Planar Chirality: Synthesis and Transannular Reactions of Unsaturated Optically Active Azoninones Bearing *E*-Olefins

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The zwitterionic aza-Claisen rearrangement of optically active *trans* 4-silyloxy-2-vinylpyrrolidines and carboxylic acid fluoride generated nine-membered ring lactams with high yields. The reaction proceeded with an almost complete 1,4-chirality transfer and the exclusive generation of the *E*-double bond in the medium sized rings to cause additional planar chiral information. The initially formed azoninones were characterized by a *pS*-arrangement of the olefin with respect to the ring. The rather kinetically stable conformation underwent a flipping of the double bond to give the *pR*-azoninones as the thermodynamically stable products. The planar diastereomers were subjected to regio- and diastereoselective transannular ring contractions to give indolizidinones. The stereochemical outcome was strongly dependent from the planar chiral information of the double bond and the lactam unit. The so-formed optically active bicycles bearing a defined substitution pattern should serve as versatile building blocks in alkaloid synthesis.

Introduction

The generation of nine-membered nitrogen heterocycles ("azonines") bearing defined constitutions and configurations is still a challenge in organic synthesis. On one hand, azonines are found as subunits in natural and pharmaceutically important products (target molecules);[1] on the other hand, the medium-sized constrained ring systems can serve as key intermediates in the synthesis of bicyclic amino compounds by selective transannular ring contractions.[2] However, an intriguing strategy to generate optically active medium-sized heterocycles is the ring enlargement of five- or six-membered rings by means of Claisen rearrangements.[3] Constrained azonines bearing *E* double bonds were efficiently built up by the so-called zwitterionic aza-Claisen rearrangement, which had been developed from a ketene Claisen reaction initially described for the synthesis of nine- or ten-membered ring lactams by Edstrom in 1991.[4] Starting from chiral 2-vinylpyrrolidines, various substituted nine-membered rings were formed.[5] The highly ordered chairlike transition state of the 3,3-sigmatopic rearrangement always induced the complete 1,3 chirality transfer from an *E*-allylamine to the corresponding γ,δ-unsaturated lactam.[5a] Furthermore, an almost complete simple diastereoselection was operative, resulting from a defined *Z*-enolate geometry in the hypothetical zwitterionic intermediate.[5b] Finally, a regio- and diastereoselective transannular reaction transferred the azoninones into indolizidinones.[4,5b]

Here we report on the 1,4-chirality[6] transfer of the zwitterionic aza-Claisen rearrangement induced by the defined enolate geometry in combination with a defined transition state geometry, which had been sparsely investigated up to now.[7] The terminal unsubstituted allylamine **1** served as the reactant and the so formed azoninones **4**−**6** were used as the key intermediates in the synthesis of the chiral indolizidinones **7**−**15**.

Results and Discussion

Allylamine **1** was efficiently generated via a six-step sequence starting from *trans*-4-hydroxy-L-(−)-proline **2**,[6] the overall yield was about 50% (Scheme 1). After esterification,[8] the *N*-benzyl group was introduced by treatment of the secondary amine with benzyl chloride

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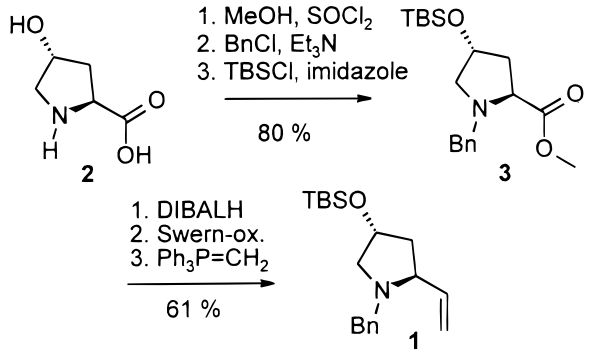
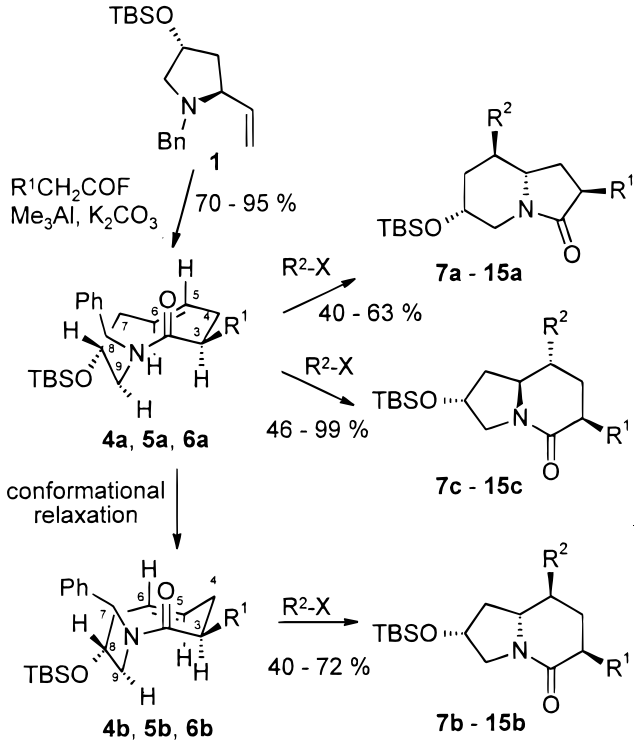
Scheme 1



in the presence of triethylamine.[9] Neither any epimerization to give the 2,4-*cis* material nor any further benzylation of the tertiary amine or the hydroxyl group was found, respectively. The high yield and the short reaction time led to the replacement of the formerly used reductive amination.[5a,6] The protection of the alcohol as a TBS ether (*tert*-butyldimethylsilyl) generated ester **3**.[10] The reduction of the carboxyl function with DIBALH yielded the primary carbinol.[11] A subsequent Swern oxidation led to the corresponding aldehyde,[12] which was immediately converted into the vinylpyrrolidine **1** by a Wittig olefination with methylenetriphenylphosphorane to avoid any epimerization to the 2,4-*cis* product.[13]

Diastereoselective Aza-Claisen Rearrangement. The vinylpyrrolidine **1** was now treated with a range of carboxylic acid fluorides under the recently reported standard conditions:[5c] The allylamine **1** was dissolved in CH_2Cl_2 in the presence of solid K_2CO_3 at an ambient temperature and treated with the acid fluoride.[14] In contrast to the reactions with carboxylic acid chlorides described earlier, no formation of a corresponding *N*-acylammonium salt was found! The rearrangement did not start up until the addition of the Me_3Al.[15] Then, a fast and highly chemoselective generation of the corresponding azoninones was observed; in some cases the addition of a further amount of the fluoride and some Me_3Al was useful to increase the yield. Overall, the reaction was found to be completed after 2 to 12 h, and the yield of isolated nine-membered ring lactams **4**−**6** varied between 70 and 95% (Scheme 2). In contrast to the investigations involving the acid chlorides, no allyl halides were formed, indicating that the competing von Braun degradation[16] had been almost efficiently suppressed. Moreover, no deactivated in situ formed amine hydrohalides decelerated the rate of the rearrangement.[5,6]

Scheme 2



R^1 = Ph, OBn, Cl R^2 = PhSe, I, Br X = I, Br

All rearrangements led diastereoselectively to single azoninones **4**−**6**, respectively, considering the stereogenic centers and the configurations of the olefins. Always, the configuration of the double bond was *E* and the relative configuration of the stereogenic centers C-3 and C-8 was found to be *trans* as proved beyond doubt by NOE analyses. Additionally, the complete description of the stereochemical aspects of the lactams needed the careful consideration of the relative arrangement of two planes of chirality (double bond and lactam function).[17] Right after the isolation 3,8-*trans*-azoninones **4a**−**6a** with conformation **a** were identified, indicating the proximity of the protons H-3, H-6, and H-9α, i.e., the double bond was arranged *pS* with respect to the medium-sized ring. The lactam unit showed a *cis* arrangement of C-3 and C-9 (about 20% NOE amplification regarding H-3 and H-9α) with respect to its partial double bond character and a *syn* arrangement of the carbonyl O-atom and H-5. The X-ray analysis of the α-chloro lactam **6a** confirmed these results.[18] Analysis of the NOE spectra indicated that irradiation at several peaks induced weak negative peaks at different ppm values. Obviously, a transfer of magnetization from the major compound to a minor diastereomer was found indicating a potential equilibri-

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(16) Cooley, J. H.; Evain, E. J. *Synthesis* **1989**, 1.
(17) The stereochemical terminology concerning the azoninones is used according to Eliel, E. L.; Wilen, S. H.; Mander; L. N. *Stereochemistry of Organic Compounds*; J. Wiley: New York, 1994; p 1121 (nomenclature *pS*, *pR*) and p 1203 (*trans* cycloalkenes). Description of *trans* cycloalkenes as planar chiral compounds: Schlögl, K. *Top. Curr. Chem.* **1984**, *125*, 27 and Nakazaki, M.; Yamamoto, K.; Naemura, K. *Top. Curr. Chem.* **1984**, *125*, 1. Alternative description as axial chiral compounds: Krow, G. *Top. Stereochem.* **1970**, *5*, 31.
(18) X-ray data of **6a**: colorless, transparent prism, crystallized from Et_2O/*n*-hexane at −20 °C, $C_{21}H_{32}NO_2Cl$ Si (M_r = 394.03); crystal data: orthorhombic; $P2_12_12_1$. For further data see Supporting Information and Figure 2.

um of at least two conformations (planar configurations) of the lactam function (partial double bond).[19]

All initially formed lactams **4a**−**6a** were characterized by conspicuous changes of their conformations, indicating a defined change of the planar chirality:[20] Keeping the lactams **4a**−**6a** at room temperature for 3−5 days or heating them to 40−60 °C for an appropriate time led to an almost complete relaxation to generate conformation **b**.[21] NOE analyses of **4b**−**6b** proved that the 3,8-*trans* configurations of the stereogenic centers and the *E*-double bonds were maintained. In contrast to the prior described lactams **4a**−**6a**, the proximity of the protons H-3, H-5, and H-9α was determined, indicating an almost complete flipping of the olefin from the *pS* to the *pR* arrangement in **4b**−**6b**. Again, the lactam unit showed a *cis* arrangement of C-3 and C-9 (about 20% NOE amplification regarding H-3 and H-9α) with respect to its partial double bond, but now a *syn* arrangement of the carbonyl O-atom and H-6 was found. The X-ray analysis of the α-chloro lactam **6b** confirmed these results.[22] Analysis of the NOE spectra resulted in no evidence concerning further species that improve almost rigid conformations of **4b**−**6b**.

Mechanistic Conclusions. The stereochemical outcome of the zwitterionic aza-Claisen rearrangement could be interpreted as follows (Figure 1): Initially, the activated carboxylic acid fluoride attacked the 2-vinylpyrrolidine *anti* with respect to the bulky TBSO substituent to give the hypothetical 1,2-*syn*-configured zwitterion with *Z*-enolate geometry as known for all amide enolates.[23] Then, the rearrangement proceeded diastereoselectively via a boatlike transition state to give the 3,8-*trans*-lactam (Figure 1).[24] Apparently, the reaction path employing a chairlike transition state was disfavored because of severe repulsive interactions (1,3 strain).[25] Furthermore, the transition state effected initially the formation of the medium-sized ring with *pS*-arrangement

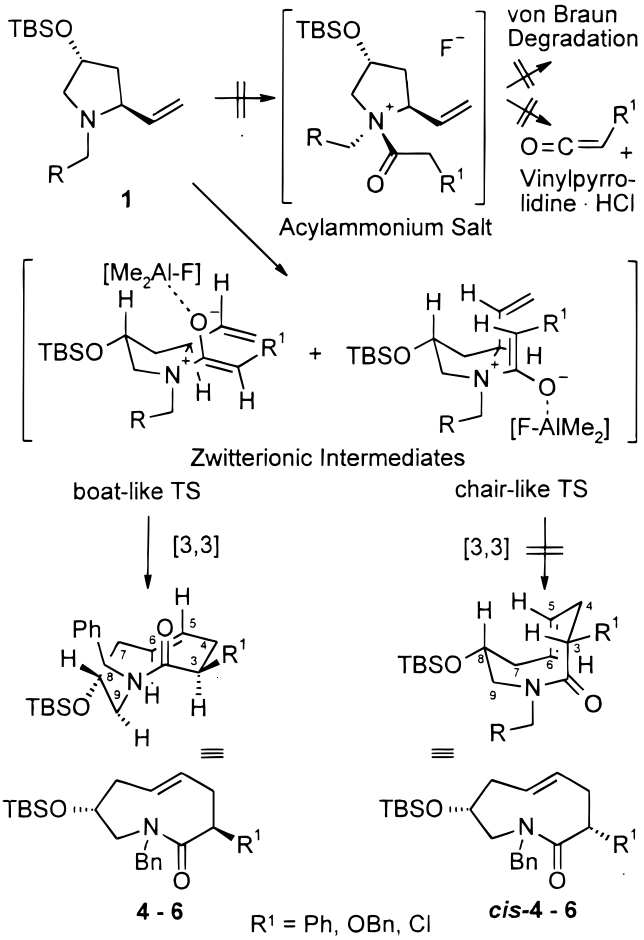

Figure 1. Chair- and boatlike intermediates of the rearrangement of allylamine **1** with carboxylic acid fluorides.

of the *E*-double bond. This planar diastereomer was obviously unstable: NMR and NOE analyses indicated the existence of one preferred (**a**) and at least one additional minor conformation (**c**?) as a highly flexible equilibrium of some arrangements of the lactam function (Figures 2, 4). Finally, the epimerization (flipping of the *E* double bond) to give the *pR* arrangement of the olefin, with respect to the ring, generated the most stable conformation (**b**) (Figures 3, 4). Preliminary force field calculations and molecular mechanics calculations of the related *E*/*Z*-1,5-nonadiene confirmed these observations.[26] Nevertheless, a high activation barrier had to be passed to achieve the change of the planar chiral information.[21,27] This fact allowed the isolation and the characterization of the conformers of the nine-membered rings. Furthermore, the reaction path starting from the allylamine via the kinetically stable to the thermodynamically stable lactam was a substantial argument that the process followed a sigmatropic rearrangement protocol.

