# Supporting Information for

## Brønsted Acid-Catalyzed Enantioselective Friedländer Condensations: Achiral

### **Amine Promoter Plays Crucial Role in the Stereocontrol**

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**General data**: NMR spectra were recorded on a Brucker-400 MHz spectrometer. Melting points were determined on a digital melting point apparatus and temperatures were uncorrected. Optical rotations were determined at 589 nm (sodium D line) by using a Perkin-Elmer-343 polarimeter. HRMS (Bio TOF Q) spectra were recorded on P-SIMS-Gly of Bruker Daltonics Inc. Infrared spectra were recorded on a Nicolet MX-1E FT-IR spectromter. HPLC analysis was performed on Waters-Breeze (2487 Dual  $\lambda$  Absorbance Detector and 1525 Binary HPLC Pump, UV detection monitored at 254 nm or 205 nm) and Agilent 1200 series instrument (auto and multiple wavelength detectors). Chiralpak AD, OD and IA columns were purchased from Daicel Chemical Industries. Toluene was dried over Na and distilled prior to use. Petroleum ether, ethyl acetate and dichloromethane for the column chromatography were distilled before use. The relative and absolute configurations of **5aa** and **5ha** were assigned by comparing with the known products.<sup>1</sup>

**Materials:** Compounds **3a**, **3e-3i** were prepared according to the methods reported previously.<sup>2-5</sup> 4-Substituted cyclohexanones **4a**, **4b** and **4c** were purchased from Alfa and Aldrich and used directly without further purification. **4d-4f** were prepared according to literature methods<sup>6</sup>





### 2-amino-5-methoxybenzaldehyde (3b)

5-Hydroxy-2-nitrobenzaldehyde (334 mg, 2 mmol),  $K_2CO_3$  (303mg, 2.2 mmol) and CH<sub>3</sub>I (0.2 mL, 3 mmol) were dissolved in DMF (10 mL) at room temperature and stirred for an additional 12 h. The reaction mixture was diluted with water (20 mL) and extracted with EtOAc (3 x 10 mL). The organic layer was washed with saturated brine (2 x 10 mL), dried over anhydrous MgSO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by column chromatography to give the 5-methoxy-2-nitrobenzaldehyde as a solid in 99% yield. (Flash column chromatography eluent, ethyl acetate / petroleum ether = 1/20).

5-methoxy-2-nitrobenzaldehyde (181 mg, 1 mmol), iron powder (560 mg, 10 mmol), and conc. HCl (2 drops), were added to a mixture of EtOH and H<sub>2</sub>O (4:1, 5 mL). The mixture was heated at reflux for 2 h and then cooled down to RT. Subsequently, it was filtered, diluted with water (10 mL) and extracted with EtOAc (3 x 10 mL). The organic layer was washed with saturated NaHCO<sub>3</sub> (2 x 10 mL) and H<sub>2</sub>O (2 x 10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and then concentrated under reduced pressure. The residue was purified by column chromatography to give **3b** as a solid in 60% yield. (Flash column chromatography eluent, ethyl acetate / petroleum ether = 1/20)

## 2-amino-5-ethoxybenzaldehyde (3c):

Starting with 5-hydroxy-2-nitrobenzaldehyde and ethyl bromide, the reaction was carried out in analogy to the preparation of **3b.** (yield: 65%, two steps) <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 9.83 (s, 1H), 7.02-6.97 (m, 2H), 6.62 (d, *J* = 8.8 Hz, 1H), 5.81 (s, 2H), 4.00 (q, *J* = 7.0 Hz, 2H), 1.40 (t, *J* = 7.0 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 193.5, 150.1, 144.7, 125.2, 118.6, 118.1, 117.6, 64.4, 14.9; IR (KBr): 3457, 3349, 2987, 2908, 1692, 1604, 1555, 1486, 1231, 1143, 1035, 820, 751; APCI FTMS exact mass calcd for (C<sub>9</sub>H<sub>11</sub>NO<sub>2</sub>)<sup>+</sup> requires m/z 166.0868, found m/z 166.0860.

