Synthesis of Optically Active Indolizidines: (–)-8a-*epi*-Dendroprimine and (–)-7,8-Dehydro-5,6-dimethylindolizidine

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Abstract: Indolizidinones can be employed as key intermediates in efficient asymmetric synthesis of naturally occurring indolizidine alkaloid analogues. The 5,7-dimethylindolizidine (–)-8a-*epi*-dendroprimine was formed by a diastereoselective methylation–reduction sequence of the lactam function. The (–)-5,6-dimethylindolizidine was generated via the same key step including an additional quasi 1,2-methyl shift: an intramolecular enamine alkylation is followed by regioselective reductive cyclopropane ring opening.

Key words: indolizidinone, indolizidine, intramolecular enamine alkylation, iminium salt, diastereoselective reduction, radical cyclopropane opening.

(–)-Dendroprimine **1** is an indolizidine alkaloid with unknown biological activity isolated and characterized by Lüning from Dendrobium primulinum Lindl (Orchidaceae) in 1965.[1] The correct relative configurations of the stereogenic centers were determined after the synthesis of the racemic compound and its diastereomers (e.g. **2**) by the same group,[1] the absolute configuration has been investigated in 1972 by measuring CD-spectra of some degradation products.[2] In 1979 Sonnet confirmed the results by NMR-spectroscopic analyses.[3] Until now, no synthesis of optically active dendroprimine **1** and its epimers like **2** has been described.

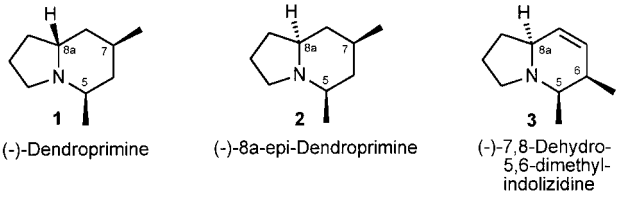
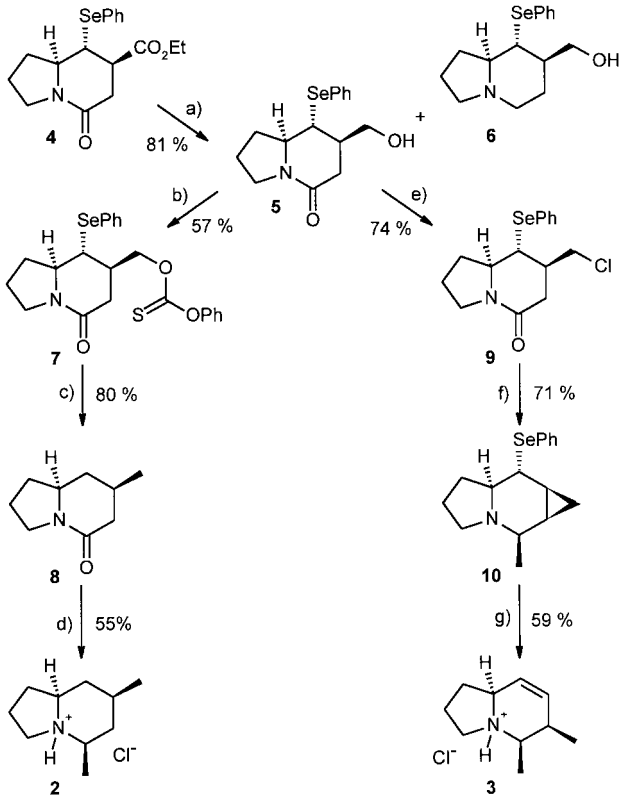


Figure 1

Our synthesis started from the known indolizidinone **4** which could be generated in six steps from L-(–)-proline including a stereoselective zwitterionic aza-Claisen rearrangement followed by a regio- and diastereoselective transannular ring junction as the key steps; overall yield was >50 %.[4] First efforts were carried out to distinguish the carboxylic groups: DIBALH-[5] or Red-Al®-reductions[6] gave unselectively the amino alcohol **6** and the desired hydroxymethyl lactam **5** in varying yields, the reaction with $NaBH_4$ in MeOH[7] led to **5** chemoselectively in the modest yield of about 50%. The best results were achieved using $Li(Et)_3BH$,[8] a reagent which is normally known to reduce amides to the corresponding primary alcohols: about 81% of the hydroxymethyl lactam **5** could be isolated, and no reduction of the amide function was observed.

