

## 3 Experimental Part

### 3.1 Materials and Methods

#### 3.1.1 General

Unless otherwise specified, materials were purchased from commercial suppliers and used without further purification. All solvents were distilled prior to use. All reactions involving organometallic reagents were carried out under argon or nitrogen. Tetrahydrofuran and diethyl ether were distilled from sodium and benzophenone. Toluene and dichloromethane were distilled from calcium hydride. Methanol was distilled from magnesium under argon.

#### 3.1.2 NMR-Spectroscopy

<sup>1</sup>H-NMR spectra were recorded on a Bruker AM 270 MHz or a Bruker AMX 500 MHz spectrometer and are reported in  $\delta$  from Me<sub>4</sub>Si ( $\delta = 0.00$  ppm) and from CDCl<sub>3</sub> ( $\delta = 7.26$  ppm). The <sup>1</sup>H-NMR chemical shifts and coupling constants were determined assuming first-order behaviour. Multiplicities are reported using the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad) or a suitable combination. The list of coupling constants (*J*; reported to the nearest 0.5 Hz) corresponds to the order of the multiplicity assignment. The assignments of proton resonances were based on <sup>1</sup>H,<sup>1</sup>H-COSY and 1D Nuclear Overhauser Enhancement (NOE) spectroscopy.

<sup>13</sup>C-NMR spectra were recorded at 68 MHz or at 125 MHz in CDCl<sub>3</sub> (unless otherwise stated) with the chemical shift relative to CHCl<sub>3</sub> (77 ppm).

#### 3.1.3 IR-Spectroscopy

IR spectra were recorded as pellets (KBr) or in solution (solvent as given) using a Perking Elmer FT-IR or a Nicolet A 320 FT-IR spectrometer and are reported using the following abbreviations: s (strong), m (medium), w (weak).

### 3.1.4 MS-Spectroscopy

Mass spectra were recorded on a Varian CH7A mass spectrometer, high resolution mass spectroscopy (HRMS) was performed using a Varian MAT 711 spectrometer (PKF served as internal reference).

### 3.1.5 Polarimetry

Optical rotations were recorded on a IBZ Messtechnik polarimeter. The specific optical rotation was calculated using the following formula:

$$[\alpha]_{\lambda}^T = \frac{\alpha \cdot 100}{c \cdot d}$$

where  $\alpha$  is the angle of optical rotation in degrees,  $\lambda$  is the wavelength of the polarized light and is normally the sodium D-line (589 nm), T is the Celsius temperature at which the measurement is made, c is the mass concentration in  $\text{g cm}^{-3}$  and d is the length of the path of the light through the solution in dm.

### 3.1.6 Chromatography

All reactions were monitored by thin layer chromatography (TLC), which was carried out on 0.25 mm Merck silica gel-60 F<sub>254</sub> precoated plates. The following reagents were used as detectors:

**Schlittler reagent:**<sup>81</sup> 3 mL of 10% aqueous H<sub>2</sub>PtCl<sub>6</sub> + 97 mL water + 100 mL 6% aqueous KI. This reagent is very specific for the detection of amides (white colour, not persistent) and amines (deep brown to black colour).

**Anisaldehyde reagent:** 1 mL anisaldehyde and 2 mL concentrated sulfuric acid dissolved in 100mL of glacial acetic acid.

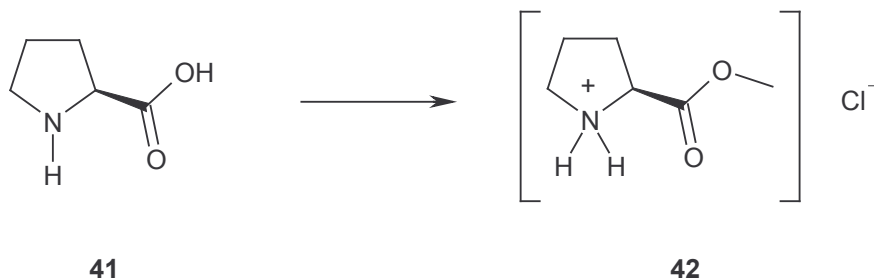
**Potassium permanganate reagent:** 0.05% aqueous KMnO<sub>4</sub>.

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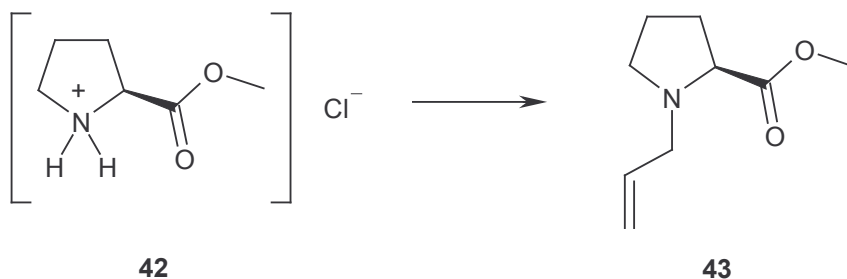
<sup>81</sup> Schlittler, E.; Hohl, J. *Helv. Chim. Acta* **1952**, *35*, 29.

**Bromokresol green reagent:** 40 mg bromokresol green indicator (3,3',5,5'-Tetrabromo-m-kresosulfon-phthalein) was dissolved in 100 ml of ethanol and treated with 0.1 M aqueous NaOH until a blue colour appeared. Basic compounds give a deep blue, acid or weak acid compounds a yellow colour.

**Ninhydrine reagent:** 0.2 g of ninhydrine was dissolved in 100 mL of ethanol.

3.2 Syntheses of *N*-Allylpyrrolidines**(*S*)-Proline methyl ester hydrochloride 42**

To a stirred solution of (*S*)-Proline **41** (10 g, 86.9 mmol) in 100 mL dry methanol at 0 °C was added carefully thionylchloride (9.8 mL). After complete addition, the solution was refluxed for 3 hours and then the solvent was removed in vacuum to give (*S*)-Proline methyl ester hydrochloride **42** as pale yellow oil, which was used without further purification.

**(*S*)-*N*-Allylproline methyl ester 43**

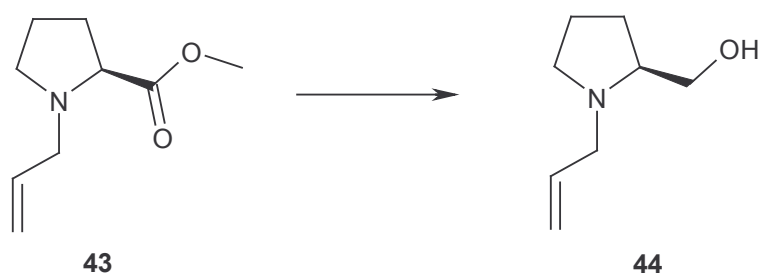
(*S*)-Proline methyl ester hydrochloride **42** (900 mg, 5.4 mmol) in DMF (80 mL) was subsequently treated with solid  $K_2CO_3$  (4 g) and fresh distilled allyl bromide (0.56 mL, 6.48 mmol). The mixture was stirred overnight at 20 °C, then  $H_2O$  (50 mL) was added. The aqueous layer was extracted with  $Et_2O$  ( $4 \times 20$  mL), the combined organic layers were dried over  $MgSO_4$  and concentrated to give the crude product. Purification by Kugelrohr distillation (140 °C / 0.01 mm Hg) gave 818 mg (89%) of (*S*)-*N*-Allylproline methyl ester **43** as colourless oil.

$^1H$ -NMR (270 MHz,  $CDCl_3$ ):  $\delta$  = 1.66-1.95 (m, 3H,  $CH_2CHH$ ), 1.97-2.10 (m, 1H,  $CH_2CHH$ ), 2.32 (ddd, 1H,  $J$  = 17.09 Hz, 7.81 Hz, 0.98 Hz,  $CH_2CHHN$ ), 3.01-3.15 (m, 3H,  $NCHCOOCH_3$ ,  $CH_2CHHN$ ,  $NCHHCH=CH_2$ ), 3.20-3.29 (ddt, 1H,  $J$  = 13.18 Hz, 6.35 Hz, 1.46 Hz, 0.98 Hz,  $NCHHCH=CH_2$ ), 3.65 (s, 3H,  $COOCH_3$ ), 5.02 (dd, 1H,  $J$  = 10.25 Hz, 0.98

Hz, CH<sub>2</sub>CH=CHH), 5.10 (dd, 1H, *J* = 17.09 Hz, 1.47 Hz, CH<sub>2</sub>CH=CHH), 5.77-5.92 (dddd, 1H, *J* = 17.09 Hz, 10.25 Hz, 6.84 Hz, 6.84 Hz, -CH<sub>2</sub>CH=CH<sub>2</sub>) ppm

<sup>13</sup>C-NMR (68 MHz, CDCl<sub>3</sub>): δ = 22.9 (CH<sub>2</sub>CH<sub>2</sub>), 29.4 (CH<sub>2</sub>CH<sub>2</sub>), 51.6 (OCH<sub>3</sub>), 53.3 (NCHCOOCH<sub>3</sub>), 57.5 (CH<sub>2</sub>CH<sub>2</sub>N), 65.1 (NCH<sub>2</sub>CH=CH<sub>2</sub>), 117.2 (CH<sub>2</sub>CH=CH<sub>2</sub>), 135.1 (CH<sub>2</sub>CH=CH<sub>2</sub>), 174.4 (COOCH<sub>3</sub>) ppm

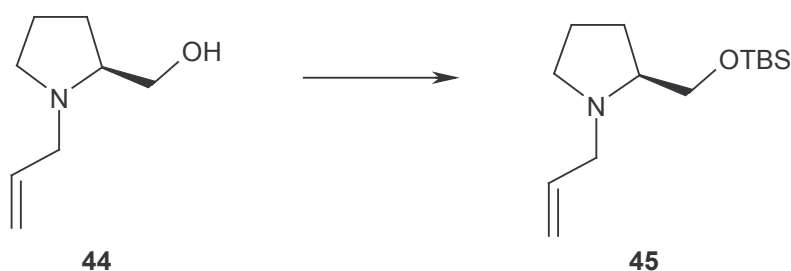
### (*S*)-*N*-Allylprolinol **44**



Allylproline methyl ester **43** (1.57 g, 9.28 mmol) in anhyd. THF (30 mL) was treated dropwise with DIBAL-H (17 mL, 20.4 mmol, 1.2 M in toluene) at 0 °C. After stirring for 3 hours at 0 °C, the reaction was quenched with MeOH (5 mL), and after a further 10 minutes of vigorous stirring, aq. sat. NaHCO<sub>3</sub> (10 mL) and 30% aq. sodium potassium tartrate (15 mL) were added. The aqueous layer was extracted with Et<sub>2</sub>O (5 × 20 mL), the combined organic layers were dried over MgSO<sub>4</sub> and concentrated to give 1.06 g (81%) of *N*-Allylprolinol **44**, which was used without further purification.

<sup>1</sup>H-NMR (270 MHz, CDCl<sub>3</sub>): δ = 1.50-1.70 (m, 3H, CH<sub>2</sub>CHH), 1.83 (m, 1H, CH<sub>2</sub>CHH), 2.29 (ddd, 1H, *J* = 8.83 Hz, 8.09 Hz, 1.47 Hz, CH<sub>2</sub>CHHN), 2.60 (m, 1H, NCHCH<sub>2</sub>OH), 2.90 (dd, 1H, *J* = 13.24 Hz, 7.36 Hz, NCHHCH=CH<sub>2</sub>), 2.92 (br s, 1H, OH), 3.06 (dd, 1H, *J* = 9.56 Hz, 4.42 Hz, CH<sub>2</sub>CHHN), 3.36 (m, 2H, NCHHCH=CH<sub>2</sub>, CHHOH), 3.61 (dd, 1H, *J* = 10.30 Hz, 3.78 Hz, CHHOH), 5.06 (dd, 1H, *J* = 10.29 Hz, 1.47 Hz, CH=CHH), 5.15 (dd, 1H, *J* = 16.91 Hz, 1.47 Hz, CH=CHH), 5.92 (dddd, 1H, *J* = 16.91 Hz, 10.30 Hz, 7.36 Hz, 5.88 Hz, CH=CH<sub>2</sub>) ppm

<sup>13</sup>C NMR (68 MHz, CDCl<sub>3</sub>): δ = 23.2 (CH<sub>2</sub>CH<sub>2</sub>), 27.5 (CH<sub>2</sub>CH<sub>2</sub>), 54.2 (NCH<sub>2</sub>CH=CH<sub>2</sub>), 57.4 (CH<sub>2</sub>CH<sub>2</sub>N), 62.4 (NCHCH<sub>2</sub>OH), 64.2 (NCHCH<sub>2</sub>OH), 116.7 (CH=CH<sub>2</sub>), 135.8 (CH=CH<sub>2</sub>) ppm

**(*S*)-*N*-Allyl-2-*tert*-butyldimethylsilyloxymethylpyrrolidine 45**

Allylprolinol **44** (1 g, 7.08 mmol), imidazole (1 g, 14.7 mmol) and DMAP (10 mg) in anhyd. THF (50 mL) were treated with TBSCl (1.7 g, 11.3 mmol) at 0 °C. After 3 hours of stirring at 20 °C (TLC control), the mixture was quenched with MeOH (20 mL) and H<sub>2</sub>O (20 mL). The aqueous layer was extracted with Et<sub>2</sub>O (4 × 10 mL) and the combined organic layers were dried over MgSO<sub>4</sub>. After removal of the solvent, the crude material was purified by Kugelrohr distillation (85 °C / 0.01 mm Hg), gave 1.77 g (98%) of **45** as colourless oil.

$[\alpha]_D^{20} = -50.1^\circ$  (c = 1.2, CHCl<sub>3</sub>)

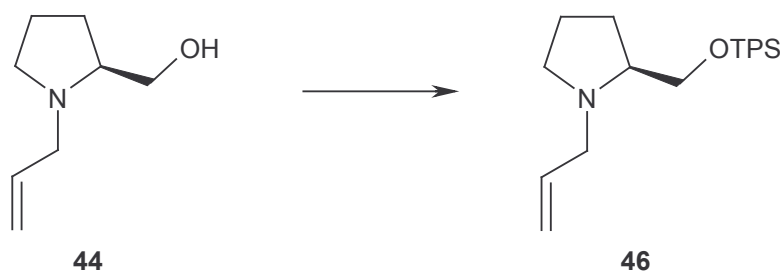
**<sup>1</sup>H-NMR** (500 MHz, CDCl<sub>3</sub>): δ = 0.00 (s, 6H, Si(CH<sub>3</sub>)<sub>2</sub>), 0.85 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>C), 1.49-1.75 (m, 3H, CH<sub>2</sub>CHH), 1.75-1.92 (m, 1H, CH<sub>2</sub>CHH), 2.20 (dd, 1H, *J* = 8.79 Hz, 8.30 Hz, -CH<sub>2</sub>CHHN), 2.55 (m, 1H, NCHCH<sub>2</sub>O), 2.88-3.05 (m, 2H, CH<sub>2</sub>CHHN, NCHCH=CH<sub>2</sub>), 3.40 (dd, 1H, *J* = 9.77 Hz, 7.32 Hz, CHHO), 3.50 (dd, 1H, *J* = 13.66 Hz, 5.86 Hz, NCHHCH=CH<sub>2</sub>), 3.65 (dd, 1H, *J* = 10.25 Hz, 5.37 Hz, CHHO), 5.04 (dd, 1H, *J* = 10.26 Hz, 1.47 Hz, CH=CHH), 5.12 (dd, 1H, *J* = 16.09 Hz, 1.47 Hz, CH=CHH), 5.85 (dddd, 1H, *J* = 16.90 Hz, 10.29 Hz, 7.35 Hz, 5.89 Hz, CH=CH<sub>2</sub>) ppm

**<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>): δ = -5.4 (Si(CH<sub>3</sub>)<sub>2</sub>), 18.2 ((CH<sub>3</sub>)<sub>3</sub>C), 22.8 (CH<sub>2</sub>CH<sub>2</sub>), 25.8 ((CH<sub>3</sub>)<sub>3</sub>C), 28.3 (CH<sub>2</sub>CH<sub>2</sub>), 54.6 (NCH<sub>2</sub>CH=CH<sub>2</sub>), 58.6 (CH<sub>2</sub>CH<sub>2</sub>N), 64.7 (NCHCH<sub>2</sub>O), 66.9 (CH<sub>2</sub>O), 116.5 (CH=CH<sub>2</sub>), 136.3 (CH=CH<sub>2</sub>) ppm

**IR** (solution, CHCl<sub>3</sub>): 1/λ = 3019 (m), 2956 (m), 2857 (m), 2805 (m), 1471 (m), 1463 (m), 1420 (w), 1389 (w), 1362 (w), 1257 (m), 1214 (s), 1096 (m) cm<sup>-1</sup>

**MS** (EI, 80 eV, 30 °C): *m/z* (%) = 255 (31, [M]<sup>+</sup>), 240 (33, [M-CH<sub>3</sub>]<sup>+</sup>), 198 (59, [M-C<sub>4</sub>H<sub>9</sub>]<sup>+</sup>), 124 (23, [M-C<sub>6</sub>H<sub>15</sub>OSi]<sup>+</sup>), 110 (100, [M-C<sub>7</sub>H<sub>17</sub>OSi]<sup>+</sup>), 41 (87, [C<sub>3</sub>H<sub>5</sub>]<sup>+</sup>).

**HRMS** (80 eV, 30 °C): *m/z* [M]<sup>+</sup> calcd. for C<sub>14</sub>H<sub>29</sub>NOSi, 255.20184; found, 255.20433

**(*S*)-*N*-Allyl-2-*tert*-butyldiphenylsilyloxymethylpyrrolidine 46**

Allylprolinol **44** (1 g, 7.08 mmol), imidazole (1 g, 14.7 mmol) and DMAP (10 mg) in anhyd. THF (50 mL) were treated with TPSCl (2.9 g, 10.5 mmol) at 0 °C. After 3 hours of stirring at 20 °C (TLC control), the mixture was quenched with H<sub>2</sub>O (20 mL). The aqueous layer was extracted with Et<sub>2</sub>O (4 × 10 mL) and the combined organic layers were dried over MgSO<sub>4</sub>. After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 4:1) to give 2.68g (99%) of **46** as colourless oil.

$[\alpha]_D^{20} = -46.2^\circ$  (c = 1.9, CHCl<sub>3</sub>)

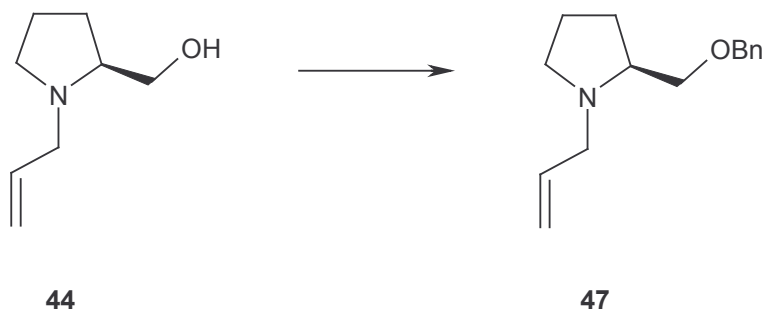
**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>): δ = 1.10 (s, 9H, SiC(CH<sub>3</sub>)<sub>3</sub>), 1.60-1.85 (m, 3H, CH<sub>2</sub>CHH), 1.85-2.01 (m, 1H, CH<sub>2</sub>CHH), 2.20-2.31 (m, 1H, NCHHCH<sub>2</sub>), 2.62-2.74 (m, 1H, NCHCH<sub>2</sub>O), 2.89-2.99 (dd, 1H, *J* = 13.18 Hz, 7.32 Hz, NCHHCH=CH<sub>2</sub>), 3.03-3.11 (m, 1H, NCHHCH<sub>2</sub>), 3.47-3.56 (m, 1H, NCHHCH<sub>2</sub>), 3.49-3.58 (dd, 1H, *J* = 10.25 Hz, 6.84 Hz, CHHOTPS), 3.73-3.81 (dd, 1H, *J* = 10.26 Hz, 6.36 Hz, CHHOTPS), 5.01-5.08 (dd, 1H, *J* = 10.26 Hz, 0.98 Hz, CH=CHH), 5.09-5.19 (dd, 1H, *J* = 17.09 Hz, 1.46 Hz, CH=CHH), 5.79-5.96 (dddd, 1H, *J* = 17.09 Hz, 10.25 Hz, 7.32 Hz, 5.86 Hz, CH=CH<sub>2</sub>), 7.30-7.55 (m, 5H, Ph), 7.65-7.82 (m, 3H, Ph) ppm

**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>): δ = 19.1 (SiC(CH<sub>3</sub>)<sub>3</sub>), 22.8 (CH<sub>2</sub>CH<sub>2</sub>), 26.8 (SiC(CH<sub>3</sub>)<sub>3</sub>), 28.4 (CH<sub>2</sub>CH<sub>2</sub>), 54.4 (NCH<sub>2</sub>CH=CH<sub>2</sub>), 58.5 (NCH<sub>2</sub>CH<sub>2</sub>), 64.6 (NCHCH<sub>2</sub>O), 67.5 (NCHCH<sub>2</sub>O), 116.4 (CH=CH<sub>2</sub>), 127.5, 129.4, 133.7, 136.2 (Ph), 135.5 (CH=CH<sub>2</sub>) ppm

**IR** (solution, CHCl<sub>3</sub>): 1/λ = 3072 (m), 3045 (m), 2807 (m), 3017 (s), 2964 (s), 2931 (s), 2859 (s), 2807 (m), 1472 (m), 1463 (w), 1428 (m), 1391 (w), 1215 (s), 1112 (s), 1050 (m) cm<sup>-1</sup>

**MS** (EI, 80 eV, 40°C): *m/z* (%) = 379 (5, [M]<sup>+</sup>), 322 (6, [M-C<sub>4</sub>H<sub>9</sub>]<sup>+</sup>), 280 (4, [M-C<sub>4</sub>H<sub>9</sub>-C<sub>3</sub>H<sub>6</sub>]<sup>+</sup>), 199 (43, [HOSiPh<sub>2</sub>]<sup>+</sup>), 110 (100, [C<sub>7</sub>H<sub>12</sub>N]<sup>+</sup>).

**HRMS** (80eV, 30-40 °C): *m/z* [M]<sup>+</sup> calcd. for C<sub>24</sub>H<sub>33</sub>NOSi, 379.23314; found, 379.23654

**(*S*)-*N*-Allyl-2-benzyloxymethylpyrrolidine 47**

To a suspension of NaH (255 mg, 10.6 mmol) in anhyd. THF (30 mL) at 0 °C was added a solution of allylprolinol **44** (1 g, 7.08 mmol) in anhyd. THF (10 mL). The deprotonation was completed within 1 hour at 0 °C. Benzyl bromide (1.3 g, 7.6 mmol) in anhyd. THF (10 mL) was added and the mixture was stirred overnight at 20 °C. The mixture was quenched with H<sub>2</sub>O (10 mL), the aqueous layer was extracted with Et<sub>2</sub>O (3 × 10 mL), the combined organic layers were dried over MgSO<sub>4</sub>, and the solvent was evaporated. The crude material was purified by kugelrohr distillation (115 °C / 0.01 mm Hg) to give 1.38 g (84%) of **47** as colourless oil.

$[\alpha]_D^{20} = -68.5^\circ$  (c = 1.4, CHCl<sub>3</sub>)

<sup>1</sup>H-NMR (270 MHz, CDCl<sub>3</sub>): δ = 1.49-1.75 (m, 3H, CH<sub>2</sub>CHH), 1.75-1.92 (m, 1H, CH<sub>2</sub>CHH), 2.21 (ddd, 1H, *J* = 8.93 Hz, 8.09 Hz, 1.47 Hz, NCHHCH<sub>2</sub>), 2.65 (m, 1H, NCHCH<sub>2</sub>O), 2.92 (dd, 1H, *J* = 13.24 Hz, 8.09 Hz, NCHHCH=CH<sub>2</sub>), 3.06 (ddd, 1H, *J* = 9.56 Hz, 6.62 Hz, 2.94 Hz, CH<sub>2</sub>CHHN), 3.36 (dd, 1H, *J* = 6.61 Hz, 5.88 Hz, CHHO), 3.50 (dd, 1H, *J* = 9.56 Hz, 5.14 Hz, CHHO), 3.56 (dd, 1H, *J* = 5.88 Hz, 1.47 Hz, NCHHCH=CH<sub>2</sub>), 4.42 (s, 2H, PhCH<sub>2</sub>), 5.06 (dd, 1H, *J* = 10.29 Hz, 1.47 Hz, CH=CHH), 5.12 (dd, 1H, *J* = 16.09 Hz, 1.47 Hz, CH=CHH), 5.85 (dddd, 1H, *J* = 16.91 Hz, 10.29 Hz, 7.35 Hz, 5.88 Hz, CH=CH<sub>2</sub>), 7.15-7.26 (m, 5H, Ph) ppm

<sup>13</sup>C NMR (68 MHz, CDCl<sub>3</sub>): δ = 22.8 (CH<sub>2</sub>CH<sub>2</sub>), 28.6 (CH<sub>2</sub>CH<sub>2</sub>), 54.4 (NCH<sub>2</sub>CH=CH<sub>2</sub>), 58.3 (NCH<sub>2</sub>CH<sub>2</sub>), 62.7 (CHCH<sub>2</sub>O), 73.2 (CH<sub>2</sub>O), 73.7 (PhCH<sub>2</sub>), 116.6 (CH=CH<sub>2</sub>), 136.2 (CH=CH<sub>2</sub>), 127.4, 127.5, 128.0, 128.2, 138.4 (Ph) ppm

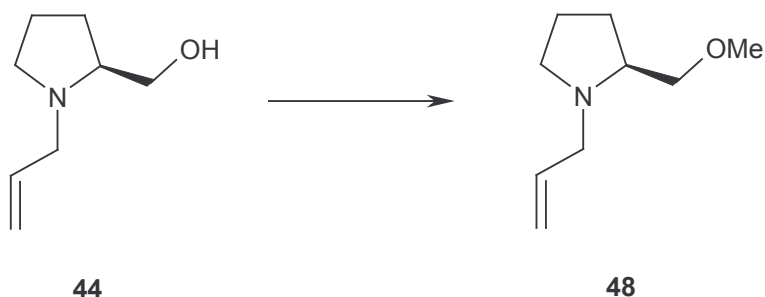
IR (solution, CHCl<sub>3</sub>): 1/λ = 3068 (m), 3015 (s), 2970 (s), 2914 (s), 2872 (s), 2803 (m), 1732 (w), 1643 (w), 1496 (m), 1454 (m), 1420 (w), 1363 (m), 1216 (s), 1097 (s) cm<sup>-1</sup>

MS (EI, 80 eV, 30 °C): *m/z* (%) = 231 (12, [M]<sup>+</sup>), 110 (100, [M-C<sub>8</sub>H<sub>9</sub>O]<sup>+</sup>), 91 (77, [C<sub>7</sub>H<sub>7</sub>]<sup>+</sup>), 41 (89, [C<sub>3</sub>H<sub>5</sub>]<sup>+</sup>).



**HRMS** (80 eV, 30 °C):  $m/z$ ,  $[M]^+$  calcd. for  $C_{15}H_{21}NO$ , 231.16231; found, 231.16482

**(*S*)-*N*-Allyl-2-methoxymethylpyrrolidine **48****



To a suspension of NaH (255 mg, 10.6 mmol) in anhyd. THF (30 mL) at 0 °C was added a solution of allylprolinol **44** (1 g, 7.08 mmol) in anhyd. THF (10 mL). The deprotonation was completed within 1 hour at 0 °C. Methyl iodide (1.2 g, 8.4 mmol) in anhyd. THF (10 mL) was added and the mixture was stirred overnight at 20 °C. The mixture was quenched with H<sub>2</sub>O (10 mL), the aqueous layer was extracted with Et<sub>2</sub>O (3 × 10 mL), the combined organic layers were dried over MgSO<sub>4</sub>, and the solvent was evaporated. The crude material was purified by kugelrohr distillation (30 °C / 0.01 mm Hg) to give 880 mg (80%) of **48** as colourless oil.

$[\alpha]_D^{20} = -85.6^\circ$  ( $c = 2.0$ , CHCl<sub>3</sub>)

**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>):  $\delta = 1.40$ - $1.65$  (m, 3H, CH<sub>2</sub>CHH),  $1.65$ - $1.85$  (m, 1H, CH<sub>2</sub>CHH),  $1.98$ - $2.16$  (dd, 1H,  $J = 8.92$  Hz,  $8.10$  Hz, NCHHCH<sub>2</sub>),  $2.38$ - $2.53$  (m, 1H, NCHCH<sub>2</sub>),  $2.70$ - $2.85$  (dd,  $J = 13.24$  Hz,  $8.10$  Hz, 1H, NCHHCH=CH<sub>2</sub>),  $2.85$ - $2.92$  (m, 1H, NCHHCH<sub>2</sub>),  $3.10$ - $3.31$  (m, 5H, OCH<sub>3</sub>, NCHCH<sub>2</sub>),  $3.31$ - $3.44$  (dd, 1H,  $J = 13.19$  Hz,  $4.40$  Hz, NCHHCH=CH<sub>2</sub>),  $4.88$ - $4.99$  (d, 1H,  $J = 10.26$  Hz, CH=CHH),  $4.99$ - $5.12$  (d, 1H,  $J = 17.09$  Hz, CH=CHH),  $5.68$ - $5.90$  (m, 1H, CH=CH<sub>2</sub>) ppm

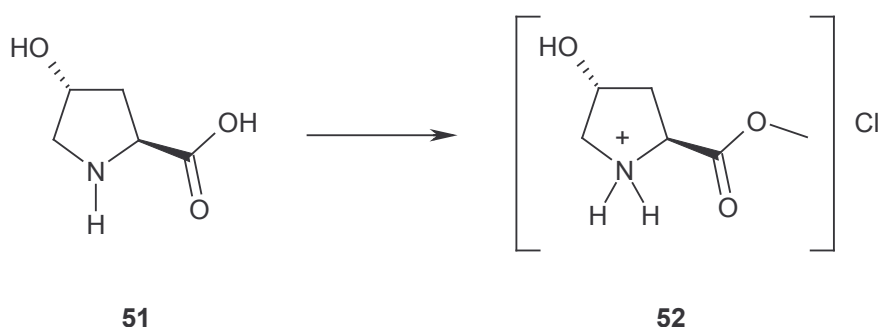
**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>):  $\delta = 22.6$  (CH<sub>2</sub>CH<sub>2</sub>),  $28.2$  (CH<sub>2</sub>CH<sub>2</sub>),  $54.2$  (NCH<sub>2</sub>CH=CH<sub>2</sub>),  $58.1$  (NCH<sub>2</sub>CH<sub>2</sub>),  $58.8$  (CHCH<sub>2</sub>O),  $75.8$  (OCH<sub>3</sub>),  $116.4$  (CH=CH<sub>2</sub>),  $136.0$  (CH=CH<sub>2</sub>) ppm

**IR** (solution, CHCl<sub>3</sub>):  $1/\lambda = 3079$  (m),  $2950$  (s),  $2900$  (s),  $2877$  (s),  $2753$  (s),  $2497$  (w),  $1675$  (m),  $1643$  (m),  $1460$  (s),  $1455$  (s),  $1420$  (m),  $1385$  (m),  $1349$  (m),  $1261$  (m),  $1217$  (s),  $1199$  (s),  $1109$  (s),  $994$  (s),  $969$  (m),  $922$  (s) cm<sup>-1</sup>

**MS** (EI, 80 eV, 30 °C):  $m/z$  (%) = 155 (1.29,  $[M]^+$ ), 124 (0.81,  $[M-CH_3O]^+$ ), 110 (100,  $[M-C_2H_5O]^+$ ), 41 (23,  $[C_3H_5]^+$ ).

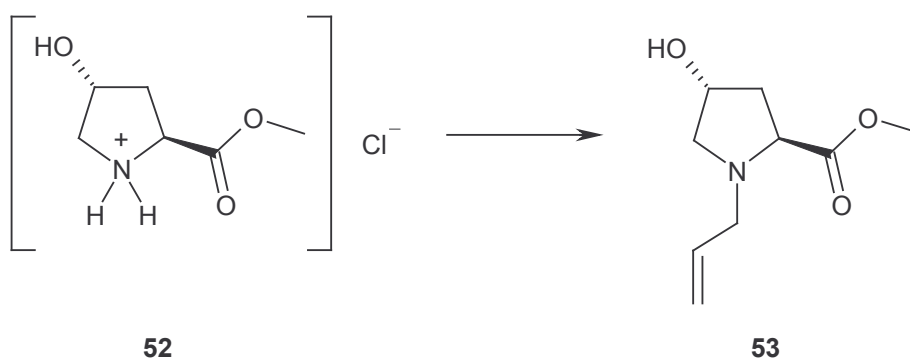
HRMS (80 eV, 30 °C):  $m/z$ ,  $[M]^+$  calcd. for  $C_9H_{17}NO$ , 155.13101; found, 155.13453

**(2*S*,4*R*)-4-Hydroxyproline methyl ester hydrochloride 52**



To a suspension of hydroxyproline **51** (5 g, 38 mmol) and dry methanol (30 mL) at 0 °C was added carefully thionylchloride (5 mL). After complete addition, the mixture was refluxed for 5 hours and then the solvent was removed in vacuum to give hydroxyproline methyl ester chloride **52** as colourless crystals, which were used without further purification.

**(2*S*,4*R*)-*N*-Allyl-4-hydroxyproline methyl ester 53**



To a suspension of hydroxyproline methyl ester **52** (2 g, 11 mmol) in dry  $CH_2Cl_2$  (50 mL) was added  $Et_3N$  (1.56 mL) and fresh distilled allyl bromide (1.12 mL, 13.2 mmol,  $d = 1.43$ ). The mixture was stirred over night at 20 °C, then  $H_2O$  (30 mL) was added. The aqueous layer was extracted with  $CH_2Cl_2$  ( $3 \times 15$  mL), the combined organic layers were dried over  $MgSO_4$ , and the solvent was removed in vacuum. The crude material was purified by column

chromatography (Ethylacetate) to give 1.66 g (81.5%) of allyl hydroxyproline methyl ester **53** as pale yellow oil.

$[\alpha]_D^{20} = -87.3^\circ$  ( $c = 1.8$ ,  $\text{CHCl}_3$ )

$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.90$ - $1.98$  (m, 1H,  $\text{HOCHCH}_2$ ),  $2.01$ - $2.09$  (m, 1H,  $\text{HOCHCH}_2$ ),  $2.29$ - $2.35$  (ddd, 1H,  $J = 9.90$  Hz,  $5.45$  Hz,  $4.45$  Hz,  $\text{NCHH}$ ),  $3.01$ - $3.07$  (m, 1H,  $\text{CHHCH}=\text{CH}_2$ ),  $3.17$ - $3.23$  (m, 1H,  $\text{CHHCH}=\text{CH}_2$ ),  $3.23$ - $3.29$  (ddd, 1H,  $J = 10.40$  Hz,  $5.45$  Hz,  $4.95$  Hz,  $\text{NCHH}$ ),  $3.34$ - $3.40$  (m, 1H,  $\text{NCH}$ ),  $3.43$ - $3.55$  (br, s, OH),  $3.55$  (s,  $\text{OCH}_3$ ),  $4.96$ - $5.01$  (dd, 1H,  $J = 10.03$  Hz,  $0.98$  Hz,  $\text{CH}=\text{CHH}$ ),  $5.03$ - $5.09$  (dd, 1H,  $J = 17.05$  Hz,  $1.24$  Hz,  $\text{CH}=\text{CHH}$ ),  $5.70$ - $5.80$  (m, 1H,  $\text{CH}=\text{CH}_2$ ) ppm

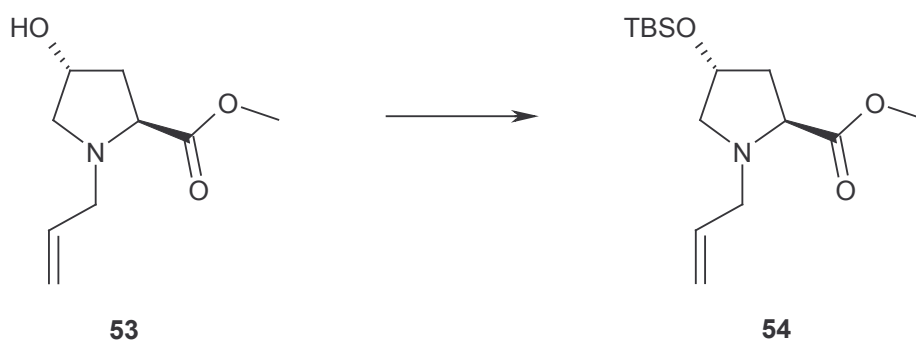
$^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ ):  $\delta = 39.3$  ( $\text{HOCHCH}_2$ ),  $51.6$  ( $\text{OCH}_3$ ),  $57.1$  ( $\text{CH}_2\text{CH}=\text{CH}_2$ ),  $61.0$  ( $\text{NCH}_2$ ),  $63.4$  ( $\text{NCHCOOCH}_3$ ),  $69.3$  ( $\text{CHOH}$ ),  $117.6$  ( $\text{CH}=\text{CH}_2$ ),  $134.4$  ( $\text{CH}=\text{CH}_2$ ),  $173.9$  ( $\text{COO}$ ) ppm

**IR** (KBr, film):  $1/\lambda = 3173$  (br, m, OH),  $3072$  (m),  $3024$  (m),  $3007$  (m),  $2985$  (m),  $2975$  (m),  $2953$  (m),  $2945$  (m),  $2866$  (m),  $2823$  (m),  $1878$  (w),  $1747$  (s, COO),  $1706$  (w),  $1644$  (w),  $1462$  (m),  $1453$  (m),  $1432$  (m),  $1377$  (m),  $1364$  (w),  $1340$  (m),  $1320$  (m),  $1287$  (w),  $1266$  (w),  $1235$  (m),  $1218$  (m),  $1196$  (s),  $1174$  (s),  $1142$  (m),  $1127$  (m),  $1091$  (s),  $1061$  (w),  $1019$  (m)  $\text{cm}^{-1}$

**MS** (EI, 80 eV,  $30^\circ\text{C}$ ):  $m/z$  (%) =  $185$  (7.4,  $[\text{M}]^+$ ),  $126$  (100,  $[\text{M}-\text{C}_2\text{H}_3\text{O}_2]^+$ ),  $108$  (7,  $[\text{M}-\text{C}_2\text{H}_5\text{O}_3]^+$ ),  $41$  (19,  $[\text{C}_3\text{H}_5]^+$ ).

**HRMS** (80 eV,  $30^\circ\text{C}$ ):  $m/z$ ,  $[\text{M}]^+$  calcd. for  $\text{C}_9\text{H}_{15}\text{NO}_3$ , 185.10519; found, 185.10733

**(2*S*,4*R*)-*N*-Allyl-4-*tert*-butyldimethylsilyloxyproline methyl ester **54****



Allyl hydroxyproline methyl ester **53** (1.4 g, 7.57 mmol), imidazole (1.13 g, 16.6 mmol) and DMAP (10 mg) in anhyd. THF (20 mL) were treated with TBSCl (2.28 g, 15.14 mmol) at 0 °C. After 3 hours of stirring at 20 °C (TLC control), the mixture was quenched with MeOH (20 mL) and H<sub>2</sub>O (20 mL). The aqueous layer was extracted with Et<sub>2</sub>O (4 × 10 mL) and the combined organic layers were dried over MgSO<sub>4</sub>. After removal of the solvent, the crude material was purified by column chromatography (hexane-EtOAc, 5:1) to give 2.2 g (98%) of **54** as pale yellow oil.

$[\alpha]_D^{20} = -47.8^\circ$  (c = 1.5, CHCl<sub>3</sub>)

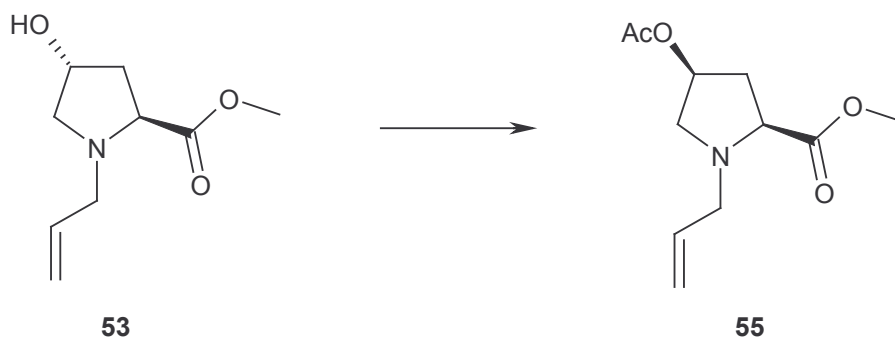
**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>): δ = 0.00 (s, 6H, Si(CH<sub>3</sub>)<sub>2</sub>), 1.35 (s, 9H, SiC(CH<sub>3</sub>)<sub>3</sub>), 1.87-1.99 (ddd, 1H, *J* = 12.69 Hz, 8.30 Hz, 3.91 Hz, NCHCHH), 1.99 (ddd, 1H, *J* = 12.70 Hz, 7.81 Hz, 7.25 Hz, NCHCHH), 2.24-2.32 (dd, 1H, *J* = 9.76 Hz, 6.88 Hz, NCHHCHO), 3.00-3.11 (dd, 1H, *J* = 13.19 Hz, 7.33 Hz, CHHCH=CH<sub>2</sub>), 3.19-3.30 (m, 2H, NHHCHO, CHHCH=CH<sub>2</sub>), 3.31-3.39 (dd, 1H, *J* = 8.30 Hz, 7.81 Hz, NCH), 3.65 (s, 3H, OCH<sub>3</sub>), 4.27-4.37 (m, 1H, TBSOCH), 4.97-5.09 (dd, 1H, *J* = 9.76 Hz, 0.98 Hz, CH=CHH), 5.09-5.15 (dd, *J* = 17.09 Hz, 1.47 Hz, CH=CHH), 5.71-5.88 (dddd, 1H, *J* = 17.09 Hz, 10.25 Hz, 9.76 Hz, 6.83 Hz, CH=CH<sub>2</sub>) ppm

**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>): δ = -5.0 (Si(CH<sub>3</sub>)<sub>2</sub>), 17.8 (Si C(CH<sub>3</sub>)<sub>3</sub>), 25.6 (SiC(CH<sub>3</sub>)<sub>3</sub>), 39.6 (OCHCH<sub>2</sub>), 51.7 (OCH<sub>3</sub>), 58.1 (NCH<sub>2</sub>CH=CH<sub>2</sub>), 61.6 (NCH<sub>2</sub>), 64.0 (NCHCOOCH<sub>3</sub>), 70.3 (OCHCH<sub>2</sub>), 117.6 (CH=CH<sub>2</sub>), 134.8 (CH=CH<sub>2</sub>), 174.2 (CO) ppm

**IR** (KBr, film): 1/λ = 3079 (w), 2954 (s), 2929 (s), 2896 (m), 2857 (s), 2803 (m), 2710 (w), 1751 (s, CO), 1659 (w), 1643 (w), 1472 (m), 1463 (m), 1436 (m), 1420 (w), 1361 (m), 1312 (w), 1257 (s), 1198 (s), 1173 (s), 1131 (m), 1099 (s), 1033 (m), 1006 (m), 995 (m) cm<sup>-1</sup>

**MS** (EI, 80 eV, 40°C): m/z (%) = 299 (3, [M]<sup>+</sup>), 284 (2, [M-CH<sub>3</sub>]<sup>+</sup>), 240 (100, [M-C<sub>2</sub>H<sub>3</sub>O<sub>2</sub>]<sup>+</sup>).

**HRMS** (80 eV, 40°C): m/z, [M]<sup>+</sup> calcd. for C<sub>15</sub>H<sub>29</sub>NO<sub>3</sub>Si, 299.19167; found, 299.19192

**(2*S*,4*S*)-*N*-Allyl-4-acetoxypyrrolidine methyl ester 55**

To a stirred solution of AcOH (120.7  $\mu$ L, 2.08 mmol) and DEAD (326  $\mu$ L, 2.08 mmol) in anhyd. Et<sub>2</sub>O (10 mL) were added allyl hydroxypyrrolidine methyl ester **53** (350 mg, 1.89 mmol) and Ph<sub>3</sub>P (556.8 mg, 2.08 mmol) in anhyd. Et<sub>2</sub>O (10 mL) at 0 °C. After 20 hours, the reaction mixture was filtered and the solvent was evaporated. The residue was purified by column chromatography (n-hexane / EtOAc, 3:1) to give 370 mg (86%) of **55** as pale yellow oil.

$[\alpha]_D^{20} = -70.2^\circ$  (c = 2.0, CHCl<sub>3</sub>)

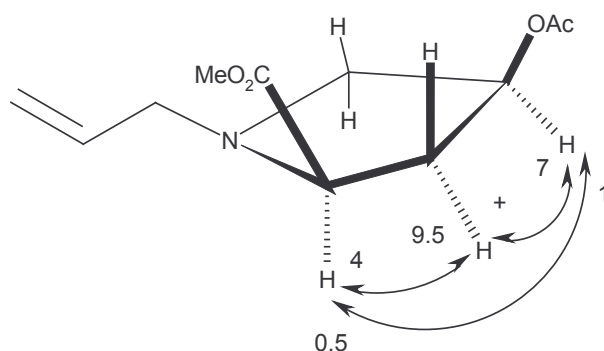
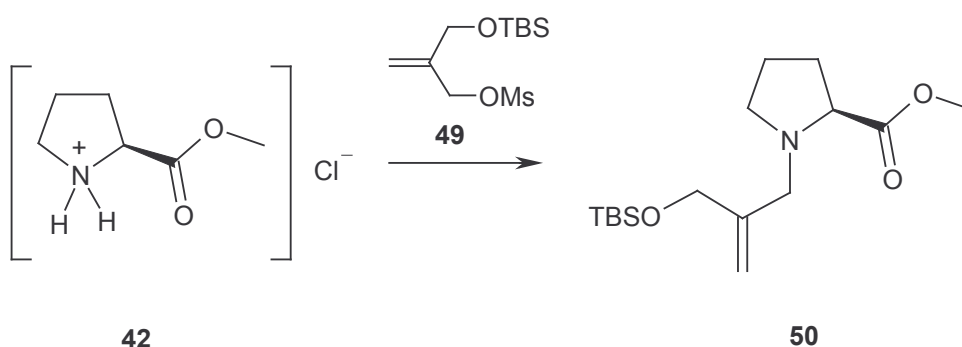
**<sup>1</sup>H-NMR** (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.96 (s, 3H, CH<sub>3</sub>CO), 1.91-2.05 (m, 1H, CHHCHCO<sub>2</sub>), 2.43-2.59 (m, 1H, CHHCHCO<sub>2</sub>), 2.48-2.55 (d, 1H, *J* = 5.37 Hz, NCHHCHOAc), 2.92-3.02 (ddd, 1H, *J* = 13.19 Hz, 7.33 Hz, 0.98 Hz, CHHCH=CH<sub>2</sub>), 3.03-3.11 (t, *J* = 8.30 Hz, CHCO<sub>2</sub>), 3.11-3.18 (d, 1H, *J* = 1.27 Hz, NCHHCHOAc), 3.24-3.36 (ddd, 1H, *J* = 13.18 Hz, 6.34 Hz, 0.98 Hz, CHHCH=CH<sub>2</sub>), 3.65 (s, 1H, OCH<sub>3</sub>), 4.30 (m, 1H, CHOH), 4.99-5.11 (m, 1H, CHOAc), 5.02-5.17 (m, 2H, CH=CH<sub>2</sub>), 5.74-5.92 (dddd, 1H, *J* = 17.09 Hz, 13.68 Hz, 10.26 Hz, 6.85 Hz, CH=CH<sub>2</sub>) ppm

**<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 21.1 (CH<sub>3</sub>CO), 36.4 (CH<sub>2</sub>CHCO<sub>2</sub>), 51.9 (OCH<sub>3</sub>), 57.3 (CH<sub>2</sub>CH=CH<sub>2</sub>), 58.9 (NCH<sub>2</sub>CHO), 64.3 (NCHCO<sub>2</sub>), 72.2 (CHOAc), 118.2 (CH=CH<sub>2</sub>), 134.0 (CH=CH<sub>2</sub>), 170.9 (CH<sub>3</sub>COO), 173.1 (COOCH<sub>3</sub>) ppm

**IR** (KBr):  $1/\lambda$  = 3077 (w), 2979 (m), 2953 (m), 2804 (m), 1738 (s, COO), 1643 (w), 1437 (m), 1367 (m), 1245 (s), 1190 (m), 1165 (m), 1057 (m), 1017 (m), 922 (m) cm<sup>-1</sup>

**MS** (EI, 80 eV, 50 °C): *m/z* (%) = 227 (0.8, [M]<sup>+</sup>), 184 (0.5, [M-C<sub>2</sub>H<sub>3</sub>O]<sup>+</sup>), 168 (19, [M-C<sub>2</sub>H<sub>3</sub>O<sub>2</sub>]<sup>+</sup>), 108 (100, [C<sub>7</sub>H<sub>10</sub>N]<sup>+</sup>).