## 2-amino-5-(benzyloxy)benzaldehyde (3d):

Starting with 5-hydroxy-2-nitrobenzaldehyde and benzyl bromide, the reaction was carried out in analogy to the preparation of **3b.** (yield: 58%, two steps) <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 9.82 (s, 1H), 7.44-7.31 (m, 5H), 7.08-7.04 (m, 2H), 6.62 (d, *J* = 7.5 Hz, 1H), 5.84 (s, 2H), 5.03 (s, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 193.5, 149.9, 145.0, 137.0, 128.6, 128.6, 128.1, 127.6, 127.0, 125.5, 118.7, 118.5, 117.7, 71.1; IR (KBr): 3461, 3332, 1664 ,1569, 1549, 1477, 1227, 1170, 1005, 805, 747, 697; APCI FTMS exact mass calcd for (C<sub>14</sub>H<sub>13</sub>NO<sub>2</sub>)<sup>+</sup> requires m/z 228.1024, found m/z 228.1013.

### **General Procedure for Preparation of Cyclohexanones (4g, 4h):**



Magnesium powder (79 mg, 3.3 mmol) and  $I_2$  (20 mg) were added to a solution of RBr (3 mmol) in drv THF (30 mL). The mixture was stirred vigorously and heated carefully until the reaction initiated, and then the reaction mixture was stirred at 60 °C until almost all magnesium powder had disappeared. After the mixture was cooled down to room temperature, 1. 4-cyclohexandionethylenketale A (471 mg, 3 mmol) in anhydrous THF (20 mL) was added dropwise and the resulting solution was refluxed for 36 h. The reaction was quenched by adding saturated NH<sub>4</sub>Cl (50 mL) and extracted with EtOAc (3 x 50 mL). The organic layers were washed with saturated brine (2 x 10 mL) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The solvent was evaporated and the residue was purified by column chromatography to give the title compound  $\mathbf{C}$  as a solid (Flash column chromatography eluent, ethyl acetate / petroleum ether = 1/20).

**B** (2 mmol) was treated with trifluoracetic acid (10 mL) and stirred at room temperature for 10-30 min. The mixture was then poured to a solution of saturated NaHCO<sub>3</sub> (20 mL) and extracted with dichloromethane. The organic layer was washed with brine (20 mL) and dried over Na<sub>2</sub>SO<sub>4</sub>, and then the solvent was evaporated. The purification of the crude product by flash chromatography gave the title compound **C** as a solid (Flash column chromatography eluent, ethyl acetate / petroleum ether = 1/20).

Palladium on carbon (Pd/C, 40 mg) and C (1 mmol) was dissolved in ethyl acetate (15 mL). The mixture was stirred under hydrogen atmosphere at room temperature for 3-6 h. After the catalyst was filtered and the solvent was evaporated, the crude product was purified by flash chromatography to give the title compound **D** as a solid (Flash column chromatography eluent, ethyl acetate / petroleum ether = 1/20).

**4-(biphenyl-4-yl)cyclohexanone (4g):** (yield: 63%, three steps) <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 7.59-7.54 (m, 4H), 7.45-7.40 (m, 2H), 7.35-7.30 (m, 3H), 3.11-3.03 (m, 1H), 2.55-2.51 (m, 4H), 2.29-2.23 (m, 2H), 2.03-1.93 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 211.1, 143.9, 140.8, 139.6, 128.8, 127.3, 127.2, 127.1, 127.0, 42.4, 41.4, 34.0; IR (KBr): 3035, 2927, 2849, 1692, 1417, 1329,

1172, 810, 770, 672, 505; APCI FTMS exact mass calcd for  $(C_{18}H_{218}O)^+$  requires m/z 251.1436, found m/z 251.1430.

**4-(naphthalen-2-yl)cyclohexanone (4h):** (yield: 81%, three steps) <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.82-7.79 (m, 3H), 7.68 (s, 1H), 7.49-7.42 (m, 2H), 7.39 (dd, J = 8.5, 1.8 Hz, 1H), 3.23-3.16 (m, 1H), 2.58-2.53 (m, 4H), 2.34-2.29 (m, 2H), 2.11-2.00 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 211.1, 142.2, 133.6, 132.4, 128.2, 127.6, 126.2, 125.6, 124.8, 42.9, 41.4, 33.9; IR (KBr): 3035, 2977, 2868, 1721, 1320, 1172, 820, 731, 486; APCI FTMS exact mass calcd for (C<sub>16</sub>H<sub>16</sub>O)<sup>+</sup> requires m/z 225.1280, found m/z 225.1272.

