Electronic Supplementary Information

Preparation of optically active cycloalkenes bearing all-carbon quaternary stereogenic centres via lipase–oxovanadium combo-catalysed dynamic kinetic resolution

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Contents

General considerations S 2
Preparation of racemic tertiary alcohols 5a-5e S 2–S 3
Dynamic kinetic resolution of (±)-5 to provide optically active esters 7 (Table 1) S 4–S 7
The optimization of the reaction conditions of DKR of (±)-5b using vinyl acetate (3A) S 8
The optimization of the reaction conditions of DKR of (±)-5c using vinyl acetate (3A) S 9–S10
The Ireland–Claisen rearrangement of optically active esters 7 S10–S12
The determination of the optical purity of (S)-4aA, (R,R)-4aB and (S)-4dA S12–S13
The determination of the relative configuration of 4aB S14
Asymmetric total synthesis of (∼)-crinane S15–S18
The optimization of the reaction conditions of DKR of (±)-5f using vinyl acetate (3A) S15
References S18
1H and 13C NMR spectra S19
General considerations

Melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. Infrared (IR) absorption spectra were recorded on a SHIMADZU FTIR-8400S spectrophotometer. $^1$H and $^{13}$C NMR spectra were measured on JEOL JNM-ECA500 ($^1$H: 500 MHz, $^{13}$C: 125 MHz), JEOL AL-400 ($^1$H: 400 MHz, $^{13}$C: 100 MHz) and JEOL AL-300 ($^1$H: 300 MHz, $^{13}$C: 75 MHz) instruments with chemical shifts reported in ppm relative to the residual deuterated solvent. The mass spectra (MS) were measured on JEOL JMS-S3000 (MALDI) and JEOL JMS-700 (FAB) instruments. Yield refers to isolated yields of compounds greater than 95% purity as determined by $^1$H NMR analysis. $^1$H NMR and melting points (where applicable) of all known compounds were taken. All new products were further characterized by $^{13}$C NMR, IR and high resolution mass spectrum (HRMS). HPLC analyses were carried out using a JASCO LC-2000Plus system (HPLC pump: PU-2080, UV detectors: MD-2018 and MD-4017) equipped with Daicel CHIRALPAK AD-3, IC-3, IE, OD-3 and OJ-H columns. All optically active compounds are detected by 254 nm wavelength absorption unless otherwise noted. Optical rotations were measured on a JASCO P-1030 polarimeter.

Immobilized *Burkholderia cepacia* lipases PS-IM and PS-CII, kindly supplied by Amano Enzyme Inc., Japan, were used as received without further purification. *Candida antarctica* lipase B (CAL-B) immobilized on a support (commercial name: Chirazyme L-2 C4) was purchased from Roche Diagnostics K. K., Japan and was used as received without further purification. V-MPS4 was prepared according to the report (it is now commercially available from Wako Pure Chemical Industries, Ltd. Japan). Kanto silica gel 60N was used for column chromatography. All reagents were of reagent grade unless otherwise stated. In general, the reactions were carried out in anhydrous solvents.

The preparation of racemic tertiary alcohols 5a–5e

A general procedure: Under an argon atmosphere, an organolithium compound (12.0 mmol) was added to a solution of an enone 1 (10.0 mmol) in anhydrous Et₂O (50 mL) at −78 °C. After being stirred for 10 min at −78 °C, the reaction mixture was warmed to 0 °C over 10 min and quenched with saturated aq. NH₄Cl (50 mL). The aqueous phase was extracted with Et₂O (3 x 25 mL), and the combined organic phases were washed with brine (50 mL), dried over MgSO₄, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel) to give (±)-5.

1-Phenylcyclohex-2-enol [(±)-5a]

According to the general procedure for the preparation of racemic 5, (±)-5a was obtained in 97% yield as a white solid. MP 44–45 °C (lit.² mp 44–45 °C). Its spectroscopic data were in good agreement with data reported previously.²

1-Butylcyclohex-2-enol [(±)-5b]

According to the general procedure for the preparation of racemic 5, (±)-5b was obtained in 95% yield as a colorless oil. Its spectroscopic data were in good agreement with data reported previously.²
2-Methyl-1-phenylcyclohex-2-enol [(±)-5c]

According to the general procedure for the preparation of racemic 5, (±)-5c was obtained in 93% yield as a colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.51-1.60 (m, 1H), 1.54 (dd, $J = 2.0$, 3.5 Hz, 3H), 1.61-1.71 (m, 1H), 1.87-2.00 (m, 2H), 2.08-2.15 (m, 2H), 5.76-5.78 (m, 1H), 7.24 (tt, $J = 1.5$, 7.5 Hz, 1H), 7.34 (br t, $J = 7.5$ Hz, 2H), 7.44 (br d, $J = 7.5$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 18.6, 19.3, 25.7, 41.3, 75.6, 125.9, 126.7, 127.3, 128.1, 136.5, 146.6; IR (neat) $\nu$ 3460 cm$^{-1}$. HRMS (MALDI) $m/z$ calcd for C$_{13}$H$_{16}$ONa [M+Na]$^+$: 211.1093. Found: 211.1096.

1-Phenylcyclohept-2-enol [(±)-5d]

According to the general procedure for the preparation of racemic 5, (±)-5d was obtained in 98% yield as a white solid. MP 42-43 °C (lit.$^3$ mp 42-43 °C). Its spectroscopic data were in good agreement with data reported previously.$^3$

1-Butylcyclohept-2-enol [(±)-5e]

According to the general procedure for the preparation of racemic 5, (±)-5e was obtained in 92% yield as a colorless oil. Its spectroscopic data were in good agreement with data reported previously.$^4$
Dynamic kinetic resolution of (+)-5 to provide optically active esters 7

\[(R)-3\text{-Phenylcyclohex-2-enyl chloroacetate }[(R)-7aD] \text{ (Table 1, entry 6)}: \text{ A typical procedure}\]

Under an argon atmosphere, *Candida antartica* lipase B (CAL-B) immobilized on a support (commercial name: Chirazyme L-2 C4; 300 mg, 3.0 w/w), V-MPS4 (29 mg, 5.7 μmol of the vanadium component) and vinyl chloroacetate (3D) (0.12 mL, 1.5 mmol) were added to a solution of (+)-5a (100 mg, 0.57 mmol) in MeCN (7.2 mL, 0.08 M) in this order at room temperature. The reaction mixture was stirred at 35 ºC for 24 h and filtered through a Celite pad. The Celite pad was washed with EtOAc, and the combined filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexanes/EtOAc = 10:1) to give \((R)-3\text{-phenylcyclohex-2-enyl chloroacetate }[(R)-7aD] \) (143 mg, 99% yield, 99% ee) as a colorless oil. Its optical purity was determined by HPLC analysis at 20 ºC, using a CHIRALCEL AD-3 column (hexanes/2-propanol = 99:1, 1.0 mL/min; retention times 9.9 (S), 10.9 min (R)). \([\alpha]^{20}_D = +90 \text{ (c 1.16, CHCl}_3\text{).} \quad \text{1H NMR (400 MHz, CD}_3\text{OD) } \delta 1.78-1.97 \text{ (m, 4H), 2.35-2.57 (m, 2H), 4.20 (s, 2H), 5.46-5.51 (m, 1H), 6.04-6.09 (m, 1H), 7.25 (tt, } J = 1.5, 7.0 \text{ Hz, 1H), 7.28-7.34 (m, 2H), 7.40 (dt, } J = 1.5, 7.0 \text{ Hz, 2H); \quad \text{IR (neat) } \nu 1748 \text{ cm}^{-1}. \quad \text{HRMS (FAB) } m/z \text{ calcd for C}_{14}H_{15}ClO_2Na [M+Na]^+: 273.0658. \text{ Found: 273.0667.} \]