Transannular Ring Contractions. Recent investigations have shown that azoninones underwent regio-

(19) The NMR spectra of lactam **5a** showed a doubled set of peaks, indicating the existence of two major diastereomeric species (ratio 3:1, independent of the temperature), and an additional minor conformer (about 5%). Several attempts to separate the compounds by means of HPLC failed because of the rapid adjustment of the equilibrium state. NOE analyses proved the conformation **5a** (first major diastereomer). The second major conformation might be the structure **5c** as shown in the Figure 4, but the NOE data left some doubts. The third compound could have represented a further lactam with an *anti* arrangement of C-3 and C-9 in respect to the partial double bond.

(20) Related effects had been reported investigating Xenicane diterpenes: (a) Guella, G.; Chiasera, G.; N′Diaye, I.; Pietra, F. *Helv. Chim. Acta* **1994**, *77*, 1203. (b) Pearson, W. H.; Hembre, E. J. *J. Org. Chem.* **1996**, *61*, 5546 (indolizidines).

(21) Preliminary kinetic investigations of the conversion of **4a** into **4b**: half-life period at 40 °C: 540 min, half-life period at 60 °C: 54 min, activation energy (Δ*G**) of the epimerization: about 24 kcal mol^{-1} (±3). Preliminary kinetic investigations of the conversion of **6a** into **6b**: half-life period at 40 °C: 540 min, half-life period at 60 °C: 54 min, activation energy (Δ*G**) of the epimerization: about 23 kcal mol^{-1} (±3).

(22) X-ray analysis of **6b**: colorless, transparent blocks, crystallized from Et_2O/*n*-hexane at −20 °C. $C_{21}H_{32}NO_2Cl$ Si (M_r = 394.03); crystal data: orthorhombic; $P2_12_12_1$. For further data see Supporting Information and Figure 3. Residual density of about 0.84 e/A^3 near the C-4/C-5 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 (**6b** in Figure 3) and a minor orientation with an occupancy factor of about 0.12 (resulting from cocrystallized **6a**, Figure 2).

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(26) Force field calculations of cyclic 1,5-nonadienes were reported by White, D. N. J.; Bowill, M. J. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1610.

(27) The activation energy (Δ*G**) of the racemisation of optically active *E*-cyclononene is about 20 kcalmol^{-1}, half-life period at 0 °C: 4 min. Cope, A. C.; Banholzer, K.; Keller, H.; Pawson, B. A.; Wang, J. J.; Winkler, H. J. S. *J. Am. Chem. Soc.* **1965**, *87*, 3644. Compare: *E*-cyclooctene: Δ*G** = 35 kcalmol^{-1}, half-life period at 133 °C: 120 h. Cope, A. C.; Pawson, B. A. *Ibid.* **1965**, *87*, 3649.

and diastereoselective ring contractions to indolizidinones.[4−6] Predominantly, the rigid conformations of the lactams involved caused a defined anti attack of an external electrophile at the unshielded face of the double bond and the intramolecular trapping of the nascent cation by the lactam nitrogen; the so-formed intermediate *N*-benzyl acylammonium ion underwent an immediate von Braun degradation to give the indolizidinone.[4,5] Preliminary investigations using the *pS* and the *pR* azoninones as reactants in transannular ring contractions, respectively, gave different bicyclic lactams. Obviously, the transannular reaction required a significantly lower activation energy than the epimerization *pS* into *pR* (conformational relaxation), i.e., the process proceeded in contrast to the dictates of the Curtin−Hammett Principle.[6]

With the intention to investigate scope and limitations of the transannular reactions, the azoninones **4**−**6** were treated with I_2, Br_2, and PhSeBr. Most of the reactions had been carried out in a NMR test tube scale to get the information concerning regio- and stereochemistry of the products **7**−**15**; an adequate number of reactions had been realized in a preparative scale to determine the more exact yields.

In the first series the *pR*-lactams **4b**−**6b** with the stable conformations **b** were treated with the reagents mentioned above. All attempts gave regio- and diastereomerically pure the indolizidinones **7b**−**15b** in acceptable yields and short reaction times; no intermediate acylammonium salts could be detected. The relative configuration of the new stereogenic centers and the position of the ring junction were proved by NOE analyses and, if necessary, by HETCOR (heteronuclear correlation). Detailed information is outlined in Table 3.

In the second series the *pS*-lactams **4a**−**6a** with the unstable conformations **a** were treated with the reagents mentioned above. Again no intermediate acylammonium salts could be detected; the reaction was found to be completed within minutes, generating the indolizidinones **7a/c**−**15a/c** in moderate to high yields. In contrast to the first series, an alternative regio- and stereochemical course was taken, and the products **a/c** were generated in varying ratios. Furthermore, the course of the reaction strongly depended on the reaction conditions: Adding slowly a solution of the reagent at room temperature to a solution of an azoninone (**4a**−**6a**), the indolizidinones **7c**−**15c** were built as the major products; the ratio of **7c**−**15c** and other diastereomers was 4:1 to >15:1. The reaction was completed at that time when the color of unreacted reagent remained. The reaction conditions were changed so that a solution of the nine-membered ring lactam **4a**−**6a** was added to a solution of the reagent at −20 °C. The regioisomeric indolizidinones **7a**−**15a** were isolated as the major products, and the ratios of **7a** to **15a** and other diastereomers were found to be 3:1 to >15:1.[28] Again, the reaction was found to be completed right after finishing the addition. The relative configuration of the new stereogenic centers and the position of the ring junction were proved by NOE analyses and, if necessary, by HETCOR (heteronuclear correlation). The results of the transannular ring contractions are summarized in Table 3.

(28) The transannular ring contraction of **5a** and I_2 followed an exceptional path despite varying reaction conditions: The selective formation of **11a** failed; only varying mixtures of **11a** and **11c** have been found to give predominantly lactam **11c**.

Table 1. Data of the Aza-Claisen Rearrangements

		transannular distance[a] [Å]			
		N→C-5		N→C-6	
azoninone	yield [%]	calcd	found	calcd	found
pS-**4a**	95	3.12		3.22	
pR-**4b**		3.35		2.99	
pS-**5a**	73	3.13		3.22	
pR-**5b**		3.31		2.97	
pS-**6a**	92	3.13	3.09	3.22	3.21
pR-**6b**		3.33	3.31	2.97	2.98

[a] Calcd: MM+ optimized structure, found: X-ray analysis.

Table 2. Nomenclature of the Indolizidinones

R^2/R^1	Ph	OBn	Cl
PhSe	7	10	13
I	8	11	14
Br	9	12	15

Mechanistic Conclusions. The interpretation of the results of the transannular reactions can be divided into a stereo- and a regiochemical part. Apparently, the stereochemical course of the ring contractions was quite reasonable; all reactions underwent well-known electrophilic *anti* additions of electrophile and nucleophile at the olefin. Regarding the *pS*-lactams **4a**−**6a**, the electrophile attacked the unshielded *Re*-face (C-5 or C-6) of the double bond, and the nascent cation was trapped by a *Si*-face attack (C-6 or C-5) of the nitrogen to generate the indolizidinones **7a/c**−**15a/c**. Due to the changed planar chirality, the double bond of the *pR*-lactams **4b**−**6b** suffered from a *Si*-face attack (C-5) of the electrophile and, consequentially, from a *Re*-attack (C-6) of the nitrogen to give **7b**−**15b**. As expected, no mixtures of the indolizidinones **7a/c**−**15a/c** on one hand and **7b**−**15b** on the other hand were found. The activation energy of the epimerization of the planar chiral information was significantly higher than that of the transannular reaction (*anti* Curtin−Hammett).[27]

The explanation of the regiochemical course of the reaction is still somewhat speculative, but a preliminary hypothesis should be submitted. All planar diastereomeric arrangements of the azoninones **4**−**6** were characterized by defined transannular distances between the nitrogen and C-5 and C-6 of the olefin (Table 1, Figure 3), respectively. The central assumption is that the shortest distance between the nitrogen and C-5 or C-6 of the olefin, respectively, determined the regiochemical outcome of the transannular reactions generating the indolizidinones **7**−**15**.

Transannular distances (Table 1, Figure 3) between the nitrogen and C-5 and C-6 of the olefin in the *pR*-lactams **4b**−**6b** were determined by X-ray analysis and some simple force field optimizations, and showed that N-1 was positioned somewhat closer to C-6 than to C-5.[22,29] Considering the rigid conformations of these lactams (no conformational mobility of both planes of chirality according NMR and NOE experiments), the ring contraction always proceeded regioselectively, the new bond forming between N-1 and C-6 as found in the indolizidinones **7b**−**15b**. Apparently, an analogous argument explicate the formation of the indolizidinones **7a**−

(29) Force field MM+ calculations had been carried out with Hyperchem arranging C-3 and C-9 *cis* with respect to the double bond character of the lactam unit. The structures are outlined in Figure 4. Transannular distances of type-**c**-conformation (N−C-5/N−C-6, [Å]): **4c**: 3.3/2.98, **5c**: 3.35/3.03, **6c**: 3.34/3.04.

Table 3. Results of the Transannular Ring Contractions[a]

							ratio indolizidinones **7** to **15**		
entry	azoninone	reagent	method**	scale*	yield [%]	product	a	b	c
a	**4a**	PhSeBr	A	p	44	7	1	−	−
b	**4a**	I_2	A	p	63	8	3	−	1
c	**4a**	Br_2	A	p	40	9	1	−	−
d	**4a**	PhSeBr	B	p	95	7	−	−	1
e	**4a**	I_2	B	p	99	8	−	−	1
f	**4a**	Br_2	B	p	55	9	1	−	4
g	**4b**	PhSeBr	A or B	p	69	7	−	1	−
h	**4b**	I_2	A or B	p	49	8	−	1	−
i	**4b**	Br_2	A or B	p	72	9	−	1	−
j	**5a**	PhSeBr	A	p	46	10	5	−	1
k	**5a**	I_2	A	a	36	11	1	−	1−>3
l	**5a**	Br_2	A	a	16	12	1	−	−
m	**5a**	PhSeBr	B	p	74	10	−	−	1
n	**5a**	I_2	B	p	70	11	−	−	1
o	**5b**	PhSeBr	A or B	a	20	10	−	1	−
p	**5b**	I_2	A or B	p	40	11	−	1	−
q	**6a**	PhSeBr	A	a	20.5	13	13	−	1
r	**6a**	Br_2	A	a	25	15	1	−	−
s	**6a**	PhSeBr	B	p	81	13	−	−	1
t	**6a**	I_2	B	a	15	14	−	−	1
u	**6a**	Br_2	B	p	82	15	−	−	1
v	**6b**	PhSeBr	A or B	p	64[6]	13	−	1	−
w	**6b**	I_2	A or B	p	64	14	−	1	−

[a] *: a = analytical scale, p = preparative scale; **methods A and B as described in the Experimental Section.

