SUPPORTING INFORMATION

General materials and methods

All non-aqueous reactions were carried out in flame- and/or oven-dried glassware using standard syringe-septum operations under argon atmosphere and magnetically stirred unless otherwise noted. All reactions were monitored by analytical thin-layer chromatography using Merck pre-coated silica gel plates with F254 indicator. Visualization was accomplished by UV light (254 nm) and phosphomolybdic acid stain. Flash column chromatography was performed using silica gel (mesh 230-400) supplied by Silicycle. Room temperature means 20±1 °C. All reactions were carried out with anhydrous solvents unless otherwise noted. Anhydrous THF (Ultra low water, 99.9%), dichloromethane, diethyl ether, acetonitrile and toluene were dried with an M BRAUN solvent purification system (A2 Alumina). Other anhydrous solvents and all other reagents were purchased from commercial vendors and used without further purification unless indicated specifically. Optical rotations were recorded on a JASCO DIP-1000 polarimeter and reported as follows: $[\alpha]_D^T \circ C$ (c = g/100 mL, solvent). High-performance liquid chromatography (HPLC) was performed on Varian ProStar series equipped with a variable wavelength detector using a Chiralpak or Chiralcel columns from Daicel, or a MICROSORB-Si-MV achiral column from Varian. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker Avance 400 (400 MHz¹H, 100 MHz¹³C), or a Bruker Avance 500 (500 MHz ¹H, 125 MHz ¹³C). Chemical shift values (δ) are reported in ppm (TMS $\delta = 0$ ppm for ¹H; residual chloroform $\delta = 77.0$ ppm for ¹³C). The proton spectra are reported as follows δ (multiplicity, coupling constant J, number of protons). Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad), and so on. Low resolution mass spectra (LRMS) were obtained on a QSTAR (Applied SCIEX Biochemistry/MDS) spectrometer.

Synthetic procedures and characterization of products

Tropone (5) (10.15 g, 95.6 mmol, 1 eq) and benzyl vinyl ether (6) (51.68 g, 385 mmol, 4 eq) were weighted in a 1 L flask, then a solution of $B(C_6F_5)_3$ (4.89 g, 9.55 mmol, 0.1 eq) in 265 mL THF was transferred into the flask via cannula at room temperature. Stirring was continued at room temperature for 85 hours, after which the reaction mixture was concentrated under vacuum to remove most of the THF and excessive benzyl vinyl ether. The residue was diluted with 100 mL hexanes and loaded on a pad of silica gel (~200 g) in a 600 mL Büchner style filter funnel under vacuum. Sequential elution (monitored by TLC) with 1000 mL hexanes, 500 mL 1:24 EtOAc/hexanes, 450 mL 1:14 EtOAc/hexanes then 260 mL 1:12 EtOAc/hexanes removed most of the less polar components. Elution with another 1200 mL 1:5 EtOAc/hexanes provided the desired products. After concentration on a rotavap, the recovered solvents were used to wash the silica gel again, and additional products obtained. This process was repeated for three times and product solutions combined. After concentration, 24.5 g products (4, 4', 106% yield) were obtained as brown oil, the regioselectivity (4/4') was estimated to be 5:1 and for the desired regioisomer 4 the diastereoselectivity (endo/exo) was estimated to be 10:3 by 1 H NMR. A smaller scale experiment and characterization of Diels-Alder products 4 and 4' have been reported in the supporting information of our previous paper (J. Am. Chem. Soc. 2009, 131, 16628-16629). Without further purification, this material was dissolved with 1 L methanol in a 2 L flask, and then 1.05 g Pd/C (10 wt%) was added under an argon atmosphere. After exchanging to a hydrogen atmosphere with a big balloon, vigorous stirring was continued at room temperature for 18 hours. The reaction mixture was filtrated through a pad of Celite, and then concentrated. After diluting the residue with 5 mL benzene, flash column chromatography (silica gel, hexanes: EtOAc 3:1 to 1:2 gradient) afforded first the regioisomers of 7 [$R_f = 0.30$ (silica gel, hexanes: EtOAc 1:1), 2.08 g, 14% yield from tropone], plus mixed fractions (342 mg), and then compound 7 (10.24 g, 69% yield from tropone) as inseparable diastereomeric mixture.

