Organocatalytic Enantioselective aza-Friedel-Crafts reaction of 2-Naphthols with benzoxathiazine 2,2-dioxides

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SUPPORTING INFORMATION

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General Experimental Methods

Reactions were carried out under nitrogen in test tubes or round bottom flasks oven-dried overnight at 120 °C. Dichloromethane, 1,2-dichloroethane and toluene were distilled from CaH₂. THF was distilled from sodium benzophenone ketyl. Reactions were monitored by TLC analysis using Merck Silica Gel 60 F-254 thin layer plates. Flash column chromatography was performed on Merck silica gel 60, 0.040-0.063 mm. Melting points were determined in capillary tubes. NMR spectra were run at 300 MHz for ¹H and at 75 MHz for ¹³C NMR using residual nondeuterated solvent as internal standard (CHCl₃: δ 7.26 and 77.0 ppm, d⁶-acetone: δ 2.05 and 29.4 ppm, d⁶-dmso: δ 2.50 and 39.5 ppm). Due to solubility reasons, NMR experiments for compounds 3 were run using CHCl₃ with -5% of d⁶-MeOH. Other solvents such as acetone, dmso or acetonitrile caused complicated spectrums possibly due to rotamers. Chemical shifts are given in ppm. The carbon type was determined by DEPT experiments. High resolution mass spectra (ESI) were recorded on a AB SCIEX Triple TOF™ spectrometer equipped with an electrospray source with a capillary voltage of 4.5 kV(ESI). Specific optical rotations were measured using sodium light (D line 589 nm). Chiral HPLC analyses were performed in a chromatograph equipped with a UV diode-array detector using chiral stationary columns from Daicel. Slow addition was performed using a kdScientific (Model 100) apparatus, a 1mL Braun syringe and a 120 mm Braun needle. Commercially available naphthols and sesamol were used as received.

Catalysts Ia, Ib, Id, Ie and If were prepared from quinine using Deng’s procedures.¹a Catalysts Ie was prepared from quinine using the method described by Chen.¹b
Typical procedures and characterization data for compounds 2

Benoxathiazine 2,2-dioxides were prepared from the corresponding salicylaldehyde as described in the literature. Products 2c, 2f, 2g and 2h were not described in the literature:

6-(tert-butyl)benzo-[e][1,2,3]oxathiazine 2,2-dioxide (2c)

Yellow solid; mp 56.5-59.2 °C. \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta = 8.60\) (d, \(J = 0.6\) Hz, 1H), 7.71 (dd, \(J = 8.7, 2.4\) Hz, 1H), 7.59 (d, \(J = 2.5\) Hz, 1H), 7.19 – 7.07 (m, 1H), 1.28 (s, 9H) ppm; \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta = 168.7\) (CH), 152.5 (C), 150.2 (C), 135.7 (CH), 127.8 (CH), 118.5 (CH), 115.3 (C), 35.2 (C), 31.5 (CH\(_3\)) ppm.

8-methylbenzo-[e][1,2,3]oxathiazine 2,2-dioxide (2f)

White solid; mp 89.5-90.9 °C. \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta = 8.56\) (s, 1H), 7.58 – 7.36 (m, 2H), 7.21 (t, \(J = 7.6\) Hz, 1H), 2.25 (t, \(J = 0.8\) Hz, 3H) ppm; \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta = 168.2\) (CH), 152.1 (C), 139.1 (CH), 128.6 (CH), 127.98 (C), 125.5 (CH), 114.9 (C), 14.2 (CH\(_3\)) ppm.

8-(tert-butyl)benzo-[e][1,2,3]oxathiazine 2,2-dioxide (2g)

White solid; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta = 8.65\) (s, 1H), 7.65 (dd, \(J = 7.9, 1.7\) Hz, 1H), 7.45 (dd, \(J = 7.6, 1.6\) Hz, 1H), 7.27 (d, \(J = 7.7\) Hz, 1H), 1.35 (s, 9H) ppm; \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta = 169.3\) (CH), 153.5 (C), 140.7 (C), 135.8 (CH), 129.7 (CH), 126.4 (CH), 116.6 (C), 35.4 (C), 30.1 (CH\(_3\)) ppm.

