Diastereoselective Synthesis of α-Hydroxy- and α-Aminoindolizidines and -quinolizidines. Evidence for a Novel Cyclization/Hydride Migration Mechanism in the $TiCl_4$-Induced Reaction of Prolinal Benzylimines by Deuterium Labeling Studies

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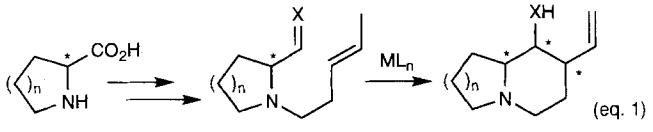
Lewis acid-catalyzed cyclization of prolinal and 2-piperidine-carbaldehyde benzylimines **11**, **12** results in the diastereoselective formation of α-amino-β-alkyl-substituted indolizidines **15**, **17**, **19**, **21** and -quinolizidines **16**, **18**, **20**, respectively. Both diastereoselectivity and constitution depend on the Lewis acid. $FeCl_3$ yields α,β-*trans*-α-(benzylamino)-β-isopropenyl derivatives **15** and **16**, probably by a cationic cyclization via carbenium ions **32a**, **b**. In contrast, $TiCl_4$ yields α,β-*cis*-α-(benzylideneamino)-β-isopropyl derivatives **19** and **20** by a novel cyclization/intermolecular hydride transfer mechanism, which was supported by deuterium labeling studies. Compounds **15**, **16**, **19**, and **20** were converted to the diastereomeric acetamides **24**, **25** and **28**, **29**. By an analogous cyclization of the aldehydes **8** and **9** only α,β-*cis*-α-hydroxy-β-isopropenylindolizidines **51** and -quinolizidines **52** were obtained irrespective of the Lewis acid used. The structures of **30** and **52** were elucidated by X-ray analysis.

Despite the many efforts spent on the stereoselective synthesis of indolizidines and quinolizidines during the last years, there is still a demand for new synthetic approaches to these alkaloids and their non-natural counterparts because of their important biological activities[1,2]. For example the hetero-substituted, i.e. hydroxylated indolizidines are potent glycosidase inhibitors[3]. Several strategies were developed for the construction of α-hydroxy-substituted indolizidines and quinolizidines[4]. The major approaches use the chiral information already present in carbohydrates to build up either the 5- or the 6-membered ring[5–9]. In alternative routes amino acids were used as synthetic precursors and were submitted to chain elongation or coupling reactions[2a–e,10,11]. The final ring closure in many cases was accomplished by a reductive amination or debenzylation/cyclization sequence[2d–e,6,8,9,12,13]. Our aim was directed toward the stereoselective synthesis of α-hetero-substituted indolizidines and quinolizidines by an intramolecular hetero-ene reaction of suitably functionalized prolinal and 2-piperidine-carbaldehyde derivatives[14–16]. As depicted in eq. (1) this strategy would allow us to use readily available amino acids **1** as chiral starting materials, which would ultimately be converted to cyclization products **3** having three adjacent stereocenters with the possibility of 1,2- and 1,3-asymmetric induction.



1a n = 1 **b** n = 2 **2** X = O, NR **3** (eq. 1)

The presence of two hetero atoms in the precursor **2** should induce the stereoselective formation of either α,β-*cis*- or α,β-*trans*-substituted indolizidines and quinolizidines by a chelation-controlled mechanism[17]. In this respect we have recently reported on the diastereoselective Lewis acid-catalyzed, intramolecular cyclization of prolinal benzylimines and the corresponding 2-piperidine-carbaldehyde derivatives to α-amino-substituted indolizidines and quinolizidines[18]. Under these conditions either the *cis* isomers were accessible by the use of $TiCl_4$ or the *trans* isomers by the use of $FeCl_3$. However, the different constitution of the *cis* and *trans* isomers suggests that this novel cyclization reaction is mechanistically not a hetero-ene reaction. It is believed to proceed by a stepwise reaction of an iminium ion[19] via a common carbenium ion intermediate, which can proceed according to two competitive pathways, depending on the relative stereochemistry at C-α and C-β of the bicyclic system. In this paper we present a full account of this work and an extension towards the stereoselective synthesis of α-hydroxyindolizidines and -quinolizidines. In addition, experimental evidence for a novel $TiCl_4$-induced cyclization/hydride migration mechanism by deuterium labeling experiments is presented.

As shown in Scheme 1, the cyclization precursors were prepared from commercially available (*S*)-prolinol (**4**) or racemic 2-piperidinylmethanol (**5**) by alkylation with 4-methyl-3-pentenyl bromide[20] followed by Swern oxidation[21] to give aldehydes **8** and **9**, which were converted to the benzylimines **11** and **12** by reaction with the appropriate benzylamines **10a–c**.

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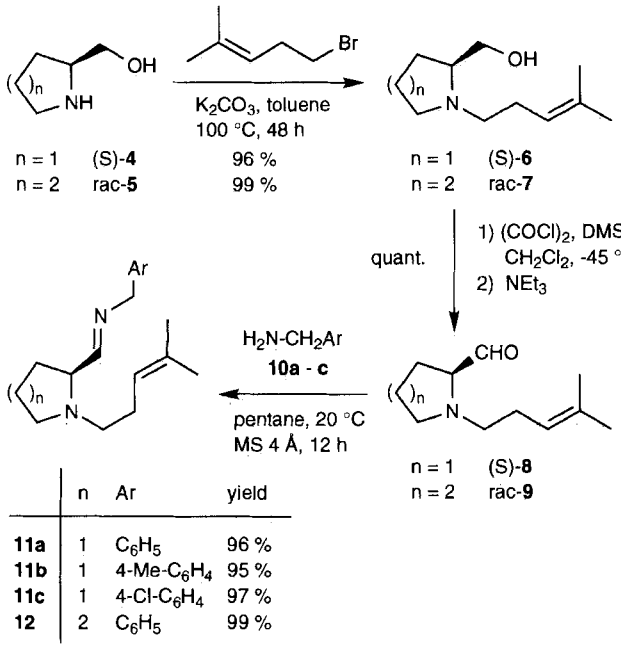
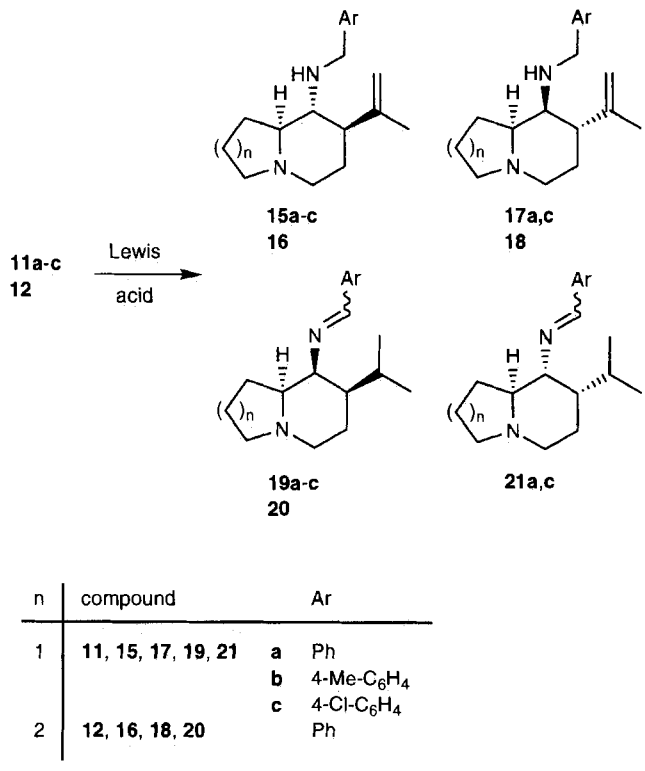
Scheme 1



	n	Ar	yield
11a	1	C_6H_5	96 %
11b	1	4-Me-C_6H_4	95 %
11c	1	4-Cl-C_6H_4	97 %
12	2	C_6H_5	99 %

Scheme 2



n	compound		Ar
1	**11, 15, 17, 19, 21**	**a**	Ph
		b	4-Me-C_6H_4
		c	4-Cl-C_6H_4
2	**12, 16, 18, 20**		Ph

Cyclization of Benzylimines 11 and 12

Treatment of the imines **11** and **12** with a Lewis acid yielded four different cyclization products, the α-(benzylamino)-β-isopropenylindolizidines **15**, **17**, the α-(benzylideneamino)-β-isopropylindolizidines **19**, **21**, and the corresponding quinolizidines **16**, **18**, and **20** (Scheme 2, Table 1)[22]. A survey of different Lewis and Brønsted acids shows that only strong Lewis acids, e.g. $SnCl_4$, $TiCl_4$, $FeCl_3$, are useful catalysts (entries 6, 9–11, 13–16). Weaker Lewis acids resulted either in low conversion or low selectivity (entries 1–4, 7, 8). This low reactivity of the benzylimines contrasts sharply with the well-established carbonyl-ene reaction[15], which requires only modest activation of the carbonyl group. When Brønsted acids like *p*-TsOH were used (entry 4), only a minor amount of the imino cyclization product **15** was found albeit with high selectivity, and the remaining imine **11a** was hydrolyzed to the corresponding aldehyde **8** which was immediately converted to the carbonyl-ene products. The most remarkable result was the "*cis*" selectivity of $TiCl_4$ and the "*trans*" selectivity of $FeCl_3$, which was almost independent of the substituents in the *para* position of the benzylimine **11** (entries 9, 11, 13–16). When the corresponding racemic benzyl(2-piperidinylmethylene)amine **12** was treated with $FeCl_3$ (2.5 equiv.) in CH_2Cl_2 for 48 h at room temperature, the cyclization products **16**, **18**, and **20** were obtained in a ratio of 71.6:14.8:13.6 and the major *rac*-**1**-(benzylamino)-2-isopropenylquinolizidine (**16**) was isolated in 68% yield. Treatment of **12** with $TiCl_4$ under the same conditions gave the three products in a ratio of 2.0:1.4:96.6, and *rac*-**1**-(benzylideneamino)-2-isopropylquinolizidine (**20**) was isolated in 50% yield.

We have established the absolute configuration of the major (7*R*,8*R*,8a*S*)-8-(benzylamino)-7-isopropenylindolizidine (**15a**) by a single-crystal X-ray structural analysis. Because the stereochemistry of the remaining cyclization products could not be established by NMR experiments, indolizidines **15a**, **19a** and quinolizidines **16**, **20** were subjected to a hydrogenation/hydrogenolysis reaction in the presence of $PdCl_2$ to yield the aminoindolizidines **22**, **26** and -quinolizidines **23**, **27**, respectively (Scheme 3). These compounds were acetylated with Ac_2O/NEt_3 to give the corresponding acetamides **24**, **28** and **25**, **29**. An X-ray crystal structure of the (1*RS*,2*SR*,9a*RS*)-(±)-1-(acetylamino)-2-isopropylquinolizidine hydrochloride **30** was obtained (Figure 1, Table 2), which supports the stereochemistry of *cis*-acetamide **29** based on NMR experiments[23].

