

# **Stereoselective Modification of *N*-( $\alpha$ -Hydroxyacyl)-glycin- esters via Palladium Catalyzed Allylic Alkylation**

## **Supporting Information**

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## 1. General Information

All air- or moisture-sensitive reactions were carried out in dried glassware (>100 °C) under an atmosphere of nitrogen. THF was dried over sodium/benzophenone and was distilled before use. Dry DCM, diethylether, DMF, DMSO, toluene and pyridine were purchased from Acros Organics. The products were purified by flash chromatography on silica gel columns (Macherey-Nagel 60, 0.04-0.063 mm) and with a Reveleris® flash chromatography system from Grace with RediSep®-columns from Teledyne Isco. Mixtures of ethyl acetate and petroleum ether (40–60°C fraction), dichloromethane and diethylether or acetonitrile and water (for reversed phase) were generally used as eluents. Analytical TLC was performed on pre-coated silica gel plates (Macherey-Nagel GmbH & Co. KG, Silica on TLC PET-foils, 4 x 8 cm). Visualization was accomplished with UV-light (254 nm), Cerium-molybdenum solution, KMnO<sub>4</sub> solution or with an iodine chamber. Melting points were determined with a MEL-TEMP II Melting point apparatus from Laboratory devices and are uncorrected. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded with a Bruker AV400 [400 MHz (<sup>1</sup>H) and 100 MHz (<sup>13</sup>C)], a Bruker AV500 [500 MHz (<sup>1</sup>H) and 125 MHz (<sup>13</sup>C)] in CDCl<sub>3</sub>, or DMSO-d<sub>6</sub>. Chemical shifts are reported in ppm relative to TMS (CDCl<sub>3</sub>) or the residual solvent signal (DMSO-d<sub>6</sub>). Diastereomeric ratios were determined by NMR and/or HPLC. Mass spectra were recorded with a Finnigan MAT 95 spectrometer (quadrupole) using the CI technique. HPLC analysis was performed on a MerckHitachi system (model LaChrom D-7000) using a Chiralcel OD-H-column (Daicel Chemical Industries, 250x4.6 mm). LCMS analyses were accomplished on a Shimadzu system (LC-10At, autoinjector SCL-6B, mass spectrometer LCMS-2020). A Phenomenex Luna C18(2) column (50x4.6 mm, grain size 3 μm) was used as the column. A GC-2010 System from Shimadzu (AOC-20i autoinjector, FID-detector) with a CP-Chirasil-Dex CB (Varian, 25 m x 0.25 mm, 0.25 μm internal diameter) was used for GC-FID analysis. Optical rotations were measured with a Perkin-Elmer polarimeter (model 341) in a thermostated (20°C ± 1 °C) cuvette. The radiation source used was a sodium vapor lamp (λ = 589 nm).

## 2. General Procedures (GP)

### General procedure 1: Preparation of α-hydroxy acids

A modified literature procedure was used.<sup>[1]</sup> A three-necked flask was equipped with a dropping funnel and an internal thermometer before the amino acid (1.0 equiv) was added. The acid was dissolved in sulfuric acid (1 M, 2 mL/mmol) and the solution was placed in an ice bath. A solution of NaNO<sub>2</sub> (6 equiv) in water (10 M) was slowly added over 2–6 hours at 0–4 °C. Afterwards, the mixture was stirred for 4 hours at 0 °C, extracted twice with Et<sub>2</sub>O and the combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>). The solvent was removed under reduced pressure to afford the desired α-hydroxy acids.

### General procedure 2: EDC coupling

A solution of acid (1.0 equiv), amine hydrochloride (1.0 equiv), HOBT (1.1 equiv) and DIPEA (2.1 equiv) in DCM (10 mL/mmol) was cooled to 0 °C and EDC·HCl (1.1 equiv) was added. The mixture was allowed to warm to room temperature, diluted with ethyl acetate and subsequently washed with 1 N HCl, sat. NaHCO<sub>3</sub> and sat. NaCl. After drying over Na<sub>2</sub>SO<sub>4</sub> the solvent was removed *in vacuo*, and the crude product was purified by column chromatography or recrystallization.

### General procedure 3: Preparation of carbonates

To a solution of the corresponding alcohol (1.0 equiv) and pyridine (1.5 equiv) in DCM (1–2 mL/mmol alcohol) ethyl chloroformate (1.2 equiv) was added at 0 °C. The mixture was then warmed to room temperature and stirred until complete conversion was observed (TLC). After addition of Et<sub>2</sub>O, the mixture was washed with HCl (1 N) and brine, and the organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>). The solvent was removed *in vacuo* and the residue purified by column chromatography.

### General procedures for Pd-catalyzed allylic alkylation

#### Procedure A

In a vacuum dried Schlenk flask the *N*-( $\alpha$ -hydroxyacyl)-glycinester (1.0 equiv) was dissolved in freshly distilled THF (6.5 mL/mmol) and a solution of ClTi(*Oi*-Pr)<sub>3</sub> (1.5 equiv, 1.0 M in hexane) was added. After stirring for 20 minutes at room temperature, the mixture was cooled to –78 °C and a solution of LHMDS (5.5 equiv, 1.0 M in THF) was added.

In a second Schlenk flask PPh<sub>3</sub> (9 mol %) and [allylPdCl]<sub>2</sub> (2 mol %) were dissolved in THF (3.0 mL/mmol) and stirred for 15 minutes at –78 °C. The allyl substrate was added to the catalyst solution and after stirring for 10 minutes at –78 °C, the mixture was slowly added to the enolate solution. After removal of the dry ice from the cooling bath, the mixture was allowed to warm to room temperature overnight. The reaction mixture was diluted with Et<sub>2</sub>O and hydrolyzed with water. After addition of KHSO<sub>4</sub> (1 N), the layers were separated, and the aqueous layer was extracted twice with Et<sub>2</sub>O. The combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>), the solvent removed *in vacuo*, and the residue was purified by column chromatography.

#### Procedure B

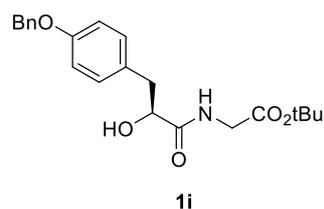
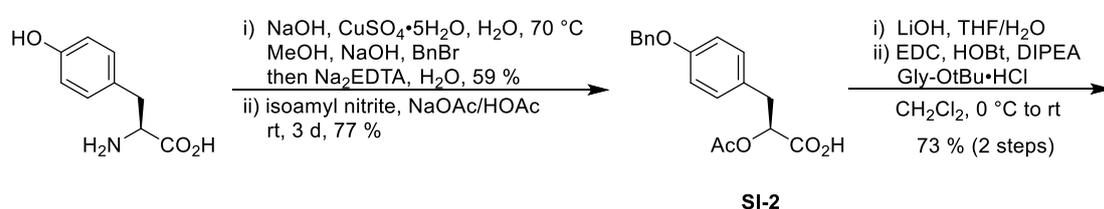
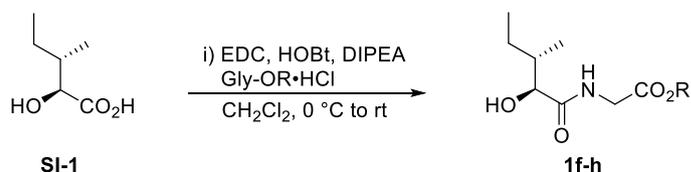
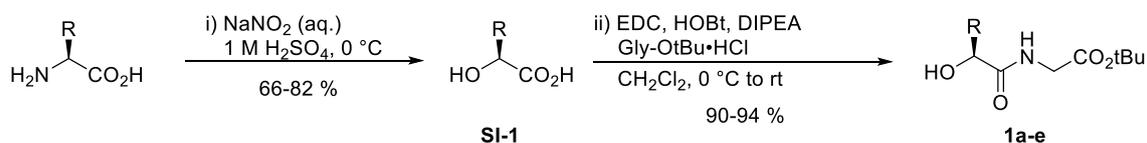
A solution of freshly distilled DIPA (3.2 equiv) in dry THF (1.5 mL/mmol) was cooled to –20 °C, and a solution of *n*-butyllithium (3.1 equiv, 2.5 M in hexane) was added. After 5 minutes at –20 °C the mixture was stirred for 20 minutes at room temperature before it was cooled to –78 °C.

In a second Schlenk flask the *N*-( $\alpha$ -hydroxyacyl)-glycinester (1.0 equiv) was dissolved in freshly distilled THF (6.5 mL/mmol), and a solution of ClTi(*Oi*Pr)<sub>3</sub> (1.5 equiv, 1.0 M in hexane) was added. After stirring for 20 minutes at room temperature, the mixture was cooled to –78 °C, and the freshly prepared LDA solution was added slowly, which resulted in a dark red solution. To ensure complete transmetalation the mixture was stirred for further 30 minutes at the same temperature.

In a third Schlenk flask PPh<sub>3</sub> (9 mol %) and [allylPdCl]<sub>2</sub> (2 mol %) were dissolved in THF (3.0 mL/mmol) and stirred for 15 minutes at –78 °C. The allyl substrate was added to the catalyst solution and after stirring for 10 minutes at –78 °C, the mixture was slowly added to the enolate solution. After removal of the dry ice from the cooling bath, the mixture was allowed to warm to room temperature overnight. The reaction mixture was diluted with Et<sub>2</sub>O and hydrolyzed with water. After addition of KHSO<sub>4</sub> (1 N), the layers were separated, and the aqueous layer was extracted twice with Et<sub>2</sub>O. The combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>), the solvent removed *in vacuo* and the residue purified by column chromatography.

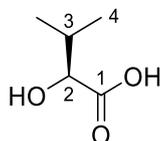
### 3. Synthesis of Starting Materials

#### 3.1 Synthesis of *N*-( $\alpha$ -hydroxyacyl)-glycinesters



#### (*S*)-2-Hydroxy-3-methylbutanoic acid (SI-1a)

According to **GP-1**, *L*-valine (10.0 g, 85.0 mmol) in sulfuric acid (170 mL, 1 M) was treated with a solution of sodium nitrite (35.3 g, 512 mmol, 6.0 equiv) in water (50 mL) at 0 °C. After aqueous work up, hydroxy acid **SI-1a** (7.53 g, 63.7 mmol, 75%) was obtained as a colorless syrup, which solidified upon vigorous drying under high vacuum.

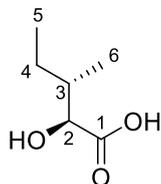


$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.94 (d,  $^3J_{4,3}$  = 6.9 Hz, 3 H, 4-H), 1.07 (d,  $^3J_{4',3}$  = 7.0 Hz, 3 H, 4-H'), 2.18 (septd,  $^3J_{3,4}$  = 6.9 Hz,  $^3J_{3,2}$  = 3.4 Hz, 1 H, 3-H), 4.19 (d,  $^3J_{2,3}$  = 3.4 Hz, 1 H, 2-H), 6.57 (bs, 2 H, OH, COOH).

$^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 15.8 (q, C-4), 18.7 (q, C-4'), 32.0 (d, C-3), 74.9 (d, C-2), 178.6 (s, C-1).

### (2S,3S)-2-Hydroxy-3-methylpentanoic acid (SI-1b)

According to **GP-1**, *L*-isoleucine (7.19 g, 54.8 mmol) in sulfuric acid (110 mL, 1 M) was treated with a solution of sodium nitrite (22.7 g, 329 mmol, 6.0 equiv) in water (35 mL) at 0 °C. After aqueous work up, hydroxy acid **SI-1b** (5.91 g, 44.7 mmol, 82%) was obtained as a white solid.

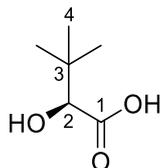


**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.93 (t, <sup>3</sup>J<sub>5,4</sub> = 7.5 Hz, 3 H, 5-H), 1.02 (d, <sup>3</sup>J<sub>6,3</sub> = 7.0 Hz, 3 H, 6-H), 1.30 (m, 1 H, 4-H<sub>a</sub>), 1.44 (m, 1 H, 4-H<sub>b</sub>), 1.89 (m, 1 H, 3-H), 4.19 (d, <sup>3</sup>J<sub>2,3</sub> = 3.7 Hz, 1 H, 2-H), 7.47 (bs, 2 H, OH, COOH).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.7 (q, C-5), 15.3 (q, C-6), 23.6 (t, C-4), 38.8 (d, C-3), 74.7 (d, C-2), 179.3 (s, C-1).

### (S)-2-Hydroxy-3,3-dimethylbutanoic acid (SI-1c)

According to **GP-1**, *L*-*tert*-leucine (7.50 g, 54.8 mmol) in sulfuric acid (115 mL, 1 M) was treated with a solution of sodium nitrite (23.7 g, 343 mmol, 6.0 equiv) in water (35 mL) at 0 °C. After aqueous work up, hydroxy acid **SI-1c** (5.01 g, 37.8 mmol, 66%) was obtained as a colorless syrup.

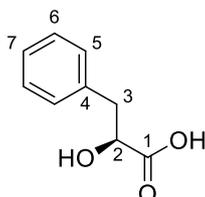


**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.02 (s, 9 H, 4-H), 3.92 (s, 1 H, 2-H), 7.53 (bs, 2 H, OH, COOH).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 25.7 (q, C-4), 35.2 (s, C-3), 78.3 (d, C-2), 178.7 (s, C-1).

### (S)-2-Hydroxy-3-phenylpropanoic acid (SI-1d)

According to **GP-1**, *L*-Phenylalanine (10.0 g, 60.5 mmol) in sulfuric acid (121 mL, 1.0 M) was treated with a solution of sodium nitrite (25.1 g, 363 mmol, 6.0 equiv) in water (35 mL) at 0 °C. After aqueous work, hydroxy acid **SI-1d** (7.90 g, 47.5 mmol, 79%) was obtained as a white solid.



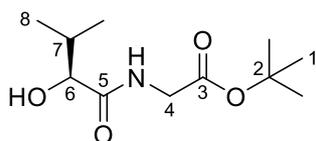
**<sup>1</sup>H-NMR** (400 MHz, DMSO-d<sub>6</sub>): δ = 2.78 (dd, <sup>2</sup>J<sub>3a,3b</sub> = 13.7 Hz, <sup>3</sup>J<sub>3a,2</sub> = 8.3 Hz, 1 H, 3-H<sub>a</sub>), 2.97 (dd, <sup>2</sup>J<sub>3b,3a</sub> = 13.7 Hz, <sup>3</sup>J<sub>3b,2</sub> = 4.4 Hz, 1 H, 3-H<sub>b</sub>), 4.15 (dd, <sup>3</sup>J<sub>2,3a</sub> = 8.3 Hz, <sup>3</sup>J<sub>2,3b</sub> = 4.5 Hz, 1 H, 2-H), 4.87 (bs, 1 H, OH), 7.26 (m, 5 H, 5-H, 6-H, 7-H), 12.57 (bs, 1 H, COOH).

<sup>13</sup>C-NMR (100 MHz, DMSO-d<sub>6</sub>): δ = 40.1 (t, C-3), 71.1 (d, C-2), 126.2 (d, C-7), 128.0 (d, C-5), 129.4 (d, C-6), 138.2 (s, C-4), 175.2 (s, C-1).

### *tert*-Butyl (S)-(2-hydroxy-3-methylbutanoyl)glycinate (**1a**)

According to **GP-2**, *tert*-butyl glycinate hydrochloride (2.00 g, 11.9 mmol), hydroxy acid **SI-1a** (1.41 g, 11.9 mmol, 1.0 equiv), HOBt (2.01 g, 13.1 mmol, 1.1 equiv), DIPEA (4.38 mL, 25.1 mmol, 2.1 equiv) and EDC·HCl (2.52 g, 13.1 mmol, 1.1 equiv) were reacted at 0 °C. After column chromatography (silica, petroleum ether/ethyl acetate 1:1), hydroxy acid peptide **1a** (2.54 g, 11.0 mmol, 92%) was obtained as a white solid.

R<sub>f</sub>(**1a**) = 0.09 (PE/EtOAc 2:1)



<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.89 (d, <sup>3</sup>J<sub>8,7</sub> = 6.9 Hz, 3 H, 8-H), 1.04 (d, <sup>3</sup>J<sub>8',7</sub> = 7.0 Hz, 3 H, 8'-H'), 1.48 (s, 9 H, 1-H), 2.17 (septd, <sup>3</sup>J<sub>7,8</sub> = 6.9 Hz, <sup>3</sup>J<sub>7,6</sub> = 3.3 Hz, 1 H, 7-H), 3.03 (bs, 1 H, OH), 3.94 (dd, <sup>2</sup>J<sub>4a,4b</sub> = 18.2 Hz, <sup>3</sup>J<sub>4a,NH</sub> = 5.3 Hz, 1 H, 4-H<sub>a</sub>), 4.01 (dd, <sup>2</sup>J<sub>4b,4a</sub> = 18.2 Hz, <sup>3</sup>J<sub>4b,NH</sub> = 5.6 Hz, 1 H, 4-H<sub>b</sub>), 4.03 (bs, 1 H, 6-H), 6.98 (bs, 1 H, NH).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 15.5 (q, C-8), 19.1 (q, C-8'), 28.0 (q, C-1), 31.9 (d, C-7), 41.5 (t, C-4), 76.3 (d, C-6), 82.4 (s, C-2), 169.0 (s, C-3), 173.6 (s, C-5).

Optical rotation:  $[\alpha]_D^{20} = -46.8$  (c = 1.0, CHCl<sub>3</sub>)

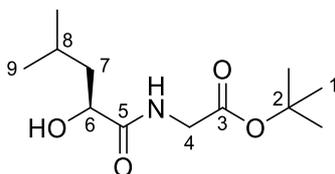
Melting point: 58–60 °C

HRMS (CI):	Calculated	Found
C <sub>11</sub> H <sub>22</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	232.1543	232.1551

### *tert*-Butyl (S)-(2-hydroxy-4-methylpentanoyl)glycinate (**1b**)

According to **GP-2**, *tert*-butyl glycinate hydrochloride (2.00 g, 11.9 mmol), (2S)-hydroxy-4-methylpentanoic acid (1.58 g, 11.9 mmol, 1.0 equiv), HOBt (2.01 g, 13.1 mmol, 1.1 equiv), DIPEA (4.38 mL, 25.1 mmol, 2.1 equiv) and EDC·HCl (2.52 g, 13.1 mmol, 1.1 equiv) were reacted at 0 °C. After column chromatography (silica, petroleum ether/ethyl acetate 1:1), hydroxy acid peptide **1b** (2.62 g, 10.7 mmol, 90%) was obtained as a colorless oil.

R<sub>f</sub>(**1b**) = 0.22 (PE/EtOAc 1:1)



<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.95 (d, <sup>3</sup>J<sub>9,8</sub> = 6.6 Hz, 3 H, 9-H), 0.97 (d, <sup>3</sup>J<sub>9',8</sub> = 6.6 Hz, 3 H, 9'-H'), 1.48 (s, 9 H, 1-H), 1.56 (ddd, <sup>2</sup>J<sub>7a,7b</sub> = 14.3 Hz, <sup>3</sup>J<sub>7a,6</sub> = 9.9 Hz, <sup>3</sup>J<sub>7a,8</sub> = 5.0 Hz, 1 H, 7-H<sub>a</sub>), 1.65 (ddd, <sup>2</sup>J<sub>7b,7a</sub> = 14.1 Hz, <sup>3</sup>J<sub>7b,6</sub> = 9.3 Hz, <sup>3</sup>J<sub>7b,8</sub> = 3.5 Hz, 1 H, 7-H<sub>b</sub>), 1.86 (m, 1 H, 8-H), 2.69 (m, 1 H, OH), 3.91 (dd, <sup>2</sup>J<sub>4a,4b</sub> = 18.2 Hz, <sup>3</sup>J<sub>4a,NH</sub> = 5.3 Hz, 1 H, 4-H<sub>a</sub>), 4.00 (dd, <sup>2</sup>J<sub>4b,4a</sub> = 18.2 Hz, <sup>3</sup>J<sub>4b,NH</sub> = 5.5 Hz, 1 H, 4-H<sub>b</sub>), 4.19 (td, <sup>3</sup>J<sub>6,7</sub> = 9.8 Hz, <sup>3</sup>J<sub>6,OH</sub> = 3.5 Hz, 1 H, 6-H), 6.93 (bs, 1 H, NH).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 21.3 (q, C-9), 23.4 (q, C-9'), 24.5 (d, C-8), 28.0 (q, C-1), 41.6 (t, C-4), 43.7 (t, C-7), 70.7 (d, C-6), 82.4 (s, C-2), 169.1 (s, C-3), 174.7 (s, C-5).

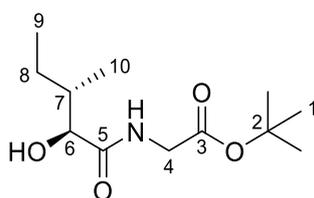
**Optical rotation:**  $[\alpha]_D^{20} = -51.8$  (c = 1.0, CHCl<sub>3</sub>)

<b>HRMS (CI):</b>	Calculated	Found
C <sub>12</sub> H <sub>23</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	246.1700	246.1703

### ***tert*-Butyl (2*S*,3*S*)-(2-hydroxy-3-methylpentanoyl)glycinate (**1c**)**

According to **GP-2**, *tert*-butyl glycinate hydrochloride (5.00 g, 29.8 mmol), hydroxy acid **SI-1b** (3.94 g, 29.8 mmol, 1.0 equiv), HOBt (5.02 g, 32.8 mmol, 1.1 equiv), DIPEA (10.9 mL, 62.6 mmol, 2.1 equiv) and EDC·HCl (6.29 g, 32.8 mmol, 1.1 equiv) were reacted at 0 °C. After column chromatography (silica, petroleum ether/ethyl acetate 1:1), hydroxy acid peptide **1c** (6.51 g, 26.5 mmol, 89%) was obtained as a white solid.

**R<sub>f</sub>(1c)** = 0.22 (PE/EtOAc 1:1)



<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.90 (t, <sup>3</sup>J<sub>9,8</sub> = 7.5 Hz, 3 H, 9-H), 1.01 (d, <sup>3</sup>J<sub>10,7</sub> = 7.0 Hz, 3 H, 10-H), 1.22 (m, 1 H, 8-H<sub>a</sub>), 1.44 (m, 1 H, 8-H<sub>b</sub>), 1.48 (s, 9 H, 1-H), 1.90 (dqt, <sup>3</sup>J<sub>7,8a</sub> = 10.6 Hz, <sup>3</sup>J<sub>7,10</sub> = 6.8 Hz, <sup>3</sup>J<sub>7,6/8b</sub> = 3.6 Hz, 1 H, 7-H), 2.95 (bs, 1 H, OH), 3.93 (dd, <sup>2</sup>J<sub>4a,4b</sub> = 18.2 Hz, <sup>3</sup>J<sub>4a,NH</sub> = 5.3 Hz, 1 H, 4-H<sub>a</sub>), 4.02 (dd, <sup>2</sup>J<sub>4b,4a</sub> = 18.2 Hz, <sup>3</sup>J<sub>4b,NH</sub> = 5.6 Hz, 1 H, 4-H<sub>b</sub>), 4.06 (dd, <sup>3</sup>J<sub>6,7</sub> = 3.3 Hz, 1 H, 6-H), 6.97 (bs, 1 H, NH).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 11.8 (q, C-9), 15.5 (q, C-10), 23.1 (t, C-8), 28.0 (q, C-1), 38.8 (d, C-7), 41.6 (t, C-4), 76.4 (d, C-6), 82.4 (s, C-2), 169.0 (s, C-3), 173.3 (s, C-5).

**Optical rotation:**  $[\alpha]_D^{20} = -40.7$  (c = 1.0, CHCl<sub>3</sub>)

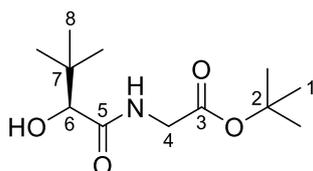
**Melting point:** 49–51 °C

<b>HRMS (CI):</b>	Calculated	Found
C <sub>12</sub> H <sub>23</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	246.1700	246.1690

### ***tert*-Butyl (S)-(2-hydroxy-3,3-dimethylbutanoyl)glycinate (**1d**)**

According to **GP-2**, *tert*-butyl glycinate hydrochloride (3.00 g, 17.9 mmol), hydroxy acid **SI-1c** (2.37 g, 17.9 mmol, 1.0 equiv), HOBt (3.01 g, 19.7 mmol, 1.1 equiv), DIPEA (6.56 mL, 37.6 mmol, 2.1 equiv) and EDC·HCl (3.77 g, 19.7 mmol, 1.1 equiv) were reacted at 0 °C. Column chromatography (silica, petroleum ether/ethyl acetate 1:1) gave rise to hydroxy acid peptide **1d** (4.01 g, 16.3 mmol, 91%) as a pale yellow solid.

**R<sub>f</sub>(1d)** = 0.17 (PE/EtOAc 2:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.01 (s, 9 H, 8-H), 1.48 (s, 9 H, 1-H), 3.25 (d, <sup>3</sup>J<sub>OH,6</sub> = 5.3 Hz, 1 H, OH), 3.78 (d, <sup>3</sup>J<sub>6,OH</sub> = 5.0 Hz, 1 H, 6-H), 3.91 (dd, <sup>2</sup>J<sub>4a,4b</sub> = 18.2 Hz, <sup>3</sup>J<sub>4a,NH</sub> = 5.1 Hz, 1 H, 4-H<sub>a</sub>), 4.02 (dd, <sup>2</sup>J<sub>4b,4a</sub> = 18.2 Hz, <sup>3</sup>J<sub>4b,NH</sub> = 5.6 Hz, 1 H, 4-H<sub>b</sub>), 6.78 (bs, 1 H, NH).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 25.9 (q, C-8), 28.0 (q, C-1), 35.0 (s, C-7), 41.6 (t, C-4), 79.6 (d, C-6), 82.4 (s, C-2), 169.0 (s, C-3), 172.8 (s, C-5).

**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = -46.9$  (c = 1.0, CHCl<sub>3</sub>)

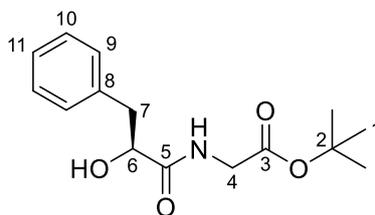
**Melting point:** 79–82 °C

<b>HRMS (CI):</b>	Calculated	Found
C <sub>12</sub> H <sub>23</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	246.1700	246.1701

### **tert-Butyl (S)-(2-hydroxy-3-phenylpropanoyl)glycinate (1e)**

According to **GP-2**, *tert*-butyl glycinate hydrochloride (2.00 g, 11.9 mmol), hydroxy acid **SI-1d** (1.98 g, 11.9 mmol, 1.0 equiv), HOBt (2.01 g, 13.1 mmol, 1.1 equiv), DIPEA (4.38 mL, 25.1 mmol, 2.1 equiv) and EDC·HCl (2.52 g, 13.1 mmol, 1.1 equiv) were reacted at 0 °C. Filtration through a pad of silica (petroleum ether/ethyl acetate 1:1) and recrystallization from petroleum ether/ethyl acetate afforded hydroxy acid peptide **1e** (3.00 g, 10.7 mmol, 90%) as colorless crystals.

**R<sub>f</sub>(1e)** = 0.14 (PE/EtOAc 2:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.47 (s, 9 H, 1-H), 2.74 (d, <sup>3</sup>J<sub>OH,6</sub> = 4.7 Hz, 1 H, OH), 2.86 (dd, <sup>2</sup>J<sub>7a,7b</sub> = 13.9 Hz, <sup>3</sup>J<sub>7a,6</sub> = 9.0 Hz, 1 H, 7-H<sub>a</sub>), 3.26 (dd, <sup>2</sup>J<sub>7b,7a</sub> = 13.9 Hz, <sup>3</sup>J<sub>7b,6</sub> = 3.5 Hz, 1 H, 7-H<sub>b</sub>), 3.88 (dd, <sup>2</sup>J<sub>4a,4b</sub> = 18.2 Hz, <sup>3</sup>J<sub>4a,NH</sub> = 5.3 Hz, 1 H, 4-H<sub>a</sub>), 3.97 (dd, <sup>2</sup>J<sub>4b,4a</sub> = 18.2 Hz, <sup>3</sup>J<sub>4b,NH</sub> = 5.4 Hz, 1 H, 4-H<sub>b</sub>), 4.33 (dt, <sup>3</sup>J<sub>6,7a</sub> = 8.9 Hz, <sup>3</sup>J<sub>6,7b/OH</sub> = 4.2 Hz, 1 H, 6-H), 7.02 (bs, 1 H, NH), 7.25 (m, 3 H, 9-H, 11-H), 7.32 (m, 2 H, 10-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 28.0 (q, C-1), 40.8 (t, C-7), 41.5 (t, C-4), 72.9 (d, C-6), 82.4 (s, C-2), 126.9 (d, C-11), 128.7 (d, C-9), 129.5 (d, C-10), 136.9 (s, C-8), 168.8 (s, C-3), 172.8 (s, C-5).

**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = -75.3$  (c = 1.0, CHCl<sub>3</sub>)

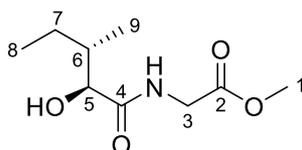
**Melting point:** 98–100 °C

<b>HRMS (CI):</b>	Calculated	Found
C <sub>15</sub> H <sub>22</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	280.1543	280.1533

### Methyl (2S,3S)-(2-hydroxy-3-methylpentanoyl)glycinate (**1f**)

According to **GP-2**, methyl glycinate hydrochloride (300 mg, 2.39 mmol), hydroxy acid **SI-1b** (316 mg, 2.39 mmol, 1.0 equiv), HOBT (403 mg, 2.63 mmol, 1.1 equiv), DIPEA (876  $\mu$ L, 5.02 mmol, 2.1 equiv) and EDC·HCl (504 mg, 2.63 mmol, 1.1 equiv) were reacted at 0 °C. Column chromatography (silica, petroleum ether/ethyl acetate 2:3) afforded hydroxy acid peptide **1f** (316 mg, 1.52 mmol, 64%) as a colorless oil.

$R_f(\mathbf{1f}) = 0.07$  (PE/EtOAc 2:1)



$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.90$  (t,  $^3J_{8,7} = 7.4$  Hz, 3 H, 8-H), 1.02 (d,  $^3J_{9,6} = 7.0$  Hz, 3 H, 9-H), 1.22 (m, 1 H, 7- $\text{H}_a$ ), 1.45 (m, 1 H, 7- $\text{H}_b$ ), 1.91 (m, 1 H, 6-H), 2.75 (bs, 1 H, OH), 3.77 (s, 3 H, 1-H), 4.06 (dd,  $^2J_{3a,3b} = 18.2$  Hz,  $^3J_{3a,\text{NH}} = 5.5$  Hz, 1 H, 3- $\text{H}_a$ ), 4.08 (m, 1 H, 5-H), 4.12 (dd,  $^2J_{3b,3a} = 18.3$  Hz,  $^3J_{3b,\text{NH}} = 5.6$  Hz, 1 H, 3- $\text{H}_b$ ), 7.02 (bs, 1 H, NH).

$^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 11.8$  (q, C-8), 15.5 (q, C-9), 23.1 (t, C-7), 38.8 (d, C-6), 40.7 (t, C-3), 52.4 (q, C-1), 76.4 (d, C-5), 170.3 (s, C-2), 173.6 (s, C-4).

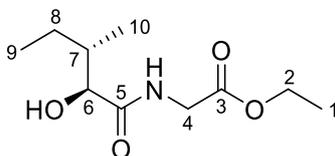
**Optical rotation:**  $[\alpha]_D^{20} = -56.0$  ( $c = 1.0$ ,  $\text{CHCl}_3$ )

<b>HRMS (CI):</b>	Calculated	Found
$\text{C}_9\text{H}_{18}\text{NO}_4$ $[\text{M}+\text{H}]^+$	204.1230	204.1238

### Ethyl (2S,3S)-(2-hydroxy-3-methylpentanoyl)glycinate (**1g**)

According to **GP-2**, ethyl glycinate hydrochloride (300 mg, 2.15 mmol), hydroxy acid **SI-1b** (284 mg, 2.15 mmol, 1.0 equiv), HOBT (362 mg, 2.36 mmol, 1.1 equiv), DIPEA (788  $\mu$ L, 4.51 mmol, 2.1 equiv) and EDC·HCl (453 mg, 2.36 mmol, 1.1 equiv) were reacted at 0 °C. After column chromatography (silica, petroleum ether/ethyl acetate 2:3), hydroxy acid peptide **1g** (298 mg, 1.34 mmol, 63%) was obtained as a white solid.

$R_f(\mathbf{1g}) = 0.10$  (PE/EtOAc 2:1)



$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.90$  (t,  $^3J_{9,8} = 7.4$  Hz, 3 H, 9-H), 1.02 (d,  $^3J_{10,7} = 7.0$  Hz, 3 H, 10-H), 1.22 (m, 1 H, 8- $\text{H}_a$ ), 1.29 (t,  $^3J_{1,2} = 7.2$  Hz, 3 H, 1-H), 1.45 (m, 1 H, 8- $\text{H}_b$ ), 1.91 (m, 1 H, 7-H), 2.73 (bs, 1 H, OH), 4.04 (dd,  $^2J_{4a,4b} = 18.2$  Hz,  $^3J_{4a,\text{NH}} = 5.5$  Hz, 1 H, 4- $\text{H}_a$ ), 4.09 (m, 2 H, 4- $\text{H}_b$ , 5-H), 4.22 (q,  $^3J_{2,1} = 7.2$  Hz, 2 H, 2-H), 6.99 (bs, 1 H, NH).

$^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 11.8$  (q, C-8), 14.1 (q, C-1), 15.5 (q, C-9), 23.1 (t, C-8), 38.8 (d, C-7), 40.9 (t, C-4), 61.6 (t, C-2), 76.4 (d, C-6), 169.8 (s, C-3), 173.6 (s, C-5).

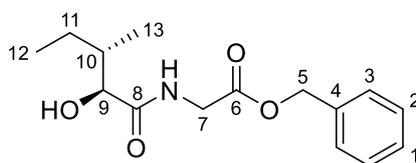
**Optical rotation:**  $[\alpha]_D^{20} = -45.0$  ( $c = 1.0$ ,  $\text{CHCl}_3$ )

<b>Melting point:</b>	51–53 °C	
<b>HRMS (CI):</b>	Calculated	Found
C <sub>10</sub> H <sub>19</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	218.1387	218.1418

### Benzyl (2S,3S)-(2-hydroxy-3-methylpentanoyl)glycinate (1h)

According to **GP-2**, phenyl glycinate hydrochloride (458 mg, 2.27 mmol, 1.0 equiv), hydroxy acid **SI-1b** (300 mg, 2.27 mmol, 1.0 equiv), HOBt (382 mg, 2.50 mmol, 1.1 equiv), DIPEA (833 μL, 4.77 mmol, 2.1 equiv) and EDC·HCl (479 mg, 2.50 mmol, 1.1 equiv) were reacted at 0 °C. Aqueous work up and column chromatography (silica, petroleum ether/ethyl acetate 3:2) afforded hydroxy acid peptide **1h** (580 mg, 2.08 mmol, 91%) as a white solid.

**R<sub>f</sub>(1h)** = 0.09 (PE/EtOAc 2:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.89 (t, <sup>3</sup>J<sub>12,11</sub> = 7.5 Hz, 3 H, 12-H), 1.00 (d, <sup>3</sup>J<sub>13,10</sub> = 7.0 Hz, 3 H, 13-H), 1.21 (m, 1 H, 11-H<sub>a</sub>), 1.44 (dq, <sup>2</sup>J<sub>11b,11a</sub> = 10.9 Hz, <sup>3</sup>J<sub>11b,12</sub> = 7.5 Hz, <sup>3</sup>J<sub>11b,10</sub> = 4.0 Hz, 1 H, 11-H<sub>b</sub>), 1.90 (qq, <sup>3</sup>J<sub>10,13</sub> = 7.1 Hz, <sup>3</sup>J<sub>10,9/11</sub> = 3.4 Hz, 1 H, 10-H), 2.59 (bs, 1 H, OH), 4.07 (d, <sup>3</sup>J<sub>9,10</sub> = 3.4 Hz, 1 H, 9-H), 4.12 (t, <sup>3</sup>J<sub>7,NH</sub> = 5.0 Hz, 2 H, 7-H), 5.19 (s, 2 H, 5-H), 6.99 (bs, 1 H, NH), 7.36 (m, 5 H, 1-H, 2-H, 3-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.8 (q, C-12), 15.5 (q, C-13), 23.1 (t, C-11), 38.7 (d, C-10), 40.9 (t, C-7), 67.3 (t, C-5), 76.4 (d, C-9), 128.4 (d, C-3), 128.5 (d, C-1), 128.6 (d, C-2), 135.1 (s, C-4), 169.7 (s, C-6), 173.6 (s, C-8).

**Optical rotation:**  $[\alpha]_D^{20} = -31.1$  (c = 1.0, CHCl<sub>3</sub>)

**Melting point:** 52–55 °C

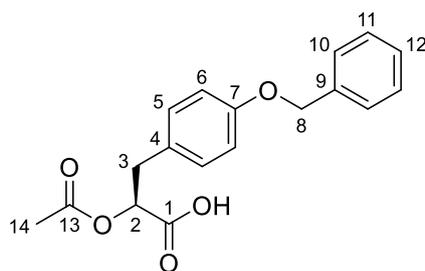
<b>HRMS (CI):</b>	Calculated	Found
C <sub>15</sub> H <sub>23</sub> NO <sub>4</sub> [M+2H] <sup>+</sup>	281.1622	281.1623

### (S)-2-Acetoxy-3-(4-(benzyloxy)phenyl)propanoic acid (SI-2)

*L*-Tyrosine (7.25 g, 40.0 mmol) was dissolved in an aqueous solution of sodium hydroxide (2 M, 20 mL, 40.0 mmol, 1.0 equiv) and warmed to 70 °C. A solution of CuSO<sub>4</sub>·5H<sub>2</sub>O (5.00 g, 20.4 mmol, 0.5 equiv) in water (35 mL) was added dropwise, and the resulting solution was stirred for another 1 hour. After successive addition of MeOH (100 mL) and NaOH (2 M, 20 mL, 40.0 mmol, 1.0 equiv), BnBr (5.00 mL, 42.0 mmol, 1.05 equiv) was added dropwise over a period of 30 minutes. After stirring overnight, the mixture was filtrated, the solid product washed with MeOH/H<sub>2</sub>O (1:3, 60 mL) three times and then added to a solution of Na<sub>2</sub>EDTA (8.74 g, 26.0 mmol) in water (100 mL). The resulting solution was stirred for 5 hours at 70 °C. After filtration and washing with water and acetone, the solid product was dried in high vacuum to afford the *O*-benzyl protected tyrosine as a beige solid (6.45 g, 23.8 mmol, 59%).

To a suspension of *O*-benzyl-*L*-tyrosine (4.30 g, 15.9 mmol) and NaOAc (4.68 g, 57.1 mmol, 3.6 equiv) in glacial HOAc (50 mL) was slowly added isoamyl nitrite (7.90 mL, 58.6 mmol, 3.7 equiv) at room temperature. The reaction mixture was stirred for 3 days at room temperature after which the mixture became clear. Hexane was added, the mixture was concentrated and the residue redissolved in EtOAc (100 mL) and H<sub>2</sub>O (70 mL). The solution was acidified to pH 1 by addition of HCl (6 M), and the layers were separated. The organic layer was washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated *in vacuo*. The residue was purified by column chromatography (silica, DCM + 1% HOAc) to afford AcO-*L*-Hpla(Bn)-OH **SI-2** (3.83 g, 12.2 mmol, 77%) as a yellow solid.

**R<sub>f</sub>(SI-2)** = 0.14 (DCM + 1% HOAc)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 2.09 (s, 3 H, 14-H), 3.06 (dd, <sup>2</sup>J<sub>3a,3b</sub> = 14.4 Hz, <sup>3</sup>J<sub>3a,2</sub> = 8.7 Hz, 1 H, 3-H<sub>a</sub>), 3.17 (dd, <sup>2</sup>J<sub>3b,3a</sub> = 14.4 Hz, <sup>3</sup>J<sub>3b,2</sub> = 4.2 Hz, 1 H, 3-H<sub>b</sub>), 5.04 (s, 2 H, 8-H), 5.21 (dd, <sup>3</sup>J<sub>2,3a</sub> = 8.7 Hz, <sup>3</sup>J<sub>2,3b</sub> = 4.2 Hz, 1 H, 2-H), 6.92 (d, <sup>3</sup>J<sub>6,5</sub> = 8.7 Hz, 2 H, 6-H), 7.16 (d, <sup>3</sup>J<sub>5,6</sub> = 8.7 Hz, 2 H, 5-H), 7.36 (m, 5 H, 10-H, 11-H, 12-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 20.5 (q, C-14), 36.3 (t, C-3), 70.0 (t, C-8), 72.6 (d, C-2), 114.9 (d, C-6), 127.5 (d, C-10), 127.9 (s, C-4), 128.0 (d, C-12), 128.6 (d, C-11), 130.4 (d, C-5), 137.0 (s, C-9), 158.0 (s, C-7), 170.4 (s, C-13), 174.5 (s, C-1).

**Optical rotation:**  $[\alpha]_D^{20} = -1.7$  (c = 1.0, CHCl<sub>3</sub>)

**Melting point:** 104–107 °C

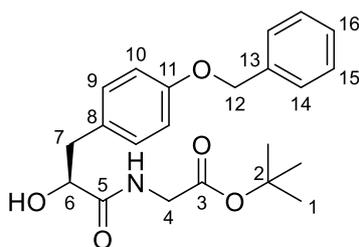
<b>HRMS (CI):</b>	Calculated	Found
C <sub>18</sub> H <sub>18</sub> O <sub>5</sub> [M] <sup>+</sup>	314.1149	314.1148

#### ***tert*-Butyl (S)-(3-(4-(benzyloxy)phenyl)-2-hydroxypropanoyl)glycinate (1i)**

To a solution of **SI-2** (3.30 g, 10.5 mmol) in THF (35 mL) was added LiOH (1 M, 31.5 mL, 31.5 mmol, 3.0 equiv) at 0 °C and the mixture was stirred overnight. The mixture was acidified by addition of HCl (1 M, aq.) and extracted two times with EtOAc. The combined organic layer was washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated *in vacuo*. The residue was directly used without further purification.

According to **GP-2**, the hydroxy acid was dissolved in DCM (105 mL) and treated with *tert*-butyl glycinate hydrochloride (1.76 g, 10.5 mmol, 1.0 equiv), EDC-HCl (2.21 g, 11.6 mmol, 1.1 equiv), HOBt (1.77 g, 11.6 mmol, 1.1 equiv) and DIPEA (3.85 mL, 22.1 mmol, 2.1 equiv) at 0 °C. Aqueous work up and column chromatography (silica, PE/EtOAc 2:1) afforded hydroxy acid dipeptide **1i** (2.95 g, 7.67 mmol, 73% over two steps) as a white solid.

**R<sub>f</sub>(1i)** = 0.09 (PE/EtOAc 2:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.47 (s, 9 H, 1-H), 2.60 (d, <sup>3</sup>J<sub>OH,6</sub> = 4.6 Hz, 1 H, OH), 2.82 (dd, <sup>2</sup>J<sub>7a,7b</sub> = 14.1 Hz, <sup>3</sup>J<sub>7a,6</sub> = 8.8 Hz, 1 H, 7-H<sub>a</sub>), 3.19 (dd, <sup>2</sup>J<sub>7b,7a</sub> = 14.1 Hz, <sup>3</sup>J<sub>7b,6</sub> = 3.8 Hz, 1 H, 7-H<sub>b</sub>), 3.06 (dd, <sup>2</sup>J<sub>4a,4b</sub> = 18.3 Hz, <sup>3</sup>J<sub>4a,NH</sub> = 5.3 Hz, 1 H, 4-H<sub>a</sub>), 3.17 (dd, <sup>2</sup>J<sub>4b,4a</sub> = 18.3 Hz, <sup>3</sup>J<sub>4b,NH</sub> = 5.5 Hz, 1 H, 4-H<sub>b</sub>), 4.28 (dt, <sup>3</sup>J<sub>6,7a</sub> = 8.8 Hz, <sup>3</sup>J<sub>6,7b/NH</sub> = 4.2 Hz, 1 H, 6-H), 5.04 (s, 2 H, 12-H), 6.93 (d, <sup>3</sup>J<sub>10,9</sub> = 8.7 Hz, 2 H, 10-H), 6.99 (t, <sup>3</sup>J<sub>NH,4</sub> = 5.0 Hz, 1 H, NH), 7.16 (d, <sup>3</sup>J<sub>9,10</sub> = 8.7 Hz, 2 H, 9-H), 7.32 (m, 1 H, 16-H), 7.40 (m, 4 H, 14-H, 15-H).

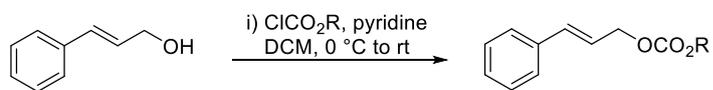
**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 28.0 (q, C-1), 39.9 (t, C-7), 41.6 (t, C-4), 70.0 (t, C-12), 73.0 (d, C-6), 82.4 (s, C-2), 115.1 (d, C-10), 127.4 (d, C-14), 127.9 (s, C-8), 128.6 (d, C-16), 128.9 (d, C-15), 130.5 (d, C-9), 136.9 (s, C-13), 157.9 (s, C-11), 168.8 (s, C-3), 172.8 (s, C-5).

**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = -53.6$  (c = 1.0, CHCl<sub>3</sub>)

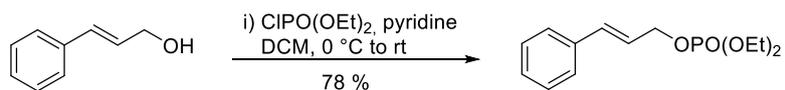
**Melting point:** 109–111 °C

<b>HRMS (CI):</b>	Calculated	Found
C <sub>22</sub> H <sub>29</sub> NO <sub>5</sub> [M+2H] <sup>+</sup>	387.2040	387.2036

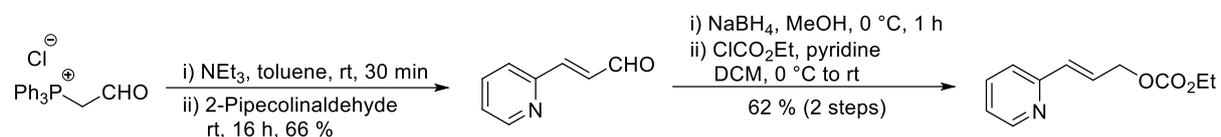
## 3.2 Synthesis of Allylic Carbonates



**SI-3** R = Me 72 %  
**SI-4** R = Et 95 %



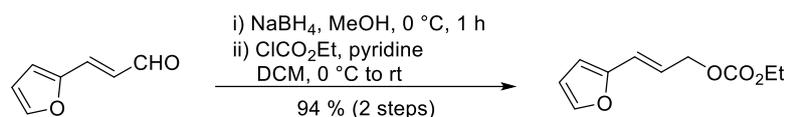
**SI-5**



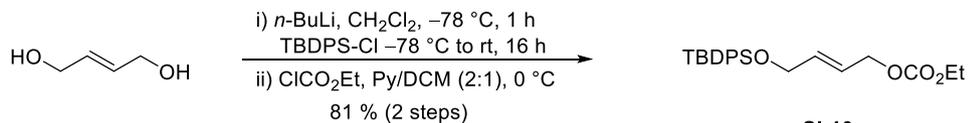
**SI-6**

**SI-7**

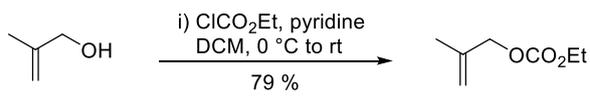
**SI-8**



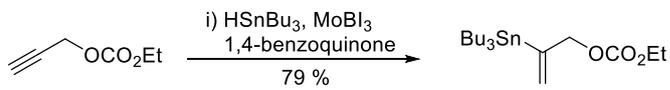
**SI-9**



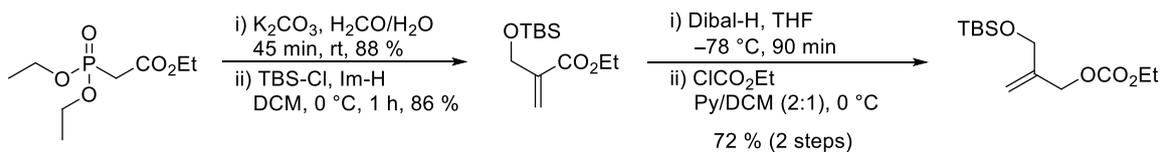
**SI-10**



**SI-11**

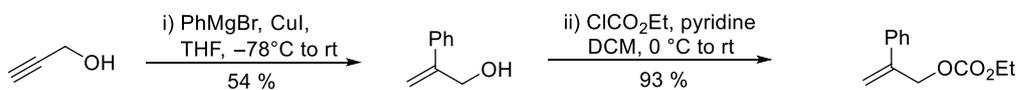


**SI-12**



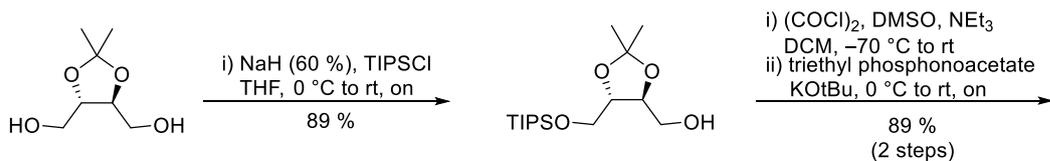
**SI-13**

**SI-14**



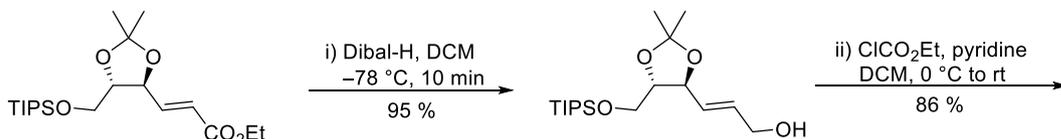
**SI-15**

**SI-16**



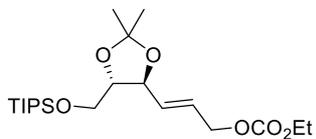
**SI-17**

**SI-18**

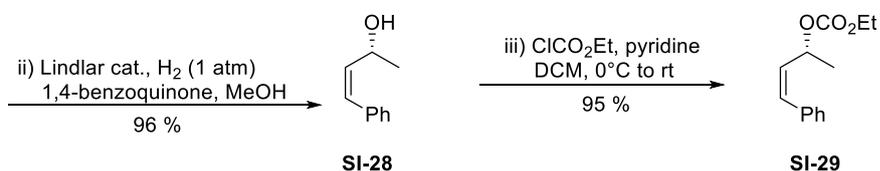
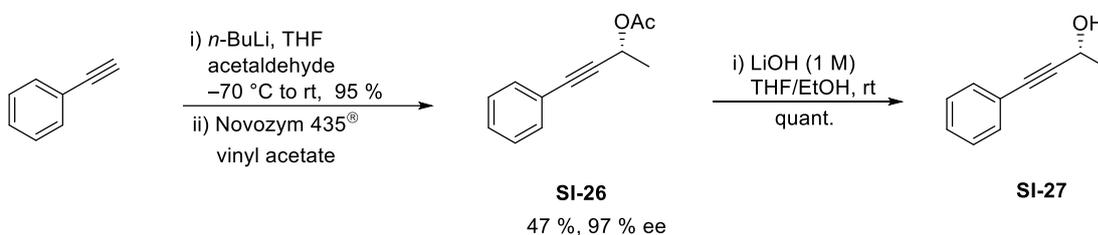
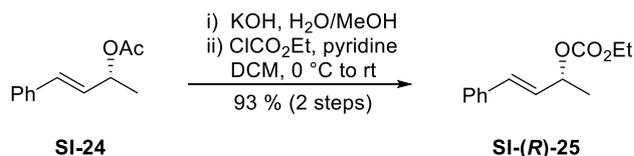
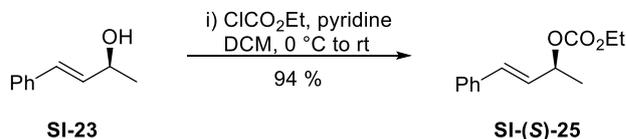
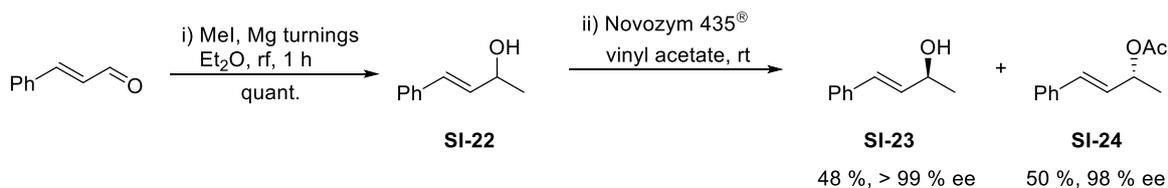


**SI-19**

**SI-20**



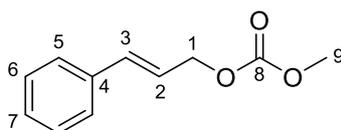
**SI-21**



### Cinnamyl methyl carbonate (SI-3)<sup>[2]</sup>

To a solution of cinnamyl alcohol (2.74 g, 20.0 mmol) in pyridine (20 mL) methyl chloroformate (3.10 mL, 40.0 mmol, 2.0 equiv) was added dropwise at 0 °C. The reaction mixture was warmed to room temperature overnight, diluted with EtOAc and washed three times with HCl (1 M, aq.). The organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>), evaporated *in vacuo* and the residue was purified by column chromatography (silica, PE/EtOAc 9:1) to afford allylic carbonate **SI-3** (2.77 g, 14.4 mmol, 72%) as a colorless liquid.

**R<sub>f</sub>(SI-3)** = 0.25 (PE/EtOAc 9:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 3.81 (s, 3 H, 9-H), 4.79 (dd, <sup>3</sup>J<sub>1,2</sub> = 6.5 Hz, <sup>4</sup>J<sub>1,3</sub> = 1.3 Hz, 2 H, 1-H), 6.30 (dt, <sup>3</sup>J<sub>2,3</sub> = 15.9 Hz, <sup>3</sup>J<sub>2,1</sub> = 6.5 Hz, 1 H, 2-H), 6.69 (d, <sup>3</sup>J<sub>3,2</sub> = 16.0 Hz, 1 H, 3-H), 7.27 (m, 1 H, 7-H), 7.33 (m, 2 H, 5/6-H), 7.40 (m, 2 H, 5/6-H).

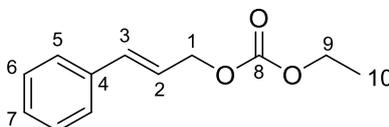
**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 54.8 (q, C-9), 68.4 (t, C-1), 122.4 (d, C-2), 126.7 (d, C-5/C-6), 128.2 (d, C-7), 128.6 (d, C-5/C-6), 134.8 (d, C-3), 136.0 (s, C-4), 155.6 (s, C-8).

<b>HRMS (CI):</b>	Calculated	Found
C <sub>11</sub> H <sub>12</sub> O <sub>3</sub> [M] <sup>+</sup>	192.0781	192.0794

#### **Cinnamyl ethyl carbonate (SI-4)**<sup>[3]</sup>

To a solution of cinnamyl alcohol (6.85 g, 50.0 mmol) in pyridine (50 mL) ethyl chloroformate (9.60 mL, 100 mmol, 2.0 equiv) was added dropwise at 0 °C. The reaction mixture was warmed to room temperature overnight, diluted with EtOAc and washed three times with HCl (1 M, aq.). The organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>), evaporated *in vacuo* and the residue was purified by column chromatography (silica, PE/EtOAc 95:5) to afford allylic carbonate **SI-4** (9.82 g, 47.6 mmol, 95%) as a colorless liquid.

**R<sub>f</sub>(SI-4)** = 0.36 (PE/EtOAc 9:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.32 (t, <sup>3</sup>J<sub>10,9</sub> = 7.2 Hz, 3 H, 10-H), 3.81 (q, <sup>3</sup>J<sub>9,10</sub> = 7.1 Hz, 2 H, 9-H), 4.78 (d, <sup>3</sup>J<sub>1,2</sub> = 6.5 Hz, 2 H, 1-H), 6.30 (dt, <sup>3</sup>J<sub>2,3</sub> = 15.9 Hz, <sup>3</sup>J<sub>2,1</sub> = 6.5 Hz, 1 H, 2-H), 6.69 (d, <sup>3</sup>J<sub>3,2</sub> = 15.9 Hz, 1 H, 3-H), 7.26 (m, 1 H, 7-H), 7.32 (m, 2 H, 5/6-H), 7.39 (m, 2 H, 5/6-H).

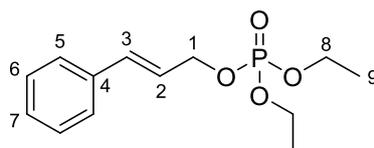
**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 14.3 (q, C-10), 64.1 (t, C-9), 68.2 (t, C-1), 122.5 (d, C-2), 126.6 (d, C-5/C-6), 128.1 (d, C-7), 128.6 (d, C-5/C-6), 134.7 (d, C-3), 136.1 (s, C-4), 155.0 (s, C-8).

<b>HRMS (CI):</b>	Calculated	Found
C <sub>12</sub> H <sub>14</sub> O <sub>3</sub> [M] <sup>+</sup>	206.0937	206.0950

#### **Cinnamyl diethyl phosphate (SI-5)**<sup>[4]</sup>

To a solution of cinnamyl alcohol (2.01 g, 15.0 mmol) in DCM (75 mL) was subsequently added pyridine (3.03 mL, 37.5 mmol, 2.5 equiv), DMAP (183 mg, 1.50 mmol, 0.1 equiv) and diethyl chlorophosphate (2.72 mL, 18.0 mmol, 1.2 equiv) at 0 °C. The mixture was warmed to room temperature overnight, diluted with DCM and hydrolyzed by addition of HCl (1 M, aq.). After separation of the layers, the aqueous layer was extracted twice with DCM and the combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated *in vacuo*. The crude product was purified by column chromatography (silica, PE/EtOAc 1:1) to afford the allylic phosphate **SI-5** (3.17 g, 11.7 mmol, 78%) as a colorless liquid.

**R<sub>f</sub>(SI-5)** = 0.13 (PE/EtOAc 1:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.35 (dt, <sup>3</sup>J<sub>9,8</sub> = 7.1 Hz, <sup>4</sup>J<sub>9,P</sub> = 0.9 Hz, 6 H, 9-H), 4.14 (dq, <sup>3</sup>J<sub>8,P</sub> = 7.9 Hz, <sup>3</sup>J<sub>8,9</sub> = 7.1 Hz, 4 H, 8-H), 4.71 (ddd, <sup>3</sup>J<sub>1,P</sub> = 8.4 Hz, <sup>3</sup>J<sub>1,2</sub> = 6.2 Hz, <sup>4</sup>J<sub>1,3</sub> = 1.3 Hz, 2 H, 1-H),

6.31 (dt,  $^3J_{2,3} = 15.9$  Hz,  $^3J_{2,1} = 6.2$  Hz, 1 H, 2-H), 6.69 (d,  $^3J_{3,2} = 15.8$  Hz, 1 H, 3-H), 7.27 (m, 1 H, 7-H), 7.33 (m, 2 H, 5-H/6-H), 7.40 (m, 2 H, 5-H/6-H).

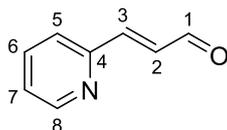
$^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 16.1$  (d,  $^3J_{9,P} = 7.1$  Hz, C-9), 63.8 (d,  $^2J_{1,P} = 5.9$  Hz, C-1), 67.9 (d,  $^2J_{8,P} = 5.1$  Hz, C-8), 123.5 (d,  $^3J_{2,P} = 6.6$  Hz, C-2), 126.6 (d, C-5/C-6), 128.1 (d, C-7), 128.6 (d, C-5/C-6), 133.9 (d, C-3), 136.0 (s, C-4).

HRMS (CI):	Calculated	Found
$\text{C}_{13}\text{H}_{19}\text{O}_4\text{P} [\text{M}]^+$	270.1015	270.1020

### (E)-3-(Pyridin-2-yl)acrylaldehyde (SI-7)

To a solution of formylmethyltriphenylphosphonium chloride (11.3 g, 33.0 mmol, 1.1 equiv) in toluene (150 mL) was added triethylamine (5.44 mL, 39.0 mmol, 1.3 equiv) and the mixture was stirred for 30 minutes at room temperature. To the mixture was then added a solution of picolinaldehyde (3.21 g, 30.0 mmol) in toluene (20 mL) and the reaction was stirred overnight. After filtration through a pad of celite the solvent was evaporated *in vacuo* and the crude product purified by column chromatography (silica, PE/EtOAc 2:1  $\rightarrow$  1:1) to afford aldehyde SI-7 (2.63 g, 19.8 mmol, 66%, 98:2 E/Z) as black crystals.

$R_f(\text{SI-7}) = 0.13$  (PE/EtOAc 2:1)



E-isomer:

$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.10$  (dd,  $^3J_{2,3} = 15.8$  Hz,  $^3J_{2,1} = 7.8$  Hz, 1 H, 2-H), 7.33 (ddd,  $^3J_{7,6} = 7.6$  Hz,  $^3J_{7,8} = 4.8$  Hz,  $^4J_{7,5} = 1.0$  Hz, 1 H, 7-H), 7.53 (d,  $^3J_{3,2} = 15.8$  Hz, 1 H, 3-H), 7.56 (d,  $^3J_{5,6} = 7.8$  Hz, 1 H, 5-H), 7.78 (td,  $^3J_{6,5/7} = 7.7$  Hz,  $^4J_{6,8} = 1.7$  Hz, 1 H, 6-H), 8.71 (dd,  $^3J_{8,7} = 4.8$  Hz,  $^4J_{8,6} = 0.7$  Hz, 1 H, 8-H), 9.80 (d,  $^3J_{1,2} = 7.8$  Hz, 1 H, 1-H).

$^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 124.1$  (d, C-5), 124.8 (d, C-7), 131.5 (d, C-2), 136.8 (d, C-6), 150.3 (d, C-8), 151.1 (d, C-3), 152.6 (s, C-4), 193.6 (d, C-1).

Z-isomer (selected signals):

$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.24$  (ddd,  $^3J_{7,6} = 7.5$  Hz,  $^3J_{7,8} = 4.8$  Hz,  $^4J_{7,5} = 0.9$  Hz, 1 H, 7-H), 7.40 (d,  $^3J_{5,6} = 7.8$  Hz, 1 H, 5-H), 7.71 (td,  $^3J_{6,5/7} = 7.7$  Hz,  $^4J_{6,8} = 1.7$  Hz, 1 H, 6-H), 8.64 (d,  $^3J_{8,7} = 4.5$  Hz, 1 H, 8-H), 9.66 (d,  $^3J_{1,2} = 7.9$  Hz, 1 H, 1-H).

$^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 123.5$  (d, C-7), 129.8 (d, C-5), 133.4 (d, C-2), 140.7 (d, C-6), 150.0 (d, C-8), 150.8 (d, C-3).

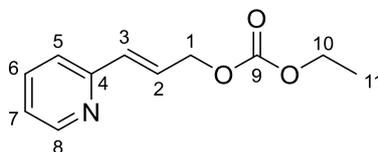
Melting point:	46–47 °C	
HRMS (CI):	Calculated	Found
$\text{C}_8\text{H}_8\text{NO} [\text{M}+\text{H}]^+$	134.0618	134.0600

### (E)-Ethyl 3-(pyridin-2-yl)allyl carbonate (SI-8)

To a solution of aldehyde **SI-7** (1.00 g, 7.51 mmol) in MeOH (22 mL) was added NaBH<sub>4</sub> (426 mg, 11.3 mmol, 1.5 equiv) at 0 °C. After stirring for 3 hours, the mixture was concentrated, the residue redissolved in water and extracted with diethylether. After drying (Na<sub>2</sub>SO<sub>4</sub>) the solvent was removed *in vacuo* and the crude product used without further purification.

The crude alcohol was dissolved in DCM (7.5 mL) and cooled to 0 °C before pyridine (911 μL, 11.3 mmol, 1.5 equiv) and ethyl chloroformate (865 μL, 9.01 mmol, 1.2 equiv) were successively added. The mixture was allowed to warm to room temperature overnight, was diluted with EtOAc, washed with sat. NaHCO<sub>3</sub> solution and brine. The organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>), the solvent removed *in vacuo* and the residue purified by column chromatography (silica, PE/EtOAc 3:2) to afford allylic carbonate **SI-8** (970 mg, 4.68 mmol, 62% over two steps) as a pale yellow oil.

R<sub>f</sub>(**SI-8**) = 0.20 (PE/EtOAc 1:1)



<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.33 (t, <sup>3</sup>J<sub>11,10</sub> = 7.2 Hz, 3 H, 11-H), 4.23 (q, <sup>3</sup>J<sub>10,11</sub> = 7.1 Hz, 2 H, 10-H), 4.85 (d, <sup>3</sup>J<sub>1,2</sub> = 4.6 Hz, 2 H, 1-H), 6.79 (m, 2 H, 2-H, 3-H), 7.16 (ddd, <sup>3</sup>J<sub>7,6</sub> = 7.5 Hz, <sup>3</sup>J<sub>7,8</sub> = 4.8 Hz, <sup>4</sup>J<sub>7,5</sub> = 0.9 Hz, 1 H, 7-H), 7.29 (d, <sup>3</sup>J<sub>5,6</sub> = 7.8 Hz, 1 H, 5-H), 7.64 (td, <sup>3</sup>J<sub>6,5/7</sub> = 7.7 Hz, <sup>4</sup>J<sub>6,8</sub> = 1.8 Hz, 1 H, 6-H), 8.57 (dd, <sup>3</sup>J<sub>8,7</sub> = 4.8 Hz, <sup>4</sup>J<sub>8,6</sub> = 0.7 Hz, 1 H, 8-H).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 14.3 (q, C-11), 64.2 (t, C-10), 67.4 (t, C-1), 122.0 (d, C-5), 122.6 (d, C-7), 127.2 (d, C-2), 133.0 (d, C-3), 136.5 (d, C-6), 149.6 (d, C-8), 154.5 (s, C-4), 155.0 (s, C-9).

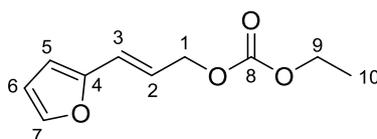
HRMS (CI):	Calculated	Found
C <sub>11</sub> H <sub>14</sub> NO <sub>3</sub> [M+H] <sup>+</sup>	208.0968	208.0970

### (E)-Ethyl 3-(furan-2-yl)allyl carbonate (SI-9)

To a solution of (*E*)-3-(furan-2-yl)acrylaldehyde (2.00 g, 16.4 mmol) in MeOH (48 mL) was added NaBH<sub>4</sub> (929 mg, 24.6 mmol, 1.5 equiv) at 0 °C. After stirring for 1 hour, the mixture was concentrated, the residue redissolved in water and extracted with diethylether. After drying (Na<sub>2</sub>SO<sub>4</sub>) the solvent was removed *in vacuo* and the crude product used without further purification.

The crude alcohol was dissolved in pyridine/DCM (2:1, 24 mL) and cooled to 0 °C before ethyl chloroformate (1.89 mL, 19.6 mmol, 1.2 equiv) was added. After 4 hours, further ethyl chloroformate (2.83 mL, 29.4 mmol, 1.8 equiv) was added, and the mixture was allowed to warm to room temperature overnight and stirred until complete consumption of the starting material was observed (TLC). The reaction was diluted with diethyl ether, washed with HCl (1 M, aq.) thrice and dried (Na<sub>2</sub>SO<sub>4</sub>). After removal of the solvent *in vacuo*, the residue was purified by column chromatography (silica, PE/EtOAc 93:7) to afford the allylic carbonate **SI-9** (3.01 g, 15.3 mmol, 94% over two steps) as a pale yellow oil.

$R_f(\text{SI-9}) = 0.27$  (PE/EtOAc 9:1)



$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.32$  (t,  $^3J_{10,9} = 7.2$  Hz, 3 H, 10-H), 4.22 (q,  $^3J_{9,10} = 7.2$  Hz, 2 H, 9-H), 4.75 (dd,  $^3J_{1,2} = 6.4$  Hz,  $^4J_{1,3} = 1.2$  Hz, 2 H, 1-H), 6.22 (dt,  $^3J_{2,3} = 15.8$  Hz,  $^3J_{2,1} = 6.4$  Hz, 1 H, 2-H), 6.29 (d,  $^3J_{5,6} = 3.3$  Hz, 1 H, 5-H), 6.37 (dd,  $^3J_{6,5} = 3.3$  Hz,  $^3J_{6,7} = 1.8$  Hz, 1 H, 6-H), 6.50 (d,  $^3J_{3,2} = 15.8$  Hz, 1 H, 3-H), 7.36 (d,  $^3J_{7,6} = 1.3$  Hz, 1 H, 7-H).

$^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 14.3$  (q, C-10), 64.1 (t, C-9), 67.7 (t, C-1), 109.1 (d, C-5), 111.3 (d, C-6), 121.0 (d, C-2), 122.5 (d, C-3), 142.5 (d, C-7), 151.7 (s, C-4), 155.0 (s, C-8).

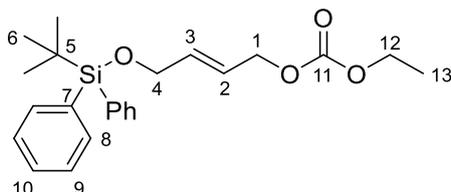
HRMS (CI):	Calculated	Found
$\text{C}_{10}\text{H}_{12}\text{O}_4$ [M] <sup>+</sup>	196.0730	196.0742

#### (E)-4-((*tert*-Butyldiphenylsilyl)oxy)but-2-en-1-yl ethyl carbonate (SI-10)<sup>[5]</sup>

To a solution of (*E*)-but-2-ene-1,4-diol (881 mg, 10.0 mmol, 2.0 equiv) in THF (40 mL) was slowly added *n*-Butyllithium (2.5 M in hexane, 2.00 mL, 5.00 mmol, 1.0 equiv) at  $-78$  °C, and the mixture was kept at the same temperature. After 1 hour, TBDPS-Cl (1.31 mL, 5.00 mmol, 1.0 equiv) was added dropwise, and the mixture was warmed to room temperature overnight. The reaction mixture was diluted with DCM and sat.  $\text{NH}_4\text{Cl}$  solution was added. The layers were separated, the aqueous layer extracted with DCM twice and the combined organic layers dried ( $\text{Na}_2\text{SO}_4$ ). After removal of the solvent *in vacuo*, the product was purified by column chromatography (silica, PE/EtOAc 85:15  $\rightarrow$  75:25) to afford the mono-protected alcohol as a colorless oil.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.07$  (s, 9 H), 4.14 (m, 2 H), 4.22 (m, 2 H), 5.78 (dtt,  $J = 15.4, 4.4, 1.3$  Hz, 1 H), 5.92 (dtt,  $J = 15.4, 5.4, 1.7$  Hz, 1 H), 7.41 (m, 6 H), 7.68 (m, 4 H). **HRMS (CI):**  $\text{C}_{20}\text{H}_{25}\text{O}_1\text{Si}$  [M-OH]<sup>+</sup> calc. 309.1669 found. 309.1671.

To a solution of the protected alcohol in pyridine/DCM (2:1, 10 mL) was added ethyl chloroformate (576  $\mu\text{L}$ , 6.00 mmol, 1.2 equiv) at 0 °C. After allowing to warm to room temperature overnight, the mixture was diluted with diethyl ether, washed with HCl (1 M, aq.) twice and dried ( $\text{Na}_2\text{SO}_4$ ). The solvent was removed *in vacuo* and the residue purified by column chromatography (silica, PE/EtOAc 95:5) to afford allylic carbonate **SI-10** (1.61 g, 4.05 mmol, 81% over two steps) as a colorless oil.

$R_f(\text{SI-10}) = 0.27$  (PE/EtOAc 9:1)



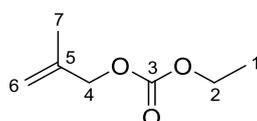
$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.06$  (s, 9 H, 6-H), 1.32 (t,  $^3J_{13,12} = 7.2$  Hz, 3 H, 13-H), 4.21 (m, 4 H, 4-H, 12-H), 4.63 (m, 2 H, 1-H), 5.90 (m, 2 H, 2-H, 3-H), 7.40 (m, 6 H, 9-H, 10-H), 7.66 (m, 4 H, 8-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 14.3 (q, C-13), 19.2 (s, C-5), 26.8 (q, C-6), 63.4 (t, C-4), 64.0 (t, C-12), 67.7 (t, C-1), 122.8 (d, C-2/C-3), 127.7 (d, C-9), 129.7 (d, C-10), 133.4 (d, C-7), 134.3 (s, C-2/C-3), 135.5 (d, C-8), 155.0 (s, C-11).

### Ethyl (2-methylallyl) carbonate (SI-11)

To a solution of methallyl alcohol (3.00 g, 41.6 mmol) in pyridine/DCM (3:1, 40 mL) was dropwise added ethyl chloroformate (7.99 mL, 83.0 mmol, 2.0 equiv) at 0 °C. The reaction mixture was warmed to room temperature overnight, diluted with diethyl ether and washed three times with HCl (1 M, aq.). The organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>), carefully evaporated *in vacuo* (40 °C, 700 mbar), and the residue was purified by column chromatography (silica, pentane/diethyl ether 95:5) to afford allylic carbonate **SI-11** (4.76 g, 33.0 mmol, 79%) as a colorless liquid.

**R<sub>f</sub>(SI-11)** = 0.50 (pentane/diethyl ether 9:1)



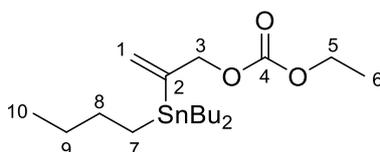
**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.32 (t, <sup>3</sup>J<sub>1,2</sub> = 7.1 Hz, 3 H, 1-H), 1.78 (s, 3 H, 7-H), 4.22 (q, <sup>3</sup>J<sub>2,1</sub> = 7.1 Hz, 2 H, 2-H), 4.55 (s, 2 H, 4-H), 4.95 (s, 1 H, 6-H<sub>a</sub>), 5.02 (s, 1 H, 6-H<sub>b</sub>).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 14.3 (q, C-1), 19.3 (q, C-7), 64.0 (t, C-2), 70.9 (t, C-4), 113.4 (t, C-6), 139.4 (s, C-5), 155.1 (s, C-3).

### Ethyl (2-(tributylstannyl)allyl) carbonate (SI-12)<sup>[6]</sup>

A preheated Schlenk flask was evacuated in high vacuum and filled with Argon. This process was repeated three times before ethyl prop-2-yn-1-yl carbonate (1.26 g, 9.83 mmol) and THF (10 mL) were added. Argon was bubbled through the solution for 5 minutes and subsequently hydroquinone (10.8 mg, 98.0 μmol, 1 mol %) and Mo(CO)<sub>3</sub>(CN-*t*-Bu)<sub>3</sub> (MoBI<sub>3</sub>) (126 mg, 293 μmol, 2 mol %) were added. Argon was bubbled through the solution for 5 minutes and the mixture was heated to 50 °C for 15 minutes. Tributylstannane (3.12 mL, 11.8 mmol, 1.2 equiv) was slowly added over 75 minutes and the mixture was stirred at 50 °C overnight. The solvent was removed under reduced pressure and the residue was purified by column chromatography (silica, PE + 1% NEt<sub>3</sub> → PE/EtOAc 99:1 + 1% NEt<sub>3</sub>) to afford vinyl stannane **SI-12** (2.26 g, 7.76 mmol, 79%, 94:6 α/β) as a colorless liquid.

**R<sub>f</sub>(SI-12)** = 0.10 (PE/EtOAc 99:1 + 1% NEt<sub>3</sub>)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.89 (t, <sup>3</sup>J<sub>10,9</sub> = 7.3 Hz, 9 H, 10-H), 0.94 (m, 6 H, 7-H), 1.31 (m, 9 H, 6-H, 9-H), 1.50 (m, 6 H, 8-H), 4.20 (q, <sup>3</sup>J<sub>5,6</sub> = 7.1 Hz, 2 H, 5-H), 4.77 (dt, <sup>3</sup>J<sub>3,Sn</sub> = 28.2 Hz, <sup>4</sup>J<sub>3,1</sub> = 1.7 Hz, 2 H, 3-H), 5.31 (dq, <sup>3</sup>J<sub>1a,Sn</sub> = 58.7 Hz, <sup>2</sup>J<sub>1a,1b</sub> = <sup>4</sup>J<sub>1a,3</sub> = 1.7 Hz, 1 H, 1-H<sub>a</sub>), 5.91 (dq, <sup>3</sup>J<sub>1b,Sn</sub> = 122.0 Hz, <sup>2</sup>J<sub>1b,1a</sub> = <sup>4</sup>J<sub>1b,3</sub> = 1.7 Hz, 1 H, 1-H<sub>b</sub>).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 9.5 (dt, <sup>1</sup>J<sub>7,Sn</sub> = 327.2 Hz, C-7), 13.7 (q, C-10), 14.3 (t, C-6), 27.3 (dt, <sup>3</sup>J<sub>9,Sn</sub> = 58.7 Hz, C-9), 29.0 (dt, <sup>2</sup>J<sub>8,Sn</sub> = 19.8 Hz, C-8), 63.8 (t, C-5), 74.0 (t, C-3), 125.6 (t, C-1), 148.8 (s, C-2), 155.1 (s, C-4).

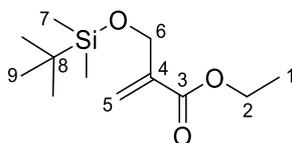
<b>HRMS (CI):</b>	Calculated	Found
C <sub>14</sub> H <sub>27</sub> O <sub>3</sub> Sn [M-C <sub>4</sub> H <sub>9</sub> ] <sup>+</sup>	363.0977	363.0942

### **Ethyl 2-(((*tert*-butyldimethylsilyl)oxy)methyl)acrylate (SI-13)<sup>[7,8]</sup>**

To a mixture of triethyl phosphonoacetate (2.24 g, 10.0 mmol) and formaldehyde (aq. 37%, 10.0 mL, 134 mmol) was added a solution of K<sub>2</sub>CO<sub>3</sub> (2.76 g, 20.0 mmol, 2.0 equiv) in 10 mL water within 15 minutes. After stirring for 30 minutes at room temperature, sat. NH<sub>4</sub>Cl solution was added, and the mixture was extracted twice with diethyl ether. The combined organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>), carefully concentrated *in vacuo* (40°C, 700 mbar) and the crude product purified by column chromatography (silica, pentane/diethyl ether 2:3) to afford ethyl 2-(hydroxymethyl)acrylate as a colorless liquid (1.14 g, 8.76 mmol, 88%).

The allylic alcohol (1.00 g, 7.68 mmol) was dissolved in DCM (15 mL) and subsequently imidazole (785 mg, 11.5 mmol, 1.5 equiv) and TBS-Cl (1.27 g, 8.45 mmol, 1.1 equiv) were added at 0 °C. After stirring for 1 hour at 0 °C, the mixture was washed with HCl (1 M, aq.), dried (Na<sub>2</sub>SO<sub>4</sub>) and the solvent removed *in vacuo*. Column chromatography (silica, PE/EtOAc 98:2 → 95:5) afforded unsaturated ester **SI-13** (1.62 g, 6.63 mmol, 86%) as a colorless liquid.

**R<sub>f</sub>(SI-13)** = 0.44 (PE/EtOAc 96:4)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.09 (s, 6 H, 7-H), 0.93 (s, 9 H, 9-H), 1.30 (t, <sup>3</sup>J<sub>1,2</sub> = 7.1 Hz, 3 H, 1-H), 4.22 (q, <sup>3</sup>J<sub>2,1</sub> = 7.1 Hz, 2 H, 2-H), 4.37 (t, <sup>4</sup>J<sub>6,5</sub> = 2.1 Hz, 2 H, 6-H), 5.90 (q, <sup>4</sup>J<sub>5a,6</sub> = <sup>2</sup>J<sub>5a,5b</sub> = 2.1 Hz, 1 H, 5-H<sub>a</sub>), 6.25 (q, <sup>4</sup>J<sub>5b,6</sub> = <sup>2</sup>J<sub>5b,5a</sub> = 2.0 Hz, 1 H, 5-H<sub>b</sub>).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = -5.4 (q, C-7), 14.2 (q, C-1), 18.3 (s, C-8), 25.9 (q, C-9), 60.5 (t, C-2/C-6), 61.5 (t, C-2/C-6), 123.6 (t, C-5), 139.9 (s, C-4), 166.0 (s, C-3).

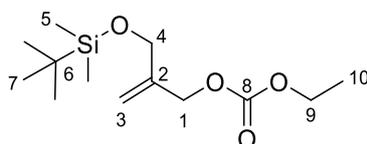
<b>HRMS (CI):</b>	Calculated	Found
C <sub>12</sub> H <sub>25</sub> O <sub>3</sub> Si [M+H] <sup>+</sup>	245.1567	245.1573

### **2-(((*tert*-Butyldimethylsilyl)oxy)methyl)allyl ethyl carbonate (SI-14)**

To a solution of **SI-13** (1.50 g, 6.14 mmol) in THF (15 mL) was added Dibal-H (1.0 M in hexane, 15.3 mL, 15.3 mmol, 2.5 equiv) at -78 °C. The mixture was stirred at -78 °C until complete consumption of the starting material was observed (TLC), and the reaction was quenched via careful addition of MeOH and sat. Na-K-tartrate solution. After warming to room temperature, the mixture was filtrated through a pad of Celite, and the aqueous layer was extracted with DCM twice. The combined organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>), the solvent removed *in vacuo*, and the crude product (1.32 g) was used without further purification.

To a solution of the crude allylic alcohol in pyridine/DCM (2:1, 10 mL) was added ethyl chloroformate (708  $\mu$ L, 7.37 mmol, 1.2 equiv) at 0 °C and the mixture was allowed to warm to room temperature overnight. After dilution with diethyl ether, the mixture was washed with HCl (1 M, aq.) twice and the organic layer was dried ( $\text{Na}_2\text{SO}_4$ ). The solvent was removed *in vacuo* and the residue purified by column chromatography (silica, PE/EtOAc 97:3) to afford the allylic carbonate **SI-14** (1.21 g, 4.42 mmol, 72% over two steps) as a colorless liquid.

$R_f(\text{SI-14}) = 0.57$  (PE/EtOAc 4:1)



$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.07$  (s, 6 H, 5-H), 0.91 (s, 9 H, 7-H), 1.31 (t,  $^3J_{10,9} = 7.2$  Hz, 3 H, 10-H), 4.18 (bs, 2-H, 4-H), 4.21 (q,  $^3J_{9,10} = 7.1$  Hz, 2 H, 9-H), 4.64 (bs, 2 H, 1-H), 5.17 (q,  $^4J_{3a,1/4} = 1.2$  Hz =  $^2J_{3a,3b} = 1.2$  Hz, 1 H, 3- $\text{H}_a$ ), 5.25 (m, 1 H, 3- $\text{H}_b$ ).

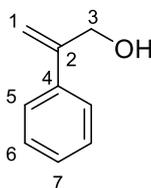
$^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = -5.5$  (q, C-5), 14.3 (q, C-10), 18.3 (s, C-6), 25.8 (q, C-7), 63.8 (t, C-4/C-9), 64.0 (t, C-4/C-9), 67.9 (t, C-1), 113.4 (t, C-3), 142.8 (s, C-2), 155.0 (s, C-8).

HRMS (CI):	Calculated	Found
$\text{C}_{13}\text{H}_{27}\text{O}_4\text{Si}$ [M+H] <sup>+</sup>	275.1673	275.1692

## 2-Phenylprop-2-en-1-ol (SI-15)<sup>[9]</sup>

Copper(I) iodide (1.91 g, 10.0 mmol, 0.5 equiv) was dried *in vacuo*, suspended in dry THF (20 mL) and prop-2-yn-1-ol (1.16 mL, 20.0 mmol) was added. After cooling to -78 °C, phenylmagnesium bromide (3 M in THF, 20.0 mL, 60.0 mmol, 3.0 equiv) was added slowly and the mixture was warmed to room temperature overnight. The reaction mixture was cooled to 0 °C, quenched with sat.  $\text{NH}_4\text{Cl}$  solution and extracted with diethyl ether thrice. The combined organic layers were washed with brine, dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated *in vacuo*. Purification via column chromatography (silica, PE/EtOAc 4:1) afforded allylic alcohol **SI-15** (1.45 g, 10.8 mmol, 54%) as a pale yellow liquid.

$R_f(\text{SI-15}) = 0.16$  (PE/EtOAc 4:1)



$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.58$  (t,  $^3J_{\text{OH},3} = 5.5$  Hz, 1 H, OH), 4.55 (d,  $^3J_{3,\text{OH}} = 5.1$  Hz, 2 H, 3-H), 5.35 (d,  $^2J_{1a,1b} = 1.2$  Hz, 1 H, 1- $\text{H}_a$ ), 5.47 (d,  $^2J_{1b,1a} = 0.7$  Hz, 1 H, 1- $\text{H}_b$ ), 7.33 (m, 3 H, 6-H, 7-H), 7.45 (m, 2 H, 5-H).

$^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 65.1$  (t, C-3), 112.6 (t, C-1), 126.1 (d, C-6), 127.9 (d, C-7), 128.5 (d, C-5), 138.5 (s, C-4), 147.3 (s, C-2).

HRMS (CI):	Calculated	Found
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C<sub>9</sub>H<sub>10</sub>O [M]<sup>+</sup>

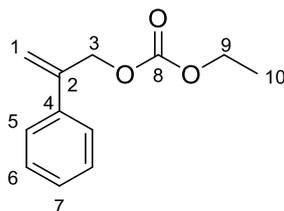
134.0726

134.0731

**Ethyl (2-phenylallyl) carbonate (SI-16)**

According to **GP-3**, alcohol **SI-15** (1.20 g, 8.94 mmol) in DCM (15 mL) was reacted with pyridine (1.09 mL, 13.4 mmol, 1.5 equiv) and ethyl chloroformate (1.03 mL, 10.7 mol, 1.2 equiv) at 0 °C. Aqueous work up and column chromatography (silica, PE/EtOAc 95:5) afforded allylic carbonate **SI-16** (1.72 g, 8.34 mmol, 93%) as a colorless liquid.

**R<sub>f</sub>(SI-16)** = 0.38 (PE/EtOAc 95:5)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.30 (t, <sup>3</sup>J<sub>10,9</sub> = 7.1 Hz, 3 H, 10-H), 4.21 (q, <sup>3</sup>J<sub>9,10</sub> = 7.1 Hz, 2 H, 9-H), 5.03 (d, <sup>4</sup>J<sub>3,1a</sub> = 0.6 Hz, 2 H, 3-H), 5.41 (d, <sup>4</sup>J<sub>1a,3</sub> = 0.9 Hz, 1 H, 1-H<sub>a</sub>), 5.47 (s, 1 H, 1-H<sub>b</sub>), 7.33 (m, 3 H, 6-H, 7-H), 7.44 (m, 2 H, 5-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 14.2 (q, C-10), 64.1 (t, C-9), 68.8 (t, C-3), 115.6 (t, C-1), 126.0 (d, C-6), 128.1 (d, C-7), 128.5 (d, C-5), 137.8 (s, C-4), 142.1 (s, C-2), 155.0 (s, C-8).

**HRMS (CI):**

Calculated

Found

C<sub>12</sub>H<sub>15</sub>O<sub>3</sub> [M+H]<sup>+</sup>

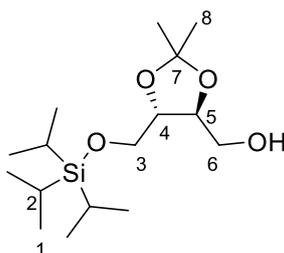
207.1016

207.1010

**((4S,5S)-2,2-Dimethyl-5-(((triisopropylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)methanol (SI-18)<sup>[10]</sup>**

To a suspension of Sodium hydride (60 w% in mineral oil, 2.40 g, 60.0 mmol, 1.2 equiv) in THF (250 mL, abs.) was added dropwise a solution of alcohol **SI-17** (7.50 g, 55.0 mmol, 1.1 equiv) in THF (25 mL, abs.) at 0 °C. The cooling bath was removed and the reaction stirred at room temperature for 1 hour. After cooling to 0 °C, a solution of TIPS-Cl (9.84 g, 50.0 mmol) in THF (25 mL, abs.) was slowly added and the reaction was stirred for 1 h. The reaction was concentrated *in vacuo*, the residue was redissolved in diethyl ether and water was added. The layers were separated, and the aqueous phase was extracted with diethyl ether twice. The combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>), and the crude product purified by column chromatography (silica, PE/EtOAc 80:20 → 50:50) to yield mono-protected alcohol **SI-18** (15.8 g, 49.6 mmol, 89%) as a colorless oil.

**R<sub>f</sub>(SI-18)** = 0.41 (PE/EtOAc 7:3)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.10 (m, 21 H, 1-H, 2-H), 1.40 (s, 3 H, 8-H), 1.42 (s, 3 H, 8-H'), 2.40 (dd, <sup>3</sup>J<sub>OH,6a</sub> = 8.3 Hz, <sup>3</sup>J<sub>OH,6b</sub> = 4.4 Hz, 1 H, OH), 3.77 (m, 3 H, 3-H<sub>a</sub>, 6-H), 3.91 (td, <sup>3</sup>J<sub>5,6</sub> = 7.6 Hz, <sup>3</sup>J<sub>5,4</sub> = 3.9 Hz, 1 H, 5-H), 3.98 (dd, <sup>2</sup>J<sub>3b,3a</sub> = 9.8 Hz, <sup>3</sup>J<sub>3b,4</sub> = 3.9 Hz, 1 H, 3-H<sub>b</sub>), 4.04 (dt, <sup>3</sup>J<sub>4,3a</sub> = 8.0 Hz, <sup>3</sup>J<sub>4,3b/5</sub> = 4.6 Hz, 1 H, 4-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.8 (d, C-2), 17.9 (q, C-1), 26.9 (q, C-8), 27.0 (q, C-8'), 62.8 (t, C-6), 64.2 (t, C-3), 78.2 (d, C-5), 80.5 (d, C-4), 109.1 (s, C-7).

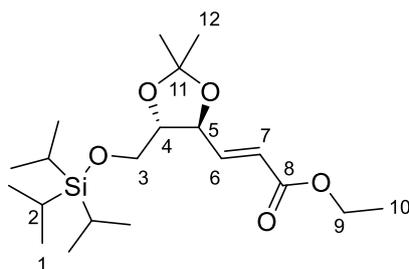
**Optical rotation:**  $[\alpha]_D^{20} = +15.6$  (c = 1.0, CHCl<sub>3</sub>)

### Ethyl (E)-3-((4S,5S)-2,2-dimethyl-5-(((triisopropylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)acrylate (SI-19)

To a solution of oxalyl chloride (2.10 ml, 24.0 mmol, 1.6 equiv) in dry DCM (60 mL) was added a solution of DMSO (3.19 ml, 45.0 mmol, 3.0 equiv) in dry DCM (12 mL) at -70 °C over 30 minutes. After complete addition, the reaction was stirred for 10 min before a solution of **SI-18** (4.78 g, 15.0 mmol) in dry DCM (15 mL) was added dropwise at -70 °C over 30 minutes. The reaction was then stirred at -70 °C for 30 min before triethylamine (10.5 ml, 75.0 mmol, 5.0 equiv) was slowly added at -70 °C. The mixture was stirred at -70 °C for 30 minutes before being warmed to room temperature over 1 hour. The reaction was diluted with diethyl ether, washed twice with HCl (1 M, aq.) and brine. After drying (MgSO<sub>4</sub>) the solvent was removed *in vacuo* and the crude aldehyde was used without further purification.

To a solution of crude aldehyde (4.75 g, 15.0 mmol) in DCM (75 mL) was added triethyl phosphonoacetate (3.60 ml, 18.0 mmol, 1.2 equiv) and KOtBu (1.85 g, 16.5 mmol, 1.1 equiv) at 0 °C. After warming to room temperature overnight, the mixture was washed with sat. sodium bicarbonate solution, HCl (1 M, sat. with NaCl) and dried (MgSO<sub>4</sub>). The solvent was evaporated *in vacuo*, and the residue purified by column chromatography (silica, PE/EtOAc 96:4) to afford unsaturated ester **SI-19** (5.16 g, 13.4 mmol, 89%) as a colorless oil.

**R<sub>f</sub>(SI-19)** = 0.11 (PE/EtOAc 98:2)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.10 (m, 21 H, 1-H, 2-H), 1.29 (t, <sup>3</sup>J<sub>10,9</sub> = 7.1 Hz, 3 H, 10-H), 1.43 (s, 3 H, 12-H), 1.44 (s, 3 H, 12-H'), 3.83 (m, 2 H, 3-H), 3.95 (q, <sup>3</sup>J<sub>4,3/5</sub> = 6.5 Hz, 1 H, 4-H), 4.20 (q, <sup>3</sup>J<sub>9,10</sub> = 7.1 Hz, 2 H, 9-H), 4.57 (t, <sup>3</sup>J<sub>5,4/6</sub> = 7.5 Hz, 1 H, 5-H), 6.13 (dd, <sup>3</sup>J<sub>7,6</sub> = 15.7 Hz, <sup>4</sup>J<sub>7,5</sub> = 1.5 Hz, 1 H, 7-H), 6.98 (dd, <sup>3</sup>J<sub>6,7</sub> = 15.7 Hz, <sup>3</sup>J<sub>6,5</sub> = 5.0 Hz, 1 H, 6-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.8 (d, C-2), 14.2 (q, C-10), 17.9 (q, C-1), 26.8 (q, C-12), 26.9 (q, C-12'), 60.4 (t, C-9), 63.4 (t, C-3), 78.1 (d, C-5), 80.8 (d, C-4), 109.8 (s, C-11), 121.8 (d, C-7), 144.8 (d, C-6), 166.1 (s, C-8).

**Optical rotation:**  $[\alpha]_D^{20} = -3.1$  (c = 1.0, CHCl<sub>3</sub>)

**HRMS (CI):** Calculated Found

C<sub>20</sub>H<sub>39</sub>O<sub>5</sub>Si [M+H]<sup>+</sup>

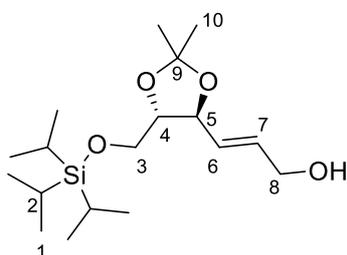
387.2561

387.2565

**(E)-3-((4S,5S)-2,2-Dimethyl-5-(((triisopropylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)prop-2-en-1-ol (SI-20)**

To a solution of **SI-19** (2.00 g, 5.17 mmol) in abs. DCM (15 mL) was dropwise added a solution of Dibal-H (1.0 M in hexane, 11.9 mL, 11.90 mmol, 2.3 equiv) at -78°C. The solution turned yellow and after 1 minute turned colorless again, which indicates full conversion. After further stirring for 15 minutes, a solution of sat. Na-K-tartrate was added and the mixture was warmed to room temperature. The mixture was extracted with EtOAc twice, the combined organic layer was dried (MgSO<sub>4</sub>) and the solvent evaporated *in vacuo*. Column chromatography of the crude product (silica, PE/EtOAc 7:3) afforded allylic alcohol **SI-20** (1.70 g, 4.93 mmol, 95%) as a colorless oil.

**R<sub>f</sub>(SI-20)** = 0.25 (PE/EtOAc 7:3)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.10 (m, 21 H, 1-H, 2-H), 1.42 (s, 3 H, 10-H), 1.43 (s, 3 H, 10-H'), 1.52 (bs, 1 H, OH), 3.78 (m, 1 H, 4-H), 3.85 (m, 2 H, 3-H), 4.17 (dd, <sup>3</sup>J<sub>8,7</sub> = 5.1 Hz, <sup>4</sup>J<sub>8,6</sub> = 1.4 Hz, 2 H, 8-H), 4.45 (t, <sup>3</sup>J<sub>5,4/6</sub> = 7.5 Hz, 1 H, 5-H), 5.86 (ddt, <sup>3</sup>J<sub>6,7</sub> = 15.5 Hz, <sup>3</sup>J<sub>6,5</sub> = 7.1 Hz, <sup>4</sup>J<sub>6,8</sub> = 1.6 Hz, 1 H, 6-H), 5.94 (dtd, <sup>3</sup>J<sub>7,6</sub> = 15.5 Hz, <sup>3</sup>J<sub>7,8</sub> = 5.1 Hz, <sup>4</sup>J<sub>7,5</sub> = 0.9 Hz, 1 H, 7-H).

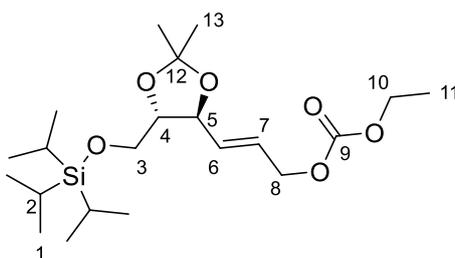
**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.8 (d, C-2), 11.9 (d, C-2'), 17.9 (q, C-1), 17.9 (q, C-1'), 26.9 (q, C-10), 27.1 (q, C-10'), 62.9 (t, C-3/C-8), 62.9 (t, C-3/C-8), 78.6 (d, C-5), 81.4 (d, C-4), 109.0 (s, C-9), 128.5 (d, C-6), 133.2 (d, C-7).

**Optical rotation:**  $[\alpha]_D^{20} = -4.5$  (c = 1.0, CHCl<sub>3</sub>)

**(E)-3-((4S,5S)-2,2-Dimethyl-5-(((triisopropylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)allyl ethyl carbonate (SI-21)**

According to **GP-3**, alcohol **SI-20** (1.50 g, 4.35 mmol) in DCM (10 mL) was treated with pyridine (528 μL, 6.53 mmol, 1.5 equiv) and ethyl chloroformate (502 μL, 5.22 mmol, 1.2 equiv) at 0 °C. After aqueous work up, the crude residue was purified by column chromatography (silica, PE/EtOAc 92:8) to afford **SI-21** (1.56 g, 3.74 mmol, 86%) as a colorless oil.

**R<sub>f</sub>(SI-21)** = 0.12 (PE/EtOAc 94:6)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.18 (m, 21 H, 1-H, 2-H), 1.31 (t, <sup>3</sup>J<sub>11,10</sub> = 7.1 Hz, 3 H, 11-H), 1.41 (s, 3 H, 13-H), 1.42 (s, 3 H, 13-H'), 3.78 (m, 1 H, 4-H), 3.83 (dd, <sup>2</sup>J<sub>3a,3b</sub> = 10.5 Hz, <sup>3</sup>J<sub>3a,4</sub> = 4.3 Hz, 1 H, 3-H<sub>a</sub>), 3.86 (dd, <sup>2</sup>J<sub>3b,3a</sub> = 10.5 Hz, <sup>3</sup>J<sub>3b,4</sub> = 4.2 Hz, 1 H, 3-H<sub>b</sub>), 4.20 (q, <sup>3</sup>J<sub>10,11</sub> = 7.1 Hz, 2 H, 10-H), 4.44 (dd, <sup>3</sup>J<sub>5,4</sub> = 7.6 Hz, <sup>3</sup>J<sub>5,6</sub> = 6.3 Hz, 1 H, 5-H), 4.63 (d, <sup>3</sup>J<sub>8,7</sub> = 5.3 Hz, 2 H, 8-H), 5.86 (dd, <sup>3</sup>J<sub>6,7</sub> = 15.7 Hz, <sup>3</sup>J<sub>6,5</sub> = 6.0 Hz, 1 H, 6-H), 5.94 (dt, <sup>3</sup>J<sub>7,6</sub> = 15.7 Hz, <sup>3</sup>J<sub>7,8</sub> = 5.3 Hz, 1 H, 7-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.9 (d, C-2), 14.3 (q, C-11), 17.9 (q, C-1), 26.9 (q, C-13), 27.0 (q, C-13'), 63.0 (t, C-3), 64.0 (t, C-10), 67.1 (t, C-8), 78.3 (d, C-5), 81.3 (d, C-4), 109.2 (s, C-12), 126.6 (d, C-7), 132.2 (d, C-6), 154.9 (s, C-9).

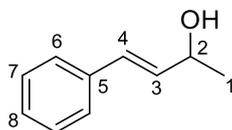
**Optical rotation:**  $[\alpha]_D^{20} = -1.7$  (c = 1.0, CHCl<sub>3</sub>)

<b>HRMS (CI):</b>	Calculated	Found
C <sub>21</sub> H <sub>40</sub> O <sub>6</sub> Si [M+H] <sup>+</sup>	416.2589	416.2586

#### **(E)-4-Phenylbut-3-en-2-ol (SI-22)**<sup>[11]</sup>

To a 500 mL three-necked flask containing Mg-turnings (2.92 g, 120 mmol, 1.2 equiv) was added a solution of methyl iodide (8.72 g, 140 mmol, 1.4 equiv) in dry diethyl ether (100 mL) at a rate at which gentle reflux of the reaction mixture occurred. After complete addition, the mixture was stirred until all magnesium was dissolved, after which a solution of cinnamaldehyde (12.6 g, 100 mmol) in dry diethyl ether (100 mL) was added. After complete conversion (TLC) the reaction was cooled to 0 °C and sat. NH<sub>4</sub>Cl solution was carefully added. The aqueous layer was extracted with diethyl ether twice, the organic layers were combined and washed with sat. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution. After drying (Na<sub>2</sub>SO<sub>4</sub>), the solvent was removed *in vacuo*, and the residue purified by column chromatography (silica, PE/EtOAc 2:1) to afford alcohol **SI-22** (14.7 g, 99.2 mmol, 99%) as a colorless oil.

