Josiphos-Catalyzed Asymmetric Homodimerization of Ketoketenes

Supporting Information

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General Information.

All reactions were carried out in flame-dried glassware under a nitrogen atmosphere using standard inert atmosphere techniques unless otherwise stated. Diethyl ether and THF were dried using sodium/benzophenone stills, CH$_2$Cl$_2$ and toluene were dried using calcium hydride stills, methanol was dried using a magnesium methoxide still, and $N,N$-dimethylethylamine was distilled from potassium hydroxide under nitrogen.$^1$ ($R$)-1-[(S)$_p$-2-(Diphenylphosphino)ferrocenyl]-ethylidicyclohexyl phosphine, ($S$)-1-[(R)$_p$-2-(diphenylphosphino)ferrocenyl]ethylidicyclohexyl phosphine, ($S$)-1-[(R)$_p$-2-[bis[3,5-bis(trifluoromethyl)phenyl]phosphino]ferrocenyl]ethylidicyclohexylphosphine, ($R$)-1-[(S)$_p$-2-[bis[3,5-bis-(trifluoromethyl)phenyl]phosphino]ferrocenyl]ethylidicyclohexylphosphine were purchased from Aldrich Chemical Co. and Strem Chemicals and used as received. ($R$)-BINAPHANE, tri-$n$-butyl phosphine, lithium iodide, $n$-butyllithium (2.5 M in hexane), and LiAlH$_4$ (1.0M in Et$_2$O) were purchased from Aldrich Chemical Co. and used as received. Iatrobeads (Bioscan, 6RS-8060, 60µM particle size) and TLC plates (Sorbent Technologies, UV254, 250µM) were used as received. Methylphenylketene, methyl-4-tolylketene, methyl-2-tolylketene, methyl-2-chlorophenylketene, ethylphenylketene, ethyl-4-chlorophenylketene, ethyl(3-thiophenyl)ketene, $n$-butylphenylketene, cyclohexylmethylketene, cyclohexylethylketene, and dimethylketene were prepared according to literature procedures.$^2,5$

NMR spectra were recorded on a Bruker DPX Avance 200 spectrometer (200 MHz for $^1$H and 50 MHz for $^{13}$C) and on a Bruker Biospin AG 400 spectrometer (400 MHz for $^1$H and 100 MHz for $^{13}$C). NMR chemical shifts were reported relative to TMS (0 ppm) for $^1$H and to CDCl$_3$ (77.23 ppm) for $^{13}$C spectra. IR spectra were recorded on a Bio Rad FTS-175C spectrometer. Optical rotations were measured on a Rudolph DigiPol 781 TDV automatic polarimeter.

Low resolution mass spectra were recorded on a GC-MS Hewlett Packard HP 6890 GC instrument with a 5973 mass selective detector. High resolution mass spectra were obtained from the College of Sciences Major Instrumentation Cluster at Old Dominion University.

Analytical high performance liquid chromatography (HPLC) was performed using a Daicel Chiralpak AD column (0.46 cm x 25 cm), a Daicel Chiralpak AS-H column (0.46 cm x 25 cm) and a Daicel Chiralcel OD-H column (0.46 cm x 25 cm) (Daicel Chemical Ind., Ltd.) on a Perkin Elmer 235C instrument attached with diode array detector (deuterium lamp, 190-600 nm) with HPLC-grade isopropanol and hexanes as the eluting solvents.
Determination of Enantiomeric Excesses, Dimer: Trimer Ratios (Table 1) and Z: E Olefin Ratios:6-7

Enantiomeric excesses were determined by assaying the β-lactones 2a-h using chiral HPLC analysis (at λ = 254 or 225 nm; details given for each compound). Authentic racemic samples for chiral HPLC analysis were generated through the PBu3-catalyzed reaction.6 The absolute configurations of 2a, 2b, 2d, and 2e were assigned on the basis of a comparison of specific rotation values with literature values.7 The absolute configurations of 2c and 2f-2h were assigned by analogy. The Dimer: Trimer Ratios (Table 1) were determined for the crude products by 1H NMR analysis or by comparing the peak areas of GC-MS data. The major diastereomer of 2a, 2b, 2d, and 2e was determined to be the Z-isomer through comparison with literature spectroscopic data.7 Z-geometry was assigned to 2c and 2f-2h by analogy. The Z:E olefin ratio for 2a-2h was determined to be >97:3 by GC-MS analysis of the crude β-lactones.

