

Catalytic Asymmetric Epoxidation of Cyclic Enones

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Supporting Information

General Remarks: All reactions were carried out under argon atmosphere in oven-dried and/or flame-dried glassware with magnetic stirring. Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All solvents employed in the reactions were distilled from appropriate drying agent prior to use. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Reactions were monitored by thin-layer chromatography (TLC) on silica gel precoated glass plates (0.25 mm thickness, 60F-254, E. Merck). Chromatograms were visualized by fluorescence quenching with UV light at 254 nm or by staining using anisaldehyde or ninhydrin stains. Flash column chromatography was performed using E. Merck silica gel 60 (particle size 0.040 - 0.063 mm). Chemical yields refer to pure isolated substances. Since most products are volatile, the isolated yields are in general slightly reduced. ¹H and ¹³C NMR spectra were recorded on either a Bruker DPX-300 or AV-400 spectrometer. Chemical shifts are reported in ppm relative to tetramethylsilane with the solvent resonance as the internal standard. The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. MS (EI): Mass spectra were measured on a Finnigan MAT 8200 (70 eV) and an Agilent 5973 (70 eV) by electron ionization, chemical ionization, of fast atom/ion

bombardment techniques. Accurate mass determinations were obtained on a Bruker APEX III FT-MS (7 T magnet). Gas chromatography (GC) was performed on Hewlett-Packard 6890 and 5890 Series or Agilent 6890N gas chromatographs equipped with a split-mode capillary injection system and flame ionization detectors using stationary columns¹ specified in the individual experiments. High performance liquid chromatography (HPLC) was performed on a Shimadzu LC-10A HPLC-system equipped with a spectrophotometric detector (monitoring at 220 nm) using a Chiralpak IA column. Optical rotations were measured on a PerkinElmer 343 polarimeter, and $[\alpha]_D$ values are reported in $10^{-1} \text{ dg cm}^2 \text{ g}^{-1}$; concentration (c) is reported in g/100 ml. Racemic epoxides described in this paper were prepared by Weitz-Scheffer epoxidation of the corresponding enones with H_2O_2 according to the procedure of Huang *et al.*² The enantiomeric ratios (*er*) of epoxides **3a-o** were determined by GC or HPLC analysis specified in the individual experiment, by comparing the samples with the appropriate racemic mixtures. The absolute configuration of **3a** was determined by measuring its optical rotation and comparison with the literature.^{3a} All other absolute configurations were assigned by analogy.

¹ BGB-176/BGB-15 (30 m × 0.25 mm): 2,3-dimethyl-6-*tert*-butyldimethylsilyl- β -cyclodextrin. BGB-178/OV-1701 (30 m × 0.25 mm): 2,3-diethyl-6-*tert*-butyl- β -cyclodextrin. Hydrodex- β -TBDAC (25 m × 0.25 mm): heptakis-(2,3-di-O-acetyl-6-O-*tert*-butyldimethylsilyl)- β -cyclodextrin. Lipodex E (25 m × 0.25 mm): octakis-(2,6-di-O-pentyl-3-O-butyryl)- γ -cyclodextrin. Optima-5-Accent (30 m × 0.25 mm) and RTX 5 (28 m × 0.25 mm): 5% diphenyl-95% dimethyl polysiloxane.

² Ouyang, X.-Y.; Jiang, H.-F.; Huang, J.-M. *Chin. J. Chem.* **2006**, *24*, 1480-1482.

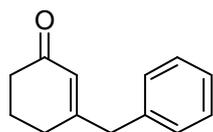
³ (a) Wynberg, H.; Marsman, B. *J. Org. Chem.* **1980**, *45*, 158-161. (b) Baba, N.; Oda, J.; Kawaguchi, M. *Agric. Biol. Chem.* **1986**, *50*, 3113-3117. (c) Aoki, M.; Seebach, D. *Helv. Chim. Acta* **2001**, *84*, 187-207.

Preparation of the Catalysts

(1*R*,2*R*)-DPEN was purchased from Aldrich. Chiral binaphthol derived phosphoric acids were prepared according or in analogy to the reported procedures.^{4,5} 9-Amino-9-deoxyepiquinine and 9-Amino-9-deoxyepiquinidine were prepared following the procedure of Soós *et al.*⁶

Preparation of the Substrates

Cyclohex-2-enone (**2a**), 4,4-dimethylcyclohex-2-enone (**2b**), isophorone (**2d**), 3-methylcyclohex-2-enone (**2e**), cyclohept-2-enone (**2i**) and cyclopent-2-enone (**2o**) were purchased from Aldrich. Other cyclic α,β -unsaturated ketones were prepared according to literature procedures⁷ or as described below and physical data were in agreement with the literature.