**R<sub>f</sub>(SI-22)** = 0.31 (pentane/diethyl ether 1:1)



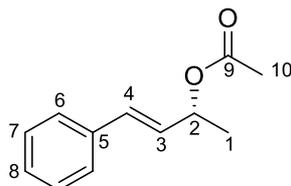
**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.38 (d, <sup>3</sup>J<sub>1,2</sub> = 6.4 Hz, 3 H, 1-H), 1.61 (bs, 1 H, OH), 4.50 (quint, <sup>3</sup>J<sub>2,1/3</sub> = 6.4 Hz, 1 H, 2-H), 6.26 (dd, <sup>3</sup>J<sub>3,4</sub> = 15.9 Hz, <sup>3</sup>J<sub>3,2</sub> = 6.4 Hz, 1 H, 3-H), 6.57 (d, <sup>3</sup>J<sub>4,3</sub> = 15.9 Hz, 1 H, 4-H), 7.24 (t, <sup>3</sup>J<sub>8,7</sub> = 7.2 Hz, 1 H, 8-H), 7.32 (t, <sup>3</sup>J<sub>7,8/6</sub> = 7.4 Hz, 2 H, 7-H), 7.38 (d, <sup>3</sup>J<sub>6,7</sub> = 7.4 Hz, 2 H, 6-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 23.4 (q, C-1), 69.0 (d, C-2), 126.4 (d, C-6), 127.6 (d, C-8), 128.6 (d, C-7), 129.4 (d, C-4), 133.5 (d, C-3), 136.7 (s, C-5).

**(S,E)-4-Phenylbut-3-en-2-ol (SI-23) and (R,E)-4-Phenylbut-3-en-2-yl acetate (SI-24)**<sup>[12]</sup>

To a solution of **SI-22** (12.0 g, 81.0 mmol) in vinyl acetate (80 mL) was added Novozym 435<sup>®</sup> and the mixture was shaken at room temperature for 5 hours. The enzyme was filtered off, washed with diethyl ether and the filtrate was evaporated *in vacuo*. Column chromatography (silica, PE/EtOAc 7:1 → 2:1) afforded alcohol **SI-23** (5.72 g, 38.6 mmol, 48%, 97% ee) as colorless crystals and acetate **SI-24** (7.45 g, 39.1 mmol, 48%, > 99% ee, determined from the corresponding alcohol after saponification) as a colorless liquid.

**R<sub>f</sub>(SI-24)** = 0.45 (PE/EtOAc 4:1)



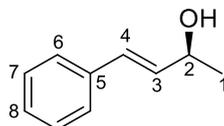
**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.41 (d, <sup>3</sup>J<sub>1,2</sub> = 6.5 Hz, 3 H, 1-H), 2.07 (s, 3 H, 10-H), 5.53 (quint, <sup>3</sup>J<sub>2,1/3</sub> = 6.5 Hz, 1 H, 2-H), 6.19 (dd, <sup>3</sup>J<sub>3,4</sub> = 16.0 Hz, <sup>3</sup>J<sub>3,2</sub> = 6.7 Hz, 1 H, 3-H), 6.60 (d, <sup>3</sup>J<sub>4,3</sub> = 15.9 Hz, 1 H, 4-H), 7.25 (m, 1 H, 8-H), 7.31 (m, 2 H, 7-H), 7.38 (m, 2 H, 6-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 20.4 (q, C-1), 21.4 (q, C-10), 71.0 (d, C-2), 126.5 (d, C-6), 127.9 (d, C-8), 128.5 (d, C-7), 128.8 (d, C-3), 131.5 (d, C-4), 136.2 (s, C-5), 170.3 (s, C-9).

**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = +149.2^{\circ}$  (c = 1.0, CHCl<sub>3</sub>)

<b>HRMS (CI)</b>	calculated	found
C <sub>12</sub> H <sub>14</sub> O <sub>2</sub> [M] <sup>+</sup>	190.0988	190.0999

**R<sub>f</sub>(SI-23)** = 0.19 (PE/EtOAc 4:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.38 (d, <sup>3</sup>J<sub>1,2</sub> = 6.4 Hz, 3 H, 1-H), 1.60 (bs, 1 H, OH), 4.50 (quint, <sup>3</sup>J<sub>2,1/3</sub> = 6.4 Hz, 1 H, 2-H), 6.26 (dd, <sup>3</sup>J<sub>3,4</sub> = 15.9 Hz, <sup>3</sup>J<sub>3,2</sub> = 6.2 Hz, 1 H, 3-H), 6.57 (d, <sup>3</sup>J<sub>4,3</sub> = 15.9 Hz, 1 H, 4-H), 7.24 (t, <sup>3</sup>J<sub>8,7</sub> = 7.4 Hz, 1 H, 8-H), 7.32 (t, <sup>3</sup>J<sub>7,8/6</sub> = 7.4 Hz, 2 H, 7-H), 7.38 (d, <sup>3</sup>J<sub>6,7</sub> = 7.4 Hz, 2 H, 6-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 23.4 (q, C-1), 69.0 (d, C-2), 126.4 (d, C-6), 127.6 (d, C-8), 128.6 (d, C-7), 129.4 (d, C-4), 133.5 (d, C-3), 136.7 (s, C-5).

**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = -37.7^{\circ}$  (c = 1.0, CHCl<sub>3</sub>)

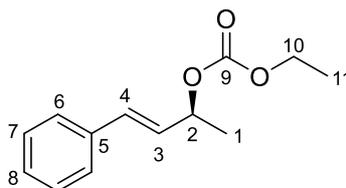
**Melting point:** 52–53 °C

<b>HRMS (CI)</b>	calculated	found
C <sub>10</sub> H <sub>12</sub> O [M] <sup>+</sup>	148.0883	148.0884

### (2*S*,3*E*)-4-Phenylbut-3-en-2-ethylcarbonate (SI-(*S*)-25)

To a solution of alcohol **SI-23** (1.48 g, 10.0 mmol) in pyridine (10 mL) was added ethyl chloroformate (1.90 mL, 20.0 mmol, 2.0 equiv) at 0 °C. The mixture was allowed to warm to room temperature overnight, diluted with EtOAc and washed with HCl (1 M, aq.) twice. After drying (Na<sub>2</sub>SO<sub>4</sub>) the solvent was removed *in vacuo* and the residue purified by column chromatography (silica, PE/EtOAc 20:1) to afford allylic carbonate **SI-(*S*)-25** (2.07 g, 9.40 mmol, 94%) as a colorless liquid.

R<sub>f</sub>(**SI-(*S*)-25**) = 0.25 (PE/EtOAc 20:1)



<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.31 (t, <sup>3</sup>J<sub>11,10</sub> = 7.1 Hz, 3 H, 11-H), 1.47 (d, <sup>3</sup>J<sub>1,2</sub> = 6.5 Hz, 3 H, 1-H), 4.20 (q, <sup>3</sup>J<sub>10,11</sub> = 7.2 Hz, 2 H, 10-H), 5.37 (quint, <sup>3</sup>J<sub>2,1/3</sub> = 6.5 Hz, 1 H, 2-H), 6.20 (dd, <sup>3</sup>J<sub>3,4</sub> = 15.9 Hz, <sup>3</sup>J<sub>3,2</sub> = 7.0 Hz, 1 H, 3-H), 6.65 (d, <sup>3</sup>J<sub>4,3</sub> = 16.0 Hz, 1 H, 4-H), 7.25 (m, 1 H, 8-H), 7.32 (m, 2 H, 7-H), 7.39 (m, 2 H, 6-H).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 14.3 (q, C-11), 20.5 (q, C-1), 63.8 (t, C-10), 75.0 (d, C-2), 126.6 (d, C-6), 128.0 (d, C-8), 128.1 (d, C-3), 128.6 (d, C-7), 132.2 (d, C-4), 136.2 (s, C-5), 154.5 (s, C-9).

Optical rotation:  $[\alpha]_D^{20} = -128.4^\circ$  (c = 1.0, CHCl<sub>3</sub>)

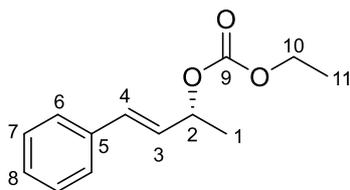
HRMS (CI)	calculated	found
C <sub>13</sub> H <sub>16</sub> O <sub>3</sub> [M] <sup>+</sup>	220.1094	220.1099

### (2*R*,3*E*)-4-Phenylbut-3-en-2-ethylcarbonate (SI-(*R*)-25)

To a solution of acetate **SI-24** (2.85 g, 15.0 mmol) in H<sub>2</sub>O/MeOH (2:1, 5 mL) was added KOH (1.03 g, 18.4 mmol, 1.2 equiv) and the mixture was stirred at 60 °C for 3 hours. The mixture was diluted with water, extracted with EtOAc thrice and the combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>). After removal of the solvent *in vacuo*, the allylic alcohol (2.24 g, 15.0 mmol, quant.) was obtained as slightly yellow crystals. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.37 (d, J = 6.4 Hz, 3 H), 1.73 (bs, 1 H), 4.48 (quintd, J = 6.4, 0.9 Hz, 1 H), 6.26 (dd, J = 15.9, 6.4 Hz, 1 H), 6.56 (d, J = 16.0 Hz, 1 H), 7.23 (m, 1 H), 7.31 (t, J = 7.4 Hz, 2 H), 7.37 (m, 2 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 23.4, 69.0, 126.4, 127.6, 128.6, 129.4, 133.5, 136.7.

To a solution of the allylic alcohol (445 mg, 3.00 mmol) in pyridine (3 mL) was added ethyl chloroformate (571 μL, 6.00 mmol, 2.0 equiv) at 0 °C. The mixture was allowed to warm to room temperature overnight, diluted with EtOAc and washed with HCl (1 M, aq.) twice. After drying (Na<sub>2</sub>SO<sub>4</sub>), the solvent was removed *in vacuo* and the residue purified by column chromatography (silica, PE/EtOAc 20:1) to afford allylic carbonate **SI-(*R*)-25** (617 mg, 2.80 mmol, 93%) as a colorless liquid.

R<sub>f</sub>(**SI-(*R*)-25**) = 0.25 (PE/EtOAc 20:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.31 (t, <sup>3</sup>J<sub>11,10</sub> = 7.1 Hz, 3 H, 11-H), 1.47 (d, <sup>3</sup>J<sub>1,2</sub> = 6.5 Hz, 3 H, 1-H), 4.20 (q, <sup>3</sup>J<sub>10,11</sub> = 7.2 Hz, 2 H, 10-H), 5.37 (quint, <sup>3</sup>J<sub>2,1/3</sub> = 6.5 Hz, 1 H, 2-H), 6.20 (dd, <sup>3</sup>J<sub>3,4</sub> = 15.9 Hz, <sup>3</sup>J<sub>3,2</sub> = 7.0 Hz, 1 H, 3-H), 6.65 (d, <sup>3</sup>J<sub>4,3</sub> = 16.0 Hz, 1 H, 4-H), 7.25 (m, 1 H, 8-H), 7.32 (m, 2 H, 7-H), 7.39 (m, 2 H, 6-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 14.3 (q, C-11), 20.5 (q, C-1), 63.8 (t, C-10), 75.0 (d, C-2), 126.6 (d, C-6), 128.0 (d, C-8), 128.1 (d, C-3), 128.6 (d, C-7), 132.2 (d, C-4), 136.2 (s, C-5), 154.5 (s, C-9).

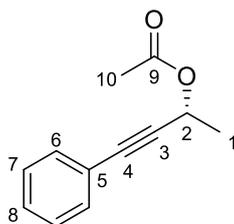
**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = +134.8^\circ$  (c = 1.0, CHCl<sub>3</sub>)

#### **(R)-4-Phenylbut-3-yn-2-yl acetate (SI-26)**<sup>[13,14]</sup>

To a solution of phenyl acetylene (2.24 mL, 20.0 mmol) in THF (40 mL) was rapidly added *n*-butyllithium (2.5 M in hexane, 8.40 mL, 21.0 mmol, 1.05 equiv) at  $-70^\circ\text{C}$ . After 30 minutes, acetaldehyde (1.69 mL, 30.0 mmol, 1.5 equiv) was added to the deep black solution of the lithium acetylide. During the addition the color changed from black to yellow and the mixture was stirred at  $-60^\circ\text{C}$  and room temperature for 30 minutes, respectively. The reaction was hydrolyzed by addition of sat. NH<sub>4</sub>Cl solution and the aqueous layer was extracted with EtOAc twice. After drying (Na<sub>2</sub>SO<sub>4</sub>) of the combined organic layers, the solvent was removed *in vacuo* and the residue purified by column chromatography (silica, PE/EtOAc 85:15) to afford the allylic alcohol (2.79 g, 19.1 mmol, 95%) as a pale yellow oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.56 (d, *J* = 6.5 Hz, 3 H), 1.89 (d, *J* = 5.4 Hz, 1 H), 4.76 (dq, *J* = 6.5, 5.4 Hz, 1 H), 7.31 (m, 3 H), 7.43 (m, 2 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 24.4, 58.9, 84.0, 90.9, 122.6, 128.3, 128.4, 131.6.

To a solution of 4-phenylbut-3-yn-2-ol (2.50 g, 17.1 mmol) in vinyl acetate (16 mL) was added Novozym 435<sup>®</sup> and the resulting mixture was shaken for 4 hours at room temperature. The enzyme was filtered off, the filtrate concentrated *in vacuo* and the residue purified by column chromatography (silica, PE/EtOAc 95:5 → 80:20) to afford acetate **SI-26** (1.50 g, 7.97 mmol, 47%, 97% ee) and the corresponding *S*-alcohol **SI-(S)-27** (1.20 g, 48%, 8.22 mmol, > 99% ee) as colorless liquids.

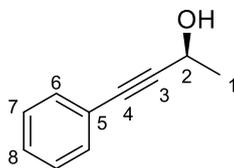
**R<sub>f</sub>(SI-26)** = 0.34 (PE/EtOAc 9:1), **R<sub>f</sub>(SI-(S)-27)** = 0.11 (PE/EtOAc 9:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.58 (d, <sup>3</sup>J<sub>1,2</sub> = 6.7 Hz, 3 H, 1-H), 2.11 (s, 3 H, 10-H), 5.69 (q, <sup>3</sup>J<sub>2,1</sub> = 6.6 Hz, 1 H, 2-H), 7.35 (m, 5 H, 6-H, 7-H, 8-H).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 21.1 (q, C-1/C-10), 21.5 (q, C-1/C-10), 60.8 (d, C-2), 84.5 (s, C-4), 87.4 (s, C-3), 122.2 (s, C-5), 128.2 (d, C-6/C-7), 128.6 (d, C-8), 131.9 (d, C-6/C-7), 170.0 (s, C-9).

<b>HRMS (CI):</b>	Calculated	Found
C <sub>12</sub> H <sub>13</sub> O <sub>2</sub> [M+H] <sup>+</sup>	189.0910	189.0904



<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.56 (d, <sup>3</sup>J<sub>1,2</sub> = 6.6 Hz, 3 H, 1-H), 1.91 (d, <sup>3</sup>J<sub>OH,2</sub> = 3.3 Hz, 1 H, OH), 4.76 (m, 1 H, 2-H), 7.31 (m, 3 H, 6-H, 8-H), 7.43 (m, 2 H, 7-H).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 24.4 (q, C-1), 58.9 (d, C-2), 84.0 (s, C-4), 90.9 (s, C-3), 122.6 (s, C-5), 128.3 (d, C-6/C-7), 128.4 (d, C-8), 131.6 (d, C-6/C-7).

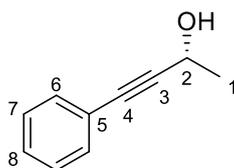
**Optical rotation:**  $[\alpha]_D^{20} = -34.2$  (c = 1.0, CHCl<sub>3</sub>)

<b>HRMS (CI):</b>	Calculated	Found
C <sub>10</sub> H <sub>10</sub> O [M] <sup>+</sup>	146.0726	146.0728

#### **(R)-4-Phenylbut-3-yn-2-ol (SI-(R)-27)**

To a solution of **SI-26** (1.30 g, 6.91 mmol) in THF/EtOH (3:1, 20 mL) was added LiOH (1 M, 13.8 mL, 13.8 mmol, 2.0 equiv) and the mixture was stirred at room temperature until complete consumption of the acetate was observed (TLC). The mixture was diluted with water and extracted with EtOAc twice. After drying (Na<sub>2</sub>SO<sub>4</sub>), the solvent was evaporated *in vacuo*, and the residue purified by column chromatography (silica, PE/EtOAc 4:1) to afford alcohol **SI-(R)-27** (1.01 g, 6.91 mmol, quant.) as a pale yellow liquid.

R<sub>f</sub>(**SI-(R)-27**) = 0.11 (PE/EtOAc 9:1)



<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.56 (d, <sup>3</sup>J<sub>1,2</sub> = 6.6 Hz, 3 H, 1-H), 1.91 (d, <sup>3</sup>J<sub>OH,2</sub> = 3.3 Hz, 1 H, OH), 4.76 (m, 1 H, 2-H), 7.31 (m, 3 H, 6-H, 8-H), 7.43 (m, 2 H, 7-H).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 24.4 (q, C-1), 58.9 (d, C-2), 84.0 (s, C-4), 90.9 (s, C-3), 122.6 (s, C-5), 128.3 (d, C-6/C-7), 128.4 (d, C-8), 131.6 (d, C-6/C-7).

**Optical rotation:**  $[\alpha]_D^{20} = +31.0$  (c = 1.0, CHCl<sub>3</sub>)

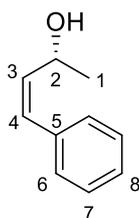
<b>HRMS (CI):</b>	Calculated	Found
C <sub>10</sub> H <sub>10</sub> O [M] <sup>+</sup>	146.0726	146.0726

### (*R,Z*)-4-Phenylbut-3-en-2-ol (SI-28)

To a solution of **SI-(*R*)-27** (850 mg, 5.81 mmol) in MeOH (15 mL) was added quinoline (225 mg, 1.74 mmol) and Lindlar catalyst (85 mg, 10 w%) and the mixture was stirred at room temperature for 10 h under an atmosphere of hydrogen (balloon). After filtration through a pad of celite, the solvent was removed *in vacuo*, and the residue purified by column chromatography (silica, PE/EtOAc 9:1 → 4:1) to afford *Z*-allylic alcohol **SI-28** (827 mg, 5.58 mmol, 96%) as a pale yellow liquid.

The corresponding (*S*)-alcohol was prepared likewise (98%).

$R_f(\text{SI-28}) = 0.11$  (PE/EtOAc 9:1)



$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.37$  (d,  $^3J_{1,2} = 6.2$  Hz, 3 H, 1-H), 1.53 (bs, 1 H, OH), 4.79 (m, 1 H, 2-H), 5.70 (dd,  $^3J_{3,4} = 11.6$  Hz,  $^3J_{3,2} = 9.1$  Hz, 1 H, 3-H), 6.51 (d,  $^3J_{4,3} = 11.6$  Hz, 1 H, 4-H), 7.26 (m, 3 H, 6-H, 8-H), 7.35 (m, 2 H, 7-H).

$^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 23.6$  (q, C-1), 64.2 (d, C-2), 127.2 (d, C-8), 128.3 (d, C-7), 128.7 (d, C-6), 130.1 (d, C-4), 135.6 (d, C-3), 136.6 (s, C-5).

**Optical rotation:**  $[\alpha]_D^{20} = -6.0$  ( $c = 1.0$ ,  $\text{CHCl}_3$ )

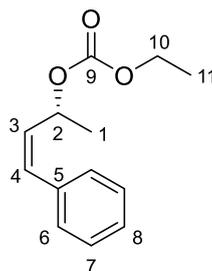
<b>HRMS (CI):</b>	Calculated	Found
$\text{C}_{10}\text{H}_{12}\text{O} [\text{M}]^+$	148.0883	148.0899

### (*R,Z*)-Ethyl (4-phenylbut-3-en-2-yl) carbonate (SI-29)

To a solution of alcohol **SI-28** (650 mg, 4.39 mmol) in DCM was added pyridine (532  $\mu\text{L}$ , 6.58 mmol, 1.5 equiv) and ethyl chloroformate (505  $\mu\text{L}$ , 5.26 mmol, 1.2 equiv) at 0 °C and the mixture was stirred at room temperature until complete consumption of the starting material was observed (TLC). The mixture was diluted with diethyl ether, washed with water and dried ( $\text{Na}_2\text{SO}_4$ ). After removal of the solvent *in vacuo* the residue was purified by column chromatography (silica, PE/EtOAc 95:5) to yield allylic carbonate **SI-29** (920 mg, 4.18 mmol, 95%) as a colorless liquid.

The corresponding (*S*)-carbonate was prepared likewise (92%).

$R_f(\text{SI-29}) = 0.37$  (PE/EtOAc 9:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.29 (t,  $^3J_{11,10}$  = 7.2 Hz, 3 H, 11-H), 1.44 (d,  $^3J_{1,2}$  = 6.1 Hz, 3 H, 1-H), 4.16 (q,  $^3J_{10,11}$  = 7.1 Hz, 2 H, 10-H), 5.67 (m, 2 H, 2-H, 3-H), 6.57 (d,  $^3J_{4,3}$  = 10.4 Hz, 1 H, 4-H), 7.27 (m, 3 H, 6-H, 8-H), 7.35 (m, 2 H, 7-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 14.2 (q, C-11), 20.8 (q, C-1), 63.8 (t, C-10), 71.5 (d, C-2), 127.4 (d, C-8), 128.4 (d, C-7), 128.6 (d, C-6), 130.8 (d, C-3), 131.3 (d, C-4), 136.1 (s, C-5), 154.3 (s, C-9).

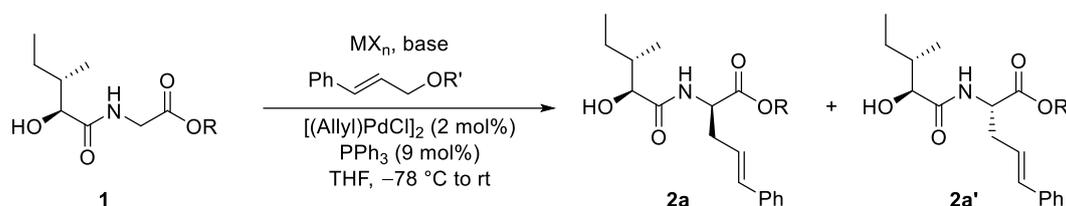
**Optical rotation:**  $[\alpha]_D^{20}$  = -55.5 (c = 1.0, CHCl<sub>3</sub>)

<b>HRMS (CI):</b>	Calculated	Found
C <sub>13</sub> H <sub>18</sub> O <sub>3</sub> [M+2H] <sup>+</sup>	222.1250	222.1246

## 4. Allylic Alkylation

Table 1 shows some of the initial optimization of several reaction parameters in the allylic alkylation, starting from the conditions used for peptides (entry 1). During the investigation we observed the formation of the opposite diastereomer when a large excess of LHMDS was used. Variation of ester functionality (entry 13, 15+16), leaving group (17-19) and metal salts (20-22) led to the best results with LHMDS (5.5 equiv) and ClTi(OiPr)<sub>3</sub> (1.5 equiv).

**Tab. 1:** Selected Examples for Reaction Optimization.



entry	Base (equiv)	MX <sub>n</sub> (equiv)	R	R'	<i>dr</i>	Y [%]
1	LHMDS (3.5)	ZnCl <sub>2</sub> (1.1)	<i>t</i> Bu	CO <sub>2</sub> Et	62/38	53
2	LHMDS (3.5)	Al(OiPr) <sub>3</sub> (1.1)	<i>t</i> Bu	CO <sub>2</sub> Et	64/36	54
3	LHMDS (3.5)	Ti(OiPr) <sub>4</sub> (1.1)	<i>t</i> Bu	CO <sub>2</sub> Et	74/26	64
4	LHMDS (3.5)	ClTi(OiPr) <sub>3</sub> (1.1)	<i>t</i> Bu	CO <sub>2</sub> Et	72/28	76
5	LHMDS (3.5)	ClTi(OiPr) <sub>3</sub> (1.5)	<i>t</i> Bu	CO <sub>2</sub> Et	73/27	84
6	LDA (3.5)	ClTi(OiPr) <sub>3</sub> (1.5)	<i>t</i> Bu	CO <sub>2</sub> Et	90/10	53
7	LDA (3.2)	ClTi(OiPr) <sub>3</sub> (1.5)	<i>t</i> Bu	CO <sub>2</sub> Et	98/2	67
8	LDA (3.1)	ClTi(OiPr) <sub>3</sub> (1.5)	<i>t</i> Bu	CO <sub>2</sub> Et	99/1	70
9	LDA (3.0)	ClTi(OiPr) <sub>3</sub> (1.5)	<i>t</i> Bu	CO <sub>2</sub> Et	99/1	71 <sup>a</sup>
10	LHMDS (3.0)	ClTi(OiPr) <sub>3</sub> (1.5)	<i>t</i> Bu	CO <sub>2</sub> Et	53/47	91
11	LHMDS (4.0)	ClTi(OiPr) <sub>3</sub> (1.5)	<i>t</i> Bu	CO <sub>2</sub> Et	38/62	46
12	LHMDS (4.5)	ClTi(OiPr) <sub>3</sub> (1.5)	<i>t</i> Bu	CO <sub>2</sub> Et	14/86	50
13	LHMDS (5.5)	ClTi(OiPr) <sub>3</sub> (1.5)	<i>t</i> Bu	CO <sub>2</sub> Et	12/88	82
14	LHMDS (6.5)	ClTi(OiPr) <sub>3</sub> (1.5)	<i>t</i> Bu	CO <sub>2</sub> Et	13/87	71
15	LHMDS (5.5)	ClTi(OiPr) <sub>3</sub> (1.5)	Me	CO <sub>2</sub> Me	47/53	41
16	LHMDS (5.5)	ClTi(OiPr) <sub>3</sub> (1.5)	Bn	CO <sub>2</sub> Et	25/75	29
17	LHMDS (5.5)	ClTi(OiPr) <sub>3</sub> (1.5)	<i>t</i> Bu	Ac	/	no rct
18	LHMDS (5.5)	ClTi(OiPr) <sub>3</sub> (1.5)	<i>t</i> Bu	Bz	18/82	43
19	LHMDS (5.5)	ClTi(OiPr) <sub>3</sub> (1.5)	<i>t</i> Bu	PO(OEt) <sub>2</sub>	23/77	47
20	LHMDS (5.5)	Ti(OiPr) <sub>4</sub> (1.5)	<i>t</i> Bu	CO <sub>2</sub> Et	14/86	52
21	LHMDS (5.5)	ZnCl <sub>2</sub> (1.5)	<i>t</i> Bu	CO <sub>2</sub> Et	51/49	71
22	LHMDS (5.5)	Al(OiPr) <sub>3</sub> (1.5)	<i>t</i> Bu	CO <sub>2</sub> Et	66/34	39

diastereomer ratios (*dr*) were determined by NMR and/or HPLC analysis, <sup>a</sup>not reproducible

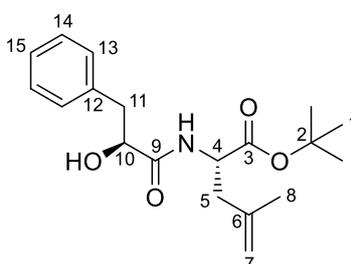
## 4.1 Determination of the absolute configuration in Allylic Alkylations

### *tert*-Butyl (*S*)-2-((*S*)-2-hydroxy-3-phenylpropanamido)-4-methylpent-4-enoate (**SI-30**)

According to general procedure A for allylic alkylation, **1e** (84.0 mg, 300  $\mu$ mol), LHMDS (1.65 mL, 1.65 mmol, 1.0 M in THF, 5.5 equiv), chlorotitanium(IV) triisopropoxide (450  $\mu$ L, 450  $\mu$ mol, 1.0 M in hexane, 1.5 equiv), carbonate **SI-11** (29.0 mg, 201  $\mu$ mol, 0.7 equiv), allylpalladiumchloride dimer (2.2 mg, 6.00  $\mu$ mol, 2 mol %) and triphenylphosphine (7.1 mg, 27.0  $\mu$ mol, 9 mol %) were reacted at  $-78$   $^{\circ}$ C. Column chromatography (silica, DCM/Et<sub>2</sub>O 9:1) afforded (*S,S*)-**SI-30** (37.1 mg, 111  $\mu$ mol, 55%) as a white solid and (*S,R*)-**SI-30** (13.8 mg, 41.0  $\mu$ mol, 21%) as a pale yellow solid separately.

$R_f$ ((*S,R*)-**SI-30**) = 0.28 (DCM/Et<sub>2</sub>O 9:1),  $R_f$ ((*S,S*)-**SI-30**) = 0.18 (DCM/Et<sub>2</sub>O 9:1)

Main diastereomer (*S,S*):



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.45 (s, 9 H, 1-H), 1.72 (s, 3 H, 8-H), 2.33 (dd,  $^2J_{5a,5b}$  = 13.8 Hz,  $^3J_{5a,4}$  = 8.0 Hz, 1 H, 5-H<sub>a</sub>), 2.45 (dd,  $^2J_{5b,5a}$  = 13.9 Hz,  $^3J_{5b,4}$  = 6.0 Hz, 1 H, 5-H<sub>b</sub>), 2.85 (dd,  $^2J_{11a,11b}$  = 13.9 Hz,  $^3J_{11a,10}$  = 8.3 Hz, 1 H, 11-H<sub>a</sub>), 2.96 (d,  $^3J_{OH,10}$  = 4.9 Hz, 1 H, OH), 3.19 (dd,  $^2J_{11b,11a}$  = 13.9 Hz,  $^3J_{11b,10}$  = 3.9 Hz, 1 H, 11-H<sub>b</sub>), 4.31 (dt,  $^3J_{10,11a}$  = 8.8 Hz,  $^3J_{10,11b/OH}$  = 4.2 Hz, 1 H, 10-H), 4.54 (td,  $^3J_{4,5a/NH}$  = 7.9 Hz,  $^3J_{4,5b}$  = 6.2 Hz, 1 H, 4 H), 4.66 (s, 1 H, 7-H<sub>a</sub>), 4.78 (s, 1 H, 7-H<sub>b</sub>), 6.95 (d,  $^3J_{NH,4}$  = 7.8 Hz, 1 H, NH), 7.23 (m, 3 H, 13-H, 15-H), 7.30 (m, 2 H, 14-H).

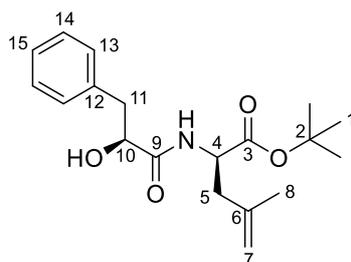
**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 21.9 (q, C-8), 27.9 (q, C-1), 40.7 (t, C-5/C-11), 40.8 (t, C-5/C-11), 50.5 (d, C-4), 72.8 (d, C-10), 82.2 (s, C-2), 114.4 (t, C-7), 126.8 (d, C-15), 128.5 (d, C-14), 129.6 (d, C-13), 137.0 (s, C-12), 140.5 (s, C-6), 171.2 (s, C-3), 172.5 (s, C-9).

**Optical rotation:**  $[\alpha]_D^{20}$  =  $-44.8$  (c = 1.0, CHCl<sub>3</sub>)

**Melting point:** 79-81  $^{\circ}$ C

<b>HRMS (CI):</b>	Calculated	Found
C <sub>19</sub> H <sub>28</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	334.2013	334.2015

Minor diastereomer (*S,R*):



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.46 (s, 9 H, 1-H), 1.77 (s, 3 H, 8-H), 2.39 (dd, <sup>2</sup>J<sub>5a,5b</sub> = 13.9 Hz, <sup>3</sup>J<sub>5a,4</sub> = 7.9 Hz, 1 H, 5-H<sub>a</sub>), 2.45 (d, <sup>3</sup>J<sub>OH,10</sub> = 4.6 Hz, 1 H, OH), 2.52 (dd, <sup>2</sup>J<sub>5b,5a</sub> = 13.9 Hz, <sup>3</sup>J<sub>5b,4</sub> = 6.1 Hz, 1 H, 5-H<sub>b</sub>), 2.86 (dd, <sup>2</sup>J<sub>11a,11b</sub> = 14.0 Hz, <sup>3</sup>J<sub>11a,10</sub> = 9.1 Hz, 1 H, 11-H<sub>a</sub>), 3.25 (dd, <sup>2</sup>J<sub>11b,11a</sub> = 14.1 Hz, <sup>3</sup>J<sub>11b,10</sub> = 3.8 Hz, 1 H, 11-H<sub>b</sub>), 4.29 (dt, <sup>3</sup>J<sub>10,11a</sub> = 9.0 Hz, <sup>3</sup>J<sub>10,11b/OH</sub> = 4.3 Hz, 1 H, 10-H), 4.59 (td, <sup>3</sup>J<sub>4,5a/NH</sub> = 7.9 Hz, <sup>3</sup>J<sub>4,5b</sub> = 6.3 Hz, 1 H, 4-H), 4.73 (s, 1 H, 7-H<sub>a</sub>), 4.83 (s, 1 H, 7-H<sub>b</sub>), 6.87 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.8 Hz, 1 H, NH), 7.25 (m, 3 H, 13-H, 15-H), 7.32 (m, 2 H, 14-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 21.9 (q, C-8), 28.0 (q, C-1), 40.9 (t, C-5/C-11), 40.9 (t, C-5/C-11), 50.7 (d, C-4), 72.9 (d, C-10), 82.2 (s, C-2), 114.4 (t, C-7), 127.0 (d, C-15), 128.8 (d, C-14), 129.4 (d, C-13), 136.8 (s, C-12), 140.7 (s, C-6), 170.9 (s, C-3), 172.1 (s, C-9).

**Optical rotation:**  $[\alpha]_D^{20} = -74.0$  (c = 1.0, CHCl<sub>3</sub>)

**Melting point:** 75-77 °C

<b>HRMS (CI):</b>	Calculated	Found
C <sub>19</sub> H <sub>28</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	334.2013	334.2017

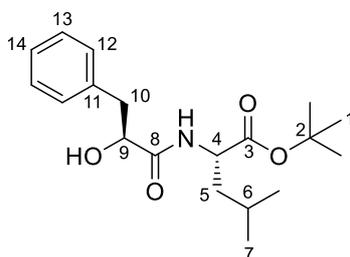
### ***tert*-Butyl ((*S*)-2-hydroxy-3-phenylpropanoyl)-*L*-leucinate (**SI-31**)**

**Preparation of reference sample:** According to **GP-2**, (*S*)-2-hydroxy-3-phenylpropanoic acid (74.3 mg, 447 μmol, 1.0 equiv), HCl-*L*-Leu-OtBu (100 mg, 447 μmol, 1.0 equiv), HOBT (75.0 mg, 492 μmol, 1.1 equiv), DIPEA (164 μL, 939 μmol, 2.1 equiv) and EDC·HCl (94.0 mg, 492 μmol, 1.1 equiv) were reacted at 0 °C. Column chromatography (silica, PE/EtOAc 2:1) afforded hydroxy acid dipeptide **SI-31** (132 mg, 394 μmol, 88%) as a white solid.

**Preparation of SI-31 by Allylic Alkylation and Hydrogenation:** To a solution of (*S,S*)-**SI-30** (20.0 mg, 60.0 μmol) in MeOH (1 mL) was added Pd/C (2.0 mg, 10 w%) and the mixture was stirred under an atmosphere of hydrogen (balloon) overnight. After filtration over celite, the solvent was removed *in vacuo* to afford (*S,S*)-**SI-31** (20.1 mg, 59.9 μmol, quant.) as a white solid.

For analytical purposes the second diastereomer was equally transformed to the saturated derivative.

**R<sub>f</sub>(SI-(*S,S*)-31)** = 0.26 (PE/EtOAc 2:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.91 (d, <sup>3</sup>J<sub>7,6</sub> = 6.2 Hz, 3 H, 7-H), 0.92 (d, <sup>3</sup>J<sub>7,6</sub> = 6.1 Hz, 3 H, 7-H'), 1.46 (s, 9 H, 1-H), 1.52 (m, 3 H, 5-H, 6-H), 2.51 (bs, 1 H, OH), 2.92 (dd, <sup>2</sup>J<sub>10a,10b</sub> = 13.9 Hz, <sup>3</sup>J<sub>10a,9</sub> = 8.1 Hz, 1 H, 10-H<sub>a</sub>), 3.22 (dd, <sup>2</sup>J<sub>10b,10a</sub> = 13.9 Hz, <sup>3</sup>J<sub>10b,9</sub> = 3.9 Hz, 1 H, 10-H<sub>b</sub>), 4.35 (dd, <sup>3</sup>J<sub>9,10a</sub> = 8.1 Hz, <sup>3</sup>J<sub>9,10b</sub> = 3.9 Hz, 1 H, 9-H), 4.48 (td, <sup>3</sup>J<sub>4,5a/NH</sub> = 8.7 Hz, <sup>3</sup>J<sub>4,5b</sub> = 5.2 Hz, 1 H, 4-H), 6.84 (d, <sup>3</sup>J<sub>NH,4</sub> = 8.2 Hz, 1 H, NH), 7.26 (m, 3 H, 12-H, 14-H), 7.32 (m, 2 H, 13-H).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 22.0 (q, C-7), 22.8 (q, C-7'), 24.8 (d, C-6), 28.0 (q, C-1), 40.7 (t, C-10), 41.7 (t, C-5), 50.9 (d, C-4), 72.8 (d, C-9), 81.9 (s, C-2), 126.9 (d, C-14), 128.6 (d, C-13), 129.6 (d, C-12), 136.7 (s, C-11), 172.1 (s, C-3/C-8), 172.2 (s, C-3/C-8).

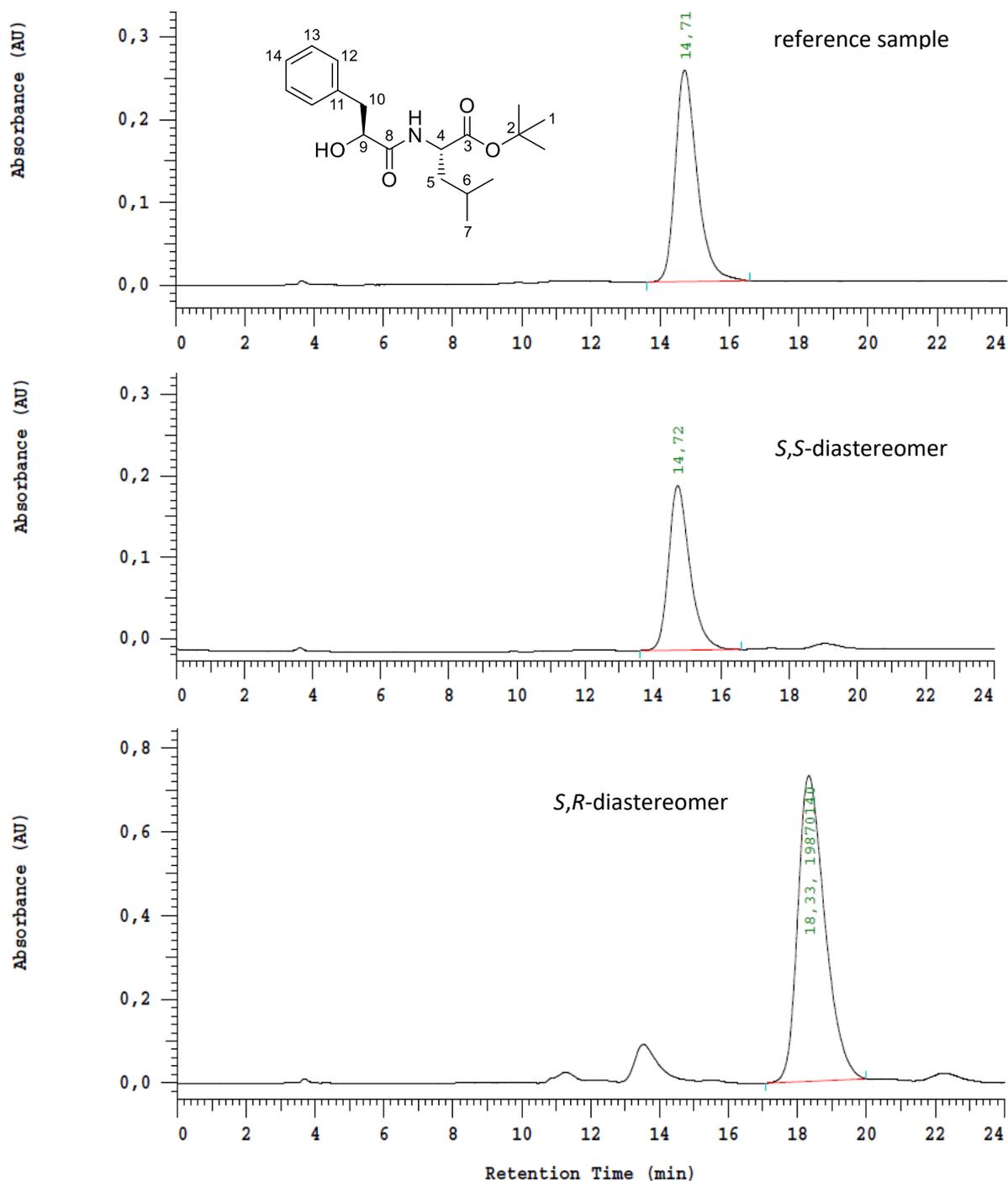
**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = -71.1$  (c = 1.0, CHCl<sub>3</sub>)

**Melting point:** 99-101 °C

<b>HRMS (CI):</b>	Calculated	Found
C <sub>19</sub> H <sub>30</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	336.2169	336.2174

## HPLC comparison

By HPLC and NMR comparison of the reference sample with both diastereomers obtained from allylic alkylation the configuration of these diastereomers could be assigned. The main diastereomer obtained by allylic alkylation with 3.1 equiv LDA possesses (*S,R*)-configuration while the use of 5.5 equiv LHMDS results in formation of the (*S,S*) diastereomer.

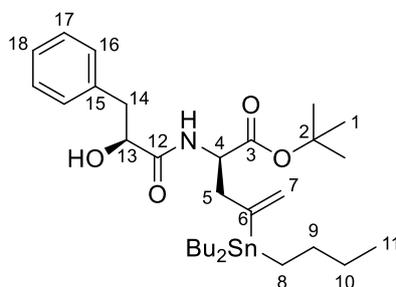


## 4.2 Allylic Alkylation in 2.0-4.0 mmol scale

### *tert*-Butyl (R)-2-((S)-2-hydroxy-3-phenylpropanamido)-4-(tributylstannyl)pent-4-enoate (2eh)

According to general procedure B for allylic alkylation, **1e** (1.00 g, 3.58 mmol), chlorotitanium(IV) triisopropoxide (5.37 mL, 5.37 mmol, 1.0 M in hexane, 1.5 equiv), DIPA (1.63 mL, 11.5 mmol, 3.2 equiv), *n*-BuLi (4.44 mL, 11.1 mmol, 3.1 equiv), ethyl carbonate **SI-12** (1.12 g, 2.40 mmol, 0.7 equiv), [AllylPdCl]<sub>2</sub> (52.0 mg, 143 μmol, 4 mol %) and PPh<sub>3</sub> (169 mg, 644 μmol, 18 mol %) in THF (36 mL) were reacted at -78 °C. Column chromatography (silica, PE/DCM/Et<sub>2</sub>O 5/5/1 + 1 % NEt<sub>3</sub>) afforded **2eh** (979 mg, 1.61 mmol, 67 %, > 99:1 *dr*) as a colorless oil.

R<sub>f</sub>(**2eh**) = 0.47 (PE/DCM/Et<sub>2</sub>O 5/5/2 + 1 % NEt<sub>3</sub>)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.90 (t, <sup>3</sup>J<sub>11,10</sub> = 7.3 Hz, 9 H, 11-H), 0.98 (m, 6 H, 8-H), 1.32 (sext, <sup>3</sup>J<sub>10,9/11</sub> = 7.3 Hz, 6 H, 10-H), 1.46 (s, 9 H, 1-H), 1.50 (m, 6 H, 9-H), 2.46 (m, 1 H, OH), 2.48 (dd, <sup>2</sup>J<sub>5a,5b</sub> = 14.0 Hz, <sup>3</sup>J<sub>5a,4</sub> = 9.1 Hz, 1 H, 5-H<sub>a</sub>), 2.78 (dd, <sup>2</sup>J<sub>5b,5a</sub> = 14.1 Hz, <sup>3</sup>J<sub>5b,4</sub> = 5.3 Hz, 1 H, 5-H<sub>b</sub>), 2.86 (dd, <sup>2</sup>J<sub>14a,14b</sub> = 14.0 Hz, <sup>3</sup>J<sub>14a,13</sub> = 9.2 Hz, 1 H, 14-H<sub>a</sub>), 3.26 (dd, <sup>2</sup>J<sub>14b,14a</sub> = 14.0 Hz, <sup>3</sup>J<sub>14b,13</sub> = 3.7 Hz, 1 H, 14-H<sub>b</sub>), 4.26 (dd, <sup>3</sup>J<sub>13,14a</sub> = 9.2 Hz, <sup>3</sup>J<sub>13,14b</sub> = 3.7 Hz, 1 H, 13-H), 4.41 (ddd, <sup>3</sup>J<sub>4,5a</sub> = 8.8 Hz, <sup>3</sup>J<sub>4,NH</sub> = 7.8 Hz, <sup>3</sup>J<sub>4,5b</sub> = 5.4 Hz, 1 H, 4-H), 5.24 (dd, <sup>3</sup>J<sub>7a,Sn</sub> = 58.2 Hz, <sup>2</sup>J<sub>7a,7b</sub> = 2.1 Hz, 1 H, 7-H<sub>a</sub>), 5.73 (d, <sup>3</sup>J<sub>7b,Sn</sub> = 128.1 Hz, 1 H, 7-H<sub>b</sub>), 6.74 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.5 Hz, 1 H, NH), 7.25 (m, 3 H, 16-H, 18-H), 7.32 (m, 2 H, 17-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 9.6 (dt, <sup>1</sup>J<sub>8,Sn</sub> = 320.0 Hz, C-8), 13.7 (q, C-11), 27.3 (dt, <sup>3</sup>J<sub>10,Sn</sub> = 58.0 Hz, C-10), 28.0 (q, C-1), 29.0 (dt, <sup>2</sup>J<sub>9,Sn</sub> = 19.8 Hz, C-9), 40.9 (t, C-14), 43.9 (dt, <sup>2</sup>J<sub>5,Sn</sub> = 40.4 Hz, C-5), 52.1 (dd, <sup>3</sup>J<sub>4,Sn</sub> = 11.0 Hz, C-4), 72.9 (d, C-13), 81.9 (s, C-2), 127.0 (d, C-18), 128.4 (dt, <sup>2</sup>J<sub>7,Sn</sub> = 24.2 Hz, C-7), 128.8 (d, C-17), 129.5 (d, C-16), 136.9 (s, C-15), 150.0 (s, C-6), 171.0 (s, C-3), 172.1 (s, C-12).

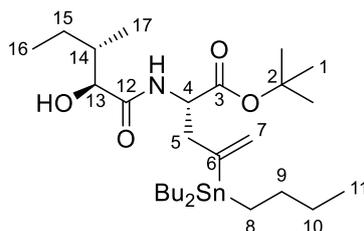
**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = -49.2$  (c = 1.0, CHCl<sub>3</sub>)

HRMS (CI):	Calculated	Found
C <sub>30</sub> H <sub>52</sub> NO <sub>4</sub> Sn [M+H] <sup>+</sup>	610.2913	610.2912

**tert-Butyl (S)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-(tributylstannyl)pent-4-enoate (2ah')**

According to general procedure A for allylic alkylation, **1c** (1.50 g, 6.11 mmol, 1.0 equiv), chlorotitanium(IV) triisopropoxide (9.17 mL, 9.17 mmol, 1.0 M in hexane, 1.5 equiv), LHMDS (33.6 mL, 33.6 mmol, 1.0 M in THF, 5.5 equiv), stannylated carbonate **SI-12** (1.91 g, 4.10 mmol, 0.7 equiv), allylpalladiumchloride dimer (89.0 mg, 245  $\mu$ mol, 4 mol %) and triphenylphosphine (289 mg, 1.10 mmol, 18 mol %) in THF (60 mL) were reacted at  $-78$  °C. After column chromatography (silica, DCM/Et<sub>2</sub>O 9:1 + 1 % NEt<sub>3</sub>), vinylstannane **6b** (1.40 g, 2.43 mmol, 59 %, 97:3 dr) was obtained as a pale yellow oil.

**R<sub>f</sub>(6b)** = 0.21 (DCM/Et<sub>2</sub>O 9:1 + 1 % NEt<sub>3</sub>)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.90 (t,  $^3J_{11,10} = ^3J_{16,15} = 7.4$  Hz, 12 H, 11-H, 16-H), 0.96 (m, 9 H, 8-H, 17-H), 1.17 (m, 1 H, 15-H<sub>a</sub>), 1.32 (sext,  $^3J_{10,9/11} = 7.3$  Hz, 6 H, 10-H), 1.46 (s, 9 H, 1-H), 1.49 (m, 7 H, 9-H, 15-H<sub>b</sub>), 1.85 (m, 1 H, 14-H), 2.48 (dd,  $^2J_{5a,5b} = 14.1$  Hz,  $^3J_{5a,4} = 9.4$  Hz, 1 H, 5-H<sub>a</sub>), 2.78 (dd,  $^2J_{5b,5a} = 14.1$  Hz,  $^3J_{5b,4} = 4.8$  Hz, 1 H, 5-H<sub>b</sub>), 3.21 (d,  $^3J_{OH,13} = 5.3$  Hz, 1 H, OH), 4.00 (dd,  $^3J_{13,OH} = 5.3$  Hz,  $^3J_{13,14} = 3.7$  Hz, 1 H, 13-H), 4.39 (ddd,  $^3J_{4,5a} = 9.3$  Hz,  $^3J_{4,NH} = 7.4$  Hz,  $^3J_{4,5b} = 5.0$  Hz, 1 H, 4-H), 5.24 (dd,  $^3J_{7a,Sn} = 59.1$  Hz,  $^2J_{7a,7b} = 2.0$  Hz, 1 H, 7-H<sub>a</sub>), 5.73 (d,  $^3J_{7b,Sn} = 128.4$  Hz, 1 H, 7-H<sub>b</sub>), 6.74 (d,  $^3J_{NH,4} = 7.3$  Hz, 1 H, NH).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 9.6 (dt,  $^1J_{8,Sn} = 320.0$  Hz, C-8), 11.8 (q, C-16), 13.7 (q, C-11), 15.5 (q, C-17), 23.2 (t, C-15), 27.3 (dt,  $^3J_{10,Sn} = 57.2$  Hz, C-10), 28.0 (q, C-1), 29.0 (dt,  $^2J_{9,Sn} = 20.5$  Hz, C-9), 38.6 (d, C-14), 43.9 (dt,  $^2J_{5,Sn} = 40.4$  Hz, C-5), 52.0 (dd,  $^3J_{4,Sn} = 11.7$  Hz, C-4), 76.2 (d, C-13), 82.0 (s, C-2), 128.3 (dt,  $^2J_{7,Sn} = 24.2$  Hz, C-7), 150.1 (s, C-6), 171.7 (s, C-3), 173.1 (s, C-12).

**Optical rotation:**  $[\alpha]_D^{20} = -3.5$  (c = 0.5, CHCl<sub>3</sub>)

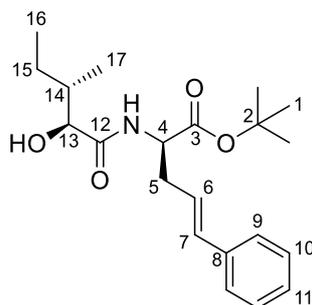
HRMS (CI):	Calculated	Found
C <sub>27</sub> H <sub>53</sub> NO <sub>4</sub> Sn [M] <sup>+</sup>	575.2997	575.2996

### 4.3 Scope of Allylic Alkylation

#### *tert*-Butyl (*R,E*)-2-((*2S,3S*)-2-hydroxy-3-methylpentanamido)-5-phenylpent-4-enoate (**2aa**)

According to general procedure B for allylic alkylation, **1c** (71.0 mg, 289  $\mu\text{mol}$ ), chlorotitanium(IV) triisopropoxide (434  $\mu\text{L}$ , 434  $\mu\text{mol}$ , 1.0 M in hexane, 1.5 equiv), DIPA (132  $\mu\text{L}$ , 926  $\mu\text{mol}$ , 3.2 equiv), *n*-BuLi (359  $\mu\text{L}$ , 897  $\mu\text{mol}$ , 3.1 equiv), cinnamyl ethyl carbonate (40.0 mg, 194  $\mu\text{mol}$ , 0.7 equiv), [AllylPdCl]<sub>2</sub> (2.1 mg, 5.8  $\mu\text{mol}$ , 2 mol %) and PPh<sub>3</sub> (6.8 mg, 26.0  $\mu\text{mol}$ , 9 mol %) in THF (3 mL) were reacted at  $-78^\circ\text{C}$ . After column chromatography (silica, DCM/Et<sub>2</sub>O 9:1), **2aa** (49.8 mg, 138  $\mu\text{mol}$ , 71%, > 99:1 dr) was obtained as an off white solid.

R<sub>f</sub>(**2aa**) = 0.26 (DCM/diethyl ether 9:1)



<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.85 (t, <sup>3</sup>J<sub>16,15</sub> = 7.5 Hz, 3 H, 16-H), 0.99 (d, <sup>3</sup>J<sub>17,14</sub> = 6.8 Hz, 3 H, 17-H'), 1.20 (m, 1 H, 15-H<sub>a</sub>), 1.41 (m, 1 H, 15-H<sub>b</sub>), 1.47 (s, 9 H, 1-H), 1.83 (dqt, <sup>3</sup>J<sub>14,15a</sub> = 10.1 Hz, <sup>3</sup>J<sub>14,17</sub> = 6.8 Hz, <sup>3</sup>J<sub>14,13/15b</sub> = 3.6 Hz, 1 H, 14-H), 2.69 (d, <sup>3</sup>J<sub>OH,13</sub> = 5.4 Hz, 1 H, OH), 2.73 (m, 2 H, 5-H), 4.01 (dd, <sup>3</sup>J<sub>13,OH</sub> = 5.3 Hz, <sup>3</sup>J<sub>13,14</sub> = 3.5 Hz, 1 H, 13-H), 4.63 (dt, <sup>3</sup>J<sub>4,NH</sub> = 7.8 Hz, <sup>3</sup>J<sub>4,5</sub> = 5.8 Hz, 1 H, 4-H), 6.06 (dt, <sup>3</sup>J<sub>6,7</sub> = 15.8 Hz, <sup>3</sup>J<sub>6,5</sub> = 7.3 Hz, 1 H, 6-H), 6.44 (d, <sup>3</sup>J<sub>7,6</sub> = 15.8 Hz, 1 H, 7-H), 6.82 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.7 Hz, 1 H, NH), 7.23 (m, 1 H, 11-H), 7.30 (m, 4 H, 9-H, 10-H).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 11.8 (q, C-16), 15.4 (q, C-17), 23.1 (t, C-15), 28.0 (q, C-1), 36.1 (t, C-5), 39.1 (d, C-14), 52.2 (d, C-4), 76.1 (d, C-13), 82.5 (s, C-2), 123.7 (d, C-6), 126.2 (d, C-9), 127.5 (d, C-11), 128.5 (d, C-10), 133.9 (d, C-7), 136.8 (s, C-8), 170.6 (s, C-3), 172.8 (s, C-12).

Optical rotation:  $[\alpha]_D^{20} = -72.4$  (c = 1.0, CHCl<sub>3</sub>)

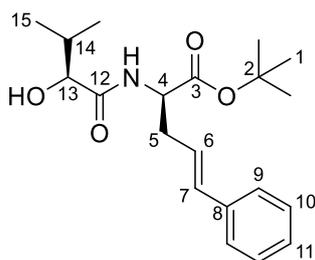
Melting point: 118–120 °C

HRMS (CI):	Calculated	Found
C <sub>21</sub> H <sub>32</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	362.2326	362.2330

#### *tert*-Butyl (*R,E*)-2-((*S*)-2-hydroxy-3-methylbutanamido)-5-phenylpent-4-enoate (**2ba**)

According to general procedure B for allylic alkylation, **1a** (67.0 mg, 289  $\mu\text{mol}$ ), chlorotitanium(IV) triisopropoxide (434  $\mu\text{L}$ , 434  $\mu\text{mol}$ , 1.0 M in hexane, 1.5 equiv), DIPA (132  $\mu\text{L}$ , 926  $\mu\text{mol}$ , 3.2 equiv), *n*-BuLi (359  $\mu\text{L}$ , 897  $\mu\text{mol}$ , 3.1 equiv), cinnamyl ethyl carbonate (40.0 mg, 194  $\mu\text{mol}$ , 0.7 equiv), [AllylPdCl]<sub>2</sub> (2.1 mg, 5.8  $\mu\text{mol}$ , 2 mol %) and PPh<sub>3</sub> (6.8 mg, 26.0  $\mu\text{mol}$ , 9 mol %) in THF (3 mL) were reacted at  $-78^\circ\text{C}$ . After column chromatography (silica, DCM/Et<sub>2</sub>O 9:1), **2ba** (49.2 mg, 142  $\mu\text{mol}$ , 73%, > 99:1 dr) was obtained as a white solid.

$R_f(\mathbf{2ba}) = 0.17$  (DCM/diethyl ether 9:1)



$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.87$  (d,  $^3J_{15,14} = 6.8$  Hz, 3 H, 15-H), 1.02 (d,  $^3J_{15',14} = 7.0$  Hz, 3 H, 15-H'), 1.47 (s, 9 H, 1-H), 2.10 (septd,  $^3J_{14,15} = 6.9$  Hz,  $^3J_{14,13} = 3.3$  Hz, 1 H, 14-H), 2.54 (d,  $^3J_{\text{OH},13} = 5.5$  Hz, 1 H, OH), 2.73 (m, 2 H, 5-H), 3.99 (dd,  $^3J_{13,\text{OH}} = 5.4$  Hz,  $^3J_{13,14} = 3.2$  Hz, 1 H, 13-H), 4.67 (dt,  $^3J_{4,\text{NH}} = 7.8$  Hz,  $^3J_{4,5} = 5.7$  Hz, 1 H, 4-H), 6.06 (dt,  $^3J_{6,7} = 15.8$  Hz,  $^3J_{6,5} = 7.3$  Hz, 1 H, 6-H), 6.45 (d,  $^3J_{7,6} = 15.8$  Hz, 1 H, 7-H), 6.76 (d,  $^3J_{\text{NH},4} = 7.6$  Hz, 1 H, NH), 7.23 (m, 1 H, 11-H), 7.30 (m, 4 H, 9-H, 10-H).

$^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 15.4$  (q, C-15), 19.1 (q, C-15'), 28.0 (q, C-1), 32.1 (d, C-14), 36.1 (t, C-5), 52.1 (d, C-4), 76.0 (d, C-13), 82.4 (s, C-2), 123.7 (d, C-6), 126.1 (d, C-9), 127.4 (d, C-11), 128.5 (d, C-10), 133.8 (d, C-7), 136.8 (s, C-8), 170.6 (s, C-3), 172.9 (s, C-12).

**Optical rotation:**  $[\alpha]_D^{20} = -72.4$  ( $c = 1.0$ ,  $\text{CHCl}_3$ )

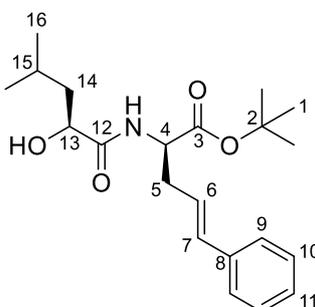
**Melting point:** 108–110 °C

<b>HRMS (CI):</b>	Calculated	Found
$\text{C}_{20}\text{H}_{30}\text{NO}_4$ $[\text{M}+\text{H}]^+$	348.2169	348.2178

### ***tert*-butyl (*R,E*)-2-((*S*)-2-hydroxy-4-methylpentanamido)-5-phenylpent-4-enoate (**2ca**)**

According to general procedure B for allylic alkylation, **1b** (71.0 mg, 289  $\mu\text{mol}$ ), chlorotitanium(IV) triisopropoxide (434  $\mu\text{L}$ , 434  $\mu\text{mol}$ , 1.0 M in hexane, 1.5 equiv), DIPA (132  $\mu\text{L}$ , 926  $\mu\text{mol}$ , 3.2 equiv), *n*-BuLi (359  $\mu\text{L}$ , 897  $\mu\text{mol}$ , 3.1 equiv), cinnamy ethyl carbonate (40.0 mg, 194  $\mu\text{mol}$ , 0.7 equiv),  $[\text{AllylPdCl}]_2$  (2.1 mg, 5.8  $\mu\text{mol}$ , 2 mol %) and  $\text{PPh}_3$  (6.8 mg, 26.0  $\mu\text{mol}$ , 9 mol %) in THF (3 mL) were reacted at  $-78$  °C. After column chromatography (silica, DCM/ $\text{Et}_2\text{O}$  9:1), **2ca** (54.0 mg, 149  $\mu\text{mol}$ , 77%, > 99:1 dr) was obtained as a colorless oil.

$R_f(\mathbf{2ca}) = 0.26$  (DCM/diethyl ether 9:1)



$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.92$  (d,  $^3J_{16,15} = 6.7$  Hz, 3 H, 16-H), 0.93 (d,  $^3J_{16',15} = 6.5$  Hz, 3 H, 16-H'), 1.47 (s, 9 H, 1-H), 1.56 (m, 2 H, 14-H), 1.84 (m, 1 H, 15-H), 2.66 (d,  $^3J_{\text{OH},13} = 5.5$  Hz, 1 H, OH), 2.72 (m, 2 H, 5-H), 4.14 (ddd,  $^3J_{13,14a} = 9.5$  Hz,  $^3J_{13,\text{OH}} = 5.4$  Hz,  $^3J_{13,14b} = 3.8$  Hz, 1 H, 13-H),

4.63 (dt,  $^3J_{4,\text{NH}} = 7.8$  Hz,  $^3J_{4,5} = 5.8$  Hz, 1 H, 4-H), 6.06 (dt,  $^3J_{6,7} = 15.8$  Hz,  $^3J_{6,5} = 7.3$  Hz, 1 H, 6-H), 6.44 (d,  $^3J_{7,6} = 15.8$  Hz, 1 H, 7-H), 6.93 (d,  $^3J_{\text{NH},4} = 7.7$  Hz, 1 H, NH), 7.23 (m, 1 H, 11-H), 7.30 (m, 4 H, 9-H, 10-H).

$^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 21.3$  (q, C-16), 23.4 (q, C-16'), 24.5 (d, C-15), 28.0 (q, C-1), 36.1 (t, C-5), 43.9 (t, C-14), 52.1 (d, C-4), 70.5 (d, C-13), 82.5 (s, C-2), 123.7 (d, C-6), 126.2 (d, C-9), 127.5 (d, C-11), 128.5 (d, C-10), 133.9 (d, C-7), 136.8 (s, C-8), 170.7 (s, C-3), 173.9 (s, C-12).

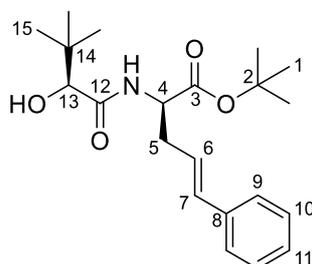
**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = -67.5$  (c = 1.0,  $\text{CHCl}_3$ )

<b>HRMS (CI):</b>	Calculated	Found
$\text{C}_{21}\text{H}_{31}\text{NO}_4$ [M+H] <sup>+</sup>	362.2326	362.2308

### ***tert*-Butyl (*R,E*)-2-((*S*)-2-hydroxy-3,3-dimethylbutanamido)-5-phenylpent-4-enoate (**2da**)**

According to general procedure B for allylic alkylation, **1d** (71.0 mg, 289  $\mu\text{mol}$ ), chlorotitanium(IV) triisopropoxide (434  $\mu\text{L}$ , 434  $\mu\text{mol}$ , 1.0 M in hexane, 1.5 equiv), DIPA (132  $\mu\text{L}$ , 926  $\mu\text{mol}$ , 3.2 equiv), *n*-BuLi (359  $\mu\text{L}$ , 897  $\mu\text{mol}$ , 3.1 equiv), cinnamy ethyl carbonate (40.0 mg, 194  $\mu\text{mol}$ , 0.7 equiv), [AllylPdCl]<sub>2</sub> (2.1 mg, 5.8  $\mu\text{mol}$ , 2 mol %) and PPh<sub>3</sub> (6.8 mg, 26.0  $\mu\text{mol}$ , 9 mol %) in THF (3 mL) were reacted at  $-78$  °C. After column chromatography (silica, DCM/Et<sub>2</sub>O 9:1), **2da** (51.0 mg, 141  $\mu\text{mol}$ , 73%, > 99:1 dr) was obtained as off white solid.

$R_f(\mathbf{2da}) = 0.26$  (DCM/diethyl ether 9:1)



$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.98$  (s, 9 H, 15-H), 1.47 (s, 9 H, 1-H), 2.68 (m, 1 H, 5-H<sub>a</sub>), 2.76 (m, 1 H, 5-H<sub>b</sub>), 3.01 (d,  $^3J_{\text{OH},13} = 5.9$  Hz, 1 H, OH), 3.71 (d,  $^3J_{13,\text{OH}} = 6.0$  Hz, 1 H, 13-H), 4.65 (dt,  $^3J_{4,\text{NH}} = 7.5$  Hz,  $^3J_{4,5} = 5.8$  Hz, 1 H, 4-H), 6.06 (dt,  $^3J_{6,7} = 15.7$  Hz,  $^3J_{6,5} = 7.3$  Hz, 1 H, 6-H), 6.45 (d,  $^3J_{7,6} = 15.7$  Hz, 1 H, 7-H), 6.65 (d,  $^3J_{\text{NH},4} = 7.5$  Hz, 1 H, NH), 7.22 (m, 1 H, 11-H), 7.29 (m, 4 H, 9-H, 10-H).

$^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 25.8$  (q, C-15), 28.0 (q, C-1), 35.1 (s, C-14), 36.1 (t, C-5), 52.4 (d, C-4), 79.4 (d, C-13), 82.5 (s, C-2), 123.8 (d, C-6), 126.1 (d, C-9), 127.5 (d, C-11), 128.5 (d, C-10), 134.0 (d, C-7), 136.8 (s, C-8), 170.6 (s, C-3), 172.0 (s, C-12).

**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = -48.0$  (c = 1.0,  $\text{CHCl}_3$ )

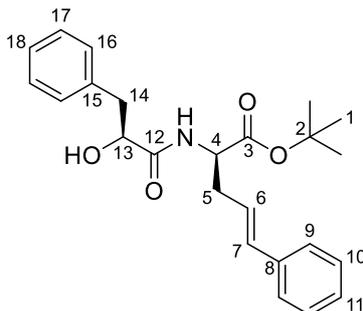
**Melting point:** 99–101 °C

<b>HRMS (CI):</b>	Calculated	Found
$\text{C}_{21}\text{H}_{31}\text{NO}_4$ [M+H] <sup>+</sup>	362.2326	362.2324

### ***tert*-Butyl (*R,E*)-2-((*S*)-2-hydroxy-3-phenylpropanamido)-5-phenylpent-4-enoate (**2ea**)**

According to general procedure B for allylic alkylation, **1e** (81.0 mg, 289  $\mu$ mol), chlorotitanium(IV) triisopropoxide (434  $\mu$ L, 434  $\mu$ mol, 1.0 M in hexane, 1.5 equiv), DIPA (132  $\mu$ L, 926  $\mu$ mol, 3.2 equiv), *n*-BuLi (359  $\mu$ L, 897  $\mu$ mol, 3.1 equiv), cinnamy ethyl carbonate (40.0 mg, 194  $\mu$ mol, 0.7 equiv), [AllylPdCl]<sub>2</sub> (2.1 mg, 5.8  $\mu$ mol, 2 mol %) and PPh<sub>3</sub> (6.8 mg, 26.0  $\mu$ mol, 9 mol %) in THF (3 mL) were reacted at -78 °C. After column chromatography (silica, DCM/Et<sub>2</sub>O 9:1), **2ea** (62.9 mg, 159  $\mu$ mol, 82%, > 99:1 dr) was obtained as an off white solid.

**R<sub>f</sub>(2ea)** = 0.29 (DCM/diethyl ether 9:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.46 (s, 9 H, 1-H), 2.53 (d, <sup>3</sup>J<sub>OH,13</sub> = 4.8 Hz, 1 H, OH), 2.69 (m, 2 H, 5-H), 2.87 (dd, <sup>2</sup>J<sub>14a,14b</sub> = 13.9 Hz, <sup>3</sup>J<sub>14a,13</sub> = 8.9 Hz, 1 H, 14-H<sub>a</sub>), 3.23 (dd, <sup>2</sup>J<sub>14b,14a</sub> = 14.0 Hz, <sup>3</sup>J<sub>14b,13</sub> = 4.1 Hz, 1 H, 14-H<sub>b</sub>), 4.30 (dt, <sup>3</sup>J<sub>13,14a</sub> = 8.9 Hz, <sup>3</sup>J<sub>13,14b/OH</sub> = 4.4 Hz, 1 H, 13-H), 4.62 (dt, <sup>3</sup>J<sub>4,NH</sub> = 7.9 Hz, <sup>3</sup>J<sub>4,5</sub> = 5.7 Hz, 1 H, 4-H), 6.03 (dt, <sup>3</sup>J<sub>6,7</sub> = 15.7 Hz, <sup>3</sup>J<sub>6,5</sub> = 7.5 Hz, 1 H, 6-H), 6.42 (d, <sup>3</sup>J<sub>7,6</sub> = 15.8 Hz, 1 H, 7-H), 7.00 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.8 Hz, 1 H, NH), 7.26 (m, 10 H, 9-H, 10-H, 11-H, 16-H, 17-H, 18-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 28.0 (q, C-1), 36.1 (t, C-5), 41.0 (t, C-14), 52.1 (d, C-4), 72.9 (d, C-13), 82.4 (s, C-2), 123.8 (d, C-6), 126.2 (d, C-9), 127.0 (d, C-11/C-18), 127.5 (d, C-11/C-18), 128.5 (d, C-10/C-17), 128.8 (d, C-10/C-17), 129.4 (d, C-16), 133.8 (d, C-7), 136.8 (s, C-15), 136.9 (s, C-8), 170.4 (s, C-3), 172.2 (s, C-12).

**Optical rotation:**  $[\alpha]_D^{20} = -85.0$  (c = 1.0, CHCl<sub>3</sub>)

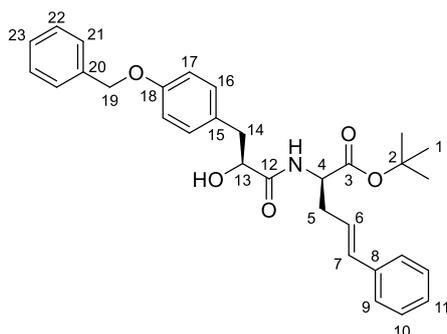
**Melting point:** 89–91 °C

<b>HRMS (CI):</b>	Calculated	Found
C <sub>24</sub> H <sub>30</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	396.2169	396.2186

### ***tert*-Butyl (*R,E*)-2-((*S*)-3-(4-(benzyloxy)phenyl)-2-hydroxypropanamido)-5-phenylpent-4-enoate (**2fa**)**

According to general procedure B for allylic alkylation, **1i** (112.0 mg, 289  $\mu$ mol), chlorotitanium(IV) triisopropoxide (435  $\mu$ L, 435  $\mu$ mol, 1.0 M in hexane, 1.5 equiv), DIPA (132  $\mu$ L, 928  $\mu$ mol, 3.2 equiv), *n*-BuLi (360  $\mu$ L, 899  $\mu$ mol, 3.1 equiv), allyl ethyl carbonate (25.3 mg, 194  $\mu$ mol, 0.7 equiv), [AllylPdCl]<sub>2</sub> (2.1 mg, 5.8  $\mu$ mol, 2 mol %) and PPh<sub>3</sub> (6.9 mg, 26.0  $\mu$ mol, 9 mol %) in THF (3 mL) were reacted at -78 °C. After column chromatography (silica, DCM/Et<sub>2</sub>O 95:5), **2fa** (67.3 mg, 134  $\mu$ mol, 69%, > 99:1 dr) was obtained as a pale yellow solid.

$R_f(\mathbf{2fa}) = 0.28$  (DCM/diethyl ether 9:1)



$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.46$  (s, 9 H, 1-H), 2.39 (d,  $^3J_{\text{OH},13} = 4.6$  Hz, 1 H, OH), 2.69 (m, 2 H, 5-H), 2.83 (dd,  $^2J_{14a,14b} = 14.1$  Hz,  $^3J_{14a,13} = 8.7$  Hz, 1 H, 14- $\text{H}_a$ ), 3.17 (dd,  $^2J_{14b,14a} = 14.1$  Hz,  $^3J_{14b,13} = 4.3$  Hz, 1 H, 14- $\text{H}_b$ ), 4.26 (dt,  $^3J_{13,14a} = 8.7$  Hz,  $^3J_{13,14b/\text{OH}} = 4.4$  Hz, 1 H, 13-H), 4.63 (dt,  $^3J_{4,\text{NH}} = 7.9$  Hz,  $^3J_{4,5} = 5.8$  Hz, 1 H, 4-H), 5.02 (s, 2 H, 19-H), 6.04 (dt,  $^3J_{6,7} = 15.8$  Hz,  $^3J_{6,5} = 7.3$  Hz, 1 H, 6-H), 6.43 (d,  $^3J_{7,6} = 15.8$  Hz, 1 H, 7-H), 6.92 (d,  $^3J_{17,16} = 8.6$  Hz, 2 H, 17-H), 6.96 (d,  $^3J_{\text{OH},13} = 7.9$  Hz, 1 H, NH), 7.15 (d,  $^3J_{16,17} = 8.6$  Hz, 2 H, 16-H), 7.30 (m, 10 H, 9-H, 10-H, 11-H, 21-H, 22-H, 23-H).

$^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 28.0$  (q, C-1), 36.1 (t, C-5), 40.1 (t, C-14), 52.1 (d, C-4), 70.0 (t, C-19), 72.9 (d, C-13), 82.4 (s, C-2), 115.2 (d, C-17), 123.8 (d, C-6), 126.2 (d, C-9), 127.4 (d, C-21), 127.5 (d, C-23), 127.9 (d, C-11), 128.5 (d, C-10/C-22), 128.6 (d, C-10/C-22), 128.8 (s, C-15), 130.5 (d, C-16), 133.8 (d, C-7), 136.9 (s, C-8/C-20), 136.9 (s, C-8/C-20), 157.9 (s, C-18), 170.4 (s, C-3), 172.2 (s, C-12).

**Optical rotation:**  $[\alpha]_D^{20} = -68.9$  ( $c = 1.0$ ,  $\text{CHCl}_3$ )

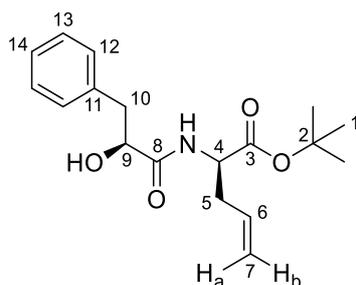
**Melting point:** 109-111 °C

<b>HRMS (CI):</b>	Calculated	Found
$\text{C}_{31}\text{H}_{35}\text{NO}_5$ $[\text{M}+\text{H}]^+$	501.2510	501.2511

### ***tert*-Butyl (*R*)-2-((*S*)-2-hydroxy-3-phenylpropanamido)pent-4-enoate (**2eb**)**

According to general procedure B for allylic alkylation, **1e** (81.0 mg, 289  $\mu\text{mol}$ ), chlorotitanium(IV) triisopropoxide (435  $\mu\text{L}$ , 435  $\mu\text{mol}$ , 1.0 M in hexane, 1.5 equiv), DIPA (132  $\mu\text{L}$ , 928  $\mu\text{mol}$ , 3.2 equiv), *n*-BuLi (360  $\mu\text{L}$ , 899  $\mu\text{mol}$ , 3.1 equiv), allyl ethyl carbonate (25.3 mg, 194  $\mu\text{mol}$ , 0.7 equiv),  $[\text{AllylPdCl}]_2$  (2.1 mg, 5.8  $\mu\text{mol}$ , 2 mol %) and  $\text{PPh}_3$  (6.9 mg, 26.0  $\mu\text{mol}$ , 9 mol %) in THF (3 mL) were reacted at  $-78$  °C. After column chromatography (silica, DCM/ $\text{Et}_2\text{O}$  95:5), **2eb** (47.0 mg, 147  $\mu\text{mol}$ , 76%, > 99:1 dr) was obtained as a colorless oil.

$R_f(\mathbf{2eb}) = 0.35$  (DCM/diethyl ether 9:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.46 (s, 9 H, 1-H), 2.52 (m, 2 H, 5-H), 2.81 (m, 1 H, OH), 2.85 (dd, <sup>2</sup>J<sub>10a,10b</sub> = 13.9 Hz, <sup>3</sup>J<sub>10a,9</sub> = 9.1 Hz, 1 H, 10-H<sub>a</sub>), 3.23 (dd, <sup>2</sup>J<sub>10b,10a</sub> = 13.9 Hz, <sup>3</sup>J<sub>10b,9</sub> = 3.9 Hz, 1 H, 10-H<sub>b</sub>), 4.29 (dt, <sup>3</sup>J<sub>9,10a</sub> = 9.1 Hz, <sup>3</sup>J<sub>9,10b/OH</sub> = 4.3 Hz, 1 H, 9-H), 4.54 (dt, <sup>3</sup>J<sub>4,NH</sub> = 8.1 Hz, <sup>3</sup>J<sub>4,5</sub> = 5.8 Hz, 1 H, 4-H), 5.10 (m, 2 H, 7-H), 5.66 (ddt, <sup>3</sup>J<sub>6,7a</sub> = 8.1 Hz, <sup>3</sup>J<sub>6,7b</sub> = 5.8 Hz, <sup>3</sup>J<sub>6,5</sub> = 8.1 Hz, 1 H, 6-H), 7.02 (d, <sup>3</sup>J<sub>NH,4</sub> = 8.0 Hz, 1 H, NH), 7.25 (m, 3 H, 12-H, 14-H), 7.31 (m, 2 H, 13-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 28.0 (q, C-1), 36.6 (t, C-5), 40.9 (t, C-10), 51.7 (d, C-4), 72.9 (d, C-9), 82.3 (s, C-2), 118.9 (t, C-7), 126.9 (d, C-14), 128.7 (d, C-13), 129.4 (d, C-12), 132.2 (d, C-6), 136.9 (s, C-11), 170.4 (s, C-3), 172.3 (s, C-8).

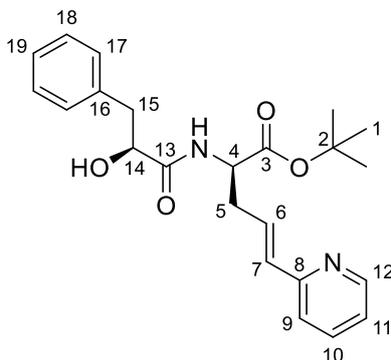
**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = -86.1$  (c = 1.0, CHCl<sub>3</sub>)

HRMS (CI):	Calculated	Found
C <sub>18</sub> H <sub>26</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	320.1856	320.1874

### **tert-Butyl (R,E)-2-((S)-2-hydroxy-3-phenylpropanamido)-5-(pyridin-2-yl)pent-4-enoate (2ec)**

According to general procedure B for allylic alkylation, **1e** (81.0 mg, 290 μmol), chlorotitanium(IV) triisopropoxide (435 μL, 435 μmol, 1.0 M in hexane, 1.5 equiv), DIPA (132 μL, 928 μmol, 3.2 equiv), *n*-BuLi (360 μL, 899 μmol, 3.1 equiv), carbonate **SI-8** (40.3 mg, 194 μmol, 0.7 equiv), [AllylPdCl]<sub>2</sub> (2.1 mg, 5.8 μmol, 2 mol %) and PPh<sub>3</sub> (6.9 mg, 26.0 μmol, 9 mol %) in THF (3 mL) were reacted at -78 °C. After reversed phase chromatography (C18-silica, H<sub>2</sub>O/MeCN 100:0 → 40:60 → 0:100), **2ec** (69.0 mg, 174 μmol, 90%, > 99:1 dr) was obtained as an off white solid.

**R<sub>f</sub>(2ec)** = 0.10 (DCM/diethyl ether 7:3)



**<sup>1</sup>H-NMR** (500 MHz, CDCl<sub>3</sub>): δ = 1.45 (s, 9 H, 1-H), 2.67 (m, 1 H, 5-H<sub>a</sub>), 2.76 (m, 1 H, 5-H<sub>b</sub>), 2.84 (dd, <sup>2</sup>J<sub>15a,15b</sub> = 13.9 Hz, <sup>3</sup>J<sub>15a,14</sub> = 9.1 Hz, 1 H, 15-H<sub>a</sub>), 3.22 (dd, <sup>2</sup>J<sub>15b,15a</sub> = 14.0 Hz, <sup>3</sup>J<sub>15b,14</sub> = 3.6 Hz, 1 H, 15-H<sub>b</sub>), 3.84 (bs, 1 H, OH), 4.30 (dd, <sup>3</sup>J<sub>14,15a</sub> = 9.1 Hz, <sup>3</sup>J<sub>14,15b</sub> = 3.8 Hz, 1 H, 14-H), 4.64 (dt, <sup>3</sup>J<sub>4,NH</sub> = 8.0 Hz, <sup>3</sup>J<sub>4,5</sub> = 6.0 Hz, 1 H, 4-H), 6.48 (m, 2 H, 6-H, 7-H), 7.07 (ddd, <sup>3</sup>J<sub>11,10</sub> = 7.5 Hz, <sup>3</sup>J<sub>11,12</sub> = 5.0 Hz, <sup>4</sup>J<sub>11,9</sub> = 1.1 Hz, 1 H, 11-H), 7.25 (m, 7 H, 9-H, 17-H, 18-H, 19-H, NH), 7.59 (td,

$^3J_{10,9/11} = 7.7$  Hz,  $^4J_{10,12} = 1.1$  Hz, 1 H, 10-H), 8.37 (ddd,  $^3J_{12,11} = 5.0$  Hz,  $^4J_{12,10} = 1.7$  Hz,  $^5J_{12,9} = 1.0$  Hz, 1 H, 12-H).

**$^{13}\text{C-NMR}$**  (125 MHz,  $\text{CDCl}_3$ ):  $\delta = 28.0$  (q, C-1), 35.9 (t, C-5), 40.8 (t, C-15), 51.9 (d, C-4), 72.9 (d, C-14), 82.4 (s, C-2), 121.0 (d, C-9), 122.1 (d, C-11), 126.8 (d, C-19), 128.6 (d, C-18), 129.0 (d, C-6), 129.5 (d, C-17), 133.5 (d, C-7), 136.6 (d, C-10), 137.3 (s, C-16), 149.2 (d, C-12), 155.1 (s, C-8), 170.2 (s, C-3), 172.8 (s, C-13).

**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = -91.2$  ( $c = 1.0$ ,  $\text{CHCl}_3$ )

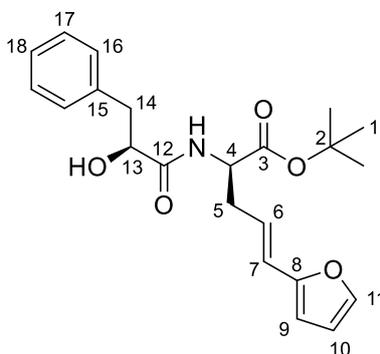
**Melting point:** 124–126 °C

<b>HRMS (CI):</b>	Calculated	Found
$\text{C}_{23}\text{H}_{29}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$	397.2122	397.2128

### ***tert*-Butyl (*R,E*)-5-(furan-2-yl)-2-((*S*)-2-hydroxy-3-phenylpropanamido)pent-4-enoate (**2ed**)**

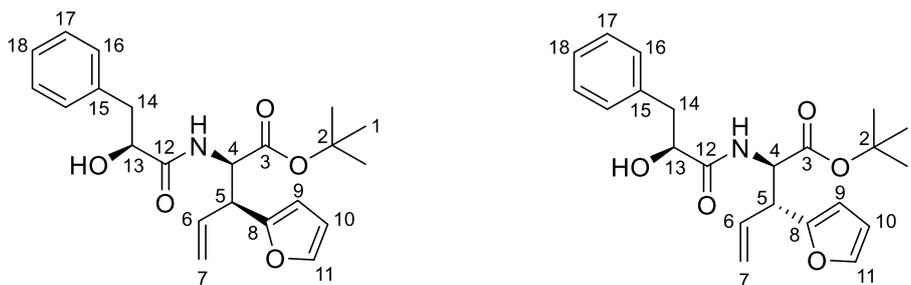
According to general procedure B for allylic alkylation, **1e** (81.0 mg, 290  $\mu\text{mol}$ ), chlorotitanium(IV) triisopropoxide (435  $\mu\text{L}$ , 435  $\mu\text{mol}$ , 1.0 M in hexane, 1.5 equiv), DIPA (132  $\mu\text{L}$ , 928  $\mu\text{mol}$ , 3.2 equiv), *n*-BuLi (360  $\mu\text{L}$ , 899  $\mu\text{mol}$ , 3.1 equiv), ethyl carbonate **SI-9** (40.3 mg, 194  $\mu\text{mol}$ , 0.7 equiv),  $[\text{AllylPdCl}]_2$  (2.1 mg, 5.8  $\mu\text{mol}$ , 2 mol %) and  $\text{PPh}_3$  (6.9 mg, 26.0  $\mu\text{mol}$ , 9 mol %) in THF (3 mL) were reacted at  $-78$  °C. Column chromatography (silica,  $\text{DCM}/\text{Et}_2\text{O}$  90:10) afforded an inseparable mixture of **2ed-I/b** (58.0 mg, 150  $\mu\text{mol}$ , 77%, 77/23 *I/b*, ca. 4/1 *dr* branched product) as a yellow oil.

$R_f(\mathbf{2ed}) = 0.27$  ( $\text{DCM}/\text{diethyl ether}$  9:1)



**$^1\text{H-NMR}$**  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.45$  (s, 9 H, 1-H), 2.65 (m, 2 H, 5-H), 2.74 (d,  $^3J_{\text{OH},13} = 6.5$  Hz, 1 H, OH), 2.85 (dd,  $^2J_{14a,14b} = 13.9$  Hz,  $^3J_{14a,13} = 8.9$  Hz, 1 H, 14- $\text{H}_a$ ), 3.22 (dd,  $^2J_{14b,14a} = 13.9$  Hz,  $^3J_{14b,13} = 3.9$  Hz, 1 H, 14- $\text{H}_b$ ), 4.29 (dt,  $^3J_{13,14a} = 9.0$  Hz,  $^3J_{13,14b/\text{OH}} = 4.4$  Hz, 1 H, 13-H), 4.59 (dt,  $^3J_{4,\text{NH}} = 7.9$  Hz,  $^3J_{4,5} = 5.7$  Hz, 1 H, 4-H), 5.97 (dt,  $^3J_{6,7} = 15.7$  Hz,  $^3J_{6,5} = 7.6$  Hz, 1 H, 6-H), 6.15 (d,  $^3J_{9,10} = 3.2$  Hz, 1 H, 9-H), 6.22 (d,  $^3J_{7,6} = 15.7$  Hz, 1 H, 7-H), 6.33 (dd,  $^3J_{10,9} = 3.3$  Hz,  $^3J_{10,11} = 1.8$  Hz, 1 H, 10-H), 7.04 (d,  $^3J_{\text{NH},4} = 7.9$  Hz, 1 H, NH), 7.28 (m, 6 H, 11-H, 16-H, 17-H, 18-H).

**$^{13}\text{C-NMR}$**  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 28.0$  (q, C-1), 35.8 (t, C-5), 40.9 (t, C-14), 52.1 (d, C-4), 72.8 (d, C-13), 82.4 (s, C-2), 107.3 (d, C-9), 111.1 (d, C-10), 122.1 (d, C-6/C-7), 122.4 (d, C-6/C-7), 126.9 (d, C-18), 128.7 (d, C-17), 129.4 (d, C-16), 136.9 (s, C-15), 141.8 (d, C-11), 152.3 (s, C-8), 170.3 (s, C-3), 172.3 (s, C-12).



Diastereomer 1 branched (selected signals)

**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.40 (s, 9 H, 1-H), 2.70 (m, 1 H, OH), 3.93 (dd, <sup>3</sup>J<sub>5,6</sub> = 8.6 Hz, <sup>3</sup>J<sub>5,4</sub> = 5.4 Hz, 1 H, 5-H), 4.89 (dd, <sup>3</sup>J<sub>13,14a</sub> = 9.0 Hz, <sup>3</sup>J<sub>13,14b</sub> = 5.4 Hz, 1 H, 13-H), 5.20 (m, 2 H, 7-H), 5.89 (m, 1 H, 6-H), 6.10 (m, 1-H, 9-H), 6.29 (m, 1 H, 10-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 27.9 (q, C-1), 40.8 (t, C-14), 46.4 (d, C-5), 82.5 (s, C-2), 107.0 (d, C-9), 110.2 (d, C-10), 141.9 (d, C-11), 152.3 (s, C-8), 169.2 (s, C-3).

Diastereomer 2 branched (selected signals)

**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.37 (s, 9 H, 1-H), 2.70 (m, 1 H, OH), 4.03 (dd, <sup>3</sup>J<sub>5,6</sub> = 7.5 Hz, <sup>3</sup>J<sub>5,4</sub> = 4.5 Hz, 1 H, 5-H), 4.93 (dd, <sup>3</sup>J<sub>13,14a</sub> = 9.3 Hz, <sup>3</sup>J<sub>13,14b</sub> = 4.8 Hz, 1 H, 13-H), 5.20 (m, 2 H, 7-H)

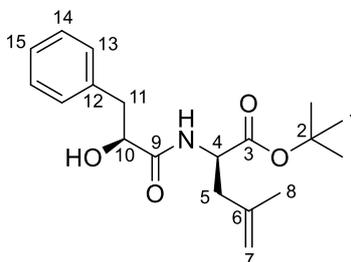
**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 27.8 (q, C-1), 82.3 (s, C-2), 107.5 (d, C-9), 142.0 (d, C-11).

HRMS (CI):	Calculated	Found
C <sub>22</sub> H <sub>28</sub> NO <sub>5</sub> [M+H] <sup>+</sup>	386.1962	386.1962

### ***tert*-Butyl (*R*)-2-((*S*)-2-hydroxy-3-phenylpropanamido)-4-methylpent-4-enoate (**2ee**)**

According to general procedure B for allylic alkylation, **1e** (81.0 mg, 290 μmol), chlorotitanium(IV) triisopropoxide (435 μL, 435 μmol, 1.0 M in hexane, 1.5 equiv), DIPA (132 μL, 928 μmol, 3.2 equiv), *n*-BuLi (360 μL, 899 μmol, 3.1 equiv), ethyl carbonate **SI-11** (28.0 mg, 194 μmol, 0.7 equiv), [AllylPdCl]<sub>2</sub> (4.2 mg, 11.6 μmol, 4 mol %) and PPh<sub>3</sub> (13.7 mg, 52.0 μmol, 18 mol %) in THF (3 mL) were reacted at -78 °C. Column chromatography (silica, DCM/Et<sub>2</sub>O 470:30) afforded **2ee** (48.1 mg, 144 μmol, 74%, > 99:1 dr) as a colorless oil.

**R<sub>f</sub>(2ee)** = 0.21 (DCM/diethyl ether 95:5)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.46 (s, 9 H, 1-H), 1.77 (s, 3 H, 8-H), 2.39 (dd, <sup>2</sup>J<sub>5a,5b</sub> = 13.9 Hz, <sup>3</sup>J<sub>5a,4</sub> = 7.9 Hz, 1 H, 5-H<sub>a</sub>), 2.45 (d, <sup>3</sup>J<sub>OH,10</sub> = 4.6 Hz, 1 H, OH), 2.52 (dd, <sup>2</sup>J<sub>5b,5a</sub> = 13.9 Hz, <sup>3</sup>J<sub>5b,4</sub> = 6.1 Hz, 1 H, 5-H<sub>b</sub>), 2.86 (dd, <sup>2</sup>J<sub>11a,11b</sub> = 14.0 Hz, <sup>3</sup>J<sub>11a,10</sub> = 9.1 Hz, 1 H, 11-H<sub>a</sub>), 3.25 (dd, <sup>2</sup>J<sub>11b,11a</sub> = 14.1 Hz, <sup>3</sup>J<sub>11b,10</sub> = 3.8 Hz, 1 H, 11-H<sub>b</sub>), 4.29 (dt, <sup>3</sup>J<sub>10,11a</sub> = 9.0 Hz, <sup>3</sup>J<sub>10,11b/OH</sub> = 4.3 Hz, 1 H, 10-H),

4.59 (td,  $^3J_{4,5a}/NH = 7.9$  Hz,  $^3J_{4,5b} = 6.3$  Hz, 1 H, 4 H), 4.73 (s, 1 H, 7-H<sub>a</sub>), 4.83 (s, 1 H, 7-H<sub>b</sub>), 6.87 (d,  $^3J_{NH,4} = 7.8$  Hz, 1 H, NH), 7.25 (m, 3 H, 13-H, 15-H), 7.32 (m, 2 H, 14-H).

**$^{13}C$ -NMR** (100 MHz, CDCl<sub>3</sub>):  $\delta = 21.9$  (q, C-8), 28.0 (q, C-1), 40.9 (t, C-5/C-11), 40.9 (t, C-5/C-11), 50.7 (d, C-4), 72.9 (d, C-10), 82.2 (s, C-2), 114.4 (t, C-7), 127.0 (d, C-15), 128.8 (d, C-14), 129.4 (d, C-13), 136.8 (s, C-12), 140.7 (s, C-6), 170.9 (s, C-3), 172.1 (s, C-9).

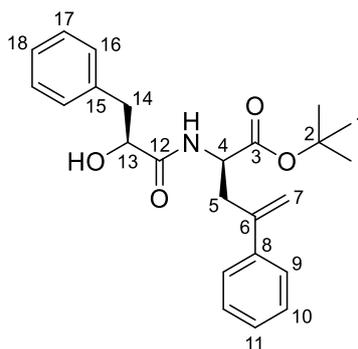
**Optical rotation:**  $[\alpha]_D^{20} = -74.0$  (c = 1.0, CHCl<sub>3</sub>)

<b>HRMS (CI):</b>	Calculated	Found
C <sub>19</sub> H <sub>28</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	334.2013	334.2017

### ***tert*-Butyl (*R*)-2-((*S*)-2-hydroxy-3-phenylpropanamido)-4-phenylpent-4-enoate (**2ef**)**

According to general procedure B for allylic alkylation, **1e** (81.0 mg, 290  $\mu$ mol), chlorotitanium(IV) triisopropoxide (435  $\mu$ L, 435  $\mu$ mol, 1.0 M in hexane, 1.5 equiv), DIPA (132  $\mu$ L, 928  $\mu$ mol, 3.2 equiv), *n*-BuLi (360  $\mu$ L, 899  $\mu$ mol, 3.1 equiv), ethyl carbonate **SI-16** (40.1 mg, 194  $\mu$ mol, 0.7 equiv), [AllylPdCl]<sub>2</sub> (4.2 mg, 11.6  $\mu$ mol, 4 mol %) and PPh<sub>3</sub> (13.7 mg, 52.0  $\mu$ mol, 18 mol %) in THF (3 mL) were reacted at  $-78$  °C. Column chromatography (silica, DCM/Et<sub>2</sub>O 92:8) afforded **2ef** (63.9 mg, 162  $\mu$ mol, 83%, > 99:1 dr) as a colorless oil.

**R<sub>f</sub>(2ef)** = 0.14 (DCM/diethyl ether 94:6)



**$^1H$ -NMR** (400 MHz, CDCl<sub>3</sub>):  $\delta = 1.42$  (s, 9 H, 1-H), 1.98 (d,  $^3J_{OH,13} = 5.9$  Hz, 1 H, OH), 2.74 (dd,  $^2J_{14a,14b} = 14.0$  Hz,  $^3J_{14a,4} = 9.2$  Hz, 1 H, 14-H<sub>a</sub>), 2.93 (dd,  $^2J_{5a,5b} = 14.2$  Hz,  $^3J_{5a,4} = 6.2$  Hz, 1 H, 5-H<sub>a</sub>), 3.09 (m, 1 H, 5-H<sub>b</sub>), 3.12 (dd,  $^2J_{14b,14a} = 13.8$  Hz,  $^3J_{14b,13} = 3.6$  Hz, 1 H, 14-H<sub>b</sub>), 4.07 (dt,  $^3J_{13,14a} = 9.3$  Hz,  $^3J_{13,14b}/OH = 4.7$  Hz, 1 H, 13-H), 4.65 (dt,  $^3J_{4,NH} = 7.7$  Hz,  $^3J_{4,5} = 6.3$  Hz, 1 H, 4-H), 5.11 (s, 1 H, 7-H<sub>a</sub>), 5.32 (d,  $^2J_{7b,7a} = 1.3$  Hz, 1 H, 7-H<sub>b</sub>), 6.82 (d,  $^3J_{NH,4} = 7.7$  Hz, 1 H, NH), 7.20 (m, 2 H, 9-H), 7.29 (m, 6 H, 10-H, 11-H, 17-H, 18-H), 7.39 (m, 2 H, 16-H).

**$^{13}C$ -NMR** (100 MHz, CDCl<sub>3</sub>):  $\delta = 28.0$  (q, C-1), 37.9 (t, C-5), 40.6 (t, C-14), 51.9 (d, C-4), 73.0 (d, C-13), 82.3 (s, C-2), 116.4 (t, C-7), 126.4 (d, C-9), 126.9 (d, C-18), 127.7 (d, C-11), 128.4 (d, C-10), 128.6 (d, C-17), 129.4 (d, C-16), 137.0 (s, C-15), 140.7 (s, C-8), 144.1 (s, C-6), 170.3 (s, C-3), 171.9 (s, C-12).

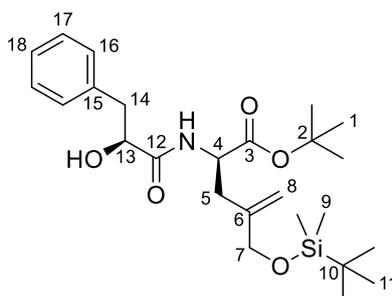
**Optical rotation:**  $[\alpha]_D^{20} = -82.7$  (c = 1.0, CHCl<sub>3</sub>)

<b>HRMS (CI):</b>	Calculated	Found
C <sub>24</sub> H <sub>29</sub> NO <sub>4</sub> [M] <sup>+</sup>	395.2091	395.2095

**tert-Butyl (R)-4-(((tert-butyldimethylsilyloxy)methyl)-2-((S)-2-hydroxy-3-phenylpropanamido)pent-4-enoate (2eg)**

According to general procedure B for allylic alkylation, **1e** (81.0 mg, 290  $\mu$ mol), chlorotitanium(IV) triisopropoxide (435  $\mu$ L, 435  $\mu$ mol, 1.0 M in hexane, 1.5 equiv), DIPA (132  $\mu$ L, 928  $\mu$ mol, 3.2 equiv), *n*-BuLi (360  $\mu$ L, 899  $\mu$ mol, 3.1 equiv), ethyl carbonate **SI-14** (53.3 mg, 194  $\mu$ mol, 0.7 equiv), [AllylPdCl]<sub>2</sub> (4.2 mg, 11.6  $\mu$ mol, 4 mol %) and PPh<sub>3</sub> (13.7 mg, 52.0  $\mu$ mol, 18 mol %) in THF (3 mL) were reacted at -78 °C. After column chromatography (silica, DCM/Et<sub>2</sub>O 95:5), **2eg** (69.0 mg, 149  $\mu$ mol, 77%, > 99:1 dr) was obtained as a colorless oil.

