Supporting Information

The First Catalytic Asymmetric Addition of Dialkylzincs to α–Ketoesters

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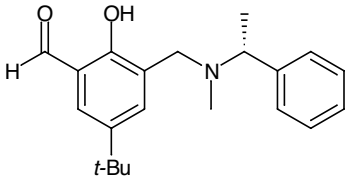
General Considerations. Unless otherwise noted, all non-aqueous reactions were carried out under an atmosphere of dry N_2 in dried glassware. All manipulations involving Et_2Zn were carried out using standard Schlenk techniques. When necessary, solvents and reagents were dried prior to use. Toluene and dioxane were distilled from Na. CH_2Cl_2 was de-oxygenated by purging with N_2 and then dried by passing through activated alumina. THF was distilled from Na/benzophenone ketyl. Ti(O*i*-Pr)$_4$ was distilled and stored as a 1.4 M solution in hexanes. Ti(O*t*-Bu)$_4$ was purchased from Acros and stored as a 1.4 M solution in hexanes. Titanium tetra[(*S*)-1-(4-methylphenyl)propoxide] was prepared as previously described[1] and used as a 1.0 M solution in hexanes. Et_2Zn was used as a freshly prepared 1.0 M solution in toluene. *n*-Bu_2Mg was used as a 1.0 M solution in heptane, purchased from Aldrich. (-)-(1*R*,2*R*)-1,2-Cyclohexanediamine and (+)-(1*S*,2*S*)-1,2-cyclohexanediamine were prepared as previously described.[2] Salen ligands for metal complexes **2**-5 and **7** were prepared as previously described (see references 9 and 10 in main text). The salen ligands for metal complexes **6**[3] and **10**[4] were prepared according to literature procedures.

Ethyl oxo(phenyl)acetate and methyl oxo(phenyl)acetate were purchased from Aldrich and distilled prior to use. Ethyl 2-oxopropanoate and ethyl 3-methyl-2-oxobutanoate were purchased from Acros and distilled prior to use. 4,4-Dimethyldihydrofuran-2,3-dione was purchased from Aldrich and used as a 0.5 M solution in toluene. Ethyl cyclohexyl(oxo)acetate,[5] *tert*-butyl oxo(phenyl)acetate,[6] ethyl (4-bromophenyl)(oxo)acetate,[5] ethyl (4-methoxyphenyl)(oxo)acetate,[5] and ethyl naphthyl(oxo)acetate[7] were prepared as previously described. Ethyl 3,3-dimethyl-2-oxobutanoate[8] was prepared from *tert*-butylmagnesium chloride and diethyl oxalate following a procedure similar to that described for ethyl cyclohexyl(oxo)acetate. Ethyl (2-methylphenyl)(oxo)acetate[9] was prepared from *o*-tolylmagnesium bromide and diethyl oxalate following a procedure similar to that described for the preparation of ethyl 2-naphthyl(oxo)acetate. Benzyl oxo(phenyl)acetate was prepared as described in a prior communication (see reference 9 in main text). All synthetic α-ketoesters were purified by distillation prior to use.

Analytical thin layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica-gel 60-F plates. Preparative thin layer chromatography was performed on EM Reagents 1.00 mm silica-gel plates. Visualization was accomplished with UV light. Chromatography on silica gel was performed using a forced flow of the indicated solvent system on EM Reagents Silica Gel 60 (230-400 mesh).[10] Conversions and enantiomeric excesses were measured using a Hewlett-Packard 5890 gas chromatograph (GC) with a Supelco β-DEX^{TM} 120 column (12 m x 0.25 mm) or a Waters 600 high performance liquid chromatography (HPLC) with UV detection at 254 nm and Daicel Chiralpak AD or OD columns (0.46 cm x 25 cm). ^{1}H NMR spectra were recorded on Bruker AM-500 (500 MHz) or AM-250 (250 MHz) spectrometers at ambient temperature. Chemical shifts are reported in ppm from the solvent resonance ($CDCl_3$ 7.26 ppm, CD_2Cl_2 5.30 ppm, DMSO-d_6 2.49 ppm, D_2O 4.80 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants, and number of protons. Proton decoupled ^{13}C NMR spectra were recorded on a Bruker AM-500 (125 MHz) spectrometer at ambient temperature.

Chemical shifts are reported in ppm from tetramethylsilane (0 ppm) or from the solvent resonance ($CDCl_3$ 77.36 ppm). Mass spectra were obtained on a low resonance Micromass Platform LC in electrospray mode and a high resonance VG autospec with an ionization mode of either CI or ES. IR spectra were taken on a Perkin-Elmer FT-IR spectrometer using a thin film on NaCl plates. Melting points were obtained on Thomas Scientific Unimelt apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer Polarimeter 341 with a sodium lamp and are reported as follows $[\alpha]^{T}_{\lambda}$, (*c* g/100 mL solvent).



