Supporting Information

Enantioselective Synthesis of γ -Hydroxyenones by Base Catalyzed Kornblum DeLaMare Rearrangement

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General Information. Unless otherwise noted all commercial materials were used without purification. Small scale reactions (< 3mL) were carried out in Fisher Scientific disposable scintillation vials. Dichloromethane used in the desymmetrization reactions was obtained from Fisher Scientific and used without purification. Dry dichloromethane was obtained by passage through a column of neutral alumina. TLC analysis of reaction mixtures was performed on Merck silica gel 60 F₂₅₄ TLC plates. Flash chromatography was carried out on Merck 60 silica gel (32-63 μ m). ¹H and ¹³C NMR spectra were recorded with Bruker AVB-400, AVQ-400 and DRX-500 spectrometers and referenced to chloroform unless otherwise noted. Mass spectral and analytical data were obtained via the Micro-Mass/Analytical Facility operated by the College of Chemistry, University of California, Berkeley. Optical rotations were determined using a Perkin-Elmer polarimeter equipped with a sodium lamp. Enantiomeric ratios were measured by chiral HPLC (Shimadzu® HPLC equipped with SPD-M10A microdiode array detector and Chiracel® OD, OD-H, AD, AD-H, AS, OJ and WHELK-01 chiral columns.

General Procedure for the Asymmetric Kornblum DeLaMare. To a solution of meso-endoperoxide in methylene chloride (0.1-2.0 M) at denoted temperature was added **11** (5-10 mol%). The solution was stirred until the reaction judged complete by tlc. Direct flash chromatography of the solution using an appropriate solvent mixture gave enantioenriched products. Procedures for specific compounds will be represented as follows: catalyst loading, concentration, temperature, reaction time; purification procedure, yield of pure product.

(S)-(+)-5. Following the general procedure: 5 mol% **11**, 2 M in CH₂Cl₂, rt, 6 h; Flash chromatography (1:1 hexanes:EtOAc), 165 mg (97%). Flushing of the column with 10% MeOH/5% NH₄OH in EtOAc gave quantitative recovery of **11**. Analytic data were similar to those previously reported.¹ ¹H NMR (400MHz, CDCl₃) δ 5.97 (dd, J = 5.8, 1.9 Hz, 1H), 5.76 (dd, J = 1.2, 5.7 Hz, 1H), 4.96 (br dd, J = 6.4, 1.5 Hz, 1H), 3.09 (s, 1H), 2.10-1.80 (m, 2H), 1.70-1.40 (m, 6H). ¹³C NMR (400MHz, CDCl₃) δ 134.58, 132.94, 111.77, 81.81, 39.33, 33.71, 24.02, 23.32. LRMS (EI): 140 (M⁺). Anal. Calcd. for C₈H₁₂O₂: C, 68.54; H, 8.63. Found: C, 68.47; H, 8.85. $[\alpha]_D^{25}$ +76.5 (c = 0.9, CHCl₃). The enantiomeric excess was determined to be >99% by chiral HPLC analysis (Chiracel AS 93:7 hexanes:ⁱPrOH, 1.0 mL/min, $t_{r-major}$ 19.1 min, $t_{r-minor}$ 15.9 min). HPLC data for racemic and 99% ee shown below.

211 nm, 4 nm Results		
Retention Time	Area	Area Percent
16.315	2543990	49.984
19.616	2545642	50.016

210 nm, 4 nm Results		
Retention Time	Area	Area Percent
17.307	11292	0.528
20.208	2128707	99.472