R<sub>f</sub>(**2eg**) = 0.34 (DCM/diethyl ether 9:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.07 (s, 3 H, 9-H), 0.08 (s, 3 H, 9-H'), 0.91 (s, 9 H, 11-H), 1.46 (s, 9 H, 1-H), 2.37 (dd, <sup>2</sup>J<sub>5a,5b</sub> = 14.3 Hz, <sup>3</sup>J<sub>5a,4</sub> = 8.4 Hz, 1 H, 5-H<sub>a</sub>), 2.63 (dd, <sup>2</sup>J<sub>5b,5a</sub> = 14.3 Hz, <sup>3</sup>J<sub>5b,4</sub> = 5.5 Hz, 1 H, 5-H<sub>b</sub>), 2.77 (d, <sup>3</sup>J<sub>OH,13</sub> = 4.8 Hz, 1 H, OH), 2.84 (dd, <sup>2</sup>J<sub>14a,14b</sub> = 14.0 Hz, <sup>3</sup>J<sub>14a,13</sub> = 9.1 Hz, 1 H, 14-H<sub>a</sub>), 3.23 (dd, <sup>3</sup>J<sub>14b,14a</sub> = 13.9 Hz, <sup>3</sup>J<sub>14b,13</sub> = 3.7 Hz, 1 H, 14-H<sub>b</sub>), 4.06 (d, <sup>2</sup>J<sub>7a,7b</sub> = 13.7 Hz, 1 H, 7-H<sub>a</sub>), 4.14 (d, <sup>2</sup>J<sub>7b,7a</sub> = 13.8 Hz, 1 H, 7-H<sub>b</sub>), 4.26 (dt, <sup>3</sup>J<sub>13,14a</sub> = 9.0 Hz, <sup>3</sup>J<sub>13,14b/OH</sub> = 4.3 Hz, 1 H, 13-H), 4.57 (td, <sup>3</sup>J<sub>4,NH/5a</sub> = 8.3 Hz, <sup>3</sup>J<sub>4,5b</sub> = 5.5 Hz, 1 H, 4-H), 4.88 (s, 1 H, 8-H<sub>a</sub>), 5.10 (d, <sup>2</sup>J<sub>8a,8b</sub> = 1.5 Hz, 1 H, 8-H<sub>b</sub>), 7.02 (d, <sup>3</sup>J<sub>NH,4</sub> = 8.1 Hz, 1 H, NH), 7.24 (m, 3 H, 16-H, 18-H), 7.30 (m, 2 H, 17-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>):  $\delta$  = -5.4 (q, C-9), 18.3 (s, C-10), 25.9 (q, C-11), 28.0 (q, C-1), 35.8 (t, C-5), 40.9 (t, C-14), 50.9 (d, C-4), 65.3 (t, C-7), 72.8 (d, C-13), 82.1 (s, C-2), 113.0 (t, C-8), 127.0 (d, C-18), 128.7 (d, C-17), 129.4 (d, C-16), 136.9 (s, C-15), 143.6 (s, C-6), 170.9 (s, C-3), 172.3 (s, C-12).

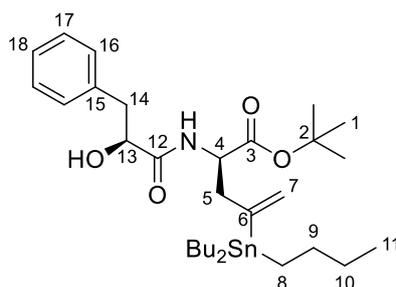
**Optical rotation:**  $[\alpha]_D^{20} = -36.5$  (c = 1.0, CHCl<sub>3</sub>)

<b>HRMS (CI):</b>	Calculated	Found
C <sub>25</sub> H <sub>42</sub> NO <sub>5</sub> Si [M+H] <sup>+</sup>	463.2731	463.2749

**tert-Butyl (R)-2-((S)-2-hydroxy-3-phenylpropanamido)-4-(tributylstannyl)pent-4-enoate (2eh)**

According to general procedure B for allylic alkylation, **1e** (81.0 mg, 290  $\mu$ mol), chlorotitanium(IV) triisopropoxide (435  $\mu$ L, 435  $\mu$ mol, 1.0 M in hexane, 1.5 equiv), DIPA (132  $\mu$ L, 928  $\mu$ mol, 3.2 equiv), *n*-BuLi (360  $\mu$ L, 899  $\mu$ mol, 3.1 equiv), ethyl carbonate **SI-12** (90.7 mg, 194  $\mu$ mol, 0.7 equiv), [AllylPdCl]<sub>2</sub> (4.2 mg, 11.6  $\mu$ mol, 4 mol%) and PPh<sub>3</sub> (13.7 mg, 52.0  $\mu$ mol, 18 mol%) in THF (3 mL) were reacted at -78 °C. Column chromatography (silica, PE/DCM/Et<sub>2</sub>O 5/5/1 + 1% NEt<sub>3</sub>) afforded **2eh** (82.8 mg, 136  $\mu$ mol, 70 %, > 99:1 dr) as a colorless oil.

$R_f(\mathbf{2eh}) = 0.47$  (PE/DCM/Et<sub>2</sub>O 5/5/2 + 1% NEt<sub>3</sub>)



<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 0.90$  (t, <sup>3</sup>J<sub>11,10</sub> = 7.3 Hz, 9 H, 11-H), 0.98 (m, 6 H, 8-H), 1.32 (sext, <sup>3</sup>J<sub>10,9/11</sub> = 7.3 Hz, 6 H, 10-H), 1.46 (s, 9 H, 1-H), 1.50 (m, 6 H, 9-H), 2.46 (m, 1 H, OH), 2.48 (dd, <sup>2</sup>J<sub>5a,5b</sub> = 14.0 Hz, <sup>3</sup>J<sub>5a,4</sub> = 9.1 Hz, 1 H, 5-H<sub>a</sub>), 2.78 (dd, <sup>2</sup>J<sub>5b,5a</sub> = 14.1 Hz, <sup>3</sup>J<sub>5b,4</sub> = 5.3 Hz, 1 H, 5-H<sub>b</sub>), 2.86 (dd, <sup>2</sup>J<sub>14a,14b</sub> = 14.0 Hz, <sup>3</sup>J<sub>14a,13</sub> = 9.2 Hz, 1 H, 14-H<sub>a</sub>), 3.26 (dd, <sup>2</sup>J<sub>14b,14a</sub> = 14.0 Hz, <sup>3</sup>J<sub>14b,13</sub> = 3.7 Hz, 1 H, 14-H<sub>b</sub>), 4.26 (dd, <sup>3</sup>J<sub>13,14a</sub> = 9.2 Hz, <sup>3</sup>J<sub>13,14b</sub> = 3.7 Hz, 1 H, 13-H), 4.41 (ddd, <sup>3</sup>J<sub>4,5a</sub> = 8.8 Hz, <sup>3</sup>J<sub>4,NH</sub> = 7.8 Hz, <sup>3</sup>J<sub>4,5b</sub> = 5.4 Hz, 1 H, 4-H), 5.24 (dd, <sup>3</sup>J<sub>7a,Sn</sub> = 58.2 Hz, <sup>2</sup>J<sub>7a,7b</sub> = 2.1 Hz, 1 H, 7-H<sub>a</sub>), 5.73 (d, <sup>3</sup>J<sub>7b,Sn</sub> = 128.1 Hz, 1 H, 7-H<sub>b</sub>), 6.74 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.5 Hz, 1 H, NH), 7.25 (m, 3 H, 16-H, 18-H), 7.32 (m, 2 H, 17-H).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 9.6$  (dt, <sup>1</sup>J<sub>8,Sn</sub> = 320.0 Hz, C-8), 13.7 (q, C-11), 27.3 (dt, <sup>3</sup>J<sub>10,Sn</sub> = 58.0 Hz, C-10), 28.0 (q, C-1), 29.0 (dt, <sup>2</sup>J<sub>9,Sn</sub> = 19.8 Hz, C-9), 40.9 (t, C-14), 43.9 (dt, <sup>2</sup>J<sub>5,Sn</sub> = 40.4 Hz, C-5), 52.1 (dd, <sup>3</sup>J<sub>4,Sn</sub> = 11.0 Hz, C-4), 72.9 (d, C-13), 81.9 (s, C-2), 127.0 (d, C-18), 128.4 (dt, <sup>2</sup>J<sub>7,Sn</sub> = 24.2 Hz, C-7), 128.8 (d, C-17), 129.5 (d, C-16), 136.9 (s, C-15), 150.0 (s, C-6), 171.0 (s, C-3), 172.1 (s, C-12).

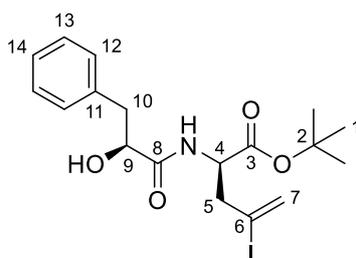
Optical rotation:  $[\alpha]_D^{20} = -49.2$  (c = 1.0, CHCl<sub>3</sub>)

HRMS (CI):	Calculated	Found
C <sub>30</sub> H <sub>52</sub> NO <sub>4</sub> Sn [M+H] <sup>+</sup>	610.2913	610.2912

### *tert*-Butyl (*R*)-2-((*S*)-2-hydroxy-3-phenylpropanamido)-4-iodopent-4-enoate (**SI-32**)

To a solution of **2eh** (500 mg, 822  $\mu$ mol) in DCM (8 mL) was added a solution of iodine (250 mg, 986  $\mu$ mol, 1.2 equiv) in DCM (8 mL) at room temperature. After 1 hour, the mixture was diluted with DCM, washed with sat. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution and the aqueous layer was extracted with DCM. The combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>), evaporated *in vacuo* and the residue purified by column chromatography (silica, DCM/Et<sub>2</sub>O 95:5) to afford vinyl iodide **SI-32** (318 mg, 714  $\mu$ mol, 87%) as colorless crystals.

$R_f(\mathbf{SI-32}) = 0.23$  (DCM/Et<sub>2</sub>O 95:5)



<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 1.48$  (s, 9 H, 1-H), 2.48 (d, <sup>3</sup>J<sub>OH,9</sub> = 4.6 Hz, 1 H, OH), 2.82 (dd, <sup>2</sup>J<sub>5a,5b</sub> = 14.8 Hz, <sup>3</sup>J<sub>5a,4</sub> = 7.5 Hz, 1 H, 5-H<sub>a</sub>), 2.86 (dd, <sup>2</sup>J<sub>10a,10b</sub> = 14.0 Hz, <sup>3</sup>J<sub>10a,9</sub> = 9.1 Hz, 1 H,

10-H<sub>a</sub>), 2.94 (dd, <sup>2</sup>J<sub>5b,5a</sub> = 14.8 Hz, <sup>3</sup>J<sub>5b,4</sub> = 5.9 Hz, 1 H, 5-H<sub>b</sub>), 3.27 (dd, <sup>2</sup>J<sub>10b,10a</sub> = 14.0 Hz, <sup>3</sup>J<sub>10b,9</sub> = 3.7 Hz, 1 H, 10-H<sub>b</sub>), 4.32 (dt, <sup>3</sup>J<sub>9,10a</sub> = 9.0 Hz, <sup>3</sup>J<sub>9,10b/OH</sub> = 4.3 Hz, 1 H, 9-H), 4.67 (td, <sup>3</sup>J<sub>4,5a/NH</sub> = 7.7 Hz, <sup>3</sup>J<sub>4,5b</sub> = 6.0 Hz, 1 H, 4-H), 5.82 (d, <sup>2</sup>J<sub>7a,7b</sub> = 1.3 Hz, 1 H, 7-H<sub>a</sub>), 6.10 (d, <sup>3</sup>J<sub>7b,7a</sub> = 1.2 Hz, 1 H, 7-H<sub>b</sub>), 7.01 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.8 Hz, 1 H, NH), 7.26 (m, 3 H, 12-H, 14-H), 7.33 (m, 2 H, 13-H).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 28.0 (q, C-1), 40.8 (t, C-10), 47.1 (t, C-5), 51.9 (d, C-4), 72.9 (d, C-9), 82.8 (s, C-2), 103.6 (s, C-6), 127.0 (d, C-14), 128.8 (d, C-13), 129.2 (t, C-7), 129.5 (d, C-12), 136.8 (s, C-11), 169.6 (s, C-3), 172.2 (s, C-8).

**Optical rotation:**  $[\alpha]_D^{20} = -47.9$  (c = 1.0, CHCl<sub>3</sub>)

**Melting point:** 70–72 °C

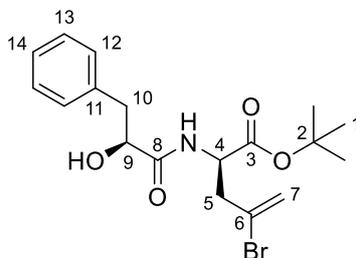
<b>HRMS (CI):</b>	Calculated	Found
C <sub>18</sub> H <sub>25</sub> INO <sub>4</sub> [M+H] <sup>+</sup>	446.0823	446.0827

### **tert-Butyl (R)-4-bromo-2-((S)-2-hydroxy-3-phenylpropanamido)pent-4-enoate (2ei)**

According to general procedure B for allylic alkylation, **1e** (81.0 mg, 290 μmol), chlorotitanium(IV) triisopropoxide (435 μL, 435 μmol, 1.0 M in hexane, 1.5 equiv), DIPA (132 μL, 928 μmol, 3.2 equiv), *n*-BuLi (360 μL, 899 μmol, 3.1 equiv), 2-bromoallyl ethyl carbonate (40.6 mg, 194 μmol, 0.7 equiv), [AllylPdCl]<sub>2</sub> (4.2 mg, 10.6 μmol, 4 mol %) and PPh<sub>3</sub> (13.7 mg, 52.0 μmol, 18 mol %) in THF (3 mL) were reacted at –78 °C. The reaction was hydrolyzed at –50 °C and after work up and column chromatography (silica, DCM/Et<sub>2</sub>O 9:1) **(S,R)-2ei** (66.5 g, 167 μmol, 86%) and **(S,S)-2ei** (7.5 mg, 19.0 μmol, 9.7%) were obtained as pale yellow solids (74.0 mg, 186 μmol, 96%, 90:10 *dr* overall).

Main diastereomer (*S,R*):

R<sub>f</sub>(**2ei**) = 0.33 (DCM/Et<sub>2</sub>O 9:1)



<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.48 (s, 9 H, 1-H), 2.70 (d, <sup>3</sup>J<sub>OH,9</sub> = 4.8 Hz, 1 H, OH), 2.86 (m, 2 H, 5-H<sub>a</sub>, 10-H<sub>a</sub>), 2.97 (dd, <sup>2</sup>J<sub>5b,5a</sub> = 14.8 Hz, <sup>3</sup>J<sub>5b,4</sub> = 5.8 Hz, 1 H, 5-H<sub>b</sub>), 3.25 (dd, <sup>2</sup>J<sub>10b,10a</sub> = 13.9 Hz, <sup>3</sup>J<sub>10b,9</sub> = 3.7 Hz, 1 H, 10-H<sub>b</sub>), 4.30 (dt, <sup>3</sup>J<sub>9,10a</sub> = 9.0 Hz, <sup>3</sup>J<sub>9,10b/OH</sub> = 4.3 Hz, 1 H, 9-H), 4.67 (td, <sup>3</sup>J<sub>4,5a/NH</sub> = 7.0 Hz, <sup>3</sup>J<sub>4,5b</sub> = 6.0 Hz, 1 H, 4-H), 5.51 (d, <sup>2</sup>J<sub>7a,7b</sub> = 1.7 Hz, 1 H, 7-H<sub>a</sub>), 5.63 (m, 1 H, 7-H<sub>b</sub>), 7.01 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.9 Hz, 1 H, NH), 7.26 (m, 3 H, 12-H, 14-H), 7.33 (m, 2 H, 13-H).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 28.0 (q, C-1), 40.8 (t, C-10), 43.3 (t, C-5), 51.1 (d, C-4), 72.8 (d, C-9), 82.8 (s, C-2), 120.4 (s, C-6), 127.0 (d, C-14), 128.0 (t, C-7), 128.7 (d, C-13), 129.4 (d, C-12), 136.9 (s, C-11), 169.6 (s, C-3), 172.4 (s, C-8).

**Optical rotation:**  $[\alpha]_D^{20} = -59.0$  (c = 1.0, CHCl<sub>3</sub>)

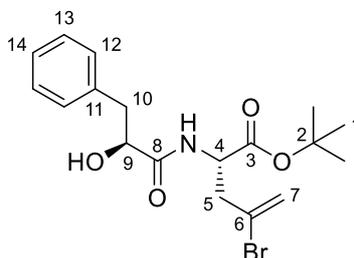
**Melting point:** 83–85 °C

<b>HRMS (CI):</b>	Calculated	Found
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C<sub>18</sub>H<sub>26</sub>NO<sub>4</sub>Br [M+2H]<sup>+</sup> 399.1040 399.1036

Minor Diastereomer (*S,S*):

R<sub>f</sub>(**2ei**) = 0.25 (DCM/Et<sub>2</sub>O 9:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.48 (s, 9 H, 1-H), 2.59 (d, <sup>3</sup>J<sub>OH,9</sub> = 4.8 Hz, 1 H, OH), 2.84 (ddd, <sup>2</sup>J<sub>5a,5b</sub> = 14.8 Hz, <sup>3</sup>J<sub>5a,4</sub> = 6.9 Hz, <sup>4</sup>J<sub>5a,7a/7b</sub> = 0.7 Hz, 1 H, 5-H<sub>a</sub>), 2.88 (dd, <sup>2</sup>J<sub>10a,10b</sub> = 13.9 Hz, <sup>3</sup>J<sub>10a,9</sub> = 8.4 Hz, 1 H, 10-H<sub>a</sub>), 2.93 (ddd, <sup>2</sup>J<sub>5b,5a</sub> = 14.8 Hz, <sup>3</sup>J<sub>5b,4</sub> = 5.8 Hz, <sup>4</sup>J<sub>5b,7a/7b</sub> = 0.6 Hz, 1 H, 5-H<sub>b</sub>), 3.23 (dd, <sup>2</sup>J<sub>10b,10a</sub> = 13.9 Hz, <sup>3</sup>J<sub>10b,9</sub> = 3.9 Hz, 1 H, 10-H<sub>b</sub>), 4.34 (dt, <sup>3</sup>J<sub>9,10a</sub> = 8.5 Hz, <sup>3</sup>J<sub>9,10b/OH</sub> = 4.2 Hz, 1 H, 9-H), 4.69 (ddd, <sup>3</sup>J<sub>4,NH</sub> = 7.9 Hz, <sup>3</sup>J<sub>4,5a</sub> = 6.7 Hz, <sup>3</sup>J<sub>4,5b</sub> = 5.9 Hz, 1 H, 4-H), 5.48 (d, <sup>2</sup>J<sub>7a,7b</sub> = 1.7 Hz, 1 H, 7-H<sub>a</sub>), 5.56 (m, 1 H, 7-H<sub>b</sub>), 7.01 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.9 Hz, 1 H, NH), 7.26 (m, 3 H, 12-H, 14-H), 7.32 (m, 2 H, 13-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 28.0 (q, C-1), 40.8 (t, C-10), 43.3 (t, C-5), 50.9 (d, C-4), 72.9 (d, C-9), 82.9 (s, C-2), 120.4 (s, C-6), 127.0 (d, C-14), 127.8 (t, C-7), 128.7 (d, C-13), 129.6 (d, C-12), 136.7 (s, C-11), 169.8 (s, C-3), 172.3 (s, C-8).

**Optical rotation:**  $[\alpha]_D^{20} = -28.8$  (c = 1.0, CHCl<sub>3</sub>)

**Melting point:** 82–84 °C

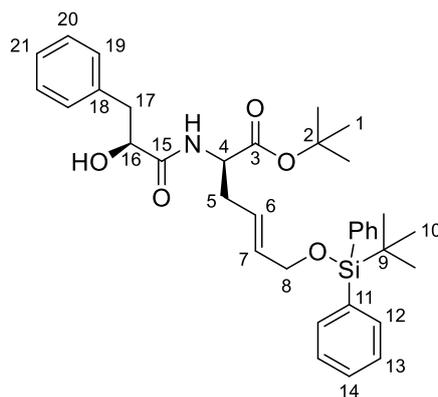
**HRMS (CI):** Calculated Found

C<sub>18</sub>H<sub>26</sub>NO<sub>4</sub>Br [M+2H]<sup>+</sup> 399.1040 399.1019

***tert*-Butyl (*R,E*)-6-((*tert*-butyldiphenylsilyl)oxy)-2-((*S*)-2-hydroxy-3-phenylpropanamido)-hex-4-enoate (**2ej**)**

According to general procedure B for allylic alkylation, **1e** (81.0 mg, 290 μmol), chlorotitanium(IV) triisopropoxide (435 μL, 435 μmol, 1.0 M in hexane, 1.5 equiv), DIPA (132 μL, 928 μmol, 3.2 equiv), *n*-BuLi (360 μL, 899 μmol, 3.1 equiv), ethyl carbonate **SI-10** (77.0 mg, 194 μmol, 0.7 equiv), [AllylPdCl]<sub>2</sub> (2.1 mg, 5.8 μmol, 2 mol %) and PPh<sub>3</sub> (6.9 mg, 26.0 μmol, 9 mol %) in THF (3 mL) were reacted at –78 °C. After column chromatography (silica, DCM/Et<sub>2</sub>O 98:2 → 93:7), **2ej** (97.1 mg, 165 μmol, 85%, > 99:1 *dr*) was obtained as a colorless oil.

R<sub>f</sub>(**2ej**) = 0.53 (DCM/diethyl ether 9:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.03 (s, 9 H, 10-H), 1.45 (s, 9 H, 1-H), 2.54 (m, 3 H, 5-H, OH), 2.84 (dd, <sup>2</sup>J<sub>17a,17b</sub> = 13.9 Hz, <sup>3</sup>J<sub>17a,16</sub> = 9.1 Hz, 1 H, 17-H<sub>a</sub>), 3.22 (dd, <sup>2</sup>J<sub>17b,17a</sub> = 13.9 Hz, <sup>3</sup>J<sub>17b,16</sub> = 3.8 Hz, 1 H, 17-H<sub>b</sub>), 4.12 (m, 2 H, 8-H), 4.26 (dt, <sup>3</sup>J<sub>16,17a</sub> = 9.1 Hz, <sup>3</sup>J<sub>16,17b/OH</sub> = 4.3 Hz, 1 H, 16-H), 4.54 (dt, <sup>3</sup>J<sub>4,5a</sub> = 7.9 Hz, <sup>3</sup>J<sub>4,5b/NH</sub> = 5.5 Hz, 1 H, 4-H), 5.60 (m, 2 H, 6-H, 7-H), 6.97 (d, <sup>3</sup>J<sub>NH,4</sub> = 5.5 Hz, 1 H, NH), 7.23 (m, 3 H, 19-H, 21-H), 7.30 (m, 2 H, 20-H), 7.39 (m, 6 H, 12-H/13-H, 14-H), 7.65 (m, 4 H, 12-H/13-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 19.2 (s, C-9), 26.7 (q, C-10), 28.0 (q, C-1), 35.0 (t, C-5), 40.9 (t, C-17), 51.9 (d, C-4), 64.0 (t, C-8), 72.9 (d, C-16), 82.2 (s, C-2), 123.7 (d, C-6), 126.9 (d, C-21), 127.6 (d, C-12/C-13), 128.7 (d, C-20), 129.4 (d, C-19), 129.6 (d, C-12/C-13), 133.4 (d, C-7), 133.5 (d, C-14), 135.5 (s, C-11), 136.9 (s, C-18), 170.4 (s, C-3), 172.2 (s, C-15).

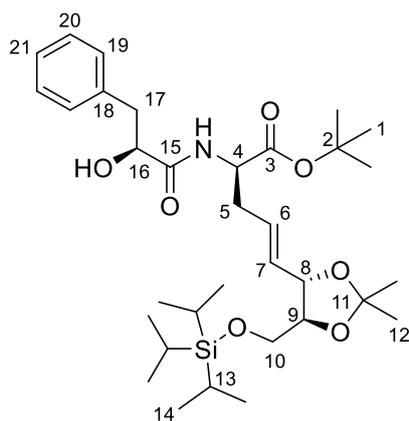
**Optical rotation:**  $[\alpha]_D^{20} = -57.5$  (c = 1.0, CHCl<sub>3</sub>)

<b>HRMS (CI):</b>	Calculated	Found
C <sub>35</sub> H <sub>46</sub> NO <sub>5</sub> Si [M+H] <sup>+</sup>	588.3140	588.3131

***tert*-Butyl (*R,E*)-5-((4*S*,5*S*)-2,2-dimethyl-5-(((triisopropylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)-2-((*S*)-2-hydroxy-3-phenylpropanamido)pent-4-enoate (**2ek**)**

According to general procedure B for allylic alkylation, **1e** (81.0 mg, 290 μmol), chlorotitanium(IV) triisopropoxide (304 μL, 304 μmol, 1.0 M in hexane, 1.05 equiv), DIPA (132 μL, 928 μmol, 3.2 equiv), *n*-BuLi (360 μL, 899 μmol, 3.1 equiv), ethyl carbonate **SI-21** (81.0 mg, 194 μmol, 0.7 equiv), [AllylPdCl]<sub>2</sub> (4.2 mg, 11.6 μmol, 4 mol %) and PPh<sub>3</sub> (13.7 mg, 52.0 μmol, 18 mol %) in THF (3 mL) were reacted at -78 °C. Column chromatography (silica, DCM/Et<sub>2</sub>O 8:2) afforded **2ek** (63.0 mg, 150 μmol, 80%, > 99:1 *dr*) as a colorless oil.

**R<sub>f</sub>(2ek)** = 0.22 (DCM/Et<sub>2</sub>O 8:2)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 1.06 (m, 21 H, 13-H, 14-H), 1.37 (s, 6 H, 12-H), 1.47 (s, 9 H, 1-H), 2.47 (dt, <sup>2</sup>J<sub>5a,5b</sub> = 14.2 Hz, <sup>3</sup>J<sub>5a,4/6</sub> = 6.6 Hz, 1 H, 5-H<sub>a</sub>), 2.61 (dt, <sup>2</sup>J<sub>5b,5a</sub> = 14.2 Hz, <sup>3</sup>J<sub>5b,4/6</sub> = 5.8 Hz, 1 H, 5-H<sub>b</sub>), 2.81 (m, 1 H, OH), 2.84 (dd, <sup>2</sup>J<sub>17a,17b</sub> = 14.1 Hz, <sup>3</sup>J<sub>17a,16</sub> = 9.2 Hz, 1 H, 17-H<sub>a</sub>), 3.23 (dd, <sup>2</sup>J<sub>17b,17a</sub> = 13.9 Hz, <sup>3</sup>J<sub>17b,16</sub> = 3.6 Hz, 1 H, 17-H<sub>b</sub>), 3.71 (dt, <sup>3</sup>J<sub>9,8</sub> = 8.1 Hz, <sup>3</sup>J<sub>9,10</sub> = 4.0 Hz, 1 H, 9-H), 3.78 (dd, <sup>2</sup>J<sub>10a,10b</sub> = 10.9 Hz, <sup>3</sup>J<sub>10a,9</sub> = 3.9 Hz, 1 H, 10-H<sub>a</sub>), 3.82 (dd, <sup>2</sup>J<sub>10b,10a</sub> = 10.9 Hz, <sup>3</sup>J<sub>10b,9</sub> = 4.8 Hz, 1 H, 10-H<sub>b</sub>), 4.28 (dt, <sup>3</sup>J<sub>16,17a</sub> = 9.3 Hz, <sup>3</sup>J<sub>16,17b/OH</sub> = 3.9 Hz, 1 H, 16-H), 4.33 (dd, <sup>3</sup>J<sub>8,9</sub> = 7.8 Hz, <sup>3</sup>J<sub>8,7</sub> = 6.9 Hz, 1 H, 8-H), 4.54 (dt, <sup>3</sup>J<sub>4,NH</sub> = 7.7 Hz, <sup>3</sup>J<sub>4,5</sub> = 6.0 Hz, 1 H, 4-H), 5.59 (m, 2 H, 6-H, 7-H), 6.98 (d, <sup>3</sup>J<sub>NH,4</sub> = 8.1 Hz, 1 H, NH), 7.25 (m, 3 H, 19-H, 21-H), 7.32 (m, 2 H, 20-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.8 (d, C-13), 17.9 (q, C-14), 26.9 (q, C-12), 27.0 (q, C-12'), 28.0 (q, C-1), 35.2 (t, C-5), 40.8 (t, C-17), 51.6 (d, C-4), 62.7 (t, C-10), 73.0 (d, C-16), 78.3 (d, C-8), 81.6 (C-9), 82.3 (s, C-2), 109.0 (s, C-11), 126.9 (d, C-21), 128.1 (d, C-6), 128.6 (d, C-20), 129.4 (d, C-19), 132.3 (d, C-7), 137.0 (s, C-18), 170.2 (s, C-3), 172.3 (s, C-15).

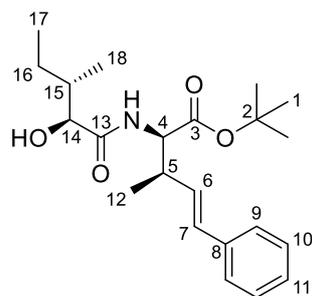
**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = -51.7$  (c = 1.0, CHCl<sub>3</sub>)

<b>HRMS (CI):</b>	Calculated	Found
C <sub>29</sub> H <sub>46</sub> NO <sub>7</sub> Si [M-C <sub>4</sub> H <sub>9</sub> ] <sup>+</sup>	548.3038	548.3032

**tert-Butyl (2R,3R,E)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-3-methyl-5-phenylpent-4-enoate (2a1-1)**

According to general procedure B for allylic alkylation, **1c** (71.0 mg, 289 μmol), chlorotitanium(IV) triisopropoxide (434 μL, 434 μmol, 1.0 M in hexane, 1.5 equiv), DIPA (132 μL, 926 μmol, 3.2 equiv), *n*-BuLi (359 μL, 897 μmol, 3.1 equiv), carbonate **SI-(R)-25** (42.7 mg, 194 μmol, 0.7 equiv), [AllylPdCl]<sub>2</sub> (2.1 mg, 5.8 μmol, 2 mol %) and PPh<sub>3</sub> (6.8 mg, 26.0 μmol, 9 mol %) in THF (3 mL) were reacted at -78 °C. After column chromatography (silica, DCM/Et<sub>2</sub>O 9:1), **2a1-1** (59.3 mg, 158 μmol, 81%, > 99:1 dr) was obtained as a white solid.

**R<sub>f</sub>(2a1-1)** = 0.24 (DCM/Et<sub>2</sub>O 9:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.86 (t, <sup>3</sup>J<sub>17,16</sub> = 7.5 Hz, 3 H, 17-H), 0.99 (d, <sup>3</sup>J<sub>18,15</sub> = 7.0 Hz, 3 H, 18-H), 1.16 (d, <sup>3</sup>J<sub>12,5</sub> = 6.8 Hz, 3 H, 12-H), 1.22 (m, 1 H, 16-H<sub>a</sub>), 1.40 (m, 1 H, 16-H<sub>b</sub>), 1.46 (s, 9 H, 1-H), 1.88 (m, 1 H, 15-H), 2.95 (m, 1 H, 5-H), 3.01 (d, <sup>3</sup>J<sub>OH,14</sub> = 5.3 Hz, 1 H, OH), 4.02 (dd, <sup>3</sup>J<sub>14,OH</sub> = 5.0 Hz, <sup>3</sup>J<sub>14,15</sub> = 3.4 Hz, 1 H, 14-H), 4.60 (dd, <sup>3</sup>J<sub>4,NH</sub> = 8.7 Hz, <sup>3</sup>J<sub>4,5</sub> = 5.0 Hz, 1 H, 4-H), 6.08 (dd, <sup>3</sup>J<sub>6,7</sub> = 15.9 Hz, <sup>3</sup>J<sub>6,5</sub> = 7.8 Hz, 1 H, 6-H), 6.44 (d, <sup>3</sup>J<sub>7,6</sub> = 15.9 Hz, 1 H, 7-H), 6.86 (d, <sup>3</sup>J<sub>NH,4</sub> = 8.7 Hz, 1 H, NH), 7.21 (m, 1 H, 11-H), 7.27 (m, 4 H, 9-H, 10-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.8 (q, C-17), 15.5 (q, C-18), 16.5 (q, C-12), 23.1 (t, C-16), 28.0 (q, C-1), 39.0 (d, C-15), 40.0 (d, C-5), 56.7 (d, C-4), 76.1 (d, C-14), 82.3 (s, C-2), 126.1 (d, C-9), 127.4 (d, C-11), 128.5 (d, C-10), 129.7 (d, C-6), 131.4 (d, C-7), 136.8 (s, C-8), 170.2 (s, C-3), 173.2 (s, C-13).

**Optical rotation:**  $[\alpha]_D^{20} = -24.0$  (c = 1.0, CHCl<sub>3</sub>)

**Melting point:** 128–129 °C

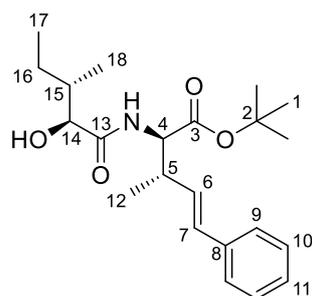
<b>HRMS (CI):</b>	Calculated	Found
C <sub>22</sub> H <sub>34</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	376.2482	376.2493

**tert-Butyl (2R,3S,E)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-3-methyl-5-phenylpent-4-enoate (2a1-2)**

According to general procedure B for allylic alkylation, **1c** (71.0 mg, 289 μmol), chlorotitanium(IV) triisopropoxide (434 μL, 434 μmol, 1.0 M in hexane, 1.5 equiv), DIPA (132 μL, 926 μmol, 3.2 equiv), *n*-BuLi (359 μL, 897 μmol, 3.1 equiv), carbonate **SI-(S)-25** (42.7 mg, 194 μmol, 0.7 equiv), [AllylPdCl]<sub>2</sub> (2.1 mg, 5.8 μmol, 2 mol %) and PPh<sub>3</sub> (6.8 mg, 26.0 μmol, 9 mol %) in THF (3 mL) were reacted at –78 °C. After column chromatography (silica, DCM/Et<sub>2</sub>O 9:1), the diastereomers **(R,S,S,S)-2a1-2** (46.0 mg, 123 μmol, 63%) and **(S,S,S,S)-2a1-2** (10.1 mg, 27.0 μmol, 14%) were separately obtained as a white solids (56.1 mg, 149 μmol, 77%, 82:18 *dr* overall)

**R<sub>f</sub>**((**R,S,S,S**)-**2a1-2**) = 0.20 (DCM/Et<sub>2</sub>O 9:1), **R<sub>f</sub>**((**S,S,S,S**)-**2a1-2**) = 0.14 (DCM/Et<sub>2</sub>O 9:1)

Main diastereomer (**R,S,S,S**)

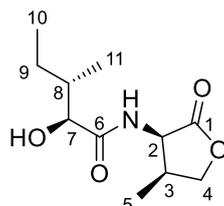




the mixture was diluted with EtOAc and HCl (1 M, aq.) and the layers were separated. The aqueous layer was extracted twice with EtOAc and the combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>), evaporated *in vacuo* and the crude product was immediately used in the next step.

The crude alcohol was dissolved in CHCl<sub>3</sub> (1 mL) and TFA (100 μL, 1.30 mmol, 9.8 equiv) was added. After stirring at room temperature for 22 hours, the mixture was concentrated *in vacuo* and the residue purified by column chromatography (silica, DCM/diethyl ether 7:3) to afford lactone **SI-33** (18.9 mg, 82.4 mmol, 62% over 2 steps) as colorless crystals.

**R<sub>f</sub>(SI-33)** = 0.19 (DCM/Et<sub>2</sub>O 7:3)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.91 (t, <sup>3</sup>J<sub>10,9</sub> = 7.5 Hz, 3 H, 10-H), 0.99 (d, <sup>3</sup>J<sub>5,3</sub> = 7.2 Hz, 3 H, 5-H), 1.04 (d, <sup>3</sup>J<sub>11,8</sub> = 7.0 Hz, 3 H, 11-H), 1.24 (m, 1 H, 9-H<sub>a</sub>), 1.45 (m, 1 H, 9-H<sub>b</sub>), 1.92 (dqt, <sup>3</sup>J<sub>8,9a</sub> = 10.1 Hz, <sup>3</sup>J<sub>8,11</sub> = 6.9 Hz, <sup>3</sup>J<sub>8,7/9b</sub> = 3.7 Hz, 1 H, 8-H), 2.69 (d, <sup>3</sup>J<sub>OH,7</sub> = 4.8 Hz, 1 H, OH), 3.03 (m, 1 H, 3-H), 4.13 (m, 2 H, 4-H<sub>a</sub>, 7-H), 4.45 (dd, <sup>2</sup>J<sub>4b,4a</sub> = 9.2 Hz, <sup>3</sup>J<sub>4b,3</sub> = 5.2 Hz, 1 H, 4-H<sub>b</sub>), 4.71 (dd, <sup>3</sup>J<sub>2,3</sub> = 7.1 Hz, <sup>3</sup>J<sub>2,NH</sub> = 6.4 Hz, 1 H, 2-H), 6.95 (d, <sup>3</sup>J<sub>NH,2</sub> = 4.9 Hz, 1 H, NH).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.8 (q, C-10), 12.8 (q, C-5), 15.5 (q, C-11), 23.2 (t, C-9), 33.9 (d, C-3), 38.9 (d, C-8), 52.9 (d, C-2), 72.7 (t, C-4), 76.3 (d, C-7), 174.1 (s, C-1), 174.9 (s, C-6).

**Optical rotation:**  $[\alpha]_D^{20} = -107.0$  (c = 1.0, CHCl<sub>3</sub>)

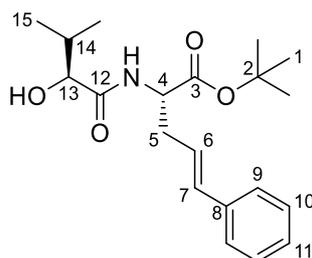
**Melting point:** 129–131 °C

<b>HRMS (CI):</b>	Calculated	Found
C <sub>11</sub> H <sub>20</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	230.1387	230.1383

#### ***tert*-Butyl (*S,E*)-2-((*S*)-2-hydroxy-3-methylbutanamido)-5-phenylpent-4-enoate (**2ba'**)**

According to general procedure A for allylic alkylation, **1a** (67.0 mg, 289 μmol, 1.0 equiv), LHMDS (1.59 mL, 1.59 mmol, 1.0 M in THF, 5.5 equiv), chlorotitanium(IV) triisopropoxide (434 μL, 439 μmol, 1.0 M in hexane, 1.5 equiv), cinnamyl ethyl carbonate (40.0 mg, 194 μmol, 0.7 equiv), allylpalladiumchloride dimer (2.1 mg, 5.79 μmol, 2 mol %) and triphenylphosphine (6.8 mg, 26.0 μmol, 9 mol %) were reacted at –78 °C. Column chromatography (silica, DCM/Et<sub>2</sub>O 9:1) afforded (**S,S**)-**2ba'** (46.2 mg, 133 μmol, 69%) and (**S,R**)-**2ba** (6.8 mg, 20.1 μmol, 10%) separately as off white solids.

**R<sub>f</sub>((S,R)-2ba)** = 0.21 (DCM/Et<sub>2</sub>O 9:1), **R<sub>f</sub>((S,S)-2ba')** = 0.16 (DCM/Et<sub>2</sub>O 9:1)



Main Diastereomer (*S,S*):

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.84 (d, <sup>3</sup>J<sub>15,14</sub> = 6.9 Hz, 3 H, 15-H), 1.00 (d, <sup>3</sup>J<sub>15',14</sub> = 6.9 Hz, 3 H, 15-H'), 1.46 (s, 9 H, 1-H), 2.15 (septd, <sup>3</sup>J<sub>14,15</sub> = 6.9 Hz, <sup>3</sup>J<sub>14,13</sub> = 3.3 Hz, 1 H, 14-H), 2.71 (m, 2 H, 5-H), 3.14 (d, <sup>3</sup>J<sub>OH,13</sub> = 3.9 Hz, 1 H, OH), 4.00 (bs, 1 H, 13-H), 4.67 (dt, <sup>3</sup>J<sub>4,NH</sub> = 7.8 Hz, <sup>3</sup>J<sub>4,5</sub> = 5.9 Hz, 1 H, 4-H), 6.07 (dt, <sup>3</sup>J<sub>6,7</sub> = 15.7 Hz, <sup>3</sup>J<sub>6,5</sub> = 7.3 Hz, 1 H, 6-H), 6.44 (d, <sup>3</sup>J<sub>7,6</sub> = 15.8 Hz, 1 H, 7-H), 7.15 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.8 Hz, 1 H, NH), 7.21 (m, 1 H, 11-H), 7.29 (m, 4 H, 9-H, 10-H).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 15.5 (q, C-15), 19.1 (q, C-15'), 28.0 (q, C-1), 31.8 (d, C-14), 36.2 (t, C-5), 52.0 (d, C-4), 76.2 (d, C-13), 82.5 (s, C-2), 123.7 (d, C-6), 126.1 (d, C-9), 127.4 (d, C-11), 128.5 (d, C-10), 133.9 (d, C-7), 136.8 (s, C-8), 170.9 (s, C-3), 173.1 (s, C-12).

**Optical rotation:**  $[\alpha]_D^{20} = +35.5$  (c = 1.0, CHCl<sub>3</sub>)

**Melting point:** 79–82 °C

<b>HRMS (CI):</b>	Calculated	Found
C <sub>20</sub> H <sub>31</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	348.2169	348.2140

Minor Diastereomer (*S,R*):

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.87 (d, <sup>3</sup>J<sub>15,14</sub> = 6.8 Hz, 3 H, 15-H), 1.02 (d, <sup>3</sup>J<sub>15',14</sub> = 7.0 Hz, 3 H, 15-H'), 1.47 (s, 9 H, 1-H), 2.10 (septd, <sup>3</sup>J<sub>14,15</sub> = 6.9 Hz, <sup>3</sup>J<sub>14,13</sub> = 3.3 Hz, 1 H, 14-H), 2.54 (d, <sup>3</sup>J<sub>OH,13</sub> = 5.5 Hz, 1 H, OH), 2.73 (m, 2 H, 5-H), 3.99 (dd, <sup>3</sup>J<sub>13,OH</sub> = 5.4 Hz, <sup>3</sup>J<sub>13,14</sub> = 3.2 Hz, 1 H, 13-H), 4.67 (dt, <sup>3</sup>J<sub>4,NH</sub> = 7.8 Hz, <sup>3</sup>J<sub>4,5</sub> = 5.7 Hz, 1 H, 4-H), 6.06 (dt, <sup>3</sup>J<sub>6,7</sub> = 15.8 Hz, <sup>3</sup>J<sub>6,5</sub> = 7.3 Hz, 1 H, 6-H), 6.45 (d, <sup>3</sup>J<sub>7,6</sub> = 15.8 Hz, 1 H, 7-H), 6.76 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.6 Hz, 1 H, NH), 7.23 (m, 1 H, 11-H), 7.30 (m, 4 H, 9-H, 10-H).

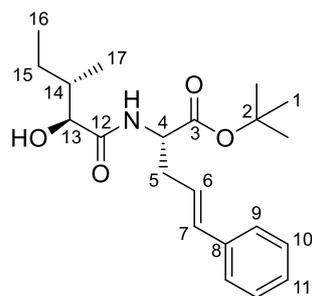
<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = 15.4 (q, C-15), 19.1 (q, C-15'), 28.0 (q, C-1), 32.1 (d, C-14), 36.1 (t, C-5), 52.1 (d, C-4), 76.0 (d, C-13), 82.4 (s, C-2), 123.7 (d, C-6), 126.1 (d, C-9), 127.4 (d, C-11), 128.5 (d, C-10), 133.8 (d, C-7), 136.8 (s, C-8), 170.6 (s, C-3), 172.9 (s, C-12).

#### ***tert*-Butyl (*S,E*)-2-((2*S*,3*S*)-2-hydroxy-3-methylpentanamido)-5-phenylpent-4-enoate (**2aa'**)**

According to general procedure A for allylic alkylation, **1c** (71.0 mg, 289 μmol, 1.0 equiv) LHMDS (1.59 mL, 1.59 mmol, 1.0 M in THF, 5.5 equiv), chlorotitanium(IV) triisopropoxide (434 μL, 434 μmol, 1.0 M in hexane, 1.5 equiv), cinnamyl ethyl carbonate (40.0 mg, 194 μmol, 0.7 equiv), allylpalladiumchloride dimer (2.1 mg, 5.79 μmol, 2 mol %) and triphenylphosphine (6.8 mg, 26.0 μmol, 9 mol %) were reacted at -78 °C. Column chromatography (silica, DCM/Et<sub>2</sub>O 9:1) afforded **2aa'** (50.6 mg, 140 μmol, 72%) and **2aa** (7.0 mg, 19.0 μmol, 10%) separately as colorless oils.

**R<sub>f</sub>(2aa)** = 0.26 (DCM/Et<sub>2</sub>O 9:1), **R<sub>f</sub>(2aa')** = 0.20 (DCM/Et<sub>2</sub>O 9:1)

Main diastereomer (*S,S*):



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.81 (t, <sup>3</sup>J<sub>16,15</sub> = 7.4 Hz, 3 H, 16-H), 0.97 (d, <sup>3</sup>J<sub>17,14</sub> = 7.4 Hz, 3 H, 17-H), 1.16 (m, 1 H, 15-H<sub>a</sub>), 1.39 (m, 1 H, 15-H<sub>b</sub>), 1.47 (s, 9 H, 1-H), 1.88 (sextd, <sup>3</sup>J<sub>14,15/17</sub> = 6.8 Hz, <sup>3</sup>J<sub>14,13</sub> = 3.9 Hz, 1 H, 14-H), 2.66 (dt, <sup>2</sup>J<sub>5a,5b</sub> = 14.2 Hz, <sup>3</sup>J<sub>5a,4/6</sub> = 7.1 Hz, 1 H, 5-H<sub>a</sub>), 2.75 (m, 1 H, 5-H<sub>b</sub>), 2.90 (d, <sup>3</sup>J<sub>OH,13</sub> = 5.3 Hz, 1 H, OH), 4.03 (dd, <sup>3</sup>J<sub>13,OH</sub> = 4.8 Hz, <sup>3</sup>J<sub>13,14</sub> = 3.7 Hz, 1 H, 13-H), 4.60 (dt, <sup>3</sup>J<sub>4,NH</sub> = 7.9 Hz, <sup>3</sup>J<sub>4,5</sub> = 6.0 Hz, 1 H, 4-H), 6.07 (dt, <sup>3</sup>J<sub>6,7</sub> = 15.7 Hz, <sup>3</sup>J<sub>6,5</sub> = 7.5 Hz, 1 H, 6-H), 6.44 (d, <sup>3</sup>J<sub>7,6</sub> = 15.7 Hz, 1 H, 7-H), 7.11 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.9 Hz, 1 H, NH), 7.26 (m, 5 H, 9-H, 10-H, 11-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.7 (q, C-16), 15.5 (q, C-17), 23.0 (t, C-15), 28.0 (q, C-1), 36.1 (t, C-5), 38.6 (d, C-14), 52.0 (d, C-4), 76.3 (d, C-13), 82.4 (s, C-2), 123.8 (d, C-6), 126.1 (d, C-9), 127.4 (d, C-11), 128.5 (d, C-10), 133.8 (d, C-7), 136.8 (s, C-8), 170.9 (s, C-3), 173.0 (s, C-12).

**Optical rotation:**  $[\alpha]_D^{20} = +40.1$  (c = 1.0, CHCl<sub>3</sub>)

<b>HRMS (CI):</b>	Calculated	Found
C <sub>21</sub> H <sub>32</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	362.2326	362.2341

Minor diastereomer (*S,R*):

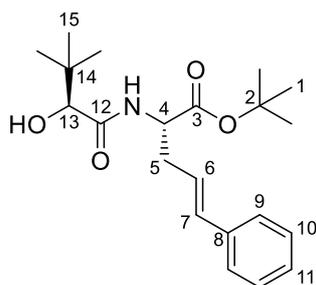
**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.85 (t, <sup>3</sup>J<sub>16,15</sub> = 7.5 Hz, 3 H, 16-H), 0.99 (d, <sup>3</sup>J<sub>17,14</sub> = 6.8 Hz, 3 H, 17-H), 1.20 (m, 1 H, 15-H<sub>a</sub>), 1.41 (m, 1 H, 15-H<sub>b</sub>), 1.47 (s, 9 H, 1-H), 1.83 (dq, <sup>3</sup>J<sub>14,15a</sub> = 10.1 Hz, <sup>3</sup>J<sub>14,17</sub> = 6.8 Hz, <sup>3</sup>J<sub>14,13/15b</sub> = 3.6 Hz, 1 H, 14-H), 2.69 (d, <sup>3</sup>J<sub>OH,13</sub> = 5.4 Hz, 1 H, OH), 2.73 (m, 2 H, 5-H), 4.01 (dd, <sup>3</sup>J<sub>13,OH</sub> = 5.3 Hz, <sup>3</sup>J<sub>13,14</sub> = 3.5 Hz, 1 H, 13-H), 4.63 (dt, <sup>3</sup>J<sub>4,NH</sub> = 7.8 Hz, <sup>3</sup>J<sub>4,5</sub> = 5.8 Hz, 1 H, 4-H), 6.06 (dt, <sup>3</sup>J<sub>6,7</sub> = 15.8 Hz, <sup>3</sup>J<sub>6,5</sub> = 7.3 Hz, 1 H, 6-H), 6.44 (d, <sup>3</sup>J<sub>7,6</sub> = 15.8 Hz, 1 H, 7-H), 6.82 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.7 Hz, 1 H, NH), 7.23 (m, 1 H, 11-H), 7.30 (m, 4 H, 9-H, 10-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.8 (q, C-16), 15.4 (q, C-17), 23.1 (t, C-15), 28.0 (q, C-1), 36.1 (t, C-5), 39.1 (d, C-14), 52.2 (d, C-4), 76.1 (d, C-13), 82.5 (s, C-2), 123.7 (d, C-6), 126.2 (d, C-9), 127.5 (d, C-11), 128.5 (d, C-10), 133.9 (d, C-7), 136.8 (s, C-8), 170.6 (s, C-3), 172.8 (s, C-12).

### **tert-Butyl (*S,E*)-2-((*S*)-2-hydroxy-3,3-dimethylbutanamido)-5-phenylpent-4-enoate (**2da'**)**

According to general procedure A for allylic alkylation, **1d** (71.0 mg, 289 μmol, 1.0 equiv), LHMDS (1.59 mL, 1.59 mmol, 1.0 M in THF, 5.5 equiv), chlorotitanium(IV) triisopropoxide (434 μL, 434 μmol, 1.0 M in hexane, 1.5 equiv), cinnamyl ethyl carbonate (40.0 mg, 194 μmol, 0.7 equiv), allylpalladiumchloride dimer (2.1 mg, 5.79 μmol, 2 mol %) and triphenylphosphine (6.8 mg, 26.0 μmol, 9 mol %) were reacted at -78 °C. Column chromatography (silica, DCM/Et<sub>2</sub>O 370:30) afforded **2da'** (43.0 mg, 119 μmol, 61%) and **2da** (4.1 mg, 11.3 μmol, 5.9%) separately as off white solids.

**R<sub>f</sub>(2da)** = 0.22 (DCM/Et<sub>2</sub>O 9:1), **R<sub>f</sub>(2da')** = 0.16 (DCM/Et<sub>2</sub>O 9:1)



Main diastereomer (*S,S*):

**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.98 (s, 9 H, 15-H), 1.46 (s, 9 H, 1-H), 2.70 (m, 2 H, 5-H), 3.14 (d, <sup>3</sup>J<sub>OH,13</sub> = 5.5 Hz, 1 H, OH), 3.74 (d, <sup>3</sup>J<sub>13,OH</sub> = 5.5 Hz, 1 H, 13-H), 4.65 (dt, <sup>3</sup>J<sub>4,NH</sub> = 7.6 Hz, <sup>3</sup>J<sub>4,5</sub> = 5.9 Hz, 1 H, 4-H), 6.07 (dt, <sup>3</sup>J<sub>6,7</sub> = 15.8 Hz, <sup>3</sup>J<sub>6,5</sub> = 7.3 Hz, 1 H, 6-H), 6.45 (d, <sup>3</sup>J<sub>7,6</sub> = 15.8 Hz, 1 H, 7-H), 6.89 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.6 Hz, 1 H, NH), 7.25 (m, 5 H, 9-H, 10-H, 11-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 25.9 (q, C-15), 28.0 (q, C-1), 35.0 (s, C-14), 36.1 (t, C-5), 52.1 (d, C-4), 79.5 (d, C-13), 82.4 (s, C-2), 123.8 (d, C-6), 126.1 (d, C-9), 127.4 (d, C-11), 128.5 (d, C-10), 133.9 (d, C-7), 136.8 (s, C-8), 170.8 (s, C-3), 172.2 (s, C-12).

**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = +21.0$  (c = 1.0, CHCl<sub>3</sub>)

**Melting point:** 70–72 °C

<b>HRMS (CI):</b>	Calculated	Found
C <sub>21</sub> H <sub>31</sub> NO <sub>4</sub> [M] <sup>+</sup>	361.2253	361.2247

Minor diastereomer (*S,R*):

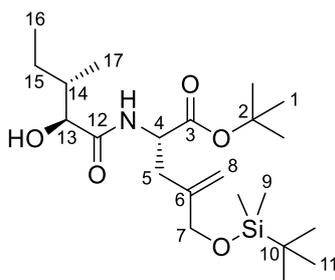
**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.98 (s, 9 H, 15-H), 1.47 (s, 9 H, 1-H), 2.68 (m, 1 H, 5-H<sub>a</sub>), 2.76 (m, 1 H, 5-H<sub>b</sub>), 3.01 (d, <sup>3</sup>J<sub>OH,13</sub> = 5.9 Hz, 1 H, OH), 3.71 (d, <sup>3</sup>J<sub>13,OH</sub> = 6.0 Hz, 1 H, 13-H), 4.65 (dt, <sup>3</sup>J<sub>4,NH</sub> = 7.5 Hz, <sup>3</sup>J<sub>4,5</sub> = 5.8 Hz, 1 H, 4-H), 6.06 (dt, <sup>3</sup>J<sub>6,7</sub> = 15.7 Hz, <sup>3</sup>J<sub>6,5</sub> = 7.3 Hz, 1 H, 6-H), 6.45 (d, <sup>3</sup>J<sub>7,6</sub> = 15.7 Hz, 1 H, 7-H), 6.65 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.5 Hz, 1 H, NH), 7.22 (m, 1 H, 11-H), 7.29 (m, 4 H, 9-H, 10-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 25.8 (q, C-15), 28.0 (q, C-1), 35.1 (s, C-14), 36.1 (t, C-5), 52.4 (d, C-4), 79.4 (d, C-13), 82.5 (s, C-2), 123.8 (d, C-6), 126.1 (d, C-9), 127.5 (d, C-11), 128.5 (d, C-10), 134.0 (d, C-7), 136.8 (s, C-8), 170.6 (s, C-3), 172.0 (s, C-12).

***tert*-Butyl (*S*)-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-2-((2*S*,3*S*)-2-hydroxy-3-methylpentanamido)pent-4-enoate (**2ag'**)**

According to general procedure A for allylic alkylation, **1c** (71.0 mg, 289 μmol), LHMDS (1.59 mmol, 1.0 M in THF, 5.5 equiv), chlorotitanium(IV) triisopropoxide (434 μL, 1.0 M in hexane, 1.5 equiv), carbonate **SI-14** (53.2 mg, 194 μmol, 0.7 equiv), allylpalladiumchloride dimer (4.2 mg, 11.6 μmol, 4 mol %) and triphenylphosphine (13.7 mg, 52.0 μmol, 18 mol %) were reacted at -78 °C. Column chromatography (silica, DCM/Et<sub>2</sub>O 9:1) afforded **2ag'** (49.1 mg, 114 μmol, 59%, 94/6 *dr*) as a colorless oil.

**R<sub>f</sub>(2ag')** = 0.30 (DCM/Et<sub>2</sub>O 9:1)



Main Diastereomer (*S,S*):

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.08 (s, 3 H, 9-H), 0.08 (s, 3 H, 9-H'), 0.88 (t, <sup>3</sup>J<sub>16,15</sub> = 7.4 Hz, 3 H, 16-H), 0.92 (s, 9 H, 11-H), 0.99 (d, <sup>3</sup>J<sub>17,14</sub> = 7.0 Hz, 3 H, 17-H), 1.18 (m, 1 H, 15-H<sub>a</sub>), 1.41 (m, 1 H, 15-H<sub>b</sub>), 1.46 (s, 9 H, 1-H), 1.85 (dq, <sup>3</sup>J<sub>14,15a</sub> = 13.4 Hz, <sup>3</sup>J<sub>14,17</sub> = 6.8 Hz, <sup>3</sup>J<sub>14,13/15b</sub> = 3.4 Hz, 1 H, 14-H), 2.41 (dd, <sup>2</sup>J<sub>5a,5b</sub> = 14.3 Hz, <sup>3</sup>J<sub>5a,4</sub> = 8.6 Hz, 1 H, 5-H<sub>a</sub>), 2.65 (dd, <sup>2</sup>J<sub>5b,5a</sub> = 14.4 Hz, <sup>3</sup>J<sub>5b,4</sub> = 5.2 Hz, 1 H, 5-H<sub>b</sub>), 2.81 (d, <sup>3</sup>J<sub>OH,13</sub> = 5.4 Hz, 1 H, OH), 4.00 (dd, <sup>3</sup>J<sub>13,OH</sub> = 5.4 Hz, <sup>3</sup>J<sub>13,14</sub> = 3.7 Hz, 1 H, 13-H), 4.08 (d, <sup>2</sup>J<sub>7a,7b</sub> = 13.8 Hz, 1 H, 7-H<sub>a</sub>), 4.16 (d, <sup>2</sup>J<sub>7b,7a</sub> = 13.7 Hz, 1 H, 7-H<sub>b</sub>), 4.59 (td, <sup>3</sup>J<sub>4,NH/5a</sub> = 8.2 Hz, <sup>3</sup>J<sub>4,5b</sub> = 5.3 Hz, 1 H, 4-H), 4.90 (s, 1 H, 8-H<sub>a</sub>), 5.11 (d, <sup>2</sup>J<sub>8a,8b</sub> = 1.2 Hz, 1 H, 8-H<sub>b</sub>), 6.94 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.7 Hz, 1 H, NH).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ = -5.4 (q, C-9), 11.8 (q, C-16), 15.4 (q, C-17), 18.3 (s, C-10), 23.1 (t, C-15), 25.9 (q, C-11), 28.0 (q, C-1), 35.8 (t, C-5), 38.8 (d, C-14), 51.0 (d, C-4), 65.2 (t, C-7), 76.2 (d, C-13), 82.2 (s, C-2), 113.0 (t, C-8), 143.6 (s, C-6), 171.2 (s, C-3), 173.0 (s, C-12).

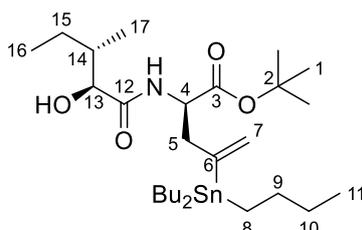
Optical rotation:  $[\alpha]_D^{20} = -3.3$  (c = 1.0, CHCl<sub>3</sub>)

HRMS (CI):	Calculated	Found
C <sub>22</sub> H <sub>44</sub> NO <sub>5</sub> Si [M+H] <sup>+</sup>	430.2983	430.2992

**tert-Butyl (R)-2-((2*S*,3*S*)-2-hydroxy-3-methylpentanamido)-4-(tributylstannyl)pent-4-enoate (**2ah**)**

According to general procedure B for allylic alkylation, **1c** (71.0 mg, 289 μmol, 1.0 equiv), chlorotitanium(IV) triisopropoxide (434 μL, 434 μmol, 1.0 M in hexane, 1.5 equiv), DIPA (132 μL, 927 μmol, 3.2 equiv), *n*-BuLi (359 μL, 898 μmol, 3.1 equiv), carbonate **SI-12** (81.0 mg, 194 μmol, 0.7 equiv), [AllylPdCl]<sub>2</sub> (4.2 mg, 11.6 μmol, 4 mol %) and PPh<sub>3</sub> (13.7 mg, 52.0 μmol, 18 mol %) in THF (3 mL) were reacted at -78 °C. After column chromatography (silica, DCM/Et<sub>2</sub>O 97:3 + 1% NEt<sub>3</sub>), **2ah** (76.0 mg, 132 μmol, 68%, > 99:1 dr) was obtained as a slightly yellow oil.

R<sub>f</sub>(**2ah**) = 0.25 (DCM/Et<sub>2</sub>O 94:6 + 1% NEt<sub>3</sub>)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.89 (t, <sup>3</sup>J<sub>16,15</sub> = 7.4 Hz, 3 H, 16-H), 0.89 (t, <sup>3</sup>J<sub>11,10</sub> = 7.3 Hz, 9 H, 11-H), 0.96 (m, 9 H, 8-H, 17-H), 1.18 (m, 1 H, 15-H<sub>a</sub>), 1.32 (sext, <sup>3</sup>J<sub>10,9/11</sub> = 7.3 Hz, 6 H, 10-H), 1.46 (s, 9 H, 1-H), 1.48 (m, 7 H, 9-H, 15-H<sub>b</sub>), 1.85 (dq, <sup>3</sup>J<sub>14,15a</sub> = 10.1 Hz, <sup>3</sup>J<sub>14,17</sub> = 6.8 Hz, <sup>3</sup>J<sub>14,13/15b</sub> = 3.6 Hz, 1 H, 14-H), 2.48 (dd, <sup>2</sup>J<sub>5a,5b</sub> = 14.2 Hz, <sup>3</sup>J<sub>5a,4</sub> = 9.3 Hz, 1 H, 5-H<sub>a</sub>), 2.71 (d, <sup>3</sup>J<sub>OH,13</sub> = 5.3 Hz, 1 H, OH), 2.80 (dd, <sup>2</sup>J<sub>5b,5a</sub> = 14.1 Hz, <sup>3</sup>J<sub>5b,4</sub> = 5.1 Hz, 1 H, 5-H<sub>b</sub>), 3.99 (dd, <sup>3</sup>J<sub>13,OH</sub> = 5.2 Hz, <sup>3</sup>J<sub>13,14</sub> = 3.4 Hz, 1 H, 13-H), 4.39 (ddd, <sup>3</sup>J<sub>4,5a</sub> = 9.1 Hz, <sup>3</sup>J<sub>4,NH</sub> = 7.9 Hz, <sup>3</sup>J<sub>4,5b</sub> = 5.2 Hz, 1 H, 4-H), 5.24 (dd, <sup>3</sup>J<sub>7a,Sn</sub> = 58.9 Hz, <sup>2</sup>J<sub>7a,7b</sub> = 2.2 Hz, 1 H, 7-H<sub>a</sub>), 5.73 (dd, <sup>3</sup>J<sub>7b,Sn</sub> = 128.3 Hz, <sup>2</sup>J<sub>7b,7a</sub> = 0.9 Hz, 1 H, 7-H<sub>b</sub>), 6.58 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.6 Hz, 1 H, NH).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 9.6 (dt, <sup>1</sup>J<sub>8,Sn</sub> = 319.9 Hz, C-8), 11.8 (q, C-16), 13.6 (q, C-11), 15.5 (q, C-17), 22.9 (t, C-15), 27.3 (dt, <sup>3</sup>J<sub>10,Sn</sub> = 58.7 Hz, C-10), 28.0 (q, C-1), 29.0 (dt, <sup>2</sup>J<sub>9,Sn</sub> = 19.8 Hz, C-9), 39.0 (d, C-14), 43.9 (dt, <sup>2</sup>J<sub>5,Sn</sub> = 41.1 Hz, C-5), 52.0 (dd, <sup>3</sup>J<sub>4,Sn</sub> = 11.7 Hz, C-4), 76.2 (d, C-13), 81.9 (s, C-2), 128.2 (dt, <sup>2</sup>J<sub>7,Sn</sub> = 24.2 Hz, C-7), 150.2 (s, C-6), 171.2 (s, C-3), 172.6 (s, C-12).

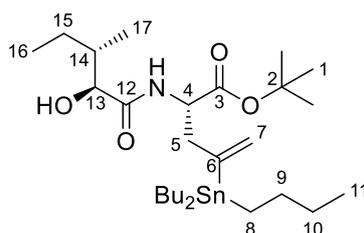
**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = -16.5$  (c = 1.0, CHCl<sub>3</sub>)

HRMS (CI):	Calculated	Found
C <sub>23</sub> H <sub>44</sub> NO <sub>4</sub> Sn [M-C <sub>4</sub> H <sub>9</sub> ] <sup>+</sup>	518.2287	518.2269

**tert-Butyl (S)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-(tributylstannyl)pent-4-enoate (2ah')**

According to general procedure A for allylic alkylation, **1c** (71.0 mg, 289 μmol, 1.0 equiv), chlorotitanium(IV) triisopropoxide (9434 μL, 434 μmol, 1.0 M in hexane, 1.5 equiv), LHMDS (1.59 mL, 1.59 mmol, 1.0 M in THF, 5.5 equiv), stannylated carbonate **SI-12** (81.0 mg, 194 μmol, 0.7 equiv), allylpalladiumchloride dimer (4.2 mg, 11.6 μmol, 4 mol %) and triphenylphosphine (13.7 mg, 52.0 μmol, 18 mol %) in THF (3 mL) were reacted at -78 °C. After column chromatography (silica, DCM/Et<sub>2</sub>O 9:1 + 1% NEt<sub>3</sub>), vinylstannane **6b** (72.4 mg, 126 μmol, 65 %, 97:3 dr) was obtained as a slightly yellow oil.

**R<sub>f</sub>(6b)** = 0.21 (DCM/Et<sub>2</sub>O 9:1 + 1% NEt<sub>3</sub>)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.90 (t, <sup>3</sup>J<sub>11,10</sub> = <sup>3</sup>J<sub>16,15</sub> = 7.4 Hz, 12 H, 11-H, 16-H), 0.96 (m, 9 H, 8-H, 17-H), 1.17 (m, 1 H, 15-H<sub>a</sub>), 1.32 (sext, <sup>3</sup>J<sub>10,9/11</sub> = 7.3 Hz, 6 H, 10-H), 1.46 (s, 9 H, 1-H), 1.49 (m, 7 H, 9-H, 15-H<sub>b</sub>), 1.85 (m, 1 H, 14-H), 2.48 (dd, <sup>2</sup>J<sub>5a,5b</sub> = 14.1 Hz, <sup>3</sup>J<sub>5a,4</sub> = 9.4 Hz, 1 H, 5-H<sub>a</sub>), 2.78 (dd, <sup>2</sup>J<sub>5b,5a</sub> = 14.1 Hz, <sup>3</sup>J<sub>5b,4</sub> = 4.8 Hz, 1 H, 5-H<sub>b</sub>), 3.21 (d, <sup>3</sup>J<sub>OH,13</sub> = 5.3 Hz, 1 H, OH), 4.00 (dd, <sup>3</sup>J<sub>13,OH</sub> = 5.3 Hz, <sup>3</sup>J<sub>13,14</sub> = 3.7 Hz, 1 H, 13-H), 4.39 (ddd, <sup>3</sup>J<sub>4,5a</sub> = 9.3 Hz, <sup>3</sup>J<sub>4,NH</sub> = 7.4 Hz, <sup>3</sup>J<sub>4,5b</sub> = 5.0 Hz, 1 H, 4-H), 5.24 (dd, <sup>3</sup>J<sub>7a,Sn</sub> = 59.1 Hz, <sup>2</sup>J<sub>7a,7b</sub> = 2.0 Hz, 1 H, 7-H<sub>a</sub>), 5.73 (d, <sup>3</sup>J<sub>7b,Sn</sub> = 128.4 Hz, 1 H, 7-H<sub>b</sub>), 6.74 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.3 Hz, 1 H, NH).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 9.6 (dt, <sup>1</sup>J<sub>8,Sn</sub> = 320.0 Hz, C-8), 11.8 (q, C-16), 13.7 (q, C-11), 15.5 (q, C-17), 23.2 (t, C-15), 27.3 (dt, <sup>3</sup>J<sub>10,Sn</sub> = 57.2 Hz, C-10), 28.0 (q, C-1), 29.0 (dt, <sup>2</sup>J<sub>9,Sn</sub> = 20.5 Hz, C-9), 38.6 (d, C-14), 43.9 (dt, <sup>2</sup>J<sub>5,Sn</sub> = 40.4 Hz, C-5), 52.0 (dd, <sup>3</sup>J<sub>4,Sn</sub> = 11.7 Hz, C-4), 76.2

(d, C-13), 82.0 (s, C-2), 128.3 (dt,  $^2J_{7,Sn} = 24.2$  Hz, C-7), 150.1 (s, C-6), 171.7 (s, C-3), 173.1 (s, C-12).

**Optical rotation:**  $[\alpha]_D^{20} = -3.5$  (c = 0.5, CHCl<sub>3</sub>)

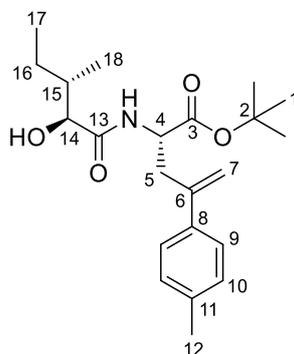
<b>HRMS (CI):</b>	Calculated	Found
C <sub>27</sub> H <sub>53</sub> NO <sub>4</sub> Sn [M] <sup>+</sup>	575.2997	575.2996

#### 4.4 Further Modification of the side chain

##### *tert*-Butyl (S)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-(p-tolyl)pent-4-enoate (**3a**)

A schlenk tube was charged with [Ph<sub>2</sub>PO<sub>2</sub>][NBu<sub>4</sub>] (64.0 mg, 139 μmol, 2.0 equiv) and the phosphinate was carefully melted *in vacuo* with a heat gun. Before solidification, dry DMF (0.3 mL, degassed with Argon) was added and 4-iodo toluene (30.4 mg, 139 μmol, 2.0 equiv), CuTC (26.6 mg, 139 μmol, 2.0 equiv) and Pd(PPh<sub>3</sub>)<sub>4</sub> (4.0 mg, 3.5 μmol, 5 mol %) were subsequently added. After addition of a solution of stannane **2ah'** (40.0 mg, 70.0 μmol, 1.0 equiv) in dry DMF (0.7 mL, degassed with Argon), the tube was sealed and stirred at room temperature for 2 hours. The reaction mixture was diluted with EtOAc and water and filtrated through a pad of celite. The layers were separated and the organic layer washed twice with water. After drying (Na<sub>2</sub>SO<sub>4</sub>), the solvent was removed under reduced pressure and the residue purified by column chromatography (silica/K<sub>2</sub>CO<sub>3</sub> 9:1, DCM/Et<sub>2</sub>O 92:8) to afford **3a** (19.3 mg, 51.5 μmol, 74%) as a white solid.

R<sub>f</sub>(**3a**) = 0.15 (DCM/Et<sub>2</sub>O 9:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.85 (t,  $^3J_{17,16} = 7.5$  Hz, 3 H, 17-H), 0.94 (d,  $^3J_{18,15} = 7.0$  Hz, 3 H, 18-H), 1.13 (m, 1 H, 16-H<sub>a</sub>), 1.33 (m, 1 H, 16-H<sub>b</sub>), 1.41 (s, 9 H, 1-H), 1.76 (dqt,  $^3J_{15,16a} = 13.5$  Hz,  $^3J_{15,18} = 6.9$  Hz,  $^3J_{15,14/16b} = 4.0$  Hz, 1 H, 15-H), 2.34 (s, 3 H, 12-H), 2.73 (bs, 1 H, OH), 2.91 (dd,  $^2J_{5a,5b} = 14.3$  Hz,  $^3J_{5a,4} = 7.5$  Hz, 1 H, 5-H<sub>a</sub>), 3.01 (dd,  $^2J_{5b,5a} = 14.3$  Hz,  $^3J_{5b,4} = 6.1$  Hz, 1 H, 5-H<sub>b</sub>), 3.87 (dd,  $^3J_{14,15} = 3.7$  Hz, 1 H, 14-H), 4.52 (td,  $^3J_{4,5a/NH} = 7.5$  Hz,  $^3J_{4,5b} = 6.2$  Hz, 1 H, 4-H), 5.09 (d,  $^2J_{7a,7b} = 0.9$  Hz, 1 H, 7-H<sub>a</sub>), 5.31 (d,  $^2J_{7b,7a} = 1.1$  Hz, 1 H, 7-H<sub>b</sub>), 6.69 (d,  $^3J_{NH,4} = 7.6$  Hz, 1 H, NH), 7.14 (d,  $^3J_{10,9} = 8.0$  Hz, 2 H, 10-H), 7.30 (d,  $^3J_{9,10} = 8.1$  Hz, 2 H, 9-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.8 (q, C-17), 15.4 (q, C-18), 21.1 (q, C-12), 23.2 (t, C-16), 27.9 (q, C-1), 38.2 (t, C-5), 38.7 (d, C-15), 51.6 (d, C-4), 76.1 (d, C-14), 82.3 (s, C-2), 115.3 (t, C-7), 126.2 (d, C-9), 129.2 (d, C-10), 137.1 (s, C-8), 137.7 (s, C-11), 143.7 (s, C-6), 171.0 (s, C-3), 172.8 (s, C-13).

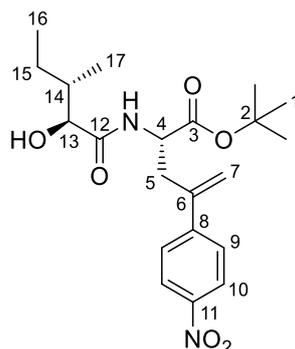
**Optical rotation:**  $[\alpha]_D^{20} = +1.4$  (c = 1.0, CHCl<sub>3</sub>)

<b>Melting point:</b>	119-121 °C	
<b>HRMS (CI):</b>	Calculated	Found
C <sub>18</sub> H <sub>26</sub> NO <sub>4</sub> [M-C <sub>4</sub> H <sub>7</sub> ] <sup>+</sup>	320.1862	320.1885

**tert-Butyl (S)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-(4-nitrophenyl)pent-4-enoate (3b)**

A schlenk tube was charged with [Ph<sub>2</sub>PO<sub>2</sub>][NBu]<sub>4</sub> (64.0 mg, 139 μmol, 2.0 equiv) and the phosphinate was carefully melted *in vacuo* with a heat gun. Before solidification, dry DMF (0.3 mL, degassed with Argon) was added and 1-iodo-4-nitrobenzene (34.7 mg, 139 μmol, 2.0 equiv), CuTC (26.6 mg, 139 μmol, 2.0 equiv) and Pd(PPh<sub>3</sub>)<sub>4</sub> (4.0 mg, 3.5 μmol, 5 mol %) were subsequently added. After addition of a solution of stannane **2ah**<sup>1</sup> (40.0 mg, 70.0 μmol, 1.0 equiv) in dry DMF (0.7 mL, degassed with Argon), the tube was sealed and stirred at room temperature for 2 hours. The reaction mixture was diluted with EtOAc and water and filtrated through a pad of celite. The layers were separated and the organic layer washed twice with water. After drying (Na<sub>2</sub>SO<sub>4</sub>), the solvent was removed under reduced pressure and the residue purified by column chromatography (silica/K<sub>2</sub>CO<sub>3</sub> 9:1, DCM/Et<sub>2</sub>O 90:10) to afford **3b** (23.6 mg, 58.1 μmol, 83%) as a white solid.

R<sub>f</sub>(**3b**) = 0.23 (DCM/Et<sub>2</sub>O 85:15)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.88 (t, <sup>3</sup>J<sub>16,15</sub> = 7.5 Hz, 3 H, 16-H), 0.96 (d, <sup>3</sup>J<sub>17,14</sub> = 7.0 Hz, 3 H, 17-H), 1.16 (m, 1 H, 15-H<sub>a</sub>), 1.32 (m, 1 H, 15-H<sub>b</sub>), 1.42 (s, 9 H, 1-H), 1.82 (m, 1 H, 14-H), 2.69 (d, <sup>3</sup>J<sub>OH,13</sub> = 5.1 Hz, 1 H, OH), 3.01 (m, 2 H, 5-H), 3.95 (t, <sup>3</sup>J<sub>13,14/OH</sub> = 4.0 Hz, 1 H, 13-H), 4.52 (q, <sup>3</sup>J<sub>4,5/NH</sub> = 7.1 Hz, 1 H, 4-H), 5.32 (s, 1 H, 7-H<sub>a</sub>), 5.50 (s, 1 H, 7-H<sub>b</sub>), 6.95 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.6 Hz, 1 H, NH), 7.60 (d, <sup>3</sup>J<sub>9,10</sub> = 8.7 Hz, 2 H, 9-H), 8.22 (d, <sup>3</sup>J<sub>10,9</sub> = 8.7 Hz, 2 H, 10-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.8 (q, C-16), 15.4 (q, C-17), 23.2 (t, C-15), 28.0 (q, C-1), 38.4 (t, C-5), 38.6 (d, C-14), 51.2 (d, C-4), 76.3 (d, C-13), 82.9 (s, C-2), 119.2 (t, C-7), 123.8 (d, C-10), 127.2 (d, C-9), 142.4 (s, C-6), 146.4 (s, C-8), 147.3 (s, C-11), 170.6 (s, C-3), 172.8 (s, C-12).

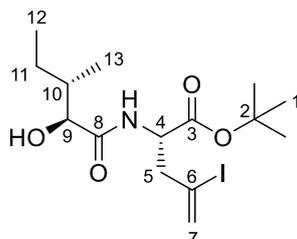
**Optical rotation:**  $[\alpha]_D^{20} = -14.6$  (c = 1.0, CHCl<sub>3</sub>)

<b>Melting point:</b>	74-76 °C	
<b>HRMS (CI):</b>	Calculated	Found
C <sub>21</sub> H <sub>31</sub> N <sub>2</sub> O <sub>6</sub> [M+H] <sup>+</sup>	407.2177	407.2170

### ***tert*-Butyl (S)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-iodopent-4-enoate (4)**

To a solution of **2ah'** (300 mg, 522  $\mu\text{mol}$ ) in DCM (5 mL) was added a solution of iodine (159 mg, 627  $\mu\text{mol}$ , 1.2 equiv) in DCM (5 mL) at room temperature. After 1 hour, the mixture was diluted with DCM, washed with sat.  $\text{Na}_2\text{S}_2\text{O}_3$  solution and the aqueous layer was extracted with DCM. The combined organic layers were dried ( $\text{Na}_2\text{SO}_4$ ), evaporated *in vacuo* and the residue purified by column chromatography (silica, DCM/ $\text{Et}_2\text{O}$  9:1) to afford vinyl iodide **4** (180 mg, 438  $\mu\text{mol}$ , 84%) as a white solid.

$R_f(\mathbf{4}) = 0.16$  (DCM/ $\text{Et}_2\text{O}$  9:1)



**$^1\text{H-NMR}$**  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.90$  (t,  $^3J_{12,11} = 7.5$  Hz, 3 H, 12-H), 1.00 (d,  $^3J_{13,10} = 7.0$  Hz, 3 H, 13-H), 1.22 (m, 1 H, 11- $\text{H}_a$ ), 1.44 (m, 1 H, 11- $\text{H}_b$ ), 1.48 (s, 9 H, 1-H), 1.89 (m, 1 H, 10-H), 2.83 (dd,  $^2J_{5a,5b} = 14.9$  Hz,  $^3J_{5a,4} = 8.1$  Hz, 1 H, 5- $\text{H}_a$ ), 2.87 (d,  $^3J_{\text{OH},9} = 5.4$  Hz, 1 H, OH), 2.95 (dd,  $^2J_{5b,5a} = 14.8$  Hz,  $^3J_{5b,4} = 5.5$  Hz, 1 H, 5- $\text{H}_b$ ), 4.05 (dd,  $^3J_{9,\text{OH}} = 5.0$  Hz,  $^3J_{9,10} = 3.7$  Hz, 1 H, 9-H), 4.70 (td,  $^3J_{4,\text{NH}/5a} = 8.0$  Hz,  $^3J_{4,5b} = 5.8$  Hz, 1 H, 4-H), 5.84 (s, 1 H, 7- $\text{H}_a$ ), 6.15 (s, 1 H, 7- $\text{H}_b$ ), 6.97 (d,  $^3J_{\text{NH},4} = 7.7$  Hz, 1 H, NH).

**$^{13}\text{C-NMR}$**  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 11.8$  (q, C-12), 15.5 (q, C-13), 23.2 (t, C-11), 28.0 (q, C-1), 38.7 (d, C-10), 47.2 (t, C-5), 51.9 (d, C-4), 76.3 (d, C-9), 82.9 (s, C-2), 103.8 (s, C-6), 129.2 (t, C-7), 170.1 (s, C-8), 173.0 (s, C-3).

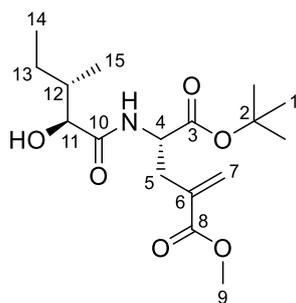
**Optical rotation:**  $[\alpha]_D^{20} = -9.1$  ( $c = 1.0$ ,  $\text{CHCl}_3$ )

<b>HRMS (CI):</b>	Calculated	Found
$\text{C}_{15}\text{H}_{26}\text{INO}_4$ $[\text{M}+\text{H}]^+$	412.0979	412.0976

### **1-(*tert*-Butyl) 5-methyl (S)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-methylenepentanedioate (5)**

To a solution of **4** (30.0 mg, 72.9  $\mu\text{mol}$ ) in dry MeOH (1 mL) was added triethylamine (41.0  $\mu\text{L}$ , 292  $\mu\text{mol}$ , 4.0 equiv) and  $\text{Pd}(\text{PPh}_3)_4$  (4.2 mg, 3.7  $\mu\text{mol}$ , 5 mol %) and CO was passed through the solution. The reaction was stirred at room temperature for 5 hours under an atmosphere of CO after which a dark red color occurred. The mixture was concentrated *in vacuo*, and the residue purified by column chromatography (silica, DCM/diethyl ether 9:1) to afford **5** (23.4 mg, 68.1  $\mu\text{mol}$ , 93%) as a colorless oil.

$R_f(\mathbf{5}) = 0.11$  (DCM/ $\text{Et}_2\text{O}$  9:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.89 (t, <sup>3</sup>J<sub>14,13</sub> = 7.5 Hz, 3 H, 14-H), 0.99 (d, <sup>3</sup>J<sub>15,12</sub> = 7.0 Hz, 3 H, 15-H), 1.19 (m, 1 H, 13-H<sub>a</sub>), 1.40 (m, 1 H, 13-H<sub>b</sub>), 1.44 (s, 9 H, 1-H), 1.83 (m, 1 H, 12-H), 2.72 (dd, <sup>2</sup>J<sub>5a,5b</sub> = 14.2 Hz, <sup>3</sup>J<sub>5a,4</sub> = 8.6 Hz, 1 H, 5-H<sub>a</sub>), 2.82 (dd, <sup>2</sup>J<sub>5b,5a</sub> = 14.2 Hz, <sup>3</sup>J<sub>5b,4</sub> = 5.4 Hz, 1 H, 5-H<sub>b</sub>), 2.90 (d, <sup>3</sup>J<sub>OH,11</sub> = 5.5 Hz, 1 H, OH), 3.78 (s, 3 H, 9-H), 4.00 (dd, <sup>3</sup>J<sub>11,OH</sub> = 5.3 Hz, <sup>3</sup>J<sub>11,12</sub> = 3.7 Hz, 1 H, 11-H), 4.66 (td, <sup>3</sup>J<sub>4,5a/NH</sub> = 8.3 Hz, <sup>3</sup>J<sub>4,5b</sub> = 5.6 Hz, 1 H, 4-H), 5.69 (s, 1 H, 7-H<sub>a</sub>), 6.27 (s, 1 H, 7-H<sub>b</sub>), 7.12 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.8 Hz, 1 H, NH).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.8 (q, C-14), 15.4 (q, C-15), 23.2 (t, C-13), 28.0 (q, C-1), 34.7 (t, C-5), 38.7 (d, C-12), 52.1 (d, C-4), 52.2 (q, C-9), 76.1 (d, C-11), 82.4 (s, C-2), 128.6 (t, C-7), 135.8 (s, C-6), 167.3 (s, C-8), 170.6 (s, C-3), 173.1 (s, C-10).

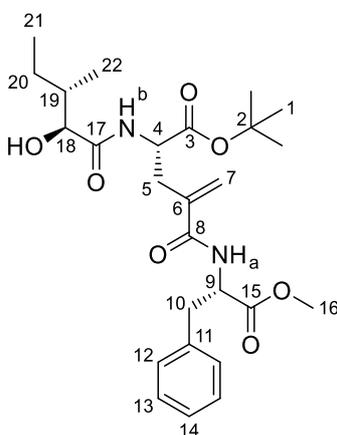
**Optical rotation:**  $[\alpha]_D^{20} = -12.1$  (c = 1.0, CHCl<sub>3</sub>)

HRMS (CI):	Calculated	Found
C <sub>17</sub> H <sub>30</sub> NO <sub>6</sub> [M+H] <sup>+</sup>	344.2068	344.2065

**tert-Butyl (S)-2-(((2S,3S)-2-hydroxy-3-methylpentanamido)-4-(((S)-1-methoxy-1-oxo-3-phenyl propan-2-yl)carbamoyl)pent-4-enoate (6a)**

To a solution of **4** (20.0 mg, 48.6 μmol), HCl-*L*-Phe-OMe (12.6 mg, 58.4 μmol, 1.2 equiv) in THF (1 mL) was subsequently added triethylamine (27.0 μL, 195 μmol, 4.0 equiv) and Pd(PPh<sub>3</sub>)<sub>4</sub> (2.8 mg, 2.43 μmol, 5 mol %) and CO was passed through the solution. The reaction was stirred at room temperature for 5 hours under an atmosphere of CO after which a dark red color occurred. The mixture was diluted with EtOAc, washed with HCl (1 M, aq.) and dried (Na<sub>2</sub>SO<sub>4</sub>). After removal of the solvent *in vacuo* the residue was purified by column chromatography (silica, DCM/MeOH 95:5) to afford **6a** (20.3 mg, 41.4 μmol, 85%) as an off white solid.

**R<sub>f</sub>(6a)** = 0.29 (DCM/MeOH 95:5)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.89 (t, <sup>3</sup>J<sub>21,20</sub> = 7.4 Hz, 3 H, 21-H), 0.99 (d, <sup>3</sup>J<sub>22,19</sub> = 6.9 Hz, 3 H, 22-H), 1.22 (m, 1 H, 20-H<sub>a</sub>), 1.42 (m, 1 H, 20-H<sub>b</sub>), 1.44 (s, 9 H, 1-H), 1.83 (m, 1 H, 19-H), 2.73 (d, <sup>3</sup>J<sub>5,4</sub> = 6.5 Hz, 2 H, 5-H), 3.00 (bs, 1 H, OH), 3.15 (dd, <sup>2</sup>J<sub>10a,10b</sub> = 13.9 Hz, <sup>3</sup>J<sub>10a,9</sub> = 6.2 Hz, 1 H, 10-H<sub>a</sub>), 3.22 (dd, <sup>2</sup>J<sub>10b,10a</sub> = 13.9 Hz, <sup>3</sup>J<sub>10b,9</sub> = 5.8 Hz, 1 H, 10-H<sub>b</sub>), 3.75 (s, 3 H, 16-H), 3.98 (t, <sup>3</sup>J<sub>18,19/OH</sub> = 4.3 Hz, 1 H, 18-H), 4.41 (q, <sup>3</sup>J<sub>4,5/NHb</sub> = 6.7 Hz, 1 H, 4-H), 4.91 (dt, <sup>3</sup>J<sub>9,NH<sub>a</sub></sub> = 7.6 Hz, <sup>3</sup>J<sub>9,10</sub> = 6.0 Hz, 1 H, 9-H), 5.43 (s, 1 H, 7-H<sub>a</sub>), 5.64 (s, 1 H, 7-H<sub>b</sub>), 6.67 (d, <sup>3</sup>J<sub>NH<sub>a</sub>,9</sub> = 7.5 Hz, 1 H, NH<sub>a</sub>), 7.12 (m, 2 H, 12-H), 7.25 (m, 3 H, 13-H, 14-H), 7.56 (d, <sup>3</sup>J<sub>NH<sub>b</sub>,4</sub> = 7.1 Hz, 1 H, NH<sub>b</sub>).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.8 (q, C-21), 15.3 (q, C-22), 23.2 (t, C-20), 28.0 (q, C-1), 34.7 (t, C-5), 37.6 (t, C-10), 38.9 (d, C-19), 52.4 (q, C-16), 52.7 (d, C-4), 53.4 (d, C-9), 75.9 (d, C-18), 82.3 (s, C-2), 122.3 (t, C-7), 127.1 (d, C-14), 128.6 (d, C-13), 129.2 (d, C-12), 135.8 (s, C-11), 140.1 (s, C-6), 167.9 (s, C-8), 170.1 (s, C-3), 171.9 (s, C-15), 173.5 (s, C-17).

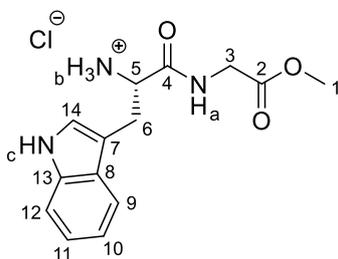
**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = +18.0$  (c = 1.0, CHCl<sub>3</sub>)

**Melting point:** 77–79 °C

<b>HRMS (CI):</b>	Calculated	Found
C <sub>26</sub> H <sub>39</sub> N <sub>2</sub> O <sub>7</sub> [M+H] <sup>+</sup>	491.2752	491.2723

**tert-Butyl (S)-4-(((S)-3-(1H-indol-3-yl)-1-((2-methoxy-2-oxoethyl)amino)-1-oxopropan-2-yl)carbamoyl)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)pent-4-enoate (6b)**

At 0 °C *N*-Boc-*L*-Trp-Gly-OMe (300 mg, 799 μmol) was treated with HCl (4.0 M in dioxane, 2.0 mL, 8.00 mmol, 10 equiv) for 2 hours until complete Boc-deprotection was observed by TLC. The solvent was removed *in vacuo* to afford HCl-*L*-Trp-Gly-OMe (249 mg, 799 μmol, quant.) as a white hygroscopic solid.

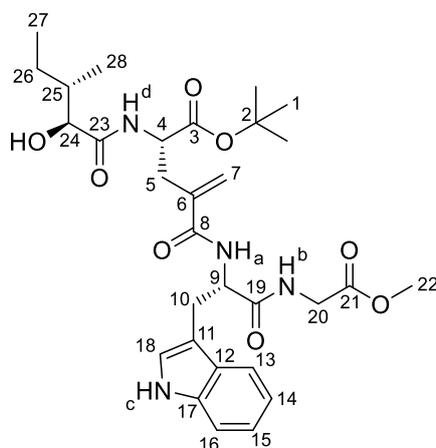


**<sup>1</sup>H-NMR** (400 MHz, DMSO-*d*<sub>6</sub>): δ = 3.13 (dd, <sup>2</sup>J<sub>6a,6b</sub> = 14.8 Hz, <sup>3</sup>J<sub>6a,5</sub> = 8.0 Hz, 1 H, 6-H<sub>a</sub>), 3.28 (dd, <sup>2</sup>J<sub>6b,6a</sub> = 14.8 Hz, <sup>3</sup>J<sub>6b,5</sub> = 5.5 Hz, 1 H, 6-H<sub>b</sub>), 3.65 (s, 3 H, 1-H), 3.92 (dd, <sup>2</sup>J<sub>3a,3b</sub> = 17.5 Hz, <sup>3</sup>J<sub>3a,NH<sub>a</sub></sub> = 5.8 Hz, 1 H, 3-H<sub>a</sub>), 3.97 (dd, <sup>2</sup>J<sub>3b,3a</sub> = 17.5 Hz, <sup>3</sup>J<sub>3b,NH<sub>a</sub></sub> = 5.8 Hz, 1 H, 3-H<sub>b</sub>), 4.05 (bs, 1 H, 5-H), 7.01 (td, <sup>3</sup>J<sub>10,9/11</sub> = 7.4 Hz, <sup>4</sup>J<sub>10,12</sub> = 0.9 Hz, 1 H, 10-H), 7.09 (td, <sup>3</sup>J<sub>11,10/12</sub> = 7.4 Hz, <sup>4</sup>J<sub>11,9</sub> = 1.0 Hz, 1 H, 11-H), 7.25 (d, <sup>3</sup>J<sub>14,NH<sub>c</sub></sub> = 2.3 Hz, 1 H, 14-H), 7.37 (d, <sup>3</sup>J<sub>12,11</sub> = 8.1 Hz, 1 H, 12-H), 7.71 (d, <sup>3</sup>J<sub>9,10</sub> = 7.8 Hz, 1 H, 9-H), 8.19 (bs, 3 H, NH<sub>3</sub><sup>+</sup>), 9.13 (t, <sup>3</sup>J<sub>NH<sub>a</sub>,3</sub> = 5.7 Hz, 1 H, NH<sub>a</sub>), 11.1 (d, <sup>3</sup>J<sub>NH<sub>c</sub>,14</sub> = 1.2 Hz, 1 H, NH<sub>c</sub>).

To a solution of **4** (20.0 mg, 48.6 μmol), HCl-*L*-Trp-Gly-OMe (16.7 mg, 53.6 μmol, 1.1 equiv) in THF (1 mL) was subsequently added triethylamine (27.0 μL, 195 μmol, 4.0 equiv) and Pd(PPh<sub>3</sub>)<sub>4</sub> (2.8 mg, 2.43 μmol, 5 mol %) and CO was passed through the solution. The reaction was stirred at room temperature for 5 hours under an atmosphere of CO after which a dark red color occurred. The mixture was diluted with EtOAc, washed with HCl (1 M) and dried (Na<sub>2</sub>SO<sub>4</sub>). After removal of the solvent *in vacuo* the residue was purified by column

chromatography (silica, DCM/MeOH 95:5) to afford **6b** (26.0 mg, 44.3  $\mu\text{mol}$ , 91%) as a colorless resin.

$R_f(\mathbf{6b}) = 0.14$  (DCM/MeOH 95:5)



$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.73$  (t,  $^3J_{27,26} = 7.5$  Hz, 3 H, 27-H), 0.85 (d,  $^3J_{28,25} = 6.9$  Hz, 3 H, 28-H), 1.06 (m, 1 H, 26- $\text{H}_a$ ), 1.27 (m, 1 H, 26- $\text{H}_b$ ), 1.41 (s, 9 H, 1-H), 1.66 (m, 1 H, 25-H), 2.31 (dd,  $^2J_{5a,5b} = 13.8$  Hz,  $^3J_{5a,4} = 9.8$  Hz, 1 H, 5- $\text{H}_a$ ), 3.10 (dd,  $^2J_{5b,5a} = 13.6$  Hz,  $^3J_{5b,4} = 3.1$  Hz, 1 H, 5- $\text{H}_b$ ), 3.24 (bs, 1 H, OH), 3.22 (dd,  $^2J_{10a,10b} = 14.8$  Hz,  $^3J_{10a,9} = 6.0$  Hz, 1 H, 10- $\text{H}_a$ ), 3.48 (dd,  $^2J_{10b,10a} = 14.9$  Hz,  $^3J_{10b,9} = 5.5$  Hz, 1 H, 10- $\text{H}_b$ ), 3.68 (s, 3 H, 22-H), 3.85 (m, 2 H, 20- $\text{H}_a$ , 24-H), 4.05 (dd,  $^2J_{20b,20a} = 17.6$  Hz,  $^3J_{20b,\text{NH}} = 6.0$  Hz, 1 H, 20- $\text{H}_b$ ), 4.55 (ddd,  $^3J_{4,5a} = 9.8$  Hz,  $^3J_{4,\text{NHd}} = 7.9$  Hz,  $^3J_{4,5b} = 3.5$  Hz, 1 H, 4-H), 4.92 (dt,  $^3J_{9,\text{NH}_a} = 7.6$  Hz,  $^3J_{9,10} = 5.9$  Hz, 1 H, 9-H), 5.20 (m, 2 H, 7-H), 6.38 (d,  $^3J_{\text{NH}_a,9} = 8.4$  Hz, 1 H,  $\text{NH}_a$ ), 7.11 (m, 1 H, 14-H), 7.17 (m, 2 H, 15-H, 18-H), 7.35 (d,  $^3J_{16,15} = 8.1$  Hz, 1 H, 16-H), 7.44 (d,  $^3J_{\text{NHd},4} = 7.8$  Hz, 1 H,  $\text{NHd}$ ), 7.61 (d,  $^3J_{13,14} = 7.8$  Hz, 1 H, 13-H), 7.67 (t,  $^3J_{\text{NHb},20} = 5.6$  Hz, 1 H,  $\text{NHb}$ ), 8.46 (bs, 1 H,  $\text{NHc}$ ).

$^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 11.6$  (q, C-27), 15.3 (q, C-28), 23.5 (t, C-26), 26.9 (t, C-10), 27.9 (q, C-1), 36.7 (t, C-5), 38.6 (d, C-25), 41.2 (t, C-20), 51.5 (d, C-4), 52.1 (q, C-22), 53.8 (d, C-9), 75.9 (d, C-24), 82.7 (s, C-2), 109.8 (s, C-11), 111.4 (d, C-16), 118.3 (d, C-13), 119.6 (d, C-14), 121.4 (t, C-7), 122.1 (d, C-15), 123.5 (d, C-18), 127.7 (s, C-12), 136.1 (s, C-17), 140.8 (s, C-6), 167.9 (s, C-8), 170.5 (s, C-21), 170.8 (s, C-3), 171.9 (s, C-19), 173.7 (s, C-23).

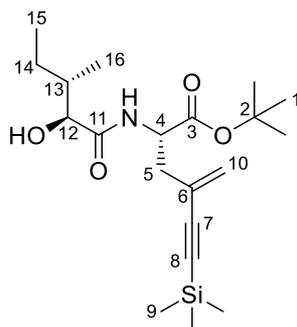
**Optical rotation:**  $[\alpha]_D^{20} = +18.0$  ( $c = 1.0$ ,  $\text{CHCl}_3$ )

<b>HRMS (CI):</b>	Calculated	Found
$\text{C}_{29}\text{H}_{37}\text{N}_4\text{O}_4$ $[\text{M}-\text{CH}_2\text{CO}_2\text{Me}]^+$	513.2713	513.2678

***tert*-Butyl (S)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-methylene-6-(trimethylsilyl)-hex-5-ynoate (7a)**

A 4 mL vial was charged with **4** (30.0 mg, 72.9  $\mu\text{mol}$ ), TMS-acetylene (31.0  $\mu\text{L}$ , 219  $\mu\text{mol}$ , 3.0 equiv) and triethylamine (31.0  $\mu\text{L}$ , 219  $\mu\text{mol}$ , 3.0 equiv). Dry THF (1.0 mL) was added, the mixture was purged with Argon and CuI (1.4 mg, 7.3  $\mu\text{mol}$ , 0.1 equiv) as well as  $\text{Pd}(\text{PPh}_3)_4$  (2.5 mg, 2.2  $\mu\text{mol}$ , 5 mol %) were added. The vial was sealed, and the mixture was stirred at 65  $^\circ\text{C}$  for 16 hours after which TLC showed full consumption of the starting material. The mixture was concentrated *in vacuo* and purified by column chromatography (silica, DCM/ $\text{Et}_2\text{O}$  9:1) to afford alkyne **7a** (25.9 mg, 67.9  $\mu\text{mol}$ , 93%) as an off white solid.

$R_f(7a) = 0.21$  (DCM/Et<sub>2</sub>O 9:1)



<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 0.20$  (s, 9 H, 9-H), 0.90 (t, <sup>3</sup>J<sub>15,14</sub> = 7.5 Hz, 3 H, 15-H), 1.00 (d, <sup>3</sup>J<sub>16,13</sub> = 6.9 Hz, 3 H, 16-H), 1.23 (m, 1 H, 14-H<sub>a</sub>), 1.44 (m, 1 H, 14-H<sub>b</sub>), 1.47 (s, 9 H, 1-H), 1.85 (m, 1 H, 13-H), 2.59 (dd, <sup>2</sup>J<sub>5a,5b</sub> = 14.2 Hz, <sup>3</sup>J<sub>5a,4</sub> = 7.5 Hz, 1 H, 5-H<sub>a</sub>), 2.67 (dd, <sup>2</sup>J<sub>5b,5a</sub> = 14.2 Hz, <sup>3</sup>J<sub>5b,4</sub> = 5.3 Hz, 1 H, 5-H<sub>b</sub>), 2.85 (bs, 1 H, OH), 4.02 (dd, <sup>3</sup>J<sub>12,OH</sub> = 4.7 Hz, <sup>3</sup>J<sub>12,13</sub> = 3.9 Hz, 1 H, 12-H), 4.69 (td, <sup>3</sup>J<sub>4,NH/5a</sub> = 7.7 Hz, <sup>3</sup>J<sub>4,5b</sub> = 5.6 Hz, 1 H, 4-H), 5.34 (d, <sup>2</sup>J<sub>10a,10b</sub> = 1.0 Hz, 1 H, 10-H<sub>a</sub>), 5.50 (d, <sup>2</sup>J<sub>10b,10a</sub> = 1.2 Hz, 1 H, 10-H<sub>b</sub>), 6.96 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.8 Hz, 1 H, NH).

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = -0.2$  (q, C-9), 11.8 (q, C-15), 15.5 (q, C-16), 23.2 (t, C-14), 28.0 (q, C-1), 38.9 (d, C-13), 39.0 (t, C-5), 51.5 (d, C-4), 76.2 (d, C-12), 82.3 (s, C-2), 95.6 (s, C-8), 104.4 (s, C-7), 125.6 (t, C-10), 126.5 (s, C-6), 170.5 (s, C-3), 173.0 (s, C-11).

