Electronic Supplementary Information

A short total synthesis of (±)-mersicarpine via visible light-induced cascade photooxygenation

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1 General information

Commercially available chemicals were used as received from suppliers unless otherwise noted. Dry solvents used were obtained from suppliers in serum-cap quality. Unless otherwise noted, reactions were performed under an atmosphere of argon. Solvents for chromatographic separation were distilled twice prior to use. Thin-layer chromatography was carried out using silica-coated aluminium plates, silica 60 F254, Merck. Column chromatography was performed with silica 60 (230-400 mesh, Macherey-Nagel). NMR spectra were recorded on Bruker AVANCE 500 NEO, Bruker AVANCE 300 III and Bruker AVANCE 250 II instruments. Spectra were calibrated against the solvent resonances of CHCl3 (δH = 7.26 ppm) and CDCl3 (δC = 77.0 ppm), as well as CD3OH (δH = 3.31 ppm) and CD3OD (δC = 49.0 ppm). 1H- and 13C-NMR peak assignments were made based on 2D NMR spectra. IR spectra were obtained using a Nicolet 380 FT-IR spectrometer by Thermo Fisher Scientific. ESI-TOF HRMS spectrometry was performed using an Agilent 1200/6210 Time-of-Flight LC-MS instrument. Optical rotation was measured with a Gyromat-HP polarimeter by Anton Paar OptoTec.

2 Experimental procedures

2.1 Synthesis of tetrahydrocarbazole 11

The synthesis of nitrile 8 starting from ethyl 4-oxocyclohexane-1-carboxylate (2) was performed along literature protocols.[1] Nitrile 8 was then further elaborated into ketone 9 and tetrahydrocarbazole 11.

Ethyl 1,4-dioxaspiro[4.5]decane-8-carboxylate (3)

A mixture of ethyl 4-oxocyclohexane-1-carboxylate (2, 4.63 mL, 4.94 g, 29.05 mmol), (+)-10-camphorsulfonic acid (682.0 mg, 2.93 mmol) and ethylene glycol (8.30 mL, 9.24 g, 148.8 mmol) in toluene (67 mL) was heated to reflux with a Dean-Stark apparatus for 10 h. The mixture was cooled to r.t., and diluted with Et2O. The mixture was washed with saturated aq. NaHCO3 (2×) and brine (1×). The layers were separated and the organic layer was washed over MgSO4, filtered and concentrated to dryness. Column chromatography (silica gel, heptane/Et2O 2:1) gave compound 3 (5.50 g, 88%) as a colorless oil.

Rf = 0.34 (heptane/Et2O 2:1).

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 1.23 (t, $J$ = 7.1 Hz, 3 H, CH$_3$), 1.47–1.60 (m, 2 H, CH$_2$), 1.71–1.81 (m, 4 H, 2 × CH$_2$), 1.86–1.97 (m, 2 H, CH$_2$), 2.31 (tt, $J$ = 3.9, 10.3 Hz, 1 H, CH), 3.92 (s, 4 H, 2 × CH$_2$), 4.10 (d, $J$ = 7.1 Hz, 2 H, CH$_2$) ppm.

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ = 14.2 (CH$_3$), 26.2 (CH$_2$), 33.7 (CH$_2$), 41.6 (CH), 60.2 (CH$_2$), 64.2 (2 × CH$_2$), 108.0 (C$_{tert}$), 175.1 (CO) ppm.

Analytical data are in agreement with the literature.$^{[1]}$

**Ethyl 8-ethyl-1,4-dioxaspiro[4.5]decane-8-carboxylate (4)**

Diisopropylamine (3.39 mL, 24.27 mmol) was dissolved in THF (30 mL) and the mixture was cooled to −78 °C. n-BuLi (10.29 mL, 25.73 mmol, 2.5 M in hexanes) was added dropwise and the mixture was stirred at −78 °C for further 30 min. The mixture was allowed to warm to 0 °C and stirred for 30 min. The mixture was again cooled to −78 °C and ethyl carboxylate 3 (2.50 g, 11.67 mmol, dissolved in 8 mL THF) was added dropwise. The mixture was allowed to warm to r.t. and stirred for 30 min. The mixture was again cooled to −78 °C and a solution of iodoethane (1.40 mL, 16.5 mmol) in THF (10 mL) was added dropwise. The mixture was stirred at −78 °C for 1 h and then allowed to reach r.t. overnight. The mixture was diluted with Et$_2$O and washed with NH$_4$Cl aq. (2 ×) and NaCl aq. (1 ×). The layers were separated and the organic layer was washed over MgSO$_4$, filtered and concentrated to dryness. Column chromatography (silica gel, heptane/Et$_2$O 2:1) gave compound 4 (2.60 g, 92%) as a colorless oil.

$R_f$ = 0.33 (heptane/Et$_2$O 2:1).

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 0.75 (t, $J$ = 7.5 Hz, 3 H, CH$_3$), 1.19 (t, $J$ = 7.1 Hz, 3 H, CH$_3$), 1.33–1.64 (m, 8 H, 4 × CH$_2$), 2.08 (m, 2 H, CH$_2$), 3.86 (m, 4 H, 2 × CH$_2$), 4.09 (q, $J$ = 7.1 Hz, 2 H, CH$_2$) ppm.

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 8.7 (CH$_3$), 14.2 (CH$_3$), 30.9 (2 × CH$_2$), 32.0 (2 × CH$_2$), 32.7 (CH$_2$), 46.3 (C$_{tert}$), 60.0 (CH$_2$), 64.1 (2 × CH$_2$), 108.6 (C$_{tert}$), 175.8 (CO) ppm.

Analytical data are in agreement with the literature.$^{[1]}$
(8-Ethyl-1,4-dioxaspiro[4.5]decan-8-yl)methanol (5)

Ethyl carboxylate 4 (1.65 g, 6.81 mmol) was dissolved in THF (30 mL) and at 0 °C, LiAlH₄ (1.04 g, 27.40 mmol) was added. The mixture was warmed to r.t. and stirred for 2 h. H₂O, 40% NaOH aq. and 1 M potassium sodium tartrate aq. were successively added and the mixture was vigorously stirred overnight. The mixture was filtered through Celite, the layers were separated and the aqueous layer was extracted with CH₂Cl₂ (4×). The combined organic layers were dried over MgSO₄, filtered and concentrated to dryness. Column chromatography (silica gel, heptane/Et₂O 2:1) gave compound 5 (1.35 g, 99%) as a colorless oil.