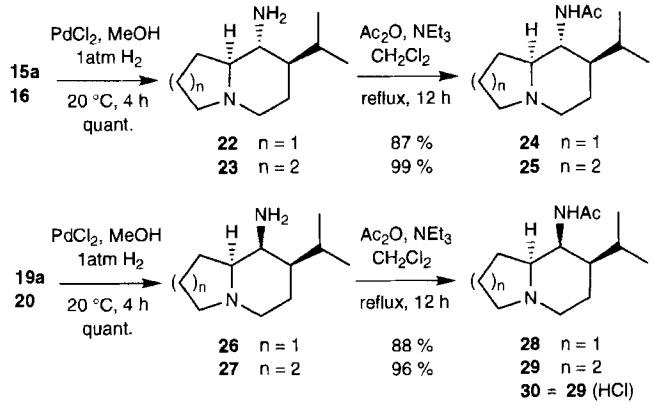
In order to explain the different constitution of the cyclization products, two different hetero-ene pathways can be assumed. The normal hetero-ene reaction should lead to products **15**–**18**, whereas a hetero-ene reaction with inverse electron demand should result in the formation of products **19**–**21**[24]. However, we propose a stepwise mechanism as an alternative to the hetero-ene pathways. As outlined in Scheme 4, the cyclization of the iminium ion **31** gives two different carbenium ions **32a,c**, depending on the reaction conditions. The relative stereochemistry between C-7 and C-8 dictates, which pathway is preferred. The 7,8-*trans*-configurated carbenium ion **32a** undergoes elimination and subsequent reprotonation followed by elimination of the Lewis acid to yield **15a**. The 7,8-*cis*-carbenium ion **32c** is able to undergo a hydride migration due to the close proximity between the isopropyl cation and the benzylic protons to give the secondary cation **33c**, which is thermodynamically more stable because of its iminium ion and

Table 1. Reaction of benzylimines **11a–c** with different Lewis acids[a]

Entry	Imine	R	Lewis acid	Solvent	Time [h]	Conversion [%] [b]	**15**	**17**	**19**	**21**	Yield [%] [c]
1	**11a**	H	$ZnCl_2$	CH_2Cl_2	23.5	32	31.6	22.3	34.9	11.1	----
2	**11a**	H	Et_2AlCl	toluene	58.5	3	29.4	41.2	29.4	----	----
3	**11a**	H	$BF_3{\cdot}OEt_2$	CH_2Cl_2	18.5	21	51.9	35.6	2.4	10.1	----
4	**11a**	H	TsOH	CH_2Cl_2	18.5	8 [d]	≥ 99.5	----	----	----	----
5	**11a**	H	$SnCl_4$	CH_2Cl_2	12	44	79.0	7.2	2.7	11.1	----
6	**11a**	H	$SnCl_4$	toluene	8	80	87.7	8.3	4.0	----	----
7	**11a**	H	$EtAlCl_2$	CH_2Cl_2	17.5	63	51.3	5.6	36.4	6.7	----
8	**11a**	H	$EtAlCl_2$	toluene	58.5	72	41.9	2.9	55.2	----	----
9	**11a**	H	$FeCl_3$	CH_2Cl_2	48	98	90.3	7.0	2.7	----	62 (**15a**)
10	**11a**	H	$FeCl_3$	toluene	8	96	88.6	8.2	3.2	----	----
11	**11a**	H	$TiCl_4$	CH_2Cl_2	21.5	95	1.2	3.7	94.7	0.3	45 (**19a**)
12	**11a**	H	$TiCl_4$	toluene	87	35	2.3	1.7	94.3	1.7	----
13	**11b**	Me	$FeCl_3$	CH_2Cl_2	96	63	97.8	----	2.2	----	52 (**15b**)
14	**11b**	Me	$TiCl_4$	CH_2Cl_2	96	58	0.3	----	99.7	----	32 (**19b**)
15	**11c**	Cl	$FeCl_3$	CH_2Cl_2	84	82	92.6	----	7.4	----	67 (**15c**)
16	**11c**	Cl	$TiCl_4$	CH_2Cl_2	84	72	6.1	2.1	90.6	1.3	42 (**19c**)

[a] Reaction conditions: 2.5 equiv. of Lewis acid, room temperature. – [b] Conversion and relative product ratio were determined by capillary GC using *n*-eicosane as an internal standard. – [c] Isolated yields of major products **15** or **19**, respectively. – [d] The carbonyl-ene product **51** was obtained as the major product.

Scheme 3



benzylic character. Subsequent elimination of the Lewis acid finally yields **19a**[25]. Pathway B in the $TiCl_4$-induced reaction was supported by a deuterium labeling experiment, in which [D_7]benzylamine **38** was converted to the imine **34** and this cyclized to the deuterated imine **35** (eq. 2). As expected, compound **35** shows no signals for the imino and the phenyl group in the ^{1}H-NMR spectrum. The doublets of the two diastereotopic methyl groups in **19a** changed to two singlets in the spectrum of **35**, because the smaller vicinal H-D coupling constant was not resolved by the 300-MHz NMR spectrometer. In addition, the ^{2}H-NMR spectrum of **35** shows only broad singlets for the imino and phenyl group and the isopropyl deuterium. The [D_7]benzylamine **38** was prepared from commercially available [D_7]benzyl chloride **36** via the *N*-phthaloyl-[D_7]benzylamine **37** by a Gabriel-type synthesis (eq. 3)[26].

Despite the incorporation of deuterium into the isopropyl position an intermolecular hydride transfer (Scheme 5) seems to be a reasonable alternative. In this mechanistic

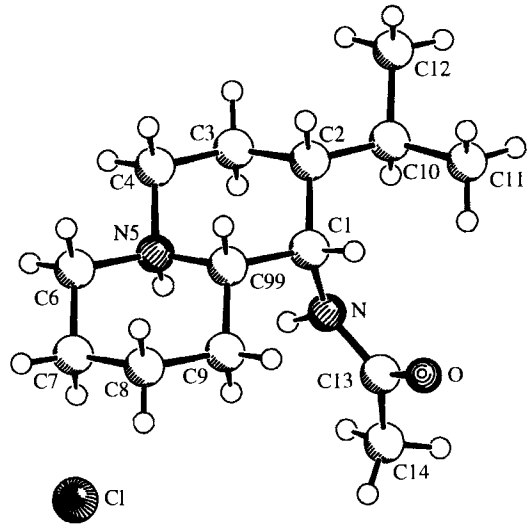


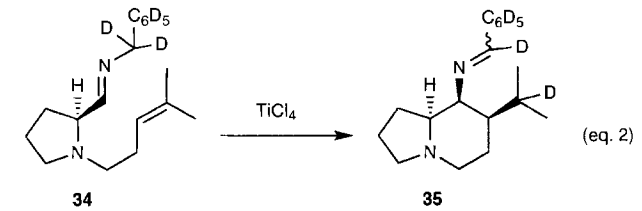
Figure 1. Molecular structure of **30** in the crystal. Selected bond lengths [Å] and angles [°]: C(1)–N(1) 1.449(3), C(1)–C(99) 1.542(2), C(1)–C(2) 1.550(2), C(2)–C(10) 1.537(2), C(4)–N(5) 1.497(2), C(6)–N(5) 1.503(2), C(99)–N(5) 1.496(2), C(9)–C(9a) 1.525(2), C(10)–C(11) 1.522(3), C(10)–C(12) 1.532(2); N(1)–C(1)–C(99) 111.29(13), N(1)–C(1)–C(2) 113.08(13), C(99)–C(1)–C(2) 110.76(12), C(10)–C(2)–C(3) 111.89(14), C(4)–N(5)–C(6) 108.74(12), C(4)–N(5)–C(99) 111.21(14), C(6)–N(5)–C(9a) 112.8(2), N(5)–C(6)–C(7) 110.55(13), N(5)–C(99)–C(9) 110.03(14), N(5)–C(99)–C(1) 111.10(13), C(9)–C(99)–C(1) 112.17(13), C(11)–C(10)–C(12) 109.2(2), C(12)–C(10)–C(2) 111.0(2)

scheme both carbenium ions **39** and **40** can operate either as hydride donor or acceptor. For clarity, only one possible intermolecular hydride transfer is outlined in detail. Thus, if **39** acts as donor and **40** as acceptor, the two new intermediate species **41** and **42** will be created. Compound **42** is unstable and might readily accept a deuteride from **43** while liberating the coordinated Lewis acid and being converted to the fully deuterated product **35**. The different combi-

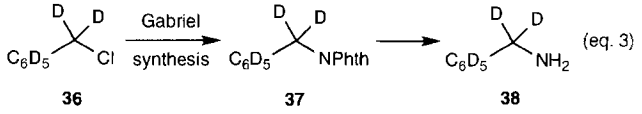
Table 2. Experimental data for the structure analyses for **30** and **52**

Compound	**30**	**52**
Formula:	$C_{14}H_{27}N_2OCl$	$C_{12}H_{21}NO$
M_r (gmol^{-1}):	274.83	195.30
Crystal system:	monoclinic	monoclinic
Space group:	$P2_1/c$	$P2_1/n$
a (Å):	8.877(2)	8.929(1)
b (Å):	12.546(3)	6.825(1)
c (Å):	14.219(3)	19.014(1)
β (°):	97.09(3)	92.17(1)
V (Å^3):	1571.5(6)	1157.9(2)
Diffractometer:	Enraf-Nonius CAD4	Enraf-Nonius CAD4
Radiation:	Cu Kα	Cu Kα
Temperature (K):	223	293
Collected reflections:	5337	2508
Independent reflections:	2671	2352
Observed reflections:	2263	2065
Refined parameters:	173	129
Refinement:	on F^2	on F^2
R:	0.053	0.057
ωR^2:	0.112	0.177
Programs used:	SHELX-86, SHELX-93, SCHAKAL-92	

nations of donor/acceptor pairs result in the formation of four different products **35**, **45**, **47**, and **19b**. Therefore, a deuterium scrambling experiment was carried out to further distinguish between the intramolecular and intermolecular pathway. Thus a mixture of prolinal [D_7]benzylimine **34** (32%) and non-deuterated prolinal 4-methylbenzylimine **11b** (68%) was treated with 2.5 equiv. of $TiCl_4$ under the usual conditions to yield a crude product which contained at least four compounds as determined by GC: 18.5% of the deuterated benzylideneamines **35** and/or **45**, 2.1% of the deuterated benzylamine **48**, 45.7% of the (4-methylbenzylidene)amines **19b** and/or **47**, and 5.3% of the (4-methylbenzyl)amine **15b**. In order to evaluate the deuterium distribution in the product mixture, the isotope pattern of the



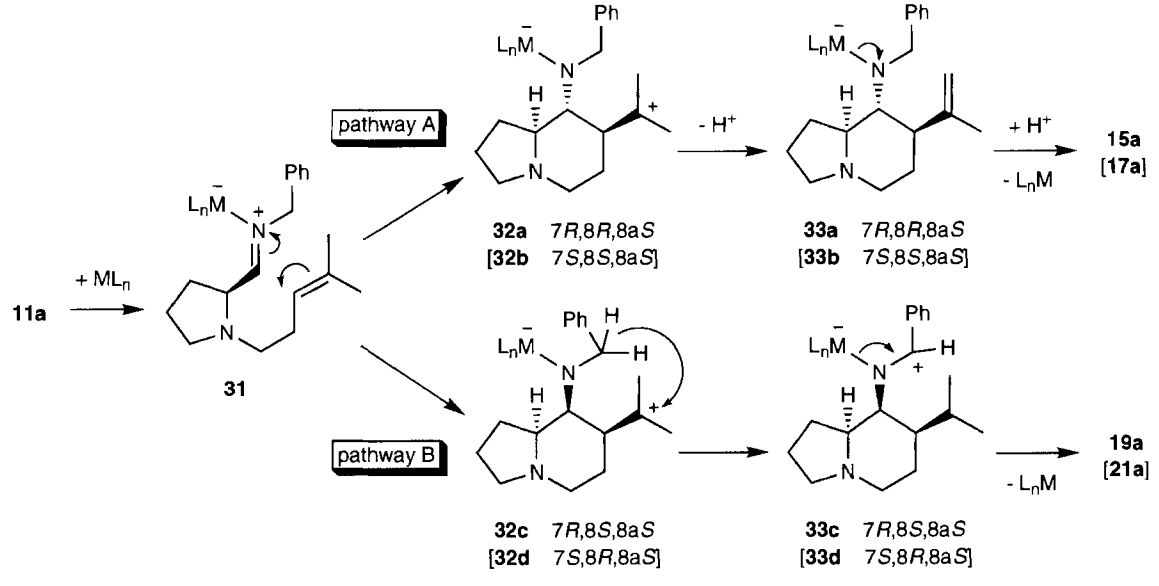
(eq. 2)



(eq. 3)

molecular ion peaks in the GC-MS (EI) spectra were analyzed in the following way. The M^+ signal of the deuterated benzylideneamine (**35**, **45**) showed the following pattern *m/z* (%): 276 (11.56), 277 (7.21), and 278 (1.15). In the first approximation any primary or secondary kinetic isotope effects were neglected and the *m/z* 276 signal (M^+ signal of **45**) was considered to be isotopically pure. The portion of ^{13}C of the *m/z* 277 signal (i.e. the $[M+1]^+$ signal of **45**) was subtracted from the intensity, thus giving the intensity of the M^+ signal of **35**. Therefore, a relative ratio of 29.8:70.2 (**35**:**45**) was calculated from the isotope pattern. When the same procedure was applied to the M^+ pattern of (4-methylbenzylidene)amine (**19b**,**47**) *m/z* (%) 284 (10.19), 285 (7.54), 286 (0.72), the ratio 65.4:34.6 (**19b**:**47**) was obtained. These deuterium distributions were taken into account in the ratio of benzylideneamine to (4-methylbenzylidene)amine, and the following total product distribution was calculated as **35**:**45**:**47**:**19b** = 8.6:20.2:24.6:46.6[27]. The relative ratios are in good agreement with those calculated for an intermolecular hydride transfer. An intramolecular pathway should result in a ratio of **35**:**19b** = 32:68[28,29].