Optical rotation:  $[\alpha]_D^{20} = -11.6$  (c = 0.5, CHCl<sub>3</sub>)

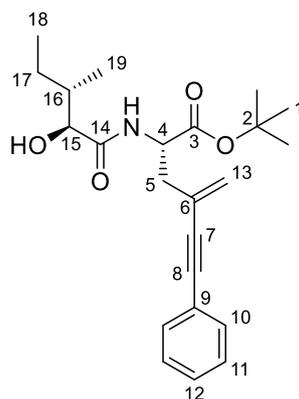
Melting point: 90–92 °C

HRMS (CI):	Calculated	Found
C <sub>20</sub> H <sub>35</sub> NO <sub>4</sub> Si [M] <sup>+</sup>	381.2330	381.2305

**tert-Butyl (R)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-methylene-6-phenylhex-5-ynoate (7b)**

A 4 mL vial was charged with **4** (20.0 mg, 48.6  $\mu$ mol), phenylacetylene (16.0  $\mu$ L, 146  $\mu$ mol, 3.0 equiv) and triethylamine (20.0  $\mu$ L, 146  $\mu$ mol, 3.0 equiv). Dry THF (1.0 mL) was added, the mixture was purged with Argon and Cu(I)I (0.9 mg, 4.9  $\mu$ mol, 0.1 equiv) as well as Pd(PPh<sub>3</sub>)<sub>4</sub> (1.7 mg, 1.5  $\mu$ mol, 5 mol %) were added. The vial was sealed, and the mixture was stirred at 65 °C for 16 hours after which TLC showed full consumption of the starting material. The mixture was concentrated *in vacuo* and purified by column chromatography (silica, DCM/Et<sub>2</sub>O 9:1) to afford alkyne **7b** (16.7 mg, 43.3  $\mu$ mol, 89%) as a colorless oil.

$R_f(7b) = 0.15$  (DCM/Et<sub>2</sub>O 9:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.83 (t, <sup>3</sup>J<sub>18,17</sub> = 7.5 Hz, 3 H, 18-H), 1.00 (d, <sup>3</sup>J<sub>19,16</sub> = 7.0 Hz, 3 H, 19-H), 1.17 (m, 1 H, 17-H<sub>a</sub>), 1.42 (m, 1 H, 17-H<sub>b</sub>), 1.46 (s, 9 H, 1-H), 1.84 (m, 1 H, 16-H), 2.70 (dd, <sup>2</sup>J<sub>5a,5b</sub> = 14.1 Hz, <sup>3</sup>J<sub>5a,4</sub> = 7.2 Hz, 1 H, 5-H<sub>a</sub>), 2.64 (dd, <sup>2</sup>J<sub>5b,5a</sub> = 14.3 Hz, <sup>3</sup>J<sub>5b,4</sub> = 5.5 Hz, 1 H, 5-H<sub>b</sub>), 2.82 (bs, 1 H, OH), 4.02 (bs, 1 H, 15-H), 4.79 (td, <sup>3</sup>J<sub>4,NH/5a</sub> = 7.6 Hz, <sup>3</sup>J<sub>4,5b</sub> = 5.5 Hz, 1 H, 4-H), 5.20 (d, <sup>2</sup>J<sub>13a,13b</sub> = 1.0 Hz, 1 H, 13-H<sub>a</sub>), 5.32 (d, <sup>2</sup>J<sub>13b,13a</sub> = 1.2 Hz, 1 H, 13-H<sub>b</sub>), 7.01 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.8 Hz, 1 H, NH), 7.31 (m, 3 H, 11-H, 12-H), 7.46 (m, 2 H, 10-H).

**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 11.8 (q, C-18), 15.4 (q, C-19), 23.2 (t, C-17), 28.0 (q, C-1), 38.8 (d, C-16), 39.3 (t, C-5), 51.5 (d, C-4), 76.3 (d, C-15), 82.4 (s, C-2), 88.6 (s, C-7), 90.6 (s, C-8), 122.7 (s, C-9), 124.8 (t, C-13), 126.5 (s, C-6), 128.3 (d, C-11), 128.4 (d, C-12), 131.6 (d, C-10), 170.6 (s, C-3), 173.0 (s, C-14).

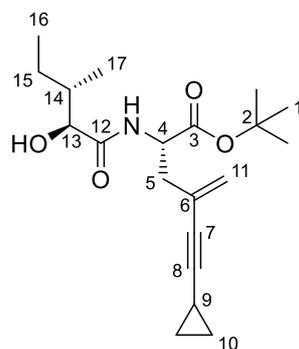
**Optical rotation:**  $[\alpha]_D^{20} = -5.7$  (c = 1.0, CHCl<sub>3</sub>)

<b>HRMS (CI):</b>	Calculated	Found
C <sub>23</sub> H <sub>32</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	386.2326	386.2322

***tert*-Butyl (*R*)-6-cyclopropyl-2-((2*S*,3*S*)-2-hydroxy-3-methylpentanamido)-4-methylenehex-5-ynoate (**7c**)**

A 4 mL vial was charged with **4** (20.0 mg, 48.6 μmol), ethynyl cyclopropane (12.0 μL, 146 μmol, 3.0 equiv) and triethylamine (20.0 μL, 146 μmol, 3.0 equiv). Dry THF (1.0 mL) was added, the mixture was purged with Argon and CuI (0.9 mg, 4.9 μmol, 0.1 equiv) as well as Pd(PPh<sub>3</sub>)<sub>4</sub> (1.7 mg, 1.5 μmol, 5 mol %) were added. The vial was sealed, and the mixture was stirred at 65 °C for 16 hours after which TLC showed full consumption of the starting material. The mixture was concentrated *in vacuo* and purified by column chromatography (silica, DCM/Et<sub>2</sub>O 9:1) to afford alkyne **7c** (15.5 mg, 44.4 μmol, 91%) as a colorless oil.

**R<sub>f</sub>(7c)** = 0.17 (DCM/Et<sub>2</sub>O 9:1)



**<sup>1</sup>H-NMR** (400 MHz, CDCl<sub>3</sub>): δ = 0.74 (m, 2 H, 10-H<sub>a</sub>), 0.81 (m, 2 H, 10-H<sub>b</sub>), 0.90 (t, <sup>3</sup>J<sub>16,15</sub> = 7.5 Hz, 3 H, 16-H), 1.00 (d, <sup>3</sup>J<sub>17,14</sub> = 7.0 Hz, 3 H, 17-H), 1.22 (m, 1 H, 15-H<sub>a</sub>), 1.34 (tt, <sup>3</sup>J<sub>9,10a</sub> = 8.1 Hz, <sup>3</sup>J<sub>9,10b</sub> = 5.1 Hz, 1 H, 9-H), 1.45 (m, 1 H, 15-H<sub>b</sub>), 1.47 (s, 9 H, 1-H), 1.86 (m, 1 H, 14-H), 2.56 (dd, <sup>2</sup>J<sub>5a,5b</sub> = 14.1 Hz, <sup>3</sup>J<sub>5a,4</sub> = 7.2 Hz, 1 H, 5-H<sub>a</sub>), 2.64 (dd, <sup>2</sup>J<sub>5b,5a</sub> = 14.1 Hz, <sup>3</sup>J<sub>5b,4</sub> = 5.3 Hz, 1 H, 5-H<sub>b</sub>), 2.93 (m, 1 H, OH), 4.03 (dd, <sup>3</sup>J<sub>13,OH</sub> = 4.4 Hz, <sup>3</sup>J<sub>13,14</sub> = 4.0 Hz, 1 H, 13-H), 4.68 (td, <sup>3</sup>J<sub>4,NH/5a</sub> = 7.6 Hz, <sup>3</sup>J<sub>4,5b</sub> = 5.5 Hz, 1 H, 4-H), 5.20 (d, <sup>2</sup>J<sub>11a,11b</sub> = 1.0 Hz, 1 H, 11-H<sub>a</sub>), 5.32 (d, <sup>2</sup>J<sub>11b,11a</sub> = 1.6 Hz, 1 H, 11-H<sub>b</sub>), 7.01 (d, <sup>3</sup>J<sub>NH,4</sub> = 7.6 Hz, 1 H, NH).

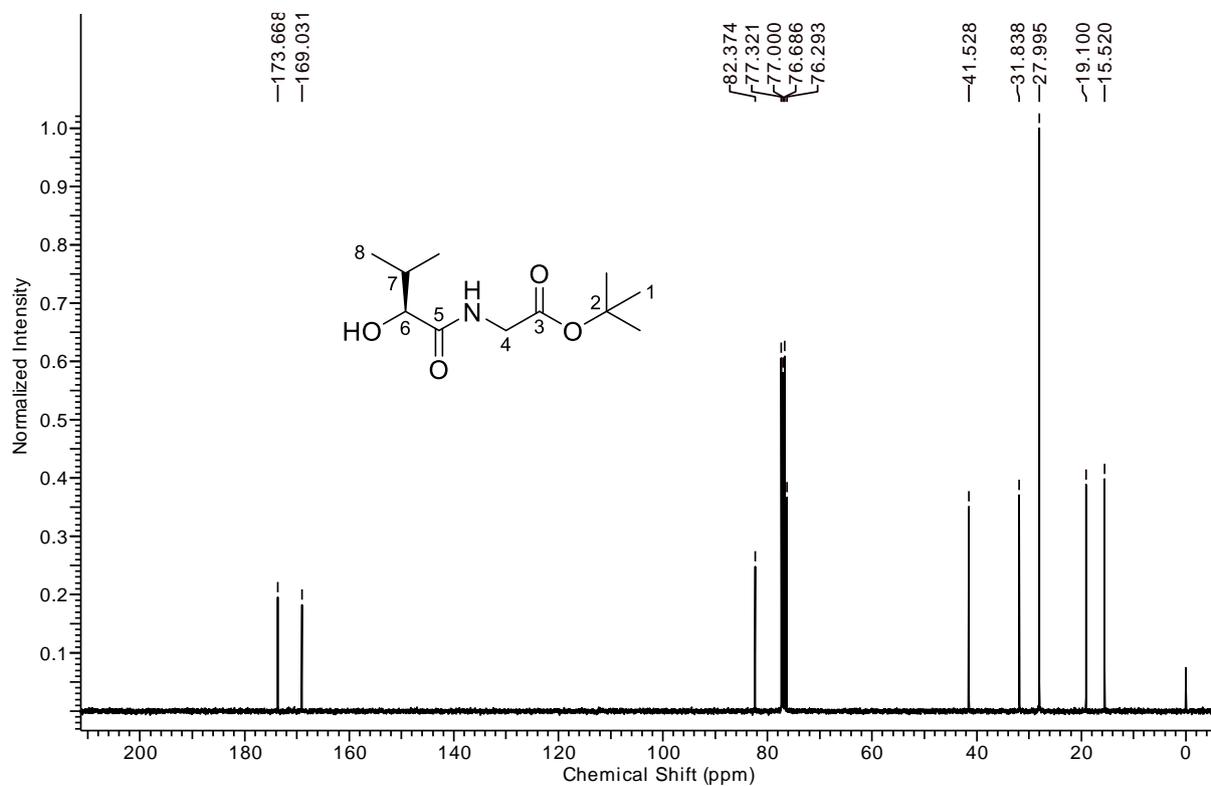
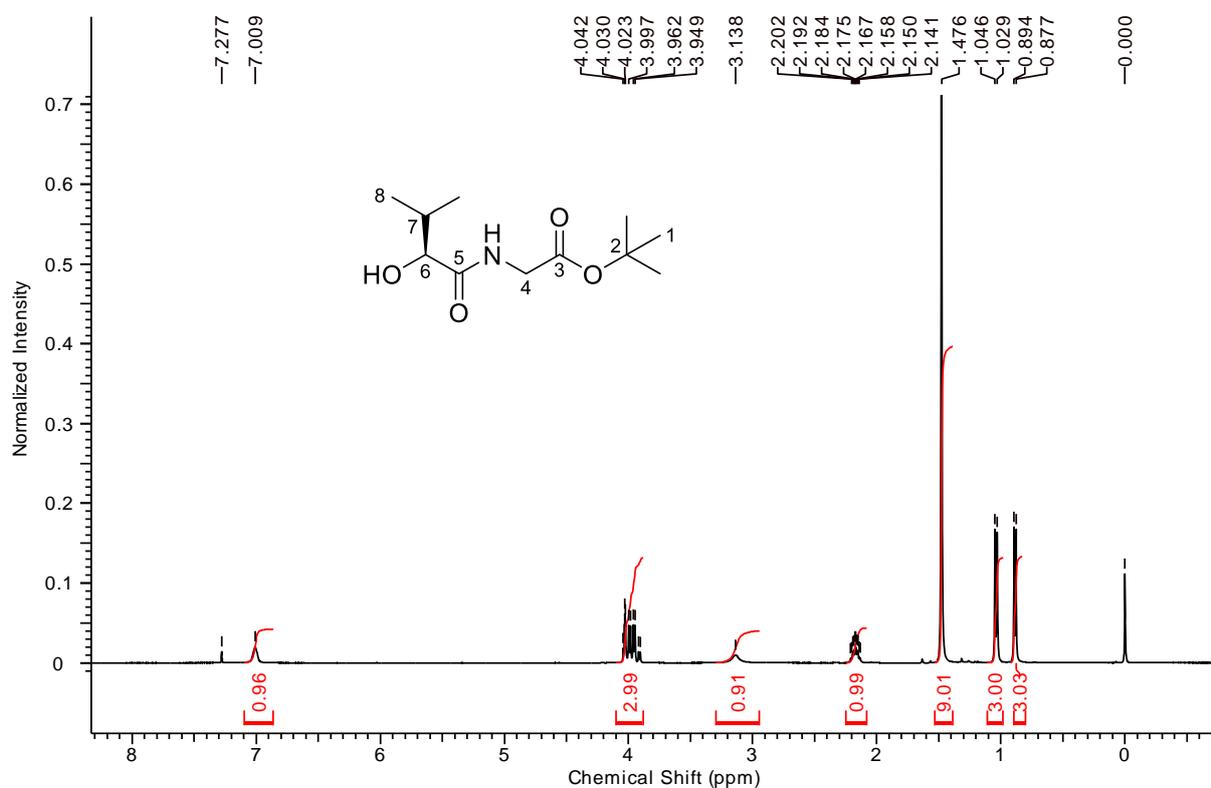
**<sup>13</sup>C-NMR** (100 MHz, CDCl<sub>3</sub>): δ = 0.0 (d, C-9), 8.5 (t, C-10), 11.8 (q, C-16), 15.5 (q, C-17), 23.2 (t, C-15), 28.0 (q, C-1), 38.8 (d, C-14), 39.4 (t, C-5), 51.4 (d, C-4), 75.2 (s, C-7), 76.3 (d, C-13), 82.3 (s, C-2), 95.0 (s, C-8), 123.4 (t, C-11), 126.7 (s, C-6), 170.6 (s, C-3), 173.0 (s, C-12).

**Optical rotation:**  $[\alpha]_{\text{D}}^{20} = -3.5$  (c = 1.0, CHCl<sub>3</sub>)

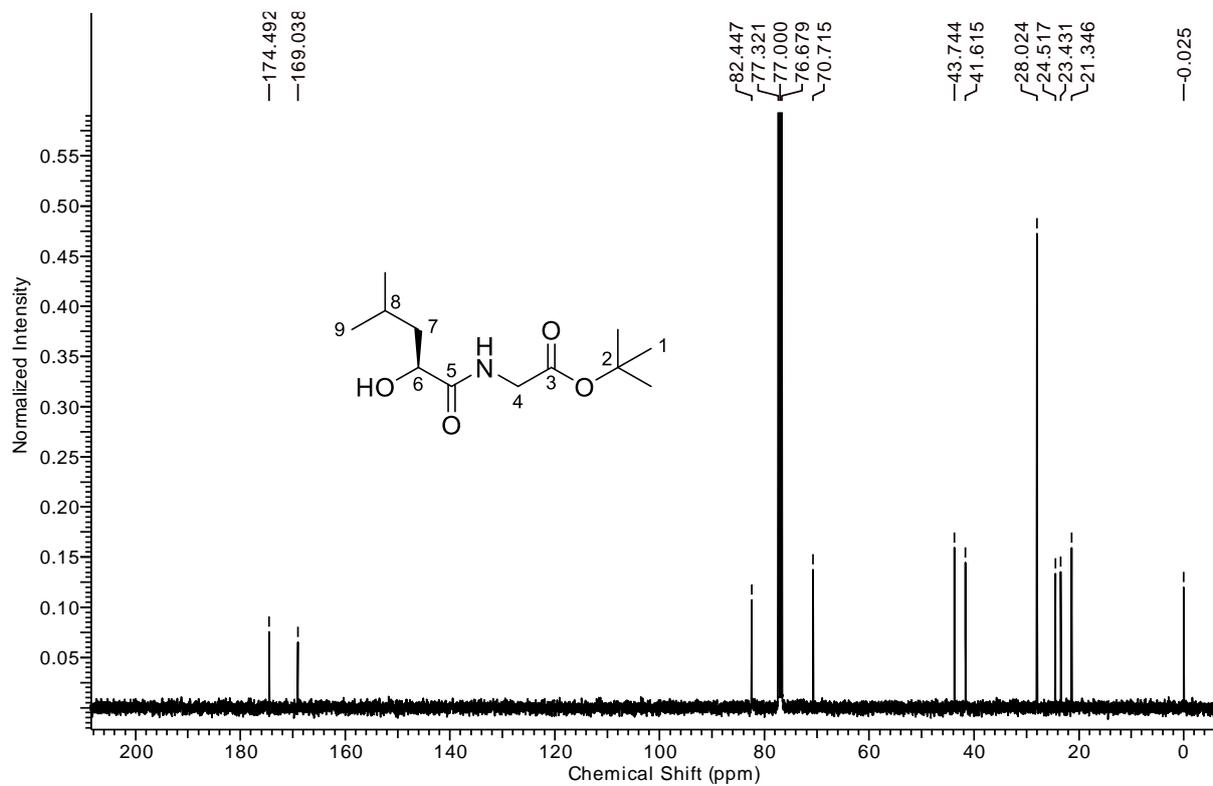
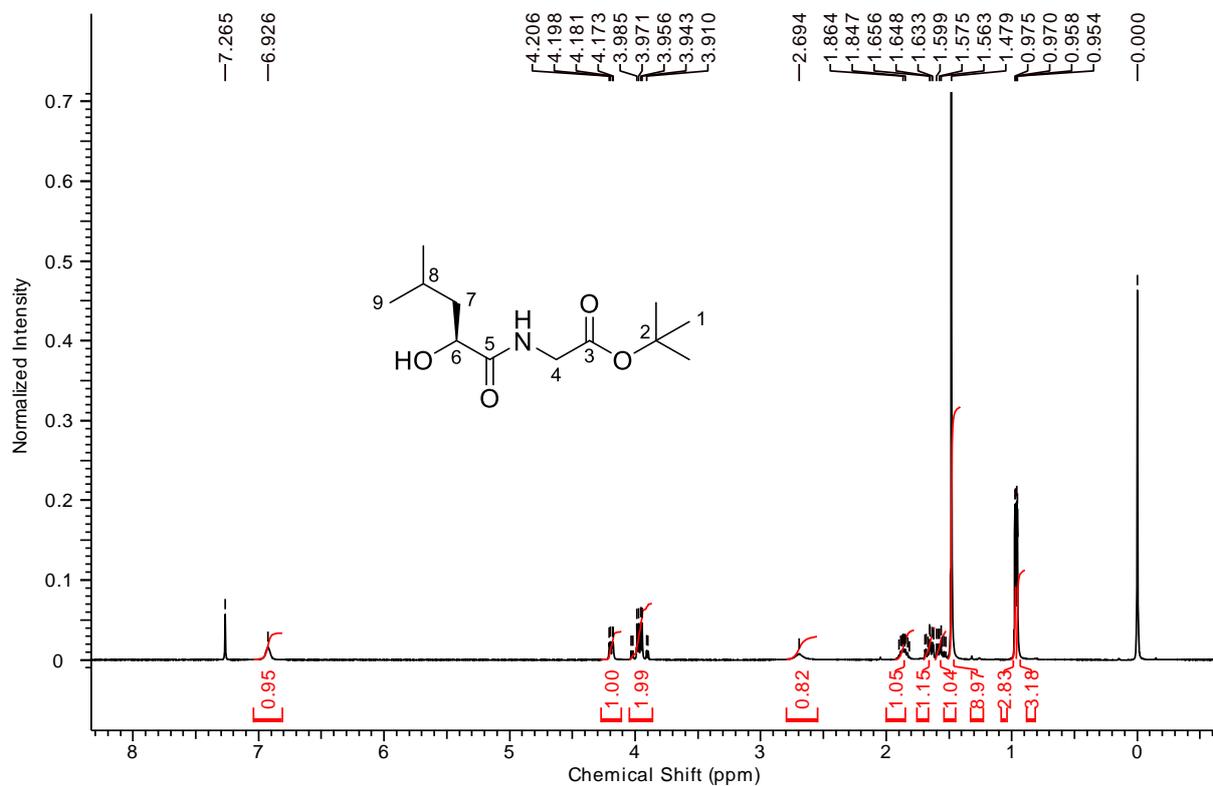
<b>HRMS (CI):</b>	Calculated	Found
C <sub>20</sub> H <sub>32</sub> NO <sub>4</sub> [M+H] <sup>+</sup>	350.2326	350.2295

## 5. NMR Spectra

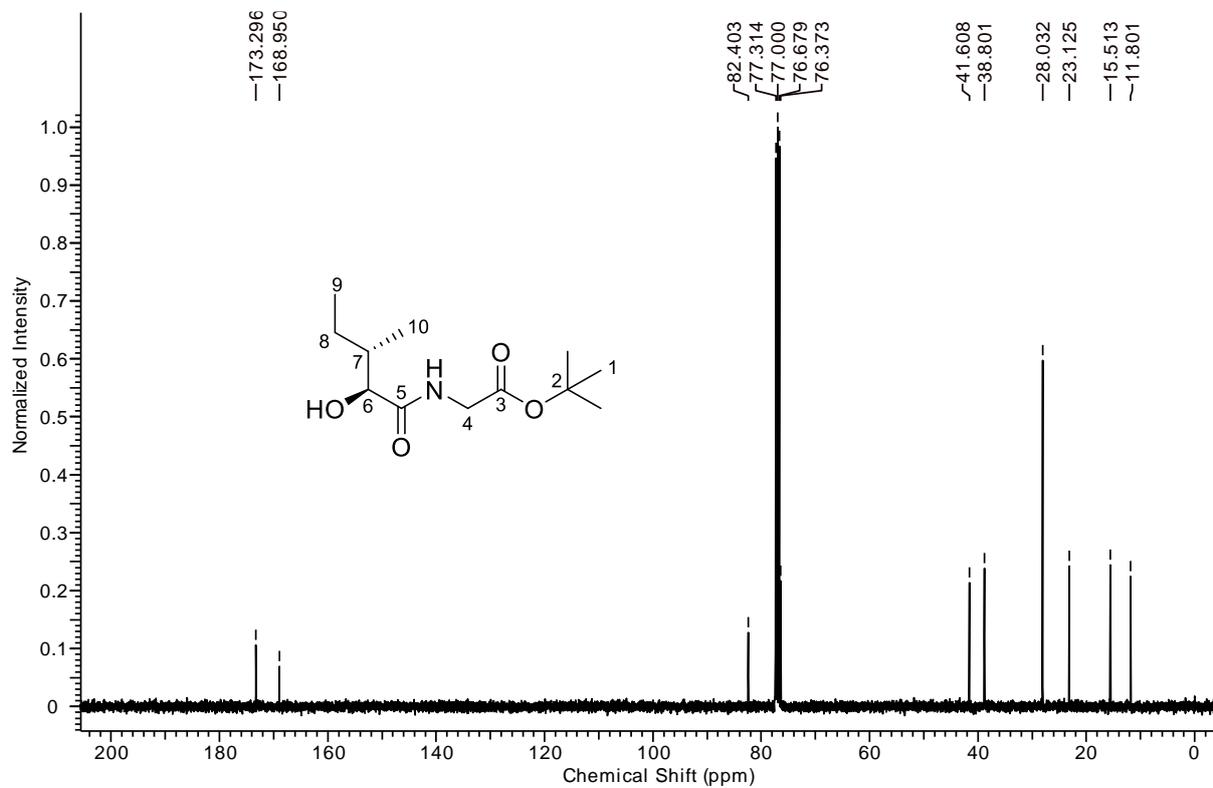
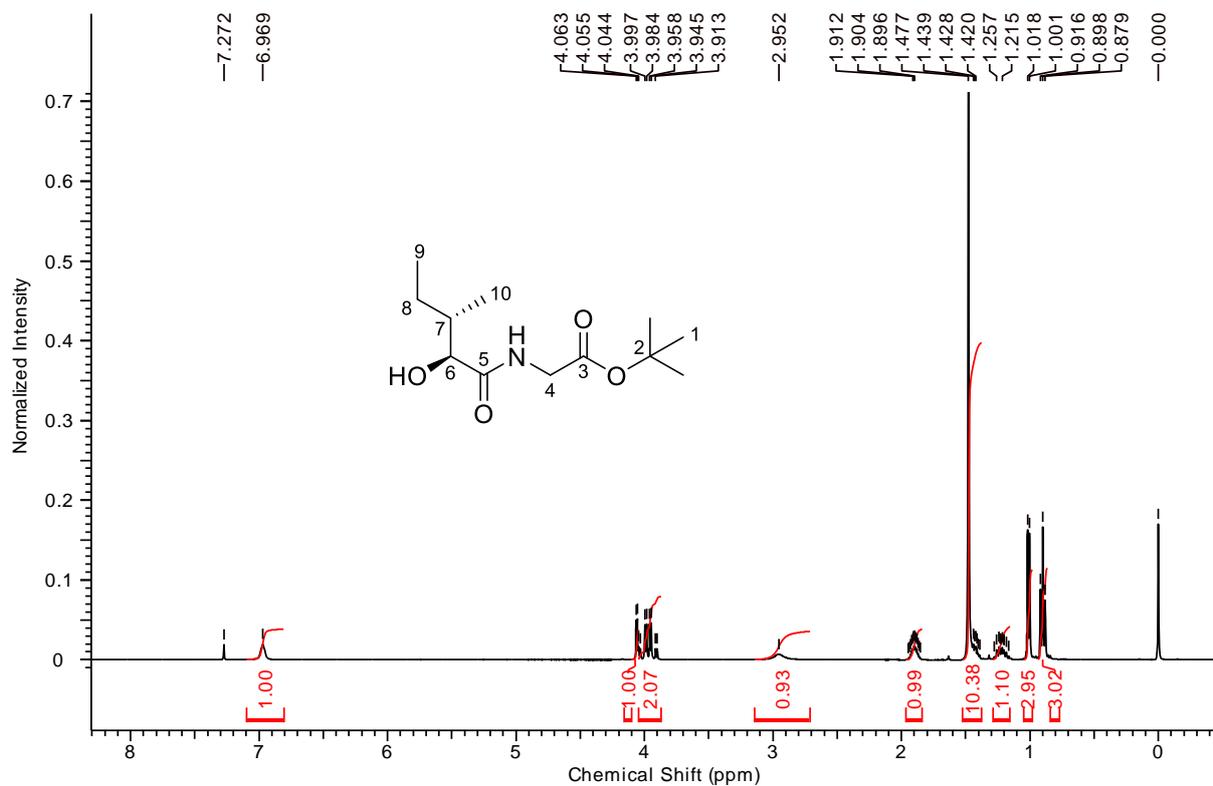
### *tert*-Butyl (*S*)-(2-hydroxy-3-methylbutanoyl)glycinate (1a)



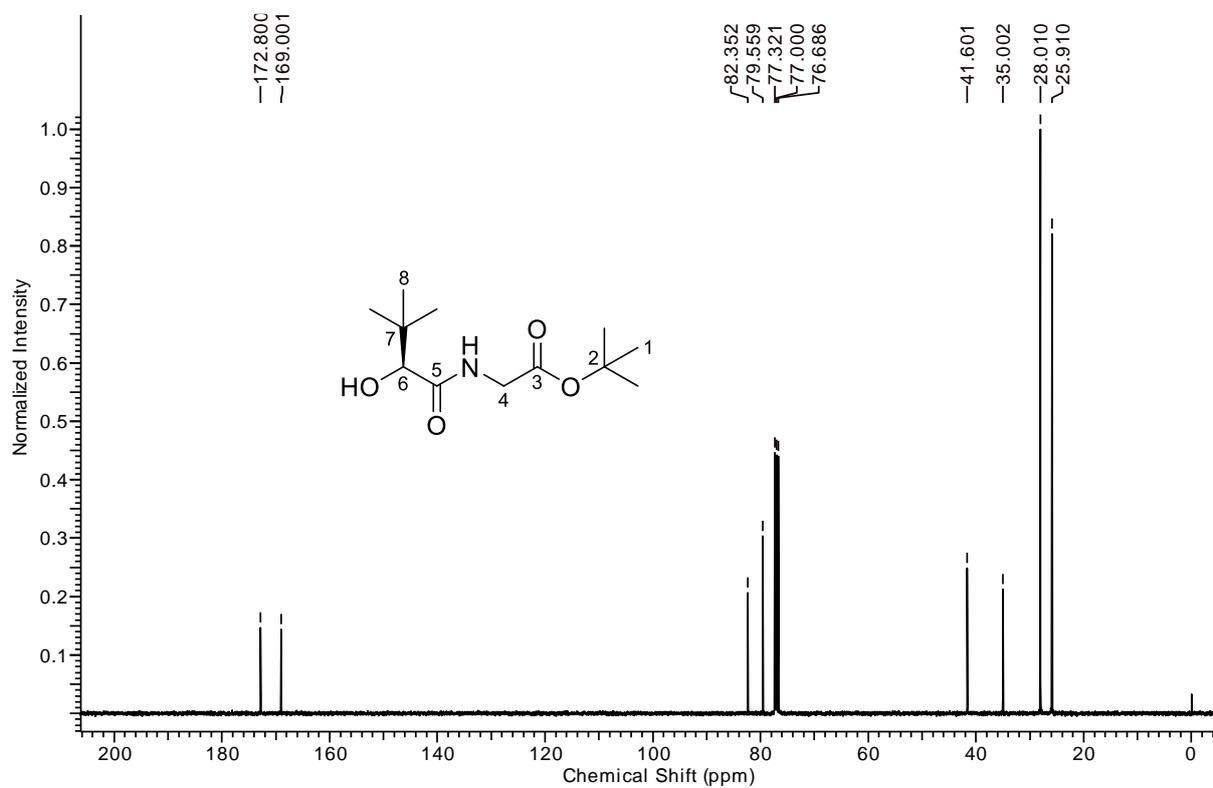
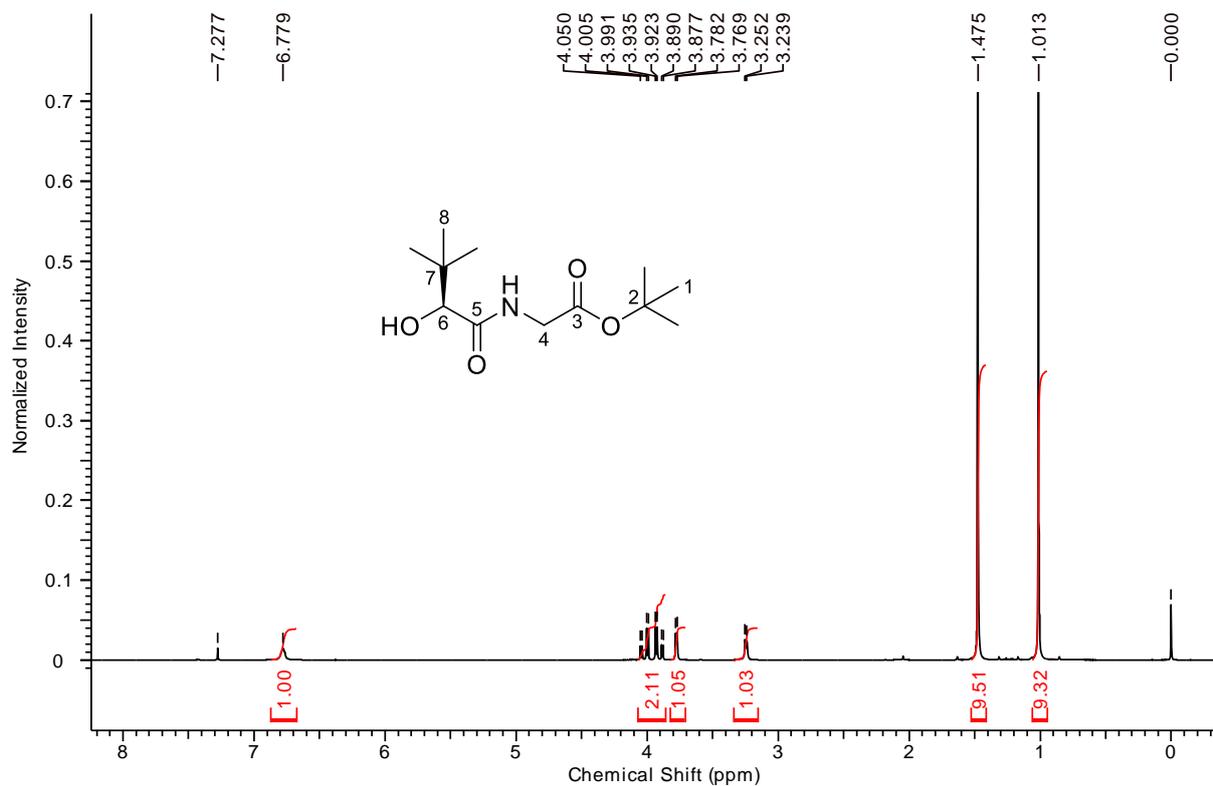
***tert*-Butyl (S)-(2-hydroxy-4-methylpentanoyl)glycinate (1b)**



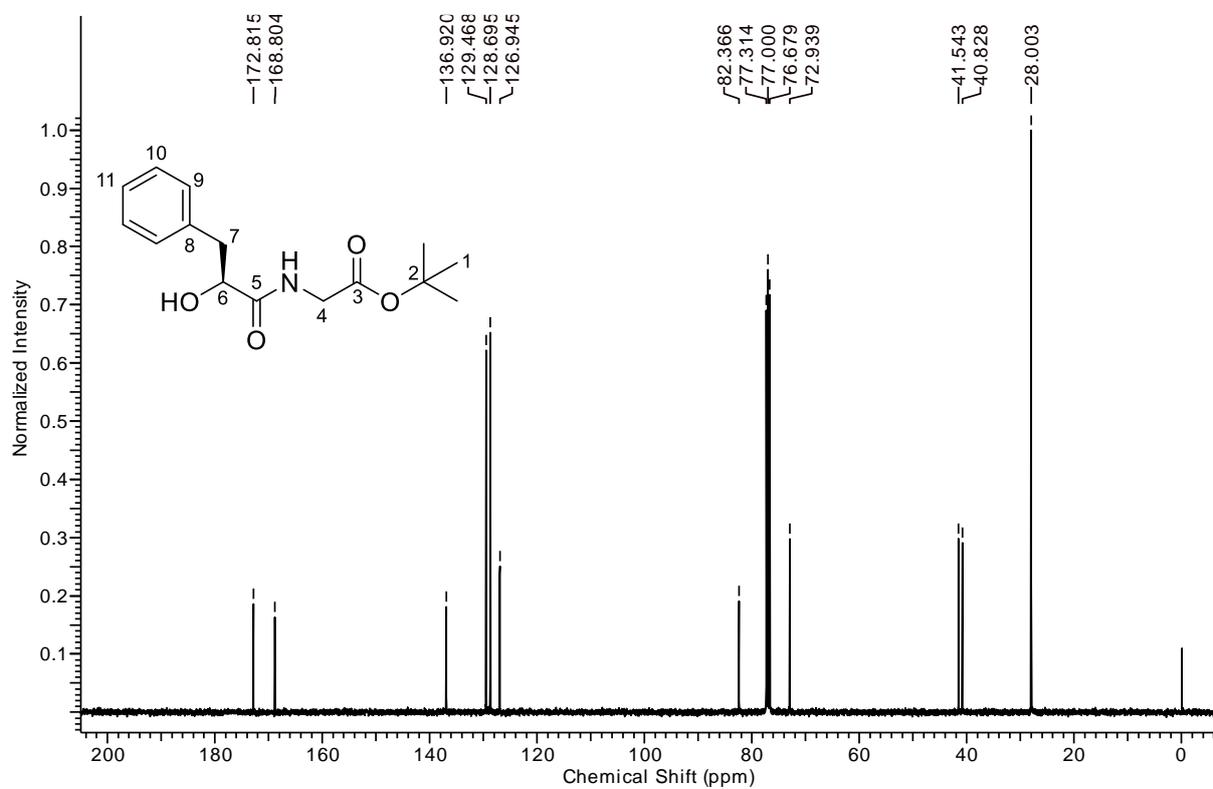
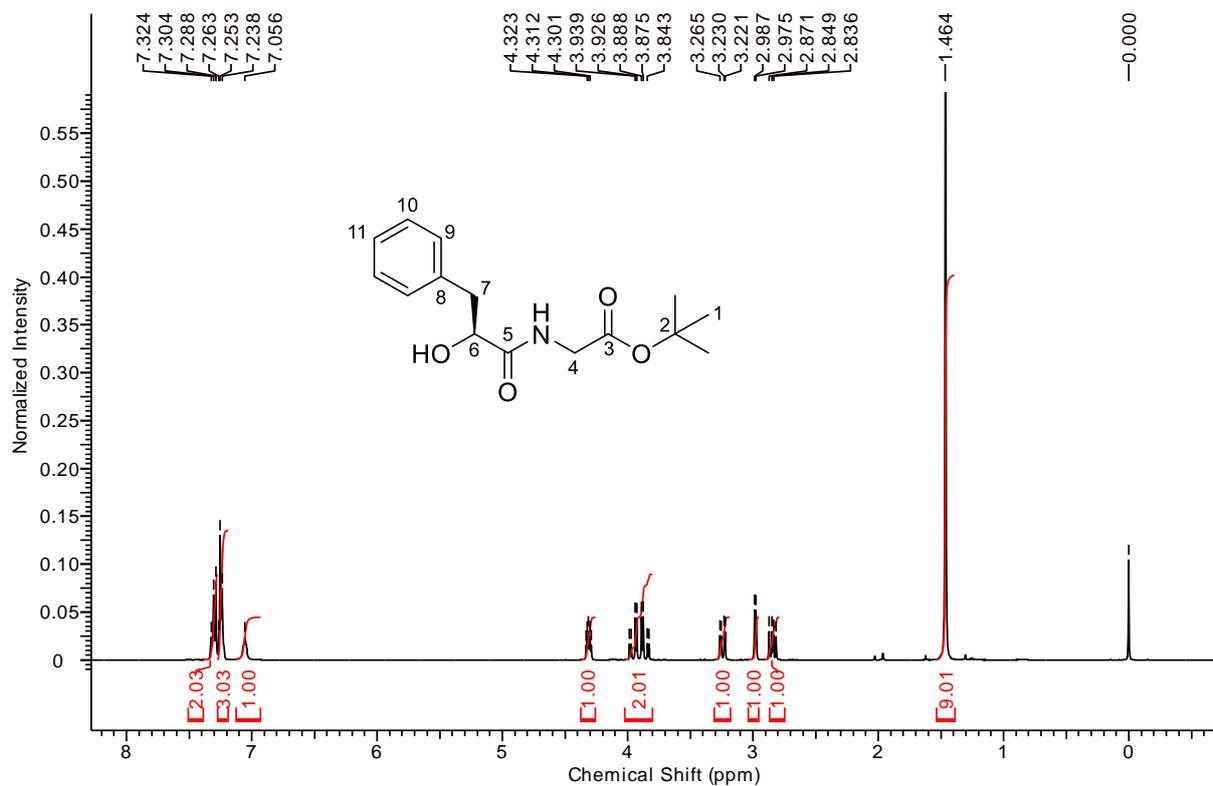
***tert*-Butyl (2*S*,3*S*)-(2-hydroxy-3-methylpentanoyl)glycinate (**1c**)**



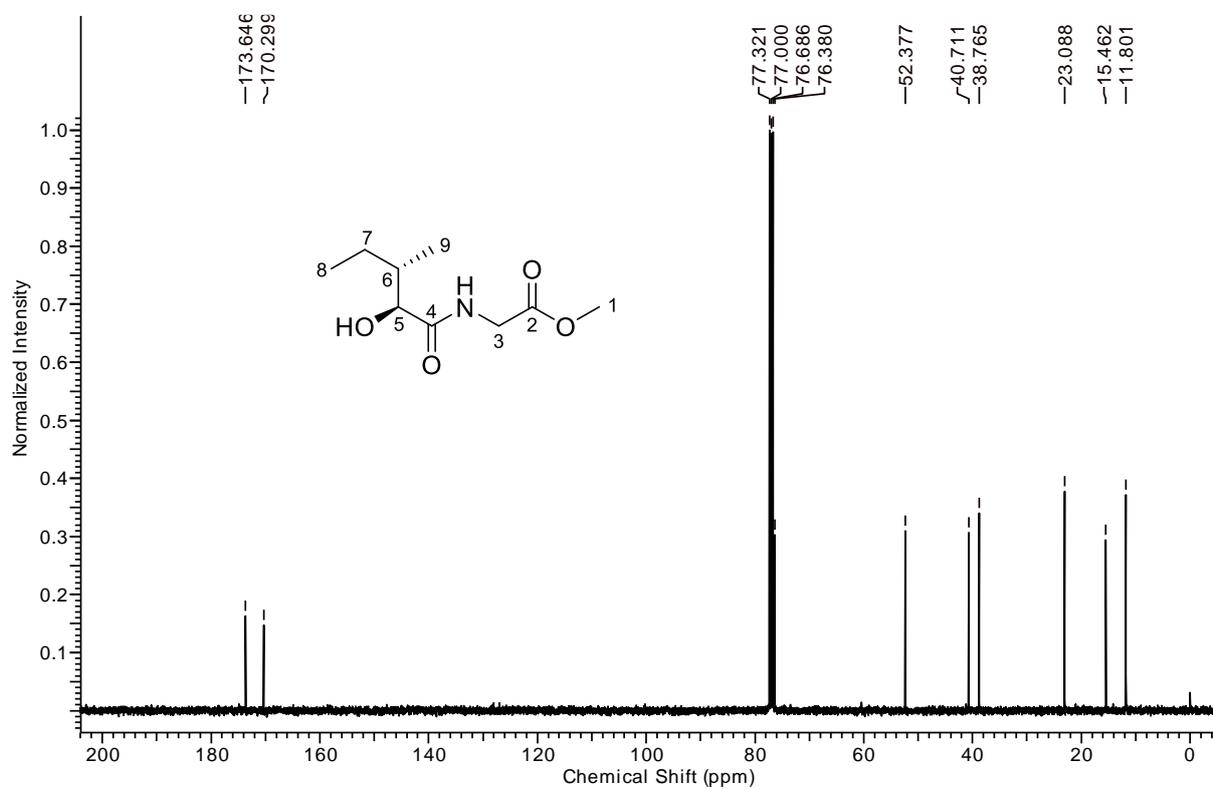
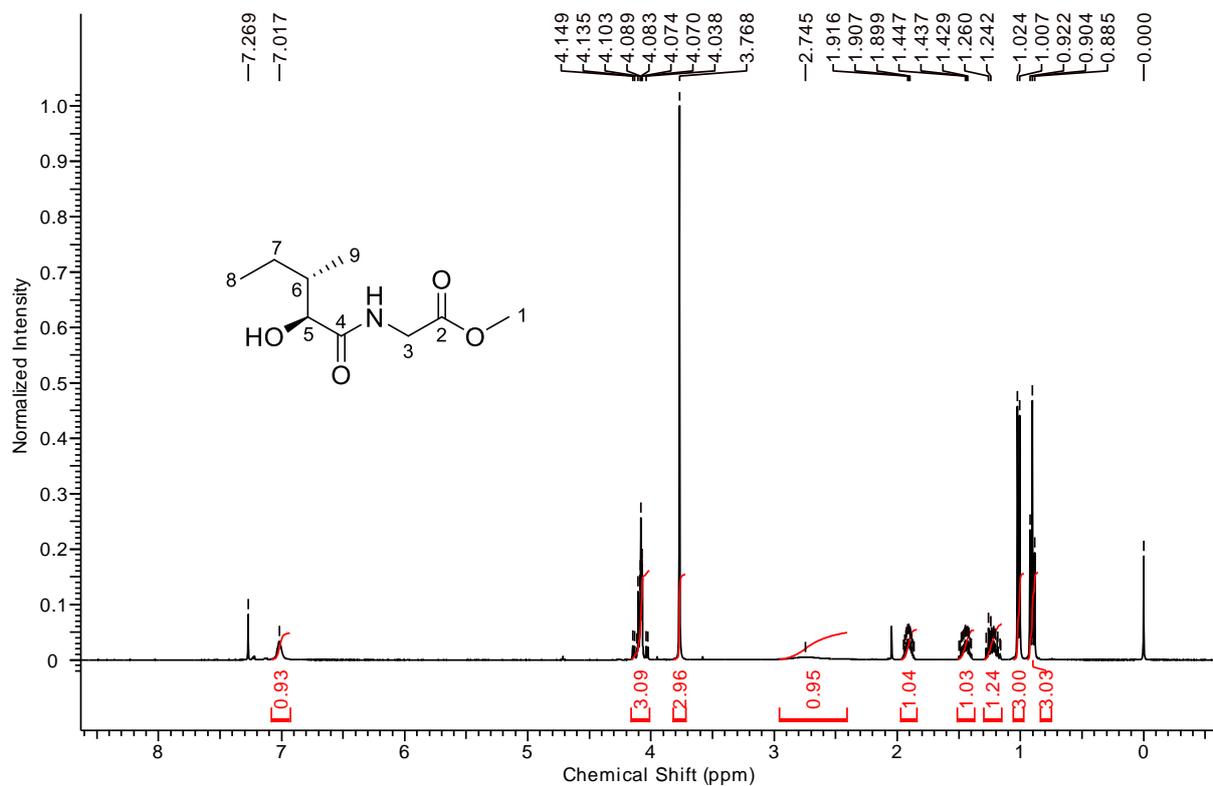
***tert*-Butyl (S)-(2-hydroxy-3,3-dimethylbutanoyl)glycinate (1d)**



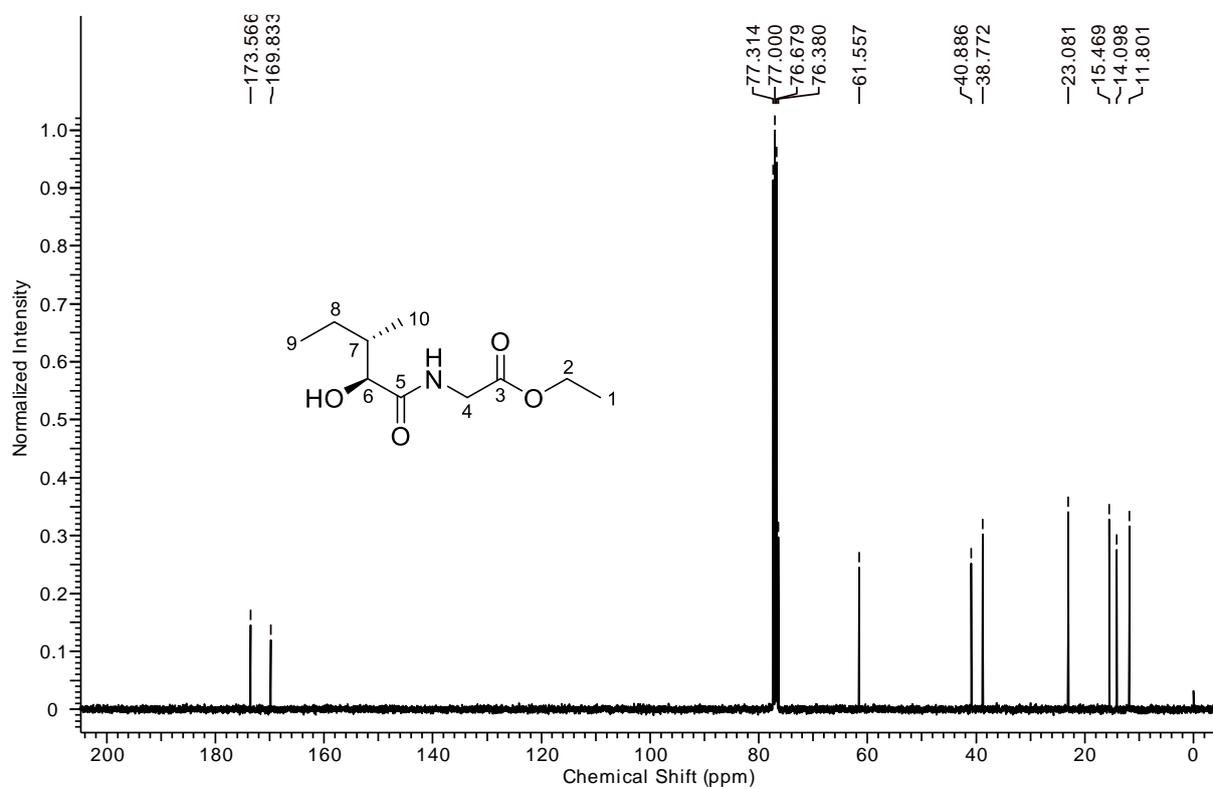
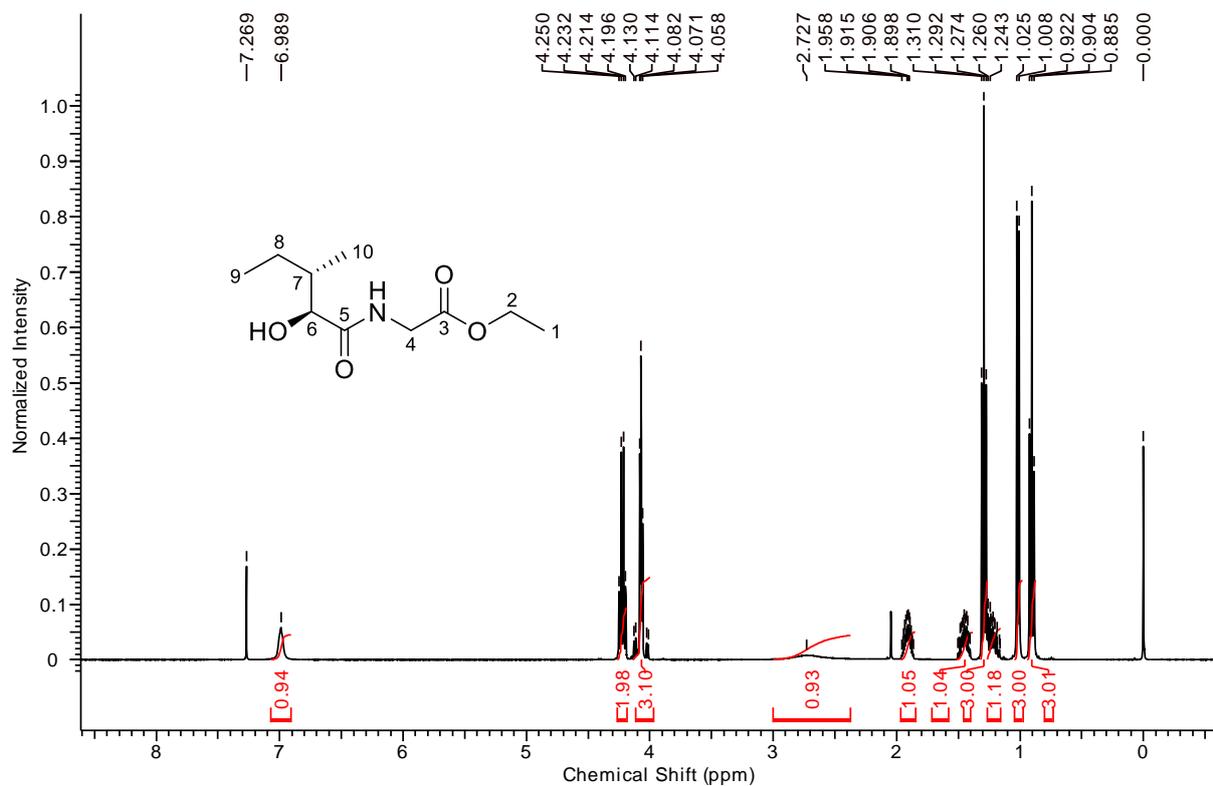
***tert*-Butyl (S)-(2-hydroxy-3-phenylpropanoyl)glycinate (1e)**



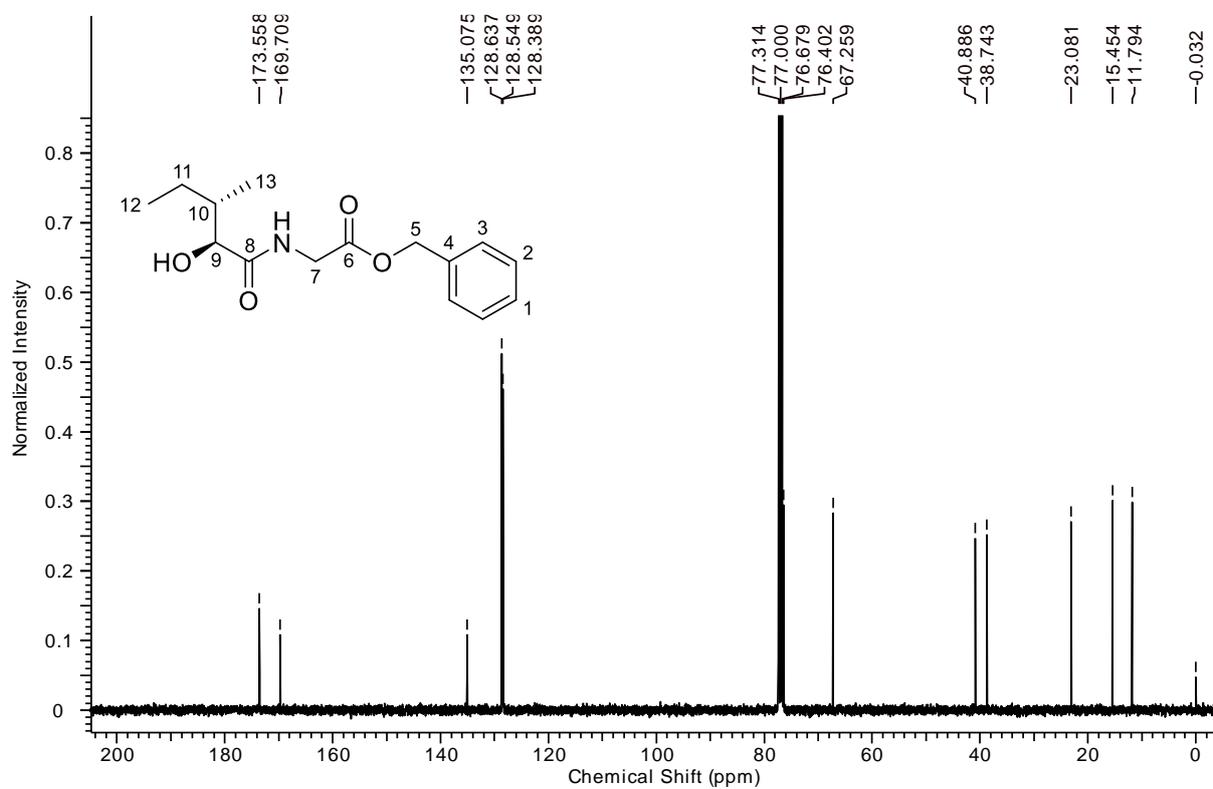
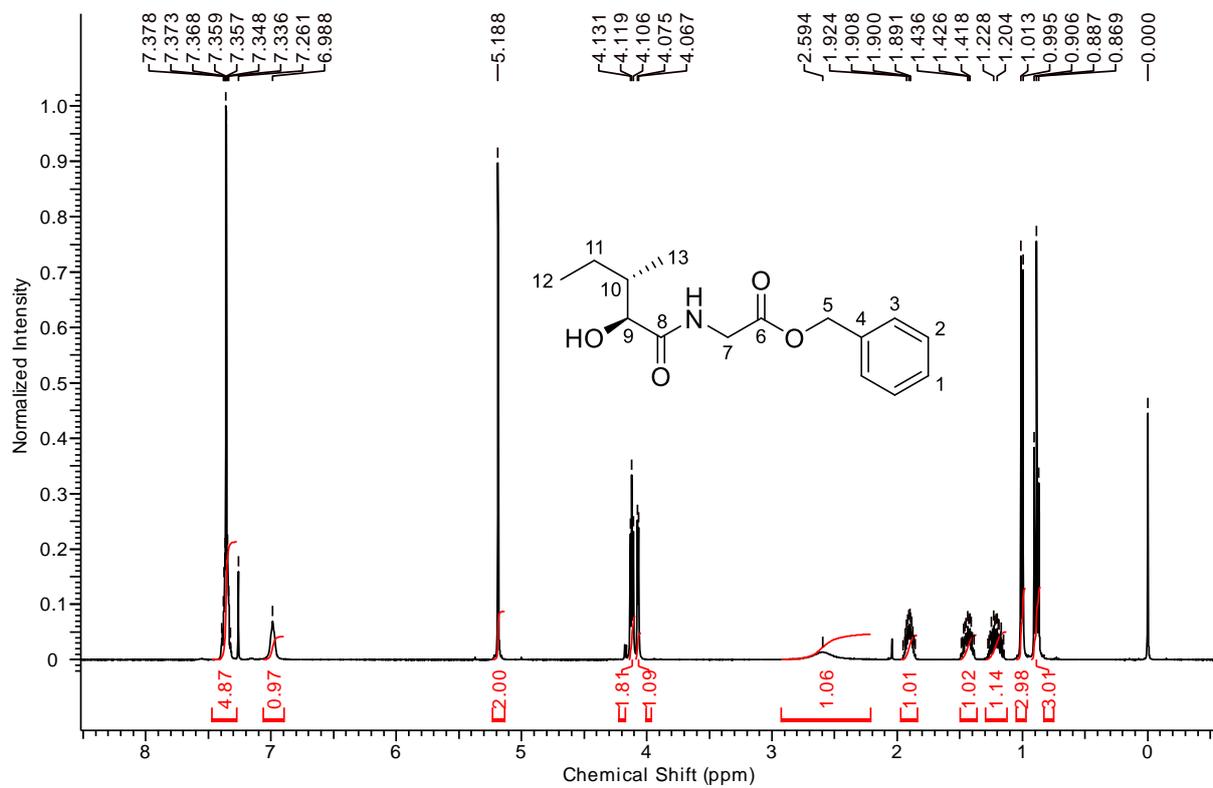
# Methyl (2S,3S)-(2-hydroxy-3-methylpentanoyl)glycinate (1f)



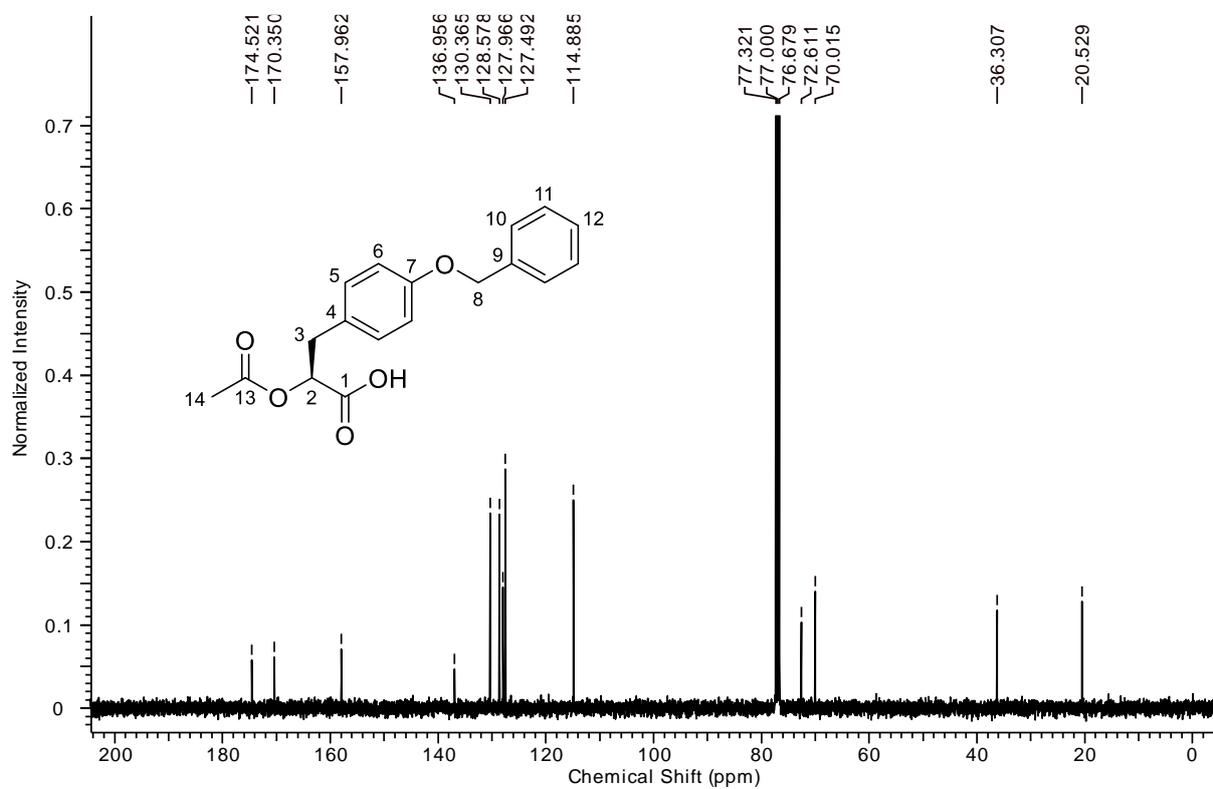
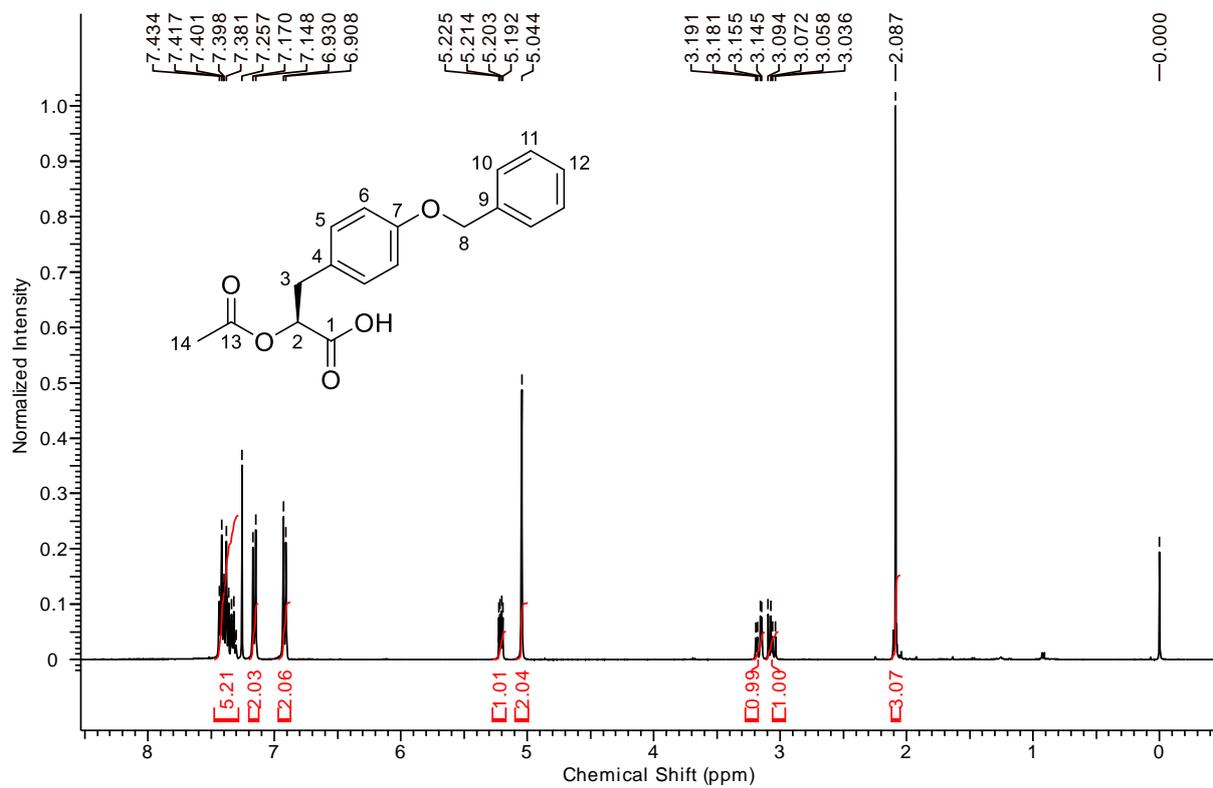
# Ethyl (2S,3S)-(2-hydroxy-3-methylpentanoyl)glycinate (1g)



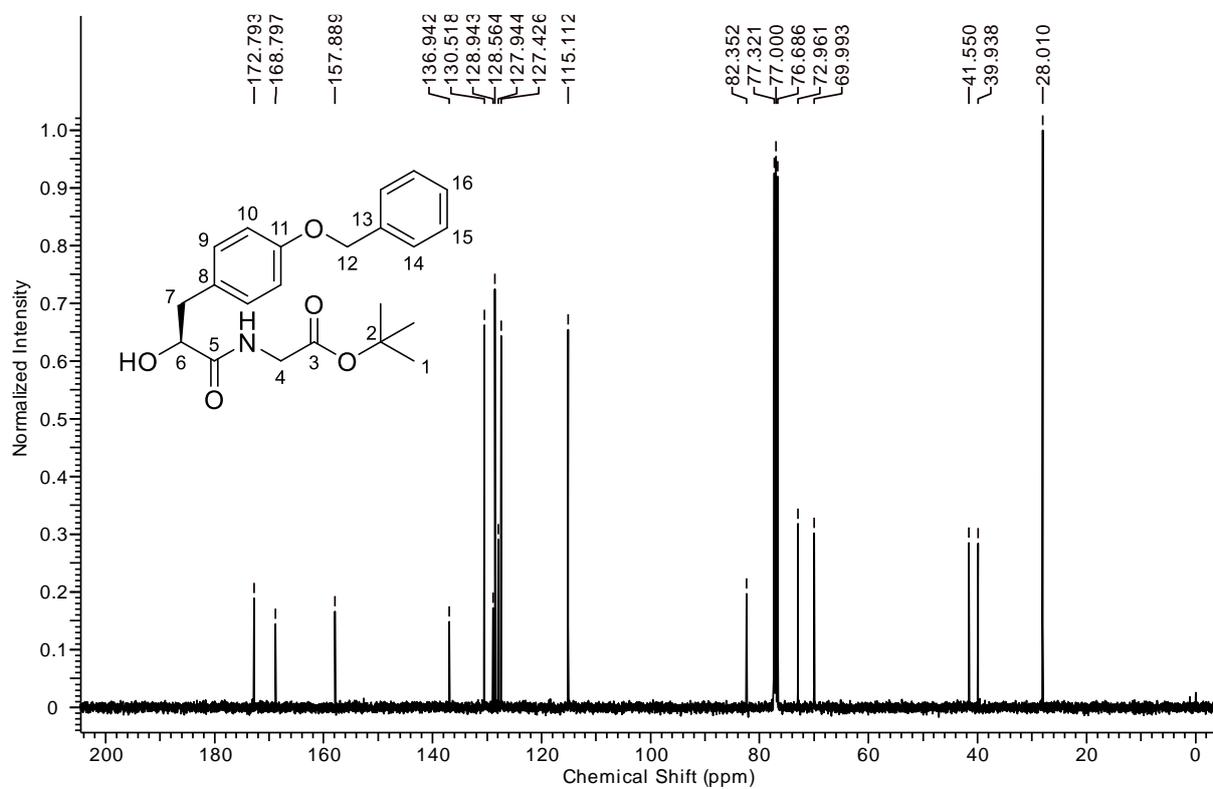
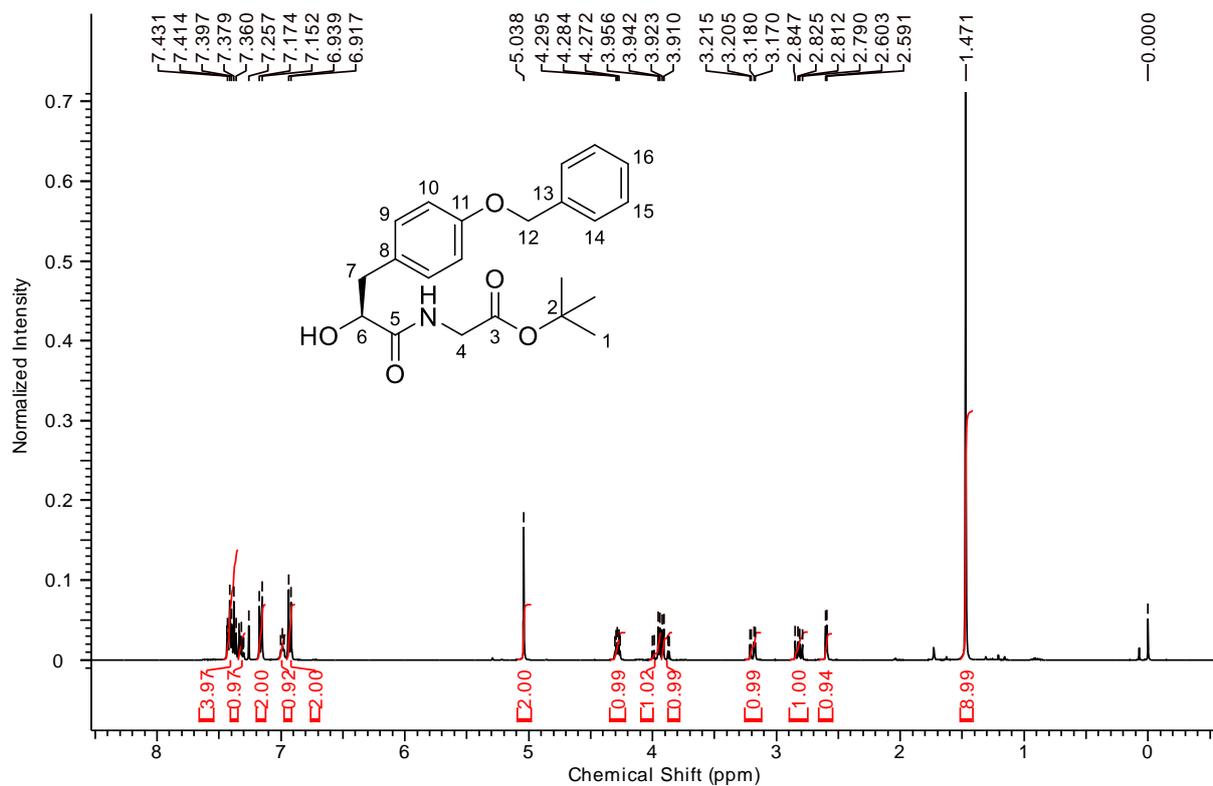
# Benzyl (2S,3S)-(2-hydroxy-3-methylpentanoyl)glycinate (1h)



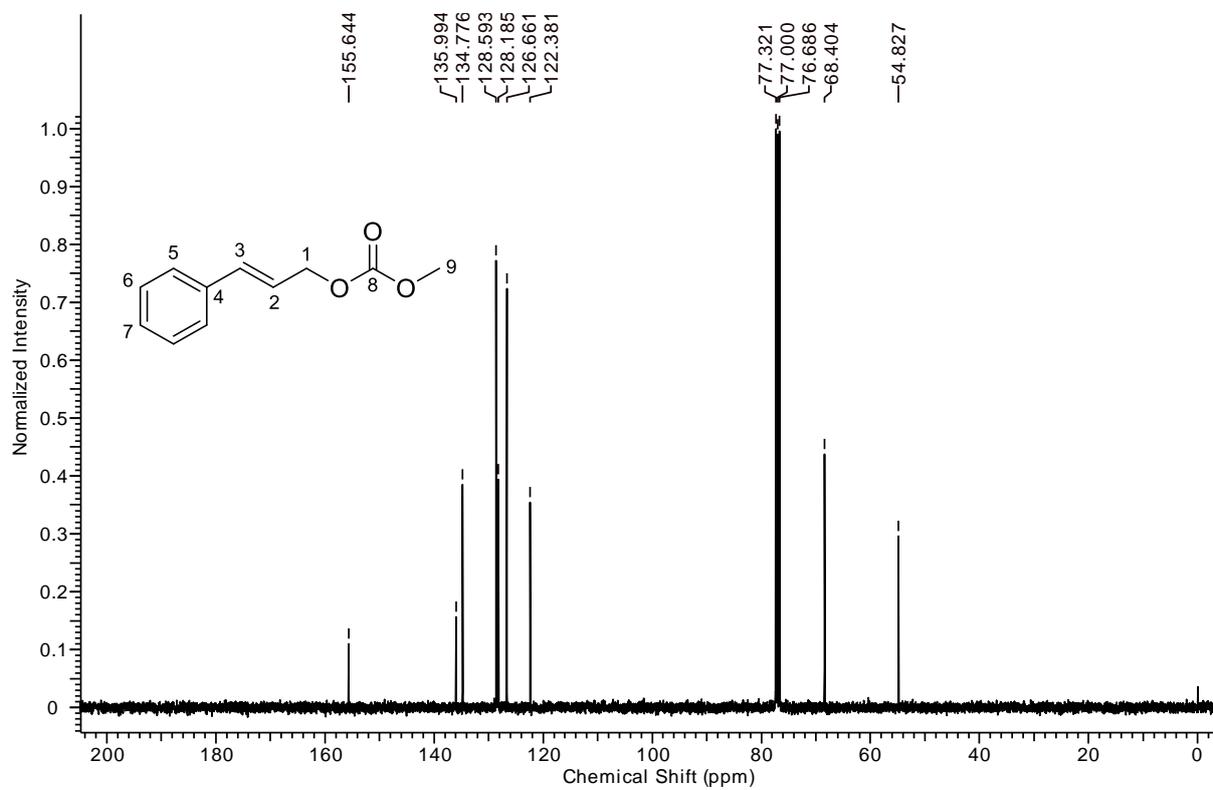
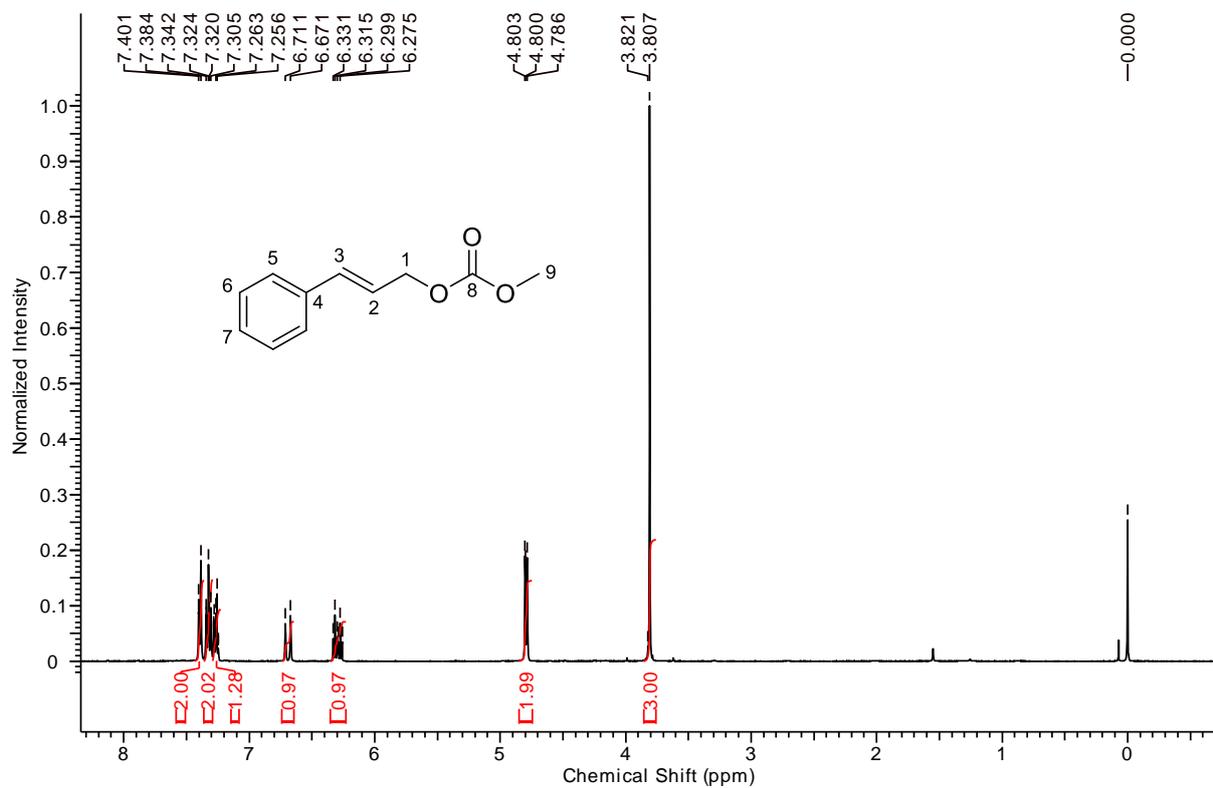
### (S)-2-Acetoxy-3-(4-(benzyloxy)phenyl)propanoic acid (SI-2)



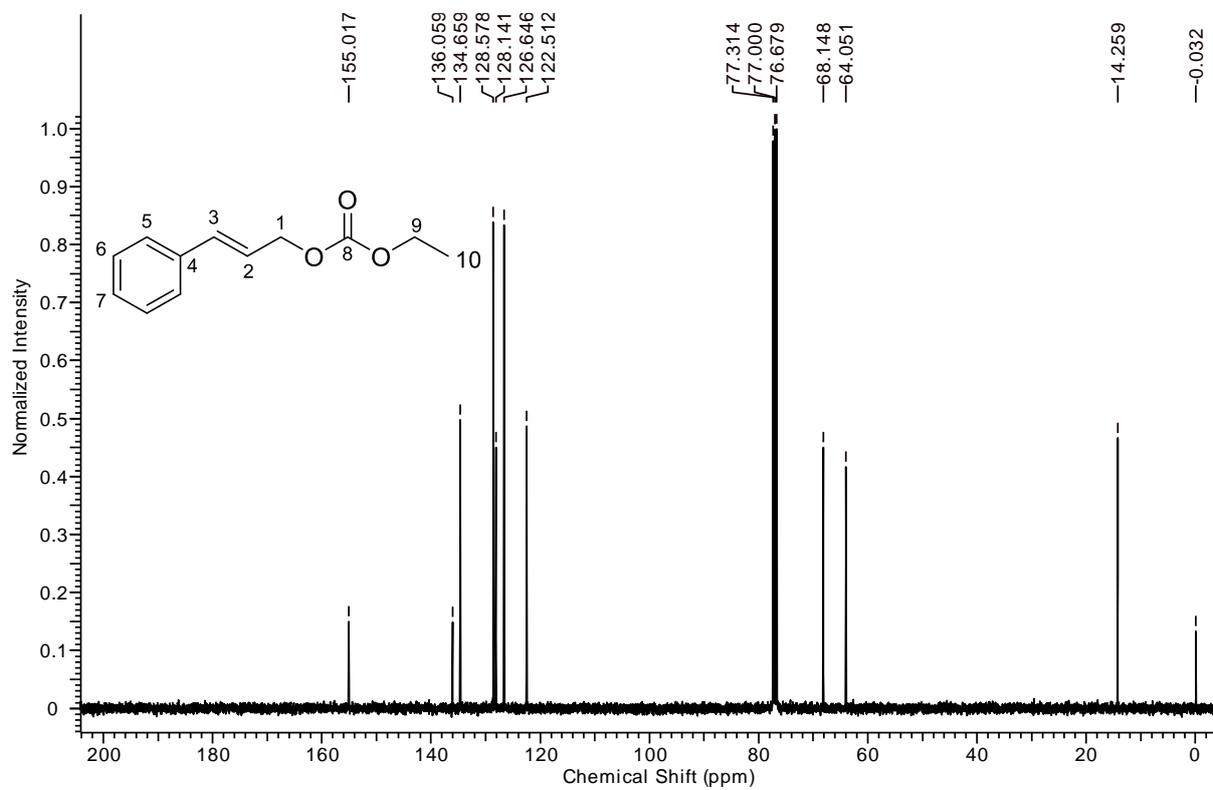
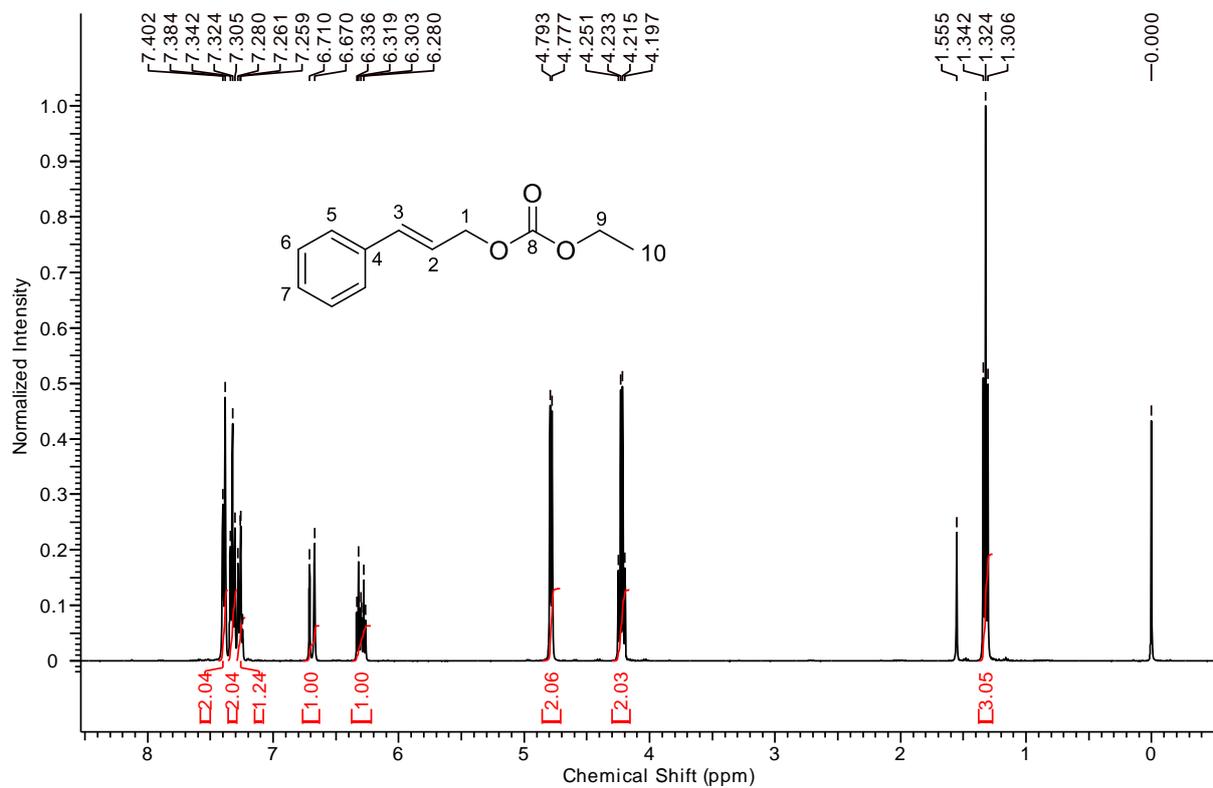
***tert*-Butyl (S)-3-(4-(benzyloxy)phenyl)-2-hydroxypropanoyl)glycinate (1i)**



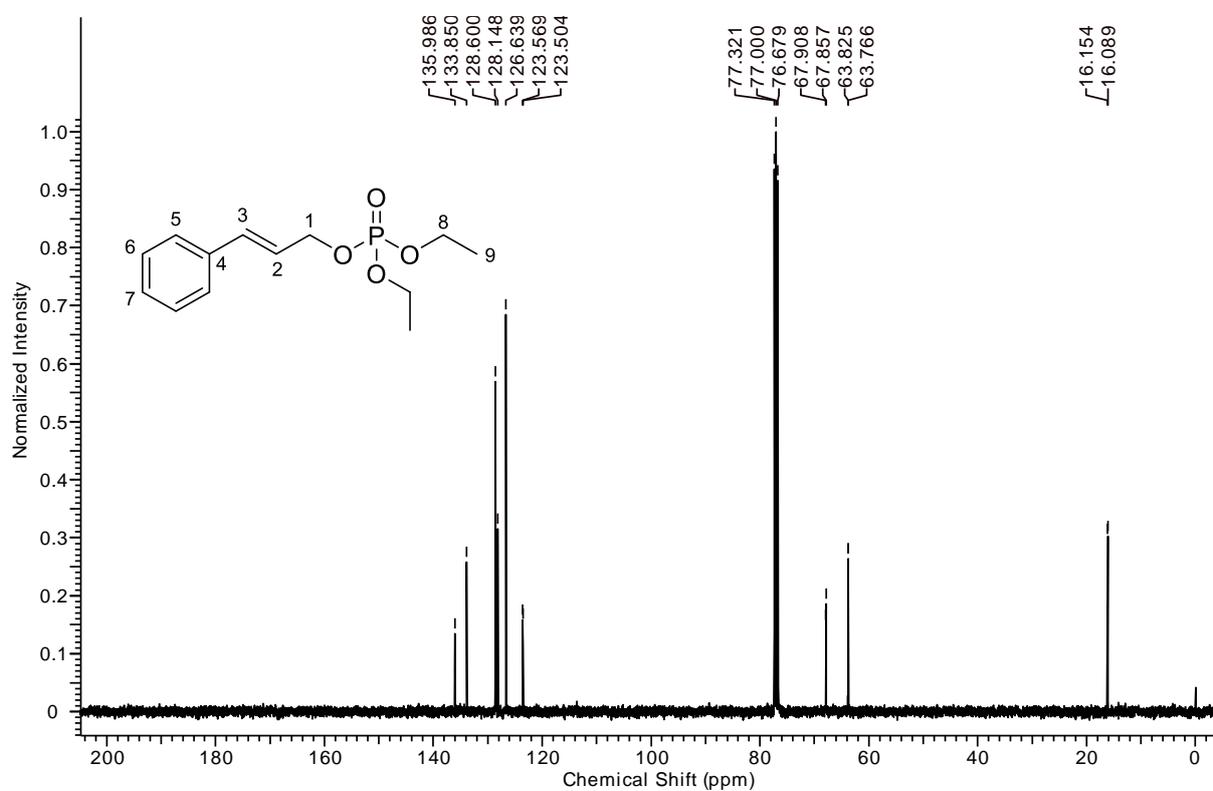
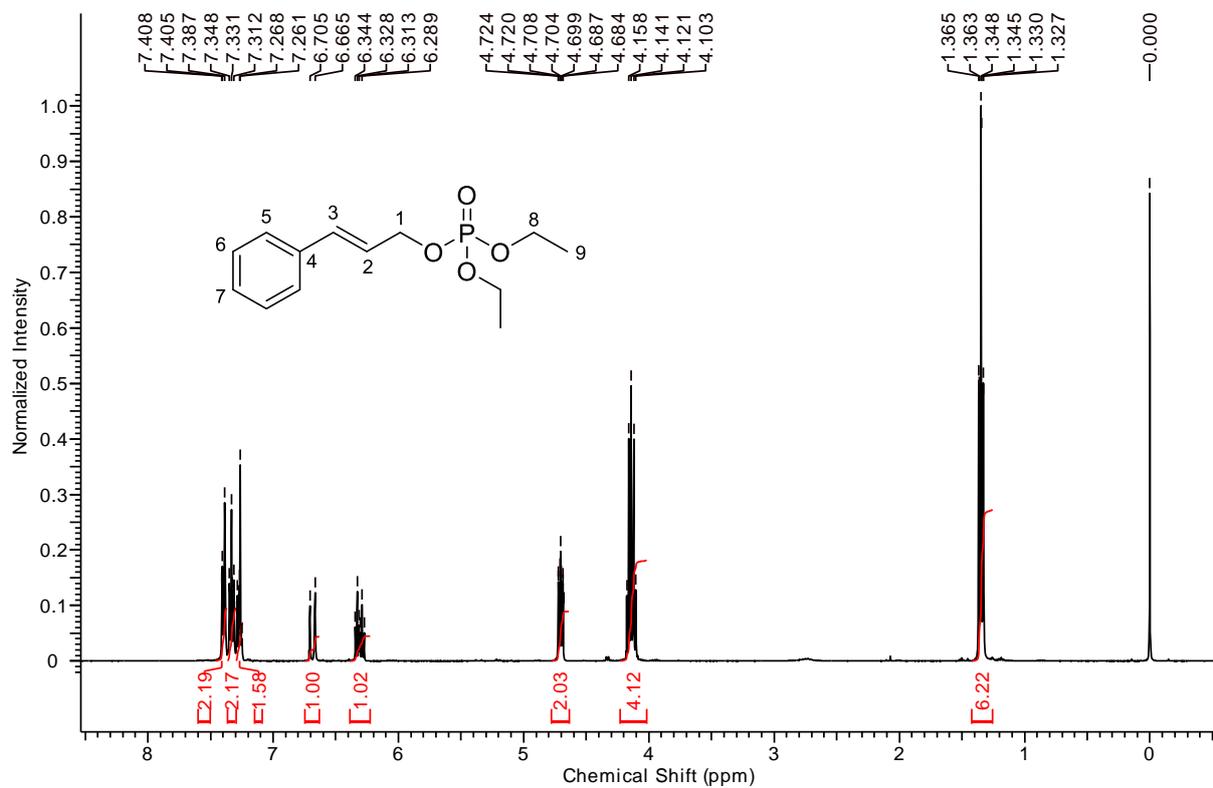
# Cinnamyl methyl carbonate (SI-3)



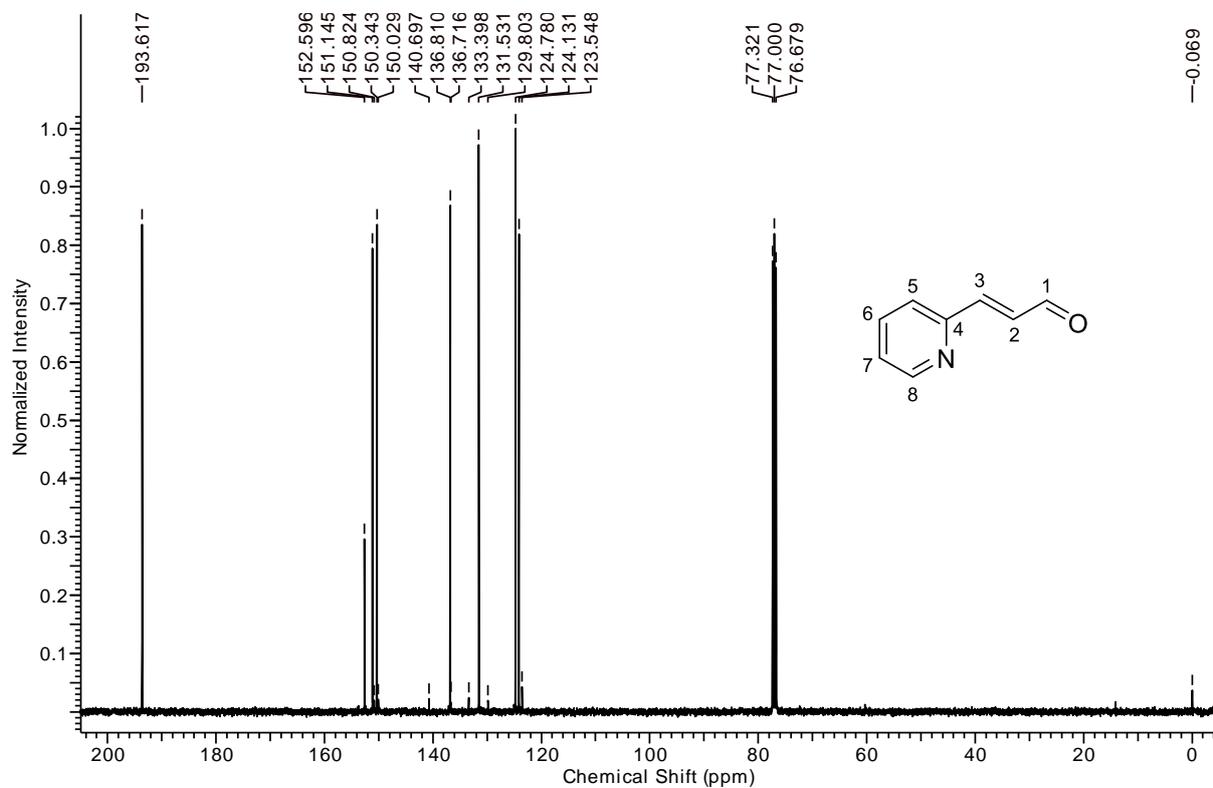
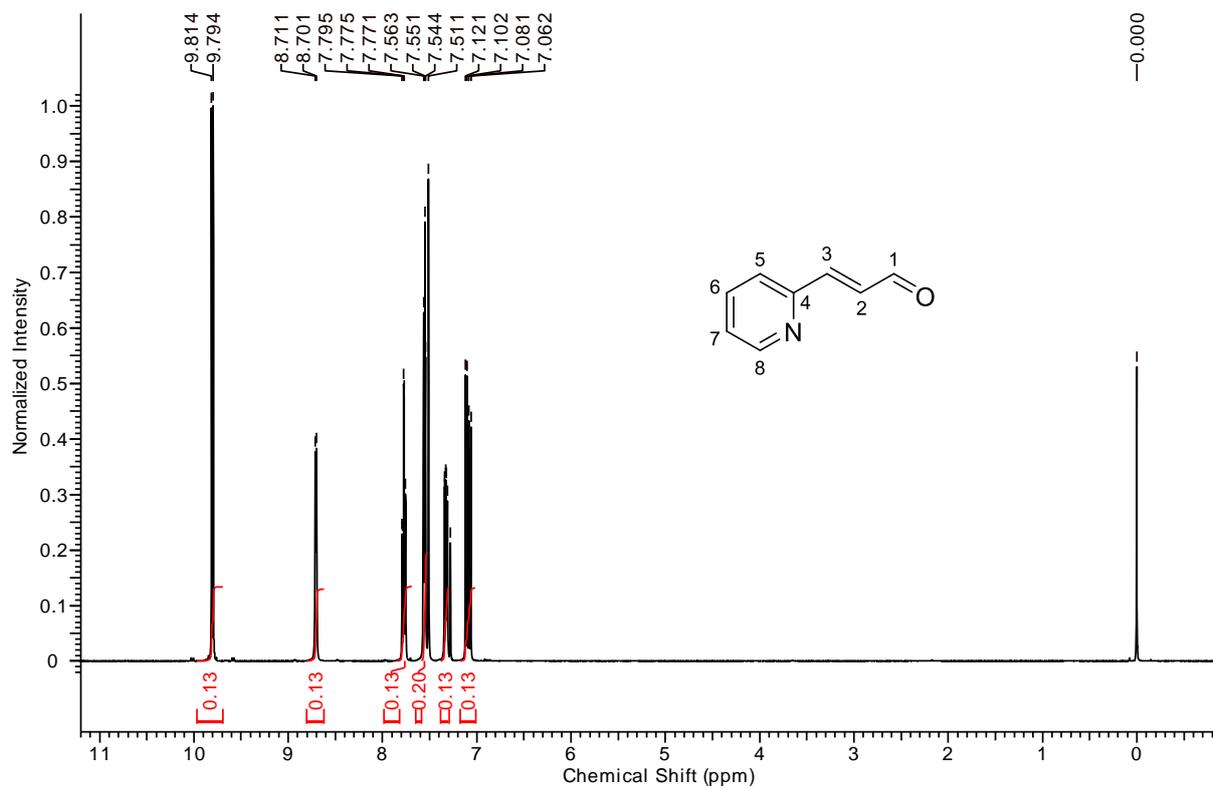
# Cinnamyl ethyl carbonate (SI-4)



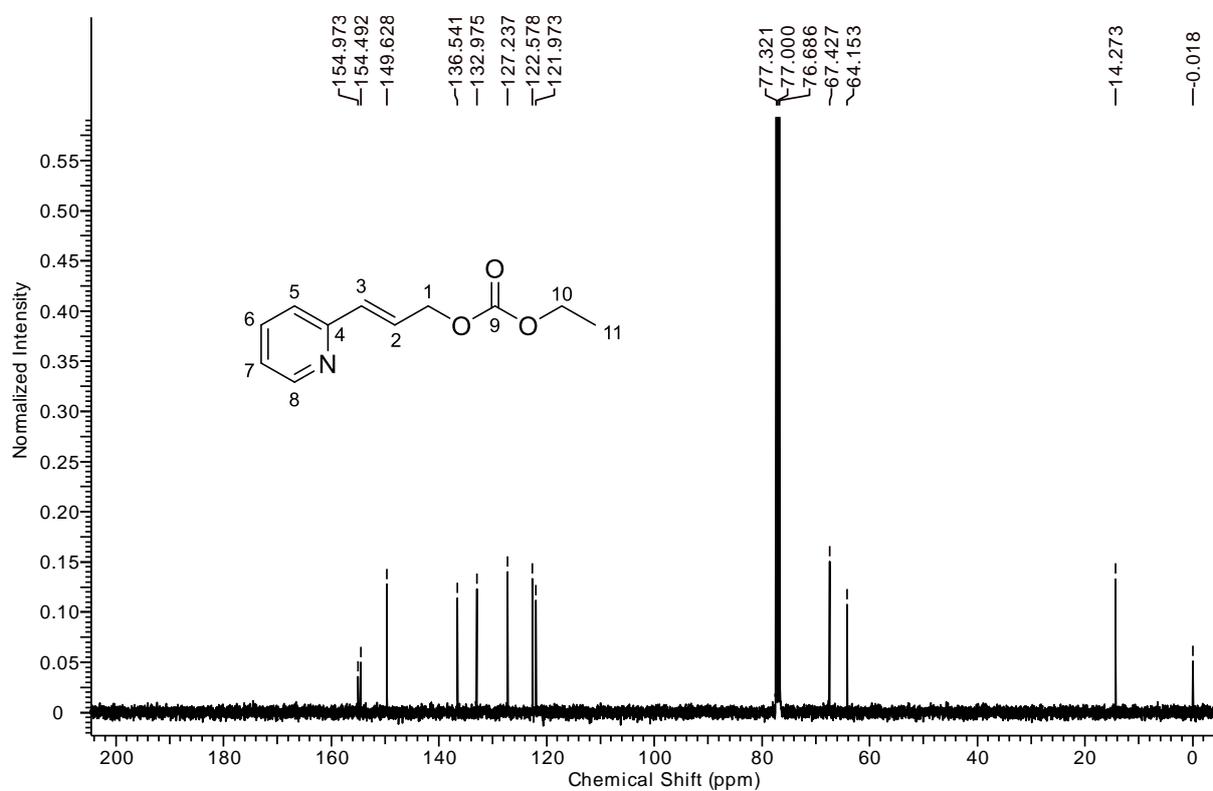
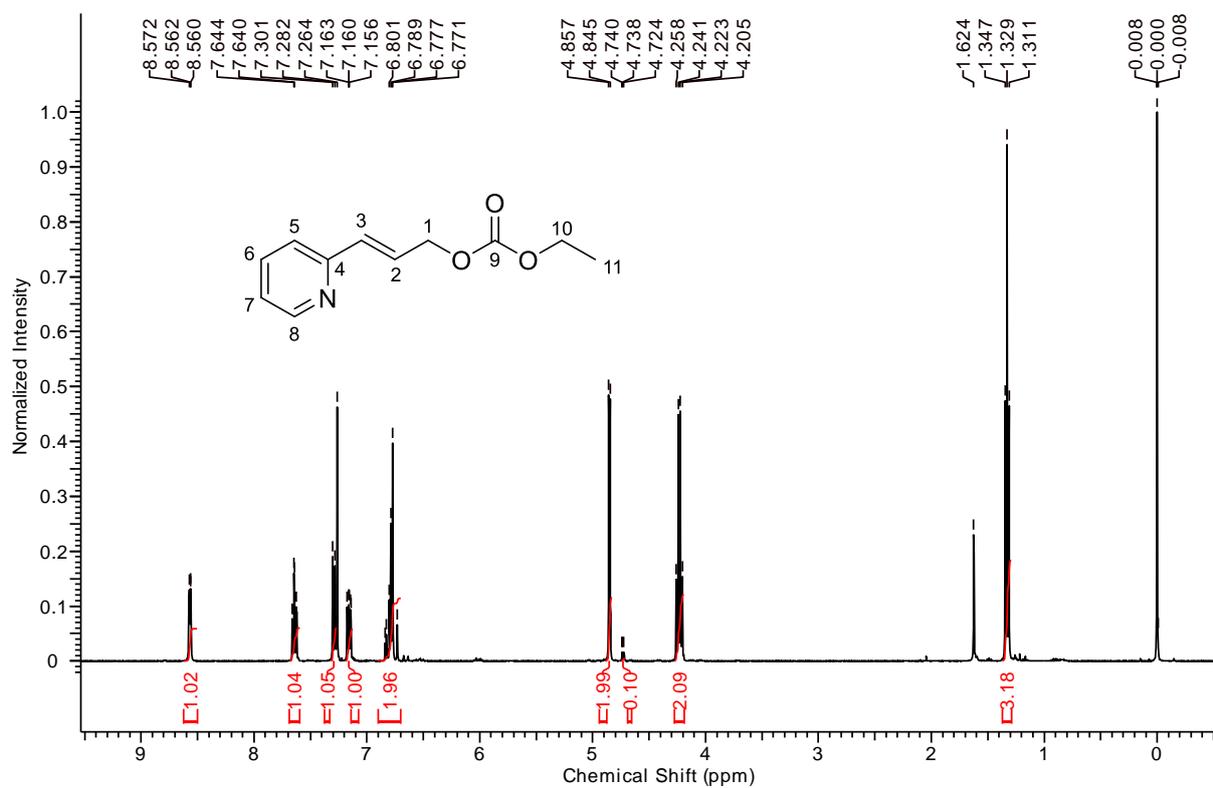
# Cinnamyl diethyl phosphate (SI-5)