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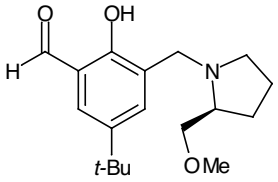

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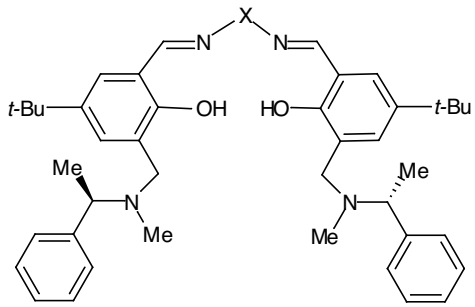
General procedure for the synthesis of (*R*)-15 and (*S*)-16. 3-Bromomethyl-5-*tert*-butyl-2-hydroxybenzaldehyde (see reference 10 in main text) (1.0 equiv) was dissolved in dry THF (5 mL) and the chiral amine (3.0 equiv) was added dropwise with the immediate formation of a precipitate in the case of **15** and a orange color in the case of **16**. After stirring for 30 min at room temperature, the slurry was filtered to remove the salt and the filtrate was concentrated. Purification with a short SiO_2 column or preparative TLC (30% EtOAc/hexanes) afforded (*R*)-**15** and (*S*)-**16**.

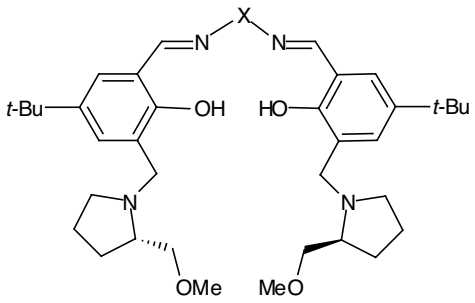
(*R*)-15. 100% yield, thick yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.8-11.1 (br s, 1H), 10.38 (s, 1H), 7.62 (d, *J* = 2.5 Hz, 1H), 7,40-7.26 (m, 6H), 3.80 (m, 2H), 3.62 (br m, 1H), 2.25 (s, 3H), 1.53 (d, *J* = 6.85 Hz, 3H), 1.28 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.0, 160.0, 142.1, 133.0, 129.0, 128.4, 128.1, 124.7, 124.2, 122.6, 116.5, 63.5, 57.3, 38.0, 34.5, 31.7, 18.1; IR(film) 3500-2500 (br), 2963, 2871, 1678, 1652, 1605, 1478, 1395, 1364 cm^{-1}; HRMS (ES) calcd *m*/*z* 326.2120 [$C_{21}H_{28}NO_2^+$], found *m*/*z* 326.2129.

(*S*)-16. 75% yield, thick orange oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.37 (s, 1H), 7.63 (d, *J* = 2.5 Hz, 1H), 7.30 (br s, 1H), 4.40 (d, *J* = 13.8 Hz, 1H), 3.55-3.48 (m, 4H), 3.47 (s, 3H), 3.06 (br s, 1H), 2.84 (br s, 1H), 2.35 (m, 1H), 2.02 (m, 1H), 1.80 (m, 1H), 1.71 (m, 1H), 1.29 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.0, 159.5, 142.2, 132.8, 132.5, 124.5, 122.4, 75.6, 64.0, 59.6, 57.8, 54.9, 34.5, 31.7, 28.4, 23.4; IR(film) 3500-2500 (br), 2959, 2871, 1678, 1604, 1478, 1395, 1363 cm^{-1}; HRMS (ES) calcd *m*/*z* 326.2069 [$C_{18}H_{28}NO_3^+$], found *m*/*z* 306.2065.



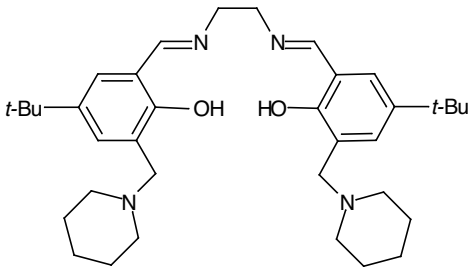
8a: X = from
(-)- (1*R*,2*R*)-1,2-cyclohexanediamine

8b: X = from
(+)- (1*S*,2*S*)-1,2-cyclohexanediamine



9a: X = from
(-)- (1*R*,2*R*)-1,2-cyclohexanediamine

9b: X = from
(+)- (1*S*,2*S*)-1,2-cyclohexanediamine



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General procedure for the synthesis of salens 8a-b, 9a-b and 11. The aldehyde (2.0 equiv) was dissolved in EtOH and 1,2-cyclohexanediamine (1.0 equiv) was added. The mixture was stirred for 24 h at room temperature, then concentrated. The salen was then taken up in CH_2Cl_2 and dried over Na_2SO_4. Filtration and reconcentration, followed by drying with gentle heat in vacuo for several hours afforded the salens in 100% yield as powdery, free-flowing solids.

