Electronic Supplementary Material (ESI) for RSC Advances.

Enantioselective Synthesis of anti-3-Alkenyl-2-amido-3-hydroxy esters: Application to the Total Synthesis of (+)-Alexine

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1. General

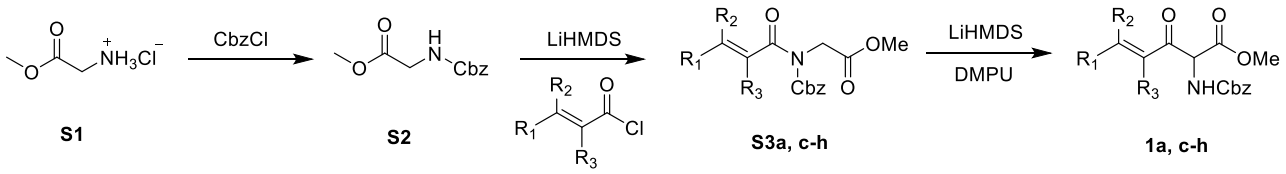
^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 MHz. Data for ^{1}H NMR are recorded as follows: chemical shift (ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quarter; m, multiplet), coupling constant (Hz), integration. Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). Optical rotations were determined on a Perkin Elmer Polarimeter 343 using the sodium D line (589 nm) at the indicated temperature. Analytical thin layer chromatography was performed on Merck silica gel 60 F254 plates; the plates were visualized with UV light or potassium permanganate stain. Flash chromatography was conducted on silica gel (230–400 mesh particle size). Air and moisture sensitive reactions were carried out in flame-dried, septum-capped flasks under an atmospheric pressure of nitrogen. Melting points were measured on a BÜCHI B-540 melting point apparatus and are uncorrected. High resolution mass spectra (HRMS) were recorded on Waters XEVO-G2 QTOF with electrospray ionization (ESI).

2. Typical procedure for the ATH/DKR reaction

The catalyst was prepared by stirring Dichloro(mesitylene)ruthenium(II) dimer (2.5 mol %) and the ligand (*S*,*S*-DPAE) (5 mmol %) in *i*-PrOH (0.3 mL) at 80°C for 1 h. After letting the catalyst mixture cool to ambient temperature, the catalyst was transferred to a vial containing the transfer-hydrogenation substrate (1 eq). Then, HCOOH (1.5 eq), Et_3N (3 eq) and corresponding dioxane (1 mL) was added to this system and stirred at room temperature for corresponding times. Then the mixture was purified by flash chromatography on silica to give the product.

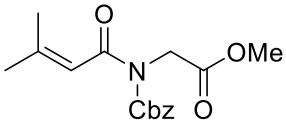
3. Synthesis and characterization of starting materials

Methods 1 (1a, 1c-d, 1i-j, 1l-n)



Methyl 2-(benzyloxycarbonylamino)ethanoate (S2) was synthesized according to the known procedure.[1]

Methyl N-((benzyloxy)carbonyl)-N-(3-methylbut-2-enoyl)glycinate (S3a)

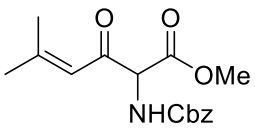


S3a

To a flask containing protected glycine ester **S2** (1.5 g, 6.7 mmol, 1 eq) and THF (30 mL) at -78°C was added LiHMDS (1.0 M solution in THF, 8.7 mL, 8.7 mmol, 1.3 eq). The

mixture was stirred at -78°C for 1.5 hours. Then the 3,3-dimethylacryloyl chloride (1.1 mL, 8.7 mmol, 1.3 eq) was added to the reaction flask via cannula and the reaction mixture was stirred at -78°C for an hour and then allowed to warm to room temperature. After diluting with EtOAc (40 mL), the mixture was washed with NH_4Cl (sat. aq. soln., 40 mL) and brine (40 mL). The combined organic layers were dried over Na_2SO_4 and then filtered and concentrated under reduced pressure. The resulting oil was subjected to column chromatography (*n*-heptane/EtOAc 5:1) to yield the desired product **S3a** (1.2 g, 3.9 mmol, 58%) as a clear oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.46 – 7.29 (m, 5H), 6.55 (q, *J* = 1.3 Hz, 1H), 5.22 (s, 2H), 4.50 (s, 2H), 3.67 (s, 3H), 2.08 (d, *J* = 1.3 Hz, 3H), 1.90 (d, *J* = 1.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.5, 167.8, 155.5, 153.8, 135.1, 128.8, 128.7, 128.4, 119.1, 68.9, 52.4, 45.2, 27.7, 21.2. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{19}NO_5$ 328.1161, found 328.1160.

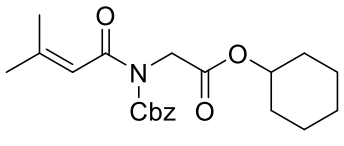
Methyl 2-(((benzyloxy)carbonyl)amino)-5-methyl-3-oxohex-4-enoate (1a)



1a

To a solution of **S3a** (1.2 g, 4 mmol) in THF (30 mL) was added DMPU (1 mL, 8 mmol) and the mixture was cooled to -78°C. Then LiHMDS (1M solution in THF, 8 mL, 8 mmol) was added drop wise to the reaction flask. The reaction was stirred for 2.5 hours at -78°C and quenched with NH_4Cl (sat. aq. soln., 30 mL). The solution was transferred to a separatory funnel and the layers were separated. The aqueous layer was EtOAc (3 × 40 mL) and the combined organic layers were washed with $NaHCO_3$ (sat. aq. soln., 40 mL) and brine (sat. aq. soln. 40 mL). The organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting oil was subjected to flash chromatography (*n*-heptane/EtOAc 5:1) to yield the desired substrate **1a** (0.63 g, 52%) as a clear oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 – 7.27 (m, 5H), 6.35 (p, *J* = 1.4 Hz, 1H), 6.10 (d, *J* = 6.9 Hz, 1H), 5.12 (d, *J* = 2.4 Hz, 2H), 5.06 (d, *J* = 6.9 Hz, 1H), 3.78 (s, 3H), 2.20 (d, *J* = 1.2 Hz, 3H), 1.97 (d, *J* = 1.3 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 188.2, 167.6, 162.6, 155.7, 136.2, 128.6, 128.3, 128.2, 120.3, 67.3, 64.4, 53.2, 28.3, 21.9. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{19}NO_5$ 328.1161, found 328.1163.

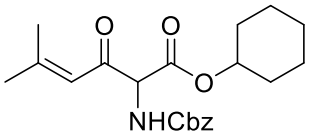
Cyclohexyl N-((benzyloxy)carbonyl)-N-(3-methylbut-2-enoyl)glycinate (S3c)



S3c

Prepared from corresponding ester[2] (0.486 g, 1.7 mmol) to give **S3c** (0.41 g, 1.1 mmol, 65%) as clear oil following the procedure for the synthesis of **S3a**. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.47 – 7.11 (m, 5H), 6.54 (p, *J* = 1.3 Hz, 1H), 5.16 (s, 2H), 4.73 (tt, *J* = 8.6, 3.7 Hz, 1H), 4.43 (s, 2H), 2.03 (d, *J* = 1.5 Hz, 3H), 1.85 (d, *J* = 1.6 Hz, 3H), 1.79 – 1.54 (m, 4H), 1.54 – 1.08 (m, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.0, 167.4, 154.4, 153.5, 134.8, 128.4, 128.3, 128.0, 119.0, 73.4, 68.4, 45.2, 31.1, 27.2, 25.1, 23.3, 20.7. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{21}H_{27}NO_5$ 396.1787, found 396.1789.

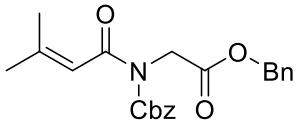
Methyl (*E*)-2-(((benzyloxy)carbonyl)amino)-4-methyl-3-oxohex-4-enoate (1c)



1c

Prepared from **S3c** (0.41 g, 1.1 mmol) to give **1c** (0.29 g, 0.8 mmol, 73%) as clear oil following the procedure for the synthesis of **1a**. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.63 – 7.03 (m, 5H), 6.38 (p, *J* = 1.3 Hz, 1H), 6.13 (d, *J* = 7.0 Hz, 1H), 5.10 (s, 2H), 5.02 (d, *J* = 7.0 Hz, 1H), 4.86 (tq, *J* = 8.4, 3.7 Hz, 1H), 2.17 (d, *J* = 1.4 Hz, 3H), 1.94 (d, *J* = 1.4 Hz, 3H), 1.87 – 1.57 (m, 4H), 1.56 – 1.15 (m, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 188.4, 166.2, 161.3, 155.5, 136.2, 128.4, 128.0, 128.0, 120.4, 74.6, 67.0, 64.67, 31.2, 31.0, 28.0, 25.2, 23.3, 23.2, 21.5. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{21}H_{27}NO_5$ 396.1787, found 396.1791.

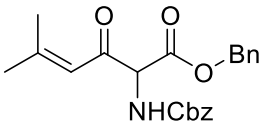
Benzyl N-((benzyloxy)carbonyl)-N-(3-methylbut-2-enoyl)glycinate (S3d)



S3d

Prepared from corresponding ester[2] (0.58 g, 1.9 mmol) to give **S3d** (0.38 g, 1 mmol, 53%) as clear oil following the procedure for the synthesis of **S3a**. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.33 (dddd, *J* = 8.9, 7.9, 5.0, 2.9 Hz, 10H), 6.61 (p, *J* = 1.3 Hz, 1H), 5.18 (s, 2H), 5.13 (s, 2H), 4.57 (s, 2H), 2.10 (d, *J* = 1.5 Hz, 3H), 1.90 (d, *J* = 1.5 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.6, 167.4, 155.0, 153.5, 135.3, 134.8, 128.5, 128.4, 128.4, 128.2, 128.0, 118.9, 68.5, 66.8, 45.1, 27.4, 20.9. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{22}H_{23}NO_5$ 404.1474, found 404.1477.

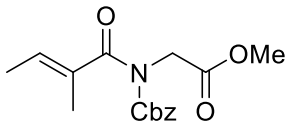
Benzyl 2-(((benzyloxy)carbonyl)amino)-5-methyl-3-oxohex-4-enoate (1d)



1d

Prepared from **S3d** (0.41 g, 1.1 mmol) to give **1c** (0.29 g, 0.8 mmol, 73%) as white solid following the procedure for the synthesis of **1a**. Melting point: 42-44 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.52 – 7.05 (m, 10H), 6.31 (p, *J* = 1.3 Hz, 1H), 6.19 (d, *J* = 6.9 Hz, 1H), 5.31 (d, *J* = 12.2 Hz, 1H), 5.23 – 4.94 (m, 4H), 2.16 (d, *J* = 1.3 Hz, 3H), 1.88 (d, *J* = 1.4 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 187.9, 166.9, 162.2, 155.6, 136.2, 135.0, 128.6, 128.5, 128.3, 128.2, 128.1, 120.3, 67.8, 67.2, 64.5, 28.1, 21.7. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{22}H_{23}NO_5$ 404.1474, found 404.1476.

Methyl (*E*)-N-((benzyloxy)carbonyl)-N-(2-methylbut-2-enoyl)glycinate (S3i)

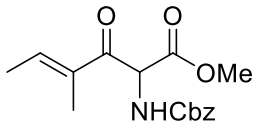


S3i

Prepared from **S2** (2 g, 9 mmol) to give **S3i** (1.5 g, 5 mmol, 56%) as clear oil following the procedure for the synthesis of **S3a**. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.45 – 7.27 (m, 5H), 6.13 (qq, *J* = 6.9, 1.4 Hz, 1H), 5.18 (s, 2H), 4.44 (s, 2H), 3.71 (s, 3H), 1.78 (p, *J* = 1.2 Hz, 3H), 1.60 (dq, *J* = 7.0, 1.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.5, 169.4, 154.2, 134.8, 134.1, 131.5, 128.8, 128.7, 128.5, 69.0, 52.4,

46.2, 13.8, 13.4. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{19}NO_5$ 328.1161, found 328.1159.

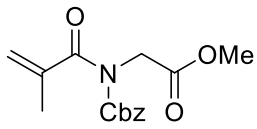
Methyl (*E*)-2-(((benzyloxy)carbonyl)amino)-4-methyl-3-oxohex-4-enoate (1i)



1i

Prepared from **S3i** (1.3 g, 4.3 mmol) to give **1d** (1.03 g, 3.4 mmol, 79%) as white solid following the procedure for the synthesis of **1a**. mp (39-41°C) **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.48 – 7.27 (m, 5H), 7.13 (qd, *J* = 6.9, 1.5 Hz, 1H), 6.07 (d, *J* = 8.1 Hz, 1H), 5.76 (d, *J* = 8.1 Hz, 1H), 5.12 (s, 2H), 3.73 (s, 3H), 2.02 – 1.89 (m, 3H), 1.89 – 1.72 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 192.1, 167.9, 155.7, 143.4, 136.1, 136.1, 128.7, 128.4, 128.2, 67.4, 58.0, 53.3, 15.5, 11.5. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{19}NO_5$ 328.1161, found 328.1165.

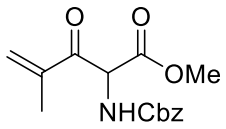
Methyl N-((benzyloxy)carbonyl)-N-methacryloylglycinate (S3j)



S3j

Prepared from **S2** (1.5 g, 6.7 mmol) to give **S3j** (1.1 g, 3.8 mmol, 57%) as clear oil following the procedure for the synthesis of **S3a**. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.44 – 7.28 (m, 5H), 5.36 (p, *J* = 1.0 Hz, 1H), 5.20 (d, *J* = 3.2 Hz, 3H), 4.46 (s, 2H), 3.71 (s, 3H), 1.94 (dd, *J* = 1.6, 1.0 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.7, 169.1, 154.0, 142.1, 134.6, 128.9, 128.7, 128.7, 128.6, 118.0, 69.2, 52.5, 45.8, 19.1. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{17}NO_5$ 314.1004, found 314.1007.

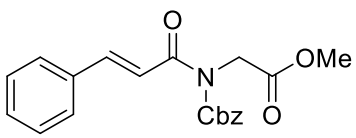
Methyl 2-(((benzyloxy)carbonyl)amino)-4-methyl-3-oxopent-4-enoate (1j)



1j

Prepared from **S3j** (1.1 g, 3.8 mmol) to give **1c** (0.6 g, 2.1 mmol, 55%) as clear oil following the procedure for the synthesis of **1a**. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.46 – 7.28 (m, 5H), 6.34 (s, 1H), 6.11 – 5.95 (m, 2H), 5.75 (d, *J* = 8.0 Hz, 1H), 5.12 (s, 2H), 3.75 (s, 3H), 1.93 (t, *J* = 1.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** 192.67, 167.47, 155.64, 142.03, 136.06, 129.56, 128.67, 128.39, 128.24, 67.50, 58.57, 53.36, 17.86. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{17}NO_5$ 314.1004, found 314.1001.

Methyl N-((benzyloxy)carbonyl)-N-cinnamoylglycinate (S3l)

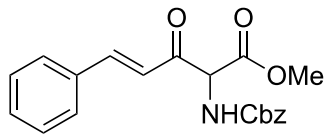


S3l

Prepared from **S2** (2 g, 9 mmol) to give **S3l** (1.82g, 5.2 mmol, 57%) as yellowish oil following the procedure for the synthesis of **S3a**. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.75 (d, *J* = 15.6 Hz, 1H), 7.60 (d, *J* = 15.6 Hz, 1H), 7.48 (dd, *J* = 7.4, 2.2 Hz, 2H), 7.40 – 7.33 (m, 8H), 5.28 (s, 2H), 4.60 (s, 2H), 3.69 (s, 3H). **^{13}C NMR (100**

MHz, $CDCl_3$) δ 169.1, 167.9, 153.7, 145.2, 134.8, 134.7, 130.3, 128.8, 128.8, 128.4, 128.3, 120.0, 69.1, 52.3, 45.6. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{20}H_{19}NO_5$ 376.1161, found 376.1159.

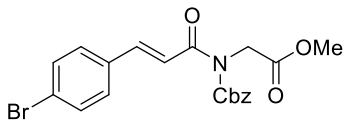
Methyl (*E*)-2-(((benzyloxy)carbonyl)amino)-3-oxo-5-phenylpent-4-enoate (1l)



1l

Prepared from **S3l** (1.8 g, 5.2 mmol) to give **1e** (1 g, 2.9 mmol, 56%) as yellowish solid following the procedure for the synthesis of **1a**. mp (84-87°C). Compound **1l** exists as keto/enol tautomers as seen by ^1H and ^{13}C NMR. **^1H NMR (400 MHz, $CDCl_3$)** δ 12.26 (s, 0.7H), 7.85 (d, *J* = 15.9 Hz, 0.3H), 7.66 – 7.32 (m, 9H), 7.05 (d, *J* = 16.0 Hz, 0.5H), 6.93 (d, *J* = 16.0 Hz, 0.5H), 6.18 (d, *J* = 7.2 Hz, 0.3H), 5.70 (s, 0.5H), 5.42 (d, *J* = 7.2 Hz, 0.3H), 5.30 – 5.09 (m, 2H), 3.83 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 189.1, 167.1, 155.6, 146.6, 139.0, 136.3, 136.0, 133.8, 131.5, 129.7, 129.1, 128.9, 128.8, 128.6, 128.3, 128.2, 128.1, 128.0, 121.6, 117.2, 67.4, 62.9, 53.4. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{20}H_{19}NO_5$ 376.1161, found 376.1157.

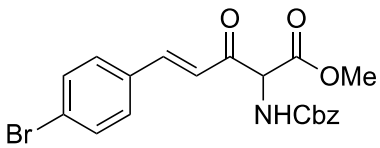
Methyl (*E*)-N-((benzyloxy)carbonyl)-N-(3-(4-bromophenyl)acryloyl)glycinate (S3m)



S3m

Prepared from **S2** (2 g, 9 mmol) to give **S3m** (1.8 g, 4.2 mmol, 46%) as yellow solid following the procedure for the synthesis of **S3a**. mp (104-106°C). **^1H NMR (400 MHz, $CDCl_3$)** δ 7.65 (d, *J* = 15.6 Hz, 1H), 7.57 (d, *J* = 15.6 Hz, 1H), 7.48 – 7.43 (m, 2H), 7.37 (d, *J* = 2.0 Hz, 5H), 7.32 – 7.26 (m, 2H), 5.27 (s, 2H), 4.59 (s, 2H), 3.68 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.1, 167.7, 153.7, 143.6, 134.7, 133.8, 132.1, 129.7, 128.9, 128.8, 128.5, 124.5, 120.8, 77.5, 77.2, 76.8, 69.2, 52.4, 45.6. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{20}H_{18}NO_5Br$ 454.0266, found 454.0270.

Methyl (*E*)-2-(((benzyloxy)carbonyl)amino)-5-(4-bromophenyl)-3-oxopent-4-enoate (1m)

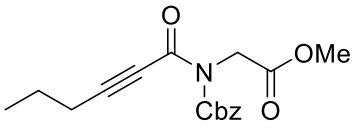


1m

Prepared from **S3m** (1.2 g, 2.8 mmol) to give **1f** (0.65 g, 1.5 mmol, 54%) as yellow solid following the procedure for the synthesis of **1a**. mp (113-116°C). Compound 1m exists as keto/enol tautomers as seen by ^1H and ^{13}C NMR. **^1H NMR (400 MHz, $CDCl_3$)** δ 12.23 (s, 0.5 H), 7.76 (d, *J* = 15.9 Hz, 0.5 H), 7.62 – 7.52 (m, 1H), 7.52 – 7.21 (m, 8H), 7.03 (d, *J* = 16.0 Hz, 0.5 H), 6.92 (t, *J* = 16.7 Hz, 0.5 H), 6.19 (d, *J* = 7.2 Hz, 0.4 H), 5.79 (s, 0.5 H), 5.41 (d, *J* = 7.2 Hz, 0.4 H), 5.32 – 5.08 (m, 2H), 3.82 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 189.2, 167.1, 155.7, 145.1, 137.5, 136.4, 136.1, 132.8, 132.5, 132.1, 130.3, 129.4, 128.7, 128.4, 128.3,

128.2, 126.0, 122.1, 117.9, 67.5, 63.1, 53.5. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{20}H_{18}NO_5Br$ 454.0266, found 454.0261.

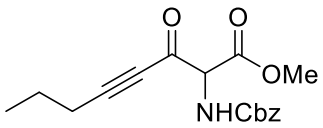
Methyl N-((benzyloxy)carbonyl)-N-(hex-2-ynoyl)glycinate (S3n)



S3n

Prepared from **S2** (1.5 g, 6.7 mmol) to give **S3n** (0.6 g, 2.7 mmol, 40%) as clear oil following the procedure for the synthesis of **S3a**. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.42 – 7.27 (m, 5H), 5.26 (s, 2H), 4.50 (s, 2H), 3.66 (s, 3H), 2.22 (t, *J* = 7.1 Hz, 2H), 1.51 (h, *J* = 7.3 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.4, 153.0, 152.6, 134.6, 128.8, 128.7, 128.7, 128.5, 128.4, 128.4, 98.3, 75.1, 69.2, 52.4, 45.0, 44.9, 21.2, 21.0, 13.5. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{17}H_{19}NO_5$ 340.1161, found 340.1158.

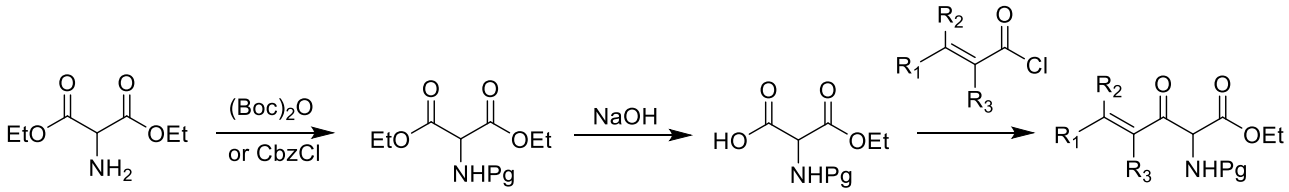
Methyl 2-(((benzyloxy)carbonyl)amino)-3-oxooct-4-ynoate (1n)



1n

Prepared from **S3h** (0.45 g, 1.4 mmol) to give **1h** (0.22 g, 0.7 mmol, 50%) as white solid following the procedure for the synthesis of **1a**. mp (97-100°C). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.48 – 7.27 (m, 5H), 5.91 (q, *J* = 1.6 Hz, 1H), 5.36 (d, *J* = 12.3 Hz, 1H), 5.19 (d, *J* = 12.3 Hz, 1H), 5.02 (dt, *J* = 1.5, 0.7 Hz, 1H), 3.62 (s, 3H), 2.38 – 2.21 (m, 2H), 1.72 – 1.44 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.8, 167.0, 160.0, 135.0, 128.5, 128.3, 128.1, 122.6, 68.0, 65.8, 52.9, 30.5, 20.3, 13.5. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{17}H_{19}NO_5$ 340.1161, found 340.1165.

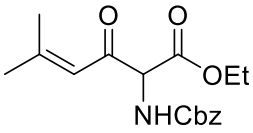
Methods 2 (1b, 1e, 1h, 1k, 1o)



Diethyl 2-(*tert*-butoxycarbonylamino)propandioate (**S4**) was synthesized according to known procedure from commercially available **diethyl aminopropanedioate**.[1]

2-(*tert*-butoxycarbonylamino)-3-ethoxy-3-oxopropanoic acid (**S5**) was synthesized according to known procedure from **S4**.[1]

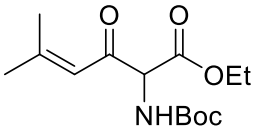
Ethyl (*E*)-2-((tert-butoxycarbonyl)amino)-3-oxohex-4-enoate (1b)



1b

To a stirred mixture of Cbz-protected malonate **S5** (10 g, 35.6 mmol, 1 eq) and $MgCl_2$ (20.4 g, 213.5 mmol, 6 eq) in THF (100 mL) was added Et_3N (12.5 mL, 89 mmol, 2.5 eq) at 0°C. The resulting mixture was stirred at 0°C for an additional 2 hours. Crotonoyl chloride (5 mL, 42.7 mmol, 1.2 equiv) was added to the malonate mixture in THF (10 mL) at 0°C. Then the reaction was brought to rt and stirred 5 days. After diluting with EtOAc (100 mL), the mixture was washed with NH_4Cl (sat. aq. soln., 100 mL) and brine (100 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude material was purified by flash chromatography on silica (*n*-heptane/EtOAc 5:1) to give the product (8.2 g, 25.7 mmol, 72%) as a yellowish oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.33 (dtd, *J* = 12.5, 4.4, 1.7 Hz, 5H), 6.37 (p, *J* = 1.4 Hz, 1H), 6.11 (d, *J* = 7.0 Hz, 1H), 5.12 (s, 2H), 5.03 (d, *J* = 7.0 Hz, 1H), 4.34 – 4.12 (m, 2H), 2.19 (d, *J* = 1.3 Hz, 3H), 1.96 (d, *J* = 1.3 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 188.4, 167.0, 162.1, 155.6, 136.3, 128.6, 128.3, 128.1, 120.3, 67.2, 64.6, 62.4, 28.2, 21.8, 14.1. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{17}H_{21}NO_5$ 342.1317, found 342.1320.

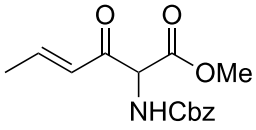
Ethyl 2-((tert-butoxycarbonyl)amino)-5-methyl-3-oxohex-4-enoate (1e)



1e

Prepared from Boc-protected **S5**(1.2 g, 4.8 mmol) to give **1e** (0.88 g, 3.1 mmol, 65%) as clear oil following the procedure for the synthesis of **1b**. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.49 – 6.16 (m, 1H), 5.83 (d, *J* = 7.1 Hz, 1H), 4.97 (d, *J* = 7.0 Hz, 1H), 4.41 – 4.06 (m, 2H), 2.21 – 2.11 (m, 3H), 1.93 (dd, *J* = 18.1, 1.3 Hz, 3H), 1.44 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 189.0, 167.5, 161.6, 155.1, 120.5, 80.4, 64.5, 62.2, 28.4, 28.3, 28.2, 21.7, 14.2. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{14}H_{23}NO_5$ 308.1474, found 308.1477.

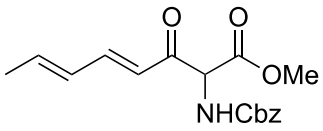
Ethyl (E)-2-((tert-butoxycarbonyl)amino)-3-oxohex-4-enoate (1h)



1h

Prepared from Cbz-protected **S5**(1.2 g, 4.8 mmol) to give **1h** (1.0 g, 3.3 mmol, 69%) as clear oil following the procedure for the synthesis of **1b**. Compound **1h** decomposed even stored in -20 °C for 2 days, and exists as keto/enol tautomers as seen by ^{1}H and ^{13}C NMR. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 12.07 (s, 0.2H), 7.06 (dq, *J* = 15.6, 6.9 Hz, 0.7H), 6.63 (dq, *J* = 15.6, 6.9 Hz, 0.3H), 6.31 (dq, *J* = 15.5, 1.6 Hz, 1H), 5.77 (d, *J* = 7.4 Hz, 0.6H), 5.49 (s, 0.3H), 5.11 (d, *J* = 7.4 Hz, 0.7H), 4.15 (tddd, *J* = 14.1, 10.8, 6.2, 3.7 Hz, 2H), 1.84 (ddd, *J* = 23.2, 6.9, 1.7 Hz, 3H), 1.37 (d, *J* = 13.8 Hz, 9H), 1.19 (dt, *J* = 10.3, 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 189.4, 171.3, 166.8, 154.9, 147.1, 146.1, 137.7, 127.7, 126.1, 121.6, 80.2, 62.2, 62.1, 60.9, 28.2, 28.1, 18.6, 18.6, 18.5, 14.1, 14.0. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{13}H_{21}NO_5$ 294.1317, found 294.1311.

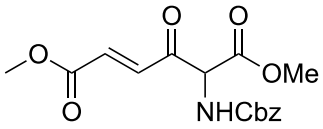
Ethyl (4E,6E)-2-((tert-butoxycarbonyl)amino)-3-oxoocta-4,6-dienoate (1k)



1k

Prepared from Cbz-protected **S5**(2 g, 7.1 mmol) to give **1k** (1.71 g, 5.2 mmol, 73%) as yellowish oil following the procedure for the synthesis of **1b**. Compound **1k** exists as keto/enol tautomers as seen by ^{1}H and ^{13}C NMR. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 12.19 (s, 0.3 H), 7.80 (dd, *J* = 15.2, 11.2 Hz, 0.1H), 7.47 – 7.29 (m, 5H), 7.09 (dd, *J* = 15.3, 10.6 Hz, 0.3H), 6.56 – 5.79 (m, 3.6H), 5.25 (d, *J* = 7.2 Hz, 0.7H), 5.15 (d, *J* = 18.4 Hz, 2H), 4.31 – 4.08 (m, 2H), 1.87 (dd, *J* = 20.7, 6.5 Hz, 3H), 1.38 – 1.09 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) **^{13}C NMR (100 MHz, $CDCl_3$)** δ 189.4, 166.8, 155.6, 146.9, 143.8, 140.9, 139.5, 137.9, 136.5, 136.2, 131.1, 130.2, 128.6, 128.3, 128.2, 127.7, 123.1, 120.6, 118.6, 67.3, 62.9, 62.5, 61.2, 32.0, 29.1, 22.8, 19.1, 18.8, 14.3, 14.2, 14.1. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{18}H_{21}NO_5$ 354.1317, found 354.1320.

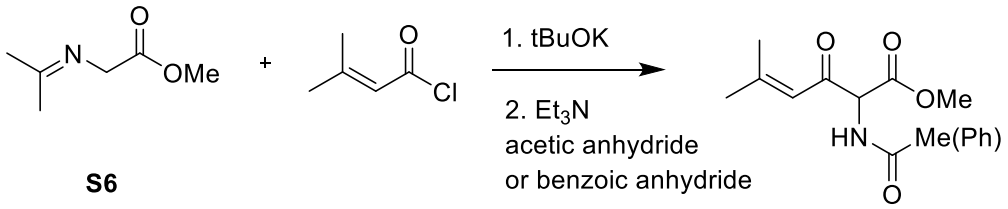
6-Ethyl 1-methyl (E)-5-(((benzyloxy)carbonyl)amino)-4-oxohex-2-enedioate (1o)



1o

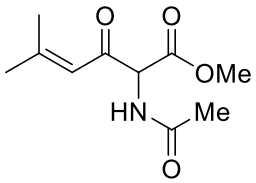
Prepared from Cbz-protected **S5**(1.5 g, 5.3 mmol) to give **1o** (1.35 g, 3.9 mmol, 70%) as white solid following the procedure for the synthesis of **1b**. mp (90-93°C). Compound **1o** exists as keto/enol tautomers as seen by ^{1}H and ^{13}C NMR.**^{1}H NMR (400 MHz, $CDCl_3$)** δ 11.95 (s, 1H), 7.47 (d, *J* = 15.6 Hz, 1H), 7.43 – 7.27 (m, 5H), 6.69 (d, *J* = 15.5 Hz, 1H), 5.73 (s, 1H), 5.15 (d, *J* = 17.2 Hz, 2H), 4.26 (d, *J* = 7.9 Hz, 2H), 3.79 (s, 3H), 1.45 – 0.94 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 155.9, 136.1, 133.1, 128.7, 128.4, 128.3, 126.9, 100.1, 67.7, 62.0, 52.2, 14.2. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{17}H_{19}NO_7$ 372.1059, found 372.1058.

Methods 3 (1f, 1g)



S6

Methyl 2-acetamido-5-methyl-3-oxohex-4-enoate (1f)



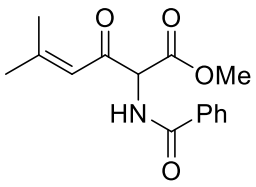
1f

To a flask was added *t*-BuOK (0.71 g, 6.33 mmol, 1.5 eq) and THF (15 mL) and cool to -78°C. Benzophenone glycine imine **S6** (1g, 4.2 mmol, 1 eq) in THF (15 mL) was then added via cannula. The reaction was stirred at -78°C for 1 hour and was then transferred to the flask containing the acid chloride (1.2

mL, 10.5 mmol, 2.5 eq) via cannula. The reaction was stirred for an additional 1 hour at -78°C and then HCl (1M aq. 30 mL) was added and the reaction was warmed to ambient temperature and stirred overnight and then concentrated to dryness. The crude material was dissolved in H_2O and washed Et_2O (3 × 30 mL). The aqueous layer was then concentrated and azeotroped two times with MeOH. At this point the crude mixture was re-suspended in anhydrous MeOH and filtered to remove KCl. The filtrate was concentrated and carried on to the next step without further purification.

The crude amine salt was dissolved in THF (30 mL) and cooled to 0°C. Acetic anhydride (0.52 mL, 5.48 mmol, 1.3 eq) was then added followed by triethylamine (0.76 mL, 5.48 mmol, 1.3 eq). The reaction was warmed to rt and then stirred overnight. The mixture was then diluted with EtOAc (30 mL) and H_2O (30 mL). The aqueous layer was EtOAc (3 × 30 mL) and the combined organic layers were dried over Na_2SO_4. The solution was filtered and concentrated to yield an oil which was then subjected to flash chromatography (*n*-heptane/EtOAc 3:1) to give product **1f** (0.47g, 2.2 mmol, 52%) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.95 (d, *J* = 6.8 Hz, 1H), 6.26 (p, *J* = 1.3 Hz, 1H), 5.14 (d, *J* = 6.6 Hz, 1H), 3.68 (s, 3H), 2.09 (d, *J* = 1.4 Hz, 3H), 1.98 (s, 3H), 1.88 (d, *J* = 1.5 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 188.5, 169.9, 167.4, 162.2, 120.3, 62.9, 52.9, 28.1, 22.6, 21.5. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{10}H_{15}NO_4$ 236.0899, found 236.0901.

Methyl 2-benzamido-5-methyl-3-oxohex-4-enoate (1g)

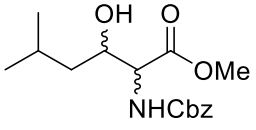


1g

Prepared from benzophenone glycine imine **S6** (1 g, 4.2 mmol) to give **1g** (0.73 g, 2.7 mmol, 63%) as colorless oil following the procedure for the synthesis of **1f**. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.87 (dq, *J* = 7.1, 1.5 Hz, 2H), 7.58 – 7.50 (m, 1H), 7.46 (ddd, *J* = 8.5, 6.6, 1.6 Hz, 2H), 6.45 (p, *J* = 1.4 Hz, 1H), 5.39 (dd, *J* = 6.3, 1.5 Hz, 1H), 3.82 (d, *J* = 1.6 Hz, 3H), 2.24 (d, *J* = 1.5 Hz, 3H), 2.00 (d, *J* = 1.5 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 188.3, 167.3, 166.7, 162.7, 133.1, 131.9, 129.9, 128.5, 128.2, 127.2, 120.2, 63.3, 53.0, 28.1, 21.6. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{17}NO_4$ 298.1055, found 298.1059.

Characterization data for products (4, 2a-2m)

Methyl 2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-methylhexanoate (4)

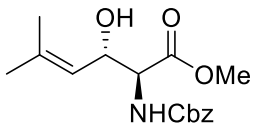


4

Prepared from **1a** (61.6 mg, 0.2 mmol) to give the over-reduction product **4** (2.5 mg, 3%) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.42-7.29 (m, 5H), 5.69 (d, J=6.8Hz, 1H), 5.12 (s, 2H), 4.44 (d, J=4.6Hz, 1H), 4.01 (s, 1H), 3.78 (s, 3H), 2.47 (s, 1H), 1.90-1.75 (m, 1H), 1.50-1.38 (m, 1H), 1.30-1.13 (m, 1H), 0.92 (dd, J=19.1Hz, 6.6Hz, 6H) **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.0, 156.4, 136.0, 128.6, 128.5, 128.3, 128.2, 128.2, 128.1, 128.1, 71.0,

67.3, 67.1, 59.0, 52.5, 52.4, 42.7, 42.2, 24.5, 24.5, 23.4, 21.8. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{21}NO_5$ 332.1474, found 332.1477.

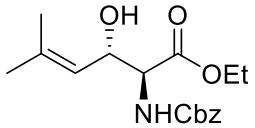
Methyl (*2S,3S*)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-methylhex-4-enoate (2a)



2a

Prepared from **1a** (61.6 mg, 0.2 mmol) to give the product **2a** (44.5 mg, 0.14 mmol, 72%) as a colorless oil. 96.5:3.5 *e.r.* determined by HPLC analysis (Chiralcel IA, 7.5% 2-propanol in hexanes, 0.75 mL/min, λ = 214 nm, t_{minor} = 49.5 min, t_{major} = 56.6min). **Optical rotation:** $[\alpha]_D^{20}$ +41.3 (c 1.7, $CHCl_3$) **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.38 – 7.29 (m, 5H), 5.68 (d, *J* = 8.0 Hz, 1H), 5.19 (dt, *J* = 9.0, 1.4 Hz, 1H), 5.11 (s, 2H), 4.75 – 4.68 (m, 1H), 4.50 (dd, *J* = 8.1, 4.2 Hz, 1H), 3.74 (s, 3H), 2.86 (s, 1H), 1.71 (d, *J* = 1.5 Hz, 3H), 1.66 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.5, 156.5, 138.3, 136.0, 128.5, 128.2, 128.1, 121.9, 69.6, 67.2, 59.0, 52.4, 25.9, 18.3. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{21}NO_5$ 330.1317, found 330.1320.

Ethyl (2S,3S)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-methylhex-4-enoate (2b)

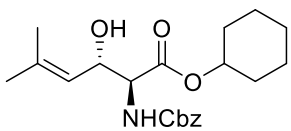


2b

Prepared from **1b** (63.8 mg, 0.2 mmol) to give the product **2b** (49.8 mg, 0.16 mmol, 78%) as a colorless oil. 97.5:2.5 *e.r.* determined by HPLC analysis (Chiralcel IA, 7.5% 2-propanol in hexanes, 0.75 mL/min, λ = 214 nm, t_{minor} = 38.3 min, t_{major} = 41.3min). **Optical rotation:** $[\alpha]_D^{20}$ +29.8 (c 6.5, CH_2Cl_2). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43 – 7.28 (m, 5H), 5.70 (d, *J* = 7.9 Hz, 1H), 5.20 (dp, *J* = 9.1, 1.4 Hz, 1H), 5.12 (s, 2H), 4.74 (dd, *J* = 9.1, 4.0 Hz, 1H), 4.49 (dd, *J* = 8.0, 4.0 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 2.80 (s, 1H), 1.71 (d, *J* = 1.5 Hz, 3H), 1.67 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.0, 156.7, 138.2, 136.1, 128.6, 128.6, 128.3, 128.2, 122.1, 69.7, 67.4, 61.8, 59.2, 26.0, 18.5, 14.2. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{17}H_{21}NO_5$ 344.1474, found 344.1470.