3-Benzylcyclohex-2-enone (2j): General Procedure: A flame-dried flask was charged with benzylmagnesium chloride (42.8 mmol, 1.0 M in Et₂O) and cooled to 0 °C.

3-Ethoxycyclohex-2-enone (3.0 g, 21.4 mmol) in THF (15 mL) was added dropwise to the Grignard reagent. Once the addition was complete the reaction mixture was left at room temperature until complete disappearance of the starting material. After 18 h the reaction was slowly quenched with 1 N HCl (100 mL) at 0 °C. The aqueous phase was separated and extracted with Et₂O (3 × 25 mL). The combined organic phase was washed successively with a saturated aqueous solution of NaHCO₃, water, and brine, dried (Na₂SO₄), filtered, and concentrated *in vacuo*. The product was purified by flash

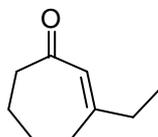
⁴ (a) Akiyama, T.; Itoh, J.; Yokota, K.; Fuchibe, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 1566-1568. (b) Akiyama, T.; Morita, H.; Itoh, J.; Fuchibe, K. *Org. Lett.* **2005**, *7*, 2583-2585; also see: (c) T. Akiyama, PCT Int. Appl. WO 200409675, 2004. (d) Akiyama, T.; Saitoh, Y.; Morita, H.; Fuchibe, K. *Adv. Synth. Catal.* **2005**, *347*, 1523-1526.

⁵ (a) Uraguchi, D.; Terada, M. *J. Am. Chem. Soc.* **2004**, *126*, 5356-5357. (b) Uraguchi, D.; Sorimachi, K.; Terada, M. *J. Am. Chem. Soc.* **2004**, *126*, 11804-11805. (c) Uraguchi, D.; Sorimachi, K.; Terada, M. *J. Am. Chem. Soc.* **2005**, *127*, 9360-9361; also see: (d) Terada, M.; Uraguchi, D.; Sorimachi, K.; Shimizu, H. PCT Int. Appl. WO 2005070875, 2005.

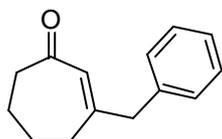
⁶ Vakulya, B.; Varga, S.; Csámpai, A.; Soós, T. *Org. Lett.* **2005**, *7*, 1967-1969.

⁷ (a) Martin, N. J. A.; List, B. *J. Am. Chem. Soc.* **2006**, *128*, 13368-13369. (b) Bergma, R.; Magnusson, G. *J. Org. Chem.* **1986**, *51*, 212-217.

chromatography (20% Et₂O in pentane) to provide the title compound as a pale yellow oil (3.0 g, 76% yield). The physical data were identical in all respect to those previously reported.⁸



3-Ethylcyclohept-2-enone (2m): The general procedure for the preparation of substrates using 3-ethoxycyclohept-2-enone (obtained from cycloheptane-1,3-dione (1.00 g, 7.93 mmol) according to the procedure of de Meijere *et al.*⁹) and ethylmagnesium bromide (15.9 mmol, 3.0 M in Et₂O) in THF (8 mL) gave after 18 h and silica gel column chromatography (20% Et₂O in pentane) the title compound as a pale yellow oil (0.57 g, 52% overall yield). ¹H NMR (400 MHz, CD₂Cl₂): δ 1.08 (t, *J* = 7.4 Hz, 3H), 1.72-1.81 (m, 4H), 2.22 (q, *J* = 7.4 Hz, 2H), 2.41 (t, *J* = 6.1 Hz, 2H), 2.52 (t, *J* = 5.8 Hz, 2H), 5.83 (s, 1H). ¹³C NMR (75 MHz, CD₂Cl₂): 204.1, 164.0, 128.4, 42.7, 34.3, 33.1, 25.7, 21.9, 12.5. MS (EI): *m/z* (%) = 138 (29), 109 (100), 96 (18), 81 (32), 79 (10), 67 (17), 53 (17), 39 (20), 27 (17). HRMS: exact mass calculated for [M]⁺ (C₉H₁₄O₁) requires *m/z* 138.104492, found *m/z* 138.104462.



