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. Tetrahydrofuran was distilled from sodium and benzophenone. Toluene and dichloromethane were distilled from calcium hydride. Methanol was distilled from Mg under argon.

3.1.2 NMR-Spectroscopy

^{1}H-NMR spectra were recorded on a Bruker AM 270 MHz or a Bruker AMX 500 MHz spectrometer and are reported in δ from Me_4Si (δ = 0.00 ppm) or from $CDCl_3$ (δ = 7.26 ppm). The ^{1}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 ^{1}H,^{1}H-COSY and 1D Nuclear Overhauser Enhancement (NOE) spectroscopy. In cyclic compounds diastereotopic protons were assigned according to their NOE analysis and marked with *o* (oberhalb, above) or *u* (unterhalb, below) referring to their 3-dimensional position with respect to the plane of the ring.

^{13}C-NMR spectra were recorded at 68 or at 125 MHz in $CDCl_3$ (unless otherwise stated) with the chemical shifts relative to $CHCl_3$ (77 ppm).

3.1.3 IR-Spectroscopy

IR spectra were recorded as pellets (KBr) or in solution (solvent as given) using a Perkin 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 the internal reference).

3.1.5 Polarimetry

Optical rotations were recorded on a IBZ Messtechnik polarimeter, at a temperature of 20 °C, using a l dm cell. The specific optical rotation was calculated using the following formula :

$$[\alpha]_{D}^{20} = \frac{\alpha \cdot 100}{c \cdot d}$$

α : optical rotation ; c : concentration (g/100mL); d : path length (1 dm); λ = 589.3 nm

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_{254} precoated plates. The following reagents were used as detectors:

Schlittler reagent [254] **:** 3 mL of 10% aqueous H_2PtCl_6 + 97 mL of water + 100mL of 6% aqueous KI. Very specific for the detection of amides (white colour, not persistent) and amines (deep brown to black colour).

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

Potassium permanganate reagent : 0.05% aqueous $KMnO_4$.

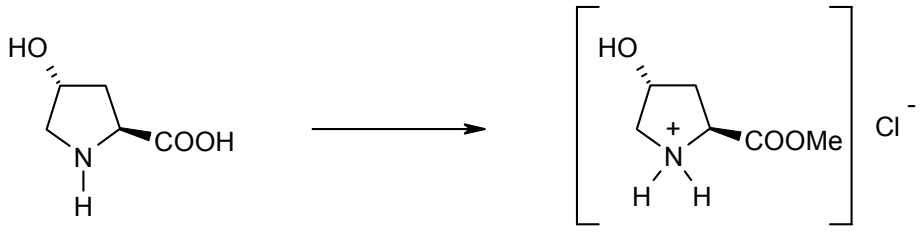
Bromokresol green reagent : 40 mg of bromokresol green indicator (3,3',5,5'-Tetrabromo-m-kresolsulfon-phthalein) was dissolved in 100 mL of ethanol and treated with 0.1 M aqueous NaOH until a blue colour appeared. Basic compounds give a deep blue, acid or weak acid compounds a yellow colour.

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

[254] Schlittler, E.; Hohl, J. *Helv. Chim. Acta* **1952**, 35, 29.

3.2 Syntheses of Vinyl pyrrolidines

2*S*,4*R*-4-Hydroxyproline methyl ester hydrochloride [2]



[1] 131.13 [$C_5H_9NO_3$] **[2]** 182.63 [$C_6H_{13}ClNO_3$]

To a suspension of hydroxyproline **[1]** (100 g, 0.76mol) and 600 mL of methanol in a 2 L three-necked flask was added carefully acetyl chloride (81 mL, 1.5 eq, 1.14mol, d = 1.105). After complete addition, the mixture was refluxed for 8 hours and then 350 mL of the solvent was removed in vacuo. After addition of diethyl ether (600 mL) and cooling to 4 °C overnight, the resulting colourless crystals were collected by filtration, washed with ether and vacuum-dried, yielding 140g (100%) of *trans*-4-hydroxy-L-proline methyl ester hydrochloride **[2]** (mp 165 °C).

$[\alpha]_D^{20}$ = -19.6° (c = 2.145, CH_3OH).

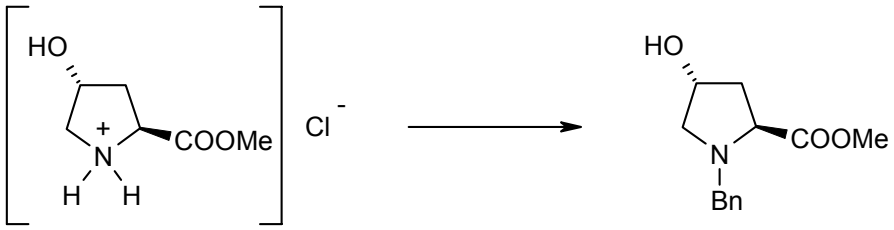
^{1}**H-NMR** (250 MHz, CD_3OD):
δ = 4.80 (s, 3H; NH and OH), 4.60 (m, 2H; H-2 and H-4), 3.75 (s, 3H; OMe), 3.4 (dd, 1H, H-3, ^3J (H,H) = 10 Hz, ^3J (H,H) = 3 Hz), 3.25 (d, 1H, H-5, ^3J (H,H) = 10 Hz), 2.35 (dd, 1H, H-5, ^3J (H,H) = 10Hz, ^3J (H,H) = 7 Hz), 2.2 (m, 1H; H-3).

^{13}**C-NMR** (62.9 MHz, CD_3OD):
δ = 170.54 (s, CO), 70.56 (d, C-4), 59.43 (d, C-2), 54.95 (t, C-5), 54.07 (q, O-CH3), 38.40 (t, C-3).

IR (KBr): υ (cm^{-1}) = 3377 (m, OH), 2948 (s, C-H), 1741 (s, C=O), 1586 (m), 1450 (m).

MS (70eV, EI, 120 °C): m/z (%): 145 (3) [M+ -Cl], 101 (8), 86 (100), 68 (25), 58 (14), 41 (11).

2*S*,4*R*-(N-Benzyl)-hydroxyproline methyl ester [3]



[2] 182.63 [$C_6H_{13}ClNO_3$] **[3]** 235.29 [$C_{13}H_{17}NO_3$]

To a suspension of proline-methyl ester hydrochloride **[2]** (140 g, 0.76 mol) in dry dichloromethane (800 mL) was added 212.6 mL (2eq, 1.52 mol, d = 0.726) of freshly distilled triethylamine and 175.8 mL (2eq, 1.52 mol, d = 1.098) of benzyl chloride. The reaction mixture was refluxed overnight and a white-brown precipitation of the amine hydrochloride was formed.

After cooling to 4 °C in an ice-bath, 5 M aqueous NaOH (200 mL) was added until the pH reached 12 - 14. The layers were separated and the aqueous phase was extracted with 400 mL of dichloromethane (2x).

The organic layers were combined and 600mL of dichloromethane was removed in vacuo to reduce the volume. The organic phase was neutralised with 600 mL of 1.65 M aqueous HCl (5%) and the phases were separated. The organic phase was extracted once more with 200 mL of 1.65 M HCl. The remaining organic layer contained unreacted benzyl chloride. The product was dissolved in the aqueous layer as hydrochloride.

The combined acid aqueous layers were carefully neutralised with 400mL of a saturated aqueous $NaHCO_3$ with ice cooling and the pH-value was subsequently adjusted to 12-14 by adding solid K_2CO_3. After stirring at room temperature for 15 min, the aqueous layer was extracted with 300mL of diethyl ether (3x). The combined organic layers were dried over Na_2SO_4 and concentrated to give 157.4g (87.6%) of N-benzyl-proline methyl ester **[3]** as a pale yellow oil.

$[\alpha]_D^{20}$ = -52.1° (c = 2.145, $CHCl_3$).

^{1}**H-NMR** (270 MHz, $CDCl_3$):

7.25-7.20 (m, 5H), 4.37 (m, 1H; H-4), 3.82 (d, 1H, H-6, ^2J (H,H) = 13 Hz), 3.59 (d, 1H, H-6, ^2J (H,H) = 13 Hz), 3.58 (s, 1H; OMe), 3.54 (dd, 1H, H-2, ^3J (H,H) = 16Hz, ^3J (H,H) = 8 Hz), 3.25 (dd, 1H, H-5, ^3J (H,H) = 10Hz, ^3J (H,H) = 6 Hz), 2.39 (dd, 1H, H-5, ^3J (H,H) = 10 Hz, ^3J (H,H) = 4 Hz), 2.4-2.3 (s, broad, 1H; OH), 2.18 (ddd, 1 H, H-3, ^2J (H,H) = 13 Hz, ^3J (H,H) = 10 Hz, ^3J (H,H) = 7Hz), 2.0 (ddd, 1 H, H-3, ^2J (H,H) = 13 Hz, ^3J (H,H) = 8 Hz, ^3J (H,H) = 3Hz).

^{13}**C-NMR** (67.9 MHz, $CDCl_3$):
174.0 (s, C=O), 137.9 (s, C-7) 129.0 (d, C-9), 128.2 (d, C-10), 127.2 (d, C-8), 70.1 (d, C-4), 63.6 (d, C-2), 61.1 (t, C-5), 58.1 (t, C-6), 51.7 (q, OCH_3), 39.5 (t, C-3).

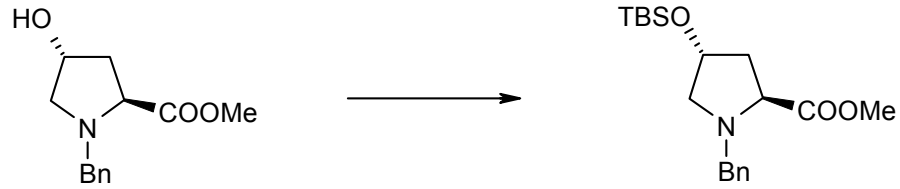
IR (KBr):
υ (cm^{-1}) = 3406 (m, OH, broad), 3062 (s), 3028 (s), 2950 (s), 2809 (s), 1734 (s), 1495 (m), 1459 (m), 1437 (s), 755 (s), 701 (s).

MS (70eV, EI, 60 °C): m/z (%): 235 (2) [$M^{+\cdot}$], 215 (2), 176 (88) [M^+ - COOMe], 91 (100) [$C_7H_7^+$].

HRMS (80eV,60 °C): found 235.12155 calc. 235.12084 (for $C_{13}H_{17}NO_3$).

$\mathbf{R}_f$ = 0.1 (hexane / ethyl acetate 2:1), black (Schlittler's reagent).

2*S*,4*R*-(N-Benzyl)-4-*tert*-butyldimethylsilyloxy-proline methyl ester [4]



[3] 235.29 [$C_{13}H_{17}NO_3$] **[4]** 349.55 [$C_{19}H_{31}NO_3Si$]

N-Benzylproline-methyl ester **[3]** (76.1g, 0.32 mol) was dissolved in 500 mL of dichloromethane (dried over CaH_2) and at 0 °C imidazole (32.7 g, 1.5 eq, 0.48mol) was added and the mixture was stirred until the imidazole was dissolved. Then, a solution of *tert*-butyldimethylsilyl chloride (53.55g, 1.1 eq, 0.36 mol) in 100mL of dry dichloromethane was added over a period of 30 min via dropping funnel. After stirring overnight at room temperature, the excess of silyl chloride was quenched with 50mL of methanol and the mixture was stirred for 20 min at room temperature.
Thereafter, 300 mL of dichloromethane was removed in vacuo to reduce the solvent volume and the remaining solution was washed with 200 mL of saturated aqueous $NaHCO_3$ (2x) and one time with brine. The organic layer was dried over Na_2SO_4 and concentrated to yield 107 g (95%) of **[4]** as a pale yellow oil.

$[\alpha]_D^{20}$ = -51.9° (c = 3.695, $CHCl_3$).

^{1}**H-NMR** (270 MHz, $CDCl_3$):

7.35-7.30 (m, 5H), 4.38 (m, 1H; H-4), 3.88 (d, 1H, H-6, ^{2}J (H,H) = 13 Hz), 3.61 (s, 1H; OMe), 3.56 (d, 1H, H-6, ^{2}J (H,H) = 13 Hz), 3.50 (dd, 1H, H-2, ^{3}J (H,H) = 8 Hz, ^{3}J (H,H) = 8 Hz), 3.23 (dd, 1H, H-5, ^{3}J (H,H) = 10 Hz, ^{3}J (H,H) = 6 Hz), 2.33 (dd, 1H, H-5, ^{3}J (H,H) = 10 Hz, ^{3}J (H,H) = 5 Hz), 2.16 (m, 1H; H-3), 2.00 (ddd, 1 H, H-3, ^{2}J (H,H) = 13 Hz, ^{3}J (H,H) = 8 Hz, ^{3}J (H,H) = 4Hz), 0.84 (s, 9H; Si-$C(CH_3)_3$), 0.00 (s, 3H; Si-CH_3), -0.01 (s, 3H; Si-CH_3).

^{13}**C-NMR** (62.9 MHz, $CDCl_3$):

174.2 (s, C=O), 138.0 (s, C-7) 129.1 (d, C-9), 128.1 (d, C-10), 127.1 (d, C-8), 70.4 (d, C-4), 64.3 (d, C-2), 61.6 (t, C-5), 59.3 (t, C-6), 51.8 (q, OCH_3), 39.5 (t, C-3), 25.7 (q, Si-$C(CH_3)_3$), 17.9 (s, Si-$C(CH_3)_3$), - 4.5 (q, Si-CH_3), - 4.9 (q, Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3063 (s), 3028 (s), 2953 (s), 2929 (s), 2897 (s), 2856 (m), 2801 (m), 1750 (s, C=O), 1495 (m), 1471 (m), 1459 (m), 1437 (m).

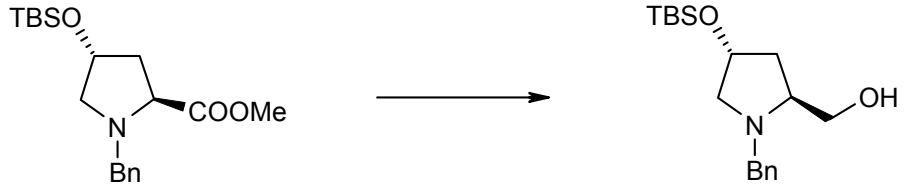
MS (70eV, EI, 60 °C):

m/z (%): 349 (2) [$M^{+\cdot}$], 334 (3) [M^{+} - CH_3], 290 (100) [M^{+} - COOMe], 158 (10) [$C_{11}H_{12}N^{+}$], 91 (80) [$C_7H_7^{+}$].

HRMS (80eV,60 °C): found 349.20996 calc. 349.207323 (for $C_{19}H_{31}NO_3Si$).

$\mathbf{R}_f$ = 0.5 (hexane / ethyl acetate 2:1), black (Schlittler's reagent).

2*S*,4*R*-(N-Benzyl)-4-*tert*-butyldimethylsilyloxy-prolinol [5]



[4] 349.55 [$C_{19}H_{31}NO_3Si$] **[5]** 321.54 [$C_{18}H_{31}NO_2Si$]

In a 2-L, three-necked round-bottom flask, fitted with a dropping funnel, mechanical stirrer and an internal thermometer, the silylprotected amino ester **[4]** (106.9 g, 0.305 mol) was dissolved in 400 mL of dry THF. Then, 0.447 L (2.2 eq, 0.67 mol) of DIBALH (1.5 M in toluene) was slowly added (the internal temperature was kept below 10 °C) with ice-cooling. The reaction mixture was stirred

overnight at room temperature. Then, the excess of DIBALH was quenched by a slow addition of 100 mL of methanol with ice-cooling. After completion of the hydrolysis, the reaction mixture was poured onto ice. The obtained aluminium hydroxide precipitates were treated with sodium potassium tartrate and saturated aqueous $NaHCO_3$ until all solids were dissolved. After warming to room temperature, 400 mL of diethyl ether was added and the layers were separated. The aqueous layer was divided into 3 parts and each part was extracted with 150 mL of diethyl ether (3x). The combined organic layers were dried with brine and Na_2SO_4 and after evaporation of the solvents, 87g (89%) of prolinol **[5]** were obtained as a clear colourless oil.

$[\alpha]_D^{20}$ = - 44.0° (c = 0.695, $CHCl_3$).

^{1}**H-NMR** (270 MHz, $CDCl_3$):
7.25-7.30 (m, 5H), 4.25 (m, 1H; H-4), 3.95 (d, 1H, H-6, ^2J (H,H) = 13 Hz), 3.63 (dd, 1H, H-11, ^2J (H,H) = 11 Hz, ^3J (H,H) = 3Hz), 3.46 (d, 1H, H-6, ^2J (H,H) = 13 Hz), 3.36 (dd, 1H, H-11, ^2J (H,H) = 11 Hz, ^3J (H,H) = 2 Hz), 3.12 (dd, 1H, H-5, ^2J (H,H) = 10 Hz, ^3J (H,H) = 5 Hz), 3.06 (m, 1H; H-2), 2.6-2.8 (s broad, 1H; OH), 2.35 (dd, 1H, H-5, ^3J (H,H) = 10 Hz, ^3J (H,H) = 6 Hz), 2.06 (m, 1H; H-3), 1.81 (ddd, 1 H, H-3, ^2J (H,H) = 13 Hz, ^3J (H,H) = 9 Hz, ^3J (H,H) = 5Hz), 0.85 (s, 9H; Si-C$(CH_3)_3$), 0.01 (s, 3H; Si-CH_3), 0.00 (s, 3H; Si-CH_3).

^{13}**C-NMR** (62.9 MHz, $CDCl_3$):
139.0 (s, C-7) 128.6 (d, C-9), 128.3 (d, C-10), 127.0 (d, C-8), 70.6 (d, C-4), 63.3 (d, C-2), 62.1 (t, C-5), 61.0 (t, C-11), 58.7 (t, C-6), 37.7 (t, C-3), 25.7 (q, Si-C$(CH_3)_3$), 17.9 (s, Si-C$(CH_3)_3$), - 4.8 (q, Si-CH_3).

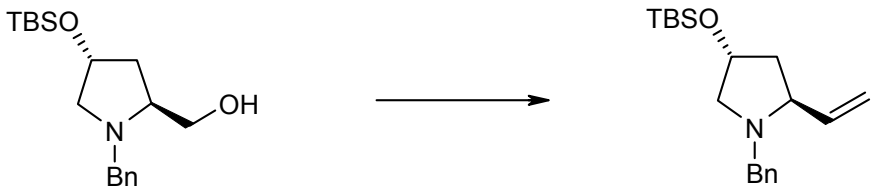
IR (KBr):
υ (cm^{-1}) = 3422 (m), 3063 (s), 3028 (s), 2954 (s), 2928 (s), 2885 (s), 2856 (s), 2803 (s), 1495 (m), 1471 (m), 1453 (m), 1437 (m), 1256 (s), 1112 (s), 1052 (s), 836 (s), 776 (s), 757 (s).

MS (70eV, EI, 60 °C):
m/z (%): 321 (2) [$M^{+\cdot}$], 306 (7) [M^+ - CH_3], 290 (100) [M^+ - CH_2OH], 158 (24) [$C_{11}H_{12}N^+$], 91 (99) [$C_7H_7^+$].

HRMS (80eV,60 °C): found 321.21255 calc. 321.212408 (for $C_{18}H_{31}NO_2Si$).

$\mathbf{R}_f$ = 0.4 - 0.5 (hexane / ethyl acetate 1:1), black (Schlittler's reagent), brown (Ninhydrine reagent).

2*S*,4*R*-(N-Benzyl)-4-*tert*-butyldimethylsilyloxy-2-vinyl pyrrolidine [6]



[5] 321.54 [$C_{18}H_{31}NO_2Si$] **[6]** 317.55 [$C_{19}H_{31}NOSi$]

(a) Swern reaction :

In a 2 l, three-necked round-bottom flask fitted with a dropping funnel, mechanical stirrer and an internal thermometer, 47.2 mL (2 eq, 0.54mol, 68.7g) of oxalyl chloride (freshly distilled, d = 1.455) was dissolved in 500 mL of dry dichloromethane (dried over CaH_2). The solution was cooled to -78 °C and a solution of dry dimethylsulfoxide (39.4 mL, 2.05 eq, 0.554 mol, 43.3 g) in 50 mL of dry dichloromethane was slowly added under argon. The internal temperature during the addition was kept below -70 °C. After complete addition, the mixture was stirred for 1 h at -60 °C. Then, the reaction mixture was cooled to -78 °C and a solution of prolinol **[5]** (87.0 g, 0.271 mol) in 50 mL of dry dichloromethane was slowly added. After stirring the reaction mixture for 2 h at -60 °C, 339 mL (9 eq, 2.43 mol) of triethylamine (d = 0.726) was slowly added and the reaction mixture was maintained for 2 h at -45 °C until TLC control showed complete conversion. The cooling bath was removed and after warming to room temperature, the suspension was treated with 150 mL of saturated $NaHCO_3$ solution. The layers were separated and the organic layer was washed with saturated aqueous $NaHCO_3$ (2x) and with brine (1x).

After drying over Na_2SO_4 (1 h stirring), the solids were removed by filtration and the solvent was evaporated to yield the crude aldehyde as a red oil which was used without further purification. The crude aldehyde could be stored at -78 °C for several days without epimerisation.

(b) Wittig reaction:

In a 2 l, three-necked round-bottom flask fitted with a dropping funnel, mechanical stirrer and an internal thermometer, 144.9 g (1.5 eq, 0.406 mol) of dry methyltriphenylphosphonium bromide was suspended in 1 L of dry THF. The mixture was cooled to -78 °C and 253.5 mL of butyl lithium (1.6 M in n-heptane) was slowly added under argon. After stirring for 2 h at -78 °C, the deep red coloured solution was transferred via a teflon tube (3mm diameter) to a cooled solution (-78 °C) of the crude aldehyde in dry THF (300 mL). The red solution changed the colour to brown and a precipitation of triphenylphoshine oxide occurred. The reaction mixture was allowed to reach room temperature overnight with continuous stirring.

Then, the reaction mixture was quenched with 200 mL of saturated aqueous $NaHCO_3$ and the triphenylphosphine oxide completely dissolved. The layers were separated and the organic layer was

washed one time with 200 mL of saturated $NaHCO_3$ solution. The combined organic layers were dried over Na_2SO_4 and the solvent was removed. During the evaporation of the solvent, the triphenylphosphine oxide precipitated. The remaining solid was taken up in diethyl ether and the triphenylphosphine oxide was removed by filtration and washed with ether until a white colour of the crystals indicated the complete exclusion of the vinyl pyrrolidine. This procedure was repeated with the mother liquor until the reaction product was a crystal-free brown oil.
The crude reaction product was purified with flash chromatography (eluent n-hexane / ethyl acetate 2:1 + 3% triethylamine) yielding the vinyl pyrrolidine **[6]** (58.7g, 69%) as a yellow oil.

$[\alpha]_D^{20}$ = -55.1° (c = 0.83, $CHCl_3$).

^{1}**H-NMR** (270 MHz, $CDCl_3$):
7.25-7.30 (m, 5H), 5.7 (ddd, 1H, H-11, ^3J (H^{11},H^{12b}) = 18 Hz, ^3J (H^{11},H^{12a}) = 10Hz, ^3J (H^{11},H^{2u}) = 8Hz), 5.22 (dd, 1H, H-12b, ^3J (H^{12b},H^{11}) = 18 Hz, ^2J (H^{12b},H^{12a}) = 2Hz), 5.13 (dd, 1H, H-12a, ^3J (H^{12a},H^{11}) = 10 Hz, ^2J (H^{12a},H^{12b}) = 2Hz), 4.30 (m, 1H; H-4o), 4.00 (d, 1H, H-6, ^2J (H^6,$H^{6'}$)= 12Hz), 3.1-3.22 (m, 3H; H-6',H-2u, H-5o); 2.11 (dd, 1H, H-5u, ^2J (H^{5u},H^{5o}) = 10 Hz, ^3J (H^{5u},H^{4o}) = 6 Hz), 1.80-1.91 (m, 2H; H-3o, H-3u), 0.84 (s, 9H; Si-C(CH_3)$_3$), 0.00 (s, 3H; Si-CH_3), - 0.02 (s, 3H; Si-CH_3).

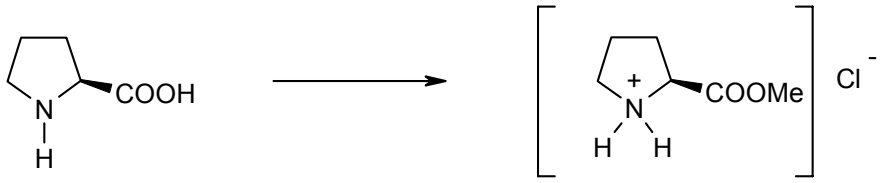
^{13}**C-NMR** (62.9 MHz, $CDCl_3$):
140.52 (d, C-11), 139.3 (s, C-7) 128.8 (d, C-9), 128.5 (d, C-10), 126.7 (d, C-8), 116.8 (t, C-12), 70.1 (d, C-4), 66.7 (d, C-2), 62.3 (t, C-5), 57.9 (t, C-6), 42.4 (t, C-3), 29.7 (q, Si-C(CH_3)$_3$), 18.1 (s, Si-C(CH_3)$_3$), - 4.8 (q, Si-CH_3).

IR (KBr):
υ (cm^{-1}) = 3063 (s), 3028 (s), 2954 (s), 2928 (s), 2856 (s), 2796 (s), 1643 (w), 1605 (w), 1495 (m), 1471 (s), 1255 (s), 1119 (s), 1050 (s), 913 (s), 836 (s), 776 (s), 698 (s).

MS (70eV, EI, 40 °C):
m/z (%): 317 (27) [$M^{+\cdot}$], 302 (4) [M^+ - CH_3], 290 (13) [M^+ - CH = CH_2], 260 (12) [M^+ - C_4H_9], 226 (27) [M^+ - CH_2Ph], 206 (8), 159 (70) [$C_{11}H_{13}N^+$], 91 (100) [$C_7H_7^+$].

HRMS (80eV,40 °C): found 317.21655 calc. 317.217493 (for $C_{19}H_{31}NOSi$).

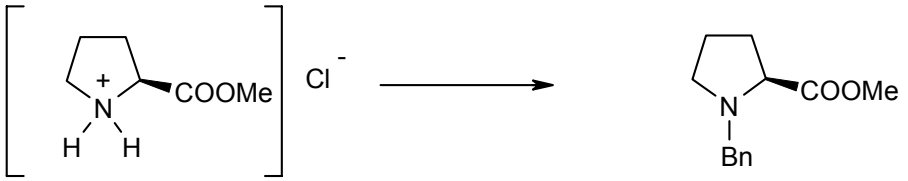
2*S*-Proline methyl ester hydrochloride [8]



[7] 115.13 [$C_5H_9NO_2$] **[8]** 165.62 [$C_6H_{12}ClNO_2$]

To a suspension of 2*S*-proline **[7]** (100 g, 0.87 mol) and 600 mL of methanol in a 2 L three-necked flask was carefully added acetyl chloride (92.6 mL, 1.5 eq, 1.30 mol, d = 1.105). After complete addition, the mixture was refluxed for 8 hours and then the solvent was removed in vacuo to yield 171g (100%) of 2*S*-proline methyl ester hydrochloride **[8]** as a colourless oil.
All spectroscopic datas were identical to prior descriptions.[255]

2*S*-(N-Benzyl)-hydroxyproline methyl ester [9]



[8] 165.62 [$C_6H_{12}ClNO_2$] **[9]** 219.29 [$C_{13}H_{17}NO_2$]

To a solution of proline methyl ester hydrochloride **[8]** (171.4 g, 0.87 mol) in 700 mL of dichloromethane (dried over Al_2O_3) in a 2 l, three-necked round-bottom flask fitted with a dropping funnel, mechanical stirrer and a reflux condenser, 242.1 mL (2eq, 1.74 mol, d = 0.726) of freshly distilled triethylamine and 200.0 mL (2eq, 1.74 mol, d = 1.098) of benzyl chloride was added. The reaction mixture was refluxed for 7 h and a pale yellow precipitation of the amine hydrochloride was formed.
After cooling to room temperature, the solvent and the excess triethylamine was completely removed under reduced pressure and then 300 mL of water was added. This solution was adjusted to a pH-value between 1 and 2 with 20% HCl. Thereafter, the mixture was extracted with 300 mL of diethyl ether (3x) to separate unreacted benzyl chloride from the product hydrochloride, dissolved in the aqueous layer. Then, 1 M aqueous NaOH (approx. 800 mL) was added to the aqueous layer until pH 11 was reached and the mixture was extracted with diethyl ether (3x). The organic layer, dried over Na_2SO_4 and evaporated, gave 155.9 g (82%) of N-benzylproline methyl ester **[9]** as a yellow oil.

[255] A. Scherrmann, Diploma Thesis, Berlin 1997

^{1}H-NMR (270 MHz, $CDCl_3$):

7.30 (m, 5H), 3.86 (d, 1H, N-Bn), 3.67 (s, 3H), 3.54 (d, 1H, N-Bn), 3.24 (m, 1H, H^2), 3.05 (m, 1H, $H^{5'}$), 2.38 (dd, 1H, H^5), 1.70-2.23 (m, 4H).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

174.42 (s), 138.12 (s), 129.10 (d), 128.02 (d), 126.96 (d), 65.14 (d), 58.62 (t), 53.13 (t), 51.55 (q), 29.21 (t), 22.82 (t).

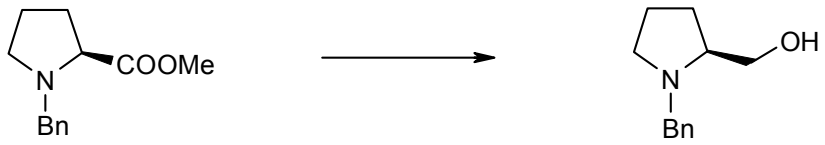
IR (KBr):

υ (cm^{-1}) = 2950 (m), 2798 (m), 1748 (s), 1733 (s), 1377 (m), 1198 (s), 1171 (s), 7447 (m), 699 (s).

MS (80 eV, EI, 40 °C): m/z (%) = 219 M^+ (6), 160 (100), 91 (83), 65 (6).

$\mathbf{R_f}$ = 0.55 (hexane / ethyl acetate 1:1), black (Schlittler's reagent).

2*S*-(N-Benzyl)-prolinol [10]



[9] 219.29 [$C_{13}H_{17}NO_2Si$] **[10]** 191.28 [$C_{12}H_{17}NO$]

In a 2-L, three-necked round-bottom flask fitted with a dropping funnel, magnetical stirrer and an internal thermometer, a solution of aminoester **[9]** (155.9 g, 0.71 mol) was dissolved in 600 mL of dry THF. Then, 20.0 g (1.3 eq, 0.92 mol) of $LiBH_4$ was added. After stirring for 2 days at 4 °C, the mixture was hydrolysed first with 100 mL of methanol then with 50 mL of water and stirred for 30 min. Then, the mixture was acidified with aqueous HCl until pH 1 was reached (at least 1 h reaction time for the dissolution of the borane-amine complexes).[256] The aqueous layer was extracted with diethyl ether (2x) and the boronic esters were removed from the aqueous layer (TLC control).[257] After separation, the acid aqueous layer was adjusted to pH 11 with 1 M aqueous NaOH and extracted three times with 150 mL of diethyl ether. The combined organic layers were dried with brine and Na_2SO_4 and the solvents were removed to yield 99.6 g (73%) of prolinol **[10]** as a clear colourless oil.

[256] At large scale reactions it could be advantageous to remove the THF before the acid treatment, since the hydrolysis of the borane-amine complexes appeared to be inhibited by large amounts of THF.

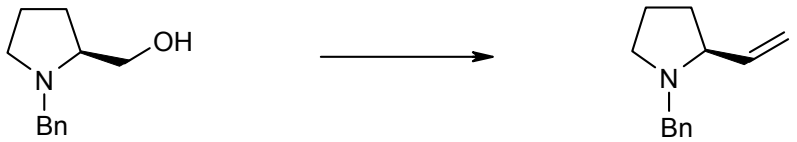
[257] With the intention to increase the yield, it was found to be necessary to extract the ethereal layer again with 20% aqueous HCl to destroy the remaining borane-amine complexes and to dissolve the product amine in the aqueous layer. The evolvement of gas shows the presence of non-hydrolysed B-H compounds.

^{1}H-NMR (270 MHz, $CDCl_3$):

7.30 (m, 5H), 3.96 (d, 1H, N-Bn), 3.60 (dd, 1H), 3.41 (dd, 1H), 3.32 (d, 1H), 2.96 (m, 1H), 2.71 (m, 1H), 2.26 (m, 1H), 1.60 - 2.00 (m, 4H).

R_f = 0.1 (hexane / ethyl acetate 1:1), black (Schlittler's reagent), brown (Ninhydrine reagent).

2*S*-(N-Benzyl)-2-vinyl pyrrolidine [11]



[10] 191.28 [$C_{12}H_{17}NO$] **[11]** 187.29 [$C_{13}H_{17}N$]

(a) Swern reaction :

In a 2 l, three-necked round-bottom flask fitted with a dropping funnel, mechanical stirrer and an internal thermometer, 89.88 mL (2 eq, 1.042 mol, 132.2 g) of freshly distilled oxalyl chloride (d = 1.455) was dissolved in 600 mL of dry dichloromethane. The solution was cooled to -78 °C and a solution of dimethylsulfoxide (75.8 mL, 2.05 eq, 1.067 mol, 83.4 g) in dry dichloromethane (50mL) was slowly added under argon. The internal temperature during this addition was kept below -70 °C. After complete addition, the mixture was stirred for 3 h at -60 °C. Then, the reaction mixture was cooled to -78 °C and a solution of prolinol **[10]** (99.6 g, 0.521 mol) in 50 mL of dry dichloromethane was slowly added. After stirring the reaction mixture for 2 h at -45 °C, 266 mL (5 eq, 2.60 mol) of triethylamine (d = 0.726) was slowly added and the reaction mixture was maintained for 1.5 h at -20 °C until TLC control showed complete conversion. The cooling bath was removed and after warming to room temperature, the suspension was treated with 300 mL of saturated $NaHCO_3$ solution. The layers were separated and the organic layer was washed two times with saturated $NaHCO_3$ and one time with brine.

After drying over Na_2SO_4 (1 h stirring), the solids were removed by filtration and the solvent was evaporated to yield the crude aldehyde as a red oil which was used without further purification. The crude aldehyde could be stored at -78 °C for several days without epimerisation.

(b) Wittig reaction:

In a 2 l, three-necked round-bottom flask fitted with a dropping funnel, mechanical stirrer and an internal thermometer, 223.5 g (1.2 eq, 0.625 mol) of dry methyltriphenylphosphonium bromide was suspended in 600 mL of dry THF. The mixture was cooled to -60 °C and 391 mL of butyl lithium (1.6 M in n-heptane) was slowly added under argon, keeping the internal temperature below -50 °C. After

stirring for 3.5 h at temperatures between -60 °C and -45 °C, a solution of the crude aldehyde in 200 mL of THF was added via the dropping funnel. The reaction mixture was allowed to reach room temperature overnight with continuous stirring.

Then, the reaction mixture was quenched with 300 mL of water and the triphenylphosphine oxide completely dissolved. The layers were separated and the organic layer was washed three times with 300 mL of water. The combined organic layers were dried over Na_2SO_4 and the solvent was removed. During the evaporation of the solvent, the triphenylphosphine oxide precipitated. The remaining solid was suspended in diethyl ether and the triphenylphosphine oxide was removed by filtration. The crude reaction product was purified by bulb-to-bulb distillation (bp 100 °C / 0.02 mbar) yielding 67.7 g (69%) of vinyl pyrrolidine **[11]** as a colourless oil.

^{1}H-NMR (270 MHz, $CDCl_3$):

7.30 (m, 5H), 5.75 - 5.85 (m 1H), 5.12 - 5.28 (m, 2H), 4.05 (d, 1H), 3.08 (d, 1H), 2.95 (m, 1H), 2.78 (m, 1H), 2.15 (m, 1H), 1.60 - 1.05 (m, 4H).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

140.92 (d), 139.37 (s), 128.93 (d), 128.05 (d), 126.65 (d), 116.55 (t), 68.42 (d), 58.03 (t), 53.21 (t), 31.38 (t), 21.91 (t).

R_f = 0.6 (hexane / ethyl acetate 1:1), black (Schlittler's reagent), brown (Ninhydrine reagent).

3.3 Preparation of Acid Fluorides

Chloroacetyl fluoride

In a 500 mL round-bottom Teflon flask equipped with a Teflon condenser, thoroughly ground KF*HF (30 g, 0.38 mol) was added to 48.0 g (0.43 mol) of chloroacetyl chloride. The mixture was heated for 1 h at 60 °C bath temperature. Thereafter, temperature of the bath was raised up to 100 °C and the chloroacetyl fluoride (bp 75-78 °C) was slowly distilled off over a period of 3 - 4 hours. Thus, 28.1 g (69%) of pure chloroacetyl fluoride were obtained as colourless liquid. The chloroacetyl fluoride could be stored without decomposition in a PFA flask at -20 °C for several months.

^{1}H-NMR (270 MHz, $CDCl_3$):
4.25 (d, 2H, ^{3}J (^{1}H,^{19}F) = 1 Hz).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
160.1 (d, C=O, ^{1}J (^{13}C,^{19}F) = 356.5 Hz), 38.6 (dt, C-2, ^{2}J (^{13}C,^{19}F) = 76.9 Hz).

Benzyloxyacetyl fluoride

A solution of benzyloxyacetic acid (3 g, 18 mmol) in dry CH_2Cl_2 (20 mL) was treated with dry pyridine (0.72 mL, 0.72 g, 9 mmol) at room temperature. After stirring for 10 min, cyanuric fluoride (0.77 mL, 1.22 g, 9 mmol) was slowly added. After a few minutes, a white solid precipitated. The mixture was stirred for additional 2 h at room temperature. Then, the precipitate was removed by filtration and the solvent was evaporated. The residue was dissolved in dry toluene and the mixture was stored at -20 °C for 10 min to precipitate a further amount of white cyanuric acid salts. After a final filtration and removal of the solvent, 2.88 g (95%, 17.1 mmol) of pure benzyloxyacetyl fluoride was isolated as a clear oil.

^{1}H-NMR (270 MHz, $CDCl_3$):
7.40-7.20 (m, 5 H), 4.65 (s, 2 H), 4.25 (d, 2H, ^{3}J (^{1}H,^{19}F) = 3.4 Hz).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
163.1 and 157.7 (d, ^{1}J (^{19}F,^{13}C) = 366 Hz, CO), 136.1 (s), 128.6 (d), 128.4 (d), 128.1 (d), 73.4 (t), 64.45 (dd, ^{2}J (^{19}F,^{13}C) = 71 Hz).

Phenylacetyl fluoride

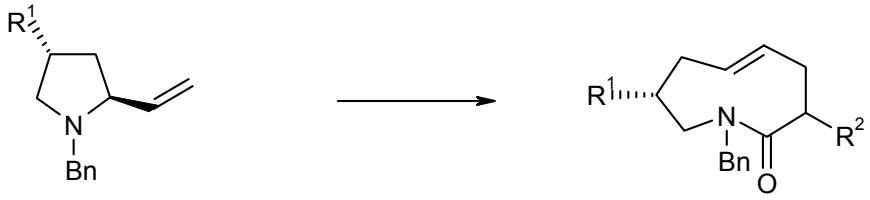
Phenylacetic acid (5g , 36.7 mmol) was dissolved in 50 mL of anhydrous dichloromethane at 0 °C. Then, pyridine (1.48 g, 1.5 mL, 18.7 mmol) and cyanuric fluoride (2.47 g, 1.56 mL, 18.3 mmol) were added and soon after the addition, a white precipitate occurred. The mixture was stirred for additional 2 h at 0 °C, then 50 mL of hexane was added and the solids were filtered off. The solvents were carefully removed to yield 4.96 g (98%) of carboxylic acid fluoride, which was pure enough for further transformations.

^{1}H-NMR (270 MHz, $CDCl_3$):
7.50- 7.20 (m, 5H), 3.84– 3.80 (d, 1H, ^{3}J (^{1}H,^{19}F) = 2.4 Hz).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
161.3 (CO, d, ^{1}J (^{13}C,^{19}F) = 361 Hz), 130.7 (s), 129.2 (d), 128.8 (d), 127.9 (d), 38.8 (t, CH_2, ^{2}J (^{13}C,^{19}F) = 53.7 Hz).

3.4 Aza-Claisen Rearrangements

Standard Procedure for the Zwitterionic Aza-Claisen Rearrangement



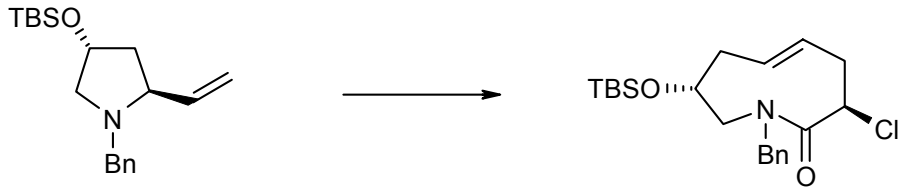
[6,11]

Under argon, dry K_2CO_3 (0.5 mmol) was suspended in dry CH_2Cl_2 (15 mL) and cooled to 0 °C. N-allylpyrrolidine **[6,11]** (1 mmol) and acid fluoride (3 to 6 mmol) were added subsequently by means of a syringe. After 15 min of stirring at 0 °C, Me_3Al (1.5-3 mmol, 2 M in n-heptane)[258] was added with a syringe and a methane evolvement started immediately.

The mixture was stirred at 4 °C until TLC showed completed reaction. The reaction was completed within hours (R^2 = Cl, Ph) or 1 to 2 days (R^2 = OBn). In several attempts, the addition of a second amount of acid fluoride and Me_3Al was necessary, to achieve a complete conversion of the reactant into the product. The workup was started by dilution of the reaction mixture with diethyl ether and filtration through a short silica gel column to remove the polar impurities. The residual organic layer was washed with saturated aqueous $NaHCO_3$ and dried (Na_2SO_4). The solvent was removed below 20 °C to isolate the *pS*-lactams **[12a]-[14a]**, heating to 40-60 °C led to a fast epimerisation to give the *pR*-lactams **[12b]-[14b]**. The crude products were purified by column chromatography. If necessary, the planar diastereomers were separated via HPLC or column chromatography on silica gel. The *pS*-lactams **[12a]-[14a]** could be stored at -20 °C without a significant epimerisation for several weeks. The crystals of **[12a]** were found to be stable even at room temperature for several days.

[258] The use of n-heptane solutions of Me_3Al in contrast to the likewise commercially available toluene preparations prevented the formation of acylated aromatic compound.

(*pS*)*E*-3*R*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-chloro-2,3,4,7,8,9-hexahydro-1H-azonin-2-one [12a]



[6] 317.55 [$C_{19}H_{31}NOSi$] **[12a]** 394.03 [$C_{21}H_{32}ClNO_2Si$]

Reaction of *anti*-vinyl pyrrolidine **[6]** (1g, 3.15 mmol) with chloroacetyl fluoride (1.5 ml), trimethylaluminium (2mL of 2 M in n-Heptane, 4 mmol) followed the standard procedure. The crude product was purified by column chromatography (SiO_2, n-hexane / ethyl acetate 3:1, $\mathbf{R_f = 0.38}$) to yield ***pS*-[12a]** as colourless crystals (1.14g, 92%) with mp = 116 °C.

$[\alpha]_D^{20}$ = -79.82° (c = 1.668, $CHCl_3$).

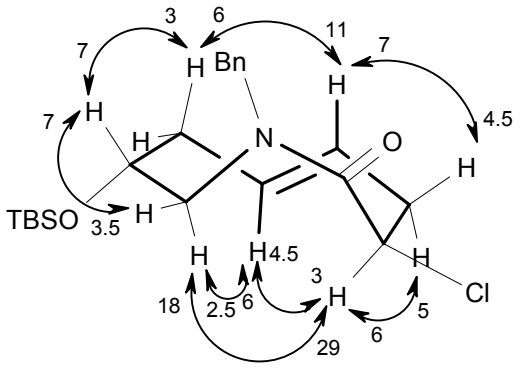
^{1}H-NMR (270 MHz, $CDCl_3$): [259]

7.25 (m, 5H), 5.76 (ddd, 1 H, H-6u, ^3J (H^{6u},H^{5o}) = 15 Hz, ^3J (H^{6u},H^{7o}) = 11 Hz, ^3J (H^{6u},H^{7u}) = 3 Hz), 5.44 (ddd, 1 H, H-5o, ^3J (H^{5o},H^{6u}) = 16 Hz, ^3J (H^{5o},H^{4}) = 9 Hz, ^3J (H^{5o},H^{4}) = 6 Hz), 5.05 (d, 1 H, CH_2-Ph, ^2J (H,H) = 14 Hz), 4.84 (dd, 1 H, H-3u, ^3J (H^{3u},H^{4o}) = 10 Hz, ^3J (H^{3u},H^{4u}) = 8 Hz), 4.17 (d, 1 H, CH_2-Ph, ^2J (H,H) = 15 Hz), 4.05 (m, 1H; H-8o), 3.55 (dd, 1 H, H-9u, ^2J (H^{9u},H^{9o}) = 16 Hz, ^3J (H^{9u},H^{8o}) = 10 Hz), 3.01 (dd, 1 H, H-9o, ^2J (H^{9o},H^{9u}) = 15 Hz, ^3J (H^{9o},H^{8o}) = 4 Hz), 2.90 (m, 1H; H-4u), 2.54 (ddd, 1 H, H-4o, ^2J (H^{4o},H^{4u}) = 17 Hz, ^3J (H^{4o},H^{3u}) = 10 Hz, ^3J (H^{4o},H^{5o}) = 6 Hz), 2.28 (m, 1H; H-7u), 2.09 (ddd, 1 H, H-7o, ^2J (H^{7o},H^{7u}) = 17 Hz, ^3J (H^{7o},H^{6u}) = 11 Hz, ^3J (H^{7o},H^{8o}) = 5 Hz), 0.81 (s, 9H; Si-$C(CH_3)_3$), -0.01 (s, 3H; Si-CH_3), -0.07 (s, 3H; Si-CH_3).

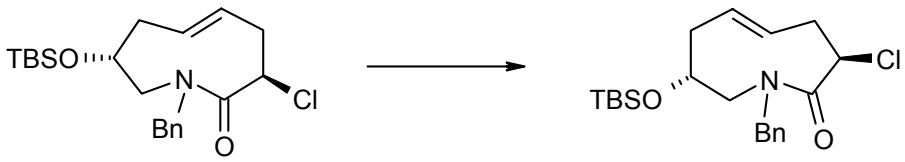
^{13}C-NMR (67.9 MHz, $CDCl_3$):

169.6 (s, C=O), 136.8, 131.2 (d, C-6), 130.7 (d, C-5), 128.5, 127.7, 66.3 (d, C-8), 55.2 (d, C-3), 51.6 (t, C-9), 49.3 (t, $\underline{C}H_2$-Ph), 39.0 (t, C-7), 36.9 (t, C-4), 25.5 (q, Si-$C(CH_3)_3$), 17.8 (s, Si-$C(CH_3)_3$), -4.9 (q, Si-CH_3), -5.1 (q, Si-CH_3).

[259] ^{1}H-NMR spectrum shows a minor conformation, saturation transfer during NOE measurement indicated a 99:1 ratio



***(pR)E*-3*R*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-chloro-2,3,4,7,8,9-hexahydro-1H-azonin-2-one [12b]**



[12a] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[12b]** 394.03 [$C_{21}H_{32}ClNO_2Si$]

Heating of azoninone **[12a]** for 4 h at 60 °C yielded conversion to **[12b]** with a ratio of 12b / 12a = 7:1. A sample of diastereomerically pure azoninone **[12b]** could be obtained by HPLC (12% ethyl acetate / n-hexane, Nucleosil 50-5, 240x32mm, flow 64mL/min).

$[\alpha]_D^{20}$ = -122.0° (c = 0.295, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.2-7.3 (m, 5H), 5.67 (ddd, 1 H, H-5u, ^3J (H^{5u},H^{6o}) = 16 Hz, ^3J (H^{5u},H^4) = 10 Hz, ^3J (H^{5u},H^4) = 6 Hz), 5.34 (ddd, 1H, H-6o, ^3J (H^{6o},H^{5u}) = 15 Hz, ^3J (H^{6o},H^{7u}) = 11 Hz, ^3J (H^{6o},H^{7o}) = 3 Hz), 5.22 (d, 1 H, CH_2-Ph, ^2J (H,H) = 15 Hz), 4.50 (dd, 1 H, H-3u, ^3J (H^{3u},H^{4o}) = 12 Hz, ^3J (H^{3u},H^{4u}) = 3 Hz), 4.09 (d, 1 H, CH_2-Ph, ^2J (H,H) = 15 Hz), 4.01 (m, 1H; H-8o), 3.62 (dd, 1 H, H-9u,^2J (H^{9u},H^{9o}) = 14 Hz, ^3J (H^{9u},H^{8o}) = 9 Hz), 2.97 (d, 1 H, H-9o,^2J (H^{9o},H^{9u}) = 14 Hz), 2.60-2.80 (m, 3H; H-4o, H-4u and H-7o), 2.02 (ddd, 1 H, H-7u, ^2J (H^{7u},H^{7o}) = 12 Hz, ^3J (H^{7u},H^{6o}) = 12 Hz, ^3J (H^{7u},H^{8o}) = 9 Hz), 0.81 (s, 9H; Si-$C(CH_3)_3$), 0.02 (s, 3H; Si-CH_3), 0.00 (s, 3H; Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

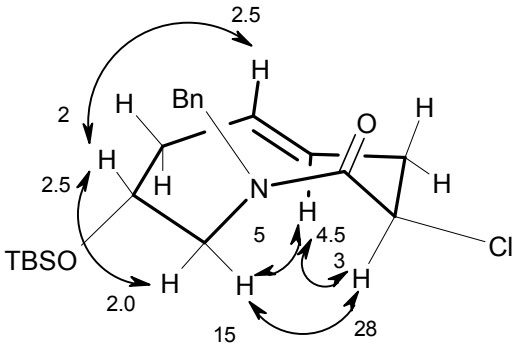
169.6 (s, C=O), 136.8 (s), 131.2 (d, C-6), 130.1 (d, C-5), 128.6 (d, C_{AR} meta), 127.9 (d, C_{AR} para), 127.6 (d, C_{AR} ortho), 69.5 (d, C-8), 56.2 (d, C-3), 54.3 (t, C-9), 49.7 (t, $\underline{C}H_2$-Ph), 42.8 (t, C-7), 40.1 (t, C-4), 25.6 (q, Si-$C(CH_3)_3$), 17.8 (s, Si-$C(CH_3)_3$), -4.5 (q, Si-CH_3), -4.9 (q, Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 2952 (s), 2929 (s), 2879 (s), 2856 (N-CH_2), 1644 (s, C=O), 1451 (m), 1421 (m), 1260 (m), 1225 (m), 1183 (m), 1099, 1084 (s), 840 (s), 778 (s).

MS (70eV, EI, 60 °C):

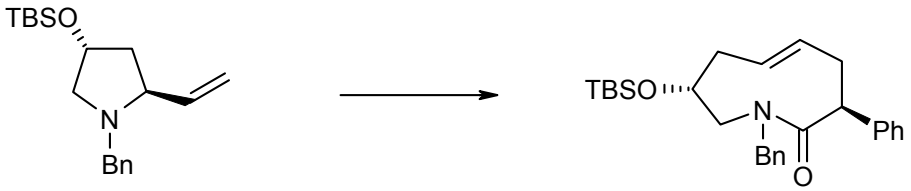
m/z (%): 393 (6) [$M^{+\cdot}$], 378 (2) [M^+ -CH_3], 358 (4) [M^+ -Cl], 336 (18) [M^+ -C_4H_9], 302 [M^+ -C_7H_7], 246 (14), 91 (100) [$C_7H_7^+$], 73 (45).



HRMS (80eV, 100 °C): found 393.18759

calc. 393.18909 (for $C_{21}H_{32}NO_2ClSi$).

***(pS)E*-3*S*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-phenyl-2,3,4,7,8,9-hexahydro-1H-azonin-2-one [13a]**



[6] 317.55 [$C_{19}H_{31}NOSi$] **[13a]** 435.69 [$C_{27}H_{37}NO_2Si$]

Reaction of vinyl pyrrolidine **[6]** (2.0 g, 6.29 mmol), phenylacetyl fluoride (2.61 g, 3 eq, 18.8 mmol) and Me_3Al (9.45 mL, 3 eq, 18.8 mmol) followed the standard procedure. After 1 h reaction time at 0 °C, no remaining vinyl pyrrolidine could be detected by TLC. Standard purification by filtration through silica gel and aqueous workup with $NaHCO_3$ yielded, after evaporation of the solvent, azoninone **[13a]** (2.28 g, 83%) as colourless oil, which crystallises storing at -20 °C. ^{1}H-NMR-spectroscopy showed that non of the thermodynamic isomer **[13b]** was formed during the reaction and the workup procedure.

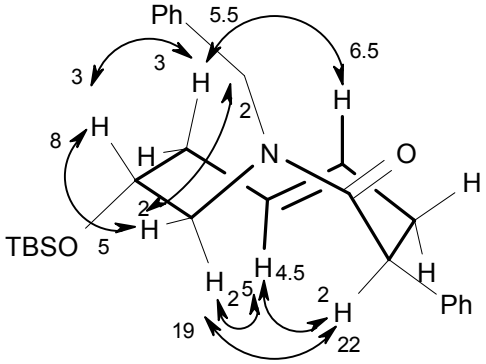
$[\alpha]_D^{20}$ = -80.67° (c = 1.4825, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$): [260]

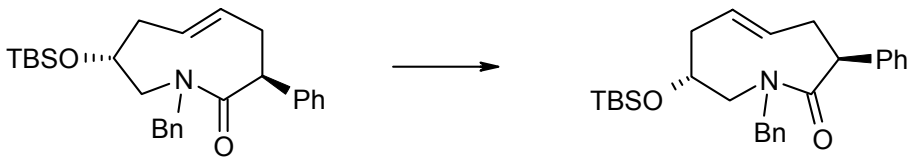
7.50 - 7.10 (m, 10H), 5.92-5.77 (m, 1 H; H-6u), 5.75-5.60 (m, 1 H; H-5o), 5.08-5.00 (d, 1 H, CH_2-Ph, ^2J (H,H) = 14 Hz), 4.30-4.22 (dd, 1 H, H-3u, ^3J (H^{3u},H^{4o}) = 10 Hz, ^3J (H^{3u},H^{4u}) = 8 Hz), 4.22-4.18 (d, 1 H, CH_2-Ph, ^2J (H,H) = 15 Hz), 4.15-4.10 (m, 1H; H-8o), 3.95-3.90 (dd, 1 H, H-9u, ^2J (H^{9u},H^{9o}) = 16 Hz, ^3J (H^{9u},H^{8o}) = 10 Hz), 3.10-3.00 (dd, 1 H, H-9o,^2J (H^{9o},H^{9u}) = 15 Hz, ^3J (H^{9o},H^{8o}) = 4 Hz), 2.70-2.60 (m, 2H; H-4u), 2.35-2.25 (dd, 1 H, H-7o, ^2J (H^{7o},H^{7u}) = 14 Hz, ^3J (H^{7o},H^{6u}) = 2 Hz), 2.22-2.10 (ddd, 1 H, H-7o, ^2J (H^{7o},H^{7u}) = 14 Hz, ^3J (H^{7o},H^{6u}) = 11 Hz, ^3J (H^{7o},H^{8o}) = 5 Hz), 0.81 (s, 9H; Si-$C(CH_3)_3$), -0.01 (s, 3H; Si-CH_3), -0.07 (s, 3H; Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

174.2 (s, C=O), 139.8 (q), 137.7 (q), 134.4 (d, C-6), 130.7 (d, C-5), 128.5, 127.7, 66.3 (d, C-8), 55.2 (d, C-3), 51.6 (t, C-9), 49.3 (t, $\underline{C}H_2$-Ph), 39.0 (t, C-7), 36.9 (t, C-4), 25.5 (q, Si-$C(CH_3)_3$), 17.8 (s, Si-$C(CH_3)_3$), - 4.9 (q, Si-CH_3), -5.1 (q, Si-CH_3).



***(pR)E*-3*S*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-phenyl-2,3,4,7,8,9-hexahydro-1H-azonin-2-one [13b]**



[13a] 435.69 [$C_{27}H_{37}NO_2Si$] **[13b]** 435.69 [$C_{27}H_{37}NO_2Si$]

Heating of azoninone **[13a]** for 4 h at 60 °C led to conversion into **[13b]**, the resulting ratio of 13b / 13a was 9:1. A sample of diastereomerically pure azoninone **[13b]** could be obtained by HPLC separation (ethyl acetate / n-hexane = 95:5, Nucleosil 50-5, 240x32mm, flow 64mL/min).

[260] According to NMR spectroscopy the compound consists of two conformers, presumably amide isomers (proven by transfer of magnetisation during the NOE measurement)

$[\alpha]_D^{20}$ = -165.1° (c = 0.57, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.2-7.3 (m,5H), 5.84 (ddd, 1 H, H-5u, ^3J (H^{5u},H^{6o}) = 16 Hz, ^3J (H^{5u},H^{4o}) = 11 Hz, ^3J (H^{5u},H^{4u}) = 5 Hz), 5.36 (ddd, 1 H, H-6o, ^3J (H^{6o},H^{5u}) = 16 Hz, ^3J (H^{6o},H^{7u}) = 12 Hz, ^3J (H^{6o},H^{7o}) = 4 Hz), 5.20 (d, 1 H, CH_2-Ph-o, ^2J (H,H) = 16 Hz), 4.15-3.95 (m, 3H; CH_2-Ph, H-8o and H-9o), 3.84 (dd, 1 H, H-9o, ^3J (H^{3u},H^{4o}) = 12 Hz, ^3J (H^{3u},H^{4u}) = 2 Hz, 1 H; H-3u), 3.04 (d,^2J (H,H) = 13 Hz), 2.81 (ddd, 1 H, H-4o, ^2J (H^{4o},H^{4u}) = 12 Hz, ^3J (H^{4o},H^{3u}) = 12 Hz, ^3J (H^{4o},H^{5u}) = 12 Hz), 2.75 (m, 1H; H-7o), 2.50 (dd, 1 H, H-4u, ^2J (H^{4u},H^{4o}) = 12 Hz, ^3J (H^{4u},H^{5u}) = 5 Hz), 2.08 (ddd, 1 H, H-7u, ^2J (H^{7u},H^{7o}) = 10 Hz, ^3J (H^{7u},H^{6o}) = 10 Hz, ^3J (H^{7u},H^{8o}) = 8 Hz), 0.84 (s, 9H; Si-C(CH_3)$_3$), 0.05 (s, 3H; Si-CH_3), 0.02 (s, 3H; Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

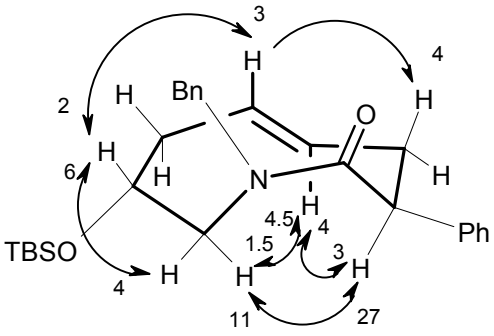
174.3 (s), 140.9 (s), 137.7 (s), 133.9 (d), 128.6 (d), 128.5 (d), 128.2 (d), 127.7 (d), 127.2 (d), 126.9 (d), 70.7 (d, C-8), 54.5 (d, C-3), 51.8 (t, C-9), 49.1 (t, $\underline{C}H_2$-Ph), 42.8 (t, C-7), 36.8 (t, C-4), 25.6 (q, Si-C(CH_3)$_3$), 17.8 (s, Si-C(CH_3)$_3$), -4.4 (q, Si-CH_3), -4.9 (q, Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3087 (m), 3063 (s), 3028 (s), 2953 (s), 2929 (s), 2887 (s), 2856 (s), 1775 (w), 1725 (w), 1637 (s), 1496 (s), 1451 (s), 1412 (s), 1255 (s), 1090 (s), 837 (s), 777 (s).

MS (70eV, EI, 60 °C):

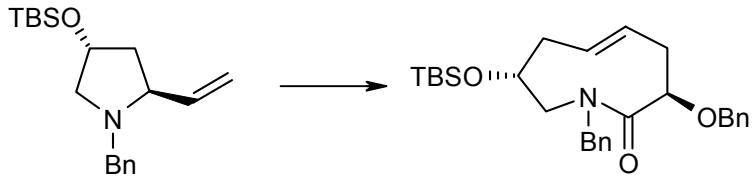
m/z (%): 435 (22) [$M^{+\cdot}$], 378 (32) [M^+ - C_4H_9], 344 (31) [M^+ -Bn], 330 (8), 290 (9), 197 (14), 184 (12), 118 (15), 91 (100), 73 (9).



HRMS (80eV,100 °C): found 435.25747

calc. 435.259358 (for $C_{27}H_{37}NO_2Si$).

(*pS*)*E*-3*R*,8*R*-1-Benzyl-3-benzyloxy-8-(*tert*-butyldimethylsilyloxy)-2,3,4,7,8,9-hexahydro-1H-azonin-2-one [14a]



[6] 317.55 [$C_{19}H_{31}NOSi$] **[14a]** 465.71 [$C_{28}H_{39}NO_3Si$]

A mixture of vinyl pyrrolidine **[6]** (1.0 g, 3.15 mmol), benzyloxyacetyl fluoride (1.93g, 1.7 mL, 3.6 eq, 11.5 mmol, d = 1.1) and 2 mL (4 mmol, 1.3 eq) of Me_3Al (2 M in n-heptane) was stirred for 8 h at 0 °C. Workup was carried out according to the standard procedure and purification by column chromatography on silica gel (n-hexane / ethyl acetate = 2:1, R_f = 0.65) yielded 0.96 g (~ 65%) of the crude azoninone **[14a]** together with a decomposition product of benzyloxyacetyl fluoride (presumably the fluoro-methyl exchange product). This crude oil was immediately used for further reactions to prevent the isomerisation to **[14b]**.

A sample of diastereomerically pure azoninone **[14a]** could be obtained by HPLC (isopropanol / n-hexane = 5:95, Nucleosil 50-5, 240x32mm, flow 64mL/min).

Azoninone **[14a]** consisted of at least three conformers [14a-1], [14a-2] and [14a-3] (ratio 12:4:1) that could not be separated via HPLC.

$[\alpha]_D^{20}$ = + 4.9° (c = 1.1, $CHCl_3$).

Major conformer [14a-1]

^{1}H-NMR (500 MHz, $CDCl_3$):

7.4 - 7.2 (m, 10H), 5.65 - 5.55 (ddd, 1H, H-6, *J* = 16, 11, 3 Hz), 5.41 - 5.33 (ddd, 1H, H-5, *J* = 16, 10, 6 Hz), 5.20 - 5.15 (d, 1H, N-Bn1, *J* = 14 Hz), 4.63 - 4.60 (d, 1H, OBn1, *J* = 12 Hz), 4.42 - 4.38 (dd, 1H, H-3, *J* = 8, 8 Hz), 4.33 - 4.30 (d, 1H, OBn-2, *J* = 12Hz), 4.08 - 4.05 (d, 1H, N-Bn2, *J* = 15 Hz), 4.03 - 3.99 (m, 1H, H-8), 3.43 - 3.35 (dd, 1H, H-9u, *J* = 15, 10 Hz), 2.88 - 2.82 (dd, 1H, H-9o, *J* = 15, 5 Hz), 2.75 - 2.68 (m, 1H, H-4u), 2.39 - 2.30 (m, 1H, H-4o), 2.27 - 2.20 (m, 1H, H-7u), 2.15 - 2.08 (ddd, 1H, H-7u, *J* = 13, 11, 6 Hz), 0.81 (s, 9H), -0.02 (s, 3H), -0.07 (s, 3H).

^{13}C-NMR (62.9 MHz, $CDCl_3$):

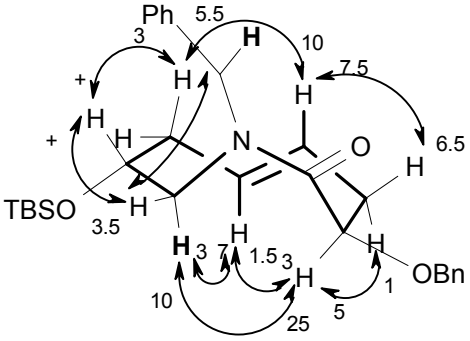
172.3 (s) , 140.0-126.0 (10C), 76.2 (d), 71.0 (t), 66.2 (d), 50.7 (t), 48.6 (t), 39.0 (t), 33.4 (t), 25.6 (q), 17.8 (s), - 4.8 (q), -5.0 (q).

Minor conformer (assignment as far as signals were detectable): **[14a-2]**

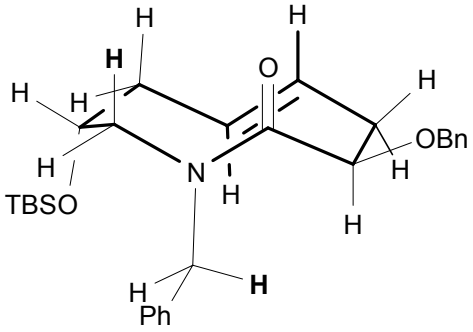
^{1}H-NMR (500 MHz, $CDCl_3$):

7.4 -7.2 (m, 10H), 5.89 - 5.82 (ddd, 1H, H-6, *J* = 16, 10, 5 Hz), 5.81 - 5.74 (ddd, 1H, H-5, *J* = 16, 10, 5 Hz), 5.41 - 5.35 (d, 1H, N-Bn1, *J* = 14 Hz), 4.65 - 4.62 (ddd, 1H, H-9o, *J* = 15, 1.4, 1.4 Hz), 4.63 - 4.60 (d, 1H, O-Bn1, *J* = 12 Hz), 4.57 - 4.55 (dd, *J* = 5, 2 Hz, 1H, H-3), 4.47 - 4.44 (d, 1H, N-Bn2, *J* = 15 Hz), 4.38 - 4.36 (m, 1H, H-8), 4.33 - 4.30 (d, 1H, O-Bn2, *J* = 12Hz), 3.31 - 3.28 (dd, 1H, H-9u, *J* = 15, 4 Hz), 2.60 - 2.55 (m, 1H, H-4o), 2.50 - 2.40 (m, 2H, H-7), 2.34 - 2.30 (m, 1H, H-7), 0.93 (s, 9H), 0.09 (s, 6H).

Major conformer

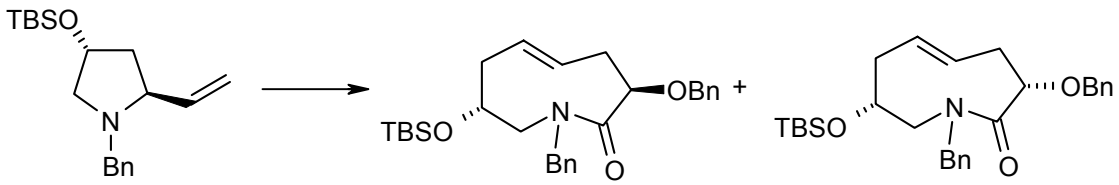


Minor conformer [261]



(*pR*)*E*-3*R*,8*R*-1-Benzyl-3-benzyloxy-8-(*tert*-butyldimethylsilyloxy)-2,3,4,7,8,9-hexahydro-1H-azonin-2-one [14b] and

(*pR*)*E*-3*S*,8*R*-1-Benzyl-3-benzyloxy-8-(*tert*-butyldimethylsilyloxy)-2,3,4,7,8,9-hexahydro-1H-azonin-2-one [15b]



[6] 317.55 [$C_{19}H_{31}NOSi$] **[14b]** 465.71 [$C_{28}H_{39}NO_3Si$] **[15b]** 465.71 [$C_{28}H_{39}NO_3Si$]

[261] the position of the protons in the spectrum could be determined by a magnetisation transfer during the NOE experiment of **[14a-1]** resulting from a fast chemical equilibration between **[14a-1]** and **[14a-2]**. The preliminary assignment of the 3-dimensional structure based on the structural correlations of the protons with the change of the characteristic ^{4}J-coupling between one H-9/N-Bn pair (proton pairs are printed in bold letter for a better visualisation) and the other one during the isomerisation. A third conformer could be observed but no structural assignment could be made due to its low concentration.