Cyclohexyl

(2S,3S)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-methylhex-4-enoate (2c)

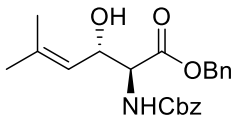


2c

Prepared from **1c** (74.6 mg, 0.2 mmol) to give the product **2c** (49 mg, 0.13 mmol, 66%) as a colorless oil. 97:3 *e.r.* determined by HPLC analysis (Chiralcel IA, 15% 2-propanol in hexanes, 0.7 mL/min, λ = 214 nm, t_{minor} = 15.5 min, t_{major}=18.3 min). **Optical rotation:** $[\alpha]_D^{20}$ +29.9 (c 4.7, CH_2Cl_2). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40 – 7.29 (m, 6H), 5.71 (d, *J* = 7.8 Hz, 1H), 5.21 (dp, *J* = 8.8, 1.5 Hz, 1H), 5.12 (s, 2H), 4.81 (dq, *J* = 8.8, 4.3 Hz, 1H), 4.77 – 4.65 (m, 1H), 4.47 (dd, *J* = 7.9, 3.8 Hz, 1H), 2.87 (s, 1H), 1.80 (dd, *J* = 11.5, 5.6 Hz, 2H), 1.71 (d, *J* = 1.5 Hz, 4H), 1.69 (s, 3H), 1.58 – 1.13 (m, 7H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.4, 156.7, 138.2, 136.2, 128.6, 128.6, 128.3,

128.3, 122.2, 74.5, 69.9, 67.4, 59.3, 31.5, 26.0, 26.0, 25.3, 23.7, 23.6, 23.6, 18.6. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{21}H_{29}NO_5$ 398.1943, found 398.2016.

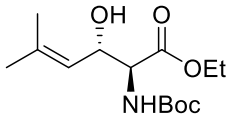
Benzyl (2S,3S)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-methylhex-4-enoate (2d)



2d

Prepared from **1d** (76.2 mg, 0.2 mmol) to give the product **2d** (55 mg, 0.14 mmol, 72%) as a colorless oil. 96.5:3.5 *e.r.* determined by HPLC analysis (Chiralcel IA, 30% 2-propanol in hexanes, 0.5 mL/min, λ=214 nm, t_{minor} = 16.1 min, t_{major} = 18.0 min). **Optical rotation:** $[\alpha]_D^{20}$ +29.0 (c 4.9, CH_2Cl_2). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.35 (d, *J* = 4.2 Hz, 10H), 5.74 (d, *J* = 8.1 Hz, 1H), 5.24 – 5.14 (m, 3H), 5.13 (s, 2H), 4.74 (dd, *J* = 9.1, 4.3 Hz, 1H), 4.56 (dd, *J* = 8.1, 4.0 Hz, 1H), 2.80 (d, *J* = 4.8 Hz, 1H), 1.66 (d, *J* = 1.4 Hz, 3H), 1.60 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.0, 156.6, 138.5, 136.1, 135.1, 128.7, 128.6, 128.6, 128.6, 128.5, 128.4, 128.3, 128.2, 122.0, 69.7, 67.4, 67.4, 59.2, 25.9, 18.4. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{22}H_{25}NO_5$ 406.1630, found 406.1630.

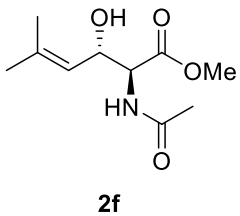
Ethyl (2S,3S)-2-((tert-butoxycarbonyl)amino)-3-hydroxy-5-methylhex-4-enoate (2e)



2e

Prepared from **1e** (57 mg, 0.2 mmol) to give the product **2d** (38 mg, 0.13 mmol, 67%) as a colorless oil. 97:3 *e.r.* determined by HPLC analysis (Chiralcel IA, 7.5% 2-propanol in hexanes, 0.8 mL/min, λ = 214 nm, t_{major} = 15.3 min, t_{minor} = 17.3min). **Optical rotation:** $[\alpha]_D^{20}$ +48.3 (c 3.0, CH_2Cl_2). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.40 (d, *J* = 7.3 Hz, 1H), 5.18 (dp, *J* = 9.1, 1.4 Hz, 1H), 4.70 (d, *J* = 9.8 Hz, 1H), 4.41 (t, *J* = 5.9 Hz, 1H), 4.18 (qd, *J* = 7.1, 1.0 Hz, 2H), 3.10 (s, 1H), 1.71 (d, *J* = 1.5 Hz, 3H), 1.67 (d, *J* = 1.4 Hz, 3H), 1.43 (s, 9H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.3, 156.4, 137.9, 122.3, 80.5, 69.9, 61.7, 58.9, 28.4, 26.0, 26.0, 18.5, 14.3, 14.2. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{14}H_{25}NO_5$ 310.1630, found 310.1630.

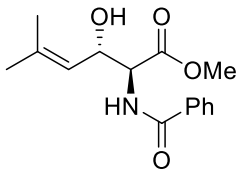
Methyl (2S,3S)-2-acetamido-3-hydroxy-5-methylhex-4-enoate (2f)



2f

Prepared from **1f** (64 mg, 0.3 mmol) to give the product **2f** (37 mg, 0.17 mmol, 58%) as a colorless oil. 81.7:18.3 *e.r.* determined by HPLC analysis (Chiralcel IA, 30% 2-propanol in hexanes, 1 mL/min, λ = 214 nm, t_{major} = 5.1 min, t_{minor} = 5.5 min). **Optical rotation:** $[\alpha]_D^{20}$ +31.1 (c 3.7, CH_2Cl_2). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.59 (d, *J* = 7.9 Hz, 1H), 5.19 (ddp, *J* = 8.7, 4.4, 1.5 Hz, 1H), 4.90 – 4.50 (m, 2H), 3.75 (d, *J* = 1.6 Hz, 3H), 2.06 (d, *J* = 1.7 Hz, 3H), 1.79 – 1.53 (m, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.4, 171.3, 170.5, 138.0, 122.8, 122.1, 69.9, 69.8, 68.6, 58.0, 57.1, 52.6, 26.0, 25.9, 23.1, 18.5, 18.4. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{10}H_{17}NO_4$ 238.1055, found 238.1056.

Methyl (2S,3S)-2-benzamido-3-hydroxy-5-methylhex-4-enoate (2g)

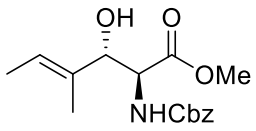


2g

Prepared from **1g** (82.5 mg, 0.3 mmol) to give the product **2g** (55 mg, 0.2 mmol, 67%) as a colorless oil. 83.4:16.6 *e.r.* determined by HPLC analysis (Chiralcel IA, 7.5% 2-propanol in hexanes, 0.8 mL/min, λ = 214 nm, t_{major} = 32.1 min, t_{minor} = 34.1min). **Optical rotation:** $[\alpha]_D^{20}$ +41.7 (c 5.1, CH_2Cl_2). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.93 – 7.75 (m, 2H), 7.54 – 7.45 (m, 1H), 7.45 – 7.36 (m, 2H), 7.12 (dd, *J* = 25.9, 7.9 Hz, 1H), 5.30 – 5.12 (m, 1H), 4.96 – 4.70 (m, 2H), 3.75 (d, *J* = 5.5 Hz, 3H), 1.94 – 1.41 (m, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.6, 168.2, 138.0, 138.0, 133.4, 132.1, 131.9, 128.7, 128.6, 128.6, 127.3, 122.8, 122.2, 70.1, 68.8, 58.4, 57.5, 52.7, 52.7, 26.0, 25.9, 18.5, 18.4. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{19}NO_4$ 300.1212, found 300.1214.

Methyl

(*2S,3S,E*)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-4-methylhex-4-enoate (2i)

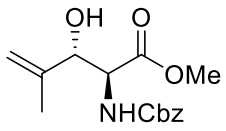


2i

Prepared from **1d** (61.6 mg, 0.2 mmol) to give the product **2d** (56.1 mg, 0.18 mmol, 91%) as a colorless oil. 98.1:1.9 *e.r.* determined by HPLC analysis (Chiralcel IA, 7.5% 2-propanol in hexanes, 0.75 mL/min, λ = 214 nm, t_{minor} = 38.5 min, t_{major} = 44.4min). **Optical rotation:** $[\alpha]_D^{20}$ +15.1 (c 4.4, CH_2Cl_2). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.39 – 7.29 (m, 5H), 5.52 (q, *J* = 6.3, 5.6 Hz, 2H), 5.19 – 5.01 (m, 2H), 4.50 (dd, *J* = 8.2, 5.7 Hz, 1H), 4.28 (d, *J* = 5.8 Hz, 1H), 3.72 (s, 3H), 2.57 (s, 1H), 1.60 (dd, *J* = 8.4, 2.2 Hz, 6H). ^{13}C **NMR (100 MHz, $CDCl_3$)** δ 171.3, 156.0, 136.0, 133.5, 128.5, 128.2, 128.0, 122.7, 77.4, 67.1, 56.9, 52.3, 13.1, 12.1. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{21}NO_5$ 330.1317, found 330.1316.

Methyl

(*2S,3S*)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-4-methylpent-4-enoate (2j)

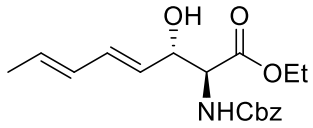


2j

Prepared from **1j** (58.2 mg, 0.2 mmol) to give the product **2j** (35.2 mg, 0.12 mmol, 60%) as a colorless oil. 98.5:1.5 *e.r.* determined by HPLC analysis (Chiralcel IA, 7% 2-propanol in hexanes, 1 mL/min, λ = 214 nm, t_{minor} = 25.9 min, t_{major} = 32.5min). **Optical rotation:** $[\alpha]_D^{20}$ +20.3 (c 2.9, CH_2Cl_2). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.45 – 7.31 (m, 5H), 5.65 (d, *J* = 8.2 Hz, 1H), 5.14 (dd, *J* = 5.6, 2.2 Hz, 2H), 5.02 (dq, *J* = 16.7, 1.3 Hz, 2H), 4.61 (dd, *J* = 8.1, 4.6 Hz, 1H), 4.41 (s, 1H), 3.76 (s, 3H), 1.79 (s, 3H).**^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.9, 156.3, 143.2, 136.1, 128.7, 128.6, 128.4, 128.3, 113.1, 76.0, 67.4, 57.0, 52.5, 18.8. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{19}NO_5$ 316.1161, found 316.1162.

Methyl

(2S,3S,4E,6E)-2-(((benzyloxy)carbonyl)amino)-3-hydroxyocta-4,6-dienoate (2k)

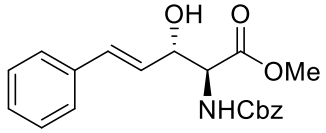


2k

Prepared from **1k** (66.2 mg, 0.2 mmol) to give the product **2k** (51.2 mg, 0.15 mmol, 77%) as a colorless oil. 92:8 *e.r.* determined by HPLC analysis (Chiralcel IB, 20% 2-propanol in hexanes, 0.5 mL/min, λ = 234 nm, t_{major} = 13.1 min, t_{minor} = 20.4 min). **Optical rotation:** $[\alpha]_D^{20}$ +16.6 (c 4.5, CH_2Cl_2). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40 – 7.29 (m, 5H), 6.24 (dd, *J* = 15.3, 10.3 Hz, 1H), 6.11 – 5.91 (m, 1H), 5.80 – 5.64 (m, 2H), 5.49 (dd, *J* = 15.2, 6.0 Hz, 1H), 5.11 (d, *J* = 2.2 Hz, 2H), 4.54 (q, *J* = 4.7, 3.9 Hz, 2H), 4.20 (pd, *J* = 7.2, 3.4 Hz, 2H), 3.09 (s, 1H), 1.74 (dt, *J* = 7.1, 2.2 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.9, 156.8, 136.1, 133.2, 131.3, 130.5, 128.6, 128.6, 128.3, 128.2, 128.1, 126.8, 73.4, 67.4, 67.4, 61.9, 59.1, 18.2, 14.3. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{18}H_{23}NO_5$ 356.1474, found 356.1476.

Methyl

(2S,3S,E)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-phenylpent-4-enoate (2l)

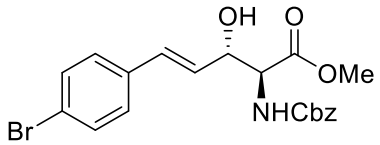


2l

Prepared from **1e** (70.6 mg, 0.2 mmol) to give the product **2e** (43.6 mg, 0.12 mmol, 61%) as a colorless oil. 88.4:11.6 *e.r.* determined by HPLC analysis (Chiralcel IA, 7.5% 2-propanol in hexanes, 0.75 mL/min, λ = 254 nm, t_{minor} = 74.9 min, t_{major} = 84.5min). **Optical rotation:** $[\alpha]_D^{20}$ +21.6 (c 3.1, CH_2Cl_2). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43 – 7.25 (m, 10H), 6.67 (d, *J* = 15.9 Hz, 1H), 6.16 (dd, *J* = 15.9, 6.0 Hz, 1H), 5.72 (d, *J* = 8.1 Hz, 1H), 5.12 (dd, *J* = 5.7, 3.2 Hz, 2H), 4.83 – 4.59 (m, 2H), 3.84 – 3.67 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.4, 156.8, 136.2, 136.0, 132.8, 128.7, 128.7, 128.6, 128.6, 128.6, 128.6, 128.4, 128.3, 128.2, 126.9, 126.8, 126.4, 73.7, 67.6, 59.2, 52.8. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{20}H_{21}NO_5$ 378.1317, found 378.1320.

Methyl

(2S,3S,E)-2-(((benzyloxy)carbonyl)amino)-5-(4-bromophenyl)-3-hydroxypent-4-enoate (2m)



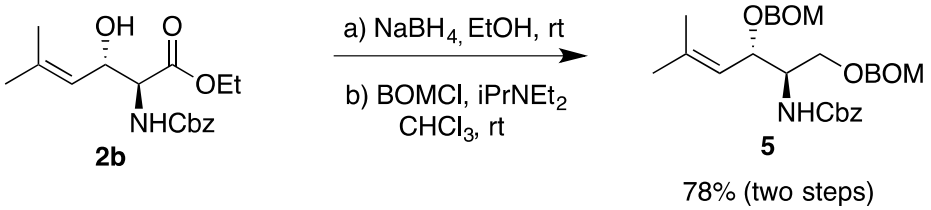
2m

Prepared from **1f** (86.4 mg, 0.2 mmol) to give the product **2f** (37.2 mg, 0.09 mmol, 43%) as a yellowish oil. 90.1:9.9 *e.r.* determined by HPLC analysis (Chiralcel IA, 7.5% 2-propanol in hexanes, 0.6 mL/min, λ = 254 nm, t_{minor} = 121.4 min, t_{major} = 141.0min). **Optical rotation:** $[\alpha]_D^{20}$ +23.5 (c 1.1, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43 (d, *J* = 8.4 Hz, 2H), 7.33 (s, 5H), 7.23 – 7.18 (m, 2H), 6.67 – 6.51 (m,

1H), 6.14 (dd, *J* = 15.9, 5.8 Hz, 1H), 5.73 (d, *J* = 7.9 Hz, 1H), 5.11 (d, *J* = 2.5 Hz, 2H), 4.78 – 4.57 (m, 2H), 3.76 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.1, 156.6, 135.8, 135.0, 131.7, 131.4, 128.5, 128.3, 128.2, 128.1, 127.1, 121.8, 73.4, 67.4. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{20}H_{20}NO_5Br$ 456.0423, found 456.0423.

4. Experimental procedures and characterization of products (5-10 and (+)-Alexine (3))

Benzyl ((5S,6R)-5-(2-methylprop-1-en-1-yl)-1,11-diphenyl-2,4,8,10-tetraoxaundecan-6-yl)carbamate (5)

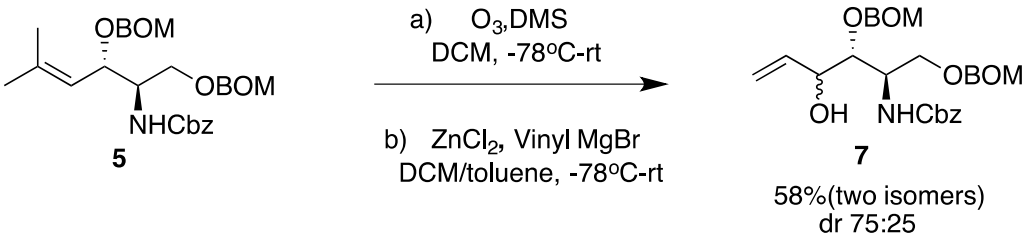


To a solution of **2b** (1.86g, 5.8 mmol, 1 eq) in EtOH (40 mL) was added $NaBH_4$ (0.44g, 11.6 mmol, 2 eq). The reaction mixture was stirred at room temperature overnight. After removing most of the solvent under reduced pressure, the crude mixture was diluted with EtOAc (50 mL). The mixture was then washed with NH_4Cl (sat. aq. soln., 50 mL) and brine (40 mL). The combined organic solvent phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude material was used directly for next step.

The crude material was dissolved in $CHCl_3$/DIPEA (45 mL. 1:1), and to it benzyl chloromethyl ether (13.4 mL, 58 mmol, 10 eq) was added. The reaction mixture was stirred at room temperature overnight. After which it was quenched with $NaHCO_3$ (sat. aq. soln., 40 mL) and extracted with EtOAc (40 mL), followed by brine wash. The organic extract was dried over Na_2SO_4, filtered, solvent evaporated under reduced pressure and the residue was purified by column chromatography (*n*-heptane/EtOAc 6:1) to furnish the corresponding di-BOM product **5** as a colorless oil (2.33g, 4.5 mmol, 78%). **Optical rotation:** $[\alpha]_D^{20}$ +58.7 (c 5.3, CH_2Cl_2). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.38 (dddd, *J* = 11.7, 8.9, 7.3, 4.9 Hz, 15H), 5.45 (d, *J* = 9.3 Hz, 1H), 5.30 – 5.11 (m, 3H), 4.92 – 4.68 (m, 6H), 4.68 – 4.61 (m, 2H), 4.56 (d, *J* = 11.8 Hz, 1H), 4.19 – 4.04 (m, 1H), 3.96 (dd, *J* = 10.3, 5.5 Hz, 1H), 3.84 (dd, *J* = 10.3, 4.0 Hz, 1H), 1.80 (d, *J* = 3.4 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.1, 139.4, 138.0, 137.8, 136.7, 128.6, 128.6, 128.5, 128.5, 128.1, 127.9, 127.8, 127.8, 127.7,

127.6, 127.0, 121.7, 95.1, 91.7, 72.2, 69.7, 69.5, 67.0, 66.7, 65.3, 54.5, 26.0, 18.5. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{31}H_{37}NO_6$ 542.2519, found 542.2518.

Benzyl ((5R,6R)-5-((R)-1-hydroxyallyl)-1,11-diphenyl-2,4,8,10-tetraoxaundecan-6-yl)carbamate (7)

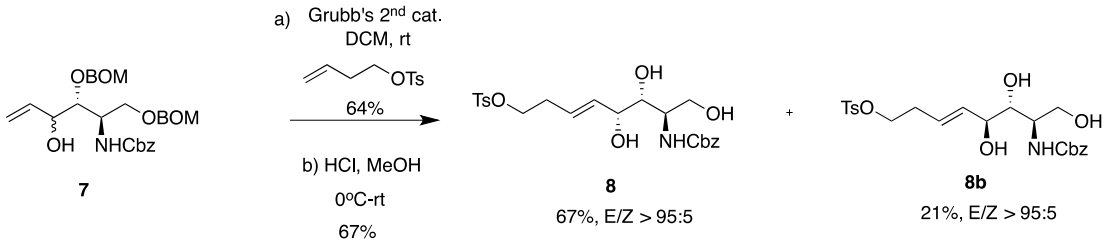


Ozone was bubbled through a vigorously stirred solution of **5** (0.2 g, 0.39 mmol, 1 eq) in DCM (15 mL) at -78°C. When TLC showed full conversion of the starting material, dimethylsulfide was added (0.29 mL, 3.9 mmol, 10eq) and the mixture was allowed to warm to room temperature for 6 h. Evaporation of the solvent afforded crude aldehyde which can be used directly in next step.

In another flammable dried round bottom flask, a commercial vinyl magnesium bromide solution (2.8 mL, 0.7 M in THF, 5 eq) was added and evaporated to dryness under reduced pressure, and the residue was dissolved in anhydrous DCM under nitrogen. This operation was repeated twice, and the obtained Grignard reagent solution in DCM (0.5 M) was combined with powered anhydrous $ZnCl_2$ (0.13 g, 0.96 mmol, 2.5 eq) at 0°C. The resulted suspension was stirred at room temperature for 5h, and then cooled to -78°C. A solution of the fresh prepared aldehyde in anhydrous toluene (0.05M) was added via cannula slowly. The reaction was stirred at -78°C for 2h, then warm to room temperature and stirred overnight. After which it was quenched with NH_4Cl (sat. aq. soln., 30 mL) and extracted with EtOAc (30 mL), followed by brine wash. The organic extract was dried over $MgSO_4$, filtered, solvent evaporated under vacuum and the residue was purified by column chromatography (*n*-heptane/ EtOAc 3:1) to furnish the corresponding mixed (3:1 *dr*) product **7 (**116 mg, 0.22 mmol, 58%) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.46 – 7.23 (m, 15H, two isomers), 5.96 (ddd, *J* = 16.4, 10.6, 5.3 Hz, 1H, two isomers), 5.72 (d, *J* = 8.9 Hz, 0.67H, major isomer), 5.56 – 5.48 (m, 0.21H, minor isomer), 5.42 (dt, *J* = 17.3, 1.6 Hz, 0.75H, major isomer), 5.39 – 5.31 (m, 0.29H, minor isomer), 5.23 (dt, *J* = 10.5, 1.6 Hz, 1H, two isomer), 5.11 (s, 1.71H, major isomer), 5.09 (s, 0.51H, minor isomer), 4.94 – 4.54 (m, 8H, two isomers), 4.36 (s, 0.2H, minor isomer), 4.31 (s, 0.79H, major isomer), 4.14 (ddt, *J* = 9.2, 6.1, 4.9 Hz, 1H, two isomers), 3.86 (ddd, *J* = 20.0, 10.1, 4.0 Hz, 1H, two isomers), 3.79 – 3.65 (m, 2H, two isomers). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.71, 137.53, 137.40, 136.59, 136.30, 128.54, 128.50, 128.48, 128.21, 128.18, 128.00, 127.86, 127.82, 127.81, 127.78, 116.52, 115.89, 96.09, 96.00,

95.08, 82.54, 81.47, 77.38, 71.92, 70.56, 70.50, 70.44, 69.94, 69.79, 67.39, 67.06, 66.96, 51.62. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{30}H_{35}NO_7$ 544.2311, found 544.2313.

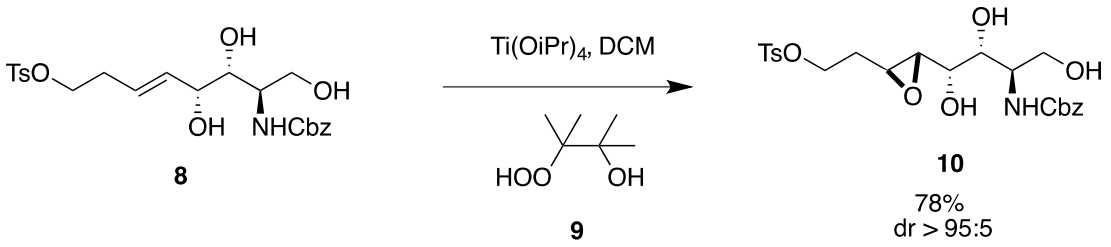
(5R,6R,7R,E)-7-(((benzyloxy)carbonyl)amino)-5,6,8-trihydroxyoct-3-en-1-yl 4-methylbenzenesulfonate (8)



Mixed starting material **7** (100 mg, 0.19 mmol, 1 eq) and 4-butenol p-tolyl-sulfonate (130 mg, 0.57 mmol, 3 eq) were added simultaneously via syringe to a stirring solution of Grubbs 2nd catalyst (16 mg, 0.02 mmol, 0.1 eq) in CH_2Cl_2 (5 mL) under nitrogen atmosphere. The flask was allowed to stir at room temperature for 1 day. The reaction mixture was then reduced in volume to 0.5 mL and purified directly by column chromatography (heptane/EtOAc 1:1) to furnish the corresponding mixed (*dr* 3:1) *trans* olefin product **(**61 mg, 44% **(**64% brsm**))** as a colorless oil.

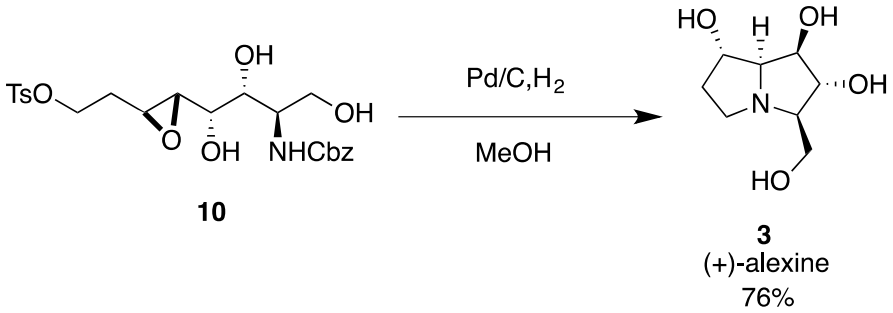
To a solution of *trans* olefin product (61 mg, 0.085 mmol, 1 eq) in MeOH (5 mL) was added HCl (35% aq., 1 mL) in 0°C. After stirring overnight, the reaction was quenched with $NaHCO_3$ (sat. aq. soln., 15 mL) and the aqueous phase was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (CH_2Cl_2/MeOH 30:1) to furnish desired product **8** (27.3 mg, 67%, *dr* > 95:5) and undesired product **8b** (8.5 mg, 21 %, *dr* > 95:5). **Optical rotation for 8:** $[\alpha]_D^{20}$ -4.5 (c 1.7, $CHCl_3$). **^{1}H NMR for 8 (400 MHz, MeOD)** δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.40 – 7.20 (m, 5H), 5.76 – 5.52 (m, 2H), 5.08 (d, *J* = 1.8 Hz, 2H), 4.15 – 3.94 (m, 3H), 3.72 (q, *J* = 7.7, 6.9 Hz, 3H), 3.48 (dd, *J* = 6.4, 3.4 Hz, 1H), 2.44 (s, 3H), 2.35 (q, *J* = 6.4 Hz, 2H). **^{13}C NMR for 8 (100 MHz, MeOD)** δ 158.8, 146.5, 138.2, 134.7, 134.4, 131.1, 129.5, 129.0, 129.0, 128.9, 127.6, 74.8, 73.1, 71.1, 67.6, 62.3, 55.8, 55.7, 32.9, 21.6. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{23}H_{29}NO_8S$ 480.1692, found 480.1690.

2-((2S,3S)-3-((1S,2R,3R)-3-(((benzyloxy)carbonyl)amino)-1,2,4-trihydroxybutyl)oxiran-2-yl)ethyl 4-methylbenzenesulfonate (10)



Starting material **8** (20 mg, 0.04 mmol, 1 eq) and β-hydroperoxy alcohol **9** (8.4 mg, 0.06 mmol, 1.5 eq) were dissolved in anhydrous CH_2Cl_2 (5 mL). Under a nitrogen atmosphere, $Ti(OiPr)_4$ (1.2 mg, 0.004 mmol, 0.1 eq) was added and the reaction mixture was stirred overnight at room temperature. The reaction was then quenched by addition of NH_4F (sat. aq. soln., 0.1 mL) and the reaction was stirred vigorously for 1h. The precipitate was removed by filtration, the filtrate concentrated under reduced pressure and the residue was purified by column chromatography (CH_2Cl_2/MeOH 30:1) to furnish the corresponding epoxide **10** (16.3 mg, 78%, *dr* > 95:5) as a colorless oil. **Optical rotation:** $[\alpha]_D^{20}$ -10.9 (c 1.1, $CHCl_3$). **^{1}H NMR (400 MHz, MeOD)** δ 7.89 – 7.71 (m, 2H), 7.50 – 7.40 (m, 2H), 7.41 – 7.22 (m, 5H), 5.18 – 5.02 (m, 2H), 4.15 (dd, *J* = 6.8, 5.7 Hz, 2H), 3.84 – 3.68 (m, 3H), 3.65 (dd, *J* = 7.7, 2.0 Hz, 1H), 3.38 (dd, *J* = 5.7, 2.0 Hz, 1H), 2.96 (ddd, *J* = 6.7, 4.1, 2.1 Hz, 1H), 2.87 (dd, *J* = 5.7, 2.2 Hz, 1H), 2.45 (s, 3H), 2.03 (dtd, *J* = 14.0, 6.8, 4.1 Hz, 1H), 1.81 – 1.62 (m, 1H). **^{13}C NMR (100 MHz, MeOD)** δ 157.5, 145.2, 136.9, 132.9, 129.7, 128.1, 127.6, 127.5, 70.6, 70.0, 67.5, 66.2, 61.0, 58.1, 54.1, 53.6, 31.2, 20.2. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_{23}H_{29}NO_9S$ 496.1641, found 496.1645.

(+)-Alexine (3)



Pd/C (16 mg, 10 wt.%, 0.1 eq) was added to **10** (76 mg, 0.15 mmol, 1 eq) in EtOH (2 mL). The reaction mixture was stirred under an atmosphere of H_2 at room temperature for 3h. The reaction was filtered over Celite and the solvent was removed *in vacuo*. The crude intermediate was purified by column chromatography (EtOAc/MeOH/$iPrNH_2$ 10:10:1) to afford (+)-Alexine **3** (22 mg, 76%) as a white solid. mp (160-162˚C). **Optical rotation:** $[\alpha]_D^{20}$ +42.1 (c 0.3, H_2O). **^{1}H NMR (400 MHz, D_2O)** δ 4.49 – 4.34 (m, 1H), 4.18 (dd, *J* = 7.7, 6.5 Hz, 1H), 3.87 – 3.80 (m, 2H), 3.77 (dd, *J* = 9.2, 6.5 Hz, 1H), 3.28 (dd, *J* = 7.7, 5.5 Hz, 1H), 3.02 – 2.75 (m, 3H), 2.18 (dtd, *J* = 12.5, 6.2, 3.1 Hz, 1H), 1.73 (ddt, *J* = 12.3, 10.0, 7.4 Hz, 1H). **^{13}C**

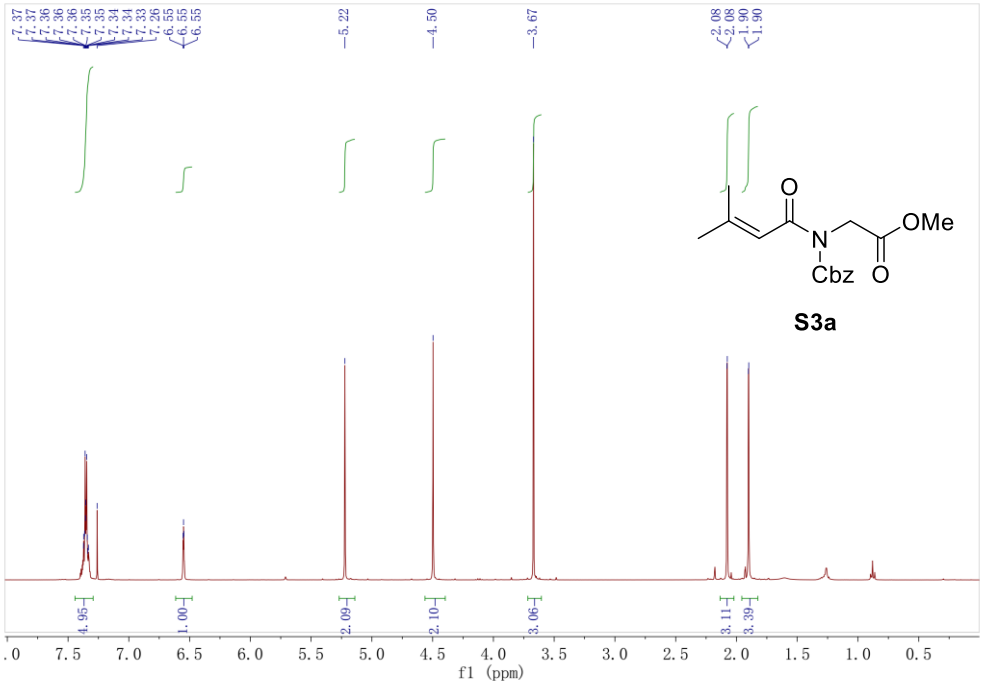
NMR (100 MHz, D_2O) δ 76.3, 76.2, 70.2, 69.9, 64.2, 59.1, 45.6, 34.2. **HRMS**: (ESI/TOF-Q) *m/z*: $[M + Na]^+$ calcd for $C_8H_{15}NO_4$ 190.1079, found 190.1087.

6. NMR spectrum

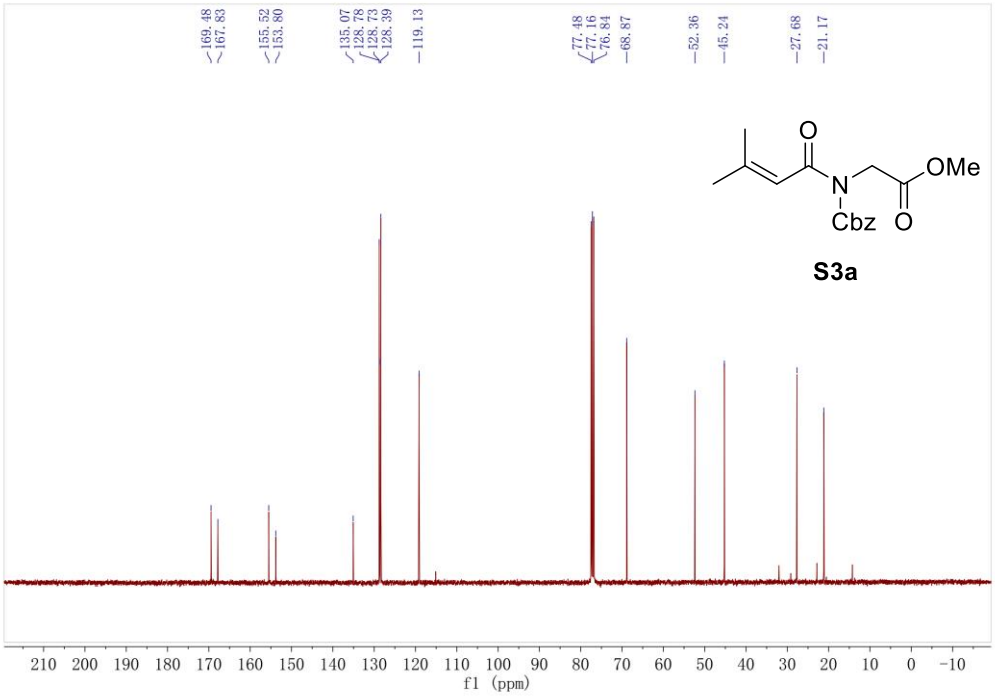
Starting material (method 1,1a, 1c-d, 1i-j, 1l-n)

Methyl N-((benzyloxy)carbonyl)-N-(3-methylbut-2-enoyl)glycinate (S3a)

^{1}H-NMR

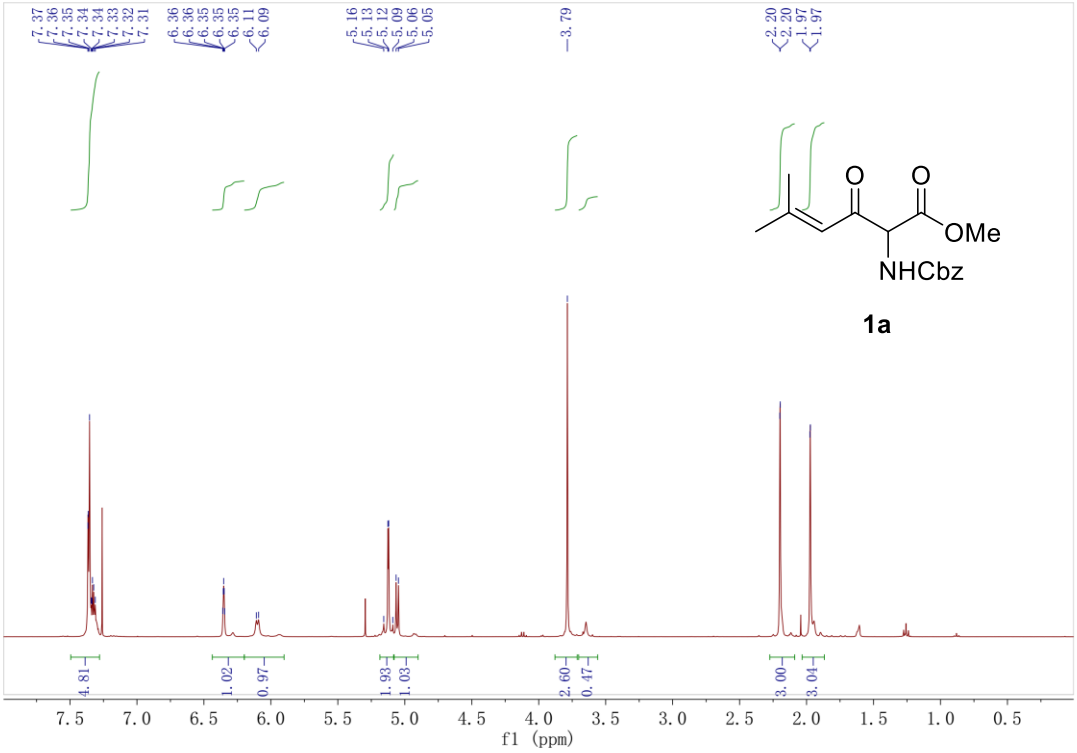


^{13}C-NMR

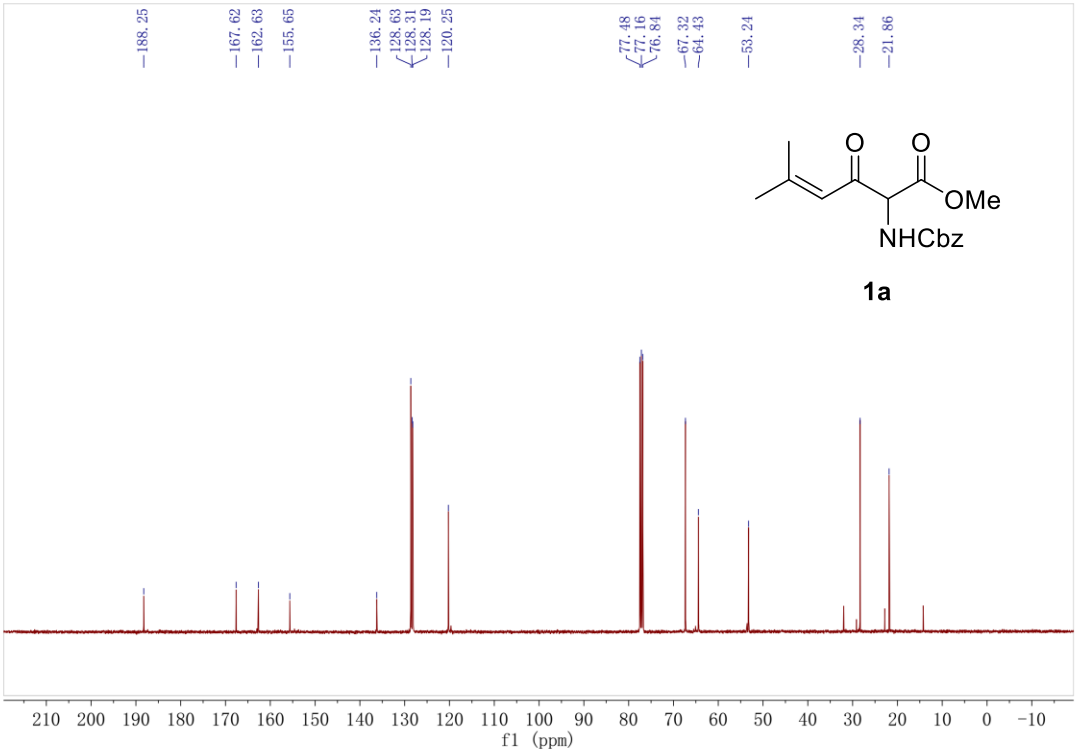


Methyl 2-(((benzyloxy)carbonyl)amino)-5-methyl-3-oxohex-4-enoate (1a)