\((R)-3\text{-Phenylcyclohex-2-enyl acetate }[(R)-7aA] \text{ (Table 1, entry 1)} \)

\((R)-7aA \) (92% yield, 96% ee) was obtained from (+)-5a and 3A. Its optical purity was determined by HPLC analysis at 20 ºC, using a CHIRALCEL AD-3 column (hexanes/2-propanol = 99:1, 1.0 mL/min; retention times 8.1 (R), 8.7 min (S)). A colorless oil. \([\alpha]^{20}_D = +189 \text{ (c 0.76, CHCl}_3\text{); (lit.}^b [\alpha]^{22}_D = +157.9 \text{ (c 0.41, CHCl}_3\text{) for } (R)-7aA \text{ (99% ee)). The spectroscopic data (1H NMR, IR) of the obtained product (R)-7aA were in agreement with those in our previous publications.}^5 \]

\((R)-3\text{-Phenylcyclohex-2-enyl butyrate }[(R)-7aB] \text{ (Table 1, entry 3)} \)

\((R)-7aB \) (95% yield, 99% ee) was obtained from (+)-5a and 3B. Its optical purity was determined by HPLC analysis at 20 ºC, using a CHIRALCEL AD-3 column (hexanes/2-propanol = 99:1, 1.0 mL/min; retention times 5.9 (R), 6.6 min (S)).

A colorless oil. \([\alpha]^{20}_D = +154 \text{ (c 0.93, CHCl}_3\text{).} \quad \text{1H NMR (400 MHz, CDCl}_3\text{) } \delta 0.96 \text{ (t, } J = 7.5 \text{ Hz, 3H), 1.68 (sext, } J = 7.5 \text{ Hz, 2H), 1.73-1.85 (m, 2H), 1.86-1.98 (m, 2H), 2.30 (t, } J = 7.5 \text{ Hz, 2H), 2.34-2.43 (m, 1H), 2.49-2.57 (m, 1H), 5.45-5.49 (m, 1H), 6.08 (td, } J = 1.5, 4.0 \text{ Hz, 1H), 7.27 (br t, } J = 7.5 \text{ Hz, 1H), 7.33 (br t, } J = 7.5 \text{ Hz, 2H), 7.41 (br d, } J = 7.5 \text{ Hz, 2H); \quad \text{13C NMR (100 MHz, CDCl}_3\text{) } \delta 13.7, 18.6, 19.4, 27.3, 28.0, 36.6, 68.6, 122.4, 125.4, 127.6, 128.3, 141.1, 142.0, 173.5; \quad \text{IR (neat) } \nu 1728 \text{ cm}^{-1}. \quad \text{HRMS (MALDI) } m/z \text{ calcd for C}_{16}H_{21}O_2Na [M+Na]^+: 273.1536. \text{ Found: 245.1542.} \)
(R)-3-Phenylcyclohex-2-enyl decanoate [(R)-7aC] (Table 1, entry 5)

(R)-7aC (97% yield, 98% ee) was obtained by conducting DKR of (±)-5a with 3C, CAL-B (1.0 w/w) and V-MPS4 (0.5 mol %). Its optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL AD-3 column (hexanes/2-propanol = 99:1, 0.5 mL/min; retention times 9.6 (R), 10.7 min (S)).

A colorless oil. [α]D20 = +104 (c 1.05, CHCl3) (lit.2 [α]D20 = +102.1 (c 0.31, CHCl3) for (R)-7aC (99% ee)). The spectroscopic data (1H NMR) of the obtained product 7aC were in good agreement with those in a previous publication, in which (R)-7aC (99% ee) was obtained in 72% yield.2

(R)-3-Butylcyclohex-2-enyl acetate [(R)-7bA] (Table 1, entry 9)

(R)-7bA (79% yield, 90% ee) was obtained by conducting DKR of (±)-5b with 3A, CAL-B (1.0 w/w) and V-MPS4 (0.5 mol %) at –10 °C for 8 days. Its optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL AD-3 column (hexanes only, 0.5 mL/min, 208 nm; retention times 12.4 (R), 13.3 min (S)).

A colorless oil. [α]D20 = +160 (c 0.90, CHCl3). 1H NMR (400 MHz, CDCl3) δ 0.89 (t, J = 7.5 Hz, 3H), 1.79 (sext, J = 7.5 Hz, 2H), 1.34-1.45 (m, 2H), 1.58-1.84 (m, 4H), 1.87-2.03 (m, 4H), 2.04 (s, 3H), 5.23-5.29 (m, 1H), 5.43-5.46 (m, 1H); 13C NMR (100 MHz, CDCl3) δ 14.0, 19.2, 21.5, 22.4, 28.3, 28.4, 29.6, 37.4, 69.0, 119.2, 145.0, 170.9; IR (neat) ν 1732 cm –1. HRMS (MALDI) m/z calcd for C12H20O2Na [M+Na]+: 219.1356. Found: 219.1355.

(R)-3-Butylcyclohex-2-enyl butyrate [(R)-7bB] (Table 1, entry 10)

(R)-7bB (93% yield, 96% ee) was obtained from (±)-5b and 3B. Its optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL OD-3 column (hexanes only, 1.0 mL/min, 208 nm; retention times 6.3 (R), 7.5 min (S)).

A colorless oil. [α]D20 = +145 (c 1.09, CHCl3) (lit.5b [α]D27 = +147.7 (c 0.47, CDCl3) for (R)-7bB (99% ee)). The spectroscopic data (1H NMR) of the obtained product (R)-7bB were in good agreement with those in our previous publication.5b

(R)-2-Methyl-3-phenylcyclohex-2-enyl acetate [(R)-7cA] (Table 1, entry 12)

7cA (77% yield, 81% ee) was obtained by conducting DKR of (±)-5c with 3A, lipase PS-IM (3.0 w/w) and V-MPS4 (1.0 mol %) in toluene at 50 °C for 24 h. Its optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL OJ-H column (hexanes/2-propanol = 99:1, 1.0 mL/min; retention times 9.8 (R),
A colorless oil. $[\alpha]_{D}^{20} = +73$ (c 0.89, MeOH). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.56 (t, $J = 2.0$ Hz, 3H), 1.69-1.95 (m, 4H), 2.11 (s, 3H), 2.19-2.38 (m, 2H), 5.34-5.39 (m, 1H), 7.16 (br d, $J = 7.5$ Hz, 2H), 7.24 (br t, $J = 7.5$ Hz, 1H), 7.34 (br t, $J = 7.5$ Hz, 2H); $^1$C NMR (100 MHz, CDCl$_3$) $\delta$ 17.4, 18.9, 21.4, 28.9, 32.1, 71.8, 72.6, 126.9, 128.0, 128.1, 139.0, 142.9, 171.1; IR (neat) v 1732 cm$^{-1}$. HRMS (FAB) m/z calcd for C$_{15}$H$_{18}$O$_2$Na [M+Na]$^+$: 253.1204. Found: 253.1208.

