A New Class of Ligands for Aqueous, Lanthanide-Catalyzed, Enantioselective Mukaiyama Aldol Reactions

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General Information

Commercial chemicals were of reagent-grade purity or better and were used without further purification. The enantiomeric excess (ee, 95%) of (S)-2-bromopropanoic acid was determined by high-performance liquid chromatography (HPLC) analysis (Chiralpak AS–H, isocratic 9:1 hexanes/2-propanol, flow rate 1.0 mL/min, \( \lambda = 210 \) nm): \( t_R = 5.69 \) min (minor, \( R \)), 6.63 min (major, \( S \)). Water was purified using a PURELAB Ultra Mk2 water purification system (ELGA). Tetrahydrofuran (THF) was purified using a solvent purification system (Vacuum Atmospheres Company). (Z)-Trimethyl(1-phenylprop-1-enyloxy)silane (\( Z/E = 12:1 \)), (Z)-trimethyl(pent-2-en-3-yloxy)silane (\( Z/E = 4.5:1 \)), and (S)-2-bromopropanoates 2–6 were synthesized using previously published procedures with minor modification (see S3).

Flash chromatography was performed using silica gel 60, 230–400 mesh (EMD Chemicals) or neutral alumina 60–325 mesh (Fisher Scientific). Analytical thin-layer chromatography (TLC) was carried out on ASTM TLC plates precoated with silica gel 60 F254 (250 μm layer thickness). TLC visualization was accomplished using a UV lamp. \(^1\)H NMR spectra were obtained using a Varian Unity 300 (300 MHz) or a Varian Mercury 400 (400 MHz) spectrometer, and \(^{13}\)C NMR spectra were obtained using a Varian Unity 300 (75 MHz) or a Varian Mercury 400 (100 MHz) spectrometer. Data for \(^1\)H NMR spectra are reported as follows: chemical shift (ppm) relative to residual CHCl3 in CDCl3 (7.27 ppm) or H2O in D2O (4.79 ppm); multiplicity (“s” = singlet, “d” = doublet, “dd” = doublet of doublets, “t” = triplet, “q” = quartet, “m” = multiplet, “brs” = broad singlet); coupling constant, \( J \), (Hz); peak assignment and integration. Italicized elements are those that are responsible for the shifts. Data for \(^{13}\)C NMR spectroscopy are reported as ppm relative to CDCl3 (77.23 ppm) or an internal standard of dimethyl sulfoxide-\( d_6 \) (39.51 ppm) in D2O. High-resolution electrospray ionization mass spectra (HRESIMS) and high-resolution atmospheric pressure chemical ionization mass spectra (HRAPCIMS) were obtained on an
electrospray time of flight Waters Micromass LCT Premier XE mass spectrometer. HPLC analysis was carried out on a Shimadzu LC–MS equipped with a Chiralpak AS-H column or Chiralcel OJ-H column (Chiral Technologies Inc, 250 × 4.6 mm) using a binary isocratic method (pump A: 2-propanol; pump B: hexanes or n-heptane). Luminescence-decay measurements for the determination of water coordination number, $q$, were performed using a HORIBA Jobin Yvon Fluoromax-4 spectrofluorometer as previously reported. Optical rotations were recorded on an Autopol III automatic polarimeter.

**Synthesis and Characterization of Chiral Ligands**

![Chemical structures](image)

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<th>R</th>
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<th>n-C$_3$H$_7$</th>
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<td>3</td>
<td>4</td>
<td>5</td>
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<tr>
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* not determined

**(S)-2-Bromopropanoates 1–6:** Under an atmosphere of Ar, a mixture of (S)-2-bromopropanoic acid (1 equiv) and thionyl chloride (1.15 equiv) was stirred at 60 °C for 12 h. After cooling to ambient temperature, the resulting solution was added over 1 min to a solution of anhydrous ROH (2.4 M, 3 equiv) and anhydrous pyridine (1.2 M, 1.5 equiv) in anhydrous CHCl$_3$ at 0 °C. After stirring for 2 h at 0 °C followed by 1 h at ambient temperature, the reaction mixture was washed successively with water, sulfuric acid (10%), and saturated aqueous NaHCO$_3$. The resulting organic layer was dried over Na$_2$SO$_4$, and then volatiles were removed under reduced pressure to yield a colorless oil. Bromopropanoates 1–6 were used without further purification.
(S)-Methyl 2-bromopropanoate (1): Yield 99%; $^1$H NMR (400 MHz, CDCl$_3$, δ): 4.43–4.36 (m, CH, 1H), 3.80 (s, OCH$_3$, 3H), 1.84 (d, J = 7.2 Hz, CHCH$_3$, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$, δ): 171.0 (C=O), 53.2 (OCH$_3$), 40.0 (CH), 21.9 (CHCH$_3$); HRAPCIMS (m/z): [M + H]$^+$ calcd for C$_4$H$_8$BrO$_2$, 166.9708; found, 166.9703; $[^{23}$D$]_D$ = 26.8 (c 1.00, CHCl$_3$).

(S)-Ethyl 2-bromopropanoate (2): Yield 99%; $^1$H NMR (300 MHz, CDCl$_3$, δ): 4.41–4.33 (m, CH, 1H), 4.28–4.20 (m, OCH$_2$, 2H), 1.84 (d, J = 6.9 Hz, CHCH$_3$, 3H), 1.31 (t, J = 6.9 Hz, CH$_2$CH$_3$, 3H); $[^{23}$D$]_D$ = 26.2 (c 1.00, CHCl$_3$).