(+)-16 Following the general procedure: 5 mol% **11**, 1 M in CH₂Cl₂, rt, 10 h; Flash chromatography (1:1 hexanes:EtOAc), 32 mg (99%). This compound exists as a mixture of ketone and hemiketal isomers. For the major (hemiketal) isomer: ¹H NMR (400 MHz, CDCl₃) δ 6.28 (d, *J* = 5.9 Hz, 1H), 6.05 (d, *J* = 5.9 Hz, 1H), 4.87 (br s, 1H), 4.31 (m, 2H), 2.64 (m, 1H), 2.52 (m, 1H), 2.33 (m, 2H), 1.50 (s, 3H), 1.31 (s, 3H). ¹³C NMR (400 MHz, CDCl₃) δ 133.24, 133.39, 107.99, 106.90, 78.86, 75.23, 42.65, 44.05, 38.74, 27.61, 24.31. HREIMS calc'd for C₁₀H₁₃O₄ (M-15)⁺: 197.0814, found: 197.0813. [α]_D²⁵ +37.3 (c = 0.5, MeOH). The enantiomeric excess was determined to be >99% by chiral HPLC analysis (Chiracel OD 80:20 hexanes:PrOH, 1.0 mL/min, *t*_{r-major} 7.3 min, *t*_{r-minor} 6.8 min). HPLC data for racemic and 99% ee samples shown below.

210 nm, 4 nm Results		
Retention Time	Area	Area Percent
6.160	2404097	52.254
7.376	2196656	47.746

210 nm, 4 nm Results		
Retention Time	Area	Area Percent
6.165	40710	0.163
7.072	24899500	99.837

(-)-18. Following the general procedure: 5 mol% **11**, 2M in CH₂Cl₂, 0°C, 24 h; Flash chromatography (1:1 hexanes:EtOAc), 38 mg (95%). ¹H NMR (400 MHz, CDCl₃) δ 6.71 (app dd, *J* = 12.4, 3.2 Hz, 1H), 6.03 (app d, *J* = 12.4 Hz, 1H), 4.73 (m, 1H), 4.07-3.75 (m, 2H), 3.00 (d, *J* = 14.8 Hz, 1H), 2.93 (d, *J* = 14.8 Hz, 1H), 2.76 (d, *J* = 6.8, 1H), 2.46 (dd, *J* = 14.0, 4.0 Hz, 1H), 2.37 (dd, *J* = 14.0, 8.8 Hz, 1H). ¹³C NMR (400 MHz, CDCl₃) δ 196.63, 149.37,

129.81, 106.13, 66.69, 64.76, 64.53, 53.84, 46.38. Anal. Calcd. for C₉H₁₂O₄: C, 58.69; H, 6.57. Found: C, 58.42; H, 6.82. LRMS (EI): 184 (M⁺). [α]_D²⁵ -51.0 (c = 1.2, CHCl₃). The enantiomeric excess was determined to be 91% by chiral HPLC analysis (Chiracel AS 85:15 hexanes:ⁱPrOH, 1.0 mL/min, *t*_{r-major} 24.9 min, *t*_{r-minor} 21.5 min). HPLC data for racemic and 91% ee samples are shown below.

210 nm, 4 nm Results		
Retention Time	Area	Area Percent
24.432	29098717	49.981
28.747	29121182	50.019

210 nm, 4 nm Results		
Retention Time	Area	Area Percent
21.525	2221652	4.422
24.880	48016859	95.578

(-)-**20**. Following the general procedure: 5 mol% **11**, 2M in CH₂Cl₂, 0°C, 24 h; Flash chromatography (5% MeOH in EtOAc), 65 mg (99%). Substrate and product were a 3.5:1 mixture of hydroxy epimers. ¹H NMR (400 MHz, acetone-d₆) δ *major diastereomer* 6.70 (dd, *J* = 12.4, 1.5 Hz, 1H), 5.84 (dd, *J* = 12.4, 1.1 Hz, 1H), 4.54 (m, 1H), 4.46 (d, *J* = 5.6 Hz, 1H), 4.27 (m, 1H), 2.98 (s, 1H), 2.80 (dd, *J* = 14.4, 3.6 Hz, 1H), 2.67 (dd, *J* = 14.4, 6.0 Hz, 1H), 2.49 (m, 1H), 1.90 (m, 1H). The following resonances could be observed for the *minor diastereomer* 5.81 (m, 1H), 4.80 (m, 1H), 4.42 (d, *J* = 5.2 Hz, 1H), 4.15 (m, 1H), 2.26 (m, 1H). ¹³C NMR (400 MHz, acetone-d₆) δ *major diastereomer* 198.26, 152.80, 129.77, 66.95, 63.44, 51.87, 45.83; *minor diastereomer* 198.67, 152.62, 129.15, 65.98, 62.90, 52.19, 45.30. Anal. Calcd. for C₇H₁₀O₃: C, 59.14; H 7.09. Found: C, 58.79; H, 7.28. [α]_D²⁵ -109.8 (c = 1.2, MeOH). The enantiomeric excess was determined to be 87% by chiral HPLC analysis (Chiracel AS 85:15 hexanes:EtOH, 1.0 mL/min, *t*_{r-major} 14.3 min, *t*_{r-minor} 8.7 min). HPLC data for racemic and 87% ee samples are shown below.