3-Benzylcyclohept-2-enone (2n): The general procedure for the preparation of substrates using 3-ethoxycyclohept-2-enone⁹ (obtained from cycloheptane-1,3-dione (0.85 g, 6.75 mmol)) and benzylmagnesium chloride (13.5 mmol, 1.0 M in Et₂O) in THF (5 mL) gave after 18 h and silica gel column chromatography (20% Et₂O in pentane) the title compound as a pale yellow oil (0.55 g, 41% overall yield). The physical data were identical in all respect to those previously reported.¹⁰

⁸ Jubert, C.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 5425-5431.

⁹ Hadjirapoglou, L.; Klein, I.; Spitzner, D.; de Meijere, A. *Synthesis* **1996**, *4*, 525-528.

¹⁰ Waske, P. A.; Mattay, J. *Tetrahedron* **2005**, *61*, 10321-10330.

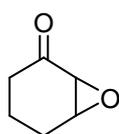
General Experimental Procedure for the Catalytic Enantioselective Epoxidation of Enones

Catalyst salts **1** were prepared in situ by stirring chiral primary amines (10 mol%) and respective acids (10-20 mol%) in dioxane (2-4 mL) for 20 minutes at room temperature. Then, the enones (**2a-o**, 0.5-1 mmol) were added followed by the addition of aqueous hydrogen peroxide (1.5 equiv., 0.75-1.5 mmol, 50% w/w in water) after another 20 minutes interval of stirring. After 20 ~ 72 h at 30 ~ 50°C, the reaction mixture was cooled to 0°C, and a 10% aqueous solution of NaHSO₃ (5 mL) was added. Then the reaction mixture was diluted with diethyl ether (10 mL), and the aqueous phase was extracted with Et₂O (3×10 mL). The combined organic phases were washed with brine, dried (Na₂SO₄) and filtered. For the highly volatile product **3o**, the resulting solution was analyzed by GC for yield (using commercially available 2,3-epoxycyclohexanone as internal standard) and enantiomeric ratio determination. Evaporation of the solvents furnished the crude products, which were purified by silica gel column chromatography to provide pure α,β -epoxyketones (**3a-o**).

Conditions A: 0.5 mmol scale with respect to the enone. Catalyst salt **1g** was used, which was prepared from (*R,R*)-DPEN (10.6 mg, 0.05 mmol, 10 mol%) and *S*-TRIP (37.6 mg, 0.05 mmol, 10 mol%).

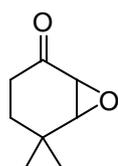
Conditions B: 1.0 mmol scale with respect to the enone. Catalyst salt **1j** was used, which was prepared from 9-amino-9-deoxyepiquinine (8.1 mg, 0.1 mmol, 10 mol%) and TFA (15.3 μ L, 0.2 mmol, 20 mol%).

Conditions C: 1.0 mmol scale with respect to the enone. Catalyst salt **1k** was used, which was prepared from 9-amino-9-deoxyepiquinidine (8.1 mg, 0.1 mmol, 10 mol%) and TFA (15.3 μ L, 0.2 mmol, 20 mol%).

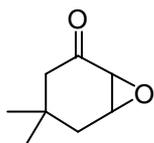


2,3-Epoxycyclohexanone (3a): **Conditions A:** The conversion was determined to be 96% by GC using Optima-5-Accent column (40 °C, 5 min at 40°C, 5.0 °C/min, until 100 °C, 25 °C/min, until 250 °C, 1.0 min at 250°C, 0.35 bar He. Starting material: t_R = 12.35 min, product: t_R = 15.66 min) after 48

h at 35 °C. **3a** was isolated and silica gel column chromatography (5-10% Et₂O in pentane) as a clear liquid (76 mg, 68%, with respect to 1.0 mmol **2a**; reduced yield due to high volatility). The physical data were identical in all respect to those previously reported.³ The enantiomeric ratio was determined to be 96:4 by GC using a chiral BGB-178/BGB-1701 column (80 °C, 1.2 °C/min, until 105 °C, 20 °C/min, until 220 °C, 10 min at 220 °C, 0.5 bar H₂). Major enantiomer: t_R = 16.62 min, minor enantiomer: t_R = 16.23 min. The absolute configuration [2*R*,3*R*] of **3a** was determined by measuring its optical rotation and comparison with literature values, [α]²³₅₈₉ = +101.2 (c 1.0, CH₂Cl₂), 92.0% ee [Lit. (2*S*,3*S*)-(-)-epoxycyclohexanone, [α]¹⁷₅₇₈ = -38.0 (c 0.82, CH₂Cl₂), 20% ee].^{3a} **Conditions B:** The conversion was determined to be 91% by GC using Optima-5-Accent column (40 °C, 5 min at 40°C, 5.0 °C/min, until 100 °C, 25 °C/min, until 250 °C, 1.0 min at 250°C, 0.35 bar He. Starting material: t_R = 12.34 min, product: t_R = 15.65 min) after 24 h at 30 °C. **3a** was isolated as a clear liquid (65 mg, 58%; reduced yield due to high volatility). The enantiomeric ratio was determined to be 97:3 by GC using a chiral BGB-178/BGB-1701 column (80 °C, 1.2 °C/min, until 105 °C, 20 °C/min, until 220 °C, 10 min at 220 °C, 0.5 bar H₂). Major enantiomer: t_R = 15.94 min, minor enantiomer: t_R = 17.02 min.

