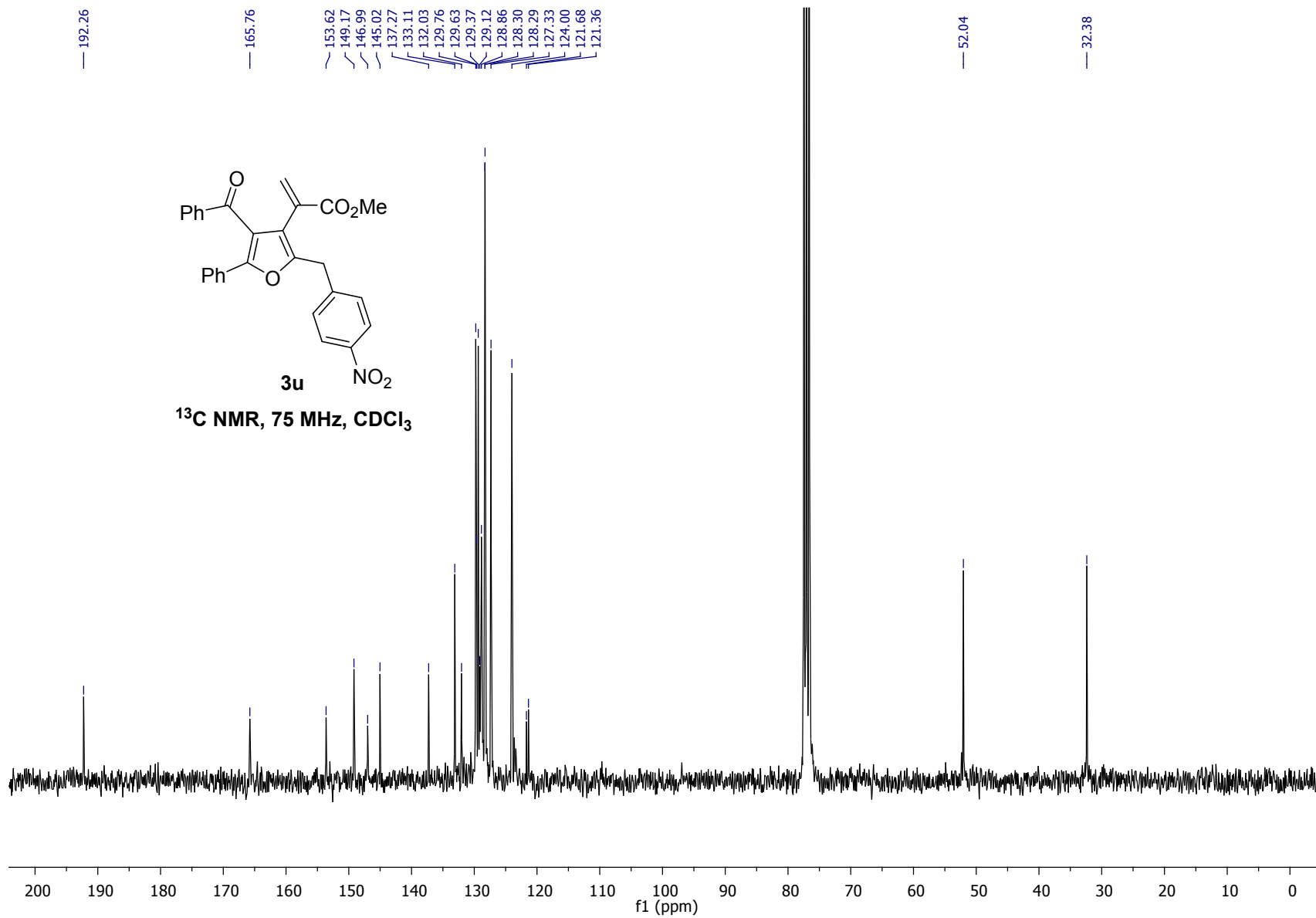


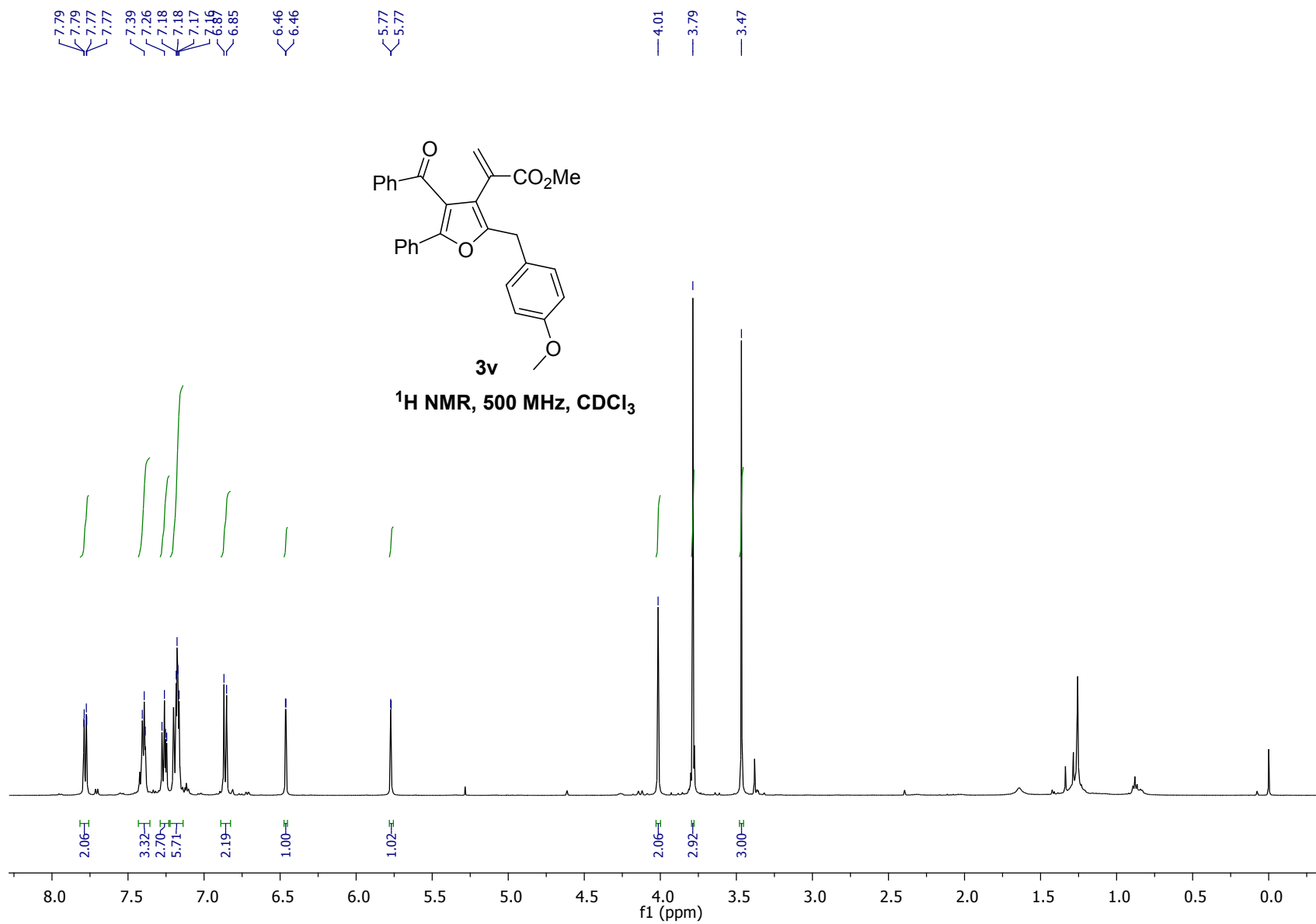
¹H NMR, 300 MHz, CDCl₃

