

## Supporting Information

### Pd(II)-catalyzed Allylic C-H Amination for the Preparation of 1,2- and 1,3-Cyclic Ureas

Yasuhiro Nishikawa, Seikou Kimura, Yuri Kato, Natsuka Yamazaki and Osamu Hara \*

*Faculty of Pharmacy, Meijo University, 150 Yagotoyama, Tempaku-ku,*

*Nagoya 468-8503, Japan*

E-mail: oshara@meijo-u.ac.jp

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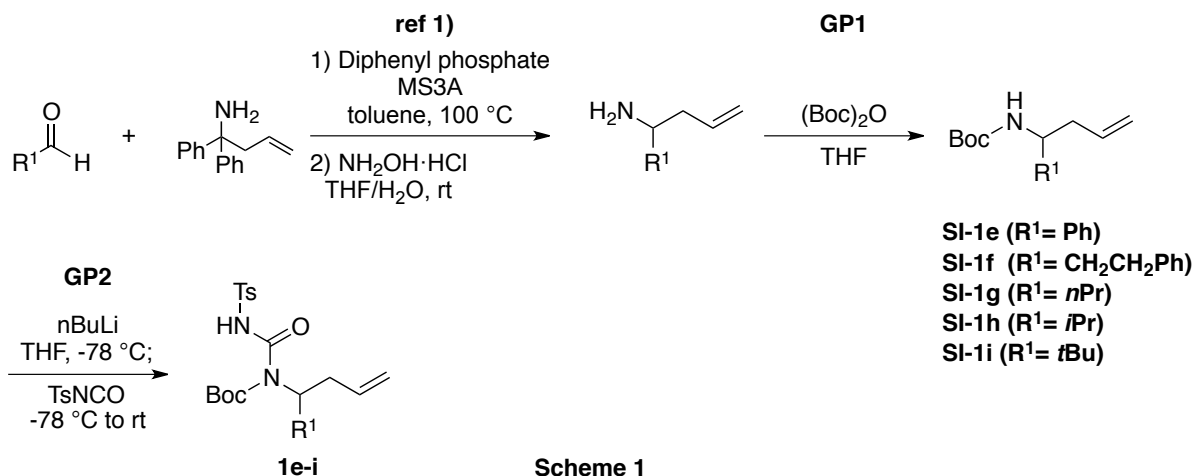
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**1. General Information.** All reactions were carried out in flame-dried glassware under argon atmosphere and stirred via magnetic stir-plates. All reactions were monitored by analytical thin-layer chromatography using Merck pre-coated silica gel plates with F254 indicator. Visualization was accomplished by UV light (254 nm), phosphomolybdic acid, ninhydrin, or anisaldehyde. Flash column chromatography was performed using Kanto Chemical silica gel 60N (spherical, neutral, 40-50  $\mu\text{m}$ ). All reactions were carried out with anhydrous solvents unless otherwise noted.  $\text{Pd}(\text{OAc})_2$  and  $\text{Pd}(\text{TFA})_2$  were purchased from Aldrich and used as received. 1,2-Bis(phenylsulfinyl)ethane was purchased from TCI Japan and used as received. All other reagents and starting materials, unless otherwise noted, were purchased from commercial vendors.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on a JEOL ECP-500 and ECA-500 spectrometer (500 MHz  $^1\text{H}$ , 125 MHz  $^{13}\text{C}$ ) or JNM A-600 (600 MHz  $^1\text{H}$ , 150 MHz  $^{13}\text{C}$ ). Chemical shift values ( $\delta$ ) are reported using tetramethylsilane ( $\delta_{\text{H}}$  0.00) and  $\text{CDCl}_3$  ( $\delta_{\text{C}}$  77.00) in  $\text{CDCl}_3$  or residual  $\text{CD}_2\text{HOD}$  ( $\delta_{\text{H}}$  3.31) and  $\text{CD}_3\text{OD}$  ( $\delta_{\text{C}}$  49.15) in  $\text{CD}_3\text{OD}$  or residual  $\text{DMSO}-d_5$  ( $\delta_{\text{H}}$  2.49) and  $\text{DMSO}-d_6$  ( $\delta_{\text{C}}$  39.50). The  $^1\text{H}$  NMR spectra are reported as follows  $\delta$  (number of protons, multiplicity, coupling constant  $J$  Hz). Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), sext (sextet), sep (septet), dd (doublet of doublet), m (multiplet) and br (broad). high-resolution mass spectra (ESI-qTOF) were obtained on a AB Sciex QSTAR pulser.

## 2. Synthesis of homoallylic ureas (**1b**, **1e-l**) as substrates for the preparation of 1,2-cyclic ureas.

### 2.1. Summary (**1e-i**)

Homoallylic ureas (**1e-i**) were prepared by amidations of the corresponding *N*-Boc amine derivatives (**SI-1e-i**)<sup>1</sup>. **SI-1e-i** were synthesized adapting known protocols from the commercially available aldehyde with achiral phosphoric acid catalyst<sup>2</sup> to afford homoallylamines, which was converted to *N*-Boc amine derivatives in a conventional manner (Scheme 1).



<sup>1</sup> Vilaivan, T.; Winotapan, C.; Banphavichit, V.; Shinada, T. Ohfuné, Y. *J. Org. Chem.* **2005**, *70*, 3464-3471.

<sup>2</sup> Rueping, M.; Antonchick, A. P. *Angew. Chem. Int. Ed.* **2008**, *47*, 10090-10093.

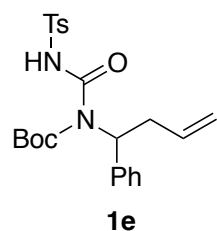
## 2.2. General procedure for the preparation of *N*-Boc amine derivatives (SI-1e-i)<sup>1</sup>. (GP1)

To a stirred solution of 1,1-diphenylbut-3-en-1-amine (2.0 g, 8.9 mmol)<sup>2</sup> and the corresponding aldehyde (1.1 equiv., 9.8 mmol) in toluene (50 mL) were added MS3A (15 g) and diphenyl phosphate (1.12 g, 4.5 mmol, 0.43 equiv.) at room temperature under argon atmosphere. The resulting suspension was heated at 100 °C. After 48 h at 100 °C, the reaction was cooled to room temperature and then filtered through celite pad. The filtrate was evaporated to afford the crude product, which was used without further purification. A part of the crude product (ca. 4.5 mmol) was dissolved in THF (80 mL) and H<sub>2</sub>O (40 mL). To the reaction mixture was added hydroxylamine hydrochloride (1.25 g, 17.9 mmol, 4.0 equiv.) at room temperature under argon atmosphere. After stirring at room temperature for 12 h, the reaction was diluted with Et<sub>2</sub>O (100 mL) and acidified with 1 M aqueous HCl. The organic layer was separated and the resulting aqueous layer was basified with 2 M aqueous NaOH to pH 10 and then extracted three times with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated at reduced pressure to give the crude product. The crude homoallylamine was converted directly to *N*-Boc derivatives without further purification because some of homoallylamines were volatile. The crude product obtained above (ca. 4.5 mmol) was dissolved in THF (8.7 mL). To the reaction mixture was added di-*tert*-butyl dicarbonate (1.07 g, 4.9 mmol) at room temperature under argon atmosphere. After stirring overnight, the reaction was quenched adding *N,N*-dimethylethylenediamine (0.43 mL, 3.9 mmol). After stirring at room temperature for 3 h, the reaction mixture was diluted with EtOAc. The mixture was washed two times with 1 M KHSO<sub>4</sub> and with brine, and dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. The resulting crude product was purified by silica gel chromatography (EtOAc/*n*-Hex) to give the title compounds (SI-1e-i), which were identified with the reported compounds<sup>1</sup>.

## 2.3. General procedure for the preparation of homoallylic urea derivatives (1e-i). (GP2)

To a stirred solution of a *N*-Boc amine derivative (2.8 mmol) prepared above in THF (14 mL) at -78 °C was added dropwise 1.6 M solution of *n*-BuLi (1.9 mL, 3.0 mmol) under argon atmosphere. After stirring at the same temperature for 30 min, *p*-toluenesulfonyl isocyanate (0.47 mL, 3.0 mmol) was added. the reaction mixture was stirred for 2 h at -78 °C and then warmed to room temperature overnight. The reaction was quenched adding saturated aqueous solution of NH<sub>4</sub>Cl and extracted two times with Et<sub>2</sub>O. The combined organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. The resulting crude product was purified by silica gel chromatography (EtOAc/*n*-Hex) to give the title compound (1b, 1e-I).

## 2.4. Characterization data of homoallylic urea derivatives (1e-i).

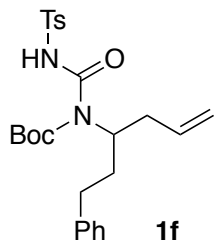


**1e:** White solid (48%), m.p. 75 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 11.66 (1H, br-s), 7.35 (2H, d, *J*=8.2), 7.35 (2H, d, *J*=8.2), 7.18-7.30 (3H, m), 7.14 (2H, d, *J*=7.3), 5.92 (1H, dd, *J*=9.9, 6.2), 5.65 (1H, m), 5.00 (1H, d, *J*=17.0), 4.94 (1H, d, *J*=10.1), 2.78-2.94 (2H, m), 2.46 (3H, s), 2.11 (2H, m), 1.56-1.67 (2H, m), 1.32 (9H, s).

<sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 154.7, 151.0, 144.6, 139.9, 136.0, 134.1, 129.4, 128.5, 128.1, 127.0, 126.3,

118.0, 85.7, 54.6, 35.4, 27.6, 21.7.

HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>23</sub>H<sub>28</sub>N<sub>2</sub>O<sub>5</sub>NaS [M+Na]<sup>+</sup>: 467.1611, found: 467.1615.

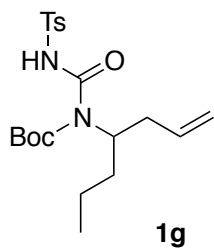


**1f**: White solid (79%), m.p. 98 °C; some signals show multiple resonance for the presence of different rotational isomers; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>, 100 °C) δ 7.61-7.83 (2H, m), 7.32-7.43 (1H, m), 7.22-7.31 (3H, m), 7.12-7.20 (3H, m), 6.23 (1H, br-s), 5.77 (1H, ddt, *J*=17.1, 10.2, 6.9), 4.95-5.06 (2H, m), 3.47 (1H, m), 2.63 (1H, ddd, *J*=14.2, 8.6, 6.0), 2.56 (1H, ddd, *J*=14.0, 9.0, 7.0), 2.40 (s) and 2.36 (3H, s), 2.19 (2H, m), 1.63-1.75 (2H, m), 1.40 (9H, s).

<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 °C) δ 154.8, 141.6, 141.2, 140.3, 135.0, 128.8, 128.6, 128.5, 127.61,

127.58, 126.7, 125.2, 125.1, 125.0, 123.8, 115.8, 76.9, 49.4, 38.6, 35.3, 31.3, 27.8, 20.2.

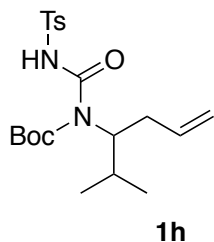
HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>25</sub>H<sub>32</sub>N<sub>2</sub>O<sub>5</sub>NaS [M+Na]<sup>+</sup>: 495.1924, found: 495.1927.



**1g**: White solid (70%), m.p. 70 °C; some signals show multiple resonance for the presence of different rotational isomers; <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 11.6 (1H, br-s), 7.95 (2H, d, *J*=8.2), 7.32 (2H, d, *J*=8.2), 5.53 (1H, m), 4.44-4.90 (3H, m), 2.40-2.50 (4H, m), 2.27 (1H, m), 1.75 (1H, m), 1.43-1.55 (10H, m), 1.15 (2H, sext, *J*=7.5), 0.81 (3H, t, *J*=7.6).

<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 °C) δ 154.7, 142.1, 141.2, 140.3, 135.2, 128.6, 128.5, 125.2, 125.1, 123.8, 115.6, 76.8, 49.4, 38.6, 35.9, 27.8, 20.2, 18.1, 13.1.

HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>20</sub>H<sub>30</sub>N<sub>2</sub>O<sub>5</sub>NaS [M+Na]<sup>+</sup>: 433.1767, found: 433.1765.

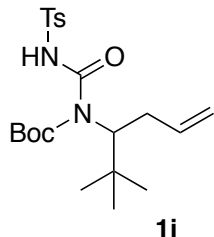


**1h**: White solid (58%), m.p. 79 °C; some signals show multiple resonance for the presence of different rotational isomers; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>, 100 °C) δ 7.62-7.79 (2H, m), 7.26-7.40 (2H, m), 6.02 (1H, br-s), 5.77 (1H, ddt, *J*=17.1, 10.3, 6.8), 5.04 (1H, dq, *J*=17.2, 1.7), 4.97 (1H, m), 3.30 (1H, m), 2.35-2.41 (3H, m), 2.15-2.23 (1H, m), 2.04-2.13 (1H, m), 1.68 (1H, m), 1.39 (9H, s), 0.86 (3H, d, *J*=6.8), 0.84 (3H, d, *J*=6.8).

<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 °C) δ 155.0, 142.1, 141.2, 140.3, 135.6, 128.7, 128.6, 128.5, 126.4,

125.2, 125.1, 123.8, 115.3, 76.8, 55.0, 35.5, 31.0, 27.8, 20.21, 20.18, 18.6, 17.5.

HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>20</sub>H<sub>30</sub>N<sub>2</sub>O<sub>5</sub>NaS [M+Na]<sup>+</sup>: 433.1767, found: 433.1772.



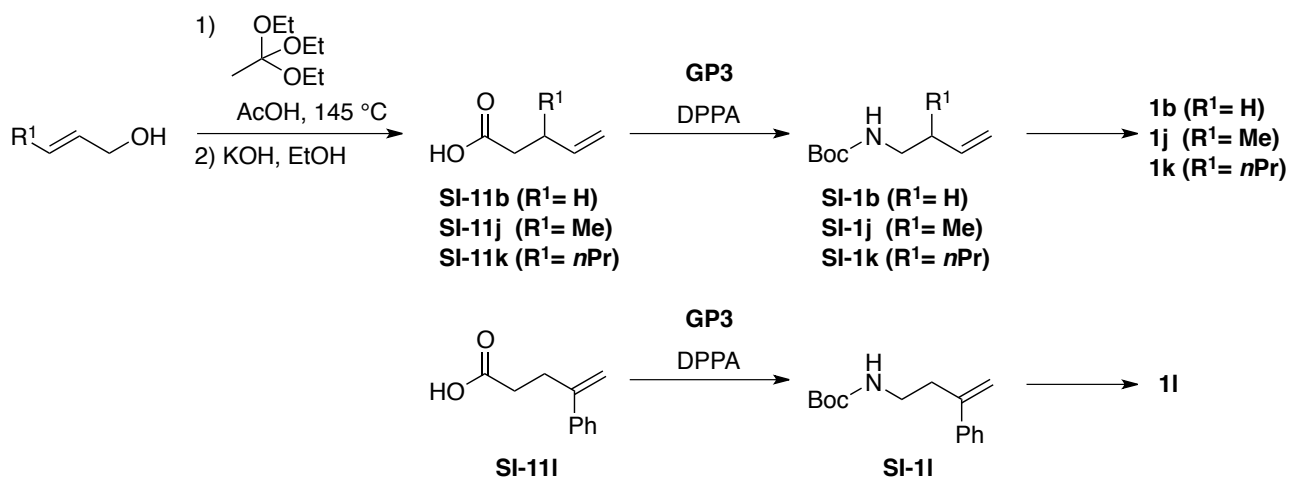
**1i**: White solid (40%), m.p. 95 °C; some signals show multiple resonance for the presence of different rotational isomers; <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 11.84 (s) and 11.50 (1H, s), 7.940 (d, *J*=8.2) and 7.936 (2H, d, *J*=8.7), 7.31 (2H, d, *J*=8.7), 5.48 (1H, m), 4.98 (d, *J*=16.5) and 4.65 (1H, d, *J*=17.0), 4.93 (d, *J*=10.1) and 4.79 (1H, d, *J*=10.1), 4.71 (dd, *J*=12.1, 5.3) and 4.15 (1H, dd, *J*=11.9, 4.1), 2.91 (ddd, *J*=13.6, 12.0, 9.3) and 2.68 (1H, ddd, *J*=14.2, 11.9, 8.7), 2.43 (3H, s), 2.33 (m) and 2.16 (1H, m), 1.56 (s) and 1.51 (9H, s), 0.89 (s) and 0.85 (9H, s).

<sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 156.2, 156.0, 152.0, 149.8, 144.4, 144.3, 136.3, 136.1, 135.3, 135.2, 129.3, 129.2, 128.45, 128.41, 117.3, 117.1, 86.1, 85.4, 66.6, 61.4, 35.6, 35.5, 32.0, 31.2, 28.6, 28.2, 28.03, 27.97, 21.64, 21.61.

HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>21</sub>H<sub>32</sub>N<sub>2</sub>O<sub>5</sub>NaS [M+Na]<sup>+</sup>: 447.1924, found: 447.1934.

## 2.5. Summary (1b, 1j-l)

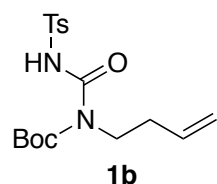
Homoallylic ureas (**1b**, **1j-l**) were prepared from the corresponding *N*-Boc amine derivatives (**SI-1b**, **SI1j-l**) by GP2. **SI-1b**<sup>3</sup> and **SI1j-l**<sup>4,5</sup> were synthesized by Curtius rearrangement of the corresponding carboxylic acids (**SI-11b**, **SI-11j-l**). **SI-11b** and **SI-11j-l**<sup>6,7</sup> were prepared adapting known protocols<sup>6</sup> from the commercially available compounds (Scheme 2).



## 2.6. General procedure for the preparation of *N*-Boc amine derivatives (**SI-1b**<sup>3</sup>, **SI-1j-l**<sup>4,5</sup>). (GP3)

To a stirred solution of a corresponding carboxylic acid (20 mmol) in *tert*-butanol (33 mL) was added triethylamine (3.4 mL, 25 mmol) and Diphenylphosphoryl azide (4.8 mL, 22 mmol) under argon atmosphere. After heating at 100 °C overnight, the reaction was cooled to room temperature. the reaction mixture was stirred for 2 h at – 78 °C and then warmed to room temperature overnight. The reaction mixture was diluted with EtOAc. The mixture was washed two times with water and brine, and dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. The resulting crude product was purified by silica gel chromatography (EtOAc/*n*-Hex) to give the title compounds (**SI-1b**<sup>3</sup>, **SI1j-l**<sup>4,5</sup>) which were identified with the reported compound.

## 2.7. Characterization data of homoallylic urea derivatives (**1b**, **1j-l**).



**1b**: White solid (78%); some signals show multiple resonance for the presence of different rotational isomers; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>, 100 °C) δ 8.19 (1H, s), 7.72 (d, *J*=8.2) and 7.68 (1H, d, *J*=7.9), 7.33 (d, *J*=7.9) and 7.16 (1H, d, *J*=7.7), 6.95 (br-s) and 6.28 (1H, br-s), 5.76 (1H, m), 4.91-5.08 (2H, m), 3.58 (1H, dd, *J*=8.5, 6.2), 3.01 (1H, td, *J*=7.0, 5.8), 2.38 (s) and 2.32 (3H, s), 2.14-2.26 (2H, m), 1.41 (s) and 1.39 (9H, s).

<sup>3</sup> Boyle, T. P.; Bremner, J. B.; Coates, J. A.; Keller, P. A.; Pyne, S. G. *Tetrahedron*, **2005**, 61, 7271-7276.

<sup>4</sup> Ziji, A. W. V.; López, F.; Minnaard, A. J.; Feringa, B. L. *J. Org. Chem.* **2007**, 72, 2558-2563.

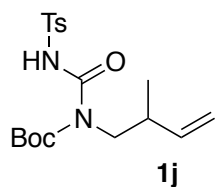
<sup>5</sup> Karila, D.; Leman, L.; Dodd, R. H. *Org. Lett.* **2011**, 13, 5830-5833.

<sup>6</sup> Heuger, G.; Kalsow, S.; Göttlich, R. *Eur. J. Org. Chem.* **2002**, 1848-1854.

<sup>7</sup> Takemiya, A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, 128, 6042-6043.

$^{13}\text{C}$  NMR (DMSO- $d_6$ , 100 °C)  $\delta$  156.8, 155.0, 153.7, 143.2, 141.2, 138.7, 135.7, 135.5, 128.6, 127.4, 126.1, 125.2, 115.3, 115.0, 79.2, 78.6, 77.0, 44.5, 33.2, 32.8, 27.8, 27.5, 20.23, 20.17.

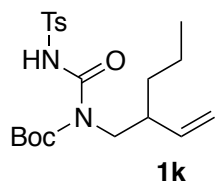
HRMS (ESI $^+$ )  $m/z$ : calcd for  $\text{C}_{17}\text{H}_{24}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 391.1298, found: 391.1286.



**1j**: White solid (44%), m.p. 90 °C; some signals show multiple resonance for the presence of different rotational isomers;  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  11.63 (1H, br-s), 7.96 (2H, d,  $J=8.3$ ), 7.32 (2H, d,  $J=8.3$ ), 5.52 (1H, ddd,  $J=16.8, 10.0, 8.5$ ), 4.86 (1H, d,  $J=16.7$ ), 4.84 (1H, d,  $J=9.8$ ), 3.56 (1H, dd,  $J=13.6, 8.3$ ), 3.51 (1H, dd,  $J=13.6, 6.8$ ), 2.38-2.46 (1H, m), 2.43 (3H, s), 1.52 (9H, s), 0.92 (3H, d,  $J=6.8$ ).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  154.9, 150.1, 144.6, 140.7, 136.0, 129.4, 128.5, 115.1, 85.3, 48.6, 37.9, 27.9, 21.6, 17.4.

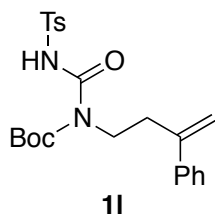
HRMS (ESI $^+$ )  $m/z$ : calcd for  $\text{C}_{18}\text{H}_{26}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 405.1454, found: 405.1452.



**1k**: White solid (77%), m.p. 70 °C;  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  11.63 (1H, br-s), 7.96 (2H, d,  $J=8.5$ ), 7.32 (2H, d,  $J=7.9$ ), 5.38 (1H, dt,  $J=17.0, 9.9$ ), 4.78-4.86 (2H, m), 3.45-3.64 (2H, m), 2.43 (3H, s), 2.23-2.33 (1H, m), 1.51 (9H, s), 1.10-1.36 (4H, m), 0.83 (3H, t,  $J=6.8$ ).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  154.9, 150.1, 144.5, 139.6, 136.1, 129.3, 128.5, 116.6, 85.2, 47.5, 43.8, 34.3, 27.9, 21.6, 20.1, 13.9.

HRMS (ESI $^+$ )  $m/z$ : calcd for  $\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 433.1778, found: 433.1780.



**1l**: White solid (48%), m.p. 85 °C; some signals show multiple resonance for the presence of different rotational isomers;  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  11.57 (1H, br-s), 7.99 (2H, d,  $J=8.5$ ), 7.22-7.40 (7H, m), 5.33 (1H, d,  $J=1.1$ ), 5.01 (1H, s), 3.73 (2H, m), 2.69 (2H, m), 2.44 (3H, s), 1.45 (9H, s).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 50 °C)  $\delta$  154.8, 149.8, 144.7, 144.6, 140.1, 136.4, 129.45, 129.41, 128.6, 128.4, 128.3, 127.6, 125.9, 114.3, 89.1, 85.5, 44.0, 37.9, 34.2, 27.9, 25.6, 23.6, 22.9, 21.6, 21.5, 13.8.

HRMS (ESI $^+$ )  $m/z$ : calcd for  $\text{C}_{23}\text{H}_{28}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 467.1611, found: 467.1612.

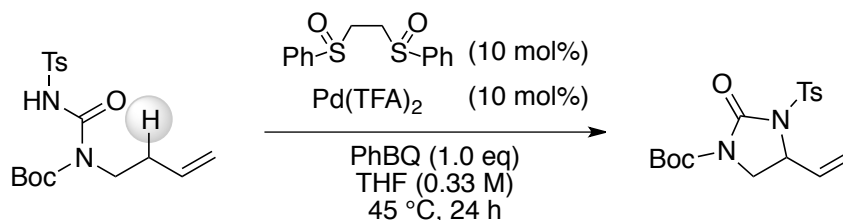
### 3. Experimental procedure for preparation of Pd(TFA) $_2$ /bis-sulfoxide catalyst.

Pd(TFA) $_2$ /bis-sulfoxide catalyst was prepared according to the procedure reported by M. C. White *et al.*<sup>8</sup>: Flame-dried 100 mL two-necked round bottom flask topped with a condenser was sequentially charged with a stir bar, 2-bis(phenylsulfinyl)ethane (92 mg, 0.33 mmol) (weighed in an other round bottom flask then transferred using 1.8 mL  $\text{CH}_2\text{Cl}_2$ ) then Pd(TFA) $_2$  (110 mg, 0.33 mmol) (weighed in the other round bottom flask then transferred using 1.8 mL  $\text{CH}_2\text{Cl}_2$ ). The reaction mixture was allowed to stir at 40 °C for 24 h. The solution was concentrated *in vacuo* and dried over a  $\text{N}_2$  stream for 2 h to give a black solid (182 mg, 90% yield) that was used without further purification.

<sup>8</sup> Fraunhofer, K. J.; White, M. C. *J. Am. Chem. Soc.* **2007**, *129*, 7274-7276.

## 4. Experimental procedure for the preparation of 1,2-cyclic ureas and characterization data

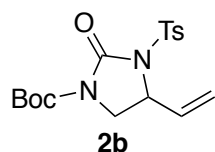
### 4.1. General procedure for preparation of 1,2-cyclic ureas (2b, 2e-l). (GP4)



**Method A:** A test tube (topped with a Teflon-lined screwed cap) was charged with  $\text{Pd(TFA)}_2$ /bis-sulfoxide catalyst (12 mg, 0.02 mmol) prepared as described above, an acyclic urea **1** (0.2 mmol), 2-phenyl-1,4-benzoquinone (36 mg, 0.2 mmol) and THF (0.3 mL, 0.66 M). The reaction was allowed to stir at 45 °C. After stirring at that temperature for 24-48 h, the reaction was diluted with  $\text{Et}_2\text{O}$ . The organic layer was washed two times with 1 M aqueous NaOH and then with brine, dried with  $\text{Na}_2\text{SO}_4$  and evaporated to give the crude product, which was purified by silica gel chromatography to give **2**.

**Method B (GP4):** A test tube (topped with a Teflon-lined screwed cap) was charged with  $\text{Pd(TFA)}_2$  (6.5 mg, 0.02 mmol), 2-bis(phenylsulfinyl)ethane (5.5 mg, 0.02 mmol) and THF (0.3 mL). The mixture was stirred at room temperature for 30 min. To the mixture was added an acyclic urea **1** (0.2 mmol), 2-phenyl-1,4-benzoquinone (36 mg, 0.2 mmol) and THF (0.3 mL). The reaction was allowed to stir at 45 °C. After stirring at that temperature for 24-48 h, the reaction was diluted with  $\text{Et}_2\text{O}$ . The organic layer was washed with 1 M aqueous NaOH and brine, dried with  $\text{Na}_2\text{SO}_4$  and evaporated to give the crude product, which was purified by silica gel chromatography to give **2**.

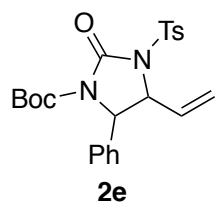
### 4.2. Characterization data of 1,2-cyclic ureas (2b, 2e-l).



**2b:** 80% yield as a white solid;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.93 (2H, d,  $J=8.2$ ), 7.30 (2H, d,  $J=8.2$ ), 5.78 (1H, ddd,  $J=17.4, 9.6, 7.6$ ), 5.45 (1H, d,  $J=17.4$ ), 5.33 (1H, d,  $J=9.8$ ), 4.77 (1H, td,  $J=8.5, 2.5$ ), 3.95 (1H, dd,  $J=10.6, 9.1$ ), 3.52 (1H, dd,  $J=10.6, 3.0$ ), 2.43 (3H, s), 1.49 (9H, s).  
 $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )

$\delta$  149.7, 148.6, 145.0, 135.5, 134.6, 129.5, 128.8, 119.7, 83.9, 55.2, 47.3, 27.9, 21.6.

HRMS ( $\text{ESI}^+$ )  $m/z$ : calcd for  $\text{C}_{17}\text{H}_{22}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 389.1142, found: 389.1140.



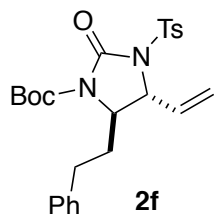
**2e:** 65% yield as diastereomer mixtures in yellowish oil (*anti* : *syn* = 1 : 1.8)

**2e (minor):**  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.89 (2H, d,  $J=8.2$ ), 7.27-7.38 (5H, m), 7.08-7.14 (2H, m), 5.94 (1H, ddd,  $J=17.1, 10.0, 7.4$ ), 5.47 (1H, d,  $J=17.0$ ), 5.39 (1H, d,  $J=10.5$ ), 4.72 (1H, d,  $J=1.8$ ), 4.52 (1H, m), 2.45 (3H, s), 1.28 (9H, s).

**2e (major):**  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.95 (2H, d,  $J=8.7$ ), 7.27-7.38 (5H, m), 7.08-7.14 (2H, m), 5.17-5.23 (3H, m), 5.03-5.07 (1H, m), 4.85 (1H, m), 2.44 (3H, s), 1.20 (9H, s).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  150.0, 148.9, 148.80, 148.78, 145.1, 139.4, 135.6, 135.3, 134.6, 132.8, 129.53, 129.49, 129.44, 129.1, 129.0, 128.84, 128.80, 128.7, 128.5, 128.3, 125.0, 120.1, 119.6, 83.9, 83.8, 63.9, 62.4, 61.3, 60.9, 27.7, 27.5, 27.4, 27.2.

HRMS ( $\text{ESI}^+$ )  $m/z$ : calcd for  $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 465.1454, found: 465.1460.



**2f**: 53% yield as diastereomer mixtures in yellowish oil (*anti* : *syn* = 2.5 : 1)

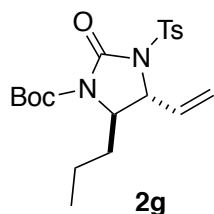
**2e (major)**:  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  7.93 (2H, d,  $J=8.7$ ), 7.10-7.34 (7H, m), 5.73 (1H, ddd,  $J=16.8$ , 10.2, 7.2), 5.41 (1H, d,  $J=17.0$ ), 5.31 (1H, d,  $J=10.5$ ), 4.51 (1H, d,  $J=7.3$ ), 3.79 (1H, dd,  $J=9.1$ , 3.2), 2.42 (3H, s), 1.44 (9H, s).

**2e (minor)**:  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  7.93 (2H, d,  $J=8.7$ ), 7.10-7.34 (7H, m), 5.94 (1H, ddd,  $J=17.1$ , 10.0, 7.4), 5.77 (1H, m), 5.57 (1H, d,  $J=17.0$ ), 5.50 (1H, d,  $J=10.1$ ), 4.78 (1H, t,  $J=8.7$ ), 4.14 (1H, ddd,  $J=9.6$ , 7.9, 3.2), 2.43 (3H, s), 1.49 (9H, s).

**unassigned signals in 2e**:  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  2.48-2.78 (2H, m), 1.66-2.12 (2H, m)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  150.1, 149.7, 149.3, 148.2, 145.08, 145.05, 140.8, 139.9, 135.5, 135.4, 134.2, 131.2, 129.52, 129.45, 128.9, 128.8, 128.7, 128.6, 128.3, 128.28, 128.16, 126.4, 126.3, 122.0, 119.2, 84.1, 83.8, 60.2, 60.1, 58.8, 56.6, 34.4, 31.2, 30.9, 29.6, 27.92, 27.89, 22.8, 21.6.

HRMS ( $\text{ESI}^+$ )  $m/z$ : calcd for  $\text{C}_{25}\text{H}_{30}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 493.1767, found: 493.1765.



**2g**: 93% yield as diastereomer mixtures in yellowish oil (*anti* : *syn* = 1.9 : 1)

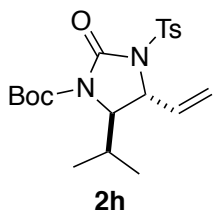
**2g (major)**:  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  7.93 (2H, d,  $J=8.5$ ), 7.30 (2H, d,  $J=8.5$ ), 5.76 (1H, ddd,  $J=17.0$ , 9.9, 7.4), 5.42 (1H, d,  $J=16.4$ ), 5.30 (1H, d,  $J=10.2$ ), 4.46 (1H, d,  $J=7.9$ ), 3.77 (1H, dd,  $J=9.1$ , 2.8), 2.43 (3H, s), 1.71 (1H, m), 1.49 (9H, s), 0.96 (3H, t,  $J=7.4$ ).

