Electronic Supplementary Information

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General Methods

All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware with magnetic stirring, unless otherwise indicated. Toluene, dichloromethane and THF were purified by a Innovative Technology Solvent Delivery System. Chemicals were used as obtained from the suppliers. Flash chromatography was performed with Silicycle silica gel 60 (0.040-0.063 μm grade). Analytical thin-layer chromatography was performed with commercial glass plates coated with 0.25 mm silica gel (E. Merck, Kieselgel 60 F254). Compounds were either visualised under UV-light at 254 nm or by dipping the plates in an aqueous potassium permanganate solution followed by heating. Proton nuclear magnetic resonance (¹H NMR) data were acquired at 400 MHz on a Bruker AV400 spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) relative to residual chloroform (s, 7.26 ppm). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; sept, septet; m, multiplet, br, broad. Proton decoupled Carbon-13 nuclear magnetic resonance (¹³C NMR) data were acquired at 100 MHz on a Bruker AV400 spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) relative to residual chloroform (77.16±0.06 ppm). Unless otherwise stated, all NMR spectra were measured at 298 K. Infrared (IR) data were recorded on an Alpha-P Bruker FT-IR Spectrometer. Absorbance frequencies are reported in reciprocal centimeters (cm⁻¹). HR-MS measurements were performed by an Agilent LC-MS TOF. High resolution mass are given in m/z. Optical rotations were measured on a Polartronic M polarimeter using a 0.5 cm cell with a Na 589 nm filter. X-ray analysis was performed by Dr. R. Scopelliti at the EPF Lausanne.
Experimental procedures and characterization data

Synthesis of Pd(dba)$_2$

Pd(dba)$_2$ was synthesized following a modified literature procedure (Y. Takahashi et al., J. Chem. Soc. D. 1970, 17, 1065):

\[
Pd(OAc)_2 + \text{Dibenzyledeneacetone} \xrightarrow{\text{NaOAc, MeOH}} Pd(dba)_2
\]

Dibenzyledeneacetone (1.72 g, 7.35 mmol, 3.3 eq) and sodium acetate (1.46 g, 17.8 mmol, 8.0 eq) were dissolved in degassed MeOH (56 ml) at 50 ºC and the mixture let cool down to rt. Palladium acetate (0.50 g, 2.23 mmol) was added in one portion under a flow of nitrogen and the reaction mixture stirred at 40 ºC for 5 h. After cooling down to rt, the mixture was filtered, the solid washed copiously with water and acetone and dried under high vacuum at rt for 24 h. Elemental analysis: C (%) calculated 71.02 found 74.12, H (%) calculated 4.91, found 5.12.

Ligand synthesis

Ligands were synthesized following literature procedures:

General procedures for the synthesis of \(N\)-(2-bromophenyl)cyclopropylamides (1)


Synthesis of II – Removal of the tert-butyl group was performed according to a literature report (A. Mehta, R. Jaouhari, T. J. Benson, K. T. Douglas, *Tetrahedron Lett.* 1992, 33, 5441.) The thus obtained carboxylic acid (1.0 eq.) was dissolved in DCM (0.3 M). Two drops of DMF were added and the reaction mixture was cooled to 0 °C. Oxalyl chloride (1.1 eq.) was added and the reaction mixture stirred at 23 °C until gas evolution ceased. This mixture was then added to a stirred solution of ortho-bromoaniline (1.2 eq.) and triethylamine (2.5 eq.) in DCM (0.3 M) at 0 °C. After stirring at 0 °C for 5 minutes, DMAP (5-10 mol%) was added. The reaction mixture was stirred overnight at 23 °C and quenched by pouring into 0.5 M aq. HCl. Et\(_2\)O was added and the layers were separated. The organic layer was washed with 0.5 M aq. HCl and then with a 1/1 mixture of brine and aq. sat. NaHCO\(_3\). The organic layer was dried over MgSO\(_4\) and the solvent removed under reduced pressure. Purification by column chromatography on silica gel afforded II.

Synthesis of 1 – A suspension of NaH (2.0 eq.) in dry THF was cooled to 0 °C and a solution of amide II (1.0 eq.) in THF (0.2 M) was added dropwise. After 5 minutes, the corresponding alkyl iodide (4.0 eq.) was added and the reaction mixture was stirred overnight at 23 °C. When an alkyl bromide or chloride was used, KI (1.0 eq.) was initially added. The reaction was quenched by slowly pouring the reaction mixture to aq. sat. NaHCO\(_3\) at 0 °C and the aq. phase extracted with Et\(_2\)O. The combined org. phases were washed with aq. sat. Na\(_2\)S\(_2\)O\(_3\), brine, dried over MgSO\(_4\) and the solvent removed under reduced pressure. Purification by column chromatography on silica gel afforded the tertiary amides 1.
N-(2-bromophenyl)-N-ethyl-1-methylcyclopropanecarboxamide (1a):

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta = 7.68\) (d, \(J = 8.1\) Hz, 1H), 7.41–7.33 (m, 1H), 7.26–7.17 (m, 2H), 4.20 (dq, \(J = 14.1, 7.0\) Hz, 1H), 3.44–2.79 (m, 1H), 1.32–1.18 (m, 1H), 1.09 (t, \(J = 7.1\) Hz, 3H), 1.03–0.60 (m, 4H), 0.51–0.19 (m, 2H) ppm; \(^{13}\)C\(^{(1)}\)H NMR (101 MHz, CDCl\(_3\)) \(\delta = 174.0, 141.2, 133.8, 131.9, 129.1, 127.9, 124.0, 44.4, 21.6, 21.1, 16.4, 14.8, 12.4\) ppm; IR (ATR): \(\tilde{\nu} = 3062, 2974, 2933, 2873, 1646, 1584, 1474, 1448, 1391, 1324, 1271, 1246, 1227, 1134, 1119, 1058, 1029, 910, 727, 646, 589\) cm\(^{-1}\); HRMS (ESI) calculated for [C\(_{13}\)H\(_{17}\)\(^{79}\)BrNO\(^{+}\)] 282.0488, found 282.0487; \(R_f: 0.40\) (pentane/EtOAc 5/1); m.p.: 69–70 °C.

1-benzyl-N-(2-bromophenyl)-N-methylcyclopropanecarboxamide (1b):

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta = 7.64\) (d, \(J = 8.6\) Hz, 1H), 7.55–6.69 (m, 8H), 3.19 (s, 3H), 2.95 (d, \(J = 14.5\) Hz, 1H), 2.65–1.98 (m, 1H), 1.40–0.13 (m, 4H) ppm; \(^{13}\)C\(^{(1)}\)H NMR (101 MHz, CDCl\(_3\)) \(\delta = 173.5, 142.9, 138.5, 133.7, 130.3, 129.4, 128.2, 126.4, 123.0, 40.4, 38.0, 25.8, 14.4, 11.8\) ppm; IR (ATR): \(\tilde{\nu} = 3084, 3061, 3025, 3004, 2921, 2861, 1647, 1583, 1494, 1477, 1453, 1439, 1369, 1331, 1301, 1241, 1117, 1089, 1055, 1029, 989, 917, 764, 728, 701, 647, 586, 520, 484, 463, 429\) cm\(^{-1}\); HRMS (ESI) calculated for [C\(_{18}\)H\(_{19}\)\(^{79}\)BrNO\(^{+}\)] 344.0645, found 344.0633; \(R_f: 0.20\) (pentane/EtOAc 5/1).

N-(2-bromophenyl)-N-methyl-1-phenylcyclopropanecarboxamide (1c):

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta = 7.68–6.58\) (m, 9H), 3.17 (s, 3H), 1.77–0.80 (m, 4H) ppm; \(^{13}\)C\(^{(1)}\)H NMR (101 MHz, CDCl\(_3\)) \(\delta = 172.9, 142.3, 140.3, 133.3, 131.2, 128.8, 128.0, 128.0, 127.8, 126.0, 123.5, 37.8, 30.8, 15.7, 14.3 ppm; IR (ATR): \(\tilde{\nu} = 3083, 3058, 3024, 3010, 2931, 1649, 1600, 1583, 1495, 1477, 1443, 1418, 1358, 1301, 1228, 1132, 1118, 1097, 1075, 1056, 1029, 951, 937, 760, 739, 727, 698, 650, 607, 544, 489, 463, 395\) cm\(^{-1}\); HRMS (ESI) calculated for [C\(_{17}\)H\(_{17}\)\(^{79}\)BrNO\(^{+}\)] 330.0488, found 330.0496; \(R_f: 0.50\) (pentane/EtOAc 3/1).
N-(2-bromophenyl)-N,1-dimethylcyclopropanecarboxamide (1d):

\[ \text{HNMR (400 MHz, CDCl}_3\text{)} \delta = 7.67 (dd, J = 8.0, 1.0 Hz, 1H), 7.37 (td, J = 7.6, 1.4 Hz, 1H), 7.33-7.27 (m, 1H), 7.22 (td, J = 8.0, 1.5 Hz, 1H), 3.21 (s, 3H), 1.35–0.25 (m, 7H) ppm; \]

\[ \text{C}^{13}\text{ (HNMR (101 MHz, CDCl}_3\text{)} \delta = 174.6, 143.2, 133.8, 129.2, 128.4, 123.3, 57.9, 21.5, 20.9, 16.4, 14.9 ppm; \]

IR (ATR): \[ \tilde{\nu} = 3062, 3005, 2965, 2931, 2874, 1647, 1584, 1477, 1419, 1386, 1369, 1357, 1235, 1130, 1118, 1090, 1055, 1029, 766, 747, 729, 586 cm^{-1}; \]

HRMS (ESI) calculated for [C\(_{12}\)H\(_{15}\)BrNO\(^+\)] 268.0332, found 268.0329; \[ R_f : 0.35 \text{ (pentane/EtOAc 5/1); m.p.: 70-71 °C.} \]

N-(2-bromophenyl)-1-methyl-N-propylcyclopropanecarboxamide (1e):

\[ \text{HNMR (400 MHz, CDCl}_3\text{)} \delta = 7.70 (d, J = 7.9 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.30-7.22 (m, 2H), 4.27–4.00 (m, 1H), 3.21–2.81 (m, 1H), 1.67–0.71 (m, 10H), 0.49–0.20 (m, 2H) ppm; \]

\[ \text{C}^{13}\text{ (HNMR (126 MHz, CDCl}_3\text{)} \delta = 174.0, 141.5, 133.8, 131.9, 129.1, 127.9, 124.0, 51.2, 21.7, 21.2, 20.5, 16.5, 14.8, 11.3 ppm; \]

IR (ATR): \[ \tilde{\nu} = 3063, 2963, 2933, 2874, 1648, 1583, 1474, 1433, 1390, 1327, 1282, 1223, 1140, 1121, 1061, 1029, 944, 769, 745, 729, 610, 450 cm^{-1}; \]

HRMS (ESI) calculated for [C\(_{14}\)H\(_{19}\)BrNO\(^+\)] 296.0645, found 296.0644; \[ R_f : 0.45 \text{ (pentane/EtOAc 5/1); m.p.: 34-35 °C.} \]

N-(2-bromophenyl)-N-(4-methoxybenzyl)-1-methylcyclopropanecarboxamide (1f):

\[ \text{HNMR (400 MHz, CDCl}_3\text{)} \delta = 7.67 (dd, J = 5.8, 3.4 Hz, 1H), 7.23–7.09 (m, 2H), 7.10–7.01 (m, 2H), 6.83–6.69 (m, 3H), 5.60 (d, J = 14.3 Hz, 1H), 4.09–3.87 (m, 1H), 3.76 (s, 3H), 1.38–1.25 (m, 1H), 1.18–0.50 (m, 4H), 0.49–0.13 (m, 2H) ppm; \]

\[ \text{C}^{13}\text{ (HNMR (101 MHz, CDCl}_3\text{)} \delta = 174.1, 158.9, 140.7, 133.7, 132.6, 130.6, 129.4, 129.2, 127.6, 123.8, 113.6, 55.2, 52.0, 21.7, 21.2, 16.4, 14.9 ppm; \]

IR (ATR): \[ \tilde{\nu} = 3063, 3001, 2960, 2934, 2876, 2835, 1645, 1611, 1584, 1511, 1473, 1439, 1389, 1323, 1302, 1246, 1229, 1175, 1109, 1060, 1031, 991, 946, 847, 801, 760, 741, 729, 706, 646, 616, 569, 549, 521, 451, 396 cm^{-1}; \]

HRMS (ESI) calculated for [C\(_{19}\)H\(_{21}\)BrNO\(^2\)] 374.0750, found 374.0737; \[ R_f : 0.10 \text{ (pentane/EtOAc 5/1); m.p.: 93-94 °C.} \]
N-(2-bromophenyl)-N-(2-methoxybenzyl)-1-methylcyclopropanecarboxamide (1g):

\[ {^1}H\text{ NMR (400 MHz, CDCl}_3\text{)} \delta = 7.73–7.55 (m, 1H), 7.39–7.23 (m, 1H), 7.22–7.16 (m, 1H), 7.16–7.04 (m, 2H), 6.97–6.79 (m, 2H), 6.72 (d, \text{J}_1 = 8.2 Hz, 1H), 5.47 (d, \text{J}_1 = 14.5 Hz, 1H), 4.63–4.19 (m, 1H), 3.54 (s, 3H), 1.35–1.22 (m, 1H), 1.22–0.54 (m, 4H), 0.52–0.09 (m, 2H) ppm; \{^{13}C\} {^1}H\text{ NMR (101 MHz, CDCl}_3\text{)} \delta = 174.1, 157.6, 141.1, 133.2, 132.1, 130.8, 128.9, 128.6, 127.3, 125.3, 124.3, 120.4, 110.0, 54.9, 46.9, 21.8, 21.3, 16.1, 14.8 ppm; IR (ATR) \nu = 3065, 3003, 2960, 2936, 2836, 1646, 1601, 1586, 1492, 1474, 1438, 1389, 1245, 1201, 1174, 1161, 1149, 1097, 987, 945, 807, 754, 726, 705, 626, 590, 453 cm\text{ }^{-1}; \text{HRMS (ESI) calculated for [C}_{19}H_{21}BrNO}_2^+ 374.0750, found 374.0740; R_f: 0.45 (pentane/EtOAc 5/1); m.p.: 81–82 °C.}

N-(2-bromophenyl)-1-methylcyclopropanecarboxamide (1h):

\[ {^1}H\text{ NMR (400 MHz, CDCl}_3\text{)} \delta = 8.41 (dd, \text{J}_1 = 8.3, 1.6 Hz, 1H), 8.18 (s, 1H), 7.56 (dd, \text{J}_1 = 8.0, 1.5 Hz, 1H), 7.33 (ddd, \text{J}_1 = 8.0, 7.5, 1.5 Hz, 1H), 6.98 (dddd, \text{J}_1 = 8.0, 7.5, 1.6 Hz, 1H), 1.56 (s, 3H), 1.36 (q, \text{J}_1 = 4.0 Hz, 2H), 0.76 (q, \text{J}_1 = 3.9 Hz, 2H) ppm; \{^{13}C\} {^1}H\text{ NMR (101 MHz, CDCl}_3\text{)} \delta = 173.3, 135.9, 128.4, 124.8, 121.4, 113.3, 20.3, 19.6, 17.0 ppm; IR (ATR) \nu = 3418, 3006, 2965, 2875, 1685, 1587, 1522, 1470, 1432, 1388, 1316, 1282, 1244, 1163, 1120, 1023, 929, 796, 751, 663, 566, 533, 436 cm\text{ }^{-1}; \text{HRMS (ESI) calculated for [C}_{11}H_{13}BrNO}_2^+ 254.0175, found 254.0173; R_f: 0.50 (pentane/EtOAc 10/1).}

N-(2-bromo-4-(trifluoromethoxy)phenyl)-N,1-dimethylcyclopropanecarboxamide (1i):

\[ {^1}H\text{ NMR (400 MHz, CDCl}_3\text{)} \delta = 7.55 (s, 1H), 7.37–7.19 (m, 2H), 3.24 (s, 3H), 1.52–0.21 (m, 7H) ppm; \{^{13}C\} {^1}H\text{ NMR (101 MHz, CDCl}_3\text{)} \delta = 174.4, 148.3, 141.9, 130.9, 126.2, 123.8, 120.7, 120.2 (q, \text{J}_{C-F} = 258.9 Hz), 37.9, 21.4, 20.8, 15.8, 14.7 ppm; IR (ATR) \nu = 3086, 2971, 2935, 2880, 1655, 1595, 1575, 1489, 1424, 1387, 1357, 1253, 1217, 1170, 1124, 1090, 1052, 943, 910, 881, 832, 677, 596, 457 cm\text{ }^{-1}; \text{HRMS (ESI) calculated for [C}_{13}H_{14}BrF_3NO}_2^+ 352.0155, found 352.0173; R_f: 0.55 (pentane/EtOAc 2/1); m.p.: 37-38 °C.}
**N-(2-bromo-4-methylphenyl)-N,1-dimethylcyclopropanecarboxamide (1j):**

\[ \text{\textsuperscript{1}H NMR (400 MHz, CDCl}_3 \text{)} \delta = 7.48 (s, 1H), 7.20-7.10 (m, 2H), 3.17 (s, 3H), 2.36 (s, 3H), 1.39-0.70 (m, 5H), 0.56-0.11 (m, 2H) ppm; \text{\textsuperscript{13}C\textsuperscript{1}H) NMR (101 MHz, CDCl}_3 \text{)} \delta = 174.7, 140.5, 139.6, 134.1, 129.9, 129.1, 122.9, 38.0, 21.6, 20.9, 20.8, 16.4, 14.9 ppm; \text{IR (ATR): } \tilde{\nu} = 3006, 2963, 2927, 2873, 1649, 1600, 1494, 1469, 1420, 1386, 1360, 1316, 1282, 1237, 1126, 1089, 1055, 1021, 946, 914, 871, 847, 826, 748, 671, 587, 515, 455, 418 \text{ cm}^{-1}; \text{HRMS (ESI) calculated for } [\text{C}_{13}\text{H}_{17}\text{BrNO}]^+ 282.0488, \text{ found 282.0491}; \text{Rf}: 0.40 (pentane/EtOAc 2/1); \text{m.p.: 46-47 °C.} \]

