Supplemental Information

Construction of poly-N-heterocyclic scaffolds via the controlled reactivity of Cu-allenylidene intermediates

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Supplementary Methods

1. General information

All reactions were performed in oven-dried glassware under a positive pressure of nitrogen or argon. Solvents were transferred via syringe and were introduced into the reaction vessels through a rubber septum. All solvents were dried by standard method. All of the reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica gel (60-F254). The TLC plates were visualized with UV light. All of the reaction products were purified by column chromatography and was carried out on a column packed with silica gel 60N spherical neutral size 50-63 mm. The \(^1\)H NMR (300 MHz and 500 MHz) and \(^1^9\)F NMR (282 MHz) spectra (with hexafluorobenzene (δ ppm -162.2) as an internal standard) as for solution in CDCl\(_3\) and DMSO were recorded on a Varian Mercury 300 and BRUKER 500 Ultra Shield TR. \(^1^3\)C NMR (126 MHz) spectra for solution in CDCl\(_3\) was recorded on a BRUKER 500 Ultra Shield TR. The chemical shifts (δ) are expressed in ppm downfield from internal TMS (δ = 0.00) and coupling constants (J) are reported in hertz (Hz). The hexafluorobenzene (C\(_6\)F\(_6\)) [δ = -162.2 (CDCl\(_3\))] was used as internal standard for \(^1^9\)F NMR. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Mass spectra were recorded on a SHIMADZU GCMS-QP5050A (EI-MS) and SHIMADZU LCMS-2020 (ESI-MS). High resolution mass spectrometry (HRMS) was carried out on an electron impact ionization mass spectrometer with a micro-TOF analyzer. Infrared spectra were recorded on a JASCO FT/IR-4100 spectrometer. Melting points were recorded on a BUCHI M-565. Optical rotations were measured on a SEPA-300 instrument (HORIBA Ltd, Kyoto, Japan). HPLC analyses were performed on a JASCOLC-2000 Plus series using 4.6 x 250 mm CHIRALPAK series. Commercially available chemicals were obtained from Aldrich Chemical Co., Alfa Aesar, TCI and used as received unless otherwise noted. Solvents acetonitrile, ethyl acetate, ethanol, Dioxane, DMF, DCM, THF and Toluene were dried and distilled before use.
2. Supplementary details for condition optimization

Supplementary Table 1. Ligand effects for copper-catalyzed annulation. $^a$

| Entry | Ligand   | $\text{dr}^b$ | Yield (%)$^b$ | ee (%)$^c$ |
|-------|----------|--------------|--------------|------------|
| 1     | L1       | $>95:5$      | 47           | 15         |
| 2     | L2       | $>99:1$      | 70           | 96         |
| 3     | L3       | -            | 28           | -          |
| 4     | L4       | $>95:5$      | 32           | 75         |
| 5     | L5       | -            | Trace        | -          |
| 6     | L6       | -            | 14           | -          |
| 7     | $R,R$-DBFOX/Ph | -     | Trace        | -          |
| 8     | (R)-BINAP | -            | NR           | -          |

$^a$ Reactions were carried out with 1a (0.1 mmol), 2a (0.1 mmol), CuOTf.1/2C$_6$H$_6$ (10 mol%), ligand (20 mol%), i-Pr$_2$NEt (DIPEA, 2.4 equiv) in Toluene at room temperature.

$^b$ Determined by $^{19}$F NMR analysis of the reaction mixture.

$^c$ The ee was determined by chiral HPLC analysis.
### Supplementary Table 2. Solvent effects for copper-catalyzed annulation. \(^a\)

| Entry | Solvent | dr\(^b\) | Yield (%\(^b\)) | ee (%\(^c\)) |
|-------|---------|----------|-----------------|-------------|
| 1     | Toluene | >99:1    | 70              | 96          |
| 2     | THF     | >99:1    | 65              | 96          |
| 3     | ACN     | >99:1    | 36              | 25          |
| 4     | DCM     | >99:1    | 42              | 25          |
| 5     | Xylene  | >99:1    | 68              | 96          |
| 6     | EA      | >99:1    | 58              | 96          |

\(^a\) Reactions were carried out with 1a (0.1 mmol), 2a (0.1 mmol), CuOTf.\(1/2\)C\(_6\)H\(_6\) (10 mol\%), L\(_2\) (20 mol\%), \(i\)-Pr\(_2\)NEt (DIPEA, 2.4 equiv) in solvent at room temperature.

\(^b\) Determined by \(^{19}\)F NMR analysis of the reaction mixture.

\(^c\) The ee was determined by chiral HPLC analysis.

### Supplementary Table 3. Screen of Cu salts for copper-catalyzed annulation. \(^a\)

| Entry | Copper salt | dr\(^b\) | Yield (%\(^b\)) | ee (%\(^c\)) |
|-------|-------------|----------|-----------------|-------------|
| 1     | CuOTf.\(1/2\)C\(_6\)H\(_6\) | >99:1    | 70              | 96          |
| 2     | Cu(OTf)_2   | >99:1    | 71              | 99          |
| 3     | CuOTf-Toluene | >99:1    | 69              | 99          |
| 4     | CuI         | -        | 21              | -           |
| 5\(^d\) | Cu(OTf)_2   | >99:1    | 68              | 98          |

\(^a\) Reactions were carried out with 1a (0.1 mmol), 2a (0.1 mmol), Cu salt (10 mol\%), L\(_2\) (20 mol\%), \(i\)-Pr\(_2\)NEt (DIPEA, 2.4 equiv) in Toluene at room temperature.

\(^b\) Determined by \(^{19}\)F NMR analysis of the reaction mixture.

\(^c\) The ee was determined by chiral HPLC analysis.

\(^d\) Using Cu salt (5 mol\%), L\(_2\) (10 mol\%).
**Supplementary Table 4. Substrate ratio effects for copper-catalyzed annulation.**

| Entry | 2a (eq mol) | dr\(^b\) | Yield (%)\(^b\) | ee (%)\(^c\) |
|-------|-------------|--------|----------------|--------|
| 1     | 1.0         | >99:1  | 68             | 98     |
| 2     | 1.1         | >99:1  | 71             | 98     |
| 3     | 1.2         | >99:1  | 65             | 98     |
| 4     | 1.5         | >99:1  | 67             | 98     |

\(^a\) Reactions were carried out with 1a (0.1 mmol), 2a, Cu(OTf)_2 (5 mol%), L2 (10 mol%), i-Pr_2NET (DIPEA, 2.4 equiv) in Toluene at room temperature.  
\(^b\) Determined by $^{19}$F NMR analysis of the reaction mixture.  
\(^c\) The ee was determined by chiral HPLC analysis.

**Supplementary Table 5. Base effect for copper-catalyzed annulation.**

| Entry | Base                | Ratio | dr\(^b\) | Yield (%)\(^c\) | ee (%)\(^d\) |
|-------|---------------------|-------|--------|----------------|--------|
| 1     | DIPEA               | 2.4   | >99:1  | 71             | 98     |
| 2     | DIPEA               | 1.2   | >99:1  | 77             | 98     |
| 3     | DIPEA               | 0.5   | >99:1  | **88**         | **98** |
| 4     | DIPEA               | 0.3   | >99:1  | 79             | 97     |
| 5     | DIPEA               | 0.15  | >99:1  | 40             | 95     |
| 6\(^d\) | -                  | -     | -     | NR             | -      |
| 7     | TEA                 | 0.5   | >99:1  | 63             | 98     |
| 8     | N-Ethylmorpholine   | 0.5   | >99:1  | 70             | 98     |
| 9     | K_2CO_3             | 0.5   | -     | 24             | -      |

\(^a\) Reactions were carried out with 1a (0.1 mmol), 2a (0.11 mmol), Cu(OTf)_2 (5 mol%), L2 (10 mol%), Base in Toluene at room temperature.  
\(^b\) Determined by $^{19}$F NMR analysis of the reaction mixture.  
\(^c\) The ee was determined by chiral HPLC analysis.  
\(^d\) No base was used.
Supplementary Table 6. Temperature effects for copper-catalyzed annulation. $^a$

| Entry | Temp (°C) | Time (h) | dr$^b$ | Yield (%)$^c$ | ee (%)$^d$ |
|-------|-----------|----------|--------|--------------|----------|
| 1     | 40        | 12       | >99:1  | 78           | 95       |
| 2     | R.T.      | 12       | >99:1  | 88           | 98       |
| 3     | 0         | 24       | >99:1  | 73           | >99      |
| 4     | 10        | 16       | >99:1  | 94           | >99      |

$^a$ Reactions were carried out with 1a (0.1 mmol), 2a (0.11 mmol), Cu(OTf)$_2$ (5 mol%), L2 (10 mol%), i-Pr$_2$NEt (DIPEA, 0.5 equiv.) in Toluene.

$^b$ Determined by $^{19}$F NMR analysis of the reaction mixture.

$^c$ The ee was determined by chiral HPLC analysis.

Supplementary Table 7. The screening of ligand for the transformation of 4a to 5a

| Ligand | Ratio | ee (%) |
|--------|-------|--------|
| L2     | 71%   | (racemic)  
2C:3C = 85:15 |
| Xphos  | N.R.  | 66%    
2C:3C = 88:12 |
| dppe   | N.R.  | 66%    
2C:3C = 88:12 |
| dppp   | N.R.  | 66%    
2C:3C = 88:12 |
| (R)-BINAP | 40% (racemic)  
2C:3C = 85:15 |
3. General experimental procedures for the synthesis of starting materials.

CF$_3$-Benzoazinanone (1),$^1$ Me-benzoazinanone (4)$^1$ and benzoazinanone$^2$ were prepared according to literature.

3.1 Synthesis of substituted ethynyl benzoazinanones (1a-1f) (Method A)

Benzoazinanones (1a-1e) were prepared according to literature$^1$. Overall reaction scheme for the synthesis of 6-methyl-4-trifluoromethyl ethynyl benzoazinanones (1f) is showing below.

Synthesis of 6-Methyl-4-((trifluoromethyl)-4-((triisopropylsilyl)ethynyl)-1,4-dihydro-2H-benzo[|][1,3]oxazin-2-one (S3f):

Under N$_2$ atmosphere, in a flame dried 20 mL round bottom flask, triisopropylethynylsilane (5.50 mmol, 5.0 equiv) and ethylmagnesium bromide (1.0 M in THF, 5.50 mol, 5.0 equiv) was stirred for 1 h at 0 ºC. To this solution a THF (5 mL) solution of S1f (1.1 mmol, 1.0 equiv) was added dropwise and the mixture was allowed to stir for 2 h at 0 ºC. After that, the reaction mixture was quenched by NH$_4$Cl aqueous solution followed by extraction with ethyl acetate (3 × 10 mL). Combined organic layers were finally washed with brine solution, dried over anhydrous Na$_2$SO$_4$ and then solvent was removed under reduced pressure. In a flame dried 30 mL round bottom flask, the crude product S2f, and dry THF (11 mL) were added. To this suspension carbonyldiimidazole (CDI) (5.5 mmol, 5.0 equiv) was added and the mixture was heated to 50 ºC for 12 h. After that, the reaction mixture was added NH$_3$ aqueous solution followed by extraction with DCM (3 × 10 mL). Combined organic layers were finally washed with brine solution, dried over anhydrous Na$_2$SO$_4$ and then solvent was removed under reduced pressure. The crude product was purified by
flash column chromatography (using 8:2 hexane/ethyl acetate) to obtain the pure product S3f as a white solid (359 mg, yield: 79% in two steps), m.p. = 153.7 – 154.7 °C. 1H NMR (500 MHz, CDCl3) δ 8.95 (s, 1H), 7.37 (s, 1H), 7.19 (m, 1H), 6.78 (d, J = 10.0 Hz, 1H), 2.34 (s, 3H), 1.11 – 1.15 (m, 21H). 13C NMR (126 MHz, CDCl3) δ 149.2, 133.7, 132.3, 132.2, 128.4, 122.3 (q, J = 287.6 Hz), 114.7, 113.0, 97.1, 93.9, 79.3 (q, J = 34.5 Hz), 20.8, 18.4, 10.9. 19F NMR (282 MHz, CDCl3) δ −81.5 (s, 3F). IR (KBr): 3158, 2948, 1727, 1617, 1515, 1346, 1251, 1189, 1170, 1045, 883, 819 cm⁻¹. HRMS (ESI) calculated for C21H28F3NO2NaSi [M+Na]⁺: 434.1739, found: 434.1726.

Synthesis of 4-ethynyl-6-methyl-4-(trifluoromethyl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one (S4f):

In 25 mL round bottom flask, compound S3f (0.83 mmol, 1.0 equiv) and THF (5 mL) was stirred at 0 °C, and TBAF solution (1.0 M in THF, 1.25 mmol, 1.5 equiv) was added dropwise. The reaction completed in 10 min by TLC followed by extraction with ethyl acetate (3 × 10 mL). Combined organic layers were finally washed with brine solution, dried over anhydrous Na2SO4 and then solvent was removed under reduced pressure. The crude product was washed by pentane to obtain the pure product S4f. Compound S4f was obtained as a white solid (228.9 mg, Yield: 97%), m.p. = 156.8 – 157.8 °C. 1H NMR (500 MHz, CDCl3) δ 8.73 (s, 1H), 7.33 (s, 1H), 7.20 (d, J = 7.9 Hz, 1H), 6.94 (d, J = 7.9 Hz, 1H), 2.94 (s, 1H), 2.36 (s, 3H). 13C NMR (126 MHz, CDCl3) δ 147.7, 133.7, 132.5, 132.4, 127.8, 122.2 (q, J = 287.0 Hz), 115.0, 112.2, 78.3, 75.2, 20.3. 19F NMR (282 MHz, CDCl3) δ −81.4 (s, 3F). IR (KBr): 3280, 2967, 2136, 2095, 1739, 1617, 1517, 1344, 1251, 1170, 1085, 827 cm⁻¹. HRMS (ESI) calculated for C12H8F3NO2Na [M+Na]⁺: 278.0405, found: 278.0403.