(S)-Propyl 2-bromopropanoate (3): Yield 99%; $^1$H NMR (400 MHz, CDCl$_3$, δ): 4.41–4.35 (m, CH, 1H), 4.19–4.08 (m, OCH$_2$, 2H), 1.83 (d, J = 6.8 Hz, CHCH$_3$, 3H), 1.75–1.66 (m, CH$_2$, 2H), 0.98 (t, J = 7.2 Hz, CH$_2$CH$_3$, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$, δ): 170.5 (C=O), 67.7 (OCH$_2$), 40.5 (CH), 22.0 (CH$_2$), 21.9 (CHCH$_3$), 10.5 (CH$_2$CH$_3$); HRAPCIMS (m/z): [M + H]$^+$ calcd for C$_6$H$_{12}$BrO$_2$, 195.0021; found, 195.0025; $[^{23}$D$]_D$ = 22.5 (c 1.00, CHCl$_3$).
(S)-Butyl 2-bromopropanoate (4): Yield 99%; \(^1\)H NMR (400 MHz, CDCl\(_3\), \(\delta\)): 4.40–4.34 (m, \(CH\), 1H), 4.22–4.14 (m, O\(CH_2\), 2H), 1.83 (d, \(J = 6.8 \text{ Hz, CHCH}_3\), 3H), 1.70–1.62 (m, \(CH_2\), 2H), 1.46–1.36 (m, \(CH_2\), 2H), 0.95 (t, \(J = 7.2 \text{ Hz, CH}_2\CH_3\), 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\), \(\delta\)): 170.6 (C=O), 66.0 (O\(CH_2\)), 40.5 (CH), 30.6 (CH\(_2\)), 21.9 (CH\(CH_3\)), 19.2 (CH\(_2\)), 13.9 (CH\(_2\)CH\(_3\)); HRAPCIMS (\(m/z\)): [M + H]\(^+\) calcd for C\(_7\)H\(_{14}\)BrO\(_2\), 209.0177; found, 209.0175; \([\alpha]_{D}^{23} -18.8 \ (c \ 1.00, \text{CHCl}_3)\).

(S)-Isopropyl 2-bromopropanoate (5): \(^3\)Yield 99%; \(^1\)H NMR (400 MHz, CDCl\(_3\), \(\delta\)): 5.09–5.02 (m, O\(CH\), 1H), 4.36–4.30 (m, Br\(CH\), 1H), 1.82 (dd, \(J = 7.2, 1.6 \text{ Hz, BrCHCH}_3\), 3H), 1.29 (d, \(J = 2.0 \text{ Hz, OCHCH}_3\), 3H), 1.27 (d, \(J = 1.6 \text{ Hz, OCHCH}_3\), 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\), \(\delta\)): 169.7 (C=O), 69.6 (O\(CH\)), 40.7 (Br\(CH\)), 21.6 (CH(CH\(_3\))\(_2\)), 21.5 (CH(CH\(_3\))\(_2\)), 21.3 (BrCHCH\(_3\)); \([\alpha]_{D}^{23} -11.7 \ (c \ 1.00, \text{CHCl}_3)\).

(S)-tert-Butyl 2-bromopropanoate (6): \(^3\)Yield 99%; \(^1\)H NMR (300 MHz, CDCl\(_3\), \(\delta\)): 4.34–4.24 (m, \(CH\), 1H), 1.79 (d, \(J = 6.6 \text{ Hz, CHCH}_3\), 3H), 1.49 (s, C(CH\(_3\))\(_3\), 9H); \([\alpha]_{D}^{23} -5.5 \ (c \ 1.00, \text{CHCl}_3)\).

Chiral ligands I–VI: Under an atmosphere of Ar, a mixture of (S)-2-bromopropanoate (6 equiv, 0.12 M), 1,7-diaza-12-crown-4 (1 equiv, 0.02 M), and Cs\(_2\)CO\(_3\) (2.3 equiv) in anhydrous CH\(_3\)CN was stirred at ambient temperature for 120 h. Upon completion of the reaction (as monitored by LC–MS), CH\(_3\)CN was
removed under reduced pressure, and CH\textsubscript{2}Cl\textsubscript{2} (5 mL) was added followed by filtration. Volatiles were removed under reduced pressure to yield a yellow oil. Racemic ligands I–VI were synthesized by using the racemic 2-bromopropanoate.

(2\textit{R},2'\textit{R})-Dimethyl 2,2’-(1,7-dioxo-4,10-diazacyclododecane-4,10-diyl)dipropanoate (I): Yield 99%; \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}, δ): 3.66 (s, OCH\textsubscript{3}, 6H), 3.62–3.53 (m, CH\textsubscript{2}O, 8H), 3.48 (q, J = 7.2 Hz, CH\textsubscript{2}CH\textsubscript{3}, 2H), 2.96–2.86 (m, NCH\textsubscript{2}, 4H), 2.77–2.70 (m, NCH\textsubscript{2}, 4H), 1.30 (d, J = 6.4 Hz, CH\textsubscript{2}CH\textsubscript{3}, 6H); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}, δ): 174.7 (C=O), 70.5 (CH\textsubscript{2}), 60.9 (CH), 53.1 (CH\textsubscript{2}), 51.3 (CH\textsubscript{3}), 16.4 (CH\textsubscript{3}); HRESIMS (m/z): [M + H]\textsuperscript{+} calcd for C\textsubscript{16}H\textsubscript{31}N\textsubscript{2}O\textsubscript{6}, 347.2182; found, 347.2190; \([\alpha]\textsubscript{D}\textsuperscript{23} +13.6 \) (c 0.50, CHCl\textsubscript{3}); HPLC (Chiralcel OJ-H, isocratic 95:5 n-heptane/2-propanol (0.3% diethylamine (DEA)), flow rate 0.3 mL/min, λ = 210 nm): >99% ee; 4:1 \textit{syn:anti}; \textit{t}\textsubscript{R} = 30.30 min [major (\textit{R},\textit{R})], 34.97 min [minor (\textit{R},\textit{S})].

(2\textit{R},2'\textit{R})-Diethyl 2,2’-(1,7-dioxo-4,10-diazacyclododecane-4,10-diyl)dipropanoate (II): Yield 99%; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}, δ): 4.12 (q, J = 7.2 Hz, C(=O)OCH\textsubscript{2}, 4H), 3.62–3.53 (m, NCH\textsubscript{2}CH\textsubscript{2}O, 8H), 3.47 (q, J = 7.6 Hz, CH\textsubscript{2}CH\textsubscript{3}, 2H), 2.93–2.86 (m, NCH\textsubscript{2}, 4H), 2.77–2.70 (m, NCH\textsubscript{2}, 4H), 1.31–1.21 (m, CH\textsubscript{2}CH\textsubscript{3} and CH\textsubscript{2}CH\textsubscript{3}, 12H); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}, δ): 174.2 (C=O), 70.5 (CH\textsubscript{2}), 60.9 (CH), 60.2 (CH\textsubscript{2}), 53.2 (CH\textsubscript{2}), 16.4 (CH\textsubscript{3}), 14.5 (CH\textsubscript{3}); HRESIMS (m/z): [M + H]\textsuperscript{+} calcd for C\textsubscript{18}H\textsubscript{35}N\textsubscript{2}O\textsubscript{6}, 375.2495;
found, 375.2502; $[\alpha]_{D}^{23} +6.8$ (c 0.50, CHCl3); HPLC (Chiralcel OJ-H, isocratic 95:5 $n$-heptane/2-propanol (0.3% DEA), flow rate 0.3 mL/min, $\lambda = 210$ nm): >99% ee; 4:1 syn:anti; $t_R = 21.78$ min [major ($R$,$R$)], 23.30 min [minor ($R$,$S$)].

