

## Supplementary Material

### Synthesis of modified miuraenamides – the Ugi approach

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## General procedures

### GP 1: Ugi reactions

To a solution of aldehyde (1.0 eq) and amine (1.0 eq) in the corresponding solvent (1.0 mL/mmol) Boc-L-alanine (1.2 eq) was added after 15 min. Methyl isocynoacetate (1.0 eq) was added at 0 °C. After stirring at room temperature or heating in a microwave the reaction mixture was hydrolyzed with saturated NaHCO<sub>3</sub> solution. The organic layer was washed with 1 M KHSO<sub>4</sub> and 0.5 M HCl solution and dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was evaporated *in vacuo* and the residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate).

### GP 2: Saponification of esters with LiOH solutions

To a solution of the ester (1.0 eq) in THF/MeOH (3:1; 5–8 mL/mmol) a solution of LiOH (1.05 eq) in dest. H<sub>2</sub>O (2 mL/mmol ester) was added at 0 °C. After complete conversion (TLC-control), the solvent was evaporated *in vacuo* and the residue was acidified with 1 M HCl solution to pH 2. The aqueous layer was extracted with ethyl acetate, the combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and the solvent was evaporated *in vacuo*.

### GP 3a: Steglich Esterifications with EDC·HCl/DMAP

To a solution of the tripeptide acid (1.0 eq) in dry CH<sub>2</sub>Cl<sub>2</sub> (8 mL/mmol) alcohol (**S**)-**6** (1.1 eq), 4-(dimethylamino)pyridine (DMAP) (0.1 eq) and *N*-(3-Dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (EDC·HCl) (1.2 eq) in dry CH<sub>2</sub>Cl<sub>2</sub> (2 mL/mmol) were added. After stirring the mixture overnight at room temperature, the solvent was evaporated *in vacuo* and the residue was dissolved in Et<sub>2</sub>O. The organic layer was washed with 1 M KHSO<sub>4</sub> and sat. NaHCO<sub>3</sub> solution and dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was evaporated *in vacuo* and the residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate).

### GP 3b: Steglich Esterifications with DCC/DMAP<sup>1</sup>

To a solution of the tripeptide acid (1.0 eq) in dry CH<sub>2</sub>Cl<sub>2</sub> (8 mL/mmol) alcohol **3** (1.0-1.2eq), 4-(dimethylamino)pyridine (DMAP) (0.1 eq) and *N,N'*-dicyclohexyl-carbodiimide (DCC) (1.2 eq) in dry CH<sub>2</sub>Cl<sub>2</sub> (3 mL/mmol) were added. After stirring the mixture overnight at room temperature, the solvent was evaporated *in vacuo* and the residue was dissolved in Et<sub>2</sub>O. The precipitated urea derivative was filtered off, the solvent was evaporated and the residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate).

### GP 4: Palladium-catalyzed allyl-cleavages

To a solution of allylester (1.0 eq) in dry THF (20 mL/mmol) Pd(PPh<sub>3</sub>)<sub>4</sub> (10 mol%) and morpholin (2.0 eq) was added. The solution was stirred overnight at room temperature, before it was diluted with ethyl acetate. The solution was washed with H<sub>2</sub>O and brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After evaporation of the solvent *in vacuo*, the residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate).

### GP 5: Macrolactamizations via the pentafluorophenyl ester method<sup>2</sup>

To a solution of the cyclization precursor (1.0 eq) and pentafluorophenol (1.1 eq) in dry CH<sub>2</sub>Cl<sub>2</sub> (10 mL/mmol) *N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (EDC·HCl) (1.0 eq) was added at 0 °C. After stirring overnight at room temperature, the mixture was diluted with ethyl acetate. The organic layer was washed with sat. NaHCO<sub>3</sub> solution, dried over Na<sub>2</sub>SO<sub>4</sub> and the solvent was evaporated *in vacuo*. The activated

<sup>1</sup> B. Neises, W. Steglich, *Angew. Chem.* **1978**, *90*, 556-557; *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 522-523.

<sup>2</sup> a) U. Schmidt, M. Kroner, H. Griesser, *Synthesis* **1991**, 294-300; b) U. Schmidt, V. Leitenberger, H. Griesser, J. Schmidt, R. Meyer, *Synthesis* **1992**, 1248-1254.

ester was then diluted in DCM/TFA (4:1, 10 mL/mmol). After complete Boc-deprotection (2-3 h, tlc-control), the reaction mixture was diluted with dry CH<sub>2</sub>Cl<sub>2</sub> (10-20 mL/mmol) and slowly added under vigorously stirring to a two-phase-mixture of CHCl<sub>3</sub>/sat. NaHCO<sub>3</sub> (7:1, 400 mL/mmol) at 40 °C. After complete addition, the mixture was heated to 60 °C and stirred overnight. The reaction mixture was diluted with H<sub>2</sub>O and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and the solvent was evaporated *in vacuo*. Column chromatography (silica gel, petroleum ether/ ethyl acetate) gave rise to the desired macrocycle.

#### GP 6: TBS-Deprotections with TBAF

To a solution of a silyl-protected depsipeptide (1.0 eq) in dry THF (3 mL/mmol) a solution of TBAF·3 H<sub>2</sub>O (1.1 eq) in dry THF (2.2 mL/mmol) was added. After complete deprotection (TLC-control), the reaction mixture was diluted with ethyl acetate, washed with 1 M HCl- and saturated NaCl solution and was dried over Na<sub>2</sub>SO<sub>4</sub>. After evaporation of the solvent and purification by column chromatography, the desired alcohol was obtained.

#### GP 7: Jones Oxidations

Jones solution (3 M): 1.0 g CrO<sub>3</sub>, 2.91 mL H<sub>2</sub>O, 0.84 mL H<sub>2</sub>SO<sub>4</sub>

To a solution of alcohol (1.0 eq) in acetone (7 mL/mmol) a 3 M Jones solution (3.0 eq) was added. After complete oxidation (TLC-control, 10–20 min), the reaction was hydrolyzed with isopropanol and the solvent was evaporated *in vacuo*. The residue was diluted with dest. H<sub>2</sub>O and extracted with ethyl acetate. The combined organic layers were washed with saturated NaCl solution and dried over Na<sub>2</sub>SO<sub>4</sub>. After evaporation of the solvent *in vacuo*, the residue was purified by column chromatography.

## Ugi Reactions

### (S)-*N*-*tert*-Butoxycarbonyl-alanyl-(*N*-methyl-phenylglycyl)-glycine methyl ester (**7b**)

According to **GP 1** 250  $\mu\text{L}$  (2.50 mmol) benzaldehyde in 0.5 mL EtOH was reacted with 310  $\mu\text{L}$  (2.50 mmol) methylamine (33 % in EtOH), 680 mg (3.00 mmol) Boc-L-alanine and 225  $\mu\text{L}$  (2.50 mmol) methyl isocynoacetate in the microwave (80 °C, 150 W, 30 min). Column chromatography (silica gel, petroleum ether/ethyl acetate 1:1) gave rise to the desired tripeptide **7b** (330 mg, 800  $\mu\text{mol}$ , 32 % diastereomer 1; 320 mg, 780  $\mu\text{mol}$ , 31 % diastereomer 2) as yellow foam. Diastereomer 1:  $R_f = 0.21$  (petroleum ether/ethyl acetate 1:1). Mp: 42–46 °C.  $[\alpha]_D^{20} = -59.6^\circ$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.32$  (d,  $J = 6.8$  Hz, 3 H), 1.44 (s, 9 H), 2.95 (s, 3 H), 3.77 (s, 3 H), 4.01 (dd,  $J = 17.8$ , 5.2 Hz, 1 H), 4.16 (dd,  $J = 17.8$ , 5.5 Hz, 1 H), 4.63 (qd,  $J = 7.0$ , 7.0 Hz, 1 H), 5.44 (d,  $J = 6.8$  Hz, 1 H), 6.34 (s, 1 H), 6.78 (bs, 1 H), 7.34–7.40 (m, 5 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 18.1$  (q), 28.3 (q), 32.3 (q), 41.2 (t), 46.8 (d), 52.3 (q), 61.1 (d), 79.8 (s), 128.4 (d), 128.8 (d), 129.5 (d), 163.1 (s), 165.0 (s), 169.2 (s) ppm. The  $^{13}\text{C}$  signal of the tertiary carbon of the phenyl group is not visible in the background noise of the spectrum. Diastereomer 2:  $R_f = 0.17$  (petroleum ether/ethyl acetate 1:1). Mp: 42–46 °C.  $[\alpha]_D^{20} = +63.1^\circ$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.38$  (d,  $J = 7.0$  Hz, 3 H), 1.44 (s, 9 H), 2.91 (s, 3 H), 4.00 (dd,  $J = 18.3$ , 5.3 Hz, 1 H), 4.16 (dd,  $J = 18.3$ , 5.5 Hz, 1 H), 4.65 (qd,  $J = 7.5$ , 7.5 Hz, 1 H), 5.49 (d,  $J = 8.0$  Hz, 1 H), 6.37 (s, 1 H), 6.27 (bs, 1 H), 7.36–7.42 (m, 5 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 18.7$  (q), 28.3 (q), 32.2 (q), 41.2 (t), 46.8 (d), 52.4 (q), 60.7 (d), 79.5 (s), 128.7 (d), 128.9 (d), 129.5 (d), 167.5 (s), 169.4 (s), 169.9 (s) ppm. The  $^{13}\text{C}$  signal of the tertiary carbon of the phenyl group is not visible in the background noise of the spectrum. HRMS (CI) calcd for:  $\text{C}_{20}\text{H}_{30}\text{N}_3\text{O}_6^+$   $[\text{M}+\text{H}]^+$ : 408.2129, found: 408.2133.

### (S)-*N*-*tert*-Butoxycarbonyl-alanyl-[*N*-methyl-(4-allyloxy-3-bromo)-phenylglycyl]-glycine methyl ester (**7c**)

According to **GP 1** 241 mg (1.00 mmol) 3-bromo-4-allyloxybenzaldehyde in 1.0 mL trifluoroethanol was reacted with 124  $\mu\text{L}$  (1.00 mmol) methylamine (33 % in EtOH), 227 mg (1.20 mmol) Boc-L-alanine and 90  $\mu\text{L}$  (1.00 mmol) methyl isocynoacetate in 0.2 mL trifluoroethanol in the microwave (100 °C, 150 W, 75 min). Column chromatography (silica gel, petroleum ether/ethyl acetate 1:1) gave rise to the desired tripeptide **7c** (129 mg, 240  $\mu\text{mol}$ , 24 % diastereomer 1; 150 mg, 280  $\mu\text{mol}$ , 28 % diastereomer 2) as brown oil. Diastereomer 1:  $R_f = 0.25$  (petroleum ether/ethyl acetate 1:1)  $[\alpha]_D^{20} = -55.4^\circ$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.32$  (d,  $J = 6.8$  Hz, 3 H), 1.44 (s, 9 H), 2.95 (s, 3 H), 3.77 (s, 3 H), 3.97 (dd,  $J = 18.2$ , 5.7 Hz, 1 H), 4.17 (m, 1 H), 4.58–4.65 (m, 3 H), 5.33 (dd,  $J = 10.5$ , 0.8 Hz, 1 H), 5.36 (bs, 1 H), 5.49 (dd,  $J = 17.3$ , 1.3 Hz, 1 H), 6.06 (ddt,  $J = 17.3$ , 10.5, 5.3 Hz, 1 H), 6.28 (s, 1 H), 6.85 (m, 1 H), 6.89 (d,  $J = 8.5$ , 1 H), 7.30 (dd,  $J = 8.8$ , 1.2 Hz, 1 H), 7.57 (d,  $J = 1.5$  Hz, 1 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 17.9$  (q), 28.3 (q), 32.1 (q), 41.3 (t), 46.8 (d), 52.4 (q), 59.6 (d), 69.7 (t), 80.0 (s), 113.3 (d), 118.0 (t), 123.4 (s), 128.9 (d), 131.3 (d), 132.3 (s), 134.5 (d), 154.3 (s), 165.6 (s), 169.1 (s), 169.3 (s), 169.9 (s) ppm. Diastereomer 2:  $R_f = 0.20$  (petroleum ether/ethyl acetate 1:1)  $[\alpha]_D^{20} = +73.4^\circ$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.39$  (d,  $J = 6.8$  Hz, 3 H), 1.45 (s, 9 H), 2.92 (s, 3 H), 3.78 (s, 3 H), 4.01 (dd,  $J = 18.1$ , 5.2 Hz, 1 H), 4.14 (dd,  $J = 18.3$ , 5.8 Hz, 1 H), 4.61–4.66 (m, 3 H), 5.34 (dd,  $J = 10.6$ , 1.3 Hz, 1 H), 5.43 (d,  $J = 8.0$  Hz, 1 H), 5.50 (dd,  $J = 17.1$ , 1.5 Hz, 1 H), 6.07 (ddt,  $J = 17.3$ , 10.5, 5.0 Hz, 1 H), 6.20 (bs, 1 H), 6.28 (s, 1 H), 6.90 (d,  $J = 8.6$  Hz, 1 H), 7.30 (dd,  $J = 8.5$ , 1.2 Hz, 1 H), 7.60 (d,  $J = 2.2$  Hz, 1 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 18.6$  (q), 28.4 (q), 32.5 (q), 41.3 (t), 46.8 (d), 52.5 (q), 59.6 (d), 69.7 (t), 80.2 (s), 113.4 (d), 118.0 (t), 123.4 (s), 128.9 (d), 131.3 (d), 132.2 (s), 134.4 (d), 154.3 (s), 165.6 (s), 169.1 (s), 169.3 (s), 169.9 (s) ppm. HRMS (CI) calcd for:  $\text{C}_{23}\text{H}_{32}\text{BrN}_3\text{O}_7^+$   $[\text{M}+\text{H}]^+$ : 543.1398, found: 543.1422.