### **General Procedure for the Enantioselective Friedländer Condensations:**

**3** (0.1 mmol), 2-naphthylamine (0.25 mmol) and MgSO<sub>4</sub> (200 mg) were mixed in toluene (1 mL) at room temperature and stirred for 2 h, then the catalyst **1b** (0.01 mmol) was added and stirred for 0.5 h. After cooling down to 0 °C, ketone (0.2 mmol) in toluene (1 mL) was added via a syringe for 1 h. The reaction mixture was stirred at this temperature until the reaction was complete (monitored by TLC, 3-7 days). Then the reaction mixture was filtered to remove MgSO<sub>4</sub>, and the solid powder was washed with ethyl acetate (5.0 mL). The resultant solution was quenched with saturated aqueous NaHCO<sub>3</sub> (5 mL) and the aqueous layer was extracted with ethyl acetate (2 x 10 mL). The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After evaporation under the reduced pressure, the residue was purified through flash column chromatography on silica gel (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1) to yield pure product.

2-phenyl-1,2,3,4-tetrahydroacridine (5aa): yellow oil. vield: 83%: (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 8.00 (d, J = 8.5 Hz, 1H), 7.80 (s, 1H), 7.70 (d, J = 8.2 Hz, 1H), 7.64-7.60 (m, 1H), 7.46-7.42 (m, 1H), 7.37-7.23 (m, 5H), 3.37-3.19 (m, 3H), 3.15-3.06 (m, 2H), 2.35-2.29 (m, 1H), 2.19-2.08 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 158.5, 146.8, 145.7, 135.1, 130.3, 128.8, 128.7, 128.4, 127.2, 127.0, 126.8, 126.5, 125.7, 40.4, 37.4, 33.6, 30.5; IR (KBr) 3027, 2929, 1601, 1492, 1415, 751, 700; Enantiomeric excess: 93%, determined by HPLC (Daicel Chirapak OD-H, hexane / isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm):  $t_R$ =11.71 min (minor),  $t_{\rm R}$  =12.68 min (major);  $[\alpha]_{\rm D}^{20}$  = +40.6 (c 1.0, CHCl<sub>3</sub>). APCI FTMS exact mass calcd for  $(C_{20}H_{19}NO)^+$  requires m/z 259.1361, found m/z 259.1335.

**7-methoxy-2-phenyl-1,2,3,4-tetrahydroacridine (5ba):** white solid, mp 106-108 °C, yield: 86%; (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.89 (d, J = 9.2 Hz, 1H), 7.73 (s, 1H), 7.37-7.25 (m, 6H), 6.98 (d, J = 2.8 Hz, 1H), 3.91 (s, 3H), 3.33-3.07 (m, 5H), 2.35-2.29 (m, 1H), 2.19-2.11 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 157.2, 155.8, 145.8, 143.0, 134.0, 130.6, 129.8, 128.6, 128.0, 126.8, 126.5, 121.5, 104.5, 55.5, 40.5, 37.4, 33.3, 30.6; IR (KBr): 3030, 2929, 1597, 1503, 1388, 1213, 1025, 823, 702, 594; Enantiomeric excess: 87%, determined by HPLC (Daicel Chirapak OD-H, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm ): t<sub>R</sub> = 10.76 min (minor), t<sub>R</sub> = 13.50 min (major);  $[\alpha]_D^{20} = +59.5$  (*c* 1.0, CDCl<sub>3</sub>); APCI FTMS exact mass calcd for (C<sub>20</sub>H<sub>19</sub>NO)<sup>+</sup> requires m/z 290.1545, found m/z 290.1535.

