Supporting Information

Pd-Catalyzed Asymmetric N-Allylation of Amino Acid Esters with Exceptional Levels of Catalyst Control: Stereo-Divergent Synthesis of ProM-15 and Related Bicyclic Dipeptide Mimetics

Stephan Dohmen,[a] Martin Reiher,[a] Dominik Albat,[a] Sema Akyol,[a] Matthias Barone,[b] Jörg-Martin Neudörfl,[a] Ronald Kühne,[b] and Hans-Günther Schmalz*[a]

chem_202000307_sm_miscellaneous_information.pdf
Table of Contents

Asymmetric N-allylation: Ligand Screening ........................................................................................................ 3
Asymmetric N-allylation: Reaction conditions optimization .................................................................................. 4
Optimization of the peptide coupling between trans-N-Boc-3-vinyl-proline (2) and N-allylated amino esters (3) ........ 5
General information .................................................................................................................................................. 6
Experimental procedures ......................................................................................................................................... 7
Synthesis of carbonate rac-4a[1–3].......................................................................................................................... 7
General procedure 1: Asymmetric Pd-catalyzed N-allylation amino acid esters ...................................................... 8
General procedure 2: Peptide coupling using Ghosez reagent .............................................................................. 26
General procedure 3: Ru-catalyzed ring closing metathesis .................................................................................. 26
NMR Spectra.......................................................................................................................................................... 50
GC Spectra of rac-3a and (S)-3a ............................................................................................................................ 88
References.............................................................................................................................................................. 89
Author Contributions.............................................................................................................................................. 97
### Asymmetric N-allylation: Ligand Screening

#### Table S1. Screening of various chiral ligands under standard conditions

| Entry | Ligand | Palladium [mol%] | Concentration [M] | Temperature [°C] | Time [h] | Conversion [%] | e.r. [S:R] |
|-------|--------|------------------|-------------------|------------------|---------|----------------|------------|
| 1     | dppe   | 2.5/6            | 10                | r.t.             | 5.5     | 100            | --         |
| 2     | S-L1   | 2.5/6            | 10                | 0                | 22      | 0              | --         |
| 3     | S-L2   | 2.5/6            | 10                | 0                | 22      | 6              | --         |
| 4     | S-L3   | 2.5/6            | 10                | 0                | 22      | 90             | 41:59      |
| 5     | S-L4   | 2.5/6            | 10                | 0                | 22      | 57             | --         |
| 6     | S-L5   | 2.5/6            | 10                | 0                | 22      | 100            | 77:23      |
| 7     | S-L6   | 2.5/6            | 10                | 0                | 22      | 0              | --         |
| 8     | S-L7   | 2.5/6            | 10                | 0                | 69      | 20             | 39:61      |
| 9     | S-L8   | 2.5/6            | 10                | 0                | 69      | 100            | 41:59      |
| 10    | S-L9   | 2.5/6            | 10                | 0                | 2.5     | 100            | 89:11      |
| 11    | S-L10  | 2.5/6            | 10                | 0                | 2.5     | 100            | 92:8       |
| 12    | S-L11  | 2.5/6            | 10                | 0                | 2.5     | 100            | 56:44      |
| 13    | L1     | 2.5/6            | 10                | r.t.             | 5       | 100            | 27:73      |
| 14    | L1     | 2.5/6            | 10                | 0                | 22      | 100            | 19:81      |
| 15    | L1     | 2.5/6            | 10                | -10              | 20      | 75             | 17:83      |
| 16    | L2     | 2.5/6            | 10                | 0                | 22      | 91             | 73:27      |
| 17    | L3     | 2.5/6            | 10                | 0                | 2.5     | 100            | 90:10      |
| 18    | L4     | 2.5/6            | 10                | 0                | 2.5     | 100            | 94:6       |
| 19    | L5     | 2.5/6            | 10                | 0                | 2.5     | 100            | 91:9       |
| 20    | L6     | 2.5/6            | 10                | 0                | 2.5     | 100            | 96:4       |
| 21    | L7     | 2.5/6            | 10                | 0                | 2.5     | 100            | 96:4       |
| 22    | L8     | 2.5/6            | 10                | 0                | 2.5     | 100            | 90:10      |

[a] Reactions were performed on a 1 mmol scale using 2 equiv. of 5a. [b] concentration of rac-4a. [c] the conversion was determined by means of GC; [d] The enantiomeric ratio was determined by means of GC using a chiral stationary phase; configurational assignments are based on the X-ray crystal structure analysis of the ProM-15 derivative 7a.
Asymmetric N-allylation: Reaction conditions optimization

**Table S2.** Screening of various conditions using diphosphine ligands L1, L4-7

| Entry | Ligand | Pd/L [mol%] | Conc [M] | Temp [°C] | Time [h] | Conv [%] | e.r. [S:R] |
|-------|--------|-------------|----------|-----------|----------|----------|-----------|
| 1     | L4     | 1/2.4       | 10       | -10       | 2.5      | 100      | 96:4      |
| 2     | L4     | 0.5/1.2     | 10       | -10       | 5        | 100      | 96:4      |
| 3     | L6     | 1/2.4       | 10       | -10       | 2.5      | 100      | 97:3      |
| 4     | L7     | 1/2.4       | 10       | -10       | 2.5      | 100      | 97:3      |
| 5     | L6     | 1/2.4       | 5        | -10       | 2.5      | 100      | 96:4      |
| 6     | L6     | 1/2.4       | 2.5      | -10       | 2.5      | 100      | 98:2      |
| 7     | L6     | 1/2.4       | 1.25     | -10       | 5        | 100      | 98:2      |
| 8     | L1     | 2.5/6       | 10       | r.t.      | 5        | 100      | 27:73     |
| 9     | L1     | 2.5/6       | 10       | -10       | 20       | 75       | 17:83     |
| 10    | L1     | 1/2.4       | 2.5      | -10       | 22       | 5        | --        |
| 11    | L4     | 1/2.4       | 25       | -10       | 2.5      | 100      | 94:6      |
| 12    | L4     | 1/2.4       | 10       | -20       | 5        | 100      | 96:4      |
| 14    | L4     | 1/2.4       | 10       | -30       | 21.5     | 100      | 97:3      |
| 15    | L4     | 1/2.4       | 1.25     | -10       | 5        | 100      | 98:2      |
| 16    | L4     | 0.25/0.6    | 10       | -10       | >5       | 100      | 96:4      |

[a] Reactions were performed on a 1 mmol scale using 2 equiv. of 5a. [b] concentration of rac-4a; [c] the conversion was determined by means of GC; [d] The enantiomeric ratio was determined by means of GC using a chiral stationary phase; configurational assignments are based on the X-ray crystal structure analysis of the ProM-15 derivative 7a.
Optimization of the peptide coupling between trans-N-Boc-3-vinyl-proline (2) and N-allylated amino esters (3)

While the glycine derivatives rac-3a and 3b afforded the expected product (6, R = H) using either PyBOP in acetonitrile or HATU in NMP as a solvent in the presence of DIPEA (Table S2, entries 1 and 2) the sterically more bulky amines (such as 3e) derived from other amino acids required the search for more powerful coupling conditions.

**Table S3.** Searching for peptide coupling conditions of the acid 2 with N-allylated amino acid esters of type 3.

| Entry | Amine | reagent | base | Temp [°C] | solvent | yield [%] |
|-------|-------|---------|------|-----------|---------|-----------|
| 1     | rac-3a| PyBOP   | DIPEA | 60        | MeCN    | 60        |
| 2     | rac-3a| HATU    | DIPEA | 85        | NMP     | 71        |
| 3     | ambo-3c| HATU | DIPEA | 85        | NMP     | --        |
| 4     | ambo-3e| HATU | DIPEA | 85        | NMP     | --        |
| 5     | ambo-3e| Pfp-OH | --   | RT        | CH$_2$Cl$_2$ | --    |
| 6     | ambo-3e| PyCloP | DIPEA | RT – 45   | CH$_2$Cl$_2$ | 12    |
| 7     | ambo-3e| PyCloP | DIPEA | RT – 80   | DMF     | --        |
| 8     | ambo-3e| EDC/DM AP | --   | 0 – 50   | CH$_2$Cl$_2$ | -- |
| 9     | ambo-3e| BTFFH | DIPEA | 0 – 85   | DMF     | --        |
| 10    | ambo-3e| BTFFH | Pyridin | 0 - RT | DMF     | --        |
| 11    | ambo-3e| cyanuric fluoride | DIPEA | RT | CH$_2$Cl$_2$ | -- |
| 12    | ambo-3e| Ghosez reagent | DIPEA | 0 - RT | CH$_2$Cl$_2$ | 66 |
| 13    | rac-3a| Ghosez reagent | DIPEA | 0 - RT | CH$_2$Cl$_2$ | 87 |

Reactions were generally performed on a 0.3 (±0.05) mmol scale. Yields refer to the purified product after chromatography.
General information
All moisture sensitive reactions were carried out under argon atmosphere using Schlenk technique. Glassware was flame-dried under vacuum (<1 mbar) and allowed to cool down under argon atmosphere. Syringes, needles and transfer cannulas were dried in an oven at 100 °C and were flushed with argon directly prior to use. Flash chromatography was performed using silica 60 (0.035 – 0.07 mm) supplied by Acros.

NMR spectroscopy: ¹H and ¹³C NMR spectra were recorded on Bruker AV 400, Bruker AV 300, or Bruker DPX 300 instruments. Chemical shifts (δ) are given in ppm relative to the solvent reference as an internal standard (¹H NMR: δ 7.26 ppm for CDCl₃ and δ 3.31 ppm for CD₃OD; ¹³C NMR: δ 77.16 ppm for CDCl₃; δ 49.00 ppm for CD₃OD). The assignments of ¹H NMR are supported by H,H-COSY, HMQC(HSQC), and HMBC spectra. Carbon multiplicity assignment is based on APT or DEPT spectra. Fourier transform infrared spectroscopy (FT-IR): IR spectra were recorded on a Perkin Elmer FT-IR Paragon 1000 spectrometer using Fourier transform infrared (FTIR) multiple-point attenuated total reflection (ATR) technique. Absorption bands are given in wave numbers (ṽ, cm⁻¹). Intensive bands are marked with (s), medium with (m), weak with (w). Broad bands are marked as (br).

Mass spectrometry: Mass spectra (ESI) were recorded on a Thermo Fischer LTQ Orbitrap XL – FTMS Analyser. GC-MS experiments were carried out on Agilent 6890 system with mass detector (MSD) 5937 N. Separation was accomplished using an Optima-5 Accent column by Macherey-Nagel. For the detection TIC as well as FID was used. Hydrogen was used as carrier gas with a flow of 1.7 ml/min. The column temperature was first held at 50 °C for 2 min and then increased to 300 °C at 25 °C/min.

For the determination of enantiomeric ratios an Agilent 6890 system with FID detection was used. The separation was performed using a CP-Chiral-Dex CB column by Varian. The carrier gas was nitrogen with a flow of 0.9 ml/min. Alternatively a Hewlett Packard 6890 system with FID detection was used with hydrogen as carrier gas and a flow of 1.5 ml/min. The used temperature programs are specified in the analytical data of the respective substance as well as the used column.
Experimental procedures

Synthesis of carbonate rac-4a\[^{1-3}\]

\[
\begin{array}{c}
\text{CH}_2\text{Cl}_2 \\
0^\circ\text{C} - \text{r.t.}, \text{o.n.}
\end{array}
\]

To a solution of 5.0 ml (51.12 mmol, 1.0 eq.) trans-2-pentenal in 75 ml abs. Et\(_2\)O 3.0 ml (66.45 mmol, 1.3 eq.) ethylmagnesium bromide were added slowly at 0°C. The reaction mixture was stirred at the same temperature for 2 h followed by the addition of 75 ml saturated NH\(_4\)Cl-solution. The phases were separated, and the aqueous layer was extracted three times with Et\(_2\)O. Combined organic layers were dried over MgSO\(_4\) and the solvent was evaporated under reduced pressure. Due to the volatility of the product the pressure should not be reduced below 200 mbar (at 40°C water bath temperature). The yellow raw product was purified by flash column chromatography (CH\(_2\)Cl\(_2\)/CHCl\(_3\) = 10/1). The resulting alcohol rac-12 was solved in 104 ml abs. CH\(_2\)Cl\(_2\) and cooled to 0°C. At this temperature 12.2 ml (150.81 mmol, 3.0 eq.) pyridine were added over 1 h followed by one additional hour of stirring at 0°C. Subsequently 7.8 ml (100.54 mmol, 2.0 eq.) methyl chloroformate was added over 1 h. After complete addition the ice bath was removed, and the reaction was stirred over night at room temperature. Afterwards saturated NaCl-solution was added, and the phases separated. The aqueous layer was diluted with H\(_2\)O until the precipitation vanished completely and then extracted three times with CH\(_2\)Cl\(_2\). The combined organic phases were dried over MgSO\(_4\) and the solvent was evaporated under reduced pressure. Due to the volatility of the carbonate pressure was not reduced below 400 mbar (at 40°C water bath temperature). The purification was performed using bulb tube distillation yielding 3.80 g (22.06 mmol, 43% over 2 steps) of the desired product as a colorless liquid.

\[
\begin{align*}
\text{C}_9\text{H}_{16}\text{O}_3 \\
\end{align*}
\]

M: 172.22 g/mol.

\(^1\text{H NMR}\) (300 MHz, CDCl\(_3\)): \(\delta\) [ppm] = 0.91 (t, \(^3\)J = 7.5 Hz, 3H, H-7); 0.99 (t, \(^3\)J = 7.5 Hz, 3H, H-1); 1.55 – 1.80 (m, 2H, H-6); 2.06 (\(\Psi_{\text{quint.}}\), \(^3\)J = 6.4 Hz, 2H, H-2); 3.76 (s, 3H, H-9); 4.95 (\(\Psi_{\text{q}}\), \(^3\)J = 6.9 Hz, 1H, H-5); 5.39 (dd, \(^3\)J = 15.4 Hz, \(^3\)J = 7.7 Hz, 1H, H-4); 5.81 (dt, \(^3\)J = 15.4 Hz, \(^3\)J = 6.2 Hz, 1H, H-3).

\(^{13}\text{C NMR}\) (75 MHz, CDCl\(_3\)): \(\delta\) [ppm] = 9.5 (C-7); 13.2 (C-1); 25.3 (C-2); 27.6 (C-6); 54.5 (C-9); 80.8 (C-5); 126.6 (C-4); 137.0 (C-3); 155.4 (C-8).

\(^{13}\text{C NMR}\) (75 MHz, CDCl\(_3\)): \(\delta\) [ppm] = 9.5 (C-7); 13.2 (C-1); 25.3 (C-2); 27.6 (C-6); 54.5 (C-9); 80.8 (C-5); 126.6 (C-4); 137.0 (C-3); 155.4 (C-8).

\(^{13}\text{C NMR}\) (75 MHz, CDCl\(_3\)): \(\delta\) [ppm] = 9.5 (C-7); 13.2 (C-1); 25.3 (C-2); 27.6 (C-6); 54.5 (C-9); 80.8 (C-5); 126.6 (C-4); 137.0 (C-3); 155.4 (C-8).

\text{IR (ATR)}: \tilde{\nu}\ [\text{cm}^{-1}] = 2967 \text{ (w)}; 2938 \text{ (w)}; 2879 \text{ (w)}; 2852 \text{ (w)}; 1744 \text{ (s)}; 1672 \text{ (w)}; 1583 \text{ (w)}; 1456 \text{ (w)}; 1442 \text{ (m)}; 1382 \text{ (w)}; 1368 \text{ (w)}; 1348 \text{ (w)}; 1304 \text{ (w)}; 1253 \text{ (s)}; 1200 \text{ (w)}; 1169 \text{ (w)}; 1137 \text{ (w)}; 1095 \text{ (w)}; 1075 \text{ (w)}; 1056 \text{ (w)}; 1034 \text{ (w)}; 968 \text{ (m)}; 946 \text{ (m)}; 921 \text{ (m)}; 884 \text{ (w)}; 828 \text{ (w)}; 792 \text{ (m)}; 742 \text{ (w)}; 714 \text{ (w)}.

\text{GC/MS (EI, 70 eV)}: m/z (%) = 172 ([M]^{+}, 1); 143 ([M]+C\(_2\)H\(_5\), 3); 96 (45); 81 (100); 67 (30); 55 ([C\(_4\)H\(_7\)]^{+}, 45).
General procedure 1: Asymmetric Pd-catalyzed N-allylation of amino acid esters

A solution of a chiral ligand L* (2.4 mol%) and [PdCl(allyl)]2 (1 mol%) in anhydrous THF (0.4 ml per mmol of the carbonate) was cooled to -10°C before carbonate rac-4a (1.0 eq.) was added by means of a syringe. After 30 min the amino acid ester (2.0 eq.) was added and stirring was continued at -10°C until complete conversion was observed by means of GC-MS (22 h if not mentioned otherwise). The clear yellow solution was then filtered with MTBE through a small pad of Celite and the solvent was evaporated. The crude product was purified by flash column chromatography as specified. In the case of glycine and serine derivatives the enantiomeric excess was determined by means of GC (FID) using a chiral stationary phase. In the case of all other amino acid derivatives the diastereomeric excess was determined by means of GC (FID) using an achiral Optima-5 Accent column.

For the synthesis of racemic reference samples 6 mol% of dppe and 2.0 mol% of [PdCl(allyl)]2 were used at room temperature.

(S,E)-Hept-4-en-3-yl-glycin tert-butyl ester ((S)-3a)

According to general procedure 1, 344 mg (2.00 mmol) of carbonate rac-4a were reacted with glycine tert-butyl ester (5a) using the chiral ligand L6 to yield 376 mg (1.65 mmol, 83%, er = 98/2) of the allylic amine (R)-3a after purification by flash column chromatography (Silica, cHex/EtOAc = 4/1) as a yellow oil.

C_{13}H_{25}NO_{2}

M: 227.34 g/mol.

TLC: Rv = 0.18 (Silica, cHex/EtOAc = 4/1), KMnO4-reagent.

1H NMR (500 MHz, CDCl3): δ [ppm] = 0.87 (t, 3J = 7.5 Hz, 3H, H-7); 0.99 (t, 3J = 7.5 Hz, 3H, H-1); 1.35 – 1.44 (m, 1H, H-6); 1.46 (s, 9H, H-11); 1.49 – 1.57 (m, 1H, H-6’); 1.85 (s, br, 1H, NH); 2.01 – 2.07 (m, 2H, H-2); 2.84 (td, 3J = 8.3 Hz, 3J = 5.3 Hz, 1H, H-5); 3.21 – 3.31 (m, 2H, H-8); 5.12 (ddt, 3J = 15.3 Hz, 3J = 8.6 Hz, 4J = 1.5 Hz, 1H, H-4); 5.70 (dt, 3J = 15.3 Hz, 3J = 6.3 Hz, 1H, H-3).

13C NMR (125 MHz, CDCl3): δ [ppm] = 10.6 (C-7); 13.9 (C-1); 25.5 (C-2); 28.3 (C-11/12/13); 29.0 (C-6); 49.3 (C-8); 62.5 (C-5); 81.1 (C-10); 131.1 (C-4); 135.2 (C-3); 172.3 (C-9).

IR (ATR): ν [cm\(^{-1}\)] = 3450 (w); 3336 (w); 3002 (w); 2964 (m); 2933 (w); 2876 (w); 2857 (w); 2812 (w); 1733 (s); 1667 (w); 1458 (w); 1421 (w); 1393 (w); 1367 (m); 1350 (w); 1251 (w); 1227 (m); 1218 (m); 1151 (s); 1089 (w); 1071 (w); 1035 (w); 970 (m); 937 (w); 917 (w); 876 (w); 850 (m); 792 (w); 755 (w); 701 (w).

GC/MS (EI, 70 eV): m/z (%) = 227 ([M]+, 2); 198 ([M]+-C\(_7\)H\(_5\), 24); 170 ([M]+-C\(_4\)H\(_10\), 10); 142 (100); 126 ([M]+-CO\(_2\)tBu, 25); 112 ([C\(_7\)H\(_{13}\)N]+, 12); 97 ([C\(_6\)H\(_{13}\)]+, 49); 83 (8); 69 (15); 55 (50).

HR/MS (ESI): calculated for [M+H]+: 228.1958; found: 228.1955; calculated for [M+Na]+: 250.1778; found: 250.1778.
Determination of enantiomeric excess: Agilent 6890N GC system using a CP-Chirasil-Dex CB column by Varian (flow (H2): 0.9 ml/min; 90 °C to 110 °C with 1 °C/min, inlet temp.: 170 °C).

(R,E)-Hept-4-en-3-ylglycin tert-butyl ester ((R)-3a)

According to general procedure 1, 517 mg (3.00 mmol) of carbonate rac-4a were reacted with glycine tert-butyl ester (5a) using the chiral ligand ent-L6 to yield 570 mg (2.51 mmol, 84%, er = 98/2) of the allylic amine (S)-3a after purification by flash column chromatography (Silica, cHex/EtOAc = 4/1) as a yellow oil.

\[C_{13}H_{25}NO_2\]

M: 227.34 g/mol.

TLC, NMR, IR and GC-MS data identical with (R)-3a

TLC: R\text{f} = 0.18 (Silica, cHex/EtOAc = 4/1), KMnO\text{4}-reagent.

\([\alpha]_{D}^{20}(\text{CHCl}_3, c = 0.515 \text{ g/100 ml}): [\alpha]_{D}^{20} = +47.6, [\alpha]_{D}^{20} = +30.9^\circ; [\alpha]_{D}^{20} = +27.3^\circ; [\alpha]_{D}^{20} = +25.8^\circ.

Determination of enantiomeric excess: Agilent 6890N GC system using a CP-Chirasil-Dex CB column by Varian (flow (H2): 0.9 ml/min; 90 °C to 110 °C with 1 °C/min, inlet temp.: 170 °C).

(S,E)-Hept-4-en-3-yl-glycin methyl ester ((S)-3b)

According to general procedure 1, 104 mg (0.604 mmol) of carbonate rac-4a were reacted with glycine methyl ester hydrochloride (5b) using the chiral ligand L6 and 0.11 ml Et\text{3}N to yield 99.6 mg (0.54 mmol, 89%, er = 98/2) of the allylic amine (R)-3b after purification by flash column chromatography (Silica, cHex/EtOAc = 2/1) as a yellow oil.

\[C_{16}H_{19}NO_2\]

M: 185.27 g/mol.

TLC: R\text{f} = 0.16 (Silica, cHex/EtOAc = 2/1), KMnO\text{4}-reagent.

\(^1\text{H NMR}\) (500 MHz, CDCl\text{3}): \(\delta [ppm] = 5.57 \text{ (dt, } ^3J = 15.3, 6.3 \text{ Hz, 1H, H-3)}, 5.13 \text{ (ddt, } ^3J = 15.3, 8.6, ^4J = 1.6 \text{ Hz, 1H, H-4)}, 3.73 \text{ (s, 3H, H-10)}, 3.52 - 3.26 \text{ (m, 2H, H-8)}, 2.85 \text{ (t, } ^2J = 8.3, 5.2 \text{ Hz, 1H, H-5)}, 2.06 \text{ (qdd, } ^3J = 7.5, 6.2, ^4J = 1.6 \text{ Hz, 2H, H-2)}, 1.71 \text{ (s, 1H, NH)}, 1.65 - 1.36 \text{ (m, 2H, H-6)}, 1.00 \text{ (t, } ^2J = 7.5 \text{ Hz, 3H, H-1)}, 0.89 \text{ (t, } ^3J = 7.5 \text{ Hz, 3H, H-7}).

\(^{13}\text{C NMR}\) (125 MHz, CDCl\text{3}): \(\delta [ppm] = 10.4 \text{ (C-7); 13.8 (C-1); 25.3 (C-2); 28.8 (C-6); 48.3 (C-8); 51.8 (C-10); 62.5 (C-5); 130.8 (C-4); 135.3 (C-3); 173.4 (C-9)
SUPPORTING INFORMATION

IR (ATR): ν [cm⁻¹] = 3329 (w), 2962 (m), 2933 (w), 2878 (w), 1742 (s), 1459 (m), 1436 (m), 1350 (w), 1200 (s), 1153 (s), 970 (s), 877 (w), 744 (m), 686 (m), 571 (w).

GC/MS (EI, 70 eV): m/z (%) = 156 ([M]⁺-C₄H₁₀, 100); 126 ([M]⁺-CO₂Bu, 6); 112 ([C₇H₁₄N]⁺, 3); 96 ([C₇H₁₃]⁺ 26, 81 (5), 55 (11), 41 (9).

Determination of enantiomeric excess: Agilent 6890N GC system using a Mega-Dex Det-Beta column by Varian (flow (H₂): 3.8 ml/min; 50 °C hold for 5 min, 50 °C to 75 °C with 1 °C/min, 75 °C to 82 °C with 0.2 °C/min, inlet temp.: 170 °C).

(R,E)-Hept-4-en-3-ylglycin tert-butyl ester ((R)-3b)
According to general procedure 1, 104 mg (0.604 mmol) of carbonate rac-4a were reacted with glycine methyl ester hydrochloride (5b) using the chiral ligand L6 and 0.11 ml Et₃N to yield 99.5 mg (0.54 mmol, 89%, er = 98/3) of the allylic amine (R)-3b after purification by flash column chromatography (Silica, cHex/EtOAc = 2/1) as a yellow oil

C₁₀H₁₉NO₂
M: 185.27 g/mol.

TLC, NMR, IR and GC-MS data identical with (S)-3b

TLC: Rf = 0.16 (Silica, cHex/EtOAc = 2/1), KMnO₄-reagent.

[α]ᵢ²⁰(CHCl₃, c = 0.939 g/100 ml): [α]ᵢ²₀ = -52.4 [α]ᵢ⁻₀ = -32.2°; [α]ᵢ⁻₀ = -28.6°; [α]ᵢ⁻₀ = -27.6°.

Determination of enantiomeric excess: Agilent 6890N GC system using a Mega-Dex Det-Beta column by Varian (flow (H₂): 3.8 ml/min; 50 °C hold for 5 min, 50 °C to 75 °C with 1 °C/min, 75 °C to 82 °C with 0.2 °C/min, inlet temp.: 170 °C).

(S)-Methyl 2-((S,E)-hept-4-en-3-ylamino)propanoate ((S,S)-3c)
According to general procedure 1, 172 mg (1.000 mmol) of carbonate rac-4a were reacted with L-alanine methyl ester ((S)-5c) using the chiral ligand L6 to yield 164 mg (0.824 mmol, 83%, dr > 2/98) of the allylic amine (S,S)-3c after purification by flash column chromatography (Silica, cHex/EtOAc = 4/1) as a yellow oil.

C₁₁H₂₁NO₂
M: 199.29 g/mol.