8a. Yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 13.4 (br s, 2H), 8.26 (s, 2H), 7.47 (br s, 2H), 7.44-7.05 (m, 12H), 7.01 (br s, 2H), 3.73-3.70 (br m, 2H), 3.56 (d, *J* = 14 Hz, 2H), 3.47 (d, *J* = 14 Hz, 2H), 3.27 (br m, 2H), 2.16 (s, 6H), 1.88 (br m, 5H), 1.52 (br m, 3H), 1.43 (d, *J* = 6.8 Hz, 6H), 1.22 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C) δ = 165.4, 157.4, 144.3, 141.0, 130.5, 128.5, 128.2, 127.1, 126.6, 118.1, 73.1, 63.5, 52.5, 38.9, 34.3, 33.7, 31.8, 24.6, 18.3; IR(film) 2962, 2860, 2784, 1629, 1599, 1478, 1467, 1451 cm^{-1}; HRMS (ES) calcd *m*/*z* 751.4927 [$C_{48}H_{64}N_4O_2Na^+$], found *m*/*z* 751.4960.

8b. Yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 13.4 (br s, 2H), 8.26 (s, 2H), 7.44-7.20 (m, 14H), 7.01 (br s, 2H), 3.81-3.70 (m, 2H), 3.65 (d, *J* = 14 Hz, 2H), 3.39 (d, *J* = 14 Hz, 2H), 3.28 (br m, 2H), 2.15 (s, 6H), 1.87 (br m, 5H), 1.68 (br m, 3H), 1.45 (d, *J* = 6.8 Hz, 6H), 1.23 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C) δ = 165.3, 157.4, 144.3, 141.0, 130.6, 128.5, 128.2, 127.1, 126.6, 118.1, 73.1, 63.5, 52.4, 38.9, 34.3, 33.7, 31.8, 24.6, 18.2; IR(film) 2962, 2861, 1680, 1629, 1471, 1362 cm^{-1}; HRMS (ES) calcd *m*/*z* 729.5107 [$C_{48}H_{65}N_4O_2^+$], found *m*/*z* 729.5095.

9a. Yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 13.3 (br s, 2H), 8.27 (s, 2H), 7.34 (br s, 2H), 7.05 (br s, 2H), 4.08 (br d, *J* = 12.2 Hz, 2H), 3.48 (br m, 4H), 3.36 (s, 6H), 3.34 (br s, 4H), 3.0 (br s, 2H), 2.74 (br s, 2H), 2.27 (br s, 2H), 1.88 (m, 7H), 1.67 (m, 9H), 1.45 (m, 3H), 1.24 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C) δ = 165.2, 142.5, 141.2, 131.2, 124.0, 121.8, 118.3, 73.0, 59.5, 58.9, 54.9, 34.8, 33.7, 31.7, 31.6, 28.2, 24.6, 23.5, 18.8; IR(film) 2956, 2868, 1629, 1470, 1362 cm^{-1}; HRMS (ES) calcd *m*/*z* 689.5006 [$C_{42}H_{65}N_4O_2^+$], found *m*/*z* 689.4984.

9b. Yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 13.7-13.1 (br s, 2H), 8.30 (s, 2H), 7.35 (br s, 2H), 7.08 (br s, 2H), 4.02 (br s, 2H), 3.58-3.20 (br m, 12H), 3.00 (br s, 2H), 2.75 (br s, 2H), 2.28 (br s, 2H), 1.93-1.40 (br m, 18H), 1.26 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C) δ = 165.3, 157.3, 140.7, 131.0, 127.0, 126.0, 118.0, 76.4, 72.9, 63.4, 59.3, 54.8, 53.2, 34.1, 33.6, 31.7, 28.9, 24.5, 23.1; IR(film) 2957, 2866, 2812, 1629, 1469, 1362 cm^{-1}; HRMS (ES) calcd *m*/*z* 689.5006 [$C_{42}H_{65}N_4O_2^+$], found *m*/*z* 689.5024.

11. Yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ = 14.4-12.2 (br s, 2H), 8.42 (s, 2H), 7.47 (br s, 2H), 7.24 (br s, 2H), 3.92 (s, 4H), 3.71 (br m, 4H), 2.53 (br m, 8H), 1.67-1.33 (br m, 14H), 1.30 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C) δ = 166.2, 157.6, 141.1, 133.0, 126.5, 118.0, 60.3, 57.5, 54.5, 34.2, 31.7, 26.0, 24.4; IR(film) 3418 (br),2936, 2856, 2792, 1632, 1467, 1362 cm^{-1}; HRMS (ES) calcd *m*/*z* 597.4144 [$C_{36}H_{54}N_4O_2Na^+$], found *m*/*z* 597.4127.

Treatment of Ethyl α–Ketoesters with EtMgBr: Formation of the α-Hydroxyester Addition/Reduction Products. Mixtures of the addition and reduction standards were prepared by reaction of the α-ketoester (1 equiv) with ethylmagnesium bromide (1 equiv) in THF at -10 °C for 1 h. (Table S1). Racemic samples of the pure α-hydroxyester reduction products were prepared by reaction of the α-ketoester (1 equiv) with the $NaBH_4$ (1 equiv) in EtOH at 0 °C for 45 min-1 h.

Table S1. Addition of EtMgBr to α–ethyl ketoesters (eq 1, M = MgBr, n = 1, R^4 = Et).