6,8-dichlorobenzo-[e][1,2,3]oxathiazine 2,2-dioxide (2h)

White solid; mp 136.0-137.3 °C. \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta = 8.62\) (s, 1H), 7.82 – 7.74 (m, 1H), 7.59 (dd, \(J = 2.4, 0.8\) Hz, 1H) ppm; \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta = 165.9\) (CH), 148.9 (C), 137.2 (CH), 131.6 (C), 128.3 (CH), 125.1 (C), 116.8 (C) ppm.
Other organocatalysts studied in the optimization process:

\[
\begin{align*}
\text{1a} + \text{2a} & \xrightarrow{\text{cat X (20 mol %)}} \text{3aa} \\
\text{A, 86\%, -2\% ee} & \\
\text{B, 92\%, -5\% ee} & \\
\text{C, 68\%, -14\% ee} & \\
\text{D, 64\%, -57\% ee} & \\
\text{E, 70\%, 81\% ee} & \\
\text{F, 72\%, 80\% ee} & \\
\text{G, 76\%, 80\% ee} & \\
\text{H, 91\%, 59\% ee} & \\
\text{I, 79\%, 72\% ee} & \\
\text{J, 93\%, 76\% ee} & \\
\text{K, 58\%, 77\% ee} & 
\end{align*}
\]
Typical procedures and characterization data for compounds 3, 6 and 7

General procedure for the enantioselective Friedel-Crafts reaction

To a solution of naphthol 1 (0.1 mmol) and catalyst Id (0.01 mmol) in 1,2-dichloroethane (1 mL) at -20 °C under inert atmosphere, was added a solution of imine 2a (0.1 mmol) in 1,2-dichloroethane (1 mL) during 12 hours using a syringe pump. Alternatively, naphthol 1a can be added to a solution of imine 2 and catalyst Id. The reaction was followed by TLC using CH₂Cl₂ as eluent. Once the reaction was complete, the mixture was directly subjected to flash chromatography eluting with CH₂Cl₂ to CH₂Cl₂/EtOAc (95:5).

General procedure for the racemic Friedel-Crafts reaction

To a solution of naphthol 1 (0.1 mmol) and imine 2 (0.1 mmol) in 1mL of CH₂Cl₂, 10 μL of Et₃N were added. The solution was stirred at room temperature. The reaction was followed and purified as described above.

(+)-(R)-4-(2-hydroxynaphthalen-1-yl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (3aa)

Enantiomeric excess (88%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer tᵣ = 7.9 min, minor enantiomer tᵣ = 6.0 min.

White solid, mp 159-161 °C, [α]D²⁰ + 102.1 (c 0.64, MeOH, 85% ee).

¹H NMR (300 MHz, CDCl₃) δ 8.00 (d, J = 8.7 Hz, 1H), 7.82 – 7.69 (m, 2H), 7.53 (ddd, J = 8.5, 7.0, 1.5 Hz, 1H), 7.41 – 7.32 (m, 1H), 7.25 – 7.14 (m, 1H), 7.06 (d, J = 9.0 Hz, 1H), 7.00 (dd, J = 8.5, 1.0 Hz, 1H), 6.86 (td, J = 7.5, 1.5 Hz, 1H), 6.66 (s, 1H), 6.55 (dt, J = 7.5, 1.5 Hz, 1H) ppm;

¹³C NMR (75 MHz, CDCl₃) δ = 153.2 (C), 151.2 (C), 132.9 (C), 131.0 (CH), 128.85 (C), 128.8 (CH), 128.5 (C), 127.8 (CH), 126.7 (CH), 124.8 (CH), 123.5 (CH), 123.05 (C), 121.3 (CH), 117.9 (CH), 114.3 (C), 54.3 (CH) ppm; HRMS (ESI): m/z: 326.0493 [M-H]⁻, C₁₇H₁₃NO₄S requires 326.0487.

(+)-(R)-4-(2-hydroxy-3-methoxynaphthalen-1-yl)-3,4-dihydrobenzo[e][1,2,3] oxathiazine 2,2-dioxide (3ba)

Enantiomeric excess (89%) was determined by chiral HPLC (Chiralpak OD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer tᵣ = 17.8 min, minor enantiomer tᵣ = 13.0 min.

Brown solid, mp 160-170 °C, [α]D²⁰ + 119.6 (c 0.83, MeOH, 89% ee).