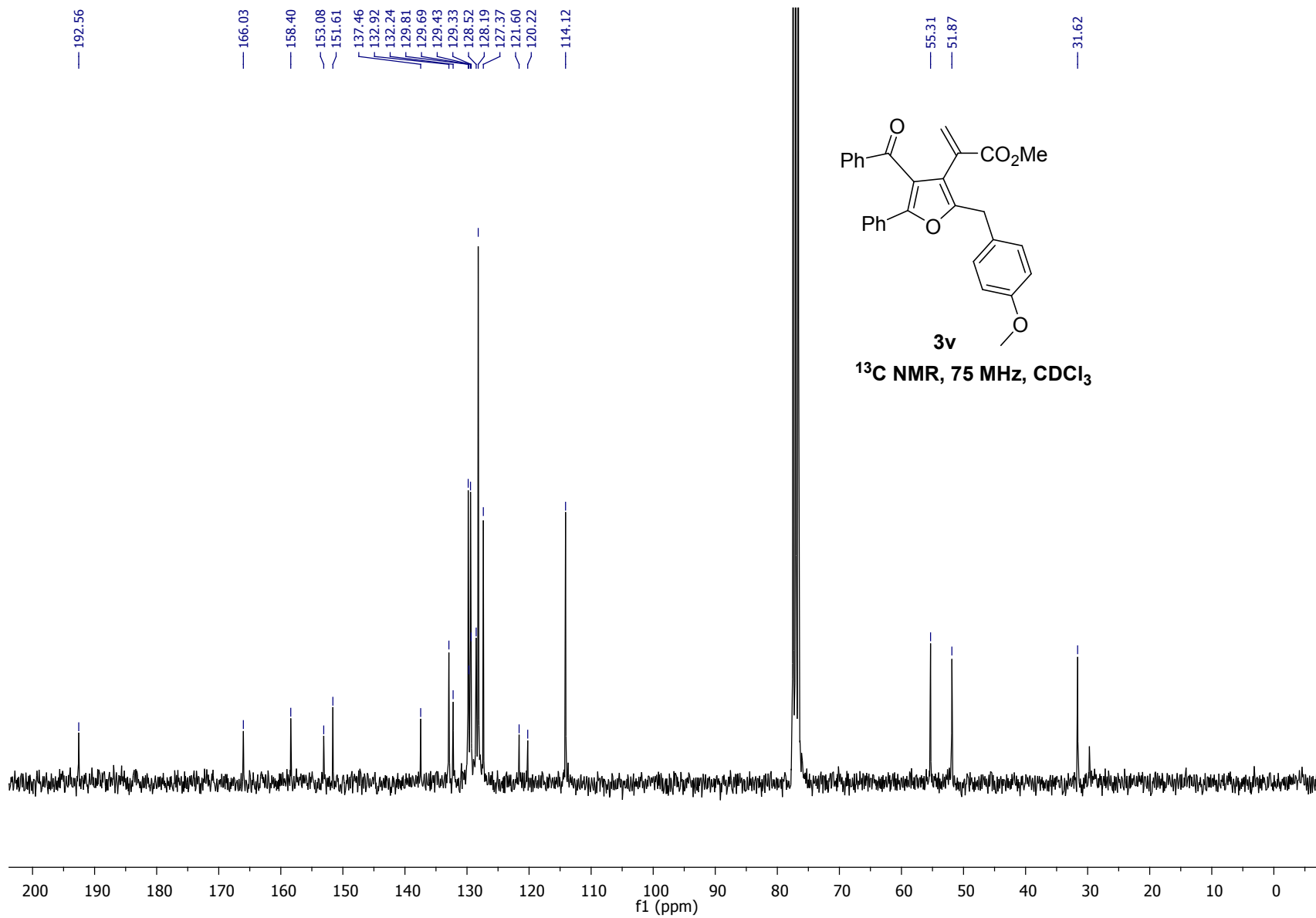


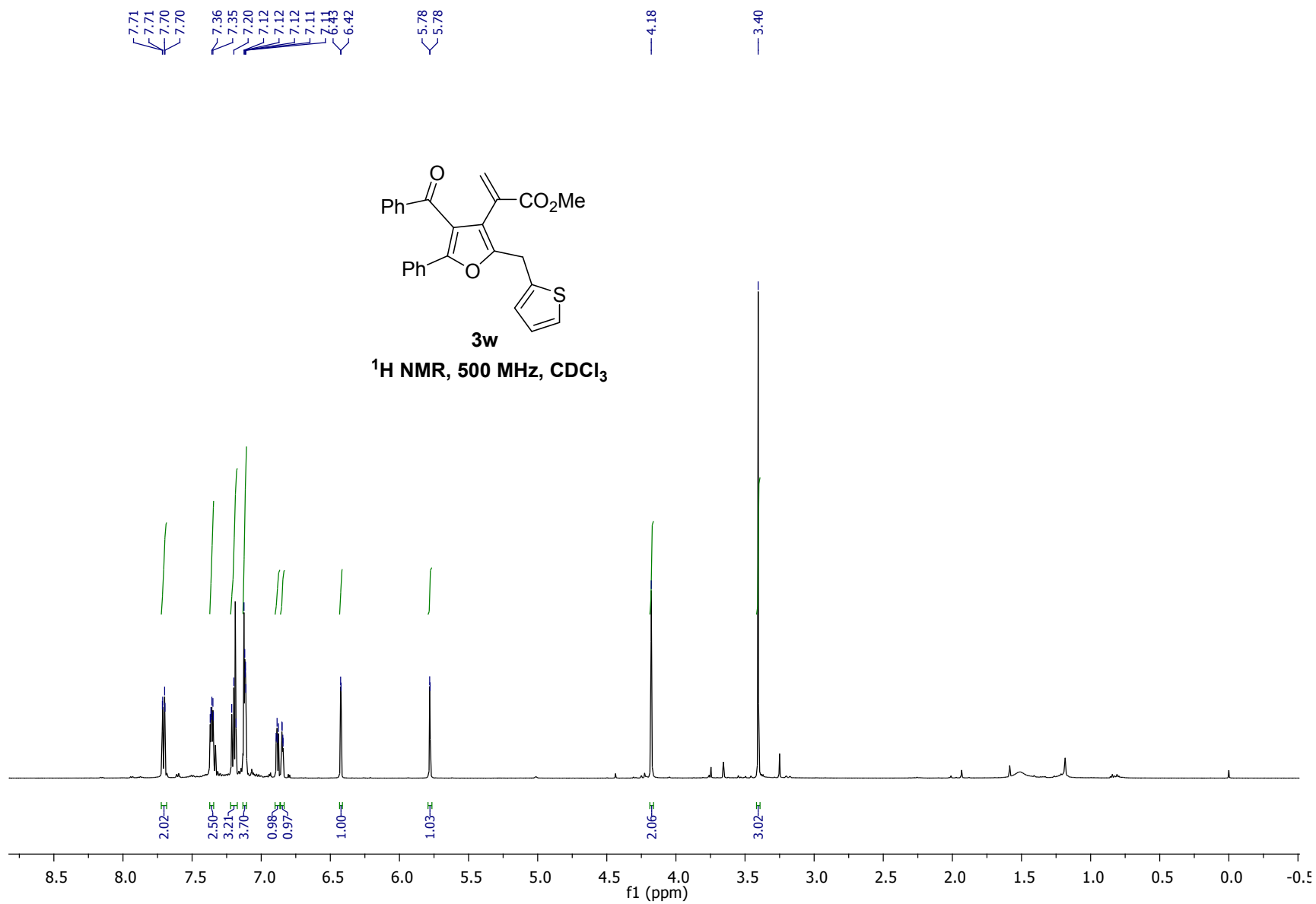


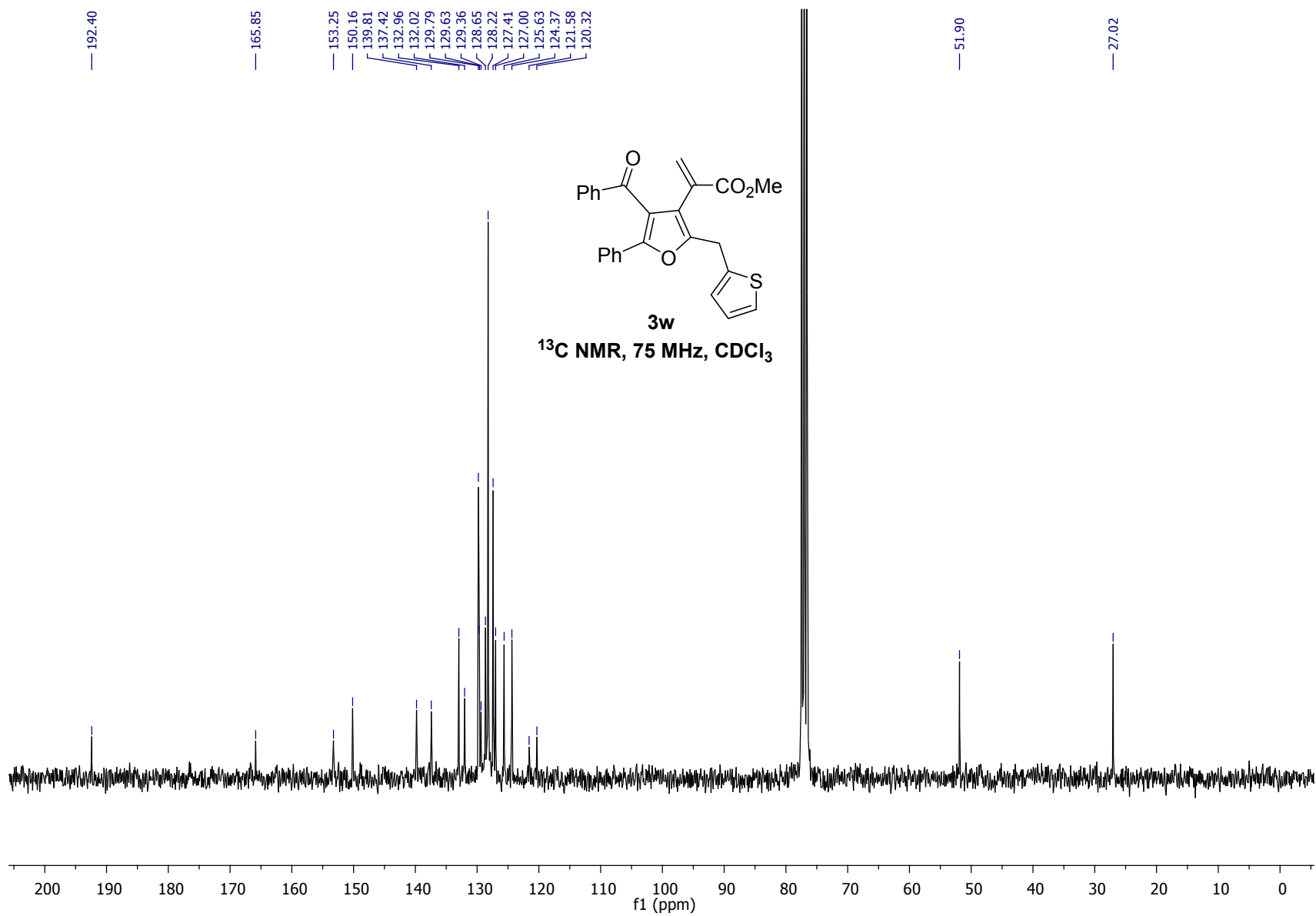