Scheme 4



Cyclization of Aldehydes

In the determination of the Lewis acid-catalyzed reversal of the diastereoselectivity in the cyclization of benzylimines **11** and **12** the question arose whether this result could be applied to the Lewis acid-catalyzed cyclization of the corresponding aldehydes **8** and **9** (eq. 4).

However, as shown in Table 3 in the studied cases the *cis* products **51** and **52** were the major products, and we were not able to revert the diastereoselectivity toward the *trans* products **49**, **50**. The *all-cis* configuration was established by an X-ray crystal structural analysis of **52** (Figure 2, Table 2)[23]. A comparison of bond lengths and angles of **52** with those of **30** shows the similarity of the two structures. The only difference is a slight elongation of the C4–N5, C6–N5, C9a–N5 bonds of **30** by about 0.02–0.03 Å, which is probably the result the result of a decreased bond order, due to the protonation of the bridging nitrogen.

The exact role of the Lewis acid in the determination of the stereochemistry of the cyclizations of the benzylimines **11a–c** and **12** remains unclear. On the contrary, it might be reasonable to explain the remarkable *cis* selectivity of the aldehyde cyclizations by a chelating transition-state model **53**. As outlined in Scheme 6, strongly chelating Lewis acids preferably direct the carbonyl oxygen into the axial position, leading to the *cis* product **52**. In the case of **55** an alternative geometry with an equatorial carbonyl oxygen chelation by the Lewis acid is not favored. The orientation of the carbonyl group and the heteroatom in the tether in transition states **53** and **55** is similar to those transition states proposed by Mikami[30]. However, in Mikami's case the steric bulk of the (binaphthol)-titanium catalyst and the use of a different heteroatom in the tether disfavor a chelation thus providing either the *trans* product or a (1 : 1) mixture of *cis* and *trans*.

In conclusion, a highly stereoselective synthesis of α-amino-β-alkylindolizidines (and -quinolizidines) by Lewis acid-catalyzed cyclization of prolinal (and 2-piperidine-carbaldehyde) benzylimines was developed, which gives access to both α,β-*cis* and α,β-*trans* isomers, presumably via a common carbenium ion intermediate. Deuterium labeling experiments support a novel cyclization/intermolecular hydride transfer mechanism leading to the *cis* product. Interestingly, the corresponding aldehyde precursors for the cyclization resulted in the stereoselective formation of α,β-*cis*-α-hydroxy-β-alkyl-indolizidines (and -quinolizidines). These compounds seem to be suitable building blocks for further elaboration into alkaloids, e.g. goniomine[31].

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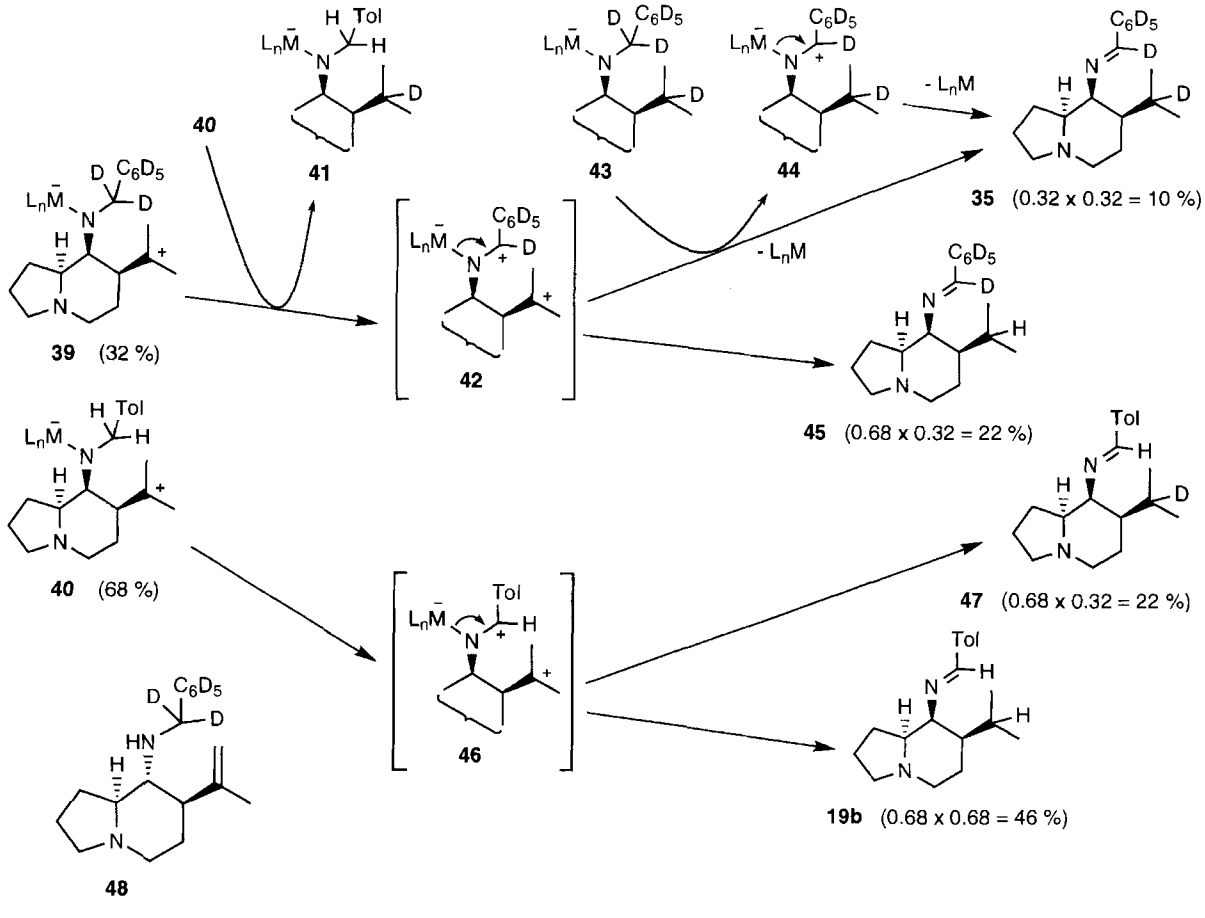
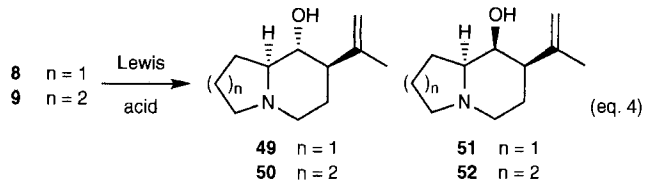
Scheme 5. Intermolecular hydride transfer between carbenium ions **39** and **40**. The values in parentheses under the product imines **35**, **45**, **47**, and **19b** represent the relative amounts calculated for a statistical hydride transfer





(eq. 4)

Table 3. Reaction of aldehydes **8** and **9** with different Lewis acids[a]

	Lewis acid	Temp. [°C]	Time [h]	Conversion [%] [b]	**49**, **50** *trans*	**51**, **52** *cis*	Yield [%] [c]
8	$EtAlCl_2$	-20	42	22	7.6	92.4	----
8	$FeCl_3$	+20	43	94	1.6	98.4	65 (**51**)
8	$FeCl_3$	-20	133	73	0.5	99.5	----
8	$SnCl_4$	+20	40	3	14.8	85.2	----
8	$TiCl_4$	+20	40	36	27.6	72.4	----
9	$FeCl_3$	+20	72	95	0.2	99.8	59 (**52**)

[a] Reaction conditions: 2.5 equiv. of Lewis acid, CH_2Cl_2. – [b] See footnote [b] in Table 1. – [c] See footnote [c] in Table 1.

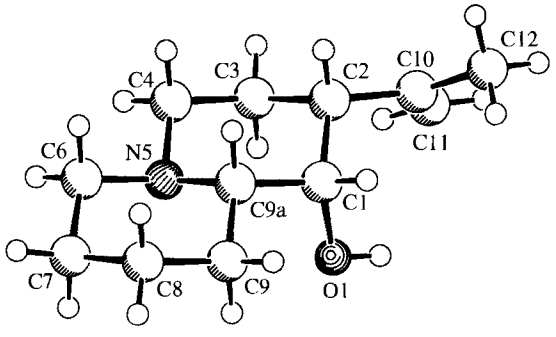


Figure 2. Molecular structure of **52** in the crystal. Selected bond lengths [Å] and angles [°]: C(1)–O(1) 1.418(2), C(1)–C(9a) 1.528(2), C(1)–C(2) 1.543(2), C(2)–C(10) 1.506(2), C(4)–N(5) 1.463(2), C(6)–N(5) 1.467(2), C(9a)–N(5) 1.479(2), C(9)–C(9a) 1.519(2), C(10)–C(11) 1.358(3), C(10)–C(12) 1.451(2); O(1)–C(1)–C(9a) 110.63(11), O(1)–C(1)–C(2) 110.43(11), C(9a)–C(1)–C(2) 110.43(11), C(10)–C(2)–C(3) 114.94(12), C(4)–N(5)–C(6) 109.14(13), C(4)–N(5)–C(9a) 110.38(11), C(6)–N(5)–C(9a) 110.33(13), N(5)–C(6)–C(7) 112.85(14), N(5)–C(9a)–C(9) 110.36(12), N(5)–C(9a)–C(1) 111.50(11), C(9)–C(9a)–C(1) 111.60(12), C(11)–C(10)–C(12) 120.5(2), C(12)–C(10)–C(2) 116.8(2)

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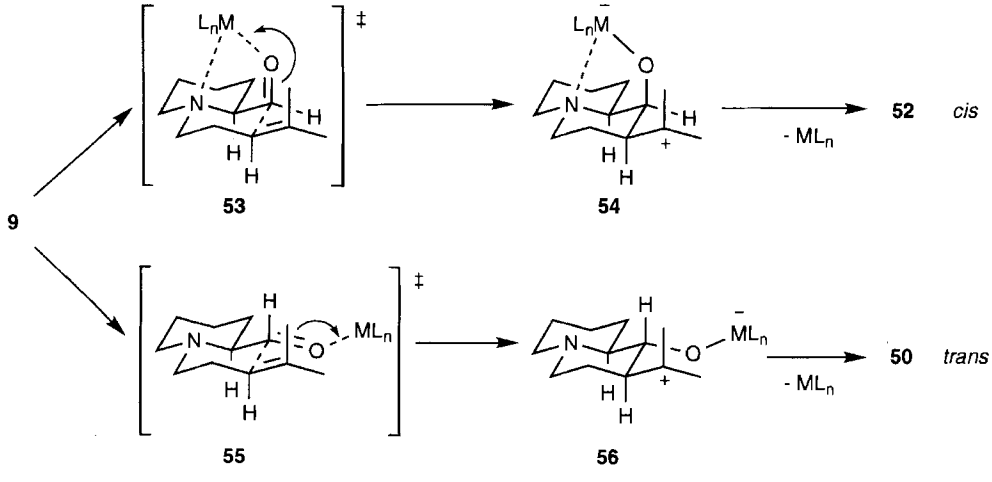
Experimental

All reactions were carried out under argon by using standard Schlenk technique. Solvents were dried and deoxygenated by standard procedures. – Analytical TLC: precoated Merck Si 254 F plates (0.25 mm thickness), products were visualized with a solution of phosphomolybdic acid in EtOH (5%, v/v). – Flash chromatography[32]: Merck silica gel 60 (230–400 mesh). – NMR: Bruker AC 200 P (200 MHz-^{1}H, 50 MHz-^{13}C), Bruker AM 360 (360 MHz-^{1}H, 90.5 MHz-^{13}C) and Bruker ARX 300 (300 MHz-^{1}H, 75.4 MHz-^{13}C). Multiplets in ^{13}C-NMR spectra were determined by DEPT and APT experiments. – Melting points (uncorrected): Gallenkamp melting point apparatus. – IR: Nicolet 5DXC FT-IR. – Optical rotations (1-dm cells, 1-ml capacity, room temp.): Perkin Elmer Model 241 polarimeter. – MS: Finnigan Model MAT 312 (EI), Finnigan Model MAT 8230 (CI, reactand gas: NH_3). – GC-MS: Varian GC 3400 coupled with a Varian Saturn 2 (ion trap) or with a Finnigan MAT 8230 (EI). – GC analysis: HP5-fused silica capillary column (ID 0.32 mm, length 25 m), HPU2-fused silica capillary column (ID 0.2 mm, length 25 m). – [D_7]benzyl chloride **36** (99% D_7) was purchased from Aldrich.