**(S)-*N*-tert-Butoxycarbonyl-alanyl-(*N*-methyl-(4-allyloxy-3-chlor)-phenylglycyl)-glycine methyl ester (7d)**

According to **GP 1** 298 mg (1.52 mmol) 3-chloro-4-allyloxybenzaldehyde in 1.5 mL trifluoroethanol was reacted with 226  $\mu\text{L}$  (1.82 mmol) methylamine (33 % in EtOH), 345 mg (1.82 mmol) Boc-L-alanine and 137  $\mu\text{L}$  (1.52 mmol) methyl isocynoacetate in 0.2 mL trifluoroethanol in the microwave (100 °C, 150 W, 60 min). Column chromatography (silica gel, petroleum ether/ethyl acetate 1:1) gave rise to the desired tripeptide **7d** (213 mg, 430  $\mu\text{mol}$ , 28 %, *dr* = 1:1) as brown foam. Diastereomer 1:  $R_f$  = 0.12 (petroleum ether/ethyl acetate 1:1).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  = 1.33 (d,  $J$  = 6.8 Hz, 3 H), 1.44 (s, 9 H), 2.95 (s, 3 H), 3.77 (s, 3 H), 3.97 (dd,  $J$  = 18.0, 5.2 Hz, 1 H), 4.17 (dd,  $J$  = 17.8, 5.8 Hz, 1 H), 4.61–4.65 (m, 3 H), 5.33 (dd,  $J$  = 10.6, 1.3 Hz, 1 H), 5.37 (m, 1 H), 5.47 (dd,  $J$  = 17.3, 1.5 Hz, 1 H), 6.07 (ddt,  $J$  = 17.3, 10.5, 5.3 Hz, 1 H), 6.28 (s, 1 H), 6.87 (t,  $J$  = 6.3 Hz, 1 H), 6.92 (d,  $J$  = 8.5 Hz, 1 H), 7.25 (dd,  $J$  = 8.5, 2.2 Hz, 1 H), 7.40 (d,  $J$  = 2.2 Hz, 1 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  = 17.9 (q), 28.3 (q), 32.1 (q), 41.3 (t), 46.8 (d), 52.4 (q), 60.0 (d), 69.7 (t), 113.6 (d), 118.1 (t), 123.2 (s), 129.0 (d), 131.9 (d), 132.3 (d), 168.9 (s), 168.9 (s), 170.0 (s) ppm. The tertiary carbons of the phenyl and silyl groups and the carboxy atom of the silyl group are in the background noise of the  $^{13}\text{C-NMR}$  spectrum. Diastereomer 2:  $R_f$  = 0.08 (petroleum ether/ethyl acetate 1:1)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  = 1.38 (d,  $J$  = 6.8 Hz, 3 H), 1.45 (s, 9 H), 2.92 (s, 3 H), 3.77 (s, 3 H), 3.99 (dd,  $J$  = 18.3, 5.3 Hz, 1 H), 4.15 (dd,  $J$  = 18.0, 5.5 Hz, 1 H), 4.62–4.65 (m, 3 H), 5.33 (dd,  $J$  = 10.5, 1.2 Hz, 1 H), 5.44 (m, 1 H), 5.48 (dd,  $J$  = 17.1, 1.3 Hz, 1 H), 6.06 (ddt,  $J$  = 17.0, 10.5, 5.0 Hz, 1 H), 6.29 (s, 1 H), 6.32 (bs, 1 H), 6.92 (d,  $J$  = 8.5 Hz, 1 H), 7.24 (d,  $J$  = 8.8 Hz, 1 H), 7.43 (d,  $J$  = 2.0 Hz, 1 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  = 18.6 (q), 28.3 (q), 32.0 (q), 41.3 (t), 46.8 (d), 52.5 (q), 59.6 (d), 69.7 (t), 113.6 (d), 118.1 (t), 123.4 (s), 128.9 (d), 131.4 (d), 132.3 (d), 154.3 (s), 165.6 (s), 169.1 (s), 169.9 (s) ppm. A tertiary carbon of the phenyl group, a tertiary carbon of the silyl group and the carboxy atom of the silyl group are in the background noise of the  $^{13}\text{C-NMR}$  spectrum. HRMS (CI) calcd for  $\text{C}_{18}\text{H}_{24}\text{ClN}_3\text{O}_5$  [ $\text{M}-\text{C}_5\text{H}_9\text{O}_2$ ] $^+$ : 397.1399, found: 397.1405.

**(S)-*N*-tert-Butoxycarbonyl-alanyl-(*N*-methyl-phenylalanyl)-glycine methyl ester (7f)**

According to **GP 1** 300 mg (2.50 mmol) 2-phenylacetaldehyde in 2.5 mL dichloroethan was reacted with 310  $\mu\text{L}$  (2.50 mmol) methylamine (33 % in EtOH), 681 mg (3.00 mmol) Boc-L-alanine and 225  $\mu\text{L}$  (2.50 mmol) methyl isocynoacetate in the microwave (100 °C, 150 W, 120 min). Column chromatography (silica gel, petroleum ether/ethyl acetate 1:1) gave rise to the desired tripeptide **7f** (351 mg, 830  $\mu\text{mol}$ , 33 %, *dr* = 1:1) as yellowish oil.  $R_f$  = 0.14 (petroleum ether/ethyl acetate 1:1). Diastereomer 1:  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.44 (m, 3 H), 1.46 (s, 9 H), 2.96 (s, 3 H), 3.00 (m, 1 H), 3.44 (dd,  $J$  = 15.0, 5.5 Hz, 1 H), 3.76 (s, 3 H), 3.86 (dd,  $J$  = 17.8, 5.3 Hz, 1 H), 4.16 (m, 1 H), 4.40 (qd,  $J$  = 7.0, 7.0 Hz, 1 H), 5.23 (m, 1 H), 5.65 (m, 1 H), 6.90 (m, 1 H), 7.13–7.31 (m, 5 H) ppm.  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 16.4 (q), 28.3 (q), 33.3 (q), 34.0 (t), 41.1 (t), 52.4 (d), 52.9 (q), 79.1 (s), 128.4 (d), 128.7 (d), 129.0 (d), 129.4 (s), 159.1 (s), 169.8 (s), 169.9 (s), 170.0 (s) ppm. Diastereomer 2 (selected signals):  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.39 (d,  $J$  = 7.0 Hz, 3 H), 1.40 (s, 9 H), 2.97 (s, 3 H), 3.05 (m, 1 H), 3.37 (dd,  $J$  = 14.6, 3.2 Hz, 1 H), 3.74 (s, 3 H), 3.95 (m, 1 H), 4.10 (m, 1 H), 4.24 (m, 1 H), 5.01 (m, 1 H), 5.23 (dd,  $J$  = 7.3, 7.3 Hz, 1 H), 7.13–7.31 (m, 5 H), 8.32 (dd,  $J$  = 5.3, 5.3 Hz, 1 H) ppm.  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 17.3 (q), 28.3 (q), 33.4 (t), 34.0 (q), 41.1 (t), 52.3 (d), 53.0 (q), 79.1 (s), 128.4 (d), 128.7 (d), 129.0 (d), 129.4 (s), 159.1 (s), 169.8 (s), 169.9 (s), 170.0 (s) ppm. HRMS (CI) calcd for:  $\text{C}_{21}\text{H}_{32}\text{N}_3\text{O}_6$  [ $\text{M}+\text{H}$ ] $^+$ : 422.2286, found: 422.2301.

## Saponification of Ugi Products

### (S)-*N*-*tert*-Butoxycarbonyl-alanyl-(*N*-methyl-phenylglycyl)-glycine (8b)

According to **GP 2** 269 mg (660  $\mu$ mol) tripeptide **7b** in 3.3 mL THF/MeOH (3:1) was reacted with 16.6 mg (693  $\mu$ mol) LiOH·H<sub>2</sub>O in 1.3 mL H<sub>2</sub>O. After aqueous workup acid **8b** (218 mg, 550  $\mu$ mol, 84 %, *dr* = 52:48) could be obtained as white foam. *R*<sub>f</sub> = 0.06 (petroleum ether/ethyl acetate 1:1). Diastereomer 1: <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta$  = 1.30 (d, *J* = 7.0 Hz, 3 H), 1.44 (s, 9 H), 2.90 (s, 3 H), 4.09 (m, 2 H), 4.66 (qd, *J* = 6.8, 6.8 Hz, 1 H), 5.51 (d, *J* = 7.3 Hz, 1 H), 6.32 (s, 1 H), 6.99 (s, 1 H), 7.30–7.37 (m, 5 H) ppm. <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta$  = 18.0 (q), 28.3 (q), 32.5 (q), 41.2 (t), 46.9 (d), 61.2 (d), 80.1 (s), 128.5 (d), 128.8 (d), 129.3 (d), 134.3 (s), 155.6 (s), 169.5 (s), 172.1 (s), 174.5 (s) ppm. Diastereomer 2: <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta$  = 1.34 (d, *J* = 6.8 Hz, 3 H), 1.43 (s, 9 H), 2.93 (s, 3 H), 4.09 (m, 2 H), 4.66 (qd, *J* = 6.8, 6.8 Hz, 1 H), 5.55 (d, *J* = 6.8 Hz, 1 H), 6.39 (s, 1 H), 6.79 (s, 1 H), 7.30–7.37 (m, 5 H) ppm. <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta$  = 18.2 (q), 28.3 (q), 32.4 (q), 41.2 (t), 46.8 (d), 60.9 (d), 79.8 (s), 128.6 (d), 128.8 (d), 129.3 (d), 134.3 (s), 155.3 (s), 169.6 (s), 171.9 (s), 174.5 (s) ppm. HRMS (CI) calcd for: C<sub>19</sub>H<sub>28</sub>N<sub>3</sub>O<sub>6</sub><sup>+</sup> [M+H]<sup>+</sup>: 394.1973, found: 394.1960.