**HRMS** (80 eV, 50 °C): *m/z*, [M]<sup>+</sup> calcd. for C<sub>11</sub>H<sub>17</sub>NO<sub>4</sub>, 227.11576; found, 227.11592

NOE data for **55****(*S*)-*N*-(2-*tert*-Butyldimethylsilyloxymethyl)prop-2-enyl proline methyl ester **50****

Proline methyl ester hydrochloride **42** (1.14 g, 6.90 mmol) in DMF (100 mL) was treated with Et<sub>3</sub>N (1.3 g, 6.90 mmol) and **49** (1.61 g, 5.75 mmol) at 0 °C. The mixture was stirred overnight at 20 °C, then H<sub>2</sub>O (50 mL) was added. The aqueous layer was extracted with Et<sub>2</sub>O (4×20 mL), the combined organic layers were dried over MgSO<sub>4</sub>. After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 5:1) to give 1.4 g (77%) of **50** as pale yellow oil.

$[\alpha]_D^{20} = -51.7^\circ$  (c = 1.7, CHCl<sub>3</sub>)

**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>): δ = 0.05 (s, 6H, Si(CH<sub>3</sub>)<sub>2</sub>), 0.90 (s, 9H, SiC(CH<sub>3</sub>)<sub>3</sub>), 1.65-1.97 (m, 3H, CH<sub>2</sub>CHH), 1.99-2.15 (m, 1H, CH<sub>2</sub>CHH), 2.26-2.38 (dd, 1H, *J* = 16.60 Hz, 8.30 Hz, NCHHCH<sub>2</sub>), 2.96-3.07 (m, 2H, NCHHCH<sub>2</sub>, NCHHCH=CH<sub>2</sub>), 3.11-3.18 (dd, 1H, *J* = 8.79 Hz, 5.37 Hz, NCHCO<sub>2</sub>), 3.20-3.28 (d, 1H, *J* = 12.70 Hz, NCHHCH=CH<sub>2</sub>), 3.65 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 4.07-4.25 (dd, 2H, *J* = 21.49 Hz, 14.65 Hz, TBSOCH<sub>2</sub>), 4.95 (s, 1H, CHH=C), 5.05 (s, 1H, CHH=C) ppm

**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>): δ = -5.4 (Si(CH<sub>3</sub>)<sub>2</sub>), 18.3 (SiC(CH<sub>3</sub>)<sub>3</sub>), 23.0 (CH<sub>2</sub>CH<sub>2</sub>), 25.8 (SiC(CH<sub>3</sub>)<sub>3</sub>), 29.3 (CH<sub>2</sub>CH<sub>2</sub>), 51.5 (OCH<sub>3</sub>), 53.3 (NCHCO<sub>2</sub>), 57.5 (NCH<sub>2</sub>CH<sub>2</sub>), 64.4 (NCH<sub>2</sub>C=CH<sub>2</sub>), 65.4 (TBSOCH<sub>2</sub>), 111.3 (CH<sub>2</sub>=C), 146.2 (CH<sub>2</sub>=C), 174.6 (CO<sub>2</sub>CH<sub>3</sub>) ppm

**IR** (KBr): 1/λ = 3092 (w), 2954 (s), 2929 (s), 2884 (m), 2856 (s), 1752 (s, COO), 1737 (s, COO), 1658 (w), 1472 (m), 1462 (m), 1435 (m), 1406 (w), 1388 (w), 1361 (m), 1251 (s), 1196 (s), 1171 (s), 1108 (s), 1040 (w), 1006 (m), 938 (w), 906 (m) cm<sup>-1</sup>

**MS** (EI, 80 eV, 40°C): m/z (%) = 313 (3, [M]<sup>+</sup>), 298 (3, [M-CH<sub>3</sub>]<sup>+</sup>), 254 (100, [M-CO<sub>2</sub>CH<sub>3</sub>]<sup>+</sup>), 185 (19, [M-C<sub>6</sub>H<sub>10</sub>NO<sub>2</sub>]<sup>+</sup>), 128 (33, [M-C<sub>6</sub>H<sub>11</sub>NO<sub>2</sub>-C<sub>4</sub>H<sub>9</sub>]<sup>+</sup>).

**HRMS** (80 eV, 40 °C): m/z, [M]<sup>+</sup> calcd. for C<sub>16</sub>H<sub>31</sub>NO<sub>3</sub>Si, 313.20732; found, 313.20722

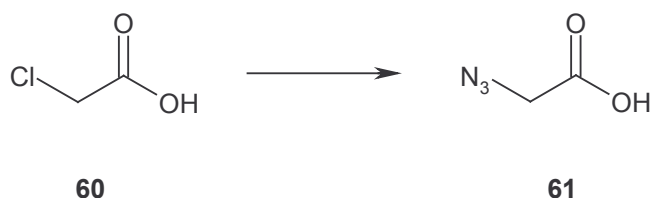
Data of **49**:

**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>): δ = 0.05 (s, 6H, Si(CH<sub>3</sub>)<sub>2</sub>), 0.90 (s, 9H, SiC(CH<sub>3</sub>)<sub>3</sub>), 3.0 (s, 3H, CH<sub>3</sub>SO<sub>3</sub>), 4.16 (s, 2H, TBSOCH<sub>2</sub>), 4.72 (s, 2H, MsOCH<sub>2</sub>), 5.25 (s, 1H, CHH=C), 5.33 (s, 1H, CHH=C) ppm

**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>): δ = -5.4 (Si(CH<sub>3</sub>)<sub>2</sub>), 18.2 (SiC(CH<sub>3</sub>)<sub>3</sub>), 25.7 (SiC(CH<sub>3</sub>)<sub>3</sub>), 37.7 (CH<sub>3</sub>SO<sub>3</sub>), 63.2 (TBSOCH<sub>2</sub>), 69.9 (MsOCH<sub>2</sub>), 115.7 (CH<sub>2</sub>=C), 141.4 (CH<sub>2</sub>=C) ppm

### 3.3 Syntheses of Carboxylic Acids

#### Azidoacetic acid **61**



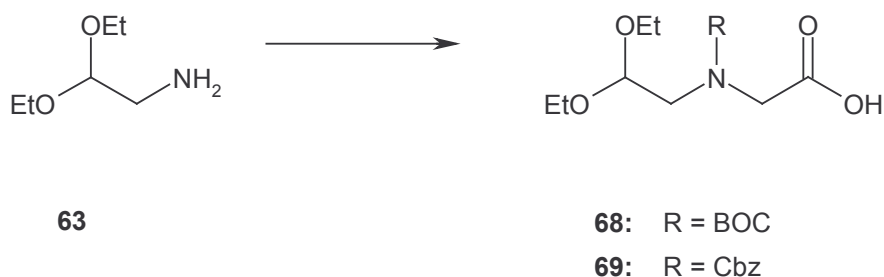
To chloroacetic acid **60** (10.4 g, 0.11 mol) in Et<sub>2</sub>O (15 mL) was added NaOH (30 mL, 3.3 M) and NaN<sub>3</sub> (8.2 g, 0.126 mol) at 0 °C. After complete dissolution, the solution was refluxed for 3 days at 60 °C. Then the solution was cooled to 0 °C and H<sub>2</sub>SO<sub>4</sub> (30 mL, 2 M) was carefully added. The aqueous layer was extracted with Et<sub>2</sub>O (10 × 200 mL), the combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent in vacuum 11 g (99%) of azidoacetic acid **61** was obtained as a colourless oil.

<sup>1</sup>H-NMR (270 MHz, CDCl<sub>3</sub>): δ = 3.90 (s, 2H, CH<sub>2</sub>), 11.4 (s, 1H, COOH) ppm

<sup>13</sup>C NMR (68 MHz, CDCl<sub>3</sub>): δ = 49.7 (CH<sub>2</sub>), 173.2 (COOH) ppm

#### *N*-*tert*-Butyloxycarbonyl-*N*-(2,2-diethoxyethyl)aminoacetic acid **68**

#### *N*-Benzyloxycarbonyl-*N*-(2,2-diethoxyethyl)aminoacetic acid **69**



Aminoacetaldehyde diethylacetal **63** (1.33 g, 10 mmol) and Et<sub>3</sub>N (1.01 g, 1.4 mL, 10 mmol) in anhyd. Et<sub>2</sub>O (100 mL) were cooled to 0 °C. Ethyl bromoacetate **65** (1.67 g, 1.11 mL, 10 mmol) in anhyd. Et<sub>2</sub>O (50 mL) was added slowly and the mixture was stirred overnight at 0 °C. Di-*tert*-butyl dicarbonate or benzyloxycarbonyl chloride (10 mmol) in anhyd. Et<sub>2</sub>O (20



mL) was added and the mixture was stirred at r.t. for 5 hours. 1 N HCl (50 mL) was added to the mixture and the aqueous layer was extracted with Et<sub>2</sub>O (4×40 mL). The combined organic layers were dried over MgSO<sub>4</sub> and the solvent was removed to give the crude protected α-amino esters.

The crude protected α-amino ester was treated with 1 N NaOH (100 mL) and LiCl (0.5 g, 11.8 mmol). After stirring at 80 °C for 3 hours and at 20 °C for 1 hour, the solution was extracted with Et<sub>2</sub>O (3×50 mL). The aqueous layer was acidified with aq. sat. KHSO<sub>4</sub> until the solution reached a pH of 4-5. The aqueous solution was extracted with Et<sub>2</sub>O (4×50 mL) and the organic layers were dried over MgSO<sub>4</sub>. After removal of the solvent, the carboxylic acids **68** and **69** were isolated pure enough for further transformations.

Data of **68**:

Yield: 2.46 g (84.5%); clear oil.

<sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>): δ = 1.15 (2×t, 6H, J = 7.35 Hz, CH<sub>3</sub>CH<sub>2</sub>O), 1.40 (2×s, 9H, (CH<sub>3</sub>)<sub>3</sub>C), 3.30 (2×d, 2H, J = 5.15 Hz, NCH<sub>2</sub>CH(OEt)<sub>2</sub>), 3.45 (m, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 3.55 (m, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 4.00 (2×s, 2H, NCH<sub>2</sub>COOH), 4.50 (2×t, 1H, J = 5.15 Hz, CH(OEt)<sub>2</sub>), 10.95 (br s, 1H, COOH) ppm

<sup>13</sup>C NMR (68 MHz, CDCl<sub>3</sub>): δ = 15.1 (CH<sub>3</sub>CH<sub>2</sub>O); 28.0, 28.2 ( (CH<sub>3</sub>)<sub>3</sub>C); 49.7, 50.7 (NCH<sub>2</sub>COOH); 50.8, 51.1 (NCH<sub>2</sub>CH(OEt)<sub>2</sub>); 63.1, 63.4 (CH<sub>3</sub>CH<sub>2</sub>O); 80.7 ( (CH<sub>3</sub>)<sub>3</sub>C); 101.8, 102.1 (CH(OEt)<sub>2</sub>); 155.2, 155.5 (NCO); 175.1 (COOH) ppm

IR (in CHCl<sub>3</sub>): 1/λ = 3019 (s), 2980 (s), 2932 (s), 2898 (s), 1730 (s, COO), 1697 (s, CON), 1477 (m), 1456 (s), 1417 (s), 1396 (s), 1369 (s), 1306 (w), 1251 (s), 1220 (s), 1159 (s), 1060 (s), 973 (m), 927 (m) cm<sup>-1</sup>

MS (neg. FAB): m/z (%) = 291 (17, [M]<sup>+</sup>), 290 (100, [M-H]<sup>+</sup>).

Data of **69**:

Yield: 2.05 g (63%); clear oil.

<sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>): δ = 1.15 (m, 6H, CH<sub>3</sub>CH<sub>2</sub>O), 3.35-3.75 (m, 6H, CH<sub>3</sub>CH<sub>2</sub>O, NCH<sub>2</sub>CH(OEt)<sub>2</sub>), 4.15 (2×s, 2H, NCH<sub>2</sub>COOH), 4.50 (2×t, 1H, J = 5.15 Hz, CH(OEt)<sub>2</sub>), 5.14 (2×s, CH<sub>2</sub>Ph), 7.24-7.36 (m, 5H, Ph), 9.90 (br s, 1H, COOH) ppm

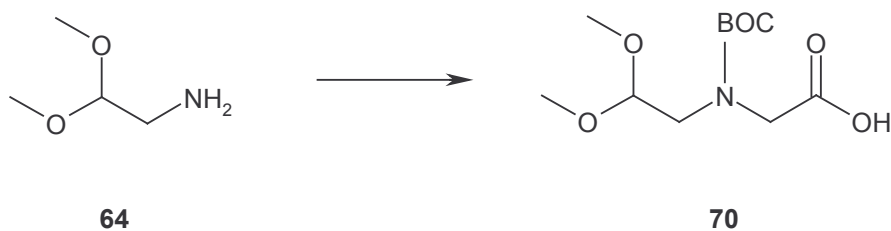
<sup>13</sup>C NMR (68 MHz, CDCl<sub>3</sub>): δ = 15.1 (CH<sub>3</sub>CH<sub>2</sub>O); 50.1 (NCH<sub>2</sub>CH(OEt)<sub>2</sub>); 51.0, 51.4 (NCH<sub>2</sub>COOH); 63.2, 63.5 (CH<sub>3</sub>CH<sub>2</sub>O); 67.6, 67.8 (CH<sub>2</sub>Ph); 101.7, 102.0 (CH(OEt)<sub>2</sub>), 126.9,

127.6, 127.9, 128.0, 128.1, 128.4, 128.5, 136.1 (Ph); 156.1, 156.3 (NCO); 174.6 (COOH) ppm

**IR** (in CHCl<sub>3</sub>):  $1/\lambda = 3019$  (s), 2979 (s), 2930 (s), 2883 (s), 2658 (m), 2548 (m), 1728 (s, COO), 1697 (s, CON), 1604 (m), 1585 (m), 1498 (m), 1454 (s), 1422 (s), 1374 (s), 1216 (s), 1126 (s), 1059 (s), 994 (m), 960 (m) cm<sup>-1</sup>

**MS** (pos. FAB):  $m/z$  (%) = 348 (1.08, [M+Na]<sup>+</sup>), 326 (1.04, [M+H]<sup>+</sup>), 280 (18, [M-CHO<sub>2</sub>]<sup>+</sup>), 236 (15, [M-C<sub>7</sub>H<sub>7</sub>]<sup>+</sup>), 103 (35, [C<sub>5</sub>H<sub>11</sub>O<sub>2</sub>]<sup>+</sup>), 91 (100, [C<sub>7</sub>H<sub>7</sub>]<sup>+</sup>).

### *N*-*tert*-Butyloxycarbonyl-*N*-(2,2-dimethoxyethyl)aminoacetic acid **70**



Aminoacetaldehyde dimethyl acetal **64** (4.60 g, 43.8 mmol) and Et<sub>3</sub>N (44.2 g, 61.3 mL, 43.8 mmol) in anhyd. Et<sub>2</sub>O (250 mL) were cooled to 0 °C. Ethyl bromoacetate **65** (73.1 g, 48.6 mL, 43.8 mmol) in anhyd. Et<sub>2</sub>O (100 mL) was added slowly and the mixture was stirred overnight at 0 °C. Di-*tert*-butyl dicarbonate (43.8 mmol) in anhyd. Et<sub>2</sub>O (50 mL) was added and the mixture was stirred at r.t. for 5 hours. 1 M HCl (150 mL) was added to the mixture and the aqueous layer was extracted with Et<sub>2</sub>O (4×80 mL). The combined organic layers were dried over MgSO<sub>4</sub> and the solvent was removed to give the crude protected α-amino esters.

The crude protected α-amino ester was treated with 1 M NaOH (438 mL) and LiCl (1.86 g, 43.8 mmol). After stirring at 80 °C for 3 hours and at 20 °C for 1 hour, the solution was extracted with Et<sub>2</sub>O (3×50 mL). The aqueous layer was acidified with aq. sat. KHSO<sub>4</sub> until the solution reached a pH of 4-5. The aqueous solution was extracted with Et<sub>2</sub>O (4×100 mL) and the organic layers were dried over MgSO<sub>4</sub>. After removal of the solvent, 7.60 g (66%) of the carboxylic acid **70** was isolated pure enough for further transformations.

**$^1\text{H}$  NMR** (270 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.25 (2  $\times$  s, 9H,  $\text{C}(\text{CH}_3)_3$ ), 3.2 (s, 6H,  $\text{OCH}_3$ ), 3.08-3.23 (m, 2H,  $\text{NCH}_2\text{CH}(\text{OCH}_3)_2$ ), 3.81 (2  $\times$  s, 2H,  $\text{NCH}_2\text{COOH}$ ), 4.15-4.50 (2  $\times$  dd, 1H,  $J$  = 5.37 Hz, 4.88 Hz,  $\text{CH}(\text{OCH}_3)_2$ ), 8.80 (br, s, 1H,  $\text{COOH}$ ) ppm

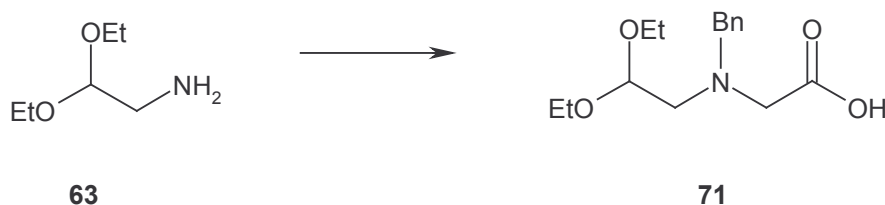
**$^{13}\text{C}$  NMR** (68 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 27.7, 27.9 ( $\text{C}(\text{CH}_3)_3$ ), 49.1, 49.6 ( $\text{CH}_2\text{CH}(\text{OCH}_3)_2$ ), 49.9, 50.0 ( $\text{CH}_2\text{COOH}$ ), 80.5, 80.6 ( $\text{C}(\text{CH}_3)_3$ ), 103.7, 103.9 ( $\text{CH}(\text{OCH}_3)_2$ ), 155.2, 155.3 ( $\text{NCO}$ ), 173.4, 173.6 ( $\text{COO}$ ) ppm

**IR** (KBr, film):  $1/\lambda$  = 3443 (br, m, OH), 3200 (br, m, OH), 2977 (s), 2939 (s), 2836 (m), 1745 (s, COO), 1702 (s, CON), 1478 (s), 1458 (s), 1395 (s), 1368 (s), 1307 (m), 1252 (m), 1166 (s), 1125 (s), 1077 (s), 1024 (m), 968 (m)  $\text{cm}^{-1}$

**MS** (EI, 80 eV, 80°C):  $m/z$  (%) = 263 (2.33,  $[\text{M}]^+$ ), 190 (6,  $[\text{M}-\text{C}_4\text{H}_9\text{O}]^+$ ), 176 (13,  $[\text{M}-\text{C}_5\text{H}_{11}\text{O}]^+$ ), 132 (11,  $[\text{M}-\text{C}_6\text{H}_{11}\text{O}_3]^+$ ), 75 (100,  $[\text{C}_3\text{H}_7\text{O}_2]^+$ ).

**HRMS** (80 eV, 40 °C):  $m/z$ ,  $[\text{M}]^+$  calcd. for  $\text{C}_{11}\text{H}_{21}\text{NO}_6$ , 263.13688; found, 263.13885

### *N*-Benzyl-*N*-(2,2-diethoxyethyl)amino acetic acid **71**



Aminoacetaldehyde diethyl acetal **63** (1.33 g, 10 mmol) and  $\text{Et}_3\text{N}$  (1.01 g, 1.4 mL, 10 mmol) in anhyd.  $\text{Et}_2\text{O}$  (100 mL) were cooled to 0 °C. Ethyl bromoacetate **65** (1.67 g, 1.11 mL, 10 mmol) in anhyd.  $\text{Et}_2\text{O}$  (50 mL) was added slowly and the mixture was stirred overnight at 0 °C. Benzyl chloride (10 mmol) in anhyd.  $\text{Et}_2\text{O}$  (20 mL) was added and the mixture was stirred at r.t. for further 24 hours.  $\text{H}_2\text{O}$  (50 mL) was added to the mixture and the aqueous layer was extracted with  $\text{Et}_2\text{O}$  (4 $\times$ 40 mL). The combined organic layers were dried over  $\text{MgSO}_4$  and the solvent was removed in vacuum. The crude material was purified by column chromatography to give  $\alpha$ -amino ester.

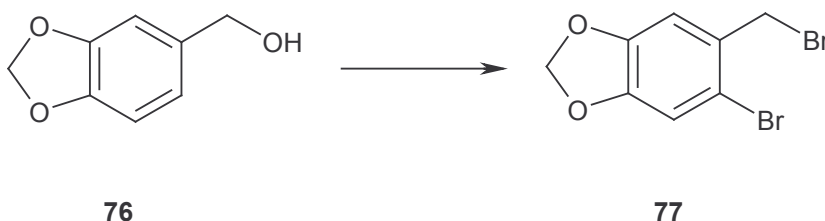
The  $\alpha$ -amino ester was treated with 1 N NaOH (100 mL) and LiCl (0.5 g, 11.8 mmol). After stirring at 80 °C for 3 hours and at 20 °C for 1 hour, the solution was extracted with  $\text{Et}_2\text{O}$  (3 $\times$ 50 mL). The aqueous layer was acidified with aq. sat.  $\text{KHSO}_4$  until the solution reached a pH of 5. The aqueous solution was extracted with  $\text{Et}_2\text{O}$  (4 $\times$ 50 mL) and the organic layers

were dried over  $\text{MgSO}_4$ . After removal of the solvent 1.2 g (65%) of the carboxylic acid **71** was isolated as a pale yellow oil.

$^1\text{H NMR}$  (270 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.20 (m, 9H,  $\text{CH}_3\text{CH}_2\text{O}$ ,  $\text{CH}_3\text{CH}_2\text{OCO}$ ), 2.86 (d, 2H,  $J$  = 5.89 Hz,  $\text{NCH}_2\text{CH}(\text{OEt})_2$ ), 3.43-3.56 (m, 4H,  $\text{NCH}_2\text{CO}$ ,  $\text{CH}_3\text{CH}_2\text{O}$ ), 3.57-3.67 (m, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 3.86 (s, 2H,  $\text{CH}_2\text{Ph}$ ), 4.13 (q, 2H,  $J$  = 7.35 Hz,  $\text{CH}_3\text{CH}_2\text{OCO}$ ), 4.54 (t,  $J$  = 5.15 Hz,  $\text{CH}(\text{OEt})_2$ ), 7.15-7.37 (m, 5H, Ph) ppm

$^{13}\text{C NMR}$  (68 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 14.2 ( $\text{CH}_3\text{CH}_2\text{OCO}$ ), 15.2 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 55.0 ( $\text{NCH}_2\text{CH}(\text{OEt})_2$ ), 56.1 ( $\text{CH}_3\text{CH}_2\text{OCO}$ ), 59.0 ( $\text{NCH}_2\text{CO}$ ), 60.0 ( $\text{CH}_2\text{Ph}$ ), 62.0 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 102.5 ( $\text{CH}(\text{OEt})_2$ ), 127.0, 128.1, 128.8, 139.1 (Ph), 171.7 ( $\text{COO}$ ) ppm

#### 4-Bromo-5-(bromomethyl)benzo (1,3)-dioxole **77**

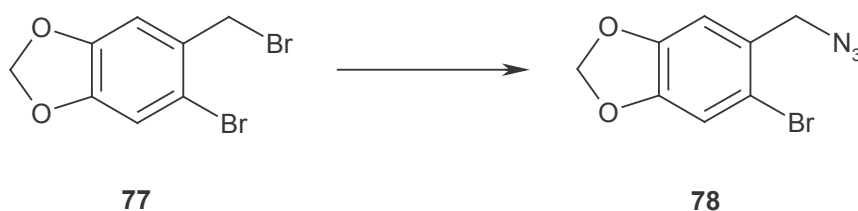


Piperonyl alcohol **76** (5 g, 32.9 mmol) was dissolved in acetic acid (10 mL) at 0 °C. A mixture of Bromine (2 mL) and acetic acid (6 mL) was added dropwise. The reaction mixture was stirred at rt for 1 hour, during this time a white solid precipitated. The mixture was filtered, and the solid residue was washed with ice water. The solid was dried in vacuum to give 9.09 g (92.5%) of **77** as colourless crystals.

$^1\text{H NMR}$  (270 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 4.53 (s, 2H,  $\text{BrCH}_2$ ), 5.98 (s, 2H,  $\text{OCH}_2\text{O}$ ), 6.88 (s, 1H,  $\text{BrCH}_2\text{CCH}$ ), 6.99 (s, 1H,  $\text{BrCCH}$ ) ppm

$^{13}\text{C NMR}$  (68 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 34.1 ( $\text{BrCH}_2$ ), 102.0 ( $\text{OCH}_2\text{O}$ ), 110.4, 113.0, 115.6, 129.7, 148.7 (Ph) ppm

For further data see (a) Naik; Wheeler, *J. Chem. Soc.* **1938**, 1780. (b) Harrowven, D.C.; Nunn, M.I.T.; Blumire, N.J.; Fenwick, D.R. *Tetrahedron Lett.* **2001**, 57, 4447.

**2-Bromopiperonyl azide 78**

Bromopiperonyl bromide **77** (500 mg, 1.7 mmol) was dissolved in anhyd. acetone (30 mL), NaN<sub>3</sub> (221 mg, 3.4 mmol) and NaI (10 mg) were added at 20 °C. The mixture was stirred overnight and H<sub>2</sub>O (20 mL) was added. The aqueous layer was extracted with Et<sub>2</sub>O (3 × 20 mL), the combined organic layers were dried over MgSO<sub>4</sub>. The removal of the solvent in vacuum delivered 410 mg (95%) of bromopiperonyl azide **78** as colourless crystals, which decomposed at 38 °C (data is identical with that lined out in the literature: (a) Padwa, A.; Cochran, J.E.; Kappe, C.O.; *J. Org. Chem.* **1996**, *61*, 3706. (b) Jin, J.; Weinreb, S.M. *J. Am. Chem. Soc.* **1997**, *119*, 5773.)

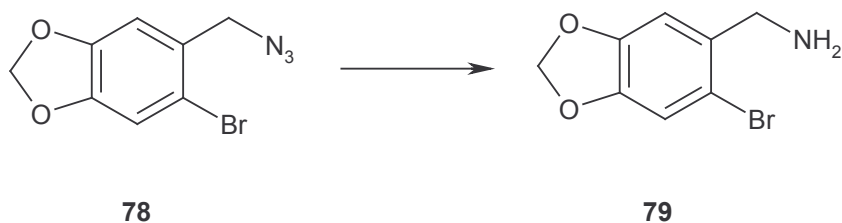
**<sup>1</sup>H NMR** (270 MHz, CDCl<sub>3</sub>): δ = 4.32 (s, 2H, N<sub>3</sub>CH<sub>2</sub>), 5.95 (s, 2H, OCH<sub>2</sub>O), 6.80 (s, 1H, N<sub>3</sub>CH<sub>2</sub>CCH), 6.96 (s, 1H, BrCCH) ppm

**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>): δ = 54.3 (N<sub>3</sub>CH<sub>2</sub>), 102.0 (OCH<sub>2</sub>O), 109.8, 112.8, 114.4, 127.8, 147.5, 148.3 (Ph) ppm

**IR** (in CHCl<sub>3</sub>): 1/λ = 2993 (s), 2901 (s), 2770 (w), 2466 (w), 2107 (s, N<sub>3</sub>), 1686 (w), 1622 (m), 1504 (s), 1475 (s), 1436 (s), 1411 (s), 1391 (s), 1364 (s), 1335 (m), 1217 (s), 1167 (m), 1116 (s) cm<sup>-1</sup>

**MS** (EI, 80 eV, 65 °C): m/z (%) = 255 (48, [M]<sup>+</sup>), 226 (14, [M-CHO]<sup>+</sup>), 213 (100, [M-N<sub>3</sub>]<sup>+</sup>), 199 (5, [M-CH<sub>2</sub>N<sub>3</sub>]<sup>+</sup>), 119 (3, [M-CH<sub>3</sub>BrN<sub>3</sub>]<sup>+</sup>), 90 (27, [C<sub>6</sub>H<sub>2</sub>O]<sup>+</sup>).

**HRMS** (80 eV, 60 °C): m/z, [M]<sup>+</sup> calcd. for C<sub>8</sub>H<sub>6</sub>N<sub>3</sub>O<sub>2</sub><sup>79</sup>Br, 254.96433; found, 254.96621

**2-Bromopiperonyl amine 79**

Bromopiperonyl azide **78** (412 mg, 1.61 mmol) in THF (20 mL) was treated with  $\text{Ph}_3\text{P}$  (633 mg, 2.41 mmol) and  $\text{H}_2\text{O}$  (1 mL). The mixture was stirred for 4 days at 20 °C. After removal of the solvent,  $\text{HCl}$  (1 M, 20 mL) was added. The aqueous layer was extracted with ethyl acetate ( $2 \times 10$  mL),  $\text{NaOH}$  (1 M) was added until the solution displayed a pH of 10. The aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  ( $4 \times 10$  mL), the combined organic layers were dried over  $\text{Na}_2\text{SO}_4$ . The solvent was evaporated to give 310 mg (84%) of bromopiperonyl amine **79** as colourless crystals with m.p. = 78-79 °C.

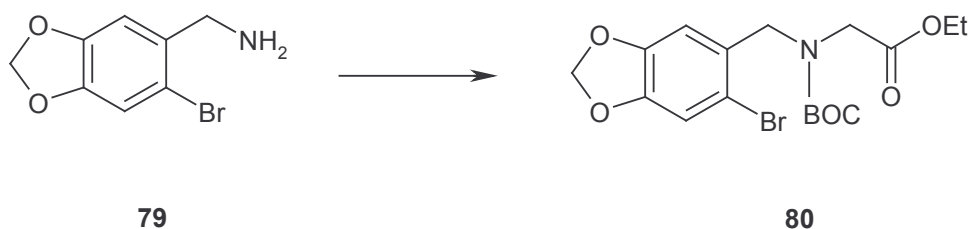
$^1\text{H NMR}$  (270 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.45 (s, 2H,  $\text{NH}_2$ ), 3.70 (s, 2H,  $\text{NCH}_2$ ), 5.88 (s, 2H,  $\text{OCH}_2\text{O}$ ), 6.75 (s, 1H,  $\text{NCCCH}$ ), 6.90 (s, 1H,  $\text{BrCCH}$ ) ppm

$^{13}\text{C NMR}$  (68 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 46.7 ( $\text{NCH}_2$ ), 101.6 ( $\text{OCH}_2\text{O}$ ), 108.9, 112.6, 113.4, 135.5, 147.0, 147.3 (Ph) ppm

**IR** (solution,  $\text{CHCl}_3$ ):  $1/\lambda$  = 3378 (br, m, NH), 3307 (br, m, NH), 3018 (s), 2973 (m), 2896 (m), 1624 (w), 1504 (s), 1476 (s), 1410 (m), 1390 (m), 1355 (w), 1336 (w), 1237 (s), 1216 (s), 1110 (m), 1040 (s), 966 (m), 936 (s)  $\text{cm}^{-1}$

**MS** (EI, 80 eV, 30 °C):  $m/z$  (%) = 229 (71,  $[\text{M}]^+$ ), 213 (20,  $[\text{M}-\text{NH}_2]^+$ ), 199 (16,  $[\text{M}-\text{CH}_4\text{N}]^+$ ), 150 (100,  $[\text{M}-\text{Br}]^+$ ), 122 (19,  $[\text{M}-\text{CH}_4\text{BrN}]^+$ ), 93 (33,  $[\text{M}-\text{C}_2\text{H}_5\text{BrN}]^+$ ).

**HRMS** (80 eV, 30 °C):  $m/z$ ,  $[\text{M}]^+$  calcd. for  $\text{C}_8\text{H}_8\text{NO}_2^{79}\text{Br}$ , 228.97384; found, 228.97543

***N*-tert-Butyloxycarbonyl-*N*-(2-bromopiperonyl)aminoacetic ethyl ester **80****

Piperonylamine **79** (300 mg, 1.31 mmol) and Et<sub>3</sub>N (132 mg, 184 μL, 1.31 mmol) in anhyd. THF (20 mL) were cooled to 0 °C. Ethyl bromoacetate **65** (219 mg, 146 μL, 1.31 mmol) in anhyd. THF (5 mL) was added slowly and the mixture was stirred overnight at 0 °C. Di-*tert*-butyl dicarbonate (1.31 mmol) in anhyd. THF (5 mL) was added and the mixture was stirred at r.t. for 5 hours. 1 N HCl (10 mL) was added to the mixture and the aqueous layer was extracted with Et<sub>2</sub>O (4×20 mL). The combined organic layers were dried over MgSO<sub>4</sub> and the solvent was removed in vacuum. The crude material was purified by column chromatography (n-hexane / ethyl acetate = 6:1) to give 540 mg (99%) of **80** as colourless oil.

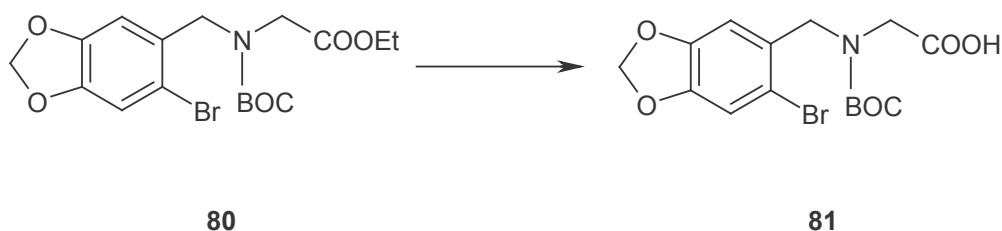
<sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>): δ = 1.20 (2 × t, 3H, *J* = 7.36 Hz, CH<sub>2</sub>CH<sub>3</sub>), 1.42 (2 × s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 3.83 (2 × s, 2H, NCH<sub>2</sub>Ar), 4.14 (q, 2H, *J* = 7.36 Hz, CH<sub>2</sub>CH<sub>3</sub>), 4.48 (2 × s, 2H, NCH<sub>2</sub>COO), 5.92 (2 × s, 2H, OCH<sub>2</sub>O), 6.80 (2 × s, 2H, NCH<sub>2</sub>CCH), 6.92 (2 × s, 2H, BrCCH) ppm

<sup>13</sup>C NMR (68 MHz, CDCl<sub>3</sub>): δ = 14.1, 14.2 (CH<sub>2</sub>CH<sub>3</sub>), 28.1, 28.2 (C(CH<sub>3</sub>)<sub>3</sub>), 47.8, 48.5 (NCH<sub>2</sub>Ar), 50.8, 51.3 (NCH<sub>2</sub>COO), 60.9 (CH<sub>2</sub>CH<sub>3</sub>), 80.6, 80.7 (C(CH<sub>3</sub>)<sub>3</sub>), 101.7 (OCH<sub>2</sub>O), 108.7, 109.5, 112.4, 112.6, 113.5, 129.7, 147.6 (Ph), 155.5 (NCO), 169.6, 169.7 (COOEt) ppm

IR (solution, CHCl<sub>3</sub>): 1/λ = 3019 (s), 2981 (s), 2935 (m), 2901 (m), 1747 (s, COO), 1697 (s, CON), 1504 (s), 1479 (s), 1410 (s), 1455 (s), 1406 (s), 1368 (s), 1216 (s), 1122 (s), 1108 (s), 1040 (s), 956 (m), 935 (s), 896 (m), 862 (m) cm<sup>-1</sup>

MS (EI, 80 eV, 90 °C): *m/z* (%) = 415 (1.6, [M]<sup>+</sup>), 336 (4.3, [M-Br]<sup>+</sup>), 314 (11, [M-C<sub>5</sub>H<sub>9</sub>O<sub>2</sub>]<sup>+</sup>), 280 (100, [M-C<sub>4</sub>H<sub>8</sub>Br]<sup>+</sup>), 234 (14, [M-C<sub>6</sub>H<sub>14</sub>BrO]<sup>+</sup>), 213 (37, [C<sub>8</sub>H<sub>6</sub>BrO<sub>2</sub>]<sup>+</sup>).

HRMS (80 eV, 30 °C): *m/z*, [M]<sup>+</sup> calcd. for C<sub>17</sub>H<sub>22</sub>NO<sub>6</sub><sup>79</sup>Br, 415.06304; found, 415.06622

***N*-tert-Butyloxycarbonyl-*N*-(2-bromopiperonyl)aminoacetic acid **81****

The protected aminoacetic ethyl ester **80** (500 mg, 1.20 mmol) was treated with NaOH (0.1 M, 12 mL) and LiCl (63 mg, 1.48 mmol). After stirring at 80 °C for 3 hours and at 20 °C for 1 hour, aq. sat. KHSO<sub>4</sub> was added until the solution displayed a pH of 4-5. The aqueous solution was extracted with Et<sub>2</sub>O (4×20 mL) and the organic layers were dried over MgSO<sub>4</sub>. The solvent was evaporated to give 433 mg (93%) of protected aminoacetic acid **81** as colourless crystal with m.p. = 122-123 °C.

**<sup>1</sup>H NMR** (270 MHz, CDCl<sub>3</sub>): δ = 1.40 (2 × s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 3.80 (2 × s, 2H, NCH<sub>2</sub>COOH), 4.40 (2 × s, 2H, NCH<sub>2</sub>Ar), 5.85 (2 × s, 2H, OCH<sub>2</sub>O), 6.70 (2 × s, 1H, NCH<sub>2</sub>CCH), 6.85 (2 × s, 1H, BrCCH), 10.3 (s, 1H, COOH) ppm

**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>): δ = 28.0, 28.1 (C(CH<sub>3</sub>)<sub>3</sub>), 47.5, 48.0 (NCH<sub>2</sub>COOH), 50.7, 51.3 (NCH<sub>2</sub>Ar), 81.0, 81.2 (C(CH<sub>3</sub>)<sub>3</sub>), 101.7 (OCH<sub>2</sub>O), 108.7, 109.4, 112.4, 112.6, 113.4, 113.8, 129.3, 147.6, 17.7 (Ph), 15.5, 155.8 (CON), 174.2, 174.3 (COOH) ppm

**IR** (in CHCl<sub>3</sub>): 1/λ = 3100 (s, br, COOH), 3018 (s), 2980 (s), 2928 (s), 2896 (s), 2703 (m), 2644 (m), 2567 (m), 1725 (s, COO), 1701 (s, CON), 1504 (s), 1476 (s), 1423 (s), 1398 (s), 1369 (s), 1265 (s), 1216 (s), 1158 (s), 1108 (s), 1040 (s), 959 (m), 934 (s) cm<sup>-1</sup>

**MS** (EI, 80 eV, 140 °C): m/z (%) = 387 (1.95, [M]<sup>+</sup>), 331 (1.86, [M-C<sub>4</sub>H<sub>8</sub>]<sup>+</sup>), 314 (2, [M-C<sub>4</sub>H<sub>9</sub>O]<sup>+</sup>), 308 (3.8, [M-Br]<sup>+</sup>), 286 (9, [M-C<sub>5</sub>H<sub>9</sub>O<sub>2</sub>]<sup>+</sup>), 252 (100, [M-C<sub>4</sub>H<sub>8</sub>Br]<sup>+</sup>), 213 (40, [C<sub>8</sub>H<sub>6</sub>BrO<sub>2</sub>]<sup>+</sup>), 57 (90, [C<sub>4</sub>H<sub>9</sub>]<sup>+</sup>).

**HRMS** (80 eV, 120 °C): m/z, [M]<sup>+</sup> calcd. for C<sub>15</sub>H<sub>18</sub>NO<sub>6</sub><sup>79</sup>Br, 387.03174; found, 387.03421



### 3.4 Syntheses of Carboxylic Acid Fluorides

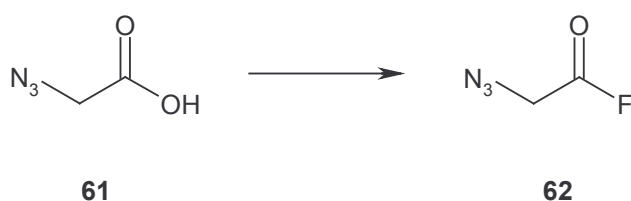
#### General Procedure of carboxylic acid fluoride:

The amino acid (500 mg) in anhyd.  $\text{CH}_2\text{Cl}_2$  (70 mL) at 0 °C was treated with pyridine (0.6 eq) and cyanuric fluoride (0.6 eq) with stirring. The mixture was stirred at 0 °C for about 1.5 hours (TLC monitoring: 0.5 mL sample of the reaction mixture was quenched with MeOH and detected on a TLC plate with n-hexane / ethyl acetate = 1:1).

Work-up method A: Dry pentane (17 mL) was added to complete the precipitation of polar compounds. The solids were filtered off to result a clear solution. The solvents were carefully removed to give the carboxylic acid fluoride, which was found to be pure enough for further transformations.

Work-up method B: The mixture was quenched with ice-water (50 mL), the aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  (3×20 mL), the combined organic layers were dried over  $\text{MgSO}_4$ , and concentrated to give the amino acid fluoride, which was immediately used without any further purification.

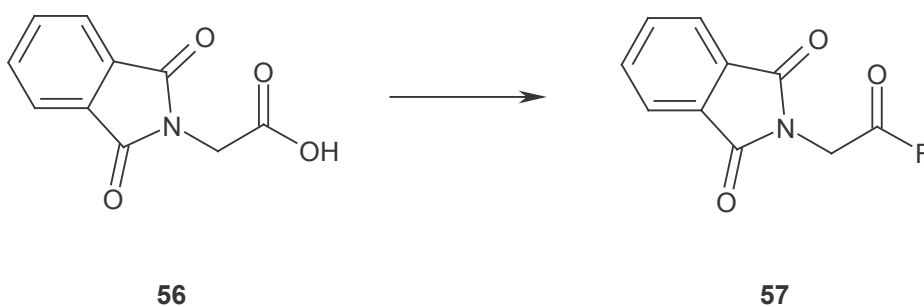
#### Azidoacetyl fluoride **62**



Reaction starting from azidoacetic acid **61** (500 mg, 4.95 mmol) following the work-up method A. Yield: 500 mg (98%) of azidoacetyl fluoride **62** as a yellow oil, which darkens after a short time.

$^1\text{H-NMR}$  (270 MHz,  $\text{CDCl}_3$ ):  $\delta = 4.07\text{-}4.12$  (d, 2H,  $^3J[{}^1\text{H}, {}^{19}\text{F}] = 2.93$  Hz,  $\text{CH}_2$ ) ppm

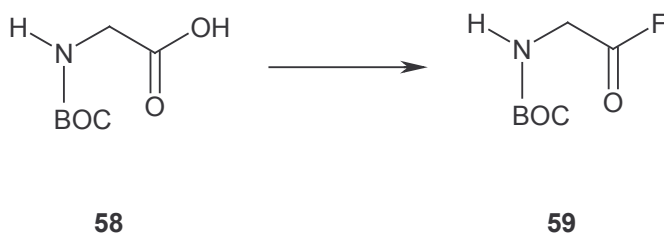
$^{13}\text{C NMR}$  (68 MHz,  $\text{CDCl}_3$ ):  $\delta = 48.2$  (d,  $^2J[{}^{13}\text{C}, {}^{19}\text{F}] = 70$  Hz,  $\text{CH}_2$ ), 158.9 (d,  $^1J[{}^{13}\text{C}, {}^{19}\text{F}] = 364$  Hz, COF) ppm

***N*-Phthaloylglycinyl fluoride 57**

Reaction starting from phthaloylglycine **56** (1 g, 4.87 mmol) following the work-up method B. Yield: 1.0 g (99%) of phthaloylglycinyl fluoride **57** as a pale yellow oil.

$^1\text{H-NMR}$  (270 MHz,  $\text{CDCl}_3$ ):  $\delta = 4.57\text{-}4.67$  (d, 2H,  $^3J [^1\text{H}, ^{19}\text{F}] = 5.15$  Hz,  $\text{CH}_2$ ), 7.72-7.80 (dd, 2H,  $J = 4.89$  Hz, 2.95 Hz, Ph), 7.83-7.92 (dd, 2H,  $J = 5.88$  Hz, 3.67 Hz, Ph) ppm

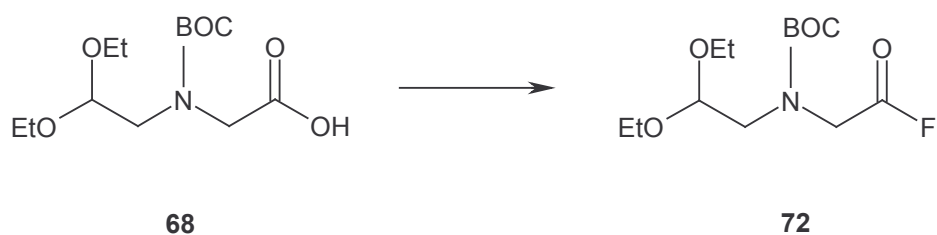
$^{13}\text{C NMR}$  (68 MHz,  $\text{CDCl}_3$ ):  $\delta = 36.8$  (d,  $^2J [^{13}\text{C}, ^{19}\text{F}] = 76$  Hz,  $\text{CH}_2$ ), 123.8, 134.6 (Ph), 157.9 (d,  $^1J [^{13}\text{C}, ^{19}\text{F}] = 363$  Hz, COF) ppm

***N-tert*-Butyloxycarbonylaminoacetyl fluoride 59**

Reaction starting from acid **58** (500 mg, 2.86 mmol) following the work-up method B. Yield: 460 mg (91%) of aminoacetyl fluoride **59** as a pale yellow oil.

$^1\text{H NMR}$  (270 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.40$  (s, 9H,  $(\text{CH}_3)_3\text{C}$ ), 3.98 (m, 2H,  $\text{NCH}_2\text{COF}$ ), 5.45 (br s, 1H,  $\text{NH}$ ) ppm

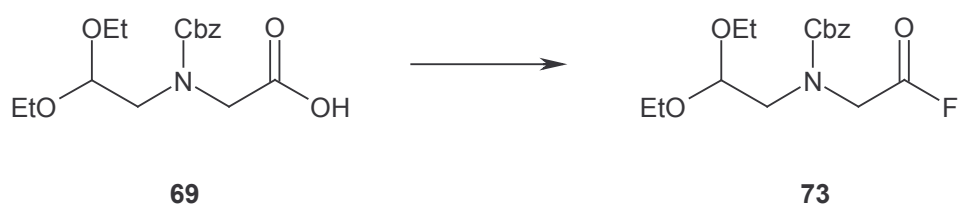
$^{13}\text{C NMR}$  (68 MHz,  $\text{CDCl}_3$ ):  $\delta = 28.0$  ( $\text{C}(\text{CH}_3)_3$ ); 40.0 (d,  $^2J [^{13}\text{C}, ^{19}\text{F}] = 74$  Hz,  $\text{NCH}_2\text{CO}$ ), 80.6 ( $\text{C}(\text{CH}_3)_3$ ); 155.7 (NCO); 158.4, 163.8 (d,  $^1J [^{13}\text{C}, ^{19}\text{F}] = 367$  Hz, COF) ppm

***N*-tert-Butyloxycarbonyl-*N*-(2,2-diethoxyethyl)aminoacetyl fluoride 72**

Reaction starting from acid **68** (500 mg, 1.72 mmol) following the work-up method B. Yield: 470 mg (93%) of **72** as a pale yellow oil.

