



Supporting Information

© Wiley-VCH 2008

69451 Weinheim, Germany

# Supporting Information

## Nickel Catalyzed Reductive Cyclization of Unactivated 1,6-Enynes in the Presence of Organozinc Reagents

Mao Chen, Yue Weng, Mian Guo, Hua Zhang and Aiwen Lei\*

*College of Chemistry and Molecular Science, Wuhan University, Wuhan, 430072, P. R. China*

[aiwenlei@whu.edu.cn](mailto:aiwenlei@whu.edu.cn)

### Experimental Details

**General.** All reactions were carried out under an atmosphere of nitrogen, unless otherwise indicated. Flasks were flame-dried and cooled under nitrogen prior to use. Dichloromethane was distilled from calcium hydride. Tetrahydrofuran (THF) was dried and distilled from sodium/benzophenone immediately prior to use under nitrogen atmosphere. CH<sub>3</sub>CN was dried over anhydrous sodium sulfate (Na<sub>2</sub>SO<sub>4</sub>).

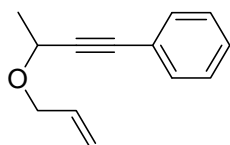
Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel in petroleum (boiling point is between 60-90°C). Gradient flash chromatography was conducted eluting with a continuous gradient from petroleum to the indicated solvent, and they are listed as volume/volume ratios.

<sup>1</sup>H and <sup>13</sup>C NMR data were recorded with a Varian Mercury (300 MHz) spectrometer with tetramethylsilane as an internal standard. All <sup>1</sup>H NMR spectra were reported in delta (δ) units, parts per million (ppm) downfield from the internal standard. Coupling constants are reported in Hertz (Hz). High resolution mass spectra (HRMS) were measured with a Waters Micromass GCT instrument or a Waters Q-ToF Premier instrument, accurate masses are reported for the molecular ion ([M]<sup>+</sup>, [M+1]<sup>+</sup>, or [M+23]<sup>+</sup>). E/Z ratios were recorded with a Varian GC 2000 gas

chromatography instrument with a FID detector. And GC yield were determined by the same instrument while naphthalene was used as the internal standard.

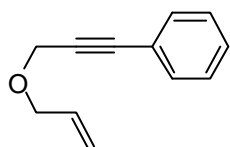
### Synthesis of the substrates for the reductive cyclization

Enynes **1a-1c**, **1e**, **3a**, **3b**, **3f** and **3g** were prepared according to the references.



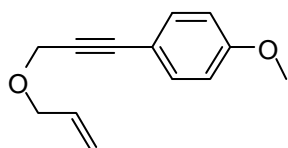
Compound **1a**

**(3-(allyloxy)but-1-ynyl)benzene (1a)**.<sup>[1]</sup>  $^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ ):  $\delta$  7.45-7.43 (m, 2H), 7.38-7.31 (m, 3H), 6.02-5.92 (m, 1H), 5.34 (d,  $J = 17.4$  Hz, 1H), 5.22 (d,  $J = 10.2$  Hz, 1H), 4.45-4.43 (m, 1H), 4.32 (dd,  $J = 12.3, 5.1$  Hz, 1H), 4.04 (dd,  $J = 12.5, 6.0$  Hz, 1H), 1.54 (d,  $J = 6.6$  Hz, 3H);  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ ):  $\delta$  134.8, 132.0, 129.0, 128.5, 123.0, 117.6, 89.3, 85.3, 69.9, 65.3, 22.4.



Compound **1b**

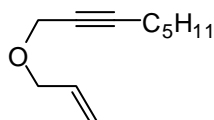
**(3-(allyloxy)prop-1-ynyl)benzene (1b)**.<sup>[2]</sup>  $^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ ):  $\delta$  7.34-7.30 (m, 2H), 7.16-7.15 (m, 3H), 5.88-5.71 (m, 1H), 5.21 (dd,  $J = 17.4, 1.5$ Hz, 1H), 5.09 (d,  $J = 10.2$  Hz, 1H), 4.23 (s, 2H), 3.99 (d,  $J = 5.7$  Hz, 2H);  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ ):  $\delta$  134.1, 131.8, 128.5, 128.4, 122.7, 117.9, 86.4, 85.2, 70.7, 57.9.



Compound **1c**

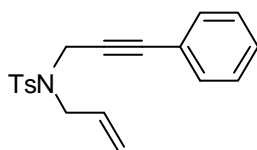
**1-(3-(allyloxy)prop-1-ynyl)-4-methoxybenzene (1c)**.<sup>[3]</sup>

$^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ ):  $\delta$  7.31 (d,  $J = 7.8$  Hz, 2H), 6.75 (d,  $J = 7.5$  Hz, 2H), 5.92-5.83 (m, 1H), 5.26 (d,  $J = 17.4$  Hz, 1H), 5.15 (d,  $J = 10.5$  Hz, 1H), 4.29 (s, 2H), 4.05 (d,  $J = 5.4$  Hz, 2H), 3.72 (s, 3H);  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ ):  $\delta$  159.9, 134.4, 133.5, 118.0, 115.0, 114.1, 86.4, 83.8, 70.9, 58.2, 55.5.



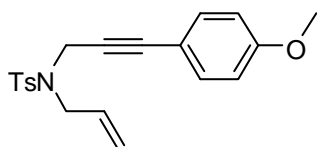
Compound **1e**

**1-(allyloxy)oct-2-yne (1e).**<sup>[4]</sup>  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.96-5.87 (m, 1H), 5.30 (dd,  $J = 17.1, 1.5$  Hz, 1H), 5.20 (d,  $J = 10.2$  Hz, 1H), 4.14 (s, 2H), 4.05 (d,  $J = 5.7$  Hz, 2H), 2.22 (t,  $J = 7.1$  Hz, 2H), 1.54-1.50 (m, 2H), 1.36-1.33 (m, 4H), 0.90 (t,  $J = 6.9$  Hz, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  134.4, 117.7, 87.3, 76.0, 70.6, 57.9, 31.3, 28.5, 22.4, 18.9, 14.1.



Compound **3a**

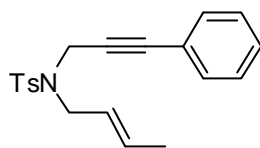
**N-allyl-4-methyl-N-(3-phenylprop-2-ynyl)benzenesulfonamide (3a).**<sup>[2]</sup>  $^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ ):  $\delta$  7.78 (d,  $J = 8.1$  Hz, 2H), 7.26-7.24 (m, 5H), 7.06 (d,  $J = 7.5$  Hz, 2H), 5.87-5.74 (m, 1H), 5.33 (d,  $J = 17.1$  Hz, 1H), 5.27 (d,  $J = 9.9$  Hz, 1H), 4.31 (s, 2H), 3.89 (d,  $J = 6.3$  Hz, 2H), 2.34 (s, 3H).



Compound **3b**

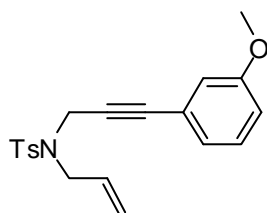
**N-allyl-N-(3-(4-methoxyphenyl)prop-2-ynyl)-4-methylbenzenesulfonamide (3b).**<sup>[2]</sup>  $^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ ):  $\delta$  7.42 (d,  $J = 7.2$  Hz, 2H), 6.89 (d,  $J = 8.1$  Hz, 2H), 6.67 (d,  $J = 8.1$  Hz, 2H), 6.42 (d,  $J = 7.5$  Hz, 2H), 5.46-5.40 (m, 1H), 4.98 (d,  $J = 17.7$  Hz, 1H), 4.90 (d,  $J = 10.2$  Hz, 1H), 3.94 (s, 2H), 3.54 (d,  $J = 6.6$  Hz, 2H), 3.42 (s, 3H), 1.99 (s,

3H);  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ ):  $\delta$  159.8, 143.6, 136.2, 133.1, 132.3, 129.7, 127.9, 119.9, 114.4, 113.9, 85.8, 80.3, 55.4, 49.4, 37.0, 21.6.



Compound **3g**

**(E)-N-(but-2-enyl)-4-methyl-N-(3-phenylprop-2-ynyl)benzenesulfonamide (3g)**.<sup>[5]</sup>  $^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ ):  $\delta$  7.76 (d,  $J = 8.1$  Hz, 2H), 7.26-7.23 (m, 5H), 7.06 (d,  $J = 6.6$  Hz, 2H), 5.80-5.69 (m, 1H), 5.48-5.39 (m, 1H), 4.29 (s, 2H), 3.81 (d,  $J = 6.6$  Hz, 2H), 2.33 (s, 3H), 1.71 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ ):  $\delta$  143.7, 136.3, 131.9, 131.8, 129.8, 128.6, 128.4, 128.1, 125.0, 122.6, 85.8, 82.2, 48.9, 36.7, 21.7, 18.1.



Compound **3c**

**N-allyl-N-(3-(3-methoxyphenyl)prop-2-ynyl)-4-methylbenzenesulfonamide (3c)**.

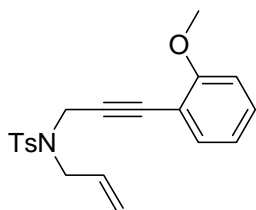
To a solution of N-allyl-4-methylbenzenesulfonamide (8.5g, 40mmol), prop-2-yn-1-ol (3.2mL, 54mmol), and triphenyl-phosphane (14.2g, 54mmol) in anhydrous THF (130mL) was added diisopropylazodicarboxylate (10.7mL, 54mmol) at  $0^\circ\text{C}$ , and the reaction mixture was gradually warmed to room temperature, and then stirred overnight. The solvent was removed under vacuum, and the residue was purified on silica gel to give compound

N-allyl-4-methyl-N-(prop-2-ynyl)benzenesulfonamide (7.6g) in 76% yield.

To a solution of N-allyl-4-methyl-N-(prop-2-ynyl)benzenesulfonamide (1.25g, 5mmol), 1-iodo-3-methoxybenzene (1.28g, 5.5mmol),  $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$  (70.2mg, 0.1mmol) and CuI (38.1mg, 0.2mmol) in dry  $\text{CH}_3\text{CN}$  (5mL) under nitrogen atmosphere was added  $\text{NEt}_3$  (1.4mL, 10mmol) at  $0^\circ\text{C}$ , and the reaction was warmed to room temperature, and then stirred overnight. The solvent was removed under

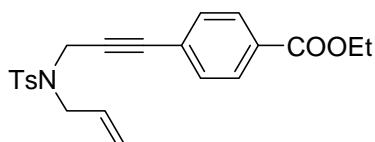
vacuum, and the residue was purified on silica gel (ethyl acetate/ petroleum = 1/40 ) to give **3c** (1.65g) in 93% yield. <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>): δ 7.67 (d, *J* = 7.8 Hz, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 7.04 (t, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 8.1 Hz, 1H), 6.56 (d, *J* = 7.8 Hz, 1H), 6.50 (s, 1H), 5.74-5.63 (m, 1H), 5.23 (d, *J* = 17.1 Hz, 1H), 5.16(d, *J* = 9.9 Hz, 1H), 4.20 (s, 2H), 3.79(d, *J* = 6.9 Hz, 2H), 3.67 (s, 3H), 2.23 (s, 3H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>): δ 159.4, 143.9, 136.2, 132.3, 129.8, 129.4, 128.0, 124.2, 123.4, 120.2, 117.2, 114.6, 85.9, 81.7, 55.5, 49.5, 36.9, 21.6; HRMS (APCI) calcd for C<sub>20</sub>H<sub>21</sub>NO<sub>3</sub>S [M]<sup>+</sup>: 355.1242; found 355.1251.

The remaining N-tethered enynes **3d** and **3e** were prepared using a procedure similar to that used to synthesize **3c**.



#### Compound **3d**

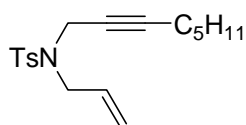
**N-allyl-N-(3-(2-methoxyphenyl)prop-2-ynyl)-4-methylbenzenesulfonamide (3d)**. 85% yield. <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>): δ 7.77 (d, *J* = 8.1 Hz, 2H), 7.28-7.19 (m, 3H), 6.93 (dd, *J* = 7.8, 1.6Hz, 1H), 6.84-6.80 (m, 2H), 5.85-5.76 (m, 1H), 5.34 (d, *J* = 15.9 Hz, 1H), 5.26 (d, *J* = 10.2 Hz, 1H), 4.36 (s, 2H), 3.91 (d, *J* = 6.6 Hz, 2H), 3.80 (s, 3H), 2.90 (s, 3H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>): δ 159.8, 143.1, 135.7, 133.2, 131.9, 129.6, 129.2, 127.6, 119.9, 119.8, 111.3, 110.2, 85.5, 82.1, 55.4, 48.9, 36.9, 21.2. HRMS (ESI) calcd for C<sub>20</sub>H<sub>21</sub>NO<sub>3</sub>S [M + Na]<sup>+</sup>:378.1140; found 378.1111.



#### Compound **3e**

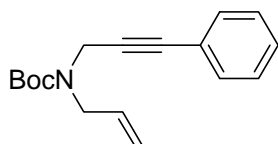
**ethyl 4-(3-(N-allyl-4-methylphenylsulfonamido)prop-1-ynyl)benzoate (3e)**. 83% yield. <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>): δ 7.91 (d, *J* = 8.1 Hz, 2H), 7.77 (d, *J* = 7.8 Hz, 2H), 7.25

(d,  $J = 7.5$  Hz, 2H), 7.11 (d,  $J = 8.1$  Hz, 2H), 5.87-5.74 (m, 1H), 5.35-5.26 (m, 2H), 4.41-4.32 (m, 4H), 3.89 (d,  $J = 6.3$  Hz, 2H), 2.34 (s, 3H), 1.40 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ ):  $\delta$  166.1, 143.8, 136.1, 132.2, 131.5, 130.3, 129.8, 129.4, 128.0, 126.9, 120.3, 85.2, 85.0, 61.5, 49.6, 36.9, 21.7, 14.5; HRMS (APCI) calcd for  $\text{C}_{22}\text{H}_{23}\text{NO}_4\text{S}$   $[\text{M}]^+$ : 397.1348; found 397.1353.



### Compound **3f**

To a solution of N-allyl-4-methylbenzenesulfonamide (2.11 g, 10mmol), oct-2-yn-1-ol (1.71g, 13.5mmol), and triphenyl-phosphane ( 3.54g, 13.5mmol) in anhydrous THF (25mL) was added diisopropylazodicarboxylate (2.9mL, 13.5mmol) at 0°C, and the reaction mixture was gradually warmed to room temperature, and then stirred overnight. The solvent was removed under vacuum. The residue was dissolved in ethyl acetate and the resulting solution was washed with brine, dried ( $\text{Na}_2\text{SO}_4$ ), filtered and concentrated in vacuum. The residue was purified on silica gel (ethyl acetate/ petroleum = 1/40) to afford **3f** (1.60g) in 50% yield.  $^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ ):  $\delta$  7.66 (d,  $J = 7.5$  Hz, 2H), 7.21 (d,  $J = 8.4$  Hz, 2H), 5.69-5.63 (m, 1H), 5.35-5.13 (m, 2H), 3.99 (s, 2H), 3.73 (d,  $J = 6.0$  Hz, 2H), 2.35 (s, 3H), 1.83-1.80 (m, 2H), 1.19-1.13 (m, 6H), 0.80 (t,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ ):  $\delta$  143.4, 136.5, 132.5, 129.5, 128.1, 119.8, 86.5, 72.5, 49.1, 36.6, 31.2, 28.3, 22.3, 21.7, 18.6, 14.2. HRMS (ESI) calcd for  $\text{C}_{18}\text{H}_{25}\text{NO}_2\text{S}$   $[\text{M} + \text{Na}]^+$ : 342.1504; found 342.1506.



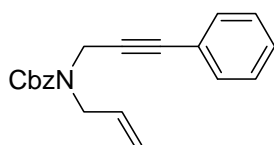
### Compound **3h**

**tert-butyl allyl(3-phenylprop-2-ynyl)carbamate (3h).**

To a solution of tert-butyl prop-2-ynylcarbamate (2.62g, 16.9mmol), iodobenzene

(3.57g, 17.5mmol), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (141.1mg, 0.2mmol) and CuI (77.3mg, 0.4mmol) in dry CH<sub>3</sub>CN (20mL) under nitrogen atmosphere was added NEt<sub>3</sub> (3.5g, 35mmol) at 0°C, and the reaction was warmed to room temperature, and then stirred overnight. The solvent was removed under vacuum, and the residue was purified on silica gel (ethyl acetate/ petroleum = 1/40) to give tert-butyl 3-phenylprop-2-ynylcarbamate (3.2g) in 82% yield.

To a solution of tert-butyl 3-phenylprop-2-ynylcarbamate (2.31g, 10mmol) in THF (50mL) was added sodium hydride (0.6g of a 60% dispersion in mineral oil, 15mmol). After stirring for 30 min, allyl bromide (1.45g, 12mmol) was added to the above solution at 0°C, and the reaction was then warmed to room temperature gradually and stirred for 2 hours. The reaction was quenched by addition of a saturated solution of NH<sub>4</sub>Cl (25 mL), and the mixture was extracted with ethyl acetate (3×20 mL). The combined organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under vacuum, and the residue was purified on silica gel (ethyl acetate/ petroleum = 1/40) to give **3h** (1.47g) in 54% yield. <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>): δ 7.43-7.40 (m, 2H), 7.31-7.29 (m, 3H), 5.89-5.76 (m, 1H), 5.24-5.16 (m, 2H), 4.25-4.20 (m, 2H), 4.00 (d, *J* = 5.4 Hz, 2H), 1.49 (s, 9H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>): δ 155.1, 133.6, 131.7, 128.6, 128.3, 123.0, 85.1, 83.4, 80.3, 48.7, 36.3, 28.5; HRMS (APCI) calcd for C<sub>17</sub>H<sub>21</sub>NO<sub>2</sub> [M]<sup>+</sup>: 271.1572; found 271.1562.



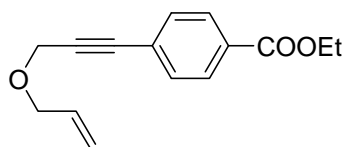
### Compound **3i**

#### **benzyl allyl(3-phenylprop-2-ynyl)carbamate (3i).**

To a solution of benzyl prop-2-ynylcarbamate (5.68g, 30mmol), iodobenzene (6.74g, 33mmol), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (306.0mg, 0.4mmol) and CuI (155.4mg, 0.8mmol) in dry CH<sub>3</sub>CN (50mL) under nitrogen atmosphere was added NEt<sub>3</sub> (6.07g, 60mmol) at 0°C, and the reaction was warmed to room temperature, and then stirred overnight. The solvent was removed under vacuum, and the residue was purified on silica gel

(ethyl acetate/ petroleum = 1/40) to give benzyl 3-phenylprop-2-ynylcarbamate (5.75g) in 72% yield.

To a solution of benzyl 3-phenylprop-2-ynylcarbamate (2.65g, 10mmol) in THF (50mL) was added sodium hydride (0.8g of a 60% dispersion in mineral oil, 20mmol). After stirring for 30 min, allyl bromide (1.45g, 12mmol) was added to the above solution at 0°C, and the reaction was then warmed to room temperature gradually and stirred for 2 hours. The reaction was quenched by addition of a saturated solution of NH<sub>4</sub>Cl (20mL), and the mixture was extracted with ethyl acetate (3×20 mL). The combined organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under vacuum, and the residue was purified on silica gel (ethyl acetate/ petroleum = 1/40) to give **3i** (1.59g) in 52% yield. <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>): δ 7.08-7.01 (m, 6H), 7.01-6.97 (m, 4H), 5.53-5.46(m, 1H), 5.00-4.86 (m, 4H), 4.03-3.95 (m, 2H), 3.75 (s, 2H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>): δ 155.6, 136.5, 132.9, 131.6, 128.4, 128.2, 127.9, 127.7, 122.6, 117.7, 117.3, 84.4, 83.6, 67.4, 48.4, 36.3. HRMS (ESI) calcd for C<sub>20</sub>H<sub>19</sub>NO<sub>2</sub> [M + Na]<sup>+</sup>: 328.1313; found 328.1321.



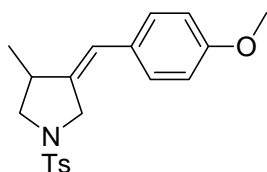
Compound **1d**

**ethyl 4-(3-(allyloxy)prop-1-ynyl)benzoate (1d).**

To a solution of sodium hydride (0.4g of a 60% dispersion in mineral oil, 10mmol) in THF (5mL) at 0 °C, was added portion drop wise ethyl 4-(3-hydroxyprop-1-ynyl) benzoate (1.0g, 4.9mmol). After stirring for 30 min, allyl bromide (0.8g, 6.6mmol) was added to the above solution at 0°C, and the reaction was then warmed to room temperature gradually and stirred for 2 hours. The reaction was quenched by addition of HCl (2M, 25mL), and the mixture was extracted with dichloromethane (3×20 mL). The combined organic phase was washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated in vacuum. The residue was purified on silica gel (ethyl acetate/ petroleum = 1/50) to give **1d** (839.1mg) in 70% yield. <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>): δ

7.89 (d,  $J = 7.8$  Hz, 2H), 7.40 (d,  $J = 8.1$  Hz, 2H), 5.92-5.79 (m, 1H), 5.25 (d,  $J = 17.1$  Hz, 1H), 5.15 (d,  $J = 10.2$  Hz, 1H), 4.30-4.24 (m, 4H), 4.04 (d,  $J = 5.7$  Hz, 2H), 1.29 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ ):  $\delta$  166.1, 134.1, 131.8, 130.3, 129.6, 127.4, 118.2, 88.3, 85.7, 71.1, 61.3, 58.0, 14.5; HRMS (ESI) calcd for  $\text{C}_{15}\text{H}_{16}\text{O}_3$  [ $\text{M} + \text{H}$ ] $^+$ : 245.1178; found 245.1166.

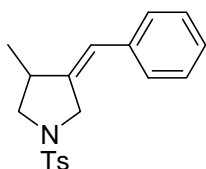
### General Procedures for the Reductive Cyclization



#### Compound **4b**

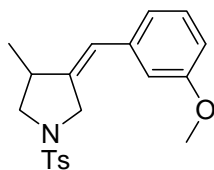
**(Z)-3-(4-methoxybenzylidene)-4-methyl-1-tosylpyrrolidine (4b).** (*i*-Pr) $_2$ Zn (6mL, 0.5M in THF) was added to a solution of **3b** (355mg, 1.0 mmol) and Ni(acac) $_2$  (25.6mg, 0.1mmol) in anhydrous THF (4mL) at  $-78^\circ\text{C}$ . The reaction mixture was stirred at  $40^\circ\text{C}$  for 18h under  $\text{N}_2$ , and then quench by adding 2M HCl (25mL). The mixture was extracted with dichloromethane and the combined organic layers were washed with saturated  $\text{NaHCO}_3$  and brine, dried ( $\text{Na}_2\text{SO}_4$ ), and then concentrated in vacuum. The residue was purified by column chromatography over silica gel (ethyl acetate/petroleum = 1/20, v/v) to give **4b** (318mg, 89%) as a colorless oil.  $^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ ):  $\delta$  7.63 (d,  $J = 8.1$  Hz, 2H), 7.20 (d,  $J = 7.8$  Hz, 2H), 6.98 (d,  $J = 8.4$  Hz, 2H), 6.78 (d,  $J = 8.7$  Hz, 2H), 6.06 (s, 1H), 4.12 (d,  $J = 14.7$  Hz, 1H), 3.93 (d,  $J = 14.4$  Hz, 1H), 3.70 (s, 3H), 3.44 (t,  $J = 7.8$  Hz, 1H), 2.78-2.71 (m, 1H), 2.62 (t,  $J = 8.4$  Hz, 1H), 2.30 (s, 3H), 1.05 (d,  $J = 6.6$  Hz, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  158.7, 143.8, 139.6, 133.0, 129.9, 129.7, 129.5, 127.9, 121.6, 114.1, 55.4, 54.1, 51.0, 39.1, 21.7, 17.1; HRMS (APCI) calcd for  $\text{C}_{20}\text{H}_{23}\text{NO}_3\text{S}$  [ $\text{M}$ ] $^+$ : 357.1399; found 357.1404.

All remaining pyrrolidine and tetrahydrofuran derivatives were prepared using a procedure similar to that used to synthesize **4b**.



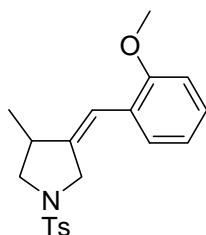
Compound **4a**

**(Z)-3-benzylidene-4-methyl-1-tosylpyrrolidine (4a)**.<sup>[6]</sup> 95% yield, Z/E > 99/1. <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>): δ 7.64 (d, *J* = 8.1 Hz, 2H), 7.28-7.20 (m, 4H), 7.17-7.12 (m, 1H), 7.05 (d, *J* = 7.2 Hz, 2H), 6.14 (d, *J* = 1.8 Hz, 1H), 4.16 (d, *J* = 14.1 Hz, 1H), 3.96 (d, *J* = 14.7 Hz, 1H), 3.47 (dd, *J* = 8.7, 7.5 Hz, 1H), 2.82-2.74 (m, 1H), 2.64 (t, *J* = 8.4 Hz, 1H), 2.32 (s, 3H), 1.08 (d, *J* = 6.6 Hz, 3H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>): δ 143.9, 142.0, 136.8, 133.2, 130.0, 128.8, 128.3, 128.0, 127.2, 122.3, 54.1, 51.1, 39.3, 21.8, 17.2.



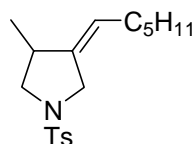
Compound **4c**

**(Z)-3-(3-methoxybenzylidene)-4-methyl-1-tosylpyrrolidine (4c)**. Colorless oil, 56% yield, Z/E > 99/1. <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>): δ 7.61 (d, *J* = 8.1 Hz, 2H), 7.21-7.12 (m, 3H), 6.70-6.64 (m, 2H), 6.62-6.57 (m, 1H), 6.09 (d, *J* = 1.8 Hz, 1H), 4.13 (d, *J* = 15.0 Hz, 1H), 3.94 (d, *J* = 15.0 Hz, 1H), 3.69 (s, 3H), 3.44 (t, *J* = 8.0 Hz, 1H), 2.78-2.71 (m, 1H), 2.63 (t, *J* = 8.4 Hz, 1H), 2.29 (s, 3H), 1.05 (d, *J* = 6.9 Hz, 3H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>): δ 159.9, 143.9, 142.4, 138.2, 133.1, 130.0, 129.8, 128.0, 122.3, 120.7, 114.2, 112.5, 55.5, 54.1, 51.1, 39.3, 21.8, 17.2; HRMS (APCI) calcd for C<sub>20</sub>H<sub>23</sub>NO<sub>3</sub>S [M]<sup>+</sup>: 357.1399; found 357.1387.



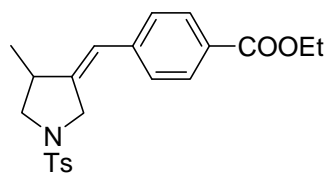
#### Compound 4d

**(Z)-3-(2-methoxybenzylidene)-4-methyl-1-tosylpyrrolidine (4d)**. Colorless oil, 36% yield, Z/E > 99/1.  $^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ ):  $\delta$  7.69 (d,  $J = 8.1$  Hz, 2H), 7.30-7.20 (m, 3H), 7.06-7.04 (m, 1H), 6.97-6.92 (m, 1H), 6.87-6.81 (m, 1H), 6.48 (d,  $J = 2.1$  Hz, 1H), 4.15 (d,  $J = 14.7$  Hz, 1H), 3.99 (d,  $J = 15.0$  Hz, 1H), 3.81 (s, 3H), 3.57-3.52 (m, 1H), 2.91-2.84 (m, 1H), 2.78-2.73 (m, 1H), 2.41 (s, 3H), 1.17 (d,  $J = 6.6$  Hz, 3H);  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ ):  $\delta$  156.9, 143.9, 142.1, 133.5, 130.0, 128.9, 128.8, 128.1, 125.9, 120.8, 117.1, 110.9, 55.8, 54.3, 51.0, 39.4, 21.9, 17.3. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{23}\text{NO}_3\text{S}$  [ $\text{M} + \text{Na}$ ] $^+$ : 380.1296; found: 380.1290.



#### Compound 4f

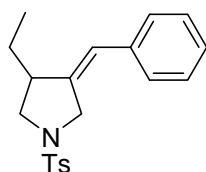
**(Z)-3-hexylidene-4-methyl-1-tosylpyrrolidine (4f)**. Colorless oil 62%, Z/E > 99/1.  $^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ ):  $\delta$  7.63 (d,  $J = 7.8$  Hz, 2H), 7.25 (d,  $J = 7.8$  Hz, 2H), 5.07 (s, 1H), 3.79 (d,  $J = 14.1$  Hz, 1H), 3.63 (d,  $J = 13.8$  Hz, 1H), 3.47-3.39 (m, 1H), 2.56 (d,  $J = 3.9$  Hz, 2H), 2.34 (s, 3H), 1.80-1.77 (m, 2H), 1.23-1.15 (m, 6H), 0.93 (d,  $J = 5.7$  Hz, 3H), 0.78 (t,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ ):  $\delta$  143.7, 139.7, 133.0, 129.8, 128.0, 122.2, 55.2, 49.9, 37.4, 31.6, 29.4, 29.1, 22.7, 21.7, 16.9, 14.2. HRMS (ESI) calcd for  $\text{C}_{18}\text{H}_{27}\text{NO}_2\text{S}$  [ $\text{M} + \text{H}$ ] $^+$ : 322.1841; found: 322.1828.



#### Compound 4e

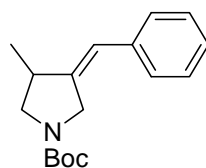
**(Z)-ethyl 4-((4-methyl-1-tosylpyrrolidin-3-ylidene)methyl)benzoate (4e)**. Colorless oil, 65% yield, Z/E = 74/26.  $^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ ):  $\delta$  8.03-8.00 (m, 2H), 7.75-7.70 (m, 2H), 7.36-7.26 (m, 2H), 7.25-7.18 (m, 2H), 6.26 (s, 1H), 4.38 (q,  $J = 6.9$  Hz, 2H), 4.27-4.15 (m, 1H), 4.03 (d,  $J = 15.0$  Hz, 0.7H), 3.80 (d,  $J = 15.9$  Hz,

0.3H), 3.57 (t,  $J = 8.1$  Hz, 0.7H), 3.28-3.20 (m, 0.9H), 2.94-2.89 (m, 0.7H), 2.74 (t,  $J = 8.7$  Hz, 0.7H), 2.43-2.41 (m, 3H), 1.40 (t,  $J = 7.2$  Hz, 3H), 1.18 (d,  $J = 6.6$  Hz, 2.1H), 1.12 (d,  $J = 6.6$  Hz, 0.9H);  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ ):  $\delta$  166.5, 144.9, 144.0, 141.1, 133.0, 130.0, 129.0, 128.1, 128.0, 122.0, 121.7, 61.2, 55.9, 54.0, 53.4, 51.1, 39.6, 35.5, 21.8, 18.6, 17.1, 14.6; HRMS (APCI) calcd for  $\text{C}_{22}\text{H}_{25}\text{NO}_4\text{S}$   $[\text{M}]^+$ : 399.1504; found 399.1501.



