

**AgAsF₆/Sm(OTf)₃ Promoted Reversal of Enantioselectivity
for the Asymmetric Friedel-Crafts Alkylations of Indoles with
 β,γ -Unsaturated α -Ketoesters**

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1. General

^1H NMR spectra were recorded on commercial instruments (400 MHz). Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (CDCl_3 , $\delta = 7.26$). Spectra are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR spectra were collected on commercial instruments (100 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard (CDCl_3 , $\delta = 77.0$). The enantiomeric excesses were determined by HPLC analysis on chiral DAICEL CHIRALCEL AS-H, OD-H, AD, OJ and AS-H column. Optical rotations were measured on a commercial polarimeter and reported as follows: $[\alpha]_D^{T_D}$ (c = g/100 mL, solvent). Reagents obtained from commercial sources were used without further purification. CH_2Cl_2 were distilled over CaH_2 before use. The other solvents were distilled over metal sodium before use.

2. General procedure for the preparation of chiral ligands

i) The N,N' -dioxdes were prepared according to the methods reported in the literature.¹⁻⁸

3. Typical experimental procedures for the asymmetric Friedel-Crafts alkylation of indoles and β,γ -unsaturated α -ketoesters

Procedure A: The mixture of ligand **1d** (1.5 mg, 0.0025 mmol), Sm(OTf)₃ (1.5 mg, 0.0025 mmol) and β,γ -unsaturated α -ketoester **3a** (95.1 mg, 0.5 mmol) in CH₂Cl₂ (0.4 mL) was stirred at room temperature for 5 to 10 minutes under nitrogen atmosphere. Then the reaction mixture was cooled to -20 °C and indole **2a** (0.5 mmol, 58.6 mg in 0.2 mL CH₂Cl₂) was added under stirring. The reaction mixture was stirred at -20 °C for 15 minutes and directly purified by flash chromatography on silica gel to give (*R*)-**4a** in 96% yield with 98% ee.

Procedure B: The mixture of ligand **1a** (17.8 mg, 0.025 mmol), AgAsF₆ (7.5 mg, 0.025 mmol) and β,γ -unsaturated α -ketoester **3a** (47.6 mg, 0.25 mmol) in THF (1.9 mL) was stirred at room temperature for 5 to 10 minutes under nitrogen atmosphere. Then the reaction mixture was cooled to -20 °C and indole **2a** (0.25 mmol, 29.3 mg in 0.1 mL THF) was added under stirring. The reaction mixture was stirred at -20 °C for 68 hours and directly purified by flash chromatography on silica gel to give (*S*)-**4a** in 82% yield with 85% ee.

4. Some representative screening results for the Friedel-Crafts alkylation of indole **2a** with β,γ -unsaturated α -ketoester **3a**.

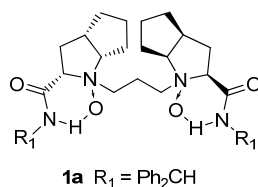
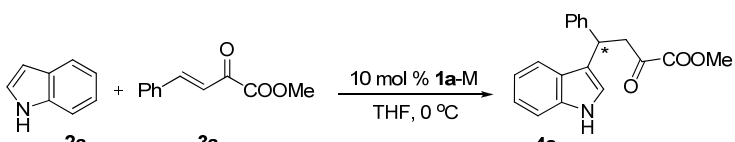


Table 1: Catalytic enantioselective Friedel-Crafts alkylation of indole **2a** with β,γ -unsaturated α -ketoesters **3a** in the presence of **1a-M**.^[a]

			
Entry	M	Yield [%] ^[b]	ee [%] ^[c]
1	Yb(OTf) ₃	87	7(<i>R</i>)
2	Y(OTf) ₃	83	17(<i>R</i>)
3	La(OTf) ₃	83	2
4	In(OTf) ₃	90	4(<i>R</i>)
5	Sc(OTf) ₃	84	0
6	Cu(OTf) ₂	11	11(<i>R</i>)
7	Zn(OTf) ₂	65	0

[a] Unless otherwise noted, reactions were carried out with **1a** (10 mol %), **M** (10 mol %), **2a** (0.25 mmol), and **3a** (0.25 mmol) in THF (0.3 mL) at 0 °C. [b] Isolated yield. [c] Determined by chiral HPLC analysis.

5. Experimental procedure for the scale-up Friedel-Crafts alkylations of indole

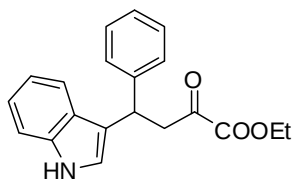
2a and β,γ -unsaturated α -ketoester 3a

i) Experimental procedure for the **mixture solution A**: The ligand **1d** (3.0 mg, 0.005 mmol), Sm(OTf)₃ (3.0 mg, 0.005 mmol) and β,γ -unsaturated α -ketoester **3a** (95.1 mg, 0.5 mmol) in CH₂Cl₂ (0.4 mL) was stirred at room temperature for 5 to 10 minutes under nitrogen atmosphere.

ii) To a solution of β,γ -unsaturated α -ketoester **3a** (4.71 g, 24.75 mmol) in CH₂Cl₂ (4 mL) was added the **mixture solution A** (0.2 mL) at room temperature. Then the reaction mixture was cooled to -20 °C and indole **2a** (25 mmol, 2.93 g in 3.8 mL CH₂Cl₂) was added under stirring. The reaction mixture was stirred at -20 °C for 43 hours and directly purified by flash chromatography on silica gel to give (*R*)-**4a** in 93% yield with 84% ee. After a simple single recrystallization, the enantiometric excess could be increased to 98% ee with 82% rescrystal yield (5.82 g).

6. Data for alkylation products

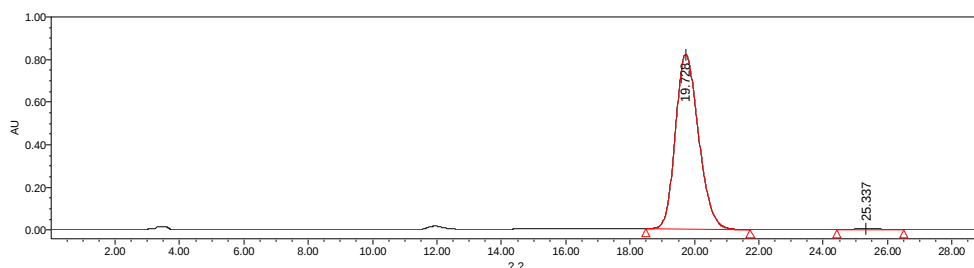
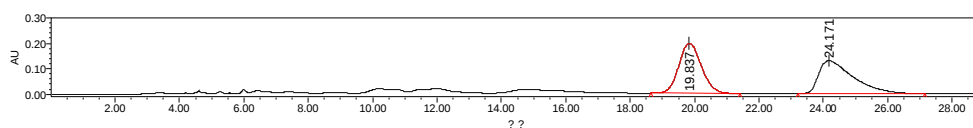
4-(1H-Indol-3-yl)-2-oxo-4-phenylbutyric acid methyl ester¹⁰



(R)-enantiomer (Table 3, entry 1): Prepared according to general **procedure A**. After 15 minutes, the crude material was directly purified by flash chromatography on silica gel

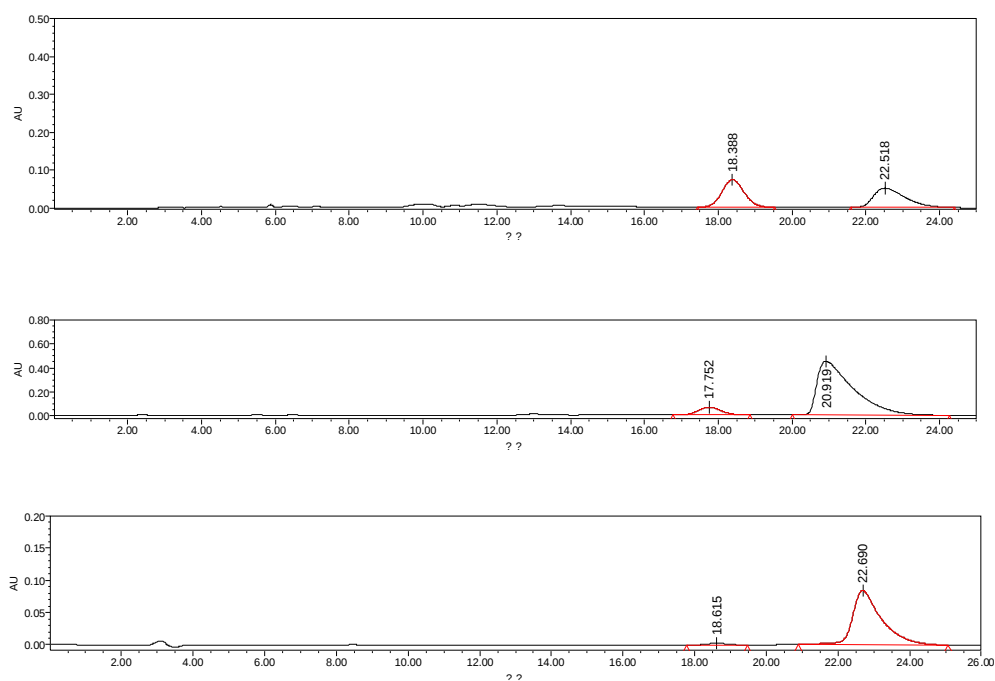
(petroleum ether/ethyl acetate, 4:1) to afford the white solid in 96% yield with 98% ee.

$[\alpha]_D^{23} = -24.0$ ($c = 0.680$, CHCl_3); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (major) = 19.728 min, t_r (minor) = 25.337 min. ^1H NMR (400 MHz, CDCl_3): $\delta = 8.06$ (s, 1H), 7.40 (d, $J = 8.0$ Hz, 1H), 7.32-7.10 (m, 7H), 7.02-6.98 (m, 1H), 6.93 (d, $J = 2.4$ Hz, 1H), 4.90 (d, $J = 7.6$ Hz, 1H), 4.17 (dq, $J = 7.6, 1.6$ Hz, 2H), 3.66 (dd, $J = 16.8, 7.2$ Hz, 1H), 3.57 (dd, $J = 16.8, 7.6$ Hz, 1H), 1.23 (t, $J = 7.2$ Hz, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 192.20, 159.93, 142.24, 135.52, 127.50, 126.74, 125.55, 125.35, 121.16, 120.61, 118.41, 118.29, 117.08, 110.20, 61.47, 44.61, 36.77, 12.84$ ppm; ES-HRMS Calcd for $\text{C}_{20}\text{H}_{20}\text{NO}_3$ $[\text{M} + \text{H}]^+$ 322.1438, Found: 322.1439.

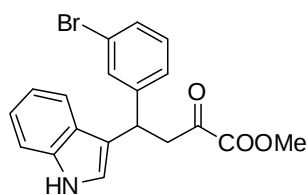


(S)-enantiomer (Table 2, entry 1): Prepared according to general **procedure B**.

After 68 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the white solid in 82% yield with 85% ee. After a simple recrystallization, the enantioselectivity could be increased to 95% ee. $[\alpha]_D^{23} = +33.1$ ($c = 0.242$, CHCl_3); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (minor) = 17.752 min, t_r (major) = 20.919 min.