^{1}H-NMR

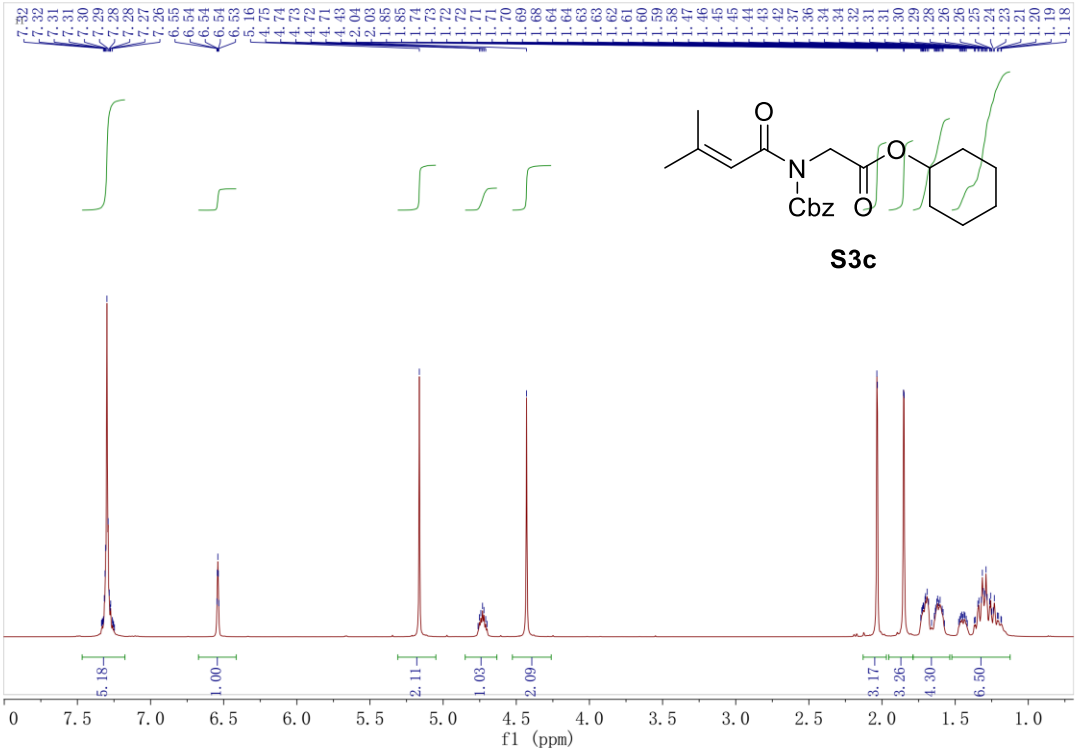


^{13}C-NMR

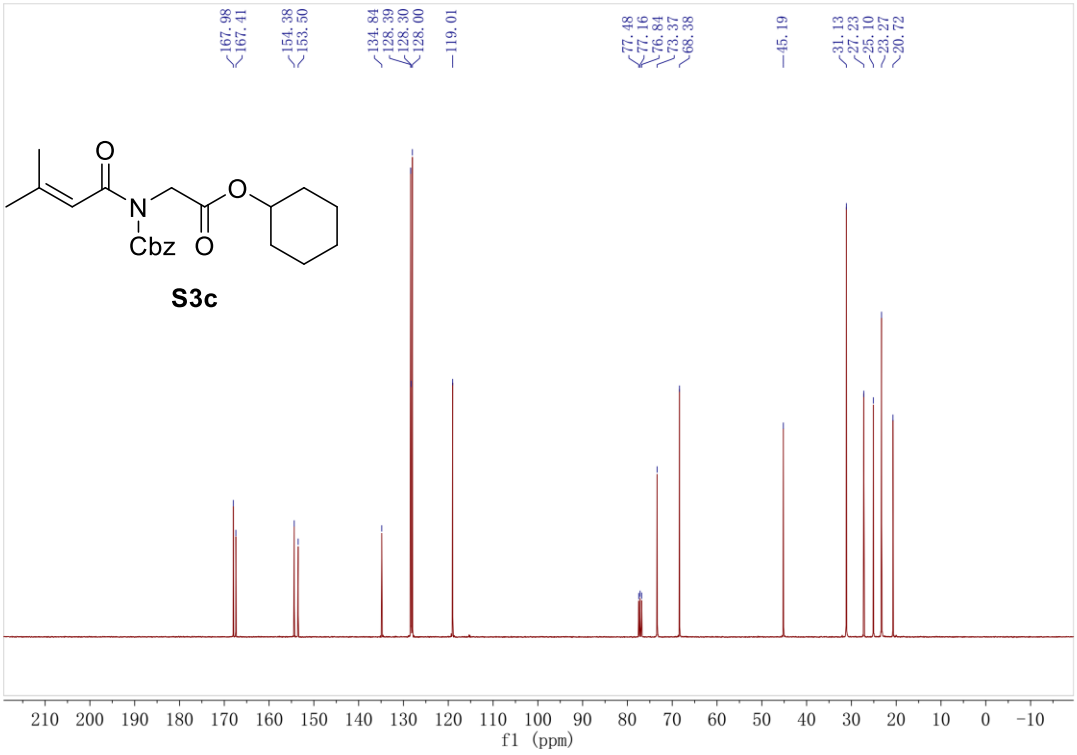


Cyclohexyl N-((benzyloxy)carbonyl)-N-(3-methylbut-2-enoyl)glycinate (S3c)

^{1}H-NMR

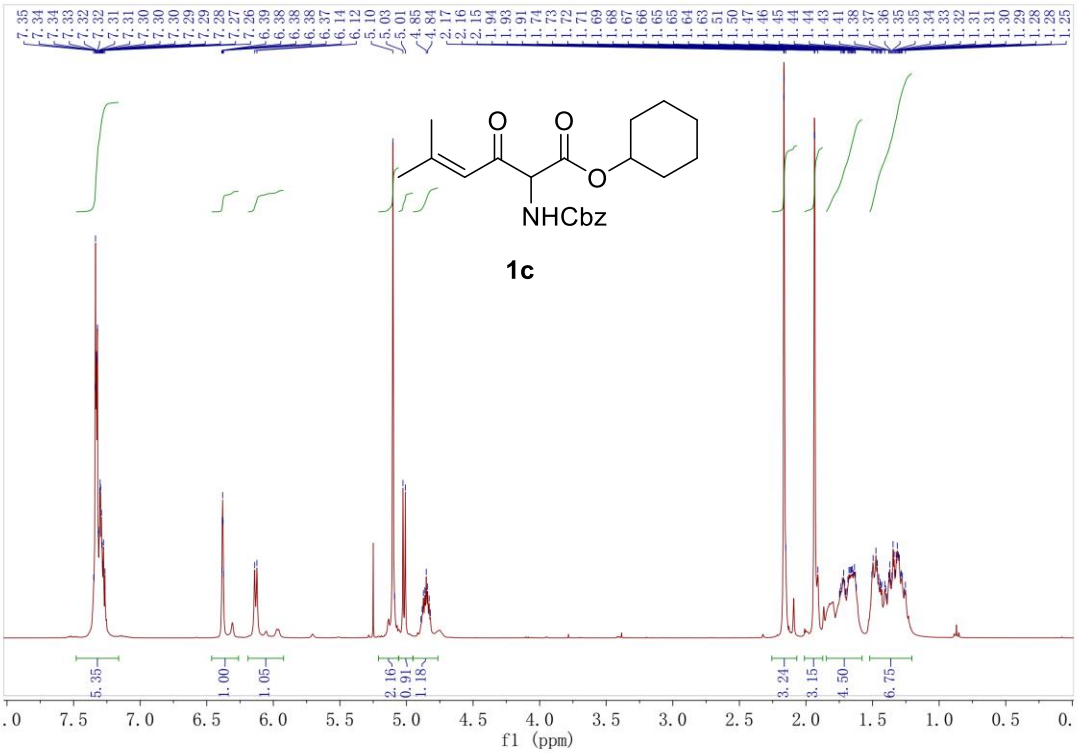


^{13}C-NMR

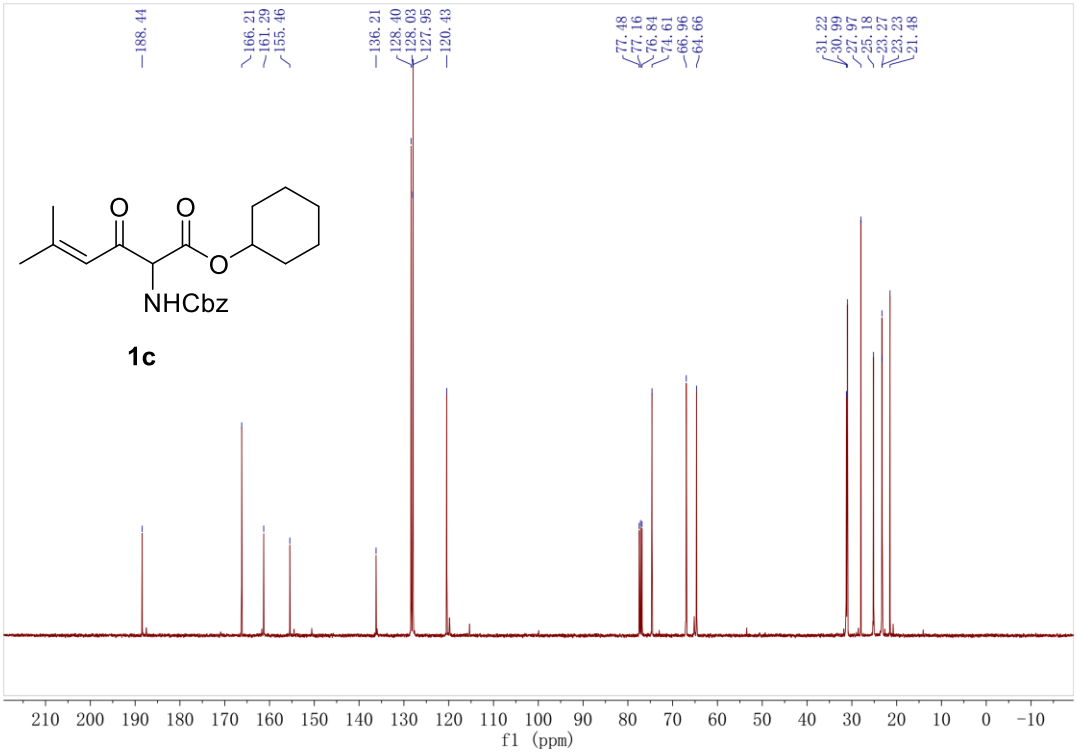


Methyl (*E*)-2-(((benzyloxy)carbonyl)amino)-4-methyl-3-oxohex-4-enoate (1c)

^{1}H-NMR

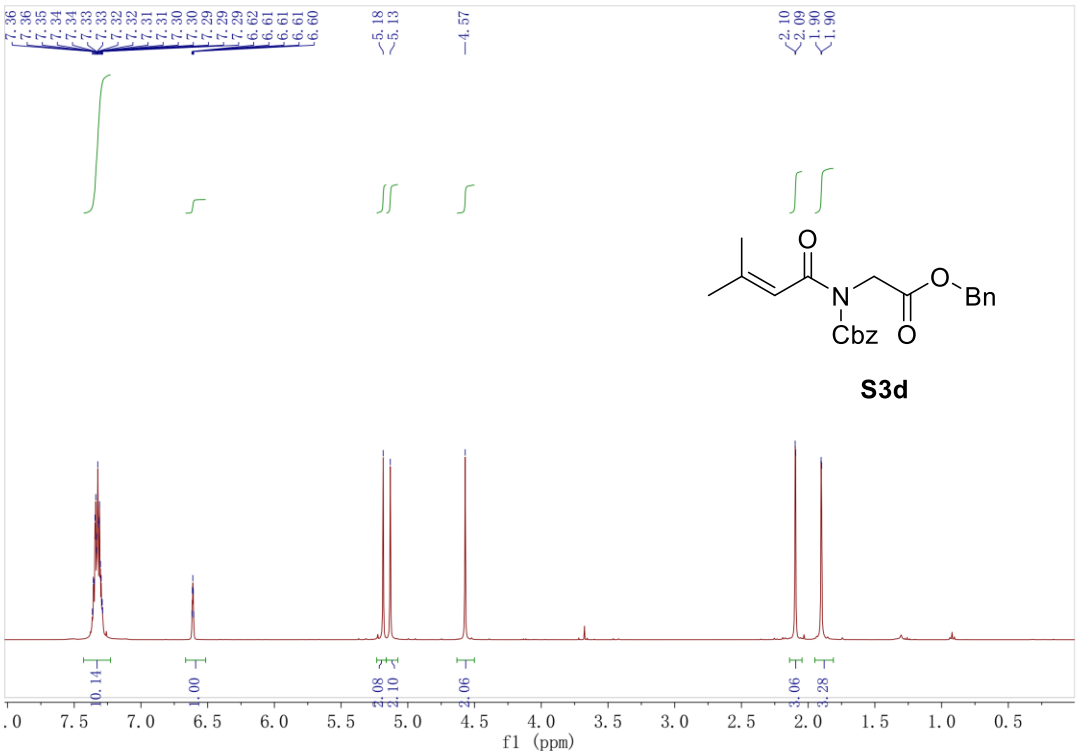


^{13}C-NMR

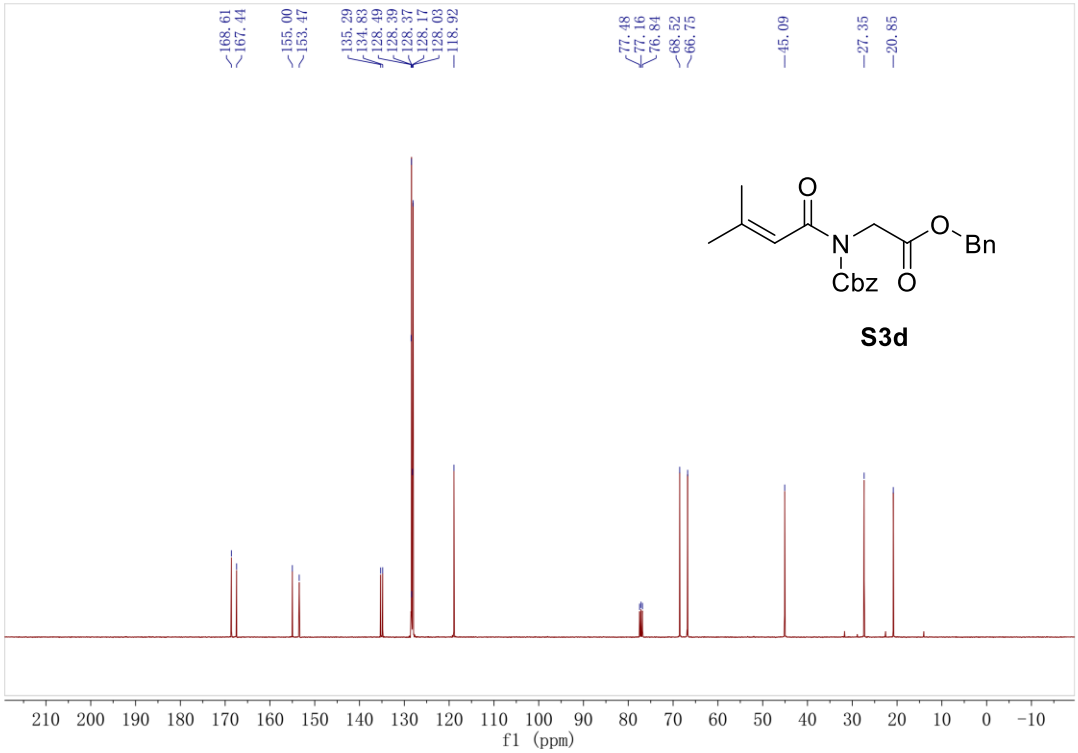


Benzyl N-((benzyloxy)carbonyl)-N-(3-methylbut-2-enoyl)glycinate (S3d)

^{1}H-NMR

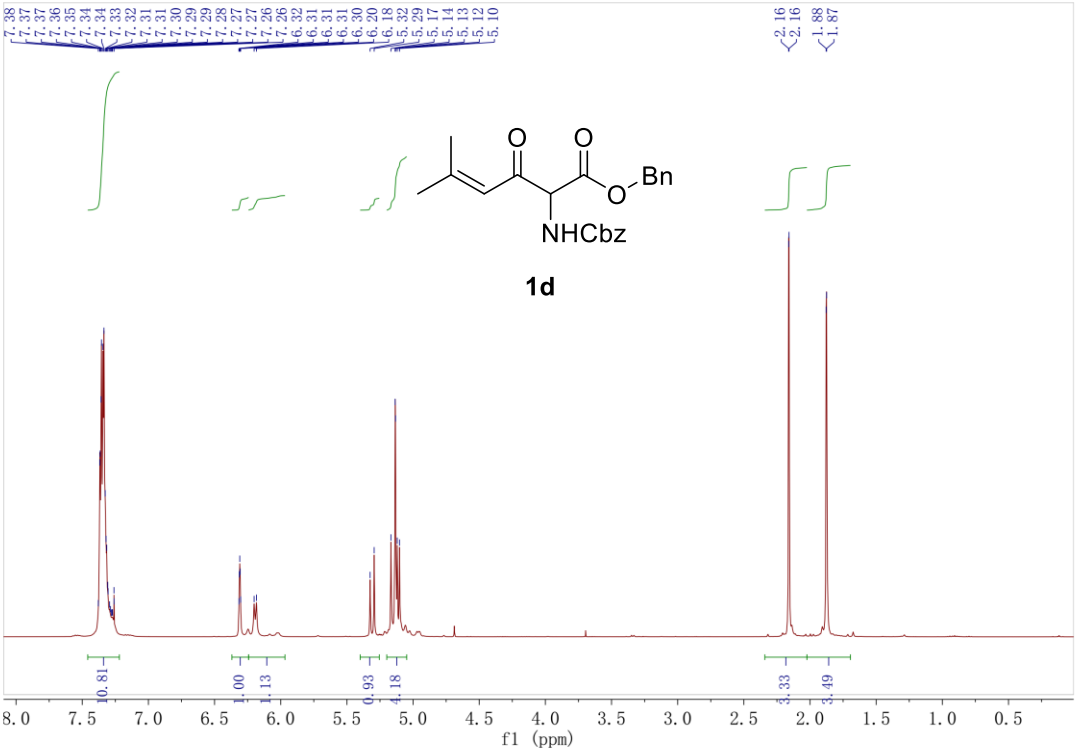


^{13}C-NMR

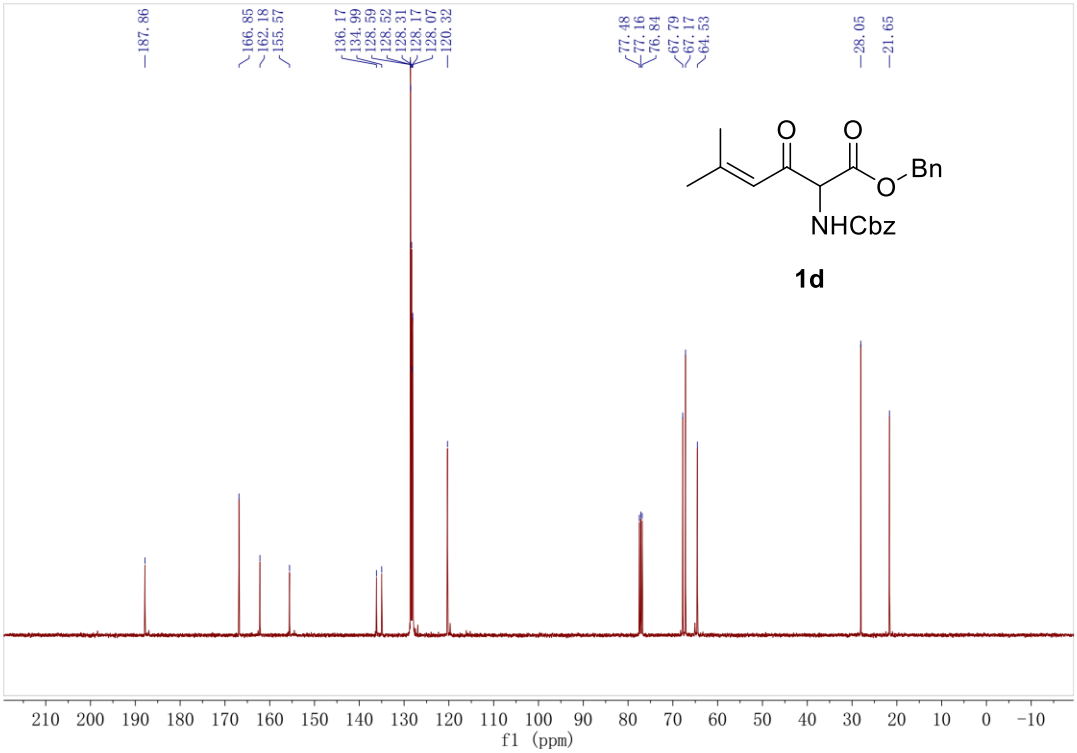


Benzyl 2-(((benzyloxy)carbonyl)amino)-5-methyl-3-oxohex-4-enoate (1d)

^{1}H-NMR

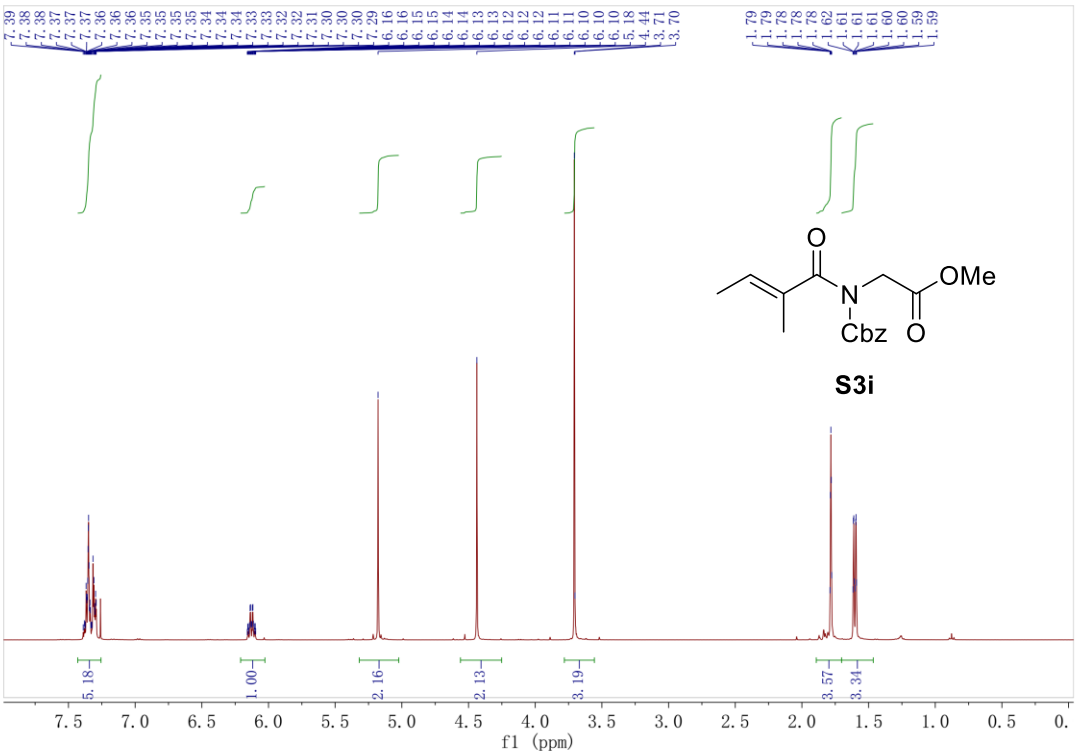


^{13}C-NMR

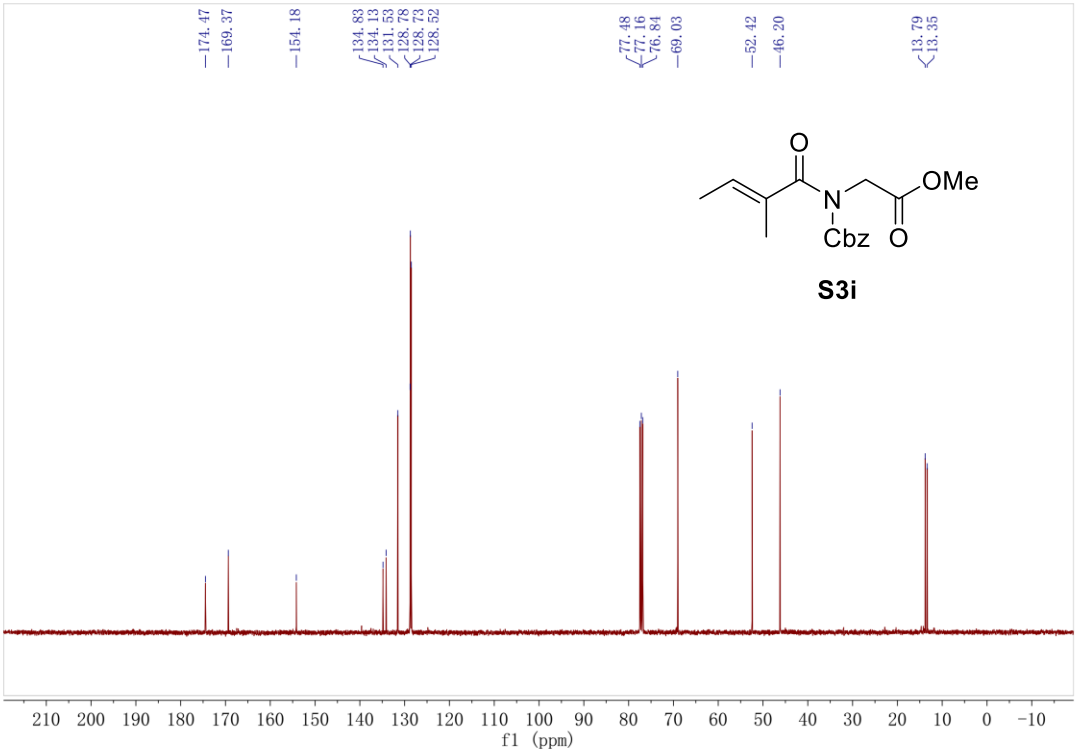


Methyl (*E*)-N-((benzyloxy)carbonyl)-N-(2-methylbut-2-enoyl)glycinate (S3i)

^{1}H-NMR

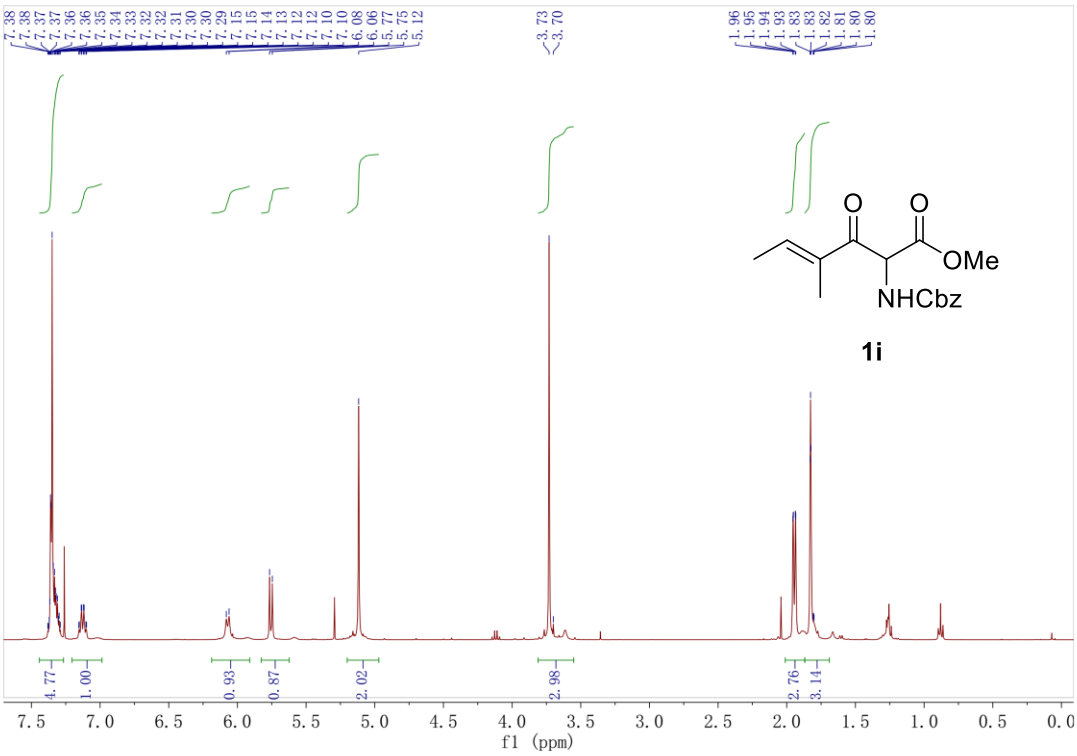


^{13}C-NMR

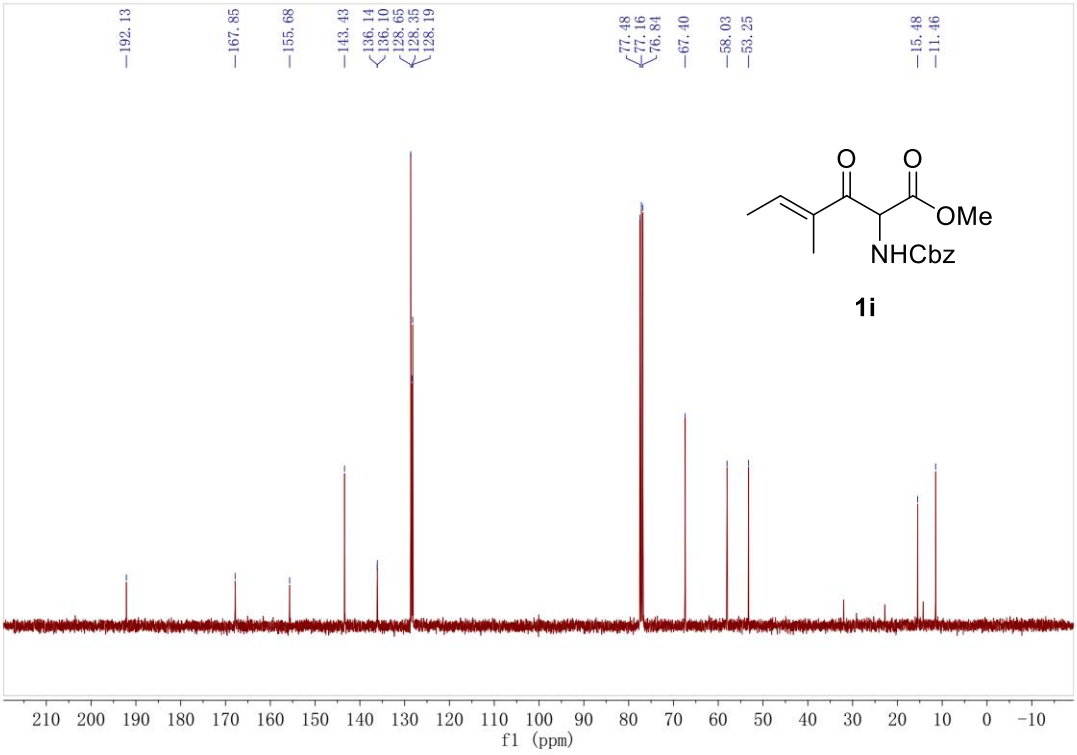


Methyl (*E*)-2-(((benzyloxy)carbonyl)amino)-4-methyl-3-oxohex-4-enoate (1i)

^{1}H-NMR

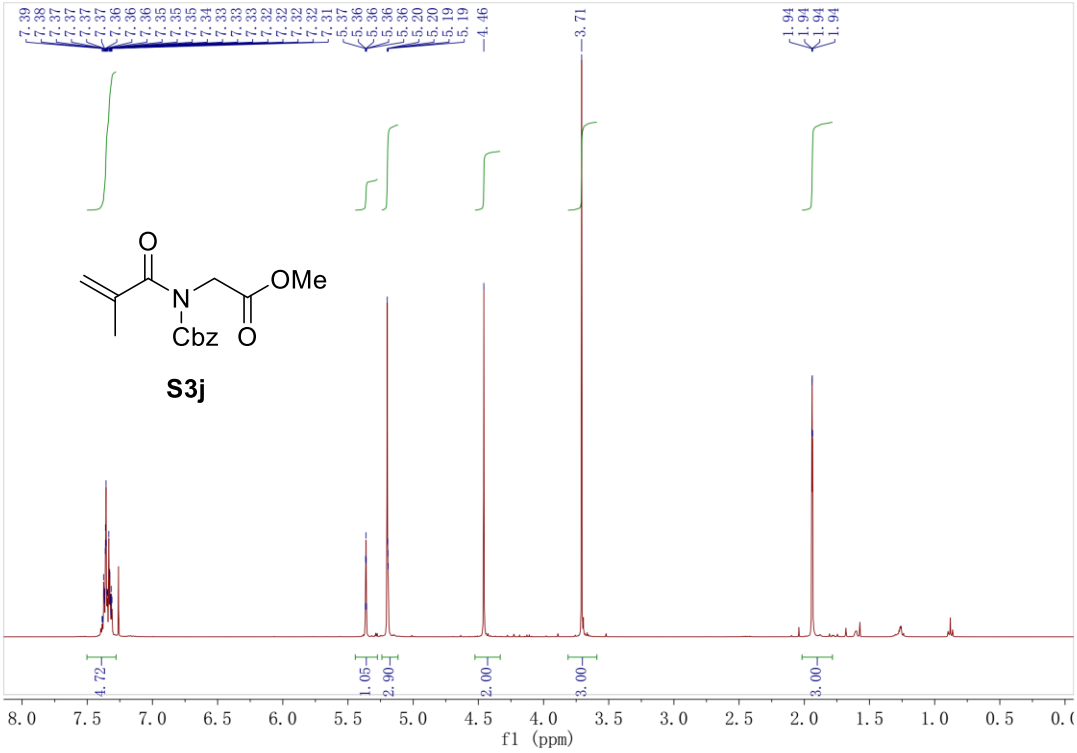


^{13}C-NMR

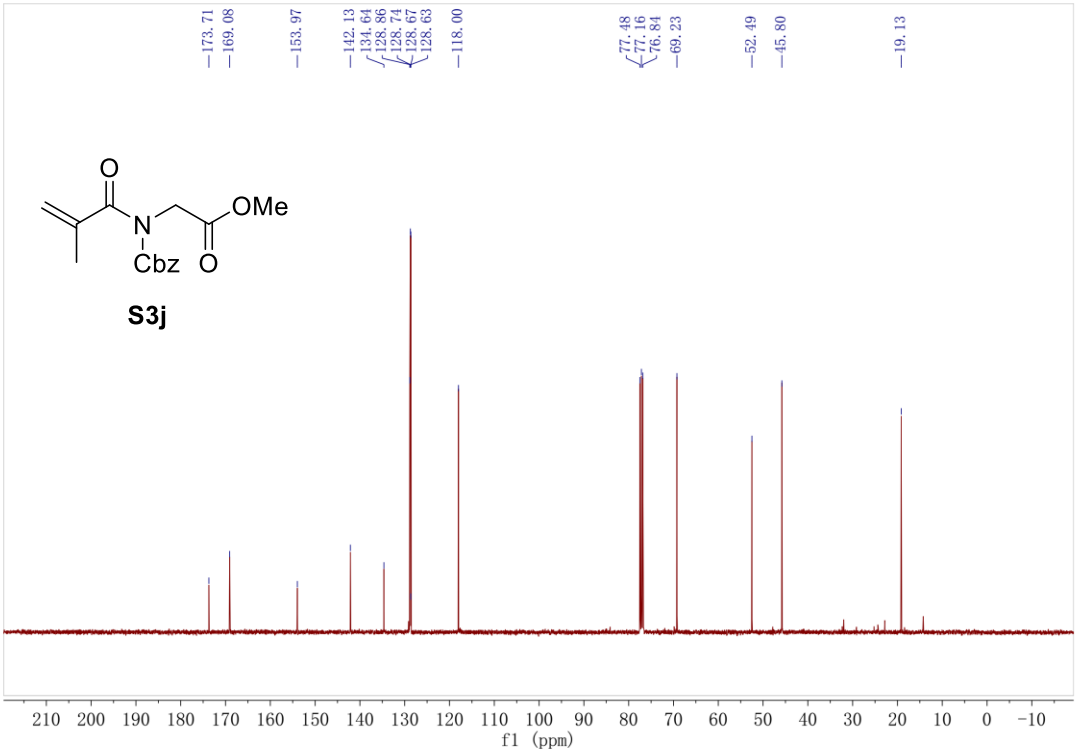


Methyl N-((benzyloxy)carbonyl)-N-methacryloylglycinate (S3j)