¹H NMR (300 MHz, CDCl₃) δ 7.99 (d, J = 8.0 Hz, 1H), 7.78 (dd, J = 7.5, 1.5 Hz, 1H), 7.50 (dd, J = 8.0, 7.0, 1.5 Hz, 1H), 7.40 (dd, J = 8.0, 7.0, 1.5 Hz, 1H), 7.28 – 7.20 (m, 3H),
7.05 (dd, J = 8.5, 1.0 Hz, 1H), 6.91 (td, J = 7.5, 1.5 Hz, 1H), 6.72 (s, 1H), 6.58 (dt, J = 8.0, 1.3 Hz, 1H), 4.03 (s, 3H) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) δ = 151.8 (C), 147.1 (C), 144.7 (C), 129.6 (CH), 129.4 (C), 128.1 (CH), 127.1 (CH), 126.3 (CH), 125.4 (CH), 125.2 (CH), 123.1 (C), 121.9 (CH), 118.6 (CH), 115.2 (C), 107.9 (CH), 56.5 (CH$_3$), 55.0 (CH) ppm; HRMS (ESI): m/z: 358.0748 [M+H]$^+$, C$_{18}$H$_{13}$NO$_5$S requires 358.0749. 

(+)-(R)-4-(2-hydroxy-6-methoxynaphthalen-1-yl)-3,4-dihydrobenzo[e][1,2,3] oxathiazine 2,2-dioxide (3ca) 

Enantiomeric excess (83%) was determined by chiral HPLC (Chiralpak AD-H), hexane-PrOH 90:10, 1.0 mL/min, major enantiomer $t_r$ = 11.2 min, minor enantiomer $t_r$ = 8.9 min. 

Brown solid, mp 163-164 °C, [α]$^20_D$ + 106.0 (c 0.89, MeOH, 83% ee), $^1$H NMR (300 MHz, CDCl$_3$) δ = 7.93 (d, J = 9.5 Hz, 1H), 7.64 (d, J = 9.0 Hz, 1H), 7.26 – 7.18 (m, 2H), 7.15 (d, J = 2.5 Hz, 1H), 7.08 – 6.99 (m, 2H), 6.94 – 6.82 (m, 2H), 6.64 (s, 1H), 6.64 (d, J = 7.5 Hz, 1H), 3.91 (s, 3H) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) δ = 155.9 (C), 151.3 (C), 151.1 (C), 129.7 (CH), 129.0 (CH), 128.2 (C), 126.7 (CH), 124.9 (CH), 123.05 (CH), 120.3 (CH), 118.5 (CH), 118.1 (CH), 114.9 (C), 107.2 (CH), 55.3 (CH$_3$), 54.9 (CH) ppm; HRMS (ESI): m/z: 358.0738 [M+H]$^+$, C$_{18}$H$_{13}$NO$_5$S requires 358.0749. 

(+)-(R)-4-(2-hydroxy-7-methoxynaphthalen-1-yl)-3,4-dihydrobenzo[e][1,2,3] oxathiazine 2,2-dioxide (3da) 

Enantiomeric excess (88%) was determined by chiral HPLC (Chiralpak OD-H), hexane-PrOH 80:20, 1.0 mL/min, major enantiomer $t_r$ = 13.6 min, minor enantiomer $t_r$ = 18.6 min. 

Brown solid, mp 167-168 °C, [α]$^20_D$ + 105.9 (c 0.81, MeOH, 88% ee), $^1$H NMR (300 MHz, CDCl$_3$) δ = 7.78 – 7.67 (m, 2H), 7.32 – 7.20 (m, 2H), 7.12 – 7.02 (m, 2H), 6.99 – 6.86 (m, 2H), 6.64 (d, J = 7.7 Hz, 1H), 6.51 (s, 1H), 3.92 (s, 3H) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) δ = 159.5 (C), 153.5 (C), 151.3 (C), 134.4 (C), 130.9 (CH), 130.5 (CH), 123.0 (CH), 126.7 (CH), 124.9 (CH), 124.1 (C), 123.1 (C), 118.1 (CH), 116.0 (CH), 115.2 (CH), 113.8 (C), 100.4 (CH), 55.4 (CH$_3$), 55.0 (CH) ppm; HRMS (ESI): m/z: 358.0755 [M+H]$^+$, C$_{18}$H$_{13}$NO$_5$S requires 358.0749. 

(+)-(R)-4-(6-bromo-2-hydroxynaphthalen-1-yl)-3,4-dihydrobenzo[e][1,2,3] oxathiazine 2,2-dioxide (3ea) 