7: mixture of endo and exo products, $R_f = 0.18$ (silica gel, hexanes: EtOAc 1:1); ¹H NMR (500 MHz, CDCl₃): $\delta = 4.16-4.03$ (m, 1H), 2.70-2.55 (m, 1H), 2.55-2.38 (m, 2H), 2.30-2.08 (m, 3H), 1.90-1.65 (m, 5H), 1.65-1.50 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): $\delta = 216.6, 216.4, 69.5, 68.3, 45.8, 44.4, 38.5, 38.2, 37.1, 35.6, 33.3, 32.7, 26.4, 23.8, 21.8, 21.2, 21.0, 19.2; LRMS (ESI) calcd for C₉H₁₅O₂⁺ (M+H)⁺ 155.1, found 155.1.$



Compound 7 (3.30 g, 21.4 mmol, 1 eq, as a diastereomeric mixture) was dissolved with 100 mL benzene in a 250 mL flask, followed by addition of ethylene glycol (13.4 mL, 240 mmol, 11 eq) and p-TsOH·H₂O (40.6 mg, 0.21 mmol, 0.01 eq) at room temperature. The flask was then placed under a Dean-Stark apparatus and refluxed for 1 hour. After cooling down to room temperature, 5.0 g solid NaHCO₃ was added, followed by 100 mL water. After extraction with 3×150 mL Et₂O, the combined organic phase was washed by 2×25 mL brine, and dried over MgSO₄. Filtration and concentration afforded 4.36 g crude product ketal [$R_f = 0.25$ (silica gel, hexanes: EtOAc 1:1)] which was used in the next step without further purifications. The crude ketal (4.36 g, calculated as 21.4 mmol, 1 eq) was dissolved with 235 mL CH₂Cl₂ at room temperature, followed by addition of NaHCO₃ (3.59 g, 42.7 mmol, 2 eq) and then Dess-Martin periodinane (10.87 g, 25.6 mmol, 1.2 eq). Stirring was continued at room temperature for 30 minutes, before 6 g solid Na₂S₂O₃ and 45 mL water were added. After about 10 minutes stirring, the gas evolving ceased. Additional 100 mL water was added and the organic phase was separated. The aqueous phase was extracted by 4×150 mL EtOAc and the combined organic phase was washed by 2×150 mL saturated aqueous Na₂S₂O₃ solution, 2×100 mL saturated aqueous NaHCO₃