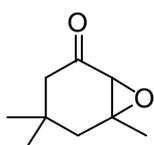


4,4-Dimethyl-2,3-epoxycyclohexanone (3b): Conditions A: The title compound was isolated after 48 h at 35 °C and silica gel column chromatography (2% Et₂O in pentane) as a clear liquid (56 mg, 80%). ¹H NMR (300 MHz, CDCl₃): δ 1.04 (s, 3H), 1.19 (s, 3H), 1.29-2.43 (m, 4H), 3.15 (dd, J₁ = 3.9 Hz, J₂ = 0.9 Hz, 1H), 3.21 (d, J = 3.9 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 206.3, 64.5, 56.3, 33.5, 31.2, 30.3, 27.8, 23.2. MS (EI): m/z (%) = 140 (14), 124 (2), 111 (20), 97 (27), 85 (58), 69 (100), 55 (73), 43 (29), 41 (95), 39 (32), 29 (31). HRMS: exact mass calculated for [M]⁺ (C₈H₁₂O₂) requires m/z 140.083903, found m/z 140.083728. The enantiomeric ratio was determined to be 97:3 by GC using a chiral Hydrodex-β-TBDAC column (80 °C, 1.5 °C/min, until 170 °C, 20 °C/min, 10 min at 220 °C, 0.6 bar H₂). Major enantiomer: t_R = 25.75 min, minor enantiomer: t_R = 21.91 min.



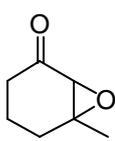
5,5-Dimethyl-2,3-epoxycyclohexanone (3c): Conditions A: The title compound was isolated after 48 h at 35 °C and silica gel column chromatography (3.3% Et₂O in pentane) as a clear liquid (53 mg, 76%).

¹H NMR (300 MHz, CD₂Cl₂): δ 0.93 (s, 3H), 1.03 (s, 3H), 1.77-2.66 (m, 4H), 3.18 (d, J = 3.6 Hz, 1H), 3.52 (t, J = 3.9 Hz, 1H). ¹³C NMR (75 MHz, CD₂Cl₂): δ 207.9, 57.7, 55.6, 49.3, 37.9, 37.8, 31.4, 28.4. HRMS: exact mass calculated for [M]⁺ (C₈H₁₂O₂) requires m/z 140.083868, found m/z 140.083731. The enantiomeric ratio was determined to be 98:2 by GC using a chiral Hydrodex-β-TBDAC column (80 °C, 1.2 °C/min, until 120 °C, 20 °C/min, until 220 °C, 10 min at 220 °C, 0.5 bar H₂). Major enantiomer: t_R = 29.57 min, minor enantiomer: t_R = 27.55 min.



3,5,5-Trimethyl-2,3-epoxycyclohexanone (3d): Conditions A: The title compound was isolated after 48 h at 50 °C and silica gel column chromatography (1.5% Et₂O in pentane) as a clear liquid (48 mg, 63%).

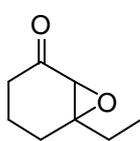
¹H NMR (300 MHz, CDCl₃): δ 0.91 (s, 3H), 1.02 (s, 3H), 1.42 (s, 3H), 1.70 (dd, J₁ = 15.0 Hz, J₂ = 1.5 Hz, 1H), 1.80 (dd, J₁ = 13.2 Hz, J₂ = 0.9 Hz, 1H), 2.07 (d, J = 15.0 Hz, 1H), 2.61 (d, J = 13.2 Hz, 1H), 3.05 (s, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 207.9, 64.2, 61.4, 48.0, 42.7, 36.1, 30.8, 27.8, 24.0. MS (EI): m/z (%) = 154 (30), 139 (33), 126 (17), 111 (12), 97 (25), 83 (100), 69 (50), 55 (39), 43 (40), 41 (64), 29 (23). HRMS: exact mass calculated for [M]⁺ (C₉H₁₄O₂) requires m/z 154.099237, found m/z 154.099382. The enantiomeric ratio was determined to be 96:4 by GC using a chiral Hydrodex-β-TBDAC column (60 °C, 1.0 °C/min, until 90 °C, 20 °C/min, until 220 °C, 10 min at 220 °C, 0.5 bar H₂). Major enantiomer: t_R = 27.80 min, minor enantiomer: t_R = 27.24 min.