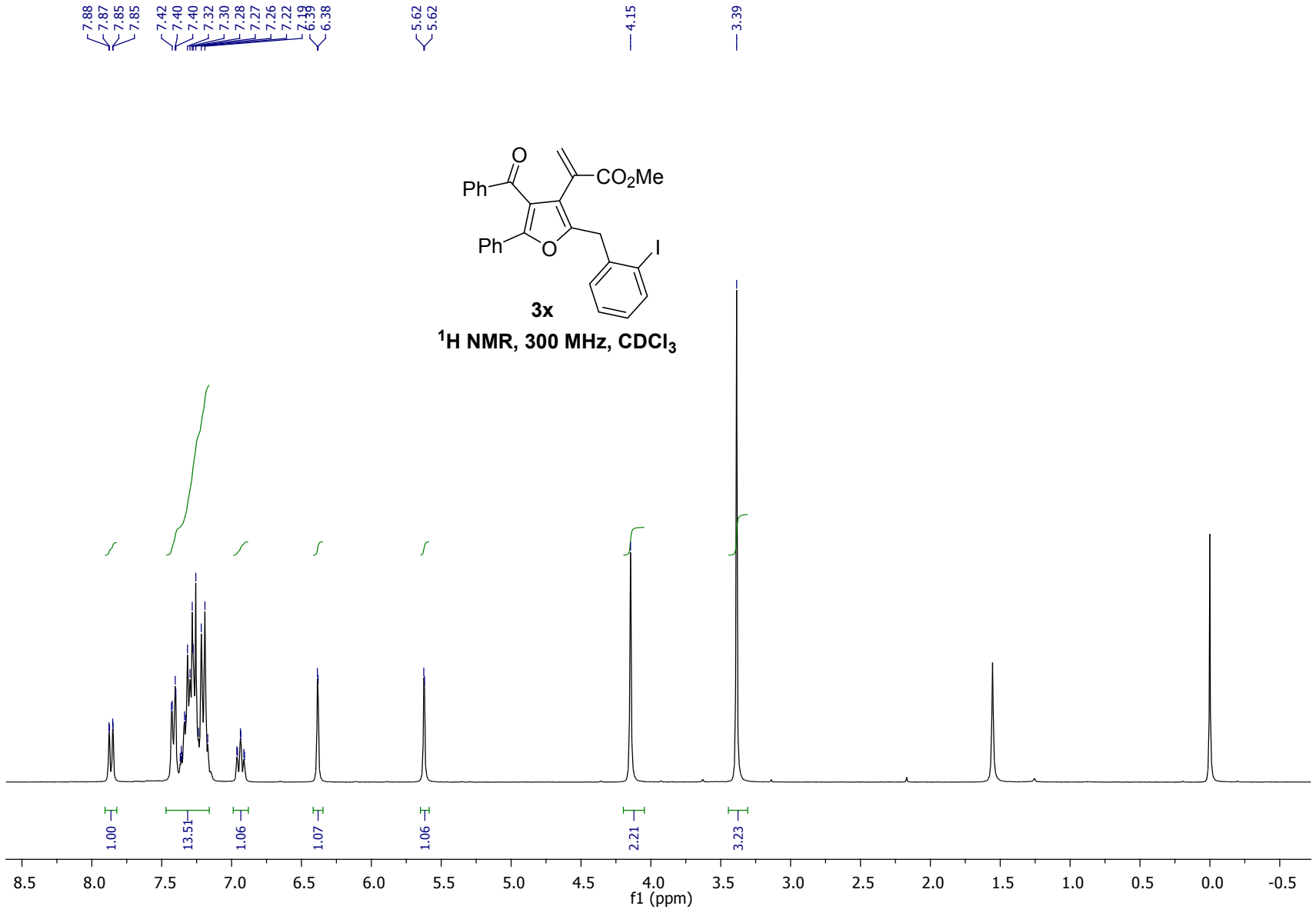


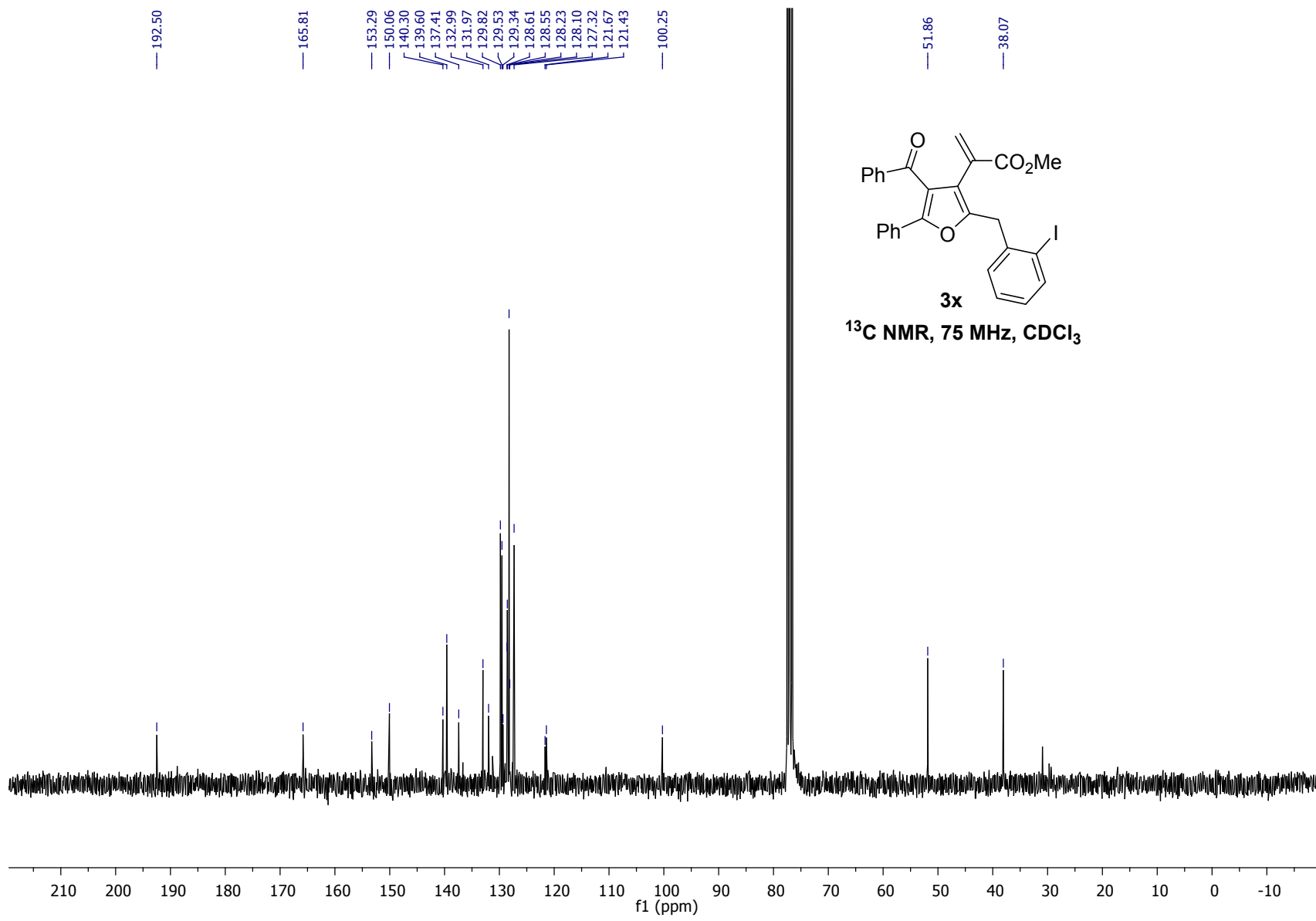


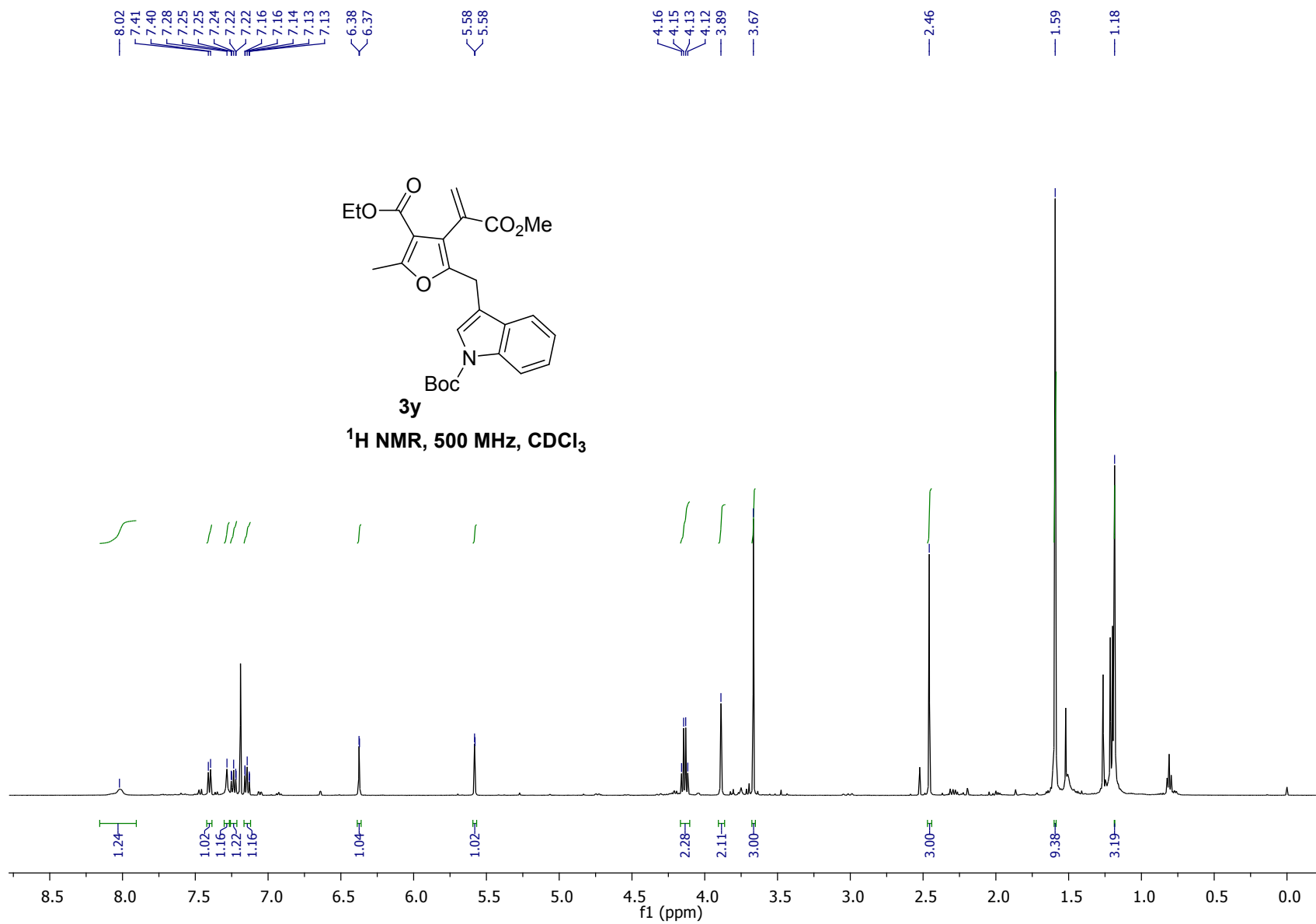