### (S)-*N*-*tert*-Butoxycarbonyl-alanyl-[*N*-methyl-(4-allyloxy-3-brom)-phenylglycyl]-glycine (8c)

According to **GP 2** 176 mg (320  $\mu$ mol) tripeptide **7c** in 1.6 mL THF/MeOH (3:1) was reacted with 7.8 mg (340  $\mu$ mol) LiOH·H<sub>2</sub>O in 0.7 mL H<sub>2</sub>O. After aqueous workup acid **8c** (159 mg, 300  $\mu$ mol, 93 %, *dr* = 1:1) could be obtained as orange foam. *R*<sub>f</sub> = 0.09 (petroleum ether/ethyl acetate 1:1). Diastereomer 1: <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta$  = 1.32 (d, *J* = 7.0 Hz, 3 H), 1.44 (s, 9 H), 2.97 (s, 3 H), 3.98 (dd, *J* = 18.6, 5.3 Hz, 1 H), 4.23 (dd, *J* = 18.3, 6.0 Hz, 1 H), 4.62 (d, *J* = 5.0 Hz, 2 H), 4.65 (m, 1 H), 5.33 (dd, *J* = 10.6, 0.8 Hz, 1 H), 5.40 (m, 1 H), 5.49 (dd, *J* = 17.3, 1.5 Hz, 1 H), 6.06 (ddt, *J* = 17.3, 10.8, 5.0 Hz, 1 H), 6.27 (s, 1 H), 6.88 (d, *J* = 8.6 Hz, 1 H), 7.00 (m, 1 H), 7.25 (m, 1 H), 7.54 (d, *J* = 2.0 Hz, 1 H) ppm. <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta$  = 18.0 (q), 28.4 (q), 32.5 (q), 41.3 (t), 46.9 (d), 60.4 (d), 69.7 (t), 113.4 (d), 118.0 (t), 123.4 (s), 127.4 (d), 129.7 (d), 132.2 (s), 155.9 (s), 156.8 (s), 169.2 (s), 169.8 (s), 174.5 (s) ppm. The <sup>13</sup>C signal of the tertiary carbon of the carbamate is not visible in the background noise of the spectrum. Diastereomer 2: <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta$  = 1.36 (d, *J* = 7.0 Hz, 3 H), 1.45 (s, 9 H), 2.93 (s, 3 H), 4.07–4.17 (m, 2 H), 4.62 (d, *J* = 5.0 Hz, 2 H), 4.65 (m, 1 H), 5.33 (dd, *J* = 10.6, 0.8 Hz, 1 H), 5.43 (m, 1 H), 5.49 (dd, *J* = 17.3, 1.5 Hz, 1 H), 6.06 (ddt, *J* = 17.3, 10.8, 5.0 Hz, 1 H), 6.32 (s, 1 H), 6.64 (m, 1 H), 6.88 (d, *J* = 8.6 Hz, 1 H), 7.25 (m, 1 H), 7.57 (d, *J* = 2.0 Hz, 1 H) ppm. <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta$  = 18.3 (q), 28.4 (q), 32.5 (q), 41.4 (t), 46.9 (d), 60.4 (d), 69.7 (t), 113.4 (d), 118.0 (t), 123.4 (s), 127.4 (d), 129.7 (d), 132.2 (s), 132.2 (d), 155.9 (s), 156.8 (s), 169.2 (s), 169.8 (s), 174.6 (s) ppm. The <sup>13</sup>C signal of the tertiary carbon of the carbamate is not visible in the background noise of the spectrum. HRMS (CI) calcd for: C<sub>17</sub>H<sub>22</sub>BrN<sub>3</sub>O<sub>5</sub><sup>+</sup> [M+H]<sup>+</sup>: 427.0737, found: 427.0759.

## Preparation of the tripeptide esters

### (S)-*N*-*tert*-Butoxycarbonyl-alanyl-(*N*-methyl-phenylglycyl)-glycine-(2*S*,6*E*)-10-(allyloxy-carbonyl)-7-methyl-dec-6-en-2-yl ester (9b)

According to **GP 3a** 190 mg (480  $\mu$ mol) acid **8b** in 3.8 mL dry CH<sub>2</sub>Cl<sub>2</sub> was reacted with 127 mg (530  $\mu$ mol) (**S**)-**6**, 6.10 mg (50.0  $\mu$ mol) DMAP and 111 mg (580  $\mu$ mol) EDC·HCl in 1.4 mL dry CH<sub>2</sub>Cl<sub>2</sub>. Purification by column chromatography (silicagel, petroleum ether/ethyl acetate 6:4) gave rise to **9b** (197 mg, 320  $\mu$ mol, 67 %, *dr* = 1:1)

as yellow resin.  $R_f = 0.25$  (petroleum ether/ethyl acetate 6:4). Diastereomer 1:  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.23$  (d,  $J = 6.5$  Hz, 3 H), 1.32 (d,  $J = 6.8$  Hz, 3 H), 1.26–1.38 (m, 4 H), 1.44 (s, 9 H), 1.60 (s, 3 H), 1.98 (td,  $J = 7.0$ , 7.0 Hz, 2 H), 2.31 (t,  $J = 8.0$  Hz, 2 H), 2.44 (t,  $J = 7.5$  Hz, 2 H), 2.92 (s, 3 H), 3.99 (m, 1 H), 4.10 (m, 1 H), 4.57 (dt,  $J = 5.8$ , 1.24 Hz, 2 H), 4.65 (qd,  $J = 7.3$ , 7.3 Hz, 1 H), 4.96 (qt,  $J = 6.0$ , 6.0 Hz, 1 H), 5.12 (m, 1 H), 5.23 (dd,  $J = 10.5$ , 1.2 Hz, 1 H), 5.31 (dd,  $J = 17.3$ , 1.5 Hz, 1 H), 5.45 (d,  $J = 8.3$  Hz, 1 H), 5.91 (ddt,  $J = 17.0$ , 10.5, 5.8 Hz, 1 H), 6.20 (dd,  $J = 5.3$ , 5.3 Hz, 1 H), 6.31 (s, 1 H), 7.34–7.43 (m, 5 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 15.9$  (q), 18.8 (q), 19.9 (q), 25.4 (t), 27.5 (t), 28.4 (q), 32.3 (q), 33.1 (t), 34.6 (t), 35.4 (t), 41.6 (t), 46.8 (d), 60.8 (d), 64.9 (t), 72.7 (d), 118.1 (t), 124.8 (d), 128.7 (d), 128.9 (q), 129.6 (q), 132.3 (s), 133.8 (s), 133.8 (d), 156.5 (s), 169.0 (s), 169.1 (s), 169.2 (s), 169.3 (s) ppm. The  $^{13}\text{C}$  signal of the tertiary carbon of the carbamate is not visible in the background noise of the spectrum. Diastereomer 2:  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.24$  (d,  $J = 6.3$  Hz, 3 H), 1.40 (d,  $J = 6.8$  Hz, 3 H), 1.26–1.38 (m, 4 H), 1.44 (s, 9 H), 1.60 (s, 3 H), 1.98 (td,  $J = 7.0$ , 7.0 Hz, 2 H), 2.31 (t,  $J = 8.0$  Hz, 2 H), 2.44 (t,  $J = 8.5$  Hz, 2 H), 2.95 (s, 3 H), 3.95 (m, 1 H), 4.15 (m, 1 H), 4.57 (dt,  $J = 5.8$ , 1.24 Hz, 2 H), 4.65 (qd,  $J = 7.3$ , 7.3 Hz, 1 H), 4.96 (qt,  $J = 6.0$ , 6.0 Hz, 1 H), 5.12 (m, 1 H), 5.23 (dd,  $J = 10.5$ , 1.2 Hz, 1 H), 5.31 (dd,  $J = 17.3$ , 1.5 Hz, 1 H), 5.47 (d,  $J = 9.0$  Hz, 1 H), 5.91 (ddt,  $J = 17.0$ , 10.5, 5.8 Hz, 1 H), 6.67 (m, 1 H), 6.36 (s, 1 H), 7.34–7.43 (m, 5 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 15.9$  (q), 18.6 (q), 19.9 (q), 25.3 (t), 27.5 (t), 28.4 (q), 32.3 (q), 32.2 (t), 34.6 (t), 35.3 (t), 41.6 (t), 46.7 (d), 60.8 (d), 64.9 (t), 72.6 (d), 118.1 (t), 124.8 (d), 128.7 (d), 128.8 (d), 129.5 (q), 132.3 (s), 133.8 (s), 133.8 (d), 156.5 (s), 169.0 (s), 169.1 (s), 169.2 (s), 169.3 (s) ppm. The  $^{13}\text{C}$  signal of the tertiary carbon of the carbamate is not visible in the background noise of the spectrum. HRMS (CI) calcd for:  $\text{C}_{33}\text{H}_{50}\text{N}_3\text{O}_8^+$  [ $\text{M}+\text{H}$ ] $^+$ : 616.3592, found: 616.3595.

**(S)-N-tert-Butoxycarbonyl-alanyl-[N-methyl-(3-brom-4-allyloxy)-phenylglycyl]-glycine-(2S,6E)-10-(allyloxy-carbonyl)-7-methyl-dec-6-en-2-yl ester (9c)**

According to **GP 3a** 319 mg (600  $\mu\text{mol}$ ) acid **8c** in 4.8 mL dry  $\text{CH}_2\text{Cl}_2$  was reacted with 160 mg (660  $\mu\text{mol}$ ) **(S)-6**, 7.3 mg (60.0  $\mu\text{mol}$ ) DMAP and 139 mg (720  $\mu\text{mol}$ ) EDC-HCl in 1.8 mL dry  $\text{CH}_2\text{Cl}_2$ . Purification by column chromatography (silicagel, petroleum ether/ethyl acetate 6:4) gave rise to **9c** (270 mg, 360  $\mu\text{mol}$ , 60 %,  $dr = 1:1$ ) as yellow resin.  $R_f = 0.25$  (petroleum ether/ethyl acetate 6:4). Diastereomer 1:  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.23$  (d,  $J = 6.2$  Hz, 3 H), 1.28–1.40 (m, 4 H), 1.32 (d,  $J = 6.8$  Hz, 3 H), 1.43 (s, 9 H), 1.60 (s, 3 H), 1.98 (td,  $J = 7.0$ , 7.0 Hz, 2 H), 2.30 (t,  $J = 7.3$  Hz, 2 H), 2.44 (t,  $J = 7.0$  Hz, 2 H), 2.92 (s, 3 H), 4.02 (m, 1 H), 4.56 (d,  $J = 5.5$  Hz, 2 H), 4.60–4.65 (m, 3 H), 4.96 (qt,  $J = 6.0$ , 6.0 Hz, 1 H), 5.13 (m, 1 H), 5.23 (dd,  $J = 10.3$ , 1.0 Hz, 1 H), 5.27–5.35 (m, 2 H), 5.40 (d,  $J = 6.5$  Hz, 1 H), 5.49 (d,  $J = 17.3$  Hz, 1 H), 5.91 (ddt,  $J = 16.8$ , 10.8, 5.5 Hz, 1 H), 6.05 (ddt,  $J = 17.1$ , 10.6, 5.0 Hz, 1 H), 6.26 (s, 1 H), 6.81 (m, 1 H), 6.88 (d,  $J = 8.5$  Hz, 1 H), 7.29 (d,  $J = 8.6$  Hz, 1 H), 7.56 (d,  $J = 2.0$  Hz, 1 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 15.9$  (q), 18.0 (q), 19.9 (q), 25.4 (t), 27.5 (t), 28.3 (q), 32.1 (q), 33.1 (t), 34.6 (t), 35.3 (t), 41.6 (t), 46.8 (d), 60.4 (d), 65.0 (t), 69.7 (t), 72.7 (d), 79.9 (s), 110.0 (s), 113.4 (d), 118.1 (t), 118.1 (t), 124.8 (s), 128.1 (d), 129.8 (d), 132.3 (s), 133.8 (s), 134.4 (d), 155.2 (s), 158.9 (s), 168.7 (s), 168.9 (s), 169.0 (s), 173.0 (s) ppm. Diastereomer 2:  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.23$  (d,  $J = 6.5$  Hz, 3 H), 1.28–1.40 (m, 4 H), 1.38 (d,  $J = 6.8$  Hz, 3 H), 1.43 (s, 9 H), 1.60 (s, 3 H), 1.98 (td,  $J = 7.0$ , 7.0 Hz, 2 H), 2.30 (t,  $J = 7.3$  Hz, 2 H), 2.44 (t,  $J = 7.0$  Hz, 2 H), 2.95 (s, 3 H), 4.02 (m, 1 H), 4.56 (d,  $J = 5.5$  Hz, 2 H), 4.60–4.65 (m, 3 H), 4.96 (qt,  $J = 6.0$ , 6.0 Hz, 1 H), 5.13 (m, 1 H), 5.23 (dd,  $J = 10.3$ , 1.0 Hz, 1 H), 5.27–5.35 (m, 2 H), 5.40 (d,  $J = 6.5$  Hz, 1 H), 5.49 (d,  $J = 17.3$  Hz, 1 H), 5.91 (ddt,  $J = 16.8$ , 10.8, 5.5 Hz, 1 H), 6.05 (ddt,  $J = 17.1$ , 10.6, 5.0 Hz, 1 H), 6.29 (s, 1 H), 6.81 (m, 1 H), 6.88 (d,  $J = 8.5$  Hz, 1 H), 7.29 (d,  $J = 8.6$  Hz, 1 H), 7.58 (d,  $J = 2.0$  Hz, 1 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 15.9$  (q), 18.0 (q), 19.9 (q), 25.3 (t), 27.5 (t), 28.3 (q), 32.0 (q), 33.1 (t), 34.6 (t), 35.3 (t), 41.5 (t), 46.8 (d), 60.4 (d), 65.0 (t),

69.7 (t), 72.5 (d), 79.9 (s), 110.0 (s), 113.3 (d), 118.1 (t), 118.1 (t), 124.8 (s), 128.1 (d), 129.7 (d), 132.3 (s), 133.8 (s), 134.4 (d), 134.4 (d), 155.2 (s), 158.9 (s), 168.7 (s), 168.9 (s), 169.0 (s), 173.0 (s) ppm.

