Stereoselective Multimodal Transformation of Planar Chiral 9-Membered Diallylic Amides

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1. General Experimental

All reactions were carried out in heat-gun-dried glassware under an argon atmosphere unless otherwise noted. Dry Et₂O, CH₂Cl₂ and CH₃CN were purchased from Kanto Chemical Co., Inc. and used without purification. ¹H NMR, ¹³C NMR, ¹⁹F NMR and ³¹P NMR spectra were recorded on a Varian Gemini-2000 (¹H, 300 MHz; ¹³C, 75 MHz), a Varian Mercury (¹H, 300 MHz; ¹³C, 75 MHz) or a JEOL Lambda 600 (¹⁹F, 565 MHz; ³¹P, 243 MHz) at ambient temperature using CDCl₃ as solvents. Chemical Shifts δ in ppm were referenced to the solvent residual peak as an internal standard CHCl₃ for ¹H NMR (δ 7.26), to the solvent signal as CDCl₃ for ¹³C NMR (δ 77.1), and to the standard resonances as external C₆F₆ for ¹⁹F NMR (δ -164.9) and external H₃PO₄ for ³¹P NMR (δ 0.00). The peak multiplicities were given as followed: s, singlet; d, doublet; q, quartet; m, multiplet; br, broad. Optical rotations were measured on a digital polarimeter (JASCO DIP-370). Infrared spectra were recorded on a Fourier transfer infrared spectrophotometer (Perkin Elmer SpectrumOne) as neat liquid on NaCl plates and as crystal used a diffuse reflector. Melting points (Mp) were measured on a Yanaco Micro Melting Point Apparatus. High performance liquid chromatography (HPLC) was performed on a SHIMADZU SPD-6A UV detector equipped with a SHIMADZU LC-9A or JASCO UV-2075 and CD-2095 detectors equipped with JASCO PU-2087 or PU-2089 using Kanto Mightysil Si 60 (5 μ m) (4.6 mm $\times$ 15 cm), (2.0 cm $\times$ 25 cm), Daicel CHIRALCEL OD-H column (4.6 mm $\times$ 25 cm), (2.0 cm $\times$ 25 cm), Daicel CHIRALPAK AD-H column (4.6 mm $\times$ 25 cm), or Daicel CHIRALPAK AS-H column (4.6 mm $\times$ 25 cm), (2.0 cm $\times$ 25 cm). Analytical thin-layer chromatography (TLC) was carried out on silica gel 60 F₂₅₄ (Merck 5715) plates and developed plates were visualized by UV (254 nm) and by heating on a hot plate after staining with a 4% solution of phosphomolybdic acid in ethanol or a 2.5% solution of *p*-anisaldehyde in ethanol. Column chromatography was performed using Kanto spherical silica gel 60N (63-210 μ m) or Fuji Silysia silica gel FL100D (neutral). X-ray crystallographic data was collected using a Rigaku Saturn CCD diffractometer with graphite monochromated Mo-K α radiation (λ = 0.7107 Å) at 123 K or a Rigaku-IP diffractometer with Cu-K α radiation (λ = 1.5418 Å) at 113 K. HRMS analyses were performed at the Analytical Center in IMCE, Kyushu University. Elemental analyses were performed by the Elemental Analysis Center, Faculty of Science, Kyushu University and by the Analytical Facility at the Research Laboratory of Resources Utilization, Tokyo Institute of Technology.

2. Detailed Reaction Procedures and Analytical Data

1) Epoxidation of cyclic amides **1a**

To a solution of $(S)\text{-1a}$ ($>98\%$ ee; 35.3 mg, 0.116 mmol) in dry CH_2Cl_2 (7 mL) at $0\text{ }^\circ\text{C}$ was added $m\text{-CPBA}$ (24.9 mg, 0.144 mmol). The reaction mixture was stirred at that temperature for 4 h. The reaction was quenched with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ and saturated aqueous NaHCO_3 . The phases were separated and the aqueous layer was extracted with CH_2Cl_2 . The combined organic phases were dried over Na_2SO_4 , filtered and the solvent was removed *in vacuo*. The residue was purified by silica gel chromatography (hexane/AcOEt = 20/1 to 2/1) to afford 27.7 mg of a mixture of mono-epoxides **2a** and **3a** (74%; **2a/3a** = 87/13 determined by ^1H NMR analysis) as a white solid and 9.7 mg (24%) of **4a** as a white solid. The mixture of **2a** and **3a** were separated by silica gel HPLC; column: Kanto Mightysil Si 60 ($5\text{ }\mu\text{m}$) ($2.0\text{ cm} \times 25\text{ cm}$), eluent: hexane/AcOEt = 4/1, flow rate: 7.0 mL/min , detection: UV 254 nm, temperature: rt. All of epoxides $(3R,4R)\text{-2a}$, $(7R,8S)\text{-3a}$ and $(3R,4R,7R,8S)\text{-4a}$ were determined as a single stereoisomer ($>98\%$ dr analyzed by ^1H NMR, $>98\%$ ee analyzed by chiral HPLC).

4,9-dimethyl-7-(*p*-toluenesulfonyl)-10-oxa-7-azabicyclo[7.1.0]dec-4-ene [(**3R,4R**)-**2a**]

^1H NMR (300 MHz, CDCl_3): δ 7.62 (d, $J = 8.3\text{ Hz}$, 2H), 7.28 (d, $J = 8.1\text{ Hz}$, 2H), 5.46 (dd, $J = 11.7, 4.7\text{ Hz}$, 1H), 4.17 (d, $J = 11.3\text{ Hz}$, 1H), 4.00 (dd, $J = 15.0, 4.7\text{ Hz}$, 1H), 3.26 (dd, $J = 15.0, 11.7\text{ Hz}$, 1H), 2.77 (dd, $J = 11.8, 2.7\text{ Hz}$, 1H), 2.41 (s, 3H), 2.41-2.31 (m, 1H), 2.11 (d, $J = 11.3\text{ Hz}$, 1H), 2.06-1.95 (m, 2H), 1.75 (s, 3H), 1.23 (s, 3H), 1.21-1.07 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3): δ 143.3, 135.9, 135.4, 129.7, 126.8, 124.4, 66.3, 57.5, 57.0, 45.7, 27.9, 25.5, 23.1, 21.6, 16.6; IR (neat, cm^{-1}): 2935, 1917, 1598, 1461, 1323, 1236, 1091, 812, 658, 550, 510; Mp: $142\text{ }^\circ\text{C}$; Analytical HPLC [column: CHIRALCEL OD-H ($4.6\text{ mm} \times 25\text{ cm}$), eluent: hexane/*i*-PrOH = 2/1, flow rate: 0.5 mL/min , detection: UV 254 nm, temperature: rt] $t_R = 14.9\text{ min}$ for (–)-(**3R,4R**)-isomer, 23.7 min for (+)-(**3S,4S**)-isomer; Optical rotation value: $[\alpha]_D^{28} -49.6$ ($c\text{ }1.03$, CHCl_3) for (**3R,4R**)-isomer ($>98\%$ ee); HRMS (EI, positive): m/z calcd for $\text{C}_{17}\text{H}_{23}\text{NO}_3\text{S}$ $[\text{M}]^+$: 321.1399, found: 321.1396; Anal. calcd for $\text{C}_{17}\text{H}_{23}\text{NO}_3\text{S}$: C, 63.52; H, 7.21; N, 4.36; S, 9.98. Found: C, 63.32; H, 7.07; N, 4.15; S, 9.86.

5,9-dimethyl-3-(*p*-toluenesulfonyl)-10-oxa-3-azabicyclo[7.1.0]dec-5-ene [(**7R,8S**)-**3a**]

^1H NMR (300 MHz, CDCl_3): δ 7.67 (d, $J = 8.1\text{ Hz}$, 2H), 7.31 (d, $J = 8.1\text{ Hz}$, 2H), 5.24 (dd, $J = 11.4, 3.6\text{ Hz}$, 1H), 4.33 (d, $J = 10.5\text{ Hz}$, 1H), 3.84 (dd, $J = 15.0, 2.1\text{ Hz}$, 1H), 2.96 (d, $J = 10.5\text{ Hz}$, 1H), 2.84 (dd, $J = 10.2, 2.1\text{ Hz}$, 1H), 2.43 (s, 3H), 2.41-2.29 (m, 1H), 2.28 (dd, $J = 15.0, 10.2\text{ Hz}$, 1H), 2.17-2.04 (m, 2H), 1.74 (s, 3H), 1.34 (s, 3H), 1.10-1.01 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3): δ 143.3, 135.8, 132.7, 129.8, 129.7, 127.0, 64.8, 61.9, 58.5, 45.5, 34.3, 25.4, 22.9, 21.7, 15.6; IR (neat, cm^{-1}): 2925, 2862, 1458, 1346, 1331, 1010, 850, 658, 548; Mp: $154\text{ }^\circ\text{C}$; Analytical HPLC [column: CHIRALCEL OD-H ($4.6\text{ mm} \times 25\text{ cm}$), eluent: hexane/*i*-PrOH = 2/1, flow rate: 0.5 mL/min , detection: UV 254 nm, temperature: rt] $t_R = 21.3\text{ min}$ for (–)-(**7S,8R**)-isomer, 38.0 min for (+)-(**7R,8S**)-isomer.

(+)-(7*R*,8*S*)-isomer; Optical rotation value: $[\alpha]_{\text{D}}^{27}$ 82.7 (*c* 0.28, EtOH) for (7*R*,8*S*)-isomer (>98% ee); HRMS (FAB, matrix: 3-nitrobenzyl alcohol, positive): *m/z* calcd for C₁₇H₂₄NO₃S [M+H]⁺: 322.1477, found: 322.1470; Anal. calcd for C₁₇H₂₃NO₃S: C, 63.52; H, 7.21; N, 4.36; S, 9.98. Found: C, 63.57; H, 7.35; N, 4.49; S, 9.90.