**N-(2-bromo-5-(trifluoromethyl)phenyl)-N,1-dimethylcyclopropanecarboxamide (1k):**

\[ \text{\textsuperscript{1}H NMR (400 MHz, CDCl}_3 \text{)} \delta = 7.81 (d, J = 8.3 Hz, 1H), 7.55 (s, 1H), 7.48 (d, J = 8.3 Hz, 1H), 3.28 (s, 3H), 1.38-0.31 (m, 7H) ppm; \text{\textsuperscript{13}C\textsuperscript{1}H) NMR (101 MHz, CDCl}_3 \text{)} \delta = 174.4, 143.8, 134.5, 131.1 (q, J_{C-F} = 33.5 Hz), 127.4, 127.3, 125.7 (q, J_{C-F} = 3.7 Hz), 123.4 (q, J_{C-F} = 272.6 Hz), 37.8, 21.3, 20.8, 16.0, 14.6 ppm; \text{IR (ATR): } \tilde{\nu} = 3068, 2972, 2934, 2913, 2883, 1655, 1603, 1575, 1480, 1415, 1387, 1333, 1297, 1257, 1235, 1172, 1128, 1078, 1048, 1029, 935, 897, 829, 748, 734, 711, 570, 519, 458, 418 \text{ cm}^{-1}; \text{HRMS (ESI) calculated for } [\text{C}_{13}\text{H}_{14}\text{BrF}_3NO]^+ 336.0205, \text{ found 336.0211}; \text{Rf}: 0.50 (pentane/EtOAc 2/1); \text{m.p.: 86-87 °C.} \]

**N-(2-bromo-5-methylphenyl)-N,1-dimethylcyclopropanecarboxamide (1l):**

\[ \text{\textsuperscript{1}H NMR (400 MHz, CDCl}_3 \text{)} \delta = 7.51 (d, J = 8.1 Hz, 1H), 7.09 (s, 1H), 7.02 (d, J = 8.1 Hz, 1H), 3.19 (s, 3H), 2.33 (s, 3H), 1.49-0.71 (m, 5H), 0.64-0.09 (m, 2H) ppm; \text{\textsuperscript{13}C\textsuperscript{1}H) NMR (101 MHz, CDCl}_3 \text{)} \delta = 174.5, 142.8, 138.7, 133.3, 130.9, 130.0, 119.6, 37.9, 21.6, 20.9, 20.8, 16.4, 14.8 ppm; \text{IR (ATR): } \tilde{\nu} = 3006, 2963, 2925, 2873, 1649, 1594, 1571, 1477, 1421, 1405, 1385, 1358, 1316, 1283, 1262, 1238, 1197, 1123, 1089, 1056, 1028, 941, 849, 811, 749, 730, 597, 563, 508, 456 \text{ cm}^{-1}; \text{HRMS (ESI) calculated for } [\text{C}_{13}\text{H}_{17}\text{BrNO}]^+ 282.0488, \text{ found 282.0492}; \text{Rf}: 0.45 (pentane/EtOAc 2/1); \text{m.p.: 66-67 °C.} \]
N-(2-bromo-4-chloro-6-fluorophenyl)-N,1-dimethylcyclopropanecarboxamide (1m):

\[ \text{\textsuperscript{1}H NMR}\ (400\ MHz,\ CDCl}_3)\ (\text{mixture\ of\ rotamers\ in\ ratio\ }= 2/1)\ \delta = 7.51\ (s,\ 0.7H),\ 7.44\ (s,\ 0.3H),\ 7.21\ (dd,\ J = 8.7,\ 1.9\ Hz,\ 0.7H),\ 7.17 - 7.11\ (m,\ 0.3H),\ 3.41\ (s,\ 1H),\ 3.12\ (s,\ 2H),\ 1.49\ (s,\ 1H),\ 1.28-1.07\ (m,\ 2H),\ 0.90\ (s,\ 2H),\ 0.69\ (s,\ 0.7H),\ 0.37\ (s,\ 1.3H)\ ppm; \text{\textsuperscript{13}C}{\text{\textsuperscript{1}H}}\ NMR\ (101\ MHz,\ CDCl}_3)\ \delta = 174.7,\ 173.8,\ 159.0\ (d,\ J_{CF} = 255.5\ Hz),\ 158.8\ (d,\ J_{CF} = 255.5\ Hz),\ 135.1\ (d,\ J_{CF} = 11.2\ Hz),\ 134.5\ (d,\ J_{CF} = 11.2\ Hz),\ 131.0\ (d,\ J_{CF} = 15.7\ Hz),\ 130.0\ (d,\ J_{CF} = 15.7\ Hz),\ 129.0\ (d,\ J_{CF} = 3.7\ Hz),\ 128.7\ (d,\ J_{CF} = 3.7\ Hz),\ 125.7,\ (d,\ J_{CF} = 1.3\ Hz),\ 124.5\ (d,\ J_{CF} = 2.5\ Hz),\ 116.8\ (d,\ J_{CF} = 24.5\ Hz),\ 116.8\ (d,\ J_{CF} = 24.2\ Hz),\ 37.0,\ 36.8\ (d,\ J_{CF} = 1.1\ Hz),\ 21.3\ (d,\ J_{CF} = 0.7\ Hz),\ 20.9,\ 20.7,\ 20.5,\ 15.6\ (d,\ J_{CF} = 3.6\ Hz),\ 15.3,\ 13.2,\ 12.8\ ppm; \text{IR (ATR):}\ \tilde{\nu} = 3083,\ 3000,\ 2967,\ 2933,\ 2875,\ 1666,\ 1606,\ 1583,\ 1485,\ 1460,\ 1387,\ 1374,\ 1354,\ 1247,\ 1194,\ 1119,\ 1107,\ 1081,\ 992,\ 925,\ 903,\ 869,\ 846,\ 800,\ 760,\ 733,\ 663,\ 578,\ 526,\ 429\ cm\ ^{-1}; \text{HRMS (ESI) calculated for} [\text{C}_{12}\text{H}_{13}\text{BrClFNO}]^+\ 319.9848,\ \text{found}\ 319.9853; R_f: 0.25\ (pentane/EtOAc 10/1).

N-(2-bromopyridin-3-yl)-N,1-dimethylcyclopropanecarboxamide (1n):

\[ \text{\textsuperscript{1}H NMR}\ (400\ MHz,\ CDCl}_3)\ \delta = 8.36\ (dd,\ J = 4.7,\ 1.8\ Hz,\ 1H),\ 7.60\ (dd,\ J = 7.7,\ 1.7\ Hz,\ 1H),\ 7.35\ (dd,\ J = 7.7,\ 4.7\ Hz,\ 1H),\ 3.28\ (s,\ 3H),\ 1.33-0.81\ (m,\ 5H),\ 0.64-0.31\ (m,\ 2H)\ ppm; \text{\textsuperscript{13}C}{\text{\textsuperscript{1}H}}\ NMR\ (101\ MHz,\ CDCl}_3)\ \delta = 174.3, 148.9,\ 143.3,\ 140.6,\ 138.3,\ 123.4,\ 37.8,\ 21.4,\ 20.7,\ 15.5,\ 14.5\ ppm; \text{IR (ATR):}\ \tilde{\nu} = 3050,\ 3006,\ 2968,\ 2931,\ 2875,\ 1650,\ 1470,\ 1449,\ 1399,\ 1368,\ 1281,\ 1242,\ 1202,\ 1137,\ 1117,\ 1090,\ 1070,\ 1053,\ 1022,\ 943,\ 908,\ 812,\ 747,\ 729,\ 695,\ 659,\ 639,\ 600,\ 561,\ 513,\ 481,\ 431\ cm\ ^{-1}; \text{HRMS (ESI) calculated for} [\text{C}_{11}\text{H}_{14}\text{BrN}_2\text{O}]^+\ 269.0284,\ \text{found}\ 269.0275; R_f: 0.35\ (pentane/EtOAc 1/1).

N-(2-bromophenyl)-N-methyl-1-(trimethylsilyl)cyclopropanecarboxamide (1o):

\[ \text{\textsuperscript{1}H NMR}\ (400\ MHz,\ CDCl}_3)\ \delta = 7.62\ (dd,\ J = 8.0,\ 1.2\ Hz,\ 1H),\ 7.34\ (td,\ J = 7.7,\ 1.4\ Hz,\ 1H),\ 7.25-7.12\ (m,\ 2H),\ 3.57-3.05\ (m,\ 3H),\ 1.42-0.99\ (m,\ 2H),\ 0.98-0.65\ (m,\ 2H),\ 0.15\ (s,\ 9H)\ ppm; \text{\textsuperscript{13}C}{\text{\textsuperscript{1}H}}\ NMR\ (101\ MHz,\ CDCl}_3)\ \delta = 176.5,\ 145.2,\ 135.7,\ 131.8,\ 131.0,\ 130.8,\ 124.9,\ 40.6,\ 16.9,\ 12.8,\ 12.8,\ 0.0\ ppm; \text{IR (ATR):}\ \tilde{\nu} = 3067,\ 2988,\ 2956,\ 2900,\ 1638,\ 1583,\ 1478,\ 1429,\ 1394,\ 1363,\ 1284,\ 1250,\ 1197,\ 1114,\ 1081,\ 1040,\ 1028,\ 936,\ 840,\ 761,\ 729,\ 691,\ 653,\ 615,\ 479\ cm\ ^{-1}; \text{HRMS (ESI) calculated for} [\text{C}_{14}\text{H}_{21}\text{BrNOSi}]^+\ 326.0570,\ \text{found}\ 326.0567; R_f: 0.20\ (pentane/EtOAc 5/1).
N-(2-bromobenzyl)-N-(2-bromophenyl)-1-methylcyclopropanecarboxamide (1p):

\[ \begin{align*}
\text{1H NMR} \ (400 \text{ MHz, CDCl}_3) \ & \delta = 7.71-7.62 \ (m, \ 1H), \ 7.43 \ (dd, \ J = 8.0, \ 1.1 \ Hz, \ 1H), \ 7.39 \ (dd, \ J = 7.7, \ 1.6 \ Hz, \ 1H), \ 7.21 \ (td, \ J = 7.5, \ 1.2 \ Hz, \ 1H), \ 7.19-7.11 \ (m, \ 2H), \ 7.07 \ (td, \ J = 7.7, \ 1.7 \ Hz, \ 1H), \ 6.94-6.88 \ (m, \ 1H), \ 5.65 \ (d, \ J = 14.8 \ Hz, \ 1H), \ 4.45 \ (d, \ J = 13.9 \ Hz, \ 1H), \ 1.37-1.28 \ (m, \ 1H), \ 1.11-0.79 \ (m, \ 4H), \ 0.52-0.21 \ (m, \ 2H) \ ppm; \ \text{13C}^{1}H) \text{ NMR} \ (101 \text{ MHz, CDCl}_3) \ & \delta = 174.2, \ 140.4, \ 136.4, \ 133.6, \ 132.6, \ 132.2, \ 131.1, \ 129.4, \ 129.0, \ 127.7, \ 127.5, \ 124.5, \ 124.4, \ 51.6, \ 21.8, \ 21.3, \ 16.1, \ 14.9 \ ppm; \ \text{IR (ATR)}: \ \tilde{\nu} = 3064, \ 3007, \ 2978, \ 2963, \ 2874, \ 1649, \ 1584, \ 1473, \ 1439, \ 1388, \ 1321, \ 1278, \ 1227, \ 1191, \ 1028, \ 988, \ 766, \ 747, \ 732, \ 624, \ 578, \ 451 \ cm^{-1}; \ \text{HRMS (ESI)} \ & \text{calculated for} \ [\text{C}_{18}\text{H}_{18}\text{Br}_{2}\text{NO}]^{+} \ 421.9750, \ \text{found} \ 421.9750; \ \text{Rf}: \ 0.45 \ (\text{pentane/EtOAc} \ 5/1); \ \text{m.p.}: \ 89-90 \ ^\circ\text{C}.
\end{align*} \]

General procedure for the enantioselective synthesis of cyclopropane containing dihydroquinolones (2):

Pd(dba)\textsubscript{2} \ (1.15 mg, \ 2.00 \mu\text{mol}, \ 2.0 \text{ mol\%}), \ \textbf{L2} \ (2.60 mg, \ 4.00 \mu\text{mol}, \ 4.0 \text{ mol\%}), \ N-(2-bromoaryl)cyclopropanecarboxamide \ (1, \ 100 \mu\text{mol}), \ PivOH \ (3.07 mg, \ 30.0 \mu\text{mol}, \ 30 \text{ mol\%}) \ and \ Cs\textsubscript{2}CO\textsubscript{3} \ (49.0 mg, \ 0.15 mmol, \ 1.5 \text{ eq.}) \ were \ weighed \ into \ a \ vial \ equipped \ with \ a \ magnetic \ stirring \ bar. \ The \ vial \ was \ sealed \ with \ a \ rubber \ septum, \ evacuated \ and \ then \ backfilled \ with \ nitrogen \ three \ times. \ Mesitylene \ (330 \mu\text{L}, \ 0.30 \text{ M}) \ was \ added. \ The \ reaction \ mixture \ was \ degassed \ by \ three \ freeze-pump-thaw \ cycles \ and \ then \ stirred \ at \ 130 \ ^\circ\text{C}. \ After \ 12 \text{ h}, \ the \ reaction \ mixture \ was \ cooled \ to \ rt \ and \ directly \ purified \ by \ chromatography \ column \ on \ silica \ gel \ to \ afford \ the \ desired \ dihydroquinolone \ 2.
(1aR,7bR)-3-ethyl-1a-methyl-3,7b-dihydro-1H-cyclopropa[c]quinolin-2(1aH)-one (2a):

95%isol. yield. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta = 7.33\) (dd, \(J = 7.4, 1.6\) Hz, 1H), 7.21 (ddd, \(J = 8.3, 7.5, 1.6\) Hz, 1H), 7.01 (td, \(J = 7.4, 1.0\) Hz, 1H), 6.94 (d, \(J = 8.3\) Hz, 1H), 4.03 (dq, \(J = 14.2, 7.1\) Hz, 1H), 3.93 (dq, \(J = 14.2, 7.1\) Hz, 1H), 2.35 (dd, \(J = 8.5, 5.1\) Hz, 1H), 1.48 (s, 3H), 1.36 (dd, \(J = 8.6, 4.3\) Hz, 1H), 1.23 (t, \(J = 7.1\) Hz, 3H), 0.70 (t, \(J = 4.7\) Hz, 1H) ppm; \(^{13}\)C\(^{(1)}\)H NMR (101 MHz, CDCl\(_3\)) \(\delta = 170.8, 136.0, 127.0, 126.7, 125.0, 122.0, 114.1, 37.1, 27.8, 24.2, 20.5, 19.1, 12.3\) ppm; IR (ATR): \(\tilde{\nu} = 2971, 2932, 1650, 1601, 1501, 1465, 1448, 1395, 1371, 1263, 1206, 1135, 1116, 1091, 1015, 910, 820, 792, 749, 679, 485, 452\) cm\(^{-1}\); HRMS (ESI) calculated for [C\(_{13}\)H\(_{16}\)NO]\(^+\) 202.1225, found 202.1226; \(R_f: 0.40\) (pentane/EtOAc 5/1); \([\alpha]_{D}^{20} = +78.5\) (c = 1.0, CHCl\(_3\)). Chiral HPLC: (Chiralpak ID, 4.6 x 250 mm; 2% i-PrOH / hexane, 1.0 mL/min, 254 nm; t\(_i\) (minor) = 14.1 min, t\(_i\) (major) = 15.5 min), 98.0/2.0 \(er\).
(1aS,7bR)-1a-benzyl-3-methyl-3,7b-dihydro-1H-cyclopropa[c]quinolin-2(1aH)-one (2b):

using [(η⁴-cinnamyl)Pd(Cp)] as the palladium source, 97% isol. yield. 

\(^1\text{H} \text{NMR} \) (400 MHz, CDCl\(_3\)) δ = 7.33–7.16 (m, 7H), 7.02 (td, \( J = 7.4, 1.0 \) Hz, 1H), 6.93 (d, \( J = 8.2 \) Hz, 1H), 3.77 (d, \( J = 14.7 \) Hz, 1H), 3.34 (s, 3H), 2.73 (d, \( J = 14.7 \) Hz, 1H), 2.42 (dd, \( J = 8.7, 5.3 \) Hz, 1H), 1.42 (dd, \( J = 8.8, 4.5 \) Hz, 1H), 0.78 (dd, \( J = 5.2, 4.6 \) Hz, 1H) ppm; 

\(^{13}\text{C}\{^1\text{H}\} \text{NMR} \) (101 MHz, CDCl\(_3\)) δ = 170.3, 138.4, 137.3, 129.5, 128.3, 127.9, 126.8, 126.4, 124.3, 122.3, 114.2, 38.9, 29.8, 28.8, 25.5, 17.2 ppm; 

**IR (ATR):** \( \tilde{\nu} = 3060, 3027, 2939, 2917, 1655, 1601, 1504, 1495, 1474, 1454, 1417, 1385, 1331, 1268, 1223, 1132, 1105, 1076, 1046, 1018, 912, 750, 680, 599, 570, 528, 488 cm\(^{-1}\); 

**HRMS (ESI) calculated for [C\(_{18}\)H\(_{18}\)NO]\(^+\) 264.1383, found 264.1373;** 

\( R_f \): 0.50 (pentane/EtOAc 3/1); \([\alpha]^{20}_D = +7.8 \) (c = 1.0, CHCl\(_3\)). Chiral HPLC: (Chiralpak ID, 4.6 x 250 mm; 10% i-ProOH / hexane, 1.0 mL/min, 214 nm; \( t \) (minor) = 12.4 min, \( t \) (major) = 14.4 min, 96.9/3.1 er.
(1aR,7bR)-3-methyl-1a-phenyl-3,7b-dihydro-1H-cyclopropa[c]quinolin-2(1aH)-one (2c):

using [(η^3-cinnamyl)Pd(Cp)] as the palladium source, 90% isol. yield. ^1H NMR (400 MHz, CDCl₃) δ = 7.46–7.26 (m, 7H), 7.09 (td, J = 7.4, 1.0 Hz, 1H), 7.02 (d, J = 8.2 Hz, 1H), 3.39 (s, 3H), 2.77 (dd, J = 9.0, 5.5 Hz, 1H), 2.60 (dd, J = 9.0, 4.5 Hz, 1H), 1.15 (dd, J = 5.4, 4.6 Hz, 1H) ppm; ^13C{^1H} NMR (101 MHz, CDCl₃) δ = 169.6, 139.7, 137.4, 130.2, 128.4, 127.9, 127.5, 127.1, 124.1, 122.5, 114.3, 33.7, 29.9, 28.0, 18.0 ppm; IR (ATR): \( \tilde{\nu} \approx 3057, 3027, 1970, 1940, 2888, 1600, 1501, 1473, 1446, 1416, 1391, 1350, 1299, 1134, 1102, 1044, 1006, 940, 776, 751, 698, 640, 604, 580, 548, 517, 482 \text{ cm}^{-1}; \) HRMS (ESI) calculated for [C_{17}H_{16}NO]^+ 250.1226, found 250.1227; \( R_f \): 0.25 (pentane/EtOAc 5/1); \([\alpha]_D^{20} = +44.5 (c = 1.0, \text{CHCl}_3)\). Chiral HPLC: (Chiralpak ID, 4.6 x 250 mm; 5% i-PrOH / hexane, 1.0 mL/min, 254 nm; tₘ (minor) = 26.1 min, tₘ (major) = 30.8 min), 95.3/4.7 er.
(1aR,7bR)-1a,3-dimethyl-3,7b-dihydro-1H-cyclopropa[c]quinolin-2(1aH)-one (2d):

90% isolated yield. ¹H NMR (400 MHz, CDCl₃) δ = 7.33 (dd, J = 7.4, 1.6 Hz, 1H), 7.22 (ddd, J = 8.2, 7.5, 1.6 Hz, 1H), 7.03 (td, J = 7.4, 1.0 Hz, 1H), 6.93 (d, J = 8.2 Hz, 1H), 3.34 (s, 3H), 2.38 (dd, J = 8.6, 5.2 Hz, 1H), 1.48 (s, 3H), 1.38 (dd, J = 8.6, 4.4 Hz, 1H), 0.76 (t, J = 4.8 Hz, 1H) ppm; ¹³C(¹H) NMR (101 MHz, CDCl₃) δ = 171.3, 137.4, 127.6, 126.7, 124.7, 112.3, 114.1, 29.7, 28.0, 24.3, 20.5, 19.3 ppm; IR (ATR): ν = 2968, 2931, 2899, 1655, 1601, 1504, n1474, 1417, 1370, 1350, 1303, 1261, 1227, 1132, 1110, 1040, 1006, 910, 750, 487, 449 cm⁻¹; HRMS (ESI) calculated for [C₁₂H₁₄NO]⁺ 188.1070, found 188.1069; Rᵣ: 0.30 (pentane/EtOAc 5/1); [α]D²⁰ = +88.8 (c = 1.0, CHCl₃). Chiral HPLC: (Chiralpak ID, 4.6 x 250 mm; 2% i-PrOH / hexane, 1.0 mL/min, 254 nm; tᵣ(minor) = 23.3 min, tᵣ(major) = 19.9 min), 97.6/2.4 er.