**2g (minor)**:  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  7.92 (2H, d,  $J=7.9$ ), 7.30 (2H, d,  $J=8.5$ ), 5.73 (1H, dt,  $J=17.2$ , 10.1), 5.46 (1H, d,  $J=17.0$ ), 5.41 (1H, d,  $J=10.2$ ), 4.70 (1H, t,  $J=8.5$ ), 4.07 (1H, ddd,  $J=9.6$ , 7.9, 3.4), 2.43 (3H, s), 1.92 (1H, m), 1.50 (9H, s), 0.89 (3H, t,  $J=7.4$ ).

**unassigned signals in 2g**:  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  1.20-1.64 (3H, m)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  150.0, 149.8, 149.4, 148.1, 144.90, 144.88, 135.6, 135.4, 134.5, 131.3, 129.4, 129.3, 128.8, 128.7, 121.3, 118.9, 83.8, 83.6, 60.4, 60.3, 59.1, 57.0, 35.0, 29.8, 27.9, 21.6, 18.1, 17.7, 13.8, 13.6.

HRMS ( $\text{ESI}^+$ )  $m/z$ : calcd for  $\text{C}_{20}\text{H}_{28}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 431.1611, found: 431.1610.



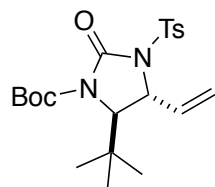
**2h**: 79% yield as a white solid, m.p. 88 °C;  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  7.93 (2H, d,  $J=8.7$ ), 7.30 (2H, d,  $J=8.2$ ), 5.78 (1H, ddd,  $J=17.2$ , 9.9, 7.6), 5.40 (1H, d,  $J=17.0$ ), 5.29 (1H, d,  $J=10.1$ ), 4.55 (1H, d,  $J=7.8$ ), 3.72 (1H, dd,  $J=4.6$ , 1.4), 2.42 (3H, s), 2.19 (1H, sextd,  $J=6.9$ , 4.4), 1.49 (9H, s), 0.97 (3H, d,  $J=6.9$ ), 0.89 (3H, d,  $J=7.3$ ).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )

$\delta$  149.8, 148.5, 144.9, 135.7, 135.2, 129.4, 128.8, 118.5, 83.7, 63.6, 56.5, 30.4, 27.9, 21.6, 17.9, 15.4.

HRMS ( $\text{ESI}^+$ )  $m/z$ : calcd for  $\text{C}_{20}\text{H}_{28}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 431.1611, found: 431.1610.





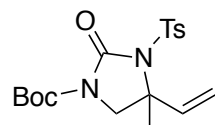
**2i**

**2i**: 69% yield as a white solid, m.p. 131 °C;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.94 (2H, d,  $J=8.5$ ), 7.30 (2H, d,  $J=7.9$ ), 5.78 (1H, ddd,  $J=17.1$ , 10.1, 7.2), 5.36 (1H, d,  $J=17.0$ ), 5.27 (1H, d,  $J=10.2$ ), 4.64 (1H, dd,  $J=7.4$ , 1.1), 3.71 (1H, s), 2.43 (3H, s), 1.49 (9H, s), 0.93 (9H, s).

$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )

$\delta$  150.5, 148.9, 144.9, 135.7, 134.9, 129.4, 128.9, 118.1, 83.7, 66.1, 57.9, 36.1, 27.9, 25.5, 21.6.

HRMS ( $\text{ESI}^+$ )  $m/z$ : calcd for  $\text{C}_{21}\text{H}_{30}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 445.1767, found: 445.1776.



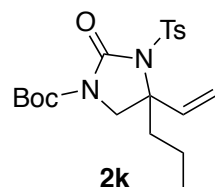
**2j**

**2j**: 78% yield as a yellowish oil;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.96 (2H, d,  $J=8.3$ ), 7.30 (2H, d,  $J=8.3$ ), 6.12 (1H, dd,  $J=17.4$ , 10.6), 5.41 (1H, d,  $J=17.4$ ), 5.35 (1H, d,  $J=11.4$ ), 3.62 (1H, d,  $J=10.6$ ), 3.50 (1H, d,  $J=10.6$ ), 2.42 (3H, s), 1.84 (3H, s), 1.49 (9H, s).

$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  149.5, 149.2, 144.8, 139.4, 136.1, 129.3, 129.1, 116.0, 83.8, 62.0, 54.7, 27.9,

24.5, 21.6.

HRMS ( $\text{ESI}^+$ )  $m/z$ : calcd for  $\text{C}_{18}\text{H}_{24}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 403.1298, found: 403.1296.



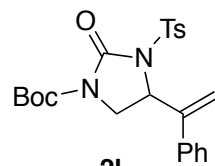
**2k**

**2k**: 85% yield as a yellowish oil;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.96 (2H, d,  $J=8.2$ ), 7.30 (2H, d,  $J=7.8$ ), 6.21 (1H, dd,  $J=17.6$ , 10.8), 5.36 (1H, d,  $J=10.5$ ), 5.36 (1H, d,  $J=17.4$ ), 3.63 (1H, d,  $J=11.0$ ), 3.60 (1H, d,  $J=10.5$ ), 2.42 (3H, s), 2.32 (1H, td,  $J=13.2$ , 4.4), 1.96 (1H, td,  $J=13.1$ , 4.6), 1.49 (9H, s), 1.28-1.49 (2H, m), 1.01 (3H, t,  $J=7.3$ ).

$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  149.5, 149.4, 144.8, 139.4, 136.0, 129.21, 129.16, 116.1, 83.8, 64.6, 51.6,

39.4, 27.9, 21.6, 16.7, 14.0.

HRMS ( $\text{ESI}^+$ )  $m/z$ : calcd for  $\text{C}_{20}\text{H}_{28}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 431.1611, found: 431.1611.



**2l**

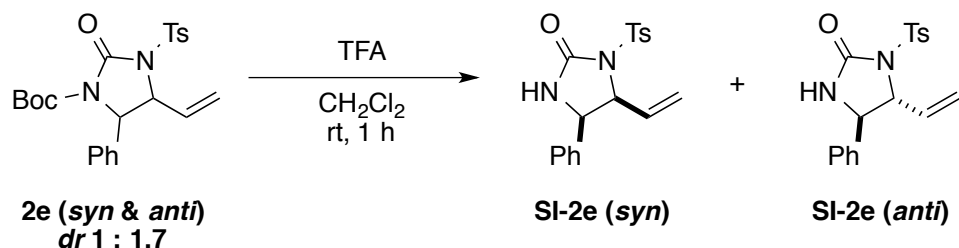
**2l**: 53% yield as a white solid, m.p. 162 °C;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.97 (2H, d,  $J=7.9$ ), 7.32-7.40 (5H, m), 7.31 (2H, d,  $J=8.5$ ), 5.37 (1H, s), 5.27 (1H, dd,  $J=9.9$ , 2.0), 5.11 (1H, s), 3.92 (1H, dd,  $J=10.5$ , 9.4), 3.50 (1H, dd,  $J=10.2$ , 2.3), 2.44 (3H, s), 1.46 (9H, s).

$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  149.6, 149.1, 145.9, 145.2, 137.7, 135.3, 129.4, 128.9, 128.8, 128.5, 126.9,

114.7, 83.8, 55.2, 48.0, 27.9, 21.7.

HRMS ( $\text{ESI}^+$ )  $m/z$ : calcd for  $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 465.1454, found: 465.1454.

### 4.3. Determination of relative stereochemistry in 2e

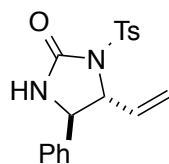


**Scheme 3**

**2e** as diastereomeric mixture were converted to deprotected derivatives **SI-2e (anti)** and **SI-2e (syn)** whose relative stereochemistries were reported as defined well (Scheme 3)<sup>9</sup>. The comparison of <sup>1</sup>H-NMR data between synthetic compounds and reported ones revealed unambiguously that the major stereoisomer of synthetic **SI-2e** was *syn* product (*syn* : *anti* = 1.6 : 1).

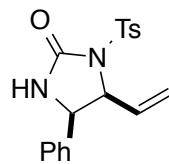
**2e** (30 mg, 0.06 mmol) was stirred for 1 h at room temperature in CH<sub>2</sub>Cl<sub>2</sub> (0.5 mL) and trifluoroacetic acid (0.5 mL). The reaction was quenched by saturated aqueous solution of NaHCO<sub>3</sub>. The mixture was extracted two times with EtOAc. The combined organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. The resulting crude product was purified by silica gel chromatography (EtOAc/CH<sub>2</sub>Cl<sub>2</sub>=1/15) to give **SI-2e** (19mg, 81%) as diastereomeric mixtures.

**SI-2e**: Diastereomeric mixtures in white solid (*anti* : *syn* = 1 : 1.6)



**SI-2e (anti)**

**SI-2e (anti)<sup>9</sup> (minor)**: <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 7.84 (2H, d, *J*=8.7), 7.26-7.33 (5H, m), 7.11 (2H, m), 5.97 (1H, ddd, *J*=17.0, 10.3, 8.0), 5.75 (1H, s), 5.36 (1H, d, *J*=17.9), 5.35 (1H, d, *J*=9.6), 4.48 (1H, dd, *J*=8.0, 3.9), 4.34 (1H, d, *J*=3.6), 2.44 (3H, s). The spectral data were identical to the ones reported in literature<sup>9</sup>.

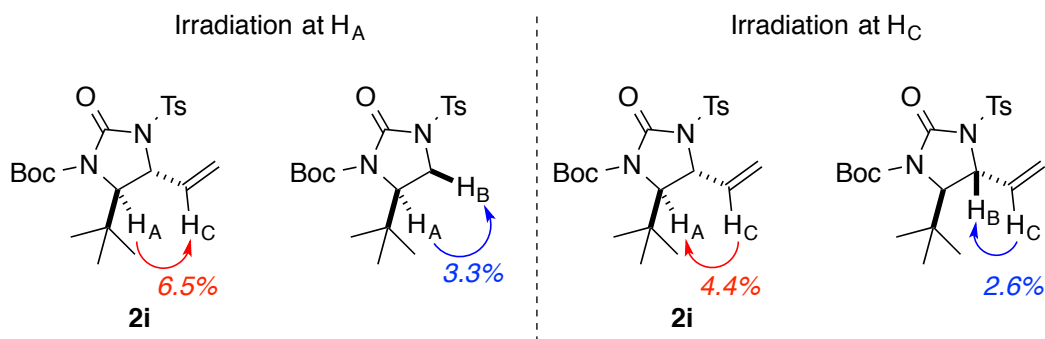


**SI-2e (syn)**

**SI-2e (syn)<sup>9</sup> (major)**: <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 7.89 (2H, d, *J* = 8.2), 7.26-7.33 (5H, m), 7.14-7.19 (2H, m), 5.59 (1H, s), 5.24 (1H, ddd, *J*=17.0, 9.9, 8.5), 5.15 (1H, dd, *J*=17.0, 1.4), 5.07 (1H, d, *J*=8.2), 5.00 (1H, br-d, *J*=11.0), 4.97 (1H, t, *J*=8.7), 2.42 (3H, s). The spectral data were identical to the ones reported in literature<sup>9</sup>.

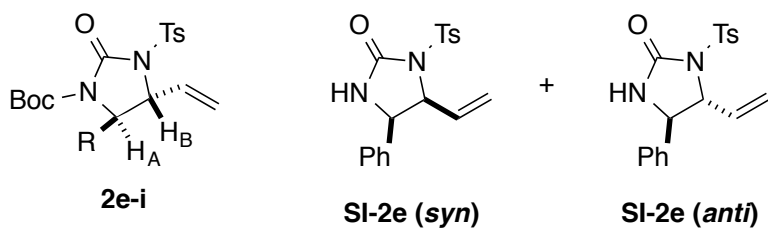
<sup>9</sup> Oshitari, T.; Akagi, R.; Mandai, T. *Synthesis*. **2004**, 9, 1325-1330

#### 4.4. Determination of relative stereochemistry in **2i** by differential NOE experiment



Differential NOE experiment clearly indicated *tert*-butyl and vinyl group on the imidazolidinone ring are arranged in *anti* stereochemistry as above.

#### 4.5. Comparison of $J$ values between $H_A$ and $H_B$ to determine relative stereochemistry in **2f-h**



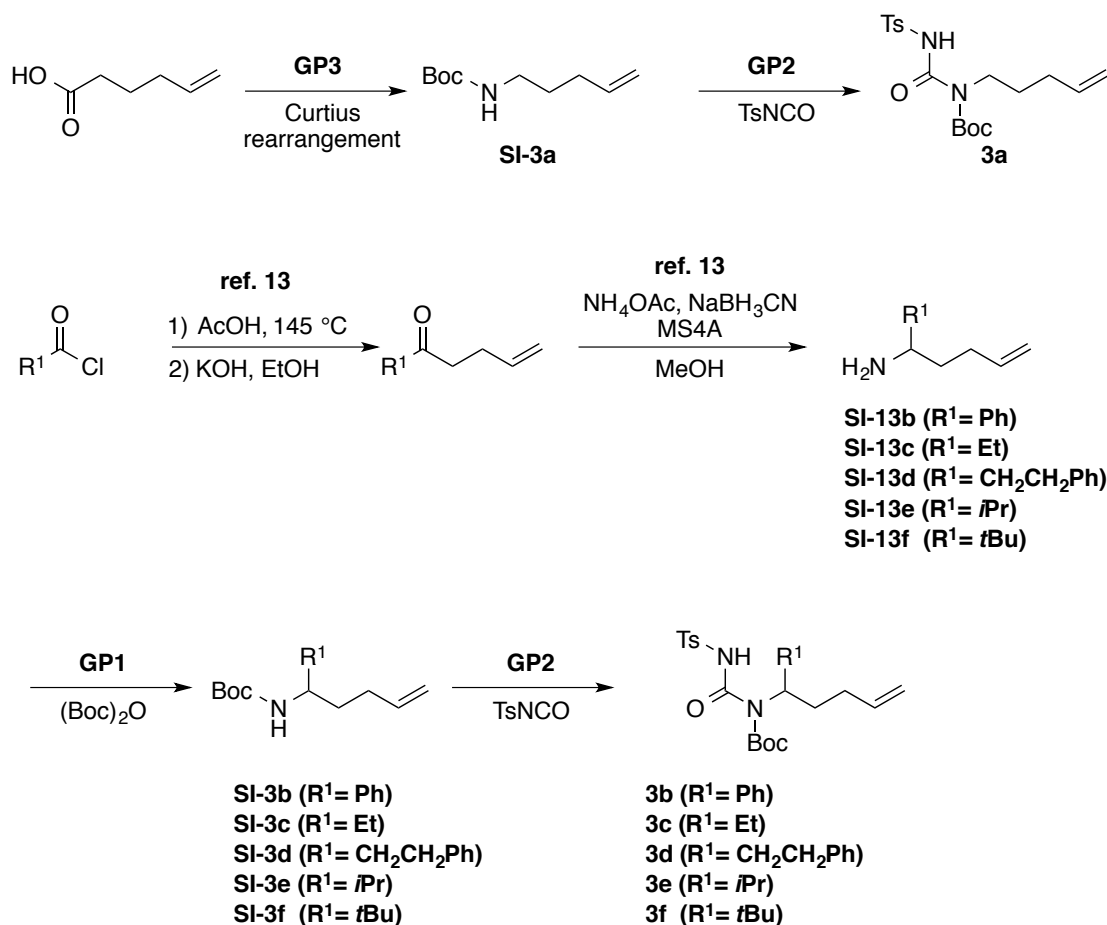
	$J$ value ( $H_A$ - $H_B$ ) in major product	$J$ value ( $H_A$ - $H_B$ ) in minor product
<b>2e</b>	unclear	1.8 ( <i>anti</i> )
<b>SI-2e</b>	8.2-8.7 ( <i>syn</i> )	3.6-3.9 ( <i>anti</i> )
<b>2f</b>	< 1.0	7.9-8.7
<b>2g</b>	< 1.0	7.9-8.5
<b>2h</b>	1.4	-
<b>2i</b>	< 1.0 ( <i>anti</i> )	-

On the basis of defined structures of **2e** and **2i**, the stereochemistry in other cyclic ureas **2f-h** was assigned by comparing  $J$  values as shown in Table above.  $J$  value between  $H_A$  and  $H_B$  in *anti* product tends to be much smaller than that of *syn* product. Thus, major product of **2f**, **2g**, and **2h** could be assigned to *anti* products.

## 5. Synthesis of bishomoallylic ureas (3a-g) as substrates for the preparation of 1,3-cyclic ureas.

### 5.1. Summary (3a, 3b-f)

Bishomoallylic ureas (**3a**) were prepared following GP3 and GP2 from commercially available 5-hexenoic acid via **SI-3a**<sup>10</sup>. Bishomoallylic ureas (**3b-f**) were prepared following GP2 from the corresponding *N*-Boc derivatives (**SI-3b-f**)<sup>11, 12</sup> which were synthesized from the corresponding bishomoallylamine (**SI-13b-f**) in a conventional manner. **SI-13b-f**<sup>13</sup> were prepared adapting known protocols<sup>13</sup> from commercially available acid chlorides (Scheme 3).



Scheme 3.

<sup>10</sup> Michael, F. E.; Cochran, B. M. *J. Am. Chem. Soc.* **2006**, *128*, 4246.

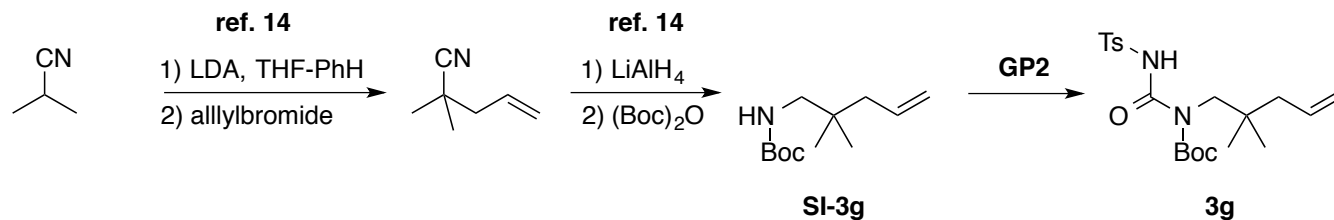
<sup>11</sup> Nicolai, S.; Waser, J. *Org. Lett.* **2011**, *13*, 6324–6327.

<sup>12</sup> Srivari, C.; Bodugam, M.; Mitta, K. *J. Org. Chem.* **2009**, *74*, 9531–9534.

<sup>13</sup> Gribkov, D. V.; Hultsch, K. C.; Hampel, F. *J. Am. Chem. Soc.* **2006**, *128*, 3748–3759.

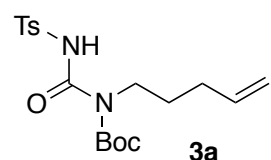
### Summary (3g)

Bishomoallylic ureas (**3g**) were prepared following GP2 from the corresponding *N*-Boc derivative (**SI-3g**)<sup>14</sup> which was prepared adapting a known protocol<sup>14</sup> from commercially available isobutyronitrile as outlined Scheme 4.



Scheme 4.

### 5.2. Characterization data of bishomoallylic urea derivatives (3a-g).

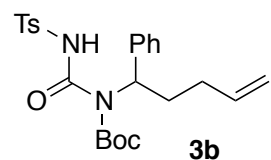


**3a**: White solid, m.p. 65-68 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 11.56 (1H, s), 7.98 (2H, d, *J*=8.5), 7.33 (2H, d, *J*=8.0), 5.72 (1H, ddt, *J*=17.0, 10.3, 6.6), 4.92-5.00 (2H, m), 3.56-3.62 (2H, m), 2.43 (3H, s), 1.99 (2H, q, *J*=7.2), 1.55-1.62 (2H, m), 1.52 (9H, s).

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 °C) δ 154.8, 150.0, 144.6, 137.3, 136.0, 129.4, 128.5, 115.2, 85.3, 43.8,

30.8, 27.9, 27.5, 21.6.

HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>18</sub>H<sub>26</sub>N<sub>2</sub>O<sub>5</sub>NaS [M+Na]<sup>+</sup>: 405.1454, found: 405.1449.

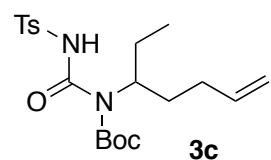


**3b**: White solid, m.p. 81-85 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 11.70 (1H, s), 8.01 (2H, d, *J*=8.5), 7.36 (2H, d, *J*=8.5), 7.19-7.29 (3H, m), 7.15 (2H, d, *J*=7.7), 5.81 (1H, t, *J*=7.8), 5.74 (1H, m), 4.87-4.92 (2H, m), 2.46 (3H, s), 2.18-2.25 (2H, m), 1.94-2.11 (2H, m), 1.23 (9H, s).

<sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 154.8, 151.0, 144.7, 140.1, 137.4, 135.9, 129.4, 128.5, 128.1, 127.0,

126.5, 115.2, 85.7, 55.3, 30.6, 29.9, 27.6, 21.7.

HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>24</sub>H<sub>30</sub>N<sub>2</sub>O<sub>5</sub>NaS [M+Na]<sup>+</sup>: 481.1767, found: 481.1767.



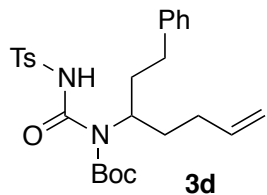
**3c**: White solid, m.p. 42-45 °C; some signals show multiple resonance for the presence of different rotational isomers: <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 50 °C) δ 11.59 (1H, s), 7.95 (2H, d, *J*=8.2), 7.30 (2H, d, *J*=8.5), 5.64 (1H, ddt, *J*=16.9, 10.5, 6.4), 4.82-4.87 (2H, m), 4.43 (1H, br-s), 2.42 (3H, s), 1.80-1.94 (3H, m), 1.68-1.79 (1H, m), 1.53-1.67 (2H, m), 1.52 (9H, s), 0.75 (3H,

t, *J*=7.4).

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 °C) δ 155.6, 150.7, 144.4, 137.7, 136.5, 129.4, 128.5, 114.9, 85.4, 32.2, 30.8, 28.1, 26.3, 21.6, 10.8.

HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>20</sub>H<sub>30</sub>N<sub>2</sub>O<sub>5</sub>NaS [M+Na]<sup>+</sup>: 433.1767, found: 433.1772.

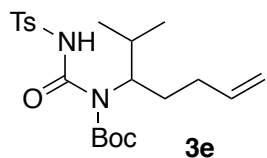
<sup>14</sup> Bender, C. F.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2005**, *127*, 1070-1071.



**3d:** Transparent oil; some signals show multiple resonance for the presence of different rotational isomers:  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 50  $^\circ\text{C}$ )  $\delta$  11.54 (1H, s), 7.97 (2H, d,  $J=8.2$ ), 7.31 (2H, d,  $J=8.5$ ), 7.18-7.22 (2H, m), 7.13 (1H, m), 7.00-7.03 (2H, m), 5.64 (1H, ddt,  $J=16.7$ , 10.5, 6.4), 4.86 (1H, br-d,  $J=16.7$ ), 4.85 (1H, d,  $J=10.5$ ), 4.56 (1H, m), 2.41 (3H, s), 2.34-2.47 (2H, m), 1.80-1.95 (4H, m), 1.59-1.70 (1H, m), 1.45-1.50 (1H, m), 1.49 (9H, s).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 50  $^\circ\text{C}$ )  $\delta$  155.1, 150.3, 144.3, 141.1, 137.3, 136.2, 129.1, 128.3, 128.2, 127.9, 125.7, 114.8, 85.4, 55.3, 34.5, 32.6, 32.2, 30.4, 27.8, 21.3.

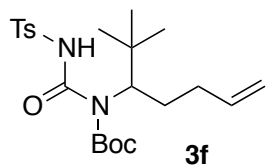
HRMS ( $\text{ESI}^+$ )  $m/z$ : calcd for  $\text{C}_{26}\text{H}_{34}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 509.2080, found: 509.2082.



**3e:** White solid, m.p. 85-86  $^\circ\text{C}$ ; some signals show multiple resonance for the presence of different rotational isomers:  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 50  $^\circ\text{C}$ )  $\delta$  11.63 (1H, s), 7.94 (2H, d,  $J=8.7$ ), 7.30 (2H, d,  $J=8.2$ ), 5.62 (1H, m), 4.75-4.87 (2H, m), 4.22 (1H, m), 2.42 (3H, s), 1.61-2.28 (5H, m), 1.52 (9H, s), 0.90 (3H, d,  $J=6.9$ ), 0.69 (3H, d,  $J=6.9$ ).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 50  $^\circ\text{C}$ )  $\delta$  155.3, 151.3, 144.4, 137.7, 136.0, 129.3, 128.4, 114.8, 85.4, 60.5, 31.4, 30.7, 30.2, 28.0, 21.6, 20.9, 19.3.

HRMS ( $\text{ESI}^+$ )  $m/z$ : calcd for  $\text{C}_{21}\text{H}_{32}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 447.1924, found: 447.1920.

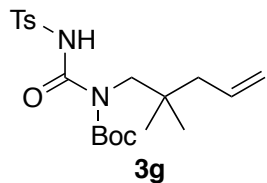


**3f:** White solid, m.p. 112-114  $^\circ\text{C}$ ; some signals show multiple resonance for the presence of different rotational isomers;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 50  $^\circ\text{C}$ )  $\delta$  11.74 (br-s) and 11.47 (1H, br-s), 7.94 (2H, d,  $J=7.9$ ), 7.29 (2H, d,  $J=7.9$ ), 5.69 (ddt,  $J=16.9$ , 10.3, 6.6) and 5.61 (1H, m), 4.80-4.92 (2H, m), 4.59 (dd,  $J=11.9$ , 4.5) and 4.08 (1H, dd,  $J=11.9$ , 4.0), 2.42 (3H, s),

2.33-2.45 (m) and 2.02-2.12 (1H, m), 1.55-1.92 (3H, m), 1.54 (s) and 1.51 (9H, s), 0.85 (s) and 0.84 (9H, s).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 50  $^\circ\text{C}$ )  $\delta$  156.3, 156.2, 151.9, 150.0, 144.34, 144.26, 138.0, 137.6, 136.5, 136.3, 129.2, 128.5, 128.4, 114.9, 86.0, 85.5, 66.6, 62.1, 35.7, 35.6, 31.2, 31.0, 28.4, 28.1, 28.0, 27.9, 26.9, 26.1, 21.5.

HRMS ( $\text{ESI}^+$ )  $m/z$ : calcd for  $\text{C}_{22}\text{H}_{34}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 461.2080, found: 461.2083.



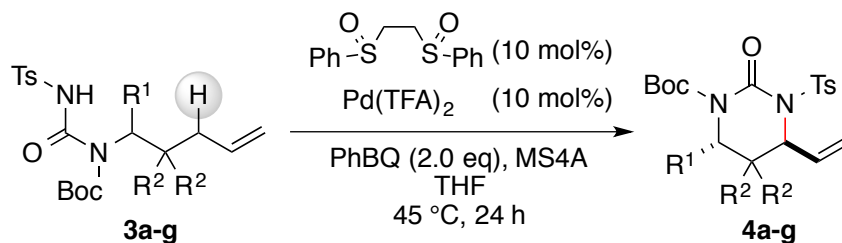
**3g:** White solid, m.p. 76-79  $^\circ\text{C}$ ; some signals show multiple resonance for the presence of different rotational isomers;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 50  $^\circ\text{C}$ )  $\delta$  11.56 (1H, s), 7.96 (2H, d,  $J=8.1$ ), 7.30 (2H, d,  $J=7.7$ ), 5.73 (1H, m), 5.00 (1H, d,  $J=10.3$ ), 4.94 (1H, d,  $J=16.9$ ), 3.61 (2H, br-s), 2.41 (3H, s), 1.87 (2H, d,  $J=7.0$ ), 1.52 (9H, s), 0.75 (6H, s).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 50  $^\circ\text{C}$ )  $\delta$  155.5, 150.6, 144.5, 136.4, 134.4, 129.4, 128.6, 117.6, 85.6, 60.3, 52.2, 45.4, 36.0, 27.9, 25.2, 21.5.

HRMS ( $\text{ESI}^+$ )  $m/z$ : calcd for  $\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_5\text{NaS}$   $[\text{M}+\text{Na}]^+$ : 433.1767, found: 433.1790.

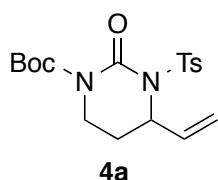
## 6. Experimental procedure for the preparation of 1,3-cyclic ureas (4a-g) and characterization data

### 6.1. General procedure for preparation of 1,3-cyclic ureas (4a-g). (GP5)

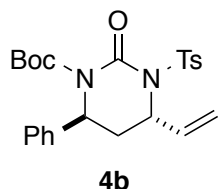


**GP5:** A test tube (topped with a Teflon-lined screwed cap) was charged with Pd(TFA)<sub>2</sub> (6.5 mg, 0.02 mmol), 2-bis(phenylsulfinyl)ethane (5.5 mg, 0.02 mmol) and THF (0.3 mL). The mixture was stirred at room temperature for 30 min. To the mixture was added an acyclic urea **3** (0.2 mmol), 2-phenyl-1,4-benzoquinone (74 mg, 0.4 mmol) and THF (0.3 mL). The reaction was allowed to stir at 45 °C. After stirring at that temperature for 24 h, the reaction was filtered through short pad of silica gel. To the filtrate was added Et<sub>2</sub>O, 10% aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>, and 1 M aqueous NaOH. The organic layer was separated and washed with brine, dried with Na<sub>2</sub>SO<sub>4</sub> and evaporated to give the crude product, which was purified by silica gel chromatography to give **4**.

### 6.2. Characterization data of 1,3-cyclic ureas (4a-g).



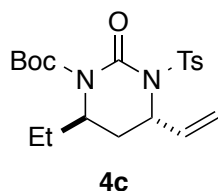
**4a:** 86% yield as a white solid, m.p. 108-111 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.93 (2H, d, *J*=8.2), 7.28 (2H, d, *J*=8.5), 5.82 (1H, ddd, *J*=17.0, 10.5, 5.1), 5.34 (1H, dd, *J*=10.5, 1.4), 5.32 (1H, dd, *J*=17.1, 1.6), 5.27 (1H, m), 3.73 (1H, dddd, *J*=12.5, 5.6, 2.8, 1.1), 3.50 (1H, td, *J*=12.6, 5.1), 2.41 (3H, s), 2.09-2.18 (1H, m), 2.04 (1H, ddt, *J*=14.0, 5.5, 2.8), 1.46 (9H, s); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 151.2, 148.7, 144.5, 136.3, 134.7, 129.3, 129.1, 118.2, 83.4, 56.2, 41.6, 27.9, 27.2, 21.6; HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>18</sub>H<sub>24</sub>N<sub>2</sub>O<sub>5</sub>NaS [M+Na]<sup>+</sup>: 403.1298, found: 403.1307.



**4b:** 46% yield as a yellow solid, m.p. 126-127 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.92 (2H, d, *J*=8.5), 7.22-7.32 (5H, m), 7.14 (2H, d, *J*=8.5), 5.92 (1H, ddd, *J*=17.1, 10.7, 5.1), 5.36 (1H, dd, *J*=10.5, 1.4), 5.32 (1H, dd, *J*=17.1, 1.6), 5.20 (1H, m), 4.94 (1H, dd, *J*=11.1, 6.5), 2.44 (3H, s), 2.40 (1H, ddd, *J*=14.3, 6.5, 3.8), 2.19 (1H, ddd, *J*=14.2, 11.1, 4.8), 1.16 (9H, s);

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 125MHz) δ 150.5, 149.0, 144.6, 141.7, 136.0, 134.4, 129.3, 129.2, 128.8, 127.6, 125.4, 118.0, 83.4, 57.2, 55.3, 38.2, 27.5, 21.6 ;

HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>24</sub>H<sub>28</sub>N<sub>2</sub>O<sub>5</sub>NaS [M+Na]<sup>+</sup>: 479.1611, found: 479.1608.