solution, 2×50 mL brine, and then dried over Na₂SO₄. Filtration and concentration afforded 3.53 g crude product ketone (ca. 84% yield over two steps) [$R_f = 0.46$ (silica gel, hexanes: EtOAc 1:1); ¹H NMR (500 MHz, CDCl₃): $\delta = 4.00-3.87$ (m, 4H), 2.64(dt, J =17.9, 2.0 Hz, 1H), 2.57-2.54 (m, 1H), 2.22 (dd, J = 19.0, 5.6 Hz, 1H), 2.18-2.14 (m, 1H), 2.10-2.03 (m, 1H), 1.94-1.82 (m, 3H), 1.80-1.63 (m, 4H); ¹³C NMR (125 MHz, CDCl₃): $\delta = 215.1, 112.6, 64.4, 64.1, 45.7, 39.3, 38.9, 32.0, 24.9, 22.4, 19.6$], which was used in the next step without further purifications. KO'Bu (11.30 g, 100.8 mmol, 5.6 eq) and MePPh₃Br (38.59g, 108 mmol, 6 eq) were dissolved in 110 mL THF at room temperature. After stirring at room temperature for 1 hour, the ylide solution was then cooled by an ice bath. The above obtained crude ketone (3.53 g, calculated as 18 mmol, 1 eq) in 110 mL THF was transferred via cannula to the ylide solution dropwise, and additional 10 mL THF was used to wash out all the substrate. The reaction mixture was gradually warmed up to room temperature over 15 hours, then quenched by 2 mL water. The solution was concentrated to a volume about 50 mL, and then 100 mL hexanes was added to precipitate out most of the triphenylphosphine oxide. Some MgSO₄ was added to dry this mixture, and then filtration through a pad of silica gel (~160 g) with Et_2O elution (totally 800 mL) afforded the crude olefin ketal after concentration [$R_{f} = 0.30$ (silica gel, hexanes: EtOAc 10:1); ¹H NMR (500 MHz, CDCl₃): $\delta = 4.72-4.68$ (m, 2H), 3.94-3.82 (m, 4H), 2.63-2.53 (m, 2H), 2.29(d of pent, J = 17.7, 2.4 Hz, 1H), 1.97-1.90 (m, 1H), 1.90-1.85 (m, 1H), 1.75-1.70 (m, 2H), 1.70-1.60 (m, 3H), 1.60-1.50 (m, 2H); ¹³C NMR (125 MHz, $CDCl_3$): $\delta = 150.2, 114.3, 107.6, 64.1 (2C), 38.8, 38.5, 32.3, 30.3, 29.3, 25.8, 20.2],$ which was used in the next step without further purifications. The crude olefin ketal (calculate as 18 mmol) was dissolved 150 mL acetone at room temperature, followed by addition of p-TsOH·H₂O (4.84 g, 25.2 mmol, 1.4 eq) and stirring was continued at room temperature for 10 minutes. After quenching with 300 mL saturated aqueous NaHCO₃ solution, the solution was concentrated under vacuum to remove most of the acetone. Extraction with 3×100 mL Et₂O, drying over MgSO₄, filtration, concentration and flash column chromatography (silica gel, hexanes: EtOAc 12:1) afforded compound 8 (2.00 g, 62% yield over four steps).

8: $R_f = 0.25$ (silica gel, hexanes: EtOAc 10:1); ¹H NMR (500 MHz, CDCl₃): $\delta =$

4.88-4.87 (m, 1H), 4.83-4.80 (m, 1H), 2.82-2.77(m, 1H), 2.63-2.40 (m, 5H), 2.00-1.60 (m, 6H; ¹³C NMR (125 MHz, CDCl₃): δ = 216.6, 147.5, 110.1, 45.6, 38.4, 38.3, 31.4, 30.1, 25.5, 21.9; LRMS (ESI) calcd for C₁₀H₁₅O⁺ (M+H)⁺ 151.1, found 151.1.



Compound 8 (0.66 g, 4.4 mmol, 1 eq) was dissolved in 120 mL CH₂Cl₂. After adding Et₃N (6.13 mL, 44 mmol, 10 eq), the solution was cooled down to -78 °C, and then TMSOTf (3.98 mL, 22 mmol, 5 eq) was added dropwise. The reaction was stirred at -78 °C for 5 h, and then gradually warmed up to room temperature overnight. After quenching with 150 mL saturated aqueous NaHCO₃ solution, it was extracted with 3×100 mL hexanes, washed by 50 mL saturated aqueous NaHCO₃ solution, 50 mL brine, and dried over MgSO₄, filtration, concentration afforded the crude silvl enol ether $[R_f = 0.81]$ (silica gel, hexanes: EtOAc 3:1)], which was used in the next step without further purifications. After dissolving the crude silvl enol ether in 13 mL CH₂Cl₂ with solid NaHCO₃ (554mg, 6.6 mmol, 1.5 eq), the mixture was cooled down to 0 °C. mCPBA (~77wt%, 1.08 g, 4.8 mmol, 1.1 eq) was added in four portions every other 15 min, and the reaction was kept at 0 °C for another 1.5 h. The solution was diluted with 11 mL CH₂Cl₂, added 1.6 g solid NaHCO₃ with 15 mL water. After separation, the aqueous phase was extracted with 2×10 mL CH₂Cl₂, the combined organic phase washed with 22 mL saturated aqueous NaHCO3 solution, 22 mL water, and dried over Na2SO4. The crude products were dissolved in 13 mL THF, and the solution was cooled down to 0 °C, and then TBAF (1.0 M in THF, 5.25 mL, 5.25 mmol, 1.2 eq) was added dropwise. After stirring at 0 °C for 1 h, the reaction was quenched by 18 mL saturated aqueous NaHCO₃ solution, extracted by 2×10 mL Et₂O, the combined organic phase washed with 27 mL brine and then dried over MgSO₄. After filtration and concentration, crude ¹H NMR indicated a 1:1 dr of two diastereomers. Flash column chromatography (silica gel, hexanes: EtOAc 7:1) afforded compound 9 as two separable while inconsequential diastereomers (combined: 573 mg, 78% yield over three steps), which were used as a mixture for the next step together.