Synthesis of 4-ethynyl-6-methyl-1-tosyl-4-(trifluoromethyl)-1,4-dihydro-2H-benzo[d][1,3] oxazin-2-one (1f):
In a flame dried 100 mL round bottom flask, compound S4f (2 mmol, 1.0 equiv) was suspended in dry DMF (6 mL) and allowed to cool to 0 °C. To this solution NaH (60% dispersion in mineral oil, 3 mmol, 1.5 equiv) was added and the mixture was allowed to stir for 30 min under N2 atmosphere. After 30 min, the solution of p-toluenesulfonyl chloride (2.2 mmol, 1.1 equiv) in dry DMF (3 mL) was added dropwise to the reaction mixture and stirred the reaction mixture at 0 °C until completion of the reaction. After that, the reaction mixture was poured into crushed ice followed by extraction with ethyl acetate (3 × 30 mL). Combined organic layers were finally washed with brine solution, dried over anhydrous Na2SO4 and then solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (using 9:1 hexane/ethyl acetate) to obtain the pure product 1f. Compound 1f was obtained as a white solid (99 mg, Yield: 30%), m.p. = 158.1 – 159.1 °C. 1H NMR (500 MHz, CDCl3) δ 8.06 (d, J = 8.5 Hz, 2H), 7.64 (d, J = 8.5 Hz, 1H), 7.42 (s, 1H), 7.38 (d, J = 7.9 Hz, 2H), 7.34 – 7.36 (m, 1H), 2.93 (s, 1H), 2.47 (s, 3H), 2.42 (s, 3H). 13C NMR (126 MHz, CDCl3) δ 146.2, 145.4, 136.6, 134.8, 131.8, 131.2, 129.6, 129.5, 127.2, 121.5 (q, J = 287.0 Hz), 120.9, 118.9, 88.2, 77.8 (q, J = 35.4 Hz), 74.1, 21.8, 20.9. 19F NMR (282 MHz, CDCl3) δ −78.5 (s, 3F). IR (KBr): 3274, 2929, 2136, 1758, 1594, 1502, 1216, 1081, 968, 935, 817, 665 cm−1. HRMS (ESI) calculated for C19H14F3NO4NaS [M+Na]+: 432.0493, found: 432.0492.

3.2 Synthesis of substituted benzoxathiazine (2a-2e, 2g-2j) (Method B)

Benzoxathiazine (2a-2e, 2g-2j) were prepared according to literature3, 4. Overall reaction scheme for the synthesis of substituted benzoxathiazine (2a-2e, 2g-2j) is showing below.

Anhydrous magnesium chloride (7.5 mmol, 1.5 equiv) was dried further by heating under vacuum. To this THF (20 mL), substituted-phenol (5.0 mmol, 1.0 equiv), triethylamine (12.5 mmol, 2.5
equiv) and paraformaldehyde (22.5 mmol, 4.5 equiv) were added at room temperature. The mixture was heated to reflux for 18 h after which the reaction was quenched via the slow addition of HCl (2M, 12 mL). The reaction was extracted with ethyl acetate, dried over anhydrous Na₂SO₄ and then solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (using 8:2 hexane/ethyl acetate) to obtain the pure product **S5**.

Anhydrous formic acid (11.6 mmol, 2.7 equiv) was added dropwise to neat chlorosulfonyl isocyanate (11.6 mmol, 2.7 equiv) at 0 °C with rapid stirring. The resulting viscous suspension was stirred at 0 °C for 1 h and afforded the ClSO₂NH₂. To a solution of **S5** (4.3 mmol, 1.0 equiv) in DMA (29 mL) at 0 °C was carefully added freshly prepared ClSO₂NH₂ in small portions and the resulting solution was stirred at room temperature for 24 h. The reaction was quenched carefully with ice-cold water and the mixture was transferred to a separating funnel containing CH₂Cl₂. The aqueous layer was separated and extracted with CH₂Cl₂, and the combined organic layers were washed with saturated NaHCO₃ aqueous solution, dried over MgSO₄, filtered through a short pad of silica using CH₂Cl₂ as eluent and concentrated in vacuum. The residue was purified via flash column chromatography on silica gel (using 8:2 hexane/ethyl acetate) to obtain the pure product **2**.

3.3 Synthesis of 5-nitrobenzoxathiazine (2f) (Method C)

5-nitrobenzoxathiazine (2f) were prepared according to literature⁴⁻⁵. Overall reaction scheme for the synthesis of 2f is showing below.

A mixture of 4-nitrophenol (5.0 mmol, 1.0 equiv), hexamethylenetetramine (6.5 mmol, 1.3 equiv) in trifluoroacetic acid (5.8 mL) was heated at 85 °C for 15 h. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The mixture was diluted with H₂O and then neutralized with Na₂CO₃ to pH 5. The precipitate formed was collected by filtration, washed with water and dried to afford the pure product **S5f** as a yellow solid.
Anhydrous formic acid (11.6 mmol, 2.7 equiv) was added dropwise to neat chlorosulfonyl isocyanate (11.6 mmol, 2.7 equiv) at 0 °C with rapid stirring. The resulting viscous suspension was stirred at 0 °C for 1 h and afforded the ClSO₂NH₂. To a solution of S5f (4.3 mmol, 1.0 equiv) in DMA (29 mL) at 0 °C was carefully added freshly prepared ClSO₂NH₂ in small portions and the resulting solution was stirred at room temperature for 24 h. The reaction was quenched carefully with ice-cold water and the mixture was transferred to a separating funnel containing CH₂Cl₂. The aqueous layer was separated and extracted with CH₂Cl₂, and the combined organic layers were washed with saturated NaHCO₃ aqueous solution, dried over MgSO₄, filtered through a short pad of silica using CH₂Cl₂ as eluent and concentrated in vacuum. The residue was purified via flash column chromatography on silica gel (using 8:2 hexane/ethyl acetate) to obtain the pure product 2f as a white solid.
4. General Procedure and Spectral Data of Products

4.1 General Procedure for the asymmetric annulation reaction (Method D)

In an argon filled glove box, a flame-dried 10 mL Schlenk tube was charged with copper(II) trifluoromethanesulfonate (1.81 mg, 0.05 mmol, 5 mol%), 2,6-bis[(4R)-phenyl-2-oxazolin-2-yl]-pyridine L2 (3.69 mg, 0.01 mmol, 10 mol%) and anhydrous Toluene (1 mL). The resulting solution was stirred for 1 h at 80 °C. In an argon filled glove box, ethynyl benzoxazinanones 1 (0.1 mmol), benzoxathiazine 2 (0.11 mmol) and DIPEA (8.7 μL, 0.05 mmol, 0.5 equiv) were added. The resulting solution was stirred at 10 °C until complete conversion of ethynyl benzoxazinanones (monitored by TLC). The reaction was quenched by saturated NH₄Cl aqueous solution (2 mL). The resulting solution was extracted with ethyl acetate (5 mL × 3). The combined organic layers were dried over Na₂SO₄, filtered and concentrated under vacuum. The diastereomeric ratio and crude yield were determined by ¹⁹F NMR analysis of the crude reaction mixture. The residue was purified by flash silica gel chromatography (Toluene) to afford the title compound 3. The characterization data of 3 are summarized below.

4.2 Characterization data of product

(13bS,13cR)-9-Tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5′,6′][1,2,3]oxathiazino[3′,4′:1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3aa):

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Following the general method D, compound 3aa was obtained as a white solid (90.8 mg, Yield: 85%), m.p. = 113.4 – 114.4 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 15.458 min, t (minor) = 30.608 min. [α]$_D^{25}$ = -113.1 (c = 0.2, CHCl$_3$, 99% ee). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.78 – 7.80 (m, 3H), 7.44 – 7.50 (m, 4H), 7.36 – 7.39 (m, 1H), 7.18 – 7.28 (m, 4H), 6.96 (s, 1H), 5.80 (s, 1H), 2.38 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 150.7, 147.1, 145.4, 134.0, 131.5, 131.1, 129.9, 128.4, 127.6, 127.3, 126.7, 126.4, 125.9, 124.7, 123.3 (q, J = 287.0 Hz), 123.7, 122.2, 120.3, 118.6, 118.4, 64.7 (q, J = 26.9 Hz), 21.7. $^{19}$F NMR (282 MHz, CDCl$_3$) δ −75.0 (s, 3F). IR (KBr): 3135, 3012, 1594, 1496, 1405, 1376, 1172, 842, 757, 665, 572 cm$^{-1}$. HRMS (ESI) calculated for C$_{24}$H$_{17}$F$_3$N$_2$O$_5$Na$_2$ [M+Na]$^+$: 557.0429, found: 557.0429.

(13bS,13cR)-2-Methyl-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ab):

Following the general method D, compound 3ab was obtained as a white solid (91.8 mg, Yield: 84%), m.p. = 112.7 – 113.7 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 18.150 min, t (minor) = 41.242 min. [α]$_D^{25}$ = -169.9 (c = 0.4, CHCl$_3$, 99% ee). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.78 – 7.80 (m, 3H), 7.46 – 7.50 (m, 1H), 7.42 (d, J = 7.3 Hz, 1H), 7.24 – 7.28 (m, 4H), 7.19 – 7.22 (m, 1H), 7.11 (d, J = 8.2 Hz, 1H), 6.95 (s, 1H), 5.73 (s, 1H), 2.43 (s, 3H), 2.37 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 148.6, 147.2, 145.4, 136.4, 134.0, 131.7, 131.5, 129.9, 128.6, 127.6, 127.3, 125.8, 124.7, 123.8, 123.3 (q, J = 287.0 Hz), 120.0, 118.7, 118.0, 114.8, 69.7, 64.6 (q, J = 26.6 Hz), 21.7, 21.0. $^{19}$F NMR (282 MHz, CDCl$_3$) δ −75.0 (s, 3F). IR (KBr): 3135, 3052, 2940, 1600, 1460, 1376, 1170, 1091, 950, 835, 761, 661 cm$^{-1}$. HRMS (ESI) calculated for C$_{25}$H$_{19}$F$_3$N$_3$O$_5$Na$_2$ [M+Na]$^+$: 571.0585, found: 571.0587.
(13bS,13cR)-2-Methoxy-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5′,6′][1,2,3]oxathiazino[3′,4′:1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ac):

Following the general method D, compound 3aa was obtained as a yellow solid (95.7 mg, Yield: 85%), m.p. = 113.2 – 114.1 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® IA (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 48.742 min, t (minor) = 62.825 min). [α]$_D^{25}$ = −159.4 (c = 0.6, CHCl$_3$, 99% ee). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.77 – 7.79 (m, 3H), 7.41 – 7.47 (m, 2H), 7.27 (d, $J$ = 7.6 Hz, 2H), 7.16 – 7.20 (m, 2H), 6.94 – 6.98 (m, 3H), 5.69 (s, 1H), 3.86 (s, 3H), 2.38 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 157.4, 147.2, 145.5, 144.3, 134.0, 131.5, 129.9, 127.5, 127.3, 125.8, 124.7, 123.7, 123.3 (q, $J$ = 287.3 Hz), 121.2, 119.3, 118.7, 115.3, 114.8, 114.2, 69.7, 64.6 (q, $J$ = 26.9 Hz), 55.9, 21.7. $^{19}$F NMR (282 MHz, CDCl$_3$) δ −74.9 (s, 3F). IR (KBr): 3135, 3012, 2840, 1596, 1496, 1405, 1376, 1230, 1172, 1091, 943, 842, 757 cm$^{-1}$. HRMS (ESI) calculated for C$_{25}$H$_{19}$F$_3$N$_2$O$_6$NaS$_2$ [M+Na]$^+$: 587.0534, found: 587.0511.

(13bS,13cR)-2-Fluoro-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5′,6′][1,2,3]oxathiazino[3′,4′:1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ad):

Following the general method D, compound 3ad was obtained as a yellow solid (78.0 mg, Yield: 71%), m.p. = 85.6 – 86.5 °C. The enantiomeric excess (95% ee) was determined by chiral HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 11.733 min, t (minor) = 23.408 min). [α]$_D^{25}$ = −104.7 (c = 0.6, CHCl$_3$, 95% ee). $^1$H NMR δ 7.77 – 7.80 (m, 3H), 7.47 – 7.50 (m, 1H), 7.41 (d, $J$ = 7.6 Hz, 1H), 7.27 (d, $J$ = 8.2 Hz, 2H), 7.16 – 7.24 (m, 4H), 6.95 (s, 1H), 5.72 (s, 1H), 2.38 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 159.8 (d,
\( J = 247.9 \text{ Hz}, 147.1, 146.7, 145.6, 133.9, 131.7, 129.9, 127.6, 127.3, 125.8, 124.8, 123.3, 123.3 \) 
\((q, J = 287.9 \text{ Hz}), 122.1 (d, J = 8.2 \text{ Hz}), 120.2 (d, J = 7.3 \text{ Hz}), 118.5, 118.2 (d, J = 23.6 \text{ Hz}), 115.2 (d, J = 25.4 \text{ Hz}), 114.8, 69.3, 64.8 (q, J = 26.9 \text{ Hz}), 21.7. \)
\( ^{19}\text{F NMR} \) (282 MHz, CDCl\(_3\)) \( \delta \) −74.9 (s, 3F), −114.3 − −114.4 (m, 1F). \textbf{IR (KBr)}: 3139, 3075, 2921, 1599, 1492, 1405, 1170, 944, 840 cm\(^{-1}\). \textbf{HRMS (ESI)} calculated for C\(_{24}\)H\(_{16}\)BrF\(_3\)N\(_2\)O\(_5\)NaS\(_2\) [M+Na\(^+\)]: 634.9534, found: 634.9532.

(13bS,13cR)-2-Bromo-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ae):

Following the general method \( D \), compound 3ae was obtained as a yellow solid (90.2 mg, Yield: 73%), m.p. = 87.5 − 88.5 °C. The enantiomeric excess (95% \( ee \)) was determined by chiral HPLC using CHIRALPAK\textsuperscript{®} IA (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, \( \lambda = 254 \text{ nm} \)) \( \tau \) (major) = 27.125 min, \( \tau \) (minor) = 34.067 min). \( [\alpha]^{25}_{25}D = −170.5 \) (c = 0.2, CHCl\(_3\), 95\% \( ee \)). \textbf{\( ^1\text{H NMR} \)} (500 MHz, CDCl\(_3\)) \( \delta \) 7.78 − 7.80 (m, 3H), 7.58 − 7.61 (m, 2H), 7.48 − 7.51 (m, 1H), 7.38 (d, \( J = 7.6 \text{ Hz}, 1H \)), 7.28 (d, \( J = 7.9 \text{ Hz}, 2\text{H} \)), 7.22 − 7.25 (m, 1H), 7.13 (d, \( J = 9.2 \text{ Hz}, 1\text{H} \)), 6.95 (s, 1H), 5.74 (s, 1H), 2.39 (s, 3H). \textbf{\( ^{13}\text{C NMR} \)} (126 MHz, CDCl\(_3\)) \( \delta \) 149.8, 147.1, 145.5, 134.2, 133.9, 131.7, 131.2, 129.9, 127.7, 127.3, 125.7, 124.9, 123.2, 123.2 (q, \( J = 282.9 \text{ Hz} \)), 122.1, 120.6, 119.2, 118.4, 114.8, 69.1, 64.8 (q, \( J = 26.9 \text{ Hz} \)), 21.7. \textbf{\( ^{19}\text{F NMR} \)} (282 MHz, CDCl\(_3\)) \( \delta \) −74.9 (s, 3F). \textbf{IR (KBr)}: 3127, 2921, 1600, 1477, 1405, 1170, 1116, 831, 782, 663, 576 cm\(^{-1}\). \textbf{HRMS (ESI)} calculated for C\(_{24}\)H\(_{16}\)BrF\(_3\)N\(_2\)O\(_5\)NaS\(_2\) [M+Na\(^+\)]: 634.9534, found: 634.9532.