**<sup>1</sup>H NMR** (270 MHz, CDCl<sub>3</sub>): δ = 1.12 (m, 6H, CH<sub>3</sub>CH<sub>2</sub>O), 1.40 (2 × s, 9H, (CH<sub>3</sub>)<sub>3</sub>C), 3.30 (2 × d, 2H, *J* = 5.15 Hz, NCH<sub>2</sub>CH(OEt)<sub>2</sub>), 3.36-3.49 (m, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 3.56-3.67 (m, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 4.13 (2 × d, 2H, <sup>3</sup>*J* [<sup>1</sup>H, <sup>19</sup>F] = 3.69 Hz, NCH<sub>2</sub>COF), 4.42 (2 × t, 1H, *J* = 5.15 Hz, CH(OEt)<sub>2</sub>) ppm

**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>): δ = 15.1 (CH<sub>3</sub>CH<sub>2</sub>O), 27.9, 28.1 (C(CH<sub>3</sub>)<sub>3</sub>), 47.6 (2 × d, <sup>2</sup>*J* = 68 Hz, NCH<sub>2</sub>COF); 50.6, 51.0 (NCH<sub>2</sub>CH(OEt)<sub>2</sub>); 63.1, 63.4 (CH<sub>3</sub>CH<sub>2</sub>O); 81.1, 81.2 (C(CH<sub>3</sub>)<sub>3</sub>); 102.0, 102.1 (CH(OEt)<sub>2</sub>); 154.4, 154.9 (NCO); 157.1 (d, <sup>1</sup>*J* [<sup>13</sup>C, <sup>19</sup>F] = 408 Hz, COF) ppm

***N*-Benzyloxycarbonyl-*N*-(2,2-diethoxyethyl)aminoacetyl fluoride 73**

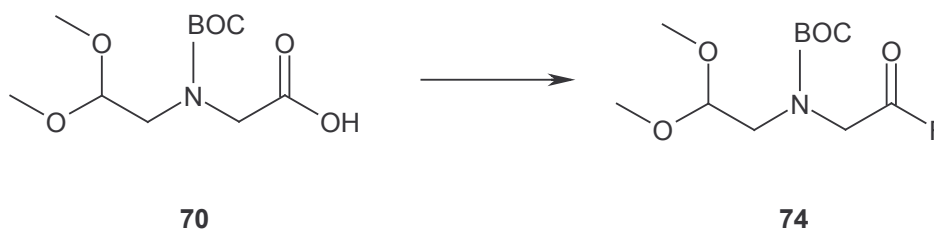
Reaction starting from acid **69** (500 mg, 1.54 mmol) following the work-up method B. Yield: 450 mg (89%) of **73** as a pale yellow oil.

**<sup>1</sup>H NMR** (270 MHz, CDCl<sub>3</sub>): δ = 1.23 (2 × t, 6H, *J* = 7.35 Hz, CH<sub>3</sub>CH<sub>2</sub>O), 3.34-3.74 (m, 6H, CH<sub>3</sub>CH<sub>2</sub>O, NCH<sub>2</sub>CH(OEt)<sub>2</sub>), 4.23 (d, 1H, <sup>3</sup>*J* [<sup>1</sup>H, <sup>19</sup>F] = 3.67 Hz, NCHHCOF), 4.26 (d, 1H, <sup>3</sup>*J* [<sup>1</sup>H, <sup>19</sup>F] = 4.41 Hz, NCHHCOF), 4.48 (2 × t, 1H, *J* = 5.15 Hz, CH(OEt)<sub>2</sub>), 5.14 (2 × s, 2H, CH<sub>2</sub>Ph), 7.26-7.35 (m, 5H, Ph) ppm

**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>): δ = 15.1 (CH<sub>3</sub>CH<sub>2</sub>O), 47.9 (2 × d, <sup>2</sup>*J* [<sup>13</sup>C, <sup>19</sup>F] = 68 Hz, NCH<sub>2</sub>COF), 50.9, 51.3 (NCH<sub>2</sub>CH(OEt)<sub>2</sub>), 63.2, 63.4 (CH<sub>3</sub>CH<sub>2</sub>O), 68.0 (CH<sub>2</sub>Ph), 101.8, 101.9

(CH(OEt)<sub>2</sub>), 127.9, 128.0, 128.2, 128.3, 128.5, 128.6, 128.7, 135.8, 135.9 (Ph), 155.4, 155.8 (NCO), 157.6 (d, <sup>1</sup>J [<sup>13</sup>C, <sup>19</sup>F] = 360 Hz, COF) ppm

***N*-tert-Butyloxycarbonyl-*N*-(2,2-dimethoxyethyl)aminoacetyl fluoride **74****

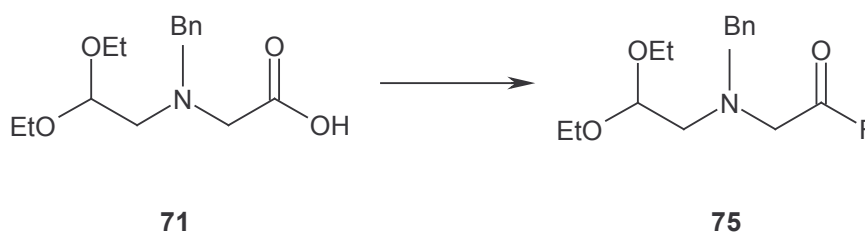


Reaction starting from acid **70** (500 mg, 1.9 mmol) following the work-up method B. Yield: 480 mg (94.5%) of **74** as a pale yellow oil.

<sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>): δ = 1.35 (2×s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 3.25 (2 × s, 6H, OCH<sub>3</sub>), 3.22-3.30 (m, 2H, NCH<sub>2</sub>CH(OCH<sub>3</sub>)<sub>2</sub>), 4.03 (2 × d, 2H, <sup>3</sup>J [<sup>1</sup>H, <sup>19</sup>F] = 3.42 Hz, CH<sub>2</sub>COF), 4.20-4.28 (2 × dd, 1H, J = 5.37 Hz, 4.88 Hz, CH(OCH<sub>3</sub>)<sub>2</sub>) ppm

<sup>13</sup>C NMR (68 MHz, CDCl<sub>3</sub>): δ = 27.7, 27.9 (C(CH<sub>3</sub>)<sub>3</sub>), 47.7 (2 × d, <sup>2</sup>J [<sup>13</sup>C, <sup>19</sup>F] = 68 Hz, CH<sub>2</sub>COF), 50.0, 50.3 (CH<sub>2</sub>CH(OCH<sub>3</sub>)<sub>2</sub>), 54.5, 54.6 (OCH<sub>3</sub>), 80.8, 81.1 (C(CH<sub>3</sub>)<sub>3</sub>), 103.9, 104.0 (CH(OCH<sub>3</sub>)<sub>2</sub>), 154.3, 154.7 (CON), 157.4 (2 × d, <sup>1</sup>J [<sup>13</sup>C, <sup>19</sup>F] = 374 Hz, COF) ppm

***N*-Benzyl-*N*-(2,2-diethoxyethyl)aminoacetyl fluoride **75****



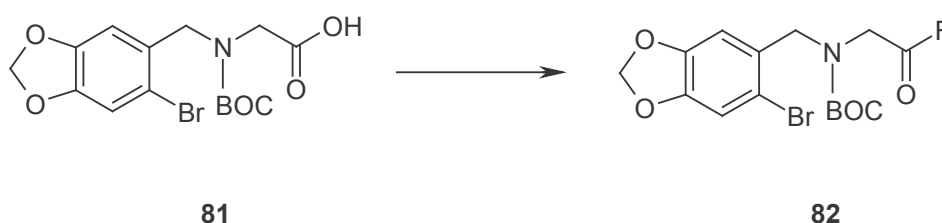
Reaction starting from acid **71** (500 mg, 1.78 mmol) following the work-up method B. Yield: 420 mg (84%) of **75** as a pale yellow oil.

<sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>): δ = 1.15 (t, 6H, J = 7.35 Hz, CH<sub>3</sub>CH<sub>2</sub>O), 2.93 (dd, 2H, J = 5.15 Hz, 1.48 Hz, NCH<sub>2</sub>CH(OEt)<sub>2</sub>), 3.44 (q, 2H, J = 7.35 Hz, CH<sub>3</sub>CH<sub>2</sub>O), 3.61 (q, 2H, J = 7.35 Hz,

$\text{CH}_3\text{CH}_2\text{O}$ ), 3.67 (d, 2H,  $^3J$  [ $^1\text{H}$ ,  $^{19}\text{F}$ ] = 2.94 Hz,  $\text{NCH}_2\text{COF}$ ), 3.90 (d, 2H,  $J$  = 1.47 Hz,  $\text{CH}_2\text{Ph}$ ), 4.53 (t, 1H,  $J$  = 5.15 Hz,  $\text{NCH}_2\text{CH}(\text{OEt})_2$ ), 7.30 (m, 5H, Ph) ppm

$^{13}\text{C}$  NMR (68 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 15.1 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 52.2 (d,  $^2J$  [ $^{13}\text{C}$ ,  $^{19}\text{F}$ ] = 61 Hz,  $\text{NCH}_2\text{COF}$ ), 55.8 ( $\text{NCH}_2\text{CH}(\text{OEt})_2$ ), 58.9 ( $\text{CH}_2\text{Ph}$ ), 62.3 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 102.2 ( $\text{NCH}_2\text{CH}(\text{OEt})_2$ ), 127.5, 128.4, 128.8, 137.8 (Ph), 158.4, 164.0 (d,  $^1J$  [ $^{13}\text{C}$ ,  $^{19}\text{F}$ ] = 380 Hz, COF) ppm

***N*-tert-Butyloxycarbonyl-*N*-(2-bromopiperonyl)aminoacetyl fluoride **82****



Reaction starting from acid **81** (1.80 g, 4.65 mmol) following the work-up method B. Yield: 1.80 g (99.5%) of **82** as a pale yellow oil.

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.40 (2 × s, 9H,  $\text{C}(\text{CH}_3)_3$ ), 3.95-4.12 (2 × d, 2H,  $^3J$  [ $^1\text{H}$ ,  $^{19}\text{F}$ ] = 2.94 Hz,  $\text{CH}_2\text{COF}$ ), 4.50 (2 × s, 2H,  $\text{NCH}_2\text{Ar}$ ), 5.92 (s, 2H,  $\text{OCH}_2\text{O}$ ), 6.70-6.85 (2 × s, 1H,  $\text{NCH}_2\text{CCH}$ ), 6.95 (2 × s, 1H,  $\text{BrCCH}$ ) ppm

$^{13}\text{C}$  NMR (68 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 28.0, 28.1 ( $\text{C}(\text{CH}_3)_3$ ), 45.4 (2 × d,  $^2J$  [ $^{13}\text{C}$ ,  $^{19}\text{F}$ ] = 68 Hz,  $\text{CH}_2\text{COF}$ ), 50.3, 50.9 ( $\text{NCH}_2\text{Ar}$ ), 81.7 ( $\text{C}(\text{CH}_3)_3$ ), 101.8 ( $\text{OCH}_2\text{O}$ ), 109.0, 109.7, 112.5, 112.7, 114.1, 128.8, 147.8, 148.0 (Ph), 154.5 (CON), 157.4 (d,  $^1J$  [ $^{13}\text{C}$ ,  $^{19}\text{F}$ ] = 367 Hz, COF) ppm

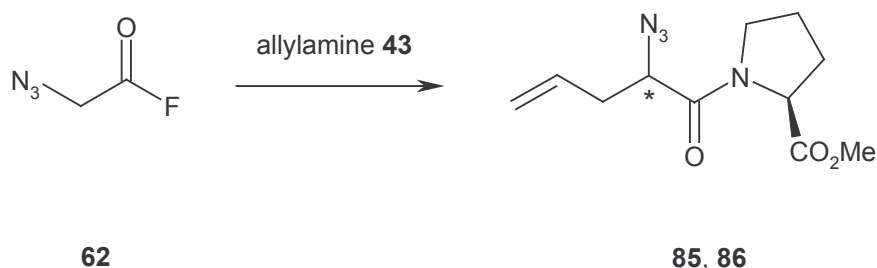
### 3.5 Zwitterionic Aza-Claisen Rearrangement

#### General Procedure:

Under Argon *N*-allylpyrrolidine and Na<sub>2</sub>CO<sub>3</sub> (3 equivalent) in anhyd. CH<sub>2</sub>Cl<sub>2</sub> were treated with freshly prepared acid fluoride in anhyd. CH<sub>2</sub>Cl<sub>2</sub>. Then AlMe<sub>3</sub> (2M in heptane) was injected slowly. A gas was evolved and the mixture darkened to light brown. The mixture was stirred until no reactant remained according TLC control. Then, MeOH was added dropwise and stirring was continued for a further 30 min at 20 °C. The polar side products and salts were filtered off by passing the mixture through a short silica gel column. The filtrate was concentrated and crude material was purified by column chromatography and HPLC (if necessary).

#### (*S*)-2-Azidopent-4-enoic acid [(2*S*)-methoxycarbonylpyrrolidinyl]amide **85**

#### (*R*)-2-Azidopent-4-enoic acid [(2*S*)-methoxycarbonylpyrrolidinyl]amide **86**



Reaction with *N*-allylproline methyl ester **43** (440 mg, 2.6 mmol) and azidoacetyl fluoride **62** (618 mg, 6 mmol) following the general procedure. Reaction temperature 20 °C, 0 °C and –20 °C, reaction time 3 hours. Purification via column chromatography (n-hexane / ethylacetate = 2:1). Yield: 480 mg (73%) (reaction at 20 °C), 510 mg (77%) (reaction at 0 °C) and 520 mg (79%) (reaction at –20 °C) of **85** and **86** as a yellow oil.

Data of **85** and **86** (reaction temperature –20 °C):

$$[\alpha]_D^{20} = -159.2^\circ \text{ (c = 1.3, CHCl}_3\text{)}$$

<sup>1</sup>H-NMR (270 MHz, CDCl<sub>3</sub>): δ = 1.70-2.00 (m, 3H, CH<sub>2</sub>CHH), 2.01-2.22 (m, 1H, CH<sub>2</sub>CHH), 2.50 (m, 2H, CH<sub>2</sub>CH=CH<sub>2</sub>), 3.35-3.79 (m, 6H, CH<sub>2</sub>CH<sub>2</sub>N, NCHCOO, COOCH<sub>3</sub>), 4.40 (2×dd, 1H, *J* = 7.30 Hz, 3.90 Hz, N<sub>3</sub>CH), 5.14 (dd, 1H, *J* = 10.26 Hz, 0.98 Hz, CH=CHH), 5.22 (dd,

$^1\text{H}$ ,  $J = 17.09$  Hz, 1.46 Hz,  $\text{CH}=\text{CHH}$ ), 5.80 (dddd, 1H,  $J = 17.09$  Hz, 10.26 Hz, 6.84 Hz, 6.83 Hz,  $\text{CH}=\text{CH}_2$ ) ppm

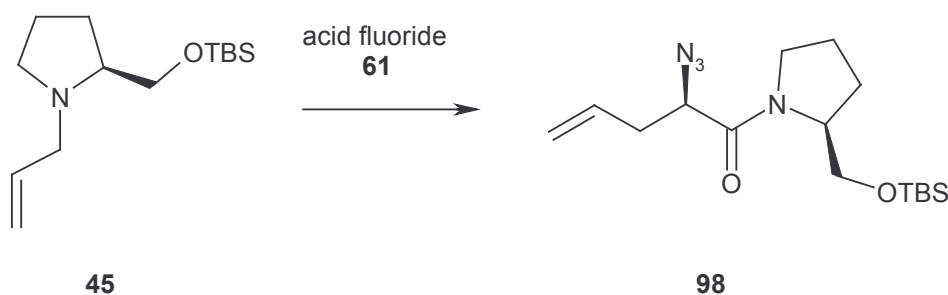
$^{13}\text{C}$  NMR (68 MHz,  $\text{CDCl}_3$ ):  $\delta = 22.0, 24.4$  ( $\text{CH}_2\text{CH}_2$ ), 28.6, 30.9 ( $\text{CH}_2\text{CH}_2$ ), 34.3, 34.5 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 46.4, 46.6 ( $\text{CH}_2\text{CH}_2\text{N}$ ), 51.9, 52.4 ( $\text{COOCH}_3$ ), 58.7 ( $\text{NCHCOO}$ ), 59.2 ( $\text{N}_3\text{CH}$ ), 118.2, 118.6 ( $\text{CH}=\text{CH}_2$ ), 132.3, 132.6 ( $\text{CH}=\text{CH}_2$ ), 167.5 ( $\text{CON}$ ), 171.7, 171.9 ( $\text{COO}$ ) ppm

IR (KBr, film):  $1/\lambda = 3079$  (w), 2980 (m), 2954 (m), 2882 (m), 2103 (s,  $\text{N}_3$ ), 1746 (s,  $\text{COO}$ ), 1653 (s,  $\text{CON}$ ), 1436 (s), 1363 (m), 1322 (m), 1280 (m), 1197 (s), 1175 (s), 1095 (m), 1043 (m), 996 (m)  $\text{cm}^{-1}$

MS (EI, 80 eV, 110°C):  $m/z$  (%) = 252 (5.2,  $[\text{M}]^+$ ), 224 (1.5,  $[\text{M}-\text{N}_2]^+$ ), 210 (8.3,  $[\text{M}-\text{N}_3]^+$ ), 193 (5.8,  $[\text{M}-\text{C}_2\text{H}_3\text{O}_2]^+$ ), 165 (3.4,  $[\text{M}-\text{C}_2\text{H}_3\text{O}_2\text{N}_2]^+$ ), 128 (100,  $[\text{C}_6\text{H}_{10}\text{NO}_2]^+$ ), 70 (31,  $[\text{C}_4\text{H}_8\text{N}]^+$ ).

HRMS (80 eV, 100 °C):  $m/z$ ,  $[\text{M}]^+$  calcd. for  $\text{C}_{11}\text{H}_{16}\text{N}_4\text{O}_3$ , 252.1222; found: 252.1236.

**(*R*)-2-Azidopent-4-enoic acid [(2*S*)-*tert*-butyldimethylsilyloxymethylpyrrolidinyl]-amide **98****



Reaction with allylamine **45** (500 mg, 1.96 mmol) and azidoacetyl fluoride **61** (605 mg, 5.87 mmol) following general procedure. Reaction temperature 0 °C, reaction time 3 hours. Purification via column chromatography (n-hexane / ethyl acetate = 5:1). Yield: 500 mg (76%) of **98** as a yellow oil.

$[\alpha]_D^{20} = -104.7^\circ$  ( $c = 1.4$ ,  $\text{CHCl}_3$ )

$^1\text{H}$ -NMR (270 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.00$  (s, 6H,  $\text{Si}(\text{CH}_3)_2$ ), 0.85 (s, 9H,  $\text{SiC}(\text{CH}_3)_3$ ), 1.72-2.11 (m, 4H,  $\text{CH}_2\text{CH}_2$ ), 2.05 (m, 2H,  $\text{CH}_2=\text{CHCH}_2$ ), 3.39-3.50 (m, 2H,  $\text{NCH}_2\text{CHH}$ ,  $\text{CHHO}$ ), 3.55-3.85 (m, 3H,  $\text{NCH}_2\text{CHH}$ ,  $\text{CHHO}$ ,  $\text{NCHCH}_2\text{O}$ ), 4.10 (m, 1H,  $\text{N}_3\text{CH}$ ), 5.11 (d, 1H,  $J = 10.30$

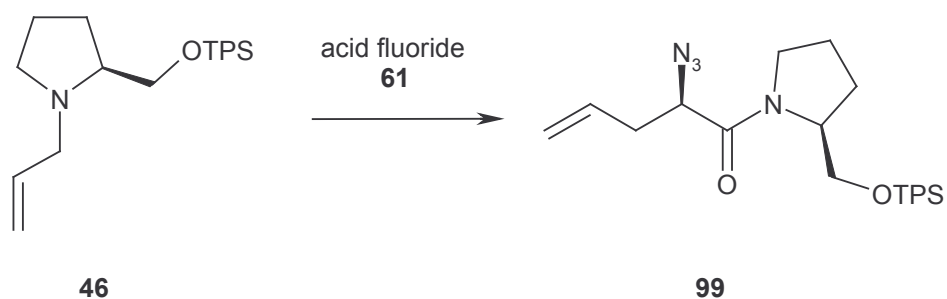
Hz, CH=CH $\mathbf{H}$ ), 5.18 (d, 1H,  $J$  = 16.92 Hz, CH=CH $\mathbf{H}$ ), 5.75 (dddd, 1H,  $J$  = 16.92 Hz, 10.30 Hz, 7.36 Hz, 6.62 Hz Hz, CH=CH $\mathbf{2}$ ) ppm

$^{13}\text{C}$  NMR (68 MHz, CDCl $_3$ ):  $\delta$  = -5.5 (SiCH $_3$ ), 18.0 (SiC(CH $_3$ ) $_3$ ), 24.1, 24.3 (CH $_2$ CH $_2$ ), 25.7 (SiC(CH $_3$ ) $_3$ ), 26.8 (CH $_2$ CH $_2$ ), 34.6, 34.8 (CH $_2$ CH=CH $_2$ ), 47.3, 47.5 (NCH $_2$ CH $_2$ ), 58.6, 58.9 (NCHCH $_2$ O), 59.5 (CH $_2$ O), 62.4 (N $_3$ CH), 118.7, 118.8 (CH=CH $_2$ ), 132.6, 132.9 (CH=CH $_2$ ), 168.9 (CON) ppm

IR (solution, CHCl $_3$ ):  $1/\lambda$  = 3013 (m), 2956 (s), 2930 (s), 2858 (m), 2101 (s, N $_3$ ), 1647 (s, CON), 1471 (m), 1462 (m), 1429 (s), 1381 (w), 1360 (w), 1319 (w), 1257 (s), 1193 (w), 1165 (w), 1103 (s), 1055 (m), 1004 (m), 956 (w), 919 (m) cm $^{-1}$

MS (pos. FAB):  $m/z$  (%) = 339 (48, [M+H] $^+$ ), 323 (3.76, [M-CH $_3$ ] $^+$ ), 281 (21, [M-C(CH $_3$ ) $_3$ ] $^+$ ).

**(*R*)-2-Azidopent-4-enoic acid [(2*S*)-*tert*-butyldiphenylsilyloxymethylpyrrolidinyl]-amide **99****



Reaction with allylamine **46** (540 mg, 1.42 mmol) and azidoacetyl fluoride **61** (510 mg, 4.95 mmol) following general procedure. Reaction temperature 0 °C, reaction time 3 hours. Purification via column chromatography (n-hexane / ethyl acetate = 5:1). Yield: 500 mg (76%) of **99** as a yellow oil.

$[\alpha]_D^{20}$  = -49.1° (c = 1.9, CHCl $_3$ )

$^1\text{H}$ -NMR (270 MHz, CDCl $_3$ ):  $\delta$  = 1.05 (s, 9H, SiC(CH $_3$ ) $_3$ ), 1.80-2.20 (m, 4H, CH $_2$ CH $_2$ ), 2.4-2.7 (2×m, 1H, NCH $\mathbf{H}$ CH $_2$ ), 3.35-3.50 (m, 2H, CH $_2$ CH=CH $_2$ ), 3.50-3.60 (m, 1H, NCH $\mathbf{H}$ CH $_2$ ), 3.70-3.82 (m, 2H, NCH $\mathbf{H}$ , OCH $\mathbf{H}$ ), 3.83-3.95 (m, 1H, OCH $\mathbf{H}$ ), 4.20-4.36 (m, 1H, N $_3$ CH), 5.12-5.19 (2×d, 1H,  $J$  = 11.23 Hz, CH=CH $\mathbf{H}$ ), 5.20-5.29 (2×d, 1H,  $J$  = 17.09 Hz, CH=CH $\mathbf{H}$ ), 5.73-5.90 (2×dddd, 1H,  $J$  = 17.09 Hz, 11.23 Hz, 7.32 Hz, 6.84 Hz, CH=CH $\mathbf{2}$ ) ppm



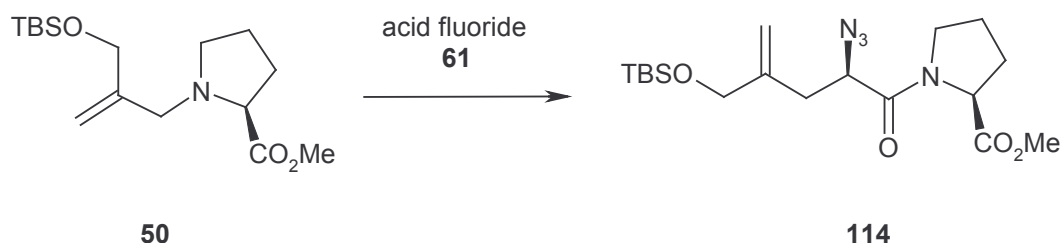
$^{13}\text{C}$  NMR (68 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 19.0, 19.1 ( $\text{SiC}(\text{CH}_3)_3$ ), 21.4, 24.1 ( $\text{CH}_2\text{CH}_2$ ), 26.7, 26.9 ( $\text{SiC}(\text{CH}_3)_3$ ), 27.9 ( $\text{CH}_2\text{CH}_2$ ), 34.6, 34.8 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 45.8, 47.2 ( $\text{NCH}_2\text{CH}_2$ ), 58.3, 58.5 ( $\text{NCH}$ ), 58.6, 59.4 ( $\text{N}_3\text{CH}$ ), 63.2, 64.8 ( $\text{CH}_2\text{O}$ ), 118.7 ( $\text{CH}=\text{CH}_2$ ), 127.5, 129.5, 129.9, 132.0, 132.6, 134.9, 135.4 (Ph), 132.7, 133.3 ( $\text{CH}=\text{CH}_2$ ), 167.4, 167.7 (CON) ppm

IR (KBr, film):  $1/\lambda$  = 3070 (m), 3048 (m), 2958 (s), 2930 (s), 2857 (s), 2245 (w), 2100 ( $\text{N}_3$ ), 1827 (w), 1749 (w), 1651 (CON), 1588 (w), 1567 (w), 1471 (m), 1428 (s), 1390 (m), 1360 (m), 1341 (m), 1260 (m), 1235 (m), 1192 (m), 1164 (w), 1113 (s), 1054 (m), 997 (m)  $\text{cm}^{-1}$

MS (EI, 80 eV,  $130^\circ\text{C}$ ):  $m/z$  (%) = 462 (0.58,  $[\text{M}]^+$ ), 447 (0.32,  $[\text{M}-\text{CH}_3]^+$ ), 434 (0.77,  $[\text{M}-\text{N}_2]^+$ ), 405 (100,  $[\text{M}-\text{C}_4\text{H}_9]^+$ ), 377 (8,  $[\text{M}-\text{C}_4\text{H}_9\text{N}_2]^+$ ), 310 (14,  $[\text{M}-\text{C}_{12}\text{H}_8]^+$ ), 280 (11,  $[\text{M}-\text{C}_{14}\text{H}_{14}]^+$ ).

HRMS (80 eV,  $130^\circ\text{C}$ ):  $m/z$ ,  $[\text{M}]^+$  calcd. for  $\text{C}_{26}\text{H}_{34}\text{N}_4\text{O}_2\text{Si}$ , 462.24510; found, 462.24298

**(*R*)-2-Azido-4-(*tert*-butyldimethylsilyloxymethyl)pent-4-enoic acid [(2*S*)-methoxycarbonylpyrrolidinyl]amide **114****



Reaction with *N*-allylproline methyl ester **50** (1g, 3.19 mmol) and azidoacetyl fluoride **61** (1g, 9.9 mmol) following general procedure. Reaction temperature  $0^\circ\text{C}$ , reaction time 3 hours. Purification via column chromatography (n-hexane / ethyl acetate = 3:1). Yield: 1.0 g (79%) of **114** as a yellow oil.

$[\alpha]_D^{20} = -75.5^\circ$  ( $c = 2.1$ ,  $\text{CHCl}_3$ )

$^1\text{H}$ -NMR (270 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.01 (s, 6H,  $\text{Si}(\text{CH}_3)_2$ ), 0.85 (s, 9H,  $\text{C}(\text{CH}_3)_3$ ), 1.65-2.24 (m, 4H,  $\text{CH}_2\text{CH}_2$ ), 2.46-2.68 (m, 2H,  $\text{N}_3\text{CHCH}_2$ ), 3.45-3.78 (m, 5H,  $\text{OCH}_3$ ,  $\text{NCH}_2\text{CH}_2$ ), 3.85-3.94 (m, 1H,  $\text{NCHCOO}$ ), 4.03-4.22 (m, 2H,  $\text{TBSOCH}_2$ ), 4.40-4.57 (m, 1H,  $\text{N}_3\text{CH}$ ), 4.99 ( $2 \times$  s, 1H,  $\text{C}=\text{CHH}$ ), 5.15 ( $2 \times$  s, 1H,  $\text{C}=\text{CHH}$ ) ppm

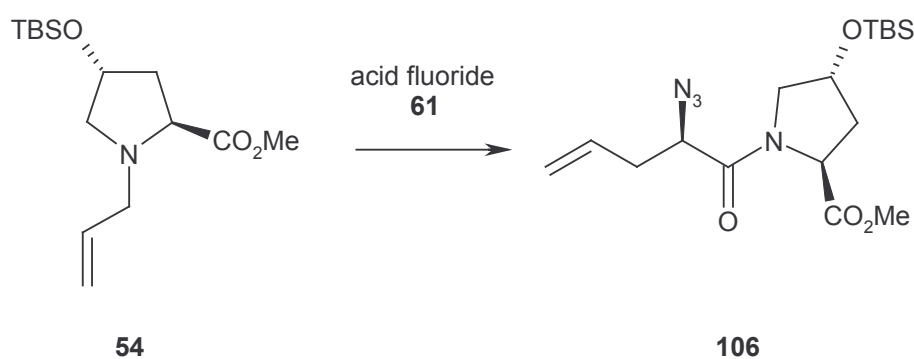
$^{13}\text{C}$  NMR (68 MHz,  $\text{CDCl}_3$ ):  $\delta = -5.4$  ( $\text{Si}(\text{CH}_3)_2$ ), 18.2 ( $\text{SiC}(\text{CH}_3)_3$ ), 23.1, 24.6 ( $\text{CH}_2\text{CH}_2$ ), 25.8 ( $\text{SiC}(\text{CH}_3)_3$ ), 28.9, 29.3 ( $\text{CH}_2\text{CH}_2$ ), 33.7 ( $\text{N}_3\text{CHCH}_2$ ), 46.8 ( $\text{NCH}_2\text{CH}_2$ ), 52.1, 51.2 ( $\text{OCH}_3$ ), 57.9, 58.3 ( $\text{NCHCOO}$ ), 58.7, 58.9 ( $\text{N}_3\text{CH}$ ), 65.3, 66.0 ( $\text{TBSOCH}_2$ ), 112.2, 113.2 ( $\text{C}=\text{CH}_2$ ), 143.2 ( $\text{C}=\text{CH}_2$ ), 168.7, 172.0 ( $\text{COOCH}_3$ ) ppm

IR (solution,  $\text{CHCl}_3$ ):  $1/\lambda = 3079$  (w), 2955 (s), 2930 (s), 2885 (m), 2857 (s), 2106 (s,  $\text{N}_3$ ), 1747 (s, COO), 1658 (s, CON), 1472 (m), 1435 (s), 1389 (m), 1362 (m), 1343 (m), 1252 (s), 1197 (s), 1176 (s), 1112 (m), 1006 (m), 939 (w), 908 (m)  $\text{cm}^{-1}$

MS (EI, 80 eV,  $80^\circ\text{C}$ ):  $m/z$  (%) = 396 (0.67,  $[\text{M}]^+$ ), 381 (0.91,  $[\text{M}-\text{CH}_3]^+$ ), 354 (5.9,  $[\text{M}-\text{N}_3]^+$ ), 339 (44,  $[\text{M}-\text{CH}_3\text{N}_3]^+$ ), 223 (100,  $[\text{M}-\text{C}_6\text{H}_{15}\text{N}_3\text{OSi}]^+$ ), 128 (58,  $[\text{C}_6\text{H}_{10}\text{NO}_2]^+$ ).

HRMS (80 eV,  $80^\circ\text{C}$ ):  $m/z$ ,  $[\text{M}]^+$  calcd. for  $\text{C}_{18}\text{H}_{32}\text{N}_4\text{O}_4\text{Si}$ , 396.21928; found, 396.21969

**(*R*)-2-Azidopent-4-enoic acid [(*2S*)-methoxycarbonyl-(*4R*)-*tert*-butyldimethylsilyloxyprolidinyl]amide **106****



Reaction with allylamine **54** (500 mg, 1.67 mmol) and azidoacetyl fluoride **61** (506 mg, 5.01 mmol) following the general procedure. Reaction temperature  $0^\circ\text{C}$ , reaction time 3 hours. Purification via column chromatography (n-hexane / ethyl acetate = 3:1). Yield: 480 mg (75%) of **106** as colourless crystals with m.p. =  $67^\circ\text{C}$ .

$[\alpha]_D^{20} = -115.4^\circ$  (c = 0.5,  $\text{CHCl}_3$ )

$^1\text{H}$ -NMR (270 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.00$  (s, 6H,  $\text{Si}(\text{CH}_3)_2$ ), 0.85 (s, 9H,  $\text{SiC}(\text{CH}_3)_3$ ), 1.95-2.06 (ddd, 1H,  $J = 13.19$  Hz, 12.69 Hz, 2.99 Hz,  $\text{CHHCHCO}_2\text{CH}_3$ ), 2.12-2.21 (m, 1H,  $\text{CHHCHCO}_2\text{CH}_3$ ), 2.47- 2.67 (ddd, 2H,  $J = 14.65$  Hz, 14.16 Hz, 3.17 Hz,  $\text{CH}_2\text{CH}=\text{CH}_2$ ), 3.32-3.42 (dd, 1H,  $J = 10.25$  Hz, 1.46 Hz,  $\text{NCHH}$ ), 3.60-3.80 (m, 5H,  $\text{OCH}_3$ ,  $\text{NCHH}$ ,  $\text{N}_3\text{CH}$ ), 4.45-4.55 (m, 1H,  $\text{TBSOCH}$ ), 4.50-4.57 (dd, 1H,  $J = 11.72$  Hz, 7.82 Hz,  $\text{NCHCO}_2\text{CH}_3$ ), 5.07- 5.17 (dd,

$^1\text{H}$ ,  $J = 10.25$  Hz,  $1.47$  Hz,  $\text{CH}=\text{CHH}$ ),  $5.17$ - $5.22$  (dd,  $1\text{H}$ ,  $J = 17.09$  Hz,  $1.47$  Hz,  $\text{CH}=\text{CHH}$ ),  $5.70$ - $5.87$  (dddd,  $1\text{H}$ ,  $J = 17.09$  Hz,  $10.25$  Hz,  $7.32$  Hz,  $6.84$  Hz,  $\text{CH}=\text{CH}_2$ ) ppm

$^{13}\text{C}$  NMR (68 MHz,  $\text{CDCl}_3$ ):  $\delta = -5.0$ ,  $-4.8$  ( $\text{Si}(\text{CH}_3)_2$ ),  $18.2$  ( $\text{SiC}(\text{CH}_3)_3$ ),  $25.5$  ( $\text{SiC}(\text{CH}_3)_3$ ),  $34.8$  ( $\text{CH}_2\text{CH}=\text{CH}_2$ ),  $37.8$ ,  $40.0$  ( $\text{CH}_2\text{CHCO}_2\text{CH}_3$ ),  $52.3$  ( $\text{OCH}_3$ ),  $55.2$  ( $\text{NCH}_2$ ),  $58.8$  ( $\text{N}_3\text{CH}$ ),  $59.6$  ( $\text{NCHCO}_2\text{CH}_3$ ),  $70.5$  ( $\text{TBSOCH}$ ),  $118.9$  ( $\text{CH}=\text{CH}_2$ ),  $132.3$ ,  $132.4$  ( $\text{CH}=\text{CH}_2$ ),  $168.1$  ( $\text{CON}$ ),  $172.1$  ( $\text{COOCH}_3$ ) ppm

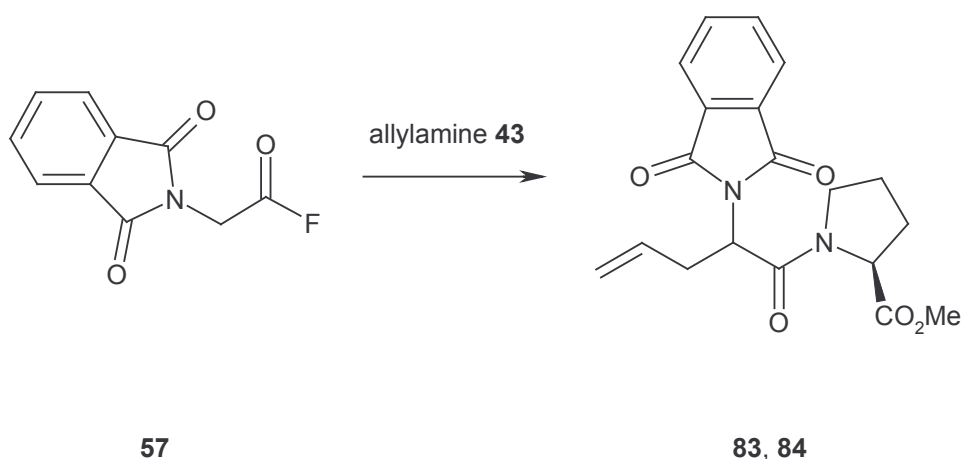
IR (in  $\text{CHCl}_3$ ):  $1/\lambda = 3087$  (w),  $2992$  (w),  $2953$  (m),  $2928$  (m),  $2893$  (w),  $2856$  (m),  $2122$  (s,  $\text{N}_3$ ),  $1765$  (s,  $\text{COO}$ ),  $1647$  (s,  $\text{CON}$ ),  $1470$  (m),  $1462$  (m),  $1434$  (s),  $1367$  (m),  $1324$  (w),  $1258$  (m),  $1240$  (m),  $1202$  (m),  $1192$  (m),  $1169$  (s),  $1150$  (m),  $1085$  (s),  $1023$  (s),  $1004$  (m),  $974$  (m),  $924$  (m),  $915$  (m)  $\text{cm}^{-1}$

MS (EI,  $80$  eV,  $90^\circ\text{C}$ ):  $m/z$  (%) =  $382$  (0.55,  $[\text{M}]^+$ ),  $367$  (1.63,  $[\text{M}-\text{CH}_3]^+$ ),  $325$  (100,  $[\text{M}-\text{C}_4\text{H}_9]^+$ ),  $258$  (12,  $[\text{C}_{12}\text{H}_{24}\text{NO}_3\text{Si}]^+$ ).

HRMS ( $80$  eV,  $90^\circ\text{C}$ ):  $m/z$ ,  $[\text{M}]^+$  calcd. for  $\text{C}_{17}\text{H}_{30}\text{N}_4\text{O}_4\text{Si}$ ,  $382.203634$ ; found,  $382.20578$   
 $[\text{M}-\text{CH}_3]^+$  calcd. for  $\text{C}_{16}\text{H}_{27}\text{N}_4\text{O}_4\text{Si}$ ,  $367.180159$ ; found,  $367.18466$   
 $[\text{M}-\text{C}_4\text{H}_9]^+$  calcd. for  $\text{C}_{13}\text{H}_{21}\text{N}_4\text{O}_4\text{Si}$ ,  $325.133209$ ; found,  $325.13534$

**(S)-2-Phthaloylamidopent-4-enoic acid [(2S)-methoxycarbonylpyrrolidinyl]amide 83**

**(R)-2-Phthaloylamidopent-4-enoic acid [(2S)-methoxycarbonylpyrrolidinyl]amide 84**



Reaction with *N*-allylproline methyl ester **43** (270 mg, 1.6 mmol) and phthaloylglycinyll fluoride **57** (660 mg, 3.61 mmol) following the general procedure. Reaction temperature  $0^\circ\text{C}$ , reaction time 16 hours. Purification and separation of the diastereomers via column

chromatography (n-hexane-EtOAc = 1:1). Yield: 220 mg (38%) of **diastereomer 1** as colourless crystals with m.p. = 111-112 °C and 230 mg (40%) of **diastereomer 2** as a pale yellow oil.

**Diastereomer 1:**

$[\alpha]_D^{20} = -104.7^\circ$  (c = 1.1, CHCl<sub>3</sub>)

**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>): δ = 1.85-2.11 (m, 4H, CH<sub>2</sub>CH<sub>2</sub>), 2.85 (ddd, 1H, J = 14.71 Hz, 5.15 Hz, 5.15 Hz, CH<sub>2</sub>=CHCHH), 3.09 (ddd, 1H, J = 14.71 Hz, 9.56 Hz, 9.56 Hz, CH<sub>2</sub>=CHCHH), 3.30 (m, 1H, CHHN), 3.60-3.72 (m, 4H, CHHN, OCH<sub>3</sub>), 4.45 (dd, 1H, J = 8.09 Hz, 2.95 Hz, CHCOO), 4.85 (dd, 1H, J = 10.29 Hz, 4.41 Hz, NCH), 4.96 (d, 1H, J = 10.30 Hz, CH=CHH), 5.01 (d, 1H, J = 16.91 Hz, CH=CHH), 5.74 (dddd, 1H, J = 16.91 Hz, 10.29 Hz, 7.32 Hz, 5.88 Hz, CH=CH<sub>2</sub>) ppm

**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>): δ = 24.8 (CH<sub>2</sub>CH<sub>2</sub>), 28.6 (CH<sub>2</sub>CH<sub>2</sub>), 32.9 (CH<sub>2</sub>=CHCH<sub>2</sub>), 46.8 (CH<sub>2</sub>N), 52.2 (NCHCOO), 52.2 (NCH), 59.3 (COOCH<sub>3</sub>), 118.6 (CH<sub>2</sub>=CH), 123.5, 131.4, 134.2 (Ar), 133.4 (CH=CH), 167.0, 167.5 (CON), 172.4 (COO) ppm

**IR** (solution, CHCl<sub>3</sub>): 1/λ = 3020 (s), 2982 (m), 2956 (m), 2882 (m), 1776 (s, COO), 1723 (s, CONCO), 1658 (s, CON), 1469 (m), 1437 (s), 1420 (s), 1383 (s), 1364 (s), 1214 (s), 1179 (s), 1116 (m), 1087 (m), 1047 (m) cm<sup>-1</sup>

**MS** (EI, 80 eV, 150 °C): m/z (%) = 356 (38.9, [M]<sup>+</sup>), 297 (18, [M-C<sub>2</sub>H<sub>3</sub>O<sub>2</sub>]<sup>+</sup>), 228 (8, [M-C<sub>6</sub>H<sub>10</sub>NO<sub>2</sub>]<sup>+</sup>), 200 (100, [M-C<sub>6</sub>H<sub>10</sub>NO<sub>2</sub>-CO]<sup>+</sup>).

**HRMS** (80 eV, 150 °C): m/z, [M]<sup>+</sup> calcd. for C<sub>19</sub>H<sub>20</sub>N<sub>2</sub>O<sub>5</sub>, 356.13722; found, 356.13565

**Diastereomer 2:**

$[\alpha]_D^{20} = +22.4^\circ$  (c = 4.3, CHCl<sub>3</sub>)

**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>): δ = 1.72-2.08 (m, 3H, CH<sub>2</sub>CHH), 2.10-2.27 (m, 1H, CH<sub>2</sub>CHH), 2.82 (m, 1H, CH<sub>2</sub>=CHCHH), 3.03 (m, 1H, CH<sub>2</sub>=CHCHH), 3.33 (dd, 1H, J = 15.35 Hz, 7.35 Hz, CHHN), 3.55 (m, 1H, CHHN), 3.63 (s, 3H, COOCH<sub>3</sub>), 4.48 (m, 1H, CHCOO), 4.97 (m, 3H, NCH, CH=CH<sub>2</sub>), 5.70 (m, 1H, CH=CH<sub>2</sub>) ppm

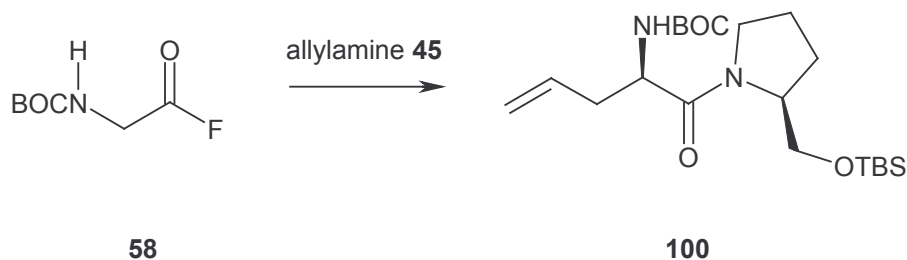
**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>): δ = 25.2 (CH<sub>2</sub>CH<sub>2</sub>), 28.6 (CH<sub>2</sub>CH<sub>2</sub>), 32.9 (CH<sub>2</sub>=CHCH<sub>2</sub>), 46.9 (CH<sub>2</sub>N), 51.7 (NCHCOO), 52.1 (NCH), 59.5 (COOCH<sub>3</sub>), 118.8 (CH=CH<sub>2</sub>), 123.5, 131.4, 134.1 (Ar), 133.4 (CH=CH<sub>2</sub>), 166.8, 167.2 (CON), 172.4 (COO) ppm

**IR** (KBr, Film):  $1/\lambda = 3079$  (w), 2980 (m), 2953 (m), 2879 (m), 2252 (m), 1775 (s, COO), 1716 (s, CONCO), 1660 (s, CON), 1468 (m), 1434 (m), 1382 (s), 1281 (m), 1196 (m), 1174 (m), 1087 (m), 1052 (m), 1027 (w), 996 (m)  $\text{cm}^{-1}$

**MS** (EI, 80 eV, 100 °C):  $m/z$  (%) = 356 (25,  $[\text{M}]^+$ ), 297 (14,  $[\text{M}-\text{C}_2\text{H}_3\text{O}_2]^+$ ), 228 (9,  $[\text{M}-\text{C}_6\text{H}_{10}\text{NO}_2]^+$ ), 200 (100,  $[\text{M}-\text{C}_6\text{H}_{10}\text{NO}_2-\text{CO}]^+$ ).

**HRMS** (80 eV, 100 °C):  $m/z$ ,  $[\text{M}]^+$  calcd. for  $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_5$ , 356.13722; found, 356.13556

**(2R)-2-(tert-Butylcarbonylamino)pent-4-enoic acid [(2S)-tert-butyl dimethylsilyloxymethylpyrrolidinyl]amide 100**



Reaction with *N*-allylprolinol silyl ether **45** (500 mg, 1.96 mmol) and *N*-BOC-glycinyll fluoride **58** (630 mg, 3.58 mmol) following the general procedure. Reaction temperature 0 °C, reaction time 16 hours. Purification via column chromatography (EtOAc). Yield: 73 mg (6%) of **100** as yellow oil.

