C₃-Symmetric Chiral Trisimidazoline-Catalyzed Friedel-Crafts (FC)-Type Reaction

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General information

$^1$H-, $^{13}$C- and $^{31}$P-NMR spectra were recorded with JEOL JMN ECS400 FT NMR, JNM ECA600 FT NMR or Bruker AVANCE II ($^1$H-NMR 400, 500, 600 or 700 MHz, $^{13}$C-NMR 100, 126, 150 or 175 MHz). $^1$H-NMR spectra are reported as follows: chemical shift in ppm relative to the chemical shift of CHCl$_3$ at 7.26 ppm, ACETONE-D$_6$ at 2.09 ppm or DMSO-D$_6$ at 2.49 ppm, integration, multiplicities (s = singlet, d = doublet, q = quartet, t = triplet, m = multiplet), and coupling constants (Hz). $^{13}$C-NMR spectra reported in ppm relative to the central line of triplet for CDCl$_3$ at 77 ppm, septet for ACETONE-D$_6$ at 30 ppm or septet for DMSO-D$_6$ at 40 ppm. FT-MS spectra were obtained with LTQ Orbitrap XL (Thermo Fisher Scientific). ESI-MS spectra were obtained with JMS-T100LC (JEOL). FAB-MS spectra were obtained with JMS-700 (JEOL). Optical rotations were measured with JASCO P-1030 polarimeter. HPLC analyses were performed on a JASCO HPLC system (JASCO PU 980 pump and UV-975 UV/Vis detector) using a mixture of hexane and 2-propanol as eluents. FT-IR spectra were recorded on a JASCO FT-IR system (FT/IR4100). Mp was measured with SHIMADZU DSC-60. Column chromatography on SiO$_2$ was performed with Kanto Silica Gel 60 (40-100 μm). Commercially available organic and inorganic compounds were used without further purification except for the solvent, which was distilled from sodium/benzophenone or CaH$_2$. N-4-Nosyl imines were prepared following the reported procedures. The products $^{4b}$, $^{4d}$, $^{4o}$ and $^{8}$ were identical in all respects with reported in the literature. Absolute configurations were assigned by comparison of optical rotation reported in the literature.

Preparation of trisimidazoline 1b

1,3,5-Triformylbenzene (35.6 mg, 0.219 mmol) and (1S,2S)-1,2-bis(4-methoxyphenyl)ethane-1,2-diamine (185 mg, 0.680 mmol) was dissolved in dioxane (6.8 mL) and stirred for 2 h at rt under N$_2$. The resulting solution was added NBS (121 mg, 0.679 mmol) at 0 °C and stirred for 24 h at rt. After the reaction was completed, sat. Na$_2$S$_2$O$_5$ aq. and 5% NaOH aq. was added to the reaction mixture and the solution was extracted with CH$_2$Cl$_2$. Organic layer was dried over Na$_2$SO$_4$, and evaporated in vacuo. After the purification via SiO$_2$ column chromatography (hexane/AcOEt/TEA = 1/2/0.3), the desired product 1b was obtained as pale yellow solid. Mp: >260 °C; [α]$_D^{24}$ = -96.9 (c 1.2, CHCl$_3$); $^1$H-NMR (CDCl$_3$) δ: 8.61 (s, 3H), 7.16 (2H, d, $J$ = 8.8 Hz), 6.82 (2H, d, $J$ = 8.8 Hz), 4.80 (brs, 6H), 3.78 (s, 18H); $^{13}$C-NMR (CDCl$_3$) δ: 161.6, 159.0, 135.1, 130.6, 128.5, 127.7, 114.0, 55.2; IR (KBr): ν 3130, 3001, 2955, 2835, 1612, 1514, 1248, 1173, 1034 cm$^{-1}$; HRMS (FAB) calcd for C$_{57}$H$_{55}$N$_6$O$_6$ m/z = 919.4183 [(M+H$^+$)], found m/z = 919.4175.
General procedure for enantioselective Friedel–Crafts (FC)-type reactions of aldmines (2) with 2-naphthols (3)

Under N₂ atmosphere, a test tube was charged with aldmine 2 (0.10 mmol), 2-naphthols 3 (0.15 mmol), and the catalyst 1 (0.005 mmol, 5 mol %) in toluene (0.4 mL). The reaction mixture was stirred at -5 °C. After the purification via SiO₂ column chromatography, the desired product 4 was obtained.