9: More polar diastereomer, $R_f = 0.24$ (silica gel, hexanes: EtOAc 3:1); ¹H NMR (500 MHz, CDCl₃): $\delta = 4.90$ -4.88 (m, 1H), 4.76-4.74 (m, 1H), 4.60 (td, J = 10.0, 4.1 Hz, 1H), 3.56 (d, J = 4.2 Hz, 1H), 2.80-2.76(m, 2H), 2.66-2.58 (m, 1H), 2.49-2.46 (m, 2H), 1.95-1.85 (m, 3H), 1.85-1.74 (m, 1H), 1.32 (t, J = 11.7 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃): $\delta = 215.7, 148.1, 110.9, 72.8, 42.5, 41.4, 36.7, 31.8, 22.6, 21.4$.

9: Less polar diastereomer, $R_f = 0.30$ (silica gel, hexanes: EtOAc 3:1); ¹H NMR (500 MHz, CDCl₃): 4.98-4.95 (m, 1H), 4.89-4.86 (m, 1H), 4.38 (td, J = 9.2, 1.7 Hz, 1H), 3.62 (d, J = 2.8 Hz, 1H), 2.82-2.75 (m, 2H), 2.66-2.45 (m, 3H), 1.95-1.77 (m, 2H), 1.77-1.58 (m, 2H), 1.30 (t, J = 12.3 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃): $\delta = 215.5$, 145.5, 110.8, 73.2, 42.4, 39.2, 36.3, 30.4, 26.9, 22.2.



Compound **9** (mixture of two diastereomers, 573 mg, 3.45 mmol, 1 eq) was dissolved in 34 mL MeOH and 34 mL benzene. The solution was cooled down to 0 °C before Pb(OAc)₄ (1.99 g, 4.48 mmol, 1.3 eq) was added. After string at 0 °C for 7 min, it was diluted with 340 mL Et₂O. The solution was filtered through ~60 g silica gel, with 450 mL Et₂O washing. The combined solution was washed with 2×100 mL saturated aqueous NaHCO₃ solution, then 50 mL brine, and dried over MgSO₄. After filtration and concentration, the crude aldehyde [R_f = 0.38 (silica gel, hexanes: EtOAc 3:1); ¹H NMR (500 MHz, CDCl₃): 9.73 (t, *J* = 2.1 Hz, 1H), 4.79-4.78 (m, 1H), 4.75-4.74 (m, 1H), 3.68 (s, 3H), 2.88 (pent, *J* = 5.2 Hz, 1H), 2.64 (ddd, *J* = 14.4, 7.8, 2.2 Hz, 1H), 2.56-2.35 (m, 4H), 1.88-1.77 (m, 2H), 1.95-1.77 (m, 2H), 1.77-1.60 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): δ = 201.8, 175.1, 147.1, 110.0, 51.7, 45.9, 43.4, 36.7, 34.7, 30.8, 24.5] was used in the next step without further purifications. Solid LiCl (366 mg, 8.62 mmol, 2.5 eq) was dried under vaccum with a heating gun for 5 min before it was suspended in 12.2 mL THF. Diethyl 2-oxopropylphosphonate (796 μ L, 4.14 mmol, 1.2 eq) dissolved in 8 mL THF was mixed with the LiCl/THF suspension *via* cannula transfer and washed with 1