Method A for dimerization of methyl substituted ketoketenes:
Ketoketene (0.34 mmol, 1.0 equiv) was dissolved in CH₂Cl₂ (2.2 mL) in a 25 mL round bottomed flask and cooled to −25 °C. (S)-1-{[(R)p]-2-[Bis[3,5-bis(trifluoromethyl)phenyl]phosphino]ferrocenyl}ethyldicyclohexylphosphine or (R)-1-{(S)p}-2-[bis[3,5-bis(trifluoromethyl)phenyl]phosphino]ferrocenyl]ethyldicyclohexylphosphine 4e (0.03 mmol, 0.1 equiv) was dissolved in CH₂Cl₂ (0.5 mL) in a 5 mL round bottomed flask, and was then transferred via syringe to the flask containing the ketoketene solution. The resulting solution (0.125 M of ketoketene in solvent) was stirred for 24 h at −25 °C before being briefly warmed to room temperature. The reaction was then quenched by the addition of aqueous H₂O₂ solution (50%, 2 drops) at room temperature. After stirring for 10 min at room temperature, the solvent was removed under reduced pressure. The crude product was dissolved in 10% EtOAc/hexane (5 mL) and dichloromethane (1 mL). The resulting solution was passed through a plug column of neutral silica (iatrobeads, 2 × 2 cm, 4 g) [50 x weight of reaction mixture]. The plug column was eluted with 10% EtOAc/hexane solvent system (100 mL), and the solvent was removed under vacuum to furnish the desired ketoketene dimer with ≥95% purity in most cases (as determined by GC-MS and ¹H NMR analysis). Further purification was carried out in some cases as specified below.

Method B for dimerization of ketoketenes:
Ketoketene (0.31 mmol, 1.0 equiv) was dissolved in CH₂Cl₂ (1 mL) in a 25 mL round bottomed flask and cooled to −25 °C. (R)-1-{(S)p}-2-(Diphenylphosphino)ferrocenyl]ethyldicyclohexylphosphine or (S)-1-{(R)p}-2-(diphenylphosphino)ferrocenyl]ethyldicyclohexylphosphine 4b (0.03 mmol, 0.1 equiv) was dissolved in CH₂Cl₂ (0.35 mL) in a 5 mL round bottomed flask, cooled to −25 °C in most cases (exceptions: formation of 2h and 5j), and was then transferred via syringe to the flask containing the ketoketene solution. The resulting solution (0.25 M of ketoketene in solvent) was stirred for 24 h at −25 °C before being briefly warmed to room temperature. The reaction was then quenched by the addition of aqueous H₂O₂ solution (50%, 2 drops) at room temperature. After stirring for 10 min at room temperature, the solvent was removed under reduced pressure. The crude product was dissolved in 10% EtOAc/hexane (5 mL) and dichloromethane (1 mL). The resulting solution was passed through a plug column of neutral silica (iatrobeads, 2 × 2 cm, 4 g) [50 x weight of reaction mixture]. The plug column was eluted with 10% EtOAc/hexane solvent system (100 mL), and the solvent was
removed under vacuum to furnish the desired ketoketene dimer with $\geq 95\%$ purity in most cases (as determined by GC-MS and $^1$H NMR analysis). Further purification was carried out in some cases as specified below.

**Method C for dimerization of ketoketenes:**
Ketoketene (0.34 mmol, 1.0 equiv) was dissolved in CH$_2$Cl$_2$ (0.35 mL) in a 25 mL round bottomed flask and was cooled to $-78\, ^\circ C$. (R)-BINAPHANE 3 (0.03 mmol, 0.1 equiv) was dissolved in CH$_2$Cl$_2$ (0.35 mL) in a 5 mL round bottomed flask, and cooled to $-78\, ^\circ C$. The phosphepine solution was then transferred via syringe to the flask containing the ketoketene solution. The reaction was stirred at $-78\, ^\circ C$ for 48 h, after which the solvent was removed under reduced pressure. The crude product was treated with dry isopropanol (3 mL) to dissolve the crude ketoketene dimer and precipitate the phosphine. The mixture was filtered under nitrogen using a Schlenk filter funnel. The precipitate was washed with dry isopropanol (2 $\times$ 3 mL), the phosphine was recovered, and the solvent was removed from the filtrate under reduced pressure. The crude product was then dissolved in 5% EtOAc/hexane (6 mL) and CH$_2$Cl$_2$ (1.5 mL), before being passed through a plug of neutral silica (3.3 g). Elution with 5% EtOAc/hexane (60 mL), followed by solvent removal under reduced pressure furnished the desired ketoketene dimer with $\geq 95\%$ purity in most cases (as determined by GC-MS and $^1$H NMR analysis). Further purification was carried out in some cases as specified below.
(S,Z)-3-methyl-3-phenyl-4-(1-phenyl-ethyldene)-oxetan-2-one ((−)-2a): (Method A)
To a cooled solution of methylphenylketene (510 mg, 3.85 mmol) in CH₂Cl₂ (28 mL) was added a solution of (S)-1-{(Rp)-2-[bis[3,5-bis(trifluoromethyl)phenyl]phosphino]ferroceny1}ethyldicyclohexylphosphine (333 mg, 0.39 mmol) in CH₂Cl₂ (3 mL). (−)-2a was isolated as a colorless oil (331 mg, 65%); HPLC analysis: 94% ee [Daicel Chiralpak AD column; 1 mL/min; solvent system: 2% isopropanol in hexane; retention times: 5.0 min (minor), 6.6 min (major)]; [α]D₁₇ = −68.3 (c = 0.41, CHCl₃); IR (thin film) 1881, 1844, 1699, 1140 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 7.50-7.10 (m, 10H), 1.90 (s, 3H), 1.85 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 171.3, 146.9, 136.2, 135.2, 129.3, 128.6, 128.6, 127.6, 127.4, 126.2, 108.6, 64.4, 19.6, 15.5; MS (EI 70 eV): m/z 264, 132, 104, 78; (M⁺ + Na) HRMS m/z calcd for C₁₈H₁₆O₂Na: 287.1043; found: 287.1039.