4a: 82% yield; ¹H-NMR (CDCl₃) δ: 7.76 (2H, d, J = 8.5 Hz), 7.76 (2H, d, J = 8.5 Hz), 7.68 (2H, d, J = 7.3 Hz), 7.45-7.41 (2H, m), 7.35-7.31 (2H, m), 7.15 (2H, d, J = 2.3 Hz), 7.10 (2H, dd, J = 8.7, 2.3 Hz), 6.57 (1H, d, J = 8.7 Hz), 4.97 (2H, bs); ¹³C-NMR (CDCl₃) δ: 155.7, 145.4, 139.0, 132.3, 132.0, 131.2, 130.4, 129.6, 129.4, 129.2, 128.8, 127.0, 123.1, 121.1, 119.9, 117.8, 114.2, 113.0, 61.5; HRMS (ESI) calcd for C₂₃H₁₆BrClNO, m/z = 436.0104 [(M-H)-], found m/z = 436.0094; IR (KBr): ν 3569, 3339, 2345, 1719, 1625, 1490, 1233, 913, 815 cm⁻¹; enantiomeric excess: Rac, determined by HPLC (Chiralpak AS-H, hexane/2-propanol = 4/1, flow rate 1.0 mL/min, 25 °C, 330 nm) first peak: t_R = 6.7 min, second peak: t_R = 9.3 min.

4b: 17% yield; ¹H-NMR (ACETONE-D₆) δ: 9.30 (1H, bs), 8.14 (1H, d, J = 8.2 Hz), 7.89 (1H, d, J = 8.2 Hz), 7.85 (1H, d, J = 8.2 Hz), 7.53 (1H, t, J = 8.2 Hz), 7.39-7.30 (6H, m), 7.00 (1H, s), 3.27 (1H, bs), 1.47 (9H, s); ¹³C-NMR (CDCl₃) δ: 156.5, 153.6, 143.0, 133.4, 132.5, 130.6, 130.0, 129.7, 128.9, 128.8, 128.0, 124.0, 123.4, 120.2, 119.3, 79.6, 50.8, 28.6; enantiomeric excess: 17%, determined by HPLC (Chiralpak IB, hexane/2-propanol = 95/5, flow rate 1.0 mL/min, 25 °C, 230 nm) minor peak: t_R = 7.6 min, major peak: t_R = 7.0 min.

4c: 88% yield; ¹H-NMR (CDCl₃) δ: 7.71 (1H, d, J = 8.2 Hz), 7.65 (1H, d, J = 8.2 Hz), 7.50 (1H, d, J = 8.7 Hz), 7.45-7.40 (3H, m), 7.30 (1H, t, J = 7.3 Hz), 7.22 (2H, d, J = 8.7 Hz), 7.15 (2H, t, J = 4.4 Hz), 7.07 (1H, t, J = 7.3 Hz), 6.89-6.82 (4H, m), 6.66 (1H, bs), 6.40 (1H, d, J = 10.1 Hz); ¹³C-NMR (CDCl₃) δ: 150.8, 139.2, 138.6, 133.1, 132.1, 130.2, 128.9, 128.6, 128.4 x 2, 128.1 x 2, 127.4, 126.4, 123.5, 121.6, 117.8, 116.9, 53.7; HRMS (ESI) calcd for C₂₃H₁₈ClNO₃SNa, m/z = 446.0594 [(M+Na)+], found m/z = 446.0584; IR (KBr): ν 3319, 1719, 1630, 1518, 1490, 1439, 1328, 1156, 1091, 1014, 751 cm⁻¹; enantiomeric excess: 22%, determined by HPLC (Chiralcel OD-3, hexane/2-propanol = 19/1, flow rate 1.0 mL/min, 25 °C, 254 nm) minor peak: t_R = 12.0 min, major peak: t_R = 16.3 min.
**4d**

70% yield; $^1$H-NMR (CDCl$_3$) $\delta$: 7.70 (1H, d, $J = 9.2$ Hz), 7.66 (1H, d, $J = 8.7$ Hz), 7.55 (1H, d, $J = 8.7$ Hz), 7.41 (1H, t, $J = 7.8$ Hz), 7.31 (2H, d, $J = 8.2$ Hz), 7.23 (2H, d, $J = 8.7$ Hz), 7.18 (2H, d, $J = 8.2$ Hz), 6.83 (1H, d, $J = 8.7$ Hz), 6.64 (2H, d, $J = 7.8$ Hz), 6.60 (1H, bs), 6.35 (1H, d, $J = 10.1$ Hz), 6.28 (1H, bs), 2.10 (3H, s); $^{13}$C-NMR (CDCl$_3$) $\delta$: 151.1, 142.8, 138.7, 135.9, 132.9, 132.1, 129.8, 128.7, 128.6, 128.4, 128.3, 128.2, 127.2, 126.4, 123.3, 121.6, 117.9, 116.9, 53.7, 21.1; enantiomeric excess: 27%, determined by HPLC (Chiralpak IC, hexane/2-propanol = 4/1, flow rate 1.0 mL/min, 25 °C, 254 nm) minor peak: $t_R = 14.1$ min, major peak: $t_R = 16.1$ min.