(13bS,13cR)-2-Nitro-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3af):

S16
Following the general method D, compound 3af was obtained as a white solid (30.2 mg, Yield: 52%), m.p. = 113.2 – 114.1 °C. The enantiomeric excess (92% ee) was determined by chiral HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 20.125 min, t (minor) = 30.692 min). [α]$_{D}^{25}$ = –66.4 (c = 0.1, CHCl$_3$, 92% ee). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.42 (d, J = 2.4 Hz, 1H), 8.38 (dd, J = 8.9, 2.7 Hz, 1H), 7.79 – 7.81 (m, 3H), 7.51 – 7.54 (m, 1H), 7.44 (d, J = 7.6 Hz, 1H), 7.42 (d, J = 8.9 Hz, 1H), 7.28 – 7.30 (m, 2H), 7.25 – 7.27 (m, 1H), 6.99 (s, 1H), 5.89 (s, 1H), 2.39 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 154.9, 147.0, 145.7, 145.2, 133.8, 132.0, 130.0, 127.9, 127.3, 126.5, 125.8, 124.3, 123.2 (q, J = 287.6 Hz), 122.7, 121.6, 120.0, 117.8, 114.9, 69.2, 65.0 (q, J = 26.6 Hz), 21.7. $^{19}$F NMR (282 MHz, CDCl$_3$) δ –74.7 (s, 3F). IR (KBr): 3127, 3052, 1537, 1409, 1376, 1172, 944, 779, 671 cm$^{-1}$. HRMS (EI) calculated for C$_{24}$H$_{16}$F$_3$N$_3$O$_7$S$_2$ [M]+: 579.0382, found: 579.0403.

(13bS,13cR)-3-Methyl-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ag):

Following the general method D, compound 3ag was obtained as a white solid (79.5 mg, Yield: 72%), m.p. = 132.4 – 133.4 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 15.975 min, t (minor) = 37.100 min). [α]$_{D}^{25}$ = –124.4 (c = 0.8, CHCl$_3$, 99% ee). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.78 – 7.80 (m, 3H), 7.42 – 7.49 (m, 2H), 7.35 (d, J = 7.9 Hz, 1H), 7.27 (d, J = 7.9 Hz, 2H), 7.16 – 7.21 (m, 2H), 7.05 (s, 1H), 6.95 (s, 1H), 5.75 (s, 1H), 2.41 (s, 3H), 2.38 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 150.5, 147.1, 145.4, 142.0, 134.0, 131.5, 129.9, 128.0, 127.6, 127.3, 125.9, 124.7, 123.8, 123.3 (q, J = 287.0 Hz), 120.7, 119.9, 118.7, 115.2, 114.8, 69.6, 64.6
(q, J = 26.9 Hz), 21.7, 21.3. \(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \(\delta -75.0\) (s, 3F). IR (KBr): 3435, 3127, 1600, 1457, 1402, 1369, 1303, 1241, 1170, 1108, 952, 798 cm\(^{-1}\). HRMS (ESI) calculated for C\(_{25}\)H\(_{19}\)F\(_3\)N\(_2\)O\(_5\)S\(_2\) [M+Na\(^+\)]: 571.0585, found: 571.0587.

(13bS,13cR)-3-Methoxy-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ah):

Following the general method D, compound 3ah was obtained as a yellow solid (93.3 mg, Yield: 83%), m.p. = 102.5 – 103.4 °C. The enantiomeric excess (97% ee) was determined by chiral HPLC using CHIRALPAK\(^{\circledast}\) IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, \(\lambda = 254\) nm) t (major) = 18.317 min, t (minor) = 37.942 min). \([\alpha]^{25}\) = -111.1 (c = 0.6, CHCl\(_3\), 97% ee). \(^{1}\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 7.78 – 7.79\) (m, 3H), 7.45 – 7.48 (m, 1H), 7.40 (d, \(J = 7.3\) Hz, 1H), 7.34 (d, \(J = 8.5\) Hz, 1H), 7.27 (d, \(J = 7.9\) Hz, 2H), 7.17 – 7.20 (m, 1H), 6.94 (s, 1H), 6.90 (d, \(J = 10.4\) Hz, 1H), 6.74 (s, 1H), 5.72 (s, 1H), 3.85 (s, 3H), 2.38 (s, 3H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta 161.4, 151.6, 147.1, 145.4, 134.0, 131.4, 129.9, 129.0, 127.8, 127.3, 125.8, 124.7, 123.8, 123.4 (q, \(J = 287.0\) Hz), 118.6, 114.8, 113.3, 109.7, 105.2, 69.5, 64.4 (q, \(J = 26.6\) Hz), 55.7, 21.7. \(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \(\delta -75.1\) (s, 3F). IR (KBr): 3135, 2937, 1627, 1510, 1459, 1402, 1170, 1089, 952, 796, 754, 659 cm\(^{-1}\). HRMS (ESI) calculated for C\(_{25}\)H\(_{19}\)F\(_3\)N\(_2\)O\(_6\)S\(_2\) [M\(^{+}\)]: 564.0637, found: 564.0615.

(13bS,13cR)-3-Chloro-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ai):

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S18
Following the general method D, compound 3ai was obtained as a yellow solid (94.3 mg, Yield: 91%), m.p. = 104.7 – 105.6 °C. The enantiomeric excess (98% ee) was determined by chiral HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 12.000 min, t (minor) = 22.567 min. \([\alpha]^{25}_D = -115.4 \text{ (c = 0.5, CHCl}_3, 98\% \text{ ee)}\). \(^1\text{H NMR}\) (500 MHz, CDCl\(_3\)) δ 7.78 – 7.79 (m, 3H), 7.47 – 7.50 (m, 1H), 7.33 – 7.42 (m, 3H), 7.26 – 7.28 (m, 3H), 7.18 – 7.21 (m, 1H), 6.95 (s, 1H), 5.76 (s, 1H), 2.39 (s, 3H). \(^{13}\text{C NMR}\) (126 MHz, CDCl\(_3\)) δ 151.0, 147.1, 145.6, 136.7, 133.9, 131.7, 129.9, 129.2, 127.7, 127.3, 126.8, 125.7, 124.7, 123.3, 123.3 (q, \(J = 287.3\) Hz), 120.9, 118.4, 117.1, 114.9, 69.3, 64.7 (q, \(J = 26.9\) Hz), 21.7. \(^{19}\text{F NMR}\) (282 MHz, CDCl\(_3\)) δ −74.9 (s, 3F). IR (KBr): 3135, 3060, 1598, 1459, 1403, 1243, 1170, 1089, 883, 796 cm\(^{-1}\). HRMS (ESI) calculated for C\(_{24}\)H\(_{16}\)ClF\(_3\)N\(_2\)O\(_5\)NaS\(_2\) [M+Na\(^+\)]: 591.0039, found: 591.0026.

(13bS,13cR)-9-Tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9\(\text{H}\)-naphthro[2''',1''':5',6']1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3aj):

Following the general method D, compound 3aj was obtained as a yellow solid (101.6 mg, Yield: 87%), m.p. = 115.2 – 116.0 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 18.683 min, t (minor) = 28.933 min. \([\alpha]^{25}_D = -99.7 \text{ (c = 0.2, CHCl}_3, 99\% \text{ ee)}\). \(^1\text{H NMR}\) (500 MHz, CDCl\(_3\)) δ 8.19 – 8.21 (m, 1H), 7.88 – 7.90 (m, 1H), 7.79 – 7.84 (m, 4H), 7.63 – 7.65 (m, 2H), 7.44 – 7.53 (m, 3H), 7.20 – 7.27 (m, 3H), 7.02 (s, 1H), 5.90 (s, 1H), 2.36 (s, 3H). \(^{13}\text{C NMR}\) (126 MHz, CDCl\(_3\)) δ 147.2, 146.6, 145.5, 143.4, 133.9, 131.6, 129.9, 129.9, 128.3, 128.0, 127.9, 127.8, 127.3, 126.3, 126.0, 125.2, 124.8, 123.6, 123.4, 123.4 (q, \(J = 287.0\) Hz), 121.5, 114.8, 113.7, 70.1, 65.0 (q, \(J = 26.9\) Hz), 21.6. \(^{19}\text{F NMR}\) (282 MHz, CDCl\(_3\)) δ −75.2 (s, 3F). IR (KBr): 3135, 3060, 1598, 1459, 1403, 1243, 1170, 1089, 883, 796 cm\(^{-1}\). HRMS (ESI) calculated for C\(_{28}\)H\(_{19}\)F\(_3\)N\(_2\)O\(_5\)NaS\(_2\) [M+Na\(^+\)]: 607.0585, found: 607.0586.
(13bS,13cR)-9-Tosyl-11,13b-bis(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ba):

Following the general method D, compound 3ba was obtained as a white solid (30.8 mg, Yield: 81%), m.p. = 128.2 – 129.1 °C. The enantiomeric excess (92% ee) was determined by chiral HPLC using CHIRALPAK® IG (n-hexane/isopropanol = 90.0/10.0, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 21.417 min, t (minor) = 25.692 min). \([\alpha]_D^{25} = -120.7 \ (c = 0.1, \text{CHCl}_3, 92\% \text{ ee})\). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 8.03 \ (s, 1H), 7.79 \ (d, \ J = 8.2 \ Hz, 2H), 7.45 – 7.56 \ (m, 4H), 7.40 – 7.41 \ (m, 1H), 7.25 – 7.31 \ (m, 3H), 7.02 \ (s, 1H), 2.40 \ (s, 3H).\) \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta 150.7, 147.7, 146.0, 133.9 \ (q, \ J = 33.0 \ Hz), 133.7, 131.4, 130.1, 128.2, 127.2, 126.9, 126.6, 126.3, 123.2 \ (q, \ J = 273.1 \ Hz), 123.0 \ (q, \ J = 287.3 \ Hz), 121.6 \ (q, \ J = 3.6 \ Hz), 120.5, 119.7, 118.0, 111.7 \ (q, \ J = 3.6 \ Hz), 69.4, 64.5 \ (q, \ J = 27.2 \ Hz), 21.7. \(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \(\delta -63.3 \ (s, 3F), -75.0 \ (s, 3F).\) IR (KBr): 3139, 2948, 1599, 1402, 1377, 1323, 1178, 1137, 962, 902, 796 cm\(^{-1}\). HRMS (ESI) calculated for C\(_{25}\)H\(_{18}\)F\(_6\)N\(_2\)O\(_5\)NaS\(_2\) [M+Na\(^+\)]: 625.0303, found: 625.0308.

Methyl (13bS,13cR)-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole-11-carboxylate 6,6-dioxide (3ca):

Following the general method D, compound 3ca was obtained as a white solid (42.4 mg, Yield: 72%), m.p. = 134.0 – 134.7 °C. The enantiomeric excess (96% ee) was determined by chiral HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 32.133 min, t (minor) = 39.2 min). \([\alpha]_D^{25} = -120.7 \ (c = 0.1, \text{CHCl}_3, 96\% \text{ ee})\). \([\alpha]_D^{25} = -88.6 \ (c = 0.3, \text{CHCl}_3).\) \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 8.39 \ (d, \ J = 1.2 \ Hz, 1H), 7.89 \ (dd, \ J = 7.9, 1.5 \ Hz, 1H), 7.81 \ (d, \ J = 8.5 \ Hz, 2H), 7.47 – 7.51 \ (m, 3H), 7.38 – 7.41 \ (m, 1H), 7.24 – 7.29 \ (m, 3H), 6.99 \ (s, 1H), 5.82 \ (s, 1H), 3.99 \ (s, 3H), 3.99 \ (s, 3H), 2.39 \ (s, 3H).\) \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta 165.7,
(13bS,13cR)-12-Fluoro-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6']
[1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3da):

Following the general method D, compound 3da was obtained as a yellow solid (50.5 mg, Yield: 91%), m.p. = 104.8 – 105.8 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85/15, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 12.333 min, t (minor) = 24.967 min). [α]$_D^{25}$ = $-131.4$ (c = 0.6, CHCl$_3$, 99% ee). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.76 – 7.78 (m, 3H), 7.47 – 7.50 (m, 1H), 7.39 – 7.43 (m, 2H), 7.13 – 7.29 (m, 5H), 6.97 (s, 1H), 5.78 (s, 1H), 2.39 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 159.5 (d, $J$ = 245.2 Hz), 150.7, 145.6, 143.3, 133.7, 131.3, 129.9, 128.2, 127.5, 127.3, 126.6, 125.0 (d, $J$ = 8.2 Hz), 123.1 (q, $J$ = 287.3 Hz), 120.4, 119.3, 118.4 (d, $J$ = 23.6 Hz), 128.1, 116.0 (d, $J$ = 8.2 Hz), 113.5 (d, $J$ = 24.5 Hz), 69.5, 64.5 (q, $J$ = 27.2 Hz), 21.7. $^{19}$F NMR (282 MHz, CDCl$_3$) δ −74.9 (s, 3F), $-116.7 – -116.8$ (m, 1F). IR (KBr): 3141, 2960, 1599, 1471, 1403, 1363, 1170, 1087, 952, 908, 815 cm$^{-1}$. HRMS (ESI) calculated for C$_{24}$H$_{16}$F$_{4}$N$_{2}$O$_{5}$NaS$_{2}$ [M+Na]$^+$: 575.0334, found: 575.0342.

(13bS,13cR)-12-Fluoro-2-methyl-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo
[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3db):
Following the general method D, compound 3db was obtained as a yellow solid (47.0 mg, Yield: 83%), m.p. = 107.2 – 108.1 °C. The enantiomeric excess (98% ee) was determined by chiral HPLC using CHIRALPAK® IG (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 69.183 min, t (minor) = 76.500 min. [α]$_D^{25}$ = −174.3 (c = 0.6, CHCl$_3$, 98% ee).$^1$H NMR (500 MHz, CDCl$_3$) δ 7.75 – 7.78 (m, 3H), 7.26 – 7.29 (m, 3H), 7.18 – 7.21 (m, 2H), 7.09 – 7.13 (m, 2H), 6.96 (s, 1H), 5.72 (s, 1H), 2.44 (s, 3H), 2.39 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 159.4 (d, $J$ = 245.2 Hz), 148.6, 145.6, 143.3, 136.7, 133.7, 131.9, 129.9, 128.4, 127.4, 127.3, 125.2 (d, $J$ = 8.2 Hz), 123.1 (q, $J$ = 287.3 Hz), 120.2, 119.5, 118.3 (d, $J$ = 23.6 Hz), 117.7, 116.0 (d, $J$ = 8.2 Hz), 113.5 (d, $J$ = 25.4 Hz), 69.5, 64.5 (q, $J$ = 26.9 Hz), 21.7, 21.1. $^{19}$F NMR (282 MHz, CDCl$_3$) δ −74.9 (s, 3F), −116.7 – −116.8 (s, 1F). IR (KBr): 3135, 2929, 1598, 1471, 1403, 1278, 1186, 1116, 1089, 950, 840, 759 cm$^{-1}$. HRMS (ESI) calculated for C$_{25}$H$_{18}$F$_4$N$_2$O$_5$Na$_2$ [M+Na]$^+$: 589.0491, found: 589.0504.