**(S)-N-tert-Butoxycarbonyl-alanyl-[N-methyl-(3-chlor-4-allyloxy)-phenylglycyl]-glycine-(2S,6E)-10-(allyloxy-carbonyl)-7-methyl-dec-6-en-2-yl ester (9d)**

According to **GP 2** 294 mg (590  $\mu$ mol) tripeptide **7d** in 3.0 mL THF/MeOH (3:1) was reacted with 26.5 mg (620  $\mu$ mol) LiOH·H<sub>2</sub>O in 0.6 mL H<sub>2</sub>O to the free acid **8d** (277 mg, 570  $\mu$ mol, 96%). According to **GP 3a** the crude acid (246 mg, 510  $\mu$ mol) in 4.1 mL dry CH<sub>2</sub>Cl<sub>2</sub> was reacted with 135 mg (560  $\mu$ mol) **(S)-6**, 6.20 mg (50.0  $\mu$ mol) DMAP and 117 mg (610  $\mu$ mol) EDC·HCl in 1.5 mL dry CH<sub>2</sub>Cl<sub>2</sub>. Purification by column chromatography (silicagel, petroleum ether/ethyl acetate 6:4) gave rise to **9d** (217 mg, 310  $\mu$ mol, 60 %, *dr* = 1:1) as brown resin. *R*<sub>f</sub> = 0.26 (petroleum ether/ethyl acetate 6:4). Diastereomer 1: <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta$  = 1.23 (d, *J* = 6.2 Hz, 3 H), 1.25–1.56 (m, 4 H), 1.32 (d, *J* = 6.8 Hz, 3 H), 1.44 (s, 9 H), 1.60 (s, 3 H), 1.98 (td, *J* = 7.0, 7.0 Hz, 2 H), 2.31 (t, *J* = 7.3 Hz, 2 H), 2.44 (t, *J* = 7.3 Hz, 2 H), 2.92 (s, 3 H), 3.97 (dd, *J* = 18.0, 5.0 Hz, 1 H), 4.09 (m, 1 H), 4.57 (d, *J* = 5.8 Hz, 2 H), 4.59–4.67 (m, 3 H), 4.96 (qt, *J* = 6.5, 6.5 Hz, 1 H), 5.13 (m, 1 H), 5.23 (dd, *J* = 10.3, 1.2 Hz, 1 H), 5.28–5.36 (m, 2 H), 5.40 (d, *J* = 6.0 Hz, 1 H), 5.47 (d, *J* = 17.3 Hz, 1 H), 5.91 (ddt, *J* = 16.6, 10.8, 5.8 Hz, 1 H), 6.06 (ddt, *J* = 17.3, 10.8, 5.0 Hz, 1 H), 6.26 (s, 1 H), 6.80 (m, 1 H), 6.92 (d, *J* = 8.5 Hz, 1 H), 7.24 (dd, *J* = 8.6, 2.2 Hz, 1 H), 7.40 (d, *J* = 2.0 Hz, 1 H) ppm. <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta$  = 15.9 (q), 18.0 (q), 19.9 (q), 25.4 (t), 27.5 (t), 28.3 (q), 32.2 (q), 33.1 (t), 34.6 (t), 35.3 (t), 41.5 (t), 46.8 (d), 60.3 (d), 65.0 (t), 69.7 (t), 72.7 (d), 79.9 (s), 113.6 (d), 118.1 (t), 118.1 (t), 123.4 (s), 124.8 (d), 131.4 (d), 132.3 (s), 132.3 (d), 133.8 (s), 133.8 (d), 155.1 (s), 158.9 (s), 168.7 (s), 168.9 (s), 169.0 (s), 173.0 (s) ppm. Diastereomer 2: <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta$  = 1.24 (d, *J* = 6.3 Hz, 3 H), 1.25–1.56 (m, 4 H), 1.38 (d, *J* = 6.8 Hz, 3 H), 1.43 (s, 9 H), 1.60 (s, 3 H), 1.98 (td, *J* = 7.0, 7.0 Hz, 2 H), 2.31 (t, *J* = 7.3 Hz, 2 H), 2.44 (t, *J* = 7.3 Hz, 2 H), 2.95 (s, 3 H), 3.92 (dd, *J* = 16.6, 5.0 Hz, 1 H), 4.13 (m, 1 H), 4.57 (d, *J* = 5.8 Hz, 2 H), 4.59–4.67 (m, 3 H), 4.96 (qt, *J* = 6.5, 6.5 Hz, 1 H), 5.13 (m, 1 H), 5.23 (dd, *J* = 10.3, 1.2 Hz, 1 H), 5.28–5.36 (m, 2 H), 5.40 (d, *J* = 6.0 Hz, 1 H), 5.47 (d, *J* = 17.3 Hz, 1 H), 5.91 (ddt, *J* = 16.6, 10.8, 5.8 Hz, 1 H), 6.06 (ddt, *J* = 17.3, 10.8, 5.0 Hz, 1 H), 6.29 (s, 1 H), 6.80 (m, 1 H), 6.92 (d, *J* = 8.5 Hz, 1 H), 7.24 (dd, *J* = 8.6, 2.2 Hz, 1 H), 7.42 (d, *J* = 2.0 Hz, 1 H) ppm. <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta$  = 15.9 (q), 18.0 (q), 19.9 (q), 25.4 (t), 27.5 (t), 28.3 (q), 32.2 (q), 33.1 (t), 34.6 (t), 35.4 (t), 41.6 (t), 46.8 (d), 60.1 (d), 65.0 (t), 69.7 (t), 72.7 (d), 79.9 (s), 113.6 (d), 118.1 (t), 123.4 (s), 124.8 (d), 131.4 (d), 132.3 (s), 132.3 (d), 133.8 (s), 133.8 (d), 155.1 (s), 158.9 (s), 168.7 (s), 168.9 (s), 169.0 (s), 173.0 (s) ppm. HRMS (CI) calcd for: C<sub>31</sub>H<sub>44</sub>ClN<sub>3</sub>O<sub>7</sub><sup>+</sup> [M+H]<sup>+</sup>: 605.2861, found: 605.2860.

**(S)-N-tert-Butoxycarbonyl-alanyl-(N-methyl-2-naphthylglycyl)-glycine-(2S,6E)-10-(allyloxycarbonyl)-7-methyl-dec-6-en-2-yl ester (9e)**

According to **GP 2** methyl ester **7e** (251 mg, 570  $\mu$ mol) in THF/MeOH (3:1, 2.8 mL) was saponified with a solution of LiOH (25.7 mg, 600  $\mu$ mol) in H<sub>2</sub>O (1.9 mL). The crude acid **8e** (250 mg, 570  $\mu$ mol, quant., *dr* 1:1) was directly used without further purification. For that, the acid (222 mg, 500  $\mu$ mol) in 4.0 mL dry CH<sub>2</sub>Cl<sub>2</sub> was converted according to **GP 3a** with 132 mg (550  $\mu$ mol) **(S)-6**, 6.1 mg (50.0  $\mu$ mol) DMAP and 115 mg (600  $\mu$ mol) EDC·HCl in 1.5 mL dry CH<sub>2</sub>Cl<sub>2</sub>. Purification by column chromatography (silicagel, petroleum ether/ethyl acetate 6:4) gave rise to **9e** (198 mg, 296  $\mu$ mol, 59 %, *dr* = 54:46) as colorless oil. Diastereomer 1: *R*<sub>f</sub> = 0.20 (petroleum ether/ethyl acetate 6:4). <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.23 (d, *J* = 6.3 Hz, 3 H), 1.27–1.56 (m, 4 H), 1.33 (d, *J* = 6.5 Hz, 3 H), 1.44 (s, 9 H), 1.60 (s, 3 H), 1.97 (td, *J* = 7.0, 7.0 Hz, 2 H), 2.30 (m, 2 H), 2.42 (m, 2 H), 2.94 (s, 3 H), 4.02 (dd, *J* = 17.6 Hz, 5.0 Hz, 1 H), 4.17 (m, 1 H), 4.55 (m, 2 H), 4.67 (dq, *J* = 7.0, 7.0 Hz, 1 H), 4.97 (m, 1 H), 5.12 (t, *J* = 6.8 Hz, 1 H), 5.22 (d, *J* = 10.3 Hz, 1 H), 5.30 (d, *J* = 17.0 Hz, 1 H), 5.50 (m, 1 H), 5.90 (m, 1 H), 6.39 (bs, 1 H), 6.50 (s, 1 H),



7.40 (m, 1 H), 7.47-7.55 (m, 2 H), 7.80-7.90 (m, 3 H), 7.94 (s, 1 H) ppm.  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 15.9 (q), 18.2 (q), 19.9 (q), 25.3 (t), 27.5 (t), 28.3 (q), 32.4 (q), 33.1 (t), 34.6 (t), 35.4 (t), 41.6 (t), 46.8 (d), 60.3 (d), 64.9 (t), 72.6 (d), 79.5 (s), 118.0 (t), 124.8 (d), 126.4, 126.5, 126.6 (3 d), 127.6 (s), 128.2 (s), 128.7 (s), 129.0 (d), 131.9 (s), 132.2 (d), 133.0 (s), 133.1 (s), 133.8 (s), 155.5 (s), 169.0 (s), 169.2 (s), 169.3 (s), 173.0 (s) ppm. Diastereomer 2:  $R_f$  = 0.16 (petroleum ether/ethyl acetate 6:4). (selected signals):  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.41 (d,  $J$  = 6.8 Hz, 3 H), 1.59 (s, 9 H), 2.30 (m, 2 H), 2.42 (m, 2 H), 2.97 (s, 3 H), 3.98 (dd,  $J$  = 17.8 Hz, 4.6 Hz, 1 H), 4.55 (m, 2 H), 5.11 (t,  $J$  = 6.2 Hz, 1 H), 5.50 (m, 1 H), 6.54 (s, 1 H), 6.82 (bs, 1 H), 7.37 (d,  $J$  = 9.6 Hz, 1 H) ppm.  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 18.7 (q), 25.3 (t), 27.5 (t), 32.2 (q), 35.3 (t), 41.6 (t), 72.5 (d), 79.8 (s), 124.8 (d), 126.6 (d), 126.7 (d), 126.7 (d), 129.0 (d), 131.5 (s), 133.0 (s), 133.1 (s), 133.8 (s), 155.1 (s) ppm. HRMS (CI) calcd for:  $\text{C}_{37}\text{H}_{52}\text{N}_3\text{O}_8^+$   $[\text{M}+\text{H}]^+$ : 666.3749, found: 666.3750.

**(S)-N-tert-Butoxycarbonyl-alanyl-(N-methyl-phenylalanyl)-glycine-(2S,6E)-10-(allyloxycarbonyl)-7-methyl-dec-6-en-2-yl ester (9f)**