(2$R$,$2'R$)-Dipropyl 2,2'-(1,7-dioxa-4,10-diazacyclododecane-4,10-diyl)dipropanoate (III): Yield 99%;
$^1$H NMR (400 MHz, CDCl$_3$, $\delta$): 4.02 (t, $J = 6.8$ Hz, C(=O)OCH$_2$, 4H), 3.61–3.51 (m, NCH$_2$CH$_2$O, 8H), 3.46 (q, $J = 7.2$ Hz, CHCH$_3$, 2H), 2.95–2.87 (m, NCH$_2$, 4H), 2.77–2.70 (m, NCH$_2$, 4H), 1.68–1.58 (m, CH$_3$CH$_2$, 4H), 1.29 (d, $J = 7.6$ Hz, CHCH$_3$, 6H), 0.91 (t, $J = 7.2$ Hz, CH$_2$CH$_3$, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$, $\delta$): 174.4 ($C=O$), 70.5 ($C$H$_2$), 65.9 ($C$H$_2$), 61.0 ($C$H), 53.2 ($C$H$_2$), 22.2 ($C$H$_2$), 16.6 ($C$H$_3$), 10.7 ($C$H$_3$); HRESIMS ($m/z$): [M + H]$^+$ calcd for C$_{20}$H$_{39}$N$_2$O$_6$, 403.2808; found, 403.2799; $[\alpha]_{D}^{23} +10.6$ (c 0.50, CHCl$_3$); HPLC (Chiralcel OJ-H, isocratic 95:5 $n$-heptane/2-propanol (0.05% DEA), flow rate 0.1 mL/min, $\lambda = 210$ nm): >99% ee; 4:1 syn:anti; $t_R = 58.65$ min [(R,$R$) + (R,$S$)].

(2$R$,$2'R$)-Dibutyl 2,2'-(1,7-dioxa-4,10-diazacyclododecane-4,10-diyl)dipropanoate (IV): Yield 99%;
$^1$H NMR (400 MHz, CDCl$_3$, $\delta$): 4.04 (t, $J = 6.4$ Hz, C(=O)OCH$_2$, 4H), 3.60–3.50 (m, NCH$_2$CH$_2$O, 8H), 3.44 (q, $J = 7.2$ Hz, CHCH$_3$, 2H), 2.92–2.85 (m, NCH$_2$, 4H), 2.75–2.68 (m, NCH$_2$, 4H), 1.61–1.53 (m, CH$_3$CH$_2$CH$_2$, 4H), 1.38–1.29 (m, CH$_3$CH$_2$, 4H), 1.27 (d, $J = 7.2$ Hz, CHCH$_3$, 6H), 0.89 (t, $J = 7.2$ Hz, CH$_2$CH$_3$, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$, $\delta$): 174.3 ($C=O$), 70.5 ($C$H$_2$), 64.1 ($C$H$_2$), 61.0 ($C$H), 53.1
(CH$_2$)$_3$, 30.9 (CH$_2$), 19.3 (CH$_2$), 16.5 (CH$_3$), 13.8 (CH$_3$); HRESIMS (m/z): [M + H]$^+$ calcd for C$_{22}$H$_{43}$N$_2$O$_6$, 431.3121; found, 431.3116; $[\alpha]_D^{23} +11.6$ (c 0.50, CHCl$_3$); HPLC (Chiralcel OJ-H, isocratic 95:5 n-heptane/2-propanol (0.3% DEA), flow rate 0.1 mL/min, $\lambda = 210$ nm): >99% ee; 4:1 syn:anti; $t_R = 48.67$ min [($R,R$) + ($R,S$)].

(2R,2'R)-Isopropyl 2,2'-(1,7-dioxa-4,10-diazacyclododecane-4,10-diyl)dipropanoate (V): Yield 99%; $^1$H NMR (400 MHz, CDCl$_3$, $\delta$): 5.05–4.96 (m, OCH, 2H), 3.64–3.53 (m, CH$_2$O, 8H), 3.43 (q, $J = 7.2$ Hz, NCH, 2H), 2.98–2.89 (m, NCH$_2$, 4H), 2.79–2.72 (m, NCH$_2$, 4H), 1.29 (d, $J = 7.6$ Hz, CHCH$_3$, 6H), 1.23 (q, $J = 3.2$ Hz, CH(CH$_3$)$_2$, 12H); $^{13}$C NMR (100 MHz, CDCl$_3$, $\delta$): 173.8 (C=O), 70.6 (CH$_2$), 67.8 (CH), 61.1 (CH), 53.2 (CH$_2$), 22.3 (CH$_3$), 22.1 (CH$_3$), 16.5 (CH$_3$). HRESIMS (m/z): [M + H]$^+$ calcd for C$_{20}$H$_{39}$N$_2$O$_6$, 403.2808; found, 403.2813; $[\alpha]_D^{23} +10.4$ (c 0.50, CHCl$_3$); HPLC (Chiralcel OJ-H, isocratic 95:5 n-heptane/2-propanol (0.3% DEA), flow rate 0.3 mL/min, $\lambda = 210$ nm): 4:1 syn:anti; $t_R = 16.71$ min [($S,S$) + ($R,S$)], 17.60 min ($R,R$).