(13bS,13cR)-12-Chloro-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5′,6′][1,2,3]oxathiazino[3′,4′:1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ea):

Following the general method D, compound 3ea was obtained as a yellow solid (48.1 mg, Yield: 84%), m.p. = 103.9 – 104.9 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 11.867 min, t (minor) = 28.683 min. [α]$_D^{25}$ = −123.7 (c = 0.4, CHCl$_3$, 99% ee).$^1$H NMR (500 MHz, CDCl$_3$) δ 7.73 – 7.78 (m, 3H), 7.41 – 7.50 (m, 4H), 7.36 (d, $J$ = 2.1 Hz, 1H), 7.24 – 7.29 (m, 3H), 6.98 (s, 1H), 5.79 (s, 1H), 2.39 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 150.7, 145.8, 145.7, 133.7, 131.6, 131.3, 130.0, 128.3, 127.3, 127.1, 126.7, 126.1, 125.2, 123.0 (q, $J$ = 287.3 Hz), 120.4, 119.4, 118.1, 115.8, 69.5, 64.5 (q, $J$ = 26.9 Hz), 21.7. $^{19}$F NMR (282 MHz, CDCl$_3$) δ −75.0 (s, 3F). IR (KBr): 3127, 2929, 1598, 1471, 1403, 1278, 1170, 1089, 950, 840, 759 cm$^{-1}$. HRMS (ESI) calculated for C$_{25}$H$_{16}$ClF$_3$N$_2$O$_5$NaS$_2$ [M+Na]$^+$: 591.0039, found: 591.0042.

S22
(13bS,13cR)-12-Chloro-2-methoxy-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'] [1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ec):

Following the general method D, compound 3ec was obtained as a yellow solid (51.7 mg, Yield: 86%), m.p. = 103.8 – 104.8 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 90.0/10.0, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 20.258 min, t (minor) = 60.733 min). [α]$_{25}^{25}$D = −170.9 (c = 0.5, CHCl$_3$, 99% ee). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.72 – 7.77 (m, 3H), 7.44 – 7.46 (m, 1H), 7.34 (d, J = 1.8 Hz, 1H), 7.26 – 7.29 (m, 2H), 7.17 – 7.19 (m, 1H), 7.02 – 7.00 (m, 1H), 7.00 – 6.97 (m, 1H), 6.90 (s, 1H), 5.70 (s, 1H), 3.87 (s, 3H), 2.39 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 157.5, 145.8, 145.7, 144.2, 133.7, 136.1, 130.0, 127.3, 127.1, 126.0, 125.3, 123.0 (q, J = 287.3 Hz), 121.3, 119.5, 119.0, 115.8, 115.4, 114.0, 69.5, 64.5 (q, J = 26.9 Hz), 55.9, 21.7. $^{19}$F NMR (282 MHz, CDCl$_3$) δ −74.9 (s, 3F). IR (KBr): 3131, 2968, 1595, 1496, 1461, 1278, 1170, 840, 728, 663, 590 cm$^{-1}$. HRMS (ESI) calculated for C$_{25}$H$_{18}$ClF$_3$N$_2$O$_6$NaS$_2$ [M+Na]$^+$: 621.0145, found: 621.0142.

(13bS,13cR)-12-Methyl-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'] [1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3fa):

Following the general method D, compound 3fa was obtained as a yellow solid (42.3 mg, Yield: 77%), m.p. = 116.7 – 117.4 °C. The enantiomeric excess (98% ee) was determined by chiral HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 15.333 min, t (minor) = 43.892 min). [α]$_{25}^{25}$D = −133.4 (c = 0.4, CHCl$_3$, 98% ee). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.78 (d, J = 8.2 Hz, 2H), 7.68 (d, J = 8.2 Hz, 1H), 7.48 – 7.50 (m, 2H), 7.40 – 7.42 (m, 1H), 7.24 – 7.29 (m, 4H), 7.20 (s, 1H), 6.94 (s, 1H), 5.76 (s, 1H), 2.39 (s, 3H), 2.38 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 150.7, 145.3, 144.8, 134.7, 133.9, 132.1, 131.1, 129.8, 128.4,
127.9, 127.3, 126.4, 126.3, 123.7, 123.3 (q, J = 287.3 Hz), 120.3, 118.5, 118.4, 114.6, 69.7, 64.7 (q, J = 26.6 Hz), 21.7, 21.1. $^{19}$F NMR (282 MHz, CDCl$_3$) δ −74.9 (s, 3F). IR (KBr): 3131, 2929, 1598, 1477, 1402, 1170, 906, 759, 665, 566 cm$^{-1}$. HRMS (ESI) calculated for C$_{25}$H$_{19}$F$_3$N$_2$O$_5$NaS$_2$ [M+Na]$^+$: 571.0585, found: 571.0572.

5. Synthetic utility I:

5.1. Synthesis of (13b$S$,13c$R$)-2-Phenyl-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-
benzo[5',6'] [1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-
dioxide (6):

In a flame dried Schlenk tube 1 mL Toluene was taken. The solvent was degassed by using standard “freeze-pump-thaw” method. The process was repeated for three times and finally the Schlenk tube was filled with argon gas. After that, Pd$_2$(dba)$_3$ (10 mol%, 9.2 mg) and triphenylphosphine (40 mol%, 10.5 mg) were taken in the tube inside the glove box and allowed to stir for 5 min. To the above mixture, bromo-indole 3ae (0.1 mmol, 1.0 equiv, 61 mg), phenylboronic acid (0.11 mmol, 1.1 equiv, 13.4 mg) and Cs$_2$CO$_3$ (0.2 mmol, 2.0 equiv, 65 mg) were added and removed from the glove box. The mixture was allowed to stir at 110 °C for 6 h under Ar. After completion, the reaction was quenched by saturated NH$_4$Cl aqueous solution (5 mL) at room temperature and extracted with CH$_2$Cl$_2$ (3×10 mL). The combined organic layers were washed with water and brine, then dried over Na$_2$SO$_4$, filtered, and concentrated under vacuum. The residue was purified by silica gel column chromatography (PE/EtOAc = 9/1) to afford the desired product 6 (48 mg, yield: 79%) as white solid. m.p. = 128.0 – 128.9 °C. The enantiomeric excess (95% ee) was determined by chiral HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, λ = 254 nm) t (major) = 19.425 min, t (minor) = 41.225 min. $[\alpha]^{25}_D = -198.1$ (c = 0.6, CHCl$_3$, 95% ee). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.79 – 7.81 (m, 3H), 7.62 – 7.66 (m, 2H), 7.40 – 7.56 (m, 7H), 7.26 – 7.31 (m, 3H), 7.19 – 7.19 (m, 1H), 6.98 (s, 1H), 5.84 (s, 1H), 2.38 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 150.0, 147.1,
145.5, 140.0, 139.2, 134.0, 128.2, 127.7, 127.3, 127.1, 127.0, 125.8, 124.8, 123.6, 123.4 (q, \( J = 287.3 \) Hz), 120.6, 118.7, 118.6, 114.8, 69.9, 64.8 (q, \( J = 26.6 \) Hz), 21.7.

\(^{19}F\) NMR (282 MHz, CDCl\(_3\)) \( \delta -74.8 \) (s, 3F). IR (KBr): 3139, 3072, 1600, 1481, 1396, 1172, 1091, 950, 842, 665, 572 cm\(^{-1}\). HRMS (ESI) calculated for \( C_{30}H_{21}F_3N_2O_5NaS_2 \) [M+Na]\(^+\): 633.0742, found: 633.0733.

5.2. General Procedure for the detosylative-methoxylation reaction (Method E):

Under argon atmosphere, a flame-dried Schlenk tube was charged with compound 3 (0.1 mmol, 1 equiv), Mg powder (1.0 mmol, 10 equiv), THF (0.3 mL) and MeOH (0.7 mL). The resulting solution was left for 6 h at room temperature under sonication. The mixture was filtered through a celite pad and concentrated under reduced pressure and purified by flash column chromatography (using Toluene) to obtain the pure product 7.

\((13bS,13cR)-8a-Methoxy-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'] [1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (7aa)\):

Following the general method E, compound 7aa was obtained as a white solid (32.2 mg, Yield: 78%), m.p. = 116.5 – 117.4°C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK\textsuperscript{\textregistered} OD-3 (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, \( \lambda = 254 \) nm) t (minor) = 18.717 min, t (major) = 29.975 min). \([\alpha]^{25}_{D} = +78.0 \) (c = 0.5, CHCl\(_3\), 99% ee). \(^1H\) NMR (500 MHz, CDCl\(_3\)) \( \delta 7.39 – 7.42 \) (m, 1H), 7.35 (d, \( J = 7.6 \) Hz, 1H), 7.28 – 7.31 (m, 1H), 7.20 – 7.23 (m, 1H), 7.11 – 7.15 (m, 2H), 6.91 – 6.94 (m, 1H), 6.83 (d, \( J = 7.9 \) Hz, 1H), 5.01 (s, 1H), 4.96 (s, 1H), 4.19 (d, \( J = 10.1 \) Hz, 1H), 4.01 (d, \( J = 10.1 \) Hz, 1H), 3.19 (s, 3H). \(^{13}C\) NMR (126 MHz, CDCl\(_3\)) \( \delta 150.7, 147.0, 130.8, 128.4, 125.6, 131.1, 129.8, 128.4, 125.6, 124.5 \) (q, \( J = 281.5 \) Hz),
123.6, 120.1, 109.7, 103.6, 71.4, 65.1 (q, J = 25.7 Hz), 57.1, 51.8. $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ −63.8 (s, 3F). IR (KBr): 3411, 3365, 2956, 1612, 1469, 1382, 1174, 964, 881, 752, 539 cm$^{-1}$. HRMS (ESI) calculated for C$_{18}$H$_{14}$F$_3$N$_2$O$_4$S [M−H]$^−$: 411.0626, found: 411.0628.

(8aS,13bS,13cR)-8a-methoxy-2-methyl-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (7ab):

Following the general method E, compound 7ab was obtained as a white solid (32 mg, Yield: 75%), m.p. = 125.1 – 126.3 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® OD-3 (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, $\lambda$ = 254 nm) t (minor) = 16.933 min, t (major) = 38.558 min. $[\alpha]_{D}^{25}$ = +74.9 (c = 0.2, CHCl$_3$, 99% ee). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.29 – 7.35 (m, 2H), 7.19 (dd, $J = 8.4$, 1.7 Hz, 1H), 7.03 (d, $J = 8.5$ Hz, 1H), 6.93 – 6.96 (m, 1H), 6.90 (s, 1H), 6.85 (d, $J = 7.9$ Hz, 1H), 4.96 (s, 1H), 4.89 (s, 1H), 4.18 (d, $J = 10.1$ Hz, 1H), 4.01 (d, $J = 10.1$ Hz, 1H), 3.19 (s, 3H), 2.33 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 148.6, 147.0, 135.4, 131.0, 130.7, 128.7, 124.5 (q, $J = 281.5$ Hz), 123.8, 123.6, 120.1, 119.5, 118.4, 109.7, 103.6, 71.5, 65.1 (q, $J = 25.7$ Hz), 57.1, 51.8, 20.9. $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ −63.74 (s, 3F). IR (KBr): 3355, 2960, 1612, 1496, 1267, 1176, 1141, 1116, 839, 821 cm$^{-1}$. HRMS (ESI) calculated for C$_{19}$H$_{16}$F$_3$N$_2$O$_4$S [M−H]$^−$: 425.0783, found: 425.0779.

(8aS,13bS,13cR)-2,8a-dimethoxy-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (7ac):

Following the general method E, compound 7ac was obtained as a white solid (36.3 mg, Yield: 82%), m.p. = 128.6 – 129.4 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC
following the general method E, compound 7ad was obtained as a white solid (27.1 mg, Yield: 63%), m.p. = 134.1 – 135.1 °C. The enantiomeric excess (85% ee) was determined by chiral HPLC using CHIRALPAK® OD-3 (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, λ = 230 nm) t (minor) = 18.117 min, t (major) = 34.392 min. [α]$_D^{25}$ = +82.2 (c = 0.2, CHCl$_3$, 85% ee). H NMR (500 MHz, CDCl$_3$) δ 7.37 (d, J = 7.6 Hz, 1H), 7.30 – 7.34 (m, 1H), 7.11 – 7.14 (m, 2H), 6.94 – 6.97 (m, 1H), 6.83 – 6.86 (m, 2H), 4.96 (s, 1H), 4.90 (s, 1H), 4.17 (d, J = 10.1 Hz, 1H), 3.92 (m, 1F). 13C NMR (126 MHz, CDCl$_3$) δ 159.4 (d, J = 246.1 Hz), 146.8 (d, J = 1.8 Hz), 131.0, 124.4 (q, J = 281.5 Hz), 123.4, 123.3, 121.5 (d, J = 8.2 Hz), 120.5 (d, J = 8.2 Hz), 120.4, 117.5 (d, J = 23.6 Hz), 115.0 (d, J = 25.4 Hz), 109.7, 103.5, 71.1, 65.1 (q, J = 25.7 Hz), 57.2, 55.7, 51.8. 19F NMR (282 MHz, CDCl$_3$) δ –63.69 (s, 3F), –115.69 – –115.74 (m, 1F). IR (KBr): 3403, 3054, 2956, 2848, 1612, 1488, 1172, 1105, 829, 750 cm$^{-1}$. HRMS (ESI) calculated for C$_{19}$H$_{16}$F$_4$N$_2$O$_4$S [M−H]: 429.0532, found: 429.0528.