A mixture of vinyl pyrrolidine **[6]** (4.0 g, 12.6 mmol), benzyloxyacetyl fluoride (5.27 g, 2.5 eq, 31.3 mmol, d = 1.1) and 12 mL (24 mmol, 2 eq) of Me_3Al (2 M in n-heptane) was stirred 5d at room temperature. Workup was carried out according to the standard procedure and purification by flash column chromatography on silica gel (n-hexane / ethyl acetate = 2:1, R_f = 0.65) yielded 6.54 g of the crude azoninones **[14b]** and **[15b]**. Separation of this crude oil with HPLC (12% ethyl acetate / n-hexane, 32x110 mm Nucleosil 50-5, 64mL/min) yielded 2.0 g (34%) of **[14b]** and 0.18 g (3%) of **[15b]** as colourless oils.

Major diastereomer [14b]

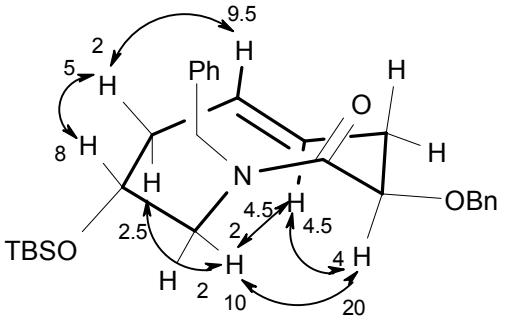
$[\alpha]_D^{20}$ = + 14.88° (c = 1.270, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
7.4 -7.2 (m, 10H; H-arom.H), 5.65 - 5.50 (m, 1H; H-5u), 5.40 - 5.20 (m, 2H; H-6o, NBn-1), 4.60 - 4.55 (d, 1H; H-OBn-1; ^2J (H^{OBn-1},H^{OBn-2}) = 12 Hz), 4.23 - 4.1.8 (d, 1H; H-OBn-2; ^2J (H^{OBn-2},H^{OBn-1}) = 12 Hz), 4.10 - 4.05 (d, 1H; H-NBn-2; ^2J (H^{NBn-2},H^{NBn-1}) = 15 Hz), 4.05 - 3.9 (m, 2H; H-8o, 3u), 3.60 - 3.50 (dd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 14 Hz, ^3J (H^{9u},H^{8o}) = 9 Hz), 2.95 - 2.88 (d, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 14 Hz), 2.78 - 2.66 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 11 Hz, ^3J (H^{7o},H) = 7 Hz, ^3J (H^{7o},H) = 4 Hz), 2.55 - 2.45 (m, 2H; H-4o, 4u), 2.05 - 1.92 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 12 Hz, ^3J (H^{7u},H) = 12 Hz, ^3J (H^{7u},H) = 8 Hz), 0.80 (s, 9H; H-Si (CMe_3)), 0.01 (s, 3H; H-Si-CH_3), 0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (62.9 MHz, $CDCl_3$):
171.6 (C=O), 137.5, 137.4, 130.2, 129.7, 128.5, 128.4, 128.2, 128.0, 127.7, 127.4, 76.7 (d, C-3), 71.1 (t, OBn), 69.4 (d, C-8), 53.7 (t), 49.0 (t), 42.8 (t), 36.8 (t), 25.6 (Si-C(CH_3)$_3$), 17.8 (Si-C(CH_3)$_3$), - 4.9 (Si-CH_3), -5.16 (Si-CH_3).

IR (KBr):
υ (cm^{-1}) = 3087 (w), 3063 (w), 3029 (w), 2925 (s), 2885 (s), 2857 (s), 1646 (s, N-CO), 1585 (w), 1495 (m), 1471 (s), 1452 (s), 1419 (s), 1374 (m), 1360 (m), 1253 (m), 1223 (m), 1118 (m), 1089 (s), 1029 (m), 1005 (m), 983 (m), 837 (s), 777 (s), 734 (s), 698 (s).

MS (70eV, EI, 130 °C):
m/z (%): 465 (7) [$M^{+\cdot}$], 450 (1), 408 (7) [M^{+} - C_4H_9], 374 (41), 359 (16), 320 (10), 302 (10), 290 (5), 267 (5), 242 (5), 91 (100), 73 (20).



HRMS (80eV, 130 °C): found. 465.26532
calc. 465.269923 (for $C_{28}H_{39}NO_3Si$).

Minor diastereomer [15b]

$[\alpha]_D^{20}$ = - 17.48° (c = 1.653, $CHCl_3$).

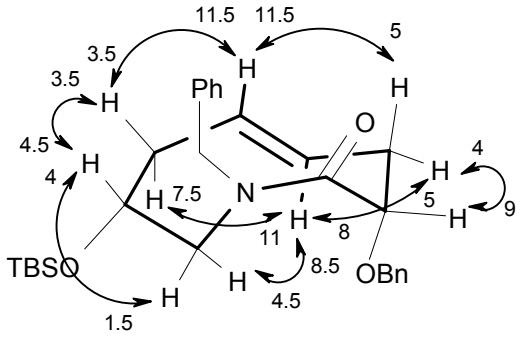
^{1}H-NMR (270 MHz, $CDCl_3$):
7.40 - 7.20 (m, 10H), 6.00-5.85 (ddd, 1H; H-5u; ^3J (H^{5u},H^{6o}) = 15.5 Hz, ^3J (H^{5u},H^{4o}) = 10 Hz, ^3J (H^{5u},H^{4u}) = 4 Hz), 5.43 - 5.30 (ddd, 1H; H-6o; ^3J (H^{6o},H^{5u}) = 15.5 Hz, ^3J (H^{6o},H^{7u}) = 12 Hz, ^3J (H^{6o},H^{7o}) = 3 Hz), 5.20 - 5.12 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 14.6 Hz), 4.78 - 4.68 (dd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 14.6 Hz, ^3J (H^{9u},H^{8o}) = 9.5 Hz), 4.60 - 4.55 (dd, 1H; H-3o; ^3J (H^{3o},H) = 5 Hz, ^3J (H^{3o},H) = 2 Hz), 4.50 - 4.45 (d, 1H; H-O-Bn1; ^2J ($H^{O\text{-}Bn1}$,$H^{O\text{-}Bn2}$) = 12 Hz), 4.38 - 4.32 (d, 1H; H-O-Bn2; ^2J ($H^{O\text{-}Bn2}$,$H^{O\text{-}Bn1}$) = 12 Hz), 4.08 - 4.02 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 14.6 Hz), 2.98 - 2.90 (d, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 14.6 Hz), 2.80 - 2.60 (m, 2H; H-7o, 4u), 2.40 - 2.30 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 11 Hz, ^3J (H^{4o},H^{5u}) = 11 Hz, ^3J (H^{4o},H^{3o}) = 2 Hz), 2.15 - 2.00 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 11 Hz, ^3J (H^{7u},H^{6o}) = 11 Hz, ^3J (H^{7u},H^{8o}) = 8 Hz), 0.90 (s, 9H; H-Si (CMe_3)), 0.06 (s, 3H; H-Si-CH_3), 0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (62.9 MHz, $CDCl_3$):
172.4 (s, CO), 137.9 (s), 137.1 (s), 132.1 (d), 129.1 (d), 128.5 (d), 128.4 (d), 128.1 (d), 127.8 (d), 127.7 (d), 127.3 (d), 87.6 (d), 71.9 (t), 71.3 (d), 53.5 (t), 50.3 (t), 43.0 (t), 34.6 (t), 25.6 (q, Si-$C(CH_3)_3$), 17.8 (s, Si-$C(CH_3)_3$), - 4.3 (q, Si-CH_3), - 4.8 (q, Si-CH_3).

IR (KBr):
υ (cm^{-1}) = 3085 (m), 3063 (m), 3031 (s), 2953 (s), 2929 (s), 2885 (s), 2857 (s), 1756 (m), 1620 (s), 1495 (m), 1471 (m), 1454 (m), 1436 (m), 1417 (m), 1330 (m), 1359 (m), 1250 (s), 1083 (s).

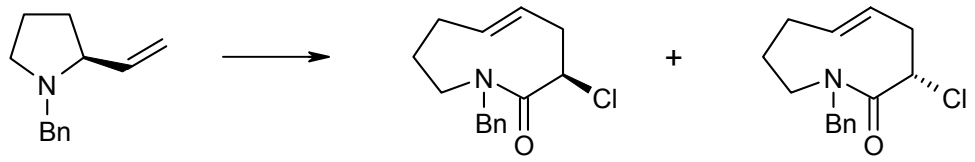
MS (70eV, EI, 130 °C):
m/z (%): 465 (7) [M^+], 408 (12) [M^+- C_4H_9], 374 (36), 359 (12), 320 (11), 302 (8), 91 (100), 73 (30).

HRMS (80eV,120 °C): found 465.26544
calc. 465.269923 (for $C_{28}H_{39}N_1O_3Si_1$ [M^+]).



(pS)E-3*R*-1-Benzyl-3-chloro-2,3,4,7,8,9-hexahydro-1H-azonin-2-one [16a] and

(*pS*)*E*-3*S*-1-Benzyl-3-chloro-2,3,4,7,8,9-hexahydro-1H-azonin-2-one [17a]



[11] 187.29 [$C_{13}H_{17}N$] **[16a]** 263.77 [$C_{15}H_{18}ClNO$] **[17a]** 263.77 [$C_{15}H_{18}ClNO$]

medium scale preparation :

In a 250 mL flask, a solution of vinyl pyrrolidine **[11]** (5.1 g, 27.2 mmol) in 100 mL of dry dichloromethane and of K_2CO_3 (1.88 g (0.5 eq, 13.6 mmol) was cooled with an ice-bath to -10 °C and under argon chloroacetyl fluoride (10.51 g, 4 eq, 7.62 mL, 0.108 mol, d = 1.3788) was added. Then, 27.3 mL (54.5 mmol, 2 eq) of Me_3Al (2 M in n-heptane)was slowly added, while the internal temperature was kept below 0 °C. After stirring overnight at 4 °C, the orange-brown suspension was slowly poured on 300 mL of diethyl ether. The precipitated aluminium salts were removed by filtration of the ethereal suspension trough silica gel. Then, the clear orange solution was washed intensively with a saturated aqueous $NaHCO_3$ and the aqueous layer was separated. After washing the organic layer with brine and drying over Na_2SO_4, the solvent was removed at temperatures <=20 °C to prevent isomerisation to the thermodynamic conformer **[16b]**. The resulting crude orange oil was purified by flash chromatography on silica gel (ethyl acetate / n-hexane = 1:1) and solvent was removed under reduced pressure. Separation of the crude product by HPLC (ethyl acetate / n-hexane = 15:85, flow 64 ml/min; 32x110 Nucleosil 50-5, UV 254 nm) yielded two main fractions : 3.22 g (44.8%) of **[16a]** with r.t. = 5 min and 2.34 g (32.5%) of **[17a]** with r.t. 6 min.

large scale preparation:

25g (0.133 mol) of vinyl pyrrolidine **[11]** was dissolved in 400 mL of dry dichloromethane (dried over Alox-B) and 36.76 g (2 eq) of K_2CO_3 was added. The mixture was cooled to 0 °C and chloroacetyl fluoride (33.6 g, 2.6 eq)[262] was added via a dropping funnel (weak heat formation). Then, 133 mL (266 mmol) of Me_3Al (2 M in n-heptane) was slowly added via a dropping funnel, the internal temperature was kept below 5 °C (formation of methane gas, heat formation!). After complete addition, the reaction mixture was stirred for 8.5 hours at 0 °C. The reaction mixture was diluted with diethyl ether (400 mL of diethyl ether per 150 mL of the reaction mixture) and filtered with suction, trough a pad of silica gel (40 mm depth) on a glass frit (70 mm i.d.).[263] The remaining aluminium salts were removed from the silica gel surface and the pad was washed three times with 200 mL of diethyl ether. After that, the combined organic layers were dried over Na_2SO_4 and the solvents were removed in vacuo under reduced pressure and lowered temperature (below 20 °C) to yield 24.28 g (70%) of azoninones **[16a]** and **[17a]**.[264] The crude oil could be stored several days at -20 °C without epimerisation by a rotation of the double bond.

Azoninone **[16a]** consists of two conformers that could not be separated via HPLC. However, their ^{1}H-NMR signals could be assigned and the nature of the conformational change was determined by NOE measurements.

$[\alpha]_D^{20} = -44.3°$ (c = 1.7, $CHCl_3$).

^{13}C-NMR (62.9 MHz, $CDCl_3$): [265]

169.2 (s) , 136.9, 135.2, 132.8, 129.8, 128.5, 128.4, 127.5, 127.3, 127.1, 64.8, 55.4, 49.1, 47.1, 45.9, 44.2, 36.6, 35.7, 32.3, 27.8, 21.9.

[262] Up to 4 equivalents of chloroacetyl fluoride were used to increase the yield.
[263] The addition of diethyl ether caused the aluminium salts to precipitate, which was necessary to achieve a good separation of phases in the subsequent aqueous workup.
[264] In some cases the crude product contained traces of the educt vinylpyrrolidine **[11]**. They were removed by washing an ethereal solution of the product once with a saturated $KHSO_4$ solution.
[265] Assignment of the signals as far as detectable, some signals of the minor and the major conformer are overlapping.

Major conformer [16a-1]

^{1}H-NMR (500 MHz, $CDCl_3$):

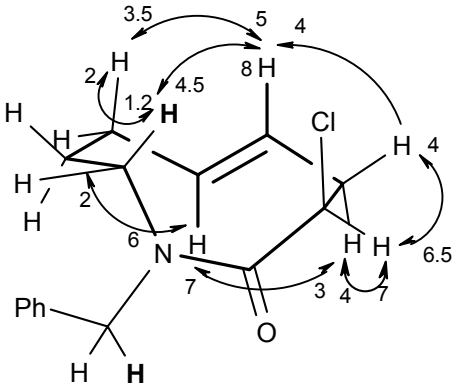
7.40 - 7.20 (m, 5H), 5.98 - 5.85 (ddd, 1H; H-5o; ^3J (H^{5o},H^{6u}) = 15 Hz, ^3J (H^{5o},H^{4u}) = 10 Hz, ^3J (H^{5o},H^{4o}) = 5 Hz), 5.62 - 5.50 (ddd, 1H; H-6u; ^3J (H^{6u},H^{5o}) = 15 Hz, ^3J (H^{6u},H^{7o}) = 9 Hz, ^3J (H^{6u},H^{7u}) = 4 Hz), 5.28 - 5.18 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 15.5 Hz), 5.04 - 5.00 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 4 Hz, ^3J (H^{3u},H^{4u}) = 2.5 Hz), 4.38 - 4.25 (m, 1H; H-9o), 3.95 - 3.88 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 15 Hz), 3.10 - 3.00 (m, 1H; H-9u), 2.82 - 2.72 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 13 Hz, ^3J (H^{4u},H^{5o}) = 13 Hz, ^3J (H^{4u},H^{3u}) = 2.5 Hz), 2.75 - 2.58 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 13 Hz, ^3J (H^{4o},H^{5o}) = 4 Hz, ^3J (H^{4o},H^{3u}) = 4 Hz), 2.45 - 2.35 (m, 1H; H-7u), 2.18 - 2.00 (m, 1H; H-7o), 1.80 - 1.70 (m, 2H; H-8o,8u).

Minor conformer [16a-2]

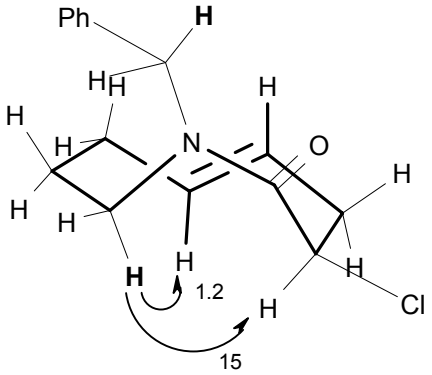
^{1}H-NMR (500 MHz, $CDCl_3$):

7.40 - 7.20 (m, 5H), 5.70 - 5.55 (m, 1H; H-6u), 5.50 - 5.38 (m, 1H; H-5o), 5.28 - 5.18 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 15.5 Hz), 4.86 - 4.80 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 10 Hz, ^3J (H^{3u},H^{4u}) = 8 Hz), 4.05 - 4.00 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 15 Hz), 3.75 - 3.60 (m, 1H; H-9u), 3.10 - 3.00 (m, 1H; H-9o), 2.90 - 2.80 (m, 1H; H-4u), 2.55 - 2.50 (m, 1H; H-4o), 2.40 - 2.28 (m, 1H; H-7u), 2.00 - 1.90 (m, 2H; H-7o,8), 1.60 - 1.50 (m, 1H; H-8').

Major conformer



Minor conformer [266]



[266] The position of the protons in the spectrum could be determined analogous to **[14a]** by transfer of magnetisation during the NOE experiment of **[16a-1]**. This transfer resulted from a fast chemical equilibration between **[16a-1]** and **[16a-2]**. The preliminary assignment of the 3-dimensional structure based on the structural correlations of the protons with their characteristic change in ^{4}J-couplings between one H-9/N-Bn pair (pairs are printed in bold letter for a better visualisation) and the other one during the isomerisation.

azoninone **[17a]** :

$[\alpha]_D^{20}$ = + 121.9° (c = 1.9, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.40 - 7.20 (m, 5H), 5.65 - 5.50 (m, 1H; H-5o), 5.55 - 5.45 (m, 1H; H-6u), 5.45 - 5.35 (d, 1H; H-Bn-1; ^2J (H^{Bn-1},H^{Bn2}) = 14.5 Hz), 4.62 - 4.55 (dd, 1H; H-3o; ^3J (H^{3o},H^{4u}) = 11.5 Hz, ^3J (H^{3o},H^{4o}) = 2 Hz), 3.95 - 3.88 (d, 1H; H-Bn-2; ^2J (H^{Bn-2},H^{Bn1}) = 14.5 Hz), 3.45 - 3.33 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 14.5 Hz, ^3J (H^{9o},H^{8u}) = 10 Hz), 3.12 - 3.02 (dd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 14.5 Hz, ^3J (H^{9u},H^{8o}) = 5 Hz), 2.84 - 2.70 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 11.5 Hz, ^3J (H^{4u},H^{5o}) = 11.5 Hz, ^3J (H^{4u},H^{3o}) = 9 Hz), 2.67 - 2.57 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4o}) = 12 Hz, ^3J (H^{4o},H^{5o}) = 5 Hz, ^3J (H^{4o},H^{3o}) = 3 Hz), 2.46 - 2.36 (m, 1H; H-7o), 2.15 - 2.00 (m, 1H; H-7u), 2.00 - 1.88 (m, 1H; H-8u), 1.75 - 1.65 (m, 1H; H-8o).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

169.5 (s), 136.7 (s), 134.8 (d), 128.5 (d), 128.2 (d), 127.4 (d), 56.3 (d, C-3), 47.6 (t, C-9), 44.7 (t), 39.3 (t), 31.6 (t), 26.0 (t).

IR (KBr): [267]

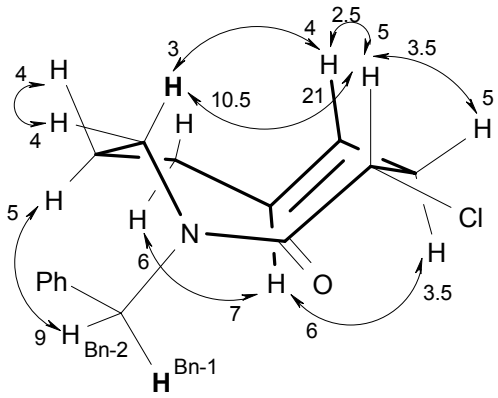
υ (cm^{-1}) = 3054 (m), 3031 (w), 2986 (m), 2940 (m), 2866 (m), 1643 (s), 1495 (w), 1453 (m), 1436 (m), 1421 (s), 1265 (s), 1185 (m), 994 (w), 896 (m).

MS (80eV, EI, 70 °C) [267] :

m/z (%): 263 (8) [$M^{+\cdot}$], 228 (4) [M^+ -Cl], 172 (14) [M^+ - C_7H_7], 136 (3), 91 (100) [$C_7H_7^+$], 65 (5), 55 (3).

HRMS (80eV, 120 °C) [267] : found 260.10934

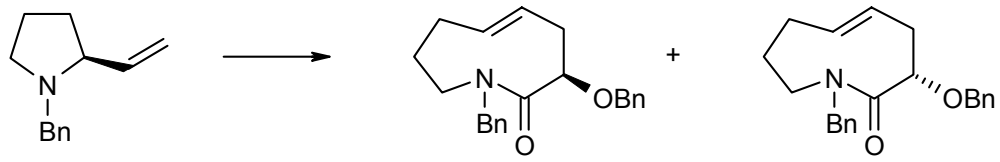
calc. 263.107692 (for $C_{15}H_{18}NOCl$).



[267] A mixture of azoninone **[16a]** and azoninone **[17a]** was used.

(pS)E-3*R*-1-Benzyl-3-benzyloxy-2,3,4,7,8,9-hexahydro-1H-azonin-2-one [18a] and

(*pS*)*E*-3*S*-1-Benzyl-3-benzyloxy-2,3,4,7,8,9-hexahydro-1H-azonin-2-one [19a]



[11] 187.29 [$C_{13}H_{17}N$] **[18a]** 335.45 [$C_{22}H_{25}NO_2$] **[19a]** 335.45 [$C_{22}H_{25}NO_2$]

In a 250 mL flask, a solution of vinyl pyrrolidine **[11]** (4.0 g, 21.4 mmol) in dry dichloromethane (100 mL) and 2.95 g (1 eq, 21.4 mmol) of K_2CO_3 was cooled with an ice bath to -10 °C and under argon, 5.4 g (1.5 eq, 32 mmol) of benzyloxyacetyl fluoride was added. Then, 21.3 mL (42 mmol, 2 eq) of Me_3Al (2 M in n-heptane) was slowly added, while the internal temperature was kept below 0 °C. After stirring overnight at 4 °C, the orange-brown suspension was slowly poured on 300 mL of diethyl ether. The following workup procedure was performed according to the standard procedure and yielded 6.86 g of the crude reaction product. Separation of this oil via HPLC (ethyl acetate / n-hexane = 15:85, flow 250 ml/min, 63x187 mm Nucleosil 50-5, UV 254 nm) yielded two main fractions : 1.81 g (25.3%) of **[18a]** with r.t. = 8 min and 0.72 g (10.0%) of **[19a]** with r.t. = 13.8 min.[268]

azoninone [18a]:

$[\alpha]_D^{20}$ = -7.9° (c = 1.684, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
5.86 - 5.75 (ddd, 1H; H-5o; ^3J (H^{5o},H^{6u}) = 15 Hz, ^3J (H^{5o},H^{4u}) = 10 Hz, ^3J (H^{5o},H^{4o}) = 4 Hz), 5.58 - 5.45 (ddd, 1H; H-6u; ^3J (H^{6u},H^{5o}) = 15 Hz, ^3J (H^{6u},H^{7o}) = 11 Hz, ^3J (H^{6u},H^{7u}) = 3.5 Hz), 5.40 -5.35 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 14.5 Hz), 4.63 - 4.60 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 5 Hz, ^3J (H^{3u},H^{4u}) = 2 Hz), 4.50 - 4.40 (m, 3H; H-9o, OBn-1, OBn-2), 3.93 - 3.85 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 14.5 Hz), 3.03 - 2.94 (dd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 15 Hz, ^3J (H^{9u},H^{8}) = 5 Hz), 2.69 - 2.58 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 13 Hz, ^3J (H^{4o},H^{5o}) = 5 Hz, ^3J (H^{4o},H^{3u}) = 5 Hz), 2.46 - 2.33 (m, 2H; H-4u, 7u), 2.15 - 2.02 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 11.5 Hz, ^3J (H^{7o},H^{6u}) = 11.5 Hz, ^3J (H^{7o},H^{8}) = 8 Hz), 2.00 - 1.80 (m, 1H; H-8u), 1.75 - 1.65 (m, 1H; H-8o).

[268] The low yield can be explained by a degradation reaction, caused by the high concentration of Me_3Al, analogous to former observed von-Braun degradation products. The yield of the reaction could be improved if a higher number of equivalents of the acid fluoride in contribution to the Me_3Al would be applied.

^{13}C-NMR (67.9 MHz, $CDCl_3$):

172.5 (s), 137.4 (s), 137.3 (s), 133.2 (d), 129.8 (d), 128.5 (d), 128.34 (d), 128.30 (d), 127.8 (d), 127.6 (d), 127.2 (d), 87.7 (d, C-3), 71.8 (t, O-Bn), 48.3 (t, N-Bn), 43.4 (t, C-9), 33.9 (t, C-4), 32.1 (t, C-7), 27.7 (t, C-8).

IR (KBr):

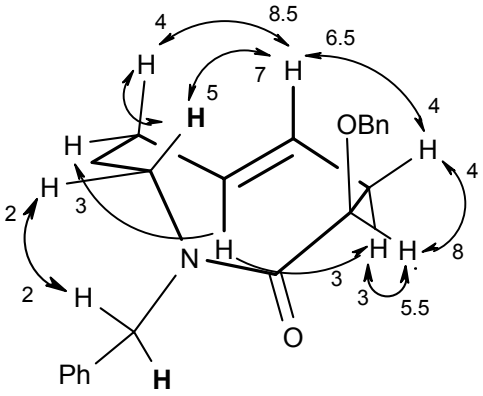
υ (cm^{-1}) = 3087 (m), 3063 (m), 3029 (m), 2929 (s), 2861 (m), 1617 (s), 1495 (m), 1453 (m), 1435 (m), 1420 (m), 1341 (m), 1245 (m), 1219 (m), 1169 (m), 1145 (m), 1090 (s), 1074 (s), 982 (m), 740 (m), 699 (s).

MS (80eV, EI, 120 °C):

m/z (%): 335 (7) [$M^{+\cdot}$], 306 (1.6), 244 (24) [M^+ -C_7H_7], 229 (20) [M^+ -C_7H_8O], 216 (3), 91 (100) [$C_7H_7^+$], 65 (5), 55 (1).

HRMS (80eV, 120 °C): found 335.18426

calc. 335.188529 (for $C_{22}H_{25}NO_2$).



azoninone [19a]:

$[\alpha]_D^{20}$ = -23.9° (c = 1.59, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):[269]

5.46 - 5.32 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 14.5 Hz), 5.42 - 5.35 (m, 2H; H-5o, 6u), 4.60 - 4.55 (d, 1H; H-O-Bn1; ^2J ($H^{O\text{-}Bn1}$,$H^{O\text{-}Bn2}$) = 11.5 Hz), 4.20 - 4.15 (d, 1H; H-O-Bn2; ^2J ($H^{O\text{-}Bn2}$,$H^{O\text{-}Bn1}$) = 11.5 Hz), 4.03 - 3.97 (dd, 1H; H-3o; ^3J (H^{3o},H$^{)}$ = 10.5 Hz, ^3J (H^{3o},H) = 3 Hz), 3.85 - 3.80 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 14.5 Hz), 3.23 - 3.15 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 14 Hz, ^3J (H^{9o},H^{8u}) = 10.5 Hz), 2.95 - 2.88 (dd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 14.5 Hz, ^3J (H^{9u},H^{8o}) = 5 Hz), 2.50 - 2.40 (m, 2H; H-4o, 4u), 2.35 - 2.28 (m, 1H; H-7o), 2.00 - 1.90 (m, 1H; H-7u), 1.87 - 1.80 (m, 1H; H-8u), 1.62 - 1.55 (m, 1H; H-8o).

[269] Compound **[19a]** showed slow conversion into **[19b]** during the NOE measurement.

^{13}C-NMR (67.9 MHz, $CDCl_3$):

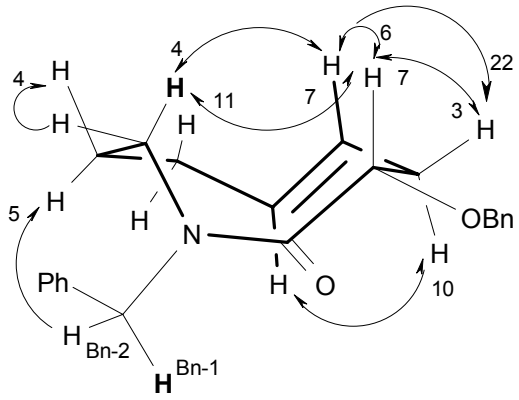
171.5 (s), 137.5 (s), 137.4 (s), 133.8 (d), 128.5 (d), 128.3 (d), 128.2 (d), 128.1 (d), 127.7 (d), 127.3 (d), 76.6 (d, C-3), 71.0 (t, O-Bn), 46.9 (t, N-Bn), 43.9 (t, C-9), 36.1 (t, C-4), 31.7 (t, C-7), 25.9 (t, C-8).

IR (KBr):

υ (cm^{-1}) = 3086 (m), 3062 (m), 3028 (m), 2932 (s), 2863 (m), 1638 (s), 1495 (m), 1453 (m), 1435 (m), 1420 (m), 1352 (m), 1233 (m), 1188 (m), 1116 (m), 1091 (m), 1077 (m), 982 (m), 751 (m), 699 (m).

MS (80eV, EI, 110 °C):

m/z (%): 335 (4) [$M^{+\cdot}$], 306 (1), 244 (14) [M^+ -C_7H_7], 229 (12) [M^+ -C_7H_8O], 216 (2), 160 (2), 137 (2), 91 (100) [$C_7H_7^+$], 65 (3).

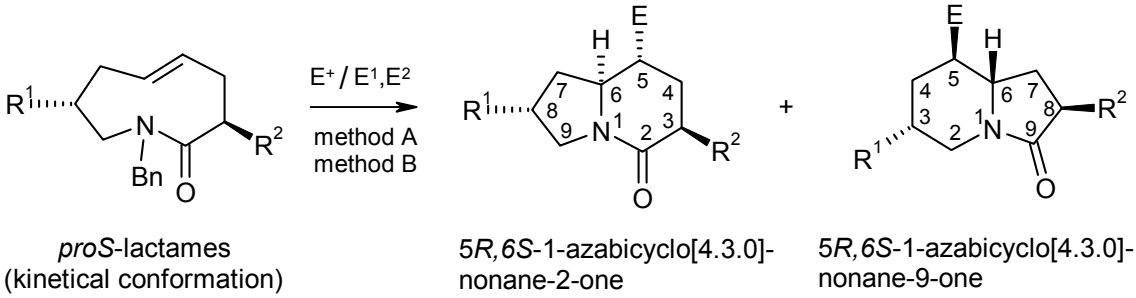


HRMS (80eV, 120 °C): found 335.18423

calc. 335.188529 (for $C_{22}H_{25}NO_2$).

3.5 Transannular Ring Contractions

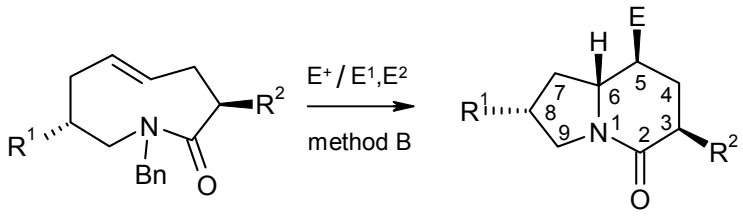
All transannular ring contractions except the two-step TMS-X (X = Br, Cl, I) induced epoxide opening reactions were performed following two main standard procedures. For an overview of the stereoselection and product ratios see Theoretical Part (chapter 2.3)



proS-lactames
(kinetical conformation)

5*R,6S*-1-azabicyclo[4.3.0]-nonane-2-one

5*R,6S*-1-azabicyclo[4.3.0]-nonane-9-one



proR-lactames
(thermodynamical conformation)

5S,*6S*-1-azabicyclo[4.3.0]-nonane-2-one

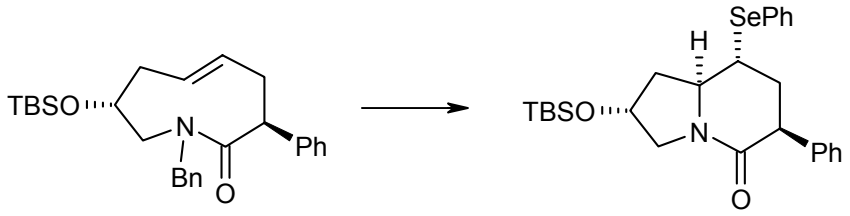
E+ = PhSeBr, J_2, Br_2 **E** = PhSe, Br, I **R1** = Cl, Ph, OBn **R2**= OTBS, H
and
E1= mCPBA **E2** = TMSI,TMSCl **E** = OH, OTMS **R1** = Cl, Ph, OBn **R2** = OTBS, H

Standard Procedure [A]: The azoninones **[12]**, **[13]**, **[14]**, **[16]** or **[17]** (1 mmol) were dissolved in dry dichloromethane (20 mL) at room temperature with stirring. Then, a solution of the electrophile (PhSeBr, I_2,or Br_2, respectively, 1 mmol) in dry dichloromethane (5 mL) was added dropwise by means of a syringe until the colour of unreacted reagent remained (quasi titration). According to most attempts, the reaction was found to be completed immediately after complete addition of the reagent (TLC monitoring). The mixture was stirred for additional 15 min at room temperature. Finally, the solvent was evaporated and the crude material was purified by column chromatography (In most cases, method A was found to give higher yields of indolizidinones than method B).

Standard procedure [B] : The electrophile (PhSeBr, I_2 or Br_2, respectively, 1mmol) was dissolved in dry dichloromethane (20mL) and the solution was cooled to -20 °C. Then, a solution of the azoninone **[12]**, **[13]**, **[14]**, **[16]** or **[17]** (1 mmol) in dry dichloromethane (5 mL) was slowly added by means of a syringe. According to most attempts, the reaction was found to be completed after finished addition

(TLC monitoring). The mixture was stirred for further 15 min at room temperature. Finally, the solvent was evaporated and the crude material was purified by column chromatography.[270]

3*S*,5*R*,6*S*,8*R*-3-Phenyl-5-phenylselanyl-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [20a]



[13a] 435.69 [$C_{27}H_{37}NO_2Si$] **[20a]** 500.62 [$C_{26}H_{35}NO_2SeSi$]

Reaction of ***pS*-[13a]** (130mg, 0.29 mmol) with PhSeBr followed the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate 3:1, R_f = 0.25) to yield **[20a]** as colourless crystals (131 mg, 88%) with mp = 109 °C.

$[\alpha]_D^{20}$ = - 12.1° (c = 1.445, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.50 -7.40 (m, 2H; o-H-SePh), 7.40 - 7.25 (m, 6H; H-arom), 7.10 - 7.00 (m, 2H; o-H-Ph), 4.45 - 4.40 (dd, 1H; H-8o; ^3J (H^{8o},H^{9o}) = 4 Hz, ^3J (H^{8o},H^{7o}) = 4 Hz), 4.00 - 3.90 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 13 Hz, ^3J (H^{9o},H^{8o}) = 4 Hz), 3.90 - 3.80 (m, 2H; H-3u,6u), 3.50 - 3.40 (d, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 13 Hz), 3.11 - 3.00 (ddd, 1H; H-5o; ^3J (H^{5o},H^{4u}) = 11 Hz, ^3J (H^{5o},H^{6u}) = 11 Hz, ^3J (H^{5o},H^{4o}) = 5 Hz), 2.38 - 2.22 (m, 3H; H-4u, 4o, 7u), 1.68 - 1.55 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 12 Hz, ^3J (H^{7o},H^{6o}) = 12 Hz, ^3J (H^{7o},H^{8o}) = 4 Hz), 0.80 (s, 9H; H-Si (CMe_3), 0.01 (s, 3H; H-Si-CH_3), 0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

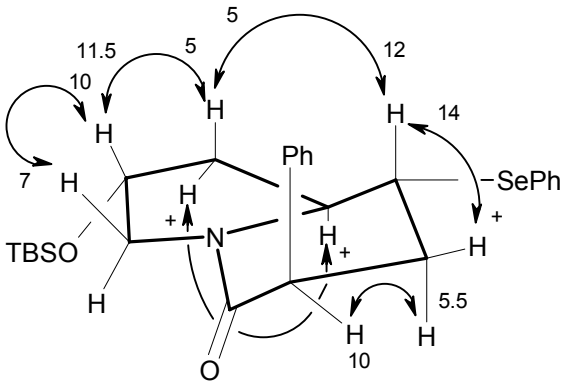
168.5 (s, C=O), 153.2 (q), 141.5 (q), 135.8 (d), 129.2 (d), 129.0 (d), 128.5 (d), 128.4 (d), 126.6 (d), 68.2 (d, C-8), 61.7 (d, C-6), 55.7 (t, C-9), 47.5 (d, C-3), 43.1 (t, C-7), 38.2 (t, C-4), 36.9 (d, C-5), 25.7 (Si-C(CH_3)$_3$), 17.9 (Si-C(CH_3)$_3$), - 4.85 (Si-CH_3), -4.89 (Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3054 (s), 2929 (s), 2885 (s), 2855 (s), 1630 (s, CO), 1437 (s), 1265 (s).

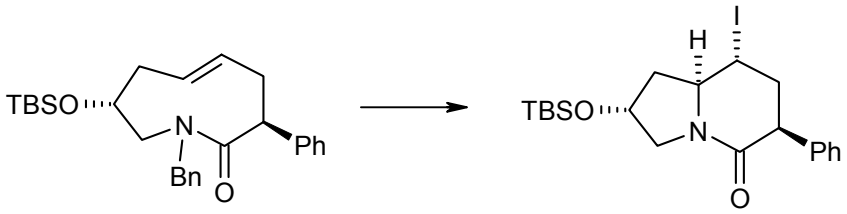
[270] Traces of iodine were removed by washing the organic layer with saturated $Na_2S_2O_3$ solution.

MS (80eV, EI, 110 °C):
m/z (%): 501 (6) [M^+], 486 (3) [M-CH_3], 444 (100) [M-C_4H_9], 344 (66), 286 (22), 222 (4), 118 (15), 91 (9), 73 (12).



HRMS (80eV,110 °C): found 501.16038
calc. 506.16022 (for $C_{26}H_{35}NO_2Si\,Se$, [M^+]).

3*S*,5*R*,6*S*,8*R*-3-Phenyl-5-iodo-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [21a]



[13a] 435.69 [$C_{27}H_{37}NO_2Si$] **[21a]** 471.46 [$C_{20}H_{30}INO_2Si$]

Reaction of ***pS*-[13a]** (120mg, 0.28 mmol) with iodine was carried out according to the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate 3:1, R_f = 0.28) to yield **[21a]** as colourless crystals (119 mg, 89%) with mp = 73 °C.

$[\alpha]_D^{20}$ = - 15.31° (c = 1.28, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
7.40 - 7.25 (m, 3H), 7.10 - 7.00 (m, 2H), 4.45 - 4.40 (dd, 1H; H-8o; ^3J (H^{8o},H^{9o}) = 4 Hz, ^3J (H^{8o},H^{7o}) = 4 Hz), 4.22 - 4.11 (ddd, 1H; H-6u; ^3J (H^{6u},H^{5o}) = 11 Hz, ^3J (H^{6u},H^{7o}) = 11 Hz, ^3J (H^{6u},H^{7u}) = 4 Hz), 4.00 - 3.92 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 13 Hz, ^3J (H^{9o},H^{8o}) = 4 Hz), 3.95 - 3.85 (ddd, 1H; H-5o; ^3J (H^{5o},H^{4u}) = 13 Hz, ^3J (H^{5o},H^{6u}) = 11 Hz, ^3J (H^{5o},H^{4o}) = 4 Hz), 3.80 - 3.76 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 6 Hz, ^3J (H^{3u},H^{4u}) = 2 Hz), 3.65 - 3.58 (d, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 13 Hz), 2.86 - 2.73 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 14 Hz, ^3J (H^{4u},H^{5o}) = 14 Hz, ^3J (H^{4u},H^{3u}) = 7 Hz), 2.65 - 2.55 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 14 Hz, ^3J (H^{4o},H^{5o}) = 4 Hz, ^3J (H^{4o},H^{3u}) = 2 Hz), 2.38 - 2.30 (dd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 13 Hz, ^3J (H^{7u},H^{6u}) = 5 Hz), 1.72 - 1.60 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 12 Hz, ^3J (H^{7o},H^{6o}) = 12 Hz, ^3J (H^{7o},H^{8o}) = 4 Hz), 0.90 (s, 9H; H-Si (CMe_3), 0.01 (s, 3H; H-Si-CH_3), 0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

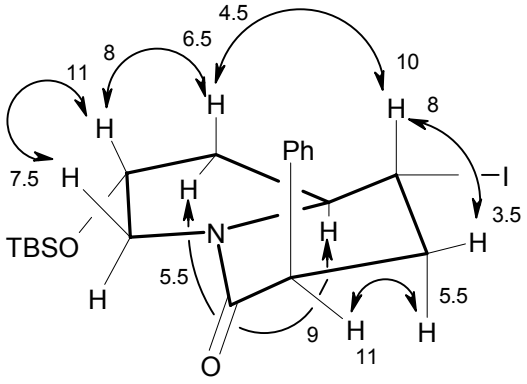
168.1 (s, C=O), 141.2 (q), 128.6 (d), 127.9 (d), 126.9 (d), 67.4 (d, C-8), 64.5 (d, C-6), 56.7 (t, C-9), 48.6 (d, C-3), 44.3 (t, C-7), 43.4 (t, C-4), 25.7 (Si-C$(CH_3)_3$), 20.5 (d, C-5), 17.9 (Si-C$(CH_3)_3$), - 4.8 (Si-CH_3), - 4.9 (Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 2957 (s), 2925 (s), 2890 (s), 2851 (s), 1630 (s, N-CO), 1438 (s), 1382 (m), 1254 (s, C=O), 1127 (m), 1087 (m), 1076 (m), 1024 (s), 846 (s), 826 (s), 779 (s), 714 (s).

MS (80eV, EI, 110 °C):

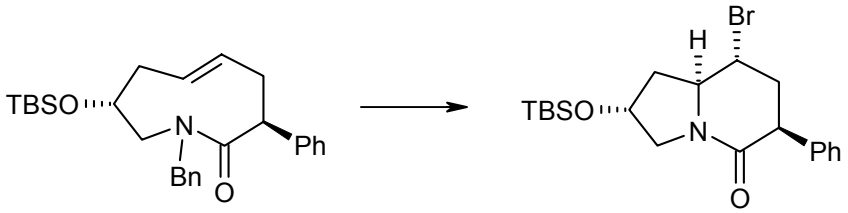
m/z (%): 470 (0.2) [M-H$^+$], 456 (4) [M$^+$-CH_3], 444 (0.8), 414 (100) [M$^+$-C_4H_9], 344 (1) [M$^+$-I], 287 (19) [M$^+$-C_4H_9-I], 244 (2) 136 (17), 134 (16), 91 (56), 87 (21), 73 (23).



HRMS (80eV,110 °C): found 456.08529

calc. 456.085460 (for $C_{19}H_{27}INO_2Si$, [M-CH_3]).

3*S*,5*R*,6*S*,8*R*-3-Phenyl-5-bromo-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [22a]



[13a] 435.69 [$C_{27}H_{37}NO_2Si$] **[22a]** 424.46 [$C_{20}H_{30}BrNO_2Si$]

Reaction of ***pS*-[13a]** (200mg, 0.45 mmol) with bromine was carried out according to the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate 3:1, R_f= 0.25) to yield **[22a]** as a colourless oil (72 mg, 37%).

$[\alpha]_D^{20}$ = - 28.33° (c = 1.92, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.40 - 7.25 (m, 3H), 7.10 - 7.00 (m, 2H; o-H-Ph), 4.48 - 4.43 (dd, 1H; H-8o; ^{3}J (H^{8o},H^{9o}) = 4 Hz, ^{3}J (H^{8o},H^{7o}) = 4 Hz), 4.13 - 4.03 (ddd, 1H; H-6u; ^{3}J (H^{6u},H^{5o}) = 11 Hz, ^{3}J (H^{6u},H^{7o}) = 11 Hz, ^{3}J (H^{6u},H^{7u}) = 4 Hz), 3.95 - 3.88 (dd, 1H; H-9o; ^{2}J (H^{9o},H^{9u}) = 13 Hz, ^{3}J (H^{9o},H^{8o}) = 5 Hz), 3.95 - 3.85 (m, 2H; H-5o, 3u), 3.58 - 3.50 (d, 1H; H-9u; ^{2}J (H^{9u},H^{9o}) = 14 Hz), 2.73 - 2.60 (ddd, 1H; H-4u; ^{2}J (H^{4u},H^{4o}) = 14 Hz, ^{3}J (H^{4u},H^{5o}) = 14 Hz, ^{3}J (H^{4u},H^{3u}) = 7 Hz), 2.56 - 2.46 (ddd, 1H; H-4o; ^{2}J (H^{4o},H^{4u}) = 14 Hz, ^{3}J (H^{4o},H^{5o}) = 4 Hz, ^{3}J (H^{4o},H^{3u}) = 2 Hz), 2.36 - 2.28 (dd, 1H; H-7u; ^{2}J (H^{7u},H^{7o}) = 13 Hz, ^{3}J (H^{7u},H^{6u}) = 5 Hz), 1.75 - 1.62 (ddd, 1H; H-7o; ^{2}J (H^{7o},H^{7u}) = 12 Hz, ^{3}J (H^{7o},H^{6o}) = 12 Hz, ^{3}J (H^{7o},H^{8o}) = 4 Hz), 0.90 (s, 9H; H-Si (CMe_3)), 0.05 (s, 3H; H-Si-CH_3), 0.09 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

168.1 (q, C=O), 141.1 (q), 128.7 (d), 127.8 (d), 126.9 (d), 68.0 (d, C-8), 63.2 (d, C-6), 56.3 (t, C-9), 47.8 (d, C-3), 44.7 (d, C-5), 42.9 (t, C-7), 41.3 (t, C-4), 25.7 (Si-C(CH_3)$_3$), 17.9 (Si-C(CH_3)$_3$), -4.8 (Si-CH_3), - 4.9 (Si-CH_3).

IR (KBr):

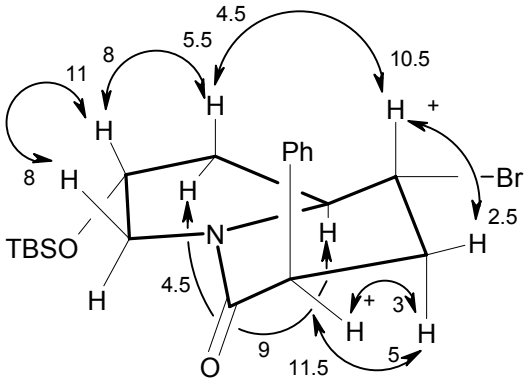
υ (cm^{-1}) = 3061 (w), 3027 (w), 2959 (s), 2883 (s), 2858 (s), 1645 (s, N-CO), 1495 (s),1439 (s), 1370 (m), 1257 (s, C=O), 1218 (m), 1085 (s), 1027 (s), 838 (s), 778 (s), 699 (s), 613 (s).

MS (80eV, EI, 120 °C):

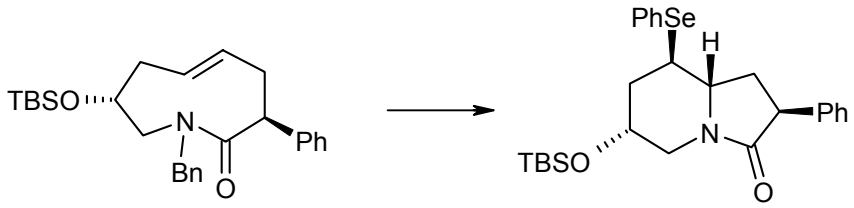
m/z (%): 424 (0.45) [M^+], 423 (0.19) [M-H], 408 (4.05) [M-CH_3], 368 (100) [M-C_4H_9], 286 (8), 184 (5), 143 (3), 91 (4), 73 (7).

HRMS (80eV,150 °C): found 408.09925

calc. 408.09945 (for $C_{19}H_{27}{}^{79}BrNO_2Si$, [M-$CH_3$]).



3*R*,5*R*,6*S*,8*S*-3-(*tert*-butyldimethylsilyloxy)-5-phenylselanyl-8-phenyl-1-azabicyclo[4.3.0]nonan-9-one [20b]



[13a] 435.69 [$C_{27}H_{37}NO_2Si$] **[20b]** 500.62 [$C_{26}H_{35}NO_2SeSi$]

Reaction of ***pS*-[13a]** (110mg, 0.25 mmol) with PhSeBr was carried out according to the standard procedure **B**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 3:1, R_f= 0.38) to yield **[20b]** as a colourless oil (56 mg, 44%).

$[\alpha]_D^{20}$ = - 29.63° (c = 0.496, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.53 - 7.56 (m, 2H), 7.15-7.35 (m, 8H), 4.06 (d, ^2J (H^{2u},H^{2o}) = 13 Hz, 1H, H-2u), 3.97 (m, 1H; H-3o), 3.71-3.65 (dd, ^3J (H^{8u},H^{7u}) = 10Hz, ^3J (H^{8u},H^{7o}) = 7 Hz, 1H; H-8u), 3.56-3.47 (ddd, ^3J (H,H) = 5Hz, ^3J (H,H) = 7Hz, ^3J (H,H) = 11 Hz, 1H; H-6o), 3.41-3.31 (ddd, ^3J (H^{5o},H^{6o}) = 12Hz, ^3J (H^{5o},H^{4o}) = 12Hz, ^3J (H^{5o} , H^{4u}) = 3 Hz, 1H; H-5o), 2.78-2.72 (dd, ^2J (H^{2o}, H^{2u}) = 13 Hz, ^3J (H^{2o}, H^{3o}) = 1.5Hz, 1H; H-2o), 2.54- 2.32 (m, 2H; H-7o, H-7u), 2.29- 2.23 (m, 1H; H-4u), 1.78-1.68 (ddd, ^2J (H^{4o},H^{4u}) = 14 Hz, ^3J (H^{4o},H^{5o}) = 13 Hz, ^3J (H^{4o},H^{3o}) = 2 Hz, 1 H; H-4o), 0.84 (s, 9H; Si-C(CH_3)$_3$), 0.05 (s, 3H; Si-CH_3), 0.00 (s, 3H; Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

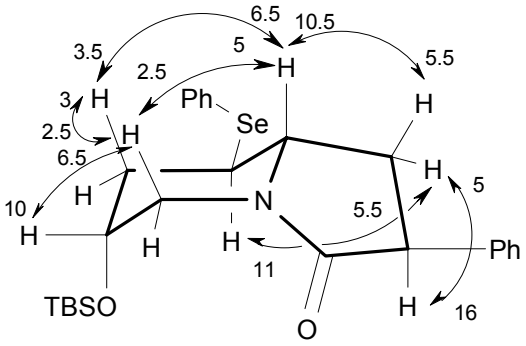
174.1 (C=O), 140.1 (q), 135.6 (d), 129.1 (d), 128.6 (d), 128.2 (d), 127.6 (d), 126.8 (d), 126.5 (q), 65.9 (d, C-3), 59.9 (d, C-8), 46.8 (d, C-6), 46.4 (t, C-2), 41.1 (d, C-5), 40.4 (t, C-7), 33.7 (t, C-4), 25.7 (Si-C(CH_3)$_3$), 17.9 (Si-C(CH_3)$_3$), - 4.9 (Si-CH_3), -5.16 (Si-CH_3).

IR (KBr):

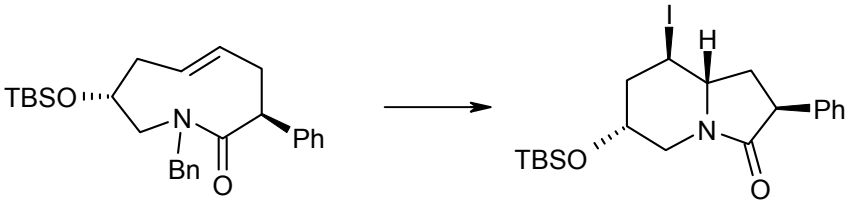
υ (cm^{-1}) = 3439 (w), 3059 (w), 3027 (w), 2951 (s), 2925 (s), 2853 (m), 2706 (m), 1695 (s, N-CO), 1578 (w),1436 (s) 1425 (m), 1360 (m), 1257 (m, C=O), 1110 (m), 1093 (m), 1051 (m), 1039 (m), 837 (m), 807 (m), 777 (m), 738 (m), 695 (m),

MS (80eV, EI, 170 °C):
m/z (%): 501 (0.5) [$M^{+\cdot}$], 486 (1.6) [M^+ - CH_3], 444 (100) [M^+ - C_4H_9], 344 (8) [M^+ - PhSe], 286 (29) [M^+ - C_4H_9 - PhSeH], 244 (5), 73 (17.6).

HRMS (80eV,160 °C): found 486.13354
calc. 486.136753 (for $C_{25}H_{32}NO_2SeSi$).



3*R*,5*R*,6*S*,8*S*-3-(*tert*-Butyldimethylsilyloxy)-5-iodo-8-phenyl-1-azabicyclo[4.3.0]nonan-9-one [21b]



[13a] 435.69 [$C_{27}H_{37}NO_2Si$] **[21b]** 471.46 [$C_{20}H_{30}INO_2Si$]

Reaction of ***pS*-[13a]** (110mg, 0.25 mmol) with iodine was carried out according to the standard procedure **B**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 3:1, R_f= 0.41) to yield **[21b]** as a colourless oil (46 mg, 40%).

$[\alpha]_D^{20}$ = - 26.0° (c = 0.650, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
7.33 - 7.19 (m, 5H; Ph-Rest), 4.30-4.20 (ddd, ^3J (H,H) = 12Hz, ^3J (H,H) = 11Hz, ^3J (H^{5o} , H^{4u}) = 4 Hz, 1H; H-5o), 4.21-4.14 (ddd, ^2J (H^{2u},H^{2o}) = 14Hz, ^3J (H^{2u},H^{3o}) = 2 Hz, ^4J (H^{2u} , H^{4u}) = 2 Hz, 1H; H-2u), 3.9-3.8 (m, 2H, H-3o, H-6o), 3.74 - 3.67 (dd, ^3J (H^{8u},H^{7u}) = 9Hz, ^3J (H^{8u},H^{7o}) = 9 Hz, 1H; H-8u), 2.95-2.89 (dd, ^2J (H^{2o}, H^{2u}) = 14 Hz, ^3J (H^{2o}, H^{3o}) = 1.5Hz, 1H; H-2o), 2.59-2.50 (dddd, ^2J (H^{4u},H^{4o}) = 14 Hz, ^3J (H^{4u},H^{5o}) = 4 Hz, ^3J (H^{4o},H^{3o}) = 4 Hz, ^4J (H^{4o},H^{2u}) = 2 Hz 1 H; H-4o), 2.43-2.37 (m, 2H; H-7o and H-7u), 2.29- 2.18 (ddd, ^2J (H^{4o},H^{4u}) = 13 Hz, ^3J (H^{4o},H^{5o}) = 11 Hz, ^3J (H^{4u},H^{3o}) = 2 Hz, 1 H; H-4u), 0.87 (s, 9H; Si-C(CH_3)$_3$), 0.07 (s, 3H; Si-CH_3), 0.05 (s, 3H; Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

174.3 (s, C=O), 139.7 (q) , 128.7 (d), 127.6 (d), 126.9 (d), 67.4 (d, C-3), 62.7 (d, C-8), 46.6 (t, C-2), 46.5 (d, C-6), 45.5 (t, C-7), 34.8 (t, C-4), 27.9 (d, C-5), 25.7 (q, Si-C$(CH_3)_3$), 17.9 (Si-C$(CH_3)_3$), - 4.9 (q, Si-CH_3), -5.16 (Si-CH_3).

IR (KBr):

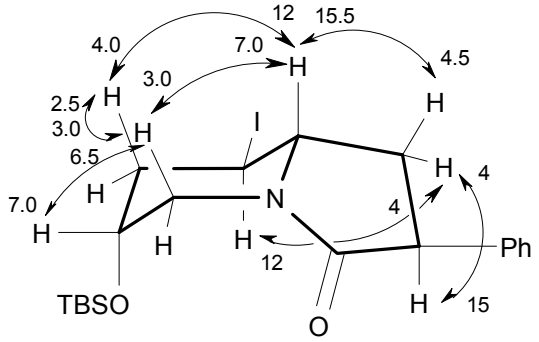
υ (cm^{-1}) = 3443 (w), 3060 (w), 3027 (w), 2949 (s), 2925 (s), 2853 (m), 2709 (w), 1697 (s, N-CO), 1601 (w),11470 (m), 1461 (m), 1447 (m) 1423 (s), 1304 (w), 1257 (m, C=O), 1109 (s), 1092 (s), 1051 (m), 1037 (m), 882 (m), 806 (m), 778 (m), 723 (m), 697 (m).

MS (70eV, EI, 150 °C):

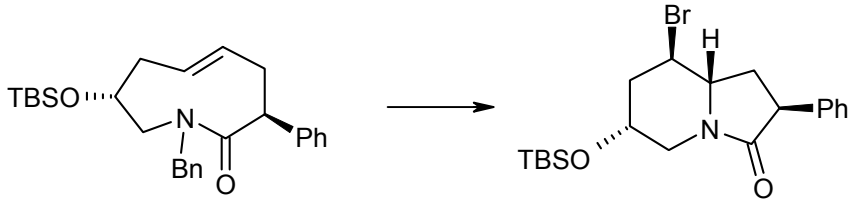
m/z (%): 470 (0.1) [$M^{+\cdot}$], 456 (3) [M^+ - CH_3], 414 (100) [M^+ - C_4H_9], 287 (14) [M^+ - C_4H_9 - I], 129 (3), 101 (2), 73 (4).

HRMS (80eV,150 °C): found 456.08212

calc. 456.08559 (for $C_{19}H_{27}NO_2ISi$).



3*R*,5*R*,6*S*,8*S*-3-(*tert*-Butyldimethylsilyloxy)-5-bromo-8-phenyl-1-azabicyclo[4.3.0]nonan-9-one [22b]



[13a]435.69[$C_{27}H_{37}NO_2Si$] **[22b]** 424.46 [$C_{20}H_{30}BrNO_2Si$]

Reaction of ***pS*-[13a]** (100mg, 0.23 mmol) with bromine was carried out according to the standard procedure **B**. The crude product was purified by column chromatography (n-hexane / ethyl acetate 5:1, R_f= 0.38) to yield **[22b]** as a colourless oil (39 mg, 40%).

$[\alpha]_D^{20}$ = - 29.3° (c = 1.935, $CHCl_3$).

^{1}H-NMR (500 MHz, $CDCl_3$):

7.4 -7.2 (m, 5H), 4.17 - 4.13 (dd, 1H; H-2u; ^{2}J (H^{2u},H^{2o}) = 14 Hz, ^{3}J (H^{2u},H^{3o}) = 4 Hz), 4.14 - 4.10 (m, 1H; H-5o), 4.05 - 4.00 (m, 1H; H-3o), 3.75 - 3.69 (m, 2H; H-6o,8u), 2.92 - 2.87 (dd, 1H; H-2o; ^{2}J (H^{2o},H^{2u}) = 14 Hz, ^{3}J (H^{2o},H^{3o}) = 2 Hz), 2.53 - 2.46 (ddd, 1H; H-7u; ^{2}J (H^{7u},H^{7o}) = 14 Hz, ^{3}J (H^{7u},H^{6o}) = 10 Hz, ^{3}J (H^{7u},H^{8u}) = 4 Hz), 2.49 - 2.42 (dddd, 1H; H-4u; ^{2}J (H^{4u},H^{4o}) = 14 Hz, ^{3}J (H^{4u},H^{5o}) = 4 Hz, ^{3}J (H^{4u},H^{3o}) = 4 Hz, ^{4}J (H^{4u},H^{2u}) = 2 Hz), 2.43 - 2.35 (ddd, 1H; H-7o; ^{2}J (H^{7o},H^{7u}) = 14 Hz, ^{3}J (H^{7o},H^{6o}) = 7 Hz, ^{3}J (H^{7o},H^{8u}) = 7 Hz), 2.08 - 2.00 (ddd, 1H; H-4o; ^{2}J (H^{4o},H^{4u}) = 14 Hz, ^{3}J (H^{4o},H^{5o}) = 12 Hz, ^{3}J (H^{4o},H^{3o}) = 2 Hz), 0.80 (s, 9H; H-Si (CMe_3)), 0.01 (s, 3H; H-Si-CH_3), 0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (62.9 MHz, $CDCl_3$):

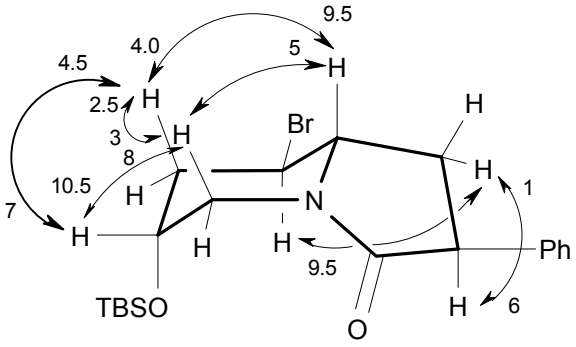
174.2 (s, C=O), 139.7 , 128.7 (d), 127.6 (d), 126.9 (d), 66.9 (d, C-3), 61.8 (d, C-6), 48.8 (d, C-5), 46.4 (d, C-8), 46.4 (t, C-2), 43.3 (t, C-4), 32.9 (t, C-7), 25.6 (q, Si-C(CH_3)$_3$), 17.9 (Si-C(CH_3)$_3$), - 4.9 (q, Si-CH_3), -5.16 (Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3062 (w), 3028 (w), 2952 (s), 2927 (s), 2855 (m), 1698 (s, N-CO), 1602 (w),1471 (m), 1422 (s), 1360 (m), 1255 (m, C=O), 1112 (s), 1109 (s), 1092 (s), 1040 (m), 885 (m), 837 (s), 806 (m), 777 (m), 729 (m), 697 (m).

MS (70eV, EI, 130 °C):

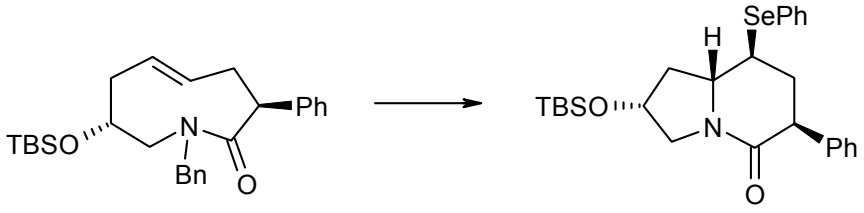
m/z (%): 424 (0.2) [$M^{+\cdot}$], 410 (2.5) [M^+ - CH_3], 384 (1.1), 368 (100) [M^+ - C_4H_9], 366 (95), 286 (10), 101 (5), 75 (5).



HRMS (80eV,130 °C): found 408.10434

calc. 408.099444 ($C_{19}H_{27}{}^{79}BrNO_2Si$ [M^+ -CH_3]).

3*S*,5*S*,6*R*,8*R*-3-Phenyl-5-phenylselanyl-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [20c]



[13b] 435.69 [$C_{27}H_{37}NO_2Si$] **[20c]** 500.62 [$C_{26}H_{35}NO_2SeSi$]

Reaction of ***pR*-[13b]** (100mg, 0.23 mmol) with PhSeBr was carried out according to the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 3:1, R_f= 0.28) to yield **[20c]** as a colourless oil (71 mg, 62%).

$[\alpha]_D^{20}$ = + 106.93° (c = 0.62, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.60 - 7.50 (m, 2H; H-o-SePh), 7.5 -7.2 (m, 8H), 4.45 - 4.35 (m, 1H; H-8o), 3.75 - 3.50 (m, 4H; H-3u, 9u, 6o, 9o), 3.25 - 3.15 (ddd, 1H; H-5u; ^3J (H^{5u},H) = 13 Hz, ^3J (H^{5u},H) = 11 Hz, ^3J (H^{5u},H^{4u}) = 3 Hz), 2.60 - 2.40 (m, 2H; H-4u, 7o), 2.10 - 1.95 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 13 Hz, ^3J (H^{4o},H) = 13 Hz, ^3J (H^{4o},H) = 12 Hz), 1.80 - 1.65 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 12 Hz, ^3J (H^{7u},H) = 11 Hz, ^3J (H^{7u},H) = 8 Hz), 0.80 (s, 9H; H-Si (CMe_3)), 0.05 (s, 3H; H-Si-CH_3), -0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (62.9 MHz, $CDCl_3$):

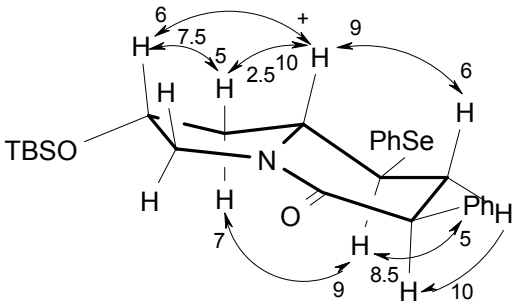
168.7 (C=O), 140.7, 135.8, 129.2, 128.6, 128.5, 128.1, 126.8, 126.5, 68.7 (d, C-8), 62.4 (d, C-6), 53.6 (t, C-9), 49.7 (d, C-3), 42.4 (t, C-7), 42.4 (d, C-5), 40.0 (t, C-4), 25.7 (Si-C(CH_3)$_3$), 17.9 (Si-C(CH_3)$_3$), - 4.8 (Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3449 (w), 3057 (w), 3026 (w), 2951 (s), 2926 (s), 2883 (m), 1643 (s, N-CO), 1577 (w),1471 (s) 1451 (s), 1436 (s), 1361 (m), 1252 (m, C=O), 1113 (m), 1073 (m), 1022 (w), 837 (m), 778 (m), 739 (m), 695 (m).

MS (80eV, EI, 170 °C):

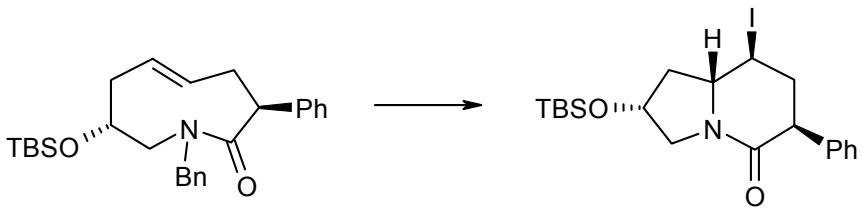
m/z (%): 500 (0.5) [$M^{+\cdot}$], 486 (1.6) [M^+ - CH_3], 444 (100) [M^+ - C_4H_9], 344 (9) [M^+ - PhSe], 287 (20) [M^+ - C_4H_9 - PhSeH], 244 (5), 73 (17.6).



HRMS (80eV,130 °C): found 486.13281

calc. 486.136753 (for $C_{25}H_{32}NO_2Si$ ^{80}Se).

3*S*,5*S*,6*R*,8*R*-3-Phenyl-5-iodo-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [21c]



[13b] 435.69 [$C_{27}H_{37}NO_2Si$] **[21c]** 471.46 [$C_{20}H_{30}INO_2Si$]

Reaction of ***pR*-[13b]** (100mg, 0.23 mmol) with iodine was carried out according to the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 6:1, R_f= 0.34) to yield **[21c]** as a colourless oil (48 mg, 45%).