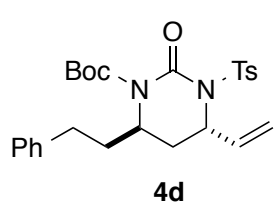


**4c:** 52% yield as dark brown oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.94 (2H, d, *J*=8.5), 7.29 (2H, d, *J*=7.9), 5.72 (1H, ddd, *J*=16.8, 10.6, 5.6), 5.20 (1H, dd, *J*=10.2, 1.4), 5.14-5.20 (2H, m), 4.06 (1H, qd, *J*=7.7, 5.2), 2.42 (3H, s), 2.25 (1H, ddd, *J*=13.9, 7.7, 4.5), 2.05 (1H, ddd, *J*=13.9, 7.4, 6.2), 1.75 (1H, m), 1.52-1.61 (1H, m), 1.42 (9H, s), 0.86 (3H, t, *J*=7.4 Hz);

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 125MHz) δ 151.7, 149.4, 144.6, 136.1, 135.5, 129.1, 117.1, 82.9, 55.5, 53.5,

34.3, 28.2, 27.9, 21.6, 9.5;

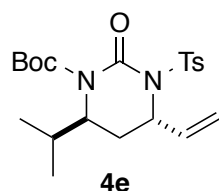
HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>20</sub>H<sub>28</sub>N<sub>2</sub>O<sub>5</sub>NaS [M+Na]<sup>+</sup>: 431.1611, found: 431.1608.



**4d**: 69% yield as ocher solid, m.p. 115-116 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.95 (2H, d, *J*=8.5), 7.25-7.29 (5H, m), 7.16-7.21 (1H, m), 7.12 (2H, m), 5.72 (1H, ddd, *J*=16.7, 10.5, 5.7), 5.20 (1H, dd, *J*=10.3, 1.3), 5.18 (1H, dd, *J*=16.4, 1.7), 5.13- 5.19 (1H, m), 4.19 (1H, qd, *J*=7.5, 5.8), 2.61 (1H, ddd, *J*=13.9, 10.5, 5.4), 2.53 (1H, ddd, *J*=13.8, 10.3, 6.2), 2.40 (3H, s), 2.28 (1H, ddd, *J*=14.0, 7.7, 4.7), 2.10 (1H, dt, *J*=13.7, 6.7), 2.04 (1H, ddt, *J*=13.6, 10.4, 6.0), 1.83 (1H, dddd, *J*=13.5, 10.3, 7.9, 5.7), 1.41 (9H, s);

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 125MHz) δ 151.6, 149.3, 144.6, 140.7, 136.0, 135.6, 129.2, 129.1, 128.4, 128.2, 126.1, 117.2, 83.1, 55.5, 52.0, 36.8, 34.8, 31.7, 27.9, 21.6 ;

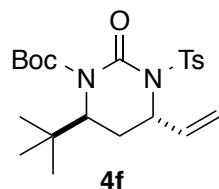
HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>26</sub>H<sub>32</sub>N<sub>2</sub>O<sub>5</sub>NaS [M+Na]<sup>+</sup>: 507.1924, found: 507.1924.



**4e**: 83% yield as yellowish oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.95 (2H, d, *J*=8.5), 7.29 (2H, d, *J*=8.5), 5.72 (1H, m), 5.13-5.21 (3H, m), 4.02 (1H, td, *J*=7.9, 6.7), 2.42 (3H, s), 2.12-2.19 (2H, m), 2.08 (1H, dt, *J*=13.7, 7.0), 1.40 (9H, s), 0.85 (3H, d, *J*=6.8), 0.78 (3H, d, *J*=6.8);

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 125MHz) δ 151.9, 149.7, 144.6, 135.9, 135.5, 129.1, 116.9, 82.7, 56.9, 55.4, 31.5, 30.7, 27.8, 21.6, 18.7, 16.6 ;

HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>21</sub>H<sub>30</sub>N<sub>2</sub>O<sub>5</sub>NaS [M+Na]<sup>+</sup>: 445.1767, found: 445.1786.

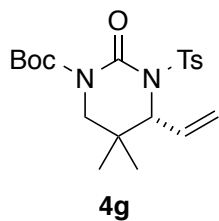


**4f**: 81% yield as orange solid, m.p. 132-135 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.96 (2H, d, *J*=8.5), 7.30 (2H, d, *J*=8.5), 5.70 (1H, ddd, *J* = 17.2, 10.7, 3.8 Hz), 5.23 (1H, ddq, *J*=6.0, 4.0, 2.0), 5.14 (1H, dd, *J*=10.7, 2.2), 5.08 (1H, dd, *J*=17.2, 2.1), 4.18 (1H, dd, *J*=10.3, 8.1), 2.42 (1H, s), 2.33 (1H, ddd, *J*=14.0, 10.3, 2.0), 2.19 (1H, ddd, *J*=14.1, 7.9, 6.0), 1.35 (9H,s), 0.80 (9H,s);

<sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 152.2, 150.6, 144.8, 135.6, 135.4, 129.13, 129.10, 116.5, 82.2, 58.3, 55.6,

36.8, 31.2, 27.9, 25.6, 21.6;

HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>22</sub>H<sub>32</sub>N<sub>2</sub>O<sub>5</sub>NaS [M+Na]<sup>+</sup>: 459.1924, found: 459.1925.



**4g**: 84% yield as yellowish solid, m.p. 134-136 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.91 (2H, d, *J*=8.2), 7.26 (2H, d, *J*=7.9), 5.84 (1H, ddd, *J* = 17.0, 10.3, 6.9 Hz), 5.40 (1H, d, *J*=10.5), 5.38 (1H, d, *J*=17.0), 4.68 (1H, d, *J*=6.8), 3.37 (1H, dd, *J*=12.6, 1.8), 3.23 (1H, d, *J*=12.5), 2.41 (3H, s), 1.46 (9H, s), 1.17 (3H, s), 1.09 (3H, s);

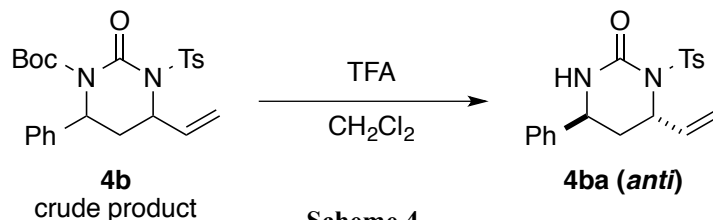
<sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 151.4, 144.3, 136.2, 133.0, 129.5, 129.0, 120.1, 83.5, 66.0, 53.2, 32.3,

27.9, 25.5, 24.2, 21.6;

HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>20</sub>H<sub>28</sub>N<sub>2</sub>O<sub>5</sub>NaS [M+Na]<sup>+</sup>: 431.1611, found: 431.1609.

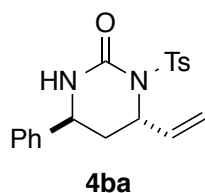


### 6.3. Determination of the relative stereochemistry in **4b**



**Scheme 4.**

The crude product of **4b** prepared by GP5 from **3b** (92 mg, 0.2 mmol) was treated with trifluoroacetic acid (0.7mL) in CH<sub>2</sub>Cl<sub>2</sub> (0.7 mL) to afford a deprotected product **4ba**<sup>15</sup> both of whose relative stereochemistry (1,3-*syn* and *anti*) was reported as defined well (Scheme 4). <sup>1</sup>H-NMR data of the crude product showed single diastereomer was produced. The crude product was purified by silica gel chromatography (Et<sub>2</sub>O/n-Hex=1/5 to 3/1) to give **4ba** (23mg, 32% in 2 steps). The comparison of <sup>1</sup>H-NMR data between synthetic compounds and reported ones<sup>11</sup> revealed unambiguously that **4ba** as well as **4b** were 1,3-*anti* product.



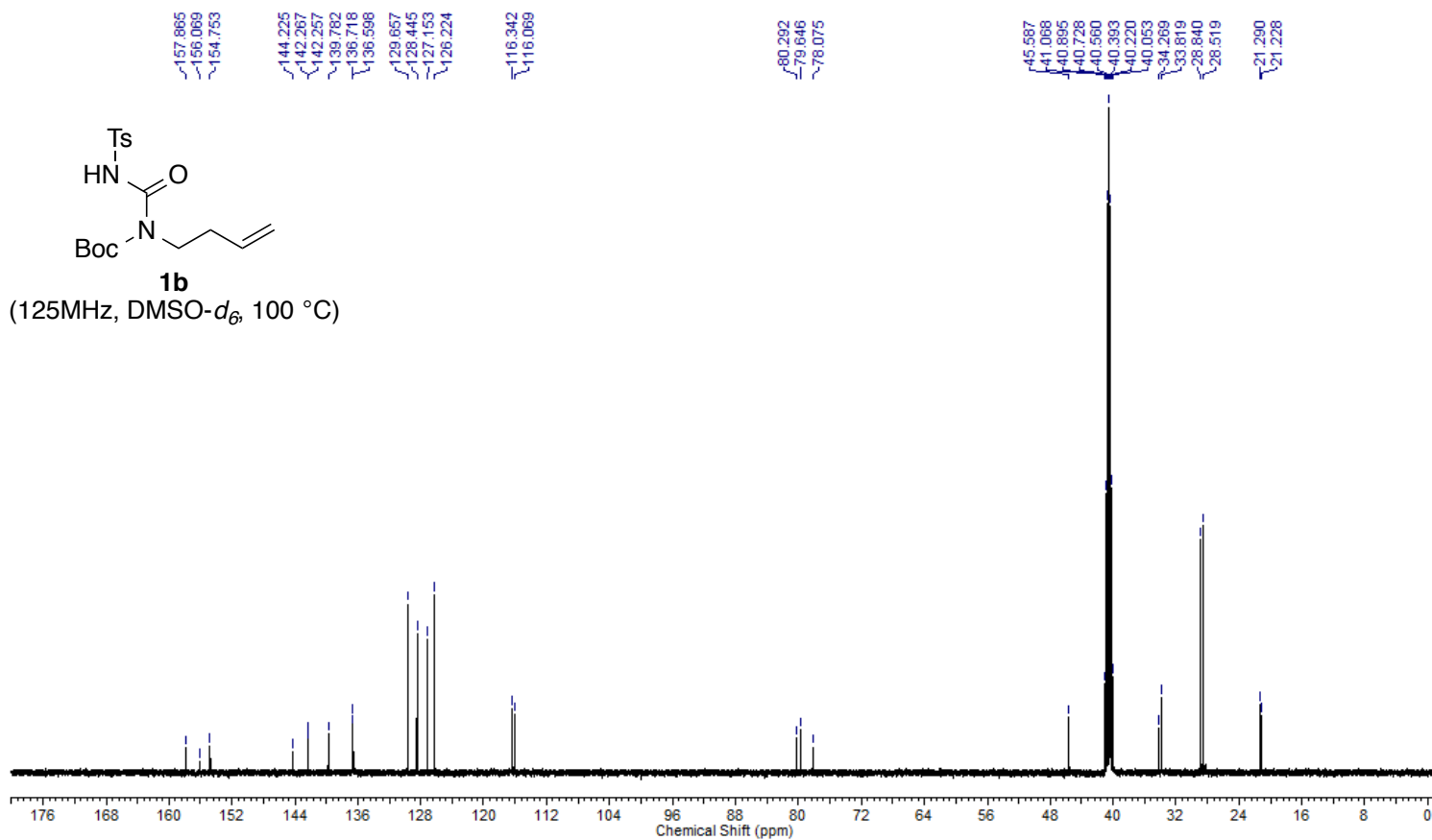
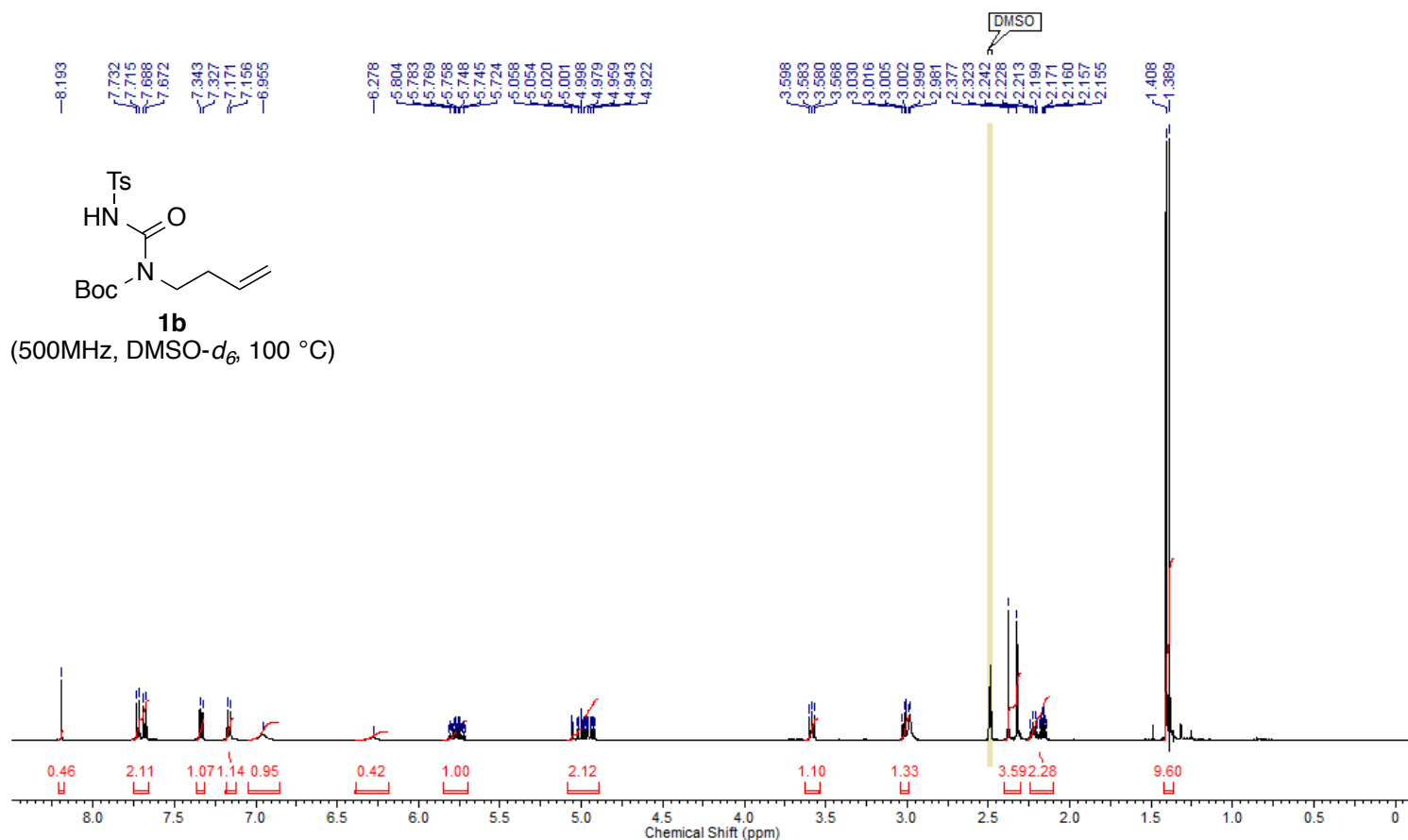
**4ba (anti)**<sup>15</sup>: 32% yield as a brown solid, m.p. 205-206 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.90 (2H, d, *J*=8.2), 7.24-7.38 (7H, m), 5.95 (1H, ddd, *J*=17.2, 10.5, 5.0), 5.40 (1H, dd, *J*=10.5, 1.4), 5.36 (1H, dd, *J*=17.0, 1.6), 5.30 (1H, m), 5.21 (1H, br-s), 4.47 (1H, dd, *J*=12.0, 4.2), 2.42 (3H, s), 2.16 (1H, m), 2.05 (1H, ddd, *J* = 13.7, 12.0, 4.7 Hz); The spectral data were identical to the ones reported in literature<sup>15</sup>.

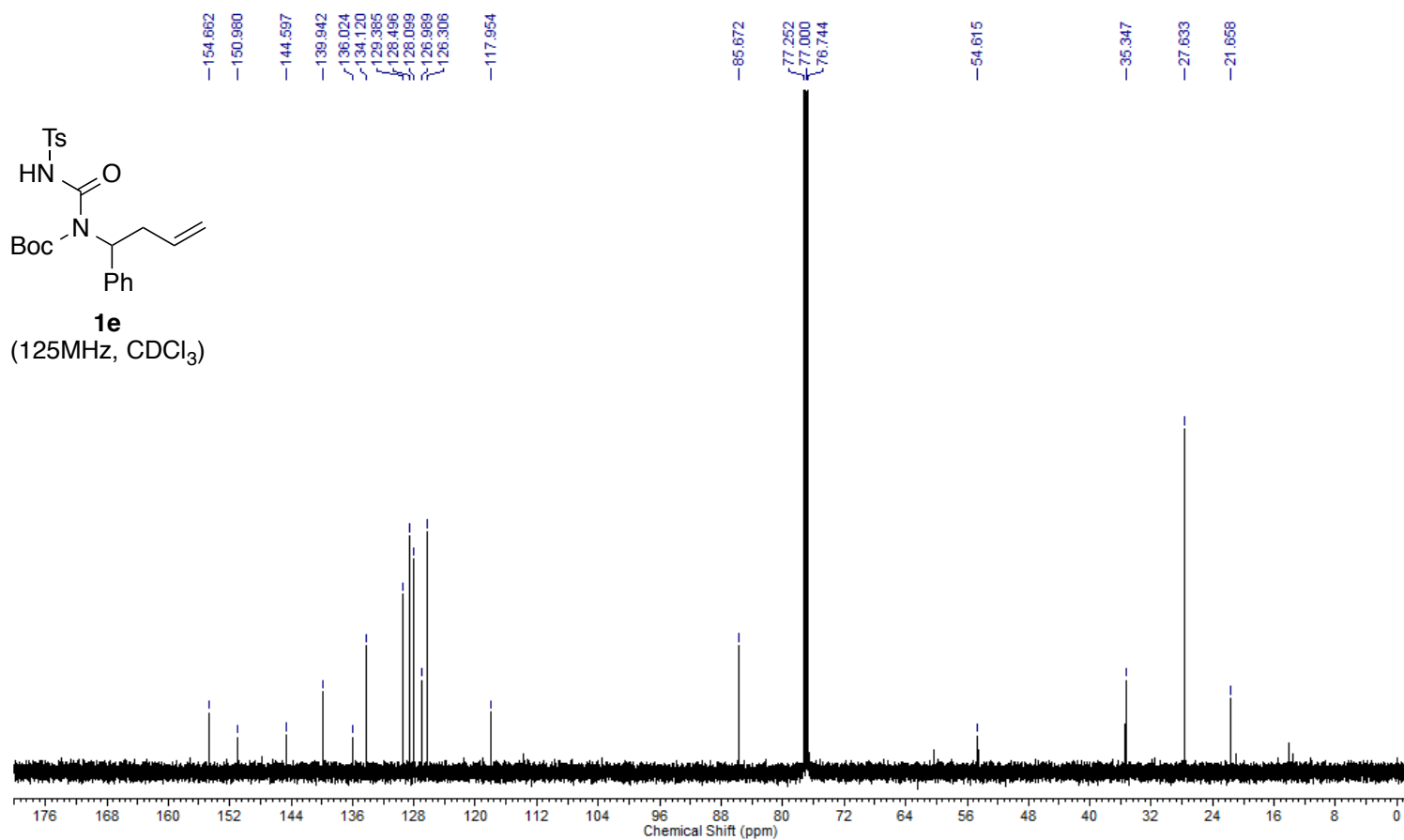
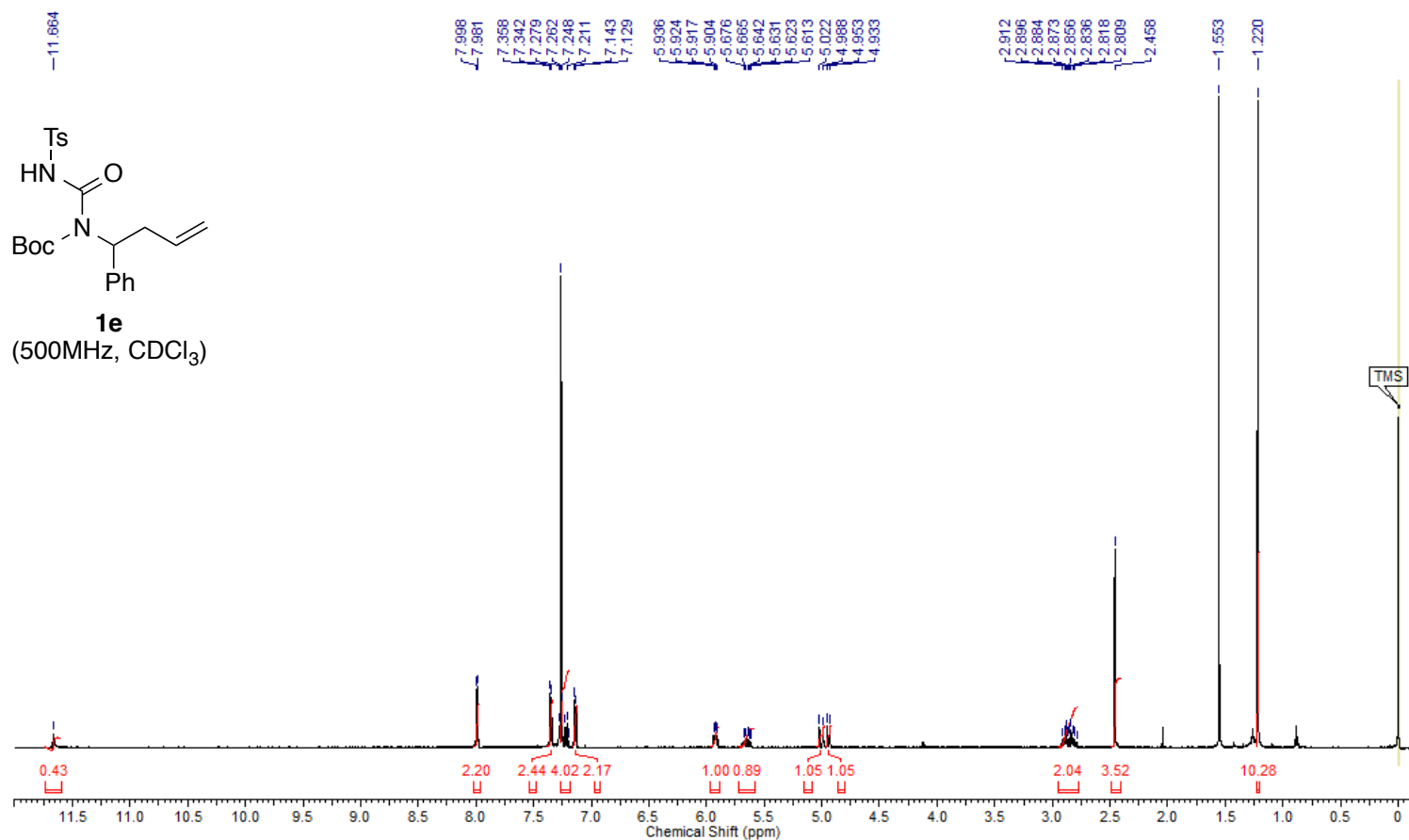
<sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 151.4, 144.3, 140.2, 136.9, 135.2, 129.1, 129.04, 129.01, 128.6, 126.2, 118.2, 56.2, 52.8, 36.4, 21.6;

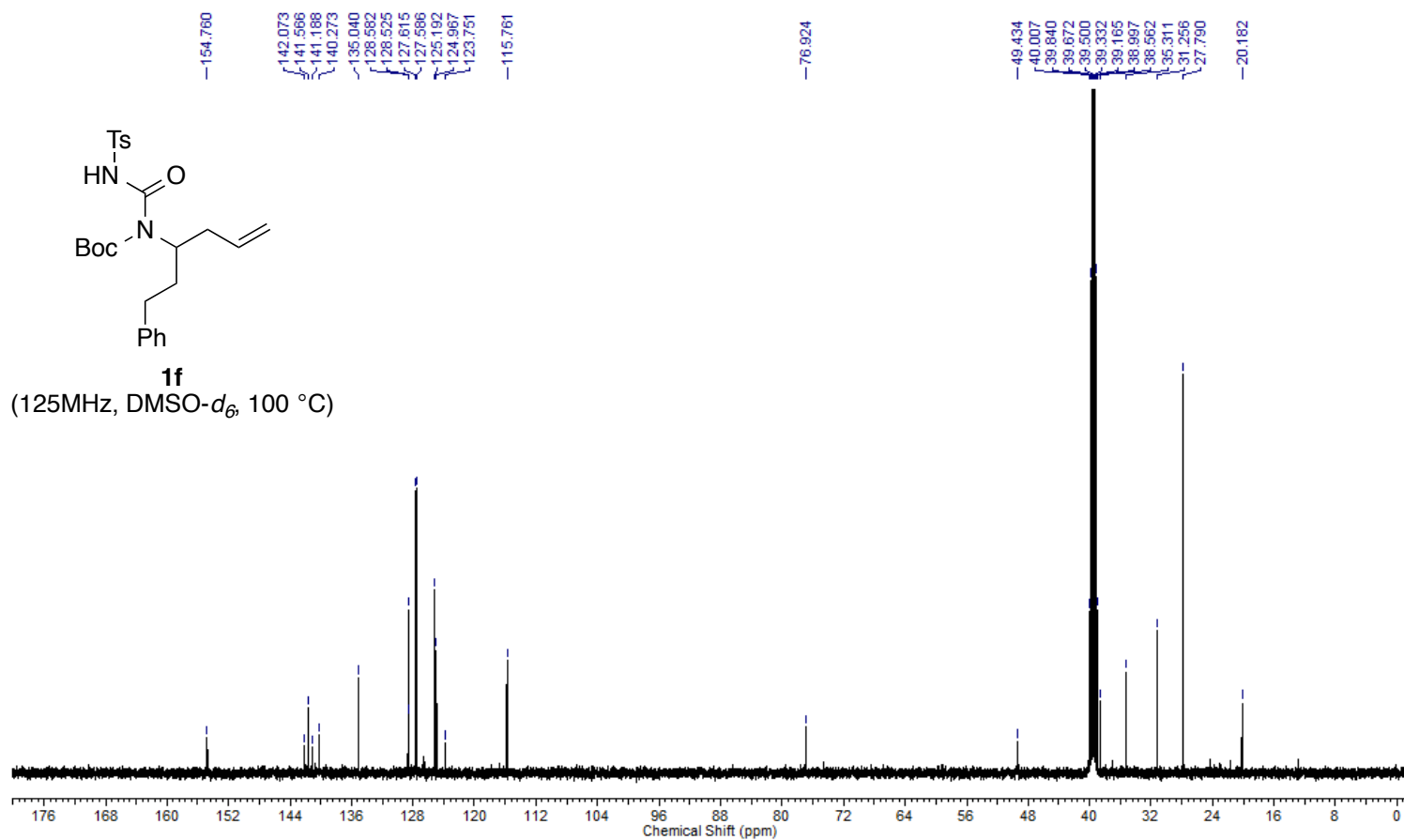
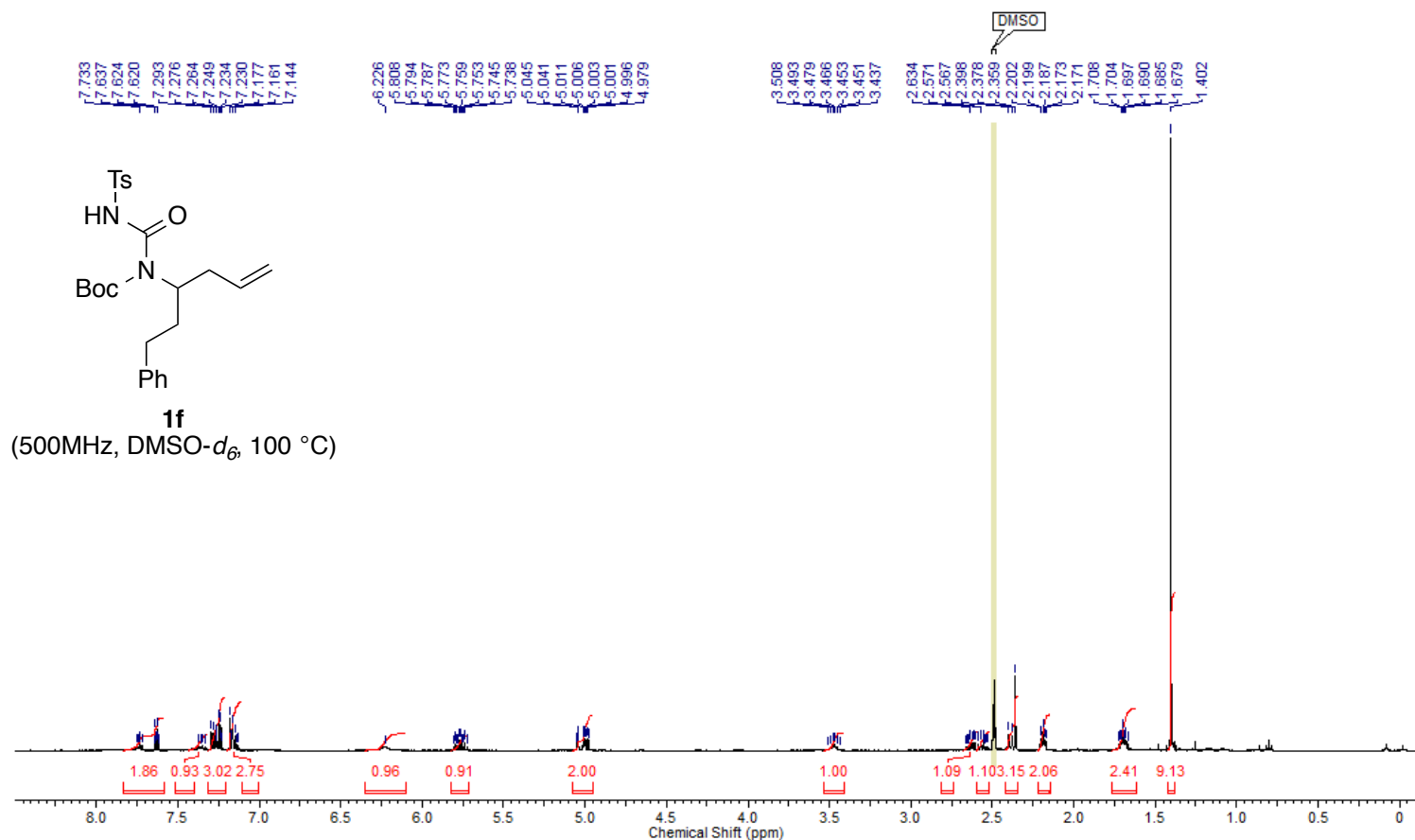
HRMS (ESI<sup>+</sup>) *m/z*: calcd for C<sub>19</sub>H<sub>20</sub>N<sub>2</sub>O<sub>3</sub>NaS [M+Na]<sup>+</sup>: 379.1087, found: 379.1084.