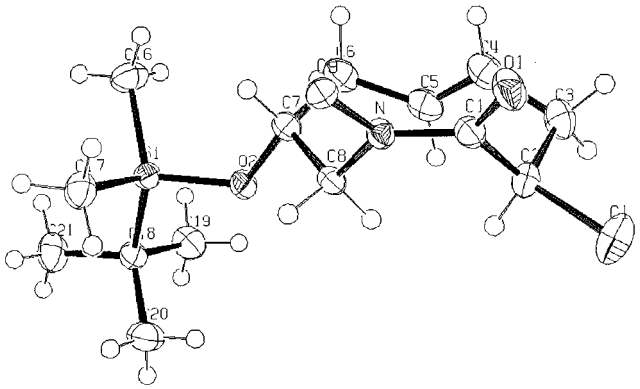

Figure 2. ORTEP plots of azoninone **6a**.

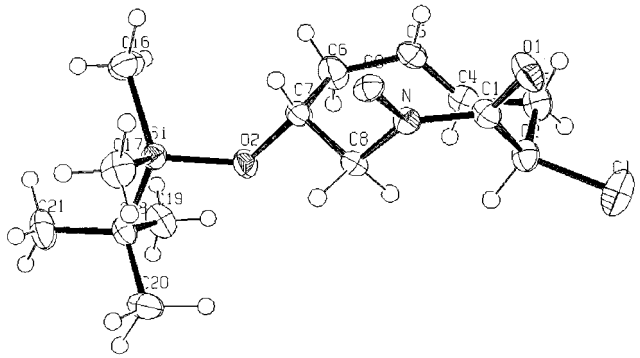

Figure 3. ORTEP plots of azoninone **6b**.

15a starting from the *pS*-lactams **4a**−**6a**: in this case the transannular distances (Table 1, Figure 2) between the nitrogen and C-5 were found to be somewhat shorter than that to C-6 according to the X-ray analysis and some simple force field calculation optimized structures.[18,29] Considering the predominant conformation of lactams **4a**−**6a** (rigid arrangement of the double bond according NMR and NOE experiments) at −20 °C, the transannular ring contraction was significantly faster than a conformational relaxation of the lactam function resulting in the regioselective formation of the indolizidinones **7a**−**15a** (*anti* Curtin−Hammett). In contrast, the reaction led to the regioisomer indolizidinones **7c**−**15c** at room temperature even though no further predominant conformation **4c**−**6c** (planar diastereomer) could be detected (all spectral data of the lactams **4a**−**6a**, respectively, measured at −20 °C, 0 °C, and room temperature were almost identical).[19] Actually, the dictates of the Curtin−Hammett Principle seemed to be the crucial point concerning the relative arrangement of the lactam function with respect to the ring. According to NOE and NMR data, the *pS*-lactams show some conformational mobility. Thus, a further conformation **c** (though sparsely populated) must have been much more reactive in respect to the transannular reaction than the predominant arrangement of type **a**. Simple force field calculation optimized structures resulted short transannular distances between N-1 and C-6 (compared to that between N-1 and C-5) in a *pS*-lactam showing a conformation of type **c**,[26,29] but severe repulsive interactions (→ low concentration) might have circumvented the occurrence of adequate peaks in the spectral analyses. Figure 4 should clarify this argument. However, the selective formation of two regioisomeric products starting from one and the same reactant presupposed the existence of at least two reactive conformations of the azoninones with (planar) diastereomeric properties.[30] Nevertheless, the exact reaction path is still unproved.

Conclusion. The zwitterionic aza-Claisen rearrangement of the *trans* 4-silyloxy-2-vinylpyrrolidine **1** to the γ,δ-unsaturated lactams **4**−**6** proceeded with an almost complete 1,4-chirality transfer and the formation of an

(30) Additionally, two corresponding (diastereomeric) *trans* arrangements of the amide function are imaginable, but, as outlined in ref 25, such *trans*/*trans* nonadienes are thought to be less stable (4−6 $kcal^{-1}$) than the *trans*/*cis* structures discussed above. Nevertheless, the existence of such structures as reactive (and diastereomeric) intermediates/transition states in the transannular ring contractions yielding **a** or **c** type products could neither be excluded nor proven. However, the presumption that diastereomeric properties caused the formation of the different bicycles was left as is. The determination of the transannular distances of N−C-5/N−C-6 would have allowed a very similar argumentation.

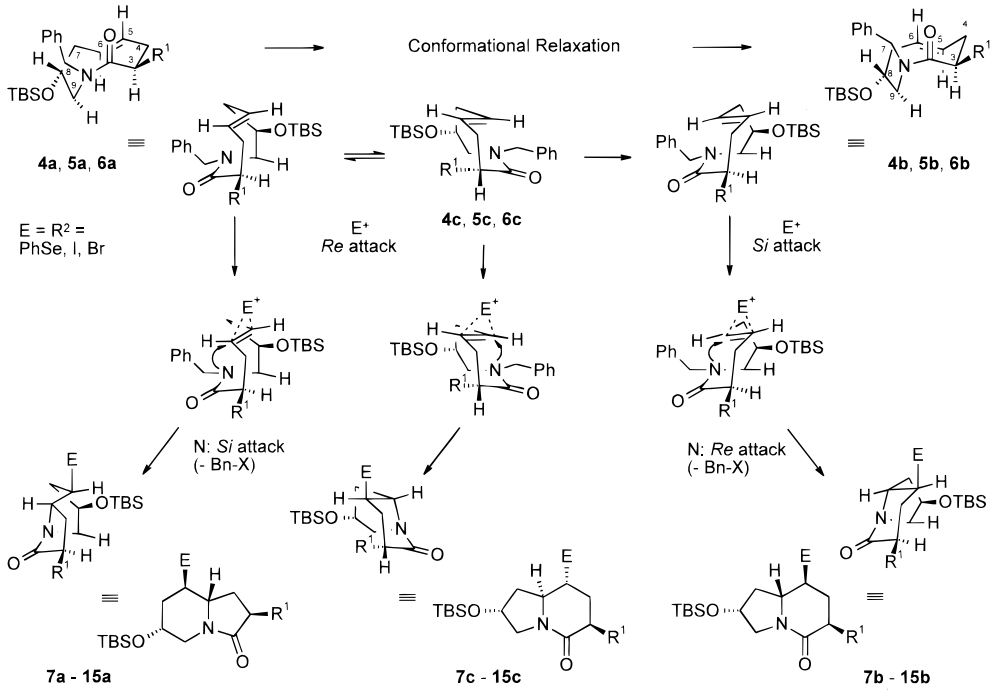

Figure 4. Regio- and diastereoselective transannular ring contraction paths of the azoninones **4**−**6**.

E-olefin in the medium-sized ring. In contrast to well-known acyclic Claisen rearrangements, an unusual diastereoselectivity was observed yielding 3,8-*trans*-lactams according to a boatlike transition state involved in the 3,3 sigmatropic process. Furthermore, the medium-sized rings were characterized by additional planar chiral properties: Right after the reaction the lactams **4**−**6** with conformations **a** (and **c**?) bearing a rigid *pS*-situation of the olefin and an almost flexible arrangement of the lactam unit were found. The relaxation from the kinetically generated conformations **a** into the thermodynamically stable forms **b** with almost rigid arrangements of lactam and olefin with respect to the ring required a significantly high activation energy.

The planar diastereomers **a** and **b** were subjected to transannular reactions to give indolizidinones with a complete stereoselectivity and a high regioselectivity. In contrast to the Curtin−Hammett−Principle lactams **4**−**6** allowed defined additions to the double bond with respect to the predominant conformation. The planar chiral information of the nine-membered ring could be transferred into defined stereogenic centers by means of the ring contraction. While the reactions of the rigid type-**b**-azoninones yielded exclusively bicycles **7b**−**15b** with a δ-valerolactam function, the type-**a**-rings used different reaction paths to generate two further products **7a/c**−**15a/c**. Obviously, the lactam function of the kinetically formed azoninones **a** showed some flexibility to generate at least two reactive conformations with diastereomeric properties under the reaction conditions. The variation of the transannular reaction conditions allowed us to pick out predominantly one of these conformations yielding either the series **7a**−**15a** or series **7c**−**15c**, respectively.

Further investigations concerning scope and limitations of the regio- and diastereoseletive transannular reactions and the use of an appropriate sequence in natural product syntheses are in progress.

(31) Nubbemeyer, U. *Synthesis* **1993**, 1120.

Experimental Section

For general experimental data see ref 31. The ^{1}H NMR spectra of **5a**, **9a** and the NOEDS analyses of **5a**, **9a** were recorded on a 500 MHz spectrometer. Satisfactory HRMS data-(± 0.4%) are reported for all new compounds. X-ray analyses were performed using $Mo_{K\alpha}$-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: $\omega(F) = 4F^2/[\,\sigma^2(F^2) + (0.03F^2)^2\,]$. The final difference density was between −0.29 and +0.36 e/A^3.

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 added slowly. 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 the white salt. After a final filtration and the removal of the solvent, the pure benzyloxyacetyl fluoride was isolated as a clear oil, yield: 2.88 g (95%, 17.1 mmol): ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.40−7.20 (m, 5 H), 4.65 (s, 2 H), 4.25 (d, $J(^{19}F,^1H)$ = 3.4 Hz, 2 H). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 163.1 and 157.7 (d, $J(^{19}F,^{13}C)$ = 366 Hz, *C*O), 136.1 (s), 128.6 (d), 128.4 (d), 128.1 (d), 73.4 (t), 64.9 and 63.9 (dd, $J(^{19}F,^{13}C)$ = 71 Hz).

Standard Procedure for the Zwitterionic Claisen Rearrangement. Under argon, dry K_2CO_3 (70 mg, 0.5 mmol) was suspended in dry CH_2Cl_2 (15 mL) and cooled to 0 °C. *N*-Allylpyrrolidine **1** (320 mg, 1 mmol) and acid fluoride (3 to 6 mmol) were added subsequently by means of a syringe. After about 15 min of stirring at 0 °C, a solution of Me_3Al (0.75−1.5 mL, 1.5−3 mmol, 2 M in *n*-heptane) was added via syringe, and CH_4 evolved. The mixture was allowed to warm to room temperature. The reaction was completed within hours (R^1 = Cl, Ph) or 1 to 2 days (R = 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. Workup was started by dilution of the reaction mixture with Et_2O 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 ($MgSO_4$). The solvent was removed below 20 °C to isolate the *pS*-lactams **4a**−**6a**, heating to 40−60 °C led to a fast epimerization to give the *pR*-lactams **4b**−**6b**. 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 **4a**−**6a** had been stored at −20 °C without a significant epimerization for several weeks. The crystals of **6a** were found to be stable even at room temperature for days.

(*pS*)*E*-3*S*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-phenyl-2,3,4,7,8,9-hexahydro-1*H*-azonin-2-one 4a.[5c] Reaction of vinylpyrrolidine **1** (0.1 g, 0.32 mmol), phenylacetyl fluoride (0.13 g, 0.95 mmol), and Me_3Al (2 mL, 4 mmol) following the standard procedure. Purification by column chromatography on silica gel (hexane/EtOAc 5:1, R_f = 0.53). Yield: azoninone **4a** (0.13 g, 95%) as crude oil. $[\alpha]^{20}_D$ −80.7 (*c* = 1.5, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.50−7.10 (m, 10 H), 5.92−5.77 (m, 1 H), 5.75−5.60 (m, 1 H), 5.08−5.00 (d, *J* = 14 Hz, 1 H), 4.30−4.22 (dd, *J* = 10, 8 Hz, 1 H), 4.22−4.18 (d, *J* = 15 Hz, 1 H), 4.15−4.10 (m, 1 H), 3.95−3.90 (dd, *J* = 16, 10 Hz, 1 H), 3.10−3.00 (dd, *J* = 15, 4 Hz, 1 H), 2.70−2.60 (m, 2 H), 2.35−2.25 (dd, *J* = 14, 2 Hz, 1 H), 2.22−2.10 (ddd, *J* = 14, 11, 5 Hz, 1 H), 0.81 (s, 9 H), −0.01 (s, 3 H), −0.07 (s, 3 H). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 174.2 (s), 139.8 (s), 137.4 (s), 134.4 (d), 128.7 (d), 128.5 (d), 128.4 (d), 128.2 (d), 127.5 (d), 127.0 (d), 67.9 (d), 52.2 (d), 52.1 (t), 48.9 (t), 39.2 (t), 34.4 (t), 25.7 (q), 18.0 (s), − 4.8 (q), − 4.9 (q). The NMR spectra show a second species (equilibrium), witch might be in accordance with azoninone **4c** (NOE analysis). In some attempts some degradation products of the phenylacetyl fluoride were found.