$[\alpha]_D^{20} = -40.8^\circ$  ( $c = 0.6$ ,  $\text{CHCl}_3$ )

**$^1\text{H-NMR}$**  (270 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.01$  (s, 6H,  $\text{Si}(\text{CH}_3)_2$ ), 0.90 (s, 9H,  $\text{SiC}(\text{CH}_3)_3$ ), 1.40 (s, 9H,  $\text{OC}(\text{CH}_3)_3$ ), 1.80-2.10 (m, 4H,  $\text{CH}_2\text{CH}_2$ ), 2.35 (m, 2H,  $\text{CH}_2=\text{CHCH}_2$ ), 3.43 (m, 1H,  $\text{NCHH}$ ), 3.52-3.78 (m, 3H,  $\text{NCHH}$ ,  $\text{CH}_2\text{O}$ ), 4.10 (br s,  $\text{NH}$ ), 4.45 (dd, 1H,  $J = 14.71$  Hz, 6.62 Hz,  $\text{NCHCH}_2\text{O}$ ), 5.05 (d, 1H,  $J = 10.30$  Hz,  $\text{CH}=\text{CHH}$ ), 5.10 (d, 1H,  $J = 16.91$  Hz,  $\text{CH}=\text{CHH}$ ), 5.33 (dd, 1H,  $J = 18.39$  Hz, 8.82 Hz,  $\text{NCHCO}$ ), 5.71 (dddd, 1H  $J = 16.91$  Hz, 10.30 Hz, 7.35 Hz, 6.62 Hz,  $\text{CH}=\text{CH}_2$ ) ppm

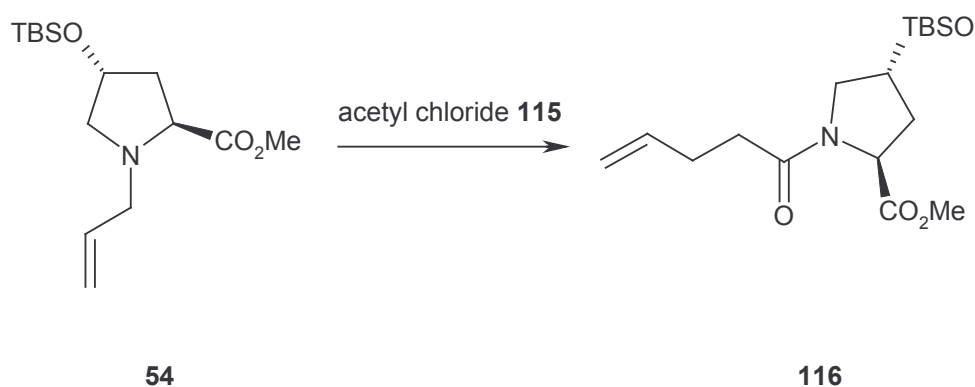
**$^{13}\text{C NMR}$**  (68 MHz,  $\text{CDCl}_3$ ):  $\delta = -5.5$  ( $\text{Si}(\text{CH}_3)_2$ ), 18.1 ( $\text{SiC}(\text{CH}_3)_3$ ), 23.9, 24.3 ( $\text{CH}_2\text{CH}_2$ ), 25.8 ( $\text{SiC}(\text{CH}_3)_3$ ), 26.6, 26.9 ( $\text{CH}_2\text{CH}_2$ ), 27.9, 28.2 ( $\text{OC}(\text{CH}_3)_3$ ), 37.4, 37.5 ( $\text{CH}_2=\text{CHCH}_2$ ), 47.2, 47.4 ( $\text{CH}_2\text{N}$ ), 51.5, 51.7 ( $\text{NCHCO}$ ), 58.4, 58.5 ( $\text{CH}_2\text{O}$ ), 62.3, 62.5 ( $\text{NCHCH}_2\text{O}$ ), 79.3 ( $\text{OC}(\text{CH}_3)_3$ ), 118.2 ( $\text{CH}=\text{CH}_2$ ), 132.8, 132.9 ( $\text{CH}=\text{CH}_2$ ), 169.9 ( $\text{CON}$ ) ppm

**IR** (KBr, Film):  $1/\lambda = 3291$  (br, m, NH), 3077 (w), 2955 (s), 2929 (s), 2883 (m), 2857 (m), 1711 (s, OCON), 1640 (s, CON), 1498 (m), 1472 (m), 1435 (s), 1390 (m), 1366 (m), 1252 (s), 1172 (s), 1101 (m), 1053 (m), 1020 (m), 915 (m)  $\text{cm}^{-1}$

**MS** (EI, 80 eV, 60°C):  $m/z$  (%) = 412 (1.47,  $[\text{M}]^+$ ), 355 (30,  $[\text{M}-\text{C}_4\text{H}_9]^+$ ), 299 (57,  $[\text{M}-\text{C}_4\text{H}_9-\text{C}_4\text{H}_8]^+$ ), 57 (100,  $[\text{C}_4\text{H}_9]^+$ ).

**HRMS** (80 eV, 150 °C):  $m/z$ ,  $[\text{M}]^+$  calcd. for  $\text{C}_{12}\text{H}_{40}\text{N}_2\text{O}_4\text{Si}$ , 412.27573; found, 412.27682

**Pent-4-enoic acid [(2*S*)-methoxycarbonyl-(4*R*)-*tert*-butyldimethylsilyloxy]pyrrolidinyl]amide **116****



Reaction with allylamine **54** (300 mg, 1.00 mmol) and acetyl chloride **115** (236 mg, 3.00 mmol) following the general procedure. Reaction temperature 0 °C, reaction time 1.5 hours. Purification via column chromatography (n-hexane / ethyl acetate = 5:1). Yield: 240 mg (70%) of **116** as pale yellow oil.

$[\alpha]_D^{20} = -53.6^\circ$  ( $c = 1.2$ ,  $\text{CHCl}_3$ )

**$^1\text{H-NMR}$**  (270 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.00$  (s, 6H,  $\text{Si}(\text{CH}_3)_2$ ), 0.80 (s, 9H,  $\text{SiC}(\text{CH}_3)_3$ ), 1.93-2.07 (m, 1H,  $\text{NCHCHH}$ ), 2.10-2.20 (m, 1H,  $\text{NCHCHH}$ ), 2.25-2.45 (m, 4H,  $\text{NCOCH}_2\text{CH}_2$ ), 3.32-3.39 (dd, 1H,  $J = 10.25$  Hz, 1.46 Hz,  $\text{NCHH}$ ), 3.68-3.75 (m, 4H,  $\text{OCH}_3$ ,  $\text{NCHH}$ ), 4.45-4.56 (m, 2H,  $\text{NCH}$ ,  $\text{TBSOCH}$ ), 5.07- 5.17 (dd, 1H,  $J = 10.25$  Hz, 1.47 Hz,  $\text{CH}=\text{CHH}$ ), 5.17-5.22 (dd, 1H,  $J = 17.09$  Hz, 1.47 Hz,  $\text{CH}=\text{CHH}$ ), 5.70-5.87 (dddd, 1H,  $J = 17.09$  Hz, 10.25 Hz, 7.32 Hz, 6.84 Hz,  $\text{CH}=\text{CH}_2$ ) ppm

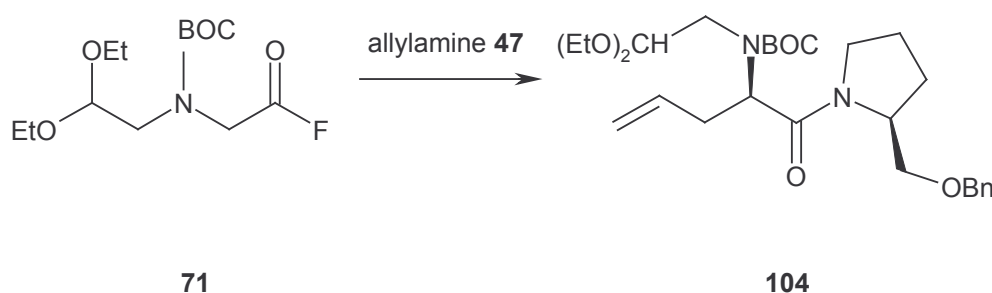
**$^1\text{H-NMR}$**  (500 MHz,  $\text{CDCl}_3$ ):  $\delta = -5.0$ ,  $-4.9$  ( $\text{Si}(\text{CH}_3)_2$ ), 17.7 ( $\text{SiC}(\text{CH}_3)_3$ ), 25.4 ( $\text{SiC}(\text{CH}_3)_3$ ), 28.5, 28.7 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 32.7, 33.5 ( $\text{NCOCH}_2$ ), 38.0, 40.2 ( $\text{NCHCH}_2$ ), 52.0, 52.4 ( $\text{OCH}_3$ ),

54.2, 55.1 (NCH<sub>2</sub>), 57.3, 58.0 (NCH), 68.8, 70.5 (TBSOCH), 115.0 (CH=CH<sub>2</sub>), 137.1 (CH=CH<sub>2</sub>), 167.5 (CON), 171.1, 172.7 (CO<sub>2</sub>CH<sub>3</sub>) ppm

IR (solution, CHCl<sub>3</sub>): 1/λ = 3077 (w), 2953 (s), 2929 (s), 2856 (s), 1750 (s, COO), 1655 (s, CON), 1472 (m), 1432 (s), 1388 (m), 1361 (m), 1321 (m), 1289 (m), 1258 (s), 1199 (s), 1177 (m), 1127 (m), 1092 (s), 1022 (m), 910 (m) cm<sup>-1</sup>

MS (EI, 80 eV, 70°C): m/z (%) = 341 (2.53, [M]<sup>+</sup>), 326 (2.66, [M-CH<sub>3</sub>]<sup>+</sup>), 284 (100, [M-C<sub>4</sub>H<sub>9</sub>]<sup>+</sup>), 202 (21, [M-C<sub>9</sub>H<sub>15</sub>O]<sup>+</sup>).

**(2R)-2-(N-tert-Butyloxycarbonyl)-N-(2,2-diethoxyethyl)aminopent-4-enoic acid-[(2S)-benzyloxymethylpyrrolidinyl]amide 104**



Reaction with *N*-allylprolinol benzyl ether **47** (1.0 g, 4.33 mmol) and acid fluoride **71** (2.5 g, 8.66 mmol) following the general procedure. Reaction temperature 0 °C, reaction time 20 hours. The crude material was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (30 mL). Et<sub>3</sub>N (1.2 mL) and Di-*tert*-butyl dicarbonate (4.5 mmol) were added. The mixture was stirred for 3 hours. H<sub>2</sub>O (20 mL) was added and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3×20 mL), and the combined organic layers were dried over MgSO<sub>4</sub>. After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 6:1). Yield: 1.70 g (78%) of **104** as a pale yellow oil.

[α]<sub>D</sub><sup>20</sup> = +20.8° (c = 2.3, CHCl<sub>3</sub>)

<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>): δ = 1.05 (2×t, 6H, CH(OCH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 1.35 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 1.68-1.93 (m, 4H, CH<sub>2</sub>CH<sub>2</sub>), 2.28-2.44 (m, 1H, CHHCH=CH<sub>2</sub>), 2.44-2.58 (ddd, 1H, J = 14.16 Hz, 7.33 Hz, 6.83 Hz, CHHCH=CH<sub>2</sub>), 2.96-3.66 (m, 10H, NCH<sub>2</sub>CH<sub>2</sub>, NCHCH<sub>2</sub>O, NCH<sub>2</sub>CH(OEt)<sub>2</sub>, CH(OCH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 4.14-4.25 (m, 1H, NCH), 4.33-4.72 (m, 3H, OCH<sub>2</sub>Ph, COCH), 4.77-4.82 (t, 1H, J = 7.81 Hz, CH(OEt)<sub>2</sub>), 4.88-4.92 (d, 1H, J = 9.76 Hz, CH=CHH),

9.76-5.13 (d, 1H,  $J = 15.58$  Hz, CH=CHH), 5.50-5.80 (m, 1H, CH=CH<sub>2</sub>), 7.10-7.29 (m, 5H, Ph) ppm

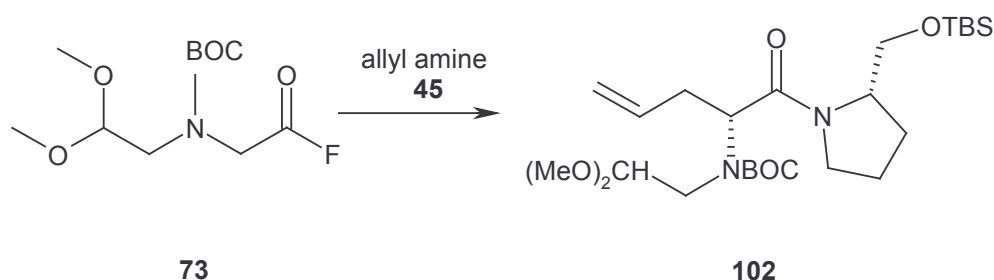
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta = 15.0, 15.1$  (CH(OCH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 24.2 (CH<sub>2</sub>CH<sub>2</sub>), 27.0 (CH<sub>2</sub>CH<sub>2</sub>), 28.1, 28.2 (C(CH<sub>3</sub>)<sub>3</sub>), 34.3, 34.6 (CH<sub>2</sub>CH=CH<sub>2</sub>), 45.2, 45.4 (NCH<sub>2</sub>CH<sub>2</sub>), 46.3, 46.5 (NCH<sub>2</sub>CH), 56.7, 56.8 (NCH), 61.8, 61.9, 62.1, 62.2 (CH(OCH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 69.4 (CH<sub>2</sub>OBn), 72.8 (OCH<sub>2</sub>Ph), 79.9, 80.0 (C(CH<sub>3</sub>)<sub>3</sub>), 100.0, 100.8 (CH(OEt)<sub>2</sub>), 116.9, 117.1 (CH=CH<sub>2</sub>), 127.1, 127.2, 127.3, 128.0, 128.1, 134.3, 138.3 (Ph), 134.7, 135.2 (CH=CH<sub>2</sub>), 155.5 (OCON), 168.8 (CON) ppm

IR (solution, CHCl<sub>3</sub>):  $1/\lambda = 3067$  (m), 3008 (s), 2978 (s), 2924 (s), 2872 (s), 1679 (s, OCON), 1635 (s, CON), 1496 (m), 1445 (s), 1309 (s), 1252 (m), 1217 (m), 1164 (s), 1063 (s), 918 (m), 876 (m) cm<sup>-1</sup>

MS (EI, 80 eV, 140 °C):  $m/z$  (%) = 504 (1.93, [M]<sup>+</sup>), 475 (11, [M-C<sub>2</sub>H<sub>5</sub>]<sup>+</sup>), 458 (4.5, [M-C<sub>2</sub>H<sub>6</sub>O]<sup>+</sup>), 431 (2, [M-C<sub>4</sub>H<sub>9</sub>O]<sup>+</sup>), 403 (6, [M-C<sub>5</sub>H<sub>9</sub>O<sub>2</sub>]<sup>+</sup>), 212 (5, [C<sub>11</sub>H<sub>18</sub>NO<sub>3</sub>]<sup>+</sup>), 190 (4, [C<sub>12</sub>H<sub>16</sub>NO]<sup>+</sup>), 184 (11, [C<sub>10</sub>H<sub>18</sub>NO<sub>2</sub>]<sup>+</sup>), 103 (100, [C<sub>5</sub>H<sub>11</sub>O<sub>2</sub>]<sup>+</sup>), 91 (17, [C<sub>7</sub>H<sub>7</sub>]<sup>+</sup>).

HRMS (80 eV, 140 °C):  $m/z$ , [M]<sup>+</sup> calcd. for C<sub>28</sub>H<sub>44</sub>N<sub>2</sub>O<sub>6</sub>, 504.31993; found, 504.31845

**(2R)-2-[(N-tert-Butyloxycarbonyl)-N-(2,2-dimethoxyethyl)]aminopent-4-enoic acid [(2S)-tert-butyldimethylsilyloxymethylpyrrolidinyl]amide 102**



Reaction with *N*-allylprolinol silyl ether **45** (500 mg, 1.96 mmol) and acid fluoride **73** (1.0 g, 3.77 mmol) following the general procedure. Reaction temperature 0 °C, reaction time 16 hours. After quenching with methanol, the mixture was filtered. The solvent was removed in vacuum and the residue was dissolved in THF (30 mL). Di-*tert*-butyl dicarbonate (2 mmol) was added and the mixture was stirred at rt for 16 hours. H<sub>2</sub>O (20 mL) was added and the aqueous layer was extracted with Et<sub>2</sub>O (4×20 mL). The combined organic layers were dried



over MgSO<sub>4</sub>. After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 1:1) to give 710 mg (72%) of **102** as a yellow oil.

$[\alpha]_D^{20} = +14.9^\circ$  (c = 1.4, CHCl<sub>3</sub>)

<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>): δ = 0.00 (s, 6H, Si(CH<sub>3</sub>)<sub>2</sub>), 0.80 (s, 9H, SiC(CH<sub>3</sub>)<sub>3</sub>), 1.40 (s, 9H, NCOOC(CH<sub>3</sub>)<sub>3</sub>), 1.71-2.05 (m, 4H, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.36-2.49 (m, 1H, CHHCH=CH<sub>2</sub>), 2.49-2.57 (m, 1H, CHHCH=CH<sub>2</sub>), 3.08-3.81 (m, 12H, CH<sub>2</sub>OSi, CH(OCH<sub>3</sub>)<sub>2</sub>, NCH<sub>2</sub>CH<sub>2</sub>, NCH<sub>2</sub>CH(OCH<sub>3</sub>)<sub>2</sub>), 4.02-4.18 (m, 1H, NCH<sub>2</sub>OSi), 4.38-4.58 (m, 1H, CH(OCH<sub>3</sub>)<sub>2</sub>), 4.60-4.67 and 4.83-4.91 (2×m, 1H, CHCH<sub>2</sub>CH=CH<sub>2</sub>), 4.94-5.02 (d, 1H, J = 10.04 Hz, CH=CHH), 5.03-5.10 (d, 1H, J = 17.18 Hz, CH=CHH), 5.62-5.77 (m, 1H, CH=CH<sub>2</sub>) ppm

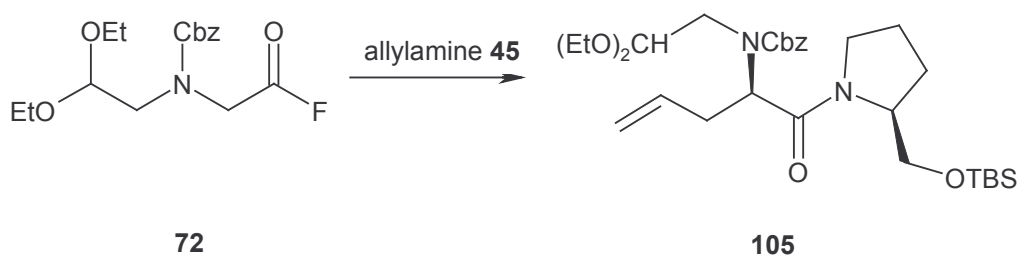
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = -5.5 (Si(CH<sub>3</sub>)<sub>2</sub>), 18.0 (SiC(CH<sub>3</sub>)<sub>3</sub>), 24.1 (NCHCH<sub>2</sub>CH<sub>2</sub>), 25.8 (SiC(CH<sub>3</sub>)<sub>3</sub>), 26.5 (NCHCH<sub>2</sub>CH<sub>2</sub>), 28.2 (NCOOC(CH<sub>3</sub>)<sub>3</sub>), 34.4 (CH<sub>2</sub>CH=CH<sub>2</sub>), 44.6, 45.6 (NCH<sub>2</sub>CH(OCH<sub>3</sub>)<sub>2</sub>), 46.8 (CH<sub>2</sub>OSi), 53.3, 53.7 (CH(OCH<sub>3</sub>)<sub>2</sub>), 53.9 (CHCH<sub>2</sub>CH=CH<sub>2</sub>), 58.7 (NCHCH<sub>2</sub>OSi), 62.3, 65.0 (CH<sub>2</sub>OSi), 80.2 (NCOOC(CH<sub>3</sub>)<sub>3</sub>), 103.1 (CH(OCH<sub>3</sub>)<sub>2</sub>), 117.0 (CH=CH<sub>2</sub>), 134.4, 134.7 (CH=CH<sub>2</sub>), 154.9, 155.7 (NCOOC(CH<sub>3</sub>)<sub>3</sub>), 176.5 (CON) ppm

IR (KBr, Film): 1/λ = 3076 (w), 2954 (s), 2930 (s), 2884 (m), 2758 (m), 1695 (s, OCON), 1648 (s, CON), 1471 (m), 1438 (m), 1402 (m), 1390 (m), 1366 (m), 1348 (w), 1308 (w), 1253 (m), 1168 (m), 1125 (s), 1079 (m), 1025 (w), 996 (w), 977 (w) cm<sup>-1</sup>

MS (EI, 80 eV, 90°C): m/z (%) = 500 (3, [M]<sup>+</sup>), 485 (10, [M-CH<sub>3</sub>]<sup>+</sup>), 468 (5, [M-CH<sub>4</sub>O]<sup>+</sup>), 443 (16, [M-C<sub>4</sub>H<sub>9</sub>]<sup>+</sup>), 429 (8, [M-C<sub>5</sub>H<sub>11</sub>]<sup>+</sup>), 413 (13, [M-C<sub>5</sub>H<sub>11</sub>O]<sup>+</sup>), 369 (23, [M-C<sub>6</sub>H<sub>11</sub>O<sub>3</sub>]<sup>+</sup>), 355 (78, [M-C<sub>7</sub>H<sub>17</sub>OSi]<sup>+</sup>), 299 (17, [M-C<sub>11</sub>H<sub>25</sub>OSi]<sup>+</sup>).

HRMS: (80 eV, 90°C): m/z, [M]<sup>+</sup> calcd. for C<sub>25</sub>H<sub>48</sub>N<sub>2</sub>O<sub>6</sub>Si, 500.32816; found, 500.32655.

**(2R)-2-(N-Benzoyloxycarbonyl)-N-(2,2-diethoxyethyl)aminopent-4-enoic acid [(2S)-tert-butyltrimethylsilyloxymethylpyrrolidinyl]amide **105****



Reaction with *N*-allylprolinol silyl ether **45** (800 mg, 3.14 mmol) and acid fluoride **72** (1.2 g, 3.67 mmol) following the general procedure. Reaction temperature 0 °C, reaction time 16 hours. Purification via column chromatography (ethyl acetate). Yield: 1.32 g (75%) of **105** as a pale yellow oil.

$[\alpha]_D^{20} = +2.4^\circ$  (c = 1.8, CHCl<sub>3</sub>)

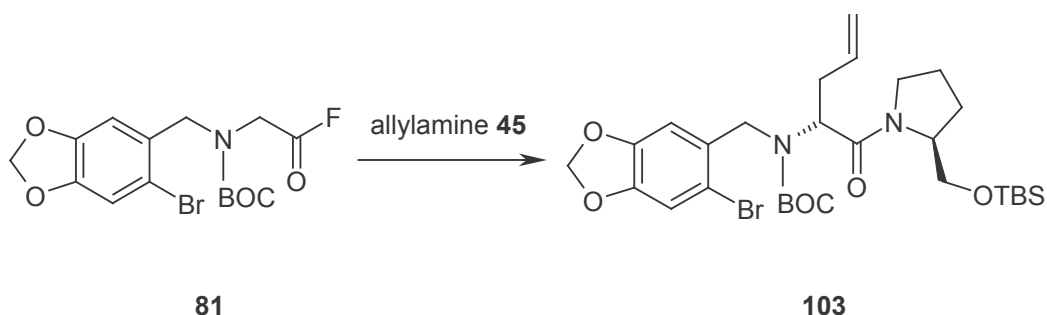
**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>): δ = 0.00 (s, 6H, Si(CH<sub>3</sub>)<sub>2</sub>), 0.84 (s, 9H, SiC(CH<sub>3</sub>)<sub>3</sub>), 1.10 (2×t, 6H, *J* = 7.35 Hz, CH<sub>3</sub>CH<sub>2</sub>O), 1.80 (m, 4H, CH<sub>2</sub>CH<sub>2</sub>), 2.50 (m, 2H, CH<sub>2</sub>CH=CH<sub>2</sub>), 3.06-3.73 (m, 10H, (CH<sub>3</sub>CH<sub>2</sub>O)<sub>2</sub>CH, CH<sub>2</sub>O, CbzNCH<sub>2</sub>CH, NCH<sub>2</sub>CH<sub>2</sub>), 4.08 (m, 1H, NCHCHO<sub>2</sub>), 4.58 (m, 1H, CH(OEt)<sub>2</sub>), 4.88-5.23 (m, 5H, CH<sub>2</sub>=CH, NCH, PhCH<sub>2</sub>), 5.70 (m, 1H, CH<sub>2</sub>=CH), 7.30 (m, 5H, Ph) ppm

**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>): δ = -5.5 (Si(CH<sub>3</sub>)<sub>2</sub>), 15.1 (CH<sub>3</sub>CH<sub>2</sub>O), 18.0 (SiC(CH<sub>3</sub>)<sub>3</sub>), 24.0, 24.2 (CH<sub>2</sub>CH<sub>2</sub>), 25.7 (SiC(CH<sub>3</sub>)<sub>3</sub>), 26.5, 26.9 (CH<sub>2</sub>CH<sub>2</sub>), 34.4, 34.6 (CH<sub>2</sub>=CHCH<sub>2</sub>), 46.1, 46.4 (NCH<sub>2</sub>CH<sub>2</sub>), 47.1, 47.4 (NCH<sub>2</sub>CH(OEt)<sub>2</sub>), 56.9, 57.3 (CHCH<sub>2</sub>O), 58.7 (NCHCH<sub>2</sub>O), 62.2, 62.3 (NCH), 62.4, 62.6 (CH<sub>3</sub>CH<sub>2</sub>O), 67.5, 67.6 (PhCH<sub>2</sub>), 100.0, 101.0 (CH(OEt)<sub>2</sub>), 117.1, 117.3 (CH<sub>2</sub>=CH), 127.9, 128.0, 128.2, 128.3, 128.5, 134.0, 136.2 (Ph), 134.5, 134.8 (CH<sub>2</sub>=CH), 156.6 (OCON), 168.5 (CON) ppm

**IR** (KBr, Film): 1/λ = 3068 (w), 3032 (w), 2955 (s), 2929 (s), 2857 (s), 1701 (s, OCON), 1648 (s, CON), 1605 (m), 1547 (w), 1517 (w), 1498 (w), 1442 (s), 1404 (s), 1375 (m), 1345 (m), 1308 (m), 1252 (s), 1102 (s), 1064 (s), 1003 (m), 913 (m) cm<sup>-1</sup>

**MS** (EI, 80 eV, 125°C): *m/z* (%) = 562 (1.6, [M]<sup>+</sup>), 547 (1.4, [M-CH<sub>3</sub>]<sup>+</sup>), 533 (11, [M-C<sub>2</sub>H<sub>5</sub>]<sup>+</sup>), 505 (20, [M-C<sub>4</sub>H<sub>9</sub>]<sup>+</sup>), 103 (100, [CH(OEt)<sub>2</sub>]<sup>+</sup>), 91 (55, [C<sub>7</sub>H<sub>7</sub>]<sup>+</sup>).

**HRMS**: (80 eV, 100°C): *m/z*, [M]<sup>+</sup> calcd. for C<sub>30</sub>H<sub>50</sub>N<sub>2</sub>O<sub>6</sub>Si, 562.34381; found: 562.34576

**(2R)-2-[N-(2-Bromo-4,5-methylenedioxyphenyl)methyl]-N-(tert-butyloxycarbonyl)-aminopent-4-enoic acid [(2S)-tert-butyltrimethylsilyloxymethyl-pyrrolidinyl]amide 103**

Reaction with *N*-allylprolinol silyl ether **45** (1.0 g, 4.33 mmol) and acid fluoride **81** (2.5 g, 8.66 mmol) following the general procedure. Reaction temperature 0 °C, reaction time 20 hours. The crude material was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (30 mL). Et<sub>3</sub>N (1.2 mL) and Di-*tert*-butyl dicarbonate (4.5 mmol) were added. The mixture was stirred for 3 hours. H<sub>2</sub>O (20 mL) was added and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3×20 mL), and the combined organic layers were dried over MgSO<sub>4</sub>. After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 6:1) to give 1.79 g (82%) of **103** as a pale yellow oil.

$[\alpha]_D^{20} = +12.5^\circ$  (c = 1.6, CHCl<sub>3</sub>)

**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>): δ = 0.00 (s, 6H, Si(CH<sub>3</sub>)<sub>2</sub>), 0.85 (s, 9H, SiC(CH<sub>3</sub>)<sub>3</sub>), 1.40, 1.50 (2×s, 9H, OC(CH<sub>3</sub>)<sub>3</sub>), 1.55-2.02 (m, 4H, CH<sub>2</sub>CH<sub>2</sub>), 2.30-2.45 (ddd, 1H, *J* = 14.71 Hz, 7.36 Hz, 7.35 Hz, CHHCH=CH<sub>2</sub>), 2.46-2.66 (dd, 1H, *J* = 13.97 Hz, 7.35 Hz, CHHCH=CH<sub>2</sub>), 2.88, 3.13 (2×m, 1H, NCHHCH<sub>2</sub>), 3.40-3.69 (m, 3H, NCHHCH<sub>2</sub>, OCH<sub>2</sub>), 4.05 (m, 1H, NCHCH<sub>2</sub>), 4.20-4.56 (m, 2H, ArCH<sub>2</sub>), 4.97-5.25 (m, 3H, BOCNCH, CH=CH<sub>2</sub>), 5.61-5.81 (m, 1H, CH=CH<sub>2</sub>), 5.90 (2×s, 2H, OCH<sub>2</sub>O), 6.35, 6.55 (2×s, 1H, NCH<sub>2</sub>CCH), 6.90 (2×s, 1H, BrCCH) ppm

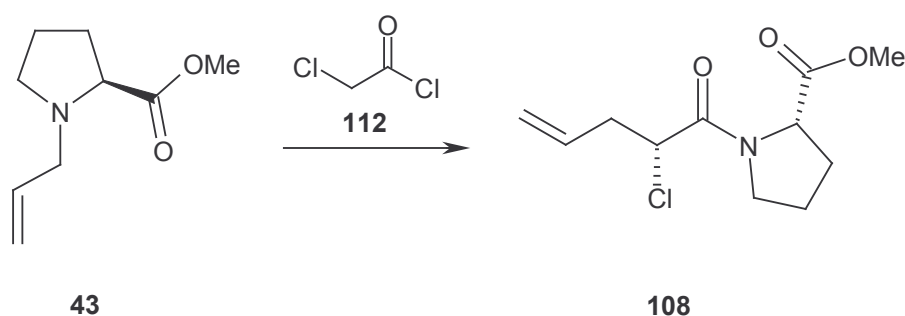
**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>): δ = -5.5 (Si(CH<sub>3</sub>)<sub>2</sub>), 18.0, 18.2 (SiC(CH<sub>3</sub>)<sub>3</sub>), 23.8 (CH<sub>2</sub>CH<sub>2</sub>), 25.8, 25.9 (SiC(CH<sub>3</sub>)<sub>3</sub>), 26.5, 27.3 (CH<sub>2</sub>CH<sub>2</sub>), 28.0, 28.2 (OC(CH<sub>3</sub>)<sub>3</sub>), 34.2 (CH<sub>2</sub>CH=CH<sub>2</sub>), 46.8, 47.1 (NCH<sub>2</sub>CH<sub>2</sub>), 55.6 (NCH), 58.1 (NCHCH<sub>2</sub>OTBS), 58.6 (TBSOCH<sub>2</sub>), 61.6 (NCH<sub>2</sub>Ar), 80.5 (OC(CH<sub>3</sub>)<sub>3</sub>), 101.4 (OCH<sub>2</sub>O), 107.0, 118.0, 133.8, 146.6 (Ar), 112.4 (CH=CH<sub>2</sub>), 133.9 (CH=CH<sub>2</sub>), 155.6 (OCON), 168.6 (CON) ppm

**IR** (KBr, Film):  $1/\lambda = 3077$  (w), 2954 (s), 2929 (s), 2883 (s), 2857 (s), 1694 (s, OCON), 1649 (s, CON), 1503 (s), 1480 (s), 1449 (s), 1412 (s), 1400 (s), 1391 (s), 1367 (s), 1342 (m), 1310 (s), 1252 (s), 1163 (s), 1102 (s), 1038 (s), 996 (m), 963 (m)  $\text{cm}^{-1}$

**MS** (EI, 80 eV, 160°C):  $m/z$  (%) = 624 (8.8,  $[\text{M}]^+$ ), 568 (8.2,  $[\text{M}-\text{C}_4\text{H}_8]^+$ ), 523 (7.4,  $[\text{M}-\text{C}_5\text{H}_9\text{O}_2]^+$ ), 511 (17,  $[\text{M}-\text{C}_6\text{H}_{15}\text{Si}]^+$ ), 489 (6.4,  $[\text{M}-\text{C}_4\text{H}_8\text{Br}]^+$ ), 445 (8.6,  $[\text{M}-\text{C}_5\text{H}_8\text{O}_2\text{Br}]^+$ ), 297 (93,  $[\text{M}-\text{C}_{14}\text{H}_{20}\text{O}_2\text{BrSi}]^+$ ), 213 (90,  $[\text{C}_8\text{H}_6\text{O}_2\text{Br}]^+$ ), 70 (100,  $[\text{C}_4\text{H}_8\text{N}]^+$ ), 57 (85,  $[\text{C}_4\text{H}_9]^+$ ).

**HRMS**: (80 eV, 160°C):  $m/z, [\text{M}]^+$  calcd. for  $\text{C}_{29}\text{H}_{45}\text{N}_2\text{O}_6\text{Si}^{79}\text{Br}$ , 624.22302; found, 624.22631

**(R)-2-Chloropent-4-enoic acid [(2S)-methoxycarbonylpyrrolidinyl]amide 108**



Reaction with allylamine **43** (500 mg, 2.95 mmol), chloroacetyl chloride **112** (470  $\mu\text{L}$ , 5.91 mmol,  $d = 1.418$ ,  $M = 113$ ) and  $\text{AlMe}_3$  (3 mL) following general procedure. Reaction temperature -20 °C, reaction time 1 hour. Purification via column chromatography (n-hexane/ethyl acetate = 3:1). Yield: 510 mg (70%) of **108** as a brown oil.

$[\alpha]_D^{20} = -93.7^\circ$  ( $c = 1.3$ ,  $\text{CHCl}_3$ )

**$^1\text{H-NMR}$**  (500 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.78\text{-}2.25$  (m, 4H,  $\text{NCH}_2\text{CH}_2\text{CH}_2$ ), 2.51-2.62 (m, 1H,  $\text{CHHCH}=\text{CH}_2$ ), 2.72-2.81 (m, 1H,  $\text{CHHCH}=\text{CH}_2$ ), 3.46-3.60 (m, 1H,  $\text{NCHH}$ ), 3.65 (2×s, 3H,  $\text{OCH}_3$ ), 3.78-3.85 (m, 1H,  $\text{NCHH}$ ), 4.01, 4.24 (2×d, 1H,  $J = 7.28$  Hz, 5.91 Hz,  $\text{ClCH}$ ), 4.45, 4.62 (2×d, 1H,  $J = 9.94$  Hz, 3.99 Hz,  $\text{NCHCO}_2\text{CH}_3$ ), 5.02-5.14 (m, 2H,  $\text{CH}=\text{CH}_2$ ), 5.66-5.79 (2×dddd, 1H,  $J = 17.18$  Hz, 10.17 Hz, 7.14 Hz, 6.88 Hz,  $\text{CH}=\text{CH}_2$ ) ppm

**$^{13}\text{C NMR}$**  (125 MHz,  $\text{CDCl}_3$ ):  $\delta = 22.2$ , 24.5 ( $\text{NCH}_2\text{CH}_2$ ), 28.8, 30.8 ( $\text{NCH}_2\text{CH}_2\text{CH}_2$ ), 38.0 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 40.7, 54.2 ( $\text{ClCH}$ ), 46.7, 46.8 ( $\text{NCH}_2$ ), 52.1, 52.7 ( $\text{CO}_2\text{CH}_3$ ), 58.9, 59.0

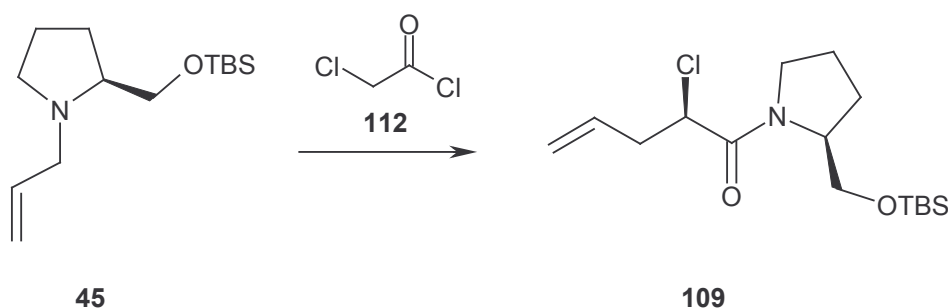
(NCHCO<sub>2</sub>), 118.4, 118.7 (CH=CH<sub>2</sub>), 132.8, 132.9 (CH=CH<sub>2</sub>), 166.7, 167.1 (CON), 171.8, 172.0 (CO<sub>2</sub>CH<sub>3</sub>) ppm

**IR** (KBr, Film):  $1/\lambda = 3079$  (w), 2980 (m), 2954 (m), 2883 (w), 1746 (s, COO), 1660 (s, CON), 1436 (s), 1364 (m), 1337 (m), 1282 (m), 1197 (s), 1175 (s), 1118 (w), 1095 (w), 1044 (w), 998 (m), 924 (m) cm<sup>-1</sup>

**MS** (EI, 80 eV, 40°C):  $m/z$  (%) = 245 (10, [M]<sup>+</sup>), 210 (11, [M-Cl]<sup>+</sup>), 186 (75, [M-C<sub>2</sub>H<sub>3</sub>O<sub>2</sub>]<sup>+</sup>), 150 (6, [M-C<sub>2</sub>H<sub>4</sub>O<sub>2</sub>Cl]<sup>+</sup>), 128 (16, [C<sub>6</sub>H<sub>10</sub>NO<sub>2</sub>]<sup>+</sup>), 89 (12, [C<sub>4</sub>H<sub>6</sub>Cl]<sup>+</sup>), 70 (100, [C<sub>4</sub>H<sub>8</sub>N]<sup>+</sup>), 41 (12, [C<sub>3</sub>H<sub>5</sub>]<sup>+</sup>).

**HRMS**: (80 eV, 40°C):  $m/z$ , [M]<sup>+</sup> calcd. for C<sub>11</sub>H<sub>16</sub>O<sub>3</sub>N<sup>35</sup>Cl, 245.08188; found, 245.08255.

**(R)-2-Chlor-4-enoic acid [(2S)-tert-butyltrimethylsilyloxymethylpyrrolidinyl]amide 109**



Reaction with allylamine **45** (500 mg, 1.96 mmol), chloroacetyl chloride **112** (310 μL, 3.89 mmol,  $d = 1.418$ ,  $M = 113$ ) and AlMe<sub>3</sub> (2 mL) following general procedure. Reaction temperature -20 °C, reaction time 1 hour. Purification via column chromatography (n-hexane/ethyl acetate = 7:1). Yield: 450 mg (69%) of **109** as a pale yellow oil.

$[\alpha]_D^{20} = -72.5^\circ$  ( $c = 3.0$ , CHCl<sub>3</sub>)

**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>):  $\delta = 0.00$  (s, 6H, Si(CH<sub>3</sub>)<sub>2</sub>), 0.70 (s, 9H, SiC(CH<sub>3</sub>)<sub>3</sub>), 1.68-2.10 (m, 4H, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.49-2.71 (m, 2H, CH<sub>2</sub>CH=CH<sub>2</sub>), 3.29-3.50 (m, 2H, NCH<sub>2</sub>), 3.50-3.71 (m, 2H, OCH<sub>2</sub>), 4.01-4.18 (m, 1H, NCH), 4.18-4.23, 4.50-4.62 (2×m, 1H, ClCH), 5.01-5.15 (m, 2H, CH=CH<sub>2</sub>), 5.64-5.81 (m, 1H, CH=CH<sub>2</sub>) ppm

**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>):  $\delta = -5.5$ ,  $-5.6$  (Si(CH<sub>3</sub>)<sub>2</sub>), 17.9, 18.2 (SiC(CH<sub>3</sub>)<sub>3</sub>), 21.7, 24.0 (NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 25.6, 25.7 (SiC(CH<sub>3</sub>)<sub>3</sub>), 26.7, 27.8 (NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 38.0, 38.1

(CH<sub>2</sub>CH=CH<sub>2</sub>), 45.7, 47.1 (NCH<sub>2</sub>), 54.5, 54.6 (NCH), 58.5, 58.7 (NCHCH<sub>2</sub>OTBS), 61.8, 65.2 (ClCH), 118.4 (CH=CH<sub>2</sub>), 133.2 (CH=CH<sub>2</sub>), 166.6, 167.3 (CON) ppm

**IR** (KBr, Film): 1/λ = 3080 (w), 2954 (s), 2929 (s), 2883 (m), 2856 (m), 1652 (s, CON), 1576 (w), 1558 (w), 1539 (w), 1521 (w), 1471 (m), 1436 (s), 1386 (w), 1360 (w), 1340 (w), 1254 (m), 1189 (w), 1165 (w), 1102 (m), 1054 (m), 997 (m), 920 (m), 836 (s, CCl) cm<sup>-1</sup>

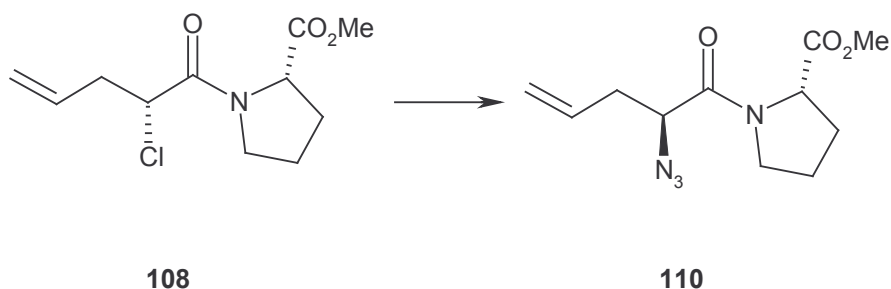
**MS** (EI, 80 eV, 70°C): m/z (%) = 331 (0.62, [M]<sup>+</sup>), 316 (3, [M-CH<sub>3</sub>]<sup>+</sup>), 296 (1, [M-Cl]<sup>+</sup>), 274 (100, [M-C<sub>4</sub>H<sub>9</sub>]<sup>+</sup>), 186 (19, [M-C<sub>7</sub>H<sub>17</sub>OSi]<sup>+</sup>), 70 (53, [C<sub>4</sub>H<sub>8</sub>N]<sup>+</sup>).

**HRMS**: (80 eV, 70°C):m/z,[M]<sup>+</sup> calcd. for C<sub>16</sub>H<sub>30</sub>NO<sub>2</sub>Si<sup>35</sup>Cl, 331.17343; found, 331.17466.

[M-CH<sub>3</sub>]<sup>+</sup> calcd. for C<sub>15</sub>H<sub>27</sub>NO<sub>2</sub>Si<sup>35</sup>Cl, 316.14996, found, 316.14866.

[M-C<sub>4</sub>H<sub>9</sub>]<sup>+</sup> calcd. for C<sub>12</sub>H<sub>21</sub>NO<sub>2</sub>Si<sup>35</sup>Cl, 274.10300; found, 274.10288.

**(S)-2-Azidopent-4-enoic acid [(2S)-methoxycarbonylpyrrolidinyl]amide 110**



To chloroamide **108** (500 mg, 2.04 mmol) in DMF (50 mL) was added NaN<sub>3</sub> (600 mg, 9.23 mmol). The mixture was stirred at room temperature for 16 hours. H<sub>2</sub>O (20 mL) was added and the aqueous layer was extracted with Et<sub>2</sub>O (4×10 mL), and the combined organic layers were dried over MgSO<sub>4</sub>. After removal of the solvent, the crude product was purified by column chromatography (n-hexane / ethyl acetate = 1:1) to give 500 mg (97%) **110** as a yellow oil.

[α]<sub>D</sub><sup>20</sup> = -26.8° (c = 1.4, CHCl<sub>3</sub>)

**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>): δ = 1.78-2.01 (m, 3H, NCH<sub>2</sub>CHHCH<sub>2</sub>), 2.01-2.20 (m, 1H, NCH<sub>2</sub>CHH), 2.45-2.66 (m, 2H, CH<sub>2</sub>CH=CH<sub>2</sub>), 3.31-3.55 (m, 2H, N<sub>3</sub>CH, NCHH), 3.60 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 3.60-3.69 (m, 1H, NCHH), 4.41-4.48 (m, 1H, NCHCO<sub>2</sub>CH<sub>3</sub>), 5.02-5.11 (d, 1H, J = 10.74 Hz, CH=CHH), 5.10-5.21 (d, 1H, J = 17.09 Hz, CH=CHH), 5.58-5.86 (2×dddd, 1H, J = 17.09 Hz, 10.25 Hz, 7.32 Hz, 6.84 Hz, CH=CH<sub>2</sub>) ppm

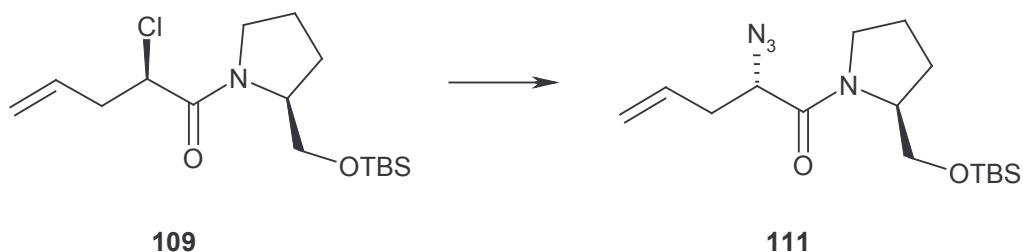
$^{13}\text{C}$  NMR (68 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 21.9, 24.6 ( $\text{NCH}_2\text{CH}_2$ ), 28.7, 31.0 ( $\text{NCH}_2\text{CH}_2\text{CH}_2$ ), 34.9, 35.5 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 46.6, 46.7 ( $\text{NCH}_2$ ), 52.0, 52.7 ( $\text{CO}_2\text{CH}_3$ ), 58.7, 58.8 ( $\text{NCHCO}_2\text{CH}_3$ ), 59.1, 59.3 ( $\text{N}_3\text{CH}$ ), 118.8, 118.9 ( $\text{CH}=\text{CH}_2$ ), 132.2 ( $\text{CH}=\text{CH}_2$ ), 168.3 ( $\text{CON}$ ), 171.9 ( $\text{CO}_2\text{CH}_3$ ) ppm

IR (KBr, Film):  $1/\lambda$  = 3078 (w), 2979 (m), 2881 (m), 2841 (w), 2101 (s,  $\text{N}_3$ ), 1746 (s, COO), 1657 (s, CON), 1435 (s), 1363 (m), 1340 (m), 1324 (m), 1280 (m), 1197 (s), 1175 (s), 1119 (w), 1095 (m), 1044 (w), 999 (m)  $\text{cm}^{-1}$

MS (EI, 80 eV,  $60^\circ\text{C}$ ):  $m/z$  (%) = 252 (1,  $[\text{M}]^+$ ), 224 (1,  $[\text{M}-\text{N}_2]^+$ ), 221 (1,  $[\text{M}-\text{CH}_3\text{O}]^+$ ), 210 (3,  $[\text{M}-\text{N}_3]^+$ ), 193 (6,  $[\text{M}-\text{C}_2\text{H}_3\text{O}_2]^+$ ), 165 (8,  $[\text{M}-\text{C}_2\text{H}_3\text{O}_2\text{N}_2]^+$ ), 137 (20,  $[\text{M}-\text{C}_3\text{H}_5\text{O}_2\text{N}_3]^+$ ), 128 (100,  $[\text{C}_6\text{H}_{10}\text{NO}_2]^+$ ), 68 (37,  $[\text{C}_4\text{H}_6\text{N}]^+$ ), 41 (36,  $[\text{C}_3\text{H}_5]^+$ ).

HRMS: (80 eV,  $60^\circ\text{C}$ ):  $m/z$ ,  $[\text{M}]^+$  calcd. for  $\text{C}_{11}\text{H}_{16}\text{N}_4\text{O}_3$ , 252.12224; found, 252.12422.

**(S)-2-Azidopent-4-enoic acid [(2S)-tert-butyltrimethylsilyloxymethylpyrrolidinyl]-amide **111****



To chloroamide **109** (200 mg, 0.60 mmol) in DMF (20 mL) was added  $\text{NaN}_3$  (200 mg, 3.07 mmol). The mixture was stirred at room temperature for 16 hours.  $\text{H}_2\text{O}$  (20 mL) was added and the aqueous layer was extracted with  $\text{Et}_2\text{O}$  ( $4 \times 10$  mL), and the combined organic layers were dried over  $\text{MgSO}_4$ . After removal of the solvent, the crude product was purified by column chromatography (n-hexane / ethyl acetate = 5:1) to give 200 mg (99%) **111** as a yellow oil.

