Supporting Information
for
A speedy route to sterically encumbered, benzene-fused derivatives of privileged, naturally occurring hexahydropyrrolo[1,2-b]isoquinoline

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Detailed experimental procedures, analytical data and copies of \(^1\)H and \(^{13}\)C NMR spectra for all new compounds; crystallographic data for compounds 10 and 13e; results of correlational and variable temperature NMR experiments

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1. EXPERIMENTAL SECTION

General information. NMR spectroscopic data were recorded with a 400 MHz (400.13 MHz for $^1$H and 100.61 MHz for $^{13}$C) and a 500 MHz (500.03 MHz for $^1$H and 125.7 MHz for $^{13}$C) spectrometers in DMSO-$d_6$ or in CDCl$_3$ and were referenced to residual solvent proton signals ($\delta_H = 7.26$ and 2.50 ppm, respectively) and solvent carbon signals ($\delta_C = 77.2$ and 39.5 ppm, respectively). Coupling constants, $J$ are reported in Hz. Melting points were determined with an automated heat block instrument and are uncorrected. Mass spectra were recorded with a HRMS-ESI-qTOF spectrometer (electrospray ionization mode). X-ray single crystal analyses were performed with monochromated Mo K\(\alpha\) or Cu K\(\alpha\) radiation, respectively. Column chromatography was performed on silica gel 60 (230–400 mesh). For TLC analysis UV$_{254}$ silica gel coated plates were used. MeCN was distilled from P$_2$O$_5$ and stored over molecular sieves 4 Å. Homophthalic anhydride was acquired from a commercial source, stored at 5 °C and used as received. All indolenines 9 were stored in sealed vials at 5 °C in the dark.

CCDC 1503093 (13e), 1503094 (anti-10e), 1503095 (anti-10d), 1503096 (anti-10g'), 1503097 (anti-10e), 1503098 (anti-10a'), 1503099 (anti-10f), 1503100 (syn-10a'), 1503101 (syn-10f), 1503102 (anti-10c'), 1503103 (anti-10n), 1503104 (anti-10i), 1503105 (syn-10e), 1503106 (anti-10l), 1470399 (anti-10b), 1470389 (anti-10h), 1461790 (anti-10j) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk.

Indolenines 9. Indolenines 9a-b [1], 9d-g [1], 9h [2], 9i [3], 9j [4], 9k [5], 9p [6] are known compounds and were prepared from the arylhydrazine hydrochlorides and respective aldehydes or ketones according to the literature protocols.

General procedure 1. Synthesis of indolenines 9c,l,n,o,q-t. To a screw-cap vial containing a suspension of the corresponding aryl hydrazine hydrochloride in glacial AcOH (15 mL) carbonyl compound (1.1 equiv) was added in one portion. The reaction mixture was stirred at 55–60 °C for 4 h (or at reflux for 2–16 h) and concentrated in vacuo at 40 °C. The residue was diluted with DCM (50 mL) and filtered through Celite. The resulting solution was passed through a short pad of silica, washed with sat. NaHCO$_3$ and water. The organic layer was dried over Na$_2$SO$_4$ and concentrated under reduced pressure to give pure indolenines 9c,l,s. Indolenines 9n,o,q-r,t were subjected to extra column chromatography.

5'-Fluorospiro[cyclohexane-1,3'-indole] (9c). The title compound was prepared from 4-fluorophenylhydrazine hydrochloride (1.51 g, 9.3 mmol) and cyclohexanecarboxaldehyde (1.14 g, 10.2 mmol) according to general procedure 1. Light yellow solid. Yield 1.39 g (74%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.34 (s, 1H), 7.59 (dd, $J$=8.4, 4.7, 1H), 7.18 – 6.92 (m, 2H), 2.00 – 1.55 (m, 10H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ = 178.1 (d, $J$=3.6), 161.6 (d, $J$=244.7), 150.3, 146.7 (d, $J$=8.8), 121.8 (d, $J$=9.0), 114.3 (d, $J$=23.8), 110.0 (d, $J$=24.7), 58.3 (d, $J$=2.2), 31.6, 25.4, 23.8. HRMS (ESI) m/z [M+H]: Calcd for C$_{13}$H$_{14}$FN: 204.1183. Found: 204.1171.

4a-Methyl-2,3,4,4a-tetrahydro-1H-carbazole (9l) [7]. The title compound was prepared from phenylhydrazine hydrochloride (0.72 g, 5 mmol) and 2-methylcyclohexanone (0.62 g, 5.5 mmol) according to general procedure 1 (reflux, 2 h). Yield 600 mg (65%). Beige solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.62 (d, $J$=7.7, 1H), 7.39 – 7.26 (m, 2H), 7.21 (t, $J$=7.4, 1H), 2.95 – 2.78 (m, 1H),
2.61 (td, J=13.3, 5.7, 1H), 2.38 – 2.13 (m, 2H), 1.91 – 1.60 (m, 2H), 1.43 (qd, J=13.2, 8.9, 1H), 1.33 (s, 3H), 1.18 (td, J=13.3, 4.2, 1H).

2-Methyl-2',3',5',6'-tetrahydrospiro[indole-3,4'-pyran] (9m). A mixture of 4-acetylpyrane (2.05 g, 16.0 mmol), phenylhydrazine (1.73 g, 16.0 mmol) and p-toluenesulfonic acid monohydrate (100 mg, 5.3 mmol) was refluxed in benzene (40 mL) with a Dean-Stark trap for 3 h. The volatiles were removed in vacuo followed by column chromatography (hexane-EtOAc from 4:1 to 5:2) affording 2.0 g of 1-phenyl-2-(1-(tetrahydro-2H-pyran-4-yl)ethylidene)hydrazine with impurity. The obtained compound was refluxed in 30 mL of AcOH for 3 h. The reaction mixture was concentrated, redissolved in CHCl₃ and washed with water. The organic layer was dried over Na₂SO₄ and concentrated to give crude 9m, which was purified by column chromatography (hexane-EtOAc from 1:1 to 2:3). Yield 550 mg (19%). Beige solid. ¹H NMR (400 MHz, CDCl₃) δ 7.84 (d, J=7.4, 1H), 7.59 (d, J=7.6, 1H), 7.38 (t, J=7.5, 1H), 7.21 (t, J=7.5, 1H), 4.20 – 3.90 (m, 4H), 2.34 (s, 3H), 2.26 – 2.12 (m, 2H), 1.28 – 1.25 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 158.9, 154.2, 143.8, 128.2, 124.8, 123.8, 120.6, 63.6, 55.1, 30.8, 16.2. HRMS (ESI) m/z [M+H]⁺: Calcd for C₁₅H₂₇NO: 202.1226. Found: 202.1246.

2'-Methylspiro[cyclohexane-1,3'-indole] (9n) [8]. The title compound was prepared from phenylhydrazine hydrochloride (1.66 g, 11.5 mmol) and cyclohexylmethylketone (1.59 g, 12.6 mmol) according to general procedure 1 (reflux, 16 h). Column chromatography (CHCl₃) afforded 685 mg (34%) of 9n as beige solid. ¹H NMR (400 MHz, CDCl₃) δ 7.74 (d, J=7.5, 1H), 7.58 (d, J=7.7, 1H), 7.36 (td, J=7.6, 1.1, 1H), 7.19 (td, J=7.5, 1.0, 1H), 2.31 (s, 3H), 2.06 – 1.88 (m, 3H), 1.88 – 1.73 (m, 4H), 1.60 – 1.40 (m, 1H), 1.41 – 1.23 (m, 2H).

3,3-Dimethyl-2-(p-tolyl)-3H-indole (9o) [9]. The title compound was prepared from phenylhydrazine hydrochloride (0.94 g, 6.5 mmol) and 2-methyl-1-(p-tolyl)propan-1-one (1.2 g, 7.2 mmol) according to general procedure 1 (reflux, 16 h). Column chromatography (CHCl₃-hexane 1:4) afforded 890 mg (58%) of 9o as viscous yellowish oil. ¹H NMR (400 MHz, CDCl₃) δ 8.07 (d, J=8.2, 2H), 7.69 (d, J=7.6, 1H), 7.41 – 7.16 (m, 5H), 2.43 (s, 3H), 1.59 (s, 6H).

3,3-Dimethyl-2-propyl-3H-indole (9q) and 2,3-dimethyl-3-propyl-3H-indole [10] (9r). The mixture of title compounds was prepared from phenylhydrazine hydrochloride (3.74 g, 26 mmol) and 2-methylhexan-3-one (3.26 g, 28.6 mmol) according to general procedure 1. Column chromatography (eluting with CHCl₃-hexane from 1:2 to 1:1) afforded pure indolines 9r and 9s.

(9q): Yield 892 mg (18%), orange oil. ¹H NMR (400 MHz, CDCl₃) δ 7.63 (d, J=7.7, 1H), 7.37 – 7.27 (m, 2H), 7.25 – 7.16 (m, 1H), 2.60 – 2.50 (m, 2H), 2.01 – 1.83 (m, 2H), 1.33 (s, 6H), 1.08 (t, J=7.4, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 191.1, 154.0, 145.8, 127.7, 125.2, 121.3, 120.2, 53.9, 31.1, 23.3, 20.0, 14.4. HRMS (ESI) m/z [M+H]⁺: Calcd for C₁₅H₁₇N: 188.1434. Found: 188.1438.

(9r): Yield 550 mg (11%), orange oil. ¹H NMR (400 MHz, CDCl₃) δ = 7.53 (d, J=7.6, 1H), 7.34 – 7.10 (m, 3H), 2.25 (s, 3H), 1.91 – 1.79 (m, 1H), 1.77 – 1.67 (m, 1H), 1.28 (s, 3H), 0.87 – 0.55 (m, 5H). ¹³C NMR (101 MHz, CDCl₃) 187.1, 154.2, 143.3, 127.4, 125.1, 121.6, 119.9, 57.7, 39.7, 22.6, 17.5, 15.5, 14.0. HRMS (ESI) m/z [M+H]⁺: Calcd for C₁₅H₁₇N: 188.1434. Found: 188.1429.

2'-Cyclohexylspiro[cyclohexane-1,3'-indole] (9s). Phenylhydrazine hydrochloride (0.86 g, 6.5 mmol) and dicyclohexylketone (1.38 g, 7.1 mmol) were reacted according to general procedure 1 (reflux, 6h). Crystallization from hexane-DCM-EtOAc mixture (2:1:2) gave 9s-hydrochloride as
light yellow solid. Yield 0.5 g (29%). The prepared compound (500 mg, 1.6 mmol) was dissolved in CHCl₃ (50 mL), washed with NaHCO₃ saturated solution (25 mL) and water. The organic layer was dried over Na₂SO₄ and concentrated in vacuo to give pure 9s. Yield 401 mg (91%). ¹H NMR (400 MHz, CDCl₃) δ 7.70 (d, J=7.4, 1H), 7.61 (d, J=7.7, 1H), 7.32 (td, J=7.6, 1.1, 1H), 7.15 (td, J=7.5, 1.0, 1H), 2.65 – 2.53 (m, 1H), 2.05 – 1.60 (m, 14H), 1.54 – 1.42 (m, 1H), 1.42 – 1.32 (m, 3H), 1.27 – 1.17 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 194.7, 144.1, 127.6, 124.4, 124.3, 120.4, 58.7, 38.5, 32.4, 30.1, 26.7, 26.0, 25.5, 21.8. HRMS (ESI) m/z [M+H]+: Calcd for C₁₉H₂₅N: 268.2060. Found: 268.2051.

**2′-(p-Tolyl)spiro[cyclohexane-1,3′-indole] (9t).** The title compound was prepared from phenylhydrazine hydrochloride (0.53 g, 3.7 mmol) and cyclohexyl(p-tolyl)methanone (0.83 g, 4.1 mmol) according to general procedure 1 (reflux, 16 h). Column chromatography (eluting with CHCl₃-hexane 1:4) afforded 650 mg (64%) of 9t as viscous yellow oil. ¹H NMR (400 MHz, DMSO-d₆) δ 8.07 (d, J=8.3, 1H), 7.87 (d, J=7.4, 1H), 7.63 (d, J=7.3, 1H), 7.39 (td, J=7.6, 1.0, 1H), 7.33 (d, J=8.1, 1H), 7.23 (td, J=7.5, 1.0, 1H), 2.38 (s, 3H), 2.34 – 2.21 (m, 2H), 2.02 – 1.88 (m, 3H), 1.81 – 1.72 (m, 2H), 1.65 – 1.50 (m, 1H), 1.27 – 1.21 (m, 2H). ¹³C NMR (101 MHz, DMSO-d₆) δ 182.1, 153.3, 146.3, 140.1, 130.1, 129.1, 128.4, 127.5, 124.7, 124.3, 120.7, 57.5, 30.8, 24.5, 21.2, 20.9. HRMS (ESI) m/z [M+H]+: Calcd for C₂₀H₂₁N: 276.1747. Found: 276.1758.

**General procedure 2. Synthesis of compounds 10.** A mixture of homophthalic anhydride (1 equiv.) and the corresponding indolenine 9a–t (1 equiv) was placed in a sealed screw-cap vial, dissolved in dry acetonitrile (2 mL per 1 mmol) and stirred at room temperature for time indicated in Table 1. The reaction mixture was cooled to –14 °C, the resulting precipitate was filtered and washed with minimum amount of cold acetonitrile to give pure compound 10.

**General procedure 3. Synthesis of methyl esters 10’.** The Castagnoli-Cushman product 10 was dissolved in dry acetonitrile (10 mL per 1 mmol). Methyl iodide (2.5 equiv) and K₂CO₃ (2.5 equiv) were added to the solution and the resulting suspension was stirred for 24 h at room temperature. The volatiles were removed in vacuo. The residue was dissolved in DCM, washed with water, brine, dried over Na₂SO₄ and concentrated to give crude methyl ester 10’, which was purified by column chromatography on silica gel.

**(RS,RS)-6’-Oxo-11’,11a’-dihydro-6’H-spirocyclohexane-1,12’-indolo[1,2-b]isoquinoline-11’-carboxylic acid (anti-10a).** The title compound was prepared according to general procedure 2 (1.9 mmol scale). The product was obtained as white solid, mp 251–252 °C (decomp.). Yield 368 mg, 56%. ¹H NMR (400 MHz, DMSO-d₆) δ 13.68 (s, 1H), 8.42 (d, J = 7.9 Hz, 1H), 8.19 – 8.00 (m, 1H), 7.74 (d, J = 7.6 Hz, 1H), 7.64 (td, J = 7.6, 1.1 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.31 – 7.25 (m, 2H), 7.10 (t, J = 7.3 Hz, 1H), 4.36 (d, J = 12.9 Hz, 1H), 4.32 (d, J = 12.8 Hz, 1H), 2.17 – 1.97 (m, 1H), 1.95 – 1.75 (m, 4H), 1.75 – 1.63 (m, 1H), 1.64 – 1.49 (m, 3H), 1.27 – 1.11 (m, 1H); ¹³C NMR (101 MHz, DMSO-d₆) δ 172.9, 161.0, 140.7, 138.8, 136.2, 132.8, 128.6, 127.8, 127.7, 127.5, 125.7, 125.6, 123.5, 116.0, 68.7, 46.3, 46.0, 34.0, 31.2, 25.1, 22.1, 20.0.; HRMS (ESI) m/z [M+H]+: Calcd for C₂₂H₂₃N₆O₃: 348.1594. Found: 348.1586.

The filtrate was concentrated and subjected to esterification according general procedure 3 and column chromatography (hexane-Me₂CO 7:1) to give some extra products anti-10a and syn-10a.
(RS,RS)-Methyl 11z,12,12-trimethyl-6-oxo-6,11,11z,12-tetrahydroindolo[1,2-b]isoquinoline-11-carboxylate (anti-10a'). Yield 84 mg, 12%. White solid, mp 158–159 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.56 (d, J=8.1, 1H), 8.25 (d, J=7.3, 1H), 7.70 (d, J=7.6, 1H), 7.62 – 7.39 (m, 2H), 7.32 (t, J=7.7, 1H), 7.16 – 6.94 (m, 2H), 4.44 (d, J=13.0, 1H), 4.39 (d, J=12.9, 1H), 3.95 (s, 3H), 2.19 – 2.01 (m, 1H), 2.01 – 1.86 (m, 2H), 1.86 – 1.71 (m, 2H), 1.70 – 1.44 (m, 4H), 1.35 – 1.18 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 172.4, 161.9, 141.2, 138.8, 135.5, 132.7, 129.2, 128.7, 128.3, 128.1, 125.8, 125.5, 123.8, 117.18, 69.4, 52.5, 46.7, 46.7, 34.5, 31.9, 25.7, 23.0, 20.6; HRMS (ESI) m/z [M+H]$^+$: Calcd for C$_{32}$H$_{33}$NO$_3$: 362.1751. Found: 362.1758.

(RS,SR)-Methyl 11z,12,12-trimethyl-6-oxo-6,11,11z,12-tetrahydroindolo[1,2-b]isoquinoline-11-carboxylate (syn-10a'). Yield 50 mg, 7%. White solid, mp 152–153 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.39 (d, J=7.9, 1H), 8.19 (dd, J=6.0, 3.0, 1H), 7.55 – 7.43 (m, 2H), 7.44 – 7.35 (m, 1H), 7.33 – 7.20 (m, 2H), 7.06 (t, J=7.5, 1H), 4.49 (d, J=3.2, 1H), 4.13 (d, J=3.2, 1H), 3.40 (s, 3H), 1.97 – 1.44 (m, 10H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.2, 162.6, 142.0, 139.5, 136.2, 132.5, 131.0, 129.3, 129.2, 128.3, 127.6, 123.8, 116.0, 70.1, 52.6, 46.9, 46.8, 42.3, 32.2, 25.5, 23.6, 22.7; HRMS (ESI) m/z [M+H]$^+$: Calcd for C$_{32}$H$_{33}$NO$_3$: 362.1751. Found: 362.1765.

(RS,RS)-2'-Methyl-6'-oxo-11',11a'-dihydro-6'H-spirocyclohexane-1,12'-indolo[1,2-b]isoquinoline-11'-carboxylic acid (anti-10b). The title compound was prepared according to general procedure 3 and column chromatography (eluent – CHCl$_3$) to give some extra product methyl ester syn-10b';

(RS,SR)-Methyl 2'-methyl-6'-oxo-11',11a'-dihydro-6'H-spirocyclohexane-1,12'-indolo[1,2-b]isoquinoline-11'-carboxylate (syn-10b'). Viscous yellow oil. Yield 48 mg, 13%. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.32 – 8.21 (m, 1H), 8.21 – 8.08 (m, 1H), 7.54 – 7.42 (m, 2H), 7.44 – 7.35 (m, 1H), 7.15 – 7.01 (m, 2H), 4.48 (d, J=3.3, 1H), 4.12 (d, J=3.3, 1H), 3.41 (s, 3H), 2.35 (s, 3H), 1.92 – 1.46 (m, 10H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.1, 162.0, 139.5, 139.5, 136.0, 133.2, 132.2, 130.9, 129.0, 129.0, 128.7, 127.4, 123.9, 115.6, 70.0, 52.5, 46.7, 46.6, 42.2, 32.1, 25.4, 23.5, 22.6, 21.5; HRMS (ESI) m/z [M+H]$^+$: Calcd for C$_{41}$H$_{33}$NO$_5$: 376.1907. Found: 376.1922.

2'-Fluoro-6'-oxo-11',11a'-dihydro-6'H-spirocyclohexane-1,12'-indolo[1,2-b]isoquinoline-11'-carboxylic acid (anti/syn-10c). The title compound was prepared according to general procedure 2 (1.2 mmol scale). The product was obtained as white solid, mp 263–265 °C (decomp.). Yield 295 mg, 66% (anti/syn = 3:3:1). Crystallization from MeCN gave anti-10c as a single isomer (151 mg, 34%). $^1$H NMR (400 MHz, DMSO-$d_6$) δ 13.71 (s, 1H), 8.41 (dd, J=8.7, 5.3, 1H), 8.06 (d, J=7.5, 1H), 7.64 (t, J=7.2, 1H), 7.58 – 7.41 (m, 2H), 7.25 (d, J=7.6, 1H), 7.16 – 6.98 (m, 1H), 4.37 (s, 2H), 2.10 – 1.94 (m, 1H), 1.92 – 1.47 (m, 8H), 1.26 – 1.06 (m, 1H); $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ = 173.1, 161.0, 158.4 (d, J$_{CF}$ =239.6), 141.1 (d, J$_{CF}$=7.7), 137.4 (d, J$_{CF}$ =1.4), 136.3, 133.0, 128.6,
128.1, 127.8, 125.8, 117.0 (d, $J_{CF} = 8.3$), 113.9 (d, $J_{CF} = 22.6$), 113.3 (d, $J_{CF} = 24.8$), 69.2, 46.5, 46.3 (d, $J_{CF} = 1.0$), 33.9, 31.2, 25.2, 22.1, 20.2; HRMS (ESI) m/z [M+H]$: Calcd for C$_{22}$H$_{28}$FNO$_3$: 366.1500. Found: 366.1509.

(RS,RS)-4'-Methyl-6'-oxo-11',11a'-dihydro-6'H-spirocyclohexane-1,12'-indolo[1,2-b]isoquinoline]-11'-carboxylic acid (anti-10d). The title compound was prepared according to general procedure 2 (3 mmol scale). The product was obtained as white solid, mp 210–212 °C (decomp.). Yield 907 mg, 84%. $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 8.04 (dd, $J = 7.8, 1.0, 1H$), 7.61 (td, $J = 7.6, 1.3, 1H$), 7.55 – 7.36 (m, 3H), 7.17 – 7.04 (m, 2H), 4.38 (d, $J = 3.3, 1H$), 4.25 (d, $J = 3.3, 1H$), 2.05 – 1.91 (m, 1H), 1.83 – 1.56 (m, 4H), 1.45 – 1.12 (m, 4H), 1.00 – 0.85 (m, 1H); $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 173.5, 161.8, 141.9, 141.8, 134.9, 132.4, 129.6, 129.1, 128.5, 128.0, 127.8, 127.5, 122.0, 71.5, 47.6, 41.7, 30.8, 29.6, 24.9, 22.4, 20.2; HRMS (ESI) m/z [M+H]$: Calcd for C$_{23}$H$_{26}$FNO$_3$: 362.1751. Found: 362.1759.

2',4'-Dichloro-6'-oxo-11',11a'-dihydro-6'H-spirocyclohexane-1,12'-indolo[1,2-b]isoquinoline]-11'-carboxylic acid (anti/syn-10e). The title compound was prepared according to general procedure 2 (1 mmol scale). The product was obtained as beige solid, yield 275 mg, 66% (anti/syn 0.8:1).

Single isomers of 10e and compound 13e were obtained via mechanical separation of monocrystals formed from the same reaction carried out without stirring (reaction conditions: 70 mg (0.28 mmol) of indolenine 9e, 45 mg (0.28 mmol) of HPA, 2.55 mL MeCN, 5 °C, 48 h).

(RS,RS)-2',4'-Dichloro-6'-oxo-11',11a'-dihydro-6'H-spirocyclohexane-1,12'-indolo[1,2-b]isonoline]-11'-carboxylic acid (anti-10e). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 13.25 (s, 1H), 8.03 (d, $J = 7.3, 1H$), 7.68 – 7.60 (m, 2H), 7.58 – 7.51 (m, 2H), 7.47 (t, $J = 7.5, 1H$), 4.45 (d, $J = 2.5, 1H$), 4.38 (d, $J = 2.7, 1H$), 2.00 – 1.84 (m, 1H), 1.81 – 1.64 (m, 4H), 1.40 (s, 1H), 1.31 – 1.15 (m, 3H), 0.94 (d, $J = 5.3, 1H$); $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ $^{13}$C NMR (101 MHz, DMSO) $\delta$ 173.2, 161.8, 146.3, 140.0, 135.0, 132.9, 130.5, 128.9, 128.0, 127.7, 127.7, 127.3, 126.3, 130.2, 41.4, 30.0, 29.3, 24.6, 22.1, 20.0; HPLC-MS-ESI m/z [M+H]$: Calcd for C$_{27}$H$_{29}$Cl$_2$N$_2$O$_3$: 416.0815. Found: 416.0818.

(RS,SR)-2',4'-Dichloro-6'-oxo-11',11a'-dihydro-6'H-spirocyclohexane-1,12'-indolo[1,2-b]isonoline]-11'-carboxylic acid (syn-10e). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 8.02 (d, $J = 7.1, 1H$), 7.61 (td, $J = 7.5, 1.2, 1H$), 7.57 – 7.48 (m, 2H), 7.40 (d, $J = 1.9, 1H$), 7.33 (d, $J = 1.9, 1H$), 4.69 (d, $J = 2.8, 1H$), 4.26 (d, $J = 2.7, 1H$), 2.09 – 1.96 (m, 1H), 1.89 – 1.33 (m, 9H); $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 171.6, 160.3, 146.1, 138.0, 137.4, 132.5, 130.1, 129.0, 128.3, 128.2, 128.1, 127.2, 122.0, 119.3, 70.2, 46.7, 45.9, 41.2, 31.0, 24.5, 23.1, 21.6; HPLC-MS-ESI m/z [M+H]$: Calcd for C$_{27}$H$_{29}$Cl$_2$N$_2$O$_3$: 416.0815. Found: 416.0818.

(SR)-4-((RS)-5',7'-Dichlorospiro[cyclohexane-1,3'-indolin]-2'-yl)isochroman-1,3-dione (13e). $^1$H NMR (500 MHz, 4% Me$_2$CO-$d_6$ in CDCl$_3$; 5 °C) $\delta$ 8.18 (d, $J = 7.7, 1H$), 7.74 (t, $J = 7.5, 1H$), 7.54 (t, $J = 7.6, 1H$), 7.37 (d, $J = 7.7, 1H$), 7.03 (s, 1H), 6.87 (s, 1H), 4.28 (s, 1H), 4.19 (s, 1H), 3.78 (s, 1H), 2.79 – 2.67 (m, 1H), 2.06 – 1.94 (m, 1H), 1.84 – 1.72 (m, 1H), 1.69 – 1.50 (m, 4H), 1.50 – 1.36 (m, 2H), 1.29 – 1.12 (m, 1H); $^{13}$C NMR (126 MHz, 4% Me$_2$CO-$d_6$ in CDCl$_3$; 5 °C) $\delta$ = 166.1, 160.8, 142.3, 140.6, 137.9, 135.6, 130.3, 128.8, 127.4, 127.0, 125.4, 123.5, 121.2, 117.2, 71.8, 51.2, 47.3, 38.6, 28.5, 25.5, 23.8, 22.7;
Methyl (11'RS,11a'RS)-2',4'-dichloro-6'-oxo-11',11a'-dihydro-6'H-spiro[cyclohexane-1,12'-indolo[1,2-b]isoquinoline]-11'-carboxylate (anti-10e'). The title compound was prepared via esterification of anti/syn-10e mixture (700 mg, 1.67 mmol, anti/syn 1:1) according to general procedure 3 and column chromatography. Yield 534 mg, 75%. Yellow foam. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.26 (dd, $J$=7.8, 1.3, 1H), 7.55 (td, $J$=7.5, 1.4, 1H), 7.51 (d, $J$=1.9, 1H), 7.46 (t, $J$=7.3, 1H), 7.38 (d, $J$=1.9, 1H), 7.34 (d, $J$=7.7, 1H), 4.43 (d, $J$=4.9, 1H), 4.26 (d, $J$=4.9, 1H), 3.83 (s, 3H), 2.04 – 1.73 (m, 4H), 1.67 – 1.15 (m, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 172.3, 161.7, 145.7, 139.4, 133.5, 132.8, 131.3, 129.0, 128.7, 128.5, 126.9, 123.7, 71.5, 52.2, 49.4, 42.9, 31.5, 30.0, 25.5, 22.9, 20.5; HRMS (ESI) m/z [M–H]$^-$: Calcd for C$_{23}$H$_{23}$Cl$_2$NO$_3$: 428.0826. Found: 428.0833.

1'-(Methylsulfonyl)-6-oxo-11,11a-di hydro-6'H-spiro[indolo[1,2-b]isoquinoline-12,4'-piperidine]-11-carboxylic acid (anti/syn-10f). The title compound was prepared according to general procedure 2 (1 mmol scale). White solid, yield 325 mg, 79% (anti/syn 2:1). This diastereomeric mixture was separated after esterification according to general procedure 3 and column chromatography (hexane-Me$_2$CO-DCM 6:2:1 to 4:2:1).

(RS,RS)-Methyl 1'-(methylsulfonyl)-6-oxo-11,11a-dihydro-6'H-spiro-[indolo[1,2-b]isoquinoline-12,4'-piperidine]-11-carboxylate (anti-10f'). White solid. Yield 191 mg, 41%. Mp 205–207 ºC. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.59 (d, $J$=7.9, 1H), 8.24 (dd, $J$=7.7, 1.3, 1H), 7.64 – 7.51 (m, 2H), 7.48 (t, $J$=7.5, 1H), 7.41 – 7.30 (m, 1H), 7.19 – 6.99 (m, 2H), 4.48 (d, $J$=12.9, 1H), 4.38 (d, $J$=12.8, 1H), 3.99 (s, 3H), 3.90 – 3.82 (m, 1H), 3.81 – 3.72 (m, 1H), 3.57 (ddd, $J$=13, 10.1, 6.0, 1H), 3.17 (td, $J$=12.5, 2.1, 1H), 2.92 (s, 3H), 2.25 (td, $J$=12.7, 4.5, 1H), 2.09 – 1.98 (m, 2H), 1.69 (d, $J$=13.1, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 172.0, 161.9, 141.3, 136.5, 135.1, 133.1, 129.0, 129.0, 128.8, 128.6, 125.6, 124.8, 124.1, 117.7, 68.6, 53.0, 46.6, 44.6, 42.8, 41.0, 36.5, 33.6, 31.3; HRMS (ESI) m/z [M+H]$^+$: Calcd for C$_{23}$H$_{24}$N$_2$O$_5$: 463.1298. Found: 463.1310.

(RS,SR)-Methyl 1'-(methylsulfonyl)-6-oxo-11,11a-dihydro-6'H-spiro-[indolo[1,2-b]isoquinoline-12,4'-piperidine]-11-carboxylate (syn-10f'). White solid. Yield 102 mg, 22%. Mp 225–226 ºC. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.42 (d, $J$=8.0, 1H), 8.26 – 8.10 (m, 1H), 7.56 – 7.46 (m, 2H), 7.44 – 7.38 (m, 1H), 7.37 – 7.29 (m, 2H), 7.09 (t, $J$=7.4, 1H), 4.50 (d, $J$=2.5, 1H), 4.03 (d, $J$=2.9, 1H), 3.73 – 3.59 (m, 2H), 3.47 – 3.24 (m, 5H), 2.91 (s, 3H), 2.15 (t, $J$=5.5, 2H), 1.97 (t, $J$=5.3, 2H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 170.6, 163.4, 135.5, 132.7, 129.4, 129.3, 129.1, 127.5, 124.0, 123.3, 116.3, 69.5, 52.8, 46.4, 44.4, 43.1, 42.5, 40.1, 35.9, 31.6; HRMS (ESI) m/z [M+H]$^+$: Calcd for C$_{23}$H$_{24}$N$_2$O$_5$: 463.1298. Found: 463.1318.

(RS,RS)- and (RS,SR)-Methyl 12,12-dimethyl-6-oxo-6,11,11a,12-tetrahydroindolo[1,2-b]isoquinoline-11-carboxylates (anti- and syn-10g'). A mixture of phenylhydrazine hydrochloride (433 mg, 3 mmol) and isobutyric aldehyde (216 mg, 3 mmol) in 15 ml of glacial acetic acid was heated at 50 ºC for 2 h in a sealed screw-cap vial. Next, the reaction mixture was gradually poured into ca. 100 ml of saturated aqueous NaHCO$_3$ and extracted with five 2 ml portions of CHCl$_3$. Combined organic extracts were washed with brine, dried over MgSO$_4$, filtered and used without purification. Solution of 3,3-dimethyldiindolene (NMR yield 1.75 mmol, 58%) was placed in a 15 ml screw-cap vial followed by addition of homopthalic anhydride (284 mg, 1.75 mmol). The reaction mixture was stirred at room temperature for 16 h, concentrated in vacuo and redissolved in Me$_2$CO (12 mL). Methyl iodide (284 mg, 2 mmol) and K$_2$CO$_3$ (276 mg, 2 mmol) were added to the solution and stirred for 24 h at r.t. The volatiles were removed in vacuo, CHCl$_3$
and water were added to the residue. The organic layer was separated, washed with brine, dried over Na₂SO₄ and concentrated to give crude mixture of anti- and syn-10g'. Column chromatography (hexane-Me₂CO from 7:1 to 4:1) afforded pure isomers.

**Anti-10g**: Yield 286 mg, 51%. Yellow foam. ¹H NMR (400 MHz, CDCl₃) δ 8.42 (d, J=8.0, 1H), 8.26 (dd, J=7.6, 1.2, 1H), 7.58 – 7.35 (m, 2H), 7.34 – 7.25 (m, 1H), 7.21 (d, J=6.9, 1H), 7.16 – 6.98 (m, 2H), 4.49 (d, J=13.0, 1H), 4.33 (d, J=12.9, 1H), 3.94 (s, 3H), 1.43 (s, 3H), 1.27 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) 172.0, 161.8, 140.3, 140.1, 135.4, 132.8, 129.4, 128.8, 128.4, 128.3, 125.4, 124.8, 121.9, 116.9, 68.9, 52.6, 47.0, 43.6, 26.3, 25.0; HRMS (ESI) m/z [M+H]^+: Calcd for C₂₉H₁₉NO₃: 322.1438. Found: 322.1439.

**Syn-10g**: Yield 202 mg, 36%. Yellow foam. ¹H NMR (400 MHz, CDCl₃) δ 8.40 (d, J=8.0, 1H), 8.30 – 8.09 (m, 1H), 7.53 – 7.45 (m, 2H), 7.42 – 7.36 (m, 1H), 7.32 – 7.27 (m, 1H), 7.18 (dd, J=7.4, 0.8, 1H), 7.10 (td, J=7.4, 0.9, 1H), 4.37 (d, J=3.7, 1H), 4.05 (d, J=3.7, 1H), 3.50 (s, 1H), 1.50 (s, 2H), 1.32 (s, 2H); ¹³C NMR (101 MHz, CDCl₃) 171.4, 162.2, 141.1, 139.5, 135.7, 132.4, 130.9, 129.3, 129.1, 128.3, 127.4, 124.3, 122.0, 116.5, 70.0, 52.6, 46.0, 43.5, 30.5, 25.1; HRMS (ESI) m/z [M+H]^+: Calcd for C₂₉H₁₉NO₃: 322.1438. Found: 322.1445.

**11a,12,12-Trimethyl-6-oxo-6,11,11a,12-tetrahydroindolo[1,2-b]isoquinoline-11-carboxylic acid (anti/syn-10h)**. The title compound was prepared according to general procedure 2 (1.9 mmol scale) and washing the residue with hexane-CCl₄ 1:1 mixture. The product was obtained as white solid. Yield 520 mg, 86% (anti/syn 4.3:1). Crystallization from MeCN gave 9h as a single diastereomer. Mp 270–271 ºC (decomp.); ¹H NMR (400 MHz, DMSO-d₆) δ 13.59 (s, 1H), 8.26 (d, J=7.8, 1H), 8.08 (dd, J=7.7, 1.1, 1H), 7.66 (td, J=7.6, 1.3, 1H), 7.52 (t, J=7.5, 1H), 7.34 (d, J=7.3, 1H), 7.30 – 7.22 (m, 2H), 7.15 (td, J=7.4, 0.9, 1H), 4.63 (s, 1H), 1.41 (s, 3H), 1.31 (s, 3H), 1.13 (s, 3H); ¹³C NMR (101 MHz, DMSO-d₆) δ 171.9, 161.0, 140.5, 138.3, 135.8, 132.8, 128.6, 127.7, 127.6, 126.7, 126.1, 124.5, 122.2, 116.2, 70.9, 49.5, 47.0, 27.1, 20.3, 17.2; HRMS (ESI) m/z [M+H]^+: Calcd for C₂₀H₁₉NO₃: 322.1438. Found: 322.1440.

**2-Fluoro-11a,12,12-trimethyl-6-oxo-6,11,11a,12-tetrahydro-indolo[1,2-b]isoquinoline-11-carboxylic acid (anti/syn-10i)**. The title compound was prepared according to general procedure 2 (1 mmol scale) as a 3:1 mixture of diastereomers. Yield 244 mg, 72%; Diastereomers were separated after esterification according to general procedure 3 and column chromatography (hexane-Me₂CO 6:1 to 4:1).

(RS,RS)-Methyl 2-fluoro-11a,12,12-trimethyl-6-oxo-6,11,11a,12-tetrahydroindolo[1,2-b]isoquinoline-11-carboxylate (anti-10i'). White foam, yield 166 mg, 47% (for two steps); ¹H NMR (400 MHz, CDCl₃) δ 8.37 (dd, J=8.8, 4.9, 1H), 8.23 (dd, J=7.6, 1.4, 1H), 7.53 (td, J=7.5, 1.5, 1H), 7.46 (t, J=7.5, 1H), 7.05 (d, J=7.6, 1H), 6.96 (td, J=8.9, 2.7, 1H), 6.89 (dd, J=8.1, 2.6, 1H), 4.65 (s, 1H), 3.95 (s, 3H), 3.36 (s, 3H), 1.34 (s, 3H), 1.27 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 171.4, 161.8, 160.3 (d, J_CF=243.4), 142.7 (d, J_CF=7.5), 135.2, 134.9 (d, J_CF=2.1), 132.8, 128.9, 128.7, 128.1, 126.1, 118.6 (d, J_CF=8.1), 114.4 (d, J_CF=22.8), 109.3 (d, J_CF=24.2), 72.1, 52.4, 50.1, 47.6 (d, J_CF=1.6), 27.4, 20.4, 17.4; HRMS (ESI) m/z [M+H]^+: Calcd for C₂₁H₂₀FNO₃: 354.1492. Found: 354.1500.
(RS,SR)-Methyl 2-fluoro-11a,12,12-trimethyl-6-oxo-6,11,11a,12-tetrahydroindolo[1,2-b]isoquinoline-11-carboxylate (syn-10i'). White foam, yield 46 mg, 13% (for two steps); $^1$H NMR (400 MHz, CDCl$_3$) δ 8.39 (dd, J=8.8, 4.9, 1H), 8.25 (dd, J=6.4, 2.5, 1H), 7.54 – 7.41 (m, 2H), 7.39 – 7.29 (m, 1H), 6.96 (td, J=8.9, 2.6, 1H), 6.86 (dd, J=8.1, 2.6, 1H), 3.96 (s, 1H), 3.52 (s, 3H), 1.49 (s, 3H), 1.27 (s, 3H), 1.12 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 172.2, 162.1, 160.1 (d, J$_{CF}$ =242.7), 141.8 (d, J$_{CF}$ =7.4), 135.9, 135.7 (d, J$_{CF}$ =1.9), 132.5, 129.7, 129.4, 128.8, 127.5, 118.2 (d, J$_{CF}$ =8.0), 114.4 (d, J$_{CF}$ =22.7), 109.2 (d, J$_{CF}$ =24.2), 70.8, 52.6, 51.7, 48.1 (d, J$_{CF}$ =1.6), 28.2, 23.9, 21.9; HRMS (ESI) m/z [M+H]$^+$: Calcd for C$_{21}$H$_{20}$FNO$_3$: 354.1492. Found: 354.1499.

(RS,RS)-11a,12,12-Trimethyl-2-nitro-6-oxo-6,11,11a,12-tetrahydro-indolo[1,2-b]isoquinoline-11-carboxylic acid (anti-10j). The title compound was prepared according to general procedure 2 (1 mmol scale). The product was obtained as light yellow solid, mp 294–296 ºC (decomp.). Yield 268 mg, 73%. $^1$H NMR (400 MHz, DMSO-d$_6$) δ 13.70 (s, 1H), 8.42 (d, J = 8.8 Hz, 1H), 8.32 – 8.16 (m, 2H), 8.11 (dd, J = 7.7, 1.1 Hz, 1H), 7.70 (td, J = 7.6, 1.4 Hz, 1H), 7.54 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 7.7 Hz, 1H), 4.75 (s, 1H), 1.49 (s, 3H), 1.38 (s, 3H), 1.18 (s, 3H); $^{13}$C NMR (101 MHz, DMSO-d$_6$) δ 171.67, 161.8, 143.9, 143.8, 142.1, 136.1, 133.5, 128.1, 127.9, 127.8, 126.3, 124.9, 118.3, 116.0, 72.1, 49.2, 47.1, 26.7, 19.9, 17.4; HRMS (ESI) m/z [M+H]$^+$: Calcd for C$_{20}$H$_{18}$N$_2$O$_3$: 367.1288. Found: 367.1296.

2-Hydroxy-11a,12,12-trimethyl-6-oxo-6,11,11a,12-tetrahydro-indolo[1,2-b]isoquinoline-11-carboxylic acid (anti/syn-10k). The title compound was prepared according to general procedure 2 (1 mmol scale). The product was obtained as a white solid. Yield 192 mg, 57% (anti/syn 6.5:1). Crystallization from MeCN gave pure anti-isomer for analysis. $^1$H NMR (400 MHz, DMSO-d$_6$) δ 13.54 (s, 1H), 9.33 (s, 1H), 8.16 – 7.98 (m, 2H), 7.62 (td, J = 7.6, 1.3 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.22 (d, J = 7.7 Hz, 1H), 6.71 (d, J = 2.4 Hz, 1H), 6.64 (dd, J = 8.6, 2.4 Hz, 1H), 4.56 (s, 1H), 1.35 (s, 3H), 1.29 (s, 3H), 1.11 (s, 4H); $^{13}$C NMR (101 MHz, DMSO-d$_6$) δ 172.0, 160.0, 154.7, 142.1, 135.5, 132.4, 130.5, 128.7, 127.5, 127.4, 126.0, 117.2, 113.5, 109.2, 70.9, 49.6, 47.0, 27.0, 20.2, 17.1; HRMS (ESI) m/z [M+H]$^+$: Calcd for C$_{20}$H$_{16}$NO$_4$: 338.1387. Found: 338.1397.

(4aRS,15SR,15aSR)-4a-Methyl-10-oxo-2,3,4,4a,10,15-hexahydro-1H-isoquinolino[3,2-k]carbazole-15-carboxylic acid (anti-10l). The title compound was prepared according to general procedure 2 (1 mmol scale). The product was obtained as white solid, mp 253–255 ºC (decomp.). Yield 280 mg, 81%. $^1$H NMR (400 MHz, DMSO-d$_6$) δ 13.59 (s, 1H), 8.32 (d, J=7.6, 1H), 8.07 (dd, J=7.7, 1.2, 1H), 7.63 (td, J=7.6, 1.4, 1H), 7.49 (t, J=7.5, 1H), 7.38 – 7.21 (m, 3H), 7.16 (td, J=7.4, 1.0, 1H), 4.68 (s, 1H), 2.25 – 2.13 (m, 2H), 1.74 (td, J=13.8, 4.0, 1H), 1.57 – 1.42 (m, 3H), 1.33 (s, 3H), 1.20 – 1.03 (m, 4H); $^{13}$C NMR (101 MHz, DMSO-d$_6$) δ 172.4, 161.2, 139.4, 138.9, 135.7, 132.6, 128.5, 127.6, 127.5, 124.5, 122.1, 116.8, 69.8, 49.4, 47.8, 30.6, 30.0, 27.2, 20.8, 20.2; HRMS (ESI) m/z [M+H]$^+$: Calcd for C$_{22}$H$_{21}$NO$_3$: 370.1414. Found: 370.1421.

11a-Methyl-6-oxo-2',3',5',6',11,11a-hexahydro-6H-spiro-[indolo[1,2-b]isoquinoline-12,4'-pyran]-11-carboxylic acid (anti/syn-10m). The title compound was prepared according to general procedure 2 (1.4 mmol scale). The product was obtained as white solid, mp 252–254 ºC. Yield 436 mg, 79% (anti/syn = 6:1). Crystallization from MeCN gave anti-10m as a single isomer (289 mg, 52%). $^1$H NMR (400 MHz, DMSO-d$_6$) δ 13.72 (s, 1H), 8.42 (d, J=7.8, 1H), 8.08 (dd, J=7.6, 0.9, 1H), 7.87 (d, J=7.5, 1H), 7.67 (td, J=7.6, 1.2, 1H), 7.52 (t, J=7.5, 1H), 7.32 (t, J=7.5, 1H), 7.24 (d, J=7.7, 1H), 7.15 (t, J=7.2, 1H), 4.64 (s, 1H), 4.23 (td, J=12.4, 2.7, 1H), 3.95 (dd, J=12.1, 6.1, 1H), 3.75 – 3.72 (m, 1H), 3.52 (t, J=11.5, 1H), 2.36 (td, J=12.6, 4.3, 1H), 1.99 (td, J=13.2, 6.5, 1H), 1.88
13C NMR (101 MHz, DMSO-\textit{d}_6) \delta = 171.8, 161.2, 139.3, 137.5, 135.6, 132.9, 128.4, 127.7, 127.7, 127.7, 125.9, 125.9, 123.6, 116.5, 71.6, 64.0, 62.0, 49.5, 47.8, 32.6, 29.2, 15.7; HRMS (ESI) m/z [M+H]^+: Calcd for C_{22}H_{21}NO_4: 386.1363. Found: 386.1356.

**RS,RS-11a'-Methyl-6'-oxo-11',11a'-dihydro-6'H-spiro[cyclohexane-1,12'-indolo[1,2-b]isoquinoline]-11'-carboxylic acid (anti-10n)**. The title compound was prepared according to general procedure 2 (0.9 mmol scale). The product was obtained as white solid, mp 239–241 °C (decomp.). Yield 336 mg, 93%.

1H NMR (400 MHz, DMSO-\textit{d}_6) \delta 13.65 (s, 1H), 8.38 (d, J=7.4, 1H), 8.07 (dd, J=7.7, 1H), 7.71 (d, J=7.4, 1H), 7.65 (t, J=7.6, 1H), 7.50 (t, J=7.5, 1H), 7.32 – 7.25 (m, 1H), 7.22 (d, J=7.7, 1H), 7.11 (td, J=7.5, 0.9, 1H), 4.63 (s, 1H), 2.17 – 1.92 (m, 3H), 1.88 – 1.74 (m, 2H), 1.64 (td, J=13.5, 5.5, 1H), 1.52 (d, 2H), 1.42 – 1.28 (m, 1H), 1.24 – 1.13 (m, 1H), 1.09 (s, 3H); 13C NMR (101 MHz, DMSO-\textit{d}_6) \delta 172.1, 161.1, 139.3, 138.5, 135.8, 132.3, 128.4, 127.6, 126.1, 126.0, 123.5, 116.4, 71.9, 49.8, 49.3, 32.7, 28.3, 25.1, 22.8, 20.7, 16.2; HRMS (ESI) m/z [M+H]^+: Calcd for C_{23}H_{23}NO_3: 384.1570. Found: 384.1558.

**RS,SR-11,12-Dimethyl-6-oxo-11a-(p-tolyl)-6,11,11a,12-tetrahydroindolo[1,2-b]isoquinoline-11'-carboxylic acid (anti-10o)**. The title compound was prepared according to general procedure 2 (0.9 mmol scale). The product was obtained as white solid, mp 236–237 °C (decomp.). Yield 208 mg, 52%.

1H NMR (400 MHz, DMSO-\textit{d}_6) \delta 13.64 (s, 1H), 8.38 (d, J=7.9, 1H), 7.77 (d, J=7.1, 1H), 7.50 (t, J=7.1, 1H), 7.37 – 7.31 (m, 2H), 7.30 – 7.21 (m, 2H), 7.19 – 7.06 (m, 2H), 6.77 (d, J=8.3, 2H), 5.26 (s, 1H), 2.04 (s, 3H), 1.47 (s, 3H), 1.15 (s, 3H); 13C NMR (101 MHz, DMSO-\textit{d}_6) \delta 172.0, 162.5, 141.0, 140.4, 136.7, 136.2, 136.0, 132.4, 129.7, 128.0, 127.9, 127.5, 127.0, 125.27, 124.7, 122.7, 114.7, 77.6, 53.0, 49.0, 28.6, 22.9, 20.2; HRMS (ESI) m/z [M+H]^+: Calcd for C_{26}H_{23}NO_3: 398.1751. Found: 398.1762.

11a,12,12-Trimethyl-11a,12-dihydroindolo[1,2-b]isoquinolin-6(11H)-one (14h). Compound \textit{anti/syn-10h} (93 mg, 0.29 mmol, 4.3:1) was dissolved in 1 mL of hexamethylphosphoramide and stirred at 205–210 °C for 1h in air. After complete consumption of starting material (controlled by TLC) the reaction mixture was diluted with 50 mL of EtOAc and washed with 5 \times 20 mL of water. The organic layer was washed with brine, dried over Na\textsubscript{2}SO\textsubscript{4} and concentrated under reduced pressure to give pure 14h (67 mg, 83%). Yellow oil. 1H NMR (400 MHz, DMSO-\textit{d}_6) \delta 8.22 (d, J=7.8, 1H), 8.03 (dd, J=7.6, 0.9, 1H), 7.56 (td, J=7.4, 1.3, 1H), 7.45 – 7.40 (m, 2H), 7.33 (dd, J=7.4, 0.8, 1H), 7.25 (td, J=7.8, 1.3, 1H), 7.12 (td, J=7.4, 1.0, 1H), 3.43 (d, J=15.6, 1H), 2.99 (d, J=15.7, 1H), 1.40 (s, 3H), 1.16 (s, 3H), 0.97 (s, 3H); 13C NMR (101 MHz, CDCl\textsubscript{3}) \delta 162.4, 140.4, 139.7, 137.1, 132.3, 129.3, 128.4, 128.3, 127.9, 127.2, 124.4, 121.9, 117.4, 69.2, 46.6, 34.3, 28.1, 20.9, 20.2; HRMS (ESI) m/z [M+H]^+: Calcd for C_{19}H_{19}NO: 278.1539. Found: 278.1537.
2. NMR studies for compounds 10d and 10e

In order to rationalize the inconsistency between $^3J_{HH}$-values and the value of dihedral angle in crystal form for compounds 10d and 10e we performed a series of NMR experiments. We reasoned that such a phenomenon could be explained by distorted molecular geometry (see section 5, crystallographic data) and different conformer population in the solution compared to solid state.

For compound 10e two sets of H-NMR spectra were recorded: at temperatures varying from 293 to 183 FIGURE K in Me$_2$CO-d$_6$ (mixture anti/syn 1:1; Figure S1) and from 293 to 393K in DMSO-d$_6$ (anti-10e; Figure S2). We observed decoalescence for the signals of $H^{11}$ and $H^{11a}$ atoms for both diastereomers at 223K (Figure S1) along with new set of signals arising: $\delta_H = 4.56$ and 4.42 ppm. It was not possible to identify these new signals by $^1$H-NMR spectrum only, due to their very low intensity, caused by small relative content of corresponding molecules. Nevertheless correlation spectroscopy provided some useful information about these sets of signals. COSY spectrum proved this pair of protons with chemical shifts 4.56 and 4.42 ppm to be a spin system (Figure S3). ROESY spectrum recorded for compound anti/syn-10e at 183K (Figure S4) revealed exchange cross-peaks between this new spin system and spin system of compound syn-10e ($\delta_H$ 4.94 and 4.59 ppm). In addition this ROESY spectrum demonstrated another two exchange cross-peaks ($\delta_H$ 5.08-4.72 and 4.80-4.51 ppm). The new signals ($\delta_H$ 5.08 and 4.80 ppm) exchanged with signals of anti-10e ($\delta_H$ 4.72 and 4.51 ppm). These facts may indicate that two new sets of signals observed at low temperatures belong to minor conformers of different isomers of 10e. In addition we observed variation in $J_{H11-H11a}$ coupling constant (anti-10e) from 2.6 to 0.7 Hz at temperature decrease (Figure S1) and from 2.9 to 3.7 Hz under heating (Figure S2). In the first case variation can be explained by increasing amount of major (thermodinamycally more stable) conformer with small $J$-value. Variation in the second case correlates with increasing amount of thermodinamycally less stable conformer with $J$-constant about 13 Hz, which is major conformer for all other cases (anti-
A similar series of NMR-experiments was carried out for compound *anti-10d* – H-NMR spectra were recorded from 292 to 182K in Me₂CO-\(d_6\) (Figure S5) and from 293 to 393K in DMSO-\(d_6\) (Figure S6). In this case \(J_{\text{H11-H11a}}\) coupling constant varied from 3.6 to 1.5 Hz under cooling and from 3.3 to 4.0 Hz under heating. \(J\)-values were obtained from \(J\)-resolved experiments.

**Table S1.** Measured dihedral angles for \(\text{C}^{11\text{H}}\)-\(\text{C}^{11\text{aH}}\) fragments for compounds 10 and corresponding \(^3J\)-coupling constants.

| Compound | Angle\(^a\) \(\text{C}^{11\text{H}}\)-\(\text{C}^{11\text{aH}}\), ° | \(J_{\text{C}^{11\text{H}}-\text{C}^{11\text{aH}}r}\), Hz | Compound | Angle\(^a\) \(\text{C}^{11\text{H}}\)-\(\text{C}^{11\text{aH}}\), ° | \(J_{\text{C}^{11\text{H}}-\text{C}^{11\text{aH}}r}\), Hz |
|----------|---------------------------------|----------------|----------|---------------------------------|----------------|
| ![Diagram](image1) | 168.7 | 13.0 | ![Diagram](image2) | 94.2 | 4.8 |
| ![Diagram](image3) | ND | 3.7 | ![Diagram](image4) | 166.7 | 2.6 |
| ![Diagram](image5) | 164.7 | 13.0 (12.9, for corresponding acid) | ![Diagram](image6) | 57.5 | 2.8 |
| ![Diagram](image7) | 58.1 | 3.2 (3.0, for corresponding acid) | ![Diagram](image8) | 169.3 | 3.3 |
| ![Diagram](image9) | 169.9 | 13.6 | ![Diagram](image10) | 171.6 | 12.9 (12.8, for corresponding acid) |
| ![Diagram](image11) | ND | 2.8 | ![Diagram](image12) | 55.5 | 2.9 (3.2, for corresponding acid) |
| ![Diagram](image13) | 170.3 | 12.9 | ![Diagram](image14) | ND | 3.3 |

\(^a\) Data obtained from X-ray single crystal analysis
**Figure S1:** Fragments of H-NMR spectra of compound 10e (anti/syn 1:1) at 293 K (top) – 183 K (bottom) in Me$_2$CO-$d_6$.

**Figure S2:** Fragments of H-NMR spectra of compound anti-10e at 393K (top) – 293K (bottom) in DMSO-$d_6$. 

$\delta$ 4.94 ppm

$\delta$ 4.72 ppm

$\delta$ 4.59 ppm

$\delta$ 4.51 ppm
Figure S3: Fragment of COSY spectrum for compound 10e (anti/syn 1:1) at 183K in Me₂CO-d₆
Figure S4: Fragment of ROESY spectrum for compound 10e (anti/syn 1:1) at 183K in Me$_2$CO-$d_6$ with different contour levels.
**Figure S5:** Fragments of H-NMR spectra of compound *anti-10d* at 293 K (top) – 183 K (bottom) in Me$_2$CO-$d_6$

**Figure S6:** Fragments of H-NMR spectra of compound *anti-10d* at 393 K (top) – 293K (bottom) in DMSO-$d_6$
3. Relative configuration determination for compounds 10k and 10m

$^{13}$C NMR spectra of 10h–k,m,n major isomers revealed chemical shifts of carbon atom in CH$_{3}^{11a}$-group to be about 16–17 ppm, while for minor isomers of 10h–k these chemical shifts lie within 23–24 ppm (Table S2). According to X-ray major isomers of 10h–i,n have anti-configuration. Thus the values of $^{13}$C chemical shifts of CH$_{3}^{11a}$-groups can serve as criterion for relative configuration assignment in CCR products 10, derived from 2-methylindolenines. The configuration of 10k and 10m major isomers was determined to be anti- according to this criterion: δC(CH$_{3}^{11a}$)= 17.1 and 15.7 ppm respectively.

![Chemical structures](image_url)

Table S2. $^{13}$C chemical shifts δ, ppm of C$^{11a}$-methyl group for compounds 10.

| Compound | δC$^{11a}$-Me (anti) | δC$^{11a}$-Me (syn) | Compound | δC$^{11a}$-Me (anti) | δC$^{11a}$-Me (syn) |
|----------|----------------------|---------------------|----------|----------------------|---------------------|
| 10h      | 17.2                 | 23.4                | 10k      | 17.1                 | 23.9                |
| 10i      | 17.7                 | 23.8                | 10n      | 16.2                 | -                   |
| 10j      | 17.4                 | 23.3                | 10m      | 15.7                 | -                   |

4. Relative configuration determination for compound 10o

Relative configuration of 11a-(p-tolyl)-substituted compound 10o was assigned to be (RS, SR)- on the basis of NOESY spectrum, which showed one cross peak from ortho-protons of p-tolyl moiety to methyl group in position 12 and another cross peak from H$^{11}$ to the second methyl group in position 12. The value of observed coupling constant between C$_{ipso}$(p-tolyl) and H$^{11}$ $^3$J$_{CH}$ 6.3 Hz also confirms this assignment (expected value of $^3$J$_{CH}$ for staggered conformation of C$_{ipso}Ar$–C$^{11a}$–C$^{11}$–H$^{11}$ fragment (anti-isomer) is 6-8 Hz and 1-3 Hz for gauche-conformation (syn-isomer); Figure S7–9) [11,12].
Figure S7 Measured coupling constants $J_{C\cdot H}^{11}$ for compound 10o.

Figure S8 Reported values of coupling constants $^3J_{C\cdot H}$ and $^2J_{C\cdot H}$ for systems with β-heteroatom.

Figure S9 Calculated dihedral angles (MM2; ChemBioOffice 2014) for anti- and syn-isomers of compound 10o.
5. Crystallographic data for compounds 10 and 13e.

X-ray single crystal analyses were performed on Agilent Technologies «Xcalibur» and «Supernova» diffractometers with monochromated Mo Kα or Cu Kα radiation, respectively. Crystals were measuring at the temperature of 100 K for all samples, except anti-10f', which destroyed at lower temperature. The structures has been solved by the Superflip [13] and ShelXS [14] structure solution programs using Charge Flipping and Direct Methods, respectively, and refined with the ShelXL [15] refinement incorporated in the OLEX2 program package [16]. The structure anti-10e' contains disordered DMSO on threefold axis. Electron density from this solvent has been suppressed using SQUEEZE/PLATON [17] program. CCDC 1503093-1503106, 1470399, 1470389, 1461790 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk.

| Table S3 Crystal data and structure refinement for anti-10e | Table S4 Crystal data and structure refinement for syn-10e |
|-------------------------------------------------------------|-------------------------------------------------------------|
| **Empirical formula** | C_{22}H_{19}ClNO_{3} | **Empirical formula** | C_{22}H_{19}ClNO_{3} |
| **Formula weight** | 416.28 | **Formula weight** | 416.28 |
| **Temperature/K** | 100(2) | **Temperature/K** | 100(2) |
| **Crystal system** | monoclinic | **Crystal system** | orthorhombic |
| **Space group** | P2_{1}/c | **Space group** | P2_{1}2_{1}2_{1} |
| **a/Å** | 15.7357(3) | **a/Å** | 15.7357(3) |
| **b/Å** | 6.94798(11) | **b/Å** | 12.2841(4) |
| **c/Å** | 17.1351(3) | **c/Å** | 15.4822(5) |
| **α/°** | 90 | **α/°** | 90 |
| **β/°** | 101.9535(17) | **β/°** | 90 |
| **γ/°** | 90 | **γ/°** | 90 |
| **Volume/Å^{3}** | 1832.78(5) | **Volume/Å^{3}** | 1876.88(11) |
| **Z** | 4 | **Z** | 4 |
| **ρ_{calc}/g/cm^{3}** | 1.509 | **ρ_{calc}/g/cm^{3}** | 1.473 |
| **μ/mm^{−1}** | 0.379 | **μ/mm^{−1}** | 0.370 |
| **F(000)** | 864.0 | **F(000)** | 864.0 |
| **Crystal size/mm^{3}** | 0.25×0.25×0.2 | **Crystal size/mm^{3}** | 0.25×0.25×0.2 |
| **Radiation** | MoKα (λ = 0.71073) | **Radiation** | MoKα (λ = 0.71073) |
| **2θ range for data** | 5.996 to 54.99 | **2θ range for data** | 5.914 to 54.99 |
| Collection/° | Collection/° |
|-------------|-------------|
| Index ranges | Index ranges |
| -20 ≤ h ≤ 20, -9 ≤ k ≤ 9, -22 ≤ l ≤ 22 | -12 ≤ h ≤ 11, -15 ≤ k ≤ 15, -20 ≤ l ≤ 20 |

| Reflections collected | 32039 | Reflections collected | 18673 |

| Independent reflections | 4193 [R_int = 0.0240, Rsigma = 0.0133] | Independent reflections | 4312 [R_int = 0.0274, Rsigma = 0.0240] |

| Data/restraints/parameters | 4193/0/254 | Data/restraints/parameters | 4312/0/254 |

| Goodness-of-fit on F² | 1.046 | Goodness-of-fit on F² | 1.047 |

| Final R indexes [I>=2σ(I)] | R₁ = 0.0340, wR₂ = 0.0841 | Final R indexes [I>=2σ(I)] | R₁ = 0.0265, wR₂ = 0.0647 |

| Final R indexes [all data] | R₁ = 0.0372, wR₂ = 0.0867 | Final R indexes [all data] | R₁ = 0.0288, wR₂ = 0.0664 |

| Largest diff. peak/hole / e Å⁻³ | 0.48/-0.22 | Largest diff. peak/hole / e Å⁻³ | 0.32/-0.19 |

| CCDC | 1503097 | CCDC | 1503105 |

Table S5 Crystal data and structure refinement for anti-10e'

| Empirical formula | C₂₃H₂₁Cl₂N₂O₃ | Empirical formula | C₂₂H₁₉Cl₂N₂O₃ |
|------------------|---------------|------------------|---------------|
| Formula weight   | 430.31        | Formula weight   | 416.28        |
| Temperature/K    | 100(2)        | Temperature/K    | 100(2)        |
| Crystal system   | trigonal      | Crystal system   | monoclinic    |
| Space group      | R3            | Space group      | P2₁/c         |
| a/Å             | 20.4043(3)    | a/Å             | 16.3985(8)    |
| b/Å             | 20.4043(3)    | b/Å             | 11.1961(6)    |
| c/Å             | 13.6622(2)    | c/Å             | 10.3370(5)    |
| α/°             | 90            | α/°             | 90            |
| β/°             | 90            | β/°             | 96.103(5)     |
| γ/°             | 120           | γ/°             | 90            |
| Volume/Å³       | 4926.02(15)   | Volume/Å³       | 1887.11(16)   |
| Z                | 9             | Z                | 4             |
| ρ_cal,g/cm³     | 1.305         | ρ_cal,g/cm³     | 1.465         |
| μ/mm⁻¹          | 2.859         | μ/mm⁻¹          | 3.297         |
| F(000)          | 2016.0        | F(000)          | 864.0         |
| Crystal size/mm³| 0.3 × 0.2 × 0.2| Crystal size/mm³| 0.2 × 0.08 × 0.08 |
| Radiation       | CuKα (λ = 1.54184) | Radiation | CuKα (λ = 1.54184) |
| 2Θ range for data collection/° | 8.18 to 144.976 | 2Θ range for data collection/° | 9.582 to 144.898 |
| Index ranges    | -25 ≤ h ≤ 25, -22 ≤ k ≤ 25, | Index ranges    | -20 ≤ h ≤ 20, -13 ≤ k |

Table S6 Crystal data and structure refinement for 13e

| Empirical formula | C₂₂H₁₉Cl₂N₂O₃ | Empirical formula | C₂₂H₁₉Cl₂N₂O₃ |
|------------------|---------------|------------------|---------------|
| Formula weight   | 430.31        | Formula weight   | 416.28        |
| Temperature/K    | 100(2)        | Temperature/K    | 100(2)        |
| Crystal system   | trigonal      | Crystal system   | monoclinic    |
| Space group      | R3            | Space group      | P2₁/c         |
| a/Å             | 20.4043(3)    | a/Å             | 16.3985(8)    |
| b/Å             | 20.4043(3)    | b/Å             | 11.1961(6)    |
| c/Å             | 13.6622(2)    | c/Å             | 10.3370(5)    |
| α/°             | 90            | α/°             | 90            |
| β/°             | 90            | β/°             | 96.103(5)     |
| γ/°             | 120           | γ/°             | 90            |
| Volume/Å³       | 4926.02(15)   | Volume/Å³       | 1887.11(16)   |
| Z                | 9             | Z                | 4             |
| ρ_cal,g/cm³     | 1.305         | ρ_cal,g/cm³     | 1.465         |
| μ/mm⁻¹          | 2.859         | μ/mm⁻¹          | 3.297         |
| F(000)          | 2016.0        | F(000)          | 864.0         |
| Crystal size/mm³| 0.3 × 0.2 × 0.2| Crystal size/mm³| 0.2 × 0.08 × 0.08 |
| Radiation       | CuKα (λ = 1.54184) | Radiation | CuKα (λ = 1.54184) |
| 2Θ range for data collection/° | 8.18 to 144.976 | 2Θ range for data collection/° | 9.582 to 144.898 |
| Index ranges    | -25 ≤ h ≤ 25, -22 ≤ k ≤ 25, | Index ranges    | -20 ≤ h ≤ 20, -13 ≤ k |
Crystal structure determination of *anti*-10n

**Crystal Data** for C<sub>23</sub>H<sub>23</sub>NO<sub>3</sub> (M =361.42 g/mol): monoclinic, space group C2/c (no. 15), a = 23.3057(6) Å, b = 12.7914(3) Å, c = 16.7508(4) Å, β = 133.0560(10)°, V = 3648.77(16) Å<sup>3</sup>, Z = 8, T = 100(2) K, μ(MoKα) = 0.087 mm<sup>-1</sup>, Deacal = 1.316 g/cm<sup>3</sup>, 30249 reflections measured (6.15° ≤ 2Θ ≤ 54.996°), 4190 unique (R<sub>int</sub> = 0.0207, R<sub>sigma</sub> = 0.0109) which were used in all calculations. The final R<sub>1</sub> was 0.0366 (I > 2σ(I)) and wR<sub>2</sub> was 0.0998 (all data).

CCDC 1503103

Crystal structure determination of *syn*-10a'

**Crystal Data** for C<sub>23</sub>H<sub>23</sub>NO<sub>3</sub> (M =361.42 g/mol): triclinic, space group P-1 (no. 2), a = 11.5749(2) Å, b = 12.2804(4) Å, c = 13.7928(4) Å, α = 68.362(3)°, β = 88.617(2)°, γ = 81.872(2)°, V = 1803.27(9) Å<sup>3</sup>, Z = 4, T = 100(2) K, μ(CuKα) = 0.703 mm<sup>-1</sup>, Deacal = 1.331 g/cm<sup>3</sup>, 51248 reflections measured (6.898° ≤ 2Θ ≤ 152.6°), 7555 unique (R<sub>int</sub> = 0.0531, R<sub>sigma</sub> = 0.0235) which were used in all calculations. The final R<sub>1</sub> was 0.0374 (I > 2σ(I)) and wR<sub>2</sub> was 0.0977 (all data).

CCDC 1503100

Crystal structure determination of *anti*-10g'

**Crystal Data** for C<sub>20</sub>H<sub>19</sub>NO<sub>3</sub> (M =321.36 g/mol): monoclinic, space group Cc (no. 9), a = 17.7696(7) Å, b = 13.3575(5) Å, c = 7.1549(3) Å, β = 109.373(2)°, V = 1602.12(11) Å<sup>3</sup>, Z = 4, T = 100(2) K, μ(MoKα) = 0.090 mm<sup>-1</sup>, Deacal = 1.332 g/cm<sup>3</sup>, 7519 reflections measured (6.1° ≤ 2Θ ≤ 54.986°), 3473 unique (R<sub>int</sub> = 0.0281, R<sub>sigma</sub> = 0.0387) which were used in all calculations. The final R<sub>1</sub> was 0.0370 (I > 2σ(I)) and wR<sub>2</sub> was 0.0926 (all data).

CCDC 1503096
Crystal structure determination of anti-10l

**Crystal Data** for C$_{22}$H$_{21}$NO$_3$ (M = 347.40 g/mol): monoclinic, space group C2/c (no. 15), a = 22.5031(6) Å, b = 13.5761(4) Å, c = 14.7923(4) Å, β = 129.571(2)°, V = 3483.49(18) Å$^3$, Z = 8, T = 100(2) K, μ(MoKα) = 0.088 mm$^{-1}$, D$_{calc}$ = 1.325 g/cm$^3$, 29448 reflections measured (5.51° ≤ 2Θ ≤ 54.998°), 4001 unique (R$_{int}$ = 0.0713, R$_{sigma}$ = 0.0318) which were used in all calculations. The final R$_1$ was 0.0410 (I > 2σ(I)) and wR$_2$ was 0.1107 (all data).

CCDC 1503106

Crystal structure determination of anti-10i

**Crystal Data** for C$_{21}$H$_{20}$FNO$_3$ (M = 353.38 g/mol): monoclinic, space group C2/c (no. 15), a = 26.5832(15) Å, b = 6.7549(2) Å, c = 21.1207(8) Å, β = 115.042(3)°, V = 3436.1(3) Å$^3$, Z = 8, T = 100(2) K, μ(MoKα) = 0.098 mm$^{-1}$, D$_{calc}$ = 1.366 g/cm$^3$, 15007 reflections measured (6.264° ≤ 2Θ ≤ 54.994°), 3943 unique (R$_{int}$ = 0.0255, R$_{sigma}$ = 0.0244) which were used in all calculations. The final R$_1$ was 0.0371 (I > 2σ(I)) and wR$_2$ was 0.0945 (all data).

CCDC 1503104

Crystal structure determination of syn-10f

**Crystal Data** for C$_{23}$H$_{24}$N$_2$O$_5$S (M = 440.50 g/mol): monoclinic, space group P2$_1$/c (no. 14), a = 11.2258(2) Å, b = 9.78991(18) Å, c = 19.3208(3) Å, β = 103.8379(19)°, V = 2061.71(7) Å$^3$, Z = 4, T = 100(2) K, μ(CuKα) = 1.730 mm$^{-1}$, D$_{calc}$ = 1.419 g/cm$^3$, 14079 reflections measured (8.112° ≤ 2Θ ≤ 139.968°), 3904 unique (R$_{int}$ = 0.0260, R$_{sigma}$ = 0.0217) which were used in all calculations. The final R$_1$ was 0.0411 (I > 2σ(I)) and wR$_2$ was 0.1052 (all data).

CCDC 1503101

Crystal structure determination of anti-10a'

**Crystal Data** for C$_{23}$H$_{23}$NO$_3$ (M = 361.42 g/mol): monoclinic, space group Cc (no. 9), a = 19.3213(7) Å, b = 13.2486(4) Å, c = 7.3482(2) Å, β = 109.212(3)°, V = 1776.24(10) Å$^3$, Z = 4, T = 100(2) K, μ(CuKα) = 0.713 mm$^{-1}$, D$_{calc}$ = 1.352 g/cm$^3$, 12942 reflections measured (8.248° ≤ 2Θ ≤ 144.844°), 2996 unique (R$_{int}$ = 0.0456, R$_{sigma}$ = 0.0265) which were used in all calculations. The final R$_1$ was 0.0353 (I > 2σ(I)) and wR$_2$ was 0.0945 (all data).

CCDC 1503098
Crystal structure determination of **anti-10c**

**Crystal Data** for C$_{22}$H$_{20}$FNO$_3$ (M = 365.39 g/mol): monoclinic, space group C2/c (no. 15), $a = 22.2110(8) \text{ Å}$, $b = 13.4818(4) \text{ Å}$, $c = 15.1581(6) \text{ Å}$, $\beta = 131.494(2)^\circ$, $V = 3399.8(2) \text{ Å}^3$, $Z = 8$, $T = 100(2) \text{ K}$, $\mu(\text{MoK} \alpha) = 0.102 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.428 \text{ g/cm}^3$, 15635 reflections measured (6.044° ≤ 2Θ ≤ 54.966°), 3905 unique ($R_{int} = 0.0254$, $R_{sigma} = 0.0218$) which were used in all calculations. The final $R_1$ was 0.0443 (I > 2σ(I)) and $wR_2$ was 0.1214 (all data).

CCDC 1503094

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Crystal structure determination of **anti-10f**

**Crystal Data** for C$_{23}$H$_{24}$N$_2$O$_5$S (M = 440.50 g/mol): monoclinic, space group P2$_1$/c (no. 14), $a = 14.5219(6) \text{ Å}$, $b = 14.0079(4) \text{ Å}$, $c = 10.9021(4) \text{ Å}$, $\beta = 109.892(4)^\circ$, $V = 2085.39(13) \text{ Å}^3$, $Z = 4$, $T = 200(2) \text{ K}$, $\mu(\text{MoK} \alpha) = 0.194 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.403 \text{ g/cm}^3$, 26903 reflections measured (5.966° ≤ 2Θ ≤ 54.998°), 4782 unique ($R_{int} = 0.0229$, $R_{sigma} = 0.0173$) which were used in all calculations. The final $R_1$ was 0.0370 (I > 2σ(I)) and $wR_2$ was 0.0989 (all data).

CCDC 1503099

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Crystal structure determination of **anti-10d**

**Crystal Data** for C$_{23}$H$_{23}$NO$_3$ (M = 361.42 g/mol): orthorhombic, space group P2$_1$2$_1$2$_1$ (no. 19), $a = 7.2945(3) \text{ Å}$, $b = 14.2074(6) \text{ Å}$, $c = 17.4589(7) \text{ Å}$, $V = 1809.36(13) \text{ Å}^3$, $Z = 4$, $T = 100(2) \text{ K}$, $\mu(\text{MoK} \alpha) = 0.088 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.327 \text{ g/cm}^3$, 14046 reflections measured (5.478° ≤ 2Θ ≤ 54.994°), 4173 unique ($R_{int} = 0.0229$, $R_{sigma} = 0.0173$) which were used in all calculations. The final $R_1$ was 0.0399 (I > 2σ(I)) and $wR_2$ was 0.0869 (all data).

CCDC 1503095

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Crystal structure determination of **anti-10h**

**Crystal Data** for C$_{20}$H$_{19}$NO$_3$ (M = 321.36 g/mol): orthorhombic, space group Pbca (no. 61), $a = 14.9929(3) \text{ Å}$, $b = 12.2708(3) \text{ Å}$, $c = 16.6823(4) \text{ Å}$, $V = 3069.13(12) \text{ Å}^3$, $Z = 8$, $T = 100(2) \text{ K}$, $\mu(\text{CuK} \alpha) = 0.755 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.391 \text{ g/cm}^3$, 21935 reflections measured (10.606° ≤ 2Θ ≤ 144.948°), 2942 unique ($R_{int} = 0.0610$, $R_{sigma} = 0.0353$) which were used in all calculations. The final $R_1$ was 0.0507 (I > 2σ(I)) and $wR_2$ was 0.1481 (all data).

CCDC 1470389
Crystal structure determination of *anti*-10b

**Crystal Data** for C_{23}H_{23}NO_{3} (M = 361.42 g/mol): monoclinic, space group P2_1/n (no. 14), a = 9.2717(2) Å, b = 11.18826(19) Å, c = 17.5072(4) Å, β = 105.013(2)°, V = 1754.11(7) Å³, Z = 4, T = 100(2) K, μ(CuKα) = 0.722 mm⁻¹, Dcalc = 1.369 g/cm³, 9756 reflections measured (9.478° ≤ 2Θ ≤ 144.978°), 3397 unique (Rint = 0.0237, Rsigma = 0.0205) which were used in all calculations. The final R₁ was 0.0516 (I > 2σ(I)) and wR₂ was 0.1243 (all data).

CCDC 1470399

Crystal structure determination of *anti*-10j

**Crystal Data** for C_{20}H_{18}N_{2}O_{5} (M = 366.36 g/mol): monoclinic, space group P2_1/c (no. 14), a = 8.8454(3) Å, b = 14.1900(4) Å, c = 13.5995(4) Å, β = 104.646(3)°, V = 1651.50(9) Å³, Z = 4, T = 100(2) K, μ(MoKα) = 0.107 mm⁻¹, Dcalc = 1.473 g/cm³, 14296 reflections measured (5.558° ≤ 2Θ ≤ 54.998°), 3807 unique (Rint = 0.0259, Rsigma = 0.0249) which were used in all calculations. The final R₁ was 0.0398 (I > 2σ(I)) and wR₂ was 0.1001 (all data).

CCDC 1461790

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7. Copies of $^1$H and $^{13}$C NMR spectra of compounds 9 and 10
anti-10m

anti-10m