**4e**

65% yield; $^1$H-NMR (CDCl$_3$) $\delta$: 7.72 (1H, d, $J = 8.7$ Hz), 7.68 (1H, d, $J = 8.1$ Hz), 7.57 (1H, d, $J = 8.7$ Hz), 7.43 (1H, t, $J = 7.3$ Hz), 7.36-7.31 (3H, m), 7.23-7.18 (4H, m), 6.83 (1H, d, $J = 8.7$ Hz), 6.33 (3H, t, $J = 8.1$ Hz), 3.62 (3H, s); $^{13}$C-NMR (CDCl$_3$) $\delta$: 162.3, 150.8, 138.7, 133.1, 132.3, 130.8, 130.0, 129.0, 128.7, 128.5, 128.4, 128.2, 127.4, 123.6, 121.8, 118.0, 117.4, 113.3, 55.3, 53.7; HRMS (ESI) calcd for C$_{24}$H$_{20}$ClNO$_4$SNa, m/z = 476.0699 [(M+Na)$^+$], found m/z = 476.0689; IR (KBr): $\nu$ 3310, 2930, 1597, 1496, 1257, 1155, 1092, 910, 815, 731 cm$^{-1}$; enantiomeric excess: 30%, determined by HPLC (Chiralpak IA, hexane/2-propanol = 9/1, flow rate 1.0 mL/min, 25 °C, 335 nm) minor peak: $t_R = 17.7$ min, major peak: $t_R = 22.6$ min.

**4f**

100% yield; $^1$H-NMR (CDCl$_3$) $\delta$: 7.74-7.71 (2H, m), 7.60 (1H, d, $J = 8.7$ Hz), 7.46 (1H, t, $J = 7.5$ Hz), 7.37 (1H, t, $J = 7.5$ Hz), 7.30-7.20 (8H, m), 6.77 (3H, d, $J = 8.7$ Hz), 6.40 (1H, s); $^{13}$C-NMR (CDCl$_3$) $\delta$: 150.7, 138.4, 138.3, 137.7, 133.2, 130.2, 129.4, 128.7, 128.5, 128.1 x 2, 127.9, 127.8, 127.6, 123.8, 121.5, 117.7, 117.0, 53.8; HRMS (ESI) calcd for C$_{23}$H$_{17}$Cl$_2$NO$_3$SNa, m/z = 480.0204 [(M+Na)$^+$], found m/z = 480.0193; IR (KBr): $\nu$ 3414, 3318, 2345, 1718, 1629, 1578, 1509, 1323, 1273, 1152, 1091, 812, 752 cm$^{-1}$; enantiomeric excess: 48%, determined by HPLC (Chiralcel OD-H, hexane/2-propanol = 19/1, flow rate 1.0 mL/min, 25 °C, 254 nm) minor peak: $t_R = 21.1$ min, major peak: $t_R = 27.7$ min.

**4g**

72% yield; $^1$H-NMR (CDCl$_3$) $\delta$: 7.73 (2H, d, $J = 8.7$ Hz), 7.61 (1H, d, $J = 8.7$ Hz), 7.46 (1H, t, $J = 7.9$ Hz), 7.37 (1H, t, $J = 7.9$ Hz), 7.27-7.20 (6H, m), 6.93 (2H, d, $J = 8.7$ Hz), 6.79 (1H, d, $J = 8.7$ Hz), 6.54 (1H, bs), 6.39 (1H, bs), 5.73 (1H, bs); $^{13}$C-NMR (CDCl$_3$) $\delta$: 150.5, 138.3 x 2, 133.3, 132.4, 131.1, 130.2, 128.8, 128.5, 128.1 x 2, 127.9 x 2, 127.7, 126.9, 123.9, 117.6, 117.1, 53.7; HRMS (ESI) calcd for C$_{23}$H$_{17}$BrClNO$_3$SNa, m/z = 523.9699 [(M+Na)$^+$], found
m/z = 523.9687; IR (KBr): ν 3403, 3317, 3089, 2925, 2853, 1903, 1719, 1629, 1575, 1544, 1326, 1273, 1153, 1089 cm⁻¹; enantiomeric excess: 63%, determined by HPLC (Chiralcel OD-H, hexane/2-propanol = 19/1, flow rate 1.0 mL/min, 25 °C, 254 nm) minor peak: t_R = 16.2 min, major peak: t_R = 22.2 min.