TLC: Rf = 0.25 (Silica, cHex/EtOAc = 3/1), KMnO₄-reagent.
**SUPPORTING INFORMATION**

**1H NMR** (500 MHz, CDCl$_3$): δ [ppm] = 0.86 (t, $^3J = 7.5$ Hz, 3H, H-7); 0.99 (t, $^3J = 7.5$ Hz, 3H, H-1); 1.26 (d, $^3J = 7.1$ Hz, 3H, H-11); 1.35 – 1.51 (m, 2H, H-6); 1.79 (s, br, 1H, NH); 2.01 – 2.07 (m, 2H, H-2); 2.76 (td, $^3J = 8.2$ Hz, $^3J = 5.6$ Hz, 1H, H-5); 3.43 (q, $^3J = 7.1$ Hz, 1H, H-8); 3.72 (s, 3H, H-10); 5.10 (ddt, $^3J = 15.3$ Hz, $^3J = 8.6$ Hz, $^3J = 1.5$ Hz, 1H, H-4); 5.50 (dt, $^3J = 15.3$ Hz, $^3J = 6.3$ Hz, 1H, H-3).

**13C NMR** (125 MHz, CDCl$_3$): δ [ppm] = 10.6 (C-7); 13.9 (C-1); 19.9 (C-11); 25.5 (C-2); 29.3 (C-6); 51.8 (C-10); 53.8 (C-8); 61.6 (C-5); 131.0 (C-4); 135.3 (C-3); 177.1 (C-9).

**IR** (ATR): $\tilde{\nu}$ [cm$^{-1}$] = 3465 (w); 3334 (w); 3030 (w); 2963 (m); 2934 (w); 2876 (w); 2857 (w); 2817 (w); 1737 (s); 1667 (w); 1455 (m); 1373 (w); 1304 (w); 1278 (w); 1201 (m); 1169 (s); 1157 (s); 1076 (m); 1058 (m); 1010 (w); 970 (s); 909 (w); 891 (w); 849 (w); 828 (w); 793 (w); 770 (w); 750 (m); 699 (w); 656 (w); 628 (w).

**GC/MS** (EI, 70 eV): m/z (%) = 198 (1); 170 ([M]+-C2H5, 100); 140 ([M]+-CO2Me, 20); 110 (30); 97 ([C7H13]+, 18); 82 (10); 67 (10); 55 (40).

**HR/MS** (ESI): calculated for [M+H]$^+$: 220.1645; found: 220.1644; calculated for [M+Na]$^+$: 222.1465; found: 222.1466.

[α]$^\circ_{D}^{20}$(CHCl$_3$, c = 0.530 g/100 ml): [α]$^\circ_{D}^{20} = -164.0$ [α]$^\circ_{D}^{20} = -97.9^\circ; [\alpha]^\circ_{D}^{20} = -87.1^\circ; [\alpha]^\circ_{D}^{20} = -84.0^\circ.$

**(S)-Methyl 2-[(R,E)-hept-4-en-3-ylamino]propanoate ((R,S)-3c)**

According to **general procedure 1**, 431 mg (2.50 mmol) of carbonate rac-4a were reacted with L-alanine methyl ester ((S)-3c) using the chiral ligand ent-L6 to yield 456 mg (2.29 mmol, 86%, $d_r > 98/2$) of the allylic amine (R,S)-3c after purification by flash column chromatography (Silica, cHex/EtOAc = 3/1) as a yellow oil.

**C$_{11}$H$_{22}$NO$_2$**

M: 199.29 g/mol.

**TLC:** R$_f = 0.25$ (Silica, cHex/EtOAc = 3/1), KMnO$_4$-reagent.

**1H NMR** (500 MHz, CDCl$_3$): δ [ppm] = 0.84 (t, $^3J = 7.5$ Hz, 3H, H-7); 0.97 (t, $^3J = 7.5$ Hz, 3H, H-1); 1.26 (d, $^3J = 6.9$ Hz, 3H, H-11); 1.30 – 1.39 (m, 1H, H-6); 1.51 – 1.59 (m, 1H, H-6'); 1.61 (s, br, 1H, NH); 1.98 – 2.05 (m, 2H, H-2); 2.85 (td, $^3J = 8.6$ Hz, $^3J = 4.8$ Hz, 1H, H-5); 3.38 (q, $^3J = 6.9$ Hz, 1H, H-8); 3.69 (s, 3H, H-10); 5.11 (ddt, $^3J = 15.3$ Hz, $^3J = 6.3$ Hz, 1H, H-3).

**13C NMR** (125 MHz, CDCl$_3$): δ [ppm] = 10.6 (C-7); 13.8 (C-1); 19.3 (C-11); 25.4 (C-2); 28.5 (C-6); 51.9 (C-10); 54.2 (C-8); 61.4 (C-5); 131.3 (C-4); 134.7 (C-3); 176.8 (C-9).

**IR** (ATR): $\tilde{\nu}$ [cm$^{-1}$] = 3460 (w); 3325 (w); 3027 (w); 2964 (m); 2934 (w); 2875 (w); 2847 (w); 1736 (s); 1666 (w); 1453 (m); 1434 (m); 1372 (w); 1348 (w); 1332 (w); 1249 (w); 1198 (m); 1164 (s); 1136 (m); 1095 (w);
(S)-Methyl 2-((S,E)-hept-4-en-3-ylamino)-3-methylbutanoate ((S,S)-3d)

According to general procedure 1, 172 mg (1.00 mmol) of carbonate rac-4a were reacted with L-alanine methyl ester ((S)-5d) using the chiral ligand L6 to yield 190 mg (0.837 mmol, 84%, dr > 98/2) of the allylic amine (S,S)-3d after purification by flash column chromatography (Silica, cHex/EtOAc = 20/1) as a yellow oil.

C_{13}H_{23}NO_{2}

M: 227.34 g/mol.

TLC: Rf = 0.25 (Silica, cHex/EtOAc = 20/1), KMnO₄-reagent.

1H NMR (500 MHz, CDCl₃): δ [ppm] = 0.85 (t, 3J = 7.5 Hz, 3H, H-7); 0.91 (ψ dd, J = 6.8 Hz, 1H, H-11); 0.98 (t, 3J = 7.5 Hz, 3H, H-1); 1.35 – 1.49 (m, 2H, H-6); 1.62 (s, br, 1H, NH); 1.81 – 1.90 (m, 1H, H-11); 2.00 – 2.06 (m, 2H, H-2); 2.67 (td, 3J = 8.0 Hz, 3J = 5.7 Hz, 1H, H-5); 3.10 (d, 3J = 5.8 Hz, 1H, H-8); 3.71 (s, 3H, H-3); 5.07 (ddt, 3J = 15.3 Hz, 3J = 8.5 Hz, 4J = 1.5 Hz, 1H, H-4); 5.49 (dt, 3J = 15.3 Hz, 3J = 6.3 Hz, 1H, H-3).

13C NMR (125 MHz, CDCl₃): δ [ppm] = 10.6 (C-7); 14.0 (C-1); 18.9 (C-12); 19.3 (C-12); 25.5 (C-2); 29.4 (C-6); 31.9 (C-11); 51.4 (C-10); 61.8 (C-5); 64.2 (C-8); 131.6 (C-4); 134.9 (C-3); 176.4 (C-9).

IR (ATR): ν [cm⁻¹] = 3455 (w); 3336 (w); 3027 (w); 2962 (m); 2934 (w); 2876 (w); 2860 (w); 2809 (w); 1734 (s); 1697 (w); 1672 (w); 1463 (m); 1434 (w); 1385 (w); 1366 (w); 1350 (w); 1335 (w); 1298 (w); 1268 (w); 1235 (w); 1198 (m); 1180 (m); 1159 (s); 1114 (m); 1080 (w); 1066 (w); 1021 (w); 997 (m); 970 (m); 927 (w); 903 (w); 886 (w); 846 (w); 831 (w); 795 (w); 765 (w); 738 (w); 695 (w); 676 (w); 651 (w); 620 (w).

GC/MS (EI, 70 eV): m/z (%) = 227 (5); 198 ([M]+-C₂H₅, 100); 168 ([M]+-CO₂Me, 24); 138 (35); 112 ([C₃H₆N]+, 12); 97 ([C₇H₁₃]+, 30); 72 (40); 55 (70).

HR/MS (ESI) calculated for [M+H]⁺: 228.1957; found: 228.1958.

[α]_{D}^{20}(CHCl₃, c = 0.515 g/100 ml): [α]_{D}^{20} = -114.8°; [α]_{D}^{36} = -70.6°; [α]_{D}^{579} = -62.6°; [α]_{D}^{589} = -61.0°.
(S)-Methyl 2-((R,E)-hept-4-en-3-ylamino)-3-methylbutanoate ((R,S)-3d)

According to general procedure 1, 172 mg (1.00 mmol) of carbonate rac-4a were reacted with L-alanine methyl ester ((S)-5d) using the chiral ligand ent-L6 to yield 181 mg (0.796 mmol, 79%, dr > 98/2) of the allylic amine (R,S)-3d after purification by flash column chromatography (Silica, cHex/EtOAc = 20/1) as a yellow oil.

C_{13}H_{23}NO_2

M: 227.34 g/mol.

TLC: Rr = 0.25 (Silica, cHex/EtOAc = 20/1), KMnO_4-reagent.

^1H NMR (500 MHz, CDCl_3): δ [ppm] 0.85 (t, ^3J = 7.4 Hz, 3H, H-7); 0.92 (V t, ^3J = 7.2 Hz, 6H, H-12); 0.96 (t, ^3J = 7.5 Hz, 3H, H-1); 1.29 – 1.37 (m, 1H, H-6); 1.48 – 1.56 (m, 2H, H-6', NH); 1.81 – 1.90 (m, 1H, H-11); 1.96 – 2.02 (m, 2H, H-2); 2.73 (td, ^3J = 8.3 Hz, ^3J = 5.2 Hz, 1H, H-5); 2.97 (d, ^3J = 5.8 Hz, 1H, H-8); 3.67 (s, 3H, H-10); 5.14 (ddt, ^3J = 15.3 Hz, ^3J = 8.7 Hz, ^4J = 1.5 Hz, 1H, H-4); 5.50 (dt, ^3J = 15.3 Hz, ^3J = 6.2 Hz, 1H, H-3).

^13C NMR (125 MHz, CDCl_3): δ [ppm] 10.6 (C-7); 13.7 (C-1); 18.9 (C-12 o. C-13); 19.2 (C-12 o. C-13); 25.4 (C-2); 28.4 (C-6); 32.1 (C-11); 51.4 (C-10); 62.9 (C-5); 65.2 (C-8); 132.0 (C-4); 133.9 (C-3); 176.5 (C-9).

IR (ATR): ν [cm^{-1}] = 3458 (w); 3330 (w); 3202 (w); 2962 (m); 2875 (w); 1735 (s); 1697 (w); 1666 (w); 1463 (m); 1434 (m); 1384 (w); 1365 (w); 1332 (w); 1309 (w); 1269 (w); 1236 (w); 1196 (m); 1179 (m); 1156 (s); 1110 (m); 1082 (w); 1064 (w); 1022 (w); 998 (m); 968 (m); 899 (w); 883 (w); 844 (w); 790 (m); 768 (m); 730 (w); 680 (w); 663 (w); 623 (w).

GC/MS (EI, 70 eV): m/z (%) = 226 (1); 198 ([M]^+ -C_2H_6, 100); 168 ([M]^+ -CO_2Me, 24); 138 (35); 112 ([C_7H_13]^+, 12); 97 ([C_7H_13]^+, 49); 72 (53); 55 (80).

HR/MS (ESI): calculated for [M+H]^+: 228.1958; found: 228.1954;

calculated for [M+Na]^+: 250.1778; found: 250.1777.

[α]_D^{19} (CHCl_3, c = 0.505 g/100 ml): [α]_D^{25} = -54.9°; [α]_D^{20} = -31.7°; [α]_D^{23} = -27.9°; [α]_D^{26} = -27.5°.

(S)-Methyl 2-((S,E)-hept-4-en-3-ylamino)-3-phenylproanoate ((S,S)-3e)

According to general procedure 1, 172 mg (1.00 mmol) of carbonate rac-4a were reacted with L-phenylalanine methyl ester ((S)-3e) using the chiral ligand L6 to yield 239 mg (0.798 mmol, 87%, dr = 97/3) of the allylic amine (S,S)-3e after purification by flash column chromatography (Silica, cHex/EtOAc = 10/1) as a yellow oil.

C_{13}H_{23}NO_2

M: 275.39 g/mol.

TLC: Rr = 0.26 (Silica, cHex/EtOAc = 10/1), KMnO_4-reagent.
SUPPORTING INFORMATION

$^{1}$H NMR (500 MHz, CDCl$_3$): $\delta$ [ppm] = 0.82 (t, $^3J$ = 7.5 Hz, 3H, H-7); 0.96 (t, $^3J$ = 7.5 Hz, 3H, H-1); 1.31 – 1.39 (m, 1H, H-6); 1.40 – 1.48 (m, 1H, H-6'); 1.64 (s, br, 1H, NH); 1.97 – 2.03 (m, 2H, H-2); 2.74 (td, $^3J$ = 8.1 Hz, $^3J$ = 5.5 Hz, 1H, H-5); 2.86 – 2.95 (m, 2H, H-11); 3.60 – 3.63 (m, 4H, H-8/10); 4.99 (ddt, $^3J$ = 15.3 Hz, $^3J$ = 8.5 Hz, $^4J$ = 1.4 Hz, 1H, H-4); 5.44 (dt, $^3J$ = 15.3 Hz, $^3J$ = 6.3 Hz, 1H, H-3); 7.15 – 7.16 (m, 2H, H-13); 7.19 – 7.22 (m, 1H, H-15); 7.25 – 7.28 (m, 2H, H-14).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ [ppm] = 10.5 (C-7); 13.9 (C-1); 25.4 (C-2); 29.3 (C-6); 40.3 (C-11); 51.6 (C-10); 60.1 (C-8); 61.3 (C-5); 126.7 (C-15); 128.4 (C-14); 129.3 (C-13); 130.8 (C-4); 135.2 (C-3); 137.6 (C-12); 175.8 (C-9).

IR (ATR): $\tilde{v}$ [cm$^{-1}$] = 3458 (w); 3334 (w); 3111 (w); 3088 (w); 3065 (w); 3029 (w); 2962 (m); 2933 (w); 2875 (w); 2855 (w); 2812 (w); 1735 (s); 1669 (w); 1604 (w); 1568 (w); 1496 (w); 1455 (m); 1434 (m); 1380 (w); 1363 (w); 1350 (w); 1272 (w); 1195 (m); 1170 (s); 1131 (m); 1078 (w); 1031 (w); 1021 (w); 971 (m); 932 (w); 889 (w); 881 (w); 846 (w); 831 (w); 793 (w); 741 (m); 699 (s); 663 (w).

GC/MS (EI, 70 eV): m/z (%) = 793 (w); 741 (m); 699 (s); 663 (w).

HR/MS (ESI): calculated for [M+H]$^+$: 276.1958; found: 276.1959;
calculated for [M+Na]$^+$: 298.1778; found: 298.1779.

$[\alpha]_{D}^{20}$(CHCl$_3$, c = 0.535 g/100 ml): $[\alpha]_{D}^{20}$ = +31.1$^\circ$; $[\alpha]_{D}^{20}$ = +6.0$^\circ$; $[\alpha]_{D}^{20}$ = -2.6$^\circ$; $[\alpha]_{D}^{20}$ = -3.6$^\circ$; $[\alpha]_{D}^{20}$ = -3.8$^\circ$.

(S)-Methyl 2-[(R,E)-hept-4-en-3-ylamino]-3-phenylpropanoate ((R,S)-3e)

According to general procedure 1, 172 mg (1.00 mmol) of carbonate rac-4a were reacted with l-phenylalanine methyl ester ((S)-5e) using the chiral ligand ent-L6 to yield 241 mg (0.875 mmol, 88%, $dr > 99/1$) of the allylic amine (R,S)-3e after purification by flash column chromatography (Silica, cHex/EtOAc = 18/1) as a yellow oil.

TLC: $R_f$ = 0.22 (Silica, cHex/EtOAc = 10/1), KMnO$_4$-reagent.

$^{1}$H NMR (500 MHz, CDCl$_3$): $\delta$ [ppm] = 0.77 (t, $^3J$ = 7.4 Hz, 3H, H-7); 0.96 (t, $^3J$ = 7.5 Hz, 3H, H-1); 1.29 – 1.37 (m, 1H, H-6); 1.43 – 1.51 (m, 1H, H-6'); 1.62 (s, br, 1H, NH); 1.97 – 2.03 (m, 2H, H-2); 2.80 (td, $^3J$ = 8.3 Hz, $^3J$ = 5.4 Hz, 1H, H-5); 2.88 – 2.95 (m, 2H, H-11); 3.53 (t, $^3J$ = 6.9 Hz, 1H, H-8); 3.58 (s, 3H, H-10); 5.11 (ddt, $^3J$ = 15.3 Hz, $^3J$ = 8.7 Hz, $^4J$ = 1.5 Hz, 1H, H-4); 5.52 (dt, $^3J$ = 15.3 Hz, $^3J$ = 6.3 Hz, 1H, H-3); 7.16 – 7.18 (m, 2H, H-13); 7.20 – 7.23 (m, 1H, H-15); 7.26 – 7.29 (m, 2H, H-14).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ [ppm] = 10.5 (C-7); 13.7 (C-1); 25.4 (C-2); 28.5 (C-6); 39.8 (C-11); 51.7 (C-10); 61.2 (C-8); 62.3 (C-5); 126.8 (C-15); 128.5 (C-14); 129.3 (C-13); 131.4 (C-4); 134.7 (C-3); 137.6 (C-12); 176.7 (C-9).

IR (ATR): $\tilde{v}$ [cm$^{-1}$] = 3455 (w); 3325 (w); 3113 (w); 3090 (w); 3066 (w); 3027 (w); 2962 (m); 2933 (w); 2875 (w); 2855 (w); 1735 (s); 1668 (w); 1604 (w); 1585 (w); 1496 (w); 1455 (m); 1434 (m); 1376 (w); 1350 (w); 1340 (w);
1268 (w); 1198 (m); 1166 (s); 1122 (m); 1077 (w); 1030 (w); 1022 (w); 970 (m); 936 (w); 907 (w); 889 (w); 881 (w); 844 (w); 831 (w); 790 (w); 743 (m); 699 (s); 667 (w); 620 (w); 602 (w).

**GC/MS (EI, 70 eV):** m/z (%) = 274 (1); 246 ([M]+ -C₂H₅, 45); 216 ([M]+ -CO₂Me, 13); 184 ([M]+ -C₃H₇, 55); 120 (30); 97 ([C₆H₃]+, 75); 91 ([C₃H₇]+, 65); 88 (35); 81 (13); 77 (13); 67 (15); 65 (18); 55 (100).

**HR/MS (ESI):** calculated for [M+H]+: 276.1958; found: 276.1957; calculated for [M+Na]+: +298.1778; found: 298.1779.

\[ [\alpha]^{20}_D (\text{CHCl}_3, c = 0.530 \text{ g/100 ml}) : [\alpha]^{20}_{356} = +88.7^\circ; [\alpha]^{20}_{446} = +48.6^\circ; [\alpha]^{20}_{579} = +42.0^\circ; [\alpha]^{20}_{589} = +39.4^\circ. \]

**SUPPORTING INFORMATION**

**GC/MS (EI, 70 eV):** m/z (%) = 274 (1); 246 ([M]+ -C₂H₅, 45); 216 ([M]+ -CO₂Me, 13); 184 ([M]+ -C₃H₇, 55); 120 (30); 97 ([C₆H₃]+, 75); 91 ([C₃H₇]+, 65); 88 (35); 81 (13); 77 (13); 67 (15); 65 (18); 55 (100).

**HR/MS (ESI):** calculated for [M+H]+: 276.1958; found: 276.1957; calculated for [M+Na]+: +298.1778; found: 298.1779.

\[ [\alpha]^{20}_D (\text{CHCl}_3, c = 0.530 \text{ g/100 ml}) : [\alpha]^{20}_{356} = +88.7^\circ; [\alpha]^{20}_{446} = +48.6^\circ; [\alpha]^{20}_{579} = +42.0^\circ; [\alpha]^{20}_{589} = +39.4^\circ. \]
C₆H₁₂NO₂

M: 215.29 g/mol.

TLC: Rf = 0.13 (Silica, CH₂Cl₂/EtOAc = 1/1), KMnO₄-reagent.

1H NMR (500 MHz, CDCl₃): δ [ppm] = 0.88 (t, 3J = 7.5 Hz, 3H, H-7); 0.98 (t, 3J = 7.5 Hz, 3H, H-1); 1.39 – 1.55 (m, 2H, H-6); 2.01 – 2.07 (m, 2H, H-2); 2.54 (s, br, 2H, NH, OH); 2.89 (td, 3J = 8.2 Hz, 3J = 5.7 Hz, 1H, H-5); 3.47 – 3.56 (m, 2H, H-8/11); 3.37 – 3.76 (m, 4H, H-11/10); 5.08 (ddt, 3J = 15.3 Hz, 3J = 8.6 Hz, 3J = 1.5 Hz, 1H, H-4); 5.53 (dt, 3J = 15.3 Hz, 3J = 6.3 Hz, 1H, H-3).

13C NMR (125 MHz, CDCl₃): δ [ppm] = 10.8 (C-7); 13.9 (C-1); 25.5 (C-2); 29.3 (C-6); 52.2 (C-10); 59.9 (C-8); 61.8 (C-5); 63.3 (C-11); 130.9 (C-4); 135.8 (C-3); 174.3 (C-9).

IR (ATR): ν [cm⁻¹] = 3438 (w, br), 3288 (sh), 3260 (m), 3032 (w), 2962 (m), 2934 (m), 2876 (w), 2857 (w), 1737 (s), 1669 (w), 1459 (m), 1435 (m), 1403 (w), 1378 (w), 1363 (w), 1347 (w), 1334 (w), 1269 (m), 1262 (m), 1199 (s), 1175 (s), 1155 (s), 1134 (m), 1093 (m), 1063 (s), 1043 (m), 971 (s), 909 (w), 891 (w), 865 (w), 851 (m), 825 (m), 793 (m), 768 (m), 734 (m), 661 (w), 647 (m).

GC/MS (EI, 70 eV): m/z (%) = 214 (1); 186 ([M⁺-C₂H₅], 100); 156 ([M⁺-CO₂Me], 12); 126 (20); 112 ([C₆H₁₁N⁺], 8); 97 ([C₅H₁₃⁺], 30); 88 (20); 81 (15); 69 (14); 60 (20); 55 (60).

HR/MS (ESI): calculated for [M+H]⁺: 216.1594; found: 226.1591;

calculated for [M+Na]⁺: 238.1414; found: 238.1415.

Determination of diastereomeric excess: Hewlett Packard 6890 GC-System using a HP-5 column by Agilent (flow (H₂): 1.5 ml/min; 50 °C to 130 °C with 1 °C/min; inlet temp.: 275 °C.

(S)-Methyl 1-((S,E)-hept-4-en-3-ylamino)-3-hydroxypropanoate ((R,S)-3f)

According to general procedure 1, 172 mg (1.00 mmol) of carbonate rac-4a were reacted with L-serine methyl ester ((S)-5k) using the chiral ligand ent-L6 to yield 166 mg (0.771 mmol, 77%, dr = 97/3) of the allylic amine (R,S)-3f after purification by flash column chromatography (Silica, CH₂Cl₂/EtOAc = 1/1) as a yellow oil.

C₆H₁₂NO₂

TLC: Rf = 0.18 (Silica, CH₂Cl₂/EtOAc = 1/1), KMnO₄-reagent.

1H NMR (500 MHz, CDCl₃): δ [ppm] = 0.88 (t, 3J = 7.4 Hz, 3H, H-7); 0.97 (t, 3J = 7.5 Hz, 3H, H-1); 1.34 – 1.43 (m, 1H, H-6); 1.53 – 1.62 (m, 1H, H-6’); 1.98 – 2.04 (m, 2H, H-2); 2.44 (s, br, 2H, NH, OH); 2.81 (td, 3J = 8.3 Hz, 3J = 5.7 Hz, 1H, H-5); 3.41 (dd, 3J = 5.9 Hz, 3J = 4.5 Hz, 1H, H-8); 3.56 (dd, 3J = 10.6 Hz, 3J = 5.9 Hz, 1H, H-11); 3.70
SUPPORTING INFORMATION

\( ^{13}C\) NMR (125 MHz, CDCl\(_3\)): \( \delta \) [ppm] = 10.8 (C-7); 13.8 (C-1); 25.4 (C-2); 28.8 (C-6); 52.3 (C-10); 60.0 (C-8); 61.8 (C-5); 62.1 (C-11); 131.1 (C-4); 135.0 (C-3); 174.3 (C-2).

IR (ATR): \( \tilde{\nu} \) [cm\(^{-1}\)] = 3434 (w, br); 3326 (w); 3007 (w); 2961 (m); 2933 (w); 2876 (m); 2854 (w); 1740 (s); 1668 (w); 1569 (m); 1450 (m); 1425 (m); 1376 (w); 1350 (m); 1260 (m); 1284 (m); 1123 (m); 1062 (s); 1031 (m); 971 (s); 912 (w); 892 (w); 854 (w); 790 (m); 733 (m); 696 (m); 661 (m); 646 (m).

GC/MS (EI, 70 eV): m/z (%) = 186 ([M]+ -C\(_2\)H\(_5\), 100); 156 ([M]+ -CO\(_2\)Me, 12); 126 (25); 112 ([C\(_7\)H\(_{12}\)N]+, 10); 97 ([C\(_7\)H\(_{12}\)]+), 50); 88 (20); 81 (12); 67 (17); 60 (27); 55 (80).

HR/MS (ESI): calculated for [M+H]+: 216.1594; found: 226.1592;
calculated for [M+Na]+: 238.1414; found: 238.1415.

\[ [\alpha]_{D}^{20} \] (CHCl\(_3\), c = 0.510 g/100 ml): \([\alpha]_{D}^{2385} = -163.4^{\circ}\); \([\alpha]_{D}^{295} = -100.6^{\circ}\); \([\alpha]_{D}^{256} = -57.7^{\circ}\); \([\alpha]_{D}^{2385} = -50.5^{\circ}\); \([\alpha]_{D}^{256} = -48.6^{\circ}\).

Determination of diastereomeric excess: Hewlett Packard 6890 GC-System using a HP-5 column by Agilent (flow \( H_2 \)): 1.5 ml/min; 50 °C to 130 °C with 1 °C/min; inlet temp.: 275 °C.

(S)-tert-Butyl 2-((S,E)-hept-4-en-3-ylamino)-4-methylpentanoate ((S,S)-3g)

According to general procedure 1, 172 mg (1.00 mmol) of carbonate rac-4a were reacted with L-leucine tert butyl ester ((S,S)-5g) using the chiral ligand L6 to yield 225 mg (0.798 mmol, 80%, 92% \( dr > 97/3 \)) of the allylic amine (S,S)-3g after purification by flash column chromatography (Silica, cHex/EtOAc = 18/1) as a yellow oil.