Enantiomeric excess (75%) was determined by chiral HPLC (Chiralpak AD-H), hexane-PrOH 80:20, 1.0 mL/min, major enantiomer $t_r$ = 10.4 min, minor enantiomer $t_r$ = 8.6 min.
Brown solid, mp 198-199 °C, $[\alpha]_D^{20} +86.0$ (c 0.72, MeOH, 75% ee), $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.96 (d, $J = 2.0$ Hz, 1H), 7.89 (d, $J = 9.0$ Hz, 1H), 7.69 (d, $J = 9.0$ Hz, 1H), 7.61 (dd, $J = 9.0$, 2.0 Hz, 1H), 7.27 – 7.20 (m, 1H), 7.06 (dd, $J = 16.0$, 8.0 Hz, 2H), 6.90 (td, $J = 7.5$, 1.0 Hz, 1H), 6.61 (s, 1H), 6.51 (d, $J = 8.0$ Hz, 1H) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 153.4 (C), 151.3 (C), 131.6 (C), 131.0 (CH), 130.7 (CH), 130.2 (CH), 129.7 (C), 129.1 (CH), 126.5 (CH), 125.0 (CH), 123.3 (CH), 122.8 (CH), 119.1 (CH), 118.1 (CH), 117.2 (C), 114.7 (C), 54.7 (CH) ppm; HRMS: m/z: 423.0008/424.9987 [M+NH$_4^+$] (+) 100/57.7, C$_{17}$H$_{17}$N$_2$O$_4$S requires 423.0014/424.9994.

(+)-(R)-Methyl 5-(2,2-dioxido-3,4-dihydrobenzo[e][1,2,3]oxathiazin-4-yl)-6-hydroxy-2-naphtoate (3fa)

Enantiomeric excess (96%) was determined by chiral HPLC (Chiralpak AD-H), hexane-$^t$PrOH 80:20, 1.0 mL/min, major enantiomer $t_r = 12.1$ min, minor enantiomer $t_r = 11.1$ min.

White solid, mp 200-205 °C, $[\alpha]_D^{20} +115.5$ (c 0.23, MeOH, 96% ee), $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.56 (s, 1H), 8.05 – 7.90 (m, 2H), 7.28 – 7.13 (m, 2H), 7.03 (d, $J = 8.6$ Hz, 1H), 6.90 (t, $J = 7.0$ Hz, 1H), 6.67 (s, 1H), 6.53 (d, $J = 7.9$ Hz, 1H), 3.97 (s, 3H) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 171.7 (C), 160.1 (C), 155.7 (C), 139.9 (CH), 137.1 (CH), 136.4 (CH), 133.4 (CH), 131.9 (C), 131.5 (CH), 130.8 (CH), 129.3 (CH), 127.2(C), 126.0 (CH), 123.2 (CH), 122.4 (CH), 118.9(C), 59.1 (CH$_3$), 56.5 (CH) ppm; HRMS (ESI): m/z: 384.1273 [M-H], C$_{19}$H$_{15}$NO$_6$S, requires 384.0542.

4-(1-hydroxynaphthalen-2-yl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (6)

Enantiomeric excess (83%) was determined by chiral HPLC (Chiralpak AD-H), hexane-$^t$PrOH 80:20, 1.0 mL/min, major enantiomer $t_r = 14.3$ min, minor enantiomer $t_r = 9.65$ min.

Brown solid, $[\alpha]_D^{20} +232.6$ (c 0.6, MeOH, 83% ee), $^1$H NMR (300 MHz, $d_6$-acetone) $\delta$ 8.43 – 8.33 (m, 1H), 8.14 (s, 1H), 7.96 – 7.86 (m, 1H), 7.64 – 7.54 (m, 2H), 7.52 (d, $J = 8.5$ Hz, 1H), 7.45 – 7.33 (m, 2H), 7.17 – 7.08 (m, 2H), 6.91 – 6.77 (m, 1H), 6.60 (s, 1H) ppm; $^{13}$C NMR (75 MHz, $d_6$-acetone) $\delta$ = 152.7 (C), 151.65 (C), 135.7 (C), 130.1 (CH), 129.1 (CH), 128.8 (CH), 127.7 (CH), 127.6 (CH), 126.6 (CH), 126.2 (C), 125.8 (CH), 124.2 (C), 122.6 (CH), 121.6 (CH), 120.0 (C), 119.0 (CH), 57.1 (CH) ppm; HRMS (ESI): m/z: 328.0638 [M+H]$^+$, C$_{17}$H$_{14}$NO$_4$S requires 328.0644.
4-(6-hydroxybenzo[d][1,3]dioxol-5-yl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (7)

Enantiomeric excess (77%) was determined by chiral HPLC (Chiralpak AD-H), hexane-PrOH 80:20, 1.0 mL/min, major enantiomer \( t_r = 14.2 \) min, minor enantiomer \( t_r = 13.4 \) min.