$[\alpha]_D^{20}$ = + 73.4° (c = 1.105, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.4 -7.1 (m, 5H), 4.45 - 4.35 (m, 1H; H-8o), 4.10 - 4.00 (ddd, 1H; H-5u; ^3J (H^{5u},H^{4o}) = 11 Hz, ^3J (H^{5u},H^{6o}) = 11 Hz, ^3J (H^{5u},H^{4u}) = 3 Hz), 4.00 - 3.90 (ddd, 1H; H-6o; ^3J (H^{6o},H^{5u}) = 11 Hz, ^3J (H^{6o},H^{7u}) = 10 Hz, ^3J (H^{6o},H^{7o}) = 5 Hz), 3.78 - 3.70 (dd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 12 Hz, ^3J (H^{9u},H^{8o}) = 6 Hz), 3.70 - 3.65 (m, 1H; H-3u), 3.65 - 3.60 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 12 Hz, ^3J (H^{9o},H^{8o}) = 6 Hz), 2.92 - 2.80 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 11 Hz, ^3J (H^{4u},H) = 7 Hz, ^3J (H^{4u},H) = 3 Hz), 2.61 - 2.50 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 12 Hz, ^3J (H^{7o},H) = 8 Hz, ^3J (H^{7o},H) = 7 Hz), 2.50 - 2.35 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 14 Hz, ^3J (H^{4o},H^{3u}) = 14 Hz, ^3J (H^{4o},H^{5u}) = 12 Hz), 1.95 - 1.75 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 11 Hz, ^3J (H^{7u},H) = 9 Hz, ^3J (H^{7u},H) = 8 Hz), 0.80 (s, 9H; H-Si (CMe_3)), 0.01 (s, 3H; H-Si-CH_3), 0.05 (s, 3H; H-Si-CH_3).

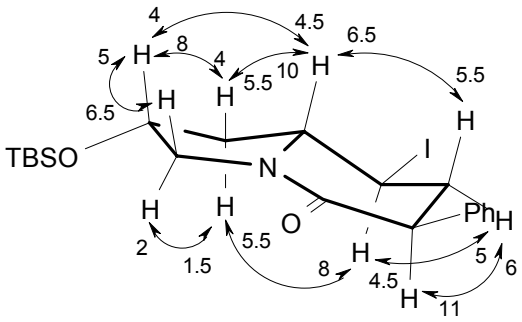
^{13}C-NMR (62.9 MHz, $CDCl_3$):

168.4 (C=O), 139.9, 128.7, 128.0, 127.0, 67.7 (d, C-8), 64.6 (d, C-6), 54.7 (t, C-9), 50.6 (d, C-3), 44.9 (t, C-7), 43.8 (t, C-4), 25.7 (Si-$C(CH_3)_3$), 24.0 (d, C-5), 17.9 (Si-$C(CH_3)_3$), - 4.9 (Si-CH_3).

IR (KBr):

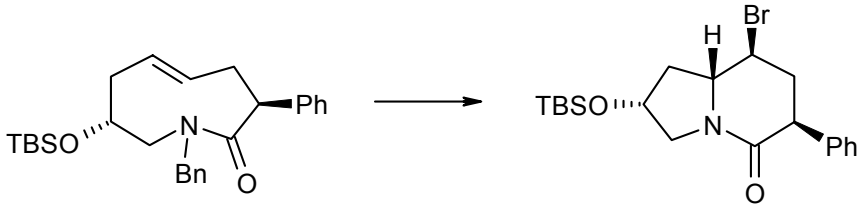
υ (cm^{-1}) = 3062 (w), 3027 (w), 2953 (s), 2928 (s), 2884 (m), 2856 (s), 1648 (s, N-CO), 1495 (m), 1471 (m), 1451 (s) 1431 (s), 1384 (m), 1252 (m, C=O), 1134 (s), 1115 (s), 1006 (w), 898 (s), 837 (s), 777 (s), 698 (m).

MS (70eV, EI, 160 °C):
m/z (%): 470 (0.5) [$M^{+\cdot}$- H^+], 456 (3) [M^+ - CH_3], 414 (100) [M^+ - C_4H_9], 287 (15) [M^+ - I - C_4H_9], 118 (5), 73 (5).



HRMS (80eV,150 °C): found 470.10574
calc. 470.101235 (for $C_{20}H_{29}NO_2SiI$ [M-H^+]).

3*S*,5*S*,6*R*,8*R*-3-Phenyl-5-bromo-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [22c]



[13b] 435.69 [$C_{27}H_{37}NO_2Si$] **[22c]** 424.46 [$C_{20}H_{30}BrNO_2Si$]

Reaction of ***pR*-[13b]** (130mg, 0.29 mmol) with bromine was carried out according to the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 3:1, R_f= 0.25) to yield **[22c]** as a colourless crystals (85.5 mg, 68%) with mp = 73 °C.

$[\alpha]_D^{20}$ = + 52.65° (c = 1.755, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
7.40 - 7.20 (m, 5H; H-H-arom), 4.46 - 4.37 (m, 1H; H-8o), 4.04 - 3.93 (ddd, 1H; H-5u; ^3J (H^{5u},H^{4o}) = 12 Hz, ^3J (H^{5u},H^{6o}) = 10 Hz, ^3J (H^{5u},H^{4u}) = 3 Hz), 3.91 - 3.81 (ddd, 1H; H-6o; ^3J (H^{6o},H^{5u}) = 10 Hz, ^3J (H^{6o},H^{7u}) = 10 Hz, ^3J (H^{6o},H^{7o}) = 6 Hz), 3.76 - 3.68 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 11 Hz, ^3J (H^{3u},H^{4u}) = 7 Hz), 3.66 - 3.63 (m, 2H; H-9o,9u), 2.83 - 2.72 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 10 Hz, ^3J (H^{4u},H^{3u}) = 6 Hz, ^3J (H^{4u},H^{5u}) = 3 Hz), 2.58 - 2.48 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 13 Hz, ^3J (H^{7o},H^{6o}) = 6 Hz, ^3J (H^{7o},H^{8o}) = 6 Hz), 2.40 - 2.25 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 13 Hz, ^3J (H^{4o},H^{5u}) = 12 Hz, ^3J (H^{4o},H^{3u}) = 12 Hz), 2.36 - 2.28 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 13 Hz, ^3J (H^{7u},H^{6o}) = 9 Hz, ^3J (H^{7u},H^{8o}) = 7 Hz), 0.90 (s, 9H; H-Si (CMe_3)), 0.05 (s, 3H; H-Si-CH_3), 0.09 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

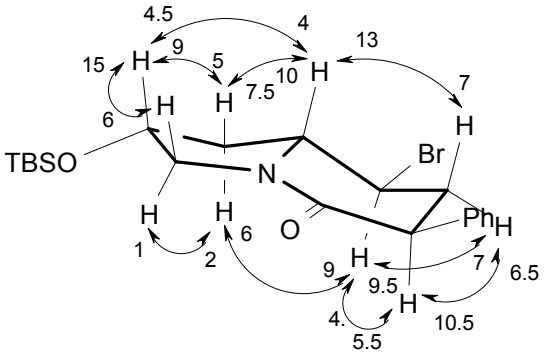
168.3 (q, C=O), 140.0 (q), 128.7 (q), 128.0 (q), 127.0 (q), 68.3 (d, C-8), 63.4 (d, C-6), 54.4 (t, C-9), 49.4 (d, C-3), 47.5 (d, C-5), 42.5 (t, C-7), 41.9 (t, C-7), 25.7 (Si-C(CH_3)$_3$), 24.0 (d, C-5), 17.9 (Si-C(CH_3)$_3$), - 4.9 (Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3065 (w), 3028 (w), 2956 (s), 2928 (s), 2884 (m), 2858 (s), 1640 (s, N-CO), 1495 (m), 1471 (m), 1460 (s), 1432 (s), 1370 (m), 1252 (m, C=O), 1173 (s), 1111 (s), 1006 (w), 899 (s), 838 (s), 777 (s), 699 (m).

MS (80eV, EI, 140 °C):

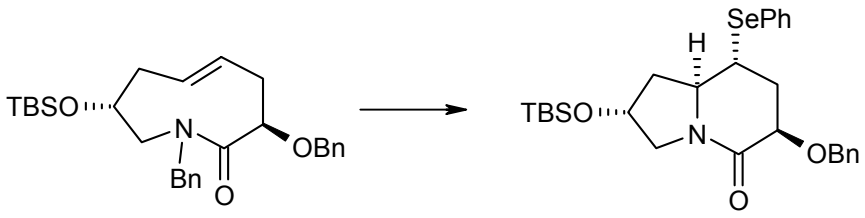
m/z (%): 425 (0.2) [M^+], 424 (0.3) [M-H], 410 (4) [M-CH_3], 368 (100) [M-C_4H_9], 286 (5), 184 (5), 143 (5), 91 (5), 73 (6).



HRMS (80eV,140 °C): found 408.09965

calc. 408.09945 (for $C_{19}H_{27}NO_2$ ^{79}Br Si , [M-CH_3]).

3*R*,5*R*,6*S*,8*R*-3-Benzyloxy-5-phenylselanyl-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [23a]



[14a] 465.71 [$C_{28}H_{39}NO_3Si$] **[23a]** 530.65 [$C_{27}H_{37}NO_3SeSi$]

Reaction of ***pS*-[14a]** (960mg, 2.06 mmol) with PhSeBr was carried out according to the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 2:1, R_f = 0.28) to yield **[23a]**, after recrystallisation from diethyl ether / n-hexane at -20 °C, as colourless needles (100 mg, 74%) with mp 77 °C.

$[\alpha]_D^{20}$ = + 2.13° (c = 1.87, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.60 - 7.50 (m, 2H; H-o-SePh), 7.4 -7.1 (m, 8H), 4.90 - 4.85 (d, 1H; H-OBn-1; ^{2}J (H^{OBn-1},H^{OBn-2}) = 12 Hz), 4.73 - 4.67 (d, 1H; H-OBn-2; ^{2}J (H^{OBn-2},H^{OBn-1}) = 12 Hz), 4.40 - 4.35 (dd, 1H; H-8o; ^{3}J (H^{8o},H^{9o}) = 5 Hz, ^{3}J (H^{8o},H^{7o}) = 5 Hz), 3.85 - 3.80 (dd, 1H; H-3u; ^{3}J (H^{3u},H^{4u}) = 4 Hz, ^{3}J (H^{3u},H^{4o}) = 2 Hz), 3.80 - 3.67 (m, 2H; H-9o, 6u), 3.78 - 3.73 (dd, 1H; H-3u; ^{3}J (H^{3u},H^{4u}) = 5 Hz, ^{3}J (H^{3u},H^{4o}) = 2 Hz), 3.37 - 3.30 (d, 1H; H-9u; ^{2}J (H^{9u},H^{9o}) = 13 Hz), 3.32 - 3.20 (ddd, 1H; H-5o; ^{3}J (H^{5o},H^{4u}) = 13 Hz, ^{3}J (H^{5o},H^{6u}) = 11 Hz, ^{3}J (H^{5o},H^{4o}) = 4 Hz), 2.50 - 2.40 (ddd, 1H; H-4o; ^{2}J (H^{4o},H^{4u}) = 14 Hz, ^{3}J (H^{4o},H^{5o}) = 3 Hz, ^{3}J (H^{4o},H^{3u}) = 3 Hz), 2.25 - 2.18 (dd, 1H; H-7u; ^{2}J (H^{7u},H^{7o}) = 13 Hz, ^{3}J (H^{7u},H^{6u}) = 4 Hz), 1.98 - 1.85 (ddd, 1H; H-4u; ^{2}J (H^{4u},H^{4o}) = 14 Hz, ^{3}J (H^{4u},H^{5o}) = 13 Hz, ^{3}J (H^{4u},H^{3u}) = 4 Hz), 1.60 - 1.49 (ddd, 1H; H-7o; ^{2}J (H^{7o},H^{7u}) = 12 Hz, ^{3}J (H^{7o},H^{6o}) = 12 Hz, ^{3}J (H^{7o},H^{8o}) = 4 Hz), 0.80 (s, 9H; H-Si (CMe_3), 0.01 (s, 3H; H-Si-CH_3), 0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

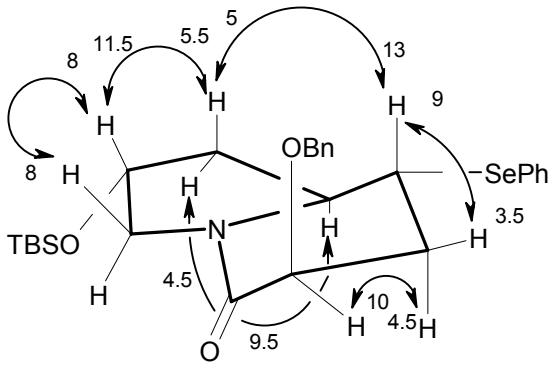
166.6 (q, C=O), 138.1 (d), 136.1 (d), 129.1 (d), 128.4 (d), 128.2 (d), 127.8 (d), 127.5 (d), 125.9 (d), 73.9 (d, C-3), 72.8 (t, C-10), 68.1 (d, C-8), 61.6 (d, C-6), 55.4 (t, C-9), 42.7 (t, C-4), 37.2 (t, C-4), 37.1 (d, C-5), 25.7 (Si-C(CH_3)$_3$), 17.9 (Si-C(CH_3)$_3$), - 4.8 (Si-CH_3), - 4.9 (Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3411.2 (w), 3061 (w), 3030 (w), 2952 (s), 2928 (s), 2883 (s), 2855 (s), 1635 (s, N-CO), 1578 (w), 1471 (s), 1454 (w), 1437 (w), 1366 (w), 1253 (s, C=O), 1216 (m), 1125 (m), 1071 (s), 1027 (s), 837 (s), 777 (s), 739 (s), 694 (s).

MS (80eV, EI, 180 °C):

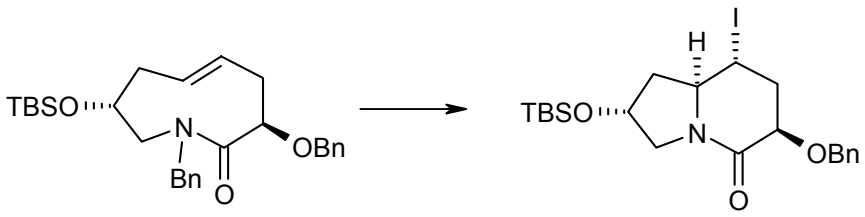
m/z (%): 531 (0.5) [M+.], 516 (2.9) [M+ -CH_3], 474 (90) [M+ - C_4H_9], 425 (45) [M+ -CH_3 -Bn], 364 (10), 344 (30), 268 (10), 226 (20), 210 (15), 91 (100), 75 (20), 73 (20).



HRMS (80eV,140 °C): Found 516.14719

calc. 516.14731 ($C_{26}H_{34}NO_3SeSi$, for [M^{+}-CH_3]).

3*R*,5*R*,6*S*,8*R*-3-Benzyloxy-5-iodo-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [24a]



[14a] 465.71 [$C_{28}H_{39}NO_3Si$] **[24a]** 501.48 [$C_{21}H_{32}INO_3Si$]

Reaction of ***pS*-[14a]** (100mg, 0.21 mmol) with iodine was carried out according to the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 3:1, R_f = 0.31) to yield **[24a]**, after recrystallisation from diethyl ether / n-hexane at -20 °C, as colourless needles (80 mg, 70%) with mp = 99 °C.

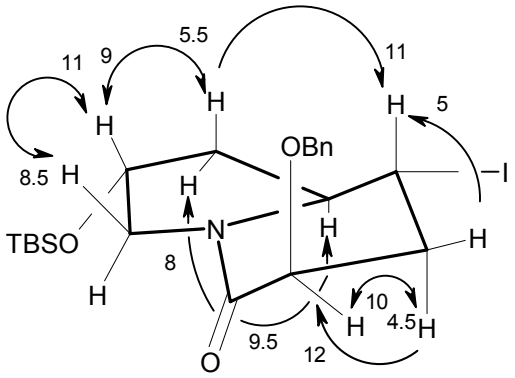
$[\alpha]_D^{20}$ = + 8.08° (c = 0.755, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
7.4 -7.1 (m, 5H), 4.94 - 4.89 (d, 1H; H-OBn-1; ^2J (H^{OBn-1},H^{OBn-2}) = 11 Hz), 4.75 - 4.70 (d, 1H; H-OBn-2; ^2J (H^{OBn-2},H^{OBn-1}) = 11 Hz), 4.40 - 4.35 (dd, 1H; H-8o; ^3J (H^{8o},H^{9o}) = 4 Hz, ^3J (H^{8o},H^{7o}) = 4 Hz), 4.10 - 3.95 (m, 2H; H-5o,6u), 3.87 - 3.78 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 13 Hz, ^3J (H^{9o},H^{8o}) = 5 Hz), 3.78 - 3.73 (dd, 1H; H-3u; ^3J (H^{3u},H^{4u}) = 5 Hz, ^3J (H^{3u},H^{4o}) = 2 Hz), 3.73 - 3.65 (d, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 13 Hz), 2.75 - 2.65 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 14 Hz, ^3J (H^{4o},H^{5o}) = 5 Hz, ^3J (H^{4o},H^{3u}) = 2 Hz), 2.50 - 2.38 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 14 Hz, ^3J (H^{4u},H^{5o}) = 12 Hz, ^3J (H^{4u},H^{3u}) = 5 Hz), 2.33 - 2.25 (m, 1H; H-7u), 1.68 - 1.75 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 12 Hz, ^3J (H^{7o},H^{6o}) = 11 Hz, ^3J (H^{7o},H^{8o}) = 4 Hz), 0.80 (s, 9H; H-Si (CMe_3)), 0.01 (s, 3H; H-Si-CH_3), 0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (62.9 MHz, $CDCl_3$):
166.4 (C=O), 137.8, 128.3, 128.0, 127.7, 74.3, 73.0, 67.4, 64.4, 56.4, 44.9, 42.5, 20.2 (C-5), 25.7 (Si-$C(CH_3)_3$), 18.0 (Si-$C(CH_3)_3$), - 4.7 (Si-CH_3), -4.8 (Si-CH_3).

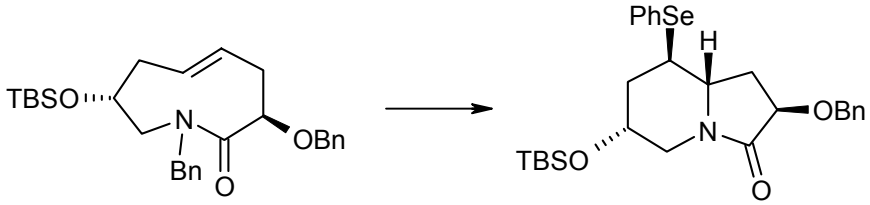
IR (KBr):
υ (cm^{-1}) = 3432 (w), 3087 (w), 3063 (w), 3029 (w), 3027 (w), 2956 (s), 2926 (s), 2903 (s), 2804 (s), 2876 (s), 2854 (s), 1637 (s, N-CO), 1631 (s), 1471 (s), 1449 (s), 1433 (m), 1373 (m), 1270 (s), 1252 (m, C=O), 1196 (m), 1169 (m), 1083 (s), 1071 (s), 1025 (s), 843 (m), 827 (m), 773 (m), 736 (m), 697 (m).

MS (70eV, EI, 130 °C):
m/z (%): 500 (0.2) [M -H^+], 486 (4) [M^+ - CH_3], 444 (35) [M^+ - C_4H_9], 395 (72) [M^+ - C_7H_7 - CH_3], 352 (6), 303 (5), 268 (100) [M- I-CH_3- C_7H_7], 226 (10), 210 (11), 91 (60), 73 (11).



HRMS (80eV,130 °C): found 486.09198
calc. 486.096149 (for $C_{20}H_{29}INO_3Si$).

3*R*,5*R*,6*S*,8*R*-3-(*tert*-Butyldimethylsilyloxy)-5-phenylselanyl-8-benzyloxy-1-azabicyclo[4.3.0]nonan-9-one [23b]



[14b] 465.71 [$C_{28}H_{39}NO_3Si$] **[23b]** 530.65 [$C_{27}H_{37}NO_3SeSi$]

Reaction of ***pS*-[14b]** (100mg, 0.21 mmol) with PhSeBr was carried out according to the standard procedure **B**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 3:1, R_f= 0.31) to yield **[23b]** as a colourless oil (43.0 mg, 38%).

$[\alpha]_D^{20}$ = - 18.25° (c = 1.09, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
7.6 (m, 2H; H-oSePh-H), 7.4 -7.2 (m, 8H), 4.94 - 4.88 (d, 1H; H-OBn-1; ^2J (H^{OBn-1},H^{OBn-2}) = 12 Hz), 4.74 - 4.66 (d, 1H; H-OBn-2; ^2J (H^{OBn-2},H^{OBn1}) = 12 Hz), 4.10 - 4.03 (dd, 1H; H-8u; ^3J (H^{8u},H^{7o}) = 8 Hz, ^3J (H^{8u},H^{7u}) = 4 Hz), 4.02 - 3.95 (m, 2H; H-3o, 2u), 3.53 - 3.42 (ddd, 1H; H-6o; ^3J (H^{6o},H^{5o}) = 11 Hz, ^3J (H^{6o},H^{7u}) = 7 Hz, ^3J (H^{6o},H^{7o}) = 6 Hz), 3.18 - 3.07 (ddd, 1H; H-5o; ^3J (H^{5o},H^{4o}) = 12 Hz, ^3J (H^{5o},H^{6o}) = 11 Hz, ^3J (H^{5o},H^{4u}) = 4 Hz), 2.73 - 2.65 (dd, 1H; H-2o; ^2J (H^{2o},H^{2u}) = 15 Hz, ^3J (H^{2o},H^{3o}) = 2 Hz), 2.40 - 2.28 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 11 Hz, ^3J (H^{7o},H^{8u}) = 7 Hz, ^3J (H^{7o},H^{6o}) = 3 Hz), 2.25 - 2.15 (dddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 14 Hz, ^3J (H^{4u},H^{5o}) = 6 Hz, ^3J (H^{4u},H^{3o}) = 6 Hz, ^4J (H^{4u},H^{2u}) = 3 Hz), 2.15 - 2.05 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 14 Hz, ^3J (H^{7u},H) = 8 Hz, ^3J (H^{7u},H) = 5 Hz), 1.70 - 1.60 (m, 1H; H-4o), 0.80 (s, 9H; H-Si (CMe_3)), 0.01 (s, 3H; H-Si-CH_3), 0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (62.9 MHz, $CDCl_3$):

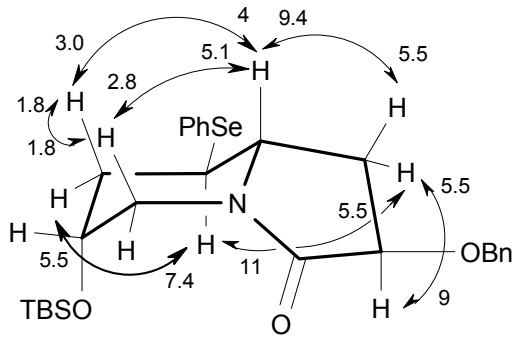
171.8 (C=O), 137.9, 135.8, 129.1, 128.3, 128.2, 128.0, 127.6, 126.4, 71.9 (C-8), 65.6 (C-3), 59.0 , 45.9, 41.6, 40.0, 33.2, 25.6 (Si-C(CH_3)$_3$), 17.9 (Si-C(CH_3)$_3$), - 4.9 (Si-CH_3), -5.16 (Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3449 (w), 3061 (w), 3031 (w), 2953 (s), 2927 (s), 2884 (m), 2856 (s), 1699 (s, N-CO), 1579 (w), 1471 (m), 1461 (m), 1453 (m), 1437 (m) 1429 (m), 1361 (w), 1258 (m, C=O), 1102 (m), 1072 (m), 1044 (m), 837 (m), 806 (w), 777 (m), 740 (m), 695 (m).

MS (80eV, EI, 160 °C):

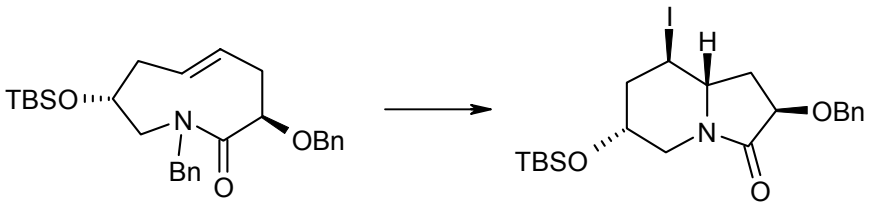
m/z (%): 516 (3) [M+ - CH_3], 474 (100) [M+ - C_4H_9], 425 (45) [M+ - CH_3 - Bn], 316 (5), 268 (10), 226 (20), 210 (15), 91 (90), 75 (20), 73 (20).



HRMS (80eV,150 °C): found 516.14337

calc. 516.147318 (for $C_{26}H_{34}NO_3SiSe$, M-CH_3).

3*R*,5*R*,6*S*,8*R*-3-(*tert*-Butyldimethylsilyloxy)-5-iodo-8-benzyloxy-1-azabicyclo[4.3.0]nonan-9-one [24b]



[14a] 465.71 [$C_{28}H_{39}NO_3Si$] **[24b]** 501.48 [$C_{21}H_{32}INO_3Si$]

Reaction of ***pS*-[14a]** (100mg, 0.21 mmol) with iodine was carried out according to the standard procedure **B**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 3:1, R_f = 0.45) to yield **[24b]** as a colourless oil (11 mg, 10%).

$[\alpha]_D^{20}$ = - 10.0° (c = 0.3, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

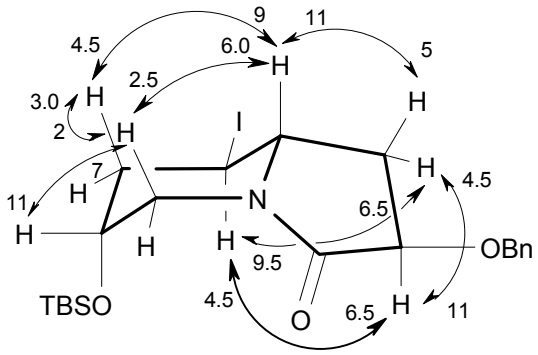
7.4 -7.2 (m, 5H), 4.94 - 4.88 (d, 1H; H-OBn-1; ^{2}J (H^{OBn-1},H^{OBn-2}) = 12 Hz), 4.74 - 4.66 (d, 1H; H-OBn-2; ^{2}J (H^{OBn-2},H^{OBn-1}) = 12 Hz), 4.14 - 4.05 (m, 2H; H-8u,2u), 4.03 - 3.93 (ddd, 1H; H-5o; ^{3}J (H^{5o},H) = 12 Hz, ^{3}J (H^{5o},H) = 11 Hz, ^{3}J (H^{5o},H) = 4 Hz), 3.90 - 3.85 (m, 1H; H-3o), 3.85 - 3.75 (ddd, 1H; H-6o; ^{3}J (H^{6o},H^{5o}) = 11 Hz, ^{3}J (H^{6o},H^{7u}) = 7 Hz, ^{3}J (H^{6o},H^{7o}) = 6 Hz), 2.90 - 2.83 (dd, 1H; H-2o; ^{2}J (H^{2o},H^{2u}) = 15 Hz, ^{3}J (H^{2o},H^{3o}) = 2 Hz), 2.51 - 2.42 (dddd, 1H; H-4u; ^{2}J (H^{4u},H^{4o}) = 14 Hz, ^{3}J (H^{4u},H^{5o}) = 6 Hz, ^{3}J (H^{4u},H^{3o}) = 6 Hz, ^{4}J (H^{4u},H^{2u}) = 3 Hz), 2.41 - 2.30 (ddd, 1H; H-7o; ^{2}J (H^{7o},H^{7u}) = 11 Hz, ^{3}J (H^{7o},H^{8u}) = 7 Hz, ^{3}J (H^{7o},H^{6o}) = 3 Hz), 2.21 - 2.10 (m, 1H; H-4o), 2.09 - 1.98 (ddd, 1H; H-7u; ^{2}J (H^{7u},H^{7o}) = 14 Hz, ^{3}J (H^{7u},H) = 8 Hz, ^{3}J (H^{7u},H) = 5 Hz), 0.80 (s, 9H; H-Si (CMe_3)), 0.01 (s, 3H; H-Si-CH_3), 0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (62.9 MHz, $CDCl_3$):

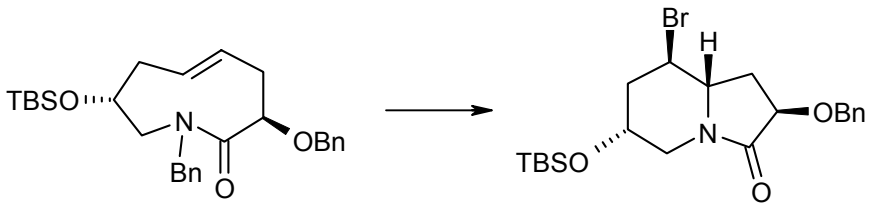
172.1 (C=O), 137.7, 128.4, 128.0, 127.7, 74.5, 72.0, 67.0 (C-8), 61.7 (C-3), 46.1, 45.2, 34.2, 27.6, 25.6 (Si-C(CH_3)$_3$), - 4.9 (Si-CH_3), -5.0 (Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3062 (w), 3031 (w), 2952 (s), 2927 (s), 2894 (m), 2855 (m), 1700 (s, N-CO), 1496 (m), 1471 (m), 1462 (m), 1453 (m), 1428 (s), 1360 (m), 1258 (m, C=O), 1138 (m), 1098 (s), 1072 (s), 1041 (m), 837 (s), 805 (w), 777 (s), 736 (m), 699 (m).



3*R*,5*R*,6*S*,8*R*-3-(*tert*-Butyldimethylsilyloxy)-5-bromo-8-benzyloxy-1-azabicyclo[4.3.0]nonan-9-one [25b]



[14a] 465.71 [$C_{28}H_{39}NO_3Si$] **[25b]** 454.48 [$C_{21}H_{32}BrNO_3Si$]

Reaction of ***pS*-[14a]** (100mg, 0.21 mmol) with iodine was carried out according to the standard procedure **B**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 5:1, R_f= 0.38) to yield **[25b]** as a colourless oil (12 mg, 8.2%).

$[\alpha]_D^{20}$ = - 4.4° (c = 1.18, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.4 -7.1 (m, 5H), 4.95 - 4.90 (d, 1H; H-OBn-1; ^2J (H^{OBn-1},H^{OBn-2}) = 12 Hz), 4.75 - 4.70 (d, 1H; H-OBn-2; ^2J (H^{OBn-2},H^{OBn-1}) = 12 Hz), 4.15 - 4.08 (dd, 1H; H-8u; ^3J (H^{8u},H^{7o}) = 8 Hz, ^3J (H^{8u},H^{7u}) = 4 Hz), 4.08 - 3.98 (m, 2H; H-3o, 2u), 3.95 - 3.85 (ddd, 1H; H-5o; ^3J (H^{5o},H^{4o}) = 12 Hz, ^3J (H^{5o},H^{6o}) = 11 Hz, ^3J (H^{5o},H^{4u}) = 4 Hz), 3.70 - 3.60 (ddd, 1H; H-6o; ^3J (H^{6o},H^{5o}) = 11 Hz, ^3J (H^{6o},H^{7u}) = 7 Hz, ^3J (H^{6o},H^{7o}) = 4 Hz), 2.88 - 2.79 (d, 1H; H-2o; ^3J (H^{2o},H^{2u}) = 12 Hz), 2.45 - 2.30 (m, 2H; H-7o, 4u), 2.22 - 2.10 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 13 Hz, ^3J (H^{7u},H^{6o}) = 8 Hz, ^3J (H^{7u},H^{8u}) = 5 Hz), 2.04 - 1.94 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 14 Hz, ^3J (H^{4o},H^{5o}) = 13 Hz, ^3J (H^{4o},H^{3o}) = 2 Hz), 0.80 (s, 9H; H-Si (CMe_3), 0.01 (s, 3H; H-Si-CH_3), 0.05 (s, 3H; H-Si-CH_3).

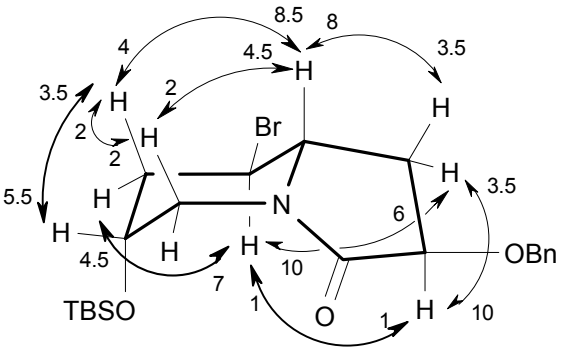
^{13}C-NMR (62.9 MHz, $CDCl_3$):

128.3, 128.0, 127.7, 74.5 (d), 72.0 (t), 66.5 (d, C-8), 60.0 (d, C-3), 49.2 (d), 46.0 (t), 43.0 (t) , 32.4 (t), 25.6 (Si-C(CH_3)$_3$), 17 (Si-C(CH_3)$_3$), - 4.9 (Si-CH_3), -5.16 (Si-CH_3).

IR (KBr):

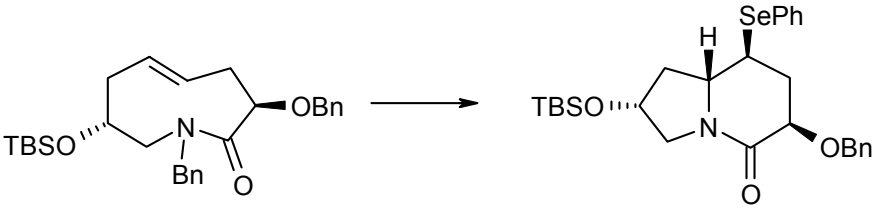
υ (cm^{-1}) = 3098 (w), 3062 (w), 3032 (w), 2955 (s), 2929 (s), 2857 (s), 1703 (s, N-CO), 1471 (s), 1430 (s), 1361 (m), 1259 (s, C=O), 1198 (m), 1170 (w), 1084 (s), 1044 (s), 1006 (w), 886 (m), 806 (m), 778 (m), 739 (m), 698 (m),

MS (70eV, EI, 110 °C):
m/z (%): 440 (4) [M^+ -CH_3], 438 (3.7) [M^+ - CH_3], 398 (100) [M^+ - C_4H_9], 396 (96) [M^+ - C_4H_9], 349 (53) 347 (52), 292 (9), 290 (9), 210 (12), 140 (12), 101 (10), 91 (88), 73 (18).



HRMS (80eV,150 °C): found 438.10519
calc. 438.11009 (for $C_{20}H_{29}BrNO_3Si$).

3*R*,5*S*,6*R*,8*R*-3-Benzyloxy-5-phenylselanyl-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [23c]



[14b] 465.71 [$C_{28}H_{39}NO_3Si$] **[23c]** 530.65 [$C_{27}H_{37}NO_3SeSi$]

Reaction of ***pR*-[14b]** (130mg, 0.28 mmol) with PhSeBr was carried out according to the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate 7:1, R_f= 0.38) to yield **[23c]** as a colourless oil (30.5 mg, 20%).

$[\alpha]_D^{20}$ = + 73.18° (c = 1.98, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
7.60 - 7.50 (m, 2H; o-PhSe), 7.40 - 7.20 (m, 8H), 4.95 - 4.85 (d, 1H; OBn1; ^2J (H^{OBn1},H^{OBn2}) = 12 Hz), 4.75 - 4.65 (d, 1H; OBn2; ^2J (H^{OBn2},H^{OBn1}) = 12 Hz), 4.38 - 4.28 (m, 1H; H-8o), 3.98 - 3.80 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 8 Hz, ^3J (H^{3u},H^{4u}) = 7 Hz), 3.70 - 3.55 (ddd, 1H; H-6o; ^3J (H^{6o},H^{5u}) = 10 Hz, ^3J (H^{6o},H^{7u}) = 10 Hz, ^3J (H^{6o},H^{7o}) = 6 Hz), 3.56 - 3.50 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 12 Hz, ^3J (H^{9o},H^{8o}) = 6 Hz), 3.50 - 3.43 (dd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 12 Hz, ^3J (H^{9u},H^{8o}) = 5 Hz), 3.10 - 3.00 (ddd, 1H; H-5u; ^3J (H^{5u},H^{6o}) = 11 Hz, ^3J (H^{5u},H^{4o}) = 11 Hz, ^3J (H^{5u},H^{4u}) = 5 Hz), 2.58 - 2.48 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 11 Hz, ^3J (H^{4u},H) = 6 Hz, ^3J (H^{4u},H) = 4 Hz), 2.45 - 2.35 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 12 Hz, ^3J (H^{7o},H^{6o}) = 6 Hz, ^3J (H^{7o},H^{8o}) = 6 Hz), 2.08 - 1.95 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 14 Hz, ^3J (H^{4o},H^{3u}) = 12 Hz, ^3J (H^{4o},H^{5u}) = 9 Hz), 1.73 - 1.60 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 13 Hz, ^3J (H^{7u},H) = 10 Hz, ^3J (H^{7u},H) = 7 Hz), 0.80 (s, 9H; H-Si (CMe_3), 0.01 (s, 3H; H-Si-CH_3), 0.05 (s, 3H; Si-CH_3).

^{13}C-NMR (62.9 MHz, $CDCl_3$):

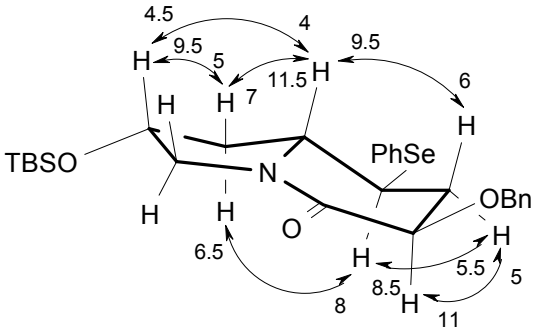
168.1 (C=O), 138.0, 136.0, 129.2, 128.5, 128.3, 127.9, 127.6, 126.5, 74.9 (d, C-3), 72.8 (t, C-OBn), 68.8 (d, C-8), 61.3 (d, C-6), 53.2 (t, C-9), 41.9 (t, C-4), 40.4 (d, C-5), 36.9 (t, C-7), 25.7 (Si-C$(CH_3)_3$), 17.9 (Si-C$(CH_3)_3$), -4.9 (Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3059 (w), 3030 (w), 2953 (s), 2927 (s), 2883 (m), 2855 (s), 1654 (s, N-CO), 1578 (w), 1471 (s) 1454 (s), 1437 (s), 1385 (m), 1258 (m, C=O), 1119 (m), 1091 (m), 1022 (w), 895 (m), 837 (m), 778 (m), 739 (m), 695 (m).

MS (80eV, EI, 170 °C):

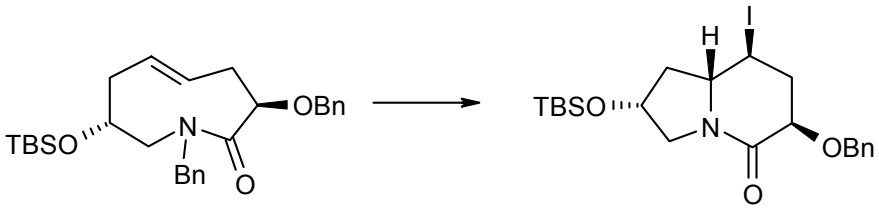
m/z = 531 (1.3) [$M^{+\cdot}$], 516 (3) [M-CH_3], 474 (40.2) [M-C_4H_9], 425 (90.1) [M-CH_3-C_7H_7], 374 (13.5) [M-SePh], 344 (37.9), 268 (10), 226 (12), 91 (100), 73 (18.3).



HRMS (80eV,170 °C): found 531.17552

calc. 531.170793 (for $C_{27}H_{37}NO_3Si\ ^{80}Se$).

3*R*,5*S*,6*R*,8*R*-3-Benzyloxy-5-iodo-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [24c]



[14b] 465.71 [$C_{28}H_{39}NO_3Si$] **[24c]** 501.48 [$C_{21}H_{32}INO_3Si$]

Reaction of ***pR*-[14b]** (130mg, 0.28 mmol) with iodine was carried out according to the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate 7:1, R_f = 0.40) to yield **[24c]** as a colourless oil (55.2 mg, 40%).

$[\alpha]_D^{20}$ = + 77.12° (c = 1.84, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.4 -7.1 (m, 5H), 4.95 - 4.88 (d, 1H; H-OBn1; ^{2}J (H^{OBn1},H^{OBn2}) = 12 Hz), 4.78 - 4.73 (d, 1H; OBn2; ^{2}J (H^{OBn2},H^{OBn1}) = 12 Hz), 4.40 - 4.30 (m, 1H; H-8o), 4.00 - 3.80 (m, 3H; H-3u, 6o, 5u), 3.65 - 3.55 (m, 2H; H-9u, 9o), 2.88 - 2.78 (ddd, 1H; H-4u; ^{2}J (H^{4u},H^{4o}) = 11 Hz, ^{3}J (H^{4u},H) = 7 Hz, ^{3}J (H^{4u},H) = 5 Hz), 2.55 - 2.40 (m, 2H; H-7u, 4o), 1.95 - 1.75 (m, 1H; H-7u), 0.80 (s, 9H; H-Si (CMe_3), 0.01 (s, 3H; H-Si-CH_3), 0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (62.9 MHz, $CDCl_3$):

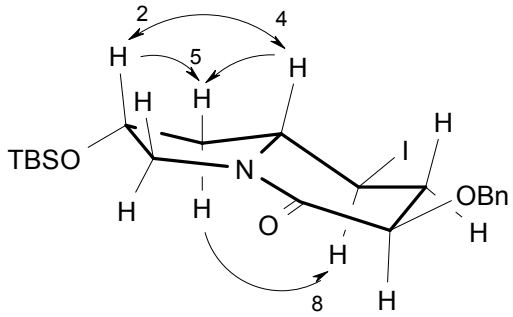
167.8 (C=O), 137.7, 128.3, 127.9, 127.7, 74.9 (d, C-3), 72.7 (t, CH2-OBn), 68.1 (d, C-8), 61.4 (d, C-6), 54.3 (t, C-9), 43.1 (t, C-7), 41.8 (t, C-4), 21.8 (d, C-5), 25.7 (Si-C(CH_3)$_3$), 17.9 (Si-C(CH_3)$_3$), - 4.8 (Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3089 (w), 3063 (w), 3030 (w), 2976 (s), 2926 (s), 2856 (m), 1641 (s, N-CO), 1496 (w),1470 (s), 1453 (s), 1383 (m), 1360 (m), 1253 (m, C=O), 1257 (m), 1195 (m), 1165 (s), 1138 (s), 1091 (m), 1024 (w), 894 (s), 838 (m), 778 (m), 734 (m), 695 (m).

MS (80eV, EI, 150 °C):

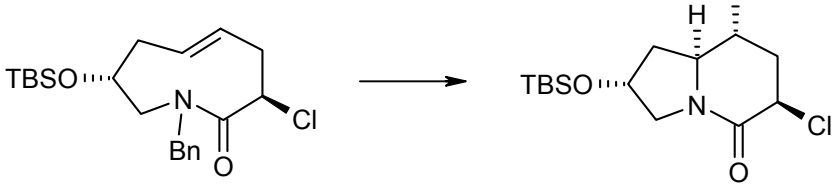
m/z (%): 500 (0.2) [M -H^+], 486 (4) [M^+ -CH_3], 444 (100) [M^+ -C_4H_9], 395 (84) [M^+ -C_7H_7 -CH_3], 268 (51) [M-I-CH_3-C_7H_7], 226 (9), 210 (10), 91 (86), 73 (19).



HRMS (80eV,130 °C): found 486.09378

calc. 486.096149 (for $C_{20}H_{29}INO_3Si$, [M-CH_3]).

3*R*,5*R*,6*S*,8*R*-3-Chloro-5-phenylselanyl-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [26a]



[12a] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[26a]** 458.97 [$C_{20}H_{30}ClNO_2SeSi$]

Reaction of ***pS*-[12a]** (200mg, 0.51 mmol) with PhSeBr was carried out according to the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 3:1, R_f= 0.34) to yield **[26a]** as a colourless oil (187.7 mg, 81%).

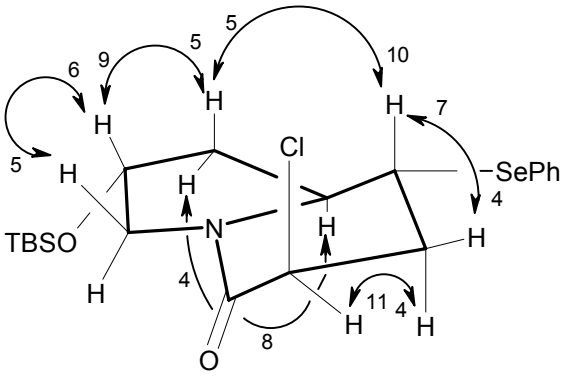
$[\alpha]_D^{20}$ = - 35.8° (c = 1.52, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
7.70 - 7.60 (m, 2H; H-o-PhSe), 7.4 -7.1 (m, 3H), 4.40 - 4.35 (m, 2H; H-8o, 3u), 3.95 - 3.70 (m, 2H; H-9o, 6u), 3.40 - 3.35 (m, 2H; H-9u, 5o), 2.62 - 2.52 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 15 Hz, ^3J (H^{4o},H^{3u}) = 2 Hz, ^3J (H^{4o},H^{5o}) = 2 Hz), 2.35 - 2.20 (m, 2H; H-7u, 4u), 1.65 - 1.55 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 12 Hz, ^3J (H^{7o},H^{6u}) = 12 Hz, ^3J (H^{7o},H^{8o}) = 4 Hz), 0.80 (s, 9H; H-Si (CMe_3), 0.01 (s, 3H; H-Si-CH_3), 0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (62.9 MHz, $CDCl_3$):
163.9 (C=O), 136.2, 129.3, 128.8, 125.2, 67.9 (d, C-8), 61.7 (d, C-6), 56.5 (t, C-9), 56.2 (d, C-3), 42.9 (t, C-7), 39.6 (t, C-4), 35.6 (d, C-5), 25.7 (Si-$C(CH_3)_3$), 17.9 (Si-$C(CH_3)_3$), - 4.9 (Si-CH_3).

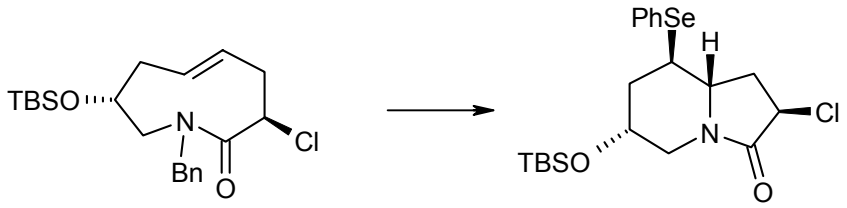
IR (KBr):
υ (cm^{-1}) = 3072 (w), 3056 (w), 2954 (s), 2928 (s), 2883 (s), 2855 (s), 1660 (s, N-CO), 1578 (w), 1448 (s), 1364 (m), 1253 (s, C=O), 1217 (m), 1125 (m), 1082 (s), 1025 (s), 837 (s), 808 (s), 777 (s), 740 (s), 692 (s), 662 (s).

MS (70eV, EI, 150 °C):
m/z (%): 459 (3) [$M^{+\cdot}$], 444 (3) [M^+ - CH_3], 402 (100) [M^+ - C_4H_9], 302 (10) [M^+ - PhSe], 244 (14) [M^+ - C_4H_9 - PhSeH], 210 (40) [$C_{10}H_{16}NO_2Si^+$], 170 (8), 134 (12), 73 (38).



HRMS (80eV,150 °C): found 459.08975
calc. 459.08996 (for $C_{20}H_{30}ClNO_2SiSe$).

3*R*,5*R*,6*S*,8*R*-3-(*tert*-Butyldimethylsilyloxy)-5-phenylselanyl-8-chloro-1-azabicyclo[4.3.0]nonan-9-one [26b]



[12a] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[26b]** 458.97 [$C_{20}H_{30}ClNO_2SeSi$]

Reaction of ***pS*-[12a]** (200mg, 0.51 mmol) with PhSeBr was carried out according to the standard procedure **B**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 3:1, R_f = 0.44) to yield **[26b]** as a colourless oil (45.5 mg, 20%).

$[\alpha]_D^{20}$ = - 50.24° (c = 1.25, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.56 - 7.50 (m,2H; o-SePh), 7.35-7.26 (m, 3H), 4.34 (dd, ^3J (H^{8u},H^{7o}) = 8 Hz, ^3J (H^{8u},H^{7u}) = 3 Hz, 1 H; H-8u), 4.03 - 3.93 (m, 2H; H-2u and H-3o), 3.60 - 3.50 (ddd, ^3J (H^{6o},H^{5o}) = 11 Hz, ^3J (H^{6o}, H^{7u}) = 6 Hz, ^3J (H^{6o},H^{7o}) = 6 Hz, 1 H; H-6o), 3.22 - 3.10 (m, 1H; H-5o), 2.75 (d, ^2J (H^{2o},H^{2u}) = 12 Hz, 1 H; H-2o), 2.63 (ddd, ^2J (H^{7o},H^{7u}) = 15 Hz, ^3J (H^{7o},H^{8u}) = 6 Hz, ^3J (H^{7o},H^{6o}) = 2 Hz, 1 H; H-7o), 2.32 - 2.25 (m, 1H; H-4u), 2.25 - 2.15 (m, 1H; H-7u), 1.68 (m, 1H; H-4o), 0.81 (s, 9H; Si-C(CH_3)$_3$), 0.02 (s, 3H; Si-CH_3), - 0.03 (s, 3H; Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

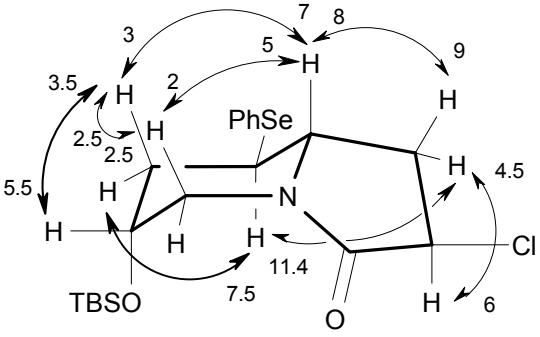
169.6 (q, C=O), 135.8 (d), 129.2 (d), 128.5 (d), 65.2 (d, C-3), 59.0 (d, C-6), 53.9 (d, C-8), 46.6 (t, C-2), 40.7 (d, C-5), 39.7 (t, C-7), 36.7 (t, C-4), 25.5 (Si-C(CH_3)$_3$), 17.9 (q, Si-C(CH_3)$_3$), - 4.9 (Si-CH_3), - 5.1 (Si-CH_3).

IR (KBr):

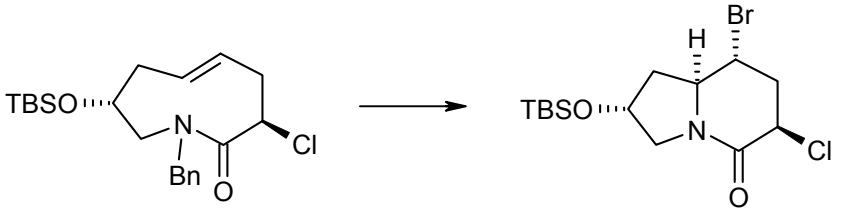
υ (cm^{-1}) = 2952 (s), 2927 (s), 2854 (s), 1714 (s, N-CO), 1578 (w),1472 (m), 1435 (m), 1257 (m, C=O), 1112 (m), 1092 (m), 1039 (m), 837 (m), 776 (m), 740 (w), 692 (w).

MS (70eV, EI, 150 °C):
m/z (%): 459 (0.1) [$M^{+\cdot}$], 444 (2) [M^+ - CH_3], 402 (100) [M^+ - C_4H_9], 244 (10) [M^+ - C_4H_9 - PhSeH], 210 (23) [$C_{10}H_{16}NO_2Si^+$], 73 (19).

HRMS (80eV,150 °C): found 444.06627
calc. 444.06647 (for $C_{19}H_{27}ClNO_2SiSe$) [M^+ - CH_3].



3*R*,5*R*,6*S*,8*R*-3-Chloro-5-bromo-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [27a]



[12a] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[27a]** 382.80 [$C_{14}H_{25}BrClNO_2Si$]

Reaction of ***pS*-[12a]** (330mg, 0.84 mmol) with bromine was carried out according to the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 3:1, R_f= 0.38) to yield **[27a]** as a colourless oil (48.6 mg, 15%).

$[\alpha]_D^{20}$ = - 30.42° (c = 1.66, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
4.46 - 4.38 (m, 2H; H-8o, 3u), 4.13 - 4.03 (ddd, 1H; H-5o; ^3J (H^{5o},H^{4u}) = 11 Hz, ^3J (H^{5o},H^{6u}) = 11 Hz, ^3J (H^{5o},H^{4o}) = 4 Hz), 4.03 - 3.90 (ddd, 1H; H-6u; ^3J (H^{6u},H^{5o}) = 11 Hz, ^3J (H^{6u},H^{7o}) = 11 Hz, ^3J (H^{6u},H^{7u}) = 5 Hz), 3.83 - 3.76 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 14 Hz, ^3J (H^{9o},H^{8o}) = 5 Hz), 3.48 - 3.40 (d, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 14 Hz), 2.80 - 2.72 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 14 Hz, ^3J (H^{4o},H^{5o}) = 4 Hz, ^3J (H^{4o},H^{3u}) = 2 Hz), 2.72 - 2.59 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 12 Hz, ^3J (H^{4o},H^{5o}) = 12 Hz, ^3J (H^{4o},H^{3u}) = 5 Hz), 2.32 - 2.25 (dd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 13 Hz, ^3J (H^{7u},H^{8o}) = 4 Hz), 1.73 - 1.60 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 11 Hz, ^3J (H^{7o},H^{6u}) = 11 Hz, ^3J (H^{7o},H^{6u}) = 4 Hz), 0.80 (s, 9H; H-Si (CMe_3)), 0.05 (s, 3H; H-Si-CH_3), 0.09 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

163.6 (q, C=O), 67.7 (d, C-8), 63.4 (d, C-6), 56.8 (t, C-9), 53.9 (d, C-3), 42.5 (t, C-7), 42.3 (t, C-4), 42.3 (d, C-5), 25.7 (Si-C$(CH_3)_3$), 17.9 (Si-C$(CH_3)_3$), - 4.9 (Si-CH_3), - 4.8 (Si-CH_3).

IR (KBr):

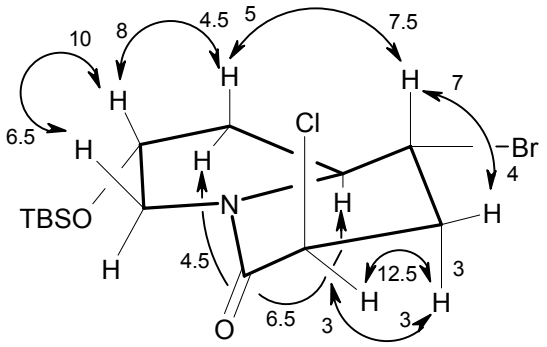
υ (cm^{-1}) = 2954 (s), 2929 (s), 2884 (s), 2856 (s), 1665 (s, N-CO), 1447 (s), 1371 (m), 1253 (s, C=O), 1218 (m), 1082 (s), 1026 (s), 837 (s), 808 (s), 777 (s).

MS (80eV, EI, 100 °C):

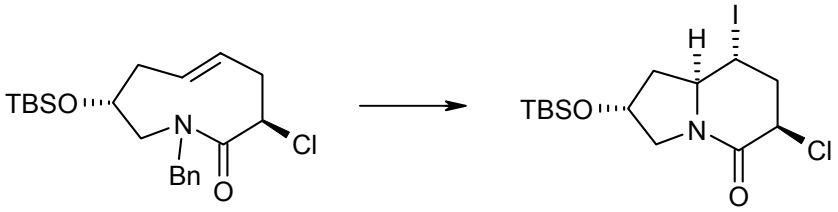
m/z (%): 368 (4.8) [M+ - CH_3], 326 (100) [M+ - C_4H_9], 244 (3), 210 (6), 75 (4), 73 (4).

HRMS (80eV,100 °C): found 366.02905

calc. 366.029180 (for $C_{13}H_{22}{}^{79}Br^{35}ClNO_2Si$, M-$CH_3$).



3*R*,5*R*,6*S*,8*R*-3-Chloro-5-iodo-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [28a]



[12a] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[28a]** 429.80 [$C_{14}H_{25}IClNO_2Si$]

Reaction of ***pS*-[12a]** (260mg, 0.66 mmol) with iodine was carried out according to the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 3:1, R_f = 0.40) to yield **[28a]**, after recrystallisation from diethyl ether/n-hexane at -20 °C, as colourless needles (230 mg, 82%) with mp = 94 °C.

$[\alpha]_D^{20}$ = - 26.48° (c = 1.412, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

4.40 - 4.34 (dd, 1H; H-8o; ^3J (H^{8o},H^{9o}) = 4 Hz, ^3J (H^{8o},H^{7o}) = 4 Hz), 4.32 - 4.26 (dd, 1H; H-3u; ^3J (H^{3u},H^{4u}) = 4 Hz, ^3J (H^{3u},H^{4o}) = 2 Hz), 4.15 - 4.05 (ddd, 1H; H-5o; ^3J (H^{5o},H^{4u}) = 11 Hz, ^3J (H^{5o},H^{6u}) = 11 Hz, ^3J (H^{5o},H^{4o}) = 4 Hz), 4.08 - 3.99 (ddd, 1H; H-6u; ^3J (H^{6u},H^{5o}) = 11 Hz, ^3J (H^{6u},H^{7o}) = 11 Hz, ^3J (H^{6u},H^{7u}) = 5 Hz), 3.85 - 3.78 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 14 Hz, ^3J (H^{9o},H^{8o}) = 5 Hz), 3.53 - 3.45 (d, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 14 Hz), 2.88 - 2.68 (m, 2H; H-4o, 4u), 2.32 - 2.25 (dd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 13 Hz, ^3J (H^{7u},H^{8o}) = 4 Hz), 1.70 - 1.57 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 11 Hz, ^3J (H^{7o},H^{6u}) = 11 Hz, ^3J (H^{7o},H^{6u}) = 4 Hz), 0.80 (s, 9H; H-Si (CMe_3)), 0.05 (s, 3H; H-Si-CH_3), 0.09 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

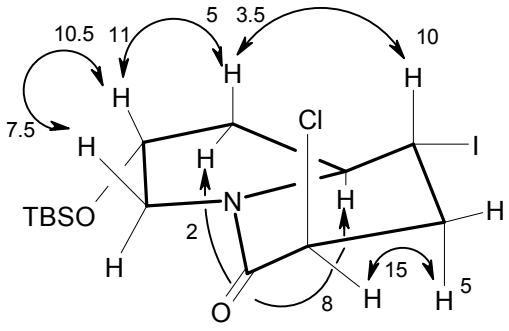
163.6 (q, C=O), 67.1 (d, C-8), 64.6 (d, C-6), 57.1 (t, C-9), 54.6 (d, C-3), 44.2 (t, C-7), 43.7 (t, C-4), 25.6 (Si-C(CH_3)$_3$), 17.9 (Si-C(CH_3)$_3$), 17.1 (d, C-5), - 4.9 (q, Si-CH_3), -5.0 (q, Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 2959 (s), 2923 (m), 2855 (m), 1659 (s, N-CO), 1651 (s), 1461 (m), 1450 (m), 1434 (m), 1371 (m), 1266 (m), 1246 (m, C=O), 1217 (s), 1078 (s), 1026 (s), 1009 (m), 840 (s), 776 (m), 661 (w).

MS (80eV, EI, 150 °C):

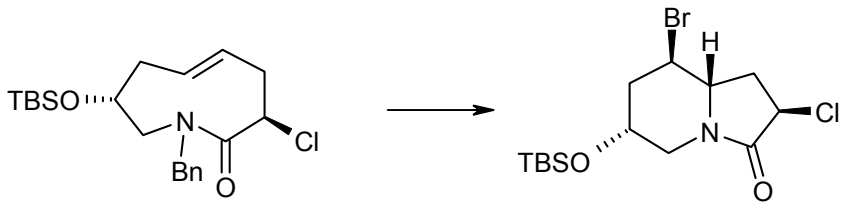
m/z (%): 414 (4) [M^+ - CH_3], 372 (100) [M^+ - C_4H_9], 245 (10) [M^+ - C_4H_9 - HI], 210 (53) [$C_{10}H_{16}NO_2Si^+$], 73 (11).



HRMS (80eV,120 °C): found 414.015140

calc. 414.015190 (for $C_{13}H_{22}ICINO_2Si$).

3*R*,5*R*,6*S*,8*R*-3-(*tert*-Butyldimethylsilyloxy)-5-bromo-8-chloro-1-azabicyclo[4.3.0]nonan-9-one [27b]



[12a] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[27b]** 382.80 [$C_{14}H_{25}BrClNO_2Si$]

Reaction of ***pS*-[12a]** (413mg, 1.05 mmol) with bromine was carried out according to the standard procedure **B**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 6:1, R_f= 0.44) to yield **[27b]** as a colourless oil (100.4 mg, 25%).

$[\alpha]_D^{20}$ = - 44.88° (c = 1.68, CH_2Cl_2).

^{1}H-NMR (270 MHz, $CDCl_3$):

4.42 - 4.36 (dd, 1H; H-8u; ^3J (H^{8u},H^{7u}) = 8 Hz, ^3J (H^{8u},H^{7u}) = 3 Hz), 4.08 - 4.02 (m, 1H; H-3o), 3.99 - 4.05 (ddd, 1H; H-2u; ^2J (H^{2u},H^{2o}) = 11 Hz, ^3J (H^{2u},H^{3o}) = 2 Hz, ^4J (H^{2u},H^{4u}) = 2 Hz), 3.98 - 3.87 (ddd, 1H; H-5o; ^3J (H^{5o},H^{4o}) = 12 Hz, ^3J (H^{5o},H^{6o}) = 10 Hz, ^3J (H^{5o},H^{4u}) = 4 Hz), 3.77 - 3.67 (ddd, 1H; H-6o; ^3J (H^{6o},H^{5o}) = 10 Hz, ^3J (H^{6o},H^{7o}) = 6 Hz, ^3J (H^{6o},H^{7u}) = 6 Hz), 2.92 - 2.85 (dd, 1H; H-2o; ^2J (H^{2o},H^{2u}) = 11 Hz, ^3J (H^{2o},H^{3o}) = 2 Hz), 2.65 - 2.55 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 15 Hz, ^3J (H^{7u},H^{8u}) = 7 Hz, ^3J (H^{7u},H^{6o}) = 4 Hz), 2.45 - 2.30 (m, 2H; H-4u, 7o), 2.05 - 1.95 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 14 Hz, ^3J (H^{4o},H^{5o}) = 13 Hz, ^3J (H^{4o},H^{3o}) = 2 Hz), 0.80 (s, 9H; H-Si (CMe_3), 0.01 (s, 3H; H-Si-CH_3), 0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (62.9 MHz, $CDCl_3$):

169.7 (C=O), 66.2 (d, C-8), 60.7 (d, C-3), 53.3 (d, C-6) , 48.0 (d, C-5), 46.6 (t, C-2), 42.7 (t, C-7), 35.9 (t, C-4), 25.6 (Si-C(CH_3)$_3$), 17.9 (Si-C(CH_3)$_3$), - 4.9 (Si-CH_3), -5.12 (Si-CH_3).

IR (KBr):

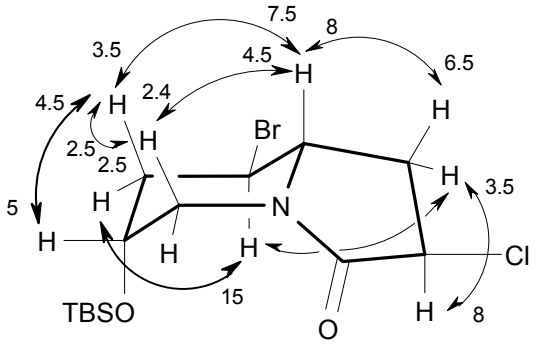
υ (cm^{-1}) = 3449 (w), 2954 (s), 2928 (s), 2885 (m), 2856 (s), 1716 (s, N-CO), 1471 (s), 1462 (s), 1427 (m), 1361 (m), 1258 (s, C=O), 1151 (s), 1098 (s), 1041 (s), 838 (s), 806 (m), 777 (s), 730 (m), 681 (m).

MS (80eV, EI, 110 °C):

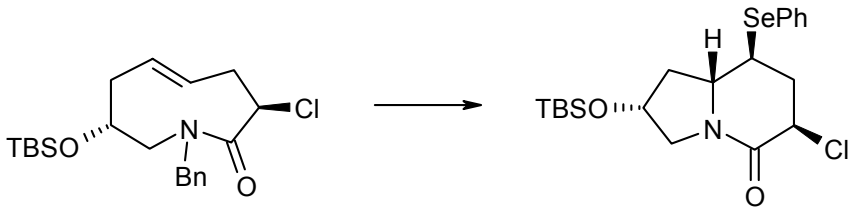
m/z (%): 382 (0.12) [M^+], 368 (3.2) [M+ - CH_3], 326 (100) [M+ - C_4H_9], 244 (8), 210 (10), 75 (10), 73 (10).

HRMS (80eV,100 °C): found 368.02520

calc. 368.027179 ($C_{13}H_{22}{}^{81}Br^{35}ClNO_2Si$, [M-CH_3]).



3*R*,5*S*,6*R*,8*R*-3-Chloro-5-phenylselanyl-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [26c]



[12b] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[26c]** 458.97 [$C_{20}H_{30}ClNO_2SeSi$]

Reaction of ***pR*-[12a]** (50mg, 0.13 mmol) with PhSeBr was carried out according to the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 10:1, R_f= 0.5) to yield **[26c]** as a colourless oil (30 mg, 64%).

$[\alpha]_D^{20}$ = + 59.4° (c = 0.4, $CHCl_3$).

^{1}H-NMR (270 MHz, C_6D_6):

7.40 (m,2H), 7.00-6.90 (m, 3H), 4.00 (dd, ^3J (H^{3u},H^{4o}) = 9 Hz, ^3J (H^{3u},H^{4u}) = 6 Hz, 1 H; H-3u), 3.84 (dddd,^3J (H^{8o},H^{7u}) = 6 Hz, ^3J (H^{8o},H^{7o}) = 6 Hz, ^3J (H^{8o},H^{9o}) = 6 Hz, ^3J (H^{8o},H^{9u}) = 6 Hz, 1 H; H-8o), 3.55 (dd, ^2J (H^{9u},H^{9o}) = 12 Hz, ^3J (H^{9u},H^{8o}) = 6 Hz, 1 H; H-9u), 3.37 (dd, ^2J (H^{9o},H^{9u}) = 12 Hz, ^3J (H^{9o},H^{8o}) = 7 Hz, 1 H; H-9o), 3.05 (ddd, ^3J (H^{6o},H^{7u}) = 10 Hz, ^3J (H^{6o},H^{5u}) = 10 Hz, ^3J (H^{6o},H^{7o}) = 5 Hz, 1 H; H-6o), 2.53 - 2.4 (m, 2H; H-5u and H-4u), 2.20 - 2.05 (m, 2H; H-7o and H-4o), 1.47 (ddd, ^2J (H^{7u},H^{7o}) = 13 Hz, ^3J (H^{7u},H^{6o}) = 10 Hz, ^3J (H^{7u},H^{8o}) = 8 Hz, 1 H; H-7u), 0.92 (s, 9H; Si-C(CH_3)$_3$), - 0.02 (s, 3H; Si-CH_3), - 0.03 (s, 3H; Si-CH_3).