(R,Z)-3-methyl-3-phenyl-4-(1-phenyl-ethyldene)-oxetan-2-one ((+)-2a): (Method A)
To a cooled solution of methylphenylketene (70 mg, 0.53 mmol) in CH₂Cl₂, was added a cooled (−25 °C) solution of (R)-1-{(Sp)-2-[bis[3,5-bis(trifluoromethyl)phenyl]phosphino]ferroceny1}ethyldicyclohexylphosphine (37 mg, 0.04 mmol) in CH₂Cl₂. Crude (+)-2a was purified by flash column chromatography over neutral silica (iatrobeads), eluting with a gradient solvent system (hexane-1.5% EtOAc/hexane), and the solvent was removed under reduced pressure to yield (+)-2a as a colorless oil (52 mg, 74%); HPLC analysis: 90% ee [Daicel Chiralpak AD column; 1 mL/min; solvent system: 2% isopropanol in hexane; retention times: 4.9 min (major), 6.7 min (minor)]; [α]D₁₇ = 62.0 (c = 0.92, CHCl₃); IR (thin film) 1881, 1844, 1699, 1140 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 7.50-7.10 (m, 10H), 1.90 (s, 3H), 1.85 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 171.3, 146.9, 136.2, 135.2, 129.3, 128.6, 128.6, 127.6, 127.4, 126.2, 108.6, 64.4, 19.6, 15.5; MS (EI 70 eV): m/z 264, 132, 104, 78; (M⁺ + Na) HRMS m/z calcd for C₁₈H₁₆O₂Na: 287.1043; found: 287.1039.
(R,Z)-3-ethyl-3-phenyl-4-(1-phenyl-propylidene)-oxetan-2-one ((+)-2b): (Method B)

To a cooled solution of ethylphenylketene (87 mg, 0.59 mmol) in CH₂Cl₂, was added a cooled (−25 °C) solution of (R)-1-[(Sp)-2-(diphenylphosphino)ferrocenyl]ethylidicyclohexylphosphine (38 mg, 0.06 mmol) in CH₂Cl₂. (+)-2b was isolated as a colorless oil (75 mg, 86%); HPLC analysis: 90% ee [Daicel Chiralpak AD column; 0.5 mL/min; solvent system: 2% isopropanol in hexane; retention times: 8.3 min (major), 10.5 min (minor)]; [α]D²⁵ = 23.0 (c = 0.20, CHCl₃); IR (thin film): 1857, 1699, 1140 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 7.42-7.20 (m, 10H), 2.34-2.10 (m, 4H), 1.15 (t, J = 7.4 Hz, 3H), 0.85 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 170.8, 144.0, 135.4, 134.7, 129.3, 128.6, 128.6, 128.2, 127.6, 126.5, 116.5, 70.2, 26.3, 23.0, 12.8, 10.0; (EI 70 eV): m/z 292, 146, 117, 104, 91, 77; MS (M⁺ + Na) HRMS m/z calcd for C₂₀H₂₀O₂Na: 315.1355; found: 315.1351.