White solid, mp 83-87 °C, \([\alpha]_D^{20} + 12.6 \) (c 0.7, MeOH, 77% ee), \(^1\)H NMR (300 MHz, CDCl₃) \( \delta \) 7.34 – 7.26 (m, 1H), 7.05 (ddd, \( J = 15.7, 7.9, 1.1 \) Hz, 2H), 6.84 (d, \( J = 7.8 \) Hz, 1H), 6.72 (s, 1H), 6.41 (s, 1H), 6.07 (d, \( J = 9.9 \) Hz, 2H), 5.81 (d, \( J = 9.8 \) Hz, 1H), 5.62 (d, \( J = 9.8 \) Hz, 1H), 5.40 (s, 1H) ppm; \(^13\)C NMR (75 MHz, CDCl₃) \( \delta \) 151.05 (C), 149.1 (C), 148.6 (C), 142.0 (C), 129.45 (CH), 127.2 (CH), 125.1 (CH), 122.4 (C), 119.45 (CH), 114.9 (C), 110.0 (CH), 101.8 (CH₂), 99.25 (CH), 59.5 (CH) ppm; HRMS (ESI): m/z: 322.0386 \([M+H]^+\), C₁₄H₁₂NO₆S requires 322.0385.

(+)-(R)-4-(2-hydroxynaphthalen-1-yl)-6-methyl-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (3ab)

Enantiomeric excess (86%) was determined by chiral HPLC (Chiralpak AD-H), hexane-PrOH 80:20, 1.0 mL/min, major enantiomer \( t_r = 8.3 \) min, minor enantiomer \( t_r = 5.65 \) min.

Orange solid, mp 152-154 °C, \([\alpha]_D^{20} + 132.8 \) (c 0.87, MeOH, 82% ee), \(^1\)H NMR (300 MHz, CDCl₃) \( \delta \) 8.03 (d, \( J = 8.5 \) Hz, 1H), 7.87 – 7.74 (m, 2H), 7.57 (ddd, \( J = 8.5, 7.0, 1.5 \) Hz, 1H), 7.47 – 7.33 (m, 1H), 7.10 – 6.99 (m, 2H), 6.93 (d, \( J = 8.5 \) Hz, 1H), 6.67 (d, \( J = 5.0 \) Hz, 1H), 6.39 – 6.31 (m, 1H), 2.04 (s, 3H) ppm; \(^13\)C NMR (75 MHz, CDCl₃) \( \delta \) 152.8 (C), 149.2 (C), 134.7 (C), 133.0 (C), 131.2 (CH), 129.6 (CH), 128.8 (CH), 128.7 (C), 127.9 (CH), 126.7 (CH), 123.7 (CH), 122.6 (CH), 121.5 (CH), 117.9 (C), 117.85 (CH), 114.6 (C), 54.7 (CH), 20.6 (CH₃) ppm; HRMS: [M+H]^+ 342.0791, C₁₈H₁₆NO₄S requires 342.0800.

(+)-(R)-6-(tert-butyl)-4-(2-hydroxynaphthalen-1-yl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (3ac)

Enantiomeric excess (82%) was determined by chiral HPLC (Chiralpak IC), hexane-PrOH 90:10, 1.0 mL/min, major enantiomer \( t_r = 10.5 \) min, minor enantiomer \( t_r = 9.1 \) min.

Brown solid, mp 154-159 °C, \([\alpha]_D^{20} + 39.0 \) (c 0.88, MeOH, 82% ee), NMR \(^1\)H (300 MHz CDCl₃) \( \delta \) 8.06 (d, \( J = 8.5 \) Hz, 1H), 7.85 (d, \( J = 7.5 \) Hz, 1H), 7.81 (d, \( J = 8.5 \) Hz, 1H), 7.65 – 7.53 (m, 1H), 7.42 (t, \( J = 7.5 \) Hz, 1H), 7.26 (dd, \( J = 8.5, 2.0 \) Hz, 1H), 7.05 (d, \( J = 8.5 \) Hz, 1H), 6.98 (d, \( J = 8.5 \) Hz, 1H), 6.72 (d, \( J = 9.0 \) Hz, 1H), 6.60 (d, \( J = 11.5 \) Hz, 1H), 0.99 (s, 9H) ppm; \(^13\)C NMR (75 MHz, CDCl₃) \( \delta \) 152.4 (C), 149.0 (C), 148.1 (C), 133.0 (CH), 131.3 (CH), 128.9 (CH), 128.0 (CH), 126.1 (CH), 123.9 (CH), 123.3 (CH), 123.1 (CH), 122.5 (CH), 117.9 (C), 117.8 (CH), 114.6 (C), 54.7 (CH), 20.6 (CH₃) ppm; HRMS: [M+H]^+ 342.0791, C₁₈H₁₆NO₄S requires 342.0800.
122.05 (CH), 121.5 (CH), 117.9 (CH), 117.6 (CH), 114.8 (C), 55.0 (CH), 34.2 (C), 31.0 (CH) ppm; **HRMS**: [M+H]+ 384.1269, C_{21}H_{22}NO_{4}S requires 384.1270.