4h: 89% yield; ¹H-NMR (DMSO-D₆) δ: 9.99 (1H, br s), 8.81 (1H, br s), 7.88 (2H, d, J = 8.7 Hz), 7.63 (2H, d, J = 8.7 Hz), 7.58 (2H, d, J = 8.2 Hz), 7.55 (1H, d, J = 9.2 Hz), 7.31 (2H, d, J = 8.7 Hz), 7.28-7.20 (3H, m), 7.16 (1H, t, J = 7.3 Hz), 6.96 (1H, d, J = 8.7 Hz), 6.52 (1H, s); ¹³C-NMR (DMSO-D₆) δ: 153.0, 148.6, 145.9, 139.9, 131.3, 131.2, 129.7, 128.2, 128.1, 128.0, 127.4, 126.3, 123.1, 122.4, 117.6, 116.1, 51.9; HRMS (ESI) calcd for C₂₃H₁₇ClN₂O₅SNa, m/z = 491.0444 [(M+Na)+], found m/z = 491.0432; IR (KBr): ν 3432, 3315, 3112, 2375, 1903, 1719, 1629, 1575, 1544, 1326, 1273, 1153, 1089 cm⁻¹; enantiomeric excess: 96%, determined by HPLC (Chiralcel OD-3, hexane/2-propanol = 9/1, flow rate 1.0 mL/min, 25 °C, 254 nm) minor peak: t_R = 8.9 min, major peak: t_R = 10.9 min; [α]D²² = +16.9 (c 1.8, CHCl₃).

4i: 92% yield; ¹H-NMR (DMSO-D₆) δ: 7.89 (2H, d, J = 9.2 Hz), 7.65 (2H, d, J = 9.2 Hz), 7.60 (2H, d, J = 7.8 Hz), 7.57 (1H, d, J = 8.7 Hz), 7.31-7.24 (4H, m), 7.17 (1H, t, J = 7.3 Hz), 7.13-7.09 (1H, m), 6.96 (1H, d, J = 8.7 Hz), 6.53 (1H, s); ¹³C-NMR (DMSO-D₆) δ: 153.1, 148.7, 146.0, 143.5, 132.8, 131.3, 130.0, 129.8, 128.3, 128.1, 127.5, 126.6, 126.4, 125.9, 125.0, 123.2, 122.9, 122.4, 117.7, 116.1, 52.1; HRMS (ESI) calcd for C₂₃H₁₇ClN₂O₅SNa, m/z = 491.0444 [(M+Na)+], found m/z = 491.0436; IR (KBr): ν 3443, 3310, 3108, 2377, 1629, 1581, 1522, 1432, 1323, 1275, 1156, 1081 cm⁻¹; enantiomeric excess: 98%, determined by HPLC (Chiralpak AD-H, hexane/2-propanol = 19/1, flow rate 1.0 mL/min, 25 °C, 254 nm) minor peak: t_R = 56.1 min, major peak: t_R = 44.9 min; [α]D²¹ = +17.7 (c 1.5, CHCl₃).

4j: 90% yield; ¹H-NMR (DMSO-D₆) δ: 10.30 (1H, br s), 7.92 (2H, d, J = 8.7 Hz), 7.77 (1H, d, J = 8.7 Hz), 7.65-7.50 (5H, m), 7.30-7.22 (2H, m), 7.18-7.11 (3H, m), 6.91 (1H, d, J = 8.7 Hz), 6.60 (1H, s); ¹³C-NMR (DMSO-D₆) δ: 154.8, 148.2, 139.3, 132.0, 131.9, 129.4, 129.1, 128.5, 128.3, 127.8, 127.4, 126.6, 126.1, 123.0, 122.2, 122.0, 118.8, 115.9, 53.1; HRMS (ESI) calcd for C₂₃H₁₇ClN₂O₅SNa, m/z = 491.0444 [(M+Na)+], found m/z = 491.0435; IR (KBr): ν 3277, 3107, 3071, 2372, 1685, 1628, 1597, 1527, 1446, 1344, 1270, 1171, 1092 cm⁻¹; enantiomeric excess: 88%, determined by HPLC (Chiralpak IC-3, hexane/2-propanol = 19/1, flow rate 1.0 mL/min, 25 °C, 254 nm) minor peak: t_R = 77.6 min, major peak: t_R = 61.2 min; [α]D²² = +92.7 (c 1.8, MeOH).
4k: 100% yield; $^1$H-NMR (ACETONE-D$_6$) $\delta$: 7.85 (1H, d, $J = 9.2$ Hz), 7.78 (2H, d, $J = 8.7$ Hz), 7.69-7.66 (3H, m), 7.60 (1H, d, $J = 8.7$ Hz), 7.43 (1H, t, $J = 7.6$ Hz), 7.29 (3H, m), 7.11 (2H, d, $J = 7.8$ Hz), 7.04 (1H, d, $J = 9.2$ Hz), 6.58 (1H, s), 2.29 (3H, s); $^{13}$C-NMR (ACETONE-D$_6$) $\delta$: 153.8, 150.4, 147.5, 138.9, 137.7, 133.6, 131.0, 130.1, 129.7, 129.0, 128.1, 127.9, 125.5, 124.3, 124.2, 119.2, 118.4, 55.1, 21.4; HRMS (ESI) calcd for C$_{24}$H$_{20}$N$_2$O$_5$SNa, m/z = 471.0991 [(M+Na) +], found m/z = 471.0984; IR (KBr): $\nu$ 3432, 3313, 3111, 2375, 1629, 1520, 1431, 1321, 1277, 1153, 1078 cm$^{-1}$; enantiomeric excess: 90%, determined by HPLC (Chiralpak AD-H, hexane/2-propanol = 4/1, flow rate 1.0 mL/min, 25 °C, 266 nm) minor peak: t$_R$ = 16.2 min, major peak: t$_R$ = 21.1 min; $[\alpha]_D^{25} = +42.4$ (c 1.2, CHCl$_3$).

4l: 95% yield; $^1$H-NMR (ACETONE-D$_6$) $\delta$: 7.86 (1H, d, $J = 8.2$ Hz), 7.79 (2H, d, $J = 8.7$ Hz), 7.70-7.66 (3H, m), 7.71 (1H, d, $J = 8.7$ Hz), 7.44 (1H, t, $J = 8.0$ Hz), 7.32-7.26 (2H, m), 7.20-7.14 (2H, m), 6.59 (1H, s), 2.27 (3H, s); $^{13}$C-NMR (ACETONE-D$_6$) $\delta$: 153.3, 150.0, 147.1, 141.5, 138.4, 133.1, 130.6, 129.6, 129.2, 128.9, 128.6, 128.5, 128.0, 127.7, 124.6, 123.8, 123.3, 118.7, 118.0, 54.7; HRMS (ESI) calcd for C$_{24}$H$_{20}$N$_2$O$_5$SNa, m/z = 471.0991 [(M+Na) +], found m/z = 471.0980; IR (KBr): $\nu$ 3452, 3316, 3107, 1620, 1534, 1323, 1281, 1156, 1079 cm$^{-1}$; enantiomeric excess: 99%, determined by HPLC (Chiralpak IC-3, hexane/2-propanol = 19/1, flow rate 1.0 mL/min, 25 °C, 231 nm) minor peak: t$_R$ = 36.9 min, major peak: t$_R$ = 41.0 min; $[\alpha]_D^{24} = +29.5$ (c 2.0, CHCl$_3$).

4m: 98% yield; $^1$H-NMR (CDCl$_3$) $\delta$: 7.75 (2H, d, $J = 8.7$ Hz), 7.65-7.47 (2H, m), 7.35 (2H, t, $J = 7.8$ Hz), 7.25 (1H, m), 7.12 (2H, d, $J = 7.8$ Hz), 7.03 (1H, d, $J = 10.1$ Hz), 6.94 (2H, t, $J = 7.8$ Hz), 6.76 (2H, d, $J = 8.7$ Hz), 6.70 (1H, s), 6.43 (1H, d, $J = 10.1$ Hz), 5.73 (1H, s); $^{13}$C-NMR (ACETONE-D$_6$) $\delta$: 164.8, 162.4, 153.4, 150.0, 147.0, 144.8, 133.0, 131.0, 130.9, 130.8, 129.6, 129.3, 128.7, 127.9, 123.9, 123.3, 118.6, 117.5, 114.6, 114.3, 114.1, 54.2; HRMS (ESI) calcd for C$_{23}$H$_{17}$FN$_2$O$_5$SNa, m/z = 475.0740 [(M+Na) +], found m/z = 475.0736; IR (KBr): $\nu$ 3419, 3304, 2375, 1696, 1619, 1526, 1439, 1346, 1256, 1165, 1086 cm$^{-1}$; enantiomeric excess: 85%, determined by HPLC (Chiralpak IE, hexane/2-propanol = 7/1, flow rate 1.0 mL/min, 25 °C, 290 nm) minor peak: t$_R$ = 11.4 min, major peak: t$_R$ = 8.6 min; $[\alpha]_D^{15} = +12.6$ (c 1.5, CHCl$_3$).