(8aS,13bS,13cR)-8a-methoxy-3-methyl-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6']/[1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (7ag):
Following the general method E, compound 7ag was obtained as a white solid (28.6 mg, Yield: 67%), m.p. = 124.4 – 125.2 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® OD-3 (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, λ = 230 nm) t (minor) = 18.892 min, t (major) = 27.700 min. [α]25D = +93.1 (c = 0.1, CHCl3, 99% ee). 1H NMR (500 MHz, CDCl3) δ 7.34 (d, J = 7.6 Hz, 1H), 7.28 – 7.32 (m, 1H), 6.98 – 7.01 (m, 2H), 6.91 – 6.95 (m, 2H), 6.84 (d, J = 7.9 Hz, 1H), 4.98 (s, 1H), 4.87 (s, 1H), 4.18 (d, J = 10.1 Hz, 1H), 4.01 (d, J = 10.1 Hz, 1H), 3.20 (s, 3H), 2.38 (s, 3H). 13C NMR (126 MHz, CDCl3) δ 150.5, 147.0, 141.2, 130.7, 128.1, 126.5, 124.5 (q, J = 281.8 Hz), 123.8, 123.7, 120.2, 120.1, 115.6, 109.6, 103.6, 71.4, 65.1 (q, J = 25.4 Hz), 57.2, 51.8, 21.2. 19F NMR (282 MHz, CDCl3) δ −63.71 (s, 3F). IR (KBr): 3384, 3045, 2954, 2850, 1612, 1508, 1257, 1189, 1170, 844 cm⁻¹. HRMS (ESI) calculated for C19H16F3N2O4S [M–H]⁻: 425.0783, found: 425.0789.

(8aS,13bS,13cR)-3,8a-dimethoxy-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (7ah):

Following the general method E, compound 7ah was obtained as a white solid (35.8 mg, Yield: 81%), m.p. = 113.9 – 114.6 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® OD-3 (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, λ = 230 nm) t (minor) = 24.617 min, t (major) = 38.833 min. [α]25D = +105.9 (c = 0.2, CHCl3, 99% ee). 1H NMR (500 MHz, CDCl3) δ 7.33 (d, J = 7.3 Hz, 1H), 7.28 – 7.31 (m, 1H), 7.00 (d, J = 8.5 Hz, 1H), 6.90 – 6.93 (m, 1H), 6.83 (d, J = 7.9 Hz, 1H), 6.77 (dd, J = 8.7, 2.6 Hz, 1H), 6.65 (d, J = 2.4 Hz, 1H), 4.96 (s, 1H), 4.89 (s, 1H), 4.18 (d, J = 10.1 Hz, 1H), 4.00 (d, J = 10.1 Hz, 1H), 3.82 (s, 3H), 3.19 (s, 3H). 13C NMR (126 MHz, CDCl3) δ 161.0, 151.5, 146.9, 130.7, 129.1, 124.5 (q, J = 281.8
Hz), 123.8, 123.6, 120.1, 112.6, 110.3, 109.6, 104.6, 103.5, 71.3, 64.9 (q, J = 25.7 Hz), 57.2, 55.6, 51.7. $^{19}$F NMR (282 MHz, CDCl$_3$) δ −63.84 (s, 3F). IR (KBr): 3334, 2958, 1616, 1583, 1510, 1284, 1168, 1141, 819, 750 cm$^{-1}$. HRMS (ESI) calculated for C$_{19}$H$_{16}$F$_{4}$N$_{2}$O$_{5}$S [M−H]$^{-}$: 441.0732, found: 441.0728.

(8aS,13bS,13cR)-12-fluoro-8a-methoxy-2-methyl-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (7db):

Following the general method E, compound 7db was obtained as a white solid (26.7 mg, Yield: 60%), m.p. = 125.1 – 126.3 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® IA (n-hexane/isopropanol = 90.0/10.0, flow rate 1.0 mL/min, λ = 254 nm) t (minor) = 7.767 min, t (major) = 13.900 min). [α]$^{25}_{D} = +68.1$ (c = 0.3, CHCl$_3$, 99% ee). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.20 – 7.22 (m, 1H), 7.08 (dd, J = 7.9, 1.8 Hz, 1H), 7.00 – 7.05 (m, 2H), 6.88 (s, 1H), 6.76 (dd, J = 8.5, 4.0 Hz, 1H), 4.97 (s, 1H), 4.88 (s, 1H), 4.17 (d, J = 10.1 Hz, 1H), 3.99 (d, J = 10.1 Hz, 1H), 3.20 (s, 3H), 2.34 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 157.0 (d, J = 237.9 Hz), 148.6, 143.2, 135.7, 131.3, 128.6, 124.9 (d, J = 8.2 Hz), 124.2 (q, J = 281.8 Hz), 119.7, 118.1, 117.2 (d, J = 23.6 Hz), 111.5 (d, J = 25.4 Hz), 110.3 (d, J = 8.2 Hz), 104.3, 71.4, 65.3 (q, J = 26.0 Hz), 57.1, 51.8, 21.0. $^{19}$F NMR (282 MHz, CDCl$_3$) δ −63.81 (s, 3F), −123.46 − −123.53 (m, 1F). IR (KBr): 3334, 3033, 2952, 1608, 1488, 1268, 1180, 838, 821 cm$^{-1}$. HRMS (ESI) calculated for C$_{19}$H$_{15}$F$_{3}$N$_{2}$O$_{4}$S [M−H]$^{-}$: 443.0689, found: 443.0686.

(8aS,13bS,13cR)-12-chloro-8a-methoxy-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (7ea):
Following the general method E, compound 7ea was obtained as a white solid (33.5 mg, Yield: 61%), m.p. = 110.2 – 111.2 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® OD-3 (n-hexane/isopropanol = 97.0/3.0, flow rate 0.8 mL/min, λ = 254 nm) t (minor) = 42.958 min, t (major) = 87.358 min). [α]_{25}^{D} = +111.1 (c = 0.2, CHCl₃, 99% ee). ¹H NMR (500 MHz, CDCl₃) δ 7.41 – 7.44 (m, 1H), 7.32 (s, 1H), 7.29 (dd, J = 8.4, 2.0 Hz, 1H), 7.25 – 7.26 (m, 1H), 7.15 (dd, J = 8.2, 0.9 Hz, 1H), 7.11 (d, J = 7.6 Hz, 1H), 6.79 (d, J = 8.2 Hz, 1H), 5.02 (s, 1H), 4.92 (s, 1H), 4.19 (d, J = 10.1 Hz, 1H), 4.02 (d, J = 10.1 Hz, 1H), 3.21 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 150.7, 145.6, 130.8, 130.6, 128.3, 125.8, 125.3, 124.9, 124.1 (q, J = 281.8 Hz), 124.0, 120.0, 118.5, 110.6, 104.0, 71.4, 65.1 (q, J = 26.0 Hz), 57.1, 51.9. ¹⁹F NMR (282 MHz, CDCl₃) δ –63.70 (s, 3F). IR (KBr): 3419, 2996, 2842, 1612, 1577, 1261, 1178, 1147, 1118, 815, 754 cm⁻¹. HRMS (ESI) calculated for C₁₈H₁₃F₃N₂O₄ScI [M–H]⁻: 445.0237, found: 445.0229.

6. Synthetic utility II:

6.1. Synthesis of (8aR,13bS,13cR)-8a-allyl-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole (8):

Under argon atmosphere, a flame-dried Schlenk tube was charged with 2-methoxy indoline 7aa (0.1 mmol) and DCM (1.0 mL) than cooled to –78 °C. To this solution, TiCl₄ (0.1 mmol, 0.1 mL of 1.0 M solution in DCM), and then trimethylallylsilane (0.4 mmol, 63.6 µL) were added slowly. The resulted solution was allowed to stir at room temperature until substrate 7aa had been consumed as indicated by TLC. The reaction mixture was quenched by adding cool water and extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layers were washed with water and brine, then dried over Na₂SO₄, filtrated, and concentrated under vacuum. The residue was purified by silica gel column chromatography (Hex/EtOAc = 19/1) to afford the desired product 8 (33 mg, yield: 79%) as white solid, m.p. = 53.2 – 54.0 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® IA (n-hexane/isopropanol = 95.0/5.0, flow rate
1.0 mL/min, λ = 254 nm) t (minor) = 14.575 min, t (major) = 46.192 min). \([\alpha]^{25}_D = +123.5 \text{ (c = 0.4, CHCl}_3, 99\% ee)\). 1H NMR (500 MHz, CDCl\(_3\)) \(\delta 7.38 – 7.41 \text{ (m, 1H)}\), 7.33 (d, \(J = 7.6 \text{ Hz, 1H})\), 7.25 – 7.29 (m, 1H), 7.20 – 7.23 (m, 1H), 7.11 – 7.15 (m, 2H), 6.90 – 6.93 (m, 1H), 6.79 (d, \(J = 7.9 \text{ Hz, 1H})\), 5.73 – 5.81 (m, 1H), 5.35 (dd, \(J = 10.1, 0.6 \text{ Hz, 1H})\), 5.20 – 5.25 (m, 2H), 4.58 (s, 1H), 4.08 (d, \(J = 10.4 \text{ Hz, 1H})\), 3.90 (d, \(J = 10.4 \text{ Hz, 1H})\), 2.44 – 2.55 (m, 2H). 13C NMR (126 MHz, CDCl\(_3\)) \(\delta 150.7, 147.8, 131.1, 130.6, 130.3, 128.6, 125.6, 125.1 \text{ (q, } J = 282.7 \text{ Hz), 124.2, 123.8, 122.3, 120.0, 119.8, 119.1, 111.3, 70.3, 67.7 \text{ (q, } J = 25.4 \text{ Hz), 58.5, 38.6, 38.5.} \) 19F NMR (282 MHz, CDCl\(_3\)) \(\delta -61.74 \text{ (s, 3F).} \) IR (KBr): 3370, 3079, 2923, 1612, 1484, 1469, 1166, 1105, 838, 752 cm\(^{-1}\). HRMS (ESI) calculated for C\(_{20}\)H\(_{16}\)F\(_3\)N\(_2\)O\(_3\)S [M – H]\(^-\): 421.0834, found: 421.0834.

6.2. Synthesis of (8aR,13bS,13cR)-13b-(trifluoromethyl)-13b,13c-dihydro-8H-benzo[5',6'] [1,2,3]oxathiazino [3',4':1,5]pyrrolo[3,4-b]indole-8a(9H)-carbonitrile 6,6-dioxide (9):

Under argon atmosphere, a flame-dried Schlenk tube was charged with 2-methoxy indoline 7aa (0.1 mmol) and DCM (1.0 mL) then cooled to 0 °C. To this solution, BF\(_3\)•OEt\(_2\) (0.2 mmol, 24.7 µL), and then trimethylsilyl cyanide (0.4 mmol, 50 µL) were added slowly. The resulted solution was allowed to stir at room temperature until substrate 7aa had been consumed as indicated by TLC. the reaction mixture was quenched by adding cool water and extracted with CH\(_2\)Cl\(_2\) (3×10 mL). The combined organic layers were washed with water and brine, then dried over Na\(_2\)SO\(_4\), filtrated, and concentrated under vacuum. The residue was purified by silica gel column chromatography (Hex/EtOAc = 4/1) to afford the desired product 9 (36 mg, yield: 88%) as white solid, m.p. = 125.1 – 126.3 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® OD-3 (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, \(\lambda = 254 \text{ nm})\) t (minor) = 26.525 min, t (major) = 37.450 min). \([\alpha]^{25}_D = +112.2 \text{ (c = 0.2, CHCl}_3, 99\% ee)\). 1H NMR (500 MHz, CDCl\(_3\)) \(\delta 7.44 – 7.48 \text{ (m, 1H)}\), 7.37 – 7.40 (m, 2H), 7.26 – 7.30 (m, 1H), 7.19 (dd, \(J = 8.2, 0.9 \text{ Hz, 1H})\), 7.16 (d, \(J = 7.6 \text{ Hz, 1H})\), 7.05 – 7.08 (m, 1H), 6.92 (d, \(J = 7.6 \text{ Hz, 1H}), 4.58 (s, 1H), 4.08 (d, \(J = 10.4 \text{ Hz, 1H})\), 3.90 (d, \(J = 10.4 \text{ Hz, 1H})\), 2.44 – 2.55 (m, 2H).
5.22 (s, 1H), 4.85 (s, 1H), 4.45 (d, $J = 11.0$ Hz, 1H), 4.22 (d, $J = 11.0$ Hz, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 150.6, 146.6, 131.6, 131.1, 128.4, 126.1, 124.1, 123.7 (q, $J = 280.3$ Hz), 122.1, 122.0, 120.2, 117.3, 115.8, 111.9, 69.8 (q, $J = 26.3$ Hz), 69.5, 69.2, 58.1. $^{19}$F NMR (282 MHz, CDCl$_3$) δ $-63.57$ (s, 3F). IR (KBr): 3378, 3068, 2923, 2852, 1612, 1486, 1469, 1176, 1103, 813 cm$^{-1}$. HRMS (ESI) calculated for C$_{18}$H$_{11}$F$_3$N$_3$O$_3$S [M$-$H$^-$]: 406.0473, found: 406.0447.

6.3. Synthesis of (8aR,13bR,13cR)-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8$H$-benzo[5',6'][1,2,3] oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (10):

![Diagram](image)

Under argon atmosphere, a flame-dried Schlenk tube was charged with 2-methoxy indoline 7aa (0.1 mmol) and DCM (1.0 mL) than cooled to 0 °C. To this solution, BF$_3$•OEt$_2$ (0.2 mmol, 24.7 µL), and then triethylsilane (0.4 mmol, 64 µL) were added slowly. The resulted solution was allowed to stir at room temperature until substrate 7aa had been consumed as indicated by TLC. The reaction mixture was quenched by adding cool water and extracted with CH$_2$Cl$_2$ (3 × 10 mL). The combined organic layers were washed with water and brine, then dried over Na$_2$SO$_4$, filtrated, and concentrated under vacuum. The residue was purified by silica gel column chromatography (Hex/EtOAc = 6/1) to afford the desired product 10 (34.8 mg, yield: 91%) as white solid, m.p. = 125.1 – 126.3 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® OD-3 (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, λ = 254 nm) t (minor) = 25.183 min, t (major) = 29.858 min. [$\alpha$]$^{25}_{D} = +113.2$ (c = 0.2, CHCl$_3$, 99% ee). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.39 – 7.42 (m, 2H), 7.34 (d, $J = 7.6$ Hz, 1H), 7.25 – 7.30 (m, 2H), 7.13 (dd, $J = 8.2$, 1.2 Hz, 1H), 6.91 – 6.94 (m, 1H), 6.80 (d, $J = 7.9$ Hz, 1H), 5.23 (s, 1H), 4.87 (t, $J = 4.6$ Hz, 1H), 4.36 (d, $J = 4.0$ Hz, 1H), 4.10 (dd, $J = 10.7$, 5.2 Hz, 1H), 3.89 (d, $J = 10.7$ Hz, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 150.7, 149.7, 130.8, 130.2, 128.4, 125.6, 125.3 (q, $J = 280.6$ Hz), 124.3, 124.2, 120.2, 119.8, 118.4, 110.9, 69.4, 67.0 (q, $J = 26.3$ Hz), 66.4, 55.7. $^{19}$F NMR (282 MHz,
CDCl$_3$ $\delta$ –62.45 (s, 1F). **IR (KBr)**: 3388, 3056, 2919, 2854, 1608, 1465, 1176, 1101, 821, 748 cm$^{-1}$. **HRMS (ESI)** calculated for C$_{17}$H$_{12}$F$_3$N$_2$O$_3$S [M–H]$^-$: 381.0521, found: 381.0522.