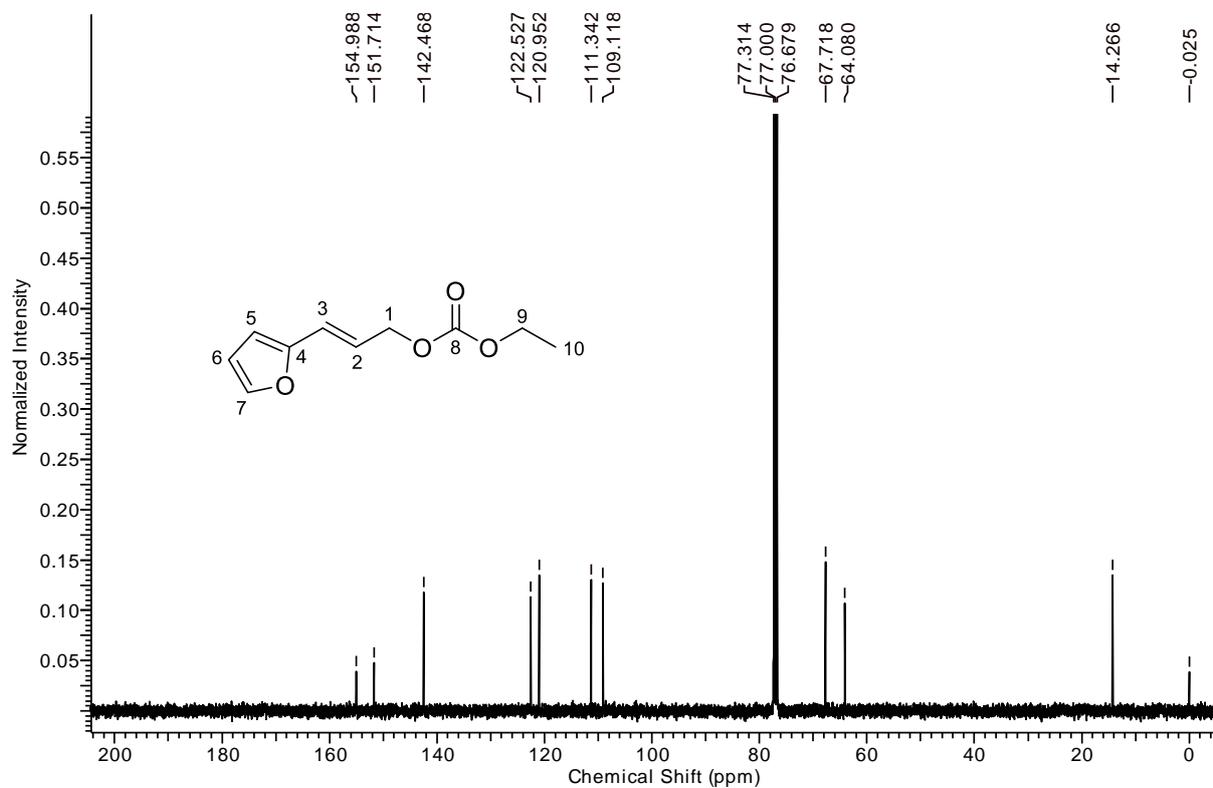
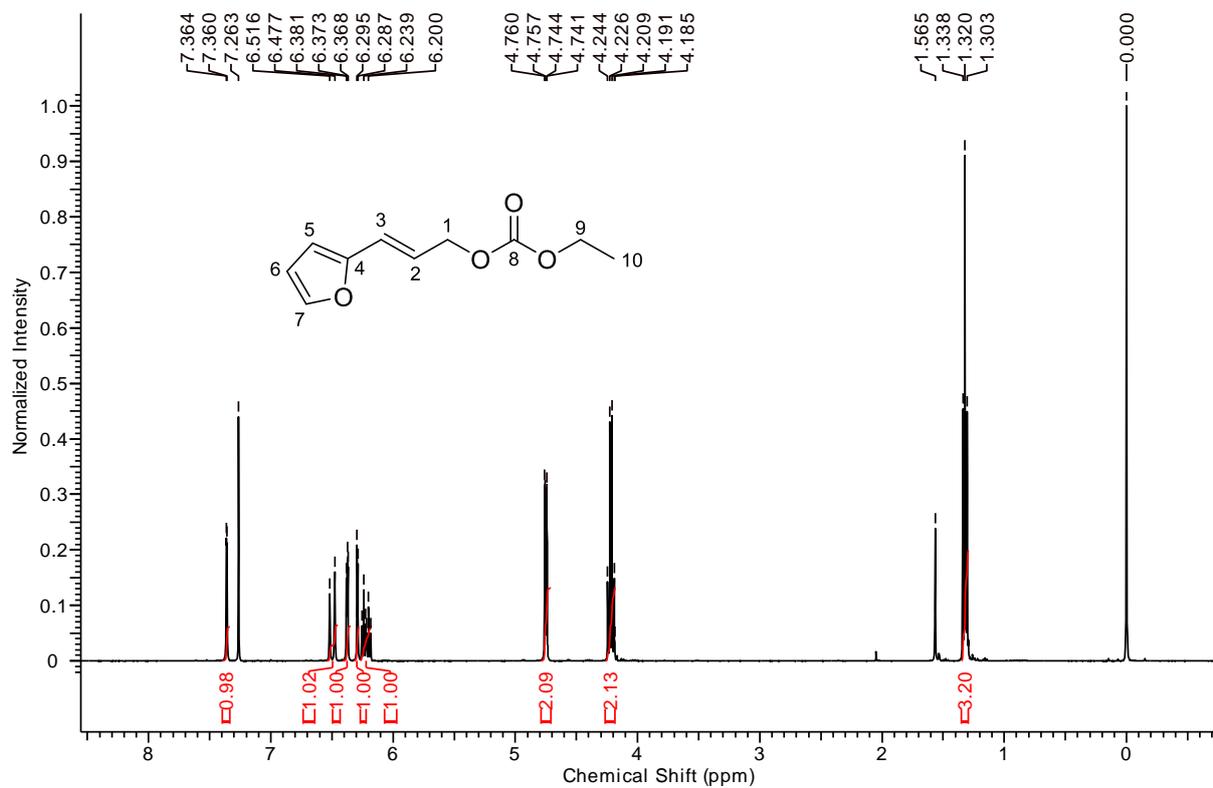
**(E)-3-(Pyridin-2-yl)acrylaldehyde (SI-7)**



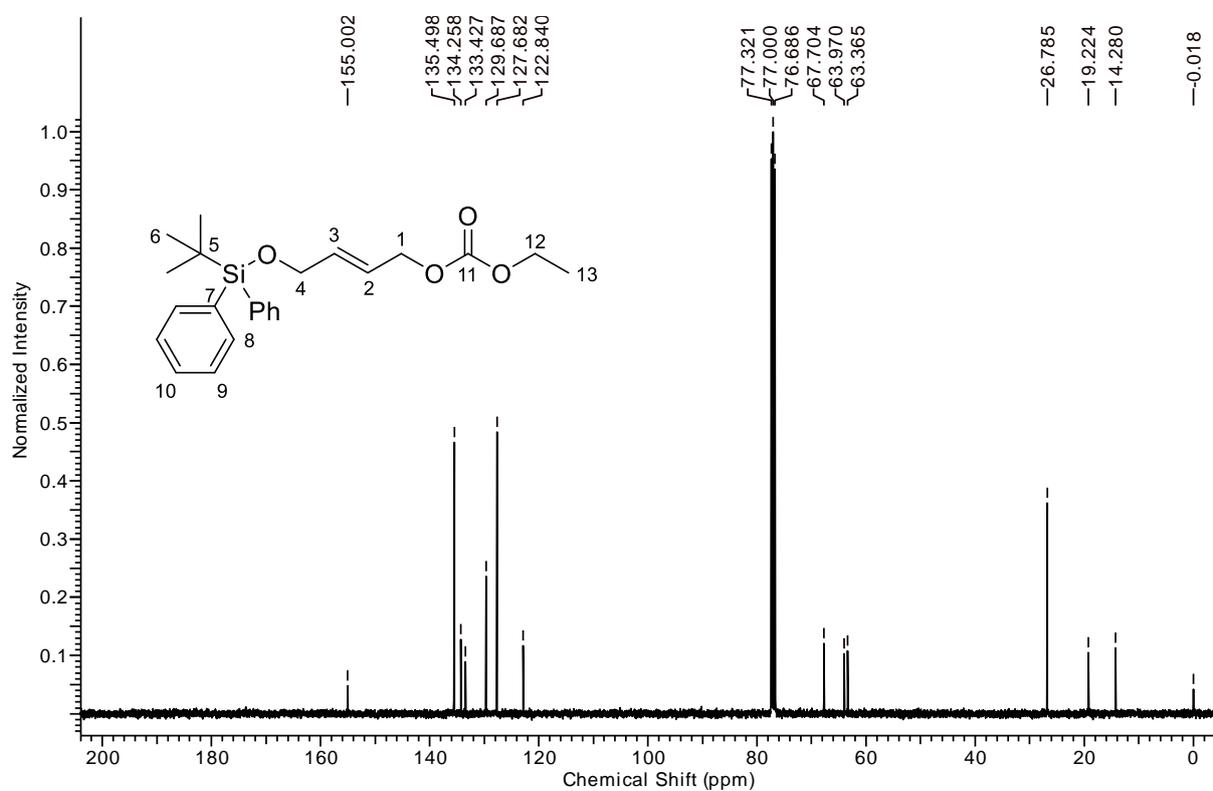
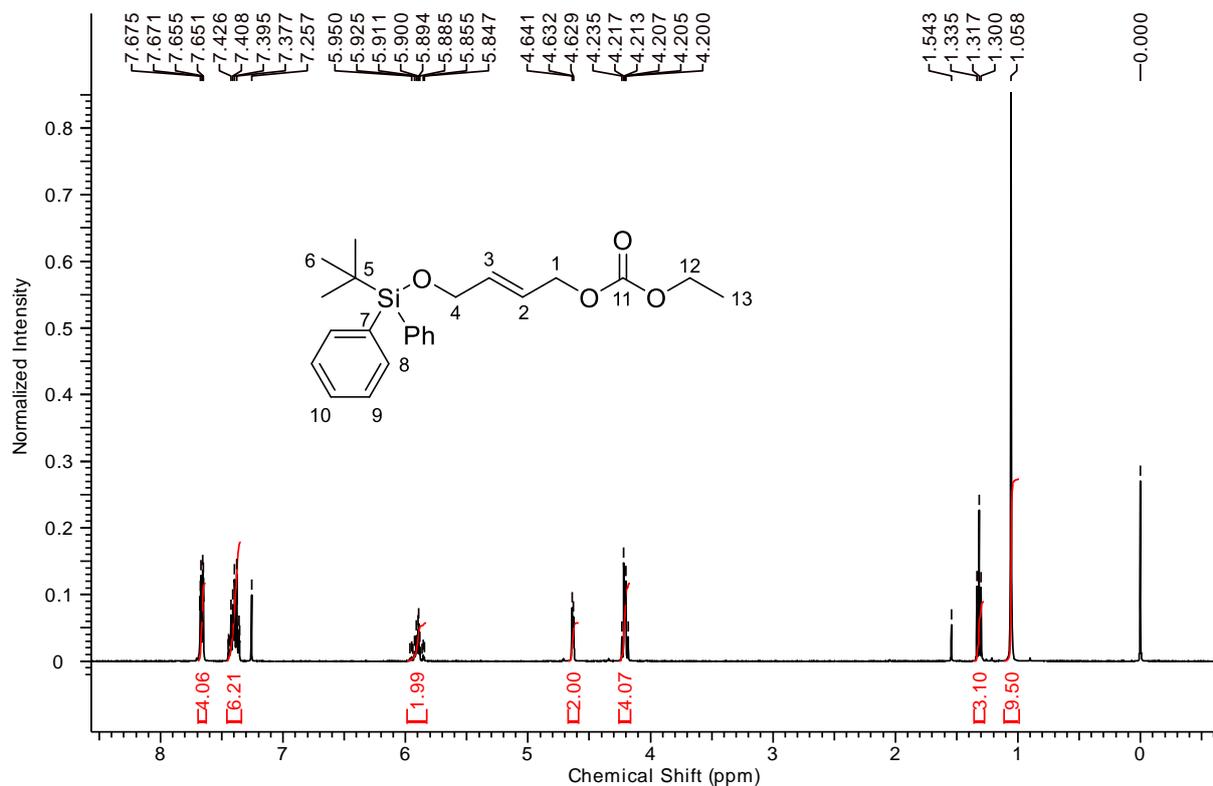
### (E)-Ethyl (3-(pyridin-2-yl)allyl) carbonate (SI-8)



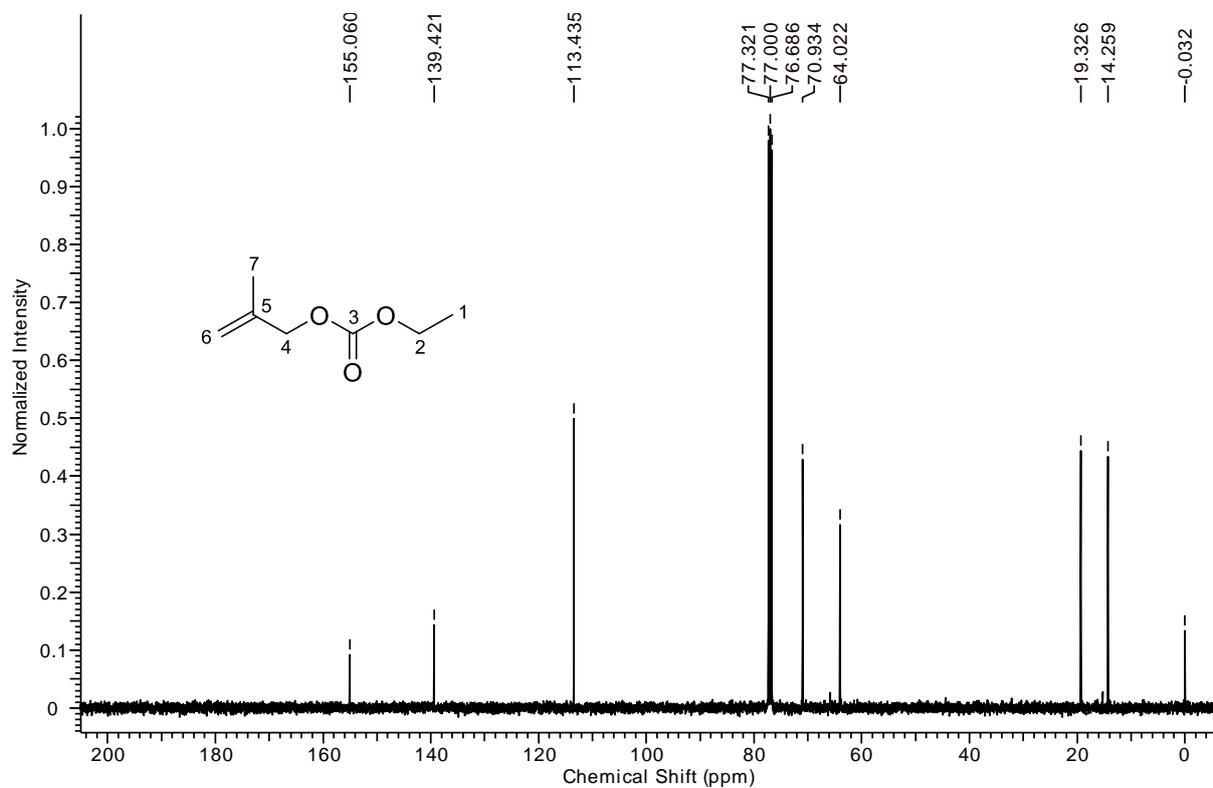
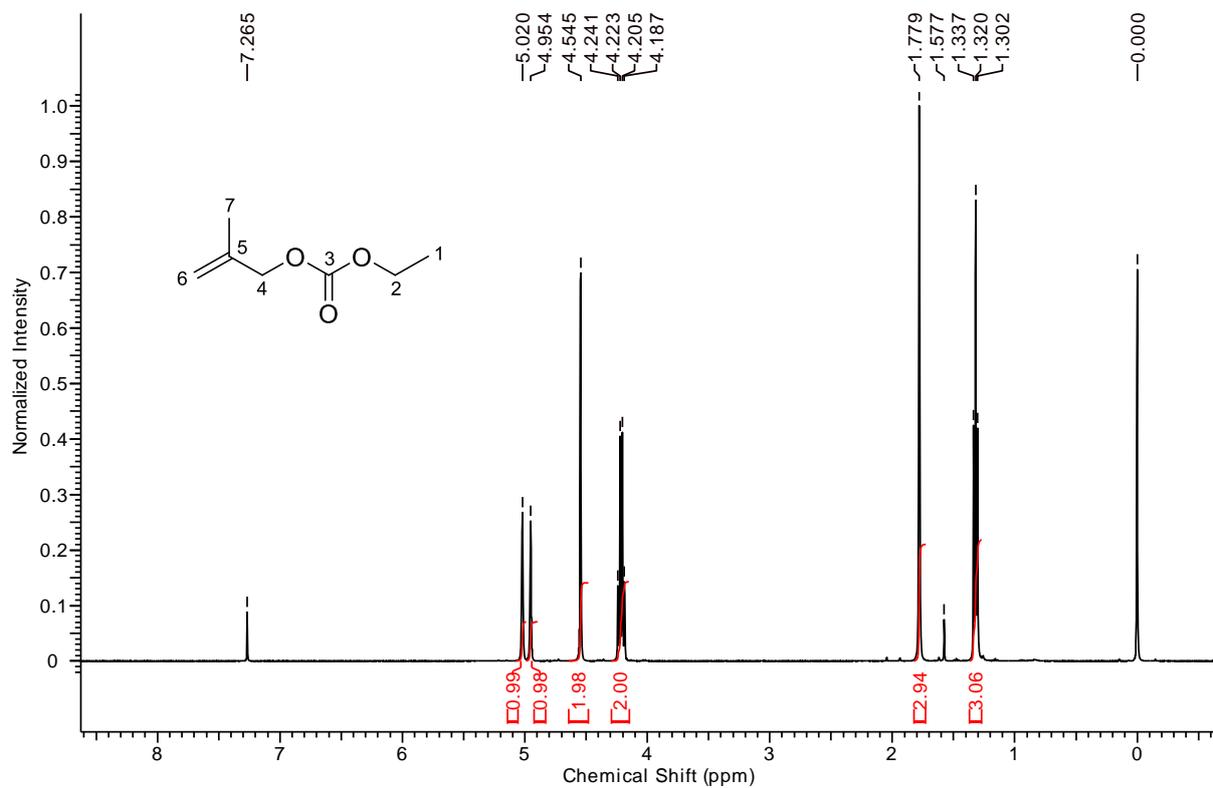
# (E)-Ethyl (3-(furan-2-yl)allyl) carbonate (SI-9)



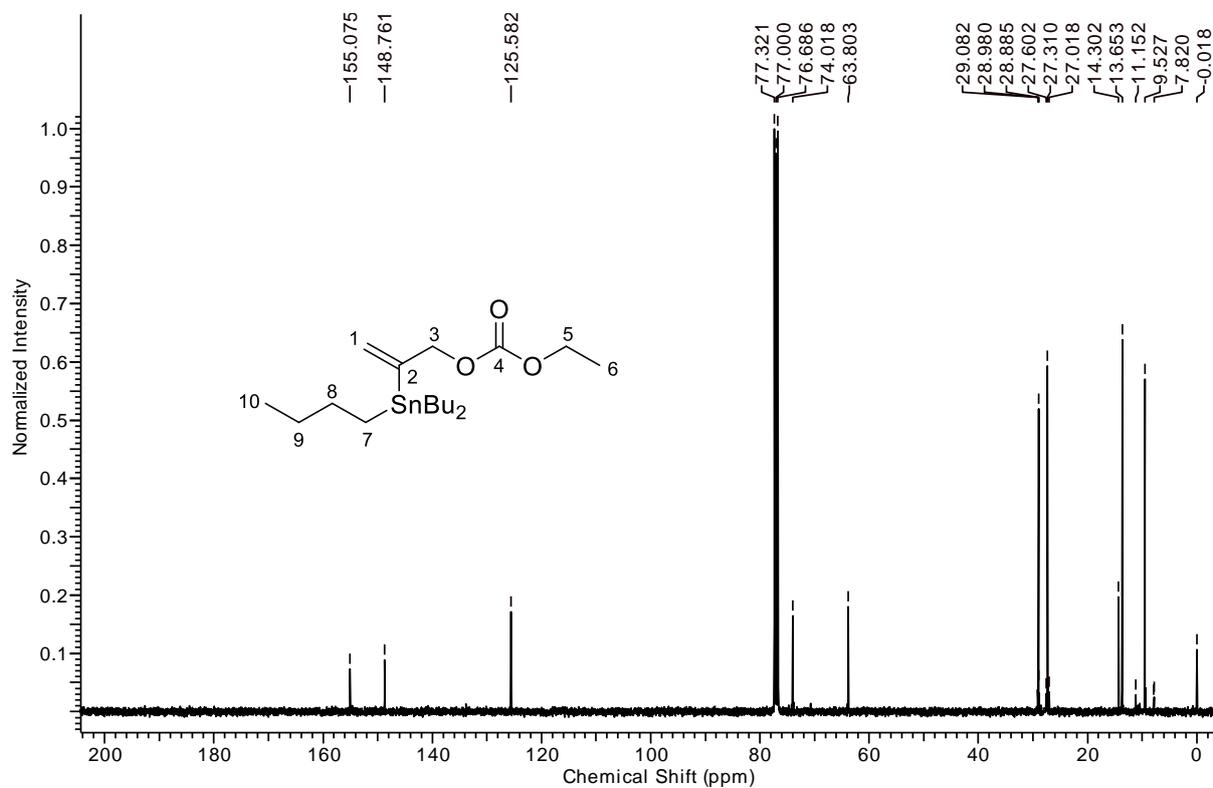
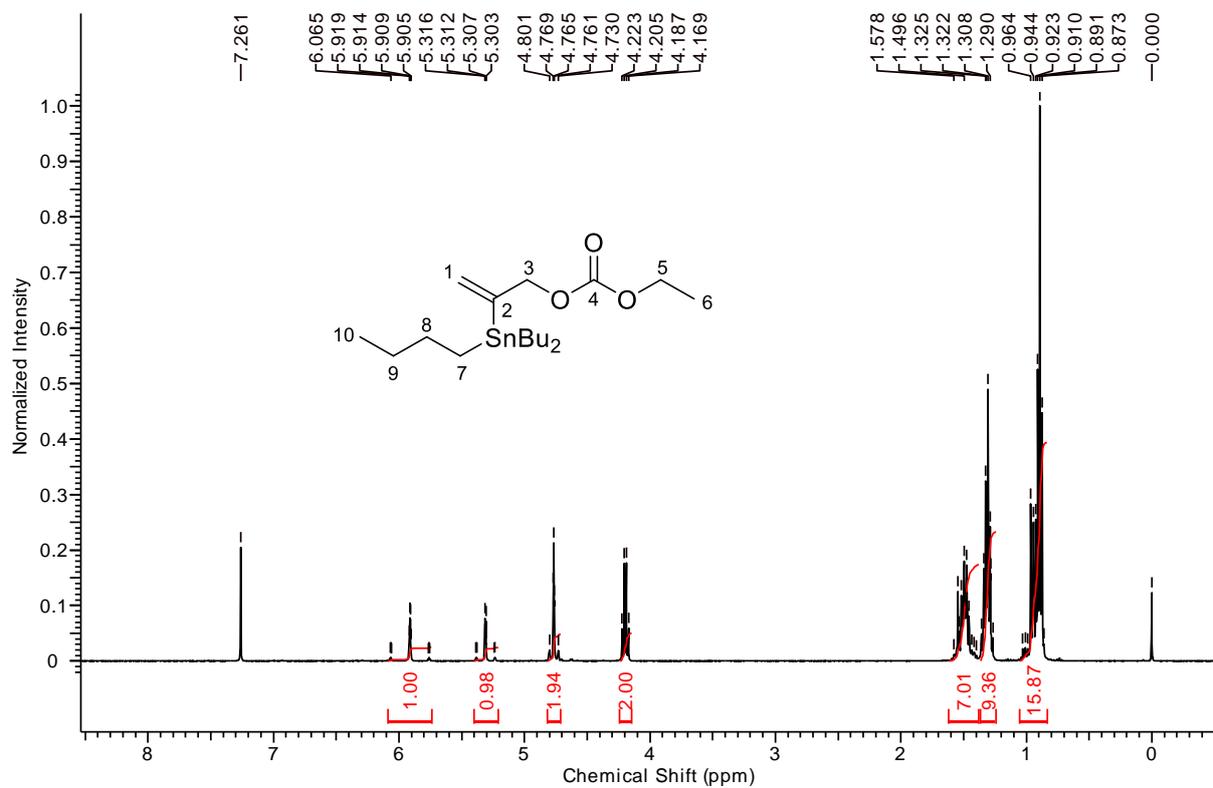
**(E)-4-((tert-Butyldiphenylsilyl)oxy)but-2-en-1-yl ethyl carbonate (SI-10)**



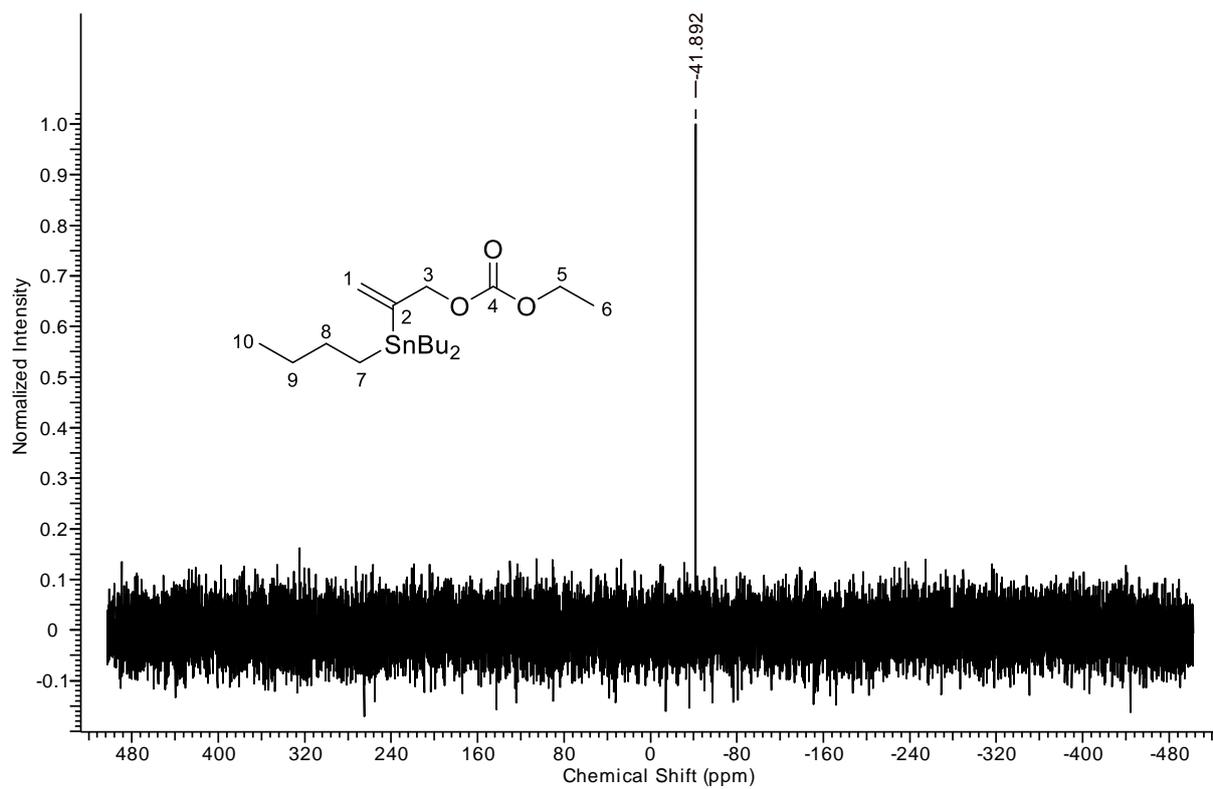
# Ethyl (2-methylallyl) carbonate (SI-11)



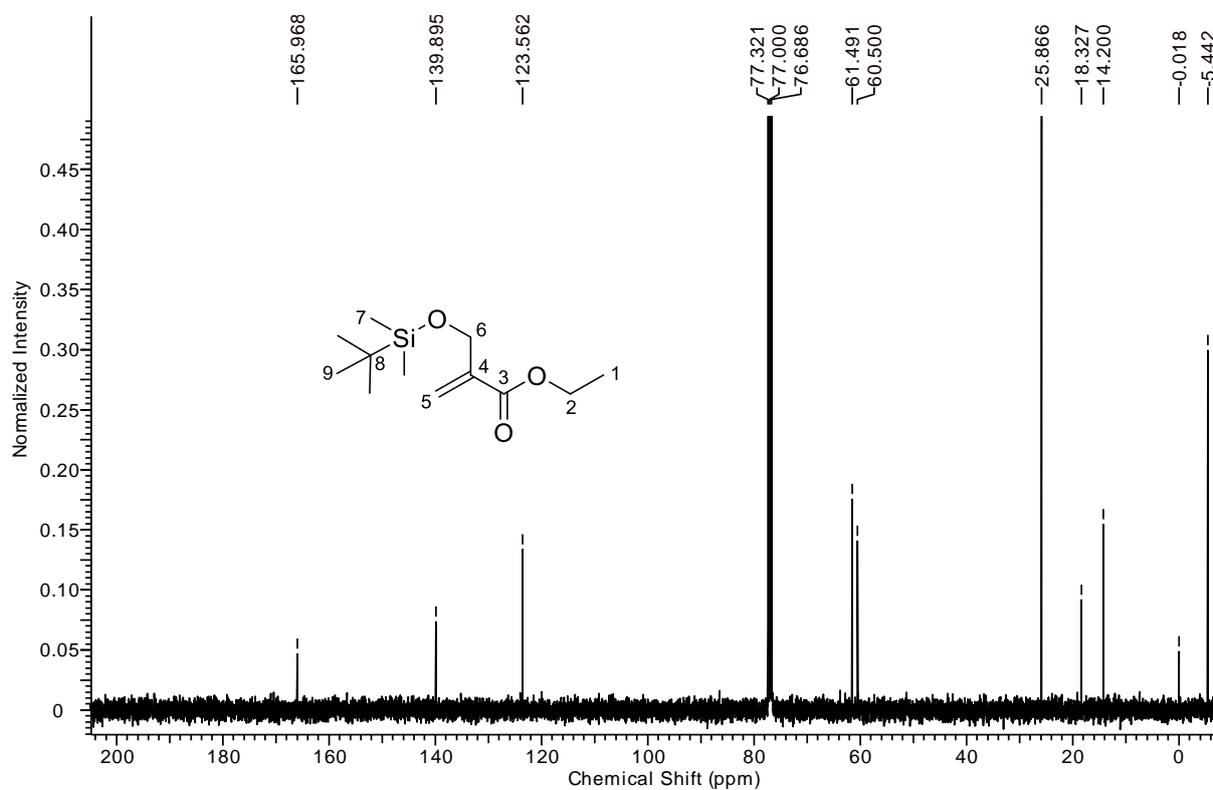
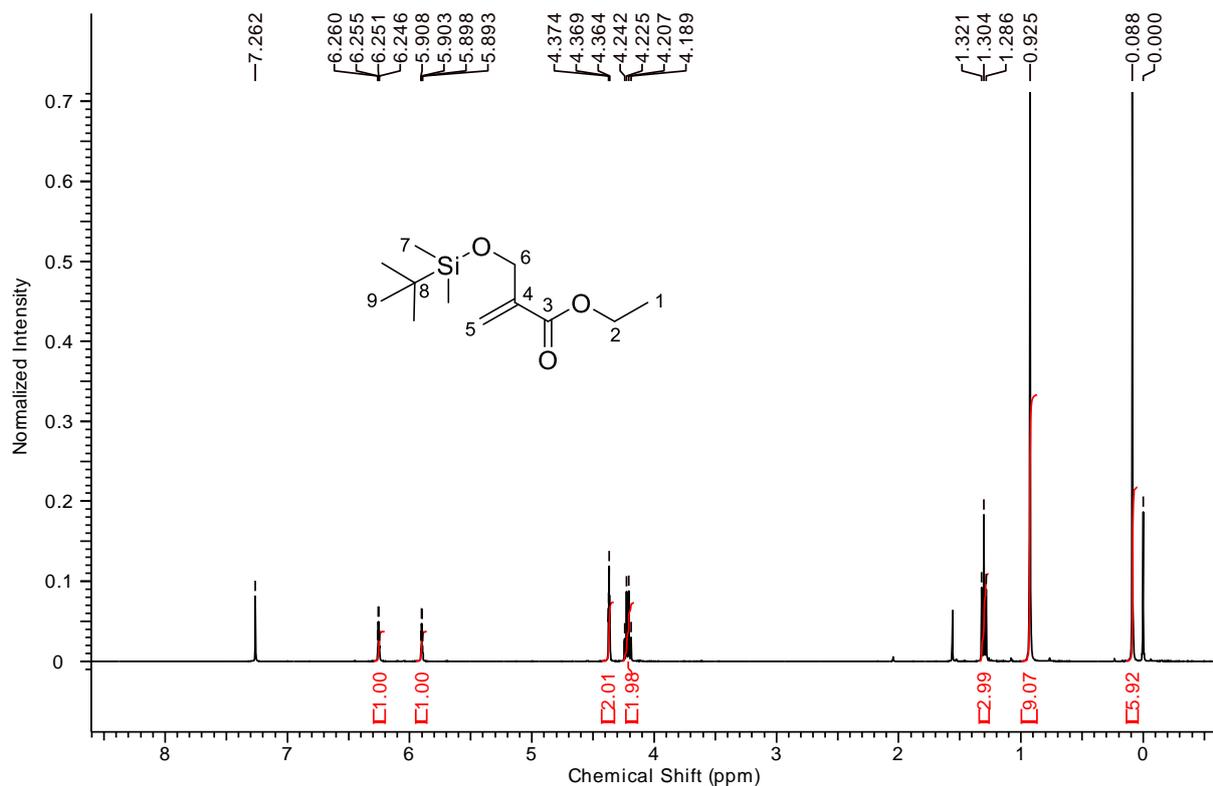
# Ethyl (2-(tributylstannyl)allyl) carbonate (SI-12)



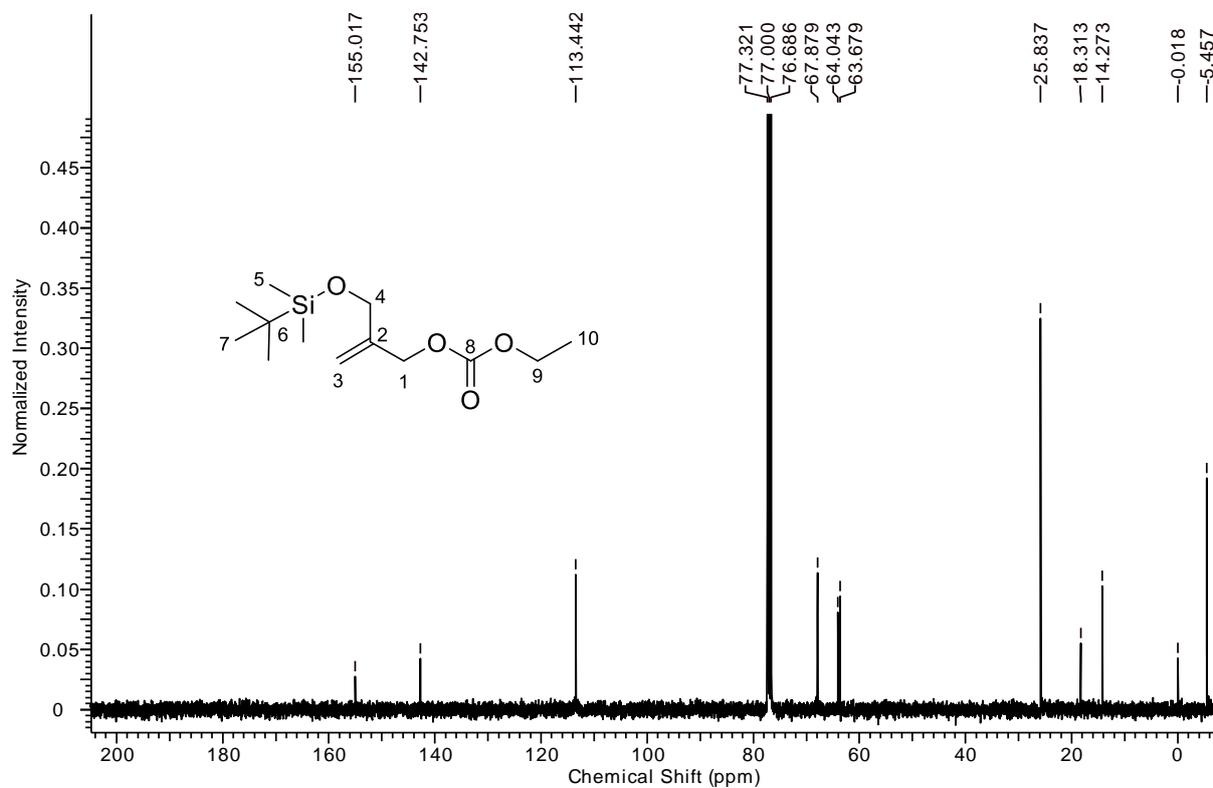
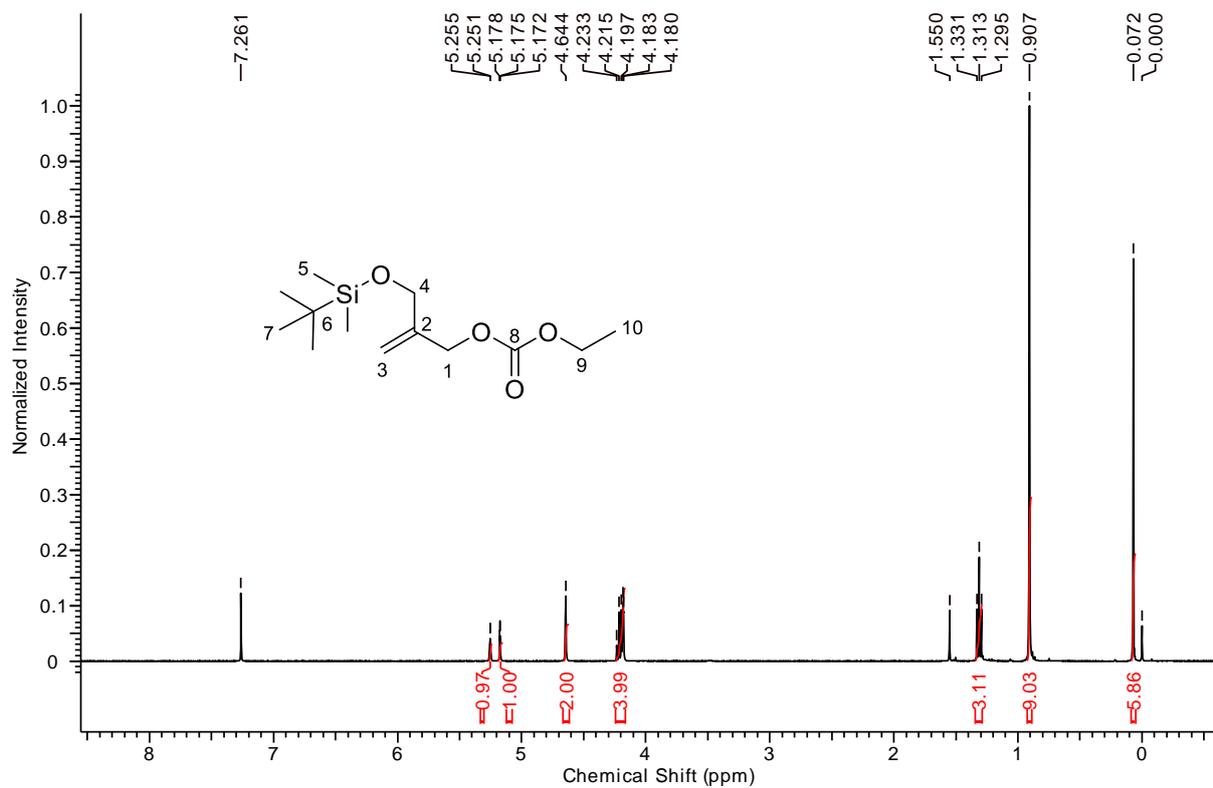
<sup>119</sup>Sn-NMR



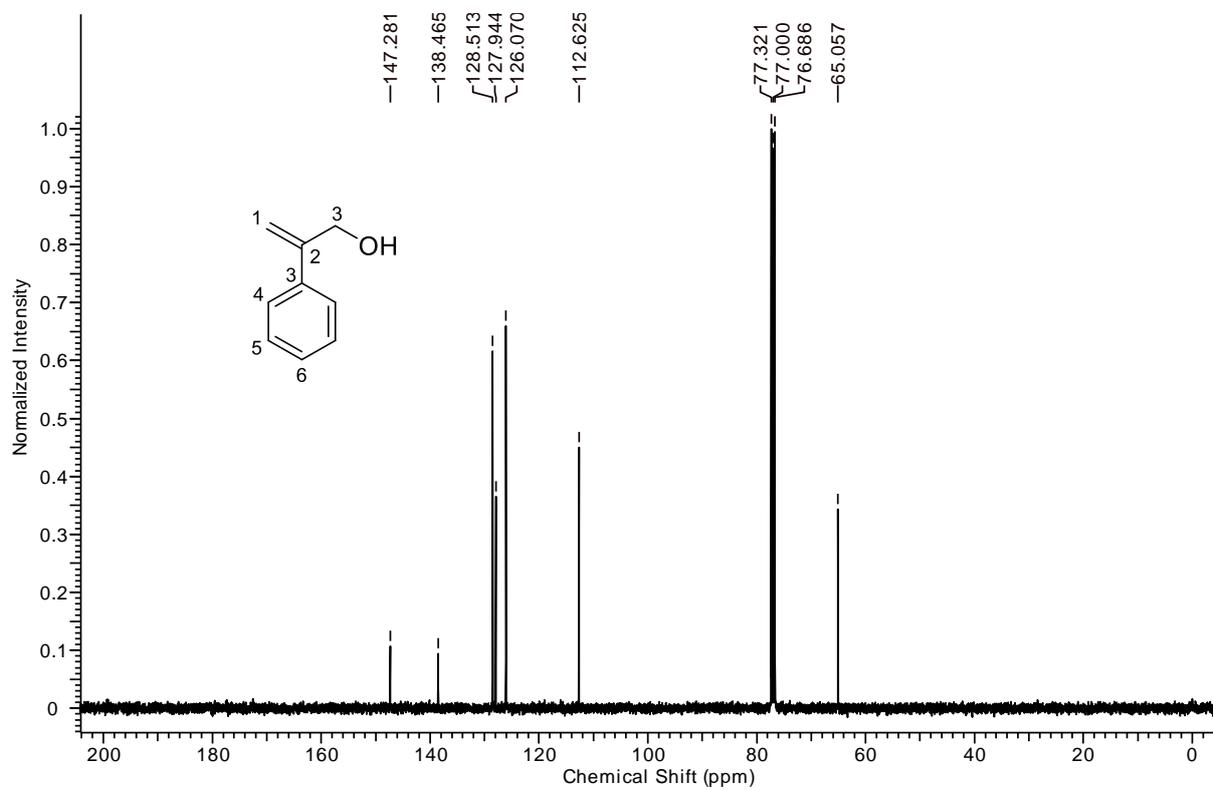
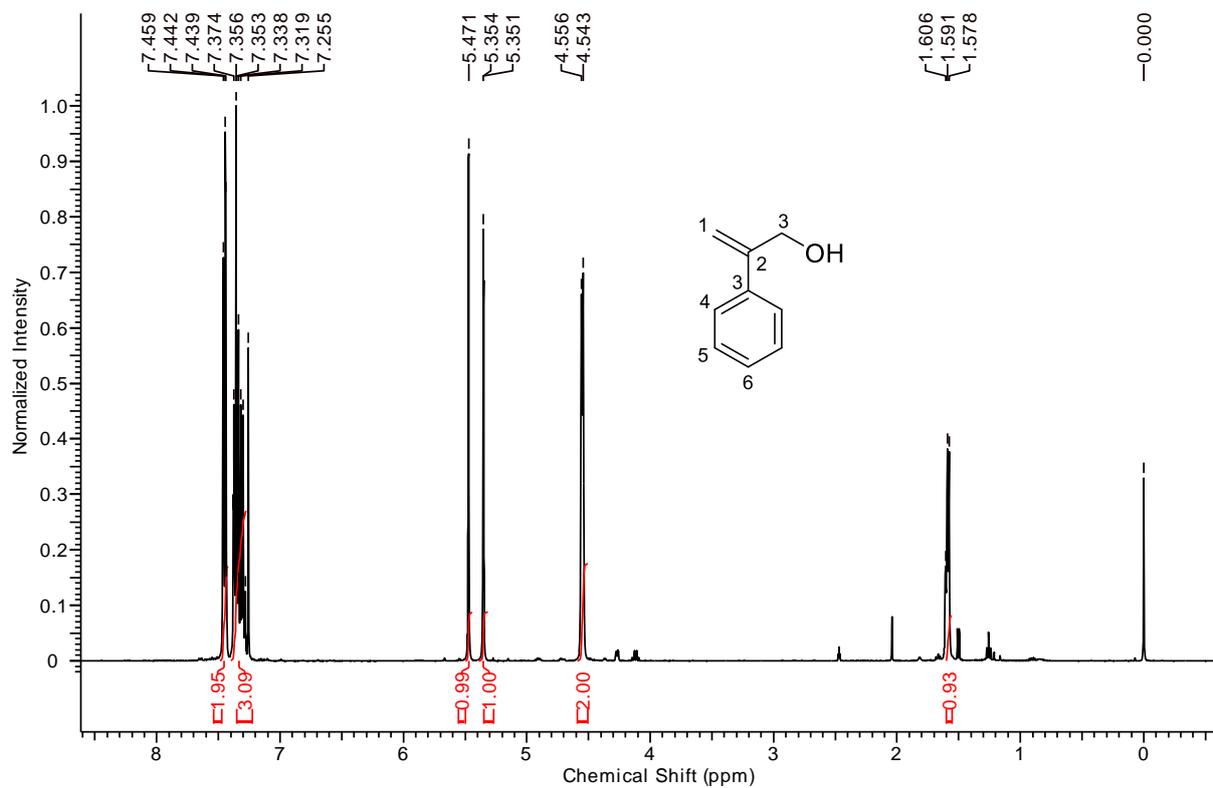
# Ethyl 2-(((*tert*-butyldimethylsilyl)oxy)methyl)acrylate (SI-13)



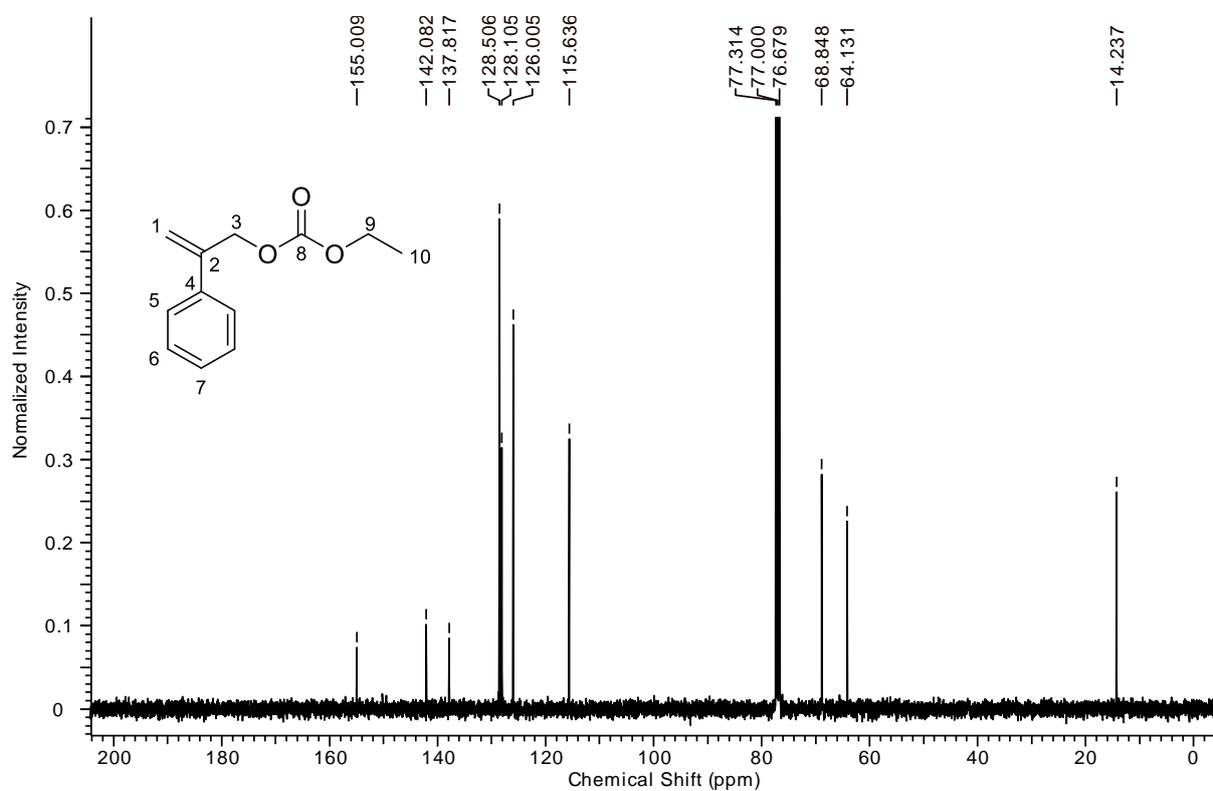
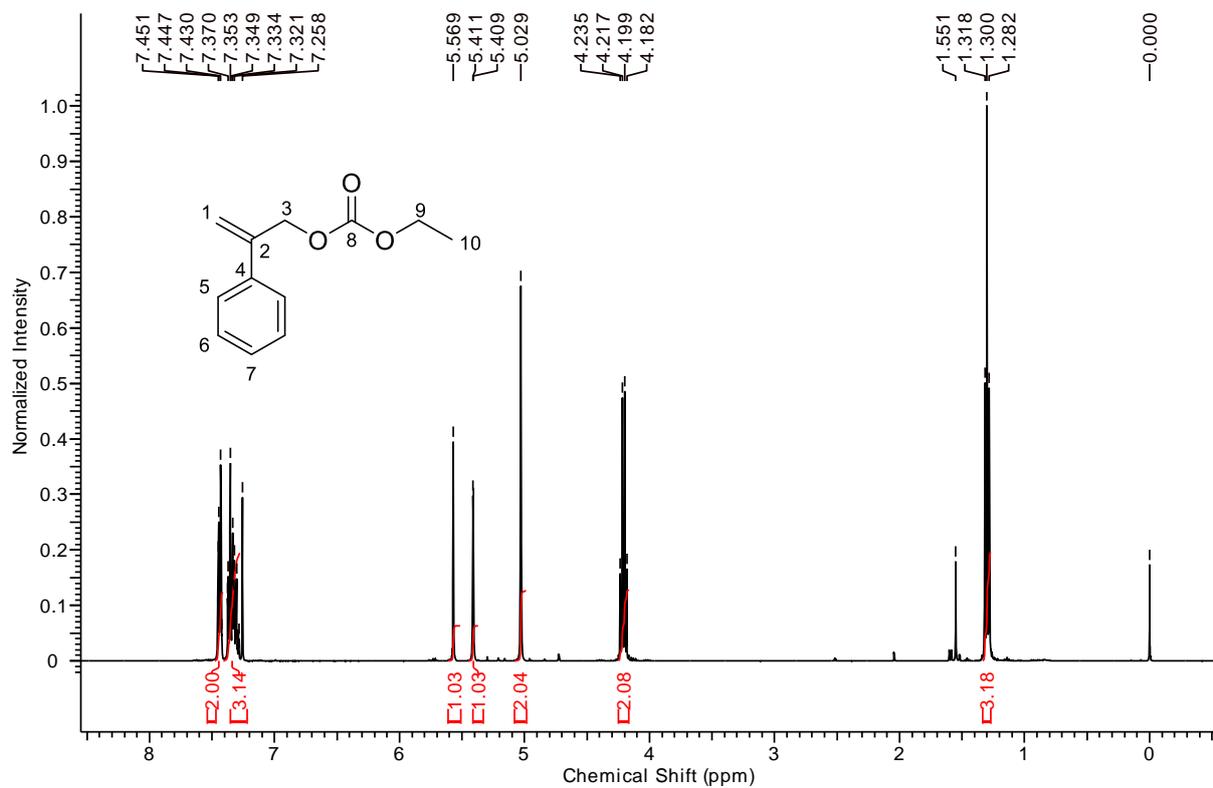
2-(((*tert*-Butyldimethylsilyloxy)methyl)allyl ethyl carbonate (SI-14)



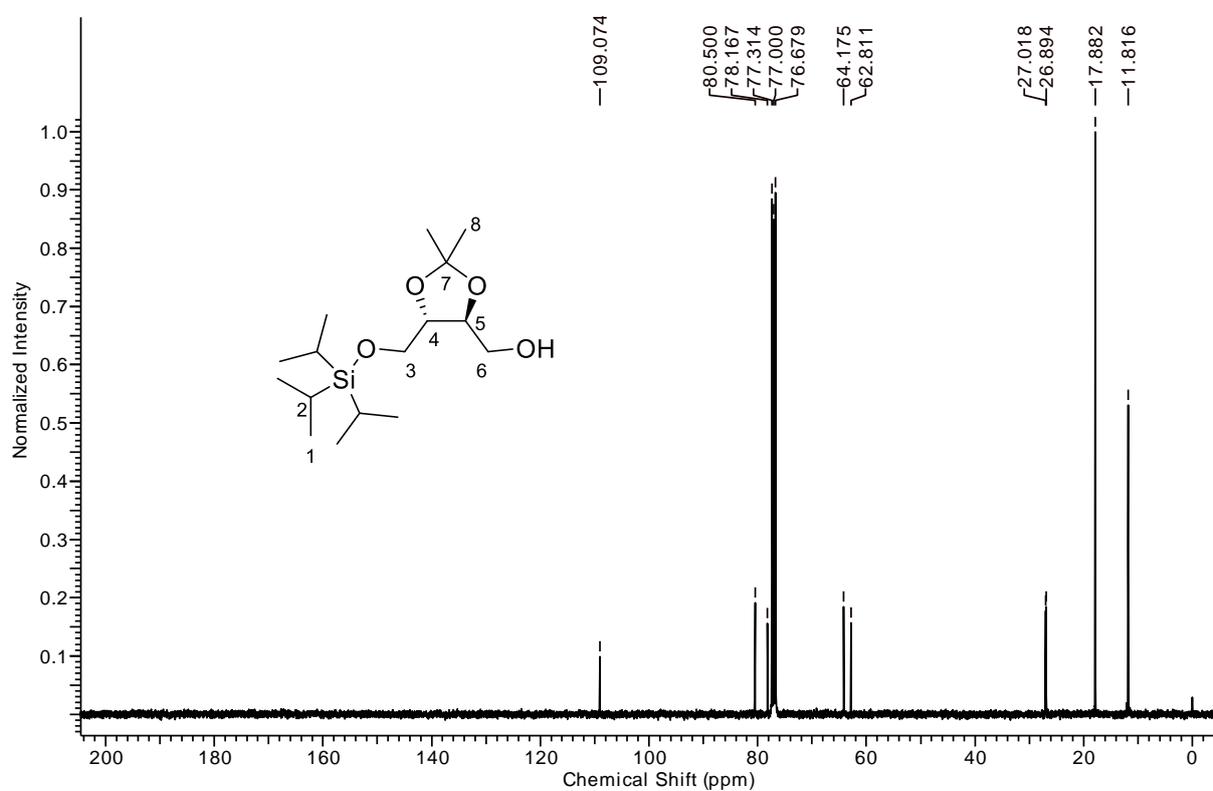
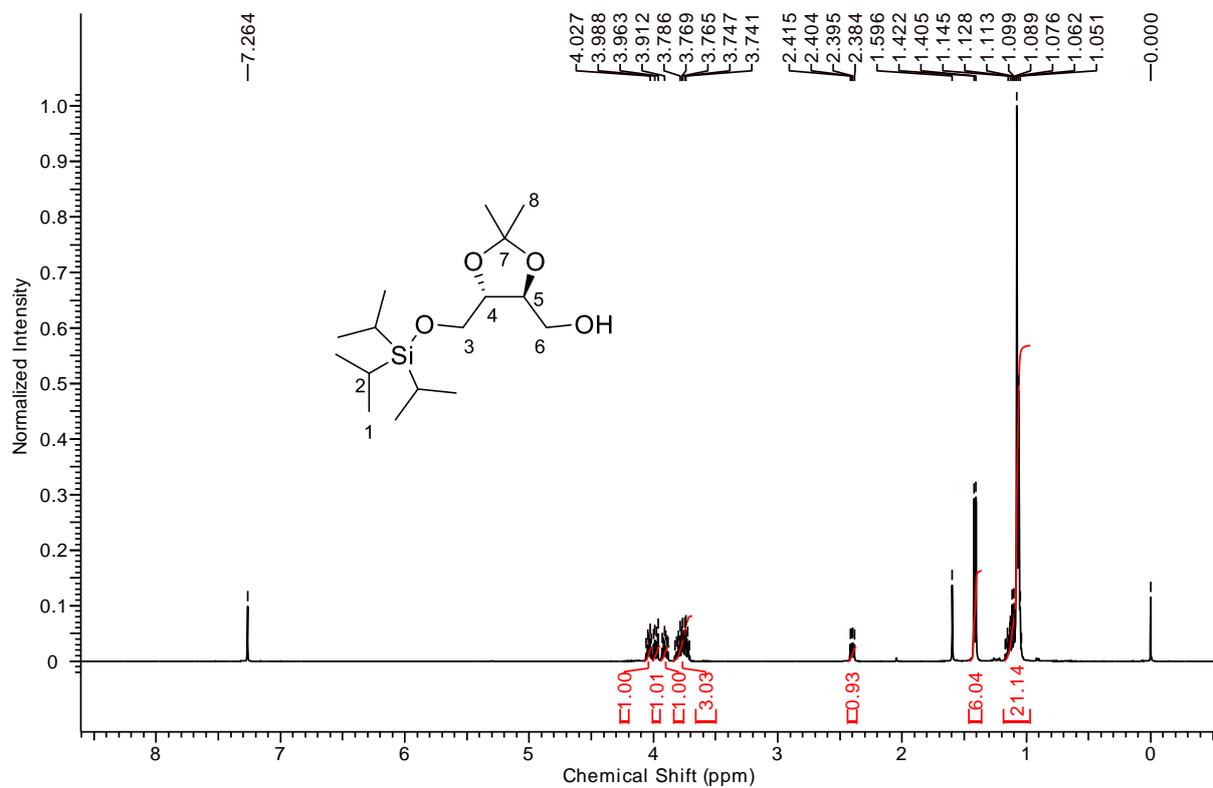
## 2-Phenylprop-2-en-1-ol (SI-15)



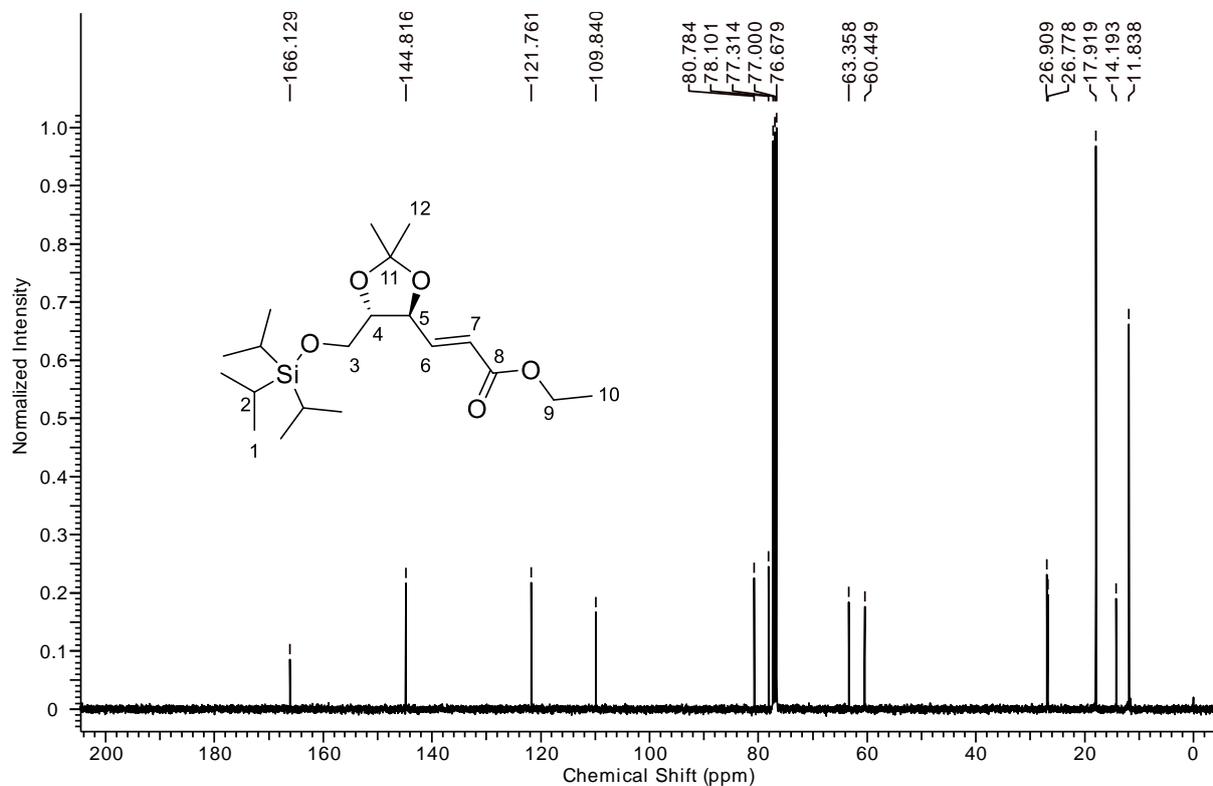
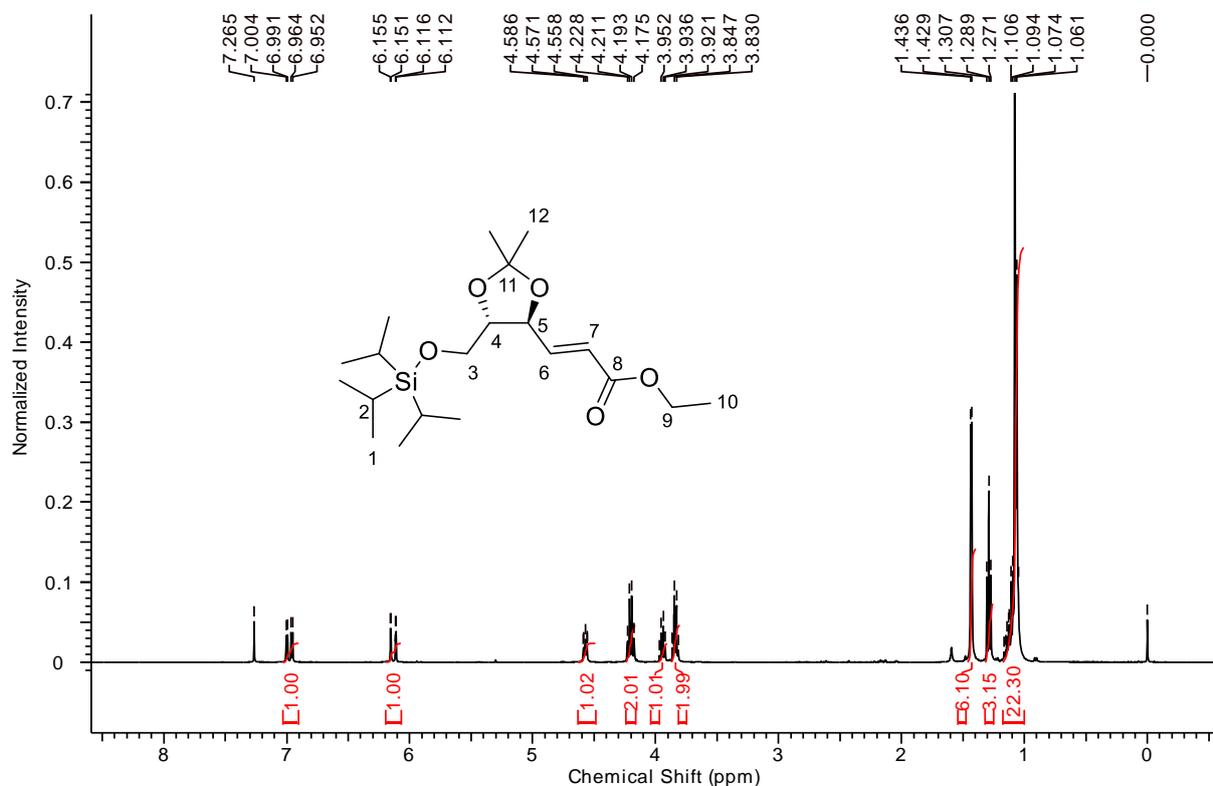
# Ethyl (2-phenylallyl) carbonate (SI-16)



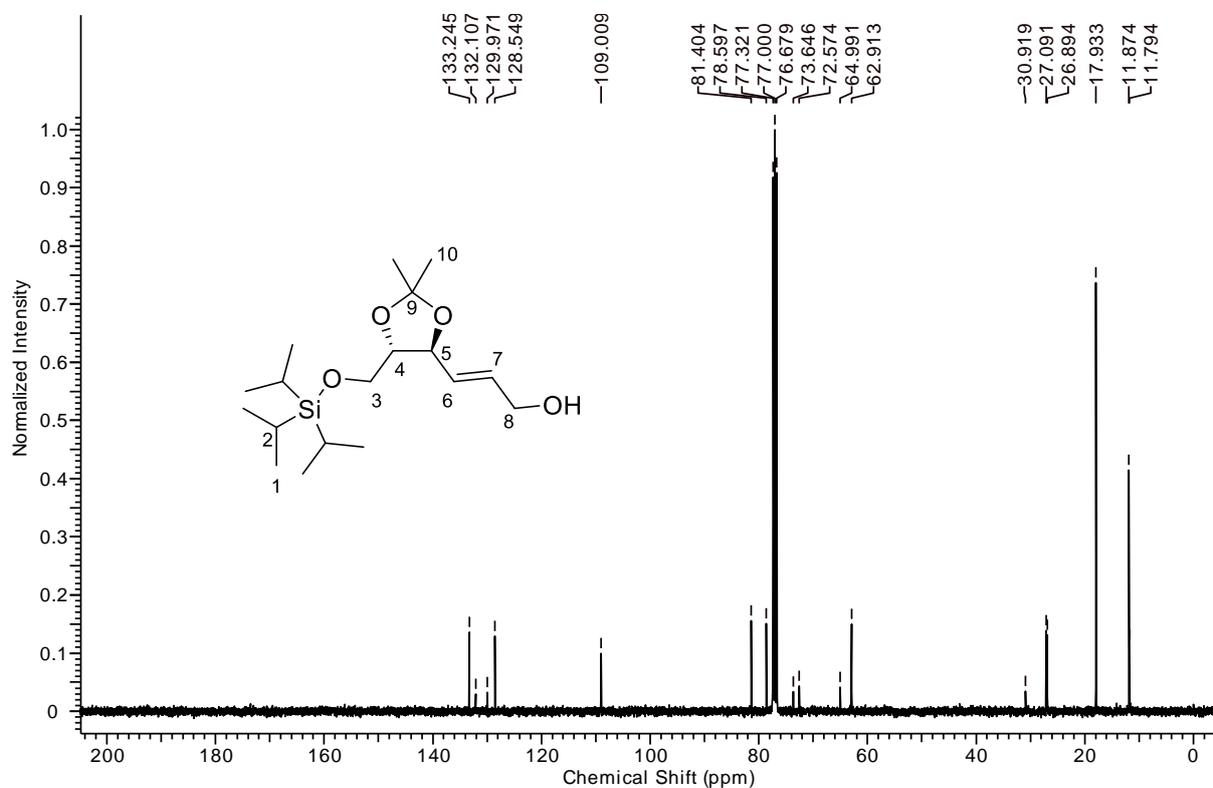
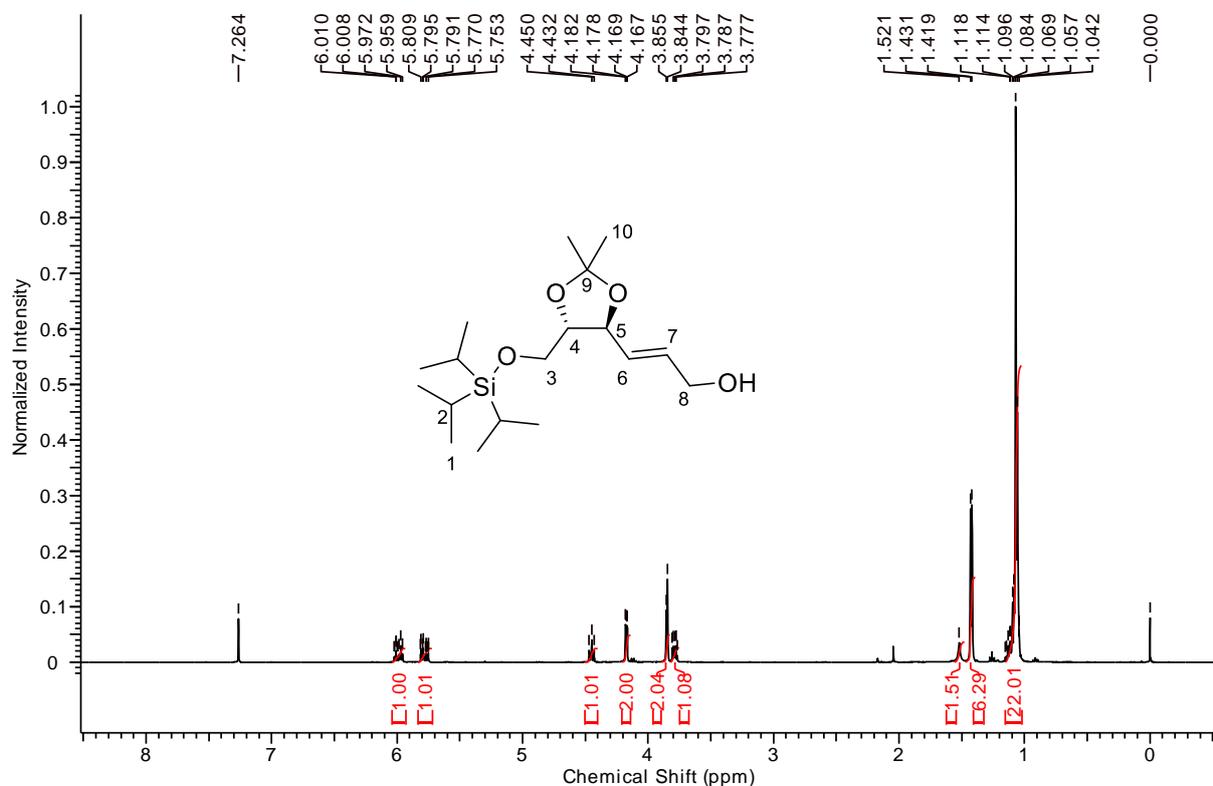
**((4*S*,5*S*)-2,2-Dimethyl-5-(((triisopropylsilyloxy)methyl)-1,3-dioxolan-4-yl)methanol (SI-18)**



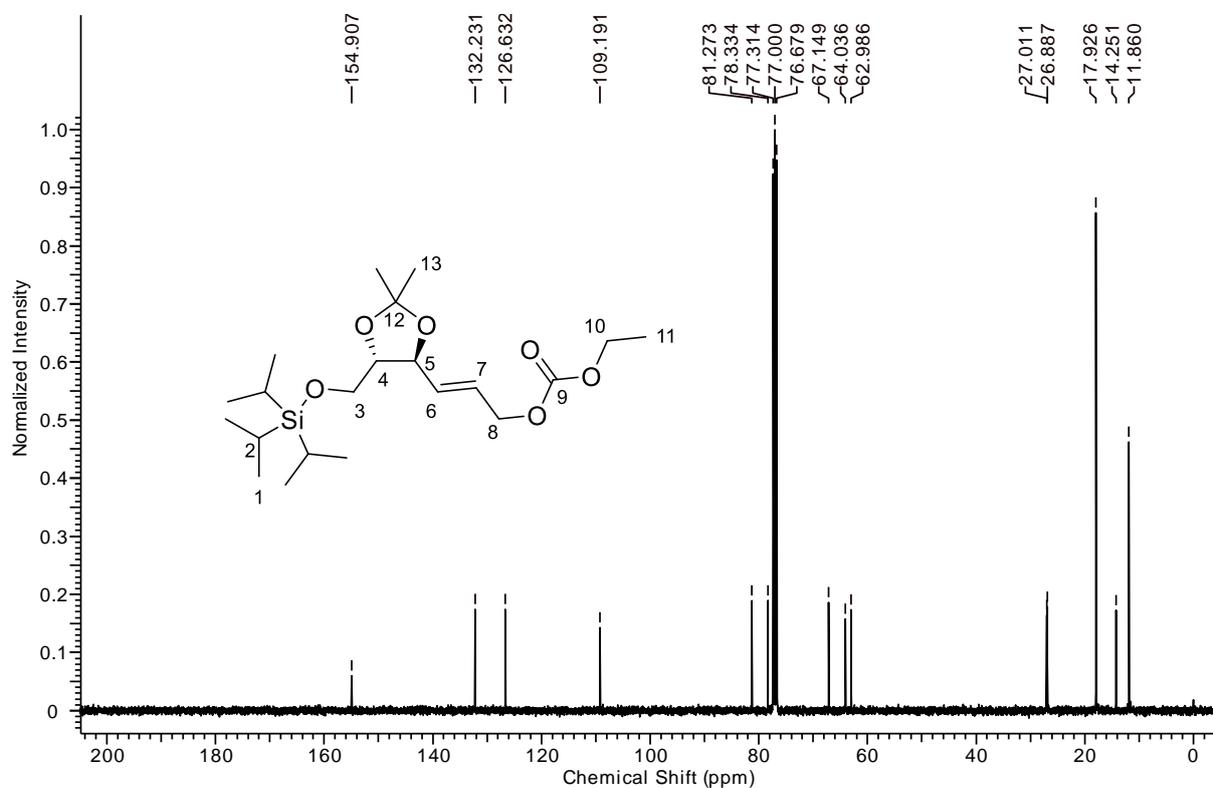
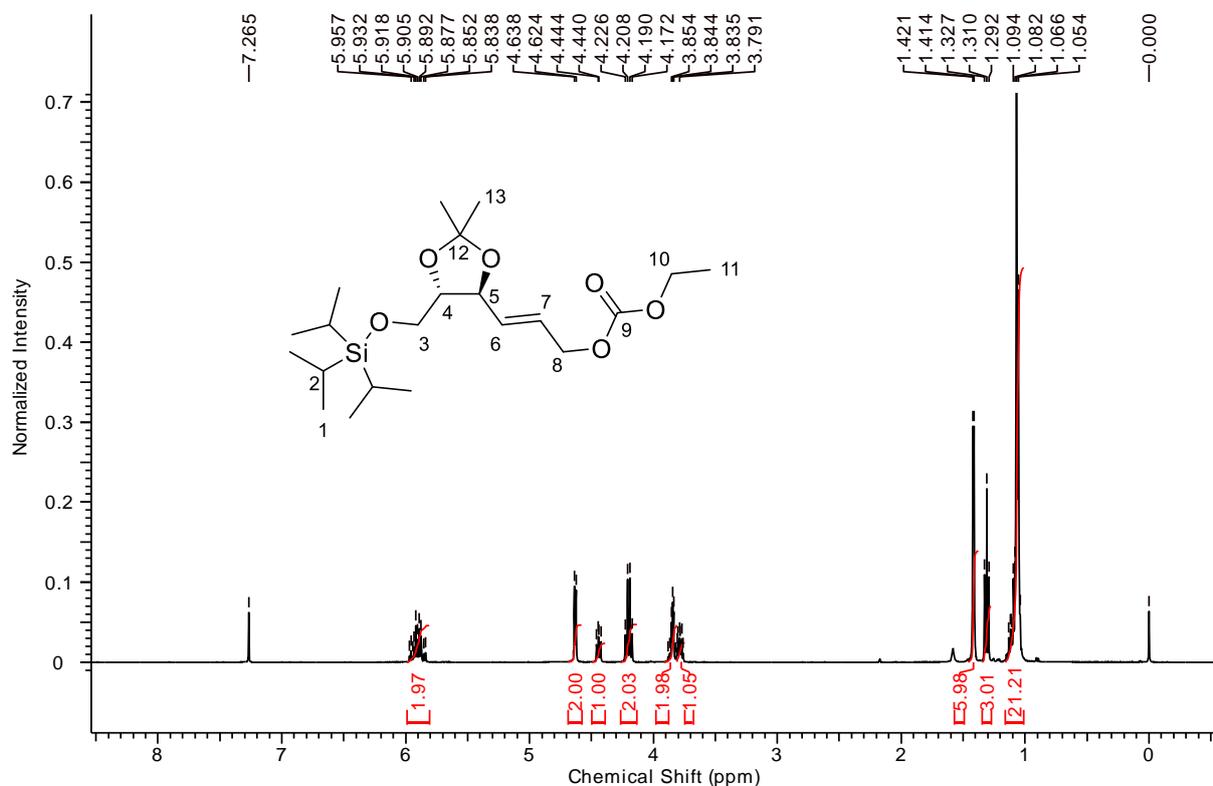
**Ethyl (E)-3-((4S,5S)-2,2-dimethyl-5-(((triisopropylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)acrylate (SI-19)**



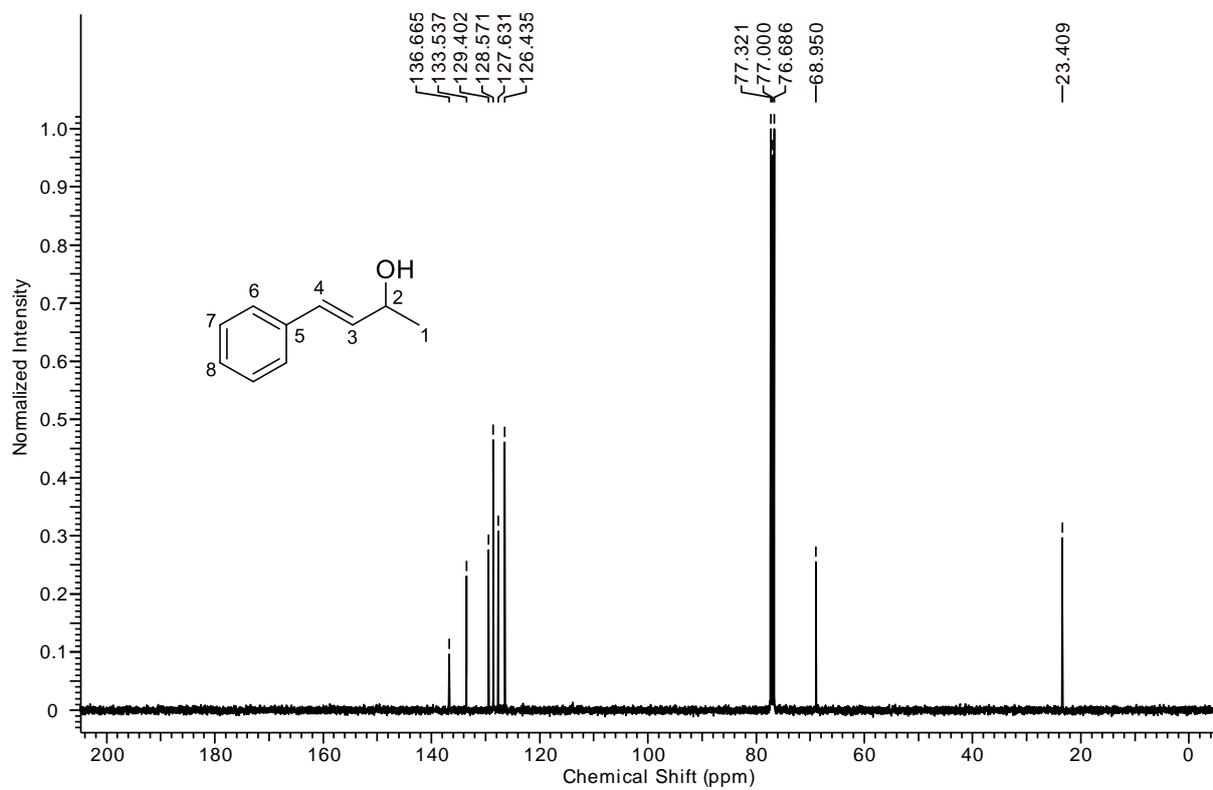
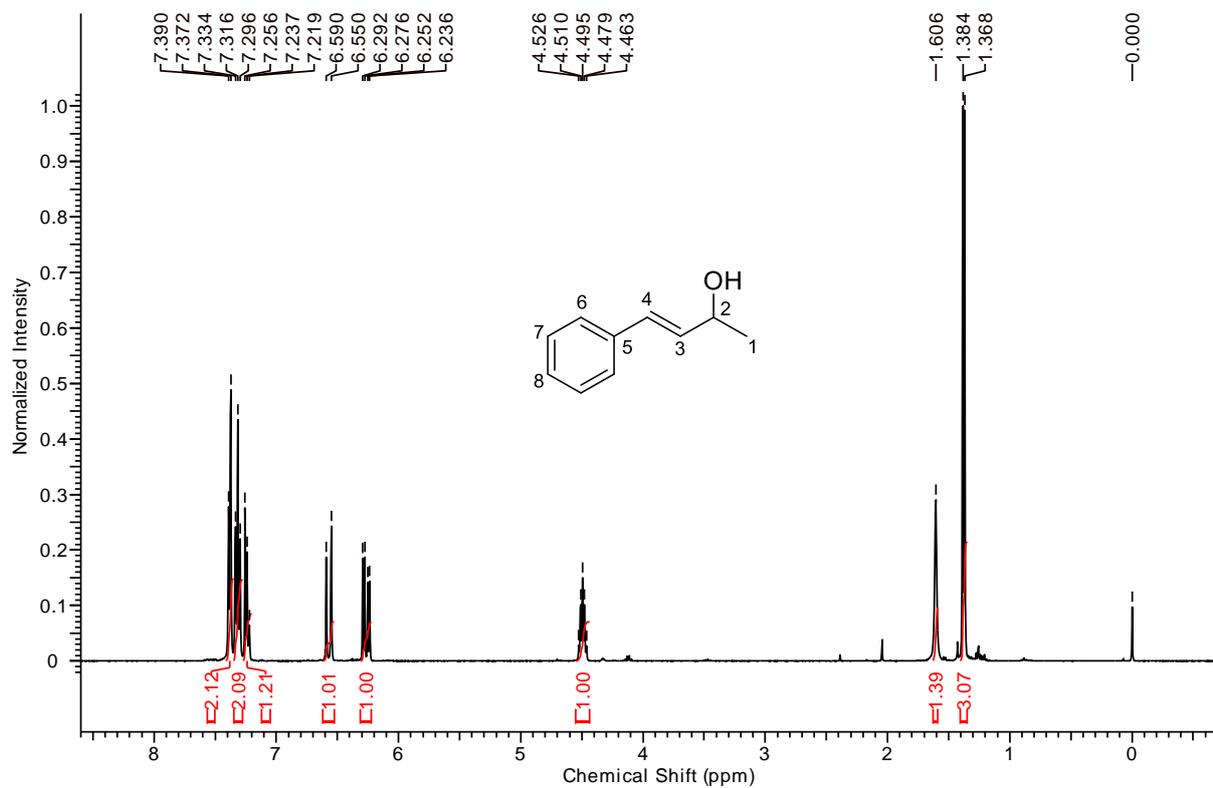
**(E)-3-((4*S*,5*S*)-2,2-Dimethyl-5-(((triisopropylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)prop-2-en-1-ol (SI-20)**



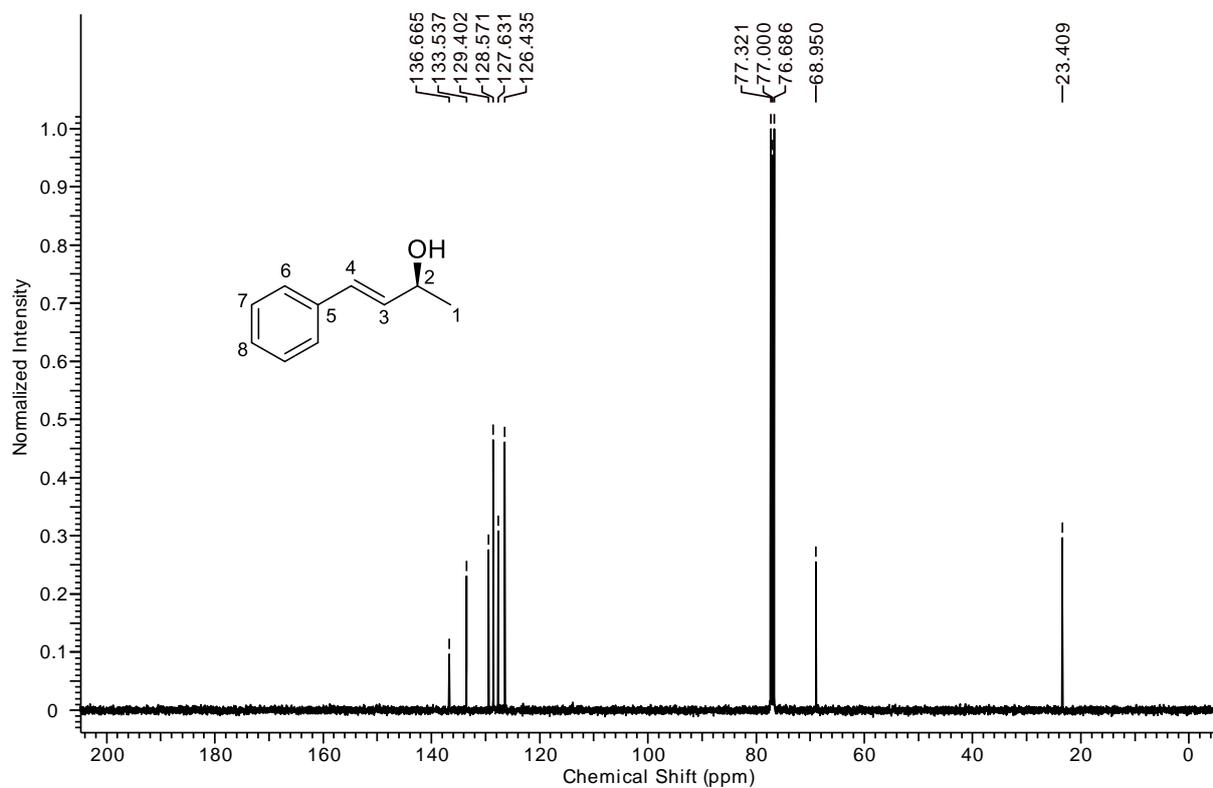
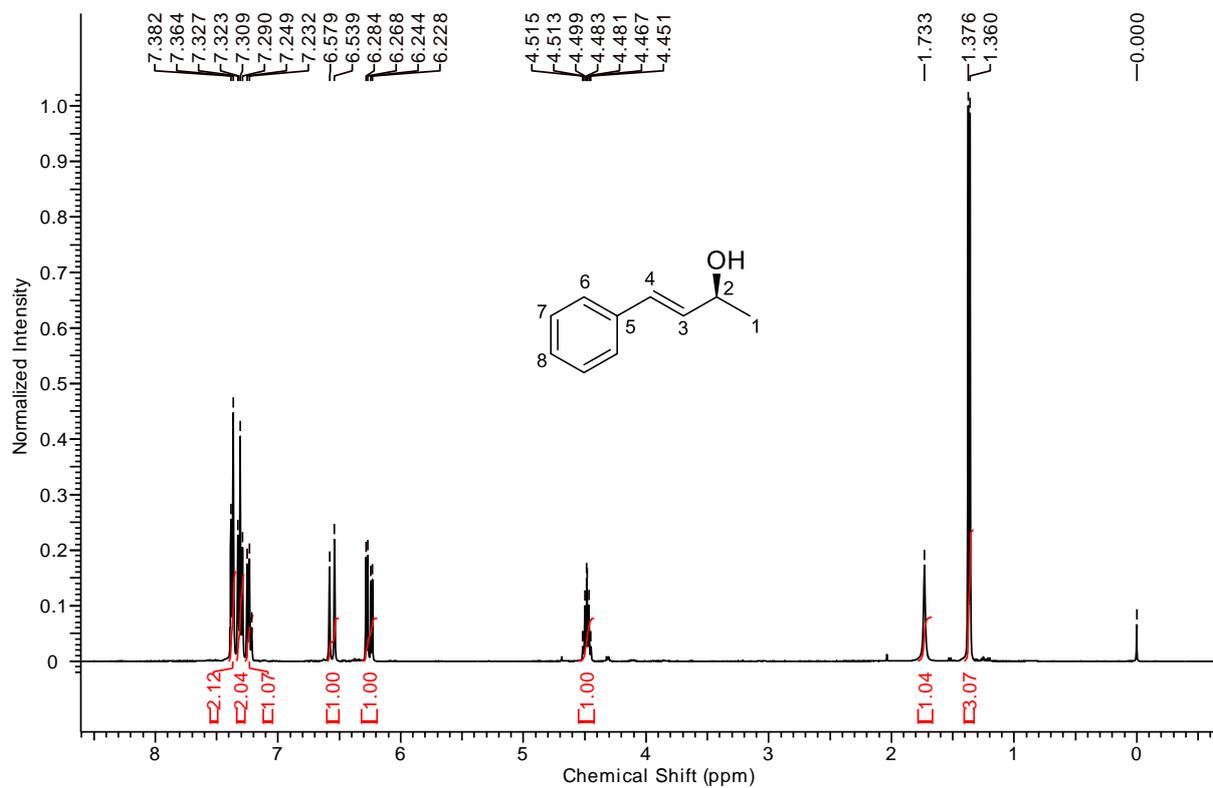
**(E)-3-((4*S*,5*S*)-2,2-Dimethyl-5-(((triisopropylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)allyl ethyl carbonate (SI-21)**



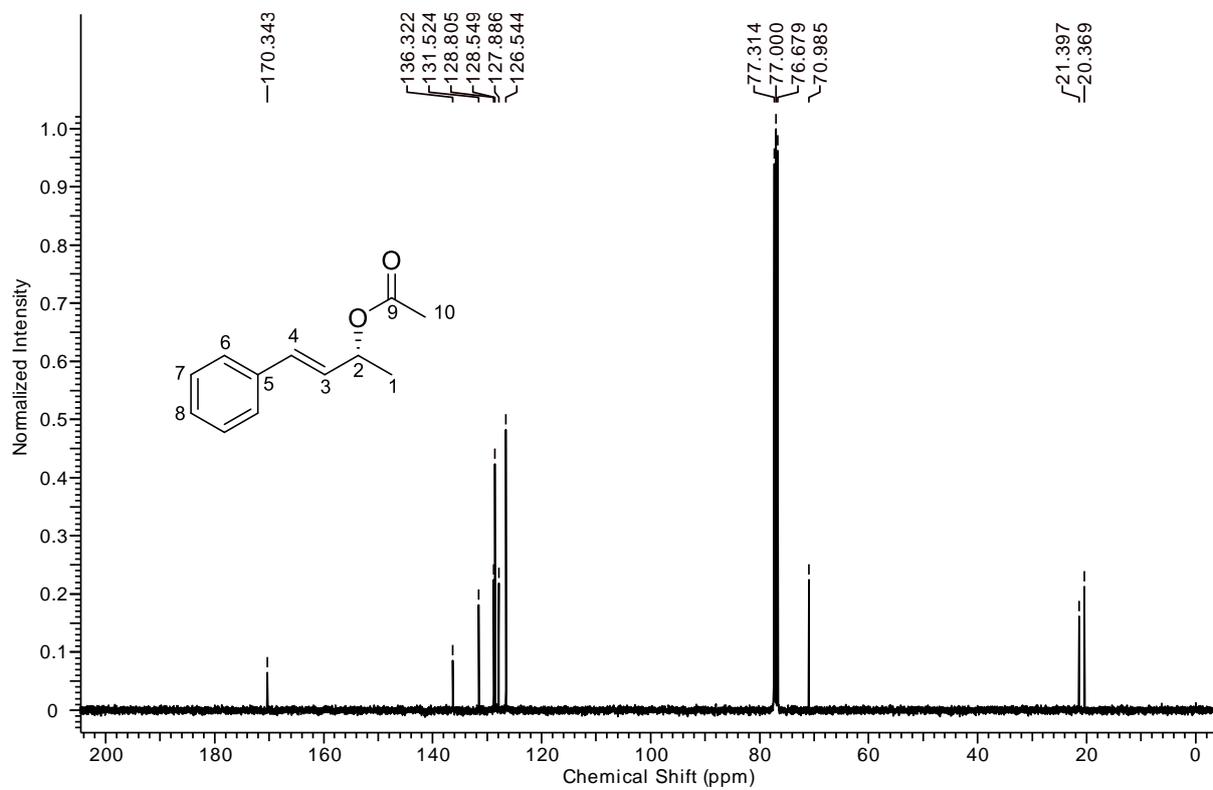
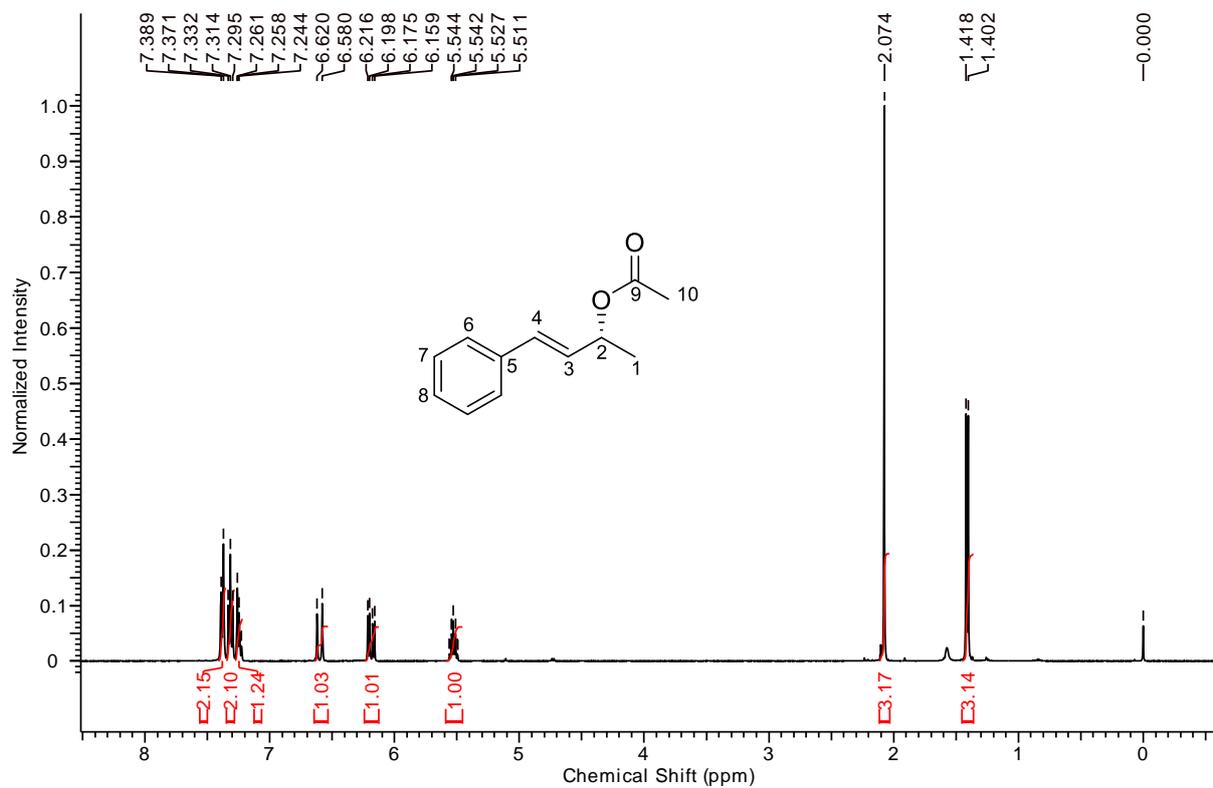
**(E)-4-Phenylbut-3-en-2-ol (SI-22)**



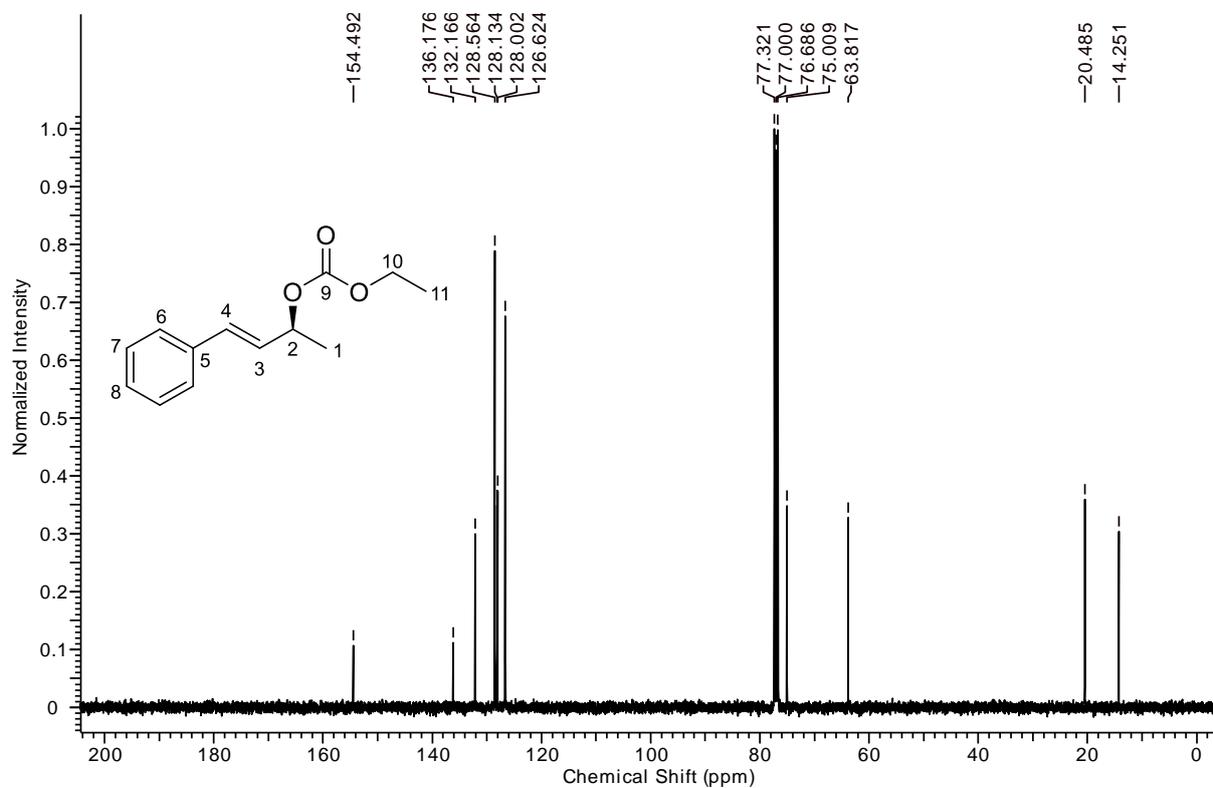
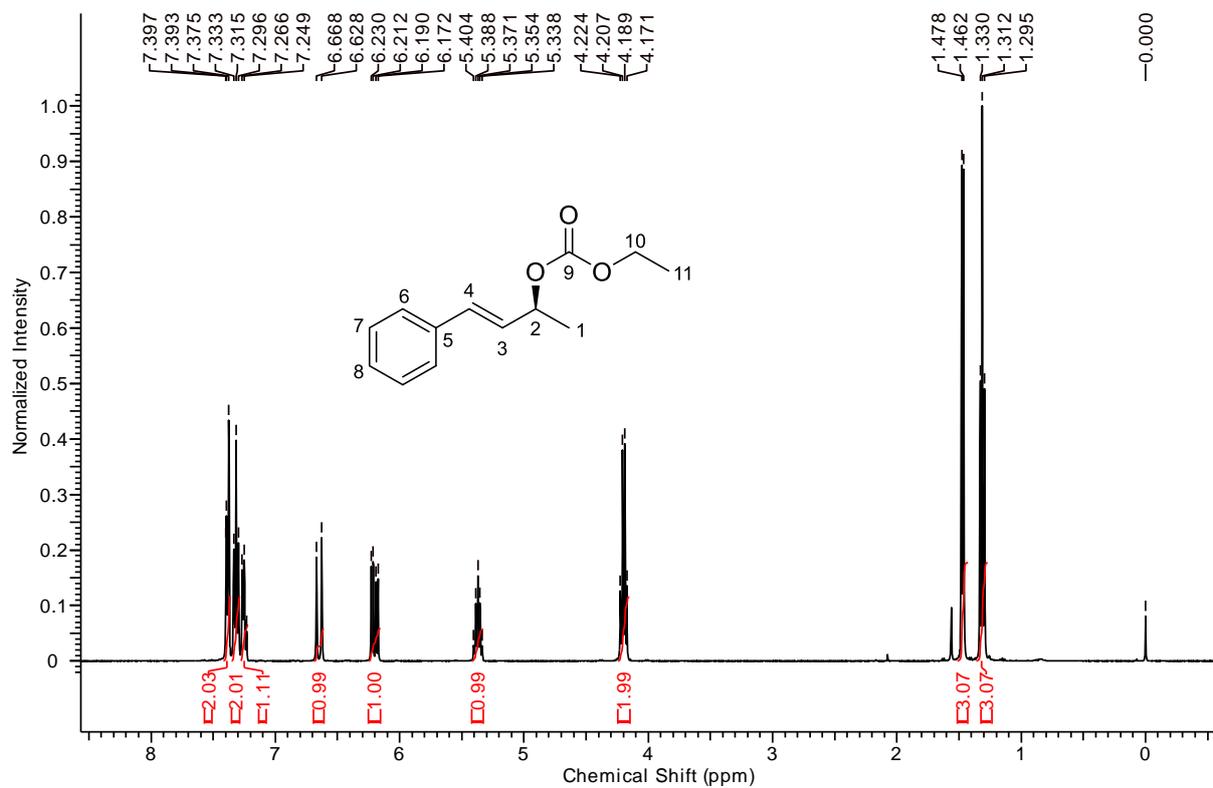
**(S,E)-4-Phenylbut-3-en-2-ol (SI-23)**