Rᵣ = 0.29 (heptane/EtOAc 1:1).

¹H NMR (300 MHz, CDCl₃) δ = 0.80 (t, J = 7.6 Hz, 3 H, CH₃), 1.34–1.48 (m, 6 H, 3 × CH₂), 1.55–1.62 (m, 4 H, 2 × CH₂), 1.74 (br. s, OH), 3.41 (s, 2 H, CH₂), 3.91 (s, 4 H, 2 × CH₂) ppm.

¹³C NMR (75 MHz, CDCl₃) δ = 7.6 (CH₃), 25.7 (CH₂), 29.2 (2 × CH₂), 30.3 (2 × CH₂), 36.2 (C₆₋₉), 64.1 (2 × CH₂), 67.0 (CH₂), 109.1 (C₆₋₉) ppm.

Analytical data are in agreement with the literature.[1]

8-Ethyl-1,4-dioxaspiro[4.5]decan-8-carbaldehyde (6)

Oxalyl chloride (1.16 mL, 1.72 g, 13.55 mmol) was dissolved in CH₂Cl₂ (17 mL) and the solution was cooled to −60 °C. A solution of DMSO (1.92 mL, 2.11 g, 27.03 mmol) in CH₂Cl₂ (17 mL) was added slowly and the mixture was stirred for 15 min. A solution of alcohol 5 (1.35 g, 6.74 mmol) in CH₂Cl₂ (17 mL) was added slowly, and the mixture was stirred for 45 min at the same temperature. Et₃N (6.58 mL, 4.78 g, 47.21 mmol) was added and the mixture was warmed to r.t. overnight. The mixture was washed with H₂O (3×), the layers were separated and the organic layer was dried over MgSO₄, filtered and evaporated to dryness. Column chromatography (silica gel, heptane/EtOAc 2:1) gave compound 6 (1.21 g, 90%) as a colorless oil.

Rᵣ = 0.55 (heptane/EtOAc 2:1).
\[ ^1H\text{ NMR} \ (300\text{ MHz, } \text{CDCl}_3) \ \delta = 0.76\ (t, \ \text{J} = 7.6\ Hz, \ 3\ H, \ CH_3),\ 1.42–1.55\ (m, \ 6\ H, \ 3 \times CH_2), \ 1.58–1.70\ (m, \ 2\ H, \ CH_2) ,\ 1.88–2.03\ (m, \ 2\ H, \ CH_2) ,\ 3.89\ (s, \ 4\ H, \ 2 \times CH_2),\ 9.40\ (s, \ 1\ H, \ CHO) \ ppm. \]

\[ ^13C\text{ NMR} \ (125\text{ MHz, } \text{CDCl}_3) \ \delta = 8.1\ (CH_3),\ 27.7\ (2 \times CH_2),\ 28.3\ (CH_2),\ 31.3\ (2 \times CH_2),\ 49.0\ (C^\text{tert}),\ 64.2\ (2 \times CH_2),\ 108.4\ (C^\text{tert}),\ 206.2\ (CHO) \ ppm. \]

Analytical data are in agreement with the literature.\[1\]

\((E)-3-(8\text{-Ethyl-1,4-dioxaspiro[4.5]decan-8-yl})\text{acrylonitrile (7)}\)

![Chemical structure of \((E)-3-(8\text{-Ethyl-1,4-dioxaspiro[4.5]decan-8-yl})\text{acrylonitrile (7)}\)]

Aldehyde 6 (1.21 g, 6.10 mmol) and diethyl cyanomethylphosphonate (1.67 mL, 1.83 g, 10.32 mmol) were dissolved in THF (64 mL). Powdered 4 Å molecular sieves were added (3.50 g) followed by solid LiOH (291.7 mg, 12.18 mmol). The mixture was heated to reflux for 21 h, then cooled to r.t. The solvent was removed under reduced pressure, and the residue was suspended in Et_2O. The mixture was washed with H_2O (2×) and NaCl aq. (1×). The layers were separated and the organic layer was dried over MgSO_4, filtered and concentrated to dryness. Column chromatography (silica gel, heptane/EtOAc 2:1) gave compound 7 (1.27 g, 94%) as a yellowish oil.

\[ R_f = 0.63\ (\text{heptane/EtOAc 2:1}). \]

\[ ^1H\text{ NMR} \ (500\text{ MHz, } \text{CDCl}_3) \ \delta = 0.77\ (t, \ \text{J} = 7.5\ Hz, \ 3\ H, \ CH_3),\ 1.44\ (q, \ \text{J} = 7.5\ Hz, \ 2\ H, \ CH_2), \ 1.51–1.70\ (m, \ 8\ H, \ 2 \times CH_2),\ 3.92\ (s, \ 4\ H, \ 2 \times CH_2),\ 5.27\ (d, \ \text{J} = 16.9\ Hz, \ 1\ H, \ CH),\ 6.57\ (d, \ \text{J} = 16.9\ Hz, \ 1\ H, \ CH) \ ppm. \]

\[ ^13C\text{ NMR} \ (75\text{ MHz, } \text{CDCl}_3) \ \delta = 7.9\ (CH_3),\ 30.8\ (2 \times CH_2),\ 31.4\ (2 \times CH_2),\ 31.6\ (CH_2),\ 40.5\ (C^\text{tert}),\ 64.11\ (CH_2),\ 64.15\ (CH_2),\ 99.0\ (CH),\ 108.2\ (C^\text{tert}),\ 117.6\ (CN),\ 162.1\ (CH) \ ppm. \]

Analytical data are in agreement with the literature.\[1\]

\(3-(8\text{-Ethyl-1,4-dioxaspiro[4.5]decan-8-yl})\text{propanenitrile (8)}\)

![Chemical structure of \(3-(8\text{-Ethyl-1,4-dioxaspiro[4.5]decan-8-yl})\text{propanenitrile (8)}\)]
Pd/C (10 wt-% Pd, 69.6 mg, 65.4 µmol) was weighed into a 2-neck flask, which was then fitted with a septum and a hose connector. The flask was evacuated and back-filled with argon (5×). Alkene 7 (669.7 mg, 3.03 mmol) was dissolved in EtOH (7 mL) and this solution was added to the flask. A balloon filled with H₂ was fitted to the hose connector and the mixture was stirred vigorously for 50 h at r.t. The mixture was filtered through a pad of Celite with the aid of EtOH, and the solvent was evaporated under reduced pressure. Column chromatography (silica gel, heptane/EtOAc 2:1) gave compound 8 (494.5 mg, 73%) as a colorless oil.