(2R,2'R)-tert-Butyl 2,2'-(1,7-dioxa-4,10-diazacyclododecane-4,10-diyl)dipropanoate (VI): Yield 99%; $^1$H NMR (400 MHz, CDCl$_3$, $\delta$): 3.65–3.53 (m, CH$_2$O, 8H), 3.36 (q, $J = 7.2$ Hz, NCH, 2H), 2.98–2.89 (m, NCH$_2$, 4H), 2.79–2.73 (m, NCH$_2$, 4H), 1.45 (s, C(CH$_3$)$_3$, 18H), 1.29–1.25 (m, CHCH$_3$, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$, $\delta$): 173.9 (C=O), 173.8 (C=O), 80.8 (C(CH$_3$)$_3$), 70.4 (CH$_2$), 70.4 (CH$_2$), 61.7
Mei, Dissanayake, and Allen  Supporting Information

(1H, 3H, 5H, 6H, 12H, 13H)-1,3,9,11-Tetramethyldodeca-1,7-diene-3,9-dione (I): The reaction mixture (1 equiv, 0.036 M) in MeOH was added a solution of NaOH (5 equiv, 0.72 M) in water. The resulting solution was stirred at ambient temperature for 48 h. Upon completion of the reaction (as monitored by LC–MS), solvent was removed under reduced pressure. The resulting white solid was dissolved in water (3 mL), loaded onto a column containing Amberlite® IR-120 (H) ion exchange resin, and eluted with water/ammonium hydroxide (28–30%, aqueous solution) (stepwise gradient of 100:0→100:0.5→100:1). Solvent was removed under reduced pressure to yield (I) (99%) as a white solid. 1H NMR (400 MHz, D2O, δ): 3.51–3.39 (m, CH2, 4H), 3.37–3.28 (m, CH2, 4H), 3.20–3.15 (m, CH, 2H), 2.62–2.50 (m, CH2, 8H), 1.04 (d, J = 7.6 Hz, CH3, 6H); 13C NMR (100 MHz, D2O, δ): 182.8 (C=O, syn), 182.5 (C=O, anti), 68.6 (CH2, anti), 68.0 (CH2, syn), 63.7 (CH, anti), 62.9 (CH, syn), 50.0 (CH2, anti), 49.5 (CH2, syn), 12.9 (CH3, anti), 12.8 (CH3, syn); HRESIMS (m/z): [M + Na]+ calcd for C14H26N2O6Na, 341.1689; found, 341.1697; [α]D23 +6.4 (c 0.5, MeOH).

(2R,2'R)-2,2'-(1,7-Dioxo-4,10-diazaacyclododecane-4,10-diyl)dipropionic acid (VII): To a solution of (I) (1 equiv, 0.036 M) in MeOH was added a solution of NaOH (5 equiv, 0.72 M) in water. The resulting solution was stirred at ambient temperature for 48 h. Upon completion of the reaction (as monitored by LC–MS), solvent was removed under reduced pressure. The resulting white solid was dissolved in water (3 mL), loaded onto a column containing Amberlite® IR-120 (H) ion exchange resin, and eluted with water/ammonium hydroxide (28–30%, aqueous solution) (stepwise gradient of 100:0→100:0.5→100:1). Solvent was removed under reduced pressure to yield VII (99%) as a white solid. 1H NMR (400 MHz, D2O, δ): 3.51–3.39 (m, CH2, 4H), 3.37–3.28 (m, CH2, 4H), 3.20–3.15 (m, CH, 2H), 2.62–2.50 (m, CH2, 8H), 1.04 (d, J = 7.6 Hz, CH3, 6H); 13C NMR (100 MHz, D2O, δ): 182.8 (C=O, syn), 182.5 (C=O, anti), 68.6 (CH2, anti), 68.0 (CH2, syn), 63.7 (CH, anti), 62.9 (CH, syn), 50.0 (CH2, anti), 49.5 (CH2, syn), 12.9 (CH3, anti), 12.8 (CH3, syn); HRESIMS (m/z): [M + Na]+ calcd for C14H26N2O6Na, 341.1689; found, 341.1697; [α]D23 +6.4 (c 0.5, MeOH).
General Procedure for Aldol Reactions

The mixture of chiral ligand (x equiv) and Eu(OTf)₃ (y equiv) in EtOH–H₂O (0.4 mL, 9:1 v/v) was stirred at 50 °C for 2 h and then cooled to –25 °C. Benzaldehyde (0.0325 mmol, 1.0 equiv) and silyl enol ether (0.0488 mmol, 1.5 equiv) were added, and the resulting mixture was stirred for a specified time at –25 °C. The mixture was purified directly using a silica gel column (1:10 ethyl acetate/hexanes), and the volatiles were removed under reduced pressure to yield a mixture of syn and anti products. The enantioselectivity and diastereoselectivity were determined by HPLC analysis.

(2R,3R)-3-Hydroxy-2-methyl-1,3-diphenylpropan-1-one (9a): Yield 92%; ¹H NMR (400 MHz, CDCl₃, δ): 7.97–7.94 (m, ArH, 2H), 7.62–7.58 (m, ArH, 1H), 7.51–7.47 (m, ArH, 2H), 7.44–7.41 (m, ArH, 2H), 7.39–7.34 (m, ArH, 2H), 7.30–7.24 (m, ArH, 1H), 5.26 (t, J = 2.4 Hz, OHCH, 1H), 3.75–3.70 (m, CH₃CH, 1H), 3.67 (d, J = 1.6 Hz, OH, 1H), 1.21 (d, J = 6.8 Hz, CH₃, 3H); ¹³C NMR (100 MHz, CDCl₃, δ): 206.0 (C=O), 142.0 (C), 135.8 (C), 133.8 (CH), 129.0 (CH), 128.7 (CH), 128.5 (CH), 127.5 (CH), 126.3 (CH), 73.3 (CH), 47.2 (CH), 11.3 (CH₃); HRESIMS (m/z): [M + Na]⁺ calcld for C₁₆H₁₆O₂Na, 263.1048; found, 263.1042; HPLC (Chiralpak AS–H, isocratic 9:1 hexanes/2-propanol, flow rate 1.0 mL/min, λ = 254 nm): 93% ee; 32:1 syn:anti; tᵣ = 8.07 min (major, syn), 12.45 min (minor, syn), 13.96 min (minor, anti), 18.53 min (major, anti). The configuration of the product was determined as 2R,3R
using a Chiralcel OJ-H column by comparison with the retention order of authentic compounds on a Chiralcel OJ column (DIACEL Chemical Industries).\(^5\)