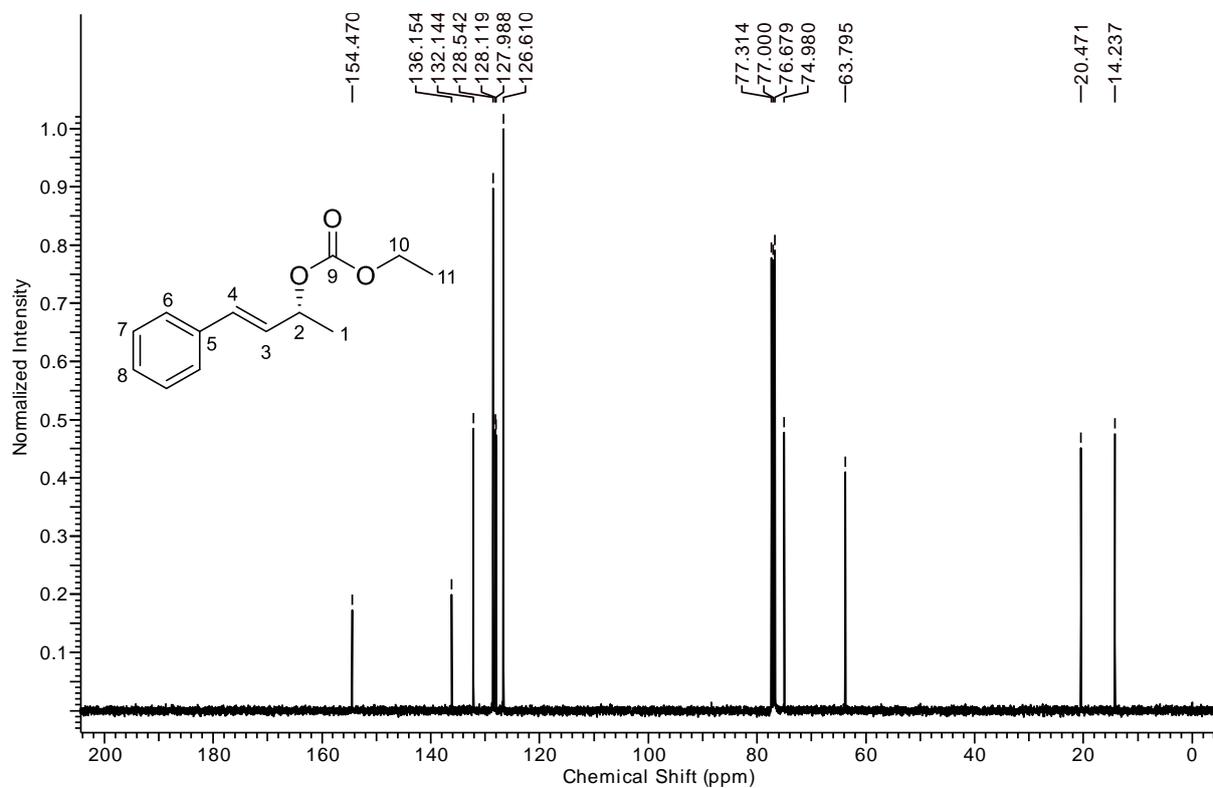
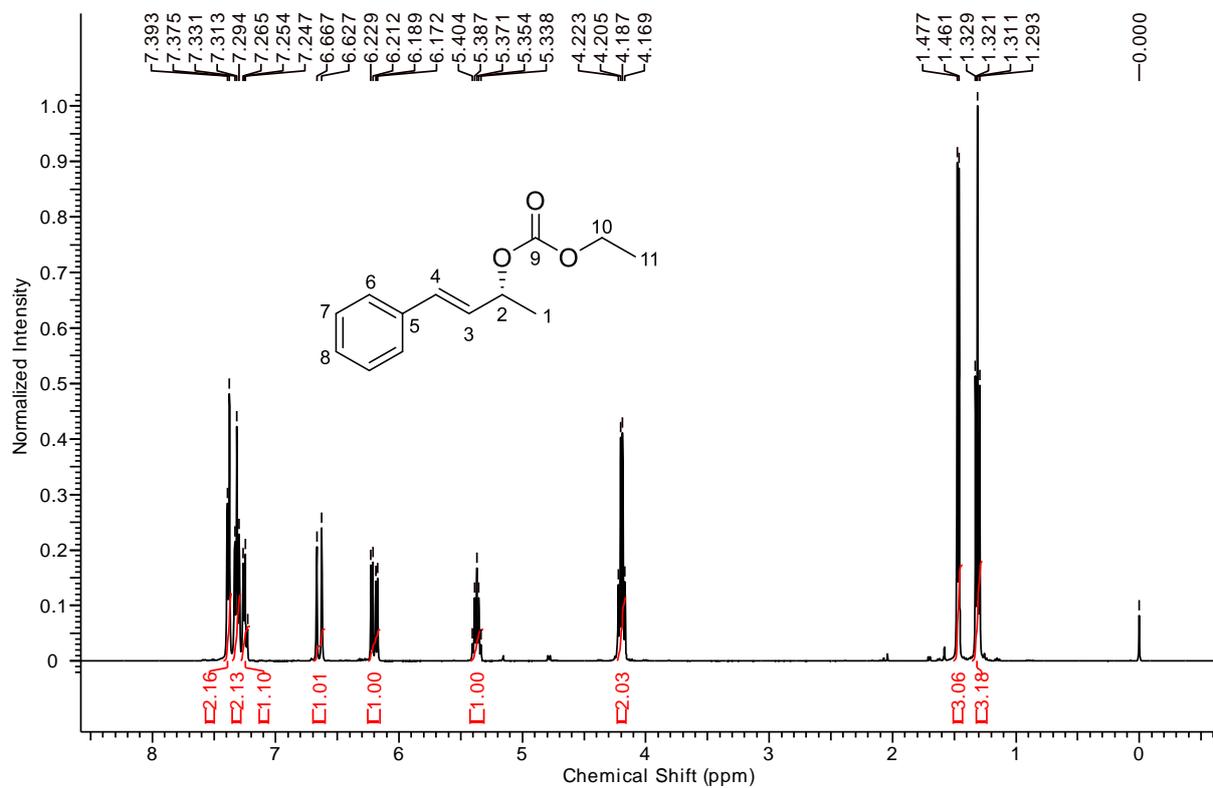
**(*R,E*)-4-phenylbut-3-en-2-yl acetate (SI-24)**



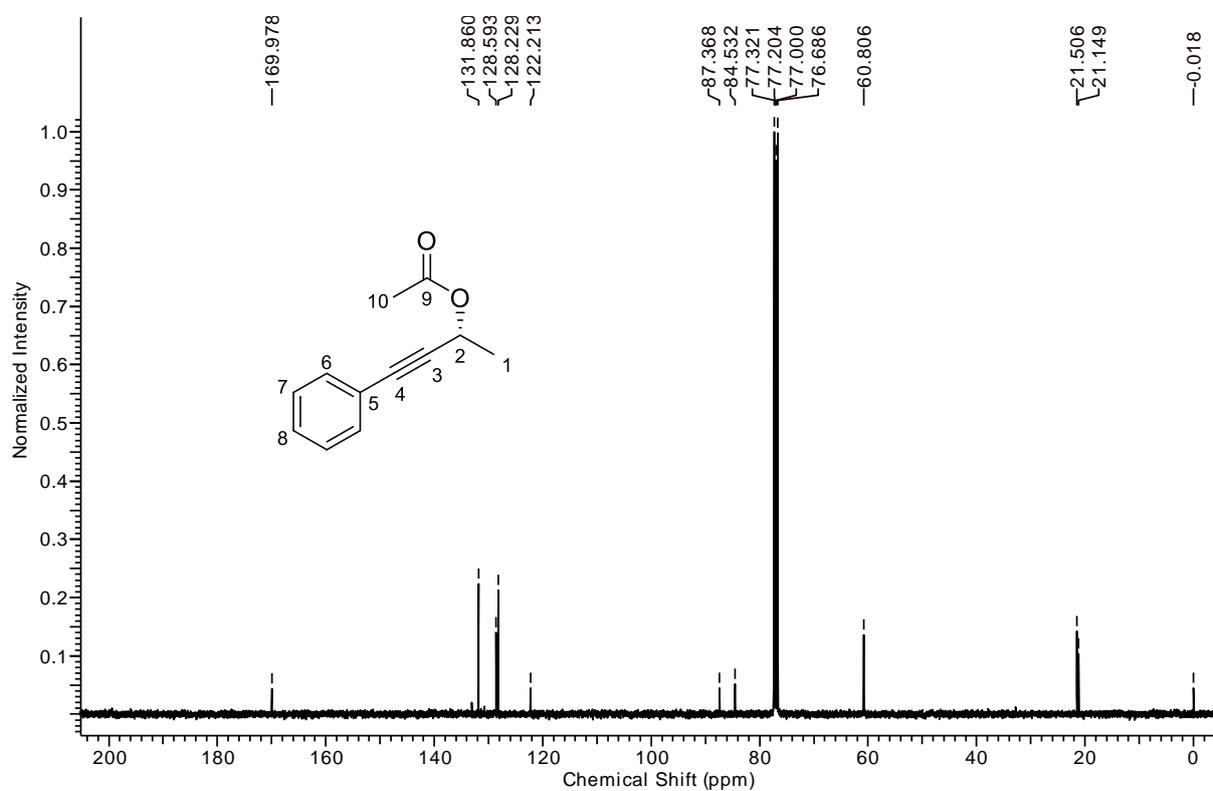
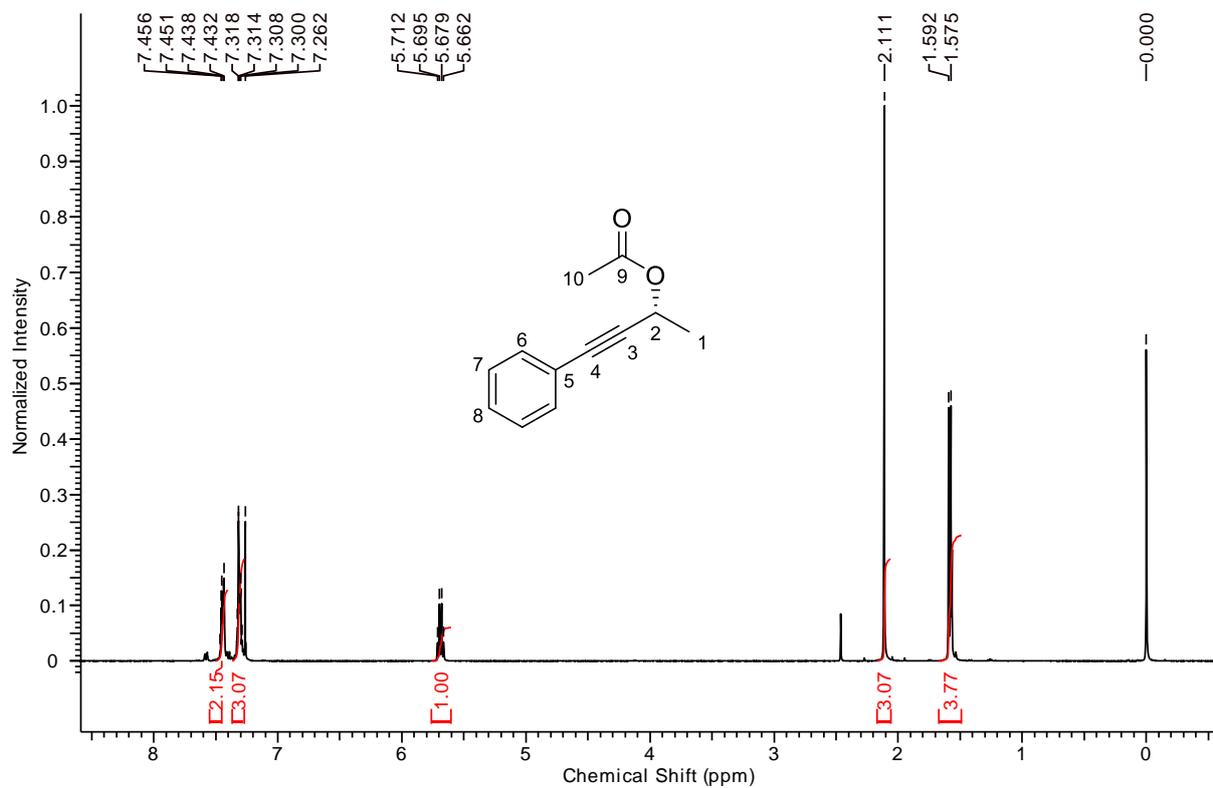
**(2*S*,3*E*)-4-Phenylbut-3-en-2-ethylcarbonate (SI-(*S*)-25)**



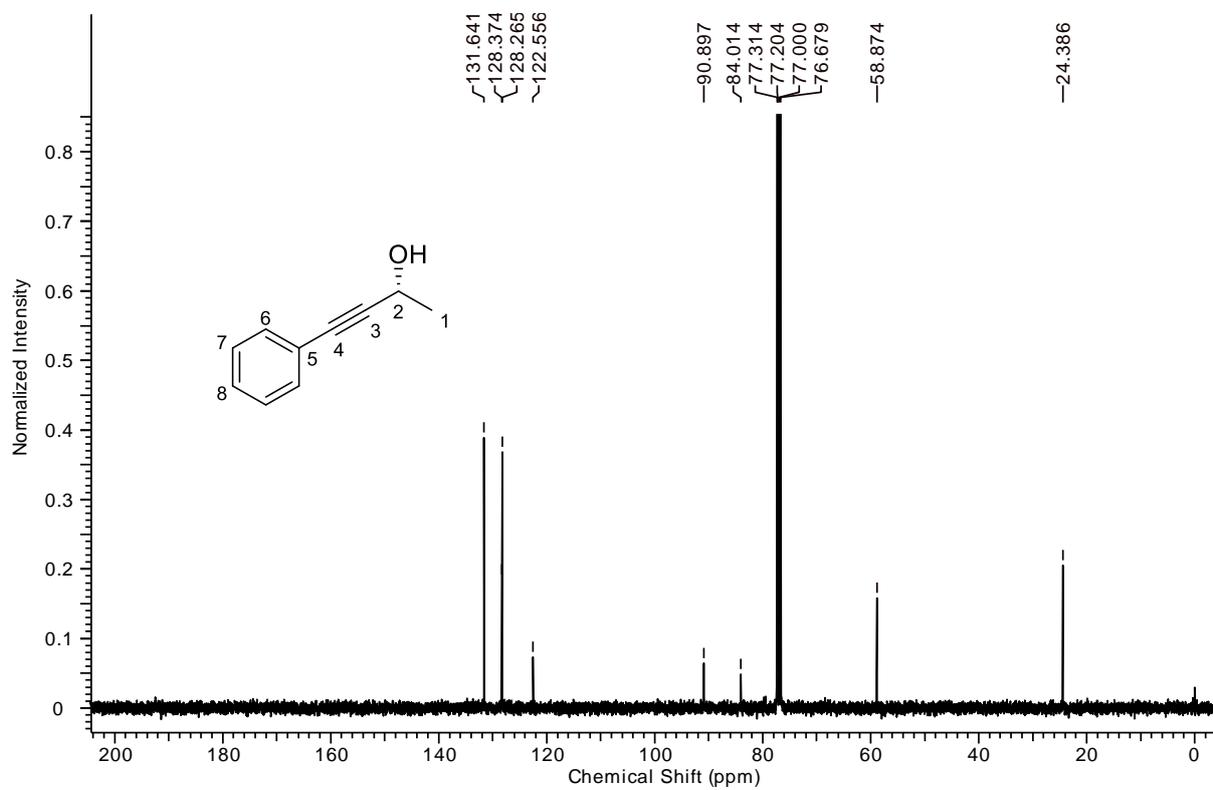
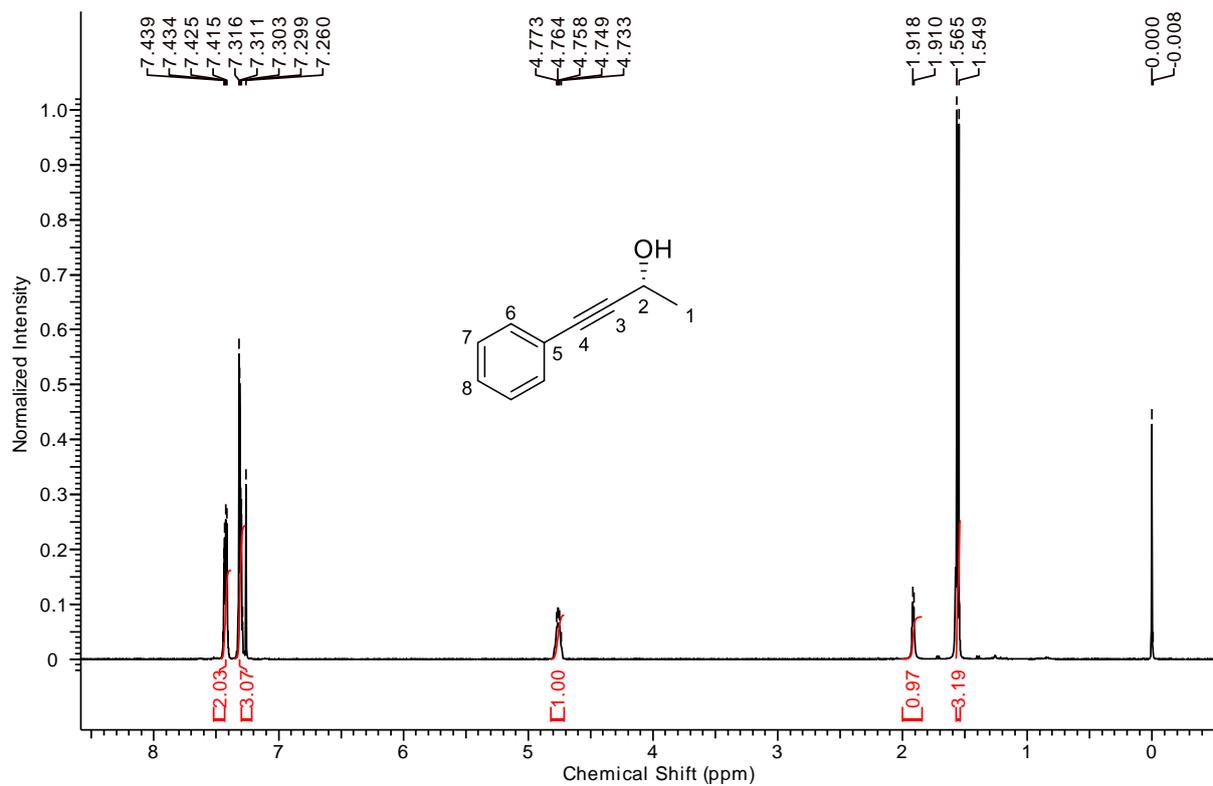
**(2*R*,3*E*)-4-Phenylbut-3-en-2-ethylcarbonate (SI-(*R*)-25)**



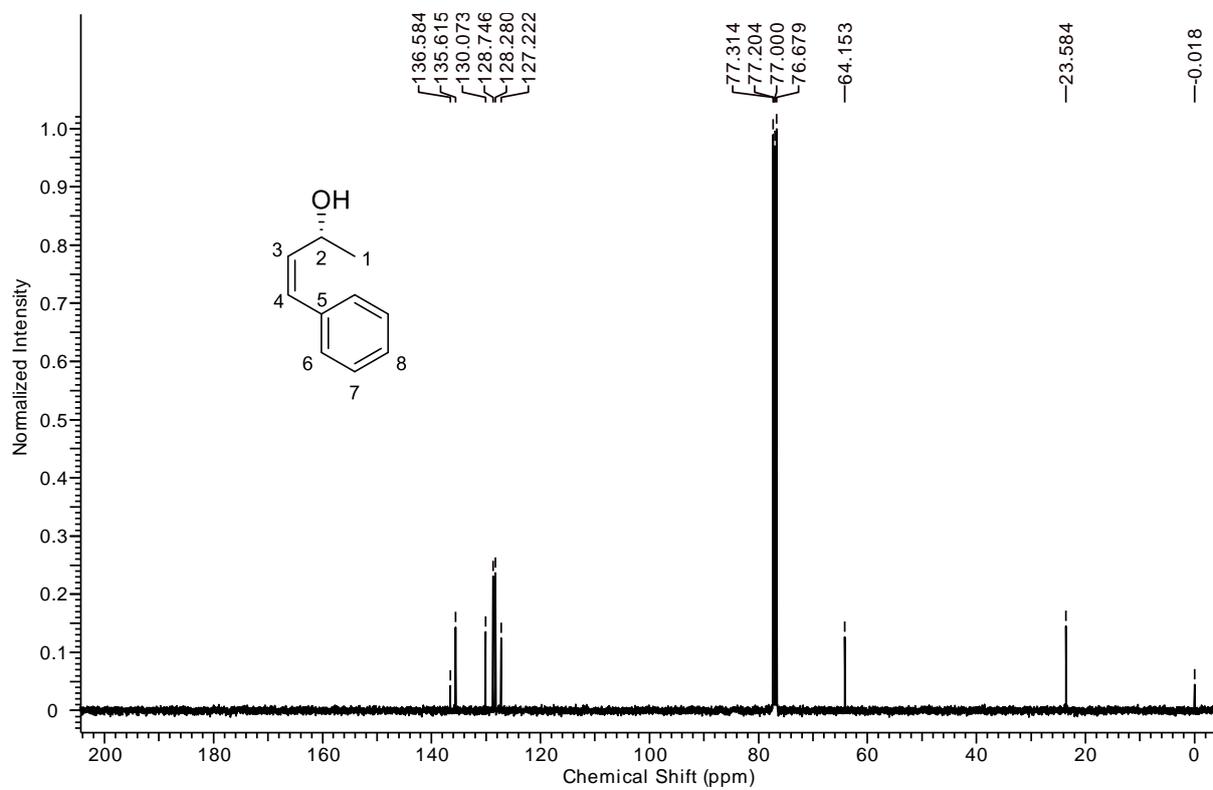
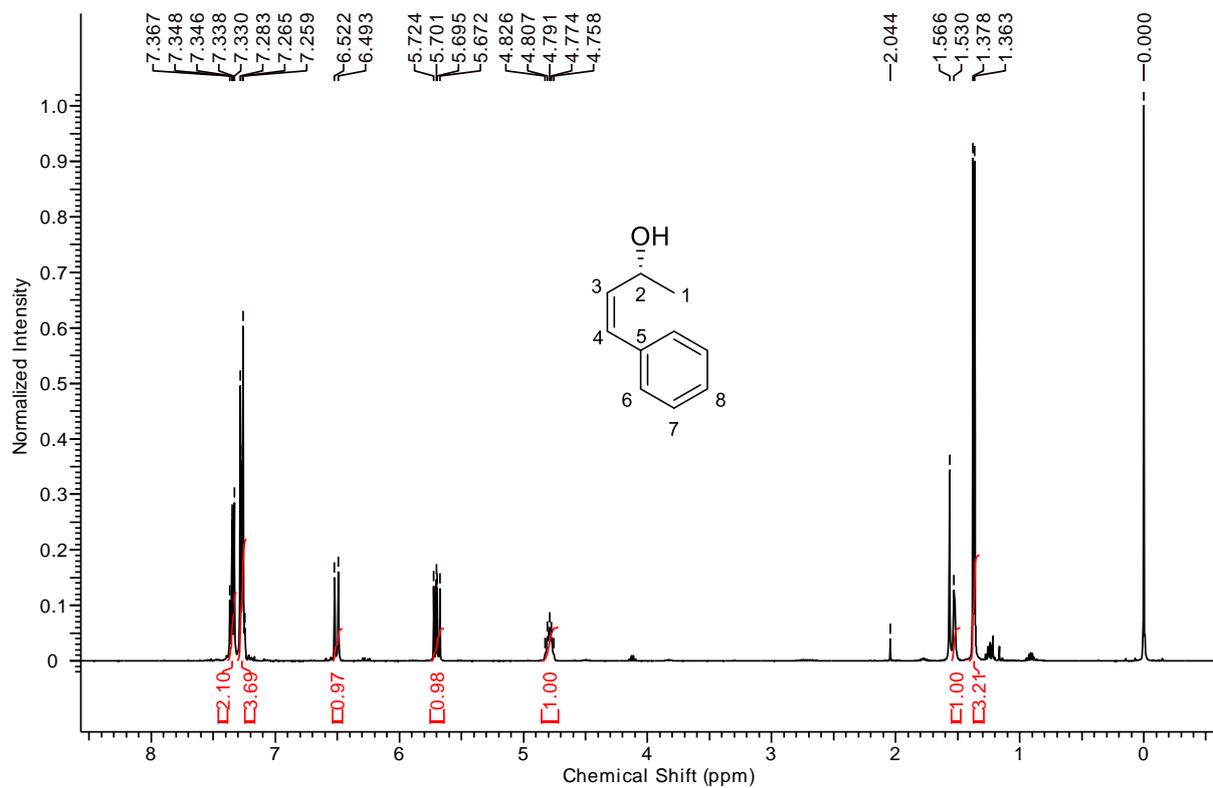
### (R)-4-Phenylbut-3-yn-2-yl acetate (SI-26)



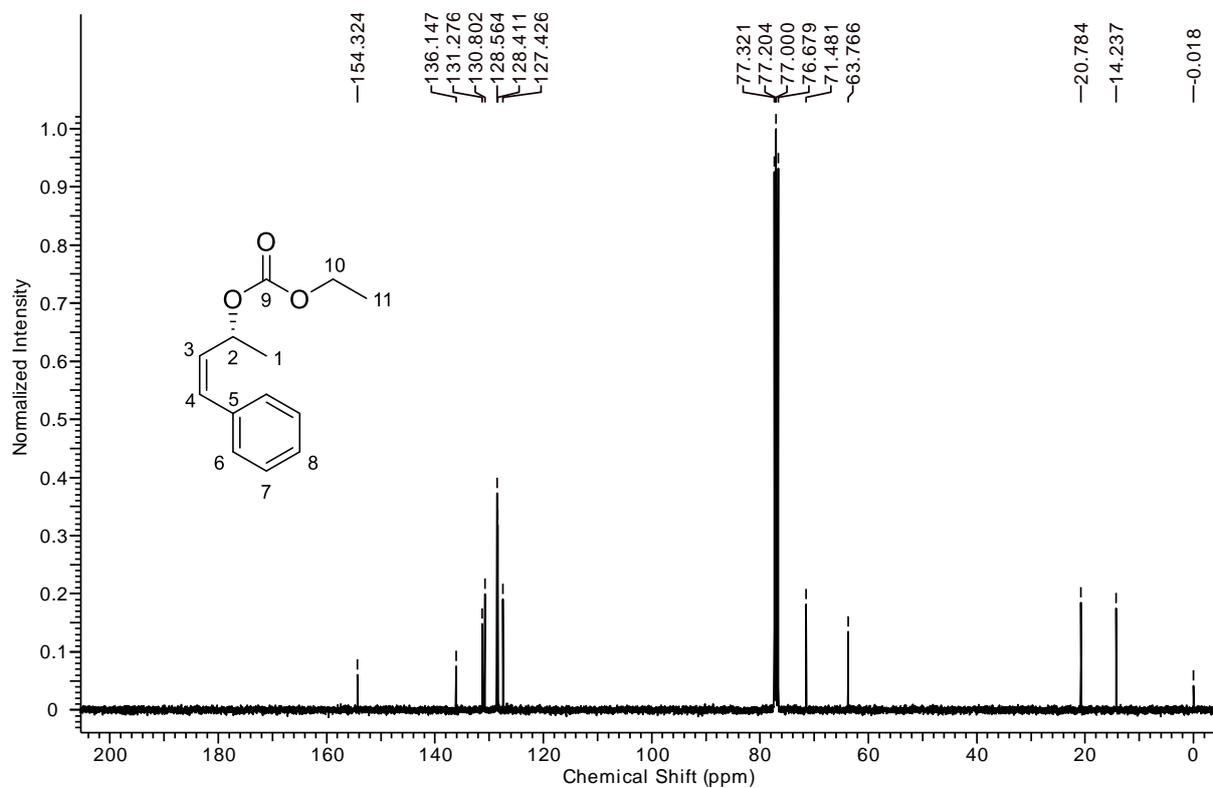
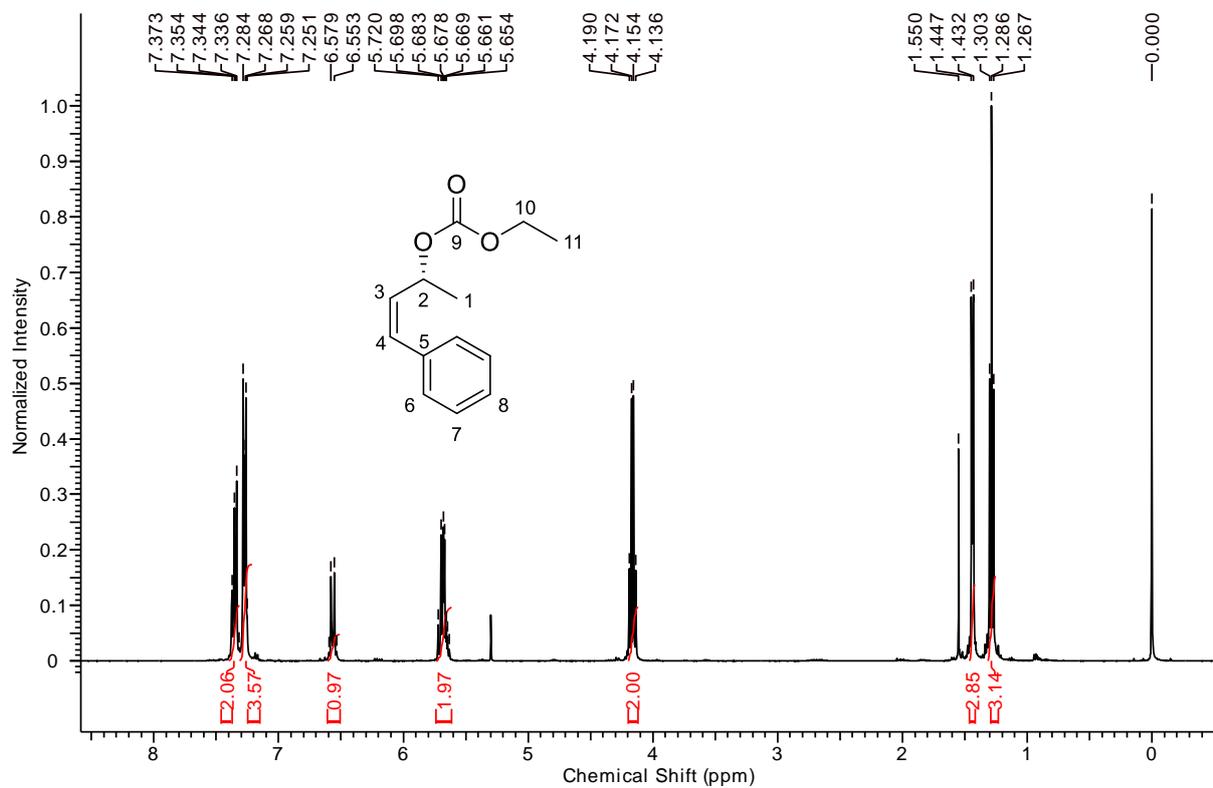
**(R)-4-Phenylbut-3-yn-2-ol (SI-(R)-27)**



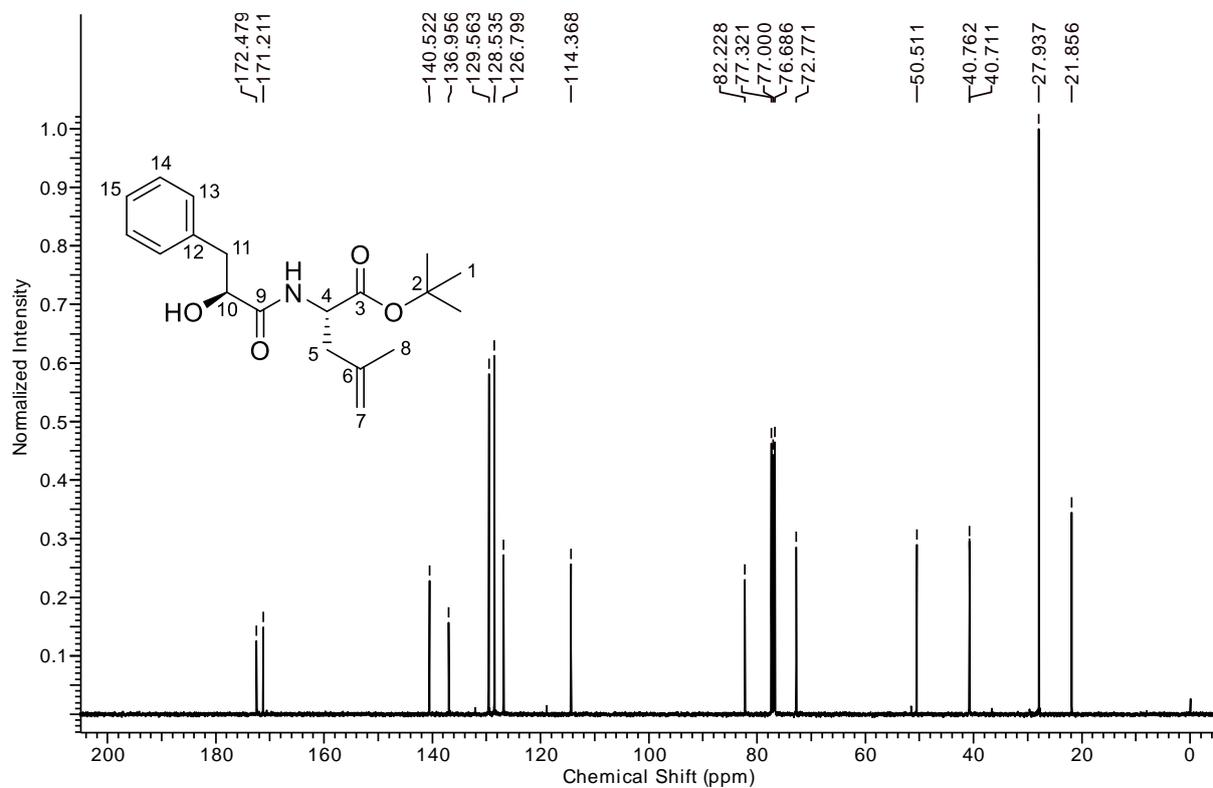
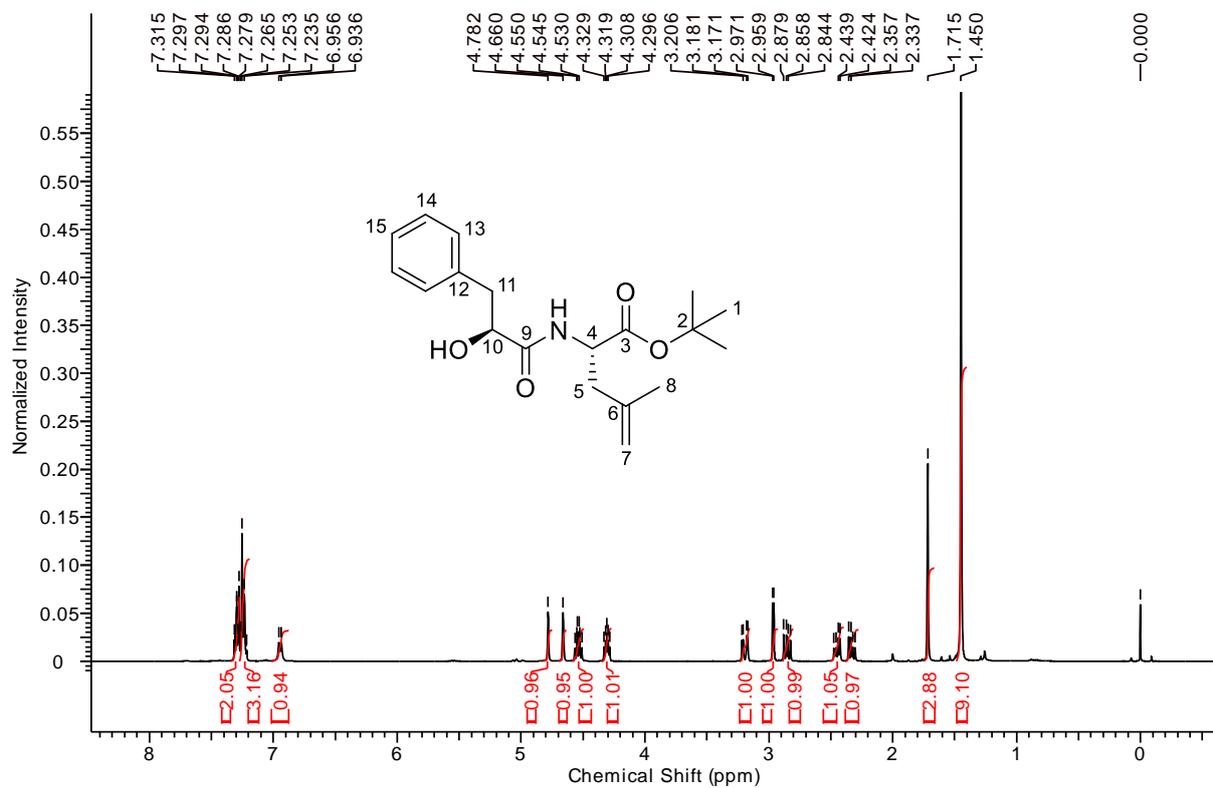
**(R,Z)-4-Phenylbut-3-en-2-ol (SI-28)**



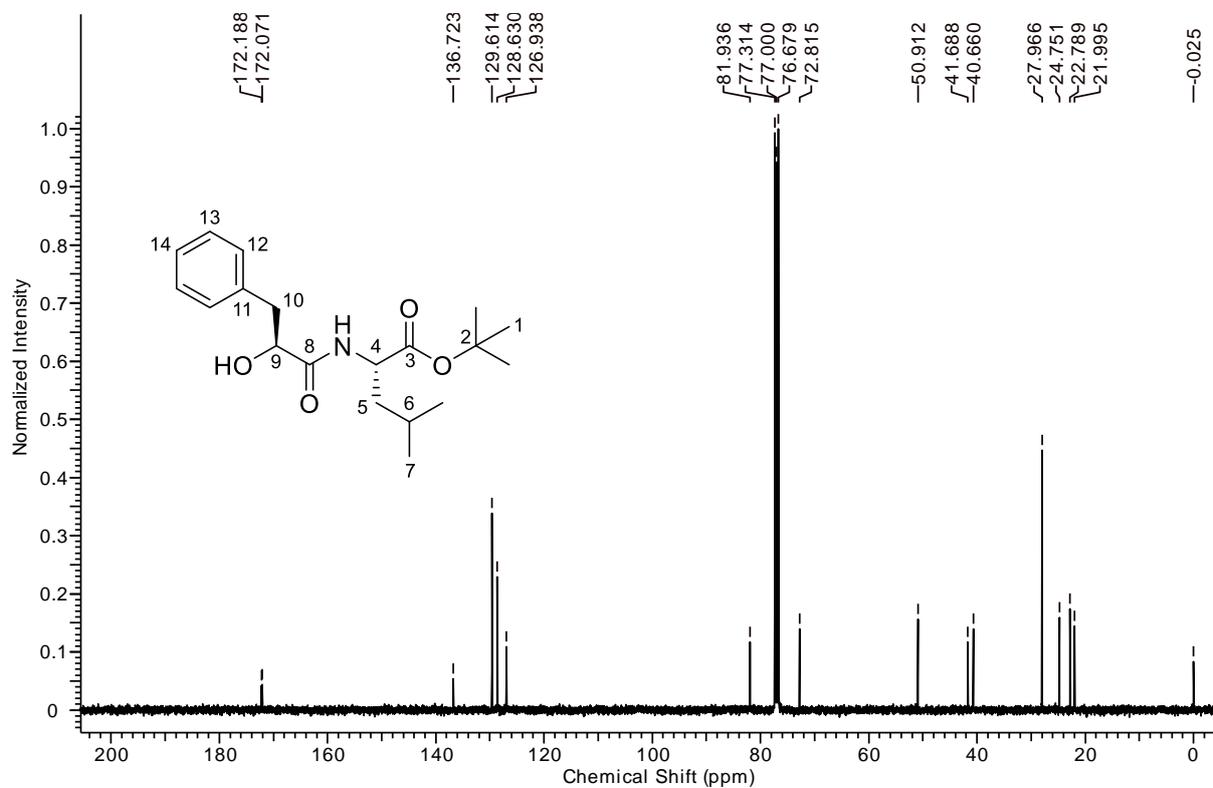
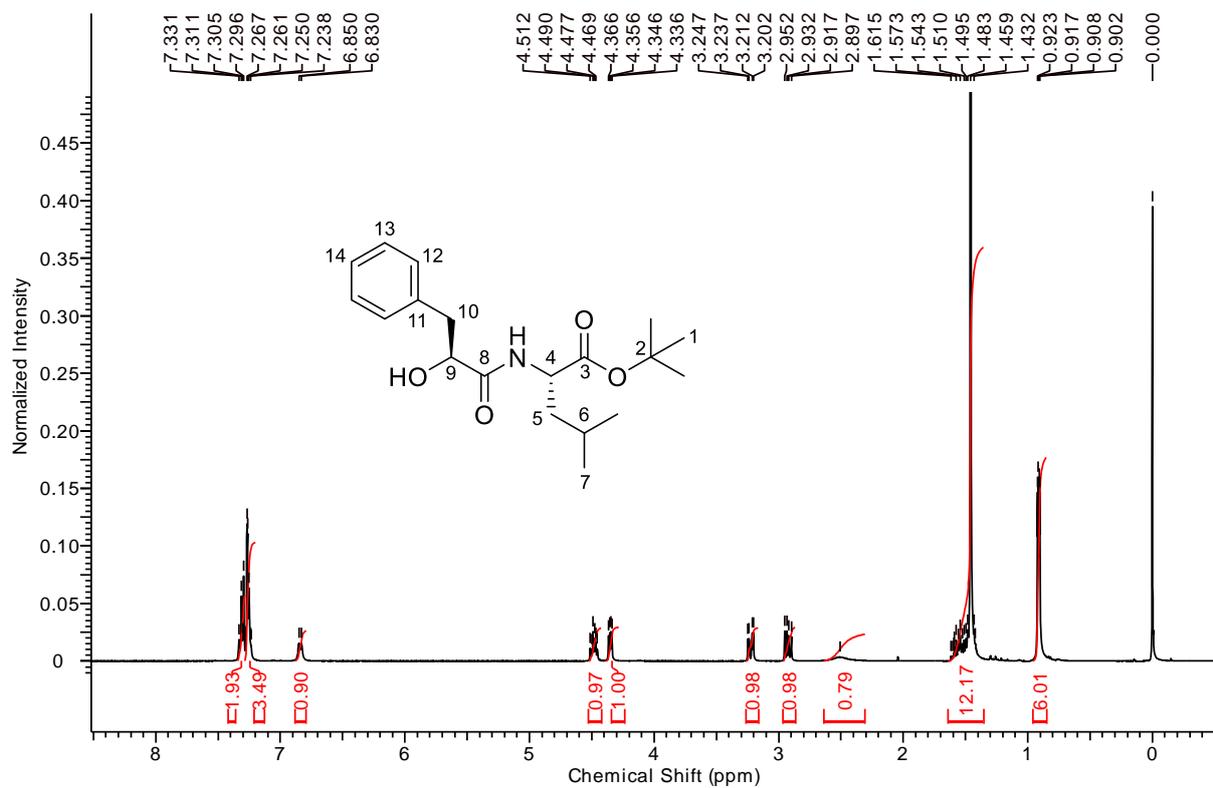
**(R,Z)-Ethyl (4-phenylbut-3-en-2-yl) carbonate (SI-29)**



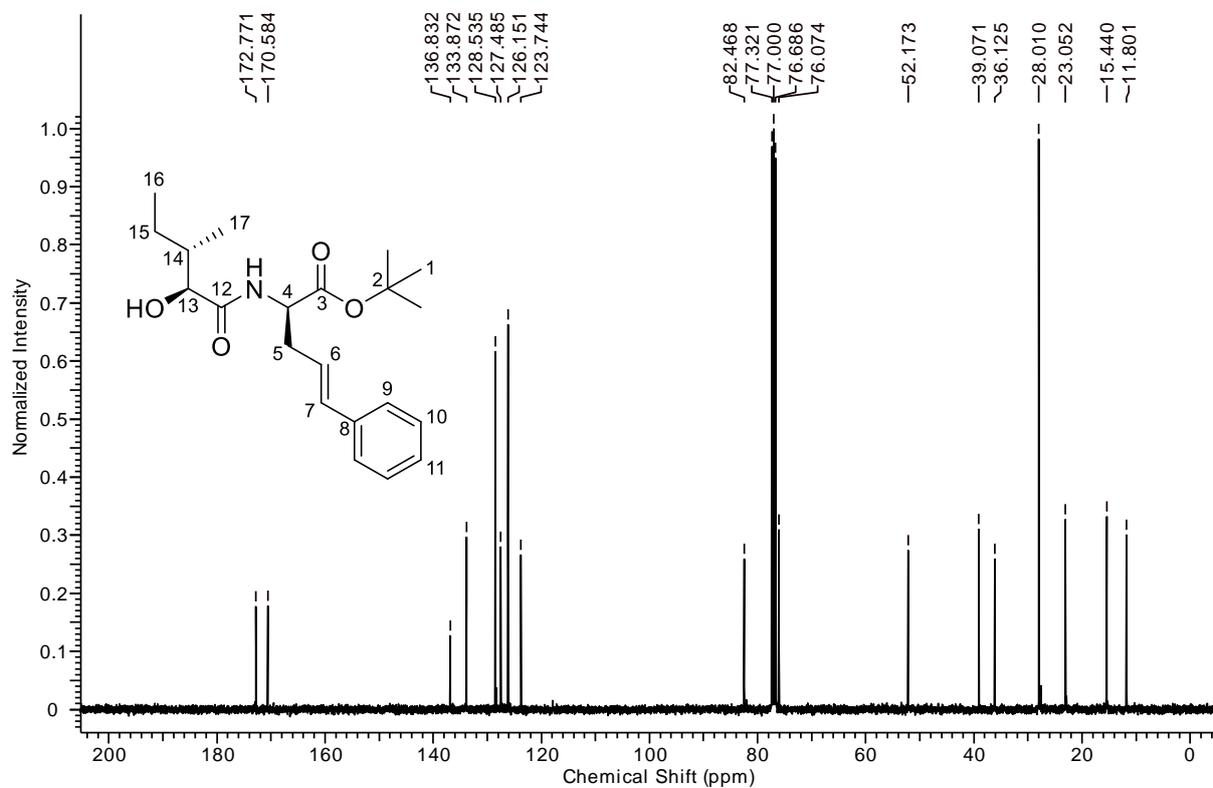
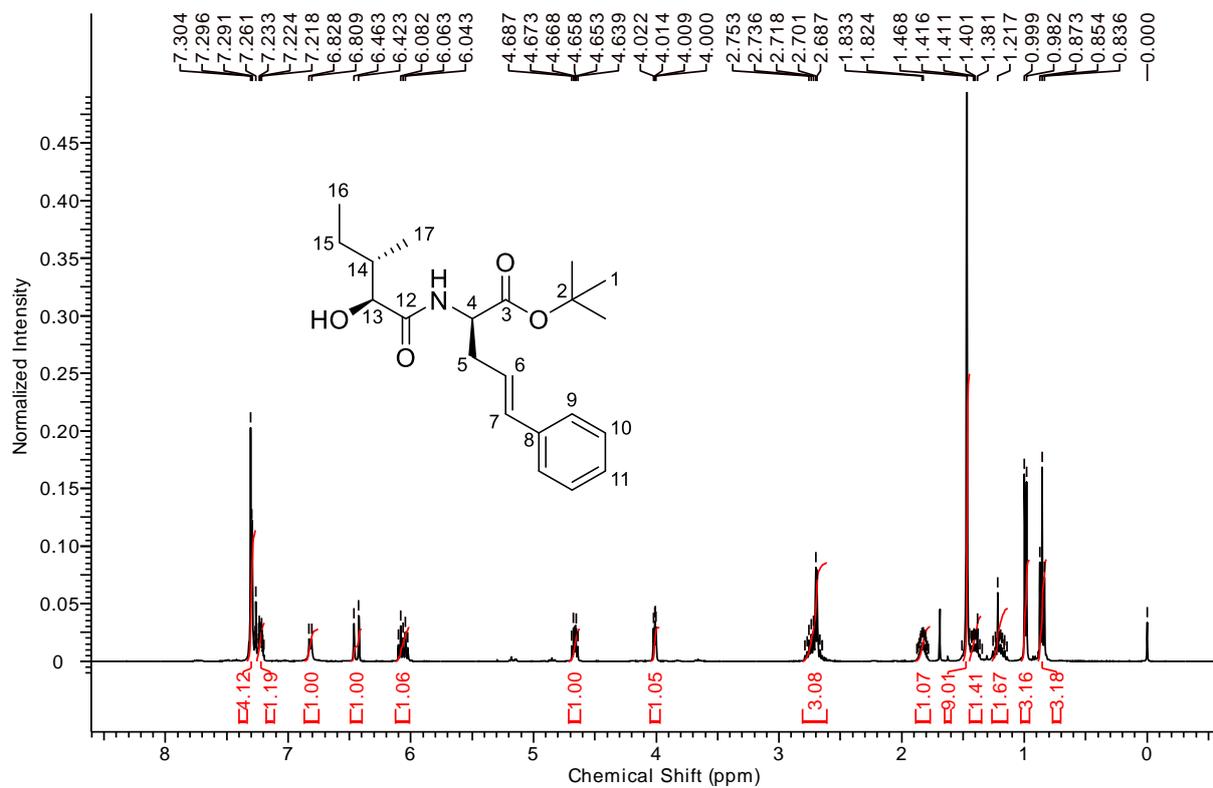
***tert*-Butyl (*S*)-2-((*S*)-2-hydroxy-3-phenylpropanamido)-4-methylpent-4-enoate (SI-30)**



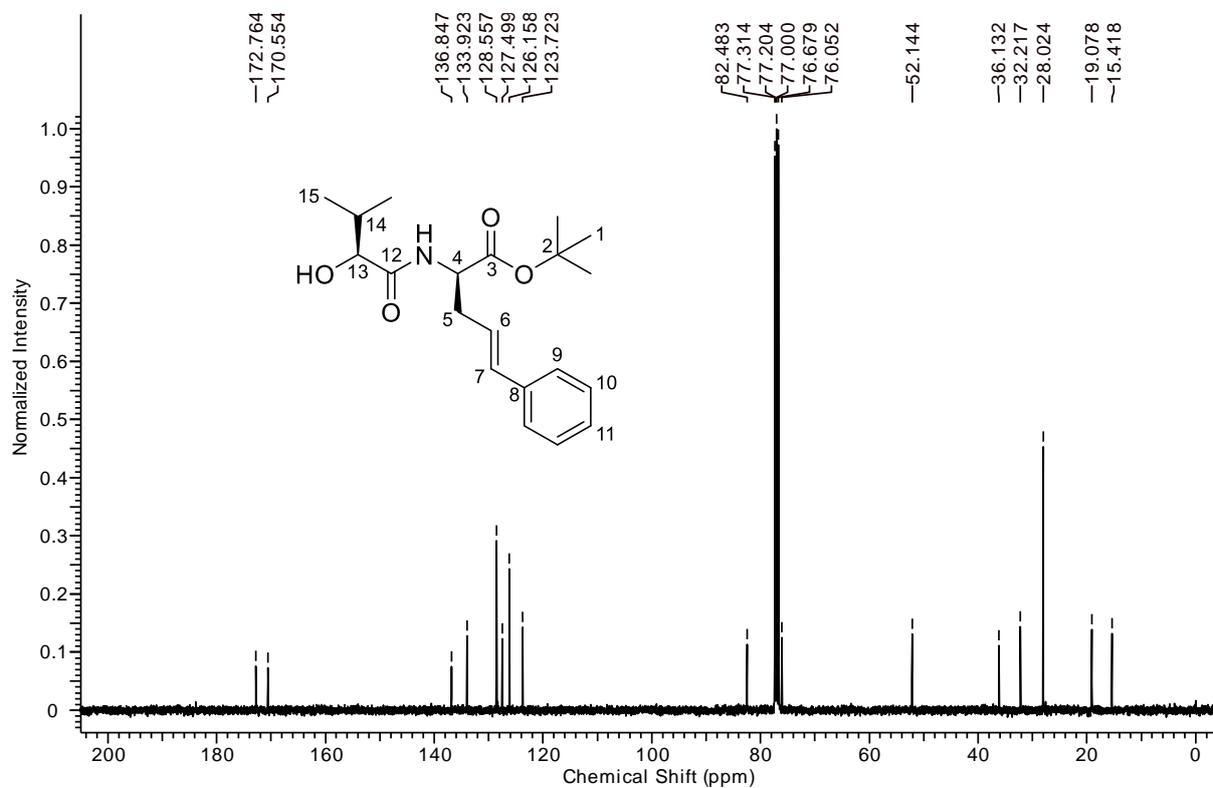
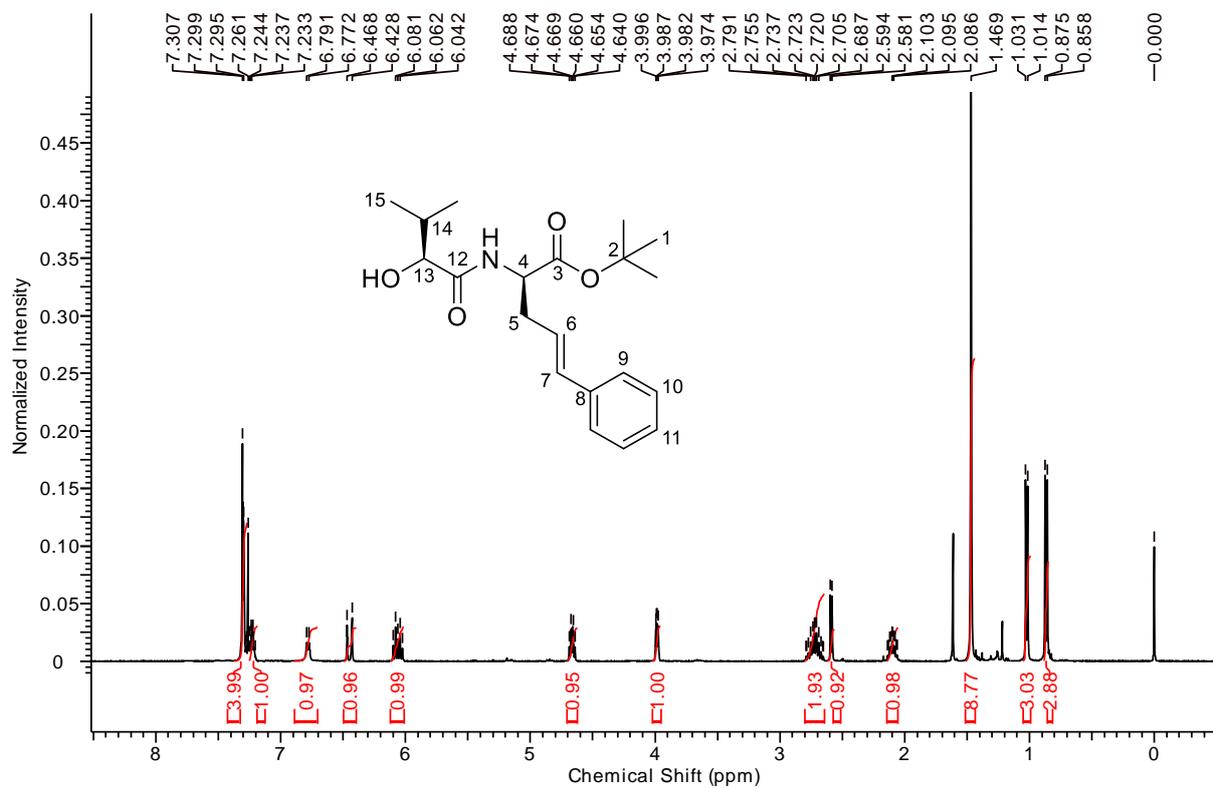
***tert*-Butyl ((*S*)-2-hydroxy-3-phenylpropanoyl)-*L*-leucinate (SI-31)**



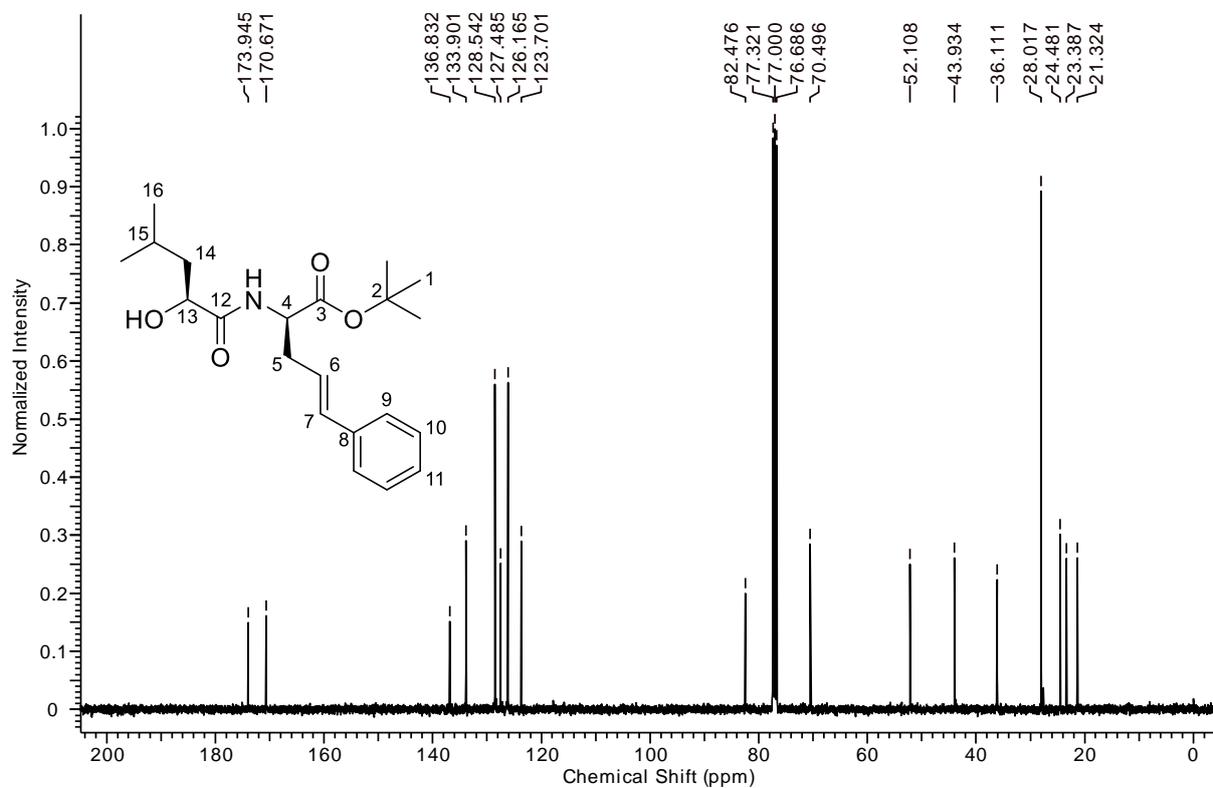
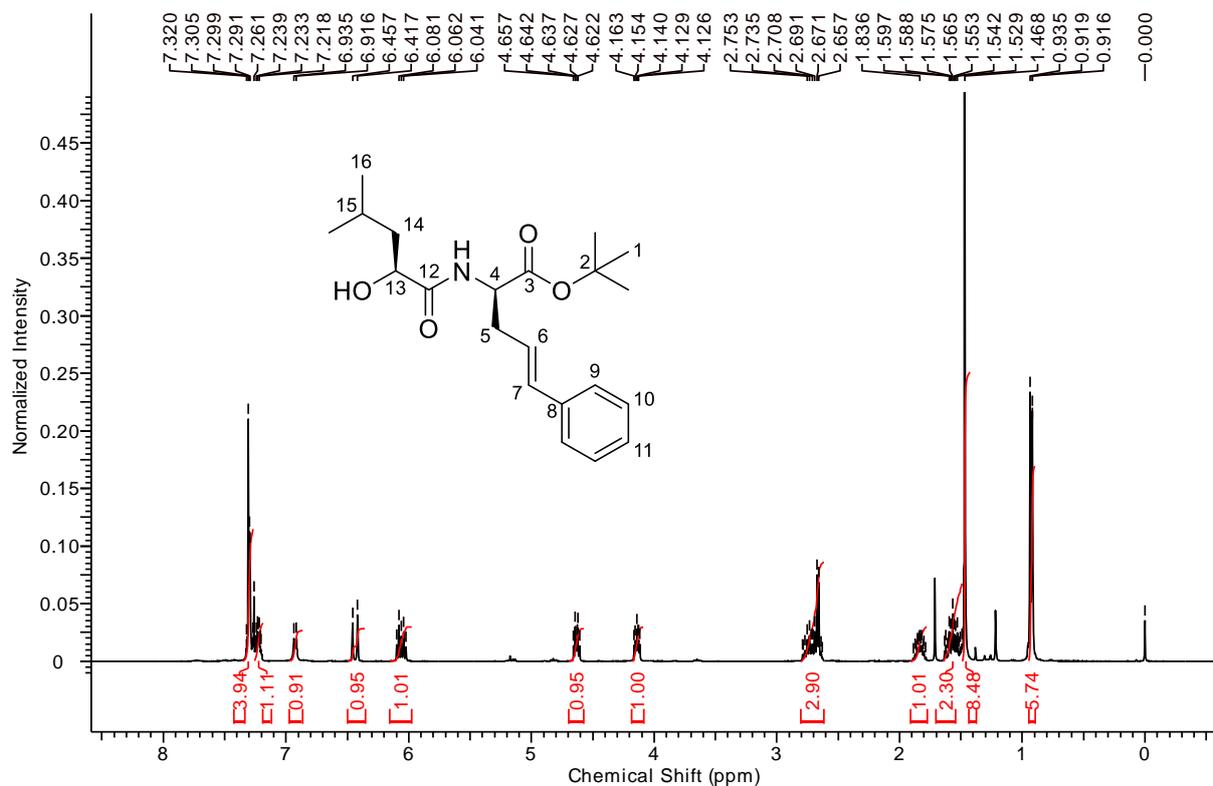
***tert*-Butyl (*R,E*)-2-((*2S,3S*)-2-hydroxy-3-methylpentanamido)-5-phenylpent-4-enoate (**2aa**)**



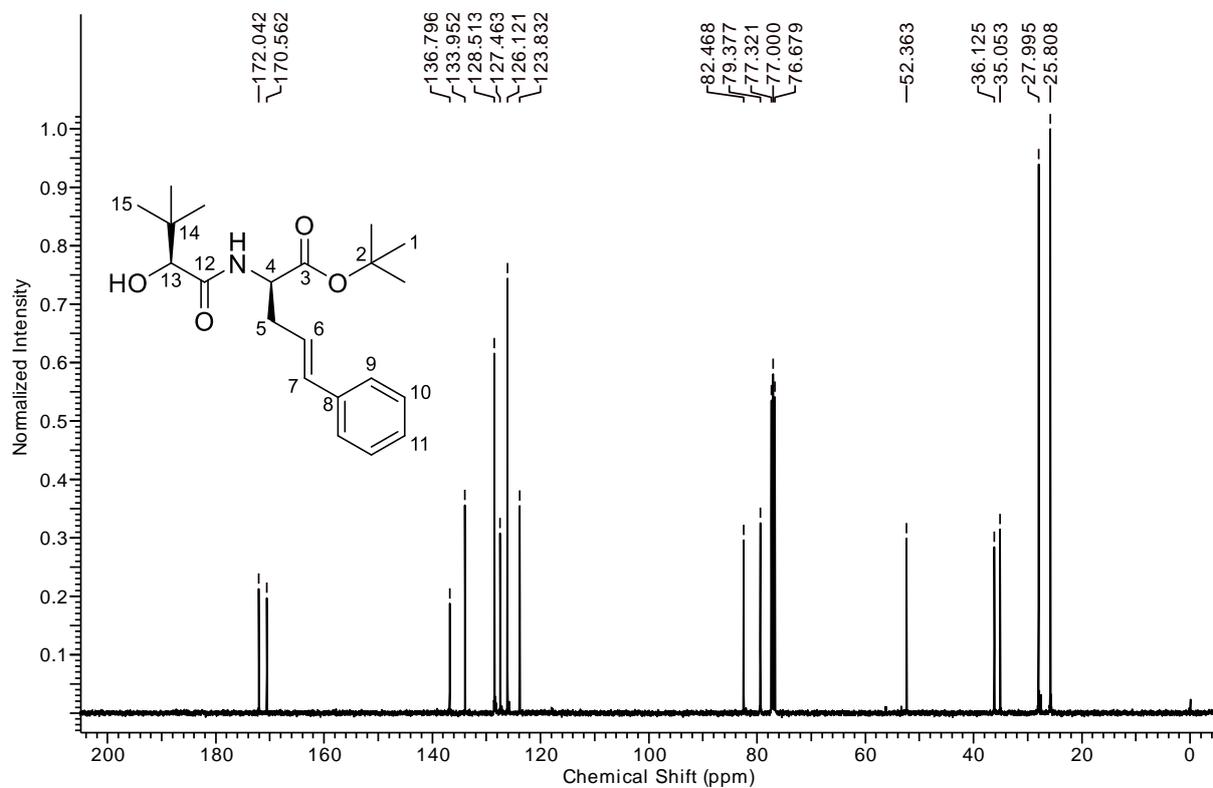
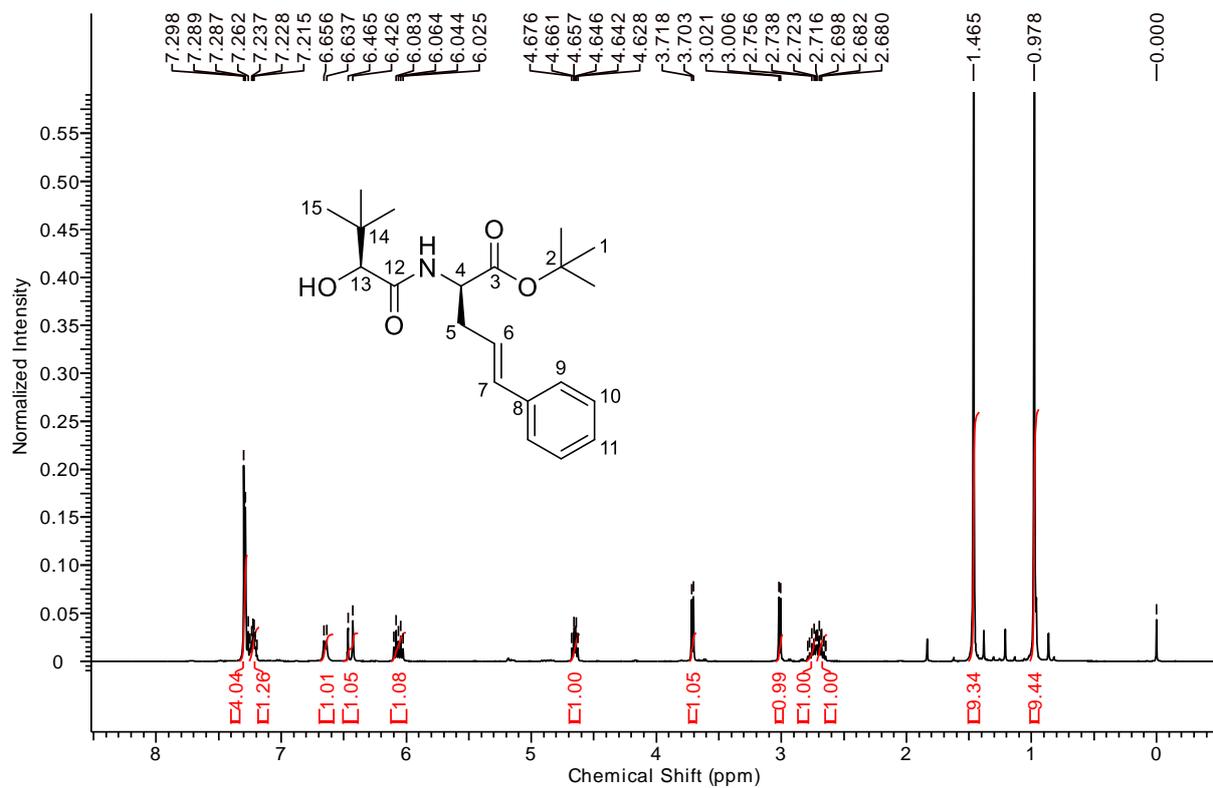
***tert*-Butyl (*R,E*)-2-((*S*)-2-hydroxy-3-methylbutanamido)-5-phenylpent-4-enoate (2ba)**



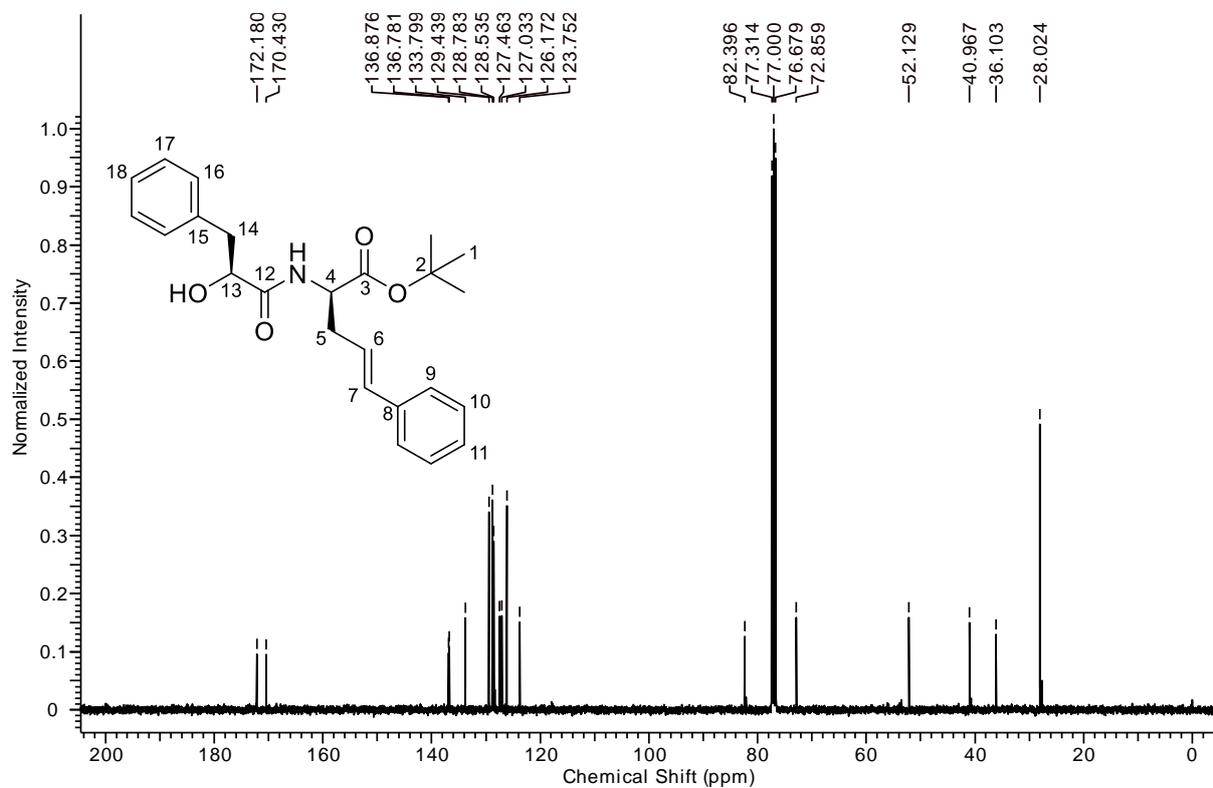
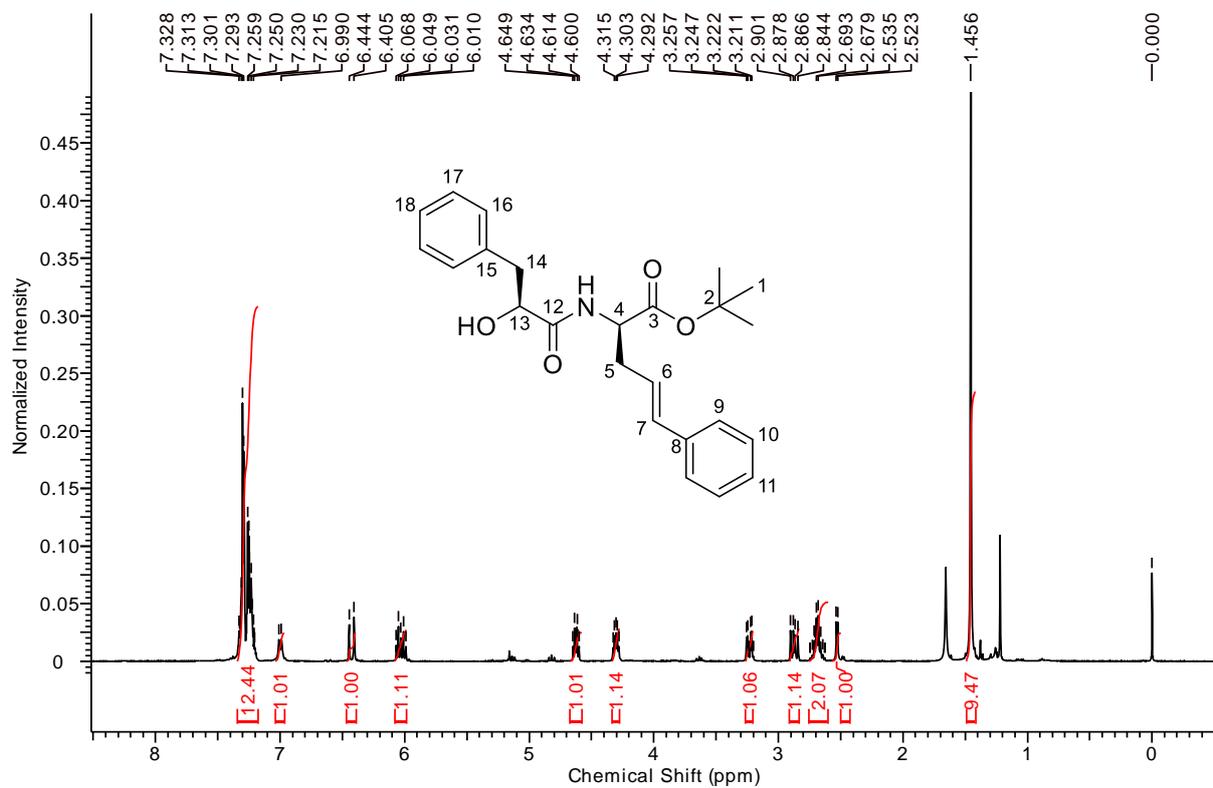
***tert*-Butyl (*R,E*)-2-((*S*)-2-hydroxy-4-methylpentanamido)-5-phenylpent-4-enoate (**2ca**)**



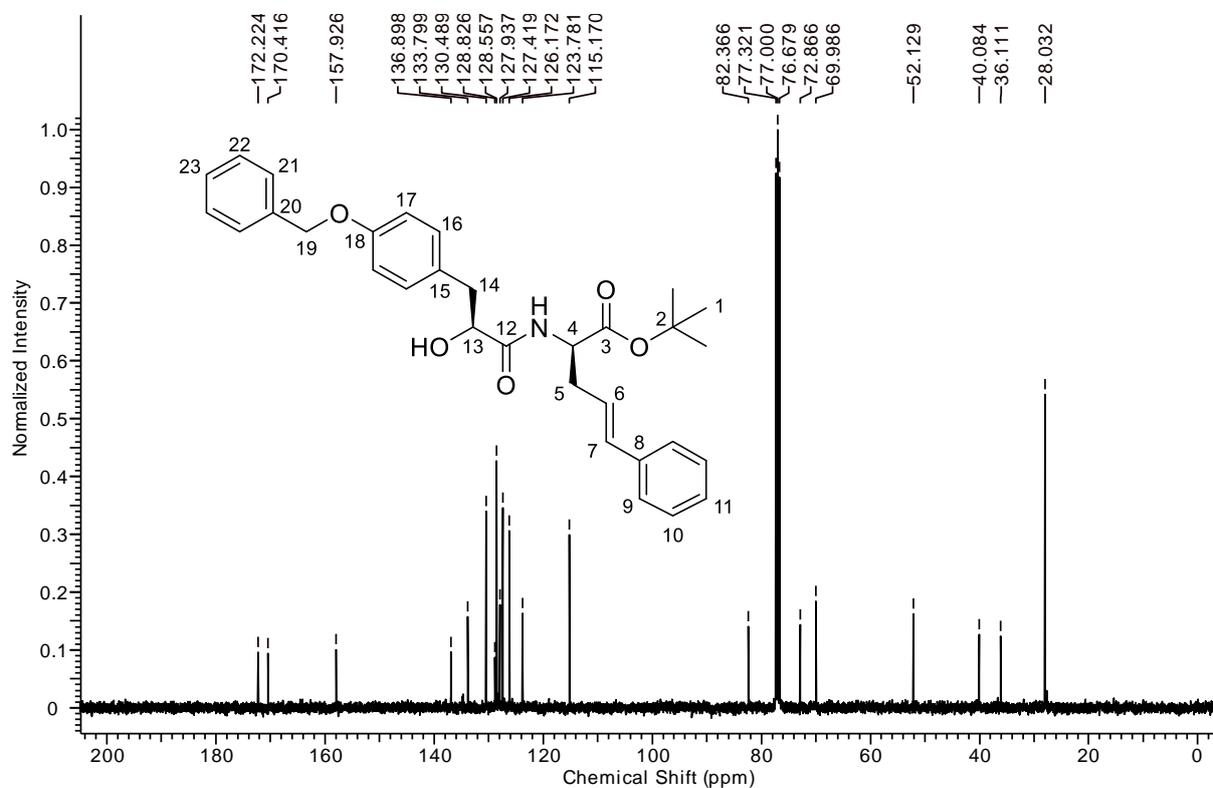
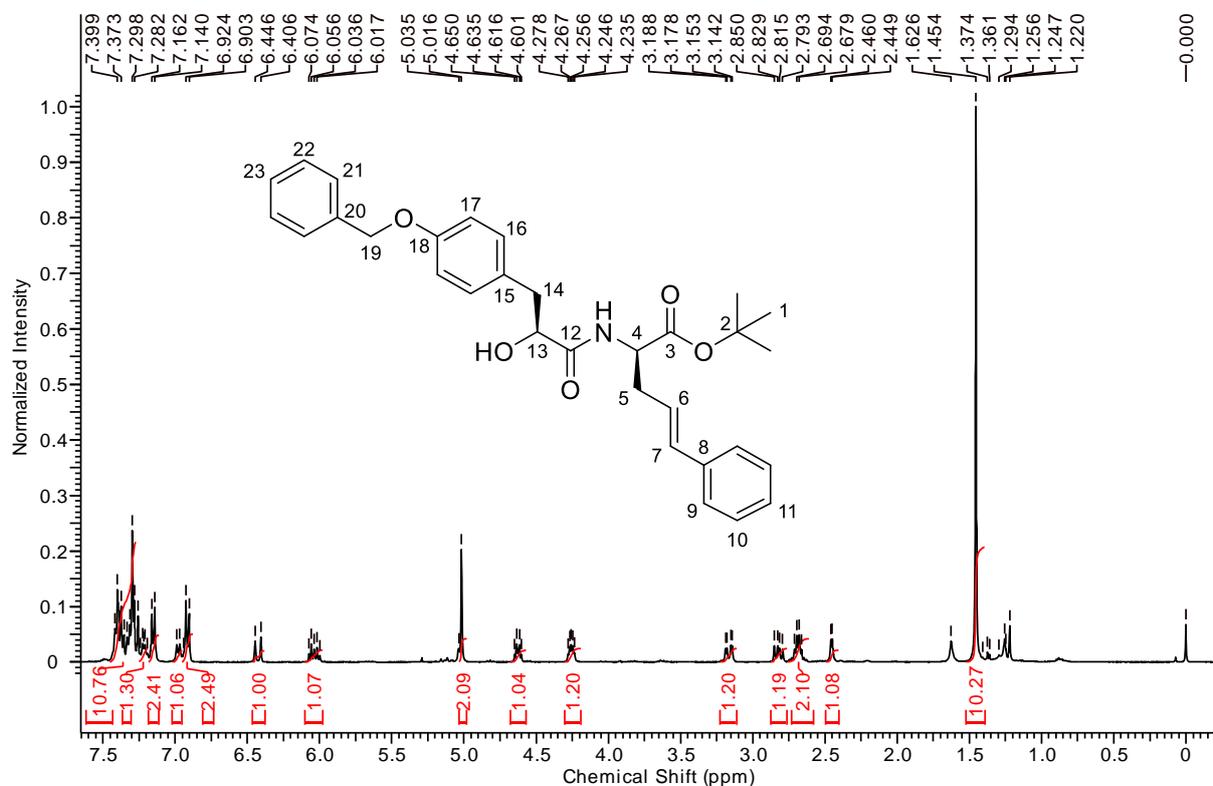
***tert*-Butyl (*R,E*)-2-((*S*)-2-hydroxy-3,3-dimethylbutanamido)-5-phenylpent-4-enoate (2da)**



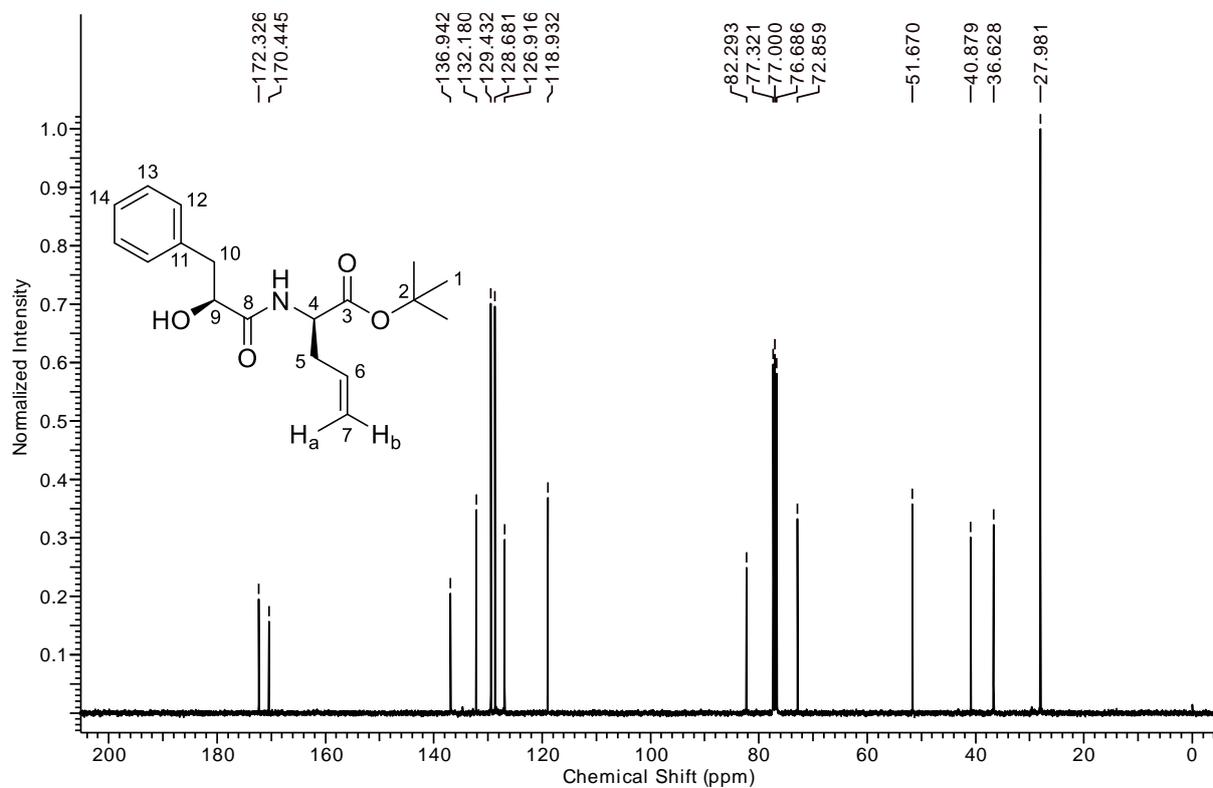
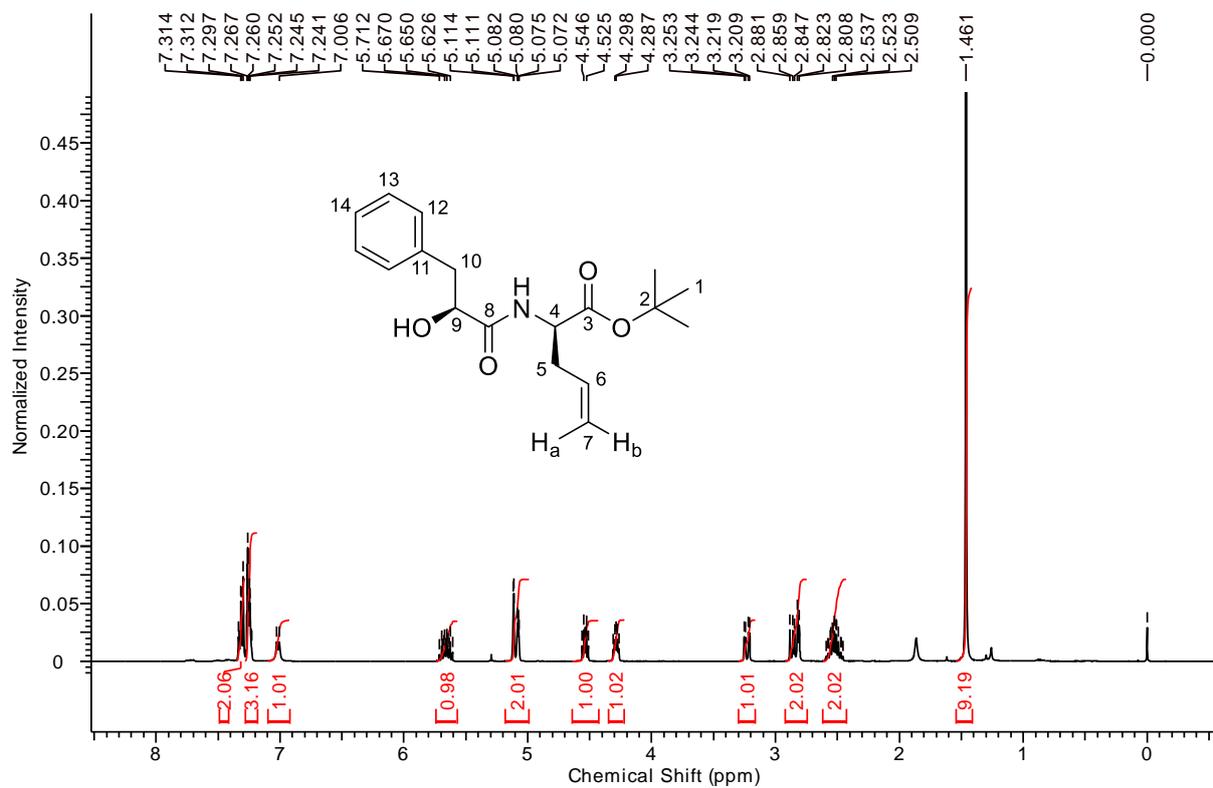
***tert*-Butyl (*R,E*)-2-((*S*)-2-hydroxy-3-phenylpropanamido)-5-phenylpent-4-enoate (**2ea**)**



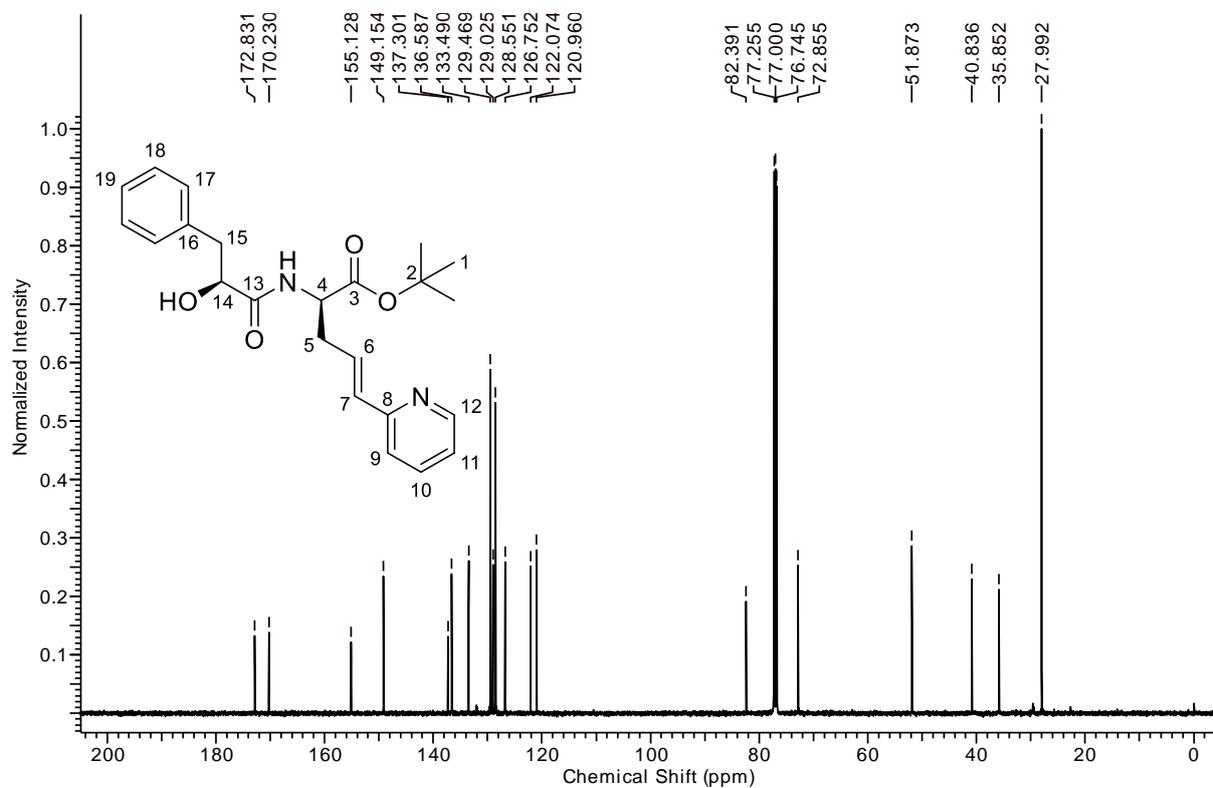
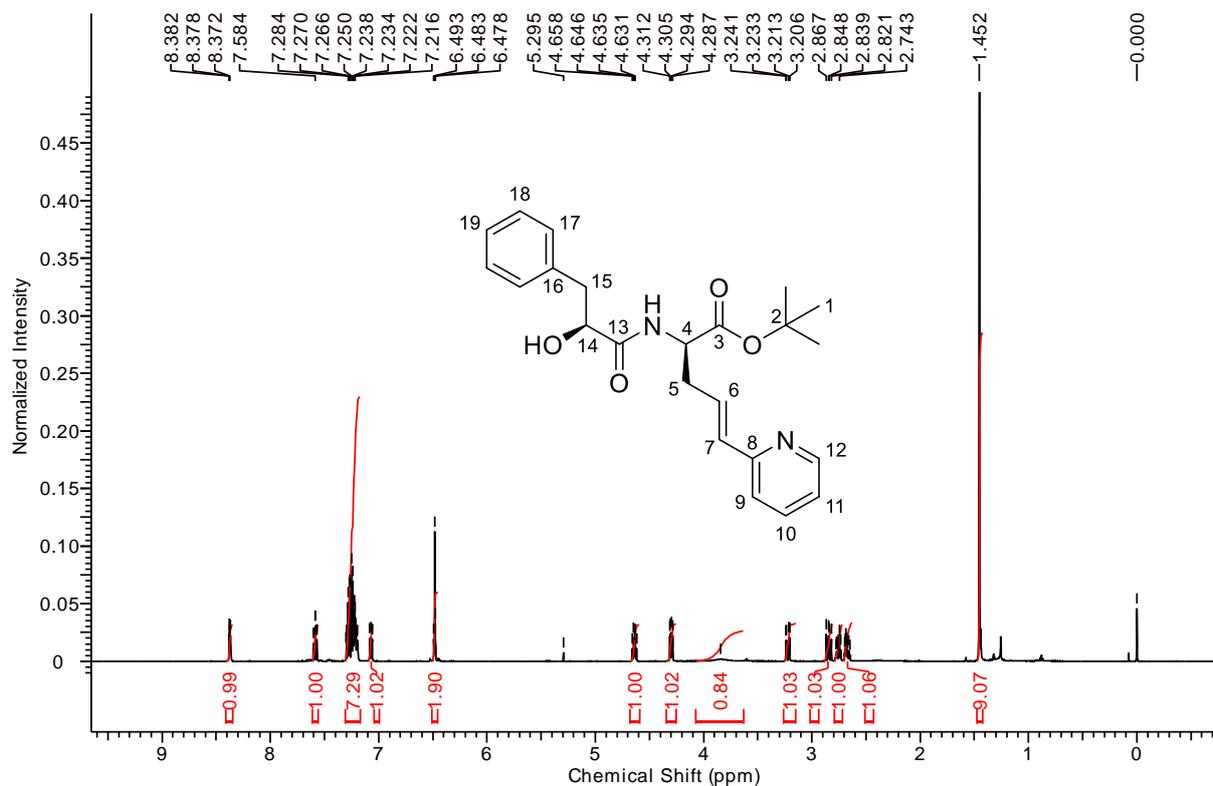
**tert-Butyl (R,E)-2-((S)-3-(4-(benzyloxy)phenyl)-2-hydroxypropanamido)-5-phenylpent-4-enoate (2fa)**



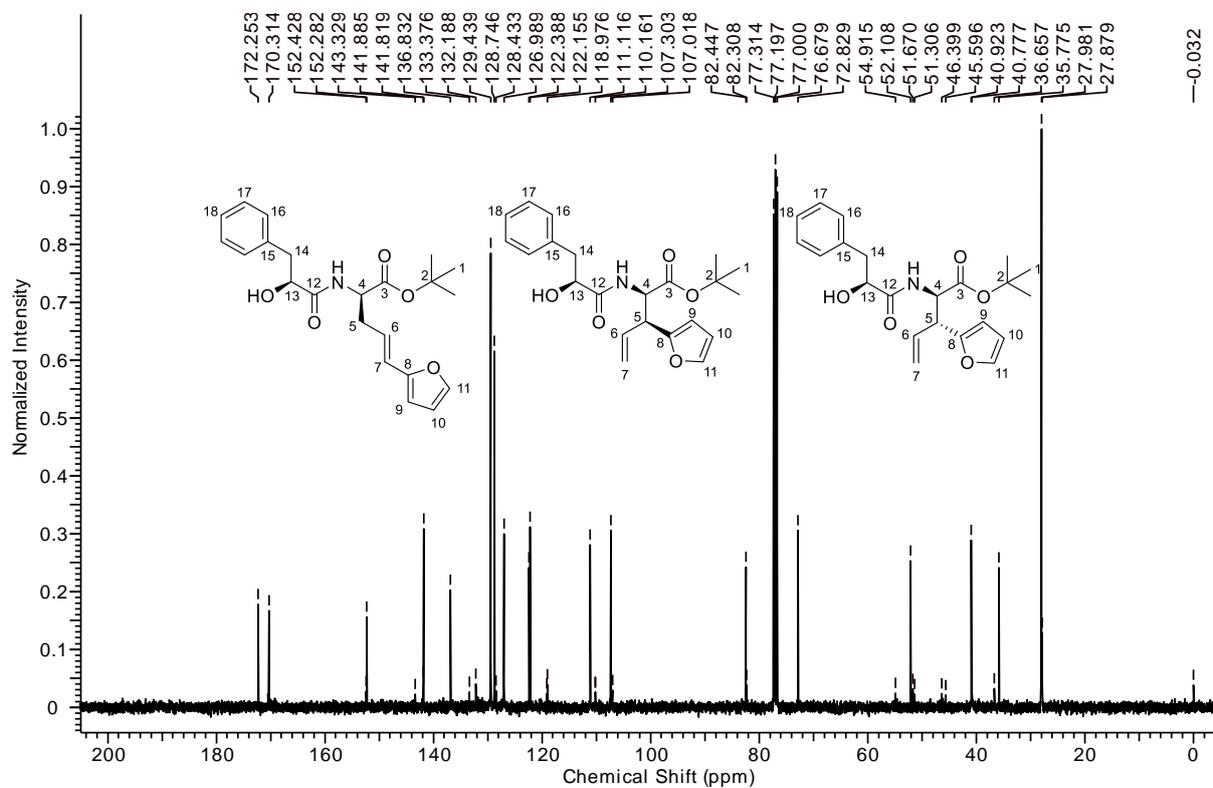
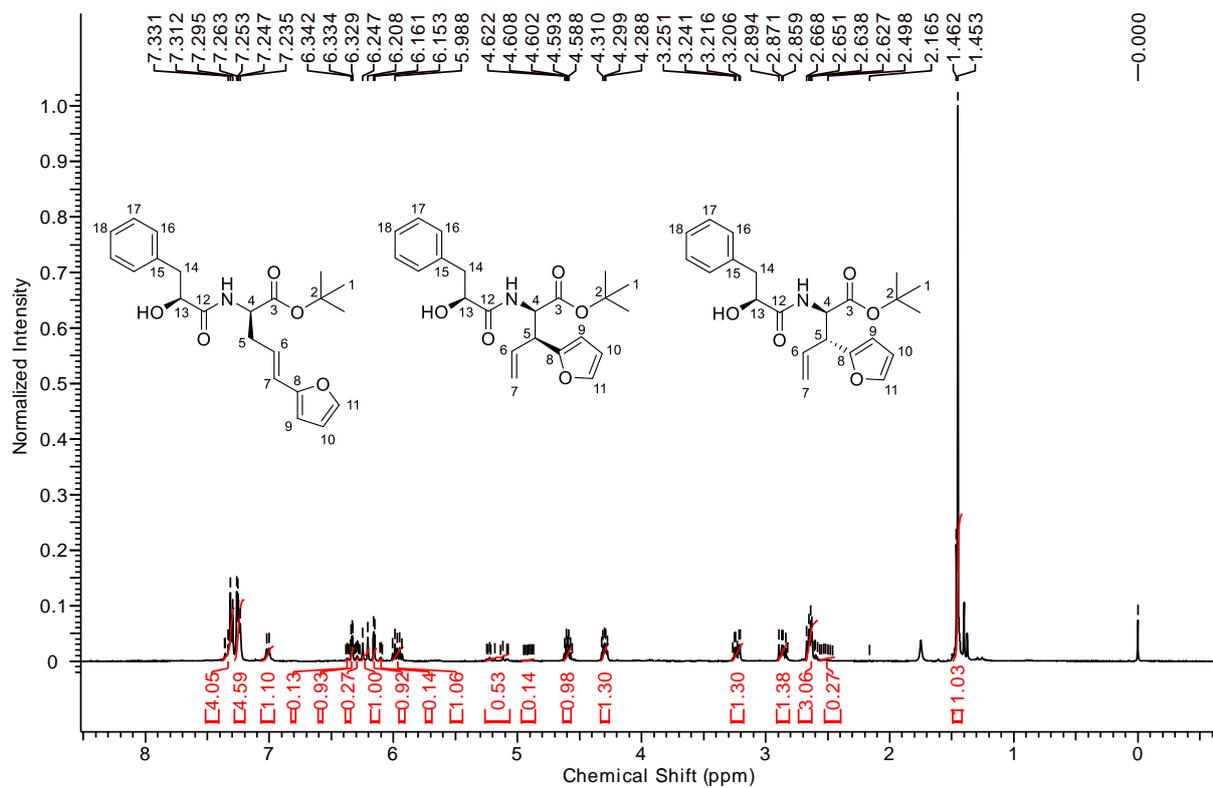
***tert*-Butyl (*R*)-2-((*S*)-2-hydroxy-3-phenylpropanamido)pent-4-enoate (**2eb**)**