**7-ethoxy-2-phenyl-1,2,3,4-tetrahydroacridine** (**5ca**): yellow oil, yield: 66%; (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.89 (d, J = 9.2 Hz, 1H), 7.72 (s, 1H), 7.38-7.30 (m, 5H), 7.28-7.24 (m, 1H), 6.97 (d, J = 2.7 Hz, 1H), 4.13 (q, J = 7.0 Hz, 2H), 3.33-3.07 (m, 5H), 2.34-2.30 (m, 1H), 2.19-2.09 (m, 1H), 1.48 (t, J = 7.0 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 156.6, 155.6, 145.8, 142.9, 134.0, 130.5, 129.8, 128.6, 128.0, 126.8, 126.5, 121.8, 105.2, 63.7, 40.5, 37.4, 33.3, 30.6, 14.8; IR (KBr): IR(KBr): 3035, 2908, 1604, 1358, 1231, 1104, 1045, 820, 741, 691; Enantiomeric excess: 92%, determined by HPLC (Daicel Chirapak OD-H, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm ): t<sub>R</sub> = 9.65 min (minor), t<sub>R</sub> = 11.17 min (major); [ $\alpha$ ]<sub>D</sub><sup>20</sup> = +39.5 (*c* 1.0, CHCl<sub>3</sub>); APCI FTMS exact mass calcd for (C<sub>21</sub>H<sub>21</sub>NO)<sup>+</sup> requires m/z 304.1701, found m/z 304.1690.

**7-(benzyloxy)-2-phenyl-1,2,3,4-tetrahydroacridine (5da):** yellow solid, mp 135-136 °C, yield: 66%; (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.92 (d, *J* = 9.2Hz, 1H), 7.72 (s, 1H), 7.49-7.47 (m, 2H), 7.43-7.30 (m, 8H), 7.28-7.23 (m, 1H), 7.07 (d, *J* = 2.8Hz, 1H), 5.17 (s, 2H), 3.34-3.07 (m, 5H), 2.35-2.29 (m, 1H), 2.19-2.09 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 156.4, 155.9, 145.8, 143.0, 136.7, 130.6, 129.9, 128.7, 128.6, 128.1, 128.0, 127.5, 126.8, 121.9, 105.9, 70.3, 40.5, 37.4, 33.3, 30.6; IR (KBr): 3035, 2957, 1633, 1486, 1437, 1398, 1221, 1153, 1035, 810, 751, 682; Enantiomeric excess: 95%, determined by HPLC (Daicel Chirapak IA-H, hexane / isopropanol = 85/15, flow rate 1.0 mL/min, T = 30 °C, 254 nm ): t<sub>R</sub> = 44.56 min (minor), t<sub>R</sub> = 49.60

min (major);  $[\alpha]_D^{20} = +30.1$  (*c* 1.0, CHCl<sub>3</sub>); APCI FTMS exact mass calcd for  $(C_{26}H_{23}NO)^+$  requires m/z 366.1858, found m/z 366.1846.

**7-fluoro-2-phenyl-1,2,3,4-tetrahydroacridine (5ea):** clolourless oil, yield: 71%; (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.97 (dd, J = 9.2 Hz, J = 5.3 Hz, 1H), 7.74 (s, 1H), 7.40-7.33 (m, 3H), 7.31-7.23 (m, 4H), 3.34-3.05 (m, 5H), 2.34-2.29 (m, 1H), 2.17-2.08 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 161.3, 158.8, 157.8 (d,  $J_{C-F} = 2.8$  Hz), 145.5, 143.9, 134.4 (d,  $J_{C-F} = 5.4$  Hz), 131.3, 130.8 (d,  $J_{C-F} = 9.1$  Hz), 128.7, 127.6 (d,  $J_{C-F} = 9.8$  Hz), 126.8, 126.6, 118.9 (d,  $J_{C-F} = 25.6$ Hz), 109.8 (d,  $J_{C-F} = 21.4$  Hz), 40.3, 37.3, 33.5, 30.4; IR (KBr): 2917, 1633, 1506, 1437, 1212, 1123, 820, 772; Enantiomeric excess: 84%, determined by HPLC (Daicel Chirapak OD-H, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm ): t<sub>R</sub> = 14.99 min (minor), t<sub>R</sub> =16.41 min (major);  $[\alpha]_D^{20} = +8.4$  (*c* 1.0, CHCl<sub>3</sub>); APCI FTMS exact mass calcd for (C<sub>19</sub>H<sub>16</sub>FN)<sup>+</sup> requires m/z 278.1345, found m/z 278.1338.