C\(_{12}\)H\(_{23}\)NO\(_2\)

M: 283.45 g/mol.

TLC: R\(_v\) = 0.21 (Silica, cHex/EtOAc = 18/1), KMnO\(_4\)-reagent.

\(^1H\) NMR (500 MHz, CDCl\(_3\)): \( \delta \) [ppm] = 0.84 – 0.88 (m, 6H, H-7/H-11); 0.91 (d, \( ^3J = 6.6 \) Hz, 3H, H-11); 1.00 (t, \( ^3J = 7.5 \) Hz, 3H, H-1); 1.32 – 1.45 (m, 4H, H-6/12); 1.47 (s, 9H, H-11); 1.60 (s, br, 1H, NH); 1.68 – 1.76 (m, 1H, H-13); 2.02 – 2.08 (m, 2H, H-2); 2.73 – 2.77 (m, 1H, H-5); 3.22 (t, \( ^3J = 7.4 \) Hz, 1H, H-8); 5.09 (ddt, \( ^3J = 15.3 \) Hz, \( ^2J = 8.6 \) Hz, \( ^4J = 1.4 \) Hz, 1H, H-4); 5.52 (dt, \( ^3J = 15.3 \) Hz, \( ^2J = 6.4 \) Hz, 1H, H-3).

\(^{13}C\) NMR (125 MHz, CDCl\(_3\)): \( \delta \) [ppm] = 10.7 (C-7); 14.1 (C-1); 22.6 (C-14); 22.7 (C-14); 25.1 (C-15); 25.5 (C-2); 28.3 (C-11); 29.5 (C-6); 43.4 (C-12); 57.7 (C-8); 61.4 (C-5); 80.6 (C-10); 131.4 (C-4); 135.0 (C-3); 176.1 (C-9).

IR (ATR): \( \tilde{\nu} \) [cm\(^{-1}\)] = 3445 (w); 3326 (w); 3007 (w); 2961 (m); 2933 (w); 2873 (w); 2852 (w); 2819 (w); 1728 (s); 1672 (w); 1459 (w); 1436 (w); 1392 (w); 1382 (w); 1367 (m); 1337 (m); 1271 (w); 1256 (w); 1242 (w);
1210 (w); 1149 (s); 1086 (w); 1066 (w); 1037 (w); 1012 (w); 969 (m); 941 (w); 921 (w); 890 (w); 850 (w); 836 (w); 800 (w); 775 (w); 756 (w); 731 (w); 701 (w); 686 (w); 646 (w).

**GC/MS** (EI, 70 eV): m/z (%): 254 ([M]+ -C2H5, 5); 198 (35); 182 ([M]+ -CO2tBu, 100); 152 (10); 112 ([C2H4N]+, 10); 110 (10); 97 ([C2H5]+, 26); 86 (75); 81 (11); 67 (11); 55 (48).

**HR/MS** (ESI): calculated for [M+H]+: 284.2584; found: 242.2583; calculated for [M+Na]+: 306.2404; found: 306.2405.

\[
\begin{align*}
\alpha\beta\gamma\delta\varepsilon\zeta\eta\theta\iota\kappa\lambda\mu
\end{align*}
\]

**TLC:** Rf = 0.21 (Silica, cHex/EtOAc = 18/1), KMnO4-reagent.

**1H NMR** (500 MHz, CDCl3): δ [ppm] = 0.83 (t, 3J = 7.4 Hz, 3H, H-7); 0.90 (d, 2J = 6.6 Hz, 3H, H-14); 0.92 (d, 3J = 6.6 Hz, 3H, H-14); 0.98 (t, 3J = 7.5 Hz, 3H, H-1); 1.26 – 1.35 (m, 1H, H-6); 1.38 – 1.41 (m, 2H, H-12); 1.45 (s, 9H, H-11); 1.53 – 1.61 (m, 1H, H-6); 1.64 (s, br, 1H, NH); 1.71 – 1.79 (m, 1H, H-13); 1.98 – 2.04 (m, 2H, H-2); 2.82 (td, 3J = 8.4 Hz, 3J = 4.5 Hz, 1H, H-5); 3.16 (t, 3J = 7.2 Hz, 1H, H-8); 5.20 (ddt, 3J = 15.3 Hz, 3J = 8.4 Hz, 4J = 1.4 Hz, 1H, H-4); 5.53 (dt, 3J = 15.3 Hz, 3J = 6.3 Hz, 1H, H-3).

**13C NMR** (125 MHz, CDCl3): δ [ppm] = 19.0 (C-7); 13.9 (C-1); 22.8 (C-14); 22.9 (C-14); 25.1 (C-13); 25.6 (C-2); 27.8 (C-6); 28.3 (C-11); 43.5 (C-12); 58.1 (C-8); 61.6 (C-5); 80.6 (C-10); 132.0 (C-4); 134.1 (C-3); 175.9 (C-9).

**IR** (ATR): ν [cm⁻¹] = 3444 (w); 3318 (w); 3005 (w); 2960 (m); 2933 (m); 2873 (w); 2846 (w); 2820 (w); 1728 (s); 1669 (w); 1462 (w); 1435 (w); 1382 (w); 1367 (m); 1336 (w); 1308 (w); 1269 (w); 1257 (w); 1206 (w); 1149 (s); 1080 (w); 1067 (w); 1033 (w); 968 (m); 944 (w); 921 (w); 910 (w); 892 (w); 850 (w); 794 (w); 775 (w); 755 (w); 729 (w); 685 (w).

**GC/MS** (EI, 70 eV): m/z (%): 254 ([M]+ -C2H5, 5); 198 (40); 182 ([M]+ -CO2tBu, 100); 152 (12); 110 (10); 97 ([C2H5]+, 35); 86 (90); 81 (12); 67 (11); 55 (50).

**HR/MS** (ESI): calculated for [M+H]+: 284.2584; found: 242.2586; calculated for [M+Na]+: 306.2404; found: 306.2406.
SUPPORTING INFORMATION

$$[\alpha]_{20}^{(d)}(\text{CHCl}_3, c = 0.520 \text{ g/100 ml})$$: $$[\alpha]_{365}^{20} = -27.9^\circ; [\alpha]_{236}^{20} = -19.2^\circ; [\alpha]_{546}^{20} = -11.5^\circ; [\alpha]_{579}^{20} = -10.3^\circ; [\alpha]_{589}^{20} = -10.2^\circ.$$

(S)-Methyl 2-((S,E)-hept-4-en-3-ylamino)-4-methylpentanoate ((S,S)-3h)

According to **general procedure 1**, 172 mg (1.00 mmol) of carbonate rac-4a were reacted with L-leucine methyl ester ((S)-5h) using the chiral ligand L6 to yield 204 mg (0.845 mmol, 84%, $$dr > 98/2$$) of the allylic amine (S,S)-3h after purification by flash column chromatography (Silica, cHex/EtOAc = 15/1) as a yellow oil.

$${\text{C}}_{14}{\text{H}}_{27}{\text{NO}}_2$$

**M**: 241.37 g/mol.

**TLC**: $$R_f = 0.25$$ (Silica, cHex/EtOAc = 15/1), KMnO$_4$ reagent.

**$^1$H NMR** (500 MHz, CDCl$_3$): $$\delta$$ [ppm] = 0.84 – 0.87 (m, 6H, H-7/H-13 o. H14); 0.90 (d, $$^3$$J = 6.7 Hz, 3H, H-13 o. H-14); 0.99 (d, $$^3$$J = 7.5 Hz, 3H, H-1); 1.34 – 1.48 (m, 4H, H-6/11); 1.60 (s, br, 1H, NH); 1.69 – 1.77 (m, 1H, H-12); 2.01 – 2.07 (m, 2H, H-2); 2.70 (td, $$^3$$J = 8.1 Hz, $$^3$$J = 5.7 Hz, 1H, H-5); 3.37 (t, $$^3$$J = 7.3 Hz, 1H, H-8); 3.71 (s, 3H, H-10); 5.08 (ddt, $$^3$$J = 15.3 Hz, $$^3$$J = 8.6 Hz, $$^4$$J = 1.5 Hz, 1H, H-4); 5.51 (dt, $$^3$$J = 15.3 Hz, $$^3$$J = 6.3 Hz, 1H, H-3).

**$^{13}$C NMR** (125 MHz, CDCl$_3$): $$\delta$$ [ppm] = 10.6 (C-7); 14.0 (C-1); 22.2 (C-13); 22.9 (C-13); 25.0 (C-12); 25.5 (C-2); 29.4 (C-6); 43.3 (C-11); 51.6 (C-10); 61.6 (C-5); 131.3 (C-4); 135.1 (C-3); 177.3 (C-9).

**IR** (ATR): $$\tilde{\nu}$$ [cm$^{-1}$] = 3457 (w); 3332 (w); 3200 (w); 2960 (m); 2934 (w); 2873 (w); 2845 (w); 2814 (w); 1737 (s); 1700 (w); 1669 (w); 1462 (m); 1434 (w); 1384 (w); 1368 (w); 1345 (w); 1330 (w); 1309 (w); 1270 (w); 1233 (w); 1196 (m); 1166 (s); 1145 (m); 1120 (m); 1088 (w); 1066 (w); 1042 (w); 1015 (w); 988 (w); 970 (m); 912 (w); 890 (w); 879 (w); 858 (w); 826 (w); 793 (w); 757 (w); 739 (w); 685 (w); 668 (w); 628 (w).

**GC/MS** (EI, 70 eV): m/z (%) = 242 (5); 212 ([M]$^+$-C$_2$H$_5$, 100); 182 ([M]$^+$-CO$_2$Me, 24); 152 (27); 110 (12); 97 ([C$_7$H$_{13}$]$^+$, 22); 86 (45); 84 (17); 67 (18); 55 (74).

**HR/MS** (ESI): calculated for [M+H]$^+$: 242.2115; found: 242.2112.

**HR/MS** (ESI): calculated for [M+Na]$^+$: 264.1934; found: 264.1934.
(S)-Methyl 2-((R,E)-hept-4-en-3-ylamino)-4-methylpentanoate ((R,S)-3h)

According to general procedure 1, 172 mg (1.00 mmol) of carbonate rac-4a were reacted with L-leucine methyl ester ((S)-5h) using the chiral ligand ent-L6 to yield 206 mg (0.863 mmol, 85%, dr > 98/2) of the allylic amine (R,S)-3h after purification by flash column chromatography (Silica, cHex/EtOAc = 15/1) as a yellow oil.

C_{14}H_{27}NO_2

M: 241.37 g/mol.

TLC: Rf = 0.21 (Silica, cHex/EtOAc = 15/1), KMnO_4-reagent.

^1H NMR (500 MHz, CDCl_3): \(\delta\) [ppm] 0.84 (t, \(^3J = 7.4\) Hz, 3H, H-7); 0.89 (d, \(^3J = 6.6\) Hz, 3H, H-13); 0.91 (d, \(^3J = 6.6\) Hz, 3H, H-13); 0.97 (t, \(^3J = 7.5\) Hz, 3H, H-1); 1.29 – 1.39 (m, 1H, H-6); 1.40 – 1.46 (m, 2H, H-11); 1.47 – 1.57 (m, 2H, H-6', NH); 1.66 – 1.75 (m, 1H, H-12); 1.97 – 2.03 (m, 2H, H-2); 2.80 (td, \(^3J = 8.4\) Hz, \(^3J = 4.9\) Hz, 1H, H-5); 3.07 (t, \(^3J = 7.2\) Hz, 1H, H-8); 3.67 (s, 3H, H-10); 5.14 (ddt, \(^3J = 15.3\) Hz, \(^3J = 8.6\) Hz, \(^4J = 1.5\) Hz, 1H, H-4); 5.53 (dt, \(^3J = 15.3\) Hz, \(^3J = 6.3\) Hz, 1H, H-3).

^13C NMR (125 MHz, CDCl_3): \(\delta\) [ppm] = 10.5 (C-7); 13.7 (C-1); 22.6 (C-13 o. C-14); 22.8 (C-13 o. C-14); 25.0 (C-12); 25.4 (C-2); 28.3 (C-6); 43.3 (C-11); 51.6 (C-10); 57.9 (C-8); 62.9 (C-5); 131.8 (C-4); 134.3 (C-3); 177.3 (C-9).

IR (ATR): \(\tilde{\nu}\) [cm\(^{-1}\)] = 3463 (w); 3325 (w); 3025 (w); 2959 (m); 2933 (m); 2873 (w); 2847 (w); 1738 (s); 1700 (w); 1666 (w); 1463 (m); 1434 (m); 1382 (w); 1368 (w); 1332 (w); 1309 (w); 1267 (m); 1230 (w); 1194 (m); 1162 (s); 1139 (m); 1118 (m); 1079 (w); 1066 (w); 1040 (w); 1022 (w); 969 (m); 915 (w); 889 (w); 876 (w); 860 (w); 842 (w); 827 (w); 790 (w); 757 (w); 732 (w); 675 (w).

GC/MS (EI, 70 eV): m/z (%) = 240 (1); 212 ([M]^+ - C\textsubscript{2}H\textsubscript{5}, 100); 182 ([M]^+ - CO\textsubscript{2}Me, 24); 152 (22); 112 ([C\textsubscript{7}H\textsubscript{14}N]^+, 10); 97 ([C\textsubscript{7}H\textsubscript{13}]^+, 49); 86 (43); 81 (10); 69 (10); 55 (45).

HR/MS (ESI): calculated for [M+H]^+: 242.2115; found: 242.2113;

calculated for [M+Na]^+: 264.1934; found: 264.193.

\([\alpha]_D^{20}\) (CHCl\textsubscript{3}, c = 0.520 g/100 ml): \([\alpha]_D^{20} = -43.2^\circ\); \([\alpha]_D^{20} = -27.0^\circ\); \([\alpha]_D^{20} = -15.3^\circ\); \([\alpha]_D^{20} = -13.5^\circ\); \([\alpha]_D^{20} = -13.0^\circ\).
(S)-Di-tert-butyl 2-((S,E)-hept-4-en-3-ylamino)glutarate ((S,S)-3i)

According to general procedure 1, 172 mg (1.00 mmol) of carbonate rac-4a were reacted with L-glutamic acid di-tert-butyl ester ((S)-5i) using the chiral ligand L6 to yield 235 mg (0.83 mmol, 84%, dr = 98/2) of the allylic amine (S,S)-3i after purification by flash column chromatography (Silica, cHex/EtOAc = 10/1) as a yellow oil.

C_{20}H_{37}NO_{4}

M: 355.51 g/mol.

TLC: R_f = 0.14 (Silica, cHex/EtOAc = 10/1), KMnO_4-reagent.

^1H NMR (500 MHz, CDCl_3): δ [ppm] = 0.85 (t, 3J = 7.4 Hz, 3H, H-7); 0.99 (t, 3J = 7.5 Hz, 3H, H-1); 1.33 – 1.44 (m, 2H, H-6); 1.44 (s, 9H, H-11 o. H-16); 1.63 (s, br, 1H, NH); 1.70 – 1.78 (m, 1H, H-12); 1.81 – 1.88 (m, 1H, H-12'); 2.00 – 2.06 (m, 2H, H-2); 2.24 – 2.39 (m, 2H, H-13); 2.74 – 2.79 (m, 1H, H-5); 3.16 (dd, 3J = 8.3 Hz, 3J = 5.8 Hz, 1H, H-8); 5.07 (ddt, 3J = 15.3 Hz, 3J = 8.6 Hz, 3J = 1.4 Hz, 1H, H-4); 5.50 (dt, 3J = 15.3 Hz, 3J = 6.4 Hz, 1H, H-3).

^13C NMR (125 MHz, CDCl_3): δ [ppm] = 10.6 (C-7); 14.0 (C-1); 25.5 (C-2); 28.2 (C-11/16); 29.2 (C-14); 29.5 (C-6); 32.5 (C-15); 58.6 (C-8); 61.5 (C-5); 80.2 (C-10 o. C-15); 81.0 (C-10 o. C-15); 131.4 (C-3); 134.9 (C-3); 172.7 (C-16); 175.2 (C-9).

IR (ATR): ν [cm^{-1}] = 3445 (w); 3327 (w); 3006 (w); 2966 (w); 2933 (w); 2876 (w); 2858 (w); 2821 (w); 1726 (s); 1671 (w); 1481 (w); 1457 (w); 1421 (w); 1392 (w); 1367 (m); 1324 (w); 1296 (w); 1255 (m); 1220 (w); 1148 (s); 1066 (w); 1037 (w); 1022 (w); 969 (m); 930 (w); 889 (w); 848 (w); 809 (w); 754 (w); 737 (w); 683 (w).

GC/MS (EI, 70 eV): m/z (%) = 355 ([M]+, 1); 326 ([M]+ - C_2H_5, 7); 298 ([M]+ - C_4H_9, 2); 270 (7); 254 ([M]+ - COOtBu, 50); 214 (52); 198 (90); 186 (10); 168 (5); 146 (12); 130 (24); 124 (10); 112 (10); 102 (100); 97 ([C_7H_13]+, 50); 84 (25); 81 (15); 67 (10); 57 (35); 56 (50); 55 (80).

HR/MS (ESI): calculated for [M+H]^+: 356.2795; found: 356.2795; calculated for [M+Na]^+ 378.2615; found: 378.2617.

[α]_{D}^{28} (CHCl_3, c = 0.515 g/100 ml): [α]_{D}^{28} = -78.3°; [α]_{D}^{28} = -53.3°; [α]_{D}^{28} = -32.6°; [α]_{D}^{28} = -28.9°; [α]_{D}^{28} = -28.4°.
According to general procedure 1, 172 mg (1.00 mmol) of carbonate rac-4a were reacted with L-glutamic acid di-tert-butyl ester ((S)-5i) using the chiral ligand ent-L6 to yield 296 mg (0.833 mmol, 83%, $\text{dr} > 99/1$) of the allylic amine ($R,S$)-3i after purification by flash column chromatography (Silica, cHex/EtOAc = 10/1) as a yellow oil.

C$_{20}$H$_{37}$NO$_{4}$

TLC: $R_f = 0.21$ (Silica, cHex/EtOAc = 10/1), KMnO$_4$-reagent.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ [ppm] = 0.84 (t, $3^J = 7.4$ Hz, 3H, H-7); 0.97 (t, $3^J = 7.5$ Hz, 3H, H-1); 1.30 – 1.36 (m, 1H, H-6); 1.44 (s, 9H, H-11 o. H-16); 1.49 – 1.58 (m, 1H, H-6’); 1.61 (s, br, 1H, NH); 1.71 – 1.78 (m, 1H, H-12); 1.83 – 1.90 (m, 1H, H-12’); 1.97 – 2.03 (m, 2H, H-2); 2.28 – 2.38 (m, 2H, H-15); 2.78 (td, $3^J = 8.3$ Hz, $4^J = 4.9$ Hz, 1H, H-5); 3.14 (dd, $3^J = 7.7$ Hz, $4^J = 5.5$ Hz, 1H, H-8); 5.15 (ddt, $3^J = 15.3$ Hz, $4^J = 8.5$ Hz, $5^J = 1.4$ Hz, 1H, H-4); 5.52 (dt, $3^J = 15.3$ Hz, $5^J = 6.3$ Hz, 1H, H-3).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ [ppm] = 10.5 (C-7); 13.9 (C-1); 25.5 (C-2); 28.2 (C-6); 28.2 (C-11 o. C-16); 29.0 (C-12); 32.0 (C-13); 58.6 (C-8); 61.7 (C-5); 80.3 (C-10 o. C-15); 81.0 (C-10 o. C-15); 131.8 (C-4); 134.1 (C-3); 172.9 (C-16); 175.1 (C-9).

IR (ATR): $\tilde{\nu}$ [cm$^{-1}$] = 3445 (w); 3325 (w); 3006 (w); 2968 (w); 2933 (w); 2873 (w); 2850 (w); 1726 (s); 1663 (w); 1475 (w); 1457 (w); 1457 (w); 1392 (w); 1367 (m); 1324 (w); 1293 (w); 1253 (m); 1217 (w); 1147 (s); 1084 (w); 1071 (w); 1037 (w); 1024 (w); 969 (m); 936 (w); 920 (w); 904 (w); 849 (m); 800 (w); 768 (w); 680 (w).

GC/MS (EI, 70 eV): m/z (%) = 355 ([M]+, 2); 326 ([M]+ -C$_2$H$_5$, 10); 298 ([M]+ -C$_4$H$_9$, 2); 270 (7); 254 ([M]+ -CO$_2$Bu, 45); 214 (70); 198 (90); 186 (8); 168 (10); 146 (15); 130 (25); 124 (10); 112 (10); 102 (98); 97 ([C$_7$H$_{13}$]+, 47); 84 (27); 81 (30); 79 (20); 67 (20); 57 (45); 56 (70); 55 (100)

HR/MS (ESI): calculated for [M+H]+: 356.2795; found: 356.2795;
 calculated for [M+Na]+: 378.2615; found: 378.2616.

$[\alpha]^{29}_{D}$(CHCl$_3$, c = 0.510 g/100 ml): $[\alpha]^{29}_{436} = -17.4^\circ$; $[\alpha]^{29}_{346} = -10.3^\circ$; $[\alpha]^{29}_{389} = -8.2^\circ$; $[\alpha]^{29}_{589} = -7.2^\circ$. 

(S)-Di-tert-butyl 2-((R,E)-hept-4-en-3-ylamino)glutarate ((R,S)-3i)
(S)-Dimethyl 2-((S,E)-hept-4-en-3-ylamino)glutarate ((S,S)-3j)

According to general procedure 1, 172 mg (1.00 mmol) of carbonate rac-4a were reacted with L-glutamic acid dimethyl ester ((S)-5j) using the chiral ligand L6 to yield 239 mg (0.881 mmol, 87%, dr = 98/2) of the allylic amine ((S,S)-3j) after purification by flash column chromatography (Silica, cHex/EtOAc = 4/1) as a yellow oil.

\[
\text{C}_{14}\text{H}_{25}\text{NO}_4
\]

M: 271.35 g/mol.

TLC: \(R_f = 0.21\) (Silica, cHex/EtOAc = 4/1), KMnO\(_4\)-reagent.

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) [ppm] = 0.85 (t, \(J = 7.5\) Hz, 3H, H-7); 0.98 (t, \(J = 7.5\) Hz, 3H, H-11); 1.34 – 1.49 (m, 2H, H-6); 1.75 (s, br, 1H, NH); 1.77 – 1.84 (m, 1H, H-3j); 1.93 – 1.99 (m, 1H, H-11‘); 2.00 – 2.06 (m, 2H, H-2); 2.37 – 2.49 (m, 2H, H-12); 2.74 (td, \(J = 8.0\) Hz, 3J = 5.9 Hz, 1H, H-5); 3.32 (dd, \(J = 8.7\) Hz, \(J = 5.3\) Hz, 1H, H-8); 3.66 (s, 3H, H-14); 3.72 (s, 3H, H-10); 5.06 (ddt, \(J = 15.3\) Hz, \(J = 8.6\) Hz, \(J = 1.3\) Hz, 1H, H-4)); 5.49 (dt, \(J = 15.3\) Hz, \(J = 6.3\) Hz, 1H, H-3j).

\(^13\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) [ppm] = 10.5 (C-7); 14.0 (C-1); 25.4 (C-2); 28.9 (C-11); 29.4 (C-6); 30.9 (C-12); 51.7 (C-14); 51.9 (C-10); 57.7 (C-8); 61.5 (C-5); 131.2 (C-4); 135.3 (C-3); 173.8 (C-13); 176.1 (C-9).

IR (ATR): \(\tilde{\nu}\) [cm\(^{-1}\)] = 3457 (w); 3330 (w); 2962 (w); 2934 (w); 2876 (w); 2866 (w); 2815 (w); 1734 (s); 1671 (w); 1460 (w); 1436 (m); 1367 (w); 1349 (w); 1326 (w); 1296 (w); 1255 (m); 1197 (s); 1169 (s); 1140 (m); 1068 (w); 1039 (w); 1017 (w); 971 (m); 943 (w); 913 (w); 891 (w); 872 (w); 821 (w); 795 (w); 773 (w); 737 (w); 670 (w).

GC/MS (EI, 70 eV): \(m/z\) (%) = 271 ([M\(^+\), 1]; 242 ([M\(^+\) - C\(_3\)H\(_5\), 100]); 212 ([M\(^+\) - CO\(_2\)Me, 20]; 182 (10); 159 (6); 150 (8); 144 (12); 122 (6); 116 (25); 97 ([C\(_7\)H\(_13\)]\(^+\), 18); 84 (20); 81 (7); 67 (10); 55 (45).

HR/MS (ESI): calculated for [M+H]\(^+\): 272.1856; found: 272.1856; calculated for [M+Na]\(^+\): 294.1676; found: 294.1678.

\[\alpha\]\(^{29}\)_D (CHCl\(_3\), c = 0.505 g/100 ml): [\(\alpha\]\(^{29}\)_D\)\(_{25\circ}\) = -120.5°; [\(\alpha\]\(^{29}\)_D\)\(_{25\circ}\) = -83.6°; [\(\alpha\]\(^{29}\)_D\)\(_{25\circ}\) = -51.4°; [\(\alpha\]\(^{29}\)_D\)\(_{25\circ}\) = -44.4°; [\(\alpha\]\(^{29}\)_D\)\(_{25\circ}\) = -41.9°.

(S)-Dimethyl 2-((R,E)-hept-4-en-3-ylamino)glutarate ((R,S)-3j)

According to general procedure 1, 172 mg (1.00 mmol) of carbonate rac-4a were reacted with L-glutamic acid dimethyl ester ((S)-5j) using the chiral ligand ent-L6 to yield 232 mg (0.856 mmol, 85%, dr = 99/1) of the allylic amine ((R,S)-3j) after purification by flash column chromatography (Silica, cHex/EtOAc = 4/1) as a yellow oil.

\[
\text{C}_{14}\text{H}_{25}\text{NO}_4
\]

TLC: \(R_f = 0.21\) (Silica, cHex/EtOAc = 4/1), KMnO\(_4\)-reagent.
SUPPORTING INFORMATION

\(^{1}\text{H NMR}\) (500 MHz, CDCl\(_3\)): \(\delta\) [ppm] = 0.84 (t, \(^3J = 7.4\) Hz, 3H, H-7); 0.96 (t, \(^3J = 7.5\) Hz, 3H, H-1); 1.28 – 1.37 (m, 1H, H-6); 1.47 – 1.55 (m, 1H, H-6'); 1.64 (s, br, 1H, NH); 1.82 – 1.89 (m, 1H, H-11); 1.91 – 2.03 (m, 3H, H-2/11'); 2.37 – 2.48 (m, 2H, H-12); 2.77 (td, \(^3J = 8.3\) Hz, \(^3J = 5.2\) Hz, 1H, H-5); 3.27 (dd, \(^3J = 7.4\) Hz, \(^3J = 5.7\) Hz, 1H, H-8); 3.67 (s, 3H, H-14); 3.69 (s, 3H, H-10); 5.09 (ddt, \(^3J = 15.3\) Hz, \(^2J = 8.8\) Hz, \(^4J = 1.5\) Hz, 1H, H-4); 5.51 (dt, \(^3J = 15.3\) Hz, \(^3J = 6.3\) Hz, 1H, H-3).

