Electronic Supplementary Information

Diastereodivergent synthesis of bispirooxindoles via asymmetric Friedel–Crafts/aldol cascade reaction: co-catalyst effects on diastereoselective outcomes

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1. General methods

All reactions were carried out under an atmosphere of nitrogen in oven-dried glasswares with magnetic stirring, unless otherwise indicated. All solvents employed in the reactions were distilled from appropriate drying agent prior to use. All other reagents were used as obtained unless otherwise noted. Flash Chromatography was performed with silica gel (300–400 mesh) from Yantai Chemical Industry Research Institute, P. R. China. Analytical thin-layer chromatography was performed with 0.2 ± 0.03 mm coated commercial silica gel plates (GF-254, particle size 0.04–0.05 mm). $^1$H and $^{13}$C NMR spectra were recorded in CDCl$_3$ on Varian Inova (400 MHz and 100 MHz, respectively) spectrometer. Chemical shifts (δ ppm) are relative to the resonance of the deuterated solvent as the internal standard (CDCl$_3$, δ 7.26 ppm for proton NMR, δ 77.23 ppm for carbon NMR). $^1$H NMR data are reported as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, q = quartet, m = multiplet), coupling constants (J) and assignment. Data for $^{13}$C NMR are reported in terms of chemical shift (δ, ppm). IR spectra were recorded on a Varian 1000 FT-IR spectrometer. Mass spectra were carried out using Agilent 6120 Quadrupole LC/MS system with ESI resource. High-resolution mass spectra (HRMS) for all the compounds were determined on Micromass GCT-TOF mass spectrometer with ESI resource. High-performance liquid chromatography (HPLC) was performed on an Agilent 1200 Series chromatographs using CHIRALCEL AD-H and OD-H columns. X-ray data were recorded on a Rigaku Mercury CCD/AFC diffractometer. Optical rotations are performed on Rudolph Aupol IV and reported as follows: $[a]_D^\circ$ (c in g per 100 mL, solvent).
2. Typical experimental procedures

2.1 Optimization of reaction conditions

Table S1. Optimization of several other reaction parameters

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*Unless otherwise noted, reactions were carried out with 1a (0.05 mmol), 2a, cat. and L6 in m-xylene at 25 °C. b Isolated yield. c Determined by 1H NMR analysis. d Determined by chiral HPLC. e Determined by TLC analysis.

2.2 General procedure for the preparation of the adduct 3
Under N\textsubscript{2} atmosphere, Cu(OTf)\textsubscript{2} (0.01 mmol, 10 mol\%) and L\textsubscript{6} (0.01 mmol, 10 mol\%) were combined into a vessel, and m-xylene (2.50 mL) was added via syringe. After the system was stirred at 25 °C for 0.5 h, the substrates 1 (0.1 mmol) and 2 (0.22 mmol, 2.2 equiv) were included. The reaction mixture was further stirred until the reaction was complete (detected by TLC). Then quinidine (0.02 mmol, 20 mol\%) was introduced into the reaction mixture at 25°C. After the reaction was detected complete (by TLC analysis), the solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel with EtOAc/petroleum ether (1/1) as eluent to give 3 as solids.

The racemic samples described in this part were synthesized according above procedure, which were catalyzed by Cu(OTf)\textsubscript{2} with mixed L\textsubscript{6} and ent-L\textsubscript{6} as ligands. Because equal amount of L\textsubscript{6} and ent-L\textsubscript{6} could not be accurately balanced, slight ee values (<15\%) were observed in their racemic HPLC spectra.

**ethyl(3R,6'S,8'S)-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3aa**

![Chemical structure of 3aa]

White solid; mp 215–216 °C; 95% yield (44.8 mg), >20:1 \textit{dr}, 95\% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min\textsuperscript{-1}, λ = 254.4 nm, t (major) = 44.771, t (minor) = 32.098]; \([\alpha]\textsubscript{D}\textsuperscript{25} = 181.5 (c 0.19, CHCl\textsubscript{3}); {\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \delta 7.66 (s, 1H), 7.44 – 7.39 (m, 2H), 7.35 – 7.11 (m, 1H), 7.25 – 7.19 (m, 2H), 7.04 – 6.96 (m, 2H), 6.87 (d, J = 7.6 Hz, 1H), 6.26 (dd, J = 2.8, 1.6 Hz, 1H), 6.06 (t, J = 3.2 Hz, 1H), 5.56 (dd, J = 3.6, 1.6 Hz, 1H), 3.81 (qd, J = 7.2, 1.6 Hz, 2H), 3.38 (s, 3H), 3.31 – 3.26 (m, 4H), 2.50 (d, J = 15.6 Hz, 1H), 0.95 (t, J = 7.2 Hz, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \delta 179.0, 171.4, 168.4, 142.9, 142.5, 132.9, 129.8, 128.8, 127.4, 125.2, 123.6, 123.3, 122.8, 122.1, 120.3, 110.4, 108.4, 108.0, 106.8, 77.9, 67.7, 61.2, 47.9, 34.2, 26.5, 26.3, 13.2; IR (KBr) \textit{v}_{\text{max}}: 3291, 3196, 2962, 2923, 2853, 1748, 1717, 1699, 1670, 1653, 1624, 1609, 1558, 1507, 1490, 1458, 1373, 1257, 1226, 1090, 1054, 1022, 801, 740, 709, 694 cm\textsuperscript{-1}; HRMS (ESI): \textit{m/z} = 472.1878 (calcd for C\textsubscript{27}H\textsubscript{25}N\textsubscript{3}O\textsubscript{5}+H\textsuperscript{+} = 472.1867).
ethyl(3R,6'S,8'S)-1''-benzyl-6'-hydroxy-1-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ba

![Structure of 3ba]

White solid; mp 110–111 °C; 85% yield (46.5 mg), 95:5 dr, 93% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 70/30, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 14.904, t (minor) = 54.561]; [α]D²⁵ = 206.1 (c 0.51, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.67 (s, 1H), 7.41 – 7.39 (m, 1H), 7.36 – 7.18 (m, 9H), 7.03 (t, J = 7.6 Hz, 1H), 6.87 (dd, J = 16.8, 7.6 Hz, 2H), 6.30 – 6.29 (m, 1H), 6.09 (t, J = 3.2 Hz, 1H), 5.58 (d, J = 3.6 Hz, 1H), 5.06 (d, J = 15.6 Hz, 1H), 4.82 (d, J = 15.6 Hz, 1H), 3.82 (q, J = 7.2 Hz, 2H), 3.39 (s, 3H), 3.35 (d, J = 15.6 Hz, 1H), 2.57 (d, J = 15.2 Hz, 1H), 0.96 (t, J = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 179.2, 171.4, 168.4, 142.5, 141.9, 134.6, 132.9, 129.9, 128.7, 128.5, 127.4, 126.9, 125.3, 123.6, 123.3, 122.8, 122.1, 120.3, 110.5, 109.5, 108.0, 106.8, 77.9, 67.7, 61.3, 47.9, 43.7, 34.3, 26.3, 13.2; IR (KBr) νmax: 2974, 2924, 2924, 1772, 1717, 1683, 1647, 1609, 1576, 1541, 1507, 1489, 1465, 1457, 1419, 1396, 1373, 1340, 1249, 1229, 1078, 929, 751, 696, 668 cm⁻¹; HRMS (ESI): m/z = 548.2174 (calcd for C₃₃H₂₉N₅O₅⁺H⁺ = 548.2180).

ethyl(3R,6'S,8'S)-1''-allyl-6'-hydroxy-1-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ca

![Structure of 3ca]

White solid; mp 207–208 °C; 95% yield (47.2 mg), >20:1 dr, 93% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 70/30, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 15.746, t (minor) = 26.650]; [α]D²⁵ = 103.6 (c 0.19, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.61 (s, 1H), 7.40 – 7.32 (m, 3H), 7.24 – 7.21 (m, 2H), 7.02 (t, J = 7.6 Hz, 1H), 6.96 (d, J = 7.6 Hz, 1H), 6.88 (d, J = 7.6 Hz, 1H), 6.27 (dd, J = 2.8, 1.6 Hz, 1H), 6.07 (t, J = 3.2 Hz, 1H), 5.85 (ddt, J = 15.6, 10.4, 5.2 Hz, 1H), 5.58 (dd, J = 3.6, 1.6 Hz, 1H), 5.28 – 5.24 (m, 2H), 4.46 – 4.40 (m, 1H), 4.34 – 4.28 (m, 1H), 3.81 (q, J = 7.2 Hz, 2H), 3.38 (s, 3H), 3.32 (d, J = 15.2 Hz, 1H), 2.52 (d, J = 15.6 Hz, 1H), 0.95 (t, J = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 178.8, 171.4, 168.4, 142.5, 142.0, 132.9, 130.1, 129.9, 128.7,
127.4, 125.3, 123.5, 123.4, 122.8, 122.1, 120.3, 117.6, 110.4, 109.3, 108.0, 106.7, 77.9, 67.7, 61.2, 47.8, 42.2, 34.3, 26.3, 13.2; IR (KBr) \( \nu_{\text{max}} \): 2961, 2922, 2850, 1733, 1717, 1683, 1652, 1636, 1609, 1558, 1541, 1507, 1472, 1457, 1419, 1372, 1340, 1250, 1231, 1089, 1074, 1035, 929, 752, 696, 668 cm\(^{-1}\); HRMS (ESI): m/z = 498.2039 (calcd for C\(_{29}\)H\(_{27}\)N\(_{3}\)O\(_{5}\)+H\(^+\) = 498.2023).

ethyl(3R,6'S,8'S)-6'-hydroxy-1''-(methoxymethyl)-1-methyl-2,2''-dioxo-6',7'-dihydropyrido[3e,6e,9f]indole-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3da

White solid; mp 106–107 °C; 88% yield (44.1 mg), >20:1 \( dr \), 92% \( ee \) [Daicel Chiralcel AD-H, hexanes/i-PrOH = 70/30, flow rate: 1.0 mL·min\(^{-1}\), \( \lambda = 254.4 \) nm, t (major) = 15.006, t (minor) = 30.067]; \( [\alpha]_D^{23} \) = 106.3 (c 0.19, CHCl\(_3\)); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.47 (t, \( J = 7.6 \) Hz, 2H), 7.42 – 7.37 (m, 2H), 7.34 – 7.30 (m, 1H), 7.27 (d, \( J = 7.6 \) Hz, 1H), 7.22 (d, \( J = 8.0 \) Hz, 1H), 7.08 (t, \( J = 7.6 \) Hz, 1H), 6.94 (d, \( J = 8.0 \) Hz, 1H), 6.32 (dd, \( J = 3.2, 1.6 \) Hz, 1H), 6.12 (t, \( J = 3.2 \) Hz, 1H), 5.66 (dd, \( J = 4.0, 2.0 \) Hz, 1H), 5.35 – 5.15 (m, 2H), 3.86 (q, \( J = 7.2 \) Hz, 2H), 3.44 (s, 3H), 3.41 – 3.33 (m, 4H), 2.59 (d, \( J = 15.6 \) Hz, 1H), 0.99 (t, \( J = 7.2 \) Hz, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 179.8, 171.4, 168.3, 142.5, 141.0, 132.3, 129.9, 128.9, 127.3, 125.3, 124.0, 123.4, 122.9, 122.2, 120.4, 110.5, 109.9, 108.1, 106.9, 77.8, 71.3, 67.6, 61.3, 56.0, 48.2, 34.5, 26.3, 13.2; IR (KBr) \( \nu_{\text{max}} \): 2973, 2923, 2851, 1733, 1698, 1671, 1647, 1609, 1558, 1541, 1507, 1489, 1472, 1457, 1373, 1340, 1249, 1090, 1074, 752 cm\(^{-1}\); HRMS (ESI): m/z = 502.1988 (calcd for C\(_{29}\)H\(_{27}\)N\(_{3}\)O\(_{5}\)+H\(^+\) = 502.1973).