According to **GP 2** 307 mg (728  $\mu\text{mol}$ ) Tripeptide **7f** in 3.6 mL THF/MeOH (3:1) was reacted with 18.3 mg (764  $\mu\text{mol}$ ) LiOH·H<sub>2</sub>O in 1.5 mL H<sub>2</sub>O. After aqueous workup, 181 mg (440  $\mu\text{mol}$ , 60%) crude acid **8f** in 3.5 mL dry  $\text{CH}_2\text{Cl}_2$  was converted directly according to **GP 3a** with 115 mg (480  $\mu\text{mol}$ ) **(S)-6**, 5.40 mg (44.0  $\mu\text{mol}$ ) DMAP and 102 mg (530  $\mu\text{mol}$ ) EDC·HCl in 3.5 mL dry  $\text{CH}_2\text{Cl}_2$ . Purification by column chromatography (silicagel, petroleum ether/ethyl acetate 6:4) gave rise to **9f** (166 mg, 263  $\mu\text{mol}$ , 60 %,  $dr$  = 63:37) as colorless oil.  $R_f$  = 0.21 (petroleum ether/ethyl acetate 6:4). Diastereomer 1:  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.84 (d,  $J$  = 6.8 Hz, 3 H), 1.27 (d,  $J$  = 7.3 Hz, 3 H), 1.30-1.58 (m, 4 H), 1.40 (s, 9 H), 1.60 (s, 3 H), 1.98 (td,  $J$  = 7.3, 7.3 Hz, 2 H), 2.31 (t,  $J$  = 7.3 Hz, 2 H), 2.44 (t,  $J$  = 7.6 Hz, 2 H), 2.96 (s, 3 H), 3.05 (m, 1 H), 3.43 (dd,  $J$  = 15.0, 5.3 Hz, 1 H), 3.85 (m, 1 H), 4.08 (m, 1 H), 4.49 (m, 1 H), 4.57 (d,  $J$  = 5.8 Hz, 2 H), 4.93 (m, 1 H), 5.13 (t,  $J$  = 6.8 Hz, 1 H), 5.23 (d,  $J$  = 10.5 Hz, 1 H), 5.24 (bs, 1 H), 5.31 (dd,  $J$  = 17.3, 1.3 Hz, 1 H), 5.64 (m, 1 H), 5.91 (ddt,  $J$  = 16.8, 10.6, 5.8 Hz, 1 H), 6.84 (m, 1 H), 7.12-7.31 (m, 5 H) ppm.  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 15.9 (q), 17.3 (q), 19.9 (q), 25.3 (t), 27.5 (t), 28.3 (3 q), 30.8 (q), 33.1 (t), 33.4 (t), 34.6 (t), 35.4 (t), 41.3 (t), 46.5 (d), 56.8 (d), 65.0 (t), 72.4 (d), 79.8 (s), 118.1 (t), 124.8 (d), 128.4 (d), 128.4 (d), 128.7 (d), 132.2 (d), 133.7 (s), 137.7 (s), 155.6 (s), 169.1 (s), 169.5 (s), 170.1 (s), 173.0 (s) ppm. Diastereomer 2 (selected signals):  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.16-1.34 (m, 6 H), 1.37 (s, 9 H), 2.97 (s, 3 H), 3.05 (m, 1 H), 3.22 (m, 1 H), 3.85 (m, 1 H), 4.08 (m, 1 H), 4.94 (m, 1 H) ppm.  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 28.2 (q), 72.1 (d), 80.6 (s), 129.4 (d), 129.4 (d) ppm. Rotamer (selected signals):  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.16-1.34 (m, 6 H), 1.36 (s, 9 H), 3.05 (m, 1 H), 3.22 (m, 1 H), 3.85 (m, 1 H), 4.08 (m, 1 H) ppm. HRMS (CI) calcd for:  $\text{C}_{34}\text{H}_{52}\text{N}_3\text{O}_8^+$   $[\text{M}+\text{H}]^+$ : 630.3749, found: 630.3755.

**(S)-(N-tert-Butoxycarbonyl-alanyl)-(R)-(O-allyl-3-bromo-N-methyl-tyrosyl)-glycine-(2S,6E)-10-(allyloxycarbonyl)-7-methyl-dec-6-en-2-yl ester (9g)**

According to **GP 3a** 180 mg (380  $\mu\text{mol}$ ) crude acid **8g**<sup>3</sup> in 3.0 mL dry  $\text{CH}_2\text{Cl}_2$  was reacted with 101 mg (420  $\mu\text{mol}$ ) **(S)-6**, 4.6 mg (38.0  $\mu\text{mol}$ ) DMAP and 88.2 mg (460  $\mu\text{mol}$ ) EDC·HCl in 1.1 mL dry  $\text{CH}_2\text{Cl}_2$ . Purification by column chromatography (silicagel, petroleum ether/ethyl acetate 1:1) gave rise to **9g** (142 mg, 186  $\mu\text{mol}$ , 49 %) as colorless oil.  $R_f$  = 0.33 (petroleum ether/ethyl acetate 1:1).  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.97 (d,  $J$  = 7.0 Hz, 3 H), 1.21 (d,  $J$  = 6.2 Hz, 3 H), 1.40 (s, 9 H), 1.25-1.37 (m, 4 H), 1.60 (s, 3 H), 1.97 (td,  $J$  = 7.3, 7.3 Hz, 2 H), 2.30 (t,  $J$  = 8.0 Hz, 2 H), 2.43 (t,  $J$  = 8.3 Hz, 2 H), 2.91 (m, 1 H), 2.96 (s, 3 H), 3.35 (dd,  $J$  = 15.3, 5.5 Hz, 1 H), 3.78 (dd,  $J$  =

<sup>3</sup> a) L. Karmann, K. Schulz, J. Herrmann, R. Müller, U. Kazmaier, *Angew. Chem.* **2015**, 127, 4585–4590; *Angew. Chem. Int. Ed.* **2015**, 54, 4502–4507. b) S. Kappler, L. Karmann, C. Prudel, J. Herrmann, G. Caddeu, R. Müller, A. M. Vollmar, S. Zahler, U. Kazmaier, *Eur. J. Org. Chem.* **2018**, 6952–6965.

17.8, 4.8 Hz, 1 H), 4.12 (m, 1 H), 4.43 (qd,  $J = 6.8, 6.8$  Hz, 1 H), 4.54–4.58 (m, 4 H), 4.93 (qt,  $J = 6.2, 6.2$  Hz, 1 H), 5.12 (t,  $J = 7.0$  Hz, 1 H), 5.19–5.34 (m, 4 H), 5.44 (dd,  $J = 17.8, 1.5$  Hz, 1 H), 5.55 (dd,  $J = 10.8, 5.8$  Hz, 1 H), 5.90 (ddt,  $J = 17.1, 11.3, 5.8$  Hz, 1 H), 6.02 (ddt,  $J = 17.3, 10.5, 5.0$  Hz, 1 H), 6.78 (d,  $J = 8.3$  Hz, 1 H), 6.88 (bs, 1 H), 7.07 (dd,  $J = 8.5, 2.0$  Hz, 1 H), 7.34 (d,  $J = 1.8$  Hz, 1 H) ppm.  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 15.9$  (q), 17.4 (q), 19.9 (q), 25.3 (t), 27.5 (t), 28.3 (q), 30.8 (q), 32.2 (t), 33.1 (t), 34.6 (t), 35.3 (t), 41.3 (t), 46.5 (d), 56.6 (d), 64.9 (t), 69.9 (t), 72.3 (d), 79.9 (s), 112.0 (s), 113.6 (d), 117.7 (t), 118.0 (t), 124.8 (d), 128.6 (d), 130.8 (s), 132.2 (d), 132.5 (d), 133.4 (d), 133.7 (s), 153.6 (s), 155.7 (s), 169.1 (s), 169.9 (s), 173.0 (s), 174.9 (s) ppm. HRMS (CI) calcd for:  $\text{C}_{37}\text{H}_{47}\text{BrN}_3\text{O}_7^+$   $[\text{M}+\text{H}]^+$ : 664.2592, found: 664.2587.

### **(S)-*N*-tert-Butoxycarbonyl-alanyl-(*N*-methyl-phenylglycyl)-glycine-(2*S*,6*E*)-10-carboxy-7-methyl-dec-6-en-2-yl ester (10b)**

According to **GP 4** 164 mg (270  $\mu\text{mol}$ ) allylester **9b** in 5.4 mL dry THF was reacted with 31.2 mg (30.0  $\mu\text{mol}$ )  $\text{Pd}(\text{PPh}_3)_4$  and 46.7  $\mu\text{L}$  (640  $\mu\text{mol}$ ) morpholin. After column chromatography (silica gel, petroleum ether/ethyl acetate 1:1) acid **10b** (80.7 mg, 140  $\mu\text{mol}$ , 52 % d. Th.,  $dr = 2:1$ ) could be isolated as yellow resin. Diastereomer 1:  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.22$  (d,  $J = 6.3$  Hz, 3 H), 1.31 (d,  $J = 6.8$  Hz, 3 H), 1.24–1.40 (m, 4 H), 1.43 (s, 9 H), 1.60 (s, 3 H), 1.98 (td,  $J = 6.8, 6.8$  Hz, 2 H), 2.30 (t,  $J = 7.0$  Hz, 2 H), 2.43 (t,  $J = 7.0$  Hz, 2 H), 2.94 (s, 3 H), 3.96 (dd,  $J = 18.0, 5.2$  Hz, 1 H), 4.13 (dd,  $J = 18.1, 6.0$  Hz, 1 H), 4.67 (qd,  $J = 7.0, 7.0$  Hz, 1 H), 4.98 (qt,  $J = 6.0, 6.0$  Hz, 1 H), 5.14 (t,  $J = 6.5$  Hz, 1 H), 5.64 (d,  $J = 7.3$  Hz, 1 H), 6.33 (s, 1 H), 6.98 (dd,  $J = 5.3, 5.3$  Hz, 1 H), 7.32–7.41 (m, 5 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 15.9$  (q), 19.7 (q), 20.8 (q), 25.0 (t), 27.3 (t), 28.3 (q), 32.4 (q), 32.9 (t), 34.6 (t), 34.9 (t), 41.6 (t), 46.8 (d), 61.2 (d), 72.4 (d), 79.6 (s), 124.8 (d), 128.4 (d), 128.5 (d), 128.8 (d), 132.0 (s), 132.1 (s), 155.6 (s), 169.2 (s), 175.9 (s) ppm. Diastereomer 2:  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.19$  (m, 3 H), 1.37 (d,  $J = 6.8$  Hz, 3 H), 1.24–1.40 (m, 4 H), 1.44 (s, 9 H), 1.60 (s, 3 H), 1.98 (td,  $J = 6.8$  Hz, 2 H), 2.30 (t,  $J = 7.0$  Hz, 2 H), 2.43 (t,  $J = 7.0$  Hz, 2 H), 2.92 (s, 3 H), 4.03 (d,  $J = 5.5$  Hz, 2 H), 4.67 (qd,  $J = 7.0, 7.0$  Hz, 1 H), 4.98 (qt,  $J = 6.0, 6.0$  Hz, 1 H), 5.14 (t,  $J = 6.5$  Hz, 1 H), 5.59 (d,  $J = 8.3$  Hz, 1 H), 6.36 (s, 1 H), 6.59 (dd,  $J = 5.3, 5.3$  Hz, 1 H), 7.32–7.41 (m, 5 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 15.9$  (q), 19.8 (q), 20.8 (q), 25.02 (t), 27.2 (t), 28.3 (3 q), 32.3 (q), 32.8 (t), 34.5 (t), 35.0 (t), 41.6 (t), 46.8 (d), 61.2 (d), 72.6 (d), 79.8 (s), 124.8 (d), 128.4 (d), 128.5 (q), 128.9 (d), 131.8 (s), 131.9 (s), 155.6 (s), 169.2 (s), 175.9 (s) ppm. HRMS (CI) calcd for:  $\text{C}_{30}\text{H}_{46}\text{N}_3\text{O}_8$   $[\text{M}+\text{H}]^+$ : 576.3279, found: 576.3286.

### **(S)-*N*-tert-Butoxycarbonyl-alanyl-[*N*-methyl-(3-brom-4-hydroxy)-phenylglycyl]-glycine-(2*S*,6*E*)-10-carboxy-7-methyl-dec-6-en-2-yl ester (10c)**

According to **GP 4** 242 mg (320  $\mu\text{mol}$ ) allylester **9c** in 6.4 mL dry THF was reacted with 37.2 mg (30.0  $\mu\text{mol}$ )  $\text{Pd}(\text{PPh}_3)_4$  and 33.5  $\mu\text{L}$  (390  $\mu\text{mol}$ ) morpholin. After aqueous workup and evaporation of the solvent acid **10c** (179 mg, 270  $\mu\text{mol}$ , 83 % d. Th.,  $dr = 1:1$ ) could be isolated as yellow resin.  $R_f = 0.11$  (petroleum ether/ethyl acetate 1:1). Diastereomer 1:  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.24$  (m, 3 H), 1.28–1.41 (m, 4 H), 1.32 (d,  $J = 7.0$  Hz, 3 H), 1.45 (s, 9 H), 1.61 (s, 3 H), 1.99 (m, 2 H), 2.31 (m, 2 H), 2.45 (t,  $J = 6.8$  Hz, 2 H), 2.95 (s, 3 H), 4.04 (m, 2 H), 4.66 (qd,  $J = 6.8$  Hz, 1 H), 4.99 (qt,  $J = 6.0$  Hz, 1 H), 5.14 (t,  $J = 7.3$  Hz, 1 H), 5.56 (d,  $J = 8.3$  Hz, 1 H), 6.27 (s, 1 H), 6.71 (dd,  $J = 5.5, 5.5$  Hz, 1 H), 6.99 (d,  $J = 8.3$  Hz, 1 H), 7.21 (d,  $J = 8.3$  Hz, 1 H), 7.52 (d,  $J = 2.0$  Hz, 1 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 15.9$  (q), 17.9 (q), 19.8 (q), 25.2 (t), 27.1 (t), 28.3 (3 q), 32.3 (q), 32.5 (t), 34.4 (t), 34.9 (t), 41.7 (t), 46.9 (d), 60.4 (d), 72.7 (d), 79.9 (s), 110.5 (s), 116.4 (d), 125.1 (d), 128.5 (d), 130.2 (s), 132.1 (d), 133.2 (s), 152.9 (s), 155.3 (s), 169.1 (s), 169.3 (s), 174.4 (s), 176.2 (s) ppm. Diastereomer 2:  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.25$  (m, 3 H), 1.28–1.41 (4 H, 17-H), 1.37 (d,  $J = 6.8$  Hz, 3 H), 1.44 (s, 9 H), 1.61 (s, 3 H), 1.99 (m, 2 H), 2.31 (m, 2 H), 2.45 (t,  $J = 6.8$  Hz, 2 H), 2.95 (s, 3 H), 4.04 (m, 2 H), 4.66 (qd,  $J = 6.8, 6.8$  Hz, 1 H), 4.99 (qt,  $J = 6.0,$

6.0 Hz, 1 H), 5.14 (t,  $J = 7.3$  Hz, 1 H), 5.65 (d,  $J = 7.3$  Hz, 1 H), 6.28 (s, 1 H), 6.71 (dd,  $J = 5.5, 5.5$  Hz, 1 H), 6.99 (d,  $J = 8.6$  Hz, 1 H), 7.21 (d,  $J = 8.5$  Hz, 1 H), 7.50 (d,  $J = 2.0$  Hz, 1 H) ppm.  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 15.9$  (q), 17.9 (q), 19.8 (q), 25.2 (t), 27.2 (t), 28.3 (3 q), 32.3 (q), 32.5 (t), 34.8 (t), 34.9 (t), 41.7 (t), 46.9 (d), 60.4 (d), 72.5 (d), 79.9 (s), 110.5 (s), 116.3 (d), 125.1 (d), 128.6 (d), 130.4 (s), 132.2 (d), 133.3 (s), 152.7 (s), 155.3 (s), 169.1 (s), 169.3 (s), 174.4 (s), 176.2 (s) ppm.