**(+)-(R)-4-(2-hydroxynaphthalen-1-yl)-6-methoxy-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (3ad)**

Enantiomeric excess (84%) was determined by chiral HPLC (Chiralpak AD-H), hexane–PrOH 80:20, 1.0 mL/min, major enantiomer t_{R} = 13.2 min, minor enantiomer t_{R} = 7.6 min.

White solid, mp 163-164 °C, [α]_{D}^{20} + 70.2 (c 0.88, MeOH, 84% ee), **1H NMR (300 MHz, CDCl_{3})**: δ 7.95 (d, J = 8.6 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.70–7.60 (m, 1H), 7.38–7.27 (m, 1H), 6.97 (d, J = 8.9 Hz, 2H), 6.91 (dd, J = 9.0 Hz, 1H), 6.69 (dd, J = 9.0, 3.0 Hz, 1H), 6.60 (d, J = 8.7 Hz, 1H), 6.45 (d, J = 10.2 Hz, 1H), 6.07–5.99 (m, 1H) ppm; **13C NMR (75 MHz, CDCl_{3})**: δ = 156.2 (C), 153.2 (C), 145.1 (C), 132.8 (C), 131.0 (CH), 128.7 (CH), 128.4 (C), 128.0 (CH), 125.3 (CH), 123.8 (C), 121.1 (CH), 119.9 (CH), 117.8 (C), 117.6 (C), 117.3 (C), 54.7 (CH) ppm; **HRMS (ESI)**: m/z: 358.0747 [M+H]+, C_{17}H_{13}NO_{4}S requires 358.0749.

**(+)-(R)-6-bromo-4-(2-hydroxynaphthalen-1-yl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (3ae)**

Enantiomeric excess (86%) was determined by chiral HPLC (Chiralpak AD-H), hexane–PrOH 80:20, 1.0 mL/min, major enantiomer t_{R} = 8.2 min, minor enantiomer t_{R} = 5.9 min.

White solid, mp 198-199 °C, [α]_{D}^{20} + 38.7 (c 0.84, MeOH, 82% ee), **1H NMR (300 MHz, CDCl_{3})**: δ 8.01 (d, J = 8.5 Hz, 1H), 7.80 (dd, J = 12.5, 8.5 Hz, 2H), 7.35 (dd, J = 8.5, 7.0 Hz, 1H), 7.17 (dd, J = 8.0, 7.2, 1.0 Hz, 1H), 7.35 (dd, J = 8.5, 2.5 Hz, 1H), 7.07 (d, J = 9.0 Hz, 1H), 6.93 (d, J = 9.0 Hz, 1H), 6.69 (d, J = 2.5 Hz, 1H), 6.66 (d, J = 3.5 Hz, 1H) ppm; **13C NMR (75 MHz, CDCl_{3})**: δ = 152.9 (C), 150.4 (C), 135.4 (C), 132.7 (C), 131.0 (CH), 129.2 (CH), 129.0 (CH), 128.7 (CH), 128.2 (CH), 125.3 (CH), 123.8 (C), 121.1 (CH), 119.9 (CH), 117.9 (C), 117.8 (C), 117.6 (CH), 113.8 (C), 54.4 (CH) ppm; **HRMS**: [M+H]+, requires.

**(+)-(R)-4-(2-hydroxynaphthalen-1-yl)-8-methyl-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (3af)**

Enantiomeric excess (83%) was determined by chiral HPLC (Chiralpak AD-H), hexane–PrOH 80:20, 1.0 mL/min, major enantiomer t_{R} = 7.25 min, minor enantiomer t_{R} = 5.6 min.

Brown solid, mp 177-179 °C, [α]_{D}^{20} + 132.8 (c 0.74, MeOH, 83% ee), **1H NMR (300 MHz, CDCl_{3})**: δ 8.01 (d, J = 8.5 Hz, 1H), 7.80 (dd, J = 12.5, 8.5 Hz, 2H), 7.55 (t, J = 7.5 Hz, 1H),
7.38 (t, J = 7.5 Hz, 1H), 7.12 – 7.03 (m, 2H), 6.78 (t, J = 7.5 Hz, 1H), 6.68 (s, 1H), 6.40 (d, J = 7.5 Hz, 1H), 2.32 (s, 3H) ppm; 13C NMR (75 MHz, CDCl3) δ = 152.95 (C), 149.9 (C), 133.0 (C), 131.05 (C), 130.5 (CH), 128.8 (CH), 128.6 (C), 127.85 (CH), 127.3 (C), 124.2 (CH), 124.1 (CH), 123.6 (CH), 122.8 (CH), 121.5 (CH), 117.9 (CH), 114.65 (C), 54.7 (CH), 15.5 (CH3) ppm; HRMS (ESI): m/z: 342.0805 [M+H]+, C18H15NO4S, requires 342.0800.