$$R_f = 0.61 \ (\text{heptane/EtOAc} \ 1:1).$$

$^{1}\text{H} \text{NMR} \ (300 \ MHz, \ CDCl_3) \ \delta = 0.79 \ (t, \ J = 7.5 \ Hz, \ 3 \ H, \ CH_3), \ 1.33 \ (q, \ J = 7.5 \ Hz, \ 2 \ H, \ CH_2), \ 1.38-1.47 \ (m, \ 4 \ H, \ 2 \times CH_2), \ 1.55-1.63 \ (m, \ 4 \ H, \ 2 \times CH_2), \ 1.63-1.72 \ (m, \ 2 \ H, \ CH_2), \ 2.17-2.25 \ (m, \ 2 \ H, \ CH_2), \ 3.91 \ (s, \ 4 \ H, \ 2 \times CH_2) \ ppm.$

$^{13}\text{C} \text{NMR} \ (75 \ MHz, \ CDCl_3) \ \delta = 7.4 \ (CH_3), \ 11.5 \ (CH_2), \ 27.0 \ (CH_2), \ 30.2 \ (2 \times CH_2), \ 31.7 \ (CH_2), \ 31.8 \ (2 \times CH_2), \ 34.0 \ (C^{\text{tert}}), \ 64.10 \ (CH_2), \ 64.13 \ (CH_2), \ 108.5 \ (C^{\text{tert}}), \ 120.3 \ (CN) \ ppm.$

Analytical data are in agreement with the literature.$^{[1]}$

3-(1-Ethyl-4-oxocyclohexyl)propanenitrile (9)

To a solution of ketal 8 (512.2 mg, 2.29 mmol) in acetone (25 mL) was added 10% aq. HCl (10 mL). To the resulting cloudy mixture, additional acetone was added dropwise until the solution became clear. The mixture was stirred at room temperature for 25 h. The mixture was diluted with NaCl aq., then it was extracted with CH₂Cl₂/Et₂O (1:2, 3×). The organic layer was washed with NaHCO₃ aq. (2×) and NaCl aq. (1×). The organic layer was dried over MgSO₄, filtered, and concentrated under reduced pressure. Column chromatography (silica gel, heptane/EtOAc 2:1) gave compound 9 (407.6 mg, 99%) as colorless oil.

$$R_f = 0.39 \ (\text{heptane/EtOAc} \ 1:1).$$

$^{1}\text{H} \text{NMR} \ (500 \ MHz, \ CDCl_3) \ \delta = 0.90 \ (t, \ J = 7.5 \ Hz, \ 3 \ H, \ CH_3), \ 1.49 \ (q, \ J = 7.5 \ Hz, \ 2 \ H, \ CH_2), \ 1.62-1.70 \ (m, \ 2 \ H, \ CH_2), \ 1.70-1.78 \ (m, \ 2 \ H, \ CH_2), \ 1.82 \ (m, \ 2 \ H, \ CH_2), \ 2.28-2.38 \ (m, \ 6 \ H, \ 3 \times CH_2) \ ppm.$

$^{13}\text{C} \text{NMR} \ (75 \ MHz, \ CDCl_3) \ \delta = 7.5 \ (CH_3), \ 11.7 \ (CH_2), \ 26.9 \ (CH_2), \ 31.6 \ (CH_2), \ 34.1 \ (2 \times CH_2), \ 34.3 \ (C^{\text{tert}}), \ 36.8 \ (2 \times CH_2), \ 119.9 \ (CN), \ 210.9 \ (CO) \ ppm.$

IR: $\tilde{\nu} = 2935, \ 2245, \ 1705, \ 1465, \ 1425, \ 1135, \ 750, \ 505, \ 415 \ \text{cm}^{-1}.$

HRMS (ESI-TOF) m/z: calc. for C₁₁H₁₆NO⁺, [M+H]⁺: 180.1388, found: 180.1392.

- ESI 6 -
3-(3-Ethyl-2,3,4,9-tetrahydro-1H-carbazol-3-yl)propanenitrile (11)

In a 10 mL crimp cap vial, phenylhydrazine (10, 244.8 µL, 2.49 mmol) was dissolved in glacial acetic acid (3.00 mL). Ketone 9 (445.8 mg, 2.49 mmol) was added and the vial was sealed. The mixture was heated to 125 °C with rapid stirring for 22 h. After cooling to r.t., the vial was fitted directly to a rotary evaporator and the mixture was concentrated to dryness. Column chromatography (silica gel, heptane/EtOAc 5:1) provided compound 11 (461.1 mg, 73%) as a colorless solid.

\[ R_f = 0.60 \text{ (heptane/EtOAc 1:1), m.p.: 67-72 °C.} \]

\[ ^1H \text{ NMR (500 MHz, CDCl}_3\] δ = 0.92 (t, \( J = 7.6 \text{ Hz, 3 H, CH}_3\), 1.39 (m, 1 H, CH\_2), 1.48 (m, 1 H, CH\_2), 1.69–1.89 (m, 4 H, 2-H, CH\_2), 2.34 (dd, \( J = 7.8, 8.2 \text{ Hz, 2 H, CH}_2\), 2.53 (m, 2 H, 4-H), 2.72 (m, 2 H, 1-H), 7.08 (td, \( J = 1.1, 7.5 \text{ Hz, 1 H, 6-H} \)), 7.13 (td, \( J = 1.1, 7.5 \text{ Hz, 1 H, 7-H} \)), 7.29 (dd, \( J = 1.1, 7.5 \text{ Hz, 1 H, 8-H} \)), 7.43 (dd, \( J = 1.1, 7.5 \text{ Hz, 1 H, 5-H} \)), 7.74 (br. s, 1 H, N-H).

\[ ^13C \text{ NMR (125 MHz, CDCl}_3\] δ = 7.7 (CH\_3), 11.9 (CH\_2), 19.9 (C-1), 28.3 (CH\_2), 31.0 (C-4), 31.4 (C-2), 31.6 (CH\_3), 35.2 (C-3), 108.1 (C-4a), 110.5 (C-8), 117.5 (C-5), 119.2 (C-6), 120.4 (CN), 121.3 (C-7), 127.8 (C-4b), 132.4 (C-9a), 136.2 (C-8a) ppm.