211 nm, 4 nm Results		
Retention Time	Area	Area Percent
7.573	4764509	22.358
8.763	8187596	38.420
14.496	8358418	39.222

210 nm, 4 nm Results		
Retention Time	Area	Area Percent
7.435	7377138	20.929
8.725	1867525	5.298
14.309	26003994	73.773

(-)-22. Following the general procedure: 5 mol% **11**, 1M in CH₂Cl₂, rt, 12 h; Flash chromatography (1:1 Et₂O:CH₂Cl₂), 83 mg (83%). ¹H NMR (400 MHz, CDCl₃) δ 6.62 (dd, *J* = 12.4, 4.0 Hz, 1H), 5.98 (d, *J* = 12.4 Hz, 1H), 4.48 (m, 1H), 4.33 (m, 1H), 3.17 (d, *J* = 8.0 Hz, 1H), 2.88 (dd, *J* = 15.2, 6.0 Hz, 1H), 2.70 (dd, *J* = 15.2, 2.8 Hz, 1H), 2.31 (m, 2H), 0.89 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 199.3, 147.8, 130.6, 68.1, 65.7, 52.2, 43.1, 25.6, 17.9, -4.9. [α]_D²⁵ -101.4 (c = 0.5, CH₂Cl₂). The enantiomeric excess was determined to be 99% by chiral HPLC analysis (Chiralcel OD-H, 98:2 hexanes/EtOH, 1.5 mL/min, 230 nm, *t*_{r-major} 9.7 min, *t*_{r-minor} 10.4 min). HPLC chromatograms for both racemic and 99% ee samples are shown below. Using pseudoenantiomeric catalyst **14** provided (4*R*,6*S*)-**X** in 91% ee.

(-)-22b. To a solution of 29 mg (0.11 mmol) of **22**, 2 mg (0.011 mmol) of 4-(*N,N*-dimethylamino)-pyridine and 50 μL (0.33 mmol) of triethylamine in 3 mL of CH₂Cl₂ was added 11 mg (0.14 mmol) of acetyl chloride dropwise at rt. After 12 h, the reaction was quenched with 1 M HCl (15 mL) and diluted with Et₂O (15 mL). The organic layer was separated and washed with saturated NaHCO₃ (15 mL), brine and dried with Na₂SO₄. Solvent was evaporated and the crude product was purified by flash chromatography with CH₂Cl₂ to afford 24 mg (73%) of the product as a clear oil. Spectral data corresponds to that previously reported.² ¹H NMR (400 MHz, CDCl₃) δ 6.53 (dt, *J* = 12.4, 1.6 Hz, 1H), 6.03 (dd, *J* = 12.4, 1.6 Hz, 1H), 5.56 (dt, *J* = 11.2, 1.6 Hz, 1H), 4.31 (m, 1H), 2.80 (m, 2H), 2.45 (m, 1H), 2.10 (s, 3H), 2.02 (m, 1H), 0.84 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); [α]_D²⁵ -30.2 (c = 1.0, CHCl₃). (Lit.: [α]_D²⁵ -30.0 (c = 1.0, CHCl₃, >95% ee) for (4*S*, 6*R*) configuration).²

(-)-24. Following the general procedure: 10 mol% **11**, 0.07M in CH₂Cl₂, rt, 24 h; Flash chromatography (Et₂O), 61 mg as a 6:1 mixture of α-epimers (90%). ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.15 (m, 10H), 6.86 (dd, *J* = 10.4, 2.4 Hz, 1H), 6.01 (dd, *J* = 10.0,