General Procedure for the N-Alkylation of **4**, **5**: To a solution of the amino alcohol (4.82 mmol) in anhydrous toluene (4 ml) were added anhydrous K_2CO_3 (540 mg, 3.91 mmol) and subsequently dropwise 5-bromo-2-methyl-2-pentene (1.89 g, 11.6 mmol) over 30 min (temp. during addition: 0–4°C for **4**, 60°C for **5**), and the mixture was heated at 110°C for 3 d. After cooling to room temp. the mixture was diluted with toluene (10 ml) and extracted with 2 N HCl (3 × 30 ml). The combined aqueous layers were washed with Et_2O (2 × 50 ml) and then treated with conc. NH_3 with ice cooling until pH 8–9 was reached. Extraction with CH_2Cl_2 (4 × 50 ml), drying of the combined extracts with $MgSO_4$, and evaporation of the solvent yielded the crude product, which was used without further purification.

N-(4-Methyl-3-pentenyl)-(S)-prolinal (**6**): 850 mg (4.63 mmol, 96%) of a pale yellow oil. $[\alpha]_D^{22} = -44.9$ (c = 1.00 in CH_2Cl_2). –

Scheme 6



IR (film): $\tilde{\nu}$ = 3409 cm^{-1} (OH). – ^1H NMR (200 MHz, $CDCl_3$): δ = 5.03 ("t", *J* = 7.5 Hz, 1H, 3'-H), 3.51 (dd, *J* = 11.0/3.0 Hz, 1H, CH_2O), 3.16–3.08 (m, 1H), 2.64 (ddd, *J* = 11.3/7.9/7.9 Hz, 2H, 1'-H), 2.51 (s, broad, 1H, OH), 2.29–2.06 (m, 4H, 2',5-H), 1.83–1.61 (m, 4H, 3,4-H), 1.61 (s, 3H, 5'-H), 1.53 (s, 3H, 6'-H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 132.7 (C-4'), 122.8 (C-3'), 64.8 (C-2), 61.9 (CH_2O), 54.4, 54.0 (C-1',5), 27.6, 27.5, 23.4 (C-2',3,4), 25.5 (C-5'), 17.6 (C-6'). – GC-MS (CI), *m/z* (%): 184 (100) [M + 1], 166 (48) [M + 1 – H_2O], 152 (22), 126 (4), 114 (18). – $C_{11}H_{22}NO$: calcd. 184.1701, found 184.1675 [GC-MS (CI)].

(±)-[1-(4-Methyl-3-pentenyl)-2-piperidyl]methanol (**7**): 1.87 g (9.54 mmol, 99%) of an orange oil (98% pure by GC). – IR (film): $\tilde{\nu}$ = 3390 cm^{-1} (OH). – ^1H NMR (200 MHz, $CDCl_3$): δ = 5.25 (d, *J* = 1.0 Hz, 1H, OH), 5.04 ("t", *J* = 7.1 Hz, 1H, 3'-H), 3.68 (dd, *J* = 10.8/4.3 Hz, 1H, CH_2O), 3.38 (dd, *J* = 10.8/4.0 Hz, 1H, CH_2O), 2.96–2.59 (m, 3H, 1',2-H), 2.42–2.23 (m, 4H, 6,3-H), 2.09 (q, *J* = 7.3 Hz, 2H, 2'-H), 1.64 (s, 3H, 5'-H), 1.57 (s, 3H, 6'-H), 1.64–1.29 (m, 4H, 4,5-H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 132.9 (C–4'), 121.9 (C-3'), 62.1 (CH_2O), 60.3 (C-2), 52.9 (C-1'), 50.8 (C-6), 27.3 (C-2'), 25.6 (C-5'), 25.2, 24.3, 23.4 (C-3,4,5), 17.7 (C-6'). – GC-MS (CI), *m/z* (%): 198 (100) [M + 1], 182 (6), 180 (24) [M + 1 – H_2O], 166 (42), 136 (3), 128 (12), 124 (6), 110 (7). – $C_{12}H_{23}NO$: calcd. 198.1858, found 198.1833 [GC-MS (CI)].

Swern Oxidation of Alcohols **6** *and* **7**: A solution of DMSO (907 mg, 11.60 mmol) in CH_2Cl_2 (2 ml) was added dropwise over 30 min at –45°C to a solution of oxalyl chloride (737 mg, 5.80 mmol) in anhydrous CH_2Cl_2 (8 ml). After stirring of the mixture for 15 min a solution of the alcohol (3.36 mmol) in anhydrous CH_2Cl_2 (5 ml) was added dropwise over 30 min, and the resulting mixture was stirred for another 8 h at –45°C. Then NEt_3 (3 ml) was added over 30 min, and the mixture was warmed to room temp. and stirred for another 1 h. It was subsequently washed with H_2O (3 × 50 ml), dried with Na_2SO_4, and concentrated to yield a crude oil, which was immediately used without further purification.

N-(4-Methyl-3-pentenyl)-(S)-prolinal (**8**): 538 mg (2.97 mmol, quant.) of a yellow oil. $[\alpha]_D^{22}$ = –63.6 (*c* = 1.00 in $CHCl_3$). – IR (film): $\tilde{\nu}$ = 1730 cm^{-1} (C=O). – ^1H NMR (200 MHz, $CDCl_3$): δ = 9.41 (d, *J* = 4.2 Hz, 1H, CHO), 5.04 (t, *J* = 7.0 Hz, 1H, 3'-H), 3.21–3.13 (m, 1H, 2-H), 2.85–2.74 (m, 2H, 1'-H), 2.59–2.36 (m, 2H, 5-H), 2.35–2.25 (m, 2H), 1.98–1.73 (m, 4H, 2',4,5-H), 1.61 (s, 3H, 5'-H), 1.54 (s, 3H, 6'-H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 203.4 (CHO), 132.8 (C-4'), 121.6 (C-3'), 72.1 (C-2), 55.5, 54.2 (C-1',5), 27.9, 26.5, 23.9 (C-2',3,4), 25.6 (C-5'), 17.7 (C-6'). – MS (70 eV), *m/z* (%): 152 (34) [M – CHO], 112 (38), 105 (35), 96 (42), 84 (44), 82 (46), 70 (71), 67 (50), 55 (100). – $C_{10}H_{17}N$ [M – CHO]: calcd. 152.1446, found 152.1439 (MS).

(±)-1-(4-Methyl-3-pentenyl)-2-piperidinecarboxaldehyde (**9**): 1.61 g (8.21 mmol, 98%) of a brown oil. – IR (film): – $\tilde{\nu}$ = 1733 cm^{-1} (C=O). – ^1H NMR (200 MHz, $CDCl_3$): δ = 9.45 (d, *J* = 3.8 Hz, 1H, CHO), 5.01 (t, *J* = 8.1 Hz, 1H, 3'-H), 2.98 (ddd, *J* = 11.5/11.5/3.3 Hz, 1H, 2-H), 2.64 (ddd, *J* = 9.6/9.6/4.1 Hz, 1H, 1a'-H), 2.46–2.09 (m, 5H, 1b',5,2a'-H), 2.01 (ddd, *J* = 11.2/8.0/5.2 Hz, 1H, 2b'-H), 1.75–1.20 (m, 6H, 3,4,5-H), 1.61 (s, 3H, 5'-H), 1.54 (s, 3H, 6'-H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 204.3 (CHO), 132.9 (C-4'), 121.4 (C-3'), 71.0 (C-2), 57.1 (C-1'), 50.9 (C-6), 46.2 (C-2'), 25.6 (C-5'), 26.1, 25.4, 22.7 (C-3,4,5), 17.6 (C-6'). – MS (70 eV), *m/z* (%): 194 (22) [M – 1], 166 (27) [M – CHO], 149 (42), 124 (69), 99 (35), 96 (62), 86 (36), 83 (43), 68 (41), 55 (100). – $C_{12}H_{21}NO$: calcd. 195.1623, found 195.1619 (MS).

General Procedure for the Preparation of Benzylimines **11a–c**, **12**: To a solution of aldehyde **8** or **9** (1.00 mmol) and benzylamine **10a–c** (1.00 mmol) in pentane (10 ml) was added powdered, freshly activated 4-Å molecular sieves (500 mg), and the mixture was stirred at room temp. for 12–24 h. The mixture was then filtered by means of a fritted funnel through Celite, and the resulting filtrate was concentrated at room temp. to give an oil in almost quantitative yield, which was used immediately without further isolation or purification.

N-(4-Methyl-3-pentenyl)-(S)-prolinal Benzylamine (**11a**): 259 mg (96%) of a pale brown oil, $[\alpha]_D^{22}$ = –55.3 (*c* = 1.00 in $CHCl_3$). – IR (film): $\tilde{\nu}$ = 1669 cm^{-1} (C=N), 1654 (C=C), 800. – ^1H NMR (300 MHz, $CDCl_3$): δ = 7.54 (dt, *J* = 6.4/6.4/1.4 Hz, 1H, HC=N), 7.27–7.13 (m, 5H, Ph), 5.03 ("t", *J* = 6.8 Hz, 1H, 3'-H), 4.51 (s, 2H, CH_2Ph), 3.15 (ddd, *J* = 10.3/8.8/2.8 Hz, 1H, 2-H), 2.94 (q, *J* = 7.9 Hz, 1H, 1a'-H), 2.66–2.57 (m, 1H, 5a-H), 2.28–2.07 (m, 4H), 2.01–1.88 (m, 1H), 1.87–1.64 (m, 3H, 3,4,2',1b',5b-H), 1.62 (d, *J* = 1.2 Hz, 3H, 5'-H), 1.52 (d, *J* = 0.4 Hz, 3H, 6'-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.1 (HC=N), 138.9 (C-*i*), 132.2 (C-4'), 128.2 (C-*o*), 127.7 (C-*m*), 126.7 (C-*p*), 121.8 (C-3'), 68.2 (C-2), 64.5 (CH_2Ph), 54.6 (C-1'), 53.7 (C-5), 28.8, 27.6, 23.0 (C-3,4,2'), 25.4 (C-5'), 17.5 (C-6'). – MS (70 eV), *m/z* (%): 270 (8) [M], 255 (6) [M – CH_3], 201 (56) [M – CH_2-CH=CMe_2], 179 (24) [M – C_7H_7], 160 (27), 152 (36), 103 (23), 91 (100), 83 (30), 70 (81), 55 (95). – $C_{18}H_{26}N_2$: calcd. 270.2096, found 270.2090 (MS).

