SUPPORTING INFORMATION

For

Asymmetric Hydrogenation of *tert*-Alkyl Ketones

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1. General Experimental

All manipulations were conducted in an oven-dried glassware using standard Schlenck techniques employing argon gas (99.998%, purified through a BASF R3-11 catalyst at 80 ^{o}C). Toluene, benzene, hexane, THF, ether, and DMF were distilled from sodium/benzophenone and stored in Schlenk tubes with a sodium mirror. CH_2Cl_2, $(CH_3)_2CHOH$, and $(CH_3)_3COH$ were freshly distilled from CaH_2 and C_2H_5OH from sodium, and stored in a Schlenk tube with molecular sieves (4A). (*R*)- and (*S*)-1-phenylethanols in >99% ee were prepared by asymmetric hydrogenation of acetophenone according to our previous report (Ohkuma, T.; Koizumi, K.; Doucet, H.; Pham, T.; Kozawa, M.; Murata, K.; Katayama, E.; Yokozawa, T.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc*. **1998**, *120*, 13529–13530), and they were distilled from CaH_2 prior to use. Anhydrous CH_3OH and DMSO purchased from Aldrich Chemical Company were used without further purification. $CDCl_3$, toluene-d_8, and benzene-d_6 were purchased from Aldrich Chemical Company, stored in Schlenk tubes (Teflon taps) over CaH_2, freshly distilled, and degassed prior to use.

$[RuCl_2(\eta^6\text{-benzene})]_2$, ethyl 2-methylacetoacetate, 2,2-dimethylcyclohexanone, CH_3I, CaH, $NaBH_4$, tetrapropylammonium perruthenate (TPAP), $KOC(CH_3)_3$ (purified by sublimation), and 1-*tert*-butyl-4,4,4-tris-(dimethylamino)-2,2-bis[tris(dimethylamino)phosphoranylidenamino]-2',4'-catenadi-(phosphazene) were purchased from Aldrich Chemical Company. Pinacolone, pivalophenone, 2-

methyl-1-tetralone, 2-methyl-1-indanone, 2-formylfuran, 1-adamantyl methyl ketone, and acetophenone were purchased from Aldrich Chemical Company and purified by distillation from CaH_2. Ethyl 3-oxo-3-phenylpropanoate and *tert*-butylmagnesium chloride (1 M THF solution) were purchased from Kanto Chemical Co., Inc. α-Picolylamine (PICA), pivaloyl chloride, and ethyl 2-methylacetoacetate were purchased from Tokyo Kasei Kogyo Co., Ltd. (TCI) and used without further purification. Thiophene was purchased from Wako Chemicals. (*R*)-, (*S*)-2,2′-bis(di-4-tolylphosphino)-1,1′-binaphthyl (TolBINAP) was purchased from AZmax. Hydrogen gas (99.99999%) was obtained from Nippon Sanaso.

Gas chromatography (GC) analysis was conducted on HP-GC equipped with a CP-Chirasil-DEX CB (df = 0.25 μm, 0.32 mm i.d. × 25 m) or an Agilent 6890N instrument equipped with a Chiramix column (T. Hasegawa Co., Ltd.; 0.25 mm i.d. × 300 mm, df: 0.25 μm). High-performance liquid chromatography (HPLC) analysis was conducted on a Shimadzu SCL10A instrument equipped with a CHIRALCEL AD (4.6 mm i.d. × 250 mm, Daicel Chemical Industries) or CHIRALCEL OD-H (4.6 mm i.d. × 250 mm, Daicel Chemical Industries) column. ^{1}H, $^{13}C\{^{1}H\}$, and $^{31}P\{^{1}H\}$ NMR data were collected on JEOL GSX-270, α-400, or α-500 FT-NMR, and Bruker DMX-500 or AMX-400 spectrometers. Chemical shifts are expressed in parts per million (ppm) relative to $Si(CH_3)_4$, benzene, or $CHCl_3$ (δ 0.0, 7.16, and 7.24 ppm for ^{1}H NMR, and δ 0.0, 128.0, and 77.0 ppm for ^{13}C NMR, respectively). All chemical shifts for $^{31}P\{^{1}H\}$ NMR data are reported downfield in ppm relative to external 85% H_3PO_4 (0.0 ppm). Signal patterns are reported as follows: s, singlet; d, doublet; dd, doublet of doublets; t, triplet; dt, doublet of triplets; q, quartet; m, multiplet; br, broad signal; v br, very broad signal; u, unresolved. Standard pulse sequences for two-dimensional (2D) acquisitions were employed for DQF–COSY, ^{1}H–^{31}P HSQC, and ^{1}H–^{13}C HMQC. Processing and analyses of the spectra were done using a JEOL or Bruker XWINNMR software. Electrospray ionization–time of flight mass spectroscopy (ESI-TOFMS) was performed on a PE Biosystems Mariner™. Optical rotation was measured on Jasco P-1010-GT Polarimeter.