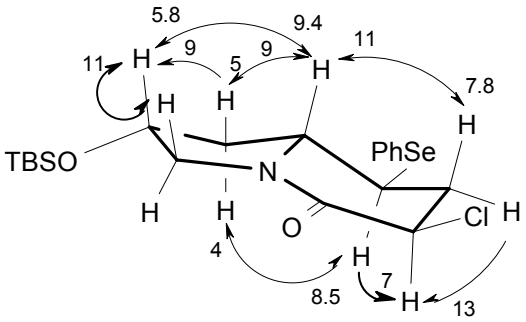
^{13}C-NMR (62.9 MHz, $CDCl_3$):

164.2 (s, C=O), 136.3 (d, ortho-C), 129.5 (d, meta-C), 125.8 (d, para-C), 125.9 (ipso-C), 68.8 (d, C-8), 61.8 (d, C-6), 54.1 (d, C-3), 53.9 (t, C-9), 42.0 (t, C-7), 40.7 (t, C-4), 40.7 (d, C-5), 22.7 (Si-C(CH_3)$_3$), 17.9 (s, Si-C(CH_3)$_3$), - 4.9 (q, Si-CH_3), -5.0 (q, Si-CH_3).

IR (KBr):

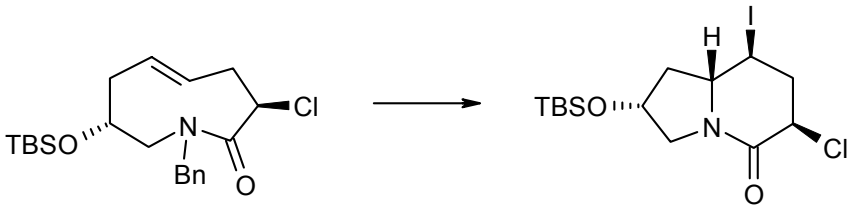
υ (cm^{-1}) = 3054 (w), 2959 (m), 2927 (m), 2880 (m), 2855 (m), 1644 (s, N-CO), 1578 (w), 1458 (m), 1434 (m), 1388 (m), 1280 (m), 1249 (m, C=O), 1135 (s), 1136 (m), 1100 (m), 851 (m), 835 (m), 773 (m), 735 (m), 690 (w), 674 (w).

MS (70eV, EI, 150 °C):
m/z (%): 459 (1) [$M^{+\cdot}$], 444 (3) [M^+ - CH_3], 436 (2), 402 (100) [M^+ - C_4H_9], 302 (11) [M^+ - PhSe], 244 (22) [M^+ - C_4H_9 - PhSeH], 210 (40), 170 (10), 134 (8), 101 (10), 73 (45).



HRMS (80eV,150 °C): found 459.08773
calc. 459.089956 (for $C_{20}H_{30}ClNO_2SiSe$).

3*R*,5*S*,6*R*,8*R*-3-Chloro-5-iodo-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo-[4.3.0]nonan-2-one [28c]



[12b] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[28c]** 429.80 [$C_{14}H_{25}ClINO_2$]

Reaction of ***pR*-[12b]** (60mg, 0.15 mmol) with iodine was carried out according to the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 10:1, R_f= 0.5) to yield **[28c]** as a colourless oil (30 mg, 64%).

$[\alpha]_D^{20}$ = + 47.0° (c = 0.04, $CHCl_3$).

^{1}H-NMR (270 MHz, C_6D_6):
3.89 (dd, ^3J (H^{3u},H^{4o}) = 10 Hz, ^3J (H^{3u},H^{4u}) = 7 Hz, 1 H; H-3u), 3.76 (dddd,^3J (H^{8o},H^{7u}) = 7 Hz, ^3J (H^{8o},H^{7o}) = 7 Hz, ^3J (H^{8o},H^{9o}) = 7 Hz, ^3J (H^{8o},H^{9u}) = 7 Hz, 1 H; H-8o), 3.54 (dd, ^2J (H^{9u},H^{9o}) = 12 Hz, ^3J (H^{9u},H^{8o}) = 6 Hz, 1 H; H-9u), 3.40 (dd, ^2J (H^{9o},H^{9u}) = 12 Hz, ^3J (H^{9o},H^{8o}) = 7 Hz, 1 H; H-9o), 3.12 (ddd, ^3J (H^{6o},H^{7u}) = 10 Hz, ^3J (H^{6o},H^{5u}) = 10 Hz, ^3J (H^{6o},H^{7o}) = 5 Hz, 1 H; H-6o), 3.01 (ddd, ^3J (H^{5u},H^{6o}) = 11 Hz, ^3J (H^{5u},H^{4o}) = 11 Hz, ^3J (H^{5u},H^{4u}) = 4 Hz, 1 H; H-5u), 2.40 (ddd, ^2J (H^{4u},H^{4o}) = 12 Hz, ^3J (H^{4u},H^{3u}) = 7 Hz, ^3J (H^{4u},H^{5u}) = 4 Hz, 1 H; H-4u), 2.30 (ddd, ^2J (H^{4o},H^{4u}) = 14 Hz, ^3J (H^{4o},H^{3u}) = 12 Hz, ^3J (H^{4o},H^{5u}) = 10 Hz, 1 H; H-4o), 2.04 (ddd, ^2J (H^{7o},H^{7u}) = 12 Hz, ^3J (H^{7o},H^{6o}) = 6 Hz, ^3J (H^{7o},H^{8o}) = 6 Hz, 1 H; H-7o), 1.38 (ddd, ^2J (H^{7u},H^{7o}) = 12 Hz, ^3J (H^{7u},H^{6o}) = 9 Hz, ^3J (H^{7u},H^{8o}) = 7 Hz, 1 H; H-7u), 0.91 (s, 9H; Si-C(CH_3)$_3$), - 0.04 (s, 3H; Si-CH_3), - 0.05 (s, 3H; Si-CH_3).

^{13}C-NMR (62.9 MHz, $CDCl_3$):

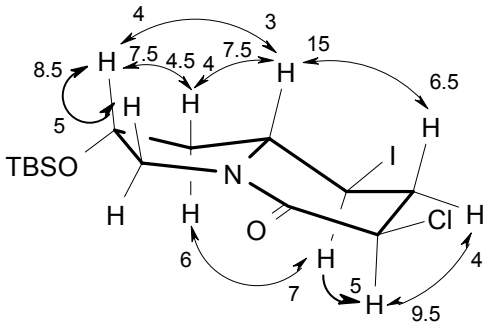
163.2 (s, C=O), 67.9 (C-8), 63.5 (C-6), 54.9 (C-3), 53.4 (C-9), 45.2 (C-4), 43.3 (C-7), 25.8 (Si-$C(CH_3)_3$), 21.2 (C-5), 18.0 (s, Si-$C(CH_3)_3$), - 4.9 (q, Si-CH_3), -5.0 (q, Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 2953 (m), 2933 (m), 2923 (m), 2883 (m), 2850 (m), 1649 (s, N-CO), 1463 (m), 1437 (m), 1386 (m), 1273 (m), 1255 (m, C=O), 1130 (s), 1112 (m), 1089 (m), 899 (s), 843 (s), 777 (m), 657 (w).

MS (70eV, EI, 150 °C):

m/z (%): 414 (3) [M^+ - CH_3], 372 (100) [M^+ - C_4H_9], 244 (5) [M^+ - C_4H_9 - HI], 210 (26) [$C_{10}H_{16}NO_2Si^+$], 170 (6), 73 (13).

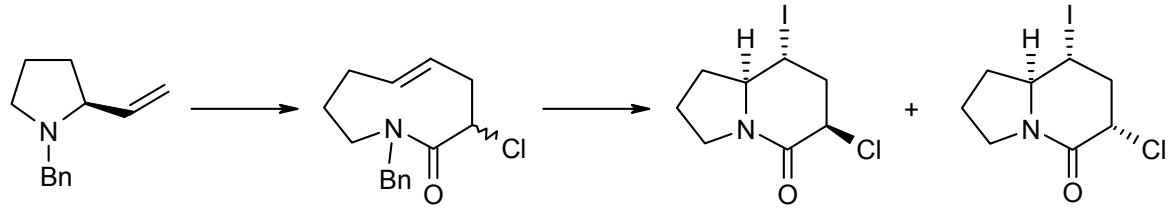


HRMS (80eV,150 °C): found 414.01514

calc. 414.01519 (for $C_{13}H_{22}NO_2Cl$ I Si) [M^+ - CH_3].

3*R*,5*R*,6*S*-3-Chloro-5-iodo-1-azabicyclo[4.3.0]nonan-2-one [29] and

3*S*,5*R*,6*S*-3-Chloro-5-iodo-1-azabicyclo[4.3.0]nonan-2-one [30]



[11] 187.29 [$C_{13}H_{17}N$] **[16,17]** 263.77 [$C_{15}H_{18}ClNO$] **[29,30]** 429.80 [$C_{14}H_{25}IClNO_2Si$]

According to standard rearrangement procedure a solution of vinyl pyrrolidine **[11]** (5.0 g, 26.7 mmol) in dry dichloromethane (100 mL) and 3.7 g (1 eq, 26.7 mmol) of K_2CO_3 was cooled with an ice bath to -10 °C and under argon chloroacetyl fluoride (10.3 g, 4 eq, 7.4 mL, 0.106 mol, d = 1.3788) was added. Then, 26.6 mL (53.4 mmol, 2 eq) of Me_3Al (2 M in n-heptane) was slowly added and further reaction and workup procedure were performed as described in **3.4**. After workup, 7.71 g of the crude product (containing **[16]** and **[17]**) was isolated and subjected to the transannular cyclisation.

Reaction of the rearrangement product with iodine followed the standard procedure **A**. The crude product was purified by column chromatography (n-hexane / ethyl acetate = 1:1, R_f = 0.14) to yield 4.23 g (53% via 2 steps) of a mixture of **[29]** and **[30]**.

An analytical sample of the mixture was separated via HPLC (32x250, Nucleosil 50-5, flow 122ml/min, UV = 254nm, ethyl acetate / n-hexane = 3:7) to yield the pure indolizidinones **[30]** (r.t. 20min) and **[29]** (r.t. 23min).

lactam [30] mp = 144-146 °C

$[\alpha]_D^{20}$ = - 45.6° (c = 1.44, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
4.40 - 4.30 (dd, 1H; H-3o; ^3J (H^{3o},H^{4u}) = 10 Hz, ^3J (H^{3o},H^{4o}) = 7 Hz), 3.90 -3.78 (ddd, 1H; H-5o; ^3J (H^{5o},H^{4u}) = 10 Hz, ^3J (H^{5o},H^{6u}) = 10 Hz, ^3J (H^{5o},H^{4o}) = 4 Hz), 3.13 - 3.04 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 13 Hz, ^3J (H^{4o},H^{3o}) = 6.5 Hz, ^3J (H^{4o},H^{5o}) = 3 Hz), 2.70 - 2.55 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 14 Hz, ^3J (H^{4u},H^{3o}) = 12.5 Hz, ^3J (H^{4u},H^{5o}) = 11 Hz), 2.48 - 2.38 (m, 1H; H-7u), 2.05 - 1.95 (m, 1H; H-8o), 1.90 - 1.70 (m, 1H; H-8u), 1.60 - 1.45 (m, 1H; H-7o).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
66.3 (d, C-3), 53.4 (d, C-6), 47.5 (t, C-9), 45.2 (t, C-4), 34.8 (t, C-7), 21.3 (t, C-8), 19.5 (d, C-5).

IR (KBr):
υ (cm^{-1}) = 3425 (s), 2939 (s), 2873 (s), 1736 (w), 1709 (w), 1636 (s), 1459 (m), 1441 (m), 1381 (w), 1332 (w), 1274 (m), 1192 (w), 1153 (w), 660 (m).

lactam [29] mp = 103-105 °C.

$[\alpha]_D^{20}$ = -11.94° (c = 1.56, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
4.28 - 4.25 (dd, 1H; H-3u; ^3J (H^{3u},H^{4u}) = 4 Hz, ^3J (H^{3u},H^{4o}) = 1.5 Hz), 4.18 - 4.08 (ddd, 1H; H-5o; ^3J (H^{5o},H^{4u}) = 10 Hz, ^3J (H^{5o},H^{6u}) = 10 Hz, ^3J (H^{5o},H^{4o}) = 3.5 Hz), 3.72 - 3.58 (m, 3H; H-6u,9o,9u), 2.86 - 2.77 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 14.5 Hz, ^3J (H^{4o},H^{5o}) = 3 Hz, ^3J (H^{4o},H^{3u}) = 1.5 Hz), 2.75 - 2.03 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 14.5 Hz, ^3J (H^{4u},H^{5o}) = 14.5 Hz, ^3J (H^{4u},H^{3u}) = 4 Hz), 2.45 - 2.35 (m, 1H; H-7u), 2.05 - 1.92 (m, 1H; H-8o), 1.85 - 1.70 (m, 1H; H-8u), 1.65 - 1.50 (m, 1H; H-7o).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
66.7 (d, C-3), 54.6 (d, C-6), 46.9 (t, C-9), 44.2 (t, C-4), 34.1 (t, C-7), 20.6 (t, C-8), 17.6 (d, C-5).

IR (KBr):

υ (cm^{-1}) = 3426 (s), 2945 (s), 2868 (s), 1673 (m), 1645 (s), 1448 (m), 1370 (w), 1321 (w), 1290 (m), 1250 (m), 1221 (w), 1192 (w), 1152 (w), 1110 (w), 657 (m).

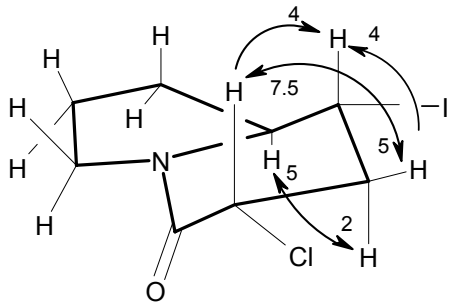
MS (80eV, EI, 80 °C)[271] :

m/z (%): 299 (12) [$M^{+\cdot}$], 264 (5) [M^+ - Cl], 172 (100) [M^+ - I], 145 (15), 136 (14), 108 (10), 82 (13), 80 (13), 70 (25), 67 (10), 55 (14), 53 (10).

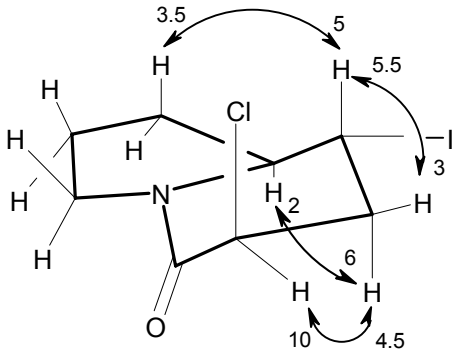
HRMS (80eV, 80 °C)[271] : found 298.95721

calc. 298.957394 (for $C_8H_{11}NO_2\,^{35}Cl^{127}I$).

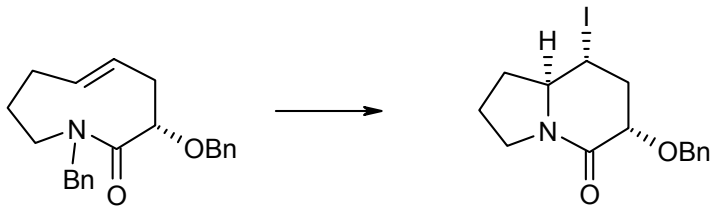
lactam **[30]**



lactam **[29]**



3*S*,5*R*,6*S*-3-Benzyloxy-5-iodo-1-azabicyclo[4.3.0]nonan-2-one [31]



[19a] 335.45 [$C_{22}H_{25}NO_2$] **[31]** 371.22 [$C_{15}H_{18}INO_2$]

Reaction of ***pS*-[19a]** (460mg, 1.37 mmol) with iodine was carried out according to the standard procedure **A**. The reaction mixture was washed with saturated aqueous $Na_2S_2O_3$ and dried over Na_2SO_4 and after evaporation of the solvent, the crude product was purified by column chromatography (n-hexane / ethyl acetate = 2:1, R_f = 0.2) to yield **[31]** as a colourless crystals (250 mg, 50%) with mp 110-112 °C.

[271] Measured from a mixture of **[29]** and **[30]**.

$[\alpha]_D^{20}$ = - 82.2° (c = 1.13, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.40 - 7.20 (m, 5H; H-Ph), 4.96 - 4.92 (d, 1H; H-O-Bn1; ^2J ($H^{O\text{-}Bn1}$,$H^{O\text{-}Bn2}$) = 11.5 Hz), 4.78 - 4.73 (d, 1H; H-O-Bn2; ^2J ($H^{O\text{-}Bn2}$,$H^{O\text{-}Bn1}$) = 11.5 Hz), 3.90 - 3.84 (dd, 1H; H-3o; ^3J (H^{3o},H^{4u}) = 9.5 Hz, ^3J (H^{3o},H^{4o}) = 7 Hz), 3.82 - 3.71 (ddd, 1H; H-6u; ^3J (H^{6u},H^{5o}) = 10 Hz, ^3J (H^{6u},H^{7o}) = 10 Hz, ^3J (H^{6u},H^{7u}) = 5 Hz), 3.70 - 3.60 (ddd, 1H; H-5o; ^3J (H^{5o},H^{4u}) = 11.5 Hz, ^3J (H^{5o},H^{6u}) = 10 Hz, ^3J (H^{5o},H^{4o}) = 3.5 Hz), 3.61 - 3.50 (m, 2H; H-9o, 9u), 2.82 - 2.72 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 13 Hz, ^3J (H^{4o},H^{3o}) = 7 Hz, ^3J (H^{4o},H^{5o}) = 3.5 Hz), 2.45 - 2.28 (m, 2H; H-4u, 7u), 1.95 - 1.83 (m, 1H; H-8o), 1.80 - 1.68 (m, 1H; H-8u), 1.52 - 1.38 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 12 Hz, ^3J (H^{7o},H^{6u}) = 10 Hz, ^3J (H^{7o},H^{8u}) = 8 Hz).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

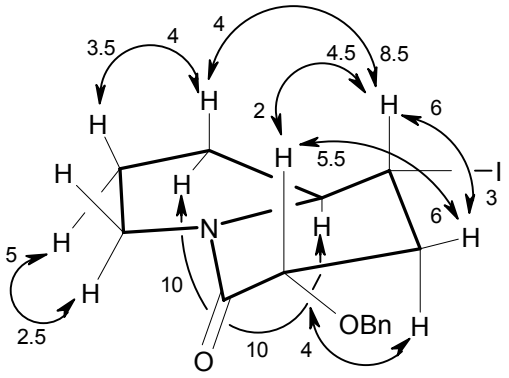
167.7 (s), 137.7 (s), 128.2 (d), 127.8 (d), 127.6 (d), 74.3 (d, C-3), 72.8 (t, OBn), 65.4 (d, C-6), 46.3 (t, C-9), 42.0 (t, C-4), 34.6 (t, C-7), 21.3 (t, C-8), 20.8 (d, C-5).

IR (solution, $CHCl_3$):

υ (cm^{-1}) = 3019 (s), 2976 (m), 2887 (m), 1729 (w), 1643 (m), 1500 (m), 1444 (m), 1418 (m), 1389 (m), 1215 (s), 1154 (m), 1047 (m), 928 (w).

MS (FAB, 3kV, MNBA):

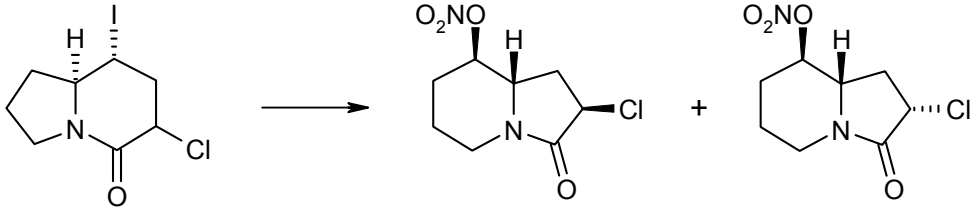
m/z (%): 372 (41) [M+], 342 (2), 265 (5), 252 (10), 91 (100).



3.6 Preparation of Hydroxy Indolizidinones by Substitution Reactions

5*R*,6*S*,*8R*-5-Nitro-8-chloro-1-azabicyclo[4.3.0]nonan-9-one [32] and

5*R*,6*S*,*8S*-5-Nitro-8-chloro-1-azabicyclo[4.3.0]nonan-9-one [33]



[29,30] 429.80 [$C_{14}H_{25}ICINO_2Si$] **[32]** 234.64 [$C_8H_{11}ClN_2O_2$] **[33]** 234.64 [$C_8H_{11}ClN_2O_2$]

A mixture of the iodo-indolizidinones **[29,30]**[272] (1.00 g, 3.34 mmol) was dissolved in 50 mL of acetone at room temperature. Then, 1.13 g (2 eq, 6.68 mmol) of thoroughly ground silver nitrate was added and the mixture was stirred for 3 days at room temperature. Then, the precipitated silver iodide was filtrated off and another equivalent of silver nitrate was added. After stirring overnight, the precipitates were filtered off and the solvent was removed. The crude product was purified on a silica gel column (ethyl acetate / n-hexane = 1:1 R_f = 0.27 and R_f = 0.13) yielding 0.72 g (92%) of a mixture of nitro-indolizidinones **[32]** and **[33]**.
An analytical sample was separated by HPLC (isopropanol / n-hexane = 5:95, 32x110 mm, Nucleosil 50-5, flow 122 mL/min, UV = 220 nm) to yield the pure compounds.

nitroindolizidinone [32] : colourless crystals : mp 75 °C

$[\alpha]_D^{20}$ = - 54.9° (c = 1.56, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
4.65 - 4.54 (ddd, 1H; H-5u; ^3J (H^{5u},H^{6o}) = 10 Hz, ^3J (H^{5u},H^{4o}) = 10 Hz, ^3J (H^{5u},H^{4u}) = 3.5 Hz), 4.42 - 4.37 (dd, 1H; H-8u; ^3J (H^{8u},H^{7u}) = 7 Hz, ^3J (H^{8u},H^{7o}) = 2 Hz), 4.17 - 4.07 (ddd, 1H; H-2u; ^2J (H^{2u},H^{2o}) = 13 Hz, ^3J (H^{2u},H^8) = 2.5 Hz, ^3J (H^{2u},$H^{8'}$) = 1 Hz), 3.68 - 3.56 (ddd, 1H; H-6o; ^3J (H^{6o},H^{5u}) = 10.5 Hz, ^3J (H^{6o},H^{7o}) = 6.5 Hz, ^3J (H^{6o},H^{7u}) = 6.5 Hz), 2.77 - 2.63 (m, 1H; H-2o), 2.61 - 2.50 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 14.5 Hz, ^3J (H^{7o},H^{6o}) = 6.5 Hz, ^3J (H^{7o},H^{8u}) = 2 Hz), 2.42 - 2.30 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 14 Hz, ^3J (H^{7u},H^{6o}) = 6.5 Hz, ^3J (H^{7u},H^{8u}) = 6.5 Hz), 2.40 - 2.30 (m, 1H; H-4u), 1.98 - 1.85 (m, 1H; H-3), 1.68 - 1.50 (m, 2H; H-3', 4o).

[272] Diastereomeric ratio at C-8 corresponded to the ratio in the isolated Claisen rearrangement products **[16a]** and **[17a]**, they were subjected to iodocyclisation without a separation of the C-8 isomers.

^{13}C-NMR (67.9 MHz, $CDCl_3$):
168.9 (s), 82.5 (d, C-5), 55.9 (d, C-6), 53.4 (d, C-8), 39.7 (t, C-2), 34.8 (t, C-7), 28.5 (t, C-4), 22.6 (t, C-3).

IR (KBr):
υ (cm^{-1}) = 2965 (w), 2917 (w), 1701 (s, CO), 1697 (s), 1639 (s, NO), 1426 (m), 1318 (m), 1271 (s), 1196 (w), 1160 (w), 1109 (w), 1054 (w), 1018 (m), 978 (m), 897 (s), 884 (s), 959 (s), 755 (m), 692 (m), 650 (m).

MS (80eV, EI, 100 °C):
m/z (%) 236 (0.2) [$M^{+\cdot}$], 234 (0.8) [$M^{+\cdot}$], 190 (15), 188 (45) [M^+ - NO_2], 172 (17) [M^+- NO_3], 160 (13), 132 (10), 124 (13), 97 (12), 71 (100), 43 (20).

HRMS (80eV,120 °C): found 234.04344
calc. 234.040735 (for $C_8H_{11}N_2O_4\,^{35}Cl_1$ [M^+]).

nitroindolizidinone [33] colourless crystals with mp = 153 °C

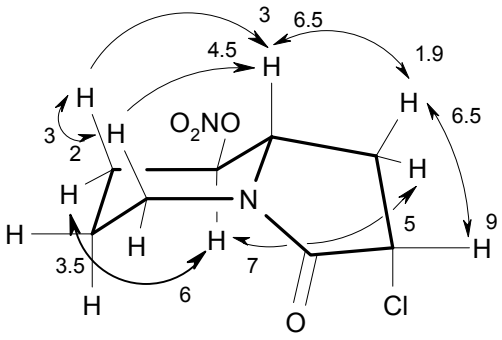
$[\alpha]_D^{20}$ = -117.8° (c = 1.25, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
4.85 - 4.75 (ddd, 1H; H-5u; ^3J (H^{5u},H^{6o}) = 9.5 Hz, ^3J (H^{5u},H^{4o}) = 9.5 Hz, ^3J (H^{5u},H^{4u}) = 3.5 Hz), 4.45 - 4.35 (ddd, 1H; H-8o; ^3J (H^{8o},H$^{)}$ = 7 Hz, ^3J (H^{8o},H) = 6 Hz, ^5J (H^{8o},H) = 0.5 Hz), 4.15 - 4.05 (m, 1H; H-2u), 3.48 - 3.40 (ddd, 1H; H-6o; ^3J (H^{6o},H^{5u}) = 9.5 Hz, ^3J (H^{6o},H^{7o}) = 7 Hz, ^3J (H^{6o},H^{7u}) = 5 Hz), 2.03 - 2.10 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 13.5 Hz, ^3J (H^{7o},H^{6o}) = 8 Hz, ^3J (H^{7o},H^8) = 6 Hz), 2.73 - 2.60 (m, 1H; H-2o), 2.40 - 2.31 (m, 1H; H-4u), 2.20 - 2.10 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 14 Hz, ^3J (H^{7u},H^{6o}) = 5.5 Hz, ^3J (H^{7u},H^8) = 5.5 Hz), 1.95 - 1.80 (m, 1H; H-3), 1.72 - 1.48 (m, 2H; H-3, 4o).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
168.9 (s), 82.2 (d, C-5), 56.3 (d, C-6), 53.1 (d, C-8), 39.9 (t, C-2), 33.4 (t, C-7), 28.8 (t, C-4), 22.8 (t, C-3).

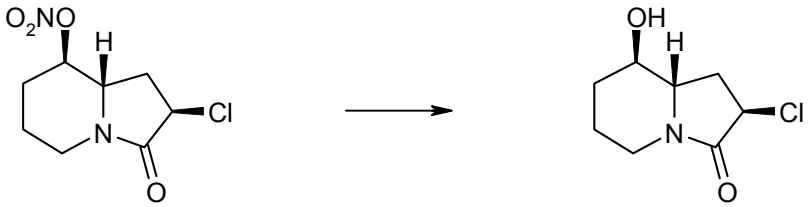
IR (KBr):
υ (cm^{-1}) = 2963 (w), 2935 (w), 2864 (m), 1702 (s, CO), 1621 (s, NO), 1447 (m), 1431 (m), 1318 (m), 1304 (m), 1277 (s), 1260 (s), 1189 (w), 1153 (m), 1118 (w), 1018 (m), 975 (m), 894 (s), 885 (s), 865 (s), 806 (m), 762 (m), 737 (m), 657 (m).

MS (80eV, EI, 90 °C):
m/z (%) 236 (0.05) [$M^{+\cdot}$], 234 (0.1) [$M^{+\cdot}$], 190 (8), 188 (24) [M^+ - NO_2], 172 (6) [M^+- NO_3], 160 (9), 132 (6), 124 (8), 97 (16), 71 (100), 43 (51), 41 (38).



HRMS (80eV,120 °C): found 234.04522
calc. 234.04735 (for $C_8H_{11}N_2O_4{}^{35}Cl_1$ [M^+]).

5*R*,6*S*,8*R*-5-Hydroxy-8-chloro-1-azabicyclo[4.3.0]nonan-9-one [34]



[32] 234.64 [$C_8H_{11}ClN_2O_2$] **[34]** 189.64 [$C_8H_{12}ClNO_2$]

Nitro-indolizidinone **[32]** (100 mg, 0.43 mmol) was dissolved in 10 mL of methanol. At 0 °C, 2mL of glacial acetic acid and 100 mg (4 mol. equiv) of zinc-powder was slowly added and after the complete addition, the cooling bath was removed and the mixture was stirred overnight at room temperature. After aqueous workup with aqueous $NaHCO_3$ and extraction of the aqueous layer with dichloromethane (3x), the combined organic layers were dried over Na_2SO_4 and the solvent was evaporated to yield 32.3 mg (40%) of **[34]** as a colourless oil.

$[\alpha]_D^{20}$ = - 49.3 ° (c = 1.61, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
4.60 - 4.40 (s, 1H; OH), 4.40 - 4.35 (dd, 1H; H-8u; ^3J (H^{8u},H^{7u}) = 7 Hz, ^3J (H^{8u},H^{7o}) = 2 Hz), 4.05 - 3.95 (dd, 1H; H-2u; ^2J (H^{2u},H^{2o}) = 13 Hz, ^3J (H^{2u},H^8) = 3.5 Hz), 3.43 - 3.32 (ddd, 1H; H-6o; ^3J (H^{6o},H^{5u}) = 9 Hz, ^3J (H^{6o},H^{7u}) = 6.5 Hz, ^3J (H^{6o},H^{7o}) = 6.5 Hz), 3.25 - 3.15 (ddd, 1H; H-5u; ^3J (H^{5u},H^{6o}) = 9.5 Hz, ^3J (H^{5u},H^{4o}) = 9.5 Hz, ^3J (H^{5u},H^{4u}) = 3.5 Hz), 2.70 - 2.60 (m, 1H; H-9o), 2.60 - 2.50 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 14.5 Hz, ^3J (H^{7o},H^{6o}) = 6 Hz, ^3J (H^{7o},H^{8u}) = 2 Hz), 2.40 - 2.30 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 13.5 Hz, ^3J (H^{7u},H^{8u}) = 7 Hz, ^3J (H^{7u},H^{6o}) = 6 Hz), 2.15 - 2.00 (m, 1H; H-4u), 1.85 - 1.70 (m, 1H; H-3), 1.50 - 1.30 (m, 2H; H-3',4o).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

169.3 (s), 72.9 (d, C-5), 60.4 (d, C-6), 54.5 (d, C-8), 39.9 (t, C-2), 34.8 (t, C-4), 32.9 (t, C-7), 22.9 (t, C-3).

IR (solution, $CHCl_3$):

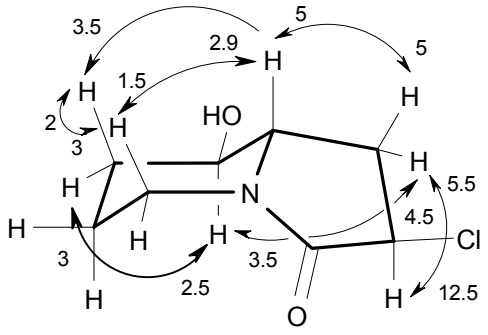
υ (cm^{-1}) = 3395 (m, broad), 2929 (m), 2861 (m), 1697 (s, C=O), 1441 (m), 1372 (m), 1272 (m), 1075 (m), 916 (s), 898 (s), 750 (s), 718 (s), 650 (s).

MS (80eV, EI, 90 °C):

m/z (%) 189 (27) [$M^{+\cdot}$], 172 (6) [M^+ -OH], 154 (100) [M^+ - Cl], 126 (32), 98 (11), 84 (25), 71 (35).

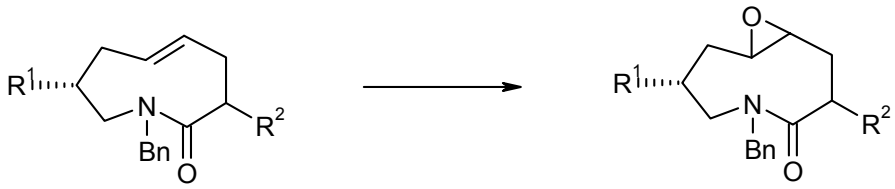
HRMS (80eV,120 °C): found 189.05392

calc. 189.055656 (for $C_8H_{12}N_1O_2\,^{35}Cl_1$ [M^+]).



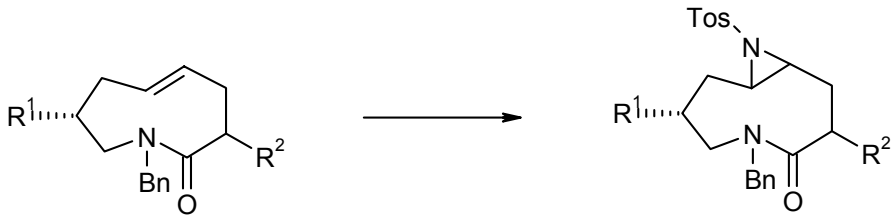
3.7 Cycloaddition Reactions

Standard Procedure for Epoxidation



Azoninone (1 mol equiv) was dissolved in a 1:1 mixture of CH_2Cl_2 and phosphate buffer (pH = 7). Then, m-Chloroperbenzoic acid (1.2 mol equiv) was added and the mixture was stirred at 4 °C or room temperature. After 3 - 5 h, the reaction was found to be complete as monitored by TLC analysis. The reaction mixture was then poured into a saturated aqueous $NaHCO_3$ /$NaHSO_3$.The organic layer was washed (saturated aqueous $NaHCO_3$ and brine) and dried (Na_2SO_4). After evaporation of the solvent, the product was purified by recrystallisation or by HPLC.[273]

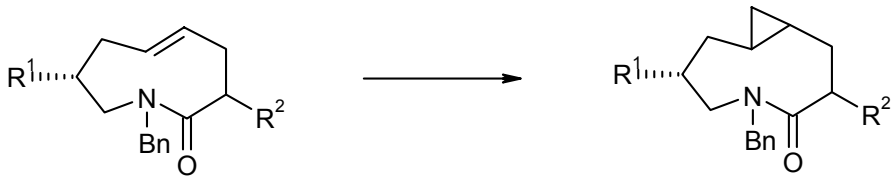
Standard Procedure for Aziridination



A solution of azoninone (1 mol equiv) in dry acetonitrile was treated with (p-toluenesulfonylimino)-phenyliodinane (1.2 - 1.4 equiv) and [Cu $(OTf)_2$] (1-5 mol%) at 10 °C. After complete conversion of the reactant (carefully monitored by TLC), the mixture was hydrolysed with aqueous $NaHCO_3$. The aqueous layer was extracted with diethyl ether and washed with brine. After drying (Na_2SO_4), the solvent was removed and the crude product was purified by column chromatography or by HPLC.

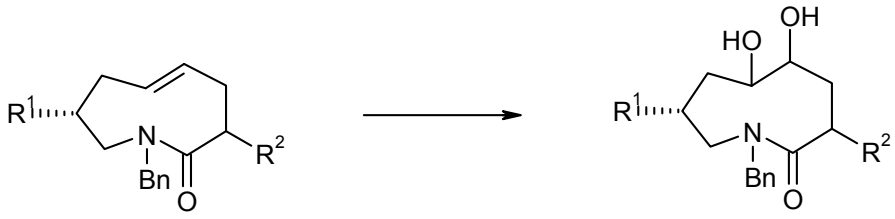
[273] All epoxides are heat sensitive, many of them could not be purified by column chromatography due to a rearrangement to more stable lactones on the silica gel column. They are stable at -20 °C for months without any decomposition.

Standard Procedure for Cyclopropanation



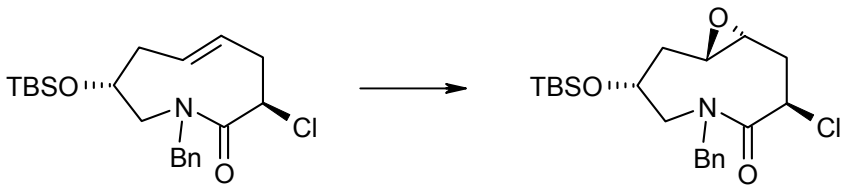
The azoninone (1 mol equiv) was dissolved in diethyl ether (10 mL) at room temperature. A saturated solution of freshly prepared diazomethane (in excess) in diethyl ether [274] and $Pd(OAc)_2$ (2.5 - 13 mol %) was subsequently added. After stirring overnight, the mixture was washed with aqueous $NaHCO_3$ and dried (Na_2SO_4). The solvent was removed and the crude product was purified by column chromatography or by recrystallisation.

Standard Procedure for Dihydroxylation



A solution of the azoninone (1 mol equiv) in acetonitrile / ethyl acetate (1:1, 18 mL) was treated with a mixture of $NaIO_4$ (1.5 equiv) and $RuCl_3$ (5 mol%) in H_2O at 0 °C. After 5 min of vigorous stirring, the reaction was stopped by the addition of an aqueous $NaHSO_3$ solution. The aqueous layer was extracted two times with ethyl acetate and dried (Na_2SO_4). After removal of the solvents, the crude dihydroxy-azonanones were subjected to the protective group insertions without any further purification.

3*R*,5*R*,6*R*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-chloro-5,6-epoxy-azonan-2-one [35a]



[12a] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[35a]** 410.03 [$C_{21}H_{32}ClNO_3Si$]

[274] Evans, D. A.; Tanis, S. P.; Hart, D. J. *J. Am. Chem. Soc.* **1981**, 103, 5813-5821.

Reaction of ***pS*-[12a]** (500mg, 1.27 mmol) with m-CPBA was carried out according to the standard epoxidation procedure. After sample workup, the product **[35a]** was isolated as colourless crystals with no need for further purification with a high yield (480 mg, 92.3%); mp = 148-152 °C.

$[\alpha]_D^{20}$ = -100.25° (c = 1.555, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.5 -7.2 (m, 5H; H-arom.H), 5.02 - 4.95 (d, 1H; H-CH2-Ph; ^2J (H^{CH2-Ph},H$^{)}$ = 14 Hz), 4.52 - 4.45 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 12 Hz, ^3J (H^{3u},H^{4u}) = 7 Hz), 4.3 - 4.25 (d, 1H; H-CH2Ph; ^2J (H^{CH2Ph},H$^{)}$ = 14 Hz), 4.25 - 4.2 (m, 1H; H-8o), 4.2 - 4.05 (dd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 14 Hz, ^3J (H^{9u},H^{8o}) = 11 Hz), 3.35 - 3.2 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 14 Hz, ^3J (H^{9o},H^{8o}) = 5 Hz), 3.03 - 2.95 (m, 1H; H-6u), 2.85 - 2.75 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 12 Hz, ^3J (H^{4o},H^{3u}) = 12 Hz, ^3J (H^{4o},H^{5o}) = 5 Hz), 2.70 - 2.60 (ddd, 1H; H-5o; ^3J (H^{5o},H$^{)}$ = 8 Hz, ^3J (H^{5o},H) = 5 Hz, ^3J (H^{5o},H) = 2 Hz), 2.25 - 2.15 (m, 1H; H-7u), 1.60 - 1.50 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 12 Hz, ^3J (H^{4u},H) = 8 Hz, ^3J (H^{4u},H) = 7 Hz), 1.10 - 1.00 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 14 Hz, ^3J (H^{7o},H^{6u}) = 11 Hz, ^3J (H^{7o},H^{8o}) = 5 Hz), 0.80 (s, 9H; H-Si (CMe_3)), 0.05 (s, 3H; H-Si-CH_3), -0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

169.3 (s, C=O), 136.2 (s), 128.8 (d), 128.7 (d), 65.9 (d, C-3), 57.4 (d, C-8), 52.0 (d), 51.5 (t), 50.2 (d), 49.9 (t), 37.6 (t), 36.7 (t), 25.6 (Si-C(CH_3)$_3$), 17.9 (Si-C(CH_3)$_3$), - 4.9 (Si-CH_3), -5.06 (Si-CH_3).

IR (KBr):

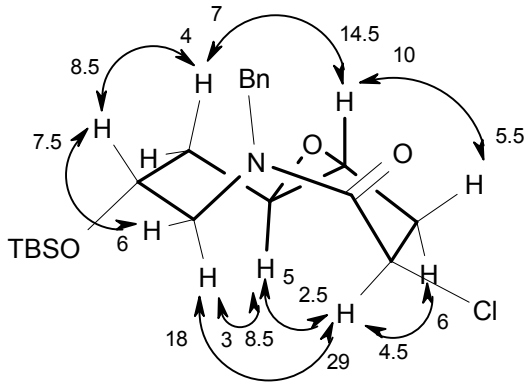
υ (cm-1) = 2932 (s), 2950 (s), 2889 (s), 2857 (m), 1650 (s, N-CO), 1453 (s), 1427 (s), 1254 (s, C-O), 1196 (s), 955 (s).

MS (80eV, EI, 130 °C):

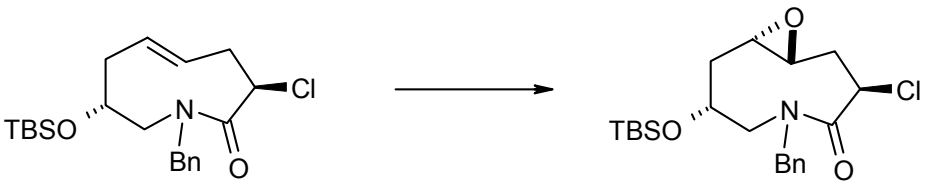
m/z (%): 409 (15) [$M^{+\cdot}$], 394 (3) [M^+ - CH_3], 374 (6) [M^+-Cl], 352 (8) [M^+ - C_4H_9], 290 (100) [M^+-$C_4H_4ClO_2$], 91 (80).

HRMS (80eV,150 °C): found. 409.18426

calc. 409.18400 (for $C_{21}H_{32}ClNO_3Si$).



3*R*,5*S*,6*S*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-chloro-5,6-epoxy-azonan-2-one [35b]



[12b] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[35b]** 410.03 [$C_{21}H_{32}ClNO_3Si$]

Reaction of ***pR*-[3]** (0.15g, 1.28 mmol) with m-CPBA was carried out according to the standard epoxidation procedure. After sample workup, the product was isolated as colourless crystals and purified by HPLC (ethyl acetate / n-hexane = 4:1). After this purification, a mixture of 95.3% **[35b]** and 4.7% **[35a]** was obtained with a high yield (0.134 g, 85.8%). This mixture of diastereomers could not be further purified neither by recrystallisation nor by HPLC.

mp = 152-154 °C.

$[\alpha]_D^{20}$ = -14.0° (c = 1.9, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
7.50 - 7.20 (m, 5H; H-Ph), 5.21 - 5.12 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 15 Hz), 5.02 - 4.95 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 12 Hz, ^3J (H^{3u},H^{4u}) = 2 Hz), 4.30 - 4.20 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 15 Hz), 4.20 - 4.10 (m, 1H; H-8o), 3.93 - 3.83 (ddd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 14.5 Hz, ^3J (H^{9u},H^{8o}) = 10 Hz, ^4J (H^{9u},$H^{N\text{-}Bn1}$) = 0.5 Hz), 3.20 - 3.13 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 14.5 Hz, ^3J (H^{9o},H^{8o}) = 1.5 Hz), 2.90 - 2.82 (ddd, 1H; H-5u; ^3J (H^{5u},H^{4o}) = 10 Hz, ^3J (H^{5u},H^{6o}) = 4 Hz, ^3J (H^{5u},H^{4u}) = 2.5 Hz), 2.73 - 2.63 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 12 Hz, ^3J (H^{4u},H^{5u}) = 4 Hz, ^3J (H^{4u},H^{3u}) = 4 Hz), 2.60 - 2.50 (m, 2H; H-7, 6o), 1.95 - 1.80 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 12.5 Hz, ^3J (H^{4o},H^{5u}) = 10 Hz, ^3J (H^{4o},H^{3u}) = 10 Hz), 1.20 - 1.00 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 13 Hz, ^3J (H^{7u},H^{6o}) = 11 Hz, ^3J (H^{7u},H^{8o}) = 8 Hz), 0.8 (s, 9H; H-Si-C(CH_3)$_3$), - 0.01 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
170.0 (s, C=O), 136.3 (s), 128.8 (d), 128.0 (d), 127.8 (d), 65.9 (d, C-8), 57.0 (d, C-3), 53.9 (t), 53.0 (d), 51.9 (d), 50.1 (t), 40.2 (t), 38.9 (t), 25.5 (q, Si-C(CH_3)$_3$), 17.7 (s, Si-C(CH_3)$_3$), - 4.5 (q, Si-CH_3), - 4.9 (q, Si-CH_3).

IR (KBr):

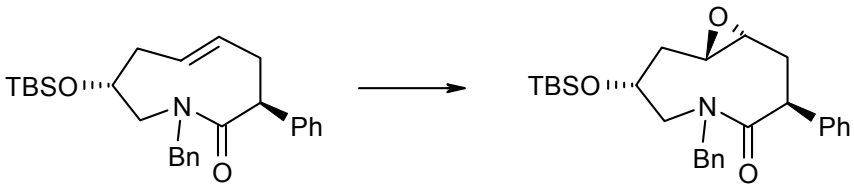
υ (cm-1) = 3427 (w), 2948 (s), 2928 (s), 2883 (s), 2856 (m), 1651 (s, C=O), 1452 (m), 1426 (m), 1259 (m, C-O), 1196 (m), 1090 (s), 957 (s), 841 (s), 776 (s).

MS (80eV, EI, 150 °C):

m/z (%): 409 (20) [M^+.], 374 (8) [M^+-Cl], 352 (14) [M^+ - C_4H_9], 318 (6), 290 (33), 120 (23), 91 (100).

HRMS (80eV,130 °C): found 409.18054 calc. 409.18400 (for $C_{21}H_{32}NO_3Cl_1Si_1$).

3*S*,5*R*,6*R*,8*R*-3-Phenyl-5,6-epoxy-1-benzyl-8-(*tert*-butyldimethylsilyloxy)-azonan-2-one [36a]



[13a] 435.69 [$C_{27}H_{37}NO_2Si$] **[36a]** 451.69 [$C_{27}H_{37}NO_3Si$]

Reaction of ***pS*-[13a]** (1.06g, 2.442 mmol) with m-CPBA was carried out according to the standard epoxidation procedure. After sample workup, the product **[36a]** was isolated as colourless crystals with no need for further purification with a high yield (1.19 g, 100%) with mp = 111-114 C.

$[\alpha]_D^{20}$ = -128.7° (c = 1.846, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.5 -7.2 (m, 5H), 5.02 - 4.95 (d, 1H; H-CH_2-Ph; ^2J (H^{CH2-Ph},H$^{)}$ = 14 Hz), 4.52 - 4.45 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 12 Hz, ^3J (H^{3u},H^{4u}) = 7 Hz), 4.3 - 4.25 (d, 1H; H-CH_2Ph; ^2J (H^{CH2Ph},H$^{)}$ = 14 Hz), 4.25 - 4.2 (m, 1H; H-8o), 4.2 - 4.05 (dd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 14 Hz, ^3J (H^{9u},H^{8o}) = 11 Hz), 3.35 - 3.2 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 14 Hz, ^3J (H^{9o},H^{8o}) = 5 Hz), 3.03 - 2.95 (m, 1H; H-6u), 2.85 - 2.75 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 12 Hz, ^3J (H^{4o},H^{3u}) = 12 Hz, ^3J (H^{4o},H^{5o}) = 5 Hz), 2.70 - 2.60 (ddd, 1H; H-5o; ^3J (H^{5o},H$^{)}$ = 8 Hz, ^3J (H^{5o},H) = 5 Hz, ^3J (H^{5o},H) = 2 Hz), 2.25 - 2.15 (m, 1H; H-7u), 1.60 - 1.50 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 12 Hz, ^3J (H^{4u},H) = 8 Hz, ^3J (H^{4u},H) = 7 Hz), 1.10 - 1.00 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 14 Hz, ^3J (H^{7o},H^{6u}) = 11 Hz, ^3J (H^{7o},H^{8o}) = 5 Hz), 0.80 (s, 9H; H-Si (CMe_3)), 0.05 (s, 3H; H-Si-CH_3), -0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

173.6 (s, C=O), 138.8 (s), 137.1 (s), 128.7 (d), 128.5 (d), 128.3 (d), 127.8 (d), 127.3 (d), 66.2 (d), 59.7 (d), 52.4 (d), 51.8 (t), 49.2 (t), 43.8 (d), 37.0 (t), 34.3 (t), 25.7 (q, Si-C(CH_3)$_3$), 17.9 (s, Si-C(CH_3)$_3$), - 4.9 (q, Si-CH_3).

IR (KBr):

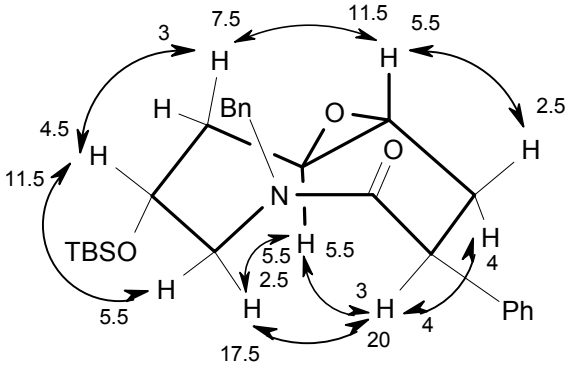
υ (cm-1) = 3426 (w), 3054 (w), 3022 (w), 2929 (s), 2950 (s), 2856 (s), 1646 (s, N-CO), 1446 (m), 1415 (m), 1252 (m, C-O), 1187 (m).

MS (80eV, EI, 110 °C):

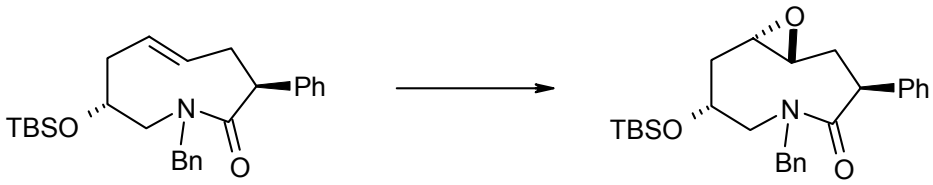
m/z (%): 451 (100) [M^+.], 436 (10) [M^+ - CH_3], 394 (20) [M^+ - C_4H_9], 360 (20), 290 (90), 91 (15), 73 (8).

HRMS (80eV,110 °C): found 451.25439

calc. 451.25427 (for $C_{27}H_{37}NO_3Si$).



3*S*,5*S*,6*S*,8*R*-3-Phenyl-5,6-epoxy-1-benzyl-8-(*tert*-butyldimethylsilyloxy)-azonan-2-one [36b]



[13b] 435.69 [$C_{27}H_{37}NO_2Si$] **[36b]** 451.69 [$C_{27}H_{37}NO_3Si$]

The educt *pS*-azoninone was heated before the reaction for 8 h at 60 °C to increase the amount of the thermodynamic *pR*-lactam. Reaction of ***pR*-[13b]** (170 mg, 0.39 mmol) with m-CPBA was carried out according to the standard epoxidation procedure and yielded 300 mg of a crude oil. This oil was purified by HPLC (ethyl acetate / n-hexane = 12:88, 32x110 mm, flow 64ml/min, r.t. 4 min) to provide 167.3 mg (0.37 mmol, 95%) of epoxy azonanones as a mixture of 81.5% **[36b]** and 13.5% **[36a]** as colourless crystals, which cannot be further purified.[275,276]

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[275] Compound **[36b]** shows the occurrence of a minor conformation (5%). Since a chemical transfer was observable during the NOE measurements of **[36b]**, the existence of amide-isomers is reasonable.

[276] The only possibility, to increase the amount of **[36b]** was to recrystallise the product from diethyl ether / n-hexane at -20 °C, **[36a]** easily crystallises therefore **[36b]** ca be enriched in the remaining solution up to 85%.

$[\alpha]_D^{20}$ = - 59.05° (c = 1.47, $CHCl_3$).

mp = 114 °C

^{1}H-NMR (270 MHz, $CDCl_3$):

7.5 -7.2 (m, 5H; H-arom.H), 5.02 - 5.10 (d, 1H; H-CH_2-Ph; ^2J (H^{CH2-Ph},H$^{)}$ = 15 Hz), 4.40 - 4.10 (m, 4H; H-3u, 9u, 8o, CH_2Ph), 3.30 - 3.20 (d, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 14 Hz), 3.03 - 2.95 (ddd, 1H; H-5u; ^3J (H^{5u},H$^{)}$ = 10 Hz, ^3J (H^{5u},H) = 6 Hz, ^3J (H^{5u},H) = 4 Hz, ^4J (H^{5u},H) = 2 Hz), 2.75 - 2.68 (ddd, 1H; H-6o; ^3J (H^{6o},H$^{)}$ = 11 Hz, ^3J (H^{6o},H) = 2 Hz, ^3J (H^{6o},H) = 2 Hz), 2.70 - 2.60 (ddd, 1H; H-5o; ^3J (H^{5o},H$^{)}$ = 8 Hz, ^3J (H^{5o},H) = 5 Hz, ^3J (H^{5o},H) = 2 Hz), 2.70 - 2.50 (m, 2H; H-7o, 4u), 2.02 - 1.98 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 13 Hz, ^3J (H^{4o},H) = 13 Hz, ^3J (H^{4o},H) = 10 Hz), 1.40 - 1.20 (m, 1H; H-7u), 0.80 (s, 9H; H-Si (CMe_3)), 0.05 (s, 3H; H-Si-CH_3), -0.05 (s, 3H; H-Si-CH_3).

^{13}C-NMR (62.9 MHz, $CDCl_3$):

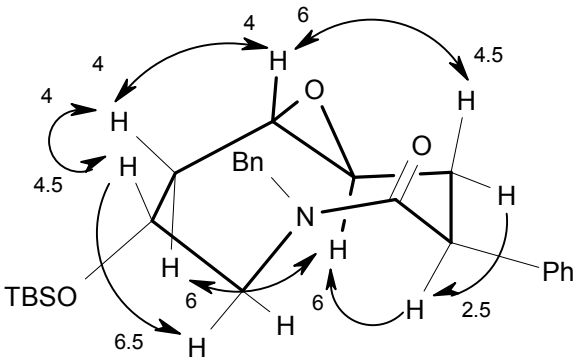
174.8 (C=O), 140.4, 137.2, 129.1, 128.6, 128.4, 127.8, 127.5, 127.2, 126.6, 66.1 (d), 59.7 (d), 54.1 (t), 53.3 (d), 49.4 (t), 44.4 (d), 40.7 (t), 34.9 (t), 25.6 (Si-C(CH_3)$_3$), 14.0 (Si-C(CH_3)$_3$), - 4.6 (Si-CH_3), -4.9 (Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3053 (m), 3027 (w), 2953 (s), 2928 (s), 2856 (m), 1641 (s, N-CO), 1495 (w), 1471 (m), 1453 (m), 1415 (m), 1383 (w), 1360 (m), 1265 (m, C-O), 1187 (w), 1091 (s), 963 (m), 838 (s), 777 (m), 738 (s), 699 (m).

MS (80eV, EI, 100-120 °C):

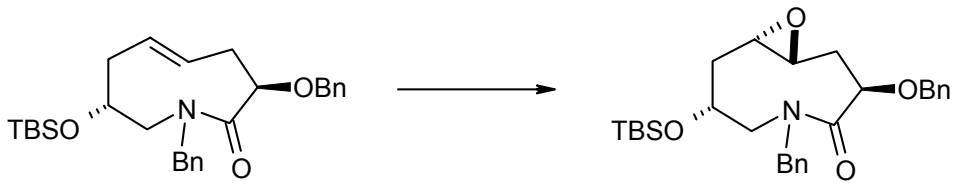
m/z (%): 451 (73) [$M^{+\cdot}$], 436 (21) [M^+ - CH_3], 394 (76) [M^+ -C_4H_9], 360 (34), 290 (100), 197 (20), 158 (65), 91 (90).



HRMS (80eV,100 °C): found 451.25073

calc. 451.254273 (for $C_{27}H_{37}NO_3Si$).

3*R*,5*S*,6*S*,8*R*-1-Benzyl-3-benzyloxy-5,6-epoxy-8-(*tert*-butyldimethylsilyloxy)- azonan-2-one [37b]



[14b] 465.71 [$C_{28}H_{39}NO_3Si$] **[37b]** 481.71 [$C_{28}H_{39}NO_4Si$]

Before the epoxidation, the reactant azoninone ***pS*-[14a]** was heated for at least 3 h to 60 °C to achieve a high degree of conversion into ***pR*-[14b]** azoninone (14a:14b = 1:12). Reaction of ***pR*-[14b]** (1.86g, 3.99 mmol) with 1.2 eq. m-CPBA followed the standard epoxidation procedure. After sample workup, the product was isolated as colourless crystals which were purified by HPLC (12% ethyl acetate / n-hexane, Nucleosil 50-5, 32x110, flow 64ml/min) to get **[37b]** with a yield (1.75 g, 91.1%) as colourless crystals with mp 119-121 °C.

$[\alpha]_D^{20} = +76.27°$ (c = 1.572, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.40 - 7.10 (m, 10 H), 5.28 - 5.19 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 14 Hz), 4.65 - 4.57 (d, 1H; H-O-Bn1; ^2J ($H^{O\text{-}Bn1}$,$H^{O\text{-}Bn2}$) = 12 Hz), 4.45 - 4.38 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 12.5 Hz, ^3J (H^{3u},H^{4u}) = 2 Hz), 4.38 - 4.21 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 14 Hz), 4.35 - 4.29 (d, 1H; H-O-Bn2; ^2J ($H^{O\text{-}Bn2}$,$H^{O\text{-}Bn1}$) = 12 Hz), 4.28 - 4.10 (m, 1H; H-8o), 3.83 - 3.70 (ddd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 14.7 Hz, ^3J (H^{9u},H^{8o}) = 9.6 Hz, ^4J (H^{9u},$H^{N\text{-}Bn1}$) = 2 Hz), 3.13 - 3.05 (d, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 14.7 Hz), 2.80 - 2.70 (m, 1H; H-5u), 2.60 - 2.50 (m, 3H; H-6o, 7o, 4u), 1.70 - 1.53 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 12.5 Hz, ^3J (H^{4o},H^{5u}) = 12.5 Hz, ^3J (H^{4o},H^{3u}) = 12.5 Hz), 1.12 - 0.99 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 15.5 Hz, ^3J (H^{7u},H^{8o}) = 12 Hz, ^3J (H^{7u},H^{6o}) = 9 Hz), 0.8 (s, 9H; H-Si-C(CH_3)$_3$), 0.01 (s, 6H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

172.2 (s, C=O), 136.9 (s), 136.8 (s), 128.6 (d), 128.6 (d), 128.1 (d), 128.0 (d), 127.8 (d), 127.6 (d), 71.4 (d), 71.0 (t), 65.9 (d), 53.2 (d), 53.0 (t), 49.3 (t), 40.2 (t), 35.3 (t), 25.4 (q, Si-C(CH_3)$_3$), 17.6 (s, Si-C(CH_3)$_3$), - 4.6 (Si-CH_3), -5.0 (Si-CH_3).

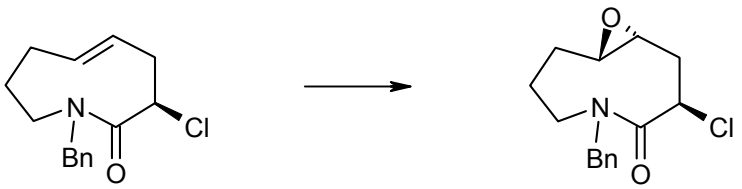
IR (KBr):

υ (cm^{-1}) = 3433 (w), 2950 (s), 2933 (s), 2858 (m), 1652 (s, N-CO), 1458 (m), 1441 (m), 1259 (m, C-O), 1129 (m), 1110 (m), 1077 (s), 838 (s).

MS (80eV, EI, 150 °C):
m/z (%): 481 (6) [$M^{+\cdot}$], 466 (1) [M^+ - CH_3], 424 (12) [M^+ - C_4H_9], 390 (38), 375 (32), 290 (50), 91 (100), 73 (20).

HRMS (80eV,130 °C): found 481.26187 calc. 481.264838 (for $C_{28}H_{39}NO_4Si$).

3*R*,5*R*,6*R*-1-Benzyl-3-chloro-5,6-epoxy-azonan-2-one [38a]



[16a] 263.77 [$C_{15}H_{18}ClNO$] **[38a]** 279.77 [$C_{15}H_{18}ClNO_2$]

Reaction of ***pS*-[16a]** (3.05g, 11.56 mmol) with m-CPBA was carried out according to the standard epoxidation procedure. After workup, the product **[38a]** was recrystallised from dichloromethane / n-hexane. The remaining mother liquor was purified by HPLC (ethyl acetate / n-hexane = 15:85, 32x250 mm Nucleosil 50-5, flow 64mL /min) to yield 2.92 g (90%) of **[38a]** as colourless crystals with mp = 139-140 °C.[277]

$[\alpha]_D^{20}$ = - 148.6° (c = 1.40, $CHCl_3$).

major conformer:

^{1}H-NMR (270 MHz, $CDCl_3$):
7.40 - 7.20 (m, 5H; H-Ph), 5.18 - 5.13 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 15 Hz), 5.15 - 5.10 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 7 Hz, ^3J (H^{3u},H^{4u}) = 3 Hz), 4.14 - 4.06 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 14.5 Hz), 4.00 - 3.80 (ddd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 15 Hz, ^3J (H^{9u},H^8) = 12 Hz, ^3J (H^{9u},H^8) = 3.5 Hz), 3.30 - 3.15 (m, 1H; H-9o), 2.80 - 2.60 (m, 2H; H-6, 4o), 2.50 - 2.40 (ddd, 1H; H-5o; ^3J (H^{5o},H^{6u}) = 8.5 Hz, ^3J (H^{5o},H^{4u}) = 5 Hz, ^3J (H^{5o},H^{4o}) = 2.5 Hz), 2.20 - 2.10 (m, 2H; H-8, 7u), 1.90 - 1.80 (m, 1H; H-4u), 0.90 - 0.70 (m, 1H; H-7o).

minor conformer:

[277] For the separation of higher quantities of these epoxides, other HPLC conditions were used : 63x187mm Nucleosil 50-5, flow 250ml/min, UV 254nm, eluent ethyl acetate / n-hexane = 20:80, injected as solution in dichloromethane, r.t. 12 and 15 min. The separation of the solvent should be performed under mild thermal conditions (30-40 °C) as the epoxides easily form the more stable lactones by rearrangement.

^{1}H-NMR (270 MHz, $CDCl_3$):

7.40 - 7.20 (m, 5H; H-Ph), 5.30 - 5.20 (d, 1H; H-N-Bn1; ^{2}J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 15 Hz), 5.08 - 5.03 (dd, 1H; H-3u; ^{3}J (H^{3u},H^{4o}) = 4.5 Hz, ^{3}J (H^{3u},H^{4u}) = 2.5 Hz), 4.65 - 4.53 (dd, 1H; H-9o; ^{2}J (H^{9o},H^{9u}) = 15 Hz, ^{3}J (H^{9o},H^{8}) = 9 Hz), 4.13 - 4.05 (d, 1H; H-Bn2; ^{2}J (H^{Bn2},$H^{Bn\text{-}1}$) = 15 Hz), 3.30 - 3.10 (m, 2H; H-5o, 9u), 2.80 - 2.60 (m, 2H; H-4o, 6u), 2.30 - 2.20 (m, 1H; H-8), 2.15 - 2.05 (m, 1H; H-7u), 1.90 - 1.50 (m, 2H; H-8, 4u), 1.20 - 1.10 (m, 1H; H-7o).

^{13}C-NMR (125.7 MHz, $CDCl_3$):[278]

169.1 (s, C-2), 168.2 (s, C-2'), 136.4 (s), 128.7 (d), 128.4 (d), 127.8 (d), 127.4 (d), 59.2 (d, C-3'), 57.1 (d, C-5), 56.5 (d, C-5'), 56.2 (d, C-6'), 54.2 (d, C-6), 50.6 (d, C-3), 49.2 (t, N-Bn'), 47.6 (t, N-Bn), 45.1 (t, C-9'), 44.2 (t, C-9), 37.4 (t, C-4), 35.4 (t, C-4'), 29.8 (t, C-7'), 26.0 (t, C-7), 22.2 (t, C-8'), 21.4 (t, C-8).

IR (KBr):

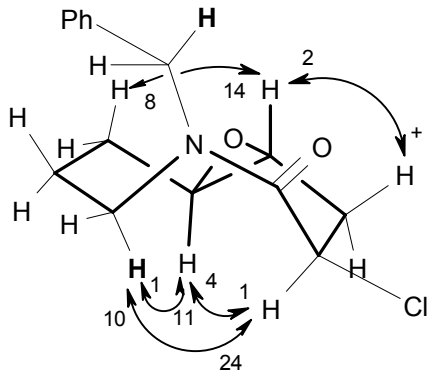
υ (cm^{-1}) = 3039 (w), 3015 (m), 2976 (m), 2940 (m), 2885 (m), 1638 (s, C=O), 1495 (m), 1475 (m), 1461 (m), 1449 (m), 1429 (m), 1366 (m), 1298 (w), 1259 (m), 1238 (w), 1210 (m), 1202 (s), 1157 (w), 1127 (w), 1107 (m), 1081 (m), 1064 (w), 971 (m), 922 (m), 908 (m), 825 (m), 796 (m), 765 (m), 792 (w), 708 (m), 634 (w), 610 (w).

MS (80eV, EI, 120 °C):

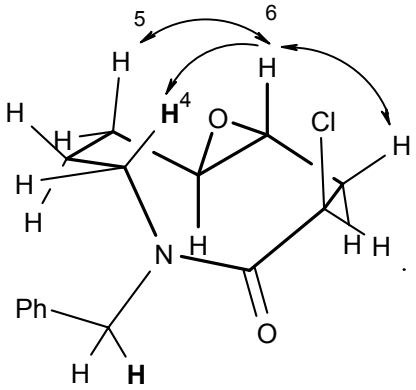
m/z (%): 281 (12) [$M^{+\cdot}$], 279 (35) [$M^{+\cdot}$], 244 (49) [M^{+} - Cl], 204 (10), 188 (8) [M^{+} - C_7H_7], 160 (23), 120 (65), 91 (100), 70 (13).

HRMS (80eV,120 °C): found 279.10409 calc. 279.1020607 (for $C_{15}H_{18}NO_2{}^{35}Cl$).

Major conformer (60%)

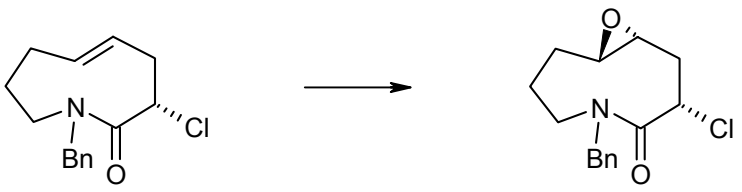


Minor conformer [279] (40%)



[278] The signal assignment based on ^{13}C-^{1}H-HMQC spectrum (500 MHz) together with DEPT and ^{1}H-^{1}H-COSY spectra (signals from the minor conformer are marked , like C-3').

3*S*,5*R*,6*R*-1-Benzyl-3-chloro-5,6-epoxy-azonan-2-one [39a]



[17a] 263.77 [$C_{15}H_{18}ClNO$] **[39a]** 279.77 [$C_{15}H_{18}ClNO_2$]

Reaction of ***pS*-[17a]** (2.55g, 9.6 mmol) with m-CPBA was carried out according to the standard epoxidation procedure. After workup, the product **[39a]** was recrystallised from dichloromethane / n-hexane to yield 2.70 g (100%) of **[39a]** as colourless oil, which slowly crystallises at -20 °C.

mp 92-95 °C.