ethyl(3R,6'S,8'S)-6'-hydroxy-1,1'',5''-trimethyl-2,2''-dioxo-6',7'-dihydropyrido[3e,6e,9f]indole-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ea

White solid; mp 133–134 °C; 90% yield (43.8 mg), >20:1 \( dr \), 60% \( ee \) [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min\(^{-1}\), \( \lambda = 254.4 \) nm, t (major) = 40.406, t (minor) = 30.586]; \( [\alpha]_D^{23} \) = 300.5 (c 0.22, CHCl\(_3\)); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.60 (s, 1H), 7.33 (t, \( J = 7.6 \) Hz, 1H),
7.24 – 7.15 (m, 3H), 7.03 (t, J = 7.2 Hz, 1H), 6.87 (dd, J = 10.8, 7.6 Hz, 2H), 6.26 (dd, J = 2.8, 1.6 Hz, 1H), 6.06 (t, J = 3.2 Hz, 1H), 5.57 (dd, J = 4.0, 2.0 Hz, 1H), 3.81 (qd, J = 7.2, 2.8 Hz, 2H), 3.38 (s, 3H), 3.27 (d, J = 15.6 Hz, 1H), 3.33 (s, 3H), 2.49 (d, J = 15.6 Hz, 1H), 2.42 (s, 3H), 0.95 (t, J = 7.2 Hz, 3H); 13C NMR (101 MHz, CDCl3) δ 178.9, 171.4, 168.5, 142.5, 140.5, 133.3, 132.8, 129.8, 129.1, 127.5, 125.5, 124.0, 122.8, 122.1, 120.2, 110.3, 108.1, 108.0, 106.6, 77.9, 67.73, 61.2, 47.9, 34.3, 29.2, 26.4, 20.8, 13.2; IR (KBr) νmax: 3219, 2962, 2923, 2854, 1733, 1718, 1697, 1653, 1636, 1608, 1558, 1541, 1506, 1490, 1472, 1457, 1419, 1371, 1340, 1246, 1070, 1030, 933, 805, 751, 697, 673 cm⁻¹; HRMS (ESI): m/z = 486.2035 (calcd for C28H37N3O5+H+ = 486.2023).

**ethyl(3R,6'S,8'S)-5″,6″-difluoro-6'-hydroxy-1,1″-dimethyl-2,2″-dioxo-6’,7'-dihydrospiro[indoline-3,5'-indolizine-8',3″-indoline]-6'-carboxylate 3fa**

White solid; mp 125–126 °C; 84% yield (42.5 mg), 97:3 dr, 86% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 70/30, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 31.166, t (minor) = 15.200]; [α]²⁰⁰° = 199.0 (c 0.21, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.44 – 7.31 (m, 2H), 7.22 (t, J = 8.0 Hz, 1H), 7.15 – 6.98 (m, 2H), 6.96 – 6.74 (m, 2H), 6.26 (s, 1H), 6.07 (t, J = 3.2 Hz, 1H), 5.58 (d, J = 3.6 Hz, 1H), 3.91 – 3.69 (m, 2H), 3.38 (s, 3H), 3.23 (s, 3H), 3.18 (d, J = 15.6 Hz, 1H), 2.51 (d, J = 15.2 Hz, 1H), 0.95 (t, J = 7.2 Hz, 3H); ¹⁹F NMR (376 MHz, CDCl₃) δ –134.8 (d, J = 19.6 Hz), –143.3 (d, J = 20.0 Hz); ¹³C NMR (101 MHz, CDCl₃) δ 178.7, 171.3, 168.2, 142.6, 139.2, 130.0, 128.098, 127.2, 124.3, 122.7, 122.2, 120.6, 113.2 (d, J = 19.6 Hz), 110.5, 108.2, 106.9, 98.8 (d, J = 23.0 Hz), 77.8, 67.5, 61.4, 47.9, 34.4, 26.7, 26.3, 13.2; IR (KBr) νmax: 3214, 2964, 2922, 1733, 1697, 1653, 1647, 1608, 1541, 1506, 1490, 1457, 1419, 1370, 1340, 1247, 1091, 1070, 1029, 933, 752, 695, 673 cm⁻¹; HRMS (ESI): m/z = 508.1668 (calcd for C29H39F2N3O5+H+ = 508.1679).

**ethyl(3R,6'S,8'S)-6″-chloro-6'-hydroxy-1,1″-dimethyl-2,2″-dioxo-6’,7'-dihydrodiospiro[indoline-3,5'-indolizine-8',3″-indoline]-6'-carboxylate 3ga**
White solid; mp 141–142 °C; 97% yield (48.9 mg), >20:1 dr, 96% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 70/30, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 41.777, t (minor) = 13.235]; [α]D° = 187.9 (c 0.31, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.41 (s, 1H), 7.37 – 7.28 (m, 2H), 7.20 (dd, J = 8.0, 2.0 Hz, 1H), 7.14 (dd, J = 7.6, 1.2 Hz, 1H), 7.05 – 6.99 (m, 1H), 6.97 (d, J = 1.6 Hz, 1H), 6.88 (d, J = 8.0 Hz, 1H), 6.26 (dd, J = 3.2, 1.8 Hz, 1H), 6.06 (t, J = 3.2 Hz, 1H), 5.57 (dd, J = 3.6, 1.6 Hz, 1H), 3.80 (qd, J = 7.2, 3.2 Hz, 2H), 3.38 (s, 3H), 3.25 (s, 3H), 3.24 (d, J = 15.2 Hz, 1H), 2.49 (d, J = 15.6 Hz, 1H), 0.95 (t, J = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 179.7, 171.3, 168.3, 144.1, 142.5, 134.6, 131.2, 129.9, 127.3, 124.6, 124.3, 123.4, 122.8, 122.1, 120.5, 110.5, 109.1, 108.1, 106.9, 77.8, 67.6, 61.3, 47.6, 34.3, 26.6, 26.3, 13.2; IR (KBr) v_max: 3219, 2962, 2924, 2852, 1732, 1696, 1684, 1607, 1491, 1472, 1458, 1371, 1341, 1245, 1221, 1089, 1069, 1051, 1027, 934, 798, 751, 696, 673 cm⁻¹; HRMS (ESI): m/z = 506.1490 (calcd for C₂₇H₄₅ClN₃O₅H⁺ = 506.1477).

**ethyl(3R,6'S,8'S)-6'-hydroxy-1',1''',7''''-trimethyl-2,2'''-dioxo-6',7'''-dihydrodispiro[indoline-3,5'-indolizine-8',3'''-indoline]-6'-carboxylate 3ha**

White solid; mp 135–136 °C; 88% yield (42.6 mg), >20:1 dr, 90% ee [Daicel Chiralcel OD-H, hexanes/i-PrOH = 70/30, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 26.760, t (minor) = 13.759]; [α]D° = 147.9 (c 0.32, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.79 (s, 1H), 7.36 – 7.29 (m, 1H), 7.25 – 7.17 (m, 2H), 7.16 – 7.07 (m, 2H), 7.09 (td, J = 7.6, 1.2 Hz, 1H), 6.87 (d, J = 7.6 Hz, 1H), 6.25 (dd, J = 2.8, 1.6 Hz, 1H), 6.06 (t, J = 3.2 Hz, 1H), 5.57 (dd, J = 3.6, 1.6 Hz, 1H), 3.79 (qd, J = 7.2, 1.2 Hz, 2H), 3.52 (s, 3H), 3.38 (s, 3H), 3.24 (d, J = 15.2 Hz, 1H), 2.65 (s, 3H), 2.47 (d, J = 15.6 Hz, 1H), 0.94 (t, J = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 179.7, 171.4, 168.4, 142.5, 140.5, 133.5, 132.5, 129.8, 127.5, 125.7, 123.4, 122.9, 122.1, 121.4, 120.2, 120.0, 110.3, 108.0, 106.7, 77.9, 67.7, 61.2, 47.3, 34.5, 29.9, 26.3, 18.5, 13.2; IR (KBr) v_max: 2973, 2927, 2891, 1748, 1716, 1684, 1670, 1576, 1541, 1507, 1489, 1457, 1418, 1374, 1087, 1047, 684, 668, 606.
ethyl(3R,6'S,8'S)-7'-fluoro-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ia

White solid; mp 108–109 °C; 91% yield (44.5 mg), >20:1 dr, 93% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 33.869, t (minor) = 31.395]; [α]D = 184.1 (c 0.22, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.49 (s, 1H), 7.33 (td, J = 7.6, 1.2 Hz, 1H), 7.24 – 7.09 (m, 4H), 7.06 (t, J = 7.6 Hz, 1H), 6.94 (d, J = 7.6 Hz, 1H), 6.26 (dd, J = 16.0, 8.0 Hz, 1H), 6.07 (t, J = 3.2 Hz, 1H), 5.60 (dd, J = 3.6, 1.6 Hz, 1H), 3.80 (qq, J = 7.2, 3.2 Hz, 2H), 3.46 (d, J = 2.4 Hz, 3H), 3.38 (s, 3H), 3.25 (d, J = 15.6 Hz, 1H), 2.52 (d, J = 15.6 Hz, 1H), 0.94 (t, J = 7.2 Hz, 3H); ¹⁹F NMR (376 MHz, CDCl₃) δ –135.7; ¹³C NMR (101 MHz, CDCl₃) δ 178.7, 171.3, 168.3, 147.2 (d, J = 243.6 Hz), 142.5, 135.6, 129.9, 129.5 (d, J = 8.7 Hz), 127.4, 124.7, 124.2 (d, J = 6.2 Hz), 122.8, 122.1, 120.4, 119.2, 116.9, 116.7, 110.4, 108.1, 106.9, 77.8, 67.6, 61.3, 48.1, 34.4, 29.1, 26.3, 13.2; IR (KBr) νmax: 2973, 2922, 1772, 1733, 1698, 1684, 1652, 1647, 1616, 1558, 1521, 1507, 1497, 1473, 1464, 1418, 1339, 883, 746, 693, 626 cm⁻¹; HRMS (ESI): m/z = 490.1779 (calcd for C₂₇H₂₄FN₃O₅+H⁺ = 490.1773).

ethyl(3R,6'S,8'S)-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-7''-(trifluoromethyl)-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ja

White solid; mp 215–216 °C; 94% yield (50.6 mg), 91:9 dr, 94% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 26.934, t (minor) = 16.233]; [α]D = 142.8 (c 0.22, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, J = 8.4 Hz, 1H), 7.58 (d, J = 7.6 Hz, 1H), 7.47 – 7.28 (m, 3H), 7.17 (d, J = 7.2 Hz, 1H), 7.03 (t, J = 7.2 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 6.27 (t, J = 2.4 Hz, 1H), 6.08 (t, J = 3.2 Hz, 1H), 5.56 (dd, J = 4.0, 1.6 Hz, 1H), 3.80 (qd, J = 7.2, 4.4 Hz, 2H), 3.46
ethyl(3R,6'S,8'S)-1-benzyl-6'-hydroxy-1''-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ab