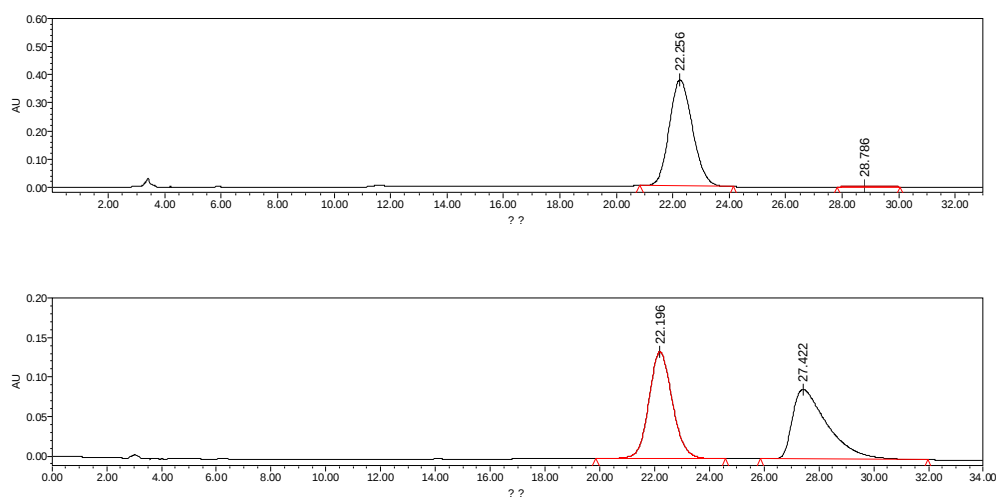


4-(1H-Indol-3-yl)-2-oxo-4-(3-bromophenyl)butyric acid methyl ester



(-)-enantiomer (Table 3, entry 2): Prepared according to general **procedure A**. After 20 minutes, the crude material

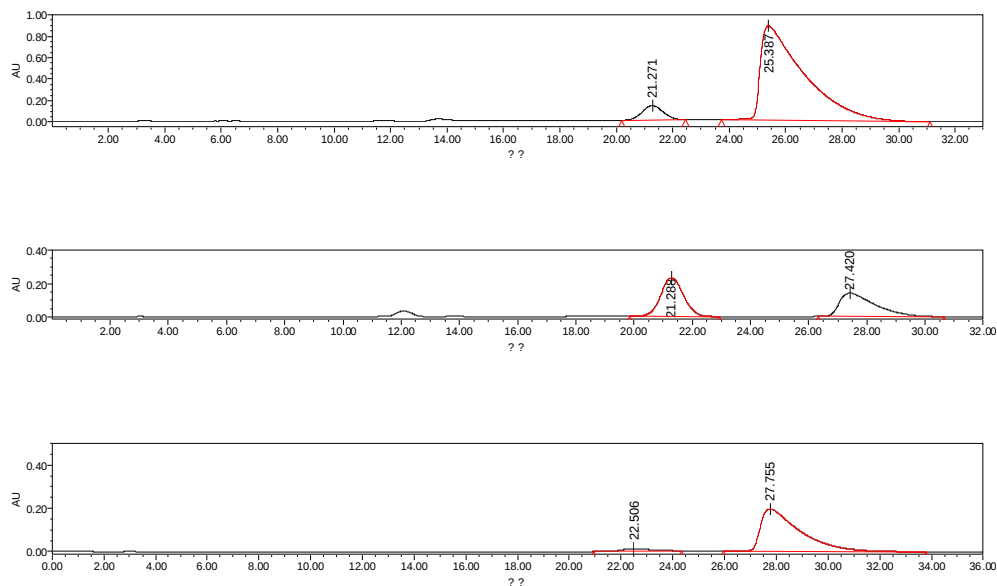
was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the white solid in 98% yield with 98% ee. M.p. 88-90 °C; $[\alpha]_D^{23} = -26.3$ ($c = 0.320$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (major) = 22.256 min, t_r (minor) = 28.786 min. ^1H NMR (400 MHz, CDCl_3): $\delta = 8.06$ (s, 1H), 7.46-7.26 (m, 5H), 7.19-7.02 (m, 4H), 4.88 (t, $J = 7.2$ Hz, 1H), 3.79 (s, 3H), 3.68 (dd, $J = 17.2, 7.2$ Hz, 1H), 3.56 (dd, $J = 17.2, 7.6$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 192.10, 161.10, 145.68, 136.54, 130.80, 130.11, 129.80, 126.55, 126.21, 122.64, 122.50, 121.51, 119.72, 119.20, 117.58, 111.23, 53.03, 45.43, 37.30$ ppm; ES-HRMS Calcd for $\text{C}_{19}\text{H}_{17}\text{NBrNO}_3$ $[\text{M} + \text{H}]^+$ 386.0386, Found: 386.0390.



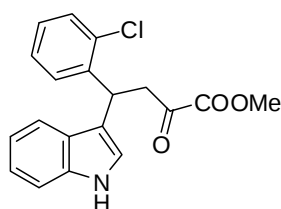
(+)-enantiomer (Table 2, entry 2): Prepared according to general **procedure B**.

After 51 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the white solid in 75% yield with 86% ee. After a simple recrystallization, the enantioselectivity could be increased to 92% ee. $[\alpha]_D^{23} = +23.7$ ($c = 0.358$, CH_2Cl_2); The ee was determined by

HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (minor) = 21.271 min, t_r (major) = 25.387 min.



4-(1H-Indol-3-yl)-2-oxo-4-(2-chlorophenyl)butyric acid methyl ester

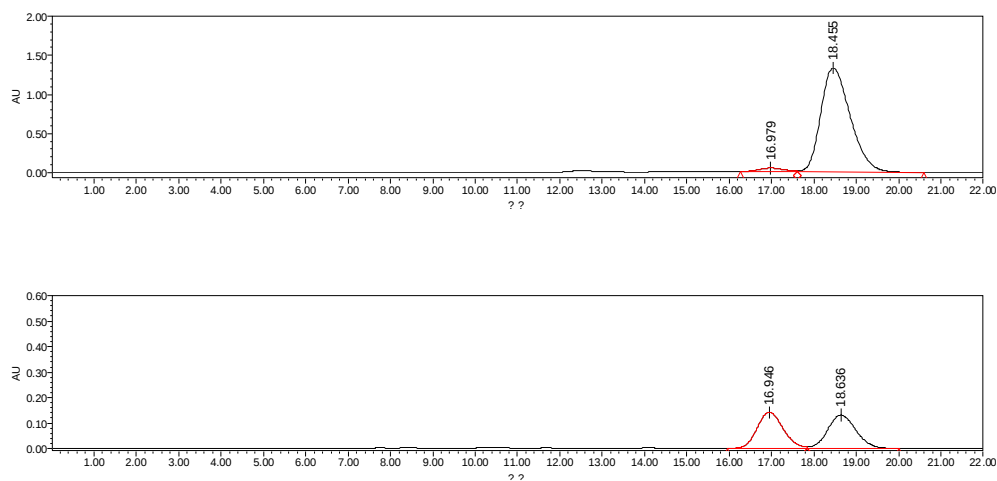


(-)-enantiomer (Table 3, entry 3): Prepared according to general **procedure A**. After 15 hours, the crude material was directly purified by flash chromatography on silica gel

(petroleum ether/ethyl acetate, 4:1) to afford the white solid in 99% yield with 95% ee.

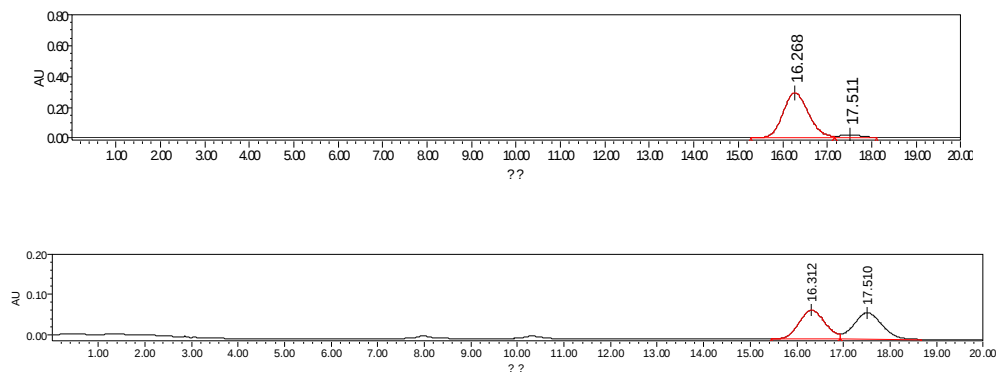
M.p. 102-103 °C; $[\alpha]_D^{23} = -95.9$ ($c = 0.296$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (minor) = 16.979 min, t_r (major) = 18.455 min. ^1H NMR (400 MHz, CDCl_3): $\delta = 8.07$ (s, 1H), 7.42 (d, $J = 8.0$ Hz, 1H), 7.39-7.36 (m, 1H), 7.31 (d, $J = 8.0$ Hz, 1H), 7.20-7.08 (m, 5H), 7.05-7.01 (m, 2H), 5.45-5.41 (m, 1H), 3.79 (s, 3H), 3.72 (dd, $J = 17.2, 8.8$ Hz, 1H), 3.47 (dd, $J = 17.2, 6.4$ Hz, 1H) ppm. ^{13}C NMR (100

MHz, CDCl₃): δ = 192.20, 161.31, 140.49, 136.54, 133.52, 129.79, 129.04, 127.93, 127.08, 126.49, 122.44, 122.07, 119.67, 119.41, 116.94, 111.20, 53.01, 44.62, 34.24 ppm; ES-HRMS Calcd for C₁₉H₁₇ClNO₃ [M + H]⁺ 342.0891, Found: 342.0906.

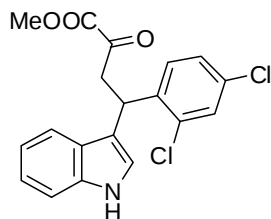


(+)-enantiomer (Table 2, entry 3): Prepared according to general **procedure**

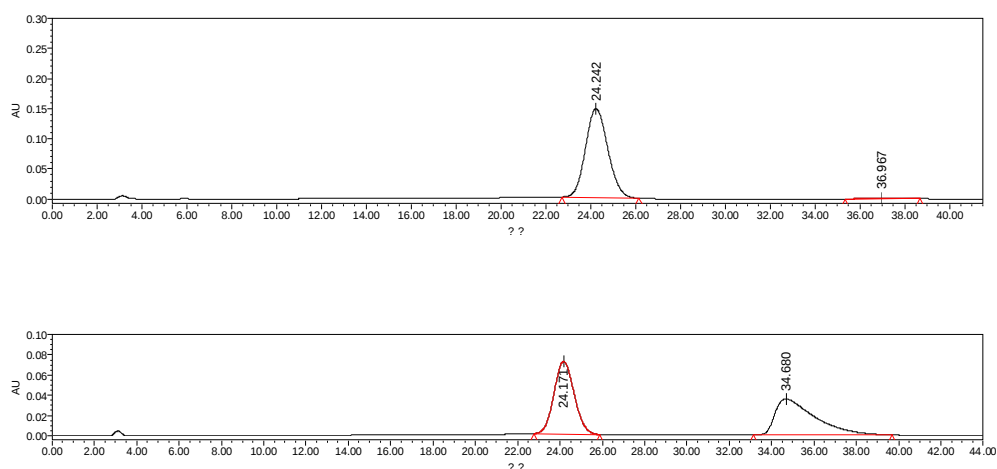
B. After 64 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the white solid in 91% yield with 90% ee. $[\alpha]_D^{23} = +87.0$ ($c = 0.208$, CH₂Cl₂); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (major) = 16.268 min, t_r (minor) = 17.511 min.



4-(1H-Indol-3-yl)-2-oxo-4-(2,4-dichlorophenyl)butyric acid methyl ester

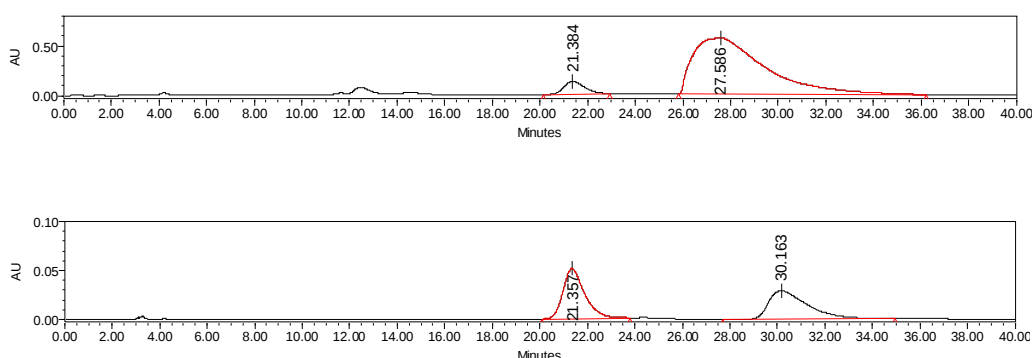


(-)-enantiomer (Table 3, entry 4): Prepared according to general procedure A. After 22 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 3:1) to afford the white solid in 94% yield with 97% ee. M.p. 126-128 °C; $[\alpha]_D^{23} = -17.5$ ($c = 0.240$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (major) = 24.242 min, t_r (minor) = 36.967 min. ^1H NMR (400 MHz, CDCl_3): $\delta = 8.10$ (s, 1H), 7.40-7.02 (m, 8H), 4.86 (t, $J = 7.2$ Hz, 1H), 3.79 (s, 3H), 3.66 (dd, $J = 17.6, 7.2$ Hz, 1H), 3.63 (dd, $J = 17.6, 8.0$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 190.90, 160.05, 142.67, 135.54, 131.46, 129.54, 129.41, 128.73, 126.30, 125.02, 121.57, 120.47, 118.76, 118.05, 116.13, 110.31, 52.08, 52.72, 44.24, 35.74$ ppm; ES-HRMS Calcd for $\text{C}_{19}\text{H}_{16}\text{Cl}_2\text{NO}_3$ $[\text{M} + \text{H}]^+$ 376.0502, Found: 376.0502.

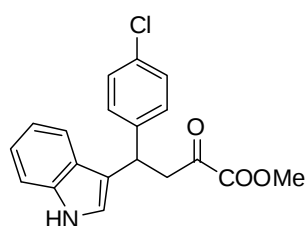


(+)-enantiomer (Table 2, entry 4): Prepared according to general **procedure**

B. After 51 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 3:1) to afford the white solid in 94% yield with 88% ee. $[\alpha]_D^{23} = +18.2$ ($c = 0.672$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, $t_r(\text{minor}) = 21.384$ min, $t_r(\text{major}) = 27.586$ min.