mL THF, and then cooled down to 0 °C, followed by addition of Et₃N (1.20 mL, 8.62 mmol, 2.5 eq). The suspension was kept at 0 °C for 10 min before the solution of crude aldehyde in 8 mL THF was transferred *via* cannula with 2×1 mL THF washing. After stirring at 0 °C for 12 h, the reaction was quenched by 35 mL saturated aqueous NH₄Cl solution, extracted by 3×15 mL Et₂O, and then the combined organic phase was washed with 10 mL brine and dried over MgSO₄. After filtration and concentration, flash column chromatography (silica gel, hexanes: EtOAc 6:1) afforded compound **10** (471.5 mg, 58% yield over two steps). The two enantiomers are then separated by preparative HPLC on an OD-H column (1 cm × 25 cm), washed by 10:1 hexanes/isopropanol, t_1 = 3.7 min, t_2 = 4.4 min, the 1st fraction is obtained in 96% ee (major peak first), $[a]_D^{24 \circ C} = -1.35$ (*c* = 1.11, CHCl₃); the 2nd fraction is obtained in 98% ee (minor peak first), $[a]_D^{26 \circ C} = +1.36$ (*c* = 1.12, CHCl₃)

10: $R_f = 0.31$ (silica gel, hexanes: EtOAc 3:1); ¹H NMR (500 MHz, CDCl₃): $\delta = 6.70$ (dt, J = 15.8, 7.4 Hz, 1H), 6.07 (d, J = 15.9 Hz, 1H), 4.79-4.77 (m, 1H), 4.72-4.70 (m, 1H), 3.69 (s, 3H), 2.50-2.34 (m, 5H), 2.34-2.26 (m, 1H), 2.23 (s, 3H), 1.82-1.74 (m, 1H), 1.70-1.63 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): $\delta = 198.5, 175.3, 147.5, 146.5, 132.2, 110.0, 51.6, 43.8, 41.7, 34.7, 34.1, 30.5, 26.9, 24.1; LRMS (ESI) calcd for C₁₄H₂₁O₃⁺ (M+H)⁺ 237.1, found 237.1.$



Compound **10** (16.1 mg, 0.0680 mmol, 1 eq) was dissolved in 1 mL THF. After cooling the solution down to 0 °C, LiAlH₄ (2.0 M in THF, 102 μ L, 3 eq) was added dropwise. The reaction mixture was warmed up to room temperature and stirred for 20 min before it was cooled down to 0 °C and quenched by 5 mL wet Et₂O. After filtration of the precipitates, the organic phase was washed with 5 mL brine and then dried over MgSO₄. After filtration and concentration, crude ¹H NMR indicated a 1:1 dr of two diastereomers. The

crude diol [R_f = 0.19 (silica gel, hexanes: EtOAc 1:1)] was dissolved in 1 mL CH₂Cl₂, solid NaHCO₃ (22.8 mg, 0.272 mmol, 4 eq) and Dess-Martin periodinane (69.2 mg, 0.163 mmol, 2.4 eq) was added at room temperature. After 15 min, the reaction was quenched by 3 mL saturated aqueous Na₂S₂O₃ solution, partitioned with 6 mL EtOAc, and separated. The aqueous phase was further extracted by 2×3 mL EtOAc. The combined organic phase was washed sequentially with 2mL saturated aqueous Na₂S₂O₃ solution, 2 mL saturated aqueous NaHCO₃ solution, 2 mL brine, and then dried over MgSO₄. After filtration and concentration, flash column chromatography (silica gel, hexanes: EtOAc 6:1) afforded compound **3** (13.6 mg, 97% yield over two steps). When (+)-10 is used, (-)-**3** is obtained, $[\alpha]_D^{22 \circ C} = -0.39$ (c = 0.74, CHCl₃); when (-)-10 is used, (+)-**3** is obtained, $[\alpha]_D^{22 \circ C} = +0.40$ (c = 0.70, CHCl₃).