**(S)-N-tert-Butoxycarbonyl-alanyl-[N-methyl-(3-chlor-4-hydroxy)-phenylglycyl]-glycine-(2S,6E)-10-carboxy-7-methyl-dec-6-en-2-yl ester (10d)**

According to **GP 4** 199 mg (280  $\mu\text{mol}$ ) allylester **9d** in 5.6 mL dry THF was reacted with 32.4 mg (30.0  $\mu\text{mol}$ )  $\text{Pd}(\text{PPh}_3)_4$  and 29.2  $\mu\text{L}$  (340  $\mu\text{mol}$ ) morpholin. After aqueous workup and evaporation of the solvent acid **10d** (173 mg, 280  $\mu\text{mol}$ , 98 % d. Th.,  $dr = 1:1$ ) could be isolated as brown resin.  $R_f = 0.11$  (petroleum ether/ethyl acetate 1:1). Diastereomer 1:  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.25$  (d,  $J = 7.3$  Hz, 3 H), 1.28–1.40 (m, 4 H), 1.31 (d,  $J = 7.0$  Hz, 3 H), 1.44 (s, 9 H), 1.60 (s, 3 H), 1.98 (m, 2 H), 2.30 (t,  $J = 6.5$  Hz, 2 H), 2.44 (m, 2 H), 2.93 (s, 3 H), 3.94 (m, 2 H), 4.64 (qd,  $J = 7.0, 7.0$  Hz, 1 H), 4.98 (qt,  $J = 6.0, 6.0$  Hz, 1 H), 5.14 (t,  $J = 7.0$  Hz, 1 H), 5.57 (d,  $J = 8.0$  Hz, 1 H), 6.25 (s, 1 H), 6.71 (dd,  $J = 5.2, 5.2$  Hz, 1 H), 6.95 (d,  $J = 6.8$  Hz, 1 H), 7.14 (d,  $J = 8.3$  Hz, 1 H), 7.35 (m, 1 H) ppm.  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 15.9$  (q), 17.9 (q), 19.8 (q), 25.2 (t), 27.2 (t), 28.3 (q), 32.3 (q), 32.6 (t), 34.4 (t), 34.9 (t), 41.7 (t), 46.9 (d), 60.3 (d), 72.6 (d), 79.9 (s), 116.7 (d), 120.4 (s), 125.0 (d), 128.5 (d), 130.3 (s), 132.0 (d), 133.6 (s), 152.0 (s), 155.4 (s), 169.2 (s), 171.2 (s), 174.5 (s), 176.5 (s) ppm. Diastereomer 2:  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.27$  (d,  $J = 7.0$  Hz, 3 H), 1.28–1.40 (m, 4 H), 1.36 (d,  $J = 7.0$  Hz, 3 H), 1.43 (s, 9 H), 1.60 (s, 3 H), 1.98 (m, 2 H), 2.30 (t,  $J = 6.5$  Hz, 2 H), 2.43 (m, 2 H), 2.95 (s, 3 H), 3.94 (m, 2 H), 4.64 (qd,  $J = 7.0$  Hz, 1 H), 4.98 (qt,  $J = 6.0, 6.0$  Hz, 1 H), 5.14 (t,  $J = 7.0$  Hz, 1 H), 5.63 (d,  $J = 7.3$  Hz, 1 H), 6.27 (s, 1 H), 6.71 (dd,  $J = 5.2, 5.2$  Hz, 1 H), 6.97 (d,  $J = 7.3$  Hz, 1 H), 7.14 (d,  $J = 8.3$  Hz, 1 H), 7.35 (m, 1 H) ppm.  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 15.8$  (q), 18.3 (q), 19.6 (q), 24.9 (t), 27.2 (t), 28.3 (3 q), 32.2 (q), 32.7 (t), 34.5 (t), 34.9 (t), 41.7 (t), 46.9 (d), 60.3 (d), 72.5 (d), 80.1 (s), 116.6 (d), 120.3 (s), 125.1 (d), 128.6 (d), 130.4 (s), 132.1 (d), 133.6 (s), 151.8 (s), 155.8 (s), 169.3 (s), 171.2 (s), 174.4 (s), 176.4 (s) ppm. HRMS (CI) calcd for:  $\text{C}_{25}\text{H}_{35}\text{ClN}_3\text{O}_7^+$  [(M-Boc)+H] $^+$ : 524.2158, found: 524.2139.

**(S)-N-tert-Butoxycarbonyl-alanyl-(N-methyl-(4-allyloxy-3-chlor)-phenylglycyl)-glycine-(2S,5E)-10-(tert-butylidimethylsiloxy)-5-methyl-dec-5-en-2-yl ester (12d)**

According to **GP 2** 294 mg (590  $\mu\text{mol}$ ) tripeptide **7d** in 3.0 mL THF/MeOH (3:1) was reacted with 26.5 mg (620  $\mu\text{mol}$ )  $\text{LiOH}\cdot\text{H}_2\text{O}$  in 0.6 mL  $\text{H}_2\text{O}$ . After aqueous workup, 277 mg (570  $\mu\text{mol}$ , 96%) crude acid **8d** in 4.6 mL dry  $\text{CH}_2\text{Cl}_2$  was converted according to **GP 3b** with 189 mg (630  $\mu\text{mol}$ ) **(S)-2**, 83.1 mg (680  $\mu\text{mol}$ ) DMAP and 140 mg (680  $\mu\text{mol}$ ) DCC in 1.7 mL dry  $\text{CH}_2\text{Cl}_2$ . Purification by column chromatography (silicagel, petroleum ether/ethyl acetate 6:4) gave rise to **12d** (206 mg, 266  $\mu\text{mol}$ , 47 %,  $dr = 1:1$ ) as colorless oil. Additionally alcohol **(S)-2** (95.4 mg, 317  $\mu\text{mol}$ , 50 %) could be reisolated.  $R_f = 0.25$  (petroleum ether/ethyl acetate 6:4). Diastereomer 1:  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.04$  (s, 6 H), 0.89 (s, 9 H), 1.25 (d,  $J = 6.1$  Hz, 3 H), 1.35 (m, 2 H), 1.38 (d,  $J = 7.0$  Hz, 3 H), 1.43 (s, 9 H), 1.50 (tt,  $J = 7.0, 7.0$  Hz, 2 H), 1.58 (s, 3 H), 1.74 (m, 2 H), 1.93–2.03 (m, 4 H), 2.92 (s, 3 H), 3.60 (t,  $J = 6.5$  Hz, 2 H), 3.96 (dd,  $J = 18.2, 5.2$  Hz, 1 H), 4.10 (dd,  $J = 19.1, 5.4$  Hz, 1 H), 4.59–4.67 (m, 3 H), 4.94 (m, 1 H), 5.12 (m, 1 H), 5.23 (d,  $J = 10.5$  Hz, 1 H), 5.40 (d,  $J = 6.6$  Hz, 1 H), 5.47 (d,  $J = 17.4$  Hz, 1 H), 6.06 (ddt,  $J = 17.1, 10.8, 5.3$  Hz, 1 H), 6.29 (s, 1 H), 6.83 (m, 1 H), 6.91 (dd,  $J = 8.4, 2.3$  Hz, 1 H), 7.24 (d,  $J = 8.4$  Hz, 1 H), 7.39 (d,  $J = 1.8$  Hz, 1 H) ppm.  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = -5.3$  (q), 15.9 (q), 18.3 (q), 19.8 (q), 26.0 (t, q, C-23), 27.6 (t), 28.3 (q), 32.1 (t), 32.5 (q), 34.2 (t), 35.3 (t), 41.6 (t), 46.8 (d), 60.0 (d), 63.1 (t), 69.7 (t), 72.6 (d), 79.9 (s), 113.6 (d), 118.0 (t), 123.4 (s), 125.1 (d), 127.7 (s), 128.9 (d), 131.3 (d), 132.3 (d), 133.8 (s), 154.3 (s), 155.6 (s), 168.7 (s), 169.0 (s),

174.1 (s) ppm. Diastereomer 2 (selected signals):  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.24 (d,  $J$  = 6.2 Hz, 3 H), 1.32 (d,  $J$  = 7.0 Hz, 3 H), 1.44 (s, 9 H), 2.95 (s, 3 H), 7.42 (d,  $J$  = 1.8 Hz, 1 H) ppm.  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 15.9 (q), 32.0 (t), 34.1 (t), 41.5 (t), 59.6 (d), 72.5 (d), 79.6 (s), 113.6 (d), 118.1 (t), 125.1 (d), 129.0 (d), 131.4 (d), 132.3 (d), 133.9 (s), 154.1 (s), 168.9 (s), 169.1 (s), 174.0 (s) ppm.

**(9S,5E)-9-((S)-(N-tert-Butoxycarbonyl-alanyl)-(N-methyl-(4-allyloxy-3-chlor)-phenylglycyl)-glycinyloxy)-6-methyldec-5-enoic acid (13d)**

According to **GP 6** 203 mg (265  $\mu\text{mol}$ ) silylester **12d** in 0.8 mL THF was reacted with 92.0 mg (292  $\mu\text{mol}$ ) TBAF-3  $\text{H}_2\text{O}$  in 0.6 mL  $\text{H}_2\text{O}$ . After complete deprotection and aqueous workup, the corresponding alcohol (159 mg, 238  $\mu\text{mol}$ , 90%) was directly subjected to Jones oxidation. According to **GP 7** 88.3 mg (135  $\mu\text{mol}$ ) alcohol in 1.0 mL acetone was reacted with 135  $\mu\text{L}$  (405  $\mu\text{mol}$ ) Jones reagent at 0 °C. Purification by column chromatography (silica gel, petroleum ether/ethyl acetate 1:1 + 1 % AcOH) gave rise to acid **13d** (41.7 mg, 63.0  $\mu\text{mol}$ , 51 %,  $dr$  = 58:42) as colorless oil.  $R_f$  = 0.26 (petroleum ether/ethyl acetate 1:1 + 1 % AcOH). Diastereomer 1:  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.24 (d,  $J$  = 6.3 Hz, 3 H), 1.33 (d,  $J$  = 7.0 Hz, 3 H), 1.43 (s, 9 H), 1.57 (s, 3 H), 1.60-1.79 (m, 4 H), 1.96-2.08 (m, 4 H), 2.24 (m, 2 H), 2.92 (s, 3 H), 3.94 (dd,  $J$  = 18.3, 5.0 Hz, 1 H), 4.08 (dd,  $J$  = 18.3, 5.3 Hz, 1 H), 4.61 (m, 2 H), 4.66 (m, 1 H), 4.90 (qt,  $J$  = 6.0, 6.0 Hz, 1 H), 5.07 (t,  $J$  = 6.5 Hz, 1 H), 5.31 (d,  $J$  = 11.3 Hz, 1 H), 5.46 (d,  $J$  = 17.3 Hz, 1 H), 5.65 (d,  $J$  = 7.6 Hz, 1 H), 6.05 (ddt,  $J$  = 16.3, 10.8, 5.3 Hz, 1 H), 6.30 (s, 1 H), 6.90 (d,  $J$  = 8.6 Hz, 1 H), 7.16 (m, 1 H), 7.22 (d,  $J$  = 8.5 Hz, 1 H), 7.37 (d,  $J$  = 1.5 Hz, 1 H) ppm.  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 15.7 (q), 18.4 (q), 20.0 (q), 24.6 (t), 27.0 (t), 28.3 (q), 32.1 (q), 33.3 (t), 33.6 (t), 35.5 (t), 41.4 (t), 46.8 (d), 60.1 (d), 69.6 (t), 72.0 (d), 79.7 (s), 113.5 (d), 118.0 (t), 123.3 (s), 124.1 (d), 127.1 (s), 128.8 (d), 131.2 (d), 132.3 (d), 134.8 (s), 154.2 (s), 155.2 (s), 169.0 (s), 169.3 (s), 174.3 (s), 177.7 (s) ppm. Diastereomer 2 (selected signals):  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.23 (d,  $J$  = 6.3 Hz, 3 H), 1.36 (d,  $J$  = 6.5 Hz, 3 H), 1.45 (s, 9 H), 2.93 (s, 3 H), 3.81 (m, 1 H), 4.22 (dd,  $J$  = 17.8, 5.0 Hz, 1 H), 5.56 (d,  $J$  = 7.5 Hz, 1 H), 6.91 (d,  $J$  = 8.8 Hz, 1 H), 7.39 (d,  $J$  = 1.5 Hz, 1 H) ppm.  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 15.6 (q), 18.1 (q), 20.2 (q), 24.7 (t), 27.1 (t), 33.6 (t), 33.6 (t), 41.5 (t), 72.3 (d), 80.2 (s), 113.6 (d), 118.0 (t), 123.2 (s), 124.2 (d), 129.0 (d), 131.4 (d), 132.3 (d), 154.0 (s), 155.8 (s) ppm.