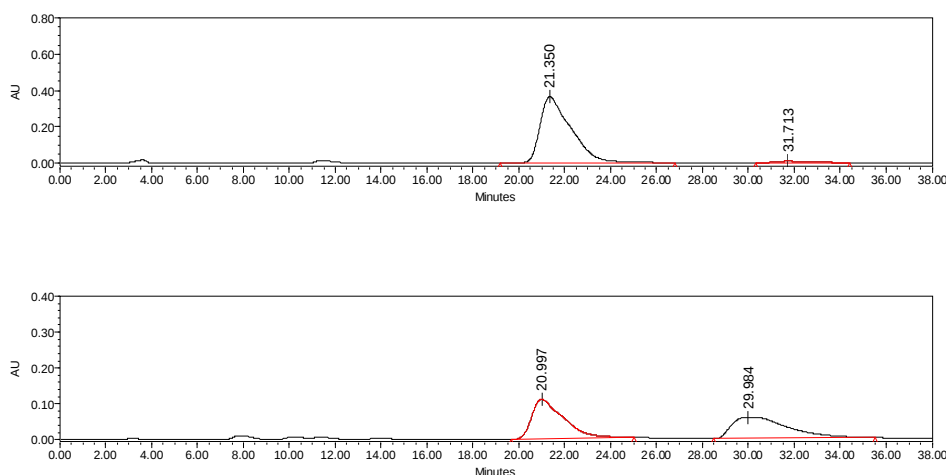
4-(1H-Indol-3-yl)-2-oxo-4-(4-chlorophenyl)butyric acid methyl ester



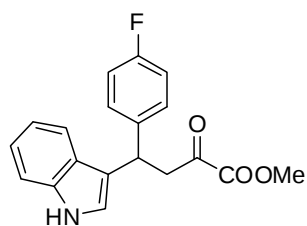
(+)-enantiomer (Table 3, entry 5): Prepared according to general **procedure A**. After 3 hours, the crude material was directly purified by flash chromatography on

silica gel (petroleum ether/ethyl acetate, 4:1) to afford the white solid in 96% yield with 93% ee. M.p. 123-125 °C; $[\alpha]_D^{23} = +10.1$ ($c = 0.240$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, $t_r(\text{major}) = 21.350$ min, $t_r(\text{minor}) = 31.713$ min. ^1H NMR (400 MHz, CDCl_3): $\delta = 8.06$ (s, 1H), 7.37-7.00 (m, 9H), 4.88 (t, $J = 7.6$ Hz, 1H), 3.78 (s, 3H), 3.66 (dd, $J = 17.2, 7.2$ Hz, 1H), 3.56 (dd, $J = 17.2, 8.0$ Hz, 1H) ppm. ^{13}C

NMR (100 MHz, CDCl_3): δ = 192.33, 161.22, 141.78, 136.60, 132.32, 129.20, 128.68, 126.21, 122.48, 121.48, 119.67, 119.27, 117.84, 111.27, 53.04, 45.47, 37.09 ppm;
 ES-HRMS Calcd for $\text{C}_{19}\text{H}_{15}\text{ClINO}_3$ $[\text{M} - \text{H}]^-$ 340.0746, Found: 340.0749.

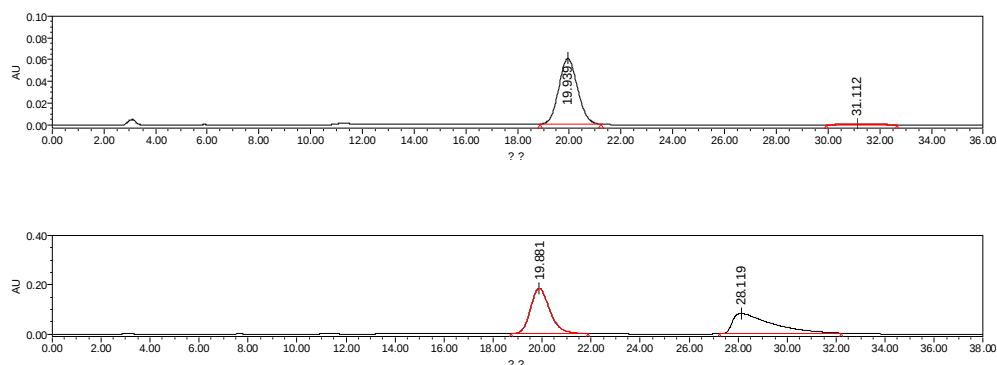


4-(1H-Indol-3-yl)-2-oxo-4-(4-fluorophenyl)butyric acid methyl ester



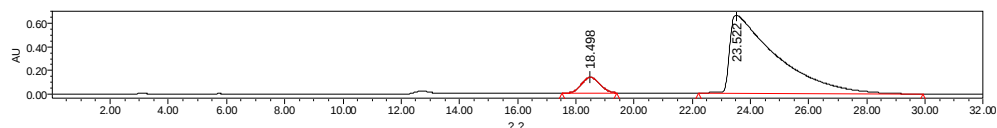
(-)-enantiomer (Table 3, entry 6): Prepared according to general **procedure A**. After 22 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the white solid in 99% yield with 96% ee. $[\alpha]_{\text{D}}^{23} = -43.6$ ($c = 0.220$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_{r} (major) = 19.939 min, t_{r} (minor) = 31.112 min. ^1H NMR (400 MHz, CDCl_3): δ = 8.04 (s, 1H), 7.38-6.89 (m, 9H), 4.90 (t, $J = 7.6$ Hz, 1H), 3.78 (s, 3H), 3.66 (dd, $J = 16.8, 7.2$ Hz, 1H), 3.57 (dd, $J = 17.2, 8.0$

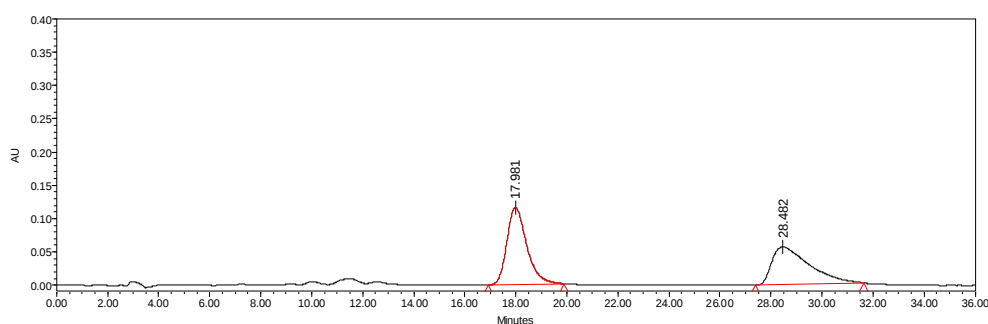
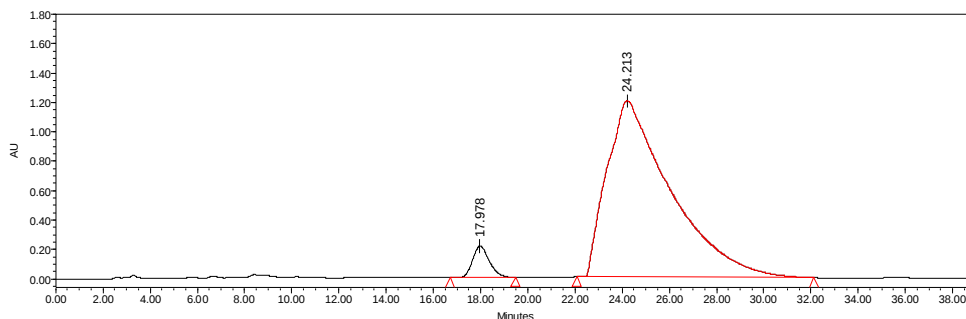
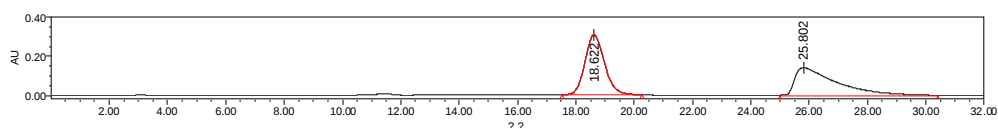
Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 192.44, 162.77, 161.26, 160.33, 138.93, 136.61, 129.32, 129.24, 126.26, 122.44, 121.40, 119.64, 119.32, 118.21, 115.43, 115.22, 111.22, 52.95, 45.69, 37.01 ppm; ES-HRMS Calcd for $\text{C}_{19}\text{H}_{15}\text{FNO}_3$ $[\text{M} - \text{H}]^-$ 324.1041, Found: 324.1044.



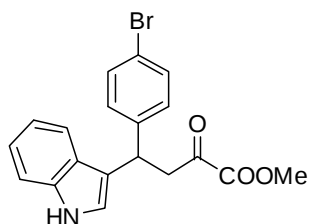
(+)-enantiomer (Table 2, entry 5): Prepared according to general **procedure**

B. After 51 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the white solid in 77% yield with 85% ee. After a simple recrystallization, the enantioselectivity could be increased to 91% ee. M.p. 142-143 °C; $[\alpha]_{\text{D}}^{23} = +40.8$ ($c = 0.228$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, $t_{\text{r}}(\text{minor}) = 18.498$ min, $t_{\text{r}}(\text{major}) = 23.522$ min.





4-(1H-Indol-3-yl)-2-oxo-4-(4-bromophenyl)butyric acid methyl ester^{10b}



(R)-enantiomer (Table 3, entry 7): Prepared according

to general **procedure A**. After 3 hours, the crude material

was directly purified by flash chromatography on silica gel

(petroleum ether/ethyl acetate, 4:1) to afford the white solid

in 90% yield with 92% ee. M.p. 124-125 °C; $[\alpha]_D^{23} = -5.1$ (c = 0.812, CHCl₃); The ee

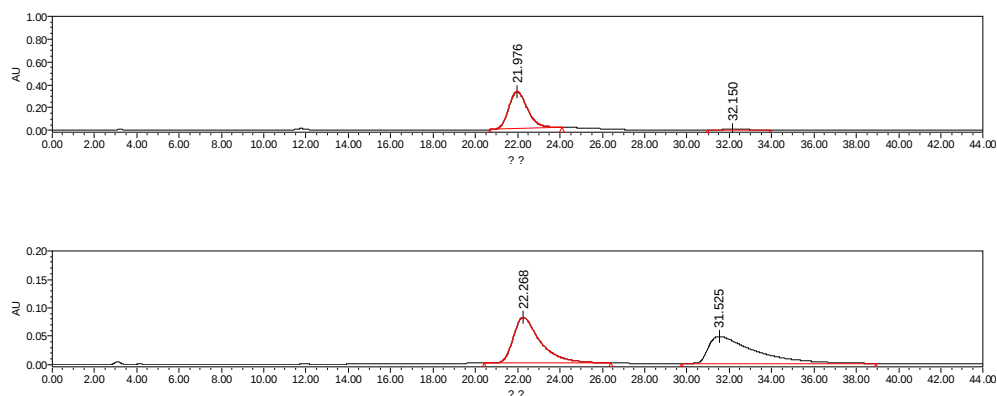
was determined by HPLC analysis using a chiralcel OD-H column

(hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, tr (major) = 21.976 min, tr (minor) =

32.150 min. ¹H NMR (600 MHz, CDCl₃): δ = 8.04 (s, 1H), 7.38-7.33 (m, 4H),

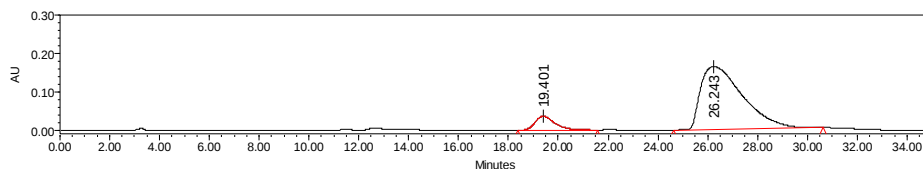
7.21-7.15 (m, 3H), 7.04-7.02 (m, 2H), 4.88 (t, J = 4.8 Hz, 1H), 3.79 (s, 3H), 3.66 (dd,

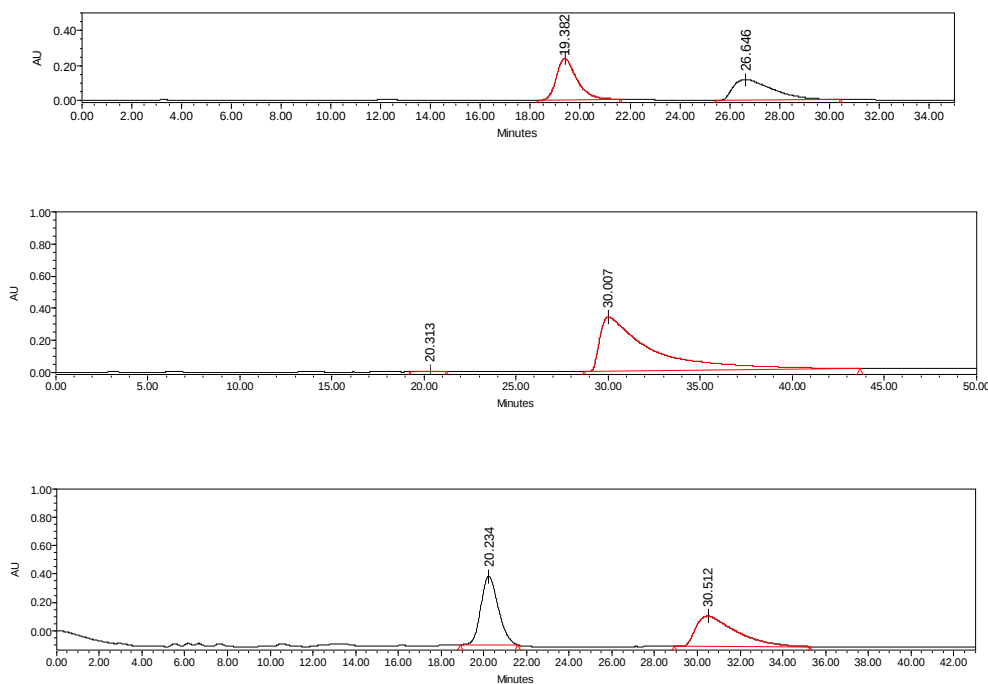
$J = 11.6, 4.8$ Hz, 1H), 3.57 (dd, $J = 11.2, 5.2$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 192.24, 161.26, 142.29, 136.62, 131.63, 129.57, 126.23, 122.50, 121.46, 120.42, 119.70, 119.26, 117.82, 111.23, 52.96, 45.41, 37.18$ ppm; ES-HRMS Calcd for $\text{C}_{19}\text{H}_{15}\text{BrNO}_3$ $[\text{M} - \text{H}]^-$ 384.0241, Found: 384.0231.