2.0 Hz, 1H), 4.79 (dd, $J = 8.4, 2.0$ Hz, 1H), 4.53 (d, $J_{AB} = 12.0$ Hz, 1H), 4.48 (d, $J_{AB} = 12.0$ Hz, 1H), 4.43 (d, $J_{AB} = 12.0$ Hz, 1H), 4.34 (d, $J_{AB} = 12.0$ Hz, 1H), 3.80 (t, $J = 9.2$ Hz, 1H), 3.68-3.56 (m, 3H), 3.46 (d, $J = 2.8$ Hz, 1H), 2.74 (dd, $J = 10.0, 5.2$ Hz, 1H), 2.60 (ddd, $J = 10.0, 8.8, 5.2$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 199.6, 152.0, 137.6, 137.2, 128.5, 128.41, 128.36, 128.0, 127.7, 127.5 (two coincident resonances in the 127-128 region), 73.5, 73.2, 71.5, 68.9, 68.5, 47.6, 44.4. Anal. Calcd. for $\text{C}_{22}\text{H}_{24}\text{O}_4$: C, 74.98; H, 6.86. Found: C, 74.68; H, 6.99. $[\alpha]_{\text{D}}^{25} -20.2$ ($c = 2.3$, CH_2Cl_2). The enantiomeric excess for major diastereomer was determined to be 96%; 99% ee for minor diastereomer (Chiralcel OD-H, 98:2 hexanes/EtOH, 1.5 mL/min, 230 nm, $t_{\text{r-major}}$ 38.0 min, $t_{\text{r-minor}}$ 35.1 min). HPLC chromatograms for both racemic and 96% ee samples are shown below.

(+)-26. Following the general procedure: 10 mol% **11**, 0.08M in CH_2Cl_2 , rt, 36 h; Flash chromatography (3:1 CH_2Cl_2 :Et₂O), 41 mg as a >50:1 mixture of α -epimers (76%). ^1H NMR (400 MHz, CDCl_3) δ 6.99 (dd, $J = 10.0, 2.0$ Hz, 1H), 5.91 (dd, $J = 10.4, 2.0$ Hz, 1H), 4.84 (broad singlet, 1H), 3.98-3.72 (m, 3H), 3.54 (dd, $J = 12.0, 4.0$ Hz, 1H), 3.39 (d, $J = 6.0$ Hz, 1H), 2.76 (dt, $J = 4.8, 4.0$ Hz, 1H), 2.26 (m, 1H), 1.34 (s, 3H), 1.31 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.7, 153.8, 128.2, 101.9, 63.5, 60.9, 59.8, 51.8, 46.4, 24.8, 24.6. We were unable to obtain satisfactory elemental analysis. $[\alpha]_{\text{D}}^{25} +3.2$ ($c = 1.7$, CH_2Cl_2). The enantiomeric excess was determined to be 89% by chiral HPLC analysis (Chiralcel OD-H, 90:10 hexanes/*iso*-propanol, 0.95 mL/min, 230 nm, $t_{\text{r-major}}$ 9.2 min, $t_{\text{r-minor}}$ 8.4 min). HPLC chromatograms for both racemic and 89% ee samples are shown below.

(-)-28. Following the general procedure: 10 mol% **11**, 2 M in CH₂Cl₂, 48 h; Flash chromatography (1:1 hexanes:EtOAc), 67 mg (89%). Analytic data were similar to those previously reported.³ ¹H NMR (400 MHz, CDCl₃) δ 6.91 (dt, *J* = 10.2, 2.0 Hz, 1H), 5.91 (app d, *J* = 10.2 Hz, 1H), 4.52 (m, 1H), 3.05 (d, *J* = 5.3 Hz, 1H), 2.52 (dt, *J* = 17.0, 3.8 Hz, 1H), 2.38-2.27 (m, 2H), 1.95 (m, 1H). ¹³C NMR (400 MHz, CDCl₃) δ 199.33, 153.44, 129.05, 66.24, 35.41, 32.40. LRMS (EI): 112 (M⁺). [α]_D²⁵ -34.4 (c = 1.1, CHCl₃). (Lit.: [α]_D²⁵ -105 (c = 0.2, CHCl₃, >95% ee) for 4S configuration³). The enantiomeric excess of this product was determined after acetylation (see below).