#### Compound 4g

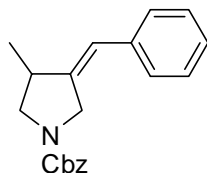
**(Z)-3-benzylidene-4-ethyl-1-tosylpyrrolidine (4g)**. 66% yield, Z/E > 99/1, and (E)-N-(but-2-enyl)-4-methylbenzenesulfonamide was obtained as a by product in 24% yield. **4g**:  $^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ ):  $\delta$  7.64 (d,  $J = 8.1$  Hz, 2H), 7.29-7.23 (m, 4H), 7.22-7.15 (m, 1H), 7.05 (d,  $J = 7.5$  Hz, 2H), 6.17 (s, 1H), 4.04 (m, 2H), 3.35 (dd,  $J = 9.0, 7.3$  Hz, 1H), 2.89 (dd,  $J = 9.3, 6.0$  Hz, 1H), 2.62-2.58 (m, 1H), 2.33 (s, 3H), 1.63-1.55 (m, 1H), 1.36-1.26 (m, 1H), 0.86 (t,  $J = 7.5$  Hz, 3H);  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ ):  $\delta$  143.9, 140.7, 136.8, 133.1, 130.0, 128.8, 128.3, 128.0, 127.2, 123.1, 52.1, 51.0, 46.5, 26.2, 21.8, 12.1. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{23}\text{NO}_2\text{S}$   $[\text{M}+\text{H}]^+$ : 342.1528; found: 342.1503. (E)-N-(but-2-enyl)-4-methylbenzenesulfonamide:  $^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ ):  $\delta$  7.75 (d,  $J = 8.1$  Hz, 2H), 7.31 (d,  $J = 8.1$  Hz, 2H), 5.63-5.52 (m, 1H), 5.38-5.28 (m, 1H), 4.44 (broad, 1H), 3.50 (t,  $J = 6.0$  Hz, 2H), 2.43 (s, 3H), 1.61 (d,  $J = 6.3$  Hz, 3H);



#### Compound 4h

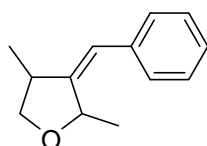
**(Z)-tert-butyl 3-benzylidene-4-methylpyrrolidine-1-carboxylate (4h)**.  $^1\text{H}$  NMR

(300MHz, CDCl<sub>3</sub>):  $\delta$  7.07-7.01 (m, 2H), 6.97-6.95 (m, 3H), 6.05 (s, 1H), 4.06-3.99(m, 2H), 3.47-3.43 (m, 1H), 2.70-2.61 (m, 2H), 1.23 (s, 9H), 0.99 (d,  $J = 6.3$  Hz, 3H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>):  $\delta$  154.7, 144.1, 143.1, 137.2, 128.5, 128.3, 126.8, 121.3, 79.6, 52.1, 51.6, 49.2, 39.2, 38.5, 28.6, 17.0; HRMS (APCI) calcd for C<sub>17</sub>H<sub>23</sub>NO<sub>2</sub> [M]<sup>+</sup>: 273.1729; found 273.1735.



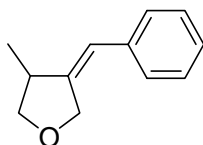
#### Compound 4i

**(Z)-benzyl 3-benzylidene-4-methylpyrrolidine-1-carboxylate (4i).** Colorless oil, 66% yield, Z/E > 99/1. <sup>1</sup>H NMR (300MHz, DMSO-D<sub>6</sub>):  $\delta$  7.34-7.30 (m, 7H), 7.23-7.20 (m, 3H), 6.35 (s, 1H), 5.07 (s, 2H), 4.33-4.12 (m, 2H), 3.69-3.65 (m, 1H), 2.93-2.90 (m, 2H), 1.16 (d,  $J = 5.7$  Hz, 3H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>):  $\delta$  154.9, 143.3, 142.4, 137.0, 128.6, 128.3, 128.0, 126.9, 121.6, 66.9, 52.1, 51.9, 49.5, 48.9, 39.2, 38.4, 16.9; HRMS (ESI) calcd for C<sub>20</sub>H<sub>21</sub>NO<sub>2</sub> [M + Na]<sup>+</sup>: 330.1470; found 330.1473.



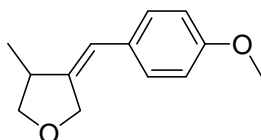
#### Compound 2a

**(Z)-3-benzylidene-2,4-dimethyltetrahydrofuran (2a).**<sup>[7]</sup> Colorless oil, 72% yield, Z/E > 99/1. <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>):  $\delta$  7.25-7.23 (m, 2H), 7.18-7.15 (m, 3H), 6.23 (s, 0.4H), 6.14 (s, 0.6H), 5.10-5.02 (m, 1H), 4.05 (t,  $J = 7.8$  Hz, 0.6H), 3.92(t,  $J = 7.7$  Hz, 0.4H), 3.47 (t,  $J = 7.5$  Hz, 0.4Hz), 3.25 (t,  $J = 8.7$  Hz, 0.6H), 2.86-2.79 (m, 1H), 1.17 (d,  $J = 6.6$  Hz, 3H), 1.11 (d,  $J = 6.9$  Hz, 3H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>):  $\delta$  151.8, 151.1, 137.4, 128.7, 126.8, 120.5, 120.0, 76.1, 73.3, 72.3, 41.2, 39.3, 19.8, 19.0, 18.6, 15.5.



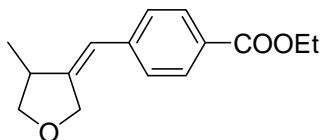
Compound **2b**

**(Z)-3-benzylidene-4-methyltetrahydrofuran (2b).**<sup>[6]</sup> Colorless oil 66% (GC yield 84%), Z/E > 99/1. <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>): δ 7.28-7.23 (m, 2H), 7.16-7.14 (m, 1H), 7.12-7.04 (m, 2H), 6.21 (d, *J* = 2.1 Hz, 1H), 4.64-4.51 (m, 2H), 3.99 (t, *J* = 7.7 Hz, 1H), 3.30 (t, *J* = 8.0 Hz, 1H), 2.86-2.79 (m, 1H), 1.14 (d, *J* = 6.6 Hz, 3H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>): δ 146.8, 137.7, 128.7, 128.1, 126.7, 120.2, 74.6, 70.5, 40.1, 16.7.



Compound **2c**

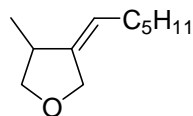
**(Z)-3-(4-methoxybenzylidene)-4-methyltetrahydrofuran (2c).** Colorless oil, 65% yield (GC yield 77%), Z/E > 99/1. <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>): δ 6.98 (d, *J* = 8.4 Hz, 2H), 6.78 (d, *J* = 8.4 Hz, 2H), 6.14 (s, 1H), 4.61-4.47 (m, 2H), 3.97 (t, *J* = 7.7 Hz, 1H), 3.70 (s, 3H), 3.27 (t, *J* = 8.0 Hz, 1H), 2.82-2.75 (m, 1H), 1.11 (d, *J* = 6.6 Hz, 3H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>): δ 158.4, 144.2, 130.5, 129.3, 119.5, 114.2, 74.5, 70.4, 55.4, 39.9, 16.7; HRMS (APCI) calcd for C<sub>13</sub>H<sub>16</sub>O<sub>2</sub> [M]<sup>+</sup>: 204.1150; found 204.1148.



Compound **2d**

**(Z)-ethyl 4-((4-methyldihydrofuran-3(2H)-ylidene)methyl)benzoate (2d).** Colorless oil, 39% yield, Z/E = 75/25. <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>): δ 7.93 (d, *J* = 7.2 Hz, 2H), 7.10 (d, *J* = 7.2 Hz, 2H), 6.25 (s, 1H), 4.65-4.47 (m, 2H), 4.30-4.27 (m, 2H), 4.00 (t, *J* = 6.9 Hz, 1H), 3.31 (t, *J* = 7.4 Hz, 1H), 2.85-2.83 (m, 1H), 1.30 (t, *J* = 5.9 Hz, 3H), 1.14 (d, *J* = 5.4 Hz, 3H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>): δ 166.6, 149.8, 142.0,

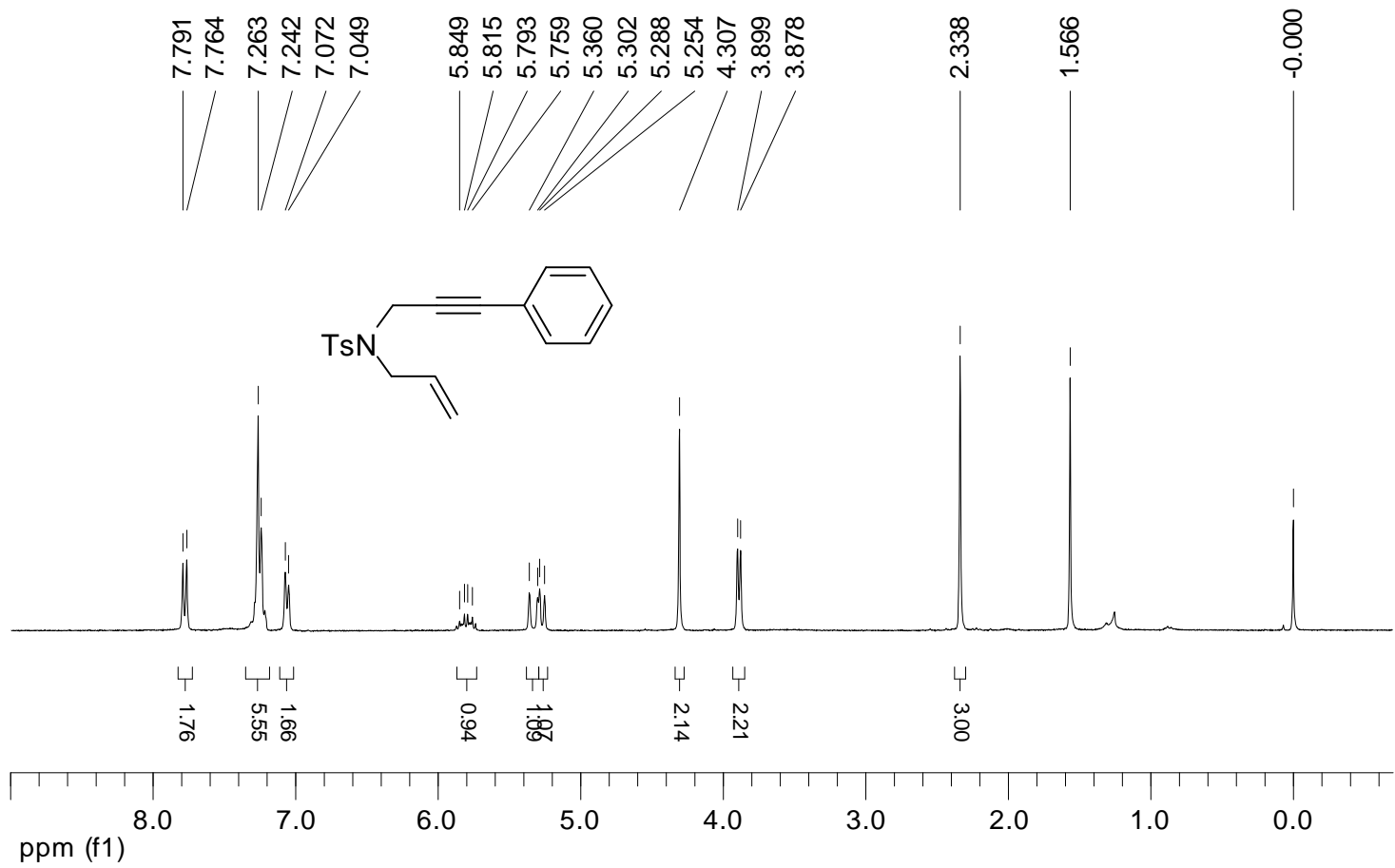
130.0, 128.1, 127.9, 119.6, 74.4, 70.5, 61.1, 40.3, 16.6, 14.6; HRMS (APCI) calcd for  $C_{15}H_{18}O_3$   $[M]^+$ : 246.1258; found 246.1256.



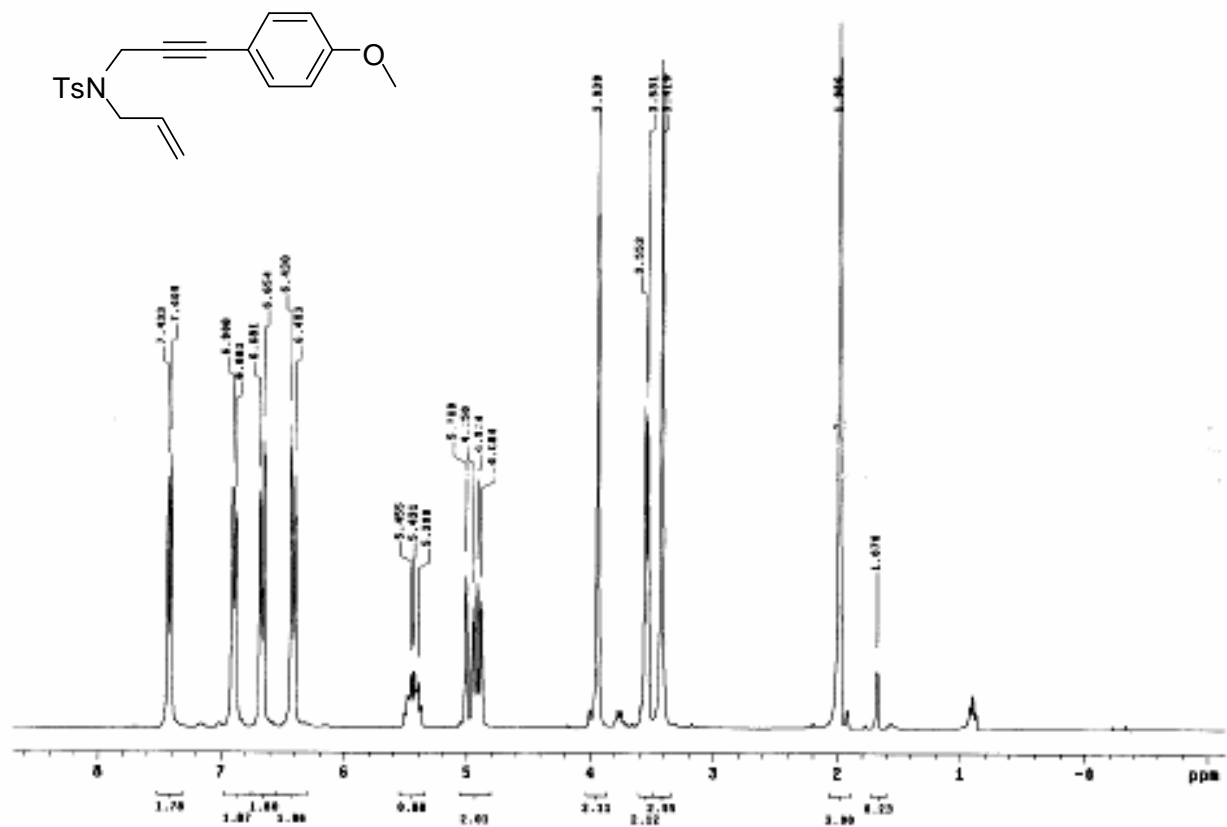
### Compound 2e

**(Z)-3-hexylidene-4-methyltetrahydrofuran (2e).** Colorless oil, 65% yield, E/Z > 99/1.  $^1H$  NMR (300MHz,  $CDCl_3$ ):  $\delta$  5.16-5.08 (m, 1H), 4.26 (s, 2H), 3.95 (t,  $J = 7.7$  Hz, 1H), 3.23 (t,  $J = 8.1$  Hz, 1H), 2.60-2.57 (m, 1H), 1.85-1.81 (m, 2H), 1.29-1.20 (m, 6H), 1.00 (d,  $J = 6.6$  Hz, 3H), 0.82 (t,  $J = 6.8$  Hz, 3H);  $^{13}C$  NMR (75MHz,  $CDCl_3$ ):  $\delta$  143.6, 119.4, 75.5, 69.4, 38.0, 31.5, 28.5, 28.3, 22.6, 16.3, 14.1; HRMS (APCI) calcd for  $C_{11}H_{20}O$   $[M]^+$ : 168.1514; found 168.1521.

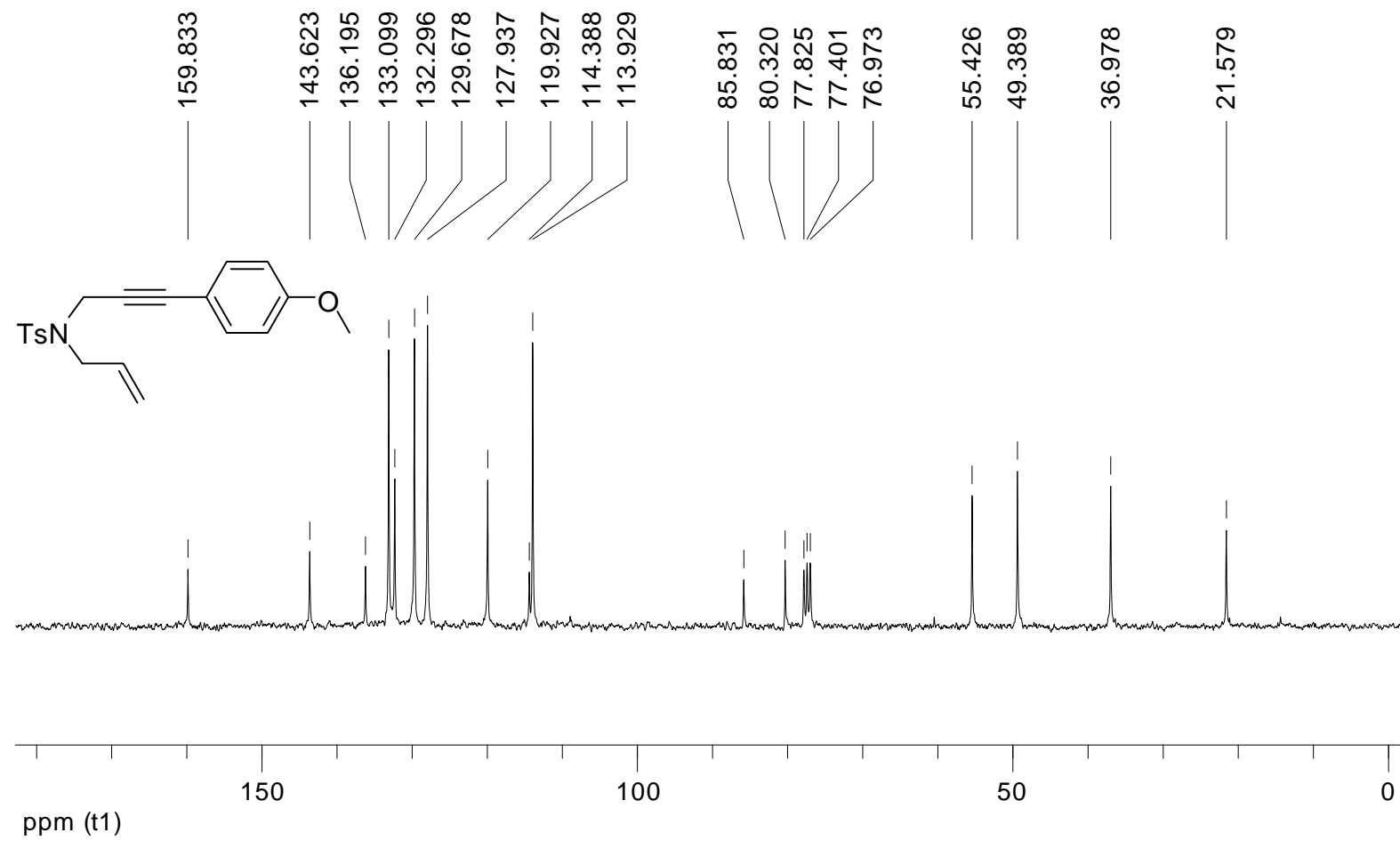
- [1] F. A. Hicks, N. M. Kablaoui, S. L. Buchwald, *J. Am. Chem. Soc.* **1999**, *121*, 5881-5898.
- [2] Y. Tang, L. Deng, Y. Zhang, G. Dong, J. Chen, Z. Yang, *Org. Lett.* **2005**, *7*, 1657-1659.
- [3] T. Shibata, N. Toshida, K. Takagi, *J. Org. Chem.* **2002**, *67*, 7446-7450.
- [4] K. M. Miller, T. F. Jamison, *J. Am. Chem. Soc.* **2004**, *126*, 15342-15343.
- [5] S. I. Lee, S. M. Kim, S. Y. Kim, Y. K. Chung, *Synlett* **2006**, 2256-2260.
- [6] H.-Y. Jang, M. J. Krische, *J. Am. Chem. Soc.* **2004**, *126*, 7875-7880.
- [7] K. Miura, M. Funatsu, H. Saito, H. Ito, A. Hosomi, *Tetrahedron Lett.* **1996**, *37*, 9059-9062.