3-Methyl-2,3-epoxycyclohexanone (3e): Conditions B: The title compound was isolated after 24 h at 30 °C and silica gel column chromatography (5-10% Et₂O in pentane) as a clear liquid (88 mg, 70%;

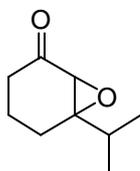
reduced yield due to high volatility). ¹H NMR (400 MHz, CD₂Cl₂): δ 1.42 (s, 3H), 1.58-1.66 (m, 1H), 1.84-2.13 (m, 4H), 2.42 (td, J₁ = 17.6 Hz, J₂ = 4.1 Hz, 1H), 3.01 (s,

1H). ¹³C NMR (75 MHz, CD₂Cl₂): 206.9, 62.8, 62.5, 36.3, 28.9, 22.5, 17.7. MS (EI): *m/z* (%) = 126 (78), 111 (8), 97 (46), 83 (35), 81 (21), 79 (5), 71 (79), 69 (26), 67 (8), 58 (3), 55 (61), 53 (12), 43 (89), 41 (100), 39 (49), 31 (2), 27 (36). HRMS: exact mass calculated for [M]⁺ (C₇H₁₀O₂) requires *m/z* 126.067971, found *m/z* 126.068078. The enantiomeric ratio was determined to be 98:2 by GC using a chiral BGB-178/OV-1701 column (80 °C, 1.2 °C/min, until 105 °C, 20 °C/min, until 220 °C, 10 min at 220 °C, 0.5 bar H₂). Major enantiomer: *t_R* = 16.79 min, minor enantiomer: *t_R* = 19.18 min.



3-Ethyl-2,3-epoxycyclohexanone (3f): Conditions B: The title compound was isolated after 30 h at 50 °C and silica gel column chromatography (5-10% Et₂O in pentane) as a clear oil (102 mg, 73%).

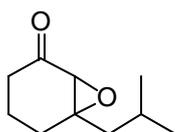
¹H NMR (400 MHz, CD₂Cl₂): δ 0.96 (t, *J* = 7.5 Hz, 3H), 1.61-1.78 (m, 3H), 1.83-1.94 (m, 2H), 1.95-2.12 (m, 2H), 2.45 (td, *J*₁ = 17.4 Hz, *J*₂ = 4.3 Hz, 1H), 3.03 (s, 1H). ¹³C NMR (100 MHz, CD₂Cl₂): 207.1, 66.4, 61.3, 36.6, 29.4, 26.7, 17.9, 9.0. MS (EI): *m/z* (%) = 140 (90), 125 (5), 111 (49), 107 (1), 97 (55), 95 (24), 85 (79), 79 (12), 67 (24), 57 (30), 55 (84), 43 (38), 41 (100), 39 (58), 29 (92), 27 (77). HRMS: exact mass calculated for [M]⁺ (C₈H₁₂O₂) requires *m/z* 140.083556, found *m/z* 140.083732. The enantiomeric ratio was determined to be 98.5:1.5 by GC using a chiral BGB-178/OV-1701 column (80 °C, 1.2 °C/min, until 115 °C, 20 °C/min, until 220 °C, 10 min at 220 °C, 0.5 bar H₂). Major enantiomer: *t_R* = 23.73 min, minor enantiomer: *t_R* = 25.43 min.



3-Isopropyl-2,3-epoxycyclohexanone (3g): Conditions B: The title compound was isolated after 48 h at 50 °C and silica gel column chromatography (5-10% Et₂O in pentane) as a clear oil (121 mg, 79%).