$(R)$-2-Methyl-3-phenylcyclohex-2-enyl decanoate [(R)-7cC] (Table 1, entry 13)

7cC (84% yield, 93% ee) was obtained by conducting DKR of (±)-5c with 3C, lipase PS-IM (3.0 w/w) and V-MPS4 (1.0 mol %) in toluene at 50 °C for 24 h. Its optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL OJ-H column (hexanes/2-propanol = 99.5:0.5, 1.0 mL/min; retention times 4.8 (S), 5.5 min (R)).

A colorless oil. $[\alpha]_{D}^{20} = +72$ (c 0.28, MeOH). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 0.87 (t, $J = 7.0$ Hz, 3H), 1.16-1.40 (m, 12H), 1.55 (t, $J = 2.0$ Hz, 3H), 1.61-1.92 (m, 6H), 2.17-2.39 (m, 4H), 5.33-5.40 (m, 1H), 7.16 (br d, $J = 7.5$ Hz, 2H), 7.24 (br t, $J = 7.5$ Hz, 1H), 7.33 (br t, $J = 7.5$ Hz, 2H); 13C NMR (100 MHz, CDCl$_3$) $\delta$ 14.1, 17.5, 19.0, 22.7, 25.2, 29.0, 29.16, 29.24, 29.3, 31.8, 32.1, 34.8, 71.5, 126.5, 127.0, 128.0, 128.1, 138.9, 143.0, 173.9; IR (neat) v 1732 cm$^{-1}$. HRMS (MALDI) m/z calcd for C$_{23}$H$_{35}$O$_2$ [M+H]$^+$: 343.2632. Found: 343.2621.

$(R)$-3-Phenylcyclohept-2-enyl acetate [(R)-7dA] (Table 1, entry 15)

(R)-7dA (82% yield, 98% ee) was obtained from (±)-5d and 3A. Its optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL AD-3 column (hexanes/2-propanol = 99:1, 1.0 mL/min; retention times 5.4 (R), 6.1 min (S)).

A colorless oil. $[\alpha]_{D}^{20} = +66$ (c 0.98, CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.44-1.54 (m, 1H), 1.68-1.93 (m, 4H), 1.99-2.06 (m, 1H), 2.09 (s, 3H), 2.50-2.71 (m, 2H), 5.54-5.62 (m, 1H), 5.87-5.92 (m, 1H), 7.23 (br t, $J = 7.0$ Hz, 1H), 7.27-7.35 (m, 4H); 13C NMR (125 MHz, CDCl$_3$) $\delta$ 21.3, 26.0, 27.6, 32.55, 32.61, 74.3, 125.6, 126.9, 128.2, 131.5, 143.0, 143.7, 170.3; IR (neat) v 1736 cm$^{-1}$. HRMS (MALDI) m/z calcd for C$_{15}$H$_{18}$O$_2$Na [M+Na]$^+$: 253.1199. Found: 253.1194.

$(R)$-3-Phenylcyclohept-2-enyl butyrate [(R)-7dB] (Table 1, entry 16)

(R)-7dB (81% yield, 98% ee) was obtained from (±)-5d and 3B. Its optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL AD-3 column (hexanes/2-propanol = 99:1, 0.5 mL/min; retention times 8.8 (S), 10.3 min (R)).

A colorless oil. $[\alpha]_{D}^{20} = +50$ (c 0.95, CHCl$_3$). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 0.97
(t, J = 7.5 Hz, 3H), 1.45-1.54 (m, 1H), 1.64-1.92 (m, 6H), 1.99-2.07 (m, 1H), 2.32 (t, J = 7.5 Hz, 2H), 2.51-2.59 (m, 1H), 2.64-2.72 (m, 1H), 5.57-5.62 (m, 1H), 5.87-5.91 (m, 1H), 7.23 (dt, J = 2.0, 7.0 Hz, 1H), 7.28-7.38 (m, 4H); 13C NMR (500 MHz, CDCl3) δ 13.7, 18.5, 26.0, 27.7, 32.6, 32.7, 36.5, 74.0, 125.8, 126.9, 128.2, 131.6, 143.0, 143.8, 173.0; IR (neat) v 1732 cm–1. HRMS (MALDI) m/z calcd for C17H23O2 [M+H]+: 259.1692. Found: 259.1690.

(R)-3-Butylcyclohept-2-enyl acetate [(R)-7eA] (Table 1, entry 17)

(R)-7eA (93% yield, 98% ee) was obtained from (±)-5e and 3A. Its optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL AD-3 column (hexanes/2-propanol = 99:1, 0.5 mL/min, 208 nm; retention times 7.6 (R), 9.4 min (S)).

A colorless oil. [α]20D = +50 (c 0.88, CHCl3). 1H NMR (500 MHz, CDCl3) δ 0.89 (t, J = 7.0 Hz, 3H), 1.23-1.39 (m, 5H), 1.57-1.71 (m, 3H), 1.76-1.82 (m, 1H), 1.86-1.99 (m, 3H), 2.03-2.15 (m, 2H), 2.05 (s, 3H), 5.28-5.45 (m, 2H); 13C NMR (125 MHz, CDCl3) δ 14.0, 21.4, 22.3, 26.0, 27.2, 29.8, 32.4, 32.9, 39.8, 74.0, 127.1, 143.9, 170.5; IR (neat) v 1736 cm–1. HRMS (MALDI) m/z calcd for C13H22O2Na [M+Na]+: 233.1512. Found: 233.1505.

(R)-3-Butylcyclohept-2-enyl butyrate [(R)-7eB] (Table 1, entry 18)

(R)-7eB (91% yield, >99% ee) was obtained from (±)-5e and 3B. Its optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL AD-3 column (hexanes/2-propanol = 99.5:0.5, 1.0 mL/min, 208 nm; retention times 5.3 (R), 6.5 min (S)).

A colorless oil. [α]20D = +47 (c 0.96, CHCl3). 1H NMR (500 MHz, CDCl3) δ 0.89 (t, J = 7.5 Hz, 3H), 0.95 (t, J = 7.5 Hz, 3H), 1.24-1.40 (m, 5H), 1.59-1.71 (m, 5H), 1.76-1.82 (m, 1H), 1.87-1.99 (m, 3H), 2.04-2.18 (m, 2H), 2.28 (t, J = 7.5 Hz, 2H), 5.34-5.41 (m, 2H); 13C NMR (125 MHz, CDCl3) δ 13.7, 14.0, 18.5, 22.4, 26.0, 27.2, 29.8, 32.4, 32.9, 39.8, 73.7, 127.2, 144.0, 173.1; IR (neat) v 1732 cm–1. HRMS (MALDI) m/z calcd for C15H27O2 [M+H]+: 239.2006. Found: 239.1999.
The optimization of the reaction conditions of DKR of (±)-5b using vinyl acetate (3A)

At first, the effect of the amount of V-MPS4 and CAL-B on the optical purity and yield of the ester (R)-7bA was examined to find the following results: The use of 5 mol % of V-MPS4 at 35 °C resulted in the decrease of the yield of (R)-7bA, while maintaining the optical purity (80% ee), due to the formation of a significant amount of the dimeric ether S1 (Table S1, entry 2). The use of a less amount (1 w/w) of CAL-B increased the optical purity to 86% ee although the chemical yield (60%) was decreased (entry 3). Therefore, 3 w/w of CAL-B and 1 mol % of V-MPS4 was found to be a good combination.