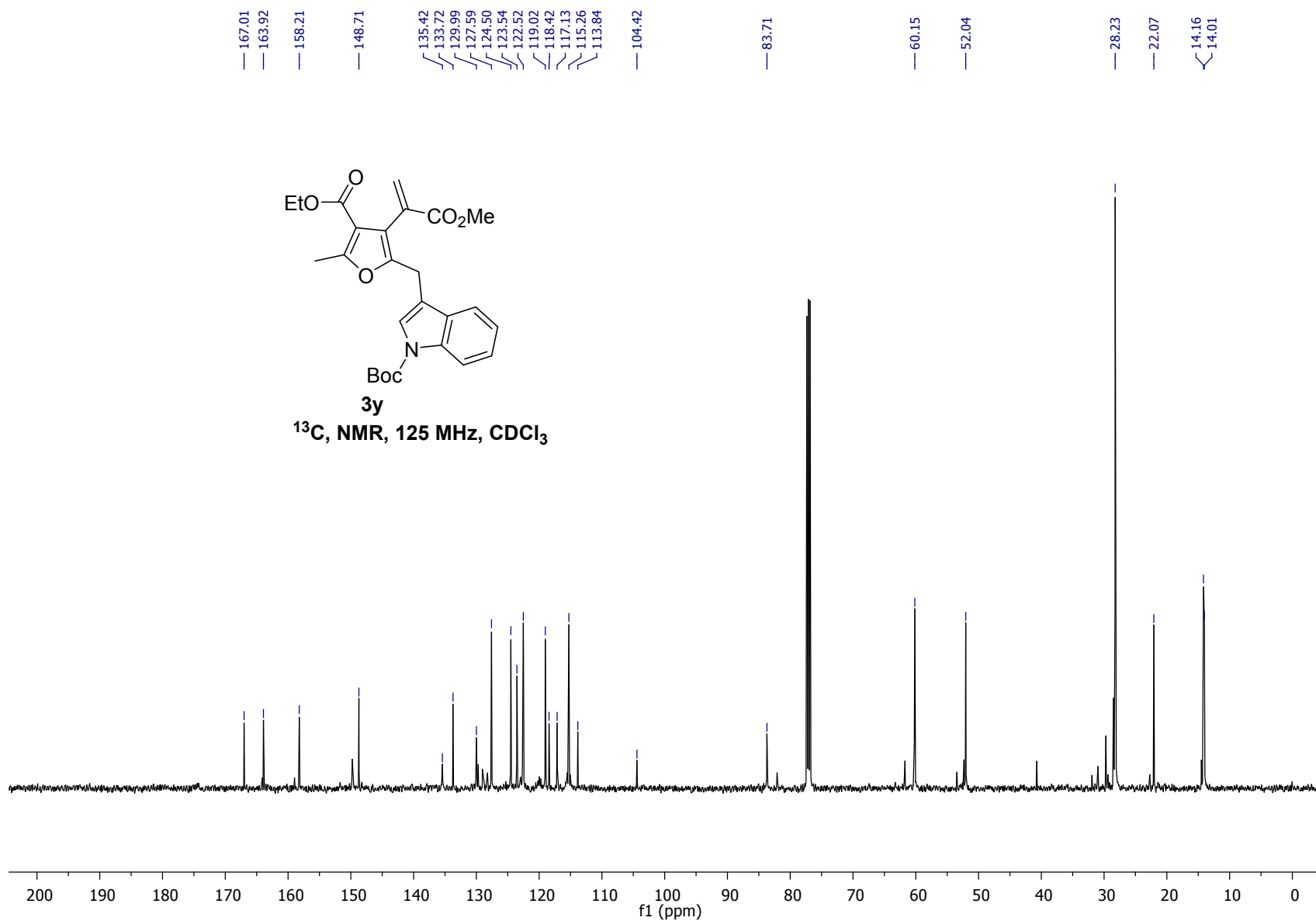


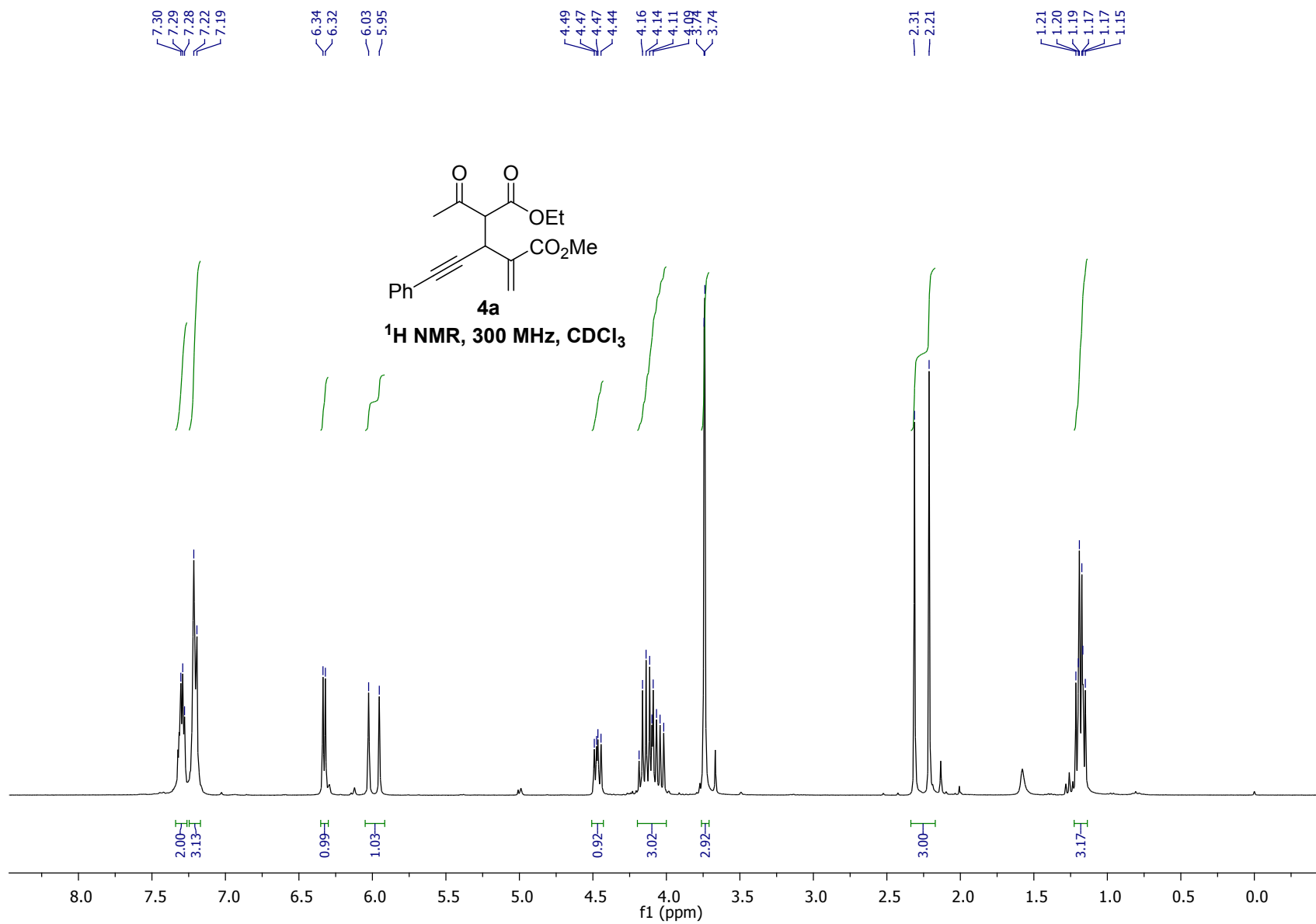