White solid; mp 109–110 °C; 89% yield (50.6 mg), 93:7 dr, 93% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 70/30, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 23.361, t (minor) = 17.937]; [α]D²⁵ = 168.1 (c 0.34, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.75 (s, 1H), 7.57 (d, J = 7.6 Hz, 2H), 7.51–7.41 (m, 4H), 7.35 (d, J = 7.6 Hz, 1H), 7.32–7.22 (m, 3H), 7.14–6.95 (m, 2H), 6.88 (d, J = 7.6 Hz, 1H), 6.37–6.23 (m, 1H), 6.11 (t, J = 3.6 Hz, 1H), 5.61 (d, J = 3.6 Hz, 1H), 5.36 (d, J = 15.2 Hz, 1H), 4.89 (d, J = 15.2 Hz, 1H), 3.87–3.66 (m, 2H), 3.36 (d, J = 15.6 Hz, 1H), 3.32 (s, 3H), 2.59 (d, J = 15.6 Hz, 1H), 0.87 (t, J = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 179.0, 171.6, 168.4, 142.9, 141.8, 135.3, 132.9, 129.7, 128.8, 128.4, 127.6, 127.6, 127.4, 125.4, 123.6, 123.3, 122.9, 122.1, 120.1, 110.5, 109.1, 108.4, 106.7, 77.8, 67.5, 61.2, 47.9, 44.3, 34.5, 26.5, 13.1; IR (KBr) νmax: 3178, 2964, 2922, 1733, 1697, 1683, 1671, 1653, 1610, 1541, 1488, 1465, 1458, 1374, 1354, 1251, 1222, 1152, 1092, 1050, 1031, 932, 752, 743, 703, 692, 683 cm⁻¹; HRMS (ESI): m/z = 570.1989 (calcld for C₃₃H₂₈N₃O₅Na⁺ = 570.1999).

ethyl(3R,6'S,8'S)-1-allyl-6'-hydroxy-1''-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ac

White solid; mp 206–207 °C; 88% yield (43.7 mg), >20:1 dr, 89% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 70/30, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 19.869, t (minor) = 12.425]; [α]D²⁵ = 208.1 (c 0.32, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.71 (s, 1H), 7.53–7.42 (m, 2H), 7.38–7.23 (m, 3H), 7.10–6.99 (m,
ethyl(3R,6'S,8'S)-6'-hydroxy-1,1''',5-trimethyl-2,2'''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3'''-indoline]-6'-carboxylate 3ad

White solid; mp 223–224 °C; 92% yield (44.8 mg), >20:1 dr, 91% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 24.439, t (minor) = 20.738]; [α]D²⁵ = 209.6 (c 0.25, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.62 (s, 1H), 7.50 – 7.33 (m, 2H), 7.24 (td, J = 7.6, 1.2 Hz, 1H), 7.12 (d, J = 8.0 Hz, 1H), 7.05 – 6.92 (m, 2H), 6.76 (d, J = 8.0 Hz, 1H), 6.26 (dd, J = 2.8, 1.6 Hz, 1H), 6.07 (t, J = 3.2 Hz, 1H), 5.57 (dd, J = 3.6, 1.6 Hz, 1H), 3.82 (qd, J = 7.2, 2.4 Hz, 2H), 3.36 (s, 3H), 3.35 (d, J = 15.6 Hz, 1H), 3.26 (s, 3H), 2.49 (d, J = 15.6 Hz, 1H), 2.31 (s, 3H), 0.96 (t, J = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 179.0, 171.4, 168.5, 142.9, 140.2, 133.0, 131.5, 130.1, 128.8, 127.4, 125.2, 123.6, 123.2, 120.3, 110.3, 108.4, 107.8, 106.6, 77.9, 67.8, 61.2, 47.9, 34.2, 26.5, 26.3, 20.9, 13.2; IR (KBr) v_max: 3177, 2987, 2971, 2906, 1733, 1698, 1653, 1609, 1558, 1541, 1506, 1472, 1457, 1418, 1374, 1346, 1249, 1226, 1092, 1080, 1051, 1037, 811, 766, 718, 696, 681, 625 cm⁻¹; HRMS (ESI): m/z = 486.2026 (calcd for C₂₉H₂₇N₃O₅+H⁺ = 486.2023).
ethyl(3R,6'S,8'S)-6'-hydroxy-1,1''-5,7-tetramethyl-2,2''-dioxo-6',7'-dihydrodispir
o[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ae

White solid; mp 221–222 °C; 94% yield (46.9 mg), >20:1 dr, 94% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 21.796, t (minor) = 24.560]; α²⁵ = 238.8 (c 0.26, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.59 (s, 1H), 7.47 – 7.35 (m, 2H), 7.23 (td, J = 7.6, 1.2 Hz, 1H), 6.97 (d, J = 7.6 Hz, 1H), 6.88 – 6.78 (m, 2H), 6.26 (dd, J = 2.8, 1.6 Hz, 1H), 6.07 (t, J = 3.2 Hz, 1H), 5.56 (dd, J = 3.6, 1.6 Hz, 1H), 3.86 (q, J = 7.2 Hz, 2H), 3.63 (s, 3H), 3.32 (d, J = 15.6 Hz, 1H), 3.26 (s, 3H), 2.54 (s, 3H), 2.43 (d, J = 15.6 Hz, 1H), 2.25 (s, 3H), 1.00 (t, J = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 179.0, 172.3, 168.5, 142.9, 137.7, 133.9, 133.0, 131.3, 128.8, 128.2, 125.3, 123.5, 123.2, 121.5, 120.4, 119.3, 110.2, 108.4, 106.5, 78.0, 67.5, 61.1, 47.9, 33.9, 29.7, 26.5, 20.5, 18.6, 13.2; IR (KBr) νmax: 3178, 2971, 2917, 1732, 1698, 1671, 1647, 1608, 1558, 1541, 1506, 1497, 1457, 1418, 1374, 1339, 1248, 1224, 1092, 1050, 811, 765 cm⁻¹; HRMS (ESI): m/z = 500.2190 (calcd for C₂₉H₉N₃O₅+H⁺ = 500.2180).

ethyl(3R,6'S,8'S)-6'-hydroxy-5-methoxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrod
ispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3af

White solid; mp 173–174 °C; 91% yield (46.5 mg), >20:1 dr, 75% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 40.833, t (minor) = 30.704]; α²⁵ = 404.0 (c 0.30, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.63 (s, 1H), 7.46 – 7.35 (m, 2H), 7.23 (t, J = 7.2 Hz, 1H), 6.96 (d, J = 7.6 Hz, 1H), 6.88 – 6.73 (m, 3H), 6.27 (dd, J = 3.2, 1.6 Hz, 1H), 6.06 (t, J = 3.2 Hz, 1H), 5.57 (dd, J = 4.0, 1.6 Hz, 1H), 3.84 (qd, J = 7.2, 2.0 Hz, 2H), 3.77 (s, 3H), 3.36 (s, 3H), 3.28 (d, J = 15.6 Hz, 1H), 3.26 (s, 3H), 2.49 (d, J = 15.6 Hz, 1H), 0.98 (t, J = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 179.0, 171.1, 168.4, 155.2, 142.9, 135.9, 132.9, 128.8, 128.6, 125.1, 123.6, 123.2, 120.4, 113.0, 111.5, 110.4, 108.4, 108.2, 106.9, 77.8, 67.9,
61.2, 55.3, 47.9, 34.1, 29.2, 26.4, 13.2; IR (KBr) \( \nu_{\text{max}}: 3219, 3197, 2965, 2921, 2649, 1733, 1698, 1653, 1636, 1609, 1558, 1507, 1490, 1464, 1457, 1419, 1373, 1290, 1247, 1232, 1091, 1053, 1030, 802, 751, 692 \text{ cm}^{-1} \); HRMS (ESI): m/z = 502.1965 (calcd for \(\text{C}_{28}\text{H}_{27}\text{N}_{3}\text{O}_{6}+\text{H}^+ = 502.1973)\).

**ethyl(3R,6'S,8'S)-6'-hydroxy-6-methoxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydropseudo[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ag**

White solid; mp 191–192 °C; 90% yield (45.1 mg), >20:1 dr, 79% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 70/30, flow rate: 1.0 mL·min\(^{-1}\), \( \lambda = 254.4 \text{ nm} \), t (major) = 23.041, t (minor) = 15.995; \( [\alpha]_D^{25} = 170.0 (c 0.20, \text{CHCl}_3) \);

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \):
- 7.60 (s, 1H)
- 7.46–7.31 (m, 2H)
- 7.26–7.16 (m, 1H)
- 7.11 (d, \( J = 8.0 \text{ Hz} \), 1H)
- 6.96 (d, \( J = 7.6 \text{ Hz} \), 1H)
- 6.49 (dd, \( J = 8.4, 2.4 \text{ Hz} \), 1H)
- 6.43 (d, \( J = 2.4 \text{ Hz} \), 1H)
- 6.25 (dd, \( J = 2.8, 1.6 \text{ Hz} \), 1H)
- 6.05 (t, \( J = 3.2 \text{ Hz} \), 1H)
- 5.54 (dd, \( J = 3.6, 1.6 \text{ Hz} \), 1H)
- 3.85 (qd, \( J = 7.2, 2.8 \text{ Hz} \), 2H)
- 3.81 (s, 3H)
- 3.36 (s, 3H)
- 3.26 (d, \( J = 15.6 \text{ Hz} \), 1H)
- 3.26 (s, 3H)
- 2.50 (d, \( J = 15.6 \text{ Hz} \), 1H)
- 0.99 (t, \( J = 7.2 \text{ Hz} \), 3H);

\(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \):
- 179.1
- 171.9
- 168.5
- 161.1
- 144.0
- 142.9
- 133.0
- 128.8
- 125.2
- 123.8
- 123.5
- 123.265
- 120.1
- 119.5
- 110.3
- 108.4
- 106.6
- 105.6
- 95.9
- 77.9
- 67.3
- 61.2
- 55.1
- 47.9
- 34.2
- 26.5
- 26.3
- 13.3;

IR (KBr) \( \nu_{\text{max}}: 3355, 2986, 2408, 1717, 1459, \)

2.3 General procedure for the preparation of the adduct 4

Under N\(_2\) atmosphere, Cu(OTf)\(_2\) (0.01 mmol, 10 mol%) and L\(_6\) (0.01 mmol, 10 mol%) were combined into a vessel, and \( m \)-xylene (2.50 mL) was added via syringe. After the catalyst system was stirred at 25 °C for 0.5 h, the substrates 1 (0.1 mmol)
and 2 (0.22 mmol, 2.2 equiv) were included and the reaction mixture was further stirred until the reaction was complete (detected by TLC). Then p-TsOH (0.02 mmol, 20 mol%) was introduced to promote the subsequent intramolecular aldol reaction at 25 °C. Once the reaction was detected complete (by TLC analysis), the solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel with EtOAc/petroleum ether (1/1) as eluent to give 4 as solids.

The racemic samples described in this part were synthesized according above procedure, which were catalyzed by Cu(OTf)$_2$ with mixed L6 and ent-L6 as ligands. Because equal amount of L6 and ent-L6 could not be accurately balanced, slight ee values (<15%) were observed in their racemic HPLC spectra.