Next, we investigated the temperature effect and found that the reaction at either higher temperature (50 °C) or lower temperature (10 °C) produced improvement of the optical purity of (R)-7bA, among which the reaction at 10 °C was more suitable for affording a higher yield of (R)-7bA albeit longer reaction time (48 h) (entries 4 and 5). The use of less amounts of V-MPS4 (1 w/w) and CAL-B (0.5 mol %) brought increase in both optical purity (88% ee) and chemical yield (92%), although the reaction was slow and needed longer time (72 h) (entry 6). The optical purity was further improved to 92% ee by performing the reaction at lower temperature (−10 °C). After 72 h, (R)-7bA was obtained in 65% yield along with racemic 3-butylcyclohex-2-enol (28% yield), which showed that V-MPS4 was active at such low temperature (entry 7). Finally, (R)-7bA (90% ee) was obtained in 79% yield by the reaction at −10 °C for 192 h (entry 8).

Table S1 The optimization of the reaction conditions of DKR of (±)-5b using vinyl acetate (3A).

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<tr>
<th>entry</th>
<th>amount of CAL-B</th>
<th>equiv of V-MPS4</th>
<th>temp.</th>
<th>reaction time</th>
<th>(R)-7bA isolated yield</th>
<th>optical puritya</th>
<th>yield of S1</th>
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<td>1 mol %</td>
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<td>24 h</td>
<td>90%</td>
<td>80% ee</td>
<td>5%</td>
</tr>
<tr>
<td>2</td>
<td>3 w/w</td>
<td>5 mol %</td>
<td>35 °C</td>
<td>24 h</td>
<td>33%</td>
<td>80% ee</td>
<td>28%</td>
</tr>
<tr>
<td>3</td>
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<td>1 mol %</td>
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<td>24 h</td>
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<td>86% ee</td>
<td>7%</td>
</tr>
<tr>
<td>4</td>
<td>3 w/w</td>
<td>1 mol %</td>
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<td>21%</td>
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<tr>
<td>5</td>
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<td>1 mol %</td>
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<td>88% ee</td>
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<td>7c</td>
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<td>0.5 mol %</td>
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a) Determined by HPLC using a chiral column.
b) Cited from entry 7 of Table 1.
c) Racemic 3-butylcyclohex-2-enol was recovered in 28% yield.
The optimization of the reaction conditions of DKR of (±)-5c using vinyl acetate (3A)

At first, some commercially available immobilized lipases were examined for the kinetic resolution of racemic secondary alcohol 6c to find that Candida antarctica lipase B (CAL-B) and Burkholderia cepacia lipases (PS-CII and PS-IM) were effective (Table S2). In particular, the use of PS-IM in a range of organic solvents produced high enantioselectivity (E value: up to 140) (entries 5-8).

Table S2 The screening of lipases and solvents for kinetic resolution of (±)-6c

<table>
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<th>lipase</th>
<th>solvent</th>
<th>conv(^a)</th>
<th>optical purity of (S)-6c</th>
<th>E value</th>
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</thead>
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<tr>
<td>1</td>
<td>CAL-B</td>
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<td>43%</td>
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</tr>
<tr>
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<td>91% ee</td>
<td>7.4</td>
</tr>
<tr>
<td>3(^b)</td>
<td>PS-CII</td>
<td>MeCN</td>
<td>54%</td>
<td>89% ee</td>
<td>24</td>
</tr>
<tr>
<td>4(^b)</td>
<td>PS-CII</td>
<td>hexane</td>
<td>60%</td>
<td>&gt;99% ee</td>
<td>30</td>
</tr>
<tr>
<td>5</td>
<td>PS-IM</td>
<td>MeCN</td>
<td>49%</td>
<td>91% ee</td>
<td>140</td>
</tr>
<tr>
<td>6</td>
<td>PS-IM</td>
<td>hexane</td>
<td>61%</td>
<td>&gt;99% ee</td>
<td>23</td>
</tr>
<tr>
<td>7</td>
<td>PS-IM</td>
<td>dPrO</td>
<td>53%</td>
<td>&gt;99% ee</td>
<td>97</td>
</tr>
<tr>
<td>8</td>
<td>PS-IM</td>
<td>toluene</td>
<td>54%</td>
<td>&gt;99% ee</td>
<td>70</td>
</tr>
</tbody>
</table>

\(^a\) Determined by \(^1\)H NMR. \(^b\) Conducted for 1.5 h.

Next, DKR was examined by using PS-IM and V-MPS4 in various organic solvents at 35 °C (Table S3, entries 1-6), in which DKR in toluene afforded the best results in terms of the yield (84%) and optical purity (71% ee) of the ester 7cA (entry 3). A similar reaction in toluene at 50 °C provided 7cA with better optical purity (81% ee) albeit in lower yield (77%) (entry 7); however, similar tendency was not observed in CH\(_2\)Cl\(_2\) (entry 8). The use of vinyl decanoate (3C) instead of vinyl acetate (3A) effected improvement of both yield (84%) and optical purity (93% ee) of the corresponding ester (R)-7cC (entry 9).
**Table S3** The optimization of the reaction conditions of DKR of 5c

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>temp.</th>
<th>reaction time</th>
<th>isolated yield</th>
<th>optical purity</th>
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<tr>
<td>1</td>
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<td>35°C</td>
<td>24 h</td>
<td>92%</td>
<td>61% ee</td>
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<tr>
<td>2a</td>
<td>hexane</td>
<td>35°C</td>
<td>48h</td>
<td>87%</td>
<td>63% ee</td>
</tr>
<tr>
<td>3</td>
<td>toluene</td>
<td>35°C</td>
<td>48h</td>
<td>84%</td>
<td>71% ee</td>
</tr>
<tr>
<td>4</td>
<td>iPr2O</td>
<td>35°C</td>
<td>48h</td>
<td>77%</td>
<td>50% ee</td>
</tr>
<tr>
<td>5</td>
<td>CH2Cl2</td>
<td>35°C</td>
<td>72h</td>
<td>58%b</td>
<td>73% ee</td>
</tr>
<tr>
<td>6</td>
<td>CH2Cl2</td>
<td>50°C</td>
<td>24h</td>
<td>62%</td>
<td>73% ee</td>
</tr>
<tr>
<td>7</td>
<td>toluene</td>
<td>50°C</td>
<td>24h</td>
<td>77%</td>
<td>81% ee</td>
</tr>
<tr>
<td>8</td>
<td>toluene</td>
<td>50°C</td>
<td>24h</td>
<td>49%</td>
<td>60% ee</td>
</tr>
<tr>
<td>9c</td>
<td>toluene</td>
<td>50°C</td>
<td>24h</td>
<td>64%</td>
<td>93% ee</td>
</tr>
</tbody>
</table>

a) PS-IM (1.5 w/w) was used. b) Alcohol 6c (88% ee) was recovered in 34% yield. c) Vinyl decanate (3C) was used instead of vinyl acetate. The isolated yield and optical purity of (R)-7cA are shown.