\[(\text{syn})-3-(4\text{-Chlorophenyl})-3\text{-hydroxy}-2\text{-methyl}-1\text{-phenylpropan-1-one (9b):}\]
Yield 75%; \(^1\)H NMR (400 MHz, CDCl\(_3\), \(\delta\)): 7.96–7.93 (m, Ar\(H\), 2H), 7.64–7.60 (m, Ar\(H\), 1H), 7.52–7.48 (m, Ar\(H\), 2H), 7.38–7.32 (m, Ar\(H\), 4H), 5.24 (t, \(J = 2.4\) Hz, OHCH, 1H), 3.77 (d, \(J = 1.6\) Hz, OH, 1H), 3.69–3.62 (m, CH\(_3\)CH, 1H), 1.18 (d, \(J = 6.4\) Hz, CH\(_3\), 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\), \(\delta\)): 205.9 (C=O), 140.5 (C), 135.6 (C), 134.0 (CH), 133.2 (C), 129.1 (CH), 128.7 (CH), 128.6 (CH), 127.7 (CH), 72.6 (CH), 47.0 (CH), 11.3(CH\(_3\));
HRESIMS (m/z): [M + Na]\(^+\) calcd for C\(_{16}\)H\(_{15}\)O\(_2\)NaCl, 297.0658; found, 297.0652; HPLC (Chiralpak AD–H, isocratic 9:1 hexanes/2-propanol, flow rate 1.0 mL/min, \(\lambda = 254\) nm): 91% ee; 21:1 syn:anti; \(t_R = 9.35\) min (major, syn), 11.00 min (minor, syn), 13.81 min (minor, anti), 17.10 min (major, anti). The configuration of the product was determined as syn by comparison with the retention order of authentic compounds on a Chiralpak AD–H column.\(^6\)

\[(\text{syn})-3\text{-Hydroxy}-2\text{-methyl}-1\text{-phenyl}-3\text{-p-tolylpropan-1-one (9c):}\]
Yield 73%; \(^1\)H NMR (400 MHz, CDCl\(_3\), \(\delta\)): 7.96–7.93 (m, Ar\(H\), 2H), 7.63–7.58 (m, Ar\(H\), 1H), 7.51–7.46 (m, Ar\(H\), 2H), 7.30 (d, \(J = 8.4\) Hz, Ar\(H\), 2H), 7.17 (d, \(J = 8.0\) Hz, Ar\(H\), 2H), 5.23 (t, \(J = 2.4\) Hz, OHCH, 1H), 3.73–3.66 (m, CH\(_3\)CH, 1H), 3.58 (d, \(J = 1.6\) Hz, OH, 1H), 2.35 (s, ArCH\(_3\), 3H), 1.20 (d, \(J = 7.6\) Hz, CH\(_3\), 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\), \(\delta\)): 205.9 (C=O), 140.5 (C), 135.6 (C), 134.0 (CH), 133.2 (C), 129.1 (CH), 128.7 (CH), 128.6 (CH), 127.7 (CH), 72.6 (CH), 47.0 (CH), 11.3(CH\(_3\))
MHz, CDCl3, δ): 206.0 (C=O), 139.0 (C), 137.1 (C), 135.9 (C), 133.8 (CH), 129.2 (CH), 129.0 (CH), 128.7 (CH), 126.2 (CH), 73.2 (CH), 47.3 (CH), 21.3 (CH3), 11.4 (CH3); HRESIMS (m/z): [M + Na]+ calcd for C17H18O2Na, 277.1204; found, 277.1201; HPLC (Chiralpak AD–H, isocratic 9:1 hexanes/2-propanol, flow rate 1.0 mL/min, λ = 254 nm): 90% ee; 24:1 syn:anti; tR = 8.86 min (major, syn), 10.15 min (minor, syn), 14.49 min (minor, anti). The configuration of the product was determined as syn by comparison with the retention order of authentic compounds on a Chiralpak AD–H column.6

![Chemical structure](image)

(2R,3S)-3-Hydroxy-2-methyl-1-phenylhex-4-en-1-one (9d): Yield 65%; 1H NMR (400 MHz, CDCl3, δ): 7.97–7.94 (m, ArH, 2H), 7.63–7.57 (m, ArH, 1H), 7.52–7.47 (m, ArH, 2H), 5.83–5.74 (m, CH=CHCH3, 1H), 5.59–5.51 (m, CH=CHCH3, 1H), 4.54 (t, J = 4.0 Hz, CHOH, 3H), 3.58–3.50 (m, CH3CH, 1H), 3.10 (d, J = 3.2 Hz, OH, 1H), 1.71 (d, J = 6.4 Hz, CH=CHCH3, 3H), 1.28 (d, J = 7.2 Hz, CHCH3, 3H); 13C NMR (100 MHz, CDCl3, δ): 205.6 (C=O), 136.3 (C), 133.6 (CH), 130.9 (CH), 129.0 (CH), 128.7 (CH), 128.1 (CH), 72.7 (CH), 45.7 (CH), 18.0 (CH3), 12.0 (CH3); HRESIMS (m/z): [M + Na]+ calcd for C13H16O2Na, 227.1048; found, 227.1042; HPLC analysis (Chiralcel OD–H, isocratic 99:1 n-heptane/2-propanol, flow rate 0.8 mL/min, λ = 254 nm): 93% ee; 21:1 syn:anti; tR = 19.90 min (major, syn), 25.45 min (minor, syn), 37.56 min (minor, anti), 39.78 min (major, anti). The configuration of the product was determined as 2R,3S on a Chiralcel OD-H column by comparison with the retention order of authentic compounds on a Chiralcel OD-H column.7
(anti)-3-Hydroxy-2-methyl-1-phenylbutan-1-one (9e): Yield 32%; $^1$H NMR (400 MHz, CDCl$_3$, $\delta$): 7.98–7.95 (m, ArH, 2H), 7.63–7.59 (m, ArH, 1H), 7.53–7.48 (m, ArH, 2H), 4.29–4.25 (m, CH$_2$OH, 1H), 3.46–3.40 (m, CH$_3$CH, 1H), 3.10 (d, $J = 2.4$ Hz, OH, 1H), 1.30–1.24 (m, CH$_3$, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$, $\delta$): 206.2 (C=O), 136.1 (C), 133.7 (CH), 129.0 (CH), 128.7 (CH), 67.6 (CH), 45.9 (CH), 20.5 (CH$_3$), 11.3 (CH$_3$); HRESIMS (m/z): [M + Na]$^+$ calcd for C$_{11}$H$_{14}$O$_2$Na, 201.0891; found, 201.0894; HPLC (Chiralpak AS–H, isocratic 95:5 $n$-heptane/2-propanol, flow rate 0.6 mL/min, $\lambda = 254$ nm): 97% ee, 22:1 anti:syn; $t_R$ = 16.65 min (major, anti), 24.35 min (minor, anti), 20.94 min (major, syn), 39.88 min (minor, syn). The configuration of the product was determined as anti by comparison with the $^1$H NMR spectra of authentic compounds.$^8$