## Cyclization towards miuraenamide derivatives

**(9S,19S,14E)-6-Phenyl-7,9,14,19-tetramethyl-1-oxa-4,7,10-triazacyclono-nadec-14-en-2,5,8,11-tetraon (11b)**

According to **GP 5** 41.8 mg (71.6  $\mu\text{mol}$ ) acid **10b**, 14.7 mg (79.9  $\mu\text{mol}$ ) pentafluorophenol and 15.3 mg (79.9  $\mu\text{mol}$ ) EDC-HCl were reacted in 0.8 mL dry  $\text{CH}_2\text{Cl}_2$ . The corresponding active ester was dissolved in 0.8 mL dry  $\text{CH}_2\text{Cl}_2$ /TFA (4:1). After Boc deprotection the reaction mixture was diluted with 1.0 mL dry  $\text{CH}_2\text{Cl}_2$  and added dropwise to 29 mL  $\text{CHCl}_3$ /sat.  $\text{NaHCO}_3$  (7:1). Column chromatography (silica gel, petroleum ether/ethyl acetate 3:7) gave rise to macrocycle **11b** (16.2 mg, 35.4  $\mu\text{mol}$ , 44 %,  $dr$  = 9:1) as colorless resin.  $R_f$  = 0.12 (petroleum ether/ethyl acetate 3:7) ppm. Diastereomer 1:  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  = 1.25 (d,  $J$  = 6.3 Hz, 3 H), 1.34 (d,  $J$  = 6.8 Hz, 3 H), 1.37–1.61 (m, 4 H), 1.64 (s, 3 H), 2.01 (td,  $J$  = 7.3, 7.3 Hz, 2 H), 2.18–2.49 (m, 4 H), 2.88 (s, 3 H), 3.76 (dd,  $J$  = 17.6, 4.5 Hz, 1 H), 4.33 (dd,  $J$  = 17.6, 7.3 Hz, 1 H), 4.93 (qd,  $J$  = 6.8 Hz, 1 H), 5.01 (m, 1 H), 5.22 (t,  $J$  = 6.0 Hz, 1 H), 6.32 (s, 1 H), 6.41 (m, 1 H), 6.79 (d,  $J$  = 6.5 Hz, 1 H), 7.32–7.41 (m, 5 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  = 16.3 (q), 18.4 (q), 20.0 (q), 24.8 (t), 27.8 (t), 32.1 (q), 33.9 (t), 34.0 (t), 35.7 (t), 42.0 (t), 45.9 (d), 60.5 (d), 72.3 (d), 126.1 (d), 128.6 (d), 128.9 (d), 129.4 (d), 133.3 (s), 134.0 (s), 168.5 (s), 169.2 (s), 172.0 (s), 173.8 (s) ppm. Diastereomer 2:  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  = 1.25 (d,  $J$  = 6.3 Hz, 3 H), 1.34 (d,  $J$  = 6.8 Hz, 3 H), 1.37–1.61 (m, 4 H), 1.64 (s, 3 H), 2.01 (td,  $J$  = 7.3, 7.3 Hz, 2 H), 2.18–2.49 (m, 4 H), 2.86 (s, 3 H), 3.76 (dd,  $J$  = 17.6, 4.5 Hz, 1

H), 4.33 (dd,  $J = 17.6, 7.3$  Hz, 1 H), 4.93 (qd,  $J = 6.8, 6.8$  Hz, 1 H), 5.01 (m, 1 H), 5.22 (t,  $J = 6.0$  Hz, 1 H), 6.32 (s, 1 H), 6.48 (m, 1 H), 6.79 (d,  $J = 6.5$  Hz, 1 H), 7.32–7.41 (m, 5 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 16.3$  (q), 18.4 (q), 20.0 (q), 24.8 (t), 27.8 (t), 32.1 (q), 33.9 (t), 34.0 (t), 35.7 (t), 42.0 (t), 45.9 (d), 60.5 (d), 72.3 (d), 126.1 (d), 128.6 (d), 128.9 (d), 129.4 (d), 133.3 (s), 134.0 (s), 168.5 (s), 169.2 (s), 172.0 (s), 173.8 (s). HRMS (CI) calcd for:  $\text{C}_{25}\text{H}_{36}\text{N}_3\text{O}_5^+$   $[\text{M}+\text{H}]^+$ : 458.2649, found: 458.2654.

**(9S,19S,14E)-6-(3-chlor-4-hydroxy)-phenyl-7,9,14,19-tetramethyl-1-oxa-4,7,10-triazacylonadec-14-en-2,5,8,11-tetraon (11d)**

According to **GP 5** 176 mg (280  $\mu\text{mol}$ ) acid **10d**, 55.9 mg (310  $\mu\text{mol}$ ) pentafluorophenol and 59.2 mg (310  $\mu\text{mol}$ ) EDC·HCl were reacted in 2.8 mL dry  $\text{CH}_2\text{Cl}_2$ . The corresponding active ester was dissolved in 2.8 mL dry  $\text{CH}_2\text{Cl}_2/\text{TFA}$  (4:1). After Boc deprotection the reaction mixture was diluted with 4.2 mL dry  $\text{CH}_2\text{Cl}_2$  and added dropwise to 112 mL  $\text{CHCl}_3/\text{sat. NaHCO}_3$  (7:1). Column chromatography (silica gel, petroleum ether/ethyl acetate 3:7) gave rise to macrocycle **11d** (54.2 mg, 110  $\mu\text{mol}$ , 38 %,  $dr = 7:3$ ) as yellow resin.  $R_f = 0.13$  (petroleum ether/ethyl acetate 3:7). Diastereomer 1:  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.24$  (m, 3 H), 1.30–1.57 (m, 4 H), 1.34 (m, 3 H), 1.62 (s, 3 H), 1.99 (td,  $J = 5.8$  Hz, 2 H), 2.29–2.56 (m, 4 H), 2.88 (s, 3 H), 3.80 (dd,  $J = 14.1, 3.8$  Hz, 2 H), 4.37 (m, 1 H), 4.90 (qd,  $J = 5.0, 5.0$  Hz, 1 H), 5.01 (m, 1 H), 5.19 (t,  $J = 5.3$  Hz, 1 H), 6.23 (s, 1 H), 6.61 (m, 1 H), 6.79 (m, 1 H), 6.99 (d,  $J = 6.8$  Hz, 1 H), 7.15 (m, 1 H), 7.36 (m, 1 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 14.6$  (q), 18.2 (q), 19.9 (q), 24.8 (t), 27.7 (t), 31.9 (q), 32.6 (t), 34.0 (t), 35.6 (t), 42.0 (t), 46.0 (d), 59.6 (d), 72.4 (d), 116.7 (d), 120.4 (s), 126.0 (d), 128.0 (d), 129.4 (s), 130.4 (d), 133.2 (s), 152.0 (s), 168.5 (s), 169.0 (s), 172.3 (s), 173.7 (s) ppm. Diastereomer 2:  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 1.24$  (m, 3 H), 1.30–1.57 (m, 4 H), 1.34 (m, 3 H), 1.60 (s, 3 H), 1.95 (td,  $J = 6.3$  Hz, 2 H), 2.29–2.56 (m, 4 H), 2.85 (s, 3 H), 3.73 (m, 2 H), 4.25 (m, 1 H), 4.86 (qd,  $J = 6.0, 6.0$  Hz, 1 H), 5.01 (m, 1 H), 5.53 (t,  $J = 5.6$  Hz, 1 H), 5.81 (s, 1 H), 6.99 (d,  $J = 6.8$  Hz, 1 H), 7.15 (m, 1 H), 7.27 (m, 1 H), 7.41 (m, 1 H), 7.89 (m, 1 H) ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 15.0$  (q), 18.2 (q), 19.9 (q), 24.8 (t), 28.4 (t), 31.9 (q), 32.9 (t), 34.0 (t), 35.6 (t), 42.1 (t), 46.4 (d), 61.3 (d), 72.8 (d), 116.7 (d), 120.5 (s), 126.0 (d), 128.0 (d), 129.6 (s), 130.4 (d), 133.5 (s), 152.3 (s), 168.7 (s), 169.2 (s), 172.3 (s), 173.7 (s) ppm. HRMS (CI) calcd for:  $\text{C}_{25}\text{H}_{34}\text{ClN}_3\text{O}_6^+$   $[\text{M}+\text{H}]^+$ : 509.2101, found: 509.2138.

**(9S,19S,14E)-7,9,14,19-tetramethyl-6-(2-naphthyl)-1-oxa-4,7,10-triazacylonadec-14-en-2,5,8,11-tetraon (11e)**

According to **GP 4** 197 mg (296  $\mu\text{mol}$ ) allylester **9e** in 5.9 mL dry THF was reacted with 34.2 mg (29.6  $\mu\text{mol}$ )  $\text{Pd}(\text{PPh}_3)_4$  and 51.2  $\mu\text{L}$  (592  $\mu\text{mol}$ ) morpholin. According to **GP 5** 197 mg (296  $\mu\text{mol}$ ) of the crude acid **10e**, 60.0 mg (326  $\mu\text{mol}$ ) pentafluorophenol and 62.5 mg (326  $\mu\text{mol}$ ) EDC·HCl were reacted in 3.0 mL dry  $\text{CH}_2\text{Cl}_2$ . The corresponding active ester was dissolved in 3.0 mL dry  $\text{CH}_2\text{Cl}_2/\text{TFA}$  (4:1). After Boc deprotection the reaction mixture was diluted with 4.4 mL dry  $\text{CH}_2\text{Cl}_2$  and added dropwise to 118 mL  $\text{CHCl}_3/\text{sat. NaHCO}_3$  (7:1). Column chromatography (silica gel, petroleum ether/ethyl acetate 3:7) gave rise to macrocycle **11e** (20.1 mg, 39.6  $\mu\text{mol}$ , 13 %,  $dr = 1:1$ ) as yellow oil.  $R_f = 0.18$  (petroleum ether/ethyl acetate 3:7). Diastereomeric mixture:  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.21$ -1.29 (m, 3 H), 1.29-1.59 (m, 7 H), 1.60, 1.68 (s, 3 H), 2.01 (m, 2 H), 2.14-2.60 (m, 4 H), 2.96 (s, 3 H), 2.99 (s, 3 H), 3.72 (m, 1 H), 4.54 (m, 1 H), 4.73-5.27 (m, 3 H), 6.39 (m, 1 H), 6.54 (s, 1 H), 6.58 (s, 1 H), 7.32-7.42 (m, 2 H), 7.47-7.55 (m, 2 H), 7.81-7.90 (m, 3 H), 7.98, 7.00 (s, 1 H) ppm.  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 15.6$  (q), 17.3, 17.5 (q), 20.5, 20.8 (q), 23.8, 24.2 (t), 26.8, 27.3 (t), 32.2 (q), 33.5 (t), 35.0 (t), 36.4 (t), 41.6 (t), 45.9, 46.2 (d), 61.3 (d), 71.3, 71.7 (d), 117.0, 117.1 (d), 126.0 (d), 126.4 (d), 126.6 (d), 127.1 (d), 127.2 (d), 127.5

(d), 127.6 (d), 128.2, 128.4 (d), 131.7 (s), 132.9 (s), 133.2 (s), 133.6 (s), 168.5 (s), 168.6 (s), 168.7 (s), 169.2 (s), 173.5 (s) ppm. HRMS (CI) calcd for:  $C_{29}H_{38}N_3O_5^+$   $[M+H]^+$ : 508.2806, found: 508.2824.