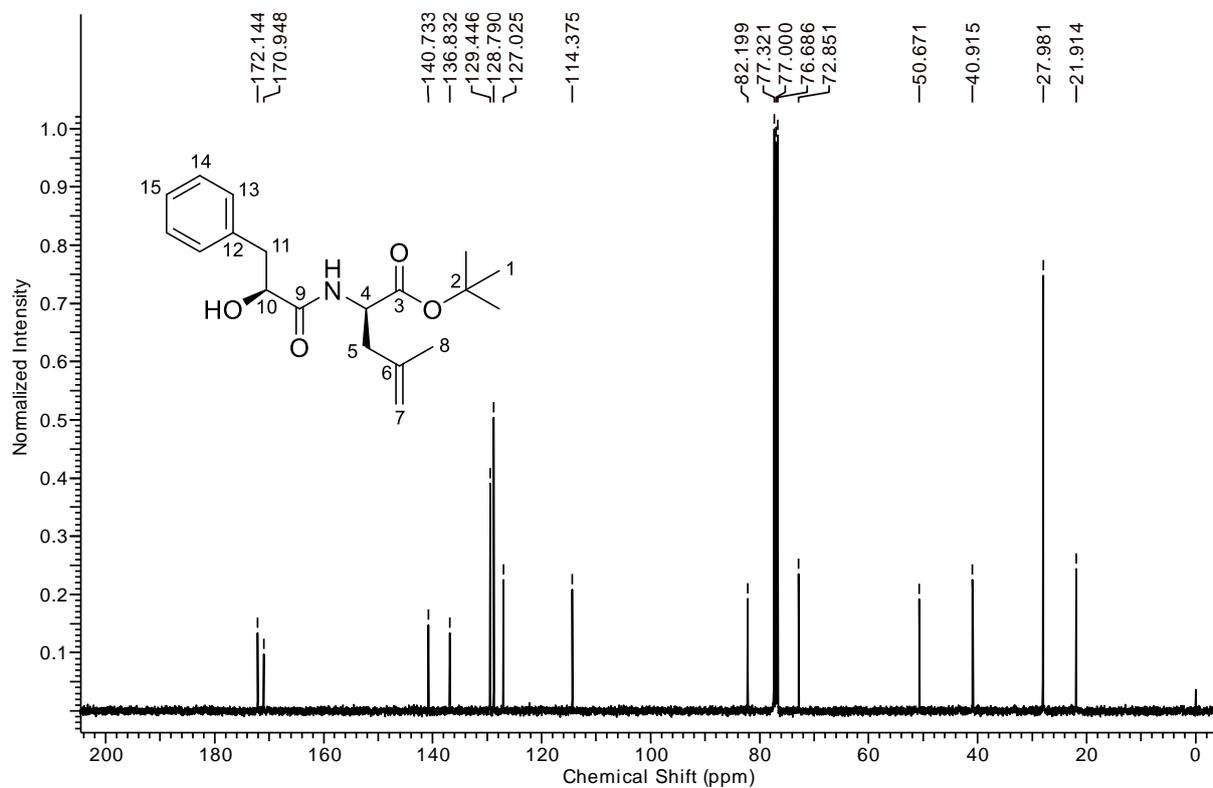
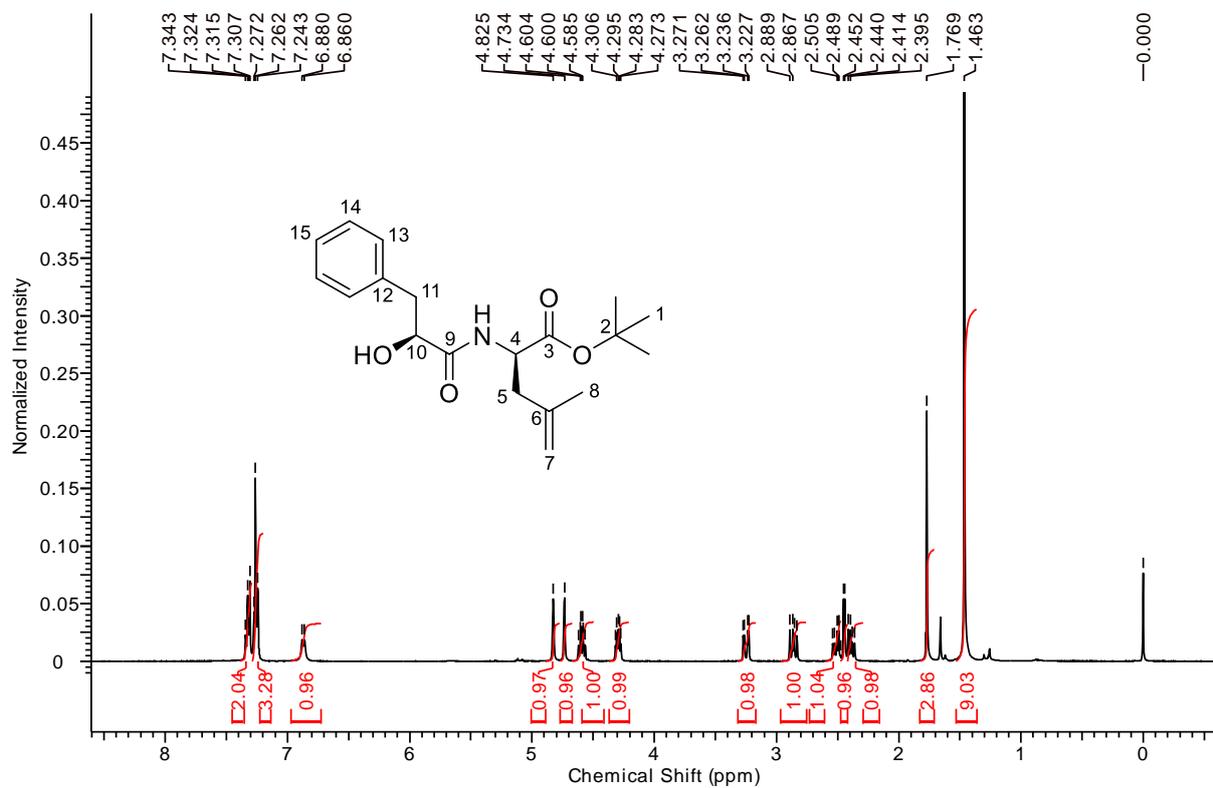
***tert*-Butyl (*R,E*)-2-((*S*)-2-hydroxy-3-phenylpropanamido)-5-(pyridin-2-yl)pent-4-enoate (**2ec**)**



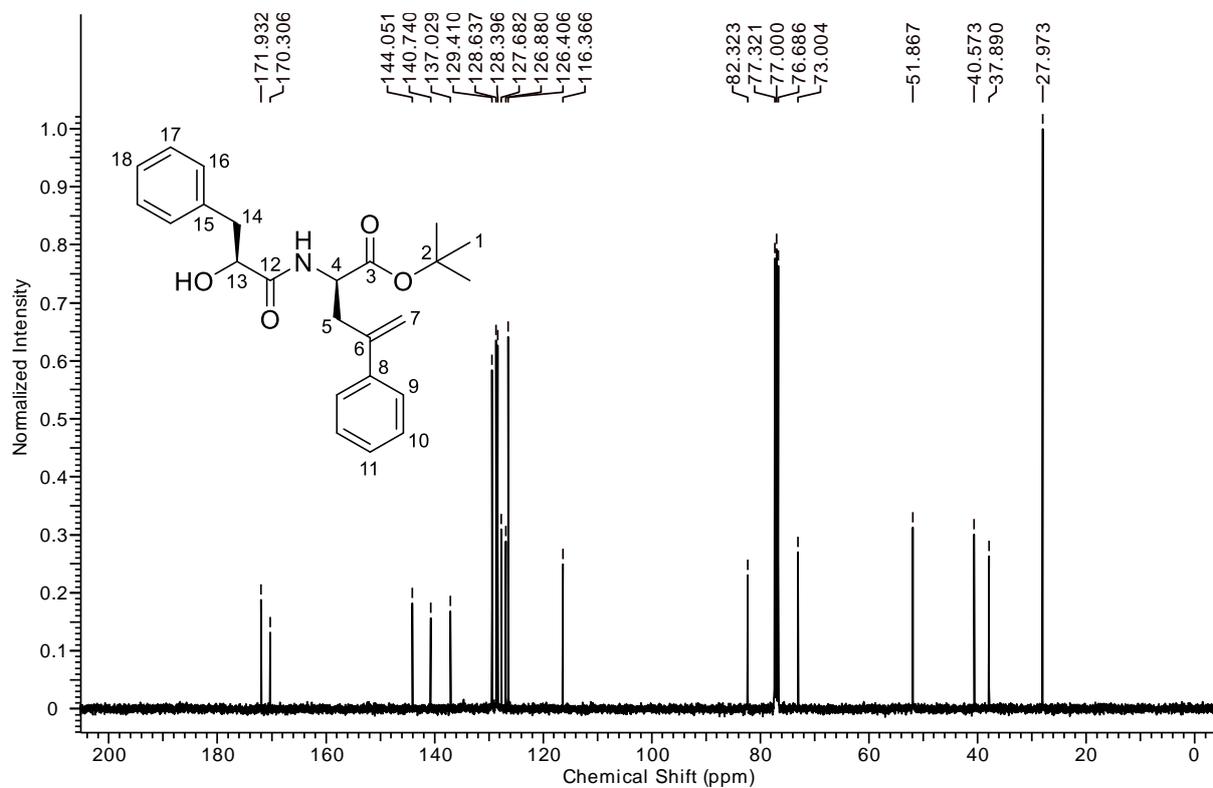
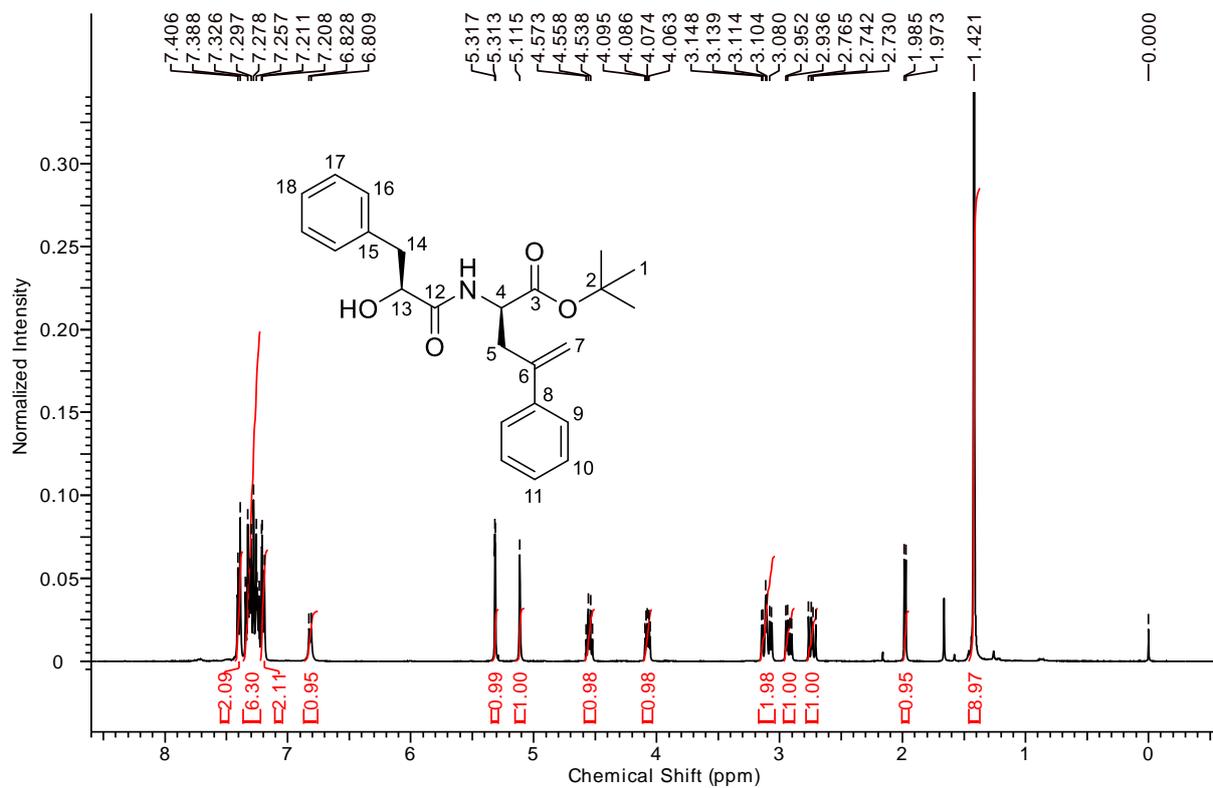
***tert*-Butyl (*R,E*)-5-(furan-2-yl)-2-((*S*)-2-hydroxy-3-phenylpropanamido)pent-4-enoate (2ed)**



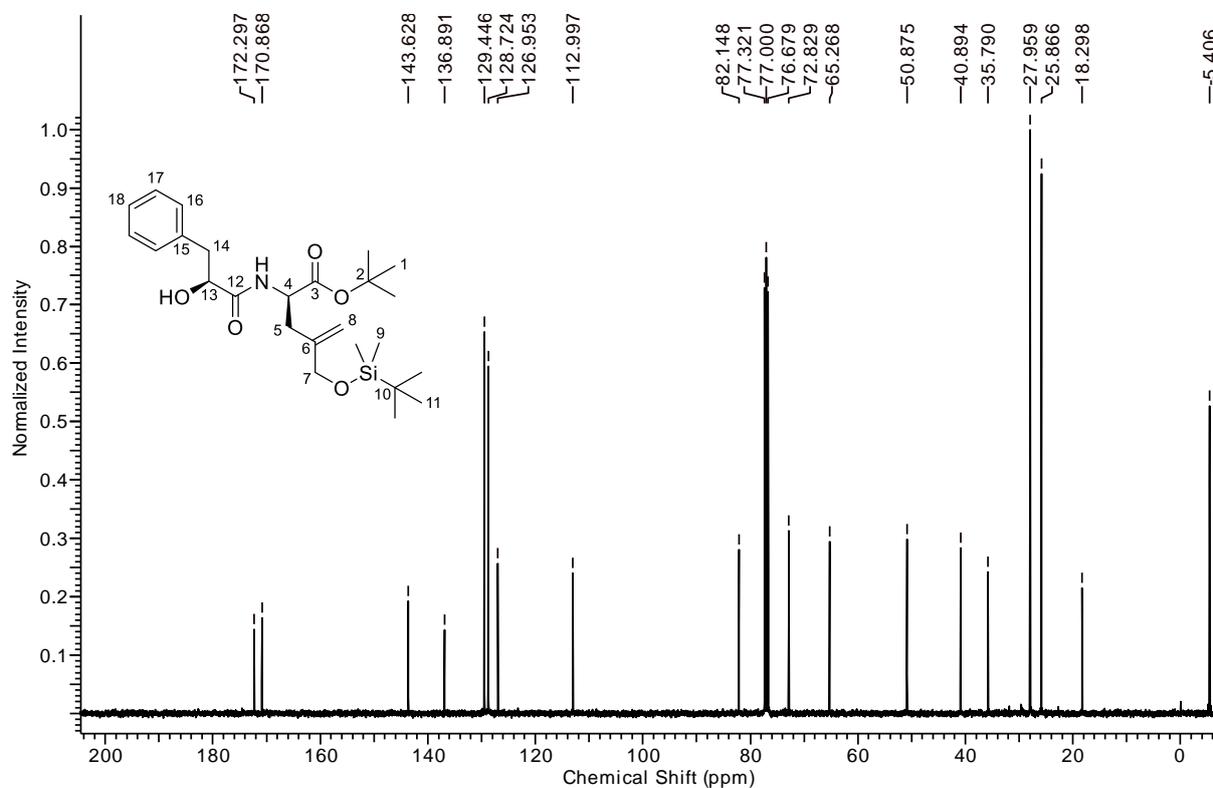
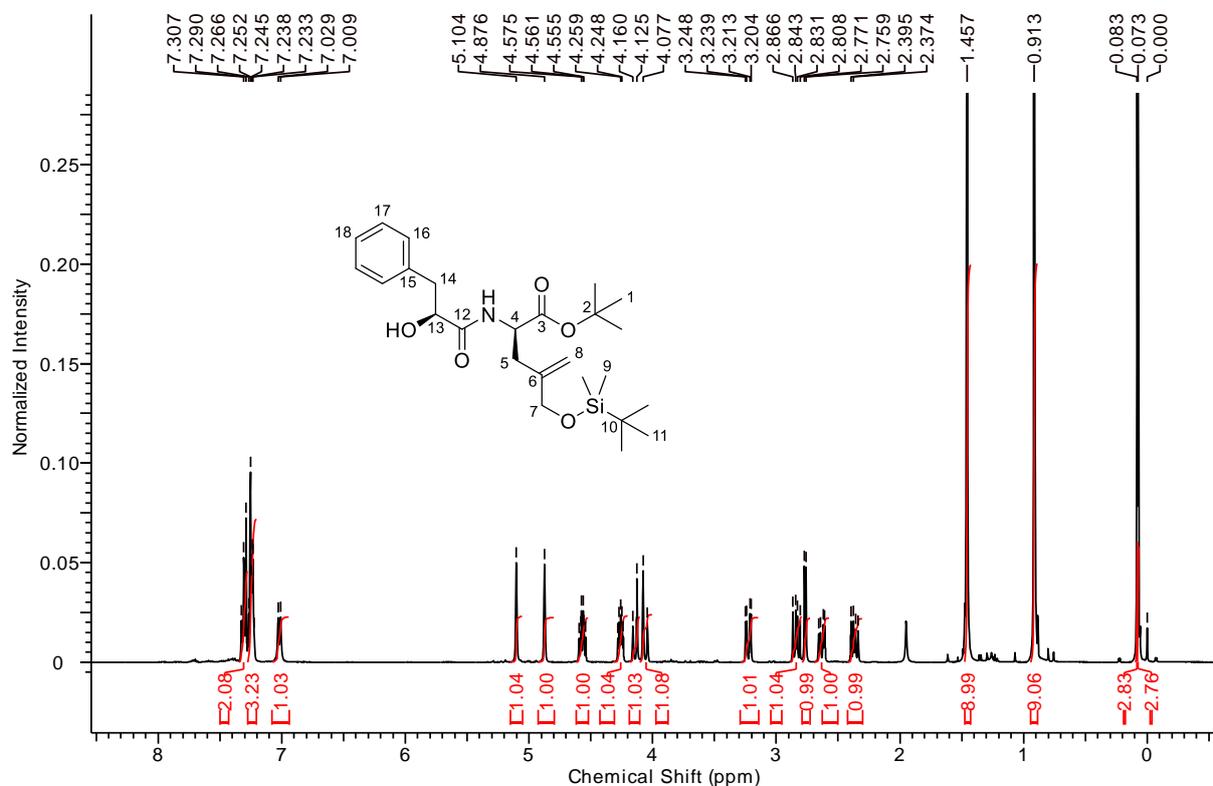
***tert*-Butyl (*R*)-2-((*S*)-2-hydroxy-3-phenylpropanamido)-4-methylpent-4-enoate (**2ee**)**



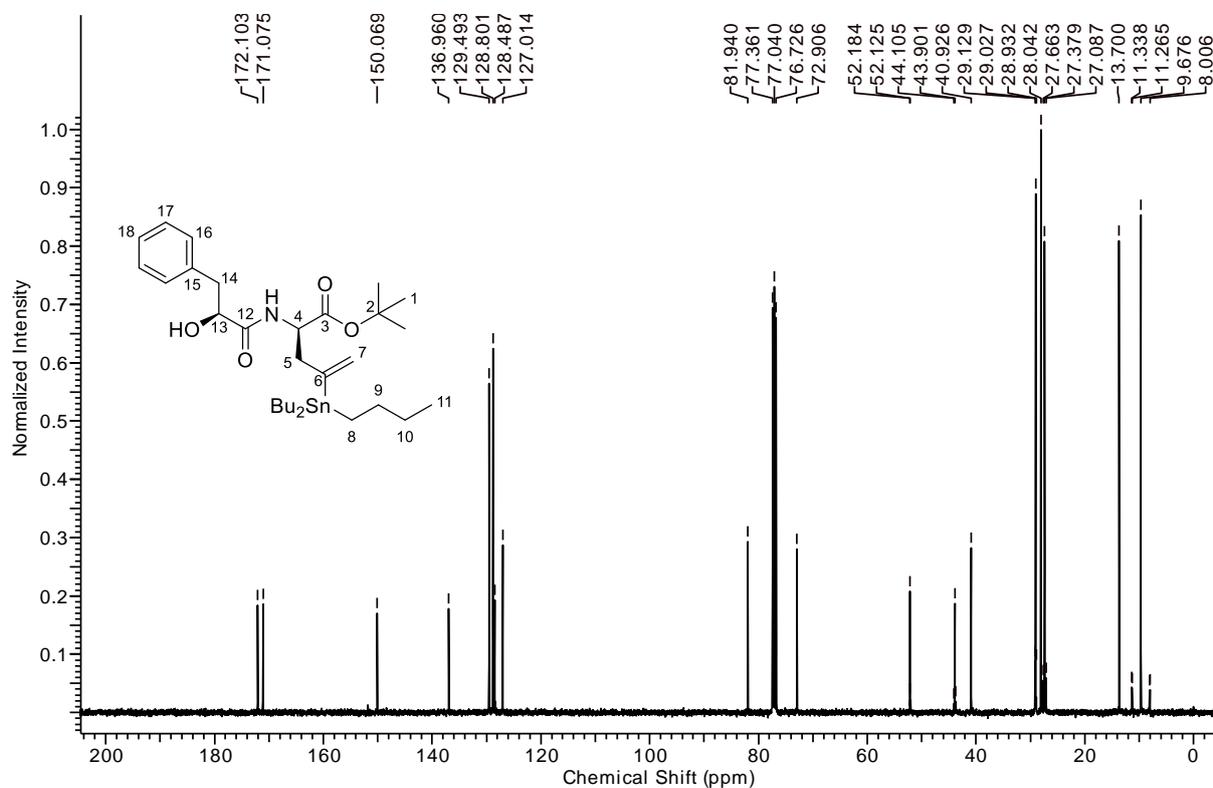
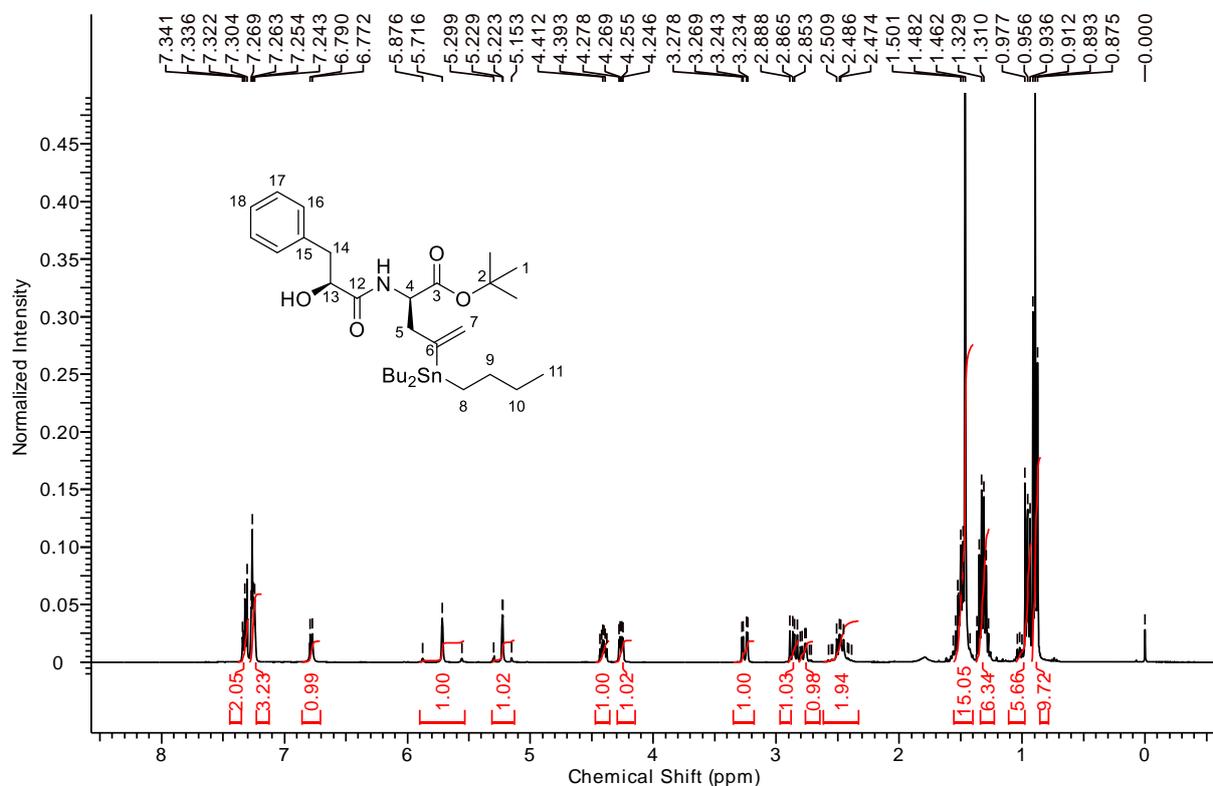
***tert*-Butyl (*R*)-2-((*S*)-2-hydroxy-3-phenylpropanamido)-4-phenylpent-4-enoate (2ef)**



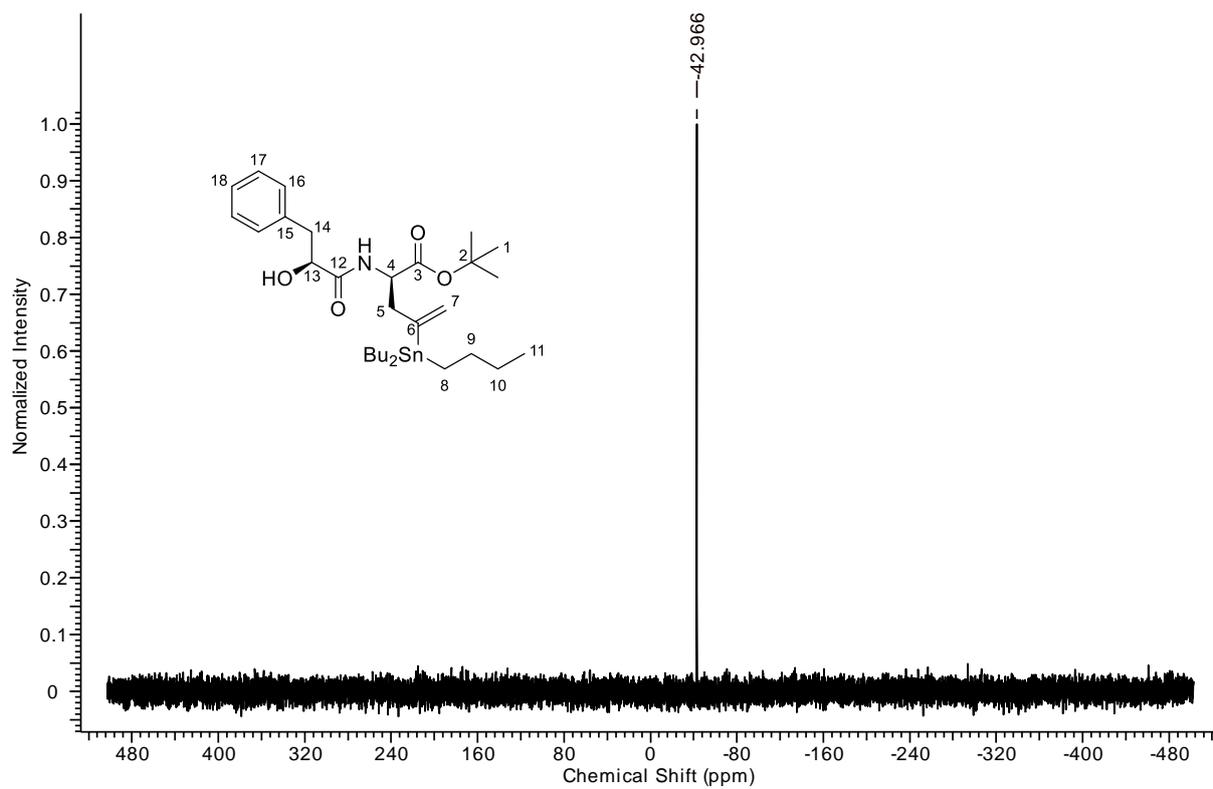
***tert*-Butyl (R)-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-2-((S)-2-hydroxy-3-phenylpropanamido)pent-4-enoate (2eg)**



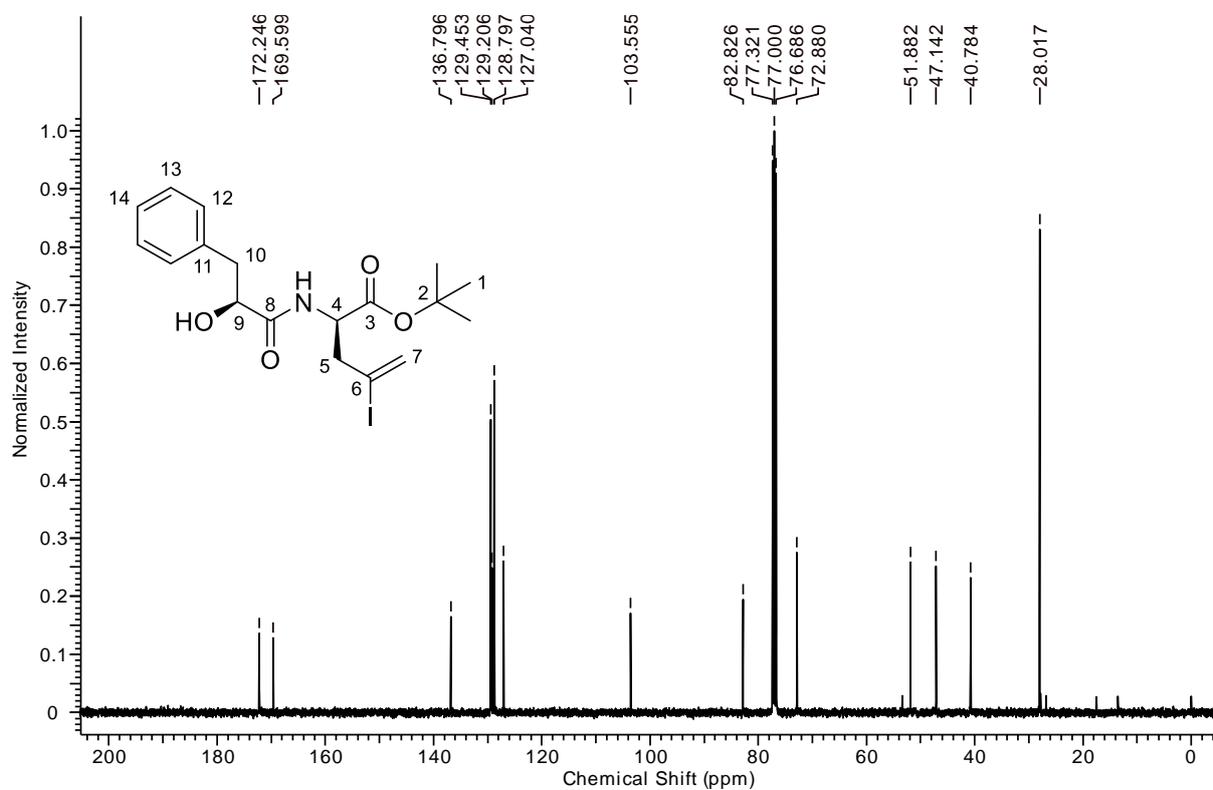
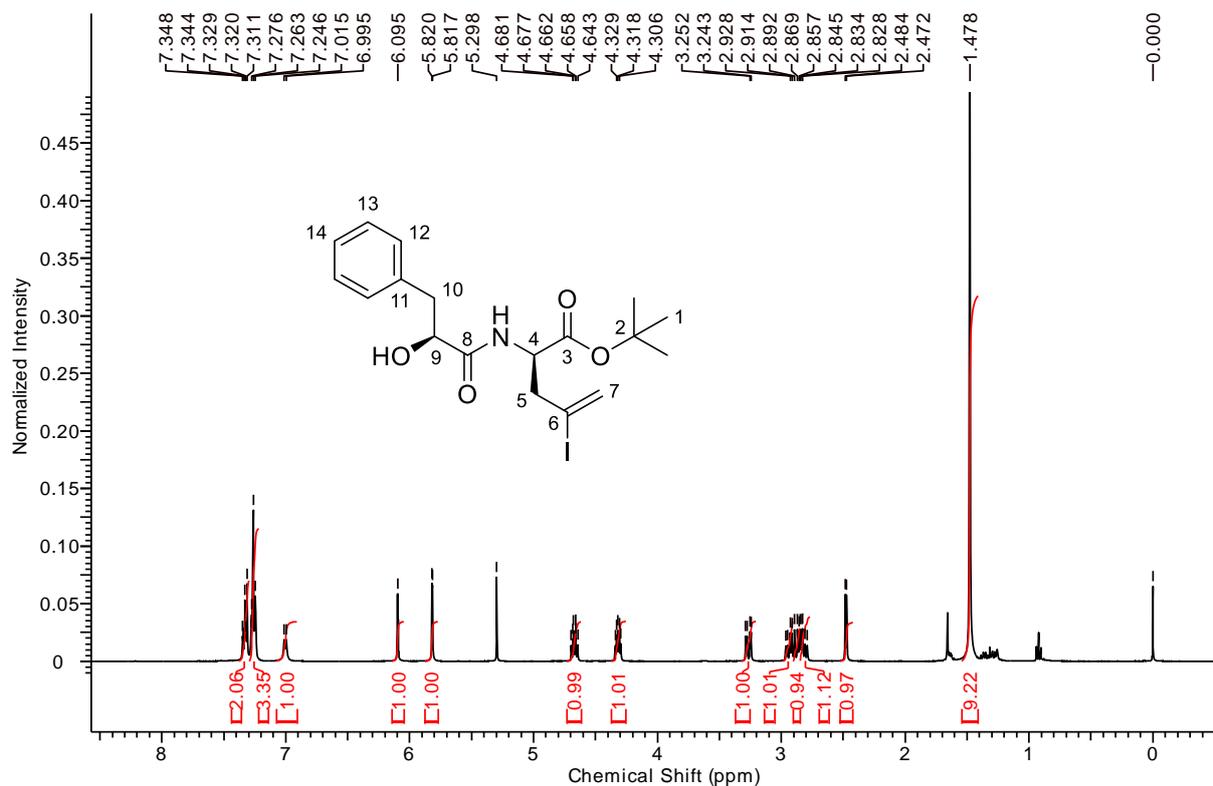
**tert-Butyl (R)-2-((S)-2-hydroxy-3-phenylpropanamido)-4-(tributylstannyl)pent-4-enoate (2eh)**



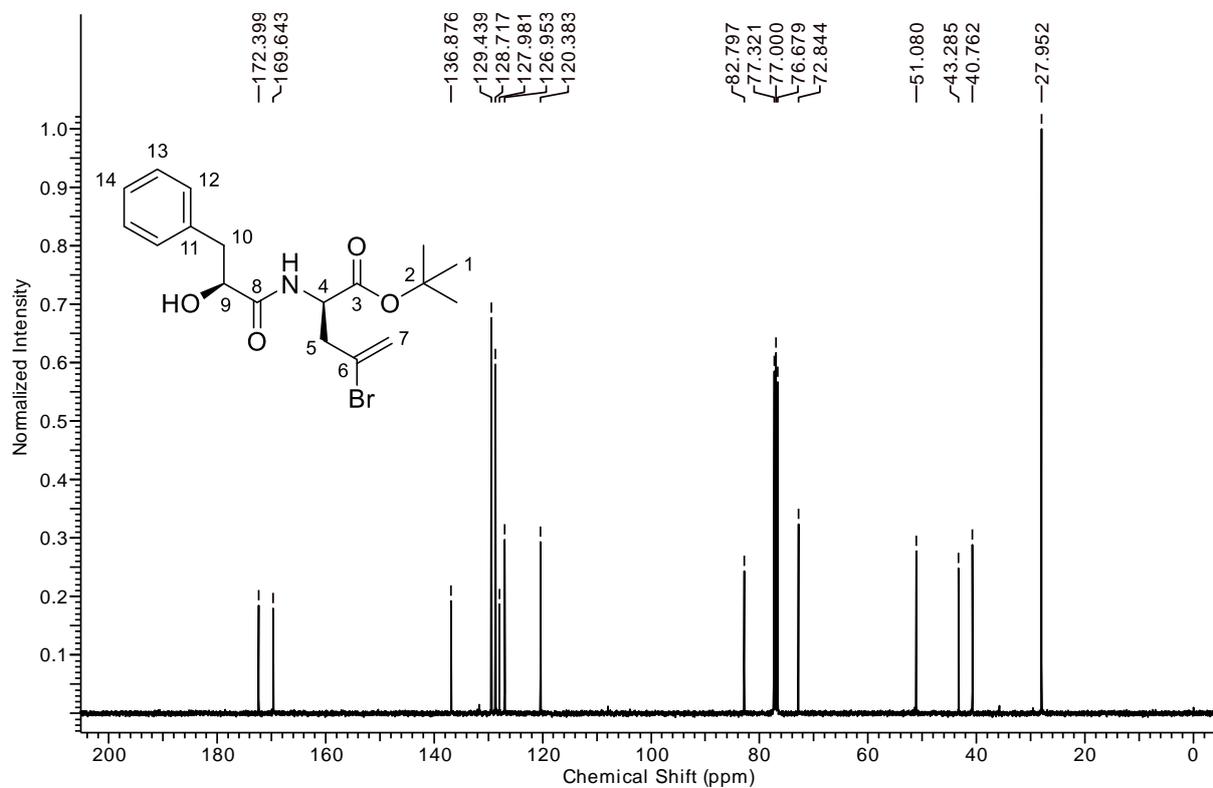
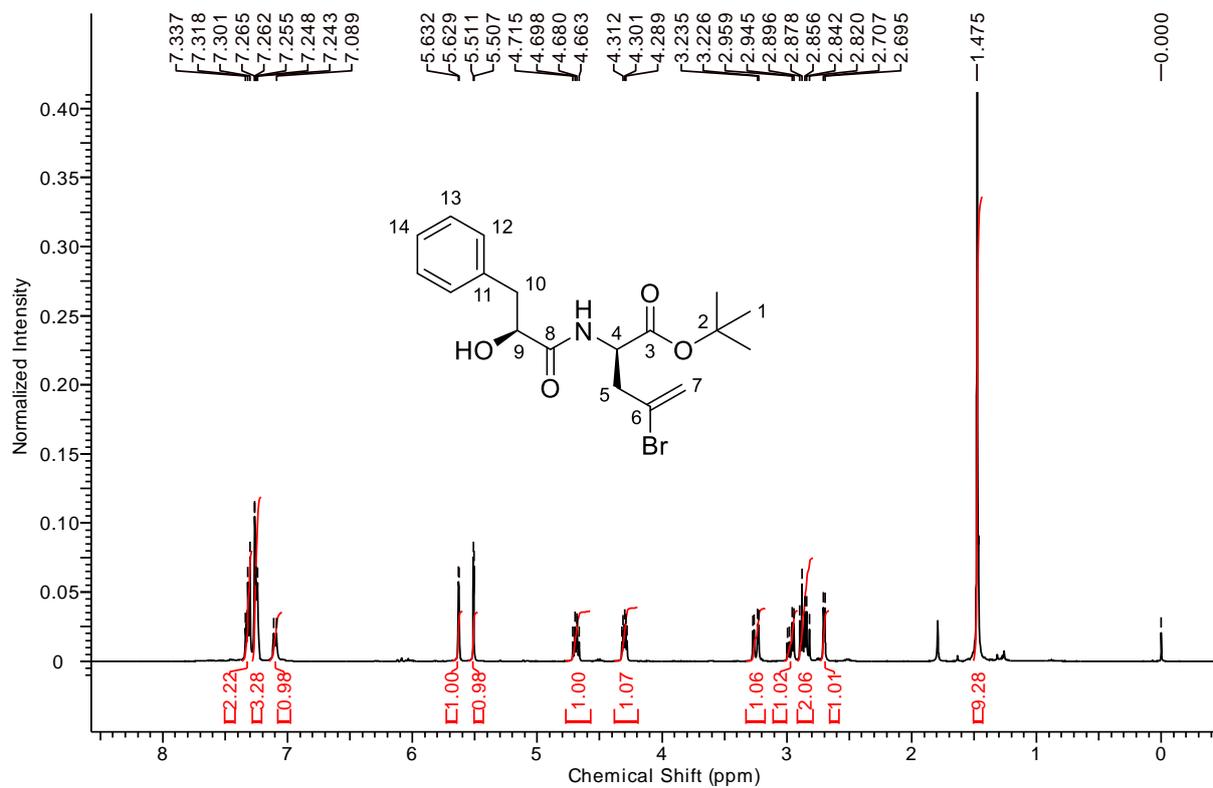
<sup>119</sup>Sn-NMR



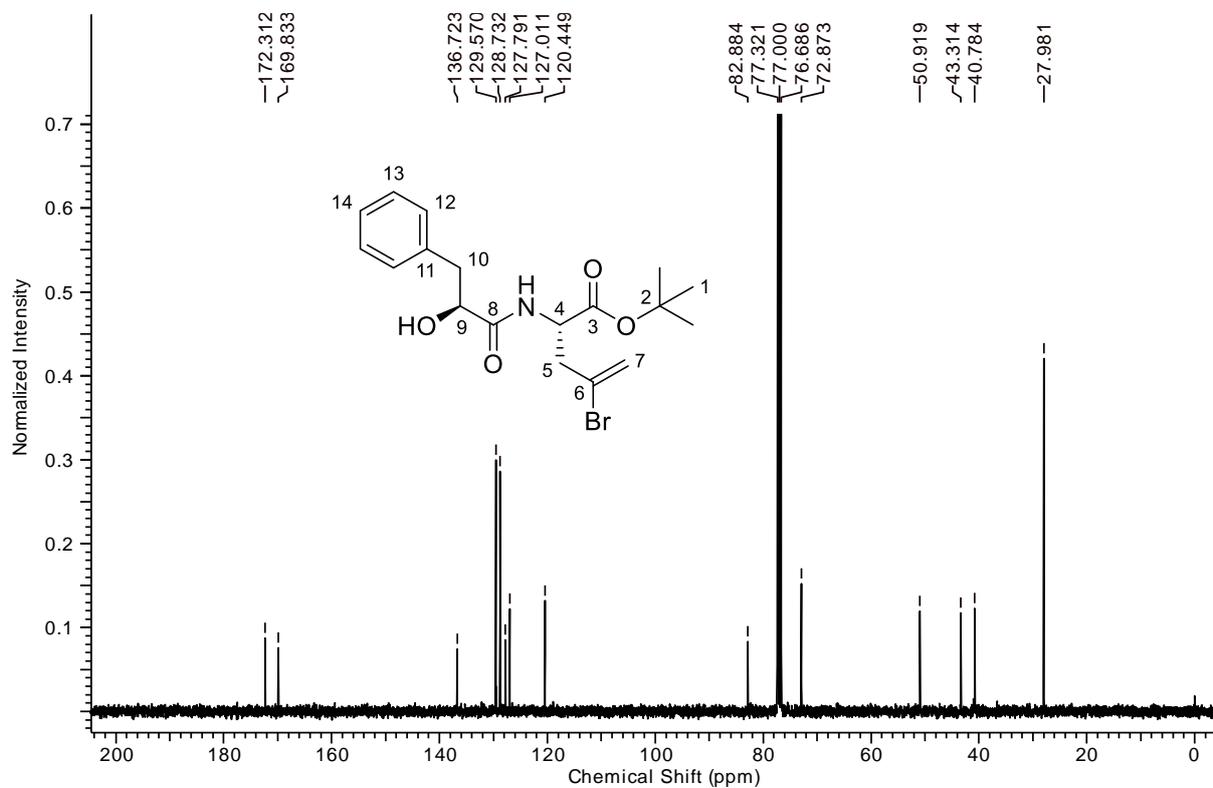
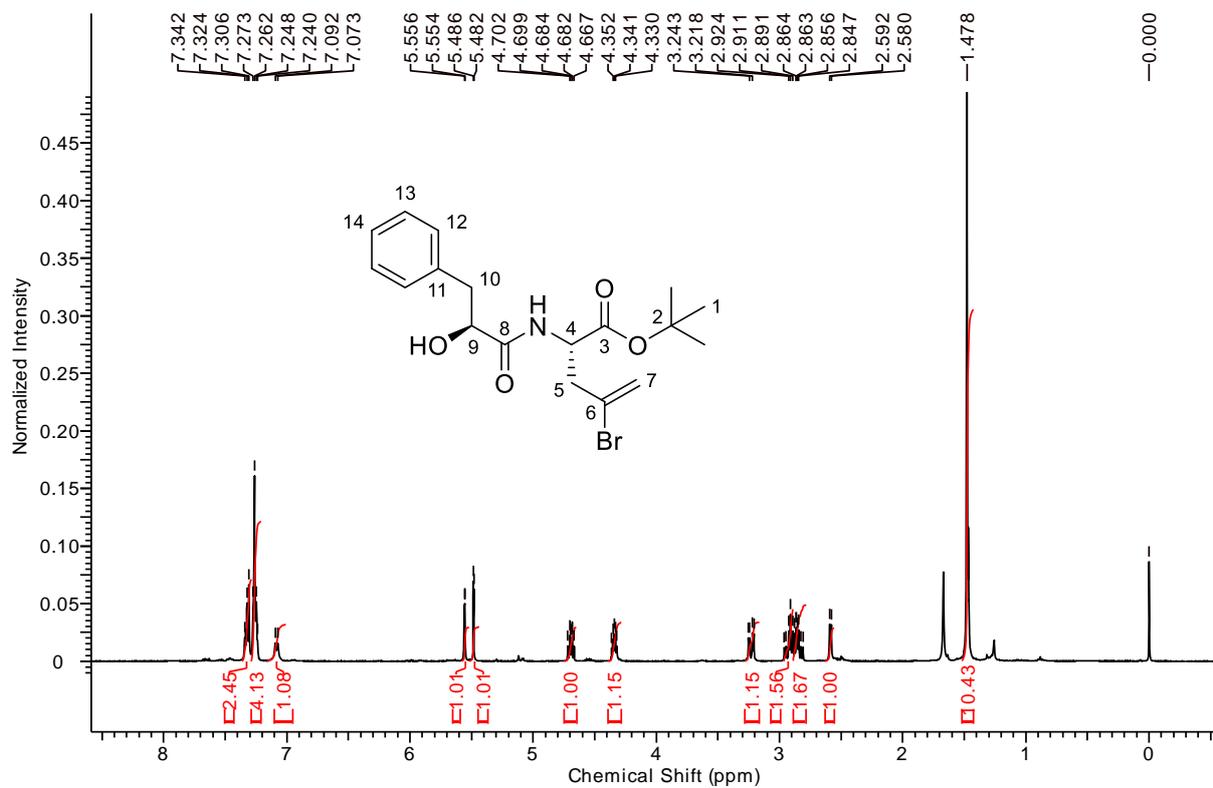
***tert*-Butyl (*R*)-2-((*S*)-2-hydroxy-3-phenylpropanamido)-4-iodopent-4-enoate (SI-32)**



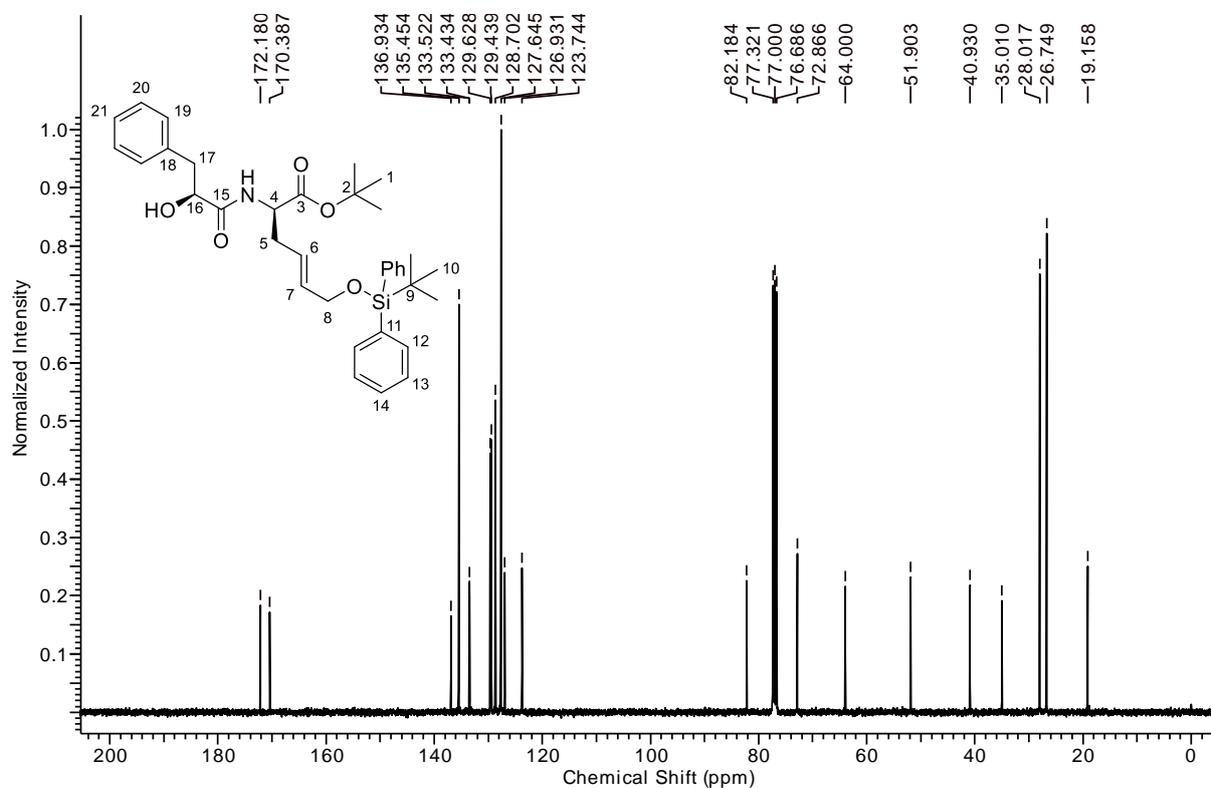
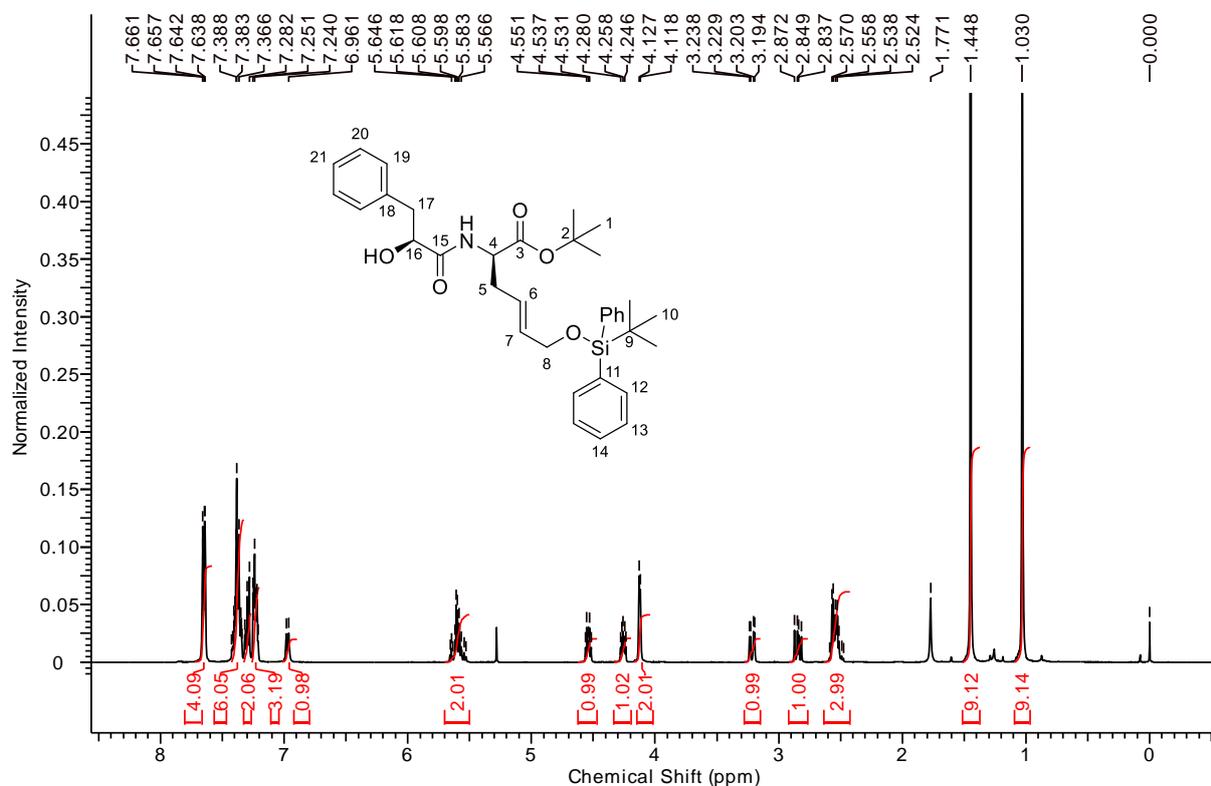
***tert*-Butyl (*R*)-4-bromo-2-((*S*)-2-hydroxy-3-phenylpropanamido)pent-4-enoate (2ei)**



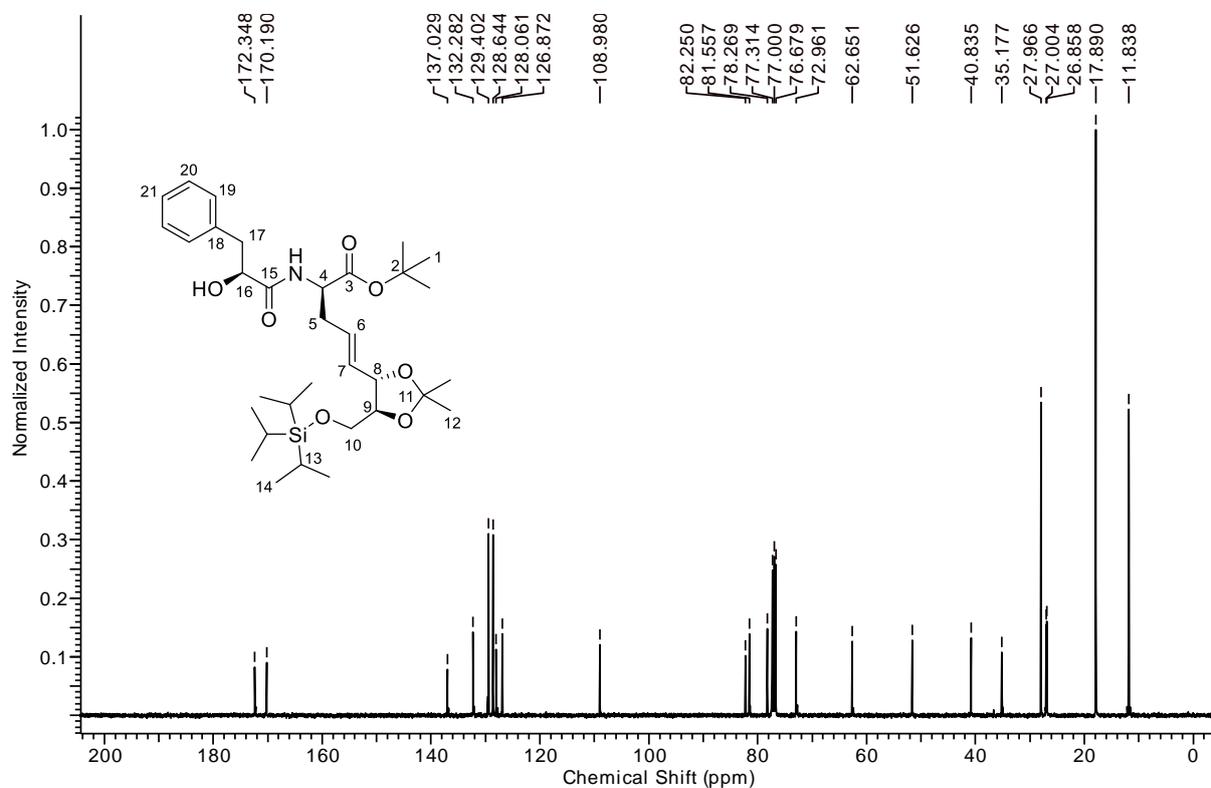
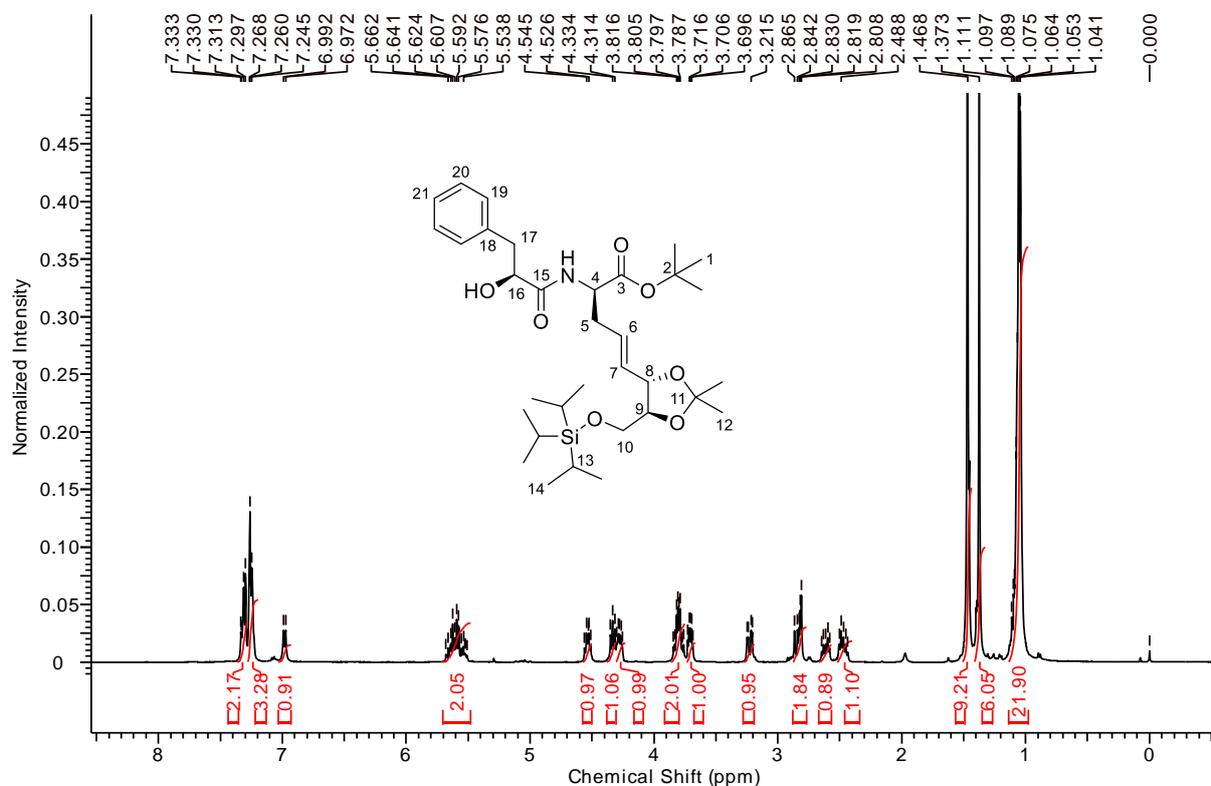
***tert*-Butyl (S)-4-bromo-2-((S)-2-hydroxy-3-phenylpropanamido)pent-4-enoate (2ei)**



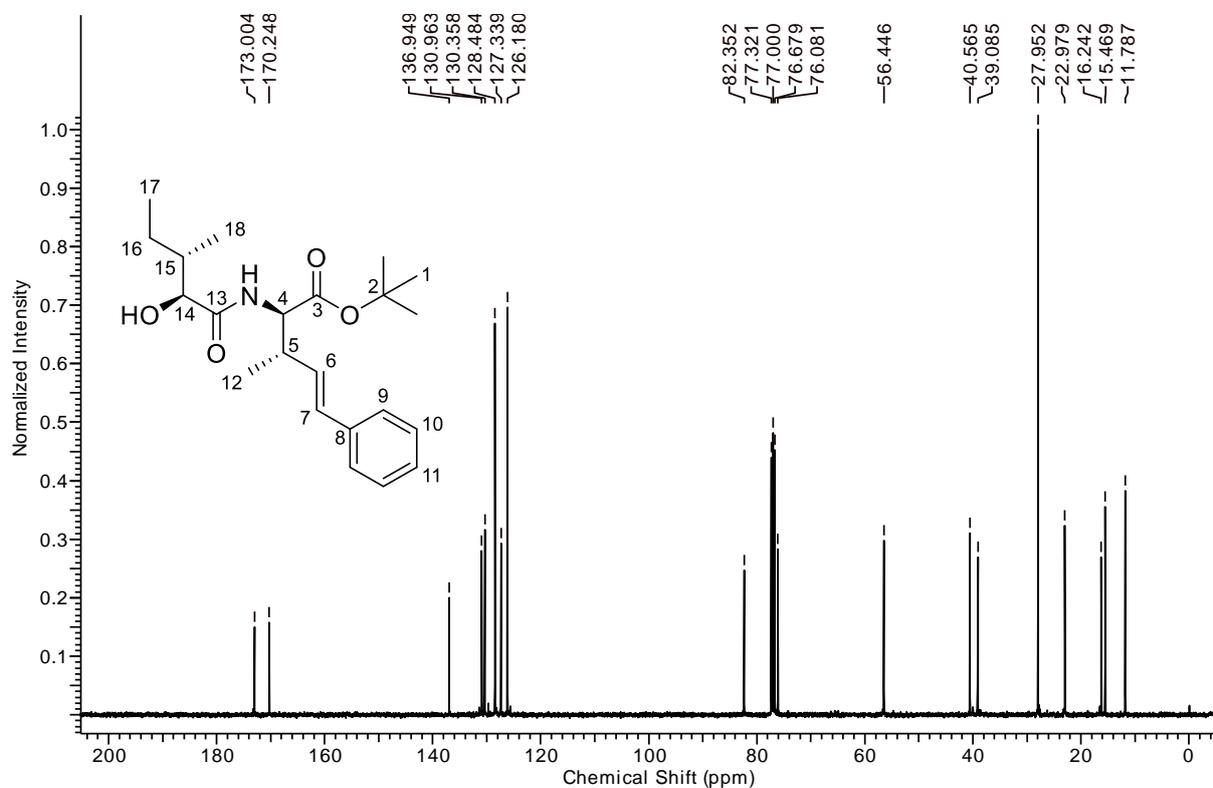
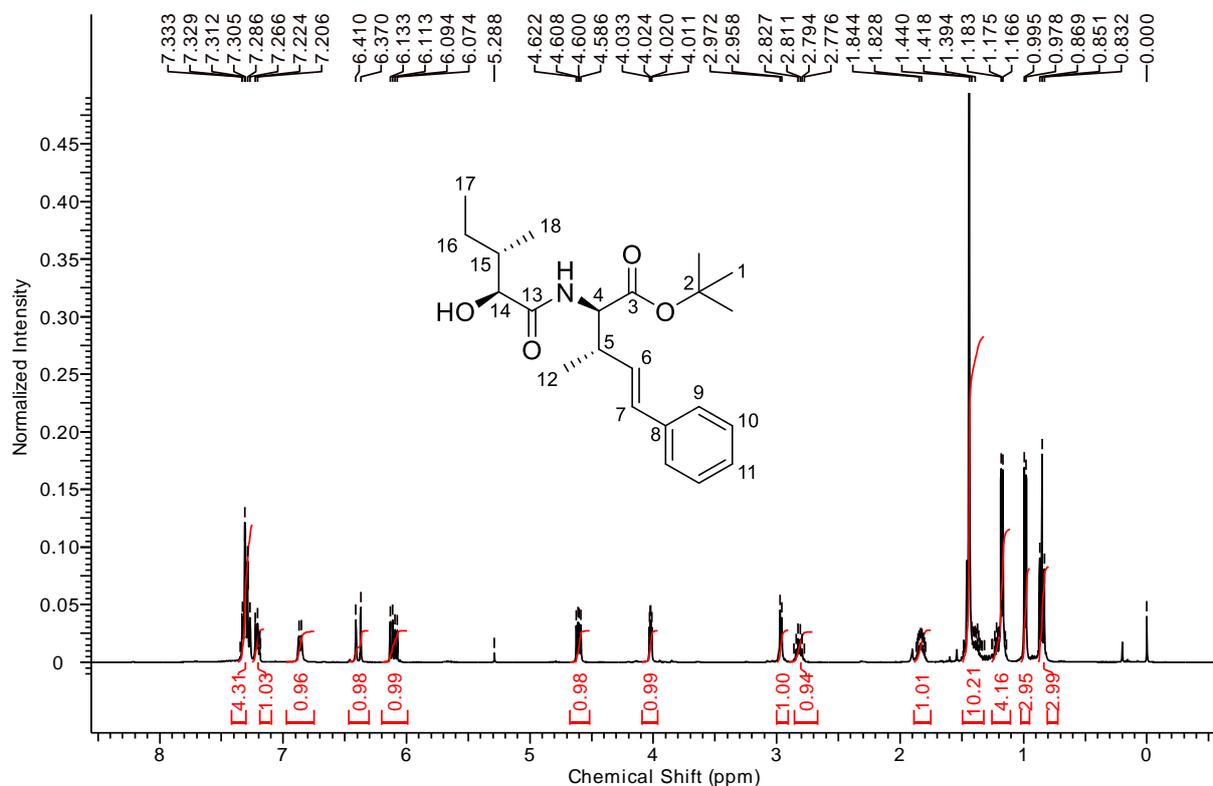
**tert-Butyl (R,E)-6-((tert-butyldiphenylsilyloxy)-2-((S)-2-hydroxy-3-phenylpropanamido)-hex-4-enoate (2ej)**



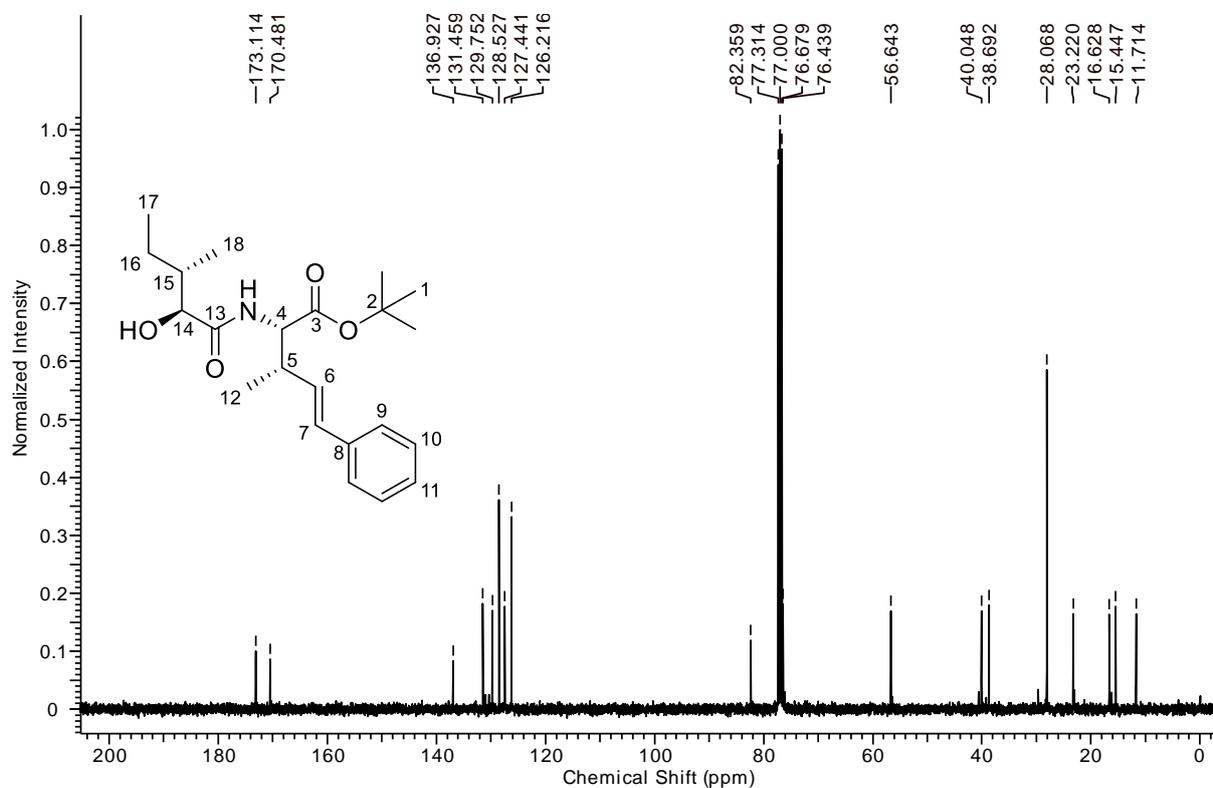
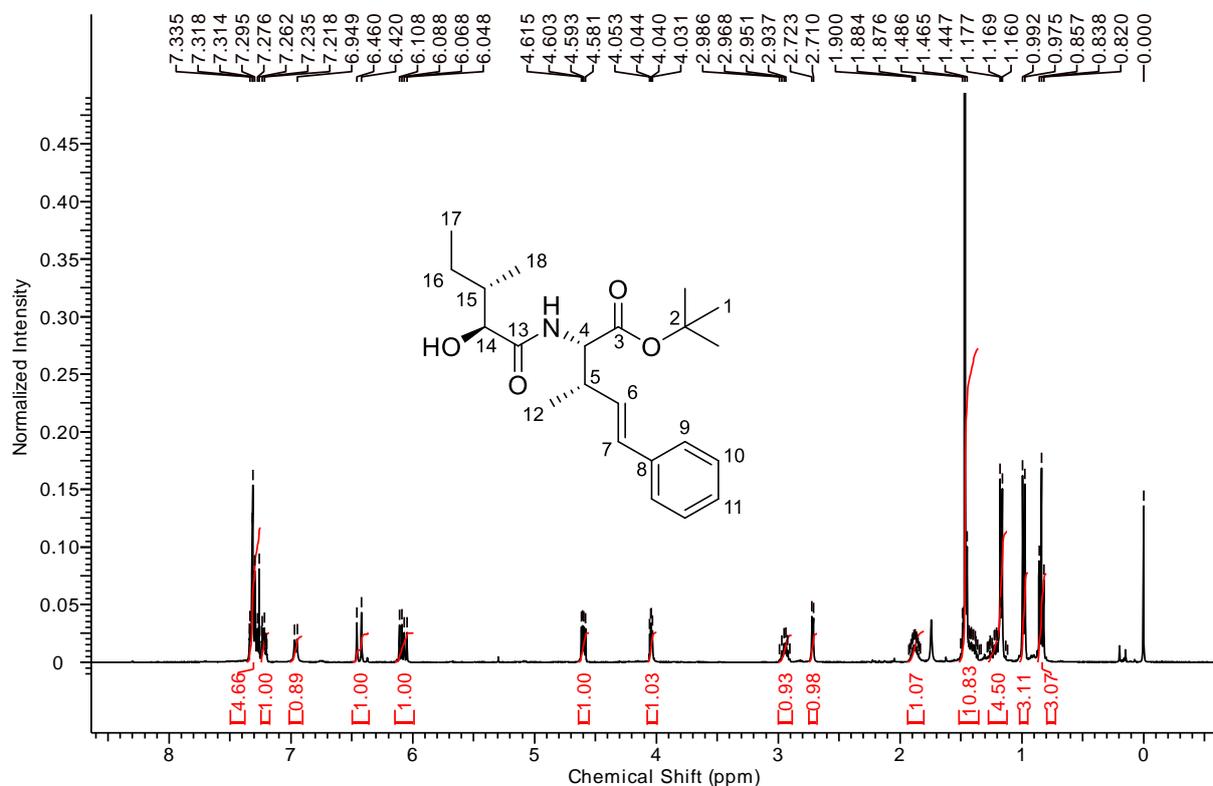
***tert*-Butyl (*R,E*)-5-((4*S,5S*)-2,2-dimethyl-5-(((triisopropylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)-2-((*S*)-2-hydroxy-3-phenylpropanamido)pent-4-enoate (2ek)**



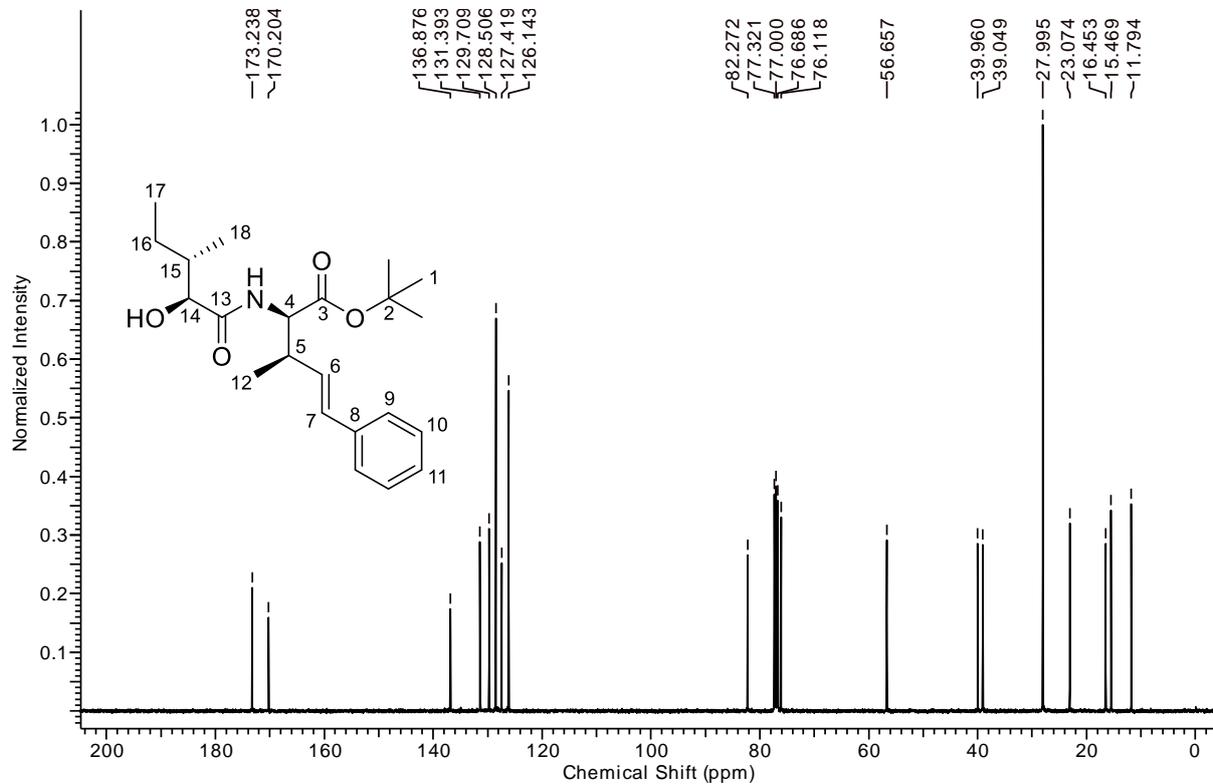
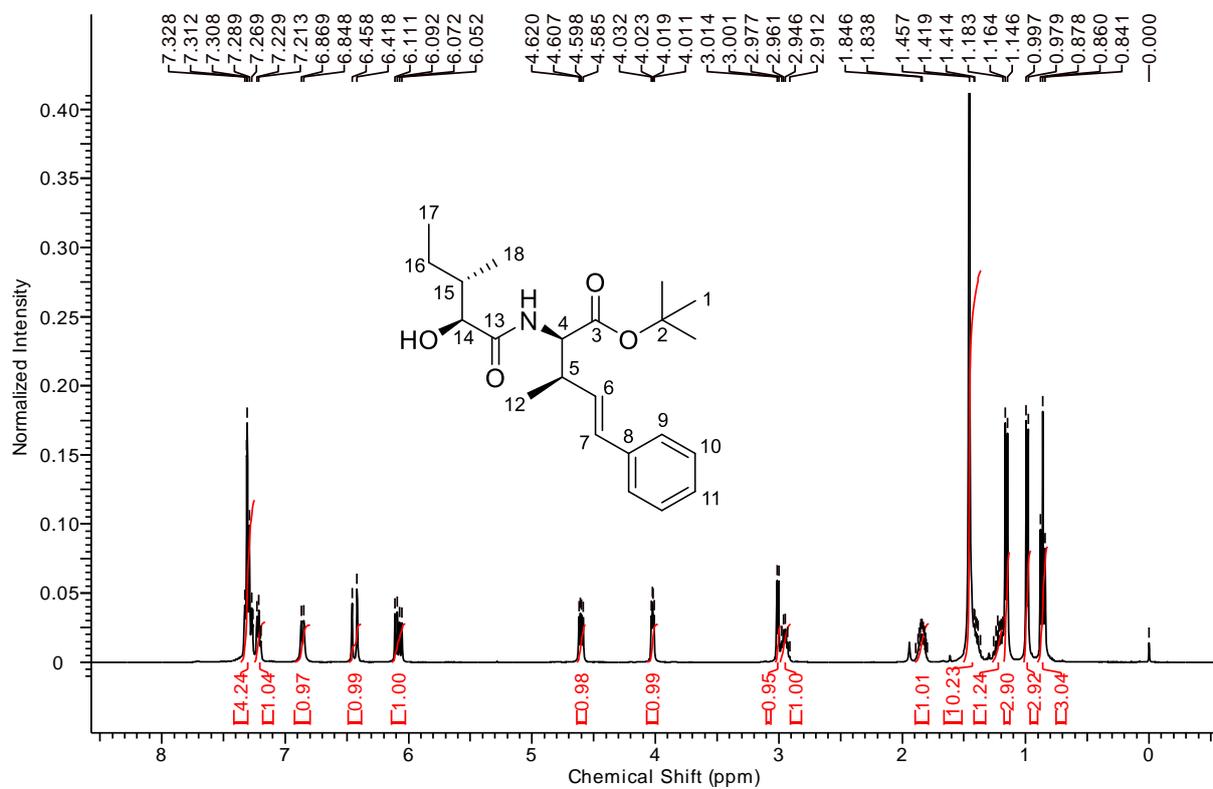
***tert*-Butyl (2*R*,3*S*,*E*)-2-((2*S*,3*S*)-2-hydroxy-3-methylpentanamido)-3-methyl-5-phenylpent-4-enoate (2aI-2)**



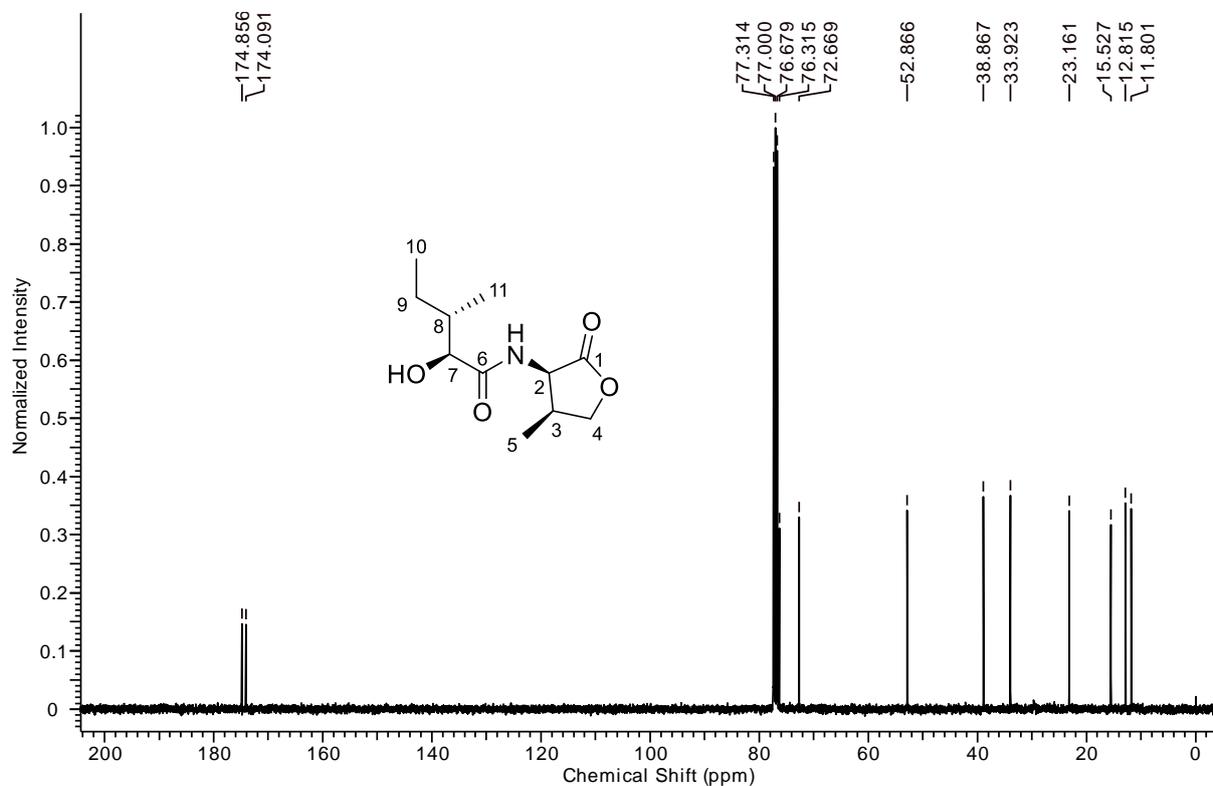
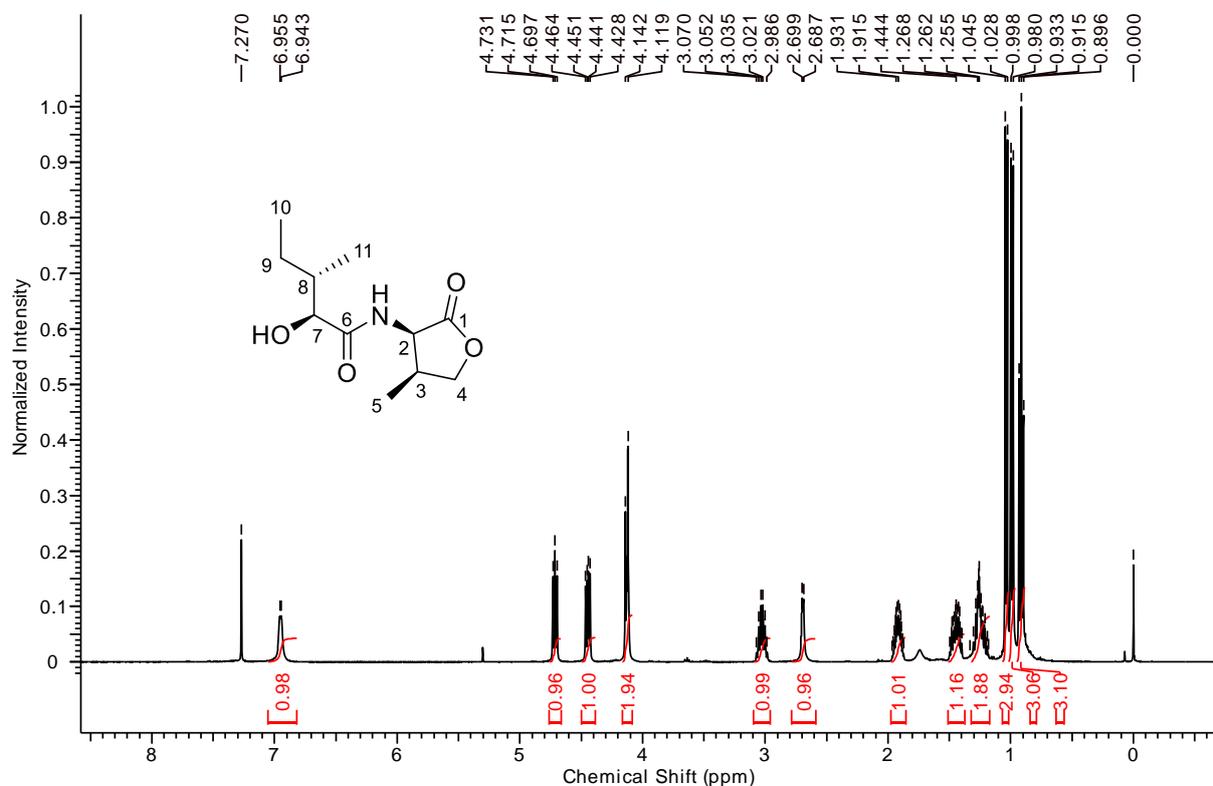
***tert*-Butyl (2*S*,3*S*,*E*)-2-((2*S*,3*S*)-2-hydroxy-3-methylpentanamido)-3-methyl-5-phenylpent-4-enoate (2aI-2)**



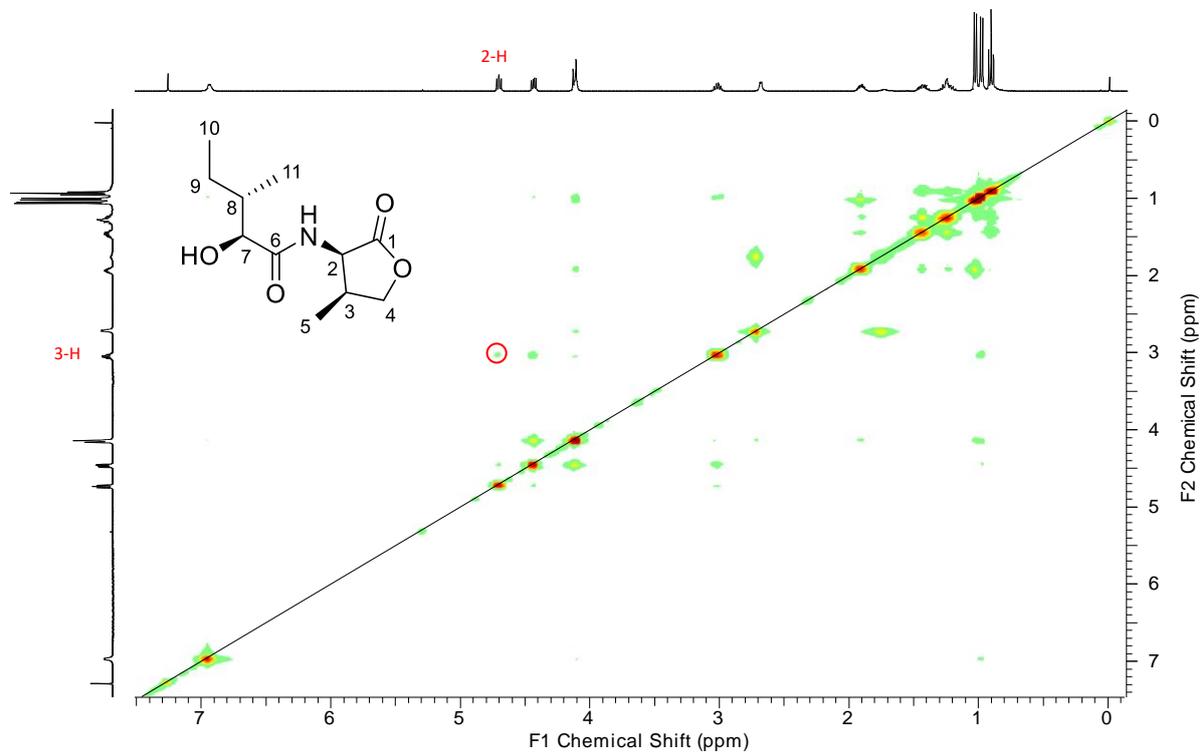
***tert*-Butyl (2*R*,3*R*,*E*)-2-((2*S*,3*S*)-2-hydroxy-3-methylpentanamido)-3-methyl-5-phenylpent-4-enoate (2a1-1)**



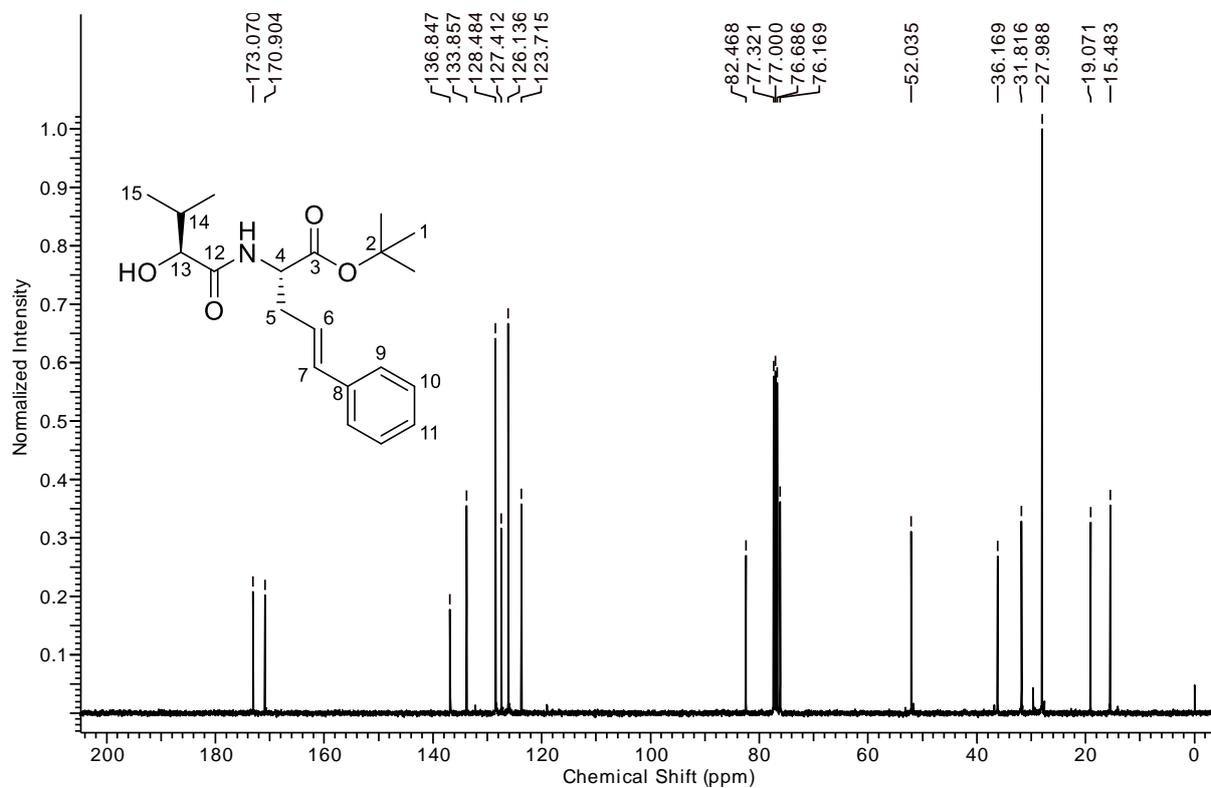
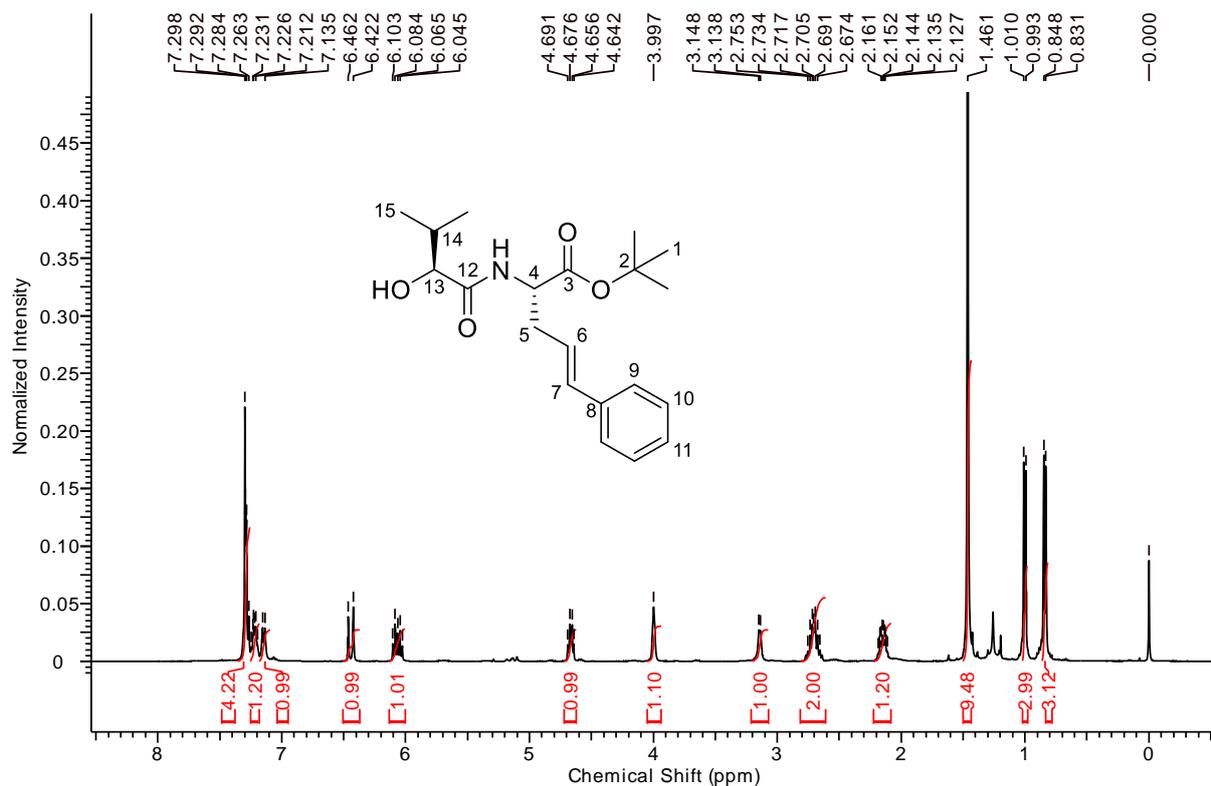
**(2*S*,3*S*)-2-Hydroxy-3-methyl-*N*-((3*R*,4*S*)-4-methyl-2-oxotetrahydrofuran-3-yl)pentanamide  
(SI-33)**



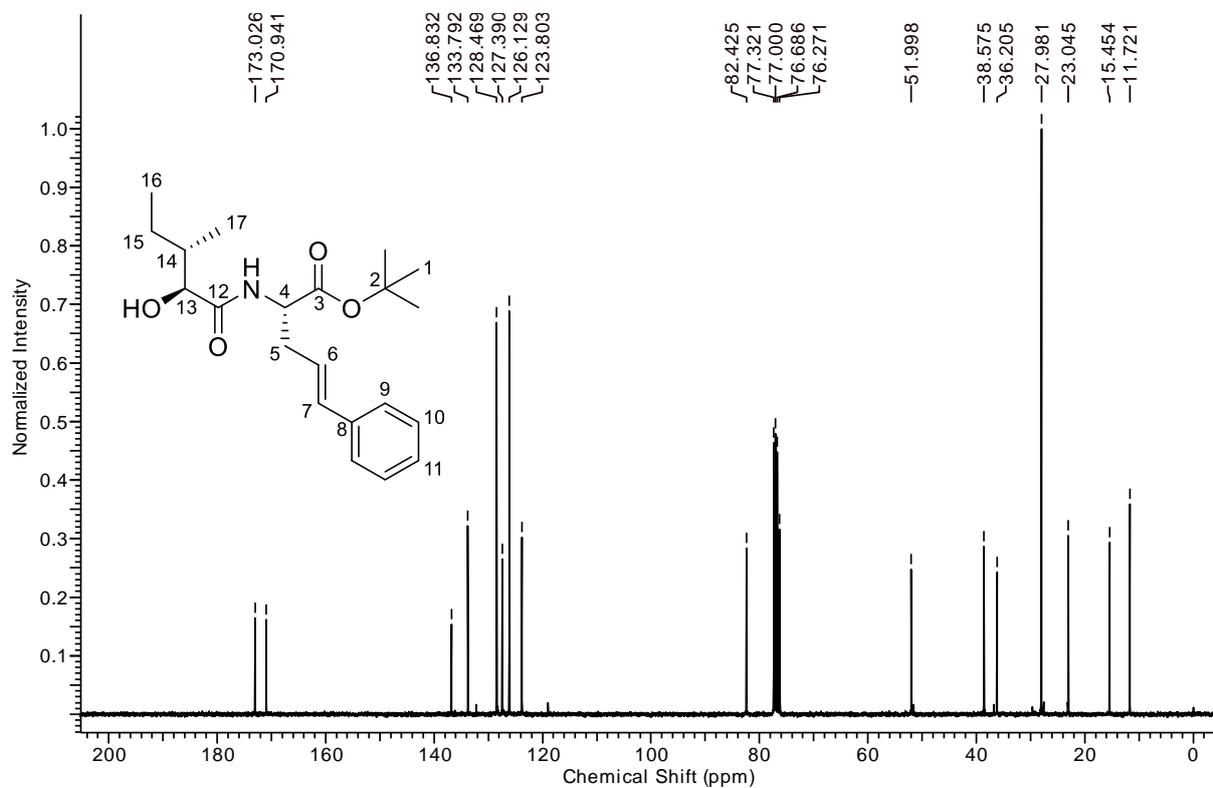
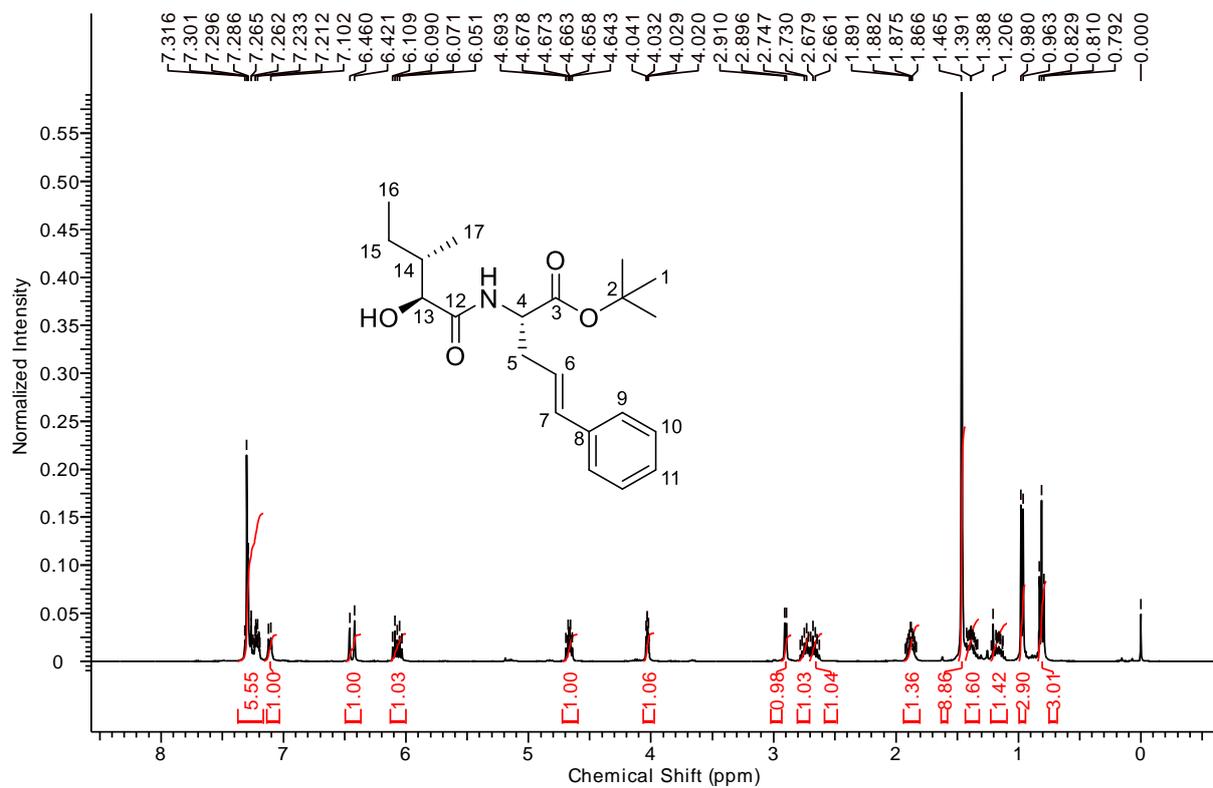
# NOESY of SI-33