\(^{13}\text{C NMR}\) (125 MHz, CDCl\(_3\)): \(\delta\) [ppm] = 10.6 (C-7); 13.8 (C-1); 25.4 (C-2); 28.5 (C-6/11); 30.4 (C-12); 51.7 (C-10 o. C-14); 51.9 (C-10 o. C-14); 58.2 (C-8); 62.0 (C-5); 131.5 (C-4); 134.5 (C-3); 173.9 (C-13); 176.1 (C-9).

IR (ATR): \(\tilde{\nu}\) [cm\(^{-1}\)] = 3434 (w, br); 3321 (w); 3026 (w); 2962 (m); 2934 (m); 2876 (m); 2853 (w); 1737 (s); 1668 (w); 1459 (m); 1435 (m); 1402 (w); 1376 (w); 1335 (m); 1265 (m); 1252 (m); 1198 (s); 1174 (s); 1123 (m); 1062 (s); 1031 (m); 971 (s); 912 (w); 892 (w); 854 (w); 790 (m); 765 (m); 696 (m); 661 (m); 646 (m).

GC/MS (EI, 70 eV): m/z (%) = 186 ([M]+ -C\(_2\)H\(_5\)), 100; 156 ([M]+ -CO\(_2\)Me, 12); 126 (25); 112 ([C\(_7\)H\(_{13}\)N]+, 10); 97 ([C\(_7\)H\(_{13}\)N]+, 50); 88 (20); 81 (12); 67 (17); 60 (27); 55 (80).

HR/MS (ESI): calculated for [M+H]+: 216.1594; found: 226.1592;

calculated for [M+Na]+: 238.1414; found: 238.1415.

\([\alpha]^{29}_{\text{d}}\) (CHCl\(_3\), c = 0.510 g/100 ml): \([\alpha]^{29}_{295} = -163.4^\circ\); \([\alpha]^{29}_{246} = -100.6^\circ\); \([\alpha]^{29}_{346} = -57.7^\circ\); \([\alpha]^{29}_{359} = -50.5^\circ\); \([\alpha]^{29}_{389} = -48.6^\circ\).

\((S)\)-Methyl 1-((S,E)-hept-4-en-3-yl)pyrrolidin-2-carboxylate ((S,S)-3k)

According to general procedure 1, 172 mg (1.00 mmol) of carbonate rac-4a were reacted with L-proline methyl ester ((S)-5k) using the chiral ligand L6 to yield 190 mg (0.843 mmol, 84%, \(dr = 99/1\)) of the allylic amine (S,S)-3k after purification by flash column chromatography (Silica, cHex/EtOAc = 3/1) as a yellow oil.

\(\text{C}_{13}\text{H}_{22}\text{NO}_{2}\)

\(M:\) 225.33 g/mol.

TLC: R\(_f\) = 0.24 (Silica, cHex/EtOAc = 3/1), K\(\text{MnO}_4\)-reagent.

\(^{1}\text{H NMR}\) (500 MHz, CDCl\(_3\)): \(\delta\) [ppm] = 0.82 (t, \(^3J = 7.4\) Hz, 3H, H-7); 0.99 (t, \(^3J = 7.5\) Hz, 3H, H-1); 1.33 – 1.42 (m, 1H, H-6); 1.62 – 1.70 (m, 1H, H-6'); 1.72 – 1.79 (m, 1H, H-9); 1.83 – 1.92 (m, 2H, H-9/10); 2.00 – 2.09 (m, 3H, H-10/2'); 2.61 – 2.66 (m, 1H, H-8); 2.90 (td, \(^3J = 9.4\) Hz, \(^3J = 4.4\) Hz, 1H, H-5); 3.01 – 3.05 (m, 1H, H-8'); 3.44 (dd, \(^3J = 9.1\) Hz, \(^3J = 4.6\) Hz, 1H, H-11); 3.69 (s, 3H, H-13); 5.27 (ddt, \(^3J = 15.3\) Hz, \(^3J = 9.3\) Hz, \(^4J = 1.5\) Hz, 1H, H-4); 5.52 (dt, \(^3J = 15.3\) Hz, \(^3J = 6.3\) Hz, 1H, H-3).

\(^{13}\text{C NMR}\) (125 MHz, CDCl\(_3\)): \(\delta\) [ppm] = 11.1 (C-7); 14.0 (C-1); 23.4 (C-9); 25.6 (C-2); 27.1 (C-6); 29.6 (C-10); 48.6 (C-8); 51.7 (C-13); 62.8 (C-5); 65.9 (C-11); 127.9 (C-4); 136.2 (C-3); 175.7 (C-12).
SUPPORTING INFORMATION

IR (ATR): $\tilde{\nu}$ [cm$^{-1}$] = 2962 (m); 2932 (m); 2874 (w); 2846 (w); 1735 (s); 1661 (w); 1459 (m); 1435 (m); 1374 (w); 1360 (w); 1343 (w); 1276 (w); 1193 (s); 1165 (s); 1106 (m); 1067 (w); 1054 (w); 1037 (w); 1019 (w); 999(w); 973 (m); 935 (w); 910 (w); 877 (w); 836 (w); 793 (w); 758 (w); 714 (w); 669 (w); 638 (w).

GC/MS (EI, 70 eV): m/z (%) = 225 ([M$^+$, 1]; 196 ([M$^+$ -C$_2$H$_5$, 100]; 166 ([M$^+$ -CO$_2$Me, 28]; 136 (10); 122 (5); 108 (8); 97 ([C$_3$H$_7$]$,^3$), 15); 81 (10); 70 (90); 55 (48).

HR/MS (ESI): calculated for [M+H]$^+$: 226.1802; found: 226.1798;
calculated for [M+Na]$^+$: 248.1621; found: 248.1621.

$[\alpha]_{20}^2$(CHCl$_3$, c = 0.520 g/100 ml): $[\alpha]_{436}^{20} = -130.5^\circ$; $[\alpha]_{546}^{20} = -79.7^\circ$; $[\alpha]_{579}^{20} = -70.6^\circ$; $[\alpha]_{589}^{20} = -68.1^\circ$.

(S)-Methyl 1-((R,E)-hept-4-en-3-yl)pyrrolidin-2-carboxylate ((R,S)-3k)

According to general procedure 1, 172 mg (1.00 mmol) of carbonate rac-4a were reacted with L-proline methyl ester ((S)-5k) using the chiral ligand ent-L6 to yield 197 mg (0.874 mmol, 88%, $dr = 98/2$) of the allylic amine (R,S)-3k after purification by flash column chromatography (Silica, cHex/EtOAc = 3/1) as a yellow oil.

C$_{13}$H$_{23}$NO$_2$

M: 225.33 g/mol.

TLC: R$_f$ = 0.18 (Silica, cHex/EtOAc = 3/1), KMnO$_4$-reagent.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ [ppm] 0.81 (t, $^3J = 7.4$ Hz, 3H, H-7); 0.98 (t, $^3J = 7.5$ Hz, 3H, H-1); 1.35 – 1.42 (m, 1H, H-6); 1.69 – 1.76 (m, 1H, H-6$^\gamma$); 1.77 – 1.97 (m, 3H, H-9/10); 1.97 – 2.05 (m, 2H, H-2); 2.06 – 2.14 (m, 1H, H-10$^\gamma$); 2.46 – 2.50 (m, 1H, H-8); 2.66 – 2.70 (m, 1H, H-5); 3.20 – 3.23 (m, 1H, H-8$^\gamma$); 3.32 – 3.38 (m, 1H, H-11); 3.68 (s, 3H, H-13); 5.22 (dd, $^3J$ = 15.3 Hz, 3J = 9.1 Hz, 1H, H-4); 5.59 (dt, $^3J$ = 15.3 Hz, $^3J$ = 6.2 Hz, 1H, H-3).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ [ppm] 11.0 (C-7); 13.6 (C-1); 23.7 (C-9); 25.4 (C-2); 26.6 (C-6); 30.4 (C-10); 51.8 (C-13); 52.3 (C-8); 63.9 (C-5); 69.5 (C-11); 129.8 (C-4); 135.8 (C-3); 176.1 (C-12).

IR (ATR): $\tilde{\nu}$ [cm$^{-1}$] = 2962 (m); 2934 (m); 2875 (w); 2846 (w); 1735 (s); 1661 (w); 1459 (m); 1435 (m); 1374 (w); 1360 (w); 1343 (w); 1276 (w); 1193 (s); 1165 (s); 1106 (m); 1067 (w); 1054 (w); 1037 (w); 1019 (w); 999(w); 973 (m); 935 (w); 910 (w); 877 (w); 836 (w); 793 (w); 758 (w); 714 (w); 669 (w); 638 (w).

GC/MS (EI, 70 eV): m/z (%) = 225 ([M$^+$, 1]; 196 ([M$^+$ -C$_2$H$_5$, 100]; 166 ([M$^+$ -CO$_2$Me, 20]; 136 (10); 122 (5); 108 (7); 97 ([C$_3$H$_7$]$,^3$), 15); 81 (10); 70 (45); 55 (30).

HR/MS (ESI): calculated for [M+H]$^+$: 226.1802; found: 226.1799;
calculated for [M+Na]$^+$: 248.1621; found: 248.1622.

$[\alpha]_{20}^2$(CHCl$_3$, c = 0.505 g/100 ml): $[\alpha]_{436}^{20} = -159.3^\circ$; $[\alpha]_{546}^{20} = -92.5^\circ$; $[\alpha]_{579}^{20} = -80.8^\circ$; $[\alpha]_{589}^{20} = -78.4^\circ$. 

25
General procedure 2: Peptide coupling using Ghosez reagent

Under inert conditions 1.1 eq. Ghosez reagent was added to a solution 1.0 eq. Zaminers acid (2) in CH₂Cl₂ (0.95 ml/mmol) at 0 °C over 1 h. Afterwards 1.1 eq. DIPEA and a solution of 1.1 eq. of amine 3 in CH₂Cl₂ (0.85 ml/mmol) was added simultaneously to the solution at 0 °C. The reaction solution was then stirred at r.t. over night. During this process the yellow solution turned to orange. After completion the solution was washed with citric acid solution (10 vol%, 22 ml/mmol Zaminers acid) and the aqueous phase was extracted three times using CH₂Cl₂. The combined organic phases were washed with sat. NaHCO₃ solution and sat. NaCl solution and dried over MgSO₄. After filtration the solvent was removed under reduced pressure and the resulting yellow raw product was purified by flash column chromatography.

General procedure 3: Ru-catalyzed ring closing metathesis

Under inert conditions a solution of 1.0 eq. of the dipeptide and 4 mol% of the Hoveyda-Grubbs II catalyst (9) in C₆F₆ (10 ml/mmol, 0.1 M) was warmed to 70 °C and stirred for 3.5 h before another 2 mol% of Hoveyda-Grubbs II catalyst (9) were added. (Note: the mixture turns dark upon heating). After complete conversion the solution was allowed to cool down before the solvent was removed under reduced pressure. The resulting dark green oil was purified by flash column chromatography. The resulting oily product was dissolved in little CH₂Cl₂ and stirred over Quadrasil AP for 15 min to remove residual ruthenium. After filtration the solvent was removed under reduced pressure and the product was dried in high vacuum to afford the desired bicyclic product.

Synthesis of (2S,3R)-tert-Butyl 2-((2-(tert-butoxy)-2-oxoethyl)-((R,E)-hept-4-en-3-yl) carbamoyl)-3-vinylpyrrolidine-1-carboxylate (6a)

The reaction was performed according to the general procedure 2 using 119 mg (0.495 mmol) of Zaminers acid (2) in combination with amine (R)-3a and stopped after 18.5 h. The crude product was purified by flash column chromatography (Silica, cHex/EtOAc = 4/1) to yield 152 mg (0.305 mmol, 62%) of the desired dipeptide 6a as a colourless viscose oil.
C_{25}H_{42}N_{2}O_{5}

M: 450.61 g/mol.

**TLC:** \( R_f = 0.19 \) (Silica, CHCl\(_3\)/EtOAc = 5/1), KMnO\(_4\)-reagent.

\(^{1}\)H NMR (500 MHz, CDCl\(_3\), rotameric mixture\(^1\)); \( \delta \) [ppm] = 0.88 – 1.01 (m, 6H, H-16/20); 1.36 – 1.54 (m, 18.6H, H-11/12/13/15\( \text{rot}_{3+4}/15\text{rot}_{3+4} \)/23/24/25); 1.61 – 1.79 (m, 2.4H, H-15\( \text{rot}_{1+2}/15\text{rot}_{1+2} \)/2); 1.99 – 2.10 (m, 2H, H-19); 2.12 – 2.19 (m, 0.35H, H-2\( \text{rot}_{1} \)); 2.20 – 2.27 (m, 0.35H, H-2\( \text{rot}_{2} \)); 2.45 – 2.53 (m, 0.15H, H-2\( \text{rot}_{3} \)); 2.58 – 2.66 (m, 0.15H, H-2\( \text{rot}_{2} \)); 2.93 – 2.96 (m, 0.7H, H-3\( \text{rot}_{1+2} \)); 3.01 – 3.07 (m, 0.3H, H-3\( \text{rot}_{3+4} \)); 3.39 – 3.50 (m, 1.35H, H-1/8\( \text{rot}_{1} \)); 3.53 – 3.65 (m, 0.85H, H-1\( \text{rot}_{1+2}/8\text{rot}_{2} \)); 3.69 – 3.75 (m, 0.8H, H-1\( \text{rot}_{2+4}/8\text{rot}_{3+4} \)); 3.98 (d, 2\( J = 16.7 \) Hz, 0.35H, H-8\( \text{rot}_{2} \)); 4.06 – 4.20 (m, 1.5H, H-4\( \text{rot}_{3+4}/8\text{rot}_{1+4}/14\text{rot}_{1+2} \)); 4.45 (s, 0.35H, H-4\( \text{rot}_{1} \)); 4.61 (s, 0.35H, H-4\( \text{rot}_{2} \)); 4.71 (d, 2\( J = 19.1 \) Hz, 0.15H, H-8\( \text{rot}_{4} \)); 4.95 – 5.05 (m, 0.9H, H-6\( \text{rot}_{3+4}/6\text{rot}_{3+4}/14\text{rot}_{3+4} \)); 5.07 – 5.19 (m, 1.4H, H-6\( \text{rot}_{1+2}/6\text{rot}_{1+2} \)); 5.27 – 5.37 (m, 0.3H, H-17\( \text{rot}_{3+4} \)); 5.38 – 5.44 (m, 0.7H, H-17\( \text{rot}_{1+2} \)); 5.60 – 5.76 (m, 1H, H-18); 5.77 – 5.85 (m, 0.3H, H-5\( \text{rot}_{3+4} \)); 5.87 – 5.95 (m, 0.7H, H-5\( \text{rot}_{1+2} \)).

\(^{13}\)C NMR (125 MHz, CDCl\(_3\), rotameric mixture\(^1\)); \( \delta \) [ppm] = 11.2, 11.3, 11.3 (C-16); 13.5, 13.5, 13.6, 13.7 (C-20); 24.6, 24.9 (C-15\( \text{rot}_{3+4} \)); 25.6, 25.7 (C-19); 26.1, 26.2 (C-15\( \text{rot}_{1+2} \)); 28.1, 28.2, 28.2 (C-11/12/13 o. C-23/24/25); 28.6, 28.7 (C-11/12/13 o. C-23/24/25); 28.5, 28.9, 28.9, 29.9 (C-2); 44.5, 44.6 (C-8\( \text{rot}_{1+2} \)); 45.4, 45.6, 45.8, 46.0 (C-1); 46.0, 46.5 (C-8\( \text{rot}_{3+4} \)); 46.1, 46.3, 47.1, 47.3 (C-3); 57.0, 57.1, 59.4, 59.4 (C-14); 61.3, 61.5, 62.0, 62.6 (C-4); 79.4, 79.6, 80.0, 80.1 (C-10 o. C-22); 81.1, 81.1, 81.8, 82.1 (C-10 o. C-22); 114.3, 114.6, 114.9, 115.0 (C-6); 126.1, 126.3, 126.4, 126.6 (C-17); 134.9, 135.8, 135.9, 136.5 (C-18); 139.1, 139.1, 139.5, 139.6 (C-5); 153.9, 154.5, 154.6, 154.7 (C-21); 168.4, 168.7, 169.0, 169.8 (C-9); 171.3, 171.5, 173.1, 174.0 (C-7).

IR (ATR): \( \bar{\nu} \) [cm\(^{-1} \)] = 3081 (w); 3005 (w); 2972 (w); 2933 (w); 2879 (w); 1746 (m); 1700 (m); 1657 (m); 1479 (w); 1452 (w); 1435 (w); 1392 (s); 1366 (s); 1308 (w); 1256 (m); 1221 (m); 1150 (s); 1117 (m); 1071 (w); 1056 (w); 992 (w); 973 (w); 945 (w); 912 (m); 866 (w); 845 (w); 820 (w); 795 (w); 771 (w); 754 (w); 737 (w); 694 (w); 661 (w).

HR/MS (ESI): calculated for [M+H]\(^+\): 451.3166; found: 451.31765; calculated for [M+Na]\(^+\): 473.2986; found: 473.2988.

\[ [\alpha]_{D}^{20}(\text{CHCl}_{3},c = 0.510 \text{ g/100 ml}): [\alpha]_{D}^{20}_{365} = +297.8^o; [\alpha]_{D}^{20}_{436} = +174.2^o; [\alpha]_{D}^{20}_{546} = +97.0^o; [\alpha]_{D}^{20}_{579} = +83.9^o; [\alpha]_{D}^{20}_{589} = +80.3^o. \]

---

\(^1\) The substance forms four rotamers: Two main rotamers (1 & 2) in 1:1 ratio and two side rotamers (3 & 4) in 1:1 ratio. The ratio between main and side rotamers is around 0.7:0.3.
Synthesis of \((2R,3S)\)-tert-Butyl 2-((2-(tert-butoxy)-2-oxoethyl)-(\((R,E)\)-hept-4-en-3-yl)carbamoyl)-3-vinyl pyrrolidine-1-carboxylate (\(\text{dia}-6a\))

To a solution of 96 mg (0.40 mmol, 1.1 eq.) \((\text{R,S})\)-Zaminer's acid (\text{ent}-2) and 167 mg (0.44 mmol, 1.1 eq.) HATU in 2.2 ml dry NMP, 0.15 ml (0.86 mmol, 1.95 eq.) DIPEA were added at r.t. under inert conditions and the solution was stirred for 20 min. 100 mg (0.44 mmol, 1.1 eq.) of Amine (\text{R})-3a were added and the reaction was heated to 85 °C for 43 h. After cooling the reaction mixture to r.t. 3.3 ml citric acid solution (10 vol%) were added and the solution was extracted four times using MTBE. The combined organic phases were washed twice with 1 m HCl and once with sat. NaHCO₃ solution and sat. NaCl solution each, dried over MgSO₄ and the solvent was removed under reduced pressure. The yellow high viscose crude product was purified by flash column chromatography (Silica, cHex/EtOAc = 5/1) yielding clean product \(\text{dia}-6a\) as a pale-yellow viscous oil in 48% yield. Furthermore 19 mg (0.042, 11%) of the product could be isolated which still contained traces of the amine (\text{R})-3a.

\[
\text{C}_{25}\text{H}_{42}\text{N}_{2}\text{O}_{5}\quad \text{M:} 450.61 \text{g/mol.}
\]

\[
\text{TLC: } R_{f} = 0.20 \quad \text{(Silica, cHex/EtOAc = 5/1), KMnO}_{4}\text{-reagent.}
\]

\[
\text{H NMR (500 MHz, CDCl}_{3}\text{, rotameric mixture)}: \delta [\text{ppm}] = 0.82 – 1.00 \text{ (m, 6H, } H-16/20); 1.39 – 1.80 \text{ (m, 21H, } H-2/11/12/13/15/23/24/25); 1.96 – 2.10 \text{ (m, 2H, } H-19); 2.15 – 2.24 \text{ (m, 0.35H, } H-2'\text{rot1}); 2.25 – 2.33 \text{ (m, 0.25H, } H-2'\text{rot2}); 2.47 – 2.54 \text{ (m, 0.15H, } H-2'\text{rot3}); 2.65 – 2.73 \text{ (m, 0.25H, } H-2'\text{rot3}); 2.89 – 2.95 \text{ (m, 0.6H, } H-3\text{rot1+2}); 3.01 – 3.08 \text{ (m, 0.4H, } H-3\text{rot3+4}); 3.38 – 3.52 \text{ (m, 1.6H, } H-1/8\text{rot1+3}); 3.57 – 3.71 \text{ (m, 1.4H, } H-1'/8\text{rot2+4}); 4.03 – 4.15 \text{ (m, 1.5H, } H-4\text{rot3+4/8'rot1+3+4/14rot1}); 4.24 – 4.27 \text{ (m, 0.25H, } H-14\text{rot3}); 4.45 \text{ (d, } ^3J = 1.6 \text{ Hz, 0.35H, } H-4\text{rot1}); 4.61 \text{ (d, } ^3J = 1.6 \text{ Hz, } 0.25H, H-4\text{rot2}); 4.68 \text{ (d, } ^3J = 19.0 \text{ Hz, 0.25H, } H-8'\text{rot2}); 4.77 \text{ (Ψ q, } J = 6.8 \text{ Hz, 0.15H, } H-14\text{rot4}); 4.96 – 5.19 \text{ (m, 2.25H, } H-6/14\text{rot2}); 5.32 – 5.42 \text{ (m, 1H, } H-17); 5.59 – 5.74 \text{ (m, 1H, } H-18); 5.76 – 5.95 \text{ (m, 1H, } H-5).
\]

\[
\text{C NMR (125 MHz, CDCl}_{3}\text{, rotameric mixture): } \delta [\text{ppm}] = 10.3, 11.2, 11.3, 11.4 \text{ (C-16); 13.5, 13.5, 13.6 (C-20); 23.9, 24.5, 25.3, 25.5 (C-15); 25.6, 25.7, 25.7, 25.7 (C-19); 28.2, 28.2 (C-11/12/13 o. C-23/24/25); 28.6, 28.6, 8.6, 28.7 (C-11/12/13 o. C-23/24/25); 29.4, 29.8, 30.3 (C-2); 44.7, 45.0, 45.4, 45.5, 45.7, 45.8, 45.9, 46.3 (C-1/8); 45.9.
\]

\(^2\) The substance forms four rotamers: Two main rotamers (1 & 2) in 0.6:0.4 ratio and two side rotamers (3 & 4) in 0.65:0.35 ratio. The ratio between main and side rotamers is around 0.6:0.4.
IR (ATR): \( \tilde{\nu} [\text{cm}^{-1}] = 3079 \) (w); 2972 (w); 2934 (w); 2879 (w); 1746 (m); 1700 (m); 1692 (m); 1655 (m); 1478 (w); 1442 (m); 1392 (s); 1366 (s); 1304 (w); 1256 (m); 1222 (m); 1150 (s); 1117 (m); 1071 (w); 1058 (w); 1043 (w); 1011 (w); 990 (w); 975 (w); 938 (w); 910 (m); 865 (w); 845 (w); 823 (w); 797 (w); 771 (w); 753 (w); 701 (w); 657 (w).

HR/MS (ESI): calculated for [M+H]\(^+\): 451.3166; found: 451.3169; calculated for [M+Na]\(^+\): 473.2986; found: 473.2983.

\([\alpha]_D^{20} (\text{XX}): (\text{CHCl}_3, c = 0.510 \text{ g/100 ml}) \): [\(\alpha\)]\(_{365}^\circ\) = -18.5°; [\(\alpha\)]\(_{546}^\circ\) = -12.9°; [\(\alpha\)]\(_{546}^\circ\) = -7.7°.

**Synthesis of (3aR,6R,8aS)-tert-Butyl 7-(2-(tert-Butoxy)-2-oxoethyl)-6-ethyl-8-oxo-3,3a,6,7,8,8a-hexahydro pyrrolo[2,3-c]azepin-1(2H)-carboxylate ((R,S,R)-7a)**

Under inert conditions a solution of 375 mg (0.832 mmol 1.0 eq.) of the dipeptide 6a and 20.9 mg (33 \(\mu\)mol, 4 mol%) of the Hoveyda-Grubbs II catalyst (9) in 8.3 ml \(\text{C}_6\text{F}_6\) (0.1 m) was warmed to 70 °C and stirred for 3.5 h before another 10.4 mg (16.5 \(\mu\)mol, 2 mol%) of Hoveyda-Grubbs II catalyst (9) were added. (Note: the mixture turns dark upon heating). After 6 h the solution was allowed to cool down before the solvent was removed under reduced pressure. The resulting dark green oil was purified by flash column chromatography (SiO\(_2\), cHex/EtOAc = 1/1). The resulting oily product was dissolved in little \(\text{CH}_2\text{Cl}_2\) and stirred over \textit{Quadrasil AP} for 15 min to remove residual ruthenium. After filtration the solvent was removed under reduced pressure and the product was dried in high vacuum to afford 266 mg (0.674, 81%) of the desired bicyclic product (R,S,R)-7a.

**C\(_{21}\)H\(_{34}\)N\(_2\)O\(_5\)**

**M**: 394.51 g/mol.

**TLC**: \(R_v = 0.20\) (Silica, cHex/EtOAc = 1/1), KMnO\(_4\)-reagent.

**Mp**: 108 – 112 °C.
**SUPPORTING INFORMATION**

**H NMR (600 MHz, CDCl₃, rotameric mixture[^3]):** δ [ppm] = 1.01 (t, ³J = 7.2 Hz, 1.5H, H-1₀(rot1)); 1.04 (t, ³J = 7.1 Hz, 1.5H, H-1₀(rot2)); 1.42 – 1.54 (m, 18H, H-14/15/16/19/20/21); 1.54 – 1.62 (m, 1H, H-9); 1.63 – 1.71 (m, 1H, H-2); 1.73 – 1.86 (m, 1H, H-9'); 2.05 (Ψ dt, ³J = 11.5 Hz, J = 5.7 Hz, 1H, H-9'); 2.89 – 3.00 (m, 1H, H-3); 3.44 (dtd, ²J = 16.5 Hz, ³J = 11.3 Hz, ⁴J = 5.6 Hz, 1H, H-5); 3.46 (d, ²J = 17.6 Hz, 0.5H, H-1₁(rot1)); 3.67 – 3.70 (m, 0.5H, H-1₁(rot2)); 3.72 (d, ²J = 17.6 Hz, 1.5H, H-1₀(rot1)); 3.79 (m, 1H, H-9); 4.25 (d, ²J = 17.4 Hz, 0.5H, H-1₁(rot2)); 4.57 – 4.62 (m, 0.5H, H-7(rot1)); 4.65 – 4.70 (m, 0.5H, H-7(rot2)); 4.81 (d, ²J = 11.8 Hz, 0.5H, H-4(rot1)); 4.85 (d, ³J = 11.8 Hz, 0.5H, H-4(rot2)); 4.91 (d, ³J = 11.8 Hz, 0.5H, H-4(rot2)); 5.56 – 5.58 (m, 1H, H-6); 5.84 (Ψ t, J = 9.5 Hz, 1H, H-5).