Entry	R^3	Reduction Conv. (%)[a]	Addition Conv. (%)[a]
1	*p*-MeO-C_6H_4	16	81
2	*p*-Br-C_6H_4	22	69
3	Ph	19	60
4	*o*-Me-C_6H_4	19	38
5	β-naphthyl	30	37
6	Me	52	38
7	Cy	54	31
8	*i*-Pr	48	21
9	*t*-Bu	63	21

[a]Determined by ^{1}H NMR spectroscopy.

General Procedure for Formation of the Metal Salen Complexes. The salen (0.030 mmol) was introduced into a dry Schlenk flask, and the system purged with N_2. The salen was dissolved in dry toluene (1 mL) and Ti(O*i*-Pr)$_4$[11] (18 μL, 1.4 M in heptanes, 0.025 mmol) was added. After stirring at room temperature for 1 h the toluene, heptanes and *i*-PrOH were removed in vacuo (removal of the *i*-PrOH was found to increase reactivity and selectivity). Fresh toluene (1 mL) was added to provide the catalyst solution which was used in the α-ketoester additions as described below. Care must be taken to avoid the introduction of water into this titanium catalyst solution as lower reactivity and selectivity results.

The other catalyst derivatives were prepared in the same manner using the following reagents: Ti(O*t*-Bu)$_2$ catalyst from Ti(O*t*-Bu)$_4$; Al(O*i*-Pr) catalyst from Al(O*i*-Pr)$_3$[12]; V(O)(O*i*-Pr) catalyst from V(O)(O*i*-Pr)$_3$[13]; Zr(O*i*-Pr)$_2$ catalyst from Zr(O*i*-Pr)$_4$·*i*-PrOH[14]. The Zn and Mg catalysts were made

from Et_2Zn[15] and *n*-Bu_2Mg[16], respectively. For these last two catalysts, it is possible to forgo the solvent removal step as no *i*-PrOH is generated during the catalyst formation.

General Procedure for the Addition of Diethylzinc to α–Ketoesters. The catalyst solution (see above) was cooled to -40 °C and Et_2Zn (305 μL, 1.0 M in toluene, 0.305 mmol) was added slowly. After 5-30 min, the α-ketoester (0.25 mmol) was added dropwise. At various intervals, 100 μL aliquots were removed from the reaction, quenched with saturated NH_4Cl, and then extracted with pentane.

The reaction progress was monitored by GC (Carrier gas: N_2; Detector: FID, 270 °C; Injector: 250 °C; Pressure: 5-7 psi). GC oven temperatures and retention times for the α-ketoesters and their corresponding α-hydroxyester addition and reduction products are listed below. Since GC and ^1H NMR integrations from the reaction mixtures were generally in agreement, percent conversion was calculated using unadjusted GC peak areas.

Where isolated yields are reported, the reaction was run for 2 h at -40 °C then quenched with saturated NH_4Cl and extracted with CH_2Cl_2. The extracts were dried over Na_2SO_4, and concentrated. Purification by preparative TLC on SiO_2 (30% EtOAc/hexanes) or flash chromatography on SiO_2 (10% EtOAC/hexanes) afforded methyl 2-hydroxy-2-phenylbutanoate and ethyl 2-hydroxy-2-phenylbutanoate as pale yellow oils. The ^1H and ^{13}C NMR spectra of these compounds were identical to those reported.[17] Absolute configurations were determined by optical rotation and comparison to the reported values.[18]

GC oven temperatures and retention times for the α-ketoesters, addition products and reduction products are listed below.

Methyl oxo(phenyl)acetate t = 19.4 min; **methyl 2-hydroxy-2-phenylbutanoate**[12] t_R = 30.8 min, t_S = 34.0 min; **methyl hydroxy(phenyl)acetate**[19] t_1 = 34.8 min, t_2 = 42.7 min; oven = 100 °C.

Ethyl oxo(phenyl)acetate t = 28.5 min; **ethyl 2-hydroxy-2-phenylbutanoate**[17] t_R = 36.9 min, t_S = 39.8 min; **ethyl hydroxy(phenyl)acetate**[19] t = 42.5 min; oven = 100 °C.

***tert*-Butyl oxo(phenyl)acetate** t = 59.1 min; ***tert*-butyl 2-hydroxy-2-phenylbutanoate**[20] t_1= 65.3 min, t_2 = 67.8 min; ***tert*-butyl hydroxy(phenyl)acetate** [21] t_1 = 74.1 min, t_2 = 86.7 min; oven = 90 °C.

Ethyl (4-methoxyphenyl)(oxo)acetate t = 47.4 min; **ethyl 2-hydroxy-2-(4-methoxyphenyl)-butanoate**[22] t_1 = 39.7 min, t_2 = 41.3 min; **ethyl hydroxy(4-methoxyphenyl)acetate** [23] t_1 = 41.4 min, t_2 = 42.9 min; oven = 130 °C.

Ethyl (4-bromophenyl)(oxo)acetate t = 24.2 min; **ethyl 2-(4-bromophenyl)-2-hydroxybutanoate**[24] t_1 = 31.0 min, t_2 = 32.4 min; **ethyl (4-bromophenyl)(hydroxy)acetate**[25] t_1 = 44.7 min, t_2 = 48.4 min; oven = 135 °C.