2. Synthesis of Ru Complexes

$RuCl_2$[(*R*)-tolbinap](pica) [(*R*)-3a]. [$RuCl_2(\eta^6$-benzene)]$_2$ (105.5 mg, 0.21 mmol) and 2 equiv of TolBINAP (286.0 mg, 0.42 mmol) were dissolved in 5.0 mL of DMF and placed in a 10-mL Schlenk tube under an argon atmosphere. Argon was bubbled through the solution for 5 min. The suspension was then heated at 100 °C for 10 min. Following solvent removal under vacuum, 45.4 mg (0.42 mmol) of α-picolylamine (PICA) was added together with 3.0 mL of CH_2Cl_2. The solution was stirred for 2 h. Reduction of the volume to ca 0.5 mL and addition of hexane (2 mL) yielded a yellow precipitation. The supernatant was removed by filtration and the resulting powder was dried in vacuo to give (*R*)-**1** in 86% yield (322.0 mg), which was used for hydrogenation without further purification. Mp >150 °C (decomp). Anal. Calcd for $C_{54}H_{48}Cl_2N_2P_2Ru$: C, 67.64; H, 5.05; N, 2.92. Found: C, 64.92; H, 4.68; N, 3.26. The precatalyst was obtained as a mixture of diastereomers. Heating it at 80 °C for 30 min in toluene results in a single dominant isomer (relative integration >90%). ^{1}H NMR (400 MHz, benzene-d_6) δ 1.78 (s, 3, CH_3), 1.90 (s, 3, CH_3), 2.28 (s, 3, CH_3), 2.33 (s, 3, CH_3), 2.86 (br s, 1, N*H*H), 3.22 (br s, 1, NH*H*), 3.95 (br s, 1, CH*H*), 4.93 (br s, 1, C*H*H), 6.19–8.36 (m, 32, aromatics). ^{31}P NMR (161.7 MHz, benzene-d_6) δ 44.2 (d, J = 35.6 Hz), 45.9 (d, J = 35.6 Hz). Importantly, the rate and enantioselectivity for ketone hydrogenation were independent of the initial diastereomeric ratio. **RuH(η^1-BH_4)[(*S*)-tolbinap](pica) [(*S*)-3b]**. (*S*)-**3a** (50.2 mg, 0.052 mmol) and $NaBH_4$ (30.1 mg, 0.81 mmol) were placed in a 20-mL Schlenk flask under an argon atmosphere. Addition of a 1:1 mixture of degassed benzene and C_2H_5OH (5 mL) immediately resulted in a pale red solution. This mixture was stirred at 40 °C for ca 1 min, and then immediately frozen in a liquid nitrogen bath. The solvent was removed in vacuo. The residue was extracted with benzene (5 mL), and the solution was filtered through a Celite® pad. The filtrate was concentrated to ca 0.3 mL, and was added hexane (3 mL) to precipitate a pale yellow solid. The supernatant was removed by filtration and the resulting powder was dried in vacuo to give (*S*)-**3b** (28.2 mg, 60%): mp >150 °C (decomp.); ^{1}H NMR (400 MHz, benzene-d_6) δ –13.82 (t, 1, J =

23.9 Hz, RuH), –0.75 (br s, 4, BH_4), 1.51 (u s, 1, N*H*H), 1.82 (u, 1, C*H*H), 1.85 (s, 3, CH_3), 1.90 (s, 3, CH_3), 2.13 (s, 3, CH_3), 2.16 (s, 3, CH_3), 2.28 (u, 1, CH*H*), 3.29 (u s, 1, NH*H*), 5.26–8.81 (m, 44, aromatics); ^{31}P (161.7 MHz, benzene-d_6) δ 71.6 (d, J = 41.4 Hz), 74.2 (d, J = 41.4 Hz). ^{1}H–^{1}H DQF-COSY aided the assignments. Other minor species were detected (<5%) but could not be characterised. The ruthenium complex (*S*)-**3b** was relatively unstable in solution (toluene-d_8, $CDCl_3$, and benzene-d_6) at RT and quickly deteriorated beyond 3–4 h.