$[\alpha]_D^{20} = -4.2^\circ$  ( $c = 2.1$ ,  $\text{CHCl}_3$ )

$^1\text{H}$ -NMR (270 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.00 (s, 6H,  $\text{Si}(\text{CH}_3)_2$ ), 0.85 (s, 9H,  $\text{Si}(\text{CH}_3)_3$ ), 1.72-2.11 (m, 4H,  $\text{CH}_2\text{CH}_2$ ), 2.05 (m, 2H,  $\text{CH}_2=\text{CHCH}_2$ ), 3.31-3.52 (m, 3H,  $\text{NCHH}$ ,  $\text{CHHO}$ ,  $\text{NCHCH}_2\text{O}$ ), 3.52-3.78 (m, 2H,  $\text{NCHH}$ ,  $\text{CHHO}$ ), 3.78-3.85, 4.08-4.10 (2×m, 1H,  $\text{N}_3\text{CH}$ ),

5.11 (d, 1H,  $J = 10.26$  Hz, CH=CH $\mathbf{H}$ ), 5.18 (dt, 1H,  $J = 17.08$  Hz, 1.47 Hz CH=C $\mathbf{H}$ H), 5.75 (dddd, 1H,  $J = 17.08$  Hz, 10.26 Hz, 7.33 Hz, 6.84 Hz, CH=CH $\mathbf{2}$ ) ppm

$^{13}\text{C}$  NMR (68 MHz,  $\text{CDCl}_3$ ):  $\delta = -5.6$  (SiCH $\mathbf{3}$ ), 17.9 (SiC(CH $\mathbf{3}$ ) $_3$ ), 21.5, 24.3 (NCH $\mathbf{2}$ CH $\mathbf{2}$ CH $\mathbf{2}$ ), 25.6, 25.7 (SiC(CH $\mathbf{3}$ ) $_3$ ), 26.7, 28.1 (NCH $\mathbf{2}$ CH $\mathbf{2}$ CH $\mathbf{2}$ ), 35.2, 35.6 (CH $\mathbf{2}$ CH=CH $\mathbf{2}$ ), 45.7, 47.4 (NCH $\mathbf{2}$ CH $\mathbf{2}$ ), 58.6, 58.8 (NCHCH $\mathbf{2}$ O), 59.1 (CH $\mathbf{2}$ OTBS), 62.3, 64.5 (N $\mathbf{3}$ CH), 118.7, 118.8 (CH=CH $\mathbf{2}$ ), 132.5 (CH=CH $\mathbf{2}$ ), 168.9 (NCO) ppm

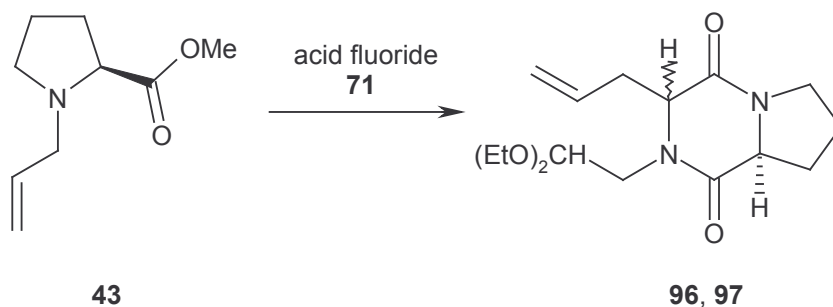
IR (KBr, Film):  $1/\lambda = 3080$  (w), 2954 (s), 2929 (s), 2883 (m), 2857 (s), 2099 (s, N $\mathbf{3}$ ), 1652 (s, CON), 1471 (m), 1462 (m), 1429 (s), 1381 (w), 1360 (w), 1319 (w), 1257 (s), 1193 (w), 1165 (w), 1103 (s), 1055 (m), 1004 (m), 956 (w), 919 (m)  $\text{cm}^{-1}$

MS (EI, 80 eV, 70°C):  $m/z$  (%) = 338 (0.36, [M] $^+$ ), 323 (1, [M-CH $\mathbf{3}$ ] $^+$ ), 310 (2, [M-N $\mathbf{2}$ ] $^+$ ), 281 (100, [M-C $\mathbf{4}$ H $\mathbf{9}$ ] $^+$ ), 253 (32, [M-C $\mathbf{4}$ H $\mathbf{6}$ N $\mathbf{3}$ ] $^+$ ), 242 (21, [C $\mathbf{12}$ H $\mathbf{24}$ NO $\mathbf{2}$ ] $^+$ ).

HRMS: (80 eV, 70°C):  $m/z$ , [M-CH $\mathbf{3}$ ] $^+$  calcd. for C $\mathbf{15}$ H $\mathbf{27}$ N $\mathbf{4}$ O $\mathbf{2}$ Si, 323.19034; found, 323.19111.  
[M-N $\mathbf{2}$ ] $^+$  calcd. for C $\mathbf{16}$ H $\mathbf{30}$ N $\mathbf{2}$ O $\mathbf{2}$ Si, 310.20764; found, 310.20833.  
[M-C $\mathbf{4}$ H $\mathbf{9}$ ] $^+$  calcd. for C $\mathbf{12}$ H $\mathbf{21}$ N $\mathbf{4}$ O $\mathbf{2}$ Si, 281.14337; found, 281.14533.



## 3.6 Syntheses of Piperazine and Furanone Derivatives

(3*S*,6*R*)-6-Allyl-1-(2,2-diethoxyethyl)-3,4-propylidene-1,4-piperazine-2,5-dione **96**(3*S*,6*S*)-6-Allyl-1-(2,2-diethoxyethyl)-3,4-propylidene-1,4-piperazine-2,5-dione **97**

Aza-Claisen rearrangement starting from *N*-allylproline methyl ester **43** (120 mg, 0.71 mmol) and acid fluoride **71** (250 mg, 0.85 mmol) following the general procedure. Reaction temperature 0 °C, reaction time 16 hours. The reaction was quenched with methanol (20 mL). After stirring for 30 min. thionyl chloride (5 mL) was added dropwise at 0°C. The solvent was removed in vacuum and the residue was purified via column chromatography (ethyl acetate) to give 160 mg (73%) of **96** / **97** as yellow oil. (Ratio **96** : **97** >15 : 1, via analytical HPLC: Nucleosil 50-5, 4×250; 20% propan-2-ol in hexane, 2 mL/min, 140 bar;  $t_{96}$  = 7.16 min,  $t_{97}$  = 7.58 min.)

$[\alpha]_D^{20} = -48.3^\circ$  ( $c = 1.1$ ,  $\text{CHCl}_3$ ) (data of **96/97**)

Data obtained from mixture, separated peaks of **96**:

**<sup>1</sup>H-NMR** (270 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.02$  (t, 3H,  $J = 7.35$  Hz,  $\text{CH}_3$ ), 1.10 (t, 3H,  $J = 7.35$  Hz,  $\text{CH}_3$ ), 1.75-1.92 (m, 3H,  $\text{CH}_2\text{CHH}$ ), 2.28 (m, 1H,  $\text{CH}_2\text{CHH}$ ), 2.49 (m, 2H,  $\text{CH}_2=\text{CHCH}_2$ ), 2.85 (dd, 1H,  $J = 13.97$  Hz, 7.35 Hz,  $\text{NCHHCH}(\text{OEt})_2$ ), 3.27-3.68 (m, 6H,  $\text{CH}_3\text{CH}_2\text{O}$ ,  $\text{CH}_2\text{NCO}$ ), 3.82 (dd, 1H,  $J = 13.97$  Hz, 3.67 Hz,  $\text{NCHHCH}(\text{OEt})_2$ ), 4.01 (dd, 1H,  $J = 7.83$  Hz, 6.62 Hz,  $\text{COCHN}$ ), 4.12 (t, 1H,  $J = 5.88$  Hz,  $\text{NCHCH}_2\text{CH}=\text{CH}_2$ ), 4.49 (dd, 1H,  $J = 7.35$  Hz, 3.67 Hz,  $\text{CH}_2\text{CH}(\text{OEt})_2$ ), 5.01(d, 1H,  $J = 9.66$  Hz,  $\text{CHH}=\text{CH}$ ), 5.06 (dd, 1H,  $J = 16.91$  Hz, 1.47 Hz,  $\text{CHH}=\text{CH}$ ), 5.68 (dddd, 1H,  $J = 16.91$  Hz, 10.30 Hz, 7.36 Hz, 7.35 Hz,  $\text{CH}_2=\text{CH}$ ) ppm

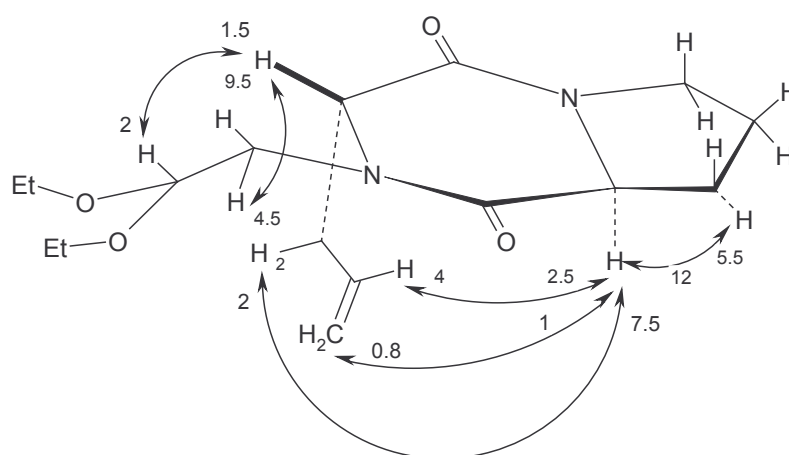
**<sup>13</sup>C NMR** (68 MHz,  $\text{CDCl}_3$ ):  $\delta = 15.1$  ( $\text{CH}_3\text{CH}_2\text{O}$ ), 22.2 ( $\text{CH}_2\text{CH}_2$ ), 29.4 ( $\text{CH}_2\text{CH}_2$ ), 35.9 ( $\text{CH}_2=\text{CHCH}_2$ ), 45.2 ( $\text{NCH}_2\text{CH}_2$ ), 48.3 ( $\text{NCH}_2\text{CH}(\text{OEt})_2$ ), 58.3 ( $\text{NCHCO}$ ), 63.1 ( $\text{CH}_3\text{CH}_2\text{O}$ ),

63.8 (NCHCH<sub>2</sub>CH=CH<sub>2</sub>), 64.2 (CH<sub>3</sub>CH<sub>2</sub>O), 100.6 (CH<sub>2</sub>CH(OEt)<sub>2</sub>), 119.9 (CH<sub>2</sub>=CH), 131.8 (CH<sub>2</sub>=CH), 165.2, 167.7 (CON) ppm

**IR** (KBr, Film):  $1/\lambda = 3077$  (w), 2975 (s), 2884 (s), 1666 (s, CON), 1454 (s), 1375 (m), 1343 (m), 1298 (m), 1261 (m), 1205 (m), 1120 (s), 1063 (s), 923 (m) cm<sup>-1</sup>

**MS** (EI, 80 eV, 90°C):  $m/z$  (%) = 310 (1.4, [M]<sup>+</sup>), 269 (6.5, [M-C<sub>3</sub>H<sub>5</sub>]<sup>+</sup>), 265 (18, [M-C<sub>2</sub>H<sub>5</sub>O]<sup>+</sup>), 103 (100, [C<sub>5</sub>H<sub>11</sub>O<sub>2</sub>]<sup>+</sup>), 75 (49, [C<sub>3</sub>H<sub>7</sub>O<sub>2</sub>]<sup>+</sup>), 70 (17, [C<sub>4</sub>H<sub>8</sub>N]<sup>+</sup>).

**HRMS**: (80 eV, 90°C):  $m/z$ , [M]<sup>+</sup> calcd. for C<sub>16</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub>, 310.18925; found, 310.18777

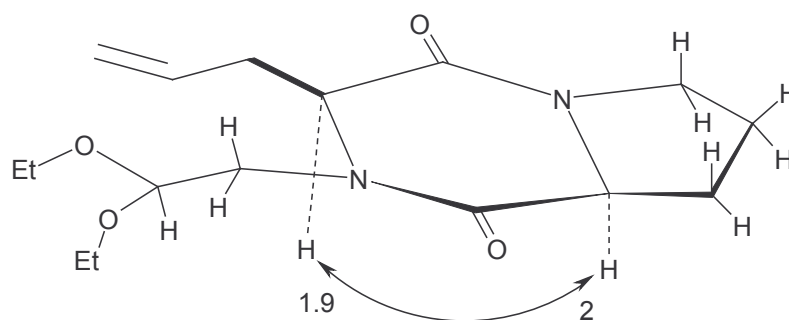


NOE data of **96**

Data obtained from mixture, separated peaks of **97**:

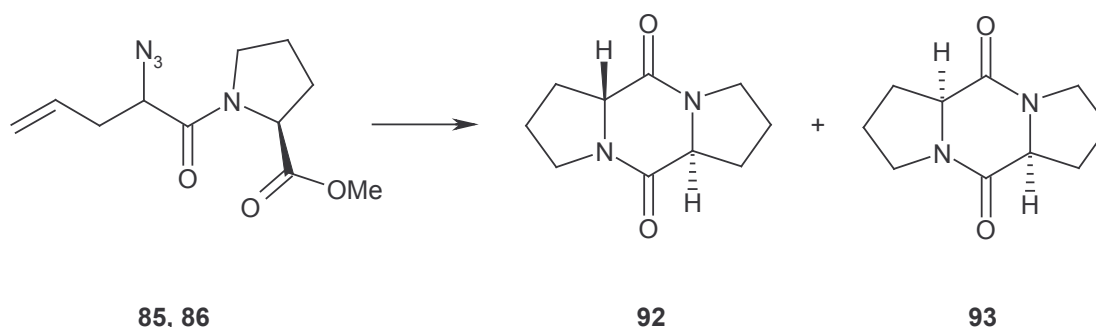
**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>):  $\delta = 1.02$  (t, 3H,  $J = 7.35$  Hz, CH<sub>2</sub>CH<sub>3</sub>), 1.10 (t, 3H,  $J = 7.35$  Hz, CH<sub>2</sub>CH<sub>3</sub>), 1.75-1.92 (m, 3H, CH<sub>2</sub>CHH), 2.28 (m, 1H, CH<sub>2</sub>CHH), 2.68 (m, 1H, CH<sub>2</sub>=CHCHH), 2.85 (m, 1H, CH<sub>2</sub>=CHCHH), 2.90 (dd, 1H,  $J = 13.97$  Hz, 7.35 Hz, NCHHCH(OEt)<sub>2</sub>), 3.27-3.68 (m, 6H, (CH<sub>3</sub>CH<sub>2</sub>O)<sub>2</sub>, CH<sub>2</sub>NCO), 3.90 (m, 1H, NCHCO), 4.11 (m, 1H, NCHH), 4.28 (m, 1H, NCHCH<sub>2</sub>CH=CH<sub>2</sub>), 4.55 (dd, 1H,  $J = 6.62$  Hz, 2.94 Hz, CH<sub>2</sub>CH(OEt)<sub>2</sub>), 4.97 (m, 2H, CH<sub>2</sub>=CH), 5.45 (dddd, 1H,  $J = 16.91$  Hz, 10.30 Hz, 7.36 Hz, 7.35 Hz, CH<sub>2</sub>=CH) ppm

**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>):  $\delta = 15.1$  (CH<sub>3</sub>CH<sub>2</sub>O), 21.7 (CH<sub>2</sub>CH<sub>2</sub>), 29.6 (CH<sub>2</sub>CH<sub>2</sub>), 33.4 (CH<sub>2</sub>=CHCH<sub>2</sub>), 44.8 (NCH<sub>2</sub>CH<sub>2</sub>), 45.3 (NCH<sub>2</sub>CH(OEt)<sub>2</sub>), 58.7 (NCHCO), 60.5 (NCHCH<sub>2</sub>CH=CH<sub>2</sub>), 63.1 (CH<sub>3</sub>CH<sub>2</sub>O), 64.2 (CH<sub>3</sub>CH<sub>2</sub>O), 100.4 (CH<sub>2</sub>CH(OEt)<sub>2</sub>), 119.4 (CH<sub>2</sub>=CH), 131.9 (CH<sub>2</sub>=CH), 164.1, 167.3 (CON) ppm

NOE data of **97**

**(3*R*,6*S*)-1,6-3,4-Bis(propylidene)-1,4-piperazine-2,5-dione 92**

**(3*S*,6*S*)-1,6-3,4-Bis(propylidene)-1,4-piperazine-2,5-dione 93**



A solution of  $\text{BH}_3 \cdot \text{S}(\text{CH}_3)_2$  (197 mg, 2.6 mmol) in anhyd.  $\text{CH}_2\text{Cl}_2$  (5 mL) was cooled to 0 °C under Argon. Cyclohexene (428 mg, 5.2 mmol) was added over a period of 5 minutes by means of syringe. After stirring at 0 °C for 3 hours,  $\alpha$ -azido amide **85** / **86** (220 mg, 0.87 mmol) in anhyd.  $\text{CH}_2\text{Cl}_2$  (5 mL) was added. The cooling bath was removed and the reaction mixture was stirred overnight at 20 °C, the colour of the mixture turned to bright yellow. The reaction was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (10 mL). After stirring for 30 minutes, sat. aq.  $\text{NaHCO}_3$  (5 mL) was added and the mixture was stirred for further 1 hour. Then, the aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  ( $5 \times 15$  mL), the combined organic layers were dried over  $\text{MgSO}_4$ , and concentrated to give crude product which was purified by column chromatography (ethyl acetate / methanol = 9 : 1) and gave 115 mg (68%) of **92** / **93** as a white solid material. Ratio of diastereomers, 4:1 (20 °C), 7:1 (0 °C), 9.5:1 (-20 °C) depending on the reaction temperature of the rearrangement.

Data of **92/93** are identical with that lined out in the literature.<sup>54</sup>

Data of **92**:

$[\alpha]_D^{20} = 0^\circ$  (c = 1.4, H<sub>2</sub>O)

**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>):  $\delta = 1.60$ - $2.02$  (m, 3H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, CHCHH),  $2.35$  (ddd, 1H,  $J = 11.03$  Hz,  $5.89$  Hz,  $5.88$  Hz, CHCHH),  $3.24$  (ddd, 1H,  $J = 12.5$  Hz,  $9.56$  Hz,  $4.41$  Hz, CHHN),  $3.84$ - $3.97$  (m, 2H, CHHN, CHCON) ppm

**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>):  $\delta = 21.6$  (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>),  $29.7$  (CHCH<sub>2</sub>),  $44.3$  (CHCON),  $60.9$  (CH<sub>2</sub>N),  $164.1$  (CON) ppm

Data of **93**:

$[\alpha]_D^{20} = -144.4^\circ$  (c = 0.2, H<sub>2</sub>O) (literature:<sup>54(c)</sup>  $[\alpha]_D^{36} -149.5^\circ$ , c = 1 in H<sub>2</sub>O)

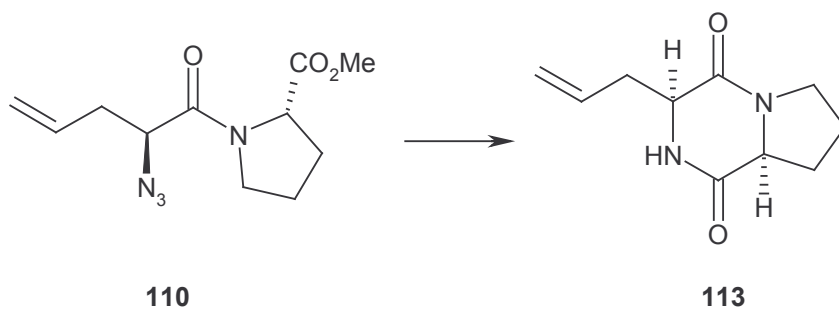
**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>):  $\delta = 2.02$ - $2.32$  (m, 4H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, CHCH<sub>2</sub>),  $3.52$  (dd, 2H,  $J = 8.79$  Hz,  $5.37$  Hz, CH<sub>2</sub>N),  $4.17$  (dd, 1H,  $J = 8.30$  Hz,  $7.81$  Hz, CHCON) ppm

**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>):  $\delta = 23.2$  (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>),  $27.5$  (CHCH<sub>2</sub>),  $45.1$  (CHCON),  $60.4$  (CH<sub>2</sub>N),  $164.1$  (CON) ppm

Data of **92** and **93**:

**IR** (KBr, Film):  $1/\lambda = 2988$  (m),  $2958$  (m),  $2876$  (m),  $1650$  (s, CON),  $1456$  (s),  $1345$  (w),  $1330$  (m),  $1300$  (m),  $1204$  (m),  $1181$  (m),  $1154$  (m),  $1073$  (w),  $1006$  (m),  $966$  (w) cm<sup>-1</sup>

**MS** (EI, 80 eV, 100°C): m/z (%) =  $194$  (33, [M]<sup>+</sup>),  $166$  (6, [M-CO]<sup>+</sup>),  $96$  (13, [C<sub>5</sub>H<sub>6</sub>NO]<sup>+</sup>),  $70$  (100, [C<sub>4</sub>H<sub>8</sub>N]<sup>+</sup>).

**(3*S*,6*S*)-6-Allyl-3,4-propylidene-1,4-piperazine-2,5-dione 113**

Azido pentenoic acid amide **110** (200 mg, 0.79 mmol) in THF (20 mL) was treated with PPh<sub>3</sub> (230 mg, 0.87 mmol) and H<sub>2</sub>O (1 mL). The mixture was stirred at 20 °C for 16 hours, H<sub>2</sub>O (20 mL) was added and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (4×15 mL). The combined organic layers were dried over MgSO<sub>4</sub>. After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 1:2) to give 140 mg (91%) of piperazine **113** as a pale yellow oil.

$[\alpha]_D^{20} = -108.8^\circ$  (c = 1.5, CHCl<sub>3</sub>)

<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>): δ = 1.77-1.90 (m, 1H, NCH<sub>2</sub>CHH), 1.90-2.07 (m, 2H, NCH<sub>2</sub>CHH, NCH<sub>2</sub>CH<sub>2</sub>CHH), 2.22-2.32 (m, 1H, NCH<sub>2</sub>CH<sub>2</sub>CHH), 2.35-2.44 (m, 1H, CHHCH=CH<sub>2</sub>), 2.77-2.85 (m, 1H, CHHCH=CH<sub>2</sub>), 3.43-3.58 (m, 2H, NCH<sub>2</sub>), 3.97-4.02 (dd, 1H, J = 8.39 Hz, 3.30 Hz, CHCH<sub>2</sub>CH=CH<sub>2</sub>), 4.02-4.09 (dd, 1H, J = 8.94 Hz, 7.56 Hz, NCHCO), 5.08-5.17 (m, 2H, CH=CH<sub>2</sub>), 5.66-5.76 (m, 1H, CH=CH<sub>2</sub>) ppm

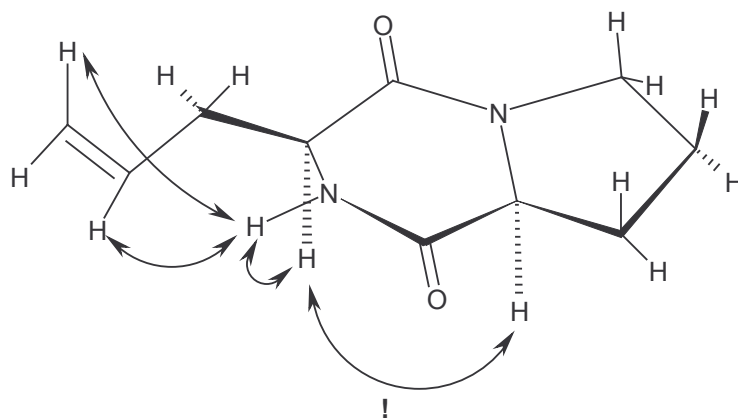
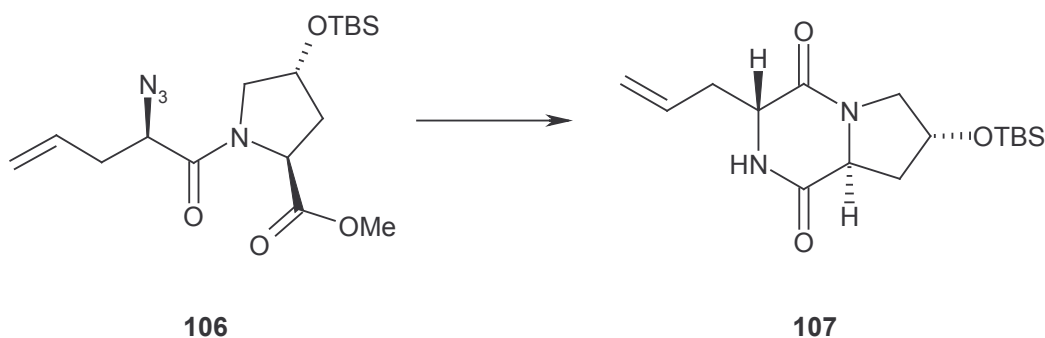
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 22.3, (NCH<sub>2</sub>CH<sub>2</sub>), 27.9 (NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 34.4 (CH<sub>2</sub>CH=CH<sub>2</sub>), 45.1 (NCH<sub>2</sub>), 53.9 (CHCH<sub>2</sub>CH=CH<sub>2</sub>), 58.8 (NCHCO), 119.5 (CH=CH<sub>2</sub>), 132.8 (CH=CH<sub>2</sub>), 164.9 (NCO), 169.7 (NHCO) ppm

IR (KBr, Film): 1/λ = 3480 (br, m, NH), 3234 (br, m, NH), 3079 (m), 2982 (m), 2954 (m), 2882 (m), 1668 (s, CONH, CON), 1558 (w), 1540 (w), 1429 (s), 1339 (m), 1305 (m), 1276 (m), 1212 (w), 1231 (w), 1212 (w), 1162 (w), 1146 (w), 1119 (w), 1002 (m), 922 (m) cm<sup>-1</sup>

MS (pos. FAB): m/z (%) = 195 (100, [M+H]<sup>+</sup>), 194 (18, [M]<sup>+</sup>), 193 (22, [M-H]<sup>+</sup>), 153 (13, [M-C<sub>3</sub>H<sub>5</sub>]<sup>+</sup>), 125 (25, [M-C<sub>4</sub>H<sub>7</sub>N]<sup>+</sup>), 69 (96, [C<sub>4</sub>H<sub>7</sub>N]<sup>+</sup>), 42 (29, [C<sub>3</sub>H<sub>6</sub>]<sup>+</sup>).

MS (EI, 80 eV, 40°C): m/z (%) = 194 (56, [M]<sup>+</sup>), 153 (18, [M-C<sub>3</sub>H<sub>5</sub>]<sup>+</sup>), 125 (50, [C<sub>6</sub>H<sub>7</sub>NO<sub>2</sub>]<sup>+</sup>), 70(100, [C<sub>4</sub>H<sub>8</sub>N]<sup>+</sup>), 41 (38, [C<sub>3</sub>H<sub>5</sub>]<sup>+</sup>).

HRMS (80 eV, 40°C): m/z, [M]<sup>+</sup> calcd for C<sub>10</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub>, 194.10553; found, 194.10633.

relevant NOE's of **113** from NOESY**(3*S*,6*R*)-6-Allyl-3,4-(2-*tert*-butyldimethylsilyloxy)propylidene-1,4-piperazine-2,5-dione **107****

Azido pentenoic acid amide **106** (110 mg, 0.28 mmol) in THF (20 mL) was treated with  $\text{PPh}_3$  (91 mg, 0.34 mmol) and  $\text{H}_2\text{O}$  (1 mL). The mixture was stirred at 20 °C for 16 hours,  $\text{H}_2\text{O}$  (10 mL) was added and the aqueous layer was extracted with  $\text{Et}_2\text{O}$  (4×15 mL). The combined organic layers were dried over  $\text{MgSO}_4$ . After removal of the solvent, the crude material was purified by column chromatography (ethyl acetate) to give 80 mg (85%) of piperazine **107** as colourless crystals with m.p. = 139-140°C.

$[\alpha]_D^{20} = -48.1^\circ$  (c = 0.6,  $\text{CHCl}_3$ )

$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.00 (s, 6H,  $\text{Si}(\text{CH}_3)_2$ ), 0.80 (s, 9H,  $\text{Si}(\text{CH}_3)_3$ ), 1.87-1.95 (ddd, 1H,  $J$  = 12.51 Hz, 12.09 Hz, 4.12 Hz,  $\text{CHHCHOTBS}$ ), 2.23-2.30 (dd, 1H,  $J$  = 12.93 Hz, 5.91 Hz,  $\text{CHHCHOTBS}$ ), 2.47-2.61 (m, 2H,  $\text{CH}_2\text{CH}=\text{CH}_2$ ), 3.37 (d, 1H,  $J$  = 12.92 Hz,  $\text{NCHHCHOTBS}$ ), 3.73-3.75 (dd, 1H,  $J$  = 12.93 Hz, 4.54 Hz,  $\text{NCHHCHOTBS}$ ), 3.93-3.99 (m,

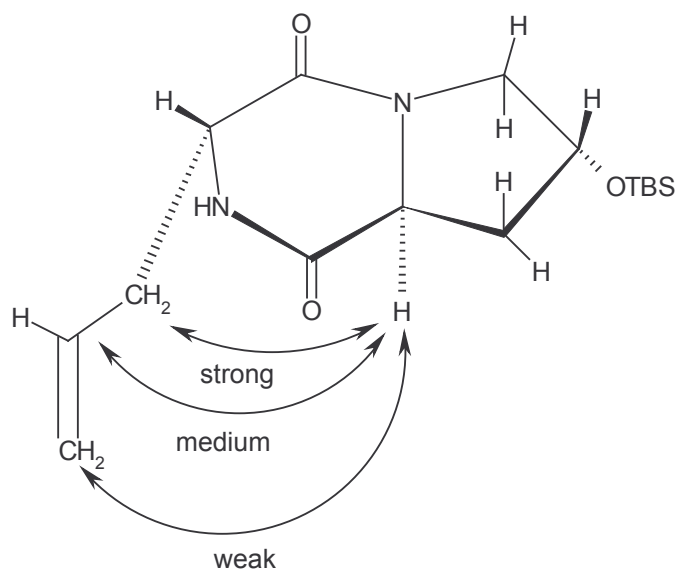
$^1\text{H}$ ,  $\text{NHCH}$ ), 4.36-4.45 (m, 2H,  $\text{NHCOCH}$ ,  $\text{CHOTBS}$ ), 5.14-5.23 (m, 2H,  $\text{CH=CH}_2$ ), 5.72-5.83 (dddd, 1H,  $J = 17.32$  Hz, 10.17 Hz, 7.44 Hz, 7.15 Hz,  $\text{CH=CH}_2$ ), 7.30 (br, s, 1H,  $\text{NH}$ ) ppm

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta = -5.0, -4.8$  ( $\text{Si}(\text{CH}_3)_2$ ), 17.8 ( $\text{SiC}(\text{CH}_3)_3$ ), 25.6 ( $\text{SiC}(\text{CH}_3)_3$ ), 38.7 ( $\text{CH}_2\text{CHOTBS}$ ), 38.9 ( $\text{CH}_2\text{CH=CH}_2$ ), 55.2 ( $\text{NCH}_2$ ), 56.5 ( $\text{CHOTBS}$ ), 57.4 ( $\text{NHCH}$ ), 68.2 ( $\text{NHCOCH}$ ), 120.2 ( $\text{CH=CH}_2$ ), 131.7 ( $\text{CH=CH}_2$ ), 165.2 ( $\text{NCO}$ ), 169.8 ( $\text{NHCO}$ ) ppm

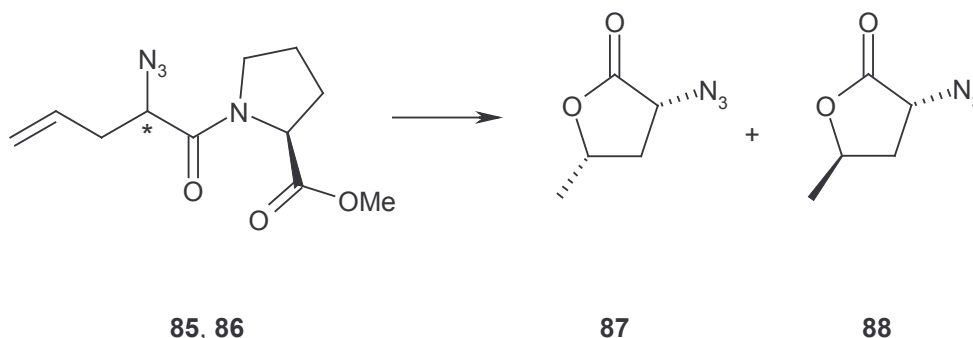
IR (KBr, Film):  $1/\lambda = 3213$  (m), 3165 (w), 3122 (w, NH), 2956 (m), 2928 (m), 2889 (w), 2856 (m), 1680 (s, CONH), 1646 (s, CON), 1498 (w), 1471 (m), 1461 (m), 1439 (m), 1419 (m), 1376 (m), 1361 (w), 1328 (w), 1308 (m), 1285 (w), 1256 (m), 1210 (w), 1161 (w), 1142 (w), 1109 (m), 1086 (m), 1026 (m), 1006 (m), 940 (w), 917 (m)  $\text{cm}^{-1}$

MS (EI, 80 eV,  $160^\circ\text{C}$ ):  $m/z$  (%) = 324 (0.17,  $[\text{M}]^+$ ), 309 (5,  $[\text{M}-\text{CH}_3]^+$ ), 267 (100,  $[\text{M}-\text{C}_4\text{H}_9]^+$ ), 239 (67,  $[\text{M}-\text{C}_6\text{H}_{13}]^+$ ).

HRMS (80 eV,  $160^\circ\text{C}$ ):  $m/z$   $[\text{M}-\text{C}_4\text{H}_9]^+$  calcd for  $\text{C}_{12}\text{H}_{19}\text{N}_2\text{O}_3\text{Si}$ , 267.11649;  
found, 267.11733.



relevant NOE's of **107** from NOESY

**(3*R*,5*S*)-3-Azido-5-methyl-2(3*H*)-furanone 87****(3*R*,5*R*)-3-Azido-5-methyl-2(3*H*)-furanone 88**

$\alpha$ -Azidoamide **85/86** (140 mg, 0.55 mmol) was heated (bath temperature 80 °C) with 6 M aq. HCl (5 mL) for 20 hours. After cooling to 20 °C, the mixture was extracted with Et<sub>2</sub>O (3 × 10 mL), the organic layers were dried over MgSO<sub>4</sub>, and the solvent was removed. Purification of the diastereomers via column chromatography (n-hexane / ethyl acetate = 4:1) afforded 20 mg (26%) of lactone **87** and 21 mg (27%) of lactone **88** as clear oils.

Data of **87**:

$$[\alpha]_D^{20} = +143.8^\circ \text{ (c = 0.3, CHCl}_3\text{)}$$

<sup>1</sup>H-NMR (270 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.45 (d, 3H,  $J$  = 5.88 Hz, **CH**<sub>3</sub>), 1.74 (ddd, 1H,  $J$  = 12.50 Hz, 11.03 Hz, 9.56 Hz, **CHH**), 2.66 (ddd, 1H,  $J$  = 13.24 Hz, 8.82 Hz, 5.88 Hz, **CHH**), 4.33 (dd, 1H,  $J$  = 11.03 Hz, 8.82 Hz, **CHN**<sub>3</sub>), 4.53 (ddt, 1H,  $J$  = 11.03 Hz, 5.88 Hz, 5.88 Hz, **CHO**) ppm

<sup>13</sup>C NMR (68 MHz, CDCl<sub>3</sub>):  $\delta$  = 20.8 (**CH**<sub>3</sub>), 36.5 (**CH**<sub>2</sub>), 58.1 (**CHN**<sub>3</sub>), 74.3 (**CHO**), 172.9 (**COO**) ppm

Data of **88**: (data is identical with those published in the literature<sup>51</sup>)

$$[\alpha]_D^{20} = +192.7^\circ \text{ (c = 0.5, CHCl}_3\text{)}$$

<sup>1</sup>H-NMR (270 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.40 (d, 3H,  $J$  = 6.62 Hz, **CH**<sub>3</sub>), 2.10 (ddd, 1H,  $J$  = 13.98 Hz, 8.09 Hz, 5.88 Hz, **CHH**), 2.25 (ddd, 1H,  $J$  = 13.24 Hz, 7.35 Hz, 5.89 Hz, **CHH**), 4.29 (dd, 1H,  $J$  = 8.09 Hz, 5.88 Hz, **CHN**<sub>3</sub>), 4.74 (ddt, 1H,  $J$  = 13.24 Hz, 6.62 Hz, 5.88 Hz, **CHO**) ppm

<sup>13</sup>C NMR (68 MHz, CDCl<sub>3</sub>):  $\delta$  = 20.9 (**CH**<sub>3</sub>), 35.6 (**CH**<sub>2</sub>), 57.3 (**CHN**<sub>3</sub>), 75.5 (**CHO**), 172.9 (**COO**) ppm



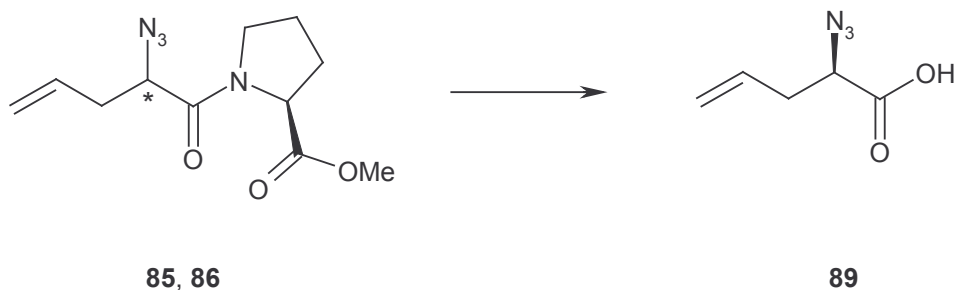
Data of **87** and **88**:

**IR** (solution, CHCl<sub>3</sub>):  $1/\lambda = 3022$  (s), 2986 (s), 2936 (s), 2127 (s, N<sub>3</sub>), 1790 (s, COO), 1321 (m), 1259 (m), 1178 (m), 955 (m) cm<sup>-1</sup>

**MS** (EI, 80 eV, 30°C):  $m/z$  (%) = 141 (8, [M]<sup>+</sup>), 126 (3, [M-CH<sub>3</sub>]<sup>+</sup>), 113 (3, [M-N<sub>2</sub>]<sup>+</sup>), 42 (100, [N<sub>3</sub>]<sup>+</sup>).

**HRMS** (80 eV, 30°C):  $m/z$  [M]<sup>+</sup> calcd for C<sub>5</sub>H<sub>7</sub>N<sub>3</sub>O<sub>2</sub>, 141.05383; found, 141.05621

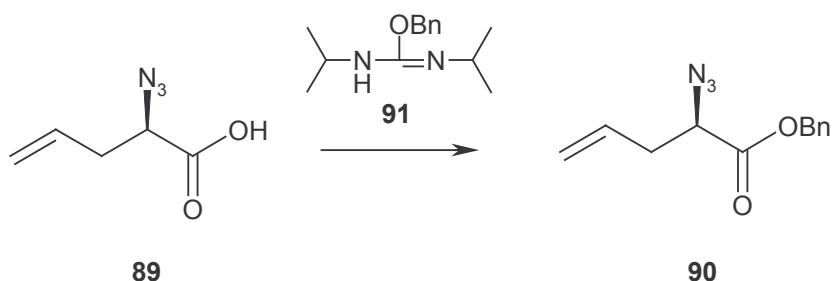
## 3.7 Syntheses of Pent-4-enoic Acid Derivatives

 $\alpha$ -Azido pent-4-enoic acid **89**

$\alpha$ -Azidoamide **85/86** (1.40 g, 5.50 mmol) was heated (bath temperature 80 °C) in 2 M aq. H<sub>2</sub>SO<sub>4</sub> (35 mL) for 20 hours. After cooling to 20 °C, the mixture was extracted with Et<sub>2</sub>O (3 × 50 mL), the organic layers were dried over MgSO<sub>4</sub>. The solvent was removed in vacuum to give 500 mg (64%) of  $\alpha$ -azido pent-4-enoic acid **89** as a pale yellow oil, which was used without further purification.

<sup>1</sup>H-NMR (270 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.48-2.73 (m, 2H, CH<sub>2</sub>CH=CH<sub>2</sub>), 3.92-4.02 (dd, 1H, *J* = 7.81 Hz, 5.37 Hz, N<sub>3</sub>CH), 5.10-5.30 (m, 2H, CH=CH<sub>2</sub>), 5.71-5.89 (m, 1H, CH=CH<sub>2</sub>) 11.7 (br, s, COOH) ppm

<sup>13</sup>C NMR (68 MHz, CDCl<sub>3</sub>):  $\delta$  = 35.5 (CH<sub>2</sub>CH=CH<sub>2</sub>), 61.1 (N<sub>3</sub>CH), 119.5 (CH=CH<sub>2</sub>), 131.6 (CH=CH<sub>2</sub>), 175.6 (COOH) ppm

*(R)*- $\alpha$ -Azido pent-4-enoic acid benzyl ester **90**

$\alpha$ -Azido pent-4-enoic acid **89** (140 mg, 1.00 mmol) was treated with *N,N'*-diisopropyl-*O*-benzylisourea **91** (281 mg, 1.20 mmol). After stirring at 20 °C for 1 hour, anhyd. THF (20 mL) was added. The mixture was stirred at 20 °C for a further 3 days. During this time a white precipitate occurred. The solids were filtered off and the solvent was removed in vacuum, the

crude material was purified by column chromatography (n-hexane / ethyl acetate = 5:1) to give 200 mg (86.5%) of  $\alpha$ -Azido pent-4-enoic acid benzyl ester **90** as a clear oil.

$[\alpha]_D^{20} = +17.2^\circ$  (c = 2.3, CHCl<sub>3</sub>)

**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.47-2.69 (m, 2H, CH<sub>2</sub>CH=CH<sub>2</sub>), 3.91-3.99 (dd, 1H, *J* = 7.81 Hz, 5.37 Hz, N<sub>3</sub>CH), 5.11-5.26 (m, 2H, CH=CH<sub>2</sub>), 5.22 (s, 2H, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 5.68-5.86 (dddd, 1H, *J* = 17.09 Hz, 10.25 Hz, 7.33 Hz, 6.83 Hz, CH=CH<sub>2</sub>), 7.35 (m, 5H, C<sub>6</sub>H<sub>5</sub>) ppm

**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>):  $\delta$  = 35.7 (CH<sub>2</sub>CH=CH<sub>2</sub>), 61.3 (N<sub>3</sub>CH), 67.4 (C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 119.2 (CH=CH<sub>2</sub>), 128.4, 128.6, 128.7, 134.9 (C<sub>6</sub>H<sub>5</sub>), 131.9 (CH=CH<sub>2</sub>), 169.8 (COOBn) ppm

**IR** (KBr, Film):  $1/\lambda$  = 3067 (m), 3034 (m), 2956 (m), 2513 (w), 2105 (s, N<sub>3</sub>), 1744 (s, COO), 1643 (m), 1608 (w), 1587 (w), 1498 (m), 1455 (m), 1438 (m), 1417 (m), 1379 (m), 1347 (m), 1268 (s), 1185 (s), 1128 (m), 1081 (w), 989 (m), 924 (m) cm<sup>-1</sup>

**MS** (EI, 80 eV, 40°C): *m/z* (%) = 231 (0.71, [M]<sup>+</sup>), 203 (0.56, [M-N<sub>2</sub>]<sup>+</sup>), 162 (3, [M-C<sub>3</sub>H<sub>5</sub>N<sub>2</sub>]<sup>+</sup>), 91 (100, [C<sub>7</sub>H<sub>7</sub>]<sup>+</sup>).

**HRMS**: (80 eV, 40°C): *m/z*, [M]<sup>+</sup> calcd. for C<sub>12</sub>H<sub>13</sub>N<sub>3</sub>O<sub>2</sub>, 231.10078; found, 231.10067

### 3.8 Syntheses of Diastereomers of $\alpha$ -Amino-pent-4-enoic Acid Derivatives

General procedure:

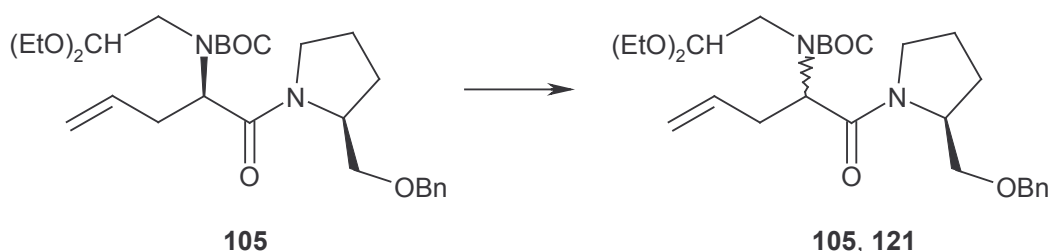
Method A:

The product of the rearrangement in anhyd. THF was cooled to  $-78$  °C. Lithium diisopropyl amide (1 eq., 1.8 M in heptane / tetrahydrofuran / ethyl benzene) was added and the mixture was stirred at  $-78$  °C for 1 hour. Then, the temperature was slowly raised to  $-40$  °C and the mixture was stirred at  $-40$  °C for a further 3 hours. The reaction was quenched with sat. aq.  $\text{NH}_4\text{Cl}$ . The aqueous layer was extracted with  $\text{Et}_2\text{O}$ , and the combined organic layers were dried over  $\text{MgSO}_4$ . After removal of the solvent, the diastereomers were separated by HPLC.

Method B:

The product of the rearrangement was dissolved in DMF and treated with  $\text{Na}_2\text{CO}_3$  (5 eq.). The reaction mixture was refluxed. After cooling to room temperature,  $\text{H}_2\text{O}$  was added and the aqueous layer was extracted with  $\text{Et}_2\text{O}$ . The combined organic layers were dried over  $\text{MgSO}_4$ . After removal of the solvent, the diastereomers were separated by means of HPLC.

#### (2*S*)-2-(*N*-*tert*-Butyloxycarbonyl)-*N*-(2,2-diethoxyethyl)aminopent-4-enoic acid [(2*S*)-benzyloxymethylpyrrolidinyl]amide **121**



Reaction starting from amide **105** (200 mg, 0.39 mmol) following the general procedure A, the diastereomers were separated by means of HPLC (2% iso-Propanol / n-hexane, Nucleosil 50-5, 32×110 mm, flow 64 mL/min, retention time:  $t_{121} = 4.40$  min,  $t_{105} = 5.65$  min). Yield: 90 mg **121** (45%) and 90 mg **105** (45%).

Reaction starting from amide **105** (200 mg, 0.39 mmol) following the general procedure B, reaction time 5 hours, the diastereomers were separated by means of HPLC to give 30 mg **121** (15%) and 150 mg **105** (75%).

Data of **121**:

$[\alpha]_D^{20} = -78.1^\circ$  ( $c = 1.4$ ,  $\text{CHCl}_3$ )

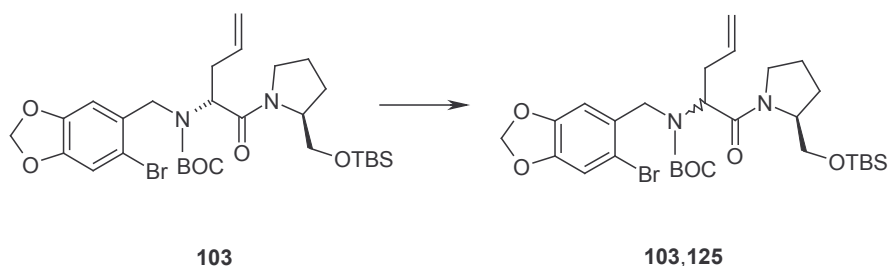
**$^1\text{H-NMR}$**  (270 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.05$  (m, 6H,  $(\text{OCH}_2\text{CH}_3)_2$ ), 1.40 (2 $\times$ s, 9H,  $\text{OC}(\text{CH}_3)_3$ ), 1.65-2.10 (m, 4H,  $\text{CH}_2\text{CH}_2$ ), 2.32-2.60 (m, 2H,  $\text{CH}_2\text{CH}=\text{CH}_2$ ), 3.10-3.67 (m, 10H,  $\text{NCH}_2\text{CH}_2$ ,  $\text{NCHCH}_2\text{O}$ ,  $\text{NCH}_2\text{CH}(\text{OEt})_2$ ,  $\text{CH}(\text{OCH}_2\text{CH}_3)_2$ ), 4.08-4.22 (m, 1H,  $\text{NCH}$ ), 4.30-4.55 (m, 3H,  $\text{OCH}_2\text{Ph}$ ,  $\text{COCH}$ ), 4.77-5.10 (m, 3H,  $\text{CH}(\text{OEt})_2$ ),  $\text{CH}=\text{CH}_2$ ), 5.53-5.73 (m, 1H,  $\text{CH}=\text{CH}_2$ ), 7.20 (m, 5H,  $\text{C}_6\text{H}_5$ ) ppm

**$^{13}\text{C NMR}$**  (68 MHz,  $\text{CDCl}_3$ ):  $\delta = 15.1$  ( $\text{CH}(\text{OCH}_2\text{CH}_3)_2$ ), 24.0 ( $\text{CH}_2\text{CH}_2$ ), 27.2, 27.3 ( $\text{CH}_2\text{CH}_2$ ), 28.1 ( $\text{C}(\text{CH}_3)_3$ ), 34.3 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 45.9 ( $\text{NCH}_2\text{CH}_2$ ), 46.3, 46.6 ( $\text{NCH}_2\text{CH}$ ), 56.0, 56.7 ( $\text{NCH}$ ), 61.2, 62.1 ( $\text{CH}(\text{OCH}_2\text{CH}_3)_2$ ), 69.7 ( $\text{CH}_2\text{OBn}$ ), 72.9 ( $\text{OCH}_2\text{Ph}$ ), 80.1 ( $\text{C}(\text{CH}_3)_3$ ), 100.0, 100.8 ( $\text{CH}(\text{OEt})_2$ ), 117.2 ( $\text{CH}=\text{CH}_2$ ), 127.2, 128.1, 134.1, 138.3 (Ph), 134.5 ( $\text{CH}=\text{CH}_2$ ), 155.7 ( $\text{OCON}$ ), 168.8 ( $\text{CON}$ ) ppm

**IR** (solution,  $\text{CHCl}_3$ ):  $1/\lambda = 3067$  (m), 3011 (s), 2978 (s), 2931 (s), 2872 (s), 1811 (m), 1751 (m), 1682 (s,  $\text{OCON}$ ), 1640 (s,  $\text{CON}$ ), 1496 (m), 1476 (m), 1452 (s), 1394 (s), 1368 (s), 1346 (m), 1310 (m), 1252 (s), 1216 (s), 1162 (s), 1122 (s), 1064 (s), 922 (m)  $\text{cm}^{-1}$

**MS** (EI, 80 eV,  $120^\circ\text{C}$ ):  $m/z$  (%) = 504 (0.59,  $[\text{M}]^+$ ), 475 (4.9,  $[\text{M}-\text{C}_2\text{H}_5]^+$ ), 458 (3.2,  $[\text{M}-\text{C}_2\text{H}_6\text{O}]^+$ ), 431 (1.2,  $[\text{M}-\text{C}_4\text{H}_9\text{O}]^+$ ), 403 (4,  $[\text{M}-\text{C}_5\text{H}_9\text{O}_2]^+$ ), 212 (5,  $[\text{C}_{11}\text{H}_{18}\text{NO}_3]^+$ ), 190 (4,  $[\text{C}_{12}\text{H}_{16}\text{NO}]^+$ ), 184 (10,  $[\text{C}_{10}\text{H}_{18}\text{NO}_2]^+$ ), 103 (100,  $[\text{C}_5\text{H}_{11}\text{O}_2]^+$ ), 91 (16,  $[\text{C}_7\text{H}_7]^+$ ).