(-)-28b. To a solution of **28** (20 mg, 0.18 mmol) in 0.4 mL dry CH₂Cl₂ at room temperature was added Et₃N (0.25 mL, excess) and DMAP (ca. 1 mg, cat.) followed by Ac₂O dropwise (80 μL, 0.9 mmol, 5 equivalents). After 1 h the mixture was diluted with ether (10 mL), washed with NaHCO₃, brine and dried (MgSO₄). Concentration and chromatography of the crude residue (3:1 hexanes:EtOAc) gave **28b** (20 mg, 72%). Analytic data were similar to those previously reported.⁴ ¹H NMR (400 MHz, CDCl₃) δ 6.87 (app d, *J* = 10.4 Hz, 1H), 6.06 (app d, *J* = 10.4 Hz, 1H), 5.58 (m, 1H), 2.62 (m, 1H), 2.50-2.32 (m, 2H), 2.12 (s, 3H), 2.11 (m, 1H). ¹³C NMR (400 MHz, CDCl₃) δ 197.89, 170.31, 147.67, 130.87, 67.78, 35.00, 28.71, 21.03. Anal. Calcd. for C₈H₁₀O₃: C, 62.33; H, 6.54. Found: C, 61.94; H, 6.69. [α]_D²⁵ -45.8 (c = 1.0, CHCl₃) (Lit.: [α]_D²⁵ -71 (c = 0.9, CHCl₃, >95% ee) for 4S configuration⁴). The enantiomeric excess was determined to be 50% by chiral HPLC analysis (Chiracel AS 80:20 hexanes:EtOH, 1.0 mL/min, *t*_{R-major} 13.1 min, *t*_{R-minor} 8.5 min). HPLC data for racemic and 50% ee shown below.

210 nm, 4 nm Results

Retention Time	Area	Area Percent
9.008	31627103	49.169
14.144	32696349	50.831

211 nm, 4 nm Results

Retention Time	Area	Area Percent
8.453	11891478	25.181
13.115	35331842	74.819

(-)-30. Following the general procedure: 5 mol% **11**, 1M in CH₂Cl₂, 0°C, 3 d; Flash chromatography (1:1 hexanes:EtOAc), 38 mg as a 4:1 mix of α-epimers (76%). ¹H NMR (400 MHz, CDCl₃) δ *major diastereomer* 6.90 (dd, *J* = 10.3, 2.7 Hz, 1H), 6.04 (d, *J* = 10.3 Hz, 1H), 4.88-4.74 (m, 4H), 4.35 (br s, 1H), 3.90 (dd, *J* = 6.6, 2.8 Hz, 1H), 3.74 (m, 1H), 3.48 (s, 3H), 3.40 (s, 3H). The following resonances could be observed for the *minor diastereomer*

6.08 (m, 1H), 4.93 (d, $J = 6.8$, 1H), 4.50 (br s, 1H), 4.22 (m, 1H), 3.53 (s, 3H), 3.50 (s, 3H). ^{13}C NMR (400 MHz, CDCl_3) δ *major diastereomer* 195.36, 148.69, 127.65, 97.10, 95.92, 82.29, 77.20, 67.74, 55.95, 55.84. *minor diastereomer* 196.10, 149.06, 127.57, 98.47, 97.04, 87.25, 77.92, 71.21, 56.14, 56.00. This compound was not suitable for mass spectral analysis (decomposition by FAB or EI methods). We were unable to obtain satisfactory elemental analysis. $[\alpha]_{\text{D}}^{25} -139.1$ ($c = 1.6$, CHCl_3). The enantiomeric excess was determined to be 70% by chiral HPLC analysis (Chiracel OJ 92:8 hexanes:EtOH, 1.0 mL/min, $t_{\text{r-major}}$ 20.2 min, $t_{\text{r-minor}}$ 16.5 min).