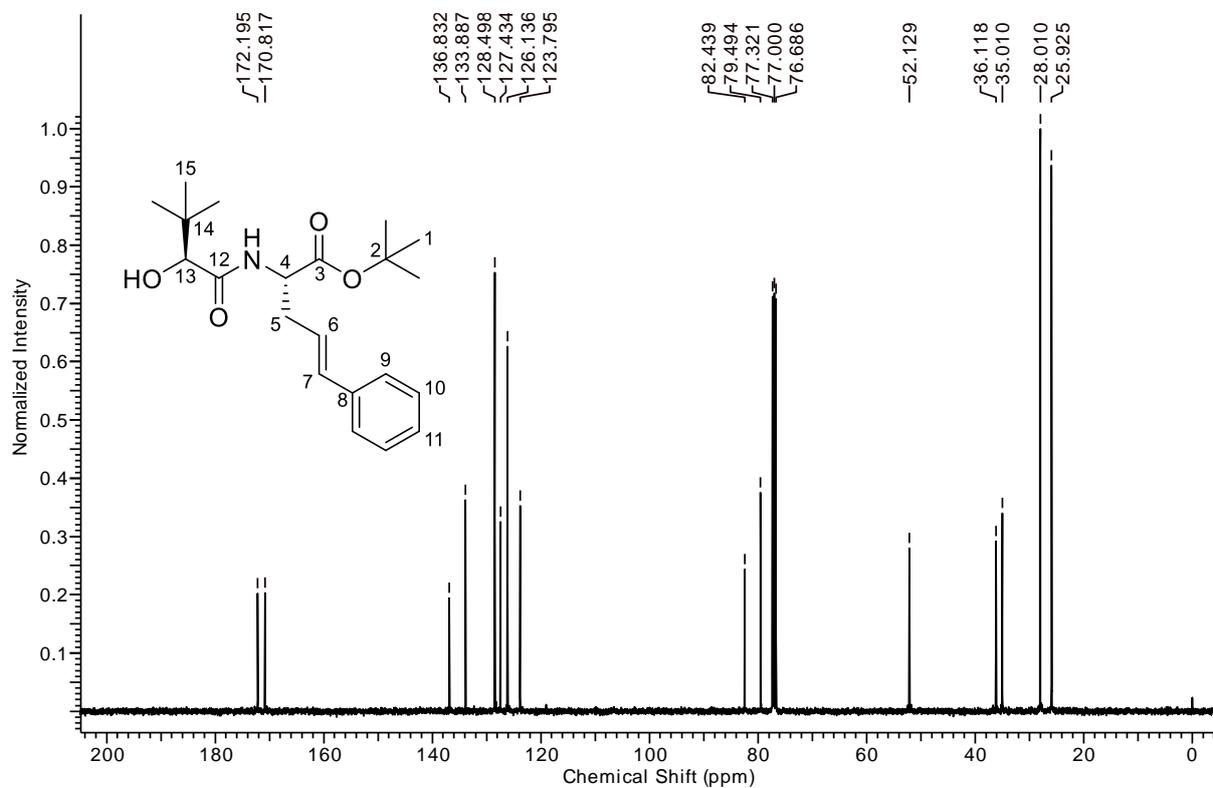
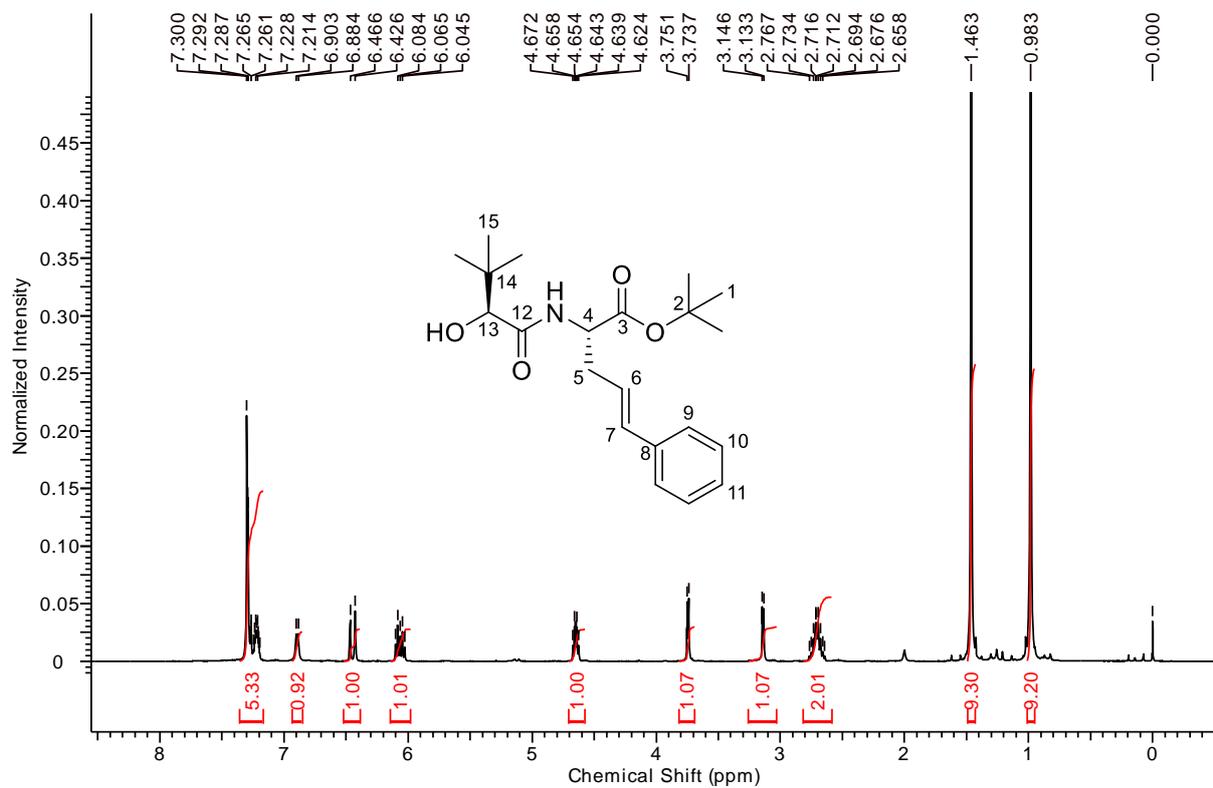
***tert*-Butyl (*S,E*)-2-((*S*)-2-hydroxy-3-methylbutanamido)-5-phenylpent-4-enoate (**2ba'**)**



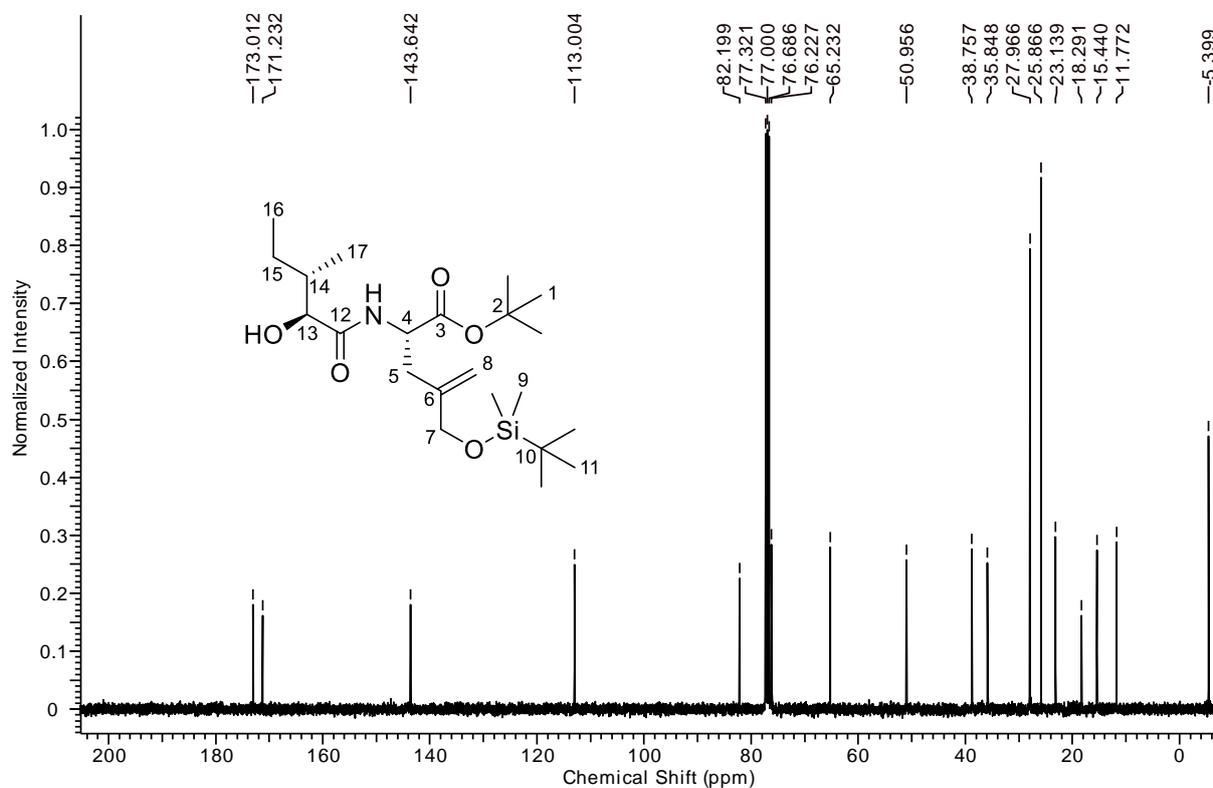
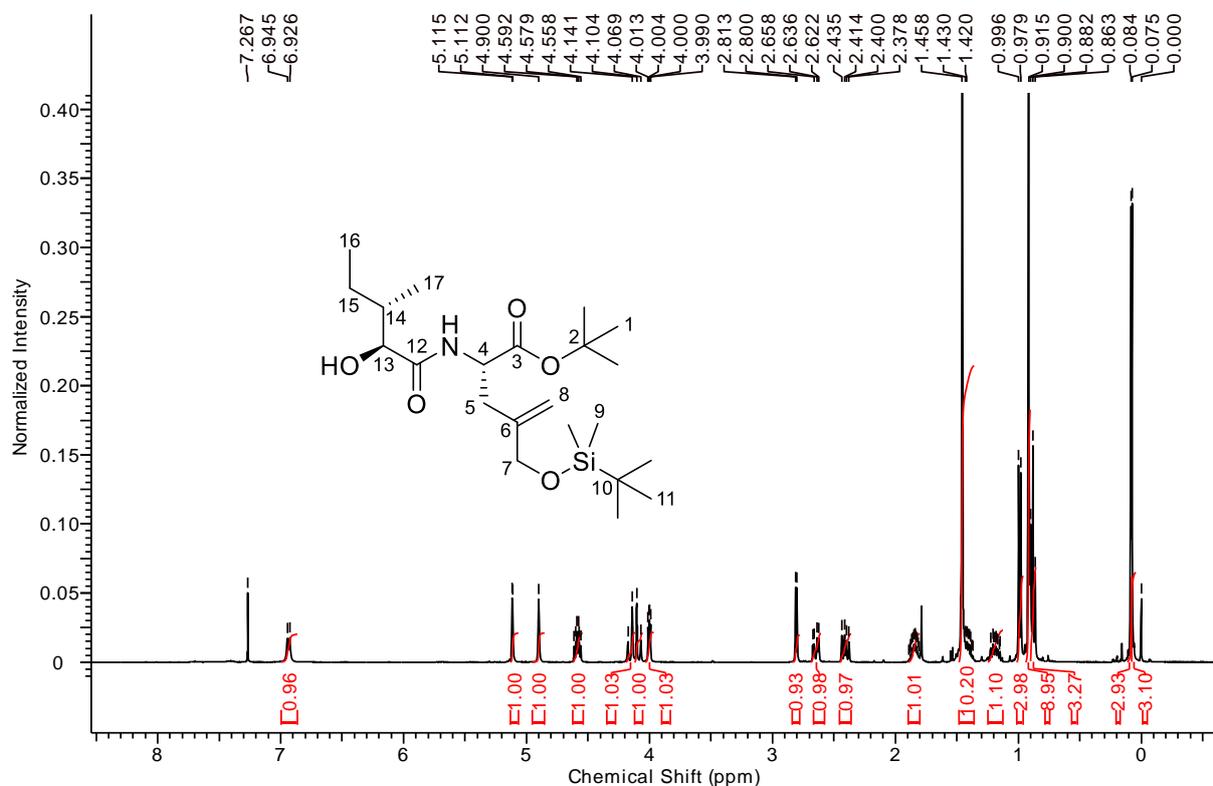
***tert*-Butyl (*S,E*)-2-((2*S*,3*S*)-2-hydroxy-3-methylpentanamido)-5-phenylpent-4-enoate (**2aa'**)**



***tert*-Butyl (*S,E*)-2-((*S*)-2-hydroxy-3,3-dimethylbutanamido)-5-phenylpent-4-enoate (**2da'**)**

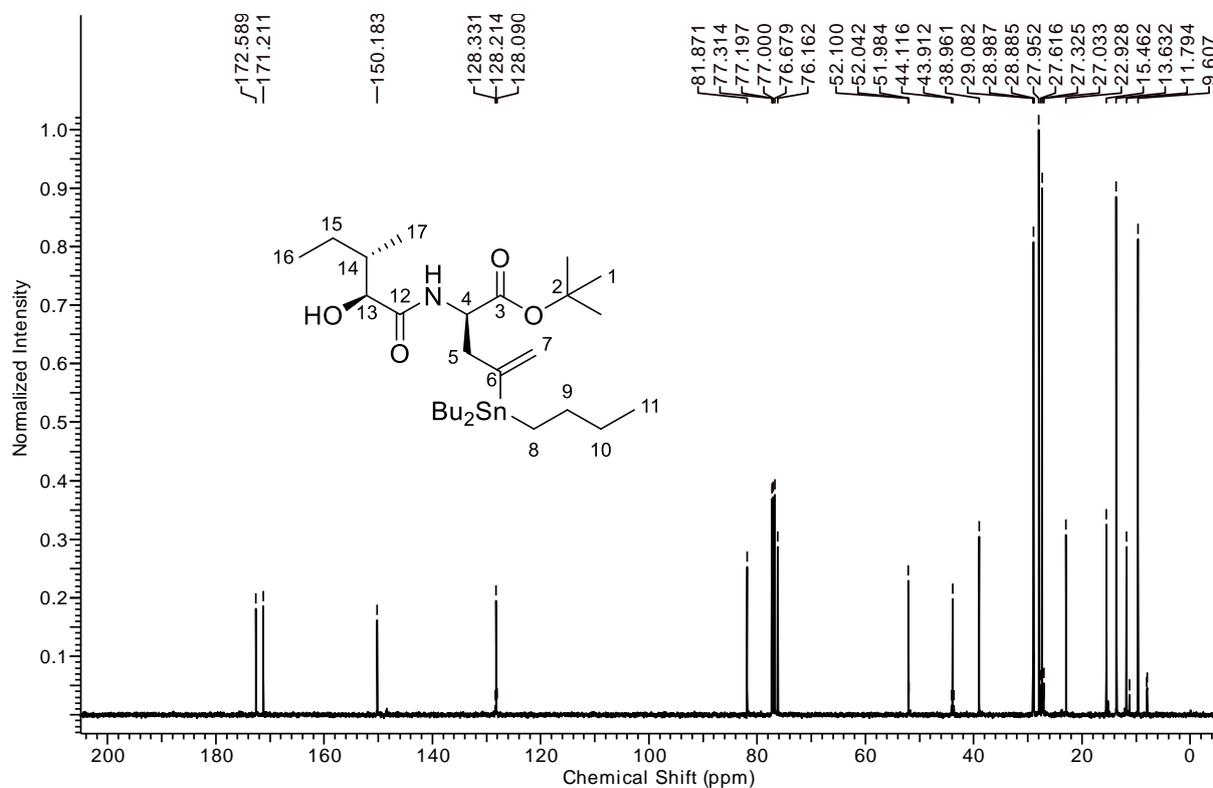
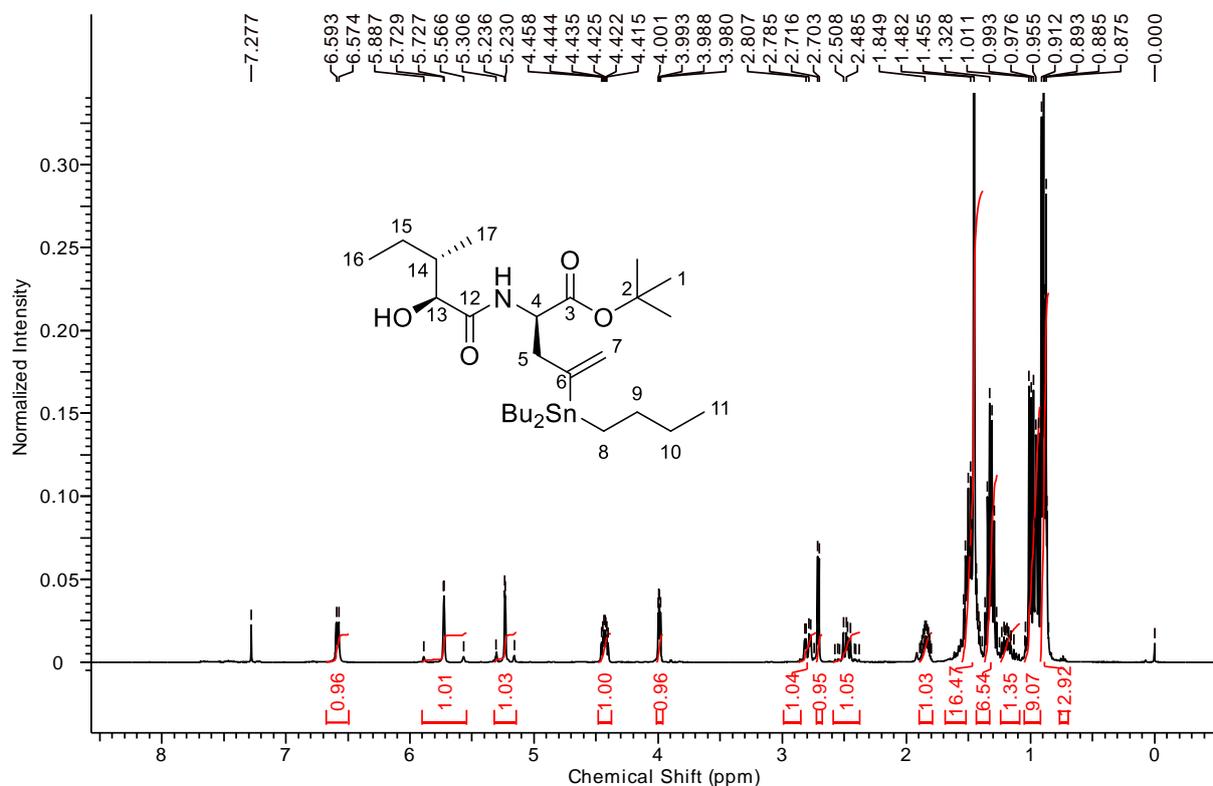


***tert*-Butyl (S)-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)pent-4-enoate (2ag')**

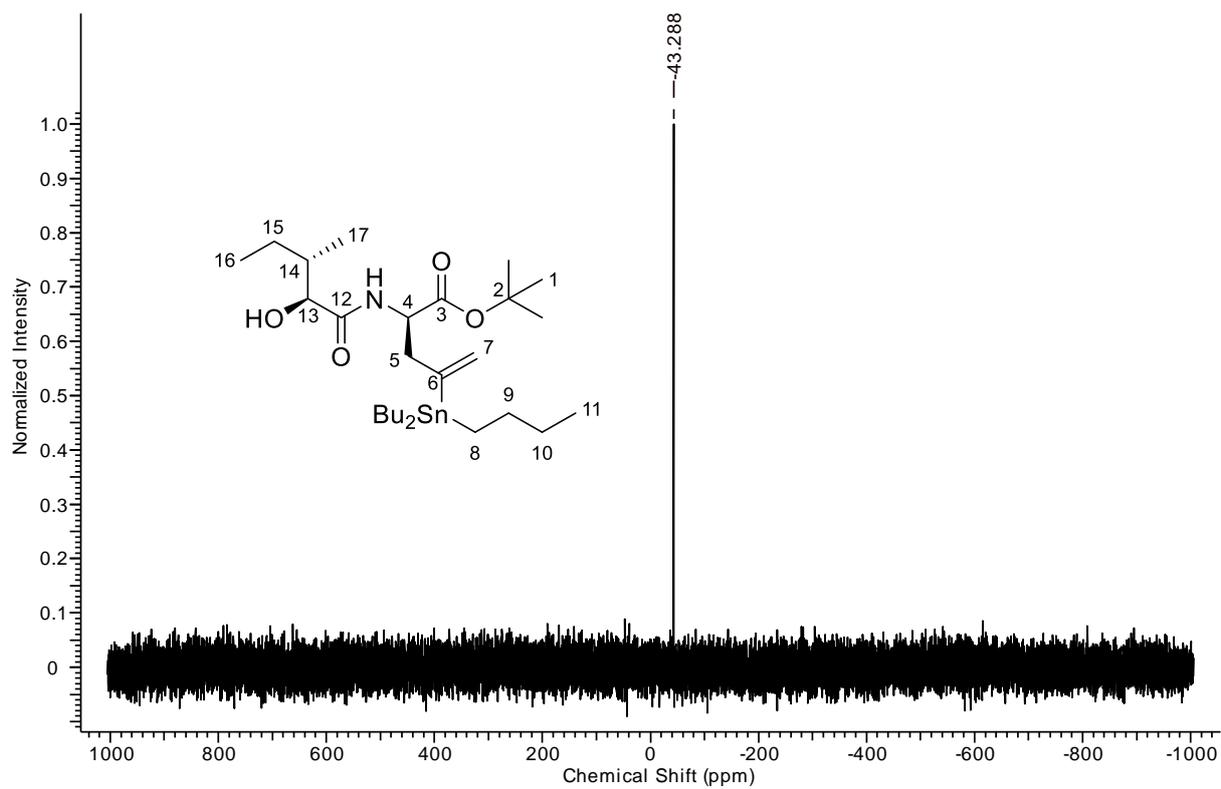


**tert-Butyl  
enoate (2ah)**

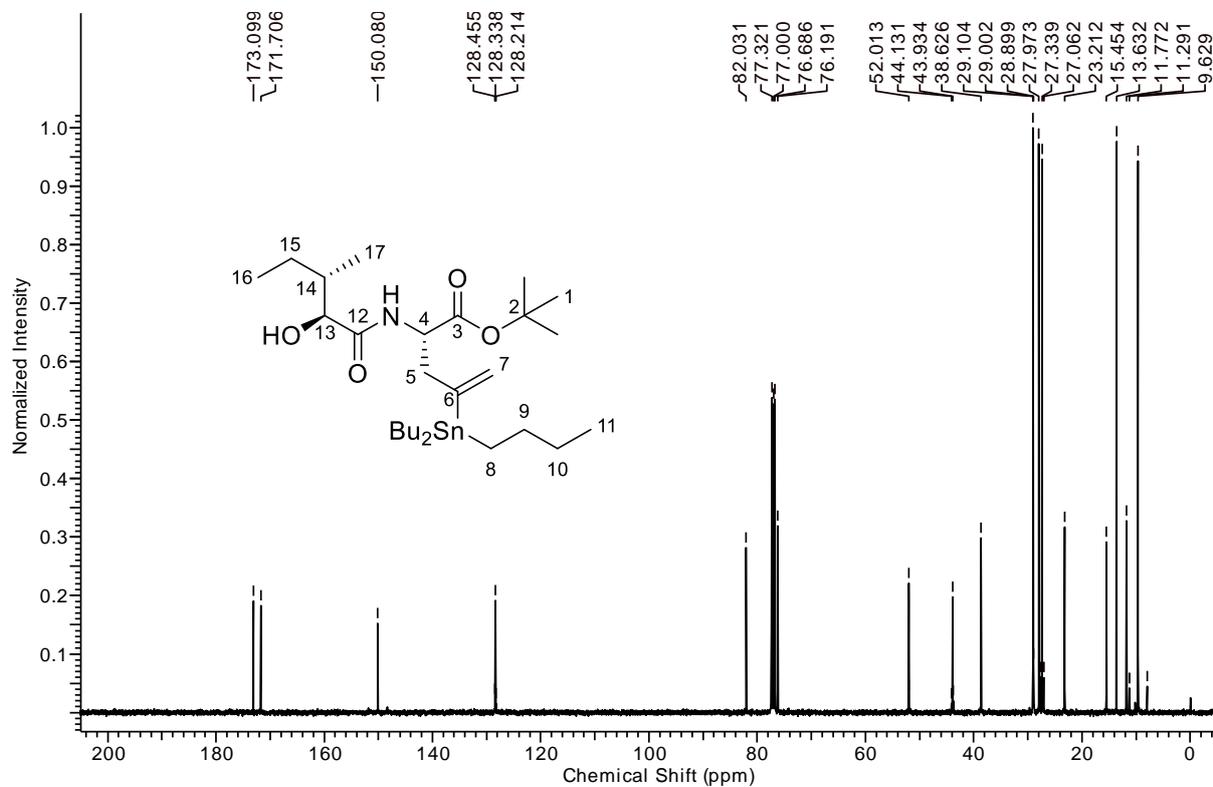
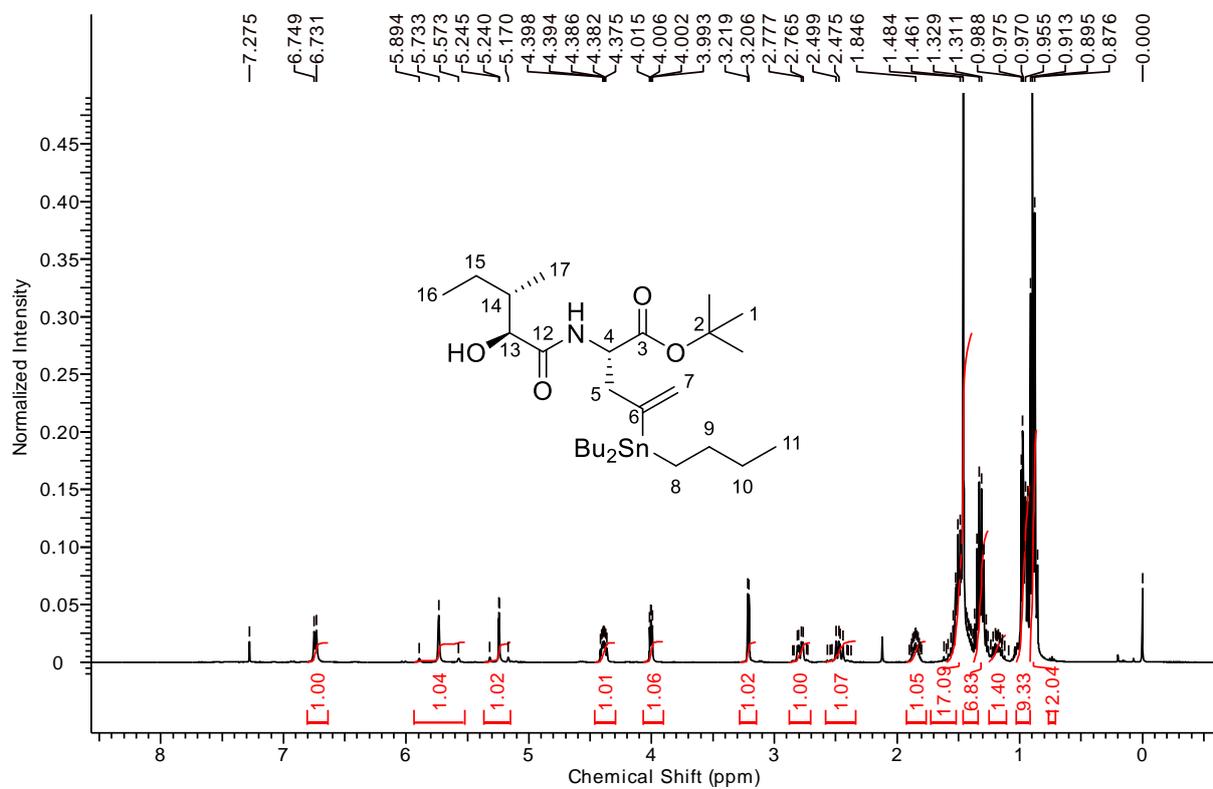
**(R)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-(tributylstannyl)pent-4-**



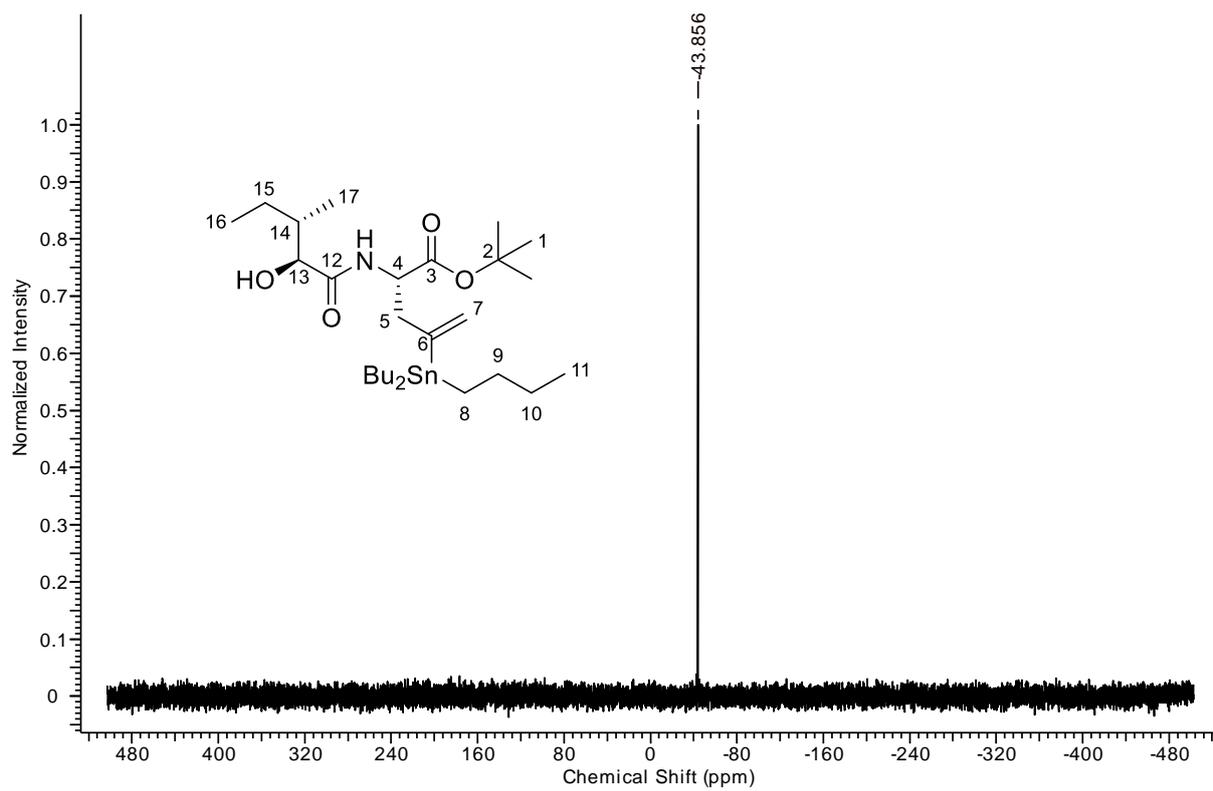
<sup>119</sup>Sn-NMR



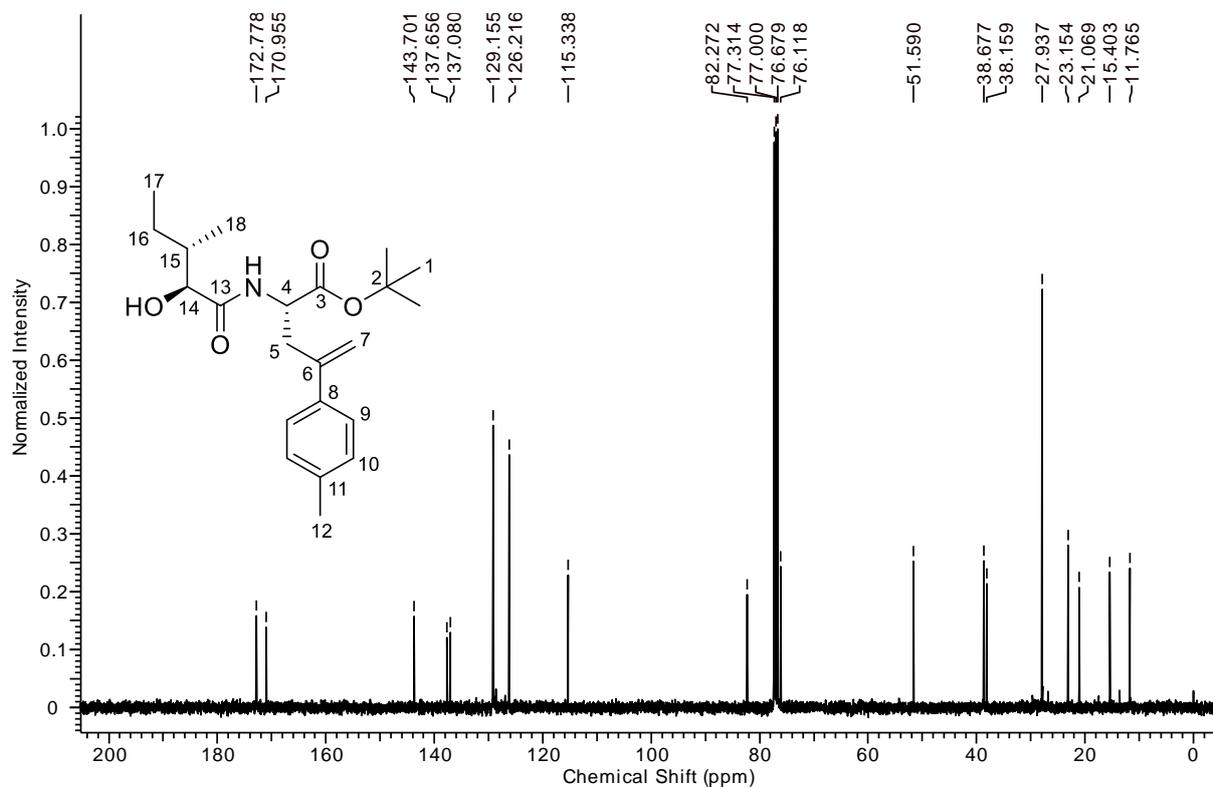
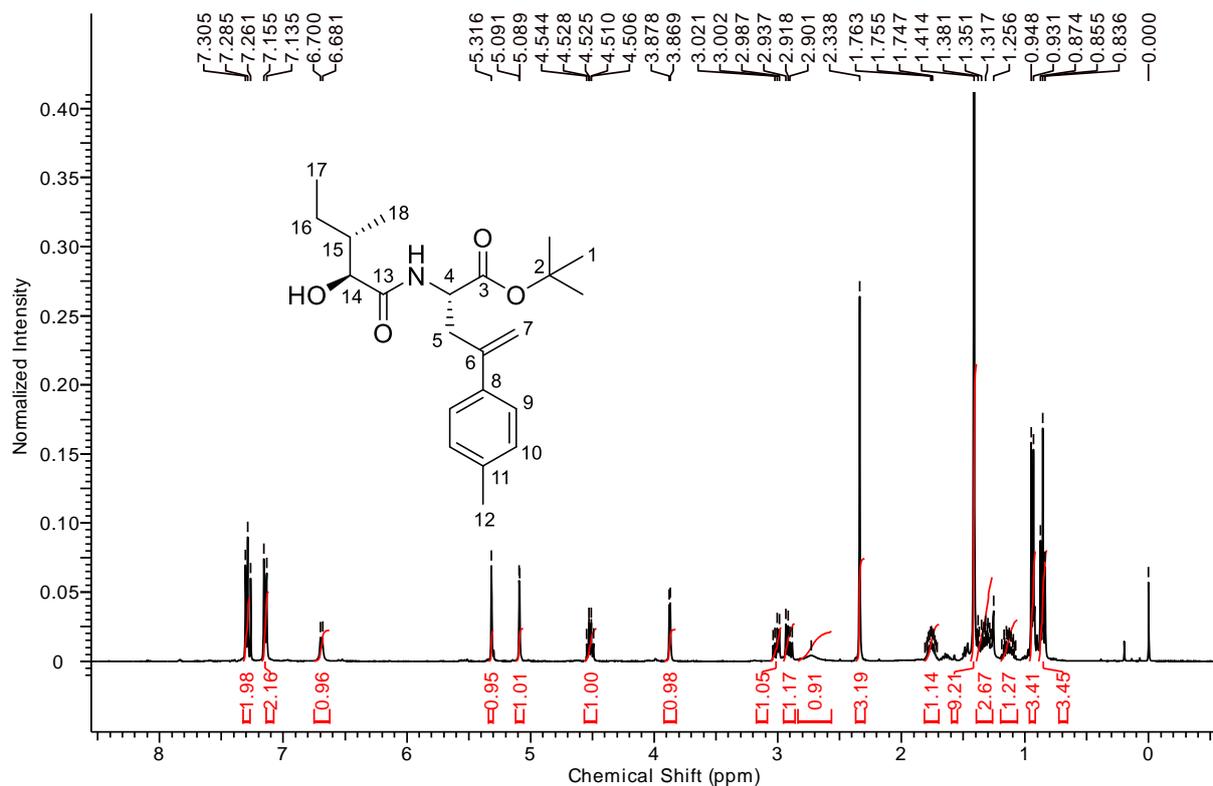
**tert-Butyl (S)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-(tributylstannyl)pent-4-enoate (2ah')**



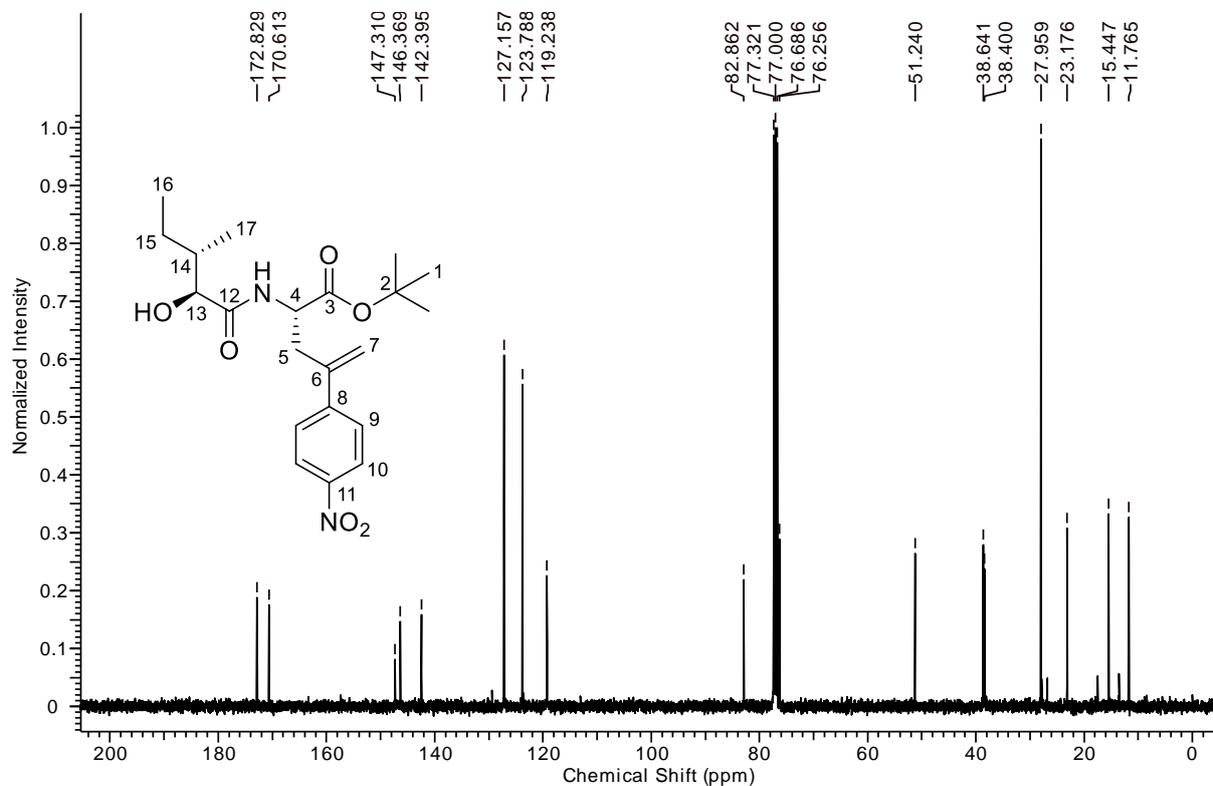
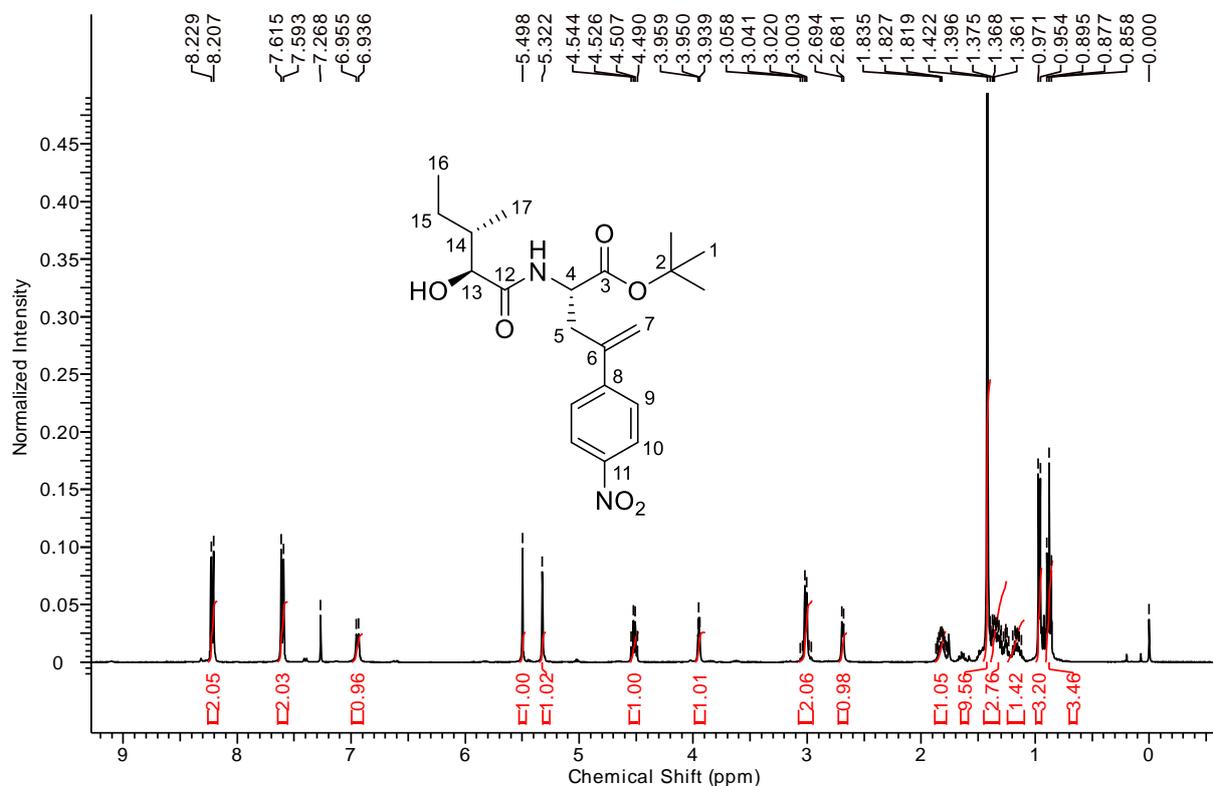
# $^{119}\text{Sn}$ -NMR



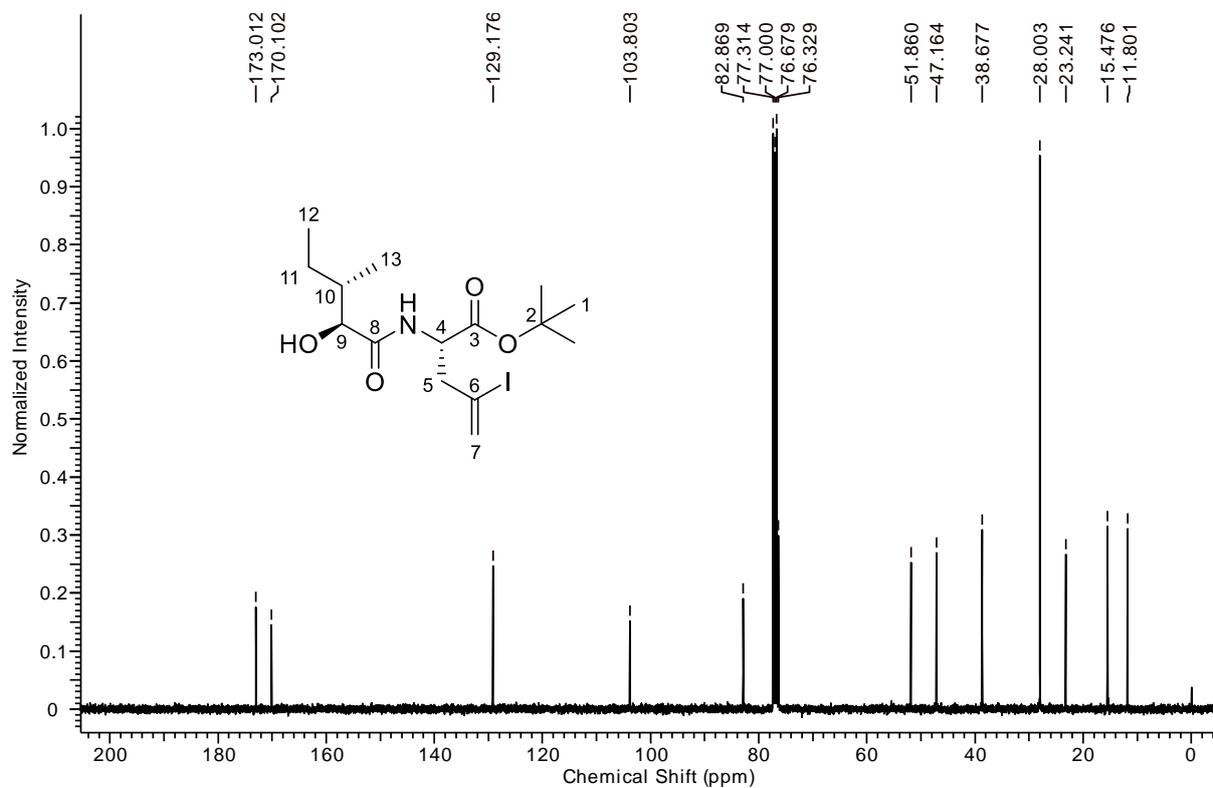
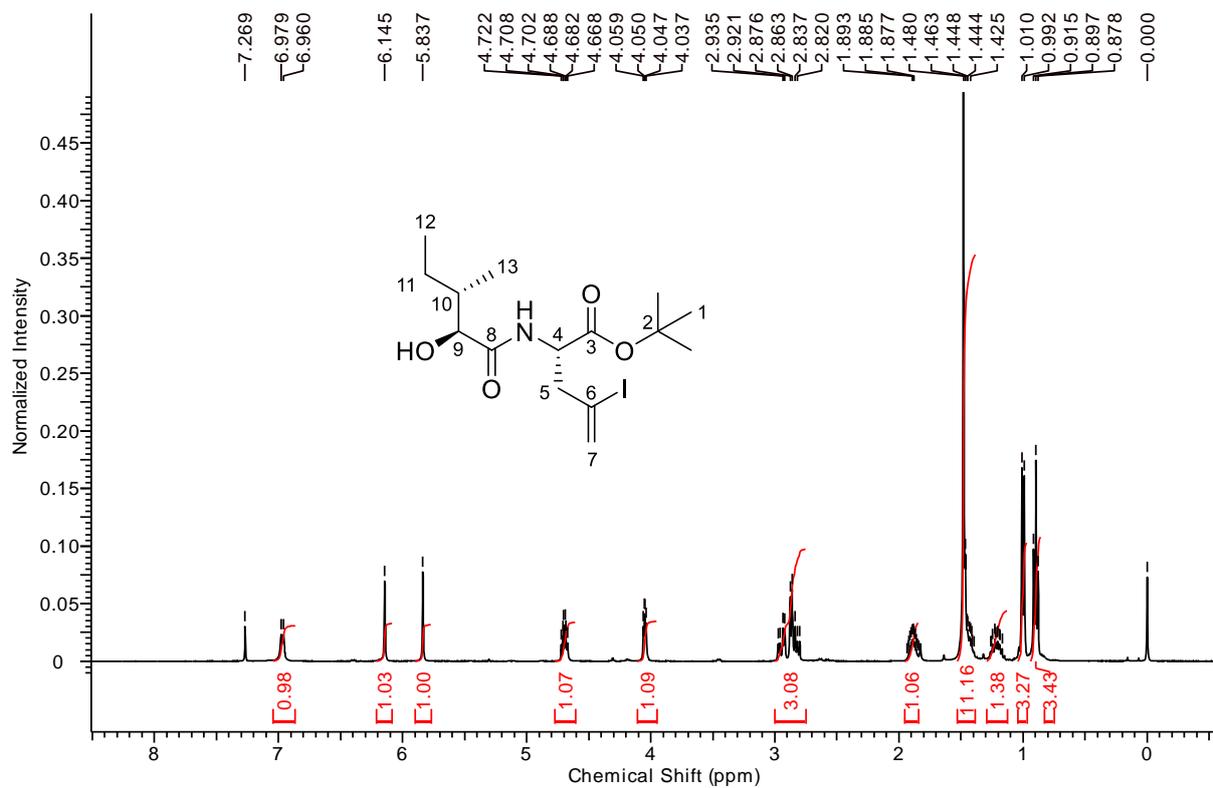
***tert*-Butyl (S)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-(*p*-tolyl)pent-4-enoate (3a)**



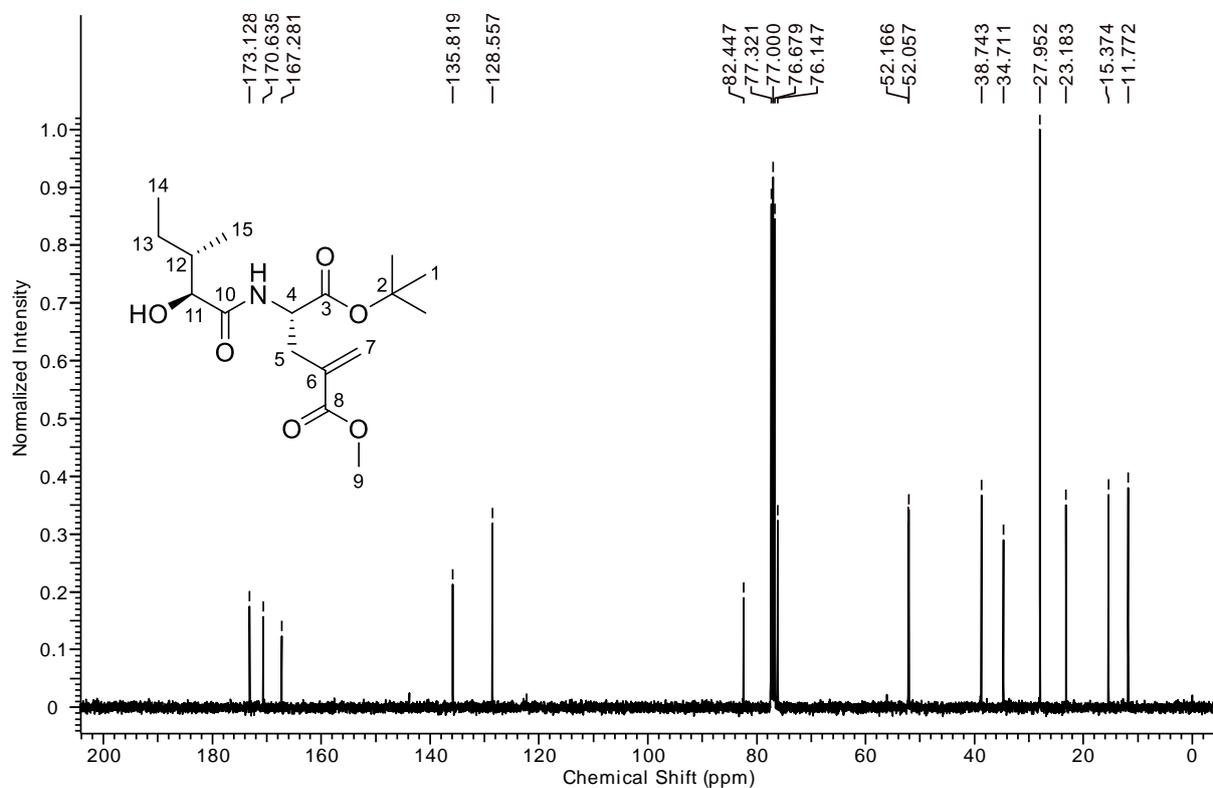
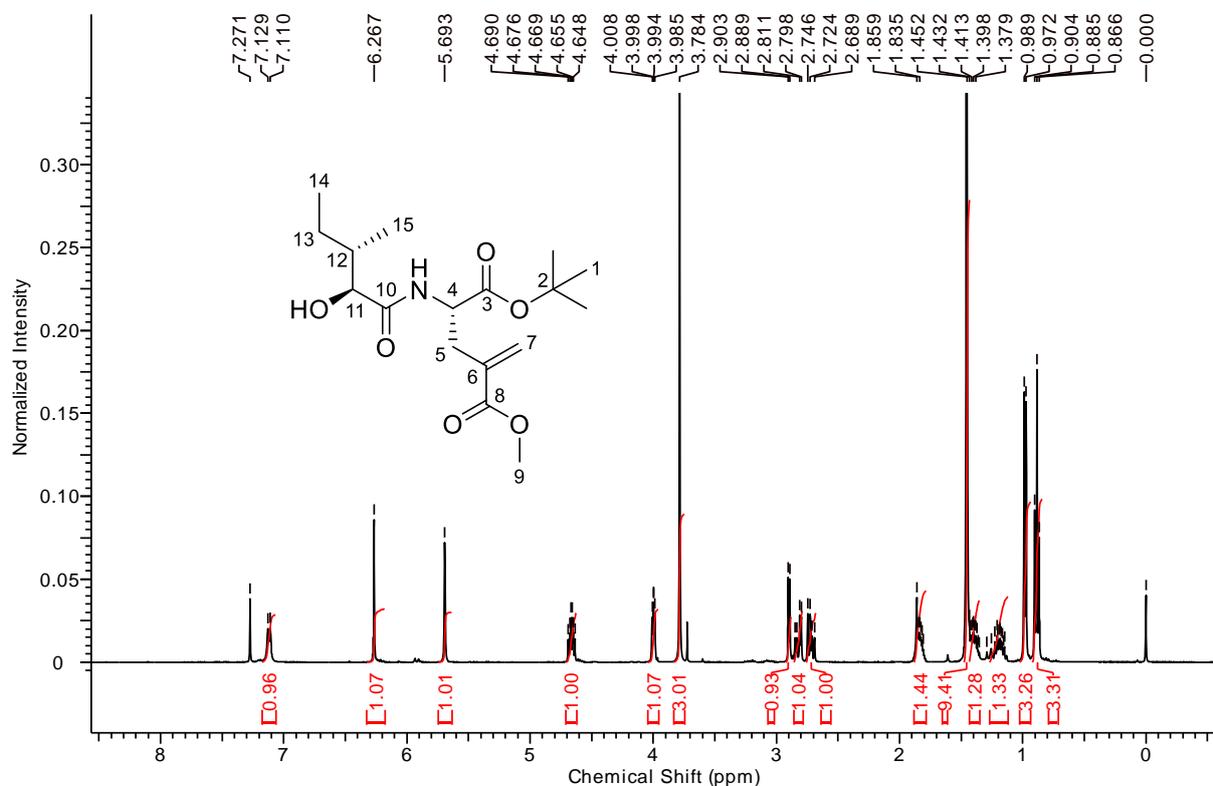
***tert*-Butyl (S)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-(4-nitrophenyl)pent-4-enoate (3b)**



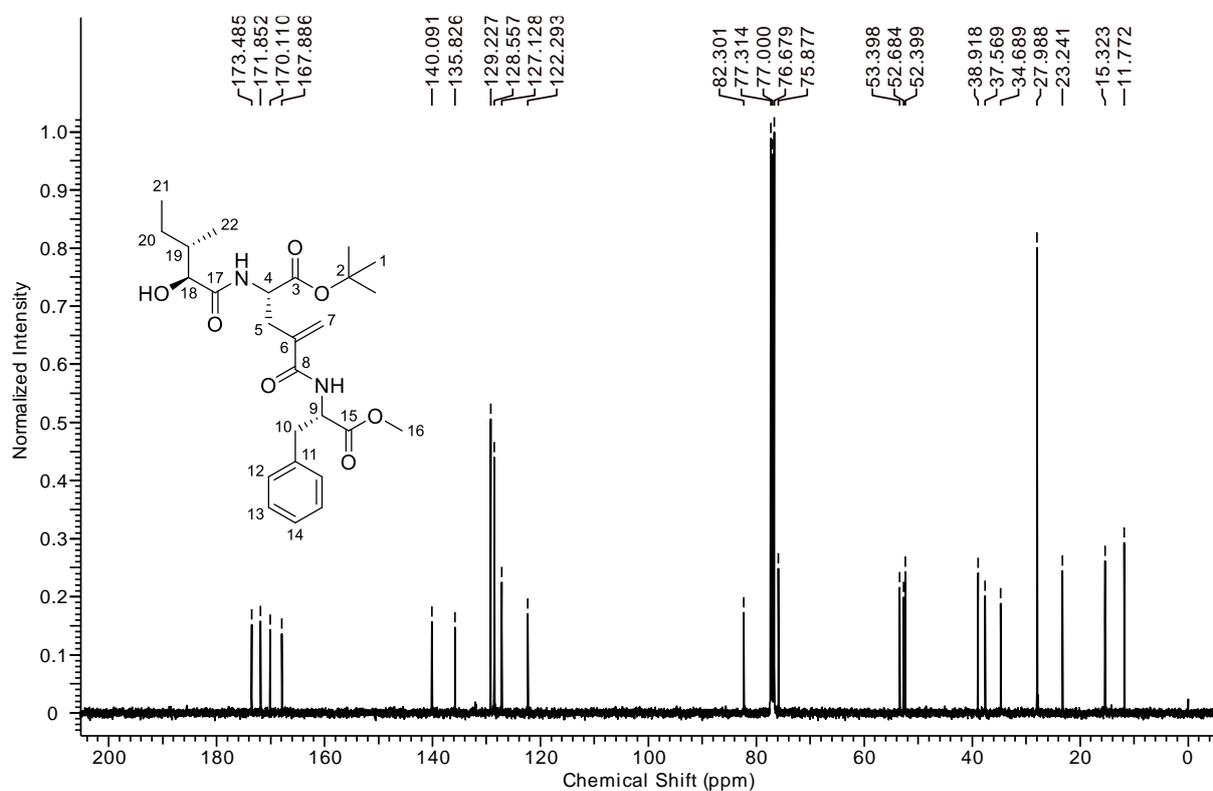
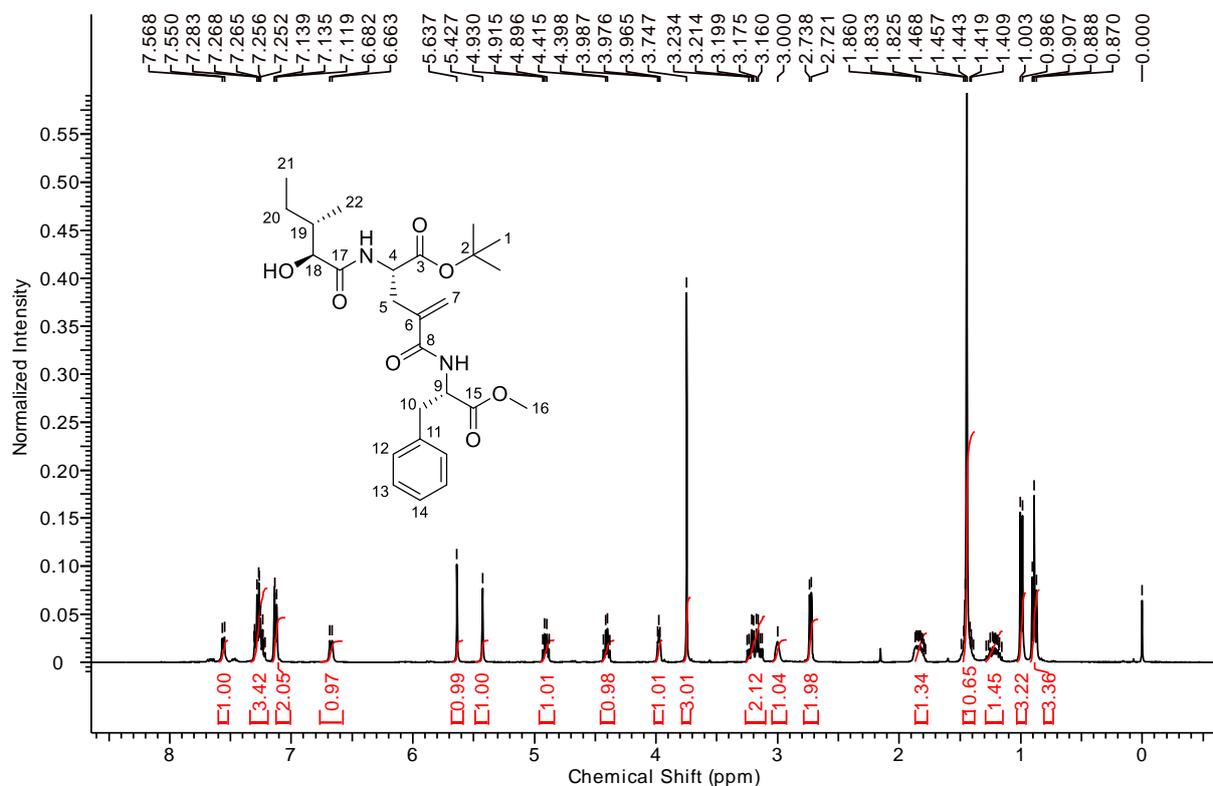
***tert*-Butyl (S)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-iodopent-4-enoate (4)**



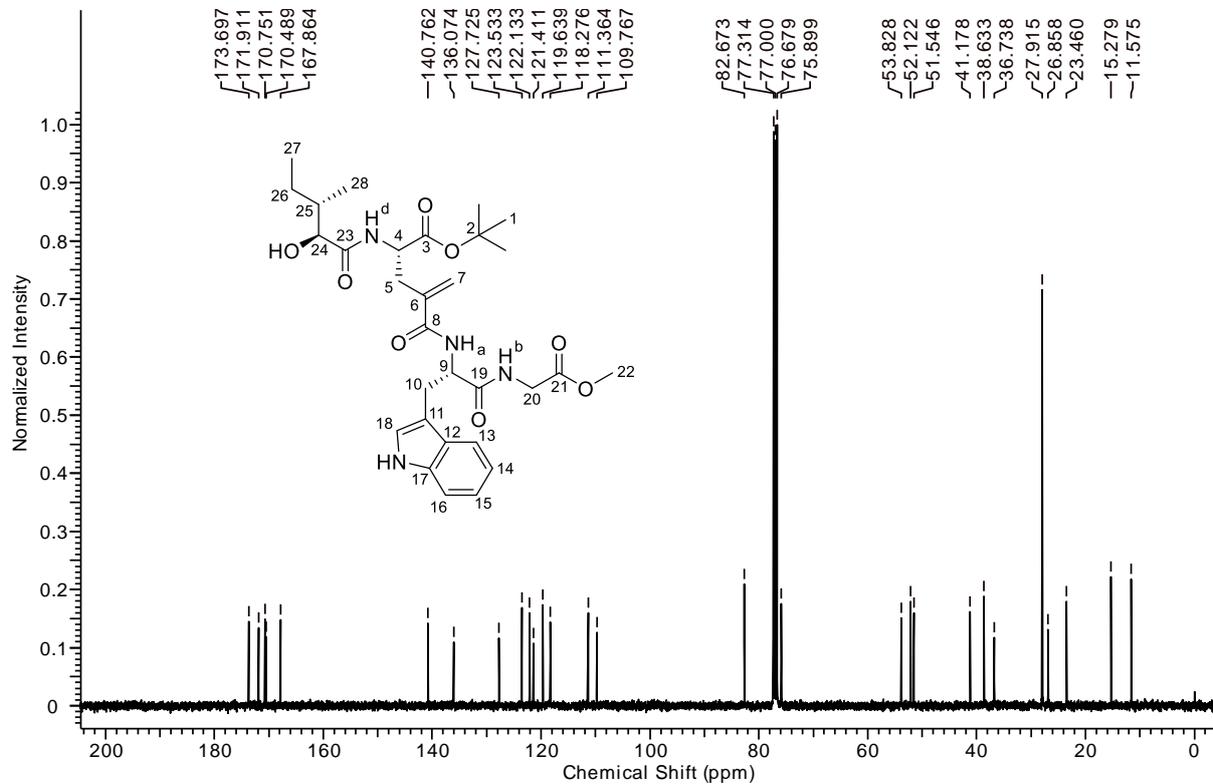
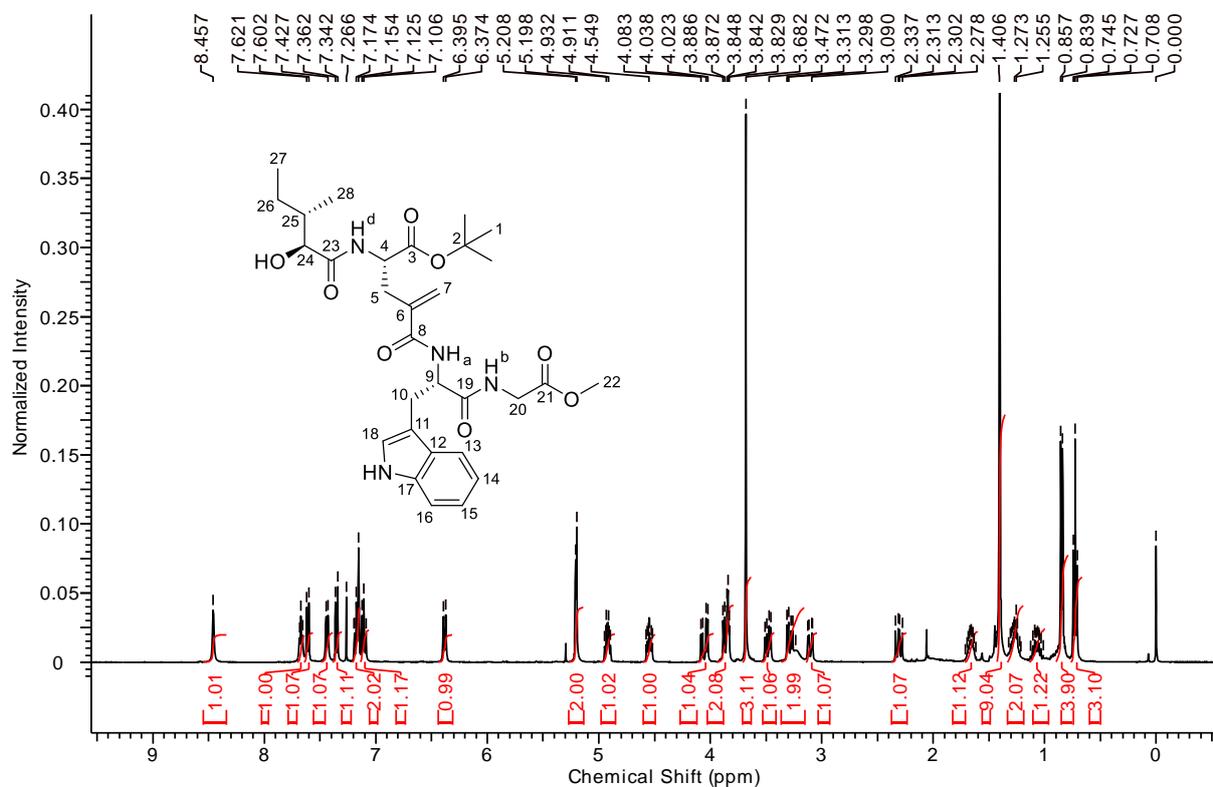
**1-(*tert*-Butyl) 5-methyl (*S*)-2-((2*S*,3*S*)-2-hydroxy-3-methylpentanamido)-4-methylenepentanedioate (5)**



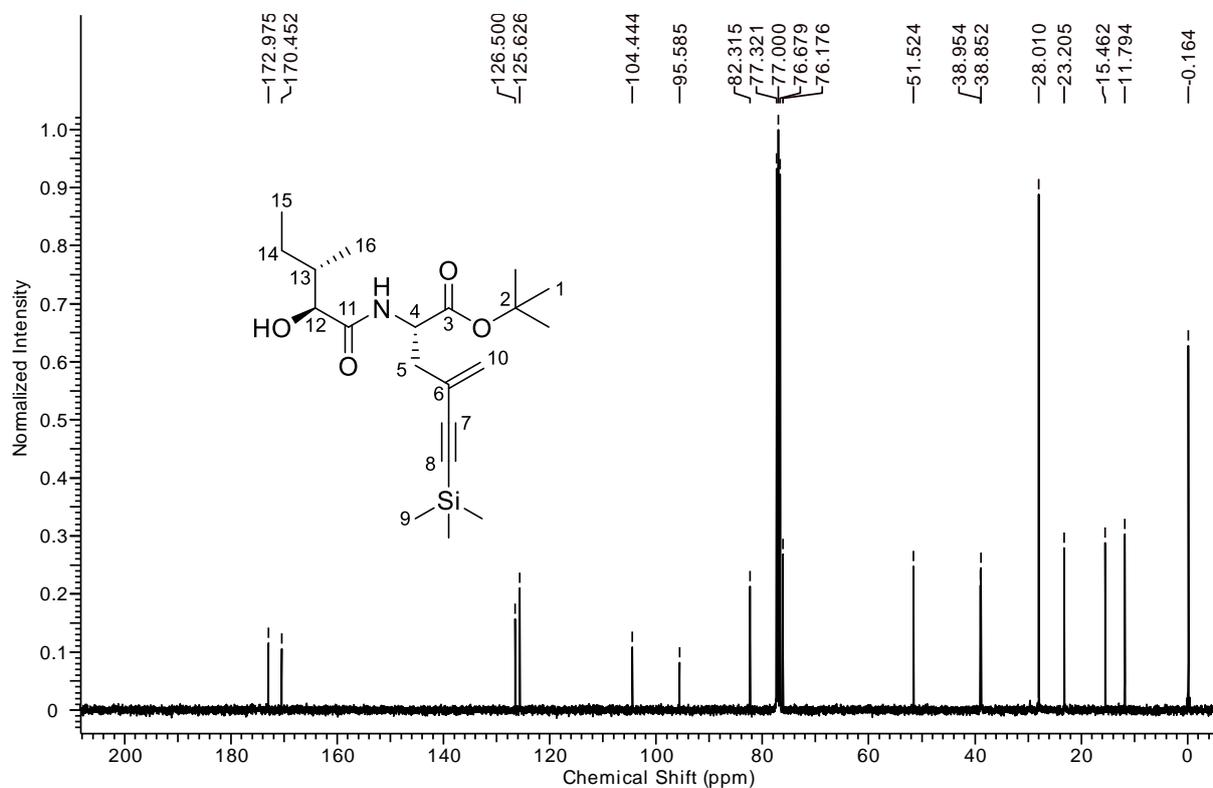
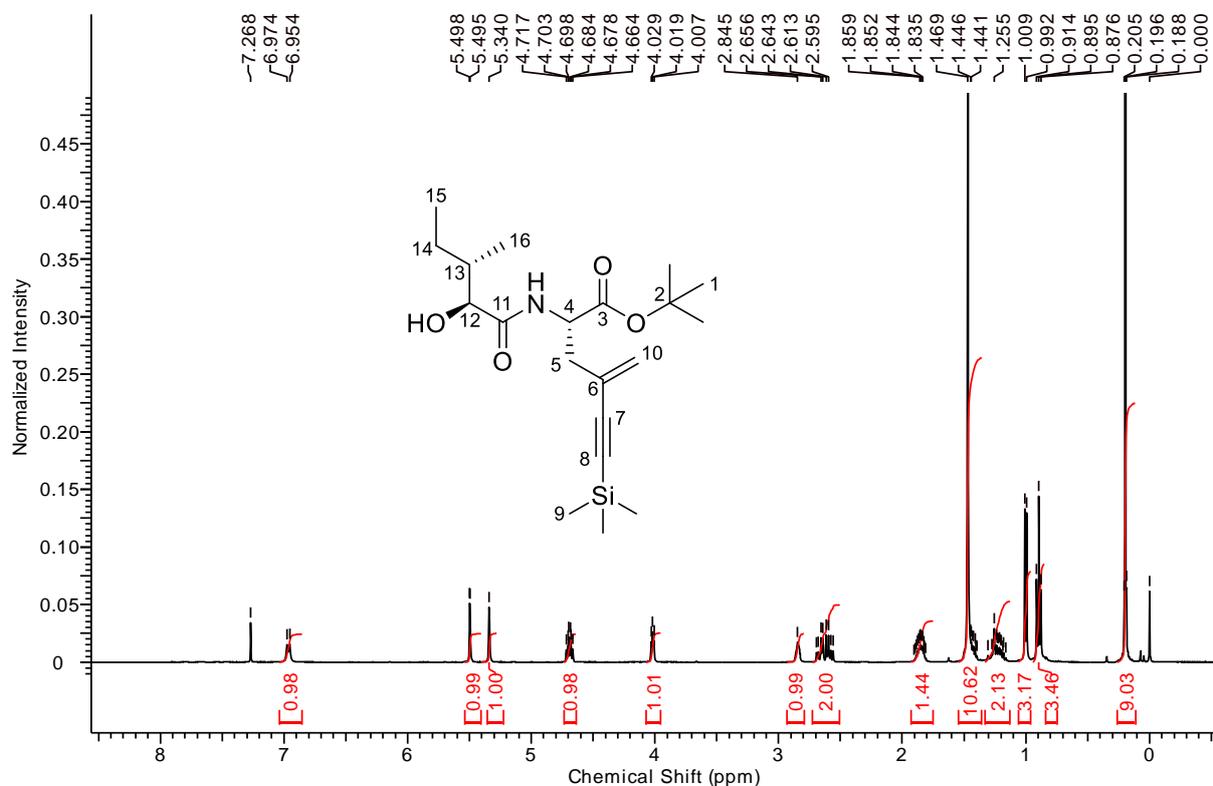
**tert-Butyl (S)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-(((S)-1-methoxy-1-oxo-3-phen-yl-propan-2-yl)carbamoyl)pent-4-enoate (6a)**



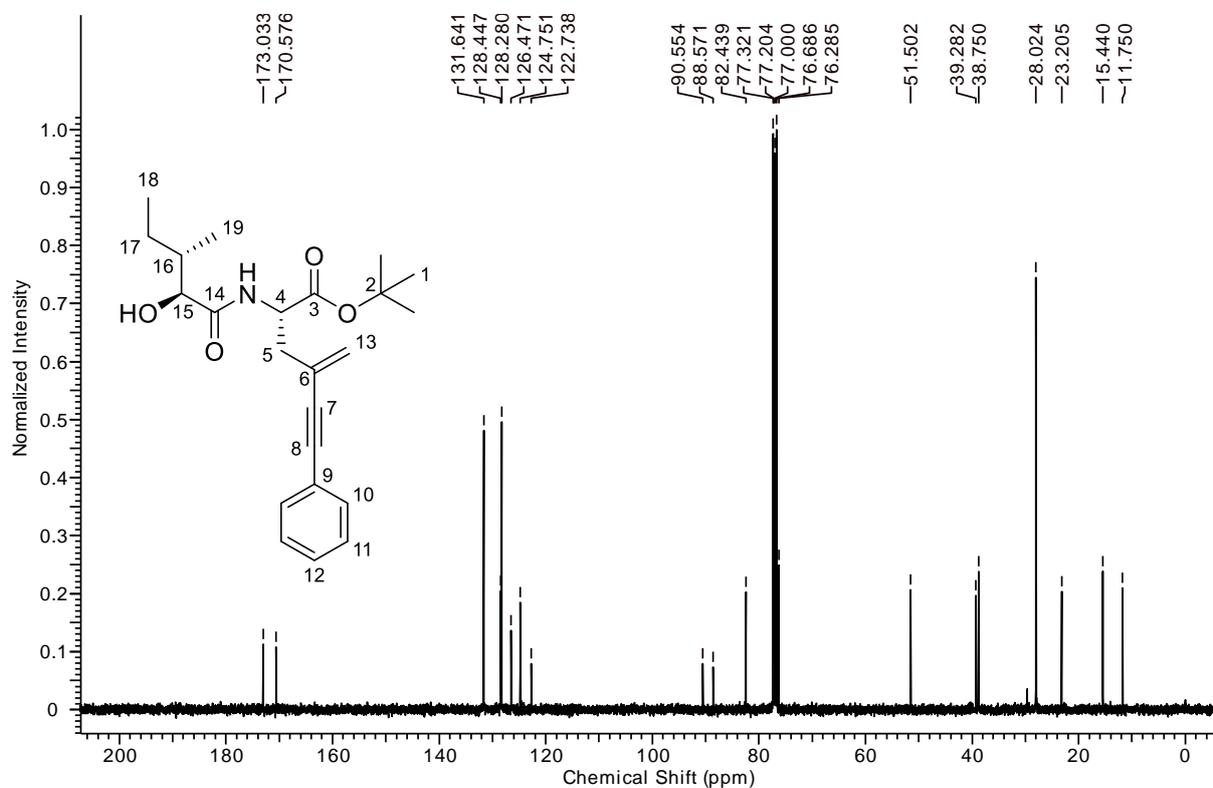
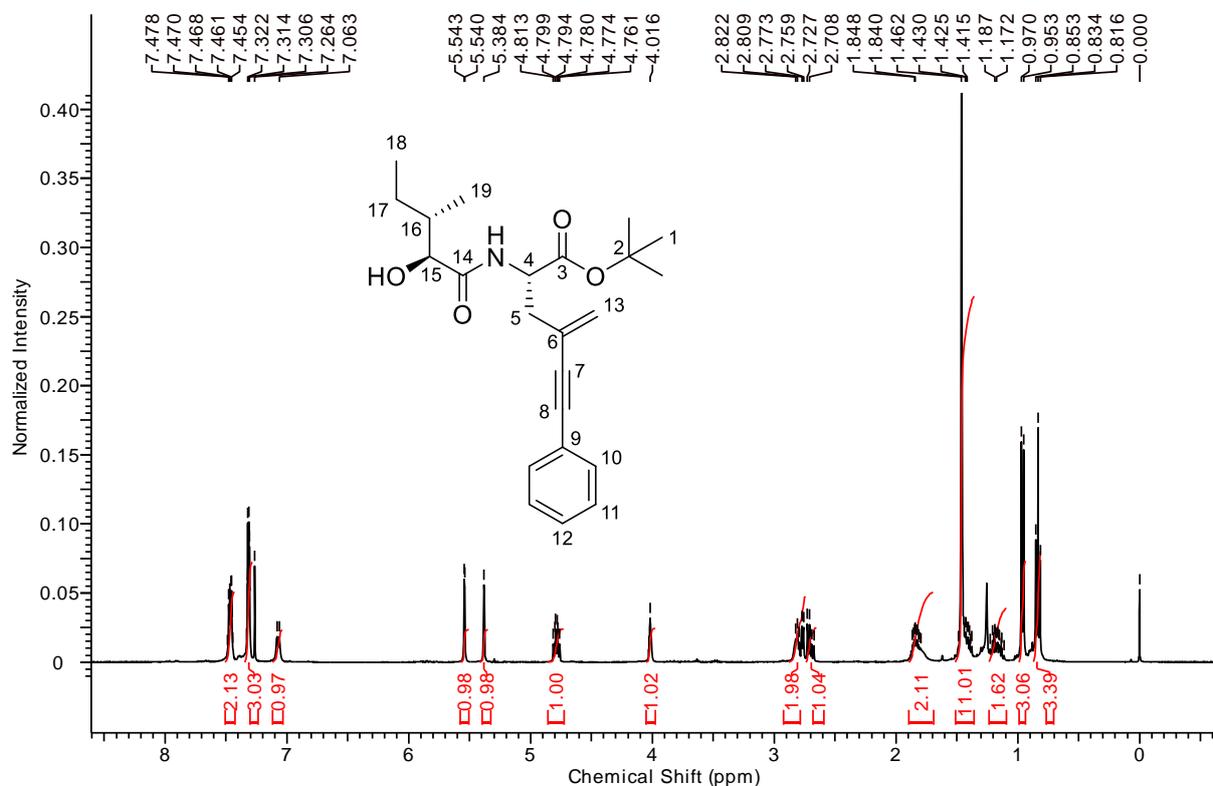
**tert-Butyl (S)-4-(((S)-3-(1H-indol-3-yl)-1-((2-methoxy-2-oxoethyl)amino)-1-oxopropan-2-yl)carbamoyl)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)pent-4-enoate (6b)**



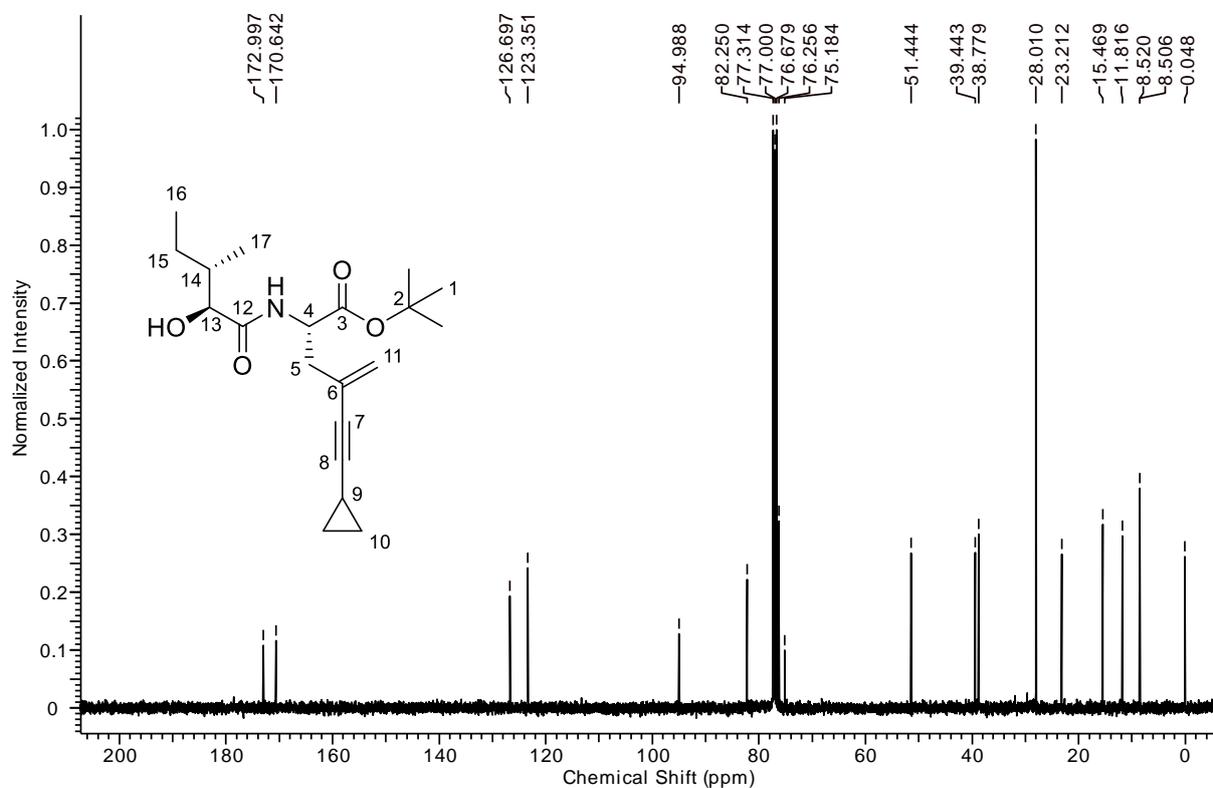
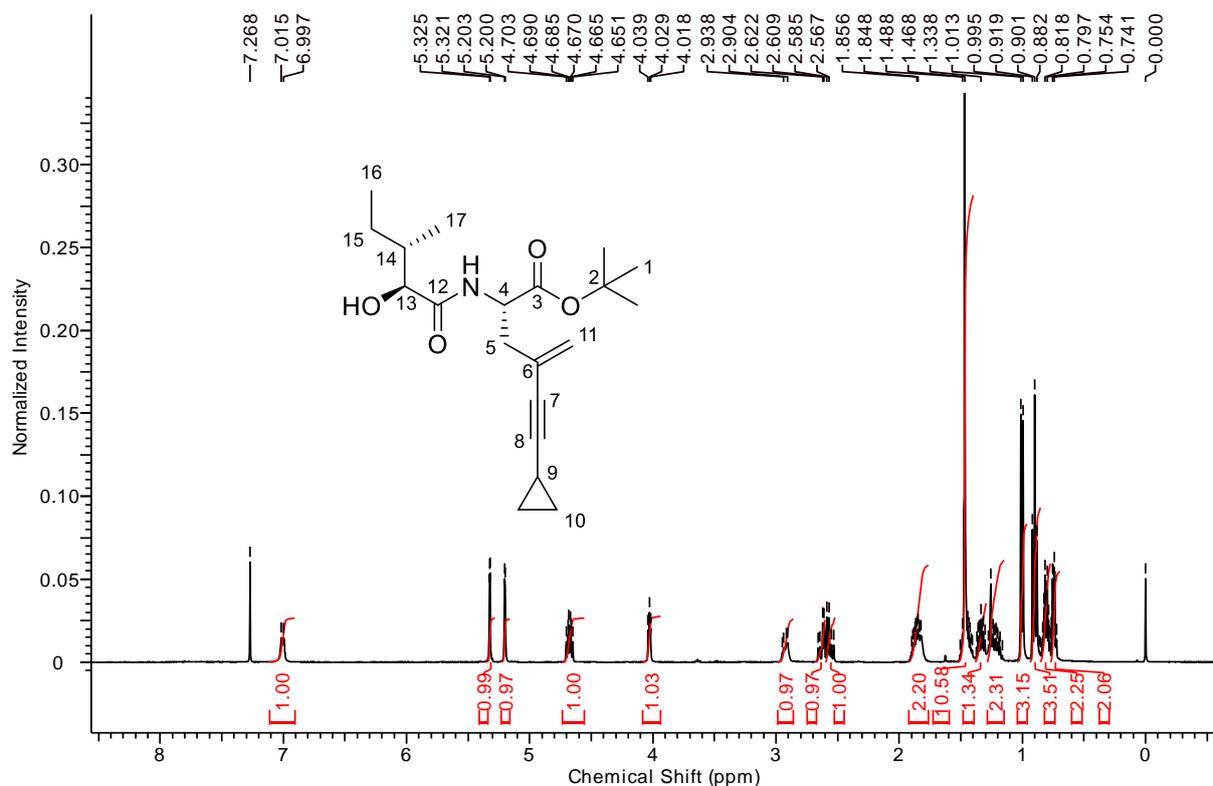
***tert*-Butyl (S)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-methylene-6-(trimethylsilyl)-hex-5-ynoate (7a)**



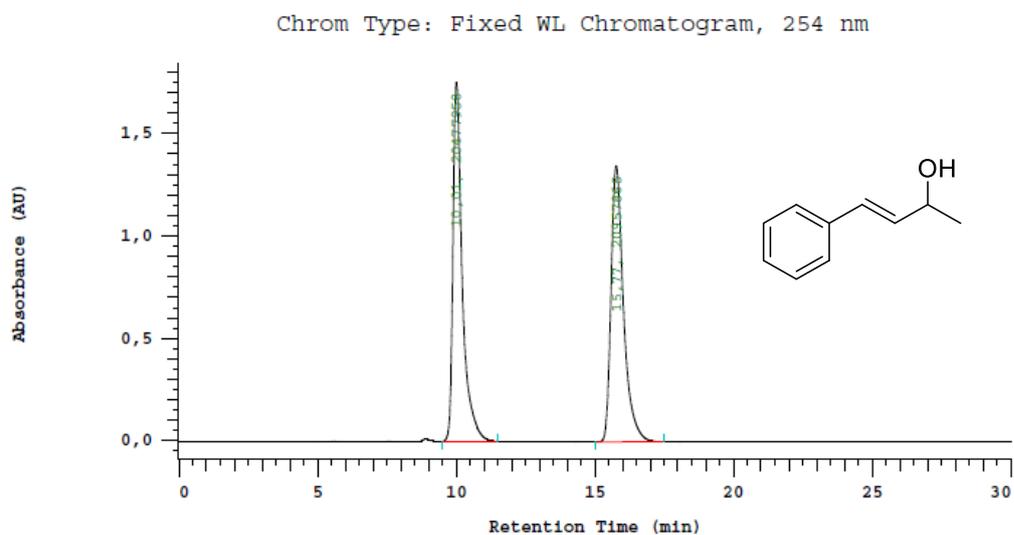
**tert-Butyl (R)-2-((2S,3S)-2-hydroxy-3-methylpentanamido)-4-methylene-6-phenylhex-5-ynoate (7b)**



***tert*-Butyl (*R*)-6-cyclopropyl-2-((2*S*,3*S*)-2-hydroxy-3-methylpentanamido)-4-methylenehex-5-ynoate (7c)**

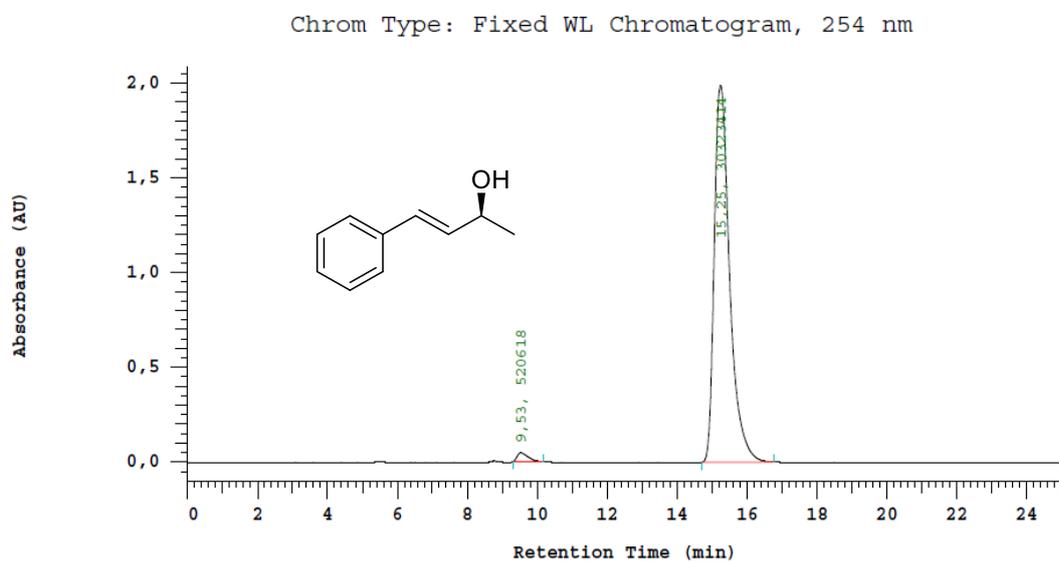


## 6. HPLC and GC Chromatograms



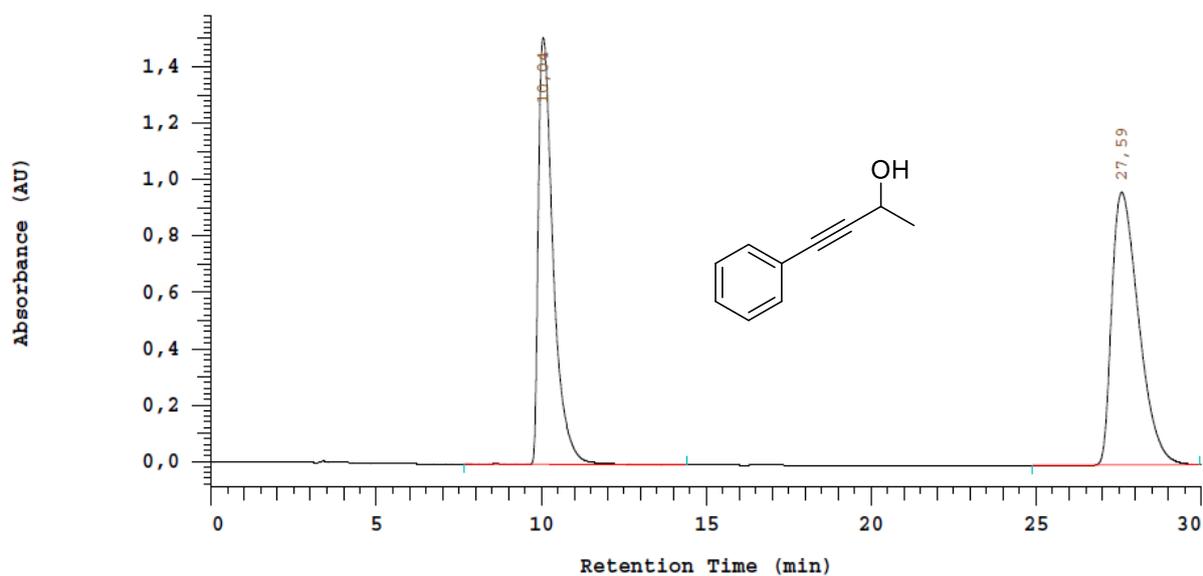
**HPLC:** Column: Chiralcel OD-H, *n*-hexane/*i*-PrOH 9:1, 30 min, 1.0 mL/min, 20 °C.

No.	RT	Area	Area %
1	10,01	20477958	49,421
2	15,77	20957865	50,579
		41435823	100,000



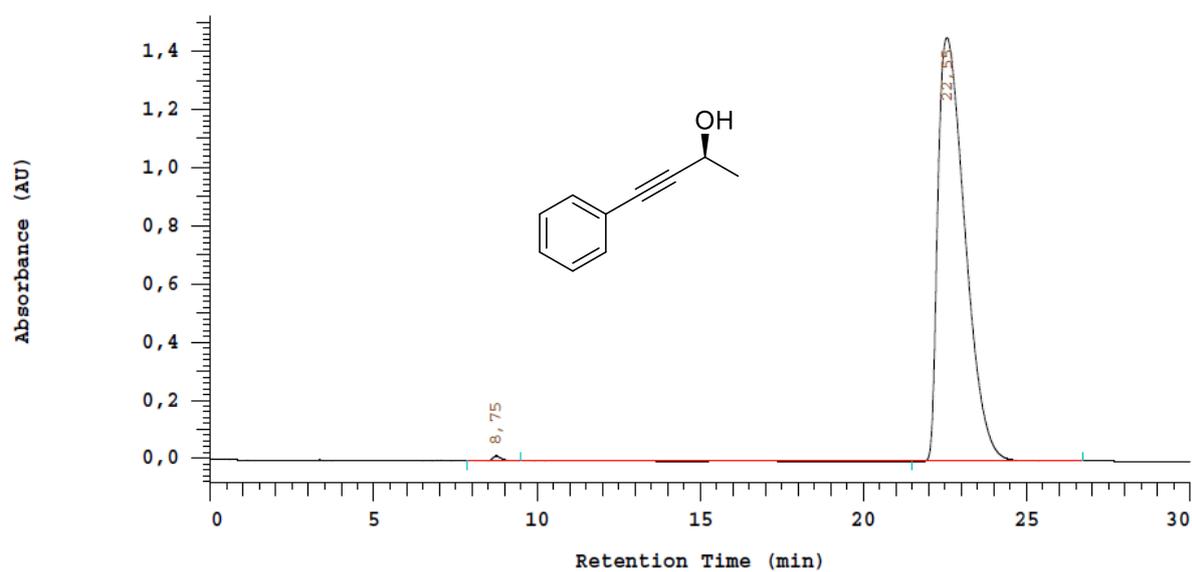
**HPLC:** Column: Chiralcel OD-H, *n*-hexane/*i*-PrOH 9:1, 30 min, 1.0 mL/min, 20 °C.

No.	RT	Area	Area %
1	9,53	520618	1,688
2	15,25	30323414	98,312
		30844032	100,000



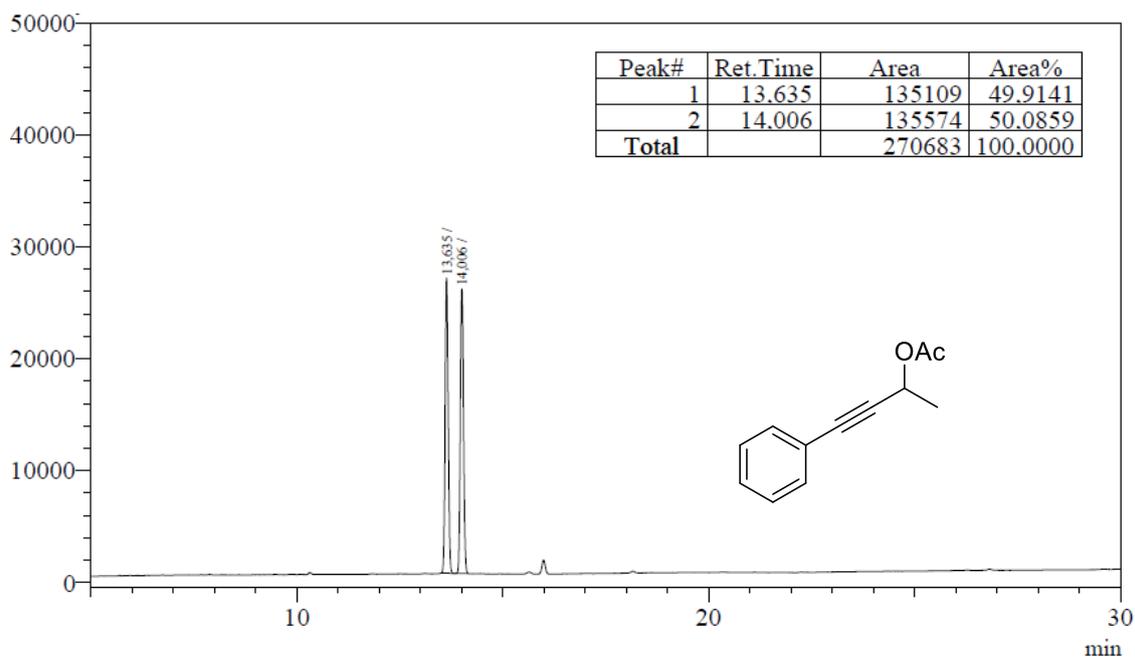
**HPLC:** Column: Chiralcel OD-H, *n*-hexane/*i*-PrOH 9:1, 30 min, 1.0 mL/min, 20 °C.

No.	RT	Area	Area %
1	10,04	23670611	46,249
2	27,59	27510387	53,751
		51180998	100,000

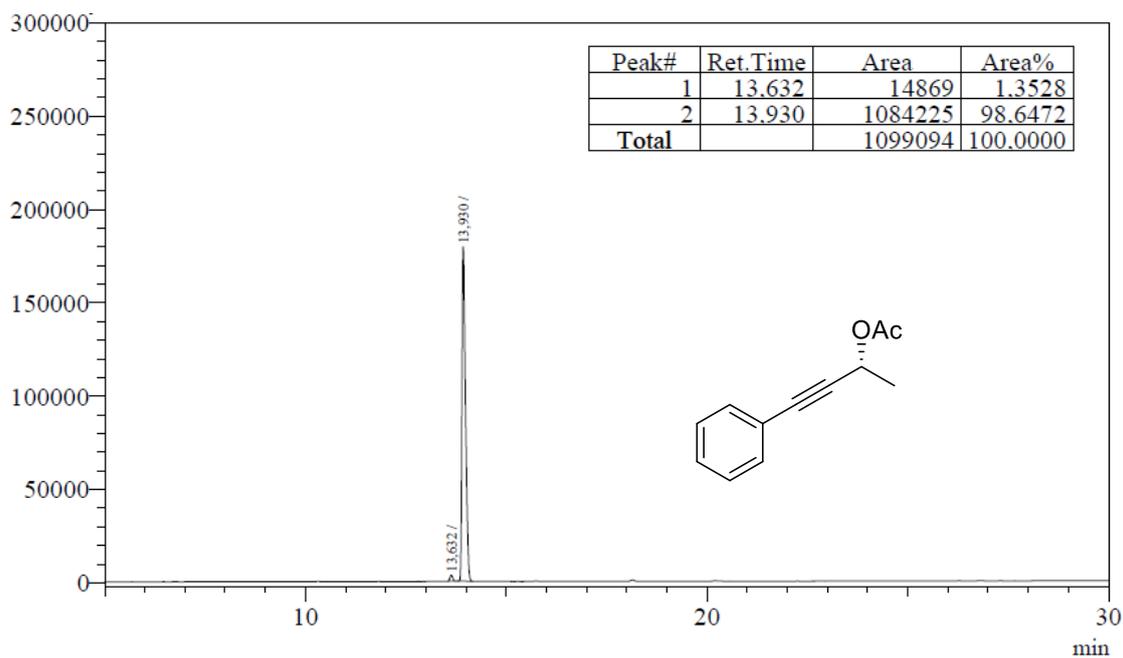


**HPLC:** Column: Chiralcel OD-H, *n*-hexane/*i*-PrOH 9:1, 30 min, 1.0 mL/min, 20 °C.

No.	RT	Area	Area %
1	8,75	159148	0,380
2	22,55	41735036	99,620
		41894184	100,000



**GC-FID:** Column: CP-Chirasil-Dex CB (Varian, 25 m x 0.25 mm, 0.25  $\mu$ m internal diameter), column flow 1.25 mL/min, injector 250  $^{\circ}$ C, T<sub>0</sub> [2 min] = 120  $^{\circ}$ C, 2  $^{\circ}$ C/min to 180  $^{\circ}$ C [2 min], 5  $^{\circ}$ C/min to 220  $^{\circ}$ C [5 min].



**GC-FID:** Column: CP-Chirasil-Dex CB (Varian, 25 m x 0.25 mm, 0.25  $\mu$ m internal diameter), column flow 1.25 mL/min, injector 250  $^{\circ}$ C, T<sub>0</sub> [2 min] = 120  $^{\circ}$ C, 2  $^{\circ}$ C/min to 180  $^{\circ}$ C [2 min], 5  $^{\circ}$ C/min to 220  $^{\circ}$ C [5 min].

## 7. References

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