1,6-dimethyl-8-(*p*-toluenesulfonyl)-5,11-dioxa-8-azatricyclo[8.1.0.0^{4,6}]undecane [(3*R*,4*R*,7*R*,8*S*)-4a]

¹H NMR (300 MHz, CDCl₃): δ 7.66 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 4.27 (d, *J* = 11.4 Hz, 1H), 4.01 (dd, *J* = 15.3, 1.7 Hz, 1H), 3.11 (dd, *J* = 10.4, 1.7 Hz, 1H), 2.61 (dd, *J* = 10.2, 2.7 Hz, 1H), 2.49 (dd, *J* = 15.3, 10.4 Hz, 1H), 2.43 (s, 3H), 2.25-2.13 (m, 2H), 2.09 (d, *J* = 11.4 Hz, 1H), 1.50-1.37 (m, 2H), 1.44 (s, 3H), 1.37 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 143.8, 135.3, 129.9, 127.0, 65.3, 64.4, 61.8, 57.3, 57.0, 46.0, 30.9, 23.5, 22.8, 21.7, 15.8; IR (neat, cm⁻¹): 2927, 1462, 1349, 1335, 1164, 1079, 1021, 657, 571, 548; Mp: 215 °C; Analytical HPLC [column: CHIRALPAK AD-H (4.6 mm × 25 cm), eluent: hexane/*i*-PrOH = 1/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] *t_R* = 23.5 min for (+)-(3*S*,4*S*,7*S*,8*R*)-isomer, 32.9 min for (–)-(3*R*,4*R*,7*R*,8*S*)-isomer; Optical rotation value: $[\alpha]_{\text{D}}^{28}$ –39.8 (*c* 0.79, CHCl₃) for (3*R*,4*R*,7*R*,8*S*)-isomer (>98% ee); HRMS (FAB, matrix: 3-nitrobenzyl alcohol, positive): *m/z* calcd for C₁₇H₂₄NO₄S [M+H]⁺: 338.1426, found: 338.1430; Anal. calcd for C₁₇H₂₃NO₄S: C, 60.51; H, 6.87; N, 4.15; S, 9.50. Found: C, 60.31; H, 6.76; N, 3.99; S, 9.31.

Recrystallization from hexane/CH₂Cl₂/AcOEt afforded a single crystal that was suitable for X-ray analysis.

Figure S1. Molecular structure of (3*R*,4*R*,7*R*,8*S*)-4a (CCDC-817441) in the solid state. Thermal ellipsoids are drawn at the 50% probability level.

2) Epoxidation of cyclic amides **1b**

To a solution of **(S)-1b** (>98% ee; 50.0 mg, 0.180 mmol) in dry CH_2Cl_2 (10 mL) at $0\text{ }^\circ\text{C}$ was added *m*-CPBA (40.4 mg, 0.234 mmol). The reaction mixture was stirred at that temperature for 45 h. The reaction was quenched with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ and saturated aqueous NaHCO_3 . The phases were separated and the aqueous layer was extracted with CH_2Cl_2 . The combined organic phases were dried over Na_2SO_4 , filtered and the solvent was removed *in vacuo*. The residue was purified by silica gel chromatography (hexane/AcOEt = 1/0 to 2/1) to afford 3.0 mg of the recovered starting material **(S)-1b** (6%; >98% ee analyzed by HPLC), 44.0 mg of a mixture of mono-epoxides **2b** and **3b** (83%; **2b/3b** = 86/14 determined by ^1H NMR analysis) as a white solid and 6.1 mg (11%) of **4b** as a white solid. The mixture of **2b** and **3b** were separated by silica gel HPLC; column: Kanto Mightysil Si 60 (5 μm) (2.0 cm $\times$ 25 cm), eluent: hexane/AcOEt = 4/1, flow rate: 7.0 mL/min, detection: UV 254 nm, temperature: rt. All of epoxides **(3R,4R)-2b**, **(7R,8S)-3b** and **(3R,4R,7R,8S)-4b** were determined as a single stereoisomer (>98% dr analyzed by ^1H NMR, >98% ee analyzed by chiral HPLC).

7-(*p*-toluenesulfonyl)-10-oxa-7-azabicyclo[7.1.0]dec-4-ene [(**3R,4R**)-**2b**]

^1H NMR (300 MHz, CDCl_3): δ 7.66 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 5.72 (ddd, J = 11.4, 11.1, 4.5 Hz, 1H), 5.65-5.55 (m, 1H), 4.34 (dd, J = 11.0, 2.7 Hz, 1H), 4.05 (dd, J = 14.7, 4.5 Hz, 1H), 3.33 (dd, J = 14.7, 11.4 Hz, 1H), 2.98 (ddd, J = 10.1, 2.7, 2.4 Hz, 1H), 2.59 (ddd, J = 10.2, 2.4, 2.1 Hz, 1H), 2.43 (s, 3H), 2.24-2.16 (m, 3H), 2.16 (dd, J = 11.0, 10.1 Hz, 1H), 0.94-0.77 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3): δ 143.5, 135.5, 130.0, 129.8, 128.6, 127.1, 60.3, 55.2, 51.7, 44.6, 27.5, 21.9, 21.7; IR (neat, cm^{-1}): 2942, 2869, 1932, 1656, 1596, 1481, 1449, 1397, 1263, 1237, 1211, 1048, 1026, 984, 708; Mp: $132\text{ }^\circ\text{C}$; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm $\times$ 25 cm), eluent: hexane/*i*-PrOH = 2/1, flow rate: 0.5 mL/min, detection: UV 236 nm, temperature: rt] t_R = 18.6 min for (–)-(**3R,4R**)- isomer, 22.7 min for (+)-(**3S,4S**)-isomer; Optical rotation value: $[\alpha]_D^{21}$ –53.3 (c 1.16, CHCl_3) for (**3R,4R**)-isomer (>98% ee); HRMS (EI, positive): m/z calcd for $\text{C}_{15}\text{H}_{19}\text{NO}_3\text{S}$ $[\text{M}]^+$: 293.1086, found: 293.1085; Anal. calcd for $\text{C}_{15}\text{H}_{19}\text{NO}_3\text{S}$: C, 61.41; H, 6.53; N, 4.77. Found: C, 61.33; H, 6.30; N, 4.77.

7-(*p*-toluenesulfonyl)-10-oxa-7-azabicyclo[7.1.0]dec-4-ene [(**7R,8S**)-**3b**]

^1H NMR (300 MHz, CDCl_3): δ 7.69 (d, J = 7.8 Hz, 2H), 7.32 (d, J = 7.8 Hz, 2H), 5.46 (ddd, J = 15.6, 10.2, 4.8 Hz, 1H), 5.30 (ddd, J = 15.6, 10.5, 4.2 Hz, 1H), 4.51 (dd, J = 10.8, 4.2 Hz, 1H), 3.91 (dd, J = 14.7, 2.1 Hz, 1H), 3.05 (ddd, J = 9.9, 3.9, 2.1 Hz, 1H), 2.99 (dd, J = 10.8, 10.5 Hz, 1H), 2.96-2.90 (m, 1H), 2.44 (s, 3H), 2.42-2.24 (m, 2H), 2.18 (dd, J = 14.7, 9.9 Hz, 1H), 2.12-1.99 (m, 1H), 0.89-0.76 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3): δ 143.5, 137.8, 135.7, 129.8, 127.1, 125.3, 57.8, 56.7, 52.1, 43.8, 28.2, 27.9, 21.7; IR (neat, cm^{-1}): 2923, 2852, 1596, 1453, 1337, 1165, 1098, 983, 916, 751, 658, 584, 548; Mp: $123\text{ }^\circ\text{C}$; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm $\times$ 25 cm), eluent: hexane/*i*-PrOH = 2/1, flow rate: 0.5 mL/min, detection: UV 236 nm, temperature: rt] t_R

= 21.9 min for (–)-(7*S*,8*R*)- isomer, 34.5 min for (+)-(7*R*,8*S*)-isomer; Optical rotation value: $[\alpha]_{\text{D}}^{20}$ 109.4 (*c* 0.49, CHCl₃) for (7*R*,8*S*)-isomer (>98% ee); HRMS (FAB, matrix: 3-nitrobenzyl alcohol, positive): *m/z* calcd for C₁₅H₂₀NO₃S [M+H]⁺: 294.1164, found: 294.1165; Anal. calcd for C₁₅H₁₉NO₃S: C, 61.41; H, 6.53; N, 4.77. Found: C, 61.74; H, 6.64; N, 4.52.

8-(*p*-toluenesulfonyl)-5,11-dioxa-8-azatricyclo[8.1.0.0^{4,6}]undecane [(3*R*,4*R*,7*R*,8*S*)-4b]

¹H NMR (300 MHz, CDCl₃): δ 7.68 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.3 Hz, 2H), 4.43 (dd, *J* = 11.1, 2.6 Hz, 1H), 4.10 (d, *J* = 15.0 Hz, 1H), 3.23–3.18 (m, 1H), 3.05–2.99 (m, 1H), 2.83 (ddd, *J* = 9.9, 2.6, 2.4 Hz, 1H), 2.51–2.39 (m, 2H), 2.47 (dd, *J* = 15.0, 10.0 Hz, 1H), 2.44 (s, 3H), 2.32–2.25 (m, 1H), 2.10 (dd, *J* = 11.1, 9.9 Hz, 1H), 1.26–1.10 (m, 2H); ¹³C NMR (75 MHz, CDCl₃): δ 143.9, 135.1, 130.0, 127.1, 60.0, 57.1, 57.0, 55.0, 51.2, 44.3, 26.5, 24.4, 21.7; IR (neat, cm^{−1}): 2931, 2870, 1597, 1492, 1474, 1450, 1301, 1264, 1239, 1215, 1181, 1160, 1073, 992, 911, 811, 600; Mp: 169 °C; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm × 25 cm), eluent: hexane/*i*-PrOH = 6/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] *t*_R = 43.5 min for (+)-(3*S*,4*S*,7*S*,8*R*)-isomer, 45.6 min for (–)-(3*R*,4*R*,7*R*,8*S*)-isomer; Optical rotation value: $[\alpha]_{\text{D}}^{27}$ −21.6 (*c* 0.37, CHCl₃) for (3*R*,4*R*,7*R*,8*S*)- isomer (>98% ee); HRMS (EI, positive): *m/z* calcd for C₁₅H₁₉NO₄S [M]⁺: 309.1035, found: 309.1036; Anal. calcd for C₁₅H₁₉NO₄S: C, 58.23; H, 6.19; N, 4.53. Found: C, 57.97; H, 5.98; N, 4.47.