**6,7-dimethoxy-2-phenyl-1,2,3,4-tetrahydroacridine** (**5fa**): yellow solid, mp 172-173 °C, yield: 50%; (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.61 (s, 1H), 7.30-7.23 (m, 5H), 7.20-7.16 (m, 1H), 6.89 (s, 1H), 3.94 (s, 3H), 3.92 (s, 3H), 3.24-2.98 (m, 5H), 2.26-2.21 (m, 1H), 2.12-2.01 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 155.8, 152.0, 149.3, 145.9, 143.7, 133.7, 128.6, 128.3, 126.8, 126.4, 122.5, 107.2, 104.5, 56.1, 56.0, 40.6, 37.3, 33.3, 30.6; IR (KBr) 2966, 2938, 1574, 1496, 1388, 1280, 1202, 1133, 1015, 869, 761, 691; Enantiomeric excess: 90%, determined by HPLC (Daicel Chirapak OD-H, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm ): t<sub>R</sub> = 12.30 min (minor), t<sub>R</sub> = 15.62 min (major);  $[\alpha]_D^{20} = +40.6$  (*c* 1.0, CHCl<sub>3</sub>); APCI-FTMS exact mass calcd for  $(C_{21}H_{21}NO_2)^+$  requires m/z 320.1651, found m/z 320.1639.

**8-phenyl-6,7,8,9-tetrahydro-[1,3]dioxolo[4,5-b]acridine (5ga):** white solid, mp 160-161 °C, yield: 55%; (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.65 (s, 1H), 7.37-7.30 (m, 5H), 7.26-7.23 (m, 1H), 6.96 (s, 2H), 3.29-3.04 (m, 5H), 2.33-2.28 (m, 1H), 2.18-2.07 (m, 1H) ; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 155.8, 150.2, 147.2, 145.9, 144.9, 134.3, 128.6, 128.4, 126.8, 126.4, 123.9, 105.0, 102.0, 101.5, 40.5, 37.1, 33.3, 30.5,; IR (KBr): 3035, 2917, 1623, 1616, 1496, 1394, 1246, 1198, 1039, 938, 866; Enantiomeric excess: 94%, determined by HPLC (Daicel Chirapak OD-H, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm ): t<sub>R</sub> = 15.72 min

(minor),  $t_R = 24.02 \text{ min (major)}; [\alpha]_D^{20} = +48.2$  (*c* 1.0, CHCl<sub>3</sub>); APCI FTMS exact mass calcd for  $(C_{20}H_{17}NO_2)^+$  requires m/z 304.1338, found m/z 304.1326.

**6-chloro-2-phenyl-1,2,3,4-tetrahydroacridine (5ha):** white solid, mp 90-92 °C, yield: 94%; (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.00 (d, *J* = 1.9 Hz, 1H), 7.82 (s, 1H), 7.65 (d, *J* = 8.7 Hz, 1H), 7.41 (dd, *J* = 8.7 Hz, *J* = 1.9 Hz, 1H), 7.38-7.34 (m, 2H), 7.32-7.30 (m, 2H), 7.28-7.24 (m, 1H), 3.36-3.30 (m, 1H), 3.27-3.08 (m, 4H), 2.37-2.31 (m, 1H), 2.22-2.10 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 159.7, 147.1, 145.5, 134.9, 134.4, 130.7, 128.7, 128.2, 127.5, 126.8, 126.8, 126.8, 126.6, 125.5, 40.3, 37.3, 33.6, 30.4; IR (KBr): 3028, 2929, 1615, 1484, 1413, 1068, 764, 699; Enantiomeric excess: 87%, determined by HPLC (Daicel Chirapak OD-H, hexane / isopropanol = 95/5, flow rate 1.0 mL/min, T = 30 °C, 254 nm ): t<sub>R</sub> = 18.88 min (minor), t<sub>R</sub> = 21.67 min (major); [α]<sub>D</sub><sup>20</sup> = +48.0 (*c* 1.0, CDCl<sub>3</sub>).