**13C NMR (150 MHz, CDCl₃, rotameric mixture[^3]):** δ [ppm] = 11.8, 11.9 (C-1₀); 26.1 (C-9); 28.1 (C-14/15/16 o. C-19/20/21); 28.3, 28.6 (C-14/15/16 o. C-19/20/21); 30.3, 30.8 (C-2); 43.2, 43.8 (C-3); 44.2, 44.5 (C-11); 46.7, 47.3 (C-1); 55.4, 55.6 (C-7); 60.3, 60.5 (C-4); 79.8, 79.9 (C-1₃ o. C-1₈); 81.4 (C-1₃ o. C-1₈); 130.8 (C-5(rot1); 130.9 (C-6); 131.3 (C-5(rot2)); 154.5, 155.0 (C-1₇); 169.1, 169.3 (C-1₂); 172.4, 172.8 (C-8).

**IR (ATR):** Ṽ [cm⁻¹] = 3022 (w); 2970 (w); 2931 (w); 2879 (w); 2855 (w); 1745 (s); 1691 (s); 1670 (s); 1573 (w); 1535 (w); 1477 (w); 1457 (w); 1429 (m); 1404 (m); 1390 (s); 1364 (m); 1335 (m); 1306 (w); 1277 (w); 1260 (m); 1247 (m); 1220 (m); 1153 (s); 1127 (s); 1116 (m); 1101 (m); 1050 (w); 1033 (w); 975 (w); 962 (w); 951 (w); 937 (w); 925 (w); 917 (w); 905 (w); 867 (w); 845 (m); 823 (w); 786 (m); 762 (w); 753 (m); 730 (w); 686 (w); 675 (w); 630 (w); 607 (w).

**GC/MS (EI, 70 eV):** m/z (%) = 394 ([M]+, 1); 338 (3); 321 ([M]+ -C₄H₉O, 13); 309 (4); 294 (20); 282 (30); 265 (37); 253 (18); 238 (40); 237 (40); 225 (13); 209 (38); 195 (16); 180 (48); 165 (13); 151 (8); 136 (46); 123 (30); 116 (36); 108 (20); 94 (14); 80 (18); 69 (21); 67 (21); 57 (100); 41 (80).

**HR/MS (ESI):** calculated for [M+H]+: 395.2540; found: 395.2545;

  calculated for [M+Na]+: 417.2360; found: 417.2361.

[^20]CHCl₃, c = 0.540 g/100 ml: [α]²⁰ [λ] = -546.2°; [α]²⁰ [λ] = -344.0°; [α]²⁰ [λ] = -200.4°; [α]²⁰ [λ] = -175.7°; [α]²⁰ [λ] = -169.3°.

[^3] The substance forms two rotamers in 1:1 ratio.
Synthesis of \((2R,3S)\text{-tert-Butyl} 2-((R,E)\text{-hept-4-en-3-yl}((S)\text{-1-methoxy-1-oxo-3-phenylpropane-2-yl})\text{-carbamoyl})\text{-3-vinylpyrrolidine-1-carboxylate})\ ((S,R,R,S)-6b)

\[
\text{ent-2} + (R,S)-3e \xrightarrow{\text{Ghosez-reagent DIPEA}} \text{(S,R,R,S)-6b}
\]

The reaction was performed according to the general procedure 2 using 80 mg (0.330 mmol) \((R,S)\text{-Zaminmer’s acid (ent-2)}\) and stopped after 17 h.

The crude product was purified by flash column chromatography (Silica, cHex/EtOAc = 4/1) to yield 104 mg (0.209 mmol, 63%) of the desired dipeptide \((R,S,R,S)-6b\) as a pale-yellow viscose oil.

**C\text{28}H\text{42}N\text{2}O\text{5}**

**M:** 489.65 g/mol.

**TLC:** \(R_f = 0.17\) (Silica, cHex/EtOAc = 4/1), KMnO\text{4}-reagent.

\(^1H\) NMR (600 MHz, CDCl\text{3}, rotameric mixture\(^5\)): \(\delta\) [ppm] = 0.86 – 0.92 (m, 4.2H, H-18/22\text{rot}/22\text{ro2}); 0.98 (t, \(^3J = 7.5\) Hz, 1.8H, H-22\text{rot}/22\text{ro1}); 1.44, 1.48 (2 × s, 9H, H-25/26/27); 1.62 – 1.92 (m, 3.8H, H-2/17/21\text{rot}/21\text{ro2}); 2.01 – 2.08 (m, 1.2H, H-21\text{rot}/21\text{ro1}); 2.13 – 2.19 (m, 0.6H, H-2’rot2); 2.27 – 2.23 (m, 0.4H, H-2’rot1); 2.81 (dd, \(^3J = 14.1\) Hz, 3J = 3.2 Hz, 0.6H, H-11-rot1); 2.85 – 2.90 (m, 1H, H-3); 3.14 (dd, \(^3J = 14.2\) Hz, 3J = 6.0 Hz, 0.4H, H-11-rot2); 3.45 – 3.52 (m, 1H, H-1); 3.60 – 3.73 (m, 4.4H, H-1’/10/11-rot2); 3.78 (ψ t, J = 6.4 Hz, 0.4H, H-8-rot2); 3.84 (dd, \(^3J = 8.4\) Hz, 3J = 3.2 Hz, 0.6H, H-8-rot1); 3.92 (dd, 2J = 14.1 Hz, \(^3J = 8.4\) Hz, 0.6H, H-11-rot1); 4.04 – 4.08 (m, 0.6H, H-16-rot1); 4.20 – 4.23 (m, 0.4H, H-16-rot2); 4.48 (s, 0.6H, H-4-rot1); 4.58 (dd, \(^3J = 2.2\) Hz, 0.4H, H-4-rot2); 4.86 (dd, \(^3J = 15.6\) Hz, 3J = 6.4 Hz, 0.4H, H-19-rot2); 5.02 – 5.23 (m, 2.6H, H-6/19-rot2); 5.57 (dt, \(^3J = 14.5\) Hz, 3J = 6.2 Hz, 0.4H, H-20-rot2); 5.71 (dt, \(^3J = 15.1\) Hz, \(^3J = 6.2\) Hz, 0.6H, H-20-rot1); 5.83 – 5.95 (m, 1H, H-5); 7.16 – 7.23 (m, 1H, H-15); 7.26 – 7.30 (m, 4H, H-13/14).

\(^13C\) NMR (150 MHz, CDCl\text{3}, rotameric mixture\(^5\)): \(\delta\) [ppm] = 11.2, 11.3 (C-18); 13.4, 13.5 (C-22); 25.2, 25.4, 25.6, 25.8 (C-17/21); 28.4, 28.5 (C-25/26/27); 29.2, 30.6 (C-2); 36.6, 38.2 (C-11); 45.5, 45.9 (C-1); 46.2, 47.1 (C-3); 52.2, 52.3 (C-10); 59.3, 59.4 (C-8); 60.5, 60.9 (C-16); 61.7, 62.5 (C-4); 79.6, 79.8 (C-24); 115.3, 115.3 (C-6); 126.3, 126.4, 126.5, 126.7 (C-15/19); 128.3, 128.5 (C-14); 129.6, 130.1 (C-13); 136.2, 136.6 (C-20); 138.9, 139.0 (C-5); 139.9, 140.2 (C-12); 154.1, 154.6 (C-23); 171.0, 171.5, 171.8, 172.1 (C-7/9).

---

\(^4\) The substance forms two rotamers in 0.6/0.4 ratio.
IR (ATR): $\tilde{v}$ [cm$^{-1}$] = 3084 (w); 3061 (w); 2969 (w); 2883 (w); 1742 (m); 1698 (s); 1652 (s); 1605 (w); 1587 (w); 1546 (w); 1497 (w); 1478 (w); 1453 (m); 1433 (m); 1392 (s); 1365 (s); 1297 (m); 1257 (m); 1237 (m); 1214 (m); 1167 (s); 1117 (s); 1081 (m); 1063 (m); 1029 (w); 1024 (w); 990 (m); 967 (m); 913 (m); 864 (w); 846 (w); 833 (w); 790 (w); 771 (m); 753 (m); 734 (w); 700 (s); 661 (w); 645 (w); 620 (w).

HR/MS (ESI): calculated for [M+Na]$^+$ 521.2086; found: 521.2988.

$[\alpha]_{\text{D}}^{20}$ (CHCl$_3$, c = 0.505 g/100 ml): $[\alpha]_{365}^{20}$ = -325.0°; $[\alpha]_{436}^{20}$ = -190.2°; $[\alpha]_{546}^{20}$ = -105.1°; $[\alpha]_{579}^{20}$ = -91.5°; $[\alpha]_{589}^{20}$ = -87.9°.

**Synthesis of (3aS,6R,8aR)-tert-Butyl 6-ethyl-7-((S)-1-methoxy-1-oxo-3-phenylpropane-2-yl)-8-oxo-3a,6,7,8,8a-hexahydropyrrolo[2,3-c]azepin-1(2H)-carboxylate ((S,R,R,S)-7b)**

Under inert conditions a solution of 125 mg (0.251 mmol 1.0 eq.) of the dipeptide (S,R,R,S)-6b and 6.3 mg (10.0 µmol, 4 mol%) of the Hoveyda-Grubbs II catalyst (9) in 2.5 ml C$_6$F$_6$ (0.1 m) was warmed to 70 °C and stirred for 3.5 h before another 3.1 mg (5.0 µmol, 2 mol%) of Hoveyda-Grubbs II catalyst (9) were added. (Note: The mixture turns dark upon heating). After 24 h the solution was allowed to cool down before the solvent was removed under reduced pressure. The resulting dark green oil was purified by flash column chromatography (SiO$_2$, cHex/EtOAc = 1/1). The resulting oily product was dissolved in little CH$_2$Cl$_2$ and stirred over QuadraSil AP for 15 min to remove residual ruthenium. After filtration the solvent was removed under reduced pressure and a second column chromatography (SiO$_2$, CH$_2$Cl$_2$/EtOAc = 4/1) was performed due to still present impurities (Note: The obtained substance was a brown solid). The product was dried in high vacuum to afford 34 mg (0.077, 31%) of the desired bicyclic product (S,R,R,S)-7b.

$\text{C}_{25}\text{H}_{34}\text{N}_2\text{O}_5$

$M$: 442.55 g/mol.

**TLC**: $R_f$ = 0.27 (Silica, cHex/EtOAc = 1/1), KMnO$_4$-reagent.

$\text{Mp}$: 173 - 177 °C.
**SUPPORTING INFORMATION**

**1H NMR** (500 MHz, CDCl₃, rotameric mixture): δ [ppm] = 0.92 (t, 3J = 7.5 Hz, 0.6H, H-10_rot2); 0.98 (t, 3J = 7.5 Hz, 2.4H, H-10_rot); 1.42 – 1.55 (m, 10H, H-2/21/22/23); 1.67 – 1.76 (m, 1H, H-9); 1.86 – 1.95 (m, 2H, H-2′/9′); 2.03 – 2.10 (m, 1H, H-3); 2.88 (dd, 3J = 14.6 Hz, 3J = 9.3 Hz, 0.8H, H-14_rot1); 2.97 (dd, 3J = 14.2 Hz, 3J = 9.4 Hz, 0.2H, H-14_rot2); 3.20 – 3.23 (m, 2H, H-1/14'); 3.59 – 3.69 (m, 4H, H-1/14_rot1); 3.62 – 3.86 (m, 1H, H-1/14_rot2); 4.28 (d, 3J = 10.8 Hz, 0.8H, H-4_rot1); 4.32 (d, 3J = 10.9 Hz, 0.2H, H-4_rot2); 5.48 – 5.51 (m, 0.2H, H-11_rot2); 5.67 – 5.75 (m, 2.8H, H-5/6/11_rot1); 7.14 – 7.18 (m, 1H, H-18); 7.20 – 7.24 (m, 4H, H-16/17).

**13C NMR** (150 MHz, CDCl₃, rotameric mixture): δ [ppm] = 12.0, 12.1 (C-10); 28.2, 28.5 (C-21/22/23); 30.8, 30.8, 31.2, 31.2 (C-2/9); 35.8, 36.3 (C-14); 41.1, 41.5 (C-3); 46.0, 46.9 (C-1); 51.9, 52.1 (C-13); 57.4, 57.8, 59.1, 59.3 (C-7/11); 63.2, 63.4 (C-2/9); 79.4, 79.6 (C-20); 126.5, 126.6 (C-18); 126.8, 125.9 (C-17); 128.6, 128.9 (C-6); 129.5, 129.7 (C-16); 129.8, 130.3 (C-5); 136.5, 137.0 (C-19); 171.6 (C-8/12).

**IR** (ATR): ν [cm⁻¹] = 3088 (w); 3058 (w); 3027 (w); 2997 (w); 2970 (w); 2954 (w); 2928 (w); 2895 (w); 2865 (w); 1735 (m); 1694 (s); 1678 (s); 1654 (m); 1607 (w); 1498 (w); 1480 (w); 1452 (m); 1407 (s); 1392 (s); 1380 (m); 1364 (m); 1345 (m); 1317 (w); 1298 (w); 1285 (w); 1268 (w); 1252 (m); 1243 (m); 1230 (m); 1216 (m); 1179 (s); 1159 (s); 1117 (s); 1098 (w); 1084 (m); 1064 (w); 1044 (w); 1027 (w); 968 (m); 953 (w); 938 (w); 868 (m); 856 (w); 820 (w); 793 (w); 744 (m); 696 (s); 619 (w).

**GC/MS** (EI, 70 eV): m/z (%) = 342 (22); 313 (10); 285 (30); 274 (9); 251 (6); 220 (100); 207 (7); 179 (17); 160 (10); 151 (5); 136 (40); 122 (30); 104 (25); 91 ([C7H7]+, 47); 77 (22); 69 (16); 51 (11); 41 (15).

**HR/MS** (ESI): calculated for [M+H]+: 443.2450; found: 443.2544; calculated for [M+Na]+: 465.2360; found: 465.2361.

[α]D²⁰ (CHCl₃, c = 0.500 g/100 ml): [α]D²⁰ = -226.9°; [α]D²⁰ = -110.3°; [α]D²⁰ = -52.0°; [α]D²⁰ = -43.9°; [α]D²⁰ = -42.5°.

**Synthesis of (2R,3S)-tert-Butyl 2-((S,E)-hept-4-en-3-yl)((S)-1-methoxy-1-oxo-3-phenylpropane-2-yl)carbamoyl)-3-vinylpyrrolidine-1-carboxylate (S,R,S)-6b**

![Chemical structure](image)

The reaction was performed according to the **general procedure 2** using 119 mg (0.495 mmol) (S,R)-Zaminier’s acid (ent-2) and stopped after 18.5 h.

---

5 The substance forms two rotamers in 0.8:0.2 ratio.
The crude product was purified by flash column chromatography (Silica, cHex/EtOAc = 4/1) to yield 152 mg (0.305 mmol, 62%) of the desired dipeptide (S,R,S,S)-6b as a colourless viscose oil.

\[
\text{C}_{28}\text{H}_{42}\text{N}_{2}\text{O}_{5}
\]

**M**: 489.65 g/mol.

**TLC**: \(R_t = 0.18\) (Silica, cHex/EtOAc = 4/1), KMnO\(_4\)-reagent.

\(^1\)H NMR (500 MHz, CDCl\(_3\), rotameric mixture\(^6\)): \(\delta\) [ppm] = 0.72 (d, \(3J = 7.3\) Hz, 1.5H, H-18\(_{\text{rot}}\)); 0.89 (d, \(3J = 7.3\) Hz, 1.5H, H-18\(_{\text{rot}}\)); 0.97 (\(\Psi\) dt, \(J = 1.1\) Hz, \(J = 7.4\) Hz, 3H, H-22); 1.03 – 1.17 (m, 1H, H-17); 1.38 – 1.56 (m, 10H, H-17/25/26/27); 1.70 – 1.76 (m, 1H, H-2); 1.97 – 2.24 (m, 3H, H-2/21); 2.87 – 2.95 (m, 1.5H, H-3/11\(_{\text{rot}}\); 3.26 (dd, \(3J = 14.2\) Hz, \(3J = 7.2\) Hz, 0.5H, H-11\(_{\text{rot}}\)); 3.42 – 3.50 (m, 1H, H-1); 3.57 – 3.68 (m, 4H, H-1\(_{\text{rot1}}\)/10/11\(_{\text{rot2}}\)); 3.69 – 3.74 (m, 0.5H, H-1\(_{\text{rot2}}\)); 3.80 – 3.83 (m, 0.5H, H-8\(_{\text{rot1}}\)); 3.86 – 3.92 (m, 1H, H-8\(_{\text{rot2}}\)/11\(_{\text{rot1}}\)); 3.99 – 4.07 (m, 1H, H-16); 4.41 (s, 0.5H, H-4\(_{\text{rot1}}\)); 4.49 (d, \(3J = 1.8\) Hz, 0.5H, H-4\(_{\text{rot2}}\)); 5.07 – 5.16 (m, 2H, H-6); 5.37 (dd, \(3J = 15.7\) Hz, \(3J = 6.4\) Hz, 0.5H, H-19\(_{\text{rot1}}\)); 5.50 (dd, \(3J = 15.7\) Hz, \(3J = 6.0\) Hz, 0.5H, H-19\(_{\text{rot2}}\)); 5.60 (dt, \(3J = 15.7\) Hz, \(3J = 6.3\) Hz, 0.5H, H-20\(_{\text{rot1}}\)); 5.69 (dt, \(3J = 15.7\) Hz, \(3J = 6.2\) Hz, 0.5H, H-20\(_{\text{rot2}}\)); 5.89 (\(\Psi\) tdd, \(J = 17.9\) Hz, \(J = 10.2\) Hz, \(J = 8.1\) Hz, 1H, H-5); 7.16 – 7.25 (m, 1H, H-15); 7.26 – 7.36 (m, 4H, H-13/14).

\(^{13}\)C NMR (125 MHz, CDCl\(_3\), rotameric mixture\(^6\)): \(\delta\) [ppm] = 11.6, 11.7 (C-18); 13.6, 13.6 (C-22); 25.6, 25.7 (C-21); 25.8, 26.5 (C-17); 28.5 (C-2\(_{\text{rot1}}\)); 28.7, 28.8 (C-25/26/27); 30.1 (C-2\(_{\text{rot2}}\)); 36.5, 38.0 (C-11); 45.6 (C-1\(_{\text{rot1}}\)); 45.7 (C-3\(_{\text{rot1}}\)); 45.8 (C-1\(_{\text{rot2}}\)); 46.5 (C-3\(_{\text{rot2}}\)); 52.2, 52.2 (C-10); 59.2, 59.5 (C-8); 60.4 (C-16); 62.4, 62.8 (C-4); 79.5, 80.0 (C-24); 115.0, 115.1 (C-6); 125.9, 126.0 (C-19); 126.4, 126.6 (C-15); 128.4, 128.5 (C-14); 129.6, 130.1 (C-13); 136.4, 136.7 (C-20); 139.0, 139.0 (C-5); 139.8, 140.1 (C-12); 154.3, 154.6 (C-23); 171.4, 171.4 (C-7\(_{\text{rot1}}\)/9\(_{\text{rot1}}\)); 171.6 (C-9\(_{\text{rot2}}\)); 172.0 (C-7\(_{\text{rot2}}\)).

**IR** (ATR): \(\bar{\nu} [\text{cm}^{-1}] = 3085 (w); 3063 (w); 3067 (w); 2997 (w); 2967 (w); 1742 (m); 1696 (s); 1653 (s); 1606 (w); 1583 (w); 1496 (w); 1478 (w); 1455 (m); 1431 (m); 1393 (s); 1365 (s); 1305 (m); 1257 (m); 1239 (m); 1215 (m); 1167 (s); 1150 (s); 1117 (m); 1082 (m); 1065 (m); 1030 (w); 977 (m); 914 (m); 864 (w); 846 (w); 829 (w); 790 (w); 770 (m); 752 (m); 701 (s); 661 (w); 643 (w); 623 (w).

**HR/MS** (ESI): calculated for [M+H]+ 499.3166; found: 499.3170, [M+Na]+ 521.2086; found: 521.2985.

\([\alpha]_{D}^{20}\) (CHCls, c = 0.500 g/100 ml): \([\alpha]_{D}^{20} = -427.4^\circ\); \([\alpha]_{D}^{20} = -249.8^\circ\); \([\alpha]_{D}^{20} = -138.3^\circ\); \([\alpha]_{D}^{20} = -120.1^\circ\); \([\alpha]_{D}^{20} = -155.5^\circ\).

---

\(^6\) The substance forms two rotamers in 1/1 ratio.
Synthesis of (3aS,6S,8aR)-tert-Butyl 6-ethyl-7-((S)-1-methoxy-1-oxo-3-phenylpropane-2-yl)-8-oxo-3,3a,6,7,8,8a-hexahydropyrrolo[2,3-c]azepin-1(2H)-carboxylate ((S,R,S,S)-7b)

Under inert conditions a solution of 142 mg (0.285 mmol, 1.0 eq.) of dipeptide (S,R,S,S)-6b and 7.1 mg (11.4 µmol, 4 mol%) of the Hoveyda-Grubbs II catalyst (9) in 2.9 ml C₆F₆ (0.1 M) was warmed to 70 °C and stirred for 3.5 h before another 3.6 mg (5.7 µmol, 2 mol%) of Hoveyda-Grubbs II catalyst (9) were added. (Note: the mixture turns dark upon heating). After 24 h the solution was allowed to cool down before the solvent was removed under reduced pressure. The resulting dark green oil was purified by flash column chromatography (Silica, cHex/EtOAc = 1/1). The resulting oily product was dissolved in little CH₂Cl₂ and stirred over QuadraSil AP for 15 min to remove residual ruthenium. After filtration the solvent was removed under reduced pressure and the product was dried in high vacuum to afford 90 mg (0.203 mmol, 71%) of the bicyclic product (S,R,S,S)-7b as a colorless viscous oil.

C₂₅H₃₄N₂O₅
M: 442.55 g/mol.

TLC: Rₛ = 0.18 (Silica, cHex/EtOAc = 1/1), KMnO₄-reagent.

Mp: 145 – 149 °C

¹H NMR (500 MHz, CDCl₃, rotameric mixture): δ [ppm] = 0.68 – 0.71 (m, 1.5H, H-1₀ rot1); 0.75 – 0.86 (m, 2H, H-1₀ rot2/9 rot1); 0.88 – 0.96 (m, 0.5H, H-9 rot2); 1.10 – 1.31 (m, 1H, H-9'); 1.50 (s, 9H, H-21/22/23); 2.03 (Ψ dt, J = 11.4 Hz, J = 5.6 Hz, 1H, H-2'); 2.82 – 2.88 (m, 1H, H-3); 3.23 (dd, ²J = 13.6 Hz, ³J = 7.0 Hz, 0.5H, H-1₄ rot1); 3.40 – 3.54 (m, 2H, H-1/14 rot2/14 rot1); 3.66 – 3.71 (m, 4H, H-1 rot1/14 rot1); 3.76 – 3.79 (m, 0.5H, H-1₀ rot2); 3.97 – 4.21 (m, br, 1H, H-11); 4.33 – 4.42 (m, 1H, H-7); 4.82 (d, ³J = 11.8 Hz, 1H, H-4); 5.45 (Ψ d, J = 10.6 Hz, 1H, H-6); 5.82 (Ψ d, J = 11.1 Hz, 1H, H-5); 7.20 – 7.33 (m, 5H, H-16/17/18).

¹³C NMR (125 MHz, CDCl₃, rotameric mixture): δ [ppm] = 11.7, 12.0 (C-10); 26.2, 26.3 (C-9); 28.7 (C-21/22/23); 30.0, 30.7 (C-2); 36.4, 37.4 (C-14); 42.5, 43.6 (C-3); 47.2, 47.5 (C-1); 52.4, 52.4 (C-13); 56.2, 56.4 (C-7); 59.2 (C-11); 60.3, 60.5 (C-4); 79.7, 80.2 (C-20); 126.5, 126.7 (C-18); 128.5 (C-16 o. C-17); 129.7, 130.0, 130.1, 130.4

The substance forms two rotamers in 1:1 ratio.
(C-6/C-16 o. C-17); 131.4, 131.7 (C-5); 139.4, 139.6 (C-15); 154.5, 155.0 (C-19); 171.5, 171.6 (C-12); 172.0, 172.2 (C-8).

**IR (ATR):** $\tilde{\nu}$ [cm$^{-1}$] = 3102 (w); 3087 (w); 3062 (w); 3026 (w); 2972 (w); 2952 (w); 2934 (w); 2882 (w); 1740 (m); 1695 (s); 1674 (s); 1655 (w); 1544 (w); 1496 (w); 1479 (w); 1392 (s); 1365 (s); 1341 (m); 1292 (m); 1257 (m); 1217 (m); 1159 (s); 1127 (s); 1104 (m); 1081 (m); 1064 (m); 976 (w); 923 (m); 865 (w); 851 (w); 829 (w); 765 (m); 751 (m); 729 (s); 704 (s); 674 (w); 661 (m); 645 (m).

**GC/MS (EI, 70 eV):** m/z (%) = 342 (17); 313 (13); 285 (22); 274 (11); 220 (100); 207 (11); 179 (28); 160 (11); 151 (13); 136 (59); 122 (38); 108 (30); 91 ([C$_7$H$_7$]+, 50); 77 (26); 69 (28); 51 (13); 41 (20).

**HR/MS (ESI):** calculated for [M+H]$^+$: 443.2450; found: 443.2543; for [M+Na]$^+$: 465.2360; found: 465.2360.

$\left[\alpha\right]_D^{20}$ (CHCl$_3$, c = 0.520 g/100 ml): $\left[\alpha\right]_{589}^{20}$ = +126.1°; $\left[\alpha\right]_{546}^{20}$ = +92.6°; $\left[\alpha\right]_{365}^{20}$ = -59.7°; $\left[\alpha\right]_{357}^{20}$ = -53.5°; $\left[\alpha\right]_{585}^{20}$ = -50.7°.