^{1}H-NMR

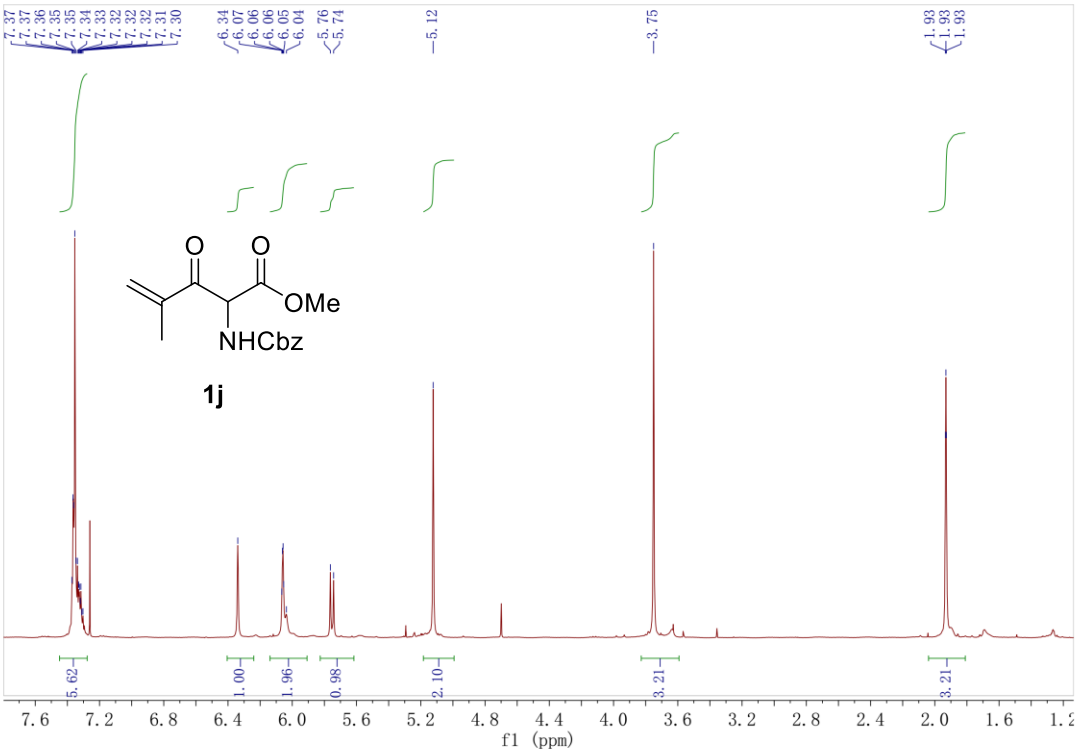


^{13}C-NMR



Methyl 2-(((benzyloxy)carbonyl)amino)-4-methyl-3-oxopent-4-enoate (1j)

^{1}H-NMR



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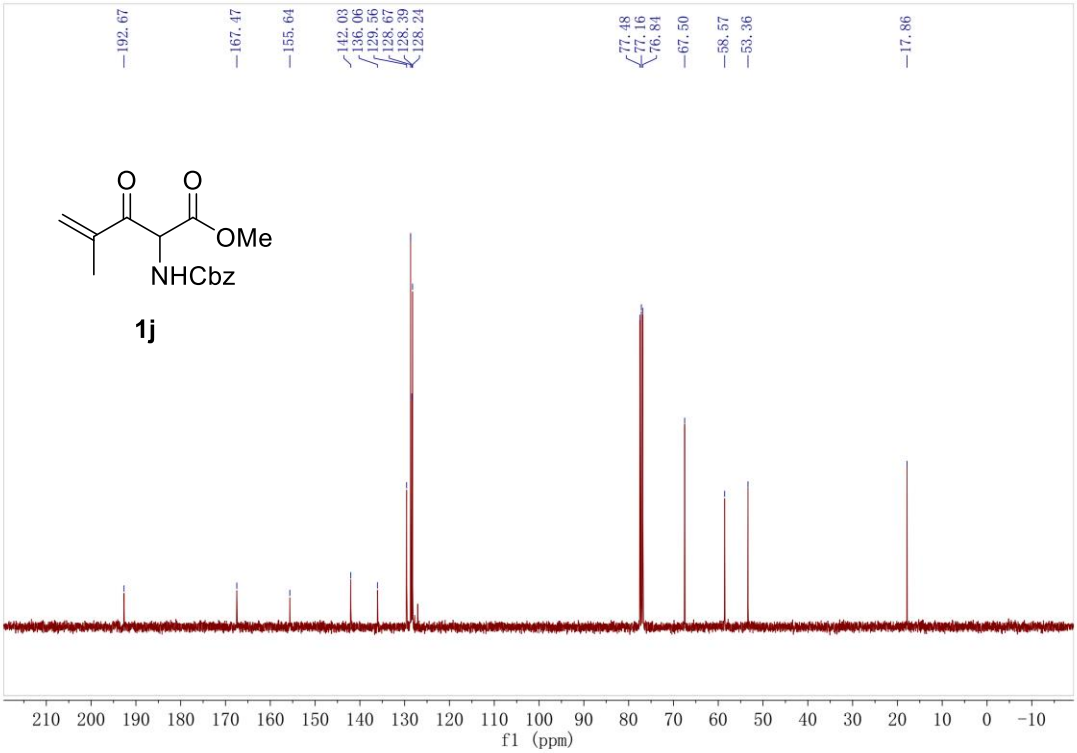
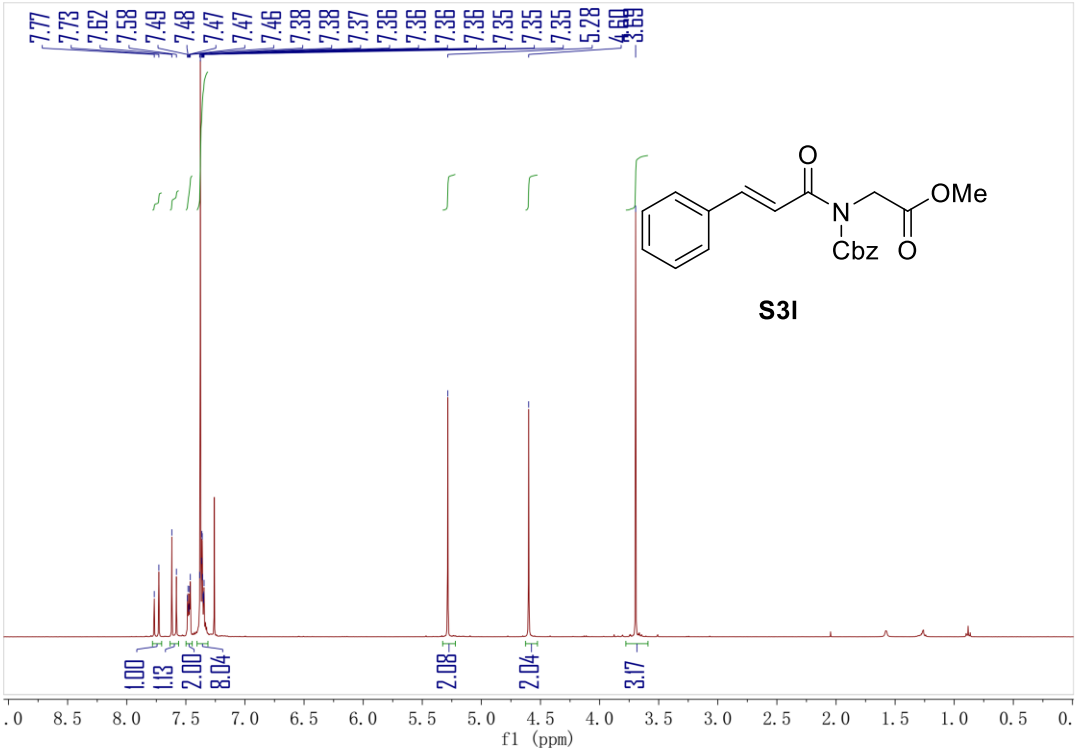
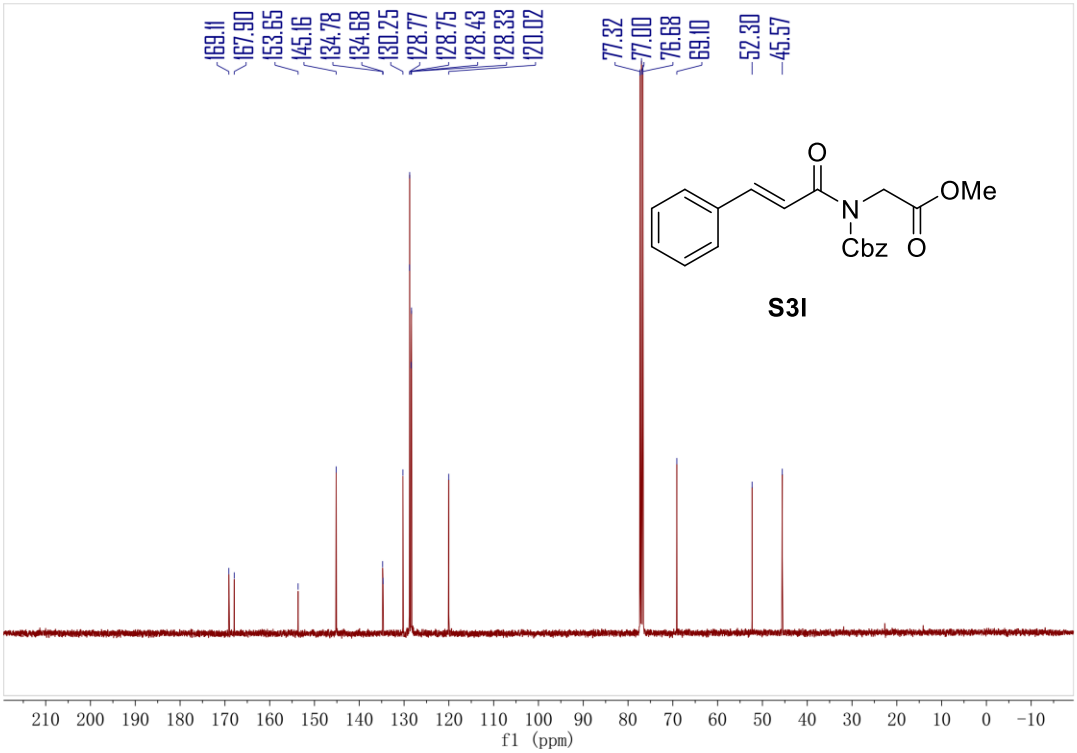


Methyl N-((benzyloxy)carbonyl)-N-cinnamoylglycinate (S3l)

^{1}H-NMR

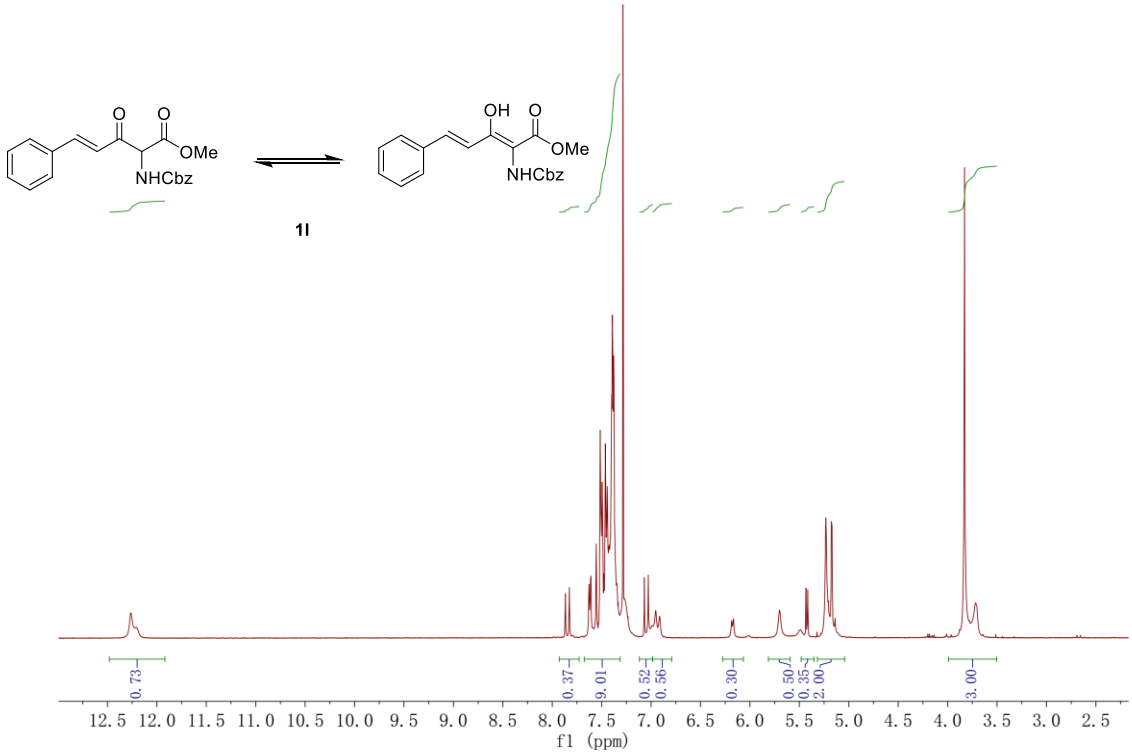


^{13}C-NMR



Methyl (*E*)-2-(((benzyloxy)carbonyl)amino)-3-oxo-5-phenylpent-4-enoate (1l)

^{1}H-NMR



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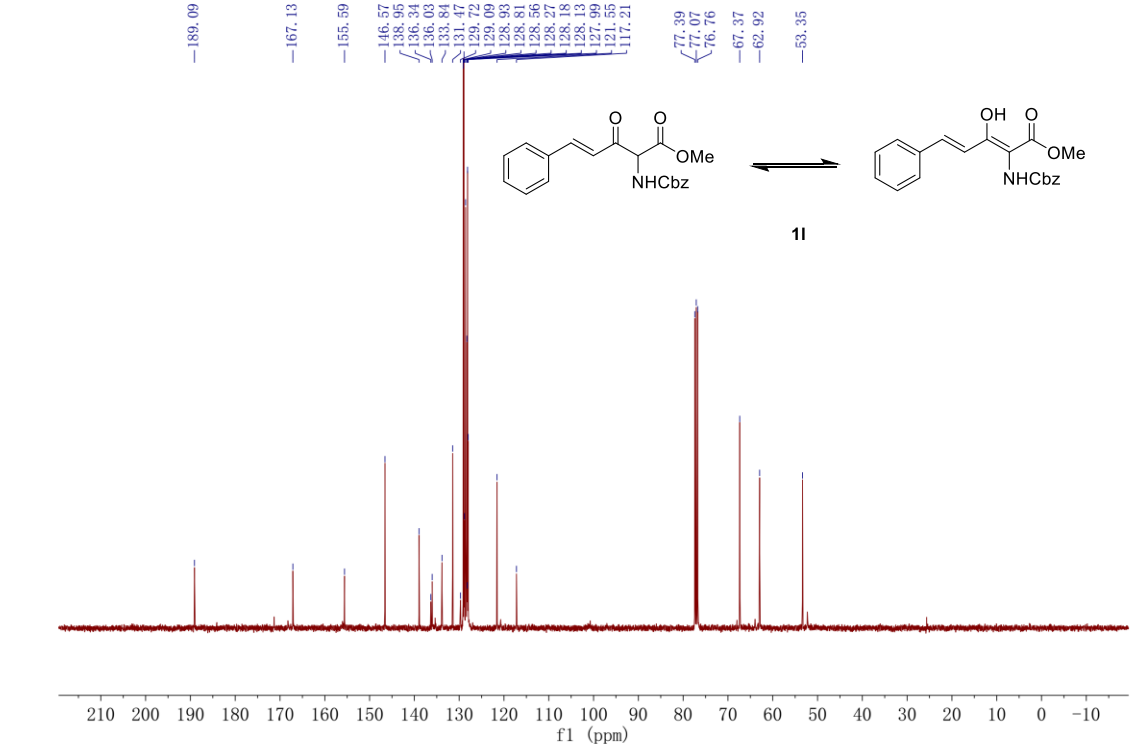
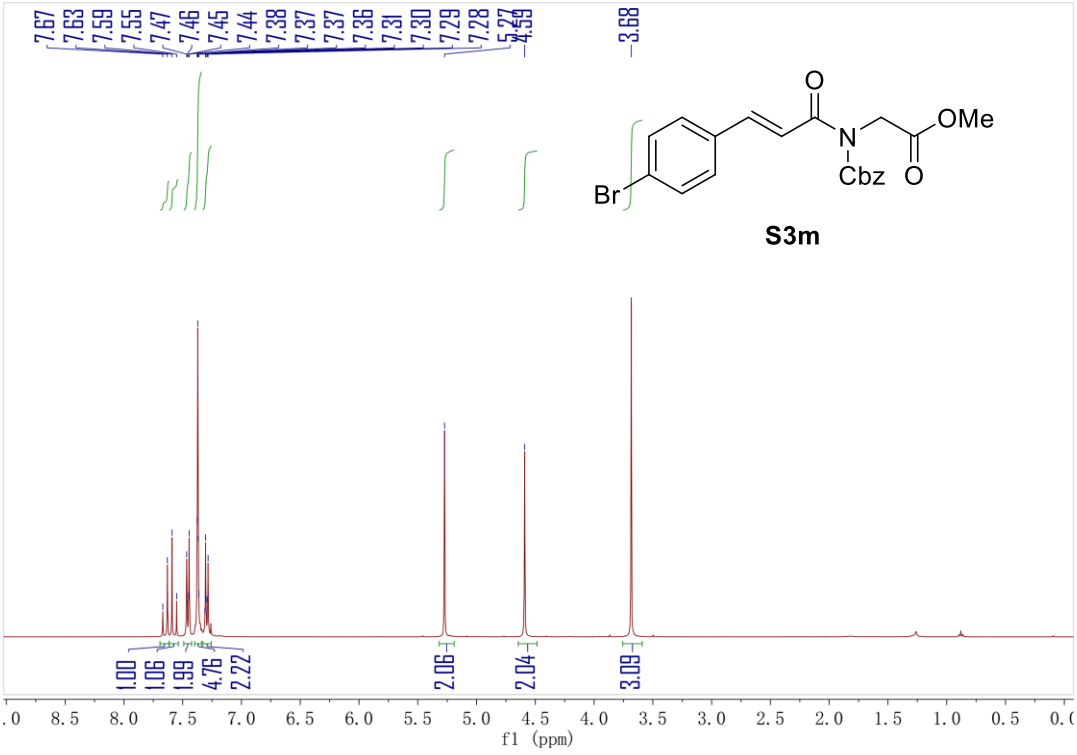
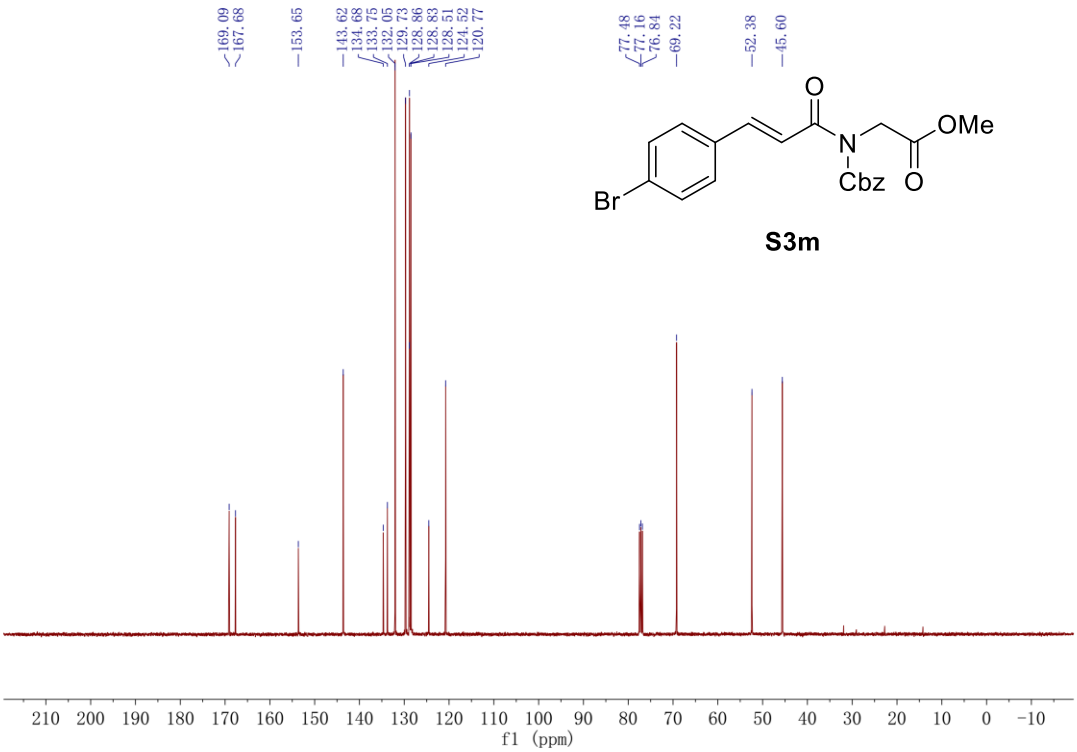


Methyl (*E*)-N-((benzyloxy)carbonyl)-N-(3-(4-bromophenyl)acryloyl)glycinate (S3m)

^{1}H-NMR

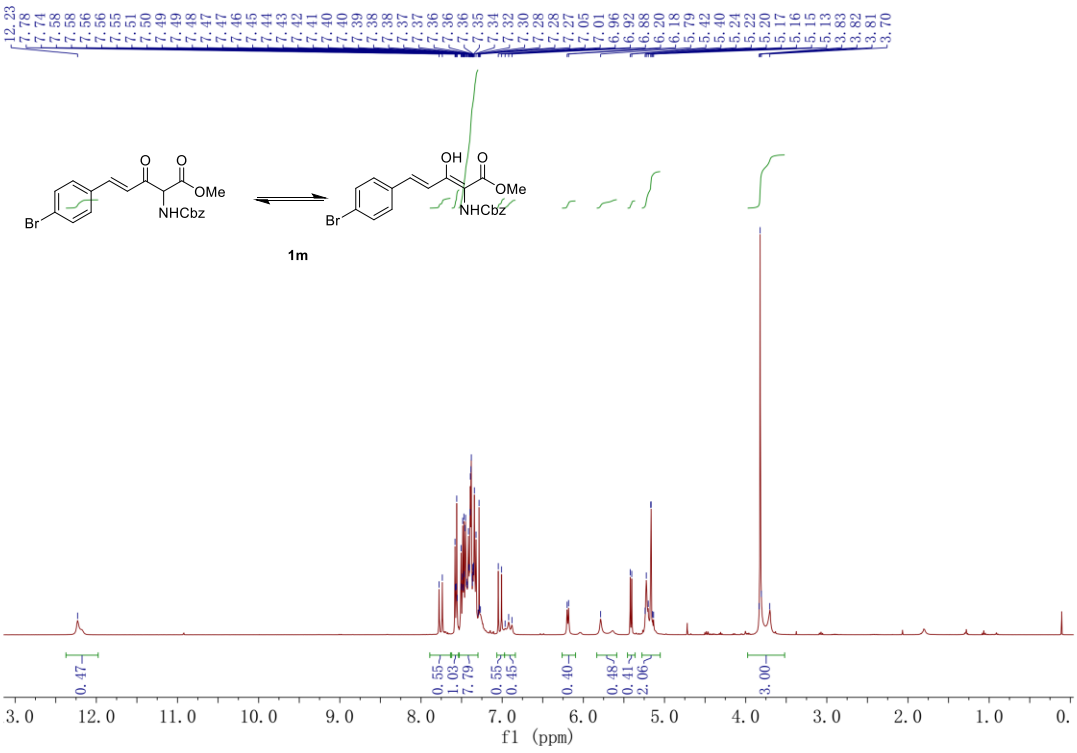


^{13}C-NMR

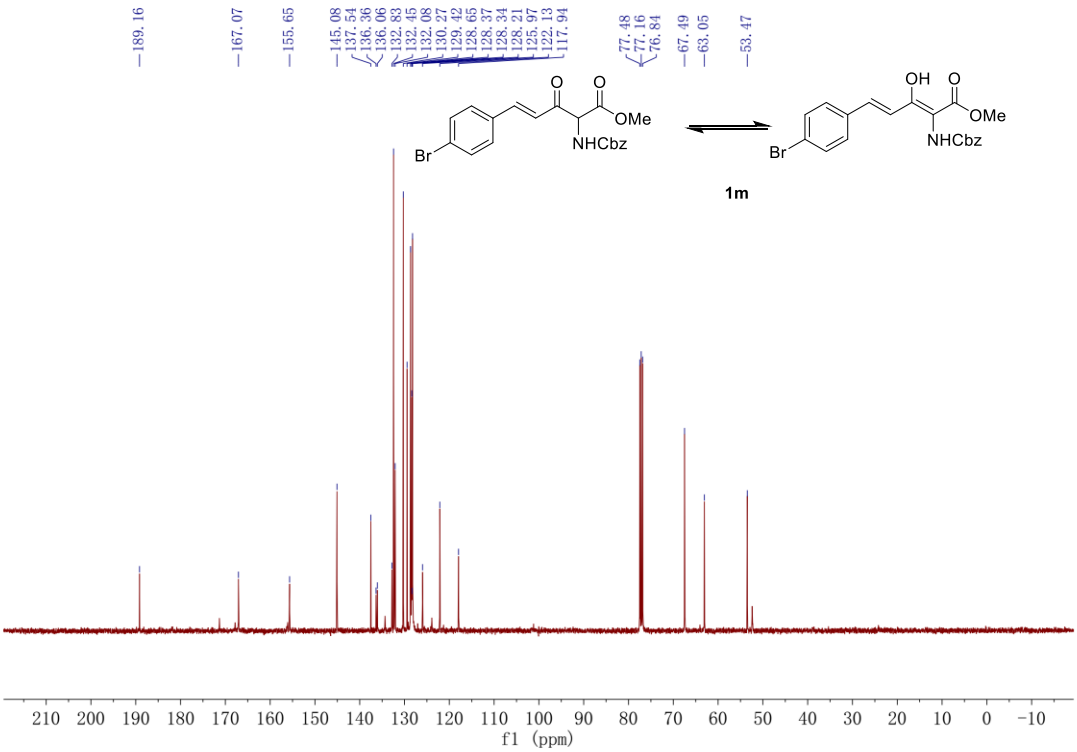


Methyl
(*E*)-2-(((benzyloxy)carbonyl)amino)-5-(4-bromophenyl)-3-oxopent-4-enoate (1m)

^{1}H-NMR

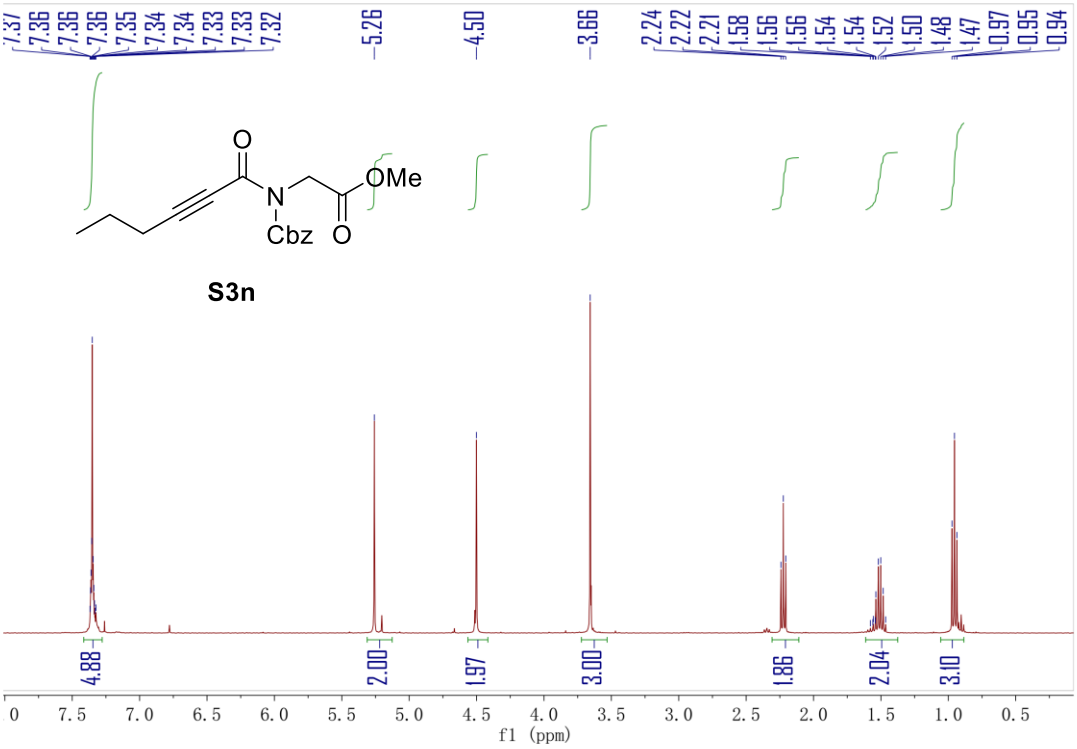


^{13}C-NMR

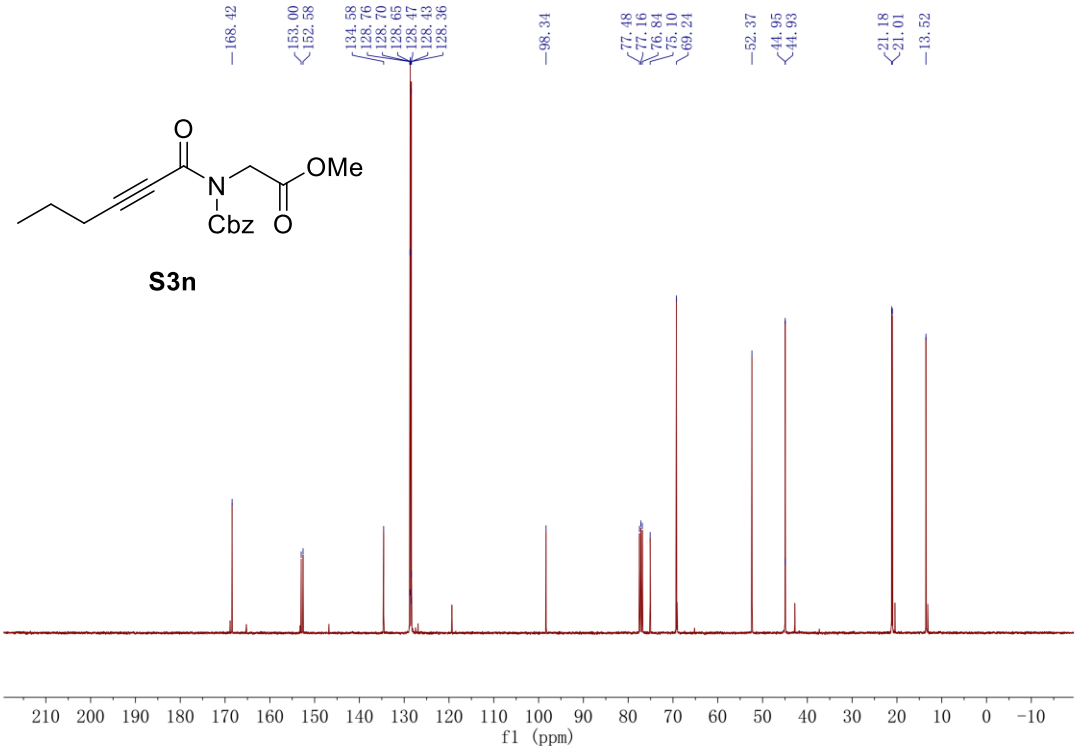


Methyl N-((benzyloxy)carbonyl)-N-(hex-2-ynoyl)glycinate (S3n)

^{1}H-NMR

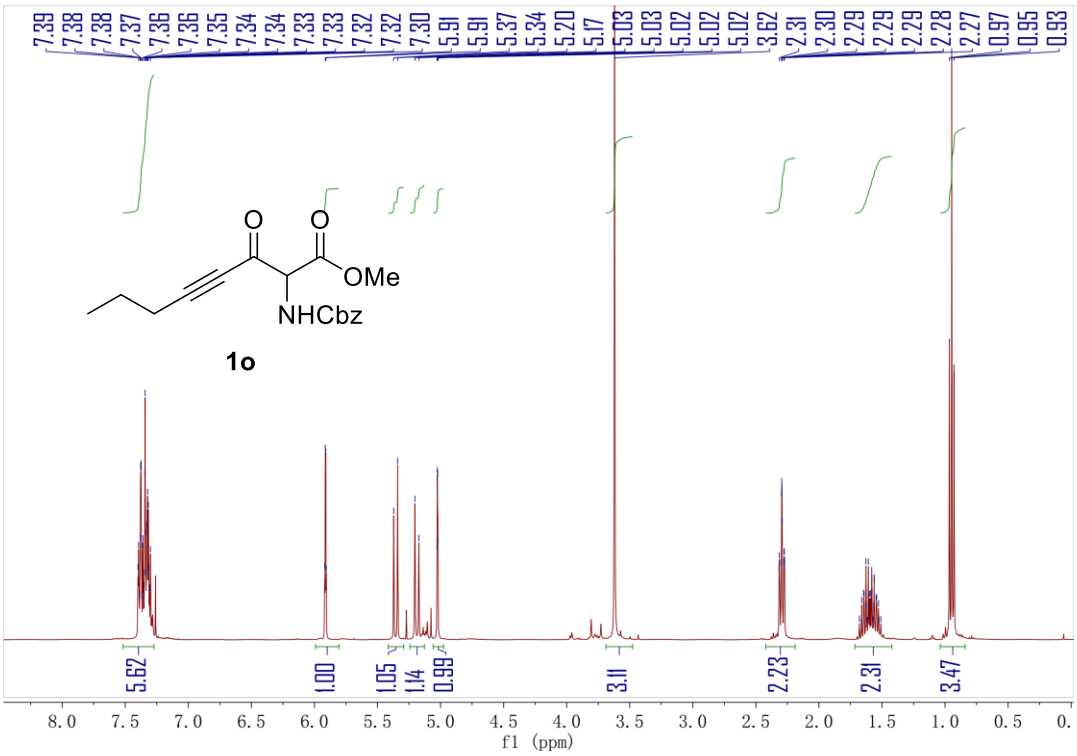


^{13}C-NMR



Methyl 2-(((benzyloxy)carbonyl)amino)-3-oxooct-4-ynoate (1n)

^{1}H-NMR



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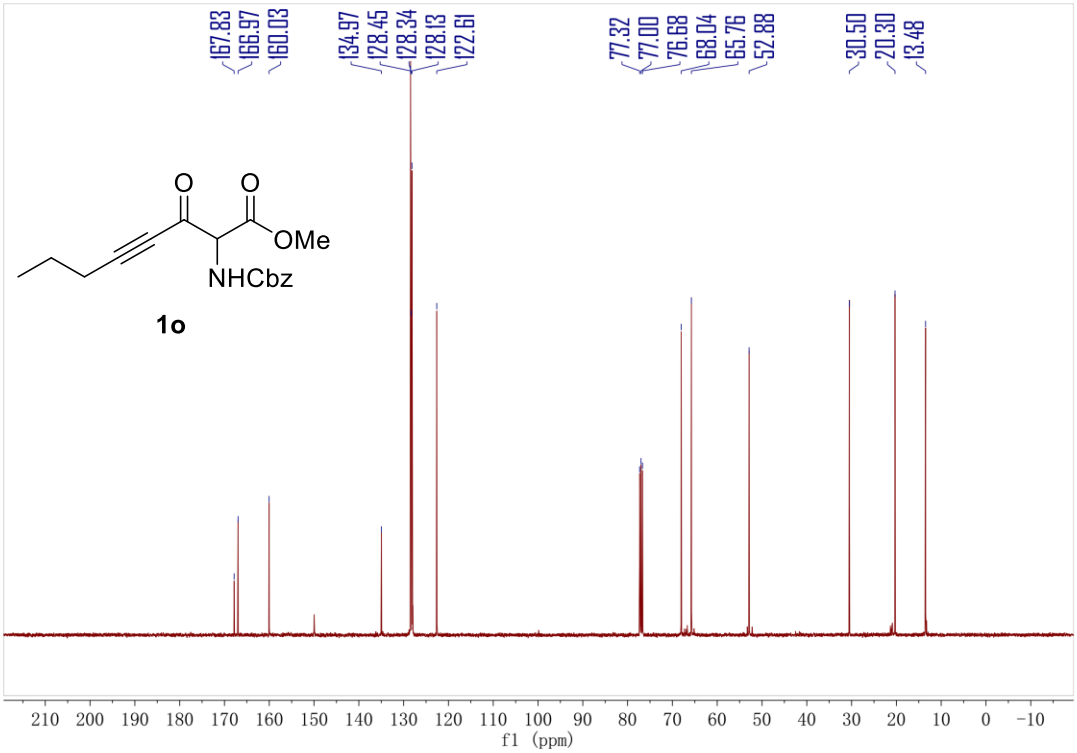
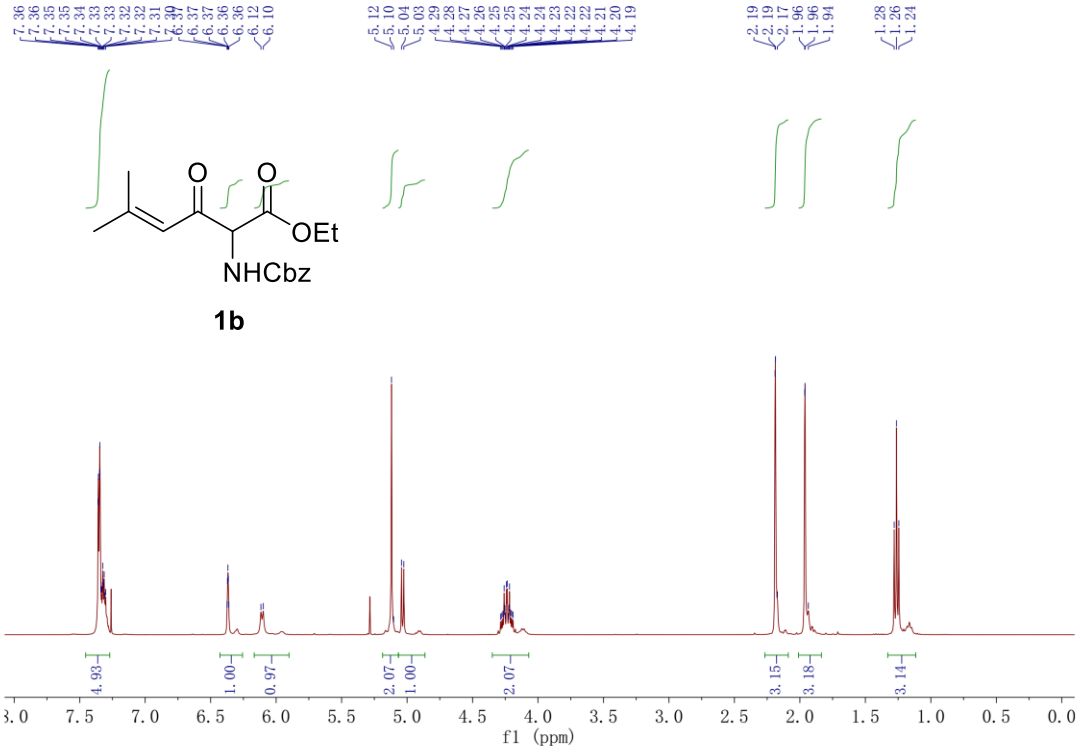