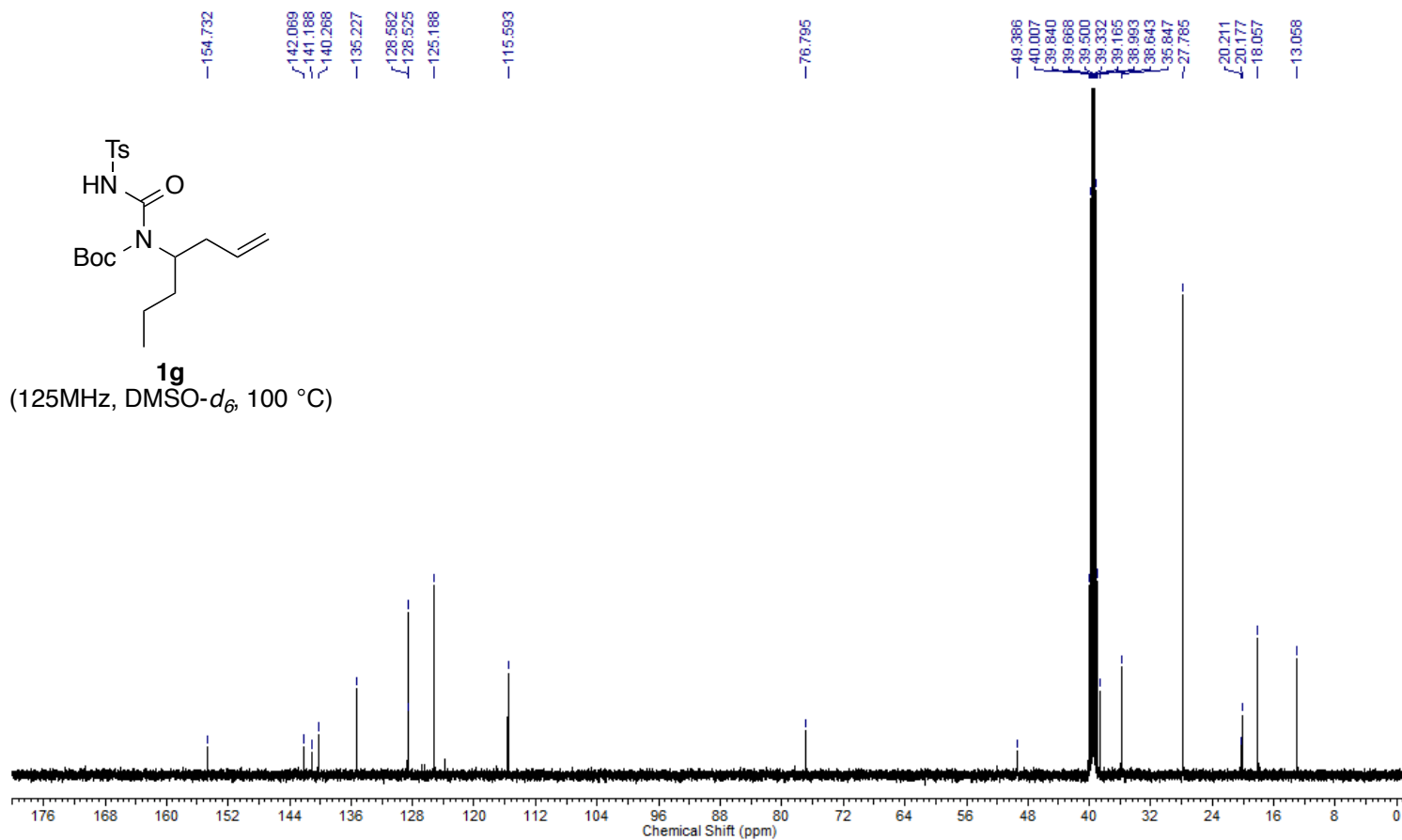
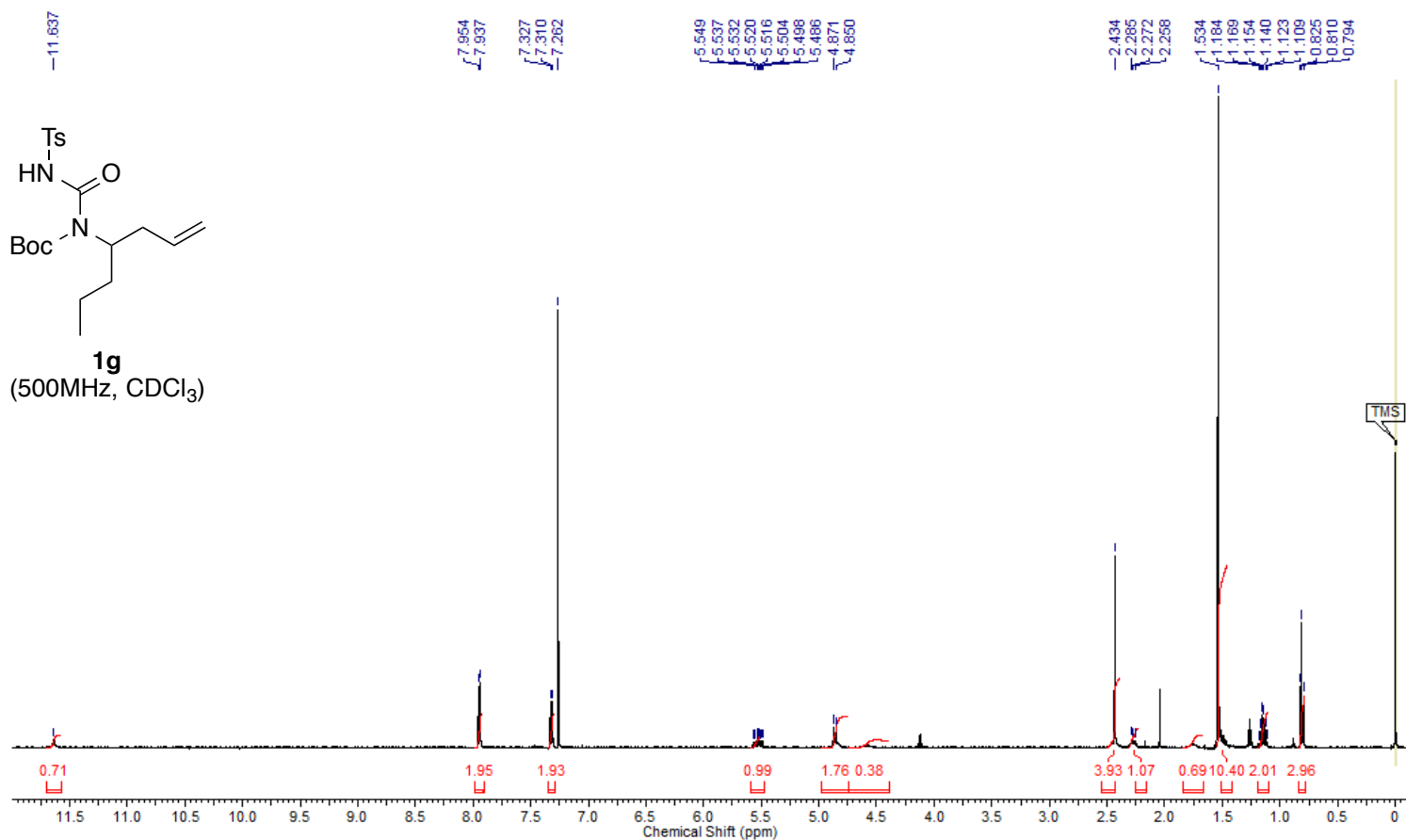
<sup>15</sup> Morgen, M.; Bretzke, S.; Li, P.; Menche, D. *Org. Lett.* **2010**, *12*, 4494-4497.

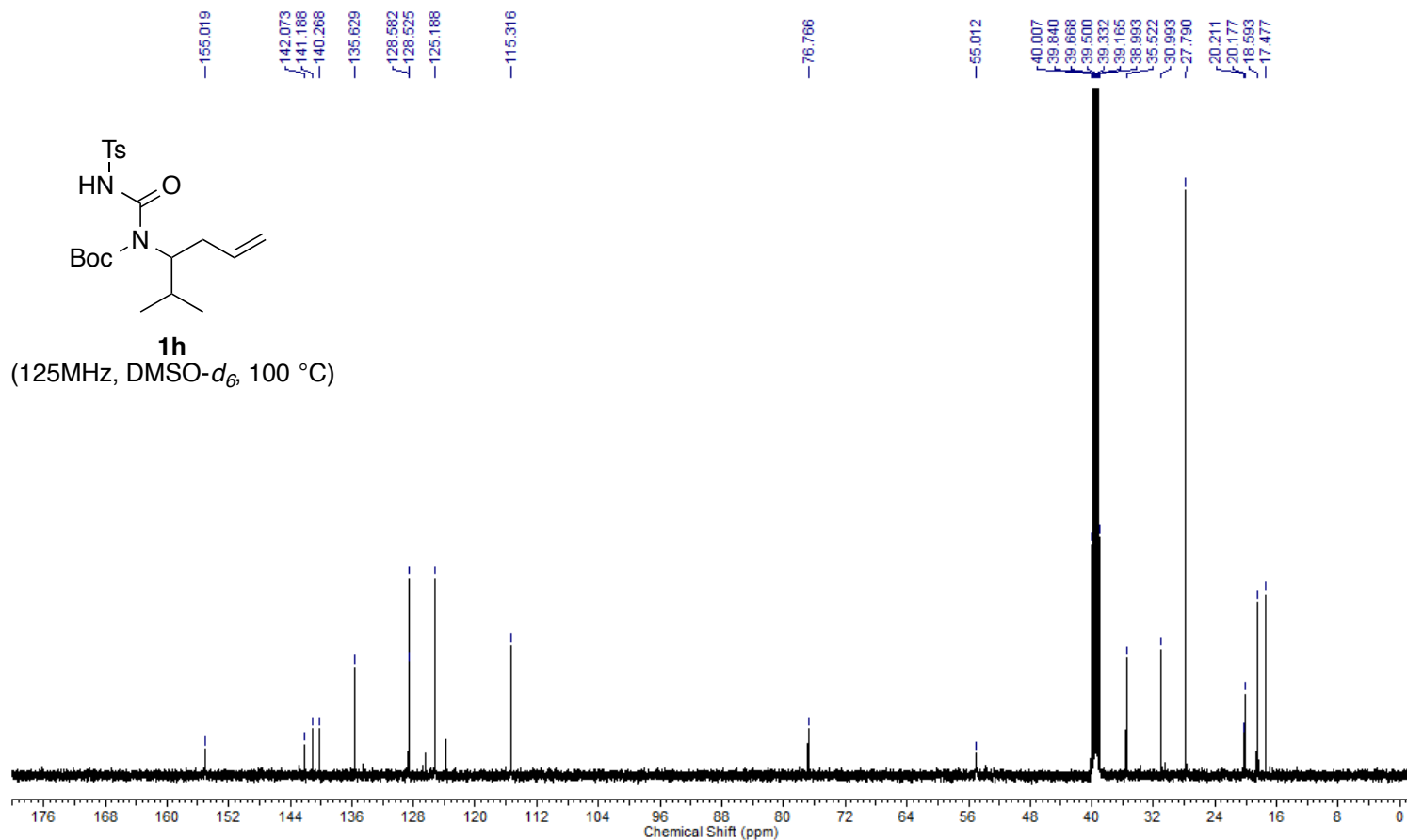
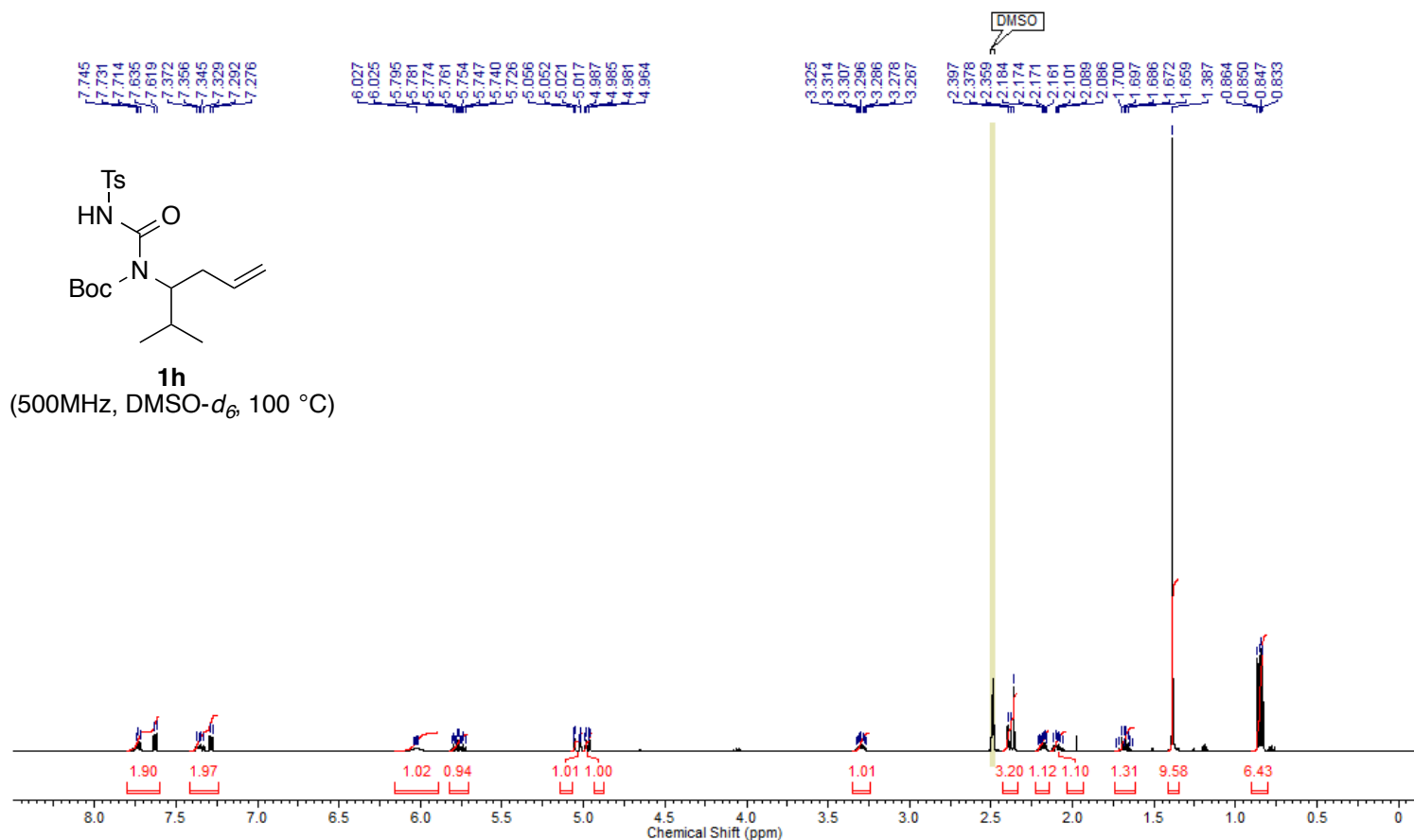
7. Copies of  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR spectra (**1b**, **1e-l**)

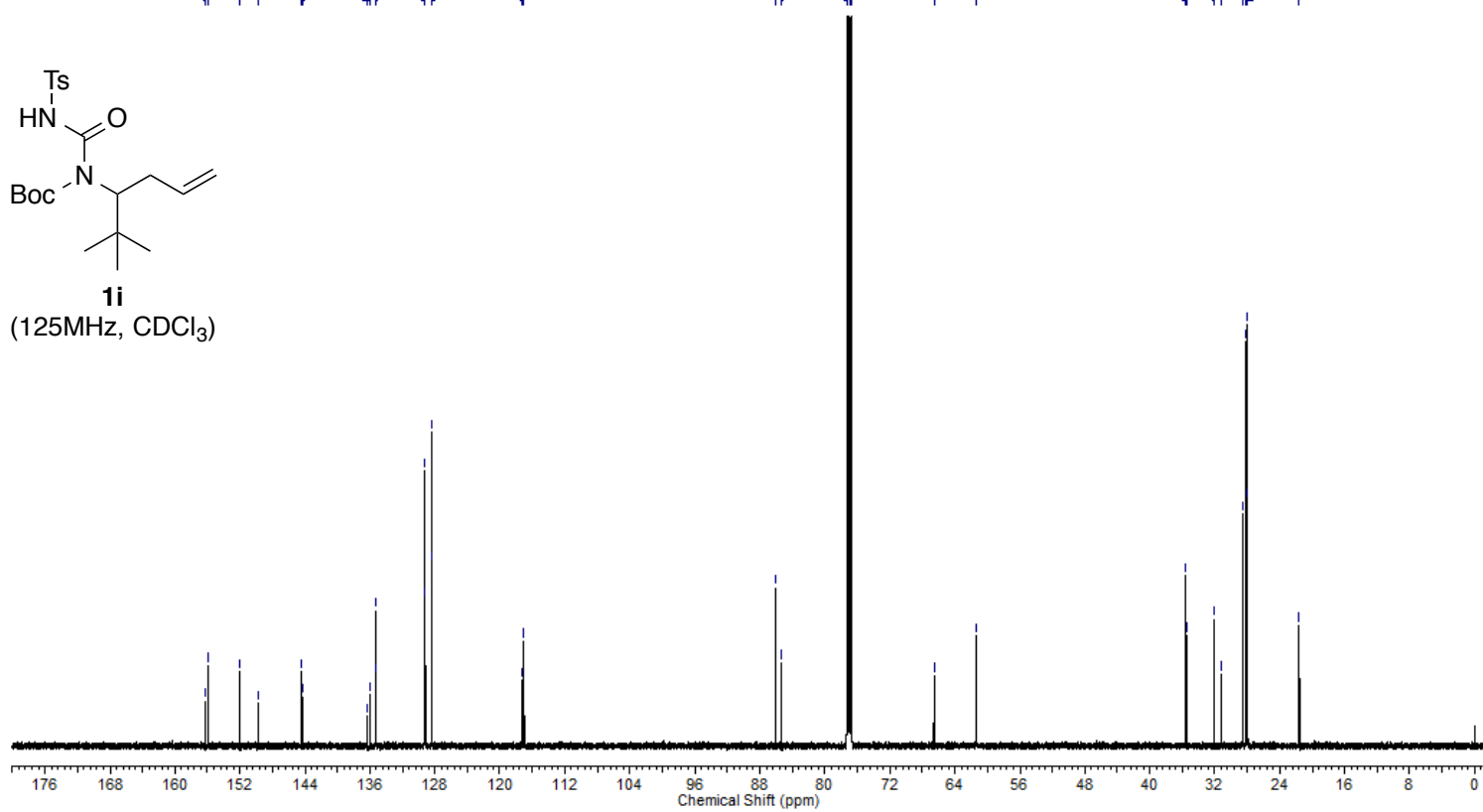
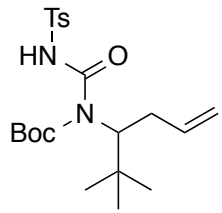
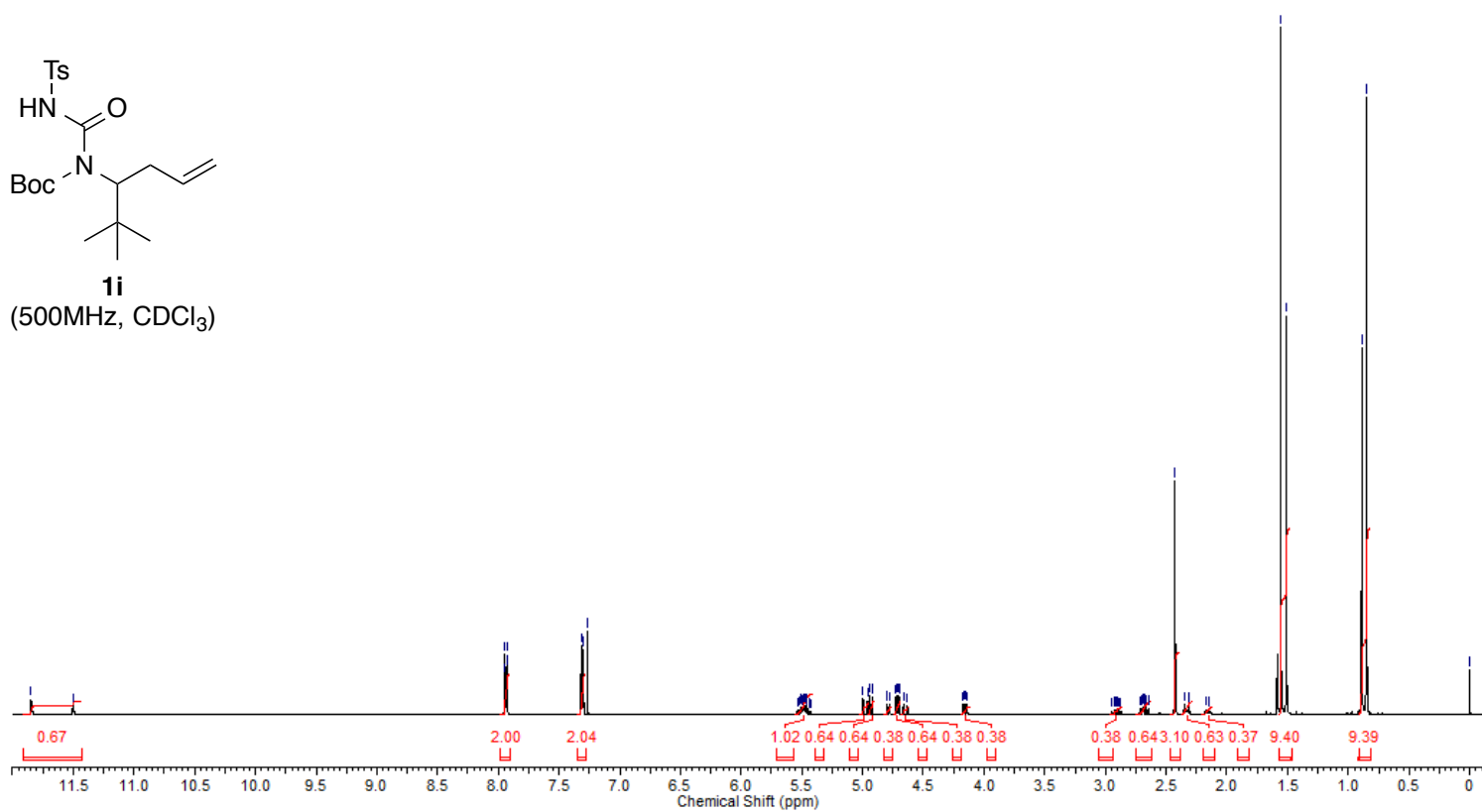
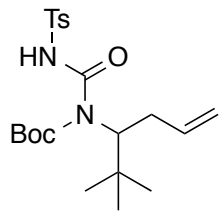


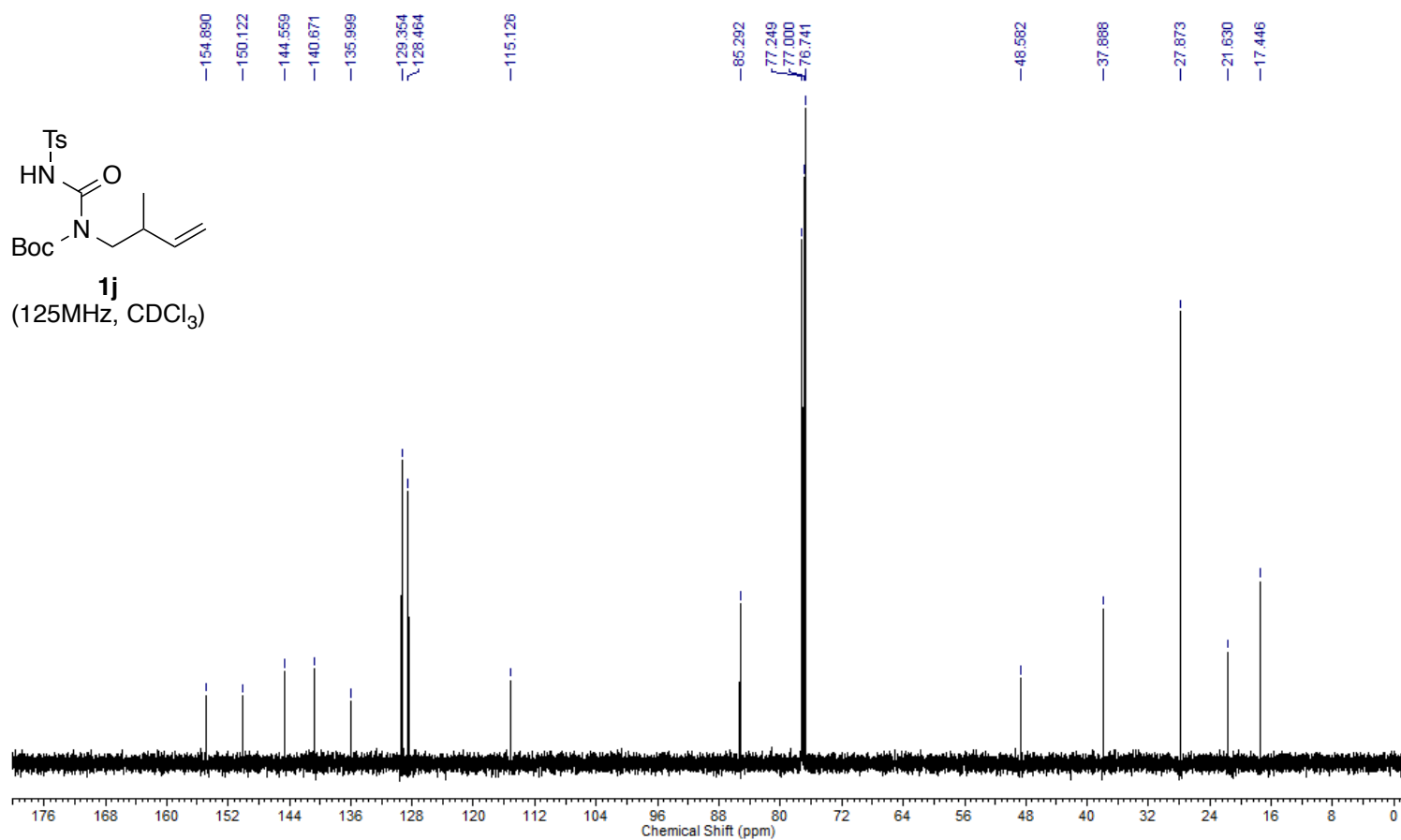
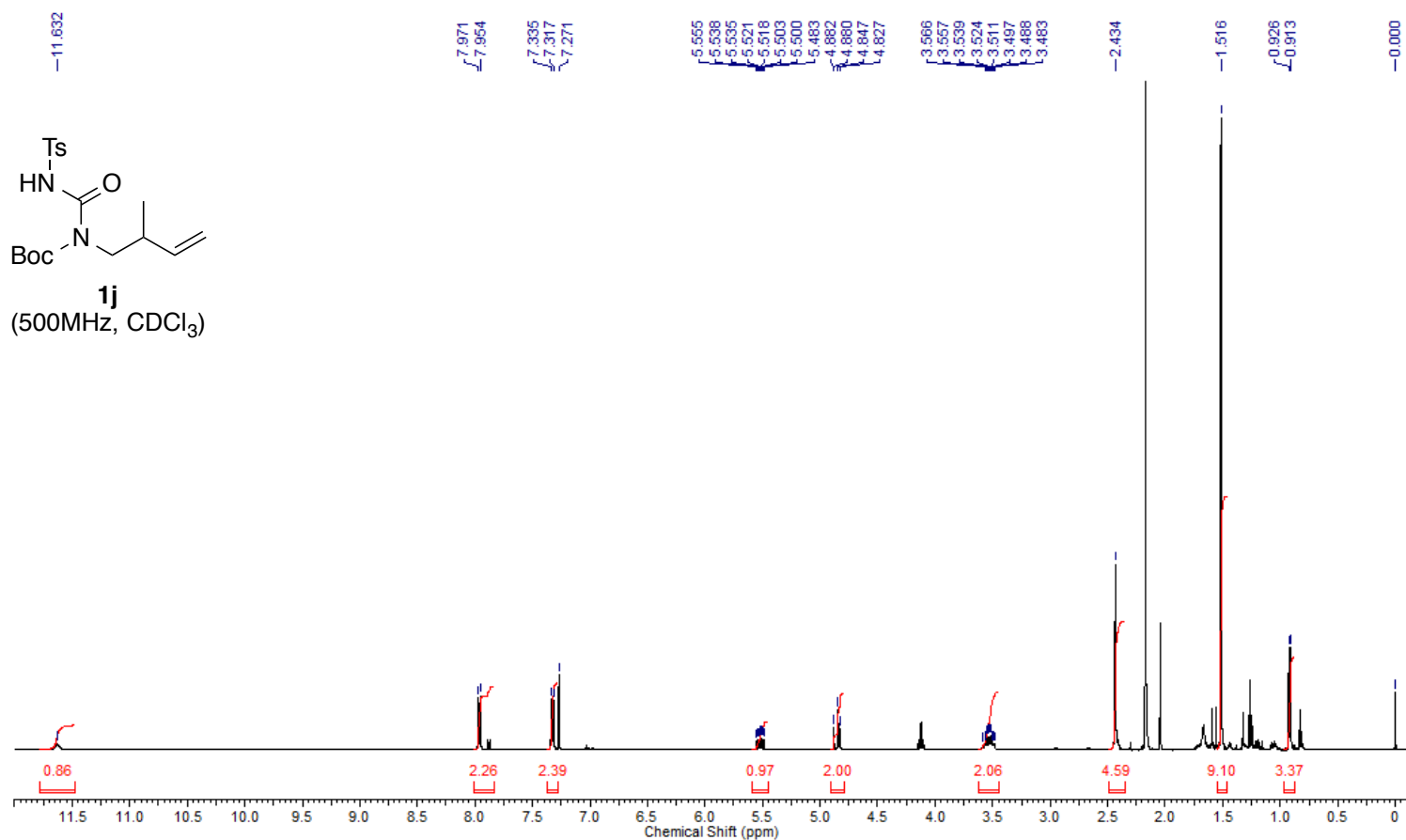




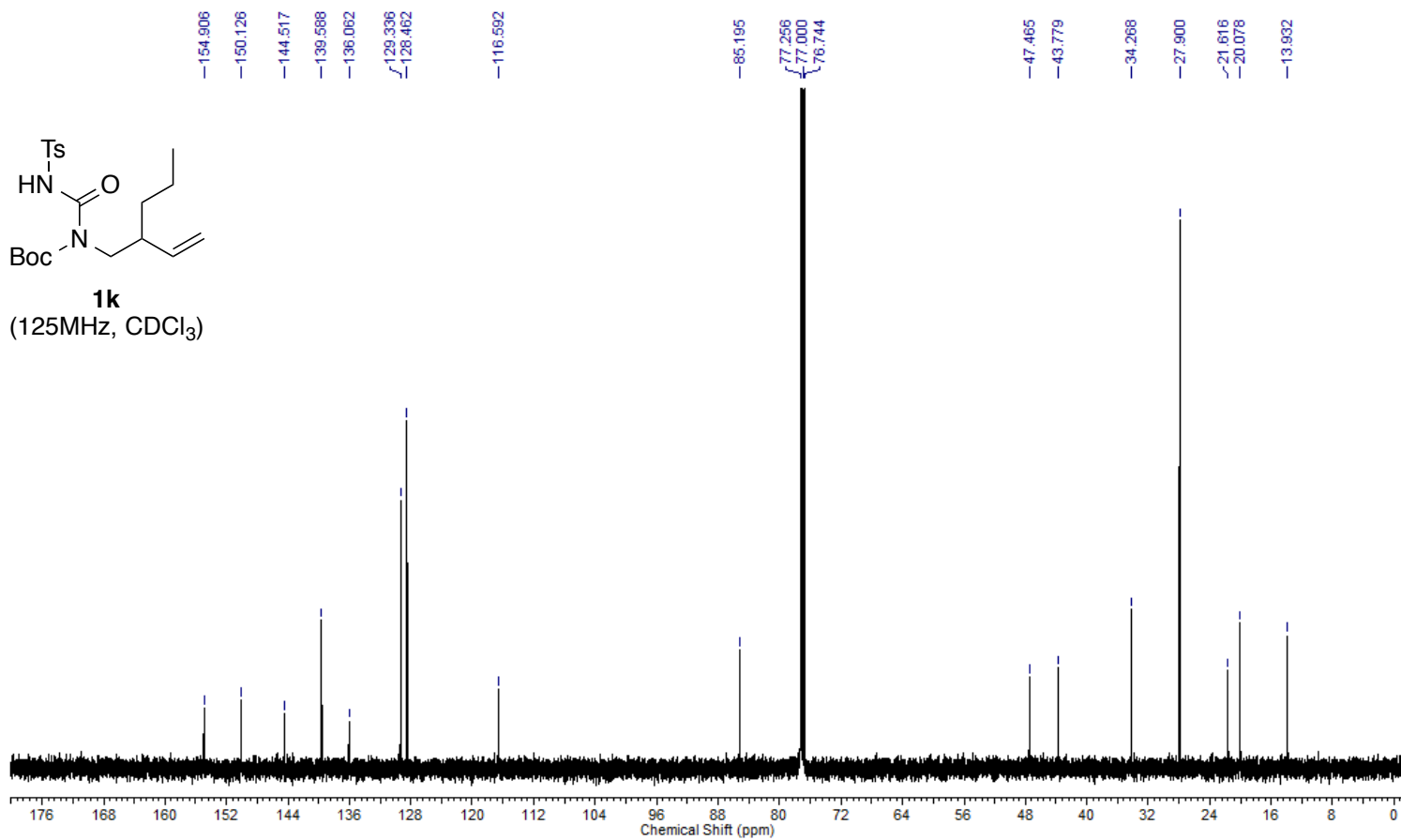
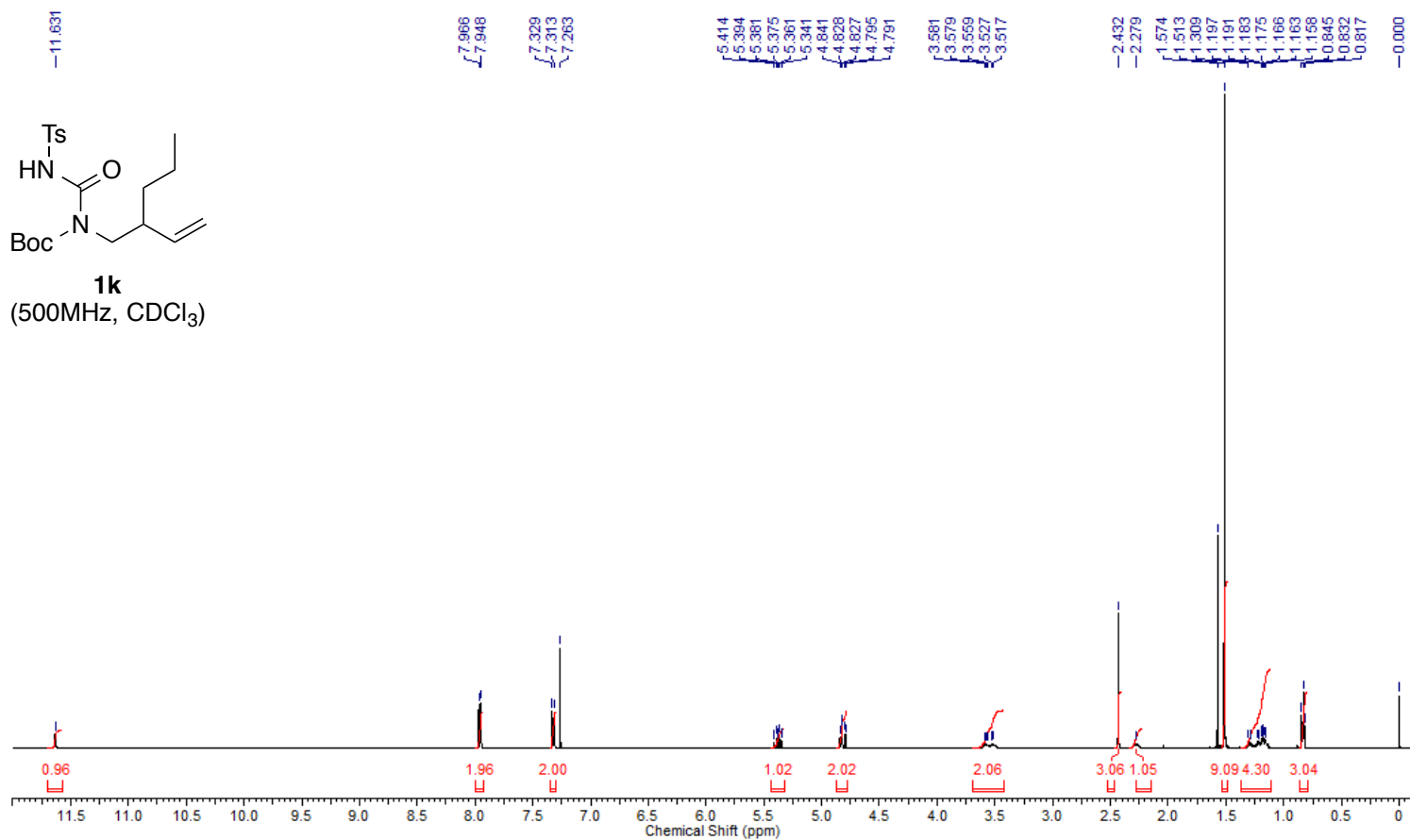