3) Cyclopropanation reaction of cyclic amide 1a

To a solution of Et₂Zn (1.10 M solution in hexane, 0.595 mL, 0.655 mmol) in dry Et₂O (10 mL) at room temperature was slowly added diiodomethane (53.7 μL, 0.668 mmol). After stirring at that temperature for 15 min, (R)-1a (>98% ee; 40.0 mg, 0.131 mmol) was added to the mixture. The mixture was stirred at room temperature for 24 h. The reaction was quenched with saturated aqueous NH₄Cl. The phases were separated and the aqueous layer was extracted with AcOEt. The combined organic phases were dried over Na₂SO₄, filtered and the solvent was removed *in vacuo*. The residue was purified by silica gel chromatography (hexane/AcOEt = 1/0 to 12/1) to afford 37.0 mg of a mixture of 5a, 6a and 7a (87%; 5a/6a/7a = 79/2/19 determined by ¹H NMR analysis) as a white solid. Di-cyclopropanated product 7a was separated from a mixture of mono-cyclopropanated products 5a and 6a by silica gel HPLC; column: Kanto Mightysil Si 60 (5 μm) (2.0 cm × 25 cm), eluent: hexane/AcOEt = 9/1, flow rate: 7.0 mL/min, detection: UV 254 nm, temperature: rt. Then the mixture of 5a and 6a were separated by chiral HPLC; column: Daicel CHIRALCEL OD-H column (2.0 cm × 25 cm), eluent: hexane/*i*-PrOH = 4/1, flow rate: 5.0 mL/min, detection: UV 254 nm, temperature: rt. All of cyclopropanated products (3*R*,4*R*)-5a, (7*R*,8*S*)-6a and (3*R*,4*R*,7*R*,8*S*)-7a were determined as a single stereoisomer (>98% dr analyzed by ¹H NMR, >98% ee analyzed by chiral HPLC).

4,9-dimethyl-7-(*p*-toluenesulfonyl)-7-azabicyclo[7.1.0]dec-4-ene [(3*R*,4*R*)-5a]

¹H NMR (300 MHz, CDCl₃): δ 7.63 (d, *J* = 7.8 Hz, 2H), 7.27 (d, *J* = 7.8 Hz, 2H), 5.49 (dd, *J* = 11.6, 4.4 Hz, 1H), 4.10 (d, *J* = 11.7 Hz, 1H), 3.96 (dd, *J* = 14.3, 4.4 Hz, 1H), 3.44 (dd, *J* = 14.3, 11.6 Hz, 1H), 2.41 (s, 3H), 2.41-2.31 (m, 1H), 1.97-1.81 (m, 3H), 1.72 (s, 3H), 0.97 (s, 3H), 0.92-0.76 (m, 1H), 0.59-0.49 (m, 1H), 0.36 (dd, *J* = 9.3, 4.8 Hz, 1H), -0.01 (dd, *J* = 6.3, 4.8 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 142.7, 136.7, 135.6, 129.6, 126.9, 123.9, 59.3, 45.6, 32.8, 28.6, 25.4, 23.3, 21.6, 17.9, 17.5, 13.8; IR (neat, cm⁻¹): 2922, 1457, 1317, 1152, 1091, 1050, 995, 946, 894, 844, 812, 752, 655; Mp: 105 °C; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm × 25 cm), eluent: hexane/*i*-PrOH = 4/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] *t*_R = 12.0 min for (-)-(3*S*,4*S*)-isomer, 22.7 min for (+)-(3*R*,4*R*)-isomer; Optical rotation value: [α]_D²³ 55.8 (*c* 1.14, CHCl₃) for (3*R*,4*R*)-isomer (>98% ee); HRMS (EI, positive): *m/z* calcd for C₁₈H₂₅NO₂S [M]⁺: 319.1606, found: 319.1612; Anal. calcd for C₁₈H₂₅NO₂S: C, 67.67; H, 7.89; N, 4.38. Found: C, 67.58; H, 7.85; N, 4.34.

5,9-dimethyl-3-(*p*-toluenesulfonyl)-3-azabicyclo[7.1.0]dec-5-ene [(7*R*,8*S*)-6a]

¹H NMR (300 MHz, CDCl₃): δ 7.66 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 5.15 (dd, *J* = 11.4, 3.0 Hz, 1H), 4.35 (d, *J* = 10.4 Hz, 1H), 3.76 (d, *J* = 14.9 Hz, 1H), 2.96 (d, *J* = 10.4 Hz, 1H), 2.50-2.36 (m, 1H), 2.43 (s, 3H), 2.18 (dd, *J* = 14.9, 9.9 Hz, 1H), 2.04-1.98 (m, 2H), 1.81 (s, 3H), 1.04 (s, 3H), 0.93-0.71 (m, 2H), 0.45 (dd, *J* = 9.6, 4.5 Hz, 1H), -0.27 (dd, *J* = 6.6, 4.5 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 142.8, 136.7, 132.6, 129.6, 128.5, 126.9, 58.8, 46.9, 34.9, 28.3, 26.0, 25.0, 21.7, 20.4, 16.9, 16.0; IR (neat, cm⁻¹): 2931, 1452, 1327, 1156, 1087, 1024, 922, 881, 809, 756, 660, 592, 546; Mp: 104 °C; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm × 25 cm), eluent: hexane/*i*-PrOH = 4/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] *t*_R = 12.0 min for (-)-(7*S*,8*R*)-isomer, 35.2 min for (+)-(7*R*,8*S*)-isomer; Optical rotation value: [α]_D²⁴ 69.8 (*c* 0.16, CHCl₃) for (7*R*,8*S*)-isomer (>98% ee); HRMS (EI, positive): *m/z* calcd for C₁₈H₂₅NO₂S [M]⁺: 319.1606, found: 319.1614.

1,6-dimethyl-8-(*p*-toluenesulfonyl)-8-azatricyclo[8.1.0.0^{4,6}]undecane [(3*R*,4*R*,7*R*,8*S*)-7a]

¹H NMR (300 MHz, CDCl₃): δ 7.65 (d, *J* = 7.8 Hz, 2H), 7.27 (d, *J* = 7.8 Hz, 2H), 4.19 (d, *J* = 12.0 Hz, 1H), 3.85 (d, *J* = 15.3 Hz, 1H), 2.47 (dd, *J* = 15.3, 9.9 Hz, 1H), 2.41 (s, 3H), 2.08 (dd, *J* = 14.4, 5.7 Hz, 1H), 1.82 (dd, *J* = 14.1, 5.7 Hz, 1H), 1.76 (d, *J* = 12.0 Hz, 1H), 1.27-1.14 (m, 2H), 1.24 (s, 3H), 1.11-1.01 (m, 1H), 1.05 (s, 3H), 0.50 (dd, *J* = 9.8, 4.5 Hz, 1H), 0.39-0.28 (m, 2H), 0.09-0.03 (m, 1H), -0.16 (dd, *J* = 6.3, 4.5 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 142.7, 136.7, 129.6, 126.8, 60.1, 47.8, 37.0, 28.8, 28.5, 24.8, 24.5, 21.7, 21.5, 18.1, 17.8, 17.7, 13.3; IR (neat, cm⁻¹): 2909, 1456, 1341, 1329, 1302, 1157, 1088, 1037, 939, 810, 747, 657; Mp: 115 °C; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm × 25 cm), eluent: hexane/*i*-PrOH = 4/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] *t*_R = 11.2 min for (-)-f-(3*S*,4*S*,7*S*,8*R*)-isomer, 11.6 min for (+)-(3*R*,4*R*,7*R*,8*S*)-isomer; Optical rotation value: [α]_D²⁴ 18.1 (*c* 0.55, CHCl₃) for (3*R*,4*R*,7*R*,8*S*)-isomer (>98% ee); HRMS (FAB, matrix: 3-nitrobenzyl alcohol, positive): *m/z* calcd for C₁₉H₂₈NO₂S [M+H]⁺: 334.1841, found: 334.1843; Anal. calcd for C₁₉H₂₇NO₂S: C, 68.43; H, 8.16; N, 4.20. Found: C, 68.14; H, 8.05; N, 4.15.

4) Dichloro-cyclopropanation reaction of cyclic amide 1a

To a solution of *(R)*-**1a** ($>98\%$ ee; 77.8 mg, 0.255 mmol) in dry CHCl_3 (6 mL) at $0\text{ }^\circ\text{C}$ was added NaOH (1.02 g, 25.5 mmol) dissolved in water (1.5 mL) and tetrabutylammonium chloride (14.2 mg, 0.0509 mmol). The mixture was stirred vigorously at that temperature for 20 h. The reaction was quenched by diluting with water. The phases were separated and the aqueous layer was extracted with CH_2Cl_2 . The combined organic phases were dried over Na_2SO_4 , filtered and the solvent was removed *in vacuo*. The residue was purified by silica gel chromatography (hexane/ CH_2Cl_2 = 10/1 to 1/1) to afford 57.1 mg of a mixture of mono-cyclopropanated products **5b** and **6b** (58%; **5b**/**6b** = 76/24 determined by ^1H NMR analysis) as a white solid and 43.3 mg (36%) of **7b** as a white solid. The mixture of **5b** and **6b** were separated by chiral HPLC; column: Daicel CHIRALPAK AS-H column (2.0 cm $\times$ 25 cm), eluent: hexane/*i*-PrOH = 2/1, flow rate: 3.0 mL/min, detection: UV 254 nm, temperature: rt. All of cyclopropanated products (*(3R,4S)*-**5b**, (*(7S,8S)*-**6b** and (*(3R,4S,7S,8S)*-**7b** were determined as a single stereoisomer ($>98\%$ dr analyzed by ^1H NMR, $>98\%$ ee analyzed by chiral HPLC).