**ethyl(3R,6'R,8'S)-6'-hydroxy-1''-dimethyl-2,2''-dioxo-6',7''-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4aa**

![Structural formula of 4aa]

White solid; mp 131–132 °C; 91% yield (43.3 mg), >20:1 dr, 97% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min$^{-1}$, $\lambda$ = 254.4 nm, t (major) = 12.056, t (minor) = 20.443]; [α]$^D_0$ = $-161.9$ (c 0.47, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.79 (d, $J = 7.6$ Hz, 1H), 7.71 (d, $J = 7.6$ Hz, 1H), 7.45 (t, $J = 7.8$ Hz, 1H), 7.29 – 7.22 (m, 1H), 7.14 (t, $J = 7.6$ Hz, 1H), 7.70 (t, $J = 7.6$ Hz, 1H), 6.88 (t, $J = 7.6$ Hz, 2H), 6.01 (t, $J = 3.2$ Hz, 1H), 5.97 – 5.88 (m, 1H), 5.63 (dd, $J = 3.6$, 2.0 Hz, 1H), 4.16 (s, 1H), 4.11 – 3.94 (m, 3H), 3.31 (s, 3H), 3.21 (s, 3H), 2.00 (d, $J = 14.0$ Hz, 1H), 1.08 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 177.5, 171.7, 170.9, 144.1, 142.4, 136.0, 130.7, 127.8, 127.4, 127.3, 126.7, 124.3, 122.5, 122.2, 116.8, 109.0, 107.6, 107.2, 105.9, 76.3, 66.7, 62.8, 47.9, 34.8, 26.3, 26.3, 13.4; IR (KBr) $\nu_{max}$: 2973, 2922, 2913, 1733, 1700, 1670, 1636, 1608, 1588, 1521, 1507, 1473, 1457, 1419, 1372, 1339, 1258, 1105, 1094, 754, 745, 700 cm$^{-1}$; HRMS (ESI): m/z = 472.1879 (calcd for C$_{27}$H$_{25}$N$_3$O$_5$H$^+$ = 472.1867).

**ethyl(3R,6'R,8'S)-1''-benzyl-6'-hydroxy-1-methyl-2,2''-dioxo-6',7''-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ba**
White solid; mp 125–126 °C; 85% yield (46.4 mg), 90:10 dr, 89% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 11.110, t (minor) = 19.014]; [α]D²⁰ = -66.2 (c 0.31, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.91 – 7.70 (m, 2H), 7.54 – 7.45 (m, 2H), 7.43 – 7.29 (m, 4H), 7.27 – 7.16 (m, 2H), 7.09 – 6.77 (m, 3H), 6.43 – 5.91 (m, 2H), 5.59 – 5.74 (m, 1H), 5.26 – 5.06 (m, 1H), 4.99 – 4.80 (m, 1H), 4.24 (s, 1H), 4.19 – 3.75 (m, 3H), 3.50 – 3.29 (s, 3H), 2.12 (d, J = 14.4 Hz, 1H), 1.14 (t, J = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 177.7, 171.7, 170.9, 144.1, 141.4, 136.1, 135.9, 130.7, 128.5, 128.2, 127.9, 127.3, 127.1, 126.9, 126.7, 124.3, 122.6, 122.2, 116.8, 109.1, 108.2, 107.6, 105.9, 76.3, 66.6, 62.9, 47.9, 43.7, 34.8, 25.9, 13.4; IR (KBr) νmax: 2962, 2629, 1733, 1717, 1685, 1608, 1489, 1466, 1457, 1363, 1341, 1259, 1174, 1129, 1084, 1055, 1024, 799, 747, 700, 669 cm⁻¹; HRMS (ESI): m/z = 548.2178 (calcd for C₃₃H₂₉N₀O₅⁺H⁺ = 548.2180).

**ethyl(3R,6'R,8'S)-1''-allyl-6''-hydroxy-1-methyl-2,2''-dioxo-6',7''-dihydrodiphenil[1
ndoline-3,5'-indizoline-8',3''-indoline]-6''-carboxylate 4ca**

White solid; mp 122–123 °C; 82% yield (40.7 mg), >20:1 dr, 94% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 10.918, t (minor) = 20.258]; [α]D²⁰ = -68.9 (c 0.22, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.80 (dd, J = 7.6, 1.2 Hz, 1H), 7.72 (dd, J = 7.6, 1.2 Hz, 1H), 7.45 (td, J = 8.0, 1.2 Hz, 1H), 7.22 (td, J = 7.6, 1.2 Hz, 1H), 7.13 (td, J = 7.6, 0.8 Hz, 1H), 6.99 (td, J = 7.6, 1.2 Hz, 1H), 6.87 (t, J = 5.2 Hz, 2H), 6.01 (t, J = 3.2 Hz, 1H), 5.98 – 5.84 (m, 2H), 5.64 (dd, J = 3.6, 1.6 Hz, 1H), 5.39 – 5.18 (m, 2H), 4.56 – 4.32 (m, 2H), 4.16 (s, 1H), 4.11 – 3.95 (m, 3H), 3.21 (s, 3H), 2.02 (d, J = 13.6 Hz, 1H), 1.08 (t, J = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 177.2, 171.7, 170.9, 144.1, 141.5, 136.1, 131.2, 130.7, 127.8, 127.3, 127.2, 126.7, 124.3, 122.5, 122.1, 117.1, 116.8, 109.0, 108.0, 107.6, 105.9, 76.3, 66.6, 62.8, 47.8, 42.2, 34.8, 25.9, 13.4; IR (KBr) νmax: 2963, 2923, 2851, 1733, 1717, 1706, 1684, 1647, 1608, 1558, 1541, 1507, 1489, 1472, 1457, 1363, 1340, 1259, 1085, 1025, 753, 713, 691, 669 cm⁻¹; HRMS (ESI): m/z = 580.2740 (calcd for C₄₀H₂₅N₀O₅⁺H⁺ = 580.2735).
ethyl(3R,6'R,8'S)-6'-hydroxy-1''-(methoxymethyl)-1-methyl-2,2''-dioxo-6',7'-dihy drodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4da

White solid; mp 102–103 °C; 89% yield (44.6 mg), >20:1 dr, 97% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 9.081, t (minor) = 19.499]; [α]₂⁵ = −116.3 (c 0.32, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.82 (d, J = 7.6 Hz, 1H), 7.71 (d, J = 7.6 Hz, 1H), 7.45 (td, J = 8.0, 1.2 Hz, 1H), 7.31 – 7.23 (m, 1H), 7.14 (td, J = 7.6, 0.8 Hz, 1H), 7.11 – 7.01 (m, 2H), 6.89 (d, J = 8.0 Hz, 1H), 6.01 (t, J = 3.6 Hz, 1H), 5.94 (dd, J = 2.8, 1.6 Hz, 1H), 5.66 (dd, J = 4.0, 1.6 Hz, 1H), 5.34 – 5.15 (m, 2H), 4.187 (s, 1H), 4.15 – 3.95 (m, 3H), 3.40 (s, 3H), 3.22 (s, 3H), 2.06 (d, J = 14.0 Hz, 1H), 1.08 (t, J = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 178.3, 171.6, 171.0, 144.0, 140.5, 135.5, 130.7, 127.7, 127.5, 127.3, 126.8, 124.3, 122.8, 122.6, 116.9, 109.1, 108.6, 107.7, 106.0, 71.3, 66.6, 62.9, 56.0, 48.2, 34.9, 29.2, 25.9, 13.4; IR (KBr) νmax: 2962, 2926, 2850, 1733, 1684, 1647, 1608, 1558, 1521, 1498, 1457, 1340, 1259, 1090, 1023, 754, 704, 692, 669 cm⁻¹; HRMS (ESI): m/z = 502.1988 (calcd for C₂₉H₂₇N₃O₆+H⁺ = 502.1973).

ethyl(3R,6'R,8'S)-5'',6''-difluoro-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihy drodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4fa

White solid; mp 226–227 °C; 85% yield (43.1 mg), >20:1 dr, 88% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 10.886, t (minor) = 15.959]; [α]₂⁵ = −230.0 (c 0.41, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.70 (t, J = 8.4 Hz, 2H), 7.46 (t, J = 7.8 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 7.6 Hz, 1H), 6.68 (dd, J = 10.0, 6.4 Hz, 1H), 6.02 (t, J = 3.2 Hz, 1H), 5.93 (dd, J = 2.8, 1.2 Hz, 1H), 5.63 (dd, J = 3.6, 1.2 Hz, 1H), 4.26 (s, 1H), 4.15 – 3.93 (m, 3H), 3.27 (s, 3H), 3.20 (s, 3H), 0.95 (d, J = 13.6 Hz, 1H), 1.08 (t, J = 7.2 Hz, 3H); ¹⁹F NMR (376 MHz, CDCl₃)
δ –138.0 (d, J = 20.7 Hz), –146.1 (d, J = 20.3 Hz); 13C NMR (101 MHz, CDCl3) δ 177.2, 171.4, 170.8, 147.1, 144.7 (d, J = 12.7 Hz), 144.0, 138.6, 131.2 130.8, 127.2, 127.0, 124.0, 122.7, 117.1, 116.7 (d, J = 21.4 Hz), 109.2, 107.7, 105.9, 97.1 (d, J = 22.7 Hz), 66.7 63.0, 47.9, 34.4, 29.2, 26.5, 26.0, 13.3; IR (KBr) νmax: 3064, 2966, 2927, 2851, 1734, 1717, 1685, 1608, 1506, 1491, 1470, 1456, 1421, 1368, 1341, 1248, 1139, 1128, 1113, 1092, 1054, 1022, 755, 711, 693, 668, 616 cm⁻¹; HRMS (ESI): m/z = 508.1694 (calcd for C27H23F2N3O5+H⁺ = 508.1679).

**ethyl(3R,6'R,8'S)-6''-chloro-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodiindole[3,5''-indolizine-3,5'-indolizin-8',3''-indoline]-6'-carboxylate 4ga**

White solid; mp 246–247 °C; 91% yield (45.9 mg), >20:1 dr, 94% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 11.515, t (minor) = 16.546]; [α]D° = −265.0 (c 0.22, CHCl3); 1H NMR (400 MHz, CDCl3) δ 7.75 – 7.65 (m, 2H), 7.45 (td, J = 8.0, 1.2 Hz, 1H), 7.14 (td, J = 7.6, 1.2 Hz, 1H), 6.96 (dd, J = 8.4, 2.0 Hz, 1H), 6.91 – 6.84 (m, 2H), 6.01 (dd, J = 3.6, 2.8 Hz, 1H), 5.93 (dd, J = 3.2, 1.6 Hz, 1H), 5.62 (dd, J = 3.6, 1.2 Hz, 1H), 4.18 (s, 1H), 4.10 – 3.94 (m, 3H), 3.29 (s, 3H), 3.204 (s, 3H), 1.96 (d, J = 13.6 Hz, 1H), 1.08 (t, J = 7.2 Hz, 3H); 13C NMR (101 MHz, CDCl3) δ 177.4, 171.6, 170.9, 144.0, 143.6, 134.3, 133.1, 130.8, 127.8, 127.3, 127.2, 124.2, 122.6, 121.9, 116.9, 109.1, 107.8, 107.7, 106.0, 76.2, 66.7, 62.9, 47.6, 34.7, 26.4, 25.9, 13.4; IR (KBr) νmax: 2962, 2922, 2851, 1733, 1705, 1684, 1670, 1652, 1636, 1558, 1521, 1490, 1457, 1419, 1366, 1258, 1081, 1023, 962, 822, 799, 753, 746, 703, 693, 679, 639 cm⁻¹; HRMS (ESI): m/z = 506.1487 (calcd for C27H24ClN3O5+H⁺ = 506.1477).