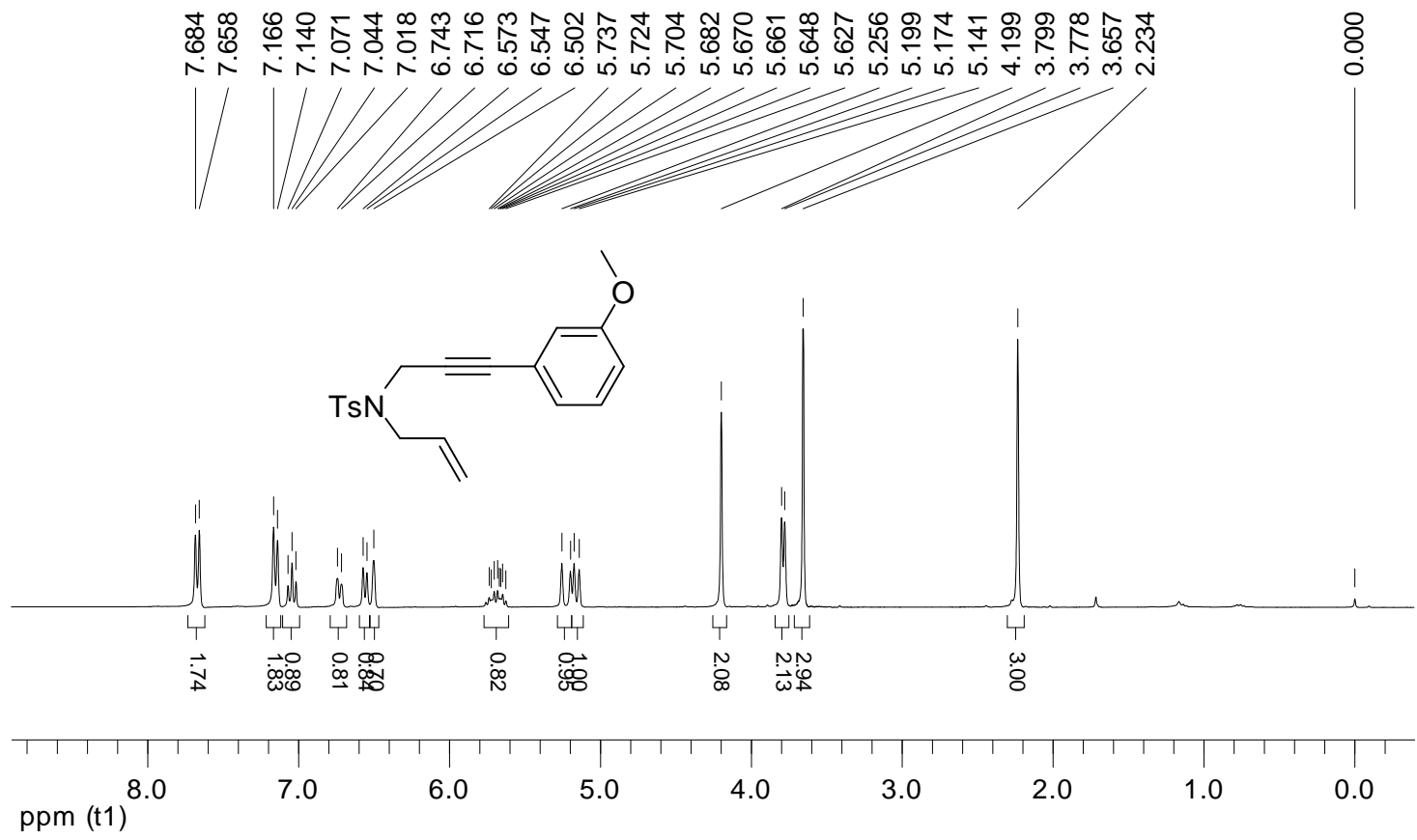
3a



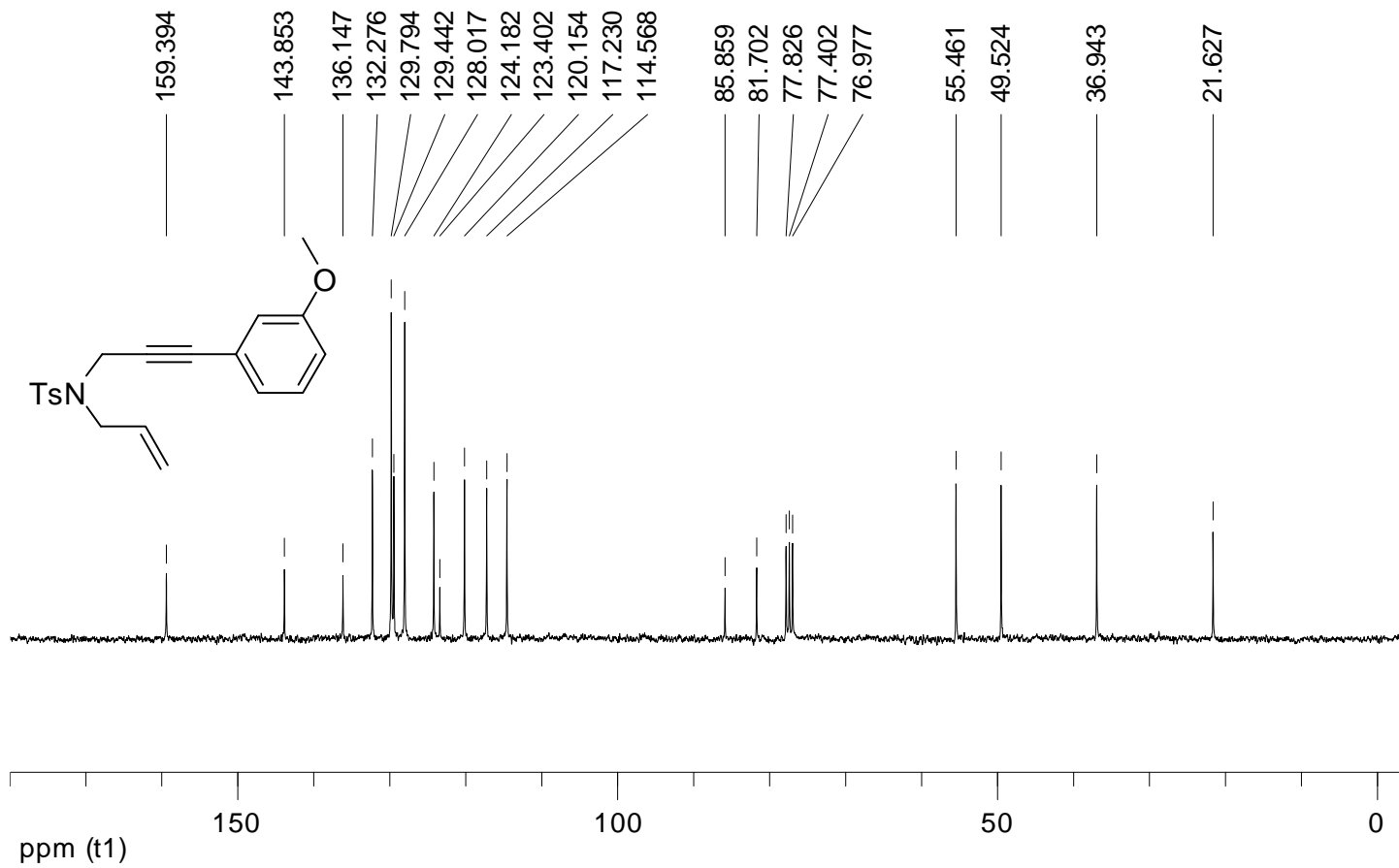
3b



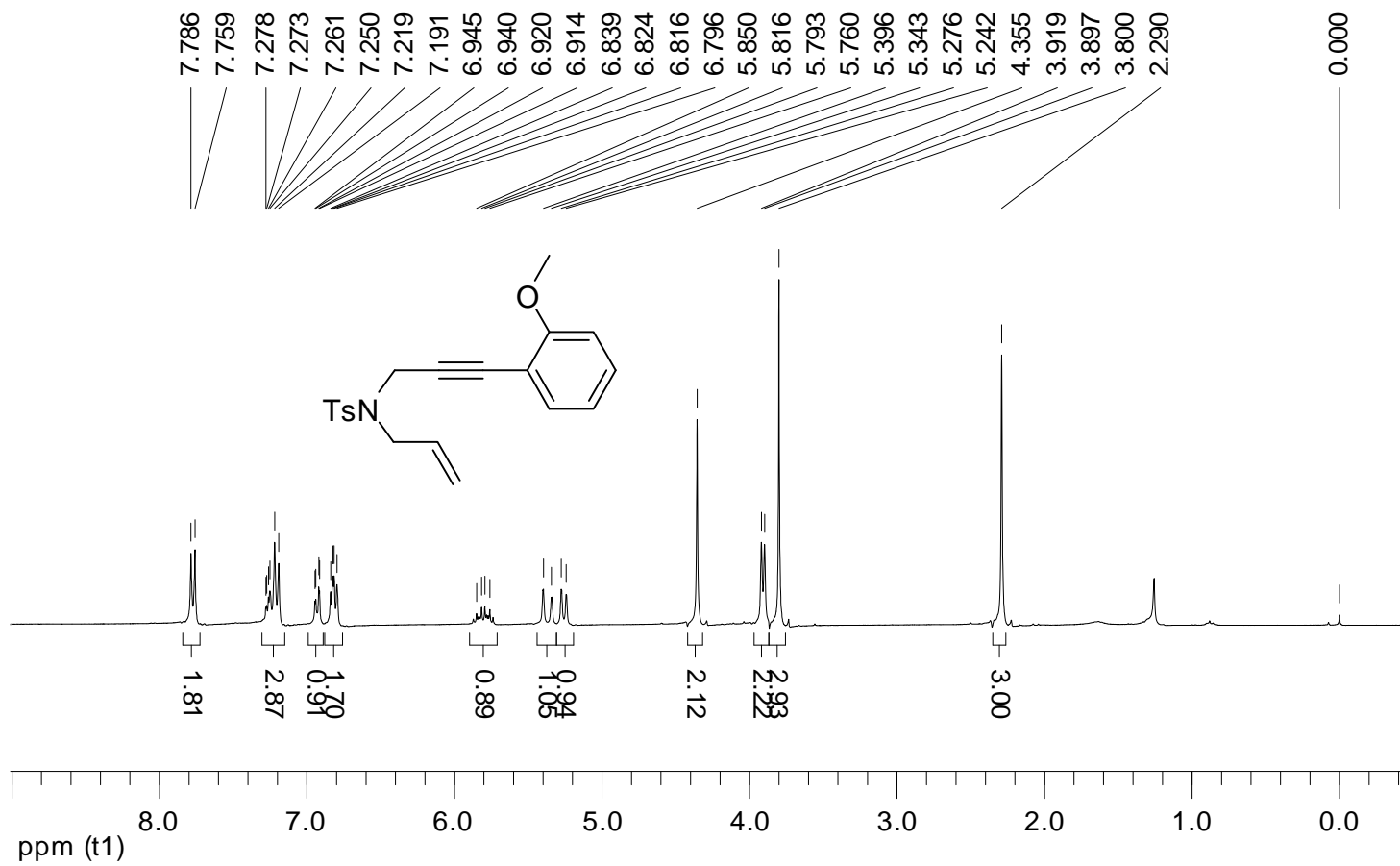
**3b**



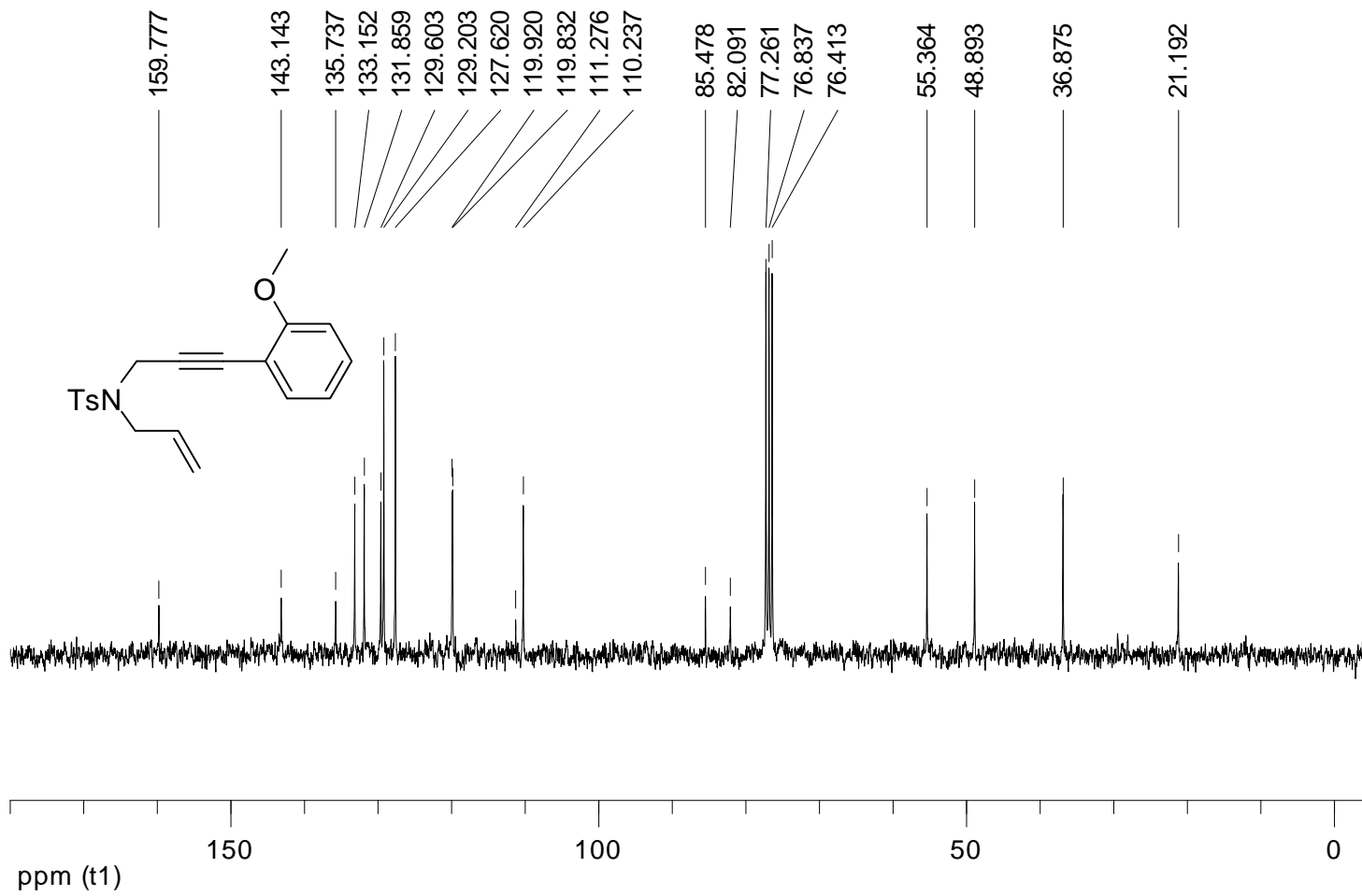
**3c**



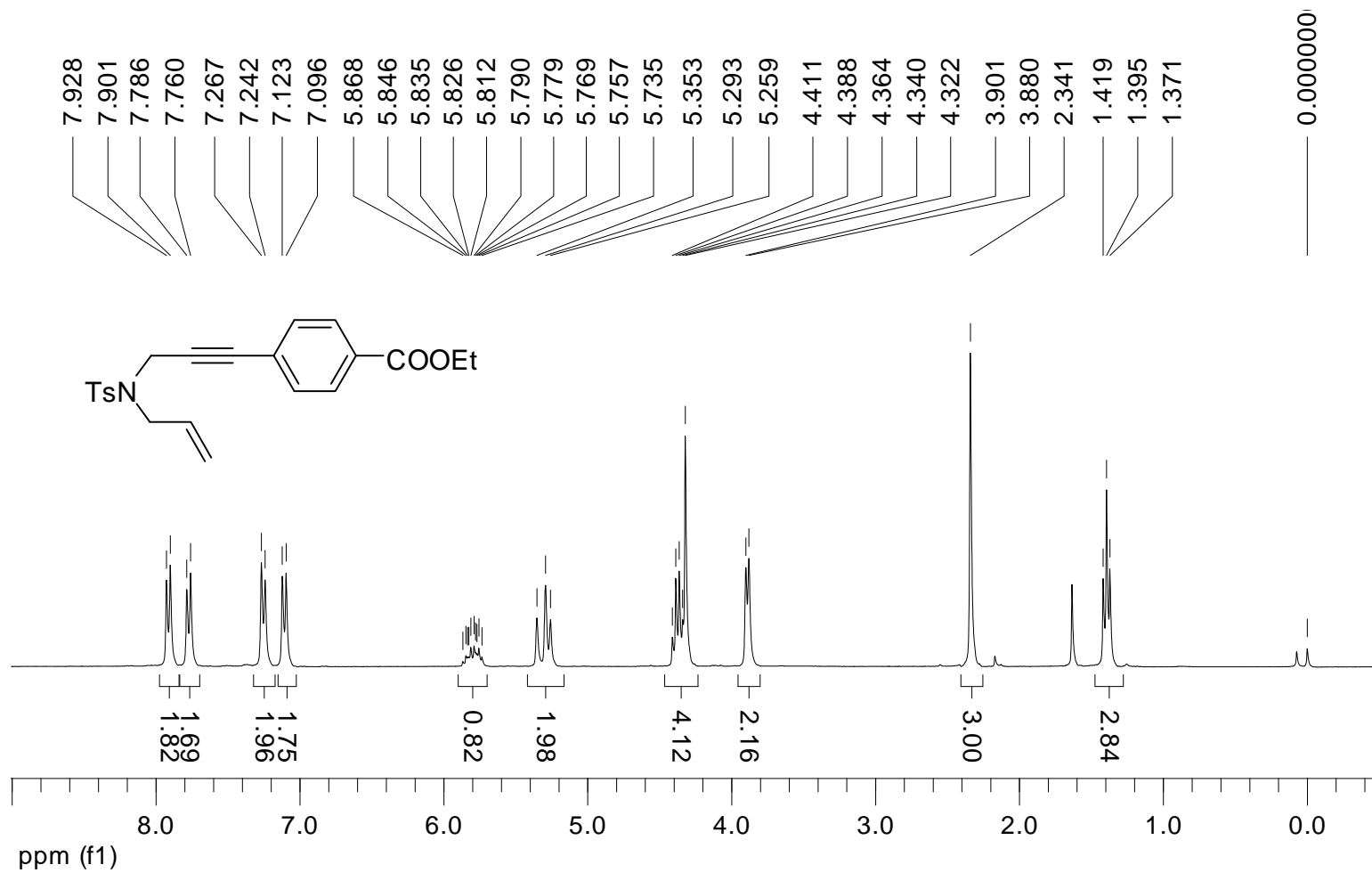
**3c**



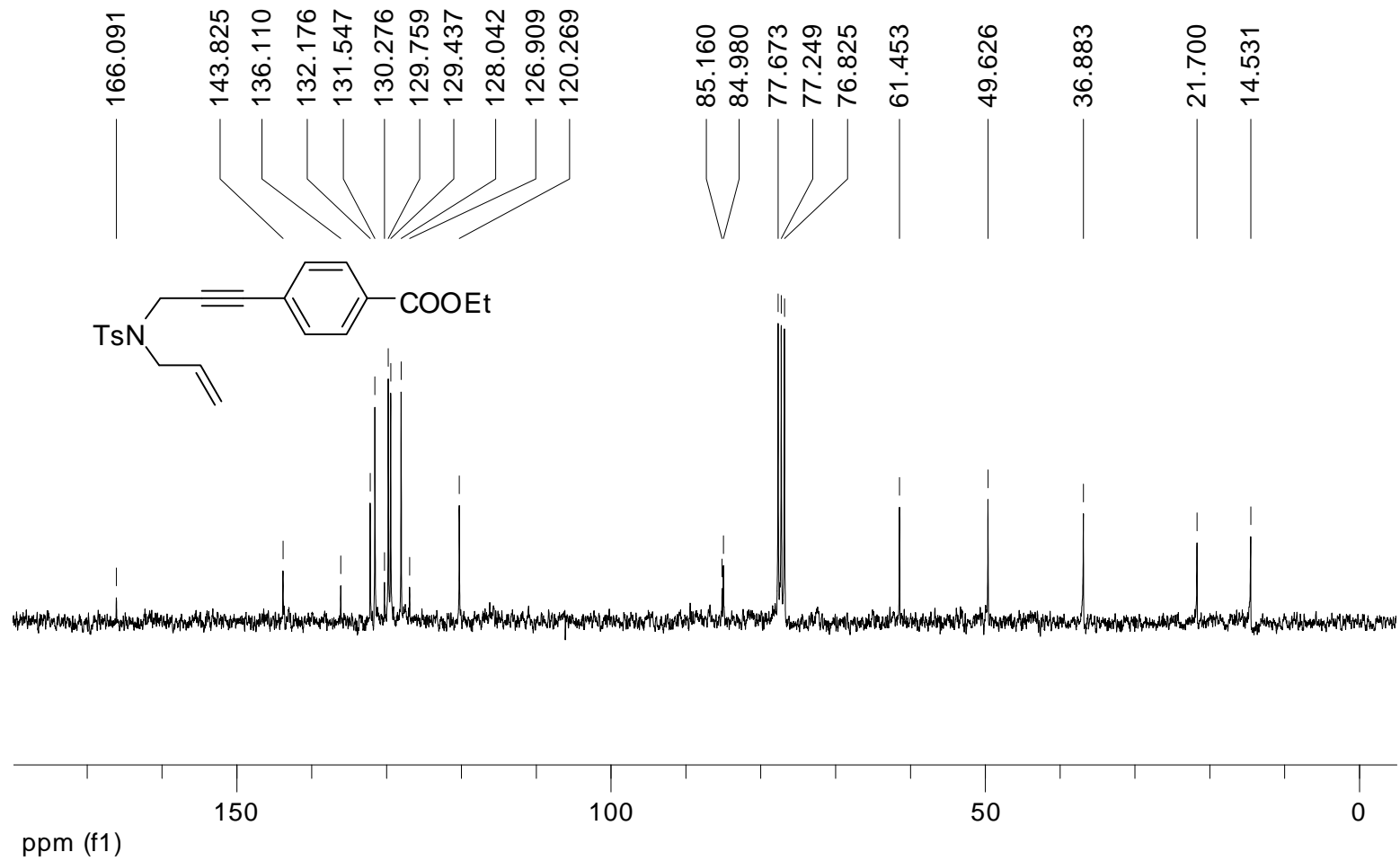
**3d**



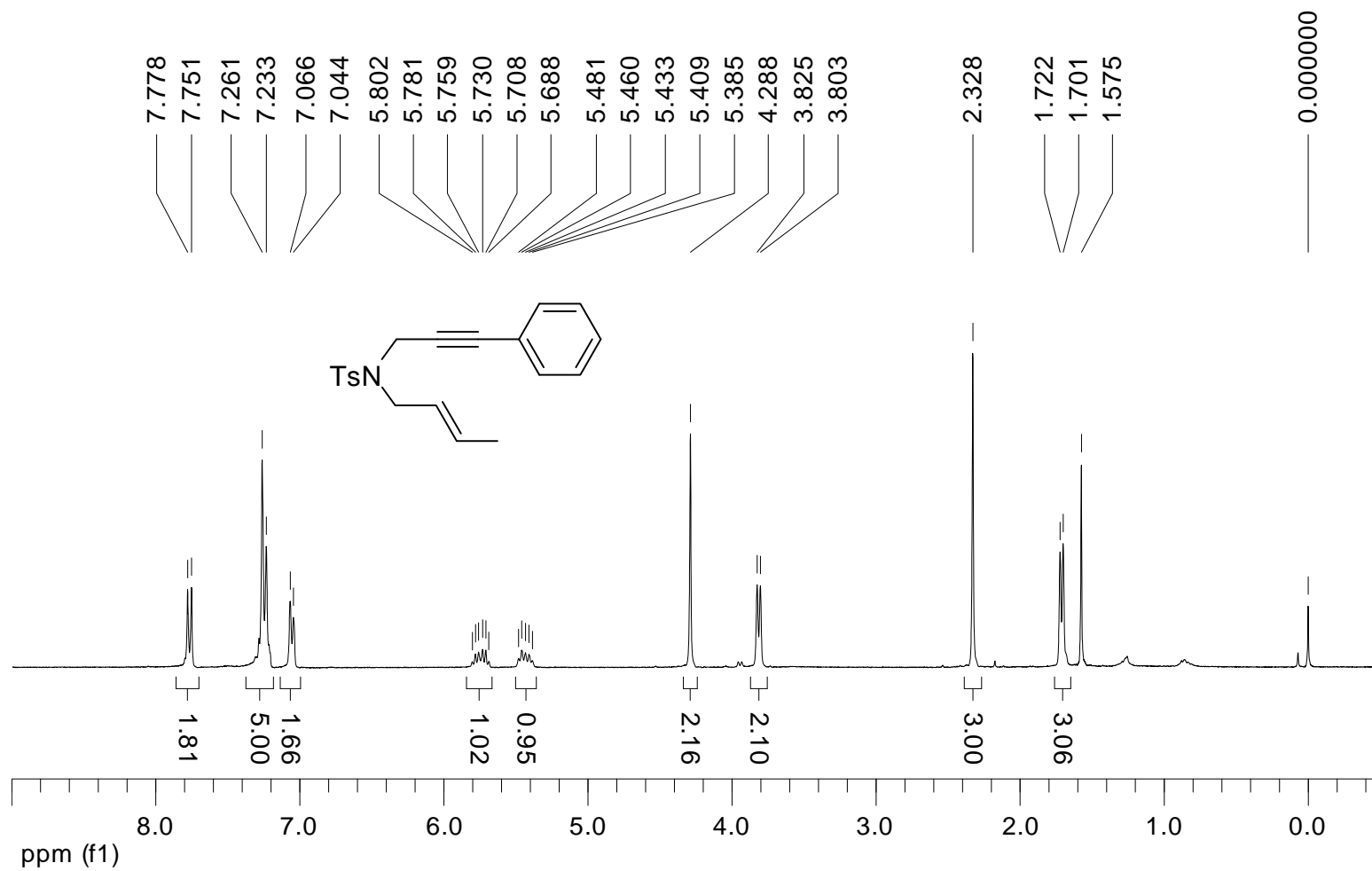
3d



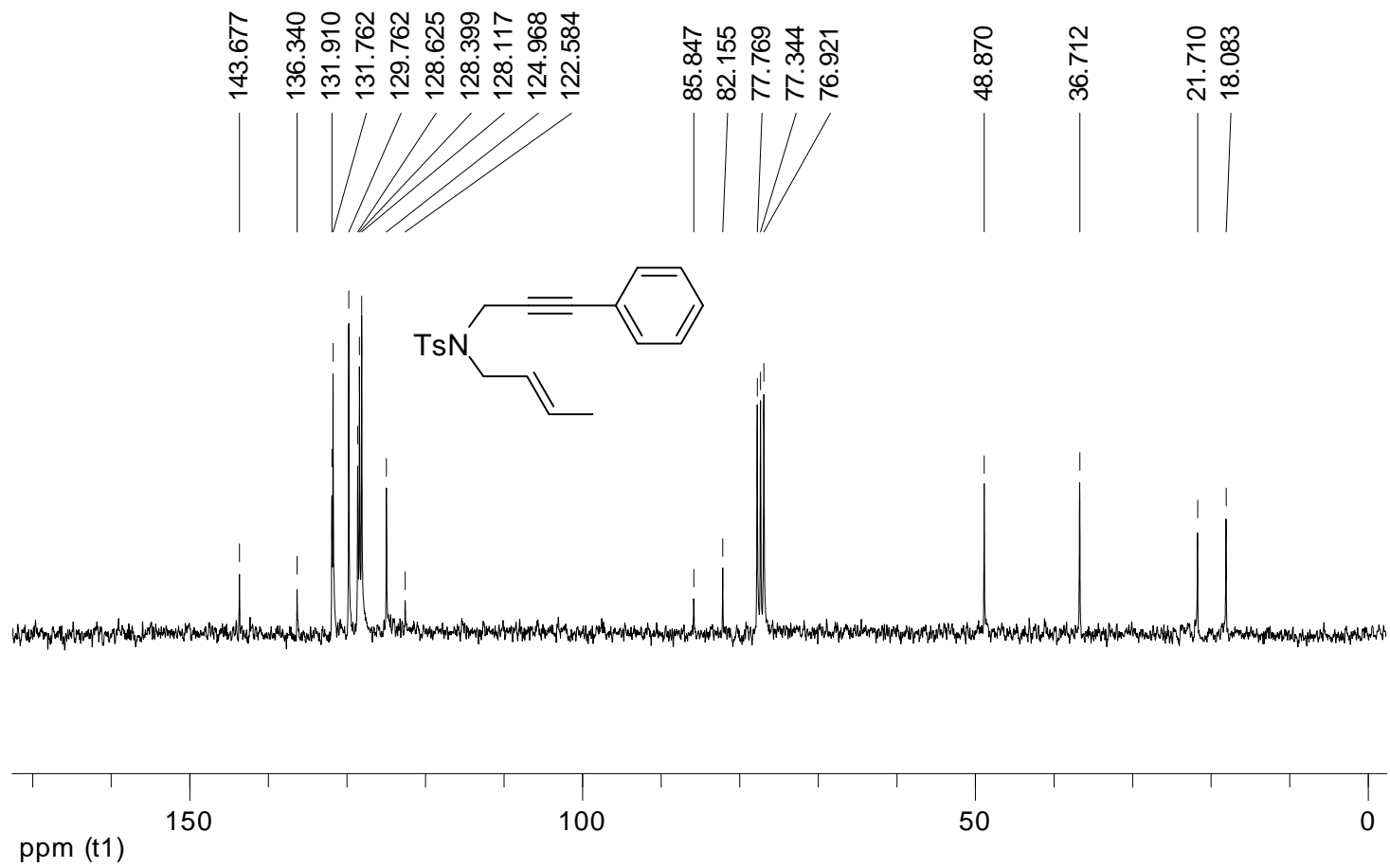
3e



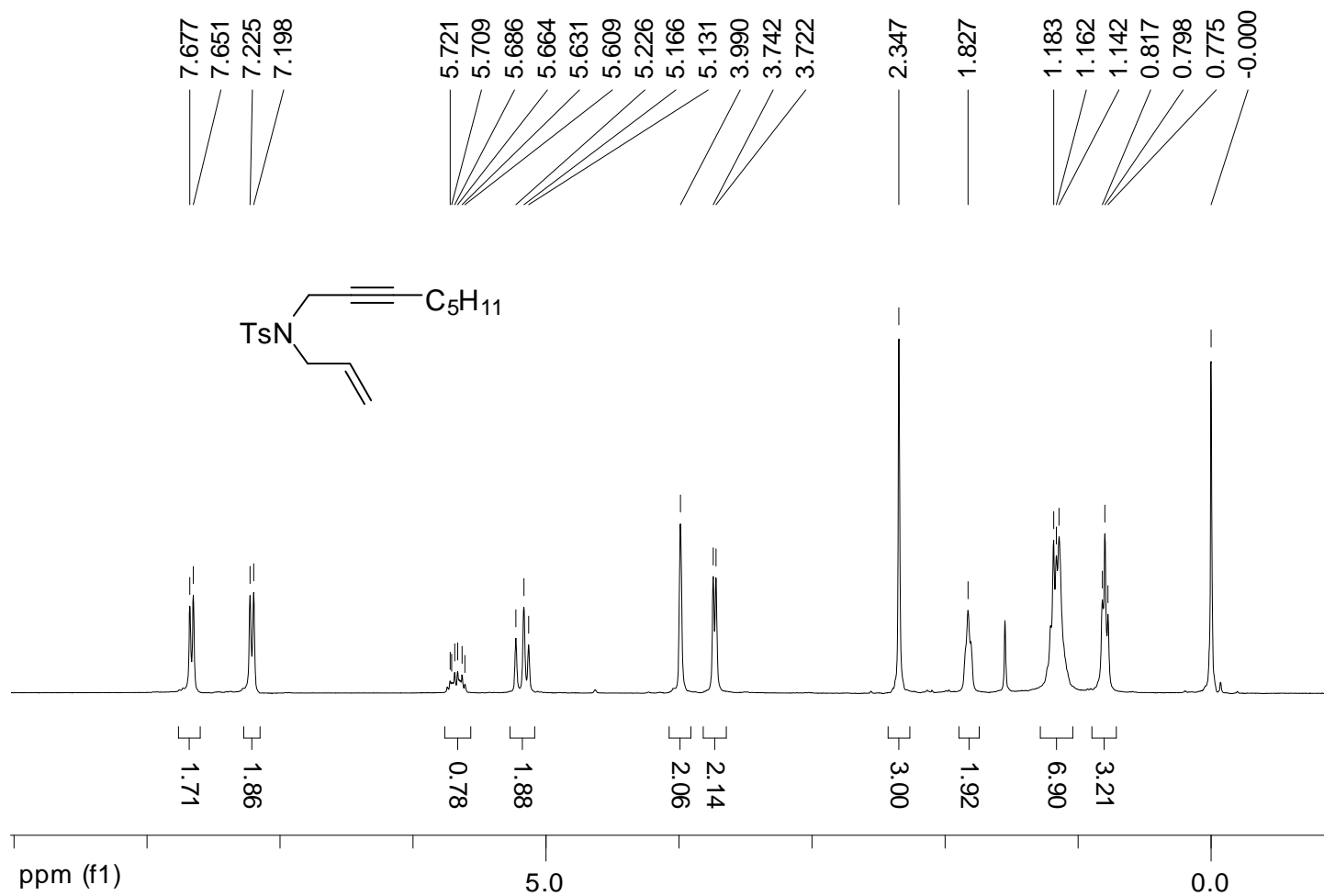