(+)-(R)-8-(tert-butyl)-4-(2-hydroxynaphthalen-1-yl)-3,4-dihydrobenzo[e][1,2,3] oxathiazine 2,2-dioxide (3ag)

Enantiomeric excess (80%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 90:10, 1.0 mL/min, major enantiomer t_r = 10.7 min, minor enantiomer t_r = 8.65 min.

Brown solid, mp 90 °C (decompose), [α]_D^20 +132.8 (c 0.74, MeOH, 80% ee). 1H NMR (300 MHz, CDCl3) δ 8.00 (d, J = 8.5 Hz, 1H), 7.80 (dd, J = 11.5, 8.5 Hz, 2H), 7.54 (t, J = 7.5 Hz, 1H), 7.45 – 7.35 (m, 1H), 7.30 – 7.22 (m, 1H), 7.07 (d, J = 9.0 Hz, 1H), 6.84 (d, J = 8.0 Hz, 1H), 6.68 (d, J = 5.5 Hz, 1H), 6.45 (d, J = 7.5 Hz, 1H), 1.47 (s, 9H) ppm; 13C NMR (75 MHz, CDCl3) δ = 152.9 (C), 150.7 (C), 139.3 (C), 132.9 (C), 131.2 (C), 131.1 (CH), 128.8 (CH), 128.7 (C), 127.9 (CH), 126.7 (CH), 124.7 (CH), 124.3 (CH), 121.5 (CH), 118.0 (CH), 114.65 (C), 54.5 (CH), 34.9 (C), 30.0 (CH3) ppm; HRMS (ESI): m/z: 384.1266 [M+H]+, C21H21NO4S, requires 384.1270.

(+)-(R)-6,8-dichloro-4-(2-hydroxynaphthalen-1-yl)-3,4-dihydrobenzo[e][1,2,3] oxathiazine 2,2-dioxide (3ah)

Enantiomeric excess (77%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 85:15, 1.0 mL/min, major enantiomer t_r = 7.85 min, minor enantiomer t_r = 6.3 min.

White solid, mp 184-186 °C, [α]_D^20 + 70.0 (c 0.90, MeOH, 77% ee). 1H NMR (300 MHz, CDCl3) δ 8.07 – 7.90 (m, 1H), 7.89 – 7.77 (m, 2H), 7.60 (dd, J = 8.5, 7.0, 1.5 Hz, 1H), 7.43 (dd, J = 8.0, 7.0, 1.0 Hz, 1H), 7.32 (dd, J = 2.5, 1.0 Hz, 1H), 7.08 (d, J = 9.0 Hz, 1H), 6.64 (d, J = 1.0 Hz, 1H), 6.46 (dd, J = 2.5, 1.0 Hz, 1H) ppm; 13C NMR (75 MHz, CDCl3) δ 153.0 (C), 146.05 (C), 132.7 (C), 131.8 (CH), 129.7 (C), 129.5 (CH), 129.0 (CH), 128.71 (C), 128.3 (CH), 126.4 (C), 124.9 (CH), 124.0 (C), 123.9 (CH), 121.0 (CH), 117.8 (CH), 113.5 (C), 54.65 (CH) ppm; HRMS (ESI) m/z: 393.9694/395.9666/397.9639 [M-H]− (100.0/70.8/15.5) C17H13NO4S requires 393.9708/395.2300/397.9649.
Procedures and characterization data for compounds 8 and 9

tert-butyl (R)-((2-hydroxynaphthalen-1-yl)(2-hydroxyphenyl)methyl)carbamate (8)

Enantiomeric excess (89%) was determined by chiral HPLC (Chiralpak AD-H), hexane-PrOH 80:20, 1.0 mL/min, major enantiomer $t_r = 7.6$ min, minor enantiomer $t_r = 5.2$ min.