N-(4-Methyl-3-pentenyl)-(S)-prolinal (4-Methylbenzyl)imine (**11b**): 270 mg (95%) of a pale brown oil, $[\alpha]_D^{22}$ = –51.8 (*c* = 1.00 in $CHCl_3$). – IR (film): $\tilde{\nu}$ = 1669 cm^{-1} (C=N), 1515, 1448, 802. – ^1H NMR (300 MHz, $CDCl_3$): δ = 7.55 (dt, *J* = 6.4/1.4/1.4 Hz, 1H, HC=N), 7.11 (s, 2H, *o*-H), 7.10 (s, 2H, *m*-H), 5.06 ("t", *J* = 6.9 Hz, 1H, 3'-H), 4.52 (s, 2H, CH_2Ph), 3.18 (td, *J* = 6.4/2.6 Hz, 2-H), 2.96 (q, *J* = 6.7 Hz, 1a'-H), 2.69–2.60 (m, 1H, 5a-H), 2.30 (s, 3H, CH_3), 2.31–2.09 (m, 4H, 1b',5b,2'-H), 2.05–1.92 (m, 1H, 3a-H), 1.88–1.71 (m, 3H, 3b,4-H), 1.66 (d, *J* = 1.2 Hz, 3H, 5'-H), 1.56 (s, 3H, 6'-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.0 (HC=N), 136.4 (C-1''), 135.9 (C-4''), 132.4 (C-4'), 129.0 (C-2'',6''), 127.9 (C-3'',5''), 121.9 (C-3'), 68.4 (C-2), 64.4 (CH_2Tol), 54.8 (C-1'), 53.8 (C-5), 28.9, 27.7, 23.1 (C-3,4,2'), 25.6 (C-5'), 20.0 (CH_3), 17.6 (C-6'). – MS (70 eV), *m/z* (%): 284 (27) [M], 269 (19) [M – CH_3], 241 (14), 215 (47) [M – CH_2CH=CMe_2], 198 (39), 179 (33), 152 (46), 149 (45), 122 (37), 105 (100) [$CH_2C_6H_4CH_3$], 96 (40), 91 (35) [C_7H_7], 83 (51), 70 (49), 55 (57). – $C_{19}H_{28}N_2$: calcd. 284.2252, found 284.2244 (MS).

N-(4-Methyl-3-pentenyl)-(S)-prolinal (4-Chlorobenzyl)imine (**11c**): 295 mg (97%) of a pale brown oil, $[\alpha]_D^{22}$ = –65.6 (*c* = 1.00 in $CHCl_3$). – IR (film): $\tilde{\nu}$ = 1669 cm^{-1} (C=N), 1491, 1091, 1019, 802. – ^1H NMR (300 MHz, $CDCl_3$): δ = 7.56 (dt, *J* = 6.7/1.2 Hz, 1H, HC=N), 7.25 (d, *J* = 8.4 Hz, 2H, 3'',5''-H), 7.15 (d, *J* = 8.4 Hz, 2H, 2'',6''-H), 5.05 (t, *J* = 6.9 Hz, 1H, 3'-H), 4.50 (s, 2H, CH_2Ph), 3.18 (ddd, *J* = 7.2/6.0/4.3 Hz, 1H, 2-H), 2.96 (q, *J* = 7.7 Hz, 1H, 5a-H), 2.72–2.58 (m, 1H, 1a'-H), 2.31–2.08 (m, 4H, 1b',5b,2'-H), 2.05–1.92 (m, 1H), 1.88–1.70 (m, 3H, 3,4-H), 1.65 (d, *J* = 1.0 Hz, 3H, 5'-H), 1.55 (s, 3H, 6'-H). – ^{13}C NMR (75 MHZ, $CDCl_3$): δ = 168.7 (HC=N), 137.6 (C-4''), 132.5 (C-4'), 129.1 (C-3'',5''), 128.4 (C-2'',6''), 128.3 (C-1''), 121.9 (C-3'), 68.2 (C-2), 63.9 (CH_2Ph), 54.8 (C-1'), 53.8 (C-5), 28.9, 27.7, 23.1 (C-3,4,2'), 25.5 (C-5'), 17.6 (C-6'). – MS (70 eV), *m/z* (%): 304 (15) [M], 286 (12), 264 (11), 235 (74), 177 (24), 165 (25), 151 (28), 125 (100) [C_7H_6Cl], 124 (33), 113 (28), 107 (27), 89 (25), 83 (46), 70 (75), 55 (90). – $C_{18}H_{25}ClN_2$: calcd. 304.1706, found 304.1700 (MS).

1-(4-Methyl-3-pentenyl)-2-piperidinecarboxaldehyde Benzylimine (**12**): 1.12 g (4.22 mmol, quant.) of a yellow oil. – IR (film): $\tilde{\nu}$ = 1672 cm^{-1} (C=N), 1496, 1453, 1100, 1029, 733, 697. – ^1H NMR (200 MHz, $CDCl_3$): δ = 7.60 (ddd, *J* = 6.7/1.4/1.3 Hz, 1H, HC=N), 7.30–7.15 (m, 5H, Ph), 5.22 (m, 1H, 3'-H), 4.54 (s, 2H,

CH_2Ph), 2.98 (ddd, J = 11.6/3.0/2.5 Hz, 1H, 6a-H), 2.86 (ddd, J = 10.2/6.7/3.2 Hz, 1H, 2-H), 2.52 (dd, J = 11.6/6.3 Hz, 1H, 6b-H), 2.27–2.05 (m, 4H), 1.77–1.23 (m, 6H, 1′,2′,3,4,5-H), 1.64 (d, J = 0.9 Hz, 3H, 5′-H), 1.52 (s, 3H, 6′-H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 168.8 (HC=N), 138.9 (C-4′), 128.3 (C-*o*), 127.8 (C-*m*), 126.9 (C-*p*), 121.7 (C-3′), 120.9 (C-*i*), 66.2 (C-2), 64.6 (CH_2Ph), 56.0 (C-1′), 51.7 (C-6), 46.1 (C-2′), 30.0, 25.4, 23.2 (C-3,4,5), 25.5 (C-5′), 17.5 (C-6′). – MS (70 eV), *m/z* (%): 284 (14) [M], 215 (69), 187 (24), 166 (32), 149 (32), 97 (32), 91 (90), 84 (67), 69 (44), 57 (91), 55 (100). – $C_{19}H_{28}N_2$: calcd. 284.2252, found 284.2244 (MS).

General Procedure for the Cyclization of Aldehydes **8** *and* **9** *and Benzylimines* **11a–c** *and* **12**: To an ice-cooled solution of aldehyde **8** or **9** or imine **11a–c**, **12** (1.00 mmol) in anhydrous CH_2Cl_2 (28 ml) was added dropwise over 30 min the Lewis acid (2.50 mmol), and the mixture was stirred at room temp. (for different reaction conditions, see Tables 1, 3), until GC showed complete conversion. Then 2 N NaOH (50 ml) was added, and the mixture was extracted with CH_2Cl_2 (3 × 100 ml). After drying of the combined organic layers with $MgSO_4$ and evaporation of the solvent the crude products were purified by flash chromatography on SiO_2 (hexanes/ethyl acetate/NEt_3, 79:16:5).

(7R,8R,8aS)-8-(Benzylamino)-7-isopropenylindolizidine (**15a**): 166 mg (62%) of an orange oil, $[\alpha]_D^{22}$ = −11.5 (*c* = 1.00 in $CHCl_3$). – IR (film): $\tilde{\nu}$ = 3441 cm^{-1} (NH), 3328 (NH), 2963, 2936, 2870, 2786, 1645 (C=C), 1495, 1260, 1137, 1091, 1028, 697. – For ^{1}H- and ^{13}C NMR data see in ref.[18]. – MS (70 eV), *m/z* (%): 270 (21) [M], 227 (20), 173 (37), 163 (25), 158 (61), 152 (25), 136 (20), 122 (33), 110 (31), 98 (42), 91 (100), 84 (88), 79 (30), 70 (38), 67 (33), 57 (55). – $C_{18}H_{26}N_2$: calcd. 270.2096, found 270.2090 (MS).

(7R,8R,8aS)-7-Isopropenyl-8-[(4-methylbenzyl)amino]-indolizidine (**15b**): 148 mg (52%) of an orange, amorphous solid, $[\alpha]_D^{22}$ = −11.8 (*c* = 1.00 in $CHCl_3$). – IR (film): $\tilde{\nu}$ = 3430 cm^{-1} (NH), 3267 (NH), 2962, 2919, 2899, 2788, 1644 (C=C), 805. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.11 (d, J = 8.4 Hz, 2H, 2′,6′-H), 7.05 (d, J = 8.4 Hz, 2H, 3′,5′-H), 4.82–4.80 (m, 2H, 10-H), 3.81 (d, J = 12.4 Hz, 1H, 12a-H), 3.59 (d, J = 12.4 Hz, 1H, 12b-H), 3.08–3.01 (m, 2H, 8,8a-H), 2.34 (dd, J = 10.3/8.6 Hz, 1H, 3-H_{eq}), 2.28 (s, 3H, Tol-CH_3), 2.18–1.92 (m, 4H), 1.86–1.55 (m, 7H, 3-H_{ax}, 5,1,2,6,7-H, NH), 1.53 (s, 3H, 11-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.5 (C-9), 137.7 (C-1′), 136.4 (C-4′), 129.0 (C-3′,5′), 128.2 (C-2′,6′), 113.5 (C-10), 70.6 (C-8a), 60.7 (C-8), 53.8 (CH_2Ph), 53.0 (C-3), 52.0 (C-5), 51.2 (C-7), 30.5 (C-6), 30.2 (C-1), 21.2 (C-2, Tol-CH_3), 18.4 (C-11). – MS (70 eV), *m/z* (%): 284 (18) [M], 239 (19), 222 (19), 200 (22), 187 (65), 172 (68), 165 (23), 149 (27), 134 (22), 110 (30), 105 (100) [$CH_2C_6H_4Me$], 98 (54), 84 (96), 77 (27), 70 (31), 55 (36). – $C_{19}H_{28}N_2$: calcd. 284.2252, found 284.2244 (MS).

(7R,8R,8aS)-8-[(4-Chlorobenzyl)amino]-7-isopropenyl-indolizidine (**15c**): 204 mg (67%) of an orange, amorphous solid, $[\alpha]_D^{22}$ = −9.6 (*c* = 1.00 in $CHCl_3$). – IR (film): $\tilde{\nu}$ = 3370 cm^{-1} (NH), 2980, 2950, 2919, 2900, 2782, 1644 (C=C). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.21 (d, J = 8.6 Hz, 2H, 2′,6′-H), 7.15 (d, J = 8.6 Hz, 2H, 3′,5′-H), 4.82–4.79 (m, 2H, 10-H), 3.79 (d, J = 12.9 Hz, 1H, 12a-H), 3.61 (d, J = 12.9 Hz, 1H, 12b-H), 3.07–3.00 (m, 2H, 8,8a-H), 2.31 (dd, J = 10.1/8.6 Hz, 1H, 3-H_{eq}), 2.17–1.91 (m, 4H), 1.87–1.55 (m, 7H, 3-H_{ax}, 5,1,2,6,7-H, NH), 1.54 (s, 3H, 11-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.1 (C-9), 139.3 (C-1′), 132.6 (C-4′), 129.6 (C-3′,5′), 128.4 (C-2′,6′), 113.5 (C-10), 70.5 (C-8a), 60.7 (C-8), 53.7 (CH_2Ph), 52.4 (C-3), 51.9 (C-5), 51.2 (C-7), 30.5 (C-6), 30.2 (C-1), 21.1 (C-2), 18.5 (C-11). – MS (70 eV), *m/z* (%): 304 (20) [M], 259 (17), 235 (7), 207 (30), 192 (28), 179 (24), 165 (27), 149 (34), 137 (28), 125 (44) [$CH_2C_6H_4Cl$], 110 (35), 98 (45), 84 (100), 71 (37), 57 (42). – $C_{18}H_{25}ClN_2$: calcd. 304.1706, found 304.1700 (MS).