**(9S,19S,14E)-6-benzyl-7,9,14,19-tetramethyl-1-oxa-4,7,10-triazacylononadec-14-en-2,5,8,11-tetraon (11f)**

According to **GP 4** 165 mg (260  $\mu$ mol) allylester **9f** in 5.2 mL dry THF was reacted with 30.0 mg (26.0  $\mu$ mol)  $Pd(PPh_3)_4$  and 27.0  $\mu$ L (310  $\mu$ mol) morpholin. According to **GP 5** the crude acid **10f** (150 mg, 258  $\mu$ mol) was reacted with 53.4 mg (290  $\mu$ mol) pentafluorophenol and 55.6 mg (290  $\mu$ mol) EDC·HCl in 2.6 mL dry  $CH_2Cl_2$ . The corresponding active ester was converted in 2.6 mL dry  $CH_2Cl_2$ /TFA (4:1). After Boc deprotection the reaction mixture was diluted with 3.9 mL dry  $CH_2Cl_2$  and added dropwise to 104 mL  $CHCl_3$ /sat.  $NaHCO_3$  (7:1). Column chromatography (silica gel, petroleum ether/ethyl acetate 3:7) gave rise to two fractions of macrocycle **11f** as colorless oils. Diastereomer 1: 33.4 mg (70.8  $\mu$ mol, 27 %).  $R_f$  = 0.27 (petroleum ether/ethyl acetate 3:7).  $^1H$ -NMR (400 MHz,  $CDCl_3$ ):  $\delta$  = 0.41 (d,  $J$  = 6.8 Hz, 3 H), 1.22 (d,  $J$  = 6.3 Hz, 3 H), 1.37-1.54 (m, 4 H), 1.56 (s, 3 H), 1.90 (td,  $J$  = 7.0, 7.0 Hz, 2 H), 2.25-2.58 (m, 4 H), 2.95 (s, 3 H), 3.07 (m, 1 H), 3.29 (m, 1 H), 3.83 (dd,  $J$  = 17.1 Hz, 5.0 Hz, 1 H), 4.23-4.44 (m, 2 H), 4.80-5.11 (m, 3 H), 5.94 (bs, 1 H), 7.12-7.32 (m, 5 H), 8.33 (t,  $J$  = 6.0 Hz, 1 H) ppm.  $^{13}C$ -NMR (100 MHz,  $CDCl_3$ ):  $\delta$  = 16.2 (q), 16.4 (q), 19.6 (q), 24.2 (t), 25.8 (t), 29.1 (q), 33.5 (t), 34.0 (t), 34.1 (t), 34.2 (t), 41.8 (t), 44.4 (d), 62.5 (d), 71.1 (d), 125.5 (d), 128.6 (d), 128.9 (d), 129.3 (d), 132.3 (s), 137.8 (s), 169.2 (s), 169.4 (s), 173.0 (s), 73.2 (s) ppm. Diastereomer 2: 32.2 mg (68.2  $\mu$ mol, 26 %).  $R_f$  = 0.17 (petroleum ether/ethyl acetate 3:7).  $^1H$ -NMR (400 MHz,  $CDCl_3$ ):  $\delta$  = 0.90 (d,  $J$  = 6.8 Hz, 3 H), 1.24 (d,  $J$  = 6.3 Hz, 3 H), 1.26-1.54 (m, 4 H), 1.59 (s, 3 H), 1.96 (td,  $J$  = 7.0, 7.0 Hz, 2 H), 2.25-2.47 (m, 4 H), 2.93 (s, 3 H), 3.04 (dd,  $J$  = 15.3, 10.5 Hz, 1 H), 3.34 (dd,  $J$  = 15.1, 6.3 Hz, 1 H), 3.82 (dd,  $J$  = 17.6, 4.5 Hz, 1 H), 4.18 (dd,  $J$  = 17.8, 7.0 Hz, 1 H), 4.74 (m, 1 H), 4.98 (m, 1 H), 5.09 (t,  $J$  = 6.8 Hz, 1 H), 5.50 (dd,  $J$  = 10.5, 6.2 Hz, 1 H), 6.57 (d,  $J$  = 6.5 Hz, 1 H), 6.67 (bs, 1 H), 7.16-7.30 (m, 5 H) ppm.  $^{13}C$ -NMR (100 MHz,  $CDCl_3$ ):  $\delta$  = 16.6 (q), 17.9 (q), 20.0 (q), 25.2 (t), 27.4 (t), 30.6 (q), 33.0 (t), 33.5 (t), 34.0 (t), 35.5 (t), 41.7 (t), 45.8 (d), 56.7 (d), 72.2 (d), 124.8 (d), 126.7 (d), 128.5 (d), 128.7 (d), 132.0 (s), 136.6 (s), 168.4 (s), 170.1 (s), 171.7 (s), 174.6 (s) ppm. HRMS (CI) calcd for:  $C_{26}H_{37}N_3O_5^+$   $[M+H]^+$ : 472.2806, found: 472.2832.

**(6R,9S,19S,14E)-6-(4-allyloxy-3-bromobenzyl)-7,9,14,19-tetramethyl-1-oxa-4,7,10-triazacylononadec-14-en-2,5,8,11-tetraon (11g)**

According to **GP 4** 143 mg (160  $\mu$ mol) allylester **9g** in 3.8 mL dry THF was reacted with 22.0 mg (19.0  $\mu$ mol)  $Pd(PPh_3)_4$  and 32.4  $\mu$ L (374  $\mu$ mol) morpholin. According to **GP 5** 130 mg (160  $\mu$ mol) of the crude acid **10g**, 32.4 mg (176  $\mu$ mol) pentafluorophenol and 33.7 mg (176  $\mu$ mol) EDC·HCl were reacted in 1.6 mL dry  $CH_2Cl_2$ . The corresponding active ester was converted in 1.6 mL dry  $CH_2Cl_2$ /TFA (4:1). After Boc deprotection the reaction mixture was diluted with 2.4 mL dry  $CH_2Cl_2$  and added dropwise to 64 mL  $CHCl_3$ /sat.  $NaHCO_3$  (7:1). Column chromatography (silica gel, petroleum ether/ethyl acetate 3:7) gave rise to macrocycle **11g** (6.6 mg, 12.0  $\mu$ mol, 9 %) as yellow oil.  $R_f$  = 0.30 (petroleum ether/ethyl acetate 3:7).  $[\alpha]_D^{20}$  =  $-21.3$  ( $c$  = 1.0,  $CHCl_3$ ).  $^1H$ -NMR (500 MHz,  $CDCl_3$ ):  $\delta$  = 1.22 (d,  $J$  = 6.0 Hz, 3 H), 1.24-1.46 (m, 4 H), 1.27 (d,  $J$  = 7.0 Hz, 3 H), 1.57 (s, 3 H), 1.91 (td,  $J$  = 7.0, 7.0 Hz, 2 H), 2.26-2.46 (m, 4 H), 2.94 (s, 3 H), 2.98 (m, 1 H), 3.22 (dd,  $J$  = 14.8, 3.5 Hz, 1 H), 3.84 (dd,  $J$  = 17.3, 5.4 Hz, 1 H), 4.38 (dd,  $J$  = 17.4, 7.6 Hz, 1 H), 4.43 (qd,  $J$  = 6.6, 6.6 Hz, 1 H), 4.74 (m, 1 H), 4.81 (qt,  $J$  = 7.0, 7.0 Hz, 1 H), 5.02 (t,  $J$  = 6.7 Hz, 1 H), 6.15 (d,  $J$  = 5.1 Hz, 1 H), 6.92 (m, 1 H), 7.02 (dd,  $J$  = 8.2, 2.2 Hz, 1 H), 7.30 (d,  $J$  = 2.2 Hz, 1 H), 6.88 (m, 1 H) ppm.  $^{13}C$ -NMR (125 MHz,  $CDCl_3$ ):  $\delta$  = 16.1 (q), 18.3 (q), 19.7 (q), 24.2 (t), 25.9 (t), 29.2 (q), 32.8 (t), 33.6 (t), 34.2 (t), 35.4 (t), 41.8 (t), 44.5 (d), 62.4 (d), 71.1 (d), 72.9 (s), 110.4 (s), 125.5 (d), 129.5 (d), 129.7 (t), 130.5 (s), 132.8 (d), 133.8 (s), 152.2 (s), 169.1 (s), 169.2 (s), 173.3 (s), 173.4 (s). HRMS (CI) calcd for:  $C_{26}H_{37}BrN_3O_6^+$   $[M+H]^+$ : 566.1860, found: 566.1859.

**(9S,19S,5E)-6-(4-allyloxy-3-chlorophenyl)-7,9,16,19-tetramethyl-1-oxa-4,7,10-triazacyclononadec-15-en-2,5,8,11-tetraon (14d)**

According to **GP 5** 41.0 mg (63.0  $\mu\text{mol}$ ) acid **13d** was reacted with 12.8 mg (69.3  $\mu\text{mol}$ ) pentafluorophenol and 13.3 mg (69.3  $\mu\text{mol}$ ) EDC·HCl in 0.6 mL dry  $\text{CH}_2\text{Cl}_2$ . The corresponding active ester was dissolved in 630  $\mu\text{L}$  dry  $\text{CH}_2\text{Cl}_2$ /TFA (4:1). After Boc deprotection the reaction mixture was diluted with 950  $\mu\text{L}$  dry  $\text{CH}_2\text{Cl}_2$  and added dropwise to 25.2 mL  $\text{CHCl}_3$ /sat.  $\text{NaHCO}_3$  (7:1). Column chromatography (silica gel, petroleum ether/ethyl acetate 1:1, 4:6, 3:7) gave rise to macrocycle **14d** (24.6 mg, 44.9  $\mu\text{mol}$ , 71 %,  $dr = 66:34$ ) as colorless foam. Diastereomer 1:  $R_f = 0.23$  (petroleum ether/ethyl acetate 3:7).  $^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.27$  (m, 3 H), 1.41 (d,  $J = 6.6$  Hz, 3 H), 1.60 (s, 3 H), 1.60-1.88 (m, 4 H), 1.95-2.28 (m, 6 H), 2.82 (s, 3 H), 4.07 (m, 1 H), 4.63 (m, 2 H), 4.93 (td,  $J = 7.0, 7.0$  Hz, 1 H), 4.97 (qt,  $J = 6.6, 6.6$  Hz, 1 H), 5.10 (t,  $J = 6.3$  Hz, 1 H), 5.33 (d,  $J = 10.75$  Hz, 1 H), 5.47 (d,  $J = 17.4$  Hz, 1 H), 5.65 (d,  $J = 7.6$  Hz, 1 H), 6.06 (m, 1 H), 6.30 (s, 1 H), 6.89 (m, 1 H), 6.92 (d,  $J = 8.5$  Hz, 1 H), 7.37 (d,  $J = 8.5$  Hz, 1 H), 7.54 (m, 1 H) ppm.  $^{13}\text{C-NMR}$  (125 MHz,  $\text{CDCl}_3$ ):  $\delta = 16.1$  (q), 17.6 (q), 19.6 (q), 25.6 (t), 26.2 (t), 31.2 (q), 32.9 (t), 34.6 (t), 35.2 (t), 41.1 (t), 46.0 (d), 58.1 (d), 69.7 (t), 71.4 (d), 113.4 (d), 118.1 (t), 123.2 (s), 125.4 (d), 126.4 (s), 128.8 (d), 131.3 (d), 132.4 (d), 134.4 (s), 154.0 (s), 168.9 (s), 170.0 (s), 173.1 (s), 173.4 (s) ppm. Diastereomer 2:  $R_f = 0.17$  (petroleum ether/ethyl acetate 3:7) (selected signals):  $^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.39$  (d,  $J = 5.6$  Hz, 3 H), 1.58 (s, 3 H), 6.91 (d,  $J = 8.2$  Hz, 1 H), 7.36 (d,  $J = 8.5$  Hz, 1 H), 7.53 (m, 1 H) ppm. HRMS (CI) calcd for:  $\text{C}_{28}\text{H}_{39}\text{ClN}_3\text{O}_6^+$   $[\text{M}+\text{H}]^+$ : 548.2522, found: 548.2550.