6.4. **Synthesis of (8a$R$,13bS,13c$R$)-8a-(1H-indol-3-yl)-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (11)$^6$: 

Under argon atmosphere, a flame-dried Schlenk tube was charged with 2-methoxy indoline 7aa (0.1 mmol), chiral phosphoric acid (0.005 mmol), 4Å MS (5 mg), and DCM (1.0 mL). The solution was stirred at room temperature for 10 min then indole (0.2 mmol) was added in one portion and continued stirring for 16 h. After the reaction was completed (monitored by TLC), the reaction mixture was quenched by adding cool water and extracted with CH$_2$Cl$_2$ (3 × 10 mL). The combined organic layers were washed with water and brine, then dried over Na$_2$SO$_4$, filtrated, and concentrated under vacuum. The residue was purified by silica gel column chromatography (MeOH/DCM = 1/1) to afford the desired product 11 (48 mg, yield: 82%) as white solid, m.p. = 129.9 – 130.5 °C. The enantiomeric excess (99% ee) was determined by chiral HPLC using CHIRALPAK® IA (n-hexane/isopropanol = 90.0/10.0, flow rate 1.0 mL/min, $\lambda$ = 254 nm) t (minor) = 29.183 min, t (major) = 63.867 min. [\(\alpha\)]$_{D}^{25}$ = +132.1 (c = 0.4, CHCl$_3$, 99% ee). **$^1$H NMR** (500 MHz, CDCl$_3$) $\delta$ 8.25 (s, 1H), 7.37 – 7.40 (m, 3H), 7.30 (d, $J$ = 7.9 Hz, 1H), 7.20 – 7.26 (m, 3H), 7.10 – 7.16 (m, 2H), 6.96 – 6.99 (m, 1H), 6.87 – 6.91 (m, 2H), 6.82 (d, $J$ = 8.2 Hz, 1H), 5.39 (s, 1H), 4.95 (d, $J$ = 10.4 Hz, 1H), 4.60 (s, 1H), 4.20 (d, $J$ = 10.4 Hz, 1H). **$^{13}$C NMR** (126 MHz, CDCl$_3$) $\delta$ 150.7, 149.4, 136.8, 130.8, 130.2, 128.9, 125.6, 125.1, 124.8, 124.6 (q, $J$ = 282.4 Hz), 124.1, 123.7, 122.5, 121.2, 120.4, 119.9, 119.7, 119.2, 113.5, 111.4, 110.4, 77.9, 72.1, 69.0 (q, $J$ = 24.8 Hz), 59.6. **$^{19}$F NMR** (282 MHz, CDCl$_3$) $\delta$ –62.45 (s, 3F). **IR (KBr)**: 3405, 3060, 2960, 1608, 1482, 1465, 1268, 1178, 1103, 835 cm$^{-1}$. **HRMS (ESI)** calculated for C$_{25}$H$_{17}$F$_3$N$_3$O$_3$S [M–H]$^-$: 496.0943, found: 496.0941.
7. General Procedure for Cu-catalyzed decarboxylative annulation reaction of Me-benzoxazinanone (Method F):

In an argon filled glove box, a flame-dried 10 mL Schlenk tube was charged with copper(II) trifluoromethanesulfonate (1.81 mg, 0.005 mmol, 5 mol%), 2,6-bis[(4R)-phenyl-2-oxazolin-2-yl]-pyridine L2 (3.69 mg, 0.01 mmol, 10 mol%) and anhydrous Toluene (1 mL). The resulting solution was stirred for 1 h at 80 °C. In an argon filled glove box, Me-benzoxazinanone 4 (0.1 mmol) and DIPEA (8.7 μL, 0.05 mmol, 0.5 equiv) were added. The resulting solution was stirred at room temperature until complete conversion of Me-benzoxazinanone 4 (monitored by TLC). The reaction was quenched by saturated NH₄Cl aqueous solution (2 mL). The resulting solution was extracted with ethyl acetate (5 mL × 3). The combined organic layers were dried over Na₂SO₄, filtered and concentrated in vacuo. The diastereomeric ratio and crude yield were determined by ¹⁹F NMR analysis of the crude reaction mixture. The residue was purified by flash silica gel chromatography (Hexane/EtOAc) to afford the title compound 5. The characterization data of 5 are summarized below.

**2'-Methylene-1',9-ditosyl-1,3,4,9-tetrahydrospiro[carbazole-2,3'-indoline] [5a (2C)]**

Following the general method F, compound 5a (2C) was obtained as a light yellow solid (21.9 mg, Yield: 71%), m.p. = 156.2 – 157.2 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.19 (d, J = 8.2 Hz, 1H), 7.93 (d, J = 8.2 Hz, 1H), 7.61 (d, J = 8.2 Hz, 2H), 7.43 (d, J = 8.5 Hz, 2H), 7.26 – 7.36 (m, 4H), 7.22 (d, J = 8.2 Hz, 2H), 7.06 (d, J = 8.2 Hz, 2H), 6.88 – 6.91 (m, 1H), 6.70 (d, J = 7.3 Hz, 1H), 5.67 (d, J = 2.1 Hz, 1H), 4.53 (d, J = 2.1 Hz, 1H), 3.10 (dd, J = 26.6, 18.3 Hz, 2H), 2.44 – 2.53 (m, 2H), 2.36 (s, 3H), 2.31 (s, 3H), 1.30 – 1.34 (m, 1H), 1.10 – 1.13 (m, 1H). ¹³C NMR (126 MHz, CDCl₃) δ 152.7, 144.8, 144.7, 140.4, 136.6, 136.6, 135.6, 134.1, 133.2, 129.7, 129.4, 129.3, 128.3,
127.2, 126.2, 124.8, 124.5, 123.5, 123.0, 118.2, 118.1, 116.7, 114.7, 97.4, 47.4, 36.7, 33.9, 21.6, 21.5, 17.6. **IR (KBr):** 3063, 2959, 2921, 1598, 1492, 1474, 1454, 1263, 866, 750 cm\(^{-1}\). **HRMS (ESI)** calculated for C\(_{34}H_{30}N_{2}O_{4}S_{2}\) \([M+Na]^{+}\): 617.1545, found: 617.1531.

**5',6-Dichloro-2'-methylene-1',9-ditosyl-1,3,4,9-tetrahydrospiro[carbazole-2,3'-indoline] [5b (2C)]:**

Following the general method F, compound 5b (2C) was obtained as a light yellow solid (22.9 mg, Yield: 67%), m.p. = 163.1 – 163.8 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.13 (d, \(J = 8.9 \) Hz, 1H), 7.87 (d, \(J = 8.9 \) Hz, 1H), 7.60 (d, \(J = 8.2 \) Hz, 2H), 7.38 (d, \(J = 8.5 \) Hz, 2H), 7.31 – 7.32 (m, 1H), 7.24 – 7.29 (m, 4H), 7.09 (d, \(J = 13.1 \) Hz, 2H), 6.55 (d, \(J = 2.1 \) Hz, 1H), 5.69 (d, \(J = 2.4 \) Hz, 1H), 4.53 (d, \(J = 2.1 \) Hz, 1H), 3.06 (s, 2H), 2.39 – 2.53 (m, 2H), 2.39 (s, 3H), 2.33 (s, 3H), 1.23 – 1.28 (m, 1H), 1.08 – 1.13 (m, 1H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 152.2, 145.3, 145.2, 139.1, 138.3, 135.2, 135.0, 134.2, 133.8, 130.4, 130.2, 129.9, 129.5, 129.5, 128.6, 127.2, 126.0, 124.7, 123.1, 118.2, 117.8, 117.4, 115.8, 97.9, 47.4, 36.5, 33.6, 21.7, 21.6, 17.4. **IR (KBr):** 3060, 2925, 2845, 1650, 1596, 1457, 1291, 909, 805, 704 cm\(^{-1}\). **HRMS (ESI)** calculated for C\(_{34}H_{28}N_{2}O_{4}S_{2}Cl_{2}\) \([M+Na]^{+}\): 685.0765, found: 685.0748.

**5,5'-Dibromo-2'-methylene-1',9-ditosyl-1,3,4,9-tetrahydrospiro[carbazole-2,3'-indoline] [5c (2C)]:**

Following the general method F, compound 5c (2C) was obtained as a light yellow solid (23.2 mg, Yield: 60%), m.p. = 169.1 – 170.0 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.07 (d, \(J = 8.9 \) Hz, 1H), 7.82 (d, \(J = 8.5 \) Hz, 1H), 7.59 (d, \(J = 7.9 \) Hz, 2H), 7.48 (s, 1H), 7.39 – 7.43 (m, 4H), 7.24 – 7.26
(m, 2H), 7.11 (d, J = 7.9 Hz, 2H), 6.73 (s, 1H), 5.67 (d, J = 1.8 Hz, 1H), 4.50 (d, J = 1.8 Hz, 1H), 3.08 (s, 2H), 2.43 – 2.54 (m, 2H), 2.39 (s, 3H), 2.34 (s, 3H), 1.24 – 1.29 (m, 1H), 1.03 – 1.08 (m, 1H). 13C NMR (126 MHz, CDCl3) δ 152.0, 145.3, 145.2, 139.6, 138.7, 135.3, 135.2, 134.0, 133.8, 131.5, 130.9, 130.0, 129.5, 127.4, 127.2, 126.0, 125.9, 121.2, 118.2, 117.8, 117.3, 117.1, 116.1, 97.9, 47.6, 36.4, 33.6, 21.7, 17.5. IR (KBr): 3066, 2923, 2845, 1650, 1492, 1456, 1273, 906, 876, 759 cm⁻¹. HRMS (ESI) calculated for C₃₄H₂₈N₂O₄Na₂S₂Br₂ [M+Na]+: 772.9755, found: 772.9729.

5',6-Dibromo-2'-methylene-1',9-ditosyl-1,2,4,9-tetrahydropyrido[carbazole-3,3'-indoline] [5c (3C)]:

Following the general method F, compound 5c (3C) was obtained as a yellow solid, m.p. = 169.1 – 170.0 °C. 1H NMR (500 MHz, CDCl3) δ 8.05 (d, J = 8.9 Hz, 1H), 7.80 (d, J = 8.9 Hz, 1H), 7.64 (d, J = 7.9 Hz, 2H), 7.56 (d, J = 7.9 Hz, 2H), 7.39 – 7.42 (m, 2H), 7.26 – 7.28 (m, 5H), 6.81 (s, 1H), 5.60 (d, J = 2.4 Hz, 1H), 4.45 (d, J = 2.1 Hz, 1H), 2.97 – 3.03 (m, 1H), 2.84 – 2.90 (m, 1H), 2.54 (s, 2H), 2.47 (s, 3H), 2.38 (s, 3H), 1.34 – 1.40 (m, 1H), 1.17 – 1.22 (m, 1H). 13C NMR (126 MHz, CDCl3) δ 152.2, 145.4, 145.1, 139.7, 139.1, 135.5, 135.3, 134.9, 133.9, 131.6, 131.1, 130.3, 129.5, 127.4, 127.3, 126.2, 125.8, 120.9, 118.4, 117.9, 117.0, 115.9, 97.8, 46.0, 34.7, 32.9, 21.8, 21.7, 20.9. IR (KBr): 3062, 2924, 2857, 1595, 1363, 1456, 1232, 813, 773, 756 cm⁻¹. HRMS (ESI) calculated for C₃₄H₂₈N₂O₄Na₂S₂Br₂ [M+Na]+: 772.9755, found: 772.9729.

6',7-Difluoro-2'-methylene-1',9-ditosyl-1,3,4,9-tetrahydropyrido[carbazole-2,3'-indoline] [5d (2C)]:
Following the general method F, compound 5d (2C) was obtained as a light yellow solid (25.5 mg, Yield: 78%), m.p. = 157.3 – 158.1 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.93 (dd, \(J = 10.2, 2.3\) Hz, 1H), 7.69 (d, \(J = 10.4\) Hz, 1H), 7.65 (s, 2H), 7.41 (d, \(J = 8.5\) Hz, 2H), 7.25 – 7.28 (m, 3H), 7.09 (d, \(J = 8.5\) Hz, 2H), 7.00 – 7.04 (m, 1H), 6.54 (dd, \(J = 7.0, 1.2\) Hz, 2H), 5.69 (d, \(J = 2.4\) Hz, 1H), 4.54 (d, \(J = 2.4\) Hz, 1H), 3.03 (s, 2H), 2.42 – 2.57 (m, 2H), 2.38 (s, 3H), 2.34 (s, 3H), 1.25 – 1.33 (m, 1H), 1.16 – 1.21 (m, 1H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 163.7, 161.8 (d, \(J = 14.5\) Hz), 159.9, 152.8, 145.2 (d, \(J = 4.5\) Hz), 141.6 (d, \(J = 11.8\) Hz), 136.8 (d, \(J = 12.7\) Hz), 135.4, 133.9, 133.1 (d, \(J = 3.6\) Hz), 131.9 (d, \(J = 2.7\) Hz), 129.9, 129.5, 127.2, 126.2, 125.5, 123.7 (d, \(J = 10.0\) Hz), 118.9 (d, \(J = 10.0\) Hz), 117.6, 111.7 (d, \(J = 23.6\) Hz), 111.3 (d, \(J = 21.8\) Hz), 104.7 (d, \(J = 28.2\) Hz), 102.4 (d, \(J = 29.1\) Hz), 97.3, 46.8, 36.8, 33.9, 21.7, 21.6, 17.6. \(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \(\delta\) −112.56 – −112.64 (m, 1F), −116.88 – −116.97 (m, 1F). IR (KBr): 3062, 2925, 2849, 1650, 1599, 1432, 1295, 931, 811, 754 cm\(^{-1}\). HRMS (ESI) calculated for C\(_{34}\)H\(_{28}\)N\(_2\)O\(_4\)F\(_2\)Na\(_2\)[M+Na]\(^+\): 653.1356, found: 653.1366.