![Graph of HPLC results](image-url)
(1aR,7bR)-1a-methyl-3-propyl-3,7b-dihydro-1H-cyclopropa[c]quinolin-2(1aH)-one (2e):

92% isol. yield. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta = 7.34\) (d, \(J = 7.4\) Hz, 1H), 7.22 (t, \(J = 7.9\) Hz, 1H), 7.02 (t, \(J = 7.4\) Hz, 1H), 6.92 (d, \(J = 8.3\) Hz, 1H), 4.03–3.90 (m, 1H), 3.88–3.79 (m, 1H), 2.36 (dd, \(J = 8.4, 5.1\) Hz, 1H), 1.78–1.59 (m, 2H), 1.49 (s, 3H), 1.38 (dd, \(J = 8.5, 4.3\) Hz, 1H), 0.99 (t, \(J = 7.4\) Hz, 3H), 0.71 (t, \(J = 4.7\) Hz, 1H) ppm; \(^{13}\)C{\(^1\)H} NMR (101 MHz, CDCl\(_3\)) \(\delta = 171.0, 136.3, 127.9, 126.6, 125.0, 122.0, 114.2, 43.6, 27.8, 24.2, 20.5, 20.2, 19.1, 11.3\) ppm; IR (ATR): \(\tilde{\nu}\) = 2963, 2932, 2875, 1657, 1602, 1500, 1468, 1395, 1369, 1338, 1305, 1258, 1241, 1201, 1138, 1120, 941, 749, 680 cm\(^{-1}\); HRMS (ESI) calculated for [C\(_{14}\)H\(_{18}\)NO]: 216.1383, found: 216.1365; \(R_f\): 0.75 (pentane/EtOAc 5/1); \([\alpha]_D^{20} = +59.5\) (c = 1.0, CHCl\(_3\)). Chiral HPLC: (Chiralpak AYH, 4.6 x 250 mm; 2% i-PrOH / hexane, 1.0 mL/min, 254 nm; \(t_c\) (minor) = 9.6 min, \(t_c\) (major) = 11.8 min), 97.9/2.1 er.
(1aR,7bR)-3-(4-methoxybenzyl)-1a-methyl-3,7b-dihydro-1H-cyclopropa[c]quinolin-2(1aH)-one (2f); using ([η³-cinnamyl]Pd(Cp)) as the palladium source, 99% isol. yield. ¹H NMR (400 MHz, CDCl₃) δ = 7.31 (d, J = 7.4 Hz, 1H), 7.16–7.11 (m, 2H), 7.05 (t, J = 7.8 Hz, 1H), 6.96 (t, J = 7.4 Hz, 1H), 6.87–6.81 (m, 3H), 5.27 (d, J = 14.2 Hz, 1H), 4.99 (d, J = 15.4 Hz, 1H), 3.77 (s, 3H), 2.42 (dd, J = 8.5, 5.1 Hz, 1H), 1.55 (s, 3H), 1.44 (dd, J = 8.5, 4.4 Hz, 1H), 0.82 (t, J = 4.7 Hz, 1H) ppm; ¹³C{¹H} NMR (101 MHz, CDCl₃) δ = 171.5, 158.6, 136.4, 129.1, 127.7, 127.7, 126.6, 124.9, 122.3, 115.2, 114.1, 55.3, 45.2, 27.9, 24.3, 20.7, 19.4 ppm; IR (ATR): ν = 2997, 2966, 2932, 2904, 2835, 1655, 1603, 1585, 1512, 1469, 1395, 1368, 1333, 1302, 1248, 1182, 1125, 1111, 1033, 997, 889, 829, 808, 751, 680, 654, 630, 595, 570, 533, 509, 448 cm⁻¹; HRMS (ESI) calculated for [C₁₉H₂₀NO₂]+= 294.1489, found 294.1492; Rᵣ: 0.65 (pentane/EtOAc 3/1); [α]D²₀ = +14.3 (c = 1.0, CHCl₃). Chiral HPLC: (Chiralpak IB, 4.6 x 250 mm; 10% i-PrOH / hexane, 1.0 mL/min, 254 nm; tᵣ (minor) = 10.4 min, tᵣ (major) = 9.6 min), 97.7/2.3 er.

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(1aR,7bR)-3-(2-methoxybenzyl)-1a-methyl-3b-dihydro-1H-cyclopropa[c]quinolin-2(1aH)-one (2g): using [(η^3-cinnamyl)Pd(Cp)] as the palladium source, 97% isol. yield. ¹H NMR (400 MHz, CDCl₃) δ = 7.32 (dd, J = 7.4, 1.6 Hz, 1H), 7.20 (ddd, J = 8.8, 7.1, 2.1 Hz, 1H), 7.05 (ddd, J = 8.2, 7.5, 1.7 Hz, 1H), 6.96 (td, J = 7.4, 1.1 Hz, 1H), 6.90 (d, J = 8.0 Hz, 1H), 6.88–6.79 (m, 2H), 6.75 (d, J = 8.2 Hz, 1H), 5.32 (d, J = 17.0 Hz, 1H), 5.05 (d, J = 17.1 Hz, 1H), 3.93 (s, 3H), 2.44 (dd, J = 8.5, 5.1 Hz, 1H), 1.56 (s, 3H), 1.46 (dd, J = 8.5, 4.4 Hz, 1H), 0.86 (t, J = 4.7 Hz, 1H) ppm; ¹³C¹H NMR (101 MHz, CDCl₃) δ = 171.5, 156.7, 136.4, 127.9, 127.6, 126.7, 126.6, 124.8, 124.7, 122.2, 120.7, 115.3, 110.2, 55.4, 40.7, 27.9, 24.4, 20.7, 19.5 ppm; IR (ATR): ν = 3110, 3076, 3036, 2997, 2963, 2934, 2837, 1658, 1602, 1588, 1492, 1462, 1439, 1395, 1366, 1334, 1302, 1285, 1242, 1188, 1164, 1125, 1111, 1050, 1028, 999, 749, 679, 498, 452 cm⁻¹; HRMS (ESI) calculated for [C₁₉H₂₀NO₂]⁺ 294.1489, found 294.1485; Rf: 0.25 (pentane/EtOAc 5/1); [α]D²⁰ = +19.8 (c = 1.0, CHCl₃). Chiral HPLC: (Chiralpak IB, 4.6 x 250 mm; 10% i-PrOH / hexane, 1.0 mL/min, 254 nm; tᵣ (minor) = 11.7 min, tᵣ (major) = 9.0 min), 98.2/1.8 er.
(1aR,7bR)-1a,3-dimethyl-6-(trifluoromethoxy)-3,7b-dihydro-1H-cyclopropa[c]quinolin-2(1H)-one (2i): using [(η3-cinnamyl)Pd(Cp)] as the palladium source, 86% isol. yield. $^1$H NMR (400 MHz, CDCl$_3$) δ = 7.20 (d, J = 2.2 Hz, 1H), 7.07 (ddd, J = 9.0, 2.7, 0.8 Hz, 1H), 6.90 (d, J = 9.0 Hz, 1H), 3.33 (s, 3H), 2.36 (dd, J = 8.6, 5.1 Hz, 1H), 1.48 (s, 3H), 1.43 (dd, J = 8.6, 4.6 Hz, 1H), 0.80 (t, J = 4.8 Hz, 1H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) δ = 170.9, 144.0 (q, $J_{C}$F = 1.9 Hz), 136.2, 126.3, 120.5 (q, $J_{C}$F = 256.3 Hz), 120.5, 119.2, 114.9, 29.9, 27.7, 24.5, 20.3, 19.4 ppm; IR (ATR): $\tilde{\nu}$ = 2970, 2933, 2902, 1662, 1611, 1507, 1472, 1419, 1370, 1356, 1251, 1158, 1109, 981, 924, 883, 861, 809, 761, 703, 666, 564, 538, 489, 476, 460 cm$^{-1}$; HRMS (ESI) calculated for [C$_{13}$H$_{13}$F$_3$NO$_2$]$^+$ 272.0893, found 272.0898; R$_f$: 0.20 (pentane/EtOAc 5/1); [α]$_D^{20}$ = +65.2 (c = 1.0, CHCl$_3$). Chiral HPLC: (Chiralpak IB, 4.6 x 250 mm; 5% i-PrOH / hexane, 1.0 mL/min, 254 nm; t$_r$ (minor) = 8.2 min, t$_r$ (major) = 8.7 min), 95.1/4.9 er.

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(1aR,7bR)-1a,3,6-trimethyl-3,7b-dihydro-1H-cyclopropa[c]quinolin-2(1aH)-one (2j):

using [{η^3-cinnamyl}Pd(Cp)] as the palladium source, 94% isol. yield. ¹H NMR (400 MHz, CDCl₃) δ = 7.14 (d, J = 1.8 Hz, 1H), 7.01 (dd, J = 8.6, 1.7 Hz, 1H), 6.82 (d, J = 8.3 Hz, 1H), 3.32 (s, 3H), 2.32 (s, 3H), 2.32 (dd, J = 8.2, 5.2 Hz, 1H), 1.47 (s, 3H), 1.35 (dd, J = 8.6, 4.3 Hz, 1H), 0.73 (t, J = 4.7 Hz, 1H) ppm; ¹³C{¹H} NMR (101 MHz, CDCl₃) δ = 171.2, 135.1, 131.8, 128.3, 127.1, 124.6, 114.0, 29.7, 27.9, 24.2, 20.5, 20.4, 19.4 ppm; IR (ATR): υ = 2967, 2929, 2902, 1655, 1617, 1590, 1509, 1459, 1416, 1360, 1319, 1299, 1269, 1229, 1108, 1011, 899, 807, 760, 633, 533, 483, 442, 429, 405 cm⁻¹; HRMS (ESI) calculated for [C₁₃H₁₆NO]⁺: 202.1226, found: 202.1232; Rf: 0.30 (pentane/EtOAc 5/1); [α]D²⁰ = +92.8 (c = 1.0, CHCl₃). Chiral HPLC: (Chiralpak IB, 4.6 x 250 mm; 10% i-PrOH / hexane, 1.0 mL/min, 254 nm; tᵣ (minor) = 15.3 min, tᵣ (major) = 14.5 min), 96.2/3.8 er.
(1aR,7bR)-1a,3-dimethyl-5-(trifluoromethyl)-3,7b-dihydro-1H-cyclopropa[c]quinolin-2(1aH)-one (2k); using [(n^3-cinnamyl)Pd(Cp)] as the palladium source, 85% isol. yield. ^1H NMR (400 MHz, CDCl₃) δ = 7.43 (d, J = 7.8 Hz, 1H), 7.31–7.26 (m, 1H), 7.12 (s, 1H), 3.37 (s, 3H), 2.43 (dd, J = 8.7, 5.1 Hz, 1H), 1.50 (s, 3H), 1.47 (dd, J = 8.7, 4.5 Hz, 1H), 0.81 (t, J = 4.8 Hz, 1H) ppm; ^13C(^1H) NMR (101 MHz, CDCl₃) δ = 171.0, 137.9, 129.1 (q, J_C-F = 32.5 Hz), 128.6 (q, J_C-F = 1.4 Hz), 128.0, 124.1 (q, J_C-F = 272.0 Hz), 118.9 (q, J_C-F = 3.9 Hz), 110.8 (q, J_C-F = 3.9 Hz), 29.9, 27.8, 24.8, 20.3, 19.5 ppm; IR (ATR): ν = 2972, 2936, 2901, 1716, 1667, 1617, 1591, 1558, 1540, 1520, 1472, 1456, 1436, 1388, 1354, 1337, 1313, 1295, 1258, 1228, 1167, 1114, 1084, 1049, 1006, 928, 867, 823, 788, 700, 662, 649, 568, 493, 459, 418 cm⁻¹; HRMS (ESI) calculated for [C₁₃H₁₃F₃NO] + 256.0944, found 256.0951; Rf: 0.25 (pentane/EtOAc 5/1); m.p.: 73-74 °C; [α]_D^20 = +47.6 (c = 1.0, CHCl₃). Chiral HPLC: (Chiralpak IB, 4.6 x 250 mm; 5% i-PrOH / hexane, 1.0 mL/min, 294 nm; t_r (minor) = 7.3 min, t_r (major) = 7.6 min), 96.5/3.5 er.
(1aR,7bR)-1a,3,5-trimethyl-3,7b-dihydro-1H-cyclopropa[c]quinolin-2(1aH)-one (2l):

using [(η³-cinnamyl)Pd(Cp)] as the palladium source, 94% isol. yield. 

**H NMR** (400 MHz, CDCl₃) δ = 7.20 (d, J = 7.6 Hz, 1H), 6.86-6.82 (m, 1H), 6.75 (s, 1H), 3.33 (s, 3H), 2.36 (dd, J = 8.5, 5.1 Hz, 1H), 2.34 (m, 1H), 1.47 (s, 3H), 1.34 (dd, J = 8.5, 4.3 Hz, 1H), 0.72 (t, J = 4.7 Hz, 1H) ppm;

**13C{¹H} NMR** (101 MHz, CDCl₃) δ = 171.6, 137.4, 136.4, 127.5, 122.9, 121.8, 114.9, 29.7, 27.7, 24.1, 21.5, 20.5, 19.4 ppm; **IR (ATR):** ν = 3018, 2966, 2930, 1655, 1613, 1584, 1518, 1469, 1418, 1356, 1314, 1300, 1267, 1230, 1110, 1014, 932, 853, 815, 791, 763, 743, 685, 601, 584, 485, 601, 584, 485, 456, 408 cm⁻¹; **HRMS (ESI) calculated for [C₁₃H₁₆NO]⁺ 202.1226, found 202.1233;**

**Rf:** 0.15 (pentane/EtOAc 5/1); **m.p.:** 92-93 °C; [α]D²⁰ = +115.2 (c = 1.0, CHCl₃). Chiral HPLC: (Chiralpak ID, 4.6 x 250 mm; 10% i-PrOH / hexane, 1.0 mL/min, 254 nm; tᵣ (minor) = 10.1 min, tᵣ (major) = 9.0 min), 96.5/3.5 e.r.
(1aR,7bR)-6-chloro-4-fluoro-1a,3-dimethyl-3,7b-dihydro-1H-cyclopropa[c]quinolin-2(1aH)-one (2m): using [(η3-cinnamyl)Pd(Cp)] as the palladium source, 74% isol. yield. 

$^1$H NMR (400 MHz, CDCl$_3$) δ = 7.08 (dd, $J = 2.3, 1.3$ Hz, 1H), 6.96 (dd, $J = 13.9, 2.4$ Hz, 1H), 3.48 (d, $J = 9.1$ Hz, 3H), 2.32 (ddd, $J = 8.7, 5.1, 1.1$ Hz, 1H), 1.46 (s, 3H), 1.41 (dd, $J = 8.7, 4.5$ Hz, 1H), 0.83 (t, $J = 4.8$ Hz, 1H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) δ = 171.6, 150.3 (d, $J_{C-F} = 248.7$ Hz), 129.1 (d, $J_{C-F} = 3.3$ Hz), 127.4 (d, $J_{C-F} = 11.4$ Hz), 124.7 (d, $J_{C-F} = 6.0$ Hz), 123.4 (d, $J_{C-F} = 3.1$ Hz), 115.8 (d, $J_{C-F} = 28.1$ Hz), 34.0 (d, $J_{C-F} = 15.6$ Hz), 28.3 (d, $J_{C-F} = 2.9$ Hz), 24.7, 20.1, 19.5 ppm; IR (ATR): $\tilde{\nu} = 3083, 3000, 2933, 2904, 1666, 1606, 1583, 1485, 1460, 1387, 1374, 1354, 1247, 1194, 1119, 1107, 1081, 992, 925, 903, 869, 846, 800, 760, 733, 663, 603, 578, 526, 429$ cm$^{-1}$; HRMS (ESI) calculated for [C$_{12}$H$_{12}$ClFNO]$^{+}$ 240.0586, found 240.0576; $R_f$: 0.75 (pentane/EtOAc 3/1); $[\alpha]_D^{20}$ = +102.5 (c = 1.0, CHCl$_3$). Chiral HPLC: (Chiralpak AYH, 4.6 x 250 mm; 5% i-PrOH / hexane, 1.0 mL/min, 254 nm; $t_1$ (minor) = 12.8 min, $t_2$ (major) = 14.9 min), 94.5/5.5 er.
(6aR,7aS)-5,6a-dimethyl-7,7a-dihydro-5H-cyclopropa[c][1,5]naphthyridin-6(6aH)-one (2n): using 10 mol% Pd(dba)$_2$, 20 mol% L$_2$, 0.50 equiv. PivOH and 2.0 equiv. Cs$_2$CO$_3$, 15% isol. yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 8.22 (dd, $J$ = 3.8, 2.3 Hz, 1H), 7.27–7.22 (m, 2H), 3.32 (s, 3H), 2.83 (dd, $J$ = 8.8, 5.2 Hz, 1H), 1.60 (dd, $J$ = 8.9, 4.7 Hz, 1H), 1.53 (s, 3H), 0.92 (t, $J$ = 4.9 Hz, 1H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) $\delta$ = 170.2, 144.6, 140.6, 134.1, 121.9, 121.5, 29.5, 29.3, 25.8, 20.1, 19.1 ppm; IR (ATR): $\tilde{\nu}$ = 3438, 3087, 2973, 2934, 1661, 1585, 1554, 1456, 1417, 1372, 1352, 1281, 1249, 1208, 1140, 1112, 1043, 1004, 946, 911, 798, 760, 685, 621, 583, 545, 492, 450 cm$^{-1}$; HRMS (ESI) calculated for [C$_{11}$H$_{13}$N$_2$O]$^+$ 189.1022, found 189.1025; $R_f$: 0.60 (EtOAc); $[\alpha]_D^{20}$ = -15.4 (c = 0.2, CHCl$_3$). Chiral HPLC: (Chiralpak ID, 4.6 x 250 mm; 10% i-PrOH / hexane, 1.0 mL/min, 254 nm; t$_r$ (minor) = 27.5 min, t$_r$ (major) = 34.3 min), 54.7/45.3 er.
(1aS,7bR)-3-methyl-1a-(trimethylsilyl)-3,7b-dihydro-1H-cyclopropa[c]quinolin-2(1aH)-one (2o): using [(η3-cinnamyl)Pd(Cp)] as the palladium source, 13% isol. yield. 1H NMR (400 MHz, CDCl3) δ = 7.34 (dd, J = 7.4, 1.6 Hz, 1H), 7.22 (dd, J = 8.2, 7.5, 1.6 Hz, 1H), 7.02 (td, J = 7.4, 1.1 Hz, 1H), 6.92 (d, J = 8.2 Hz, 1H), 3.31 (s, 3H), 2.38 (dd, J = 8.0, 4.9 Hz, 1H), 1.44 (dd, J = 8.0, 4.0 Hz, 1H), 0.84 (dd, J = 4.9, 4.1 Hz, 1H), 0.14 (s, 9H) ppm; 13C{1H} NMR (101 MHz, CDCl3) δ = 172.0, 137.6, 128.1, 126.8, 124.4, 122.1, 114.0, 29.2, 23.9, 18.3, 14.5, -2.6 ppm; IR (ATR): ν = 2952, 2929, 2898, 1645, 1600, 1504, 1472, 1415, 1378, 1344, 1304, 1280, 1246, 1211, 1186, 1104, 1046, 1013, 939, 907, 841, 774, 749, 680, 629, 489 cm⁻¹; HRMS (ESI) calculated for [C14H20NOSi]⁺ 246.1309, found 246.1310; Rf: 0.70 (pentane/EtOAc 5/1); [α]D20 = +162.5 (c = 0.2, CHCl3). Chiral HPLC: Chiralpak ID, 4.6 x 250 mm; 10% i-PrOH / hexane, 1.0 mL/min, 254 nm; t, (minor) = 5.5 min, t, (major) = 6.0 min, 84.2/15.8 er.