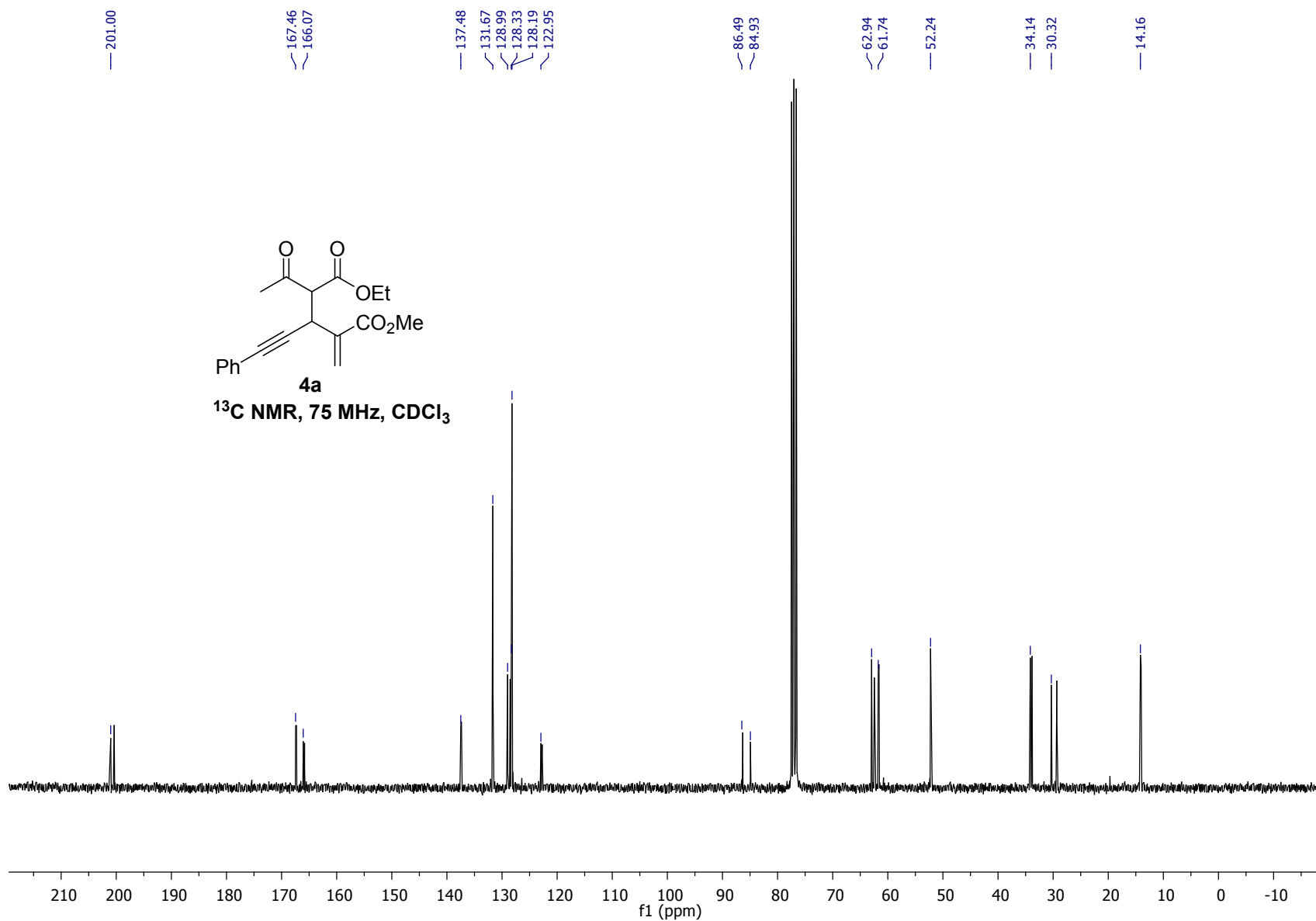


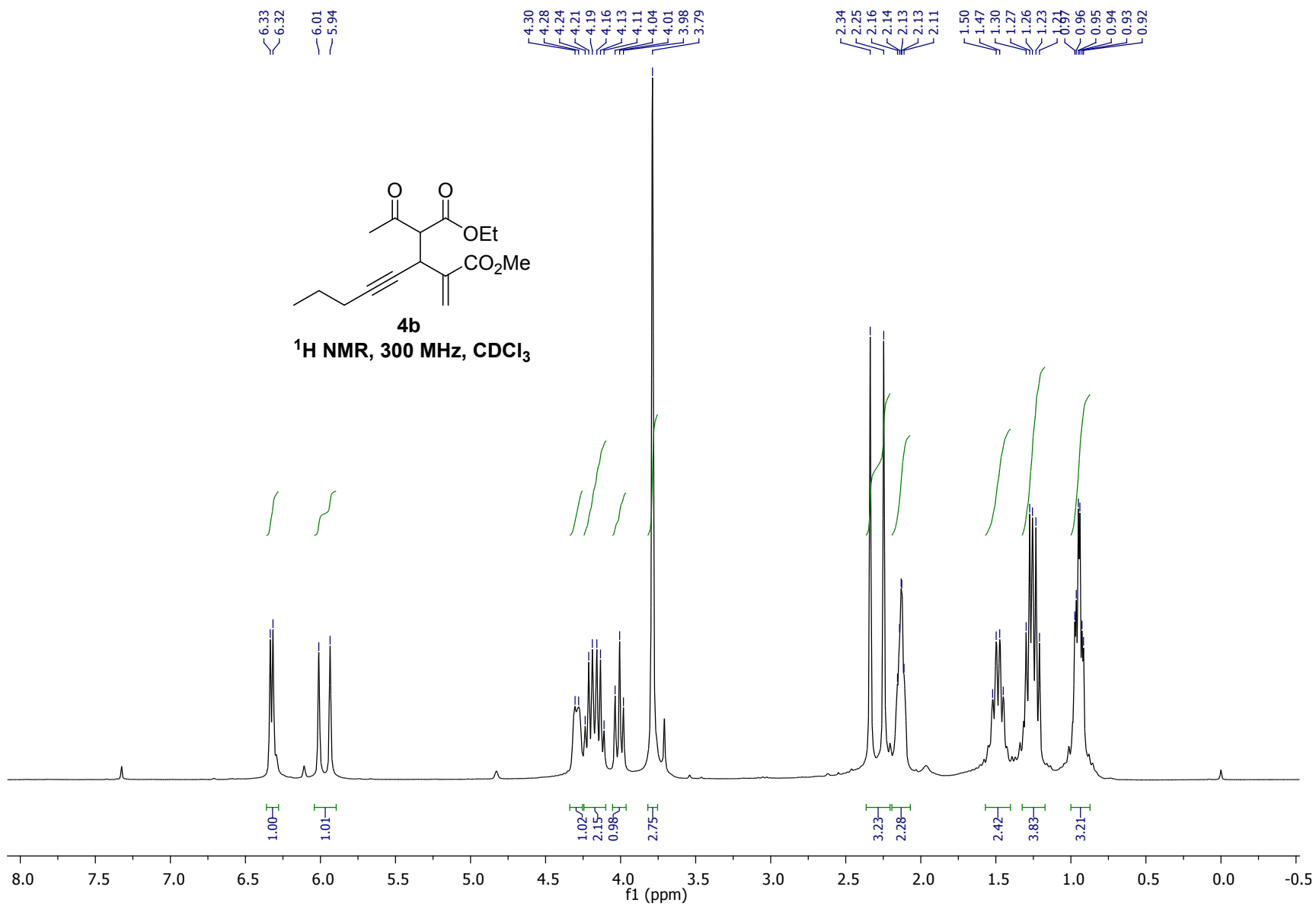


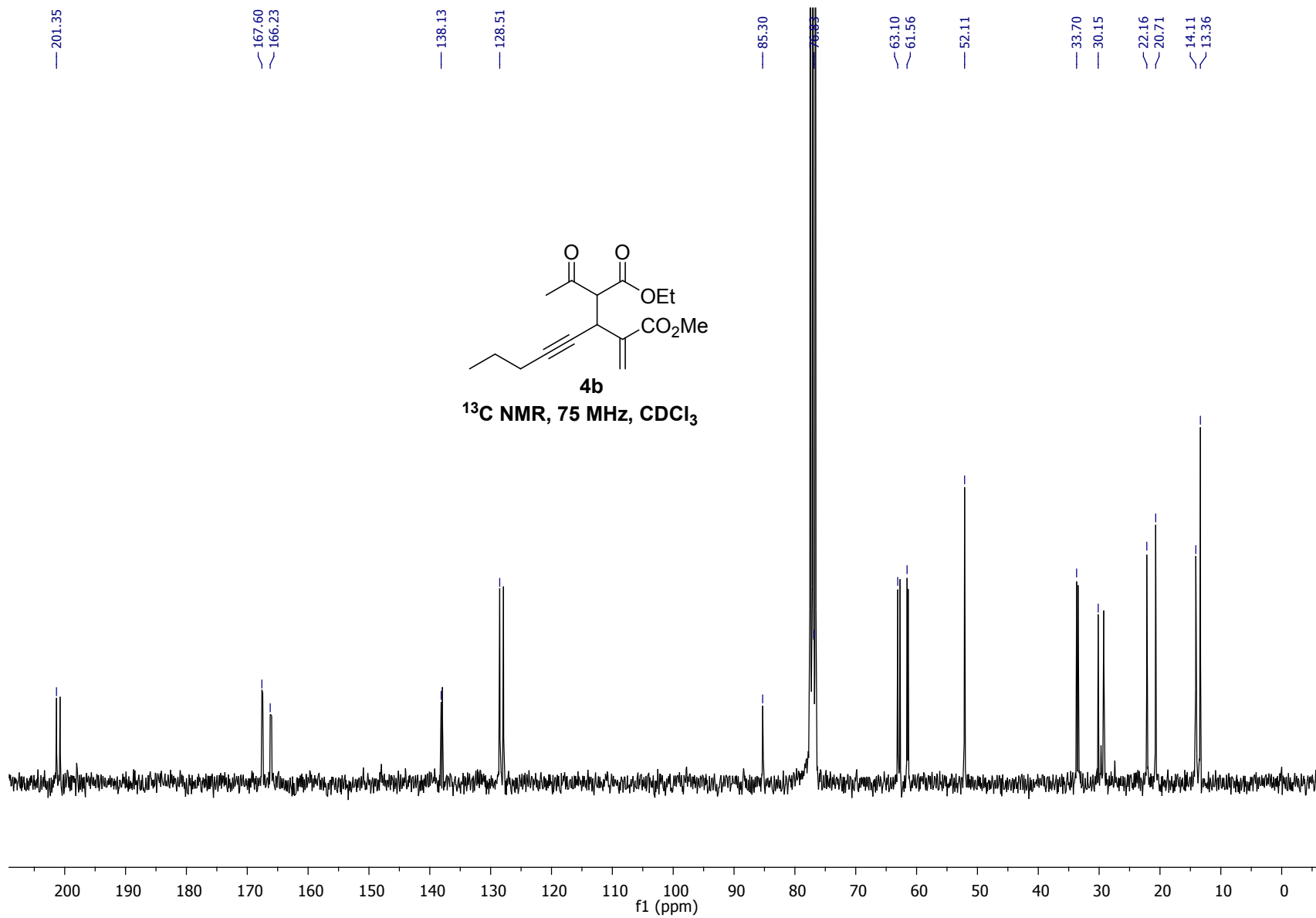