**ethyl(3R,6'R,8'S)-6'-hydroxy-1,1''-trimethyl-2,2''-dioxo-6',7'-dihydrodispiro[indole-3,5''-indolizine-8',3''-indoline]-6'-carboxylate 4ha**

White solid; mp 175–176 °C; 62% yield (30.1 mg), >20:1 dr, 97% ee [Daicel Chiralcel OD-H, hexanes/i-PrOH = 70/30, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 71.191, t (minor) = 69.357]; [α]D° = −135.7 (c 0.34, CHCl3); 1H NMR (400 MHz, CDCl3) δ 7.79 – 7.67 (m, 2H), 7.44 (td, J = 8.0, 1.2 Hz, 1H), 7.13 (td, J = 7.6, 1.2 Hz, 1H), 6.91 – 6.84 (m, 2H), 6.01 (dd, J = 3.6, 2.8 Hz, 1H), 5.93 (dd, J = 3.2, 1.6 Hz, 1H), 5.62 (dd, J = 3.6, 1.2 Hz, 1H), 4.18 (s, 1H), 4.10 – 3.94 (m, 3H), 3.29 (s, 3H), 3.204 (s, 3H), 1.96 (d, J = 13.6 Hz, 1H), 1.08 (t, J = 7.2 Hz, 3H); 13C NMR (101 MHz, CDCl3) δ 177.4, 171.6, 170.9, 144.0, 143.6, 134.3, 133.1, 130.8, 127.8, 127.3, 127.2, 124.2, 122.6, 121.9, 116.9, 109.1, 107.8, 107.7, 106.0, 76.2, 66.7, 62.9, 47.6, 34.7, 26.4, 25.9, 13.4; IR (KBr) νmax: 2962, 2922, 2851, 1733, 1705, 1684, 1670, 1652, 1636, 1558, 1521, 1490, 1457, 1419, 1366, 1258, 1081, 1023, 962, 822, 799, 753, 746, 703, 693, 679, 639 cm⁻¹; HRMS (ESI): m/z = 506.1487 (calcd for C27H24ClN3O5+H⁺ = 506.1477).
ethyl(3R,6'R,8'S)-7''-fluoro-6''-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ia

White solid; mp 94—95 °C; 90% yield (44.0 mg), >20:1 dr, 97% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 7.506, t (minor) = 9.978]; [α]D²⁰ = −260.8 (c 0.24, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.69 (d, J = 7.2 Hz, 1H), 7.60 (d, J = 7.6 Hz, 1H), 7.45 (t, J = 7.6 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H), 7.02 – 6.86 (m, 3H), 6.01 (t, J = 3.2 Hz, 1H), 5.97 – 5.88 (m, 1H), 5.67 (dd, J = 3.6, 1.6 Hz, 1H), 4.17 (s, 1H), 4.11 – 3.92 (m, 3H), 3.52 (d, J = 2.8 Hz, 3H), 3.21 (s, 3H), 2.00 (d, J = 14.0 Hz, 1H), 1.08 (t, J = 7.2 Hz, 3H); ¹⁹F NMR (376 MHz, CDCl₃) δ −137.5; ¹³C NMR (101 MHz, CDCl₃) δ 177.2, 171.6, 170.8, 148.1, 145.7, 144.0, 138.7, 130.7, 129.1, 127.3, 127.2, 124.2, 122.5, 122.4 (d, J = 6.7 Hz), 117.0, 115.2 (d, J = 18.9 Hz), 109.1, 107.7, 106.1, 76.2, 66.7, 62.9, 48.1, 34.9, 28.9, 25.9, 13.4; IR (KBr) νmax: 2965, 2931, 1733, 1717, 1684, 1670, 1652, 1647, 1609, 1558, 1541, 1507, 1489, 1472, 1435, 1364, 1340, 1258, 1175, 1129, 1111, 1086, 1023, 753, 701, 668 cm⁻¹; HRMS (ESI): m/z = 490.1781 (calcd for C₂₇H₂₄FN₃O₅+H⁺ = 490.1773).

ethyl(3R,6'R,8'S)-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-7''-(trifluoromethyl)-6',7''-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ja
White solid; mp 211–212 °C; 90% yield (48.5 mg), 91:9 dr, 95% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 26.934, t (minor) = 16.233]; [α]D = −165.9 (c 0.32, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 8.04 (dd, J = 7.6, 1.2 Hz, 1H), 7.70 (dd, J = 7.6, 1.2 Hz, 1H), 7.54 (dd, J = 8.0, 1.2 Hz, 1H), 7.46 (td, J = 7.6, 1.2 Hz, 1H), 7.14 (td, J = 7.6, 0.8 Hz, 1H), 7.05 (t, J = 8.0 Hz, 1H), 6.90 (d, J = 8.0 Hz, 1H), 6.02 (t, J = 3.6 Hz, 1H), 5.96 (dd, J = 3.2, 1.6 Hz, 1H), 5.62 (dd, J = 3.6, 1.6 Hz, 1H), 4.23 (s, 1H), 4.14 – 3.92 (m, 3H), 3.52 (q, J = 2.4 Hz, 3H), 3.21 (s, 3H), 1.99 (d, J = 14.0 Hz, 1H), 1.08 (t, J = 7.2 Hz, 3H); ¹⁹F NMR (376 MHz, CDCl₃) δ −52.6; ¹³C NMR (101 MHz, CDCl₃) δ 178.4, 171.5, 170.8, 144.0, 140.3, 138.4, 130.8, 130.5, 127.2, 127.1, 125.4, 125.3, 124.1, 122.6, 121.4, 117.1, 111.5, 109.1, 107.7, 106.2, 76.2, 66.7, 63.0, 46.4, 35.2, 29.0, 26.0, 13.4; IR (KBr) νmax: 2973, 2921, 2849, 1733, 1699, 1652, 1647, 1541, 1507, 1489,1457, 1339, 1261, 1135, 1095, 1083, 1044, 752, 744, 711, 697 cm⁻¹; HRMS (ESI): m/z = 540.1754 (calcd for C₂₈H₂₄F₃N₃O₅+H⁺ = 540.1741).

ethyl(3R,6'R,8'S)-1-allyl-6'-hydroxy-1''-methyl-2,2''-dioxo-6',7''-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indolone]-6''-carboxylate 4ac

White solid; mp 124–125 °C; 88% yield (43.7 mg), >20:1 dr, 94% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 10.282, t (minor) = 17.245]; [α]D = −229.7 (c 0.15, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.79 (dd, J = 7.6, 1.2 Hz, 1H), 7.73 (dd, J = 7.6, 1.2 Hz, 1H), 7.41 (td, J = 8.0, 1.2 Hz, 1H), 7.29 – 7.23 (m, 1H), 7.13 (td, J = 7.6, 0.8 Hz, 1H), 7.00 (td, J = 7.6, 1.2 Hz, 1H), 6.88 (t, J = 8.8 Hz, 2H), 6.01 (dd, J = 3.6, 3.2 Hz, 1H), 5.93 (dd, J = 3.2, 1.6 Hz, 1H), 5.88 – 5.75 (m, 1H), 5.64 (dd, J = 3.6, 1.6 Hz, 1H), 5.37 – 5.18 (m, 2H), 4.50 – 4.37 (m, 1H), 4.26 – 4.18 (m, 1H), 4.15 – 4.13 (m, 1H), 4.11 – 3.94 (m, 3H), 3.31 (s, 3H), 2.01 (d, J = 14.0 Hz, 1H), 1.07 (t, J = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 177.5, 171.6, 170.6, 143.3, 142.4, 136.0, 130.6, 130.5, 127.8, 127.4, 127.3, 126.6,
ethyl(3R,6′R,8′S)-6′-hydroxy-1,1″,5-trimethyl-2,2″-dioxo-6′,7′-dihydrodispiro[indoline-3,5′-indolizine-8′,3″-indoline]-6′-carboxylate 4ad

White solid; mp 223–224 °C; 86% yield (41.2 mg), >20:1 dr, 96% ee [Daicel Chiralcel OD-H, hexanes/i-PrOH = 90/10, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 87.491, t (minor) = 77.586]; [α]D²⁵ = −331.4 (c 0.25, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.80 (dd, J = 7.6, 1.2 Hz, 1H), 7.52 (d, J = 1.6 Hz, 1H), 7.28 – 7.23 (m, 2H), 6.99 (td, J = 7.6, 1.2 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 6.77 (d, J = 8.0 Hz, 1H), 6.01 (t, J = 3.2 Hz, 1H), 5.94 (dd, J = 3.2, 1.6 Hz, 1H), 5.63 (dd, J = 4.0, 1.6 Hz, 1H), 4.16 (s, 1H), 4.09 – 3.91 (m, 3H), 3.31 (s, 3H), 3.18 (s, 3H), 2.37 (s, 3H), 1.99 (d, J = 14.0 Hz, 1H), 1.09 (t, J = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 177.6, 171.8, 170.9, 142.4, 141.6, 136.1, 132.1, 130.9, 127.9, 127.4, 126.7, 124.3, 122.1, 116.8, 108.9, 107.4, 107.1, 105.8, 99.5, 66.8, 62.8, 47.9, 34.7, 26.3, 26.0, 20.7, 13.4; IR (KBr) νmax: 2972, 2926, 2864, 1717, 1699, 1684, 1652, 1647, 1605, 1558, 1541, 1521, 1506, 1498, 1489, 1472, 1457, 1362, 1340, 1252, 1138, 1096, 700 cm⁻¹; HRMS (ESI): m/z = 486.2019 (calcd for C₂₈H₂₇N₃O₅+H⁺ = 486.2023).

ethyl(3R,6′R,8′S)-6′-hydroxy-1,1″,5,7-tetramethyl-2,2″-dioxo-6′,7′-dihydrodispiro[indoline-3,5′-indolizine-8′,3″-indoline]-6′-carboxylate 4ae

White solid; mp 133–134 °C; 88% yield (43.9 mg), >20:1 dr, 94% ee [Daicel Chiralcel OD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 34.228, t (minor) = 22.621]; [α]D²⁵ = −138.0 (c 0.36, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.79 (dd, J = 7.6, 1.2 Hz, 1H), 7.37 – 7.33 (m, 1H), 7.28 – 7.22
ethyl(3R,6'R,8'S)-6'-hydroxy-6-methoxy-1,1''-dimethyl-2,2''-dioxo-6',7''-dihydrod 

ispido[4ag]

White solid; mp 125–126 °C; 64% yield (32.1 mg), >20:1 dr, 90% ee [Daicel Chiralcel OD-H, hexanes/i-PrOH = 75/25, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 26.342, t (minor) = 22.684]; [α]D²⁵ = −273.0 (c 0.12, CHCl₃);

1H NMR (400 MHz, CDCl₃) δ 7.78 (dd, J = 7.6, 1.2 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.28 – 7.22 (m, 1H), 6.99 (td, J = 7.6, 1.2 Hz, 1H), 6.86 (dd, J = 8.0, 1.2 Hz, 1H), 6.61 (dd, J = 8.4, 2.4 Hz, 1H), 6.44 (d, J = 2.4 Hz, 1H), 6.00 (dd, J = 3.6, 2.8 Hz, 1H), 5.96 (dd, J = 3.2, 1.6 Hz, 1H), 5.62 (dd, J = 3.6, 2.0 Hz, 1H), 4.14 (s, 1H), 4.11 – 3.94 (m, 3H), 3.87 (s, 3H), 3.30 (s, 3H), 3.18 (s, 3H), 1.98 (d, J = 14.0 Hz, 1H), 1.10 (t, J = 7.2 Hz, 3H); 13C NMR (101 MHz, CDCl₃) δ 177.6, 171.9, 171.4, 161.8, 145.5, 142.4, 136.1, 128.2, 127.8, 127.3, 126.6, 122.1, 116.7, 116.1, 108.9, 107.1, 106.0, 105.9, 95.6, 76.4, 66.3, 62.8, 55.1, 47.9, 34.9, 26.6, 25.9, 13.4; IR (KBr) νmax: 3289, 2962, 2922, 2850, 1733, 1700, 1652, 1647, 1624, 1558, 1541, 1506, 1489, 1457, 1431, 1372, 1258, 1207, 1138, 1128, 1090, 1056, 1046, 1022, 979, 963, 801, 790, 754, 709, 684, 661 cm⁻¹; HRMS (ESI): m/z = 502.1987 (calcd for C₂₈H₂₇ClN₃O₆+H⁺ = 502.1973).