IR: \( \tilde{\nu} = 3390, 2920, 2245, 1465, 1325, 735, 635, 430 \text{ cm}^{-1}. \)

HRMS (ESI-TOF) m/z: calc. for \( C_{17}H_{21}N_2^+ \), [M+H]^+: 253.1704, found: 253.1705.

2.2 Completion of the synthesis of (±)-mersicarpine (1)

\[ \text{tert-Butyl [3-(3-ethyl-2,3,4,9-tetrahydro-1H-carbazol-3-yl)propyl]carbamate (12)} \]

Tetrahydrocarbazole 11 (63.1 mg, 250.0 µmol) was dissolved in EtOH (5.00 mL) in a round-bottomed flask equipped with magnetic stirrer and a three-way valve. CHCl\_3 (4 drops) and Pt\_2O
(8.5 mg, 37.4 µmol) were added. A balloon filled with H₂ was fitted to the three-way valve, and the headspace was evacuated, then purged with H₂ (5×). The reaction mixture was stirred vigorously for 24 h at r.t. A second portion of Pt₂O (8.5 mg, 37.4 µmol) was added and the mixture was stirred for 16 h. A third portion of Pt₂O (8.5 mg, 37.4 µmol) was added and the mixture was stirred for 2 h, whereupon TLC showed complete consumption of the starting material. The mixture was filtered through Celite with the aid of EtOH and EtOAc. The filtrate was concentrated to dryness and the crude product was dried in high vacuum. The crude product was dissolved in CH₂Cl₂ (2.00 mL). A solution of Boc₂O (632 mg, 2.90 mmol) in CH₂Cl₂ (1.00 mL) was added followed by Et₃N (69.3 µL, 500 µmol). The mixture was stirred at r.t. for 4 h, then poured into 5% HCl aq. and extracted with CH₂Cl₂ (3×). The combined organic layers were washed with NaCl aq. (3×), dried over MgSO₄, filtered, and concentrated to dryness. Column chromatography (silica gel, heptane/EtOAc 5:1 + 1 vol-% Et₃N) gave compound 12 (86.4 mg, 97%) as a yellowish solid.

**R<sub>r</sub>** = 0.65 (heptane/EtOAc 1:1), m.p.: 63-66°C

**¹H NMR** (500 MHz, CD₂OD) δ = 0.92 (t, J = 7.4 Hz, 3 H, CH₃), 1.25–1.34 (m, 2 H, CH₂), 1.40 (s, 9 H, t-Bu), 1.43–1.54 (m, 4 H, 2 × CH₂), 1.70 (t, J = 6.4 Hz, 2 H, 2-H), 2.46 (m, 2 H, 4-H), 2.64–2.70 (m, 2 H, 1-H), 2.98 (t, J = 6.7 Hz, 2 H, CH₂), 3.09 (br. s, 1 H, N-H), 6.91 (t, J = 7.5 Hz, 1 H, 6-H), 6.98 (t, J = 7.5 Hz, 1 H, 7-H), 7.21 (d, J = 7.5 Hz, 1 H, 8-H), 7.31 (d, J = 7.5 Hz, 1 H, 5-H), 7.89 (s, 1 H, NH) ppm.

**¹³C NMR** (125 MHz, CDCl₃) δ = 7.8 (CH₃), 20.0 (C-1), 24.1 (CH₂), 28.4 (t-Bu), 28.8 (CH₂), 31.6 (C-4), 31.9 (C-2), 32.9 (CH₂), 35.0 (C-3), 41.4 (CH₂), 79.0 (t-Bu), 108.9 (C-4a), 110.4 (C-8), 117.5 (C-5), 118.9 (C-6), 120.9 (C-7), 128.1 (C-4b), 133.0 (C-9a), 136.1 (C-8a), 155.9 (CO) ppm.

**IR:** ν = 3325, 2925, 1685, 1510, 1455, 1365, 1240, 1160, 735 cm⁻¹.

**HRMS** (ESI-TOF) m/z: calc. for C₂₂H₃₆N₂O₂⁺; [M+H]^⁺: 357.2542, found: 357.2543.

**tert-Butyl [3-(9-ethyl-9a-hydroxy-6,10-dioxo-6,7,8,9,9a,10-hexahydropyrido[1,2-ajindol-9-yl])propyl]carbamate (13)**

![Image](image_url)

d.r. = 1:1

In a Pyrex tube (length ca. 15 cm, Ø = 3.0 cm), tetrahydrocarbazole 12 (45.9 mg, 128.7 µmol) and rose bengal disodium salt (2.6 mg, 2.57 µmol, 2 mol-%) were dissolved in MeOH (2.60 mL). 40% NaOH aq. (108.0 µL, 12 equiv.) was added, and the vial was sealed with a septum. An O₂ balloon was fitted (septum pierced by needle), and the mixture was irradiated with green LEDs (λ<sub>em</sub> = 530 nm, 10 W total power) with rapid stirring, at r.t. for 36 h. H₂O (10 mL) and 1 M HCl aq. (ca. 2 mL, until the mixture was pH neutral) were added and the mixture was extracted with CH₂Cl₂ (4×). The combined organic layers were dried with MgSO₄, filtered and
evaporated. Column chromatography (silica gel, heptane/EtOAc 3:2→0:1) provided compound 13 (31.4 mg, 61%) as a colorless solid, as a 1:1 mixture of diastereomers. As a byproduct, tert-butyl [3-(1-ethyl-9-oxo-2,3,4,9-tetrahydro-1H-cyclopenta[b]quinolin-1-yl)propyl]carbamate was isolated (8.0 mg, 17%) as a colorless solid.

R<sub>T</sub> = 0.37+0.31 (heptane/EtOAc 1:1), m.p.: 58-60 °C.