**3e**



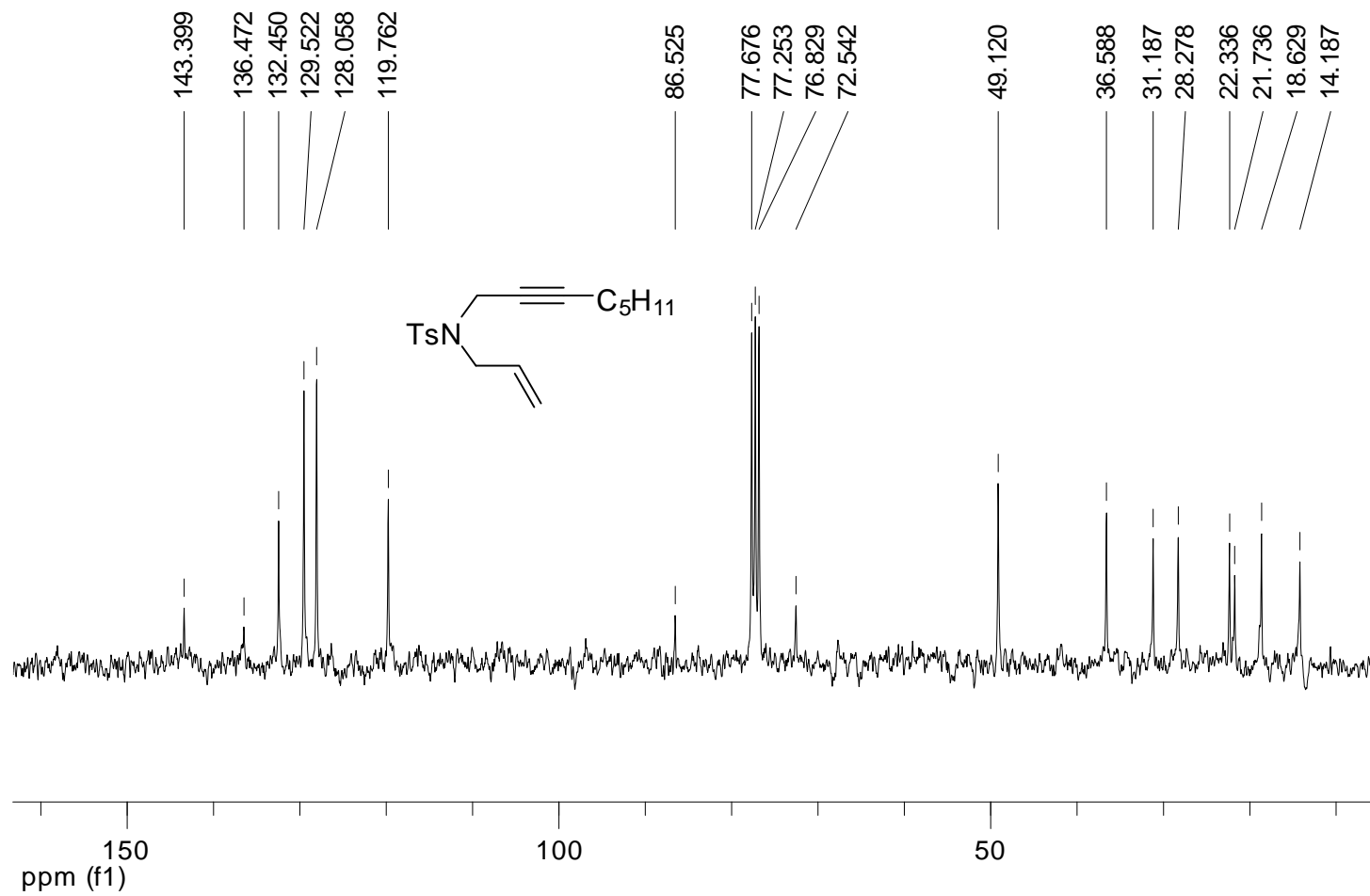
3g



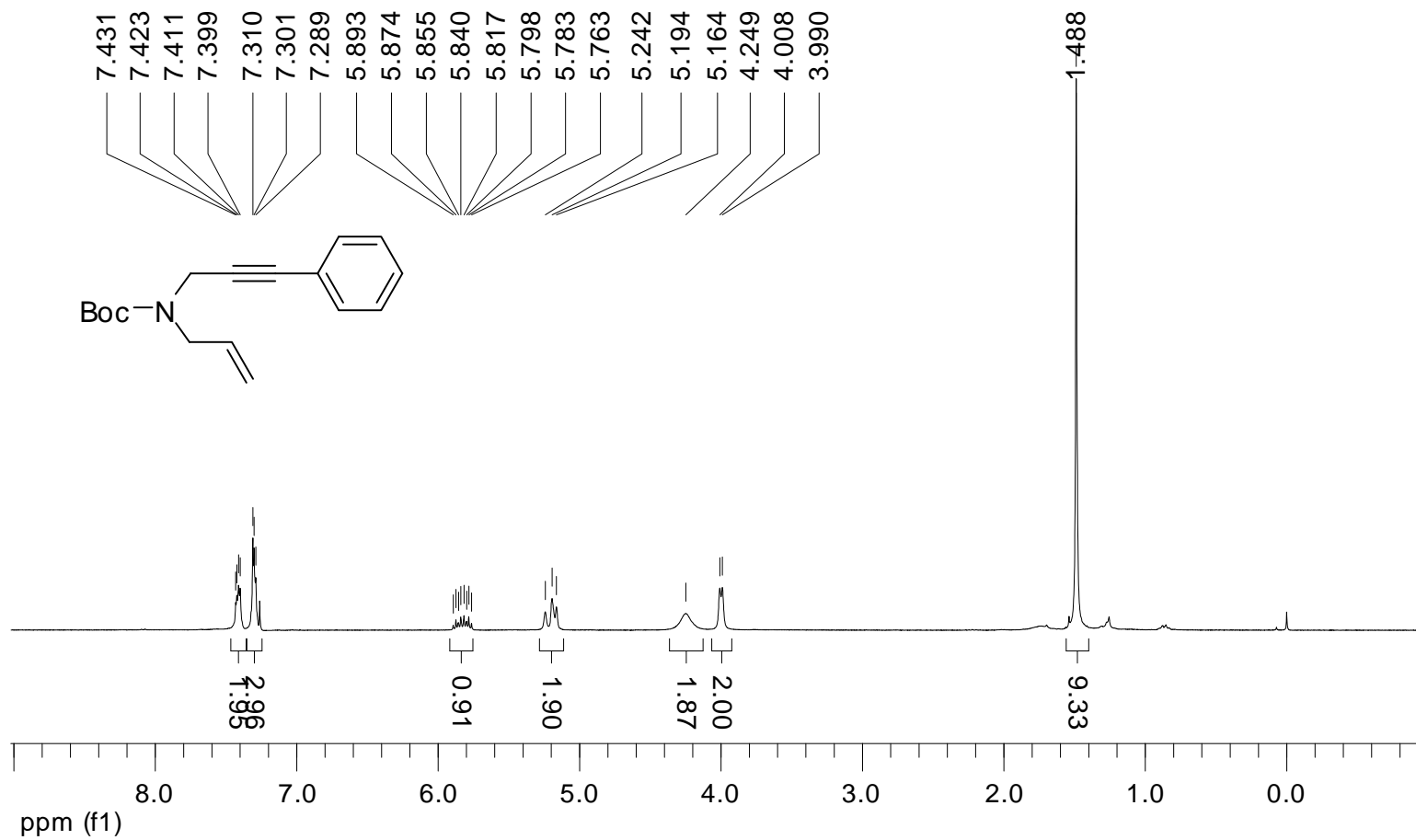
3g



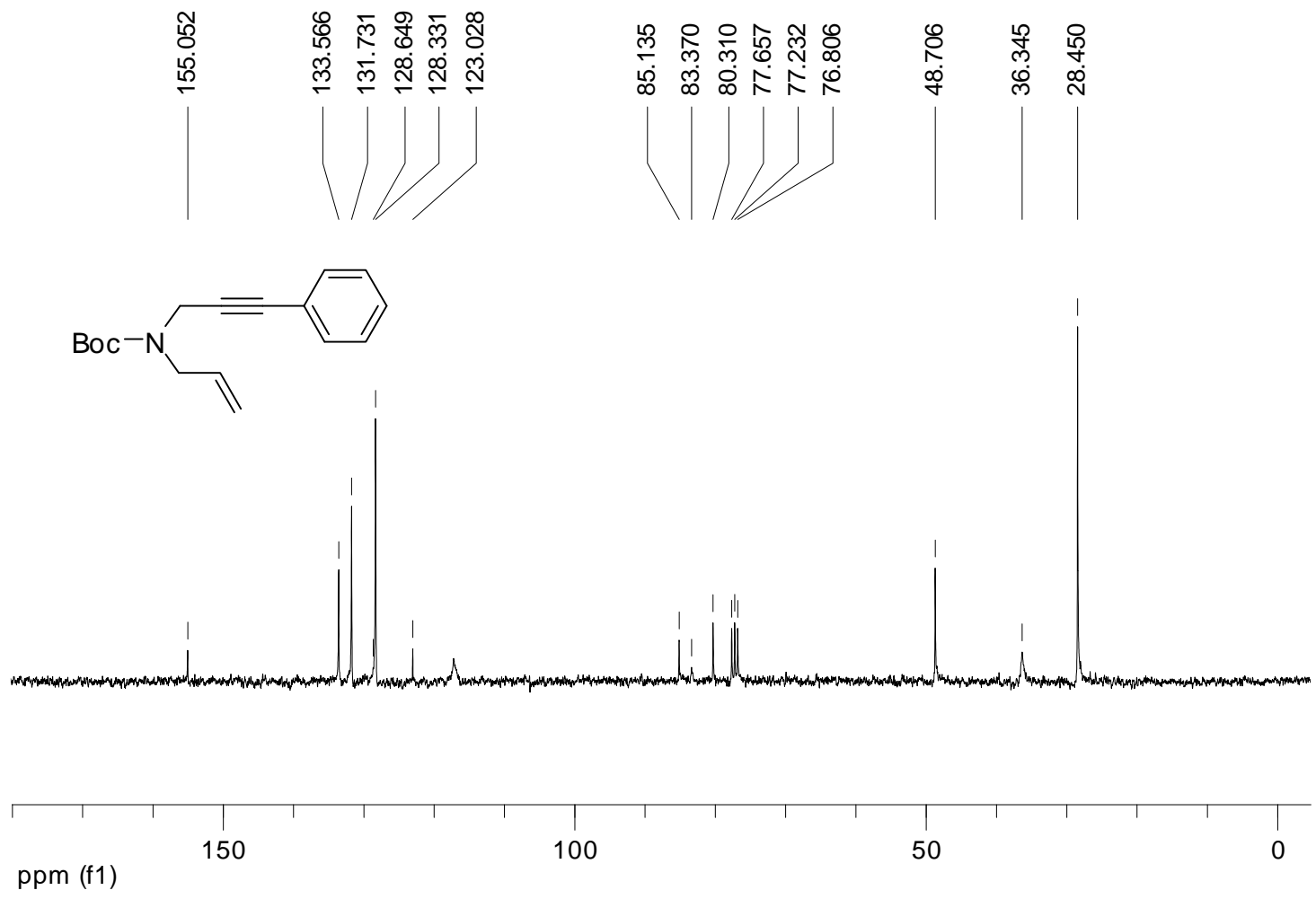
**3f**



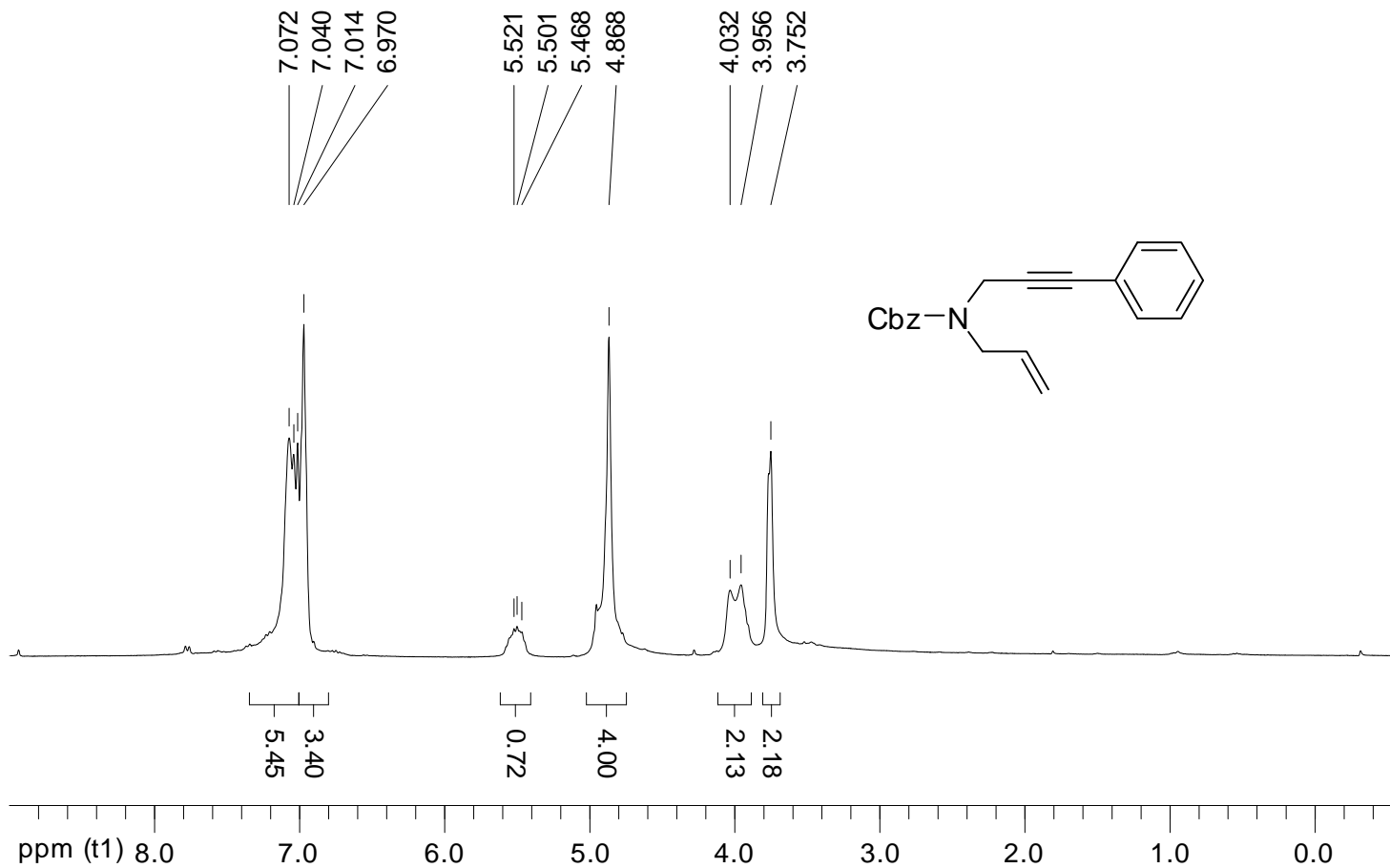
**3f**



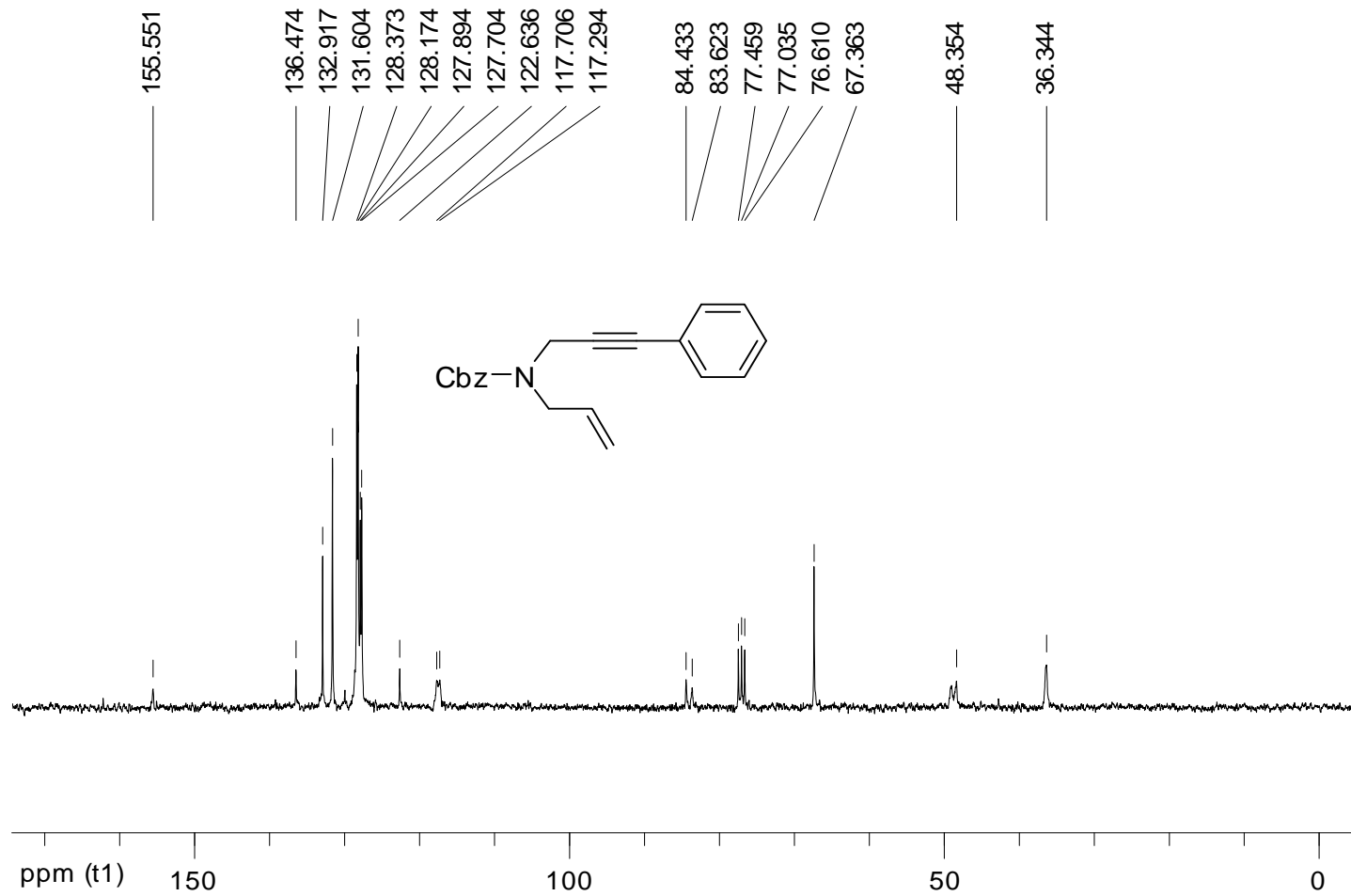
**3h**



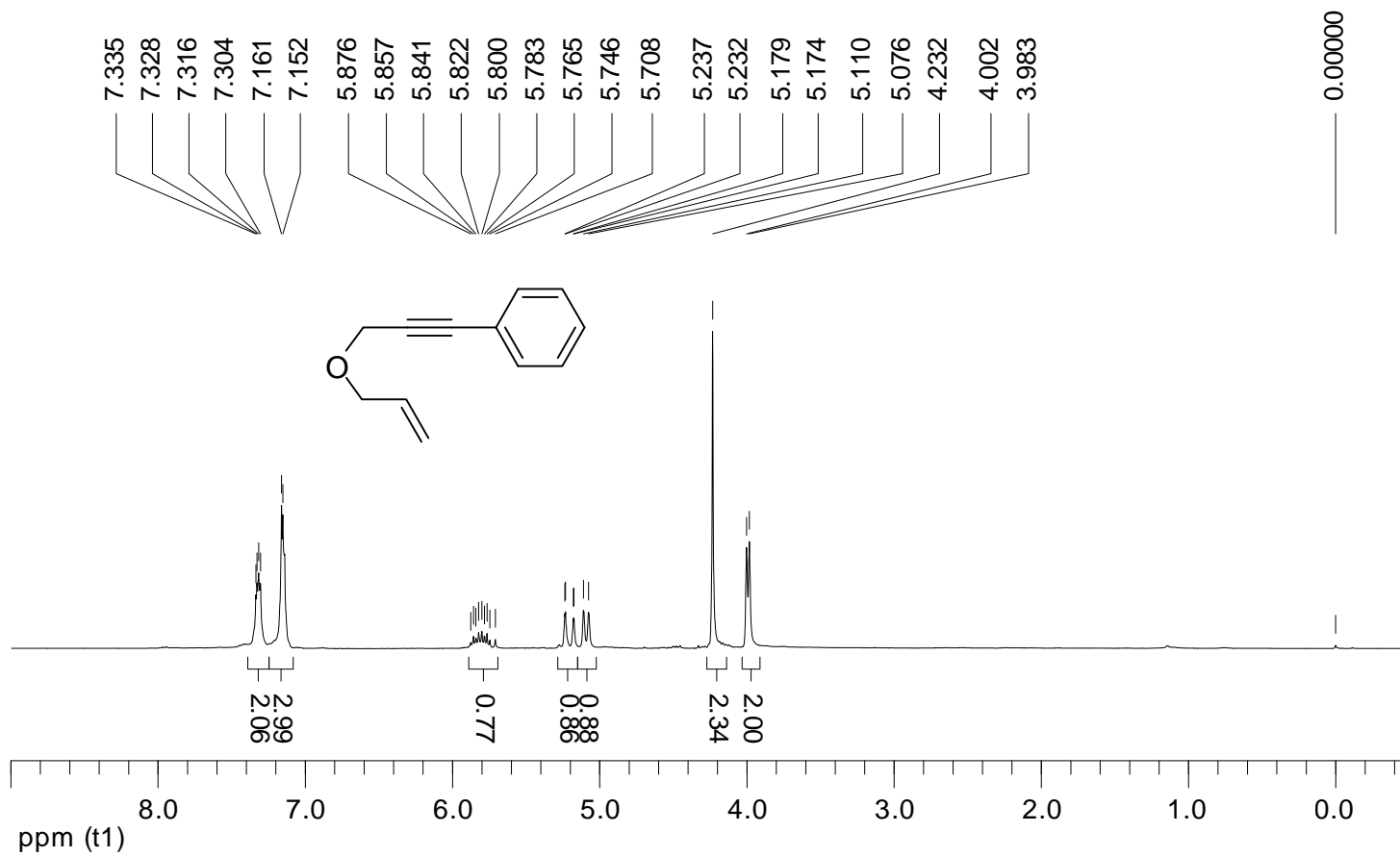
**3h**



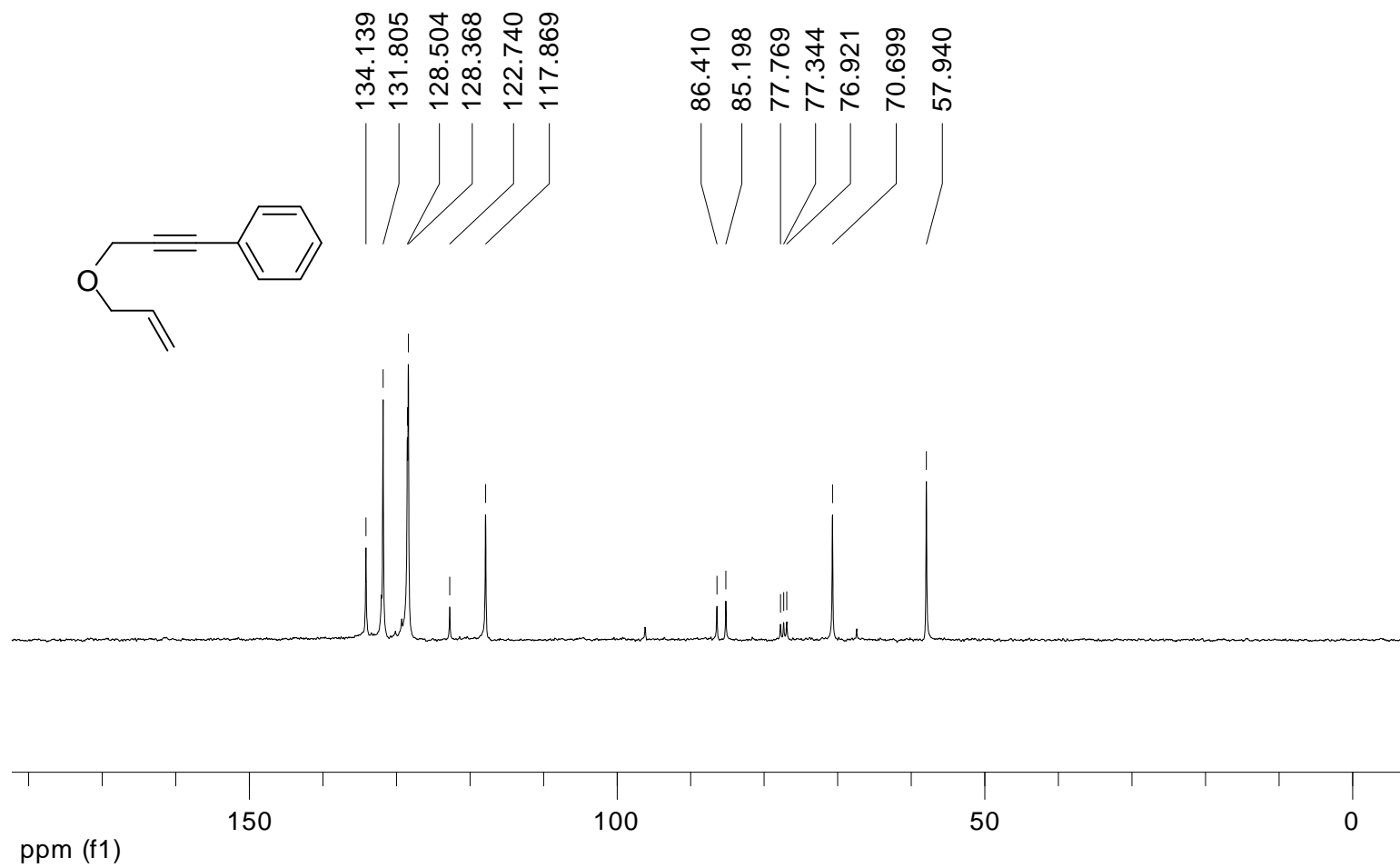
3i



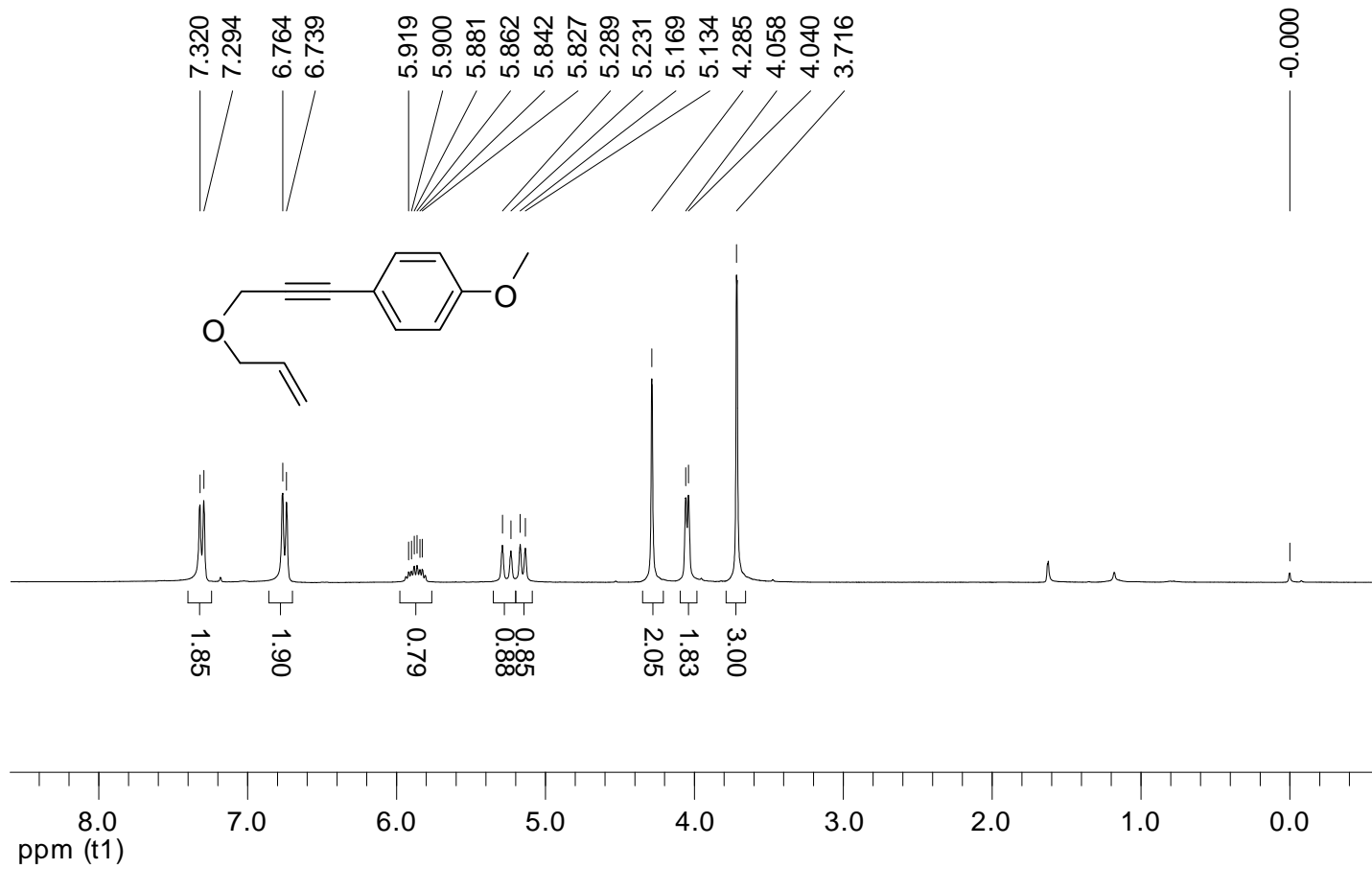