**Synthesis of (2R,3S)-tert-Butyl 2-((S,E)-hept-4-en-3-yl((R)-1-methoxy-1-oxo-3-phenylpropane-2-yl)carbamoyl)-3-vinylpyrrolidine-1-carboxylate ((S,R,S,R)-6b)**

\[
\begin{align*}
&\text{Boc} & \text{CO}_2\text{H} & \quad + & \text{ent-2} & \quad \text{(S,R)-3e} \\
&\text{N} & \text{H} & \text{CO}_2\text{Me} & \quad \text{Ph} & \quad \text{Ghozez-reagent} & \quad \text{DIPEA} \\
&\text{CH}_2\text{Cl}_2, 0^\circ\text{C} - \text{r.t.} & \quad 63\% & \quad \text{6b} \\
\end{align*}
\]

The reaction was performed according to the general procedure 2 using 80 mg (0.330 mmol) (S,R)-Zaminer’s acid (ent-2) and stopped after 17 h.

The crude product was purified by flash column chromatography (Silica, cHex/EtOAc = 4/1) to yield 104 mg (0.209 mmol, 63%) of the desired dipeptide (S,R,S,R)-6b as a pale-yellow viscose oil.

**C$_{29}$H$_{42}$N$_2$O$_5$**

M: 489.65 g/mol.

**TLC:** $R_f$ = 0.17 (Silica, cHex/EtOAc = 4/1), KMnO$_4$-reagent.

$^1$H NMR (500 MHz, CDCl$_3$, rotameric mixture): $\delta$ [ppm] = 0.90 – 0.96 (m, 6H, H-18/22); 1.45, 1.46 (2 x s, 9H, H-25/26/27); 1.61 – 1.72 (m, 1H, H-17); 1.75 – 1.80 (m, 1H, H-2); 1.82 – 2.10 (m, 3H, H-17/21); 2.16 – 2.28 (m, 1H, 18).  

The substance forms two rotamers in 0.6/0.4 ratio.
H-2); 2.74 – 2.78 (m, 1H, H-3); 2.99 (dd, $^2J_1$ = 13.9 Hz, $^3J_1$ = 6.1 Hz, 0.4H, H-11$_{rot2}$); 3.06 (dd, $^2J_2$ = 14.1 Hz, $^3J_2$ = 6.8 Hz, 0.6H, H-11$_{rot1}$); 3.44 – 3.53 (m, 1H, H-1); 3.59 – 3.75 (m, 5H, H-1'/10'/11'); 3.83 (Ψ t, J = 6.6 Hz, 0.4H, H-8$_{rot2}$); 3.86 – 3.94 (m, 1.2H, H-8$_{rot1}$/16$_{rot1}$); 3.99 – 4.03 (m, 0.4H, H-16$_{rot2}$); 4.43 (s, 0.6H, H-4$_{rot1}$); 4.53 (d, $^4J_2$ = 2.0 Hz, 0.4H, H-4$_{rot2}$); 4.73 – 4.82 (m, 1H, H-19); 5.06 – 5.14 (m, 2H, H-6); 5.49 – 5.55 (m, 1H, H-20); 5.85 – 5.93 (m, 1H, H-5); 7.16 – 7.22 (m, 3H, H-13/15); 7.24 – 7.30 (m, 2H, H-14).

$^{13}$C NMR (125 MHz, CDCl$_3$, rotameric mixture$^b$): $\delta$ [ppm] = 11.6, 11.7 (C-18); 13.5 (C-22); 25.8, 25.8, 25.8, 26.2 (C-17/21); 28.4, 28.6 (C-25/26/27); 28.7, 30.2 (C-2); 36.3, 36.7 (C-11); 45.3, 45.7 (C-1); 46.6, 47.3 (C-3); 52.1, 52.3 (C-10); 58.4, 58.5 (C-8); 61.0, 61.1 (C-16); 62.2, 62.8 (C-4); 79.3, 80.1 (C-24); 115.0, 115.2 (C-6); 125.8, 126.2 (C-19); 126.5, 126.6 (C-15); 128.3, 128.3 (C-14); 129.8, 129.9 (C-13); 136.7, 136.9 (C-20); 139.0, 139.1 (C-5); 139.3, 139.6 (C-12); 154.3, 154.4 (C-23); 171.3, 171.3, 171.8, 171.8 (C-7/9).

IR (ATR): $\tilde{\nu}$ [cm$^{-1}$] = 3087 (w); 3064 (w); 3028 (w); 2966 (w); 2932 (w); 2876 (w); 2851 (w); 2817 (m); 1741 (m); 1698 (s); 1654 (s); 1605 (w); 1587 (w); 1544 (w); 1496 (w); 1480 (w); 1453 (m); 1431 (m); 1392 (s); 1364 (s); 1331 (m); 1304 (m); 1254 (m); 1239 (m); 1217 (m); 1166 (s); 1116 (s); 1080 (w); 1064 (m); 1030 (w); 991 (m); 968 (m); 914 (m); 864 (w); 844 (w); 828 (w); 821 (w); 790 (w); 770 (m); 752 (m); 701 (s); 648 (w).

HR/MS (ESI): calculated for [M+H]$^+$ 499.3166; found: 499.3168, [M+Na]$^+$ 521.2086; found: 521.2988.

[$\alpha$]$^\circ_20$ (CHCl$_3$, c = 0.510 g/100 ml): $\delta$; [$\alpha$]$^\circ_20$ = +41.5$^\circ$; [$\alpha$]$^\circ_546$ = +25.8$^\circ$; [$\alpha$]$^\circ_579$ = +22.7$^\circ$; [$\alpha$]$^\circ_589$ = +21.2$^\circ$.

**Synthesis of (3aS,6S,8aR)-tert-Butyl 6-ethyl-7-(((R)-1-methoxy-1-oxo-3-phenylpropane-2-yl)-8-oxo-3,3a,6,7,8,8a-hexahydropyrrolo[2,3-c]azepin-1(2H)-carboxylate ((S,R,S,R)-7b)**

Under inert conditions a solution of 140 mg (0.281 mmol, 1.0 eq.) of dipeptide (S,R,S,R)-6b and 7.0 mg (11.2 µmol, 4 mol%) of the *Hoveyda-Grubbs II* catalyst (9) in 2.8 ml C$_6$F$_6$ (0.1 m) was warmed to 70 °C and stirred for 3.5 h before another 3.5 mg (5.7 µmol, 2 mol%) of *Hoveyda-Grubbs II* catalyst (9) were added. (Note: the mixture turns dark upon heating). After 24 h the solution was allowed to cool down before the solvent was removed under reduced pressure. The resulting dark green oil was purified by flash column chromatography (Silica, cHex/ EtOAc = 1/1). The resulting oily product was dissolved in little CH$_2$Cl$_2$ and stirred over *QuadraSil AP* for 15 min to remove residual ruthenium. After filtration the solvent was removed under reduced pressure and the product was dried in high vacuum to afford 77 mg (0.174 mmol, 62%) of the bicyclic product (S,R,S,R)-7b as a colorless viscous oil.
SUPPORTING INFORMATION

C₂₂H₃₄N₂O₅

M: 442.55 g/mol.

TLC: Rᵣ = 0.24 (Silica, cHex/EtOAc = 1/1), KMnO₄-reagent.

Mp: 161 - 165 °C.

¹H NMR (500 MHz, CDCl₃, rotameric mixture⁹): δ [ppm] = 0.92 – 1.02 (m, 3H, H-10); 1.36 – 1.48 (m, 10H, H-9/21/22/23); 1.54 – 1.62 (m, 1H, H-2); 1.75 – 1.81 (m, 1H, H-9'); 1.98 (Ψ dt, J = 11.3 Hz, J = 5.5 Hz, 1H, H-2'); 2.69 – 2.75 (m, 1H, H-3); 3.12 – 3.22 (m, 1H, H-14); 3.38 – 3.43 (Ψ td, J = 11.3 Hz, J = 5.4 Hz, 1H, H-14); 3.54 (dd, ²J = 14.1 Hz, ³J = 5.2 Hz, 1H, H-14'); 3.63 – 3.76 (m, 4H, H-1/13); 4.13 – 4.16 (m, 1H, H-11); 4.48 – 4.56 (m, br, 0.75H, H-7_rot1); 4.56 – 4.67 (m, br, 0.25H, H7_rot2); 4.78 (d, ³J = 11.9 Hz, 1H, H-4); 4.94 – 5.03 (m, 1H, H-6); 5.41 (Ψ d, J = 10.9 Hz, 1H, H-5); 7.14 – 7.18 (m, 3H, H-17/18); 7.21 – 7.24 (m, 2H, H-16).

¹³C NMR (125 MHz, CDCl₃, rotameric mixture¹⁰): δ [ppm] = 11.7 (C-10); 26.7, 26.9 (C-9); 28.3, 28.5 (C-21/22/23); 30.2, 30.7 (C-2); 35.1, 35.3 (C-14); 43.3, 44.0 (C-3); 46.9, 47.5 (C-1); 52.5 (C-13); 55.6, 56.0 (C-7); 58.0, 58.2 (C-11); 60.1, 60.4 (C-4); 79.9 (C-20); 126.5 (C-18); 128.4 (C-17); 129.6 (C-16); 130.3, 130.6, 131.0 (C-5/6); 139.1 (C-15); 154.5 (C-19); 171.5 (C-12); 172.0 (C-8).

IR (ATR): υ [cm⁻¹] = 3087 (w); 3060 (w); 3026 (w); 3005 (w); 2966 (w); 2932 (w); 2869 (w); 1752 (m); 1734 (m); 1693 (s); 1672 (s); 1645 (w); 1604 (w); 1585 (w); 1541 (w); 1496 (w); 1478 (w); 1453 (m); 1426 (m); 1404 (s); 1388 (s); 1365 (m); 1333 (w); 1296 (w); 1279 (w); 1252 (m); 1233 (m); 1218 (s); 1178 (m); 1162 (s); 1125 (m); 1116 (m); 1103 (m); 1081 (m); 1060 (m); 1041 (m); 1033 (m); 1000 (w); 987 (w); 977 (w); 966 (w); 939 (w); 919 (m); 863 (w); 852 (m); 824 (w); 782 (m); 764 (m); 745 (s); 727 (m); 696 (s); 676 (w); 652 (m); 623 (w); 610 (m).

GC/MS (EI, 70 eV): m/z (%) = 342 (15); 313 (14); 285 (21); 274 (8); 251 (4); 220 (100); 207 (10); 179 (23); 160 (11); 151 (12); 136 (55); 122 (35); 108 (26); 91 ([C₇H₇]+), 40); 77 (24); 69 (25); 51 (10); 41 (20).

HR/MS (ESI): calculated for [M+H]+: 443.2450; found: 443.2544; for [M+Na]+: 465.2360; found: 465.2360.

[α]⁺²⁰ (CHCl₃, c = 0.520 g/100 ml): [α]⁺²⁰ = +780.0°; [α]⁺²⁰ = +479.7°; [α]⁺²⁰ = -275.6°; [α]⁺²⁰ = -239.6°; [α]⁺²⁰ = -229.6°.

Synthesis of (2R,3S)-tert-Butyl 2-((R,E)-hept-4-en-3-yl)((R)-1-methoxy-1-oxo-3-phenylpropane-2-yl)carbamoyl)-3-vinylpyrrolidine-1-carboxylate ((S,R,R,R)-6b)

---

⁹ The substance forms two rotamers in 0.75:0.25 ratio.
The reaction was performed according to the general procedure 2 using 119 mg (0.495 mmol) (S,R)-Zaminier’s acid (ent-2) and stopped after 18.5 h.

The crude product was purified by flash column chromatography (Silica, cHex/EtOAc = 4/1) to yield 106 mg (0.213 mmol, 43%) of the desired dipeptide (S,R,R,R)-6b as a white solid. The product still contained minor amounts of impurities which could not be separated by repetitive column chromatographic purification.

\[ \text{C}_{29}\text{H}_{42}\text{N}_{2}\text{O}_{5} \]

M: 489.65 g/mol.

TLC: \( R_f = 0.19 \) (Silica, cHex/EtOAc = 4/1), KMnO\(_4\)-reagent.

Mp.: 101 – 103 °C.

\(^1\)H NMR (500 MHz, CDCl\(_3\), rotameric mixture\(^{10}\)): δ [ppm] = 0.70 – 0.73 (m, 3H, H-18); 0.83 – 1.03 (m, 4H, H-17/22); 1.19 – 1.34 (m, 1H, H-17’); 1.45, 1.45 (2 × s, 9H, H-25/26/27); 1.73 – 1.79 (m, 1H, H-2); 1.99 – 2.07 (m, 2H, H-21); 2.21 – 2.28 (m, 0.6H, H-2’\(\text{rot1}\)); 2.31 – 2.38 (m, 0.4H, H-2’\(\text{rot2}\)); 2.69 – 2.72 (m, 0.6H, H-3\(\text{rot1}\)); 2.78 – 2.86 (m, 0.4H, H-3\(\text{rot2}\)); 3.04 (dd, 3\(J = 14.0 \text{ Hz}, \ 3J = 6.7 \text{ Hz}, 0.4H, H-11\(\text{rot1}\)); 3.14 (dd, 3\(J = 14.1 \text{ Hz}, \ 3J = 7.2 \text{ Hz}, 0.6H, H-11\(\text{rot2}\)); 3.46 – 3.55 (m, 1H, H-1); 3.59 – 3.73 (m, 5H, H-1’/10/11’); 3.79 (Ψ t, J, \(J = 6.7 \text{ Hz}, 0.4H, H-8\(\text{rot2}\)); 3.83 (Ψ t, J, \(J = 6.9 \text{ Hz}, 0.6H, H-8\(\text{rot1}\)); 3.89 – 3.93 (m, 0.6H, H-16\(\text{rot1}\)); 4.23 – 4.27 (m, 0.4H, H-16\(\text{rot2}\)); 4.47 (s, 0.6H, H-4\(\text{rot1}\)); 4.54 (d, 4\(J = 2.4 \text{ Hz}, 0.4H, H-4\(\text{rot2}\)); 5.03 – 5.10 (m, 2H, H-6); 5.41 – 5.66 (m, 2H, H-19/20); 5.79 – 5.91 (m, 1H, H-5); 7.19 – 7.23 (m, 3H, H-13/15); 7.26 – 7.30 (m, 2H, H-14).

\(^13\)C NMR (125 MHz, CDCl\(_3\), rotameric mixture\(^{11}\)): δ [ppm] = 11.5, 11.6 (C-18); 13.3, 13.5 (C-22); 25.4, 25.6, 25.6 (C-17/21); 28.4, 28.6 (C-25/26/27); 29.1, 30.6 (C-2); 36.3, 36.6 (C-11); 45.2, 45.9 (C-1); 47.0, 47.8 (C-3); 51.9, 52.3 (C-10); 58.9, 59.0 (C-8); 60.4, 61.0 (C-16); 61.7, 62.9 (C-4); 79.3, 79.9 (C-24); 115.1, 115.3 (C-6); 126.1, 126.4 (C-19); 126.5, 126.7 (C-15); 128.4 (C-14); 129.8 (C-13); 135.3, 135.9 (C-20); 139.0, 139.0 (C-5); 139.5, 139.9 (C-12); 154.3, 154.3 (C-23); 171.0, 171.6, 171.8, 172.5 (C-7/9).

IR (ATR): \( \tilde{\nu} [\text{cm}^{-1}] = 3104 (w); 3084 (w); 3064 (w); 3031 (w); 2962 (w); 2952 (w); 2934 (w); 2874 (w); 2846 (w); 1746 (m); 1731 (m); 1684 (s); 1653 (s); 1606 (w); 1541 (w); 1497 (w); 1482 (w); 1456 (m); 1445 (m); 1405 (s); 1363 (m); 1351 (m); 1331 (w); 1301 (m); 1278 (m); 1232 (m); 1215 (m); 1208 (m); 1194 (m); 1185 (m); 1167 (s); 1150

\(^{10}\) The substance forms two rotamers in 0.6/0.4 ratio.
(m); 1125 (s); 1080 (w); 1062 (m); 1028 (m); 1013 (m); 997 (m); 988 (m); 969 (m); 914 (m); 865 (m); 829 (w); 816 (w); 797 (w); 767 (m); 756 (m); 705 (s); 644 (m).

HR/MS (ESI): calculated for [M+Na]⁺ 521.2986; found: 521.2988.

\[ \alpha_{D}^{20} \text{ (CHC}l_3, c = 0.500 \text{ g/100 ml): } [\alpha]_{D}^{20} = +172.3^\circ; \ [\alpha]_{D}^{20} = +106.7^\circ; \ [\alpha]_{D}^{20} = +61.8^\circ; \ [\alpha]_{D}^{20} = +53.8^\circ; \ [\alpha]_{D}^{20} = +51.2^\circ. \]

Synthesis of (3aS,6R,8aR)-tert-Butyl 6-ethyl-7-((R)-1-methoxy-1-oxo-3-phenylpropane-2-yl)-8-oxo-3,3a,6,7,8,8a-hexahydropyrrolo[2,3-c]azepin-1(2H)-carboxylate ((S,R,R,R)-7b)

Under inert conditions a solution of 120 mg (0.241 mmol, 1.0 eq.) of dipeptide (S,R,R,R)-6b and 6.0 mg (9.6 µmol, 4 mol%) of the Hoveyda-Grubbs II catalyst (9) in 2.4 ml C₆F₆ (0.1 M) was warmed to 70 °C and stirred for 3.5 h before another 3.0 mg (4.8 µmol, 2 mol%) of Hoveyda-Grubbs II catalyst (9) were added. (Note: the mixture turns dark upon heating). After 24 h the solution was allowed to cool down before the solvent was removed under reduced pressure. The resulting dark green oil was purified by flash column chromatography (Silica, cHex/ EtOAc = 1/1). The resulting oily product was dissolved in little CH₂Cl₂ and stirred over QuadraSil AP for 15 min to remove residual ruthenium. After filtration the solvent was removed under reduced pressure and the product was dried in high vacuum to afford 66 mg (0.149 mmol, 62%) of the bicyclic product (S,R,R,R)-7b as a colorless viscous oil.

C₂₅H₃₄N₂O₅

M: 442.55 g/mol.

TLC: Rf = 0.24 (Silica, cHex/EtOAc = 1/1), KMnO₄-reagent.

Mp: 132 – 135 °C.

¹H NMR (500 MHz, CDCl₃, rotameric mixture¹¹): δ [ppm] = 0.96 (t, ³J = 7.2 Hz, 0.6H, H-10rot₂); 1.01 (t, ³J = 7.5 Hz, 2.4H, H-10rot₁); 1.38, 1.47 (2 × s, 9H, H-21/22/23); 1.52 – 1.59 (m, 1H, H-2); 1.77 – 1.86 (m, 1H, H-9); 1.89 – 1.98 (m, 1H, H-9’); 2.03 (Ψ dt, ³J = 11.4 Hz, J = 5.6 Hz, 1H, H-2’); 2.69 – 2.75 (m, 1H, H-3); 3.08 – 3.18 (m, 1H, H-14); 3.29 – 3.43 (m, 3H, H-1/7/14’); 3.65 – 3.78 (m, 4H, H-1’/13); 4.24 (d, ³J = 10.6 Hz, 0.8H, H-4rot₁); 4.28 (d, ³J = 10.7

¹¹ The substance forms two rotamers in 0.8:0.2 ratio.
Hz, 0.2H, H-4_rot2): 4.57 (dd, \(^3J = 9.3\) Hz, \(^3J = 5.4\) Hz, 1H, H11); 5.32 – 5.40 (m, 1H, H-6); 5.67 – 5.73 (m, 1H, H-5); 7.17 – 7.27 (m, 5H, H-16/17/18).

\(^13C\) NMR (125 MHz, CDCl\(_3\), rotameric mixture\(^{12}\)): \(\delta [ppm] = 11.9, 11.9\) (C-10); 28.3, 28.6 (C-21/22/23); 30.3, 30.4 (C-9); 31.1, 31.6 (C-2); 35.5, 35.6 (C-14); 41.3, 42.0 (C-3); 46.5, 47.1 (C-1); 52.1, 52.3 (C-13); 62.8, 63.3, 63.5 (C-4_rot2/7_rot2/11_rot2); 63.8, 63.8, 64.3 (C-4_rot1/7_rot1/11_rot1); 79.5, 79.8 (C-20); 126.6, 126.7 (C-18); 128.6, 128.7 (C-17); 128.9, 128.9 (C-6); 129.1, 129.2 (C-5); 129.3, 129.5 (C-16); 137.8, 138.0 (C-15); 154.3, 154.5 (C-19); 170.9, 171.0 (C-12); 171.3, 171.4 (C-8).

IR (ATR): \(\tilde{\nu} [cm^{-1}] = 3088\) (w); 3047 (w); 3028 (w); 3012 (w); 2973 (w); 2934 (w); 2906 (w); 2878 (w); 2857 (w); 1738 (s); 1698 (s); 1660 (s); 1654 (s); 1605 (s); 1497 (w); 1484 (m); 1435 (m); 1394 (s); 1384 (s); 1367 (m); 1330 (m); 1290 (m); 1288 (m); 1273 (w); 1251 (m); 1239 (m); 1227 (m); 1218 (m); 1190 (m); 1163 (s); 1118 (s); 1094 (m); 1081 (m); 1042 (m); 1029 (w); 992 (w); 968 (w); 938 (w); 917 (w); 876 (w); 848 (w); 837 (w); 824 (w); 771 (w); 754 (m); 743 (m); 730 (m); 705 (m); 694 (m); 666 (w); 631 (w).

GC/MS (EI, 70 eV): \(m/z (\%) = 342 (17); 313 (10); 285 (25); 274 (11); 251 (6); 220 (100); 207 (7); 179 (17); 160 (10); 151 (6); 136 (40); 122 (24); 91 ([C7H7]+, 47); 77 (22); 69 (19); 51 (10); 41 (15).

HR/MS (ESI): calculated for \([M+H]^+\): 443.2450; found: 443.2543; for \([M+Na]^+\): 465.2360; found: 465.2361.

[\(\alpha\)]\(_D^{20}\) (CHCl\(_3\), \(c = 0.515\) g/100 ml): [\(\alpha\)]\(_D^{365}\) = +459.8°; [\(\alpha\)]\(_D^{436}\) = +284.7°; [\(\alpha\)]\(_D^{546}\) = -165.1°; [\(\alpha\)]\(_D^{1579}\) = -144.5°; [\(\alpha\)]\(_D^{359}\) = -137.9°.

**Synthesis of \((2S,3R)-\text{tert-Butyl} 2-((R,E)-hept-4-en-3-yl)((S)-1-methoxy-1-oxo-3-phenylpropane-2-yl)carbamoyl)-3-vinylpyrrolidine-1-carboxylate (6c) and \((2R,3S)-\text{tert-Butyl} 2-((R,E)-hept-4-en-3-yl)((S)-1-methoxy-1-oxo-3-phenylpropane-2-yl)carbamoyl)-3-vinylpyrrolidine-1-carboxylate (dia-6c)\)**

The reaction was performed according to the **general procedure 2** using 330 mg (1.37 mmol) racemic Zaminer’s acid (rac-2) and stopped after 17 h.

The crude product was purified by flash column chromatography (Silica, cHex/EtOAc = 3/2) to yield 208 mg (0.376 mmol, 36%) of desired dipeptide 6c as paly-yellow oil and 159 mg (0.376 mmol, 28%) of the diastereomer dia-6c as a pale yellow solid. Additional 82 mg (0.194 mmol, 14%) of a mixture of both products was isolated.
SUPPORTING INFORMATION

C_{23}H_{38}N_{2}O_{5}

M: 422.56 g/mol.

Analytical data for 6c:

**TLC:** Rf = 0.27 (Silica, cHex/EtOAc = 3/2), KMnO₄-reagent.

**¹H NMR** (500 MHz, CDCl₃, rotameric mixture[^12^]): δ [ppm] = 0.99 – 1.04 (m, 6H, H-14/18); 1.39 – 1.41 (m, 3H, H-11); 1.44, 1.45 (2 × s, 9H, H-21/22/23); 1.67 – 1.76 (m, 2H, H-2/13); 1.79 – 1.87 (m, 0.6H, H-13’rot1); 1.91 – 2.00 (m, 0.4H, H-13’rot2); 2.05 – 2.20 (m, 3H, H-2/17); 2.71 – 2.77 (m, 1H, H-3); 3.41 – 3.49 (m, 1H, H-1); 3.57 – 3.73 (m, 5H, H-1’/8/10); 4.02 (Ψ q, J = 7.2 Hz, 0.6H, H-12’rot1); 4.10 (Ψ q, J = 7.0 Hz, 0.4H, H-12’rot2); 4.43 (s, 0.6H, H-4’rot1); 4.52 (d, 4 J = 2.1 Hz, 0.4H, H-4’rot2); 5.09 – 5.17 (m, 2H, H-6); 5.37 – 5.43 (m, 1H, H-15); 5.71 – 5.78 (m, 1H, H-16); 5.86 – 5.95 (m, 1H, H-5).

**¹³C NMR** (125 MHz, CDCl₃, rotameric mixture[^13^]): δ [ppm] = 11.3, 11.4 (C-14); 13.5 (C-18); 15.7, 15.8 (C-11); 25.6, 25.8, 26.2 (C-13/17); 28.4, 28.5 (C-21/22/23); 28.7, 30.2 (C-2); 45.2, 45.7 (C-1); 46.7, 47.3 (C-3); 51.8, 51.9, 52.0, 52.2 (C-8/10); 60.4, 60.5 (C-12); 61.9, 62.6 (C-4); 79.2, 80.0 (C-20); 115.1, 115.2 (C-6); 126.0, 126.4 (C-15); 136.8, 137.0 (C-16); 138.9, 139.0 (C-5); 154.3, 154.4 (C-19); 170.0, 170.6 (C-7); 171.9, 172.5 (C-9).

**IR** (ATR): \( \nu [\text{cm}^{-1}] = 3078 (\text{w}); 2967 (\text{w}); 2934 (\text{w}); 2877 (\text{w}); 2847 (\text{w}); 1743 (s); 1698 (s); 1653 (s); 1545 (w); 1480 (w); 1453 (m); 1432 (m); 1365 (s); 1215 (s); 1168 (s); 1060 (m); 1047 (w); 1024 (w); 976 (m); 933 (w); 914 (m); 863 (m); 824 (w); 790 (w); 771 (m); 760 (w); 702 (w); 661 (w); 617 (w); 608 (w).

**HR/MS** (ESI): calculated for [M+Na]^+ 445.2673; found: 445.2676.

\[ [\alpha]_{D}^{20} (\text{CHCl}_{3}, \text{c} = 0.525 \text{ g/100 ml}): [\alpha]_{D}^{20} = +185.8^{b}; [\alpha]_{D}^{20} = +103.8^{b}; [\alpha]_{D}^{20} = +55.9^{b}; [\alpha]_{D}^{20} = +48.1^{b};\]

**TLC:** Rf = 0.19 (Silica, cHex/EtOAc = 3/2), KMnO₄-reagent.

**Mp.:** 88 – 91 °C.

**¹H NMR** (500 MHz, CDCl₃, rotameric mixture[^13^]): δ [ppm] = 0.92 – 0.97 (m, 3H, H-14); 1.01 (t, 3J = 7.5 Hz, 3H, H-18); 1.39 – 1.47 (m, 9.9H, H-11rot2/21/22/23); 1.53 (d, 3J = 6.8 Hz, 2.1H, H-11rot1); 1.67 – 1.77 (m, 2.3H, H-2/13/13’rot2); 1.80 – 1.88 (m, 0.7H, H-13’rot1); 2.05 – 2.19 (m, 2.7H, H-2’rot1/17); 2.23 – 2.30 (m, 0.3H, H-2’rot2); 2.84 – 2.91 (m, 1H, H-3); 3.42 – 3.49 (m, 1H, H-1); 3.53

[^12^] The substance forms two rotamers in 0.6/0.4 ratio.