***E*(*pR*)-3*S*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-phenyl-2,3,4,7,8,9-hexahydro-1*H*-azonin-2-one 4b.**[5c] Heating of azoninone **4a** to 40−60 °C yields conversion to **4b**, ratio **4b**/**4a**: 7/1 to 10/1. $[\alpha]^{20}_D$ −165.1 (*c* = 0.6, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.2−7.3 (m, 5 H), 5.84 (ddd, *J* = 16, 11, 5 Hz, 1 H), 5.36 (ddd, *J* = 16, 12, 4 Hz, 1 H), 5.20 (d, *J* = 16 Hz, 1 H), 4.15−3.95 (m, 3 H), 3.84 (dd, *J* = 12, 2 Hz, 1 H), 3.04 (d, *J* = 13 Hz, 1 H), 2.81 (ddd, *J* = 12, 12, 12 Hz, 1 H), 2.75 (m, 1 H), 2.50 (dd, *J* = 12, 5 Hz, 1 H), 2.08 (ddd, *J* = 10, 10, 8 Hz, 1 H), 0.84 (s, 9 H), 0.05 (s, 3 H), 0.02 (s, 3 H). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 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), 54.5 (d), 51.8 (t), 49.1 (t), 42.8 (t), 36.8 (t), 25.6 (q), 17.8 (s), − 4.4 (q), −4.9 (q). IR (KBr) 3063 (s), 3028 (s), 2953 (s), 2929 (s), 2887 (s), 2856 (s), 1775 (w), 1725 (w), 1637 (s, C═O), 1255 (s) cm^{-1}. MS (70 eV, EI, 60 °C): *m*/*z* 435 (22) [M^+], 378 (32) [M^+ − C_4H_9], 344 (31) [M^+ − Bn], 91 (100). HRMS: Calcd for $C_{27}H_{37}NO_2Si$: 435.25936 (M^+), found 435.25747 (M^+).

(*pS*)*E*-3*R*,8*R*-1-Benzyl-3-benzyloxy-8-(*tert*-butyldimethylsilyloxy)-2,3,4,7,8,9-hexahydro-1*H*-azonin-2-one 5a. Reaction of vinylpyrrolidine **1** (0.3 g, 0.95 mmol), benzyloxyacetyl fluoride (1 g, 5.7 mmol), and Me_3Al (1.4 mL, 3 mmol) following the standard procedure. Purification by column chromatography on silica gel (hexane/EtOAc 3:1, R_f = 0.51). Yield: Inseparable 3:1 mixture of azoninones **5a** (major conformer) and **5c** (minor conformer, structure had not been undoubtedly proved) (0.32 g, 73%) as pale yellow oil. $[\alpha]^{20}_D$ 4.9 (*c* = 1.1, $CHCl_3$). Major compound **5a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.4−7.2 (m, 10 H), 5.65−5.55 (ddd, *J* = 16, 11, 3 Hz, 1 H), 5.41−5.33 (ddd, *J* = 16, 10, 6 Hz, 1 H), 5.20−5.15 (d, *J* = 14 Hz, 1 H), 4.63−4.60 (d, *J* = 12 Hz, 1 H), 4.42−4.38 (dd, *J* = 8, 8 Hz, 1 H), 4.33−4.30 (d, *J* = 12 Hz, 1 H), 4.08−4.05 (d, *J* = 15 Hz, 1 H), 4.03−3.99 (m, 1 H), 3.43−3.35 (dd, *J* = 15, 10 Hz, 1 H), 2.88−2.82 (dd, *J* = 15, 5 Hz, 1 H), 2.75−2.68 (m, 1 H), 2.39−2.30 (m, 1 H), 2.27−2.20 (m, 1 H), 2.15−2.08 (ddd, *J* = 13, 11, 6 Hz, 1 H), 0.81 (s, 9 H), −0.02 (s, 3 H), −0.07 (s, 3 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 172.3 (s), 140.0−126.0 (10 C), 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 compound (assignment as far as possible): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.4−7.2 (m, 10 H), 5.89−5.82 (ddd, *J* = 16, 10, 5 Hz, 1 H), 5.81−5.74 (ddd, *J* = 16, 10, 5 Hz, 1 H), 5.41−5.35 (d, *J* = 14 Hz, 1 H), 4.65−4.62 (ddd, *J* = 15, 1.4, 1.4 Hz, 1 H), 4.63−4.60 (d, *J* = 12 Hz, 1 H), 4.57−4.55 (dd, *J* = 5, 2 Hz, 1 H), 4.47−4.44 (d, *J* = 15 Hz, 1 H), 4.38−4.36 (m, 1 H), 4.33−4.30 (d, *J* = 12 Hz, 1 H), 3.31−3.28 (dd, *J* = 15, 4 Hz, 1 H), 2.60−2.55 (m, 1 H), 2.50−2.40 (m, 2 H), 2.34−2.30 (m, 1 H), 0.93 (s, 9 H), 0.09 (s, 6 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 173.3 (s), 140.0−126.0 (10 C), 76.6 (d), 71.7 (t), 51.9 (t), 48.5 (t), 41.9 (t), 34.3 (t), 25.9 (q), 17.9 (s), −4.6 (q), −4.8 (q).

(*pR*)*E*-3*R*,8*R*-1-Benzyl-3-benzyloxy-8-(*tert*-butyldimethylsilyloxy)-2,3,4,7,8,9-hexahydro-1*H*-azonin-2-one 5b. Heating of azoninone **5a** to 40−60 °C yields conversion to **5b**, ratio **5b**/**5a**: 7/1 to 10/1. $[\alpha]^{20}_D$ 14.9 (*c* = 1.3, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.4−7.2 (m, 10 H), 5.65−5.50 (m, 1 H), 5.40−5.20 (m, 2 H), 4.60−4.55 (d, *J* = 12 Hz, 1 H), 4.23−4.1.8 (d, *J* = 12 Hz, 1 H), 4.10−4.05 (d, *J* = 15 Hz, 1 H), 4.05−3.9 (m, 2 H), 3.60−3.50 (dd, *J* = 14, 9 Hz, 1 H), 2.95−2.88 (d, *J* = 14 Hz, 1 H), 2.78−2.66 (ddd, *J* = 11, 7, 4 Hz, 1 H), 2.55−2.45 (m, 2 H), 2.05−1.92 (ddd, *J* = 12, 12, 8 Hz, 1 H), 0.80 (s, 9 H), 0.01 (s, 3 H), 0.05 (s, 3 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 171.6 (s), 137.5 (s), 137.4 (s), 130.2 (d), 129.7 (d), 128.5 (d), 128.4 (d), 128.2 (d), 128.0 (d), 127.7 (d), 127.4 (d), 76.7 (d), 71.1 (t), 69.4 (d), 53.7 (t), 49.0 (t), 42.8 (t), 36.8 (t), 25.6 (q), 17.8 (s), −4.9 (q), −5.16 (q). IR (KBr) 2925 (s), 2885 (s), 2857 (s), 1646 (s), 1471 (s), 1452 (s) cm^{-1}. MS (70 eV, EI, 130 °C): *m*/*z* 465 (7) [M^+], 408 (7) [M^+ − C_4H_9], 374 (41), 359 (16), 91 (100). HRMS: calcd for $C_{28}H_{39}NO_3Si$: 465.26992 (M^+), found 465.26532 (M^+).

(*pS*)*E*-3*R*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-chloro-2,3,4,7,8,9-hexahydro-1*H*-azonin-2-one 6a.[6] Reaction of vinylpyrrolidine **1** (1 g, 3.15 mmol), chloroacetyl fluoride (1.5 mL, 2 mmol), and Me_3Al (2 mL, 4 mmol) following the standard procedure. Purification by column chromatography on silica gel (hexane/EtOAc 3:1, R_f = 0.38). Yield: Azoninone **6a** (1.14 g, 92%) as colorless crystals, mp 116 °C. $[\alpha]^{20}_D$ −79.8 (*c* = 1.7, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.25 (m, 5 H), 5.76 (ddd, *J* = 15, 11, 3 Hz, 1 H), 5.44 (ddd, *J* = 16, 9 Hz, 6 Hz, 1 H), 5.05 (d, *J* = 14 Hz, 1 H), 4.84 (dd, *J* = 10, 8 Hz, 1 H), 4.17 (d, *J* = 15 Hz, 1 H), 4.05 (m, 1 H), 3.55 (dd, *J* = 16, 10 Hz, 1 H), 3.01 (dd, *J* = 15, 4 Hz, 1 H), 2.90 (m, 1 H), 2.54 (ddd, *J* = 17,10, 6 Hz, 1 H), 2.28 (m, 1 H), 2.09 (ddd, *J* = 17,11, 5 Hz, 1 H), 0.81 (s, 9 H), −0.01 (s, 3 H), −0.07 (s, 3 H). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 169.6 (s), 136.8 (s), 131.2 (d), 130.7 (d), 128.5 (d), 127.7 (d), 66.3 (d), 55.2 (d), 51.6 (t), 49.3 (t), 39.0 (t), 36.9 (t), 25.5 (q), 17.8 (s), −4.9 (s), −5.1 (s).

(*pR*)*E*-3*R*,8*R*-1-Benzyl-8-(*tert*-butyldimethylsilyloxy)-3-chloro-2,3,4,7,8,9-hexahydro-1*H*-azonin-2-one 6b.[6] $[\alpha]^{20}_D$ −122 (*c* = 0.3, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.2−7.3 (m, 5 H), 5.67 (ddd, *J* = 16, 10, 6 Hz, 1 H), 5.34 (ddd, *J* = 15, 11, 3 Hz, 1 H), 5.22 (d, *J* = 15 Hz, 1 H), 4.50 (dd, *J* = 12, 3 Hz, 1 H), 4.09 (d, *J* = 15 Hz, 1 H), 4.01 (m, 1 H), 3.62 (dd, *J* = 14, 9 Hz, 1 H), 2.97 (d, *J* = 14 Hz, 1 H), 2.60−2.80 (m, 3 H), 2.02 (ddd, *J* = 12, 12, 9 Hz, 1 H), 0.81 (s, 9 H), 0.02 (s, 3 H), 0.00 (s, 3 H). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 169.6 (s), 136.8 (s), 131.2 (d), 130.1 (d), 128.6 (d), 127.9 (d), 127.6 (d), 69.5 (d), 56.2 (d), 54.3 (t), 49.7 (t), 42.8 (t), 40.1 (t), 25.6 (q), 17.8 (s), −4.5 (s), −4.9 (s). IR (KBr) 2952 (s), 2879 (s), 1644 (s, CO) cm^{-1}. MS (80 eV, EI, 100 °C): *m*/*z* 393 (6) [M^+], 378 (2) [M^+ −CH_3], 358 (4) [M^+ − Cl], 336 (18) [M^+ − C_4H_9]. HRMS: calcd for $C_{21}H_{32}NO_2ClSi$: 393.18909 (M^+), found 393.18759 (M^+).

Standard Procedure A. The electrophile (PhSeBr, I_2 or Br_2, respectively, 1 mmol) was dissolved in dry CH_2Cl_2 (20 mL), and the solution was cooled to −20 °C with stirring. Then a solution of the azoninone **4**, **5**, or **6** (1 mmol) in dry CH_2Cl_2 (5 mL) was added slowly by means of a syringe. According to most attempts, the reaction was found to be completed right after the finish of the addition (TLC monitoring). The mixture was stirred for a further 15 min at room temperature. Finally, the solvent was evaporated, and the crude material was purified by column chromatography.

Standard Procedure B. The azoninone **4**, **5**, or **6** (1 mmol) was dissolved in dry CH_2Cl_2 (20 mL) at room temperature with stirring. Then a solution of the electrophile (PhSeBr, I_2, or Br_2, respectively, 1 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise by means of a syringe until the color of unreacted reagent remained (quasi titration). According to most attempts, the reaction was found to be completed right after the finish of

the addition (TLC monitoring). The mixture was stirred for a further 15 min at room temperature. Finally, the solvent was evaporated, and the crude material was purified by column chromatography. (In most cases, method B was found to give the higher yields of indolizidinones compared to method A.)