**3i**



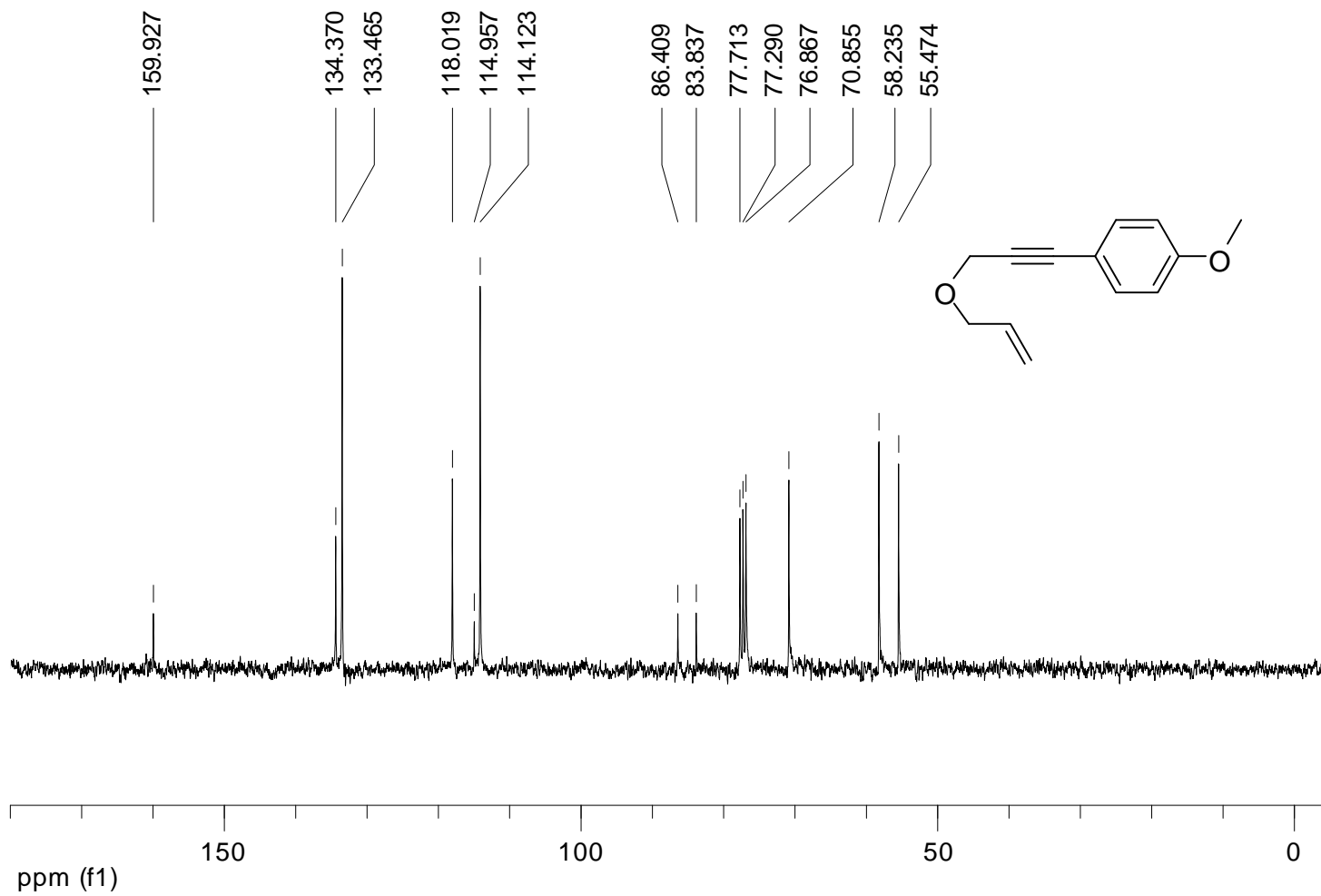
**1b**



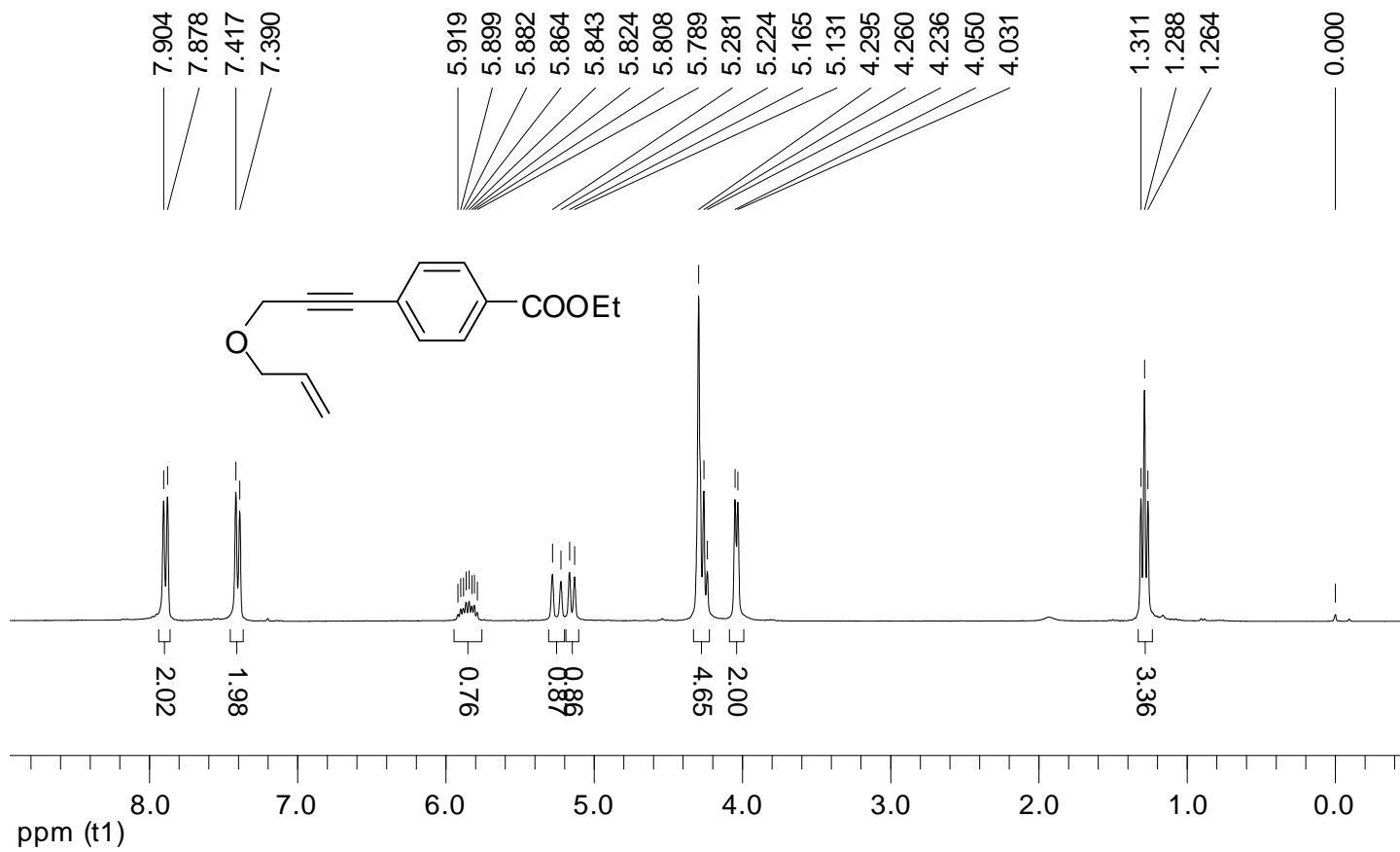
**1b**



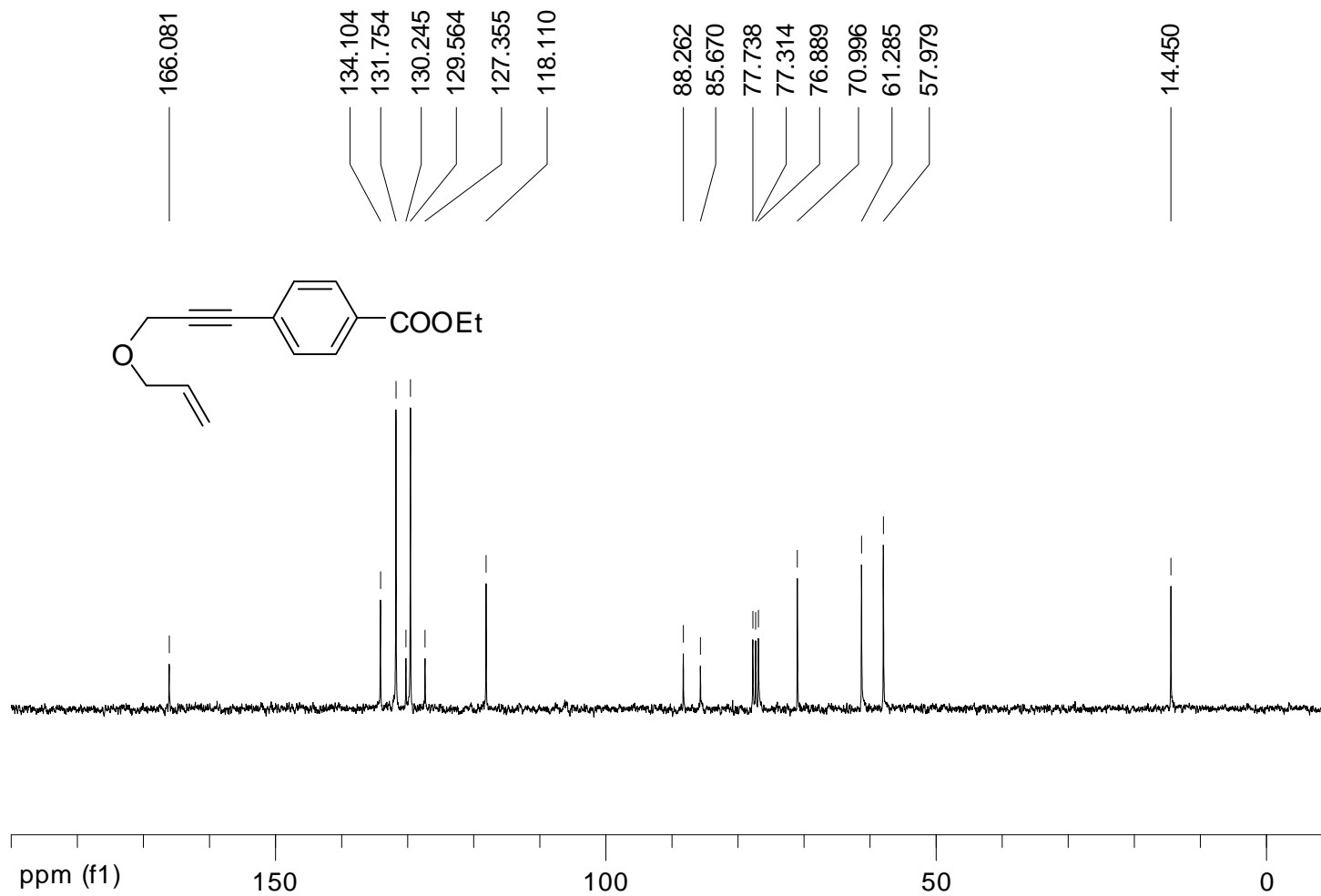
**1c**



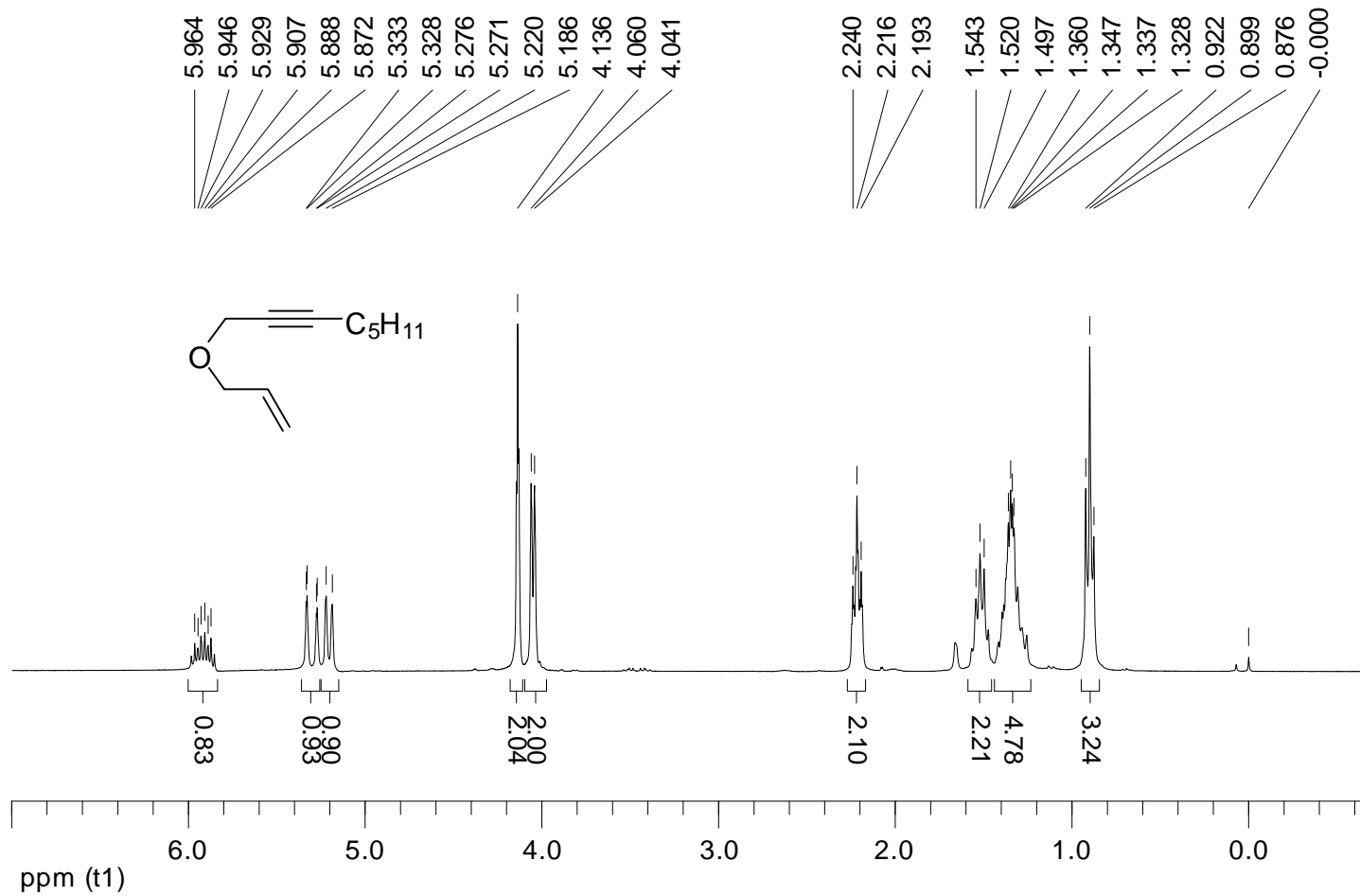
**1c**



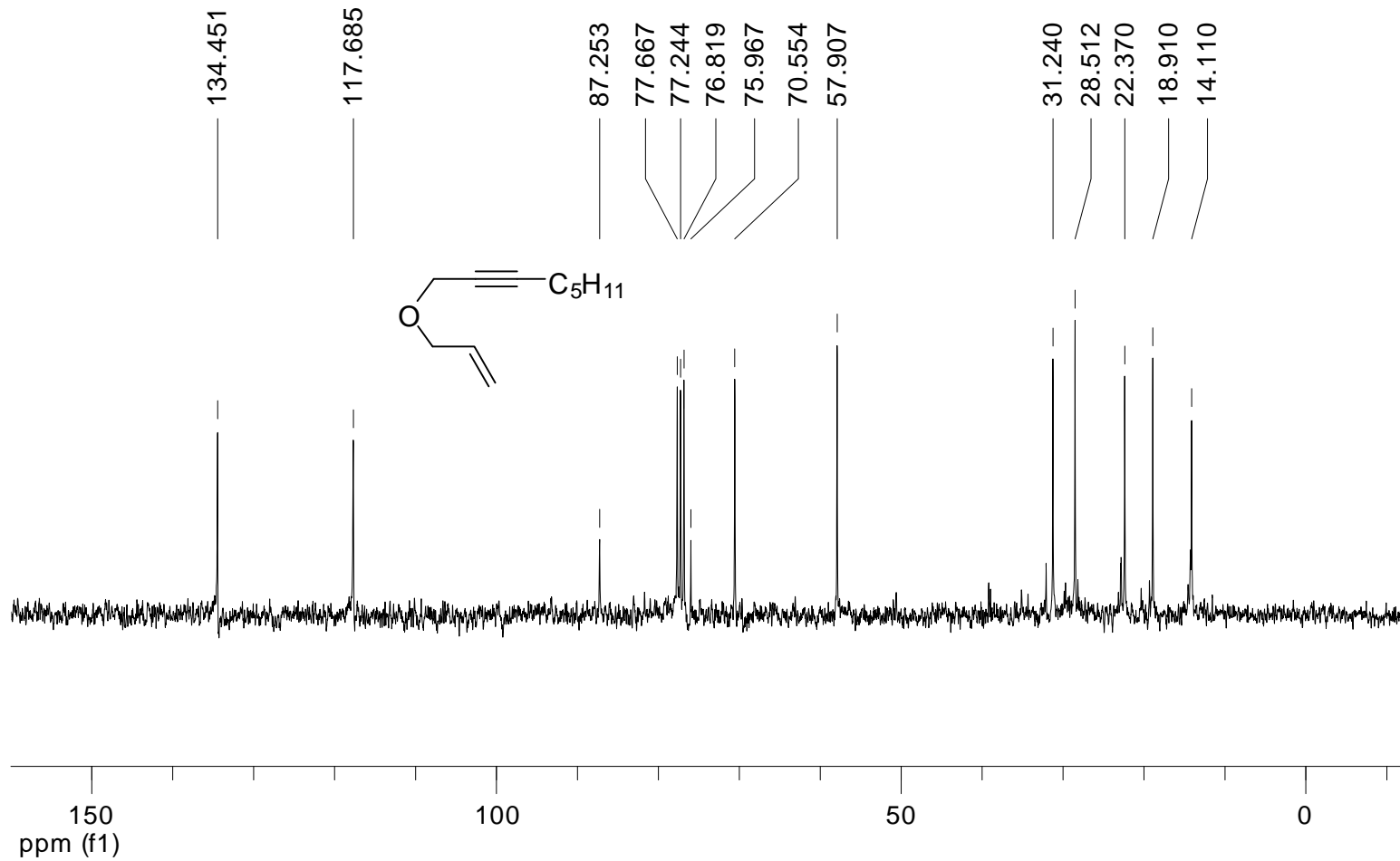
**1d**



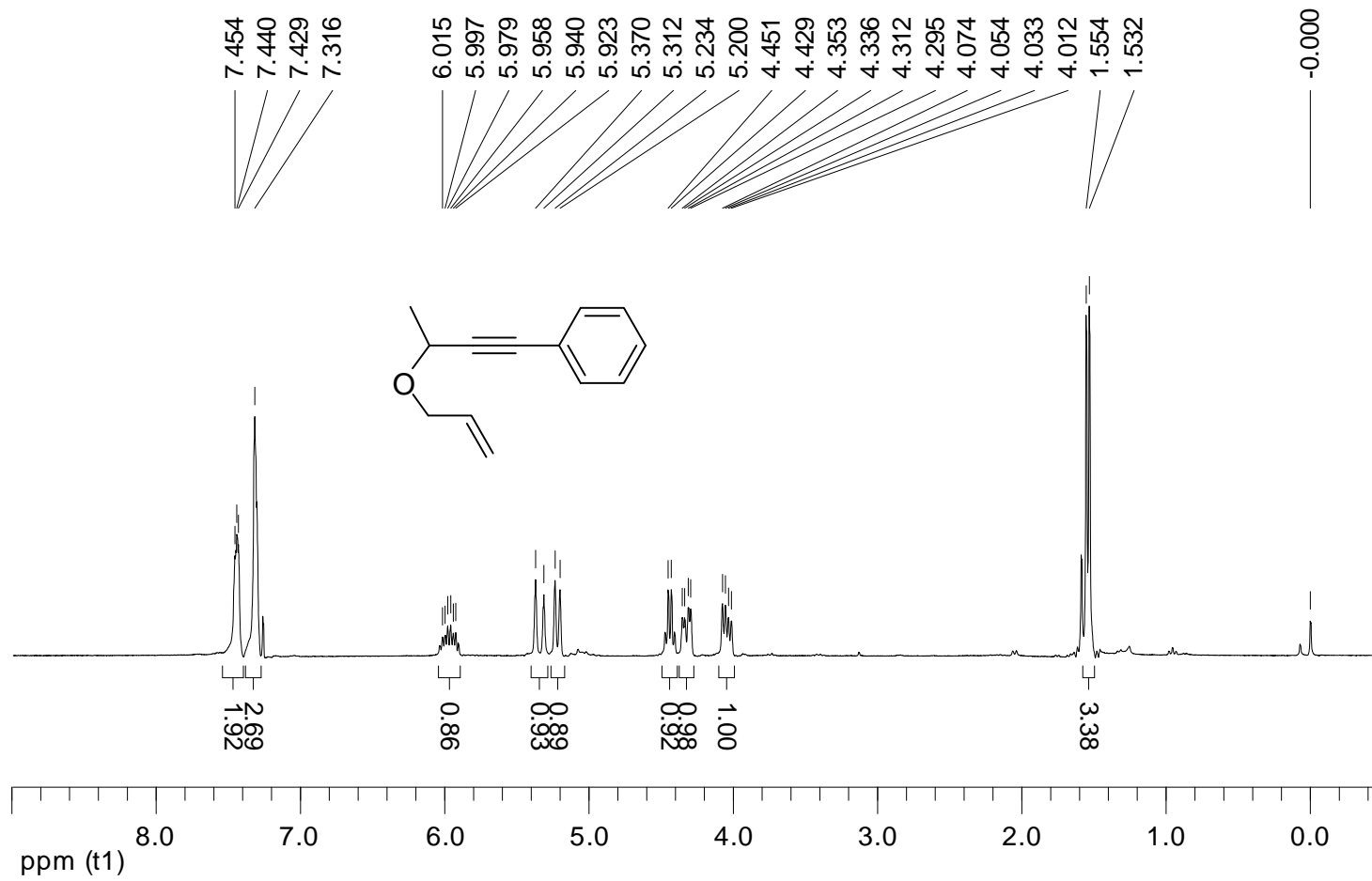
**1d**



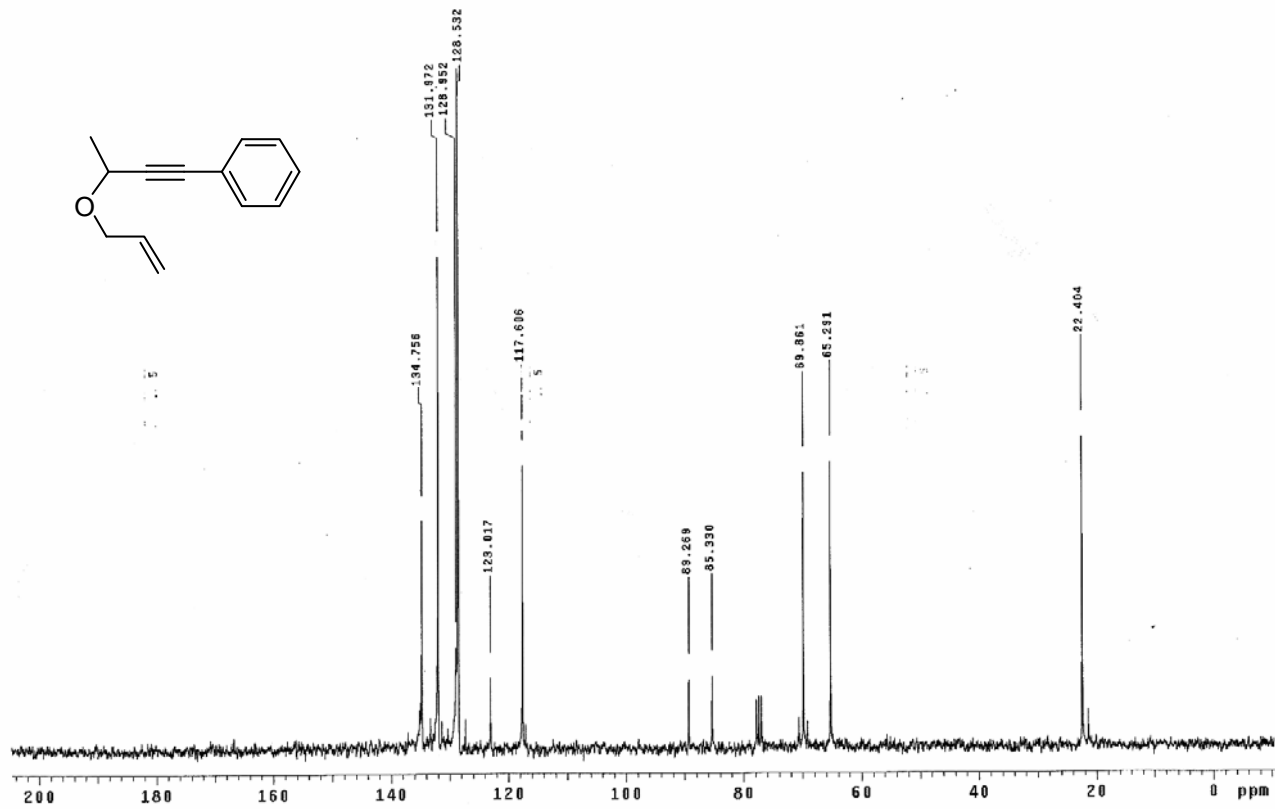
**1e**



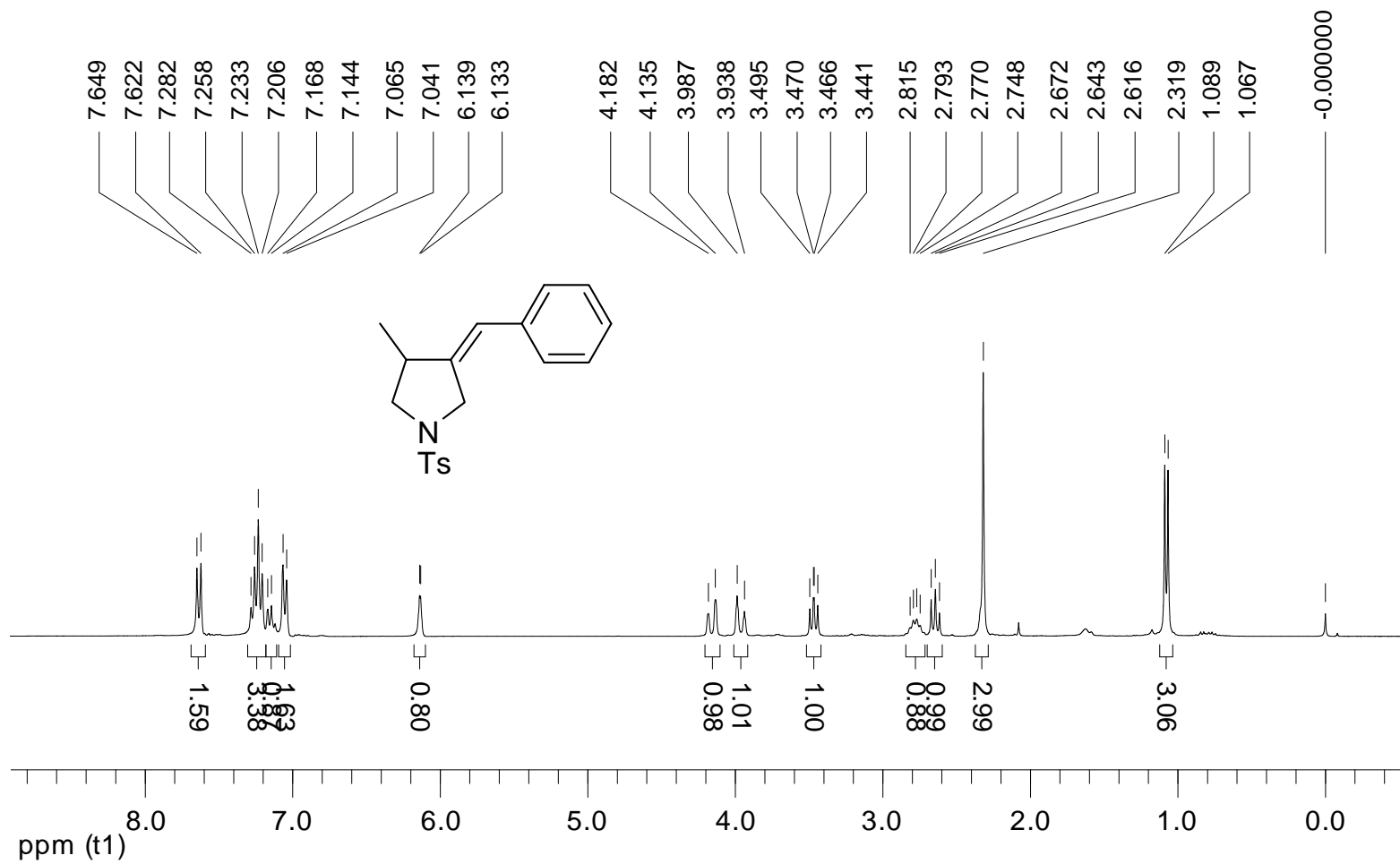