(S,Z)-3-ethyl-3-phenyl-4-(1-phenyl-propylidene)-oxetan-2-one: ((−)-2b): (Method B)

To a cooled solution of ethylphenylketene (81 mg, 0.55 mmol) in CH₂Cl₂, was added a cooled (−25 °C) solution of (S)-1-[(Rp)-2-(diphenylphosphino)ferrocenyl]ethylidicyclohexylphosphine (35 mg, 0.06 mmol) in CH₂Cl₂. Crude (−)-2b was purified by flash column chromatography over neutral silica (iatrobeads), eluting with a gradient solvent system (hexane-1.5% EtOAc/hexane), and the solvent was removed under reduced pressure to yield (−)-2b as a colorless oil (75 mg, 93%); HPLC analysis: 86% ee [Daicel Chiralpak AD column; 0.5 mL/min; solvent system: 2% isopropanol in hexane; retention times: 8.0 min (minor), 10.2 min (major)]; [α]D²⁵ = −22.3 (c = 0.56, CHCl₃); IR (thin film): 1857, 1699, 1140 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 7.42-7.20 (m, 10H), 2.34-2.10 (m, 4H), 1.15 (t, J = 7.3 Hz, 3H), 0.85 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 170.8, 144.0, 135.4, 134.7, 129.3, 128.6, 128.6, 128.2, 127.6, 126.5, 116.5, 70.2, 26.3, 23.0, 12.8, 10.0; (EI 70 eV): m/z 292, 146, 117, 104, 91, 77; MS (M⁺ + Na) HRMS m/z calcd for C₂₀H₂₀O₂Na: 315.1355; found: 315.1351.
(R,Z)-3-butyl-3-phenyl-4-(1-phenylpentylidene)-oxetan-2-one (2c):

(Method B)

To a cooled solution of n-butylphenylketene (103 mg, 0.59 mmol) in CH₂Cl₂ was added a cooled (−25 °C) solution of (R)-1-[(S)p]-2-(diphenylphosphino)ferrocenyl]ethylidicyclohexylphosphine (37 mg, 0.06 mmol) in CH₂Cl₂. Crude 2c was purified by flash column chromatography over neutral silica (iatrobeads), eluting with a gradient solvent system (0.5-1.5% EtOAc/hexane), and the solvent was removed under reduced pressure to yield 2c as a colorless oil (93 mg, 90%); HPLC analysis: 89% ee [Daicel Chiralpak AD column; 0.5 mL/min; solvent system: 2% isopropanol in hexane; retention times: 9.1 min (major), 7.4 min (minor)]; [α]D²³ = 20.7 (c = 1.53, CHCl₃); IR (thin film): 1869, 1703 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 7.38-7.19 (m, 10H), 2.30-2.19 (m, 2H), 2.12-2.04 (m, 2H), 1.61-1.36 (m, 2H), 1.28-1.02 (m, 2H), 0.90 (t, J = 7.2 Hz, 3H), 0.86-0.74 (m, 4H), 0.69 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 171.1, 144.8, 135.6, 135.1, 129.3, 128.6, 128.5, 128.2, 127.6, 126.5, 115.3, 69.3, 32.9, 30.4, 29.5, 27.6, 23.0, 22.8, 14.1, 14.0; MS (EI 70 eV): m/z 348, 264, 205, 174, 131, 117, 103; (M⁺ + Na) HRMS calcd for C₂₄H₂₈O₂Na: 371.1982; found: 371.1984.

(S,Z)-3-ethyl-3-p-tolyl-4-(1-p-tolyl-ethylidene)-oxetan-2-one (2d):

(Method B)

To a cooled solution of ethyl-4-tolylketene (83 mg, 0.52 mmol) in CH₂Cl₂ was added a cooled (−25 °C) solution of (S)-1-[(R)p]-2-(diphenylphosphino)ferrocenyl]ethylidicyclohexylphosphine (33 mg, 0.05 mmol) in CH₂Cl₂. 2d was isolated as a colorless oil (82 mg, 99%); HPLC analysis: 85% ee [Daicel Chiralpak AD column; 0.5 mL/min; solvent system: 2% isopropanol in hexane; retention times: 9.1 min (minor), 16.1 min (major)]; [α]D²³ = −28.2 (c = 0.80, CHCl₃); IR (thin film): 1862, 1734, 1700 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 7.30-7.12 (m, 8H), 2.34-2.22 (m, 2H), 2.29 (s, 3H), 2.29 (s, 3H), 2.11-2.05 (m, 2H), 1.14 (t, J = 7.4, 3H), 0.84 (t, J = 7.4, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 171.1, 143.8, 138.3, 137.3, 132.5, 131.8, 129.9, 129.3, 128.1, 126.3, 116.1, 69.8, 26.2, 22.8, 21.4, 21.2, 12.8, 9.9; MS (EI 70 eV) m/z 320, 263, 160, 132, 117; (M⁺ + Na) HRMS m/z calcd for C₂₂H₂₄O₂Na: 343.1669; found: 343.1667.
(S,Z)-3-(4-chlorophenyl)-4-(1-(4-chlorophenyl)-propylidene)-3-ethyloxetan-2-one (2e): (Method B)