$[\alpha]_D^{20} = +5.5°$ (c = 1.39, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.40 - 7.20 (m, 5H; H-Ph), 5.40 -5.30 (d, 1H; N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 14.5 Hz), 5.03 - 4.94 (dd, 1H; H-3o; ^3J (H^{3o},H^{4u}) = 12.5 Hz, ^3J (H^{3o},H^{4o}) = 1.5 Hz), 4.07 - 4.02 (d, 1H; N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 14.5 Hz), 3.70 - 3.58 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 15 Hz, ^3J (H^{9o},H^{8}) = 11 Hz), 3.25 - 3.15 (dd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 15 Hz, ^3J (H^{9u},H^{8}) = 5.5 Hz), 2.80 - 2.73 (ddd, 1H; H-5o; ^3J (H^{5o},H^{4u}) = 10 Hz, ^3J (H^{5o},H^{6u}) = 4 Hz, ^3J (H^{5o},H^{4o}) = 2 Hz), 2.73 - 2.60 (m, 2H; H-4o, 6u), 2.30 - 2.18 (m, 1H; H-7u), 2.15 - 1.95 (m, 1H; H-8), 1.95 - 1.80 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 12.5 Hz, ^3J (H^{4u},H^{3o}) = 12.5 Hz, ^3J (H^{4u},H^{5o}) = 10 Hz), 1.80 - 1.65 (m, 1H; H-8'), 1.20 - 1.00 (m, 1H; H-7o).

^{13}C-NMR (62.9 MHz, $CDCl_3$):

169.5 (s, C-2), 136.1 (s), 128.6 (d), 128.1 (d), 127.6 (d), 57.0 (d, C-5), 55.2 (d, C-6), 52.0 (d, C-3), 47.9 (t, N-Bn), 44.6 (t, C-9), 38.9 (t, C-4), 29.4 (t, C-7), 21.6 (t, C-8).

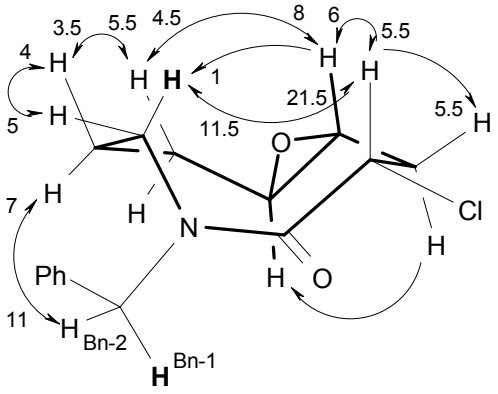
[279] The position of the protons in the spectrum could be determined in analogy to **[14a]** by a magnetisation transfer during the NOE experiment of **[16a-1]** (dynamic equilibrium between **[16a-1]** and **[16a-2]**). The preliminary assignment of the 3-dimensional structure bases on the structural correlations of the protons with the change of the characteristic ^{4}J-coupling between both H-9/N-Bn pairs (pairs are printed in bold letters for a better visualisation) during the isomerisation.

MS (80eV, EI, 120 °C):

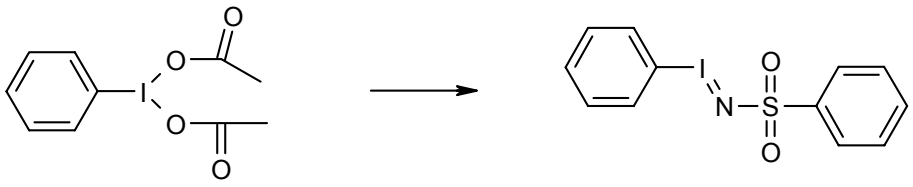
m/z (%): 281 (11) [$M^{+\cdot}$], 279 (30) [$M^{+\cdot}$], 244 (40) [M^{+} - Cl], 188 (5) [M^{+} - C_7H_7], 160 (24), 158 (18), 156 (52), 141 (18), 139 (57), 120 (15), 111 (25), 91 (100), 75 (12).

HRMS (80eV,120 °C): found 279.10434

calc. 279.1020607 (for $C_{15}H_{18}NO_2{}^{35}Cl$).



N-(*p*-Tolylsulfonylimino)-phenyl iodinane (modified procedure)



A solution of KOH (0.7 g, 12.5 mmol, 2.5 mol-eq.) in MeOH (10 mL) was treated with p-toluenesulfone amide (0.86 g, 5 mmol). The resulting clear and colourless solution was stirred for 10 min at 0 °C, then, a white precipitate of the potassium p-toluenesulfonates appeared. Diacetoxy-iodosobenzene (1.6 g, 5 mmol) was added at 0 °C. After 5-10 min of stirring at 0 °C, all solids were dissolved to result a clear yellow solution. After a further 30 min of stirring at 0 °C, a yellow precipitate of the N-(p-tolylsulfonylimino)-phenyl iodinane occurred. Stirring was continued for 30 min at 0 °C and 1 h at room temperature. Workup started by addition of H_2O (25 mL, 0 °C) and cooling for 45 min at 4 °C. The solid product was filtered off and dried in vacuo to give pure N-(p-tolylsulfonylimino)-phenyl iodinane (0.85 g, 48%) as a pale yellow solid with mp = 104 °C (lit.: 102 - 104 °C).

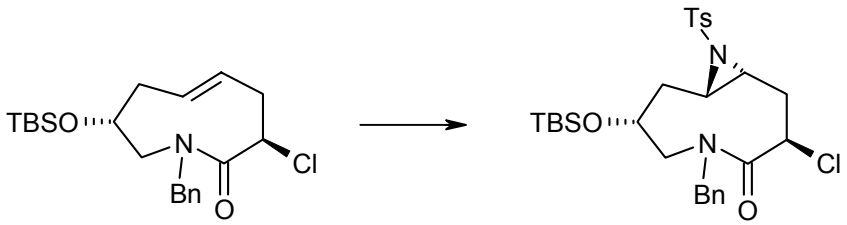
^{1}H-NMR (270 MHz, DMSO-D_6): 7.80-7.20 (m, 9H), 2.25 (s, 3H).

IR (KBr):[280]

υ (cm^{-1}) = 1266 (s, υ_{as} SO_2), 1132 (s, υ_s SO_2), 1081 (s), 989 (m), 866 (s).

[280] The purity of the phenyl iodinane was controlled by the absence of characteristic IR bands of p-tosyl amide; IR (KBr): υ(cm^{-1}) = : 1305 (s, υ_{as} SO_2), 1155 (s, υ_s SO_2) according Yamamoto et al.

3*R*,5*R*,6*R*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-chloro-5,6-(N-tosyl)-epiminoazonan-2-one [40a]



[12a] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[40a]** 563.24 [$C_{28}H_{39}ClN_2O_4S_1Si$]

Reaction of ***pS*-[12a]** (0.15g, 0.38 mmol) proceeded with 1.3 eq of PhI=NTs and 6 mg (5 mol%) of $Cu(OTf)_2$ in 15 mL of dry acetonitrile under stirring at 10 °C. After 3 h reaction time, the solvent was evaporated under reduced pressure and the crude product was dissolved in ethyl acetate and filtered through a short silica gel column to remove polar impurities (p-$TsNH_2$). Pure product could be obtained by HPLC (ethyl acetate / n-hexane = 12:88, Nucleosil 50-5, 32*250, 64ml/min flow, r.t. 13 min) to yield 0.12 g (56.1%) of **[40a]** as a colourless oil.

$[\alpha]_D^{20}$ = - 31.58° (c = 1.624, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.85 - 7.75 (m, 2H; H-o-Ts), 7.50 - 7.10 (m, 7H), 5.20 - 5.15 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 14 Hz), 5.15 - 5.08 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 10 Hz, ^3J (H^{3u},H^{4u}) = 7 Hz), 4.30 - 4.19 (m, 1H; H-8o), 4.15 - 4.05 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 14 Hz), 3.72 - 3.60 (dd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 15 Hz, ^3J (H^{9u},H^{8o}) = 10 Hz), 3.38 - 3.28 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 15 Hz, ^3J (H^{9o},H^{8o}) = 6 Hz), 2.85 - 2.75 (dd, 1H; H-6u; ^3J (H^{6u},H^{7o}) = 11 Hz, ^3J (H^{6u},H^{5o}) = 5 Hz), 2.65 - 2.50 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 12 Hz, ^3J (H^{4o},H^{3u}) = 12 Hz, ^3J (H^{4o},H^{5o}) = 5 Hz), 2.50 - 2.38 (m, 1H; H-5o), 2.42 (s, 3H; H-p-Ts-CH_3), 2.35 - 2.25 (m, 1H; H-4u), 2.25 - 2.20 (d, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 14.6 Hz), 1.58 - 1.45 (m, 1H; H-7o), 0.83 (s, 9H; H-Si-C(CH_3)$_3$), 0.00 (s, 3H; H-Si-CH_3), - 0.06 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

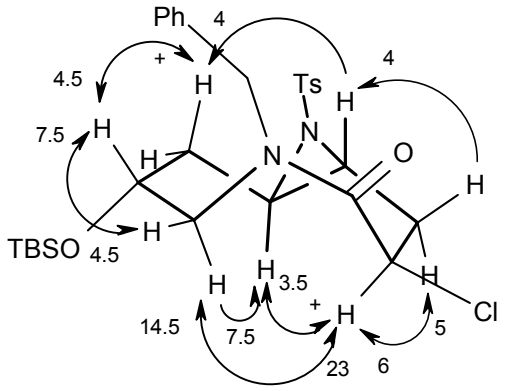
168.8 (q, C=O), 144.5 (s), 136.6 (s), 135.9 (s), 129.7 (d), 128.9 (d), 128.6 (d), 128.2 (d), 127.3 (d), 66.1 (d, C-8), 50.7 (t), 50.2 (d), 49.5 (t), 46.5 (d), 41.1 (d), 34.7 (t, 2 peaks ?), 25.6 (q, Si-C(CH_3)$_3$), 21.5 (q), 17.8 (Si-C(CH_3)$_3$), - 5.0 (q, Si-CH_3), -5.1 (q, Si-CH_3).

IR (KBr):

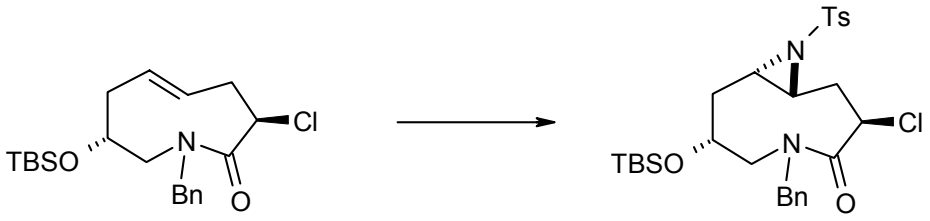
υ (cm^{-1}) = 2954 (s), 2929 (m), 2857 (m), 1747 (m), 1656 (s, CO), 1598 (m), 1495 (m), 1471 (s), 1447 (s), 1325 (s), 1258 (s), 1161 (s), 1090 (s), 968 (m), 837 (s).

MS (80eV, EI, 60-100 °C):
m/z (%): 562 (0.6) [$M^{+\cdot}$], 547 (2) [M^+ - CH_3], 527 (0.7) [M^+ -Cl], 505 (2) [M^+ - C_4H_9], 290 (100), 281 (8), 157 (4), 126 (3), 91 (42), 75 (9), 73 (4).

HRMS (80eV,120 °C): found 547.18194
calc. 547.185361 (for $C_{27}H_{36}N_2O_4S_1Cl_1Si_1$ [M^+ - CH_3]).



3*R*,5*S*,6*S*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-chloro-5,6-(N-tosyl)-epiminoazonan-2-one [40b]



[12b] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[40b]** 563.24 [$C_{28}H_{39}ClN_2O_4S_1Si$]

Reaction of ***pR*-[12b]** (0.20g, 0.507 mmol) proceeded with 1.2 eq of PhI=NTs and 9 mg of $Cu(OTf)_2$ (5 mol%) in 15 mL of dry acetonitrile and stirring at room temperature. After 2 h reaction time, the solvent was evaporated under reduced pressure and the crude product was dissolved in ethyl acetate and filtered through a short silica gel column to remove polar impurities (p-$TsNH_2$). Pure product could be obtained with HPLC (ethyl acetate / n-hexane = 12:88, Nucleosil 50-5, 32*250, 64ml/min flow, r.t. 13.5min) to yield 0.15 g (52.5%) of **[40b]** as a colourless oil.

The NMR spectra of **[40b]** showed a second set of minor peaks that originated from a minor conformation (ratio 3:7, flexible amide geometry?). NOE experiments indicated a fast interconversion of *minor*-**[40b]** and *major*-**[40b]**.

$[\alpha]_D^{20}$ = - 26.48° (c = 1.412, $CHCl_3$).

major conformer :

^{1}H-NMR (270 MHz, $CDCl_3$):

7.85 - 7.75 (m, 2H; H-o-Ts), 7.50 - 7.10 (m, 7H; H-arom.), 5.13 - 5.05 (d, 1H; H-N-Bn1; ^{2}J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 14.6 Hz), 5.00 - 4.90 (dd, 1H; H-3u; ^{3}J (H^{3u},H^{4o}) = 12 Hz, ^{3}J (H^{3u},H^{4u}) = 1.5 Hz), 4.35 - 4.30 (d, 1H; H-N-Bn2; ^{2}J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 14.6 Hz), 4.13 - 4.05 (m, 1H; H-8o), 3.95 - 3.83 (dd, 1H; H-9u; ^{2}J (H^{9u},H^{9o}) = 14.6 Hz, ^{3}J (H^{9u},H^{8o}) = 9 Hz), 3.35 - 3.25 (d, 1H; H-9o; ^{2}J (H^{9o},H^{9u}) = 14.6 Hz), 2.90 - 2.80 (ddd, 1H; H-5u; ^{3}J (H^{5u},H^{4o}) = 11 Hz, ^{3}J (H^{5u},H^{6o}) = 4 Hz, ^{3}J (H^{5u},H^{4o}) = 4 Hz), 2.70 - 2.45 (m, 3H; H-6o, 7o, 4u), 2.43 (s, 3H; H-p-Ts), 2.25 - 2.10 (ddd, 1H; H-4o; ^{2}J (H^{4o},H^{4u}) = 12 Hz, ^{3}J (H^{4o},H^{3u}) = 12 Hz, ^{3}J (H^{4o},H^{5u}) = 12 Hz), 1.70 - 1.58 (ddd, 1H; H-7u; ^{2}J (H^{7u},H^{7o}) = 12 Hz, ^{3}J (H^{7u},H^{8o}) = 12 Hz, ^{3}J (H^{7u},H^{6o}) = 10 Hz), 0.8 (s, 9H; H-Si-C(CH_3)$_3$), 0.01 (s, 6H; H-Si-CH_3).

minor conformer:

^{1}H-NMR (270 MHz, $CDCl_3$):

7.85 - 7.75 (m, 2H; H-o-Ts), 7.50 - 7.10 (m, 7H; H-arom.), 5.12 - 5.05 (d, 1H; H-N-Bn1; ^{2}J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 15 Hz), 5.05 - 5.00 (m, 1H; H-3u), 4.68 - 4.52 (m, 1H; H-8o), 4.45 - 4.35 (d, 1H; H-N-Bn2; ^{2}J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 15 Hz), 4.20 - 4.15 (m, 1H; H-9o), 2.70 - 2.45 (m, 3H; H-9u, 4u, 5u), 2.43 (s, 3H; H-p-Ts), 2.32 - 2.25 (m, 1H; H-7o), 1.95 - 1.80 (m, 2H; H-7u,4o), 0.83 (s, 9H; H-Si-C(CH_3)$_3$), 0.04 (s, 6H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

δ 169.4 (s), 144.5 (s), 136.7 (s), 136.3 (s), 135.5 (s), 129.7 (d), 128.8 (d), 127.9 (d), 127.3 (d), 126.6 (d), 66.3 (d), 54.3 (t), 52.5 (d), 50.1 (t), 46.5 (d), 42.7 (d), 37.6 (t), 36.3 (t), 25.4 (q, Si-C(C$\underline{H_3}$)$_3$), 21.5 (q), 17.6 (s, Si-C(CH_3)$_3$), - 4.5 (q, Si-CH_3), -4.9 (q, Si-CH_3).

IR (KBr):

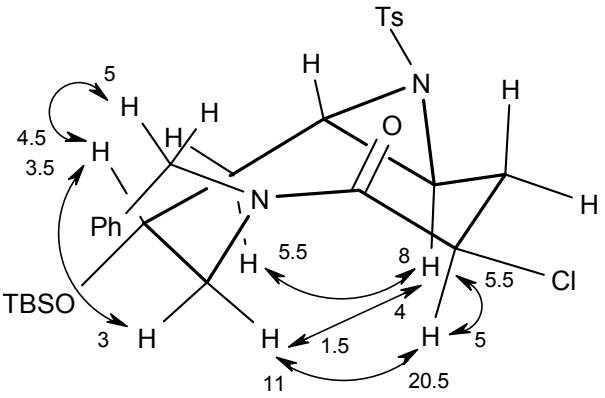
υ (cm^{-1}) = 2954 (s), 2929 (m), 2857 (m), 1656 (s, CO), 1598 (m), 1495 (m), 1471 (s), 1449 (s), 1325 (s), 1260 (s), 1161 (s), 1090 (s), 1006 (m), 968 (m), 837 (s).

MS (80eV, EI, 150 °C):

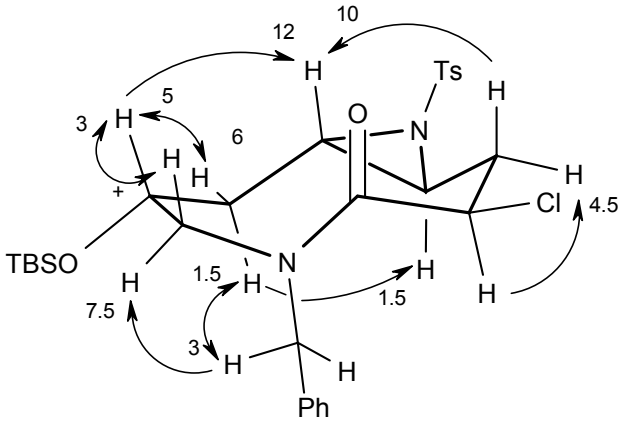
m/z (%): 563 (0.85) [$M^{+\cdot}$], 562 (0.8) [$M^{+\cdot}$], 547 (3) [M^{+} - CH_3], 527 (0.8) [M^{+} -Cl], 505 (4) [M^{+} - C_4H_9], 290 (100), 281 (88), 157 (14), 126 (27), 91 (93), 75 (34), 73 (11).

HRMS (80eV,120 °C): found 547.18377 calc. 547.185361 (for $C_{27}H_{36}N_2O_4S_1Cl_1Si_1$ [M^{+} CH_3]).

major conformer (70%)

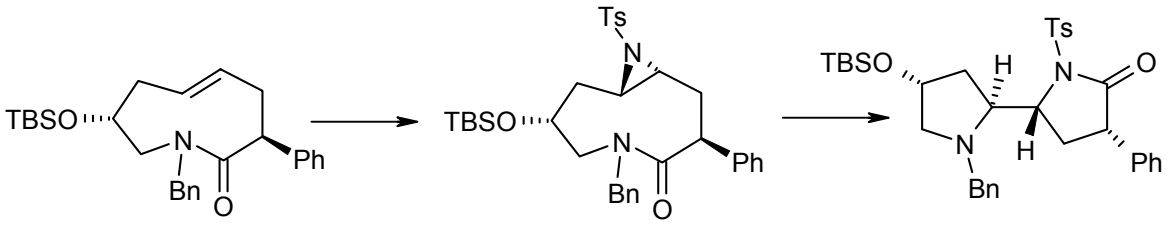


minor conformer (30%)



3*S*,5*R*,6*R*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)- 5,6-(N-tosyl)-epimino-3-phenylazonan-2-one [41a] and

3*S*,5*R*,5-(1*S*,4*R*-2-Benzyl-4-(*tert*-butyldimethylsilyloxy)-2-pyrrolidinyl)-3-phenyl-1-tosyl-3,4,5-trihydro-pyrrolidine-2-one [41b]



[13a] 435.69 [$C_{27}H_{37}NO_2Si$] **[41a]** 604.89 [$C_{34}H_{44}N_2O_4S_1Si$] **[41b]** 604.89 [$C_{34}H_{44}N_2O_4S_1Si$]

A solution of ***pS*-[13a]** (0.15 g, 0.34 mmol), PhI=NTs (1.4 equiv) and [$Cu(OTf)_2$] (2 mg, 1.2 mol%) in dry MeCN (15 mL) was stirred for 30 min at 0 °C. For the purification, the crude oil was dissolved in diethyl ether, whereas most of the p-toluenesulfonylamide (originating from decomposed PhI=NTs) precipitated, after addition of excess hexane (→ diethyl ether/ n-hexane 1:5). After filtration, the crude oil was purified by means of HPLC (ethyl acetate / n-hexane = 12:88) and 0.12 g (0.2 mmol, 57.7%) of **[41a]** were obtained as a colourless oil. Compound **[41a]** was found to be unstable and completely rearranged to **[41b]** when stored at room temperature.

aziridino azonanone [41a]:

$[\alpha]_D^{20}$ = - 54.80° (c = 1.472, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
7.90 - 7.80 (d, 2 H; H-o-Ts; ^{3}J ($H^{o\text{-}Ts}$,$H^{m\text{-}Ts}$) = 8 Hz), 7.60 - 7.10 (m, 12H; H-arom.H), 5.20 - 5.10 (d, 1H; H-N-Bn1; ^{2}J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 14 Hz), 4.55 - 4.45 (m, 1H; H-3u), 4.30 - 4.20 (m, 1H; H-8o), 4.28 - 4.10 (d, 1H; H-N-Bn2; ^{2}J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 14 Hz), 4.11 - 4.01 (dd, 1H; H-9u; ^{2}J (H^{9u},H^{9o}) = 15 Hz, ^{3}J (H^{9u},H^{8o}) = 10 Hz), 3.36 - 3.26 (dd, 1H; H-9o; ^{2}J (H^{9o},H^{9u}) = 15 Hz, ^{3}J (H^{9o},H^{8o}) = 6 Hz), 3.00 - 2.90 (dd, 1H; H-6u; ^{3}J (H^{6u},H$^{)}$ = 10 Hz, ^{3}J (H^{6u},H) = 4 Hz), 2.80 - 2.60 (m, 2H; H-4o, 5o), 2.44 (s, 3H; H-p-Ts-CH_3), 2.32 - 2.25 (d, 1H; H-7u; ^{2}J (H^{7u},H^{7o}) = 14.6 Hz), 2.10 - 1.95 (m, 1H; H-4u), 1.65 - 1.50 (m, 1H; H-7o), 0.8 (s, 9H; H-Si-C(CH_3)$_3$), 0.01 (s, 3H; H-Si-CH_3), - 0.01 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$): 173.3 (s, C=O), 144.2 (s), 138.5 (s), 137.1 (s), 136.8 (s), 129.6 (d), 128.7 (d), 128.5 (d), 128.4 (d), 127.9 (d), 127.4 (d), 127.3 (d), 66.5 (d, C-8), 51.0 (t), 48.96 (t), 48.90 (d), 43.7 (d), 41.8 (t), 35.1 (t), 31.8 (t), 25.7 (q, Si-C(CH_3)$_3$), 21.6 (q, p-Ts-CH_3), 17.9 (s, Si-C(CH_3)$_3$), -4.9 (q, Si-CH_3).

pyrrolidinone [41b]:

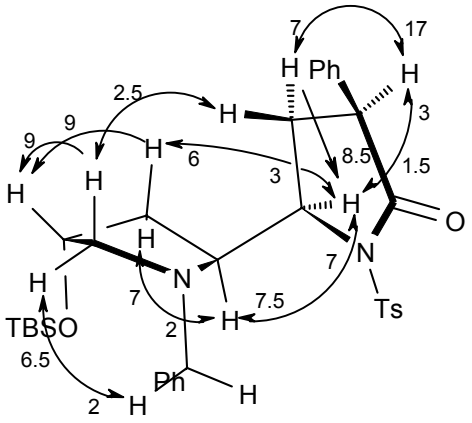
$[\alpha]_D^{20}$ = - 43.98° (c = 1.573, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
8.05 - 7.95 (m, 2H; H-o-Ts), 7.40 - 7.20 (m, 13H; H-arom), 4.52 - 4.43 (dd, 1H; H-5; ^{3}J (H^{5},H^{4o}) = 8 Hz, ^{3}J (H^{5},H^{4u}) = 8 Hz), 4.18 - 4.10 (m, 2H; H-8o, 6u), 4.10 - 4.00 (d, 1H; H-N-Bn1; ^{2}J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 13 Hz), 3.65 - 3.58 (d, 1H; H-3u; ^{3}J (H^{3u},H^{4o}) = 11 Hz), 3.55 - 3.48 (d, 1H; H-N-Bn2; ^{2}J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 13 Hz), 2.98 - 2.90 (dd, 1H; H-9o; ^{2}J (H^{9o},H^{9u}) = 11 Hz, ^{3}J (H^{9o},H^{8o}) = 4 Hz), 2.70 - 2.60 (ddd, 1H; H-4o; ^{2}J (H^{4o},H^{4u}) = 12.7 Hz, ^{3}J (H^{4o},H^{3u}) = 12.7 Hz, ^{3}J (H^{4o},H^{5}) = 8 Hz), 2.53 - 2.40 (m, 2H; H-9u, 4u), 2.40 (s, 3H; H-CH_3), 2.05 - 1.95 (ddd, 1H; H-7u; ^{2}J (H^{7u},H^{7o}) = 12.7 Hz, ^{3}J (H^{7u},H) = 9 Hz, ^{3}J (H^{7u},H) = 3 Hz), 1.63 - 1.53 (ddd, 1H; H-7o; ^{2}J (H^{7o},H$^{)}$ = 13 Hz, ^{3}J (H^{7o},H) = 8 Hz, ^{3}J (H^{7o},H) = 6 Hz), 0.90 (s, 9H; H-Si (CMe_3)), 0.06 (s, 3H; H-Si-CH_3), 0.04 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
174.9 (s, CO), 145.0 (s), 139.9 (s), 137.4 (s), 135.6 (s), 129.4 (d), 128.6 (d), 128.4 (d), 128.0 (d), 127.4 (d), 126.6 (d), 71.1 (d), 64.4 (d), 62.5 (t), 61.5 (t), 61.2 (d), 48.1 (d), 38.4 (t), 26.5 (t), 25.8 (q, Si-C(CH_3)$_3$), 21.6 (q), 17.9 (s, Si-C(CH_3)$_3$), - 4.8 (q, Si-CH_3).

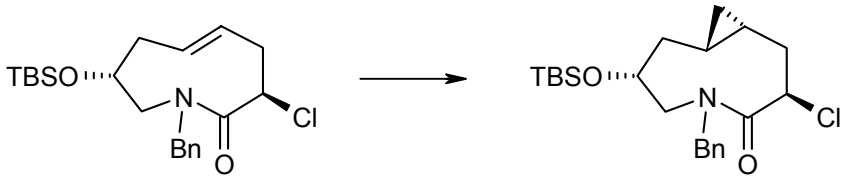
IR (KBr):
υ (cm^{-1}) = 3027 (m), 2927 (s), 2854 (s), 1731 (s, N-CO), 1597 (m), 1494 (s), 1471 (s), 1453 (s), 1361 (s), 1253 (m, C-O), 1210 (m), 1166 (s).

MS (80eV, EI, 150 °C):
m/z (%): 604 (0.3) [$M^{+\cdot}$], 589 (0.5) [M^+ - CH_3], 547 (0.1) [M^+ - C_4H_9], 449 (0.66) [M^+ - Ts], 290 (100), 91 (18), 75 (11).



HRMS (80eV,120 °C): found 604.27722
calc. 604.279109 (for $C_{34}H_{44}N_2O_4S_1Si_1$, [M^+]).

3*R*,5*R*,6*R*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-chloro-5,6-methano-azonan-2-one [42a]



[12a] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[42a]** 408.06 [$C_{22}H_{34}ClNO_2Si$]

Reaction of ***pS*-[12a]** (200mg, 0.507 mmol) with 13mol% Pd $(OAc)_2$/diazomethane was carried out according to the standard cyclopropanation procedure. The crude product was purified by column chromatography (n-hexane/ ethyl acetate = 3:1, R_f = 0.42) to yield **[42a]** as colourless crystals (189.8 mg, 91.7%) with mp = 133-134 °C.

$[\alpha]_D^{20}$ = - 96.05° (c = 1.62, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
7.50 - 7.20 (m, 5H; H-Ph), 5.20 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 14 Hz), 5.20 - 5.10 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 10 Hz, ^3J (H^{3u},H^{4u}) = 10 Hz), 4.20 - 4.10 (m, 1H; H-8o), 4.08 - 4.00 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 14 Hz), 3.88 - 3.78 (dd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 15 Hz, ^3J (H^{9u},H^{8o}) = 9.6 Hz, ^4J (H^{9u},$H^{N\text{-}Bn1}$) = 0.5 Hz), 3.18 - 3.08 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 15 Hz, ^3J (H^{9o},H^{8o}) = 5 Hz), 2.60 - 2.50 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 12.5 Hz, ^3J (H^{4o},H^{3u}) = 10 Hz, ^3J (H^{4o},H^{5o}) = 5 Hz), 2.02 - 1.95 (d, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 14 Hz), 1.55 - 1.42 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 12.5 Hz, ^3J (H^{4u},H^{5o}) = 11 Hz, ^3J (H^{4u},H^{3u}) = 7 Hz), 0.8 (s, 9H; Si-C$(CH_3)_3$), 0.75 - 0.40 (m, 4H; H-7o, 5a-o, 5a-u, 6u), 0.30 - 0.10 (m, 1H; H-5o), - 0.01 (s, 3H; Si-CH_3), - 0.10 (s, 3H; Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

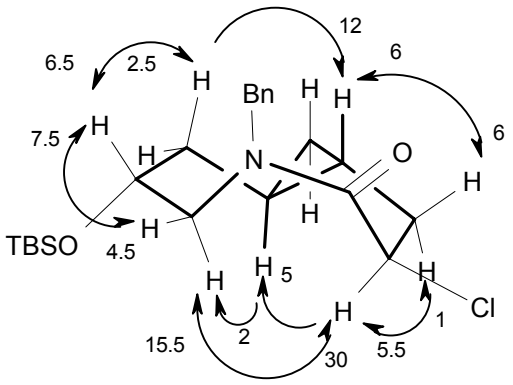
170.1 (s, C=O), 136.6 (s), 128.7 (d), 128.6 (d), 127.8 (d), 67.7 (d, C-8), 52.4 (d, C-3), 50.9 (t, C-9), 49.0 (t, N-Bn), 39.3 (t, C-7), 39.2 (t, C-4), 25.7 (q, Si-C$(CH_3)_3$), 20.4 (d, C-5), 17.9 (s, Si-C$(CH_3)_3$), 11.7 (t, methano C-5a), 9.9 (d, C-6), - 4.9 (q, Si-CH_3), - 5.0 (q, Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3426 (m), 3028 (w), 2928 (s), 2855 (s), 1656 (s, N-CO), 1449 (s), 1254 (m, C-O), 1197 (s), 1099 (s), 1080 (s), 838 (s), 776 (s), 704 (m).

MS (80eV, EI, 80 °C):

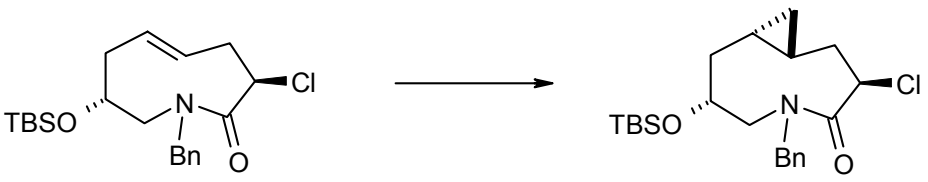
m/z (%): 407 (9) [M^+], 392 (16) [M^+-CH_3], 372 (44) [M^+-Cl], 350 (94) [M^+-C_4H_9], 336 (100), 314 (15), 302 (50), 127 (40), 91 (90), 73 (55).



HRMS (80eV, 80 °C): found 407.20742

calc. 407.204736 (for $C_{22}H_{34}NO_2Si$ ^{35}Cl [M^+]).

3*R*,5*S*,6*S*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-chloro-5,6-methanoazonan-2-one [42b]



[12b] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[42b]** 408.06 [$C_{22}H_{34}ClNO_2Si$]

Before the cyclopropanation, the reactant azoninone ***pS*-[12a]** was heated for at least 3 h at 65 °C to achieve a high degree of conversion into azoninone ***pR*-[12b]** (12a:12b ~ 1:4.3). Reaction of azoninone ***pR*-[12b]** (0.42 g, 1.06 mmol) and [$Pd(OAc)_2$] (5 mg, 2 mol%) according to the standard cyclopropanation procedure, followed by chromatography (hexane / ethyl acetate = 3:1, R_f = 0.42) gave 0.41 g (1.02 mmol, 95.7%) of a colourless oil as a mixture of **[42b]** and **[42a]** (4.3:1). Fractional crystallisation of **[42a]** (solid) from diethyl ether / n-hexane gave **[42b]** (oil, purity 96%).

$[\alpha]_D^{20}$ = - 20.1° (c = 1.95, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):[281]

7.50 - 7.20 (m, 5H; H-Ph), 5.40 - 5.30 (d, 1H; H-N-Bn1; ^{2}J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 15 Hz), 5.00 (dd, 1H; H-3u; ^{3}J (H^{3u},H^{4o}) = 12 Hz, ^{3}J (H^{3u},H^{4u}) = 2 Hz), 4.20 - 4.00 (m, 3H; H-N-Bn2, 8o, 9u), 3.18 - 3.10 (d, 1H; H-9o; ^{2}J (H^{9o},H^{9u}) = 12 Hz), 2.55 - 2.45 (ddd, 1H; H-4u; ^{2}J (H^{4u},H^{4o}) = 13 Hz, ^{3}J (H^{4u},H^{5u}) = 3 Hz, ^{3}J (H^{4u},H^{3u}) = 3 Hz), 2.40 - 2.30 (dd, 1H; H-7u; ^{2}J (H^{7u},H^{7o}) = 14 Hz, ^{3}J (H^{7u},H) = 6 Hz), 0.8 (s, 9H; Si-C(CH_3)$_3$), 0.75 - 0.40 (m, 5H; H-7o, 5a-o, 5a-u, 6u, 5o), - 0.01 (s, 3H; Si-CH_3), - 0.10 (s, 3H; Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

171.1 (s, C=O), 136.6 (s), 128.6 (d), 127.9 (d), 127.5 (d), 67.4 (d, C-8), 55.7 (d, C-3), 53.5 (t, C-9), 49.2 (t, C-NBn), 41.9 (t, C-7), 39.6 (t, C-4), 25.5 (q, Si-C(CH_3)$_3$), 20.6 (d, C-5), 17.7 (s, Si-C(CH_3)$_3$), 12.5 (d, C-6), 9.3 (t, C-5a), - 4.4 (q, Si-CH_3), - 4.9 (q, Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3028 (w), 2953 (s), 2928 (s), 2857 (s), 1654 (s, N-CO), 1447 (s), 1257 (m, C-O), 1197 (m), 1090 (s), 834 (s), 776 (s).

MS (80eV, EI, 80 °C):

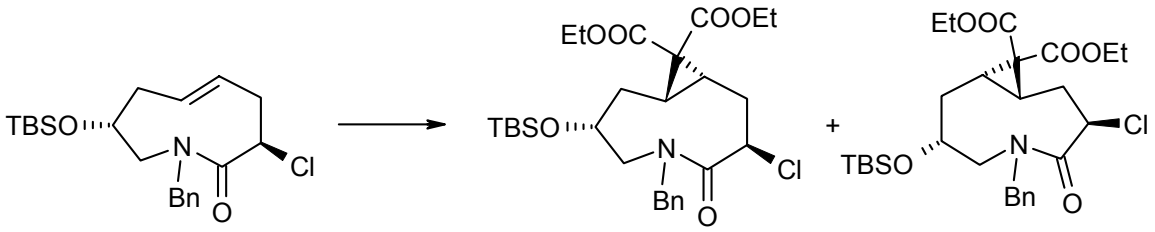
m/z (%): 407 (13) [M^+], 392 (7) [M^+-CH_3], 372 (34) [M^+-Cl], 350 (100) [M^+-C_4H_9], 314 (14), 224 (10), 195 (12), 91 (45), 73 (13).

HRMS (80eV, 80 °C): found 407.20196 calc. 407.204736 (for $C_{22}H_{34}NO_2SiCl$ [M^+]).

[281] NOE spectrum of compound **[42b]** could not be interpreted due to the overlapping signals of H-5 and H-6 in the ^{1}H-NMR spectrum, the comparison with **[42a]** confirmed the structure, since inversion of the stereogenic centers at C-3 and C-8 could be excluded.

3*R*,5*R*,6*R*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-5,6-bis-(ethyloxycarbonyl)-methano-3-chloroazonane-2-one [43a] and

3*R*,5*S*,6*S*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-5,6-bis-(ethyloxycarbonyl)-methano-3-chloroazonan-2-one [43b]



[12a,b] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[43a]** 552.19 [$C_{28}H_{42}ClNO_6Si$] **[43b]** 552.19 [$C_{28}H_{42}ClNO_6Si$]

Reaction of **[12a,b]**[282] (0.16 g, 0.414 mmol), diethyl diazomalonate (2 equiv)[283] and [$Pd(OAc)_2$] (10 mg, 10 mol%) in dry toluene (20 mL) at 60 °C, otherwise following the standard cyclopropanation procedure. The reaction mixture was purified by filtration through a short silica gel column. Separation by HPLC (ethyl acetate / n-hexane = 8:92, Nucleosil 50-5, 32x238 mm, 128ml/min flow, r.t. 15min) yielded 28.5 mg (0.05 mmol, 12.4%) of **[43a]** and 40.4 mg (0.07 mmol, 17.7%) of **[43b]** as colourless oils.

azonan-2-one [43a] :

$[\alpha]_D^{20}$ = - 46.1° (c = 1.425, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
7.50 - 7.20 (m, 5H; H-Ph), 5.25 - 5.15 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 14 Hz), 5.12 - 5.05 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 10 Hz, ^3J (H^{3u},H^{4u}) = 6 Hz), 4.30 - 4.10 (m, 5H; H-Ester-CH_2, 8o), 4.05 - 3.95 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 14 Hz), 3.80 - 3.75 (ddd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 15 Hz, ^3J (H^{9u},H^{8o}) = 10 Hz, ^4J (H^{9u},$H^{N\text{-}Bn1}$) = 0.5 Hz), 3.20 - 3.10 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 15 Hz, ^3J (H^{9o},H^{8o}) = 6 Hz), 2.50 - 2.40 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 12 Hz, ^3J (H^{4o},H^{3u}) = 11 Hz, ^3J (H^{4o},H^{5o}) = 6 Hz), 1.90 - 1.76 (m, 3H; H-6u, 4u, 7u), 1.60 - 1.50 (ddd, 1H; H-5o; ^3J (H^{5o},H^{6u}) = 11 Hz, ^3J (H^{5o},H^{4u}) = 8 Hz, ^3J (H^{5o},H^{4o}) = 6 Hz), 1.30 - 1.20 (m, 6H; H-Ester-CH_3), 1.02 - 0.90 (m, 1H; H-7o), 0.8 (s, 9H; H-Si-C(CH_3)$_3$), - 0.01 (s, 3H; H-Si-CH_3), - 0.10 (s, 3H; H-Si-CH_3).

[282] During the reaction conditions a mixture of **[12a]** and **[12b]** was formed.
[283] Prepared from diethyl malonate and tosylazide in acetonitrile acc. to : Regitz, M.; Liedhegener, A. *Chem. Ber.* **1966**, 99, 3128. Tosyl azide was prepared from tosyl chloride and sodium azide acc. to Tietze, L. F.; Eicher, Th.; *Reaktionen and Synthesen*, Georg Thieme Stuttgart, 2nd edition **1991**, p. 270.

^{13}C-NMR (67.9 MHz, $CDCl_3$):

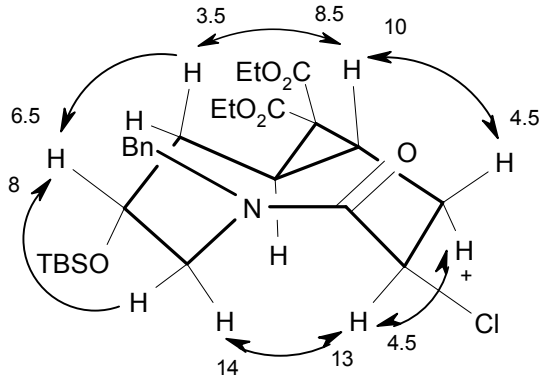
168.3 (s, C=O), 167.7 (s, C=O), 167.2 (s, C=O), 136.2 (s), 128.7 (d), 128.6 (d), 127.9 (d), 66.9 (d, C-8), 61.8 (t, ester-CH_2), 61.5 (t, ester-CH_2), 51.6 (d, C-3), 50.7 (t, C-9), 49.2 (t, N-Bn), 39.6 (s), 34.6 (t, C-7), 32.6 (t, C-4), 32.1 (d), 25.7 (Si-C$(CH_3)_3$), 23.7 (d), 17.9 (Si-C$(CH_3)_3$), 14.2 (q, ester-CH_3), 14.1 (q, ester-CH_3), - 4.9 (Si-CH_3), -5.0 (Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3444 (w), 2954 (s), 2935 (s), 2856 (s), 1726 (s, Ester-CO), 1661 (s, N-CO), 1443 (s), 1366 (s), 1292 (s), 1074 (s).

MS (80eV, EI, 110 °C):

m/z (%): 551 (23) [M^+], 536 (4) [M^+ -CH_3], 516 (8) [M^+ -Cl], 506 (17) [M^+ - C_2H_5O], 494 (100) [M^+ - C_4H_9], 460 (8), 394 (10), 356 (8), 296 (28), 290 (11), 211 (5), 184 (83), 91 (54), 73 (26).



HRMS (80eV,110 °C): found 551.24730

calc. 551.24700 (for $C_{28}H_{42}NO_6Si_1Cl_1$ [M^+]).

azonan-2-one [43b] :

$[\alpha]_D^{20}$ = + 16.42° (c = 1.346, $CHCl_3$).

^{1}H-NMR (500 MHz, $CDCl_3$): [284]

7.50 - 7.20 (m, 5H; H-Ph), 5.16 - 5.12 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 15 Hz), 5.00 - 4.96 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 12 Hz, ^3J (H^{3u},H^{4u}) = 2 Hz), 4.34 - 4.28 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 15 Hz), 4.25 - 4.10 (m, 5H; H-Ester-CH_2), 4.10 - 4.00 (m, 1H; H-8o), 3.80 - 3.75 (ddd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 14.5 Hz, ^3J (H^{9u},H^{8o}) = 9 Hz), 3.20 - 3.15 (d, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 14.5 Hz), 2.45 - 2.40 (d, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 13 Hz), 2.15 - 2.09 (dd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 13 Hz, ^3J (H^{7o},H^{8o}) = 6 Hz), 1.93 - 1.85 (ddd, 1H; H-5u; ^3J (H^{5u},H^{4o}) = 12 Hz, ^3J (H^{5u},H^{6o}) = 8 Hz, ^3J (H^{5u},H^{4u}) = 4 Hz), 1.85 - 1.78 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 12 Hz, ^3J (H^{4o},H^{5u}) = 12 Hz, ^3J (H^{4o},H^{3u}) = 12 Hz), 1.62 - 1.58 (dd, 1H; H-6o; ^3J (H^{6o},H^{7u}) = 11 Hz, ^3J (H^{6o},H^{5u}) = 8 Hz), 1.30 - 1.20 (m, 6H; H-Ester-CH_3), 1.05 - 0.98 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 13 Hz, ^3J (H^{7u},H^{6o}) = 10 Hz, ^3J (H^{7u},H^{8o}) = 10 Hz), 0.8 (s, 9H; H-Si-C$(CH_3)_3$), - 0.01 (s, 3H; H-Si-CH_3), - 0.10 (s, 3H; H-Si-CH_3).

[284] Compound **[43b]** consists of two rotamers with a 5/1 ratio, presumably two amide isomers as detected by NOE-measurements, in analogy to conformers of compound **[40b]**.

^{13}C-NMR (67.9 MHz, $CDCl_3$):

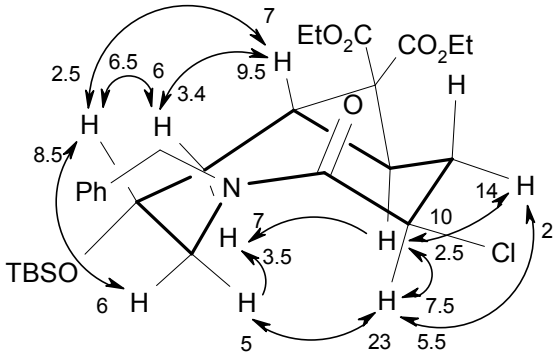
169.8 (s, C=O), 167.4 (s, C=O), 166.9 (s, C=O), 136.6 (s), 128.7 (d), 128.0 (d), 127.6 (d), 67.3 (d, C-8), 61.8 (t, ester-CH_2), 61.7 (t, ester-CH_2), 54.6 (d, C-3), 54.4 (t, C-9), 49.9 (t, N-Bn), 37.6 (s), 36.4 (t, C-7), 34.1 (t, C-4), 32.3 (d), 25.7 (Si-C$(CH_3)_3$), 25.5 (d), 17.7 (Si-C$(CH_3)_3$), 14.2 (q, ester-CH_3), - 4.4 (Si-CH_3), -4.8 (Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 3443 (w), 3065 (m), 3032 (m), 2932 (s), 2858 (s), 1727 (s, ester-CO), 1660 (s, N-CO), 1449 (s), 1368 (s), 1213 (s), 1094 (s).

MS (80eV, EI, 120 °C):

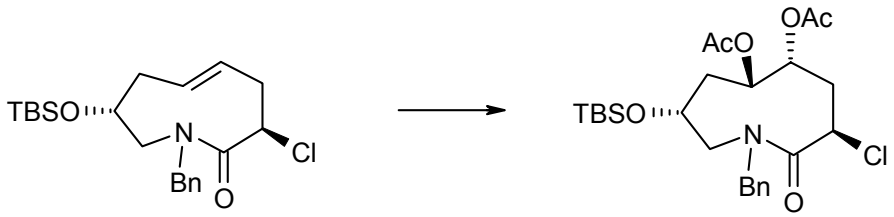
m/z (%): 551 (7) [M^+], 536 (2) [M^+ -CH_3], 516 (5) [M^+ -Cl], 506 (11) [M^+ - C_2H_5O], 494 (100) [M^+ - C_4H_9], 460 (13), 394 (10), 356 (10), 296 (20), 290 (7), 211 (11), 185 (42), 91 (97), 73 (10).



HRMS (80eV,120 °C): found 551.24762

calc. 551.24700 (for $C_{28}H_{42}NO_6Si_1Cl_1$ [M^+]).

3*R*,5*R*,6*R*,8*R*-1-Benzyl-5,6-bis-acetoxy-8-(*tert*-butyldimethylsilyloxy)-3-chloro-azonan-2-one [44a]



[12a] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[44a]** 512.12 [$C_{25}H_{38}ClNO_6Si$]

Reaction of ***pS*-[12a]** (0.10g, 0.254 mmol) with 1.5 eq of sodium periodate and $RuCl_3$ (7 mol%) in a mixture of acetonitrile and ethyl acetate (18mL, 1:1) proceeded according the standard dihydroxylation procedure. After standard workup, the brown oil was dissolved in dry dichloromethane and 4 eq. of pyridine, 4 eq of acetic acid anhydride and 20 mg of DMAP were added. After 3 h at room temperature and standard workup conditions, the crude reactions product was purified using column chromatography (ethyl acetate / n-hexane 1:4, R_f 0.28) to yield 0.092 g (70.5%) of **[44a]** as a colourless oil.

$[\alpha]_D^{20}$ = - 16.38° (c = 1.550, $CHCl_3$).

^{1}H-NMR (500 MHz, 287 K, C_6D_6): **major conformation** [285]

7.40 - 7.10 (m, 5H; H-arom.), 5.13 - 5.05 (m, 2H; H-5o,6u), 4.80 - 4.75 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 15 Hz), 4.65 - 4.60 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 10 Hz, ^3J (H^{3u},H^{4u}) = 4 Hz), 4.15 - 4.05 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 15 Hz), 3.60 - 3.52 (m, 1H; H-8o), 2.90 - 2.80 (dd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 15 Hz, ^3J (H^{9u},H^{8o}) = 10 Hz), 2.75 - 2.68 (d, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 15 Hz), 2.55 - 2.46 (dd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 12 Hz, ^3J (H^{4o},H^{3u}) = 12 Hz), 2.15 - 2.08 (m, 1H; H-4u), 1.85 - 1.78 (d, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 16 Hz), 1.72 (s, 3H;$COCH_3$), 1.60 (s, 3H; $COCH_3$), 0.83 (s, 9H; H-Si-$C(CH_3)_3$), -0.14 (s, 3H; H-Si-CH_3), -0.17 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, 293 K, C_6D_6): **major conformation** [285]

169.2 (s), 168.8 (s), 137.3 (d), 129.2 (d), 128.9 (d), 71.7 (d), 71.4 (d), 65.3 (d), 54.3 (t), 51.2 (t), 49.6 (d), 39.6 (t), 38.4 (t), 25.7 (q, Si-$C(CH_3)_3$), 20.6 (q, $OCOCH_3$), 20.4 (q, $OCOCH_3$), 17.9 (s, Si-$C(CH_3)_3$), - 4.8 (q, Si-CH_3), -5.0 (q, Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 2954 (s), 2930 (s), 2886 (s), 2857 (s), 1745 (s, ester-CO), 1667 (s, N-CO), 1471 (m), 1446 (m), 1368 (m), 1243 (s, C-O), 1082 (s), 1032 (s).

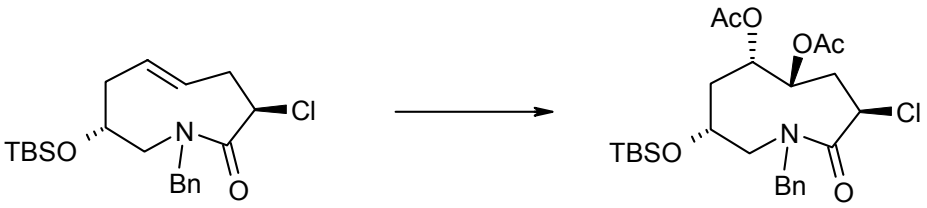
MS (80eV, EI, 130 °C):

m/z (%): 511 (0.7) [$M^{+\cdot}$], 496 (0.3) [M^+ - CH_3], 476 (3) [M^+ - Cl], 468 (0.7) [M^+ - OCH_3], 454 (26) [M^+ - C_4H_9], 394 (10), 304 (47), 244 (15), 200 (25), 117 (6), 91 (100), 73 (12).

HRMS (80eV,130 °C): found 511.21911 calc. 511.215694 (for $C_{25}H_{38}N_1O_6Si_1Cl_1$ [M^+]).

[285] At room temperature, ^{1}H and ^{13}C- NMR spectra of **[44b]** were characterised by broad lines. At 10 °C, a second set of minor peaks appeared that originated from a minor conformation. A NOE measurement could not be performed due to the high flexibility of the compound (at room temperature).

3*R*,5*S*,6*S*,8*R*-1-Benzyl-5,6-bis-acetoxy-8-(*tert*-butyldimethylsilyloxy)-3-chloro-azonan-2-one [44b]



[12b] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[44b]** 512.12 [$C_{25}H_{38}ClNO_6Si$]

Reaction with ***pR*-[12b]** (150 mg, 0.38 mmol), $NaIO_4$ (1.5 equiv) and $RuCl_3$ (7 mol%) followed the standard dihydroxylation / bisacetate protection procedure. Chromatography (ethyl acetate / n-hexane 1:4, Rf = 0.28) yielded 172 mg (0.38 mmol, 88.2%) of **[44b]** as colourless crystals (mp 131-133 °C) and 20 mg (0.04 mmol, 10%) of **[44a]** that were separated in an additional fraction.

$[\alpha]_D^{20} = +6.9°$ (c = 1.412, $CHCl_3$).

^{1}H-NMR (500 MHz, 263K, CD_2Cl_2): **major conformation**[286]

7.40 - 7.20 (m, 5H), 5.50 - 5.40 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 15 Hz), 5.20 - 5.15 (m, 1H; H-3u), 5.10 - 5.05 (m, 1H; H-5), 4.95 - 4.85 (m, 1H; H-6), 4.15 - 4.05 (m, 1H; H-8o), 3.85 - 3.80 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 15 Hz), 3.65 - 3.59 (dd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 12 Hz, ^3J (H^{9u},H^{8o}) = 5 Hz), 3.20 - 3.15 (m, 1H; H-9o), 2.70 - 2.60 (m, 2H; H-4o, 4u), 2.20 - 2.05 (m, 2H; H-7o, 7u), 2.01 (s, 6H; O-$COCH_3$), 0.80 (s, 9H; H-Si (CMe_3), 0.06 (s, 3H; H-Si-CH_3), 0.03 (s, 3H; H-Si-CH_3).

^{1}H-NMR (500 MHz, 263K, CD_2Cl2): **minor conformation**

7.40 - 7.20 (m, 5H), 5.45 - 5.40 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 15 Hz), 5.00 - 4.80 (m, 2H; H-3u, 5), 4.47 - 4.43 (m, 1H; H-6), 4.25 - 4.15 (m, 2H; H-8, 9), 4.05 - 4.00 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 15 Hz), 3.20 - 3.10 (m, 1H; H-9), 2.35 - 2.30 (m, 1H; H-4), 2.20 - 2.00 (m, 2H; H-7, 4), 2.04 (s, 6H; O-$COCH_3$), 1.90 - 1.85 (m, 1H; H-7), 0.84 (s, 9H; H-Si (CMe_3), 0.01 (s, 3H; H-Si-CH_3), 0.00 (s, 3H; H-Si-CH_3).

^{13}C-NMR (125.76 MHz, 263K, CD_2Cl_2): both conformers

169.7, 169.6, 167.3, 136.3, 136.2, 128.8, 128.6, 128.2, 127.9, 127.8, 127.4, 77.8, 71.6, 70.5, 70.2, 68.8, 65.3, 56.9, 54.4, 51.7, 50.4, 50.0, 49.6, 41.8, 40.6, 38.1, 37.6, 25.5, 25.4, 21.0, 17.8, -5.2, -5.3.

[286] At room temperature, the ^{1}H and ^{13} C-NMR spectra of **[44b]** were characterised by broad lines. At -10 °C, a second set of minor peaks appeared that originated from a minor conformation (1: 2.6).

IR(KBr):

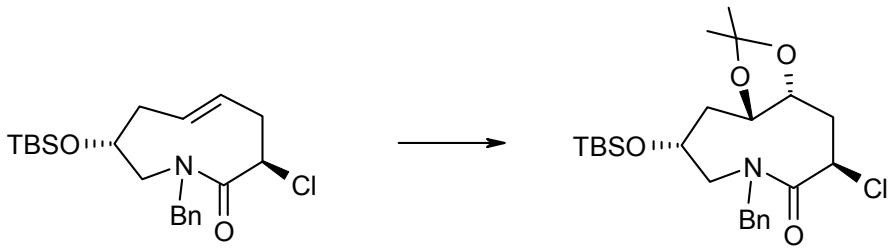
υ (cm^{-1}) = 2954 (s), 2930 (s), 2857 (s), 1744 (s), 1646 (s, N-CO), 1657 (s, N-CO), 1462 (s), 1453 (s), 1366 (s), 1240 (s), 1218 (s).

MS (80eV, EI, 135 °C):

m/z (%): 511 (6) [$M^{+\cdot}$], 496 (3) [M^+ - CH_3], 476 (6) [M^+ - Cl], 454 (38) [M^+ - C_4H_9], 394 (91), 304 (33), 200 (25), 117 (26), 91 (100).

HRMS (80eV, 130 °C): Found 511.21415 calc. 511.215694 (for $C_{25}H_{38}N_1O_6Si_1Cl_1$ [M^+]).

3*R*,5*R*,6*R*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-chloro-5,6-isopropylidendioxyazonan-2-one [45a]



[12a] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[45a]** 468.11 [$C_{24}H_{38}ClNO_4Si$]

Reaction of ***pS*-[12a]** (0.15g, 0.381 mmol) with 1.5 eq of sodium periodate and 4.6 mol% $RuCl_3$ in a mixture of acetonitrile and ethyl acetate (18mL, 1:1) proceeded according to the dihydroxylation procedure. After standard workup, the brown oil was dissolved in acetone and 5 eq. of dimethoxypropane and 10 mg of p-TsOH were added. After 2 h at room temperature and standard workup conditions, the crude reactions product was purified using column chromatography (ethyl acetate / n-hexane 1:4, R_f 0.48) to yield 0.128 g (70.9%) of **[45a]** as a colourless oil.

$[\alpha]_D^{20}$ = - 42.78° (c = 1.615, $CHCl_3$).

^{1}H-NMR (270 MHz, CD_2Cl_2): [287]

7.40 - 7.10 (m, 5H; H-arom.), 5.10 - 5.00 (m, 2H; H-N-Bn1, 3u), 4.20 - 4.10 (m, 1H; H-8o), 4.10 - 4.00 (m, 2H; H-6u, N-Bn2), 3.65 - 3.55 (m, 1H; H-5o), 3.55 - 3.45 (dd, 1H; H-9u; ^{2}J (H^{9u},H^{9o}) = 15.6 Hz, ^{3}J (H^{9u},H^{8o}) = 8 Hz), 3.45 - 3.30 (m, 1H; H-9o), 2.75 - 2.65 (dd, 1H; H-4o; ^{2}J (H^{4o},H^{4u}) = 12 Hz, ^{3}J (H^{4o},H^{3u}) = 12 Hz, ^{3}J (H^{4o},H^{5o}) = 4 Hz), 2.28 - 2.15 (ddd, 1H; H-4u; ^{2}J (H^{4u},H^{4o}) = 12.6 Hz, ^{3}J (H^{4u},H) = 11 Hz, ^{3}J (H^{4u},H) = 6 Hz), 2.19 - 2.09 (ddd, 1H; H-7u; ^{2}J (H^{7u},H^{7o}) = 15.6 Hz, ^{3}J (H^{7u},H^{8o}) = 6 Hz, ^{3}J (H^{7u},H^{6u}) = 2 Hz), 1.80 - 1.68 (dd, 1H; H-7o; ^{2}J (H^{7o},H^{7u}) = 15.6 Hz, ^{3}J (H^{7o},H^{6u}) = 6 Hz), 1.35 (s, 3H; H-O-C(CH_3)$_2$), 1.31 (s, 3H; H-O-C(CH_3)$_2$), 0.83 (s, 9H; H-Si-C(CH_3)$_3$), 0.08 (s, 3H; H-Si-CH_3), - 0.00 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, CD_2Cl2): [287]

169.8 (s, C=O), 136.8 (s), 129.4 (d), 129.0 (d), 128.5 (d), 108.05 (s, acetonide-C), 79.8 (d), 75.2 (d), 67.4 (d, C-8), 53.9 (t), 50.8 (t), 49.4 (d), 41.1 (t), 40.2 (t), 26.9 (q), 26.8 (q), 26.0 (q, Si-C(CH_3)$_3$), 18.3 (Si-C(CH_3)$_3$), - 4.5 (q, Si-CH_3), -4.7 (q, Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 2985 (s), 2953 (s), 2930 (s), 2886 (s), 2857 (s), 1662 (s, N-CO), 1472 (s), 1450 (s), 1432 (m), 1380 (s), 1369 (s), 1259 (s, C-O), 1209 (s), 1169 (s), 1098 (s), 1061 (s), 1028 (s).

MS (80eV, EI, 110 °C):

m/z (%): 467 (3) [$M^{+\cdot}$], 452 (8) [M^{+} - CH_3], 431 (3) [M^{+} -HCl], 410 (13) [M^{+} -C_4H_9], 394 (2), 373 (7), 352 (60), 277 (11), 242 (20), 91 (100) 73 (9).

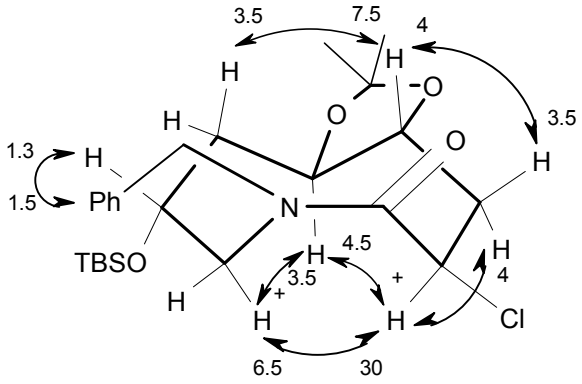
HRMS (80eV,120 °C): found 467.22723 calc. 467.225865 (for $C_{24}H_{38}N_1O_4Si_1Cl_1$; [$M^{+\cdot}$]).

[287] Although most of the signals appeared as sharp lines in the ^{1}H-NMR spectrum, line broadening of some signal indicated the existence of a second conformer (flexible amide geometry?). NOE experiments indicated a fast interconversion of both species. Furthermore, broad lines with a weak signal intensity were found in the ^{13}C-NMR spectrum for C6/C5 and C7/C4.

possible major conformation[288]

MM-Plus : 25.35 kcal

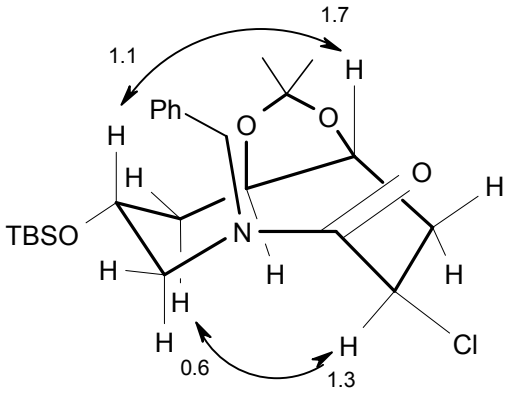
distance H5o-H8o 4.47Å´; distance H7u-H3u 4.66Å



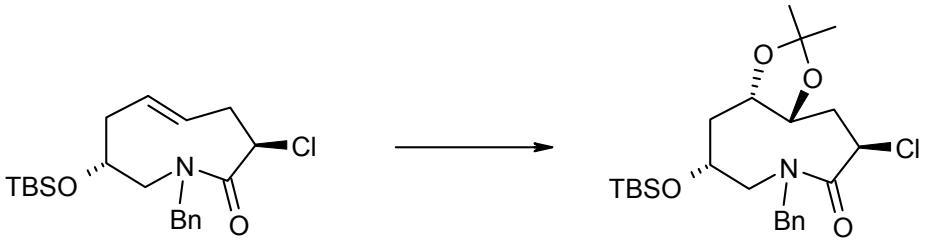
possible minor conformation

MM-Plus : 30.81 kcal

distance H5o-H8o 2.33Å; distance H7u-H3u 2.21Å



3*R*,5*S*,6*S*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-chloro-5,6-isopropylidendioxyazonan-2-one [45b]



[12b] 394.03 [$C_{21}H_{32}ClNO_2Si$] **[45b]** 468.11 [$C_{24}H_{38}ClNO_4Si$]

Before the reaction, ***pS*-[12a]** was heated for 1 h at 65 °C to achieve a high degree of conversion into azoninone ***pR*-[12b]** (12b:12a ~ 1:3.5). Reaction of ***pR*-[12b]** (0.15g, 0.381 mmol) with 1.5 eq of sodium periodate and 4.6 mol% $RuCl_3$ in a mixture of acetonitrile and ethyl acetate (18 mL, 1:1) proceeded according to the standard dihydroxylation procedure. After standard workup, the brown oil was dissolved in acetone and 5 eq. of dimethoxypropane and 10 mg of p-TsOH was added. After 2 h at room temperature and standard workup conditions, the crude reactions product was purified using column chromatography (ethyl acetate / n-hexane 1:5, R_f 0.56) to yield 0.098 g (55.5%) of **[45b]** as a colourless oil.

$[\alpha]_D^{20} = +28.04°$ (c = 1.6975, $CHCl_3$).

[288] Some of the observed NOE spectra indicate that the minor conformation is formed by a conformational change at C-7 and not as in earlier cases, an amide-isomerisation.

^{1}H-NMR (500 MHz, 233K, CD_2Cl_2): **major conformation** [289]

7.40 - 7.10 (m, 5H; H-arom.), 5.30 - 5.25 (d, 1H; H-N-Bn1 ; ^{2}J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 15 Hz), 4.85 - 4.78 (dd, 1H; H-8o ; ^{3}J (H^{8o} ,H^{4o}) = 10.6 Hz, ^{3}J (H^{8o} ,H^{4u}) = 10.6 Hz), 4.48 - 4.43 (d, 1H; H-N-Bn2; ^{2}J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 15 Hz), 4.06 - 4.00 (m, 1H; H-8o), 3.90 - 3.85 (m, 1H; H-9u), 3.55 - 3.48 (m, 2H; H-5u,6o), 3.29 - 3.24 (d, 1H; H-9o; ^{2}J (H^{9o},H^{9u}) = 16 Hz), 2.80 - 2.73 (dd, 1H; H-4o; ^{2}J (H^{4o},H^{4u}) = 16 Hz, ^{3}J (H^{4o},H^{3u}) = 10 Hz), 2.18 - 2.08 (m, 2H; H-7,4u), 2.05 - 1.95 (m, 1H; H-7'), 1.32 (s, 3H; H-O-C$(CH_3)_2$), 1.28 (s, 3H; H-O-C$(CH_3)_2$), 0.79 (s, 9H; H-Si-C$(CH_3)_3$), 0.04 (s, 3H; H-Si-CH_3), - 0.08 (s, 3H; H-Si-CH_3).

^{1}H-NMR (500 MHz, 233K, CD_2Cl_2): **minor conformation** [289]

7.40 - 7.10 (m, 5H; H-arom.), 5.28 - 5.22 (d, 1H; H-N-Bn1 ; ^{2}J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 15 Hz), 4.92 - 4.88 (d, 1H; H-8o ; ^{3}J (H^{8o} ,H^{4u}) = 10.1 Hz), 3.98 - 3.93 (m, 1H; H-5u), 3.93 - 3.85 (m, 2H; H-8o, N-Bn2), 3.72 - 3.67 (m, 1H; H-6o), 3.62 - 3.55 (dd, 1H; H-9; ^{2}J (H^{9},$H^{9'}$) = 15.5 Hz, ^{3}J (H^{9},H^{8o}) = 10 Hz), 3.17 - 3.12 (d, 1H; H-9'; ^{2}J ($H^{9'}$,H^{9}) = 15.3 Hz), 2.65 - 2.55 (m, 2H; H-4o, 4u), 2.25 - 2.18 (d, 1H; H-7; ^{2}J (H^{7},$H^{7'}$) = 15 Hz), 2.03 - 1.93 (m, 1H; H-7'), 1.31 (s, 3H; H-O-C$(CH_3)_2$), 1.26 (s, 3H; H-O-C$(CH_3)_2$), 0.79 (s, 9H; H-Si-C$(CH_3)_3$), 0.04 (s, 3H; H-Si-CH_3), 0.02 (s, 3H; H-Si-CH_3).

^{13}C-NMR (125.76 MHz, 233K, CD_2Cl_2):

171.9, 169.0, 137.4, 137.3, 130.0, 129.7, 129.2, 129.1, 128.2, 128.1, 109.2, 107.7, 81.0, 80.8, 79.1, 78.6, 75.1, 71.3, 67.5, 58.1, 56.1, 51.8, 51.3, 49.5, 48.5, 44.6, 41.9, 38.9, 36.5, 27.8, 27.7, 27.5, 26.6, 26.5, 19.0, 18.9, -3.9, -4.0, -4.1, -4.2.

IR (KBr):

υ (cm-1) = 2985 (s), 2953 (s), 2930 (s), 2857 (s), 1652 (s, N-CO), 1472 (s), 1452 (s), 1432 (m), 1379 (s), 1369 (s), 1254 (s, C-O), 1209 (s), 1165 (s), 1056 (s).