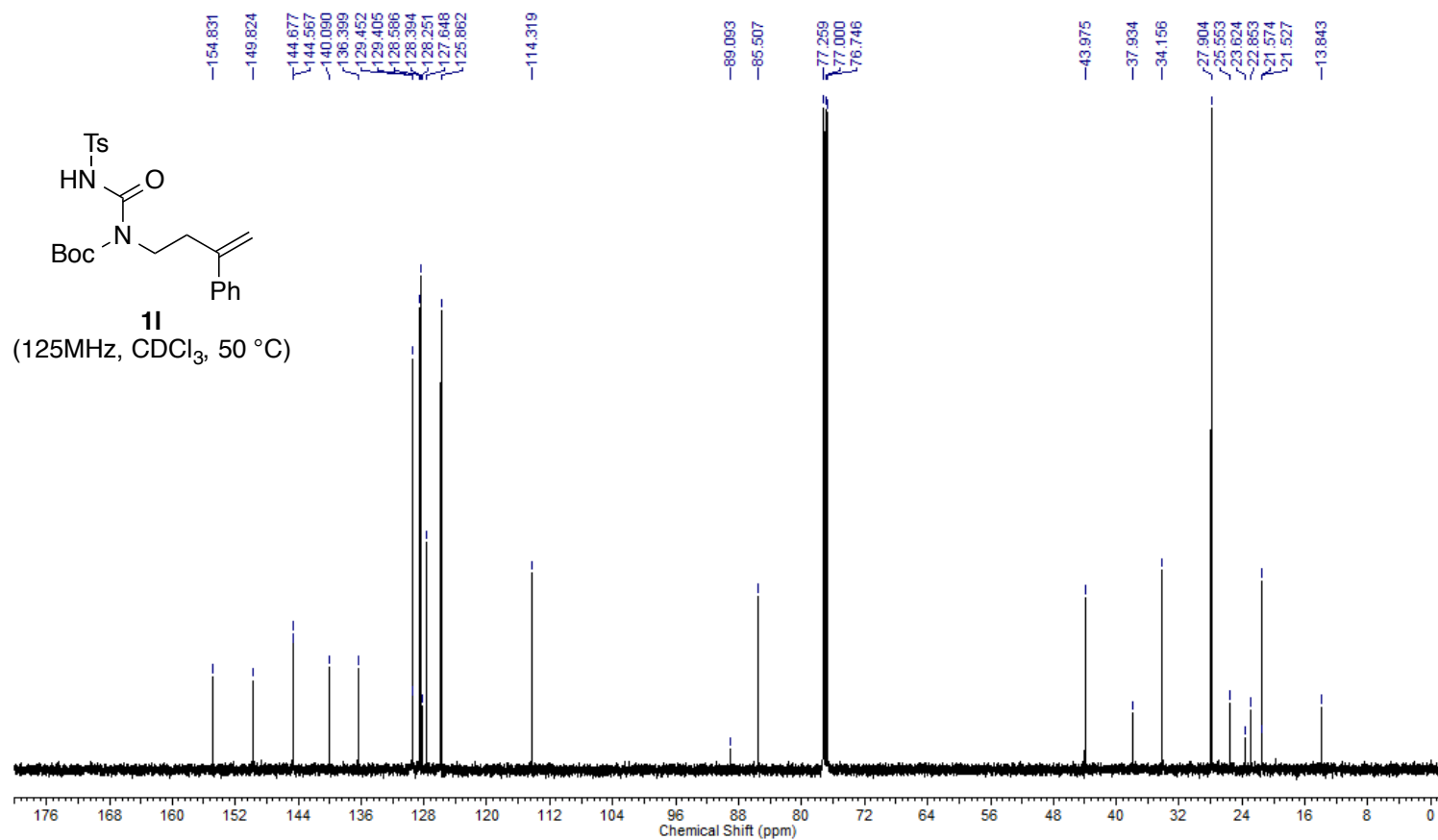
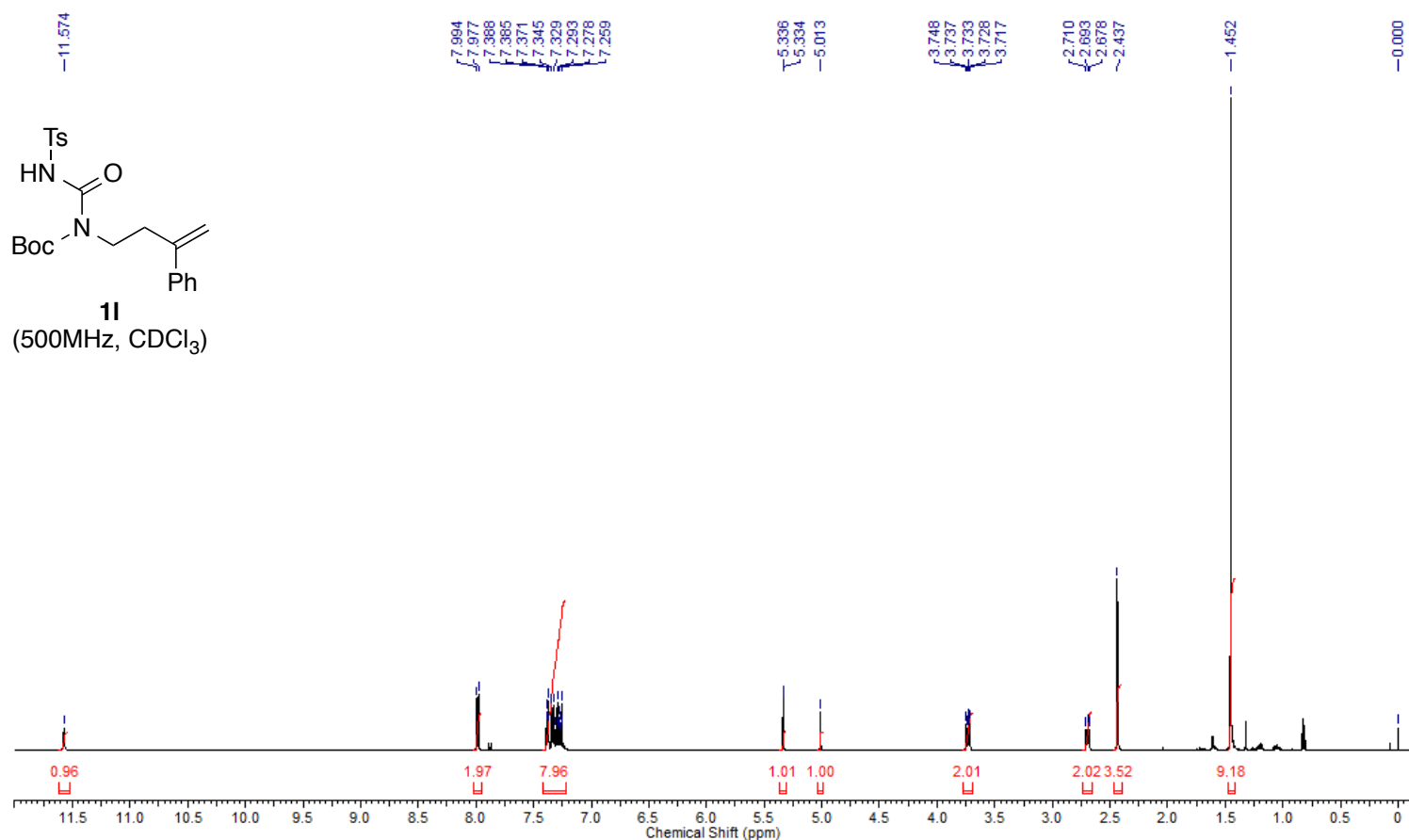




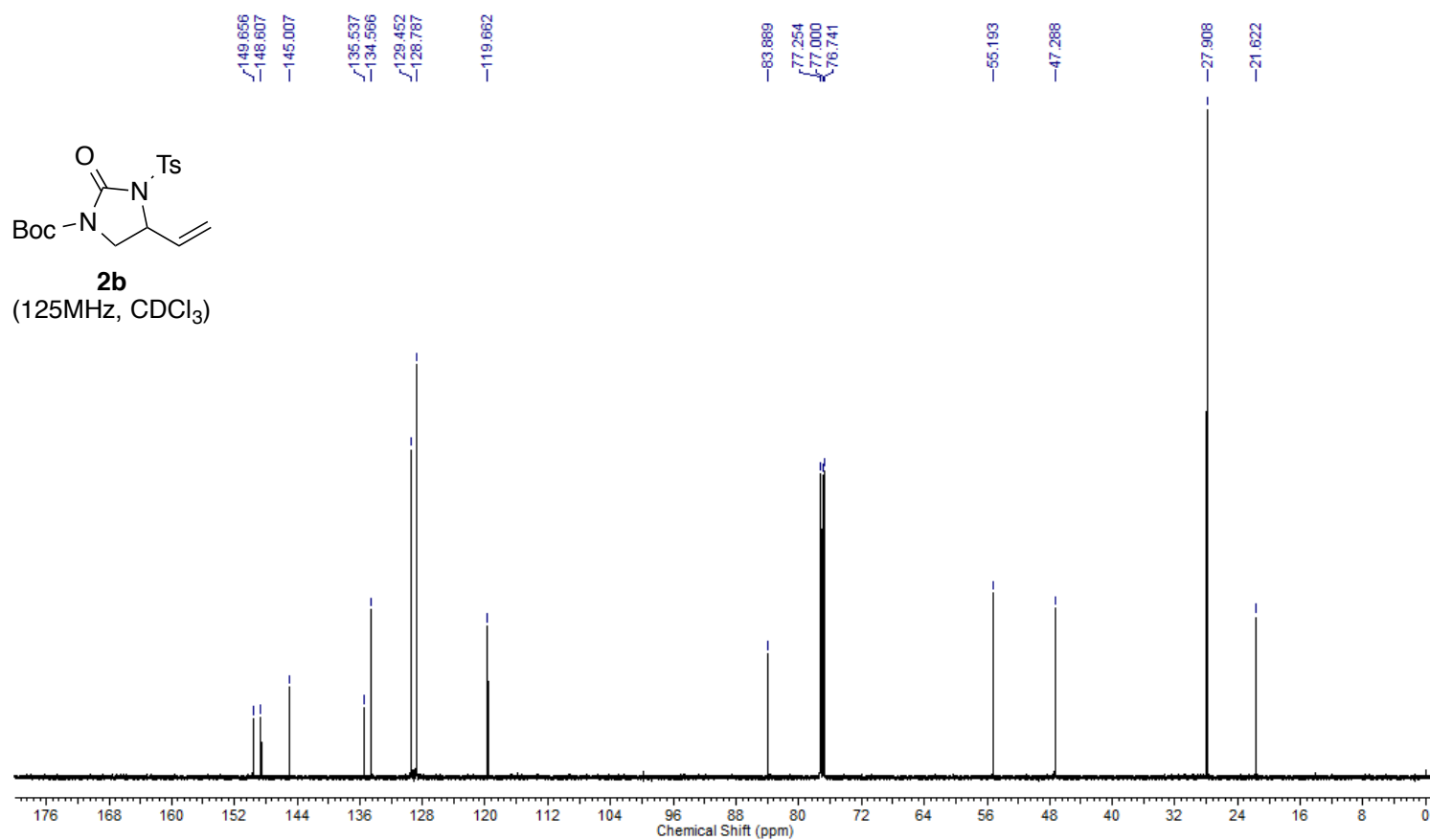
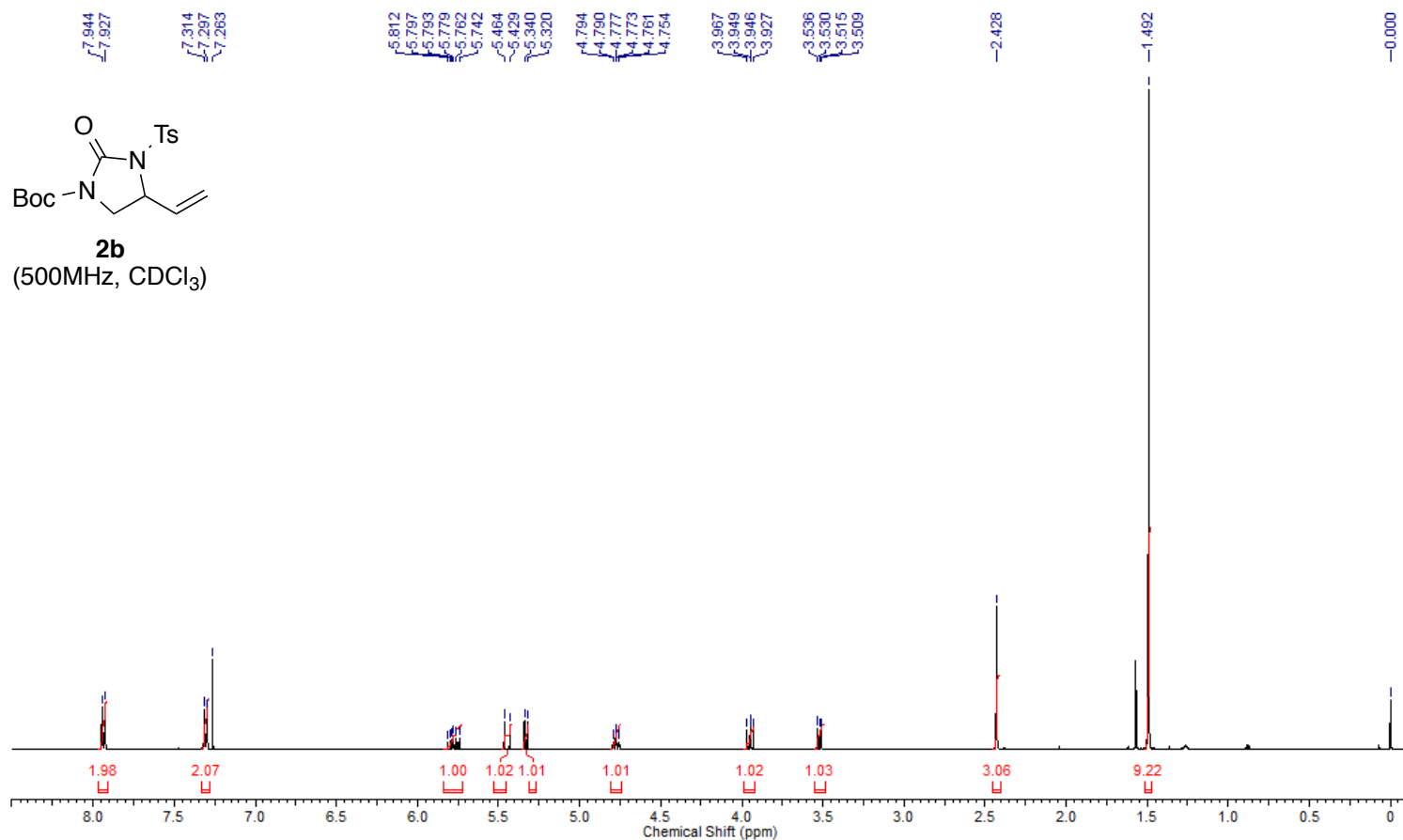


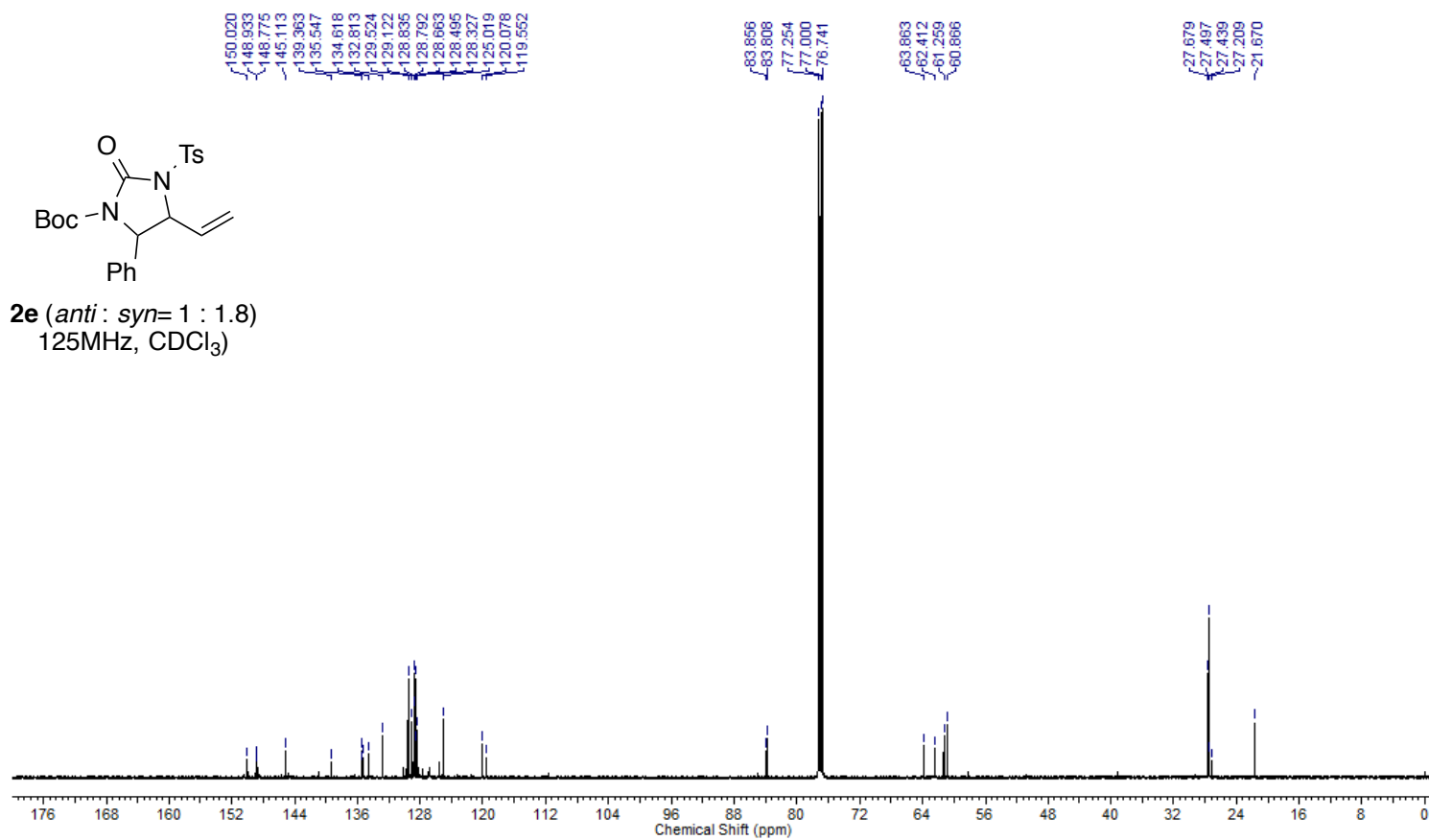
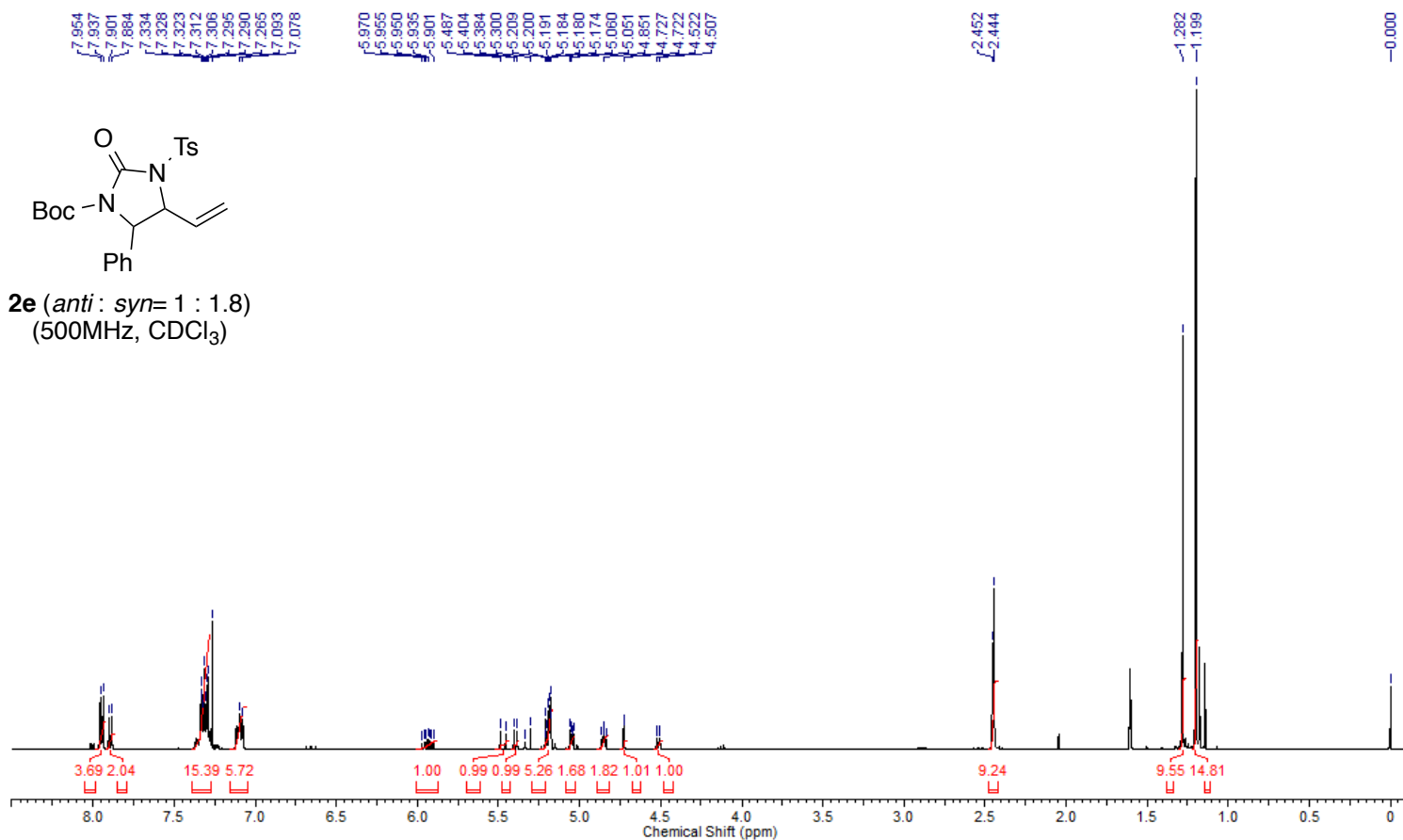


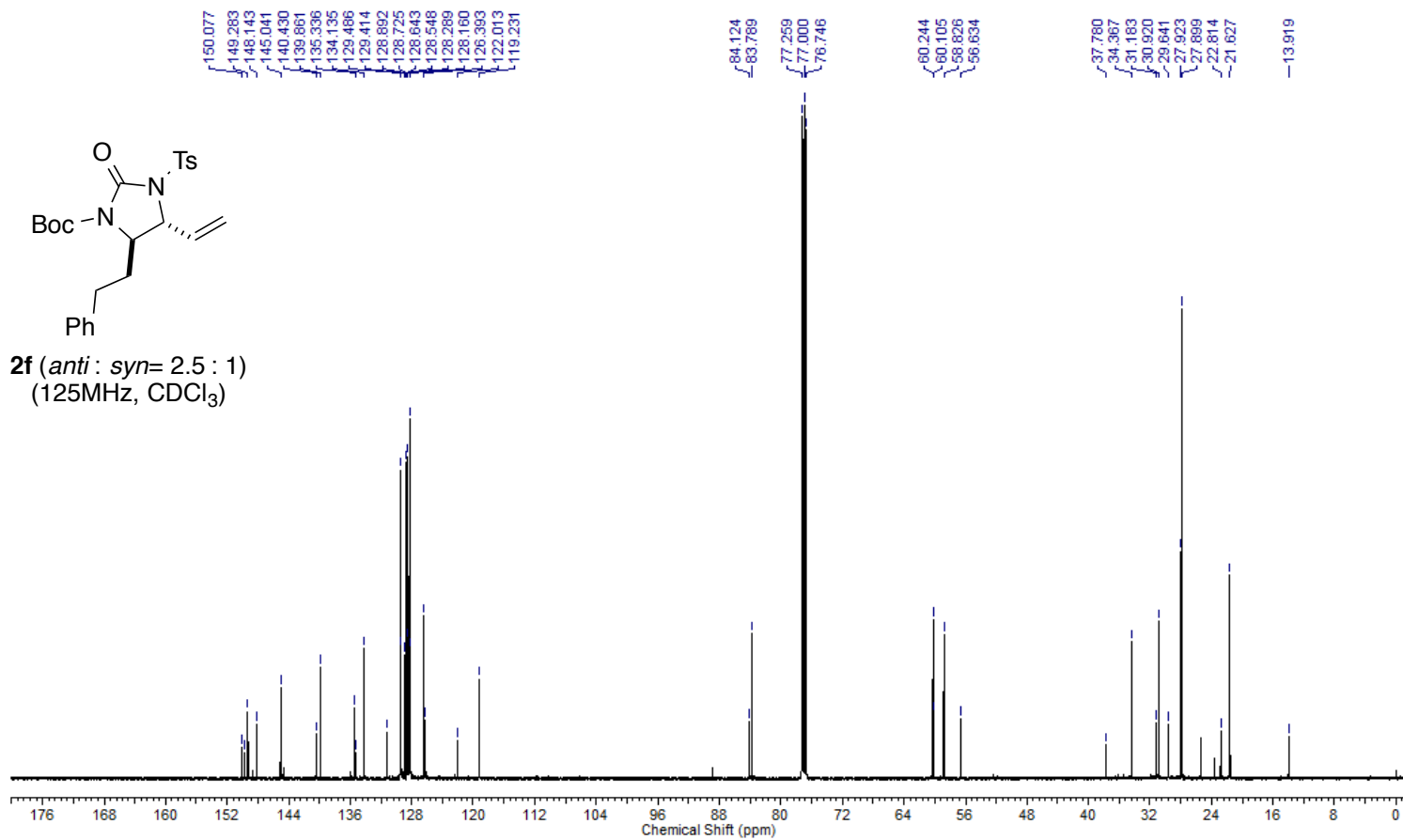
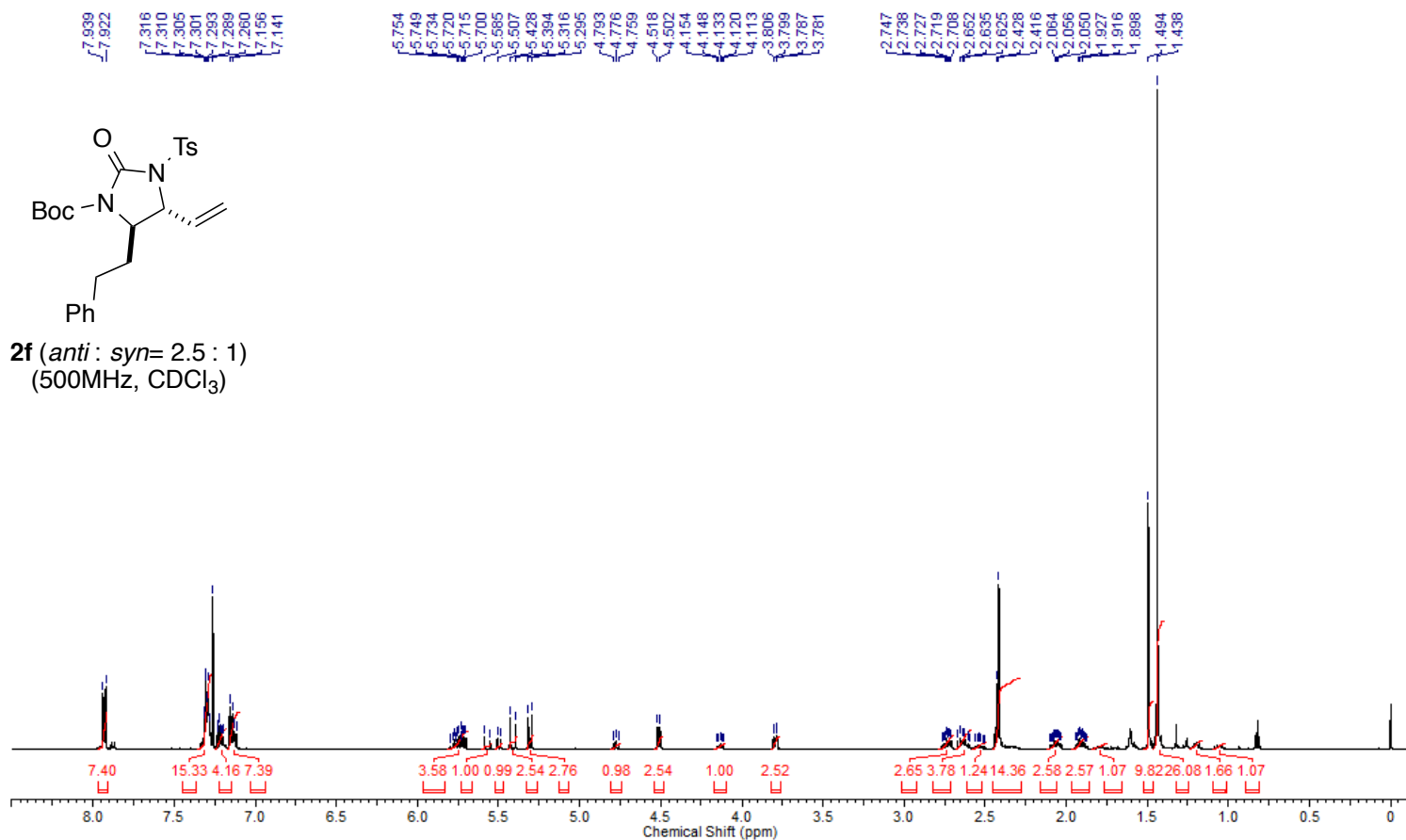