dispiro[4ah]

ethyl(3R,6'R,8'S)-5,6-difluoro-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7''-dihydrod 

ispido[4ah]
White solid; mp 108–109 °C; 92% yield (46.6 mg), >20:1 dr, 96% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 7.685, t (minor) = 13.880]; [α]²⁰₀° = −218.9 (c 0.28, CHCl₃);

¹H NMR (400 MHz, CDCl₃) δ 7.74 (d, J = 7.6 Hz, 1H), 7.64 (dd, J = 9.6, 7.6 Hz, 1H), 7.30 – 7.24 (m, 1H), 7.00 (t, J = 7.6 Hz, 1H), 6.87 (d, J = 2.8, 1.6 Hz, 1H), 6.73 (dd, J = 9.6, 6.0 Hz, 1H), 6.02 (t, J = 3.2 Hz, 1H), 5.90 (dd, J = 9.6, 6.0 Hz, 1H), 5.63 (dd, J = 3.6, 16 Hz, 1H), 4.21 – 3.99 (m, 3H), 3.92 (d, J = 14.0 Hz, 1H), 3.30 (s, 3H), 3.18 (s, 3H), 1.99 (d, J = 14.0 Hz, 1H), 1.11 (t, J = 7.2 Hz, 3H); ¹⁹F NMR (376 MHz, CDCl₃) δ −131.9 (d, J = 19.6 Hz), −144.4 (d, J = 19.9 Hz); ¹³C NMR (101 MHz, CDCl₃) δ 177.4, 171.5, 170.6, 150.7, 147.3, 144.8, 142.4, 140.8, 135.8, 127.8, 127.5, 126.5, 122.2, 119.6, 117.5 (d, J = 20.6 Hz), 116.4, 109.6, 107.3, 106.3, 97.8 (d, J = 23.1 Hz), 76.3, 66.2, 63.1, 47.8, 35.1, 26.3, 26.2, 13.4; IR (KBr) νmax: 2973, 2924, 2927, 1772, 1747, 1733, 1701, 1684, 1652, 1636, 1624, 1608, 1558, 1521, 1507, 1489, 1473, 1436, 1396, 1362, 1350, 1339, 1261, 1093, 1052, 1022, 702, 694 cm⁻¹; HRMS (ESI): m/z = 508.1689 (calcd for C₂₇H₂₅F₂N₃O₅+H⁺ = 508.1679).

**ethyl(3R,6'R,8'S)-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-7-(trifluoromethyl)-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ai**

White solid; mp 242–243 °C; 87% yield (46.9 mg), >20:1 dr, 81% ee [Daicel Chiralcel OD-H, hexanes/i-PrOH = 75/25, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 13.914, t (minor) = 12.219]; [α]²⁰₀° = −20.0 (c 0.18, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.94 (d, J = 7.6 Hz, 1H), 7.75 (t, J = 7.2 Hz, 2H), 7.29 – 7.26 (m, 1H), 7.21 (t, J = 7.6 Hz, 1H), 7.00 (t, J = 7.6 Hz, 1H), 6.88 (d, J = 8.0 Hz, 1H), 6.04 (t, J = 3.2 Hz, 1H), 5.92 (dd, J = 2.8, 1.6 Hz, 1H), 5.66 (dd, J = 3.6, 1.6 Hz, 1H), 4.14 (s, 1H), 4.10 – 3.98 (m, 2H), 3.93 (d, J = 14.0 Hz, 1H), 3.42 (q, J = 2.4 Hz, 3H), 3.31 (s, 3H), 2.01 (d, J = 14.0 Hz, 1H), 1.12 (t, J = 7.2 Hz, 3H); ¹⁹F NMR (376 MHz, CDCl₃) δ −53.3; ¹³C NMR (101 MHz, CDCl₃) δ 177.4, 171.8, 171.5, 142.4, 142.1, 135.8, 130.9, 128.5, 128.1, 127.5,
126.9, 126.6, 122.2, 121.7, 116.6, 112.0, 109.5, 107.3, 106.2, 76.3, 65.1, 63.3, 47.8, 34.8, 28.8, 26.3, 13.2; IR (KBr) \( \nu_{\text{max}} \): 2973, 2935, 1747, 1733, 1716, 1706, 1699, 1684, 1652, 1558, 1541, 1507, 1489, 1473, 1457, 1338, 1256, 1116, 1094, 1051, 744, 685 cm\(^{-1}\); HRMS (ESI): \( m/z = 540.1758 \) (calcd for C\(_{28}\)H\(_{24}\)F\(_3\)N\(_3\)O\(_5\)+H\(^+\) = 540.1741).

**2.4 Procedure for the preparation the stereoisomeric products**

![Chemical structure](image)

<table>
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<tr>
<th>Compound</th>
<th>Reaction Conditions</th>
<th>Yield</th>
<th>Remarks</th>
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<tr>
<td>3gd: L6 + QD, (2 + 8) h</td>
<td>85% yield, &gt;20:1 dr, 93% ee</td>
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<tr>
<td>3ge: L6 + QD, (2 + 8) h</td>
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<tr>
<td>ent-3gd: L2 + QD, (2 + 8) h</td>
<td>88% yield, &gt;20:1 dr, 92% ee</td>
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<tr>
<td>ent-3ge: L2 + QD, (2 + 8) h</td>
<td>91% yield, &gt;20:1 dr, 95% ee</td>
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<tr>
<td>4gd: L6 + p-TsOH, (2 + 8) h</td>
<td>75% yield, &gt;20:1 dr, 95% ee</td>
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<tr>
<td>4ge: L6 + p-TsOH, (2 + 8) h</td>
<td>88% yield, &gt;20:1 dr, 94% ee</td>
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<td></td>
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<tr>
<td>ent-4gd: L2 + p-TsOH, (2 + 8) h</td>
<td>85% yield, &gt;20:1 dr, 95% ee</td>
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<tr>
<td>ent-4ge: L2 + p-TsOH, (2 + 8) h</td>
<td>84% yield, &gt;20:1 dr, 92% ee</td>
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<td></td>
</tr>
</tbody>
</table>

* QD = Quinidine: 20 mol%, p-TsOH: 20 mol%

Under N\(_2\) atmosphere, Cu(OTf)\(_2\) (0.01 mmol, 10 mol%) and L6 or L2 (0.01 mmol, 10 mol%) were combined into a vessel, and m-xylene (2.50 mL) was added via syringe. After the reaction system was stirred at 25 °C for 0.5 h, the substrates 1g (0.1 mmol) and 2d or 2e (0.22 mmol, 2.2 equiv) were added and the reaction mixture was stirred until the reaction was complete (detected by TLC). Then quinidine (0.02 mol, 20 mol%) or p-TsOH (0.02 mmol, 20 mol%) was introduced into the reaction mixture to promote the intramolecular aldol reaction at 25°C. After the reaction was detected complete (by TLC analysis), the solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel with EtOAc/petroleum ether (1/1) as eluent to give 3 or 4 as white solids.
“Racemic” samples described in this part were obtained via mixing two isomer of corresponding chiral product 3 or 4.

**ethyl(3R,6'S,8'S)-6''-chboro-6'-hydroxy-1,1'',5-trimethyl-2,2''-dioxo-6',7'-dihydrd**

**dispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3gd**

White solid; mp 155–156 °C; 85% yield (44.2 mg), >20:1 dr, 93% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 70/30, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 19.234, t (minor) = 9.665; [α]d 25 = 201.3 (c 0.15, CHCl₃);

1H NMR (400 MHz, CDCl₃) δ 7.42 (s, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.29 – 7.24 (m, 1H), 7.18 (d, J = 7.6 Hz, 1H), 7.03 (d, J = 1.6 Hz, 1H), 6.98 (d, J = 1.6 Hz, 1H), 6.82 (d, J = 8.0 Hz, 1H), 6.31 (dd, J = 3.2, 1.6 Hz, 1H), 6.13 (t, J = 3.2 Hz, 1H), 5.63 (dd, J = 3.6, 1.6 Hz, 1H), 3.87 (p, J = 7.2 Hz, 2H), 3.41 (s, 3H), 3.30 (s, 3H), 3.29 (d, J = 15.6 Hz, 1H), 2.54 (d, J = 15.6 Hz, 1H), 2.36 (s, 3H), 1.01 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl₃) δ 178.9, 171.3, 168.3, 144.1, 140.2, 134.6, 131.6, 131.3, 130.2, 127.3, 124.6, 124.2, 123.6, 123.4, 120.4, 110.4, 109.2, 107.9, 106.7, 77.8, 67.6, 61.3, 47.6, 34.3, 26.6, 26.3, 20.9, 13.2; IR (KBr) νₘₐₓ: 2962, 2924, 2855, 1732, 1687, 1605, 1497, 1463, 1364, 1244, 1225, 1093, 1051, 1031, 943, 905, 798, 700 cm⁻¹; HRMS (ESI): m/z = 542.1452 (calcd for C₂₈H₂₆ClN₅O₅Na⁺ = 542.1453).

**ethyl(3S,6'R,8'R)-6''-chboro-6'-hydroxy-1,1'',5-trimethyl-2,2''-dioxo-6',7'-dihydrd**

**odispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate ent-3gd**

White solid; mp 151–152 °C; 88% yield (45.7 mg), >20:1 dr, 92% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 70/30, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 9.332, t (minor) = 21.266]; [α]d 25 = 204.1 (c 0.10, CHCl₃); HRMS (ESI): m/z = 542.1460 (calcd for C₂₈H₂₆ClN₅O₅Na⁺ = 542.1453).

**ethyl(3R,6'R,8'S)-6''-chboro-6'-hydroxy-1,1'',5-trimethyl-2,2''-dioxo-6',7'-dihydrd**

**odispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4gd**

White solid; mp 255–256 °C; 75% yield (39.0 mg), >20:1 dr, 95% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t
(major) = 8.008, t (minor) = 12.580; [α]_{D}^{25} = −201.4 (c 0.07, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, J = 8.0 Hz, 1H), 7.50 (s, 1H), 7.24 (d, J = 8.0 Hz, 1H), 6.95 (dd, J = 8.0, 2.0 Hz, 1H), 6.86 (d, J = 2.0 Hz, 1H), 6.77 (d, J = 8.0 Hz, 1H), 6.01 (t, J = 3.2 Hz, 1H), 5.94 (t, J = 2.4 Hz, 1H), 5.62 (dd, J = 3.6, 2.0 Hz, 1H), 4.19 (s, 1H), 4.11 – 3.90 (m, 3H), 3.29 (s, 3H), 3.18 (s, 3H), 2.37 (s, 3H), 1.95 (d, J = 14.0 Hz, 1H), 1.09 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 177.4, 171.7, 170.8, 143.7, 141.6, 134.4, 133.1, 132.2, 131.0, 127.8, 127.8, 127.3, 124.1, 121.9, 117.0, 109.0, 107.8, 107.4, 105.9, 76.1, 66.8, 62.9, 47.6, 34.6, 26.4, 26.0, 20.7, 13.4; IR (KBr) ν_max: 2965, 2925, 1732, 1699, 1604, 1498, 1364, 1246, 1094, 1070, 1054, 794, 703 cm⁻¹; HRMS (ESI): m/z = 542.1456 (calcd for C₂₁H₂₆Cl₂N₃O₅+Na⁺ = 542.1453).

ethyl(3S,6'S,8'R)-6''-chboro-6'-hydroxy-1',1''-5-trimethyl-2,2''-dioxo-6',7''-dihydro dispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate ent-4gd