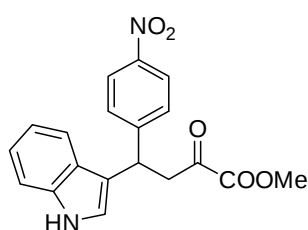
(S)-enantiomer (Table 2, entry 6): Prepared according to general **procedure**

B. After 51 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the white solid in 73% yield with 83% ee. After a simple recrystallization, the enantioselectivity could be increased to 99% ee. $[\alpha]_{\text{D}}^{23} = +4.2$ ($c = 0.402$, CHCl_3); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, $t_{\text{r}}(\text{minor}) = 19.401$ min, $t_{\text{r}}(\text{major}) = 26.243$ min.



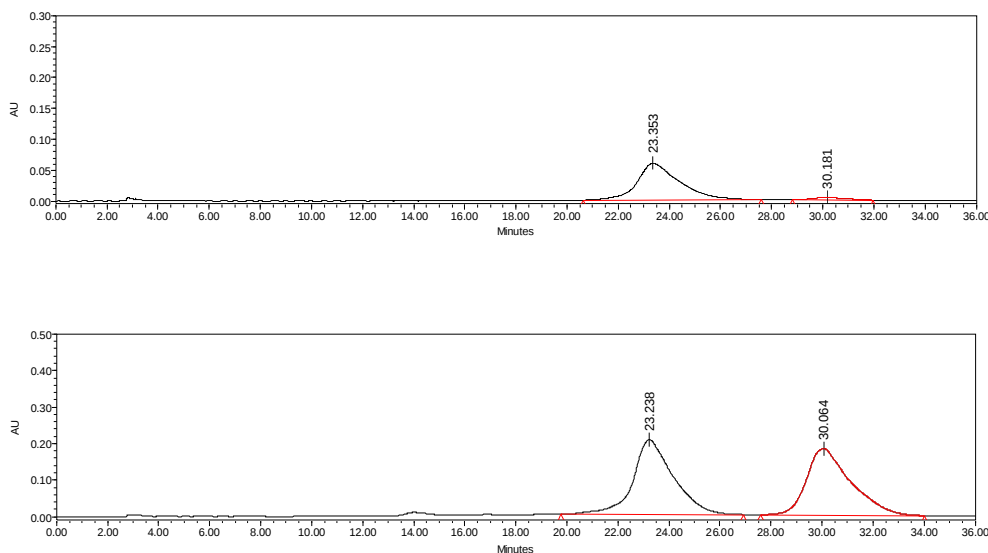


4-(1H-Indol-3-yl)-2-oxo-4-(4-nitrophenyl)butyric acid methyl ester

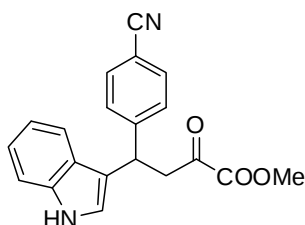


(-)-enantiomer (Table 3, entry 8): Prepared according to general **procedure A**. After 39 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 2:1) to afford the white solid in 77% yield with 90% ee. M.p. 118-119 °C; $[\alpha]_D^{23} = -1.9$ ($c = 0.876$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel AD column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, tr (major) = 23.353 min, tr (minor) = 30.181 min. ^1H NMR (400 MHz, CDCl_3): $\delta = 8.25$ (s, 1H), 8.12-8.07 (m, 2H), 7.50-7.00 (m, 7H), 5.01 (t, $J = 7.6$ Hz, 1H), 3.80 (s, 3H), 3.74 (dd, $J = 18.0, 6.8$ Hz, 1H), 3.63 (dd, $J = 18.0, 8.0$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 191.79, 161.06, 151.07, 146.67, 136.62, 128.87, 128.78, 126.00, 123.85, 122.69, 121.65,$

119.87, 118.94, 116.75, 111.48, 53.20, 45.07, 37.37 ppm; ES-HRMS Calcd for $C_{19}H_{17}N_2O_5 [M + H]^+$ 353.1132, Found: 353.1081.



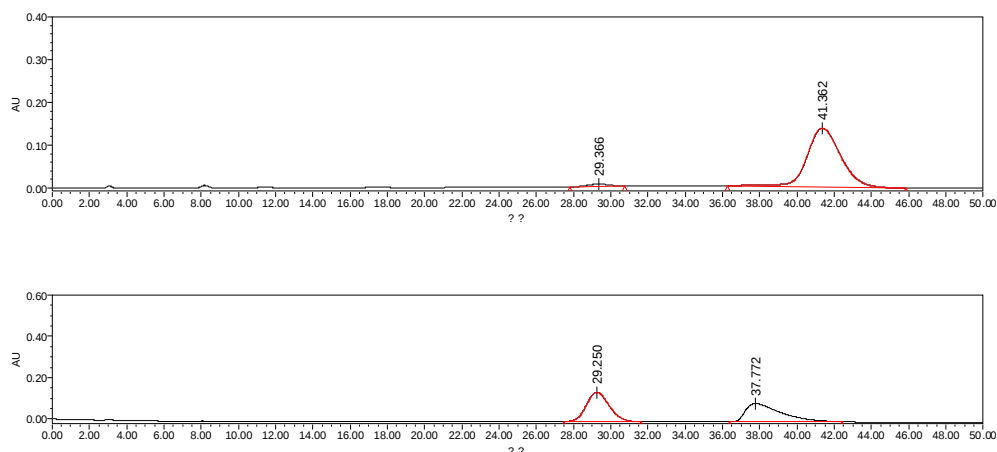
4-(1H-Indol-3-yl)-2-oxo-4-(4-cyanophenyl)butyric acid methyl ester



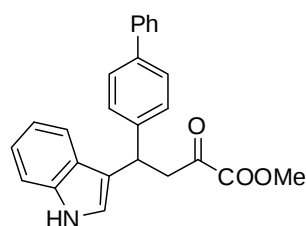
(-)-enantiomer (Table 3, entry 9): Prepared according to general **procedure A**. After 15 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 3:1) to afford the yellow solid

in 92% yield with 95% ee. M.p. 121-123 °C; $[\alpha]_D^{23} = -11.5$ ($c = 0.322$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (minor) = 29.366 min, t_r (major) = 41.362 min. 1H NMR (400 MHz, $CDCl_3$): δ = 8.06 (s, 1H), 7.48 (d, $J = 8.0$ Hz, 1H), 7.30 (d, $J = 8.0$ Hz, 1H), 7.20-6.99 (m, 7H), 4.91 (t, $J = 7.6$ Hz, 1H), 3.77 (s, 3H), 3.70 (dd, $J = 16.8, 7.2$ Hz, 1H), 3.61 (dd, $J = 17.2, 8.0$ Hz, 1H) ppm. ^{13}C NMR (100

MHz, CDCl₃): δ = 192.83, 161.37, 143.21, 138.13, 136.59, 128.59, 128.45, 127.44, 126.48, 124.78, 122.26, 121.62, 119.50, 119.41, 118.31, 111.24, 52.96, 45.79, 37.72, 21.52 ppm; ES-HRMS Calcd for C₂₀H₁₅N₂O₃ [M - H]⁻ 331.1088, Found: 331.1081.



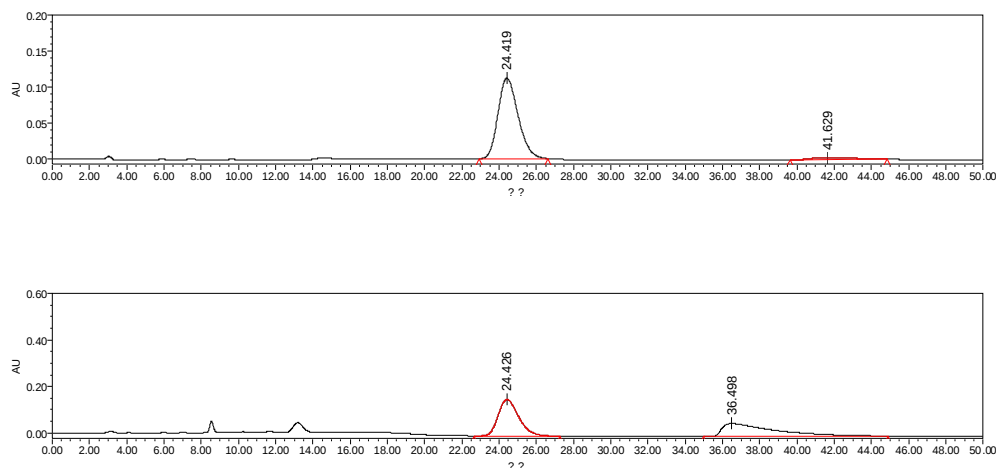
4-(1H-Indol-3-yl)-2-oxo-4-(4-phenylphenyl)butyric acid methyl ester



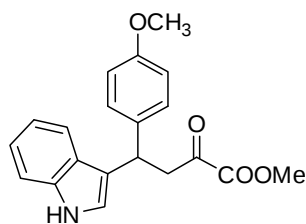
(+)-enantiomer (Table 3, entry 10): Prepared according to general **procedure A**. After 15 hours, the crude material was directly purified by flash chromatography on silica gel

(petroleum ether/ethyl acetate, 4:1) to afford the yellow solid in 91% yield with 90% ee. M.p. 107-108 °C; $[\alpha]_D^{23}$ = + 6.1 (c = 0.228, CH₂Cl₂); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, tr (major) = 24.419 min, tr (minor) = 41.629 min. ¹H NMR (400 MHz, CDCl₃): δ = 8.04 (s, 1H), 7.54-7.28 (m, 12H), 7.17-7.13 (m, 1H), 7.06-7.02 (m, 2H), 4.96 (t, *J* = 7.6 Hz, 1H), 3.76 (s, 3H), 3.71 (dd, *J* = 17.2, 7.2 Hz, 1H), 3.63 (dd, *J* = 17.2, 8.0 Hz, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 192.65, 161.33, 142.32, 140.84, 139.47, 136.61, 128.74, 128.21, 127.29, 127.17, 127.01, 126.42, 122.38,

121.60, 119.60, 119.44, 118.24, 111.24, 53.00, 45.66, 37.41 ppm; ES-HRMS Calcd for C₂₅H₂₂NO₃ [M + H]⁺ 384.1594, Found: 384.1594.