The Ireland–Claisen rearrangement of optically active esters 7

(S)-(1-Phenylcyclohex-2-enyl)acetic acid (4aA) (Table 2, entry 1): A typical procedure

Under an argon atmosphere, HMPA (0.13 mL, 5% of total volume of THF) was added to a solution of LDA (0.55 mmol) in THF (1.0 mL) at −78 °C. Then, a solution of (R)-7aA (96% ee, 100 mg, 0.46 mmol) in THF (1.0 mL) was added via a cannula. After the reaction mixture was stirred at the same temperature for 15 min, a solution of TBSCl (105 mg, 0.69 mmol) in THF (0.5 mL) was added. After being stirred at −78 °C for 15 min, the reaction mixture was warmed to room temperature over 1 h and then refluxed for 15 h. After cooling to room temperature, aqueous hydrochloric acid (1.0 M, 1.0 mL) was added to the solution, and the mixture was stirred at room temperature for 3 h. Et2O (5 mL) was added, and the organic phase was separated. The aqueous phase was extracted with Et2O (2 x 5 mL). The combined organic phases were washed with brine (5 mL), dried over MgSO4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexanes/EtOAc = 3:1) to give (S)-4aA (79 mg, 79%, 96% ee). Its optical purity was determined by HPLC analysis of the alcohol S2 obtained by the reduction of (S)-4aA (vide infra).

(S)-4aA. A white solid. Mp 87-88 °C. [α]D20 = +39 (c 0.86, CHCl3). 1H NMR (500 MHz, CDCl3) δ 1.30-1.41 (m, 1H), 1.51-1.58 (m, 1H), 1.87 (ddd, J = 3.0, 11.5, 13.0 Hz, 1H), 1.95 (ddd, J = 2.5, 6.5, 13.0 Hz, 1H), 1.99-2.08 (m, 2H), 2.73 (d, J = 14.0 Hz, 1H), 2.83 (d, J = 14.0 Hz, 1H), 5.95 (td, J = 3.5, 10.0 Hz, 1H), 6.07 (ddd, J = 2.5, 3.5, 10.0 Hz, 1H), 7.18 (dt, J = 1.5, 7.5 Hz, 1H), 7.30 (br t, J = 7.5 Hz, 2H), 7.34 (br d, J = 7.5 Hz, 2H); 13C NMR (125 MHz, CDCl3) δ 18.6, 25.0, 37.0, 41.7, 46.4, 126.0, 126.7, 128.0, 128.8, 131.8, 146.6,
176.8; IR (neat) ν 1713, 3024 cm \(^{-1}\). HRMS (MALDI) \textit{m/z} calculated for C\(_{14}H_{16}O_2Na [M+Na]^+\): 239.1043. Found: 239.1043.

\((R)-2\cdot[(R)-1-Phenylcyclohex-2-enyl]butanoic acid (4aB) and (S)-2\cdot[(R)-1-phenylcyclohex-2-enyl]-butanoic acid (4aB') (Table 2, entry 2)\)

4aB (63% yield, 99% ee) and 4aB' (6% yield, optical purity was not determined) were obtained from (R)-7aB (99% ee) by column chromatography (silica gel, hexanes/EtOAc = 7:1).

4aB. A white solid. Mp 145-146 °C. \([\alpha]_{D}^{20} = +28\) (c 0.96, CHCl\(_3\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 0.82\) (t, \(J = 7.0\) Hz, 3H), 1.14-1.28 (m, 2H), 1.49-1.57 (m, 1H), 1.63-1.74 (m, 1H), 1.89 (dt, \(J = 2.0, 13.0\) Hz, 1H), 1.94-2.06 (m, 2H), 2.20 (dt, \(J = 5.0, 6.5\) Hz, 1H), 2.71 (dd, \(J = 3.0, 13.0\) Hz, 1H), 5.96 (td, \(J = 3.0, 11.0\) Hz, 1H), 6.01 (ddd, \(J = 1.5, 3.5, 11.0\) Hz, 1H), 7.19 (t, \(J = 7.0\) Hz, 1H), 7.28-7.37 (m, 4H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 12.7, 18.8, 20.8, 25.4, 33.9, 45.6, 58.8, 126.0, 127.3, 128.1, 129.3, 130.0, 146.3, 180.1; IR (neat) \(\nu\) 1704, 3025 cm \(-1\). HRMS (MALDI) \textit{m/z} calculated for C\(_{16}H_{20}O_2Na [M+Na]^+\): 267.1356. Found: 267.1350. Its optical purity was determined by the HPLC analysis of the alcohol S3 obtained from the reduction of (S)-4aB (vide infra) and its relative configuration was determined by the derivatization of 4aB into the iodo lactone S5 (vide infra).

4aB'. A colorless oil. \([\alpha]_{D}^{20} = +72\) (c 1.07, CHCl\(_3\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 0.88\) (t, \(J = 7.0\) Hz, 3H), 1.21-1.34 (m, 2H), 1.49-1.69 (m, 2H), 1.90-2.04 (m, 4H), 2.63 (dd, \(J = 3.5, 11.0\) Hz, 1H), 5.89-5.93 (m, 1H), 6.20-6.24 (m, 1H), 7.15 (br t, \(J = 7.5\) Hz, 1H), 7.26 (br t, \(J = 7.5\) Hz, 2H), 7.33 (br d, \(J = 7.5\) Hz, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 12.8, 18.7, 21.4, 25.2, 32.4, 45.1, 57.7, 126.0, 127.5, 127.8, 129.0, 130.8, 145.9, 178.9; IR (neat) \(\nu\) 1703, 3031 cm \(-1\). HRMS (MALDI) \textit{m/z} calculated for C\(_{16}H_{20}O_2Na [M+Na]^+\): 267.1356. Found: 267.1353.

\((R)-2\cdot[(R)-1-Phenylcyclohex-2-enyl]decanoic acid (4aC) and (S)-2\cdot[(R)-1-phenylcyclohex-2-enyl]-decanoic acid (4aC') (Table 2, entry 3)\)

An 11:1 mixture of 4aC and 4aC' was obtained from (R)-7aC (98% ee), whose ratio was determined by \(^1\)H NMR analysis of a crude product. Pure 4aC (77% yield) was isolated by column chromatography (silica gel, hexanes/EtOAc = 7:1).

4aC. A colorless oil. \([\alpha]_{D}^{20} = +28\) (c 1.21, CHCl\(_3\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 0.85\) (t, \(J = 7.0\) Hz, 3H), 1.04-1.33 (m, 1H), 1.48-1.57 (m, 1H), 1.62-1.74 (m, 1H), 1.82-2.06 (m, 3H), 2.20 (br d, \(J = 14.0\) Hz, 1H), 2.78 (br d, \(J = 12.0\) Hz, 1H), 5.93-6.03 (m, 2H), 7.19 (br t, \(J = 7.5\) Hz, 1H), 7.28-7.36 (m, 4H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 14.1, 18.8, 22.6, 25.3, 27.4, 28.2, 29.16, 29.22, 29.3, 31.8, 33.7, 45.6, 56.9, 126.0, 127.3, 128.0, 129.2, 130.1, 146.2, 181.1; IR (neat) \(\nu\) 1701, 3031 cm \(-1\). HRMS (MALDI) \textit{m/z} calculated for C\(_{16}H_{30}O_2Na [M+Na]^+\): 267.1356. Found: 267.1356.
267.1350.

4aC’. Some typical $^1$H NMR data (500 MHz, CDCl$_3$) $\delta$ 5.89-5.93 (m, 1H), 6.24-6.29 (m, 1H).

(R)-2-(1-Butylcyclohex-2-enyl)acetic acid (4bA) (Table 2, entry 4)

(R)-4bA (78% yield) was obtained from (R)-7bA (90% ee).
A colorless oil. $[\alpha]_{D}^{20} =$ +2.4 (c 1.04, CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 0.89 (t, $J = 7.0$ Hz, 3H), 1.18-1.34 (m, 4H), 1.37-1.71 (m, 6H), 1.87-2.02 (m, 2H), 2.33 (d, $J = 16.0$ Hz, 1H), 2.36 (d, $J = 16.0$ Hz, 1H), 5.53 (td, $J = 2.0, 10.0$ Hz, 1H), 5.70 (td, $J = 3.5, 10.0$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 14.1, 18.8, 23.4, 24.9, 26.0, 32.5, 36.8, 39.6, 44.0, 127.1, 133.9, 178.4; IR (neat) $\nu$ 1709, 3020 cm$^{-1}$. HRMS (MALDI) $m/z$ calcd for C$_{12}$H$_{20}$O$_2$Na [M+Na]$^+$: 219.1356. Found: 219.1360.

(S)-2-(1-Phenylcyclohex-2-enyl)acetic acid (4dA) (Table 2, entry 6)

(S)-4dA (63% yield, 98% ee) was obtained from (R)-7dA (99% ee) by conducting Ireland-Claisen rearrangement with HMPA, KN(SiMe$_3$)$_2$ and TBSCl in THF. Its optical purity was determined by the HPLC analysis of the alcohol S4 obtained by the reduction of (S)-4dA (vide infra).
A white solid. Mp 110 °C. $[\alpha]_{D}^{20} =$ +90 (c 1.00, CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.29-1.53 (m, 3H), 1.58-1.70 (m, 1H), 1.89-2.21 (m, 4H), 2.68 (d, $J = 14.0$ Hz, 1H), 2.70 (d, $J = 14.0$ Hz, 1H), 6.00-6.04 (m, 2H), 7.20 (tt, $J = 1.5, 7.5$ Hz, 1H), 7.31 (br t, $J = 7.5$ Hz, 2H), 7.37 (br d, $J = 7.5$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 25.0, 26.3, 27.9, 38.6, 47.5, 49.6, 126.0, 126.9, 128.2, 132.6, 136.2, 144.7, 177.0; IR (neat) $\nu$ 1705, 3021 cm$^{-1}$. HRMS (MALDI) $m/z$ calcd for C$_{15}$H$_{18}$O$_2$Na [M+Na]$^+$: 253.1199. Found: 253.1194.

The determination of the optical purity of (S)-4aA, (R,R)-4aB and (S)-4dA

(S)-2-(1-Phenylcyclohex-2-enyl)ethanol (S2)
A solution of (S)-4aA (10 mg, 0.046 mmol) in THF (1.0 mL) was added to a suspension of LiAlH$_4$ (1.8 mg, 0.046 mmol) in THF (1.0 mL) at 0 °C. Then, the reaction mixture was stirred at 60 °C for 2 h, cooled to 0 °C, and quenched with aqueous hydrochloric acid (1.0 M, 1.0 mL). The aqueous phase was extracted with Et$_2$O (3 x 1.0 mL), and the combined organic phases were washed with brine (1.0 mL), dried over MgSO$_4$, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexanes/EtOAc = 3:1) to give S2 (9.4 mg, quantitative yield). Its optical purity was determined by HPLC
analysis at 20 °C, using a CHIRALCEL IE column (hexanes/2-propanol = 95:5, 1.0 mL/min, 208 nm; retention times 11.0 (R), 11.7 min (S)).

A colorless oil. [α]$_D^{20}$ = +62 (c 1.00, CHCl$_3$). ¹H NMR (400 MHz, (CD$_3$)$_2$SO) δ 1.14-1.28 (m, 1H), 1.45-1.57 (m, 1H), 1.63-1.73 (m, 1H), 1.79-2.04 (m, 5H), 3.12-3.19 (m, 1H), 3.26-3.30 (m, 1H), 5.81-5.92 (m, 2H), 7.13-7.19 (m, 1H), 7.26-7.34 (m, 4H); ¹³C NMR (100 MHz, (CD$_3$)$_2$SO) δ 18.5, 24.9, 36.5, 41.3, 45.1, 57.4, 126.0, 126.7, 127.3, 128.1, 133.2, 147.8; IR (neat) ν 3337 cm$^{-1}$. HRMS (MALDI) m/z calcd for C$_{14}$H$_{18}$ONa [M+Na]$^+$: 225.1250. Found: 225.1251.

(R)-2-[(R)-1-Phenylcyclohex-2-enyl]butanol (S3)

According to the procedure of preparation of S2, S3 was obtained from (R,R)-4aB in 99% yield. Its optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL IC-3 column (hexanes/2-propanol = 97.5:2.5, 1.0 mL/min, 208 nm; retention times 7.5 (R,R), 8.2 min (S,S)).

A colorless oil. [α]$_D^{20}$ = +109 (c 0.50, CHCl$_3$). ¹H NMR (500 MHz, CDCl$_3$) δ 0.85 (t, $J = 7.5$ Hz, 3H), 1.16-1.37 (m, 3H), 1.51-1.58 (m, 1H), 1.68-1.74 (m, 1H), 1.92-2.09 (m, 4H), 3.745 (dd, $J = 4.0$, 11.5 Hz 1H), 3.754 (dd, $J = 4.0$, 11.5 Hz, 1H), 5.85-5.94 (m, 2H), 7.12 (tt, $J = 2.5$, 6.5 Hz, 1H), 7.28-7.34 (m, 4H); ¹³C NMR (100 MHz, CDCl$_3$) δ 13.5, 18.8, 20.2, 25.6, 32.9, 46.5, 52.9, 62.6, 125.6, 127.3, 128.0, 129.6, 132.2, 147.9; IR (neat) ν 3375 cm$^{-1}$. HRMS (MALDI) m/z calcd for C$_{16}$H$_{22}$ONa [M+Na]$^+$: 253.1563. Found: 253.1562.

(S)-2-(1-Phenylcyclohept-2-enyl)ethan-1-ol (S4)

According to the procedure of preparation of S2, S4 was obtained from (S)-4dA in 99% yield. Its optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL OJ-H column (hexanes/2-propanol = 95:5, 1.0 mL/min, 208 nm; retention times 10.7 (R), 19.7 min (S)).

A colorless oil. [α]$_D^{20}$ = +115 (c 0.88, CHCl$_3$). ¹H NMR (400 MHz, (CD$_3$)$_2$SO) δ 1.16-1.43 (m, 3H), 1.50-1.63 (m, 1H), 1.70-1.94 (m, 4H), 2.00-2.15 (m, 2H), 3.07-3.17 (m, 1H), 3.30-3.43 (m, 1H), 5.76-5.82 (m, 1H), 5.89-5.97 (m, 1H), 7.12-7.20 (m, 1H), 7.26-7.34 (m, 4H); ¹³C NMR (100 MHz, (CD$_3$)$_2$SO) δ 25.6, 27.0, 28.4, 39.2, 48.0, 49.2, 58.6, 126.4, 127.6, 129.0, 132.4, 138.6, 146.9; IR (neat) ν 3345 cm$^{-1}$. HRMS (MALDI) m/z calcd for C$_{15}$H$_{20}$ONa [M+Na]$^+$: 239.1406. Found: 239.1406.
The determination of the relative configuration of the major isomer 4aB

The relative configuration of the major isomer 4aB was determined based on the nOe experiment of the iodo lactone S5 obtained by the reaction with iodine under basic reaction conditions (Scheme S1).

**Scheme S1.** Determination of the relative configuration of 4aB.

(3R,3aR,7S,7aS)-3-Ethyl-7-iodo-3a-phenylhexahydrobenzofuran-2(3H)-one (S5)

Iodine (20 mg, 0.082 mmol) was added to a solution of 4aB (10 mg, 0.041 mmol) in THF/aq. NaHCO₃ (1:1, 1.0 mL) at 0 °C. Then, the solution was warmed to room temperature over 30 min and quenched with saturated aq. Na₂S₂O₃ (1.0 mL). The aqueous phase was extracted with EtOAc (3 x 5.0 mL), and the combined organic phases were washed with brine (1.0 mL), dried over MgSO₄, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexanes/EtOAc = 5:1) to give S5 (11.8 mg, 78%).

A white solid. Mp 129-130 °C. [α]₂₀ D = +65 (c 0.90, CHCl₃). ¹H NMR (500 MHz, CDCl₃) δ 0.95-1.13 (m, 5H), 1.50-1.58 (m, 1H), 1.63-1.72 (m, 1H), 1.83-1.97 (m, 2H), 2.34-2.41 (m, 1H), 2.48-2.54 (m, 1H), 2.60 (dd, J = 5.0, 8.0 Hz, 1H), 4.07 (ddd, J = 4.5, 9.0, 13.0 Hz, 1H), 4.96 (d, J = 9.0 Hz, 1H), 7.21 (br t, J = 6.5 Hz, 1H), 7.23-7.32 (m, 4H); ¹³C NMR (125 MHz, CDCl₃) δ 12.5, 19.4, 23.3, 28.1, 31.3, 36.0, 47.2, 50.5, 88.4, 126.2, 127.4, 128.7, 142.0, 176.5; IR (neat) ν 1779 cm⁻¹. HRMS (MALDI) m/z calcd for C₁₆H₁₉O₂NaI [M]+: 393.0322. Found: 393.0321.
Asymmetric total synthesis of (−)-crinane

1-(3,4-methylenedioxyphenyl)cyclohex-2-enol [(±)-5f]

Under an argon atmosphere, nBuLi (2.6 M in hexane; 12 mL, 31 mmol) was added to a solution of 4-bromo-1,2-methylenedioxybenzene (6.3 g, 31 mmol) in Et₂O (60 mL) and THF (30 mL) at −78 °C. After 30 min at −78 °C, a solution of cyclohex-2-enone (2.5 g, 26 mmol) in THF (10 mL) was added. The reaction mixture was warmed to room temperature over 15 min and quenched with saturated aq. NH₄Cl (70 mL). The organic phase was separated and the aqueous phase was extracted with EtOAc (3 x 50 mL). The combined organic phases were washed with brine (50 mL), dried over MgSO₄, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexanes/EtOAc = 5:1) to give 5f (5.5 g, 96%).

A white solid. Mp 52–53 °C (lit.6 mp 55–56 °C). The 1H NMR data of the obtained product 5f was in good agreement with those in a previous publication.6

The optimization of the reaction conditions of DKR of (±)-5f using vinyl acetate (3A)

At first, the DKR of (±)-5f (50 mg) was conducted under standard conditions at 35 °C for 24 h to give the ester (R)-7fA with 89% ee in 79% yield (Table S4, entry 1). A similar reaction performed at −5 °C by using CAL-B (1.0 w/w) and V-MPS4 (0.5 mol %) provided the increase of both yield (87%) and optical purity (95% ee) of (R)-7fA (entry 2). At lower temperature (−10 and −20 °C) the optical purity of (R)-5fA was further improved to 97–98% ee (entries 3 and 4). A similar reaction of 1 g of (±)-5f also afforded the same chemical and optical yields of (R)-7fA (entry 5).

Table S4 The optimization of the reaction conditions of DKR of (±)-5f using vinyl acetate (3A)

<table>
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<th>amount of CAL-B</th>
<th>equiv of V-MPS4</th>
<th>temp.</th>
<th>reaction time</th>
<th>(R)-7fA</th>
<th>isolated yield</th>
<th>optical purity</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>3.0 w/w</td>
<td>1.0 mol %</td>
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<td>24 h</td>
<td>79%</td>
<td>89% ee</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.0 w/w</td>
<td>0.5 mol %</td>
<td>−5 °C</td>
<td>65 h</td>
<td>87%</td>
<td>95% ee</td>
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</tr>
<tr>
<td>3</td>
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<td>−30 °C</td>
<td>120 h</td>
<td>89%</td>
<td>97% ee</td>
<td></td>
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a) The reaction was conducted by using 50 mg of (±)-5f, otherwise noted.
b) One gram of (±)-5f was used.
(R)-3-(3,4-methylenedioxyphenyl)cyclohex-2-enyl acetate [(R)-7fA]

Under an argon atmosphere, CAL-B (100 mg), V-MPS4 (11 mg, 2.3 μmol of the vanadium component) and vinyl acetate (85 μL, 0.92 mmol) were added to a solution of (±)-5f (100 mg, 0.46 mmol) in MeCN (5.7 mL, 0.08 M) in this order at –20 ºC. The reaction mixture was stirred at –20 ºC for 78 h and then filtered through a Celite pad. The Celite pad was washed with EtOAc, and the combined filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexanes/EtOAc = 7:1) to give (R)-7fA (105 mg, 88% yield, 98% ee). Its optical purity was determined by HPLC analysis at 20 ºC, using a CHIRALCEL AD-3 column (hexanes/2-propanol = 99:1, 1.0 mL/min; retention times 22.9 (R), 24.6 min (S)).

A colorless oil. [α]_{D}^{20} = +144 (c 0.99, CHCl3). 1H NMR (400 MHz, CDCl3) δ 1.69-1.98 (m, 4H), 2.07 (s, 3H), 2.27-2.36 (m, 1H), 2.42-2.51 (m, 1H), 5.40-5.46 (m, 1H), 5.93-6.00 (m, 3H), 6.76 (d, J = 8.0 Hz, 1H), 6.88 (d, J = 2.0 Hz, 1H), 6.91 (dd, J = 2.0, 8.0 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ 19.4, 21.5, 27.6, 28.0, 68.9, 101.0, 106.0, 108.0, 119.0, 121.2, 135.4, 141.6, 147.1, 147.7, 170.9; IR (neat) ν 1729 cm –1. HRMS (MALDI) m/z calcd for C15H16O4 [M] +: 260.1043. Found: 260.1045.

(S)-1-(3,4-methylenedioxyphenyl)cyclohex-2-enyl]acetic acid [(S)-4fA]

Similarly to the preparation of (S)-4aA, (S)-4fA was obtained in 70% yield.

A white solid. Mp 118-119 ºC. [α]_{D}^{20} = +43 (c 0.91, CHCl3). 1H NMR (500 MHz, CDCl3) δ 1.31-1.41 (m, 1H), 1.50-1.57 (m, 1H), 1.78-1.91 (m, 2H), 1.96-2.04 (m, 2H), 2.67 (d, J = 15.0 Hz, 1H), 2.77 (d, J = 15.0 Hz, 1H), 5.89-5.95 (m, 3H), 6.03 (dd, J = 1.0, 10.0 Hz, 1H), 6.73 (d, J = 8.0 Hz, 1H), 6.78 (dd, J = 2.0, 8.0 Hz, 1H), 6.84 (d, J = 2.0 Hz, 1H); 13C NMR (125 MHz, CDCl3) δ 18.5, 25.0, 37.3, 41.5, 46.5, 100.9, 107.5, 107.7, 120.0, 128.9, 131.7, 140.6, 145.6, 147.4, 177.1; IR (neat) ν 3021, 1705 cm –1. HRMS (MALDI) m/z calcd for C15H16O4 [M] +: 260.1043. Found: 260.1045.