1<sup>H</sup> NMR (300 MHz, CDCl<sub>3</sub>): 1:1 mixture of diastereomers, δ = 0.64 (t, J = 7.7 Hz, 3 H, CH<sub>3</sub>), 0.93 (t, J = 7.5 Hz, 3 H, CH<sub>3</sub>), 1.16–1.23 (m, 4 H, CH<sub>2</sub>), 1.33 (s, 9 H, t-Bu), 1.39 (s, 9 H, t-Bu), 1.46–1.72 (m, 8 H, 8-H, CH<sub>2</sub>), 1.76–1.90 (m, 2 H, CH<sub>2</sub>), 1.96–2.10 (m, 2 H, CH<sub>2</sub>), 2.13–2.32 (m, 4 H, 8-H, CH<sub>2</sub>), 2.41–2.57 (m, 2 H, 7-H), 2.67–2.84 (m, 4 H, 7-H, CH<sub>2</sub>), 3.00–3.24 (m, 2 H, CH<sub>2</sub>), 4.25 (m, 1 H, N-H), 4.73 (br. s, 1 H, N-H), 7.17 (td, J = 0.7, 7.5 Hz, 1 H, 2-H), 7.18 (td, J = 0.7, 7.5 Hz, 1 H, 2-H), 7.58-7.65 (m, 2 H, 3-H), 7.65–7.70 (m, 2 H, 1-H), 8.36 (dt, J = 0.7, 8.3 Hz, 1 H, 4-H), 8.37 (dt, J = 0.7, 8.3 Hz, 1 H, 4-H) ppm.

1<sup>3</sup>C NMR (75 MHz, CDCl<sub>3</sub>): 1:1 mixture of diastereomers, δ = 8.18, 9.43 (CH<sub>3</sub>), 24.00 (CH<sub>2</sub>), 24.45 (CH<sub>2</sub>), 24.50 (CH<sub>2</sub>), 25.66 (CH<sub>2</sub>), 26.35, 26.59 (C-8), 28.27, 28.35 (t-Bu), 28.48 (CH<sub>2</sub>), 29.39, 29.47 (C-7), 35.31, 35.39 (C-9), 42.92, 43.03 (CH<sub>2</sub>), 79.20 (t-Bu), 89.88, 89.95 (C-9a), 117.85, 117.89 (C-4), 121.36, 121.52 (C-10a), 124.31, 124.38 (C-1), 124.46, 124.57 (C-2), 137.81, 137.98 (C-3), 151.11, 151.15 (C-4a), 155.74, 156.15 (CO), 169.75, 169.83 (C-6), 197.82, 197.86 (C-10) ppm.

IR: ν = 2925, 1675, 1465, 1365, 1160, 755 cm<sup>-1</sup>.

HRMS (ESI-TOF) m/z: calc. for C<sub>22</sub>H<sub>30</sub>N<sub>2</sub>O<sub>5</sub>, [M]<sup>+</sup>: 402.2149, found: 402.2147.

The NMR spectroscopic data are in agreement with the literature.<sup>[2]</sup>

Analytical data for tert-butyl [3-(1-ethyl-9-oxo-2,3,4,9-tetrahydro-1H-cyclopenta[b]quinolin-1-yl)propyl]carbamate:

![Diagram](image)

R<sub>T</sub> = 0.65 (EtOAc/MeOH 10:1), m.p.: 330 °C (decomp.).

1<sup>H</sup> NMR (500 MHz, CD<sub>3</sub>OD) δ = 0.80 (t, J = 7.4 Hz, 3 H, CH<sub>3</sub>), 1.20–1.27 (m, 1 H, 2-H), 1.40 (s, 9 H, t-Bu), 1.41–1.52 (m, 1 H, 2-H), 1.63–1.75 (m, 2 H, 3-H, CH<sub>2</sub>), 1.95–2.12 (m, 4 H, 3-H, CH<sub>2</sub>), 2.93–3.04 (m, 4 H, CH<sub>2</sub>), 7.35 (ddd, J = 1.4, 7.0, 8.2 Hz, 1 H, 7-H), 7.50 (dd, J = 1.4, 8.2 Hz, 1 H, 5-H), 7.63 (ddd, J = 1.4, 7.0, 8.2 Hz, 1 H, 6-H), 8.24 (dd, J = 1.4, 8.2 Hz, 1 H, 8-H) ppm.

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\[^{13}\text{C} \text{NMR}\] (126 MHz, CD\textsubscript{3}OD) \(\delta = 9.6\) (CH\textsubscript{3}), 26.6 (C-2), 28.8 (t-Bu), 31.2 (CH\textsubscript{2}), 32.3 (CH\textsubscript{2}), 32.4 (CH\textsubscript{2}), 37.1 (C-3), 42.1 (CH\textsubscript{2}), 52.8 (C-1), 79.7 (t-Bu), 118.9 (C-5), 124.3 (C-7), 124.7 (C-9a), 126.1 (C-8), 126.9 (C-8a), 132.4 (C-6), 141.7 (C-4a), 157.3 (CO), 158.5 (C-3a), 177.6 (C-9) ppm.

\[\text{IR}\] \(\tilde{\nu} = 2935, 1685, 1630, 1565, 1505, 1470, 1365, 1165, 1020, 760\ \text{cm}^{-1}.

\[\text{HRMS (ESI-TOF)}\] m/z: calc. for C\textsubscript{22}H\textsubscript{31}N\textsubscript{2}O\textsubscript{3}+: [M+H]\(^+\): 371.2335, found: 371.2338.

(\textpm)-Mersicarpine (1)

Numbering for: (4aR\(^*\),12cS\(^*\))-4a-Ethyl-3,4,4a,5,6,12c-hexahydro-12c-hydroxyazepino[4,3,2-\text{h}]benz[\text{b}]indolizin-7(2\text{H})-one

Compound 13 (30.0 mg, 74.5 \(\mu\)mol) was dissolved in CH\textsubscript{2}Cl\textsubscript{2} (3.50 mL) and the mixture was cooled to 0 °C. 2.6-Lutidine (432.0 \(\mu\)L, 399.6 mg, 3.73 mmol) and TBSOTf (342.0 \(\mu\)L, 393.3 mg, 1.49 mmol) were added and the mixture was stirred at r.t. for 25 h. The reaction was quenched by the addition of 5% HCl \(\text{aq.}\), the layers were separated and the aqueous layer was extracted with CH\textsubscript{2}Cl\textsubscript{2} (4×). The combined organic layers were dried with MgSO\textsubscript{4}, filtered and evaporated to dryness. The crude product was dried in high vacuum, then dissolved in THF (3.50 mL). A solution of TBAF (1 M in THF, 223.6 \(\mu\)L, 223.6 \(\mu\)mol,) was added and the mixture was stirred at r.t. for 20 h. The mixture was evaporated onto silica, and column chromatography (heptane/EtOAc 1:1 provided (\textpm)-mersicarpine (1) as a colorless solid (11.7 mg, 55%).