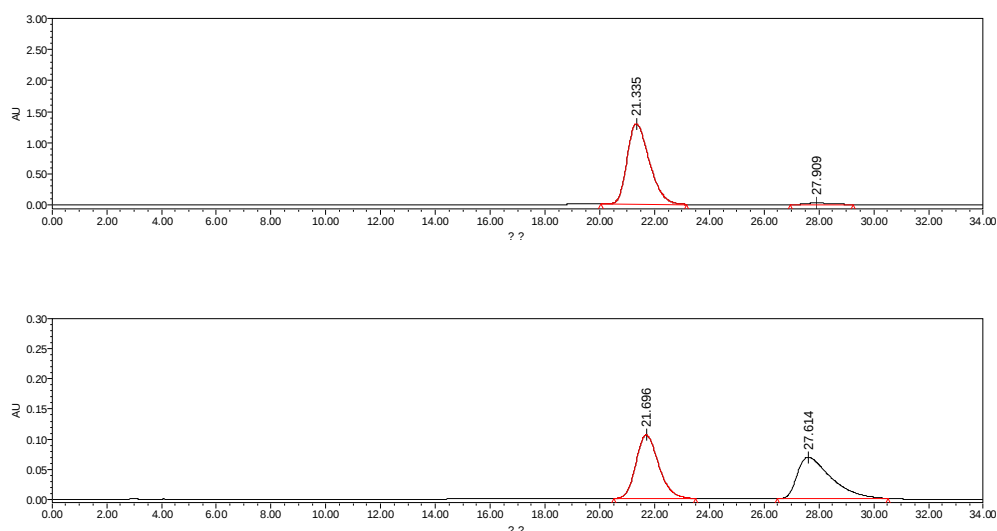
4-(1H-Indol-3-yl)-2-oxo-4-(4-methoxyphenyl)butyric acid methyl ester



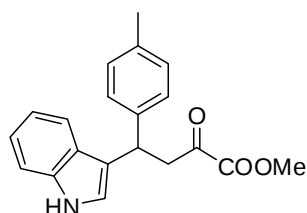
(-)-enantiomer (Table 3, entry 11): Prepared according to general **procedure A**. After 36 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the white solid

in 93% yield with 96% ee. $[\alpha]_D^{23} = -31.2$ ($c = 0.852$, CH₂Cl₂); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (major) = 21.335 min, t_r (major) = 27.909 min. ¹H NMR (400 MHz, CDCl₃): δ = 8.08 (s, 1H), 7.45 (dd, J = 8.0, 0.8 Hz, 1H), 7.33 (dd, J = 8.0, 0.8 Hz, 1H), 7.28-7.26 (m, 2H), 7.18 (dt, J = 6.8, 0.8 Hz, 1H), 7.08-7.04 (m, 1H), 7.01 (dd, J = 2.4, 0.8 Hz, 1H), 6.85-6.82 (m, 2H), 4.91 (t, J = 7.6 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.69 (dd, J = 16.8, 7.2 Hz, 1H), 3.61 (dd, J = 16.8, 8.0 Hz, 1H) ppm. ¹³C

NMR (100 MHz, CDCl_3): δ = 192.84, 161.36, 158.21, 136.62, 135.32, 128.78, 126.40, 122.28, 121.44, 119.50, 119.45, 118.63, 113.92, 111.19, 55.23, 52.95, 45.85, 37.03 ppm; ES-HRMS Calcd for $\text{C}_{20}\text{H}_{18}\text{NO}_4$ $[\text{M} - \text{H}]^-$ 336.1241, Found: 336.1248.



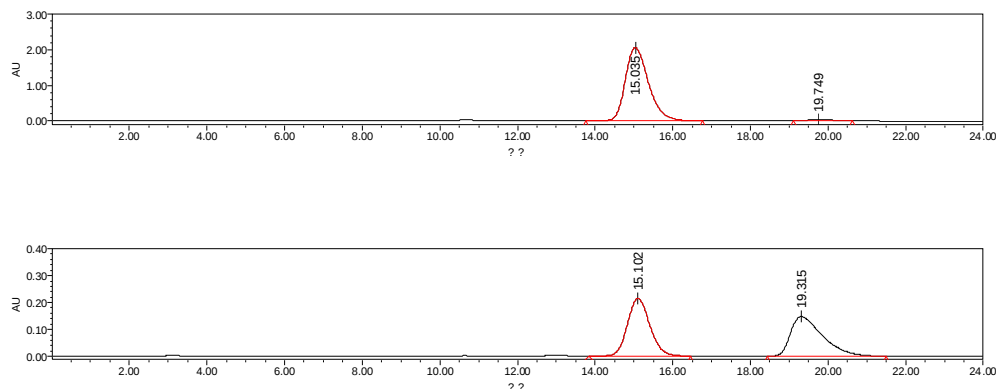
4-(1H-Indol-3-yl)-2-oxo-4-(4-methylphenyl)butyric acid methyl ester^{10b}



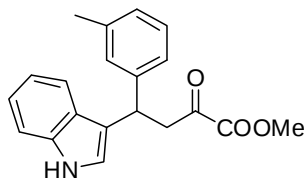
(-)-enantiomer (Table 3, entry 12): Prepared according to general **procedure A**. After 22 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the white solid

in 96% yield with 96% ee. M.p. 94-96 °C; $[\alpha]_D^{23}$ = - 21.6 (c = 0.306, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (major) = 15.035 min, t_r (major) = 19.749 min. ^1H NMR (400 MHz, CDCl_3): δ = 8.06 (s, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.33 (dd, J = 8.4, 0.8 Hz, 1H), 7.28-7.25 (m, 2H), 7.19 (dt, J = 8.0, 1.2 Hz, 1H), 7.12-7.05 (m, 3H), 7.02 (d, J = 2.0 Hz, 1H), 4.93 (t, J = 7.6 Hz, 1H), 3.80 (s, 3H),

3.75-3.60 (m, 2H), 2.33 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 192.81, 161.36, 140.20, 136.59, 136.12, 129.25, 127.65, 126.44, 122.26, 121.52, 119.50, 119.43, 118.48, 111.19, 52.93, 45.79, 37.39, 21.02 ppm; ES-HRMS Calcd for $\text{C}_{20}\text{H}_{18}\text{NO}_3$ $[\text{M} - \text{H}]^-$ 320.1292, Found: 320.1288.



4-(1H-Indol-3-yl)-2-oxo-4-(3-methylphenyl)butyric acid methyl ester

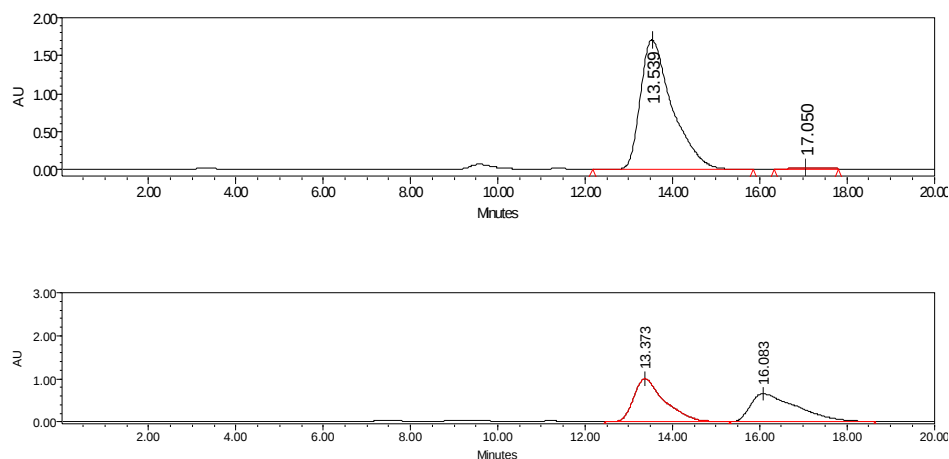


(-)-enantiomer (Table 3, entry 13): Prepared according to general **procedure A**. After 22 hours, the crude material was directly purified by flash chromatography on silica gel

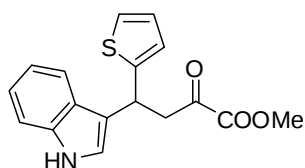
(petroleum ether/ethyl acetate, 4:1) to afford the white solid in 83% yield with 97% ee.

M.p. 95-96 °C; $[\alpha]_D^{23}$ = - 36.6 (c = 0.399, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (major) = 13.539 min, t_r (major) = 17.050 min. ^1H NMR (400 MHz, CDCl_3): δ = 8.06 (s, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.20-6.99 (m, 7H), 4.91 (t, J = 7.6 Hz, 1H), 3.77 (s, 3H), 3.70 (dd, J = 16.8, 7.2 Hz, 1H), 3.61 (dd, J = 17.2, 8.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 192.83, 161.37, 143.21, 138.13, 136.59, 128.59, 128.45, 127.44, 126.48, 124.78, 122.26, 121.62, 119.50,

119.41, 118.31, 111.24, 52.96, 45.79, 37.72, 21.52 ppm; ES-HRMS Calcd for $C_{20}H_{20}NO_3$ $[M + H]^+$ 322.1438, Found: 322.1447.

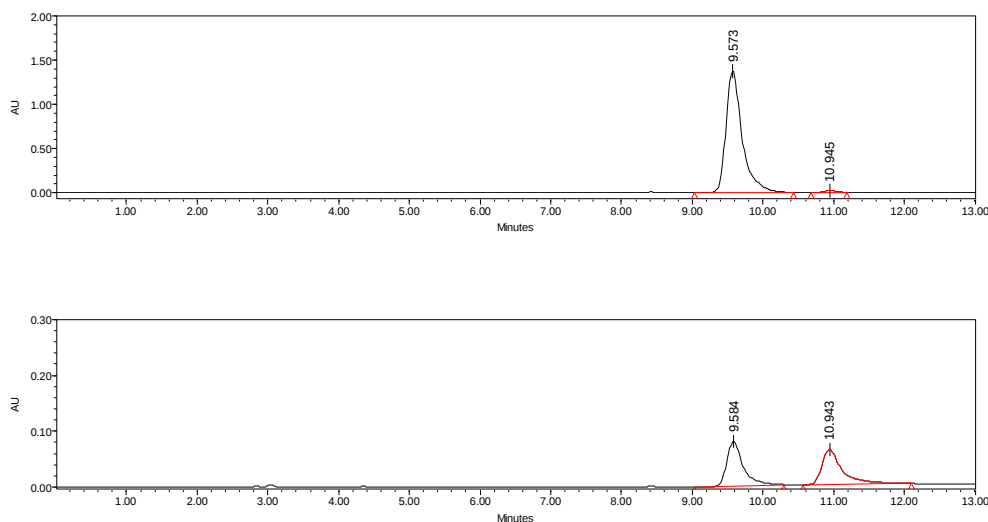


4-(1H-Indol-3-yl)-2-oxo-4-(2-thienyl)butyric acid methyl ester



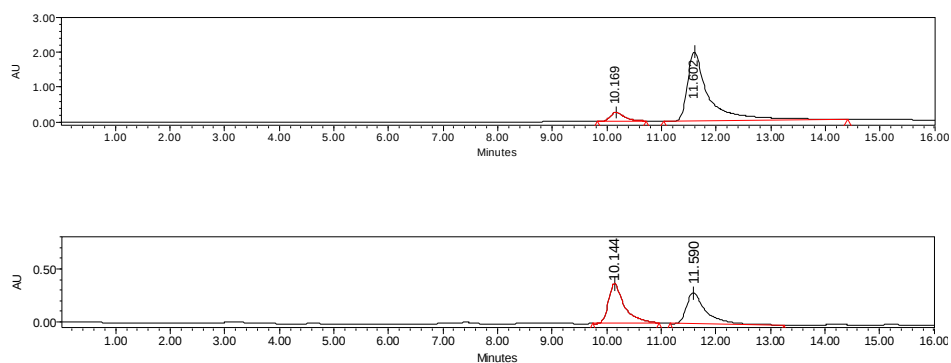
(-)-enantiomer (Table 3, entry 14): Prepared according to general **procedure A**. After 36 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the white solid in 87% yield with 98% ee. M.p. 88-89 °C; $[\alpha]_D^{23} = -17.7$ ($c = 0.940$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel IA column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (major) = 9.573 min, t_r (major) = 10.945 min. 1H NMR (400 MHz, DMSO): $\delta = 10.94$ (d, $J = 1.6$ Hz, 1H), 7.44 (d, $J = 8.0$ Hz, 1H), 7.36-7.33 (m, 1H), 7.28 (d, $J = 2.4$ Hz, 1H), 7.24 (dd, $J = 5.2, 1.2$ Hz, 1H), 7.08-7.04 (m, 1H), 6.98 (dt, $J = 6.4, 0.8$ Hz, 1H), 6.96-6.92 (m, 1H), 6.88 (dd, $J = 3.6, 5.2$ Hz, 1H), 5.03 (t, $J = 7.6$ Hz, 1H), 3.74 (s, 3H), 3.78-3.65 (m, 2H), ppm. ^{13}C NMR (100 MHz, DMSO): $\delta = 192.20, 161.24, 149.32, 136.88, 127.03, 126.35, 124.45, 124.36, 122.73, 121.64, 119.13, 118.97,$

117.39, 112.01, 53.12, 46.41, 32.66 ppm; ES-HRMS Calcd for $C_{17}H_{16}NO_3S [M + H]^+$
314.0845, Found: 314.0858.

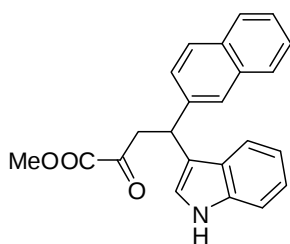


(+)-enantiomer (Table 2, entry 7): Prepared according to general **procedure B**.

After 93 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the white solid in 51% yield with 84% ee. $[\alpha]_D^{23} = +13.4$ ($c = 0.186$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel IA column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (minor) = 10.169 min, t_r (major) = 11.602 min.