**7-methyl-2-phenyl-1,2,3,4-tetrahydroacridine (5ia):** clolourless oil , yield: 94%; (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.89 (d, *J* = 8.3 Hz, 1H), 7.74 (s, 1H), 7.47-7.44 (m, 2H), 7.37-7.30 (m, 4H), 7.27-7.23 (m, 1H), 3.35-3.07 (m, 5H), 2.51 (s, 3H), 2.35-2.29 (m, 1H), 2.20-2.09 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 157.4, 145.8, 145.5, 134.5, 131.1, 130.3, 128.6, 128.1, 127.2, 126.8, 126.5, 125.8, 40.5, 27.4, 33.5, 30.5, 21.6; IR (KBr): 3045, 2917, 2388, 1604, 1525, 1447, 388, 829, 761, 702; Enantiomeric excess: 95%, determined by HPLC (Daicel Chirapak OD-H, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm ): t<sub>R</sub> = 9.46 min (minor), t<sub>R</sub> = 12.80 min (major); [ $\alpha$ ]<sub>D</sub><sup>20</sup> = +48.1 (*c* 1.0, CHCl<sub>3</sub>); APCI FTMS exact mass calcd for (C<sub>20</sub>H<sub>19</sub>N)<sup>+</sup> requires m/z 274.1596, found m/z 274.1586.

**2,7-dimethyl-1,2,3,4-tetrahydroacridine** (**5ib**): white solid, mp 100-103 °C , yield: 70%; (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.86 (d, J = 8.4 Hz, 1H), 7.68 (s, 1H), 7.44-7.41 (m, 2H), 3.23-3.17 (m, 1H), 3.12-2.98 (m, 2H), 2.61-2.55 (m, 1H), 2.49 (s, 3H), 2.09-1.95 (m, 2H), 1.65-1.55 (m, 1H), 1.12 (d, J = 6.6 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 158.0, 145.3, 135.2, 134.3, 130.8, 130.5, 128.0, 127.2, 125.7, 37.9, 33.0, 31.5, 29.2, 21.7, 21.5; IR (KBr): 2949, 2914, 2860, 1610, 1496, 1455, 1372, 937, 813; Enantiomeric excess: 87%, determined by HPLC (Daicel Chirapak OD-H, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm ):

 $t_R = 4.55 \text{ min (minor)}, t_R = 7.02 \text{ min (major)}; [\alpha]_D^{20} = +81.6 (c \ 1.0, \text{ CHCl}_3); \text{ APCI FTMS exact}$ mass calcd for  $(C_{15}H_{17}N)^+$  requires m/z 212.1439, found m/z 212.1431.

**2-ethyl-7-methyl-1,2,3,4-tetrahydroacridine** (**5ic**): clolourless oil, yield: 73%; (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.86 (d, J = 8.4 Hz, 1H), 7.70 (s, 1H), 7.44-7.41 (m, 2H), 3.24-3.17 (m, 1H), 3.10-3.01 (m, 2H), 2.61-2.55 (m, 1H), 2.49 (s, 3H), 2.15-2.10 (m, 1H), 1.78-1.69 (m, 1H), 1.62-1.52 (m, 1H), 1.49-1.42 (m, 2H), 1.02 (t, J = 7.4 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 158.3, 145.3, 135.2, 134.4, 130.8, 130.6, 128.0, 127.2, 125.7, 35.8, 35.6, 33.0, 29.1, 28.9, 21.5, 11.6; IR (KBr): 2976, 2917, 1604, 1496, 1437, 1369, 1153, 918, 820, 613; Enantiomeric excess: 88%, determined by HPLC (Daicel Chirapak OD-H, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm ): t<sub>R</sub> = 4.52 min (minor), t<sub>R</sub> = 6.65 min (major);  $[\alpha]_D^{20} = +68.0$  (*c* 1.0, CHCl<sub>3</sub>); APCI-FTMS exact mass calcd for (C<sub>16</sub>H<sub>19</sub>N)<sup>+</sup> requires m/z 226.1596, found m/z 226.1587.