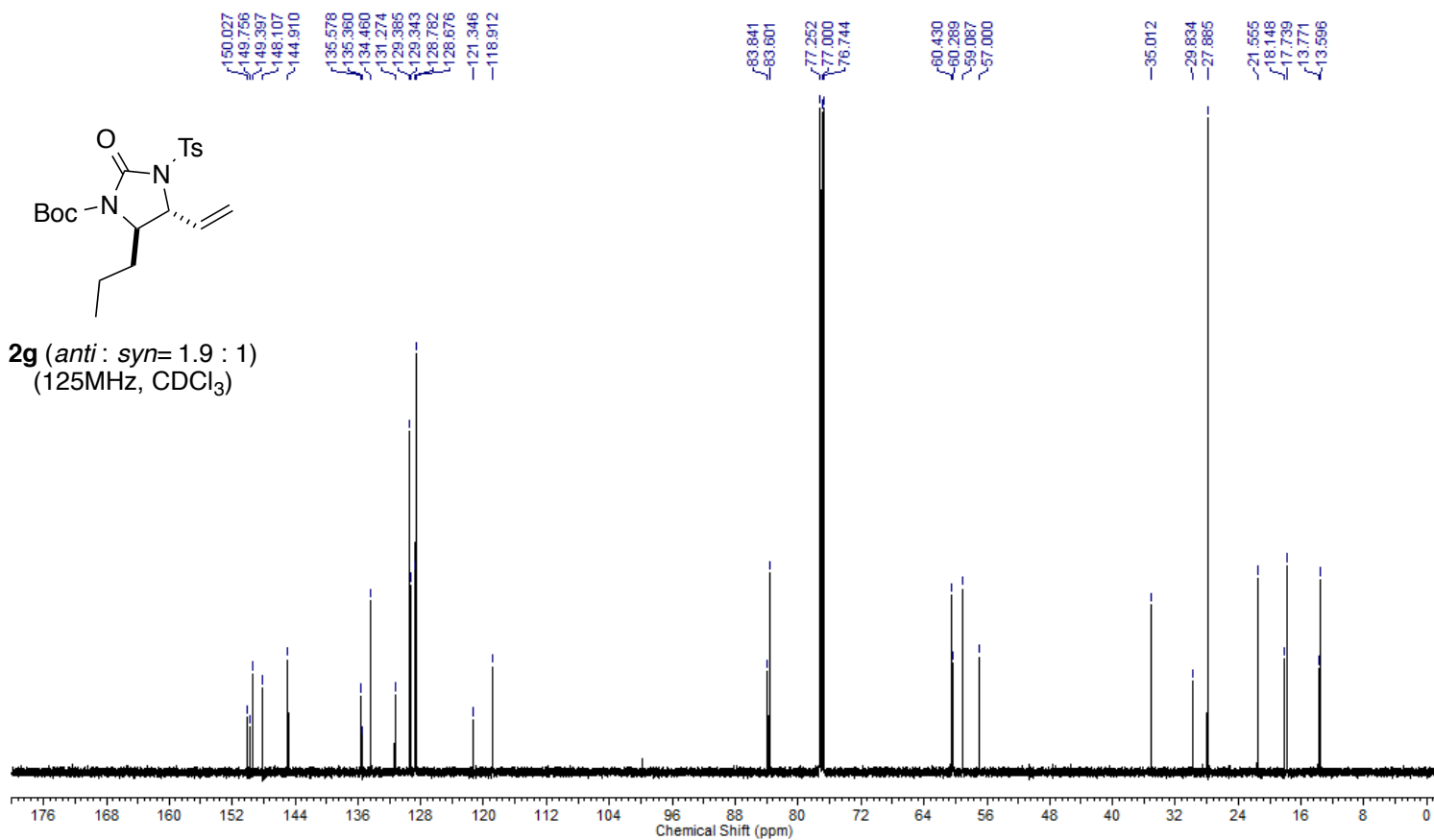
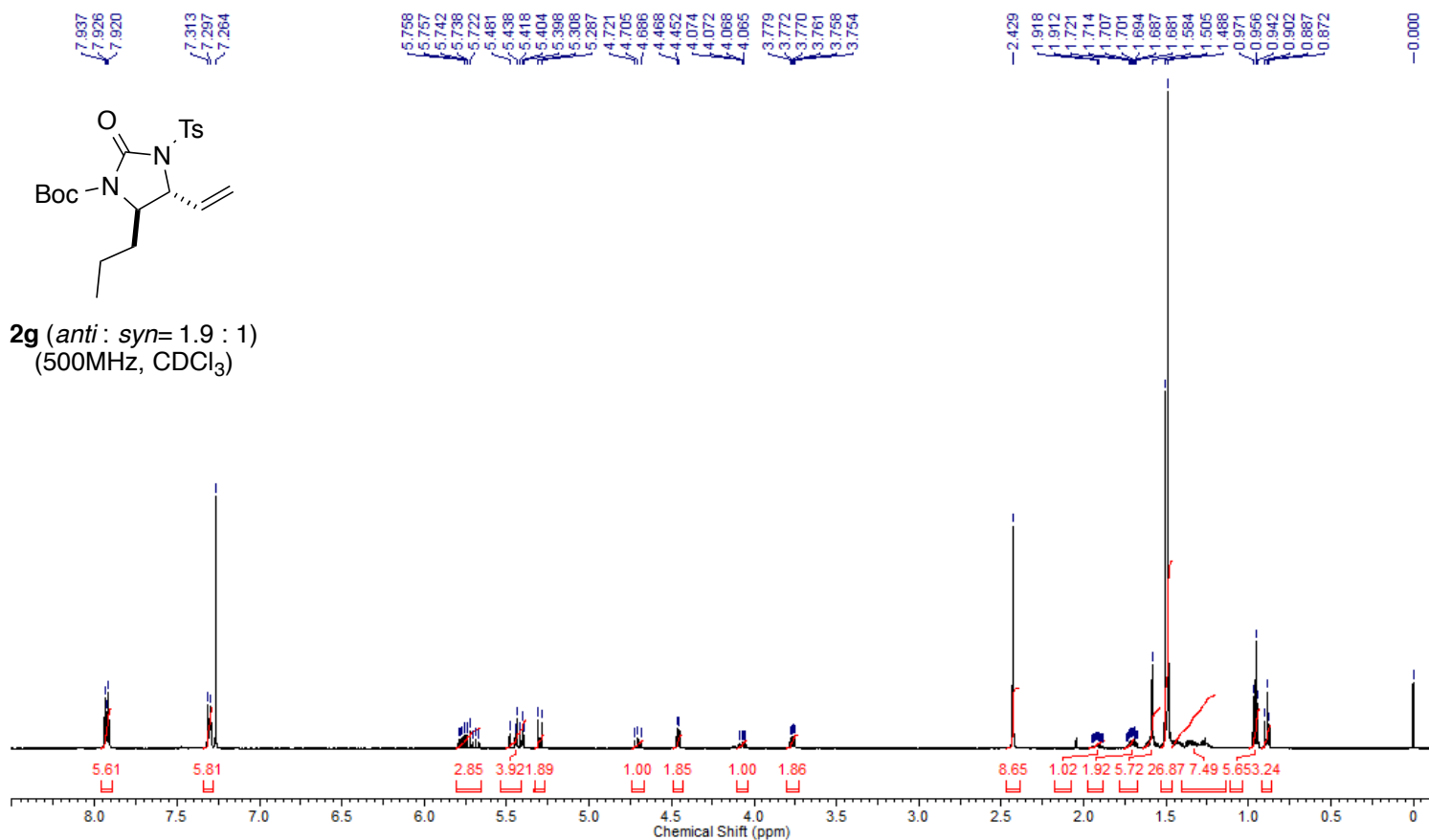


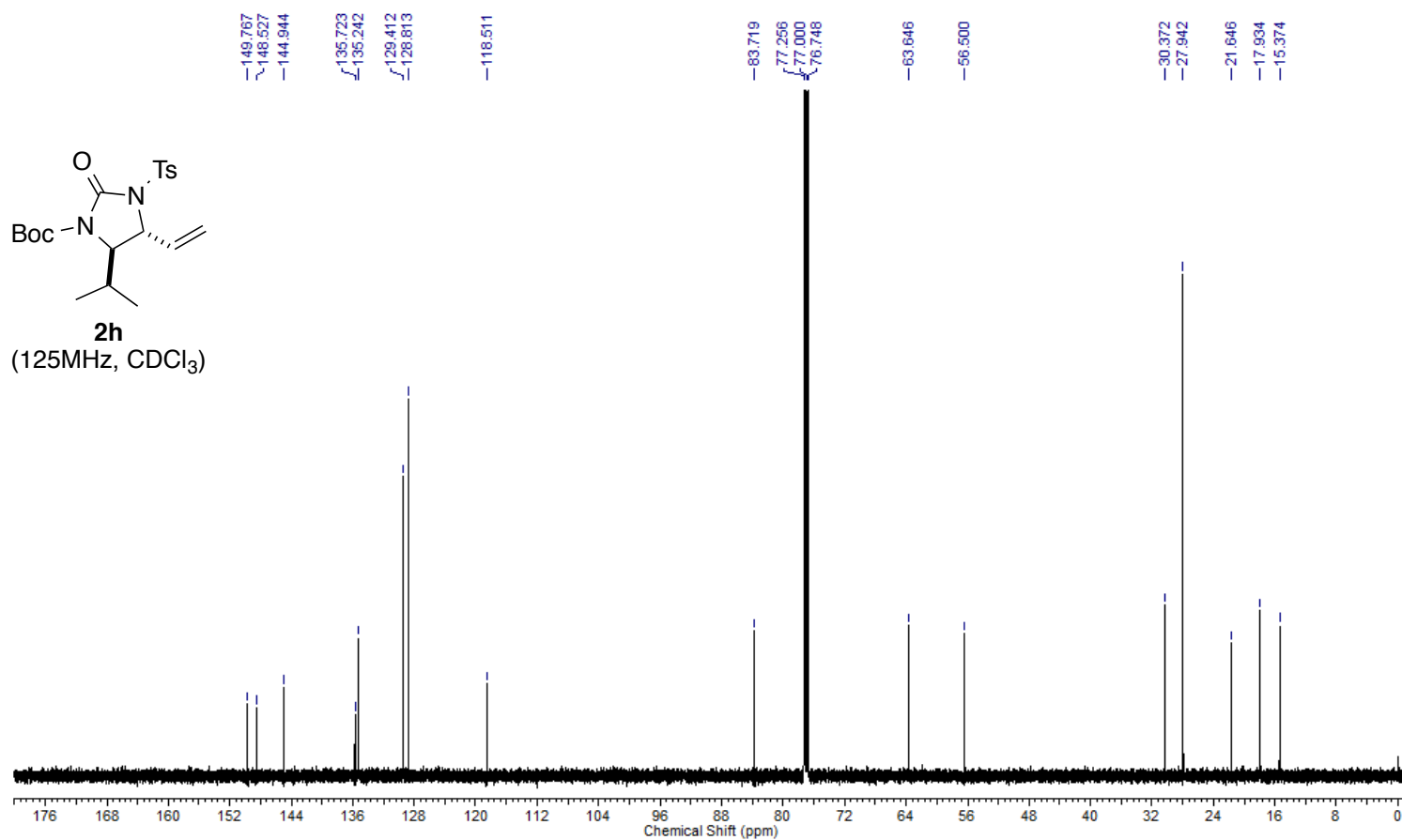
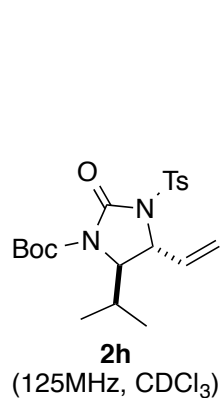
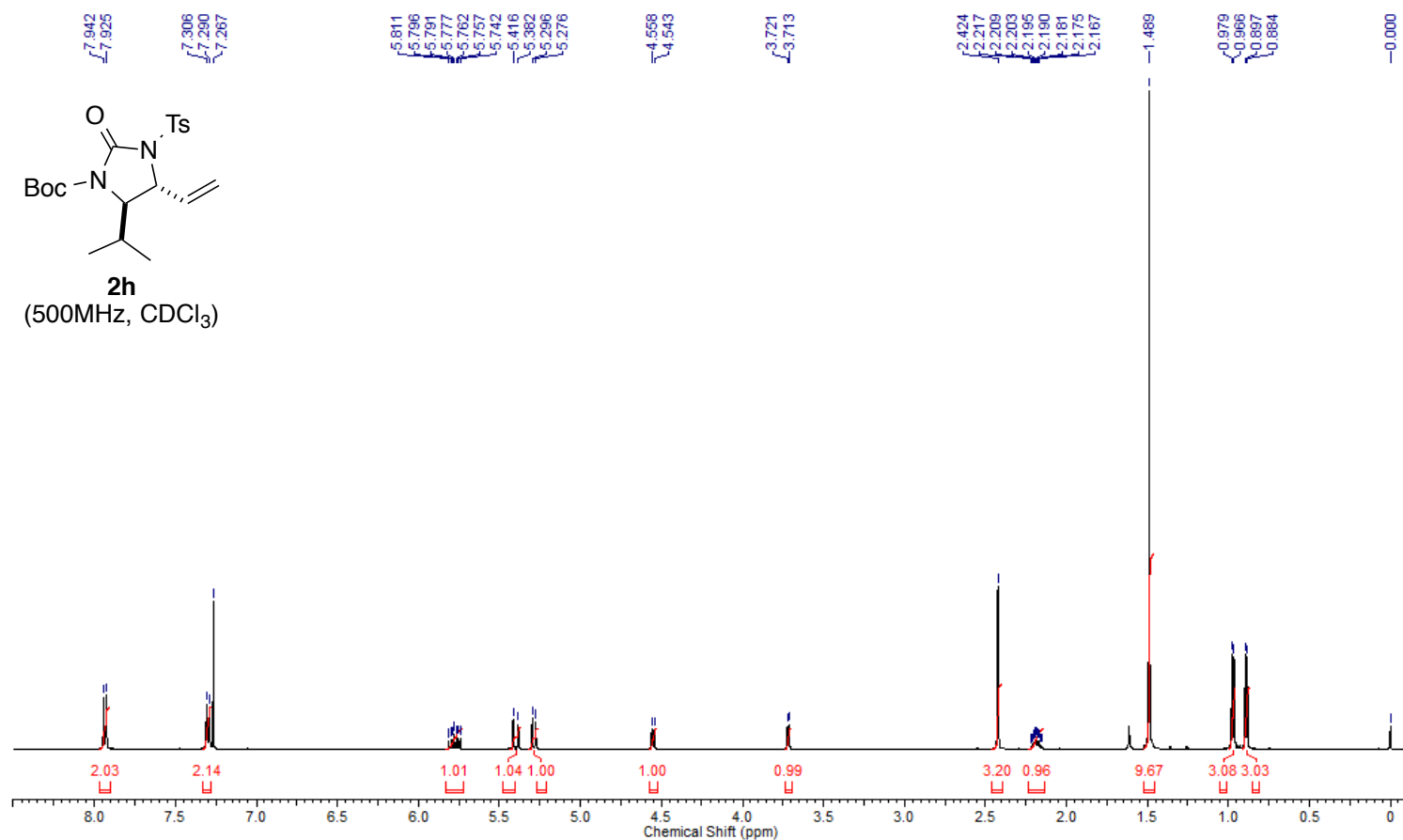
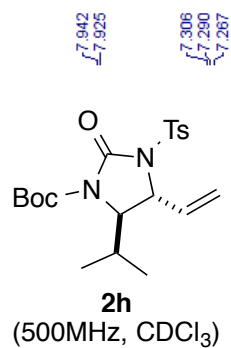
8. Copies of  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR spectra (**2b**, **2e-l**)

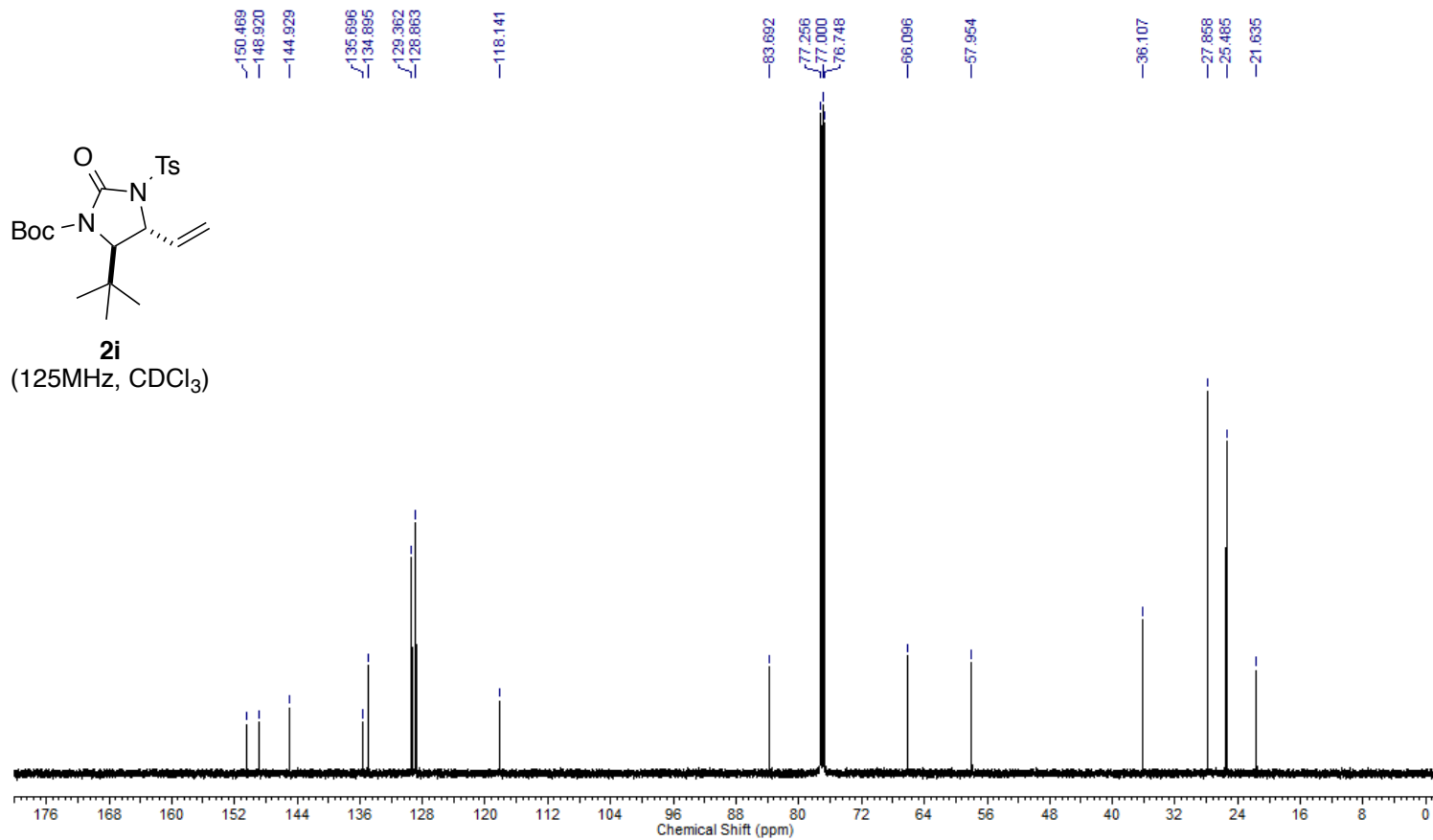
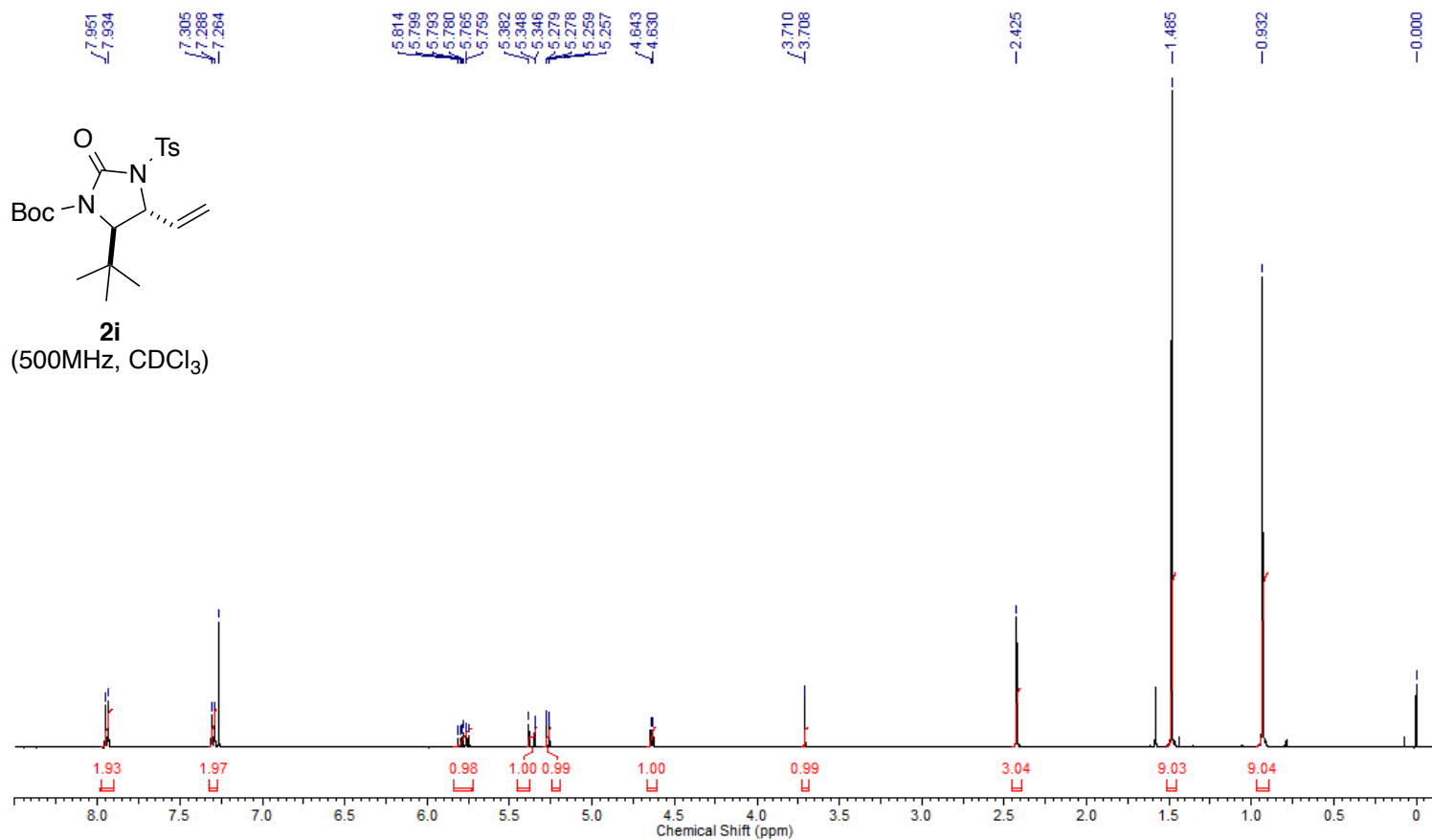




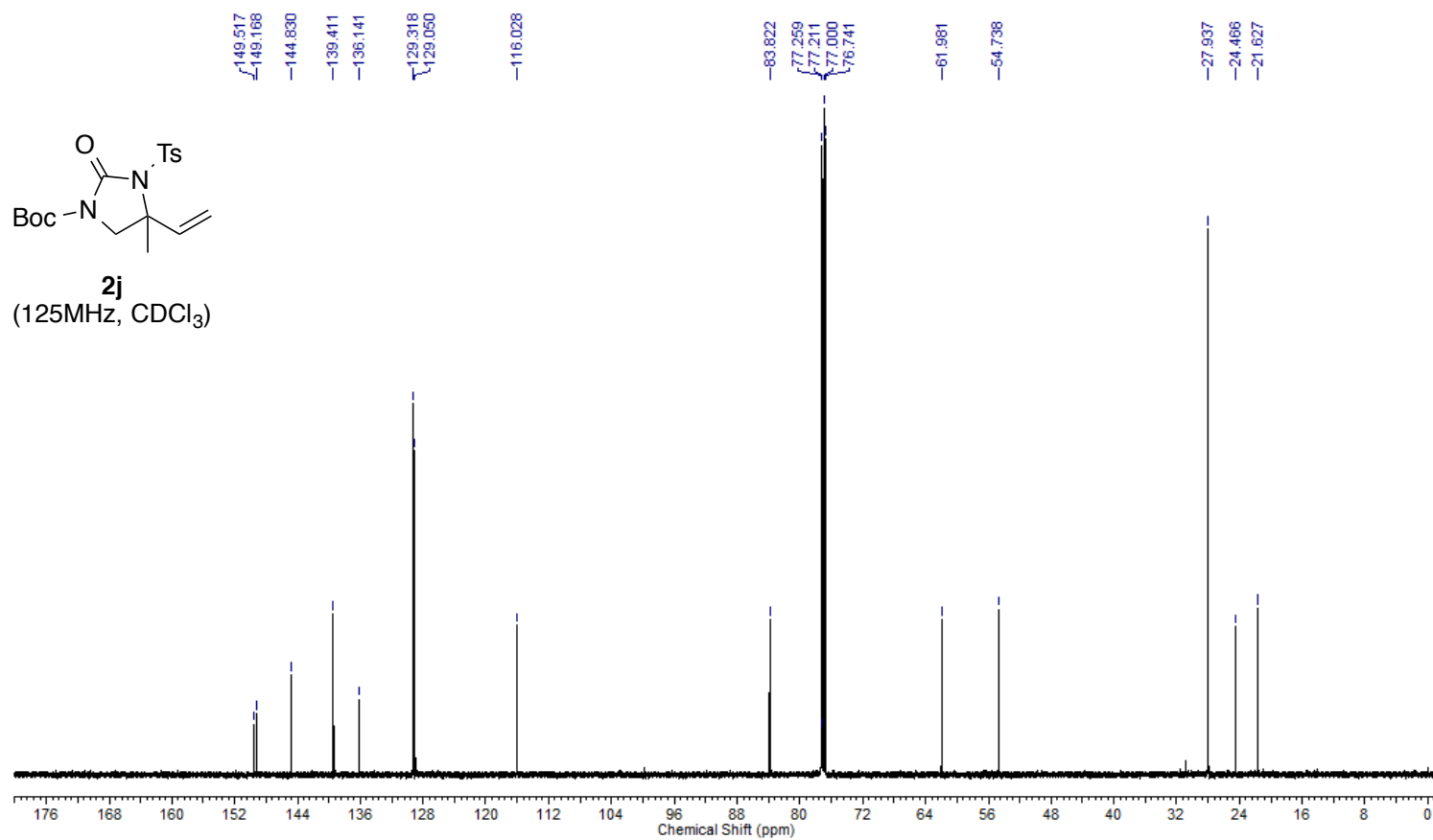
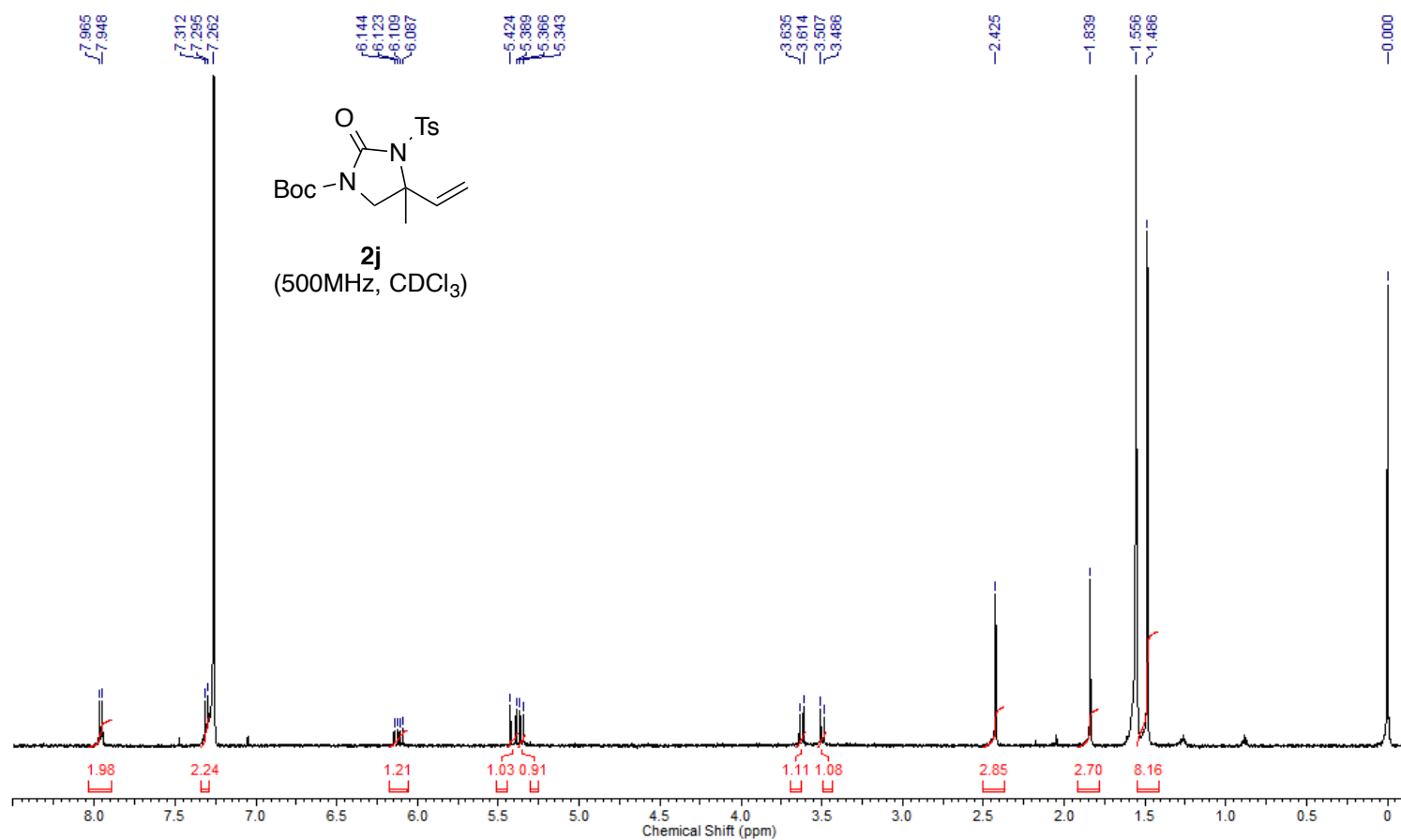