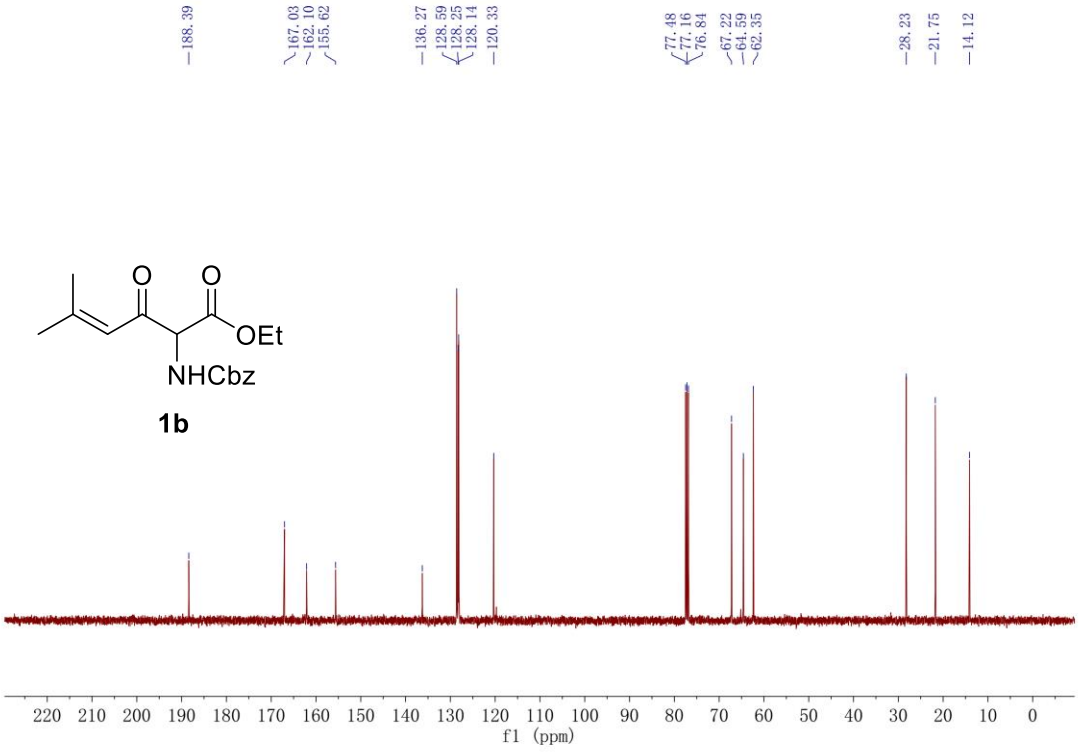
Method 2 (1b, 1e, 1h, 1k, 1o)

Ethyl (*E*)-2-((tert-butoxycarbonyl)amino)-3-oxohex-4-enoate (1b)

^{1}H-NMR

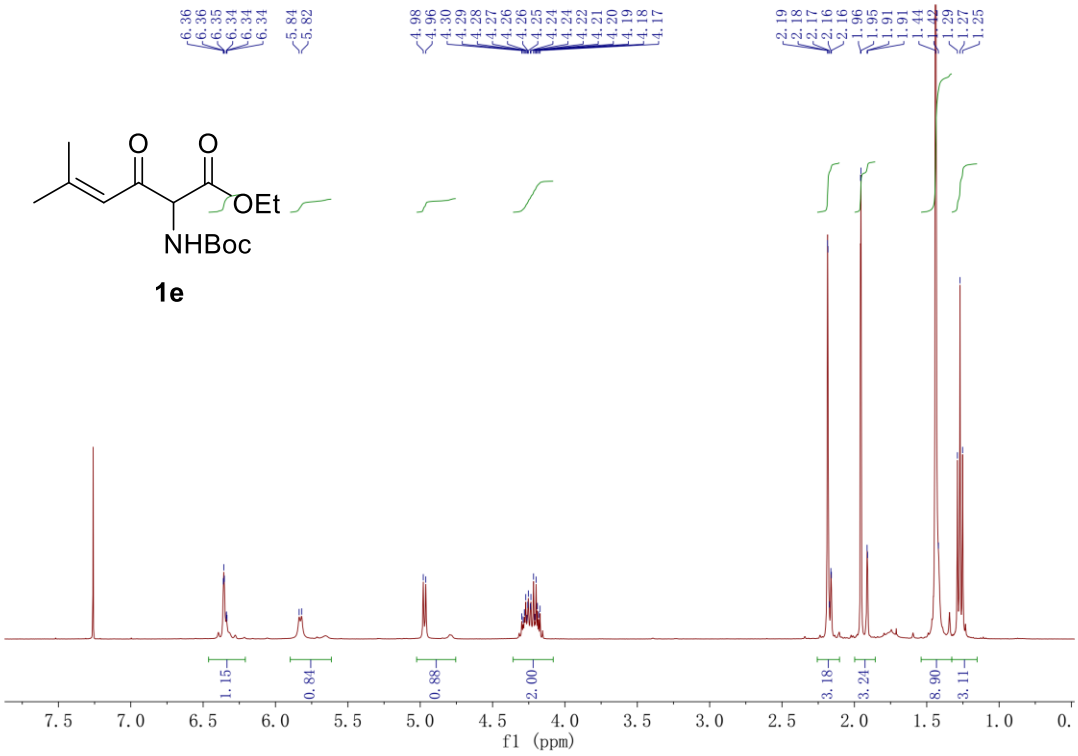


^{13}C-NMR

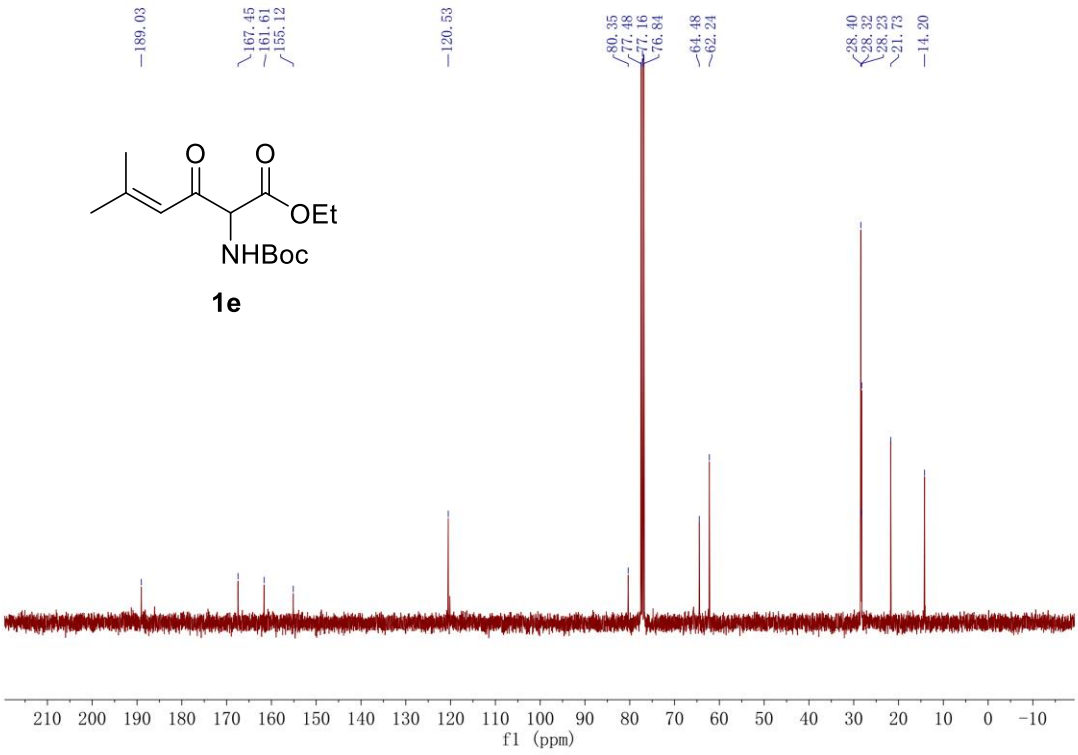


Ethyl 2-((tert-butoxycarbonyl)amino)-5-methyl-3-oxohex-4-enoate (1e)

^{1}H-NMR

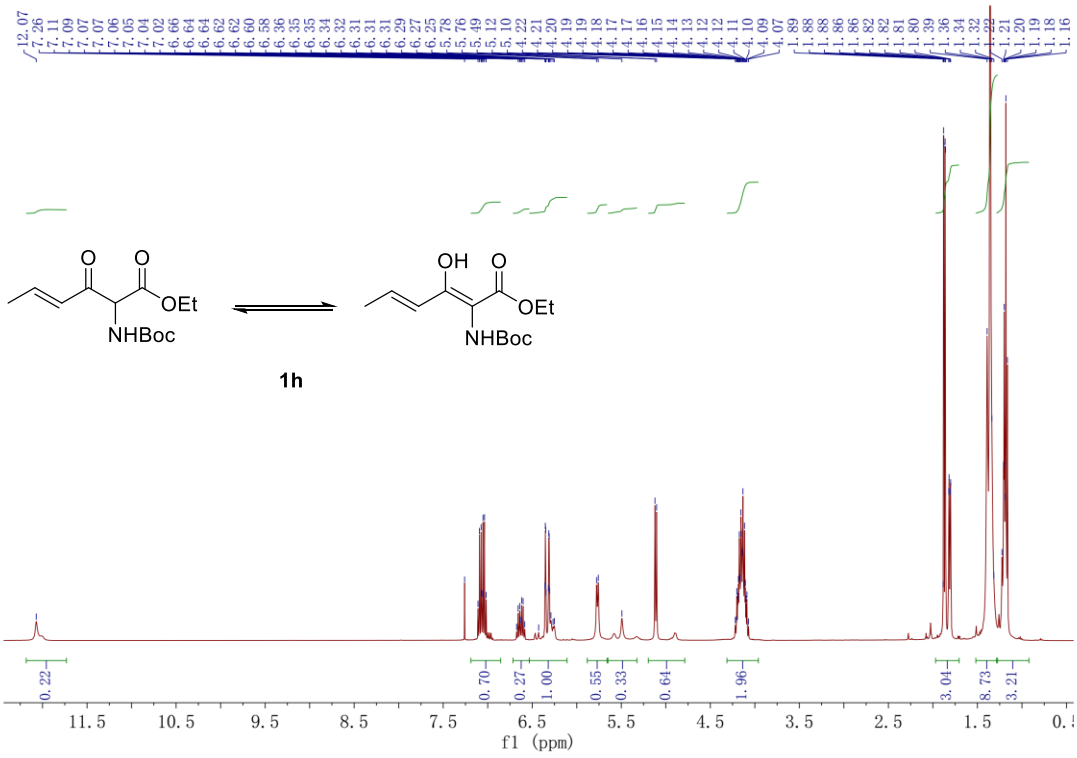


^{13}C-NMR

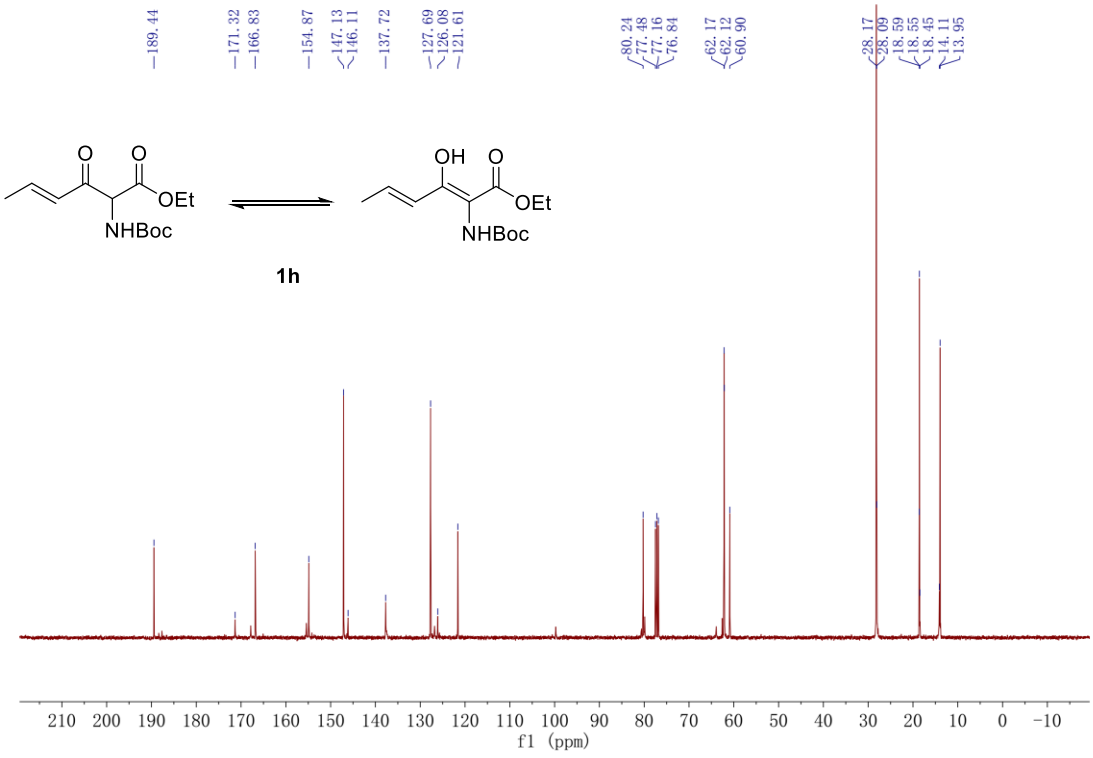


Ethyl (E)-2-((tert-butoxycarbonyl)amino)-3-oxohex-4-enoate (1h)

^{1}H-NMR

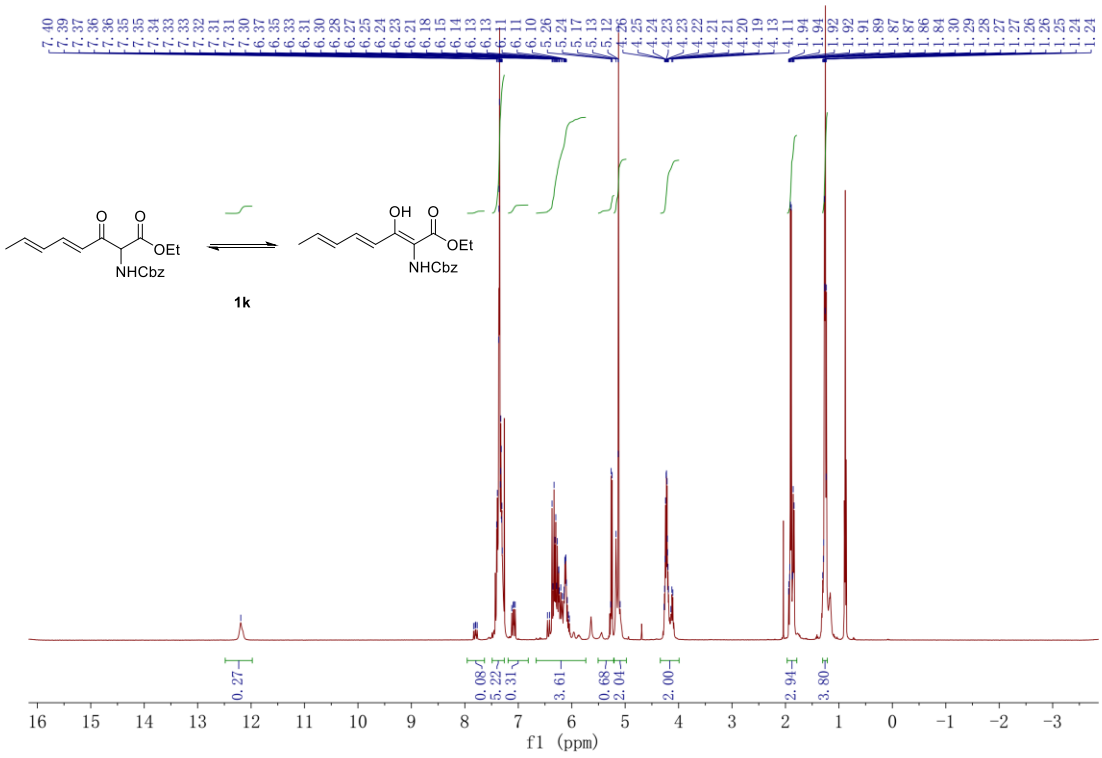


^{13}C-NMR

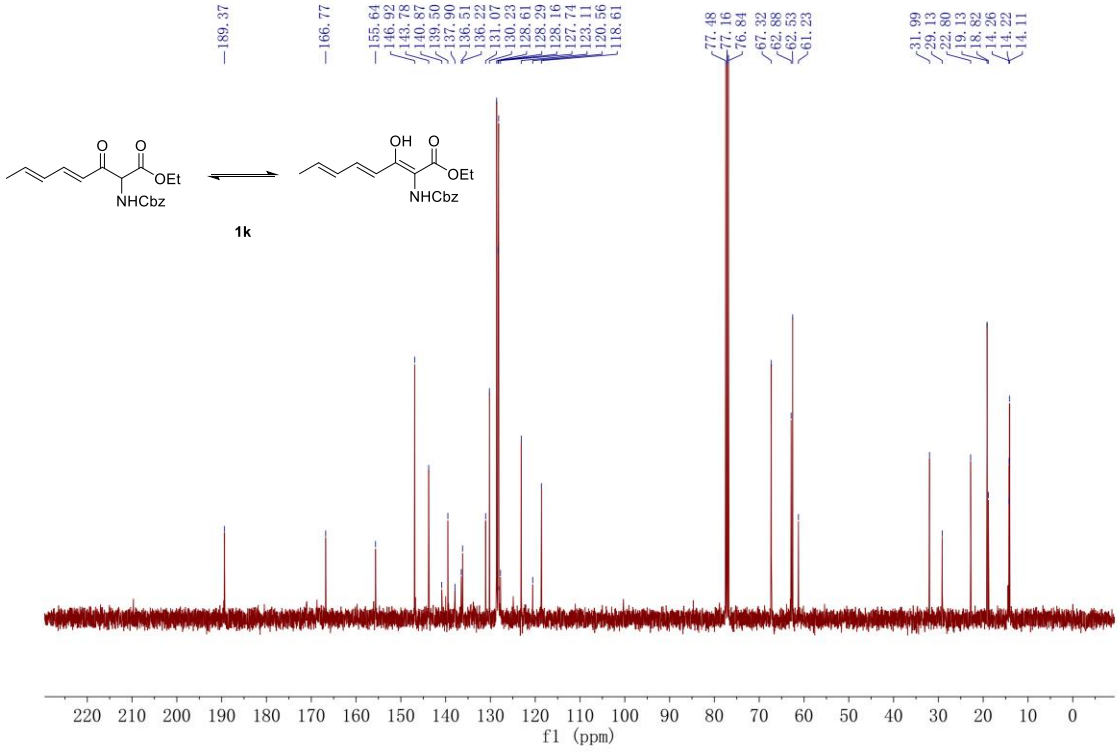


Ethyl (4E,6E)-2-((tert-butoxycarbonyl)amino)-3-oxoocta-4,6-dienoate (1k)

^{1}H-NMR

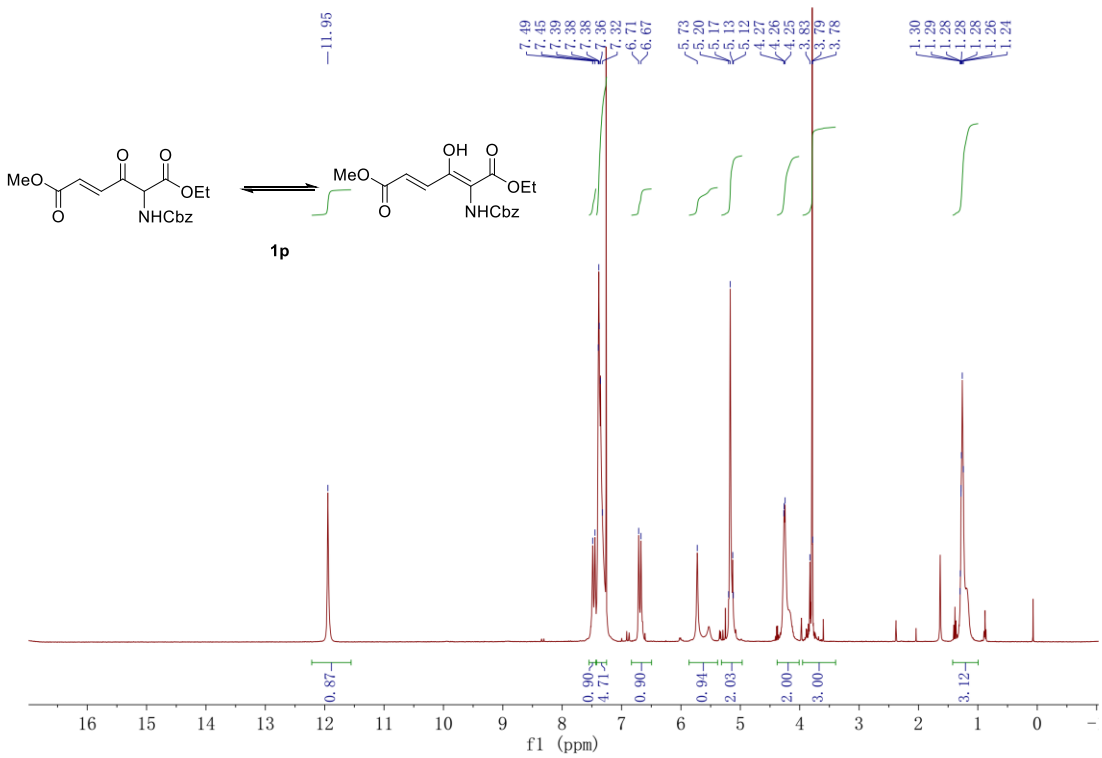


^{13}C-NMR

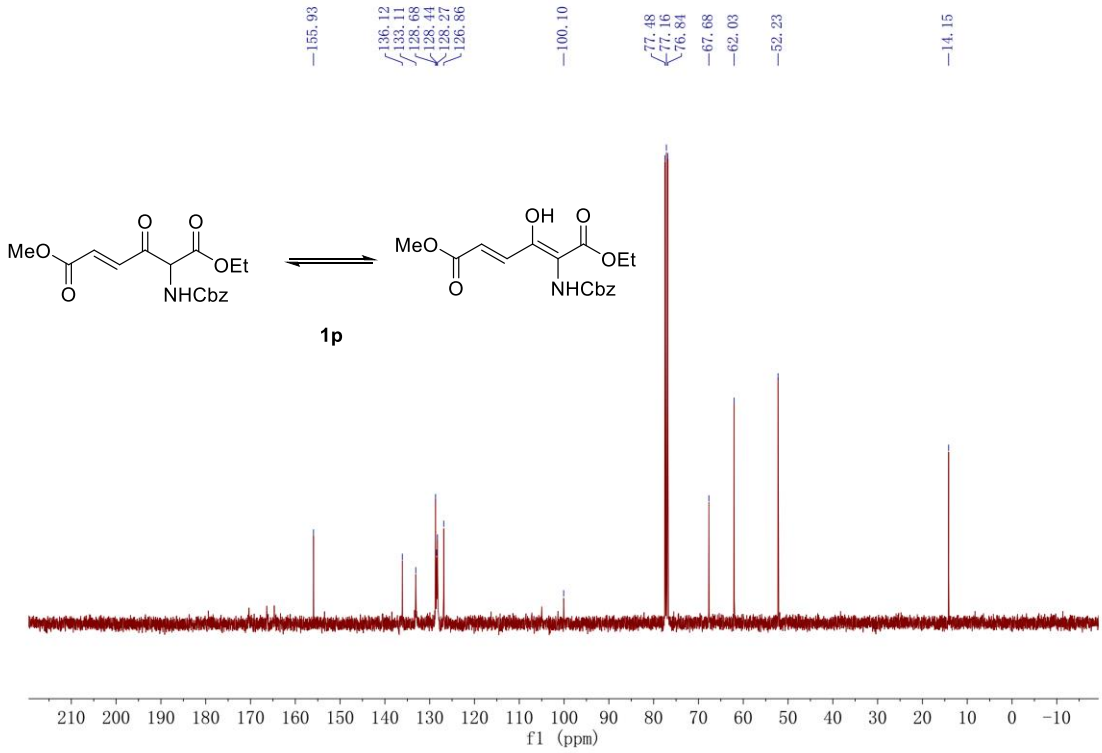


6-Ethyl 1-methyl (E)-5-(((benzyloxy)carbonyl)amino)-4-oxohex-2-enedioate (1o)

^{1}H-NMR



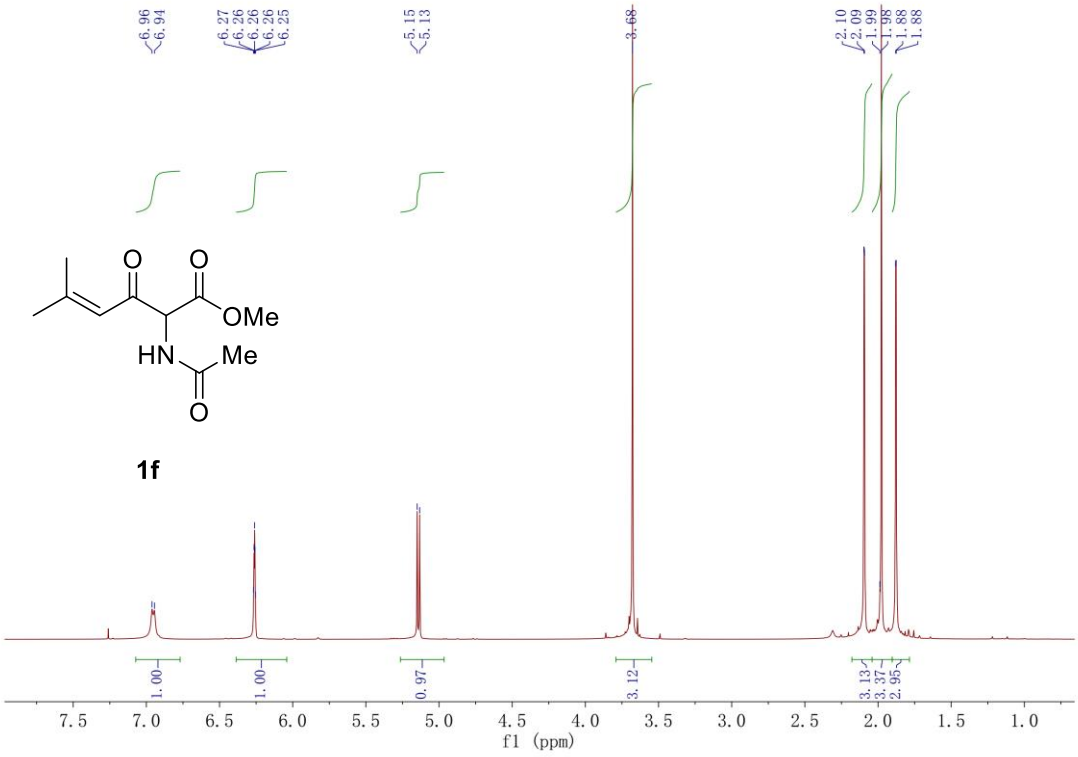
^{13}C-NMR



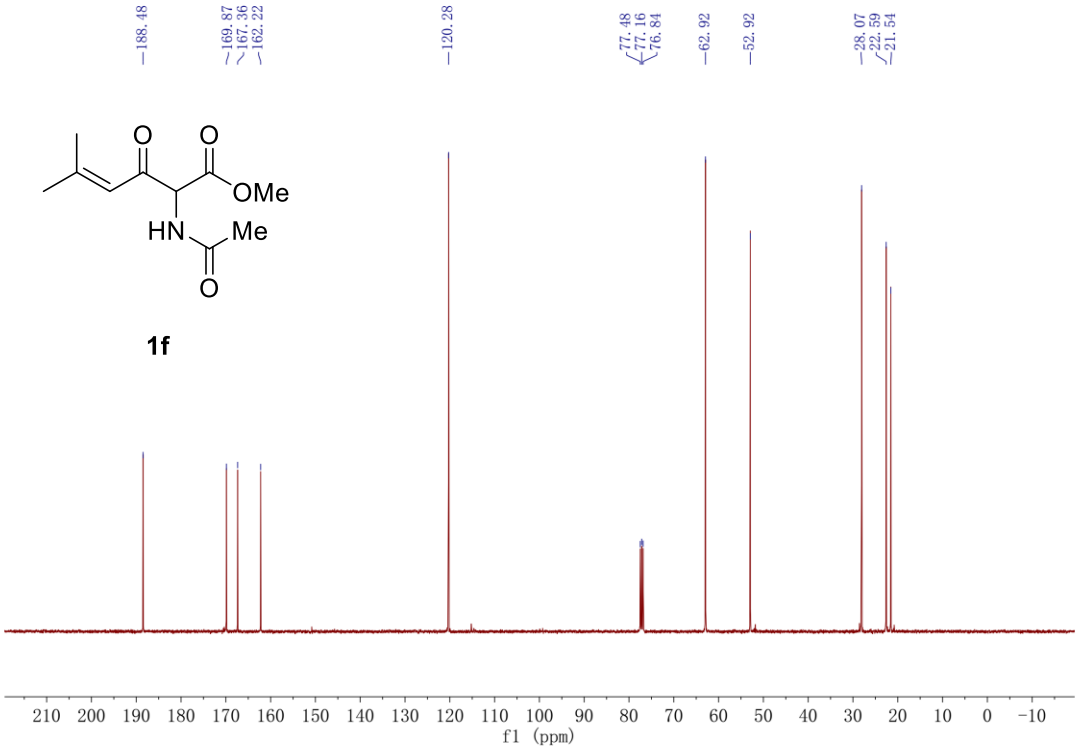
Method 3(1f. 1g)

Methyl 2-acetamido-5-methyl-3-oxohex-4-enoate (1f)

^{1}H-NMR

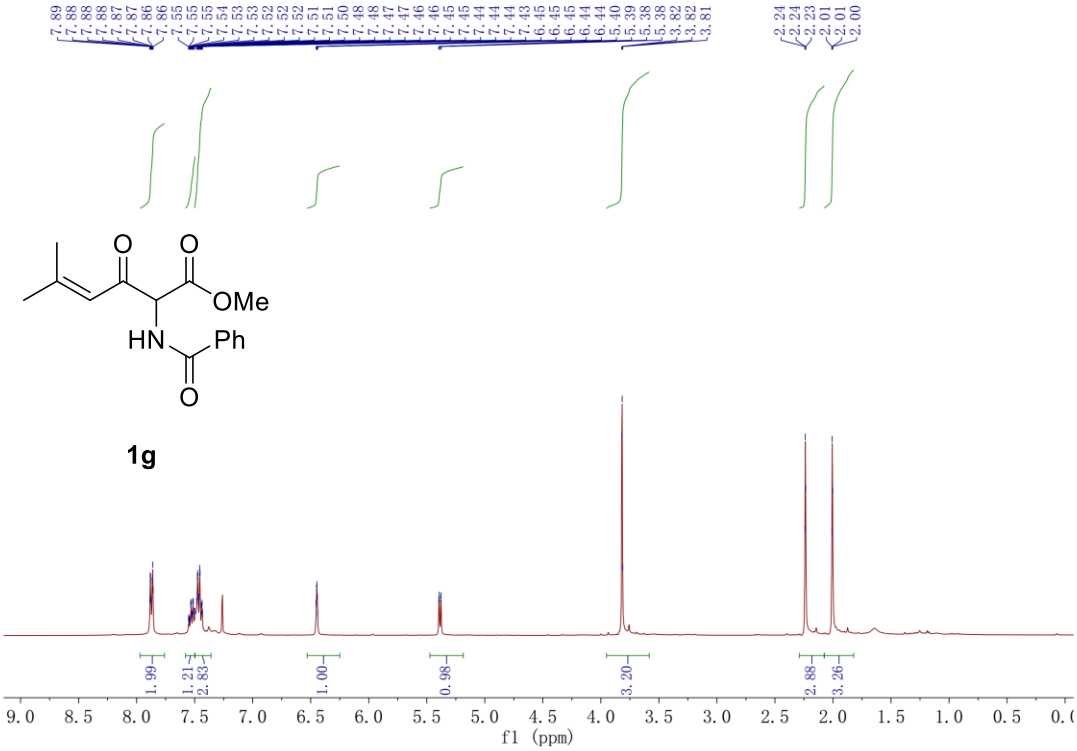


^{13}C-NMR

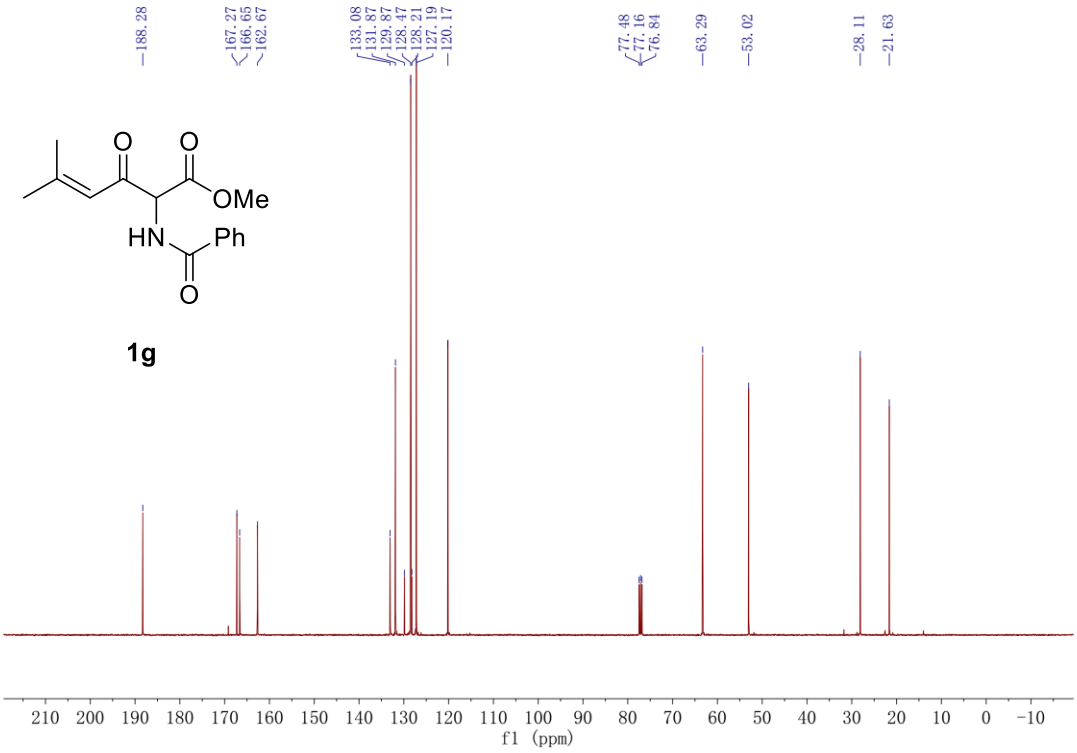


Methyl 2-benzamido-5-methyl-3-oxohex-4-enoate (1g)

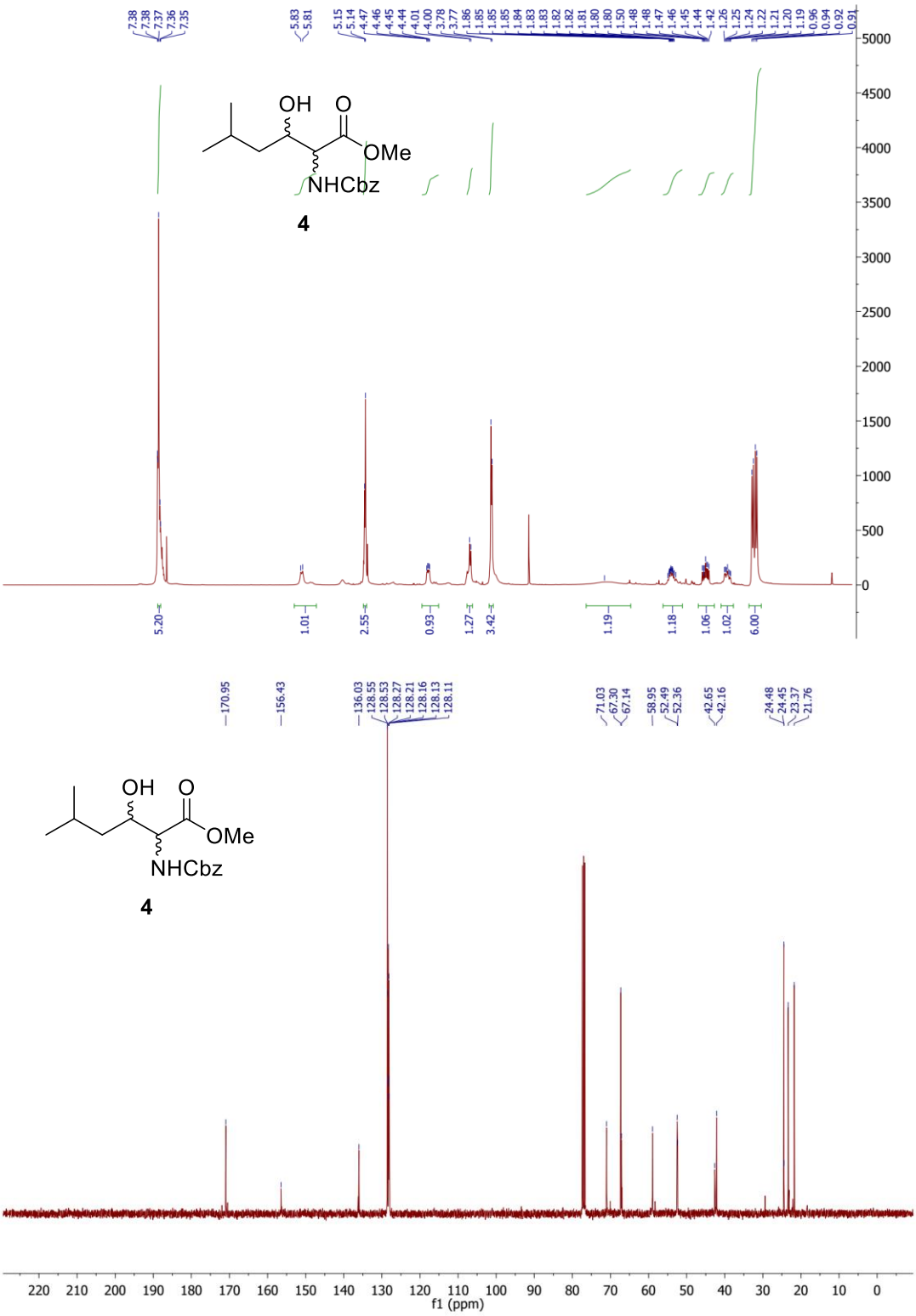
^{1}H-NMR



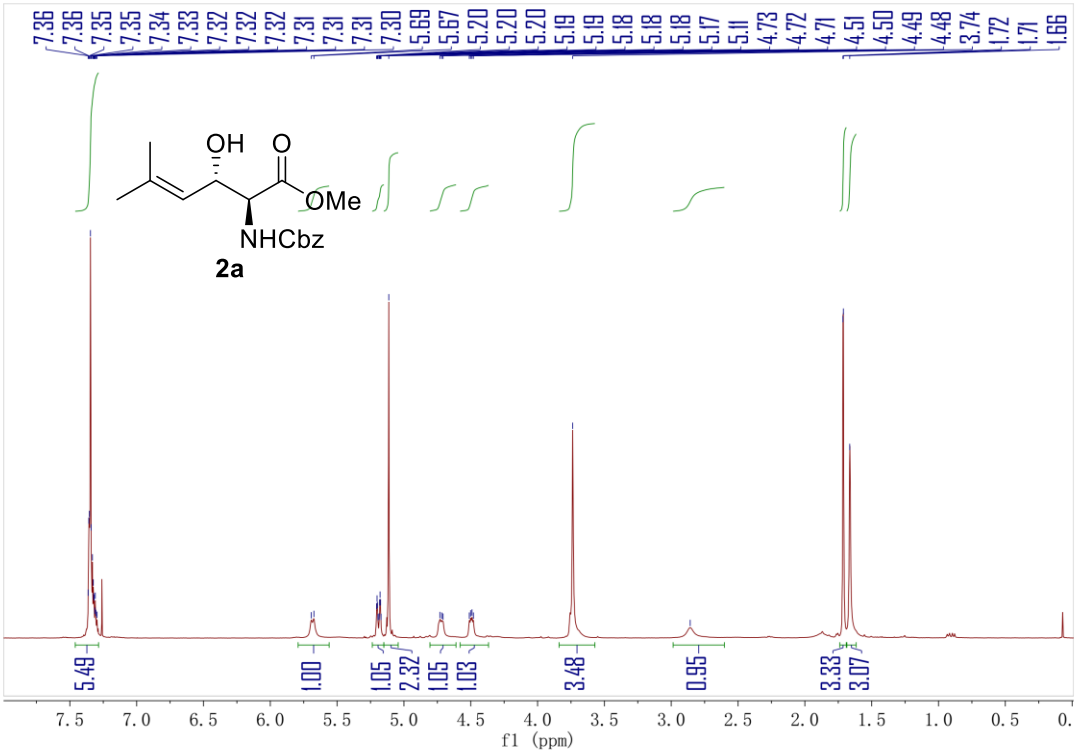
^{13}C-NMR

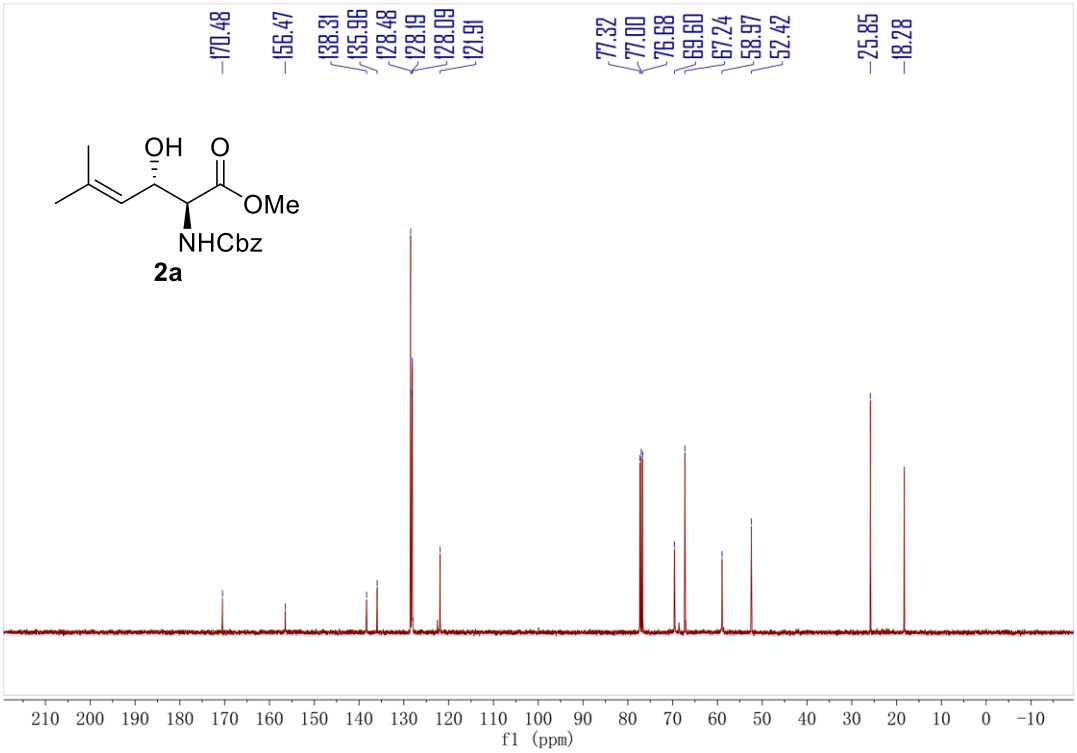


NMR Specturm of product (2a-2m, 4, 5, 7, 8, 10 amd (+)-Alexine (3))
Methyl 2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-methylhexanoate (4)