(syn)-3-Hydroxy-2-methyl-1-phenylnonan-1-one (9f): Yield 22%; $^1$H NMR (400 MHz, CDCl$_3$, $\delta$): 7.97–7.94 (m, ArH, 2H), 7.63–7.58 (m, ArH, 1H), 7.52–7.48 (m, ArH, 2H), 4.07–4.02 (m, OHCH$_2$, 1H), 3.51–3.44 (m, CH$_3$CH, 1H), 3.11 (d, $J = 2.4$ Hz, OH, 1H), 1.61–1.20 (m, CH$_2$ and CHCH$_3$, 13H), 0.89 (t, $J = 7.2$ Hz, CH$_2$CH$_3$, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$, $\delta$): 206.2 (C=O), 136.1 (C), 133.7 (CH), 129.0 (CH), 128.7 (CH), 71.5 (CH), 44.6 (CH), 34.5 (CH$_2$), 32.0 (CH$_2$), 29.5 (CH$_2$), 26.3 (CH$_2$), 22.8 (CH$_2$), 14.3 (CH$_3$), 11.2 (CH$_3$); HRESIMS (m/z): [M + H]$^+$ calcd for C$_{16}$H$_{25}$O$_2$, 249.1855; found, 249.1847; HPLC (Chiralpak AS–H, isocratic 95:5 $n$-heptane/2-propanol, flow rate 0.7 mL/min, $\lambda = 254$ nm): 96% ee; 23:1 syn:anti; $t_R$ = 8.87 min (major, syn), 11.75 min (minor, syn), 9.35 min (major, anti), 22.48 min
(minor, anti). The configuration of the product was determined as syn by comparison with the retention order of authentic compounds on a Chiralpak AS–H column.

\[(\text{anti})-3\text{-Cyclohexyl}-3\text{-hydroxy}-2\text{-methyl}-1\text{-phenylpropan-1-one (9g)}: \text{Yield 12\%; } ^1\text{H NMR } 300\text{ MHz, CDCl}_3, \delta: 7.96–7.93 \text{ (m, } \text{ArH, 2H}), 7.63–7.57 \text{ (m, } \text{ArH, 1H}), 7.52–7.46 \text{ (m, } \text{ArH, 2H}), 3.72–3.64 \text{ (m, CH}_3\text{CH and CHOH, 2H}), 3.11–3.09 \text{ (m, OH, 1H)}, 2.12 (d, } J = 12.9 \text{ Hz, OH, 1H}), 1.84–0.92 \text{ (m, CHCH}_3\text{ and CH}_2, 13\text{H}); ^{13}\text{C NMR } 70\text{ MHz, CDCl}_3, \delta: 206.2 \text{ (C=O), 136.1 } (C), 133.6 \text{ (CH), 129.0 } (CH), 128.7 \text{ (CH), 75.6 } (CH), 41.5 \text{ (CH), 40.4 } (CH), 29.7 \text{ (CH}_2\text{), 29.4 } (CH)_2\text{, 26.6 } (CH)_2\text{, 26.3 } (CH)_2\text{, 26.1 } (CH)_2\text{, 10.7 } (CH); \text{ HRESIMS } (m/z): [M + Na]^+ \text{ calcd for C}_{16}\text{H}_{22}\text{O}_2\text{Na, 269.1517; found, 269.1525; HPLC (Chiralpak AS–H, isocratic 95:5 } n\text{-heptane/2-propanol, flow rate 0.6 mL/min, } \lambda = 254 \text{ nm): 95\% ee; 49:1 anti:syn; } t_R = 12.60 \text{ min (major, anti), 22.35 min (minor, anti), 11.70 min (minor, syn), 30.12 min (major, syn). The configuration of the product was determined as anti by comparison with the } ^1\text{H NMR spectra of authentic compounds.}\]

\[(\text{syn})-1\text{-hydroxy}-2\text{-methyl}-1\text{-phenylpentan-3-one (9i)}: \text{Yield 61\%; } ^1\text{H NMR } 400\text{ MHz, CDCl}_3, \delta: 7.37–7.24 \text{ (m, } \text{ArH, 5H}), 5.09–5.06 \text{ (m, OHCH, 1H)}, 3.14 (d, } J = 2.8 \text{ Hz, OH, 1H}), 2.89–2.82 \text{ (m, CH}_3\text{CH, 1H}), 2.58–2.47 \text{ (m, CH}_3\text{CH}_2\text{, 1H}), 2.41–2.30 \text{ (m, CH}_2\text{CH}_2\text{, 1H}), 1.09 (d, } J = 7.2 \text{ Hz, CHCH}_3\text{, 3H}), 1.02 (t, } J = 6.8 \text{ Hz, CH}_2\text{CH}_3\text{, 3H}); ^{13}\text{C NMR } 100\text{ MHz, CDCl}_3, \delta: 216.6 \text{ (C=O), 142.0 } (C), 128.5\]
(CH), 127.6 (CH), 126.1 (CH), 73.4 (CH), 52.4 (CH), 35.6 (CH₂), 10.7 (CH₃), 7.7 (CH₃); HRESIMS (m/z): [M + Na]^+ calcd for C₁₂H₁₆O₂Na, 215.1048; found, 215.1048; HPLC (Chiralpak AS–H, isocratic 90:10 n-heptane/2-propanol, flow rate 0.6 mL/min, λ = 210 nm): 84% ee; 11:1 anti:syn; tₚ = 12.65 min (major, syn), 14.86 min (minor, syn), 13.75 min (minor, anti), 19.18 min (major, anti). The configuration of the product was determined as syn by comparison with the retention order of authentic compounds on a Chiralpak AS–H column and the ^1H NMR spectra of authentic compounds.⁶

Procedure for q Measurements

Metalated Chiral Ligand Solutions (I´–V´): A mixture of chiral ligand (I, II, III, IV, or V) (1.2 mM, 1.2 equiv) and Eu(OTf)₃ (1 mM, 1 equiv) was stirred at ambient temperature for 5 h in a solution of H₂O and THF (10% v/v). This procedure was repeated using D₂O in THF (10% v/v). These solutions were used directly in the luminescence-decay measurements.