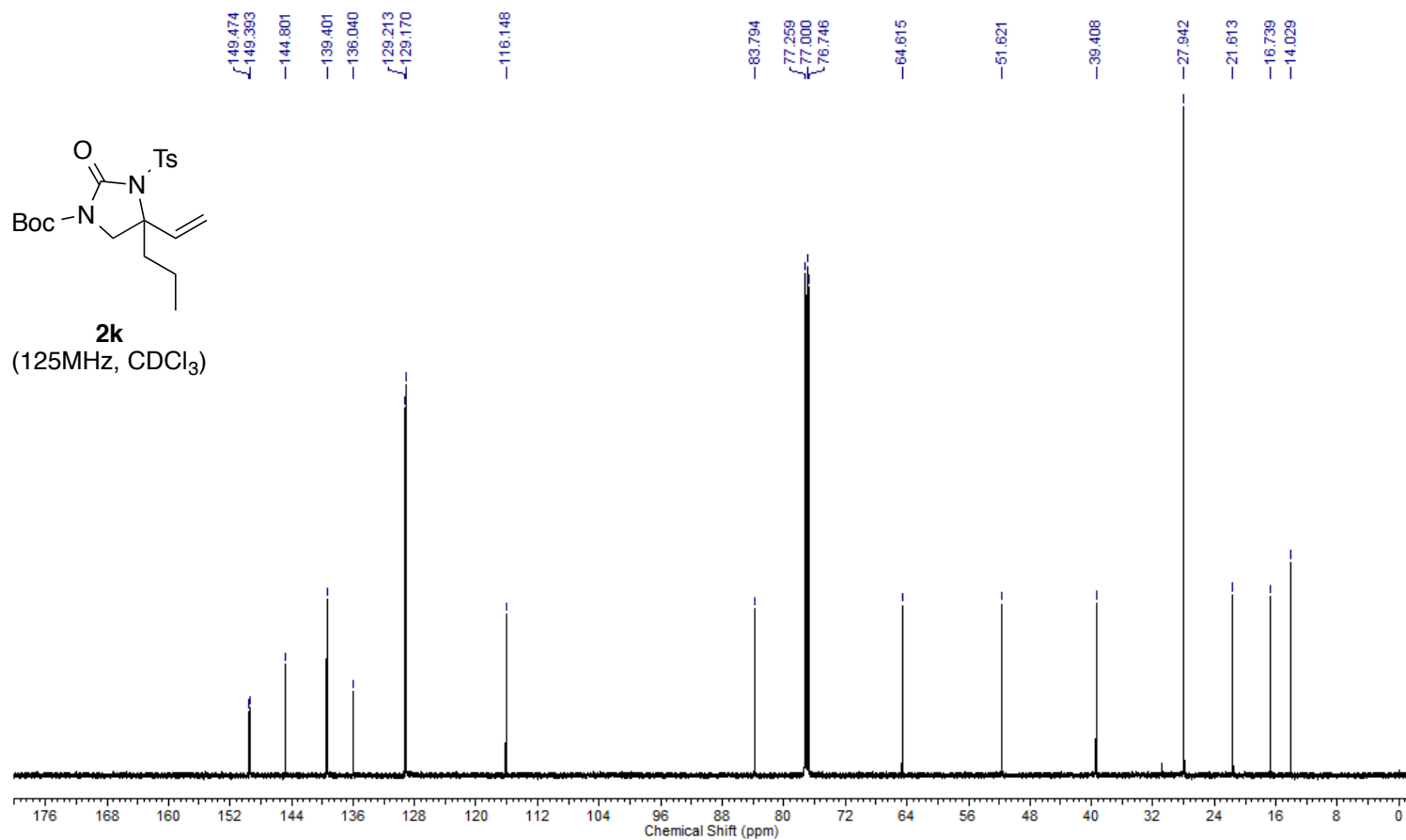
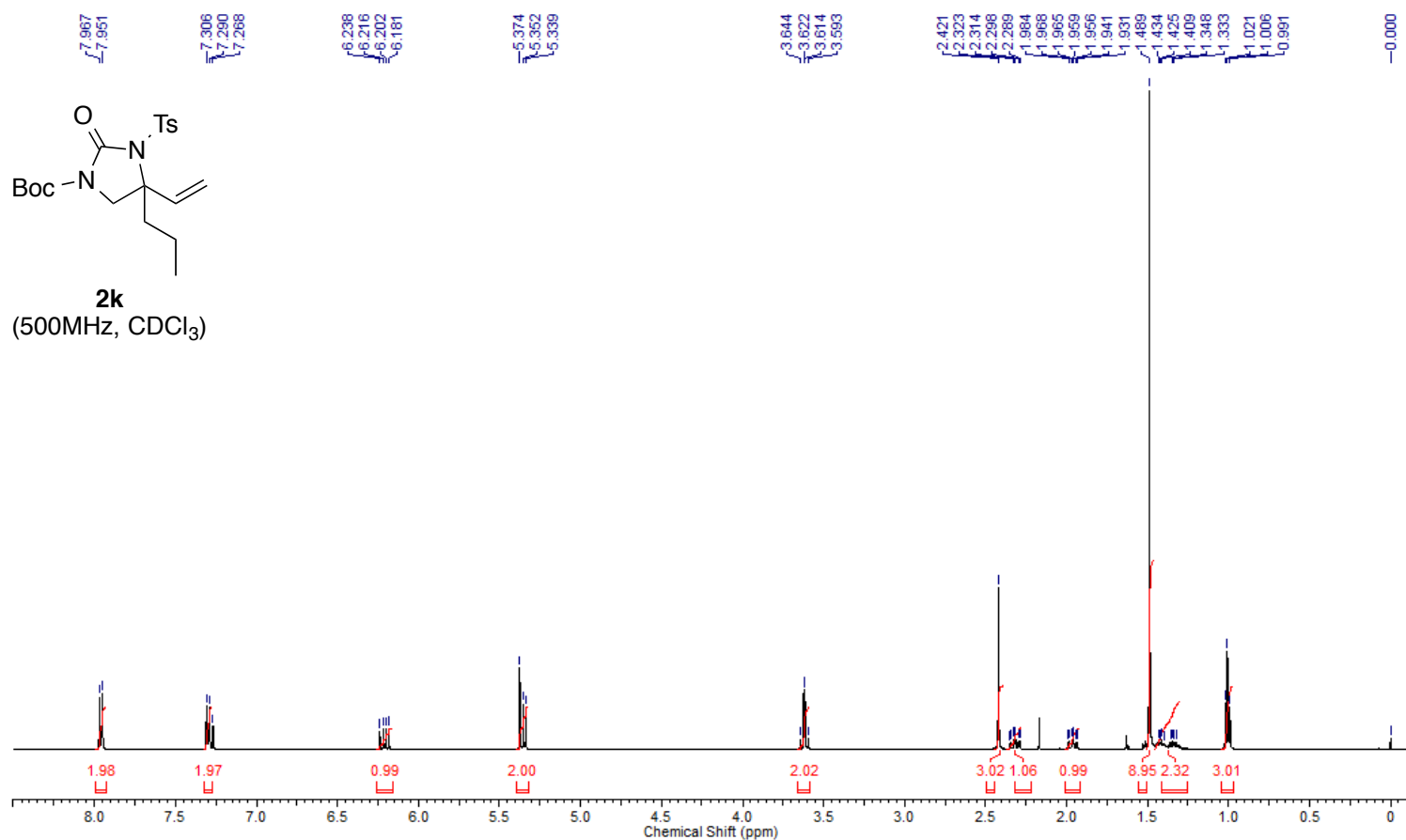


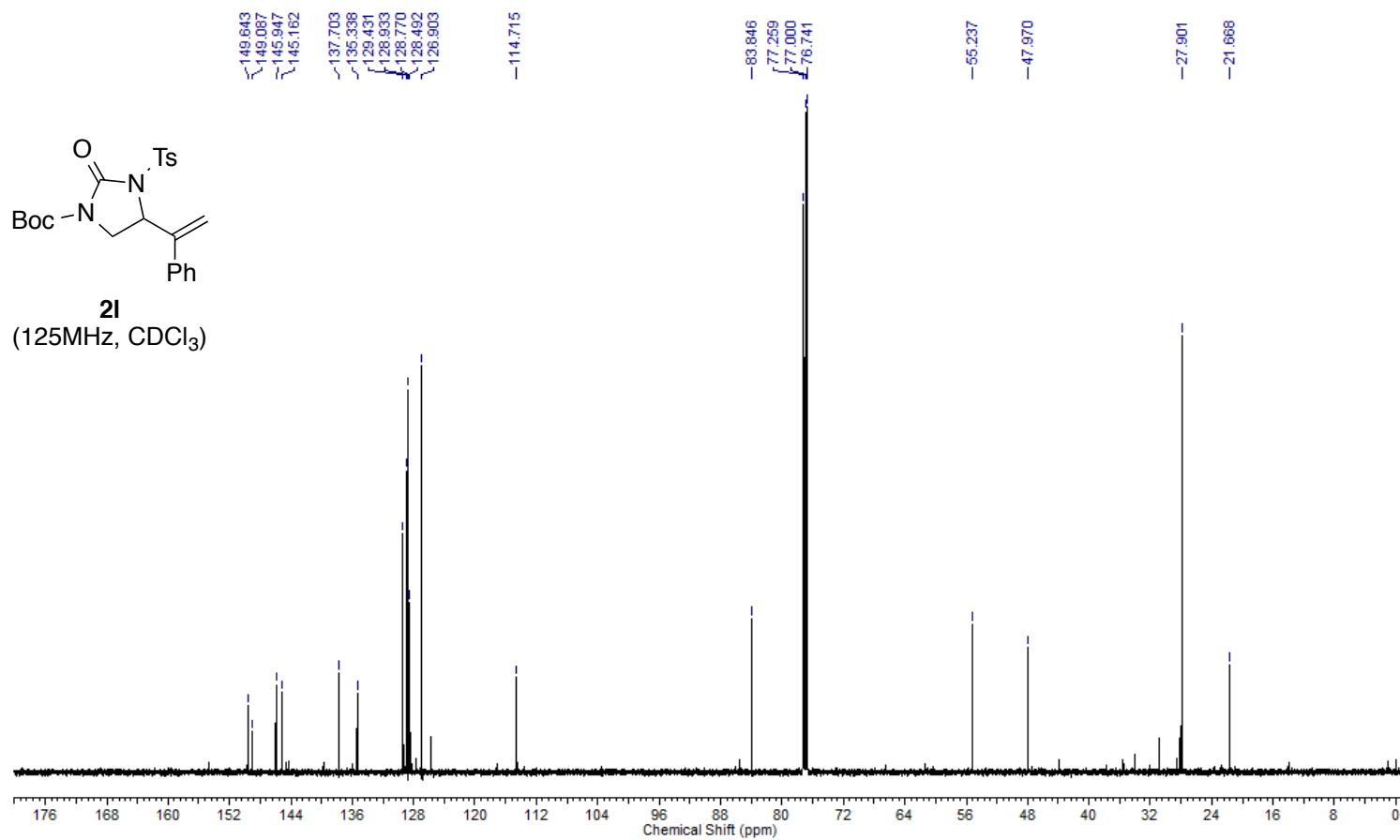
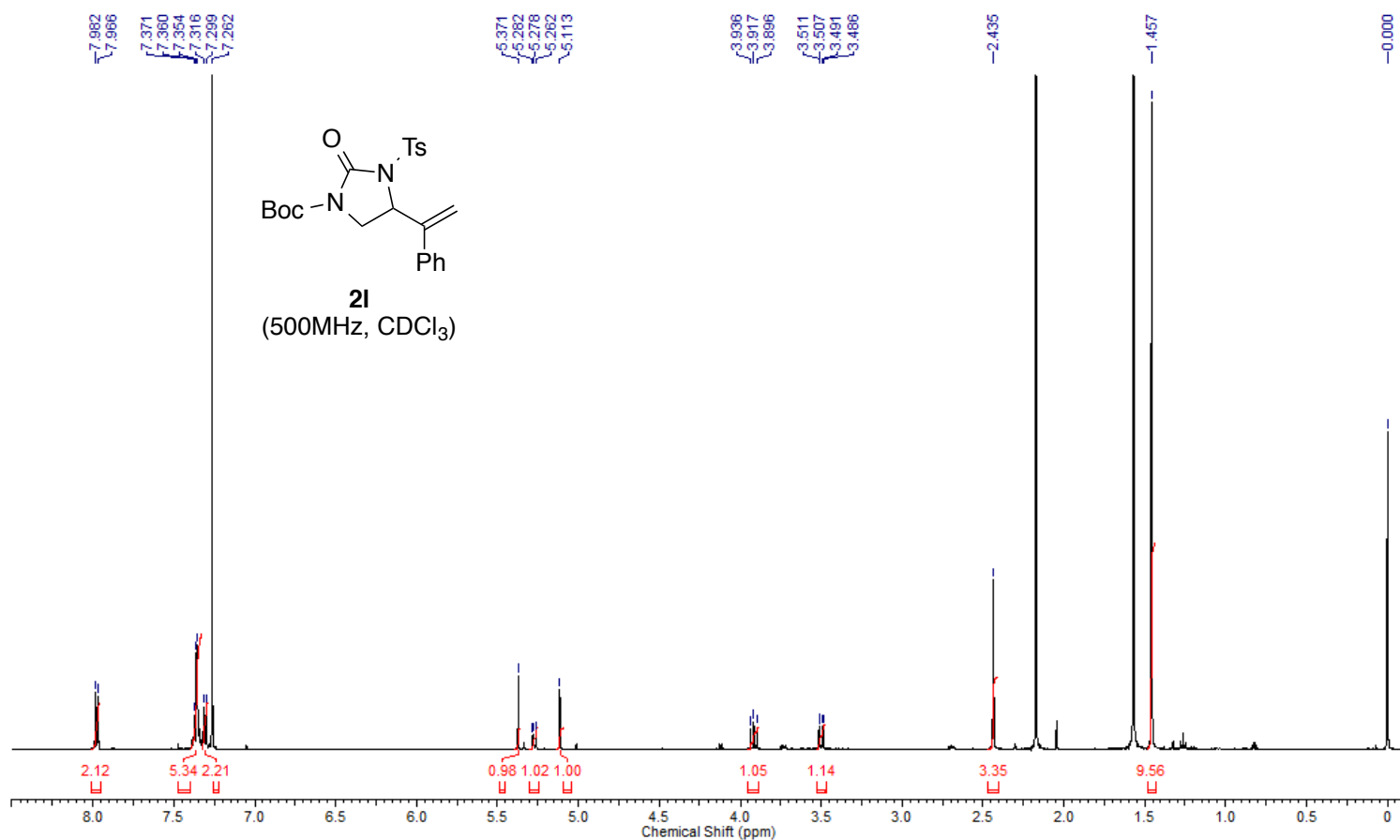




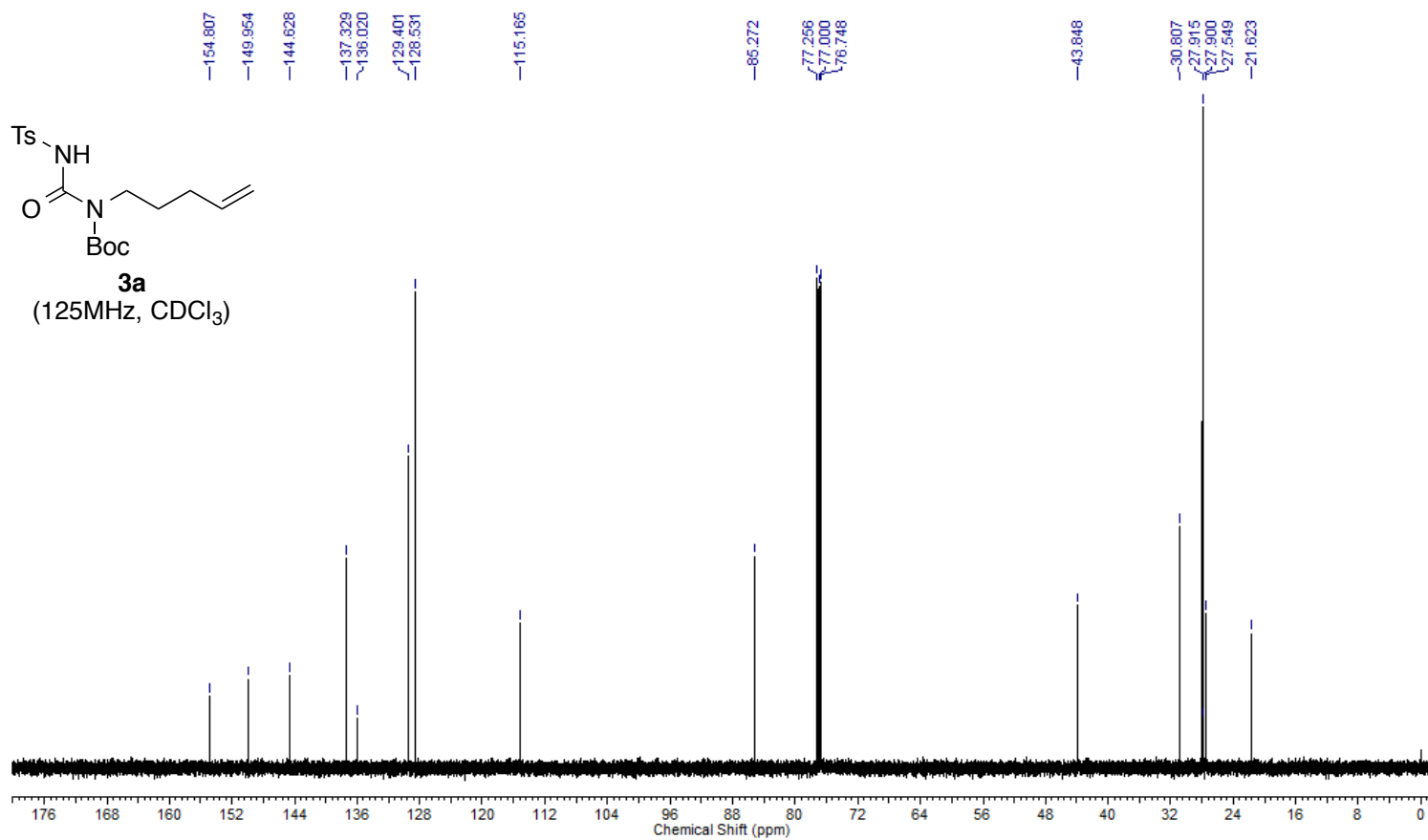
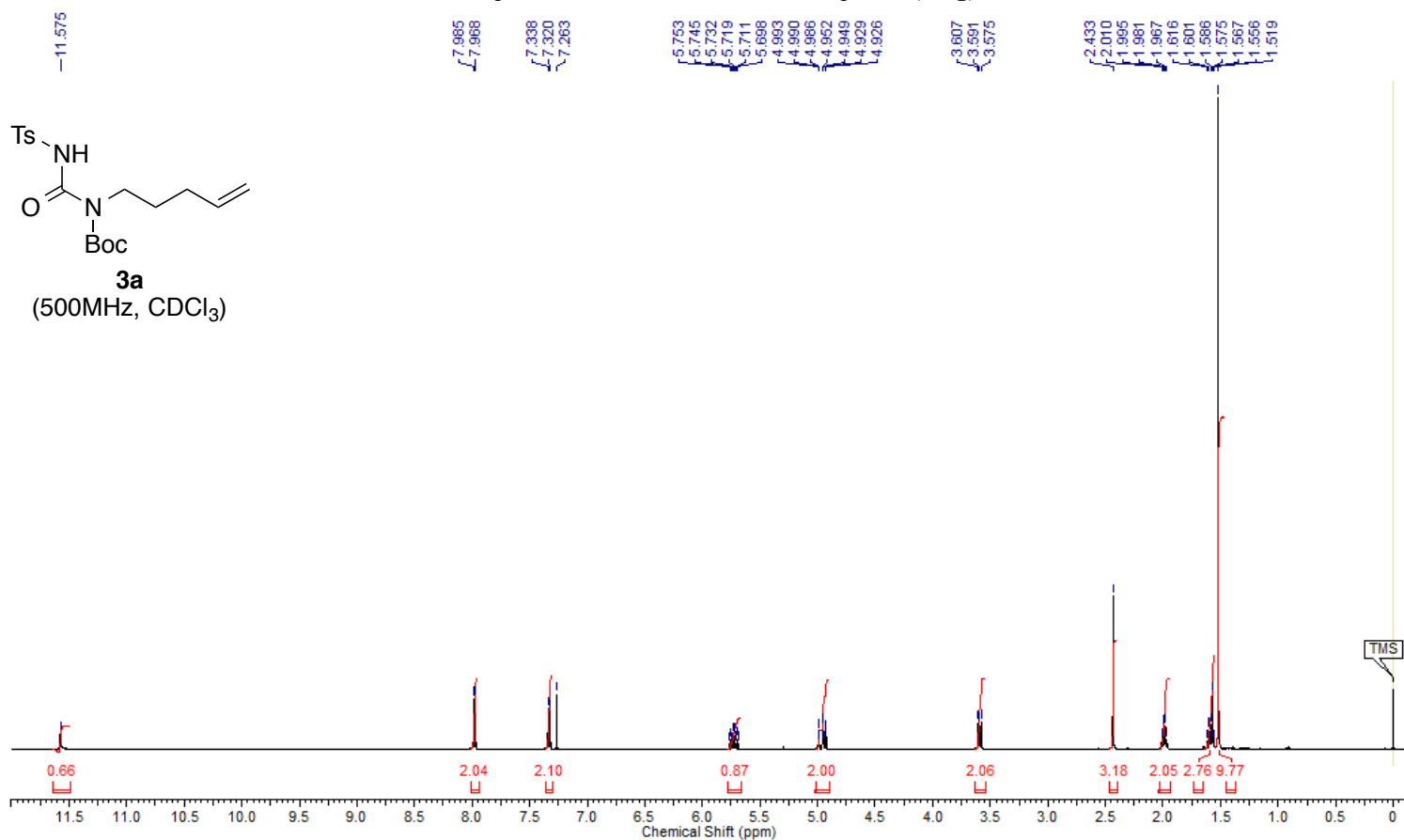


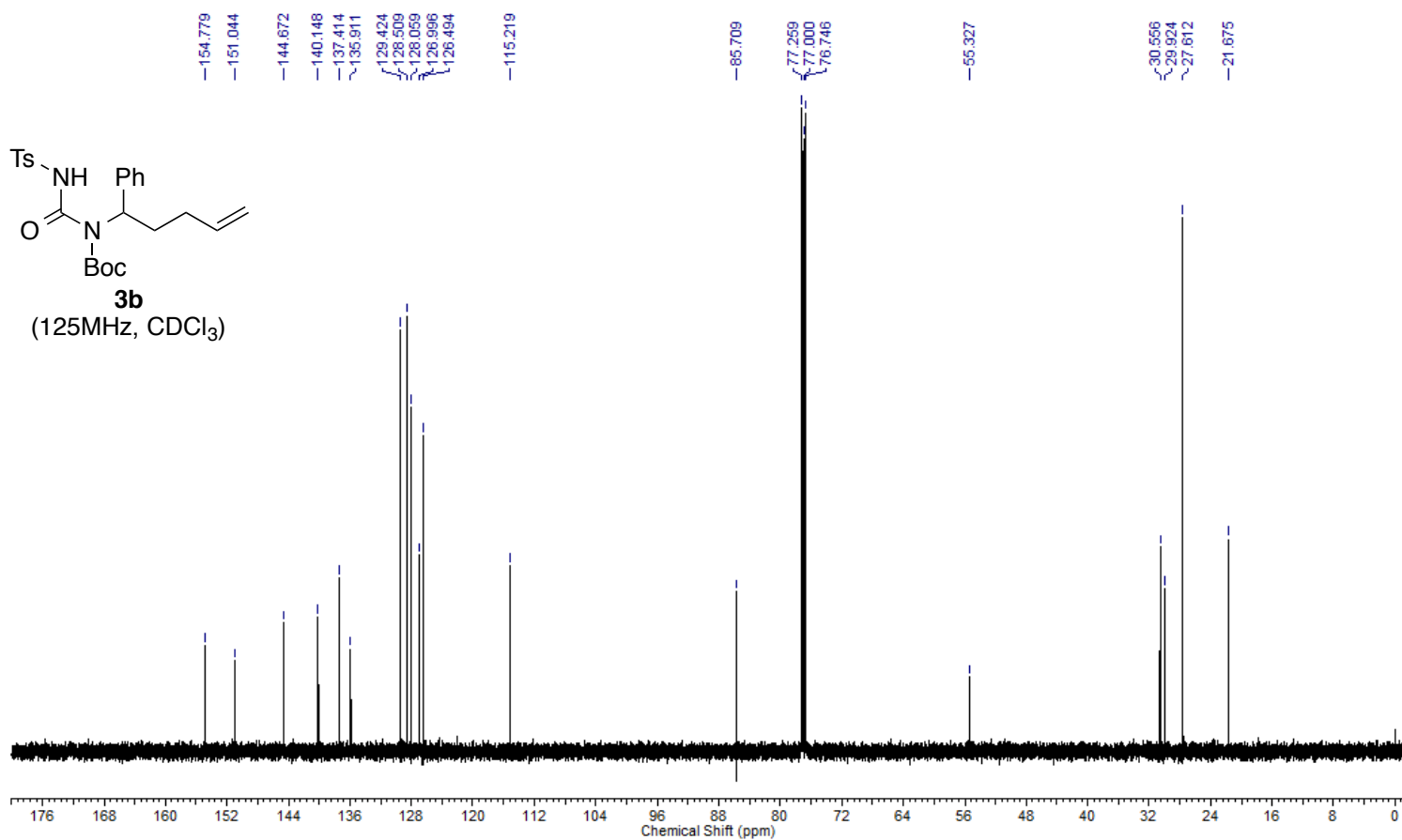
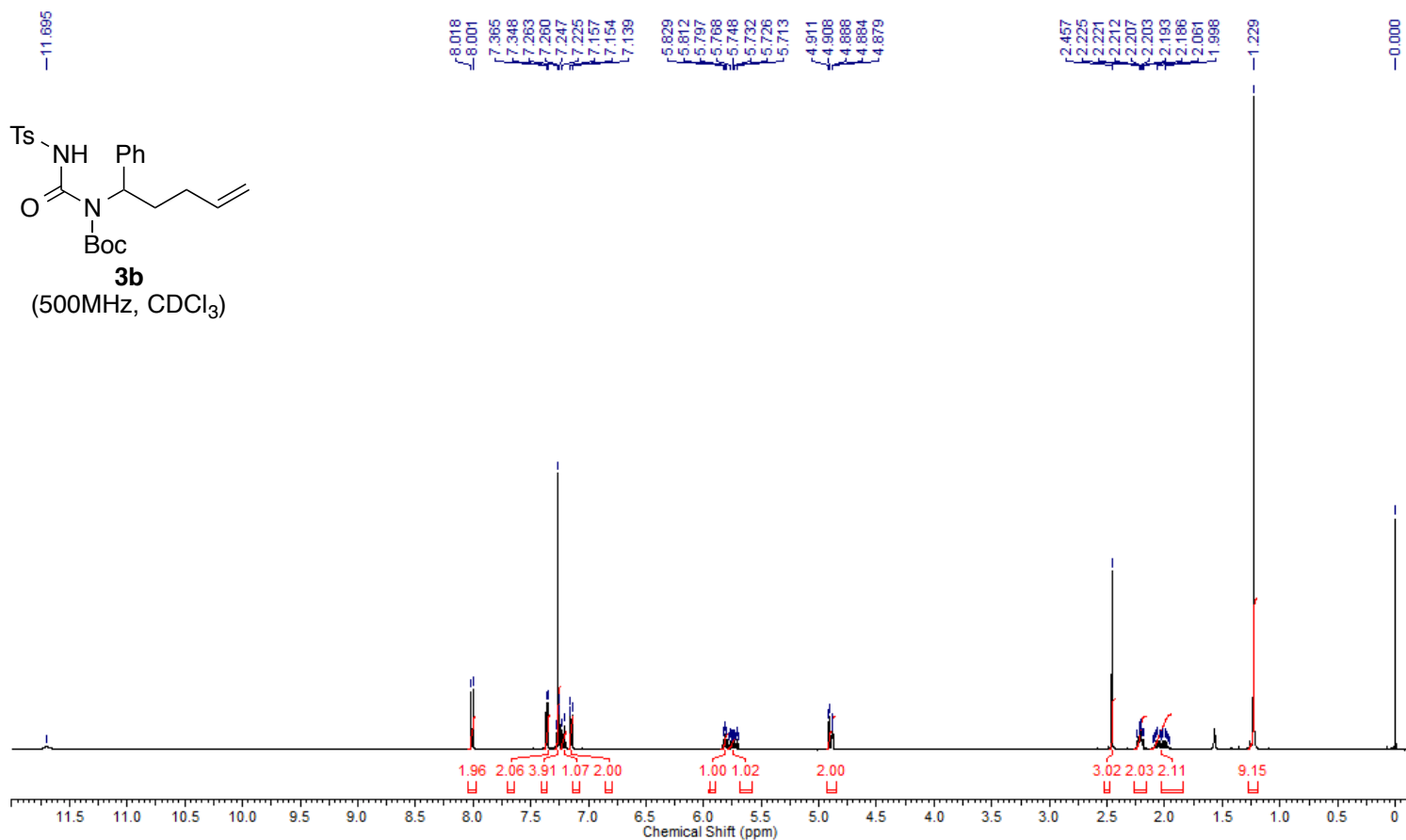


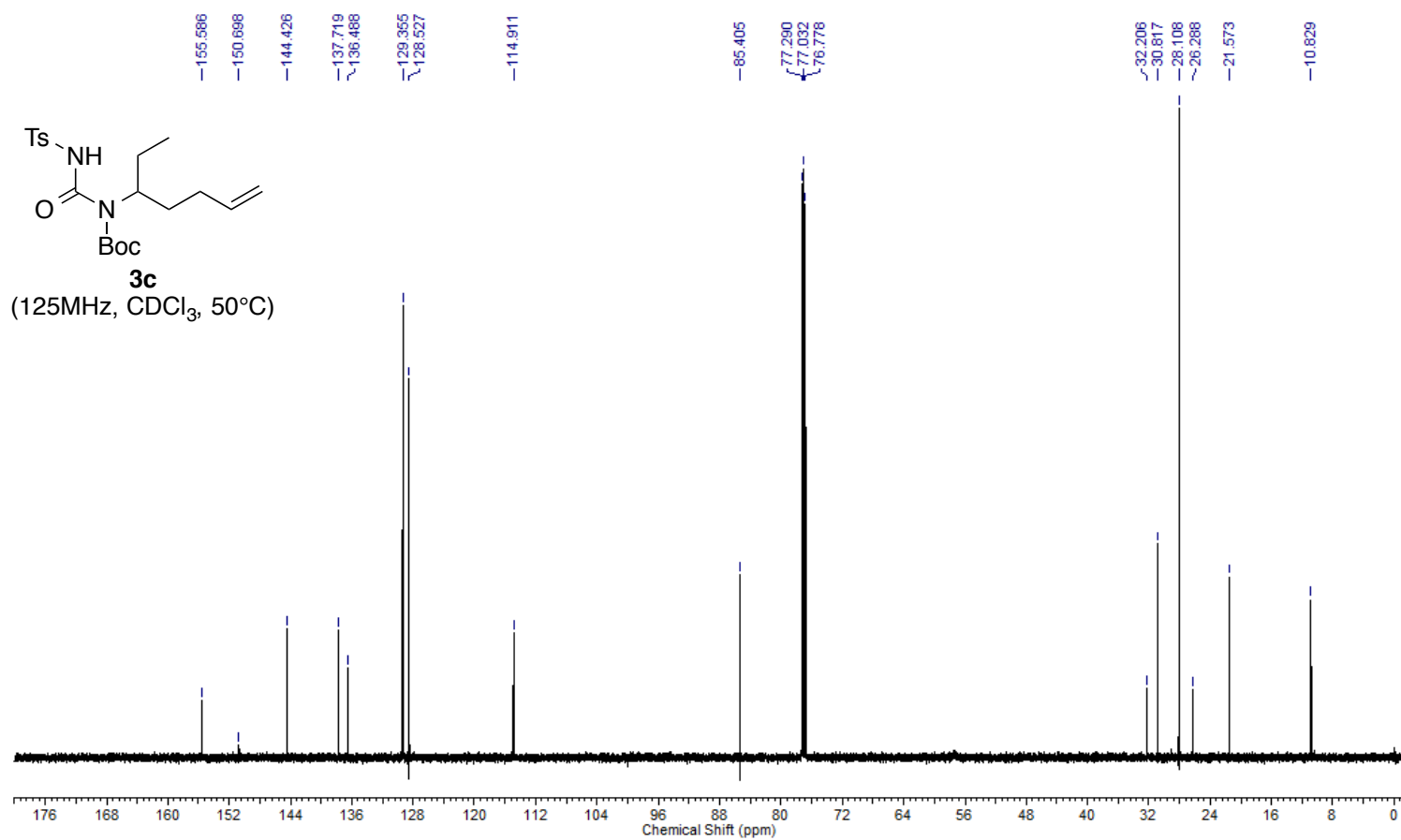
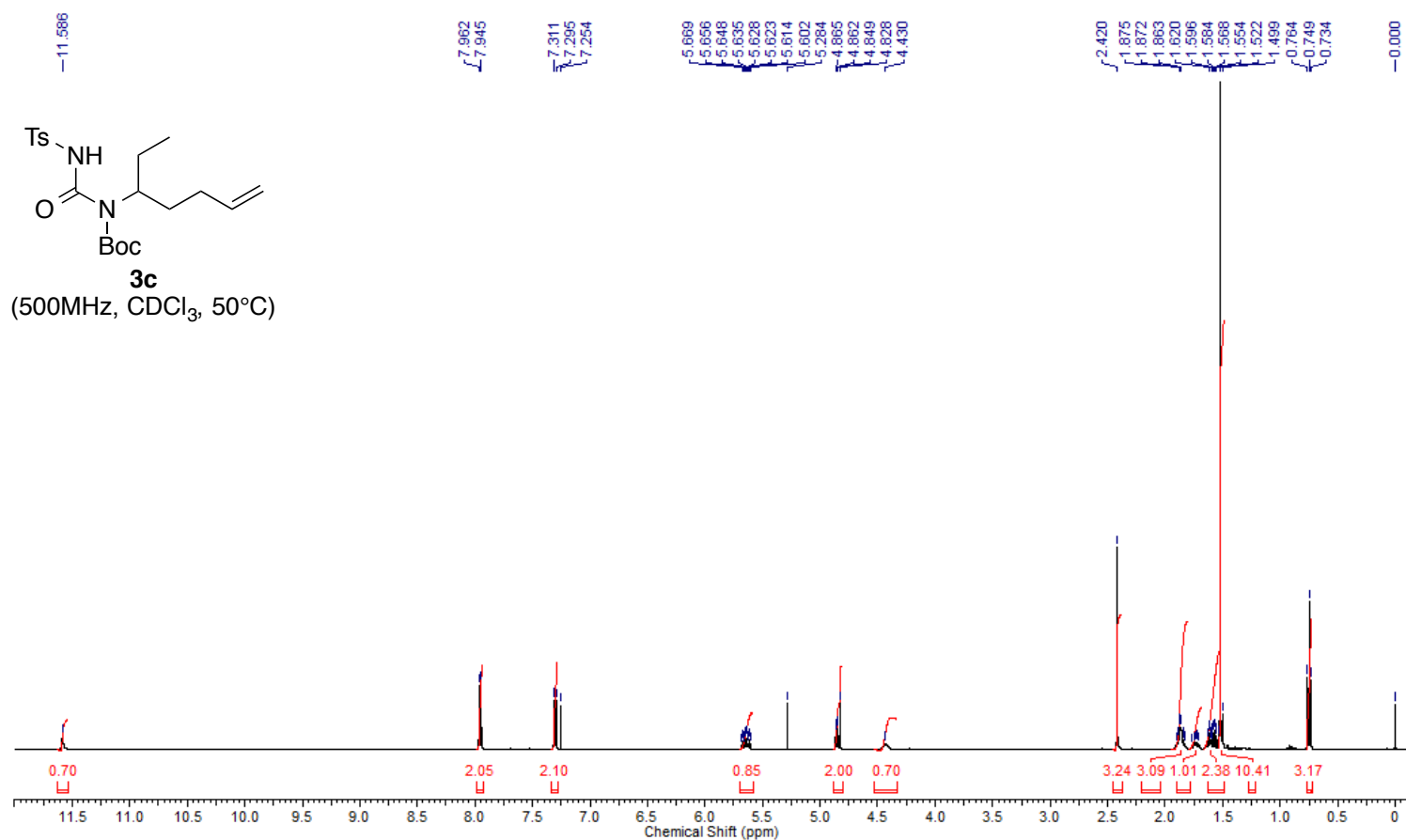