(1RS,2RS,9aSR)-1-(Benzylamino)-2-isopropenylquinolizidine (**16**): 193 mg (68%) of a deep yellow oil. – IR (film): $\tilde{\nu}$ = 3334 cm^{-1} (NH), 3063, 3028, 2933, 2854, 2802, 2755, 2677, 1644 (C=C), 1465, 1452, 1443, 1120, 698. – ^{1}H NMR (300 MHz, C_6D_6): δ = 7.46 (d, J = 6.8 Hz, 2H, *o*-H), 7.34–7.18 (m, 3H, *m*-, *p*-H), 4.86 (d, J = 1.5 Hz, 1H, 11a-H), 4.84 (s, 1H, 11b-H), 3.85 (d, J = 12.1 Hz, 1H, 13a-H), 3.78 (d, J = 12.1 Hz, 1H, 13b-H), 3.10–2.41 (m, 4H, 1,9a-H, 6-H_{eq}), 4-H_{eq}), 2.33–1.15 (m, 12H, 2,3-H, 4-H_{ax}, 6-H_{ax}, 7,8,9-H, NH), 1.68 (s, 3H, 12-H). – ^{13}C NMR (75 MHz, C_6D_6): δ = 147.6 (C-10), 141.8 (C-1′), 128.5 (C-3′,5′), 128.4 (C-2′,6′), 127.0 (C-4′), 112.6 (C-11), 68.7 (C-9a), 61.4 (C-1), 56.8 (C-4), 56.3 (C-6), 53.4 (CH_2Ph), 51.6 (C-2), 30.6 (C-3), 26.3 (C-9), 25.3 (C-8), 24.8 (C-7), 18.8 (C-12). – MS (70 eV), *m/z* (%): 284 (53) [M], 241 (43), 213 (35), 181 (60), 173 (75), 158 (82), 149 (60), 138 (62), 110 (79), 98 (91), 91 (84) [C_7H_7], 82 (88), 69 (96), 55 (100). – $C_{19}H_{28}N_2$: calcd. 284.2252, found 284.2244 (MS).

(7R,8S,8aS)-8-(Benzylideneamino)-7-isopropylindlizidine (**19a**): 122 mg (45%) of a yellow oil, $[\alpha]_D^{22}$ = −85.7 (*c* = 1.00 in $CHCl_3$). – IR (film): $\tilde{\nu}$ = 3386 cm^{-1} (H–C=N), 2955, 2850, 2783, 2681 (H–C=N), 1644 (C=N), 761, 694. – For ^{1}H and ^{13}C NMR data see ref.[18]. – MS (70 eV), *m/z* (%): 270 (38) [M], 225 (77), 201 (15), 173 (32), 167 (47), 158 (100), 122 (76), 96 (50), 91 (90), 84 (68), 70 (49). – $C_{18}H_{26}N_2$: calcd. 270.2096, found 270.2098 (MS).

(7R,8S,8aS)-8-[(4-Methylbenzylidene)amino]-7-isopropyl-indolizidine (**19b**): 91 mg (32%) of a yellow oil, $[\alpha]_D^{22}$ = −88.1 (*c* = 1.00 in $CHCl_3$). – IR (film): $\tilde{\nu}$ = 3375 cm^{-1} (H–C=N), 2954, 2868, 2849, 2780, 2740, 2680, 1645 (C=N), 1609 (C=C), 814. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.17 (s, 1H, HC=N), 7.68 (d, J = 7.9 Hz, 2H, 2′,6′-H), 7.16 (d, J = 7.9 Hz, 2H, 3′,5′-H), 3.44 (t, J = 2.4 Hz, 1H, 8-H), 3.34–3.28 (m, 1H, 8a-H), 3.16–3.08 (m, 1H), 2.34 (s, 3H, Tol-CH_3), 2.16–1.91 (m, 4H), 1.71–1.45 (m, 4H), 1.39–1.27 (m, 2H), 1.26–1.12 (m, 1H, 1,2,3,5,6,7,9-H), 0.85 (d, J = 6.4 Hz, 3H, 10-H), 0.79 (d, J = 6.4 Hz, 3H, 11-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.1 (HC=N), 140.4 (C-1′), 133.7 (C-4′), 129.2 (C-2′), 128.9 (C-6′), 128.2 (C-3′,5′), 69.4 (C-8), 68.7 (C-8a), 54.4 (C-3), 53.3 (C-5), 48.7 (C-7), 28.7 (C-9), 25.6 (C-1), 25.3 (C-6), 21.4 (Tol-CH_3), 20.7 (C-10,2), 20.0 (C-11). – MS (70 eV), *m/z* (%): 284 (23) [M], 239 (48), 179 (26), 172 (100), 167 (47), 149 (33), 122 (96), 105 (100) [$CH_2C_6H_4Me$], 96 (44), 84 (98), 69 (46), 55 (58). – $C_{19}H_{28}N_2$: calcd. 284.2252, found 284.2244 (MS).

(7R,8S,8aS)-8-[(4-Chlorobenzylidene)amino]-7-isopropylindolizidine (**19c**): 128 mg (42%) of a yellow oil, $[\alpha]_D^{22}$ = −90.4 (*c* = 1.00 in $CHCl_3$). – IR (film): $\tilde{\nu}$ = 3366 cm^{-1} (H–C=N), 2954, 2888, 2870, 2850, 2782, 2740, 2680, 1643 (C=N), 1595 (C=C), 829, 821. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.16 (s, 1H, HC=N), 7.70 (d, J = 8.6 Hz, 2H, 2′,6′-H), 7.31 (d, J = 8.6 Hz, 2H, 3′,5′-H), 3.46 (t, J = 2.4 Hz, 1H, 8-H), 3.32–3.27 (m, 1H, 8a-H), 3.14–3.08 (m, 1H), 2.19–1.91 (m, 4H), 1.71–1.48 (m, 4H), 1.34–1.14 (m, 3H, 1,2,3,5,6,7,9-H), 0.84 (d, J = 6.5 Hz, 3H, 10-H), 0.78 (d, J = 6.5 Hz, 3H, 11-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.8 (HC=N), 136.2 (C-1′), 134.7 (C-4′), 129.8 (C-2′,6′), 128.5 (C-3′,5′), 69.3 (C-8), 68.7 (C-8a), 54.3 (C-3), 53.3 (C-5), 48.7 (C-7), 28.8 (C-9), 25.7 (C-1), 25.3 (C-6), 20.7 (C-2), 20.1 (C-10,11). – MS (70 eV), *m/z* (%): 304 (33) [M], 261 (47), 192 (63), 166 (72), 125 (28) [$CH_2C_6H_4Cl$], 122 (84), 111 (88), 96 (88), 91 (70), 83 (100), 69 (81), 55 (86). – $C_{18}H_{25}ClN_2$: calcd. 304.1706, found 304.1700 (MS).

^{1}H- and ^{13}C-NMR signals of the minor isomers **17a**, **c**, **18** and **21a**, **c** from crude product mixtures were only incompletely visible.

(1RS,2SR,9aRS)-1-(Benzylideneamino)-2-isopropylquinolizidine (**20**): 142 mg (50%) of a deep yellow oil. – IR (film): $\tilde{\nu}$ = 3386 cm^{-1} (H–C=N), 2955, 2867, 2850, 2782, 2740, 2681, 1644 (C=N), 1451, 1389. – ^1H NMR (300 MHz, C_6D_6): δ = 8.12 (s, 1H, HC=N), 7.84–7.78 (m, 2H, *o*-H), 7.19–7.08 (m, 3H, *m*-, *p*-H), 3.13 (s, broad, 1H, 1-H), 3.03 (ddd, *J* = 10.9/3.4/3.4 Hz, 1H, 9a-H), 2.84 (d, broad, *J* = 11.3 Hz, 1H), 2.39 (qd, *J* = 12.4/12.4/12.4/3.7 Hz, 1H), 2.09 (ddd, *J* = 11.3/11.3/2.7 Hz, 1H), 1.90–1.79 (m, 2H), 1.66–1.11 (m, 9H, 2,3,4,6,7,8,9,10-H), 0.86 (d, *J* = 6.8 Hz, 3H, 11-H), 0.82 (d, *J* = 6.4 Hz, 3H, 12-H). – ^{13}C NMR (75 MHz, C_6D_6): δ = 159.5 (HC=N), 137.1 (C-*i*), 130.4 (C-*m*), 128.5 (C-*o*,*p*), 72.8 (C-1), 66.9 (C-9a), 58.0 (C-4), 57.5 (C-6), 49.2 (C-2), 30.4 (C-9), 28.8 (C-10), 26.0 (C-3), 25.7 (C-7), 25.2 (C-8), 20.7 (C-11), 20.2 (C-12). – MS (70 eV), *m/z* (%): 284 (47) [M], 241 (57) [M – CH_3CHCH_3], 200 (21), 181 (78), 158 (100), 138 (82), 109 (43), 98 (67), 91 (55) [C_7H_7], 55 (51). – $C_{19}H_{28}N_2$: calcd. 284.2252, found 284.2261 (MS).

Hydrogenation/Hydrogenolysis: To a solution of **15a**, **16**, **19a**, or **20** (1.23 mmol) in anhydrous MeOH (15 ml) was added under argon $PdCl_2$ (218 mg, 1.23 mmol), and the remaining mixture was presaturated (3×) with H_2, then stirred under H_2 at 1 atm for 4 h at room temp. The mixture was filtered through Celite, and the solvent was evaporated to yield the crude amines, which were used without further purification.

(7R,8R,8aS)-8-Amino-7-isopropylindolizidine (**22**): 200 mg (1.10 mmol, quant.) of a pale brown, amorphous solid, $[\alpha]_D^{22}$ = –1.1 (*c* = 1.00 in MeOH). – IR (film): $\tilde{\nu}$ = 3400 cm^{-1} (NH), 2963, 2941, 2819. – ^1H NMR (200 MHz, CD_3OD): δ = 6.78 (s, broad, 4H, NH_2), 5.90–5.40 (m, broad, 4H, 8,8a-H, 3-H_{eq}, 5-H_{eq}), 5.40–5.00 (m, broad, 2H, 3-H_{ax}, 5-H_{ax}), 4.55 (m, 1H, 7-H), 4.30–3.70 (m, 7H, 1,2,6,9-H), 3.05 (d, *J* = 6.0 Hz, 3H, 10-H), 2.91 (d, *J* = 6.0 Hz, 3H, 11-H). – ^{13}C NMR (50 MHz, CD_3OD): δ = 67.3 (C-8), 53.9 (C-3), 53.0 (C-8a), 51.4 (C-5), 44.5 (C-7), 27.6 (C-1), 26.3 (C-9), 21.9 (C-6), 21.2 (C-10), 20.9 (C-2), 15.3 (C-11). – MS (70 eV), *m/z* (%): 182 (27) [M], 149 (58), 139 (29), 97 (80), 84 (73), 70 (100), 58 (51), 55 (78). – $C_{11}H_{22}N_2$: calcd. 182.1783, found 182.1787 (MS).

(1RS,2RS,9aSR)-1-Amino-2-isopropylquinolizidine (**23**): 507 mg (2.59 mmol, quant.) of a pale brown, amorphous solid. – IR (film): $\tilde{\nu}$ = 3394 cm^{-1} (NH), 2960, 2873, 2751, 2701, 2583, 1527. – ^1H NMR (200 MHz, CD_3OD): δ = 6.82 (s, broad, 6H, NH_2), 5.57–5.38 (m, 4H, 1,9a-H, 6-H_{eq}, 4-H_{eq}), 5.20–5.07 (m, 2H, 6-H_{ax}, 4-H_{ax}), 4.35–3.65 (m, 10H, 2,3,7,8,9,10-H), 3.05 (d, *J* = 6.7 Hz, 3H, 11-H), 2.90 (d, *J* = 6.7 Hz, 3H, 12-H). – ^{13}C NMR (50 MHz, CD_3OD): δ = 64.7 (C-1), 56.8 (C-6), 55.2 (C-4), 53.9 (C-9a), 43.9 (C-2), 27.6 (C-9), 26.7 (C-10), 23.7 (C-3), 22.7 (C-8), 20.8 (C-11), 20.7 (C-7), 15.1 (C-12). – MS (70 eV), *m/z* (%): 196 (49) [M], 166 (18), 149 (66), 121 (65), 111 (69), 97 (73), 83 (73), 69 (100), 67 (58), 55 (97). – $C_{12}H_{24}N_2$: calcd. 196.1939, found 196.1934 (MS).