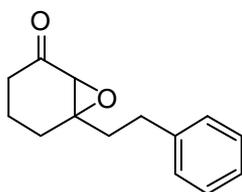
¹H NMR (400 MHz, CD₂Cl₂): δ 0.96 (d, *J* = 7.0 Hz, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 1.60-1.70 (m, 2H), 1.83-1.95 (m, 2H), 1.99-2.11 (m, 2H), 2.46 (td, *J*₁ = 17.3 Hz, *J*₂ = 4.7 Hz, 1H), 3.03 (s, 1H). ¹³C NMR (100 MHz, CD₂Cl₂): 207.2, 69.5, 61.3, 36.8, 34.7, 23.5, 18.3, 18.2, 18.2. MS (EI): *m/z* (%) = 154 (61), 139 (4), 125 (24), 111 (78), 99 (34), 81 (41), 71 (6), 69 (30), 55 (93), 53 (18), 43 (84), 41 (100), 29 (32), 27 (56). HRMS:

exact mass calculated for $[M]^+$ ($C_9H_{14}O_2$) requires m/z 154.099324, found m/z 154.099377. The enantiomeric ratio was determined to be 99:1 by GC using a chiral BGB-178/OV-1701 column (80 °C, 1.2 °C/min, until 120 °C, 20 °C/min, until 220 °C, 10 min at 220 °C, 0.5 bar H_2). Major enantiomer: t_R = 27.79 min, minor enantiomer: t_R = 29.24 min.



3-Isobutyl-2,3-epoxycyclohexanone (3h): Conditions B: The title compound was isolated after 48 h at 50 °C and silica gel column chromatography (5-10% Et_2O in pentane) as a clear oil (123 mg, 73%).

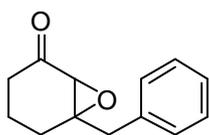
1H NMR (400 MHz, CD_2Cl_2): δ 0.91 (d, J = 6.6 Hz, 3H), 0.96 (d, J = 6.6 Hz, 3H), 1.40 (dd, J_1 = 14.0 Hz, J_2 = 8.1 Hz, 1H), 1.60-1.67 (m, 2H), 1.81-2.11 (m, 5H), 2.45 (td, J_1 = 17.4 Hz, J_2 = 4.3 Hz, 1H), 2.98 (s, 1H). ^{13}C NMR (75 MHz, CD_2Cl_2): 207.1, 65.0, 62.0, 45.6, 36.6, 26.7, 25.6, 23.4, 22.9, 17.9. MS (EI): m/z (%) = 168 (45), 153 (7), 139 (7), 126 (36), 112 (31), 79 (32), 67 (43), 55 (56), 41 (100), 39 (43), 27 (54). HRMS: exact mass calculated for $[M]^+$ ($C_{10}H_{16}O_2$) requires m/z 168.114911, found m/z 168.115034. The enantiomeric ratio was determined to be 98:2 by GC using a chiral BGB-178/OV-1701 column (80 °C, 0.8 °C/min, until 120 °C, 20 °C/min, until 220 °C, 10 min at 220 °C, 0.5 bar H_2). Major enantiomer: t_R = 43.77 min, minor enantiomer: t_R = 45.20 min.



3-Phenethyl-2,3-epoxycyclohexanone (3i): Conditions B: The title compound was isolated after 48 h at 50 °C and silica gel column chromatography (5-10% Et_2O in pentane) as a clear oil (195 mg, 84%).

1H NMR (400 MHz, CD_2Cl_2): δ 1.62-1.71 (m, 1H), 1.87-2.08 (m, 5H), 2.12-2.20 (m, 1H), 2.46 (td, J_1 = 17.0 Hz, J_2 = 4.7 Hz, 1H), 2.74 (t, J = 8.3 Hz, 2H), 3.01 (s, 1H), 7.18-7.23 (m, 3H), 7.27-7.31 (m, 2H). ^{13}C NMR (100 MHz, CD_2Cl_2): 206.7, 141.7, 129.0, 128.8, 126.7, 65.3, 61.6, 38.4, 36.5, 31.4, 27.1, 18.0. MS (EI): m/z (%) = 216 (2), 198 (2), 187 (1), 169 (3), 154 (1), 143 (11), 128 (4), 104 (100), 97 (13), 91 (69), 79 (13), 69 (5), 65 (17), 55 (12), 41 (31). HRMS: exact mass calculated for $[M]^+$ ($C_{14}H_{16}O_2$) requires m/z 216.114905, found m/z 216.115027.

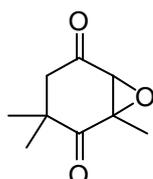
The enantiomeric ratio was determined to be 98.5:1.5 by GC using a chiral BGB-176/BGB-15 column (100 °C, 1.2 °C/min, until 180 °C, 20 °C/min, until 220 °C, 10 min at 220 °C, 0.5 bar H₂). Major enantiomer: t_R = 56.99 min, minor enantiomer: t_R = 58.46 min.