Metalated Chiral Ligand Solution (VI´): A mixture of chiral ligand (VI) (3 mM, 3 equiv) and Eu(OTf)₃ (1 mM, 1 equiv) was stirred at 40 °C for 45 min and then at ambient temperature for 24 h in a solution of H₂O and THF (10% v/v). This procedure was repeated using D₂O and THF (10% v/v). The resulting solution was used directly in the luminescence-decay measurements.

Metalated Chiral Ligand (VII´): A mixture of chiral ligand (VII) (34 mg, 5.4 μM, 1.0 equiv) and Eu(OTf)₃ (70 mg, 5.9 μM, 1.1 equiv) was stirred at ambient temperature for 12 h and then at 80 °C for 12 h in a solution of H₂O, and the pH of the reaction mixture was maintained between 6.9 and 7.1 by addition of 0.1 M aqueous NH₄OH. After cooled to ambient temperature, the pH of the mixture was increased to 11 using 0.1 M aqueous NH₄OH to precipitate excess Eu³⁺ as Eu(OH)₃. After removing
Eu(OH)$_3$ by filtration through a 0.2 μm filter (Millipore, IC Millex-LG), volatiles were removed under reduced pressure. The resulting white solid was dissolved in H$_2$O (5 mL) and dialyzed against H$_2$O (cellulose ester, 100–500 Dalton molecular weight cut off, Spectra/Por Biotech). After dialysis, the solution inside the membrane was freeze dried to yield 62 mg (93%) of VII’ as a white solid: HRESIMS (m/z): [M]$^+$ calcd for C$_{14}$H$_{24}$N$_2$O$_6$Eu, 467.0833; found, 467.0825. Solutions (1 mM in H$_2$O and THF (10% v/v) or D$_2$O and THF (10% v/v)) of this solid were used in the luminescence-decay measurements.

**Determination of q Values:** The luminescence-decay measurements for the metalated chiral ligand solutions (1 mM) of I’–VII’ were acquired using the parameters listed in the next paragraph, and the excitation and emission wavelengths are listed in Table S1. Then, benzaldehyde (5 mM) was added to each solution, and the measurements were repeated. All solutions were prepared and measured 3–6 times, and the results of these measurements are listed in Table S2.

The following parameters were kept constant during luminescence-decay measurements: excitation and emission slit width (5 nm), flash count (100), initial delay (0.001 ms), maximum delay (2.0 ms), and delay increment (0.02 ms). The natural log of the intensity of the scan was plotted against time, and the resulting slope was used as the decay rate ($\tau^{-1}$). The decay rates were used in eq 1 to determine the number of water molecules, $q$, coordinated to the Eu$^{3+}$ ion.$^{4,10}$

$$\text{eq 1: } q = 1.1 \left( \left| \frac{\tau_{H_2O}^{i}}{\tau_{D_2O}^{i}} - 0.3 \right| \right)$$


Table S1. Excitation and emission wavelengths used in the determination of \( q \) values.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Excitation wavelength (nm)</th>
<th>Emission wavelength (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I’</td>
<td>395</td>
<td>590</td>
</tr>
<tr>
<td>I’ + benzaldehyde</td>
<td>395</td>
<td>590</td>
</tr>
<tr>
<td>II’</td>
<td>395</td>
<td>590</td>
</tr>
<tr>
<td>II’ + benzaldehyde</td>
<td>395</td>
<td>590</td>
</tr>
<tr>
<td>III’</td>
<td>394</td>
<td>590</td>
</tr>
<tr>
<td>III’ + benzaldehyde</td>
<td>394</td>
<td>590</td>
</tr>
<tr>
<td>IV’</td>
<td>394</td>
<td>590</td>
</tr>
<tr>
<td>IV’ + benzaldehyde</td>
<td>394</td>
<td>590</td>
</tr>
<tr>
<td>V’</td>
<td>395</td>
<td>590</td>
</tr>
<tr>
<td>V’ + benzaldehyde</td>
<td>395</td>
<td>590</td>
</tr>
<tr>
<td>VI’</td>
<td>395</td>
<td>591</td>
</tr>
<tr>
<td>VI’ + benzaldehyde</td>
<td>395</td>
<td>591</td>
</tr>
<tr>
<td>VII’</td>
<td>395</td>
<td>589</td>
</tr>
<tr>
<td>VII’ + benzaldehyde</td>
<td>395</td>
<td>589</td>
</tr>
</tbody>
</table>

Table S2. Number of H\(_2\)O molecules, \( q \), coordinated to complexes of Eu\(^{3+}\) with chiral ligands I–VII.*

<table>
<thead>
<tr>
<th>Chiral ligand</th>
<th>( q ) (complex)</th>
<th>( q ) (complex plus benzaldehyde)</th>
<th>( \Delta q )</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (syn:anti = 4:1)</td>
<td>2.39 ± 0.02</td>
<td>1.77 ± 0.01</td>
<td>–0.62</td>
</tr>
<tr>
<td>I (syn:anti = 5:1)</td>
<td>2.49 ± 0.02</td>
<td>1.93 ± 0.01</td>
<td>–0.56</td>
</tr>
<tr>
<td>I (R, R)</td>
<td>2.58 ± 0.02</td>
<td>1.90 ± 0.01</td>
<td>–0.68</td>
</tr>
<tr>
<td>II (syn:anti = 4:1)</td>
<td>2.20 ± 0.02</td>
<td>1.80 ± 0.02</td>
<td>–0.40</td>
</tr>
<tr>
<td>III (syn:anti = 4:1)</td>
<td>2.25 ± 0.02</td>
<td>1.80 ± 0.02</td>
<td>–0.45</td>
</tr>
<tr>
<td>IV (syn:anti = 4:1)</td>
<td>2.41 ± 0.01</td>
<td>1.92 ± 0.01</td>
<td>–0.49</td>
</tr>
<tr>
<td>V (syn:anti = 4:1)</td>
<td>2.81 ± 0.01</td>
<td>2.62 ± 0.02</td>
<td>–0.19</td>
</tr>
<tr>
<td>VI (syn:anti &gt; 1:1)</td>
<td>2.83 ± 0.01</td>
<td>2.69 ± 0.02</td>
<td>–0.14</td>
</tr>
<tr>
<td>VII (syn:anti = 3:1)</td>
<td>2.61 ± 0.04</td>
<td>2.52 ± 0.03</td>
<td>–0.09</td>
</tr>
</tbody>
</table>