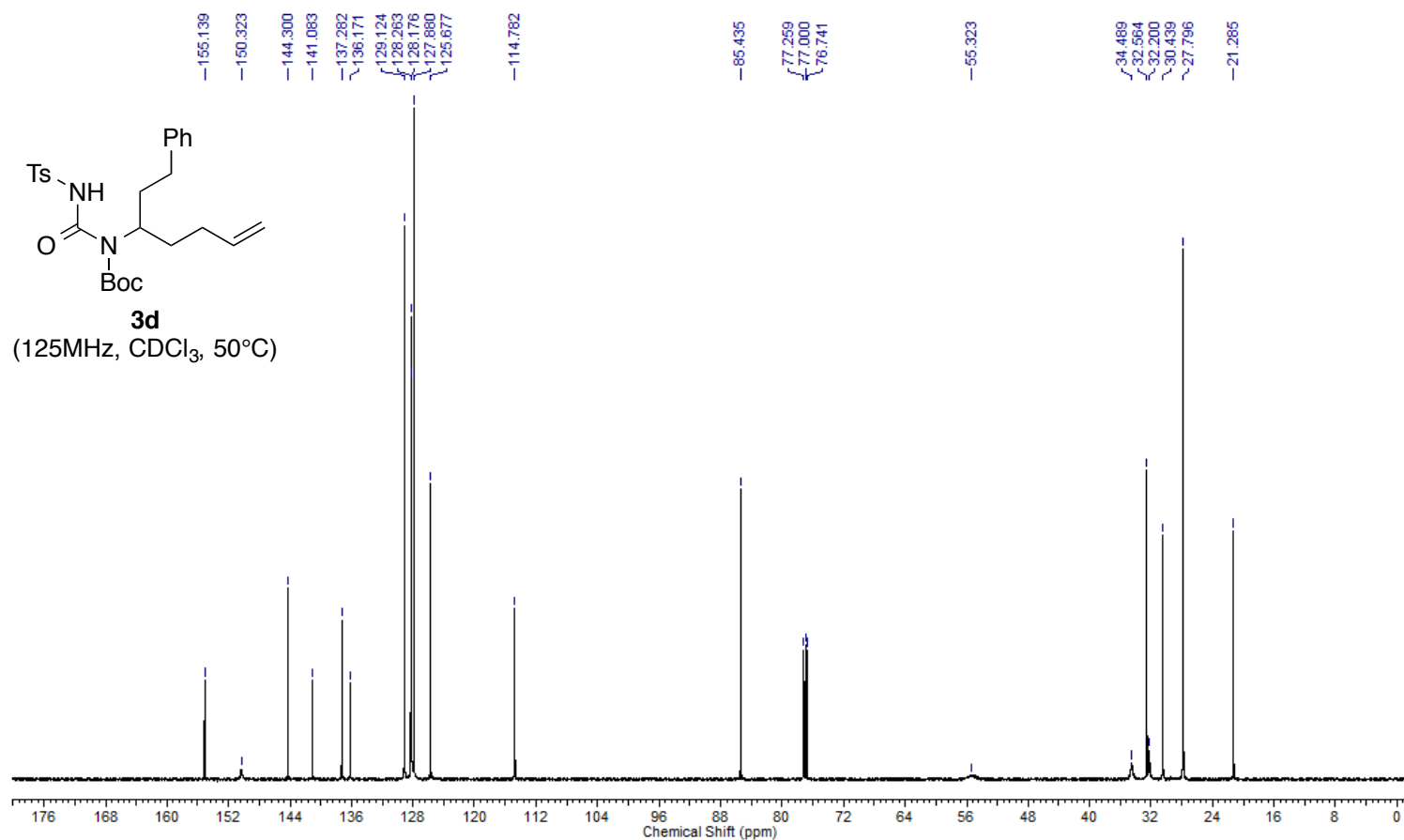
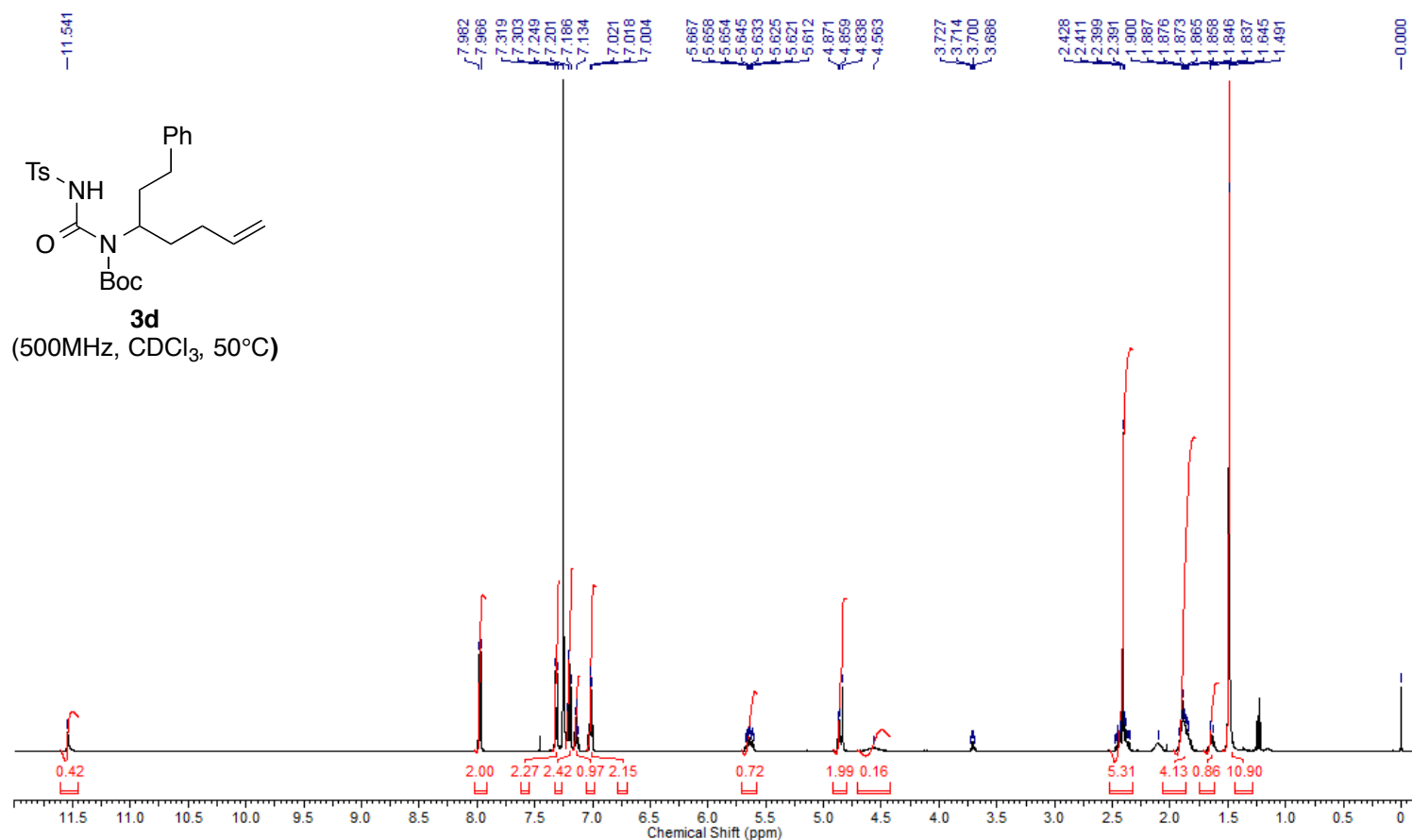


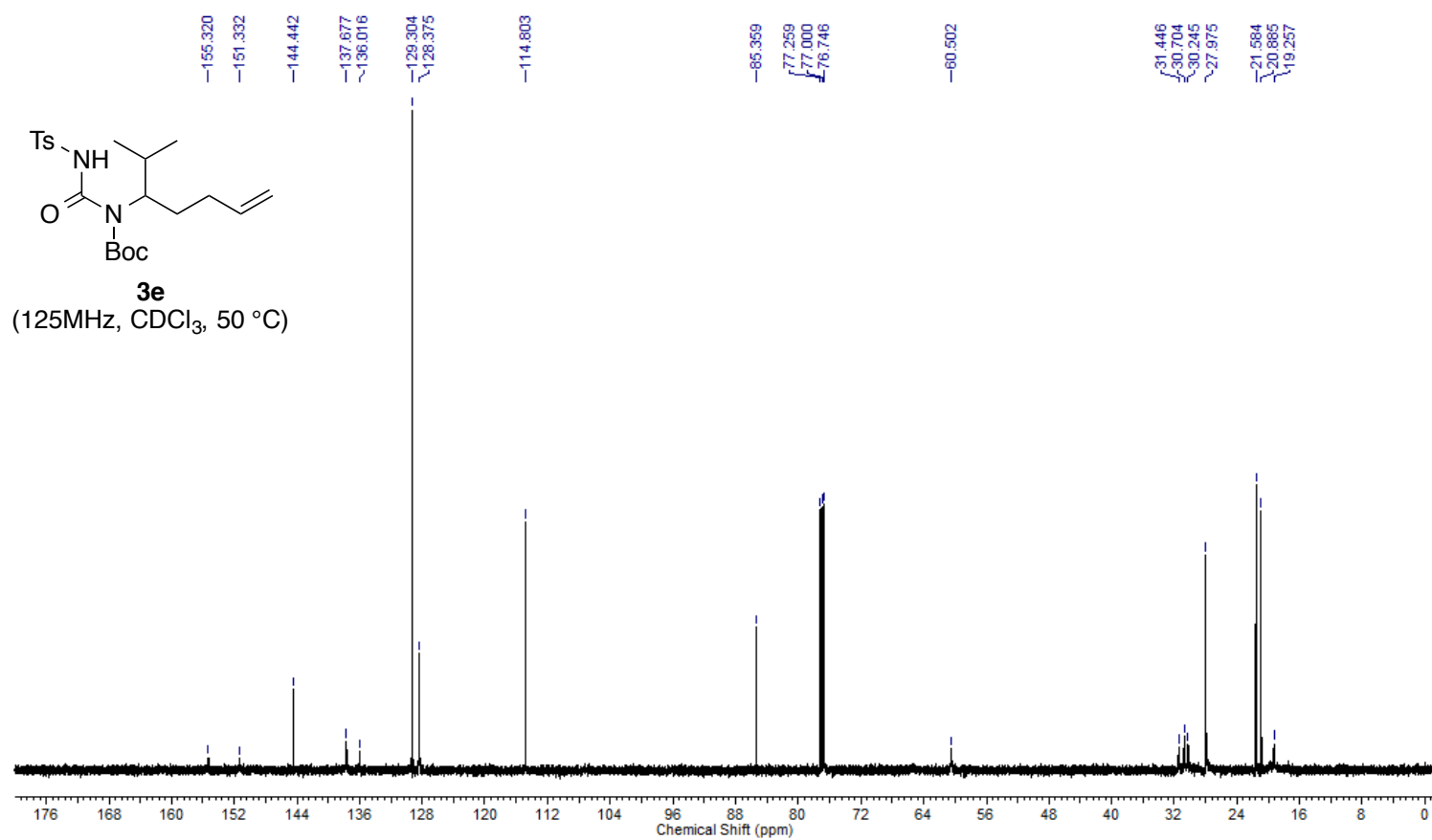
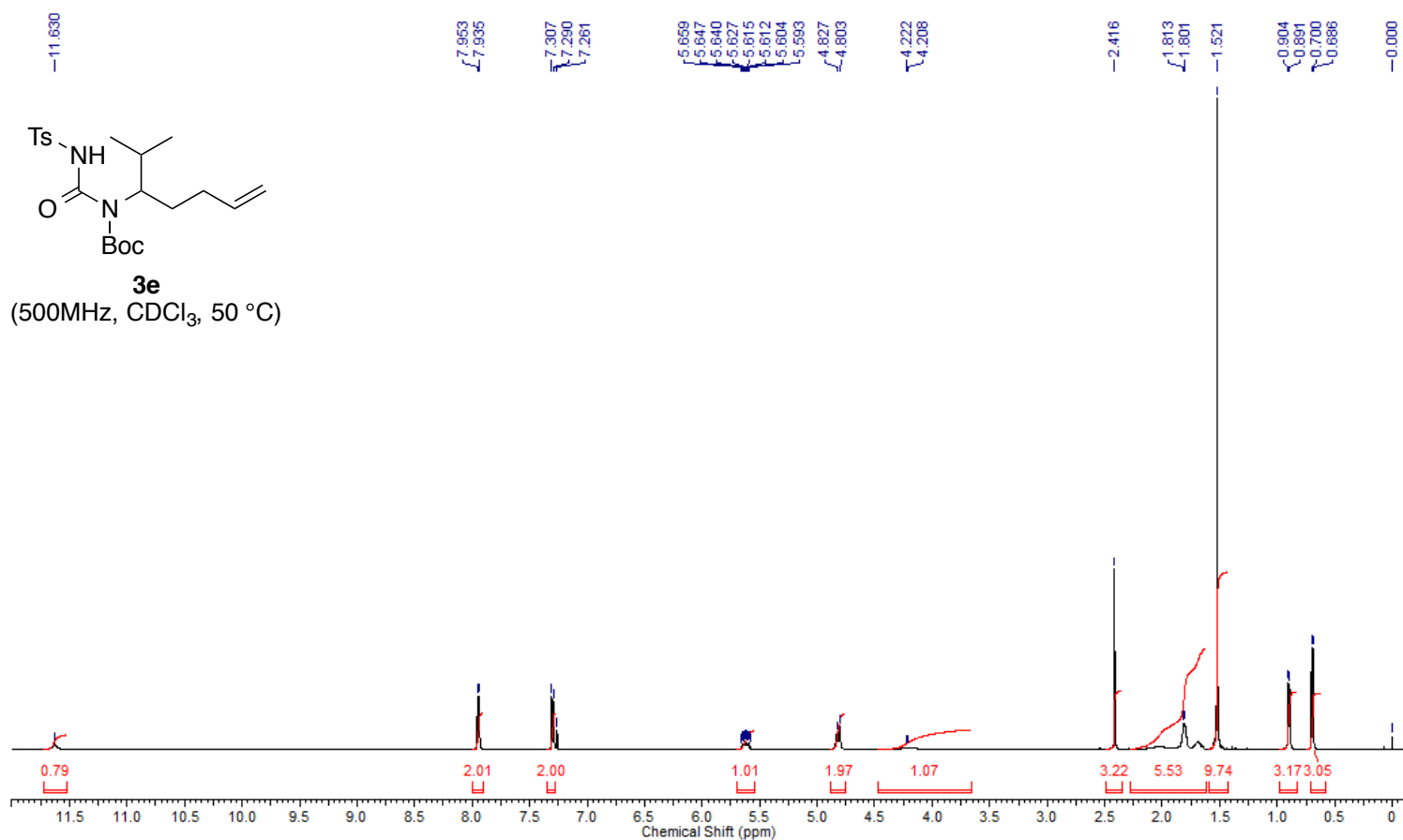
9. Copies of  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR spectra (**3a-g**)



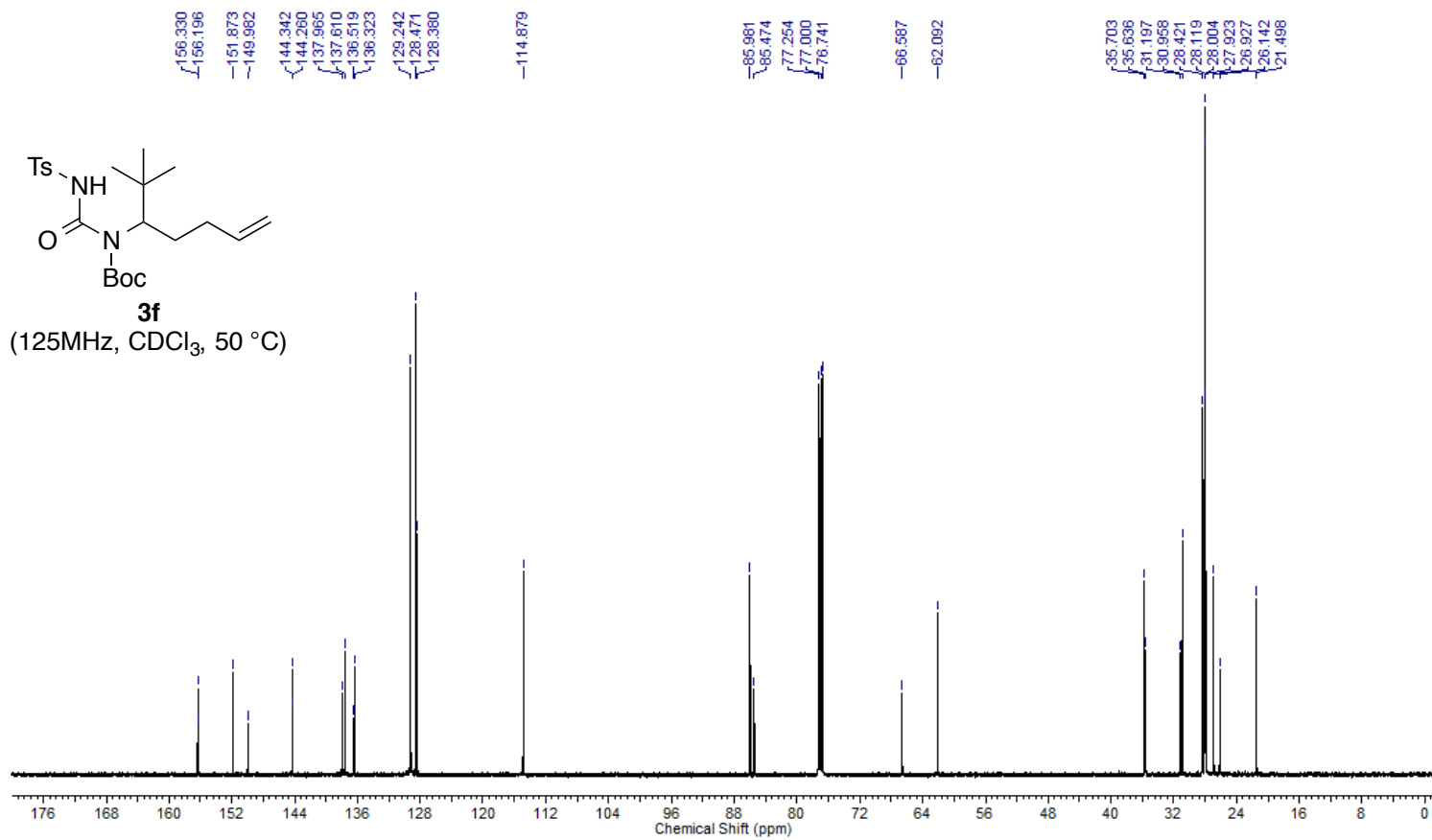
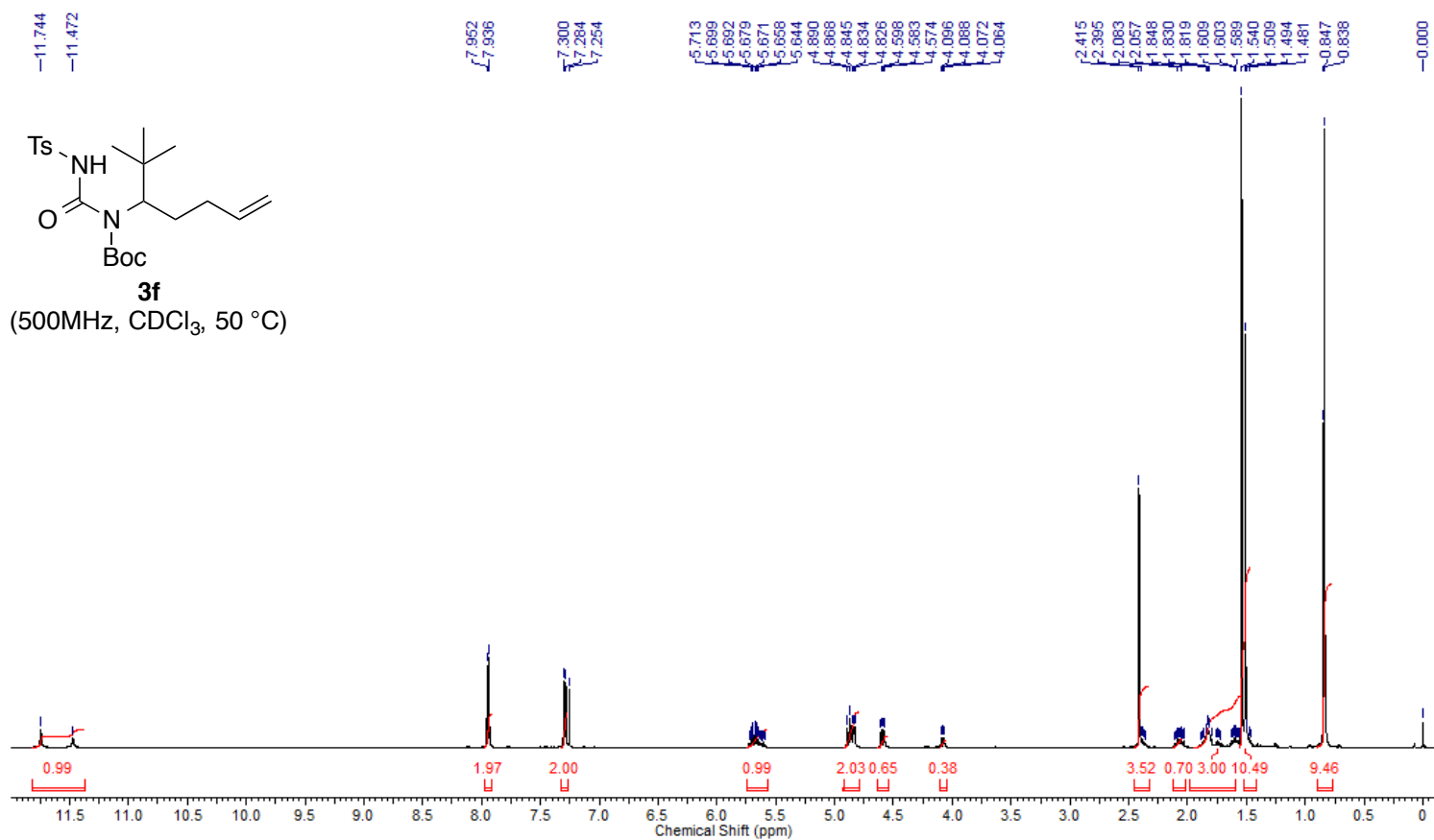


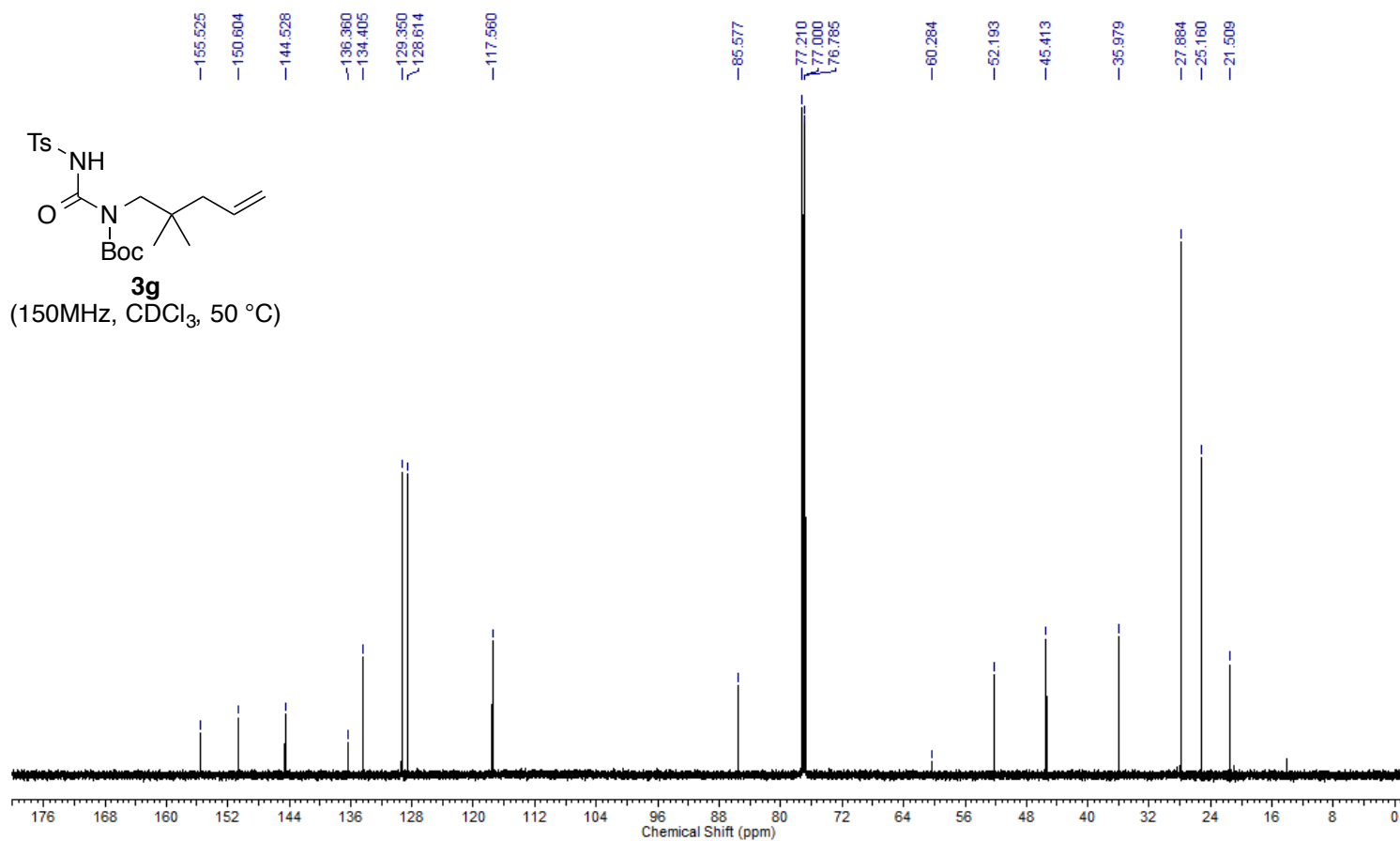
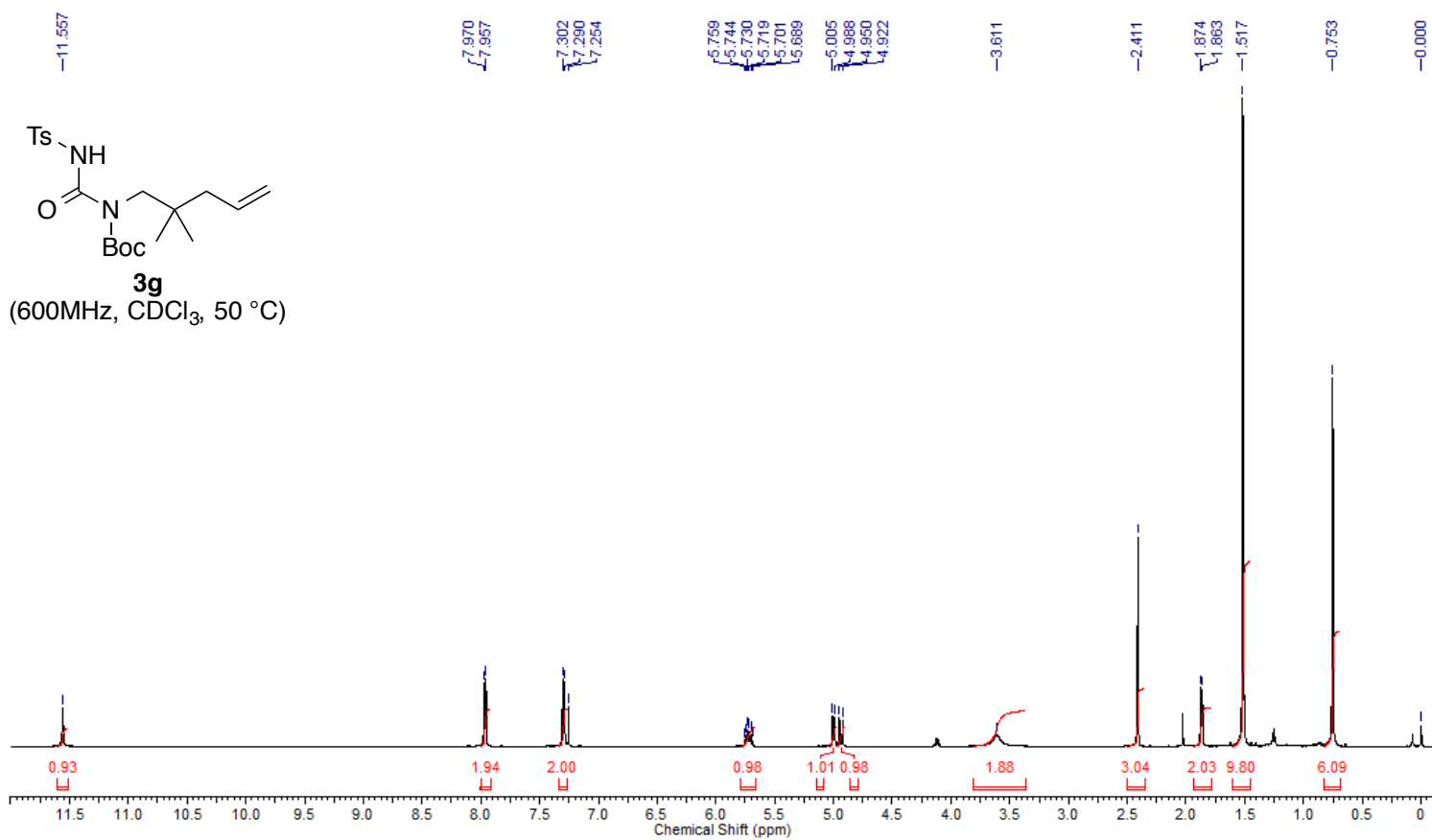












10. Copies of  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR spectra (4a-g)