10,10-dichloro-4,9-dimethyl-7-(*p*-toluenesulfonyl)-7-azabicyclo[7.1.0]dec-4-ene [(*(3R,4S)*)-**5b**]

^1H NMR (300 MHz, CDCl_3): δ 7.65 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 5.51 (dd, J = 10.8, 3.9 Hz, 1H), 4.16 (br, 1H), 3.96 (br, 1H), 3.23 (br, 1H), 2.50-2.30 (m, 2H), 2.43 (s, 3H), 2.05-1.98 (m, 2H), 1.74 (s, 3H), 1.40-1.32 (m, 1H), 1.16 (s, 3H), 1.08-0.97 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3): δ 143.2, 136.3, 135.1, 129.8, 126.9, 123.9, 67.3, 56.5, 45.5, 42.5, 30.8, 29.9, 25.2, 21.7, 20.2, 15.0; IR (neat, cm^{-1}): 2928, 1598, 1457, 1334, 1160, 1092, 1045, 934, 907, 862, 846, 798, 765, 661; Mp: $106\text{ }^\circ\text{C}$; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm $\times$ 25 cm), eluent: hexane/EtOH = 10/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] t_R = 14.2 min for (–)-(*(3S,4R)*)-isomer, 31.9 min for (+)-(*(3R,4S)*)-isomer; Optical rotation value: $[\alpha]_D^{24}$ 94.1 (c 1.40, CHCl_3) for (*(3R,4S)*)-isomer ($>98\%$ ee); HRMS (EI, positive): m/z calcd for $\text{C}_{18}\text{H}_{23}\text{Cl}_2\text{NO}_2\text{S}$ $[\text{M}]^+$: 387.0827, found: 387.0819; Anal. calcd for $\text{C}_{18}\text{H}_{23}\text{Cl}_2\text{NO}_2\text{S} \cdot 1/8(\text{C}_6\text{H}_{14})$: C, 56.42; H, 6.25; N, 3.51. Found: C, 56.47; H, 6.22; N, 3.50.

10,10-dichloro-5,9-dimethyl-3-(*p*-toluenesulfonyl)-3-azabicyclo[7.1.0]dec-5-ene [(*(7S,8S)*)-**6b**]

^1H NMR (300 MHz, CDCl_3): δ 7.69 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 5.15 (dd, J = 11.7, 3.6 Hz, 1H), 4.33 (d, J = 10.5 Hz, 1H), 3.86 (d, J = 15.2 Hz, 1H), 2.95 (d, J = 10.5 Hz, 1H), 2.57-2.44 (m, 1H), 2.44 (s, 3H), 2.31 (dd, J = 15.2, 9.3 Hz, 1H), 2.22-2.14 (m, 1H), 1.93-1.81 (m, 1H), 1.77 (s, 3H), 2.59-1.39 (m, 2H), 1.37 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 143.2, 136.3, 131.7, 129.8, 129.1, 126.9, 69.5, 58.9, 44.7, 41.0, 31.9, 30.3, 25.9, 23.5, 21.7, 15.9; IR (neat, cm^{-1}): 2932, 1456, 1347, 1161, 1096, 1009, 921, 886, 840, 756, 662, 592; Mp: $167\text{ }^\circ\text{C}$; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm $\times$ 25 cm), eluent: hexane/EtOH = 10/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] t_R = 12.6 min for (+)-(*(7S,8S)*)-isomer, 34.2 min for

(-)-(7*R*,8*R*)-isomer; Optical rotation value: $[\alpha]_D^{24}$ 130.6 (*c* 0.24, CHCl₃) for (7*S*,8*S*)-isomer (>98% ee); HRMS (FAB, matrix: 3-nitrobenzyl alcohol, positive): *m/z* calcd for C₁₈H₂₄Cl₂NO₂S [M+H]⁺: 388.0905, found: 388.0901; Anal. calcd for C₁₈H₂₃Cl₂NO₂S: C, 55.67; H, 5.97; N, 3.61. Found: C, 55.66; H, 5.98; N, 3.57.

5,5,11,11-tetrachloro-1,6-dimethyl-8-(*p*-toluenesulfonyl)-8-azatricyclo[8.1.0.0^{4,6}]undecane [(3*R*,4*S*,7*S*,8*S*)-7b]

¹H NMR (300 MHz, CDCl₃): δ 7.70 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.3 Hz, 2H), 4.26 (d, *J* = 12.5 Hz, 1H), 3.95 (d, *J* = 15.8 Hz, 1H), 2.44 (s, 3H), 2.40 (d, *J* = 12.5 Hz, 1H), 2.38 (dd, *J* = 15.8, 9.3 Hz, 1H), 2.19-2.12 (m, 1H), 2.08-2.01 (m, 1H), 1.85 (dd, *J* = 9.3, 1.2 Hz, 1H), 1.77 (d, *J* = 13.5 Hz, 1H), 1.48-1.37 (m, 1H), 1.37 (s, 6H), 1.17 (dd, *J* = 11.1, 1.8 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 143.7, 135.8, 130.0, 126.9, 69.0, 66.3, 57.3, 45.8, 41.5, 40.5, 32.1, 30.7, 30.1, 22.9, 21.72, 21.69, 14.5; IR (neat, cm⁻¹): 2989, 2963, 2921, 2862, 1599, 1454, 1321, 1155, 930, 766, 666, 551, 531; Mp: 166 °C; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm × 25 cm), eluent: hexane/EtOH = 30/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] *t_R* = 15.5 min for (-)-(3*S*,4*R*,7*R*,8*R*)-isomer, 16.8 min for (+)-(3*R*,4*S*,7*S*,8*S*)-isomer; Optical rotation value: $[\alpha]_D^{28}$ 6.27 (*c* 1.38, CHCl₃) for (3*R*,4*S*,7*S*,8*S*)-isomer (>98% ee); HRMS (FAB, matrix: 3-nitrobenzyl alcohol, positive): *m/z* calcd for C₁₉H₂₄Cl₄NO₂S [M+H]⁺: 472.0252, found: 472.0253; Anal. calcd for C₁₉H₂₃Cl₄NO₂S: C, 48.42; H, 4.92; N, 2.97. Found: C, 48.35; H, 5.02; N, 2.99.

Recrystallization from hexane/CH₂Cl₂ afforded a single crystal that was suitable for X-ray analysis.

Figure S2. Molecular structure of *rac*-7b (CCDC-817442) in the solid state. Thermal ellipsoids are drawn at the 50% probability level.

5) Cyclobutanation reaction of cyclic amide **1a**

To a solution of (*S*)-**1a** ($>98\%$ ee; 31.9 mg, 0.104 mmol) in dry CH_2Cl_2 (7 mL) at 0°C was added, successively, ethyldiisopropylamine (54.6 μL , 0.312 mmol), methoxyacetyl chloride (19.1 μL , 0.209 mmol) and $\text{BF}_3\cdot\text{OEt}_2$ (26.4 μL , 0.209 mmol). The reaction mixture was allowed to warm up to room temperature and was stirred for 3 days. The reaction was quenched with saturated aqueous NaHCO_3 . The phases were separated and the aqueous layer was extracted with CH_2Cl_2 . The combined organic phases were dried over Na_2SO_4 , filtered and the solvent was removed *in vacuo*. The residue was purified by silica gel chromatography (hexane/ AcOEt = 30/1 to 6/1) to afford 32.0 mg of (*3S,4R*)-**8** (81%; $>98\%$ dr analyzed by ^1H NMR, $>98\%$ ee analyzed by chiral HPLC) as a white solid and 6.1 mg of the recovered starting material (*S*)-**1a** (19%; $>98\%$ ee analyzed by HPLC).

10-methoxy-4,9-dimethyl-7-(*p*-toluenesulfonyl)-7-azabicyclo[7.2.0]undec-4-en-11-one [(*3S,4R*)-**8**]

^1H NMR (300 MHz, CDCl_3): δ 7.71 (d, J = 8.3 Hz, 1H), 7.33 (d, J = 8.3 Hz, 1H), 5.53 (dd, J = 8.6, 8.0 Hz, 1H), 4.54 (brs, 1H), 3.77 (dd, J = 13.8, 8.6 Hz, 1H), 3.73 (d, J = 14.7 Hz, 1H), 3.54 (s, 3H), 3.37 (dd, J = 13.8, 8.0 Hz, 1H), 3.13 (d, J = 14.7 Hz, 1H), 2.95 (d, J = 11.7 Hz, 1H), 2.44 (s, 3H), 2.12–1.99 (m, 2H), 1.91–1.82 (m, 1H), 1.73 (s, 3H), 1.48–1.37 (m, 1H), 0.89 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 205.4, 143.5, 141.3, 135.8, 129.8, 127.1, 121.7, 89.8, 59.5, 59.2, 56.7, 48.6, 38.3, 29.8, 23.6, 21.7, 18.6, 14.0; IR (reflection, cm^{-1}): 2940, 1781, 1597, 1452, 1334, 1221, 1156, 1040, 811, 760, 552; Mp: 132°C ; Analytical HPLC [column: CHIRALPAK AD-H (4.6 mm $\times$ 25 cm), eluent: hexane/*i*-PrOH = 4/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] t_R = 33.4 min for (+)-(*3R,4S*)-isomer, 34.4 min for (–)-(*3S,4R*)-isomer; Optical rotation value: $[\alpha]_D^{29}$ –35.1 (c 0.76, CHCl_3) for (*3S,4R*)-isomer ($>98\%$ ee); HRMS (FAB, matrix: 3-nitrobenzyl alcohol, positive): m/z calcd for $\text{C}_{20}\text{H}_{28}\text{NO}_4\text{S}$ $[\text{M}+\text{H}]^+$: 378.1739, found: 378.1732; Anal. calcd for $\text{C}_{20}\text{H}_{27}\text{NO}_4\text{S}$: C, 63.63; H, 7.21; N, 3.71. Found: C, 63.53; H, 7.14; N, 3.67.