**HRMS**: (80 eV,  $120^\circ\text{C}$ ):  $m/z$ ,  $[\text{M}]^+$  calcd. for  $\text{C}_{28}\text{H}_{44}\text{N}_2\text{O}_6$ , 504.31993; found, 504.31765  
 $[\text{M}-\text{C}_2\text{H}_5]^+$  calcd. for  $\text{C}_{26}\text{H}_{39}\text{N}_2\text{O}_6$ , 475.28081; found, 475.28332

**(2S)-2-[N-(2-Bromo-4,5-methylenedioxyphenyl)methyl]-N-(tert-butyloxycarbonyl)-aminopent-4-enoic acid [(2S)-tert-butyldimethylsilyloxymethyl-pyrrolidinyl]amide **125****

Reaction starting from amide **103** (250 mg, 0.24 mmol) following the general procedure B, reaction time 20 hours. The diastereomers were separated by HPLC (20% ethyl acetate / n-hexane, Nucleosil 50-5, 32×110 mm, flow 64 mL/min, retention time:  $t_{125} = 6.86$  min,  $t_{103} = 8.09$  min). Yield: 90 mg **125** (36%) and 140 mg **103** (56%).

Data of **125**:

$[\alpha]_D^{20} = -52.8^\circ$  ( $c = 1.6$ ,  $\text{CHCl}_3$ )

**$^1\text{H-NMR}$**  (500 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.00$  (s, 6H,  $\text{Si}(\text{CH}_3)_2$ ), 0.80 (s, 9H,  $\text{SiC}(\text{CH}_3)_3$ ), 1.30 (s, 9H,  $\text{OC}(\text{CH}_3)_3$ ), 1.70-2.15 (m, 4H,  $\text{CH}_2\text{CH}_2$ ), 2.35- 2.58 (m, 2H,  $\text{CH}_2\text{CH}=\text{CH}_2$ ), 3.36-3.62 (m, 2H,  $\text{NCHHCH}_2$ ,  $\text{OCHH}$ ), 3.62-3.81 (m, 2H,  $\text{NCHHCH}_2$ ,  $\text{OCHH}$ ), 3.90 (m, 1H,  $\text{BOCNCH}$ ), 4.35 (d, 1H,  $J = 16.92$  Hz,  $\text{NCHHAr}$ ), 4.51 (d, 1H,  $J = 16.92$  Hz,  $\text{NCHHAr}$ ), 4.96-5.15 (m, 3H,  $\text{NCH}$ ,  $\text{CH}=\text{CH}_2$ ), 5.60-5.77 (m, 1H,  $\text{CH}=\text{CH}_2$ ), 5.90 (s, 2H,  $\text{OCH}_2\text{O}$ ), 6.50 (s, 1H, Ar-H), 6.90 (s, 1H, Ar-H) ppm

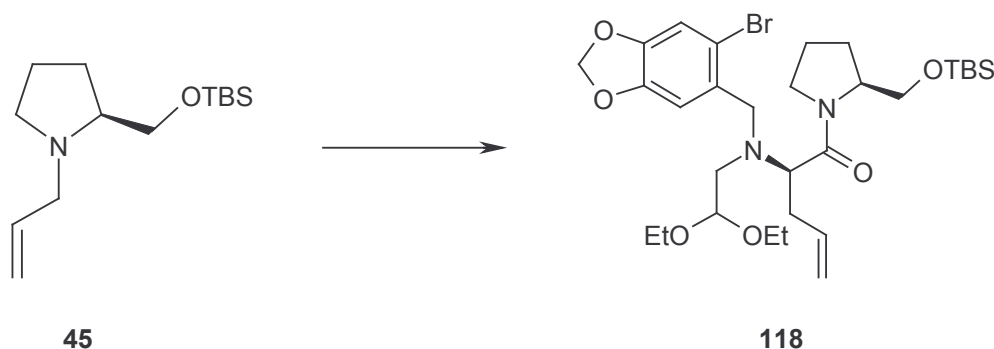
**$^{13}\text{C NMR}$**  (125 MHz,  $\text{CDCl}_3$ ):  $\delta = -5.5$  ( $\text{Si}(\text{CH}_3)_2$ ), 18.0 ( $\text{SiC}(\text{CH}_3)_3$ ), 22.1, 24.5 ( $\text{CH}_2\text{CH}_2$ ), 25.7 ( $\text{SiC}(\text{CH}_3)_3$ ), 26.8, 27.3 ( $\text{CH}_2\text{CH}_2$ ), 28.0 ( $\text{OC}(\text{CH}_3)_3$ ), 31.5 ( $\text{NCHCH}_2\text{OTBS}$ ), 34.3 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 46.9, 47.4 ( $\text{NCH}_2\text{CH}_2$ ), 55.2 ( $\text{NCH}$ ), 58.6 ( $\text{TBSOCH}_2$ ), 62.4 ( $\text{NCH}_2\text{Ar}$ ), 80.5 ( $\text{OC}(\text{CH}_3)_3$ ), 101.4 ( $\text{OCH}_2\text{O}$ ), 106.7, 118.1, 132.1, 147.1 (Ar), 112.3 ( $\text{CH}=\text{CH}_2$ ), 133.5 ( $\text{CH}=\text{CH}_2$ ), 155.6 ( $\text{OCON}$ ), 168.6 ( $\text{CON}$ ) ppm

**IR** (solution,  $\text{CHCl}_3$ ):  $1/\lambda = 3070$  (w), 3017 (s), 2976 (s), 2956 (s), 2930 (s), 2885 (s), 2858 (s), 1812 (w), 1682 (s,  $\text{OCON}$ ), 1642 (s,  $\text{CON}$ ), 1504 (s), 1480 (s), 1452 (s), 1412 (s), 1368 (s), 1340 (m), 1313 (m), 1216 (s), 1161 (s), 1105 (s), 1041 (s), 999 (m)  $\text{cm}^{-1}$

**MS** (EI, 80 eV,  $140^\circ\text{C}$ ):  $m/z$  (%) = 624 (16,  $[\text{M}]^+$ ), 567 (11,  $[\text{M}-\text{C}_4\text{H}_9]^+$ ), 523 (13,  $[\text{M}-\text{C}_5\text{H}_9\text{O}_2]^+$ ), 511 (30,  $[\text{M}-\text{C}_6\text{H}_{15}\text{Si}]^+$ ), 297 (100,  $[\text{M}-\text{C}_{14}\text{H}_{20}\text{O}_2\text{BrSi}]^+$ ), 213 (97,  $[\text{C}_8\text{H}_6\text{O}_2\text{Br}]^+$ ), 70 (25,  $[\text{C}_4\text{H}_8\text{N}]^+$ ), 57 (15,  $[\text{C}_4\text{H}_9]^+$ ).

**HRMS** (80 eV,  $140^\circ\text{C}$ ):  $m/z$ ,  $[\text{M}]^+$  calcd. for  $\text{C}_{29}\text{H}_{45}\text{N}_2\text{O}_6\text{Si}^{79}\text{Br}$ , 624.22302; found, 624.22564

## 3.9 Syntheses of Isoquinolone Derivatives

**(2R)-2-[N-(2-Bromo-4,5-methylenedioxyphenyl)methyl]-N-(2,2-diethoxyethyl)aminopent-4-enoic acid [(2S)-tert-butyl dimethylsilyloxymethyl-pyrrolidinyl]amide 118**

Reaction starting from *N*-allylprolinol silyl ether **45** (700 mg, 2.74 mmol) and *N*-BOC glycyl fluoride **71** (965 mg, 3.29 mmol) following the general procedure as described for the zwitterionic aza-Claisen rearrangement. Reaction temperature 0 °C, reaction time 16 hours. The major part of the BOC-protective group had been removed during the course of the workup. The crude amide in EtOH (10 mL) cooled to 0 °C. SOCl<sub>2</sub> (5 mL) was added and the mixture was stirred at 20 °C for 16 hours. Aq. NaHCO<sub>3</sub> (20 mL) was added, then, the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were dried over MgSO<sub>4</sub> and the solvent was evaporated to give the crude amide. The TBS group was reintroduced following the procedure as described for the silyl ether **45**: Imidazole (380 mg, 5.59 mmol), DMAP (10 mg), TBSCl (650 mg, 4.33 mmol), anhyd. CH<sub>2</sub>Cl<sub>2</sub> (30 mL), reaction time 16 hours.

The crude silyl ether and K<sub>2</sub>CO<sub>3</sub> (3 g, 21.7 mmol) in anhyd. MeCN (20 mL) were treated with 2-bromopiperonyl bromide **77** (1 g, 3.4 mmol). The mixture was refluxed overnight. After cooling to 20 °C, H<sub>2</sub>O (20 mL) was added and the aqueous layer was extracted with Et<sub>2</sub>O (4×10 mL). After drying over MgSO<sub>4</sub>, the solvent was removed and the crude benzyl ether was purified via column chromatography (n-hexane / ethyl acetate = 7:1) to give 900 mg (51%) of **118** as a yellow oil.

$[\alpha]_D^{20} = -13.5^\circ$  (c = 0.9, CHCl<sub>3</sub>)

<sup>1</sup>H-NMR (270 MHz, CDCl<sub>3</sub>): δ = 0.00 (s, 6H, Si(CH<sub>3</sub>)<sub>2</sub>), 0.84 (s, 9H, SiC(CH<sub>3</sub>)<sub>3</sub>), 1.15 (2xt, 6H, *J* = 7.35 Hz, CH<sub>3</sub>CH<sub>2</sub>O), 1.70-1.98 (m, 4H, CH<sub>2</sub>CH<sub>2</sub>), 2.40 (ddd, 1H, *J* = 13.97 Hz, 7.36 Hz, 6.61 Hz, CH<sub>2</sub>=CHCHH), 2.55 (ddd, 1H, *J* = 13.97 Hz, 7.35 Hz, 6.61 Hz, CH<sub>2</sub>=CHCHH), 2.88 (dd, 2H, *J* = 13.97 Hz, 5.15 Hz, NCH<sub>2</sub>CH(OEt)<sub>2</sub>), 3.17 (m, 1H, NCHHCH<sub>2</sub>), 3.31-3.70

(m, 8H, NCH $\overline{H}$ HCH $\overline{2}$ , NCH $\overline{H}$ CH $\overline{2}$ CH=CH $\overline{2}$ , (CH $\overline{3}$ CH $\overline{2}$ O) $\overline{2}$ , CH $\overline{2}$ O), 3.79 (d, 1H,  $J$  = 14.81 Hz, ArCH $\overline{H}$ ), 3.93 (d, 1H,  $J$  = 15.44 Hz, ArCH $\overline{H}$ ), 4.13 (m, 1H, NCH $\overline{H}$ CH $\overline{2}$ O), 4.31 (t, 1H,  $J$  = 5.15 Hz, CH(OEt) $\overline{2}$ ), 4.97 (d, 1H,  $J$  = 10.30 Hz, CH=CH $\overline{H}$ ), 5.05 (d, 1H,  $J$  = 16.91 Hz, CH=CH $\overline{H}$ ), 5.75 (dddd, 1H,  $J$  = 16.91 Hz, 10.30 Hz, 7.36 Hz, 6.61 Hz, CH=CH $\overline{2}$ ), 5.91 (s, 2H, OCH $\overline{2}$ O), 6.90 (s, 1H, Ar-H), 7.05 (s, 1H, Ar-H) ppm

$^{13}$ C NMR (68 MHz, CDCl $\overline{3}$ ):  $\delta$  = -5.4 (Si(CH $\overline{3}$ ) $\overline{2}$ ), 15.2 (CH $\overline{3}$ CH $\overline{2}$ O), 18.0 (SiC(CH $\overline{3}$ ) $\overline{3}$ ), 24.3 (CH $\overline{2}$ CH $\overline{2}$ ), 25.7 (SiC(CH $\overline{3}$ ) $\overline{3}$ ), 26.8 (CH $\overline{2}$ CH $\overline{2}$ ), 31.7 (CH $\overline{2}$ =CHCH $\overline{2}$ ), 46.8 (NCH $\overline{2}$ CH $\overline{2}$ ), 54.5 (NCH $\overline{2}$ CH(OEt) $\overline{2}$ ), 55.3 (CHCH $\overline{2}$ O), 58.3 (NCHCH $\overline{2}$ O), 61.9 (CH $\overline{2}$ =CHCH $\overline{2}$ CHN), 62.1 (ArCH $\overline{2}$ ), 62.4, 62.6 (CH $\overline{3}$ CH $\overline{2}$ O), 101.4 (CH(OEt) $\overline{2}$ ), 103.0 (OCH $\overline{2}$ O), 116.7 (CH $\overline{2}$ =CH), 110.2, 112.2, 113.8, 132.8, 146.9, 147.2 (Ar), 135.4 (CH $\overline{2}$ =CH), 170.7 (CON) ppm

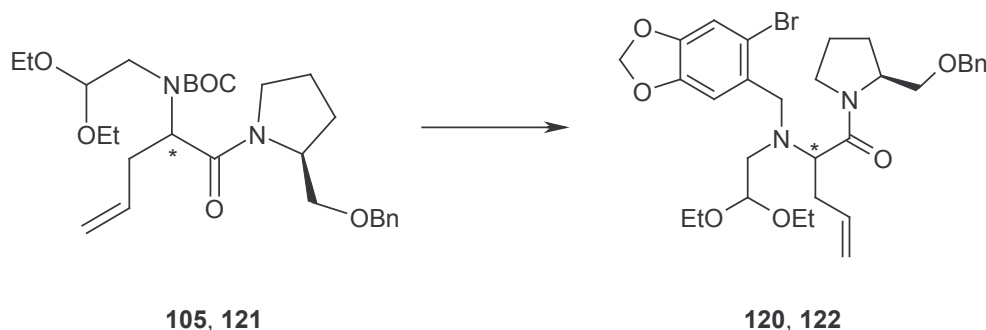
IR (solution, CHCl $\overline{3}$ ):  $1/\lambda$  = 3078 (w), 3017 (s), 2977 (s), 2952 (s), 2930 (s), 2897 (s), 2885 (s), 2853 (s), 1632 (s, CON), 1504 (s), 1475 (s), 1440 (s), 1409 (m), 1375 (m), 1252 (s), 1233 (s), 1214 (s), 1106 (s), 1041 (s), 1001 (m), 965 (w), 936 (m) cm $^{-1}$

MS (EI, 80 eV, 160°C):  $m/z$  (%) = 640 (3.6, [M] $^{+}$ ), 594 (4, [M-CH $\overline{2}$ O $\overline{2}$ ] $^{+}$ ), 537 (17, [M-C $\overline{5}$ H $\overline{11}$ O $\overline{2}$ ] $^{+}$ ), 398 (83, [M-C $\overline{12}$ H $\overline{24}$ NO $\overline{2}$ Si] $^{+}$ ), 213 (100, [C $\overline{8}$ H $\overline{6}$ O $\overline{2}$ Br] $^{+}$ ), 103 (24, [C $\overline{5}$ H $\overline{11}$ O $\overline{2}$ ] $^{+}$ ).

HRMS (80 eV, 160 °C):  $m/z$ , [M] $^{+}$  calcd. for C $\overline{30}$ H $\overline{49}$  $^{79}$ BrN $\overline{2}$ O $\overline{6}$ Si, 640.25432; found, 640.25744

**(2R)-2-[N-(2-Bromo-4,5-methylenedioxyphenyl)methyl]-N-(2,2-diethoxyethyl)aminopent-4-enoic acid [(2S)-benzyloxymethylpyrrolidinyl]amide 120**

**(2S)-2-[N-(2-Bromo-4,5-methylenedioxyphenyl)methyl]-N-(2,2-diethoxyethyl)aminopent-4-enoic acid [(2S)-benzyloxymethylpyrrolidinyl]amide 122**



The benzyl ether **105** (1 g, 1.98 mmol) or **121** (90 mg, 0.17 mmol) in dry EtOH (30 mL) was treated with SOCl $\overline{2}$  (0.5 mL) at 0 °C. The mixture was stirred at 20 °C for 16 hours. Aq. NaHCO $\overline{3}$  (20 mL) was added, then the mixture extracted with CH $\overline{2}$ Cl $\overline{2}$ . The combined organic layers were dried over MgSO $\overline{4}$  and the solvent was evaporated to give the crude amide. The



crude silyl ether and  $K_2CO_3$  (3 g, 21.7 mmol) in anhyd. MeCN (20 mL) was treated with 2-bromopiperonyl bromide **77** (1 g, 3.4 mmol). The mixture was refluxed overnight. After cooling to 20 °C,  $H_2O$  (20 mL) was added and the aqueous layer was extracted with  $Et_2O$  (4×10 mL). After drying over  $MgSO_4$ , the solvent was removed and the crude benzyl ether was purified via column chromatography (n-hexane / ethyl acetate = 7:1) to give 1.06 g (87%) of **120** or 90 mg (82%) of **122** as yellow oils.

Data of **120**:

$$[\alpha]_D^{20} = -39.3^\circ \text{ (c = 0.8, } CHCl_3\text{)}$$

**$^1H$ -NMR** (500 MHz,  $CDCl_3$ ):  $\delta$  = 1.25 (2×t, 6H,  $J$  = 7.35 Hz,  $(CH_3CH_2O)_2$ ), 1.75-1.85 (m, 2H,  $CHHCHH$ ), 1.85-2.02(m, 2H,  $CHHCHH$ ), 2.32-2.45 (m, 1H,  $CHHCH=CH_2$ ), 2.49-2.63 (m, 1H,  $CHHCH=CH_2$ ), 2.72-2.82 (m, 1H,  $CHHCH(OEt)_2$ ), 2.82-2.92 (m, 1H,  $CHHCH(OEt)_2$ ), 3.15 (m, 1H,  $NCHHCH_2$ ), 3.23-3.70 (m, 8H,  $(CH_3CH_2O)_2$ ,  $BnOCH_2$ ,  $NCOCH$ ,  $NCHHCH_2$ ), 3.75-3.82 (d, 2H,  $J$  = 1.96 Hz,  $ArCH_2$ ), 4.20-4.37 (m, 3H,  $CONCH$ ,  $CH(OEt)_2$ ,  $OCHHC_6H_5$ ), 4.45 (s, 1H,  $OCHHC_6H_5$ ), 4.89-5.01 (2×dd, 1H,  $J$  = 10.11 Hz, 0.95 Hz,  $CH=CHH$ ), 4.90-5.11 (2×dd, 1H,  $J$  = 17.16 Hz, 1.53 Hz,  $CH=CHH$ ), 5.60-5.69, 5.72-5.82 (2×dddd, 1H,  $J$  = 17.16 Hz, 10.11 Hz, 7.25 Hz, 6.96 Hz,  $CH=CH_2$ ), 5.85-5.90 (2×s, 2H,  $OCH_2O$ ), 6.89 (2×s, 1H, Ar-H), 7.05 (2×s, 1H, Ar-H), 7.18-7.32 (m, 5H,  $C_6H_5$ ) ppm

**$^{13}C$  NMR** (125 MHz,  $CDCl_3$ ):  $\delta$  = 15.2 ( $(CH_3CH_2O)_2$ ), 18.3, 21.7 ( $CH_2CH_2$ ), 24.0, 27.2 ( $CH_2CH_2$ ), 28.5, 30.0 ( $CH_2CH=CH_2$ ), 45.4, 46.7 ( $NCH_2CH_2$ ), 54.0, 54.2 ( $CH_2CH(OEt)_2$ ), 55.0, 55.1 ( $NCH_2Ar$ ), 55.5, 56.4 ( $CONCH$ ), 61.5, 61.6, 61.9, 62.0 ( $(CH_3CH_2O)_2$ ), 62.1, 62.4 ( $COCHN$ ), 69.6, 71.6 ( $BnOCH_2$ ), 72.9 ( $OCH_2C_6H_5$ ), 101.4 ( $OCH_2O$ ), 102.6, 102.9 ( $CH(OEt)_2$ ), 112.1, 112.2, 113.7, 113.8, 137.8, 138.4, 146.9, 147.2 (Ar), 116.7, 116.9 ( $CH=CH_2$ ), 127.3, 127.4, 127.5, 128.1, 128.2, 132.5 ( $C_6H_5$ ), 135.5, 135.6 ( $CH=CH_2$ ), 170.3, 170.5 (CON) ppm

**IR** (solution,  $CHCl_3$ ):  $1/\lambda$  = 3064 (w), 3018 (s), 2978 (s), 2887 (m), 1630 (s, CON), 1503 (m), 1476 (s), 1453 (m), 1409 (m), 1375 (m), 1328 (w), 1213 (s), 1107 (m), 1041 (s), 966 (w)  $cm^{-1}$

**MS** (EI, 80 eV, 170°C):  $m/z$  (%) = 618 (3.4,  $[M]^+$ ), 616 (3,  $[M]^+$ ), 577 (8,  $[M-C_3H_5]^+$ ), 575 (8,  $[M-C_3H_5]^+$ ), 515 (31,  $[M-C_5H_{11}O_2]^+$ ), 513 (30,  $[M-C_5H_{11}O_2]^+$ ), 400 (85,  $[M-C_{13}H_{16}NO_2]^+$ ), 398 (83,  $[M-C_{13}H_{16}NO_2]^+$ ), 215 (99,  $[C_8H_6O_2Br]^+$ ), 213 (100,  $[C_8H_6O_2Br]^+$ ), 103 (16,  $[C_5H_{11}O_2]^+$ ), 91 (29,  $[C_7H_7]^+$ ).

**HRMS** (80 eV, 170 °C): $m/z$ ,  $[M]^+$  calcd. for  $C_{31}H_{41}N_2O_6^{79}Br$ , 616.21479; found, 616.21673

Data of **122**:

$$[\alpha]_D^{20} = -21.2^\circ \text{ (c = 1.1, CHCl}_3\text{)}$$

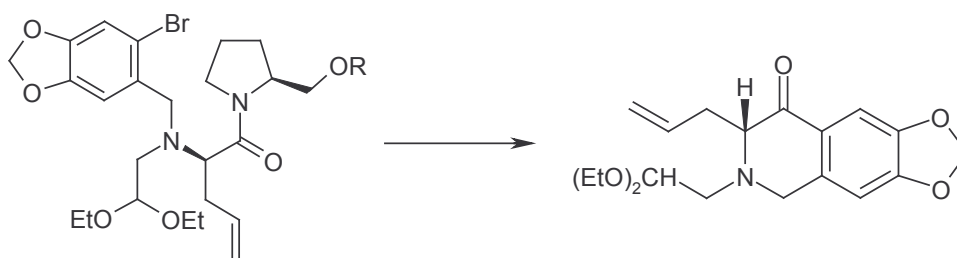
**<sup>1</sup>H-NMR** (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.10 (2×t, 6H,  $J$  = 7.35 Hz, (CH<sub>3</sub>CH<sub>2</sub>O)<sub>2</sub>), 1.75-1.80 (m, 1H, CH<sub>2</sub>CHH), 1.85-2.02(m, 3H, CH<sub>2</sub>CHH), 2.32-2.44 (ddd, 1H,  $J$  = 13.19 Hz, 6.84 Hz, 6.34 Hz, CHHCH=CH<sub>2</sub>), 2.48-2.61 (ddd, 1H,  $J$  = 14.16 Hz, 7.82 Hz, 6.34 Hz, CHHCH=CH<sub>2</sub>), 2.77-2.94 (dd, 2H,  $J$  = 5.37 Hz, 4.88 Hz, CH<sub>2</sub>CH(OEt)<sub>2</sub>), 3.02 (m, 1H, NCHHCH<sub>2</sub>), 3.26-3.68 (m, 8H, (CH<sub>3</sub>CH<sub>2</sub>O)<sub>2</sub>, BnOCH<sub>2</sub>, NCOCH, NCHHCH<sub>2</sub>), 3.76 (d, 1H,  $J$  = 15.13 Hz, ArCHH), 3.93 (d, 1H,  $J$  = 15.14 Hz, ArCHH), 4.19-4.28 (m, 1H, CONCH), 4.29 (dd, 1H,  $J$  = 5.37 Hz, 4.88 Hz, CH(OEt)<sub>2</sub>), 4.36-4.43(d, 1H,  $J$  = 12.21 Hz, OCHHC<sub>6</sub>H<sub>5</sub>), 4.43-4.51 (d, 1H,  $J$  = 12.21 Hz, OCHHC<sub>6</sub>H<sub>5</sub>), 4.89-4.91 (dd, 1H,  $J$  = 10.25 Hz, 1.95 Hz, CH=CHH), 4.90-5.11 (dd, 1H,  $J$  = 17.09 Hz, 1.46 Hz, CH=CHH), 5.63-5.78 (dddd, 1H,  $J$  = 17.09 Hz, 10.25 Hz, 7.33 Hz, 6.83 Hz, CH=CH<sub>2</sub>), 5.86-5.90 (2×s, 2H, OCH<sub>2</sub>O), 6.89 (s, 1H, Ar-H), 7.05 (s, 1H, Ar-H), 7.15-7.39 (m, 5H, C<sub>6</sub>H<sub>5</sub>) ppm

**<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 15.2 ((CH<sub>3</sub>CH<sub>2</sub>O)<sub>2</sub>), 24.2 (CH<sub>2</sub>CH<sub>2</sub>), 27.4 (CH<sub>2</sub> CH<sub>2</sub>), 31.7 (CH<sub>2</sub>CH=CH<sub>2</sub>), 46.5 (NCH<sub>2</sub>CH<sub>2</sub>), 54.3 (CH<sub>2</sub>CH(OEt)<sub>2</sub>), 55.3 (NCH<sub>2</sub>Ar), 56.4 (CONCH), 61.8, 61.9, 62.0, 62.1 ((CH<sub>3</sub>CH<sub>2</sub>O)<sub>2</sub>), 62.5 (COCHN), 69.8 (BnOCH<sub>2</sub>), 73.0 (OCH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 101.4 (OCH<sub>2</sub>O), 103.0 (CH(OEt)<sub>2</sub>), 110.1, 112.1, 113.7, 138.4, 146.9, 147.1 (Ar), 116.7 (CH=CH<sub>2</sub>), 127.2, 128.1, 128.2, 132.6 (C<sub>6</sub>H<sub>5</sub>), 135.1 (CH=CH<sub>2</sub>), 170.7 (CON) ppm

**IR** (solution, CHCl<sub>3</sub>):  $1/\lambda$  = 3062 (w), 3026 (m), 3007 (s), 2978 (s), 2881 (s), 1632 (s, CON), 1503 (s), 1476 (s), 1453 (s), 1409 (m), 1375 (m), 1235 (s), 1107 (m), 1041 (s), 966 (w) cm<sup>-1</sup>

**MS** (EI, 80 eV, 170°C):  $m/z$  (%) = 618 (4.1, [M]<sup>+</sup>), 616 (3.9, [M]<sup>+</sup>), 577 (6, [M-C<sub>3</sub>H<sub>5</sub>]<sup>+</sup>), 575 (7, [M-C<sub>3</sub>H<sub>5</sub>]<sup>+</sup>), 515 (33, [M-C<sub>5</sub>H<sub>11</sub>O<sub>2</sub>]<sup>+</sup>), 513 (33, [M-C<sub>5</sub>H<sub>11</sub>O<sub>2</sub>]<sup>+</sup>), 400 (86, [M-C<sub>13</sub>H<sub>16</sub>NO<sub>2</sub>]<sup>+</sup>), 398 (87, [M-C<sub>13</sub>H<sub>16</sub>NO<sub>2</sub>]<sup>+</sup>), 215 (96, [C<sub>8</sub>H<sub>6</sub>O<sub>2</sub>Br]<sup>+</sup>), 213 (100, [C<sub>8</sub>H<sub>6</sub>O<sub>2</sub>Br]<sup>+</sup>), 103 (16, [C<sub>5</sub>H<sub>11</sub>O<sub>2</sub>]<sup>+</sup>), 91 (27, [C<sub>7</sub>H<sub>7</sub>]<sup>+</sup>).

**HRMS** (80 eV, 170 °C): $m/z$ , [M]<sup>+</sup> calcd. for C<sub>31</sub>H<sub>41</sub>N<sub>2</sub>O<sub>6</sub><sup>79</sup>Br, 616.21479; found, 616.21679

**(3*R*)-3-Allyl-*N*-(2,2-diethoxyethyl)-6,7-methylenedioxy-1,2,3,4-tetrahydro-4-isoquinolone 119**

**118: R = TBS**  
**120: R = Bn**

**119**

Under argon, *N*-piperonylprolinol silyl ether amide **118** (550 mg, 0.86 mmol) in anhyd. THF (20 mL) was cooled to  $-78\text{ }^{\circ}\text{C}$ . BuLi (650  $\mu\text{L}$ , 1.04 mmol, 1.6 M in hexane) was injected dropwise. The temperature was raised to  $-40\text{ }^{\circ}\text{C}$  and the mixture was stirred under these conditions for a further 3 hours (TLC-monitoring). Sat. aq.  $\text{NH}_4\text{Cl}$  (10 mL) was added to the mixture and the aqueous layer was extracted with  $\text{Et}_2\text{O}$  ( $4 \times 10\text{ mL}$ ), and the combined organic layers were dried over  $\text{MgSO}_4$ . After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 5:1) gave 210 mg (81%) of **119** as a yellow oil.

Reaction with **120** (700 mg, 1.13 mmol) as described above for **118**. Yield: 290 mg (83%) of **119** as a yellow oil.

$[\alpha]_D^{20} = -6.1^{\circ}$  ( $c = 1.3$ ,  $\text{CHCl}_3$ )

**$^1\text{H-NMR}$**  (270 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.10$  (2x t, 6H,  $J = 7.35\text{ Hz}$ ,  $(\text{CH}_3\text{CH}_2\text{O})_2$ ), 2.45 (ddd, 2H,  $J = 13.97\text{ Hz}$ , 7.36 Hz, 6.62 Hz,  $\text{CH}_2=\text{CHCH}_2$ ), 2.73 (dd, 2H,  $J = 13.97\text{ Hz}$ , 5.15 Hz,  $\text{NCH}_2\text{CH}(\text{OEt})_2$ ), 3.35-3.43 (m, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ,  $\text{NCHCO}$ ), 3.51-3.64 (m, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 3.86 (d, 1H,  $J = 16.91\text{ Hz}$ ,  $\text{ArCHH}$ ), 4.18 (d, 1H,  $J = 16.91\text{ Hz}$ ,  $\text{ArCHH}$ ), 4.48 (t, 1H,  $J = 5.15\text{ Hz}$ ,  $\text{CH}(\text{OEt})_2$ ), 4.99 (d, 1H,  $J = 10.29\text{ Hz}$ ,  $\text{CH}=\text{CHH}$ ), 5.03 (dd, 1H,  $J = 16.92\text{ Hz}$ , 2.21 Hz,  $\text{CH}=\text{CHH}$ ), 5.82 (dddd, 1H,  $J = 16.92\text{ Hz}$ , 10.30 Hz, 7.35 Hz, 6.62 Hz,  $\text{CH}=\text{CH}_2$ ), 5.94 (s, 2H,  $\text{OCH}_2\text{O}$ ), 6.53 (s, 1H, Ar-H), 7.35 (s, 1H, Ar-H) ppm

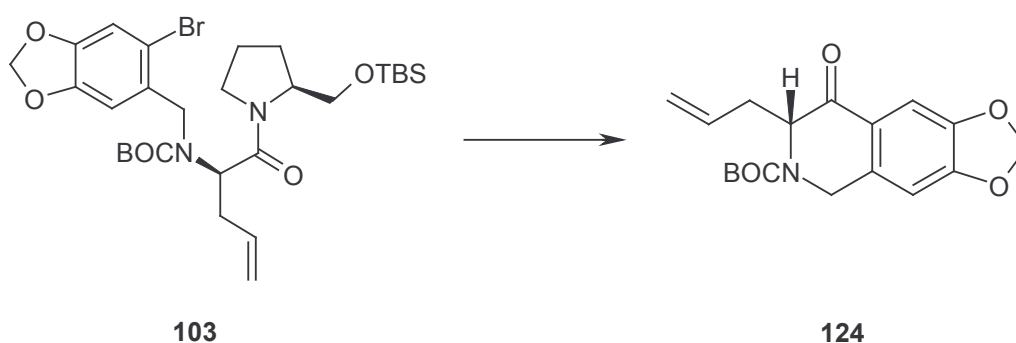
**$^{13}\text{C NMR}$**  (68 MHz,  $\text{CDCl}_3$ ):  $\delta = 15.2$  ( $(\text{CH}_3\text{CH}_2\text{O})_2$ ), 31.8 ( $\text{CH}_2=\text{CHCH}_2$ ), 50.7 ( $\text{NCH}_2\text{CH}(\text{OEt})_2$ ), 56.2 ( $\text{NCHCO}$ ), 62.1, 62.2 ( $(\text{CH}_3\text{CH}_2\text{O})_2$ ), 68.4 ( $\text{NCH}_2\text{Ar}$ ), 101.5 ( $\text{CH}(\text{OEt})_2$ ), 102.4 ( $\text{OCH}_2\text{O}$ ), 105.7, 125.0, 125.0, 137.7, 147.2, 152.2 (Ar), 116.7 ( $\text{CH}=\text{CH}_2$ ), 135.0 ( $\text{CH}=\text{CH}_2$ ), 195.1 ( $\text{CO}$ ) ppm

**IR** (solution, CHCl<sub>3</sub>):  $1/\lambda = 3017$  (s), 2978 (s), 2899 (s), 1732 (m), 1673 (s, CO), 1617 (m), 1504 (s), 1481 (s), 1376 (m), 1323 (m), 1263 (s), 1214 (s), 1124 (s), 1041 (s), 938 (m) cm<sup>-1</sup>

**MS** (EI, 80 eV, 130°C):  $m/z$  (%) = 347 (0.23, [M]<sup>+</sup>), 306 (100, [M-C<sub>3</sub>H<sub>5</sub>]<sup>+</sup>), 103 (75, [C<sub>5</sub>H<sub>11</sub>O<sub>2</sub>]<sup>+</sup>).

**HRMS** (80 eV, 120°C):  $m/z$  [M-C<sub>3</sub>H<sub>5</sub>]<sup>+</sup> calcd. for C<sub>16</sub>H<sub>20</sub>NO<sub>5</sub>, 306.13414; found, 306.13733

**(3*R*)-3-Allyl-(*N*-tert-butyloxycarbonyl)-6,7-methylenedioxy-1,2,3,4-tetrahydro-4-isoquinolone 124**



Under argon, *N*-piperonylprolinol silyl ether amide **103** (500 mg, 0.80 mmol) in anhyd. THF (20 mL) was cooled to -78 °C. BuLi (575 μL, 0.92 mmol, 1.6 M in hexane) was injected dropwise. The temperature was raised to -40 °C and the mixture was stirred under these conditions for a further 3 hours (TLC-monitoring). Sat. aq. NH<sub>4</sub>Cl (10 mL) was added to the mixture and the aqueous layer was extracted with Et<sub>2</sub>O (4×10 mL), and the combined organic layers were dried over MgSO<sub>4</sub>. After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 5:1) to give 110 mg (41.5%) of **124** as a yellow oil.

$[\alpha]_D^{20} = -4.7^\circ$  (c = 1.3, CHCl<sub>3</sub>)

**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>): δ = 1.40 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 2.30-2.55 (m, 2H, CH<sub>2</sub>=CHCH<sub>2</sub>), 4.12-4.35 (m, 1H, NCHCO), 4.65-5.25 (m, 4H, NCH<sub>2</sub>Ar, CH=CH<sub>2</sub>), 5.62-5.87 (m, 1H, CH=CH<sub>2</sub>), 5.98 (s, 2H, OCH<sub>2</sub>O), 6.60 (s, 1H, Ar-H), 7.35 (s, 1H, Ar-H) ppm

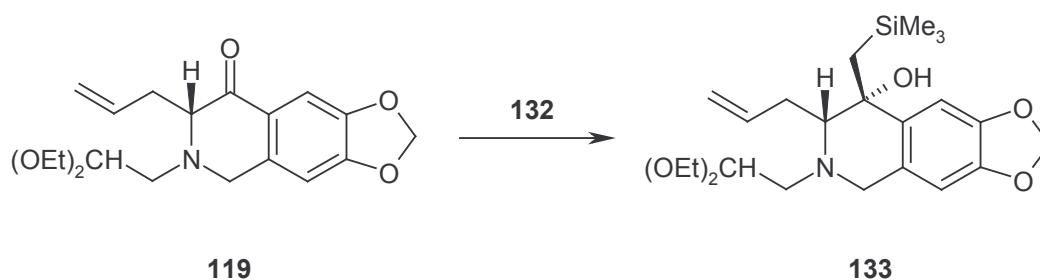
**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>): δ = 28.2 (C(CH<sub>3</sub>)<sub>3</sub>), 34.4 (CH<sub>2</sub>=CHCH<sub>2</sub>), 40.8 (NCHCO), 60.1 (NCH<sub>2</sub>Ar), 80.7 (C(CH<sub>3</sub>)<sub>3</sub>), 101.9 (OCH<sub>2</sub>O), 105.3, 106.1, 147.6, 152.7, 154.2 (Ar), 118.3 (CH=CH<sub>2</sub>), 133.5 (CH=CH<sub>2</sub>), 192.8 (CO) ppm

**IR** (solution,  $\text{CHCl}_3$ ):  $1/\lambda = 3019$  (s), 2978 (m), 2900 (w), 1681 (s, CO), 1619 (m), 1505 (m), 1482 (s), 1412 (s), 1369 (m), 1350 (w), 1316 (m), 1282 (m), 1245 (s), 1215 (s), 1162 (s), 1122 (w), 1041 (m)  $\text{cm}^{-1}$

**MS** (EI, 80 eV,  $110^\circ\text{C}$ ):  $m/z$  (%) = 331 (1.26,  $[\text{M}]^+$ ), 290 (17,  $[\text{M}-\text{C}_3\text{H}_5]^+$ ), 274 (1.59,  $[\text{M}-\text{C}_4\text{H}_9]^+$ ), 258 (3,  $[\text{M}-\text{C}_4\text{H}_9\text{O}]^+$ ), 234 (12,  $[\text{M}-\text{C}_7\text{H}_{13}]^+$ ), 190 (62,  $[\text{M}-\text{C}_8\text{H}_{13}\text{O}]^+$ ), 57 (100,  $[\text{C}_4\text{H}_9]^+$ ).

**HRMS** (80 eV,  $100^\circ\text{C}$ ):  $m/z$   $[\text{M}]^+$  calcd. for  $\text{C}_{18}\text{H}_{21}\text{NO}_5$ , 331.14197; found, 331.14422

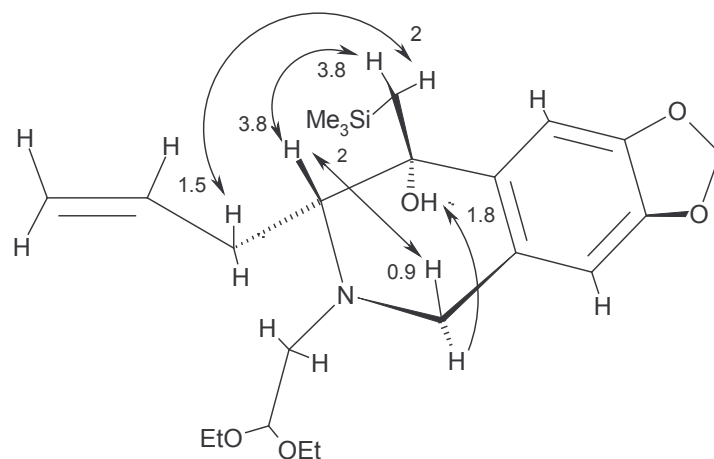
**(3*R*,4*R*)-3-Allyl-*N*-(2,2-diethoxyethyl)-4-hydroxy-4-trimethylsilylmethyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline 133**



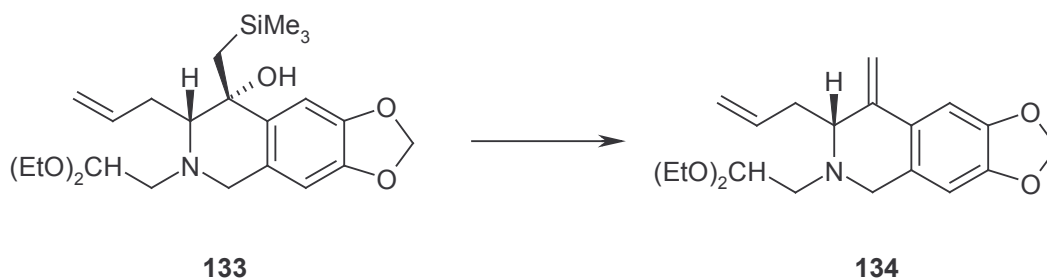
Under argon, isoquinolone **119** (250 mg, 0.72 mmol) in anhyd. THF (10 mL) was cooled to  $-78^\circ\text{C}$ . Trimethylsilyl methyl lithium **132** (870  $\mu\text{L}$ , 0.87 mmol, 1 M in heptane) was injected dropwise. The mixture was stirred at  $-78^\circ\text{C}$  for 3 hours (TLC-monitoring). Sat. aq.  $\text{NH}_4\text{Cl}$  (10 mL) was added to the mixture and the aqueous layer was extracted with  $\text{Et}_2\text{O}$  ( $4 \times 10$  mL), and the combined organic layers were dried over  $\text{MgSO}_4$ . After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 7:1) to result 240 mg (76.6%) of **133** as a yellow oil.

**$^1\text{H-NMR}$**  (500 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.00$  (s, 9H,  $\text{Si}(\text{CH}_3)_3$ ), 1.12 (2xt, 6H,  $J = 7.35$  Hz,  $(\text{CH}_3\text{CH}_2\text{O})_2$ ), 1.35 (d, 1H,  $J = 4.71$  Hz,  $\text{SiCHH}$ ), 1.63 (d, 1H,  $J = 5.44$  Hz,  $\text{SiCHH}$ ), 1.84 (s, 1H,  $\text{OH}$ ), 2.10-2.19 (m, 1H,  $\text{CHHCH}=\text{CH}_2$ ), 2.28-2.36 (m, 1H,  $\text{CHHCH}=\text{CH}_2$ ), 2.68-2.75 (dd, 1H,  $J = 13.24$  Hz, 5.15 Hz,  $\text{NCHHCH}$ ), 2.78-2.85 (dd, 1H,  $J = 13.24$  Hz, 5.15 Hz,  $\text{NCHHCH}$ ), 2.99-3.03 (dd, 1H,  $J = 6.61$  Hz, 5.89 Hz,  $\text{NCH}$ ), 3.46-3.57 (m, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 3.60-3.70 (m, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ,  $\text{NCHHAr}$ ), 3.82 (d, 1H,  $J = 5.44$  Hz,  $\text{NCHHAr}$ ), 4.57 (t, 1H,  $J = 5.15$  Hz,  $\text{CH}(\text{OEt})_2$ ), 4.93-5.05 (m, 2H,  $\text{CH}=\text{CH}_2$ ), 5.85 (2xs, 2H,  $\text{OCH}_2\text{O}$ ), 5.90-6.00 (m, 1H,  $\text{CH}=\text{CH}_2$ ), 6.40 (s, 1H, Ar-H), 7.04 (s, 1H, Ar-H) ppm

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.4, 0.6$  ( $\text{Si}(\text{CH}_3)_3$ ), 15.3 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 28.8 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 34.0 ( $\text{SiCH}_2$ ), 51.2 ( $\text{NCH}_2\text{Ar}$ ), 57.7 ( $\text{NCH}_2\text{CH}$ ), 61.6, 62.1 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 67.6 ( $\text{NCH}$ ), 76.7 ( $\text{HO}$ ), 100.6 ( $\text{OCH}_2\text{O}$ ), 100.9 ( $\text{CH}(\text{OEt})_2$ ), 105.1, 106.8, 126.0, 136.5, 146.1, 146.4 ( $\text{Ar}$ ), 115.7 ( $\text{CH}=\text{CH}_2$ ), 138.7 ( $\text{CH}=\text{CH}_2$ ) ppm

NOE data of **79**

**(3R)-3-Allyl-N-(2,2-diethoxyethyl)-4-methylene-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline 134**



Method A:

Under argon, NaH (14 mg, 0.47 mmol, in 80% mineral oil) in anhyd. THF (10 mL) was cooled to 0 °C. Isoquinoline **133** (170 mg, 0.39 mmol) in anhyd. THF (10 mL) was added. The mixture was stirred at 0 °C for 1 hour and then refluxed for a further 3 hours. The mixture was cooled to 0 °C again, sat. aq.  $\text{NH}_4\text{Cl}$  (10 mL) was added dropwise. The aqueous layer was extracted with  $\text{Et}_2\text{O}$  (4×10 mL), and the combined organic layers were dried over  $\text{MgSO}_4$ .

After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethylacetate = 6:1) to give 110 mg (81.5%) of **134** as a yellow oil.

Method B:

Isoquinoline **133** (150 mg, 0.34 mmol) in dry  $\text{CHCl}_3$  (10 mL) was treated with acetic acid (5 mL). The mixture was stirred at 20 °C for 3 hours (TLC-monitoring). Sat. aq.  $\text{K}_2\text{CO}_3$  was added until the solution reached a pH of 10. The aqueous layer was extracted with  $\text{CHCl}_3$  (4 × 10 mL), the combined organic layers were dried over  $\text{Na}_2\text{SO}_4$ . The solvent was evaporated, and the crude material was purified by column chromatography (n-hexane / ethylacetate = 6:1) to give 100 mg (85%) of **134** as yellow oil.