**1e**



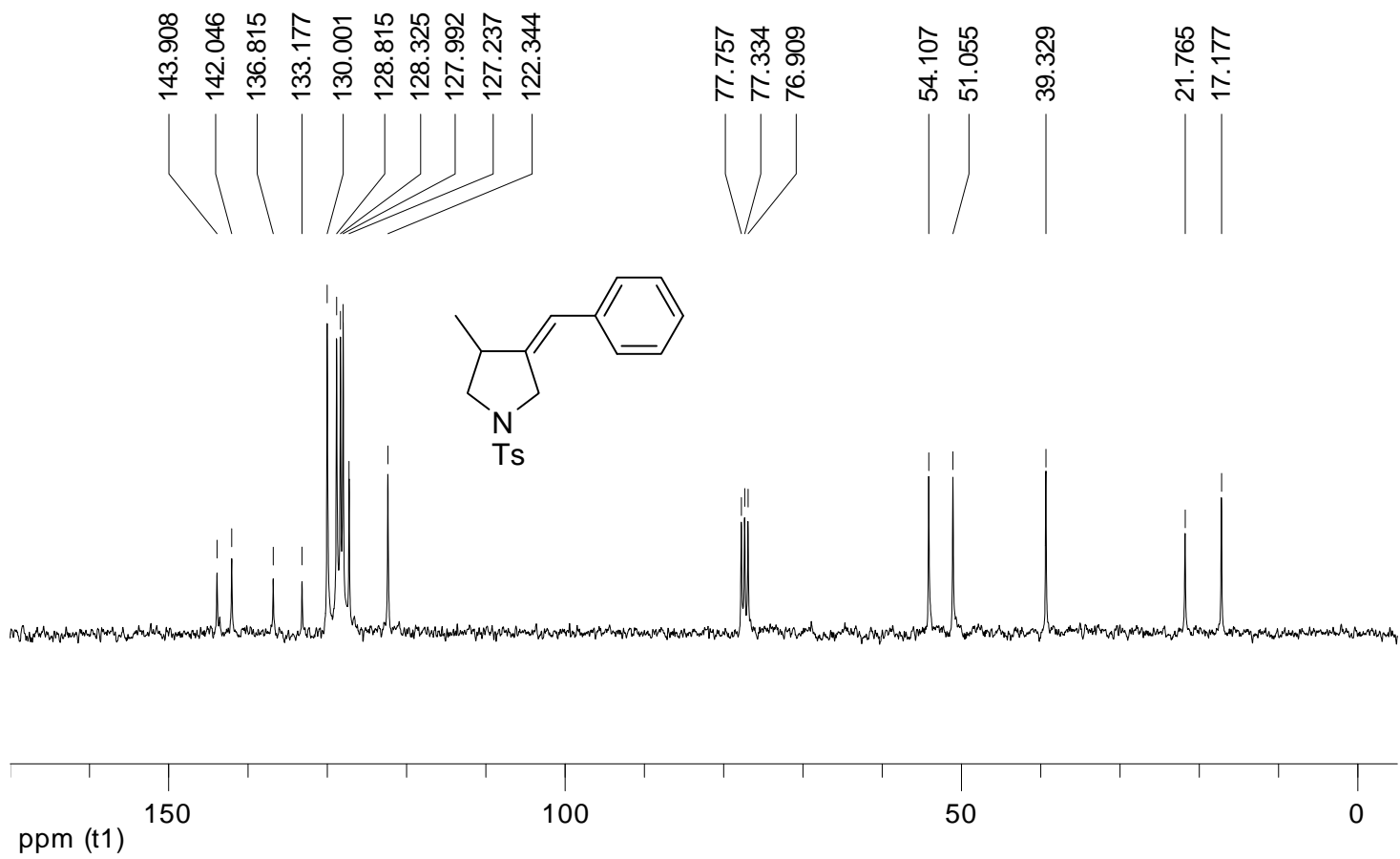
**1a**



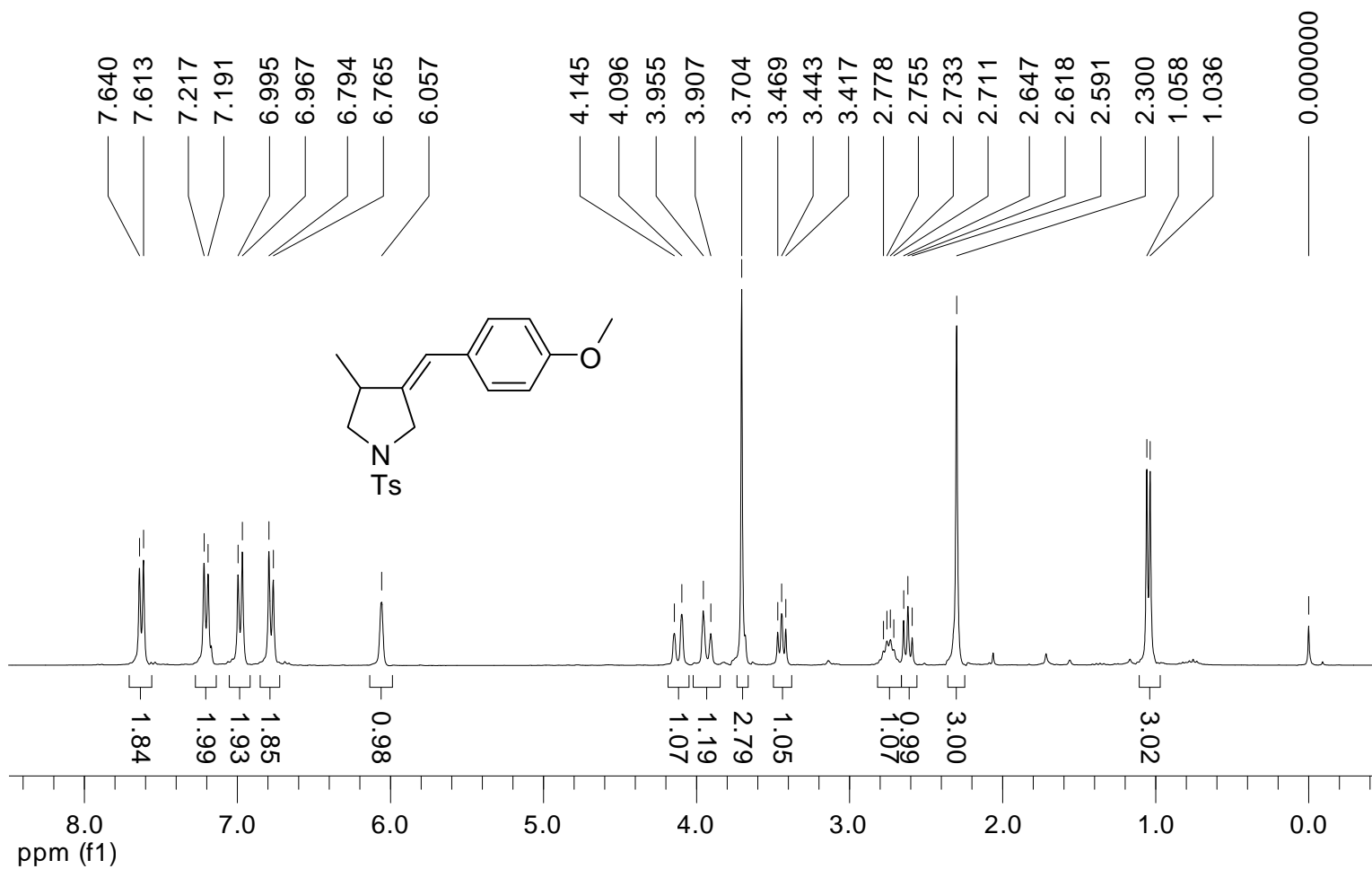
1a



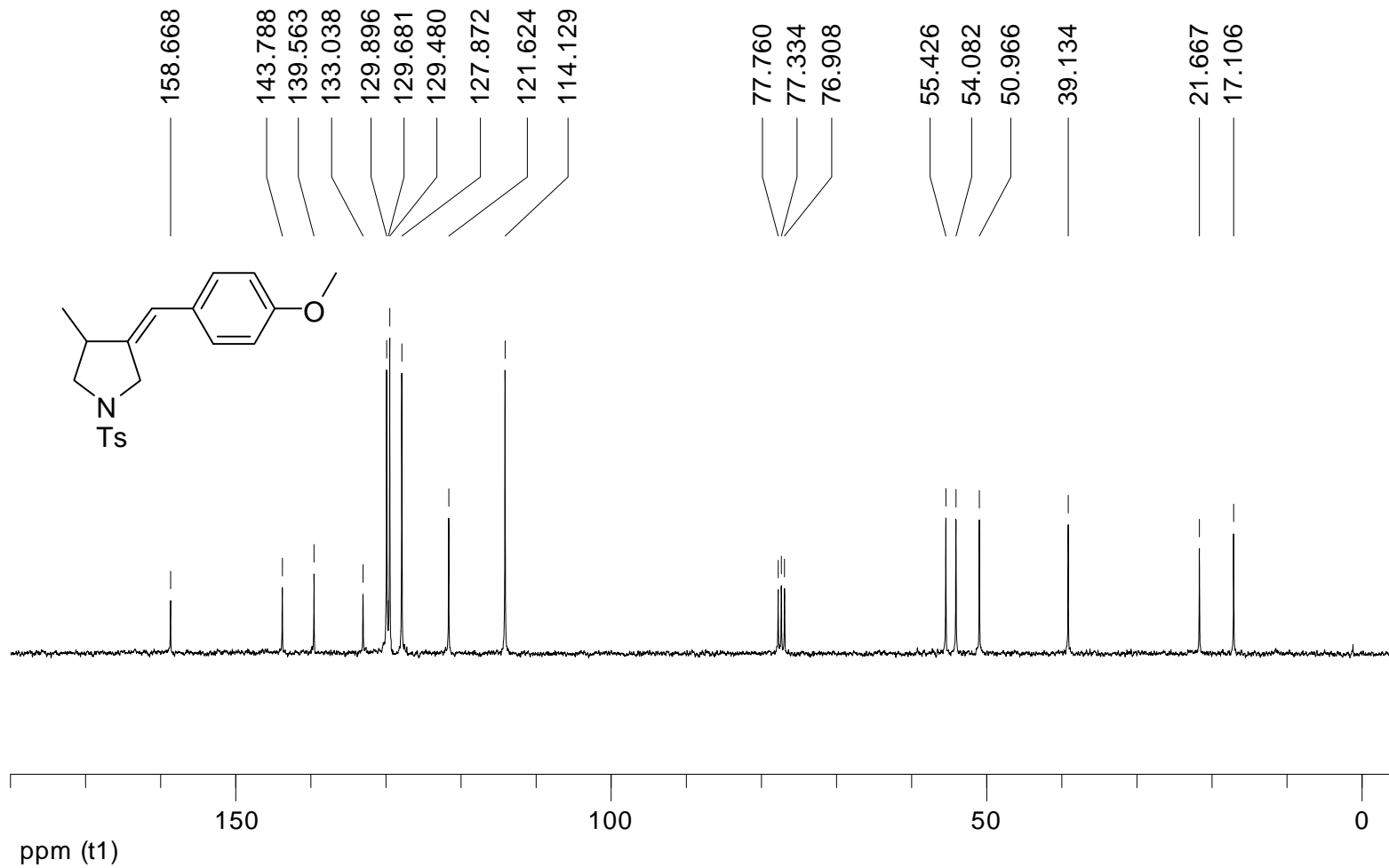
4a



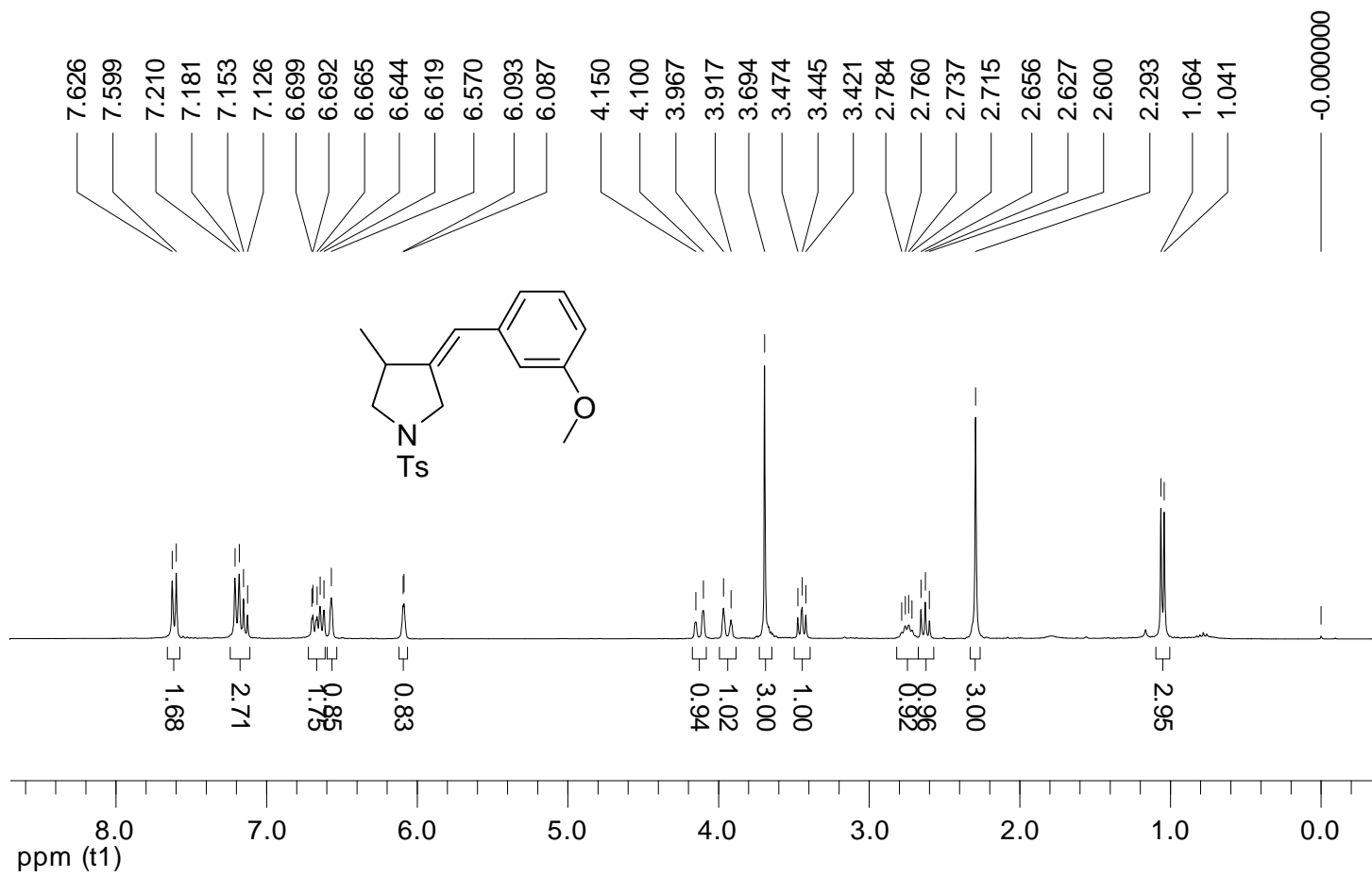
4a



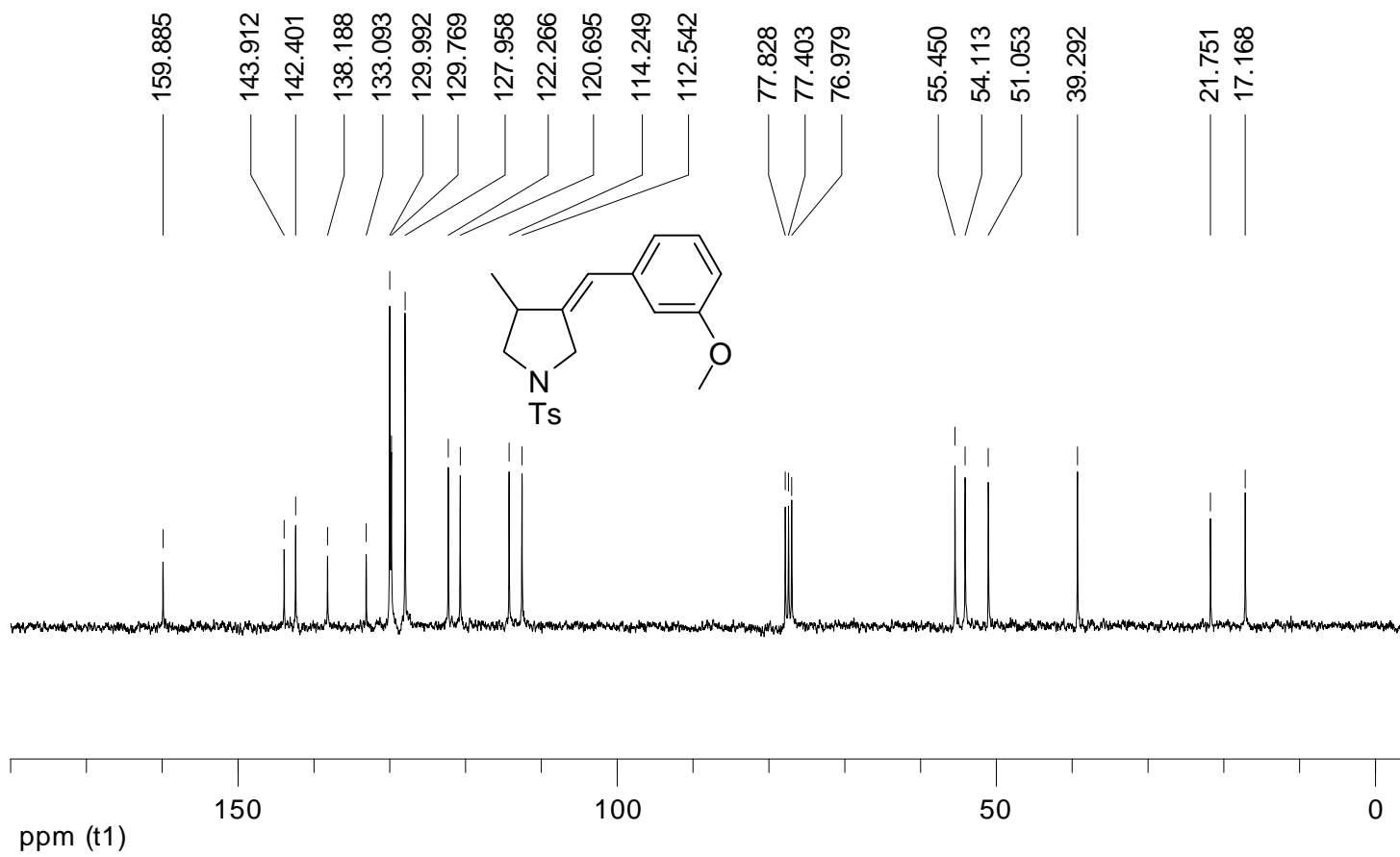
4b



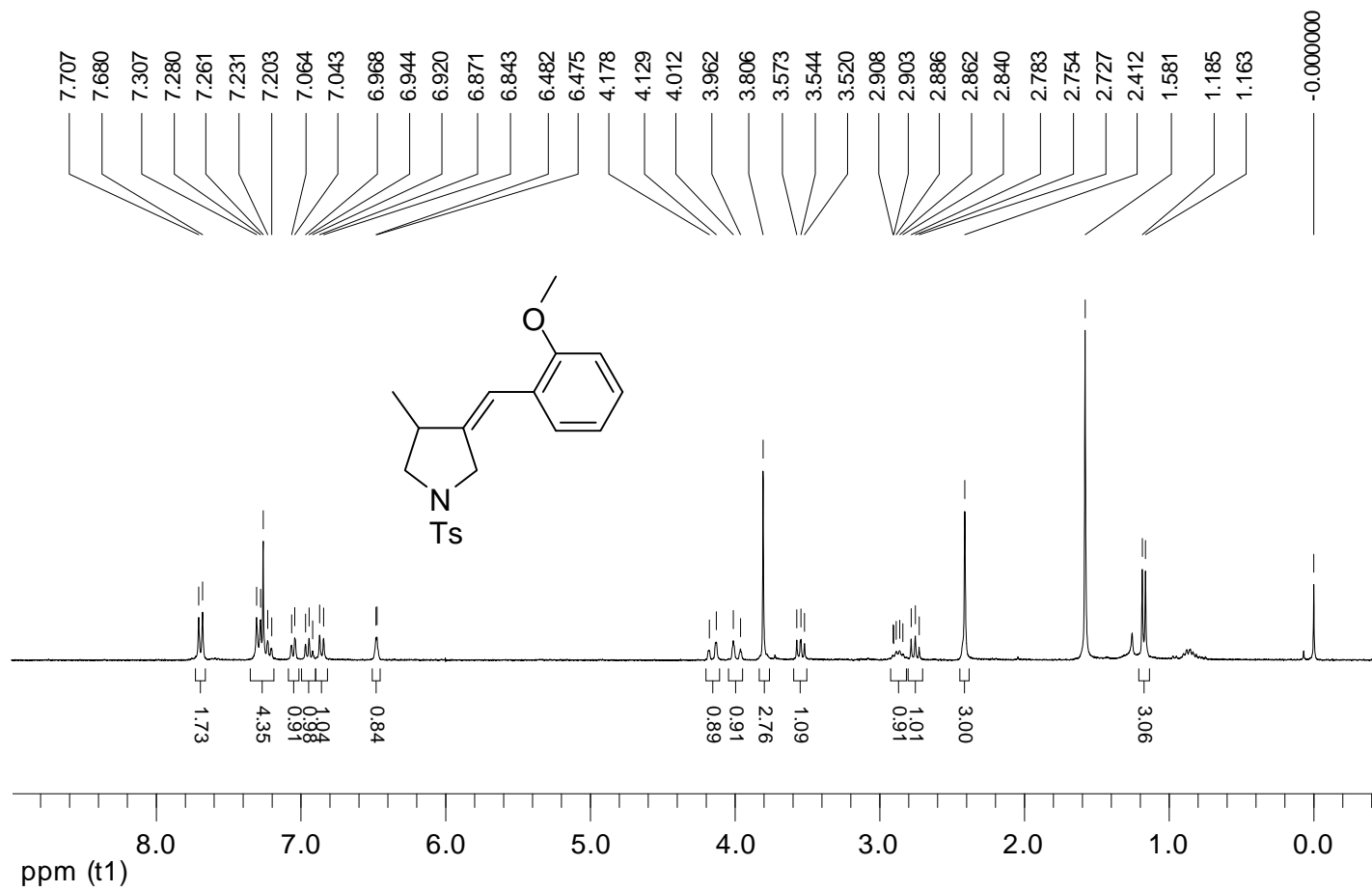
4b



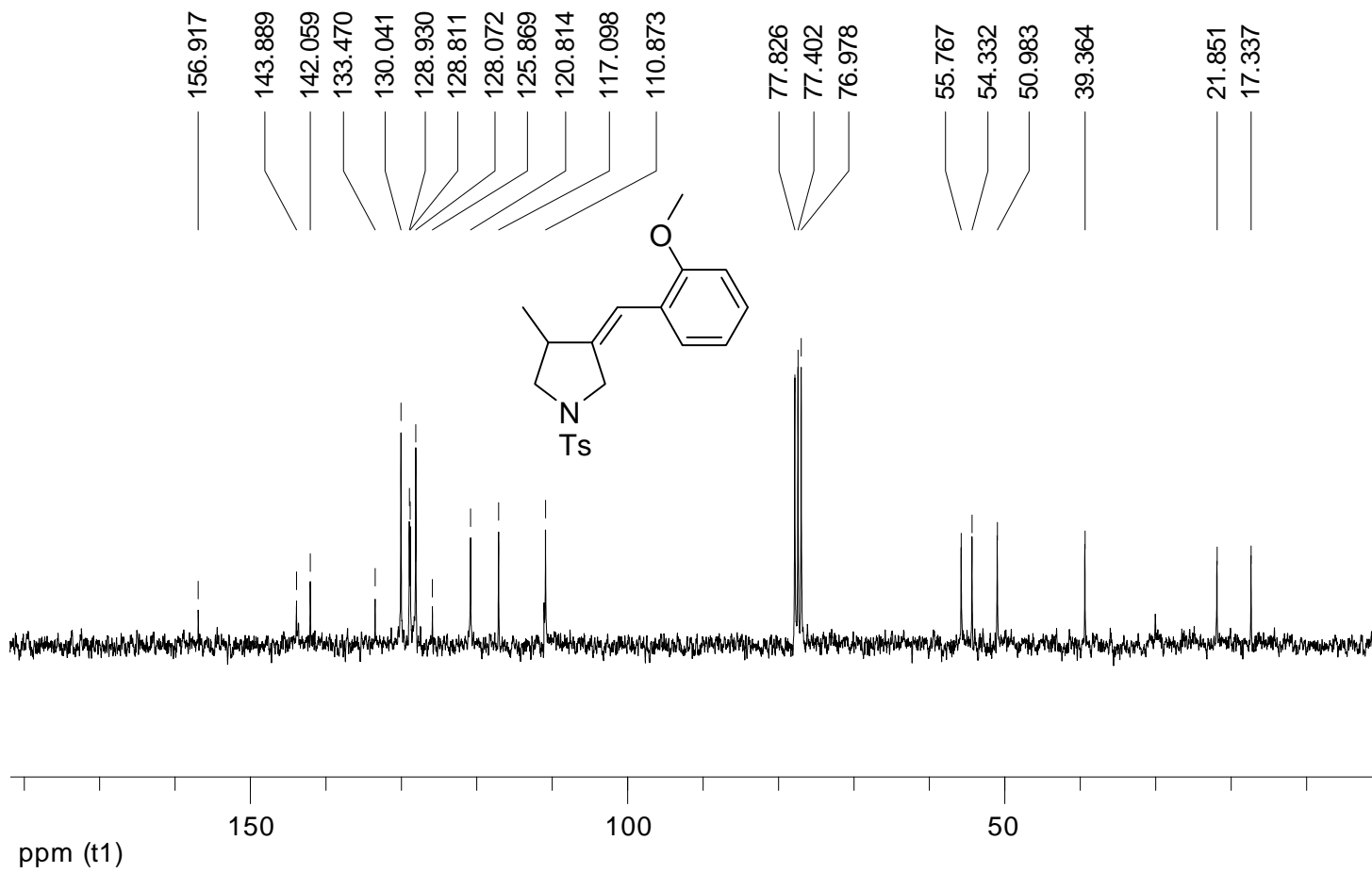
**4c**



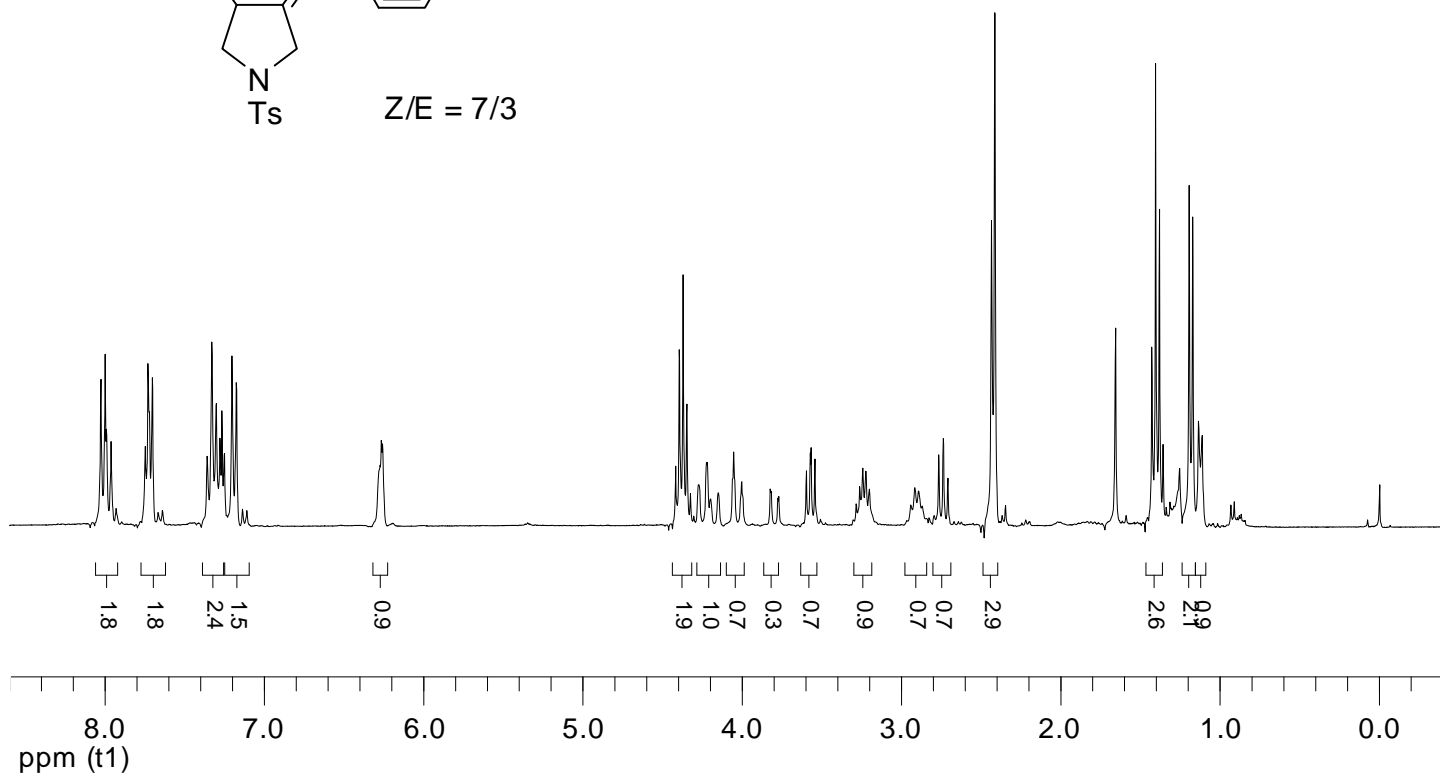
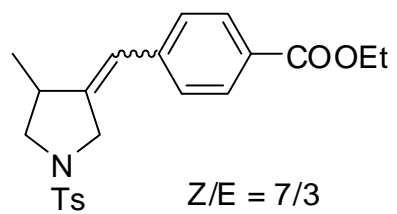
4c