White solid, mp 171-173 °C, $[\alpha]^{20}_D - 228.3$ (c 0.45, MeOH, 89% ee). $^1$H NMR (300 MHz, $d^6$-dmsO) $\delta$ 10.02 (s, 1H), 9.46 (s, 1H), 8.25 (d, $J = 8.7$ Hz, 1H), 7.76 (d, $J = 7.9$ Hz, 1H), 7.70 (d, $J = 8.8$ Hz, 1H), 7.42 (t, $J = 8.0$ Hz, 2H), 7.26 (t, $J = 7.2$ Hz, 1H), 7.15 (d, $J = 8.8$ Hz, 1H), 6.97 (dt, $J = 18.1$, 8.1 Hz, 3H), 6.69 (dd, $J = 13.4$, 7.2 Hz, 2H), 1.56 – 1.16 (m, 10H) ppm; $^{13}$C NMR (75 MHz, $d^6$-dmsO) $\delta$ 154.67 (C), 154.3 (C), 152.8 (C), 132.3 (C), 128.6 (C), 128.5 (CH), 128.4 (C), 128.1 (CH), 127.6 (CH), 127.5 (C), 125.9 (CH), 123.4 (CH), 122.4 (CH), 119.5 (C), 118.7 (CH), 118.4 (CH), 114.95 (CH), 78.0 (C), 39.7 (CH), 28.1 (CH$_3$) ppm; HRMS (ESI) m/z: 364.1542 [M-H]$_-^{C_{22}H_{22}NO_4}$ requires 364.1549.

(R)-4H,11cH-benzo[e]naphtho[1’,2’:5,6][1,3]oxazino[3,4-c][1,2,3]oxathiazine 2,2-dioxide (9)

Enantiomeric excess (85%) was determined by chiral HPLC (Chiralpak AD-H), hexane-PrOH 95:05, 1.0 mL/min, major enantiomer $t_r = 9.7$ min, minor enantiomer $t_r = 10.65$ min.

White solid, mp 203-206 °C, $[\alpha]^{20}_D + 343.4$ (c 0.90, CHCl$_3$, 85% ee). $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.93 – 7.82 (m, 2H), 7.77 (dd, $J = 8.5$, 0.7 Hz, 1H), 7.58 (ddd, $J = 8.4$, 6.9, 1.4 Hz, 1H), 7.48 (ddd, $J = 8.1$, 6.9, 1.2 Hz, 1H), 7.36 (ddddd, $J = 8.3$, 5.9, 3.1, 0.8 Hz, 1H), 7.17 (d, $J = 8.9$ Hz, 1H), 7.15 – 7.10 (m, 1H), 7.07 – 6.99 (m, 2H), 6.68 (s, 1H), 5.47 (dd, $J = 7.9$, 1.5 Hz, 1H), 4.83 (d, $J = 7.9$ Hz, 1H) ppm $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 150.2 (C), 150.0 (C), 131.8 (C), 131.0 (CH), 130.3 (CH), 129.6 (CH), 129.5 (C), 128.9 (CH), 127.8 (CH), 125.5 (CH), 124.6 (CH), 122.3 (CH), 121.4 (C), 118.51 (CH), 118.46 (CH), 110.25 (C), 73.35 (CH$_2$), 54.9 (CH) ppm; HRMS (ESI) m/z: 340.0636 [M+H]$^+$, C$_{18}$H$_{14}$NO$_4$S requires 340.0644.
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\(^{13}\text{C} \text{NMR, CDCl}_3, \text{75 MHz}\)
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X-ray data for compound 3aa: crystallized from ethyl acetate/n-hexane; C_{17}H_{13}NSO_4; Mr=327.35; Diffraction data on prismatic crystals were collected at 293 K with a Nonius Kappa-CCD single crystal diffractometer using Mo K\alpha (\lambda = 0.71073 Å). The structures were solved by direct methods using SHELXS97 and refined by full-matrix least squares on F^2 using SHELXL97. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed at calculated positions, refined using a riding model and assigned fixed isotropically displacement parameters. The H1 atom was located in a difference map and refined isotropically.

Figure 1. ORTEP plot for the X-ray structure of compound 3aa.
X-ray data for compound 9: crystallized from ethyl acetate/n-hexane; C_{18}H_{13}NSO_{4}; Mr=339.37; Diffraction data on prismatic crystals were collected at 293 K with a Nonius Kappa-CCD single crystal diffractometer using Mo Kα (λ = 0.71073 Å). The structures were solved by direct methods using SHELXS97 and refined by full-matrix least squares on F^2 using SHELXL97. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed at calculated positions, refined using a riding model and assigned fixed isotropically displacement parameters. The H1 atom was located in a difference map and refined isotropically.

Figure 2. ORTEP plot for the X-ray structure of compound 9.
References