The next sequence removed the hydroxyl group as well as the phenylselenyl substituent. After activating the hydroxyl group as a thiocarboxylic ester **7** and radical reduction with AIBN and tributyl stannane (Barton–McCombie),[9] the 7-methylindolizidinone **8** was generated in about 50% over two steps.

The second methyl group at C-5 was stereoselectively introduced employing a one-pot procedure: After initial treatment of the lactam **8** with one equivalent of methylmagnesium chloride, the in situ formed iminium salt was reduced with $NaBH_4$/HOAc.[11] The stereoselectivity was efficiently directed by the "open book effect", the hydride ion exclusively attacks from the less hindered face parallel to the bridgehead hydrogen. The (–)-8a-*epi*-dendroprimine **2** was isolated as the hydrochloride in 55% yield, all spectral data were in good agreement with those published in the literature.[10]



(a) $Li(Et)_3BH$, THF, 0 °C, 4 h; (b) ClC(S)OPh, pyridine, CH_2Cl_2, r.t., 2 h; (c) Bu_3SnH, AIBN, PhMe, 75 °C, 3 h; (d) 1. MeMgCl, Et_2O, 0 °C to r.t., 1 h, 2. $NaBH_4$, HOAc, 0 °C 1.5 h; (e) PPh_3, CCl_4, 77 °C, 2.5 h; (f) 1. MeMgCl, THF, 65 °C, 6 h, 2. $NaBH_4$, HOAc, r.t., 1 h; (g) Bu_3SnH, AIBN, PhMe, 110 °C, 4 h.

Scheme

Alternatively, the C-7 hydroxyl group in **5** could be activated by a chlorination following Appels procedure[12] to give the chloromethyl lactam **9** in 74% yield. With intent to introduce the C-5 methyl group prior to the removal of the phenylselenyl substituent, the methylmagnesium chloride addition/$NaBH_4$ reduction sequence was carried out with **9** to give low amounts of the tricyclic **10** and some side products. The yield of **10** could be significantly increased by heating **9** in presence of the Grignard reagent for several hours before treating the mixture with $NaBH_4$ and HOAc. The reaction path was interpreted as follows (Figure 2): Initially, the carbonyl group of lactam **9** was methylated by the Grignard reagent, the in situ formed iminium salt was deprotonated to form an enamine,[13] which underwent an intramolecular alkylation to generate the cyclopropane. Finally the resulting iminium species was reduced stereoselectively with $NaBH_4$ according to the prerequisites of the open-book effect discussed above. The removal of the phenylselenyl substituent with tributyl stannane and AIBN simultaneously effected the opening of the cyclopropane to give the 7,8-dehydro-5,6-dimethylindolizidine **3** which was isolated as the hydrochloride in 59 % yield. Obviously, the intermediately formed secondary alkyl radical adjacent to the cyclopropane underwent ring opening with decrease of ring strain. Finally, the methyl group was built up after H-transfer from the Bu_3SnH. The relative configurations of all stereogenic centers of the indolizidine **3** were determined by NOE-analysis.

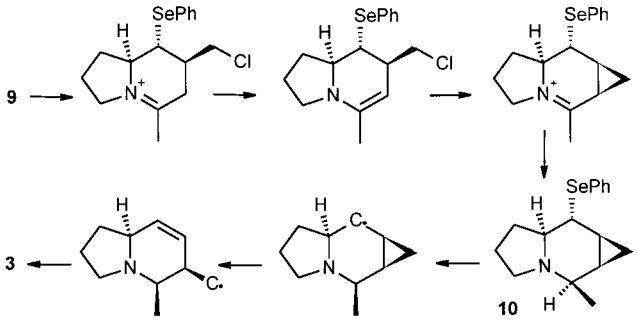


Figure 2

In summary, indolizidine alkaloid analogues bearing alkyl substituents at the positions 5 and 6 or 5 and 7, respectively, with defined configurations, were synthesized starting from an optically active indolizidinone. The stereogenic center C-5 was generated by an alkylation/reduction sequence, the configuration was controlled by the open book effect of the bicycle. On achieving the synthesis of 8a-*epi*-dendropimine (5,7-dialkylindolizidine) the functional groups at C-8 and C-7-CH_2 were removed by a radical reduction. The migration of the substituent of C-7 to C-6 started with an intramolecular enamine alkylation, the so-formed cyclopropane was regioselectively cleaved by a final radical reduction. Further investigations to realize the total synthesis of the natural dendroprimine **1** and to test scope and limitations of the alkyl shift are in progress.[14]