4n: 90% yield; $^1$H-NMR (DMSO-D$_6$) $\delta$: 9.96 (1H, br s), 8.81 (1H, br s), 7.88 (2H, d, $J = 8.7$ Hz), 7.64 (2H, d, $J = 8.7$ Hz), 7.58 (2H, d, $J = 7.3$ Hz), 7.55 (1H, d, $J = 9.2$ Hz), 7.44 (2H, d, $J = 8.7$ Hz), 7.25 (1H, t, $J = 8.2$ Hz), 7.19-7.13 (3H, m), 6.95 (1H, d, $J = 9.2$ Hz), 6.49 (1H, s); $^{13}$C-NMR (DMSO-D$_6$) $\delta$: 153.0, 148.6, 146.0, 140.4, 131.3, 131.0, 129.7, 128.4, 6
128.2, 127.4, 126.3, 123.1, 122.4, 119.7, 117.6, 116.1, 52.0; HRMS (ESI) calcd for C_{23}H_{17}BrN_{2}O_{5}SNa, m/z = 534.9939 [(M+Na)^+] , found m/z = 534.9926; IR (KBr): ν 3426, 3315, 3110, 2544, 2465, 2374, 1618, 1522, 1318, 1280, 1157, 1112 cm⁻¹; enantiomeric excess: 90%, determined by HPLC (Chiralcel OD-H, hexane/2-propanol = 19/1, flow rate 1.0 mL/min, 25 °C, 250 nm) minor peak: t_R = 47.5 min, major peak: t_R = 61.2 min; [α]_{D}^{20} = +21.8 (c 1.6, CHCl₃).

4o: 80% yield; \textsuperscript{1}H-NMR (CDCl₃) δ: 8.12 (1H, s), 8.06 (1H, d, J = 7.8 Hz), 7.75-7.67 (3H, m), 7.59 (1H, d, J = 8.6 Hz), 7.45 (1H, t, J = 7.1 Hz), 7.39 (1H, t, J = 7.1 Hz), 7.34 (3H, d, J = 6.85 (1H, d, J = 8.6 Hz), 6.68 (3H, d, J = 7.8 Hz), 6.45 (1H, d, J = 10.1 Hz), 5.99 (1H, s), 2.11 (3H, s); \textsuperscript{13}C-NMR (CDCl₃) δ: 151.2, 148.1, 143.0, 142.8, 135.8, 133.1, 132.0, 130.2, 129.1, 128.8, 128.7, 128.5, 127.5, 126.4, 123.5, 122.2, 121.6, 121.3, 117.8, 116.4, 53.5, 21.1; enantiomeric excess: 73%, determined by HPLC (Chiralpak IC-3, hexane/2-propanol = 4/1, flow rate 1.0 mL/min, 25 °C, 335 nm) minor peak: t_R = 12.4 min, major peak: t_R = 15.4 min.

4p: 100% yield; \textsuperscript{1}H-NMR (ACETONE-D₆) δ: 7.87 (1H, d, J = 8.7 Hz), 7.81 (2H, d, J = 8.7 Hz), 7.70 (2H, d, J = 8.7 Hz), 7.69 (1H, d, J = 8.7 Hz), 7.63 (1H, d, J = 8.7 Hz), 7.46-7.41 (3H, m), 7.34-7.23 (4H, m), 7.04 (1H, d, J = 8.7 Hz), 6.64 (1H, s); \textsuperscript{13}C-NMR (ACETONE-D₆) δ: 153.3, 150.0, 147.0, 141.5, 133.1, 130.7, 129.6, 129.2, 129.0 x 2, 128.6, 127.8, 127.4, 123.8, 123.3, 118.6, 117.9, 54.7; HRMS (ESI) calcd for C_{23}H_{18}N_{2}O_{5}SNa, m/z = 457.0834 [(M+Na)^+], found m/z = 457.0827; IR (KBr): ν 3305, 2359, 1698, 1528, 1430, 1348, 1312, 1162, 1090, 1028 cm⁻¹; enantiomeric excess: 73%, determined by HPLC (Chiralpak AD-H, hexane/2-propanol = 7/1, flow rate 1.0 mL/min, 25 °C, 268 nm) minor peak: t_R = 18.3 min, major peak: t_R = 21.4 min; [α]_{D}^{20} = +22.4 (c 2.3, CHCl₃).