Spectroscopic data for compound 5 was in complete agreement with the reported values: C. L. Ladd, D. Sustac Roman, A. B. Charette, Org. Lett. 2013, 15, 1350.
(3bR,4aR)-4a-methyl-4,4a-dihydro-3bH-cyclopropa[4,5]pyrido[3,2,1-de]phenanthridin-5(7H)-one (2p): using 4 mol% Pd(db)2, 8 mol% L2 and 2.5 equiv. Cs2CO3, 95% isol. yield. \( ^1H \) NMR (400 MHz, CD2Cl2) \( \delta = 7.74-7.68 \) (m, 2H), 7.40-7.25 (m, 4H), 7.08 (t, \( J = 7.7 \) Hz, 1H), 5.15 (d, \( J = 16.5 \) Hz, 1H), 4.76 (d, \( J = 16.4 \) Hz, 1H), 2.43 (dd, \( J = 8.5, 5.1 \) Hz, 1H), 1.48 (s, 3H), 1.45 (dd, \( J = 8.5, 4.4 \) Hz, 1H), 0.71 (t, \( J = 4.7 \) Hz, 1H) ppm; \( ^{13}C\{^1H\} \) NMR (101 MHz, CD2Cl2) \( \delta = 170.4, 132.8, 130.6, 130.2, 127.9, 127.9, 127.2, 126.6, 125.2, 122.6, 122.5, 122.2, 121.0, 45.0, 27.7, 24.9, 20.2, 19.6 ppm; \( \text{IR (ATR): } \tilde{\nu} = 3036, 2969, 2929, 2835, 1655, 1604, 1478, 1433, 1374, 1357, 1298, 1196, 1177, 1129, 755, 657, 601 \text{ cm}^{-1}; \) HRMS (ESI) calculated for [\( \text{C}_{18}\text{H}_{16}\text{NO}\)]\(^+\) 262.1226, found 262.1225; \( R_f \): 0.50 (pentane/EtOAc 5/1); \( [\alpha]_D^{20} = +9.5 \) (c = 1.0, CHCl3). Chiral HPLC: (Chiralpak IB, 4.6 x 250 mm; 10% \( \text{i-PrOH} / \text{hexane}, 1.0 \text{ mL/min}, 296 \text{ nm}; t_\text{r} \) (minor) = 10.6 min, \( t_\text{r} \) (major) = 16.9 min), 96.6/3.4 \text{ er}. 

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Cleavage of PBM-protecting group

\[
\text{O} \quad \text{PMB} \quad \text{N} \quad \text{O} \\
\text{2f} \quad \text{4 equiv anisole} \quad \text{TFA, 50°C} \quad \text{2h}
\]

Compound 2f (21.3 mg, 73.0 μmol) was weighed into a vial equipped with a magnetic stirring bar and sealed with a rubber septum. Anisole (32.0 μl, 4 equiv.) and TFA (1.45 mL) were added. The mixture was stirred at 50°C for 14 h and the volatiles removed under reduced pressure. Purification by column chromatography on silica gel afforded the free amide 2h (11.3 mg, 65.0 μmol, 90%) as a colourless oil.

(1aR,7bR)-1a-methyl-3,7b-dihydro-1H-cyclopropa[c]quinolin-2(1aH)-one (2h):

\(^1\text{H} \text{NMR} \) (400 MHz, CDCl\(_3\)) \( \delta = 8.50 \) (s, 1H), 7.31 (d, \( J = 7.5, 1.1 \) Hz, 1H), 7.13 (d, \( J = 7.7, 1.5 \) Hz, 1H), 6.99 (td, \( J = 7.5, 1.2 \) Hz, 1H), 6.80–6.75 (m, 1H), 2.36 (d, \( J = 8.6, 5.4 \) Hz, 1H), 1.47 (s, 3H), 1.45 (d, \( J = 8.6, 4.6 \) Hz, 1H), 0.85 (t, \( J = 4.9 \) Hz, 1H) ppm; \(^{13}\text{C}\{^1\text{H}\} \text{NMR} \) (101 MHz, CDCl\(_3\)) \( \delta = 172.6, 134.9, 127.4, 126.7, 123.6, 122.6, 115.1, 28.2, 24.1, 19.6, 19.1 \) ppm; IR (ATR): \( \tilde{\nu} = 3200, 3121, 3060, 2966, 2928, 2861, 1661, 1593, 1558, 1505, 1491, 1458, 1435, 1405, 1379, 1363, 1203, 1024, 942, 869, 829, 749, 673, 570, 528, 487, 446, 430 \) cm\(^{-1}\); HRMS (ESI) calculated for \([\text{C}_{11}\text{H}_{12}\text{NO}]^+\) 174.0913, found 174.0913; \( [\alpha]_D^{20} = +67.5 \) (c = 1.0, CHCl\(_3\)); \( R_f: 0.15 \) (pentane/EtOAc 3/1).

Determination of the absolute configuration of the dihydroquinolones (2):

Amide 2c (22.0 mg, 88.0 μmol) was dissolved in DCM (880 μL) and DIBAL-H (1.2 M solution in toluene, 290 μL, 353 μmol) was added. The reaction was stirred at 23°C for 14 h,
quenched with a saturated solution of Rochelle’ salt (10 mL) and diluted with ether (25 mL). The biphasic mixture was vigorously stirred for 30 min. The organic layer was washed with aq. NaOH (0.5 M, 25 mL), brine (25 mL) and then dried over MgSO₄. The solvent was removed in vacuo and the residue was purified by chromatography on silica gel to afford 9 (15.2 mg, 65.0 μmol, 73%).

Compound 10 (68.5 mg, 194 μmol) was weighed into a vial equipped with a magnetic stirring bar, sealed with a rubber septum. The vial was evacuated and then backfilled with nitrogen. Dry toluene (1.45 mL) and Red-Al (3.5 M solution in toluene, 550 μL, 10.0 equiv.) were added. The reaction was stirred for 5 min at 23 °C and heated at 50 °C for 10 h. The reaction mixture was diluted with ether (50 mL) and poured into a saturated Rochelle’ salt solution (25 mL). After stirring for 20 min, the layers were separated and the organic layer was washed with aq. NaOH (2 M, 50 mL) and brine (50 mL). The organic layer was dried over MgSO₄ and evaporated in vacuo. Purification by column chromatography on silica gel afforded the free aniline in 99% yield. The thus obtained aniline (30.0 mg, 136 μmol) and NaBH(OAc)₃ (144 mg, 678 μmol, 4.9 eq.) were weighed into a vial equipped with a magnetic stirring bar, sealed with a rubber septum and dissolved in THF (2.7 mL). Aqueous CH₂O (37%, 600 μl, 8.13 mmol, 60 eq.) and AcOH (8.00 μL, 136 μmol, 1.0 eq.) were added and the mixture stirred at 23 °C for 14 h, then diluted with Et₂O (25 mL). The organic layer was washed with aq. NaOH (2 M, 25 mL), brine (25 mL) and then dried over MgSO₄. The solvent was removed in vacuo and the residue was purified by chromatography on silica gel to afford 9 (22.6 mg, 96.0 μmol, 71%).

(1aR,7bS)-3-methyl-1a-phenyl-1a,2,3,7b-tetrahydro-1H-cyclopropa[c]quino- line (9): ¹H-NMR (400 MHz, CDCl₃) δ = 7.45–7.39 (m, 2H), 7.39–7.33 (m, 2H), 7.31–7.24 (m, 2H), 7.18–7.12 (m, 1H), 6.80 (td, J = 7.4, 1.1 Hz, 1H), 6.68 (d, J = 8.0 Hz, 1H), 3.44 (d, J = 10.5 Hz, 1H), 3.18 (d, J = 10.5 Hz, 1H), 2.85 (s, 3H), 2.24 (dd, J = 8.9, 4.8 Hz, 1H), 2.02 (t, J = 4.5 Hz, 1H), 1.21 (ddd, J = 8.9, 4.1, 0.7 Hz, 1H) ppm; ¹³C(¹H) NMR (101 MHz, CDCl₃) δ = 144.5, 143.0, 128.5, 128.2, 127.8, 127.1, 126.7, 126.3, 118.3, 111.5, 54.9, 38.7, 34.2, 23.8, 14.7 ppm; IR (ATR): ν = 3057, 3023, 2950, 2852, 2800, 1602, 1579, 1498, 1477, 1452, 1422, 1390, 1365, 1327, 1285, 1239, 1202, 1136, 1121, 1096, 1077, 1043, 1030, 968, 938, 895, 861, 746, 720, 698, 639, 588, 555, 543, 514, 480 cm⁻¹; HRMS (ESI) calculated for [C₁₁H₁₈N⁺]+ 236.1434, found 236.1429; [α]₀ᵇ⁻²⁰ = +303 (c = 1.0, CHCl₃) from 2c; [α]₀ᵇ⁻²⁰ = +307 (c = 1.0, CHCl₃) from 10; Rf: 0.35 (pentane/EtOAc 5/1).
General procedures for the synthesis of 2-bromo benzamides (3)

1. Ti(OiPr)$_4$, R$_2^\text{NH}$
2. NaBH$_4$, EtOH


Synthesis of II — To a solution of I in THF (0.25 M) were added aldehyde (1.0 eq.) and Ti(OiPr)$_4$ (1.1 eq.) at rt and the mixture stirred overnight (12-16 h) under N$_2$. After addition of NaBH$_4$ (2.0 eq.) and EtOH (20 eq.) the mixture was stirred at rt for further 12-16 h, then cooled down to 0 °C, 6 M aq. HCl was added and the cooling bath removed after 30 min. After stirring for 1 h at rt the reaction mixture was basified with 10% aq. NaOH and extracted with DCM, the combined organic phases washed with brine and dried over Na$_2$SO$_4$, the solvent removed under reduced pressure and the crude product analysed by $^1$H NMR. If necessary, the crude product was purified by column chromatography on silica gel (eluent: DCM/MeOH/NH$_3$ 600/15/1 to 150/15/1).
Synthesis of III and IV (R² ≠ H)

a) X = Cl: to a solution of I or II in DCM (0.4 M) were added DIPEA (1.2 eq.) and acid chloride (1.0 eq.) at −20 °C and the reaction mixture allowed to warm up to rt within 3-4 h. After stirring for further 2-10 h at rt, the reaction mixture was diluted with Et₂O and washed successively with 2 M aq. HCl, aq. sat. NaHCO₃ and brine, the organic phase dried over MgSO₄ and the solvent removed under reduced pressure. The crude product was purified by column chromatography on silica gel (eluent: pentane/EtOAc 10/1 to 1/1).

b) X = OH: to a solution of primary or secondary amine in DCM (0.2 M) was added DIPEA (2.5 eq.), carboxylic acid (1.0 eq.), EDC·HCl (1.1 eq.) and HOBT (0.2 eq.) at 0 °C and the reaction mixture allowed to warm up to rt overnight. After stirring for further 5-7 h at rt, the reaction mixture was diluted with Et₂O and washed successively with 2 M aq. HCl, aq. sat. NaHCO₃ and brine, the organic phase dried over MgSO₄ and the solvent removed under reduced pressure. The crude product was purified by column chromatography on silica gel (eluent: pentane/EtOAc 10/1 to 1/1).

Synthesis of IV (R² = H)

A solution of III in THF (0.2 M) was added dropwise to a suspension of NaH (1.1 eq.) in THF (0.2 M) at 0 °C. After 30 min, MeI (1.2 eq) was added and the reaction mixture allowed to warm up to rt within 2-3 h and stirred for further 1-2 h. The reaction mixture was cooled to 0 °C and quenched with H₂O, the aq. phase extracted with Et₂O, the combined organic phases washed with brine and dried over MgSO₄ and the solvent removed under reduced pressure. The crude product was purified by column chromatography on silica gel (eluent: pentane/EtOAc 10/1 to 1/1).

2-bromo-N-cyclopropyl-N-methylbenzamide (3a):

Obtained as a yellow oil. \(^1\)H NMR (400 MHz, CDCl₃) (mixture of rotamers in ratio 3.8/1) δ 7.59 – 7.50 (m, 1H), 7.36 – 7.30 (m, 1H), 7.26 – 7.18 (m, 2H), 3.11 (s, 2.4H), 2.92 – 2.85 (m, 0.2H), 2.77 (s, 0.6H), 2.71 (dt, J = 11.4, 5.2 Hz, 0.8H), 1.00 - 0.73 (br m, 1H), 0.71 – 0.31 (m, 3H) ppm; \(^{13}\)C\(^{1}\)H NMR (101 MHz, CDCl₃) δ = 171.4, 170.9, 140.1, 139.1, 132.8, 132.7, 130.3, 130.0, 128.1, 127.9, 127.8, 127.3, 119.2, 36.5, 34.2, 32.1, 30.1 ppm; IR (ATR): \(^\tilde{\nu}\) 3012, 1642, 1590, 1454, 1424, 1384, 1364, 1289, 1106, 1024, 931, 859, 829, 768, 749, 702, 652, 575, 448, 411 cm\(^{-1}\); HRMS (ESI) calculated for [C\(_{11}\)H\(_{13}\)\(^{79}\)BrNO]\(^+\) 254.0175, found 254.0170; Rᵣ: 0.39 (pentane/EtOAc 1/1).
2-bromo-N-methyl-N-(1-(3-phenylpropyl)cyclopropyl)benzamide (3b):

Obtained as a colourless oil. $^1$H NMR (400 MHz, CDCl$_3$) (mixture of rotamers in ratio 4/1) δ 7.57 (d, $J = 9.1$ Hz, 0.2H), 7.53 (d, $J = 7.9$ Hz, 0.8H), 7.37 – 7.03 (m, 8H), 3.12 (s, 0.6H), 2.76 (s, 2.4H), 2.67 (t, $J = 7.1$ Hz, 1.6H), 2.59 (d, $J = 4.5$ Hz, 0.4H), 2.15 – 1.47 (m, 4H), 1.17 – 0.35 (m, 4H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) δ = 169.8, 142.5, 141.9, 139.9, 139.6, 133.0, 132.8, 130.0, 129.8, 128.6, 128.4, 127.9, 127.5, 126.8, 126.1, 125.8, 120.2, 119.0, 41.5, 40.2, 38.1, 36.7, 36.2, 36.0, 35.3, 28.7 ppm; IR (ATR): $\tilde{\nu}$ 2937, 1646, 1591, 1495, 1475, 1452, 1437, 1381, 1210, 1076, 1025, 768, 748, 699, 683, 635, 449 cm$^{-1}$; HRMS (ESI) calculated for [C$_{20}$H$_{23}$BrNO]$^+$ 372.0958, found 372.0955; R$_f$: 0.39 (pentane/EtOAc 3/1).

2-bromo-N-cyclopropyl-N-(4-methoxybenzyl)benzamide (3c):

Obtained as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) (mixture of rotamers in ratio 5/1) δ 7.57 – 7.52 (m, 1H), 7.39 (d, $J = 8.6$ Hz, 1.7H), 7.35 – 7.29 (m, 1.2H), 7.24 – 7.18 (m, 1.8H), 7.08 (d, $J = 8.6$ Hz, 0.3H), 6.88 (d, $J = 8.7$ Hz, 1.7H), 6.84 (d, $J = 8.6$ Hz, 0.3H), 4.71 (d, $J = 71.2$ Hz, 1.7H), 4.30 – 4.16 (m, 0.3H), 3.82 (s, 2.5H), 3.79 (s, 0.5H), 2.64 – 2.58 (m, 0.3H), 2.50 (ddd, $J = 11.5$, 7.0, 4.6 Hz, 0.7H), 1.03 – 0.39 (m, 4H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) δ = 171.3, 159.1, 140.0, 132.9, 130.1, 129.9, 129.8, 128.7, 128.1, 127.3, 119.3, 114.1, 113.9, 55.4, 52.7, 49.6, 30.5, 28.4 ppm; IR (ATR): $\tilde{\nu}$ 3007, 2937, 1643, 1612, 1588, 1512, 1432, 1402, 1302, 1287, 1247, 1176, 1109, 1029, 983, 833, 759, 605, 556 cm$^{-1}$; HRMS (ESI) calculated for [C$_{18}$H$_{19}$BrNO$_2$]$^+$ 360.0594, found 360.0599; R$_f$: 0.28 (pentane/EtOAc 3/1); m.p.: 67.6-71.2 °C.