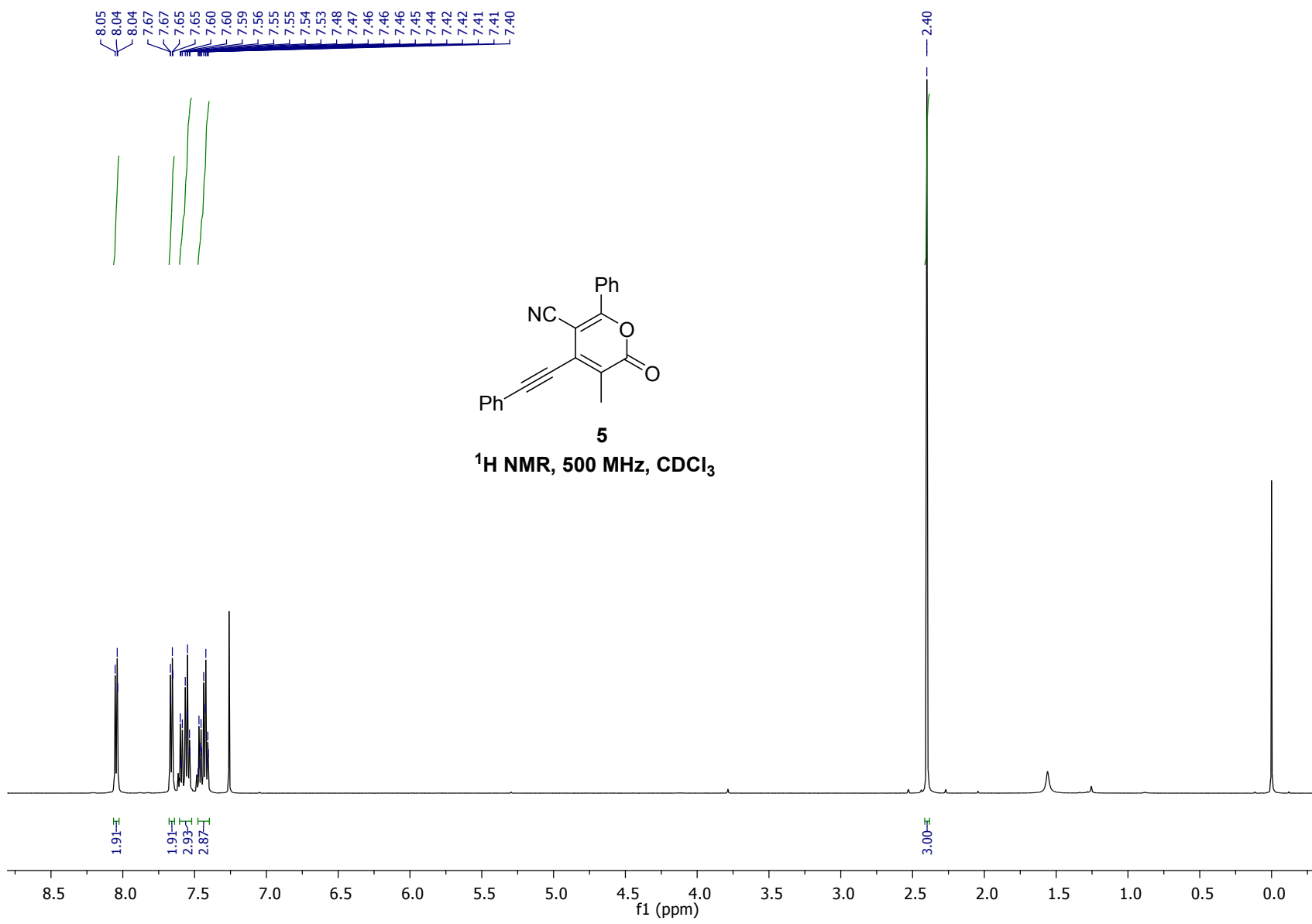


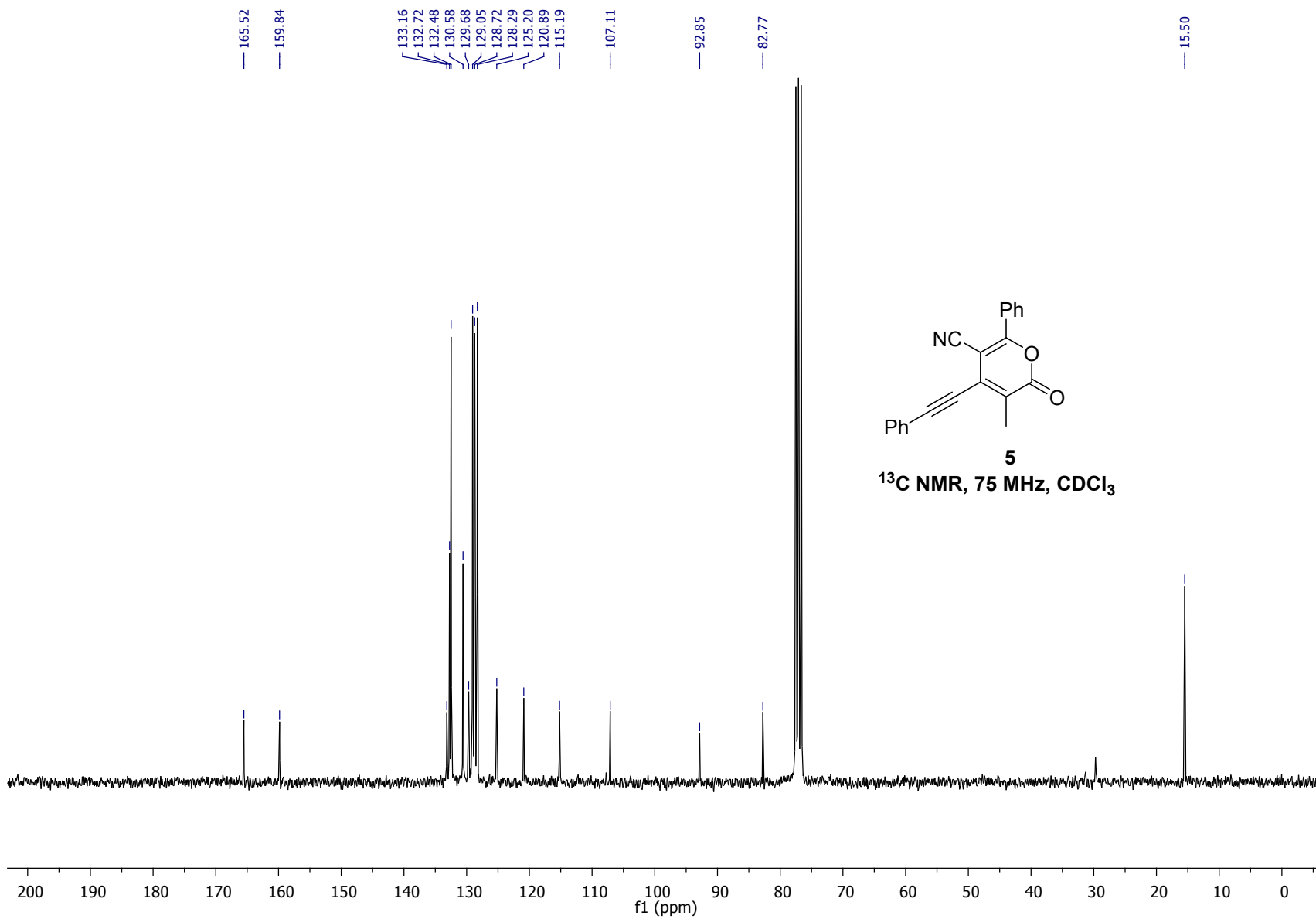


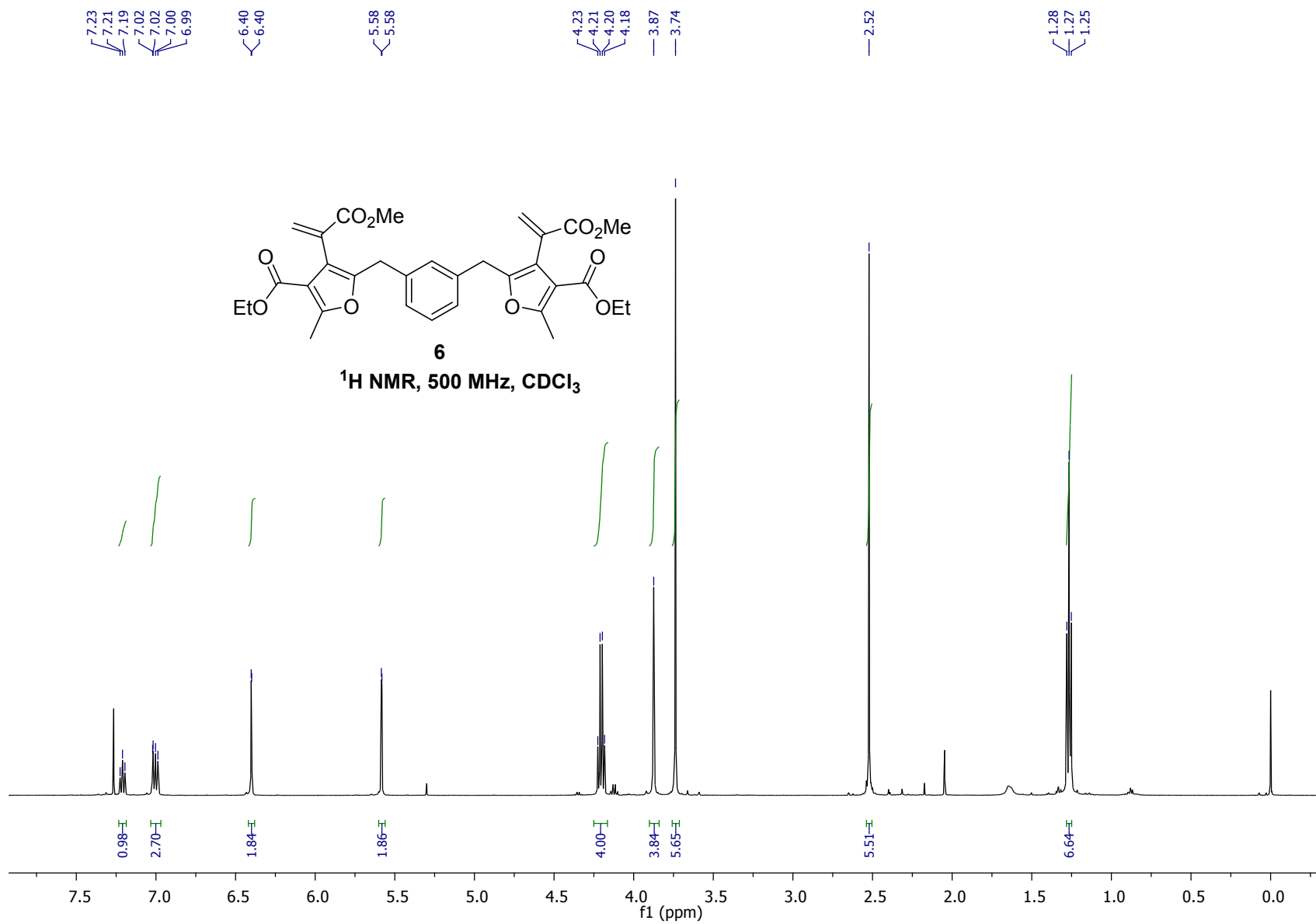