Ethyl 2-naphthyl(oxo)acetate t = 70.2 min; **ethyl 2-hydroxy-2-(2-naphthyl)butanoate**[26] t_1 = 76.7 min, t_2 = 78.8 min; **ethyl hydroxy(2-naphthyl)acetate**[23] t_1 = 81.4 min, t_2 = 82.0 min; oven = 145 °C.

Ethyl cyclohexyl(oxo)acetate t = 18.9 min; **ethyl 2-cyclohexyl-2-hydroxybutanoate**[27] t_1= 28.9 min, t_2 = 32.7 min; **ethyl cyclohexyl(hydroxy)acetate**[5] t_1 = 25.6 min, t_2 = 26.2 min; oven = 100 °C.

Ethyl 3,3-dimethyl-2-oxobutanoate t = 8.4 min; **ethyl 2-ethyl-2-hydroxy-3,3-dimethyl-butyrate**[28] t_1 = 30.9 min, t_2 = 42.7 min; **ethyl 2-hydroxy-3,3-dimethylbutanoate**[29] t_1 = 5.3 min, t_2 = 7.1 min; oven = 60 °C.

Ethyl 3-methyl-2-oxobutanoate t = 14.5 min; **ethyl 2-ethyl-2-hydroxy-3-methylbutanoate**[30] t_1 = 36.5 min, t_2 = 40.3 min; **ethyl 2-hydroxy-3-methylbutanoate**[31] t_1 = 26.7 min, t_2 = 27.5 min; oven[32]

Ethyl (2-methylphenyl)(oxo)acetate t = 25.8 min; **ethyl 2-hydroxy-2-(2-methylphenyl)butanoate**[33] t = 44.4 min; **ethyl hydroxy(2-methylphenyl)acetate** [34] t_1 = 36.8 min, t_2 = 38.5 min; oven = 110 °C. Enantiomeric excess measured by HPLC (OD hexanes, 0.5 mL/min) after conversion to the trifluoroacetylated derivative (**ethyl 2-(2-methylphenyl)-2-[trifluoroacetyl)oxy]butanoate**) t_1 = 19.2 min, t_2 = 23.9 min.

Ethyl 2-oxopropanoate t = 4.7 min; **ethyl 2-hydroxy-2-methylbutanoate**[35] t = 15.0 min; **ethyl 2-hydroxypropanoate**[36] t_1 = 8.2 min, t_2 = 9.8 min; oven = 50 °C. The ee was measured on the acetylated derivative (**ethyl 2-acetoxybutanoate**) t_1 = 11.7, t_2 = 13.4 min; oven = 40 °C.

Benzyl oxo(phenyl)acetate t = 8.3 min; **benzyl 2-hydroxy-2-phenylbutanoate**[37] t_1 = 8.9 min, t_2 = 11.7 min; **benzyl hydroxy(phenyl)acetate**[38] t_1 = 12.7 min, t_2 = 14.9 min; Conversion measured by ^{1}H NMR. Enantiomeric excess measured by HPLC (AD 10% *i*-PrOH/hexane, 1.0 mL/min).

3-Ethyl-3-hydroxy-4,4-dimethyldihydrofuran-2(3*H*)-one[39] Conversion measured by 1H NMR. Ee measured on the benzoylated derivative (**3-ethyl-4,4-dimethyl-2-oxotetrahydrofuran-3-yl benzoate**)[40] by HPLC (OD 10% iPrOH/hexane, 0.5 mL/min) t_1 = 12.4 min, t_2 = 14.4 min.

Ethyl oxo(phenyl)acetate t = 31.9 min; **ethyl 2-hydroxy-2-phenylpropanoate**[41] t_1 = 48.7 min, t_2 = 50.0 min; oven = 90 °C.

Enrichment of the $PhCOCO_2Me/Et_2Zn$ Adduct by Recrystallization. A portion (600 mg, 3.14 mmol, 78% ee) of the isolated adduct from a reaction employing 5 mmol of $PhCOCO_2Me$ and 5 mol% of **2** with 1.2 equiv of Et_2Zn was treated with ethanolic KOH to provide the α-hydroxy acid (**10**) in quantitative yield. This material was recrystallized four times from CCl_4 to provide 72% of the α-hydroxy acid (400 mg, 2.26 mmol). A portion of this material was treated with diazomethane to provide the corresponding methyl ester (98% ee) which was analyzed by GC as described above.

Nonlinear Effects Study. These experiments were done at -78 °C due to technical difficulties at -40 °C. When the reaction from Table 3, entry 9 was performed at -78 °C, 96% conversion and 74% ee (*R*) were observed after 2 h. Two different procedures were employed for the nonlinear studies. In the first, (**A**), catalyst solutions made separately from the (*S,S*)- and (*R,R*)-salens were combined in the appropriate proportions to provide the catalyst solution of the indicated catalyst enantiomeric excess. In the second, (**B**), catalyst solutions made separately from the racemic and (*R,R*)-salens were combined in the appropriate proportions to provide the catalyst solution of the indicated catalyst enantiomeric excess. The results from both trials were similar (see Figures S1 and S2 below) indicating that the catalyst species were equilibrating to the same starting point under the reaction conditions. For example, an unreactive species was not irreversibly formed from the racemic salen upon treatment with titanium to form the catalyst.

A. (*R,R*)-Cyclohexanediamine piperidine salen, (*R,R*)-**1** (85 mg, 0.136 mmol), was dissolved in toluene (1 mL) in a 10 mL Schlenk flask in an inert atmospheres glove box. Neat Ti(O*i*-Pr)$_4$ was added (40.6 μL, 0.136 mmol) and the solution was allowed to stir for 1 h. The toluene and *i*-PrOH were then removed in vacuo and the dry catalyst was redissolved in fresh toluene (0.54 mL) to make a 0.25 M solution of (*R,R*)-**2**. This procedure was simultaneously performed using the (*S,S*)-cyclohexanediamine piperidine salen, (*S,S*)-**1**, to make a 0.25 M solution of (*S,S*)-**2**. The subsequent ketoester alkylation reactions were performed simultaneously in flame dried, N_2 purged test-tubes. The test-tubes were each charged with a total volume of 100 μL (0.025 mmol) of these freshly prepared catalyst solutions as outlined in Table S2.

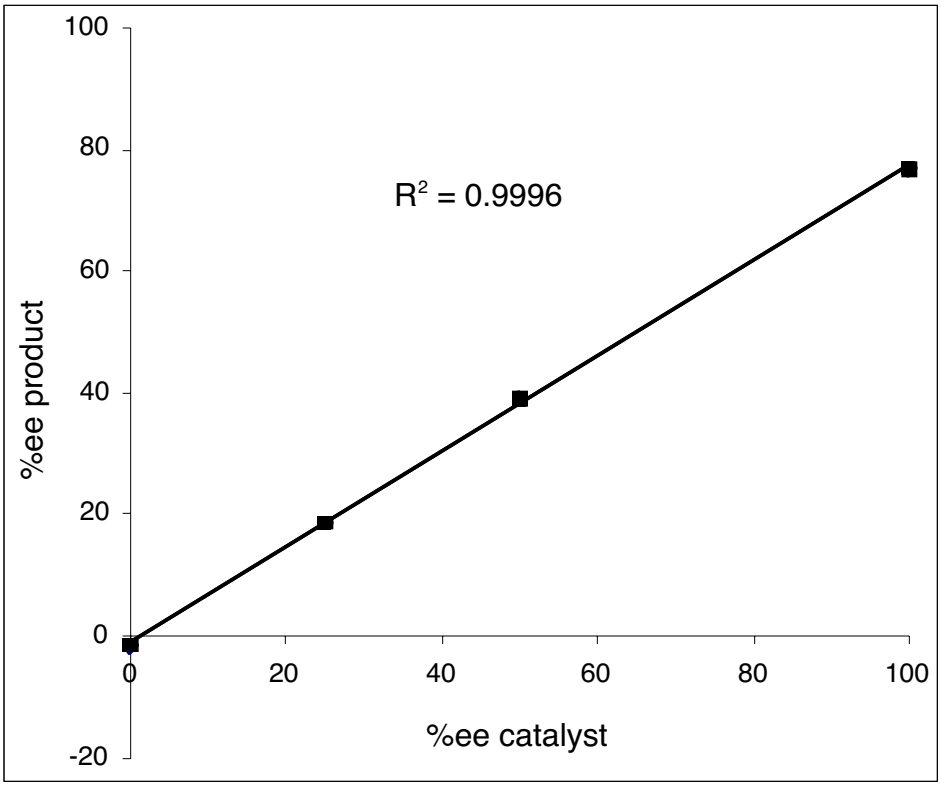
Additional toluene (0.9 mL) was added to each test-tube and the tubes were removed from the glove box. After cooling to -78 °C, Et_2Zn (300 μL of a 1.0 M soln. in hexanes, 0.3 mmol) was slowly added to each test tube. After stirring for 30 min, methyl oxo(phenyl)acetate (35.5 μL, 0.25 mmol) was added dropwise to each tube. After 2 h, the reactions were quenched by injection of 1.5 mL cold water. After extraction with pentane, the crude reaction mixtures were analyzed by GC (see Table S2) as described in the General Procedure above.

Table S2. Nonlinear effect study (method A) using (*S,S*)-**2** and (*R,R*)-**2** catalyst solutions in the addition of Et_2Zn to $PhCOCO_2Me$.

Tube	μL (*S,S*)-**2** solution	μL (*R,R*)-**2** solution	catalyst %ee in (*S,S*)-**2**	addition product[a] % ee
1	50	50	0	1.6 (*R*)[b]
2	62.5	37.5	25	18.7 (*S*)
3	75	25	50	39.0 (*S*)
4	0	100	100	76.8 (*S*)

[a] No reduction product was observed. [b]The non-zero reading arises from a small amount of error in volumes of the catalyst solutions combined or in the GC assay.