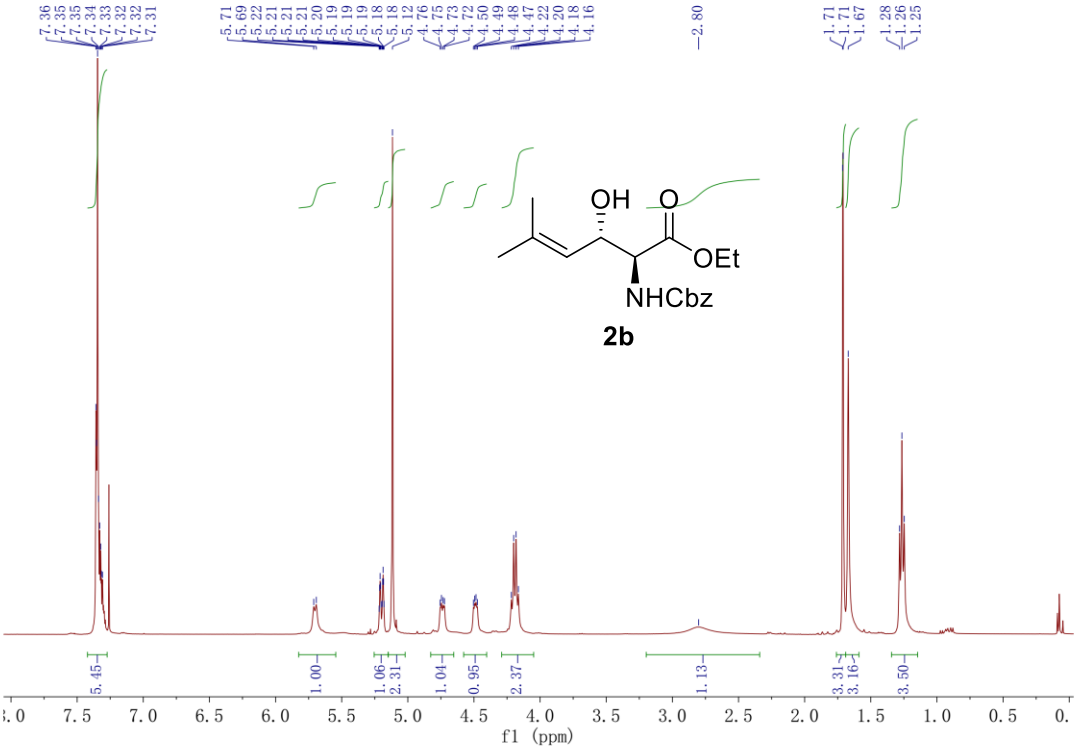


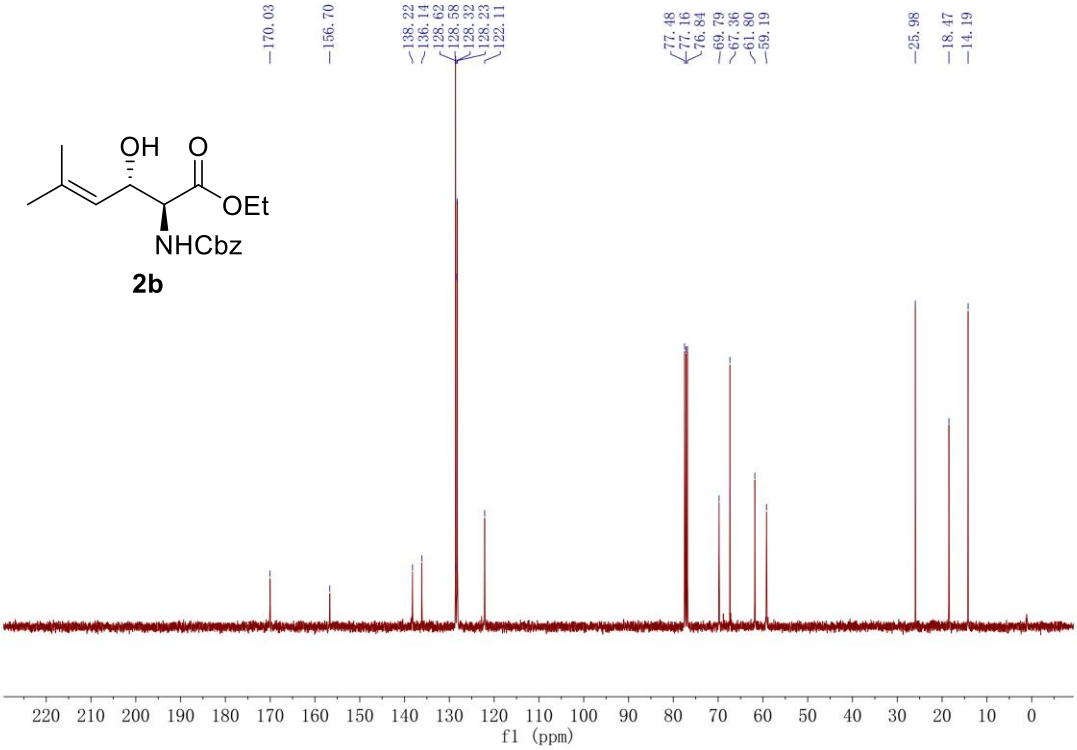
Methyl (*2S,3S*)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-methylhex-4-enoate (2a)



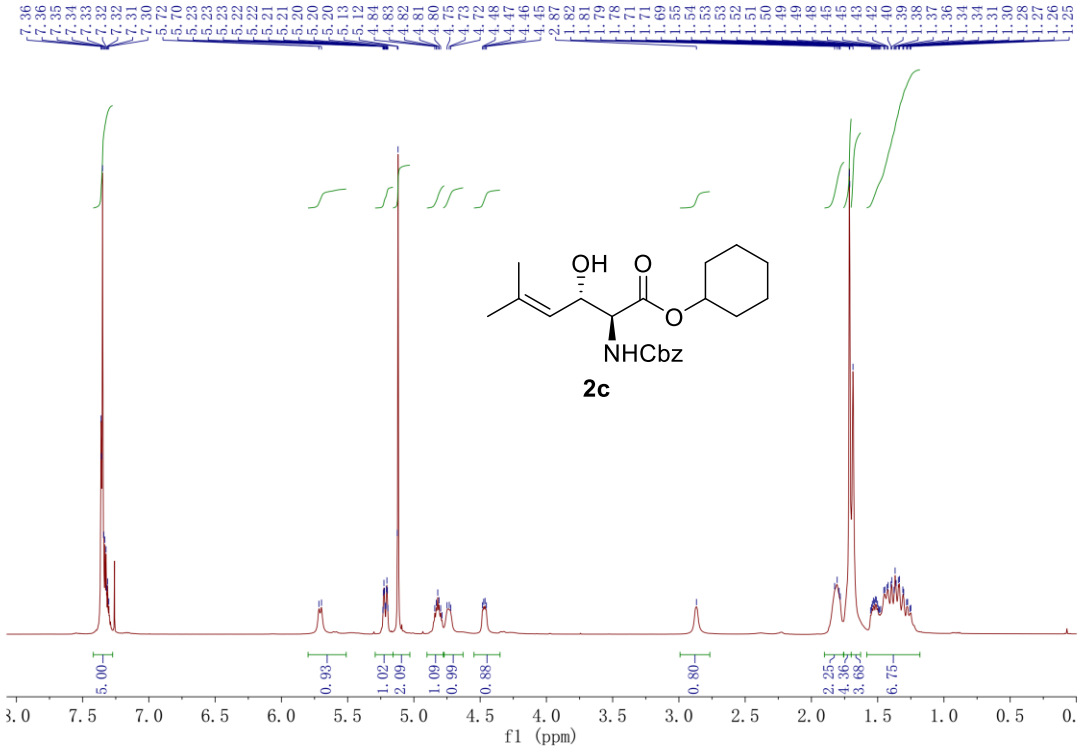


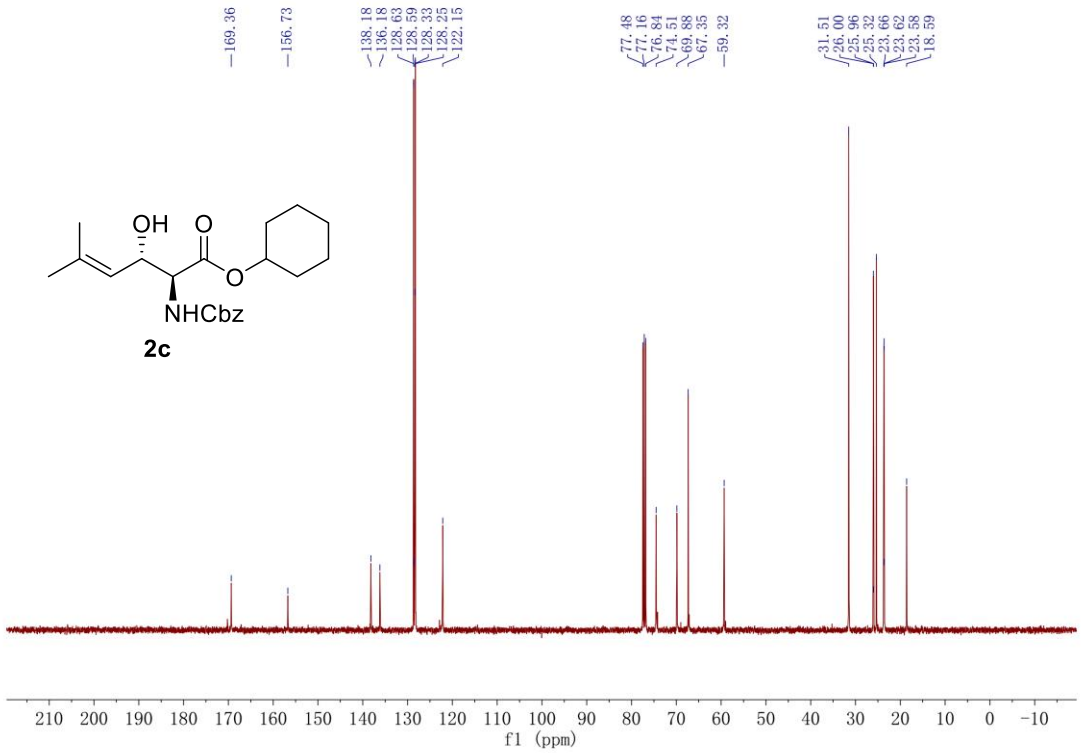
Ethyl (2S,3S)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-methylhex-4-enoate (2b)



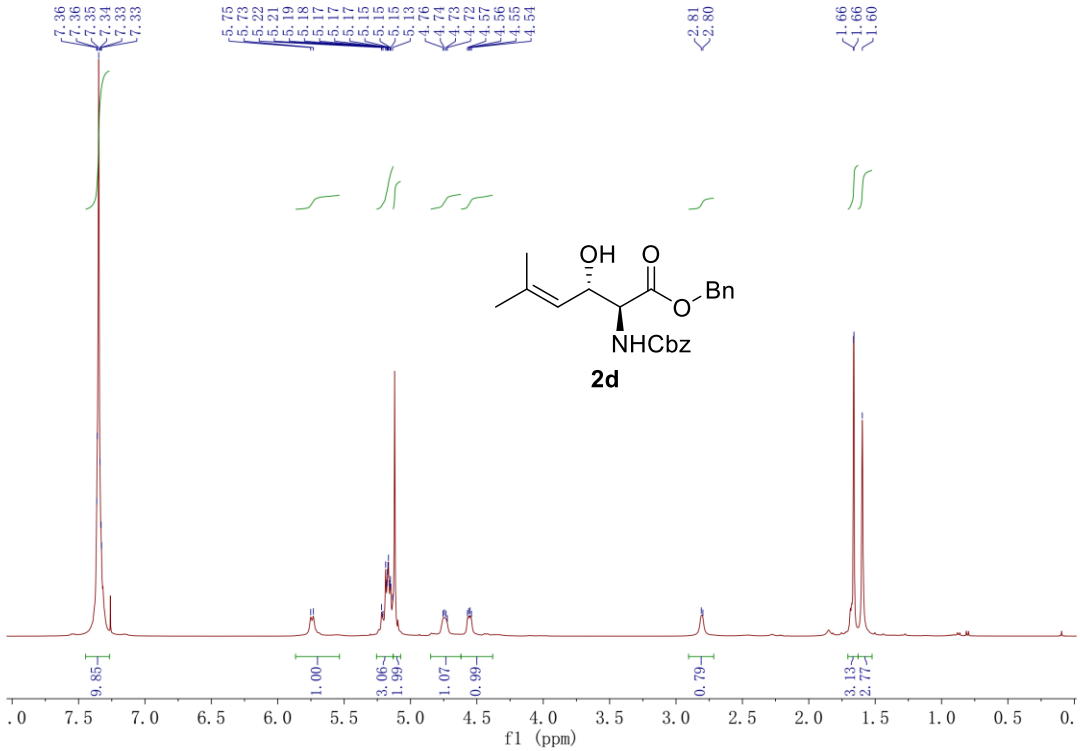


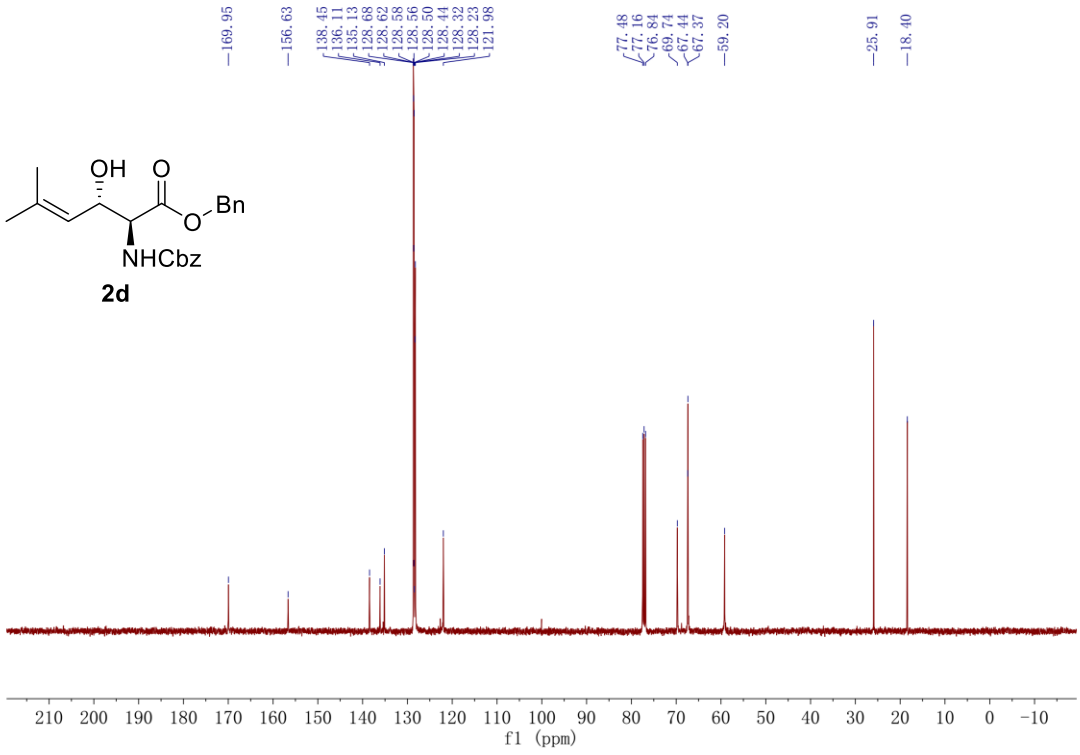
Cyclohexyl (2S,3S)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-methylhex-4-enoate (2c)



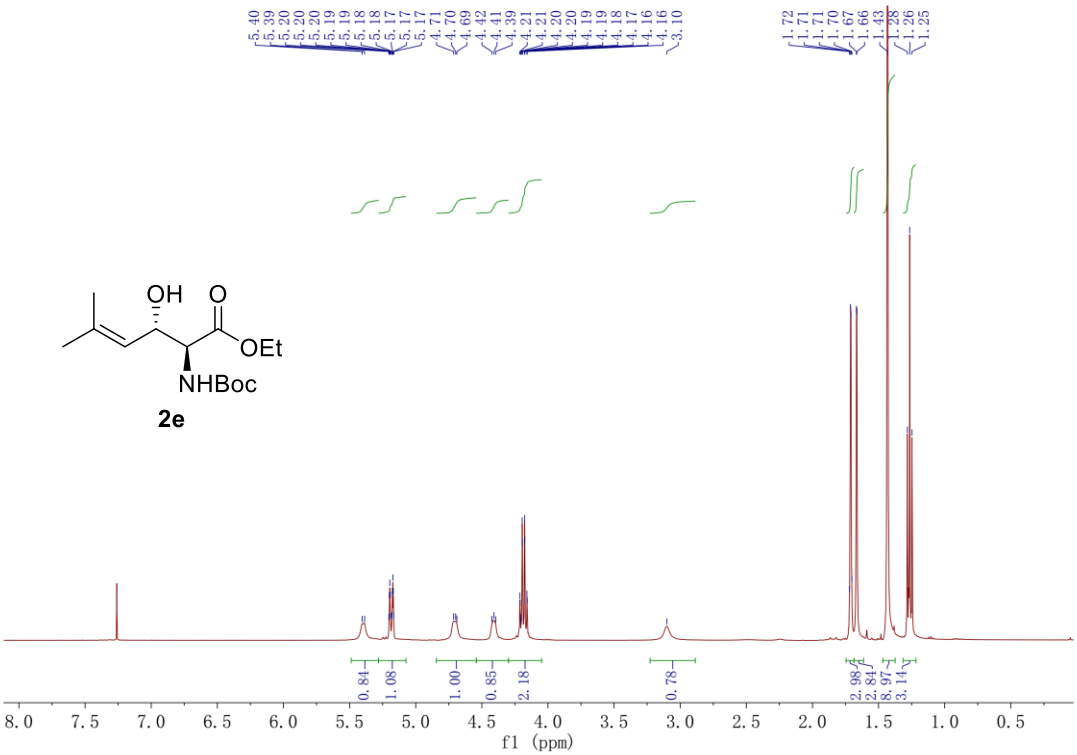


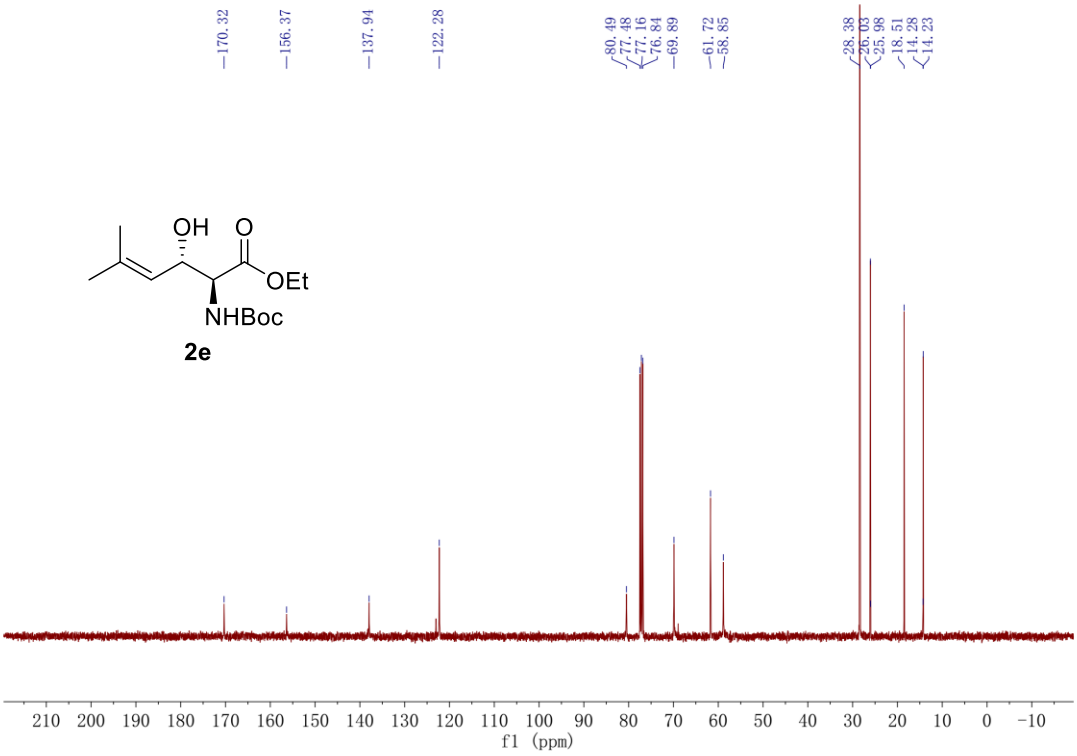
Benzyl (2S,3S)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-methylhex-4-enoate (2d)



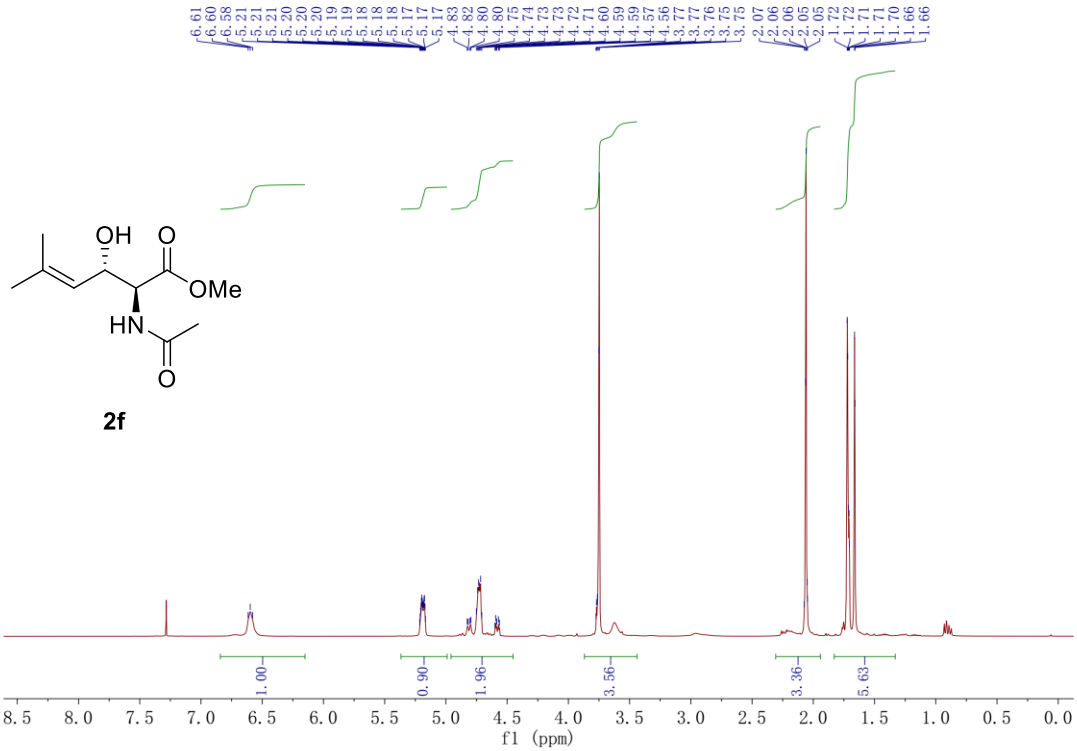


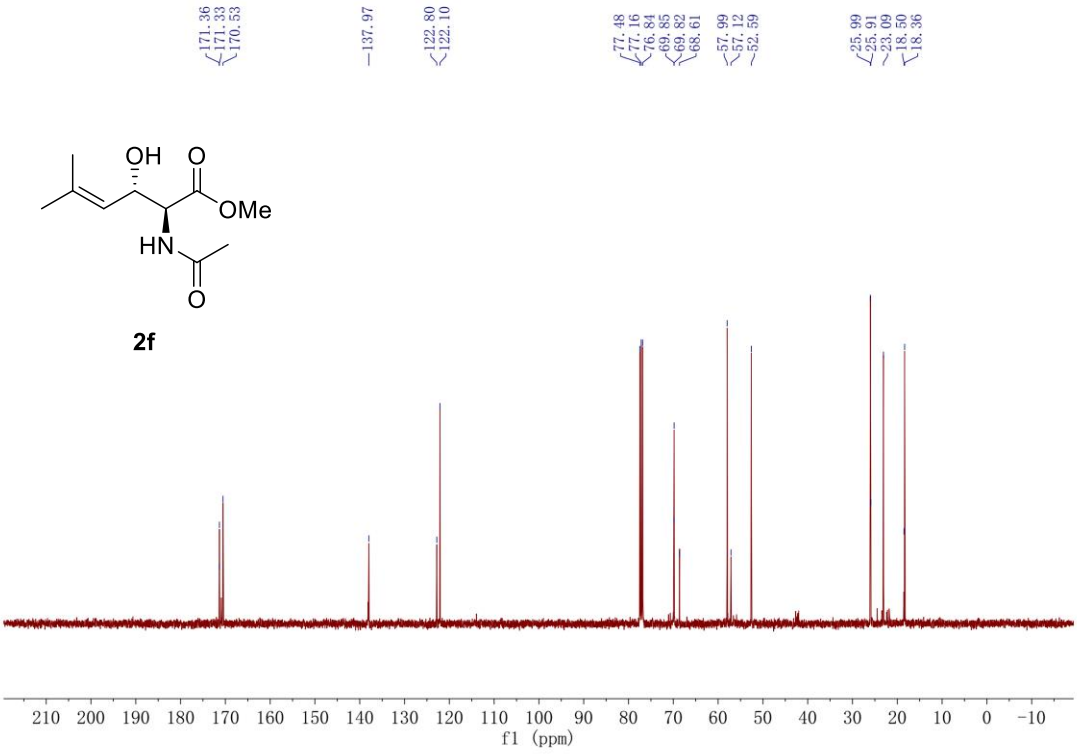
Ethyl (2S,3S)-2-((tert-butoxycarbonyl)amino)-3-hydroxy-5-methylhex-4-enoate (2e)



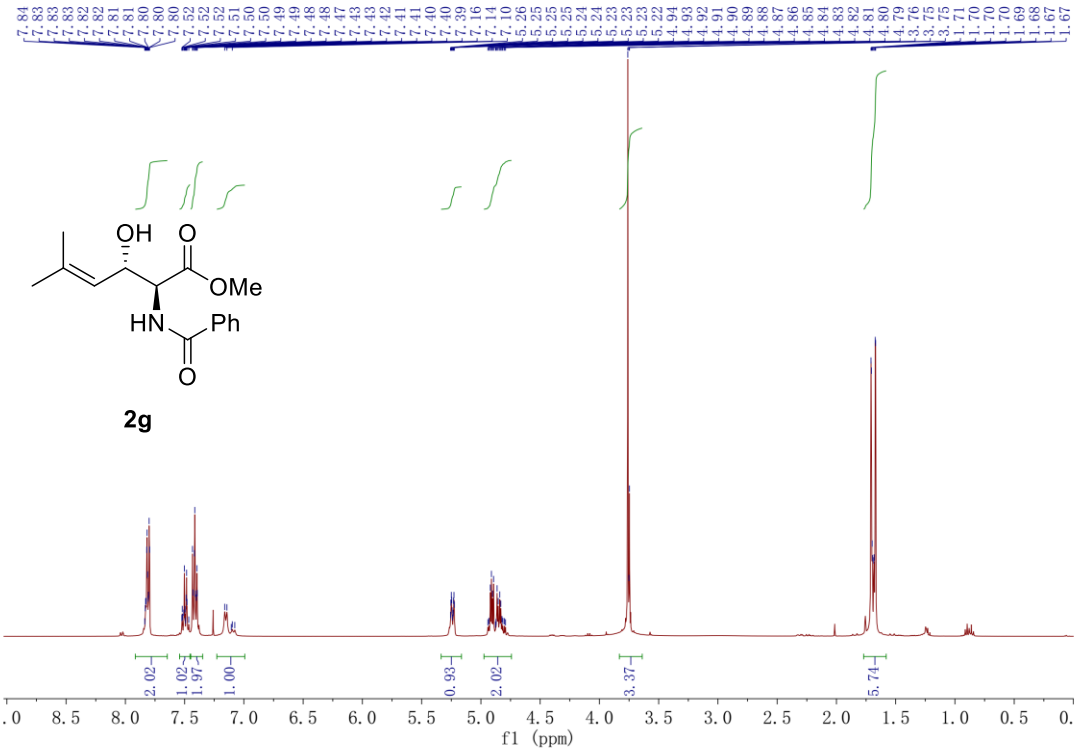


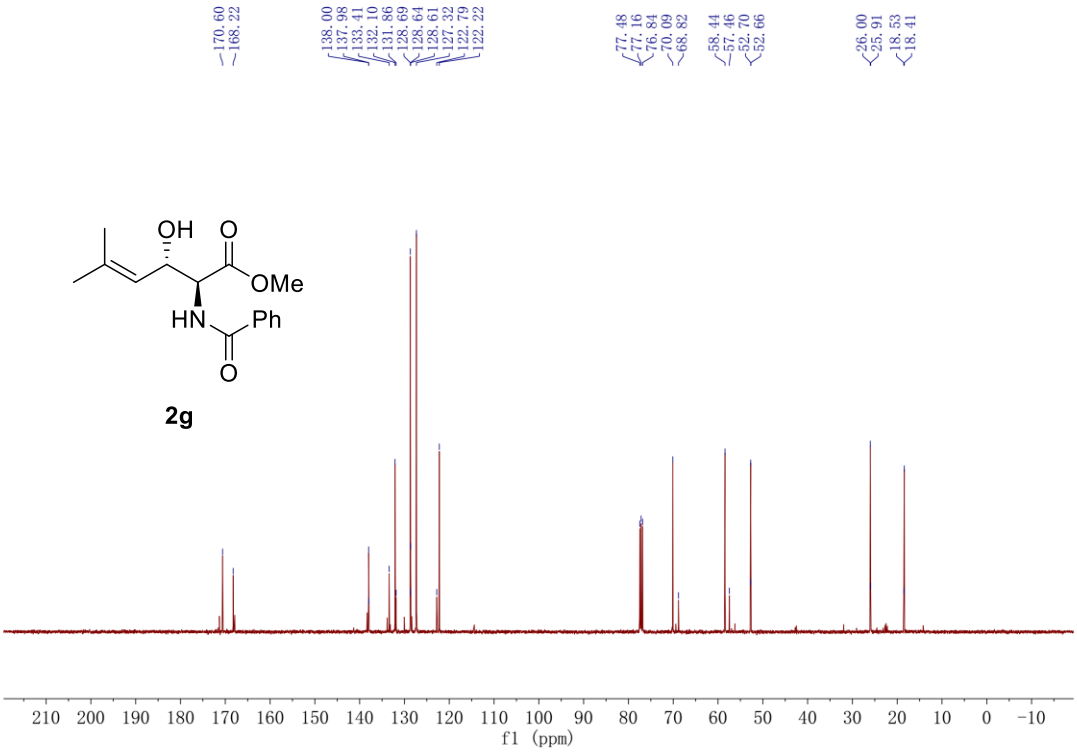
Methyl (2S,3S)-2-acetamido-3-hydroxy-5-methylhex-4-enoate (2f)



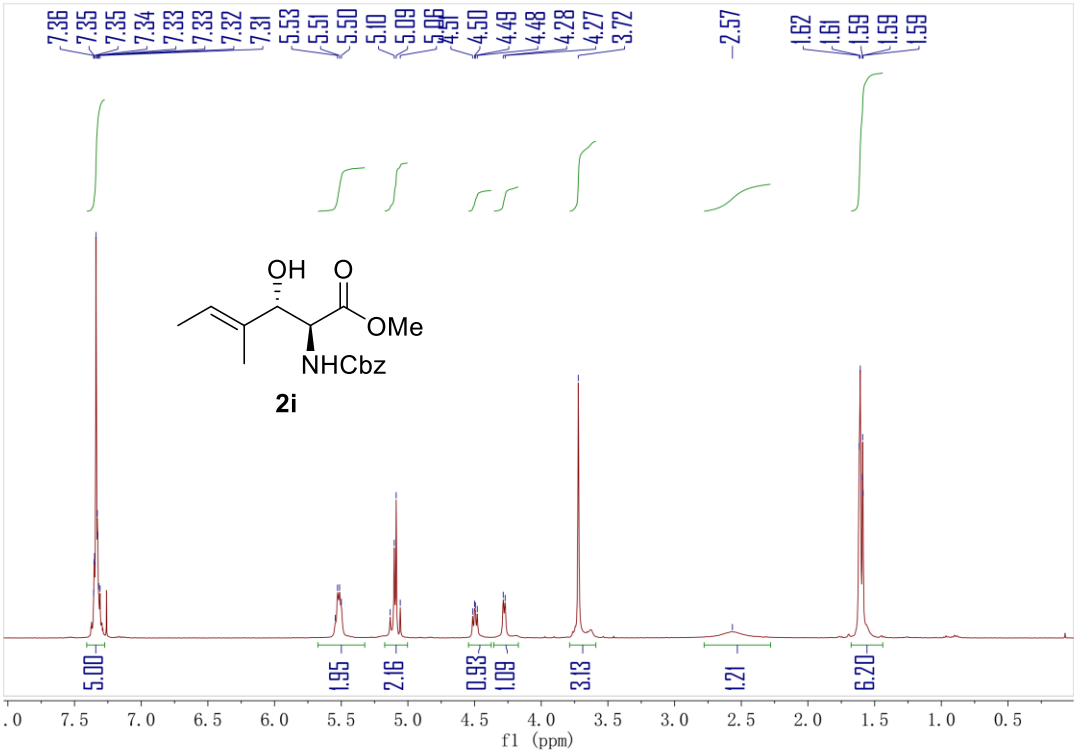


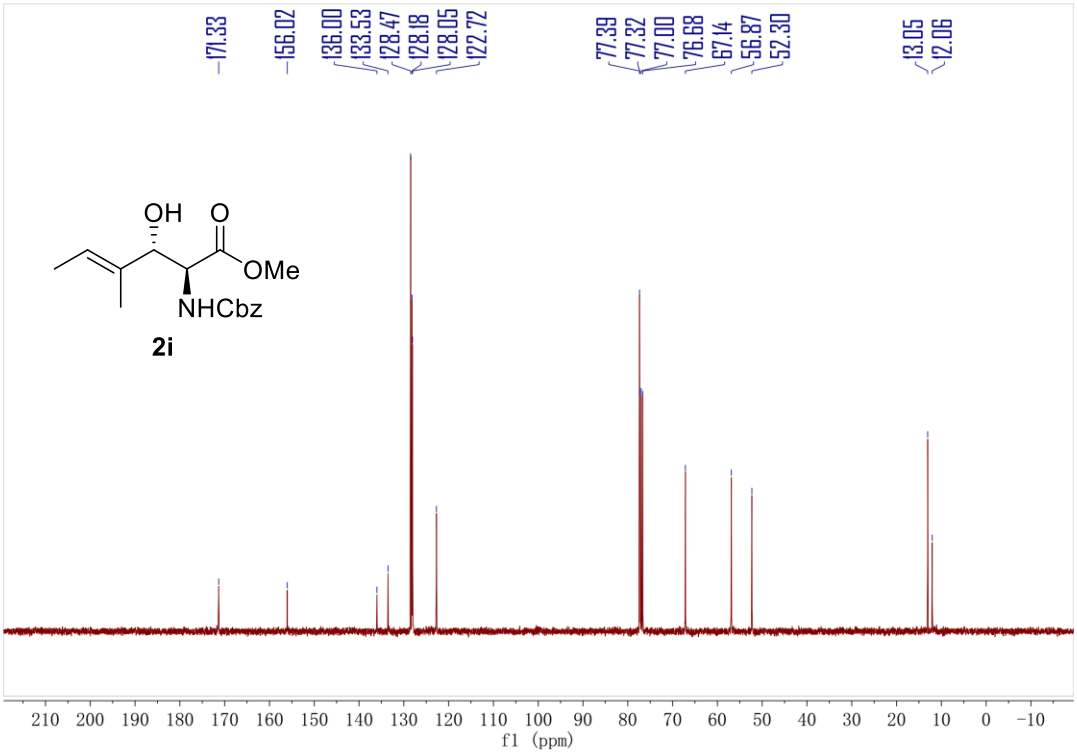
Methyl (2S,3S)-2-benzamido-3-hydroxy-5-methylhex-4-enoate (2g)