2-bromo-N-cyclopropyl-N-(2,4,6-trimethylbenzyl)benzamide (3d):

Obtained as a colourless wax. $^1$H NMR (400 MHz, CDCl$_3$) (mixture of rotamers in ratio 7.3/1) δ 7.58 (d, $J = 8.0$ Hz, 1H), 7.38 – 7.26 (m, 2H), 7.24 – 7.17 (m, 1H), 6.88 (s, 1.75H), 6.81 (s, 0.25H), 5.38 – 4.09 (m, 2H), 2.45 – 2.23 (m, 10H), 0.86 – 0.79 (m, 1H), 0.39 – 0.14 (m, 3H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) δ = 170.5, 140.3, 138.2, 137.2, 133.2, 130.3, 130.0, 129.4, 127.9, 127.1, 119.9, 44.2, 30.0, 21.0, 20.5 ppm; IR (ATR): $\tilde{\nu}$ 2951, 2923, 1645, 1468, 1432, 1403, 1373, 1300, 1253, 1027, 769, 746, 400 cm$^{-1}$; HRMS (ESI) calculated for [C$_{20}$H$_{23}$BrNO]$^+$ 372.0958, found 372.0953; R$_f$: 0.28 (pentane/EtOAc 2/1).
2-bromo-N-cyclopropyl-N-methylbenzamide (3e):

Obtained as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) 7.56 (dd, $J = 8.0$, 0.9 Hz, 1H), 7.52 (dd, $J = 7.6$, 1.7 Hz, 1H), 7.34 (td, $J = 7.5$, 1.1 Hz, 1H), 7.29 – 7.22 (m, 1H), 6.06 (s, 1H), 2.92 (tq, $J = 7.1$, 3.7 Hz, 1H), 0.88 (dt, $J = 6.9$, 3.3 Hz, 2H), 0.69 – 0.64 (m, 2H) ppm; $^{13}$C{$_1$H} NMR (101 MHz, CDCl$_3$) $\delta$ = 169.1, 137.8, 133.4, 131.4, 129.7, 127.7, 119.4, 23.2, 6.9 ppm; IR (ATR): $\tilde{\nu}$ 3249, 1641, 1590, 1539, 1452, 1430, 1361, 1322, 1309, 1260, 859, 773, 756, 687 cm$^{-1}$; HRMS (ESI) calculated for [C$_{10}$H$_{11}$BrNO]$^+$ 240.0019, found 240.0013; R$_f$: 0.37 (pentane/EtOAc 1/1); m.p.: 121.3-123.2 °C.

2-bromo-N-(4-methoxybenzyl)-N-(1-(3-phenylpropyl)cyclopropyl)benzamide (3f):

Obtained as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) (mixture of rotamers in ratio 2.5/1) $\delta$ 7.61 – 7.56 (m, 0.25H), 7.50 – 7.45 (m, 0.75H), 7.35 – 6.96 (m, 9.5H), 6.86 (dd, $J = 13.6$, 8.6 Hz, 2H), 6.73 (d, $J = 8.7$ Hz, 1.5H), 5.11 (br s, 0.25H), 4.52 – 4.16 (m, 1.75H), 3.80 (s, 0.85H), 3.77 (s, 2.15H), 2.55 (t, $J = 7.5$ Hz, 2H), 2.07 – 0.69 (m, 8H) ppm; $^{13}$C{$_1$H} NMR (101 MHz, CDCl$_3$) $\delta$ = 170.5, 159.0, 158.7, 142.6, 139.3, 133.1, 132.6, 131.2, 130.4, 129.9, 129.8, 128.6, 128.4, 128.2, 127.4, 126.7, 126.1, 125.8, 119.0, 113.9, 55.4, 53.5, 40.7, 36.3, 36.2, 36.0, 28.6 ppm; IR (ATR): $\tilde{\nu}$ 2936, 1644, 1612, 1512, 1453, 1440, 1427, 1398, 1357, 1302, 1248, 1175, 1029, 771, 749, 700 cm$^{-1}$; HRMS (ESI) calculated for [C$_{27}$H$_{29}$BrNO$_2$]$^+$ 478.1376, found 478.1378; R$_f$: 0.32 (pentane/EtOAc 3/1); m.p.: 62.1-63.2 °C.

2-bromo-N-(1-isopropylcyclopropyl)-N-methylbenzamide (3g):

Obtained as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) (mixture of rotamers in ratio 9/1) $\delta$ 7.60 – 7.49 (m, 8.1 Hz, 1H), 7.37 – 7.30 (m, 1H), 7.23 – 7.15 (m, 2H), 3.14 (s, 0.3H), 2.80 (s, 2.7H), 1.92 (dt, $J = 13.8$, 6.9 Hz, 1H), 1.09 – 0.81 (m, 10H) ppm; $^{13}$C{$_1$H} NMR (101 MHz, CDCl$_3$) $\delta$ = 170.1, 132.9, 130.5, 129.9, 128.5, 127.9, 127.5, 126.1, 118.8, 44.8, 38.1, 34.3, 34.0, 20.1, 20.0 ppm; IR (ATR): $\tilde{\nu}$ 3013, 2963, 2872, 1652, 1591, 1468, 1439, 1378, 1209, 1077, 1026, 769, 749, 673, 636 cm$^{-1}$; HRMS (ESI) calculated for [C$_{14}$H$_{15}$BrNO]$^+$ 296.0645, found 296.0646; R$_f$: 0.53 (pentane/EtOAc 3/1); m.p.: 62.1-63.2 °C.
2-bromo-N-methyl-N-(1-phenylcyclopropyl)benzamide (3h): Obtained as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) (mixture of rotamers in ratio 2.0/1) δ 7.59 – 7.52 (m, 1H), 7.39 – 7.29 (m, 4.7H), 7.23 (ddd, J = 7.4, 4.9, 1.7 Hz, 1.7H), 7.12 (td, J = 7.8, 1.7 Hz, 0.3H), 7.00 – 6.92 (m, 1H), 6.86 (dd, J = 7.7, 1.6 Hz, 0.3H), 3.31 (s, 1H), 2.86 (s, 2H), 1.71 – 1.31 (m, 4.3H), 1.03 (s, 0.7H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) δ = 171.2, 170.0, 143.2, 140.9, 139.5, 139.1, 133.0, 132.9, 130.4, 130.0, 128.9, 128.7, 128.0, 128.0, 126.9, 126.8, 126.7, 126.4, 126.1, 123.8, 120.3, 119.2, 43.9, 42.3, 36.4, 35.2, 19.4, 17.6 ppm; IR (ATR): $\tilde{\nu}$ 3059, 1650, 1602, 1591, 1497, 1479, 1459, 1437, 1382, 1330, 1211, 1080, 1030, 751, 699, 680, 665, 636, 556 cm$^{-1}$; HRMS (ESI) calculated for [C$_{17}$H$_7^{79}$BrNO]$^+$ 330.0488, found 330.0490; R$_f$: 0.36 (pentane/EtOAc 3/1); m.p.: 72.6-73.7 °C.

2-bromo-N-(1-(4-chlorophenyl)cyclopropyl)-N-(4-methoxybenzyl)benzamide (3i): Obtained as a colourless wax. $^1$H NMR (400 MHz, CDCl$_3$) (mixture of rotamers in ratio 1/1) 7.59 – 7.55 (m, 0.5H), 7.51 (dd, J = 7.8, 1.1 Hz, 0.5H), 7.39 (d, J = 8.7 Hz, 1H), 7.33 – 7.29 (m, 2H), 7.25 – 7.12 (m, 3H), 7.00 (t, J = 7.5 Hz, 0.5H), 6.90 – 6.84 (m, 2H), 6.81 (d, J = 6.9 Hz, 0.5H), 6.72 (d, J = 8.7 Hz, 1H), 6.65 – 6.56 (m, 1H), 5.98 – 5.38 (br s, 0.5H), 4.49 – 4.02 (br m, 1.5H), 3.81 (s, 1.5H), 3.73 (s, 1.5H), 1.48 – 1.22 (m, 3H), 0.84 (br s, 1H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) δ = 171.9, 170.7, 159.1, 159.0, 142.4, 140.5, 139.3, 138.8, 133.1, 132.8, 132.6, 132.2, 130.5, 130.3, 130.1, 129.9, 129.2, 129.0, 128.5, 128.1, 127.7, 126.7, 126.7, 125.3, 120.2, 119.2, 114.0, 113.8, 55.4, 55.4, 53.2, 51.7, 43.6, 42.0 ppm; IR (ATR): $\tilde{\nu}$ 2932, 1644, 1612, 1588, 1512, 1492, 1463, 1428, 1396, 1359, 1329, 1303, 1248, 1176, 1109, 1096, 1031, 1011, 983, 946, 910, 821, 772, 752, 732, 698, 676, 646, 566, 527 cm$^{-1}$; HRMS (ESI) calculated for [C$_{24}$H$_{22}^{79}$BrCINO$_2$]$^+$ 470.0517, found 470.0519; R$_f$: 0.38 (pentane/EtOAc 3/1).

N-(1-benzylcyclopropyl)-2-bromo-N-methylbenzamide (3j): Obtained as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) (mixture of rotamers in ratio 4/1) δ = 7.58 (d, J = 7.8 Hz, 0.2H), 7.55 – 7.47 (m, 0.8H), 7.37 – 7.27 (m, 5H), 7.25 – 7.14 (m, 2H), 7.08 (m, 0.8H), 6.95 (br s, 0.2H), 3.35 (br s, 1H), 2.95 (s, 0.6H), 2.89 (br s, 1H), 2.37 (s, 2.4H), 1.17 – 0.24 (m, 4H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) δ = 170.7, 170.0, 139.4, 138.8, 137.4, 133.1, 132.9, 130.1, 130.0, 128.7, 128.4, 127.9, 127.6, 127.1, 126.8, 126.7, 119.0, 42.7, 41.7, 40.6, 36.8, 34.8 ppm; IR (ATR): $\tilde{\nu}$ 3026, 1648, 1591, 1494, 1478, 1454, 1440, 1383, 1075, 1027, 769, 747, 703, 637 cm$^{-1}$; HRMS (ESI) calculated for [C$_{18}$H$_{19}^{79}$BrNO]$^+$ 344.0645, found 344.0649; R$_f$: 0.33 (pentane/Et$_2$O 1/1).
Ethyl 1-(2-bromo-N-methylbenzamido)cyclopropanecarboxylate (3k):

Obtained as a colourless oil. $^1$H NMR (400 MHz, CDCl$_3$) (mixture of rotamers in ratio 1.5/1) $\delta$ 5.78 (d, $J = 7.6$ Hz, 0.4H), 7.54 (d, $J = 8.0$ Hz, 0.6H), 7.37 (td, $J = 7.5$, 0.9 Hz, 0.6H), 7.30 (d, $J = 6.7$ Hz, 0.4H), 7.26 – 7.18 (m, 2H), 4.29 – 4.12 (m, 2H), 3.18 (s, 1.2H), 2.86 (s, 1.8H), 1.91 – 1.11 (m, 7H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) $\delta$ = 172.4, 171.9, 170.9, 170.6, 139.5, 138.7, 133.3, 132.9, 130.5, 130.3, 128.1, 127.9, 127.2, 126.7, 119.8, 119.0, 61.9, 61.6, 43.3, 40.7, 37.1, 34.9, 20.8, 18.7, 14.4 ppm; IR (ATR): $\tilde{\nu}$ 2981, 1728, 1657, 1591, 1476, 1437, 1385, 1369, 1328, 1298, 1214, 1189, 1136, 1080, 1024, 771, 749, 448 cm$^{-1}$; HRMS (ESI) calculated for [C$_{14}$H$_{17}$BrNO$_3$]$^+$ 326.0386, found 326.0390; $R_1$: 0.19 (pentane/EtOAc 3/1).

2-bromo-N-(1-cyanocyclopropyl)-N-methylbenzamide (3i):

Obtained as a pale yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) (mixture of rotamers in ratio 1.5/1) $\delta$ 7.63 (d, $J = 8.0$ Hz, 0.4H), 7.58 – 7.49 (m, 1H), 7.48 – 7.36 (m, 1H), 7.31 (dd, $J = 13.6$, 7.5 Hz, 1.6H), 3.22 (s, 1.2H), 2.90 (s, 1.8H), 1.81 – 1.09 (m, 4H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) $\delta$ = 170.5, 138.1, 137.2, 133.4, 133.0, 131.1, 131.0, 128.1, 127.7, 127.5, 120.0, 119.5, 119.3, 119.1, 36.4, 34.1, 30.7, 27.9, 17.5 ppm; IR (ATR): $\tilde{\nu}$ 2237, 1659, 1590, 1476, 1431, 1371, 1323, 1214, 1158, 1077, 1048, 1029, 771, 750, 673, 636, 566 cm$^{-1}$; HRMS (ESI) calculated for [C$_{12}$H$_{12}$BrN$_2$O]$^+$ 279.0128, found 279.0132; $R_1$: 0.16 (pentane/EtOAc 3/1).

2-bromo-4-chloro-N-(4-methoxybenzyl)-N-(1-(3-phenylpropyl)cyclopropyl)benzamide (3m):

Obtained as a colourless oil. $^1$H NMR (400 MHz, CDCl$_3$) (mixture of rotamers in ratio 2.75/1) $\delta$ 7.54 – 7.50 (m, 0.25H), 7.40 – 7.36 (m, 0.75H), 7.32 – 7.26 (m, 2.5H), 7.24 – 7.10 (m, 3.75H), 7.06 (dd, $J = 8.6$, 2.5 Hz, 0.75H), 6.88 – 6.77 (m, 2.5H), 6.77 – 6.71 (m, 1.5H), 5.05 (br s, 0.25H), 4.55 – 4.21 (m, 1.75H), 3.80 (s, 0.75H), 3.78 (s, 2.25H), 2.67 – 2.46 (m, 2H), 2.06 – 0.39 (m, 8H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) $\delta$ = 169.1, 159.1, 158.8, 142.5, 140.6, 134.4, 133.7, 133.0, 130.8, 130.1, 130.0, 128.7, 128.6, 128.4, 128.2, 126.2, 125.9, 116.7, 114.1, 114.0, 55.5, 55.4, 53.8, 41.1, 36.2, 36.2, 36.0, 28.6 ppm; IR (ATR): $\tilde{\nu}$ 2935, 1646, 1612, 1512, 1496, 1454, 1425, 1405, 1372, 1356, 1322, 1302, 1248, 1175, 1095, 1032, 815, 749, 700, 504 cm$^{-1}$; HRMS (ESI) calculated for [C$_{27}$H$_{28}$BrClNO$_2$]$^+$ 512.0986, found 512.0967; $R_1$: 0.55 (pentane/EtOAc 3/1).
2-bromo-5-methoxy-N-(4-methoxybenzyl)-N-(1-(3-phenylpropyl)cyclopropyl)benzamide (3n):

Obtained as a colourless oil. $^1$H NMR (400 MHz, CDCl$_3$) (mixture of rotamers in ratio 2.8/1) δ 7.46 (d, $J = 8.6$ Hz, 0.2H), 7.37 – 7.23 (m, 3.8H), 7.22 – 7.09 (m, 3H), 6.89 – 6.80 (m, 2H), 6.76 – 6.70 (m, 1.5H), 6.66 (dd, $J = 8.8$, 3.0 Hz, 0.75H), 6.43 (br s, 0.75H), 5.09 (s, 0.3H), 4.33 (d, $J = 4.9$ Hz, 1.7H), 3.79 (s, 0.8H), 3.76 (s, 2.2H), 3.66 (s, 0.8H), 3.56 (s, 2.2H), 2.57 (t, $J = 7.6$ Hz, 2H), 2.23 – 1.60 (m, 3H), 1.24 – 0.37 (m, 5H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) δ = 170.4, 159.0, 158.8, 158.3, 142.6, 139.9, 133.9, 133.3, 130.7, 128.6, 128.6, 128.4, 128.2, 126.1, 125.8, 117.0, 113.9, 113.1, 109.1, 55.6, 55.4, 53.7, 41.0, 38.4, 36.3, 36.1, 28.7 ppm; IR (ATR): $\tilde{\nu}$ 2937, 2836, 1649, 1612, 1591, 1571, 1513, 1496, 1462, 1412, 1386, 1356, 1290, 1248, 1175, 1112, 1021, 817, 749, 701, 600 cm$^{-1}$; HRMS (ESI) calculated for [C$_{28}$H$_{31}$BrNO$_3$]$^+$ 508.1482, found 508.1488; $R_f$: 0.22 (pentane/EtOAc 3/1).

3-bromo-N-(4-methoxybenzyl)-N-(1-(3-phenylpropyl)cyclopropyl)isonicotinamide (3o):

Obtained as a colourless oil. $^1$H NMR (400 MHz, CDCl$_3$) (mixture of rotamers in ratio 2/1) δ 8.82 – 8.59 (m, 1H), 8.49 – 8.22 (m, 1H), 7.35 – 7.09 (m, 6H), 6.87 – 6.71 (m, 4H), 5.08 (br s, 0.25H), 4.46 – 4.18 (m, 1.75H), 3.80 (s, 1H), 3.77 (s, 2H), 2.69 – 2.48 (m, 2H), 2.19 – 0.10 (m, 8H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) δ = 169.1, 168.2, 159.2, 158.9, 152.4, 151.9, 148.1, 147.8, 147.1, 146.3, 142.4, 141.6, 130.5, 129.8, 128.8, 128.6, 128.6, 128.5, 127.9, 126.3, 125.9, 122.4, 117.1, 114.1, 114.0, 55.4, 55.4, 53.5, 51.9, 41.2, 37.9, 36.2, 36.1, 35.8, 28.7, 28.1 ppm; IR (ATR): $\tilde{\nu}$ 2937, 1649, 1612, 1513, 1453, 1425, 1404, 1303, 1249, 1176, 1030, 839, 750, 701 cm$^{-1}$; HRMS (ESI) calculated for [C$_{28}$H$_{28}$BrN$_2$O$_2$]$^+$ 479.1329, found 479.1335; $R_f$: 0.29 (pentane/EtOAc 1/1).