Figure S1. Nonlinear effect study (method A) using (*S,S*)-**2** and (*R,R*)-**2** catalyst solutions in the addition of Et_2Zn to $PhCOCO_2Me$.



B. (*R,R*)-Cyclohexanediamine piperidine salen, (*R,R*)-**1** (100 mg, 0.16 mmol) was dissolved in toluene (1 mL) in a 10 mL Schlenk flask in an inert atmospheres glove box. Neat Ti(O*i*-Pr)$_4$ (48 μL, 0.16 mmol) was then added and the solution was allowed to stir for 1 h. The toluene and *i*-PrOH were then removed in vacuo and the dry catalyst was redissolved in fresh toluene (1.94 mL) to make a 0.083 M solution of (*R,R*)-**2**. This procedure was simultaneously performed using racemic cyclohexanediamine piperidine salen , (+/-)-**1**, to make a 0.083 M solution of (+/-)-**2**. This racemic solution was slightly cloudy. The ketoester alkylation reactions were performed simultaneously in flame dried, N_2 purged test-tubes. The test-tubes were each charged with a total volume of 300 μL (0.025 mmol) of freshly prepared catalyst solutions as outlined in Table S3.

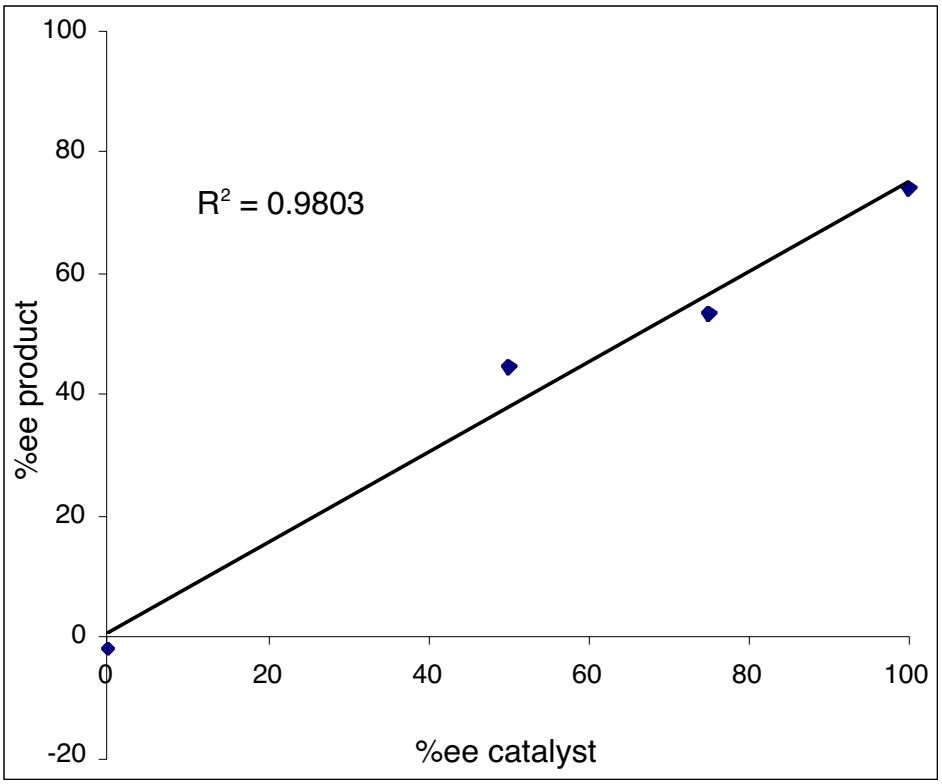
Toluene (0.7 mL) was then added to each test-tube and the tubes were removed from the glove box. After cooling to -78 °C, Et_2Zn (300 μL of a 1.0 M soln. in hexanes, 0.3 mmol) was slowly added to each test tube. After stirring for 30 min, methyl oxo(phenyl)acetate (35.5 μL, 0.25 mmol) was added dropwise to each tube. After 2 h, the reactions were quenched by injection of 1.5 mL cold water. After extraction with pentane, the crude reaction mixtures were analyzed by GC (see Table S3) as described in the General Procedure above.

Table S3. Nonlinear effect study (method B) using rac-**2** and (*R,R*)-**2** catalyst solutions in the addition of Et_2Zn to $PhCOCO_2Me$.