6',7-Dimethyl-2'-methylene-1',9-ditosyl-1,3,4,9-tetrahydrospiro[carbazole-2,3'-indoline] [5e (2C)]:

Following the general method F, compound 5e (2C) was obtained as a white solid (25.5 mg, Yield: 79%), m.p. = 155.7 – 156.4 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.00 (s, 1H), 7.76 (s, 1H), 7.61 (d, \(J = 8.5\) Hz, 2H), 7.43 (d, \(J = 8.2\) Hz, 2H), 7.21 – 7.23 (m, 3H), 7.06 – 7.09 (m, 3H), 6.69 (d, \(J = 7.6\) Hz, 1H), 6.56 (d, \(J = 7.9\) Hz, 1H), 5.62 (d, \(J = 2.1\) Hz, 1H), 4.49 (d, \(J = 2.1\) Hz, 1H), 2.99 – 3.08 (m, 2H), 2.50 (s, 3H), 2.44 – 2.48 (m, 2H), 2.40 (s, 3H), 2.36 (s, 3H), 2.32 (s, 3H), 1.24 – 1.31 (m, 1H), 1.04 – 1.09 (m, 1H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 153.0, 144.7, 144.6, 140.5, 138.4, 137.0, 135.8, 134.5, 134.2, 133.8, 132.5, 129.7, 129.4, 127.4, 127.1, 126.2, 125.5, 124.8, 122.7, 118.0, 117.8, 117.1, 114.9, 97.3, 47.1, 36.7, 33.9, 22.0, 21.8, 21.6, 21.6, 17.7. IR (KBr): 3061, 2920, 2849, 1651, 1597, 1455, 1295, 868, 811, 778 cm\(^{-1}\). HRMS (ESI) calculated for C\(_{36}\)H\(_{34}\)N\(_2\)O\(_4\)Na\(_2\)[M+Na]\(^+\): 645.1845, found: 645.1858.
8. Applications of spiro carbazole/indole skeleton

**Synthesis of (S)-2'-methyl-1,3,4,9-tetrahydrospiro[carbazole-2,3'-indole] (12):**

Under argon atmosphere, a flame-dried Schlenk tube was charged with compound 5a (0.1 mmol, 1 equiv), Mg powder (1.0 mmol, 10 equiv), THF (0.3 mL) and MeOH (0.7 mL). The resulting solution was left for 24 h at room temperature under sonication. The mixture was filtered through a celite pad and concentrated under reduced pressure and purified by flash column chromatography (using Toluene) to obtain the pure product 12 as a pale yellow solid (9.2 mg, Yield: 32%), m.p. = 169.3 – 170.1 °C. 

**1H NMR** (500 MHz, CDCl$_3$) δ 7.82 (s, 1H), 7.57 – 7.60 (m, 2H), 7.35 – 7.37 (m, 1H), 7.29 – 7.32 (m, 1H), 7.16 – 7.23 (m, 2H), 6.99 – 7.00 (m, 2H), 3.30 (d, $J = 15.9$ Hz, 1H), 3.07 – 3.12 (m, 1H), 2.99 – 3.03 (m, 1H), 2.48 (d, $J = 15.9$ Hz, 1H), 2.38 (s, 3H), 2.25 – 2.31 (m, 1H), 1.60 – 1.62 (m, 1H). 

**13C NMR** (126 MHz, CDCl$_3$) δ 186.1, 154.0, 142.8, 136.2, 131.0, 128.0, 127.1, 125.1, 123.2, 121.8, 120.0, 119.5, 118.2, 110.7, 109.6, 56.7, 28.8, 28.8, 18.6, 16.2. 

**IR** (KBr): 3415, 3060, 2927, 2846, 1590, 1452, 1379, 1258, 871, 758 cm$^{-1}$. 

**HRMS (ESI)** calculated for C$_{20}$H$_{19}$N$_2$ [M+H]$^+$: 287.1548, found: 287.1548.

**Synthesis of (S)-2'-methylene-5',6-diphenyl-1',9-ditosyl-1,3,4,9-tetrahydrospiro[carbazole-2,3'-indoline] (13):**

In a flame dried Schlenk tube 1 mL Toluene was taken. The solvent was degassed by using standard “freeze-pump-thaw” method. The process was repeated for three times and finally the
Schlenk tube was filled with argon gas. After that, Pd$_2$(dba)$_3$ (10 mol%, 2.7 mg) and triphenylphosphine (40 mol%, 3.1 mg) were taken in the tube inside the glove box and allowed to stir for 5 min. To the above mixture, 5c (2C) (0.03 mmol, 1.0 equiv, 22.6 mg), phenylboronic acid (0.063 mmol, 2.1 equiv, 7.7 mg) and Cs$_2$CO$_3$ (0.12 mmol, 4.0 equiv, 39 mg) were added and removed from the glove box. The mixture was allowed to stir at 110 °C for 6 h under Ar. After completion, the reaction was quenched by saturated NH$_4$Cl aqueous solution (2 mL) at room temperature and extracted with CH$_2$Cl$_2$ (3×5 mL). The combined organic layers were washed with water and brine, then dried over Na$_2$SO$_4$, filtrated, and concentrated under vacuum. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 19/1) to afford the desired product 13 (12.5 mg, yield: 56 %) as pale yellow solid. m.p. = 192.1 – 192.7 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.24 (d, $J$ = 7.9 Hz, 1H), 8.00 (d, $J$ = 5.5 Hz, 1H), 7.63 – 7.66 (m, 4H), 7.55 – 7.58 (m, 3H), 7.44 – 7.50 (m, 4H), 7.28 – 7.37 (m, 6H), 7.24 – 7.25 (m, 2H), 7.05 (d, $J$ = 2.1 Hz, 1H), 7.00 (d, $J$ = 7.9 Hz, 2H), 5.65 (d, $J$ = 2.1 Hz, 1H), 4.51 (d, $J$ = 2.1 Hz, 1H), 3.23 (dd, $J$ = 43.3, 18.6 Hz, 2H), 2.54 – 2.56 (m, 2H), 2.38 (s, 3H), 2.19 (s, 3H), 1.39 – 1.44 (m, 1H), 1.00 – 1.05 (m, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 152.5, 144.9, 141.1, 140.1, 139.8, 137.9, 137.5, 136.9, 136.0, 135.6, 134.2, 133.7, 129.8, 129.5, 128.8, 127.3, 127.3, 127.2, 127.1, 126.6, 126.2, 123.9, 121.3, 118.3, 116.9, 116.7, 114.8, 97.7, 47.5, 36.5, 33.8, 21.7, 21.5, 17.6. IR (KBr): 3059, 2955, 2854, 1596, 1459, 1365, 1259, 898, 810, 746 cm$^{-1}$. HRMS (ESI) calculated for C$_{46}$H$_{38}$N$_2$O$_4$NaS$_2$ [M+Na]$^+$: 769.2171, found: 769.2181.

9. General Procedure for Cu-catalyzed decarboxylative annulation reaction of 4-ethynyl benzoxazinanone (Method G):

\[ \begin{align*}
4 & \quad \text{Cu(OTf)$_2$ (5 mol\%),} \\
6 & \quad \text{L2 (10 mol\%),} \\
8 & \quad \text{i-Pr$_2$NEt (0.5 equiv), Toluene, 10 °C}
\end{align*} \]

In an argon filled glove box, a flame-dried 10 mL Schlenk tube was charged with copper(II) trifluoromethanesulphonate (1.81 mg, 0.005 mmol, 5 mol%), 2,6-bis[(4R)-phenyl-2-oxazolin-2-yl]-pyridine L2 (3.69 mg, 0.01 mmol, 10 mol%) and anhydrous Toluene (1 mL). The resulting solution was stirred for 1 h at 80 °C. In an argon filled glove box, 4-ethynyl benzoxazinanone 14 (0.1 mmol), sulfamate-derived cyclic imine 2 (0.11 mmol) and DIPEA (8.7 μL, 0.05 mmol, 0.5 equiv) were
added. The resulting solution was stirred at 10 °C until complete conversion of ethynyl benzoxazinanones (monitored by TLC). The reaction was quenched by saturated NH₄Cl aqueous solution (2 mL). The resulting solution was extracted with ethyl acetate (5 mL × 3). The combined organic layers were dried over Na₂SO₄, filtered and concentrated in vacuo. The diastereomeric ratio and crude yield were determined by ¹H NMR analysis of the crude reaction mixture. The residue was purified by flash silica gel chromatography to afford the title compound 15. The characterization data of 3 are summarized below.

8-Ethynyl-13-tosyl-13a-dihydro-8H-benzo[5,6][1,2,3]oxathiazino[4,3-b]quinazoline 6,6 dioxide (15a):

Following the general method G, compound 15a was obtained as a white solid (25.4 mg, Yield: 52%), m.p. = 172.1 – 173.1 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.05 (d, J = 9.2 Hz, 1H), 7.39 – 7.44 (m, 4H), 7.31 – 7.34 (m, 1H), 7.25 – 7.28 (m, 2H), 7.18 – 7.19 (m, 3H), 7.10 (t, J = 7.8 Hz, 1H), 6.92 (d, J = 7.3 Hz, 1H), 4.86 (d, J = 2.4 Hz, 1H), 2.39 (s, 3H), 2.12 (d, J = 2.7 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ 152.6, 145.1, 133.3, 131.1, 130.2, 129.5, 128.9, 128.3, 128.1, 127.6, 127.4, 126.2, 125.1, 124.9, 117.5, 117.1, 79.4, 74.8, 66.8, 45.6, 21.7. IR (KBr): 3290, 3077, 2959, 1595, 1455, 1250, 924, 863, 772, 704 cm⁻¹. HRMS (ESI) calculated for C₂₃H₁₈N₂O₅NaS₂ [M+Na]^+: 489.0555, found: 489.0550.

2-Bromo-8-ethynyl-13-tosyl-13a-dihydro-8H-benzo[5,6][1,2,3]oxathiazino[4,3-b] quinazoline 6,6-dioxide (15e):
Following the general method G, compound 15e was obtained as a white solid (36.3 mg, Yield: 64%), m.p. = 177.7 – 178.4 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.06 – 8.07 (m, 1H), 7.55 – 7.55 (m, 1H), 7.42 – 7.48 (m, 2H), 7.37 – 7.40 (m, 3H), 7.29 – 7.32 (m, 1H), 7.18 – 7.21 (m, 3H), 6.81 (d, $J = 8.5$ Hz, 1H), 4.86 (d, $J = 2.4$ Hz, 1H), 2.39 (s, 3H), 2.16 (d, $J = 2.4$ Hz, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 151.5, 145.3, 134.2, 133.1, 129.6, 129.2, 129.0, 128.3, 128.0, 127.9, 127.4, 124.6, 119.4, 119.0, 118.8, 117.8, 79.2, 75.3, 66.4, 45.6, 21.7. IR (KBr): 3301, 3063, 2966, 1597, 1492, 1453, 1249, 905, 855, 704 cm$^{-1}$. HRMS (ESI) calculated for C$_{23}$H$_{17}$N$_2$O$_5$NaS$_2$Br [M+Na]$^+$: 566.9660, found: 566.9653.

10. X-Ray crystallographic analysis of products

![Diagram of 3aa](CCDC: 2026703)

![Diagram of 7aa](CCDC: 2026704)

![Diagram of 5c (2C)](CCDC: 2026705)

![Diagram of 15a](CCDC: 2026702)
11. Computational methods

Two-types of potential conformations of zwitterionic Cu-allenylidene intermediates I (X=CF₃), I’ (X= Me), and I” (X=H) were used as initial structures for geometry optimizations. Ligand L₁ was used instead of L₂ for computation to simplify their calculations. The Gaussian 16 program was used for the DFT calculations. The geometry optimizations and energy calculations were carried out at the B3LYP/6-311G** level with Grimme’s dispersion correction methods of the D3. Atomic charge distributions were calculated from the B3LYP/6-311G** level wave functions by electrostatic potential fitting using the Merz-Singh-Kollman scheme.

Supplementary Figure 1. a) The optimized geometries of I and Ia (with L₁) with their relative energy. b) The optimized geometries of I’ and I’a (with L₁) with their relative energy. c) The optimized geometries of I” and I”a (with L₁) with their relative energy.
**Supplementary Figure 2.** Atomic charge distributions of a) I (with L1), I’ (with L1) and I” (with L1).

**Supplementary Figure 3.** a) The optimized geometry of II (with L1) with its atomic charge distributions. b) The optimized geometry of II’ (II”) (with L1) with its atomic charge distributions.
12. HPLC Data and NMR Data:

(13b$S$,13c$R$)-9-Tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3aa):

HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, $\lambda = 254$ nm)

Supplementary Figure 4. Determination of enantiomeric excess of 3aa.

(13b$S$,13c$R$)-2-Methyl-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo [5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ab):

HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, $\lambda = 254$ nm).
Supplementary Figure 5. Determination of enantiomeric excess of 3ab.

(13bS,13cR)-2-Methoxy-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo [5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ac):

HPLC using CHIRALPAK® IA (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, \( \lambda = 254 \text{ nm} \)).

Supplementary Figure 6. Determination of enantiomeric excess of 3ac.
(13b$S$,13c$R$)-2-Fluoro-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9$H$-benzo [5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-$b$]indole 6,6-dioxide (3ad):

HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, $\lambda = 254$ nm).

Supplementary Figure 7. Determination of enantiomeric excess of 3ad.

(13b$S$,13c$R$)-2-Bromo-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9$H$-benzo [5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-$b$]indole 6,6-dioxide (3ae):

HPLC using CHIRALPAK® IA (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, $\lambda = 254$ nm).
Supplementary Figure 8. Determination of enantiomeric excess of 3ae.

(13bS,13cR)-2-Nitro-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3af):

HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, λ = 254 nm).
**Supplementary Figure 9.** Determination of enantiomeric excess of 3af. 

(13b$^S$,13c$^R$)-3-Methyl-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo [5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ag): 

HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, \( \lambda = 254 \text{ nm} \)).

**Supplementary Figure 10.** Determination of enantiomeric excess of 3ag. 

(13b$^S$,13c$^R$)-3-Methoxy-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo [5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ah): 

HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, \( \lambda = 254 \text{ nm} \)).
Supplementary Figure 11. Determination of enantiomeric excess of 3ah.

(13bS,13cR)-3-Chloro-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ai):

HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, \( \lambda = 254 \text{ nm} \)).
Supplementary Figure 12. Determination of enantiomeric excess of 3ai.

(13bS,13cR)-9-Tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-naphtho[2'',1''':5',6''][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-6]indole 6,6-dioxide (3aj):

HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, λ = 254 nm).

```
| No. | tR (min) | Area (%) | Height (%) |
|-----|----------|----------|------------|
| 1   | 18.600   | 50.084   | 60.843     |
| 2   | 28.750   | 49.916   | 39.157     |
```

Supplementary Figure 13. Determination of enantiomeric excess of 3aj.

(13bS,13cR)-9-Tosyl-11,13b-bis(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'] [1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-6]indole 6,6-dioxide (3ba):

HPLC using CHIRALPAK® IG (n-hexane/isopropanol = 90.0/10.0, flow rate 1.0 mL/min, λ = 254 nm).
Supplementary Figure 14. Determination of enantiomeric excess of 3ba.

Methyl (13bS,13cR)-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3] oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole-11-carboxylate 6,6-dioxide (3ca):

HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, \( \lambda = 254 \text{ nm} \)).