2*S*,6*R*,8*R*,8a*S*-6-(*tert*-Butyldimethylsilyloxy)-2-phenyl-8-phenylselanyl-3-(8*H*)-indolizidinone 7a. Reaction of azoninone **4a** (110 mg, 0.25 mmol) and PhSeBr following the standard procedure A. Purification by column chromatography on silica gel (hexane/EtOAc 3:1, $R_f = 0.38$). Yield: indolizidinone **7a** (56 mg, 44%) as a colorless oil. $[\alpha]^{20}_D$ −29.6 ($c = 0.5$, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.53−7.56 (m, 2 H), 7.15−7.35 (m, 8 H), 4.06 (d, $J = 13$ Hz, 1 H), 3.97 (m, 1 H), 3.71−3.65 (dd, $J = 10$, 7 Hz, 1 H), 3.56−3.47 (ddd, $J = 5$, 7, 11 Hz, 1 H), 3.41−3.31 (ddd, $J = 12$, 12, 3 Hz, 1 H), 2.78−2.72 (dd, $J = 13$, 1.5 Hz, 1 H), 2.54−2.32 (m, 2 H), 2.29−2.23 (m, 1 H), 1.78−1.68 (ddd, $J = 14$, 13, 2 Hz, 1 H), 0.84 (s, 9 H), 0.05 (s, 3 H), 0.00 (s, 3 H). ^{13}C NMR δ (67.9 MHz, $CDCl_3$) 174.1 (s), 140.1 (s), 135.6 (d), 129.1 (d), 128.6 (d), 128.2 (d), 127.6 (d), 126.8 (d), 126.5 (s), 65.9 (d), 59.9 (d), 46.8 (d), 46.4 (t), 41.1 (d), 40.4 (t), 33.7 (t), 25.7 (q), 17.9 (s), −4.9 (q), −5.16 (q). IR (KBr) 2951 (s), 1695 (s, CO), 1257 (m) cm^{-1}. MS (80 eV, EI, 170 °C): *m*/*z* 501 (0.5) [M^+], 486 (1.6) [$M^+ - CH_3$], 444 (100) [$M^+ - C_4H_9$], 344 (8) [M^+ − PhSe]. HRMS calcd for $C_{25}H_{32}NO_2SeSi$: 486.13675 ($M^+ - CH_3$), found 486.13354 ($M^+ - CH_3$).

2*R*,6*S*,8*S*,8a*R*-2-(*tert*-Butyldimethylsilyloxy)-6-phenyl-8-phenylselanyl-5(8*H*)-indolizidinone 7b. Reaction of azoninone **4b** (100 mg, 0.23 mmol) and PhSeBr following the standard procedure B. Purification by column chromatography on silica gel (hexane/EtOAc 3:1, $R_f = 0.28$). Yield: indolizidinone **7b** (79 mg, 69%) as a colorless oil. $[\alpha]^{20}_D$ 106.9 ($c = 0.6$, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.60−7.50 (m, 2 H), 7.5−7.2 (m, 8 H), 4.45−4.35 (m, 1 H), 3.75−3.50 (m, 4 H), 3.25−3.15 (ddd, $J = 13$, 11, 3 Hz, 1 H), 2.60−2.40 (m, 2 H), 2.10−1.95 (ddd, $J = 13$, 13, 12 Hz, 1 H), 1.80−1.65 (ddd, $J = 12$, 11, 8 Hz, 1 H), 0.80 (s, 9 H), 0.05 (s, 3 H), −0.05 (s, 3 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 168.7 (s), 140.7, 135.8, 129.2, 128.6, 128.5, 128.1, 126.8, 126.5, 68.7 (d), 62.4 (d), 53.6 (t), 49.7 (d), 42.4 (t), 42.4 (d), 40.0 (t), 25.7 (q), 17.9 (s), −4.8 (q). IR (KBr) 2951 (s), 2926 (s), 1643 (s), 1252 (m) cm^{-1}. MS (80 eV, EI, 170 °C) *m*/*z* 500 (0.5) [M^+], 486 (1.6) [$M^+ - CH_3$], 444 (100) [$M^+ - C_4H_9$], 344 (9) [M^+ − PhSe], 287 (20) [$M^+ - C_4H_9$ − PhSeH]. HRMS calcd for $C_{25}H_{32}NO_2Si\ ^{80}Se$: 486.13675 ($M^+ - CH_3$), found 486.13281 ($M^+ - CH_3$).

2*R*,6*S*,8*R*,8a*S*-2-(*tert*-Butyldimethylsilyloxy)-6-phenyl-8-phenylselanyl-5(8*H*)-indolizidinone 7c. Reaction with azoninone **4a** (130 mg, 0.29 mmol) and PhSeBr following the standard procedure B. Purification by column chromatography on silica gel (hexane/EtOAc 3:1, $R_f = 0.25$). Yield: indolizidinone **7c** (141 mg, 95%) as colorless crystals, mp 109 °C. $[\alpha]^{20}_D$ −12.1 ($c = 1.4$, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.50−7.40 (m, 2 H), 7.40−7.25 (m, 6 H), 7.10−7.00 (m, 2 H), 4.45−4.40 (dd, $J = 4$, 4 Hz, 1 H), 4.00−3.90 (dd, $J = 13$, 4 Hz, 1 H), 3.90−3.80 (m, 2 H), 3.50−3.40 (d, $J = 13$ Hz, 1 H), 3.11−3.00 (ddd, $J = 11$, 11, 5 Hz, 1 H), 2.38−2.22 (m, 3 H), 1.68−1.55 (ddd, $J = 12$, 12, 4 Hz, 1 H), 0.80 (s, 9 H), 0.05 (s, 3 H), 0.01 (s, 3 H). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 168.5 (s), 153.2 (s), 141.5 (s), 135.8 (d), 129.2 (d), 129.0 (d), 128.5 (d), 128.4 (d), 126.6 (d), 68.2 (d), 61.7 (d), 55.7 (t), 47.5 (d), 43.1 (t), 38.2 (t), 36.9 (d), 25.7 (q), 17.9 (s), −4.85 (q), −4.89 (q). IR (KBr) 3054 (s), 2929 (s), 2885 (s), 2855 (s), 1630 (s, CO), 1437 (s), 1265 (s) cm^{-1}. MS (80 eV, EI, 110 °C) *m*/*z* 501 (6) [M^+], 486 (3) [$M^+ - CH_3$], 444 (100) [$M^+ - C_4H_9$]. HRMS calcd for $C_{26}H_{35}NO_2SiSe$ 501.16022 (M^+), found 501.16038 (M^+).

2*S*,6*R*,8*R*,8a*S*-6-(*tert*-Butyldimethylsilyloxy)-8-iodo-2-phenyl-3-(8*H*)-indolizidinone 8a. Reaction of azoninone **4a** (110 mg, 0.25 mmol) and I_2 following the standard procedure A. Purification by column chromatography on silica gel (hexane/EtOAc 3:1, $R_f = 0.41$). Yield: indolizidinones **8a/c** (72.5 mg, 63%, ratio 3:1) as a colorless oil. Separation **8a/8c** via HPLC. $[\alpha]^{20}_D$ −26.0 ($c = 0.7$, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.33−7.19 (m, 5 H), 4.30−4.20 (ddd, $J = 12$, 11, 4 Hz, 1 H), 4.21−4.14 (ddd, $J = 14$, 2, 2 Hz, 1 H), 3.9−3.8 (m, 2 H), 3.74−3.67 (dd, $J = 9$, 9 Hz, 1 H), 2.95−2.89 (dd, $J = 14$, 1.5 Hz, 1 H), 2.59−2.50 (dddd, $J = 14$, 4, 4, 2 Hz, 1 H), 2.43−2.37 (m, 2 H), 2.29−2.18 (ddd, $J = 13$, 11, 2 Hz, 1 H), 0.87 (s, 9 H), 0.07 (s, 3 H), 0.05 (s, 3 H). ^{13}C NMR δ (67.9 MHz, $CDCl_3$) δ 174.3 (s), 139.7 (s), 128.7 (d), 127.6 (d), 126.9 (d), 67.4 (d), 62.7 (d), 46.6 (t), 46.5 (d), 45.5 (t), 34.8 (t), 27.9 (d), 25.7 (q), 17.9 (s), −4.9 (q), −5.16 (q). IR (KBr) 2949 (s), 2925 (s), 1697 (s, CO), 1257 (m) cm^{-1}. MS (70 eV, EI, 150 °C) *m*/*z* 470 (0.1) [M^+], 456 (3) [$M^+ - CH_3$], 414 (100) [$M^+ - C_4H_9$], 287 (14) [$M^+ - C_4H_9$ − I]. HRMS calcd for $C_{19}H_{27}NO_2ISi$: 456.08559 ($M^+ - CH_3$), found 456.08212 ($M^+ - CH_3$).

2*R*,6*S*,8*S*,8a*R*-2-(*tert*-Butyldimethylsilyloxy)-8-iodo-6-phenyl-5(8*H*)-indolizidinone 8b. Reaction of azoninone **4b** (100 mg, 0.23 mmol) with I_2 following the standard procedure B. Purification by column chromatography on silica gel (hexane/EtOAc 6:1, $R_f = 0.34$). Yield: indolizidinone **8b** (53 mg, 49%) as a colorless oil. $[\alpha]^{20}_D$ 73.4 ($c = 1.1$, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.4−7.1 (m, 5 H), 4.45 −4.35 (m, 1 H), 4.10−4.00 (ddd, $J = 11$, 11, 3 Hz, 1 H), 4.00−3.90 (ddd, $J = 11$, 10, 5 Hz, 1 H), 3.78−3.70 (dd, $J = 12$, 6 Hz, 1 H), 3.70−3.65 (m, 1 H), 3.65−3.60 (dd, $J = 12$, 6 Hz, 1 H), 2.92−2.80 (ddd, $J = 11$, 7, 3 Hz, 1 H), 2.61−2.50 (ddd, $J = 12$, 8, 7 Hz, 1 H), 2.50−2.35 (ddd, $J = 14$, 14, 12 Hz, 1 H), 1.95−1.75 (ddd, $J = 11$, 9, 8 Hz, 1 H), 0.80 (s, 9 H), 0.05 (s, 3 H), 0.01 (s, 3 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 168.4 (s), 139.9, 128.7, 128.0, 127.0, 67.7 (d), 64.6 (d), 54.7 (t), 50.6 (d), 44.9 (t), 43.8 (t), 25.7 (q), 24.0 (d), 17.9 (s), −4.9 (q). IR (KBr) 2953 (s), 2928 (s), 2856 (s), 1648 (s, CO), 1451 (s) 1431 (s), 1252 (m) cm^{-1}. MS (70 eV, EI, 160 °C) *m*/*z* 470 (0.5) [$M^{+\cdot}$- H^+], 456 (3) [$M^+ - CH_3$], 414 (100) [$M^+ - C_4H_9$], 287 (15) [$M^+ - I - C_4H_9$]. HRMS calcd for $C_{20}H_{29}NO_2SiI$ 470.10124 (M^+ − H), found 470.10574 (M^+ − H).

2*R*,6*S*,8*R*,8a*S*-2-(*tert*-Butyldimethylsilyloxy)-8-iodo-6-phenyl-5(8*H*)-indolizidinone 8c. Reaction of azoninone **4a** (120 mg, 0.28 mmol) and I_2 following the standard procedure B. Purification by column chromatography on silica gel (hexane/EtOAc 3:1, $R_f = 0.28$). Yield: indolizidinone **8c** (132 mg, 99%) as colorless crystals, mp 73 °C. $[\alpha]^{20}_D$ −15.3 ($c = 1.3$, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.40−7.25 (m, 3 H), 7.10−7.00 (m, 2 H), 4.45−4.40 (dd, $J = 4$, 4 Hz, 1 H), 4.22−4.11 (ddd, $J = 11$, 11, 4 Hz, 1 H), 4.00−3.92 (dd, $J = 13$, 4 Hz, 1 H), 3.95−3.85 (ddd, $J = 13$, 11, 4 Hz, 1 H), 3.80−3.76 (dd, $J = 6$, 2 Hz, 1 H), 3.65−3.58 (d, $J = 13$ Hz, 1 H), 2.86−2.73 (ddd, $J = 14$, 14, 7 Hz, 1 H), 2.65−2.55 (ddd, $J = 14$, 4, 2 Hz, 1 H), 2.38−2.30 (dd, $J = 13$, 5 Hz, 1 H), 1.72−1.60 (ddd, $J = 12$, 12, 4 Hz, 1 H), 0.90 (s, 9 H), 0.05 (s, 3 H), 0.01 (s, 3 H). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 168.1 (s), 141.2 (s), 128.6 (d), 127.9 (d), 126.9 (d), 67.4 (d), 64.5 (d), 56.7 (t), 48.6 (d), 44.3 (t), 43.4 (t), 25.7 (q), 20.5 (d), 17.9 (s), −4.8 (q), −4.9 (q). IR (KBr) 2957 (s), 2925 (s), 2890 (s), 2851 (s), 1630 (s, CO), 1438 (s), 1254 (s) cm^{-1}. MS (80 eV, 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]. HRMS calcd for $C_{19}H_{27}INO_2Si$ 456.08546 ($M^+ - CH_3$), found 456.08529 ($M^+ - CH_3$).