(S)-2-[1-(3,4-methylenedioxyphenyl)cyclohex-2-enyl]ethanol [(S)-8]

Similarly to the preparation of S2, (S)-8 was obtained in quantitative yield with 98% ee. Its optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL AD-3 column (hexanes/2-propanol = 90:10, 1.0 mL/min; retention times 11.1 (R), 12.0 min (S)).

A colorless oil. [α]_{D}^{20} = +58 (c 0.74, CHCl3). 1H NMR (400 MHz, CDCl3) δ 1.30-1.39 (m, 1H), 1.51-1.59 (m, 1H), 1.71 (ddd, J = 3.0, 11.0, 13.0 Hz, 1H), 1.83-1.90 (m, 1H), 1.92-2.06 (m, 4H), 3.51-3.64 (m, 2H), 5.80-5.85 (m, 1H), 5.87-5.91 (m, 1H), 5.92 (s, 2H), 6.73 (d, J = 8.5 Hz, 1H), 6.77 (dd, J = 2.0, 8.5 Hz,
1H), 6.85 (d, J = 2.0 Hz, 1H); 13C NMR (125 MHz, CDCl3) δ 18.6, 25.3, 37.4, 41.5, 45.2, 59.7, 100.8, 107.5, 107.7, 120.0, 128.4, 132.6, 141.8, 145.4, 147.6; IR (neat) ν 3348 cm⁻¹. HRMS (MALDI) m/z calcld for C15H18O3 [M]+: 246.1250. Found: 246.1248.

(S)-3a-(3,4-methylenedioxyphenyl)-3,3a,4,5,6,7-hexahydro-2H-indole [(S)-9]

DPPA (53 μL, 0.24 mmol) and DBU (37 μL, 0.24 mmol) were added to a solution of (S)-8 (50 mg, 0.20 mmol) in toluene (0.70 mL) at 30 °C. After the reaction mixture was stirred at 30 °C for 1 h, TMSN₃ (27 μL, 0.20 mmol) and DBU (30 μL, 0.20 mmol) were added to the solution. The reaction mixture was refluxed for 24 h and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, CH₂Cl₂/MeOH = 7:1) to give (S)-9 (39 mg, 78% yield).

A colorless oil. [α]D²⁰ = –43 (c 1.57, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 1.33–1.65 (m, 4H), 1.85–1.95 (m, 3H), 2.19–2.30 (m, 1H), 2.57–2.76 (m, 2H), 3.62 (ddt, J = 4.0, 8.5, 15.0 Hz, 1H), 3.86 (dddd, J = 1.5, 3.5, 8.0, 15.0 Hz, 1H), 5.94 (s, 2H), 6.54 (dd, J = 2.0, 8.0 Hz, 1H), 6.65 (d, J = 2.0 Hz, 1H), 6.76 (d, J = 8.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 22.4, 27.5, 30.2, 39.2, 41.9, 57.5, 58.5, 101.0, 106.6, 108.4, 119.1, 137.0, 145.8, 148.3, 180.8; IR (neat) ν 1651 cm⁻¹. HRMS (MALDI) m/z calcld for C15H18NO2 [M+H]+: 244.1332. Found: 244.1331.

(3aR,7aR)-3a-(3,4-methylenedioxyphenyl)octahydro-1H-indole (10)

NaBH₃CN (11 mg, 0.16 mmol) was added to a solution of (S)-9 (20 mg, 0.082 mmol) in acetic acid (0.33 mL) at room temperature. The reaction mixture was stirred at room temperature for 30 min, and 15% aq. NaOH (2 mL) and Et₂O (10 mL) were added. The organic phase was separated, and the aqueous phase was extracted with Et₂O (3 x 5 mL). The combined organic phases were washed with brine (10 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, CH₂Cl₂/MeOH = 5:1) to give 10 (17.7 mg, 88% yield).

A colorless oil. [α]D²⁰ = +11 (c 0.86, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 1.15–1.32 (m, 1H), 1.40–1.58 (m, 3H), 1.62–1.94 (m, 5H), 2.00 (ddd, J = 4.0, 8.5, 13.0 Hz, 1H), 2.07 (br s, 1H), 3.00 (dt, J = 4.5, 10.0 Hz, 1H), 3.09–3.17 (m, 1H), 3.42 (t, J = 4.0 Hz, 1H), 5.93 (s, 2H), 6.76 (d, J = 8.0 Hz, 1H), 6.82 (dd, J = 2.0, 8.0 Hz, 1H), 6.88 (d, J = 2.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 21.1, 22.1, 26.3, 33.9, 41.4, 43.1, 47.9, 61.0, 100.8, 107.6, 107.7, 119.4, 141.0, 145.2, 147.6; IR (neat) ν 3339 cm⁻¹. HRMS (MALDI) m/z calcld for C15H₂₀NO₂ [M+H]+: 246.1489. Found: 246.1493.
(–)-Crinane

$N,N$-Dimethylmethyleneammonium iodide (15 mg, 0.082 mmol) was added to a solution of 10 (10 mg, 0.041 mmol) in THF (2 mL) and the mixture was stirred at 50 °C for 36 h. THF was removed under reduced pressure, and Et$_2$O (5 mL) was added. 15% aq. NaOH was added until the solution became basic. The aqueous phase was extracted with Et$_2$O (3 x 5 mL). The organic phases were combined and washed with brine (5 mL), dried over Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, CH$_2$Cl$_2$/MeOH = 10:1) to give (–)-crinane (10.1 mg, 96% yield).

A colorless oil. $[\alpha]_D^{20} = –8.6 \ (c \ 0.77, \ CHCl_3)$ [ref.$^7$ $[\alpha]_D^{20} = –12.2 \ (c \ 0.66, \ CHCl_3)$, ref.$^8$ $[\alpha]_D^{20} +7.0 \ (c \ 1.0, \ CHCl_3)$ for (+)-crinane with 94% ee]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.12-1.32 (m, 2H), 1.43-1.67(m, 2H), 1.68-1.81 (m, 4H), 2.16-2.26 (m, 1H), 2.34 (d, $J = 13.0$ Hz, 1H), 2.75-2.90 (m, 2H), 3.29-3.41 (m, 1H), 3.75 (d, $J = 17.0$ Hz, 1H), 4.35 (d, $J = 17.0$ Hz, 1H), 5.88 (s, 2H), 6.46 (s, 1H), 6.71 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 21.8, 24.4, 27.6, 29.0, 37.9, 29.0, 52.0, 62.1, 67.4, 100.7, 103.4, 106.3, 126.0, 142.2, 145.6, 146.3. ; IR (neat) ν 3460 cm$^{-1}$. HRMS (MALDI) $m/z$ calcd for C$_{16}$H$_{20}$NO$_2$ [M+H]$^+$: 258.1489. Found: 258.1484.

References
Et₄COOH
Ph
4aB'}