[^13^] The substance forms two rotamers in 0.7/0.3 ratio.
- 3.77 (m, 5H, H-1’/8/10); 4.01 – 4.05 (m, 0.7H, H-12_{rot1}); 4.32 (\Psi \ q, J = 6.8 \ Hz, 0.3H, H-12_{rot2}); 4.40 (d, 4J = 1.2 \ Hz, 0.7H, H-4_{rot1}); 4.54 (d, 4J = 2.5 \ Hz, 0.3H, H-4_{rot2}); 5.03 – 5.19 (m, 2H, H-6); 5.37 (dd, 3J = 15.5 \ Hz, 3J = 7.5 \ Hz, 0.7H, H-15_{rot1}); 5.50 (dd, 3J = 15.7 \ Hz, 3J = 6.0 \ Hz, 0.3H, H-15_{rot2}); 5.73 (dt, 3J = 15.5 \ Hz, 3J = 6.3 \ Hz, 0.7H, H-16_{rot1}); 5.77 – 5.95 (m, 1.3H, H-5/16_{rot2}).

\[^{13}\text{C}\] NMR (125 MHz, CDCl\(_3\), rotameric mixture\(^{13}\)): \(\delta \ [ppm] = 11.1, 11.2 \ (C-14)\); 13.4, 13.6 \ (C-18)\); 15.9, 16.4 \ (C-11)\); 25.0, 25.4, 25.5, 25.7 \ (C-13/17)\); 28.5 \ (C-21/22/23)\); 29.3, 30.6 \ (C-2)\); 45.4, 45.9 \ (C-1)\); 46.4, 47.2 \ (C-3)\); 52.1, 52.2, 52.3, 52.5 \ (C-8/10)\); 59.7, 60.3 \ (C-12)\); 61.3, 62.4 \ (C-4)\); 79.4, 79.7 \ (C-20)\); 115.2, 115.3 \ (C-6)\); 126.3, 126.7 \ (C-15)\); 136.2, 136.3 \ (C-16)\); 138.9, 138.9 \ (C-5)\); 154.0, 154.5 \ (C-19)\); 170.2, 170.9 \ (C-7)\); 172.0, 172.4 \ (C-9)\).

IR (ATR): \(\tilde{\nu} \ [cm^{-1}] = 3091 \ (w)\); 2965 \ (w)\); 2950 \ (w)\); 2935 \ (w)\); 2920 \ (w)\); 2874 \ (w)\); 2847 \ (w)\); 1750 \ (s)\); 1698 \ (s)\); 1636 \ (s)\); 1549 \ (w)\); 1481 \ (w)\); 1459 \ (m)\); 1439 \ (m)\); 1392 \ (s)\); 1365 \ (s)\); 1337 \ (m)\); 1320 \ (m)\); 1209 \ (s)\); 1248 \ (m)\); 1206 \ (s)\); 1164 \ (s)\); 1109 \ (s)\); 1049 \ (m)\); 1070 \ (w)\); 1060 \ (m)\); 1048 \ (w)\); 1028 \ (w)\); 993 \ (s)\); 974 \ (m)\); 951 \ (w)\); 921 \ (m)\); 888 \ (w)\); 865 \ (m)\); 838 \ (w)\); 817 \ (w)\); 786 \ (w)\); 773 \ (m)\); 761 \ (m)\); 730 \ (w)\); 658 \ (w)\).

HR/MS (ESI): calculated for [M+Na]\(^{+}\) 445.2673; found: 445.2676.

\([\alpha]_{\text{d}}^{20} (\text{CHCl}_3, \ c = 0.525 \text{ g/100 ml}): [\alpha]_{365}^{20} = -104.0^\circ; [\alpha]_{436}^{20} = -59.2^\circ; [\alpha]_{546}^{20} = -32.1^\circ; [\alpha]_{579}^{20} = -27.7^\circ; [\alpha]_{590}^{20} = -26.7^\circ.\)

**Synthesis of (3aR,6R,8aS)-**tert-**Butyl 6-ethyl-7-((S)-1-methoxy-1-oxo-3-phenylpropane-2-yl)-8-oxo-3,3a,6,7,8,8a-hexahydropyrrolo[2,3-c]azepin-1(2H)-carboxylate (7c)**

Under inert conditions a solution of 120 mg (0.285 mmol, 1.0 eq.) of dipeptide 6c and 7.1 mg (11.4 µmol, 4 mol%) of the Hoveyda-Grubbs II catalyst (9) in 2.9 ml \(\text{C}_6\text{F}_6\) (0.1 m) was warmed to 70 °C and stirred for 3.5 h before another 3.6 mg (5.7 µmol, 2 mol%) of Hoveyda-Grubbs II catalyst (9) were added. (Note: the mixture turns dark upon heating). After 6 h the solution was allowed to cool down before the solvent was removed under reduced pressure. The resulting dark green oil was purified by flash column chromatography (Silica, cHex/ EtOAc = 1/1). The resulting oily product was dissolved in little CH\(_2\)Cl\(_2\) and stirred over QuadraSil AP for 15 min to remove residual ruthenium. After filtration the solvent was removed under reduced pressure and the product was dried in high vacuum to afford 64 mg (0.175 mmol, 61%) of the bicyclic product 7c as a colorless viscous oil.
C₁₉H₃₀N₂O₅

M: 366.45 g/mol.

TLC: Rᵣ = 0.29 (Silica, cHex/EtOAc = 1/1), KMnO₄-reagent.

Mp: 149 - 153 °C

¹H NMR (500 MHz, CDCl₃, rotameric mixture¹⁴): δ [ppm] = 1.04 – 1.12 (m, 3H, H-10); 1.36 (d, ³J = 6.7 Hz, 3H, H-14); 1.43 – 1.47 (m, 9H, H-17/18/19); 1.61 – 1.72 (m, 2H, H-2/9); 1.83 (Ψ dq, J = 14.8 Hz, J = 7.4 Hz, 1H, H-9'); 2.05 (Ψ dt, J = 11.3 Hz, J = 5.5 Hz, 1H, H-2'); 2.71 – 2.78 (m, 1H, H-3); 3.39 (Ψ td, J = 11.2 Hz, J = 5.6 Hz, 1H, H-1'); 3.63 – 3.74 (m, 1H, H-3); 3.92 (q, J = 6.7 Hz, 0.8H, H₁-11₁); 3.95 – 4.01 (m, 0.2H, H₁-11₂); 4.88 (d, ³J = 11.8 Hz, 1H, H-4'); 5.60 (Ψ dt, J = 11.1 Hz, J = 2.8 Hz, 1H, H-6'); 5.79 (Ψ dt, J = 11.1 Hz, J = 2.1 Hz, 1H, H-5').

¹³C NMR (125 MHz, CDCl₃, rotameric mixture¹⁵): δ [ppm] = 11.5, 11.6 (C-10); 14.3, 14.6 (C-14); 26.8 (C-9); 28.2, 28.5 (C-17/18/19); 30.2, 30.7 (C-2); 43.4, 44.0 (C-3); 46.6, 47.4 (C-1); 51.0 (C-11); 52.2 (C-13); 55.3, 55.5 (C-7); 60.1, 60.2 (C-4); 79.7, 79.9 (C-16); 131.1, 131.3 (C-5); 131.8, 131.9 (C-6); 154.3, 154.7 (C-15); 171.5, 171.9 (C-12); 172.0, 172.3 (C-8).

IR (ATR): "[cm⁻¹] = 3026 (w); 2980 (w); 2965 (w); 2949 (w); 2941 (w); 2884 (w); 2870 (w); 2842 (w); 1736 (s); 1699 (s); 1666 (s); 1653 (w); 1565 (w); 1535 (w); 1479 (w); 1461 (w); 1433 (m); 1404 (s); 1389 (s); 1373 (m); 1273 (m); 1263 (m); 1220 (s); 1159 (s); 1130 (s); 1120 (s); 1104 (m); 1085 (m); 1070 (m); 1056 (m); 1036 (w); 996 (w); 969 (m); 945 (w); 926 (w); 863 (m); 834 (m); 822 (w); 783 (m); 758 (m); 752 (m); 728 (m); 673 (w); 640 (m); 610 (m).

GC/MS (EI, 70 eV): m/z (%) = 366 ([M]+, 2); 337 ([M⁺⁻C₂H₅, 4); 310 (24); 293 ([M⁺⁻C₄H₆O, 28); 281 (32); 266 (38); 253 (29); 237 (30); 223 (15); 209 (23); 193 (7); 180 (44); 179 (40); 167 (16); 151 (11); 144 (95); 136 (42); 122 (41); 108 (29); 94 (20); 80 (21); 79 (22); 67 (32); 57 (100); 41 (95).

HR/MS (ESI): calculated for [M+H]⁺: 367.2227; found: 367.2233; calculated for [M+Na]⁺: 389.2047; found: 389.2094.

[α]₂⁰° (CHCl₃, c = 0.510 g/100 ml): [α]₂⁰° = -456.9°; [α]₂⁰° = -295.8°; [α]₂⁰° = -175.2°; [α]₂⁰° = -153.9°; [α]₂⁰° = -148.6°.

¹⁴ The substance forms two rotamers in 0.8:0.2 ratio.
Synthesis of tert-Butyl (R,E)-N-(hept-3-en-3-yl)-N-(pent-4-enoyl)glycinate (13a)

\[

\begin{align*}
\text{CH}_2\text{Cl}_2, 0^\circ \text{C} & \quad \text{DIPEA} \\
& \quad \text{Ghosez-reagent} \\
\end{align*}
\]

The reaction was performed according to the general procedure 2 using 80 µl (0.800 mmol) 4-Pentenoic acid (10) and stopped after 2.5 h.

The crude product was purified by flash column chromatography (Silica, cHex/EtOAc = 6/1) to yield 224 mg (0.724 mmol, 90%) of the desired dipeptide 12a as a colorless oil.

\[
\text{C}_{18}\text{H}_{31}\text{NO}_3
\]

**M**: 309.45 g/mol.

**TLC**: \( R_f = 0.21 \) (Silica, cHex/EtOAc = 6/1), KMnO₄-reagent.

**\(^1\)H NMR** (500 MHz, CDCl₃, rotameric mixture\(^{15}\)): \( \delta [\text{ppm}] = 0.87 \) (\( \text{t}, \text{ } ^3\text{J} = 7.4 \text{ Hz}, \text{ } 1.2\text{H}, \text{ } \text{H-7}_\text{rot2} \)); 0.94 – 1.00 (m, 4.8H, H-1/7\_rot1); 1.42 – 1.51 (m, 9.4H, H-6\_rot2/11/12/13); 1.51 – 1.66 (m, 1.6H, H-6\_rot1/6'); 2.00 – 2.08 (m, 2H, H-2); 2.30 – 2.33 (m, 0.8H, H-15\_rot2/15'\_rot2); 2.40 – 2.45 (m, 2H, H-15\_rot1/16/16'\_rot2); 2.48 – 2.51 (m, 1.2H, H-15'\_rot1/16'\_rot1); 3.71 – 3.82 (m, 2H, H-8); 4.17 (\( \Psi q, ^3\text{J} = 6.4 \text{ Hz}, 0.6\text{H}, \text{ } \text{H-5}_\text{rot1} \)); 4.96 – 5.00 (m, 1H, H-18); 5.03 – 5.09 (m, 1.4H, H-5\_rot2/18'); 5.32 (ddt, \( ^3\text{J} = 15.6 \text{ Hz}, ^3\text{J} = 6.1 \text{ Hz}, ^4\text{J} = 1.5 \text{ Hz}, 0.6\text{H}, \text{ } \text{H-4}_\text{rot2} \)); 5.50 (ddt, \( ^3\text{J} = 15.6 \text{ Hz}, ^3\text{J} = 5.6 \text{ Hz}, ^4\text{J} = 1.5 \text{ Hz}, 0.4\text{H}, \text{ } \text{H-4}_\text{rot1} \)); 5.60 – 5.67 (m, 1H, H-3); 5.82 – 5.92 (m, 1H, H-17).

**\(^13\)C NMR** (125 MHz, CDCl₃, rotameric mixture\(^{17}\)): \( \delta [\text{ppm}] = 11.0, 11.2 \) (C-7); 13.6, 13.6 (C-1); 24.4 (C-6\_rot2); 25.6, 25.7 (C-2); 25.8 (C-6\_rot1); 28.1, 28.2 (C-11/12/13); 29.4, 29.4 (C-16); 32.7, 33.0 (C-15); 44.6, 46.1 (C-8); 56.0, 60.1 (C-5); 81.1, 82.2 (C-10); 115.1, 115.2 (C-18); 127.1, 127.1 (C-4); 135.1, 135.6 (C-3); 137.8, 137.9 (C-17); 168.7, 169.1 (C-9); 172.6, 172.9 (C-14).

**IR** (ATR): \( \tilde{\nu} [\text{cm}^{-1}] = 3078 \) (w); 3005 (w); 2967 (w); 2935 (w); 2878 (w); 2855 (w); 1746 (m); 1647 (m); 1437 (m); 1408 (m); 1395 (w); 1368 (m); 1304 (w); 1255 (w); 1219 (m); 1150 (s); 1058 (w); 1032 (w); 975 (m); 940 (w); 910 (m); 848 (w); 793 (w); 783 (w); 749 (w); 641 (w).

**GC/MS** (EI, 70 eV): \( m/z (\%) = 309 \) ([M]\(^+\), 2); 280 ([M]\(^+\)-C₇H₅, 7); 253 (13); 238 (8); 224 (12); 210 (8); 208 ([M]\(^+\)-CO₂Bu, 9); 198 (16); 194 (11); 170 (48); 142 (100); 112 (25); 97 ([C₇H₅]\(^+\), 52); 81 (10); 69 (10); 57 (40); 55 (75); 41 (30).

\(^{15}\) The substance forms two rotamers in 0.6/0.4 ratio.
HR/MS (ESI): calculated for [M+Na]+ 310.2377; found: 310.2380; [M+Na]+ 332.2196; found: 332.2196.

$[\alpha]^{20}_d$ (CHCℓ₃, c = 0.500 g/100 ml): $[\alpha]^{20}_d$ = +216.4°; $[\alpha]^{20}_{436}$ = +125.9°; $[\alpha]^{20}_{546}$ = +69.5°; $[\alpha]^{20}_{579}$ = +60.5°; $[\alpha]^{20}_{359}$ = +57.4°.

Synthesis of tert-Butyl (R)-2-(ethyl-2-oxo-2,3,4,7-tetrahydro-1H-azepin-1-yl)acetate (11a)

Under inert conditions a solution of 150 mg (0.485 mmol, 1.0 eq.) of peptide 12a and 3.0 mg (4.9 µmol, 1 mol%) of the Hoveyda-Grubbs II catalyst (9) in 24.3 ml toluene (0.02 M) was stirred for 1 h at room temperature. After completion 200 mg QuadraSil® was added and the solution stirred for another 1 h. The mixture was filtrated and the solvent was removed under reduced pressure before the colorless crude product was purified by flash column chromatography (Silica, cHex/EtOAc = 2/1). The product 11a was isolated as viscose colorless oil in 92% (113 mg, 0.446 mmol) yield and crystallized at 4 °C to a white solid.

C_{14}H_{23}NO₃

M: 253.34 g/mol.

TLC: $R_f = 0.20$ (Silica, cHex/EtOAc = 3/2), KMnO₄-reagent.

Mp.: 56 – 58 °C.

$^1$H NMR (500 MHz, CDCl₃): δ [ppm] = 1.00 (t, $^3J = 7.4$ Hz, 3H, H-7); 1.45 (s, 9H, H-12/13/14); 1.75 – 1.84 (m, 1H, H-6); 1.86 – 1.94 (m, 1H, H-6'); 2.25 – 2.32 (m, 1H, H-2); 2.37 – 2.46 (m, 1H, H-2'); 2.61 – 2.65 (m, 1H, H-1); 2.80 – 2.86 (m, 1H, H-1'); 3.56 (d, $^3J = 17.1$ Hz, 1H, H-9); 3.67 (Ψ q, $^3J = 6.9$ Hz, 1H, H-5); 4.53 (d, $^3J = 17.1$ Hz, 1H, H-9'); 5.68 – 5.72 (m, 1H, H-4); 5.79 – 5.83 (m, 1H, H-3).

$^{13}$C NMR (125 MHz, CDCl₃): δ [ppm] = 11.8 (C-7); 24.5 (C-2); 28.1 (C-12/13/14); 29.5 (C-6); 5.2 (C-1); 51.8 (C-9); 61.8 (C-5); 81.7 (C-11); 128.5 (C-4); 129.7 (C-3); 168.8 (C-10); 174.1 (C-8).

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 3429 (w); 3262 (w); 3028 (w); 3003 (w); 2974 (m); 2940 (w); 2924 (w); 2899 (w); 2881 (w); 2848 (w); 1723 (s); 1671 (w); 1634 (s); 1600 (w); 1491 (m); 1465 (w); 1455 (m); 1404 (w); 1392 (w); 1364 (m); 1327 (m); 1295 (m); 1267 (m); 1255 (m); 1214 (m); 1181 (m); 1156 (s); 1193 (w); 1044 (w); 1035 (w); 1014 (w); 986 (w); 972 (w); 949 (m); 931 (m); 872 (w); 861 (w); 852 (m); 825 (w); 784 (w); 759 (w); 750 (w); 696 (m); 648 (w); 618 (w); 604 (w).
SUPPORTING INFORMATION

GC/MS (EI, 70 eV): m/z (%) = 309 ([M]+, 2); 280 ([M]+-C₂H₅, 7); 253 (13); 238 (8); 224 (12); 210 (8); 208 ([M]+-CO₂Bu, 9); 198 (16); 194 (11); 170 (48); 142 (100); 112 (25); 97 ([C₇H₁₃]+, 52); 81 (10); 69 (10); 57 (40); 55 (75); 41 (30).

HR/MS (ESI): calculated for [M+Na]+ 254.1751; found: 254.1752; [M+Na]+ 276.1570; found: 276.1572.

[α]D²⁰(CHCl₃, c = 0.510 g/100 ml): [α]D⁰₂⁰ = -308.6°; [α]D²⁰ = -183.7°; [α]D²⁰ = -102.8°; [α]D²⁰ = -89.7°; [α]D²⁰ = -86.1°.

Synthesis of tert-Butyl (R,E)-N-(hept-3-en-3-yl)-N-(pent-4-enoyl)-L-phenylalaninate (11b)

The reaction was performed according to the general procedure 2 using 50 µl (0.495 mmol) 4-Pentenoic acid (10) and stopped after 1 h. The crude product was purified by flash column chromatography (Silica, cHex/EtOAc = 5/1) to yield 131 mg (0.366 mmol, 74%) of the desired peptide 12b as a colorless oil.

C₂₂H₃₁NO₃

M: 357.49 g/mol.

TLC: Rf = 0.20 (Silica, cHex/EtOAc = 5/1), KMnO₄-reagent.

¹H NMR (500 MHz, CDCl₃, rotameric mixture): δ [ppm] = 0.90 – 0.94 (m, 6H, H-1/7); 1.57 – 1.74 (m, 2H, H-6); 1.89 (Ψ quint., ²J = 7.2 Hz, 2H, H-2); 2.41 – 2.50 (m, 4H, H-17/18); 3.06 (dd, ³J = 14.0 Hz, ²J = 6.8 Hz, 1H, H-11); 3.64 (dd, ³J = 14.0 Hz, ²J = 7.0 Hz, 1H, H-11¹); 3.69 (s, 3H, H-10); 3.82 (Ψ t, ³J = 6.6 Hz, 1H, H-8); 4.04 (Ψ q, ³J = 7.0 Hz, 1H, H-5); 4.75 (ddt, ²J = 15.6 Hz, ³J = 6.8 Hz, ⁴J = 1.4 Hz, 1H, H-4); 5.01 – 5.10 (m, 2H, H-20); 5.52 (dt, ²J = 15.6 Hz, ³J = 6.4 Hz, 1H, H-3); 5.86 – 5.94 (m, 1H, H-19); 7.18 – 7.20 (m, 3H, H-13/15); 7.14 – 7.27 (m, 2H, H-14).

¹³C NMR (125 MHz, CDCl₃, rotameric mixture): δ [ppm] = 11.4 (C-7); 13.5 (C-1); 25.6 (C-6); 25.7 (C-2); 29.1 (C-18); 33.1 (C-17); 36.5 (C-11); 52.1 (C-10); 58.6 (C-8); 61.2 (C-5); 115.2 (C-20); 126.3 (C-15); 127.1 (C-4); 128.2 (C-14); 129.7 (C-13); 135.9 (C-3); 137.6 (C-19); 139.6 (C-12); 171.7 (C-9); 172.0 (C-16).

The substance forms two rotamers in 1.0/0.8 ratio. Because of the weak signal intensity only the main rotamer is given.
**SUPPORTING INFORMATION**

IR (ATR): $\tilde{\nu}$ [cm$^{-1}$] = 3107 (w); 3084 (w); 3065 (w); 3028 (w); 2963 (w); 2934 (w); 2875 (w); 2851 (w); 1740 (s); 1639 (s); 1605 (w); 1585 (w); 1497 (w); 1455 (m); 1430 (s); 1378 (w); 1351 (w); 1300 (m); 1217 (s); 1182 (m); 1162 (m); 1153 (m); 1115 (w); 1080 (m); 1065 (m); 1030 (m); 1021 (m); 977 (m); 910 (m); 846 (w); 796 (w); 751 (m); 700 (s); 646 (w); 623 (w).

GC/MS (El, 70 eV): $m/z$ (%) = 357 ([M$^+$], 8); 342 ([M$^+$]-CH$_3$, 5); 328 ([M$^+$]-C$_2$H$_5$, 6); 298 ([M$^+$]-CO$_2$Me, 7); 274 ([M$^+$]-C$_6$H$_5$O, 18); 246 (73); 202 (10); 194 (15); 184 (22); 170 (16); 166 (10); 162 (7); 120 (12); 103 (11); 97 ([C$_7$H$_3$]$^+$, 35); 91 (30); 81 (14); 67 (13); 55 (100).

HR/MS [(ESI): calculated for [M+Na]$^+$ 358.2377; found: 358.2377; [M+Na]$^+$ 380.2169; found: 380.2194.

$[\alpha]^2$ (CHCl$_3$, $c$ = 0.505 g/100 ml): $[\alpha]^2_{365}$ = -231.2$^\circ$; $[\alpha]^2_{236}$ = -136.0$^\circ$; $[\alpha]^2_{546}$ = -75.5$^\circ$; $[\alpha]^2_{375}$ = -65.7$^\circ$; $[\alpha]^2_{589}$ = -63.7$^\circ$.

**Synthesis of tert-Butyl (S)-(R)-7-ethyl-2-oxo-2,3,4,7-tetrahydro-1H-azepin-1-yl)-3-phenylpropanoate (11b)**

Under inert conditions a solution of 125 mg (0.350 mmol, 1.0 eq.) of peptide 12b and 4.4 mg (7.0 $\mu$mol, 2 mol%) of the *Hoveyda-Grubbs II* catalyst (9) in 24.3 ml toluene (0.02 m) was heated to 70 $^\circ$C and stirred for 3 h. After completion 200 mg *QuadraSil AP* was added and the solution stirred for another 1 h. The solution was allowed to cool down before the solvent was removed under reduced pressure. The resulting dark green oil was purified by flash column chromatography (Silica, cHex/ EtOAc = 3/2). The resulting oily product was dissolved in little CH$_2$Cl$_2$ and stirred over *QuadraSil AP* for 15 min to remove residual ruthenium. After filtration the solvent was removed under reduced pressure and the product was dried in high vacuum to afford 101 mg (0.335 mmol, 96%) of the cyclic product 11b as a colorless viscous oil.

**C$_{18}$H$_{23}$NO$_3$**

M: 301.38 g/mol.

TLC: $R_f$ = 0.24 (Silica, cHex/EtOAc = 3/2), KMnO$_4$-reagent.

Mp.: 75 – 76 $^\circ$C

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ [ppm] = 0.90 (t, $^3$J = 7.5 Hz, 3H, H-7); 1.53 – 1.61 (m, 1H, H-6); 1.71 – 1.80 (m, 1H, H-6$^\circ$); 2.10 – 2.16 (m, 1H, H-3$^\circ$); 2.49 (ddd, $^2$J = 13.5 Hz, $^3$J = 5.7 Hz, $^3$J = 3.0 Hz, 1H, H-1$^\circ$); 2.84 ($\Psi$ td, $^2$J = 13.1 Hz, $^3$J = 3.6 Hz, 1H, H-1$^\circ$); 2.99 (dd, $^2$J = 14.3 Hz, $^3$J = 9.1 Hz, 1H, H-12$^\circ$); 3.29 (dd, $^2$J = 14.3 Hz, $^3$J = 9.1 Hz, 1H, H-12$^\circ$); 3.44 (s, 3H, NCH$_3$); 4.92, 4.97 (d, $^1$J = 10.5 Hz, 1H, H-2$^\circ$); 5.01 (s, 1H, H-2$^\circ$); 5.93, 5.95 (d, $^1$J = 10.5 Hz, 1H, H-6$^\circ$); 6.87, 6.88 (d, $^1$J = 10.5 Hz, 2H, ArH); 7.07, 7.29 (d, $^1$J = 10.5 Hz, 2H, ArH); 7.30, 7.32, 7.48, 7.49, 7.53, 7.59 (m, 3H, ArH); 7.68, 7.70 (d, $^1$J = 10.5 Hz, 2H, ArH); 7.88, 7.91 (d, $^1$J = 10.5 Hz, 2H, ArH); 8.36, 8.39 (d, $^1$J = 10.5 Hz, 2H, ArH).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ [ppm] = 0.90 (t, $^3$J = 7.5 Hz, 3H, H-7); 1.53 – 1.61 (m, 1H, H-6); 1.71 – 1.80 (m, 1H, H-6$^\circ$); 2.10 – 2.16 (m, 1H, H-3$^\circ$); 2.49 (ddd, $^2$J = 13.5 Hz, $^3$J = 5.7 Hz, $^3$J = 3.0 Hz, 1H, H-1$^\circ$); 2.84 ($\Psi$ td, $^2$J = 13.1 Hz, $^3$J = 3.6 Hz, 1H, H-1$^\circ$); 2.99 (dd, $^2$J = 14.3 Hz, $^3$J = 9.1 Hz, 1H, H-12$^\circ$); 3.29 (dd, $^2$J = 14.3 Hz, $^3$J = 9.1 Hz, 1H, H-12$^\circ$); 3.44 (s, 3H, NCH$_3$); 4.92, 4.97 (d, $^1$J = 10.5 Hz, 1H, H-2$^\circ$); 5.01 (s, 1H, H-2$^\circ$); 5.93, 5.95 (d, $^1$J = 10.5 Hz, 1H, H-6$^\circ$); 6.87, 6.88 (d, $^1$J = 10.5 Hz, 2H, ArH); 7.07, 7.29 (d, $^1$J = 10.5 Hz, 2H, ArH); 7.30, 7.32, 7.48, 7.49, 7.53, 7.59 (m, 3H, ArH); 7.68, 7.70 (d, $^1$J = 10.5 Hz, 2H, ArH); 7.88, 7.91 (d, $^1$J = 10.5 Hz, 2H, ArH); 8.36, 8.39 (d, $^1$J = 10.5 Hz, 2H, ArH).
14.3 Hz, $^{3}J = 6.4$ Hz, 1H, H-12'); 3.69 – 3.74 (m, 4H, H-5/11); 5.31 (dd, $^{3}J = 9.1$ Hz, $^{3}J = 6.4$ Hz, 1H, H-9); 5.59 – 5.66 (m, 2H, H-3/4); 7.15 – 7.24 (m, 5H, H-14/15/16).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ [ppm] = 12.0 (C-7); 24.3 (C-2); 30.7 (C-6); 35.2 (C-1); 35.8 (C-12); 52.1 (C-11); 57.3 (C-5); 59.3 (C-9); 126.6 (C-16); 128.0 (C-4); 128.2 (C-15); 129.5 (C-14); 130.1 (C-3); 137.3 (C-13); 171.7 (C-10); 174.3 (C-8).