**7-methyl-2-p-tolyl-1,2,3,4-tetrahydroacridine (5id):** clolourless oil, yield: 93%; (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.89 (d, *J* = 8.3 Hz, 1H), 7.74 (s, 1H), 7.47-7.44 (m, 2H), 7.22-7.15 (m, 4H), 3.35-3.17 (m, 3H), 3.13-3.04 (m, 2H), 2.51 (s, 3H), 2.35 (s, 3H), 2.33-2.27 (m, 1H), 2.19-2.07 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 157.5, 145.5, 142.8, 136.0, 125.4, 134.5, 131.0, 130.3, 129.3, 128.1, 127.2, 126.7, 125.8, 40.1, 37.5, 33.6, 30.7, 21.6, 21.0; IR (KBr): 3016, 2938, 1599, 1492, 1423, 1370, 927, 820, 538; Enantiomeric excess: 93%, determined by HPLC (Daicel Chirapak OD-H, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm ): t<sub>R</sub> = 6.54 min (minor), t<sub>R</sub> = 8.41 min (major);  $[\alpha]_D^{20}$  = +40.0 (*c* 1.0, CHCl<sub>3</sub>); APCI FTMS exact mass calcd for (C<sub>21</sub>H<sub>21</sub>N)<sup>+</sup> requires m/z 228.1752, found m/z 228.1741.

**2-(4-methoxyphenyl)-7-methyl-1,2,3,4-tetrahydroacridine** (**5ie**): clolourless oil, yield: 79%; (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.89 (d, J = 8.3 Hz, 1H), 7.73 (s, 1H), 7.47-7.44 (m, 2H), 7.25-7.21 (m, 2H), 6.91-6.88 (m, 2H), 3.81 (s, 3H), 3.33-3.17 (m, 3H), 3.11-3.03 (m, 2H), 2.51 (s, 3H), 2.32-2.27 (m, 1H), 2.15-2.05 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 158.2, 157.5, 145.4, 137.9, 135.4, 134.4, 131.0, 130.3, 128.0, 127.7, 127.2, 125.8, 114.0, 55.3, 39.6, 37.6, 33.5, 30.8, 21.5; IR (KBr): 3025, 2917, 1702, 1594, 1525, 1417, 1202, 1172, 1055, 829, 564; Enantiomeric excess: 93%, determined by HPLC (Daicel Chirapak OD-H, hexane / isopropanol =

80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm ):  $t_R = 7.82 \text{ min (minor)}, t_R = 11.48 \text{ min (major)};$  $[\alpha]_D^{20} = +30.0 \ (c \ 1.0, \ CHCl_3);$  APCI FTMS exact mass calcd for  $(C_{21}H_{21}NO)^+$  requires m/z 304.1701, found m/z 304.1690.

**2-(4-chlorophenyl)-7-methyl-1,2,3,4-tetrahydroacridine (5if):** clolourless oil, yield: 80%; (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.89 (d, *J* = 9.2 Hz, 1H), 7.74 (s, 1H), 7.48-7.45 (m, 2H), 7.33-7.30 (m, 2H), 7.25-7.22 (m, 2H), 3.34-3.03 (m, 5H), 2.51 (s, 3H), 2.33-2.27 (m, 1H), 2.16-2.06 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 157.1, 145.5, 144.2, 135.5, 134.5, 132.1, 131.2, 129.8, 128.7, 128.2, 128.0, 127.2, 125.8, 39.9, 37.3, 33.4, 30.5, 21.5; IR (KBr): 3025, 2917, 1614, 1477, 1378, 1085, 1005, 875, 820, 721 Enantiomeric excess: 95%, determined by HPLC (Daicel Chirapak OD-H, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm ): t<sub>R</sub> = 8.34 min (minor), t<sub>R</sub> = 15.71 min (major);  $[\alpha]_D^{20} = +33.1$  (*c* 1.0, CHCl<sub>3</sub>); APCI-FTMS exact mass calcd for (C<sub>20</sub>H<sub>18</sub>ClN)<sup>+</sup> requires m/z 308.1206, found m/z 308.1195.