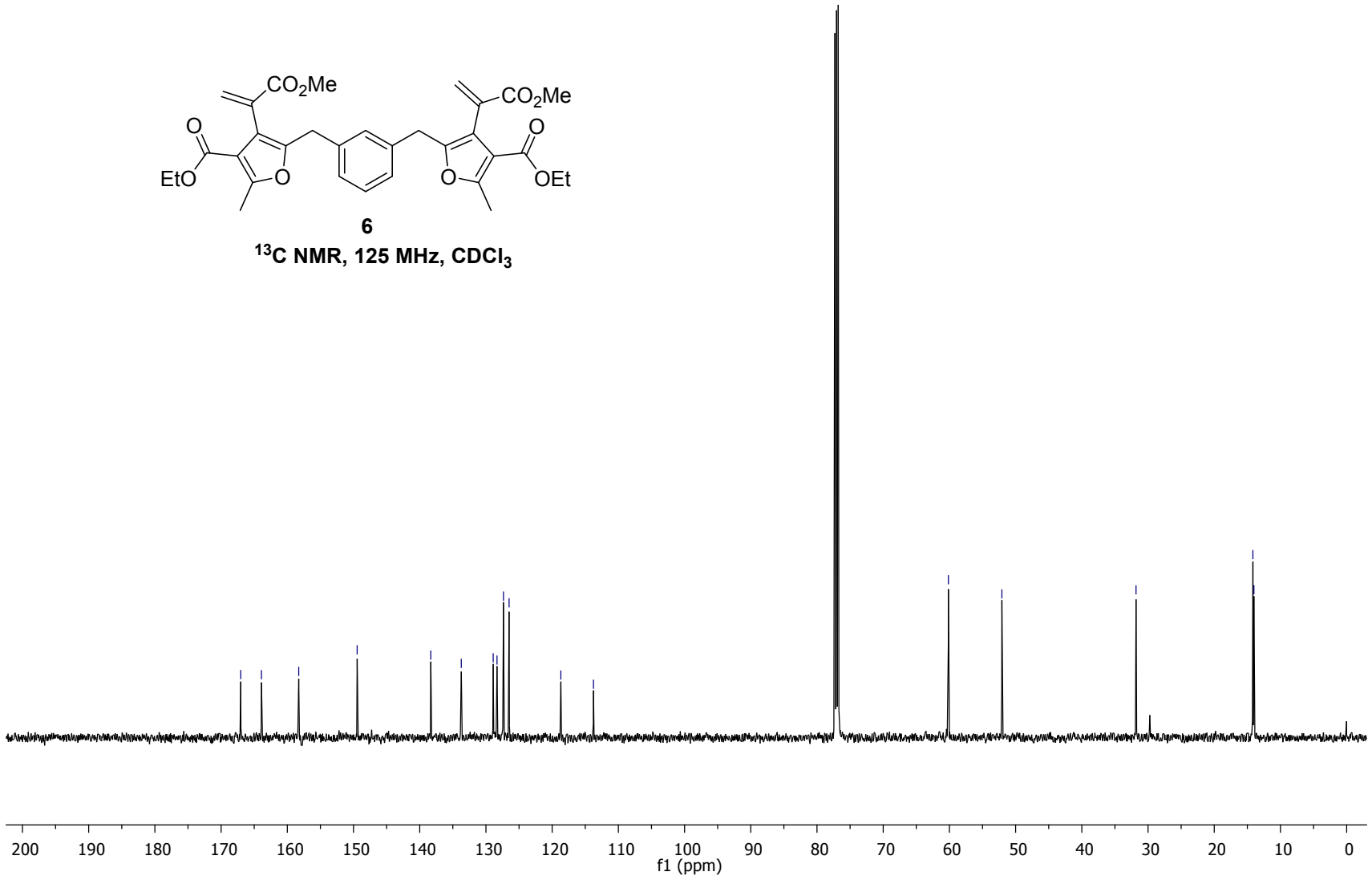
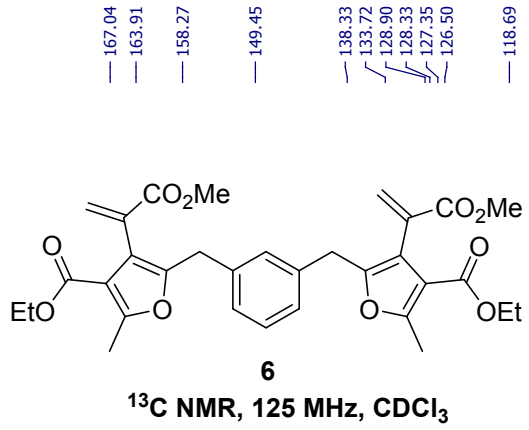