4q: 100% yield; \textsuperscript{1}H-NMR (ACETONE-D₆) δ: 7.99 (1H, d, J = 8.7 Hz), 7.86 (2H, d, J = 8.7 Hz), 7.72 (2H, d, J = 8.7 Hz), 7.68 (1H, d, J = 8.2 Hz), 7.62 (1H, d, J = 8.7 Hz), 7.48-7.42 (2H, m), 7.29 (1H, t, J = 7.5 Hz), 7.05 (1H, d, J = 8.7 Hz), 6.69 (1H, s), 6.34 (1H, dd, J = 3.2, 1.8 Hz), 6.23 (1H, d, J = 3.2 Hz); \textsuperscript{13}C-NMR (ACETONE-D₆) δ: 153.8, 153.7, 150.0, 147.1, 143.0, 132.9, 130.9, 129.6, 129.2, 128.6, 127.6, 123.8, 123.2, 118.6, 115.7, 111.2, 108.4, 50.0; HRMS (ESI) calced for C_{21}H_{16}N_{2}O_{6}SNa, m/z = 447.0627 [(M+Na)^+], found m/z = 447.0617; IR (KBr): ν 3396, 3324, 3162, 3104, 3067, 1702, 1614, 1525, 1411, 1345, 1310, 1281, 1160, 1078 cm⁻¹; enantiomeric excess: 72%, determined by HPLC (Chiralpak AD-H, hexane/2-propanol = 7/1, flow rate 1.0 mL/min, 25 °C, 268 nm) minor peak: t_R = 45.3 min, major peak: t_R = 25.6 min; [α]_{D}^{20} = +37.0 (c 3.9, CHCl₃).
 Procedure for enantioselective Friedel–Crafts (FC)-type reaction of ketimine (2r) with 2-naphthol (3a)

Under N₂ atmosphere, a test tube was charged with imine 2r (0.10 mmol), 2-naphthol 3a (0.15 mmol), and the catalyst 1b (0.005 mmol, 5 mol %) in toluene (0.4 mL). The reaction mixture was stirred at -35 °C. After the purification via SiO₂ column chromatography (hexane/AcOEt = 3/1), the desired product 4 was obtained in 70% yield (33.6mg, 0.07 mmol) with 43% ee. 4t: 70% yield; ^1H-NMR (CDCl₃) δ: 10.02 (1H, s), 7.68 (2H, dd, J = 7.8, 3.7 Hz), 7.34-7.16 (9H, m), 7.05 (1H, t, J = 7.8 Hz), 6.97 (1H, t, J = 7.8 Hz), 6.80 (2H, d, J = 7.8 Hz), 5.87 (1H, s), 5.18 (1H, d, J = 15.8 Hz), 4.87 (1H, d, J = 15.8 Hz), 1.31 (9H, s); ^13C-NMR (CDCl₃) δ: 179.7, 153.8, 143.0, 138.6, 138.2, 135.0, 131.9, 130.7, 130.2, 129.6, 128.8 x 2, 127.6, 127.1, 125.5 x 2, 124.3, 123.5, 122.8, 121.5,
114.2, 110.0, 80.7, 46.4, 28.1; HRMS (ESI) calcd for C_{30}H_{28}N_{2}O_{4}Na, m/z = 503.1947 [(M+Na)^+], found m/z = 503.1932; IR (KBr): ν = 3269, 1696, 1610, 1490, 1349, 1274, 1161, 1048, 818, 738 cm^{-1}; enantiomeric excess: 43%, determined by HPLC (Chiralpak AD-H, hexane/2-propanol = 4/1, flow rate 1.0 mL/min, 25 °C, 231 nm) minor peak: t_R = 17.7 min, major peak: t_R = 36.9 min; [α]D^24_2 = +8.0 (c 1.1, CHCl_3).

**Procedures for the deprotection of sulfonamide group**

![Chemical structure](image)

To a solution of compound 4p (50 mg, 0.12 mmol) in MeOH (0.2 mL) and DCM (0.2 mL), TMSCHN₂ (2N solution in Et₂O, 0.44 mL, 1.0 mmol) was added in 10 portions over 1 h at rt. The reaction mixture was then stirred at 45 °C for 0.5 h. The solvent was evaporated in vacuo. After the purification via SiO₂ column chromatography (hexane/AcOEt = 2/1), the methyl-capped product was obtained (18 mg, 0.04 mmol, 40% yield); \(^1\)H-NMR (CDCl₃) δ: 7.78 (1H, d, J = 8.4 Hz), 7.64 (2H, d, J = 9.2 Hz), 7.56 (2H, d, J = 8.4 Hz), 7.49-7.42 (3H, m), 7.35 (1H, t, J = 7.5 Hz), 7.28-7.20 (4H, m), 6.99 (1H, d, J = 9.2 Hz), 6.62 (1H, bs), 6.47 (1H, d, J = 10.5 Hz), 5.67 (3H, s); \(^1^3\)C-NMR (CDCl₃) δ: 154.3, 148.9, 145.4, 139.6, 132.0, 130.3, 128.3, 128.1, 128.3, 127.8, 127.6, 127.3, 126.3, 124.3, 122.7, 121.8, 120.4, 113.4, 56.5, 54.1; HRMS (ESI) calcd for C_{24}H_{20}N_{2}O_{5}SNa, m/z = 471.0991 [(M+Na)^+], found m/z = 471.0966; IR (KBr): ν = 3435, 3302, 3104, 2917, 2352, 1523, 1348, 1156, 1022 cm^{-1}. Subsequently PhSH (44 μL, 0.43 mmol) was added to a solution of the methyl-capped product (10 mg, 0.022 mmol) and K₂CO₃ (55.2 mg, 0.40 mmol) in DMF (0.2 mL) and CH₃CN (0.2 mL). The mixture was stirred at 50 °C for 4 h. Water was added to the reaction mixture and the solution was extracted with AcOEt. The combined organic layer was back extracted with 1N HCl and then the aqueous layer was basified with NaOH and extracted with AcOEt. Organic layer was dried over Na₂SO₄, and evaporated in vacuo. After the purification via SiO₂ column chromatography (AcOEt), the desired product 8 was obtained (5.9 mg, 0.022 mmol, quant) without racemization. [α]D^23_2 = -145 (73% ee, c 0.85, CHCl₃) (lit. \[^6\] [α]D^25_2 = +196 (> 99% ee, c 1.6, CHCl₃)); \(^1\)H-NMR (CDCl₃) δ: 8.02 (1H, d, J = 8.7 Hz), 7.80 (2H, d, J = 8.7 Hz), 7.42-7.36 (3H, m), 7.34-7.22 (4H, m), 7.18-7.13 (1H, m), 6.13 (1H, s), 3.79 (3H, s), 2.15 (2H, br s); \(^1^3\)C-NMR (CDCl₃) δ: 154.8, 145.4, 132.0, 129.6, 129.2, 128.7, 127.9, 126.8, 126.6, 126.0, 125.9, 123.5, 123.4, 114.2, 56.5, 50.9.
References


$^1$H-NMR and $^{13}$C-NMR charts
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**1H NMR Spectra**

**Compound: 4n**

**Assignments**:
- **3.48 ppm (0.97)**: 
  -4-Br-NH
- **7.66 ppm (0.97)**: 
  - OH
- **7.45 ppm (0.97)**: 
  -OH
- **7.18 ppm (4.00)**: 
  -OH

**13C NMR Spectra**

**Assignments**:
- **130.97 ppm**: 
  - C
- **129.65 ppm**: 
  - C
- **128.26 ppm**: 
  - C
- **127.43 ppm**: 
  - C
- **123.17 ppm**: 
  - C
- **119.78 ppm**: 
  - C
- **117.63 ppm**: 
  - C
- **116.07 ppm**: 
  - C
- **115.07 ppm**: 
  - C

**Spectral Parameters**
- **ObnuC**: 1H
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- **Obset**: 4.19 kHz
- **Obfin**: 7.29 Hz
- **Point**: 13120
- **Freqq**: 100.53 MHz
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- **Frequ**: 31407.04 Hz
- **Scans**: 13312
- **Acqtm**: 1.0433 sec
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- **Irnuc**: 1H
- **Ctemp**: 25.0 c
- **Slvnt**: DMSO
- **Exref**: 39.50 ppm
- **Bf**: 0.10 Hz
- **Rgain**: 54
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SLVNT  ACETN
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BF     0.10 Hz
RGAIN  40

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### Table 1: Peak Area Analysis

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**Note:**

- **Cl**: Chlorine
- **OH**: Hydroxyl
- **NHBoc**: N-Benzylcarbonylamine
- **HSO2Ph**: Benzenesulfonyl
- **ee**: Enantiomeric excess
- **rac-4c**: Racemic 4c
Cl\_\text{NHSO}_2\_\text{OH}

4e, 30% ee

\text{rac-4e}

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\text{rac-4f}
4t, 43% ee

rac-4t

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