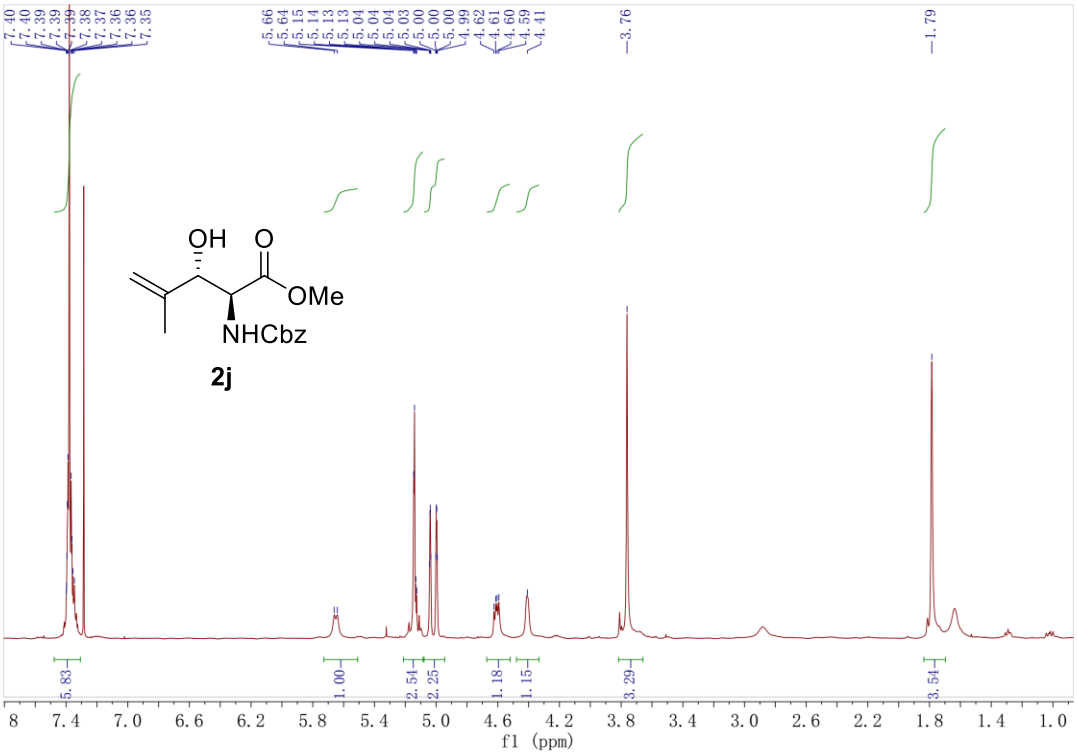


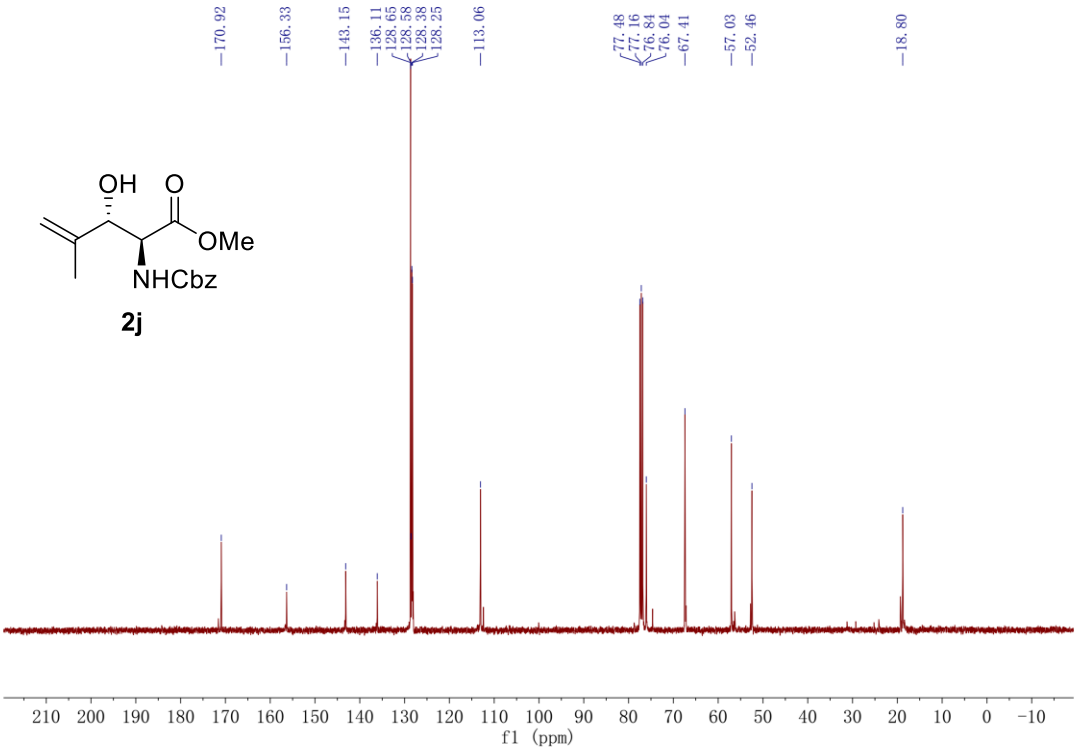
Methyl (*2S,3S,E*)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-4-methylhex-4-enoate (2i)



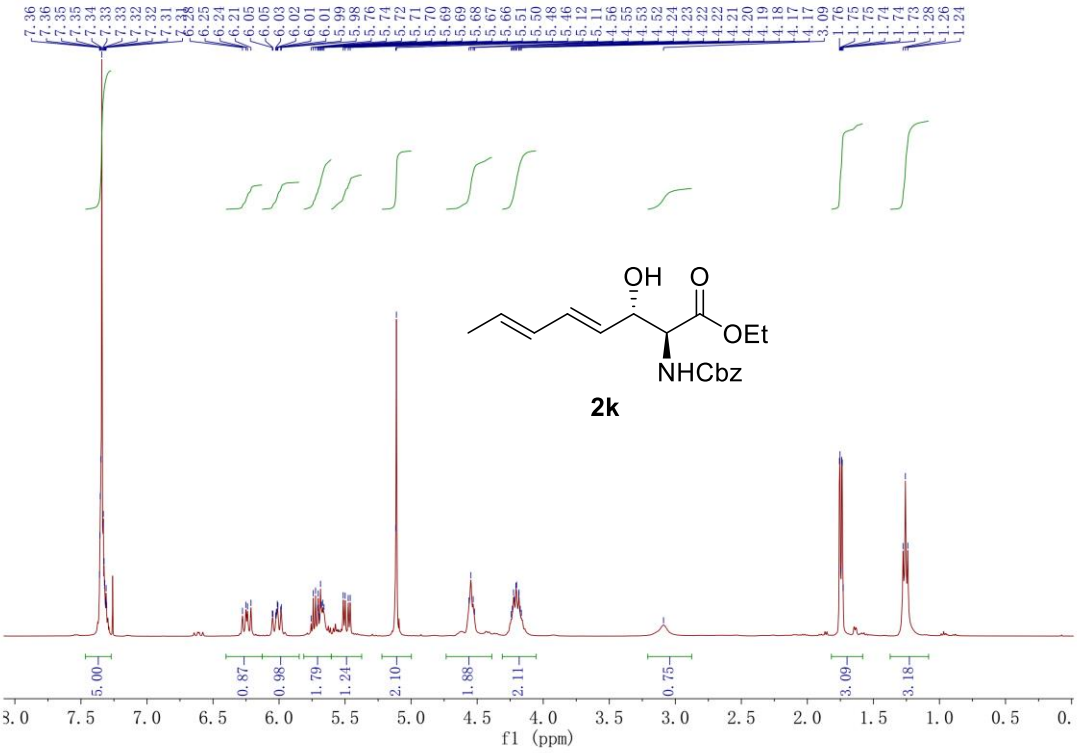


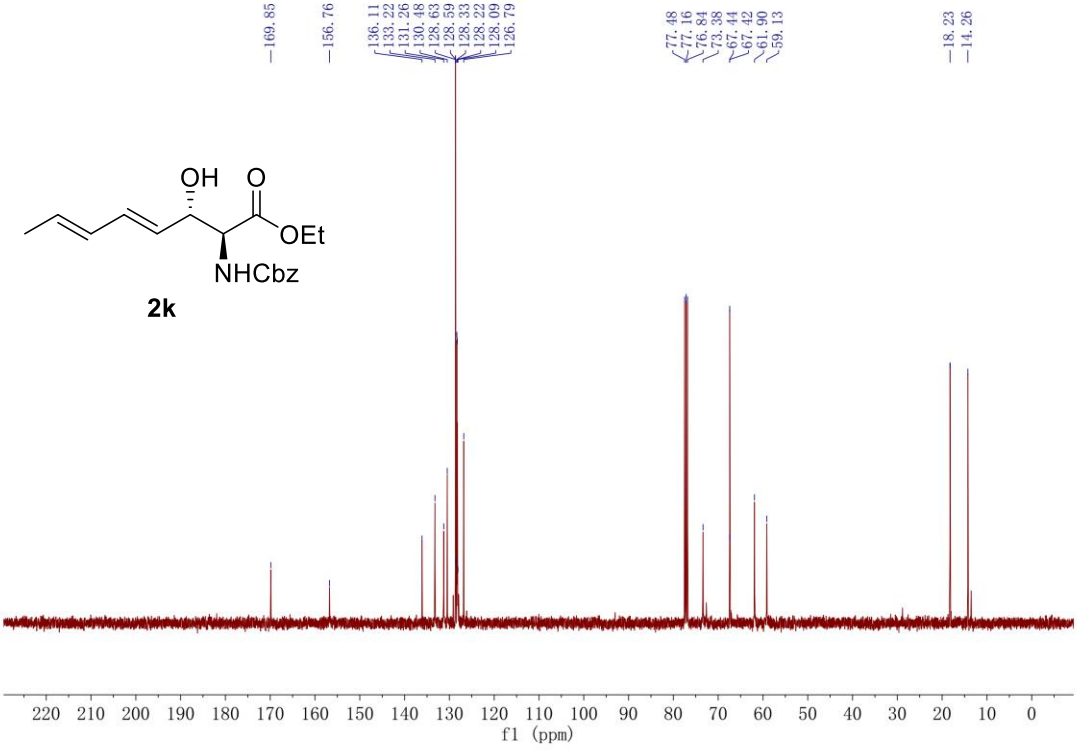
Methyl (*2S,3S*)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-4-methylpent-4-enoate (2j)



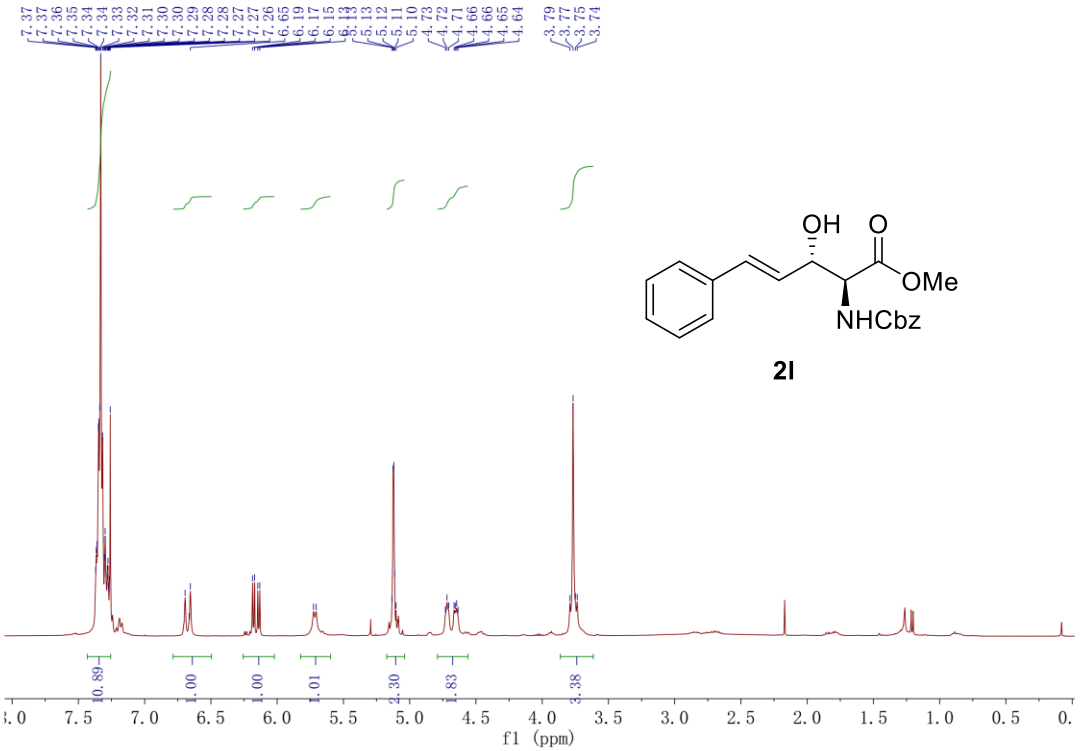


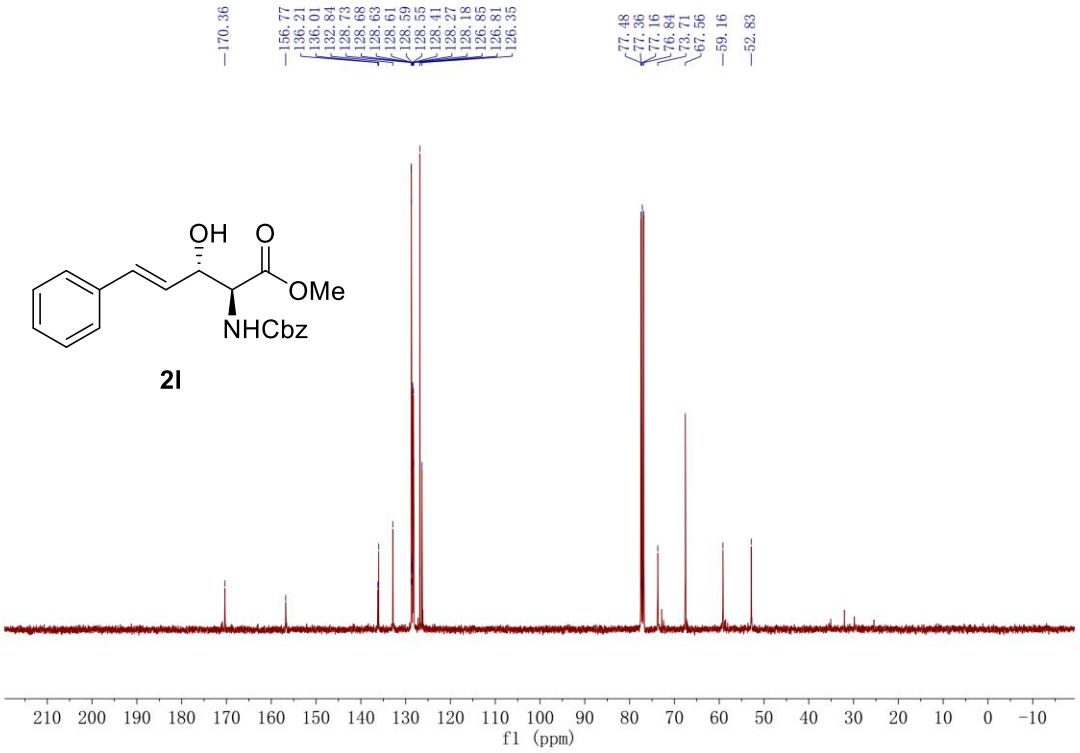
Methyl (2S,3S,4E,6E)-2-(((benzyloxy)carbonyl)amino)-3-hydroxyocta-4,6-dienoate (2k)



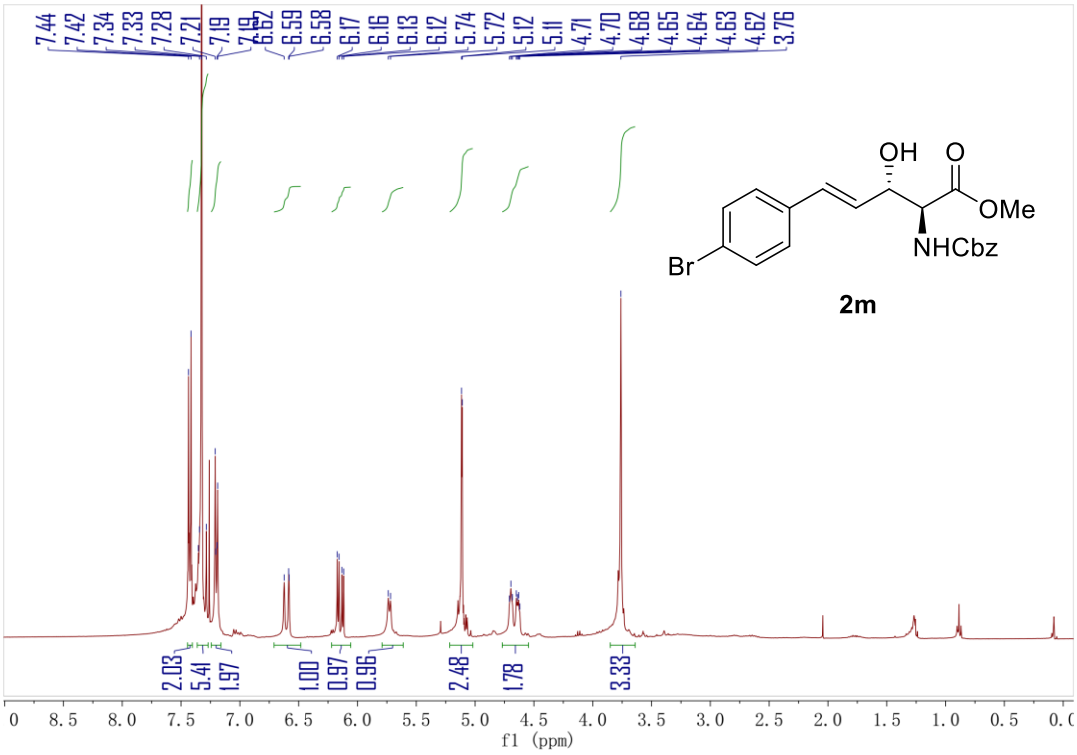


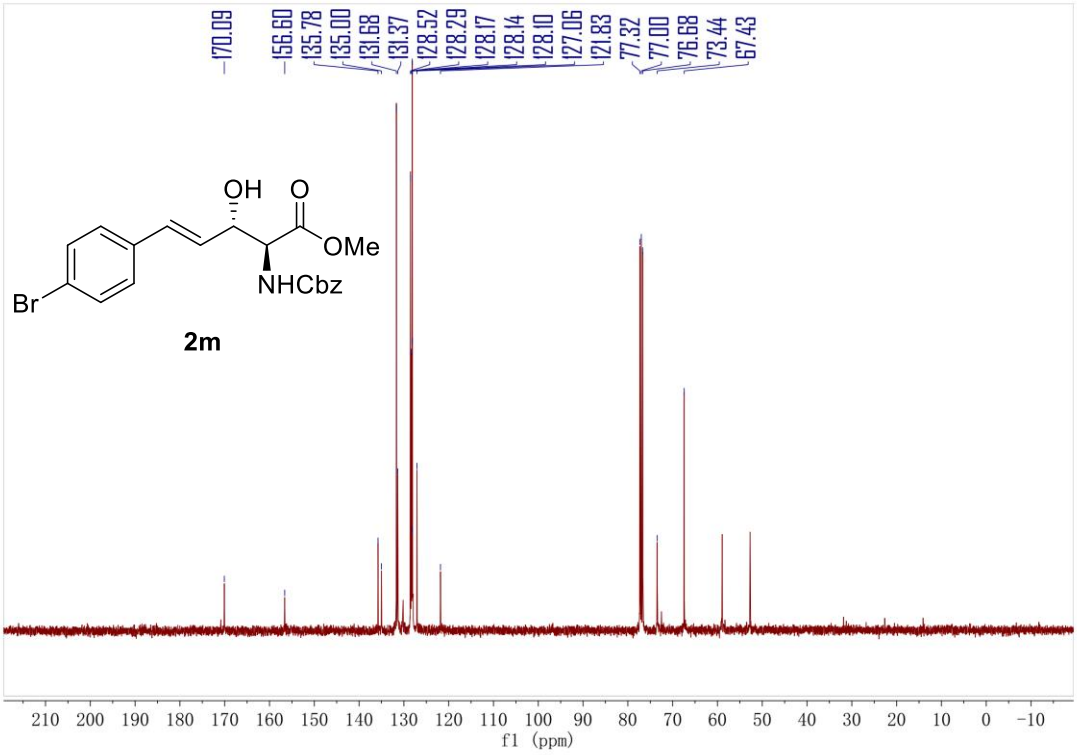
Methyl (2S,3S,E)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-phenylpent-4-enoate (2l)



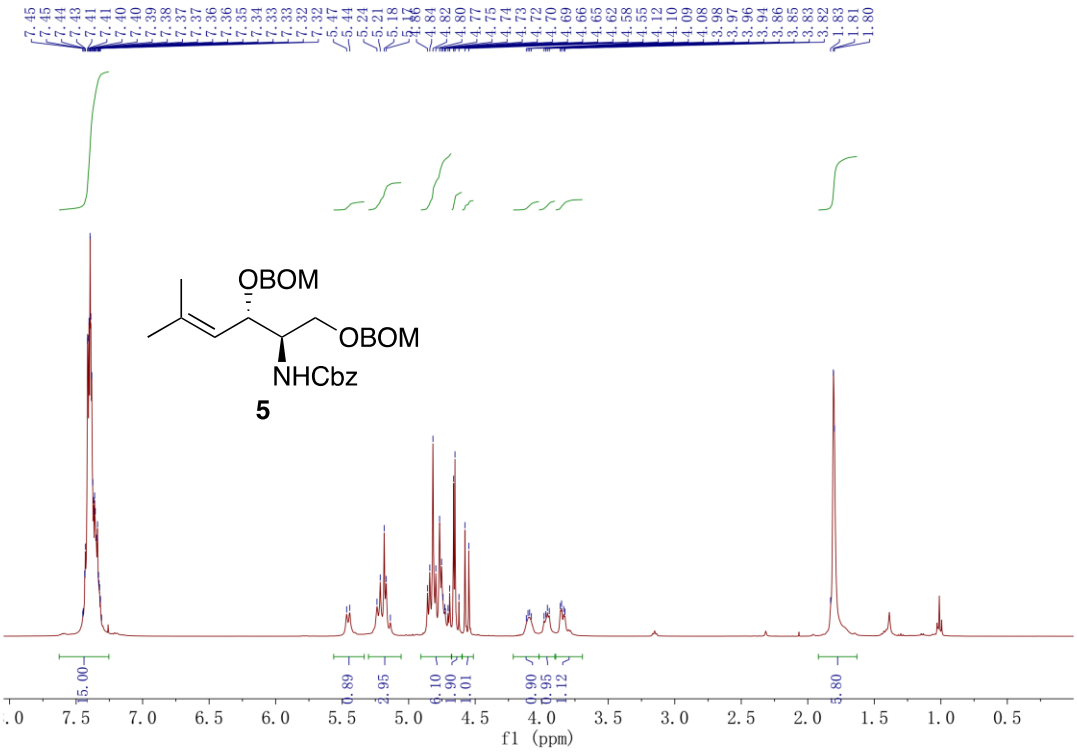


Methyl (2S,3S,E)-2-(((benzyloxy)carbonyl)amino)-5-(4-bromophenyl)-3-hydroxypent-4-enoate (2m)

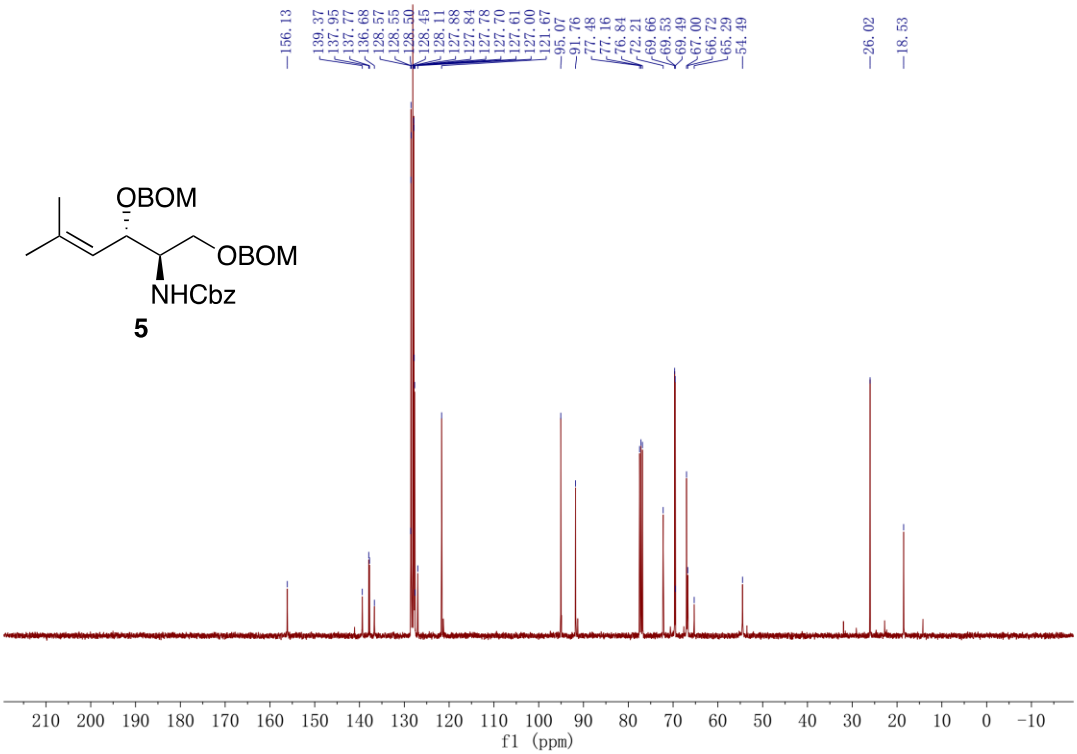




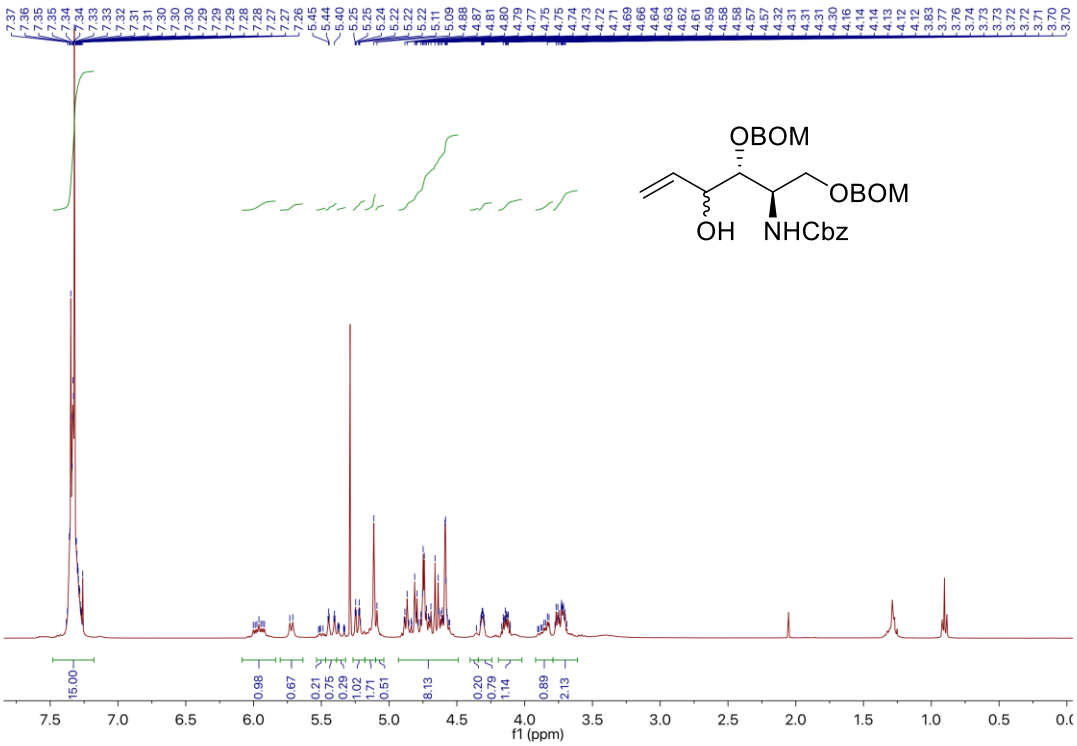
Benzyl ((5S,6R)-5-(2-methylprop-1-en-1-yl)-1,11-diphenyl-2,4,8,10-tetraoxaundecan-6-yl)carbamate (5)

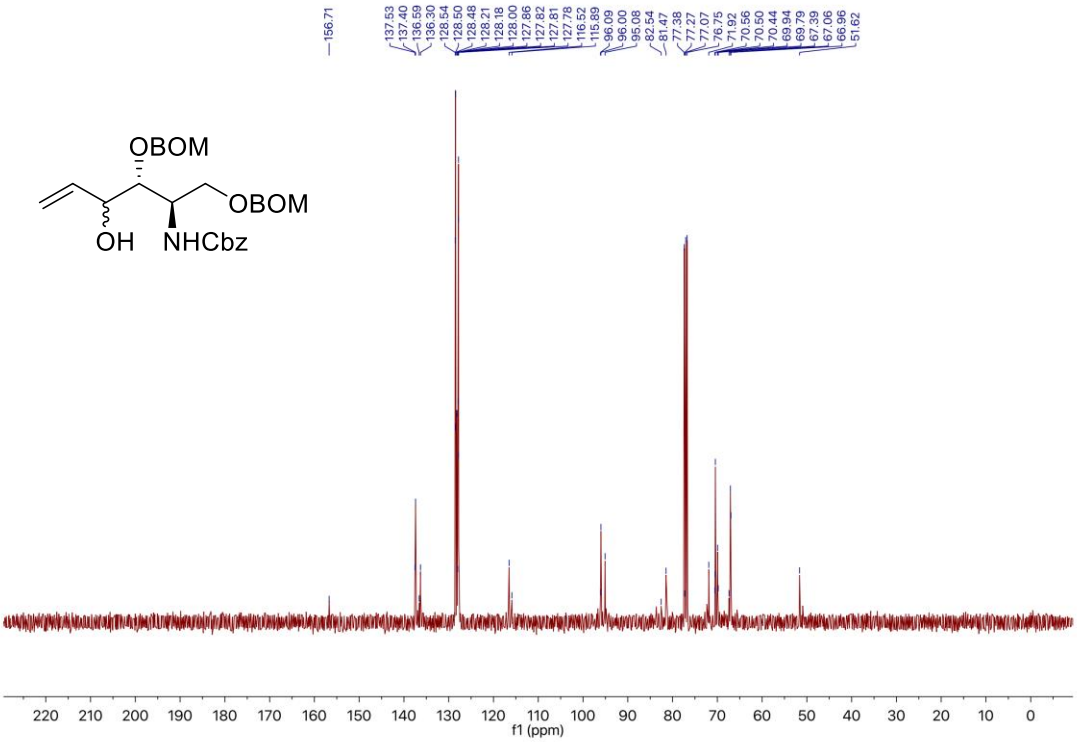


^{13}C-NMR

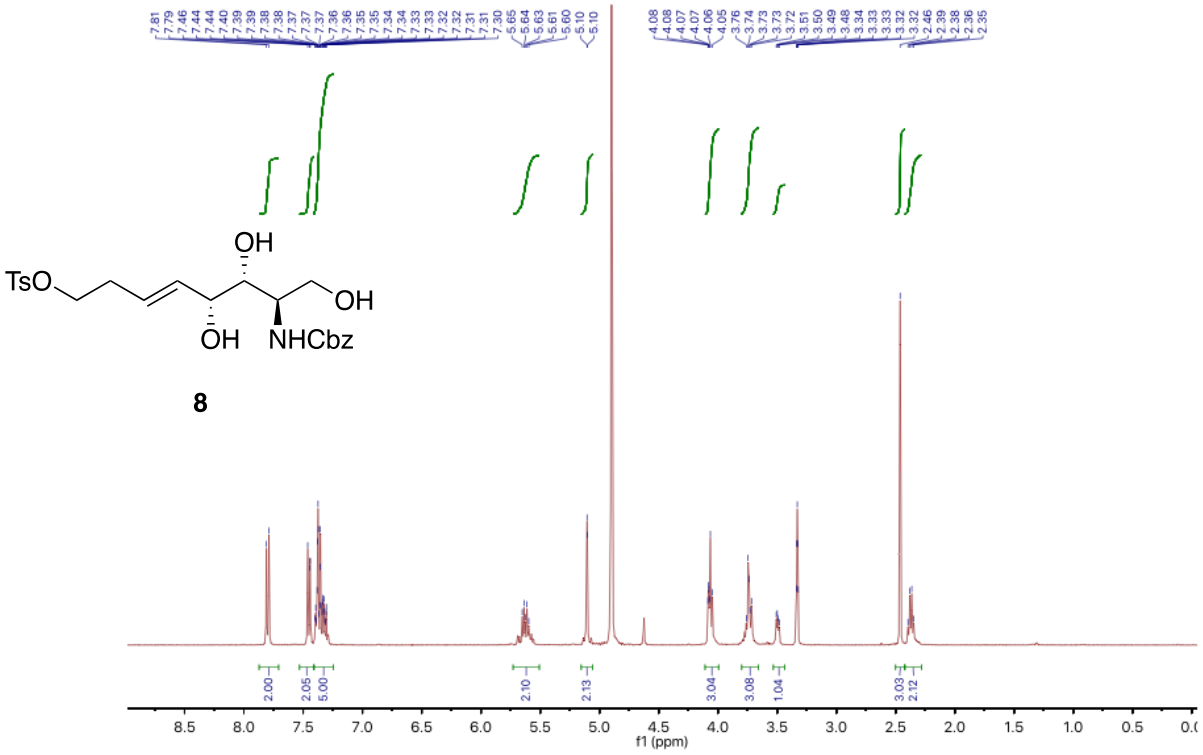


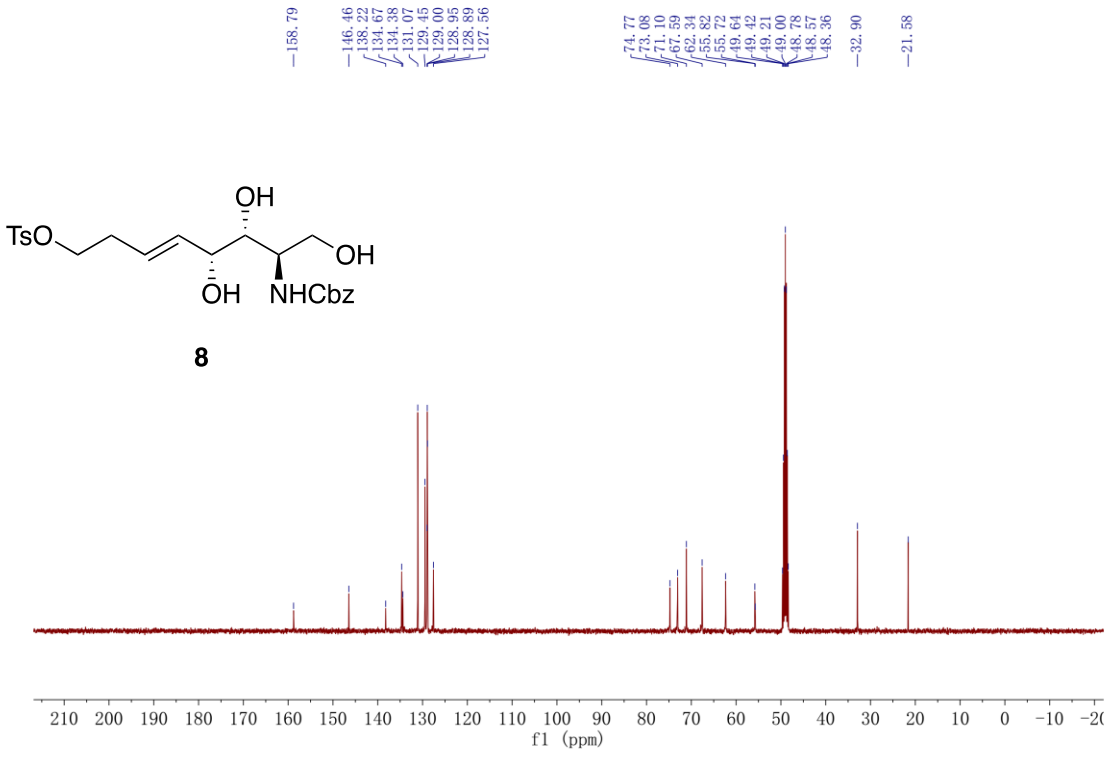
Benzyl ((5R,6R)-5-((R)-1-hydroxyallyl)-1,11-diphenyl-2,4,8,10-tetraoxaundecan-6-yl)carbamate (7)