To a cooled solution of ethyl-4-chlorophenylketene (73 mg, 0.41 mmol) in CH$_2$Cl$_2$ was added a cooled (−25 °C) solution of (S)-1-[(Rp)-2-(diphenylphosphino)ferrocenyl]ethyldicyclohexylphosphine (26 mg, 0.04 mmol) in CH$_2$Cl$_2$. Crude 2e was purified by flash column chromatography over neutral silica (iatrobeads), eluting with a gradient solvent system (1-2% EtOAc/hexane), and the solvent was removed under reduced pressure to yield 2e as a colorless oil (59 mg, 81%); HPLC analysis: 94% ee [Daicel Chiralcel OD-H column; 0.5 mL/min; solvent system: 2% isopropanol in hexane; retention times: 9.2 min (major), 9.8 min (minor)]; [α]$_D^{23}$ = −19.3 (c = 0.43, CHCl$_3$); IR (thin film): 1862, 1734, 1700 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$, TMS): δ 7.34-7.12 (m, 8H), 2.33-1.98 (m, 4H), 1.14 (t, $J$ = 7.4 Hz, 3H), 0.84 (t, $J$ = 7.4 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 170.0, 144.1, 134.8, 133.7, 133.5, 132.9, 129.6, 129.5, 128.9, 127.9, 115.7, 69.8, 26.3, 22.8, 12.8, 9.9; MS (EI 70 eV): m/z 360, 180, 152, 117; (M$^+$ + Na) HRMS m/z calcd for C$_{20}$H$_{18}$O$_2$Cl$_2$Na: 383.0576; found: 383.0580.

(R,Z)-3-methyl-3-o-toly-4-(1-o-tolyethylidene)oxetan-2-one (2f): (Method A)

To a cooled solution of methyl-2-tolylketene (50 mg, 0.34 mmol) in CH$_2$Cl$_2$ was added a solution of (R)-1-{[(Sp)-2-[bis[3,5-bis(trifluoromethyl)phenyl]phosphino]-ferrocenyl]ethyldicyclohexylphosphine (30 mg, 0.04 mmol) in CH$_2$Cl$_2$. Crude 2f was purified by flash column chromatography over neutral silica (iatrobeads), eluting with a gradient solvent system (0.5-1.5% EtOAc/hexane), and the solvent was removed under reduced pressure to yield 2f as a colorless oil (40 mg, 80%); HPLC analysis: 94% ee [Daicel Chiralpak AS-H column; 0.5 mL/min; solvent system: 10% isopropanol in hexane; retention times: 8.8 min (major), 11.1 min (minor)]; [α]$_D^{23}$ = 71.0 (c = 0.04, CHCl$_3$); IR (thin film): 1883, 1844, 1717, 1456, 1112 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$, TMS): δ 7.43-7.10 (m, 8H), 2.26 (s, 3H), 2.15 (s, 3H), 2.10 (s, 3H), 1.79 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 171.2, 145.3, 137.7, 136.8, 136.0, 133.1, 132.7, 130.6, 128.7, 128.5, 128.0, 127.1, 126.6, 126.1, 110.3, 63.3, 20.6, 20.5, 19.9, 17.5; MS (EI 70 eV): m/z 292, 264, 249, 146, 117, 91; (M$^+$ + Na) HRMS m/z calcd for C$_{20}$H$_{20}$O$_2$Na: 315.1356; found: 315.1359.
(S,Z)-3-(2-chlorophenyl)-4-(1-(2-chlorophenyl)ethylidene)-3-methyloxetan-2-one: (2g) (Method A)

To a cooled solution of methyl-2-chlorophenylketene (46 mg, 0.28 mmol) in CH₂Cl₂ was added a solution of (S)-1-{[(Rp)-2-[bis[3,5-bis(trifluoromethyl)phenyl]-phosphino]ferrocenyl}ethylidicyclohexylphosphine (24 mg, 0.03 mmol) in CH₂Cl₂. Crude 2g (54% 2g, 46% cyclobutanedione 5g by GC-MS analysis) was purified by flash column chromatography over neutral silica (iatrobeads), eluting with a gradient solvent system (hexane to 0.25% EtOAc/hexane). The solvent was removed under reduced pressure to yield 2g as a colorless oil (21 mg, 45%); HPLC analysis: 96% ee [Daicel Chiralpak AS-H column; 1 mL/min; solvent system: 10% isopropanol in hexane; retention times: 7.3 min (major), 15.5 min (minor)]; [α]D²³ = -44.4 (c = 0.19, CHCl₃); IR (thin film): 1890, 1843, 1725, 1647 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 7.48-7.12 (m, 8H), 2.06 (s, 3H), 1.68 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 169.8, 145.7, 136.0, 134.9, 133.4, 132.0, 131.5, 130.7, 130.3, 130.0, 129.3, 128.8, 127.5, 127.1, 108.5, 62.1, 20.0, 16.1; MS (EI 70 eV): m/z 332, 166, 138, 103; (M⁺ + Na)HRMS m/z calcd for C₁₈H₁₄Cl₂O₂Na: 355.0263; found: 355.0266.