(7R,8S,8aS)-8-Amino-7-isopropylindolizidine (**26**): 680 mg (4.20 mmol, quant.) of a pale brown, amorphous solid, $[\alpha]_D^{22}$ = –13.1 (*c* = 1.00 in MeOH). – IR (KBr): $\tilde{\nu}$ = 3536 cm^{-1} (NH), 3429 (NH), 2957, 2932, 2863, 2765, 2618, 2543, 1508. – ^1H NMR (200 MHz, CD_3OD): δ = 6.82 (s, broad, 5H, NH_2), 6.15 (s, broad, 1H, 8-H), 5.75–5.63 (m, 3H, 8a-H, 3-H_{eq}, 5-H_{eq}), 5.15–5.08 (m, 2H, 3-H_{eq}, 5-H_{eq}), 4.25–3.60 (m, 8H, 1,2,6,7,9-H), 3.07 (d, *J* = 6.9 Hz, 3H, 10-H), 3.02 (d, *J* = 6.9 Hz, 3H, 11-H), 2.95–2.91 (m, 1H). – ^{13}C NMR (50 MHz, CD_3OD): δ = 67.6 (C-8), 53.0 (C-3), 51.8 (C-5), 49.7 (C-8a), 45.2 (C-7), 28.9 (C-9), 24.9 (C-1), 23.4 (C-6), 21.3 (C-10), 20.5 (C-2), 20.3 (C-11). – MS (70 eV, DCI – NH_3), *m/z* (%): 198 (2) [M + 1 + NH_3], 183 (100) [M + 1]. – $C_{11}H_{22}N_2$ + H: calcd. 183.1861, found 183.1856 [MS (DCI)].

(1RS,2SR,9aRS)-1-Amino-2-isopropylquinolizidine (**27**): 355 mg (1.81 mmol, quant.) of a colorless, amorphous solid. – IR (KBr): $\tilde{\nu}$ = 3436 cm^{-1} (NH), 2962, 2875, 2745, 2691, 2640, 2578, 1533. – ^1H NMR (200 MHz, CD_3OD): δ = 6.82 (s, broad, 5H, NH_2), 5.88 (s, broad, 1H, 1-H), 5.63–5.48 (m, 3H, 9a-H, 6-H_{eq}, 4-H_{eq}), 5.18–5.05 (m, 2H, 6-H_{ax}, 4-H_{ax}), 4.18–3.57 (m, 10H, 2,3,7,8,9,10-H), 3.04 (d, *J* = 5.7 Hz, 3H, 11-H), 3.01 (d, *J* = 5.7 Hz, 3H, 12-H). – ^{13}C NMR (50 MHz, CD_3OD): δ = 64.9 (C-1), 56.9 (C-6), 55.4 (C-4), 52.4 (C-9a), 44.9 (C-2), 28.7 (C-10), 27.9 (C-9), 24.0 (C-3), 23.3 (C-8), 22.7 (C-7), 20.9 (C-11), 20.1 (C-12). – MS (70 eV), *m/z* (%): 196 (8) [M], 136 (20), 124 (16), 112 (33), 111 (86), 98 (100), 83 (60), 70 (52), 55 (39). – $C_{11}H_{24}N_2$ + H: calcd. 197.2018, found 197.2043 [MS (DCI)].

Acetylation of Amines: To a solution of amine **22**, **23**, **26**, or **27** (4.20 mmol) in anhydrous CH_2Cl_2 (42 ml) were successively added dropwise NEt_3 (1.28 g, 12.6 mmol) and then Ac_2O (493 mg, 4.83 mmol), and the remaining yellow solution was refluxed for ca. 12 h. After cooling to room temp. MeOH (10 ml) was added, and the solution was stirred for an additional 1 h. Evaporation of the solvent yielded a pale brown solid, which was adsorbed on SiO_2 and purified by flash chromatography on SiO_2 ($CHCl_3$/MeOH, 5:1).

(7R,8R,8aS)-8-Acetamido-7-isopropylindolizidine (**24**): 304 mg (1.36 mmol, 87%) of colorless crystals, m.p. 165°C, $[\alpha]_D^{22}$ = +27.0 (*c* = 0.60 in $CHCl_3$). – IR (film): $\tilde{\nu}$ = 3409 cm^{-1} (NH), 3253 (NH), 3076 (NH), 2964, 2873, 2849, 2802, 1637 (C=O), 1567 (C=O). – For ^1H- and ^{13}C NMR data see ref.[18]. – MS (70 eV), *m/z* (%): 223 (16) [M – 1], 181 (32) [M – $COCH_3$], 122 (100), 119 (32), 112 (27), 97 (35), 84 (43), 70 (90), 57 (90), 55 (38). – $C_{13}H_{23}N_2O$: calcd. 223.1810, found 223.1814 (MS).

(1RS,2RS,9aSR)-1-Acetamido-2-isopropylquinolizidine (**25**): Flash chromatography yielded 38 mg (0.16 mmol, 7%) of brown oil as the first fraction (86.9% of **29**, 2.9% of **25**, determined by GC) and 492 mg (2.07 mmol, 92%) of a brown oil as the second fraction (30.0% of **29**, 61.8% of **25**). – IR (film): $\tilde{\nu}$ = 3233 cm^{-1} (NH), 3198 (NH), 2960, 2940, 2682, 2652, 2593, 2525, 2497, 1667 (C=O), 1553 (C=O). – ^1H NMR (300 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 9.4 Hz, 1H, NH), 4.02 (s, 1H, 1-H), 3.23 (t, *J* = 7.9 Hz, 2H, 4-H_{eq}, 6-H_{eq}), 2.88 (q, *J* = 13.2 Hz, 2H, 9a-H, 4-H_{ax}), 2.02–1.59 (m, 10H, 2,3-H, 6-H_{ax}, 7,8,9,10-H), 1.94 (s, 3H, $COCH_3$), 1.48–1.25 (m, 1H), 0.79 (d, *J* = 6.8 Hz, 3H, 11-H), 0.71 (d, *J* = 6.8 Hz, 3H, 12-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.7 (CO), 65.8 (C-9a), 55.2 (C-6), 54.5 (C-4), 46.0 (C-1,2), 26.5 (C-9), 26.3 (C-10), 22.8 (C-3), 22.2 (C-8), 20.6 (C-7), 20.5 (C-11), 15.7 (C-12). – GC-MS (70 eV), R_t = 23.27 min (**25**), *m/z* (%): 239 (25) [M + 1], 195 (3) [M – $COCH_3$], 179 (20), 136 (100), 84 (10), 43 (15) [$COCH_3$]. – $C_{14}H_{26}N_2O$ + H: calcd. 239.2123, found 239.2138 [MS (CI)].

(7R,8S,8aS)-8-Acetamido-7-isopropylindolizidine (**28**): 810 mg (3.65 mmol, 87%) of a brown oil, $[\alpha]_D^{22}$ = –64.9 (*c* = 1.00 in $CHCl_3$). – IR (KBr): $\tilde{\nu}$ = 3434 cm^{-1} (NH), 3111 (NH), 3090 (NH), 2970, 2951, 2933, 2875, 2786, 1631, 1542 (C=O). – For ^1H- and ^{13}C-NMR data see ref.[18]. – MS (70 eV), *m/z* (%): 223 (70) [M – 1], 136 (34), 122 (100), 97 (38), 83 (38), 70 (89), 55 (38). – $C_{13}H_{23}N_2O$: calcd. 223.1810, found 223.1814 (MS).

(1RS,2SR,9aRS)-1-Acetamido-2-isopropylquinolizidine (**29**): Flash chromatography yielded 269 mg (1.13 mmol, 75%) of a brown amorphous solid as the first fraction (87.8% of **29**, 1.5% of **25**, determined by GC) and 77 mg (0.32 mmol, 22%) of a brown oil as the second fraction (47.9% of **29**, 44.0% of **25**). – IR (film): $\tilde{\nu}$ = 3268 cm^{-1} (NH), 3066 (NH), 2939, 2868, 2807, 2763, 2678, 2590, 2557, 2514, 1660 (C=O), 1545 (C=O), 1537, 1290, 1277. – ^1H NMR (300 MHz, $CDCl_3$): δ = 6.84 (d, broad, *J* = 10.6 Hz, 1H,

NH), 4.28 (d, J = 10.6 Hz, 1H, 1-H), 3.07–2.98 (m, 2H, 4-H_{eq}, 6-H_{eq}), 2.23 (ddd, J = 12.0/12.0/3.0 Hz, 2H, 4-H_{ax}, 6-H_{ax}), 2.28–2.14 (m, 1H), 2.00 (s, 3H, $COCH_3$), 1.76–1.45 (m, 7H), 1.39–1.23 (m, 1H), 1.14–1.03 (m, 1H), 0.89 (d, J = 6.7 Hz, 3H, 11-H), 0.79 (d, J = 6.7 Hz, 3H, 12-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.6 (CO), 66.5 (C-9a), 56.1 (C-4,6), 48.5 (C-1), 46.6 (C-2), 28.7 (C-10), 27.7 (C-9), 24.2 (C-3), 23.8 (C-7), 23.1 ($COCH_3$), 23.0 (C-8), 20.9 (C-11), 20.2 (C-12). – GC-MS (70 eV), R_t = 22.25 min (**29**), *m/z* (%): 239 (9) [M + 1], 195 (4) [M – $COCH_3$], 179 (15), 136 (100), 84 (12), 55 (8), 43 (20) [$COCH_3$]. – $C_{14}H_{26}N_2O$ + H: calcd. 239.2123, found 239.2130 [MS (CI)].

Hydrochloride **30**: Heating of **29** in CH_2Cl_2 for 12 h followed by recrystallization from EtOH yielded **30** as colorless crystals, which were suitable for X-ray analysis[33]. – $C_{14}H_{27}ClN_2O$ (274.7): calcd. C 61.18, H 9.90, N 10.19; found C 61.40, H 8.89, N 10.15.

N-(4-Methyl-3-pentenyl)-(S)-prolinal[D_7]Benzylimine **34**: 485 mg (1.75 mmol, quant.) of a pale brown oil, $[\alpha]_D^{22}$ = –104.9 (c = 1.00 in $CHCl_3$). – IR (film): $\tilde{\nu}$ = 2966 cm^{-1}, 2926, 2873, 2854, 2834, 2796, 2275 (=C–D), 2173 (=C–D), 2095 (=C–D), 1668 (HC=N). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58 (d, J = 6.7 Hz, 1H, *H*C=N), 5.06 (t, J = 5.6 Hz, 1H, 3′-H), 3.19 (ddd, J = 10.3/7.2/2.9 Hz, 1H, 2-H), 2.97 (q, J = 7.9 Hz, 1H, 5-H_{eq}), 2.69–2.60 (m, 1H, 1′a-H), 2.30–2.11 (m, 4H, 5-H_{ax}, 1′b,2′-H), 2.06–1.92 (m, 1H, 3-H_{eq}), 1.89–1.71 (m, 1H, 4-H_{eq}), 1.69–1.58 (m, 2H, 3-H_{ax}, 4-H_{ax}), 1.65 (d, J = 1.4 Hz, 3H, 5′-H), 1.56 (d, J = 0.5 Hz, 3H, 6′-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.4 (HC=N), 132.6 (C–4′), 128.4–126.0 (several small multiplets), 121.9 (C-3′), 68.5 (C-2), 64.2 (m, CD_2), 54.9 (C-1′), 53.9 (C-5), 28.9 (C-2′), 27.7 (C-3), 25.6 (C-5′), 23.2 (C-4), 17.7 (C-6′). – MS (70 eV), *m/z* (%): 278 (9) [M + 1], 277 (21) [M], 262 (18) [M – CH_3], 208 (95) [M – $CH_2CH{=}CMe_2$], 178 (24) [M + 1 – C_7D_7], 167 (26), 152 (36), 108 (33), 98 (100) [C_7D_7], 84 (35), 83 (53), 55 (81) [$HC{=}CMe_2$]. – $C_{18}H_{19}D_7N_2$: calcd. 277.2535, found 277.2542 (MS).