IR (ATR): $\tilde{\nu}$ [cm$^{-1}$] = 3463 (w); 3259 (w); 3111 (w); 3087 (w); 3072 (w); 3028 (w); 2970 (w); 2947 (w); 2928 (w); 2911 (w); 2891 (w); 2855 (w); 2839 (w); 1740 (s); 1700 (w); 1608 (s); 1498 (m); 1449 (m); 1384 (m); 1345 (m); 1322 (w); 1309 (w); 1295 (m); 1283 (m); 1263 (m); 1245 (m); 1223 (s); 1209 (m); 1192 (s); 1176 (m); 1162 (m); 1153 (m); 1124 (m); 1100 (w); 1081 (m); 1047 (w); 1029 (s); 1010 (m); 993 (w); 962 (w); 954 (w); 941 (w); 930 (w); 920 (w); 907 (m); 869 (w); 853 (w); 819 (m); 771 (m); 747 (s); 703 (s); 672 (w); 658 (w); 618 (s); 602 (w).

GC/MS (EI, 70 eV): m/z (%) = 301 ([M]$^+$, 12); 272 ([M]$^+$-C$_2$H$_5$, 100); 242 ([M]$^+$-CO$_2$Me, 50); 210 ([M]$^+$-C$_7$H$_7$, 87); 206 (55); 182 (73); 180 (26); 178 (72); 162 (23); 150 (25); 146 (60); 139 (34); 138 (35); 131 (20); 128 (22); 120 (55); 110 (35); 103 (27); 95 (60); 93 (38); 91 ([C7H7]$^+$, 95); 81 (27); 77 (30); 67 (78); 65 (34); 59 (20); 55 (35); 53 (25).

HR/MS (ESI): calculated for [M+Na]$^+$ 302.1751; found: 302.1753; [M+Na]$^+$ 324.1570; found: 324.1569.

$[\alpha]_{D}^{20}$ (CHCl$_3$, c = 0.510 g/100 ml): $[\alpha]_{D}^{20} = -818.2^\circ$; $[\alpha]_{D}^{20} = -475.8^\circ$; $[\alpha]_{D}^{20} = -262.5^\circ$; $[\alpha]_{D}^{20} = -228.1^\circ$; $[\alpha]_{D}^{20} = -219.1^\circ$. 


**SUPPORTING INFORMATION**

**NMR Spectra**

$^1$H NMR (300 MHz) of rac-12 in CDCl$_3$

$^{13}$C-NMR (75 MHz) of rac-12 in CDCl$_3$
$^1$H NMR (300 MHz) of rac-4a in CDCl$_3$

$^{13}$C-NMR (75 MHz) of rac-4a in CDCl$_3$
$^1$H NMR (300 MHz) of rac-3a in CDCl$_3$

$^{13}$C-NMR (75 MHz) of rac-3a in CDCl$_3$
$^1$H NMR (300 MHz) of rac-3b in CDCl$_3$

$^{13}$C-NMR (75 MHz) of rac-3b in CDCl$_3$
**SUPPORTING INFORMATION**

$^1$H NMR (500 MHz) of (R,S)-3c in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (R,S)-3c in CDCl$_3$
$^1$H NMR (500 MHz) of (S,S)-3c in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (S,S)-3c in CDCl$_3$
$^1$H NMR (500 MHz) of (R,S)-3d in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (R,S)-3d in CDCl$_3$
$^1$H NMR (500 MHz) of (S,S)-3d in CDCl$_3$ 

$^{13}$C-NMR (125 MHz) of (S,S)-3d in CDCl$_3$
$^1$H NMR (500 MHz) of (R,S)-3e in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (R,S)-3e in CDCl$_3$
$^1$H NMR (500 MHz) of (S,S)-3e in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (S,S)-3e in CDCl$_3$
$^1$H NMR (500 MHz) of (R,S)-3f in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (R,S)-3f in CDCl$_3$
$^1$H NMR (500 MHz) of (S,S)-3f in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (S,S)-3f in CDCl$_3$
$^1$H NMR (500 MHz) of (R,S)-3g in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (R,S)-3g in CDCl$_3$
$^1$H NMR (500 MHz) of (S,S)-3g in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (S,S)-3g in CDCl$_3$
$^1$H NMR (500 MHz) of (R,S)-3h in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (R,S)-3h in CDCl$_3$
$^1$H NMR (500 MHz) of (S,S)-3h in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (S,S)-3h in CDCl$_3$
$^1$H NMR (500 MHz) of (R,S)-3i in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (R,S)-3i in CDCl$_3$
$^1$H NMR (500 MHz) of (S,S)-3i in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (S,S)-3i in CDCl$_3$
$^1$H NMR (500 MHz) of (R,S)-3j in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (R,S)-3j in CDCl$_3$
$^1$H NMR (500 MHz) of (S,S)-3j in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (S,S)-3j in CDCl$_3$
$^1$H NMR (500 MHz) of (R,S)-3k in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (R,S)-3k in CDCl$_3$
$^1$H NMR (500 MHz) of (S,S)-3k in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (S,S)-3k in CDCl$_3$
$^1$H NMR (500 MHz) of 6a in CDCl$_3$.

$^{13}$C NMR (125 MHz) of 6a in CDCl$_3$. 
$^1$H NMR (500 MHz) of \textit{dia-6a} in CDCl$_3$ 

$^{13}$C-NMR (125 MHz) of \textit{dia-6a} in CDCl$_3$
$^1$H NMR (500 MHz) of (S,R,R,R)-6b in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (S,R,R,R)-6b in CDCl$_3$
SUPPORTING INFORMATION

$^1$H NMR (500 MHz) of (S,R,R,S)-6b in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (S,R,R,S)-6b in CDCl$_3$
$^1$H NMR (500 MHz) of (S,R,S,S)-6b in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (S,R,S,S)-6b in CDCl$_3$
$^1$H NMR (500 MHz) of (S,R,S,R)-6b in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (S,R,S,R)-6b in CDCl$_3$
$^1$H NMR (500 MHz) of 6c in CDCl$_3$

$^{13}$C-NMR (125 MHz) of 6c in CDCl$_3$
$^1$H NMR (500 MHz) of dia-6c in CDCl$_3$

$^{13}$C-NMR (125 MHz) of dia-6c in CDCl$_3$
$^1$H NMR (500 MHz) of ($R,S,R$)-$6a$ in CDCl$_3$

$^{13}$C-NMR (125 MHz) of ($R,S,R$)-$7a$ in CDCl$_3$
H NMR (500 MHz) of (S,R,R,R)-7b in CDCl₃

13C-NMR (125 MHz) of (S,R,R,R)-7b in CDCl₃
$^1$H NMR (500 MHz) of (S,R,R,S)-7b in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (S,R,R,S)-7b in CDCl$_3$
$^1$H NMR (500 MHz) of (S,R,S,R)-7b in CDCl$_3$

$^{13}$C-NMR (125 MHz) of (S,R,S,R)-7b in CDCl$_3$
\textsuperscript{1}H NMR (500 MHz) of (S,R,S,S)-7b in CDCl\textsubscript{3}

\textsuperscript{13}C-NMR (125 MHz) of (S,R,S)-7b in CDCl\textsubscript{3}
$^1$H NMR (500 MHz) of 7c in CDCl$_3$

$^{13}$C-NMR (125 MHz) of 7c in CDCl$_3$
$^1$H NMR (500 MHz) of 11a in CDCl$_3$

$^{13}$C-NMR (125 MHz) of 11a in CDCl$_3$
$^1$H NMR (500 MHz) of 11b in CDCl$_3$

$^{13}$C-NMR (125 MHz) of 11b in CDCl$_3$
Gas chromatograms of rac-3a and (S)-3a
X-ray crystallographic data:

Data for 7a

Identification code  sd759
Empirical formula  C_{21}H_{34}N_{13}O_{5}
Moiety formula  C_{21}H_{34}N_{13}O_{5}
Formula weight  394.50
Temperature  100(2) K
Wavelength  1.54178 Å
Crystal system  Monoclinic
Space group  P2_1
Unit cell dimensions

\begin{align*}
a &= 10.5339(14) \text{ Å} \\
b &= 9.6639(12) \text{ Å} \\
c &= 11.0835(19) \text{ Å} \\
\alpha &= 90^\circ \\
\beta &= 104.865(11)^\circ \\
\gamma &= 90^\circ
\end{align*}

Volume  1090.5(3) Å³
Z  2
Density (calculated)  1.201 Mg/m³
Absorption coefficient  0.693 mm⁻¹
F(000)  428
Crystal size  0.250 x 0.200 x 0.040 mm³
Theta range for data collection  4.127 to 65.226°
Index ranges  -12<=h<=12, -11<=k<=11, -13<=l<=13
Reflections collected  13096
Independent reflections  3700 [R(int) = 0.0520]
Completeness to theta = 65.226°  99.9%
Absorption correction  Semi-empirical from equivalents
Max. and min. transmission  0.7526 and 0.4523
Refinement method  Full-matrix least-squares on F²
Data / restraints / parameters  3700 / 1 / 260
Goodness-of-fit on F²  1.067
Final R indices [I>2sigma(I)]  R1 = 0.0405, wR2 = 0.0985
R indices (all data)  R1 = 0.0433, wR2 = 0.1012
Absolute structure parameter  0.14(11)
Extinction coefficient  n/a
Largest diff. peak and hole  0.178 and -0.286 e.Å⁻³
**Data for 7c**

| Property                                      | Value                                      |
|-----------------------------------------------|--------------------------------------------|
| Identification code                           | sd665n                                     |
| Empirical formula                             | C_{19}H_{30}N_{2}O_{5}                     |
| Moiety formula                                | C_{19}H_{30}N_{2}O_{5}                     |
| Formula weight                                | 366.45                                     |
| Temperature                                   | 100(2) K                                   |
| Wavelength                                    | 1.54178 Å                                  |
| Crystal system                                | Orthorhombic                               |
| Space group                                   | P_{21}2_{1}2_{1}                           |
| Unit cell dimensions                          | a = 10.7523(3) Å, b = 12.4063(3) Å, c = 14.8461(4) Å |
|                                              | α = 90°, β = 90°, γ = 90°                  |
| Volume                                        | 1980.41(9) Å^{3}                          |
| Z                                             | 4                                          |
| Density (calculated)                          | 1.229 Mg/m^{3}                             |
| Absorption coefficient                        | 0.726 mm^{−1}                              |
| F(000)                                        | 792                                        |
| Crystal size                                  | 0.200 x 0.160 x 0.120 m^{3}                |
| Theta range for data collection               | 4.645 to 77.610°                          |
| Index ranges                                  | -13<=h<=13, -15<=k<=15, -16<=l<=18         |
| Reflections collected                         | 60691                                      |
| Independent reflections                       | 4216 [R(int) = 0.0335]                     |
| Completeness to theta = 67.679°               | 100.0%                                     |
| Absorption correction                         | Semi-empirical from equivalents            |
| Max. and min. transmission                    | 0.8646 and 0.8047                          |
| Refinement method                             | Full-matrix least-squares on F^{2}         |
| Data / restraints / parameters                 | 4216 / 0 / 242                             |
| Goodness-of-fit on F^{2}                      | 1.047                                      |
| Final R indices [I>2sigma(I)]                 | R1 = 0.0233, wR2 = 0.0604                  |
| R indices (all data)                          | R1 = 0.0238, wR2 = 0.0608                  |
| Absolute structure parameter                  | 0.01(2)                                    |
| Extinction coefficient                        | 0.0035(3)                                  |
| Largest diff. peak and hole                   | 0.246 and -0.133 e.Å^{3}                   |
Data for \((S,R,S,S)-7b\)

| Property                          | Value                      |
|----------------------------------|----------------------------|
| Identification code              | sd626_1                    |
| Empirical formula                | \(C_{25}H_{34}N_2O_5\)     |
| Moiety formula                   | \(C_{25}H_{34}N_2O_5\)     |
| Formula weight                   | 442.54                     |
| Temperature                      | 100(2) K                   |
| Wavelength                       | 1.54178 Å                  |
| Crystal system                   | Orthorhombic               |
| Space group                      | \(P2_12_1_2_1\)            |
| Unit cell dimensions             |                           |
| a                                | 8.4270(2) Å               |
| \(\alpha\)                       | 90°                        |
| b                                | 9.3160(2) Å               |
| \(\beta\)                       | 90°                        |
| c                                | 31.6237(8) Å              |
| \(\gamma\)                      | 90°                        |
| Volume                           | 2482.65(10) Å\(^3\)       |
| Z                                | 4                          |
| Density (calculated)             | 1.184 Mg/m\(^3\)          |
| Absorption coefficient           | 0.666 mm\(^{-1}\)         |
| \(F(000)\)                      | 952                        |
| Crystal size                     | 0.150 x 0.150 x 0.030 mm\(^3\) |
| Theta range for data collection  | 4.949 to 72.203°          |
| Index ranges                     | -10<=h<=10, -11<=k<=11, -39<=l<=38 |
| Reflections collected            | 31065                      |
| Independent reflections          | 4897 [R(int) = 0.0366]     |
| Completeness to theta = 67.679°  | 100.0%                     |
| Absorption correction            | Semi-empirical from equivalents |
| Max. and min. transmission       | 0.7536 and 0.6626          |
| Refinement method                | Full-matrix least-squares on \(F^2\) |
| Data / restraints / parameters   | 4897 / 0 / 294             |
| Goodness-of-fit on \(F^2\)       | 1.068                      |
| Final R indices [I>2sigma(I)]    | \(R_1 = 0.0452, \)w\(R_2 = 0.1125\) |
| R indices (all data)             | \(R_1 = 0.0468, \)w\(R_2 = 0.1137\) |
| Absolute structure parameter     | 0.07(4)                    |
| Extinction coefficient           | n/a                        |
| Largest diff. peak and hole      | 0.593 and -0.268 e.Å\(^{-3}\) |
Data for \((S,R,R,S)-7b\)

| Identification code | sd620 |
|---------------------|-------|
| Empirical formula   | \(\text{C}_{25}\text{H}_{34}\text{N}_{2}\text{O}_{5}\) |
| Moiety formula      | \(\text{C}_{25}\text{H}_{34}\text{N}_{2}\text{O}_{5}\) |
| Formula weight      | 442.54 |
| Temperature         | 100(2) K |
| Wavelength          | 1.54178 Å |
| Crystal system      | Monoclinic |
| Space group         | \(P2_1\) |
| Unit cell dimensions| \(a = 9.3016(3)\) Å, \(b = 21.2294(7)\) Å, \(c = 12.1312(4)\) Å, \(\alpha = 90^\circ\), \(\beta = 92.7160(10)^\circ\), \(\gamma = 90^\circ\). |
| Volume              | 2392.83(14) Å\(^3\) |
| Z                   | 4 |
| Density (calculated) | 1.228 Mg/m\(^3\) |
| Absorption coefficient | 0.691 mm\(^{-1}\) |
| F(000)              | 952 |
| Crystal size        | 0.200 x 0.200 x 0.100 mm\(^3\) |
| Theta range for data collection | 3.647 to 72.365\(^\circ\). |
| Index ranges        | \(-11\leq h\leq 11, -26\leq k\leq 26, -13\leq l\leq 14\) |
| Reflections collected | 27458 |
| Independent reflections | 9274 [R(int) = 0.0351] |
| Completeness to theta = 67.679\(^\circ\) | 99.2% |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.7536 and 0.5586 |
| Refinement method   | Full-matrix least-squares on F\(^2\) |
| Data / restraints / parameters | 9274 / 1 / 587 |
| Goodness-of-fit on F\(^2\) | 1.074 |
| Final R indices [I>2sigma(I)] | R1 = 0.0330, wR2 = 0.0888 |
| R indices (all data) | R1 = 0.0343, wR2 = 0.0935 |
| Absolute structure parameter | 0.13(5) |
| Extinction coefficient | n/a |
| Largest diff. peak and hole | 0.718 and -0.230 e.Å\(^{-3}\) |
### Data for (S,R,S,R)-7b

| Property                      | Value          |
|-------------------------------|----------------|
| **Identification code**       | sd758          |
| **Empirical formula**         | C$_{25}$H$_{34}$N$_2$O$_5$ |
| **Moiety formula**            | C$_{25}$H$_{34}$N$_2$O$_5$ |
| **Formula weight**            | 442.54         |
| **Temperature**               | 100(2) K       |
| **Wavelength**                | 1.54178 Å      |
| **Crystal system**            | Orthorhombic   |
| **Space group**               | P2$_1$2$_1$2$_1$ |
| **Unit cell dimensions**      |                |
| a                             | 9.5447(11) Å   |
| b                             | 14.5784(17) Å  |
| c                             | 16.887(3) Å    |
| **Volume**                    | 2349.8(5) Å$^3$|
| **Z**                         | 4              |
| **Density (calculated)**      | 1.251 Mg/m$^3$ |
| **Absorption coefficient**    | 0.704 mm$^{-1}$|
| **F(000)**                    | 952            |
| **Crystal size**              | 0.150 x 0.030 x 0.020 mm$^3$ |
| **Theta range for data collection** | 4.006 to 72.348° |
| **Index ranges**              | -11<=h<=11, -18<=k<=12, -20<=l<=20 |
| **Reflections collected**     | 24130          |
| **Independent reflections**   | 4623 [R(int) = 0.0580] |
| **Completeness to theta = 67.679°** | 100.0%         |
| **Absorption correction**     | Semi-empirical from equivalents |
| **Max. and min. transmission**| 0.7536 and 0.5330 |
| **Refinement method**         | Full-matrix least-squares on F$^2$ |
| **Data / restraints / parameters** | 4623 / 0 / 294 |
| **Goodness-of-fit on F$^2$**   | 1.091          |
| **Final R indices [l>$\sigma$(l)]** | R1 = 0.0302, wR2 = 0.0749 |
| **R indices (all data)**      | R1 = 0.0320, wR2 = 0.0761 |
| **Absolute structure parameter** | 0.05(6)          |
| **Extinction coefficient**    | n/a            |
| **Largest diff. peak and hole** | 0.277 and -0.226 e.Å$^{-3}$ |
Data for \((S,R,R,R)-7b\)

Identification code: sd777
Empirical formula: \(C_{30}H_{46}N_{2}O_{6}\)
Moieity formula: \(C_{25}H_{34}N_{2}O_{5}, C_{5}H_{12}O\)
Formula weight: 530.69
Temperature: 100(2) K
Wavelength: 1.54178 Å
Crystal system: Orthorhombic
Space group: \(P2_12_12_1\)
Unit cell dimensions:
\[
\begin{align*}
    a &= 10.2223(5) \text{ Å} \\
    b &= 10.4398(5) \text{ Å} \\
    c &= 27.5410(13) \text{ Å}
\end{align*}
\]
\(\alpha = 90^\circ\)
\(\beta = 90^\circ\)
\(\gamma = 90^\circ\)
Volume: 2939.1(2) Å³
\(Z\): 4
Density (calculated): 1.199 Mg/m³
Absorption coefficient: 0.666 mm⁻¹
\(F(000)\): 1152
Crystal size: 0.070 x 0.070 x 0.010 mm³
Theta range for data collection: 3.209 to 66.652°
Index ranges:
\(-11\leq h\leq12, -12\leq k\leq11, -30\leq l\leq32\)
Reflections collected: 21611
Independent reflections: 5107 [\(R(int) = 0.0526\)]
Completeness to theta = 66.652°: 99.5%
Absorption correction: Semi-empirical from equivalents
Max. and min. transmission: 0.7528 and 0.4728
Refinement method: Full-matrix least-squares on \(F^2\)
Data / restraints / parameters: 5107 / 0 / 352
Goodness-of-fit on \(F^2\): 1.135
Final R indices [\(I>2\sigma(I)\)]: \(R1 = 0.0707, wR2 = 0.2043\)
R indices (all data): \(R1 = 0.0775, wR2 = 0.2106\)
Absolute structure parameter: 0.28(11)
Extinction coefficient: n/a
Largest diff. peak and hole: 0.609 and -0.642 e.Å⁻³
**Supporting Information**

Data for 11a

| Property                          | Value                         |
|----------------------------------|-------------------------------|
| Identification code              | sd726                         |
| Empirical formula                | C₁₄H₂₃NO₃                    |
| Moiety formula                   | C₁₄H₂₃NO₃                    |
| Formula weight                   | 253.33                        |
| Temperature                      | 100(2) K                      |
| Wavelength                       | 1.54178 Å                     |
| Crystal system                   | Monoclinic                    |
| Space group                      | P₂₁                           |
| Unit cell dimensions             |                               |
| a                                | 8.6307(10) Å                  |
| b                                | 9.7649(14) Å                  |
| c                                | 9.1877(19) Å                  |
| α                                | 90°                           |
| β                                | 106.921(8)°                   |
| γ                                | 90°                           |
| Volume                           | 740.8(2) Å³                   |
| Z                                | 2                             |
| Density (calculated)             | 1.136 Mg/m³                   |
| Absorption coefficient           | 0.637 mm⁻¹                    |
| F(000)                           | 276                           |
| Crystal size                     | 0.600 x 0.200 x 0.200 mm³     |
| Theta range for data collection  | 6.194 to 72.224°              |
| Index ranges                     | -10<=h<=10, -10<=k<=11, -11<=l<=11 |
| Reflections collected            | 24734                         |
| Independent reflections          | 2827 [R(int) = 0.0383]         |
| Completeness to theta = 67.679° | 99.6%                         |
| Absorption correction            | Semi-empirical from equivalents |
| Max. and min. transmission       | 0.7536 and 0.5623             |
| Refinement method                | Full-matrix least-squares on F² |
| Data / restraints / parameters   | 2827 / 1 / 168                |
| Goodness-of-fit on F²            | 1.054                         |
| Final R indices [l>2sigma(l)]    | R₁ = 0.0284, wR₂ = 0.0805     |
| R indices (all data)             | R₁ = 0.0287, wR₂ = 0.0807     |
| Absolute structure parameter     | 0.04(5)                       |
| Extinction coefficient           | 0.059(5)                      |
| Largest diff. peak and hole      | 0.218 and -0.178 e.Å⁻³        |
### Supporting Information

**Data for 11e**

![Molecular Structure](image)

| Property                          | Value                                      |
|-----------------------------------|--------------------------------------------|
| Identification code               | sd678                                      |
| Empirical formula                 | C<sub>18</sub>H<sub>23</sub>NO<sub>3</sub>  |
| Moiety formula                    | C<sub>18</sub>H<sub>23</sub>NO<sub>3</sub>  |
| Formula weight                    | 301.37                                     |
| Temperature                       | 100(2) K                                   |
| Wavelength                        | 1.54178 Å                                  |
| Crystal system                    | Monoclinic                                 |
| Space group                       | P<sub>2</sub>₁                           |
| Unit cell dimensions              |                                           |
|                                   | a = 7.4223(9) Å                           |
|                                   | b = 10.3697(13) Å                         |
|                                   | c = 10.3426(10) Å                         |
|                                   | 796.01(16) Å                              |
|                                   |                                           |
| Volume                            |                                           |
| Z                                 | 2                                          |
| Density (calculated)              | 1.257 Mg/m³                                |
| Absorption coefficient            | 0.683 mm⁻¹                                 |
| F(000)                            | 324                                        |
| Crystal size                      | 0.500 x 0.100 x 0.100 mm³                  |
| Theta range for data collection   | 6.043 to 72.179°                           |
| Index ranges                      | -9≤h≤9, -11≤k≤12, -12≤l≤11                 |
| Reflections collected             | 10683                                      |
| Independent reflections           | 3036 [R(int) = 0.0354]                     |
| Completeness to theta = 67.679°   | 99.5%                                      |
| Absorption correction             | Semi-empirical from equivalents           |
| Max. and min. transmission        | 0.7536 and 0.5982                          |
| Refinement method                 | Full-matrix least-squares on F²           |
| Data / restraints / parameters    | 3036 / 1 / 202                             |
| Goodness-of-fit on F²             | 1.038                                      |
| Final R indices [I>2sigma(I)]     | R1 = 0.0292, wR2 = 0.0743                 |
| R indices (all data)              | R1 = 0.0296, wR2 = 0.0748                 |
| Absolute structure parameter      | -0.02(6)                                   |
| Extinction coefficient            | 0.025(2)                                   |
| Largest diff. peak and hole       | 0.230 and -0.195 e Å⁻³                    |
References

[1] Y. Dai, F. Wu, Z. Zang, H. You, H. Gong, *Chem. Eur. J.* **2012**, *18*, 808–812.

[2] X. Fu, J. M. Cook, *J. Org. Chem.* **1993**, *58*, 661–672.

[3] P. Y. Hayes, S. Chow, F. Rahm, P. V. Bernhardt, J. J. De Voss, W. Kitching, *J. Org. Chem.* **2010**, *75*, 6489–6501.

Author Contributions

Stephan Dohmen performed the majority of the experiments and developed the methodology. Martin Reiher contributed to data collection and to manuscript preparation. Dominik Albat performed experiments. Sema Akyol contributed to ligand synthesis. Matthias Barone and Ronald Kühne designed the ProM scaffolds. Jörg-Martin Neudörfl performed X-ray crystal structure analyses. Hans-Günther Schmalz conceived and supervised the research and wrote the manuscript.