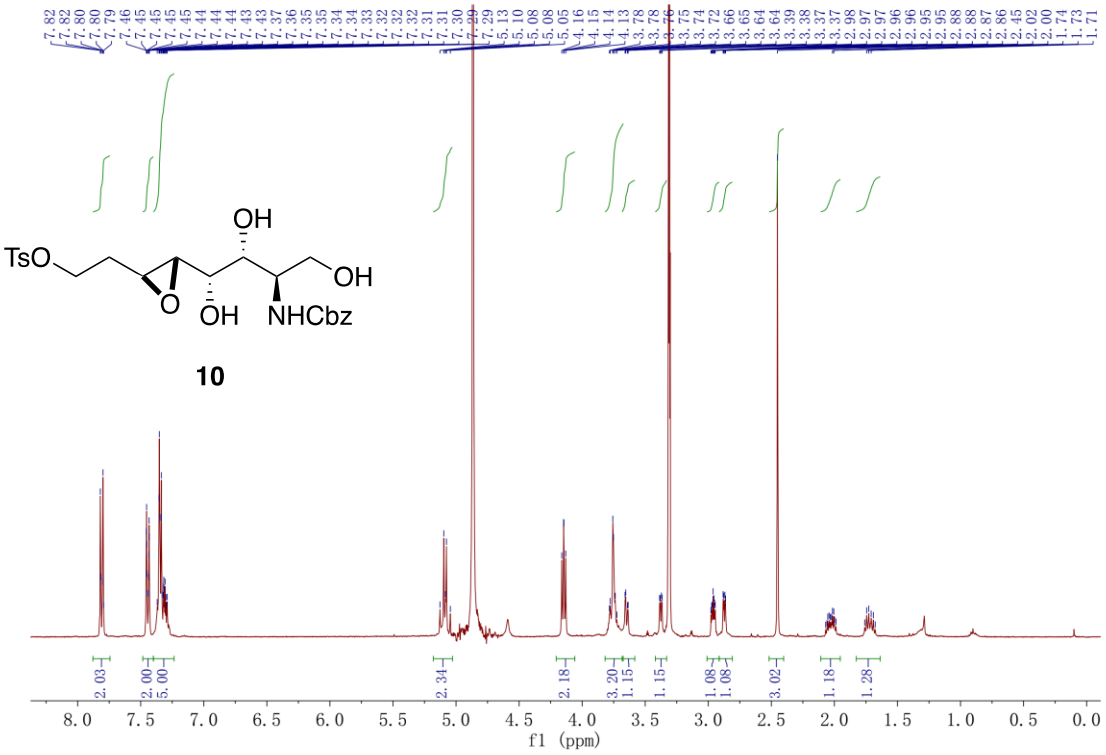


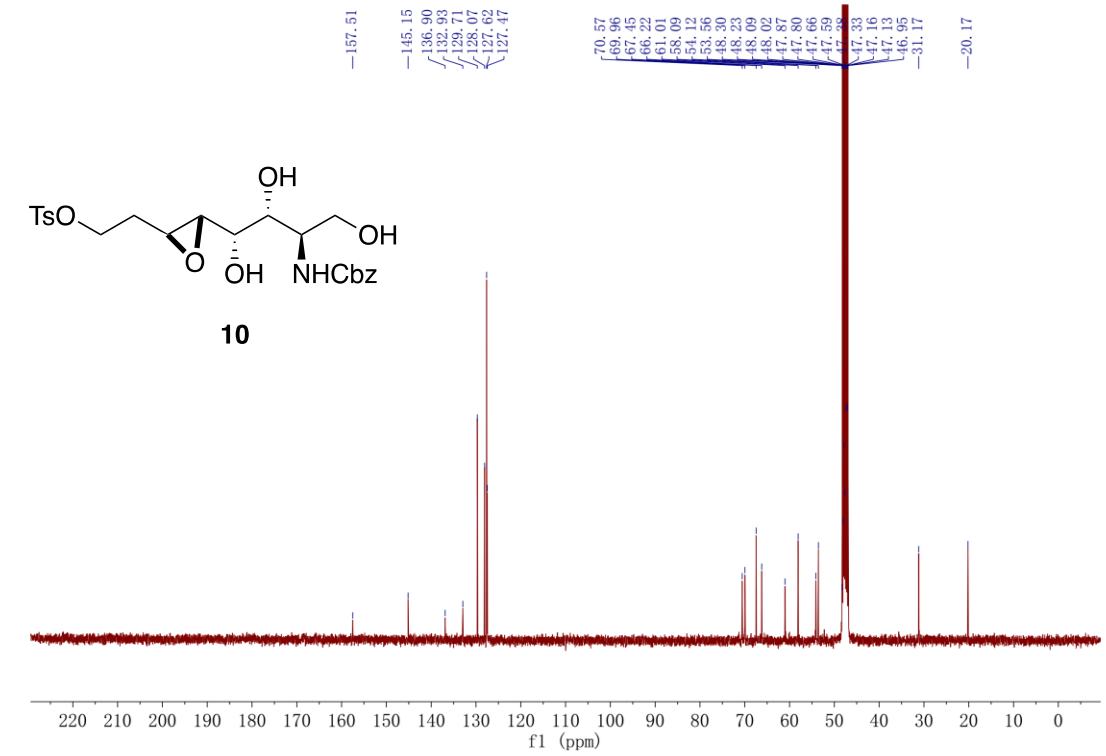
(5R,6R,7R,E)-7-(((benzyloxy)carbonyl)amino)-5,6,8-trihydroxyoct-3-en-1-yl 4-methylbenzenesulfonate (8)



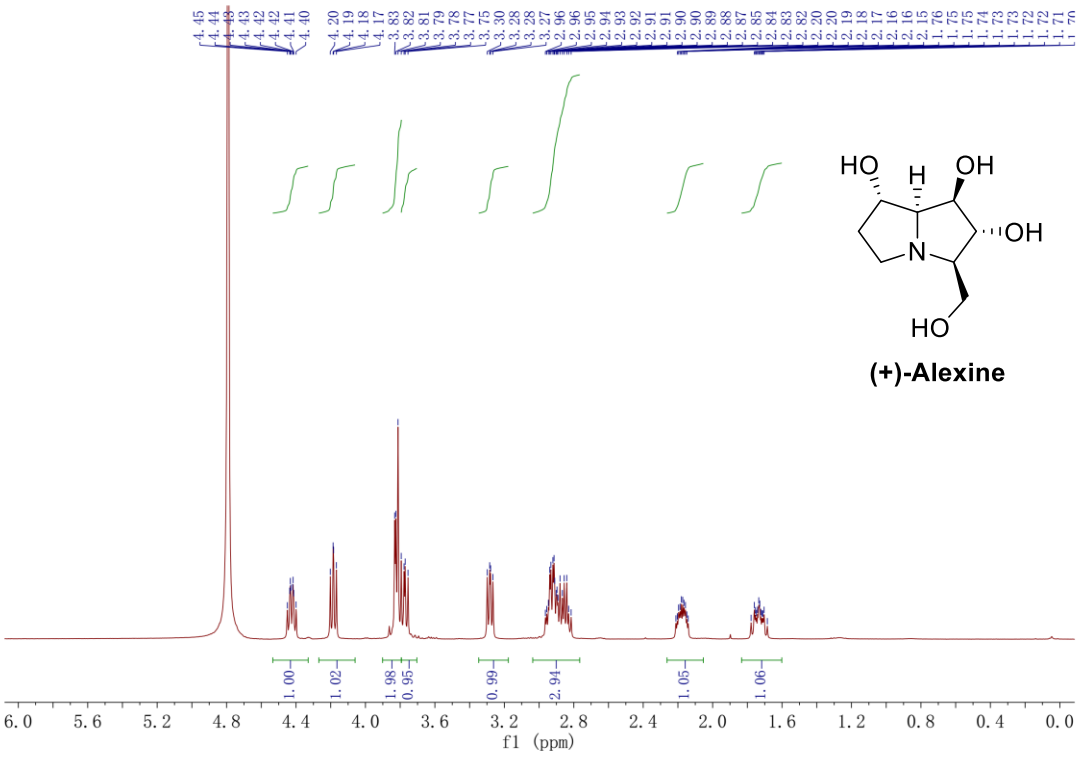


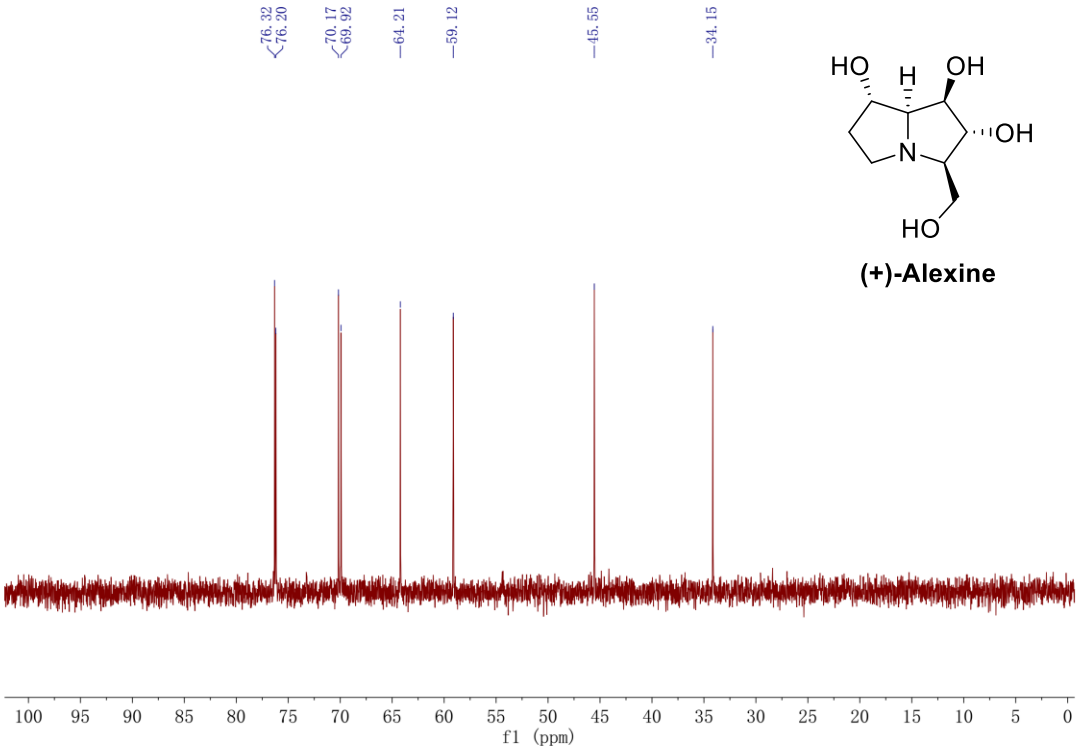
2-((2S,3S)-3-((1S,2R,3R)-3-(((benzyloxy)carbonyl)amino)-1,2,4-trihydroxybutyl)oxiran-2-yl)ethyl 4-methylbenzenesulfonate (10)





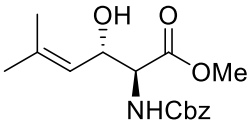
(+)-Alexine (3)



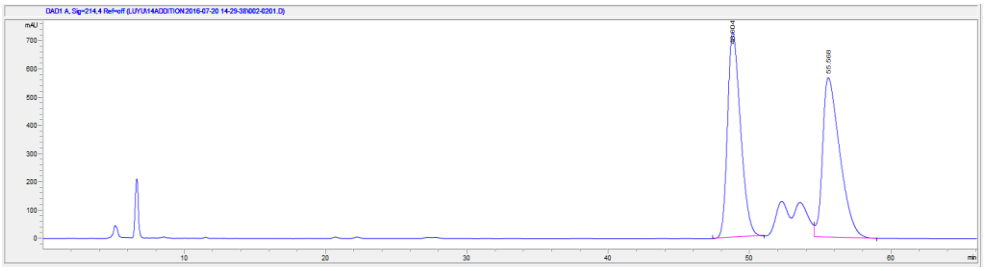


7. HPLC spectrum of products (2a-2g, 2i-2m)

Methyl (*2S,3S*)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-methylhex-4-enoate (2a)



2a



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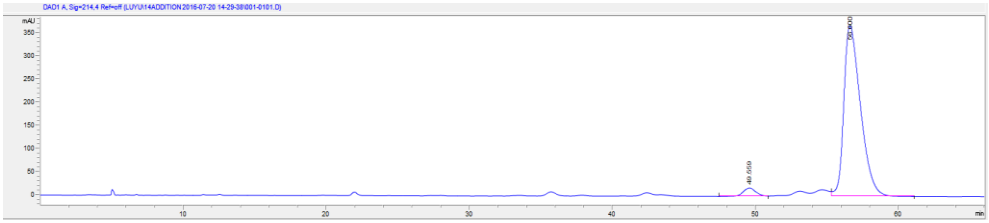
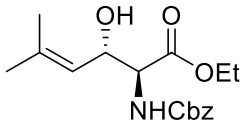
1	48.804	46791.7	729.7	0.9921	49.338	0.647
2	55.568	48046.8	567.6	1.2796	50.662	0.477

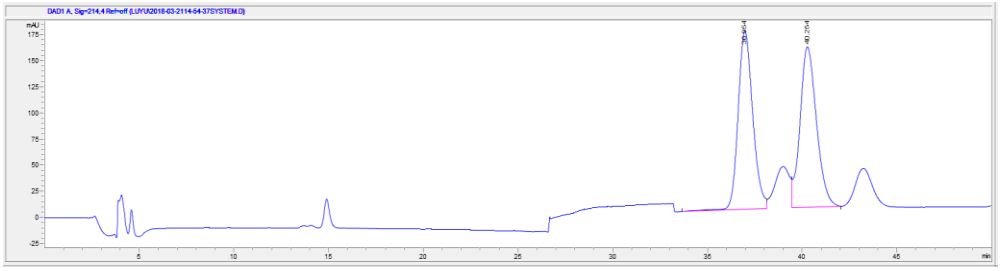


#	Time	Area	Height	Width	Area%	Symmetry
1	49.559	1062.4	17.5	0.9282	3.444	0.958
2	56.6	29786	368.6	1.2387	96.556	0.546

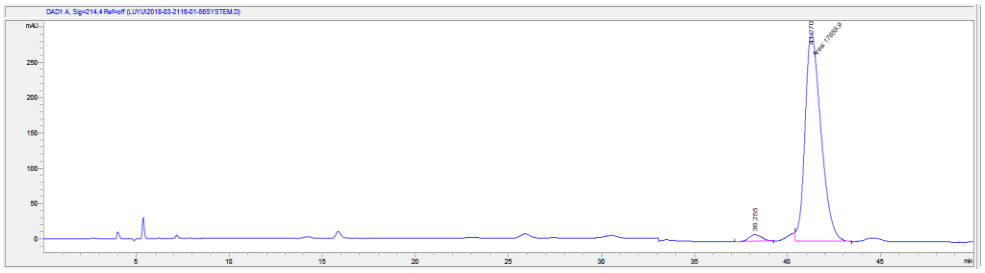
Ethyl (2S,3S)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-methylhex-4-enoate (2b)



2b

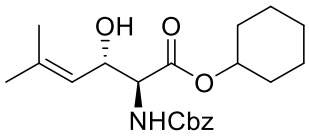


#	Time	Area	Height	Width	Area%	Symmetry
1	36.954	9172.1	170.3	0.8245	49.880	0.828
2	40.254	9216.3	153	0.9227	50.120	0.774

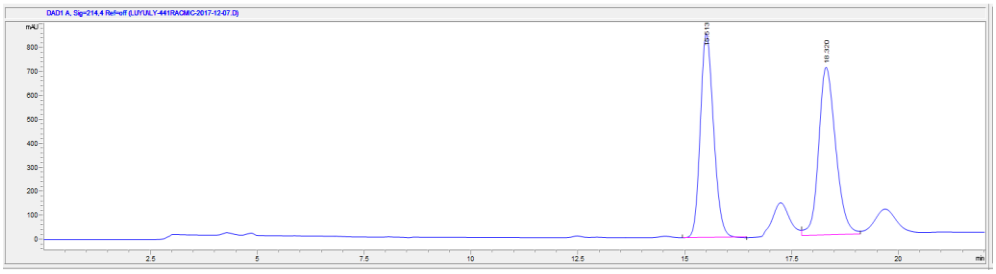


#	Time	Area	Height	Width	Area%	Symmetry
1	38.255	455.6	9.5	0.7436	2.515	0.976
2	41.27	17659.9	296.2	0.9937	97.485	0.644

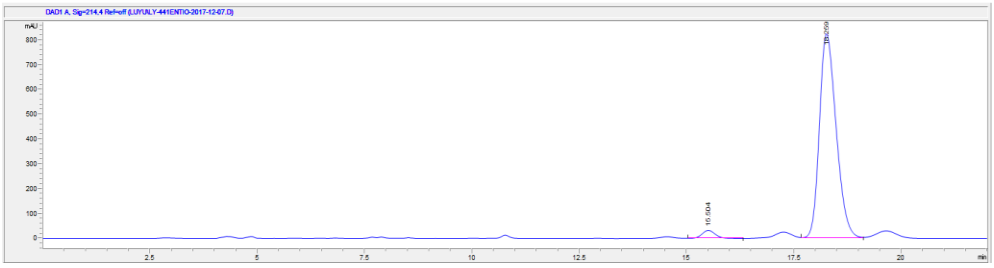
Cyclohexyl
(2S,3S)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-methylhex-4-enoate (2c)



2c

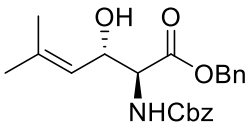


#	Time	Area	Height	Width	Area%	Symmetry
1	15.513	18429.7	852.1	0.3323	48.406	0.778
2	18.32	19643.6	702	0.4305	51.594	0.762

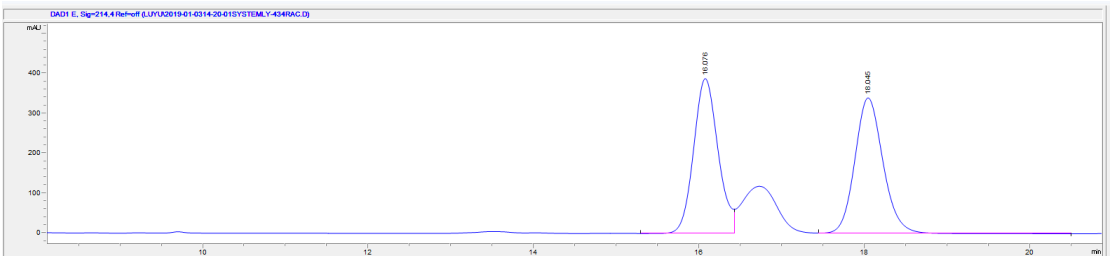


#	Time	Area	Height	Width	Area%	Symmetry
1	15.504	711	32.7	0.3373	3.053	0.888
2	18.259	22581.6	830.1	0.4214	96.947	0.711

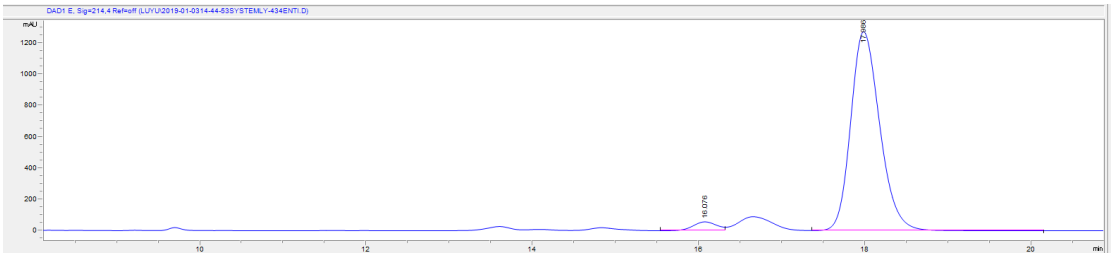
Benzyl (2S,3S)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-methylhex-4-enoate (2d)



2d

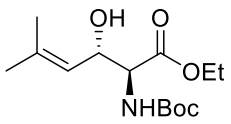


#	Time	Area	Height	Width	Area%	Symmetry
1	16.076	7996	388.7	0.316	49.656	0.878
2	18.045	8106.9	340.6	0.3657	50.344	0.847

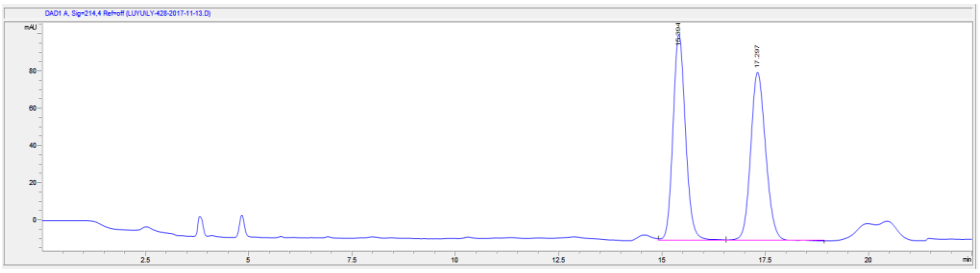


#	Time	Area	Height	Width	Area%	Symmetry
1	16.076	1138.9	56.7	0.3062	3.541	0.957
2	17.986	31028	1278.7	0.3751	96.459	0.764

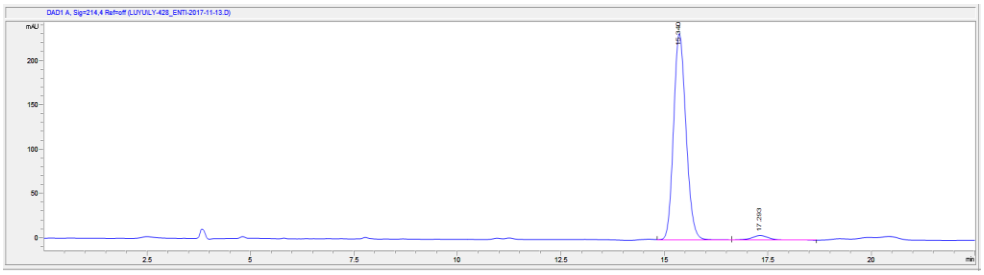
Ethyl (2S,3S)-2-((tert-butoxycarbonyl)amino)-3-hydroxy-5-methylhex-4-enoate (2e)



2e

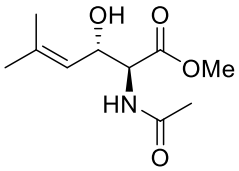


#	Time	Area	Height	Width	Area%	Symmetry
1	15.394	2362.3	111.1	0.328	50.601	0.825
2	17.297	2306.2	90.8	0.3925	49.399	0.823

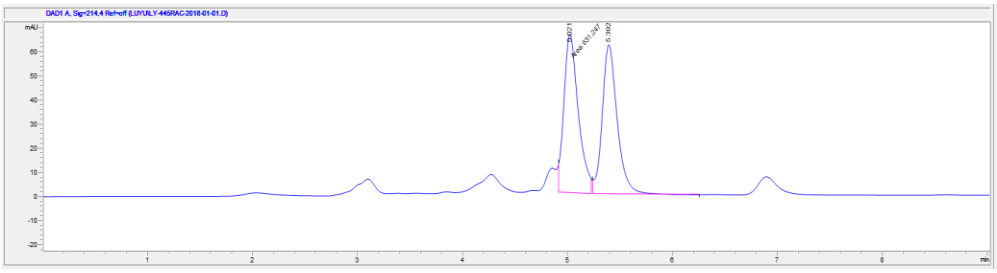


#	Time	Area	Height	Width	Area%	Symmetry
1	15.34	4922.4	233.8	0.3296	96.441	0.808
2	17.293	181.6	5.4	0.4849	3.559	0.866

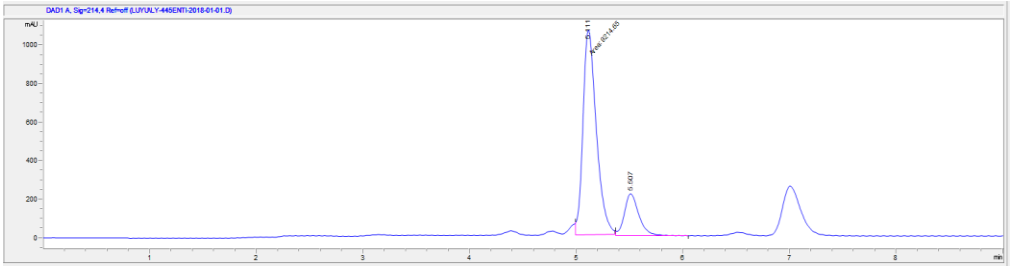
Methyl (2S,3S)-2-acetamido-3-hydroxy-5-methylhex-4-enoate (2f)



2f

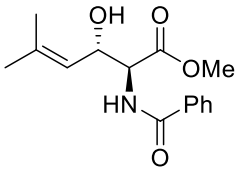


#	Time	Area	Height	Width	Area%	Symmetry
1	5.021	631.2	66.3	0.1588	50.350	0.727
2	5.392	622.5	62.1	0.149	49.650	0.728

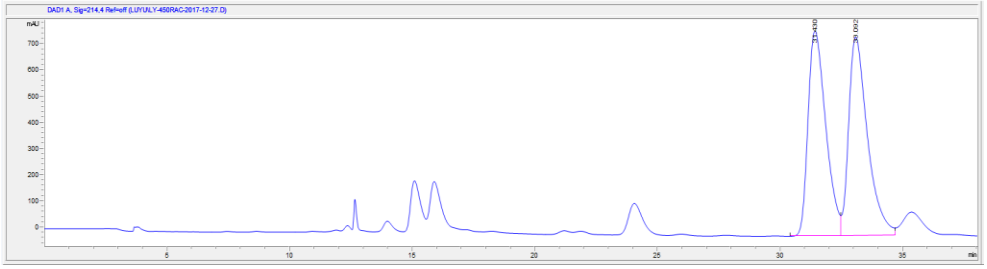


#	Time	Area	Height	Width	Area%	Symmetry
1	5.111	9214.6	1062.3	0.1446	81.740	0.709
2	5.507	2058.4	215.9	0.1432	18.260	0.71

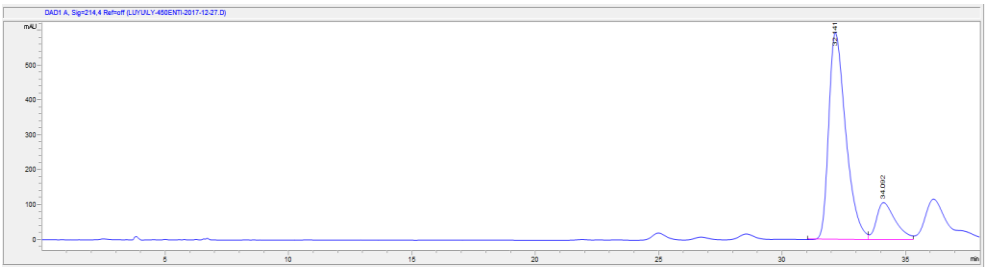
Methyl (2S,3S)-2-benzamido-3-hydroxy-5-methylhex-4-enoate (2g)



2g

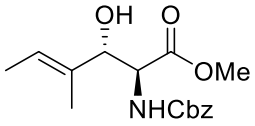


#	Time	Area	Height	Width	Area%	Symmetry
1	31.43	39425	784.3	0.7784	49.291	0.607
2	33.092	40559.6	759	0.8074	50.709	0.554

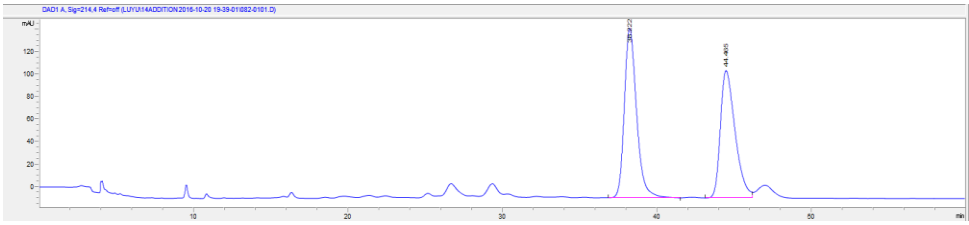


#	Time	Area	Height	Width	Area%	Symmetry
1	32.141	28547.4	592.7	0.7299	83.407	0.604
2	34.092	5679.4	106.5	0.7983	16.593	0.558

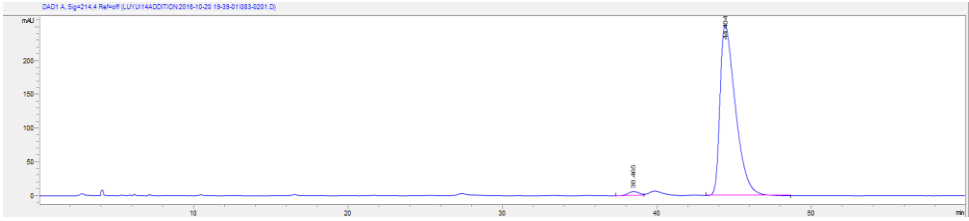
Methyl
(*2S,3S,E*)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-4-methylhex-4-enoate (2i)



2i

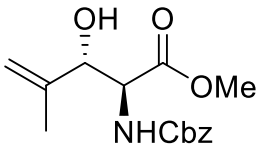


#	Time	Area	Height	Width	Area%	Symmetry
1	38.222	8301.6	150.8	0.8503	52.444	0.727
2	44.465	7527.8	113.5	1.0219	47.556	0.596

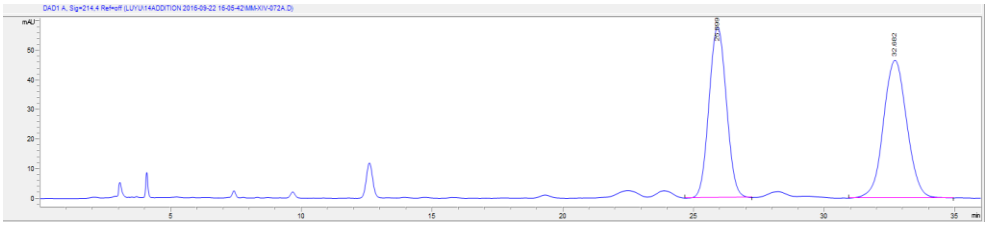


#	Time	Area	Height	Width	Area%	Symmetry
1	38.465	334.9	6.3	0.8215	1.865	0.942
2	44.404	17624.1	252.4	1.0626	98.135	0.469

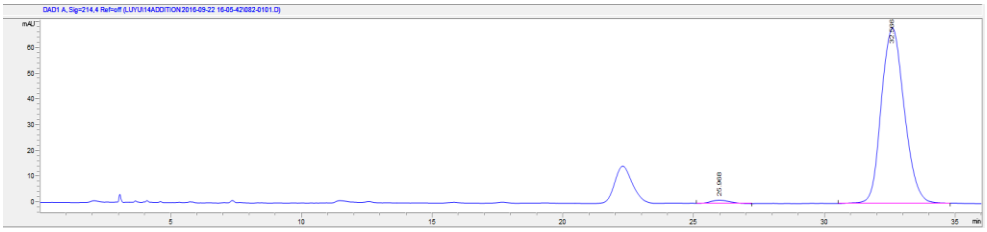
Methyl (*2S,3S*)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-4-methylpent-4-enoate (2j)



2j

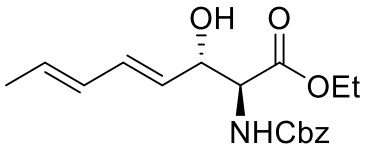


#	Time	Area	Height	Width	Area%	Symmetry
1	25.899	2677.7	57.9	0.732	47.953	0.937
2	32.682	2906.3	46.7	0.9746	52.047	0.948

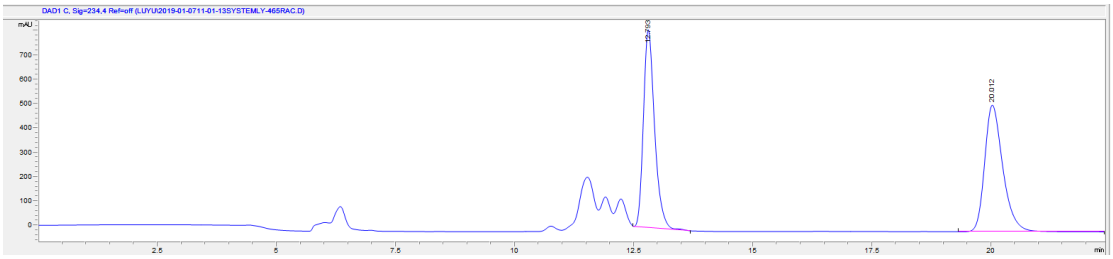


#	Time	Area	Height	Width	Area%	Symmetry
1	25.968	63	1.3	0.6704	1.503	0.805
2	32.566	4129.6	67.8	0.9511	98.497	0.896

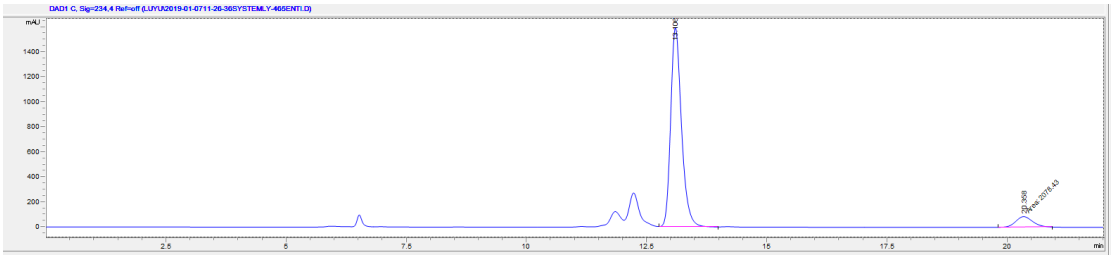
Methyl (2S,3S,4E,6E)-2-(((benzyloxy)carbonyl)amino)-3-hydroxyocta-4,6-dienoate (2k)



2k

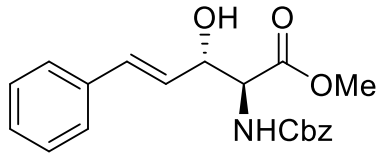


#	Time	Area	Height	Width	Area%	Symmetry
1	12.793	13160.5	808.2	0.248	48.921	0.724
2	20.012	13740.8	517.4	0.4018	51.079	0.688

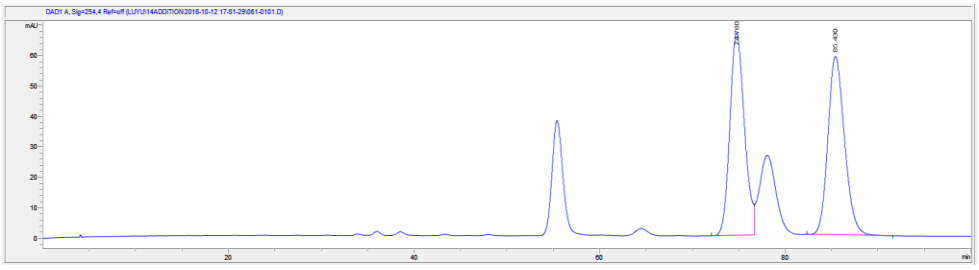


#	Time	Area	Height	Width	Area%	Symmetry
1	13.106	24839.1	1586.6	0.2386	92.279	0.734
2	20.358	2078.4	84.4	0.4106	7.721	0.867

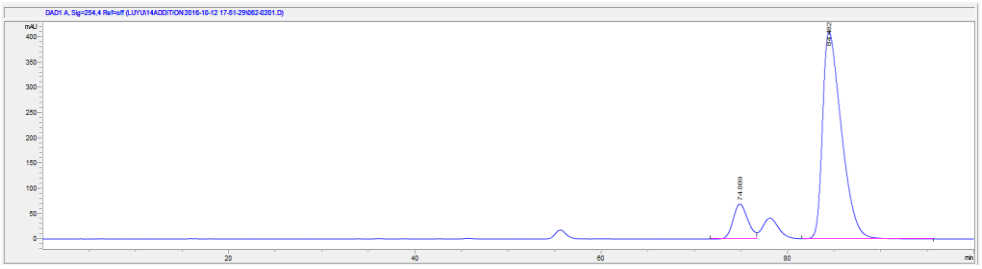
Methyl (2S,3S,E)-2-(((benzyloxy)carbonyl)amino)-3-hydroxy-5-phenylpent-4-enoate (2l)



2l

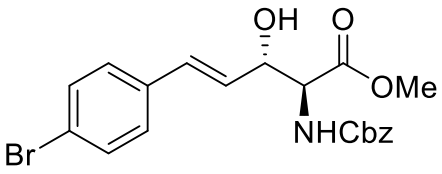


#	Time	Area	Height	Width	Area%	Symmetry
1	74.76	7304	66.8	1.6764	49.871	0.807
2	85.43	7341.8	58.8	1.8725	50.129	0.793

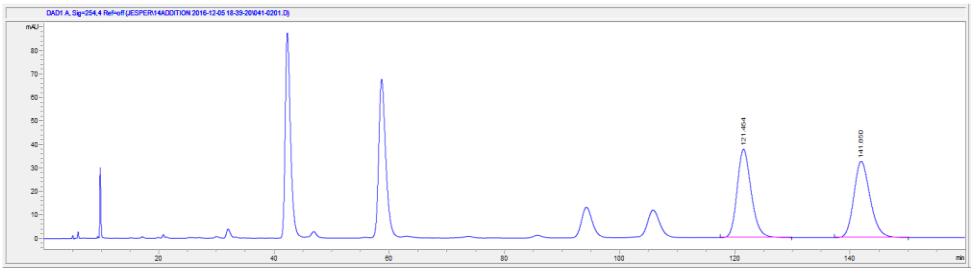


#	Time	Area	Height	Width	Area%	Symmetry
1	74.889	7506.6	68.8	1.6616	11.606	0.816
2	84.482	57171.8	407.3	2.0657	88.394	0.503

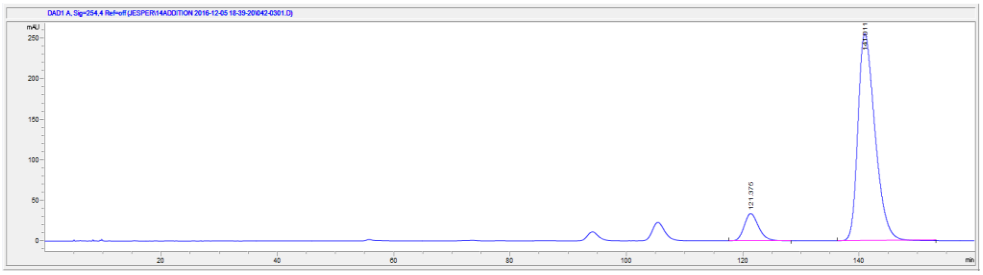
Methyl(2S,3S,E)-2-(((benzyloxy)carbonyl)amino)-5-(4-bromophenyl)-3-hydroxypent-4-enoate (2m)



2m



#	Time	Area	Height	Width	Area%	Symmetry
1	121.454	6363.7	37.6	2.5516	50.030	0.809
2	141.85	6356.1	32.4	2.9478	49.970	0.773



#	Time	Area	Height	Width	Area%	Symmetry
1	121.375	5714.5	33.5	2.4617	9.870	0.787
2	141.011	52182.7	255.5	3.1265	90.130	0.637

1. Seashore-Ludlow, B.; Villo, P.; Somfai, P., *Chemistry – A European Journal* **2012,** *18*, 7219-7223.
2. Iwasaki, T.; Maegawa, Y.; Hayashi, Y.; Ohshima, T.; Mashima, K., *The Journal of Organic Chemistry* **2008,** *73*, 5147-5150.