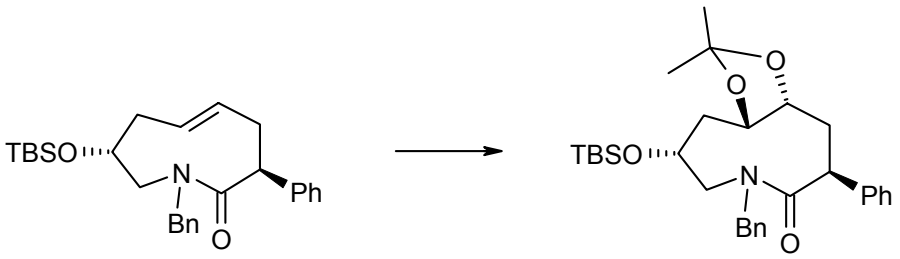
MS (80eV, EI, 130 °C):

m/z (%): 467 (2) [$M^{+\cdot}$], 452 (3) [M^{+} - CH_3], 431 (1) [M^{+} -HCl], 410 (9) [M^{+} -C_4H_9], 316 (1), 373 (3), 352 (16), 277 (5), 242 (13), 91 (100) 73 (4).

HRMS (80eV,120 °C): found 467.22934 calc. 467.225865 (for $C_{24}H_{38}N_1O_4Si_1Cl_1$ [$M^{+\cdot}$]).

[289] The ^{1}H- and ^{13}C-NMR spectra of **[45b]** showed an unseparated mixture of at least two conformers at room temperature (very broad lines). At 233 K two discrete conformers appeared. NOE experiments indicated a fast interconversion of both species (flexible amide geometry?).

3*S*,5*R*,6*R*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-5,6-isopropylidendioxy-3-phenylazonan-2-one [46a]



[13a] 435.69 [$C_{27}H_{37}NO_2Si$] **[46a]** 509.77 [$C_{30}H_{43}NO_4Si$]

Reaction of ***pS*-[13a]** (0.35g, 0.803 mmol) with 1.3 eq of sodium periodate and 4.2 mol% $RuCl_3$ in a mixture of acetonitrile and ethyl acetate (18 mL, 1:1) was performed according to the standard dihydroxylation procedure. After standard workup, the brown oil was dissolved in acetone and 4 eq. of dimethoxypropane and 10 mg of p-TsOH were added. After 3 h at room temperature and standard workup conditions, the crude reactions product was purified using column chromatography (eluent ethyl acetate / n-hexane 1:3, R_f 0.48) to yield 0.39 g (95.2%) **[46a]** as a colourless oil.

$[\alpha]_D^{20}$ = - 85.15° (c = 1.32, $CHCl_3$).

^{1}H-NMR (270 MHz, CD_2Cl_2):

7.50 - 7.40 (m, 2H; H-o-Ph), 7.40 - 7.10 (m, 8H; H-arom), 5.10 - 5.00 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 14 Hz), 4.35 - 4.25 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 12.7 Hz, ^3J (H^{3u},H^{4u}) = 5 Hz), 4.20 - 4.10 (m, 2H; H-8o, 6u), 4.10 - 4.00 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 14 Hz), 3.72 - 3.60 (dd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 15.6 Hz, ^3J (H^{9u},H^{8o}) = 8 Hz), 3.81 - 3.72 (ddd, 1H; H-5o; ^3J (H^{5o},H^{6o}) = 11 Hz, ^3J (H^{5o},H^{4u}) = 8 Hz, ^3J (H^{5o},H^{4o}) = 5 Hz), 3.42 - 3.35 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 15.6 Hz, ^3J (H^{9o},H^{8o}) = 6 Hz), 2.82 - 2.70 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 12.7 Hz, ^3J (H^{4o},H^{3u}) = 12.7 Hz, ^3J (H^{4o},H^{5o}) = 5 Hz), 2.25 - 2.15 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 16 Hz, ^3J (H^{7u},H) = 6 Hz, ^3J (H^{7u},H) = 2 Hz), 1.98 - 1.85 (m, 2H; H-4u, 7o) = Hz), 1.35 (s, 3H; H-O-C(CH_3)$_2$), 1.34 (s, 3H; H-O-C(CH_3)$_2$), 0.83 (s, 9H; H-Si-C(CH_3)$_3$), 0.08 (s, 3H; H-Si-CH_3), - 0.00 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, CD_2Cl_2):

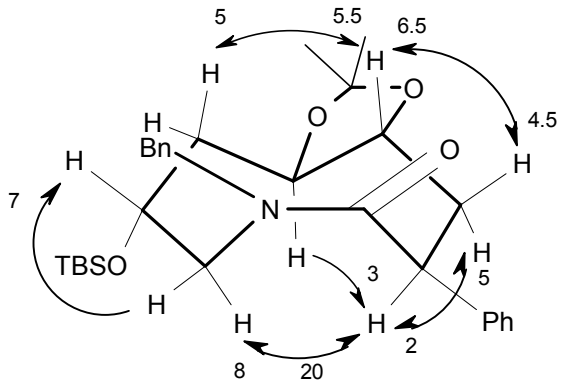
174.2 (s, C=O), 140.4 (s), 137.7 (s), 129.2 (d), 128.9 (d), 128.8 (d), 128.6 (d), 128.2 (d), 127.7 (d), 107.8 (s), 81.1 (d), 75.7 (d), 68.0 (d, C-8), 54.6 (t), 50.4 (t), 42.2 (d), 41.5 (t), 38.5 (t), 27.0 (q), 26.9 (q), 26.1 (q, Si-C(CH_3)$_3$), 18.5 (s, Si-C(CH_3)$_3$), - 4.5 (q, Si-CH_3), -4.6 (q, Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 2984 (s), 2929 (s), 2885 (s), 2855 (s), 1649 (s, N-CO), 1495 (m), 1471 (m), 1453 (m), 1379 (m), 1253 (m, C-O), 1209 (s), 1096 (s), 1057 (s), 1028 (s), 838 (s).

MS (80eV, EI, 120 °C):

m/z (%): 509 (15) [$M^{+\cdot}$], 494 (16) [M^+ - CH_3], 451 (38) [M^+ -C_3H_6O], 436 (8), 394 (100) [M^+ - C_4H_9 - C_3H_6O], 319 (63), 252 (43), 197 (75), 91 (62) 73 (35).

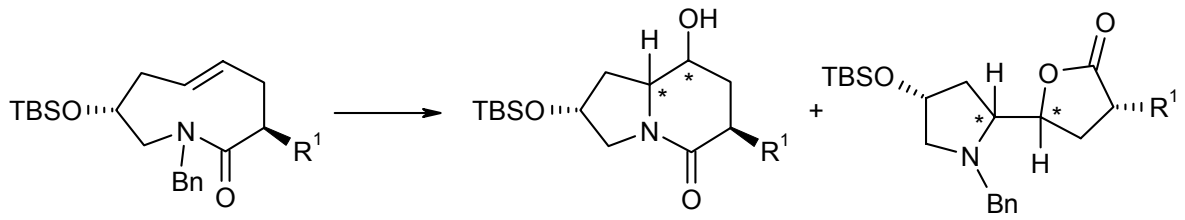


HRMS (80eV,120 °C): found 509.29627

calc. 509.296140 (for $C_{30}H_{43}NO_4Si$).

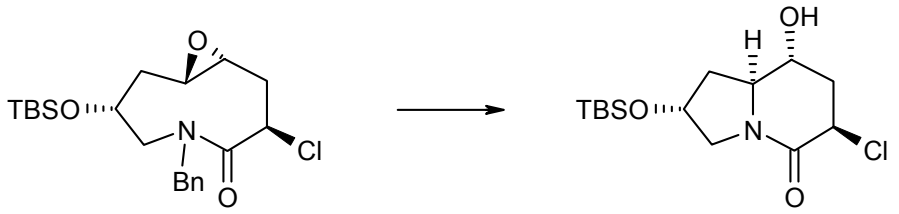
3.8 Synthesis of Hydroxy Indolizidinones by Ring Opening Reactions of Epoxy Azonanones

Standard Procedure for Lewis Acid Mediated Transannular Epoxide Opening



The epoxy azonanones (1 mol equiv), dissolved in $CHCl_3$ (10 mL), were treated with anhydrous LiI (1.2 equiv) and TMSI (1.3 equiv) at room temperature. After max. 5 min of vigorous stirring, the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ and 10% aqueous $Na_2S_2O_3$ (3:1); after a few minutes, a clear colourless solution was obtained. The aqueous layer was extracted two times with diethyl ether, after drying (Na_2SO_4) and removal of the solvent, the crude indolizidinones **[47]** - **[54]** and lactones **[48]**, **[50]**, **[52]**, **[55]** were purified by column chromatography or by HPLC.

3*R*,5*R*,6*S*,8*R*-3-Chloro-5-hydroxy-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [47-1]



[35a] 410.03 [$C_{21}H_{32}ClNO_3Si$] **[47-1]** 319.91 [$C_{14}H_{26}ClNO_3Si$]

Reaction with **[35a]** (0.5 g, 1.22 mmol) , anhydrous LiI (1.2 eq) and TMSI (1.2 equiv) followed the standard transannular epoxide opening procedure. Reaction time was kept <90 s to avoid most of the chlorine - iodine exchange (in some attempts up to 10% of 6-iodo compounds were detected by NMR spectroscopy and MS). Chromatography (ethyl acetate / n-hexane = 1:1, R_f = 0.15) yielded 124 mg (0.39 mmol, 32%) of **[47-1]** as colourless crystals with mp = 152 °C.

$[\alpha]_D^{20}$ = - 61.98° (c = 1.92, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):[290]

4.55 - 4.50 (dd, 1H; H-3u; ^{3}J (H^{3u},H^{4o}) = 5 Hz, ^{3}J (H^{3u},H^{4u}) = 2 Hz), 4.48 - 4.42 (dd, 1H; H-8o; ^{3}J (H^{8o},H) = 12.8 Hz, ^{3}J (H^{8o},H) = 12.8 Hz), 4.10 - 3.96 (ddd, 1H; H-5o; ^{3}J (H^{5o},H) = 14 Hz, ^{3}J (H^{5o},H) = 8.8 Hz, ^{3}J (H^{5o},H) = 4 Hz), 3.81 - 3.72 (dd, 1H; H-9o; ^{2}J (H^{9o},H^{9u}) = 13.6 Hz, ^{3}J (H^{9o},H^{8o}) = 5 Hz), 3.72 - 3.62 (m, 1H; H-6u), 3.40 - 3.33 (d, 1H; H-9u; ^{2}J (H^{9u},H^{9o}) = 13.6 Hz), 3.10 - 3.05 (s, 1H; H-OH), 2.51 - 2.42 (ddd, 1H; H-4o; ^{2}J (H^{4o},H^{4u}) = 14 Hz, ^{3}J (H^{4o},H^{3u}) = 4 Hz, ^{3}J (H^{4o},H^{5o}) = 2 Hz), 2.40 - 2.20 (m, 2H; H-4u, 7u), 1.73 - 1.61 (ddd, 1H; H-7o; ^{2}J (H^{7o},H^{7u}) = 12 Hz, ^{3}J (H^{7o},H^{6u}) = 12 Hz, ^{3}J (H^{7o},H^{8o}) = 4 Hz), 0.90 (s, 9H; H-Si (CMe_3)), 0.01 (s, 6H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

164.4 (s, C=O), 68.6 (d), 66.9 (d), 62.2 (d), 56.3 (t), 53.7 (d), 41.3 (t), 40.2 (t), 25.7 (q, Si-$C(CH_3)_3$), 17.9 (s, Si-$C(CH_3)_3$), -4.8 (q, Si-CH_3), - 4.9 (q, Si-CH_3).

IR (KBr):

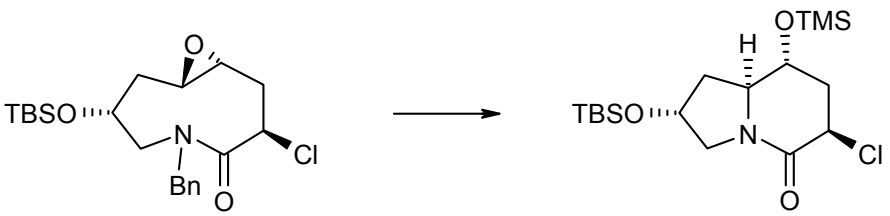
υ (cm^{-1}) = 3319 (s, broad, OH), 2956 (s), 2929 (s), 2856 (s), 1629 (s, N-CO), 1472 (s), 1274 (s), 1258 (m, C-O), 1094 (m), 1078 (m), 1024 (s), 837 (s).

MS (70eV, EI, 140 °C): [290]

m/z (%): 304 (3) [M^+- CH_3], 262 (100) [M^+- C_4H_9], 228 (10), 186 (5), 116 (5).

HRMS (80eV,130 °C): found 304.11690 calc. 304.113575 (for $C_{13}H_{23}NO_3Si_1Cl_1$ [M^+-CH_3]).

3*R*,5*R*,6*S*,8*R*-3-Chloro-5-(trimethylsilyloxy)-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [47-2]



[35a] 410.03 [$C_{21}H_{32}ClNO_3Si$] **[47-2]** 392.09 [$C_{17}H_{34}ClNO_3Si_2$]

Reaction with **[35a]** (0.15 g, 0.37 mmol) and TMSI (1 equiv) followed the standard transannular epoxide opening procedure. Reaction time was kept <90 s to avoid most of the chlorine - iodine

[290] ^{1}H-NMR and MS showed the presence of a minor compound, presumably the iodo-exchange product (~10%)

exchange. Chromatography (ethyl acetate / n-hexane = 2:1, R_f = 0.38) yielded 67 mg (0.17 mmol, 47%) of **[47-2]** as colourless oil.

$[\alpha]_D^{20}$ = - 38.075° (c = 1.663, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

4.50 – 4.45 (dd, 1H; H-3u; ^3J (H^{3u},H^{4u}) = 4 Hz, ^3J (H^{3u},H^{4o}) = 4 Hz), 4.42 – 4.35 (dd, 1H; H-8o; ^3J (H^{8o},H^{7u}) = 4 Hz, ^3J (H^{8o},H^{9o}) = 4 Hz), 3.97 – 3.87 (ddd, 1H; H-5o; ^3J (H^{5o},H^{6u}) = 8 Hz, ^3J (H^{5o},H^{4o}) = 8 Hz, ^3J (H^{5o},H^{4u}) = 8 Hz), 3.78 – 3.70 (dd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 13 Hz, ^3J (H^{9o},H^{8o}) = 4 Hz), 3.73 – 3.60 (ddd, 1H; H-6u,; ^2J (H^{6u},H^{7o}) = 12 Hz, ^2J (H^{6u},H^{5o}) = 9 Hz, ^2J (H^{6u},H^{7u}) = 4 Hz), 3.35 – 3.30 (d, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 13 Hz), 2.30 – 2.25 (m, 2H; H-4o, 4u), 2.15 – 2.05 (dd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 12.5 Hz, ^3J (H^{7u},H^{8o}) = 4 Hz), 1.60 – 1.48 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 12 Hz, ^3J (H^{7o},H^{6u}) = 12 Hz, ^3J (H^{7o},H^{8o}) = 4 Hz), 0.83 (s, 9H; H-Si-C(CH_3)$_3$), 0.13 (s, 9H; H-Si (CH_3)$_3$), 0.03 (s, 3H; H-Si-CH_3), 0.02 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

164.1 (q, C=O), 68.5 (d), 67.6 (d), 62.2 (d), 56.3 (t), 53.9 (d), 41.5 (t), 40.8 (t), 25.7 (q, Si-C(CH_3)$_3$), 17.9 (s, Si-C(CH_3)$_3$), 0.0 (q, Si (CH_3)$_3$), - 4.5 (q, Si-CH_3).

IR (KBr):

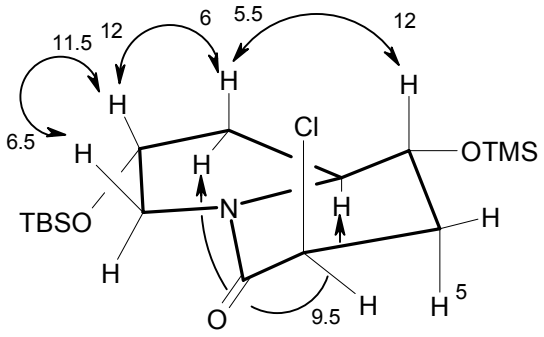
υ (cm^{-1}) = 2955 (s), 2928 (s), 2895 (s), 2857 (s), 1664 (s, CO), 1449 (s), 1356 (m), 1253 (m), 1130 (m), 1099 (m), 1024 (m), 888 (s), 841 (s).

MS (70eV, EI, 90 °C):

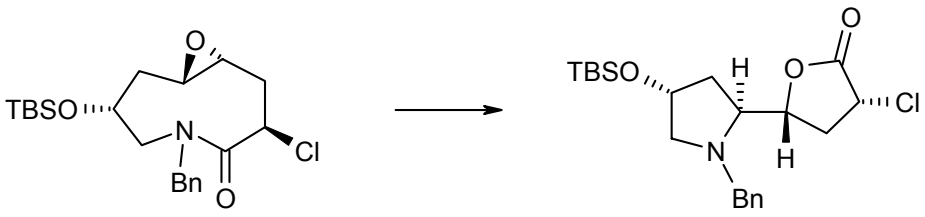
m/z (%): 391 (0.1) [M^+- H^+], 376 (8) [M^+ - CH_3], 356 (1) [M^+ - Cl], 334 (100) [M^+ - C_4H_9].

HRMS (80eV,90 °C): found 376.15301

calc. 376.15310 (for $C_{16}H_{31}NO_3Si_2Cl_1$ [M^+ -CH_3]).



3*R*,5*R*,5-(1*S*,4*R*-2-Benzyl-4 (*tert*-butyldimethylsilyloxy)-2-pyrrolidinyl)-3-chloro-3,4,5-trihydro-furan-2-one [48]



[35a] 410.03 [$C_{21}H_{32}ClNO_3Si$] **[48]** 410.03 [$C_{21}H_{32}ClNO_3Si$]

All tests for the lewis-acid mediated oxirane opening showed the formation of lactones. When less active silyl halogenides (TMSBr, TMSCl) were used during the oxirane opening without addition of LiI, the amount of formed lactones was substantially higher.

In an analytical test, oxirane **[35a]** was dissolved in dichloromethane and 2 eq of TMSCl were added at room temperature. After stirring for 2 h and workup according to the standard epoxidation procedure, the complete rearrangement of **[35a]** into **[48]** could be detected via ^{1}H- and ^{13}C-NMR spectroscopy.[291]

$[\alpha]_D^{20}$ = - 22.47° (c = 1.455, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.40 - 7.20 (m, 10H; H-arom), 4.60 - 4.50 (dd, 1H; H-3u; ^{3}J (H^{3u},H^{4o}) = 11 Hz, ^{3}J (H^{3u},H^{4u}) = 9 Hz), 4.45 - 4.35 (ddd, 1H; H-5; ^{3}J (H^{5},H^{4o}) = 10 Hz, ^{3}J (H^{5},H^{4u}) = 5 Hz, ^{3}J (H^{5},H^{6}) = 4 Hz), 4.35 - 4.28 (m, 1H; H-8o), 4.30 - 4.23 (d, 1H; H-N-Bn1; ^{2}J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 13.7 Hz), 3.70 - 3.65 (d, 1H; H-N-Bn2; ^{2}J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 13.7 Hz), 3.45 - 3.35 (ddd, 1H; H-6u; ^{3}J (H^{6u},H^{7o}) = 8 Hz, ^{3}J (H^{6u},H^{7u}) = 8 Hz, ^{3}J (H^{6u},H^{5}) = 4 Hz), 3.08 - 3.00 (dd, 1H; H-9o; ^{2}J (H^{9o},H^{9u}) = 11 Hz, ^{3}J (H^{9o},H^{8o}) = 5 Hz), 2.84 - 2.74 (ddd, 1H; H-4u; ^{2}J (H^{4u},H^{4o}) = 12.7 Hz, ^{3}J (H^{4u},H^{3u}) = 9 Hz, ^{3}J (H^{4u},H^{5}) = 5 Hz), 2.52 - 2.38 (m, 2H; H-9u, 4o), 2.00 - 1.90 (ddd, 1H; H-7u; ^{2}J (H^{7u},H^{7o}) = 12.7 Hz, ^{3}J (H^{7u},H) = 8 Hz, ^{3}J (H^{7u},H) = 4 Hz), 1.80 - 1.70 (m, 1H; H-7o), 0.90 (s, 9H; H-Si (CMe_3)), 0.06 (s, 3H; H-Si-CH_3), 0.04 (s, 3H; H-Si-CH_3).

^{13}C-NMR (62.9 MHz, $CDCl_3$):

171.9 (s, CO), 139.3 (s), 128.6 (d), 128.3 (d), 127.0 (d), 80.0 (d), 71.0 (d), 64.0 (d), 62.2 (t), 61.5 (t), 51.5 (d), 36.9 (t), 34.8 (t), 25.7 (Si-C(CH_3)$_3$), 17.9 (Si-C(CH_3)$_3$), - 4.8 (Si-CH_3).

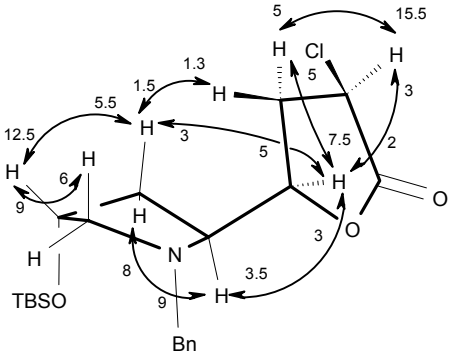
[291] In some cases an identical transformation was observed when the epoxides were purified by column chromatography.

IR (KBr):

υ (cm^{-1}) = 2953 (s), 2928 (s), 2885 (s), 2856 (m), 1787 (s, N-CO), 1494 (m), 1462 (m), 1471 (m), 1453 (m), 1387 (m), 1361 (m), 1255 (m, C-O), 1184 (m), 1116 (m).

MS (70eV, EI, 130 °C):

m/z (%): 409 (1) [$M^{+\cdot}$], 394 (1) [M^{+}- CH_3], 352 (1) [M^{+} - C_4H_9], 290 (100) [$M^{+\cdot}$- $C_4H_4Cl_1O_2$], 226 (5), 158 (4), 91 (36).

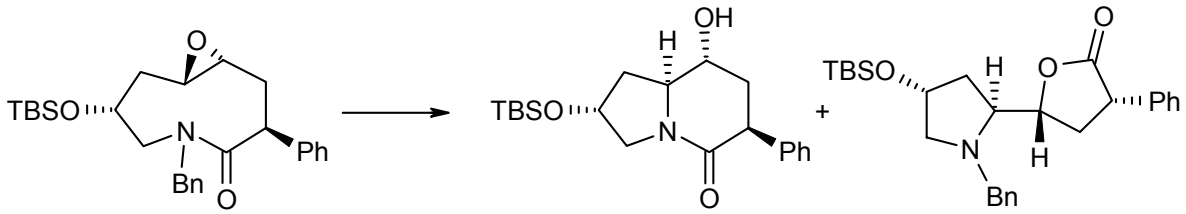


HRMS (80eV,130 °C): found 409.18533

calc. 409.1840 (for $C_{21}H_{32}N_1O_3Si_1Cl_1$ [M^{+}]).

3*S*,5*R*,6*S*,8*R*-3-Phenyl-5-hydroxy-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [49] and

3*S*,5*R*,5-(1*S*,4*R*-2-Benzyl-4 (*tert*-butyldimethylsilyloxy)-2-pyrrolidinyl)-3-phenyl-3,4,5-trihydro-furan-2-one [50]



[36a] 451.69 [$C_{27}H_{37}NO_3Si$] **[49]** 361.56 [$C_{20}H_{31}NO_3Si$] **[50]** 451.69 [$C_{27}H_{37}NO_3Si$]

Reaction with **[36a]** (1.1 g, 2.44 mmol), TMSI (1.1 equiv) followed the standard transannular epoxide opening procedure. Chromatography (gradient ethyl acetate / n-hexane = 1:3 to ethyl acetate, R_f = 0.28) yielded 530 mg (1.47 mmol, 60%) of **[49]** (recrystallised from n-hexane/ diethyl ether = 3:1, first fraction: 250 mg, 0.69 mmol, 28.3%) and 170 mg (0.38 mmol, 15.4%) of **[50]** as a colourless oil.

indolizidinone [49] :

Colourless crystals with mp = 143 - 145 °C

$[\alpha]_D^{20}$ = - 60.75° (c = 1.98, $CHCl_3$).

^{1}H-NMR (270 MHz, CD_2Cl_2):

7.30 - 7.15 (m, 3H; H-p-,m-arom.), 7.10- 7.00 (m, 2H; H-o-arom), 4.45 - 4.40 (dd, 1H; H-8o; ^{3}J (H^{8o},H^{7u}) = 5 Hz, ^{3}J (H^{8o},H^{9o}) = 5 Hz), 3.80 - 3.68 (dd, 1H; H-9o; ^{2}J (H^{9o},H^{9u}) = 13 Hz, ^{3}J (H^{9o},H^{8o}) = 5 Hz), 3.70 - 3.55 (m, 3H; H-6u, 3u, 5o), 3.42 - 3.35 (s, broad, 1H; OH), 3.35 - 3.30 (d, 1H; H-9u; ^{2}J (H^{9u},H^{9o}) = 13 Hz), 2.25 - 2.15 (dd, 1H; H-7u; ^{2}J (H^{7u},H^{7o}) = 12.7 Hz, ^{3}J (H^{7u},H) = 4 Hz), 2.10 - 2.00 (m, 2H; H-4o, 4u), 1.62 - 1.50 (ddd, 1H; H-7o; ^{2}J (H^{7o},H^{7u}) = 12.7 Hz, ^{3}J (H^{7o},H^{6u}) = 10.7 Hz, ^{3}J (H^{7o},H^{8o}) = 4 Hz), 0.89 (s, 9H; H-Si-C(CH_3)$_3$), -0.09 (s, 6H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, CD_2Cl_2):

169.6 (s, C=O), 142.8 (s), 128.9 (d), 128.8 (d), 127.1 (d), 69.7 (d), 68.2 (d), 62.3 (d), 56.1 (t), 46.8 (d), 42.1 (t), 39.4 (t), 26.1 (Si-C(CH_3)$_3$), 18.5 (Si-C(CH_3)$_3$), - 4.5 (Si-CH_3), -4.6 (Si-CH_3).

IR (KBr):

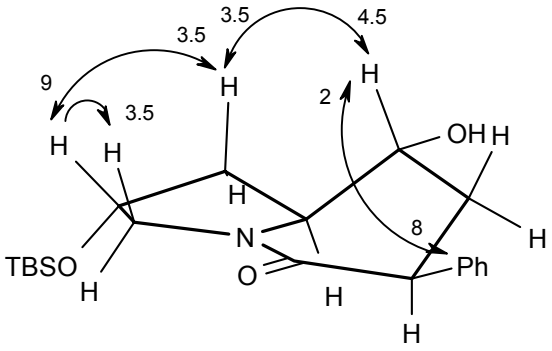
υ (cm^{-1}) = 3307 (s, broad), 2955 (s), 2928 (s), 2885 (m), 2856 (s), 1613 (s, N-CO), 1450 (s), 1278 (m), 1257 (m, C-O), 1128 (m), 1095 (m), 1072 (m), 1024 (m), 836 (s), 776 (s).

MS (70eV, EI, 100 °C):

m/z (%): 360 (0.1) [M^+ -H^+], 346 (4) [M^+- CH_3], 304 (100) [M^+ - C_4H_9], 286 (13), 258 (29), 116 (11).

HRMS (80eV,100 °C): found 346.18722

calc. 346.183847 (for $C_{19}H_{28}NO_3Si$ [M^+ - CH_3]).



lactone [50] :

$[\alpha]_D^{20}$ = - 25.83° (c = 1.916, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.40 - 7.20 (m, 10H; H-arom), 4.55 - 4.48 (ddd, 1H; H-5o; ^{3}J (H^{5o},H^{4o}) = 10 Hz, ^{3}J (H^{5o},H^{4o}) = 5 Hz, ^{3}J (H^{5o},H) = 4 Hz), 4.35 - 4.28 (m, 1H; H-8o), 4.16 - 4.10 (d, 1H; H-N-Bn1; ^{2}J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 13 Hz), 3.92 - 3.83 (dd, 1H; H-3o; ^{3}J (H^{3o},H^{4u}) = 12.7 Hz, ^{3}J (H^{3o},H^{4o}) = 9 Hz), 3.50 - 3.40 (ddd, 1H; H-6u; ^{3}J (H^{6u},H) = 8 Hz, ^{3}J (H^{6u},H) = 8 Hz, ^{3}J (H^{6u},H) = 4 Hz), 3.13 - 3.07 (dd, 1H; H-9u; ^{2}J (H^{9u},H^{9o}) = 10 Hz, ^{3}J (H^{9u},H^{8o}) = 5 Hz), 2.70 - 2.60 (ddd, 1H; H-4o; ^{2}J (H^{4o},H^{4u}) = 12.7 Hz, ^{3}J (H^{4o},H^{3o}) = 9 Hz, ^{3}J (H^{4o},H^{4o}) = 6 Hz), 2.50 - 2.42 (dd, 1H; H-9o; ^{2}J (H^{9o},H^{9u}) = 10 Hz, ^{3}J (H^{9o},H^{8o}) = 6 Hz), 2.45 - 2.35 (ddd, 1H; H-4u; ^{2}J (H^{4u},H^{4o}) = 12.7 Hz, ^{3}J (H^{4u},H^{3o}) = 12.7 Hz, ^{3}J (H^{4u},H^{5o}) = 11 Hz), 2.05 - 1.95 (ddd,

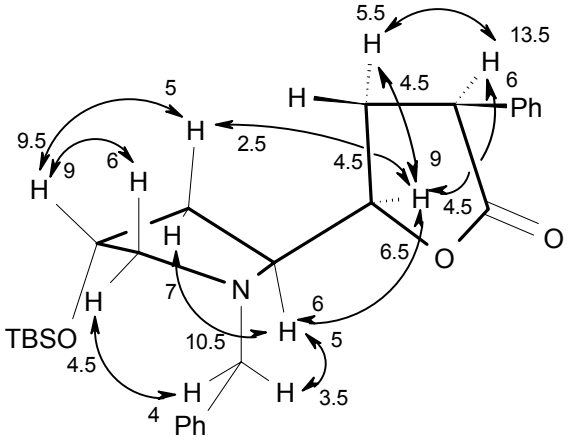
1H; H-7u; ^{2}J (H^{7u},H^{7o}) = 13 Hz, ^{3}J (H^{7u},H) = 8 Hz, ^{3}J (H^{7u},H) = 4 Hz), 1.90 - 1.80 (ddd, 1H; H-7o; ^{2}J (H^{7o},H^{7u}) = 13 Hz, ^{3}J (H^{7o},H) = 7 Hz, ^{3}J (H^{7o},H^{8o}) = 7 Hz), 0.90 (s, 9H; H-Si (CMe_3), 0.06 (s, 3H; H-Si-CH_3), 0.04 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
176.6 (s, C=O), 139.8 (s), 136.7 (s), 128.8 (d), 128.5 (d), 128.2 (d), 128.1 (d), 127.5 (d), 126.8 (d), 80.5 (d), 70.9 (d), 64.0 (d), 62.4 (t), 61.3 (t), 47.0 (d), 37.0 (t), 33.7 (t), 25.7 (q, Si-C(CH_3)$_3$), 17.9 (s, Si-C(CH_3)$_3$), - 4.8 (q, Si-CH_3).

IR (KBr):
υ (cm^{-1}) = 2953 (s), 2927 (s), 2855 (s), 1773 (s, CO), 1495 (m), 1471 (m), 1453 (m), 1388 (m), 1361 (m), 1253 (m, C-O), 1160 (m), 1019 (m), 837 (m).

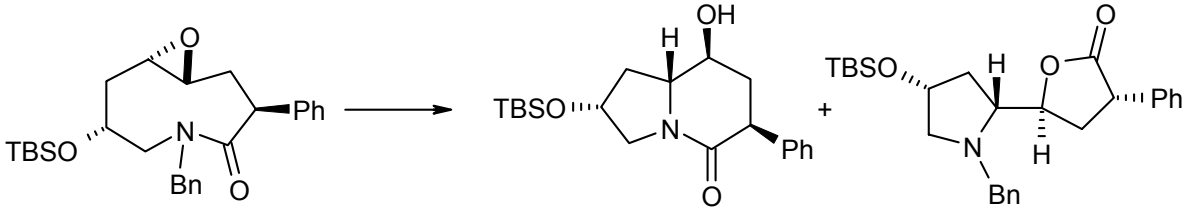
MS (80eV, EI, 130 °C):
m/z (%): 451 (0.4) [$M^{+\cdot}$], 436 (1.2) [M^{+}- CH_3], 394 (0.65) [M^{+} - C_4H_9], 376 (0.3), 352 (0.5), 290 (100), 91 (15), 75 (8).

HRMS (80eV,130 °C): found 451.25921
calc. 451.254273 (for $C_{27}H_{37}NO_3Si$ [M^{+}]).



3*S*,5*S*,6*R*,8*R*-3-Phenyl-5-hydroxy-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [51] and

3*S*,5S,5-(1*R*,4*R*-2-Benzyl-4 (*tert*-butyldimethylsilyloxy)-2-pyrrolidinyl)-3-phenyl-3,4,5-trihydro-furan-2-one [52]



[36b] 451.69 [$C_{27}H_{37}NO_3Si$] **[51]** 361.56 [$C_{20}H_{31}NO_3Si$] **[52]** 451.69 [$C_{27}H_{37}NO_3Si$]

Reaction with **[36b]** (160 mg, 0.35 mmol) followed the standard transannular epoxide opening procedure. Chromatography (ethyl acetate / n-hexane = 1:1, R_f = 0.13) yielded 41 mg (0.11 mmol, 32%) of **[51]** as colourless crystals (mp 170 - 178 °C) and 21 mg (18%) of **[52]** as colourless oil.

$[\alpha]_D^{20}$ = + 37.21° (c = 1.94, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
7.50 - 7.20 (m, 5H; H-arom), 4.41 - 4.31 (m, 1H; H-8o), 3.60 - 3.40 (m, 5H; H-5u, 3u, 9u, 9o, 6o), 2.42 - 2.32 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 12 Hz, ^3J (H^{7o},H^{8o}) = 6 Hz, ^3J (H^{7o},H^{6o}) = 6 Hz), 2.22 - 2.12 (m, 1H; H-4u), 1.85 - 1.75 (dd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 11 Hz, ^3J (H^{4o},H) = 11 Hz, ^3J (H^{4o},H) = 2 Hz), 1.71 - 1.61 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 12 Hz, ^3J (H^{7u},H) = 11 Hz, ^3J (H^{7u},H) = 8 Hz), 0.90 (s, 9H; H-Si (CMe_3)), 0.01 (s, 3H; H-Si-CH_3), 0.00 (s, 3H; H-Si-CH_3).

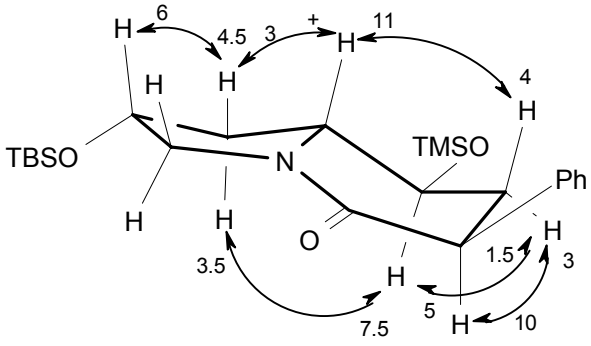
^{13}C-NMR (67.9 MHz, $CDCl_3$):
169.2 (s, C=O), 141.0 (s), 128.5 (d), 128.1 (d), 126.7 (d), 70.2 (d), 69.2 (d), 62.5 (d), 53.5 (t), 47.7 (d), 40.3 (t), 40.2 (t), 25.7 (q, Si-C(CH_3)$_3$), 17.9 (s, Si-C(CH_3)$_3$), - 4.9 (q, Si-CH_3).

IR (KBr):
υ (cm^{-1}) = 3442 (s), 2956 (s), 2929 (s), 2895 (m), 2857 (s), 1616 (s, N-CO), 1465 (s), 1445 (s), 1260 (s, C-O), 1235 (m), 1101 (m), 1070 (m), 836 (m).

MS (80eV, EI, 140 °C):
m/z (%): 361 (0.1) [M^+], 346 (2) [M^+ - CH_3], 304 (100) [M^+ - C_4H_9], 200 (3), 176 (5), 118 (5).

HRMS (80eV,140 °C): found 346.18634
calc. 346.183847 (for $C_{19}H_{28}NO_3Si_1$ [M-CH_3]).

NOE measurement of the TMS protected **[51]**

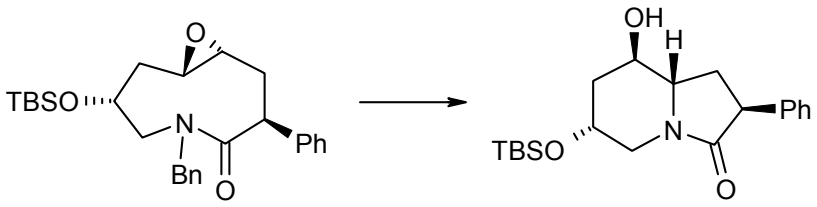


lactone [52]

^{1}H-NMR (270 MHz, $CDCl_3$) :

4.82 - 4.73 (ddd, 1H; H-5; $^3J(H^5,H)$=7.5 Hz, $^3J(H^5,H)$=5 Hz, $^3J(H^5,H)$=5 Hz), 4.37 - 4.30 (m, 1H; H-8o), 4.18 - 4.11 (d, 1H; H-N-Bn1; $^2J(H^{N\text{-}Bn1},H^{N\text{-}Bn2})$=14 Hz), 4.08 - 4.01 (dd, 1H; H-3u; $^3J(H^{3u},H^{4o})$=9.5 Hz, $^3J(H^{3u},H^{4u})$=7.5 Hz), 3.57 - 3.51 (d, 1H; H-N-Bn2; $^2J(H^{N\text{-}Bn2},H^{N\text{-}Bn1})$=14 Hz), 3.30 - 3.21 (ddd, 1H; H-6o; $^3J(H^{6o},H^{5u})$=9 Hz, $^3J(H^{6o},H^{7u})$=4 Hz, $^3J(H^{6o},H^{7o})$=4 Hz), 3.15 - 3.02 (ddd, 1H; H-4u; $^2J(H^{4u},H^4)$=12.5 Hz, $^3J(H^{4u},H^{5u})$=10 Hz, $^3J(H^{4u},H^{3u})$=4.5 Hz), 2.99 - 2.92 (ddd, 1H; H-9o; $^2J(H^{9o},H^{9u})$=10.5 Hz, $^3J(H^{9o},H^{8o})$=1.5 Hz, $^4J(H^{9o},H^{N\text{-}Bn1})$=1.5 Hz), 2.58 - 2.51 (dd, 1H; H-9u; $^2J(H^{9u},H^{9o})$=10.5 Hz, $^3J(H^{9u},H^{8o})$=4.5 Hz), 2.45 - 2.33 (ddd, 1H; H-4o; $^2J(H^{4o},H^{4u})$=13 Hz, $^3J(H^{4o},H^5)$=13 Hz, $^3J(H^{4o},H^{3u})$=7.5 Hz), 2.32 - 2.19 (m, 1H; H-7), 1.75 - 1.65 (m, 1H; H-7'), 0.87 (s, 9H; H-Si (CMe_3)), 0.05 (s, 3H; H-Si-CH_3), 0.01 (s, 3H; H-Si-CH_3).

3*R*,5*R*,6*S*,8*S*-3-(*tert*-Butyldimethylsilyloxy)-5-hydroxy-8-phenyl-1-azabicyclo[4.3.0]nonan-9-one [53]



[36a] 451.69 [$C_{27}H_{37}NO_3Si$] **[53]** 361.56 [$C_{20}H_{31}NO_3Si$]

Reaction with epoxy azonanone **[36a]** (190 mg, 0.42 mmol) and LiI (1.2 equiv) proceeded with fast addition of TMSI (1.2 equiv) at -10 °C. After 3 min reaction time, workup was performed following the standard transannular epoxide opening procedure. Chromatography (ethyl acetate / n-hexane = 1:3, R_f = 0.1) yielded 29 mg (0.08 mmol, 19%) of **[53]** as colourless crystals (mp 145 °C).

$[\alpha]_D^{20}$ = - 39.39° (c = 1.485, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.50 - 7.20 (m, 5H; H-arom), 4.10 - 4.08 (m, 1H; H-8o), 4.03 - 3.98 (d, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 13 Hz), 3.82 - 3.70 (ddd, 1H; H-6u; ^3J (H^{6u},H^{5o}) = 10 Hz, ^3J (H^{6u},H^{7o}) = 10 Hz, ^3J (H^{6u},H^{7u}) = 4 Hz), 3.70 - 3.60 (dd, 1H; H-3u; ^3J (H^{3u},H^{4u}) = 10 Hz, ^3J (H^{3u},H^{4o}) = 8 Hz), 3.32 - 3.23 (ddd, 1H; H-5o; ^3J (H^{5o},H^{6u}) = 12 Hz, ^3J (H^{5o},H^{4o}) = 8 Hz, ^3J (H^{5o},H^{4u}) = 4 Hz), 2.78 - 2.72 (d, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 13 Hz), 2.67 - 2.60 (s, 1H; H-OH), 2.52 - 2.40 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 13.6 Hz, ^3J (H^{4u},H^{3u}) = 10

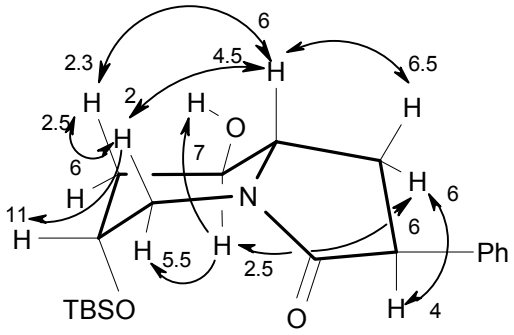
Hz, ^{3}J (H^{4u},H^{5o}) = 4 Hz), 2.30 - 2.20 (ddd, 1H; H-4o; ^{2}J (H^{4o},H^{4u}) = 13.6 Hz, ^{3}J (H^{4o},H^{3u}) = 8 Hz, ^{3}J (H^{4o},H^{5o}) = 8 Hz), 2.15 - 2.05 (m, 1H; H-7u), 1.52 - 1.42 (ddd, 1H; H-7o; ^{2}J (H^{7o},H^{7u}) = 13 Hz, ^{3}J (H^{7o},H^{6u}) = 12 Hz, ^{3}J (H^{7o},H^{8o}) = 2 Hz), 0.90 (s, 9H; H-Si (CMe_3)), 0.01 (s, 3H; H-Si-CH_3), 0.00 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
174.4 (s, C=O), 140.3 (s), 128.6 (d), 127.8 (d), 126.8 (d), 67.4 (d), 66.3 (d), 61.3 (d), 46.9 (d), 46.4 (t), 40.8 (t), 31.4 (t), 25.7 (q, Si-C(CH_3)$_3$), 17.9 (s, Si-C(CH_3)$_3$), -4.98 (q, Si-CH_3), -5.13 (q, Si-CH_3).

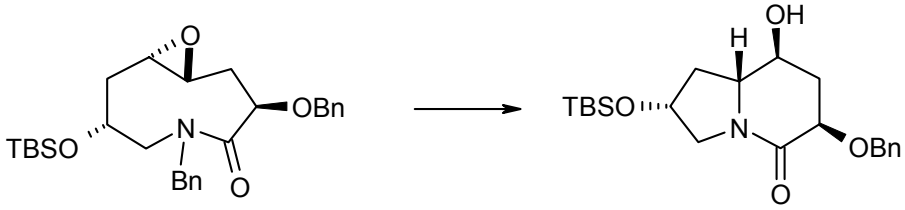
IR (KBr):
υ (cm^{-1}) = 3312 (s, broad, OH), 2954 (s), 2926 (s), 2852 (s), 1652 (s, N-CO), 1473 (s), 1463 (s), 1255 (s, C-O), 1078 (s), 1039 (s), 839 (s), 774 (s).

MS (80eV, EI, 145 °C):
m/z (%): 361 (0.1) [$M^{+\cdot}$], 346 (2) [M^{+}- CH_3], 304 (100) [M^{+} - C_4H_9].

HRMS (80eV,140 °C): found 346.18588
calc. 346.183847 (for $C_{19}H_{28}NO_3Si_1$ [M-CH_3]).



3*R*,5*S*,6*R*,8*R*-3-Benzyloxy-5-hydroxy-8-(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.3.0]nonan-2-one [54]



[34b] 481.71 [$C_{28}H_{39}NO_4Si$] **[54]** 391.59 [$C_{21}H_{33}NO_4Si$]

Reaction with **[37b]** (2.8 g, 5.81 mmol) followed the standard transannular epoxide opening procedure. A reaction time <2 min was applied to avoid a cleavage of the benzylether. Chromatography (ethyl acetate / n-hexane = 1:1, R_f = 0.13) yielded 1.3 g (3.32 mmol, 57%) as colourless crystals (mp 140 - 143 °C).

$[\alpha]_D^{20}$ = + 69.84° (c = 1.93, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.40 - 7.20 (m, 5H; H-arom), 4.85 - 4.80 (d, 1H; H-OBn1; ^2J ($H^{H\text{-}OBn1}$,$H^{H\text{-}OBn2}$) = 12 Hz), 4.70 - 4.65 (d, 1H; H-OBn2; ^2J ($H^{H\text{-}OBn2}$,$H^{H\text{-}OBn1}$) = 12 Hz), 4.40 - 4.30 (m, 1H; H-8o), 4.00 - 3.95 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 7 Hz, ^3J (H^{3u},H^{4u}) = 5 Hz), 3.75 - 3.68 (ddd, 1H; H-5u; ^3J (H^{5u},H^{6o}) = 8 Hz, ^3J (H^{5u},H^{4o}) = 8 Hz, ^3J (H^{5u},H^{4u}) = 6 Hz), 3.60 - 3.50 (ddd, 1H; H-6o; ^3J (H^{6o},H^{5u}) = 8 Hz, ^3J (H^{6o},H^{7u}) = 8 Hz, ^3J (H^{6o},H^{7o}) = 8 Hz), 3.45 - 3.40 (m, 2H; H-9u, 9o), 3.00 - 2.80 (s, broad, 1H; OH), 2.45 - 2.35 (ddd, 1H; H-7o; ^2J (H^{7o},H^{7u}) = 12 Hz, ^3J (H^{7o},H^{6o}) = 6 Hz, ^3J (H^{7o},H^{8o}) = 6 Hz), 2.35 - 2.28 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 14 Hz, ^3J (H^{4u},H^{5u}) = 6 Hz, ^3J (H^{4u},H^{6}) = 6 Hz), 2.00 - 1.90 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 14 Hz, ^3J (H^{4o},H^{3u}) = 8 Hz, ^3J (H^{4o},H^{5u}) = 8 Hz), 1.82 - 1.70 (ddd, 1H; H-7u; ^2J (H^{7u},H^{7o}) = 13 Hz, ^3J (H^{7u},H^{6o}) = 8 Hz, ^3J (H^{7u},H^{8o}) = 7 Hz), 0.85 (s, 9H; H-Si (CMe_3)), 0.05 (s, 6H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

168.2 (s, C=O), 137.6 (s), 128.3 (d), 127.9 (d), 127.7 (d), 74.7 (d), 72.5 (t, C-OBn), 69.6 (d, C-8), 69.2 (d), 61.8 (d), 52.9 (t, C-9), 40.1 (t), 37.4 (t), 25.7 (q, Si-C(CH_3)$_3$), 17.9 (s, Si-C(CH_3)$_3$), -4.9 (q, Si-CH_3).

IR (KBr):

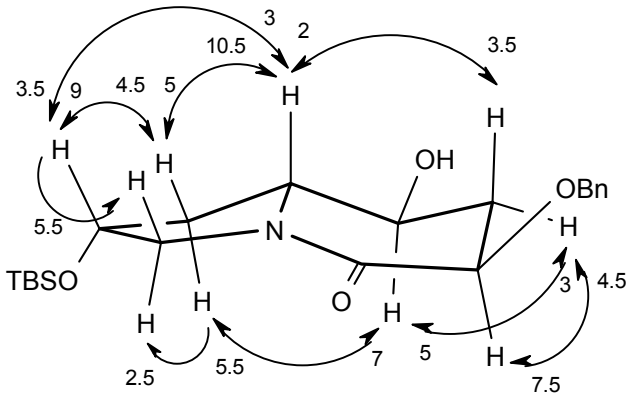
υ (cm^{-1}) = 3327 (s, broad), 2953 (s), 2928 (s), 2896 (s), 2856 (s), 1622 (s, N-CO), 1470 (m) 1454 (m), 1385 (m), 1359 (m), 1265 (m, C-O), 1251 (m), 1142 (m), 1069 (m), 837 (m), 778 (m).

MS (80eV, EI, 130 °C):

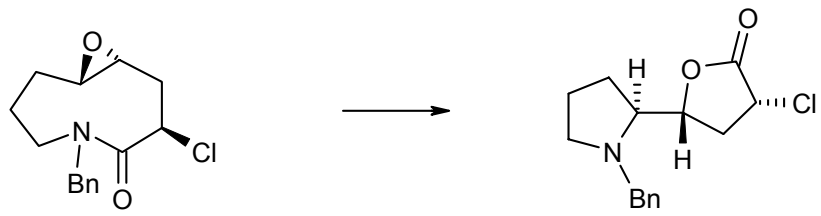
m/z = 390 (0.2) [$M^{+\cdot}$], 376 (2) [M-CH_3], 334 (100) [M-C_4H_9], 285 (97) [M-CH_3-C_7H_7], 228 (15), 91 (62).

HRMS (80eV,120 °C): found 334.14364

calc. 334.147462 (for $C_{17}H_{24}NO_4Si_1$, [M^+-C_4H_9]).



3*R*,5*R*,5-(1*S*-2-Benzyl-pyrrolidinyl)-3-chloro-3,4,5-trihydro-furan-2-one [55]



[38a] 279.77 [$C_{15}H_{18}ClNO_2$] **[55]** 279.77 [$C_{15}H_{18}ClNO_2$]

Reaction with 200 mg (0.71 mmol) oxirane **[38a]** and 1.2 eq TMSCl at room temperature for 1 h and standard workup according to **3.7.1** yielded 200 mg (100%) of pure **[55]** as a colourless oil.

^{1}H-NMR (270 MHz, $CDCl_3$):

7.40 - 7.20 (m, 5H; H-Ph), 4.60 - 4.52 (dd, 1H; H-3u; ^3J (H^{3u},H^{4o}) = 10.5 Hz, ^3J (H^{3u},H^{4u}) = 8.5 Hz), 4.42 - 4.34 (ddd, 1H; H-5o; ^3J (H^{5o},H^{4o}) = 9.5 Hz, ^3J (H^{5o},H^{4u}) = 5 Hz, ^3J (H^{5o},H^{6u}) = 5 Hz), 4.08 - 4.02 (d, 1H; H-N-Bn1; ^2J ($H^{N\text{-}Bn1}$,$H^{N\text{-}Bn2}$) = 13 Hz), 3.54 - 3.48 (d, 1H; H-N-Bn2; ^2J ($H^{N\text{-}Bn2}$,$H^{N\text{-}Bn1}$) = 13 Hz), 3.17 - 3.10 (m, 1H; H-6u), 3.00 - 2.90 (m, 1H; H-9o), 2.86 - 2.76 (ddd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 14.5 Hz, ^3J (H^{4u},H^{3u}) = 8.5 Hz, ^3J (H^{4u},H^{5o}) = 5.5 Hz), 2.59 - 2.46 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 12.5 Hz, ^3J (H^{4o},H^{3u}) = 10.5 Hz, ^3J (H^{4o},H^{5o}) = 9.5 Hz), 2.41 - 2.31 (m, 1H; H-9u), 2.04 - 1.91 (m, 1H; H-7u), 1.80 - 1.60 (m, 3H; H-7o, 8o, 8u).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

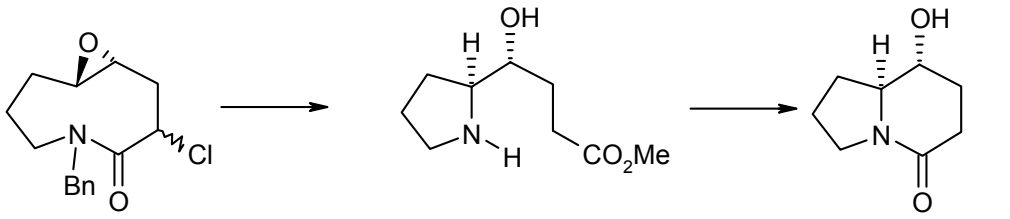
172.1 (s), 139.4 (s), 128.5 (d), 128.2 (d), 126.9 (d), 80.4 (d, C-5), 64.2 (d, C-6), 60.7 (t, C-9), 51.6 (d, C-3), 34.6 (t, C-4), 27.1 (t, C-7), 23.8 (t, C-8).

IR (KBr):

υ (cm^{-1}) = 3085 (w), 3062 (m), 3028 (m), 2957 (s), 2877 (m), 2798 (m), 1786 (s, lactone C=O), 1653 (s), 1494 (m), 1453 (s), 1385 (m), 1368 (m), 1327 (m), 1276 (m), 1253 (m), 1188 (s), 1135 (m), 1101 (m), 1027 (m), 1012 (m), 935 (m), 885 (m), 844 (m), 701 (s).

3.9 Total Syntheses of Pumiliotoxins (Part I) - Preparation of the Bicyclic Core

5*R*,6*S*-5-Hydroxy-azabicyclo[4.3.0]nonan-2-one [57]



[38a, 39a] 279.77 [$C_{15}H_{18}ClNO_2$] **[56]** 187.24 [$C_9H_{17}NO_3$] **[57]** 155.20 [$C_8H_{13}NO_2$]

In a 1 L flask, a mixture of the epoxy azonanones **[38a, 39a]**[292] (22.3 g, 0.08 mol) was dissolved in 500 mL of methanol. Then, a suspension of Pearlman's catalyst (2g, 10% Pd $(OH)_2$ on carbon) in 20 mL of methanol was added to the flask and the reaction mixture was cooled to 5 °C in an ice-bath. Then, the flask was evacuated (70-80 mbar) and filled with hydrogen. This procedure was repeated three times to remove all oxygen from the reaction flask. After stirring for 5 h in the cooling bath, the bath was removed and the mixture was stirred for 7 days until ^{1}H-NMR showed the complete disappearance of the dd at 4.63 ppm (H-3, chloro substituted). Depending on the purity of the reactant epoxy azonanones all signals in the aromatic section (8-7 ppm in ^{1}H-NMR) disappeared.

After completed hydrogenation, the flask was charged with 26 g (0.19 mol) of K_2CO_3 and the mixture was heated for 6 h at 45 °C. Then, the methanol was completely removed and the black residue was suspended into 300 mL of dichloromethane. The black suspension was filtered and the precipitates were again extracted with 2x200 mL of dichloromethane. The combined clear dichloromethane extracts were evaporated and 9.7 g of the crude hydroxy indolizidinone was obtained. The crude solid was ground using a mortar and washed with 200 mL of cold diethyl ether yielding 7.29 g (59%) of **[56]** as nearly colourless crystals (mp 99 - 101 °C).[293]

pyrrolidine [56][294]

^{13}C-NMR (67.9 MHz, $CDCl_3$):

173.7 (s), 67.1 (d), 64.0 (d), 51.5 (q), 45.7 (t), 30.1 (t), 28.5 (t), 24.4 (t), 23.0 (t).

---

[292] Usually, the crude epoxy azonanones were used. Depending on their purity, some signals of the m-chloro-benzoic acid remained during the hydrogenation (~ 8 ppm in ^{1}H spectrum).

[293] When purified epoxy azonanones were used, the yield of **[57]** was higher (78%), the product was purified using flash chromatography on silica gel (ethyl acetate / methanol 6:1).

[294] The pyrrolidine intermediate was not isolated and purified due to its high polarity, the given ^{13}C-NMR data refer to a spectrum measured from the crude intermediate. The ^{1}H-NMR spectrum of **[56]** was characterised by very broad lines, effected by the presence of the protonated form.

IR (KBr):

υ(cm^{-1})= 3302.4 (s, broad), 2929 (s), 2772 (m), 1735 (s), 1596 (m), 1446 (m), 1405 (m), 1347 (m), 1261 (m), 1220 (m), 1167 (s), 1119 (m), 1085 (m).

MS (80eV, EI, 220 - 250 °C):

m/z (%) 187 (0.3) [$M^{+\cdot}$], 156 (4), 141 (0.6), 126 (2), 96 (2), 91 (2), 85 (2), 71(6), 70 (100).

lactam [57]

$[\alpha]_D^{20}$ = -37.7° (c = 1.27, ethanol).

^{1}H-NMR (270 MHz, $CDCl_3$):

3.60 - 3.43 (m, 3H; H-5o, 9o, 9u), 3.32 - 3.21 (ddd, 1H; H-6u; ^3J (H^{6u},H$^{)}$ = 14 Hz, ^3J (H^{6u},H) = 8.5 Hz, ^3J (H^{6u},H) = 3.5 Hz), 2.60 - 2.48 (ddd, 1H; H-3u; ^2J (H^{3u},H$^{)}$ = 18 Hz, ^3J (H^{3u},H) = 7 Hz, ^3J (H^{3u},H) = 2 Hz), 2.47 -2.28 (m, 2H; H-3o,7u), 2.13 - 2.00 (m, 1H; H-4o), 2.00 - 1.91 (m, 1H; H-8o), 1.85 - 1.70 (m, 2H; H-4u, 8u), 1.60 - 1.45 (m, 1H; H-7o).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

168.7 (s), 70.7 (d, C-5), 63.9 (d, C-6), 45.5 (t, C-9), 31.6 (t, C-3), 29.9 (t, C-4 and C-7), 22.1 (t, C-8).

IR (KBr):

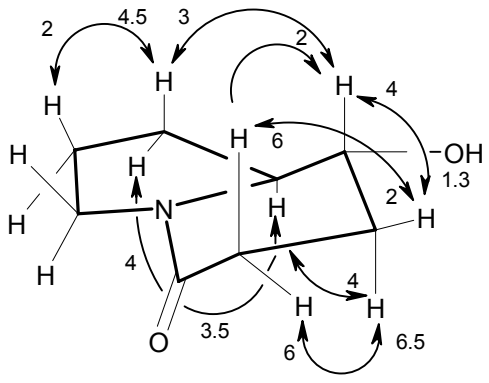
υ (cm^{-1}) = 3267 (s, OH), 2969 (m), 2952 (m), 2885 (m), 1601 (s, C=O), 1479 (m), 1454 (m), 1442 (m), 1412 (m), 1339 (m), 1320 (w), 1287 (m), 1265 (s), 1224 (w), 1209 (w), 1167 (w), 1142 (w), 1132 (w), 1093 (m), 1063 (m), 990 (w), 960 (m), 843 (w), 770 (w), 667 (m).

MS (80eV, EI, 130 °C):

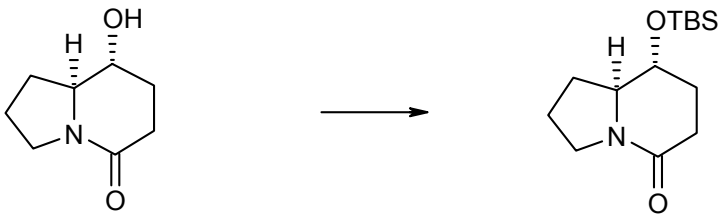
m/z (%) 155 (36) [$M^{+\cdot}$], 138 (3) [M^+ - OH], 127 (6), 111 (21), 99 (11), 83 (100), 70 (81), 55 (26), 41 (24).

HRMS (80eV, 130 °C): found 155.09567

calc. 155.094629 (for $C_8H_{13}N_1O_2$ [M^+])



5*R*,6*S*-5-*tert*-Butyldimethylsilyloxy-azabicyclo[4.3.0]nonan-2-one [58]



[57] 155.20 [$C_8H_{13}NO_2$] **[58]** 269.46 [$C_{14}H_{27}NO_2Si$]

In a 200 mL flask, 500 mg (3.22 mmol) of indolizidinone **[57]** and 395 mg (5.79 mmol, 1.8 eq.) of imidazole was dissolved in 50 mL of dichloromethane. Then, 534 mg (3.54 mmol, 1.1 eq) of *tert*-butyldimethylsilyl chloride was added and the mixture was stirred overnight at ambient temperature. The excess TBSCl was quenched with 10 mL of methanol followed by stirring for 30 minutes at room temperature. Thereafter, solvent was evaporated (30 °C water bath temperature) and the residue was suspended in 150 mL of diethyl ether. The organic phase was washed with saturated aqueous NH_4Cl to remove the imidazole.[295] The organic phase was dried (Na_2SO_4) and evaporated to yield 780 mg (90%) of **[58]** as a colourless oil.

$[\alpha]_D^{20}$ = - 36.2° (c = 0.85, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
3.50 - 3.30 (m, 3H; H-5o, 9o, 9u), 3.23 - 3.13 (ddd, 1H; H-6u; ^3J (H^{6u},H$^{)}$ = 14 Hz, ^3J (H^{6u},H) = 8.5 Hz, ^3J (H^{6u},H) = 3.5 Hz), 2.50 - 2.35 (ddd, 1H; H-3u; ^2J (H^{3u},H$^{)}$ = 18 Hz, ^3J (H^{3u},H) = 7 Hz, ^3J (H^{3u},H) = 2 Hz), 2.35 -2.10 (m, 2H; H-3o,7u), 1.95 - 1.85 (m, 2H; H-4o, 8o), 1.75 - 1.60 (m, 2H; H-4u, 8u), 1.45 - 1.30 (m, 1H; H-7o), 0.81 (s, 9H; Si-C(CH_3)$_3$), 0.00 (s, 6H; Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
168.0 (s), 72.0 (d, C-5), 63.9 (d, C-6), 45.4 (t, C-9), 31.9 (t, C-3), 30.6 (t, C-4), 29.9 (t, C-7), 25.4 (Si-C(CH_3)$_3$), 21.9 (t, C-8), 17.6 (Si-C(CH_3)$_3$), - 4.5 (q, Si-CH_3), -4.9 (q, Si-CH_3).

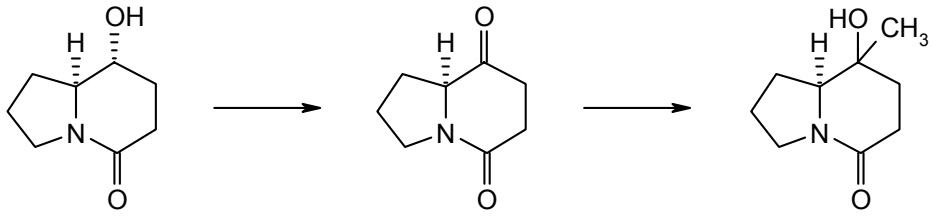
IR (solution, $CHCl_3$):
υ (cm^{-1}) = 3018 (s), 1956 (s), 1930 (s), 2885 (m), 2858 (m), 1624 (m), 1470 (m), 1463 (m), 1416 (m), 1387 (w), 1361 (m), 1273 (m), 1257 (m), 1221 (s), 1210 (s), 1128 (m), 1104 (m). 867 (m), 837 (m).

[295] When dichloromethane was used, traces of imidazole remained in the organic phase and further purification of the silyl ether with column chromatography was necessary.

MS (80eV, EI, 50 °C):
m/z (%) 269 (1) [$M^{+\cdot}$], 254 (3) [M^+ - CH_3], 212 (100) [M^+ - C_4H_9], 156 (4), 138 (18), 129 (19), 115 (9), 101 (7), 83 (18), 73 (12).

6*S*-5-Oxo-azabicyclo[4.3.0]nonan-2-one [59] and

5-(*R*,*S*)-6*S*-5-Hydroxy-5-methyl-azabicyclo[4.3.0]nonan-2-one [60]



[57] 155.20 [$C_8H_{13}NO_2$] **[59]** 153.18 [$C_8H_{11}NO_2$] **[60]** 169.23 [$C_9H_{15}NO_2$]

Swern oxidation :

In a 250 mL, three-necked round-bottom flask fitted with a rubber septum, magnetical stirrer and an internal thermometer, 2.81 mL (2 eq, 0.032 mol, 4.09 g) of oxalyl chloride (freshly distilled, d = 1.455) was dissolved in 100 mL of dry dichloromethane (dried over CaH_2). The solution was cooled to -78 °C and a solution of anhydrous dimethylsulfoxide (2.34 mL, 2.05 eq, 0.033 mol, 2.58 g) in 5 mL of dry dichloromethane was slowly added under argon. The internal temperature during the addition was kept below -70 °C. After complete addition, the mixture was stirred for 1 h at -70 °C. Then, the reaction mixture was cooled to -78 °C and a solution of hydroxy indolizidinone **[57]** (2.5 g, 0.016 mol) in 50 mL of dry dichloromethane was slowly added. Stirring was continued for 2 h at temperatures between -60 °C and -55 °C, then 11.0 mL (5 eq, 0.08 mol) of triethylamine (d = 0.726) was slowly added at -65 °C and the reaction mixture was allowed to reach room temperature over a period of 1 hour. During the warm-up of the suspension, the solvent was removed under reduced pressure.[296] The remaining residue was suspended in 300 mL of ethyl acetate and the white precipitation of triethylamine hydrochloride was removed by filtration. The clear filtrate was purified from traces of the hydrochloride by filtration through a frit with a plug of silica gel. After this manipulation, TLC control showed no further polar impurities in the remaining ethyl acetate solution. The solvent was evaporated (bath temperature 30 °C) to yield 2.5g (100%) of the crude ketone **[59]** as a colourless oil which was used without further purification.

[296] Other attempts to isolate the very polar product by a standard aqueous workup resulted in low yields due to the high solubility of the product in water.

Grignard addition with methylmagnesium iodide

Preparation of methylmagnesium iodide: To a 50 mL flask filled with 5.1 g (0.193 mol) of magnesium was added a small amount of diethyl ether in that manner that the magnesium turnings were just covered by the solvent. Then, 10.6 mL (0.161 mol) methyl iodide was added in single portions via a dropping funnel. After complete addition of the methyl iodide, the mixture was heated under reflux for another 30min (in some cases diethyl ether had to be added before refluxing) and a grey coloured solution was formed.[297]

Grignard addition : In a 1-L, three-necked round-bottom flask fitted with a rubber septum, mechanical stirrer and an internal thermometer was dissolved the crude ketone **[59]** (2.5 g) in 250 mL of dry THF. The mixture was set under argon and cooled to -78 °C and the freshly prepared methylmagnesium iodide solution was transferred slowly into the reaction mixture with a teflon tube (the internal temperature was kept below -60 °C). Immediately, a white precipitation of magnesium salts occurred. The mixture was stirred overnight at -78 °C and then allowed to reach room temperature. Then, the excess of methylmagnesium iodide was quenched by a slow addition of 100 mL saturated NH_4Cl solution. Thereafter, all solvents (including the water) were evaporated (water bath temperature <40 °C) under reduced pressure. [298] The remaining solids were extracted several times with 250 mL of dichloromethane and the solvent was evaporated. The crude oil was first purified on silica gel (ethyl acetate / methanol = 3:1) followed by HPLC (isopropanol / hexane = 25:75, 32x110 mm Nucleosil 50-5, UV = 220 nm, flow 64 mL/min) to separate the product from the unreacted ketone and finally 4.21 g (77%) of tertiary alcohol **[60]** could be obtained as mixture of C-5 diastereomers.

Addition of Methyllithium, Methylmagnesium chloride, Methylmagnesium bromide

Some analytical test were performed to determine the diastereomeric ratio in the addition of methylanion equivalents (see Table 13, page 85). In these tests, the applied reaction conditions were analogous to the addition of methylmagnesium iodide.

compound [59] [299]

$[\alpha]_D^{20}$ = - 245° (c = 1.56, $CHCl_3$).