Tube	μL (+/-)-**2** solution	μL (*R,R*)-**2** solution	catalyst %ee in (*R,R*)-**2**	addition product[a] % ee
1	300	0	0	1.8 (*S*)[b]
2	150	150	50	44.6 (*R*)
3	75	225	75	53.5 (*R*)
4	0	300	100	75.8 (*R*)

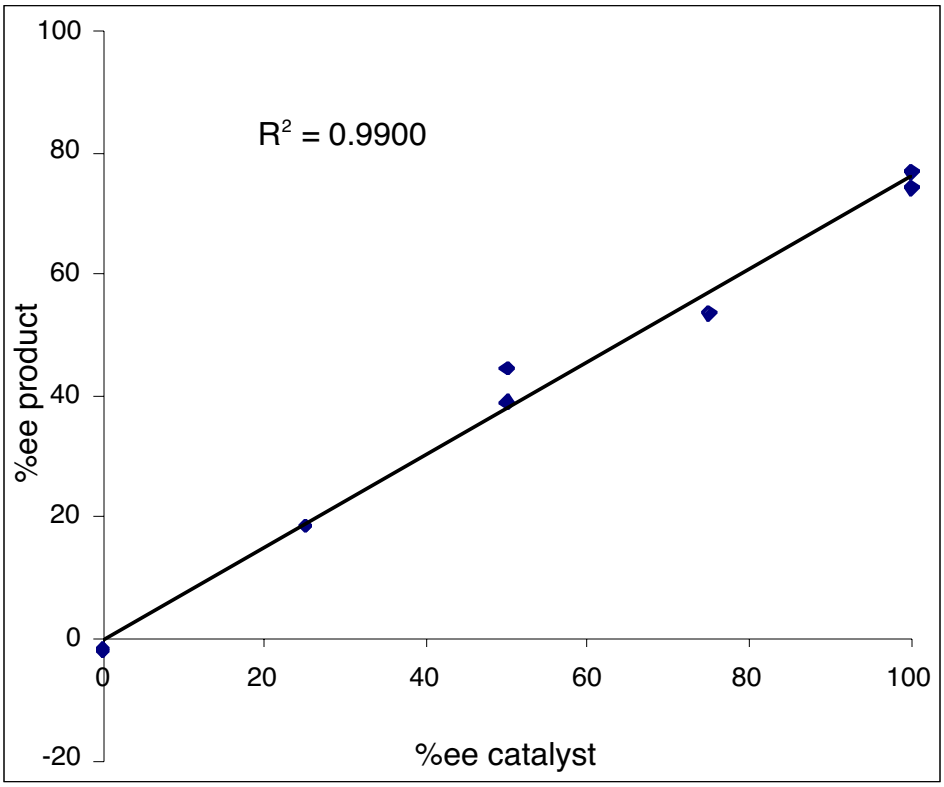
[a] No reduction product was observed. [b]The non-zero reading with catalyst from racemic salen arises from a small amount of error in the GC assay.

Figure S2. Nonlinear effect study (method B) using rac-**2** and (*R,R*)-**2** catalyst solutions in the addition of Et_2Zn to $PhCOCO_2Me$.



A plot combining the catalyst ee vs product ee results from methods A and B is shown in below in Figure S3. The reaction is characterized by the absence of a nonlinear effect, which is somewhat unusual for titanium containing catalysts.[42]

Figure S3. Nonlinear effect study combining the results from methods A and B.



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(26) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.10 (s, 1H), 7.83 (m. 3H), 7.48 (m, 3H), 4.31-4.15 (m, 2H), 2.33 (dq, *J* = 14.2, 7.1 Hz, 1H), 2.14 (dq, *J* = 14.2, 7.1 Hz,1H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.3 Hz, 3H).

(27) Mallinckrodt Chem. Works US Patent 2349796, **1942**.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 4.3 (q, *J* = 7.2 Hz, 2H), 3.2 (br s, 1H), 1.77 (dq, *J* = 14.8, 7.4 Hz, 1H), 1.66 (dq, *J* = 14.8, 7.4 Hz, 1H), 1.36 (t, *J* = 7.2 Hz, 3H), 1.34-1.10 (m, 11H), 0.82 (t, *J* = 7.4 Hz, 3H).

(28) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 4.2 (q, *J* = 7.2 Hz, 2H), 3.3 (br s, 1H), 1.9 (q, *J* =7.3 Hz, 1H), 1.65 (q, *J* = 7.3 Hz, 1H), 1.34 (t, *J* = 7.2 Hz, 3H), 1.1 (s, 9H), 0.80 (t, *J* = 7.3 Hz, 3H).

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(32) HP 6890 GC; Supelco β-DEX™ 120 (30 m x 0.25 mm); pressure = 12.7 psi; flow = 1.0 mL/min

(33) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.45-7.05 (m, 4H), 4.29-4.15 (m, 2H), 2.36 (s, 3H), 2.24 (m, 2H), 1.23 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.3 Hz, 3H).

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^{1}H NMR (500 MHz, $CDCl_3$) δ = 4.23 (q, *J* = 5.6 Hz, 2H), 1.85 (q, *J* = 6.6 Hz, 1H), 1.65 (q, *J* = 6.6 Hz, 1H), 1.39 (s, 3H), 1.30 (t, *J* = 6.5 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H).

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(40) ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 8.09 (d, *J* = 8.1 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 4.04 (d, *J* = 8.8 Hz, 1H), 3.95 (d, *J* = 8.8 Hz, 1H), 2.53 (sextet, *J* = 7.4 Hz, 1H), 1.87 (sextet, *J* = 7.4 Hz, 1H), 1.37 (s, 3H), 1.16 (s, 3H), 1.07 (t, *J* = 7.4 Hz, 3H).

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