Supplementary Figure 15. Determination of enantiomeric excess of 3ca.
(13bS,13cR)-12-Fluoro-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3da):

HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, $\lambda = 254$ nm).

Supplementary Figure 16. Determination of enantiomeric excess of 3da.

(13bS,13cR)-12-Fluoro-2-methyl-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3db):

HPLC using CHIRALPAK® IG (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, $\lambda = 254$ nm).
Supplementary Figure 17. Determination of enantiomeric excess of 3db.

(13bS,13cR)-12-Chloro-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo [5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ea):

HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, \( \lambda = 254 \text{ nm} \)).

Supplementary Figure 18. Determination of enantiomeric excess of 3ea.
(13bS,13cR)-12-Chloro-2-methoxy-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3ec):

HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 90.0/10.0, flow rate 1.0 mL/min, \( \lambda = 254 \text{ nm} \)).

Supplementary Figure 19. Determination of enantiomeric excess of 3ec.

(13bS,13cR)-12-Methyl-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (3fa):

HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, \( \lambda = 254 \text{ nm} \)).
Supplementary Figure 20. Determination of enantiomeric excess of 3fa.

(13bS,13cR)-2-Phenyl-9-tosyl-13b-(trifluoromethyl)-13b,13c-dihydro-9H-benzo
[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (6):

| No. | tR (min) | Area (%) | Height (%) |
|-----|----------|----------|------------|
| 1   | 15.367   | 50.033   | 75.347     |
| 2   | 43.650   | 49.967   | 24.653     |

| No. | tR (min) | Area (%) | Height (%) |
|-----|----------|----------|------------|
| 1   | 15.333   | 99.200   | 99.619     |
| 2   | 43.892   | 0.800    | 0.381      |

HPLC using CHIRALPAK® IC (n-hexane/isopropanol = 85.0/15.0, flow rate 1.0 mL/min, \( \lambda = 254 \text{ nm} \)).
Supplementary Figure 21. Determination of enantiomeric excess of 6.

(13b$\text{S}$,13c$\text{R}$)-8a-Methoxy-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (7aa):

HPLC using CHIRALPAK® OD-3 (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, $\lambda$ = 254 nm).
Supplementary Figure 22. Determination of enantiomeric excess of 7aa.

(8aS,13bS,13cR)-8a-methoxy-2-methyl-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole-6,6-dioxide (7ab):

HPLC using CHIRALPAK® OD-3 (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, λ = 254 nm).

Supplementary Figure 23. Determination of enantiomeric excess of 7ab.

(8aS,13bS,13cR)-2,8a-dimethoxy-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (7ac):

HPLC using CHIRALPAK® IA (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, λ = 254 nm).
Supplementary Figure 24. Determination of enantiomeric excess of 7ac.

\[(8aS,13bS,13cR)-2-fluoro-8a-methoxy-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (7ad):

HPLC using CHIRALPAK® OD-3 (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, λ = 230 nm).

Supplementary Figure 25. Determination of enantiomeric excess of 7ad.

| No. | tR (min) | Area (%) | Height (%) |
|-----|----------|----------|------------|
| 1   | 17.942   | 50.007   | 66.814     |
| 2   | 35.458   | 49.993   | 33.186     |

| No. | tR (min) | Area (%) | Height (%) |
|-----|----------|----------|------------|
| 1   | 18.767   | 0.183    | 0.475      |
| 2   | 35.225   | 99.817   | 99.525     |
(8aS,13bS,13cR)-8a-methoxy-3-methyl-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (7ag):

HPLC using CHIRALPAK® OD-3 (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, λ = 230 nm).

![Supplementary Figure 26: Determination of enantiomeric excess of 7ag.](image)

| No. | tR (min) | Area (%) | Height (%) |
|-----|---------|----------|------------|
| 1   | 18.750  | 50.052   | 61.368     |
| 2   | 27.442  | 49.948   | 38.612     |

Supplementary Figure 26. Determination of enantiomeric excess of 7ag.

(8aS,13bS,13cR)-3,8a-dimethoxy-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (7ah):

HPLC using CHIRALPAK® OD-3 (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, λ = 230 nm).
Supplementary Figure 27. Determination of enantiomeric excess of 7ah.

(8aS,13bS,13cR)-12-fluoro-8a-methoxy-2-methyl-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (7db):

HPLC using CHIRALPAK® IA (n-hexane/isopropanol = 90.0/10.0, flow rate 1.0 mL/min, \( \lambda = 254 \, \text{nm} \)).

Supplementary Figure 28. Determination of enantiomeric excess of 7db.
(8aS,13bS,13cR)-12-chloro-8a-methoxy-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (7ea):

HPLC using CHIRALPAK® OD-3 (n-hexane/isopropanol = 97.0/3.0, flow rate 0.8 mL/min, λ = 254 nm).

Supplementary Figure 29. Determination of enantiomeric excess of 7ea.

(8aR,13bS,13cR)-8a-allyl-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-8H-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole (8):

HPLC using CHIRALPAK® IA (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, λ = 254 nm).
Supplementary Figure 30. Determination of enantiomeric excess of **8**.

(8aR,13bS,13cR)-13b-(trifluoromethyl)-13b,13c-dihydro-8H-benzo[5',6'][1,2,3]oxathiazino [3',4':1,5]pyrrolo[3,4-b]indole-8a(9H)-carbonitrile 6,6-dioxide (9):

HPLC using CHIRALPAK® OD-3 (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, \( \lambda = 254 \) nm).
**Supplementary Figure 31.** Determination of enantiomeric excess of 9.

(8a\(R\),13b\(R\),13c\(R\))-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-\(8H\)-benzo[5',6']\[1,2,3\]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (10):

HPLC using CHIRALPAK® OD-3 (n-hexane/isopropanol = 95.0/5.0, flow rate 1.0 mL/min, \(\lambda = 254\) nm).

| No. | tR (min) | Area (%) | Height (%) |
|-----|----------|----------|------------|
| 1   | 25.250   | 49.994   | 54.705     |
| 2   | 29.992   | 50.006   | 45.295     |

**Supplementary Figure 32.** Determination of enantiomeric excess of 10.

(8a\(R\),13b\(S\),13c\(R\))-8a-(1\(H\)-indol-3-yl)-13b-(trifluoromethyl)-8a,9,13b,13c-tetrahydro-\(8H\)-benzo[5',6'][1,2,3]oxathiazino[3',4':1,5]pyrrolo[3,4-b]indole 6,6-dioxide (11):

HPLC using CHIRALPAK® IA (n-hexane/isopropanol = 90.0/10.0, flow rate 1.0 mL/min, \(\lambda = 254\) nm).

| No. | tR (min) | Area (%) | Height (%) |
|-----|----------|----------|------------|
| 1   | 25.183   | 0.108    | 0.237      |
| 2   | 29.858   | 99.892   | 99.763     |
Supplementary Figure 33. Determination of enantiomeric excess of 11.

| No. | t_R (min) | Area (%) | Height (%) |
|-----|-----------|----------|------------|
| 1   | 29.092    | 50.057   | 68.518     |
| 2   | 63.442    | 49.943   | 31.482     |

| No. | t_R (min) | Area (%) | Height (%) |
|-----|-----------|----------|------------|
| 1   | 29.183    | 0.527    | 1.239      |
| 2   | 63.867    | 99.473   | 98.761     |
Supplementary Figure 34. $^1$H NMR of 1f.
Supplementary Figure 35. $^{13}$C NMR of 1f.
Supplementary Figure 36. $^{19}$F NMR of 1f.
Supplementary Figure 37. $^1$H NMR of 3aa.
Supplementary Figure 38. $^{13}$C NMR of 3aa.
Supplementary Figure 39. $^{19}$F NMR of 3aa.
Supplementary Figure 40. $^1$H NMR of 3ab.
Supplementary Figure 41. $^{13}$C NMR of 3ab.
Supplementary Figure 42. $^{19}$F NMR of 3ab.
Supplementary Figure 43. $^1$H NMR of 3ac.
Supplementary Figure 44. $^{13}$C NMR of 3ac.
Supplementary Figure 45. $^{19}$F NMR of 3ac.
Supplementary Figure 46. $^1$H NMR of 3ad.
Supplementary Figure 47. $^{13}$C NMR of 3ad.
Supplementary Figure 48. $^{19}\text{F}$ NMR of 3ad.
Supplementary Figure 49. $^1$H NMR of 3ae.
Supplementary Figure 50. $^{13}$C NMR of 3ae.
Supplementary Figure 51. $^{19}$F NMR of 3ae.
Supplementary Figure 52. $^1$H NMR of 3af.
Supplementary Figure 53. $^{13}$C NMR of 3af.

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Supplementary Figure 54. $^{19}$F NMR of 3af.
Supplementary Figure 55. $^1$H NMR of 3ag.
Supplementary Figure 56. $^{13}$C NMR of 3ag.
Supplementary Figure 57. $^{19}$F NMR of 3ag.
Supplementary Figure 58. $^1$H NMR of 3ah.
Supplementary Figure 59. $^{13}$C NMR of 3ah.
Supplementary Figure 60. $^{19}$F NMR of 3ah.
Supplementary Figure 61. $^1$H NMR of 3ai.
Supplementary Figure 62. $^{13}\text{C}$ NMR of 3ai.
Supplementary Figure 63. $^{19}$F NMR of 3ai.
Supplementary Figure 64. $^1$H NMR of 3aj.
Supplementary Figure 65. $^{13}$C NMR of 3aj.
Supplementary Figure 66. $^{19}$F NMR of 3aj.
Supplementary Figure 67. $^1$H NMR of 3ba.
Supplementary Figure 68. $^{13}$C NMR of 3ba.
Supplementary Figure 69. $^{19}$F NMR of 3ba.
Supplementary Figure 70. $^1$H NMR of 3ca.
Supplementary Figure 71. $^{13}$C NMR of 3ca.
Supplementary Figure 72. $^{19}$F NMR of 3ca.
Supplementary Figure 73. $^1$H NMR of 3da.
Supplementary Figure 74. \(^{13}\text{C}\) NMR of 3da.
Supplementary Figure 75. $^{19}$F NMR of 3da.
Supplementary Figure 76. $^1$H NMR of 3db.
Supplementary Figure 77. $^{13}$C NMR of 3db.
Supplementary Figure 78. $^{19}$F NMR of 3db.
Supplementary Figure 79. $^1$H NMR of 3ea.
Supplementary Figure 80. $^{13}$C NMR of 3ea.
Supplementary Figure 81. $^{19}$F NMR of 3ea.
Supplementary Figure 82. $^1$H NMR of 3ec.
Supplementary Figure 83. $^{13}$C NMR of 3ec.
Supplementary Figure 84. $^{19}$F NMR of 3ec.

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Supplementary Figure 85. $^1$H NMR of 3fa.
Supplementary Figure 86. $^{13}$C NMR of 3fa.
Supplementary Figure 87. $^{19}$F NMR of 3fa.
Supplementary Figure 88. $^1$H NMR of 6.
Supplementary Figure 89. $^{13}$C NMR of 6.
Supplementary Figure 90. $^{19}$F NMR of 6.
Supplementary Figure 91. $^1$H NMR of 7aa.
Supplementary Figure 92. $^{13}$C NMR of 7aa.
Supplementary Figure 93. $^{19}$F NMR of 7aa.
Supplementary Figure 94. $^1$H NMR of 7ab.
Supplementary Figure 95. $^{13}$C NMR of 7ab.
Supplementary Figure 96. $^{19}$F NMR of 7ab.
Supplementary Figure 97. $^1$H NMR of 7ac.
Supplementary Figure 98. $^{13}$C NMR of 7ac.
Supplementary Figure 99. $^{19}$F NMR of 7ac.
Supplementary Figure 100. $^1$H NMR of 7ad.
Supplementary Figure 101. $^{13}$C NMR of 7ad.
Supplementary Figure 102. $^{19}$F NMR of 7ad.
Supplementary Figure 103. $^1$H NMR of 7ag.
Supplementary Figure 104. $^{13}$C NMR of 7ag.
Supplementary Figure 105. $^{19}$F NMR of 7ag.
Supplementary Figure 106. $^1$H NMR of 7ah.
Supplementary Figure 107. $^{13}$C NMR of 7ah.
Supplementary Figure 108. $^{19}$F NMR of 7ah.
Supplementary Figure 109. $^1$H NMR of 7db.
Supplementary Figure 110. $^{13}$C NMR of 7db.
Supplementary Figure 111. $^{19}\text{F}$ NMR of 7db.
Supplementary Figure 112. $^1$H NMR of 7ea.
Supplementary Figure 113. $^{13}$C NMR of 7ea.
Supplementary Figure 114. $^{19}$F NMR of 7ea.
Supplementary Figure 115. $^1$H NMR of 8.
Supplementary Figure 116. $^{13}$C NMR of 8.
Supplementary Figure 117. $^{19}$F NMR of 8.
Supplementary Figure 118. $^1$H NMR of 9.
Supplementary Figure 119. $^{13}$C NMR of 9.
Supplementary Figure 120. $^{19}$F NMR of 9.
Supplementary Figure 121. $^1$H NMR of 10.
Supplementary Figure 122. $^{13}$C NMR of 10.
Supplementary Figure 123. $^{19}$F NMR of 10.
Supplementary Figure 124. $^1$H NMR of 11.
Supplementary Figure 125. $^{13}$C NMR of 11.
Supplementary Figure 126. $^{19}$F NMR of 11.
Supplementary Figure 127. $^1$H NMR of 5a (2C).
Supplementary Figure 128. $^{13}$C NMR of 5a (2C).
Supplementary Figure 129. $^1$H NMR of 5b (2C).

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Supplementary Figure 130. $^{13}$C NMR of 5b (2C).
Supplementary Figure 131. $^1$H NMR of 5c (2C).
Supplementary Figure 132. $^{13}$C NMR of 5c (2C).
Supplementary Figure 134. $^{13}$C NMR of 5c (3C).
Supplementary Figure 135. $^1$H NMR of 5d (2C).
Supplementary Figure 136. $^{13}\text{C}$ NMR of 5d (2C).
Supplementary Figure 137. $^{19}$F NMR of 5d (2C).
Supplementary Figure 138. $^1$H NMR of 5e (2C).
Supplementary Figure 139. $^{13}$C NMR of 5e (2C).
Supplementary Figure 140. $^1$H NMR of 12.
Supplementary Figure 141. $^{13}$C NMR of 12.
Supplementary Figure 142. $^1$H NMR of 13.
Supplementary Figure 143. $^{13}$C NMR of 13.
Supplementary Figure 144. $^1$H NMR of 15a.
Supplementary Figure 145. $^{13}$C NMR of 15a.
Supplementary Figure 146. $^1$H NMR of 15e.
Supplementary Figure 147. $^1$H NMR of 15e.
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