(S,Z)-3-ethyl-3-(thiophen-3-yl)propylidene)oxetan-2-one (2h): (Method B)

To a cooled solution of ethyl(3-thiophenyl)ketene (50 mg, 0.33 mmol) in CH₂Cl₂ was added a solution of (S)-1-{[(Rp)-2-(diphenylphosphino)ferrocenyl]ethylidicyclohexylphosphine (21 mg, 0.03 mmol) in CH₂Cl₂. 2h was isolated as a colorless oil (34 mg, 68%); HPLC analysis: 46% ee [Daicel Chiralpak AD column; 1 mL/min; solvent system: 5% isopropanol in hexane; retention times: 5.4 min (minor), 8.7 min (major)]; [α]D²³ = -9.0 (c = 0.17, CHCl₃); IR (thin film): 1859, 1695, 1411 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 7.31-7.05 (m, 6H), 2.39-2.01 (m, 4H), 1.09 (t, J = 7.4 Hz, 3H), 0.92 (t, J = 7.5 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 170.1, 144.6, 136.1, 135.5, 127.4, 127.2, 126.1, 125.5, 122.6, 122.4, 111.3, 67.5, 26.2, 22.7, 13.5, 9.7; MS (EI 70 eV): m/z 152, 123, 97; (M⁺ + Na)HRMS m/z calcd for C₁₆H₁₆O₂S₂Na: 327.0484; found: 327.0485.
(S,Z)-3-ethyl-3-(thiophen-3-yl)-4-(1-(thiophen-3-yl)propylidene)oxetan-2-one (2h): (Method C)

To a cooled solution of ethyl(3-thiophenyl)ketene (82 mg, 0.54 mmol) in CH$_2$Cl$_2$ was added a cooled solution of (R)-BINAPHANE (38 mg, 0.05 mmol) in CH$_2$Cl$_2$. 2h was isolated as a colorless oil (50 mg, 61%); HPLC analysis: 78% ee [Daicel Chiralpak AD column; 1 mL/min; solvent system: 2% isopropanol in hexane; retention times: 5.0 min (minor), 8.2 min (major)]; $[\alpha]_D^{23}$ = -14.6 ($c$ = 0.18, CHCl$_3$); IR (thin film): 1859, 1695, 1411 cm$^{-1}$; $^1$H NMR (200 MHz, CDCl$_3$, TMS) $\delta$ 7.31-7.05 (m, 6H), 2.39-2.01 (m, 4H), 1.09 (t, J = 7.4 Hz, 3H), 0.92 (t, J = 7.5 Hz, 3H); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ 170.1, 144.6, 136.1, 135.5, 127.4, 127.2, 126.1, 125.5, 122.6, 122.4, 111.3, 67.5, 26.2, 22.7, 13.5, 9.7; MS (EI 70 eV): m/z 152, 123, 97; (M$^+$ + Na)HRMS m/z calcd for C$_{16}$H$_{16}$O$_2$S$_2$Na: 327.0484; found: 327.0485.

2,4-dicyclohexyl-2,4-dimethylcyclobutane-1,3-dione (5i): (variation of Method A)