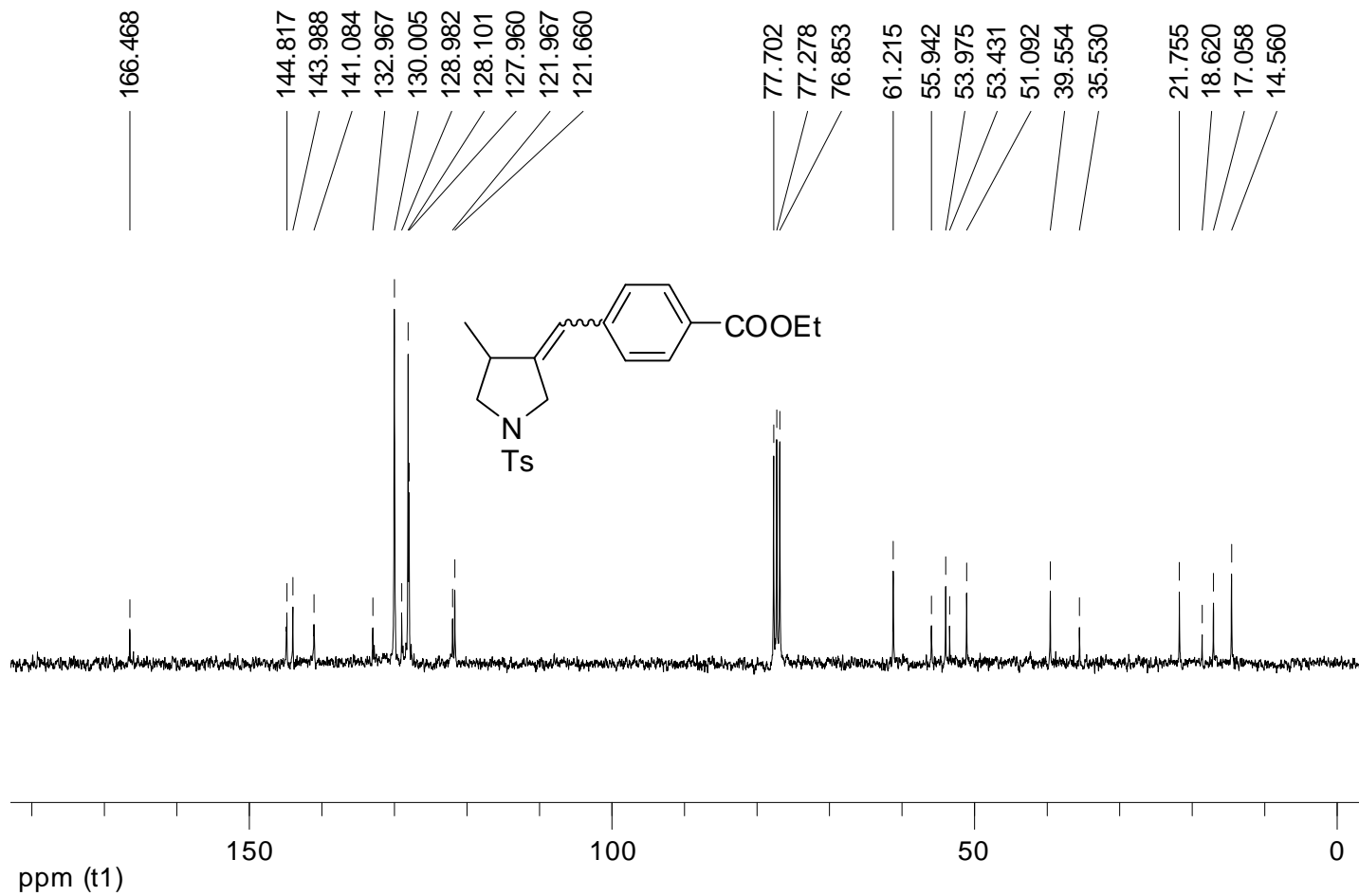
**4d**



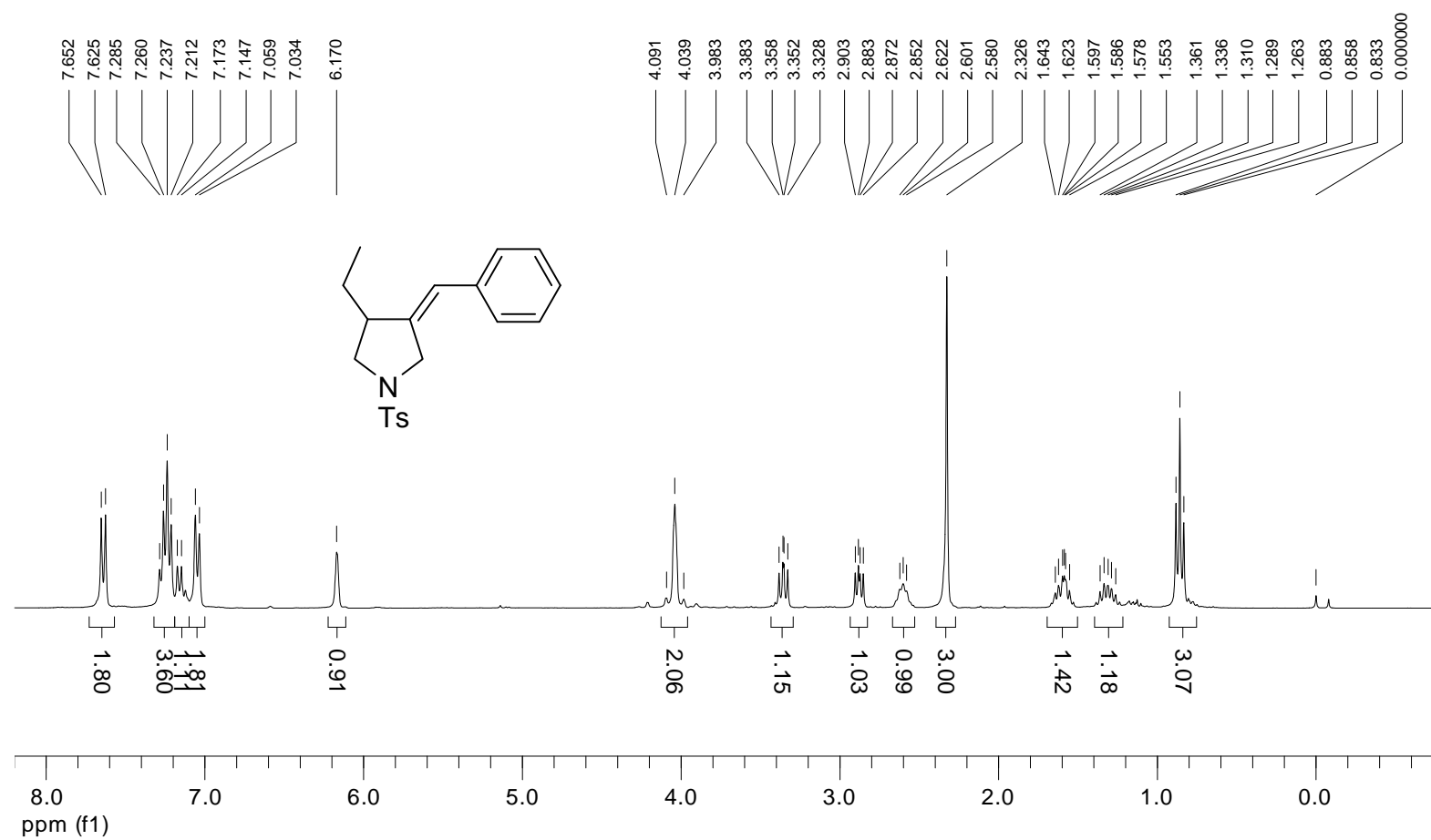
4d



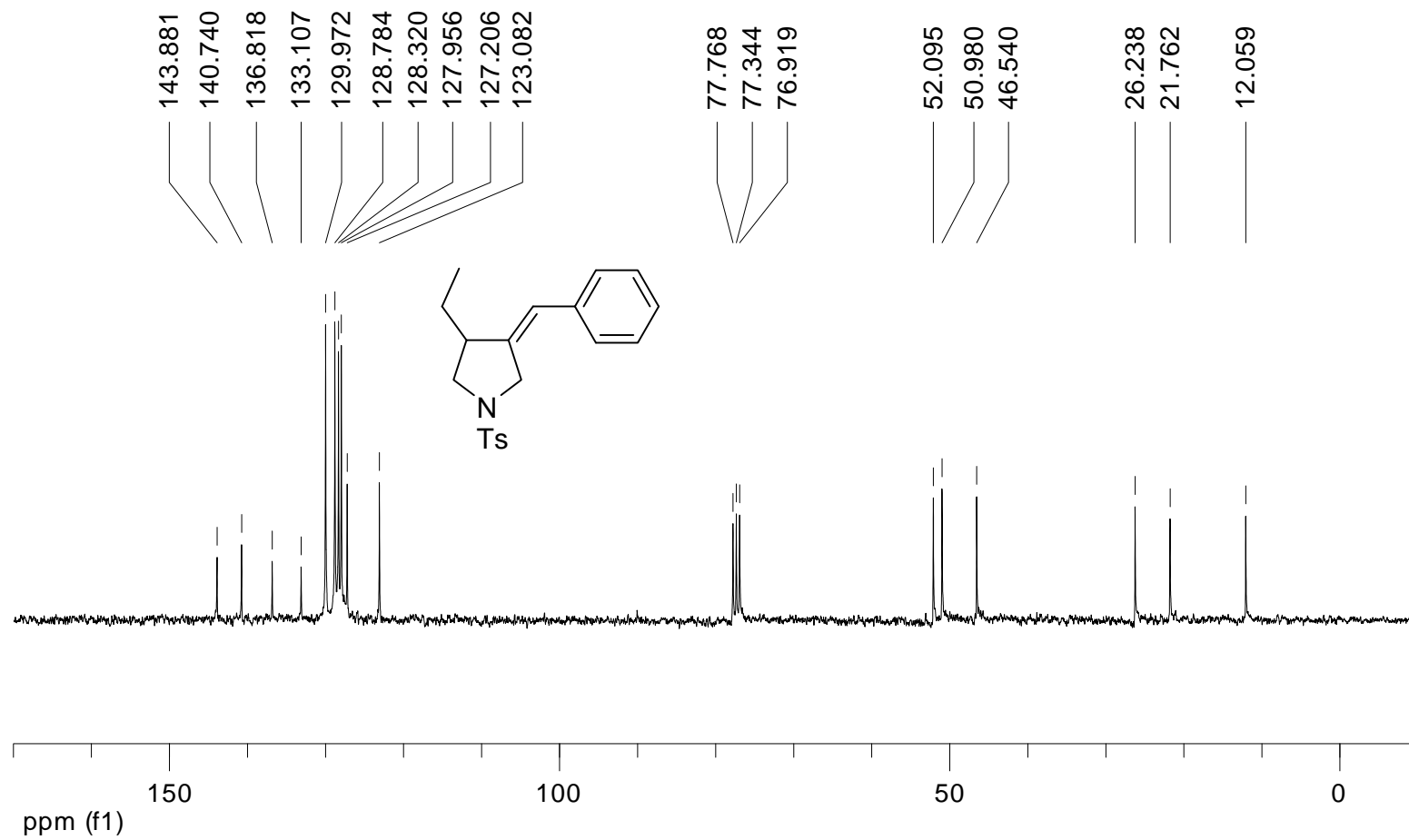
**4e**



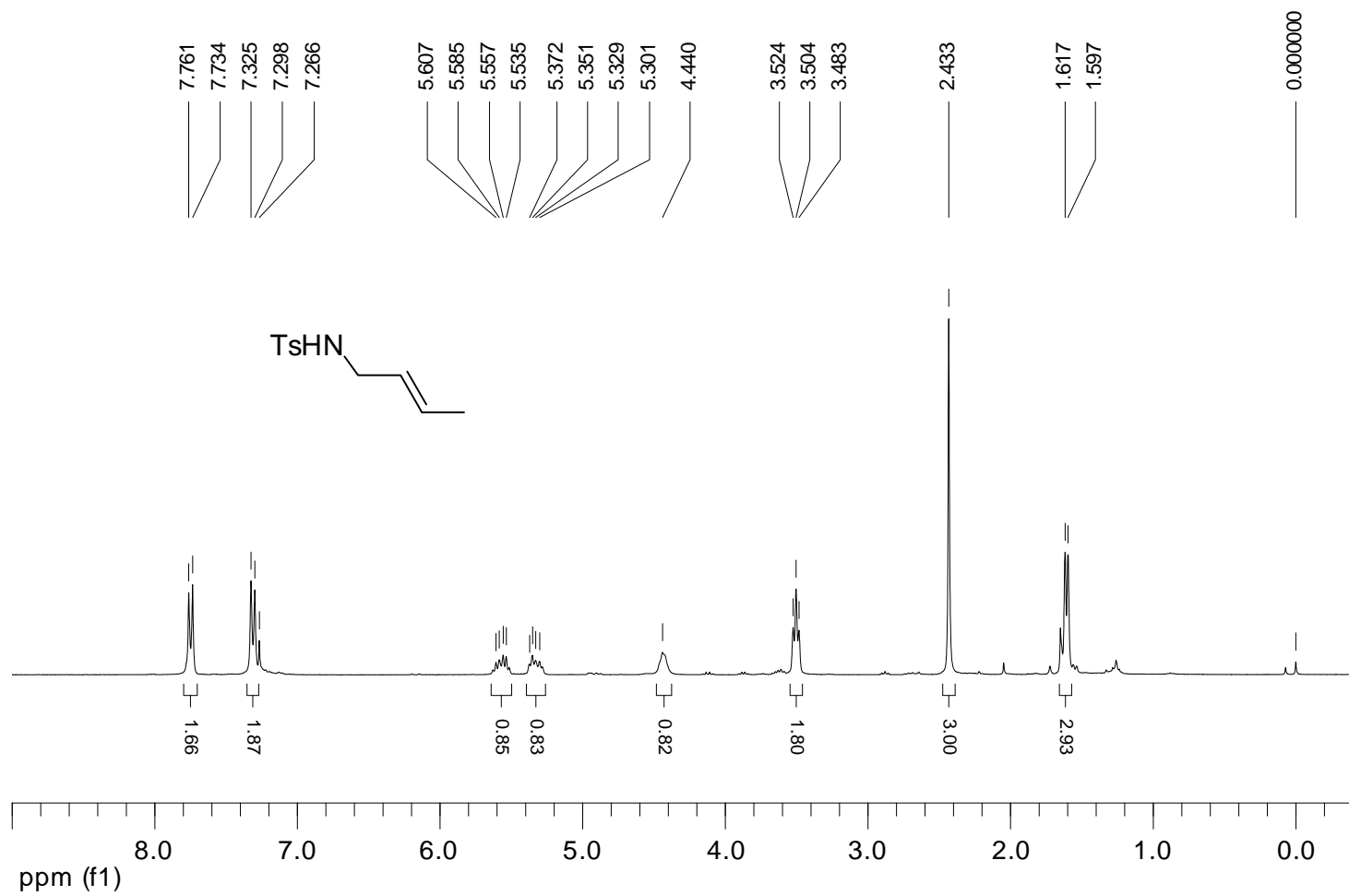
4e



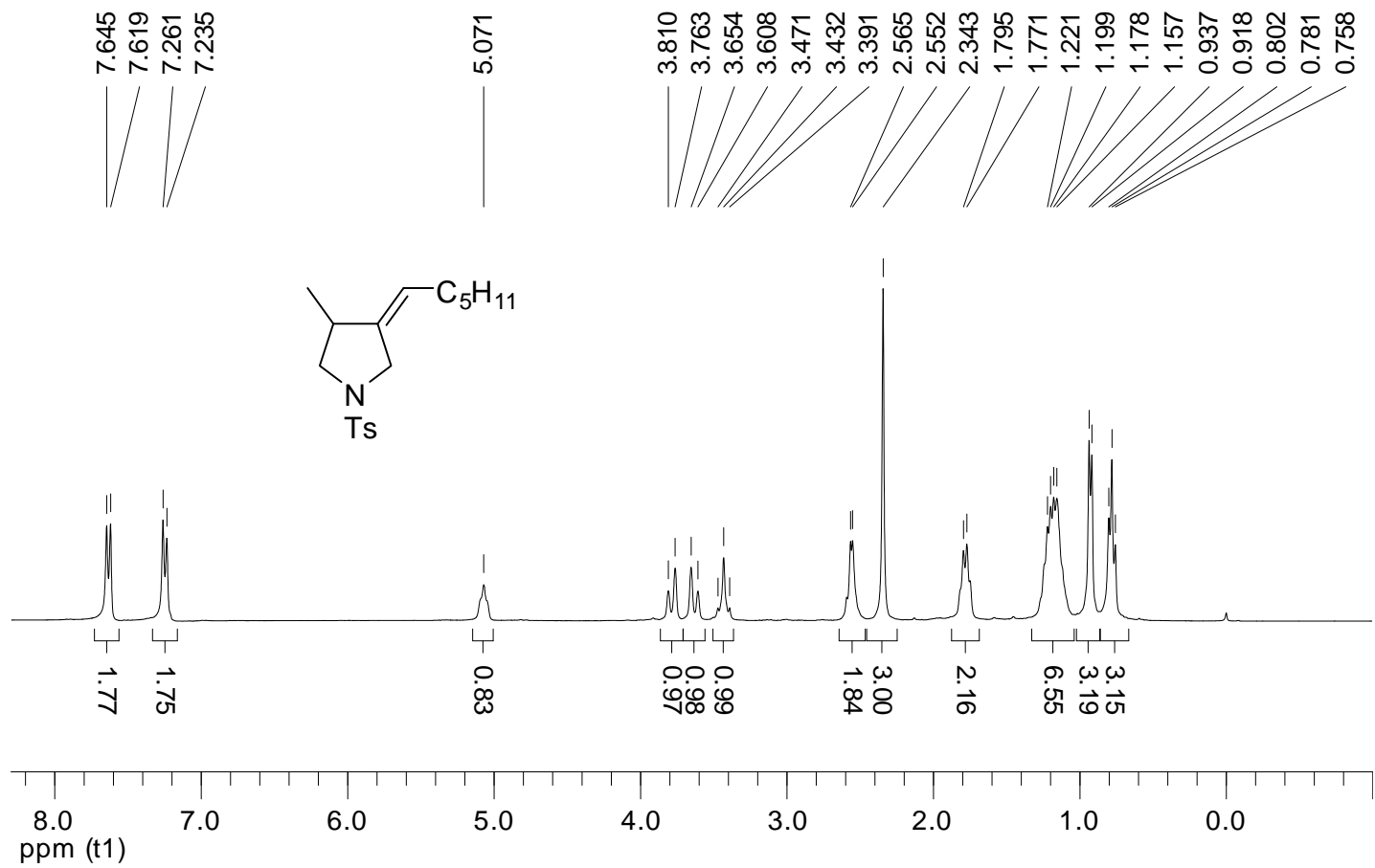
4g



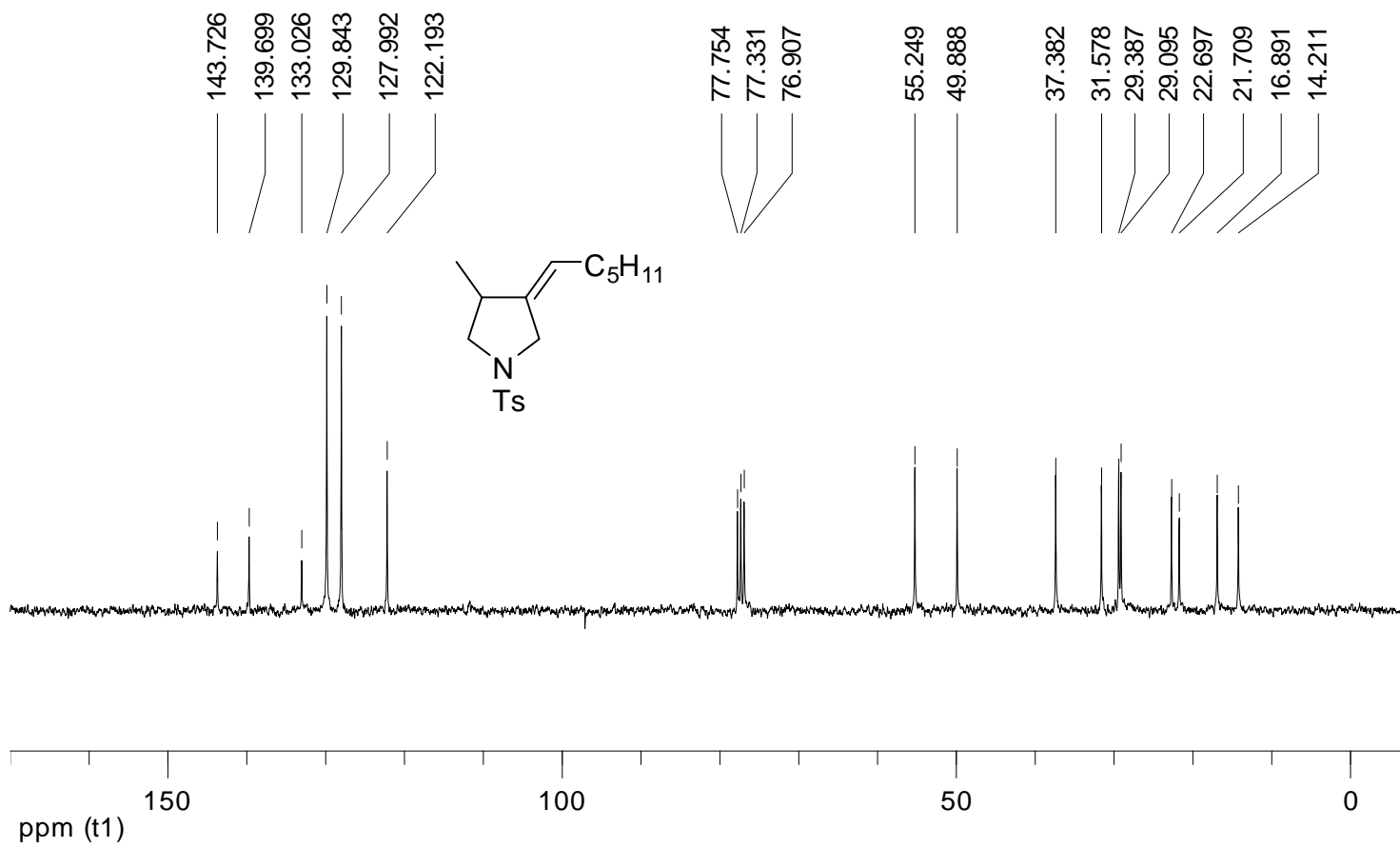
4g



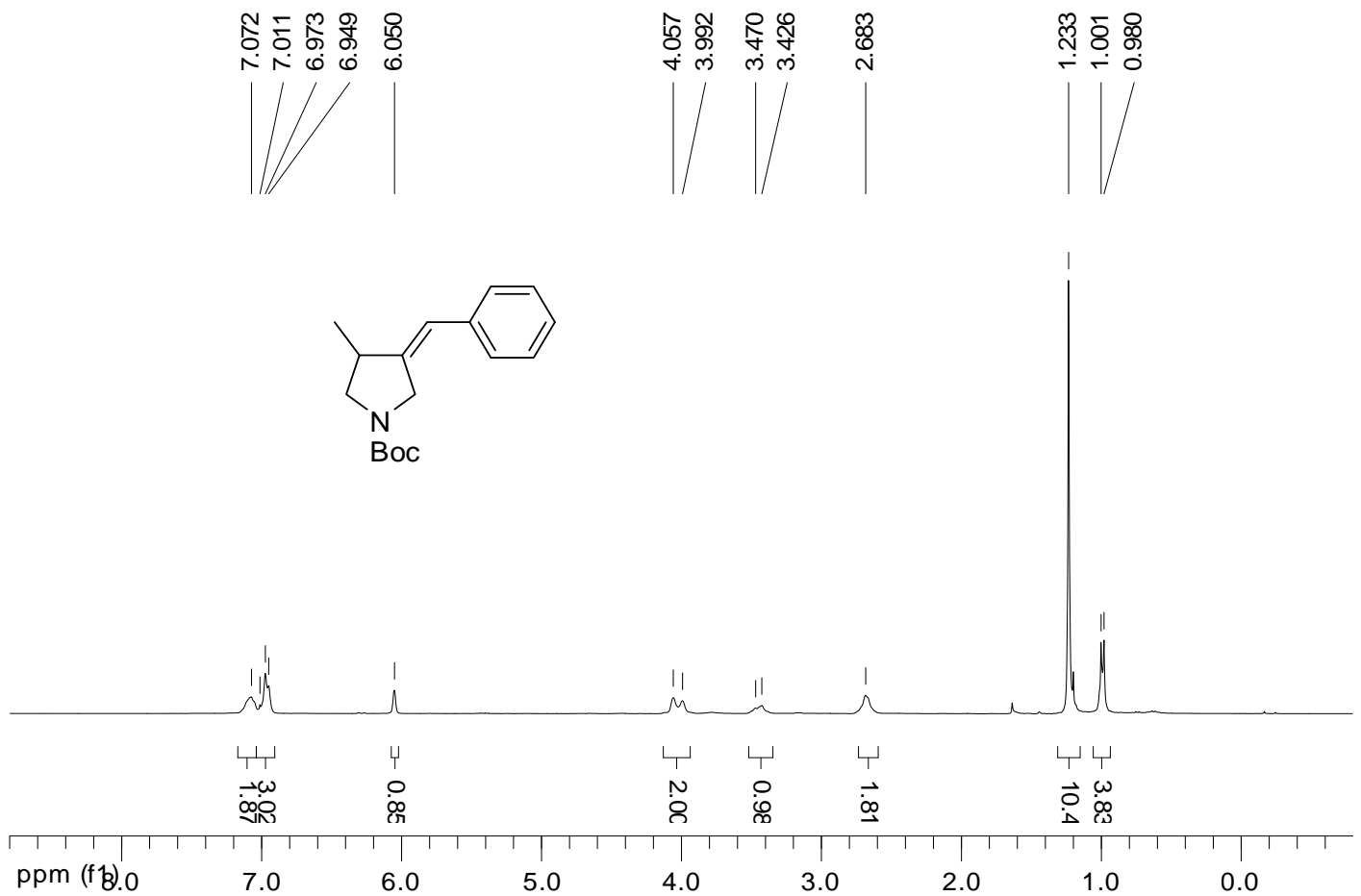
4j



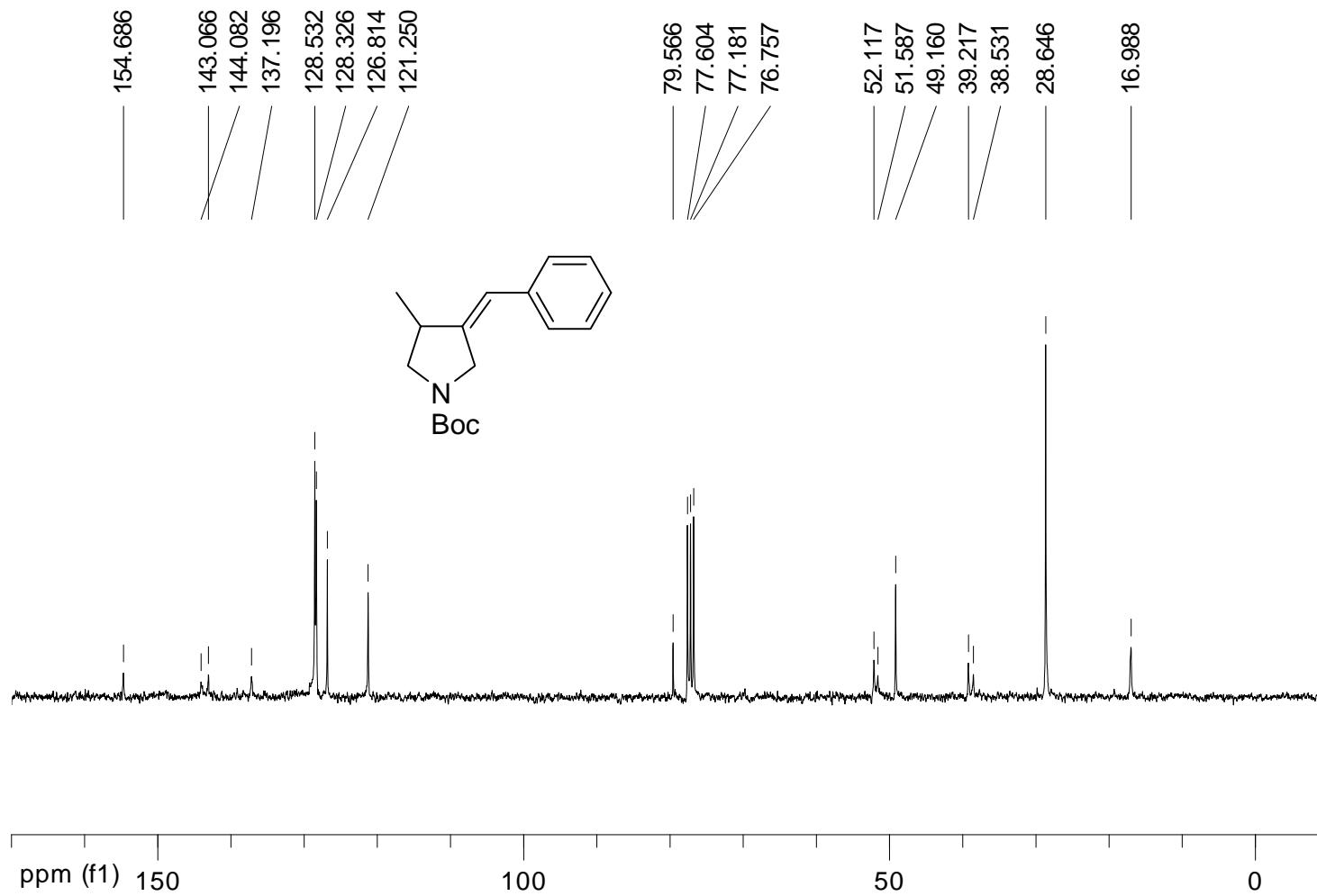
4f



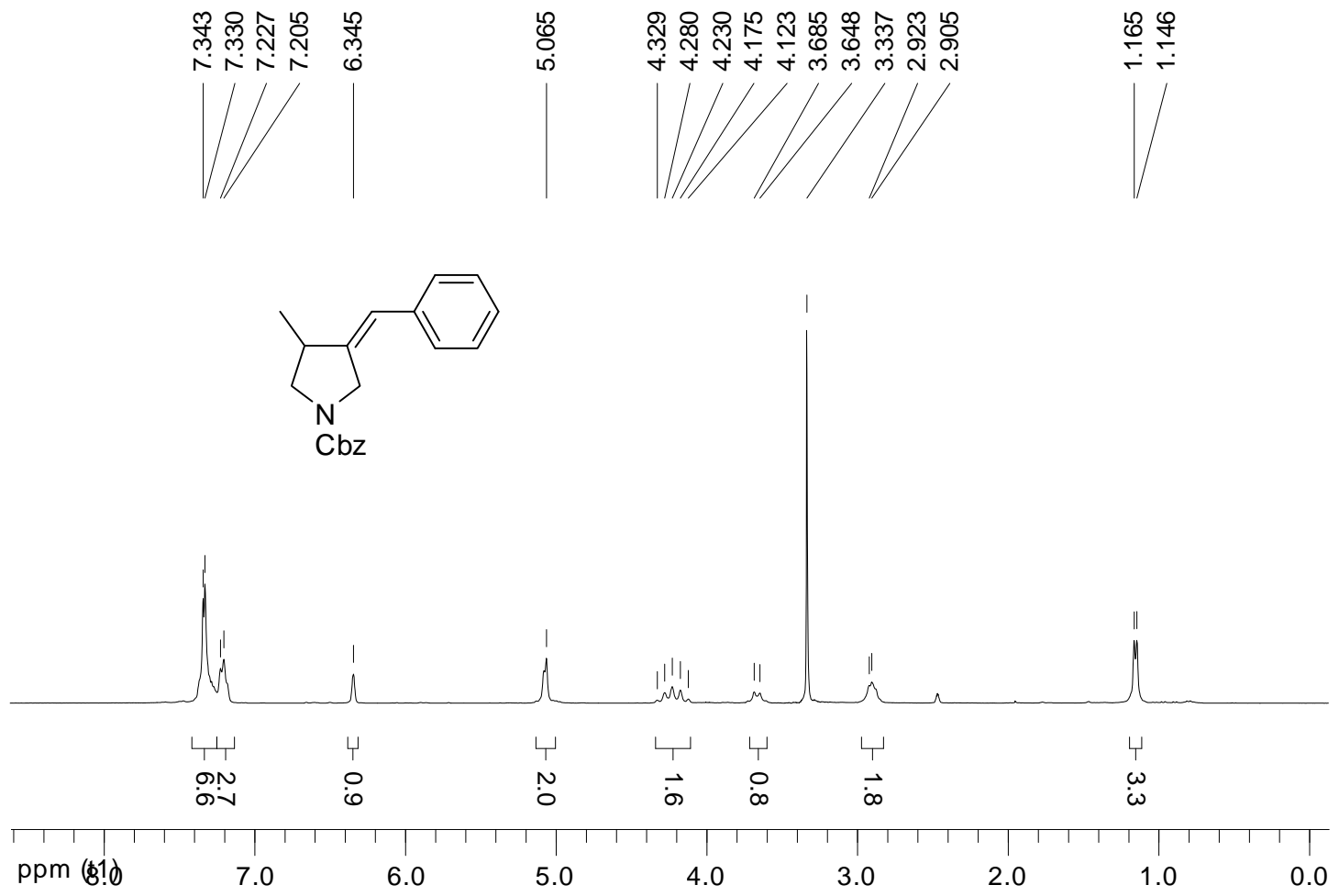
**4f**



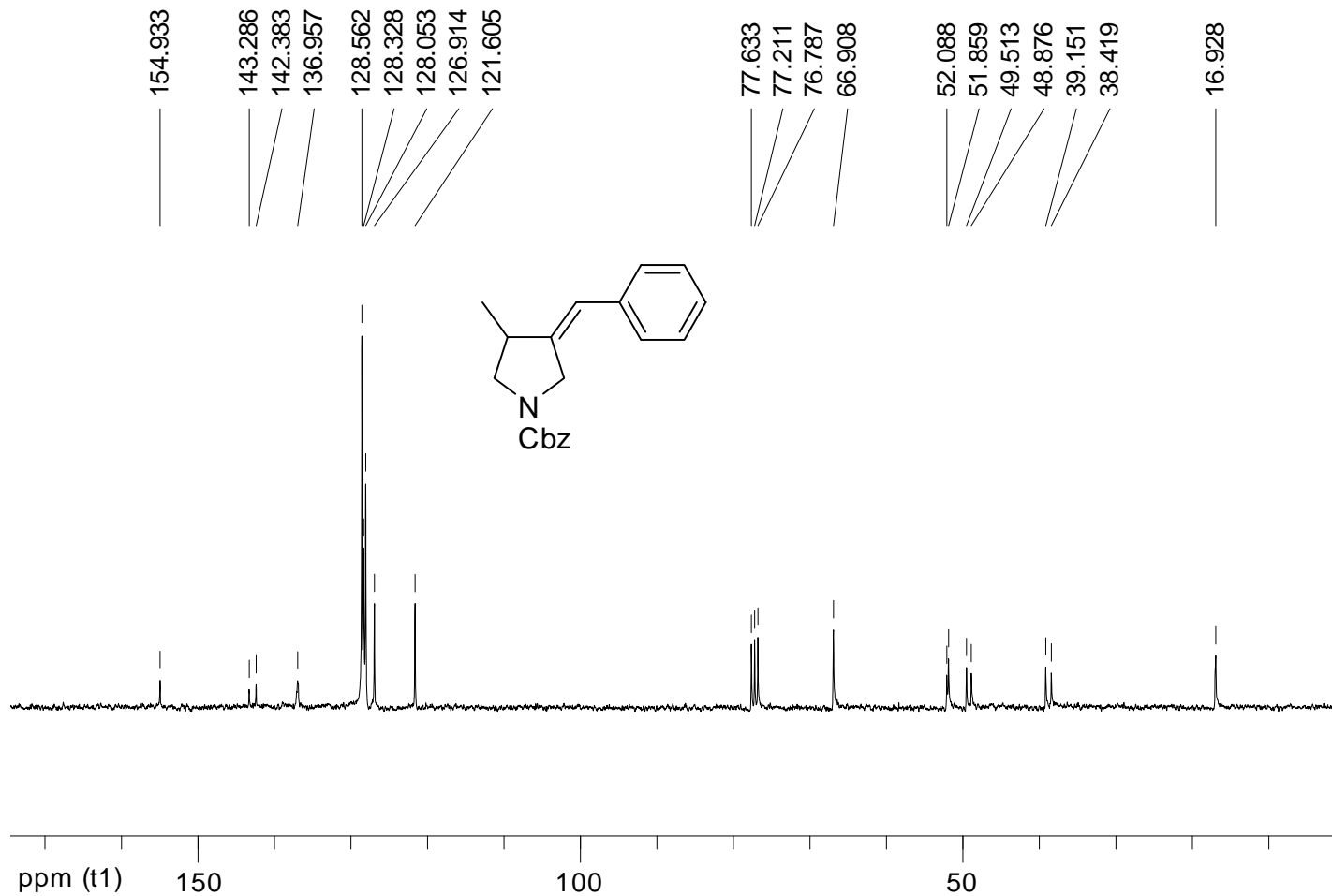
4h



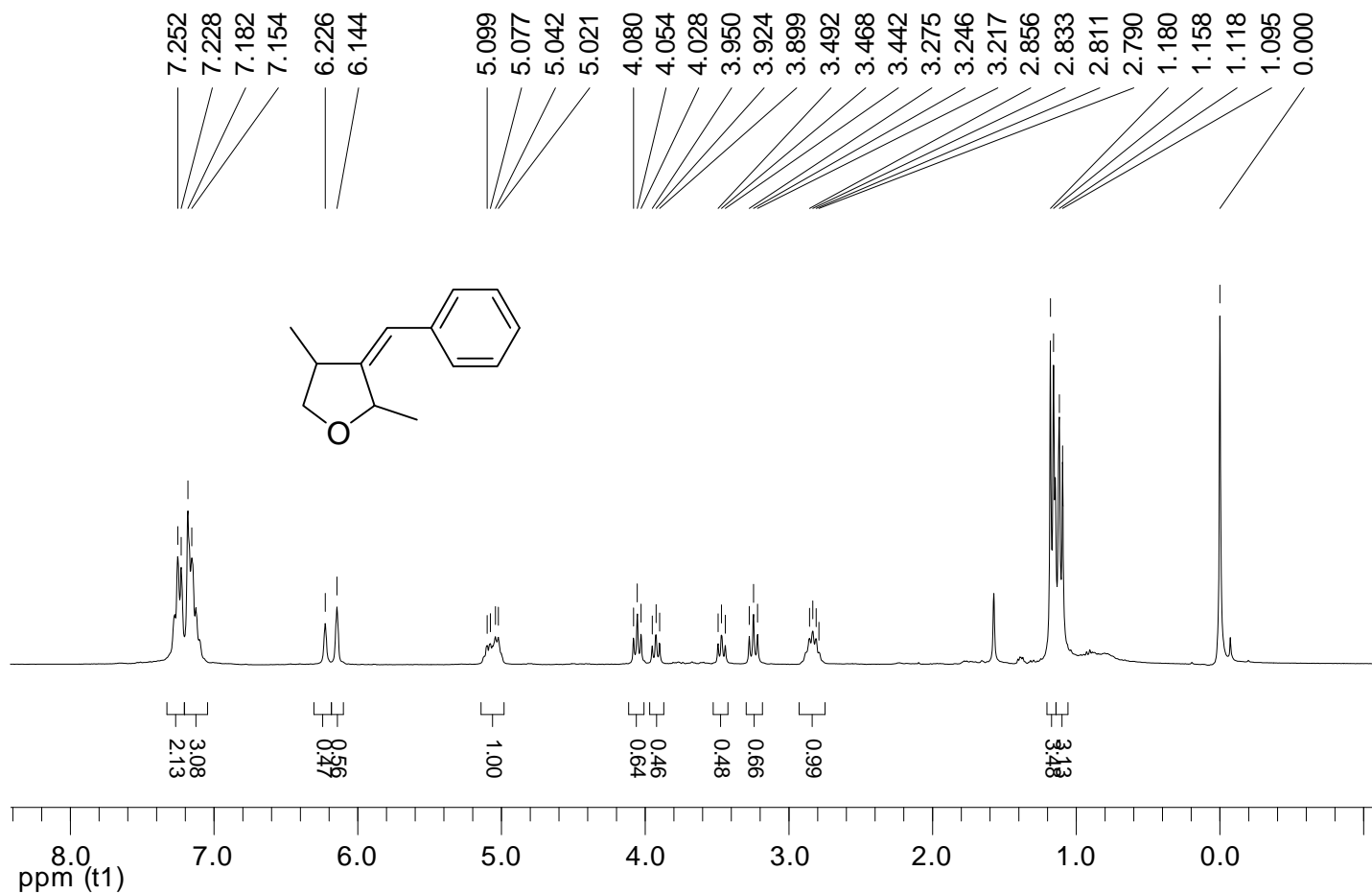
4h



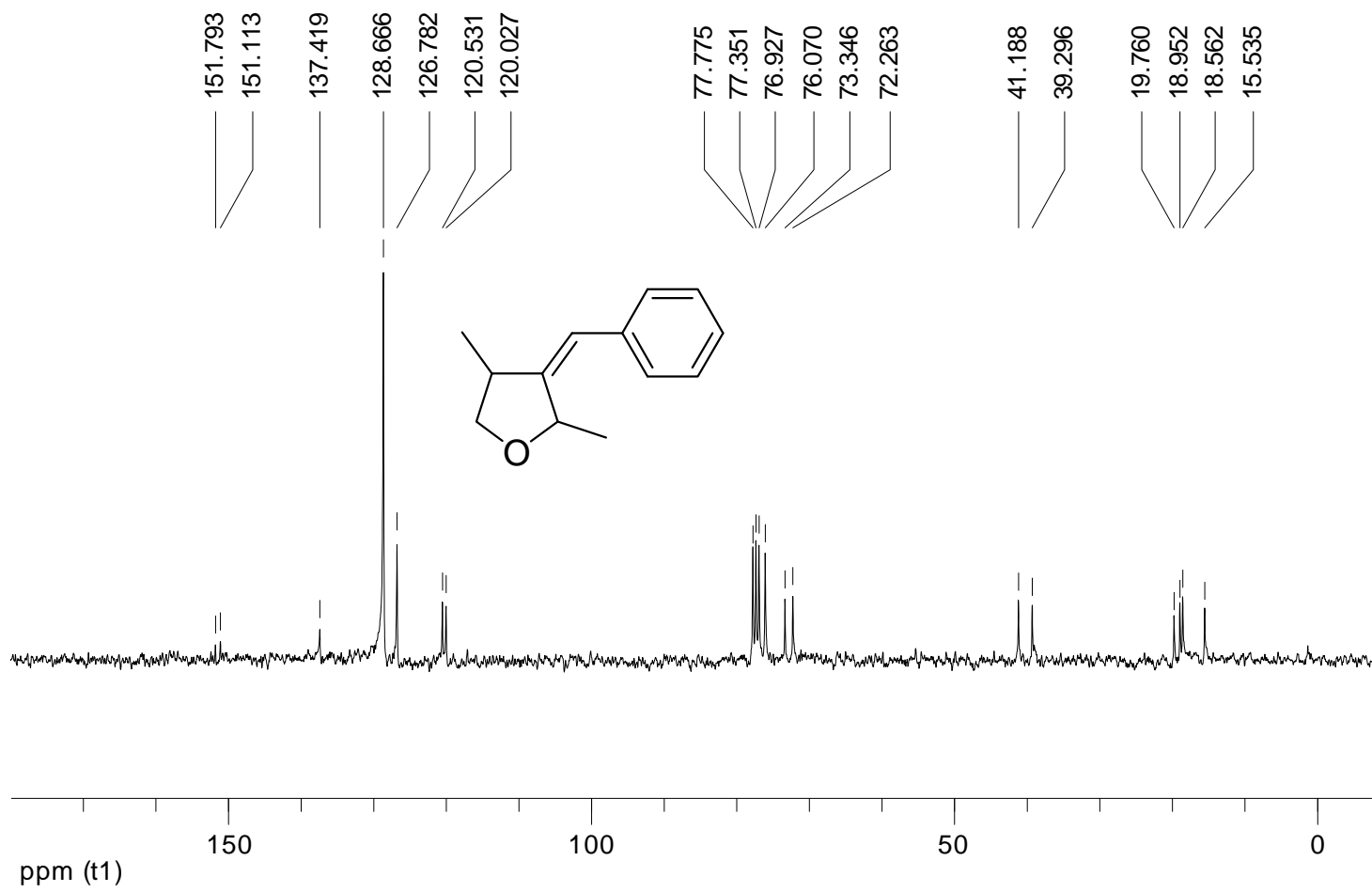
**4i**



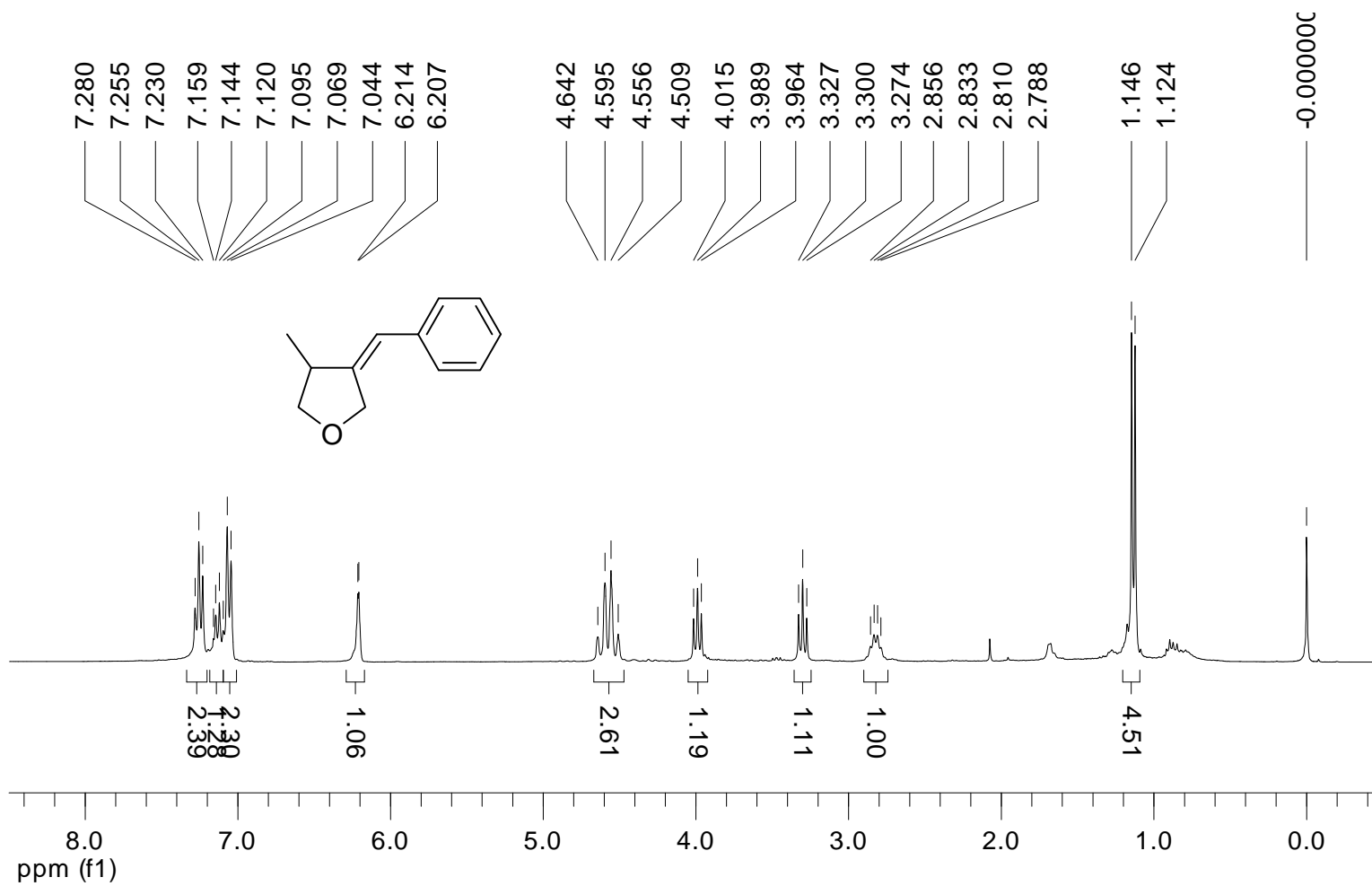
4i



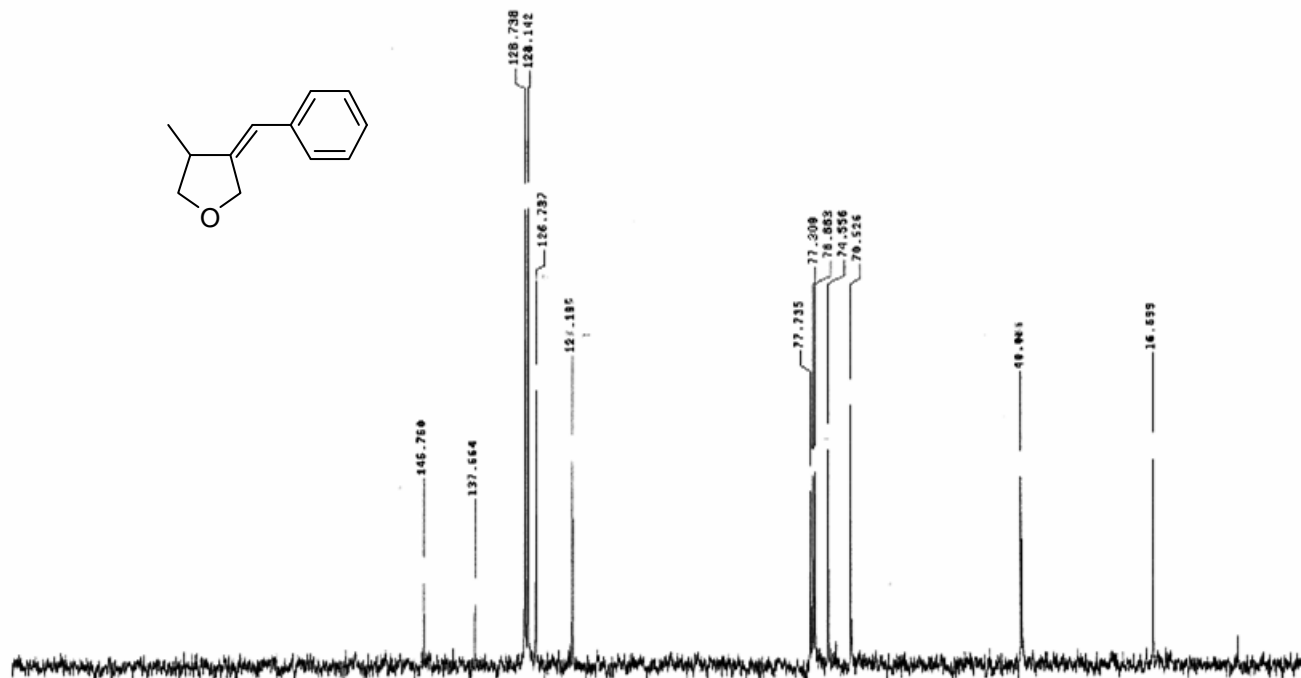
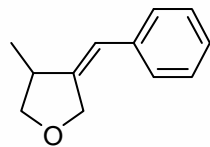
**2a**