3-Benzyl-2,3-epoxycyclohexanone (3j): Conditions B: The title

compound was isolated after 48 h at 50 °C and silica gel column chromatography (5-10% Et₂O in pentane) as a clear oil (158 mg, 78%). ¹H NMR (400 MHz, CD₂Cl₂): δ 1.58-1.65 (m, 1H), 1.80-1.89 (m, 2H), 1.95-2.10 (m, 2H), 2.44 (td, J_1 = 18.0 Hz, J_2 = 4.4 Hz, 1H), 2.98 (s, 2H), 3.04 (s, 1H), 7.21-7.34 (m, 5H). ¹³C NMR (100 MHz, CD₂Cl₂): 206.6, 136.4, 130.2, 129.0, 127.5, 65.6, 61.0, 42.6, 36.6, 26.9, 17.8. MS (EI): m/z (%) = 202 (60), 184 (5), 173 (53), 156 (4), 145 (12), 129 (46), 117 (21), 91 (100), 78 (11), 65 (28), 55 (28), 51 (15), 39 (36). HRMS: exact mass calculated for [M]⁺ (C₁₃H₁₄O₂) requires m/z 202.099081, found m/z 202.099380. The enantiomeric ratio was determined to be 99:1 by GC using a chiral Hydrodex-β-TBDAC column (100 °C, 1.2 °C/min, until 175 °C, 20 °C/min, until 220 °C, 10 min at 220 °C, 0.4 bar H₂). Major enantiomer: t_R = 45.74 min, minor enantiomer: t_R = 46.65 min.

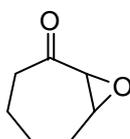
Conditions C: The title compound was isolated after 48 h at 50 °C and silica gel column chromatography (5-10% Et₂O in pentane) as a clear oil (156 mg, 77%). The enantiomeric ratio was determined to be 98.5:1.5 by GC using a chiral Hydrodex-β-TBDAC column (100 °C, 1.2 °C/min, until 175 °C, 20 °C/min, until 220 °C, 10 min at 220 °C, 0.4 bar H₂). Major enantiomer: t_R = 46.37 min, minor enantiomer: t_R = 45.88 min.



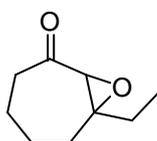
3,5,5-trimethyl-2,3-Epoxycyclohexane-1,4-dione (3k): Conditions B:

The title compound was isolated with 65% yield after silica gel column chromatography (2.5 % Et₂O in pentane) as a clear oil (82 mg, 49%). ¹H NMR (300 MHz, CDCl₃) δ = 1.05 (s, 3H), 1.25 (s, 3H), 1.52 (s, 3H), 2.12 (dd, J_1 = 13.5 Hz, J_2 = 0.9 Hz, 1H), 3.13 (d, J = 14.8 Hz, 1H), 3.46 (s, 1H). ¹³C NMR (75 MHz,

CDCl₃) δ 206.0, 204.5, 65.2, 63.2, 47.4, 45.9, 27.3, 26.4, 16.3. MS (EI): m/z (%) = 168 (59), 153 (27), 125 (65), 85 (77), 83 (21), 69 (34), 56 (100), 43 (91), 41 (95), 39 (41), 27 (34). HRMS: exact mass calculated for [M]⁺ (C₉H₁₂O₃) requires m/z 168.078475, found m/z 168.078643. The enantiomeric ratio was determined to be 96:4 by GC using a chiral BGB-178/OV-1701 column (80 °C, 1.2 °C/min, until 130°C, 20 °C/min, until 220°C, 10 min at 220 °C, 0.5 bar H₂). Major enantiomer: t_R = 19.27 min, minor enantiomer: t_R = 22.67 min.



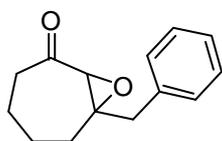
2,3-Epoxycycloheptanone (3l): Conditions A: The title compound was isolated after 20 h at 30 °C and silica gel column chromatography (3.3% Et₂O in pentane) as a clear liquid (43 mg, 82%). The physical data were identical in all respect to those previously reported.¹¹ The enantiomeric ratio was determined to be >99:1 by GC using a chiral Hydrodex- β -TBDAC column (80 °C, 1.5 °C/min, until 120 °C, 20 °C/min, until 220 °C, 10 min at 220°C, 0.6 bar H₂). Major enantiomer: t_R = 23.46 min, minor enantiomer: t_R = 20.62 min.