[297] Some magnesium turnings remained in the flask, the supernatant solution was used for the Grignard addition.
[298] The complete removal of the water under mild thermal conditions was necessary for a good yield.
[299] ^{1}H-NMR and ^{13}C-NMR showed minor impurities, maybe the methylthiomethylether of the alcohol was formed during the oxidation in a small extent.

^{1}H-NMR (270 MHz, $CDCl_3$): [299]
3.98 - 3.90 (dd, 1H; H-6; ^{3}J (H^{6},H^{7o}) = 8 Hz, ^{3}J (H^{6},H^{7u}) = 8 Hz), 3.60 - 3.30 (m, 2H; H-9o, 9u), 2.70 - 2.40 (m, 4H; H-3o, 3u, 4o, 4u), 2.20 - 2.10 (m, 1H; H-7), 2.00 - 1.70 (m, 3H; H-7',8o, 8u).

^{13}C-NMR (67.9 MHz, $CDCl_3$): [299]
207.0 (s, C=O), 168.7 (s), 64.5 (d, C-6), 45.0 (t), 34.4 (t), 30.5 (t), 27.4 (t), 22.6 (t).

IR (solution, $CHCl_3$):
υ (cm^{-1}) = 2983 (m), 2970 (m), 2916 (m), 2891 (m), 1732 (s, C=O), 1653 (s, N-C=O), 1450 (s), 1381 (m), 1346 (m), 1330 (m), 1321 (m), 1290 (m), 1203 (m), 1177 (m), 1132 (m), 1103 (m).

MS (80eV, EI, 30 °C):
m/z (%) 153 (100) [$M^{+\cdot}$], 141 (12), 125 (77), 110 (16), 97 (50), 91 (34), 84 (44), 78 (30), 75 (14), 70 (20).

HRMS (80eV, 30 °C): found 153.07655 calc. 153.078979 (for $C_8H_{11}NO_2$ [M^{+}]).

compound [60]

$[\alpha]_D^{20}$ = - 47.97° (c = 1.78, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
3.50 - 3.35 (m, 4H; H-2x9,2x9'), 3.30 - 3.25 (m, 1H; H-6), 3.20 - 3.10 (m, 1H; H-6'), 3.00 - 2.90 (s, 2H; H-OH), 2.50 - 2.40 (m, 2H; H-4), 2.35 - 2.20 (m, 2H; H-4'), 2.08 - 1.89 (m, 2H; H-7), 1.90 - 1.60 (m, 10H; H-2x7',2x8, 2x8', 2x3, 2x3'), 1.25 (s, 3H; H-CH_3), 1.08 (s, 3H; H-CH_3').

^{13}C-NMR (67.9 MHz, $CDCl_3$):
168.3 (s), 69.5 (s, C-5), 67.3 (s, C-5'), 66.4 (d, C-6), 66.2 (d, C-6'), 45.8 (t, C-9, C-9'), 36.6 (t, C-3), 34.9 (t, C-3'), 30.0 (t, C-4), 28.0 (t, C-4'), 27.1 (t, C-7), 26.3 (q, Me'), 26.2 (t, C-7'), 22.1 (t, C-8), 21.9 (t, C-8'), 19.5 (q, Me).

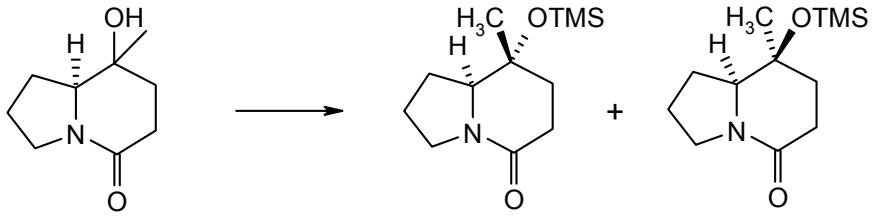
IR (solution, $CHCl_3$):
υ (cm^{-1}) = 3365 (m), 3053 (s), 2981 (s), 2882 (m), 1620 (s, C=O), 1471 (s), 1452 (s), 1418 (s), 1301 (m), 1265 (s), 1149 (m), 1125 (m), 1050 (w), 972 (m), 896 (m).

MS (80eV, EI, 30 °C):
m/z (%) 169 (73) [$M^{+\cdot}$], 154 (6), 152 (5), 140 (5), 112 (18), 111 (26), 99 (14), 83 (65), 70 (100).

HRMS (80eV, 70 °C): found 169.11355 calc. 169.110279 (for $C_9H_{15}NO_2$ [M^+]).

5*R*,6*S*-5-Trimethylsilyloxy-5-methyl-azabicyclo[4.3.0]nonan-2-one [61] and

5*S*,6*S*-5-Trimethylsilyloxy-5-methyl-azabicyclo[4.3.0]nonan-2-one [62]



[60] 169.23 [$C_9H_{15}NO_2$] **[61]** 241.41 [$C_{12}H_{23}NO_2Si$] **[62]** 241.41 [$C_{12}H_{23}NO_2Si$]

In a 100 mL flask, 1.85 g (0.011 mol) of indolizidinone **[60]**[300] and 1.48 g (0.022 mol, 2 eq.) of imidazole was dissolved in 50 mL of dichloromethane. Then, 1.76 mL (0.013 mol, 1.2 eq) of trimethylsilyl chloride was added and the mixture was stirred overnight at ambient temperature. The excess TMSCl was quenched with 5 mL of methanol and the solution was stirred for 30 minutes at room temperature. Thereafter, the solvent was evaporated (30 °C water bath temperature) and the residue was taken up in 150 mL of diethyl ether. The organic phase was washed with saturated aqueous NH_4Cl to remove the imidazole. Then, the organic phase was dried (Na_2SO_4) and evaporated to yield 2.14 g of a mixture of **[61]** and **[62]** as a colourless oil. This mixture was separated by HPLC (isopropanol / hexane = 1:9, 32x110 mm Nucleosil 50-5, UV = 220 nm, flow 95 mL/ min) and 1.23 g (46.6% ; r.t. 2.8 min) of **[61]** and 0.54 g (20.5%; r.t. 5.5 min) of **[62]** were obtained as colourless oils.

indolizidinone [61]:

$[\alpha]_D^{20}$ = -38.02° (c = 1.30, $CHCl_3$).

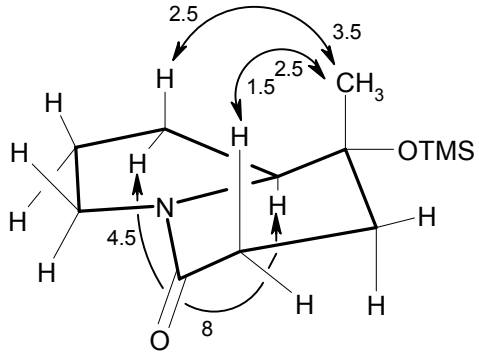
^{1}H-NMR (270 MHz, $CDCl_3$):
3.50 - 3.30 (m, 3H; H-9o, 9u, 6u), 2.52 - 2.40 (m, 1H; H-3u), 2.33 - 2.18 (m, 1H; H-3o), 2.00 - 1.90 (m, 1H; H-7u), 1.90 - 1.80 (m, 3H; H-4o, 4u, 8o), 1.75 - 1.60 (m, 1H; H-8u), 1.60 - 1.50 (m, 1H; H-7o), 1.12 (s, 3H; H-5-CH_3), 0.07 (s, 9H; H-Si $(CH_3)_3$).

[300] Diastereomeric ratio according to the Grignard addition (MeMgI).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
167.9 (s), 72.74 (s, C-5), 66.9 (d, C-6), 45.8 (t, C-9), 37.2 (t, C-3), 30.2 (t, C-7), 27.3 (t, C-4), 22.1 (t, C-8), 19.8 (q, CH_3), 2.54 (q, Si $(CH_3)_3$).

IR (solution, $CHCl_3$):
υ (cm^{-1}) = 2976 (m), 2951 (m), 2884 (m), 1624 (s, C=O), 1649 (m), 1417 (m), 1382 (m), 1299 (w), 1282 (w), 1252 (m), 1216 (m), 1159 (s), 1127 (m), 1072 (m), 1023 (m), 995 (w).

MS (80eV, EI, 30 °C):
m/z (%) 241 (100) [$M^{+\cdot}$], 226 (20) [M^+ - CH_3], 206 (8), 198 (28), 144 (43), 143 (44), 130 (18), 129 (28), 111 (64), 83 (75), 75 (48), 73 (59), 70 (48).



HRMS (80eV, 30 °C): found 241.14787
calc. 241.149808 (for $C_{12}H_{23}N_1O_2Si$ [M^+]).

indolizidinone [62] :

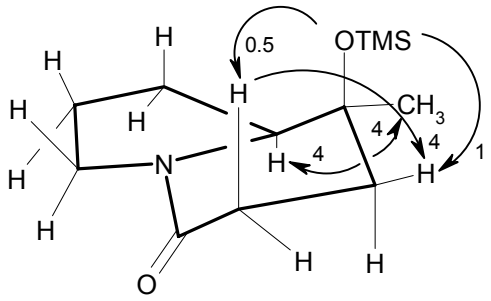
$[\alpha]_D^{20}$ = -35.14° (c = 1.08, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
3.48 - 3.38 (m, 2H; H-9o, 9u), 3.21 - 3.14 (dd, 1H; H-6u; ^3J (H^{6u},H^{7o}) = 10 Hz, ^3J (H^{6u},H^{7u}) = 5.5 Hz), 2.48 - 2.35 (m, 1H; H-3o), 2.35 - 2.21 (m, 1H; H-3u), 1.90 - 1.60 (m, 6H; H-8o, 8u, 7o, 7u, 4o, 4u), 1.25 (s, 3H; H-5-CH_3), 0.05 (s, 9H; H-Si $(CH_3)_3$).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
168.9 (s), 70.4 (s, C-5), 67.4 (d, C-6), 45.7 (t, C-9), 35.2 (t, C-3), 28.3 (t, C-7), 26.3 (q, 5-CH_3), 26.2 (t, C-4), 21.9 (t, C-8), 2.2 (q, Si $(CH_3)_3$).

IR (solution, $CHCl_3$):
υ (cm^{-1}) = 2975 (m), 2955 (m), 2880 (w), 1621 (s, C=O), 1470 (m), 1413 (m), 1378 (m), 1316 (w), 1273 (m), 1265 (m), 1253 (m), 1224 (w), 1134 (m), 1068 (m), 1021 (m).

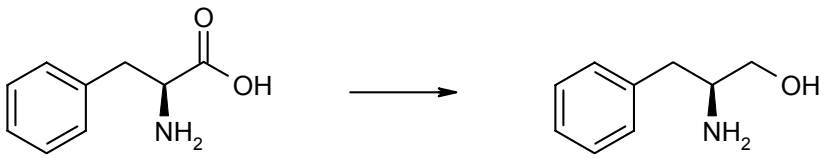
MS (80eV, EI, 30 °C):
m/z (%) 241 (100) [$M^{+\cdot}$], 226 (30) [M^{+} - CH_3], 198 (28), 178 (7), 171 (13), 144 (43), 143 (42), 130 (16), 129 (25), 111 (65), 83 (76), 75 (29), 73 (47), 70 (50).



HRMS (80eV, 30 °C): found 241.14755
calc. 241.149808 (for $C_{12}H_{23}N_1O_2Si$ [M^{+}]).

3.10 Total Syntheses of Pumiliotoxins (Part II) - Preparation of the Side Chain

(*S*)-Phenylalanol [63]



165.19 [$C_9H_{11}NO_2$] **[63]** 151.21 [$C_9H_{13}NO$]

A dry, 1L, three-necked flask was equipped with a mechanical stirrer, an internal thermometer and a reflux condenser connected to a mineral oil bubbler. The flask was loaded with 40.0 g (0.242 mol) of (S)-phenylalanine and 500 mL of anhydrous tetrahydrofurane and cooled in an ice-bath until a temperature below 4 °C was reached. Under continuous stirring 20.2 g (0.53 mol, 2.2 eq.) of $LiAlH_4$ was added in small portions.[301] After complete addition and almost complete stopping of the gas formation, the mixture was refluxed for 15 hours with continuous stirring.

After cooling down the reaction mixture to 4 °C, the excess $LiAlH_4$ was quenched with crunched ice (slow addition and control of the internal temperature !) until the colour of the suspension turned from grey to white. Then, the suspension was filtered with vacuum and the remaining precipitate was suspended in 150mL of a THF - water mixture (4:1) and heated for 1 hour under reflux. This procedure was repeated three times until the solvent remained colourless. The combined aqueous THF extracts were evaporated under reduced pressure and the aqueous solution was extracted three times with 100 mL of dichloromethane. The combined dichloromethane layers were dried (brine , Na_2SO_4) and the solvent was removed in vacuo. To the crude oil, 100 mL of toluene was added and thereafter the toluene was removed under reduced pressure. This procedure was repeated two times yielding the crude amino alcohol **[63]** as colourless solid. The crude product was recrystallised from 80 mL of ethyl acetate to yield 18.56 g (51%) of **[63]** as colourless crystals (mp 89-91 °C).

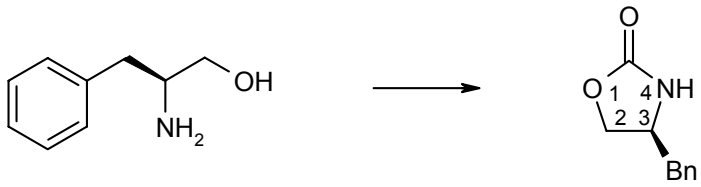
$[\alpha]_D^{20}$ = - 24.6° (c = 1.38, ethanol)[302]

All other spectroscopic datas were identical to those earlier reported. [302]

[301] After addition of each portion the internal temperature must be observed, because the exothermic reaction often started with some time delay.

[302] $[\alpha]_D$= - 24.7° (c = 1.03, ethanol) with mp = 88.5-91 °C taken from : Gage. R. J., Evans D. A., *Org. Synth. Coll. Vol.* **1989**, 68, 77-82.

(*S*)-4-(Phenylmethyl)-2-oxazolidinone [64]



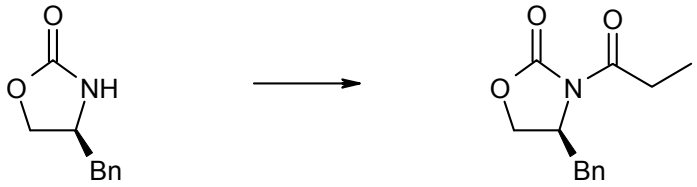
[63] 151.21 [$C_9H_{13}NO$] **[64]** 177.2 [$C_{10}H_{11}NO_2$]

A dry 250 mL of three-necked flask was equipped with a magnetical stirrer, a 12mm Vigreux column fitted with a distillation head and a 50 mL of receiver flask connected to an argon source and bubbler. The flask was charged with 25.4 g (0.168 mol) of (S)-phenylalanol, 2.31 g (0.1 eq, 0.017 mol) of anhydrous potassium carbonate and 45 mL (2.2 eq, 0.369 mol) of diethyl carbonate. The mixture was lowered into an oil bath, preheated to 135 °C and was stirred until dissolution was achieved (ca. 5 min). The distillation receiver was cooled in an ice bath and ca 28 mL of ethanol was collected from the reaction over a 2-hr period. The oil bath was removed upon cessation of the ethanol distillation. After this, the light yellow solution was cooled to ambient temperature, it was diluted with 100 mL of dichloromethane, transferred to a separatory funnel and washed with 150 mL of water. The organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated on the rotatory evaporator affording 31.4 g (110%) of a colourless oil. This material was take up into 100 mL of a hot 1.5:1 ethyl acetate-hexane solution, filtered, while hot, the allowed to crystallise to afford 22.2 g (75%) of **[64]** as colourless crystals (mp 85 °C).

$[\alpha]_D^{20}$ = - 61.2 ° (c = 1.25, $CHCl_3$).[303]

all other spectroscopic datas were identical to those earlier reported [302]

(*S*)-3-(1-Oxopropyl)-4-(phenylmethyl)-2-oxazolidinone [65]



[64] 177.2 [$C_{10}H_{11}NO_2$] **[65]** 233.27 [$C_{13}H_{15}NO_3$]

[303] $[\alpha]_D$ = -62.5° ($CHCl_3$) taken from: Ishizuka, T.; Kimura, K.; Ishibuchi, S.; Kunieda, T. *Chem.Lett.* **1992**, 991-994.

A dry, 1L three-necked flask equipped with a magnetic stirring bar was charged with 22.2 g (0.125 mol) of oxazolidinone **[64]**, capped with a rubber septum and flushed with argon. Anhydrous THF (400mL) was the added to the flask and the resulting solution was cooled to -78 °C in an acetone-dry ice bath. A solution of 82.1 mL (0.131 mol, 1.05 eq) of 1.5 M butyl lithium in hexane was transferred via a cannula first to a dry , septum stoppered, 100 mL of graduated cylinder then to the reaction flask over a 20-min period. During the addition the internal temperature was kept below -60 °C. After stirring for 45 min at -78 °C, freshly distilled propionyl chloride (12 mL, 0.137 mol, 1.1 eq) was added in one portion by syringe. The resulting clear, nearly colourless solution was stirred for 30 min at -78 °C, then allowed to warm to room temperature over a 45-min period. Excess propionyl chloride was quenched by the addition of 60 mL of saturated aqueous ammonium chloride. The bulk of the THF was removed on a rotatory evaporator (bath temperature ca. 30 °C) and the resulting slurry was extracted with two 100-mL of portions of dichloromethane. The combined organic extracts were washed with 100 mL of an aqueous 1 M NaOH and 100 mL of brine, dried over anhydrous Na_2SO_4 and filtered. The solvent was removed by rotary evaporation and the residue was placed in a refrigerator overnight to crystallise.

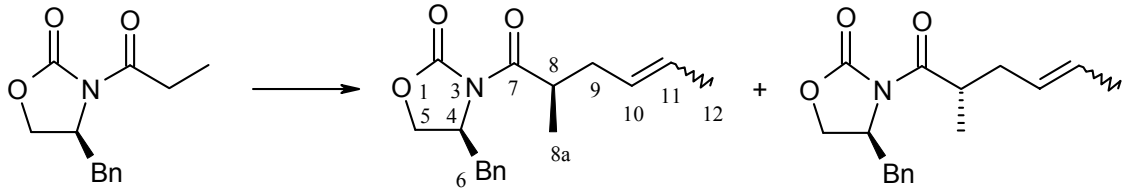
The resulting crystalline solid was pulverised and triturated with a minimum quantity of cold hexane. After filtration and drying, 28.5 g (98%) of **[65]** was obtained as a colourless crystalline solid with mp = 43 °C.

$[\alpha]_D^{20} = + 98.95°$ (c = 1.334, ethanol)[304]

all other spectroscopic datas were identical to those earlier reported. [304]

(*S*)-3-(2*R*-1-Oxo-2-methyl-hex-4-enyl)-4-(phenylmethyl)-2-oxazolidinone [66] and

(*S*)-3-(2*S*-1-Oxo-2-methyl-hex-4-enyl)-4-(phenylmethyl)-2-oxazolidinone [67]



[65] 233.27 [$C_{13}H_{15}NO_3$] **[66]** 287.36 [$C_{17}H_{21}NO_3$] **[67]** 287.36 [$C_{17}H_{21}NO_3$]

[304] $[\alpha]_D = + 99.5°$ (c = 1.01, ethanol) taken from: Gage. R. J., Evans D. A., *Org. Synth. Coll. Vol.* **1989**, 68, 83-91.

A dry, 250mL of three-necked flask equipped with a magnetic stirring bar was charged with 300 mL of anhydrous THF, capped with a rubber septum and flushed with argon. The solvent was cooled to -78 °C in an acetone-dry ice bath. A solution of 60 mL (0.06 mol, 2.0 eq) of 1.0 M sodium hexamethyldisilazide in THF was added with a syringe. Then, a solution of the precooled acylated oxazolidinone **[65]** in 50 mL of anhydrous THF was transferred into the solution via a teflon tube. The solution was stirred for 2 hours at -78 °C and then 12.34 mL (0.12 mol, 4 eq) of crotyl bromide[305] was slowly added with a syringe. After stirring at -60 to -50 °C for 4 hours, the reaction mixture was cooled to -78 °C and stirred overnight. On the next day, stirring was continued at -50 °C until TLC showed complete conversion of the reactant **[65]**. The reaction mixture was allowed to warm to room temperature and the excess sodium hexamethyldisilazide was quenched with saturated NH_4Cl solution. The mixture was transferred into a separatory funnel and the phases were separated. The aqueous phase was extracted with diethyl ether and the combined organic extracts were dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude oil was purified with flash chromatography on silica gel (hexane / ethyl acetate 2:1, $R_f = 0.45$) and the diastereomers were separated via HPLC (ethyl acetate / n-hexane = 12:88, Nucleosil 50-5, 32x110 mm, flow 64mL / min, UV = 254 nm) and 6.16g 71.5%) of **[66]** and 0.64 g (7.4%) of **[67]** were isolated as clear colourless oils.

oxazolidinone [66]

$[\alpha]_D^{20} = +34.6°$ (c = 1.468, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$): [306]

7.20 - 7.10 (m, 5H; H-Ph), 5.60 - 5.40 (m, 2H; H-10,11), 4.71 - 4.60 (m, 1H; H-4), 4.20 - 4.10 (m, 2H; H-6,6'), 3.85 - 3.75 (m, 1H; H-8), 3.30 - 3.20 (dd, 1H; H-5; ^2J (H^5,$H^{5'}$) = 13 Hz, ^3J (H^5,H^4) = 3 Hz), 2.85 - 2.65 (m, 1H; H-5'), 2.55 - 2.38 (m, 1H; H-9), 2.30 - 2.10 (m, 1H; H-9'), 1.65 - 1.60 (m, 3H; 12-CH_3), 1.20 - 1.10 (t, 3H; 8a-CH_3 ; ^3J ($H^{8a\text{-}CH3}$,H^8) = 6.5 Hz).

^{13}C-NMR (67.9 MHz, $CDCl_3$): [306]

176.6 (s, C-7), 152.9 (s, C-2), 135.3 (s), 129.9 (d), 128.8 (d), 127.7 (d), 127.6 (d), 127.1 (d), 126.8 (d), 126.2 (d), 65.8 (t, C-5), 55.1 (d, C-4), 37.9 (t, C-6), 37.9 (t, C-6'), 37.6 (d, C-8), 37.5 (d, C-8'), 36.8 (t, C-9), 31.0 (t, C-9'), 17.9 (q, C-12), 16.2 (q, C-8a and C8a'), 12.8 (q, C-12').

[305] The purity was technical grade : ca. 87% *(E,Z)*-1-bromo-2-butene + 13% 1-bromo-3-butene.
[306] The compounds **[66]** and **[67]** consist of two double bond isomers.

IR (KBr):

υ (cm^{-1}) = 3541 (w), 3381 (w), 3087 (m), 3064 (m), 3028 (s), 2975 (s), 2934 (s), 2857 (s), 1780 (s, C=O), 1698 (s, C=O), 1604 (w), 1498 (s), 1481 (s), 1454 (s), 1385 (s), 1350 (s), 1290 (s), 1208 (s), 1099 (s), 1076 (m), 1051 (m), 1017 (m), 969 (m), 924 (m), 838 (w), 762 (s), 750 (s), 703 (s), 507 (m).

MS (80eV, EI, 80 °C):

m/z (%) 287 (62) [$M^{+\cdot}$], 272 (3) [M^+ -CH_3], 233 (16) [M^+ - C_4H_9], 178 (80), 134 (8), 117 (54), 111 (56), 91 (30), 83 (100), 82 (72), 67 (17), 55 (62).

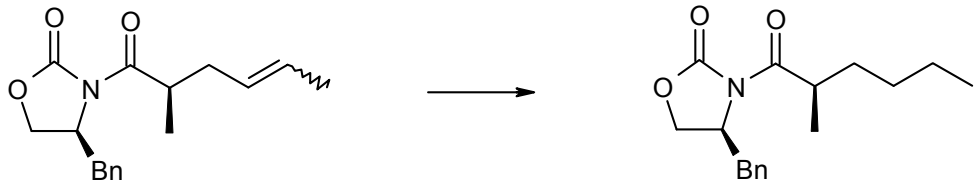
HRMS (80eV, 80 °C): found 287.15298 calc. 287.152144 (for $C_{17}H_{21}N_1O_3$ [M^+]).

oxazolidinone [67]

^{1}H-NMR (270 MHz, $CDCl_3$):[306]

7.20 - 7.10 (m, 5H; H-Ph), 5.60 - 5.40 (m, 2H; H-10,11), 4.73 - 4.63 (m, 1H; H-4), 4.20 - 4.10 (m, 2H; H-6,6'), 3.96 - 3.76 (m, 1H; H-8), 3.30 - 3.22 (dd, 1H; H-5; ^2J (H^5,$H^{5'}$) = 13 Hz, ^3J (H^5,H^4) = 3 Hz), 2.75 - 2.65 (m, 1H; H-5'), 2.55 - 2.38 (m, 1H; H-9), 2.30 - 2.10 (m, 1H; H-9'), 1.65 - 1.60 (m, 3H; 12-CH_3), 1.20 - 1.10 (t, 3H; 8a-CH_3 ; ^3J ($H^{8a\text{-}CH3}$,H^8) = 6.5 Hz).

(*S*)-3-(2*S*-1-Oxo-2-methyl-hexyl)-4-(phenylmethyl)-2-oxazolidinone [68]



[66] 287.36 [$C_{17}H_{21}NO_3$] **[68]** 289.38 [$C_{17}H_{23}NO_3$]

In a 250 mL flask, 5.72 g (0.02 mol) of imide **[66]** was dissolved in 50 mL of methanol and then 0.1g of palladium on carbon (10%) was added. The mixture was slowly evacuated and set under hydrogen at normal pressure. This procedure was repeated three times and then the mixture was stirred at ambient temperature for 15 hours until TLC-control showed complete disappearance of the double bond ($KMnO_4$ reagent). After completed hydrogenation, the methanol was evaporated with the rotatory evaporator and re-extracted with 100 mL of diethyl ether. Then, the black suspension was filtered through a frit with a plug of silica gel, to remove the catalyst. After evaporation of the solvent, 5.88 g (100%) of **[68]** as a clear colourless oil were obtained.

$[\alpha]_D^{20}$ = + 26.4 (c = 1.73, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

7.40 - 7.20 (m, 5H; H-arom.), 4.65 - 4.61 (m, 1H; H-4), 4.20 - 4.15 (m, 2H; H-6), 3.80 - 3.65 (m, 1H; H-8), 3.30 - 3.20 (dd, 1H; H-5; ^2J (H^5,$H^{5'}$) = 13 Hz, ^3J (H^5,H^4) = 3 Hz), 2.77 - 2.66 (dd, 1H; H-5'; ^2J ($H^{5'}$,H^5) = 13 Hz, ^3J ($H^{5'}$,H^4) = 9.5 Hz), 1.85 - 1.70 (m, 1H; H-9), 1.50 - 1.25 (m, 5H; H-9', 10,11), 1.20 - 1.15 (d, 3H; H-8a; ^3J (H^{8a},H^8) = 6 Hz), 0.95 - 0.85 (m, 3H; H-12).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

177.2 (s, C-7), 152.9 (s, C-2), 135.2 (s), 129.3 (d), 128.8 (d), 127.2 (d), 65.8 (t, C-5), 55.2 (d, C-4), 37.9 (t, C-6), 37.3 (d, C-8), 33.4 (t, C-9), 29.1 (t, C-10), 22.6 (t, C-11), 16.6 (q, C-8a), 13.8 (q, C-12).

IR (KBr):

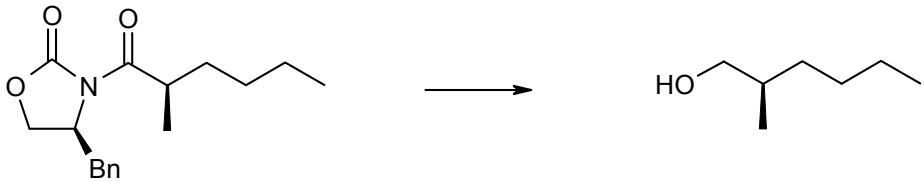
υ (cm^{-1}) = 3536 (w), 3374 (w), 3086 (w), 3062 (m), 3028 (m), 2957 (s), 2932 (s), 2859 (s), 1782 (s, C=O), 1699 (s, C=O), 1604 (w), 1497 (m), 1481 (m), 1385 (s), 1349 (s), 1288 (m), 1208 (s), 1097 (s), 1076 (m), 1053 (m), 1018 (m), 968 (m), 922 (w), 838 (w), 762 (m), 748 (m), 703 (s). 507 (m).

MS (80eV, EI, 80 °C):

m/z (%) 289 (16) [$M^{+\cdot}$], 233 (6) [M^+ - C_4H_9], 198 (25), 178 (10), 134 (5), 117 (11), 113 (100), 91 (13), 86 (22), 85 (62), 69 (6), 55 (5), 43 (21).

HRMS (80eV, 80 °C): found 289.16345 calc. 289.167794 (for $C_{17}H_{23}N_1O_3$ [M^+]).

(*R*)-2-Methylhexanol [69]



[68] 289.38 [$C_{17}H_{23}NO_3$] **[69]** 116.2 [$C_7H_{16}O$]

In a 250 mL flask, 5.88 g (0.02 mol) of imide **[68]** was dissolved in100 mL of anhydrous THF and the solution was cooled to 0 °C in an ice-bath. Then, 1.52 g (0.04 mol, 2 eq) of $LiAlH_4$ was slowly added within 30 min. After complete addition, the mixture was stirred for 1 h at 0 °C and then, the excess $LiAlH_4$ was quenched first with crunched ice followed by a saturated NH_4Cl solution. After the colour of the precipitate had turned to white, the solution was filtered and the precipitate was washed two

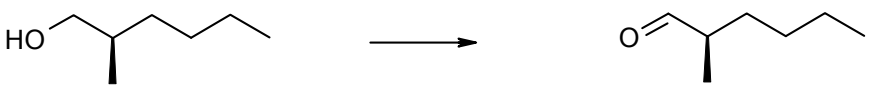
times with 100 mL of diethyl ether. The combined organic fractions were dried (Na_2SO_4) and solvent was evaporated (100 mbar , room temperature). The remaining oil was subjected to bulb-to-bulb distillation (20-30 mbar, bp 130 °C) and 1.78 g (77%) of hexanol **[69]** was obtained. The remaining distillation residue was taken up in a hexane-ethyl acetate solution (2:1) were it began to crystallise. After addition of pure hexane and filtration, 2.05 g (70%) of Evans-auxiliary could be reisolated as colourless crystals.

$[\alpha]_D^{20}$ = + 13.98° (c = 1.18, methanol).[307]

^{1}H-NMR (270 MHz, $CDCl_3$):
3.52 -3.44 (dd, 1H; H-1; ^2J (H^1,$H^{1'}$) = 10.5 Hz, ^3J (H^1,H^2) = 5.5 Hz), 3.42 - 3.34 (dd, 1H; H-1'; ^2J ($H^{1'}$,H^1) = 10.5 Hz, ^3J ($H^{1'}$,H^2) = 6.5 Hz), 1.90 - 1.80 (s, 1H; H-OH), 1.62 - 1.50 (m, 1H; H-2), 1.40 - 1.10 (m, 6H; H-3,4,5), 0.90 - 0.80 (m, 3H; H-6).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
68.3 (t, C-1), 35.66 (d, C-2), 32.8 (t, C-3), 29.1 (t, C-4), 22.9 (t, C-5), 16.5 (q, C-2a), 14.0 (q, C-6).

(*R*)-2-Methylhexanal [70]



[69] 116.2 [$C_7H_{16}O$] **[70]** 114.2 [$C_7H_{14}O$]

In a 250 mL, three-necked round-bottom flask fitted with a rubber septum, magnetical stirrer and an internal thermometer, 2.55 mL (2 eq, 0.029 mol, 3.71 g) of oxalyl chloride (freshly distilled, d = 1.455) was dissolved in 50 mL of dry dichloromethane (dried over CaH_2). The solution was cooled to -78 °C and a solution of anhydrous dimethylsulfoxide (2.12 mL, 2.05 eq, 0.03 mol, 2.34 g) in 5 mL of anhydrous dichloromethane was slowly added under argon. The internal temperature during the addition was kept below -70 °C. After complete addition, the mixture was stirred for 1 h at -60 °C. Then, the reaction mixture was cooled to -78 °C and a solution of hexanol **[69]** (1.7 g, 0.0146 mol) in 5 mL of dry dichloromethane was slowly added. After stirring the reaction mixture for 2 h at -45 °C, 10.2 mL of triethylamine (5 eq, 0.073 mol, d = 0.726) was slowly added at -78 °C and the reaction mixture was allowed to reach room temperature over a period of 2 hours.

[307] $[\alpha]_D$ = + 14.5 ° (c = 2.25, methanol) taken from: Mori, K.; Horikiri, H. *Liebigs Ann. Org. Bioorg. Chem.* **1996**, 501-506.

The suspension was then treated with 100 mL of saturated $NaHCO_3$ solution. The layers were separated and the organic layer was washed two times with saturated $NaHCO_3$ and one time with brine. After drying over Na_2SO_4, the solids were removed by filtration and the solvent was evaporated (bath temperature 20 °C, 50 mbar) to yield 1.62 g (97%) of the crude aldehyde **[70]** as an orange oil which was used without further purification. The crude aldehyde could be stored at -78 °C for several days without changing the optical rotatory value. [308]

$[\alpha]_D^{20}$ = - 19.95° (c = 1.12, $CHCl_3$).[309]

^{1}H-NMR (270 MHz, $CDCl_3$):
9.59 - 9.57 (d, 1H, H-1, ^3J (H^1,H^2) = 2 Hz), 2.40 - 2.30 (m, 1H, H-2), 1.80 - 1.20 (m, 6H; H-3,4,5), 1.10 - 0.90 (d, 3H, ^3J (H^{2a},H^2) = 7 Hz) 0.90 - 0.80 (m, 3H; H-6).

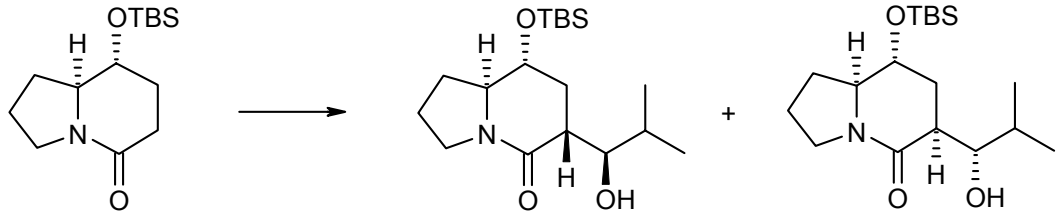
^{13}C-NMR (67.9 MHz, $CDCl_3$):
205.4 (s), 46.2 (d, C-2), 30.1 (t, C-3), 29.0 (t, C-4), 22.6 (t, C-5), 13.8 (q, C-2a), 13.3 (q, C-6).

[308] All attempts, to purify the crude aldehyde by high-vacuum condensation or column chromatography were unsuccessful. The optical purity of the aldehyde was not determined, some epimerisation during the Swern reaction could be possible due to variable optical rotation values (- 26.6° to - 19.95° observed).
[309] Lit : $[\alpha]_D$ = - 19.7° taken from: Goldstein, S. W.; Overman, L. E.; Rabinowitz, M. H. *J. Org. Chem.* **1992**, 57 1179-1190.

3.11 Total Syntheses of Pumiliotoxins (Part III) - Aldol approach

3*R*,5*R*,6*S*-3-(1*R*-1-Hydroxy-2-methyl-propyl)-5-*tert*-butyldimethylsilyloxy-azabicyclo[4.3.0]nonan-2-one [71] and

3*S*,5*R*,6*S*-3-(1*S*-1-Hydroxy-2-methyl-propyl)-5-*tert*-butyldimethylsilyloxy-azabicyclo[4.3.0]nonan-2-one [72]



[58] 269.46 [$C_{14}H_{27}NO_2Si$] **[71]** 341.57 [$C_{18}H_{35}NO_3Si$] **[72]** 341.57 [$C_{18}H_{35}NO_3Si$]

A dry 10mL flask equipped with a magnetic stirring bar was charged with 2 mL of anhydrous THF, capped with a rubber septum and flushed with argon. The solvent was cooled to -78 °C in an acetone-dry ice bath. A solution of 101µl (0.204 mmol, 1.1 eq) lithium diisopropylamide (2.0 M in THF) was added with a syringe. Then, a solution of indolizidinone **[58]** (50 mg, 0.185 mmol) in 1 mL of anhydrous THF was transferred into the solution with a syringe over 5 min. The solution was stirred for 1 hours at -78 °C and then 76µl (0.75 mmol, 4 eq) of isobutyraldehyde was slowly added with a syringe. After stirring at -78° to -60 °C for 3 hours, the cooling bath was removed and the excess lithium diisopropylamide was quenched with a saturated NH_4Cl solution. The mixture was transferred into a separatory funnel and the phases were separated. The aqueous phase was extracted with diethyl ether and the combined organic extracts were dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude oil was purified by flash chromatography on silica gel (hexane / ethyl acetate 1:1, R_f = 0.37) and 18 mg (27%) of product was obtained as a 1.4:1 mixture of diastereomers **[71]** and **[72]**. The diastereomers were separated via HPLC (isopropanol / n-hexane = 4:96, Nucleosil 50-5, 32x237 mm, flow 64mL / min, UV = 225nm).

aldol adduct [72] - HPLC 1

$[\alpha]_D^{20}$ = -43.6° (c = 1.68, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

4.98 - 4.94 (d, 1H; OH; ^{3}J (H^{OH},H^{3a}) = 1.5 Hz), 3.65 - 3.42 (m, 4H; H-3a, 5o, 9o, 9u), 3.41 - 3.32 (ddd, 1H; H-6u; ^{3}J (H^{6u},H^{5}) = 8 Hz, ^{3}J (H^{6u},H^{4o}) = 8 Hz, ^{3}J (H^{6u},H^{4u}) = 6 Hz), 2.60 - 2.48 (ddd, 1H; H-3; ^{3}J (H^{3},H^{3a}) = 8 Hz, ^{3}J (H^{3},H^{4o}) = 8 Hz, ^{3}J (H^{3},H^{4o}) = 8 Hz), 2.30 - 2.18 (m, 1H; H-7u), 2.00 - 1.70 (m, 4H; H-8o, 4, 8u, 3b), 1.65 - 1.49 (m, 1H; H-7o), 1.05 - 1.00 (d, 3H; H-3c; ^{3}J (H^{3c},H^{3b}) = 6.5 Hz), 0.92 - 0.87 (d, 3H; H-3c'; ^{3}J ($H^{3c'}$,H^{3b}) = 6.5 Hz), 0.87 (s, 9H; H-Si- $(CH_3)_3$), 0.05 (s, 6H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$): [310]

172.8 (s), 75.6 (d, C-3a), 70.7 (d, C-5), 62.9 (d, C-6), 45.1 (t, C-9), 41.3 (t, C-3), 33.1 (t, C-4), 31.5 (t, C-7), 29.5 (d, C-3b), 25.5 (Si-$C(CH_3)_3$), 22.6 (t, C-8), 20.1 (q, C-3c), 17.6 (Si-$C(CH_3)_3$), 14.2 (q, C-3c'), - 4.4 (q, Si-CH_3), -4.8 (q, Si-CH_3).

aldol adduct [71] - HPLC 2

$[\alpha]_D^{20}$ = -35.2° (c = 1.67, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

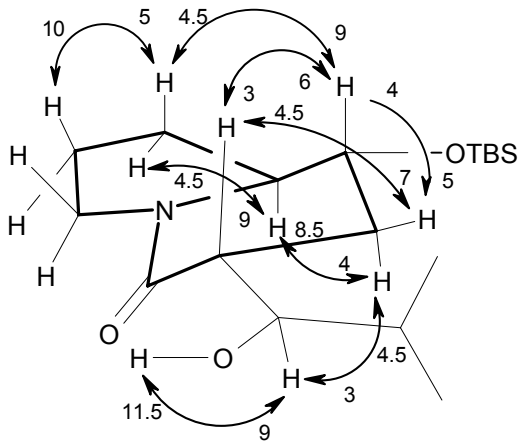
5.85 - 5.80 (s, 1H; H-OH), 3.60 - 3.40 (m, 4H; H-3a, 5, 9, 9'), 3.30 - 3.20 (ddd, 1H; H-6u; ^{3}J (H^{6u},H^{5o}) = 8 Hz, ^{3}J (H^{6u},H^{4o}) = 8 Hz, ^{3}J (H^{6u},H^{4u}) = 6 Hz), 2.40 - 2.20 (m, 2H; H-3, 7u), 2.00 - 1.80 (m, 2H; H-8o, 4o), 1.80 - 1.60 (m, 2H; H-8u, 3b), 1.50 - 1.30 (m, 2H; H-7o, 4u), 1.03 - 0.98 (d, 3H; H-3c; ^{3}J (H^{3c},H^{3b}) = 6.5 Hz), 0.85 - 0.80 (d, 3H; H-3c'; ^{3}J ($H^{3c'}$,H^{3b}) = 6.5 Hz), 0.85 (s, 9H; H-Si- $(CH_3)_3$), 0.00 (s, 6H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$): [310]

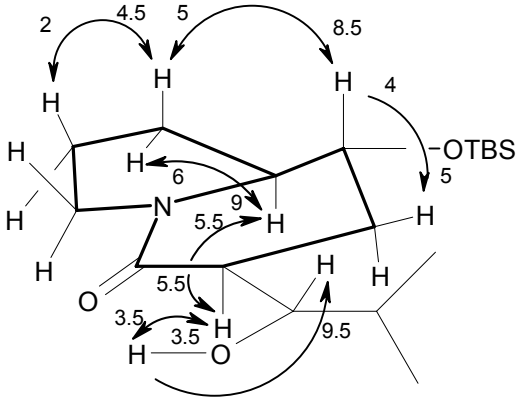
171.9 (s), 76.3 (d, C-3a), 71.5 (d, C-5), 64.2 (d, C-6), 45.8 (t, C-9), 42.5 (t, C-3), 33.8 (t, C-4), 32.0 (t, C-7), 28.9 (d, C-3b), 25.5 (Si-$C(CH_3)_3$), 22.1 (t, C-8), 19.9 (q, C-3c), 17.7 (Si-$C(CH_3)_3$), 13.4 (q, C-3c'), - 4.4 (q, Si-CH_3), -4.8 (q, Si-CH_3).

[310] Determined from a mixture of **[71]** and **[72]**.

NOE measurement [71] [311]



NOE measurement [72]



IR (KBr): [310]

υ (cm^{-1}) = 3364 (m), 2956 (s), 2930 (s), 2883 (s), 2858 (s), 1712 (w), 1616 (s, C=O), 1463 (s), 1428 (s), 1388 (m), 1362 (m), 1341 (m), 1258 (m), 1176 (w), 1132 (m), 1103 (s), 1003 (m), 940 (m), 917 (m), 901 (m), 865 (s), 838 (s), 777 (s), 736 (w), 672 (w).

MS (80eV, EI, 90 °C): [310]

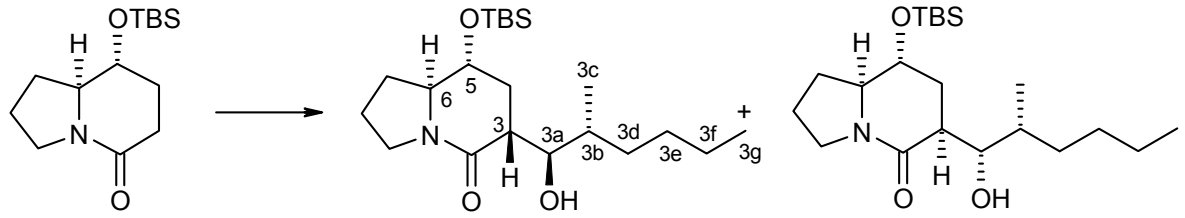
m/z (%) 341 (1) [$M^{+\cdot}$], 340 (1) [M^+ - H^+], 326 (10) [M^+ - CH_3], 323 (48) [M^+ - H_2O], 298 (100) [M^+ - C_3H_7], 284 (74) [M^+ -C_4H_9], 269 (28), 266 (17), 254 (6), 212 (27), 209 (36), 192 (10), 166 (42), 138 (40), 125 (12), 96 (18), 75 (32), 73 (44), 70 (44).

HRMS (80eV, 90 °C): [310] found 341.23645 calc. 341.238623 (for $C_{18}H_{35}N_1O_3Si$ [M^+]).

[311] ^{1}H-NMR, H,H-COSY and NOE-measurements indicated the presence of a fixated side chain by a strong hydrogen bridge between OH and C=O, the configuration could therefore be unambiguously determined.

3*R*,5*R*,6*S*-3-(1*R*-1-Hydroxy-2-methyl-propyl)-5-*tert*-butyldimethylsilyloxy-azabicyclo[4.3.0]nonan-2-one [73] and

3*S*,5*R*,6*S*-3-(1*S*-1-Hydroxy-2-methyl-propyl)-5-*tert*-butyldimethylsilyloxy-azabicyclo[4.3.0]nonan-2-one [74]



[58] 269.46 [$C_{14}H_{27}NO_2Si$] **[73]** 383.65 [$C_{21}H_{41}NO_3Si$] **[74]** 383.65 [$C_{21}H_{41}NO_3Si$]

A dry 10mL flask equipped with a magnetic stirring bar was charged with 2 mL of anhydrous THF, capped with a rubber septum and flushed with argon. The solvent was cooled to -78 °C in an acetone-dry ice bath. A solution of 100µl (0.204 mmol, 1.1 eq) lithium diisopropylamide (2.0 M in THF) was added with a syringe. Then, a solution of indolizidinone **[58]** (50 mg, 0.185 mmol) in 1 mL of anhydrous THF was transferred into the solution with a syringe over 5 min. The solution was stirred for 15 min at -78 °C and then 42.2 mg (0.37 mmol, 2 eq) of (R)-2-methylhexanal **[69]** was slowly added with a syringe. After stirring at -78° to -60 °C for 20 min, the cooling bath was removed and the excess lithium diisopropylamide was quenched with saturated NH_4Cl solution. The mixture was transferred into a separatory funnel and the phases were separated. The aqueous phase was extracted with diethyl ether and the combined organic extracts were dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude oil was purified with flash chromatography on silica gel (n-hexane / ethyl acetate = 1:1, R_f = 0.45) and 26.8 mg (38%) of a 1.1:1 mixture of diastereomers **[73]** and **[74]** and 5.2 mg (7%) of a third diastereomer **[75]**[312] could be obtained. The diastereomers were separated via HPLC (isopropanol / n-hexane = 5:95, Nucleosil 50-5, 32x250 mm, flow 64mL / min, UV = 225nm).

aldol adduct [73] :

$[\alpha]_D^{20}$ = - 20.54 ° (c = 1.48, $CHCl_3$).

[312] Due to the stereogenic centre at the side chain (free rotation of the C-3b to C-3g part of the side chain), the structure of **[75]** could not be unambiguously determined, some NOE enhancements indicated an epimerisation of the methyl stereogenic centre (C-3b).

^{1}H-NMR (270 MHz, $CDCl_3$):
3.67 - 3.60 (dd, 1H; H-3a; ^{3}J (H^{3a},H^{3}) = 8.5 Hz, ^{3}J (H^{3a},H^{3b}) = 2 Hz), 3.60 - 3.40 (m, 3H; H-9o,9u, 5), 3.32 - 3.20 (ddd, 1H; H-6u; ^{3}J (H^{6u},H^{5o}) = 11 Hz, ^{3}J (H^{6u},H^{7o}) = 11 Hz, ^{3}J (H^{6u},H^{7u}) = 5 Hz), 2.50 - 2.38 (ddd, 1H; H-3; ^{3}J (H^{3},H^{4u}) = 11.5 Hz, ^{3}J (H^{3},H^{3a}) = 10 Hz, ^{3}J (H^{3},H^{4o}) = 6.5 Hz), 2.30 - 2.20 (m, 1H; H-7u), 2.05 - 1.85 (m, 2H; H-8o, 4o), 1.85 - 1.70 (m, 1H; H-8u), 1.60 - 1.50 (m, 1H; H-3b), 1.50 - 1.20 (m, 11H; H-4u,7o, 3d-g), 1.05 - 1.00 (d, 3H; H-3c; ^{3}J (H^{3c},H^{3b}) = 6.5 Hz), 0.90 (s, 9H; H-Si-$(CH_3)_3$), 0.08 (s, 6H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
172.1 (s), 71.7 (d, C-3a), 64.5 (d, C-5), 45.9 (t, C-9), 42.6 (d, C-6), 34.2 (d, C-3), 34.1 (t, C-4), 32.1 (t), 29.9 (t), 27.7 (t), 25.6 (q, Si-C$(CH_3)_3$), 22.9 (t, C-8), 22.3 (t), 17.9 (s, Si-C$(CH_3)_3$), 17.1 (d), 14.1 (q), - 4.3 (q, Si-CH_3), -4.6 (q, Si-CH_3).

IR (solution, $CHCl_3$):
υ (cm^{-1}) = 3366 (w), 3019 (s), 2957 (m), 2931 (m), 1609 (m, C=O), 1523 (w), 1471 (m), 1425 (m), 1365 (w), 1217 (s), 1132 (m), 1103 (m), 987 (w), 931 (w), 861 (w), 838 (w).

aldol adduct [74]

$[\alpha]_D^{20}$ = - 39.82° (c = 1.73, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
3.75 - 3.70 (dd, 1H; H-3a; ^{3}J (H^{3a},H^{3}) = 9.5 Hz, ^{3}J (H^{3a},H^{3b}) = 2 Hz), 3.65 - 3.45 (m, 3H; H-9o,9u, 5), 3.45 - 3.33 (ddd, 1H; H-6u; ^{3}J (H^{6u},H^{5o}) = 8.5 Hz, ^{3}J (H^{6u},H^{7o}) = 8.5 Hz, ^{3}J (H^{6u},H^{7u}) = 6.5 Hz), 2.60 - 2.50 (ddd, 1H; H-3; ^{3}J (H^{3},H^{4u}) = 8 Hz, ^{3}J (H^{3},H^{3a}) = 8 Hz, ^{3}J (H^{3},H^{4o}) = 8 Hz), 2.30 - 2.20 (m, 1H; H-7u), 2.00 - 1.90 (m, 1H; H-8o), 1.85 - 1.70 (m, 3H; H-4o, 4u, 8u), 1.65 - 1.43 (m, 2H; H-7o, 3b), 1.40 - 1.20 (m, 9H; H-3d-3g), 0.90 (m, 3H; H-3c), 0.90 (s, 9H; H-Si- $(CH_3)_3$), 0.08 (s, 6H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
173.1 (s), 73.6 (d, C-3a), 70.7 (d, C-5), 63.2 (d, C-6), 45.3 (t, C-9), 41.4 (d, C-3), 34.4 (d, C-3b), 33.8 (t, C-4), 32.9 (t, C-7), 31.6 (t), 29.9 (t), 25.6 (q, Si-C$(CH_3)_3$), 22.9 (t, C-8), 22.7 (t), 17.9 (s, Si-C$(CH_3)_3$), 14.1 (q, 3c), 12.1 (q, 3g), - 4.3 (q, Si-CH_3), - 4.8 (q, Si-CH_3).

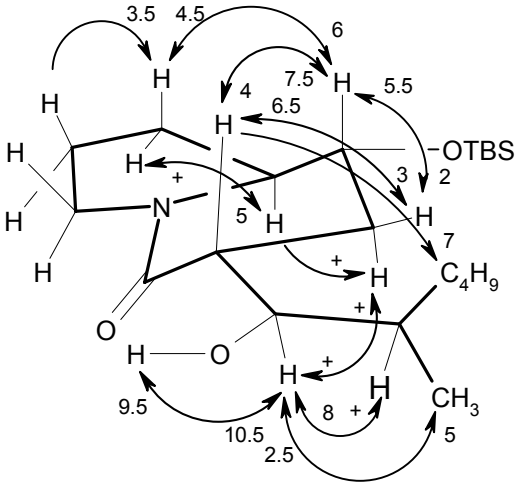
IR (solution, $CHCl_3$):
υ (cm^{-1}) = 3413 (w), 3020 (s), 2957 (m), 2931 (m), 2886 (m), 2858 (m), 1627 (m, C=O), 1517 (w), 1471 (m), 1424 (m), 1364 (w), 1217 (s), 1108 (m).

MS (80eV, EI, 90 °C): [313]

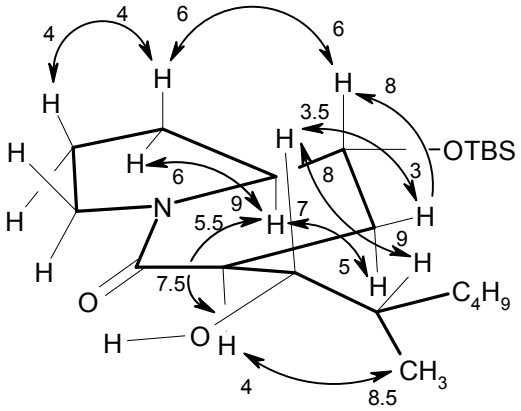
m/z (%) 383 (1) [$M^{+\cdot}$], 365 (34) [M^+ - H_2O], 326 (26) [M^+ -C_4H_9], 308 (5), 298 (100) [M^+ - C_6H_{13}], 269 (27), 251 (7), 213 (10), 212 (10), 166 (25), 138 (18), 96 (8), 75 (15), 73 (17), 70 (20).

HRMS (80eV, 90 °C) [313] : found 383.28332 calc. 383.285573 (for $C_{21}H_{41}N_1O_3Si$ [M^+]).

NOE measurement [73] [314]



NOE measurement [74]



aldol adduct [75] [315]

$[\alpha]_D^{20}$ = + 19.6° (c = 0.31, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

3.75 - 3.65 (dd, 1H; H-3a; ^3J (H^{3a},H^3) = 9.5 Hz, ^3J (H^{3a},H^{3b}) = 1.5 Hz), 3.60 - 3.45 (m, 3H; H-9o,9u, 5), 3.35 - 3.23 (ddd, 1H; H-6u; ^3J (H^{6u},H^{5o}) = 8.5 Hz, ^3J (H^{6u},H^{7o}) = 8.5 Hz, ^3J (H^{6u},H^{7u}) = 6.5 Hz), 2.42 - 2.30 (m, 1H; H-3), 2.30 - 2.20 (m, 1H; H-7u), 2.00 - 1.90 (m, 1H; H-8o), 1.85 - 1.2 (m, 14H), 0.90 (m, 3H; H-3c), 0.90 (s, 9H; H-Si- $(CH_3)_3$), 0.08 (s, 6H; H-Si-CH_3).

^{13}C-NMR (62.9 MHz, $CDCl_3$):

172.3 (s), 74.7 (d, C-3a), 71.8 (d, C-5), 64.5 (d, C-6), 45.9 (t, C-9), 42.6 (d, C-3), 34.2 (d, C-3b), 34.0 (t, C-4), 33.8 (t, C-7), 32.2 (t), 29.8 (t), 25.7 (q, Si-$C(CH_3)_3$), 22.9 (t, C-8), 22.3 (t), 17.9 (s, Si-$C(CH_3)_3$), 14.1 (q, 3c), 11.7 (q, 3g), - 4.3 (q, Si-CH_3), - 4.8 (q, Si-CH_3).

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[313] Determined from a mixture of **[73]** and **[74]**.

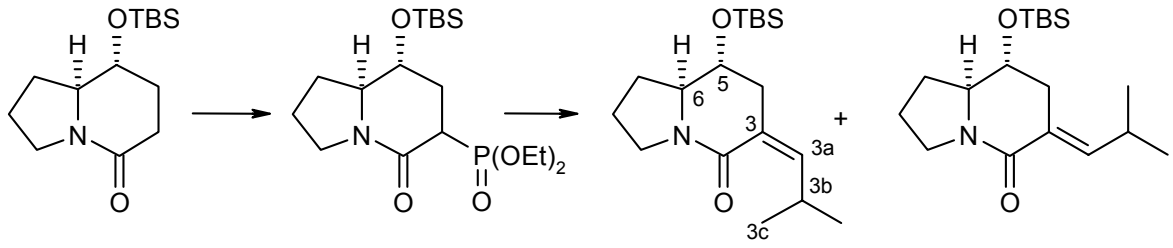
[314] ^{1}H-NMR, H,H-COSY and NOE-measurements indicated the presence of a fixated side chain, presumably by a strong hydrogen bridge between OH and C=O, the stereoconfiguration could therefore be unambiguously determined.

3.12 Total Syntheses of Pumiliotoxins (Part IV) - Horner Approach

5*R*,6*S*-3-(Diethoxyphosphinyl)-5-*tert*-butyldimethylsilyloxy-azabicyclo[4.3.0]nonan-2-one [76] and

***(3Z)*-5*R*,6*S*-3-(Isobutylidene)-5-*tert*-butyldimethylsilyloxy-azabicyclo[4.3.0]nonan-2-one [77] and**

***(3E)*-5*R*,6*S*-3-(Isobutylidene)-5-*tert*-butyldimethylsilyloxy-azabicyclo[4.3.0]nonan-2-one [78]**



[58] 269.46
[$C_{14}H_{27}NO_2Si$]

[76] 405.55
[$C_{18}H_{36}NO_5PSi$]

[77] 323.56
[$C_{18}H_{33}NO_2Si$]

[78] 323.56
[$C_{18}H_{33}NO_2Si$]

Two step-procedure - intermediate isolation of the β-ketophosphonate :

A dry 25mL flask equipped with a magnetic stirring bar was charged with 10 mL of anhydrous THF, capped with a rubber septum and flushed with argon. The solvent was cooled to -78 °C in an acetone-dry ice bath. A solution of 1.53 mL (3.07 mmol, 1.2 eq) lithium diisopropylamide (2.0 M in THF) was added with a syringe. Then, a solution of indolizidinone **[58]** (690 mg, 2.56 mmol) in 3 mL of anhydrous THF was transferred into the solution with a syringe over 5 min. The solution was stirred for 30 min at -78 °C and then 0.74 mL (5.12 mmol, 883 mg, 2 eq) of diethyl chlorophosphate (d = 1.2), dissolved in 2mL of anhydrous THF, was slowly added with a syringe. After stirring at -78° to -70 °C for 2.5 hours, a solution of 2.0 mL (4.0 mmol, 1.6 eq) lithium diisopropylamide (2.0 M in THF) was added with a syringe. After 3.5 h stirring at -78 °C, the cooling bath was removed and the excess lithium diisopropylamide was quenched with saturated NH_4Cl solution. The mixture was transferred into a separatory funnel and the phases were separated. The aqueous phase was extracted with diethyl ether and the combined organic extracts were dried over anhydrous Na_2SO_4. After evaporation of the solvent, 1.13 g (100%) of **[76]** was isolated as crude oil. An analytical sample was

[315] Structure could not be undoubtedly determined, some NOE hints indicated that **[75]** had the same structure as **[73]** but with inverted position at C-3b.

purified with flash chromatography on silica gel (hexane / ethyl acetate = 1:1, R_f = 0.1) and pure **[76]** as mixture of both C-3 diastereomers was obtained.

Horner-Wittig reaction :

A dry 50mL flask equipped with a magnetic stirring bar was charged with 10 mL of anhydrous THF, capped with a rubber septum and flushed with argon. The solvent was cooled to -78 °C in an acetone-dry ice bath and 1.13 g (2.56 mmol) of ketophosphonate **[76]** was added. Then, a solution of 1.66 mL (3.32 mmol, 1.3 eq) lithium diisopropylamide (2.0 M in THF) was transferred into the solution with a syringe over 5 min. The solution was stirred for 1 h at -78 °C and then 0.930 mL (10.2 mmol, 738 mg, 4 eq) of isobutyraldehyde (d = 0.794) was slowly added with a syringe. After stirring at -78° overnight, the cooling bath was removed and the excess lithium diisopropylamide was quenched with saturated NH_4Cl solution. The mixture was transferred into a separatory funnel and the phases were separated. The aqueous phase was extracted with diethyl ether and the combined organic extracts were dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude oil was purified with flash chromatography on silica gel (hexane / ethyl acetate = 1:1, R_f = 0.55) and 540 mg (65.2%) of **[77]** were obtained. The (*E*/*Z*) ratio, determined with ^{1}H-NMR spectroscopy was 1:13.5.

one-pot procedure - intermediate formation of β-ketophosphonate and Horner coupling :

In a 50 mL flask, 0.65 mL (1.29 mmol, 1.2 eq) of lithium diisopropylamide (2.0 M in THF) was dissolved in 20 mL of anhydrous THF and flushed with argon. At -78 °C a solution of indolizidinone **[58]** (290 mg, 1.08 mmol) in 2mL of anhydrous THF was slowly added within 5 min. The mixture was stirred for 40 min at -78 °C. Thereafter, a solution of diethyl chlorophosphate (309 µl, 2.152 mmol, 2 eq) in 1 mL of anhydrous THF was added. After stirring for 2 h between -78 °C and -70 °C, another 0.85 mL (1.7 mmol) of 2.0 M lithium diisopropylamide in THF was added and the mixture was stirred for 1 h at -78 °C after completed addition. After TLC control showed complete formation of the β-ketophosphonate, 390 µL (4.3 mmol, 4 eq) of isobutyraldehyde (d = 0.794) was added. After stirring at -78° overnight, the cooling bath was removed and the excess lithium diisopropylamide was quenched with a saturated NH_4Cl solution. The mixture was transferred into a separatory funnel and the phases were separated. The aqueous phase was extracted with diethyl ether and the combined organic extracts were dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude oil was purified with flash chromatography on silica gel (n-hexane / ethyl acetate = 2:1) and 170 mg (49%) of **[77]** were obtained. The *(E/Z)* ratio, determined with ^{1}H-NMR spectroscopy, was 1:12.8.

ketophosphonate [76] :

^{1}H-NMR (500 MHz, $CDCl_3$): [316]

4.25 - 4.00 (m, 8H; H-2 x O-CH_2 and O-$CH_{2'}$), 4.00 - 3.93 (m, 1H; H-5), 3.55 - 3.38 (m, 5H; H-9o, 9u, 9o', 9u', 5'), 3.37 - 3.30 (m, 1H; H-6'), 3.20 - 3.15 (m, 1H; H-6), 3.05 - 2.90 (m, 2H; H-3, 3'), 2.37 - 2.29 (m, 1H; H-4), 2.23 - 2.10 (m, 2H; H-7, 7'), 2.07 - 1.95 (m, 2H; H-4,4'), 1.95 - 1.85 (m, 3H; H-8,8',4'), 1.75 - 1.60 (m, 2H; H-8,8'), 1.50 - 1.40 (m, 1H; H-7'), 1.45 - 1.35 (m, 1H; H-7), 1.30 - 1.25 (m, 12H; H-2x CH_2-CH_3), 0.82 (s, 9H; H-Si- $(CH_3)_3$), 0.81 (s, 9H; H-Si- $(CH_3)_3$), 0.06 (s, 6H; H-Si-CH_3), 0.04 (s, 6H; H-Si-CH_3), 0.01 (s, 6H; H-Si-CH_3), 0.00 (s, 6H; H-Si-CH_3).

^{13}C-NMR (125.8 MHz, $CDCl_3$): [316]

163.25 (s), 163.20 (s), 72.00 (dd, C-5', ^{3}J (^{31}P,^{13}C) = 13 Hz), 69.08 (d, C-5), 64.40 (d, C-6), 63.43 (d, C-6'), 63.20 (dt, O-CH_2, ^{2}J (^{31}P,^{13}C) = 6 Hz), 63.10 (dt, O-CH_2, ^{2}J (^{31}P,^{13}C) = 6 Hz), 61.95 (dt, O-CH_2', ^{2}J (^{31}P,^{13}C) = 7.5 Hz), 61.75 (dt, O-$CH_{2'}$, ^{2}J (^{31}P,^{13}C) = 7.5 Hz), 46.52 (t, C-9), 45.88 (t, C-9'), 40.53 (dd, C-3, ^{1}J (^{31}P,^{13}C) = 135.8 Hz), 40.43 (dd, C-3', ^{1}J (^{31}P,^{13}C) = 138.9 Hz), 32.15 (t, C-7 and C-7' and C-4), 31.83 (t, C-4'), 25.56 (q, Si-C$(CH_3)_3$), 25.50 (q, Si-C$(CH_3)_3$), 22.25 (t, C-8), 22.01 (t, C-8'), 17.77 (s, Si-C$(CH_3)_3$), 16.45 and 16.38 and 16.33 and 16.22 and 16.17 (multiple signals, no definite structure, O-CH_2-CH_3 and O-CH_2-CH_3', 4 sets of doublets from quartet), - 4.35 (q, Si-CH_3), - 4.51 (q, Si-CH_3), - 4.87 (q, Si-CH_3), - 4.91 (q, Si-CH_3).

^{31}P-NMR (202.5 MHz, $CDCl_3$):

22.72, 22.32

IR (solution, $CHCl_3$):

υ (cm^{-1}) = 3019 (m), 2982 (m), 2956 (m), 2931 (m), 1886 (m), 2858 (m), 1636 (s, C=O), 1462 (m), 1443 (m), 1389 (m), 1362 (m), 1252 (s), 1216 (s), 1128 (m), 1103 (m), 1028 (s), 965 (m).

MS (80eV, EI, 90 °C):

m/z (%) 405 (8) [M^{+}], 390 (5) [M^{+} - CH_3], 348 (84) [M^{+} -C_4H_9], 320 (26), 302 (4), 292 (10), 274 (15), 263 (10), 235 (7), 212 (96), 181 (35), 155 (18), 136 (100) [PO $(OEt)_2$], 129 (20), 109 (15), 99 (59), 84 (35), 75 (31), 73 (40), 70 (36).

HRMS (80eV, 80 °C): found 405.21331 calc. 405.21004 (for $C_{18}H_{36}N_1O_5PSi$ [M^{+}]).

[316] Signal assignment was complicated by two C-3 diastereomers (presumably fast equilibration between both isomers) and the presence of ^{1}H,^{31}P and ^{31}P,^{13}C couplings. Assignments based on ^{13}C-^{1}H-HMQC, ^{31}P-^{1}H-HMQC and H,H-COSY spectra.

(*Z*)-alkylidene indolizidinone [77]

$[\alpha]_D^{20}$ = - 61.35° (c = 1.71, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

5.60 - 5.55 (ddd, 1H; H-3a; ^3J (H^{3a},H^{3b}) = 9.5 Hz, ^4J (H^{3a},H^{4o}) = 1.5 Hz, ^4J (H^{3a},H^{4u}) = 1.5 Hz), 3.90 - 3.75 (m, 1H; H-3b), 3.60 - 3.40 (m, 3H; H-9o, 9u, 5o), 3.33 - 3.23 (ddd, 1H; H-6u; ^3J (H^{6u},H^{5o}) = 10 Hz, ^3J (H^{6u},H^{7o}) = 10 Hz, ^3J (H^{6u},H^{7u}) = 5 Hz), 2.53 - 2.45 (m, 2H; H-4o, 4u), 2.25 - 2.15 (m, 1H; H-7u), 2.00 - 1.85 (m, 1H; H-8o), 1.80 - 1.60 (m, 1H; H-8u), 1.52 - 1.38 (m, 1H; H-7o), 1.00 - 0.90 (m, 6H; H-3c), 0.86 (s, 9H; H-Si-C(CH_3)$_3$), 0.05 (s, 3H; H-Si-CH_3), 0.04 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

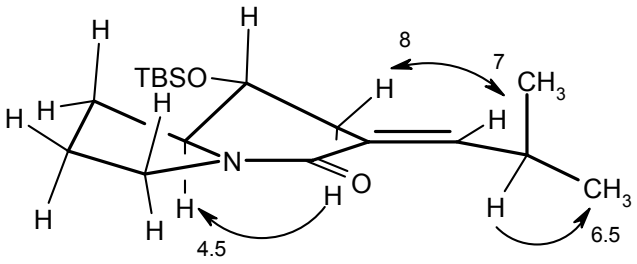
163.7 (s), 150.4 (d, C-3a), 123.6 (s, C-3), 71.9 (d, C-5), 64.2 (d, C-6), 45.6 (t, C-9), 41.9 (t, C-7), 32.0 (t, C-4), 27.2 (d, C-3b), 25.6 (q, Si-C(CH_3)$_3$), 22.81 (q, C-3c), 22.78 (q, C-3c'), 22.5 (t, C-8), 17.8 (s, Si-C(CH_3)$_3$), -4.3 (q, Si-CH_3), -4.8 (q, Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 2955 (s), 2860 (s), 1658 (s), 1620 (s), 1464 (m), 1472 (m), 1445 (s), 1423 (s), 1389 (m), 1378 (m), 1349 (m), 1258 (s), 1146 (m), 1115 (s), 1057 (w), 1023 (w), 1005 (m), 991 (m), 939 (m), 901 (m), 865 (s), 838 (s), 777 (s), 735 (m), 680 (m), 573 (w), 483 (w).

MS (80eV, EI, 90 °C):

m/z (%) 323 (100) [$M^{+\cdot}$], 308 (6) [M^+ - CH_3], 266 (34) [M^+ -C_4H_9], 192 (8), 183 (5), 156 (9), 148 (7), 136 (5), 96 (7), 81 (16), 75 (31), 73 (43), 70 (12).



HRMS (80eV, 90 °C): found 323.22644

calc. 323.228058 (for $C_{18}H_{33}N_1O_2Si$ [M^+])

(*E*)-alkylidene indolizidinone [78]

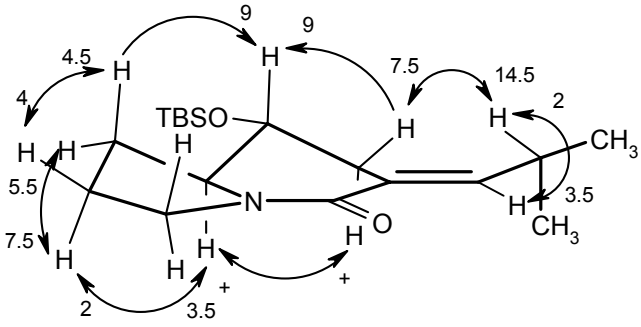
$[\alpha]_D^{20}$ = - 33.4° (c = 0.84, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
6.68 - 6.60 (ddd, 1H; H-3a; ^2J (H^{3a},H^{3b}) = 9 Hz, ^4J (H^{3a},H^{4u}) = 2.5 Hz, ^4J (H^{3a},H^{4o}) = 1.5 Hz), 3.60 - 3.40 (m, 3H; H-5,9o,9u), 3.40 - 3.28 (m, 1H; H-6u), 2.83 - 2.73 (ddd, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 15.5 Hz, ^3J (H^{4o},H^{5o}) = 5 Hz, ^4J (H^{4o},H^{3a}) = 1.5 Hz), 2.58 - 2.43 (m, 1H; H-3b), 2.31 - 2.18 (m, 2H; H-7u, 4u), 2.00 - 1.90 (m, 1H; H-8o), 1.80 - 1.65 (m, 1H; H-8u), 1.53 - 1.40 (m, 1H; H-7o), 1.02 (d, 3H; H-3c; ^3J (H^{3c},H^{3b}) = 5.5 Hz), 0.99 (d, 3H; H-3c'; ^3J ($H^{3c'}$,H^{3b}) = 5.5 Hz), 0.88 (s, 9H; H-Si-C(CH_3)$_3$), 0.08 (s, 3H; H-Si-CH_3), 0.07 (s, 3H; H-Si-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
163.6 (s), 145.5 (d, C-3a), 125.0 (s, C-3), 72.0 (d, C-5), 63.6 (d, C-6), 46.1 (t, C-9), 34.6 (t, C-7), 32.2 (t, C-4), 27.5 (d, C-3b), 25.7 (q, Si-C(CH_3)$_3$), 22.5 (t, C-8), 22.0 (q, C-3c), 21.8 (q, C-3c'), 17.9 (s, Si-C(CH_3)$_3$), -4.2 (q, Si-CH_3), -4.7 (q, Si-CH_3).

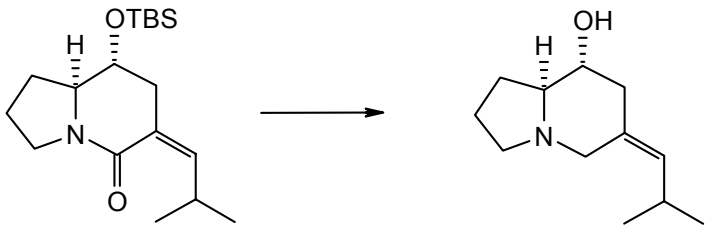
IR (KBr):
υ (cm^{-1}) = 3409 (m), 2958 (s), 2929 (s), 2858 (s), 1664 (s), 1622 (s), 1443 (s), 1425 (s), 1384 (m), 1361 (m), 1337 (m), 1306 (w), 1257 (s), 1208 (m), 1190 (m), 1126 (s), 1102 (s), 1054 (m), 1030 (m), 1006 (m), 985 (m), 928 (m), 900 (m), 881 (m), 864 (m), 837 (s), 777 (s), 733 (s), 681 (m), 670 (s), 563 (m).

MS (80eV, EI, 80 °C):
m/z (%) 323 (14) [$M^{+\cdot}$], 308 (5) [M^+ - CH_3], 266 (100) [M^+ -C_4H_9], 237 (10), 222 (80), 194 (12), 180 (68), 155 (15), 124 (38), 99 (10), 75 (25), 73 (25).



HRMS (80eV, 90 °C): found 323.22838
calc. 323.228058 (for $C_{18}H_{33}N_1O_2Si$ [M^+])

(3Z)-5*R*,6*S*-3-(Isobutylidene)-5-hydroxy-azabicyclo[4.3.0]nonane [79]



[77] 323.56 [$C_{18}H_{33}NO_2Si$] **[79]** 195.31 [$C_{12}H_{21}NO$]

In a 50 mL flask, 80 mg (2.1 mmol, 3.75 eq.) of $LiAlH_4$ was dissolved in 10 mL of anhydrous diethyl ether, flushed with argon and cooled to 0 °C. Then, a solution of anhydrous $AlCl_3$ (93 mg, 0.7 mmol, 1.25 eq) in 2 mL of anhydrous diethyl ether was added with a syringe. After addition, the cooling bath was removed and the mixture was stirred for 1 h at room temperature. During the addition of the $AlCl_3$ solution, the grey colour of $LiAlH_4$ turned to light grey and a grainy suspension was formed. [317]
Then, the mixture was cooled to 0 °C and a solution of indolizidinone **[77]** (180 mg, 0.56 mmol) in 2mL of anhydrous diethyl ether was added. The cooling bath was removed and the mixture was stirred overnight at ambient temperature.[318] For the workup, 0.3 mL of water was carefully added and the formed white precipitate was stirred for 15 min at 0 °C. Then, 0.3 mL of a 2.5 M aqueous KOH was added forming a colourless supernatant. The supernatant was decanted and the precipitate was again extracted with 40 mL of diethyl ether. The combined organic extracts were dried (Na_2SO_4) and the solvent was evaporated. The crude indolizidine was purified on silica gel (methanol / ethyl acetate = 1:4) and 86.5 mg (79.1%) of indolizidine **[79]** were obtained as clear colourless oil.

TLC : methanol / ethyl acetate = 1:3; R_f = 0.25 - 0.37 ($KMnO_4$ reagent, Schlittler).

$[\alpha]_D^{20}$ = - 23.01° (c = 1.45, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
5.08 - 5.00 (d, 1H; H-3a; ^3J (H^{3a},H^{3b}) = 8.5 Hz), 3.75 - 3.67 (d, 1H; H-2o; ^2J (H^{2o},H^{2u}) = 12.5 Hz), 3.35 - 3.25 (ddd, H; H-5o; ^3J (H^{5o},$H^{)}$ = 13 Hz, ^3J (H^{5o},H) = 8.5 Hz, ^3J (H^{5o},H) = 4 Hz), 3.20 - 3.00 (s, 1H; H-OH), 3.05 - 2.95 (ddd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 8.5 Hz, ^2J (H^{9o},H^{8}) = 8.5 Hz, ^2J (H^{9o},H^{8}) = 2 Hz), 2.60 - 2.40 (m, 2H; H-4o, 3b), 2.35 - 2.30 (d, 1H; H-2u; ^2J (H^{2u},H^{2o}) = 12.5 Hz), 2.24 - 2.13 (ddd, 1H; H-9u; ^2J (H^{9u},H^{9o}) = 8.5 Hz, ^2J (H^{9u},H^{8o}) = 8.5 Hz, ^2J (H^{9u},H^{8u}) = 8.5 Hz), 2.05 - 1.45 (m, 5H; H-8o, 8u, 6u, 7u, 7o), 0.94 (d, 3H; H-3c; ^3J (H^{3c},H^{3b}) = 6.5 Hz), 0.87 (d, 3H; H-3c'; ^3J ($H^{3c'}$,H^{3b}) = 6.5 Hz).

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[317] The quality of the $LiAlH_4$ was crucial for a successful reduction, since the exact molar ratio of $LiAlH_4$: $AlCl_3$ (3:1) must be kept. In case that, after addition of $AlCl_3$, no grainy suspension but a sticky precipitate was formed (stirring impossible), the reduction failed.
[318] In other experiments, the reaction was found to be complete within hours.

^{13}C-NMR (67.9 MHz, $CDCl_3$):

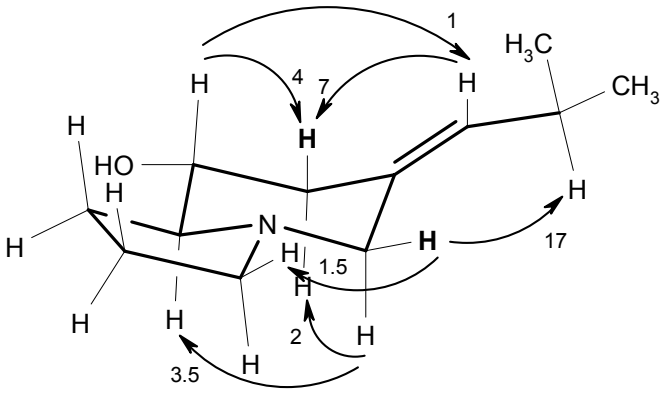
133.9 (d, C-3a), 129.8 (s, C-3), 72.5 (d, C-5), 70.0 (d, C-6), 53.8 (t, C-2), 51.8 (t, C-9), 43.7 (t, C-4), 27.9 (t, C-7), 26.7 (d, C-3b), 23.5 (q, C-3c), 23.1 (q, C-3c'), 21.1 (t, C-8).

IR (solution, $CHCl_3$):

υ (cm^{-1}) = 3618 (m), 2961 (s), 2935 (m), 2870 (m), 2804 (m), 1465 (m), 1447 (m), 1378 (m9, 1215 (w), 1153 (w), 1127 (w), 1095 (w), 1059 (w), 1020 (w).

MS (80eV, EI, 80 °C):

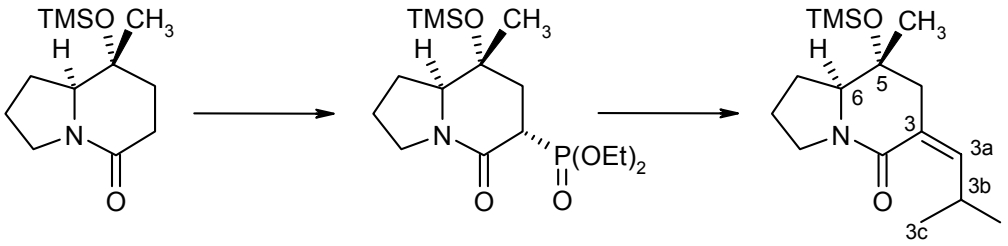
m/z (%) 195 (37) [$M^{+\cdot}$], 180 (18) [M^+ - CH_3], 152 (96) [M^+ -C_3H_7], 134 (12), 111 (12), 108 (17), 98 (16), 82 (17), 70 (100), 55 (31).



HRMS (80eV, 30 °C): found 195.16433 calc. 195.162314 (for $C_{12}H_{21}N_1O_1$ [M^+]).

5*R*,6*S*-3-(Diethoxyphosphinyl)-5-*tert*-butyldimethylsilyloxy-azabicyclo[4.3.0]nonan-2-one [80] and

***(3Z)*-5*R*,6*S*-3-(Isobutylidene)-5-*tert*-butyldimethylsilyloxy-azabicyclo[4.3.0]nonan-2-one [81]**



[61] 241.41 [$C_{12}H_{23}NO_2Si$] **[80]** 377.50 [$C_{16}H_{32}NO_5PSi$] **[81]** 295.50 [$C_{16}H_{29}NO_2Si$]

Preparation of the β-ketophosphonate [80] :

A dry 250mL flask equipped with a magnetic stirring bar was charged with 100 mL of anhydrous THF, capped with a rubber septum and flushed with argon. The solvent was cooled to -78 °C in an acetone-dry ice bath. A solution of 1.566 mL (3.1 mmol, 1.2 eq) lithium diisopropylamide (2.0 M in THF) was added with a syringe. Then, a solution of indolizidinone **[61]** (630 mg, 2.60 mmol) in 5 mL of anhydrous THF was transferred into the solution with a syringe within 5 min. The solution was

stirred for 50 min at -78 °C and then 0.75 mL (5.2 mmol, 900 mg, 2 eq) of diethyl chlorophosphate (d = 1.2) was slowly added with a syringe. After stirring at -78° to -70 °C for 2.5 h, a solution of 2.34 mL (4.7 mmol, 1.8 eq) lithium diisopropylamide (2.0 M in THF) was added with a syringe. After 40 min stirring at -78 °C, the cooling bath was removed and the excess lithium diisopropylamide was quenched with saturated NH_4Cl solution. The mixture was transferred into a separatory funnel and the phases were separated. The aqueous phase was extracted with diethyl ether and the combined organic extracts were dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude oil was purified with flash chromatography on silica gel (methanol / ethyl acetate = 1:9, R_f = 0.3) and 0.73 g (74%) of **[80]** was isolated.

One-pot procedure - intermediate formation of β-ketophosphonate and Horner coupling :

In a 250 mL flask 2.83 mL (5.66 mmol, 1.2 eq) of lithium diisopropylamide (2.0 M in THF) was dissolved in 100 mL of anhydrous THF and flushed with argon. At -78 °C, a solution of indolizidinone **[61]** (1.14 g, 4.72 mmol) in 10 mL of anhydrous THF was slowly added within 5 min. The mixture was stirred for 50 min at -78 °C. Thereafter, a solution of diethyl chlorophosphate (1.36 mL, 9.44 mmol, 2 eq) in 1 mL of anhydrous THF was added. After stirring for 2.5 h between -78 °C and -70 °C, another 4.24 mL (8.5 mmol, 1.8 eq) of 2.0 M lithium diisopropylamide in THF was added and the mixture was stirred for 30 min at -78 °C after completed addition. After TLC control showed complete formation of the β-ketophosphonate, 1.72 mL (18.8 mmol, 4 eq) of isobutyraldehyde (d = 0.794) was added. After stirring first at -65° for 3 h, then overnight at -78 °C, the cooling bath was removed and the excess lithium diisopropylamide was quenched with saturated NH_4Cl solution. The mixture was transferred into a separatory funnel and the phases were separated. The aqueous phase was extracted with diethyl ether and the combined organic extracts were dried with anhydrous Na_2SO_4. After evaporation of the solvent, the crude oil was purified with flash chromatography on silica gel (hexane / ethyl acetate = 2:1) and 600 mg (43%) of **[81]** were obtained. The *(E/Z)* ratio, determined with ^{1}H-NMR spectroscopy, was 1:6.

β-ketophosphonate [80] :

$[\alpha]_D^{20}$ = - 15.17° (c = 1.38, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

4.28 - 3.93 (m, 4H; H-PO-CH_2), 3.50 - 3.30 (m, 3H; H-9o, 9u, 6u), 2.95 - 2.76 (ddd, 1H; H-3o; ^2J (H^{3o},P) = 26.5 Hz, ^3J (H^{3o},H^{4u}) = 11 Hz, ^3J (H^{3o},H^{4o}) = 8 Hz), 2.20 - 2.00 (m, 2H; H-4o, 4u), 2.00 - 1.90 (m, 1H; H-7o), 1.90 - 1.60 (m, 2H; H-8o, 8u), 1.60 - 1.46 (m, 1H; H-7u), 1.30 - 1.20 (m, 6H; H-PO-CH_2-CH_3), 1.05 (s, 3H; H-5-CH_3), 0.05 (s, 9H; H-Si $(CH_3)_3$).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

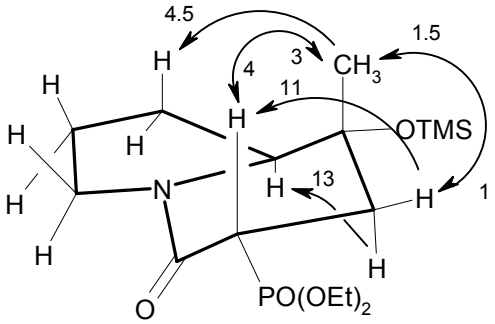
163.1 (dd, C-1, ^2J (^{13}C,^{31}P) = 5 Hz), 72.8 (d, C-5, ^3J (^{13}C,^{31}P) = 13Hz), 66.3 (d, C-6), 63.3 (dt, PO-CH2, ^2J (^{13}C,^{31}P) = 6 Hz), 61.8 (dt, PO-CH2, ^2J (^{13}C,^{31}P) = 7 Hz), 46.7 (t, C-9), 40.8 (dd, C-3, ^1J (^{13}C,^{31}P) = 139 Hz), 38.9 (dt, C-4, ^2J (^{13}C,^{31}P) = 3.5 Hz), 27.3 (t, C-7), 22.1 (t, C-8), 19.5 (q, C-5-CH_3), 16.4 and 16.35 and 16.3 and 16.2 and 16.1 and 16.1 (multiple signals, no definite structure, O-CH_2-CH_3 , 2 sets of doublets from quartet), 2.43 (q, Si-CH_3).

IR (KBr):

υ (cm^{-1}) = 2996 (s), 2884 (m), 1634 (s), 1456 (m), 1441 (m), 1385 (m), 1296 (m), 1284 (m), 1252 (s), 1215 (s), 1161 (s), 1123 (m), 1028 (s), 974 (m), 909 (s), 876 (m), 843 (s).

MS (80eV, EI, 85 °C):

m/z (%) 377 (2) [$M^{+\cdot}$], 362 (4) [M^+ - CH_3], 332 (2), 288 (8), 280 (3), 251 (1), 240 (5), 237 (3), 219 (3), 198 (2), 170 (1), 150 (100), 110 (5), 73 (8).



HRMS (80eV, 80 °C): found 377.17645

calc. 377.17874 (for $C_{16}H_{32}N_1O_5PSi$ [M^+]).

(*Z*)-alkylidene indolizidinone [81] :

$[\alpha]_D^{20}$ = - 35.94° (c = 1.56, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

5.57 - 5.53 (dd, 1H; H-3a; ^3J (H^{3a},H^{3b}) = 9.5 Hz, ^3J (H^{3a},H^{4o}) = 2 Hz), 3.95 - 3.83 (m, 1H; H-3b), 3.55 - 3.43 (m, 3H; H-9o, 9u, 6u), 2.70 - 2.65 (dd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 14 Hz, ^3J (H^{4u},H^{3a}) = 2 Hz), 2.40 - 2.34 (d, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 14.5 Hz), 2.00 - 1.50 (m, 4H; H-7o, 7u, 8o, 8u), 1.08 (s, 5-CH_3), 0.98 - 0.96 (d, 3H; H-3c; ^3J (H^{3c},H^{3b}) = 3.5 Hz), 0.96 - 0.94 (d, 3H; H-3c'; ^3J ($H^{3c'}$,H^{3b}) = 3.5 Hz), 0.12 (s, 9H; Si (CH_3)$_3$).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

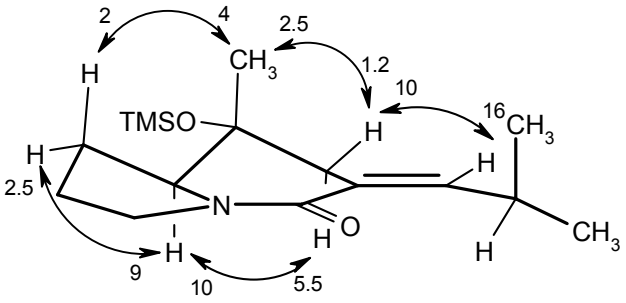
163.6 (s), 150.5 (d, C-3a), 124.3 (s, C-3), 72.7 (s, C-5), 67.4 (d, C-6), 49.3 (t, C-9), 45.6 (t, C-4), 27.2 (t, C-7), 27.1 (d, C-3b), 22.9 (q, C-3c), 22.8 (q, C-3c'), 22.3 (t, C-8), 20.3 (q, C-5-Me), 2.6 (q, Si (CH_3)$_3$).

IR (solution, $CHCl_3$):

υ (cm^{-1}) = 3019 (s), 2968 (w), 2863 (w), 1651 (w), 1602 (w), 1522 (w), 1429 (w), 1223 (s), 1210 (s), 1158 (w), 1125 (w), 1017 /w), 929 (w), 844 (w).

MS (80eV, EI, 50 °C):

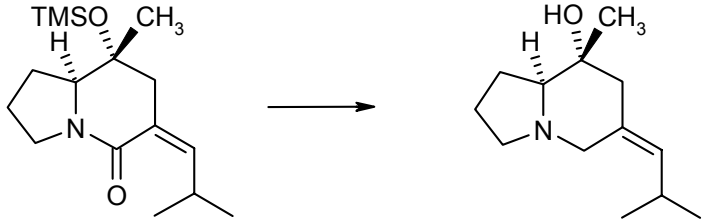
m/z (%) 295 (100) [$M^{+\cdot}$], 280 (14) [M^+ - CH_3], 252 (40) [M^+ -C_3H_7], 224 (15), 223 (14), 183 (20), 155 (9), 143 (7), 142 (6), 96 (9), 81 (13), 75 (17), 73 (54), 70 (27).



HRMS (80eV, 90 °C): found 295.19488

calc. 295.19676 (for $C_{16}H_{29}N_1O_2Si$ [M^+]).

(3Z)-5*R*,6*S*-3-(Isobutylidene)-5-hydroxy-5-methyl-azabicyclo[4.3.0]nonane [82] 5-(*epi*)-Pumiliotoxin 209 F



[81] 295.50 [$C_{16}H_{29}NO_2Si$] **[82]** 209.33 [$C_{13}H_{23}NO$]

In a 100 mL flask, 329 mg (8.67 mmol, 7.5 eq.) of $LiAlH_4$ was dissolved in 40 mL of anhydrous diethyl ether, flushed with argon and cooled to 0 °C. Then, a solution of anhydrous $AlCl_3$ (385 mg, 2.89 mmol, 2.5 eq) in 10 mL of anhydrous diethyl ether was added with a syringe. After addition, the cooling bath was removed and the mixture was stirred for 30 min at room temperature. During the addition of the $AlCl_3$ solution, the grey colour of $LiAlH_4$ turned to light grey and a grainy suspension was formed. [317]

Then, the mixture was cooled to 0 °C and a solution of indolizidinone **[81]** (342 mg, 1.15 mmol) in 2mL of anhydrous diethyl ether was added. The cooling bath was removed and the mixture was stirred for 15 min at ambient temperature.

For the workup, 0.5 mL of water was carefully added and the formed white precipitate was stirred for 15 min at 0 °C. Then, 0.5 mL of 2.5 M aqueous KOH was added and the volume of the precipitate decreased, forming a colourless supernatant. The supernatant was decanted and the precipitate was extracted with 40 mL of diethyl ether. The combined organic extracts were dried (Na_2SO_4) and the

solvent was evaporated. The crude indolizidine was purified on silica gel (methanol / ethyl acetate = 1:9) and 192.6 mg (79.6%) of **5-*epi*-pumiliotoxin 209 [82]** were obtained as colourless crystals (mp 73-77 °C).

TLC : methanol / ethyl acetate = 1:3; R_f = 0.25 - 0.37 ($KMnO_4$ reagent, Schlittler).

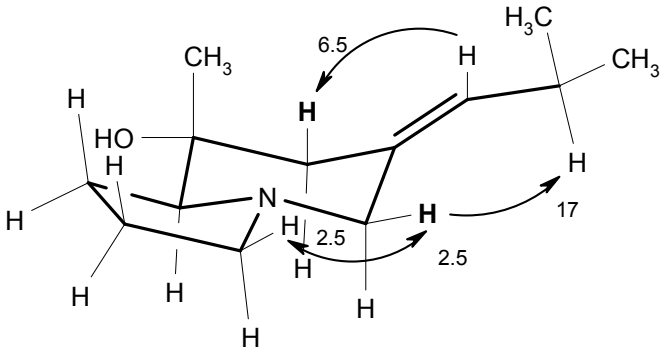
$[\alpha]_D^{20}$ = - 20.58° (c = 1.38, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
5.02 - 4.95 (d, 1H; H-3a; ^2J (H^{3a},H^{3b}) = 9.5 Hz), 3.70 - 3.65 (d, 1H; H-2o; ^2J (H^{2o},H^{2u}) = 12.5 Hz), 3.06 - 2.97 (ddd, 1H; H-9o; ^2J (H^{9o},H^{9u}) = 8.5 Hz, ^3J (H^{9o},H^{8u}) = 8.5 Hz, ^3J (H^{9o},H^{8o}) = 2 Hz), 2.58 - 2.42 (m, 1H; H-3b), 2.37 - 2.30 (d, 1H; H-2u; ^2J (H^{2u},H^{2o}) = 12.5 Hz), 2.20 - 2.00 (m, 3H; H-9u, 4o, 4u), 1.85 - 1.50 (m, 5H; H-8o, 8u, 7o, 7u, 6u), 1.08 (s, 3H; 5-CH_3), 0.92 - 0.90 (d, 3H; H-3c; ^3J (H^{3c},H^{3b}) = 6.5 Hz), 0.87 - 0.85 (d, 3H; H-3c'; ^3J ($H^{3c'}$,H^{3b}) = 6.5 Hz).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
133.95 (d, C-3a), 130.2 (s, C-3), 72.8 (d, C-6), 71.3 (s, C-5), 54.7 (t, C-2), 52.8 (t, C-9), 50.4 (t, C-4), 26.7 (q, 5-CH_3), 23.8 (t, C-7), 23.4 (q, C-3c), 23.3 (q, C-3c'), 20.9 (t, C-8), 20.4 (d, C-3b).

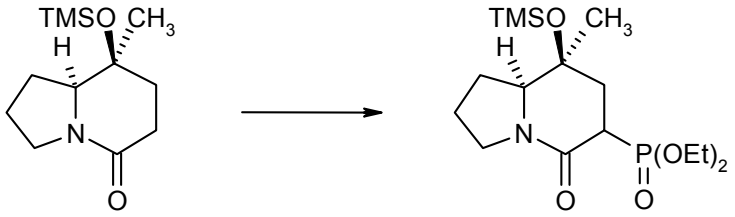
IR (solution, $CHCl_3$):
υ (cm^{-1}) = 3019 (m), 2961 (m), 2880 (w), 2795 (w), 1637 (w), 1519 (w), 1464 (m), 1429 (w), 1382 (w), 1216 (s, C-O), 1149 (w), 1106 (m), 912 (s).

MS (80eV, EI, 30 °C):
m/z (%) 209 (42) [$M^{+\cdot}$], 194 (18) [M^+ - CH_3], 176 (10), 166 (99) [M^+ -C_3H_7], 148 (11), 136 (6), 108 (10), 96 (11), 84 (35), 70 (100), 55 (12).



HRMS (80eV, 30 °C): found 209.17488
calc. 209.177965 (for $C_{13}H_{23}N_1O_1$ [M^+]).

5*S*,6*S*-3-(Diethoxyphosphinyl)-5-trimethylsilyloxy-5-methyl-azabicyclo[4.3.0]nonan-2-one [83]



[62] 241.41 [$C_{12}H_{23}NO_2Si$] **[83]** 377.50 [$C_{16}H_{32}NO_5PSi$]

A dry 250mL flask equipped with a magnetic stirring bar was charged with 100 mL of anhydrous THF, capped with a rubber septum and flushed with argon. The solvent was cooled to -78 °C in an acetone-dry ice bath. A solution of 0.82 mL (1.64 mmol, 1.2 eq) lithium diisopropylamide (2.0 M in THF) was added with a syringe. Then, a solution of indolizidinone **[62]** (350 mg, 1.45 mmol) in 2 mL of anhydrous THF was transferred into the solution with a syringe within 5 min. The solution was stirred for 50 min at -78 °C and then a solution of diethyl chlorophosphate (0.39 mL, 2.73 mmol, 471 mg, 2 eq) in 1.5 mL of diethyl ether was slowly added with a syringe. After stirring at -78° to -70 °C for 2.5 hours, a solution of 1.23 mL (2.45 mmol, 1.8 eq) lithium diisopropylamide (2.0 M in THF) was added with a syringe. After stirring for 40 min at -78 °C, the cooling bath was removed and the excess lithium diisopropylamide was quenched with saturated NH_4Cl solution. The mixture was transferred into a separatory funnel and the phases were separated. The aqueous phase was extracted with diethyl ether and the combined organic extracts were dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude oil was purified by flash chromatography on silica gel (methanol / ethyl acetate = 1:9, R_f = 0.25) and 533.7 mg (97.5%) of **[83]** was isolated.

$[\alpha]_D^{20}$ = - 10.7 ° (c = 1.58, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):

4.23 - 3.98 (m, 4H; PO-CH_2), 3.45 - 3.20 (m, 3H; H-9o, 9u, 6u), 3.02 - 2.85 (ddd, 1H; H-3o; ^2J (H^{3o},^{31}P) = 25.5 Hz, ^3J (H^{3o},H^{4u}) = 10 Hz, ^3J (H^{3o},H^{4o}) = 8 Hz), 2.05 - 1.93 (m, 2H; H-7, 4), 1.85 - 1.45 (m, 4H; H-4', 7', 8, 8'), 1.30 - 1.15 (m, 9H; 5-CH_3, $POCH_2$-CH_3), 0.02 (s, 9H; Si $(CH_3)_3$).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

163.9 (d, C-1, ^2J (^{13}C,^{31}P) = 4.5 Hz), 70.5 (d, C-5, ^3J (^{13}C,^{31}P) = 9.5 Hz), 66.9 (d, C-6), 63.1 (dt, PO-CH_2 , ^2J (^{13}C,^{31}P) = 7 Hz), 61.5 (dt, PO-CH_2 , ^2J (^{13}C,^{31}P) = 6 Hz), 46.5 (t, C-9), 39.0 (dd, C-3, ^1J (^{13}C,^{31}P) = 139 Hz), 37.3 (dt, C-4, ^2J (^{13}C,^{31}P) = 3.5 Hz), 26.3 (t, C-7), 25.5 (q, C-5-CH_3), 22.0 (t, C-8),

16.24 (qd, $POCH_2$-CH_3, ^3J (^{13}C,^{31}P) = 6 Hz), 16.10 (qd, $POCH_2$-CH_3, ^3J (^{13}C,^{31}P) = 6 Hz), 2.00 (q, Si $(CH_3)_3$).

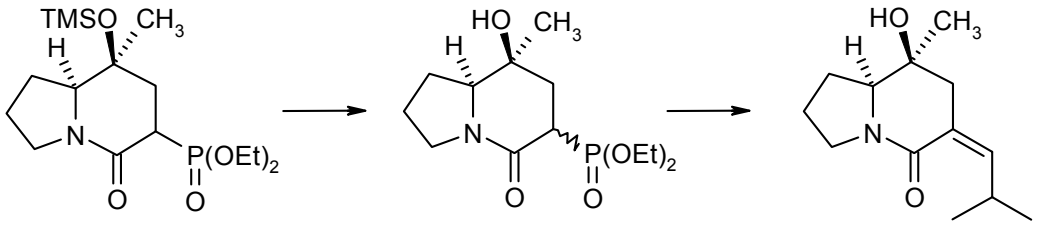
IR (solution, $CHCl_3$):
υ (cm^{-1}) = 2980 (s), 2953 (s), 2909 (m), 2881 (m), 1633 (s, C=O), 1460 (s), 1393 (m), 1378 /m), 1364 (m), 1340 (w), 1319 (w), 1295 (m), 1253 (s, C-O), 1217 (s, C-O), 1151 (m), 1130 (m), 1050 (s), 1028 (s), 979 (s), 969 (s).

MS (80eV, EI, 50 °C):
m/z (%) 377 (22) [$M^{+\cdot}$], 362 (10) [M^+ - CH_3], 288 (38), 286 (22), 241 (15), 240 (9), 219 (6), 198 (7), 170 (8), 153 (20), 150 (33), 126 (79), 109 (22), 98 (88), 80 (100), 75 (20), 73 (32), 70 (34).

HRMS (80eV, 40 °C): found 377.17682 calc. 377.17874 (for $C_{16}H_{32}N_1O_5PSi$ [M^+]).

5*S*,6*S*-3-(Diethoxyphosphinyl)-5-hydroxy-5-methyl-azabicyclo[4.3.0]nonan-2-one [84] and

(3Z)-5*S*,6*S*-3-(Isobutylidene)-5-hydroxy-5-methyl-azabicyclo[4.3.0]nonan-2-one [85]



[83] 377.50 [$C_{16}H_{32}NO_5PSi$] **[84]** 305.31 [$C_{13}H_{24}NO_5P$] **[85]** 223.32 [$C_{13}H_{21}NO_2$]

In a 10 mL flask, 49.0 mg (0.13 mmol) of ketophosphonate **[83]** was dissolved in 2 mL of a 1 M methanolic HCl solution. After stirring the clear solution for 1 h at room temperature, the solvent was evaporated under reduced pressure and 32.5 mg (84%) of hydroxy ketophosphonate **[84]** was obtained. Preceding the Horner reaction, the ketophosphonate **[84]** was dissolved in 2 mL of anhydrous THF and stirred over molecular sieves (4Å) for 30 min.
In a 10 mL flask, 136 µL (0.27 mmol, 2.5 eq) of lithium diisopropylamide (2.0 M in THF) was dissolved in 2 mL of anhydrous THF and flushed with argon. At -78 °C a solution of the ketophosphonate **[84]** in anhydrous THF was slowly added within 5 min. The mixture was stirred for 30 min at -78 °C and then 40µl (0.4 mmol, 4 eq) of isobutyraldehyde (d = 0.794) was added. After stirring at -78° for 2.5 h, the cooling bath was removed and the excess lithium diisopropylamide was quenched with saturated NH_4Cl solution. The mixture was transferred into a separatory funnel and the

phases were separated. The aqueous phase was extracted with diethyl ether and the combined organic extracts were dried over anhydrous Na_2SO_4. After evaporation of the solvent, 10.0 mg (42%) of the crude **[85]** was obtained as colourless oil. The (*E*/*Z*) ratio, determined with ^{1}H-NMR spectroscopy, was 1:10. The crude product was purified on silica gel (ethyl acetate / methanol = 3:1).

ketophosphonate [84]

^{1}H-NMR (270 MHz, $CDCl_3$): [319]
4.40 - 4.00 (m, 4 H, PO-CH_2), 3.60 - 3.40 (m, 3H, 9o, 9u, 6), 3.40 and 3.05 (m, 2xH-3), 2.40 - 1.60 (m, 6H, H-4,7,8), 1.40 - 1.30 (m, 9H, 5-CH_3 and $POCH_2$-CH_3).

^{13}C-NMR (67.9 MHz, $CDCl_3$): [319]
166.3 (s, C=O), 67.3 (dd, C5 and C-5', ^3J (^{13}C,^{31}P) = 8.5 Hz), 67.0 (d, C-6'), 66.8 (d, C-6), 64.8 (dt, $POCH_2$', ^2J (^{13}C,^{31}P) = 6 Hz), 63.7 (dt, $POCH_2$, ^2J (^{13}C,^{31}P) = 7 Hz), 63.9 (dt, $POCH_2$, ^2J (^{13}C,^{31}P) = 7 Hz), 62.2 (dt, $POCH_2$', ^2J (^{13}C,^{31}P) = 7 Hz), 47.7 (t, C-9), 46.5 (t, C-9'), 39.3 (dd, C-3', ^1J (^{13}C,^{31}P) = 135.5 Hz), 38.3 (dd, C-3, ^1J (^{13}C,^{31}P) = 137.5 Hz), 36.6 (dt, C-4, ^2J (^{13}C,^{31}P) = 3 Hz), 36.3 (dt, C-4', ^2J (^{13}C,^{31}P) = 3.5 Hz), 26.3 (t, C-7'), 26.2 (q, C-5-CH_3'), 26.1 (t, C-7), 25.6 (q, C-5-CH_3), 22.2 (t, C-8), 21.8 (t, C-8'), 16.4 and 16.3 and 16.2 and 16.1 (q, 2x$POCH_2$-CH_3 and 2x $POCH_2$'-CH_3').

MS (80eV, EI, 120 °C):
m/z (%) 305 (14) [$M^{+\cdot}$], 288 (6) [M^+ - OH], 265 (5), 260 (19), 234 (5), 222 (6), 208 (5), 195 (5), 168 (5), 155 (12), 151 (100), 136 (18), 127 (8), 111 (16), 99 (13), 96 (9), 83 (24), 70 (47).

HRMS (80eV, 120 °C): found 305.13687 calc. 305.139212 (for $C_{13}H_{24}N_1O_5P$ [M^+]).

(*Z*)-alkylidene indolizidinone [85]

$[\alpha]_D^{20}$ = - 68.68° (c = 0.91, $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
5.65 - 5.60 (dd, 1H; H-3a; ^3J (H^{3a},H^{3b}) = 9.5 Hz, ^4J (H^{3a},H^{4u}) = 2 Hz), 3.92 - 3.80 (m, 1H; H-3b), 3.55 - 3.45 (m, 2H; H-9o, 9u), 3.43 - 3.37 (dd, 1H; H-6u; ^3J (H^{6u},H^{7o}) = 9.5 Hz, ^3J (H^{6u},H^{7u}) = 5.5 Hz), 2.65 - 2.60 (dd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 14.5 Hz, ^4J (H^{4u},H^{3a}) = 2.5 Hz), 2.42 - 2.37 (d, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 14.5 Hz), 2.0 - 1.70 (m, 4H; H-8o, 8u, 7o, 7u), 1.24 (s, 3H; H-5-CH_3), 1.00 - 0.95 (m, 6H; H-3c, 3c').

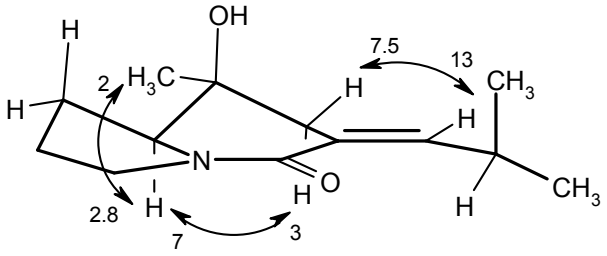
[319] Compound **[84]** consisted of two C-3 diastereomers (3:1 acc. ^{13}C-NMR) , described with C and C'.

^{13}C-NMR (67.9 MHz, $CDCl_3$):

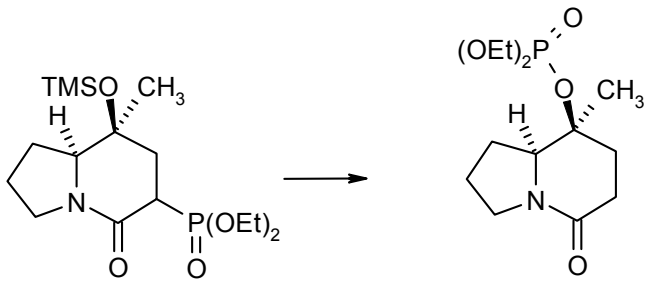
163.7 (s), 152.8 (d, C-3a), 122.3 (s, C-3), 67.7 (s, C-5), 66.5 (d, C-6), 46.9 (t, C-9), 45.5 (t, C-4), 27.5 (d, C-3b), 26.1 (t, C-7), 25.2 (q, C-5-CH_3), 22.9 (q, C-3c), 22.7 (q, C-3c'), 22.1 (t, C-8).

IR (solution, $CHCl_3$):

υ (cm^{-1}) = 2977 (m), 2932 (w), 2899 (w), 2866 (w), 1729 (w), 1653 (m), 1604 (m), 1468 (m), 1451 (m), 1437 (m), 1381 (m), 1295 (w), 1252 (w), 1099 (w), 919 (s), 899 (s), 751 (s), 718 (s), 651 (s).



5*S*,6*S*-5-Diethoxyphosphoryl-5-methyl-azabicyclo[4.3.0]nonan-2-one [86]



[83] 377.50 [$C_{16}H_{32}NO_5PSi$] **[86]** 305.31 [$C_{13}H_{24}NO_5P$]

To a solution of ketophosphonate **[83]** (50mg) in 2 mL of THF was added TBAF trihydrate (50 mg) and the solution was stirred for 10 min at room temperature. Thereafter, solvent was evaporated and the crude oil was filtered over a short silica gel column. The ^{13}C and ^{1}H-NMR spectrum undoubtedly showed the presence of compound **[86]** that was earlier isolated from the two step desilylation-Horner reaction procedure and that origin should be clarified. [320]

^{1}H-NMR (270 MHz, $CDCl_3$):

4.20 - 3.90 (m, 4 H, PO-CH_2), 3.50 - 3.40 (m, 2H, 9o, 9u), 3.36 - 3.29 (dd, 1H, H-6, ^{3}J (H^6,H^7) = 9.5 Hz, ^{3}J (H^6,H^7) = 4 Hz), 2.60 and 2.30 (m, 2H, H-3), 2.00 - 1.60 (m, 6H, H-4,7,8), 1.50 (s, 3H, 5-CH_3), 1.30 - 1.10 (m, 6H, $POCH_2$-CH_3).

[320] In this reaction, 67% of **[86]** were isolated after a desilylation with TBAF and Horner reaction.

^{13}C-NMR (67.9 MHz, $CDCl_3$):
168.5 (s), 79.3 (d, C-5, ^2J (^{13}C,^{31}P) = 6 Hz), 66.70 (dd, C-6, ^3J (^{13}C,^{31}P) = 11Hz), 63.7 (dt, PO-CH_2, ^2J (^{13}C,^{31}P) = 6 Hz), 63.6 (dt, PO-CH_2, ^2J (^{13}C,^{31}P) = 6 Hz), 45.7 (t, C-9), 33.0 (t, C-3), 27.8 (t, C-7), 26.4 (t, C-4), 23.5 (q, C-5-CH_3), 21.7 (t, C-8), 16.0 and 15.93 (q, PO-CH_2CH_3).

IR (KBr):
υ (cm^{-1}) = 3019 (s), 2987 (s), 2888 (w), 1627 (m), 1521 (w), 1471 (w), 1416 (w), 1265 (m), 1215 (s), 1035 (s).

MS (80eV, EI, 120 °C):
m/z (%) 305 (10) [$M^{+\cdot}$], 288 (3), 260 (1), 223 (1), 208 (1), 194 (4), 155 (11), 151 (100), 136 (18), 127 (8), 111 (16), 99 (13), 96 (9), 83 (24), 70 (47).

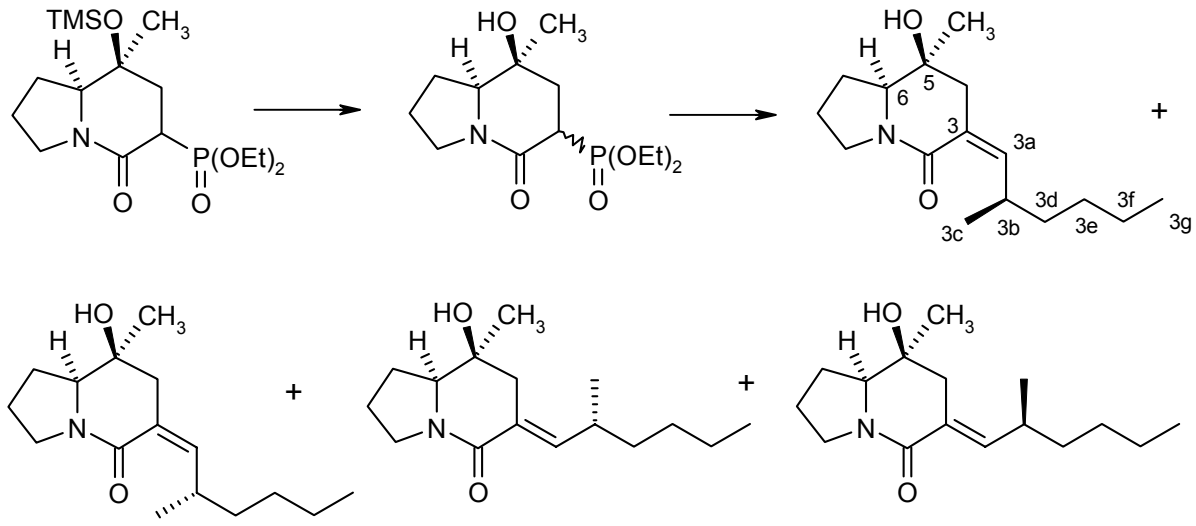
HRMS (80eV, 120 °C): found 305.13754 calc. 305.139212 (for $C_{13}H_{24}N_1O_5P$ [M^+]).

(3*Z*)-5*S*,6*S*-3-(*R*-2-Methyl-hexylidene)-5-hydroxy-5-methyl-azabicyclo[4.3.0]nonan-2-one [87] and

(3*Z*)-5*S*,6*S*-3-(*S*-2-Methyl-hexylidene)-5-hydroxy-5-methyl-azabicyclo[4.3.0]nonan-2-one [88] and

(3*E*)-5*S*,6*S*-3-(*R*-2-Methyl-hexylidene)-5-hydroxy-5-methyl-azabicyclo[4.3.0]nonan-2-one [89] and

(3*E*)-5*S*,6*S*-3-(*S*-2-Methyl-hexylidene)-5-hydroxy-5-methyl-azabicyclo[4.3.0]nonan-2-one [90]



[83] 377.50 [$C_{16}H_{32}NO_5PSi$] **[84]** 305.31 [$C_{13}H_{24}NO_5P$] **[87-90]** 265.40 [$C_{16}H_{27}NO_2$]

In a 50 mL flask, 433.0 mg (0.13 mmol) of ketophosphonate **[83]** was dissolved in 10 mL of a 1 M methanolic HCl solution. After stirring of the clear solution for 1 h at room temperature, the solvent was evaporated under reduced pressure. The residue was dissolved in dichloromethane, filtered through a plug of silica gel (ethyl acetate / methanol = 3:1) and 359 mg (100%) of hydroxy ketophosphonate **[84]** was obtained.

In a 50 mL flask, 1.36 mL (2.7 mmol, 2.1 eq) of lithium diisopropylamide (2.0 M in THF) was dissolved in 15 mL of anhydrous THF and flushed with argon. At -78 °C, a solution of the ketophosphonate **[84]** in 2 mL of anhydrous THF was slowly added within 5 min. The mixture was stirred for 30 min at -65 °C and then 648µl (4.5 mmol, 4 eq) (R)-2-methylhexanal (d = 0.804) **[70]** was added. After stirring at -78° for 4 h, the cooling bath was removed and the excess lithium diisopropylamide was quenched with saturated NH_4Cl solution. The mixture was transferred into a separatory funnel and the phases were separated. The aqueous phase was extracted with diethyl ether and the combined organic extracts were dried over anhydrous Na_2SO_4. After evaporation of the

solvent, the crude oil was purified on a silica gel column (ethyl acetate / methanol = 9:1). The diastereomers were separated by HPLC (10% isopropanol/hexane, 32x110 mm, Nucleosil 50-5, UV = 254nm, flow 64ml/min) yielding 4 isomers :

56.3 mg (16.4%) of **[88]** with r.t. 2.7 min
97.9 mg (28.5%) of **[87]** with r.t. 3.3 min
14.2 mg (4.1%) of **[89]** with r.t. 4.5 min
16.2 mg (4.7%) of **[90]** with r.t. 5.8 min.

(*Z*)-alkylidene indolizidinone [87]

$[\alpha]_D^{20}$ = - 67.58° (c = 1.644, $CHCl_3$).

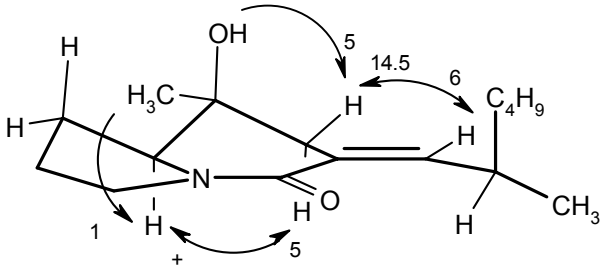
mp = 135-140 °C.

^{1}H-NMR (270 MHz, $CDCl_3$):
5.64 - 5.60 (dd, 1H; H-3a; ^3J (H^{3a},H^{3b}) = 10 Hz, ^{4u}J (H^{3a},H^4) = 2 Hz), 3.87 - 3.72 (m, 1H; H-3b), 3.58 - 3.51 (dd, 2H; H-9o, 9u; ^2J ($H^{9o,9u}$,H^9) = 8.5 Hz, ^3J ($H^{9o,9u}$,H^8) = 5 Hz), 3.47 - 3.40 (dd, 1H; H-6u; ^3J (H^{6u},H^{7o}) = 9.5 Hz, ^3J (H^{6u},H^{7u}) = 5.5 Hz), 2.73 - 2.63 (dd, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 14.5 Hz, ^3J (H^{4u},H^{3a}) = 2 Hz), 2.47 - 2.38 (d, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 15 Hz), 2.04 - 1.65 (m, 4H; H-7o, 7u, 8o, 8u), 1.36 - 1.18 (m, 6H; H-3d, 3e, 3f), 0.98 - 0.93 (d, 3H; H-3c; ^3J (H^{3c},H^{3b}) = 6.5 Hz), 0.89 - 0.80 (t, 3H; H-3g; ^3J (H^{3g},H^{3f}) = 6.5 Hz).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
163.7 (s, C=O), 152.4 (d, C-3a), 122.8 (s, C-3), 67.7 (s, C-5), 66.5 (d, C-6), 47.0 (t, C-9), 45.5 (t, C-4), 37.2 (t, C-3c), 32.5 (d, C-3b), 29.6 (t, C-3d), 26.1 (t, C-7), 25.2 (q, C-5-CH_3), 22.9 (t, C-3e), 22.1 (t, C-8), 20.8 (q, C-3c), 14.08 (q, C-3g).

IR (solution, $CHCl_3$):
υ (cm^{-1}) = 3019 (s), 1650 (w), 1600 (w), 1522 (w), 1472 (w), 1425 (w), 1215 (s), 1031 (w), 929 (w).

MS (80eV, EI, 50 °C):
m/z (%) 265 (73) [$M^{+\cdot}$], 250 (3) [M^+ - CH_3], 236 (10) [M^+ - C_2H_5], 222 (100) [M^+ - C_3H_7], 208 (6) [M^+ -C_4H_9], 180 (8), 169 (27), 153 (19), 126 (72), 109 (15), 108 (15), 98 (66), 80 (61), 70 (24).



HRMS (80eV, 50 °C): found 265.20523
calc. 265.204179 (for $C_{16}H_{27}N_1O_2$ [M^+]).

(*Z*)-alkylidene indolizidinone [88]

$[\alpha]_D^{20}$ = + 55.02° (c = 1.79, $CHCl_3$).

mp = 85 °C.

^{1}H-NMR (270 MHz, $CDCl_3$):

5.60 - 5.54 (d, 1H; H-3a; ^3J (H^{3a},H^{3b}) = 10 Hz), 3.80 - 3.65 (m, 1H; H-3b), 3.53 - 3.45 (m, 2H; H-9o, 9u), 3.43 - 3.35 (dd, 1H; H-6u; ^3J (H^{6u},H^{7o}) = 9.5 Hz, ^3J (H^{6u},H^{7u}) = 5.5 Hz), 2.65 - 2.60 (d, 1H; H-4u; ^2J (H^{4u},H^{4o}) = 14.5 Hz), 2.43 - 2.38 (d, 1H; H-4o; ^2J (H^{4o},H^{4u}) = 15 Hz), 2.04 - 1.65 (m, 4H; H-7o, 7u, 8o, 8u), 1.30 - 1.15 (m, 6H; H-3d, 3e, 3f), 0.95 - 0.90 (d, 3H; H-3c; ^3J (H^{3c},H^{3b}) = 6.5 Hz), 0.85 - 0.79 (t, 3H; H-3g; ^3J (H^{3g},H^{3f}) = 6.5 Hz).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

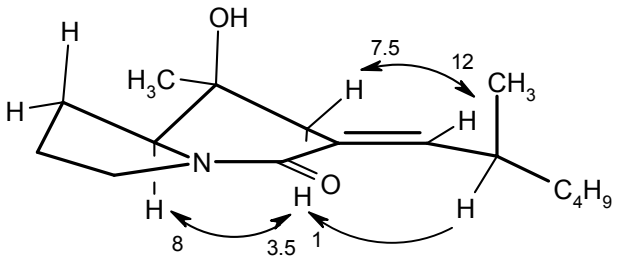
163.7 (s, C=O), 151.9 (d, C-3a), 123.0 (s, C-3), 67.5 (s, C-5), 66.5 (d, C-6), 47.0 (t, C-9), 45.4 (t, C-4), 37.2 (t, C-3c), 32.5 (d, C-3b), 29.6 (t, C-3d), 26.0 (t, C-7), 25.1 (q, C-5-CH_3), 22.8 (t, C-3e), 22.0 (t, C-8), 20.4 (q, C-3c), 13.9 (q, C-3g).

IR (solution, $CHCl_3$):

υ (cm^{-1}) = 3019 (s), 2977 (m), 2929 (m), 1653 (m), 1604 (m), 1523 (w), 1450 (m), 1437 (m), 1426 (m), 1294 (m), 1265 (s), 1215 (s), 1046 (m), 929 (w).

MS (80eV, EI, 50 °C):

m/z (%) 265 (59) [M^+], 250 (3) [M^+ - CH_3], 236 (7) [M^+ - C_2H_5], 222 (100) [M^+ - C_3H_7], 208 (6) [M^+ - C_4H_9], 180 (4), 169 (29), 81 (7), 70 (22).



HRMS (80eV, 50 °C): found 265.20733

calc. 265.204179 (for $C_{16}H_{27}N_1O_2$ [M^+]).

(*E*)-alkylidene indolizidinone [89]

$[\alpha]_D^{20}$ = - 65.1° (c = 1.40, $CHCl_3$).

mp = 150-153 °C.

^{1}H-NMR (270 MHz, $CDCl_3$):

6.81 - 6.73 (dd, 1H; H-3a; ^3J (H^{3a},H^{3b}) = 10 Hz, ^4J (H^{3a},H^{4u}) = 2 Hz), 3.63 - 3.40 (m, 3H; H-9o, 9u, 6u), 2.78 - 2.70 (d, 1H; H-4o; ^2J (H^{4o},H^{4o}) = 16 Hz), 2.43 - 2.38 (d, 1H; H-4u; ^2J (H^{4u},H^{4u}) = 16 Hz, ^4J (H^{4u},H^{3a}) = 2.5 Hz), 2.48 - 2.30 (m, 1H; H-3b), 2.04 - 1.70 (m, 4H; H-7o, 7u, 8o, 8u), 1.40 - 1.20 (m, 6H; H-3d, 3e, 3f), 0.98 - 0.92 (d, 3H; H-3c; ^3J (H^{3c},H^{3b}) = 6.5 Hz), 0.88 - 0.80 (t, 3H; H-3g; ^3J (H^{3g},H^{3f}) = 6.5 Hz).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

163.7 (s, C=O), 147.3 (d, C-3a), 124.3 (s, C-3), 67.7 (s, C-5), 65.7 (d, C-6), 46.1 (t, C-9), 39.5 (t, C-4), 36.5 (t, C-3c), 32.7 (d, C-3b), 29.6 (t, C-3d), 26.4 (t, C-7), 25.3 (q, C-5-CH_3), 22.8 (t, C-3e), 22.2 (t, C-8), 19.7 (q, C-3c), 14.0 (q, C-3g).

IR (solution, $CHCl_3$):

υ (cm^{-1}) = 3019 (s), 2976 (m), 2895 (w), 1601 (w), 1521 (w), 1476 (w), 1420 (w), 1215 (s), 1046 (m), 929 (w).

MS (80eV, EI, 80 °C):

m/z (%) 265 (53) [M^+], 236 (7) [M^+ - C_2H_5], 222 (100) [M^+ - C_3H_7], 208 (6) [M^+ -C_4H_9], 194 (5), 180 (20), 169 (17), 138 (15), 126 (8), 92 (13), 86 (23), 70 (88).

HRMS (80eV, 80 °C): found 265.20654 calc. 265.204179 (for $C_{16}H_{27}N_1O_2$ [M^+]).

(*E*)-alkylidene indolizidinone [90]

$[\alpha]_D^{20}$ = + 38.1° (c = 1.63, $CHCl_3$).

mp = 105-110 °C.

^{1}H-NMR (270 MHz, $CDCl_3$):

6.80 - 6.70 (ddd, 1H; H-3a; ^3J (H^{3a},H^{3b}) = 10 Hz, ^4J (H^{3a},H^{4u}) = 3 Hz, ^4J (H^{3a},H^4) = 1.5 Hz), 3.62 - 3.42 (m, 3H; H-9o, 9u, 6u), 2.79 - 2.70 (d, 1H; H-4o; ^2J (H^{4o},H^{4o}) = 16 Hz), 2.39 - 2.30 (d, 1H; H-4u; ^2J (H^{4u},H^{4u}) = 16 Hz, ^4J (H^{4u},H^{3a}) = 2 Hz), 2.43 - 2.28 (m, 1H; H-3b), 2.05 - 1.75 (m, 4H; H-7o, 7u, 8o, 8u), 1.40 - 1.10 (m, 6H; H-3d, 3e, 3f), 1.01 - 0.97 (d, 3H; H-3c; ^3J (H^{3c},H^{3b}) = 6.5 Hz), 0.88 - 0.80 (t, 3H; H-3g; ^3J (H^{3g},H^{3f}) = 6.5 Hz).

^{13}C-NMR (67.9 MHz, $CDCl_3$):

163.8 (s, C=O), 147.3 (d, C-3a), 124.3 (s, C-3), 67.7 (s, C-5), 65.7 (d, C-6), 46.2 (t, C-9), 39.7 (t, C-4), 36.5 (t, C-3c), 32.8 (d, C-3b), 29.7 (t, C-3d), 26.4 (t, C-7), 25.3 (q, C-5-CH_3), 22.7 (t, C-3e), 22.2 (t, C-8), 20.3 (q, C-3c), 14.0 (q, C-3g).

IR (solution, $CHCl_3$):

υ (cm^{-1}) = 3390 (w), 3019 (s), 2976 (m), 2930 (m), 1658 (m), 1600 (m), 1522 (w), 1450 (m), 1439 (m), 1386 (w), 1296 (w), 1215 (s), 1046 (m), 929 (w).

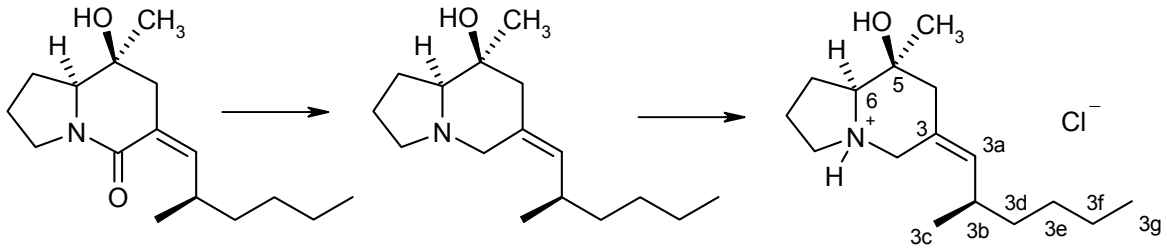
MS (80eV, EI, 115 °C):

m/z (%) 265 (35) [M^+], 222 (100) [M^+ - C_3H_7], 208 (4) [M^+ -C_4H_9], 180 (20), 152 (3), 70 (30).

HRMS (80eV, 100 °C): found 265.20822 calc. 265.204179 (for $C_{16}H_{27}N_1O_2$ [M^+]).

(3*Z*)-5*S*,6*S*-3-(*R*-2-Methyl-hexylidene)-5-hydroxy-5-methyl-azabicyclo[4.3.0]nonane [91] - Pumiliotoxin 251D - and

(3*Z*)-5*S*,6*S*-3-(*R*-2-methyl-hexylidene)-5-hydroxy-5-methyl-azabicyclo[4.3.0]nonane hydrochloride [92] - Pumiliotoxin 251 D hydrochloride



[87] 265.40 [$C_{16}H_{27}NO_2$] **[91]** 251.42 [$C_{16}H_{29}NO$] **[92]** 287.88 [$C_{16}H_{30}ClNO$]

In a 50 mL flask 39 mg (1.03 mmol, 7.4 eq.) of $LiAlH_4$ was dissolved in 15 mL of anhydrous diethyl ether, flushed with argon and cooled to 0 °C. Then, a solution of anhydrous $AlCl_3$ (46 mg, 0.34 mmol, 2.4 eq) in 2 mL of anhydrous diethyl ether was added with a syringe. After addition, the cooling bath was removed and the mixture was stirred for 30 min at room temperature. During the addition of the $AlCl_3$ solution the grey colour of $LiAlH_4$ turned to light grey and a grainy suspension was formed. [317] Then, the mixture was cooled to 0 °C and a solution of indolizidinone **[87]** (36.6 mg, 0.14 mmol) in 2mL of anhydrous diethyl ether was added. The cooling bath was removed and the mixture was stirred for 10 min at ambient temperature.

For the workup, 0.5 mL of water was carefully added and the formed white precipitate was stirred for 15 min at 0 °C. Then, 0.5 mL of 2.5 M aqueous KOH was added and the volume of the precipitate decreased, forming a colourless supernatant. The supernatant was decanted and the precipitate was again extracted with 40 mL of diethyl ether. The combined organic extracts were dried (Na_2SO_4) and the solvent was evaporated. The crude indolizidine was purified on silica gel (methanol / ethyl acetate = 1:9) followed by HPLC (isopropanol / hexane = 1:9, 4x250 mm, Nucleosil 50-5, UV = 210 nm, flow 2mL/min)[321] to remove minor impurities. After HPLC purification, 19.7 mg (56.8%) of pure **(+)-Pumiliotoxin 251D** was obtained.

[321] HPLC behaviour of PTX 251D strongly depended on the injected concentration, the product was purified using its tendency of a decreasing retention time when the column was overloaded.

For the preparation of the hydrochloride, 19.7 mg of (+)-pumiliotoxin 251D was dissolved in 4 mL of a 1 M methanolic HCl solution. After evaporation of the solvent, 21.8 mg (97%) of **(+)-Pumiliotoxin 251 hydrochloride** was obtained. Recrystallisation from dichloromethane / ethyl acetate yielded colourless needles (mp 203-205 °C; 205-206 ref.[322] ; 200-201 °C ref.[323]) that were used for X-Ray structure analysis.

(+)-Pumiliotoxin 251 D [91] :

$[\alpha]_D^{20}$ = - 8.47° (c = 1.05 , $CHCl_3$).

^{1}H-NMR (270 MHz, $CDCl_3$):
5.04 - 4.97 (d, 1H; H-3a; ^3J (H^{3a},H^{3b}) = 9.5 Hz), 3.78 - 3.73 (d, 1H; H-2o; ^2J (H^{2o},H^{2u}) = 12 Hz), 3.07 - 3.00 (m, 1H; H-9o), 2.65 (s, 1H; OH), 2.43 - 2.40 (m, 1H; H-3b), 2.35 - 2.29 (d, 1H; H-2u; ^2J (H^{2u},H^{9o}) = 12 Hz), 2.25 - 2.15 (m, 1H; H-9u), 2.12 - 2.08 (s, 2H; H-4o, 4u), 1.99 - 1.92 (m, 1H; H-6u), 1.78 - 1.60 (m, 4H; H-7o, 7u, 8o, 8u), 1.30 - 1.10 (m, 6H; H-3d, 3e, 3f), 1.11 (s, 3H; H-5-CH_3), 0.96 - 0.93 (d, 3H; H-3c; ^3J (H^{3c},H^{3b}) = 6.5 Hz), 0.87 - 0.80 (t, 3H; H-3g; ^3J (H^{3g},H^{3f}) = 6.5 Hz).

^{13}C-NMR (67.9 MHz, $CDCl_3$):
134.6 (d, C-3a), 129.8 (s, C-3), 71.7 (d, C-6), 68.3 (s, C-5), 54.5 (t, C-2), 53.2 (t, C-9), 48.8 (t, C-4), 37.4 (t, C-7), 32.0 (d, C-3b), 29.9 (t, C-8), 24.2 (q, C-5-CH_3), 23.2 (t, C-3d), 22.8 (t, C-3e), 21.6 (q, C-3c), 21.0 (t, C-3f), 14.1 (q, C-3g).

IR (solution, $CHCl_3$):
υ (cm^{-1}) = 2959 (m), 2929 (m), 2871 (m), 2857 (w), 2797 (w), 1794 (w), 1642 (w), 1466 (m), 1382 (m).

MS (80eV, EI, 30 °C):
m/z (%) 251 (26) [M^+], 236 (5) [M^+ - CH_3], 208 (17) [M^+ - C_3H_7], 206 (12), 194 (20) [M^+ -C_4H_9], 176 (5), 166 (100), 148 (7), 137 (9), 123 (9), 112 (12), 84 (18), 70 (76).

HRMS (80eV, 30 °C): found 251.22622 calc. 251.224915 (for $C_{16}H_{29}N_1O_1$ [M^+]).

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[323] Fox, D. N. A.; Lathbury, D.; Mahon, M. F.; Molloy, K. C.; Gallagher, T. *J. Am. Chem. Soc.* **1991**, 113, 2652-2656.

(+)-Pumiliotoxin 251 D hydrochloride [92] :

$[\alpha]_D^{20}$ = + 27.98° (c = 1.09 , methanol).

^{1}H-NMR (270 MHz, CD_3OD):
5.35 - 5.28 (d, 1H; H-3a; ^3J (H^{3a},H^{3b}) = 9.5 Hz), 4.42 - 4.33 (d, 1H; H-2o; ^2J (H^{2o},H^{2u}) = 13 Hz), 3.64 - 3.52 (m, 1H; H-9o), 3.45 - 3.39 (d, 1H; H-2u; ^2J (H^{2u},H^{2o}) = 11 Hz), 3.34 (s, 1H; H-NH), 3.20 - 3.05 (m, 1H; H-3b), 2.50 - 2.30 (m, 2H; H-4o, 4u), 2.20 - 1.95 (m, 6H; H-6u, 9u, 7o, 7u, 8o, 8u), 1.40 - 1.20 (m, 6H; H-3d, 3e, 3f), 1.28 (s, 3H; H-5-CH3), 1.05 - 1.01 (d, 3H; H-3c; ^3J (H^{3c},H^{3b}) = 5.5 Hz), 0.91 - 0.84 (t, 3H; H-3g; ^3J (H^{3g},H^{3f}) = 6.5 Hz).

^{13}C-NMR (67.9 MHz, CD_3OD):
140.9 (d, 3a), 125.7 (s, C-3), 74.1 (d, C-6), 68.9 (s, C-5), 54.3 (t, C-2), 52.6 (t, C-9), 47.7 (t, C-4), 38.6 (t, C-7), 33.7 (d, C-3b), 31.0 (t, C-8), 26.3 (q, C-5-CH_3), 24.1 (t, C-3d), 23.0 (t, C-3e), 21.7 (q, C-3c), 20.8 (t, C-3f), 14.7 (q, C-3g).