Recrystallization from hexane/ CH_2Cl_2 afforded a single crystal that was suitable for X-ray analysis.

Figure S3. Molecular structure of *rac*-**8** (CCDC-817443) in the solid state. Thermal ellipsoids are drawn at the 50% probability level.

6) Transannular reaction of epoxide 2a

To a solution of (3R,4R)-**2a** ($>98\%$ dr, $>98\%$ ee; 53.8 mg, 0.167 mmol) in dry Et_2O (10 mL) at $-78\text{ }^\circ\text{C}$ was added $\text{BF}_3 \cdot \text{OEt}_2$ (63.3 μL , 0.502 mmol). The reaction mixture was allowed to warm up to $0\text{ }^\circ\text{C}$ over a period of 1 h and was stirred for 2 h. The reaction was quenched with saturated aqueous NaHCO_3 . The phases were separated and the aqueous layer was extracted with Et_2O . The combined organic phases were washed with brine, dried over Na_2SO_4 , filtered and the solvent was removed *in vacuo*. The residue was purified by silica gel chromatography (hexane/AcOEt = 10/1 to 2/1) to afford 48.3 mg of a mixture of **9a** and **9b** (90%; **9a**/**9b** = 81/19 determined by ^1H NMR analysis) as a white solid and 2.1 mg (4%) of **9c** as a white solid. The mixture of **9a** and **9b** were separated by silica gel HPLC; column: Kanto Mightysil Si 60 (5 μm) (2.0 cm $\times$ 25 cm), eluent: hexane/AcOEt = 2/1, flow rate: 7.0 mL/min, detection: UV 254 nm, temperature: rt. All of transannular products **9a**, **9b** and **9c** were determined as a single stereoisomer ($>98\%$ dr analyzed by ^1H NMR, $>98\%$ ee analyzed by chiral HPLC).

3a,7-dimethyl-2-(*p*-toluenesulfonyl)-2,3,3a,4,5,7a-hexahydro-1*H*-isoindol-4-ol (**9a**)

^1H NMR (300 MHz, CDCl_3): δ 7.72 (d, $J = 8.1$ Hz, 2H), 7.33 (d, $J = 8.1$ Hz, 2H), 5.24 (d, $J = 5.1$ Hz, 1H), 3.71 (d, $J = 10.2$ Hz, 1H), 3.63 (dd, $J = 9.6, 9.3$ Hz, 1H), 3.41 (dd, $J = 9.9, 6.0$ Hz, 1H), 2.91 (dd, $J = 9.6, 9.4$ Hz, 1H), 2.86 (d, $J = 10.2$ Hz, 1H), 2.44 (s, 3H), 2.24 (dd, $J = 9.4, 9.3$ Hz, 1H), 2.21–2.12 (m, 1H), 2.03–1.94 (m, 1H), 1.92 (s, 1H), 1.60 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 143.4, 133.7, 132.1, 129.6, 127.4, 119.7, 67.2, 56.7, 52.7, 51.0, 44.7, 31.3, 22.8, 21.7, 16.2; IR (neat, cm^{-1}): 3518, 2965, 2921, 2879, 1598, 1441, 1339, 1159, 1093, 1056, 813, 686, 663; Mp: $104\text{ }^\circ\text{C}$; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm $\times$ 25 cm), eluent: hexane/*i*-PrOH = 15/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] $t_R = 27.2$ min for (–)-isomer, 32.3 min for (+)-isomer; Optical rotation value: $[\alpha]_D^{27} -20.1$ (c 0.67, CHCl_3) for (–)-isomer ($>98\%$ ee); HRMS (EI, positive): m/z calcd for $\text{C}_{17}\text{H}_{23}\text{NO}_3\text{S}$ $[\text{M}]^+$: 321.1399, found: 321.1389; Anal. calcd for $\text{C}_{17}\text{H}_{23}\text{NO}_3\text{S} \cdot 1/5(\text{C}_6\text{H}_{14})$: C, 64.55; H, 7.68; N, 4.14. Found: C, 65.54; H, 7.65; N, 4.09.

3a-methyl-7-methylene-2-(*p*-toluenesulfonyl)-octahydroisoindol-4-ol (**9b**)

^1H NMR (300 MHz, CDCl_3): δ 7.73 (d, $J = 8.0$ Hz, 2H), 7.34 (d, $J = 8.0$ Hz, 2H), 4.81 (s, 1H), 4.73 (s, 1H), 3.76 (d, $J = 9.8$ Hz, 1H), 3.48 (dd, $J = 12.0, 4.2$ Hz, 1H), 3.34 (dd, $J = 10.2, 9.9$ Hz, 1H), 3.26 (dd, $J = 10.7, 10.2$ Hz, 1H), 2.77 (d, $J = 9.8$ Hz, 1H), 2.47 (dd, $J = 10.7, 9.9$ Hz, 1H), 2.45 (s, 3H), 2.22–2.17 (m, 2H), 1.76–1.69 (m, 1H), 1.67 (s, 1H), 1.54–1.39 (m, 1H), 0.90 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 143.4, 141.9, 134.3, 129.7, 127.3, 113.9, 69.2, 57.6, 53.7, 50.1, 47.2, 31.4, 29.5, 21.8, 15.2; IR (neat, cm^{-1}): 3517, 2936, 1651, 1598, 1444, 1338, 1156, 1094, 1066, 709, 663; Mp: $115\text{ }^\circ\text{C}$; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm $\times$ 25 cm), eluent: hexane/*i*-PrOH = 15/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] $t_R = 35.8$ min for (+)-isomer, 43.0 min for (–)-isomer; Optical rotation value: $[\alpha]_D^{24} 24.4$ (c 0.52, CHCl_3) for (+)-isomer ($>98\%$ ee); HRMS (EI, positive): m/z calcd for $\text{C}_{17}\text{H}_{23}\text{NO}_3\text{S}$ $[\text{M}]^+$: 321.1399, found: 321.1401; Anal. calcd

for C₁₇H₂₃NO₃S: C, 63.52; H, 7.21; N, 4.36. Found: C, 63.38; H, 7.20; N, 4.27.

3a,7-dimethyl-2-(*p*-toluenesulfonyl)-2,3,3a,4,5,6-hexahydro-1*H*-isoindol-4-ol (9c)

¹H NMR (300 MHz, CDCl₃): δ 7.72 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 3.99 (d, *J* = 13.2 Hz, 1H), 3.73 (d, *J* = 13.2 Hz, 1H), 3.57 (d, *J* = 8.9 Hz, 1H), 3.47 (dd, *J* = 10.8, 5.1 Hz, 1H), 2.75 (d, *J* = 8.9 Hz, 1H), 2.44 (s, 3H), 2.10-2.01 (m, 2H), 1.75-1.64 (m, 2H), 1.49 (s, 3H), 0.98 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 143.3, 133.7, 132.0, 129.6, 127.6, 125.3, 74.1, 60.9, 49.1, 45.7, 30.9, 27.7, 21.8, 19.1, 18.0; IR (neat, cm⁻¹): 3513, 2936, 1725, 1598, 1465, 1342, 1159, 1094, 1047, 814, 709, 667; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm × 25 cm), eluent: hexane/*i*-PrOH = 15/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] *t*_R = 50.4 min, 54.5 min; HRMS (EI, positive): *m/z* calcd for C₁₇H₂₃NO₃S [M]⁺: 321.1399, found: 321.1403.

7) Transannular reaction of cyclobutanation product 8

To a solution of (3*S*,4*R*)-**8** (>98% dr, >98% ee; 8.5 mg, 0.0225 mmol) in dry CH₂Cl₂ (5 mL) at 0 °C was added BF₃·OEt₂ (28.4 μL, 0.225 mmol). The reaction mixture was stirred at that temperature for 24 h. The reaction was quenched with saturated aqueous NaHCO₃. The phases were separated and the aqueous layer was extracted with CH₂Cl₂. The combined organic phases were dried over Na₂SO₄, filtered and the solvent was removed *in vacuo*. The residue was purified by silica gel chromatography (hexane/AcOEt = 10/1 to 2/1) to afford 4.4 mg (52%) of **10a** as a white solid and 1.5 mg (18%) of **10c** as a colorless oil. Both transannular products **10a** and **10c** were determined as a single stereoisomer (>98% dr analyzed by ¹H NMR, >98% ee analyzed by chiral HPLC).

1-[3a,7-dimethyl-2-(*p*-toluenesulfonyl)-2,3,3a,4,5,7a-hexahydro-1*H*-isoindol-4-yl]-2-methoxyethanone (10a)

¹H NMR (300 MHz, CDCl₃): δ 7.70 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.3 Hz, 2H), 5.40-5.35 (m, 1H), 3.98 (s, 2H), 3.59 (dd, *J* = 9.4, 9.2 Hz, 1H), 3.43 (d, *J* = 10.5 Hz, 1H), 3.39 (s, 3H), 3.09 (dd, *J* = 9.5, 9.4 Hz, 1H), 2.85 (d, *J* = 10.5 Hz, 1H), 2.65 (dd, *J* = 9.9, 6.6 Hz, 1H), 2.45 (s, 3H), 2.18-2.13 (m, 2H), 2.03 (dd, *J* = 9.5, 9.2 Hz, 1H), 1.62 (s, 3H), 1.04 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 209.1, 143.5, 133.8, 132.2, 129.7, 127.5, 120.0, 78.2, 59.3, 58.0, 51.9, 51.1, 43.5, 41.7, 25.8, 22.9, 21.7, 18.7; IR (neat, cm⁻¹): 2926, 1726, 1598, 1449, 1344, 1160, 1093, 1055, 814, 665; Mp: 82 °C; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm × 25 cm), eluent: hexane/*i*-PrOH = 10/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] *t*_R = 33.9 min for (–)-isomer, 36.1 min for (+)-isomer; Optical rotation value: [α]_D²⁶ 5.31 (*c* 0.31, CHCl₃) for (+)-isomer (>98% ee); HRMS (FAB, matrix: 3-nitrobenzyl alcohol, positive): *m/z* calcd for C₂₀H₂₈NO₄S [M+H]⁺: 378.1739, found: 378.1733; Anal. calcd for C₂₀H₂₇NO₄S: C, 63.63; H, 7.21; N, 3.71; S, 8.49. Found: C, 63.38; H, 7.10; N, 3.64; S, 8.34.