To a cooled solution of cyclohexylmethylketene (51 mg, 0.37 mmol) in CH$_2$Cl$_2$ was added a solution of (R)-1-{[(Sp)-2-[bis[3,5-bis(trifluoromethyl)phenyl]phosphino]ferrocenyl}ethyl)dicyclohexylphosphine (32 mg, 0.04 mmol) in CH$_2$Cl$_2$. The crude product was treated with dry hexane (3 mL) to dissolve crude 5i and precipitate the phosphine. The mixture was filtered using a Schlenk filter funnel. The precipitate was washed with dry hexane (2 × 3 mL) and the phosphine was recovered. The solvent was removed from the filtrate under reduced pressure to yield 5i as a colorless oil (50 mg, 97%), and as an inseparable mixture of diastereomers (cis: trans = ca. 1:1 as determined by $^1$H NMR analysis); IR (thin film): 1743, 1704 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$, TMS) for both diastereomers: $\delta$ 2.28 (m, 4H), 1.70-1.52 (m, 20H), 1.24-1.16 (m, 20H), 1.10 (s, 6H), 1.08 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) for both diastereomers: $\delta$ 172.3, 172.3, 70.7, 70.7, 46.7, 46.7, 40.7, 40.7, 31.3, 29.5, 26.5, 26.4, 13.4, 13.4; MS (EI 70 eV): m/z 276, 183, 139, 111.
2,4-dicyclohexyl-2,4-diethylcyclobutane-1,3-dione (5j): (Method B)
To a cooled solution of cyclohexylethylketene (53 mg, 0.35 mmol) in CH₂Cl₂ was added a solution of (S)-1-[(Rp)-2-(diphenylphosphino)ferrocenyl]ethyl-dicyclohexylphosphine (22 mg, 0.03 mmol) in CH₂Cl₂. Crude 5j was purified by flash column chromatography over neutral silica (iatrobeads), eluting with a gradient solvent system (hexane to 0.5% EtOAc/hexane). The solvent was removed under reduced pressure to yield 5j as a colorless oil (41 mg, 77%), and as an inseparable mixture of diastereomers (cis: trans = ca. 1:1 as determined by NMR analysis); IR (thin film): 1754, 1714 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS) for both diastereomers: δ 2.11-2.05 (m, 4H), 1.74-1.51 (m, 32H), 1.19-1.02 (m, 16H), 0.88 (t, J = 7.4 Hz, 12H); ¹³C NMR (100 MHz, CDCl₃) for both diastereomers: δ 171.5, 171.5, 55.0, 55.0, 40.0, 40.0, 31.3, 31.3, 30.6, 30.6, 26.5, 26.5, 22.3, 22.3, 12.2, 12.2; MS (EI 70 eV): m/z 304, 153, 125, 83; HRMS analysis obtained for 1,3-diol derivative 5k (through LiAlH₄ reduction of 5j) (M⁺ + Na)HRMS m/z calcd for C₂₀H₃₆O₂Na: 331.2608; found: 331.2607.

3,3-dimethyl-4-(propan-2-ylidene)oxetan-2-one (2k): (variation of Method A)
(R)-1-[(S₆)-2-[bis[3,5-bis(trifluoromethyl)phenyl]phosphino]ferrocenyl]ethyldicyclohexylphosphine (35 mg, 0.04 mmol) in THF (1 mL) was added to a solution of dimethylketene (57 mg, 0.81 mmol) in THF (7.1 mL) at −25 °C, and stirred for one hour at the same temperature. The reaction was then quenched by the addition of aqueous H₂O₂ solution (50%, 1 drop) at room temperature. The solution was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude product was dissolved in 50% CH₂Cl₂/pentane (10 mL) and passed through a plug of neutral silica (7 g, 2 × 2 cm), eluting with 50% CH₂Cl₂/pentane (40 mL). The solvent was removed under reduced pressure to afford 2k as a colorless oil (43 mg, 75 %); IR (thin film): 1880, 1825, 1624 cm⁻¹; ¹H NMR (400 MHz, CDCl₃,TMS): δ 1.64 (s, 3H), 1.60 (s, 3H), 1.43 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 174.0, 145.7, 103.7, 54.1, 20.4, 16.4, 16.2; MS (EI 70 eV): m/z 140, 81, 70; (M⁺ + Na) HRMS m/z calcd for (C₈H₁₂O₂)₂Na⁺: 303.1567; Found: 303.1569.
(+)-4-methyl-2,4-diphenylnonane-3,5-dione (8a):  
(−)-2a (48 mg, 0.18 mmol) was dissolved in THF (1.5 mL), and n-BuLi (2.5 M in hexane, 0.14 mL, 0.36 mmol) was added dropwise over two minutes at −78 °C. The reaction was stirred for 15 min and was then quenched by adding water (2 mL) at −78 °C. The reaction was then warmed up to room temperature, brine (8 mL) and CH₂Cl₂ (5 mL) were added, and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (2 × 5 mL), and the combined organics were dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure to yield a colorless oil (59 mg, >99%), with a dr = 88:12 as determined by ¹H NMR analysis; [α]_D^{23} = 16.3 (c = 0.73, CHCl₃); IR (thin film): 1713, 1710 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS) for the major diastereomer: δ 7.31-6.78 (m, 10H), 3.88 (q, J = 6.8 Hz, 1H), 2.37-2.27 (m, 2H), 1.57 (s, 3H), 1.48-1.45 (m, 2H), 1.31 (d, J = 6.8 Hz, 3H), 1.22-1.16 (m, 2H), 0.76 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) for the major diastereomer: δ 210.8, 210.6, 141.1, 137.8, 128.9, 128.6, 128.6, 128.2, 128.1, 127.5, 126.7, 70.7, 49.8, 39.4, 26.4, 22.4, 21.4, 20.0, 14.1; MS (EI 70 eV): m/z 322, 238, 190, 132, 105, 77; (M^+ + Na) HRMS m/z calcd for C₂₂H₂₆O₂Na: 345.1825; found: 345.1819.
(S,Z)-4-methyl-5-oxo-2,4-diphenylnon-2-en-3-ylpropionate (9a):