2*S*,6*R*,8*R*,8a*S*-8-Bromo-6-(*tert*-butyldimethylsilyloxy)-2-phenyl-3(8*H*)-indolizidinone 9a. Reaction of azoninone **4a** (100 mg, 0.23 mmol) and Br_2 following the standard procedure A. Purification by column chromatography on silica gel (hexane/EtOAc 5:1, $R_f = 0.38$). Yield: indolizidine **9a** (39 mg, 40%) as a colorless oil. $[\alpha]^{20}_D$ −29.3 ($c = 1.9$, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.4−7.2 (m, 5 H), 4.17−4.13 (dd, $J = 14$, 4 Hz, 1 H), 4.14−4.10 (m, 1 H), 4.05−4.00 (m, 1 H), 3.75−3.69 (m, 2 H), 2.92−2.87 (dd, $J = 14$, 2 Hz, 1 H), 2.53−2.46 (ddd, $J = 14$, 10, 4 Hz, 1 H), 2.49 −2.42 (dddd, $J = 14$, 4, 4, 2 Hz, 1 H), 2.43−2.35 (ddd, $J = 14$, 7, 7 Hz, 1 H), 2.08−2.00 (ddd, $J = 14$, 12, 2 Hz, 1 H), 0.80 (s, 9 H), 0.05 (s, 3 H), 0.01 (s, 3 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 174.2 (s), 139.7 (s), 128.7 (d), 127.6 (d), 126.9 (d), 66.9 (d), 61.8 (d), 48.8 (d), 46.4 (d), 46.4 (t), 43.3 (t), 32.9 (t), 25.6 (q), 17.9 (s), −4.9 (q), −5.16 (q). IR (KBr) 2952 (s), 1698 (s, CO), 1255 (m) cm^{-1}. MS (70 eV, EI, 130 °C) *m*/*z* 424 (0.2) [M^+], 410 (2.5) [$M^+ - CH_3$], 384 (1.1), 368 (100) [$M^+ - C_4H_9$]. HRMS calcd for $C_{19}H_{27}{}^{79}BrNO_2Si$: 408.09944 ($M^+ - CH_3$), found 408.10434 ($M^+ - CH_3$).

2*R*,6*S*,8*S*,8a*R*-8-Bromo-2-(*tert*-butyldimethylsilyloxy)-6-phenyl-5(8*H*)-indolizidinone 9b. Reaction of azoninone **4b** (130 mg, 0.29 mmol) with Br_2 following the standard procedure B. Purification by column chromatography on silica gel (hex-

ane/EtOAc 3:1, $R_f = 0.25$). Yield: indolizidinone **9b** (90.5 mg, 72%) as colorless crystals, mp 73 °C. $[\alpha]^{20}_D$ 52.7 (c = 1.8, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.40−7.20 (m, 5 H), 4.46−4.37 (m, 1 H), 4.04−3.93 (ddd, J = 12, 10, 3 Hz, 1 H), 3.91−3.81 (ddd, J = 10, 10, 6 Hz, 1 H), 3.76−3.68 (dd, J = 11, 7 Hz, 1 H), 3.66−3.63 (m, 2 H), 2.83−2.72 (ddd, J = 10, 6, 3 Hz, 1 H), 2.58−2.48 (ddd, J = 13, 6, 6 Hz, 1 H), 2.40−2.25 (ddd, J = 13, 12, 12 Hz, 1 H), 2.36−2.28 (ddd, J = 13, 9, 7 Hz, 1 H), 0.90 (s, 9 H), 0.09 (s, 3 H), 0.05 (s, 3H). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 168.3 (s), 140.0 (s), 128.7 (s), 128.0 (s), 127.0 (s), 68.3 (d), 63.4 (d), 54.4 (t), 49.4 (d), 47.5 (d), 42.5 (t), 41.9 (t), 25.7 (q), 24.0 (d), 17.9 (s), −4.9 (q). IR (KBr) 2956 (s), 2928 (s), 1640 (s, CO), 1252 (m) cm^{-1}. MS (70 eV, EI, 160 °C) m/z 425 (0.18) [M^+], 424 (0.27) [$M^+ - H$], 410 (4.17) [$M^+ - CH_3$], 368 (100) [$M^+ - C_4H_9$]. HRMS calcd for $C_{19}H_{27}NO_2$ ^{79}Br Si 408.09945 ($M^+ - CH_3$), found 408.09965 ($M^+ - CH_3$).

2*R*,6*S*,8*R*,8a*S*-8-Bromo-2-(*tert*-butyldimethylsilyloxy)-6-phenyl-5(8*H*)-indolizidinone 9c: Reaction of azoninone **4a** (0.2 g, 0.45 mmol) and Br_2 following the standard procedure B. Purification by column chromatography on silica gel (hexane/EtOAc 3:1, $R_f = 0.25$). Yield: indolizidinone **9a/c** (107 mg, 55%, ratio 1:4) as a colorless oil. Separation of **9a** and **9c** via HPLC. $[\alpha]^{20}_D$ −28.3 (c = 1.9, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.40−7.25 (m, 3 H), 7.10−7.00 (m, 2 H), 4.48−4.43 (dd, J = 4, 4 Hz, 1 H), 4.13−4.03 (ddd, J = 11, 11, 4 Hz, 1 H), 3.95−3.88 (dd, J = 13, 5 Hz, 1 H), 3.95−3.85 (m, 2 H), 3.58−3.50 (d, J = 14 Hz, 1 H), 2.73−2.60 (ddd, J = 14, 14, 7 Hz, 1 H), 2.56−2.46 (ddd, J = 14, 4, 2 Hz, 1 H), 2.36−2.28 (dd, J = 13, 5 Hz, 1 H), 1.75−1.62 (ddd, J = 12, 12, 4 Hz, 1 H), 0.90 (s, 9 H), 0.09 (s, 3 H), 0.05 (s, 3 H). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 168.1 (s), 141.1(s), 128.7 (d), 127.8 (d), 126.9 (d), 68.0 (d), 63.2 (d), 56.3 (t), 47.8 (d), 44.7 (d), 42.9 (t), 41.3 (t), 25.7 (q), 17.9 (s), −4.8 (q), −4.9 (q). IR (KBr) 2959 (s), 2883 (s), 2858 (s), 1645 (s, CO), 1257 (s) cm^{-1}. MS (80 eV, EI, 130 °C) m/z 424 (0.45) [M^+], 423 (0.2) [$M^+ - H$], 408 (4.1) [$M^+ - CH_3$], 368 (100) [$M^+ - C_4H_9$]. HRMS: calcd for $C_{19}H_{27}{}^{79}BrNO_2Si$: 408.09945 ($M^+ - CH_3$), found 408.09925 ($M^+ - CH_3$).

2*R*,6*R*,8*R*,8a*S*-2-Benzyloxy-6-(*tert*-butyldimethylsilyloxy)-8-phenylselanyl-3-(8*H*)-indolizidinone 10a. Reaction of azoninone **5a** (100 mg, 0.21 mmol) and PhSeBr following the standard procedure A. Purification by column chromatography on silica gel (hexane/EtOAc 5:1, $R_f = 0.31$). Yield: indolizidinone **10a/c** (52 mg, 46%, ratio 5:1) as a colorless oil. Separation of **10a** and **10c** via HPLC. $[\alpha]^{20}_D$ −18.3 (c = 1.1, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.6 (m, 2 H), 7.4−7.2 (m, 8 H), 4.94−4.88 (d, J = 12 Hz, 1 H), 4.74−4.66 (d, J = 12 Hz, 1 H), 4.10−4.03 (dd, J = 8, 4 Hz, 1 H), 4.02−3.95 (m, 2 H), 3.53−3.42 (ddd, J = 11, 7, 6 Hz, 1 H), 3.18−3.07 (ddd, J = 12, 11, 4 Hz, 1 H), 2.73−2.65 (dd, J = 15, 2 Hz, 1 H), 2.40−2.28 (ddd, J = 11, 7, 3 Hz, 1 H), 2.25−2.15 (dddd, J = 14, 6, 6, 3 Hz, 1 H), 2.15−2.05 (ddd, J = 14, 8, 5 Hz, 1 H), 1.70−1.60 (m, 1 H), 0.80 (s, 9 H), 0.05 (s, 3 H), 0.01 (s, 3 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 171.8, 137.9, 135.8, 129.1, 128.3, 128.2, 128.0, 127.6, 126.4, 71.9, 65.6, 59.0, 45.9, 41.6, 40.0, 33.2, 25.6, 17.9, −4.9, −5.16. IR (KBr) 2953 (s), 2927 (s), 1699 (s, CO), 1258 (m) cm^{-1}. MS (80 eV, EI, 160 °C) m/z 516 (2.9) [$M^+ - CH_3$], 474 (100) [$M^+ - C_4H_9$], 425 (45) [$M^+ - CH_3 - Bn$]. HRMS calcd for $C_{26}H_{34}NO_3SiSe$: 516.14732 ($M^+ - CH_3$), found 516.14337 ($M^+ - CH_3$).

2*R*,6*R*,8*S*,8a*R*-2-Benzyloxy-6-(*tert*-butyldimethylsilyloxy)-8-phenylselanyl-5(8*H*)-indolizidinone 10b. Reaction of azoninone **5b** (13 mg, 0.03 mmol) and PhSeBr following the standard procedure B. Purification by column chromatography on silica gel (hexane/EtOAc 7:1, R_f = 0.38). Yield: indolizidinone **10b** (3.5 mg, 20%) as a colorless oil. $[\alpha]^{20}_D$ 73.2 (c = 2, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.60−7.50 (m, 2 H), 7.40−7.20 (m, 8 H), 4.95−4.85 (d, J = 12 Hz, 1 H), 4.75−4.65 (d, J = 12 Hz, 1 H), 4.38−4.28 (m, 1 H), 3.98−3.80 (dd, J = 8, 7 Hz, 1 H), 3.70−3.55 (ddd, J = 10, 10, 6 Hz, 1 H), 3.56−3.50 (dd, J = 12, 6 Hz, 1 H), 3.50−3.43 (dd, J = 12, 5 Hz, 1 H), 3.10−3.00 (ddd, J = 11, 11, 5 Hz, 1 H), 2.58−2.48 (ddd, J = 11, 6, 4 Hz, 1 H), 2.45−2.35 (ddd, J = 12, 6, 6 Hz, 1 H), 2.08−1.95 (ddd, J = 14, 12, 9 Hz, 1 H), 1.73−1.60 (ddd, J = 13, 10, 7 Hz, 1 H), 0.80 (s, 9 H), 0.05 (s, 3 H), 0.01 (s, 3 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 168.1 (s), 138.0, 136.0, 129.2, 128.5, 128.3, 127.9, 127.6, 126.5, 74.9 (d), 72.8 (t), 68.8 (d), 61.3 (d), 53.2 (t), 41.9 (t), 40.4 (d), 36.9 (t), 25.7 (q), 17.9 (s), −4.9 (q). IR (KBr) 2927 (s), 2855 (s), 1654 (s, CO), 1258 (m) cm^{-1}. MS (80 eV, EI, 170 °C) m/z 531(1.3) [M^+], 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]. HRMS calcd for $C_{27}H_{37}NO_3Si^{80}Se$: 531.17079 ($M^+$), found 531.17552 ($M^+$).