3: $R_f = 0.50$ (silica gel, hexanes: EtOAc 1:1); ¹H NMR (500 MHz, CDCl₃): $\delta = 9.67$ (s, 1H), 6.72 (dt, J = 15.8, 7.3 Hz, 1H), 6.07 (d, J = 15.9 Hz, 1H), 4.84-4.81 (m, 1H), 4.74-4.71 (m, 1H), 2.50-2.30 (m, 5H), 2.30-2.20 (m, 1H), 2.24 (s, 3H), 1.88-1.77 (m, 2H), 1.77-1.66 (m, 1H), 1.58-1.50 (m, 1H); ¹³C NMR (125 MHz, CDCl₃): $\delta = 203.8$, 198.5, 147.1, 146.3, 132.4, 109.8, 50.1, 41.8, 34.8, 32.4, 30.4, 26.9, 22.2; LRMS (ESI) calcd for $C_{13}H_{19}O_2^+$ (M+H)⁺ 207.1, found 207.1.



(*S*)-3-(2-naphthyl)-*L*-alanine (286.6 mg, 1.332 mmol, 1 eq) and cesium hydroxide monohydrate (223.6 mg, 1.332 mmol, 1 eq) were dissolved in 10 mL MeOH by ultrasonication at room temperature for 5 minutes. It was then concentrated under vacuum and azeotropically dried with 3×10 mL benzene and finally high vacuum for 30 minutes. The residue was dissolved in 10 mL Et₂O, 10 mL MeOH and added 1.019 g silica gel. After concentration under vacuum and drying under high vacuum, 1.51 g white color fine powder of silica gel absorbed cesium salt of (*S*)-3-(2-naphthyl)-*L*-alanine (**11**) was obtained and used as such. For calculating the amount of catalyst, we assumes quantitative conversion of this acid-base reaction, so that the formal "molecular weight"

is 1.51 g/1.332 mmol = 1134 mg/mmol.



Compound (+)-3 (9.2 mg, 0.0446 mmol, 1 eq) and the silica gel absorbed cesium salt of (*S*)-3-(2-naphthyl)-*L*-alanine (11) (25.3 mg, calculated as 0.0223 mmol, 0.5 eq) were suspended in 0.6 mL diethyl ether at room temperature for 113 h. After filtration and evaporation of solvent, the crude products (2, 2', and corresponding intermediate Michael adducts) were dissolved in 1 mL EtOH, then added a solution of 130 μ L 5% KOH in EtOH and stirred at room temperature for 2 h. Flash column chromatography (silica gel, hexanes: EtOAc 10:1) afforded tricyclic compound 2 and 2' as inseparable diastereomeric mixture (7.2 mg, 86% combined yield, 9:1 dr, favoring the desired diastereomer (–)-2). The two diastereomers can be separated by preparative HPLC (MICROSORB-Si-MV achiral column, hexane/*i*-PrOH 100:0.2, 30 mL/min, detect 235 nm, collect ~27-32 min fractions) to afford a pure sample of (–)-2, $[\alpha]_D^{23 \circ C} = -22.7$ (c = 0.59, CHCl₃).

2: $R_f = 0.41$ (silica gel, hexanes: EtOAc 3:1); ¹H NMR (500 MHz, CDCl₃): $\delta = 6.56$ (d, J = 10.0 Hz, 1H), 5.87 (d, J = 10.0, 1H), 4.85-4.80 (m, 1H), 4.71-4.67 (m, 1H), 2.48-2.37 (m, 2H), 2.37-2.27 (m, 2H), 2.19-2.06 (m, 2H), 2.03-1.95 (m, 1H), 1.82-1.66 (m, 3H), 1.54-1.46 (m, 1H), 1.20 (dd, J = 12.5, 8.0 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃): $\delta = 200.1$, 156.7, 148.9, 127.7, 106.9, 41.6, 40.9, 36.0, 35.6, 35.5, 34.9, 26.4, 24.5; LRMS (ESI) calcd for $C_{13}H_{17}O^+$ (M+H)⁺ 189.1, found 189.1.





ppm 225 200 175 150 125 100 75 50 25

