^1H and ^{13}C NMR spectra were recorded on Bruker spectrometers AC 250, AM 270 or AMX 500. IR spectra were obtained on a Nicolet FTIR-Interferrometer 5 SXC. Mass spectra were recorded on a Varian MAT 711. Optical rotations were measured with a Perkin Elmer P 241 in a 1 dm cell. Elemental analyses were obtained from a Perkin Elmer 240 Elemental Analyzer. Melting points (not corrected) were determined with a Büchi SMP 20.

(5*R*, 7*S*, 8*aS*)-5,7-Dimethylindolizidine (2) ((–)-8*a*-*epi*-Dendroprimine)

Under Ar, indolizidinone **8** (60 mg, 0.39 mmol) in anhyd Et_2O (2 mL) was cooled to 0 °C. A solution of MeMgCl (0.4 mL, 1.2 mmol, 3 M in THF) was added dropwise with stirring. The cooling bath was removed and the mixture was stirred at r.t. for 0.5 to 1 h (TLC control). Then, the mixture was cooled again to 0 °C and HOAc (1.8 mL) as well as $NaBH_4$ (30 mg, 0.78 mmol) were added subsequently. After stirring for a further 1.5 h, the reaction was quenched with Et_2O (20 mL), and sat. aq Na_2CO_3 (10 mL). The mixture was extracted with Et_2O (3 × 20 mL) the combined organic layers were washed with brine (5 mL) and dried ($MgSO_4$). The $MgSO_4$ was filtered off and concd aq HCl (0.1 mL) was added. The solvents were evaporated and the remaining H_2O was removed by distilling twice with toluene. Yield: 33 mg (0.21 mmol, 55 %) of the hydrochloride of **2** as a pale yellow oil, which did not crystallize. $[\alpha]_D^{20}$ = –45.8 (*c* = 0.72, $CHCl_3$).

MS (EI, 70 eV, 40 °C): *m/z* (%) = 153 (15, $[M]^+$), 138 (100), 110 (13), 96 (20), 70 (9), 36 (9).

^1H NMR (500 MHz, 323 K, DMSO, D_2O): δ = 0.92 (d, 3 H, *J* = 6 Hz, 7-CH_3), 1.28 (d, 3 H, *J* = 7 Hz, 5-CH_3), 1.35 (m_C, 2 H, 6-H^1, 8-H^1), 1.62–1.75 (m, 2 H, 1-H^1, 7-H), 1.79 (dd, br s, 1 H, *J* = 11 Hz, 6-H^2), 1.82–1.95 (m, 3 H, 2-H^1, 2-H^2, 8-H^2), 2.08 (m_C, 1 H, 1-H^2), 2.88 (m_C, 1 H, 3-H^1), 3.09 (m_C, 2 H, 5-H, 8a-H), 3.49 (m_C, 1 H, 3-H).

^{13}C NMR (68 MHz, $CDCl_3$): δ = 17.8 (C-9), 19.4 (C-2), 20.7 (C-10), 28.1 (C-1), 30.2 (C-7), 34.9 (C-8), 39.2 (C-6), 49.8 (C-3), 60.0 (C-5), 67.3 (C-8a).

^1H–^{13}C COSY (DMSO, 323 K): crosspeak δC /δH (No.) = 17.5/0.92 (10), 19.0/1.9 (2), 21.0/1.25 (9), 27.7/1.65, 2.1 (1), 29.2/1.7 (7), 35.0/1.35, 19.5 (8), 39.0/1.35, 1.8 (6), 49.0/2.9, 3.5 (3), 58.2/3.15 (5), 66.0/3.1 (8a).