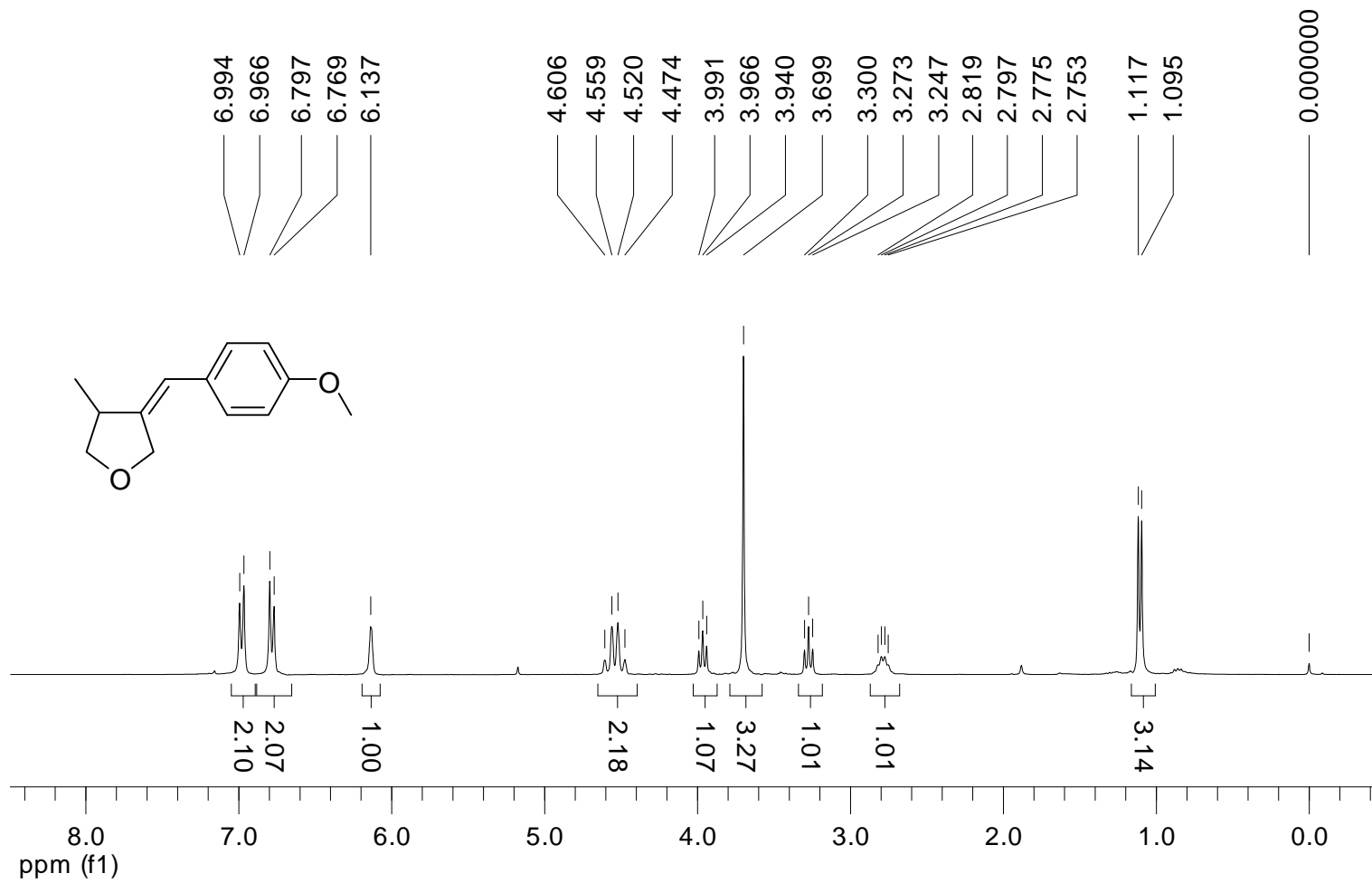
2a



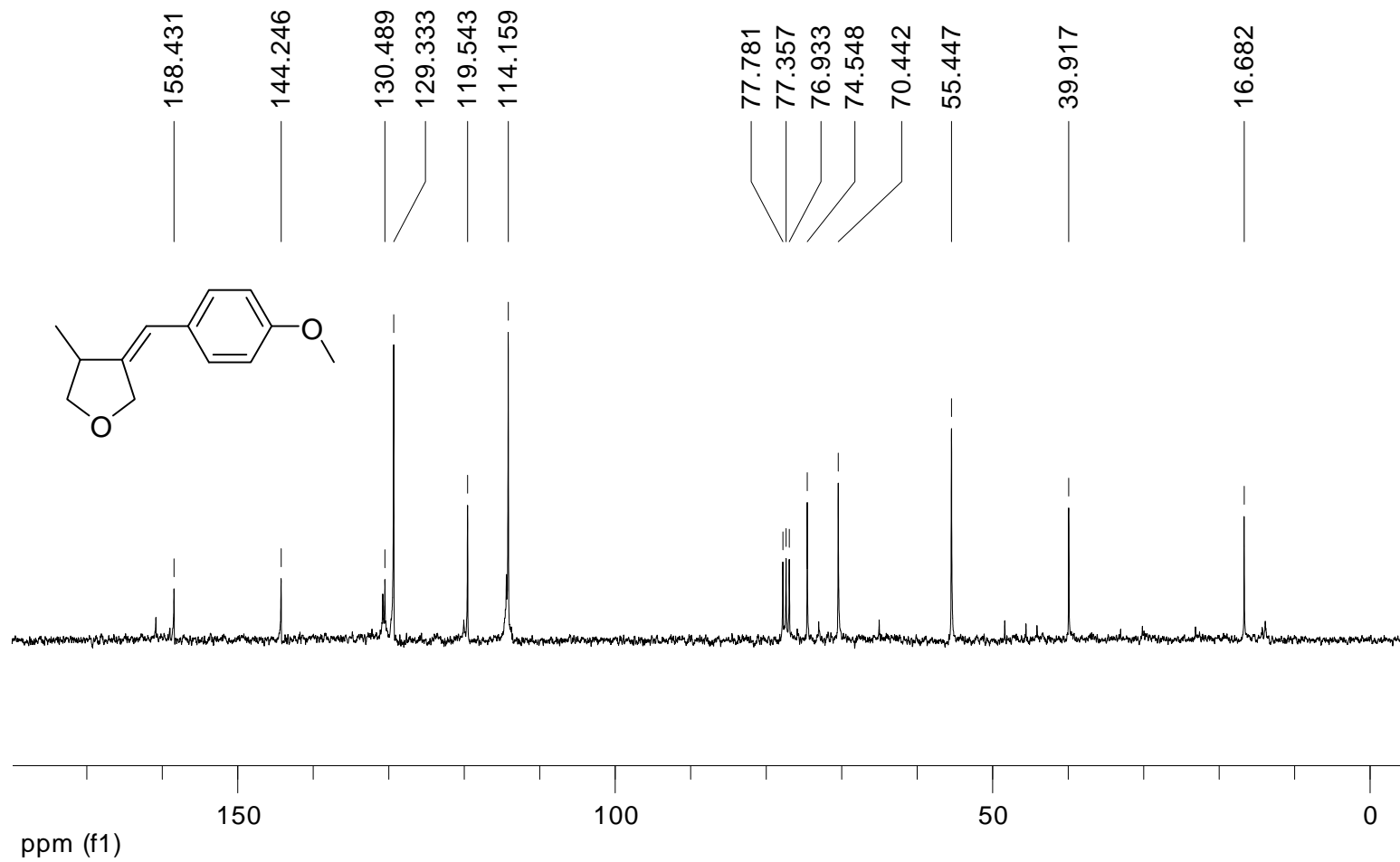
2b



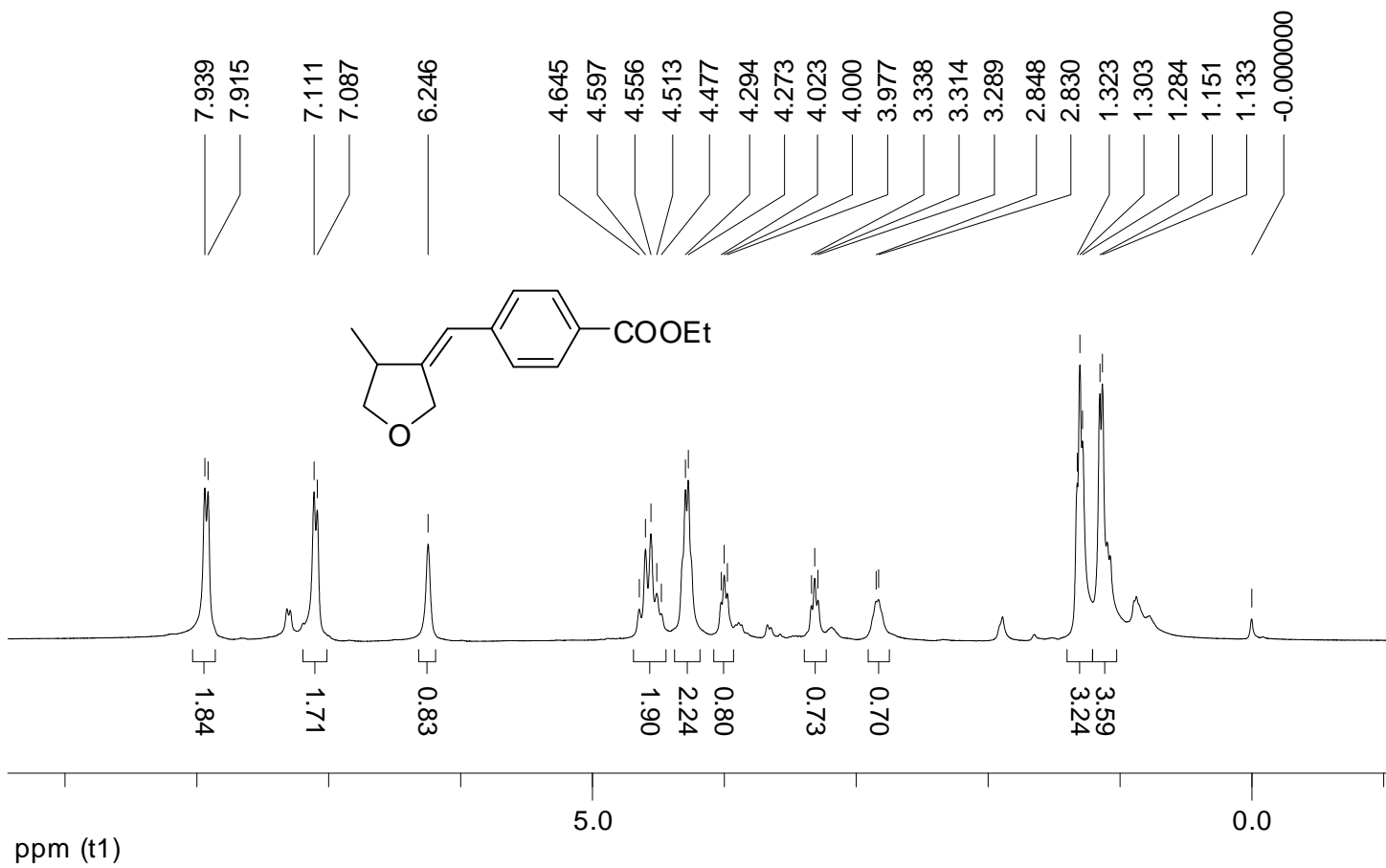
2b



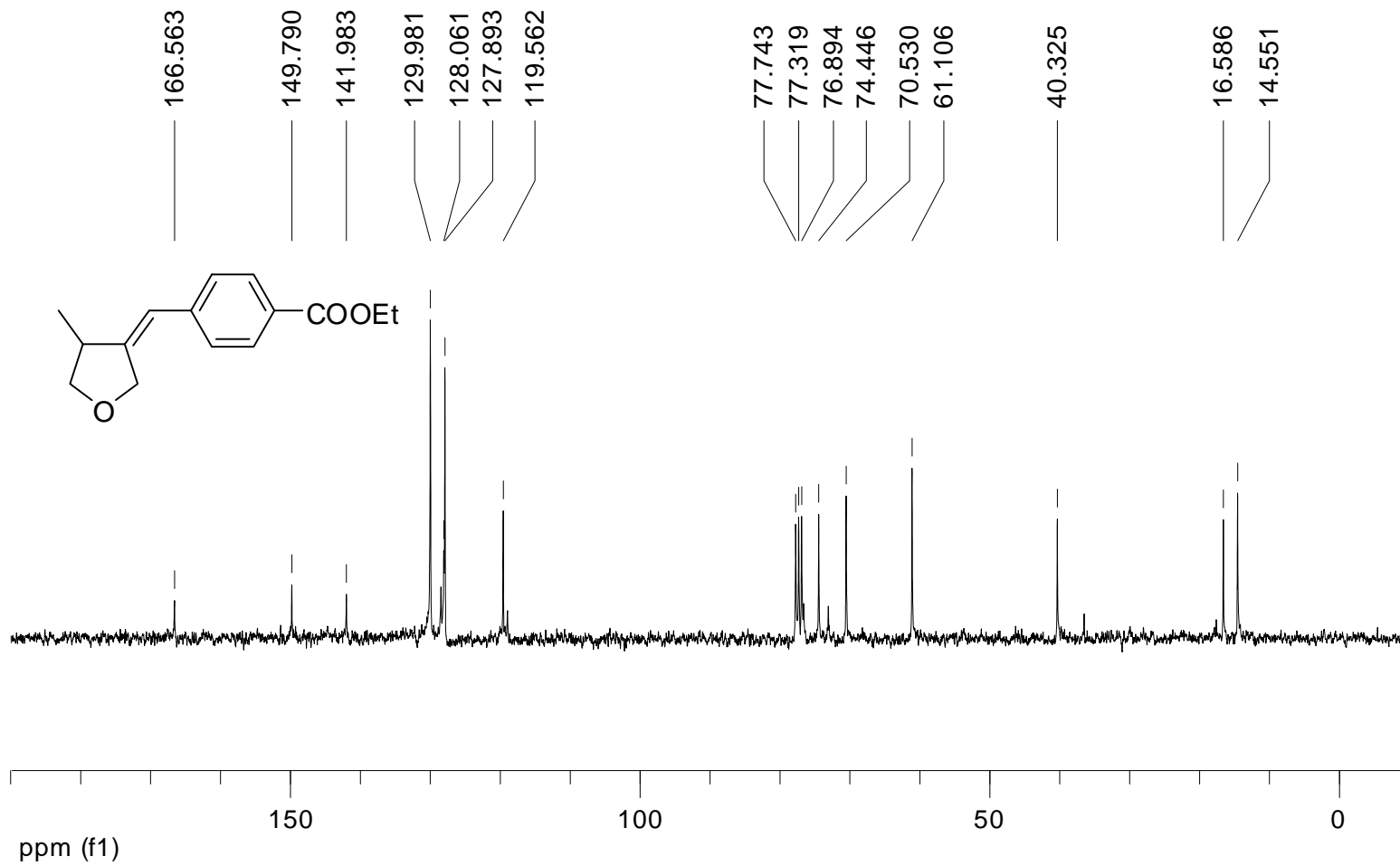
2c



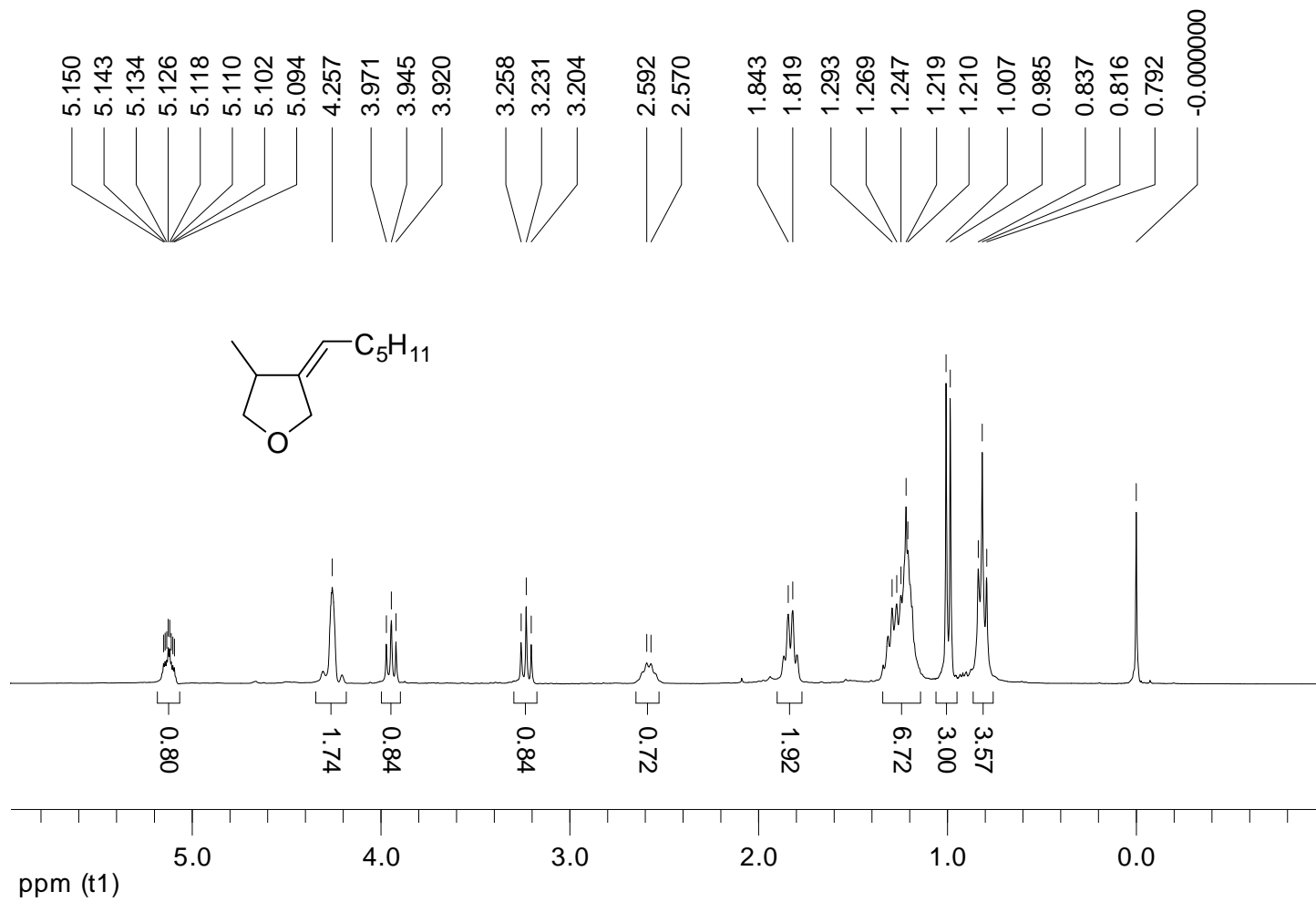
2c



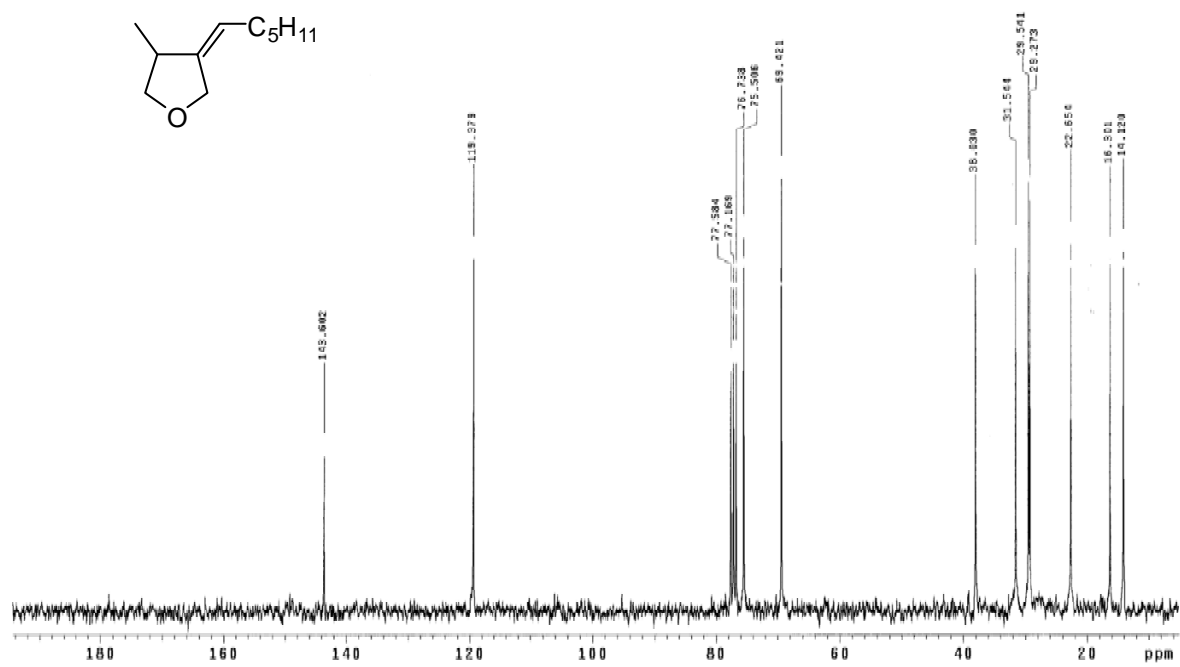
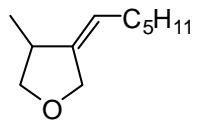
**2d**



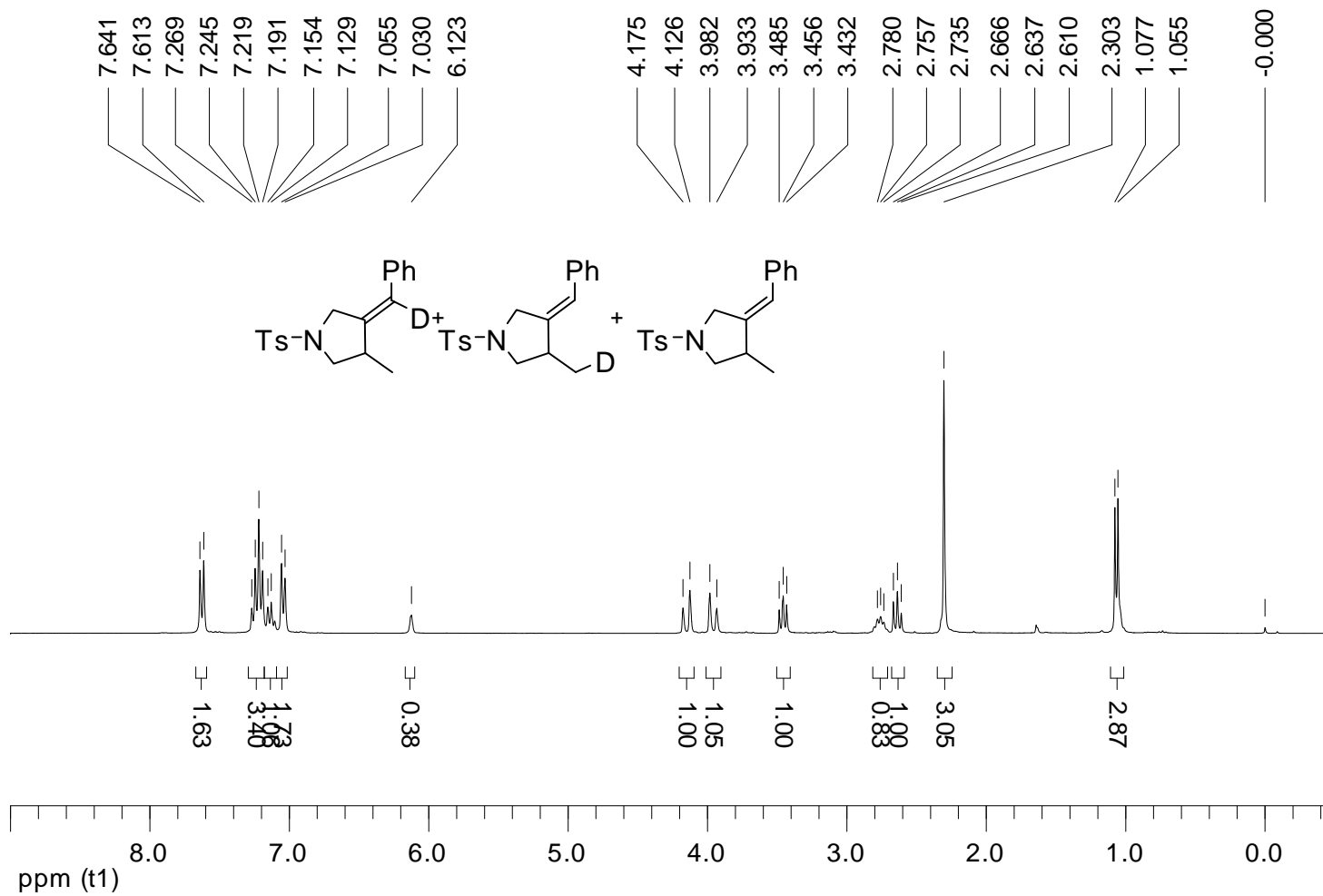
2d

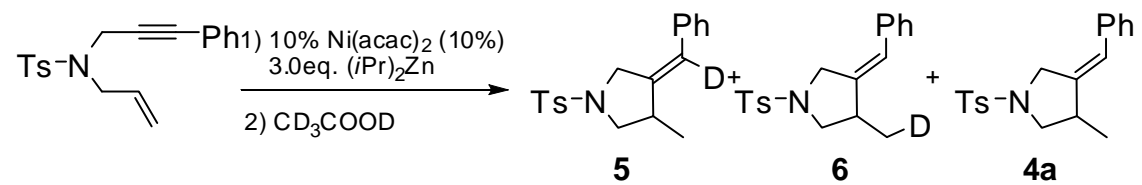


2e



2e

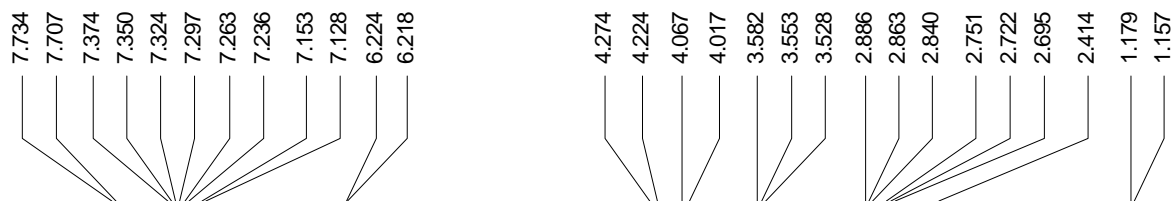




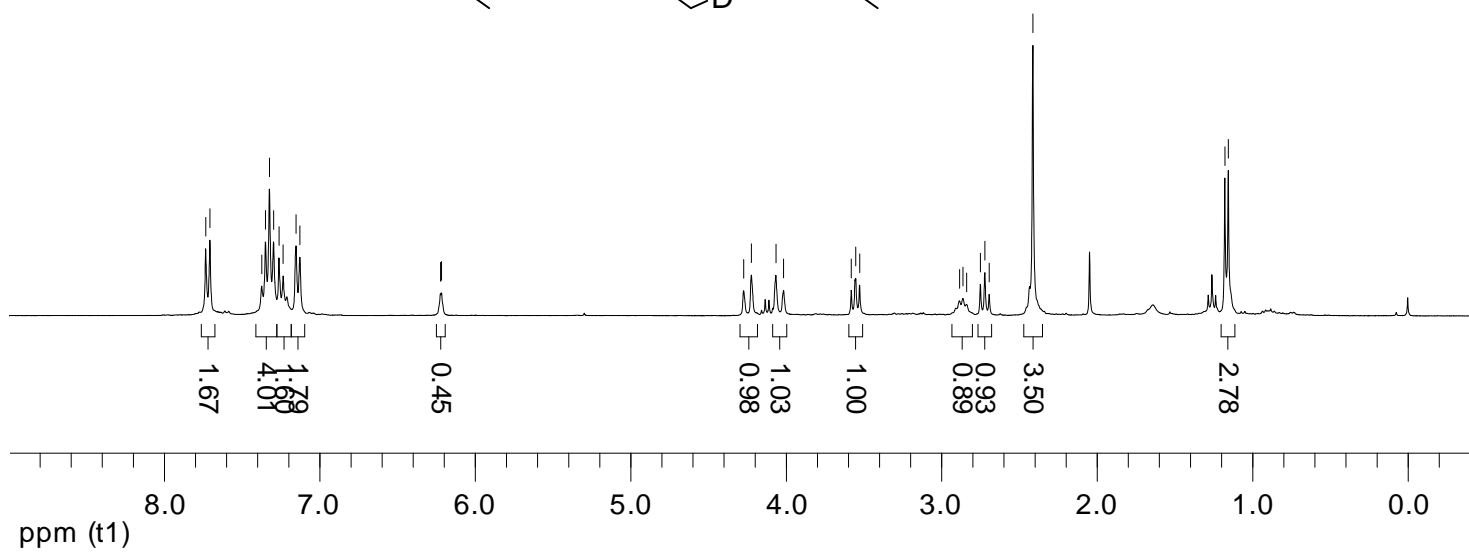
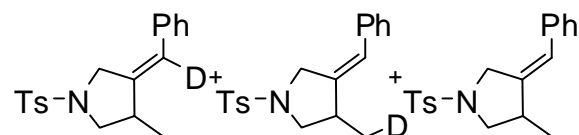
$$\mathbf{5\%} = [1 * (0.80 - 0.38) / 0.8] * 100\% = 53\%$$

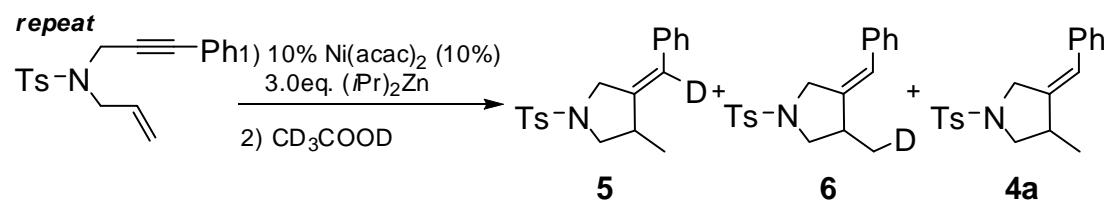
$$\mathbf{6\%} = [3 * (3.06 - 2.87) / 3.06] * 100\% = 19\%$$

$$\mathbf{4a\%} = (100\% - \mathbf{5\%} - \mathbf{6\%}) = 28\%$$



repeat





$$\mathbf{5\%} = [1 \cdot (0.80 - 0.45) / 0.8] \cdot 100\% = 44\%$$

$$\mathbf{6\%} = [3 \cdot (3.06 - 2.78) / 3.06] \cdot 100\% = 27\%$$

$$\mathbf{4a\%} = (100\% - \mathbf{5\%} - \mathbf{6\%}) = 29\%$$

# NOE experiment