$[\alpha]_D^{20} = +31.0^\circ$  (c = 1.7,  $\text{CHCl}_3$ )

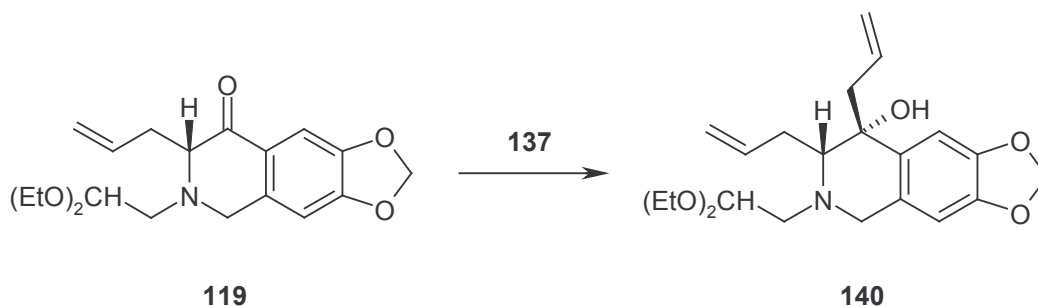
$^1\text{H-NMR}$  (270 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.20$  (2xt, 6H,  $J = 7.35$  Hz,  $(\text{CH}_3\text{CH}_2\text{O})_2$ ), 2.06-2.20 (m, 1H,  $\text{CHHCH}=\text{CH}_2$ ), 2.30-2.42 (m, 1H,  $\text{CHHCH}=\text{CH}_2$ ), 2.60-2.66 (dd, 2H,  $J = 5.15$  Hz, 4.68 Hz,  $\text{NCH}_2\text{CH}$ ), 3.36-3.44 (dd, 1H,  $J = 8.09$  Hz, 6.62 Hz,  $\text{NCH}$ ), 3.44-3.68 (m, 4H,  $(\text{CH}_3\text{CH}_2\text{O})_2$ ), 3.68-3.78 (d, 1H,  $J = 6.91$  Hz,  $\text{NCHHAr}$ ), 3.96-4.07 (d, 1H,  $J = 7.65$  Hz,  $\text{NCHHAr}$ ), 4.59 (t, 1H,  $J = 5.15$  Hz,  $\text{CH}(\text{OEt})_2$ ), 4.79 (s, 1H,  $\text{CHH}=\text{C}$ ), 4.91-5.03 (m, 2H,  $\text{CH}=\text{CH}_2$ ), 5.35 (s, 1H,  $\text{CHH}=\text{C}$ ), 5.70-5.90 (m, 1H,  $\text{CH}=\text{CH}_2$ ), 5.85 (s, 2H,  $\text{OCH}_2\text{O}$ ), 6.43 (s, 1H, Ar-H), 7.04 (s, 1H, Ar-H) ppm

$^{13}\text{C NMR}$  (68 MHz,  $\text{CDCl}_3$ ):  $\delta = 15.3$  ( $(\text{CH}_3\text{CH}_2\text{O})_2$ ), 35.0 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 50.6 ( $\text{NCH}_2\text{CH}$ ), 56.7 ( $\text{NCH}_2\text{Ar}$ ), 61.9, 62.0 ( $(\text{CH}_3\text{CH}_2\text{O})_2$ ), 65.1 ( $\text{NCH}$ ), 100.7 ( $\text{OCH}_2\text{O}$ ), 102.6 ( $\text{CH}(\text{OEt})_2$ ), 103.8, 106.0, 125.6, 127.2, 146.6, 147.6 (Ar), 107.8 ( $\text{CH}_2=\text{C}$ ), 115.8 ( $\text{CH}=\text{CH}_2$ ), 136.1 ( $\text{CH}=\text{CH}_2$ ), 140.1 ( $\text{CH}_2=\text{C}$ ) ppm

**IR** (solution,  $\text{CHCl}_3$ ):  $1/\lambda = 3019$  (s), 2977 (m), 2896 (m), 1504 (m), 1482 (s), 1421 (w), 1389 (w)  $\text{cm}^{-1}$

**MS** (EI, 80 eV, 80-100°C):  $m/z$  (%) = 344 (0.1,  $[\text{M-H}]^+$ ), 304 (100,  $[\text{M}-\text{C}_3\text{H}_5]^+$ ), 300 (15,  $[\text{M}-\text{OC}_2\text{H}_5]^+$ ), 242 (32,  $[\text{M}-\text{C}_5\text{H}_{11}\text{O}_2]^+$ ), 103 (24,  $[\text{C}_5\text{H}_{11}\text{O}_2]^+$ ), 75 (25,  $[\text{C}_3\text{H}_7\text{O}_2]^+$ ).

**HRMS** (80 eV, 100°C):  $m/z$   $[\text{M}-\text{C}_3\text{H}_5]^+$  calcd. for  $\text{C}_{17}\text{H}_{22}\text{NO}_4$ , 304.15488; found, 304.15643

**(3*R*,4*R*)-3,4-Diallyl-*N*-(2,2-diethoxyethyl)-4-hydroxy-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline 140**

Under argon, allyltriphenyltin **136** (576 mg, 1.47 mmol) was dissolved in anhyd. THF (3 mL). Phenyllithium **135** (816  $\mu\text{L}$ , 1.47 mmol, 1.8 M in cyclohexane / ether) was added. The mixture was stirred at 20 °C for 30 minutes, during this time a white precipitate occurred and the colour of the mixture was changed from colourless to green.

The so formed allyllithium **137** was then cooled to  $-78^\circ\text{C}$  and isoquinolone **119** (390 mg, 1.27 mmol) was injected dropwise. The mixture was stirred at  $-60^\circ\text{C}$  for a further 1 hour (TLC-monitoring). Methanol (10 mL) was added and the solid was filtered off. The solvent was evaporated, and the crude material was purified by column chromatography (n-hexane / ethylacetate = 6:1) to give 390 mg (88%) of **140** as a yellow oil.

$[\alpha]_D^{20} = +87.2^\circ$  (c = 0.4,  $\text{CHCl}_3$ )

**$^1\text{H-NMR}$**  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.12 (2xt, 6H,  $J$  = 6.59 Hz,  $(\text{CH}_3\text{CH}_2\text{O})_2$ ), 2.05 (s, 1H, OH), 2.09-2.16 (m, 1H, NCHCHH), 2.16-2.25 (m, 1H, NCHCHH), 2.40-2.46 (dd, 1H,  $J$  = 12.93 Hz, 6.98 Hz, CHHCH=CH<sub>2</sub>), 2.64-2.70 (dd, 1H,  $J$  = 12.80 Hz, 4.78 Hz, NCHHCH), 2.77-2.82 (dd, 1H,  $J$  = 12.93 Hz, 5.17 Hz, NCHHCH), 2.77-2.82 (dd, 1H,  $J$  = 12.93 Hz, 6.98 Hz, CHHCH=CH<sub>2</sub>), 2.98-3.02 (dd, 1H,  $J$  = 6.09 Hz, 5.43 Hz, NCH), 3.40-3.50 (m, 2H,  $(\text{CH}_3\text{CH}_2\text{O})_2$ ), 3.56-3.65 (m, 3H,  $(\text{CH}_3\text{CH}_2\text{O})_2$ , NCHHAr), 3.78 (d, 1H,  $J$  = 14.74 Hz, NCHHAr), 4.50 (t, 1H,  $J$  = 5.04 Hz, CH(OEt)<sub>2</sub>), 4.87-4.96 (m, 2H, NCHCH<sub>2</sub>CH=CH<sub>2</sub>), 5.05-5.12 (m, 2H, HOCCH<sub>2</sub>CH=CH<sub>2</sub>), 5.80 (s, 2H, OCH<sub>2</sub>O), 5.80-5.91 (m, 2H, 2 $\times$ CH=CH<sub>2</sub>), 6.38 (s, 1H, Ar-H), 6.92 (s, 1H, Ar-H) ppm

**$^{13}\text{C NMR}$**  (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 15.1, 15.2 ( $(\text{CH}_3\text{CH}_2\text{O})_2$ ), 28.3 (NCHCH<sub>2</sub>CH=CH<sub>2</sub>), 47.4 (HOCCH<sub>2</sub>CH=CH<sub>2</sub>), 50.7 (NCH<sub>2</sub>Ar), 58.4 (NCH<sub>2</sub>CH(OEt)<sub>2</sub>), 61.8, 61.9 ( $(\text{CH}_3\text{CH}_2\text{O})_2$ ), 64.6 (NCH), 75.3 (HOCAr), 100.6 (OCH<sub>2</sub>O), 102.0 (CH(OEt)<sub>2</sub>), 105.0, 106.1, 126.9, 133.5, 146.2, 146.3 (Ar), 115.7 (NCHCH<sub>2</sub>CH=CH<sub>2</sub>), 119.0 (HOCCH<sub>2</sub>CH=CH<sub>2</sub>), 134.2 (HOCCH<sub>2</sub>CH=CH<sub>2</sub>), 138.7 (NCHCH<sub>2</sub>CH=CH<sub>2</sub>) ppm

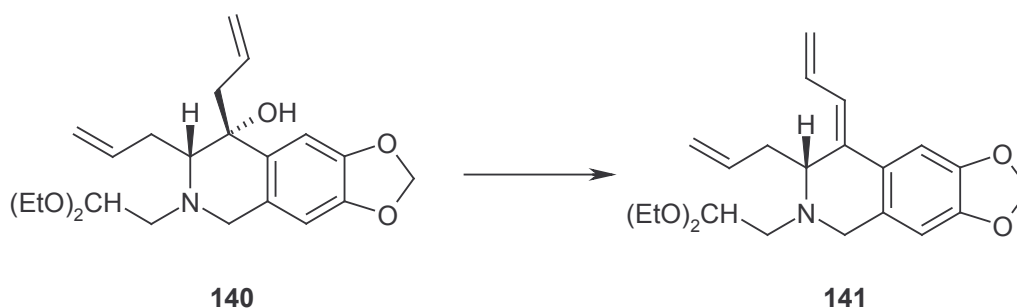


**IR** (solution, CHCl<sub>3</sub>):  $1/\lambda = 3019$  (s), 2977 (m), 2896 (w), 1637 (w), 1503 (w), 1483 (m), 1433 (w), 1390 (w), 1216 (s), 1127 (w), 1042 (m), 929 (w) cm<sup>-1</sup>

**MS** (EI, 80 eV, 80-100°C):  $m/z$  (%) = 389 (0.4, [M]<sup>+</sup>), 348 (100, [M-C<sub>3</sub>H<sub>5</sub>]<sup>+</sup>), 307 (53, [M-C<sub>6</sub>H<sub>10</sub>]<sup>+</sup>), 245 (23, [M-C<sub>8</sub>H<sub>16</sub>O<sub>2</sub>]<sup>+</sup>), 204 (25, [M-C<sub>11</sub>H<sub>21</sub>O<sub>2</sub>]<sup>+</sup>), 103 (20, [C<sub>5</sub>H<sub>11</sub>O<sub>2</sub>]<sup>+</sup>).

**HRMS** (80 eV, 100°C):  $m/z$  [M-C<sub>3</sub>H<sub>5</sub>]<sup>+</sup> calcd. for C<sub>19</sub>H<sub>26</sub>NO<sub>5</sub>, 348.18110; found, 348.18123

**Z-(3R)-3-Allyl-4-allylidene-N-(2,2-diethoxyethyl)-6,7-methylenedioxy-1,2,3,4-tetrahydro isoquinoline 141**



Under argon, allyl isoquinoline **140** (100 mg, 0.25 mmol) in anhyd. DMSO (10 mL) was treated with MsCl (35 mg, 0.30 mmol) and KOC(CH<sub>3</sub>)<sub>3</sub> (34 mg, 0.30 mmol). The mixture was stirred at 20 °C for 2 days. H<sub>2</sub>O (10 mL) and Et<sub>2</sub>O (10 mL) were added, the aqueous layer was extracted with Et<sub>2</sub>O (4×10 mL), and the combined organic layers were dried over MgSO<sub>4</sub>. After removal of the solvent in vacuum, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 5:1) to give 37 mg (38%) of **141** as a brown oil, which easily tended to decompose.

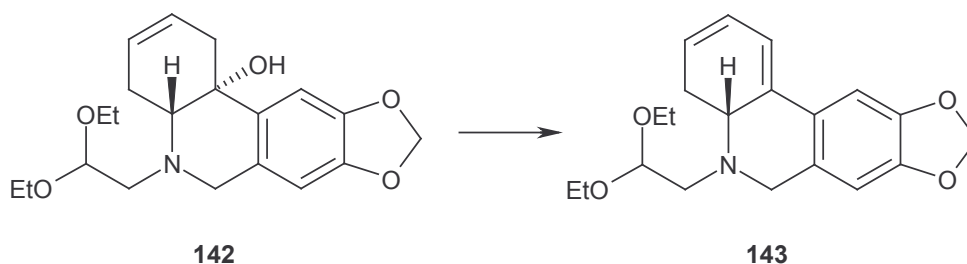
**<sup>1</sup>H-NMR** (500 MHz, CDCl<sub>3</sub>):  $\delta = 1.13$  (2×t, 6H,  $J = 6.83$  Hz, (CH<sub>3</sub>CH<sub>2</sub>O)<sub>2</sub>), 2.01-2.15 (m, 1H, CHHCH=CH<sub>2</sub>), 2.29-2.42 (m, 1H, CHHCH=CH<sub>2</sub>), 2.51-2.57 (dd, 1H,  $J = 13.67$  Hz, 4.88 Hz, NCHHCH), 2.58-2.65 (dd, 1H,  $J = 13.67$  Hz, 5.38 Hz, NCHHCH), 3.38-3.50 (m, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 3.53-3.65 (m, 3H, CH<sub>3</sub>CH<sub>2</sub>O, NCHHAr), 3.93-3.98 (dd, 1H,  $J = 7.81$ Hz, 7.32 Hz, NCH), 4.01 (d, 1H,  $J = 17.09$  Hz, NCHHAr), 4.51-4.59 (dd, 1H,  $J = 5.37$  Hz, 4.88 Hz, CH(OEt)<sub>2</sub>), 4.88-4.98 (m, 2H, CH<sub>2</sub>CH=CH<sub>2</sub>), 5.06-5.10 (dd, 1H,  $J = 9.77$  Hz, 1.95 Hz, C=CHCH=CHH), 5.21-5.26 (dd, 1H,  $J = 16.11$  Hz, 1.95 Hz, C=CHCH=CHH), 5.70-5.80 (dddd, 1H,  $J = 17.09$  Hz, 9.77 Hz, 7.32 Hz, 6.84 Hz, CH<sub>2</sub>CH=CH<sub>2</sub>), 5.81 (s, 2H, OCH<sub>2</sub>O), 6.38 (s, 1H, Ar-H), 6.45 (d, 1H,  $J = 11.23$  Hz, C=CHCH=CH<sub>2</sub>), 6.54-6.63 (ddd, 1H,  $J = 16.11$  Hz, 11.23 Hz, 9.77 Hz, C=CHCH=CH<sub>2</sub>), 6.99 (s, 1H, Ar-H) ppm

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 15.2 ( $(\text{CH}_3\text{CH}_2\text{O})_2$ ), 34.7 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 49.9 ( $\text{NCH}_2\text{Ar}$ ), 57.3 ( $\text{NCH}_2\text{CH}$ ), 58.4 ( $\text{NCH}$ ), 61.8, 62.0 ( $(\text{CH}_3\text{CH}_2\text{O})_2$ ), 100.7 ( $\text{OCH}_2\text{O}$ ), 102.5 ( $\text{CH}(\text{OEt})_2$ ), 103.4, 106.0, 127.3, 133.9, 135.7, 146.7, 147.3 (Ar), 116.0 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 117.7 ( $\text{C}=\text{CHCH}=\text{CH}_2$ ), 123.2 ( $\text{C}=\text{CHCH}=\text{CH}_2$ ), 126.0 ( $\text{C}=\text{CHCH}=\text{CH}_2$ ), 132.5 ( $\text{C}=\text{CHCH}=\text{CH}_2$ ), 135.7 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ) ppm

IR (solution,  $\text{CHCl}_3$ ):  $1/\lambda$  = 3076 (m), 3018 (s), 2978 (s), 2933 (s), 2897 (s), 2775 (w) 1639 (m), 1616 (m), 1504 (s), 1481 (s), 1444 (m), 1375 (m), 1332 (m), 1231 (s), 1217 (s), 1175 (m), 1126 (m), 1042 (s), 987 (m)  $\text{cm}^{-1}$

MS (EI, 80 eV,  $100^\circ\text{C}$ ):  $m/z$  (%) = 330 (100,  $[\text{M}-\text{C}_3\text{H}_5]^+$ ), 284 (15,  $[\text{M}-\text{C}_4\text{H}_7\text{O}_2]^+$ ), 268 (16,  $[\text{M}-\text{C}_5\text{H}_{11}\text{O}_2]^+$ ), 212 (41,  $[\text{M}-\text{C}_9\text{H}_{19}\text{O}_2]^+$ ), 103 (13,  $[\text{C}_5\text{H}_{11}\text{O}_2]^+$ ), 75 (14,  $[\text{C}_3\text{H}_7\text{O}_2]^+$ ), 41 (12,  $[\text{C}_3\text{H}_5]^+$ ).

**(3R)-N-(2,2-Diethoxyethyl)-8,9-methylenedioxy-4,4a,5,6-tetrahydrophenanthridine 143**



Under argon, allyl isoquinoline **142** (100 mg, 0.27 mmol) in anhyd. DMSO (10 mL) was treated with  $\text{MsCl}$  (35 mg, 0.30 mmol) and  $\text{KOC}(\text{CH}_3)_3$  (34 mg, 0.30 mmol). The mixture was stirred at  $20^\circ\text{C}$  for 2 days.  $\text{H}_2\text{O}$  (10 mL) and  $\text{Et}_2\text{O}$  (10 mL) were added, the aqueous layer was extracted with  $\text{Et}_2\text{O}$  ( $4 \times 10$  mL), and the combined organic layers were dried over  $\text{MgSO}_4$ . After removal of the solvent in vacuum, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 1:1) to give 20 mg (21%) of **143** as a brown oil, which easily tended to decompose.

$[\alpha]_D^{20} = +162.9^\circ$  ( $c = 0.47$ ,  $\text{CHCl}_3$ )

$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.15 (2xt, 6H,  $J = 7.33$  Hz,  $\text{CH}_3\text{CH}_2$ ), 2.11-2.28 (m, 1H,  $\text{CHHCHN}$ ), 2.44-2.57 (m, 1H,  $\text{CHHCHN}$ ), 2.61-2.69 (dd, 1H,  $J = 14.16$  Hz, 5.37 Hz,  $\text{NCHHCH}(\text{OEt})_2$ ), 2.69-2.77 (dd, 1H,  $J = 14.16$  Hz, 4.88 Hz,  $\text{NCHHCH}(\text{OEt})_2$ ), 3.40-3.50 (m, 2H,  $\text{CH}_3\text{CH}_2$ ), 3.53-3.65 (m, 2H,  $\text{CH}_3\text{CH}_2$ ), 3.65-3.78 (d, 1H,  $J = 15.63$  Hz,  $\text{NCHHAr}$ ), 3.83-3.92

(d, 1H,  $J = 15.13$  Hz, NCHHAr), 4.52-4.59 (dd, 1H,  $J = 5.37$  Hz, 4.88 Hz, CH(OEt)<sub>2</sub>), 5.82 (2×s, 2H, OCH<sub>2</sub>O), 5.80-5.88 (m, 1H, CH<sub>2</sub>CH=CH), 5.95-6.02 (m, 1H, CH=CHCH=C), 6.02-6.24 (m, 1H, CH=CHCH=C), 6.43 (s, 1H, CHCCH<sub>2</sub>N), 6.97 (s, 1H, CHCC=CH) ppm

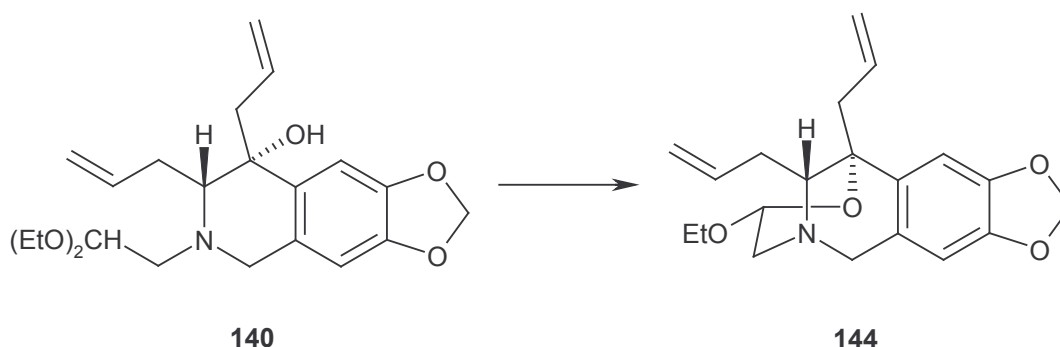
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta = 15.2$  (CH<sub>3</sub>CH<sub>2</sub>), 28.2 (CH<sub>2</sub>CHN), 53.6 (NCH<sub>2</sub>CH(OEt)<sub>2</sub>), 56.2 (NCH<sub>2</sub>Ar), 59.9 (NCH), 61.8, 62.0 (CH<sub>3</sub>CH<sub>2</sub>), 100.6 (OCH<sub>2</sub>O), 102.0 (CH(OEt)<sub>2</sub>), 102.4, 106.7, 128.9, 132.9, 146.8, 146.9 (Ar), 115.7 (CH<sub>2</sub>CH=CH), 124.7 (CH=CHCH=C), 125.7 (CH=CHCH=C), 126.3 (CH=C) ppm

IR (solution, CHCl<sub>3</sub>):  $1/\lambda = 3019$  (s), 2977 (m), 2928 (m), 2897 (m), 2413 (w), 1602 (w), 1503 (m), 1481 (s), 1377 (w), 1215 (s), 1122 (m), 1043 (m), 939 (m) cm<sup>-1</sup>

MS (EI, 80 eV, 100°C):  $m/z$  (%) = 343 (100, [M]<sup>+</sup>), 298 (8, [M-C<sub>2</sub>H<sub>5</sub>O]<sup>+</sup>), 240 (25, [M-C<sub>5</sub>H<sub>11</sub>O<sub>2</sub>]<sup>+</sup>), 211 (30, [M-C<sub>6</sub>H<sub>14</sub>NO<sub>2</sub>]<sup>+</sup>), 181 (60, [M-C<sub>7</sub>H<sub>14</sub>O<sub>4</sub>]<sup>+</sup>), 103 (35, [C<sub>5</sub>H<sub>11</sub>O<sub>2</sub>]<sup>+</sup>), 75 (25, [C<sub>3</sub>H<sub>7</sub>O<sub>2</sub>]<sup>+</sup>).

HRMS (80 eV, 100°C):  $m/z$  [M]<sup>+</sup> calcd. for C<sub>20</sub>H<sub>25</sub>NO<sub>4</sub>, 343.17835; found, 343.17654

**(5*R*,9*R*)-3,4-Diallyl-2,4-(2-ethoxy-3-oxapropylidene)-6,7-methylenedioxy isoquinoline 144**



**Method A:**

Under argon, diallyl compound **140** (200 mg, 0.51 mmol) was dissolved in anhyd. CHCl<sub>3</sub> (30 mL) and SmCl<sub>3</sub> (5 mg) and acetyl chloride (140  $\mu$ L) was added at room temperature. The reaction mixture was stirred for 30 min. (TLC monitoring) at room temperature. NaOH (1 M) was added until pH reached 9-10 and the aqueous layer was extracted with CHCl<sub>3</sub> (4×10 mL). The combined organic layers were dried over MgSO<sub>4</sub> and the solvent was removed. The residue was purified by column chromatography (n-hexane / ethyl acetate = 3:1) to give 150 mg (85%) of **144** as a yellow oil.

## Method B:

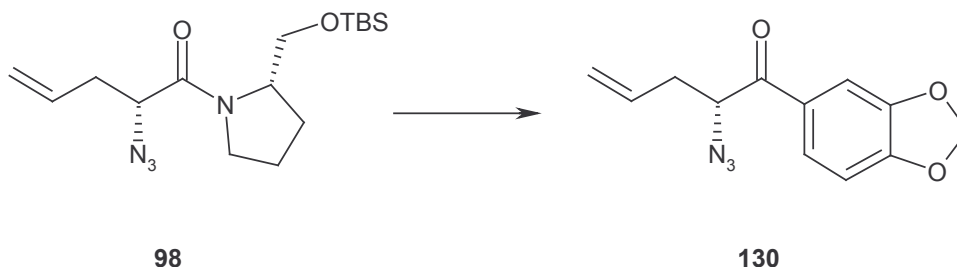
Diallyl compound **140** (200 mg, 0.51 mmol) was treated with aq. HCl (1M, 20 mL). The reaction mixture was heated to 50°C for 20 hours. NaOH (1 M) was added until pH reached 9-10 and the aqueous layer was extracted with CHCl<sub>3</sub> (4×10 mL). The combined organic layers were dried over MgSO<sub>4</sub> and the solvent was removed. The residue was purified by column chromatography (n-hexane / ethyl acetate = 3:1) to give 110 mg (62%) of **144** as a yellow oil.

<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>): δ = 1.05 (t, 3H, *J* = 7.33 Hz, CH<sub>3</sub>CH<sub>2</sub>), 2.40-2.60 (m, 3H, CHHCAr, CHHCHN, NCHHCH), 2.70-2.92 (m, 4H, CH<sub>2</sub>CHN, CHHCAr, CHHCHN, NCHHCH), 3.12-3.26 (m, 1H, CH<sub>3</sub>CHH), 3.64-3.76 (m, 1H, CH<sub>3</sub>CHH), 3.77-3.85 (d, 1H, *J* = 17.58 Hz, NCHHAr), 4.23-4.30 (m, 2H, NCH<sub>2</sub>CH(OEt), NCHHAr), 4.91-5.15 (m, 4H, CH<sub>2</sub>=CHCH<sub>2</sub>CHN, CH<sub>2</sub>=CHCH<sub>2</sub>CAr), 5.31-5.47 (m, 1H, CH<sub>2</sub>=CHCH<sub>2</sub>CAr), 5.72-5.88 (m, 1H, CH<sub>2</sub>=CHCH<sub>2</sub>N), 5.91 (s, 2H, OCH<sub>2</sub>O), 6.42 (s, 1H, Ar-H), 6.92 (s, 1H, Ar-H) ppm

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 15.0 (CH<sub>3</sub>CH<sub>2</sub>O), 29.8 (NCHCH<sub>2</sub>CH=CH<sub>2</sub>), 38.3 (ArCCH<sub>2</sub>CH=CH<sub>2</sub>), 50.5 (NCH<sub>2</sub>Ar), 57.4 (NCH<sub>2</sub>CH), 57.8 (CH<sub>3</sub>CH<sub>2</sub>), 64.3 (NCH), 71.9 (CH<sub>2</sub>CAr), 94.3 (NCH<sub>2</sub>CH(OEt)<sub>2</sub>), 100.8 (OCH<sub>2</sub>O), 104.6, 105.9, 131.6, 131.7, 146.8, 147.0 (Ar), 115.9 (NCHCH<sub>2</sub>CH=CH<sub>2</sub>), 118.5 (ArCCH<sub>2</sub>CH=CH<sub>2</sub>), 128.3 (ArCHCH<sub>2</sub>CH=CH<sub>2</sub>), 138.7 (NCHCH<sub>2</sub>CH=CH<sub>2</sub>) ppm

IR (solution, CHCl<sub>3</sub>): 1/λ = 3079 (m), 3017 (s), 2979 (s), 2932 (m), 2896 (m), 1713 (w), 1641 (m), 1504 (s), 1486 (s), 1454 (m), 1440 (m), 1380 (m), 1332 (m), 1310 (m), 1266 (m), 1243 (s), 1215 (s), 1163 (m), 1129 (m), 1105 (m), 1041 (s), 939 (m) cm<sup>-1</sup>

MS (EI, 80 eV, 80°C): m/z (%) = 343 (50, [M]<sup>+</sup>), 284 (27, [M-C<sub>3</sub>H<sub>7</sub>O]<sup>+</sup>), 269 (44, [M-C<sub>3</sub>H<sub>6</sub>O<sub>2</sub>]<sup>+</sup>), 228 (77, [M-C<sub>6</sub>H<sub>11</sub>O<sub>2</sub>]<sup>+</sup>), 202 (100, [M-C<sub>9</sub>H<sub>17</sub>O]<sup>+</sup>).

3.10 Syntheses of Acyclic  $\alpha$ -Amino Ketone Derivatives**(R)-2-Azido-1-(3,4-methylenedioxyphenyl)-4-penten-1-one 130**

Under argon, 1-Bromo-3,4-methylenedioxybenzene **126** (170  $\mu$ L, 1.42 mmol,  $d = 1.678$ ,  $M = 201$ ) in anhyd. THF (20 mL) was cooled to  $-78$   $^{\circ}\text{C}$ . Butyl lithium (568  $\mu$ L, 1.42 mmol, 2.5 M in hexane) was injected dropwise. The mixture was stirred at  $-78$   $^{\circ}\text{C}$  for 15 min. A solution of amide **98** (400 mg, 1.18 mmol) in 5 mL anhyd. THF was added slowly. The mixture was stirred at  $-78$   $^{\circ}\text{C}$  for a further 30 min (TLC-monitoring). Sat. aq.  $\text{NH}_4\text{Cl}$  (10 mL) was added to the mixture and the aqueous layer was extracted with  $\text{Et}_2\text{O}$  ( $4 \times 10$  mL). The combined organic layers were dried over  $\text{MgSO}_4$ . After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethylacetate = 7:1) to give 250 mg (78%) of **130** as a yellow oil.

$[\alpha]_D^{20} = +1.2^{\circ}$  ( $c = 1.3$ ,  $\text{CHCl}_3$ )

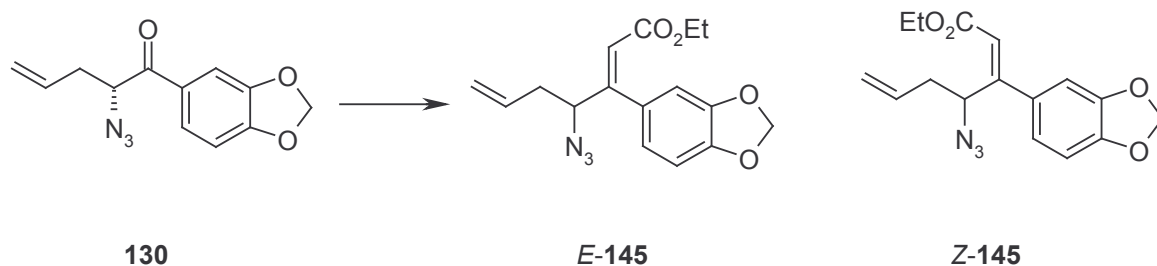
**$^1\text{H-NMR}$**  (270 MHz,  $\text{CDCl}_3$ ):  $\delta = 2.5$ - $2.73$  (m, 2H,  $\text{CH}_2=\text{CHCH}_2$ ), 4.48-4.57 (dd, 1H,  $J = 8.30$  Hz, 5.37 Hz,  $\text{CHN}_3$ ), 5.15-5.28 (m, 2H,  $\text{CH}_2=\text{CH}$ ), 5.75-5.91 (dddd, 1H,  $J = 17.09$  Hz, 10.25 Hz, 6.83 Hz, 6.83 Hz,  $\text{CH}_2=\text{CH}$ ), 6.07 (s, 2H,  $\text{OCH}_2\text{O}$ ), 6.85-6.90 (d, 1H,  $J = 7.81$  Hz, Ar-H), 7.41 (d, 1H,  $J = 1.96$  Hz, Ar-H), 7.49-7.55 (dd, 1H,  $J = 8.30$  Hz, 1.95 Hz, Ar-H) ppm

**$^{13}\text{C NMR}$**  (68 MHz,  $\text{CDCl}_3$ ):  $\delta = 35.4$  ( $\text{CH}_2=\text{CHCH}_2$ ), 61.7 ( $\text{CHN}_3$ ), 101.9 ( $\text{OCH}_2\text{O}$ ), 108.0, 108.1, 124.9, 129.1, 148.4, 152.4 (Ph), 118.9 ( $\text{CH}_2=\text{CH}$ ), 132.3 ( $\text{CH}_2=\text{CH}$ ), 193.7 ( $\text{CO}$ ) ppm

**IR** (KBr Film):  $1/\lambda = 3079$  (w), 2980 (w), 2907 (m), 2785 (w), 2612 (w), 2500 (w), 2103 (s,  $\text{N}_3$ ), 1680 (s, CO), 1641 (m), 1603 (s), 1504 (s), 1489 (s), 1445 (s), 1363 (m), 1323 (w), 1259 (s), 1141 (w), 1105 (m), 1039 (s), 994 (w)  $\text{cm}^{-1}$

**MS** (EI, 80 eV,  $70^{\circ}\text{C}$ ):  $m/z$  (%) = 245 (24,  $[\text{M}]^+$ ), 217 (8,  $[\text{M}-\text{N}_2]^+$ ), 149 (100,  $[\text{M}-\text{C}_4\text{H}_6\text{N}_3]^+$ ), 121 (85,  $[\text{M}-\text{C}_5\text{H}_6\text{N}_3\text{O}]^+$ ), 91 (13,  $[\text{C}_6\text{H}_3\text{O}]^+$ ).

**HRMS** (80 eV,  $70^{\circ}\text{C}$ ):  $m/z$   $[\text{M}]^+$  calcd. for  $\text{C}_{12}\text{H}_{11}\text{N}_3\text{O}_3$ , 245.08005; found, 245.08222.

**(*R,S*)-Ethyl *E*-3-(3,4-methylenedioxyphenyl)-4-azido-2,6-heptadienoate *E*-145****(*R,S*)-Ethyl *Z*-3-(3,4-methylenedioxyphenyl)-4-azido-2,6-heptadienoate *Z*-145**

Under argon, triethyl phosphonoacetate (400  $\mu$ L, 2.0 mmol,  $d = 1.120$ ,  $M = 224$ ) in anhyd. THF (20 mL) was cooled to  $-78$   $^{\circ}$ C. Lithium diisopropyl amide (1.10 mL, 2.0 mmol, 1.8 M in hexane) was injected. The mixture was stirred at  $-78$   $^{\circ}$ C for 1 hour. A solution of azid ketone **130** (240 mg, 0.98 mmol) in 5 mL anhyd. THF was added slowly. The mixture was stirred at  $-20$   $^{\circ}$ C for a further 20 hours (TLC-monitoring). Sat. aq.  $\text{NH}_4\text{Cl}$  (20 mL) was added to the mixture. The aqueous layer was extracted with  $\text{Et}_2\text{O}$  (4 $\times$ 20 mL), and the combined organic layers were dried over  $\text{MgSO}_4$ . After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 7:1) to give 120 mg (38.8%) of *E*-**145** and 60 mg (19.4%) of *Z*-**145** as yellow oils.

Data of *E*-**145**:

$^1\text{H-NMR}$  (270 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.25$  (t, 3H,  $J = 6.84$  Hz,  $\text{CH}_2\text{CH}_3$ ), 2.10-2.39 (m, 2H,  $\text{CH}_2\text{CH}=\text{CH}_2$ ), 4.10-4.22 (q, 2H,  $J = 6.84$  Hz,  $\text{CH}_2\text{CH}_3$ ), 4.91-5.08 (m, 2H,  $\text{CH}=\text{CH}_2$ ), 5.59-5.75 (dddd, 1H,  $J = 17.58$  Hz, 10.75 Hz, 6.83 Hz, 6.35 Hz,  $\text{CH}=\text{CH}_2$ ), 5.82-5.96 (m, 3H,  $\text{OCH}_2\text{O}$ ,  $\text{N}_3\text{CH}$ ), 5.98 (s, 1H,  $\text{C}=\text{CHCO}_2\text{Et}$ ), 6.75 (d, 1H,  $J = 7.81$  Hz, Ar-H), 6.84-6.99 (m, 2H, Ar-H) ppm

$^{13}\text{C NMR}$  (68 MHz,  $\text{CDCl}_3$ ):  $\delta = 14.0$  ( $\text{CH}_2\text{CH}_3$ ), 37.4 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 58.9 ( $\text{N}_3\text{CH}$ ), 60.4 ( $\text{CH}_2\text{CH}_3$ ), 101.2 ( $\text{OCH}_2\text{O}$ ), 108.0, 108.3, 121.5, 121.9, 147.4, 148.1 (Ar), 117.9 ( $\text{CH}=\text{CH}_2$ ), 128.0 ( $\text{C}=\text{CHCO}_2$ ), 133.3 ( $\text{CH}=\text{CH}_2$ ), 154.8 ( $\text{C}=\text{CHCO}_2$ ), 165.5 ( $\text{COO}$ ) ppm

**IR** (KBr Film):  $1/\lambda = 3077$  (w), 2980 (m), 2902 (m), 2777 (w), 2466 (w), 2098 (s,  $\text{N}_3$ ), 1849 (w), 1712 ( $\text{COO}$ ), 1604 (m), 1503 (s), 1488 (s), 1438 (m), 1371 (m), 1356 (w), 1322 (w), 1231 (s), 1179 (s), 1143 (m), 1107 (m), 1040 (s), 994 (w)  $\text{cm}^{-1}$

**MS** (EI, 80 eV, 70°C):  $m/z$  (%) = 315 (15,  $[M]^+$ ), 287 (16,  $[M-N_2]^+$ ), 273 (49,  $[M-N_3]^+$ ), 258 (24,  $[M-C_2H_5N_2]^+$ ), 246 (100,  $[M-C_3H_5N_3]^+$ ), 214 (74,  $[M-C_3H_5N_2O_2]^+$ ), 200 (40,  $[M-C_3H_5N_3O_2]^+$ ).

**HRMS** (80 eV, 70°C):  $m/z$   $[M]^+$  calcd. for  $C_{16}H_{17}N_3O_4$ , 315.12192; found, 315.12266.

Data for **Z-145**:

**$^1H$ -NMR** (270 MHz,  $CDCl_3$ ):  $\delta$  = 1.09 (t, 3H,  $J$  = 7.33 Hz,  $CH_2CH_3$ ), 2.05-2.38 (m, 2H,  $CH_2CH=CH_2$ ), 4.10-4.22 (q, 2H,  $J$  = 7.33 Hz,  $CH_2CH_3$ ), 4.13-4.21 (ddd, 1H,  $J$  = 7.82 Hz, 5.37 Hz, 0.97 Hz,  $N_3CH$ ), 4.97-5.13 (m, 2H,  $CH=CH_2$ ), 5.60-5.78 (ddt, 1H,  $J$  = 17.09 Hz, 10.25 Hz, 6.83 Hz,  $CH=CH_2$ ), 5.90 (s, 2H,  $OCH_2O$ ), 6.01 (s, 1H,  $C=CHCO_2Et$ ), 6.55-6.67 (m, 2H, Ar-H), 6.77 (d, 1H,  $J$  = 7.81 Hz, Ar-H) ppm

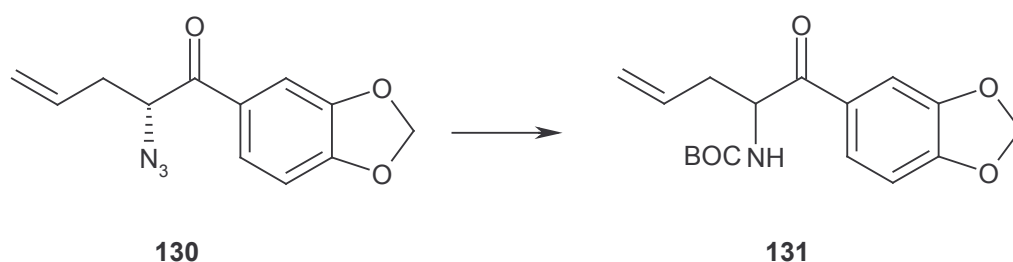
**$^{13}C$  NMR** (68 MHz,  $CDCl_3$ ):  $\delta$  = 13.8 ( $CH_2CH_3$ ), 36.8 ( $CH_2CH=CH_2$ ), 60.1 ( $CH_2CH_3$ ), 67.1 ( $N_3CH$ ), 101.0 ( $OCH_2O$ ), 108.0, 108.3, 119.8, 121.2, 147.3, 147.6 (Ar), 118.6 ( $CH=CH_2$ ), 129.9 ( $C=CHCO_2$ ), 132.6 ( $CH=CH_2$ ), 153.5 ( $C=CHCO_2$ ), 165.2 ( $COO$ ) ppm

**IR** (KBr Film):  $1/\lambda$  = 3078 (w), 2981 (m), 2903 (m), 2100 (s,  $N_3$ ), 1711 (s, COO), 1641 (m), 1605 (m), 1503 (s), 1488 (s), 1441 (s), 1372 (m), 1240 (s), 1179 (s), 1143 (m), 1107 (m), 1039 (s), 995 (w), 933 (m)  $cm^{-1}$

**MS** (EI, 80 eV, 70°C):  $m/z$  (%) = 315 (12,  $[M]^+$ ), 273 (4,  $[M-N_3]^+$ ), 246 (15,  $[M-C_3H_5N_3]^+$ ), 214 (10,  $[M-C_3H_5N_2O_2]^+$ ), 149 (100,  $[M-C_8H_{10}N_2O_2]^+$ ), 121 (13,  $[C_7H_5O_2]^+$ ).

**HRMS** (80 eV, 70°C):  $m/z$   $[M]^+$  calcd. for  $C_{16}H_{17}N_3O_4$ , 315.12192; found, 315.12233.

**(*R,S*)-2-(*N*-*tert*-Butyloxycarbonyl)amino-1-(3,4-methylenedioxyphenyl)-4-penten-1-one 131**



Ketone **130** (100 mg, 0.31 mmol) in THF (10 mL) and  $H_2O$  (0.5 mL) was treated with  $Ph_3P$  (100 mg, 0.38 mmol) and di-*tert*-butyl dicarbonate (80  $\mu$ L, 0.36 mmol,  $d$  = 1.02,  $M$  = 218).

The reaction mixture was stirred at room temperature for 16 hours. H<sub>2</sub>O (10 mL) was added and the aqueous layer was extracted with Et<sub>2</sub>O (4×50 mL). The combined organic layers were dried over MgSO<sub>4</sub> and the solvent was removed. The residue was purified by column chromatography (n-hexane / ethyl acetate = 7:1) to give 100 mg (81%) carbamate **131** as a yellow oil.

$$[\alpha]_D^{20} = 0^\circ \text{ (c = 0.6, CHCl}_3\text{)}$$

**<sup>1</sup>H-NMR** (270 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.40 (s, 9H, OC(CH<sub>3</sub>)<sub>3</sub>), 2.23-2.37 (ddd, 1H,  $J$  = 14.16 Hz, 6.84 Hz, 6.83 Hz, CHHCH=CH<sub>2</sub>), 2.52-2.66 (m, 1H, CHHCH=CH<sub>2</sub>), 4.91-5.04 (m, 2H, CH=CH<sub>2</sub>), 5.15-5.25 (m, 1H, NCH), 5.38-5.46 (2×s, br, 1H, NH), 5.52-5.69 (dddd, 1H,  $J$  = 17.58 Hz, 10.25 Hz, 7.33 Hz, 6.83 Hz, CH=CH<sub>2</sub>), 6.79-6.83 (d, 1H,  $J$  = 8.30 Hz, Ar-H), 7.70 (d, 1H,  $J$  = 1.96 Hz, Ar-H), 7.50-7.56 (dd, 1H,  $J$  = 8.31 Hz, 1.96 Hz, Ar-H) ppm

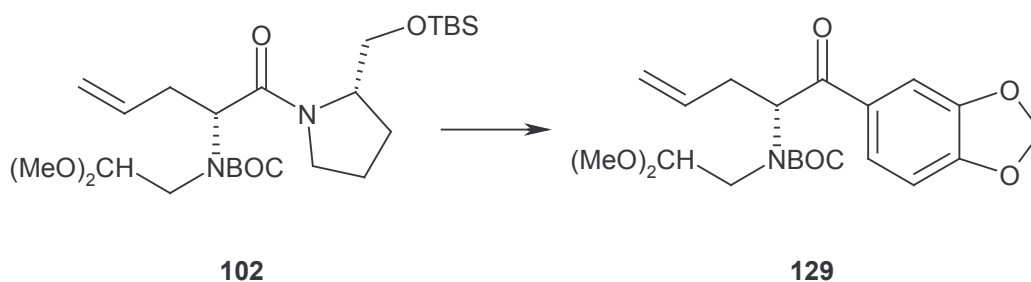
**<sup>13</sup>C NMR** (68 MHz, CDCl<sub>3</sub>):  $\delta$  = 28.1 (OC(CH<sub>3</sub>)<sub>3</sub>), 37.6 (CH<sub>2</sub>CH=CH<sub>2</sub>), 54.1 (NCH), 79.5 (OC(CH<sub>3</sub>)<sub>3</sub>), 101.8 (OCH<sub>2</sub>O), 107.9, 108.1, 124.8, 129.2, 148.2, 152.1 (Ar), 118.6 (CH=CH<sub>2</sub>), 132.1 (CH=CH<sub>2</sub>), 155.1 (NCO), 196.3 (CO) ppm

**IR** (KBr Film):  $1/\lambda$  = 3420 (br, m, NH), 3351 (br, m, NH), 3078 (w), 3004 (m), 2978 (s), 2929 (s), 1711 (s, CO), 1676 (s, NCO), 1641 (m), 1605 (m), 1504 (s), 1443 (s), 1391 (m), 1366 (s), 1330 (m), 1253 (s), 1169 (s), 1106 (m), 1039 (s), 994 (m), 932 (s) cm<sup>-1</sup>

**MS** (EI, 80 eV, 140°C):  $m/z$  (%) = 319 (8.4, [M]<sup>+</sup>), 278 (15, [M-C<sub>3</sub>H<sub>5</sub>]<sup>+</sup>), 246 (11, [M-C<sub>4</sub>H<sub>9</sub>O]<sup>+</sup>), 170 (59, [M-C<sub>8</sub>H<sub>5</sub>O<sub>3</sub>]<sup>+</sup>), 149 (100, [C<sub>8</sub>H<sub>5</sub>O<sub>3</sub>]<sup>+</sup>), 70 (45, [C<sub>4</sub>H<sub>8</sub>N]<sup>+</sup>), 57 (48, [C<sub>4</sub>H<sub>9</sub>]<sup>+</sup>).

**HRMS** (80 eV, 70°C):  $m/z$  [M]<sup>+</sup> calcd. for C<sub>17</sub>H<sub>21</sub>NO<sub>5</sub>, 319.14197; found: 319.14244.