Analysis: $C_{10}H_{19}N$ (153.27) calculated: C 74.46, H 11.18. found: C 74.11, H 10.89.

(5*R*, 6*S*, 8a*S*)-5,6-Dimethyl-1,2,3,5,6,8a-hexahydroindolizine Hydrochloride (3)

Under Ar, the cyclopropane **10** (300 mg, 1 mmol) was dissolved in anhyd toluene (25 mL). While Ar was slowly bubbled through the solution, Bu_3SnH (580 mg, 2 mmol) and AIBN (10 mg, 0.07 mmol) were added and the mixture was heated to 110 °C for 4 h. After cooling to r.t., aq HCl (5 mL, 12.5 %) was added and the aqueous layer was extracted with Et_2O (3 × 10 mL) to remove the tin salts. Then, the H_2O was removed by distillation with toluene (3 × 10 mL). Yield: 110 mg (0.59 mmol, 59 %) of **3** as a yellow oil, that did not crystallize.$[\alpha]_D^{20}$ = –36.8 (*c* = 0.78, $CHCl_3$).

IR (KBr, Film): ν = 3419, 3032, 2974, 2943, 2880, 2828, 2738, 2645, 2581, 2517, 1624, 1451, 1387, 1083 cm^{-1}.

MS (DMSO/Glyc./Xenon, CH_5 DF//FAB POS): *m/z* (%) = 339 (10, $[M + C_{10}H_{18}N]^+$), 185 (10), 153 (26), 152 (100, $[C_{10}H_{18}N]^+$), 151 (11), 150 (11), 93 (36), 75 (12), 70 (12).

^1H NMR (270 MHz, $CDCl_3$, TMS): δ = 1.05 (d, *J* = 7 Hz, 3 H, 6-CH_3) 1.35 (d, *J* = 7 Hz, 3 H, 5-CH_3), 1.75 (m_C, 1 H, 1-H^1), 2.05 (m_C, 2 H, 2-H), 2.30 (m_C, 1 H, 1-H^2), 2.65 (m_C, 1 H, 6-H), 3.15 (m_C, 1 H, 3-H^1), 3.55 (m_C, 1 H, 3-H^2), 3.65 (m_C, 1 H, 5-H), 4.30 (m_C, 1 H, 8a-

H), 5.55 (d, br s, J = 11 Hz, 1 H, 8-H), 5.80 (m_C, 1 H, 7-H), 12.20 (s, 1 H, N^+-H).

NOE-analysis: irradiation at H-X ⇒ amplification at H-Y [%]: H-3α ⇒ H-6α (8); H-3β ⇒ CH_3-6β (1); H-5α ⇒ H-3α (8); CH_3-5β ⇒ CH_3-6β (2); CH_3-6β ⇒ H-3β (6), CH_3-5β (1), H-7 (1); H-7 ⇒ CH_3-6β (1).

^{13}C NMR (68 MHz, $CDCl_3$): δ = 13.1 (CH_3), 15.3 (CH_3), 21.9 (C-2), 29.9 (C-1), 30.8 (C-6), 47.1 (C-3), 54.0 (C-5), 59.3 (C-8a), 122.5 (C=C), 130.6 (C=C).

$C_{10}H_{17}N$•HCl (187.70) calc.: C 62.74, H 6.91. found: C 62.92, H 7.31.

(7R, 8R, 8aS)-7-Hydroxymethyl-8-phenylselenylindolizidin-5-one (5)

Under Ar, the ester **4** (3.7 g, 10 mmol) was dissolved in anhyd THF (50 mL) and cooled to 0°C. A solution of $Li(Et)_3BH$ (21 mL, 21 mmol, 1 M in THF) was added dropwise, with stirring. After 3 to 4 h at this temperature, the reaction was detected to be complete (TLC). Sat. aq $KHSO_4$ (4 mL) and H_2O (8 mL) were added to reach a pH < 2. After extraction with Et_2O (4 × 30 mL) the combined organic layers were washed with brine (20 mL) and dried ($MgSO_4$). The solvent was removed, the crude material was purified via column chromatography (EtOAc, R_f = 0.1). Yield: 2.7 g (8.1 mmol, 81%) of **5** as a white foam, mp 83°C. $[\alpha]_D^{20}$ = –39.1 (c = 0.85, $CHCl_3$).