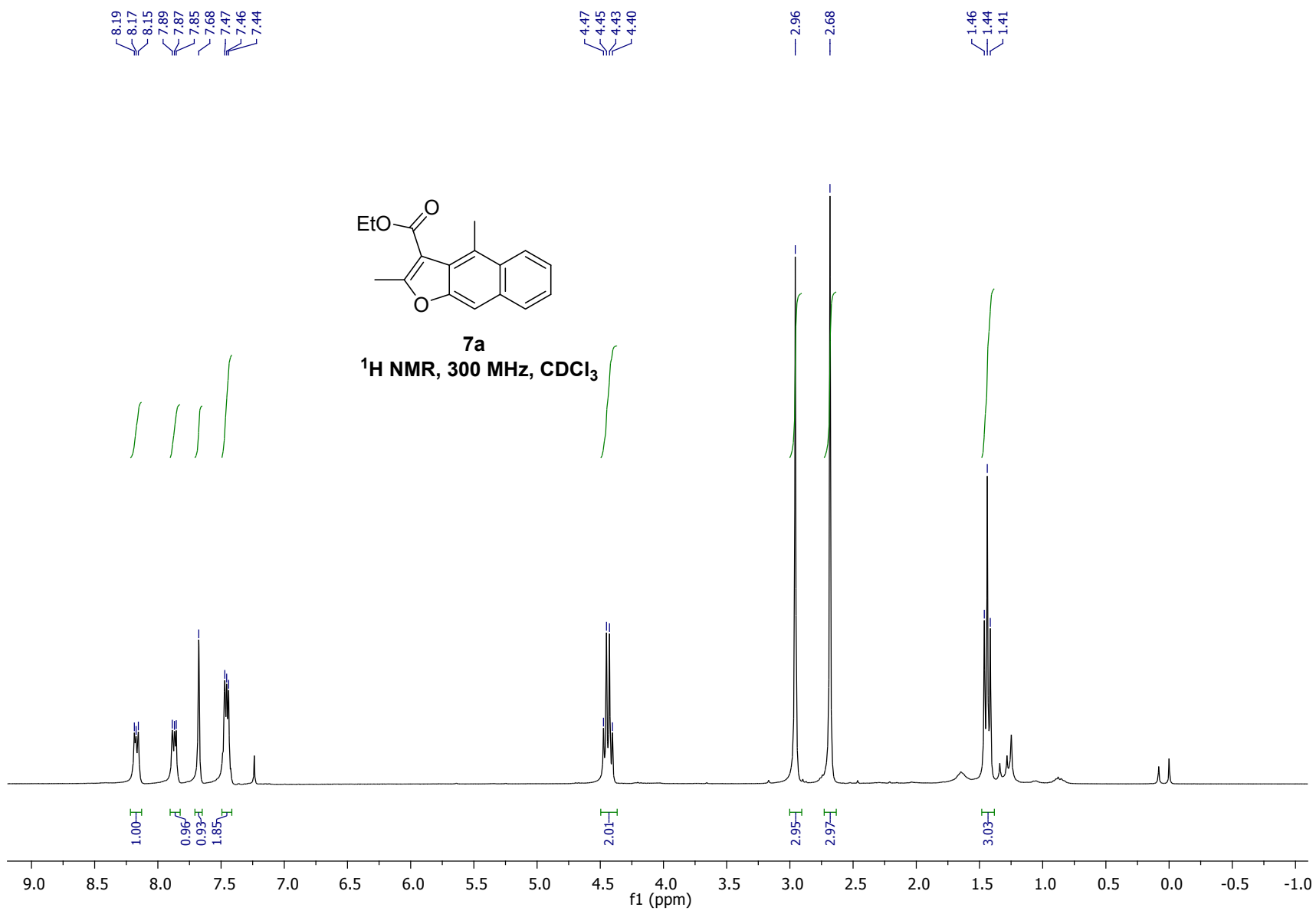


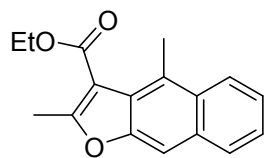












7a

¹³C NMR, 75 MHz, CDCl₃