(−)-2a (31 mg, 0.12 mmol) was dissolved in THF (1.0 mL), and n-BuLi (2.5 M in hexane, 0.05 mL, 0.12 mmol) was added dropwise over 2 min at −78 °C. The reaction was then stirred for 5 min at −78 °C and warmed up to room temperature for 30 min. The reaction was then quenched by adding propionyl chloride (0.02 mL, 0.24 mmol) at −78 °C. The reaction was taken out of the cooling bath and warmed up to room temperature over 1 h. Brine (8 mL) and CH₂Cl₂ (5 mL) were added, and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (2 × 5 mL), and the combined organics were dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure to yield a colorless oil (27 mg, 61%), with a dr >99:1 as determined by ¹H NMR analysis; [α]₀° = 29.4 (c = 0.22, CHCl₃); IR (thin film): 1756, 1715 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 7.49-7.14 (m, 10H), 2.58-2.54 (m, 2H), 1.83-1.78 (m, 2H), 1.70 (s, 3H), 1.57 (s, 3H), 1.50-1.37 (m, 2H), 1.23-1.21 (m, 2H), 0.79 (t, J = 7.3 Hz, 3H), 0.66 (t, J = 7.5 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 210.3, 172.7, 143.7, 141.6, 141.2, 129.9, 128.5, 128.3, 128.3, 127.8, 127.1, 127.1, 127.1, 61.6, 39.2, 27.3, 27.0, 23.6, 22.6, 21.1, 14.1, 8.8; MS (EI 70 eV): m/z 322, 293, 237, 220, 205, 190; (M⁺ + Na) HRMS m/z calcd for C₂₅H₃₀O₃Na: 401.2087; found: 401.2084
(3S,5S)-3-(hydroxymethyl)-3,5-diphenylheptan-4-one (10b):

(+)-2b (38 mg, 0.13 mmol) was dissolved in THF (0.6 mL) and the solution was cooled to −78 °C. After five minutes, LiAlH₄ (1M in Et₂O, 0.13 mL, 0.13 mmol) was added at −78 °C. The reaction was stirred for 2 h until TLC showed complete consumption of 2b and then the reaction was quenched with aqueous saturated NH₄Cl solution (5 mL) at −78 °C. Aqueous saturated NaCl (2 mL) solution was added to aid separation of the phases. The aqueous phase was extracted with CH₂Cl₂ (3 × 5 mL), and the combined organic layers were dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure. The resulting crude product was purified on a plug of neutral silica (iatribeads), eluting with a gradient solvent system (10% EtOAc/hexane to 20% EtOAc/hexane). The solvent was removed to afford 10b as a white solid (32 mg, 84%), with a dr >99:1 as determined by 1H NMR analysis; HPLC analysis: 91% ee [Daicel Chiralpak AD column; 0.5 mL/min; solvent system: 2% isopropanol in hexane; retention times: 19.6 min (major), 24.3 min (minor)]; [α]D²³ = −31.9 (c = 0.19, CHCl₃); IR (thin film): 3460, 1697, 1030 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 7.05-6.78 (m, 10H), 4.15 (d, J = 11.8 Hz, 1H), 3.76 (d, J = 11.8 Hz, 1H), 3.44 (dd, J = 6.2, 8.7 Hz, 1H), 2.16-2.12 (m, 2H), 1.72-1.66 (m, 2H), 0.84 (t, J = 7.4 Hz, 3H), 0.52 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 213.5, 139.5, 137.9, 128.8, 128.5, 128.1, 128.0, 127.5, 126.9, 63.8, 61.9, 56.2, 28.5, 23.6, 12.1, 8.6; MS (EI 70 eV): m/z 266, 147, 119, 91, 77; (M⁺ + Na) HRMS m/z calcd for C₂₀H₂₄O₂Na: 319.1669; found: 319.1662.