4-(1H-Indol-3-yl)-2-oxo-4-(2-naphthyl)butyric acid methyl ester



(+)-enantiomer (Table 2, entry 8): Prepared according to

general **procedure B**. After 93 hours, the crude material was

directly purified by flash chromatography on silica gel

(petroleum ether/ethyl acetate, 4:1) to afford the white solid

in 62% yield with 84% ee. After a simple recrystallization, the enantioselectivity

could be increased to 90% ee. M.p. 140-141 °C; $[\alpha]_D^{23} = +16.3$ ($c = 0.208$, CH_2Cl_2);

The ee was determined by HPLC analysis using a chiralcel OD-H column

(hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, $t_r(\text{minor}) = 22.517$ min, $t_r(\text{major}) =$

27.885 min. ^1H NMR (400 MHz, DMSO): $\delta = 10.96$ (s, 1H), 7.90 (s, 1H), 7.85-7.76

(m, 3H), 7.52-7.32 (m, 6H), 7.04-7.00 (dt, $J = 6.8, 1.2$ Hz, 1H), 6.89-6.85 (dt, $J = 7.2,$

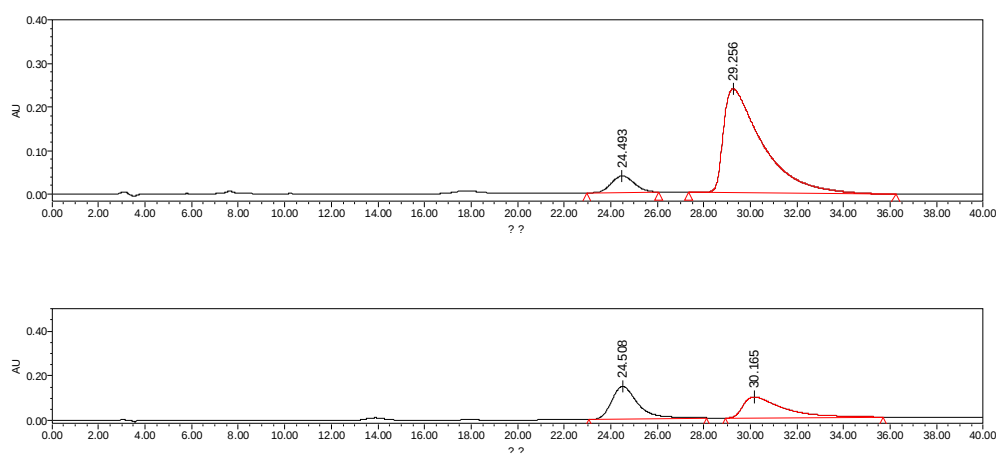
0.8 Hz, 1H), 4.91 (t, $J = 6.8$ Hz, 1H), 3.84 (ddd, $J = 17.6, 7.2, 1.2$ Hz, 1H), 3.75-3.68

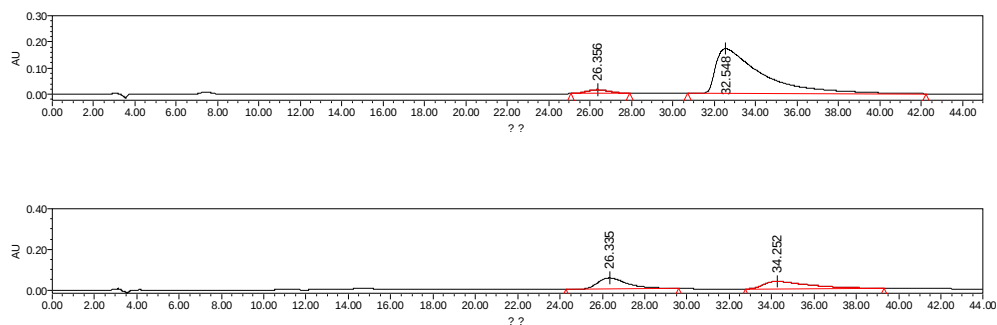
(m, 1H) ppm. ^{13}C NMR (100 MHz, DMSO): $\delta = 192.75, 161.42, 142.39, 136.91,$

133.45, 132.21, 128.21, 128.01, 127.85, 126.97, 126.69, 125.88, 122.65, 121.57,

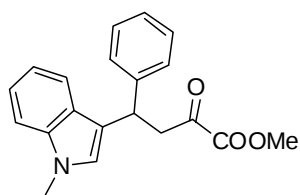
119.08, 118.84, 117.49, 111.91, 53.08, 45.34, 37.57 ppm; ES-HRMS Calcd for

$\text{C}_{23}\text{H}_{20}\text{NO}_3$ $[\text{M} + \text{H}]^+$ 358.1438, Found: 358.1442.





4-(1-Methylindol-3-yl)-2-oxo-4-phenylbutyric acid methyl ester^{10,11}



(-)-enantiomer (Table 3, entry 15): Prepared according to

general **procedure A**. After 1 hour, the crude material was

directly purified by flash chromatography on silica gel

(petroleum ether/ethyl acetate, 4:1) to afford the yellow solid in 86% yield with 93%

ee. $[\alpha]_D^{23} = -47.1$ ($c = 0.350$, CH_2Cl_2); The ee was determined by HPLC analysis

using a chiralcel AS-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r

(major) = 11.363 min, t_r (major) = 13.166 min. ^1H NMR (400 MHz, CDCl_3): $\delta =$

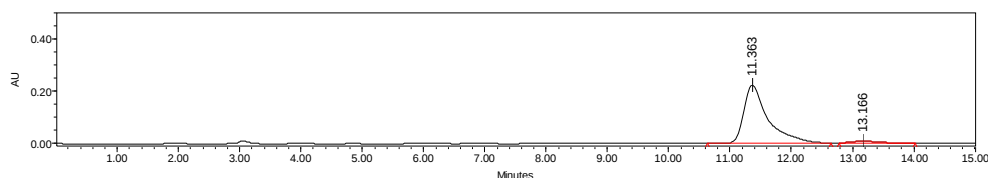
7.44-6.88 (m, 10H), 4.93-4.90 (m, 1H), 3.76 (d, $J = 1.6$ Hz, 3H), 3.73 (s, 3H),

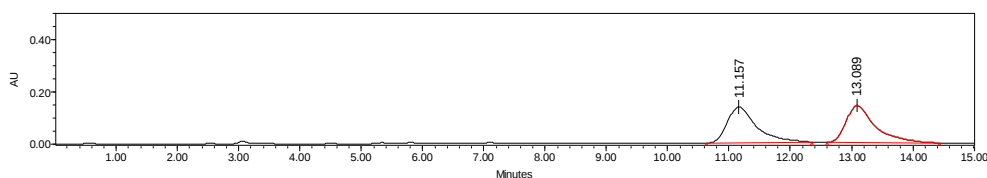
3.68-3.58 (m, 2H) ppm. ^{13}C NMR (150 MHz, CDCl_3): $\delta = 192.15, 160.85, 142.91,$

136.84, 128.07, 127.29, 126.35, 126.09, 125.85, 121.37, 119.00, 118.54, 116.32,

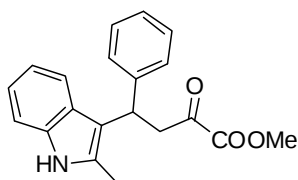
108.78, 52.42, 45.32, 37.22, 32.23 ppm; ES-HRMS Calcd for $\text{C}_{20}\text{H}_{19}\text{NO}_3$ $[\text{M} - \text{H}]^-$

320.1292, Found: 320.1285.





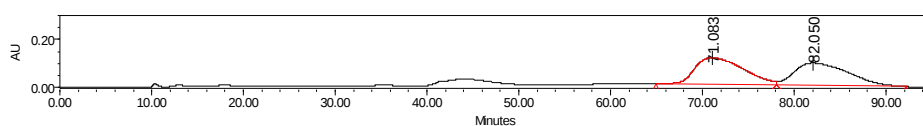
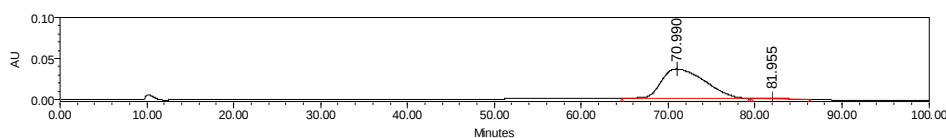
4-(2-Methylindol-3-yl)-2-oxo-4-phenylbutyric acid methyl ester^{10b}



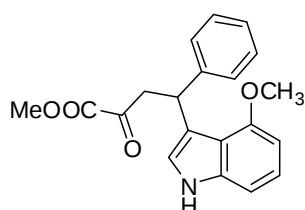
(+)-enantiomer (Table 3, entry 16): Prepared according to general **procedure A**. After 1 hour, the crude material was directly purified by flash chromatography on silica gel

(petroleum ether/ethyl acetate, 3:1) to afford the yellow oil in 99% yield with 98% ee.

$[\alpha]_D^{23} = +37.5$ ($c = 0.296$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OJ column (hexane/2-propanol 60:40, 0.3 mL/min, 220 nm, t_r (major) = 70.990 min, t_r (major) = 82.067 min. ^1H NMR (400 MHz, CDCl_3): $\delta = 7.81$ (s, 1H), 7.41 (d, $J = 7.6$ Hz, 1H), 7.31 (d, $J = 7.6$ Hz, 2H), 7.26-7.13 (m, 4H), 7.07-6.96 (m, 2H), 4.90 (dd, $J = 9.2, 6.0$ Hz, 1H), 3.90 (dd, $J = 17.2, 9.2$ Hz, 1H), 3.69 (dd, $J = 17.2, 6.0$ Hz, 1H), 3.62 (s, 3H), 2.37 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 193.10, 161.06, 143.16, 135.45, 132.20, 128.44, 127.35, 127.16, 126.24, 120.95, 119.33, 119.10, 112.28, 110.47, 52.79, 44.01, 36.27, 12.14$ ppm; ES-HRMS Calcd for $\text{C}_{20}\text{H}_{18}\text{NO}_3$ $[\text{M} - \text{H}]^-$ 320.1292, Found: 320.1297.



4-(4-Methoxyindol-3-yl)-2-oxo-4-phenylbutyric acid methyl ester^{10b}



(+)-enantiomer (Table 3, entry 17): Prepared

according to general **procedure A**. After 27 hours, the crude material was directly purified by flash

chromatography on silica gel (petroleum ether/ethyl acetate, 3:1) to afford the yellow

oil in 83% yield with 92% ee. $[\alpha]_D^{23} = +30.6$ ($c = 0.222$, CH_2Cl_2); The ee was

determined by HPLC analysis using a chiralcel OJ column (hexane/2-propanol 60:40,

1.0 mL/min, 220 nm, t_r (major) = 28.734 min, t_r (major) = 73.935 min. ^1H NMR (400

MHz, CDCl_3): $\delta = 7.95$ (s, 1H), 7.32 (d, $J = 7.6$ Hz, 2H), 7.28-7.14 (m, 3H), 7.06 (t, J

= 8.0 Hz, 1H), 6.90 (d, $J = 8.0$ Hz, 1H), 6.68 (d, $J = 2.0$ Hz, 1H), 6.44 (d, $J = 7.6$ Hz,

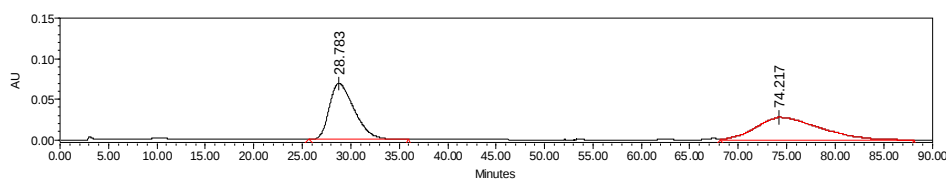
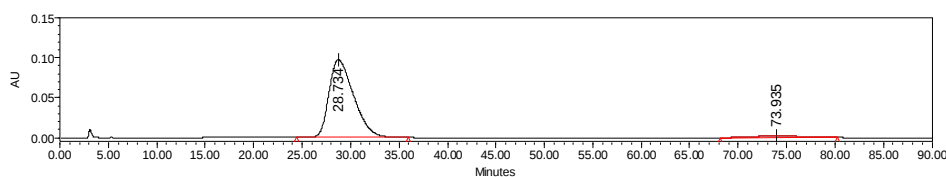
1H), 5.25 (t, $J = 8.0$ Hz, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 3.69 (dd, $J = 17.2, 7.2$ Hz,

1H), 3.63 (dd, $J = 17.2, 8.8$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 191.11,$

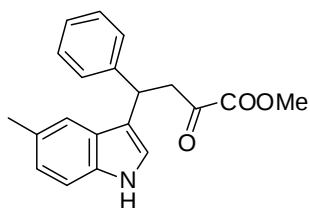
161.67, 154.57, 143.86, 138.21, 128.22, 128.05, 126.21, 123.16, 120.69, 119.59,

116.63, 104.41, 99.84, 54.96, 52.72, 46.65, 38.41 ppm; ES-HRMS Calcd for

$\text{C}_{20}\text{H}_{18}\text{NO}_4$ $[\text{M} - \text{H}]^-$ 336.1241, Found: 336.1241.