White solid; mp 252–253 °C; 85% yield (44.2 mg), >20:1 dr, 95% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 11.774, t (minor) = 9.693]; [α]_{D}^{25} = 212.4 (c 0.14, CHCl₃); HRMS (ESI): m/z = 542.1459 (calcd for C₂₁H₂₆Cl₂N₃O₅+Na⁺ = 542.1453).

ethyl(3R,6'S,8'S)-6''-chloro-6'-hydroxy-1',1''-5,7-tetramethyl-2,2''-dioxo-6',7''-dihydro dispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ge

White solid; mp 235–236 °C; 82% yield (43.7 mg), >20:1 dr, 96% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 70/30, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 19.557, t (minor) = 11.141]; [α]_{D}^{25} = 52.3 (c 0.14, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.34 (s, 1H), 7.28 (d, J = 8.0 Hz, 1H), 7.20 (dd, J = 8.0, 2.0 Hz, 1H), 6.96 (d, J = 1.6 Hz, 1H), 6.85 (s, 1H), 6.74 (d, J = 2.0 Hz, 1H), 6.26 (dd, J = 2.8, 1.6 Hz, 1H), 6.07 (t, J = 3.2 Hz, 1H), 5.57 (dd, J = 3.6, 1.6 Hz, 1H), 3.85 (q, J = 7.2 Hz, 2H), 3.63 (s, 3H), 3.25 (d, J = 15.6 Hz, 1H), 3.24 (s, 3H), 2.54 (s, 3H), 2.43 (d, J = 15.6 Hz, 1H), 2.24 (s, 3H), 1.00 (t, J = 7.2 Hz,
ethyl(3S,6'R,8'R)-6''-chloro-6'-hydroxy-1'',5,7-tetramethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate ent-3ge

White solid; mp 230–231 °C; 91% yield (48.5 mg), >20:1 dr, 97% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 70/30, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 11.035, t (minor) = 20.444]; [α]D²⁵ = −49.6 (c 0.12, CHCl₃); HRMS (ESI): m/z = 556.1614 (calcd for C₂₀H₂₇ClN₃O₅Na⁺ = 556.1610).

ethyl(3R,6'R,8'S)-6''-chloro-6'-hydroxy-1'',5,7-tetramethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ge

White solid; mp 263–264 °C; 88% yield (46.9 mg), >20:1 dr, 94% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 8.703, t (minor) = 13.148]; [α]D²⁵ = −130.5 (c 0.15, CHCl₃); IH NMR (400 MHz, CDCl₃) δ 7.76 (d, J = 8.0 Hz, 1H), 7.38 (s, 1H), 7.16 – 6.75 (m, 3H), 6.04 (d, J = 16.8 Hz, 2H), 5.67 (s, 1H), 4.29 – 3.95 (m, 4H), 3.50 (s, 3H), 3.34 (s, 3H), 2.59 (s, 3H), 2.36 (s, 3H), 1.99 (d, J = 14.0 Hz, 1H), 1.18 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl₃) δ 177.5, 171.7, 171.6, 143.7, 139.2, 134.9, 134.4, 133.0, 131.9, 127.9, 127.3, 125.5, 124.8, 121.9, 118.9, 117.1, 108.9, 107.7, 105.8, 76.1, 66.4, 62.8, 47.6, 34.5, 29.4, 26.4, 20.4, 18.5, 13.4; IR (KBr) νmax: 2926, 2871, 1723, 1707, 1603, 1468, 1366, 1247, 105, 1078, 692, 702 cm⁻¹; HRMS (ESI): m/z = 556.1620 (calcd for C₂₀H₂₇ClN₃O₅Na⁺ = 556.1610).

ethyl(3S,6'S,8'R)-6''-chloro-6'-hydroxy-1'',5,7-tetramethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate ent-4ge

S26
White solid; mp 260–261 °C; 84% yield (44.8 mg), >20:1 dr, 92% ee [Daicel Chiralcel AD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 12.008, t (minor) = 9.417]; [α]D²⁵ = 128.2 (c 0.11, CHCl₃); HRMS (ESI): m/z = 566.1618 (calcd for C₂⁹H₂₈ClN₃O₅+Na⁺ = 556.1610).

2.5 Procedure for the preparation of 4aa from 3aa

The compound 3aa (0.1 mmol) was introduced into a vessel, and toluene (1 mL) was added via syringe. Then DBU (0.025 mmol, 25 mol%) was added and the system was stirred at 25°C for 16 h. Followed evaporation of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel with EtOAc/petroleum ether (1/1) as eluent to give 4aa as a white solid.

2.6 Procedure for the preparation of the adduct 6

Under N₂ atmosphere, Cu(OTf)₂ (0.01 mmol, 10 mol%) and L₆ (0.01 mmol, 10 mol%) were combined into a vessel, and m-xylene (2.50 mL) was added via syringe. After the catalyst system was stirred at 25°C for 0.5 h, the substrates 1a (0.1 mmol) and 5 (0.22 mmol, 2.2 equiv) were added and the reaction mixture was stirred until the reaction was complete (detected by TLC). Then DBU (0.1 mmol, 1 equiv) was introduced to promote the intramolecular aldol reaction at 25°C. After the reaction
was detected complete (by TLC analysis), the solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel with EtOAc/petroleum ether (1/3) as eluent to give 6 as a white solid.

**triethyl-6'-hydroxy-1-methyl-2-oxo-6',7'-dihydro-5'H-spiro[indoline-3,8'-indolizine]-5',5',6'-tricarboxylate 6**

White solid; mp 123–124 °C; 87% yield (42.1 mg), >20:1 dr, 9% ee [Daicel Chiralcel OD-H, hexanes/i-PrOH = 80/20, flow rate: 1.0 mL·min⁻¹, λ = 254.4 nm, t (major) = 9.898, t (minor) = 16.001; [α]D²⁵ = −11.6 (c 0.37, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 8.15 (s, 1H), 7.35 (t, J = 7.6 Hz, 2H), 7.22–7.17 (m, 1H), 7.13 (t, J = 7.6 Hz, 1H), 6.90 (d, J = 7.6 Hz, 1H), 6.15 (t, J = 3.2 Hz, 1H), 5.48 (dd, J = 3.6, 1.6 Hz, 1H), 4.50–4.15 (m, 6H), 3.32 (d, J = 14.4 Hz, 1H), 3.23 (s, 3H), 2.29 (d, J = 14.8 Hz, 1H), 1.39–1.24 (m, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 179.5, 171.3, 166.0, 165.2, 142.5, 133.4, 128.6, 126.1, 123.9, 123.9, 123.6, 110.2, 108.1, 107.3, 99.5, 76.8, 74.1, 62.0, 61.7, 47.8, 35.2, 26.4, 13.6, 13.5, 13.4; IR (KBr) νmax cm⁻¹: 2986, 2901, 1734, 1668, 1609, 1541, 1507, 1472, 1379, 1259, 1150, 1097, 1039, 800, 757, 684, 613 cm⁻¹; HRMS (ESI): m/z = 498.1927 (calcd for C₂₅H₂₈N₃O₈+H⁺ = 485.1918).

3. X-ray data

**3.1 Crystal structure determination of chiral 3ae:**

Crystal data and structure refinement for chiral 3ae:

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Figure S3. OPTEP drawing of chiral 3ae (40% thermal ellipsoids)

Figure S4. Packing of molecules in a unit cell of chiral 3ae

The crystal was prepared from the solution of chiral 3ae in DCM and n-hexane. CCDC 1548552 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data request/cif.
### 3.2 Crystal structure determination of compound racemic 3ae (7% ee):

Crystal data and structure refinement for racemic 3ae:

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<tr>
<td></td>
<td>a = 8.851(5) Å, alpha = 90 deg.</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>b = 10.081(6) Å, beta = 91.989(15) deg.</td>
</tr>
<tr>
<td></td>
<td>c = 28.437(14) Å, gamma = 90 deg.</td>
</tr>
<tr>
<td>Volume</td>
<td>2536(2) Å³</td>
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<tr>
<td>Z, Calculated density</td>
<td>4, 1.308 Mg/m³</td>
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<tr>
<td>Absorption coefficient</td>
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<tr>
<td>F(000)</td>
<td>1056</td>
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<tr>
<td>Crystal size</td>
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<tr>
<td>Radiation</td>
<td>MoKα (λ = 0.71073)</td>
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<tr>
<td>Theta range for data collection</td>
<td>2.302 to 27.640 deg.</td>
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<tr>
<td>Limiting indices</td>
<td>-10 ≤ h ≤ 11, -13 ≤ k ≤ 12, -33 ≤ l ≤ 36</td>
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<tr>
<td>Reflections collected / unique</td>
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<tr>
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<td>Goodness-of-fit on F²</td>
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<tr>
<td>Final R indexes [I&gt;=2σ (I)]</td>
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<td>Final R indexes [all data]</td>
<td>R₁ = 0.1351, wR₂ = 0.1057</td>
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<tr>
<td>Largest diff. peak/hole / eÅ⁻³</td>
<td>0.280 and −0.303</td>
</tr>
<tr>
<td>Absolute structure parameter</td>
<td>0.3(13)</td>
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</table>
Figure S5. OPTEP drawing of racemic 3ae (40% thermal ellipsoids)

Figure S6. Packing of molecules in a unit cell of racemic 3ae

The crystal was prepared from the solution of racemic 3ae in DCM and n-hexane. CCDC 1539269 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data request/cif.
### 3.3 Crystal structure determination of racemic 4ia:

Crystal data and structure refinement for racemic 4ia:

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<th>Property</th>
<th>Value</th>
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<tr>
<td>Formula weight</td>
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</tr>
<tr>
<td>Temperature</td>
<td>293(2) K</td>
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<tr>
<td>Wavelength</td>
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<td>Crystal system, space group</td>
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<td>a = 12.2486(5) Å, alpha = 90 deg.</td>
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<td>Unit cell dimensions</td>
<td>b = 10.5812(5) Å, beta = 93.509(2) deg.</td>
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<td>c = 21.0573(11) Å, gamma = 90 deg.</td>
</tr>
<tr>
<td>Volume</td>
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<tr>
<td>Z, Calculated density</td>
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<td>Absorption coefficient</td>
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<td>F(000)</td>
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<td>Crystal size</td>
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<td>Radiation</td>
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<td>Final R indexes [all data]</td>
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<td>Largest diff. peak/hole / eÅ&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>1.147 and −1.638</td>
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Figure S7. OPTEP drawing of racemic 4ia (40% thermal ellipsoids)

Figure S8. Packing of molecules in a unit cell of racemic 4ia

The crystal was prepared from the solution of racemic 4ia in DCM and n-hexane. CCDC 1539270 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data request/cif.
4. $^1$H NMR, $^{19}$F NMR and $^{13}$C NMR spectra

ethyl(3R,6'S,8'S)-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3aa
ethyl(3R,6'S,8'S)-1''-benzyl-6'-hydroxy-1-methyl-2,2''-dioxo-6',7'-dihydrodispiro
[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ba
ethyl(3R,6'S,8'S)-1''-allyl-6'-hydroxy-1-methyl-2,2''-dioxy-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ca
ethyl(3R,6'S,8'S)-6'-hydroxy-1''-(methoxymethyl)-1-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3da
ethyl(3R,6'S,8'S)-6'-hydroxy-1''',5'''-trimethyl-2,2'''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3'''-indoline]-6'-carboxylate 3ea
ethyl(3R,6'S,8'S)-5'',6''-difluoro-6''-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7''-dihydrodispiro[indoline-3,5'-'-indolizine-8',3''-indoline]-6'-carboxylate 3fa

\[
\begin{array}{cccccccc}
0.094 & 0.096 & 0.092 & 0.094 & 0.092 & 0.096 \\
\end{array}
\]

\[
\begin{array}{cccccccc}
7.344 & 7.343 & 7.344 & 7.343 \\
7.240 & 7.240 & 7.240 & 7.240 \\
7.053 & 7.053 & 7.053 & 7.053 \\
7.014 & 7.014 & 7.014 & 7.014 \\
\end{array}
\]

\[
\begin{array}{cccccccc}
7.4 & 7.3 & 7.2 & 7.1 & 7.0 & 6.9 & 6.8 & 6.7 \\
0 & 100 & 200 & 300 & \\
\end{array}
\]

\[
\begin{array}{cccccccc}
1.98 & 1.98 & 1.98 & 1.98 \\
1.86 & 1.86 & 1.86 & 1.86 \\
0.93 & 0.93 & 0.93 & 0.93 \\
0.93 & 0.93 & 0.93 & 0.93 \\
1.80 & 1.80 & 1.80 & 1.80 \\
1.80 & 1.80 & 1.80 & 1.80 \\
2.83 & 2.83 & 2.83 & 2.83 \\
2.83 & 2.83 & 2.83 & 2.83 \\
\end{array}
\]

\[
\begin{array}{cccccccc}
7.5 & 7.0 & 6.5 & 6.0 & 5.5 & 5.0 & 4.5 & 4.0 \\
3.5 & 3.0 & 2.5 & 2.0 & 1.5 & 1.0 & 0.5 & 0.0 \\
\end{array}
\]

\[
\begin{array}{cccccccc}
\end{array}
\]

133.5 -134.5 -135.5 -136.5 -137.5 -138.5 -139.5 -140.5 -141.5 -142.5 -143.5 -144.5 -145.5 -14
ethyl(3R,6'S,8'S)-6''-chloro-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodi
spiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ga
ethyl(3R,6'S,8'S)-6'-hydroxy-1,1'',7''-trimethyl-2,2''-dioxo-6',7''-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ha
ethyl(3R,6'S,8'S)-7''-fluoro-6'-hydroxy-1''-dimethyl-2,2''-dioxo-6',7''-dihydrodis piro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ia
ethyl(3R,6'S,8'S)-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-7''-(trifluoromethyl)-6',7' -dihydropyprodinoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ja
ethyl(3R,6'S,8'S)-1-benzyl-6'-hydroxy-1''-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ab
ethyl(3R,6'S,8'S)-1-allyl-6'-hydroxy-1''-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ac
ethyl(3R,6'S,8'S)-6'-hydroxy-1,1''-5-trimethyl-2,2''-dioxo-6'7'-dihy drodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ad

S48
ethyl(3R,6’S,8’S)-6’-hydroxy-1,1’’,5,7-tetramethyl-2,2’’-dioxo-6’,7’-dihydrodispir
o[indoline-3,5’-indolizine-8’,3’’-indoline]-6’-carboxylate3ae
ethyl(3R,6'S,8'S)-6'-hydroxy-5-methoxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodi

spiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3af
ethyl(3R,6'S,8'S)-6'-hydroxy-6-methoxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrod
ispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ag
ethyl(3R,6'R,8'S)-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4aa
ethyl(3R,6'R,8'S)-1''-benzyl-6''-hydroxy-1-methyl-2,2''-dioxo-6',7'-dihydrodispir o[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ba
ethyl(3R,6'R,8'S)-1''-allyl-6'-hydroxy-1-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-'indolizine-8',3''-indoline]-6'-carboxylate 4ca
ethyl(3R,6'R,8'S)-6'-hydroxy-1''-(methoxymethyl)-1-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4da
ethyl(3R,6'R,8'S)-5'',6''-difluoro-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4fa
ethyl(3R,6'R,8'S)-6''-chloro-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodi
spiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ga
ethyl(3R,6'R,8'S)-6'-hydroxy-1,1'',7''-trimethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ha
ethyl(3R,6'R,8'S)-7''-fluoro-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodi
spiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ia
ethyl(3R,6'R,8'S)-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-7''-(trifluoromethyl)-6',7' -dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ja
ethyl(3R,6'R,8'S)-1-allyl-6'-hydroxy-1''-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ac
ethyl(3R,6'R,8'S)-6'-hydroxy-1,1'',5-trimethyl-2,2''-dioxo-6',7'-dihydrodispiro[...
doline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ad

ethyl(3R,6'R,8'S)-6'-hydroxy-1,1''',5,7-tetramethyl-2,2''-dioxo-6',7'-dihydrodipr
 o[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ae
ethyl(3R,6'R,8'S)-6'-hydroxy-6-methoxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydropyrido[2,1-b][1,4]oxazepine-8',3''-indoline]-6'-carboxylate 4ag
ethyl(3R',6'R,8'S)-5,6-difluoro-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydro
dispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ah

S66
ethyl(3R,6'R,8'S)-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-7-(trifluoromethyl)-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ai
ethyl(3R,6'R,S,S')-6''-chloro-6'-hydroxy-1,1'',5-trimethyl-2,2''-dioxo-6',7'-dihydro
dispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3hd or ent-3gd

ethyl(3R,6'R,R,S')-6''-chloro-6'-hydroxy-1,1'',5-trimethyl-2,2''-dioxo-6',7'-dihydr
dispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4hd or ent-4gd

S70
ethyl(3R,6'S,8'S)-6''-chloro-6'-hydroxy-1,1'',5,7-tetramethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3he or ent-3ge
ethyl(3R,6'R,8'S)-6''-chloro-6'-hydroxy-1,1'',5,7-tetramethyl-2,2''-dioxo-6',7'-dih
ydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6''-carboxylate 4he or ent-4ge

triethyl6'-hydroxy-1-methyl-2-oxo-6',7'-dihydro-5'H-spiro[indoline-3,8'-indolin]
e]-5',5',6'-tricarboxylate 6
5. HPLC spectra

ethyl(3R,6'R,8'S)-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3aa

| Peak RetTime Type Width Area Height Area |
|---------|---------|---------|---------|---------|
| #       | [min]   | [min]   | [mAU*]   | [mAU]   | %       |
| 1        | 11.663  | BB      | 0.4046   | 128.82217 | 4.74679 | 1.4542 |
| 2        | 16.174  | MM R    | 0.6156   | 70.79432  | 1.91667 | 0.7991 |
| 3        | 30.806  | BB      | 1.0100   | 4768.95068| 67.68413| 53.8332|
| 4        | 43.623  | BB      | 1.4102   | 3890.19458| 38.06848| 43.9135|

ethyl(3R,6'S,8'S)-1''-benzyl-6'-hydroxy-1-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ba

| Peak RetTime Type Width Area Height Area |
|---------|---------|---------|---------|---------|
| #       | [min]   | [min]   | [mAU*]   | [mAU]   | %       |
| 1        | 32.098  | MM R    | 0.8896   | 52.65709 | 9.86549e-1| 2.3816 |
| 2        | 44.771  | MM R    | 1.6991   | 2158.37769| 21.17238| 97.6184|
ethyl(3R,6'S,8'S)-1''-allyl-6'-hydroxy-1-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ca
ethyl(3R,6'S,8'S)-6'-hydroxy-1''-(methoxymethyl)-1-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-'indolizine-8',3''-indoline]-6'-carboxylate 3da

ethyl(3R,6'S,8'S)-6'-hydroxy-1',1''-,5''-trimethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-'indolizine-8',3''-indoline]-6'-carboxylate 3ea
ethyl(3R,6'S,8'S)-5''',6'''-difluoro-6'-hydroxy-1'''-dimethyl-2,2'''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3'''-indoline]-6'-carboxylate 3fa
ethyl(3R,6’S,8’S)-6’-chboro-6’-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodi
spiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ga

ethyl(3R,6'S,8'S)-6'-hydroxy-1,1''-7''-trimethyl-2,2''-dioxo-6',7'-dihyrodiospiro[i
ndoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ha
ethyl(3R,6'S,8'S)-7''-fluoro-6''-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodis
piro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ia
ethyl(3R,6'S,8'S)-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-7''-(trifluoromethyl)-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ja

ethyl(3R,6'S,8'S)-1-benzyl-6'-hydroxy-1''-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ab
ethyl(3R,6'S,8'S)-1-allyl-6'-hydroxy-1''-methyl-2,2''-dioxo-6',7'-dihydrodipiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ac
ethyl(3R,6'S,8'S)-6'-hydroxy-1,1'',5-trimethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ad
ethyl(3R,6'S,8'S)-6'-hydroxy-1,1''-5,7-tetramethyl-2,2''-dioxo-6',7'-dihydropirindoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ae

ethyl(3R,6'S,8'S)-6'-hydroxy-5-methoxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydroidispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3af
ethyl(3R,6'S,8'S)-6'-hydroxy-6-methoxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrod

ispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ag
ethyl(3R,6'R,8'S)-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4aa

ethyl(3R,6'R,8'S)-1''-benzyl-6'-hydroxy-1-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ba
ethyl(3R,6'R,8'S)-1''-allyl-6'-hydroxy-1-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ca
ethyl(3R,6'R,8'S)-6'-hydroxy-1''-(methoxymethyl)-1-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4da

ethyl(3R,6'R,8'S)-5'',6''-difluoro-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4fa
ethyl(3R,6'R,8'S)-6''-chloro-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodi
spiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ga

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<th>Area</th>
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<td>[min]</td>
<td>[min]</td>
<td>[mAU*s]</td>
<td>[mAU]</td>
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<td>BB</td>
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<table>
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<th>Type</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area</th>
<th>%</th>
</tr>
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<tr>
<td>#</td>
<td>[min]</td>
<td>[min]</td>
<td>[mAU*s]</td>
<td>[mAU]</td>
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S89
ethyl(3R,6'R,8'S)-6'-hydroxy-1,1''-7''-trimethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ha

ethyl(3R,6'R,8'S)-7''-fluoro-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydrodi
spiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ia
ethyl(3R,6'R,8'S)-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-7''-(trifluoromethyl)-6',7''-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ja
ethyl(3R,6'R,8'S)-1-allyl-6'-hydroxy-1''-methyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ac

ethyl(3R,6'R,8'S)-6'-hydroxy-1,1'',5-trimethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ad
ethyl(3R,6'R,8'S)-6'-hydroxy-1,1'',5,7-tetramethyl-2,2''-dioxo-6',7'-dihydrodispir
o[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ae
ethyl(3R,6'R,8'S)-6'-hydroxy-6-methoxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydro
dispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ag

ethyl(3R,6'R,8'S)-5,6-difluoro-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-6',7'-dihydro
dispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ah
ethyl(3R,6'R,8'S)-6'-hydroxy-1,1''-dimethyl-2,2''-dioxo-7-(trifluoromethyl)-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ai
ethyl(3R,6'S,8'S)-6''-chloro-6'-hydroxy-1,1'',5-trimethyl-2,2''-dioxo-6',7'-dihydro dispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3gd or ent-3gd
ethyl(3R,6'R,8'S)-6''-chloro-6'-hydroxy-1,1''-5-trimethyl-2,2''-dioxo-6',7'-dihydra
dispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4gd or ent-4gd
ethyl(3R,6'S,8'S)-6''-chloro-6'-hydroxy-1,1'',5,7-tetramethyl-2,2''-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 3ge or ent-3ge
ethyl(3R,6'R,8'S)-6''-chloro-6'-hydroxy-1,1'',5,7-tetramethyl-2,2'-dioxo-6',7'-dihydrodispiro[indoline-3,5'-indolizine-8',3''-indoline]-6'-carboxylate 4ge or ent-4ge
triethyl6'-hydroxy-1-methyl-2-oxo-6',7'-dihydro-5'H-spiro[indoline-3,8'-indolizin]
e]-5',5',6'-tricarboxylate 6