Recrystallization from hexane/CH₂Cl₂ afforded a single crystal that was suitable for X-ray analysis.

Figure S4. Molecular structure of (–)-**10a** (CCDC-817444) in the solid state. Thermal ellipsoids are drawn at the 50% probability level.

1-[3a,7-dimethyl-2-(*p*-toluenesulfonyl)-2,3,3a,4,5,6-hexahydro-1*H*-isoindol-4-yl]-2-methoxyethanone (10c**)**

^1H NMR (300 MHz, CDCl_3): δ 7.73 (d, $J = 8.1$ Hz, 2H), 7.33 (d, $J = 8.1$ Hz, 2H), 4.02 (d, $J = 17.1$ Hz, 1H), 3.96 (d, $J = 17.1$ Hz, 1H), 3.93 (d, $J = 13.2$ Hz, 1H), 3.78 (d, $J = 13.2$ Hz, 1H), 3.55 (d, $J = 9.0$ Hz, 1H), 3.41 (s, 3H), 2.90 (d, $J = 9.0$ Hz, 1H), 2.47–2.41 (m, 1H), 2.44 (s, 3H), 2.09–1.71 (m, 4H), 1.51 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 208.8, 143.4, 133.8, 132.8, 129.7, 127.5, 125.5, 77.7, 60.8, 59.3, 50.4, 48.2, 42.7, 30.1, 21.7, 20.5, 20.2, 19.3; IR (neat, cm^{-1}): 2921, 1720, 1598, 1450, 1343, 1159, 1094, 1058, 814, 709, 663; Analytical HPLC [column: CHIRALPAK AS-H (4.6 mm $\times$ 25 cm), eluent: hexane/ *i*-PrOH = 2/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] $t_R = 36.2$ min for (+)-isomer, 56.4 min for (–)-isomer; Optical rotation value: $[\alpha]_D^{23} -5.69$ (c 0.22, CHCl_3) for (–)-isomer (>98% ee); HRMS (EI, positive): m/z calcd for $\text{C}_{20}\text{H}_{27}\text{NO}_4\text{S}$ $[\text{M}]^+$: 377.1661, found: 377.1664; Anal. calcd for $\text{C}_{20}\text{H}_{27}\text{NO}_4\text{S}$: C, 63.63; H, 7.21; N, 3.71. Found: C, 63.94; H, 7.07; N, 3.45.

8) Transannular reaction of epoxide **3a**

To a solution of (7*R*,8*S*)-**3a** (>98% dr, >98% ee; 19.9 mg, 0.0619 mmol) in dry CH_2Cl_2 (10 mL) at -78°C was added $\text{BF}_3 \cdot \text{OEt}_2$ (11.7 μL , 0.0929 mmol). The reaction mixture was allowed to warm up to room temperature over a period of 1 h and was stirred for 1 h. The reaction was quenched with saturated aqueous NaHCO_3 . The phases were separated and the aqueous layer was extracted with CH_2Cl_2 . The combined organic phases were dried over Na_2SO_4 , filtered and the solvent was removed *in vacuo*. The residue was purified by silica gel chromatography (hexane/ AcOEt = 20/1 to 5/1) to afford 16.3 mg of **11** (82%; >98% dr analyzed by ^1H NMR, >98% ee analyzed by chiral HPLC) as a white solid.

1,2-dimethyl-4-(*p*-toluenesulfonyl)-7-oxa-4-azatricyclo[4.4.0.0^{2,8}]decane (11)

¹H NMR (300 MHz, CDCl₃): δ 7.70 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 3.73 (d, *J* = 3.3 Hz, 1H), 3.66 (brs, 1H), 3.45 (d, *J* = 12.6 Hz, 1H), 3.40 (dd, *J* = 12.3, 3.6 Hz, 1H), 3.08 (d, *J* = 12.3, 1.2 Hz, 1H), 3.02 (d, *J* = 12.6 Hz, 1H), 2.43 (s, 3H), 1.73-1.43 (m, 4H), 0.92 (s, 3H), 0.83 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 143.1, 134.7, 129.4, 127.4, 83.9, 81.0, 48.1, 47.1, 46.1, 43.7, 33.5, 30.1, 21.7, 15.0, 11.8; IR (reflection, cm⁻¹): 2938, 1921, 1598, 1470, 1394, 1332, 1154, 1058, 1010, 815, 717, 592, 547; Mp: 92 °C; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm × 25 cm), eluent: hexane/*i*-PrOH = 4/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] *t*_R = 17.4 min for (+)-isomer, 24.9 min for (–)-isomer; Optical rotation value: [α]_D²⁸ –16.3 (*c* 0.36, CHCl₃) for (–)-isomer (>98% ee); HRMS (FAB, matrix: 3-nitrobenzyl alcohol, positive): *m/z* calcd for C₁₇H₂₄NO₃S [M+H]⁺: 322.1477, found: 322.1472; Anal. calcd for C₁₇H₂₃NO₃S: C, 63.52; H, 7.21; N, 4.36. Found: C, 63.37; H, 7.03; N, 4.28.

Recrystallization from hexane afforded a single crystal that was suitable for X-ray analysis.

Figure S5. Molecular structure of *rac*-**11** (CCDC-817445) in the solid state. Thermal ellipsoids are drawn at the 40% probability level.

9) Transannular reaction of cyclic amide **1a using NBS**

To a solution of (*R*)-**1a** (>98% ee; 20.0 mg, 0.0655 mmol) in dry CH₂Cl₂ (5 mL) at 0 °C was added *N*-bromosuccinimide (17.5 mg, 0.0982 mmol). The mixture was stirred at that temperature for 3 h. The reaction was quenched with saturated aqueous NaHCO₃. The phases were separated and the aqueous layer was extracted with CH₂Cl₂. The combined organic phases were dried over Na₂SO₄, filtered and the solvent was removed *in vacuo*. The residue was purified by silica gel chromatography (hexane/AcOEt = 1/0 to 12/1) to afford 24.7 mg of a mixture of **12a**, **12b** and **12c** (98%; **12a**/**12b**/**12c** = 54/19/27 determined by ¹H NMR analysis) as a white solid. The mixture of **12a**, **12b** and **12c** were separated by silica gel HPLC; column: Kanto Mightysil Si 60 (5 μm) (2.0 cm × 25 cm), eluent: hexane/AcOEt = 9/1, flow rate: 7.0 mL/min, detection: UV 254 nm, temperature: rt. All of transannular products **12a**, **12b** and **12c** were determined as a single stereoisomer (>98% dr analyzed by ¹H NMR, >98% ee analyzed by chiral HPLC).

4-bromo-3a,7-dimethyl-2-(*p*-toluenesulfonyl)-2,3,3a,4,5,7a-hexahydro-1*H*-isoindole (12a)

¹H NMR (300 MHz, CDCl₃): δ 7.73 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 5.21 (brs, 1H), 3.81 (dd, *J* = 8.7, 7.8 Hz, 1H), 3.76 (d, *J* = 10.5 Hz, 1H), 3.68 (dd, *J* = 9.5, 9.2 Hz, 1H), 3.00 (d, *J* = 10.5 Hz, 1H), 2.87 (dd, *J* = 10.1, 9.5 Hz, 1H), 2.49-2.45 (m, 2H), 2.45 (s, 3H), 2.41 (dd, *J* = 10.1, 9.2 Hz, 1H), 1.60 (d, *J* = 1.5 Hz, 3H), 1.07 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 143.6, 133.5, 132.3, 129.7, 127.5, 120.8, 59.1, 54.8, 52.4, 50.7, 45.4, 34.3, 22.7, 21.8, 18.8; IR (neat, cm⁻¹): 2970, 1440, 1345, 1160, 1093, 1051, 814, 691, 664, 604, 582, 548, 528; Mp: 142 °C; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm × 25 cm), eluent: hexane/*i*-PrOH = 10/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] *t*_R = 22.4 min for (+)-isomer, 23.1 min for (–)-isomer; Optical rotation value: [α]_D²³ 57.8 (*c* 0.50, CHCl₃) for (+)-isomer (>98% ee); HRMS (FAB, matrix: 3-nitrobenzyl alcohol, positive): *m/z* calcd for C₁₇H₂₃BrNO₂S [M+H]⁺: 384.0633, found: 384.0631; Anal. calcd for C₁₇H₂₂BrNO₂S: C, 53.13; H, 5.77; N, 3.64. Found: C, 53.04; H, 5.78; N, 3.62.

Recrystallization from hexane/CH₂Cl₂ afforded a single crystal that was suitable for X-ray analysis.

Figure S6. Molecular structure of *rac*-12a (CCDC-817446) in the solid state. Thermal ellipsoids are drawn at the 50% probability level.

4-bromo-3a-methyl-7-methylene-2-(*p*-toluenesulfonyl)octahydroisoindole (12b)

¹H NMR (300 MHz, CDCl₃): δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.3 Hz, 2H), 4.84 (s, 1H), 4.78 (s, 1H), 3.88 (dd, *J* = 12.9, 4.2 Hz, 1H), 3.78 (d, *J* = 10.2 Hz, 1H), 3.35 (dd, *J* = 10.4, 9.8 Hz, 1H), 3.25 (dd, *J* = 10.8, 10.4 Hz, 1H), 2.86 (d, *J* = 10.2 Hz, 1H), 2.67 (dd, *J* = 10.8, 9.8 Hz, 1H), 2.46 (s, 3H), 2.20-2.05 (m, 3H), 1.98-1.83 (m, 1H), 1.08 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 143.6, 140.4, 134.0, 129.8, 127.4, 114.8, 59.2, 56.1, 54.1, 49.5, 48.0, 34.1, 31.7, 21.8, 18.5; IR (neat, cm⁻¹): 2945, 1597, 1473, 1345, 1304, 1168, 1092, 1044, 892, 810, 708, 664, 598; Mp: 170 °C; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm × 25 cm), eluent: hexane/*i*-PrOH = 10/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] *t*_R = 25.1 min for (–)-isomer, 29.1 min for (+)-isomer; Optical rotation value: [α]_D²² –20.2 (*c* 0.16, CHCl₃) for (–)-isomer (>98% ee); HRMS (EI, positive): *m/z* calcd for C₁₇H₂₂BrNO₂S [M]⁺: 383.0555, found: 383.0557.