2*R*,6*R*,8*R*,8a*S*-6-Benzyloxy-2-(*tert*-butyldimethylsilyloxy)-8-phenylselanyl-5(8*H*)-indolizidinone 10c. Reaction of azoninone **5a** (960 mg, 2.06 mmol) and PhSeBr following the standard procedure B. Purification by column chromatography on silica gel (hexane/EtOAc 2:1, $R_f = 0.28$). Yield: indolizidinone **10c** (820 mg, 74%) as colorless needles, mp 77 °C (recrystallization from Et_2O/hexane). $[\alpha]^{20}_D$ 2.1 (c = 1.9, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.60−7.50 (m, 2 H), 7.4−7.1 (m, 8 H), 4.90−4.85 (d, J = 12 Hz, 1 H), 4.73−4.67 (d, J = 12 Hz, 1 H), 4.40−4.35 (dd, J = 5, 5 Hz, 1 H), 3.85−3.80 (dd, J = 4, 2 Hz, 1 H), 3.80−3.67 (m, 2 H), 3.78−3.73 (dd, J = 5, 2 Hz, 1 H), 3.37 −3.30 (d, J = 13 Hz, 1 H), 3.32−3.20 (ddd, J = 13, 11, 4 Hz, 1 H), 2.50−2.40 (ddd, J = 14, 3, 3 Hz, 1 H), 2.25−2.18 (dd, J = 13, 4 Hz, 1 H), 1.98−1.85 (ddd, J = 14, 13, 4 Hz, 1 H), 1.60−1.49 (ddd, J = 12, 12, 4 Hz, 1 H), 0.80 (s, 9 H), 0.05 (s, 3 H), 0.01 (s, 3 H). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 166.6 (s), 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), 72.8 (t, C-10), 68.1 (d), 61.6 (d), 55.4 (t), 42.7 (t), 37.2 (t), 37.1 (d), 25.7 (q), 17.9 (s), −4.8 (q), −4.9 (q). IR (KBr) 2952 (s), 2883 (s), 1635 (s, CO), 1253 (s) cm^{-1}. MS (80 eV, EI, 180 °C): m/z 531 (0.5) [M^+], 516 (2.9) [$M^+ - CH_3$], 474 (90) [$M^+ - C_4H_9$], 425 (45) [$M^+ - CH_3 - Bn$]. HRMS: calcd for $C_{26}H_{34}NO_3SeSi$: 516.14731 ($M^+ - CH_3$), found 516.14719 ($M^+ - CH_3$).

2*R*,6*R*,8*R*,8a*S*-2-Benzyloxy-6-(*tert*-butyldimethylsilyloxy)-8-iodo-3-(8*H*)-indolizidinone 11a. Reaction of azoninone **5a** (31 mg, 0.07 mmol) and I_2 following the standard procedure A. Purification by column chromatography on silica gel (hexane/EtOAc 3:1, $R_f = 0.45$). Yield: indolizidinone **11a/c** (12 mg, 36%, ratio 1:3) as a colorless oil. Separation of **11a** and **11c** via HPLC. $[\alpha]^{20}_D$ −10° (c = 0.3, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.4−7.2 (m, 5 H), 4.94−4.88 (d, J = 12 Hz, 1 H), 4.74−4.66 (d, J = 12 Hz, 1 H), 4.14−4.05 (m, 2 H), 4.03−3.93 (ddd, J = 12, 11, 4 Hz, 1 H), 3.90−3.85 (m, 1 H), 3.85−3.75 (ddd, J = 11, 7, 6 Hz, 1 H), 2.90−2.83 (dd, J = 15, 2 Hz, 1 H), 2.51−2.42 (dddd, J = 14, 6, 6, 3 Hz, 1 H), 2.41−2.30 (ddd, J = 11, 7, 3 Hz, 1 H), 2.21−2.10 (m, 1 H), 2.09−1.98 (ddd, J = 14, 8, 5 Hz, 1 H), 0.80 (s, 9 H), 0.05 (s, 3 H), 0.01 (s, 3 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 172.1, 137.7, 128.4, 128.0, 127.7, 74.5, 72.0, 67.0, 61.7, 46.1, 45.2, 34.2, 27.6, 25.6, −4.9, −5.0. IR (KBr) 2952 (s), 2927 (s), 1700 (s), 1258 (m) cm^{-1}. MS (70 eV, EI, 130 °C): m/z 500 (0.2) [$M - H^+$], 486 (4) [$M^+ - CH_3$], 444 (35) [$M^+ - C_4H_9$], 395 (72) [$M^+ - C_7H_7 - CH_3$].

2*R*,6*R*,8*S*,8a*R*-2-Benzyloxy-6-(*tert*-butyldimethylsilyloxy)-8-iodo-5(8*H*)-indolizidinone 11b. Reaction of azoninone **5b** (130 mg, 0.28 mmol) with I_2 following the standard procedure B. Purification by column chromatography on silica gel (hexane/EtOAc 7:1, R_f = 0.4). Yield: indolizidinone **11b** (55.2 mg, 40%) as a colorless oil. $[\alpha]^{20}_D$ 77.1 (c = 1.8, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.4−7.1 (m, 5 H), 4.95−4.88 (d, J = 12 Hz, 1 H), 4.78−4.73 (d, J = 12 Hz, 1 H), 4.40−4.30 (m, 1 H), 4.00−3.80 (m, 3 H), 3.65−3.55 (m, 2 H), 2.88−2.78 (ddd, J = 11, 7, 5 Hz, 1 H), 2.55−2.40 (m, 2 H), 1.95−1.75 (m, 1 H), 0.80 (s, 9 H), 0.05 (s, 3 H), 0.01 (s, 3 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 167.8 (s), 137.7, 128.3, 127.9, 127.7, 74.9 (d), 72.7 (t), 68.1(d), 61.4 (d), 54.3 (t), 43.1 (t), 41.8 (t), 21.8 (d), 25.7 (q), 17.9 (s), −4.8 (q). IR (KBr) 2976 (s), 2926 (s), 1641 (s, CO), 1257 (m) cm^{-1}. MS (80 eV, 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) [$M^+ - J - CH_3 - C_7H_7$]. HRMS calcd for $C_{20}H_{29}INO_3Si$: 486.09615 ($M^+ - CH_3$), found 486.09378 ($M^+ - CH_3$).

2*R*,6*R*,8*R*,8a*S*-2-Benzyloxy-6-(*tert*-butyldimethylsilyloxy)-8-iodo-5(8*H*)-indolizidinone 11c. Reaction of azoninone **5a** (100 mg, 0.21 mmol) and I_2 following the standard procedure B. Purification by column chromatography on silica gel (hexane/EtOAc 3:1, R_f = 0.31). Yield: indolizidinone **11c** (80 mg, 70%) as colorless needles, mp 99 °C (recrystallization

from Et_2O/hexane). $[\alpha]^{20}_D$ 8.1 (c = 0.8, $CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$) δ 7.4−7.1 (m, 5 H), 4.94−4.89 (d, J = 11 Hz, 1 H), 4.75−4.70 (d, J = 11 Hz, 1 H), 4.40−4.35 (dd, J = 4, 4 Hz, 1 H), 4.10−3.95 (m, 2 H), 3.87−3.78 (dd, J = 13, 5 Hz, 1 H), 3.78−3.73 (dd, J = 5, 2 Hz, 1 H), 3.73−3.65 (d, J = 13 Hz, 1 H), 2.75−2.65 (ddd, J = 14, 5, 2 Hz, 1 H), 2.50−2.38 (ddd, J = 14, 12, 5 Hz, 1 H), 2.33−2.25 (m, 1 H), 1.68−1.75 (ddd, J = 12, 11, 4 Hz, 1 H), 0.80 (s, 9 H), 0.05 (s, 3 H), 0.01 (s, 3 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 166.4, 137.8, 128.3, 128.0, 127.7, 74.3, 73.0, 67.4, 64.4, 56.4, 44.9, 42.5, 20.2, 25.7, 18.0, −4.7, −4.8. IR (KBr) 2956 (s), 2926 (s), 1637 (s, CO), 1270 (s) cm^{-1}. MS (70 eV, EI, 130 °C) m/z 500 (0.2) [$M - H^+$], 486 (4) [$M^+ - CH_3$], 444 (35) [$M^+ - C_4H_9$], 395 (72) [$M^+ - C_7H_7 - CH_3$]. HRMS calcd for $C_{20}H_{29}INO_3Si$: 486.09615 ($M^+ - CH_3$), found 486.09198 ($M^+ - CH_3$).

2*R*,6*R*,8*R*,8a*S*-2-Benzyloxy-8-bromo-6-(*tert*-butyldimethylsilyloxy)-3-(8*H*)-indolizidinone 12a. Reaction of azoninone **5a** (10 mg, 0.02 mmol) with Br_2 following the standard procedure A. Purification by column chromatography on silica gel (hexane/EtOAc 5:1, R_f = 0.38). Yield: indolizidinone **12a** (2.4 mg, 16%) as a colorless oil. $[\alpha]^{20}_D$ −4.4 (c = 1.2, $CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$) δ 7.4−7.1 (m, 5 H), 4.95−4.90 (d, J = 12 Hz, 1 H), 4.75−4.70 (d, J = 12 Hz, 1 H), 4.15−4.08 (dd, J = 8, 4 Hz, 1 H), 4.08−3.98 (m, 2 H), 3.95−3.85 (ddd, J = 12, 11, 4 Hz, 1 H), 3.70−3.60 (ddd, J = 11, 7, 4 Hz, 1 H), 2.88−2.79 (d, J = 12 Hz, 1 H), 2.45−2.30 (m, 2 H), 2.22−2.10 (ddd, J = 13, 8, 5 Hz, 1 H), 2.04−1.94 (ddd, J = 14, 13, 2 Hz, 1 H), 0.80 (s, 9 H), 0.05 (s, 3 H), 0.01 (s, 3 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 128.3, 128.0, 127.7, 74.5, 72.0, 66.5, 60.0, 49.2, 46.0, 43.0, 32.4, 25.6, 17.0, −4.9, −5.16. IR (KBr) 2955 (s), 2929 (s), 1703 (s), 1259 (s) cm^{-1}. MS (70 eV, EI, 110 °C): m/z 440 (3.9) [$M^+ - CH_3$], 438 (3.7) [$M^+ - CH_3$], 398 (100) [$M^+ - C_4H_9$], 396 (96) [$M^+ - C_4H_9$]. HRMS calcd for $C_{20}H_{29}BrNO_3Si$ 438.11009 ($M^+ - CH_3$), found 438.10519 ($M^+ - CH_3$).

2*R*,6*R*,8*R*,8a*S*-6-(*tert*-Butyldimethylsilyloxy)-2-chloro-8-phenylselanyl-3(8*H*)-indolizidinone 13a.[6] Reaction of azoninone **6a** (23 mg, 0.06 mmol) and PhSeBr following the standard procedure A. Purification by column chromatography on silica gel (hexane/EtOAc 3:1, R_f = 0.44). Yield: indolizidinone **13a/c** (5.5 mg, 20.5%, ratio 13:1) as a colorless oil. Separation of **13a** and **13c** via HPLC. $[\alpha]^{20}_D$ −50.2 (c = 1.3, $CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$) δ 7.56−7.50 (m, 2 H), 7.35−7.26 (m, 3 H), 4.34 (dd, J = 8, 3 Hz, 1 H), 4.03−3.93 (m, 2 H), 3.60−3.50 (ddd, J = 11, 6, 6 Hz, 1 H), 3.22−3.10 (m, 1 H), 2.75 (d, J = 12 Hz, 1 H), 2.63 (ddd, J = 15, 6, 2 Hz, 1 H), 2.32−2.25 (m, 1 H), 2.25−2.15 (m, 1 H), 1.68 (m, 1 H), 0.81 (s, 9 H), 0.02 (s, 3 H), −0.03 (s, 3 H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 169.6 (s), 135.8 (d), 129.2 (d), 128.5 (d), 65.2 (d), 59.0 (d), 53.9 (d), 46.6 (t), 40.7 (d), 39.7(t), 36.7 (t), 25.5 (q), 17.9 (s), −4.9 (q), −5.1 (q). IR (KBr) 2952 (s), 2927 (s), 1714 (s), 1257 (m) cm^{-1}. MS (70 eV, EI, 150 °C) m/z 459 (0.1) [M^+], 444 (2) [$M^+ - CH_3$], 402 (100) [$M^+ - C_4H_9$], 244 (10) [$M^+ - C_4H_9$ − PhSeH]. HRMS calcd for $C_{19}H_{27}ClNO_2SiSe$: 444.06647 ($M^+ - CH_3$), found 444.06627 ($M^+ - CH_3$).