Retention Time	Area	Area Percent
11.771	248933	2.544
12.603	274175	2.802
15.723	4622942	47.246
19.141	4638805	47.408

Retention Time	Area	Area Percent
16.533	1082787	15.134
20.224	6071749	84.866

(-)-32. Following the general procedure: 10 mol% **11**, 0.08M in CH_2Cl_2 , rt, 24 h; Flash chromatography (2:1 CH_2Cl_2 : Et_2O), 90 mg as a 9:1 mixture of α -epimers (99%). ^1H NMR (400 MHz, CDCl_3) δ 7.69 (d, $J = 8.4$ Hz, 2H), 7.34 (d, $J = 8.4$ Hz, 2H), 6.88 (dd, $J = 10.4$, 2.4 Hz, 1H), 5.92 (dd, $J = 10.0$, 1.6 Hz, 1H), 4.28 (broad singlet, 1H), 3.57 (dd, $J = 10.0$, 2.8 Hz, 1H), 3.50 (t, $J = 10.4$ Hz, 1H), 3.40 (dd, $J = 10.4$, 8.4 Hz, 1H), 3.28 (dd, $J = 10.0$, 5.6 Hz, 1H), 3.11 (d, $J = 5.6$ Hz, 1H), 2.87 (dd, $J = 16.0$, 8.8 Hz, 1H), 2.67 (m, 1H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 195.3, 151.5, 144.1, 133.0, 129.9, 127.9, 127.4, 64.6, 50.8, 48.4, 46.4, 46.2, 21.5. Anal. Calcd. for $\text{C}_{15}\text{H}_{17}\text{NO}_4\text{S}$: C, 58.61; H, 5.57; N, 4.56. Found: C, 58.44; H, 5.69; N, 4.47. $[\alpha]_{\text{D}}^{25} -15.0$ ($c = 2.0$, CH_2Cl_2). The enantiomeric excess of this product was determined after conversion to its TBS ether (see below).

(-)-32b. To a solution of 48 mg (0.16 mmol) of **32** and 50 μL (0.32 mmol) of 2,6-lutidine in 2 mL of CH_2Cl_2 was added 55 μL (0.24 mmol) of *tert*-butyldimethylsilyl chloride at room temperature. After 30 min the reaction was treated with 5 mL of 1 M of HCl and 10 mL of Et_2O . The organic layer was separated and washed with NaHCO_3 (15 mL), brine and dried with Na_2SO_4 . Solvent was evaporated and the crude product was purified by flash chromatography with CH_2Cl_2 to afford the product as colorless crystals. ^1H NMR (400 MHz, CDCl_3) δ 7.70 (d, $J = 8.4$ Hz, 2H), 7.32 (d, $J = 8.4$ Hz, 2H), 6.75 (dd, $J = 10.0$, 2.8 Hz, 1H), 5.90 (dd, $J = 10.4$, 1.6 Hz, 1H), 4.30 (dt, $J = 6.8$, 2.4 Hz, 1H), 3.54-3.43 (m 2H), 3.37 (dd, $J = 10.0$, 4.0 Hz, 1H), 3.25 (dd, $J = 10.0$, 6.0 Hz, 1H), 2.85 (dd, $J = 15.2$, 8.4 Hz, 1H), 2.65 (m, 1H), 2.43 (s, 3H), 0.89 (s, 6H), 0.12 (s, 3H), 0.11 (s,

3H); ^{13}C NMR (100 MHz, CDCl_3) δ 195.3, 151.3, 143.8, 133.4, 129.8, 127.6, 127.5, 65.3, 50.5, 48.4, 46.8, 46.1, 25.6, 21.5, 17.9, -4.5, -4.8. Anal. Calcd. for $\text{C}_{21}\text{H}_{31}\text{NO}_4\text{SSi}$: C, 59.82; H, 7.41; N, 3.32. Found: C, 60.10; H, 7.70; N, 3.26. $[\alpha]_{\text{D}}^{25}$ -37.5 ($c = 0.32$, CH_2Cl_2). The enantiomeric excess was determined to be 89% by chiral HPLC analysis (Chiralcel OD-H, 98:2 hexanes/*iso*-propanol, 1.5 mL/min, 230 nm, $t_{\text{r-major}}$ 23.5 min, $t_{\text{r-minor}}$ 17.2 min). HPLC chromatograms for both racemic and 73% ee samples are shown below.