IR (KBr): ν = 3452 (br), 1630, 1475, 1455, 1398 cm^{-1}.

MS (EI; 70 eV, 100°C): *m/z* = 325 (7), 323 (3), 214 (3), 169 (11), 168 (100), 158 (5), 157 (4), 150 (5), 136 (22), 108 (7), 84 (7), 83 (7), 80 (5), 70 (24).

^{1}H NMR (270 MHz, $CDCl_3$, TMS): δ = 1.40, (m_C, 1 H, 1-H^1), 1.60 (m_C, 1 H, 2-H^1),1.75 (m_C, 1 H, 2-H^2), 2.00 (m_C, 1 H, 1-H^2), 2.40 (m_C, 1 H, 7-H), 2.50 (m_C, 2 H, 6-H), 2.75 (dd, J = 10 Hz, 10 Hz, 1 H, 8-H), 3.40–3.50 (m, 3 H, 8a-H, 3-H), 3.80 (m_C, 1 H, 9-H^1), 3.95 (m_C, 1 H, 9-H^2), 4.10 (s, 1 H, OH), 7.25 (m_C, 3 H, ArH), 7.55 (m_C, 2 H, ArH).

^{13}C NMR (68 MHz, $CDCl_3$): δ = 21.7 (C-2), 33.5 (C-1), 34.0 (C-6), 39.9 (C-7), 45.5 (C-8), 45.9 (C-9), 126.8, 128.1, 130.0, 135.5 (C-Ar), 168.8 (C=O).

$C_{15}H_{19}NO_2Se$ (324.28) calc.: C 55.56, H 5.91. found: C 55.10, H 5.47.

(7*R*, 8*R*, 8a*S*)-7-(Phenyloxythiocarbonyloxymethyl)-8-phenylselenylindolizidin-5-one (7)

Under Ar, alcohol **5** (1.9 g, 5.9 mmol) in anhyd CH_2Cl_2 (40 mL) was treated with pyridine (1.8 mL, 21.9 mmol) and phenylchlorothiono formate (1.2 mL, 6.5 mmol) with stirring. After 2 h the solvent was removed and the residue was dissolved in Et_2O (40 mL). The organic layer was washed with aq $KHSO_4$ (2 × 20 mL, 0.1 M), sat. aq $NaHCO_3$ (2 × 20 mL) and dried ($MgSO_4$). After removal of the solvent, the crude material was purified by column chromatography (gradient EtOAc/hexane 1: 5 to EtOAc, R_f (EtOAc) = 0.2). Yield: 1.56 g (3.4 mmol, 57%) thioformate **7** as pale yellow crystals, mp: 159°C. $[\alpha]_D^{20}$ = –32.0 (c = 0.87, $CHCl_3$).

IR (KBr, Film): ν = 1627, 1455, 1477, 1326, 1289 cm^{-1}.

MS (EI, 70 eV, 120–150°C): *m/z* (%) = 461 (17, $[M]^+$), 307 (27), 305 (36), 304 (60), 230 (20), 156 (45), 151 (58), 150 (100, $[O_2SC_5H_6]^+$), 149 (58), 136 (58), 122 (45), 109 (27), 108 (44), 95 (25), 91 (45), 83 (58), 70 (91), 65 (56).

^{1}H NMR (250 MHz, $CDCl_3$, TMS): δ = 1.50 (m_C, 1 H, 1-H^1), 1.75 (m_C, 1 H, 2-H^1), 1.90 (m, 1 H, 2-H^2), 2.40 (m_C, 1 H, 7-H), 2.50–2.75 (m, 3 H, 1-H^2, 6-H^1, 6-H^2), 2.80 (dd, J = 10Hz, 10 Hz, 1 H, 8-H), 3.40–3.60 (m, 3 H, 8a-H, 3-H^1, 3-H^2), 4.7 (dd, J = 10 Hz, 1 Hz, 1 H, 9-H^1), 4.9 (dd, J = 10 Hz, 1 Hz, 1 H, 9-H^2), 7.05 (m_C, 2 H, ArH), 7.20–7.45 (m, 6 H, ArH), 7.60 (m_C, 2 H, ArH).