4-bromo-3a,7-dimethyl-2-(*p*-toluenesulfonyl)-2,3,3a,4,5,6-hexahydro-1*H*-isoindole (12c)

¹H NMR (300 MHz, CDCl₃): δ 7.72 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 4.06 (d, *J* = 13.5 Hz, 1H), 3.90 (dd, *J* = 10.2, 5.7 Hz, 1H), 3.77 (d, *J* = 13.5 Hz, 1H), 3.53 (d, *J* = 9.0 Hz, 1H), 2.69 (d, *J* = 9.0 Hz, 1H), 2.45 (s, 3H), 2.23-2.02 (m, 4H), 1.45 (s, 3H), 1.15 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 143.5, 133.5, 131.8, 129.7, 127.6, 125.4, 61.4, 57.3, 49.8, 46.0, 32.0, 30.0, 21.8, 20.5, 19.1; IR (neat, cm⁻¹): 2917, 1598, 1449, 1346, 1160, 1095, 1053, 1000, 813, 709, 681, 660; Mp: 154 °C; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm × 25 cm), eluent: hexane/*i*-PrOH = 10/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] *t*_R = 19.3 min for (–)-isomer, 20.2 min for (+)-isomer; Optical rotation value: [α]_D²³ –1.19 (*c* 0.30, CHCl₃) for (–)-isomer (>98% ee); HRMS (EI, positive): *m/z* calcd for C₁₇H₂₂BrNO₂S [M]⁺: 383.0555, found: 383.0551; Anal.

calcd for C₁₇H₂₂BrNO₂S: C, 53.13; H, 5.77; N, 3.64. Found: C, 53.03; H, 5.78; N, 3.61.
Recrystallization from hexane/CH₂Cl₂ afforded a single crystal that was suitable for X-ray analysis.

Figure S7. Molecular structure of (-)-**12c** (CCDC-817447) in the solid state. Thermal ellipsoids are drawn at the 50% probability level.

10) Transannular reaction of cyclic amide **1a** using NIS

To a solution of (*S*)-**1a** (>98% ee; 20.0 mg, 0.0655 mmol) in dry CH₂Cl₂ (5 mL) at 0 °C was added *N*-iodosuccinimide (22.1 mg, 0.0982 mmol). The mixture was stirred at that temperature for 2.5 h. The reaction was quenched with saturated aqueous NaHCO₃. The phases were separated and the aqueous layer was extracted with CH₂Cl₂. The combined organic phases were dried over Na₂SO₄, filtered and the solvent was removed *in vacuo*. The residue was purified by silica gel chromatography (hexane/AcOEt = 1/0 to 12/1) to afford 27.4 mg of a mixture of **13a**, **13b** and **13c** (97%; **13a**/**13b**/**13c** = 55/32/13 determined by ¹H NMR analysis) as a white solid. The mixture of **13a**, **13b** and **13c** were separated by silica gel HPLC; column: Kanto Mightysil Si 60 (5 μm) (2.0 cm × 25 cm), eluent: hexane/AcOEt = 9/1, flow rate: 7.0 mL/min, detection: UV 254 nm, temperature: rt. All of transannular products **13a**, **13b** and **13c** were determined as a single stereoisomer (>98% dr analyzed by ¹H NMR, >98% ee analyzed by chiral HPLC).

4-iodo-3a,7-dimethyl-2-(*p*-toluenesulfonyl)-2,3,3a,4,5,7a-hexahydro-1*H*-isoindole (**13a**)

¹H NMR (300 MHz, CDCl₃): δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 5.11 (brs, 1H), 3.98 (dd, *J* = 11.1, 6.0 Hz, 1H), 3.68 (dd, *J* = 9.6, 9.0 Hz, 1H), 3.61 (d, *J* = 10.8 Hz, 1H), 3.05 (d, *J* = 10.8 Hz, 1H), 2.88 (dd, *J* = 9.8, 9.6 Hz, 1H), 2.76-2.52 (m, 2H), 2.46 (s, 3H), 2.43 (dd, *J* = 9.8, 9.0 Hz, 1H), 1.60 (d, *J* = 0.9 Hz, 3H), 1.09 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 143.6, 133.6, 132.3, 129.8, 127.5, 121.9, 61.7, 52.5, 48.7, 45.3, 37.1, 36.9, 22.8, 21.8, 21.5; IR (neat, cm⁻¹): 2967, 1438, 1345, 1159, 1092, 1051, 813, 709, 685, 662, 600, 574, 549; Mp: 91 °C; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm × 25 cm), eluent: hexane/*i*-PrOH = 10/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] *t*_R = 22.4 min for (+)-isomer, 23.1 min for (-)-isomer; Optical rotation value: [α]_D²³ -54.0 (*c* 1.16, CHCl₃) for (-)-isomer (>98% ee); HRMS (FAB, matrix: 3-nitrobenzyl alcohol, positive): *m/z* calcd for C₁₇H₂₃INO₂S [M+H]⁺: 432.0494, found: 432.0496; Anal. calcd for C₁₇H₂₂INO₂S: C, 47.34; H, 5.14; N, 3.25. Found: C, 47.53; H, 5.14; N, 3.00.

4-iodo-3a-methyl-7-methylene-2-(*p*-toluenesulfonyl)octahydroisoindole (13b)

^1H NMR (300 MHz, CDCl_3): δ 7.75 (d, $J = 8.1$ Hz, 2H), 7.36 (d, $J = 8.1$ Hz, 2H), 4.82 (s, 1H), 4.77 (s, 1H), 4.06 (dd, $J = 12.0, 4.2$ Hz, 1H), 3.64 (d, $J = 10.2$ Hz, 1H), 3.34 (dd, $J = 10.1, 9.8$ Hz, 1H), 3.27 (dd, $J = 10.8, 10.1$ Hz, 1H), 2.88 (d, $J = 10.2$ Hz, 1H), 2.73 (dd, $J = 10.8, 9.8$ Hz, 1H), 2.47 (s, 3H), 2.28-1.98 (m, 4H), 1.12 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 143.6, 140.5, 134.0, 129.9, 127.4, 114.7, 61.2, 52.6, 49.4, 48.1, 38.1, 36.8, 32.9, 21.82, 21.80; IR (neat, cm^{-1}): 2942, 1598, 1441, 1345, 1167, 1092, 1045, 907, 809, 680, 662, 597; Mp: 155 $^\circ\text{C}$; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm $\times$ 25 cm), eluent: hexane/*i*-PrOH = 10/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] t_R = 25.6 min for (–)-isomer, 27.8 min for (+)-isomer; Optical rotation value: $[\alpha]_D^{22}$ 26.7 (c 0.84, CHCl_3) for (+)-isomer (>98% ee); HRMS (EI, positive): m/z calcd for $\text{C}_{17}\text{H}_{22}\text{INO}_2\text{S}$ $[\text{M}]^+$: 431.0416, found: 431.0421; Anal. calcd for $\text{C}_{17}\text{H}_{22}\text{INO}_2\text{S}$: C, 47.34; H, 5.14; N, 3.25. Found: C, 47.49; H, 5.16; N, 3.18.

Recrystallization from hexane/ CH_2Cl_2 afforded a single crystal that was suitable for X-ray analysis.

Figure S8. Molecular structure of *rac*-**13b** (CCDC-818009) in the solid state. Thermal ellipsoids are drawn at the 50% probability level.

4-iodo-3a,7-dimethyl-2-(*p*-toluenesulfonyl)-2,3,3a,4,5,6-hexahydro-1*H*-isoindole (13c)

^1H NMR (300 MHz, CDCl_3): δ 7.72 (d, $J = 8.1$ Hz, 2H), 7.34 (d, $J = 8.1$ Hz, 2H), 4.09 (d, $J = 13.4$ Hz, 1H), 4.02 (dd, $J = 12.0, 5.1$ Hz, 1H), 3.81 (d, $J = 13.4$ Hz, 1H), 3.48 (d, $J = 9.0$ Hz, 1H), 2.63 (d, $J = 9.0$ Hz, 1H), 2.45 (s, 3H), 2.38-2.24 (m, 2H), 2.14-2.00 (m, 1H), 1.94-1.83 (m, 1H), 1.48 (s, 3H), 1.18 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 143.5, 133.5, 130.3, 129.7, 127.6, 125.4, 62.6, 50.2, 45.7, 36.7, 32.6, 32.4, 22.9, 21.8, 19.2; IR (neat, cm^{-1}): 2967, 1598, 1447, 1346, 1160, 1095, 1051, 812, 676, 658; Mp: 154 $^\circ\text{C}$; Analytical HPLC [column: CHIRALCEL OD-H (4.6 mm $\times$ 25 cm), eluent: hexane/*i*-PrOH = 10/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] t_R = 19.4 min for (+)-isomer, 20.8 min for (–)-isomer; Optical rotation value: $[\alpha]_D^{24}$ –45.4 (c 0.15, CHCl_3) for (–)-isomer (>98% ee); 3-nitrobenzyl alcohol, positive): m/z calcd for $\text{C}_{17}\text{H}_{23}\text{INO}_2\text{S}$ $[\text{M}+\text{H}]^+$: 432.0494, found: 432.0494.

11) Preparation of *N*-(trifluoromethanesulfonyl)phosphoramidic acid diphenyl ester¹

To a mixture of trifluoromethanesulfonamide (1.31 g, 8.80 mmol) and K₂CO₃ (1.22 g, 8.80 mmol) in dry CH₃CN (15 mL) at 0 °C was slowly added diphenyl chlorophosphate (2.0 mL, 9.68 mmol). The mixture was allowed to warm up to room temperature and was stirred for 15 h. The reaction was quenched with water. The phases were separated and the aqueous layer was extracted with Et₂O. The combined organic phases were washed with saturated aqueous NaHCO₃ and aqueous HCl (6N), respectively. After the HCl layer was extracted with Et₂O once again, the combined organic phases were dried over MgSO₄, filtered and the solvent was removed *in vacuo* to afford 1.95 g (98%) of the expected pure *N*-Tf-phosphoramidate as a white solid.

¹H NMR (300 MHz, CDCl₃): δ 9.21 (br, 1H), 7.35-7.30 (m, 4H), 7.25-7.17 (m, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 149.52 (d, *J*_{C-P} = 8.0 Hz), 129.99 (d, *J*_{C-P} = 0.6 Hz), 126.28 (d, *J*_{C-P} = 1.2 Hz), 120.06 (d, *J*_{C-P} = 4.9 Hz), 119.10 (q, *J*_{C-F} = 319.1 Hz); ³¹P NMR (243 MHz, CDCl₃): δ -15.7; ¹⁹F NMR (565 MHz, CDCl₃): δ -75.3; IR (neat, cm⁻¹): 2945, 2698, 1590, 1490, 1436, 1375, 1203, 1014, 947, 754, 688; Mp: 67 °C; HRMS (FAB, matrix: 3-nitrobenzyl alcohol, positive): *m/z* calcd for C₁₃H₁₂F₃NO₅PS [M+H]⁺: 382.0126, found: 382.0125.

12) Transannular reaction of cyclic amide **1a** using phosphoramidate

To a solution of (*R*)-**1a** (>98% ee; 20.0 mg, 0.0655 mmol) in dry CH₂Cl₂ (5 mL) at 0 °C was added *N*-Tf-phosphoramidate (37.5 mg, 0.0982 mmol). The mixture was allowed to warm up to room temperature and was stirred for 30 h. The reaction was quenched with saturated aqueous NaHCO₃. The phases were separated and the aqueous layer was extracted with CH₂Cl₂. The combined organic phases were dried over Na₂SO₄, filtered and the solvent was removed *in vacuo*. The residue was purified by silica gel chromatography (hexane/AcOEt = 1/0 to 12/1) to afford 17.5 mg of a mixture of **14a** and **14b** (88%; **14a**/**14b** = 67/33 determined by ¹H NMR analysis) as a white solid. The mixture of **14a** and **14b** were separated by chiral HPLC; column: Daicel CHIRALPAK AS-H column (2.0 cm × 25 cm), eluent: hexane/EtOH = 2/1, flow rate: 4.0 mL/min, detection: UV 254 nm, temperature: rt. Both transannular products **14a** and **14b** were determined as a single stereoisomer (>98% dr analyzed by ¹H NMR, >98% ee analyzed by chiral HPLC).

3a,7-dimethyl-2-(*p*-toluenesulfonyl)-2,3,3a,4,5,7a-hexahydro-1*H*-isoindole (**14a**)

¹ (a) Rueping, M.; Nachtsheim, B. J.; Moreth, S. A.; Bolte, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 593-596. (b) Schneekloth, Jr., J. S.; Kim, J.; Sorensen, E. J. *Tetrahedron* **2009**, *65*, 3096-3101.

^1H NMR (300 MHz, CDCl_3): δ 7.70 (d, $J = 8.1$ Hz, 2H), 7.32 (d, $J = 8.1$ Hz, 2H), 5.35-5.32 (m, 1H), 3.67 (dd, $J = 9.6, 9.0$ Hz, 1H), 3.17 (d, $J = 9.8$ Hz, 1H), 3.06 (d, $J = 9.8$ Hz, 1H), 2.95 (dd, $J = 9.6, 9.2$ Hz, 1H), 2.44 (s, 3H), 2.03 (dd, $J = 9.2, 9.0$ Hz, 1H), 1.98-1.83 (m, 2H), 1.59 (d, $J = 1.5$ Hz, 3H), 1.28-1.12 (m, 2H), 0.92 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 143.2, 133.9, 131.7, 129.5, 127.4, 121.4, 60.5, 53.0, 48.7, 39.4, 28.8, 23.2, 22.6, 22.5, 21.7; IR (neat, cm^{-1}): 2923, 1598, 1448, 1343, 1160, 1094, 813, 709, 666, 583; Mp: 105 $^\circ\text{C}$; Analytical HPLC [column: CHIRALCEL AS-H (4.6 mm $\times$ 25 cm), eluent: hexane/EtOH = 2/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] t_R = 14.9 min for (+)-isomer, 16.5 min for (–)-isomer; Optical rotation value: $[\alpha]_{\text{D}}^{20}$ 8.77 (c 0.85, CHCl_3) for (+)-isomer (>98% ee); HRMS (EI, positive): m/z calcd for $\text{C}_{17}\text{H}_{23}\text{NO}_2\text{S}$ $[\text{M}]^+$: 305.1449, found: 305.1445.

3a-methyl-7-methylene-2-(*p*-toluenesulfonyl)octahydroisindole (14b)

^1H NMR (300 MHz, CDCl_3): δ 7.72 (d, $J = 8.3$ Hz, 2H), 7.33 (d, $J = 8.3$ Hz, 2H), 4.77 (s, 1H), 4.68 (s, 1H), 3.37 (dd, $J = 10.4, 10.1$ Hz, 1H), 3.33 (dd, $J = 10.4, 9.6$ Hz, 1H), 3.26 (d, $J = 9.5$ Hz, 1H), 2.91 (d, $J = 9.5$ Hz, 1H), 2.45 (s, 3H), 2.33 (dd, $J = 10.1, 9.6$ Hz, 1H), 2.15-1.96 (m, 2H), 1.63-1.52 (m, 1H), 1.46-1.22 (m, 3H), 0.92 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 143.7, 143.2, 134.4, 129.6, 127.3, 112.4, 61.1, 52.6, 50.3, 42.5, 31.6, 30.3, 23.4, 21.78, 21.75; IR (neat, cm^{-1}): 2933, 1344, 1159, 1094, 810, 665, 600, 544; Mp: 76 $^\circ\text{C}$; Analytical HPLC [column: CHIRALCEL AS-H (4.6 mm $\times$ 25 cm), eluent: hexane/EtOH = 2/1, flow rate: 0.5 mL/min, detection: UV 254 nm, temperature: rt] t_R = 17.6 min for (+)-isomer, 22.1 min for (–)-isomer; Optical rotation value: $[\alpha]_{\text{D}}^{20}$ –32.8 (c 0.39, CHCl_3) for (–)-isomer (>98% ee); HRMS (EI, positive): m/z calcd for $\text{C}_{17}\text{H}_{23}\text{NO}_2\text{S}$ $[\text{M}]^+$: 305.1449, found: 305.1448; Anal. calcd for $\text{C}_{17}\text{H}_{23}\text{NO}_2\text{S}$: C, 66.85; H, 7.59; N, 4.59. Found: C, 66.88; H, 7.55; N, 4.54.

Recrystallization from hexane/ CH_2Cl_2 afforded a single crystal that was suitable for X-ray analysis.

Figure S9. Molecular structure of (–)-**14b** (CCDC-817448) in the solid state. Thermal ellipsoids are drawn at the 50% probability level.

3. ^1H , ^{13}C , ^{19}F and ^{31}P NMR Spectra

^1H NMR Chart of **2a**

^{13}C NMR Chart of **2a**

¹H NMR Chart of **3a**

¹³C NMR Chart of **3a**

¹H NMR Chart of **4a**

^{13}C NMR Chart of **4a**

¹H NMR Chart of **2b**

^{13}C NMR Chart of **2b**

¹H NMR Chart of **3b**

^{13}C NMR Chart of **3b**

¹H NMR Chart of **4b**

^{13}C NMR Chart of **4b**

¹H NMR Chart of **5a**

^{13}C NMR Chart of **5a**

¹H NMR Chart of **6a**

^{13}C NMR Chart of **6a**

¹H NMR Chart of **7a**

^{13}C NMR Chart of **7a**

¹H NMR Chart of **5b**

^{13}C NMR Chart of **5b**

¹H NMR Chart of **6b**

^{13}C NMR Chart of **6b**

¹H NMR Chart of **7b**

¹³C NMR Chart of **7b**

¹H NMR Chart of **8**

^{13}C NMR Chart of **8**

¹H NMR Chart of **9a**

^{13}C NMR Chart of **9a**

¹H NMR Chart of **9b**

^{13}C NMR Chart of **9b**

¹H NMR Chart of **9c**

^{13}C NMR Chart of **9c**

¹H NMR Chart of **10a**

¹³C NMR Chart of **10a**

¹H NMR Chart of **10c**

¹³C NMR Chart of **10c**

¹H NMR Chart of **11**

^{13}C NMR Chart of **11**

^1H NMR Chart of **12a**

^{13}C NMR Chart of **12a**

^1H NMR Chart of **12b**

^{13}C NMR Chart of **12b**

¹H NMR Chart of **12c**

^{13}C NMR Chart of **12c**

¹H NMR Chart of **13a**

^{13}C NMR Chart of **13a**

^1H NMR Chart of **13b**

^{13}C NMR Chart of **13b**

¹H NMR Chart of **13c**

^{13}C NMR Chart of **13c**

^1H NMR Chart of *N*-Tf-phosphoramidate

¹³C NMR Chart of *N*-Tf-phosphoramidate

¹⁹F NMR Chart of *N*-Tf-phosphoramidate

³¹P NMR Chart of *N*-Tf-phosphoramidate

¹H NMR Chart of **14a**

^{13}C NMR Chart of **14a**

¹H NMR Chart of **14b**

^{13}C NMR Chart of **14b**