Procedure for a one pot asymmetric 1,4-dioxygenation. A solution of 1,3-cycloheptadiene (100 μL , 0.92 mmol) in 2 mL CH_2Cl_2 with added 5,10,15,20-tetraphenyl-21H,23H-porphine (TPP, 1 mg) was cooled to 0°C . The reaction mixture was photolyzed (projection lamp attached to variable voltage supply, 80V) while oxygen was bubbled through the solution. After 30 min, oxygen addition and photolysis were ceased and the solution was treated with **11** (17 mg, 5 mol%). After 12 h no endoperoxide was visible by TLC. The reaction was concentrated and the crude residue purified by flash column chromatography (1:1 hexanes:EtOAc) to give **36** (104 mg, 90%). Analytic data were similar to those previously reported.⁵ (-)-**36**. ^1H NMR (400 MHz, CDCl_3) δ 6.56 (dd, $J = 12.4, 2.8$ Hz, 1H), 5.91 (dd, $J = 12.4, 2.4$ Hz, 1H), 4.54 (br s, 1H), 2.86 (m, 1H), 2.56 (m, 2H), 2.19 (m, 1H), 1.82 (m, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 203.7, 149.7, 129.7, 70.4, 43.1, 35.1, 18.3, $[\alpha]_{\text{D}}^{25}$ -117.1 ($c = 0.7$, CH_2Cl_2). The enantiomeric excess of this product was determined after acetylation (see below).

(-)-**36b**. To a solution of (-)-**36** (104 mg, 0.83 mmol) in 3 mL dry CH_2Cl_2 was added DMAP (1 mg, cat.) and Et_3N (400 μL , 2.7 mmol) followed by acetic anhydride (180 μL , 1.9 mmol) dropwise. After 2 h, the reaction mixture was diluted with ether and saturated NaHCO_3 . After separation, the aqueous layer was extracted with ether (2X, 20 mL) and the combined organics were washed with saturated NaHCO_3 and brine and dried (MgSO_4). Concentration and flash

chromatography provided **36b** (130 mg, 94%) as a colorless oil. Analytic data were similar to those previously reported.⁶ ¹H NMR (300 MHz, CDCl₃) δ 6.43 (ddd, *J* = 12.6, 3.3, 0.9 Hz, 1H), 6.02 (dd, *J* = 12.6, 2.1 Hz, 1H), 5.57 (m, 1H), 2.62 (m, 2H), 2.20 (m, 1H), 2.10 (s, 3H), 1.85 (m, 3H); [α]_D²⁵ -101.4 (c = 0.5, CH₂Cl₂) (Lit.: [α]_D²⁵ +106.9 (c = 1.0, CHCl₃, >98% ee) for (4*R*) configuration⁶). The enantiomeric excess was determined to be 92% by chiral HPLC analysis (Chiracel AD-H 96:4 hexanes:ⁱPrOH, 1.5 mL/min, *t*_{r-major} 7.3 min, *t*_{r-minor} 10.0 min). HPLC data for racemic and 92% ee traces are shown below. Note: retention time changes are a result of a new AD-H column and guard column. Alternatively **36** was prepared by reaction of the pure isolated endoperoxide in similar ee (91%).

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Appendix A. Additional screening data for the desymmetrization of endoperoxide **27**.

Table 1. Selected Chiral Base Catalyzed Desymmetrizations of 3,6-Epiperoxycyclohexane.

	Entry	Base	Solvent	ee
B	1	A	MeCN	N.R.
	2	B	DCM/ MeOH	N.R.
	3	C	DCM	N.R.
	4	C	MeCN	N.R.
	5	C	THF	N.R.
	6	D	Benzene	N.R.
D	7	D	DCM	N.R.
	8	D	THF	N.R.
	9	D	MeOH	N.R.
	10	E	Acetone	0 %
F	11	F	DCM	0 %
	12	G	THF	0 %
	13	H	MeCN	0 %
	14	I	MeOH	6 %
	15	J	EtOAc	9 %
	16	K	DCM	N.R.
H	17	K	MeCN	6 %
	18	L	DCM	N.R.
	19	L	Acetone	17 %
	20	L	EtOAc	19 %
	21	M	MeOH	8 %
	22	N	EtOAc	N.R.