^{13}C NMR (68 MHz, $CDCl_3$): δ = 21.7 (C-1), 33.9 (C-2), 34.4 (C-6), 38.0 (C-7), 45.8 (C-3), 46.0 (C-8a), 63.2 (C-8), 75.1 (C-9), 121.7, 126.5, 128.5, 129.3, 135.7 (ArC), 153.2 (OCAr), 167.0 (C=O), 194.6 (C=S).

$C_{22}H_{23}NO_3SSe$ (460.45) calc.: C 57.39, H 5.03. found: C 57.03, H 5.37.

(7*R*, 8a*S*)-7-Methylindolizidin-5-one (8)

Under Ar, the thioformate **7** (1 g, 2.2 mmol) was dissolved in anhyd toluene (80 mL). While Ar was slowly bubbled through the solution Bu_3SnH (1.54 mL, 5.4 mmol) and AIBN (130 mg, 0.8 mmol) were added and the mixture was heated to 75°C for 3 h. Then, the solvent was removed (low temperature, because product might be distilled) and the crude material was purified by column chromatography (EtOAc/hexane, 1 : 2, R_f = 0.12) and preparative HPLC (Nucleosil 50–5 µm, 4 × 125 mm. UV: 220 nm. RI: Range 8. Flow: 2 ml/min. solvent: 10% isopropanol/hexane, retention time = ~ 6.7 min (amide **8**) and 8.3 min (thioformate **7**)). Yield: 270 mg (1.76 mmol, 80 %) of **8** as a colorless liquid. $[\alpha]_D^{20}$ = –2.9 (c = 1.2, $CHCl_3$).

IR ($CHCl_3$): ν = 1620 (vs).

MS (EI, 70 eV, 40°C): *m/z* (%) = 153 (100, $[M]^+$), 125 (24), 111 (45), 83 (100), 70 (90), 56 (34), 41 (39).

^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ = 1.05 (m_C, 4 H, 7-H, 7-CH_3), 1.40 (m_C, 1 H, 1-H^1), 1.70-1.80 (m, 1 H, 2-H^1); 1.85–2.00 (m, 3 H, 2-H^2, 8-H^1, 8-H^2), 2.00–2.10 (m, 2 H, 1-H^2, 6-H^1), 2.50 (dd, J = 15 Hz, 1 Hz, 1 H, 6-H^2), 3.35–3.45 (m, 2 H, 3-H^1, 8a-H); 3.55 (m_C, 1 H, 3-H^2).

^{13}C NMR (68 MHz, $CDCl_3$): δ = 21.5 (7-CH_3), 22.1 (C-2), 28.4 (C-7), 33.2 (C-1), 37.4 (C-8), 39.6 (C-6), 44.4 (C-3), 58.9 (C-8a), 168.8 (C=O).

$C_9H_{15}NO$ (153.23) calc.: C 70.55, H 9.87. found: C 71.17, H 10.24.

(7*R*, 8*R*, 8a*S*)-7-Chloromethyl-8-phenylselenylindolizidin-5-one (9)

Under Ar, alcohol **5** (3.2 g, 10 mmol) in anhyd CCl_4 (20 mL) was treated with PPh_3 (2.6 g, 10 mmol) and the mixture was heated to reflux for 2–3 h. Then, the solvent was evaporated and the crude material was purified by column chromatography (EtOAc/MeOH, 10:1, R_f = 0.2). Yield: 2.5 g (7.4 mmol, 74%) of **9** as a white foam, mp: 95°C. $[\alpha]_D^{20}$ = 23.2 (c = 0.76, $CHCl_3$).

IR (KBr): ν = 1620, 1478, 1468, 1417 cm^{-1}.

MS (100°C, EI; 70 eV): *m/z* = 345 (4), 343 (8), 341 (4), 188 (36), 187 (13), 186 (100), 136 (16), 70 (12).