**(2R)-2-[(*N*-*tert*-Butyloxycarbonyl)-*N*-(2,2-dimethoxyethyl)]amino-3,4-methylenedioxyphenyl-4-penten-1-one **129****





Under argon, 1-Bromo-3,4-methylenedioxybenzene **126** (110  $\mu$ L, 0.91 mmol,  $d = 1.678$ ,  $M = 201$ ) in anhyd. THF (20 mL) was cooled to  $-78$  °C. Butyllithium (360  $\mu$ L, 0.90 mmol, 2.5 M in hexane) was injected dropwise. The mixture was stirred at  $-78$  °C for 15 min. A solution of amide **102** (400 mg, 0.80 mmol) in 5 mL anhyd. THF was added slowly. The mixture was stirred at  $-78$  °C for a further 30 min (TLC-monitoring). Sat. aq.  $\text{NH}_4\text{Cl}$  (10 mL) was added to the mixture and the aqueous layer was extracted with  $\text{Et}_2\text{O}$  ( $4 \times 10$  mL), and the combined organic layers were dried over  $\text{MgSO}_4$ . After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 5:1) to give 220 mg (67.5%) of **129** as a yellow oil.

$$[\alpha]_D^{20} = +110.7^\circ \text{ (c = 1.2, CHCl}_3\text{)}$$

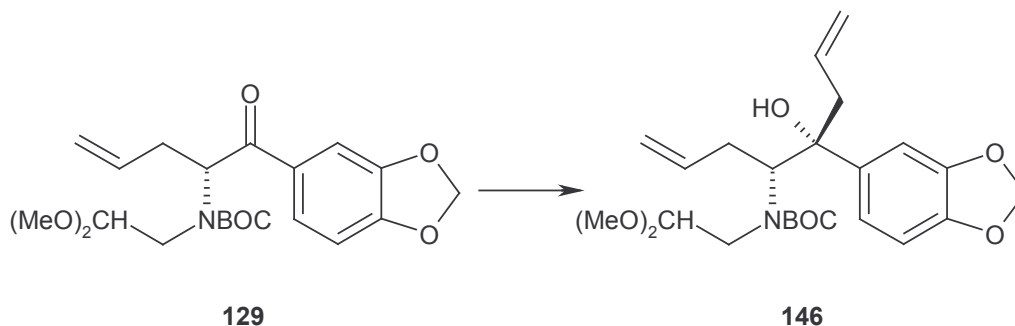
**$^1\text{H-NMR}$**  (270 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.40$  (s, 9H,  $\text{OC}(\text{CH}_3)_3$ ), 2.44-2.59 (m, 2H,  $\text{CH}_2\text{CH}=\text{CH}_2$ ), 2.95, 3.06 (2 $\times$ s, 3H,  $\text{OCH}_3$ ), 2.98-3.17 (m, 2H,  $\text{CH}_2\text{CH}(\text{OCH}_3)_2$ ), 3.19, 3.27 (2 $\times$ s, 3H,  $\text{OCH}_3$ ), 4.20-4.27, 4.37-4.45 (2 $\times$ dd, 1H,  $J = 4.88$  Hz, 4.39 Hz,  $\text{CH}(\text{OCH}_3)_2$ ), 4.92-4.98 (d, 1H,  $J = 11.23$  Hz,  $\text{CH}=\text{CHH}$ ), 5.01-5.09 (d, 1H,  $J = 17.09$  Hz,  $\text{CH}=\text{CHH}$ ), 5.43-5.52 (dd, 1H,  $J = 7.82$  Hz, 6.83 Hz,  $\text{CHCON}$ ), 5.61-5.84 (m, 1H,  $\text{CH}=\text{CH}_2$ ), 5.94 (2 $\times$ s, 2H,  $\text{OCH}_2\text{O}$ ), 6.71-6.79 (d, 1H,  $J = 8.30$ , Ar-H), 7.39-7.45 (d, 1H,  $J = 5.86$  Hz, Ar-H), 7.50-7.67 (dd, 1H,  $J = 24.90$  Hz, 8.30 Hz, Ar-H) ppm

**$^{13}\text{C NMR}$**  (68 MHz,  $\text{CDCl}_3$ ):  $\delta = 28.1$  ( $\text{OC}(\text{CH}_3)_3$ ), 32.8, 33.4 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 46.2, 48.0 ( $\text{CH}_2\text{CH}(\text{OCH}_3)_2$ ), 54.3, 54.5, 54.6 ( $\text{OCH}_3$ ), 58.2, 61.1 ( $\text{CHCON}$ ), 80.6, 81.0 ( $\text{OC}(\text{CH}_3)_3$ ), 101.5 ( $\text{OCH}_2\text{O}$ ), 103.1, 103.5 ( $\text{CH}(\text{OCH}_3)_2$ ), 107.6, 108.1, 124.1, 124.6, 130.7, 147.8, 151.4 (Ar), 117.3 ( $\text{CH}=\text{CH}_2$ ), 134.2, 134.5 ( $\text{CH}=\text{CH}_2$ ), 154.8, 155.4 ( $\text{NCOO}$ ), 194.6, 195.3 (ArCO) ppm

**IR** (KBr,  $\text{CHCl}_3$ ):  $1/\lambda = 3076$  (w), 2977 (m), 2932 (m), 1685 (s, CO, NCO), 1642 (w), 1605 (w), 1505 (m), 1489 (m), 1447 (s), 1402 (m), 1367 (m), 1305 (w), 1252 (s), 1166 (m), 1123 (m), 1075 (m), 1039 (m)  $\text{cm}^{-1}$

**MS** (EI, 80 eV,  $110^\circ\text{C}$ ):  $m/z$  (%) = 407 (2,  $[\text{M}]^+$ ), 334 (4,  $[\text{M}-\text{C}_4\text{H}_9\text{O}]^+$ ), 276 (9,  $[\text{M}-\text{C}_6\text{H}_{11}\text{O}_3]^+$ ), 258 (78,  $[\text{M}-\text{C}_8\text{H}_5\text{O}_3]^+$ ), 202 (28,  $[\text{M}-\text{C}_{12}\text{H}_{13}\text{O}_3]^+$ ), 158 (100,  $[\text{M}-\text{C}_{13}\text{H}_{13}\text{O}_5]^+$ ).

**HRMS** (80 eV,  $110^\circ\text{C}$ ):  $m/z$   $[\text{M}]^+$  calcd. for  $\text{C}_{21}\text{H}_{29}\text{NO}_7$ , 407.19440; found, 407.19533.

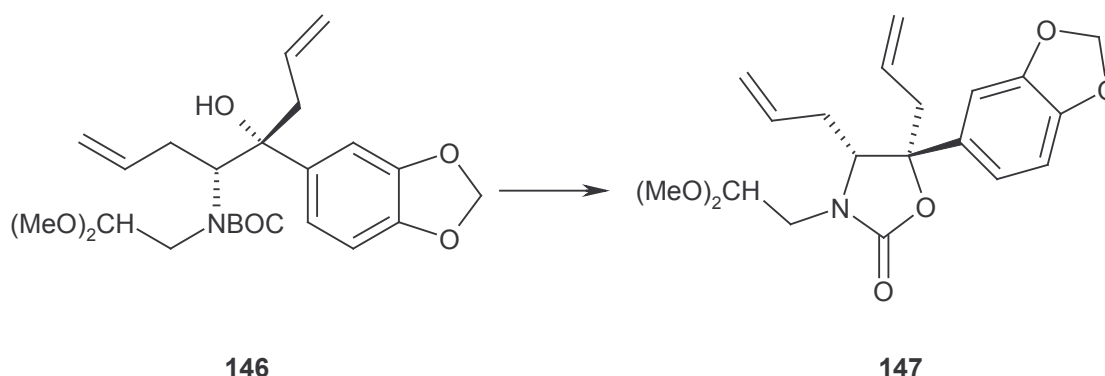
**(4*R*,5*R*)-4-(3,4-Methylenedioxyphenyl)-5-*N*-(*tert*-butyloxycarbonyl)-*N*-(2,2-dimethoxyethyl)amino-1,7-octadien-4-ol 146**

Under argon, allyltriphenyltin **136** (210 mg, 0.53 mmol) was dissolved in anhyd. THF (10 mL). Phenyllithium **135** (298  $\mu$ L, 0.53 mmol, 1.8 M in cyclohexane / ether) was added. The mixture was stirred at 20 °C for 30 minutes, during this time a white precipitate occurred and the colour of the mixture was changed from colourless to green.

The so formed allyllithium **137** was then cooled to -78 °C and ketone **129** (200 mg, 0.49 mmol) was injected dropwise. The mixture was stirred at -60 °C for a further 1 hour (TLC-monitoring). Methanol (10 mL) was added and the solid was filtered off. The solvent was evaporated to give diallyl **146** as a yellow oil, which was used without further purification.

**$^1\text{H-NMR}$**  (270 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.40 (2 $\times$ s, 9H,  $\text{OC}(\text{CH}_3)_3$ ), 2.09 (m, 1H,  $\text{OH}$ ), 2.25-2.90 (m, 4H,  $\text{CHCH}_2\text{CH}=\text{CH}_2$ ,  $\text{CCH}_2\text{CH}=\text{CH}_2$ ), 2.90-3.37 (m, 8H,  $\text{NCH}_2$ ,  $\text{CH}(\text{OCH}_3)_2$ ), 3.95-4.12 (2 $\times$ m, 1H,  $\text{CH}(\text{OCH}_3)_3$ ), 4.21-4.35, 4.50-4.61 (2 $\times$ m, 1H,  $\text{NCH}$ ), 4.76-5.11 (m, 4H,  $\text{CHCH}_2\text{CH}=\text{CH}_2$ ,  $\text{CCH}_2\text{CH}=\text{CH}_2$ ), 5.73-5.98 (m, 2H,  $\text{CHCH}_2\text{CH}=\text{CH}_2$ ,  $\text{CCH}_2\text{CH}=\text{CH}_2$ ), 6.81 (s, 2H,  $\text{OCH}_2\text{O}$ ), 6.60-7.01 (m, 3H, Ar-H) ppm

**$^{13}\text{C NMR}$**  (68 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 28.0 ( $\text{OC}(\text{CH}_3)_3$ ), 30.9, 32.0 ( $\text{CHCH}_2\text{CH}=\text{CH}_2$ ), 44.0, 45.7 ( $\text{CCH}_2\text{CH}=\text{CH}_2$ ), 46.7, 46.9 ( $\text{CH}_2\text{CH}(\text{OCH}_3)_2$ ), 53.8, 54.5 ( $\text{OCH}_3$ ), 58.5, 60.4 ( $\text{NCH}$ ), 78.8, 79.0 ( $\text{OC}(\text{CH}_3)_3$ ), 79.7 (ArC), 100.6 ( $\text{OCH}_2\text{O}$ ), 104.0, 104.2 ( $\text{CH}(\text{OCH}_3)_2$ ), 106.7, 106.9, 115.9, 116.9, 128.4, 128.9, 136.6, 137.0, 138.8, 139.1, 146.8, 147.3 (Ar), 117.2, 117.8 ( $\text{CHCH}_2\text{CH}=\text{CH}_2$ ), 118.9, 119.1 ( $\text{CCH}_2\text{CH}=\text{CH}_2$ ), 133.8, 134.9 ( $\text{CHCH}_2\text{CH}=\text{CH}_2$ ), 136.6, 137.0 ( $\text{CCH}_2\text{CH}=\text{CH}_2$ ), 156.3, 157.4 ( $\text{NCO}$ ) ppm

**(4*R*,5*R*)-3-(2,2-Dimethoxyethyl)-4,5-diallyl-5-(3,4-methylenedioxyphenyl)-2-oxazolidinone 147**

Under argon, the crude diallyl **146** in anhyd. THF (20 mL) was treated with KHMDS (1.0 mL, 0.5 M in toluene) at 0°C. The reaction mixture was stirred at 0°C for 30 min (TLC control). Sat. aq. NH<sub>4</sub>Cl (20 mL) was added to the mixture. The aqueous layer was extracted with Et<sub>2</sub>O (4×10 mL). The combined organic layers were dried over MgSO<sub>4</sub>. After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 5:1) to give 150 mg (81.4% from ketone **129**) of **147** as a pale yellow oil.

$[\alpha]_D^{20} = +10.0^\circ$  (c = 2.4, CHCl<sub>3</sub>)

**<sup>1</sup>H-NMR** (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.46-2.57 (m, 2H, CHCH<sub>2</sub>CH=CH<sub>2</sub>), 2.57-2.62 (dd, 1H,  $J$  = 14.43 Hz, 7.42 Hz, ArCCHH), 2.75-2.81 (dd, 1H,  $J$  = 14.44 Hz, 6.32 Hz, ArCCHH), 2.92-2.98 (dd, 1H,  $J$  = 14.71 Hz, 7.01 Hz, NCHHCH(OCH<sub>3</sub>)<sub>2</sub>), 3.01 (s, 3H, OCH<sub>3</sub>), 3.21 (s, 3H, OCH<sub>3</sub>), 3.54-3.59 (dd, 1H,  $J$  = 14.71 Hz, 3.99 Hz, NCHHCH(OCH<sub>3</sub>)<sub>2</sub>), 3.91-3.96 (dd, 1H,  $J$  = 6.46 Hz, 5.50 Hz, NCH), 4.10-4.14 (dd, 1H,  $J$  = 7.01 Hz, 3.99 Hz, CH(OCH<sub>3</sub>)<sub>2</sub>), 5.43-5.53 (dddd, 1H,  $J$  = 17.58 Hz, 10.26 Hz, 7.32 Hz, 6.35 Hz, ArCCH<sub>2</sub>CH=CH<sub>2</sub>), 5.73-5.82 (dddd, 1H,  $J$  = 17.09 Hz, 10.17 Hz, 7.02 Hz, 6.88 Hz, NCHCH<sub>2</sub>CH=CH<sub>2</sub>), 5.90 (s, 2H, OCH<sub>2</sub>O), 6.71-6.74 (d, 1H,  $J$  = 6.11 Hz, Ar-H), 6.75-6.80 (m, 2H, Ar-H) ppm

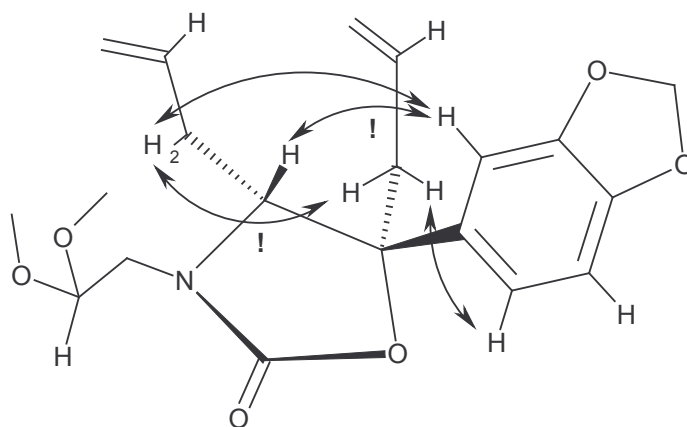
**<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 33.0 (CHCH<sub>2</sub>CH=CH<sub>2</sub>), 39.6 (ArCCH<sub>2</sub>CH=CH<sub>2</sub>), 44.0 (CH<sub>2</sub>CH(OCH<sub>3</sub>)<sub>2</sub>), 54.3, 55.1 (CH(OCH<sub>3</sub>)<sub>2</sub>), 65.9 (NCH), 84.9 (NCOOC), 101.0 (OCH<sub>2</sub>O), 103.1 (CH(OCH<sub>3</sub>)<sub>2</sub>), 105.6, 107.9, 118.1, 136.9, 146.7, 147.7 (Ar), 118.8, 118.9 (CH=CH<sub>2</sub>), 131.3 (ArCCH<sub>2</sub>CH=CH<sub>2</sub>), 133.2 (CHCH<sub>2</sub>CH=CH<sub>2</sub>), 156.7 (NCO) ppm

**IR** (KBr, Film):  $1/\lambda$  = 3086 (w), 3052 (w), 2992 (m), 2948 (s), 2898 (s), 2835 (m), 1732 (br, s, NCOO), 1635 (w), 1612 (m), 1507 (s), 1490 (s), 1438 (s), 1420 (s), 1392 (m), 1383 (m), 1357

(m), 1347 (m), 1316 (m), 1296 (m), 1283 (m), 1251 (s), 1210 (m), 1192 (m), 1178 (m), 1145 (m), 1121 (s), 1071 (s), 1035 (s), 1020 (s), 999 (m), 972 (m), 964 (m), 928 (m)  $\text{cm}^{-1}$

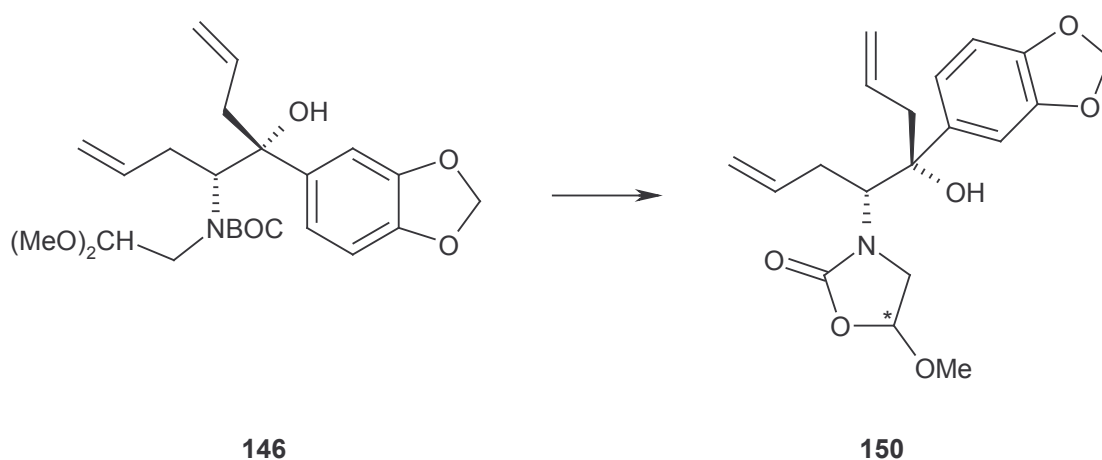
**MS** (EI, 80 eV, 110°C):  $m/z$  (%) = 375 (13.9,  $[\text{M}]^+$ ), 344 (4,  $[\text{M}-\text{CH}_3\text{O}]^+$ ), 334 (14,  $[\text{M}-\text{C}_3\text{H}_5]^+$ ), 315 (10,  $[\text{M}-\text{C}_2\text{H}_4\text{O}_2]^+$ ), 293 (3,  $[\text{M}-\text{C}_6\text{H}_{10}]^+$ ), 274 (4,  $[\text{M}-\text{C}_5\text{H}_9\text{O}_2]^+$ ), 258 (23,  $[\text{M}-\text{C}_5\text{H}_9\text{O}_3]^+$ ), 228 (7,  $[\text{M}-\text{C}_6\text{H}_{11}\text{O}_4]^+$ ), 75 (100,  $\text{C}_3\text{H}_7\text{O}_2$ ).

**HRMS** (80 eV, 110°C):  $m/z$   $[\text{M}]^+$  calcd. for  $\text{C}_{20}\text{H}_{25}\text{O}_6\text{N}$ , 375.16818; found, 375.16911.



relevant NOE's of **147** from NOESY

**(4*R*,5*R*)-4-(3,4-Methylenedioxyphenyl)-5-(4-methoxy-2-oxazolidinonyl)-1,7-octadien-4-ol 150**



## Method A:

Diallyl **146** (150 mg, 0.33 mmol) in DMSO (30 mL) and H<sub>2</sub>O (1 mL) was heated to 80-90°C for 20 hours. The mixture was then cooled to room temperature and H<sub>2</sub>O (10 mL) was added. The aqueous layer was extracted with Et<sub>2</sub>O (4×10 mL), and the combined organic layers were dried over MgSO<sub>4</sub>. After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 2:1) to give 90 mg (74% from ketone **129**) of **150** as a yellow oil.

## Method B:

Under argon, the crude diallyl **146** (150 mg, 0.33 mmol) in anhyd. CHCl<sub>3</sub> (20 mL) was treated with cat. SmCl<sub>3</sub> and acetyl chloride (90  $\mu$ L) at room temperature. The reaction mixture was stirred for 30 min (TLC monitoring). Sat. aq. NaHCO<sub>3</sub> (20 mL) was added until pH was reached to 9-10 and the aqueous layer was extracted with CHCl<sub>3</sub> (4×10 mL). The combined organic layers were dried over MgSO<sub>4</sub> and the solvent was removed. The residue was purified by column chromatography (n-hexane / ethyl acetate = 2:1) to give 80 mg (66% from ketone **129**) of **150** as a yellow oil.

## Method C:

Diallyl **146** (150 mg, 0.33 mmol) in anhyd. CH<sub>3</sub>OH (30 mL) at 0°C was treated with SOCl<sub>2</sub> (1 mL). The mixture was stirred at 0°C for 3 hours. After removal of the solvent, Na<sub>2</sub>CO<sub>3</sub> (10 mL) was added. The aqueous layer was extracted with Et<sub>2</sub>O (4×10 mL), and the combined organic layers were dried over MgSO<sub>4</sub>. After removal of the solvent, the crude material was purified by column chromatography (n-hexane / ethyl acetate = 2:1) to give 70 mg (58% from ketone **129**) of **150** as a yellow oil.

Data obtained from mixture, separated peaks of diastereomer 1:

<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.39-2.70 (m, 4H, 2×CH<sub>2</sub>CH=CH<sub>2</sub>), 3.02-3.08 (dd, 1H, *J* = 10.59 Hz, 3.02 Hz, NCHH), 3.29 (s, 3H, OCH<sub>3</sub>), 3.49-3.54 (dd, 1H, *J* = 10.59 Hz, 6.60 Hz, NCHH), 3.80-3.90 (m, 1H, NCH), 4.93-5.09 (m, 5H, 2×CH=CH<sub>2</sub>, CHOCH<sub>3</sub>), 5.22-5.30 (m, 1H, ArCCH<sub>2</sub>CH=CH<sub>2</sub>), 5.60-5.71 (m, 1H, NCHCH<sub>2</sub>CH=CH<sub>2</sub>), 5.82 (2×s, 2H, OCH<sub>2</sub>O), 6.62-6.67 (d, 1H, *J* = 1.46 Hz, Ar-H), 6.73-6.78 (dd, 1H, *J* = 8.31 Hz, 1.96 Hz, Ar-H), 6.80-6.84 (d, 1H, *J* = 7.81 Hz, Ar-H) ppm

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 30.4 (NCHCH<sub>2</sub>), 44.4 (ArCCH<sub>2</sub>CH=CH<sub>2</sub>), 55.4 (OCH<sub>3</sub>), 61.0 (NCH), 78.4 (ArC), 98.4 (OCHOCH<sub>3</sub>), 100.8 (OCH<sub>2</sub>O), 106.8, 107.7, 120.1, 137.6, 146.4, 147.7 (Ar), 118.2 (CH=CH<sub>2</sub>), 118.9 (CH=CH<sub>2</sub>), 132.6 (CH=CH<sub>2</sub>), 134.5 (CH=CH<sub>2</sub>), 157.5 (CON) ppm

Data obtained from mixture, separated peaks of diastereomer 2:

$^1\text{H}$ -NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 2.39-2.70 (m, 4H, 2 $\times$ CH<sub>2</sub>CH=CH<sub>2</sub>), 3.22-3.28 (dd, 1H,  $J$  = 10.17 Hz, 2.20 Hz, NCHH), 3.22-3.28 (m, 4H, OCH<sub>3</sub>, NCHH), 3.90-4.00 (m, 1H, NCH), 4.93-5.09 (m, 5H, 2 $\times$ CH=CH<sub>2</sub>, CHOCH<sub>3</sub>), 5.30-5.39 (m, 1H, ArCCH<sub>2</sub>CH=CH<sub>2</sub>), 5.60-5.71 (m, 1H, NCHCH<sub>2</sub>CH=CH<sub>2</sub>), 5.82 (2 $\times$ s, 2H, OCH<sub>2</sub>O), 6.62-6.67 (d, 1H,  $J$  = 1.46 Hz, Ar-H), 6.73-6.78 (dd, 1H,  $J$  = 8.31 Hz, 1.96 Hz, Ar-H), 6.80-6.84 (d, 1H,  $J$  = 7.81 Hz, Ar-H) ppm

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 30.4 (NCHCH<sub>2</sub>), 45.0 (ArCCH<sub>2</sub>CH=CH<sub>2</sub>), 55.7 (OCH<sub>3</sub>), 61.5 (NCH), 78.3 (ArC), 98.6 (OCHOCH<sub>3</sub>), 100.8 (OCH<sub>2</sub>O), 106.1, 107.8, 120.3, 137.3, 146.5, 147.6 (Ar), 117.6 (CH=CH<sub>2</sub>), 118.3 (CH=CH<sub>2</sub>), 132.3 (CH=CH<sub>2</sub>), 134.0 (CH=CH<sub>2</sub>), 156.8 (CON) ppm

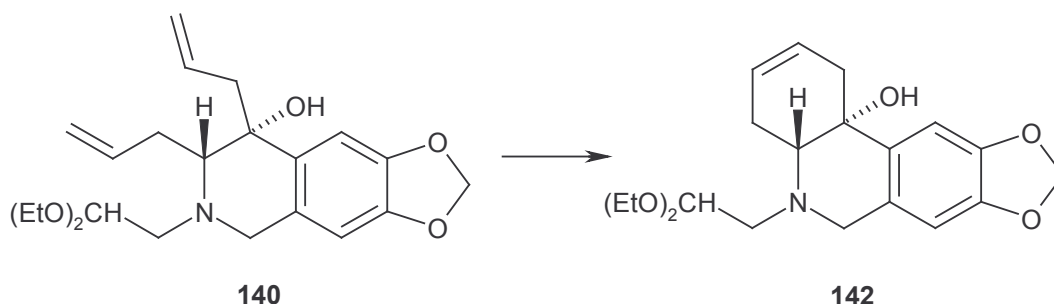
Data of diastereomers 1 and 2:

IR (KBr, Film):  $1/\lambda$  = 3423 (br, m, OH), 3077 (m), 3005 (m), 2977 (m), 2957 (m), 2938 (m), 2843 (w), 2777 (w), 2249 (w), 1734 (s, CON), 1640 (m), 1610 (w), 1504 (s), 1488 (s), 1433 (s), 1377 (s), 1335 (m), 1238 (s), 1183 (m), 1125 (m), 1074 (m), 1040 (s), 1017 (m), 971 (m), 915 (m)  $\text{cm}^{-1}$

MS (EI, 80 eV, 150°C):  $m/z$  (%) = 361 (8, [M]<sup>+</sup>), 343 (1, [M-H<sub>2</sub>O]<sup>+</sup>), 330 (2, [M-CH<sub>3</sub>O]<sup>+</sup>), 288 (2, [M-C<sub>3</sub>H<sub>5</sub>O<sub>2</sub>]<sup>+</sup>), 191 (47, [M-C<sub>8</sub>H<sub>10</sub>O<sub>4</sub>]<sup>+</sup>), 149 (100, [C<sub>8</sub>H<sub>5</sub>O<sub>3</sub>]<sup>+</sup>), 121 (6, [C<sub>7</sub>H<sub>5</sub>O<sub>2</sub>]<sup>+</sup>).

HRMS (80 eV, 150°C):  $m/z$  [M]<sup>+</sup> calcd. for C<sub>19</sub>H<sub>23</sub>NO<sub>6</sub>, 361.15253; found, 361.15366.

## 3.11 Ring-Closing Olefin Metathesis

**(4a*R*,10b*R*)-*N*-(2,2-Diethoxyethyl)-8,9-methylenedioxy-1,4,4a,5,6,10b-hexahydro phenanthridine 142**

Diallyl **140** (100 mg, 0.25 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (50 mL) was treated with Benzyldienebis(tricyclohexylphosphine) dichlororuthenium **40** (10 mg, 0.012 mmol). The mixture was refluxed at 60°C. Another portion of Grubbs catalyst **40** (10 mg, 0.012 mmol) was added every 24 hours. After 96 hours, the reaction mixture was stirred at room temperature for 2 hours. The mixture was filtered over silica gel and the solvent was evaporated. The residue was purified by HPLC (ethyl acetate / n-hexane = 1:1, Nucleosil 50-5, 32×110 mm, flow 64 mL/min, retention time: 5.0 min) to give 60 mg (66%) of **142** as a brown oil.

$[\alpha]_D^{20} = -144.5^\circ$  (c = 1.6, CHCl<sub>3</sub>)

**<sup>1</sup>H-NMR** (500 MHz, CDCl<sub>3</sub>): δ = 1.15 (2xt, 6H, *J* = 7.01 Hz, CH<sub>3</sub>CH<sub>2</sub>), 2.10-2.20 (m, 2H, CHHCHN, CHHCOH), 2.34-2.42 (m, 1H, CHHCHN), 2.51-2.57 (dd, 1H, *J* = 13.88 Hz, 4.81 Hz, NCHHCH(OEt)<sub>2</sub>), 2.67-2.73 (dd, 1H, *J* = 10.76 Hz, 5.50 Hz, NCH), 2.78-2.85 (m, 1H, CHHCOH), 2.86 (s, br, 1H, OH), 3.02-3.08 (dd, 1H, *J* = 13.88 Hz, 5.67 Hz, NCHHCH(OEt)<sub>2</sub>), 3.48-3.56 (m, 2H, CH<sub>3</sub>CH<sub>2</sub>), 3.56-3.61 (d, 1H, *J* = 14.85 Hz, NCHHAr), 3.62-3.74 (m, 2H, CH<sub>3</sub>CH<sub>2</sub>), 3.91-3.97 (d, 1H, *J* = 14.99 Hz, NCHHAr), 4.62-4.66 (dd, 1H, *J* = 5.49 Hz, 5.09 Hz, CH(OEt)<sub>2</sub>), 5.63-5.68 (m, 1H, CH=CHCH<sub>2</sub>COH), 5.69-5.75 (m, 1H, CH=CH-CHN), 5.88 (d, 2H, *J* = 1.37 Hz, OCH<sub>2</sub>O), 6.39 (s, 1H, Ar-H), 6.89 (s, 1H, Ar-H) ppm

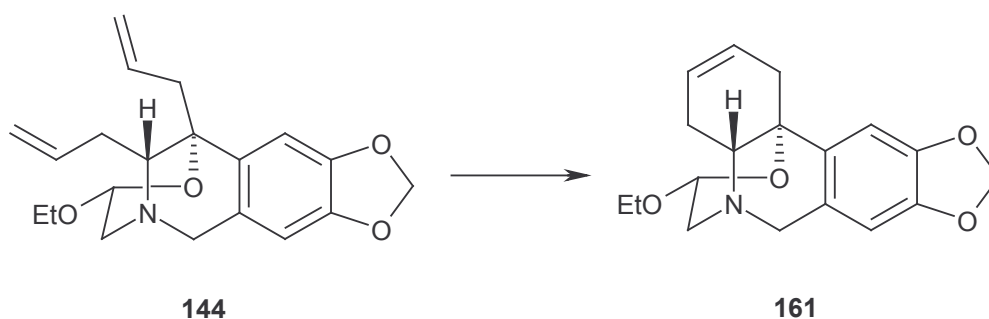
**<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>): δ = 15.31, 15.32 (CH<sub>3</sub>CH<sub>2</sub>), 26.4 (CH<sub>2</sub>CHN), 35.8 (CH<sub>2</sub>COH), 53.5 (NCH<sub>2</sub>CH(OEt)<sub>2</sub>), 56.3 (NCH<sub>2</sub>Ar), 61.4 (CH<sub>3</sub>CH<sub>2</sub>), 61.6 (CH<sub>2</sub>CHN), 62.4 (CH<sub>3</sub>CH<sub>2</sub>), 68.1 (COH), 100.7 (OCH<sub>2</sub>O), 101.4 (CH(OEt)<sub>2</sub>), 105.3, 105.5, 127.4, 133.7, 146.5, 146.6 (Ar), 123.5 (CH=CHCH<sub>2</sub>COH), 124.2 (CH=CHCH<sub>2</sub>CHN) ppm

**IR** (solution, CHCl<sub>3</sub>): 1/λ = 3320 (w, OH), 3019 (s), 2978 (m), 2897 (m), 1605 (w), 1504 (m), 1486 (m), 1389 (w), 1294 (w), 1215 (s), 1126 (m), 1043 (m), 909 (s) cm<sup>-1</sup>

**MS** (EI, 80 eV, 120°C):  $m/z$  (%) = 361 (1.37,  $[M]^+$ ), 343 (9,  $[M-H_2O]^+$ ), 316 (6,  $[M-C_2H_5O]^+$ ), 258 (100,  $[M-C_5H_{11}O_2]^+$ ), 103 (7,  $[C_5H_{11}O_2]^+$ ).

**HRMS** (80 eV, 100°C):  $m/z$   $[M]^+$  calcd. for  $C_{20}H_{27}NO_5$ , 361.18892; found, 361.18744.  
 $[M-H_2O]^+$  calcd. for  $C_{20}H_{25}NO_4$ , 343.17835; found, 343.17654.  
 $[M-C_2H_5O]^+$  calcd. for  $C_{18}H_{22}NO_4$ , 316.15488; found, 316.15622.  
 $[M-C_5H_{11}O_2]^+$  calcd. for  $C_{15}H_{16}NO_3$ , 258.11301; found, 258.11633.

**(4a*R*,10b*R*)-4,10b-(2-Ethoxy-3-oxapropylidene)-8,9-methylenedioxy-1,4,4a,5,6,10b-hexahydro phenanthridine 161**



Diallyl **144** (120 mg, 0.35 mmol) in  $CH_2Cl_2$  (80 mL) was treated with Benzylidene-bis(tricyclohexylphosphine) dichlororuthenium **40** (14 mg, 0.017 mmol), the mixture was refluxed at 60°C. Another portion of Grubb's Carbene **40** (14 mg, 0.017 mmol) was added every 24 hours. After 96 hours, the reaction mixture was stirred at room temperature for 2 hours. The mixture was filtered over silica gel and the solvent was evaporated. The residue was purified by HPLC (ethyl acetate / n-hexane = 3:1, Nucleosil 50-5, 32×110 mm, flow 64 mL/min, retention time: 5.0 min) to give 75 mg (68%) of **161** as a brown crystal with m.p. = 138-139°C.

$[\alpha]_D^{20} = -49.1^\circ$  (c = 1.3,  $CHCl_3$ )

**$^1H$ -NMR** (500 MHz,  $CDCl_3$ ):  $\delta$  = 1.02 (t, 3H,  $J$  = 7.15 Hz,  $CH_3CH_2$ ), 2.11-2.19 (m, 1H,  $CH=CHCHHCHN$ ), 2.36-2.44 (m, 1H,  $CH=CHCHHCAr$ ), 2.59-2.65 (dd, 1H,  $J$  = 14.57 Hz, 3.57 Hz,  $NCHHCHOEt$ ), 2.75-2.84 (m, 2H,  $CH=CHCHHCHN$ ,  $CH=CHCHHCAr$ ), 2.94-2.99 (dd, 1H,  $J$  = 10.86 Hz, 6.19 Hz,  $NCHCH_2$ ), 3.09-3.15 (dd, 1H,  $J$  = 14.57 Hz, 10.03 Hz,  $NCHHCHOEt$ ), 3.18-3.25 (m, 1H,  $CH_3CHH$ ), 3.71-3.77 (m, 1H,  $CH_3CHH$ ), 3.81-3.87 (d, 1H,  $J$  = 17.05 Hz,  $NCHHAr$ ), 4.24-4.35 (d, 1H,  $J$  = 17.05 Hz,  $NCHHAr$ ), 4.33-4.37 (dd, 1H,  $J$  = 10.05 Hz, 3.71 Hz,  $EtOCHO$ ), 5.50-5.60 (m, 1H,  $CH=CHCH_2CAr$ ), 5.65-5.75 (m, 1H,  $CH=CHCH_2CHN$ ), 5.90 (s, 2H,  $OCH_2O$ ), 6.42 (s, 1H, Ar), 6.85 (s, 1H, Ar) ppm



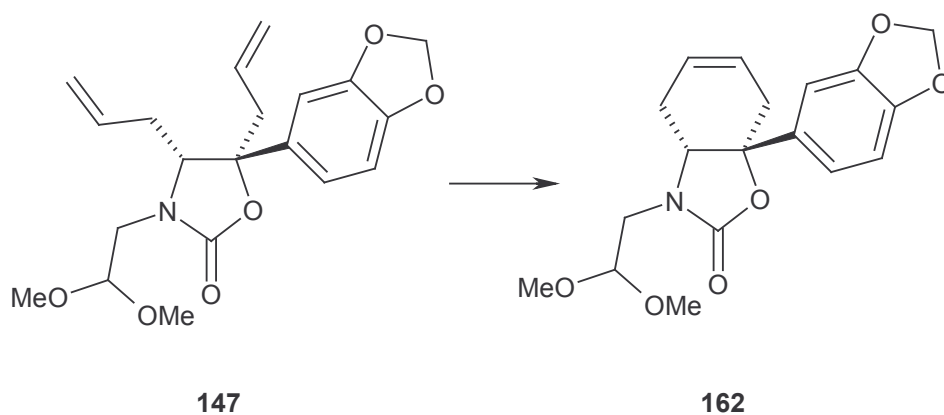
$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 15.0 ( $\text{CH}_3\text{CH}_2$ ), 24.7 ( $\text{NCHCH}_2$ ), 36.3 ( $\text{CH}=\text{CHCH}_2\text{CAr}$ ), 51.1 ( $\text{NCH}_2\text{CH}$ ), 54.6 ( $\text{NCHCH}_2$ ), 57.7 ( $\text{NCH}_2\text{Ar}$ ), 64.3 ( $\text{CH}_3\text{CH}_2$ ), 67.4 ( $\text{OCAr}$ ), 95.2 ( $\text{NCH}_2\text{CHOEt}$ ), 100.8 ( $\text{OCH}_2\text{O}$ ), 104.4, 105.4, 130.3, 131.0, 146.9, 147.0 (Ar), 122.9 ( $\text{CH}=\text{CHCH}_2\text{CAr}$ ), 124.7 ( $\text{CH}=\text{CHCH}_2\text{CHN}$ ) ppm

IR (solution,  $\text{CHCl}_3$ ):  $1/\lambda$  = 3016 (s), 2978 (s), 2928 (s), 2896 (s), 2775 (w), 2654 (w), 1665 (w), 1622 (w), 1504 (s), 1483 (s), 1450 (m), 1424 (m), 1380 (m), 1349 (m), 1333 (m), 1307 (m), 1260 (m), 1237 (s), 1214 (s), 1185 (m), 1161 (m), 1141 (m), 1111 (s), 1040 (s), 991 (w), 970 (w)  $\text{cm}^{-1}$

MS (EI, 80 eV,  $110^\circ\text{C}$ ):  $m/z$  (%) = 315 (7,  $[\text{M}]^+$ ), 270 (1,  $[\text{M}-\text{C}_2\text{H}_5\text{O}]^+$ ), 241 (51,  $[\text{M}-\text{C}_3\text{H}_6\text{O}_2]^+$ ), 226 (21,  $[\text{M}-\text{C}_4\text{H}_9\text{O}_2]^+$ ), 212 (100,  $[\text{M}-\text{C}_4\text{H}_9\text{NO}_2]^+$ ).

HRMS (80 eV,  $100^\circ\text{C}$ ):  $m/z$   $[\text{M}]^+$  calcd. for  $\text{C}_{18}\text{H}_{21}\text{NO}_4$ , 315.14705; found, 315.14932

**(3*aR*,7*aR*)- 3-(2,2-Dimethoxyethyl)-7*a*-(3,4-methylenedioxyphenyl)-3*a*,4,7,7*a*-tetrahydrobenzo oxazol-2-one 162**



Diallyl **147** (100 mg, 0.27 mmol) in  $\text{CH}_2\text{Cl}_2$  (80 mL) was treated with Benzylidene-bis(tricyclohexylphosphine) dichlororuthenium **40** (11 mg, 0.013 mmol). The reaction mixture was refluxed at  $60^\circ\text{C}$  for 3 hours (TLC control). After removal of the solvent, the residue was purified by column chromatograph (n-hexane / ethyl acetate = 3:1) to give 80 mg (86%) **162** as a pale yellow oil.

$[\alpha]_D^{20} = -37.3^\circ$  (c = 1.7,  $\text{CHCl}_3$ )

$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 2.17-2.25 (m, 1H,  $\text{NCHCHH}$ ), 2.36-2.43 (m, 1H,  $\text{ArCCCHH}$ ), 2.48-2.53 (ddd, 1H,  $J$  = 15.63 Hz, 5.37 Hz, 2.93 Hz,  $\text{NCHCHH}$ ), 2.58-2.65 (dd,

1H,  $J = 16.60$  Hz, 5.86 Hz, ArCCHH), 2.91-2.96 (dd, 1H,  $J = 14.65$  Hz, 6.35 Hz, NCHH), 3.21 (s, 3H, OCH<sub>3</sub>), 3.32 (s, 3H, OCH<sub>3</sub>), 3.51-3.56 (dd, 1H,  $J = 14.65$  Hz, 4.39 Hz, NCHH), 4.07-4.12 (dd, 1H,  $J = 4.89$  Hz, 2.93 Hz, NCH), 4.33-4.38 (dd, 1H,  $J = 5.86$  Hz, 4.40 Hz, CH(OCH<sub>3</sub>)<sub>2</sub>), 5.89-5.93 (m, 1H, CH=CH), 5.92 (s, 2H, OCH<sub>2</sub>O), 5.93-6.01 (m, 1H, CH=CH), 6.67-6.71 (d, 1H,  $J = 8.30$  Hz, Ar-H), 6.78-6.83 (dd, 1H,  $J = 8.30$  Hz, 1.96 Hz, Ar-H), 6.83-6.85 (d, 1H,  $J = 1.46$  Hz, Ar-H) ppm

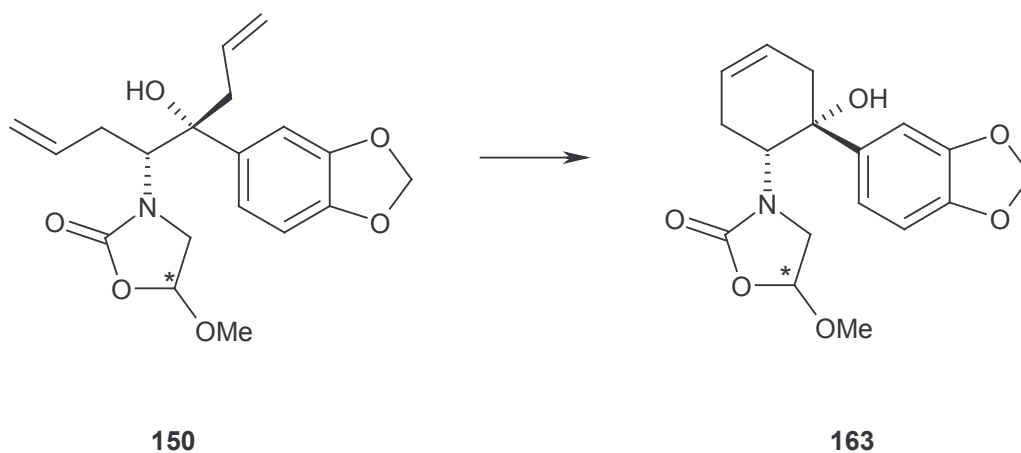
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta = 25.6$  (NCHCH<sub>2</sub>), 36.0 (ArCCH<sub>2</sub>), 43.5 (NCH<sub>2</sub>), 54.4, 55.1 (OCH<sub>3</sub>), 63.0 (NCHCH<sub>2</sub>), 82.9 (NCOOC), 101.1 (OCH<sub>2</sub>O), 102.9 (CH(OCH<sub>3</sub>)<sub>2</sub>), 105.0, 107.9, 117.2, 138.6, 147.0, 147.8 (Ar), 125.8 (CH=CH), 127.4 (CH=CH), 157.3 (NCO) ppm

IR (KBr, Film):  $1/\lambda = 3086$  (w), 3052 (w), 2992 (w), 2948 (m), 2898 (m), 2835 (m), 1847 (w), 1732 (s, CON), 1635 (w), 1612 (w), 1507 (s), 1490 (s), 1438 (s), 1420 (s), 1392 (m), 1383 (m), 1357 (m), 1347 (m), 1326 (m), 1316 (m), 1296 (s), 1283 (m), 1251 (s), 1210 (m), 1192 (m), 1178 (m), 1145 (m), 1121 (m), 1071 (s), 1035 (s), 1020 (s), 999 (m), 972 (m), 964 (m), 928 (s) cm<sup>-1</sup>

MS (EI, 80 eV, 120°C):  $m/z$  (%) = 347 (8, [M]<sup>+</sup>), 200 (8, [C<sub>13</sub>H<sub>12</sub>O<sub>2</sub>]<sup>+</sup>), 75 (100, [C<sub>3</sub>H<sub>7</sub>O<sub>2</sub>]<sup>+</sup>).

HRMS (80 eV, 120°C):  $m/z$  [M]<sup>+</sup> calcd. for C<sub>18</sub>H<sub>21</sub>NO<sub>6</sub>, 347.13690; found, 347.13588.

**(1*R*,6*R*)-1-(3,4-Methylenedioxyphenyl)-6-*N*-(4-methoxy-2-oxazolidinonyl)-3-cyclohexen-1-ol 163**



Diallyl **150** (160 mg, 0.44 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (100 mL) was treated with Benzylidene-bis(tricyclohexylphosphine) dichlororuthenium **40** (16 mg, 0.022 mmol). The reaction mixture was refluxed at 60°C for 3 hours (TLC control). After removal of the solvent, the

residue was purified by column chromatograph (ethyl acetate) to give 130 mg (88%) **163** as colourless crystals with m.p. = 188-189°C.

Data obtained from mixture, separated peaks of diastereomer 1:

**<sup>1</sup>H-NMR** (500 MHz, CDCl<sub>3</sub>): δ = 2.13-2.36 (m, 2H, NCHC**HH**, ArC**C**H**H**), 2.48-2.63 (m, 2H, NCHC**HH**, ArC**C**H**H**), 3.18-3.25 (dd, 1H, *J* = 10.74 Hz, 2.44 Hz, N**CH**H), 3.37 (s, 3H, O**C**H****<sub>3</sub>), 3.50-3.56 (dd, 1H, *J* = 10.74 Hz, 6.34 Hz, N**CH**H), 4.29-4.37 (dd, 1H, *J* = 10.72 Hz, 5.91 Hz, N**CH**), 5.07-5.10 (dd, 1H, *J* = 6.46 Hz, 2.47 Hz, CH<sub>3</sub>O**C**H**O**), 5.54-5.64 (m, 1H, ArC**C**H****<sub>2</sub>**C**H**=CH**), 5.72-5.82 (m, 1H, ArC**C**H****<sub>2</sub>**C**H**=CH**), 5.90 (s, 2H, O**C**H****<sub>2</sub>O), 6.75 (d, 1H, *J* = 7.81 Hz, Ar-H), 6.88-6.93 (dd, 1H, *J* = 8.31 Hz, 1.96 Hz, Ar-H), 7.01 (d, 1H, *J* = 1.46 Hz, Ar-H) ppm

**<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>): δ = 25.9 (NCH**C**H****<sub>2</sub>), 43.9 (Ar**C**C**H****<sub>2</sub>), 50.8 (N**C**H****<sub>2</sub>), 55.2 (N**C**H****), 55.3 (O**C**H****<sub>3</sub>), 74.8 (Ar**C**C**H****<sub>2</sub>), 98.4 (CH<sub>3</sub>O**C**H**O**), 100.9 (O**C**H****<sub>2</sub>O), 105.9, 107.9, 118.0, 138.8, 146.5, 147.6 (Ar), 124.2 (Ar**C**C**H****<sub>2</sub>**C**H**=CH**), 125.7 (Ar**C**C**H****<sub>2</sub>**C**H**=CH**) ppm********

Data obtained from mixture, separated peaks of diastereomer 2:

**<sup>1</sup>H-NMR** (500 MHz, CDCl<sub>3</sub>): δ = 2.13-2.36 (m, 2H, NCHC**HH**, ArC**C**H**H**), 2.48-2.60 (m, 1H, ArC**C**H**H**), 2.62-2.73 (m, 1H, NCHC**HH**), 3.32-3.36 (dd, 1H, *J* = 10.45 Hz, 2.61 Hz, N**CH**H), 3.29 (s, 3H, O**C**H****<sub>3</sub>), 3.41-3.49 (dd, 1H, *J* = 10.45 Hz, 6.35 Hz, N**CH**H), 4.01-4.07 (dd, 1H, *J* = 10.45 Hz, 5.37 Hz, N**CH**), 5.14-5.17 (dd, 1H, *J* = 6.32 Hz, 2.61 Hz, CH<sub>3</sub>O**C**H**O**), 5.54-5.64 (m, 1H, ArC**C**H****<sub>2</sub>**C**H**=CH**), 5.72-5.82 (m, 1H, ArC**C**H****<sub>2</sub>**C**H**=CH**), 5.90 (s, 2H, O**C**H****<sub>2</sub>O), 6.77 (d, 1H, *J* = 8.31 Hz, Ar-H), 6.88-6.93 (dd, 1H, *J* = 8.31 Hz, 1.96 Hz, Ar-H), 7.01 (d, 1H, *J* = 1.96 Hz, Ar-H) ppm

**<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>): δ = 25.7 (NCH**C**H****<sub>2</sub>), 43.2 (Ar**C**C**H****<sub>2</sub>), 49.0 (N**C**H****<sub>2</sub>), 55.7 (O**C**H****<sub>3</sub>), 57.2 (N**C**H****), 75.0 (Ar**C**C**H****<sub>2</sub>), 98.4 (CH<sub>3</sub>O**C**H**O**), 100.9 (O**C**H****<sub>2</sub>O), 106.3, 107.8, 118.2, 138.2, 146.5, 147.7 (Ar), 124.5 (Ar**C**C**H****<sub>2</sub>**C**H**=CH**), 125.1 (Ar**C**C**H****<sub>2</sub>**C**H**=CH**) ppm********

Data of diastereomers 1 and 2:

**IR** (KBr, Film): 1/λ = 3375 (br, m, OH), 3073 (w), 3063 (w), 3031 (w), 3000 (w), 2962 (w), 2925 (w), 2904 (m), 2836 (w), 1733 (s, CON), 1654 (w), 1612 (w), 1505 (s), 1483 (s), 1447 (s), 1424 (s), 1389 (s), 1364 (s), 1347 (w), 1338 (w), 1329 (w), 1315 (w), 1271 (s), 1247 (s), 1236 (s), 1216 (s), 1192 (m), 1151 (w), 1133 (w), 1125 (w), 1112 (m), 1100 (w), 1091 (w), 1068 (w), 1047 (s), 1040 (s), 1020 (s), 977 (s) cm<sup>-1</sup>

**MS** (EI, 80 eV, 150°C):  $m/z$  (%) = 333 (37,  $[M]^+$ ), 216 (26,  $[M-C_4H_7NO_3]^+$ ), 149 (100,  $[C_8H_5O_3]^+$ ), 121 (8,  $[C_7H_5O_2]^+$ ).

**HRMS** (80 eV, 150°C):  $m/z$   $[M]^+$  calcd. for  $C_{17}H_{19}NO_6$ , 333.12125; found, 333.12322.