^aReactions run using ~10 mol % catalyst loadings ~0.5 M in peroxide (0.2-0.3 mmol of peroxide) at room temperature

^b ee's determined by HPLC (chiralpak AS)

Appendix B. Additional screening data for the desymmetrization of endoperoxide **4**.

Table 2. Examples of other chiral bases/conditions for the desymmetrization.

Reaction scheme showing the conversion of an endoperoxide (a cyclooctane ring with two adjacent peroxide bridges) to a cyclooct-2-en-1-ol-8-one derivative (a cyclooctane ring with a double bond, a hydroxyl group, and a ketone group).

Chemical structure of (DHQD)(9-PHEN), showing a fluorene derivative with an OR group at the 9-position.

Chemical structure of (DHQD)(MeQ), showing a quinoline derivative with an OR group at the 2-position.

Chemical structure of endoperoxide **4**, showing a complex bicyclic peroxide with a quinoline moiety.

R = dihydroquinidine

Chemical structure of chiral base **1**, a bis-dimethylammonium salt with two methoxy groups.

Chemical structure of chiral base **2**, a chiral diol derivative with a dimethylammonium group.

Chemical structure of chiral base **3**, a cyclic amide derivative.

Entry	Base	Solvent	Yield	ee
1	(DHQD) ₂ AQN	acetone	56 %	68 %
2	(DHQD) ₂ AQN	DCE	27 %	62 %
3	(DHQD) ₂ AQN	MeCN	67 %	63 %
4	(DHQD) ₂ AQN	MeOH	60 %	74 %
5	(DHQD) ₂ AQN	EtOAc	67 %	72 %
6	(DHQD) ₂ AQN	CF ₃ CH ₂ OH	83 %	54 %
7	(DHQD) ₂ AQN	iPrOAc	67 %	72 %
8 ^a	Quinidine	EtOAc	51 %	10 %
9	(DHQD) ₂ PHAL	EtOAc	38 %	32 %
10	(DHQD) ₂ PYR	EtOAc	N.D.	
11	(DHQD)(9-PHEN)	DCM	50 %	55 %
12	(DHQD)(9-PHEN)	EtOAc	50 %	49 %
13	(DHQD)(9-PHEN)	MeOH	75 %	26 %
14	(DHQD)(9-PHEN)	THF	81 %	46 %
15	(DHQD)(MeQ)	DCM	94 %	14 %
16	(DHQD)(MeQ)	EtOAc	30 %	21 %
17	(DHQD)(MeQ)	MeOH	100 %	5 %
18	Nicotine	DCM	38 %	0 %
19	Nicotine	MeOH	88 %	0 %
20	1	DCM	75 %	0 %
21	1	MeOH	88 %	0 %
22	2	DCM	38 %	0 %
23	3	DCM	75 %	0 %
24	4	DCM	94 %	25 %
25	4	EtOAc	89 %	28 %
26	4	MeOH	98 %	26 %

Appendix C. ^1H and ^{13}C NMR data for the γ -hydroxyenone products.

^1H NMR (CDCl_3) of (+)-5

^{13}C NMR (CDCl_3) of (+)-5

¹H NMR (CDCl₃) of (+)-16

¹³C NMR (CDCl₃) of (+)-16

¹H NMR (CDCl₃) of (-)-18

¹³C NMR (CDCl₃) of (-)-18

¹H NMR (CDCl₃) of (-)-20

¹³C NMR (CDCl₃) of (-)-20

¹H NMR (CDCl₃) of (-)-22

¹³C NMR (CDCl₃) of (-)-22

¹H NMR (CDCl₃) of (-)-24

¹³C NMR (CDCl₃) of (-)-24

¹H NMR (CDCl₃) of (+)-26

^{13}C NMR (CDCl_3) of (+)-26

¹H NMR (CDCl₃) of (-)-28

¹³C NMR (CDCl₃) of (-)-28

¹H NMR (CDCl₃) of (-)-30

¹³C NMR (CDCl₃) of (-)-30

¹H NMR (CDCl₃) of (-)-32

¹³C NMR (CDCl₃) of (-)-32

¹H NMR (CDCl₃) of (-)-36

¹³C NMR (CDCl₃) of (-)-36