2*R*,6*R*,8*S*,8a*R*-2-(*tert*-Butyldimethylsilyloxy)-6-chloro-8-phenylselanyl-5(8*H*)-indolizidinone 13b.[6] Reaction of azoninone **6b** (0.25 g, 0.65 mmol) and PhSeBr following the standard procedure B. Purification by column chromatography on silica gel (hexane/EtOAc 10:1, R_f = 0.5). Yield: indolizidinone **13b** (150 mg, 64%) as a colorless oil. $[\alpha]^{20}_D$ 59.4 (c = 0.4, $CHCl_3$). ^1H NMR (270 MHz, C_6D_6) δ 7.40 (m, 2 H), 7.00−6.90 (m, 3 H), 4.00 (dd, J = 9, 6 Hz, 1 H), 3.84 (m, 1 H), 3.55 (dd, J = 12, 6 Hz, 1 H), 3.37 (dd, J = 12, 7 Hz, 1 H), 3.05 (ddd, J = 10, 10, 5 Hz, 1 H), 2.53−2.4 (m, 2 H), 2.20−2.05 (m, 2 H), 1.47 (ddd, J = 13, 10, 8 Hz, 1 H), 0.92 (s, 9 H), −0.02 (s, 3 H), −0.03 (s, 3 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 164.2 (s), 136.3 (d), 129.5 (d), 125.8 (d), 125.9 (s), 68.8 (d), 61.8 (d), 54.1 (d), 53.9 (t), 42.0 (t), 40.7 (t), 40.7(d), 22.7 (q), 17.9 (s), −4.9 (q), −5.0 (q). IR (KBr) 2855 (m), 1644 (s, CO) cm^{-1}. MS (70 eV, EI, 150 °C) m/z 459 (1) [M^+], 444 (3) [$M^+ - CH_3$], 436 (2), 402 (100) [$M^+ - C_4H_9$], 302 (11) [M^+ − PhSe], 244 (22) [$M^+ - C_4H_9$ − PhSeH]. HRMS calcd for $C_{20}H_{30}ClNO_2SiSe$: 459.08996 (M^+), found 459.08773 (M^+).

2*R*,6*R*,8*R*,8a*S*-2-(*tert*-Butyldimethylsilyloxy)-6-chloro-8-phenylselanyl-5(8*H*)-indolizidinone 13c.[6] Reaction of azoninone **6a** (0.2 g, 0.51 mmol) and PhSeBr following the standard procedure B. Purification by column chromatography on silica gel (hexane/EtOAc 3:1, R_f = 0.34). Yield: indolizidinone **13c** (187.7 mg, 81%) as a colorless oil. $[\alpha]^{20}_D$ −35.8 (c = 1.5, $CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$) δ 7.70−7.60 (m, 2 H), 7.4−7.1 (m, 3 H), 4.40−4.35 (m, 2 H), 3.95−3.70 (m, 2 H), 3.40−3.35 (m, 2 H), 2.62−2.52 (ddd, J = 15, 2, 2 Hz, 1 H), 2.35−2.20 (m, 2 H), 1.65−1.55 (ddd, J = 12, 12, 4 Hz, 1 H), 0.80 (s, 9 H), 0.05 (s, 3 H), 0.01 (s, 3 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 163.9 (s), 136.2, 129.3, 128.8, 125.2, 67.9 (d), 61.7 (d), 56.5 (t), 56.2 (d), 42.9 (t), 39.6 (t), 35.6 (d), 25.7 (q), 17.9 (s), −4.9 (q). IR (KBr) 2954 (s), 2855 (s), 1660 (s, CO), 1253 (s) cm^{-1}. MS (70 eV, EI, 150 °C) m/z 459 (3) [M^+], 444 (3) [$M^+ - CH_3$], 402 (100) [$M^+ - C_4H_9$], 302 (10) [M^+ − PhSe], 244 (14) [$M^+ - C_4H_9$ − PhSeH]. HRMS calcd for $C_{20}H_{30}ClNO_2SiSe$: 459.08996 (M^+), found 459.08975 (M^+).

2*R*,6*R*,8*S*,8a*R*-2-(*tert*-Butyldimethylsilyloxy)-6-chloro-8-iodo-5(8*H*)-indolizidinone 14b. Reaction of azoninone **6b** (300 mg, 0.75 mmol) and I_2 following the standard procedure B. Purification by column chromatography on silica gel (hexane/EtOAc 10:1, R_f = 0.5). Yield: indolizidinone **14b** (150 mg, 64%) as a colorless oil. $[\alpha]^{20}_D$ 47 (c = 0.04, $CHCl_3$). ^1H NMR (270 MHz, C_6D_6) δ 3.89 (dd, J = 10, 7 Hz, 1 H), 3.76 (m, 1 H), 3.54 (dd, J = 12, 6 Hz, 1 H), 3.40 (dd, J = 12, 7 Hz, 1 H), 3.12 (ddd, J = 10, 10, 5 Hz, 1 H), 3.01 (ddd, J = 11, 11, 4 Hz, 1 H), 2.40 (ddd, J = 12, 7, 4 Hz, 1 H), 2.30 (ddd, J = 14, 12, 10 Hz, 1 H), 2.04 (ddd, J = 12, 6, 6 Hz, 1 H), 1.38 (ddd, J = 12, 9, 7 Hz, 1 H), 0.91 (s, 9 H), −0.04 (s, 3 H), −0.05 (s, 3 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 163.2 (s), 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 (q), 21.2 (C-5), 18.0 (s), −4.9 (q), −5.0 (q). IR (KBr) 2850 (m), 1649 (s, CO), 1273 (m) cm^{-1}. MS (70 eV, EI, 150 °C) m/z 414 (3) [$M^+ - CH_3$], 372 (100) [$M^+ - C_4H_9$], 244 (5) [$M^+ - C_4H_9$ − HJ]. HRMS calcd for $C_{13}H_{22}NO_2ClISi$ 414.01519 ($M^+ - CH_3$), found 414.01514 ($M^+ - CH_3$).

2R,6*R*,8*R*,8a*S*-2-(*tert*-Butyldimethylsilyloxy)-6-chloro-8-iodo-5(8*H*)-indolizidinone 14c. Reaction of azoninone **6a** (260 mg, 0.66 mmol) and I_2 following the standard procedure B. Purification by column chromatography on silica gel (hexane/EtOAc 3:1, R_f = 0.4). Yield: indolizidinone **14c** (230 mg, 82%) as colorless needles, mp 94 °C (recrystallization from Et_2O/hexane). $[\alpha]^{20}_D$ −26.5 (c = 1.4, $CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$) δ 4.40−4.34 (dd, J = 4, 4 Hz, 1 H), 4.32−4.26 (dd, J = 4, 2 Hz, 1 H), 4.15−4.05 (ddd, J = 11, 11, 4 Hz, 1 H), 4.08−3.99 (ddd, J = 11, 11, 5 Hz, 1 H), 3.85−3.78 (dd, J = 14, 5 Hz, 1 H), 3.53−3.45 (d, J = 14 Hz, 1 H), 2.88−2.68 (m, 2 H), 2.32−2.25 (dd, J = 13, 4 Hz, 1 H), 1.70−1.57 (ddd, J = 11, 11, 4 Hz, 1 H), 0.80 (s, 9 H), 0.09 (s, 3 H), 0.05 (s, 3 H). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 163.6 (s), 67.1 (d), 64.6 (d), 57.1 (t), 54.6 (d), 44.2 (t), 43.7 (t), 25.6 (q), 17.9 (s), 17.1 (d), −4.9 (s), −5.0 (s). IR (KBr) 2959 (s), 1659 (s, CO), 1651 (s), 1266 (m) cm^{-1}. MS (80 eV, EI, 150 °C) m/z 414 (4) [$M^+ - CH_3$], 372 (100) [$M^+ - C_4H_9$], 245 (10) [$M^+ - C_4H_9$ − HJ]. HRMS calcd for $C_{13}H_{22}I$ Cl NO_2Si: 414.01519 ($M^+ - CH_3$), found 414.01514 ($M^+ - CH_3$).

2*R*,6*R*,8*R*,8a*S*-8-Bromo-6-(*tert*-butyldimethylsilyloxy)-2-chloro-3-(8*H*)-indolizidinone 15a. Reaction of azoninone **6a** (41 mg, 0.11 mmol) and Br_2 following the standard procedure A. Purification by column chromatography on silica gel (hexane/EtOAc 6:1, R_f = 0.44). Yield: indolizidinone **15a** (10 mg, 25%) as a colorless oil. $[\alpha]^{20}_D$ −44.9° (c = 1.7, CH_2Cl_2). ^1H NMR (270 MHz, $CDCl_3$) δ 4.42−4.36 (dd, J = 8, 3 Hz, 1 H), 4.08−4.02 (m, 1 H), 3.99−4.05 (ddd, J = 11, 2, 2 Hz, 1 H), 3.98−3.87 (ddd, J = 12, 10, 4 Hz, 1 H), 3.77−3.67 (ddd, J = 10, 6, 6 Hz, 1 H), 2.92−2.85 (dd, J = 11, 2 Hz, 1 H), 2.65−2.55 (ddd, J = 15, 7, 4 Hz, 1 H), 2.45−2.30 (m, 2 H), 2.05−1.95 (ddd, J = 14, 13, 2 Hz, 1 H), 0.80 (s, 9 H), 0.05 (s, 3 H), 0.01 (s, 3 H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 169.7 (s), 66.2 (d), 60.7 (d), 53.3 (d), 48.0 (d), 46.6 (t), 42.7 (t), 35.9 (t), 25.6 (q), 17.9 (s), −4.9 (q), −5.12 (q). IR (KBr) 2954 (s), 2928 (s), 1716 (s, CO), 1258 (s) cm^{-1}. MS (80 eV, EI, 110 °C) m/z 382 (0.12) [M^+], 368 (3.2) [$M^+ - CH_3$], 326 (100) [$M^+ - C_4H_9$]. HRMS calcd for $C_{13}H_{22}{}^{81}Br\,{}^{35}ClNO_2Si$: 368.02718 ($M^+ - CH_3$), found 368.02520 ($M^+ - CH_3$).

2*R*,6*R*,8*R*,8a*S*-8-Bromo-2-(*tert*-butyldimethylsilyloxy)-6-chloro-5(8*H*)-indolizidinone 15c. Reaction of azoninone **6a** (33 mg, 0.08 mmol) and Br_2 following the standard procedure B. Purification by column chromatography on silica gel (hexane/EtOAc 3:1, $R_f = 0.38$). Yield: indolizidinone **15c** (4.9 mg, 15%) as a colorless oil. $[\alpha]^{20}_D$ −30.4 ($c = 1.7$, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.46−4.38 (m, 2 H), 4.13−4.03 (ddd, $J = 11, 11, 4$ Hz, 1 H), 4.03−3.90 (ddd, $J = 11, 11, 5$ Hz, 1 H), 3.83−3.76 (dd, $J = 14, 5$ Hz, 1 H), 3.48−3.40 (d, $J = 14$ Hz, 1 H), 2.80−2.72 (ddd, $J = 14, 4, 2$ Hz, 1 H), 2.72−2.59 (ddd, $J = 12, 12, 5$ Hz, 1 H), 2.32−2.25 (dd, $J = 13, 4$ Hz, 1 H), 1.73−1.60 (ddd, $J = 11, 11, 4$ Hz, 1 H), 0.80 (s, 9 H), 0.09 (s, 3 H), 0.05 (s, 3 H). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 163.6 (s), 67.7 (d), 63.4 (d), 56.8 (t), 53.9 (d), 42.5 (t), 42.3 (t), 42.3 (d), 25.7 (q), 17.9 (s), −4.9 (q), −4.8 (q). IR (KBr) 2954 (s), 2884 (s), 2856 (s), 1665 (s, CO), 1253 (s) cm^{-1}. MS (80 eV, EI, 100 °C) *m*/*z* 368 (4.8) [$M^+ - CH_3$], 326 (100) [$M^+ - C_4H_9$]. HRMS calcd for $C_{13}H_{22}{}^{79}Br^{35}ClNO_2Si$ 366.02918 ($M^+ - CH_3$), found 366.02905 ($M^+ - CH_3$).

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Supporting Information Available: ^{13}C NMR spectra, NOEDS data for all new compounds, and crystallographic data including ORTEP plots for **6a** and **6b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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