\[R_f = 0.23\] (heptane/ EtOAc 1:1), m.p.: 232-235 °C (lit.: 150 °C decomp.)\textsuperscript{[3]}

\[^{1}\text{H} \text{NMR}\] (500 MHz, CDCl\textsubscript{3}) \(\delta = 0.74\) (t, \(J = 7.4\) Hz, 3 H, CH\textsubscript{3}), 1.04–1.15 (m, 1 H, CH\textsubscript{2}), 1.25–1.35 (m, 1 H, CH\textsubscript{2}), 1.60–1.71 (m, 3 H, 3-H, 5-H), 1.75 (dt, \(J = 3.4, 14.7\) Hz, 1 H, 4-H), 1.86–1.96 (m, 1 H, 5-H), 2.00–2.11 (m, 1 H, 4-H), 2.38 (ddd, \(J = 8.7, 8.7, 18.1\) Hz, 1 H, 6-H), 2.57 (ddd, \(J = 1.5, 9.5, 18.1\) Hz, 1 H, 6-H), 3.76–3.90 (m, 2 H, 2-H), 5.59 (br. s, 1 H, OH), 7.06 (t, \(J = 7.8\) Hz, 1 H, 11-H), 7.37 (t, \(J = 7.8\) Hz, 1 H, 10-H), 7.60–7.73 (m, 1 H, 12-H), 8.11 (d, \(J = 7.8\) Hz, 1 H, 9-H) ppm.

\[^{13}\text{C} \text{NMR}\] (125 MHz, CDCl\textsubscript{3}) \(\delta = 6.8\) (CH\textsubscript{3}), 21.0 (CH\textsubscript{2}), 22.8 (C-3), 25.5 (C-5), 29.1 (C-6), 34.2 (C-4), 39.4 (C-4a), 50.0 (C-2), 94.0 (C-12c), 116.8 (C-9), 122.7 (C-12), 123.6 (C-12a), 124.4 (C-11), 134.0 (C-10), 146.9 (C-8a), 169.4 (C-7), 169.8 (C-12b) ppm.

The signals at 122.7, 123.6, 134.0, 146.9, 169.8 ppm were of low intensity. Their presence was unambiguously confirmed by an HMBC experiment.

IR: $\tilde{\nu} = 2920, 1600, 1500, 1215, 1155, 900, 810, 755, 575, 500$ cm$^{-1}$.

HRMS (ESI-TOF) m/z: calc. for C$_{17}$H$_{21}$N$_2$O$_2^+$, [M+H]$^+$: 285.1603, found: 285.1596.

The NMR spectroscopic data are in agreement with the literature.$^{[2][4]}$

3 Chiral Brønsted acid-catalyzed Fischer indolization of hydrazones 16 and 17 to enantioenriched tetrahydrocarbazoles 19 and 20

3.1 Preparation of hydrazones 16 and 17

3-(4-(2-Benzyl-2-phenylhydrazineylidene)-1-ethylcyclohexyl)propanenitrile (16)

\[ \text{1-Benzyl-1-phenylhydrazine (14, 99.1 mg, 0.50 mmol) and ketone 9 (90.0 mg, 0.50 mmol) were dissolved in EtOH (1.00 mL). One drop of glacial AcOH was added and the mixture was stirred at 60 °C for 3 h. The mixture was concentrated to dryness and the crude product was purified by column chromatography on silica gel (heptane/Et$_2$O 1:1) to give compound 16 (161.0 mg, 90%) as a colorless oil.} \]

$R_f = 0.25$ (heptane/Et$_2$O 1:1).

$^1$H NMR (250 MHz, CDCl$_3$) $\delta = 0.76$ (t, $J = 7.6$ Hz, 3 H, CH$_3$), 0.91–1.01 (m, 1 H, CH$_2$), 1.07–1.18 (m, 1 H, CH$_2$), 1.30 (qd, $J = 1.2, 7.9$ Hz, 2 H, CH$_2$), 1.37–1.55 (m, 2 H, CH$_2$), 1.61 (m, 2 H, CH$_2$), 2.10–2.21 (m, 3 H, CH$_3$), 2.28–2.34 (m, 1 H, CH$_2$), 2.40 (t, $J = 6.7$ Hz, 2 H, CH$_2$), 4.49–4.62 (m, 2 H, CH$_2$), 6.82–6.90 (m, 3 H, Ar-H), 7.19–7.28 (m, 3 H, Ar), 7.28–7.34 (m, 4 H, Ar) ppm.

$^{13}$C NMR (63 MHz, CDCl$_3$) $\delta = 7.4$ (CH$_3$), 11.5 (CH$_2$), 24.9 (CH$_2$), 27.0 (CH$_2$), 30.1 (CH$_2$), 31.6 (CH$_2$), 33.4 (CH$_2$), 34.5 (CH$_2$), 34.6 (C$_{\text{tert}}$), 60.6 (CH$_2$), 115.9 (Ar), 120.1 (CN), 120.2 (Ar), 126.9 (Ar), 128.2 (Ar), 128.7 (Ar), 128.9 (Ar), 138.8 (Ar), 150.5 (Ar), 175.8 (CN) ppm.

IR: $\tilde{\nu} = 3085, 3060, 2960, 2930, 1710, 1635, 1545, 1455, 1215, 1200, 910, 750$ cm$^{-1}$.

HRMS (ESI-TOF) m/z: calc. for C$_{24}$H$_{30}$N$_6^+$, [M+H]$^+$: 360.2440, found: 360.2433.

3-(1-Ethyl-4-(2-(4-iodobenzyl)-2-phenylhydrazineylidene)cyclohexyl)propanenitrile (17)

1-(4-Iodobenzyl)-1-phenylhydrazine[5] (15, 97.3 mg, 0.30 mmol) and ketone 9 (54.0 mg, 0.30 mmol) were dissolved in EtOH (1.00 mL). One drop of glacial AcOH was added and the mixture was stirred at 60 °C for 5 h. The mixture was concentrated to dryness and the crude product was purified by column chromatography on silica gel (PhCH₃/ EtOAc 8:1) to give compound 17 (93.0 mg, 63%) as a colorless solid.