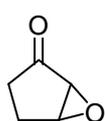
3-Ethyl-2,3-epoxycycloheptanone (3m): Conditions B: The title compound was isolated after 20 h at 50 °C and silica gel column chromatography (5% Et₂O in pentane) as a clear oil (127 mg, 82%). ¹H NMR (400 MHz, CD₂Cl₂): δ 0.93 (t, J = 7.5 Hz, 3H), 1.02-1.13 (m, 1H), 1.49-1.59 (m, 1H), 1.66-1.87 (m, 5H), 2.12-2.18 (m, 1H), 2.18-2.24 (m, 1H), 2.67 (ddd, J_1 = 13.5 Hz, J_2 = 11.0 Hz, J_3 = 4.1 Hz, 1H), 3.20 (d, J = 1.3 Hz, 1H). ¹³C NMR (75 MHz, CD₂Cl₂): 210.9, 65.2, 65.1, 41.3, 32.1, 31.6, 25.5, 24.1, 9.2. MS (EI): m/z (%) = 154 (1), 138 (1), 125 (11), 109 (12), 98 (68), 93 (8), 83 (29), 67 (35), 55 (100), 53 (16), 41 (65), 29 (57), 27 (23). HRMS: exact mass calculated for [M]⁺ (C₉H₁₄O₂) requires m/z 154.099489, found m/z 154.099382. The enantiomeric ratio was determined to be >99.5:0.5 by GC using a chiral BGB-176/BGB-15 column (80 °C, 1.2 °C/min, until 220 °C, 10 min at 220 °C, 0.5 bar H₂). Major enantiomer: t_R = 18.25 min, minor enantiomer: t_R = 19.50

¹¹ Aljarilla, A.; Córdoba, R.; Csaky, A. G.; Fernández, I.; López Ortiz, F.; Plumet, J.; Ruiz Gómez, G. *Eur. J. Org. Chem.* **2006**, 17, 3969-3976.

min.



3-Benzyl-2,3-epoxycycloheptanone (3n): Conditions B: The title compound was isolated after 20 h at 50 °C and flash chromatography (5-10% Et₂O/pentane) as a clear oil (183 mg, 85%). ¹H NMR (400 MHz, CD₂Cl₂): δ 1.00-1.11 (m, 1H), 1.63-1.86 (m, 4H), 2.16-2.25 (m, 2H), 2.67 (ddd, *J*₁ = 13.5 Hz, *J*₂ = 11.0 Hz, *J*₃ = 4.0 Hz, 1H), 2.90-2.98 (m, 2H), 3.20 (d, *J* = 1.2 Hz, 1H), 7.22-7.27 (m, 3H), 7.29-7.33 (m, 2H). ¹³C NMR (75 MHz, CD₂Cl₂): 210.5, 136.7, 130.3, 129.0, 127.4, 64.8, 64.3, 44.8, 41.3, 31.9, 25.4, 24.1. MS (ED): *m/z* (%) = 216 (22), 198 (3), 187 (19), 169 (6), 159 (3), 143 (7), 129 (12), 118 (30), 104 (4), 97 (20), 91 (100), 78 (8), 65 (18), 55 (11), 41 (23). HRMS: exact mass calculated for [M]⁺ (C₁₄H₁₆O₂) requires *m/z* 216.115217, found *m/z* 216.115027. The enantiomeric ratio was determined to be >99.5:0.5 by HPLC using a chiral Chiralpak IA column (n-heptane/2-propanol = 98:2, flow rate = 0.5 mL/min, wavelength = 220 nm). Major enantiomer: *t*_R = 13.74 min, minor enantiomer: *t*_R = 14.83 min.



2,3-Epoxy-cyclopentenone (3o): Conditions A: The conversion was determined to be 33% by GC using RTX 5 column, and 2,3-epoxycyclohexanone as internal standard (60 °C, 6.0 °C/min, until 290 °C, 10.0 min at 290°C, 0.5 bar H₂. Starting material: *t*_R = 3.90 min, product: *t*_R = 4.99 min, internal standard material: *t*_R = 7.98 min) after 48 h. The physical data were identical in all respect to those previously reported.² The enantiomeric ratio was determined to be 89:11 by GC using a chiral Lipodex E column (60 °C, 1.2 °C/min, until 90 °C, 18 °C/min, until 220 °C, 10 min at 220°C, 0.5 bar H₂). Major enantiomer: *t*_R = 14.49 min, minor enantiomer: *t*_R = 13.33 min.

Scheme 1. Extended Catalyst Screening.



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