^{1}H NMR (270 MHz, $CDCl_3$, TMS): δ = 1.50 (m_C, 1 H, 1-H^1) 1.75 (m_C, 1 H, 2-H^1), 1.90–2.05 (m, 1 H, 2-H^2), 2.35 (m_C, 1 H, 7-H), 2.45–2.65 (m, 3 H, 6-H^1, 6-H^2, 1-H^2), 2.90 (dd, 1H, J= 10 Hz, 1 Hz, 8-H), 3.40–3.60 (m, 3 H, 3-H^1, 3-H^2, 8a-H), 3.80 (dd, J = 10 Hz, 3 Hz, 1 H, 9-H^2), 4.20 (dd, J= 10 Hz, 5 Hz, 1 H, 9-H^2), 7.35 (m_C, 3 H, ArH), 7.60 (m_C, 2 H, ArH).

^{13}C NMR (68 MHz, $CDCl_3$): δ = 21.7 (ring-CH_2) 33.9 (ring-CH_2), 34.4 (C-6), 39.4 (C-7), 45.8 (CH_2X), 46.8 (C-8), 48.3 (CH_2X), 63.3 (C-9), 126.4, 128.6, 129.3, 135.8 (C-Ar), 167.2 (C=O).

$C_{15}H_{18}NOSe$ (342.73) calc.: C 48.78, H 5.63. found: C 48.97, H 5.88.

(5*R*, 6*S*, 7*S*, 8*R*, 8a*S*)-6,7-Cyclopropa-8-phenylselenylindolizidin-5-one (10)

Under Ar, chloride **9** (3.4 g, 10 mmol) in anhyd THF (20 mL) was treated with MeMgCl (7.2 mL, 24 mmol, 3 M in THF) with stirring. After heating to reflux for 6 h, the mixture was cooled to r.t. and HOAc (15 mL) and $NaBH_4$ (380 mg, 10 mmol) were added subsequently. The mixture was stirred for 1 h at r.t. Then, the excess of acid was neutralized by quenching with sat. aq $NaHCO_3$ (20 mL)

and the addition of solid $NaHCO_3$ until the pH was raised to 7–8. The mixture was extracted with EtOAc (5 × 20 mL), the combined organic layers were dried ($MgSO_4$). Finally, the crude brownish oil was purified by column chromatography (EtOAc / hexane, 1 : 5, *Rf* = 0.12). Yield: 2.2 g (7.2 mmol, 71 %) of **10** as yellow amorphous needles, mp: 66 °C. $[\alpha]_D^{20} = -12.2$ (*c* = 0.55, $CHCl_3$).

IR (KBr): ν = 2962, 2924, 2865, 2789, 1580, 1481, 1430, 1369, 1155, 1075 cm^{-1}.

MS (100 °C, EI; 70 eV): *m/z* (%) = 307 (6), 238 (41), 236 (20), 157 (10), 150 (43), 134 (17), 120 (11), 97 (47), 81 (100), 80 (17), 79 (23), 78 (10), 77 (19), 70 (13), 69 (10).

^{1}H NMR (270 MHz, $CDCl_3$, TMS): δ = 0.55 (m_C, 1 H, 6a-H^1), 0.65 (m_C, 1 H, 6a-H^2), 1.10 (m_C, 1 H, 6-H), 1.25 (d, 3H, *J* = 6 Hz, 5-CH_3), 1.35 (m_C, 1 H, 1-H), 1.45 (m_C, 2 H, 7-H), 1.60–1.80 (m, 3 H, 2-H^1, 1-H, 2-H^2), 2.05 (dd, 1 H, *J* = 10 Hz, 10 Hz, 3-H^1), 2.1–2.25 (m, 1 H, 8a-H), 2.60 (m_C, 1 H, 5-H), 3.25 (m_C, 1 H, 3-H^2, 8-H^2), 7.25 (m_C, 3 H, ArH), 7.60 (m_C, 2 H, ArH).

^{13}C NMR (68 MHz, $CDCl_3$): δ = 9.0 (C-6a), 18.3 (CH_3), 20.2 (CH), 20.5 (C-2), 20.7 (CH), 31.2 (C-1), 45.9 (C-8), 52.9 (C-3), 56.9 (C-5), 66.9 (C-8a), 126.7, 128.8, 129.9, 133.1 (CAr).

$C_{16}H_{21}NSe$ (306.31) calc.: C 62.74, H 6.91. found: C 62.92, H 7.31

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