Rᵣ = 0.33 (PhCH₃/ EtOAc 5:1), m.p.: 104-106 °C.

¹H NMR (300 MHz, CDCl₃) δ = 0.81 (t, J = 7.6 Hz, 3 H, CH₃), 0.97–1.06 (m, 1 H, CH₂), 1.13–1.22 (m, 1 H, CH₂), 1.33 (qd, J = 2.9, 7.7 Hz, 2 H, CH₂), 1.42–1.58 (m, 2 H, CH₂), 1.67 (m, 2 H, CH₂), 2.14–2.23 (m, 3 H, CH₂), 2.29–2.38 (m, 1 H, CH₂), 2.24 (t, J = 6.7 Hz, 2 H, CH₂), 4.46–4.56 (m, 2 H, CH₂), 6.85 (m, 2 H, Ar-H), 6.90 (tt, J = 1.1, 7.3 Hz, 1 H, Ar-H), 7.10 (dt, J = 1.8, 8.4 Hz, 2 H, Ar-H), 7.25 (dd, J = 7.3, 8.6 Hz, 2 H, Ar-H), 7.65 (dt, J = 1.8, 8.4 Hz, 2 H, Ar-H) ppm.

¹³C NMR (75 MHz, CDCl₃) δ = 7.4 (CH₃), 11.6 (CH₂), 24.9 (CH₂), 27.0 (CH₂), 30.1 (CH₂), 31.6 (CH₂), 33.5 (CH₂), 34.64 (C[tert]), 60.3 (CH₂), 92.3 (Ar), 116.1 (Ar), 120.0 (Ar), 120.6 (Ar), 129.0 (Ar), 130.7 (Ar), 137.3 (Ar), 138.5 (Ar), 150.3 (Ar), 175.6 (CN) ppm.

IR: ν = 3060, 3035, 2930, 2835, 1710, 1635, 1595, 1490, 1200, 1010, 790 cm⁻¹.

HRMS (ESI-TOF) m/z: calc. for C₂₄H₂₉IN₃⁺, [M+H]⁺: 486.1406, found: 486.1414.

3.2 Fischer indole synthesis

Note: Prior to their use, all commercially available phosphoric acid catalysts were dissolved in CH₂Cl₂ and the solutions were washed with 4 M HCl aq. After phase separation, the organic layers were immediately evaporated and the respective catalyst was dried in high vacuum.

The cyclization of hydrazone 16 to N-benzyl tetrahydrocarbazole 19 was first investigated utilizing diphenyl phosphate (DPP) as the Brønsted acid catalyst (Table ESI-1).

Table ESI-1. Fischer indolization of hydrazone 16 catalyzed by diphenyl phosphate (DPP).

<table>
<thead>
<tr>
<th>entry</th>
<th>mol-% DPP</th>
<th>additive</th>
<th>T (°C)</th>
<th>t (h)</th>
<th>conversion of 16 (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>NMR yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>isolated yield (%)</th>
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<tbody>
<tr>
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<td>none</td>
<td>40</td>
<td>48</td>
<td>12</td>
<td>10</td>
<td>-/-</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>none</td>
<td>40</td>
<td>48</td>
<td>25</td>
<td>21</td>
<td>-/-</td>
</tr>
<tr>
<td>3</td>
<td>100</td>
<td>none</td>
<td>40</td>
<td>48</td>
<td>94</td>
<td>86</td>
<td>79</td>
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<tr>
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<td>0</td>
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<td>40</td>
<td>48</td>
<td>12</td>
<td>5</td>
<td>-/-</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
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<tr>
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<td>16</td>
<td>11</td>
<td>-/-</td>
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<td>25</td>
<td>48</td>
<td>100</td>
<td>48</td>
<td>44</td>
</tr>
</tbody>
</table>

All reactions were performed on 0.10 mmol scale. a) Conversion determined by ¹H NMR analysis. b) NMR yield determined against 1,3,5-trimethoxybenzene standard.

As can be seen from Table ESI-1, DPP alone showed no catalytic turnover even at 40 °C. Amberlite® CG 50 H⁺ resin alone at 40 °C does induce the cyclization of 16 to 19 only to a very minor extend. However Amberlite® IR-120 H⁺ resin alone efficiently promotes the reaction at 40 °C, but to a much lesser extend at 25 °C. Combining DPP with Amberlite® CG 50 H⁺ resin<sup>[5]</sup> was not successful. Combining DPP with Amberlite® IR-120 H⁺ resin<sup>[6]</sup> led to a catalytic

turnover and full conversion at r.t., when using 30 mol-% of DPP. The addition of ZnCl$_2$ did not lead to further improvements.

Subsequently, the cyclizations of 16 to 19 and 17 to 20 were attempted using chiral phosphate catalysts, under the conditions of entry 10 in Table ESI-1. The results are summarized in Table ESI-2.

**Table ESI-2.** Asymmetric Fischer indolization of hydrazones 16 and 17 catalyzed by chiral phosphoric acids.

<table>
<thead>
<tr>
<th></th>
<th>catalyst</th>
<th>substrate 16</th>
<th></th>
<th>substrate 17</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>conversion (%)$^a$</td>
<td>NMR yield (%)$^b$</td>
<td>isolated yield of 19 (%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>35</td>
<td>16</td>
<td>100</td>
</tr>
<tr>
<td></td>
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<td>23</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14</td>
<td>17</td>
<td>15</td>
</tr>
</tbody>
</table>

$^a$ Conversion determined by $^1$H NMR analysis. $^b$ NMR yield determined against 1,3,5-trimethoxybenzene standard. $^c$ Determined by chiral HPLC.
As can be seen from Table ESI-2, only catalyst 18 offers any asymmetric induction and acceptable product yields.

3.2.1 Synthetic procedures and analytical data

3-(9-Benzyl-3-ethyl-2,3,4,9-tetrahydro-1H-carbazol-3-yl)propanenitrile (−)-(19)

In a 5 mL Schlenk flask, hydrazone 16 (36.0 mg, 0.10 mmol) was dissolved in PhCH3 (1 mL). Powdered 4Å molecular sieves (50 mg) were added, followed by catalyst 18 (CAS 1345628-08-1, 20.0 mg, 30.0 μmol) and Amberlite® IR 120 H+ (CAS 39389-20-3, 200 mg). The mixture was stirred at 25 °C for 72 h (TLC showed complete consumption of starting material), then filtered through a small bed of Celite with the aid of EtOAc. The filtrate was concentrated to dryness and the crude product was purified by column chromatography on silica gel (heptane/EtOAc 5:1) to give compound (−)-19 (19.2 mg, 56%) as a colorless oil. HPLC on chiral stationary phase showed e.r. = 68:32.