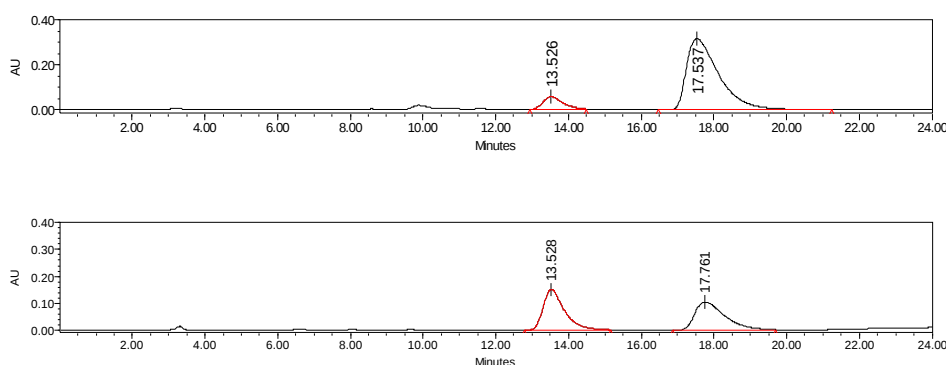


4-(5-Methylindol-3-yl)-2-oxo-4-phenylbutyric acid methyl ester

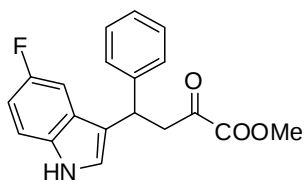


(+)-enantiomer (Table 2, entry 9): Prepared according to general **procedure B**. After 64 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the white solid

in 70% yield with 81% ee. M.p. 112-114 °C; $[\alpha]_D^{23} = +10.4$ ($c = 0.278$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, $t_r(\text{minor}) = 13.526$ min, $t_r(\text{major}) = 17.537$ min. ^1H NMR (400 MHz, CDCl_3): $\delta = 7.91$ (s, 1H), 7.32 (d, $J = 7.6$ Hz, 2H), 7.28-7.17 (m, 5H), 6.98-6.95 (m, 2H), 4.89 (t, $J = 7.6$ Hz, 1H), 3.75 (s, 3H), 3.66 (dd, $J = 17.2, 7.6$ Hz, 1H), 3.58 (dd, $J = 16.8, 8.0$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 192.70, 161.35, 143.26, 134.89, 128.78, 128.54, 127.77, 126.66, 126.57, 123.96, 121.72, 118.94, 117.81, 110.84, 52.93, 45.77, 37.70, 21.53$ ppm; ES-HRMS Calcd for $\text{C}_{20}\text{H}_{18}\text{NO}_3$ $[\text{M} - \text{H}]^-$ 320.1292, Found: 320.1296.



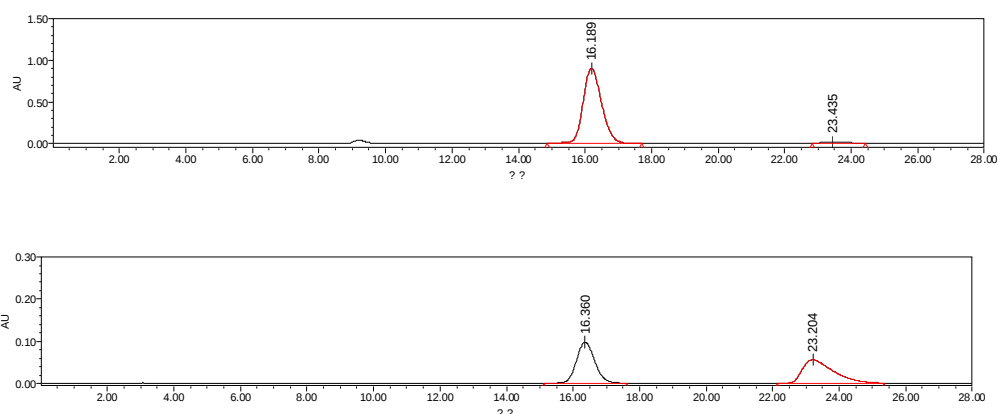
4-(5-floroindol-3-yl)-2-oxo-4-phenylbutyric acid methyl ester



(-)-enantiomer (Table 3, entry 18): Prepared according

to general **procedure A**. After 58 hours, the crude material was directly purified by flash chromatography

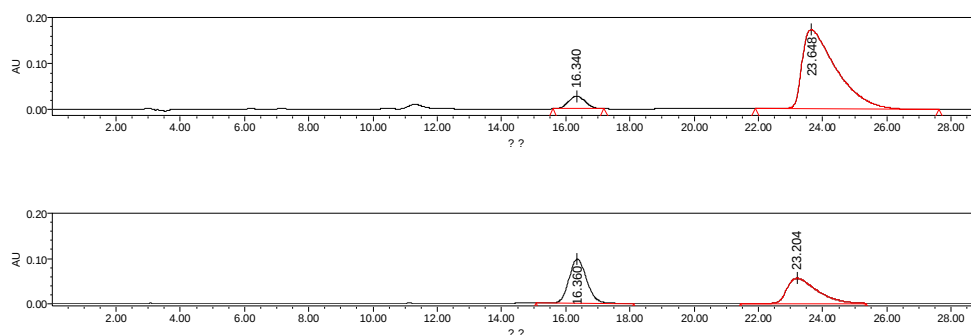
on silica gel (petroleum ether/ethyl acetate, 3:1) to afford the yellow solid in 90% yield with 95% ee. M.p. 129-130 °C; $[\alpha]_D^{23} = -30.4$ ($c = 0.388$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (major) = 16.189 min, t_r (major) = 23.435 min. ^1H NMR (400 MHz, CDCl_3): $\delta = 8.04$ (s, 1H), 7.35-7.16 (m, 6H), 7.08 (d, $J = 2.8$ Hz, 1H), 7.02 (dd, $J = 9.6, 2.4$ Hz, 1H), 6.92-6.86 (m, 1H), 4.83 (t, $J = 7.6$ Hz, 1H), 3.78 (s, 3H), 3.66 (dd, $J = 17.2, 7.6$ Hz, 1H), 3.57 (dd, $J = 17.2, 7.6$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 192.47, 161.27, 158.80, 156.47, 142.84, 133.05, 128.65, 127.70, 126.78, 123.19, 118.47, 118.43, 111.84, 111.74, 110.90, 110.63, 104.49, 104.26, 52.99, 45.51, 37.66$ ppm; ES-HRMS Calcd for $\text{C}_{19}\text{H}_{15}\text{FNO}_3$ $[\text{M} - \text{H}]^-$ 324.1041, Found: 324.1033.



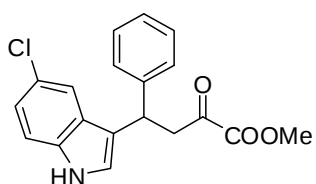
(+)-enantiomer (Table 2, entry 10): Prepared according to general **procedure**

B. After 64 hours, the crude material was directly purified by flash chromatography

on silica gel (petroleum ether/ethyl acetate, 3:1) to afford the white solid in 68% yield with 85% ee. $[\alpha]_D^{23} = +29.6$ ($c = 0.260$, CHCl_3); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (minor) = 16.340 min, t_r (major) = 23.648 min.



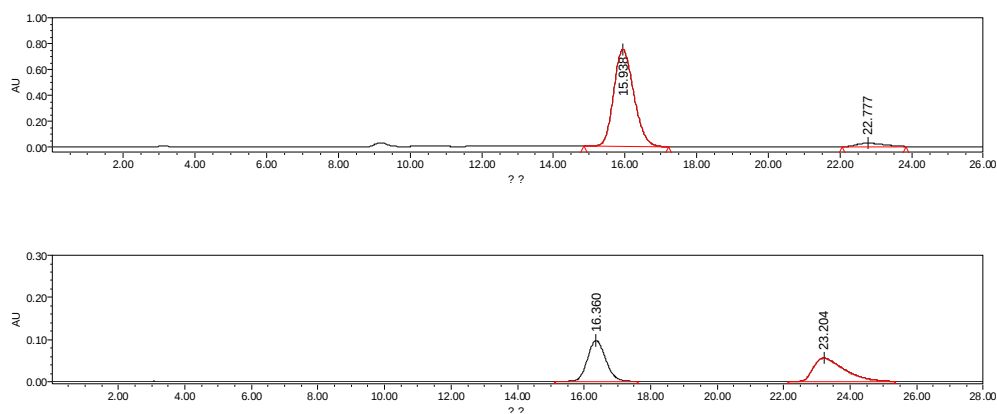
4-(1H-5-chloroindol-3-yl)-2-oxo-4-phenylbutyric acid methyl ester^{10b}



(+)-enantiomer (Table 3, entry 19): Prepared according to general **procedure A**. After 58 hours, the crude material was directly purified by flash

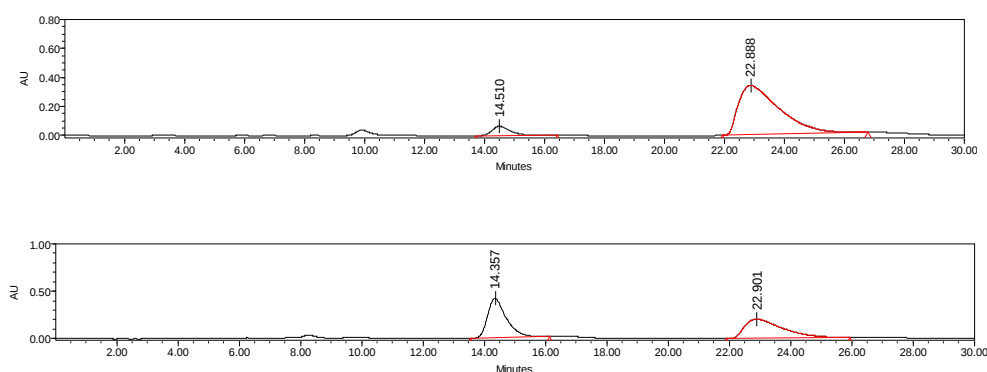
chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the yellow solid in 82% yield with 90% ee. $[\alpha]_D^{23} = +29.4$ ($c = 0.286$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (minor) = 15.938 min, t_r (major) = 22.777 min. ^1H NMR (400 MHz, CDCl_3): $\delta = 8.16$ (s, 1H), 7.37 (d, $J = 1.6$ Hz, 1H), 7.32-7.07 (m, 8H), 4.85 (t, $J = 7.6$ Hz, 1H), 3.79 (s, 3H), 3.65 (dd, $J = 16.8, 7.6$ Hz, 1H), 3.58 (dd, $J = 17.2, 7.6$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 192.38, 161.24, 142.75, 134.90, 128.67, 127.66, 127.51, 126.80, 122.85, 122.69, 118.83, 118.08, 112.17,$

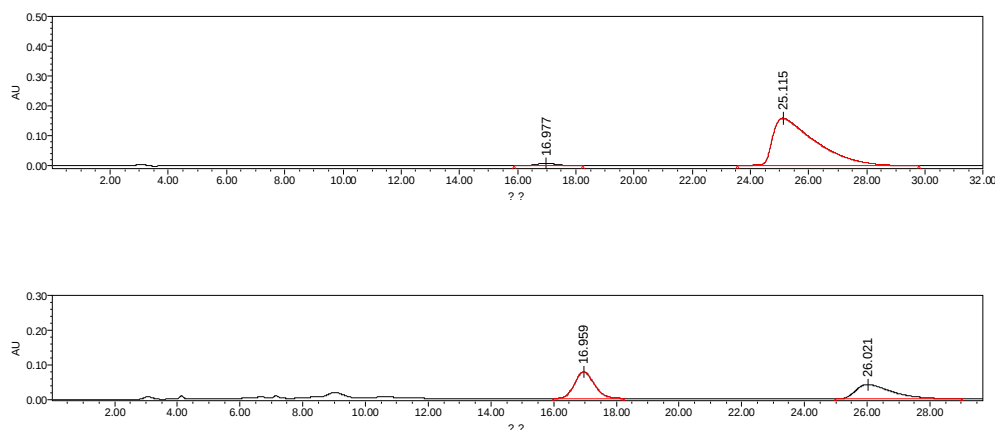
53.00, 45.60, 37.52 ppm; ES-HRMS Calcd for $C_{19}H_{16}ClNO_3$ $[M - H]^-$ 340.0746,
Found: 340.0744.



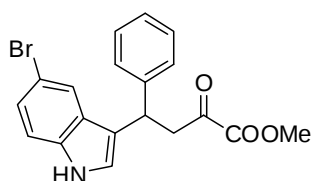
(+)-enantiomer (Table 2, entry 11): Prepared according to general **procedure**

B. After 68 hours, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the white solid in 80% yield with 85% ee. After a simple recrystallization, the enantioselectivity could be increased to 96% ee. $[\alpha]_D^{23} = -10.1$ ($c = 0.198$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (minor) = 14.510 min, t_r (major) = 22.888 min.