*\( q \) values are listed as mean ± standard error
**Derivation of Equation for $K$**

$LEu(H_2O)_{q_i}(aq) \rightleftharpoons LEuB(H_2O)_{q_b}(aq)$

For the equilibrium above, B is benzaldehyde; L is the non-H$_2$O ligands; $q_i$ is the measured number of water molecules coordinated to Eu$^{3+}$ prior to the addition of B; $q_b$ is the number of water molecules coordinated to Eu$^{3+}$ after the addition of B, and $q_e$ is the measured number of water molecules coordinated to Eu$^{3+}$ at equilibrium.

Assume that L is not labile; that B can replace H$_2$O; that at equilibrium both B and H$_2$O are in excess; that no other Eu$^{3+}$-containing species exist in solution; that the maximum number of B that can coordinate per Eu$^{3+}$ is one ($q_b = q_i - 1$); and that the volume change of the system upon addition of benzaldehyde is negligible.

Then at equilibrium,

$$K = \frac{\left[ LEuB\left( H_2O \right)_{q_b} \right]}{\left[ LEu\left( H_2O \right)_{q_i} \right]}$$

because the volume is a constant,

$$K = \frac{\text{number of } LEuB\left( H_2O \right)_{q_e} \text{ molecules}}{\text{number of } LEu\left( H_2O \right)_{q_i} \text{ molecules}} = \frac{N_b}{N_i}.$$

The measured value $q_e$ is the weighted average of the species in solution; thus, $q_e = \frac{N_b(q_b) + N_i(q_i)}{(N_b + N_i)}$.

Rearranging the equation for $q_e$ yields $\frac{N_b}{N_i} = \frac{q_i - q_e}{q_e - q_b}$.

Substituting for $q_b$ yields $\frac{N_b}{N_i} = \frac{q_i - q_e}{q_e - q_i + 1}$.

Because $\Delta q = q_e - q_i$ and $K = \frac{N_b}{N_i}$, $K = \frac{-\Delta q}{\Delta q + 1}$. 
References

Br

OCH₃

OCH₃
Supporting Information

Figure S1: NMR spectrum showing the 9a position.
Chiral High-Performance Liquid Chromatography (HPLC) Chromatograms of Aldol Products and Ligands:

**Aldol Products:**

- **Ph**
- **CH₃**
- **Ph**
- **O**
- **OH**

**syn (racemic)**

- Retention time: 7.789/137108
- 0.0
- 2.5
- 5.0
- 7.5
- 10.0
- 12.5
- 15.0
- 17.5
- 20.0
- 22.5
- 25.0
- 27.5

**anti (racemic)**

- Retention time: 11.836/238261
- 7.884/125960
- 12.121/43548
- 13.556/17313
- 18.158/23131

**93% ee; syn:anti = 32:1**

**9a**
0.0 2.5 5.0 7.5 10.0 12.5 15.0 17.5 20.0 22.5 min

0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 mAU

254nm, 2nm (1.00)

9.433/589776
11.117/609938
13.871/1242585
17.021/1246390

Ph
Cl
CH3
O
OH

syn (racemic)

Ph
Cl
CH3
O
OH

anti (racemic)

S53
90% ee; syn:anti = 24:1
Ph CH₃

O
OH

syn (racemic)

Ph

CH₃

O
OH

anti (racemic)

Ph

CH₃

O
OH

9d

93% ee; syn:anti = 21:1
97% ee; \textit{anti:syn} = 22:1
Ph \[\text{CH}_3\]

**syn** (racemic)

\[\begin{align*}
\text{O} & \quad \text{OH} \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}\]

\[\text{5}\]

Ph \[\text{CH}_3\]

**anti** (racemic)

\[\begin{align*}
\text{O} & \quad \text{OH} \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}\]

\[\text{5}\]

9f

96% ee; **syn**:**anti** = 23:1
Ph\[\text{CH}_3\]O\[\text{OH}\]
syn (racemic)

Ph\[\text{CH}_3\]O\[\text{OH}\]
anti (racemic)

$9g$
95% ee; $anti: syn = 49:1$
84% ee; syn:anti = 11:1
Ligand I:

Racemic

>99% ee; syn:anti = 4:1
>99% ee; syn:anti = 5:1
Ligand II:

Racemic

>99% ee; syn:anti = 4:1
Ligand III:

Racemic

$>99\% \text{ ee; syn:anti } = 4:1$
Ligand IV:

Racemic

>99% ee; syn:anti = 4:1

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

S

R

H₃C

O

N

O

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Ligand V:

Racemic

syn:anti = 4:1
Ligand VI:

**Racemic**

**Syn:anti > 1:1**
Ligand VII:

\[ \text{syn:anti} = 3:1 \]

Control Experiments without Metal*

\[ [I \ (x \ \text{mol}) + \text{Eu(OTf)}_3 \ (y \ \text{mol})] \]

EtOH/H\(_2\)O (0.4 mL, 9:1 v/v)

-25 °C, 168 h

<table>
<thead>
<tr>
<th>x:y yield (%)(^b)</th>
<th>syn:anti(^c)</th>
<th>ee (%) (syn)(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0:0</td>
<td>trace</td>
<td>nd(^d)</td>
</tr>
<tr>
<td>72:0</td>
<td>trace</td>
<td>nd(^d)</td>
</tr>
<tr>
<td>0:0.06</td>
<td>93</td>
<td>1:1 rac(^e)</td>
</tr>
</tbody>
</table>

\(^a\) Reaction conditions: To a mixture of I (x mol\%) and Eu(OTf)\(_3\) (y mol\%), which was stirred at 50 °C for 2 h then cooled to -25 °C, was added 7 (48.8 \(\mu\)mol, 1.5 equiv) and 8 (32.5 \(\mu\)mol, 1.0 equiv); \(^b\) isolated yields; \(^c\) determined by chiral HPLC analysis; \(^d\) not determined; \(^e\) racemic.