Rf = 0.33 (heptane/EtOAc 5:1).

[α]D22 = −4.80° (c 0.8, CHCl3).

1H NMR (250 MHz, CDCl3) δ = 0.82 (t, J = 7.6 Hz, 3 H, CH3), 1.33 (dq, J = 7.6, 10.6 Hz, 2 H, CH2), 1.56–1.80 (m, 4 H, 2-H, CH2), 2.23 (t, J = 8.2 Hz, 2 H, CH2), 2.43–2.59 (m, 4 H, 1-H, 4-H), 5.17 (s, 2 H, CH2), 6.85–6.92 (m, 2 H, Ar-H), 6.97–7.07 (m, 2 H, 6-H, 8-H), 7.07–7.22 (m, 4 H, 7-H, Ar-H), 7.35–7.43 (m, 1 H, 5-H) ppm.

13C NMR (63 MHz, CDCl3) δ = 7.7 (CH3), 11.9 (CH2), 18.9 (C-1), 28.2 (CH2), 31.1 (C-4), 31.4 (C-2), 31.6 (CH2), 35.1 (C-3), 46.3 (CH2), 107.7 (C-4a), 109.1 (C-8), 117.6 (C-5), 119.0 (C-6), 120.3 (CN), 121.1 (C-7), 126.0 (Ar), 127.3 (Ar), 127.5 (C-4b), 128.7 (Ar), 133.9 (C-9a), 137.0 (C-8a), 138.0 (Ar) ppm.

IR: ν = 3085, 3050, 2960, 1615, 1465, 1455, 1355, 1180, 735, 705, 695 cm⁻¹.

The racemic reference sample (±)-19 could be base-line separated by using a Lux Cellulose-1 column, EtOH/heptane 5:95, flow rate 1.0 mL/min. The individual enantiomers eluted at retention times of 23 and 26 min, respectively.
Reaction product (−)-19, e.r. 68:32

Lux Cellulose-1 column, EtOH/heptane 5:95, flow rate 1.0 mL/min.
3-(3-Ethyl-9-(4-iodobenzyl)-2,3,4,9-tetrahydro-1H-carbazol-3-yl)propanenitrile (–)-(20)

In a 5 mL Schlenk flask, hydrazone 17 (48.0 mg, 0.10 mmol) was dissolved in PhCH₃ (1 mL). Powdered 4Å molecular sieves (50 mg) were added, followed by catalyst 18 (CAS 1345628-08-1, 20.0 mg, 30.0 μmol) and Amberlite® IR 120 H⁺ (CAS 39389-20-3, 200 mg). The mixture was stirred at 25 °C for 48 h (TLC showed complete consumption of starting material), then filtered through a small bed of Celite with the aid of EtOAc. The filtrate was concentrated to dryness and the crude product was purified by column chromatography on silica gel (heptane/EtOAc 5:1) to give compound (–)-20 (26.0 mg, 56%) as a colorless oil. HPLC on chiral stationary phase showed e.r. = 66:34. 

Rᵣ = 0.34 (heptane/EtOAc 5:1).

[α]²²ₒ = −4.63° (c 1.0, CHCl₃).

¹H NMR (250 MHz, CDCl₃) δ = 0.91 (t, J = 7.6 Hz, 3 H, CH₃), 1.42 (dq, J = 7.6, 10.6 Hz, 2 H, CH₂), 1.65–1.90 (m, 4 H, 2-H, CH₂), 2.34 (t, J = 8.2 Hz, 2 H, CH₂), 2.52–2.65 (m, 4 H, 1-H, 4-H), 5.19 (s, 2 H, CH₂), 6.71 (dt, J = 2.0, 8.3 Hz, 2 H, Ar-H), 7.07–7.20 (m, 3 H, 6-H, 7-H, 8-H), 7.45–7.51 (m, 1 H, 5-H), 7.59 (dt, J = 2.0, 8.3 Hz, 2 H, Ar-H) ppm.

¹³C NMR (63 MHz, CDCl₃) δ = 7.7 (CH₃), 11.9 (CH₂), 18.9 (C-1), 28.1 (CH₂), 31.1 (C-4), 31.4 (C-2), 31.6 (CH₂), 35.1 (C-3), 45.9 (CH₂), 92.6 (Ar), 108.0 (C-4a), 109.0 (C-8), 117.7 (C-5), 119.2 (C-6), 120.3 (CN), 121.2 (C-7), 127.5 (C-4b), 127.9 (Ar), 133.7 (C-9a), 136.9 (C-8a), 137.7 (Ar), 137.8 (Ar) ppm.

IR: ν = 3050, 3030, 2960, 1465, 1180, 1005, 740 cm⁻¹.

HRMS (ESI-TOF) m/z: calc. for C₂₄H₂₂IN₂⁺, [M+H]⁺: 469.1141, found: 469.1140.
The racemic reference sample (±)-20 could be base-line separated by using a Lux Cellulose-1 column, EtOH/heptane 5:95, flow rate 1.0 mL/min. The individual enantiomers eluted at retention times of 30 and 36 min, respectively.

Racemate (±)-20

<table>
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<th>Signalname</th>
<th>Retention (min)</th>
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<th>Höhe (mAU)</th>
<th>Fläche (%)</th>
<th>Höhe (%)</th>
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</table>

Lux Cellulose-1 column, EtOH/heptane 5:95, flow rate 1.0 mL/min.
Reaction product (−)-20, e.r. 66:34

Lux Cellulose-1 column, EtOH/heptane 5:95, flow rate 1.0 mL/min.
4 NMR spectra

300 MHz, CDCl$_3$

125 MHz, CDCl$_3$

- ESI 21 -
500 MHz, CDCl$_3$

75 MHz, CDCl$_3$
$d.r. = 1:1$

300 MHz, CDCl$_3$

75 MHz, CDCl$_3$
$^3$J coupling between 2-H and C-12b confirms ring closure.
250 MHz, CDCl₃

63 MHz, CDCl₃