**2-(biphenyl-4-yl)-7-methyl-1,2,3,4-tetrahydroacridine (5ig):** white solid, mp 160-162 °C, yield: 99%; (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.90 (d, *J* = 8.4 Hz, 1H), 7.77 (s, 1H), 7.62-7.58 (m, 4H), 7.48-7.32 (m, 7H), 3.38-3.12 (m, 5H), 2.52 (s, 3H), 2.40-2.34 (m, 1H), 2.24-2.14 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 157.4,145.5, 144.9, 141.0, 139.5, 135.4, 134.5, 131.1, 130.2, 128.8, 128.1, 127.4, 127.3, 127.2, 127.2, 127.1, 125.8, 40.2, 37.4, 33.5, 30.6, 21.6; IR (KBr): 3045, 2927, 1614, 1477, 1398, 839, 741, 691;Enantiomeric excess: 93%, determined by HPLC (Daicel Chirapak OD-H, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm ): t<sub>R</sub> = 10.27 min (minor), t<sub>R</sub> = 13.89 min (major); [ $\alpha$ ]<sub>D</sub><sup>20</sup> = +12.2 (*c* 1.0, CHCl<sub>3</sub>); APCI FTMS exact mass calcd for (C<sub>26</sub>H<sub>23</sub>N)<sup>+</sup> requires m/z 350.1909, found m/z 350.1895.

**7-methyl-2-(naphthalen-2-yl)-1,2,3,4-tetrahydroacridine** (**5ih**): clolourless oil, yield: 99%; (Flash column chromatography eluent, dichloromathane 200 mL, and then petroleum ether / ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.91 (d, *J* = 8.4 Hz, 1H), 7.85-7.74 (m, 5H), 7.50-7.43 (m, 5H), 3.40-3.18 (m, 5H), 2.52 (s, 3H), 2.45-2.38 (m, 1H), 2.30-2.19 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 157.4,145.5, 143.2, 135.4, 133.6, 132.4, 131.1, 130.2, 128.2, 128.1, 127.7, 127.6, 127.2, 126.1, 125.8, 125.7, 125.4, 124.9, 40.6, 37.3, 33.6, 30.5, 21.5; IR (KBr): 3055, 2917, 1594, 1486, 1420, 1358, 810, 741; Enantiomeric excess: 94%, determined by HPLC (Daicel Chirapak OD-H, hexane / isopropanol = 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm ): t<sub>R</sub> =

17.37 min (minor),  $t_R = 20.45$  min (major);  $[\alpha]_D^{20} = +16.0$  (*c* 1.0, CHCl<sub>3</sub>); APCI FTMS exact mass calcd for  $(C_{24}H_{21}N)^+$  requires m/z 324.1752, found m/z 324.1741.

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# NMR and HPLC Spectra















### 2-phenyl-1,2,3,4-tetrahydroacridine (5aa)





# 7-ethoxy-2-phenyl-1,2,3,4-tetrahydroacridine (5ca)













### 8-phenyl-6,7,8,9-tetrahydro-[1,3]dioxolo[4,5-b]acridine (5ga)



## 6-chloro-2-phenyl-1,2,3,4-tetrahydroacridine (5ha)



## 7-methyl-2-phenyl-1,2,3,4-tetrahydroacridine (5ia)



f1 (ppm) 



# 2,7-dimethyl-1,2,3,4-tetrahydroacridine (5ib)



## 7-methyl-2-p-tolyl-1,2,3,4-tetrahydroacridine (5id)







## 2-(biphenyl-4-yl)-7-methyl-1,2,3,4-tetrahydroacridine (5ig)

<sup>2</sup> 7, 2088 <sup>2</sup> 7, 2088 <sup>2</sup> 7, 2026 <sup>2</sup> 7, 2026 <sup>2</sup> 7, 2026 <sup>2</sup> 7, 2679	•	• •	• • • •	·	
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# 7-methyl-2-(naphthalen-2-yl)-1,2,3,4-tetrahydroacridine (5ih)

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Peak	RetTime	Type	Width	Area	Height	Area
#	[min]		[min]	mAU *s	[mAU ]	8
1	10.754	BB	0.3539	828.75641	34.93535	6.3264
2	13.498	BB	0.4202	1.22713e4	451.89020	93.6736









Peak	RetTime	Type	Width	Area	Height	Area
#	[min]		[min]	mAU *s	[mAU ]	8
1	14.994	BB	0.3835	1302.2542	27 52.58776	8.0131
2	16.412	BB	0.4804	1.49493e4	4 466.16827	91.9869















	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	4.531	1246514	50.92	123501	53.39
2	6.682	1201361	49.08	107800	46.61