4-bromo-N-(4-methoxybenzyl)-N-(1-(3-phenylpropyl)cyclopropyl)thiophene-3-carboxamide (3p):

Obtained as a colourless oil. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.36 – 7.07 (m, 7H), 7.02 – 6.75 (m, 4H), 5.04 (br s, 0.5H), 4.37 (br s, 1.5H), 3.78 (s, 3H), 2.55 (t, $J = 7.2$ Hz, 2H), 1.98 – 1.44 (m, 3H), 1.18 – 0.38 (m, 5H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) δ = 167.2, 159.0, 142.6, 141.9, 138.7, 130.8, 128.6, 128.4, 127.6, 126.2, 125.8, 124.7, 123.7, 123.3, 114.0, 55.4, 53.8, 51.8, 41.2, 38.2, 36.3, 35.9, 28.6, 28.2 ppm; IR (ATR): $\tilde{\nu}$ 3084, 3025, 2937, 1643, 1613, 1585, 1512, 1453, 1427, 1387, 1357, 1301, 1248, 1175, 1031, 852, 803, 749, 701 cm$^{-1}$; HRMS (ESI) calculated for [C$_{25}$H$_{27}$BrNO$_2$S]$^+$ 484.0940, found 484.0936; $R_f$: 0.35 (pentane/EtOAc 3/1).
General procedure for the enantioselective synthesis of cyclopropane containing dihydroisoquinolones (4):

Pd(dba)$_2$ (1.44 mg, 2.50 μmol, 2.5 mol%), L2 (3.26 mg, 5.0 μmol, 10 mol%), benzamide (3, 0.10 mmol), AdCO$_2$H (3.60 mg, 0.02 mmol, 20 mol%), and Cs$_2$CO$_3$ (49.0 mg, 0.15 mmol, 1.5 eq) were weighed in a tube containing a magnetic stirring bar. The tube was sealed with a rubber septum, evacuated and refilled with nitrogen. After addition of toluene (0.4 ml, 0.25 M) the reaction mixture was degassed by three freeze-pump-thaw cycles and stirred for 12 h at 110 °C. After cooling to rt the mixture was filtered over a pad of silica gel (eluted with EtOAc) and the crude analysed by $^1$H NMR (2.5 – 5.0 μmol 1,3,5-trimethoxybenzene added as internal standard). The crude mixture was chromatographed on silica gel (eluted with pentane/EtOAc 10/1 to 1/1) to afford the corresponding dihydroisoquinolone 4.
(1aR,7bR)-2-methyl-1a,2-dihydro-1H-cyclopropa[c]isoquinolin-3(7bH)-one (4a):

Obtained as a colourless oil in 64% yield (11.0 mg). $^1$H NMR (400 MHz, CDCl$_3$) $\delta = 8.16$ (d, $J = 7.8$ Hz, 1H), 7.42 (ddd, $J = 16.7, 11.5, 3.8$ Hz, 2H), 7.33 – 7.27 (m, 1H), 3.25 (s, 3H), 3.15 (ddd, $J = 8.2, 6.5, 3.9$ Hz, 1H), 2.31 (ddd, $J = 9.5, 8.3, 5.8$ Hz, 1H), 1.35 (ddd, $J = 9.8, 6.4, 5.2$ Hz, 1H), 0.27 (td, $J = 5.4, 4.0$ Hz, 1H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) $\delta = 161.5, 139.3, 131.9, 129.1, 128.2, 126.6, 125.6, 36.3, 34.9, 15.0, 13.8$ ppm; IR (ATR): $\tilde{\nu} = 2917, 1644, 1604, 1577, 1483, 1441, 1428, 1395, 1377, 1359, 1275, 1173, 1103, 1033, 822, 761, 710, 693, 553$ cm$^{-1}$; HRMS (ESI) calculated for [C$_{11}$H$_{12}$NO]+ 174.0913, found 174.0913; R$_f$: 0.30 (pentane/EtOAc 1/1); [$\alpha$]$_D^{20}$: -116.7° ($c = 0.1, \text{CHCl}_3$). Chiral HPLC: (Chiralpak IA, 4.6 x 250 mm; 20% i-PrOH / hexane, 1.0 mL/min, 254 nm; $t_r$(minor) = 10.2 min, $t_r$(major) = 7.0 min), 93.7/6.3 er.
(1αR,7bR)-2-methyl-1α-(3-phenylpropyl)-1α,2-dihydro-1H-cyclopropa[c]isoquinolin-3(7bH)-one (4b): obtained as a colourless oil in 93% yield (27.0 mg). $^1$H NMR (400 MHz, CDCl$_3$) δ = 8.12 (d, J = 7.8 Hz, 1H), 7.42 (td, J = 7.5, 1.3 Hz, 1H), 7.32 (d, J = 7.5 Hz, 1H), 7.30 - 7.22 (m, 3H), 7.21 - 7.08 (m, 3H), 3.14 (s, 3H), 2.69 - 2.55 (m, 2H), 2.45 (ddd, J = 14.8, 10.6, 4.3 Hz, 1H), 2.09 - 2.03 (m, 1H), 1.85 - 1.67 (m, 2H), 1.19 (dd, J = 9.9, 4.8 Hz, 1H), 0.92 (ddd, J = 14.8, 11.0, 6.1 Hz, 1H), 0.49 (dd, J = 5.8, 5.0 Hz, 1H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) δ = 162.9, 141.8, 138.7, 131.9, 129.1, 128.5, 128.4, 128.0, 126.7, 126.1, 125.2, 43.6, 35.8, 35.4, 30.8, 27.6, 22.7, 19.3 ppm; IR (ATR): $\tilde{\nu}$ 2935, 1641, 1603, 1579, 1481, 1453, 1413, 1396, 1369, 1280, 1161, 1030, 750, 697, 562 cm$^{-1}$; HRMS (ESI) calculated for [C$_{20}$H$_{22}$NO$^+$] $^{292.1696}$, found 292.1699; R$_f$: 0.28 (pentane/EtOAc 3/1); [α]$^0_{D}$: -68.3° ($c = 0.1$, CHCl$_3$). Chiral HPLC: (Chiralpak IA, 4.6 x 250 mm; 20% i-PrOH / hexane, 1.0 mL/min, 254 nm; t$_r$(minor) = 7.9 min, t$_r$(major) = 7.0 min), 93.6/6.4 er.
(1aR,7bR)-2-(4-methoxybenzyl)-1a,2-dihydro-1H-cyclopropa[c]isoquinolin-3(7bH)-one (4c):

Obtained as a colourless oil in 70% yield (19.6 mg). $^1$H NMR (400 MHz, CDCl$_3$) $\delta = 8.22$ (d, $J = 7.8$ Hz, 1H), 7.43 (dd, $J = 10.5, 4.3$ Hz, 1H), 7.38 – 7.29 (m, 4H), 6.87 (d, $J = 8.6$ Hz, 2H), 5.00 (d, $J = 14.4$ Hz, 1H), 4.70 (d, $J = 14.4$ Hz, 1H), 3.80 (s, 3H), 3.11 (ddd, $J = 8.2, 6.6, 4.0$ Hz, 1H), 2.29 – 2.21 (m, 1H), 1.31 – 1.23 (m, 1H), 0.18 (dd, $J = 9.5, 5.4$ Hz, 1H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) $\delta = 161.3, 159.2, 139.3, 132.0, 130.0, 129.4, 129.2, 128.3, 126.6, 125.7, 114.1, 55.4, 50.2, 34.2, 14.8, 14.4$ ppm; IR (ATR): $\tilde{\nu} = 2931, 1639, 1604, 1577, 1511, 1477, 1443, 1415, 1373, 1350, 1301, 1276, 1245, 1176, 1158, 1111, 1033, 986, 919, 846, 820, 761, 708, 692, 604, 586, 570, 551, 522$ cm$^{-1}$; HRMS (ESI) calculated for [C$_{18}$H$_{18}$NO$_2$]$^+$ 280.1332, found 280.1338; $R_f$: 0.27 (pentane/EtOAc 3/1); $[\alpha]_D^{20}$: -63.3° ($c = 0.1$, CHCl$_3$). Chiral HPLC: (Chiralpak IA, 4.6 x 250 mm; 20% i-PrOH / hexane, 1.0 mL/min, 254 nm; $t_r$(minor) = 14.7 min, $t_r$(major) = 10.6 min), 92.3/7.7 er.

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(1aR,7bR)-2-(2,4,6-trimethylbenzyl)-1a,2-dihydro-1H-cyclopropa[c]isoquinolin-3(7bH)-one (4d): obtained as a colourless oil in 82% yield (24.0 mg) employing 5.0 mol% Pd(dba)$_2$ and 10 mol% L2. $^1$H NMR (400 MHz, CDCl$_3$) δ = 8.28 – 8.18 (m, 1H), 7.43 (td, J = 7.5, 1.4 Hz, 1H), 7.37 – 7.29 (m, 2H), 6.89 (s, 2H), 5.50 (d, J = 14.4 Hz, 1H), 4.50 (d, J = 14.4 Hz, 1H), 2.80 (dd, J = 8.3, 6.6, 4.1 Hz, 1H), 2.35 (s, 6H), 2.29 (s, 3H), 2.20 – 2.14 (m, 1H), 1.18 (ddd, J = 9.7, 6.5, 5.1 Hz, 1H), 0.22 (dd, J = 9.6, 5.2 Hz, 1H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) δ = 161.1, 139.2, 138.7, 137.6, 132.0, 129.4, 129.3, 129.0, 128.2, 126.6, 125.6, 43.3, 31.7, 21.1, 20.2, 15.0, 14.2 ppm; IR (ATR): $\tilde{\nu}$ 2954, 2921, 1642, 1578, 1476, 1415, 1377, 1293, 1266, 1245, 1155, 761, 694 cm$^{-1}$; HRMS (ESI) calculated for [C$_{20}$H$_{22}$NO]$^+$ 292.1696, found 292.1697; R$_f$: 0.35 (pentane/EtOAc 5/1); $[\alpha]_D^{20}$: -70.0° (c = 0.1, CHCl$_3$, sample of 97.5/2.5 er). Chiral HPLC: (Chiralpak IC, 4.6 x 250 mm; 20% i-PrOH / hexane, 1.0 mL/min, 254 nm; t$_r$(minor) = 10.4 min, t$_r$(major) = 11.3 min), 91.6/8.4 er.
(1aR,7bR)-2-(4-methoxybenzyl)-1a-(3-phenylpropyl)-1a,2-dihydro-1H-cyclopropa[c]isoquinoline-3(7bH)-one (4f): obtained as a colourless oil in 98% yield (39.1 mg). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 8.24 – 8.16 (m, 1H), 7.45 – 7.39 (m, 1H), 7.33 – 7.24 (m, 6H), 7.17 (dd, $J$ = 8.4, 6.3 Hz, 1H), 7.05 (d, $J$ = 7.0 Hz, 2H), 6.86 – 6.79 (m, 2H), 5.29 (d, $J$ = 15.5 Hz, 1H), 4.38 (d, $J$ = 14.8 Hz, 1H), 3.79 (s, 3H), 2.56 – 2.45 (m, 2H), 2.43 – 2.35 (m, 1H), 1.94 (dd, $J$ = 9.8, 6.1 Hz, 1H), 1.69 – 1.61 (m, 2H), 1.09 (dd, $J$ = 9.9, 5.0 Hz, 1H), 0.83 (ddd, $J$ = 14.9, 10.9, 6.6 Hz, 1H), 0.29 (dd, $J$ = 5.9, 5.2 Hz, 1H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) $\delta$ = 163.2, 158.9, 141.9, 139.0, 132.1, 130.1, 130.0, 129.4, 128.5, 128.0, 126.6, 126.0, 125.3, 113.8, 55.4, 46.7, 42.6, 35.9, 35.4, 27.8, 21.4, 21.3 ppm; IR (ATR): $\bar{\nu}$ 2936, 1640, 1605, 1581, 1495, 1474, 1403, 1381, 1337, 1302, 1248, 1176, 1035, 752, 699 cm$^{-1}$; HRMS (ESI) calculated for [C$_{27}$H$_{28}$NO$_2$]$^+$ 398.2115, found 398.2106; $R_f$: 0.42 (pentane/EtOAc 3/1); $[\alpha]_D^{20}$: -85.0° ($c$ = 0.1, CHCl$_3$). Chiral HPLC: (Chiralpak IB, 4.6 x 250 mm; 20% i-PrOH / hexane, 1.0 mL/min, 254 nm; t$_r$ (minor) = 8.2 min, t$_r$ (major) = 9.3 min), 94.4/5.6 er.
(1aS,7bR)-1a-isopropyl-2-methyl-1a,2-dihydro-1H-cyclopropa[c]isoquinolin-3(7bH)-one (4g):

Obtained as a colourless oil in 85% yield (18.2 mg) employing 5.0 mol% Pd(dba)$_2$ and 10 mol% L2. $^1$H NMR (400 MHz, CDCl$_3$) $\delta = 8.15 – 8.09$ (m, 1H), 7.42 (td, $J = 7.5$, 1.4 Hz, 1H), 7.35 (d, $J = 6.6$ Hz, 1H), 7.29 (td, $J = 7.8$, 1.3 Hz, 1H), 3.20 (s, 3H), 2.52 – 2.44 (m, 1H), 2.16 (dd, $J = 10.2$, 6.4 Hz, 1H), 1.42 (dd, $J = 10.2$, 5.0 Hz, 1H), 0.99 (d, $J = 6.6$ Hz, 3H), 0.77 (d, $J = 6.9$ Hz, 3H), 0.48 (dd, $J = 6.3$, 5.1 Hz, 1H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) $\delta = 163.1$, 138.8, 131.9, 128.9, 128.2, 126.6, 125.4, 48.9, 31.7, 28.6, 19.6, 17.1, 17.0, 16.9 ppm; IR (ATR): $\tilde{\nu}$ 2964, 2929, 1603, 1581, 1483, 1415, 1374, 1275, 1141, 1110, 1031, 748, 695 cm$^{-1}$; HRMS (ESI) calculated for [C$_{14}$H$_{18}$NO]$^+$ 216.1383, found 216.1379; R$_f$: 0.31 (pentane/EtOAc 3/1); $[\alpha]_D^{20}$: -61.7° ($c = 0.1$, CHCl$_3$). Chiral HPLC: (Chiralpak IA, 4.6 x 250 mm; 20% i-PrOH / hexane, 1.0 mL/min, 254 nm; t (minor) = 6.7 min, t (major) = 7.3 min), 93.5/6.5 er.
(1aR,7bR)-2-methyl-1a-phenyl-1a,2-dihydro-1H-cyclopropa[c]isoquinolin-3(7bH)-one (4h):

Obtained as a colourless oil in 99% yield (24.8 mg) after 24 h reaction time.

**1H NMR** (400 MHz, CDCl₃) δ = 8.27 – 8.16 (m, 1H), 7.46 (td, J = 7.5, 1.4 Hz, 1H), 7.40 – 7.27 (m, 7H), 2.96 (s, 3H), 2.30 (dd, J = 10.2, 6.5 Hz, 1H), 2.12 (dd, J = 10.2, 5.2 Hz, 1H), 0.80 (dd, J = 6.4, 5.3 Hz, 1H) ppm; **13C(1H) NMR** (101 MHz, CDCl₃) δ = 162.7, 139.8, 138.2, 132.1, 129.1, 129.0, 128.1, 128.0, 126.9, 125.1, 47.4, 32.9, 25.9, 17.7 ppm; **IR (ATR):** ν = 3058, 3029, 1640, 1602, 1579, 1475, 1447, 1416, 1393, 1367, 1307, 1195, 1156, 1100, 1082, 1047, 1030, 968, 937, 921, 906, 886, 797, 761, 747, 695, 679, 606, 580, 542, 514, 496, 467, 412 cm⁻¹; **HRMS (ESI)** calculated for [C₁₇H₁₆NO]⁺ 250.1226, found 250.1228; Rₚ: 0.35 (pentane/EtOAc 3/1); [α]₀²⁰: +36.7° (c = 0.1, CHCl₃). Chiral HPLC: (Chiralpak IB, 4.6 x 250 mm; 20% i-PrOH / hexane, 1.0 mL/min, 254 nm; tₘ (minor) = 6.7 min, tₘ (major) = 6.2 min, 91.3/8.7 ee.
(1aR,7bR)-1a-(4-chlorophenyl)-2-(4-methoxybenzyl)-1a,2-dihydro-1H-cyclopropa[c]isoquinolin-3(7bH)-one (4i): obtained as a yellow oil in 99% yield (38.5 mg) after 24 h reaction time employing 5.0 mol% Pd(dba)$_2$ and 10 mol% L2. $^1$H NMR (400 MHz, CDCl$_3$) δ = 8.29 (d, $J = 7.7$ Hz, 1H), 7.46 (td, $J = 7.4$, 1.1 Hz, 1H), 7.38 (dd, $J = 11.0$, 4.0 Hz, 1H), 7.28 (dt, $J = 11.6$, 8.6 Hz, 5H), 7.05 (d, $J = 8.6$ Hz, 2H), 6.75 (d, $J = 8.6$ Hz, 2H), 5.43 (d, $J = 14.5$ Hz, 1H), 3.88 (d, $J = 14.5$ Hz, 1H), 3.77 (s, 3H), 2.13 (dd, $J = 10.2$, 6.7 Hz, 1H), 1.93 (dd, $J = 10.3$, 5.6 Hz, 1H), 0.51 (t, $J = 6.1$ Hz, 1H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) δ = 162.4, 158.9, 138.3, 138.0, 133.9, 132.3, 130.4, 130.0, 129.5, 129.3, 129.0, 128.1, 127.0, 125.2, 113.6, 55.3, 47.3, 45.2, 24.4, 19.2 ppm; IR (ATR): $\tilde{\nu}$ 2954, 2929, 1643, 1605, 1582, 1511, 1489, 1469, 1439, 1397, 1378, 1356, 1323, 1303, 1273, 1247, 1176, 1163, 1110, 1093, 1034, 1013, 979, 830, 807, 751, 692, 570, 523 cm$^{-1}$; HRMS (ESI) calculated for [C$_{24}$H$_{21}$ClNO$_2$]$^+$ 390.1255, found 390.1255; $R_f$: 0.33 (pentane/EtOAc 5/1); [$\alpha$]$_D^{20}$: +18.3$^\circ$ (c = 0.1, CHCl$_3$). Chiral HPLC: (Chiralpak IB, 4.6 x 250 mm; 20% i-PrOH / hexane, 1.0 mL/min, 254 nm; t (minor) = 10.3 min, t (major) = 11.3 min), 95.2/4.8 er.
(1aS,7bR)-1-benzyl-2-methyl-1a,2-dihydro-1H-cyclopropa[c]isoquinolin-3(7bH)-one (4j):