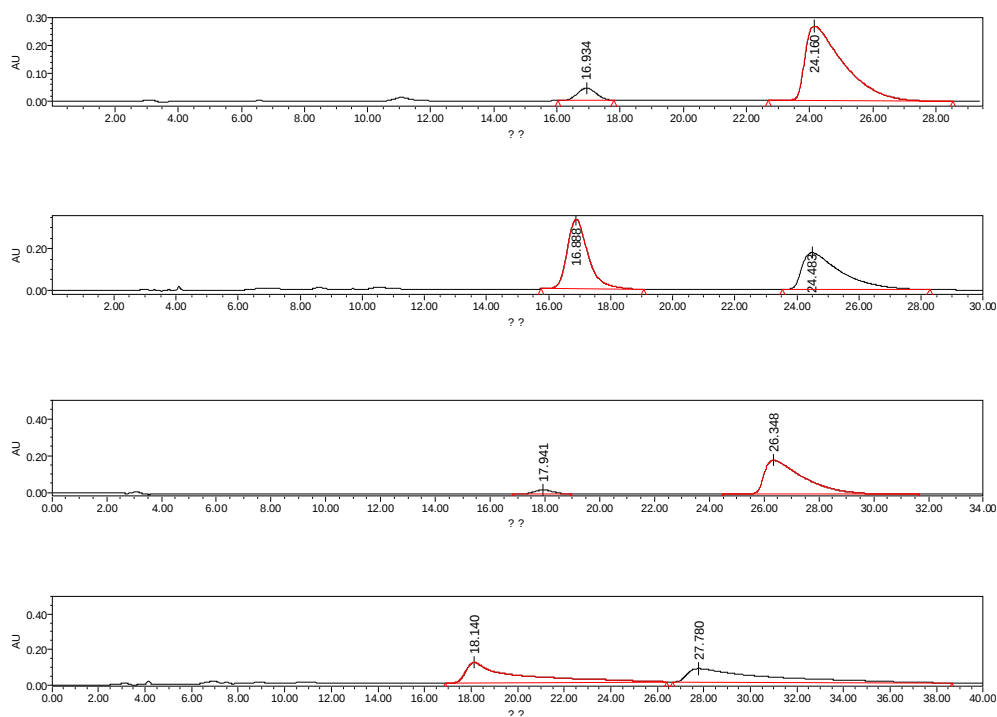
4-(1H-5-bromoindol-3-yl)-2-oxo-4-phenylbutyric acid methyl ester



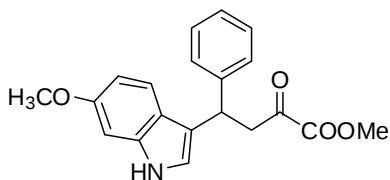
(+)-enantiomer (Table 2, entry 12): Prepared according

to general **procedure B**. After 68 hours, the crude material was directly purified by flash chromatography on

silica gel (petroleum ether/ethyl acetate, 4:1) to afford the white solid in 75% yield with 85% ee. M.p. 78-80 °C; After a simple recrystallization, the enantioselectivity could be increased to 90% ee. $[\alpha]_D^{23} = +23.1$ ($c = 0.208$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (minor) = 16.481 min, t_r (major) = 23.123 min. ^1H NMR (400 MHz, CDCl_3): $\delta = 8.08$ (s, 1H), 7.53 (d, $J = 1.6$ Hz, 1H), 7.32-7.16 (m, 7H), 7.03 (d, $J = 2.4$ Hz, 1H), 4.85 (t, $J = 7.6$ Hz, 1H), 3.78 (s, 3H), 3.64 (dd, $J = 16.8$, 7.2 Hz, 1H), 3.57 (dd, $J = 17.2$, 7.6 Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 192.37$, 161.24, 142.72, 135.16, 128.69, 128.18, 127.65, 126.83, 125.27, 122.70, 121.91, 118.03, 112.88, 112.62, 53.01, 45.64, 37.49 ppm; ES-HRMS Calcd for $\text{C}_{19}\text{H}_{17}\text{BrNO}_3$ $[\text{M} + \text{H}]^+$ 386.0386, Found: 386.0394.

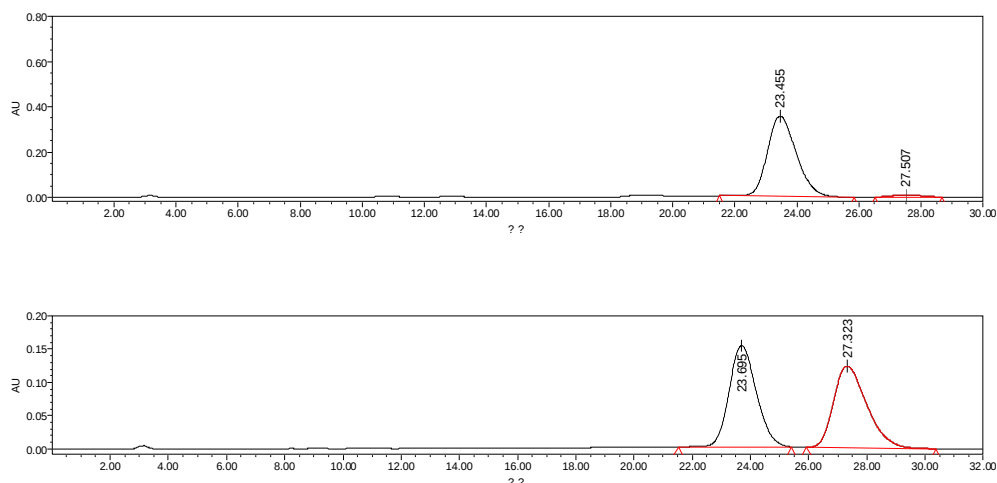


4-(6-Methoxyindol-3-yl)-2-oxo-4-phenylbutyric acid methyl ester

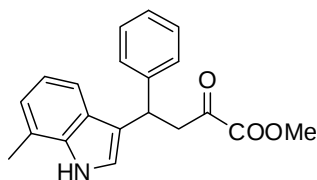


(-)-enantiomer (Table 3, entry 20): Prepared according to general **procedure A**. After 30 minutes, the crude material was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 2:1) to afford the yellow solid in 99% yield with 95% ee. M.p. 118-119 °C; $[\alpha]_D^{23} = -23.3$ ($c = 0.240$, CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (major) = 23.455 min, t_r (major) = 27.507 min. ^1H NMR (400 MHz, CDCl_3): $\delta = 7.92$ (s, 1H), 7.32-7.15 (m, 6H), 6.88 (dd, $J = 2.4, 0.8$ Hz, 1H), 6.78 (d, $J = 2.0$ Hz, 1H), 6.67 (dd, $J = 8.8, 2.4$ Hz, 1H), 4.86 (t, $J = 7.6$ Hz, 1H), 3.78 (s, 3H), 3.75 (s, 3H), 3.65 (dd, $J = 16.8, 7.2$ Hz, 1H), 3.56 (dd, $J = 16.8, 7.6$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 192.71, 161.34, 156.61,$

143.28, 137.38, 128.55, 127.76, 126.62, 120.87, 120.32, 120.01, 118.25, 109.48, 94.68, 55.63, 52.95, 45.69, 37.82 ppm; ES-HRMS Calcd for C₂₀H₂₀NO₄ [M + H]⁺ 338.1387, Found: 338.1397.



4-(7-methylindol-3-yl)-2-oxo-4-phenylbutyric acid methyl ester

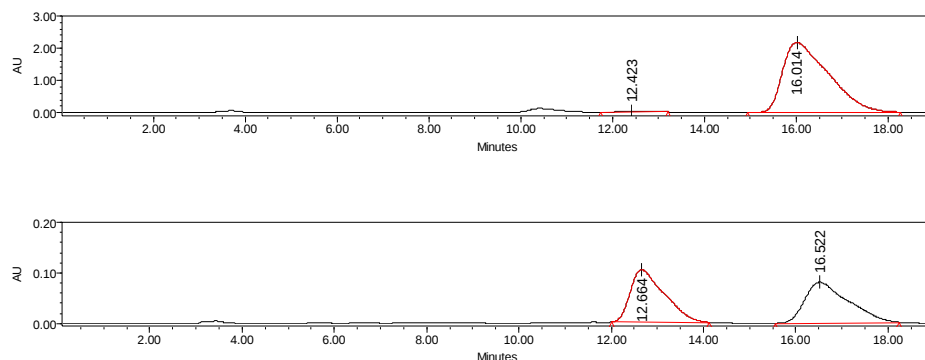


(-)-enantiomer (Table 3, entry 21): Prepared according to general **procedure A**. After 27 hours, the crude material was directly purified by flash chromatography

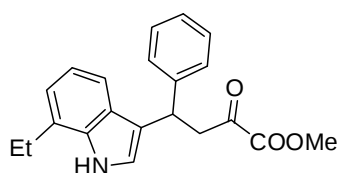
on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the yellow solid in 99% yield with 98% ee. M.p. 97-99 °C; [α]_D²³ = - 53.6 (c = 0.302, CH₂Cl₂); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (major) = 12.423 min, t_r (major) = 16.014 min. ¹H NMR (600 MHz, CDCl₃): δ = 7.95 (s, 1H), 7.32-7.15 (m, 6H), 7.01 (d, *J* = 1.6 Hz, 1H), 6.95-6.93 (m, 2H), 4.91 (t, *J* = 4.8 Hz, 1H), 3.75 (s, 3H), 3.67 (dd, *J* = 11.2, 4.8 Hz, 1H), 3.60 (dd, *J* = 11.2, 5.2 Hz, 1H), 2.43 (s, 3H) ppm. ¹³C NMR (150 MHz, CDCl₃): δ = 192.65, 161.31, 143.22, 136.13, 128.51, 127.76, 126.56, 125.93, 122.82,

121.24, 120.32, 119.76, 118.79, 117.12, 52.91, 45.65, 37.83, 16.51 ppm; ES-HRMS

Calcd for $C_{20}H_{20}NO_3$ $[M + H]^+$ 322.1438, Found: 322.1449.



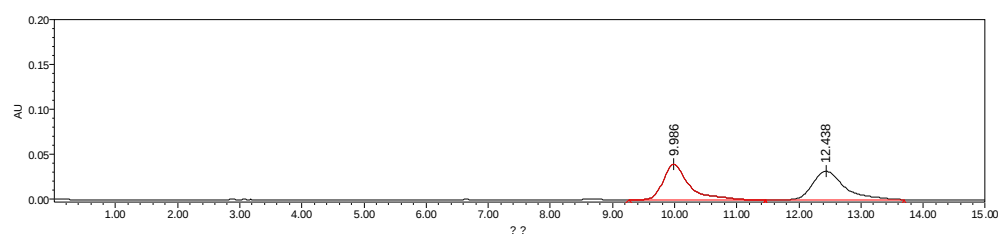
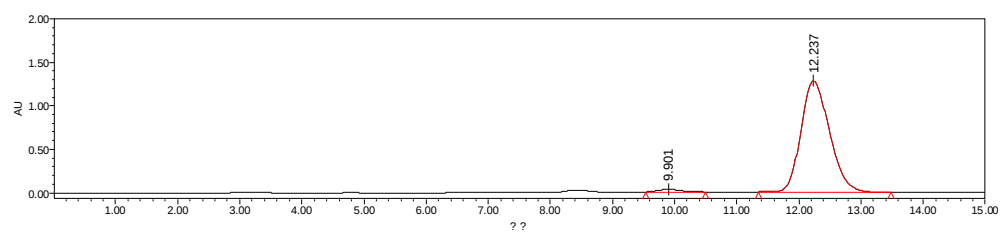
4-(7-ethylindol-3-yl)-2-oxo-4-phenylbutyric acid methyl ester



(-)-enantiomer (Table 3, entry 22): Prepared

according to general **procedure A**. After 10 hours, the crude material was directly purified by flash

chromatography on silica gel (petroleum ether/ethyl acetate, 4:1) to afford the yellow solid in 99% yield with 96% ee. $[\alpha]_D^{23} = -35.3$ ($c = 0.238$ CH_2Cl_2); The ee was determined by HPLC analysis using a chiralcel OD-H column (hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, t_r (major) = 9.901 min, t_r (major) = 12.237 min. 1H NMR (400 MHz, $CDCl_3$): δ = 7.99 (s, 1H), 7.32-7.15 (m, 6H), 6.98-6.95 (m, 3H), 4.90 (t, J = 7.6 Hz, 1H), 3.73 (s, 3H), 3.67 (dd, J = 16.8, 7.2 Hz, 1H), 3.59 (dd, J = 16.8, 7.6 Hz, 1H), 2.77 (q, J = 7.6 Hz, 2H), 1.30 (t, J = 7.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.67, 160.28, 142.20, 134.38, 127.48, 125.51, 125.10, 120.18, 119.71, 118.76, 117.65, 116.06, 51.86, 44.64, 36.80, 22.83, 12.69 ppm; ES-HRMS Calcd for $C_{21}H_{20}NO_3$ $[M - H]^-$ 334.1449, Found: 334.1436.



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- (11) M. Rueping, B. J. Nachtsheim, S. A. Moreth, M. Bolte, *Angew. Chem. Int. Ed.* **2008**, 47, 593.

8. Copy of ^1H NMR and ^{13}C NMR spectra for products:

