

## 4 Appendix

## 4.1 X-ray Data

comp.	structure	CCDC number	comp.	structure	CCDC number
[12a]		-	[39a]		172937
[12b]		-	[37b]		145068
[32]		172938	[42a]		145065
[35a]		145066	[54]		145069
[35b]		145067	[92]		172939
[38a]		172936			

#### 4.1.1 Crystallographic Data of *pS*-Azoninone [12a]

colourless, transparent prism from diethyl ether / n-hexane at  $-20^{\circ}\text{C}$   $\text{C}_{21}\text{H}_{32}\text{NO}_2\text{Cl}$  Si ( $M_r = 394.03$ ); crystal dimensions  $0.18 \times 0.40 \times 0.65 \text{ mm}^3$ ; orthorhombic;  $\text{P}2_12_12_1$ ,  $a = 11.343(1)$ ,  $b = 12.342(2)$ ,  $c = 15.815(2) \text{ \AA}$ ,  $Z = 4$ ,  $V = 2210.7 \text{ \AA}^3$ ,  $\rho_{\text{calc.}} = 1.184 \text{ g/cm}^3$ ,  $T = 135\text{K}$ ,  $2\Theta_{\text{max}} = 65.7^{\circ}$ ; of the 43029 reflections measured, were 7375 independent reflections ( $R_{\text{int}} = 0.086$ ,  $\omega R = 0.039$  and  $S = 0.65$ ); Siemens-SMART-diffractometer,  $\text{MoK}\alpha$ -radiation ( $\lambda = 0.71073 \text{ \AA}$ ). The structure was determined by direct methods using program SHELXS.<sup>324</sup> The H atoms were taken from a difference Fourier synthesis and were refined with isotropic thermal parameters. The non-H atoms were refined with anisotropic thermal parameters. The structure was refined on F values using weighting scheme:  $\omega(F) = 4 * F^2 / [\sigma^2(F^2) + (0.03 * F^2)^2]$ . The final difference density was between  $-0.29$  and  $+0.36 \text{ e/\AA}^3$ .

Discussion of the structure:

The nine-membered lactam ring has a *trans* conformation for the C5-C6 double bond and a *cis* conformation for the amide bond. The amide bond shows only a small deviation from planarity with a C9-N-C2-C3 torsion angle of  $3.9^{\circ}$  (3). The C5-C6 double bond shows a considerable deviation from planarity: the C4-C5-C6-C7 torsion angle is  $147.4^{\circ}$  (2) rather than  $180^{\circ}$  expected for a planar bond. This shows the nine-membered ring to be considerably strained. This is also reflected by the C-C single bonds which deviate considerably from the ideal gauche conformation. The initial conformation of the nine-membered ring differs considerably from the final conformation which was determined in a previous study. Large differences between the two conformations are observed in the section C4-C5-C6-C7-C8. Small conformational differences up to about  $5^{\circ}$  are observed in the remaining structure. Both conformations crystallise with isostructural crystal structures. The molecule shows a number of short intramolecular contacts: a repulsive H...H contact between H-3 and H-9u ( $1.97(2) \text{ \AA}$ ) and a number of attractive O...H contacts: O1...H (N-Bn1):  $2.33(1) \text{ \AA}$ , O2...H6:  $2.37(2) \text{ \AA}$  and O2...H-9u:  $2.42(1) \text{ \AA}$ . The shortest intermolecular O...H distance is  $2.54(2) \text{ \AA}$ . Two intermolecular Cl...H contacts of  $3.02(2)$  and  $3.04(2) \text{ \AA}$  are only slightly longer than the van der Waals contact distance of  $2.85 \text{ \AA}$ .

<sup>324</sup> (a) G. M. Sheldrick, SHELXS-97, program for the Solution of Crystal Structures, Göttingen, 1997; (b) G. M. Sheldrick, SHELXL-97, program for the Refinement of Crystal Structures, Göttingen, 1997.

### 4.1.2 Crystallographic Data of *pS*-Azoninone [12b]

colourless, transparent blocks from diethyl ether / n-hexane at -20°C C<sub>21</sub>H<sub>32</sub>NO<sub>2</sub>Cl Si (M<sub>r</sub> = 394.03); crystal dimensions 0.68 × 0.80 × 0.82 mm<sup>3</sup>; orthorhombic; P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>, a = 11.523(2), b = 12.336(1), c = 15.641(1) Å, Z = 4, V = 2223.4 Å<sup>3</sup> (4), ρ<sub>calc.</sub> = 1.177 g/cm<sup>3</sup>, T = 135K, 2Θ<sub>max</sub> = 65.7°; of the 43625 reflections measured, were 7534 independent reflections (R<sub>int</sub> = 0.054, ωR = 0.042 and S = 1.10); Siemens-SMART-diffractometer, MoK<sub>α</sub>-radiation (λ = 0.71073 Å). The structure was determined by direct methods using program SHELXS. The H atoms were taken from a difference Fourier synthesis and were refined with isotropic thermal parameters. The non-H atoms were refined with anisotropic thermal parameters. The structure was refined on F values using weighting scheme: ω(F) = 4 \* F<sup>2</sup> / [σ<sup>2</sup>(F<sup>2</sup>) + (0.03 \* F<sup>2</sup>)<sup>2</sup>]. The final difference density was between -0.29 and +0.36 e/Å<sup>3</sup>. Residual density of about 0.84 e/Å<sup>3</sup> near the C5-C6 double bond showed this bond to be slightly disordered. A careful inspection of the data showed two possible orientations for this bond: a major orientation with an occupancy factor of about 0.88 and a minor orientation with an occupancy factor of about 0.12 (resulting from cocrystallised kinetic conformer [12a]).

#### Discussion of the structure

The nine-membered lactam ring has a *trans* conformation for the C5-C6 double bond and a *cis* conformation for the amide bond. The amide bond is almost planar with a C9-N-C2-C3 torsion angle of -2.2°(2). The C5-C6 double bond shows a considerable deviation from planarity: the C3-C4-C5-C6 torsion angle is -150.0°(2) rather than 180° expected for a planar bond. This shows the nine-membered ring to be considerably strained. This is also reflected by the C-C single bonds which deviate considerably from the ideal gauche conformation. The conformation of the nine-membered ring is very similar to a related ring in a crystal structure reported by Edstrom<sup>57a</sup>. This structure also contains a benzyl substituent at the N atom. A very different conformation has been reported by Olson<sup>56a</sup> for a related nine-membered ring with no substituent at the N atom. In that case a *trans* amide conformation and a *cis* olefinic bond occurs. The molecule shows a number of short intramolecular contacts: a repulsive H...H contact between H3 and H9u (1.91(2) Å) and a number of attractive O...H contacts: O1...H-NBn1: 2.28(2) Å, O2...H7o: 2.42(2) Å and O2...H9o: 2.39(1) Å. The crystal packing shows an intermolecular distance of 2.43(2) Å between O1 and H15 (symmetry code: 1-x, y-0.5, 0.5-z) which approaches the van der Waals contacts distance of 2.4 Å between O and H. Two intermolecular Cl...H contacts of about 2.94(2) Å are only slightly longer than the van der Waals contact distance of 2.85 Å.

### 4.1.3 Crystallographic Data of Nitroindolizidinone [52]

Crystal data for the nitro-exchange product: colourless, transparent blocks from dichloromethane / n-hexane  $C_8H_{11}N_2O_4Cl$  Si ( $M_r = 234.64$ ); crystal dimensions  $0.64 \times 0.64 \times 0.14 \text{ mm}^3$ ; monoclinic;  $P2_1$ ,  $a = 8.8883 (18)$ ,  $b = 9.1550 (14)$ ,  $c = 12.5246 (18) \text{ \AA}$ ,  $Z = 4$ ,  $V = 1006.9 \text{ \AA}^3 (3)$ ,  $\rho_{\text{calc.}} = 1.548 \text{ g/cm}^{-3}$ ,  $T = 146 (2) \text{ K}$ ,  $2\Theta_{\text{max}} = 65.7^\circ$ ; of the 20797 reflections measured, were 6262 independent reflections ( $R_{\text{int}} = 0.025$ ,  $\omega R = 0.0632$  and  $S = 1.325$ ); Siemens-SMART-diffractometer,  $Mo_{K\alpha}$ -radiation ( $\lambda = 0.71073 \text{ \AA}$ ). The structure was determined by direct methods using program SHELXS. The H atoms were taken from a difference Fourier synthesis and were refined with isotropic thermal parameters. The non-H atoms were refined with anisotropic thermal parameters. The structure was refined on F values using weighting scheme:

$\omega(F) = 4 * F^2 / [\sigma^2(F^2) + (0.03 * F^2)^2]$ . The final difference density was between  $-0.18$  and  $+0.23 \text{ e/\AA}^3$ .

#### Discussion of the structure

The structure contains two crystallographically independent molecules. The dimensions of both molecules are very similar. A small difference of  $6^\circ$  is found for the torsion angle about the N-O single bond of the nitrate side chains. The conformation of the 1-aza-bicyclo[4.3.0]nonan-9-one group is similar to the conformation of this group found in other crystal structures (CSD ref codes: GONJEY, HIHKAK and PAWTAI): the six-membered ring has a chair conformation, the five-membered ring has a 7-envelope conformation. The nitrate group is in an equatorial position with respect to the six-membered ring. The Cl atoms is in a pseudo-axial position with respect to the five-membered ring. The aza-nitrogen atoms are almost planar. The molecules show no significant intramolecular interactions. The crystal packing shows three intermolecular C-H...Cl interactions with H...Cl distances between 2.93 and 3.03  $\text{\AA}$  and six intermolecular C-H...O interactions with H...O distances between 2.48 and 2.61  $\text{\AA}$ .

### 4.1.4 Crystallographic Data of Epoxy Azonanone [35a]

Crystal data for the epoxidation product of the kinetic conformer : colourless, transparent prism from diethyl ether / n-hexane at room temperature  $C_{21}H_{32}NO_3Cl$  Si ( $M_r = 410.02$ ); crystal dimensions  $0.38 \times 0.52 \times 0.64 \text{ mm}^3$ ; orthorhombic;  $P_{212121}$ ,  $a = 11.6502(12)$ ,  $b = 12.2039(10)$ ,  $c = 16.000(2) \text{ \AA}$ ,  $Z = 4$ ,  $V = 2274.9 \text{ \AA}^3 (5)$ ,  $\rho_{\text{calc.}} = 1.197 \text{ g/cm}^{-3}$ ,  $T = 136\text{K}$ ,  $2\Theta_{\text{max}} = 66.3^\circ$ ; of the 43338 reflections measured, were 8017 independent reflections ( $R_{\text{int}} = 0.048$ ,  $\omega R = 0.1019$  und  $S = 1.32$ ); Siemens-SMART-diffractometer,  $Mo_{K\alpha}$ -radiation ( $\lambda = 0.71073 \text{ \AA}$ ). The structure was determined by direct methods using program SHELXS. The H atoms were taken from a difference Fourier synthesis and were

refined with isotropic thermal parameters. The non-H atoms were refined with anisotropic thermal parameters. The structure was refined on F values using weighting scheme:

$w(F) = 4 * F^2 / [s^2(F^2) + (0.03 * F^2)^2]$ . The final difference density was between -0.205 and +0.414 e/Å<sup>3</sup>.

#### Discussion of the structure

The conformation of the nine-membered ring is very similar to that found in the corresponding unsaturated compound. The largest difference (about 12°) is found for the torsion angle about the C6-C7 bond. The title compound and the corresponding unsaturated compound have isomorphous crystal structures. Small differences between the title compound and the unsaturated compound are found for the relative orientations of the side chains: differences up to 14 deg are found for the torsion angles about the O-Si bond. Differences up to 6 deg are also found for the torsion angles about the N-C9 and C9-C10 bonds. The molecule shows a short repulsive intramolecular distance of 1.96 Å between H2 and H8Å. The crystal packing only shows very weak, intermolecular electrostatic interactions: Cl...H17C: 3.09 Å (x, y-1, z) and O1...H17B: 2.69 Å (1-x, y-0.5, 0.5-z). There are no other significant intra- or intermolecular contacts.

#### 4.1.5 Crystallographic Data of Epoxy Azonanone [35b]

Crystal data for the epoxidation product of the thermodynamic conformer : colourless, transparent prism from diethyl ether/n-hexane at room temperature C<sub>21</sub>H<sub>32</sub>NO<sub>3</sub>Cl Si (Mr = 410.02); crystal dimensions 0.56 x 0.56 x 0.52 mm<sup>3</sup>; orthorhombic; P<sub>21 21 21</sub>, a = 11.7627(13), b = 12.3161(14), c = 15.553(2) Å, Z = 4, V = 2253.2 Å<sup>3</sup>(5), ρ<sub>calc.</sub> = 1.209 g/cm<sup>3</sup>, T = 136K, 2Θ<sub>max</sub> = 66.3°; of the 43001 reflections measured, were 7790 independent reflections (R<sub>int</sub> = 0.0351, ωR = 0.0914 und S = 1.37); Siemens-SMART-diffractometer, MoK<sub>α</sub>-radiation (λ = 0.71073 Å). The structure was determined by direct methods using program SHELXS. The H atoms were taken from a difference Fourier synthesis and were refined with isotropic thermal parameters. The non-H atoms were refined with anisotropic thermal parameters. The structure was refined on F values using weighting scheme:

$w(F) = 4 * F^2 / [s^2(F^2) + (0.03 * F^2)^2]$ . The final difference density was between -0.51 and +0.61 e/Å<sup>3</sup>.

#### Discussion of the structure

The title compound and the corresponding unsaturated compound have isomorphous crystal structures. The conformation of the molecule is very similar to that of the corresponding unsaturated compound.

Torsion angles about corresponding bonds agree within 4°, except for the C3-C4-C5-C6 bond which has a torsion angle of -142.3°(1) in the title compound and -149.3°(2) in the unsaturated compound. The molecule shows a short repulsive intramolecular distance of 2.01 Å between H2 and H8B. The crystal packing only shows very weak, intermolecular electrostatic interactions: Cl...H17A: 3.05 Å (x, y-1, z), Cl...H19B: 3.03 Å (x-0.5, 0.5-y, -z), O1...H15: 2.56 Å (1-x, y-0.5, 0.5-z), O1...H17C: 2.60 Å (1-x, y-0.5, 0.5-z) and O3...H13: 2.60 Å (x+1, y, z). There are no other significant intra- or intermolecular contacts.

#### 4.1.6 Crystallographic Data of Epoxy Azonanone [38a]

Crystal data for the epoxidation product of the kinetic conformer : colourless, transparent prism from diethyl ether/n-hexane at room temperature C<sub>15</sub>H<sub>18</sub>NO<sub>2</sub>Cl (Mr = 279.75); crystal dimensions 0.19 x 0.40 x 0.50 mm<sup>3</sup> ; orthorhombic; P<sub>21 21 21</sub>, a = 9.5482 (16), b = 9.5691 (8), c = 15.0739 (17) Å, Z = 4, V = 1377.3 Å<sup>3</sup> (3) , ρ<sub>calc.</sub> = 1.349 g/cm<sup>-3</sup>, T = 144K (2), 2Θ<sub>max</sub> = 66.3°; of the 25245 reflections measured, were 4509 independent reflections (R<sub>int</sub> = 0.038, ωR = 0.0719 und S = 1.203); Siemens-SMART-diffractometer, MoK<sub>α</sub>-radiation (λ = 0.71073 Å). The structure was determined by direct methods using program SHELXS. The H atoms were taken from a difference Fourier synthesis and were refined with isotropic thermal parameters. The non-H atoms were refined with anisotropic thermal parameters. The structure was refined on F values using weighting scheme:

$w(F) = 4 * F^2 / [s^2(F^2) + (0.03 * F^2)^2]$ . The absolute configuration of the structure was determined by a refinement of the Flack x - parameter [ x = 0.00(3); x = 0 for the correct and +1 for the wrong absolute configuration ]. The final difference density was between -0.18 and +0.27 e/Å<sup>3</sup>.

#### Discussion of the structure

The conformation of the nine-membered ring is very similar to that found in the corresponding compound with a TBSO group attached to C7. Large differences (about 10°) are only found for the torsion angles about the C6-C7 and C7-C8 bonds. Small differences of about 5° are found for the torsion angles about the N-C9 and C9-C10 bonds. The molecule shows a short repulsive intramolecular distance of 2.04 Å between H3 and H9u. The intramolecular O1...N-Bn1 distance of 2.28 Å approaches the van der Waals contact distance.

#### 4.1.7 Crystallographic Data of Epoxy Azonanone [39a]

Crystal data for epoxidation product: colourless, transparent block from product oil at  $-20^{\circ}\text{C}$ ;  $\text{C}_{15}\text{H}_{18}\text{NO}_2\text{Cl}$  ( $M_r = 275.75$ ); crystal dimensions  $1.00 \times 0.80 \times 0.43 \text{ mm}^3$ ; orthorhombic;  $P_{21\ 21\ 21}$ ,  $a = 8.9639$  (16),  $b = 11.9771$  (13),  $c = 13.5890$  (15) Å,  $Z = 4$ ,  $V = 1458.9 \text{ Å}^3$ (3),  $\rho_{\text{calc.}} = 1.247 \text{ g/cm}^3$ ,  $T = 202\text{K}$ ,  $2\Theta_{\text{max}} = 62^{\circ}$ ; of the 30222 reflections measured, were 4621 independent reflections ( $R_{\text{int}} = 0.0268$ ,  $\omega R = 0.1522$  and  $S = 1.049$ ); Siemens-SMART-diffractometer,  $\text{Mo}_{K\alpha}$ -radiation ( $\lambda = 0.71073 \text{ Å}$ ). The structure was determined by direct methods using program SHELXS. The H atoms were taken from a difference Fourier synthesis and were refined with isotropic thermal parameters. The non-H atoms were refined with anisotropic thermal parameters. The structure was refined on F values using weighting scheme:  $w(F) = 4 * F^2 / [s^2(F^2) + (0.03 * F^2)^2]$ . The absolute configuration of the structure was determined by a refinement of the Flack  $x$  - parameter [ $x = 0.05$  (10);  $x = 0$  for the correct and  $+1$  for the wrong absolute configuration]. The final difference density was between  $-0.349$  and  $+0.252 \text{ e/Å}^3$ .

#### Discussion of the structure

The molecules shows rather large displacement parameters even at  $-71^{\circ}\text{C}$ . Large displacement parameters are often observed in the high temperature phase of compounds which undergo phase transitions.<sup>325</sup> The title compound shows a phase transition at about  $-80^{\circ}\text{C}$ . Below the phase transition temperature additional reflections appear with indices  $h + 1/6$  and  $h - 1/6$ . Thus the structure appears to be incommensurate below  $-80^{\circ}\text{C}$ . No additional phase transition was found on cooling to  $-157^{\circ}\text{C}$ .

The N atom is perfectly planar: the sum of the three valence angles about N is  $360^{\circ}\text{C}$ . The amide bond is almost planar: The torsion angle about the N-C2 bond is  $7.5^{\circ}$ . A number of C-C bonds in the nine-membered ring show considerable deviations from a staggered conformation. Thus the nine-membered ring appears strained. The shortest intramolecular contact distances are H3...H9o :  $1.92 \text{ Å}$ ; H-6...N-Bn1:  $2.04 \text{ Å}$  and N-Bn2...O1:  $2.28 \text{ Å}$ .

The crystal packing shows a rather short intermolecular C-H...O contact with a H...O distance of  $2.4 \text{ Å}$ , two intermolecular C-H... $\pi$  (phenyl) interactions and an intermolecular C-H...Cl interaction.

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<sup>325</sup> J. W. Bats; private communication to A. S.

### 4.1.8 Crystallographic Data of Epoxy Azonanone [37b]

Crystal data for the epoxidation product of the kinetic conformer : colourless, transparent rod from dichloromethane / n-hexane at -20°C C<sub>28</sub>H<sub>39</sub>NO<sub>4</sub>Si (Mr = 481.69); crystal dimensions 0.65 x 0.26 x 0.22 mm<sup>3</sup> ; monoclinic; P<sub>21</sub>, a = 13.152 (2), b = 7.9712 (11), c = 13.4576 (16) Å, Z = 2, V = 1366.9 Å<sup>3</sup> (3) , ρ<sub>calc.</sub> = 1.170 g/cm<sup>-3</sup>, T = 137 K (2), 2Θ<sub>max</sub> = 66.3°; of the 25495 reflections measured, were 8511 independent reflections (R<sub>int</sub> = 0.0325, ωR = 0.1076 und S = 1.277); Siemens-SMART-diffractometer, MoK<sub>α</sub>-radiation (λ = 0.71073 Å). The structure was determined by direct methods using program SHELXS.

The H atoms were taken from a difference Fourier synthesis and were refined with isotropic thermal parameters. The non-H atoms were refined with anisotropic thermal parameters. The structure was refined on F values using weighting scheme:

$w(F) = 4 * F^2 / [s^2(F^2) + (0.03 * F^2)^2]$ . The absolute configuration of the structure was determined by a refinement of the Flack x - parameter [ x = 0.04 (8); x = 0 for the correct and +1 for the wrong absolute configuration ]. The final difference density was between 0.330 and -0.225 e/Å<sup>3</sup>.

The structure was determined by direct methods using program SHELXS. Residual density up to 0.7 e/Å<sup>3</sup> revealed a second possible position for C2 and the O-benzyl group attached to it. Those atoms were entered as C2', O4', C22', C23', C24', C25', C26', C27' and C28'. The occupancy factor for those partially occupied atoms refined to 0.107(3), while the occupancy factor of the main conformation was 0.893(3). H atoms at C2 and the O-benzyl group were placed at calculated positions and were not refined. The remaining H atoms were taken from a difference Fourier synthesis and were refined with isotropic thermal parameters.

#### Discussion of the structure

The conformation of the nine-membered ring is very similar to that found in the corresponding chloride. The molecule shows a short repulsive intramolecular distances of 1.98 Å between H3 and H9u and of 2.03 Å between H8 and H9o. The crystal packing shows weak, intermolecular electrostatic C-H...O and C-H...π (phenyl) interactions.



### 4.1.9 Crystallographic Data of Methano Azonanone [42a]

Crystal data for cyclopropanation product of kinetic conformer [12a]: colourless, transparent prism from diethyl ether/n-hexane at -20°C C<sub>22</sub>H<sub>34</sub>NO<sub>2</sub>Cl Si (Mr = 408.06); crystal dimensions 0.40 x 0.45 x 0.52 mm<sup>3</sup>; monoclinic; P<sub>21</sub>, a = 8.5018(8), b = 15.124(2), c = 9.068(1) Å, Z = 4, V = 1108.7 Å<sup>3</sup>(3), ρ<sub>calc.</sub> = 1.222 g/cm<sup>3</sup>, T = 135K, 2Θ<sub>max</sub> = 66.3°; of the 22972 reflections measured, were 7240 independent reflections (R<sub>int</sub> = 0.027, ωR = 0.037 und S = 1.50); Siemens-SMART-diffractometer, MoK<sub>α</sub>-radiation (λ = 0.71073 Å). The structure was determined by direct methods using program SHELXS. The H atoms were taken from a difference Fourier synthesis and were refined with isotropic thermal parameters. The non-H atoms were refined with anisotropic thermal parameters. The structure was refined on F values using weighting scheme: w (F) = 4 \* F<sup>2</sup> / [ s<sup>2</sup>(F<sup>2</sup>) + ( 0.03 \* F<sup>2</sup> )<sup>2</sup> ]. A refinement of the Flack x - parameter gave x = 0.00(3) . This confirms the absolute configuration of the molecule ( x = 0 for the correct and x = +1 for the wrong absolute structure ). The final difference density was between -0.18 and +0.22 e/Å<sup>3</sup> .

#### Discussion of the structure

The conformation of the bicyclo[7.1.0]decane ring differs considerably from similar rings found in other crystal structures.<sup>326</sup> The C4-C5-C6-C7 torsion angle of 134.1° (1) is slightly smaller than the value of about 143° found for a larger ring<sup>327</sup>. Several C-C bonds deviate significantly from a gauche conformation. Thus the nine-membered ring appears considerably strained. Both the N and C1 atoms deviate slightly from planarity: N lies 0.07 Å outside the plane through C1, C9 and C-NBn; C2 lies 0.04 Å outside the plane through N, O1 and C3. The intramolecular H3...H9u distance of 1.91(2) Å is very short and indicates a steric repulsion between those atoms. Another short intramolecular contact distance is found between O1 and N-Bn1 (2.28(1) Å). The crystal packing shows only very weak intermolecular electrostatic interactions.

<sup>326</sup> Mihailovic M. L. *Tetrahedron Lett.* **1979**, 4917.

<sup>327</sup> Mash, E. A.; Gregg, T. M.; Kaczynski, M. A. *J. Org. Chem.* **1996**, 61, 2743-2752.

#### 4.1.10 Crystallographic Data of Hydroxy Indolizidinone [54]

Crystal data for the epoxide opening product of epoxide [37b]: colourless, transparent prism from diethyl ether / n-hexane at room temperature  $C_{21}H_{33}NO_4$  Si (Mr = 391.57); crystal dimensions 0.76 x 0.50 x 0.34 mm<sup>3</sup>; monoclinic;  $P_{21}$ , a = 7.4054 (14), b = 8.3590 (10), c = 18.2498 (14) Å, Z = 2, V = 1123.9 Å<sup>3</sup> (3),  $\rho_{\text{calc.}} = 1.157 \text{ g/cm}^3$ , T = 200K,  $2\Theta_{\text{max}} = 66.3^\circ$ ; of the 20991 reflections measured, were 6837 independent reflections ( $R_{\text{int}} = 0.0199$ ,  $\omega R = 0.1975$  und  $S = 1.491$ ); Siemens-SMART-diffractometer,  $Mo_{K\alpha}$ -radiation ( $\lambda = 0.71073 \text{ \AA}$ ). The dimethyl-t-butyl-silyl group was found to be disordered. Two possible orientations were found for this group. The occupancy factor of the group labeled Si, C16, C17, C18, C19, C20 and C21 was 0.494 (6). The occupancy factor of the group labeled Si', C16', C17', C18', C19', C20' and C21' was 0.506 (6). Even the split atoms had very large displacement parameters. H atoms were placed at calculated positions and were treated as riding atoms. The H atom of the hydroxyl group was taken from a difference Fourier synthesis and was refined with isotropic thermal parameters. The structure was refined on  $F^2$  values using program SHELXL-96. The absolute configuration of the structure was confirmed by a refinement of the Flack x - parameter [ x = -0.05(20) ]. The final difference density was between -0.47 and +0.49 e/Å<sup>3</sup>. Below about -85°C additional reflections appear with indices h+0.50, k+0.39, l+0.50, corresponding to a modulated phase. The structure remains modulated upon cooling to at least -170°C, which was the lowest temperature reachable with low temperature device.

#### Discussion of the structure

The five-membered ring approximately has an envelope conformation with atom C6 0.57 Å outside the plane through C5, N, C8 and C7. The saturated six-membered ring approximately has an unsymmetrical twist (half-chair) conformation with atoms C3 and C4 0.27 and 0.48 Å in opposite directions outside the plane through C2, C1, N and C5. The hydroxyl group is in a pseudo-equatorial position with respect to this ring. Conformations for the 2-oxo-1-azabicyclononane group similar to that in the title compound have been observed by Polyak and Lubell<sup>328</sup> and Lindemann *et al.*<sup>329</sup> Slightly different conformations were found by Austin *et al.*<sup>330</sup> and Hua *et al.*<sup>331</sup> The molecules are connected by an intermolecular hydrogen bond to infinite chains in the a - direction. A weak, intermolecular C-H...O interaction also contributes to this chain formation. There are no other significant intra- or intermolecular contacts.

<sup>328</sup> Polyak, F.; Lubell, W. D. *J. Org. Chem.* **1998**, 63, 5937.

<sup>329</sup> Lindemann, U.; Reck, G.; Wulff-Molder, D.; Wessig, P. *Tetrahedron* **1998**, 54, 2529-2544.

<sup>330</sup> Austin, G.N.; Fleet, G.W. J.; Peach, J.M.; Smith, P. W.; Watkin, D. J. *Tetrahedron* **1987**, 43, 3095.

<sup>331</sup> Hua, D. H. *Acta Cryst.* **1995**, C51, 2301.

#### 4.1.11 Crystallographic Data of (+)-Pumiliotoxin 251D-hydrochloride [92]

Crystal data for pumiliotoxin 251D hydrochloride: colourless, transparent needles from ethyl acetate / dichloromethane at room temperature;  $C_{16}H_{30}NOCl$  (Mr = 287.86); crystal dimensions 1.50 x 0.06 x 0.05 mm<sup>3</sup>; monoclinic;  $P_{21}$ , a = 10.2863 (16), b = 6.9189 (13), c = 11.959 (2) Å, Z = 2, V = 842.9 Å<sup>3</sup>(3),  $\rho_{\text{calc.}} = 1.134 \text{ g/cm}^3$ , T = 146K,  $2\Theta_{\text{max}} = 62^\circ$ ; of the 11029 reflections measured, were 4707 independent reflections ( $R_{\text{int}} = 0.0880$ ,  $\omega R = 0.1092$  and  $S = 0.973$ ); Siemens-SMART-diffractometer,  $Mo_{K\alpha}$ -radiation ( $\lambda = 0.71073 \text{ \AA}$ ). The structure was determined by direct methods using program SHELXS. The H atoms were taken from a difference Fourier synthesis and were refined with isotropic thermal parameters. The non-H atoms were refined with anisotropic thermal parameters. The structure was refined on F values using weighting scheme:

$w(F) = 4 * F^2 / [s^2(F^2) + (0.03 * F^2)^2]$ . The final difference density was between -0.278 and +0.386 e/Å<sup>3</sup>.

#### Discussion of the structure

The structure is identical to the hydrochloride of the natural product<sup>332</sup> (CCDC-code HMXZB).

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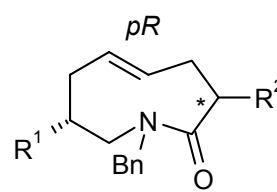
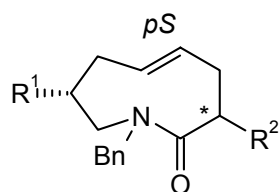
<sup>332</sup> Daly, J. W.; Tokuyama, T.; Fujiwara, T.; Highet, R. J.; Karle I.L. *J. Am. Chem. Soc.* **1980**, 102, 830.

## 4.2 List of Compounds

## 4.2.1 Pyrrolidines

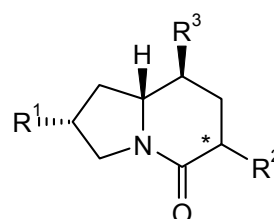
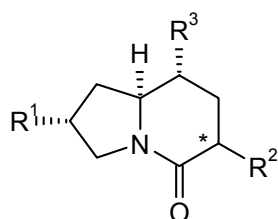
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	[4]	116		[5]	117
	[6]	119		[8]	121
	[9]	121		[10]	122
	[11]	123		[41b]	197
	[48]	216		[50]	217
	[52]	219		[55]	224

## 4.2.2 Azoninones

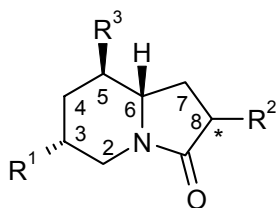


no	R <sup>1</sup>	R <sup>2</sup>	planar chirality	chirality at C-3	page	no	R <sup>1</sup>	R <sup>2</sup>	planar chirality	chirality at C-3	page
[12a]	OTBS	Cl	<i>pS</i>	R (β)	128	[12b]	OTBS	Cl	<i>pR</i>	R (β)	129
[13a]	OTBS	Ph	<i>pS</i>	S (β)	130	[13b]	OTBS	Ph	<i>pR</i>	S (β)	131
[14a]	OTBS	OBn	<i>pS</i>	R (β)	133	[14b]	OTBS	OBn	<i>pR</i>	R (β)	134
[16a]	H	Cl	<i>pS</i>	R (β)	137	[15b]	OTBS	OBn	<i>pR</i>	S (α)	134
[17a]	H	Cl	<i>pS</i>	S (α)	137						
[18a]	H	OBn	<i>pS</i>	S (β)	141						
[19a]	H	OBn	<i>pS</i>	R (α)	141						

## 4.2.3 Indolizidinones

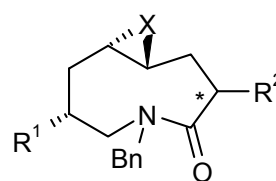
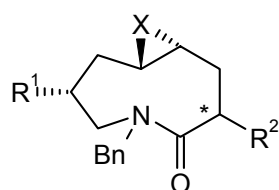


no	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	chirality at C-3	page	no	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	chirality at C-3	page
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[23a]	OTBS	OBn	SePh	R (β)	156	[23c]	OTBS	OBn	SePh	R (β)	163
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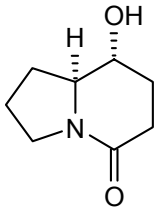
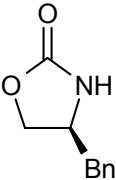
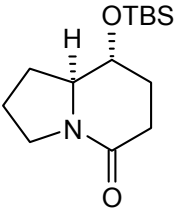
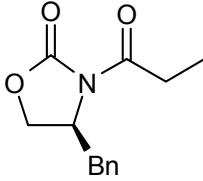
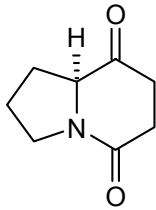
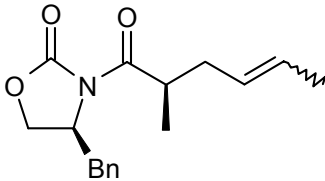
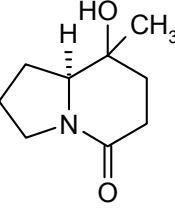
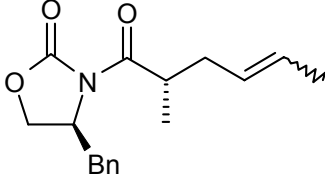
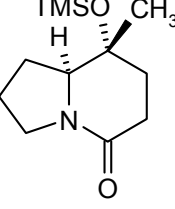
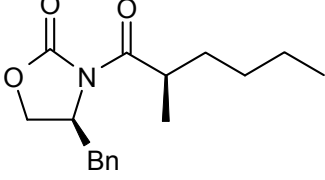
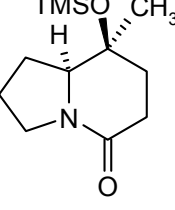
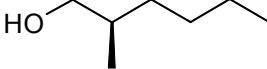
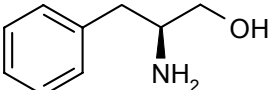
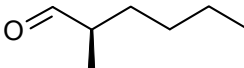
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[22b]	OTBS	Ph	Br	S (β)	151	[32]	H	Cl	ONO <sub>2</sub>	R (β)	178
[23b]	OTBS	OBn	SePh	R (β)	159	[33]	H	Cl	ONO <sub>2</sub>	S (α)	178
[24b]	OTBS	OBn	I	R (β)	160	[34]	H	Cl	OH	R (β)	180
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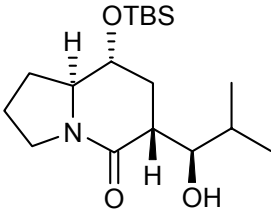
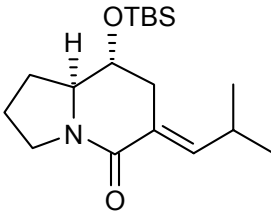
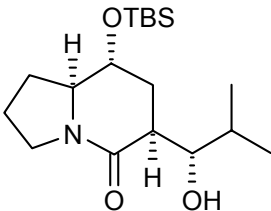
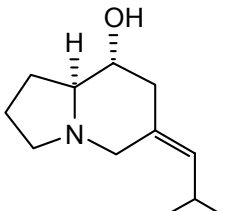
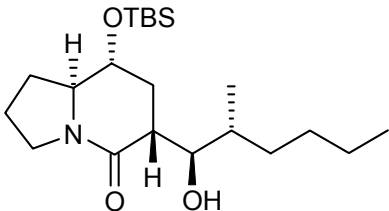
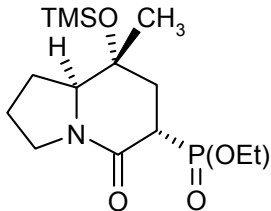
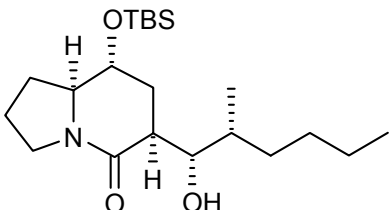
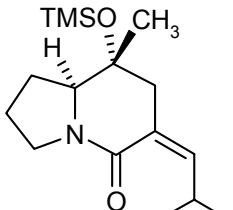
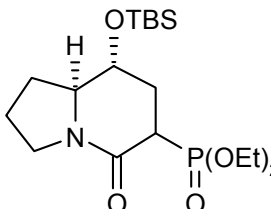
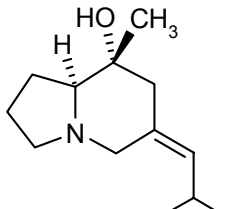
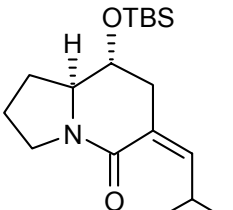
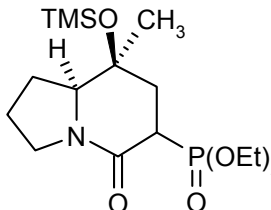
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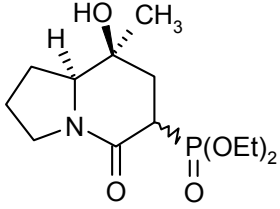
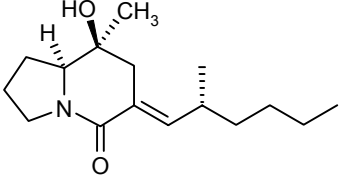
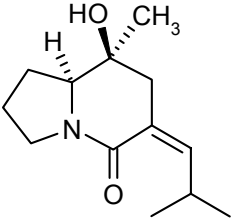
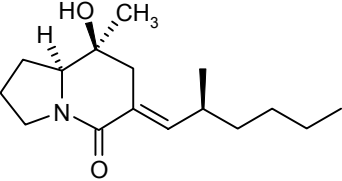
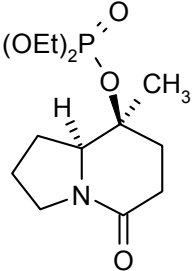
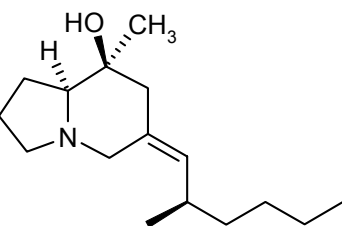
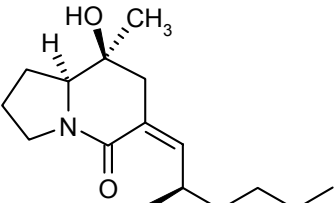
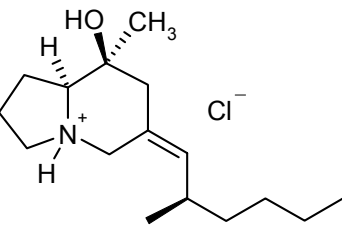
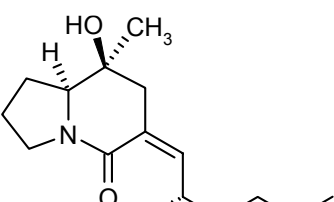
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[36a]	OTBS	Ph	O	S (β)	186	[36b]	OTBS	Ph	O	S (β)	187
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[39a]	H	Cl	O	S (α)	192	[40b]	OTBS	Cl	N-Ts	R (β)	195
[40a]	OTBS	Cl	N-Ts	R (β)	194	[42b]	OTBS	Cl	CH <sub>2</sub>	R (β)	200
[41a]	OTBS	Ph	N-Ts	S (β)	197	[43b]	OTBS	Cl	C(CO <sub>2</sub> Et) <sub>2</sub>	R (β)	202
[42a]	OTBS	Cl	CH <sub>2</sub>	R (β)	199	[44b]	OTBS	Cl	OAc bisacetate	R (β)	206
[43a]	OTBS	Cl	C(CO <sub>2</sub> Et) <sub>2</sub>	R (β)	202	[45b]	OTBS	Cl	O(CMe <sub>2</sub> )O acetonide	R (β)	209
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[46a]	OTBS	Ph	O(CMe <sub>2</sub> )O acetonide	S (β)	211						

## 4.2.5 Compounds described in the part Total Synthesis of Pumiliotoxins

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	[57]	225		[64]	235
	[58]	227		[65]	235
	[59]	228		[66]	236
	[60]	228		[67]	236
	[61]	231		[68]	238
	[62]	231		[69]	239
	[63]	234		[70]	240

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	[71]	242		[78]	248
	[72]	242		[79]	253
	[73]	245		[80]	254
	[74]	245		[81]	254
	[76]	248		[82]	257
	[77]	248		[83]	259



compound	number	page	compound	number	page
	[84]	260		[89]	264
	[85]	260		[90]	264
	[86]	262		[91]	269
	[87]	264		[92]	269
	[88]	264			