Obtained as a pale yellow oil in 89% yield (23.5 mg). $^1$H NMR (400 MHz, CDCl$_3$) δ = 8.12 (d, J = 7.7 Hz, 1H), 7.44 (td, J = 7.5, 1.0 Hz, 1H), 7.38 – 7.15 (m, 7H), 3.67 (d, J = 15.8 Hz, 1H), 3.20 (s, 3H), 2.60 (d, J = 15.8 Hz, 1H), 2.33 (dd, J = 9.9, 6.1 Hz, 1H), 1.32 (dd, J = 9.9, 4.9 Hz, 1H), 0.59 – 0.52 (m, 1H) ppm; $^{13}$C{H} NMR (101 MHz, CDCl$_3$) δ = 162.7, 138.3, 136.8, 132.0, 129.2, 128.8, 128.1, 126.9, 126.8, 125.2, 43.2, 41.7, 31.2, 22.8, 17.9 ppm; IR (ATR): $\tilde{\nu}$ 3028, 2922, 1639, 1579, 1479, 1454, 1438, 1413, 1394, 1370, 1279, 1141, 1049, 1030, 757, 743, 696, 615, 574, 559 cm$^{-1}$; HRMS (ESI) calculated for [C$_{18}$H$_{18}$NO]$^+$ 264.1383, found 264.1379; $R$: 0.19 (pentane/EtOAc 3/1); $[\alpha]_D^{20}$: -218.3° (c = 0.1, CHCl$_3$). Chiral HPLC: (Chiralpak IA, 4.6 x 250 mm; 20% i-PrOH / hexane, 1.0 mL/min, 254 nm; t $(\text{minor}) = 8.1$ min, t $(\text{major}) = 7.4$ min, 92.2/7.8 er.
(1aR,7bR)-ethyl 2-methyl-3-oxo-1a,2,3,7b-tetrahydro-1H-cyclopropa[c]isoquinoline-1a-carboxylate (4k): obtained as a colourless oil in 99% yield (25.0 mg). $^1$H NMR (400 MHz, CDCl$_3$) δ = 8.15 (d, $J = 7.9$ Hz, 1H), 7.50 – 7.43 (m, 1H), 7.39 – 7.32 (m, 2H), 4.34 – 4.16 (m, 2H), 3.25 (s, 3H), 2.74 (dd, $J = 10.4, 7.2$ Hz, 1H), 2.17 (dd, $J = 10.4, 4.6$ Hz, 1H), 1.31 (t, $J = 7.1$ Hz, 3H), 0.88 (dd, $J = 7.2, 4.6$ Hz, 1H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) δ = 170.1, 162.3, 136.4, 132.2, 129.2, 128.2, 127.6, 125.2, 62.1, 45.0, 34.8, 26.5, 20.1, 14.3 ppm; IR (ATR): $\tilde{\nu}$ 2981, 1729, 1652, 1605, 1583, 1471, 1445, 1421, 1367, 1336, 1288, 1249, 1202, 1176, 1135, 1107, 1077, 1053, 1021, 858, 750, 725, 694, 676, 565 cm$^{-1}$; HRMS (ESI) calculated for [C$_{14}$H$_{16}$NO$_3$]$^+$ 246.1125, found 246.1126; $R_f$: 0.23 (pentane/EtOAc 3/1); $[\alpha]_D^{20}$: +115.0° ($c = 0.1$, CHCl$_3$). Chiral HPLC: (Chiralpak IA, 4.6 x 250 mm; 20% $i$-PrOH / hexane, 1.0 mL/min, 254 nm; $t$ (minor) = 19.0 min, $t$ (major) = 12.7 min), 91.5/8.5 er.

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(1aR,7bR)-2-methyl-3-oxo-1a,2,3,7b-tetrahydro-1H-cyclopropa[c]isoquinoline-1a-carbonitrile (4l): obtained as a white solid in 89% yield (18.9 mg) employing 5.0 mol% Pd(dba)$_2$ and 10 mol% L2. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 8.22 – 8.08 (m, 1H), 7.56 – 7.50 (m, 1H), 7.45 – 7.37 (m, 2H), 3.38 (s, 3H), 3.00 (dd, $J$ = 10.5, 7.4 Hz, 1H), 1.99 (dd, $J$ = 10.5, 5.6 Hz, 1H), 0.98 (dd, $J$ = 7.4, 5.6 Hz, 1H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) $\delta$ = 160.8, 134.6, 132.9, 129.6, 128.4, 128.3, 124.4, 117.7, 33.3, 23.7, 21.6 ppm; IR (ATR): $\tilde{\nu}$ 2920, 2243, 1658, 1605, 1582, 1473, 1420, 1392, 1369, 1324, 1150, 1052, 1033, 753, 692 cm$^{-1}$; HRMS (ESI) calculated for [C$_{12}$H$_7$N$_2$O]$^+$ 199.0866, found 199.0865; $R_\ell$: 0.23 (pentane/EtOAc 3/1); m.p.: 163.0-165.7 °C; $[\alpha]_{D}^{20}$: +55.0° (c = 0.1, CHCl$_3$). Chiral HPLC: (Chiralpak IA, 4.6 x 250 mm; 20% i-PrOH / hexane, 1.0 mL/min, 254 nm; t (minor) = 18.3 min, t (major) = 9.6 min), 93.5/6.5 $\text{er}$.

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(1aR,7bR)-6-chloro-2-(4-methoxybenzyl)-1a-(3-phenylpropyl)-1a,2-dihydro-1H-cyclopropa[c]-isoquinolin-3(7bH)-one (4m): obtained as a yellow oil in 98% yield (42.5 mg). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta = 8.17\) (m, 1H), 7.37 (dd, \(J = 8.1, 2.2\) Hz, 1H), 7.29 – 7.15 (m, 6H), 7.05 (d, \(J = 7.9\) Hz, 2H), 6.82 (d, \(J = 8.6\) Hz, 2H), 5.27 (d, \(J = 14.7\) Hz, 1H), 4.33 (d, \(J = 14.7\) Hz, 1H), 3.79 (s, 3H), 2.56 – 2.35 (m, 3H), 1.90 (dd, \(J = 9.8, 6.1\) Hz, 1H), 1.74 – 1.60 (m, 2H), 1.10 (dd, \(J = 9.8, 5.1\) Hz, 1H), 0.87 – 0.78 (m, 1H), 0.26 (t, \(J = 5.6\) Hz, 1H) ppm; \(^{13}\)C\(^1\)H NMR (101 MHz, CDCl\(_3\)) \(\delta = 162.0, 159.0, 141.7, 137.3, 132.7, 132.1, 130.1, 129.7, 129.5, 129.4, 128.5, 128.5, 126.9, 126.1, 113.9, 55.4, 46.7, 42.7, 35.8, 35.4, 27.8, 21.4, 20.9 ppm; IR (ATR): \(\tilde{\nu}\) 2935, 1643, 1611, 1599, 1512, 1487, 1459, 1425, 1377, 1334, 1302, 1248, 1176, 1033, 819, 750, 700 cm\(^{-1}\); HRMS (ESI) calculated for [C\(_{27}\)H\(_{27}\)ClNO\(_2\)]\(^+\) 432.1725, found 432.1731; \(R_f: 0.38\) (pentane/EtOAc 5/1); [\(\alpha\)]\(_D\)\(^{20}\): -57.8° (c = 0.1, CHCl\(_3\)). Chiral HPLC: (Chiralpak IB, 4.6 x 250 mm; 20% i-PrOH / hexane, 1.0 mL/min, 290 nm; t (minor) = 8.3 min, t (major) = 9.6 min), 94.2/5.8 er.

### Table 1

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(1aR,7bR)-5-methoxy-2-(4-methoxybenzyl)-1a-(3-phenylpropyl)-1a,2-dihydro-1H-cyclopropa-
c[isoquinolin-3(7bH)-one (4n): obtained as a colourless oil in 99% yield (42.5 mg). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta = 7.80\) (d, \(J = 2.7\) Hz, 1H), 7.37 – 7.21 (m, 6H), 7.11 (d, \(J = 7.1\) Hz, 2H), 7.07 (dd, \(J = 8.3, 2.8\) Hz, 1H), 6.89 (d, \(J = 8.6\) Hz, 2H), 5.32 (d, \(J = 14.7\) Hz, 1H), 4.46 (d, \(J = 14.7\) Hz, 1H), 3.92 (s, 3H), 3.86 (s, 3H), 2.62 – 2.40 (m, 3H), 1.97 (dd, \(J = 9.6, 6.1\) Hz, 1H), 1.76 – 1.66 (m, 2H), 1.10 (dd, \(J = 9.7, 5.0\) Hz, 1H), 0.93 – 0.85 (m, 1H), 0.29 (t, \(J = 5.5\) Hz, 1H) ppm; \(^{13}\)C\(^{1}\)H NMR (101 MHz, CDCl\(_3\)) \(\delta = 163.2, 158.9, 158.5, 141.9, 131.2, 130.0, 129.1, 128.5, 128.5, 126.3, 126.0, 120.2, 113.8, 112.0, 55.7, 55.4, 46.8, 42.4, 36.0, 35.4, 27.8, 20.9, 20.7 ppm; IR (ATR): \(\tilde{\nu}\) 2933, 1640, 1608, 1581, 1504, 1461, 1441, 1428, 1380, 1332, 1300, 1276, 1244, 1176, 1150, 1102, 1034, 829, 780, 752, 701 cm\(^{-1}\); HRMS (ESI) calculated for [C\(_{28}\)H\(_{30}\)NO\(_3\)]\(^+\) 428.2220, found 428.2215; R\(_f\): 0.30 (pentane/EtOAc 3/1); [\(\alpha\)]\(^D\)\(^{20}\): -88.3° (c = 0.1, CHCl\(_3\)). Chiral HPLC: (Chiralpak IB, 4.6 x 250 mm; 20% i-PrOH / hexane, 1.0 mL/min, 254 nm; \(t\) (minor) = 8.5 min, \(t\) (major) = 9.5 min), 93.9/6.1 er.
(1aR,7bR)-2-(4-methoxybenzyl)-1a-(3-phenylpropyl)-1a,2-dihydro-1H-cyclopropa[c][2,6]-
naphthyridin-3(7bH)-one (4o): obtained as a yellow oil in 99% yield (39.6 mg). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 8.65 (s, 1H), 8.60 (d, $J$ = 5.1 Hz, 1H), 7.95 (d, $J$ = 5.1 Hz, 1H), 7.30 – 7.16 (m, 6H), 7.08 – 7.03 (m, 2H), 6.85 – 6.80 (m, 2H), 5.29 (d, $J$ = 14.7 Hz, 1H), 4.32 (d, $J$ = 14.7 Hz, 1H), 3.79 (s, 3H), 2.52 (tt, $J$ = 10.1, 6.3 Hz, 2H), 2.45 – 2.37 (m, 1H), 1.96 (dd, $J$ = 9.9, 6.1 Hz, 1H), 1.69 – 1.59 (m, 2H), 1.18 (dd, $J$ = 9.9, 5.3 Hz, 1H), 0.87 (ddd, $J$ = 15.0, 10.7, 6.7 Hz, 1H), 0.30 (t, $J$ = 5.7 Hz, 1H) ppm; $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) $\delta$ = 161.4, 159.1, 150.0, 148.5, 141.6, 133.3, 131.8, 130.1, 129.2, 128.6, 128.5, 126.2, 121.8, 113.9, 55.4, 46.7, 43.0, 35.6, 35.3, 27.8, 21.5, 18.6 ppm; IR (ATR): $\tilde{\nu}$ 2935, 1645, 1612, 1571, 1512, 1497, 1460, 1425, 1395, 1380, 1359, 1336, 1302, 1247, 1213, 1176, 1112, 1032, 848, 815, 751, 700 cm$^{-1}$; HRMS (ESI) calculated for [C$_{26}$H$_{27}$N$_2$O$_2$]$^+$ 399.2067, found 399.2067; $R_f$: 0.13 (pentane/EtOAc 1/1); $[^{[\alpha]}]_D$^20: -153.3° ($c$ = 0.1, CHCl$_3$). Chiral HPLC: (Chiralpak IA, 4.6 x 250 mm; 20% i-PrOH / hexane, 1.0 mL/min, 254 nm; t (minor) = 12.0 min, t (major) = 13.9 min), 96.4/3.6 er.

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(5aR,6aR)-5-(4-methoxybenzyl)-5a-(3-phenylpropyl)-5,5a,6,6a-tetrahydro-4H-cyclopropa[b]-thieno[3,4-d]pyridin-4-one (4p): obtained as a colourless wax 29% yield (11.1 mg) employing 5.0 mol% Pd(dba)₂ and 10 mol% L₂ in mesitylene (0.1 M) at 130 °C. "H NMR (400 MHz, CDCl₃) δ = 8.08 (d, J = 3.1 Hz, 1H), 7.29 – 7.15 (m, 5H), 7.07 – 7.02 (m, 3H), 6.82 (d, J = 8.6 Hz, 2H), 5.24 (d, J = 14.8 Hz, 1H), 4.30 (d, J = 14.8 Hz, 1H), 3.79 (s, 3H), 2.54 – 2.33 (m, 3H), 1.99 (dd, J = 9.6, 6.3 Hz, 1H), 1.68 – 1.59 (m, 2H), 1.02 (dd, J = 9.6, 5.3 Hz, 1H), 0.80 (ddd, J = 14.9, 10.5, 6.9 Hz, 1H), 0.36 (t, J = 5.8 Hz, 1H) ppm; "C{"H} NMR (101 MHz, CDCl₃) δ = 160.8, 158.9, 141.9, 137.5, 131.2, 130.1, 130.0, 129.8, 128.5, 126.1, 120.3, 113.8, 55.4, 45.9, 44.0, 36.0, 35.4, 27.9, 21.7, 18.9 ppm; IR (ATR): ν 2931, 1635, 1556, 1512, 1466, 1454, 1396, 1322, 1301, 1248, 1176, 1033, 816, 772, 752, 700 cm⁻¹; HRMS (ESI) calculated for [C₂₅H₂₆NO₂S]⁺ 404.1679, found 404.1673; Rf: 0.29 (pentane/EtOAc 3/1); [α]D²⁰: -60.0° (c = 0.1, CHCl₃). Chiral HPLC: (Chiralpak IB, 4.6 x 250 mm; 20% i-PrOH / hexane, 1.0 mL/min, 254 nm; tr (minor) = 8.8 min, tr (major) = 9.5 min), 86.0/14.0 er.
Cleavage of PBM-protecting group

To a mixture of isoquinolinone 4 and anisole (5.0 eq.) was added TFA (43 eq.) and the resulting clear yellow solution stirred at 65 °C for 12 h. After cooling down to rt, TFA was removed under reduced pressure and the residue chromatographed on silica gel to afford the corresponding secondary amide.

(1aR,7bR)-1a-(4-chlorophenyl)-1a,2-dihydro-1H-cyclopropa[c]isoquinolin-3(7bH)-one (4q):

Obtained as a white solid in quantitative yield (29.0 mg, 0.11 mmol scale). \( ^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta = 8.11 \) (d, \( J = 7.7 \) Hz, 1H), 7.42 (td, \( J = 7.6, 1.3 \) Hz, 1H), 7.29 (dd, \( J = 14.4, 6.5 \) Hz, 2H), 7.16 (s, 4H), 6.18 (s, 1H), 2.36 – 2.26 (m, 1H), 1.99 (dd, \( J = 10.2, 5.5 \) Hz, 1H), 0.75 (dd, \( J = 5.9, 5.5 \) Hz, 1H) ppm; \( ^{13}\)C\( (^1\)H) NMR (101 MHz, CDCl\(_3\)) \( \delta = 163.1, 139.6, 138.8, 134.2, 133.0, 129.3, 129.0, 128.5, 128.3, 127.1, 124.3, 42.2, 25.5, 20.6 \) ppm; IR (ATR): \( \tilde{\nu} \) 3188, 3074, 2964, 2922, 1660, 1604, 1575, 1478, 1384, 1261, 1096, 1014, 800, 751, 520 cm\(^{-1}\); HRMS (ESI) calculated for [C\(_{16}\)H\(_{13}\)ClNO\(^+\)] 270.0680, found 270.0678; \( R_\text{f} \): 0.75 (EtOAc); m.p.: 140.7-142.1 °C; \([\alpha]_D^{20} \): +115.0° (c = 0.1, CHCl\(_3\)). This compound was crystallised from i-Pr\(_2\)O/Et\(_2\)O and its absolute configuration assigned by X-ray crystallography as \( R,R \).
(1aR,7bR)-1a,2-dihydro-1H-cyclopropa[c]isoquinolin-3(7bH)-one (4e):

Obtained as a white wax in quantitative yield (0.25 g, 1.6 mmol scale). ¹H NMR (400 MHz, CDCl₃) δ = 8.14 (d, J = 7.6 Hz, 1H), 7.44 (ddt, J = 18.7, 14.8, 3.9 Hz, 2H), 7.30 (dt, J = 13.0, 2.9 Hz, 1H), 3.18 (ddd, J = 10.5, 7.1, 3.6 Hz, 1H), 2.26 (ddd, J = 9.5, 8.3, 5.0 Hz, 1H), 1.38 – 1.27 (m, 1H), 0.26 (td, J = 5.4, 4.1 Hz, 1H) ppm; ¹³C(¹H) NMR (101 MHz, CDCl₃) δ = 163.6, 140.5, 132.7, 129.0, 128.4, 126.6, 124.8, 30.0, 14.8, 14.5 ppm; IR (ATR): ν 3197, 3040, 1658, 1604, 1574, 1479, 1409, 1352, 1203, 1182, 1153, 1136, 861, 802, 758, 731 cm⁻¹; HRMS (ESI) calculated for [C₁₀H₁₀NO]⁺ 160.0757, found 160.0759; Rᵣ: 0.32 (EtOAc); [α]₂⁰: -106.7° (c = 0.1, CHCl₃).

Chiral HPLC: (Chiralpak AYH, 4.6 x 250 mm; 20% i-PrOH / hexane, 1.0 mL/min, 254 nm; tᵣ(minor) = 14.9 min, tᵣ(major) = 10.5 min), 93.5/6.5 er.
Enantioselective C-H functionalization strategy towards the BMS-791325 ring system

Synthesis of ethyl 1-acetyl-2-(2-bromo-4-methoxyphenyl)-3-cyclohexyl-1H-indole-6-carboxylate (19):

A mixture of ethyl 3-acetamidobenzoate (17, 104 mg, 0.5 mmol), 2-bromo-1-(cyclohexylethynyl)-4-methoxybenzene (18, 161 mg, 1.1 eq.), [Cp’RhCl₂]₂ (18 mg, 5 mol%), AgSbF₆ (34 mg, 20 mol%) and Cu(OAc)₂•H₂O (36 mg, 40 mol%) in t-amyl alcohol (2.5 mL) was stirred at 60 °C under O₂ atmosphere (1 atm - balloon) for 24 h. Upon completion of the reaction time the volatiles were removed in vacuo. The residue was suspended in DCM (5 mL) and filtered through celite. The filtrate was concentrated under reduced pressure and the residue subjected to column chromatography on silica gel to afford pure 19 as yellowish oil in 68% yield (170 mg).

¹H-NMR (400 MHz, CDCl₃): δ = 9.16 (d, J = 1.4 Hz, 1H), 7.98 (dd, J₁ = 8.4 Hz, J₂ = 1.5 Hz, 1H), 7.80 (d, J = 8.3 Hz, 1H), 7.25-7.28 (m, 2H), 6.99 (dd, J₁ = 8.5 Hz, J₂ = 2.6 Hz, 1H), 4.42 (qd, J₁ = 7.2 Hz, J₂ = 1.3 Hz, 2H), 3.90 (s, 3H), 2.27-2.40 (m, 1H), 2.02 (s, 3H), 1.63-1.88 (m, 7H), 1.42 (t, J = 7.1 Hz, 3H), 1.12-1.34 (m, 3H); ¹³C{¹H}-NMR (100 MHz, CDCl₃): δ = 170.3, 167.3, 160.9, 136.5, 135.3, 133.0, 132.1, 127.4, 126.9, 126.7, 126.5, 124.3, 120.1, 118.8, 118.4, 113.9, 61.0, 55.8, 37.0, 32.0, 31.8, 26.9, 26.7, 26.2, 14.5; IR (ATR): ν = 2977, 2929, 2852, 1710, 1604, 1582, 1555, 1491, 1475, 1425, 1368, 1306, 1287, 1230, 1160, 1128, 1095, 1031, 950, 912, 843, 777, 750; HRMS (ESI) calculated for [C₂₆H₂₇BrNO₄]⁺ 498.1271, found 498.1274; Rf: 0.27 (pentane/EtOAc 5/1).
Synthesis of ethyl 2-(2-bromo-4-methoxyphenyl)-3-cyclohexyl-1H-indole-6-carboxylate:

Acetyl chloride (0.345 ml, 10 eq.) was added dropwise to a solution of 19 (242 mg, 0.486 mmol) in EtOH (4 mL) at 0 °C. The obtained solution was heated at 70 °C for 4 h, whereupon all volatiles were removed in vacuo. The residue was dissolved in DCM (5 mL), stirred with K₂CO₃ (500 mg) for 20 min, filtered through celite and concentrated under reduced pressure. Purification of the residue by column chromatography on silica gel afforded ethyl 2-(2-bromo-4-methoxyphenyl)-3-cyclohexyl-1H-indole-6-carboxylate as yellowish oil (201 mg, 91%).

^1H-NMR (400 MHz, CDCl₃): δ = 8.10 (s, 1H), 7.77-7.84 (m, 2H), 7.29 (d, J = 8.5 Hz, 1H), 7.25 (d, J = 2.8 Hz, 1H), 6.94 (dd, J₁ = 8.4 Hz, J₂ = 2.6 Hz, 1H), 4.40 (q, J = 7.1 Hz, 2H), 3.88 (s, 3H), 2.60 (p, J = 7.9 Hz, 1H), 1.67-1.90 (m, 7H), 1.41 (t, J = 7.1 Hz, 3H), 1.21-1.35 (m, 3H);

^13C{^1H}-NMR (100 MHz, CDCl₃): δ = 167.8, 160.5, 135.6, 135.2, 133.2, 130.5, 126.4, 125.0, 123.7, 120.5, 120.14, 120.13, 118.3, 113.4, 113.3, 60.7, 55.8, 36.7, 33.1, 27.2, 26.3, 14.6; IR (ATR): ʋ = 3324, 2978, 2926, 2849, 1687, 1605, 1555, 1492, 1460, 1438, 1392, 1368, 1319, 1286, 1212, 1141, 1118, 1095, 1033, 987, 949, 888, 863, 844, 820, 775, 748; HRMS (ESI) calculated for [C₂₄H₂₂⁷BrNO₃]⁺ 456.1169, found 456.1148; Rₜ 0.34 (pentane/EtOAc 5/1).

Synthesis of ethyl 2-(2-bromo-4-methoxyphenyl)-3-cyclohexyl-1-((1-(ethoxycarbonyl)cyclopropyl)methyl)-1H-indole-6-carboxylate (16):

A mixture of ethyl 2-(2-bromo-4-methoxyphenyl)-3-cyclohexyl-1H-indole-6-carboxylate (163 mg, 0.358 mmol) and Cs₂CO₃ (233 mg, 2 eq.) in DMF (3.6 mL) was stirred at 23 °C for 30 min followed by addition of 4-chloro-2-methylenebutanoate (20, 87 mg, 1.5 eq.). The mixture was stirred at 23 °C for 17 h, whereupon all volatiles were removed in vacuo. The residue was suspended in EtOAc (5 mL), filtered through celite and concentrated under reduced pressure. Purification of the residue by column chromatography on silica gel afforded pure 16 (201 mg, 96%) as colourless oil.
\textbf{1H-NMR} (500 MHz, CDCl\textsubscript{3}): $\delta = 8.16$ (s, 1H), 7.78 (s, 2H), 7.26 (d, $J = 2.6$ Hz, 1H), 7.19 (d, $J = 8.5$ Hz, 1H), 6.96 (dd, $J_1 = 8.5$ Hz, $J_2 = 2.6$ Hz, 1H), 4.64 (d, $J = 15.6$ Hz, 1H), 4.36-4.46 (m, 2H), 4.27 (d, $J = 15.6$ Hz, 1H), 4.01 (q, $J = 7.1$ Hz, 2H), 3.89 (s, 3H), 3.89 (s, 3H), 2.35-2.47 (m, 1H), 1.66-1.86 (m, 7H), 1.42 (t, $J = 7.1$ Hz, 3H), 1.17-1.28 (m, 3H), 1.10 (t, $J = 7.1$ Hz, 3H), 1.03-1.06 (m, 2H), 0.30-0.43 (m, 2H); \textbf{13C{\textsuperscript{1}}H}NMR (125 MHz, CDCl\textsubscript{3}): $\delta = 173.6, 167.9, 160.6, 138.3, 136.8, 133.9, 129.8, 126.6, 125.5, 123.4, 120.7, 120.0, 119.8, 118.1, 113.5, 112.7, 61.0, 60.7, 55.7, 44.4, 37.0, 33.2, 33.1, 27.1, 26.3, 24.0, 15.1, 15.0, 14.6, 14.1; \textbf{IR (ATR)}: $\tilde{\nu} = 2978, 2926, 2851, 1707, 1605, 1556, 1490, 1459, 1376, 1342, 1286, 1262, 1234, 1217, 1194, 1173, 1147, 1104, 1031, 982, 910, 889, 862, 843, 827, 774, 748, 734; \textbf{HRMS (ESI)} calculated for [C\textsubscript{31}H\textsubscript{37}79BrNO\textsubscript{5}]\textsuperscript{+} 582.1815, found 582.1827; \textbf{Rf}: 0.27 (pentane/EtOAc 5/1).

\textbf{Synthesis of (4bR,5aS)-diethyl 12-cyclohexyl-3-methoxy-4b,5,5a,6-tetrahydrobenzo[3,4]-cyclopropa[5,6]azepino[1,2-a]indole-5a,9-dicarboxylate (ent-15):}

![Diagram of the synthesis](image.png)

Pd(dba\textsubscript{2}) (7.24 mg, 13 µmol, 10 mol%), L6 (17.2 mg, 25 µmol, 20 mol%), AdCO\textsubscript{2}H (9.1 mg, 50 µmol, 40 mol%) and Cs\textsubscript{2}CO\textsubscript{3} (61.5 mg, 0.19 mmol, 1.5 eq.) were weighed in a microwave tube containing a magnetic stirring bar. The tube was closed with a cap, evacuated and backfilled with N\textsubscript{2}. Ethyl 2-(2-bromo-4-methoxyphenyl)-3-cyclohexyl-1-(1-(ethoxycarbonyl)-cyclopropyl)methyl)-1H-indole-6-carboxylate (16, 73.3 mg, 0.126 mmol, 1.0 eq.) was added as a solution in mesitylene (2.5 ml, 0.05 M) and the reaction mixture degassed by three freeze-pump-thaw cycles. The tube was sealed and placed in a pre-heated oil bath. The reaction mixture was stirred at 130 \degree C for 9 h. After cooling down to rt, the mixture was chromatographed on silica gel to afford pure ent-15 as a yellow foam in 80% yield (50.5 mg) and 94.5/5.5 er.

\textbf{1H-NMR} (500 MHz, CDCl\textsubscript{3}) mixture of atropisomers in ratio 1.5/1 $\delta = 8.32$ (d, $J = 0.9$ Hz, 0.6H), 8.14 (s, 0.4H), 7.87 - 7.69 (m, 2H), 7.27 (dd, $J = 11.5$, 8.5 Hz, 2H), 7.14 (d, $J = 2.2$ Hz, 0.6H), 7.02 (d, $J = 2.6$ Hz, 0.4H), 6.97 - 6.88 (m, 1H), 5.45 (d, $J = 15.0$ Hz, 0.6H), 5.20 (d, $J = 15.1$ Hz, 0.4H), 4.50 - 4.35 (m, 2H), 4.33 - 4.19 (m, 0.8H), 4.12 - 4.02 (m, 1.2H), 3.93 (dt, $J = 7.2$, 5.4 Hz, 0.6H), 3.89 (s, 3H), 3.44 (d, $J = 15.0$ Hz, 0.6H), 2.98 - 2.87 (m, 1.2H), 2.79 (tt, $J = 12.0$, 3.5 Hz, 0.4H), 2.64 (dd, $J = 10.0$, 6.9 Hz, 0.4H), 2.14 - 1.89 (m, 4H), 1.84 - 1.71 (m, 2.8H), 1.68 (dd, $J = 9.5$, 4.0 Hz, 0.6H), 1.46 - 1.32 (m, 6H), 1.21 (dd, $J = 6.1$, 4.1 Hz, 2H).
Hz, 0.6H), 1.13 (t, J = 7.2 Hz, 2H), 0.44 – 0.38 (m, 0.4H); $^{13}$C{(^1}H)-NMR (101 MHz, CDCl$_3$): δ = 173.0, 172.3, 168.0, 167.9, 159.9, 159.7, 139.0, 137.3, 136.8, 136.5, 135.4, 135.3, 133.1, 133.0, 130.3, 130.1, 123.2, 123.1, 122.5, 120.6, 120.2, 119.9, 119.7, 119.6, 119.2, 118.7, 117.6, 117.5, 113.4, 113.0, 112.3, 111.5, 61.7, 61.6, 60.9, 60.7, 55.5, 44.5, 39.8, 37.0, 36.6, 35.3, 33.4, 33.3, 33.2, 33.1, 32.8, 32.3, 27.3, 27.3, 27.2, 26.5, 26.4, 22.2, 15.0, 14.7, 14.4, 14.1; IR (ATR): ν = 2927, 2851, 1706, 1610, 1463, 1403, 1379, 1304, 1272, 1234, 1214, 1196, 1168, 1148, 1095, 1027, 774, 746; HRMS (ESI) calculated for [C$_{31}$H$_{36}$NO$_5$]$^+$ 502.2588, found 502.2576; Rf: 0.50 (pentane/EtOAc 5/1); [α]$_D^{20}$: +230.0° (c = 0.1, CHCl$_3$). Chiral HPLC: (Chiralpak IC, 4.6 x 250 mm; 10% i-PrOH / hexane, 1.0 mL/min, 320 nm; tr (minor) = 17.1 min, tr (major) = 14.4 min), 94.5/5.5 er.

Aqueous (40wt%) Bu₄POH (62 μL, 1.3 eq.) was added to a solution of ent-15 (34 mg, 0.068 mmol) in THF (2.5 mL). After stirring for 1 h at 23 °C, 1M HCl (1 mL) was added and the mixture was extracted with EtOAc. Combined organic phases were dried (Na₂SO₄) and concentrated. Purification of the residue by column chromatography on silica gel (gradient elution from DCM to DCM/EtOAc 1/1) afforded 21 (26 mg, 81%) as yellowish film.

¹H-NMR (600 MHz, CDCl₃): mixture of atropisomers in ratio 1.4/1 - δ = 8.37 (d, J = 1.2 Hz, 0.42H), 8.13 (d, J = 1.2 Hz, 0.58H), 7.85 (d, J = 8.5 Hz, 0.58H), 7.82 (d, J = 8.5 Hz, 0.42H), 7.78 (dd, J₁ = 1.4 Hz, J₂ = 8.5 Hz, 0.58H), 7.73 (dd, J₁ = 1.4 Hz, J₂ = 8.5 Hz, 0.42H), 7.26-7.30 (m, 1H), 7.14 (dd, J₁ = 0.8 Hz, J₂ = 2.8 Hz, 0.42H), 7.02 (d, J = 2.8 Hz, 0.58H), 6.90-6.96 (m, 1H), 5.45 (d, J = 15.0 Hz, 0.42H), 5.20 (d, J = 15.0 Hz, 0.58H), 4.35-4.49 (m, 2H), 4.07 (d, J = 15.0 Hz, 0.58H), 3.89 (s, 3H), 3.43 (d, J = 3.6 Hz, J₂ = 12.2 Hz, 0.42H), 2.93 (tt, J₁ = 3.6 Hz, J₂ = 12.2 Hz, 0.42H), 2.79 (tt, J₁ = 3.6 Hz, J₂ = 12.2 Hz, 0.58H), 2.74 (dd, J₁ = 6.9 Hz, J₂ = 10.1 Hz, 0.58H), 1.88-2.13 (m, 4H), 1.68-1.83 (m, 3H), 1.53-1.61 (m, 0.58H), 1.18-1.50 (m, 8H), 0.46-0.51 (m, 0.58H); ¹³C{¹H}-NMR (150 MHz, CDCl₃): δ = 178.5, 178.1, 168.2, 167.9, 159.9, 159.6, 138.5, 137.0, 136.6, 135.8, 135.5, 135.2, 133.1, 133.0, 130.2, 129.9, 123.3, 123.0, 122.8, 120.6, 120.1, 120.0, 119.7, 119.2, 118.8, 117.5, 117.4, 113.5, 113.1, 112.7, 111.5, 60.9, 60.6, 55.54, 55.53, 44.3, 39.4, 37.0, 36.6, 34.9, 33.5, 33.4, 33.3, 33.19, 33.14, 32.0, 27.38, 27.30, 27.27, 27.23, 27.1, 26.4, 26.3, 22.3, 15.5, 14.66, 14.61; IR (ATR): ν = 2974, 2926, 2850, 1690, 1609, 1561, 1491, 1461, 1423, 1382, 1368, 1344, 1321, 1273, 1237, 1216, 1164, 1104, 1073, 1041, 980, 908, 878, 827, 773, 731; HRMS (ESI) calculated for [C₂₈H₃₂NO₅]⁺ 474.2275, found 474.2280; Rf: 0.28 (DCM/EtOAc 1/1); [α]D⁰₂⁰ = +191.5° (c = 1.0, CHCl₃).
Determination of the absolute configuration


1) KOH (29.6 mg, 20 eq.) was added to a solution of 21 (13 mg, 0.027 mmol) in a mixture of EtOH (0.5 mL) and H₂O (0.5 mL) at 23 °C. After stirring for 2 h at 23 °C the mixture was evaporated under reduced pressure and the residue was partitioned between 4M HCl and EtOAc. The aqueous layer was extracted with EtOAc, combined organic phases dried (Na₂SO₄) and concentrated under reduced pressure affording the crude diacid (10 mg, 0.022 mmol, 85%), which was used in the next step without purification.

2) A mixture of the above diacid (10 mg, 0.022 mmol) and 1,1′-carbonyldiimidazole (10.9 mg, 3 eq.) in THF (0.1 mL) was stirred at 50 °C for 30 min. Upon cooling to 23 °C a solution of N,N-dimethylsulfamide (8.9 mg, 3.2 eq.) and DBU (13.7 mg, 4 eq.) in THF (0.2 mL) was added at once and the mixture was stirred at 23 °C for 16 h. Then the reaction mixture was partitioned between 4M HCl and EtOAc. The aqueous layer was extracted with EtOAc, combined organic phases dried (Na₂SO₄) and concentrated under reduced pressure affording the crude diamide, which was used in the next step without purification.

3) A solution of the above diamide in a mixture of 4M HCl (0.5 mL) and AcOH (0.5 mL) was stirred at 80 °C for 3 h. Upon cooling to 23 °C the reaction mixture was concentrated under reduced pressure and extracted with EtOAc. Combined organic phases were dried (Na₂SO₄) and concentrated. The title compound (3 mg, 25%) was isolated from the crude product mixture by preparative HPLC (Agilent 1260 Infinity Series) on reversed-phase C18 column (Phenomenex Kinetex EVO, 150 mm X 21.2 mm, 100 Å, 5 μm). Elution was performed using a linear gradient of 50 % B to 98 % B over 25 min at a flow rate of 25 mL/min with UV detection at 254 nm (Solvent A = H₂O + 0.1 % FA; Solvent B = 95 : 5 MeCN : H₂O + 0.1 % FA). Retention time 10.1 min.
Spectroscopic data for this compound was in complete agreement with the reported values for the opposite enantiomer: R. G. Gentles et al. *J. Med. Chem.* 2014, **57**, 1855:

$^1\text{H-NMR}$ (600 MHz, CD$_3$OD): mixture of atropisomers in ratio 1.6/1 - δ = 8.28 (d, $J = 1.6$ Hz, 0.62H), 8.09 (d, $J = 1.6$ Hz, 0.38H), 7.89 (d, $J = 8.5$ Hz, 0.38H), 7.85 (d, $J = 8.4$ Hz, 0.62H), 7.61 (dd, $J_1 = 8.5$ Hz, $J_2 = 1.6$ Hz, 0.38H), 7.52 (dd, $J_1 = 8.5$ Hz, $J_2 = 1.6$ Hz, 0.62H), 7.31 (d, $J = 8.5$ Hz, 0.38H), 7.27 (d, $J = 8.6$ Hz, 0.62H), 7.21 (d, $J = 2.6$ Hz, 0.62H), 7.14 (d, $J = 2.6$ Hz, 0.38H), 6.97-7.01 (m, 1H), 5.46 (d, $J = 15.0$ Hz, 0.62H), 5.27 (d, $J = 15.2$ Hz, 0.38H), 4.03 (d, $J = 15.2$ Hz, 0.38H), 3.44 (d, $J = 15.0$ Hz, 0.62H), 3.02 (s, 3.72H), 3.01 (s, 2.28H), 2.96 (tt, $J_1 = 12.3$ Hz, $J_2 = 3.6$ Hz, 0.62H), 2.80-2.90 (m, 1H), 2.74 (dd, $J_1 = 10.0$ Hz, $J_2 = 6.7$ Hz, 0.38H), 1.98-2.18 (m, 2.76H), 1.91-1.97 (m, 1H), 1.74-1.85 (m, 2H), 1.63-1.71 (m, 1.24H), 1.21-1.55 (m, 5H), 0.23-0.27 (m, 0.38H); HRMS (ESI) calculated for [C$_{29}$H$_{34}$N$_3$O$_6$S]$^+$ 552.2163, found 552.2172; [α]$_D^{20}$ = +167.1° ($c = 0.33$, MeOH) – reported value for the opposite enantiomer: [α]$_D^{20}$ = -166.99° ($c = 1.0$, MeOH).
$^{1}H$ and $^{13}C$-NMR spectra