(7R,8S,8aS)-8-{([D_6]Benzylidene)amino}-7-(1-methyl[1D]-ethyl)indolizidine (**35**): Flash chromatography yielded 166 mg (0.60 mmol, 37%) of a pale brown oil, $[\alpha]_D^{22}$ = –97.0 (c = 1.00 in $CHCl_3$). – IR (film): $\tilde{\nu}$ = 2953 cm^{-1}, 2866, 2850, 2780, 2748, 2272 (=C–D), 2115 (=C–D), 1685 (HC=N), 1629 (C=C). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.47 (t, J = 2.4 Hz, 1H, 8-H), 3.31 ("ddd", J = 10.5/4.6/2.6 Hz, 1H, 5-H_{eq}), 3.16–3.10 (m, 1H, 3-H_{eq}), 2.21–1.86 (m, 3H), 1.85–1.48 (m, 5H), 1.38–1.28 (m, 1H), 1.26–1.16 (m, 1H, 1,2-H, 3-H_{ax}, 5-H_{ax}, 6,7-H), 0.85 (s, 3H, 10-H), 0.79 (s, 3H, 11-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.8 (t, DC=N), 136.2 (s, C-*i*), 129.7 (t, C-*m*), 128.4, 128.1, 127.7, 127.3 (C-*o*,*p*), 69.2 (C-8), 68.6 (C-8a), 54.3 (C-3), 53.1 (C-5), 48.5 (C-7), 28.2 (t, C-9), 25.6 (C-1), 25.1 (C-6), 20.7 (C-2), 20.6 (C-10), 19.9 (C-11). – ^{2}H NMR (55 MHz, $CHCl_3$): δ = 7.99 (s, broad, 1D, DC=N), 7.57 (s, broad, 2D, *o*-D), 7.15 (s, broad 3D, *m*-,*p*-D), 1.07 (s, broad, 1D, $CDMe_2$). – MS (70 eV), *m/z* (%): 278 (43) [M + 1], 277 (55) [M], 233 (57) [M – CH_3CDCH_3], 179 (63) [M – C_7D_7], 169 (68), 164 (82), 149 (87), 122 (82), 112 (77), 98 (87) [C_7D_7], 84 (94), 82 (71) [C_6D_5], 69 (83) [$CH_2CH{=}CMe_2$], 55 (100) [$HC{=}CMe_2$]. – $C_{18}H_{19}D_7N_2$: calcd. 277.2535, found 277.2542 (MS).

N-Phthaloyl[D_7]benzylamine (**37**): To a solution of [D_7]benzyl chloride (**36**) (1.00 g, 7.48 mmol) and cetylphosphonium bromide (380 mg, 0.75 mmol) in anhydrous toluene (3.7 ml) was added potassium phthalimide (1.73 g, 9.35 mmol) in one portion, and the mixture was heated at 60°C for 6 h. The precipitated potassium chloride was removed by filtration by means of a fritted funnel and washed with Et_2O (2 × 10 ml). The solvent was evaporated from the combined filtrates to yield a colorless, crystalline residue, which was purified by flash chromatography (SiO_2, hexanes/Et_2O, 5:1, then 2:1) to yield 1.70 g (93%) of colorless crystals, m.p. 117°C. – IR (KBr): $\tilde{\nu}$ = 3095 cm^{-1}, 2272 (=CD), 2159 (=C–D), 2127 (=C–D), 1771 (C=O), 1702 (C=C), 1612 (C=C), 1394, 1190, 917, 718. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.80 (dd, J = 5.3/3.1 Hz, 2H, 3′,6′-H), 7.66 (dd, J = 5.3/3.1 Hz, 2H, 4′,5′-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.9 (CO), 136.0 (C-1), 133.8 (C-3′,6′), 132.1 (C-1′,2′), 128.5 ("m", C-2,6), 128.4 ("m", C-3,5), 127.7 ("m", C-4), 123.2 (C-4′,5′), 41.1 (quint, $CD_2C_6D_5$). – MS (70 eV), *m/z* (%): 245 (10) [M + 1], 244 (67) [M], 243 (4) [M – 1], 224 (39) [M – D_2O], 187 (18), 149 (37), 135 (31), 111 (36), 110 (43), 109 (55), 95 (53), 81 (77), 77 (49), 71 (80), 56 (100). – $C_{15}H_4D_7NO_2$: calcd. 244.1229, found 244.1223 (MS).

[D_7]Benzylamine **38**: To a boiling solution of **37** (1.61 g, 6.61 mmol) in 38 ml of EtOH and 2 ml of H_2O was added hydrazine hydrate (450 mg, 8.99 mmol), and the mixture was refluxed for 5 h. Then the pH of the mixture was adjusted to 1 by the addition of conc. HCl to the ice-cooled mixture. The resulting was refluxed for another 30 min and after cooling to room temp. the precipitated *N*-phthaloylhydrazine was removed by filtration and washed with water. The combined filtrates were concentrated at 40°C and 25 mbar to yield a pale yellow crystalline residue, which was dissolved in 2 N HCl (50 ml). The aqueous layer was washed with toluene (2 × 30 ml) and Et_2O (2 × 30 ml). Then concd. NH_3 was added dropwise with stirring to the ice-cooled mixture until pH 8–9, and the resulting mixture was extracted with CH_2Cl_2 (4 × 50 ml). The combined extracts were dried with $MgSO_4$ and evaporated (while the bath temp. was kept below 50°C at 600 mbar) to yield 964 mg (quant). of a pale yellow oil (99% as determined by GC), which was used without further purification and characterization.

Deuterium Scrambling Experiment: To an ice-cooled mixture of **11b** (605 mg, 2.13 mmol) and **34** (277 mg, 1.00 mmol) in CH_2Cl_2 (85 ml) was added dropwise over 30 min $TiCl_4$ (7.83 ml, 7.83 mmol of a 1.0 M solution in CH_2Cl_2), and the dark brown solution was stirred for 60 h at room temp. Workup as described above yielded 950 mg of a dark brown oil, which was directly subjected to GC-MS analysis. – GC-MS (EI, 70 eV), R_t = 29.6 min (**35**, **45**), *m/z* (%): 278 (1.15), 277 (7.21), 276 (11.56), 233 (21), 179 (13), 164 (100), 137 (12), 122 (49), 110 (14), 96 (33), 84 (41), 69 (14), 55 (14), 41 (14); R_t = 30.4 min (**48**), *m/z* (%): 277 (7.9), 233 (2.0), 193 (17), 180 (91), 164 (32), 137 (11), 122 (21), 110 (38), 98 (100), 84 (78), 70 (30), 55 (28), 44 (33); R_t = 31.6 min (**47**, **17b**), *m/z* (%): 286 (0.72), 285 (7.54), 284 (10.19), 241 (20), 172 (100), 122 (56), 105 (28), 97 (20), 84 (50), 69 (13), 55 (19), 41 (22); R_t = 32.0 min (**15b**), *m/z* (%): 285 (3), 284 (7), 241 (9), 187 (89), 172 (54), 122 (14), 120 (19), 110 (33), 105 (82), 96 (39), 84 (100), 70 (27), 55 (31), 41 (27).

(7R,8S,8aS)-8-Hydroxy-7-isopropenylindolizidine (**51**): Flash chromatography yielded 117 mg (65%) of a brown oil as a mixture of diastereomers (98.6:1.4, determined by GC). $[\alpha]_D^{22}$ = –28.7 (c = 1.00 in $CHCl_3$). – IR (film): $\tilde{\nu}$ = 3220 cm^{-1} (OH), 2965, 2949, 2929, 2914, 2796, 2750, 2714, 1650 (C=C). – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.86 (s, broad, 1H, 10a-H), 4.76 (s, broad, 1H, 10b-H), 3.81 (s, broad, 1H, OH), 3.08–2.95 (m, 2H, 8,8a-H), 2.14–1.45 (m, 11H, 2,3,4,7,8,9-H), 1.74 (s, broad, 3H, 11-H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 146.4 (C-9), 110.8 (C-10), 68.2 (C-8a), 66.7 (C-8), 54.1 (C-3), 52.0 (C-5), 48.0 (C-7), 25.2 (C-1), 24.0 (C-6), 22.1 (C-11), 21.3 (C-2). – ^{1}H- and ^{13}C-NMR spectra of **49** (from crude mixtures of **49** and **51**): signals were only incompletely visible. – MS (70 eV), *m/z* (%): 181 (63) [M], 149 (82), 112 (63), 99 (73), 84 (68), 71 (94), 55 (100) [$HC{=}CMe_2$]. – $C_{11}H_{19}NO$: calcd. 181.1467, found 181.1471 (MS).

(1RS,2SR,9aSR)-(±)-1-Hydroxy-2-isopropenylquinolizidine (**52**): Flash chromatography yielded 2.30 g (11.80 mmol, 59%) of a yellow oil as a mixture of **52** and **50** (99.8:0.2, determined by GC). Recrystallization from Et_2O/CH_2Cl_2 yielded colorless needles (m.p. 82°C), which are sufficient for X-ray analysis. – IR (KBr): $\tilde{\nu}$ = 3233 cm^{-1} (OH), 2934, 2901, 2873, 2852, 2801, 2756, 1656 (C=C), 1351, 1131, 1121, 1100, 1087, 883. – ^1H NMR (300 MHz, $CDCl_3$): δ = 4.88 (s, 1H, 11a-H), 4.74 (s, 1H, 11b-H), 3.54 (d, *J* = 5.7 Hz, 1H, OH), 2.84–2.79 (m, 2H, 1,9a-H), 1.76 (s, 3H, 12-H), 2.08–1.87 (m, 5H), 1.85–1.66 (m, 3H), 1.57–1.42 (m, 4H), 1.31–1.13 (m, 1H, 2,3,4,5,6,7,8,9-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.2 (C-10), 111.1 (C-11), 69.5 (C-9a), 66.3 (C-1), 56.2 (C-6), 56.1 (C-4), 47.9 (C-2), 28.9 (C-3), 25.6 (C-9), 24.3 (C-8), 23.7 (C-7), 22.1 (C-12). – ^1H- and ^{13}C-NMR spectra of **50** (from crude mixtures of **50** and **52**): signals were only incompletely visible. – MS (70 eV), *m/z* (%): 195 (43) [M], 180 (48) [M – CH_3], 169 (42), 152 (46), 149 (85), 131 (67), 119 (74), 105 (60), 99 (69), 83 (84), 71 (80), 55 (100) [$HC{=}CMe_2$]. – $C_{12}H_{21}NO$: calcd. 195.1623, found 195.1619 (MS). – calcd. C 73.79, H 10.84, N 7.17; found C 73.68, H 10.98, N 7.47.

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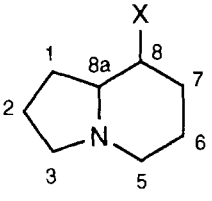

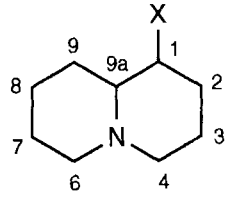

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D-76344 Eggenstein-Leopoldshafen, on quoting the depository number CSD-58190, the names of the authors, and the journal citation.

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[27] The ratio of isotopically pure and mixed products was calculated as follows (natural abundance of ^{13}C = 1.108%): amount of **45** (containing 18 C-atoms) = 11.56; amount of **35** = 7.21 − [11.56 · (18 · 0.01108)] = 4.9045; **45**:**35** = 70.21:29.79; **45**+**35** = 18.5% (from GC); amount of **19b** = 10.19; amount of **47** = 7.54 − [10.19 · (19 · 0.01108)] = 5.3948; **19b**:**47** = 65.38:34.62; **19b**+**47** = 45.7% (from GC); amount of **45** = 0.7021 · 18.5 = 12.9889 (= 20.23%); analogous procedure for **35** (8.59%), **19b** (46.54%), and **47** (24.64%).

[28] One possible rationalization for an intermolecular pathway might be the formation of dimers which is induced by coordination of $TiCl_4$ to two different imines.

[29] Deuterium scrambling of the product imines **19b** and **35** was not observed, when a mixture of **19b** and **35** was treated with $TiCl_4$.

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[31] A. Chiaroni, L. Raudriambola, C. Riche, H. P. Husson, *J. Am. Chem. Soc.* **1980**, *102*, 5920–5921.

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[33] A similar case of unexpected hydrochloride formation caused by CH_2Cl_2 was observed during isolation of alkaloids from plants: J. E. Saxton, *Nat. Prod. Rep.*, **1992**, *8*, 393–446 [see p. 439, isolation of (+)-melonine].

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