3. General Hydrogenation Procedure

A typical hydrogenation procedure using pinacolone (**1a**) is described as an example. Accurately weighed amounts of precatalyst (*S*)-**3a** (2.5 mg, 2.6 μmol) and solid $KOC(CH_3)_3$ (14.5 mg, 0.13 mmol) were placed in a pre-oven-dried (120 °C) 100-mL glass autoclave containing a magnetic stirring bar. They were placed under high vacuum for at least 5 min before purging with argon. Freshly distilled C_2H_5OH (6.0 mL) and purified substrate **1a** (0.521 g, 5.20 mmol) were degassed by running argon through the solution (5 min), and then added to the autoclave under an argon atmosphere. Hydrogen was introduced under 8 atm pressure with several quick release–fill cycles before being reduced to the desired pressure (typically 5 atm). The solution was vigorously stirred at 25 °C, while hydrogen consumption was monitored. Following hydrogenation (typically 5 h), a small aliquot of the crude product mixture was analyzed by chiral GC to determine conversion and percent enantiomeric excess (ee) of the chiral alcohol product. The product was then purified by chromatography and/or bulb-to-bulb distillation to give the final isolated yield. As outlined below, all isolated products were characterized by various chromatography and spectrometric methods, ^{1}H and ^{13}C NMR analysis.

4. Hydrogenation of Pinacolone (1a) (S/C = 100 000)

Accurately weighed amounts of precatalyst (*S*)-**3a** (2.0 mg, 2.1 μmol) and solid $KOC(CH_3)_3$ (83.0 mg, 0.74 mmol) were placed in a pre-oven-dried (120 °C) 100-mL glass autoclave containing a magnetic

stirring bar with a plastic cover and subjected to high vacuum for 10 min before purging with argon. Freshly distilled C_2H_5OH (15.0 mL) and purified substrate **1a** (21.13 g, 0.21 mol) were degassed by three freeze–thaw cycles and then syringed into the autoclave. Hydrogen was introduced under 8 atm pressure with several quick release–fill cycles before the pressure being increased to 20 atm. The solution was vigorously stirred at 25 °C, and hydrogen consumption was monitored. Following hydrogenation for 22–24 h, a small aliquot of the crude product mixture was analyzed by chiral GC showing 100% conversion and 98% ee. The crude product was then purified by bulb-to-bulb distillation to give (*S*)-3,3-dimethyl-2-butanol [(*S*)-**2a**] (20.28 g, 96% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (s, 9, $C(CH_3)_3$), 1.13 (d, 3, J = 6.4 Hz, $CHCH_3$), 1.67 (br s, 1, OH), 3.45 (q, 1, J = 6.4 Hz, C*H*OH). $^{13}C\{^1H\}$ NMR (67.8 MHz, $CDCl_3$) δ 17.85 ($CHCH_3$), 25.32 ($C(CH_3)_3$), 34.81 ($C(CH_3)_3$), 75.55 (COH). GC conditions: CP-Chirasil-DEX CB column, P = 41 kPa, T(column) = 60 °C, T(injection) = 200 °C, T(detector) = 200 °C, t_R of (*R*)-**2a** = 17.2 min, t_R of (*S*)-**2a** = 17.9 min, 98% ee. Absolute configuration: found $[\alpha]^{22}_D$ +7.8° (neat), lit. $[\alpha]^{22}_D$ +8.1° (neat) for (*S*)-**2a** (Newman, P.; Lutkin, P.; Mislow, K. *J. Am. Chem. Soc.* **1958**, *80*, 465–473).

5. Substrate Syntheses and Hydrogenation Details

Pinacolone (1a). a) Hydrogenation conditions: (*S*)-**3a** (2.5 mg, 2.6 μmol); **1a** (0.521 g, 5.20 mmol); S/C = 2000; $KOC(CH_3)_3$ (14.5 mg, 0.13 mmol); C_2H_5OH (6.0 mL); P_{H_2} = 5 atm; T = 25 °C; t = 5 h. The solvent was removed under vacuum and the product was extracted with hexane (5 mL) and filtered through a Celite® pad, giving (*S*)-**2a** (0.47 g, 98% yield, 97% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (s, 9, $C(CH_3)_3$), 1.12 (d, 3, J = 6.4 Hz, $CHCH_3$), 1.65 (br s, 1, OH), 3.47 (q, 1, J = 6.4 Hz, C*H*OH). $^{13}C\{^1H\}$ NMR (67.8 MHz, $CDCl_3$) δ 17.80 ($CHCH_3$), 25.33 ($C(CH_3)_3$), 34.81 ($C(CH_3)_3$), 75.54 (COH). GC conditions: CP-Chirasil-DEX CB column, P = 41 kPa, T(column) = 60 °C, T(injection) = 200 °C, T(detector) = 200 °C, t_R of (*R*)-**2a** = 17.3 min, t_R of (*S*)-**2a** = 17.9 min, 97% ee. Absolute configuration:

found $[\alpha]^{25}_{D}$ +5.8° (neat), lit. $[\alpha]^{22}_{D}$ +8.1° (neat) for (*S*)-**2a** (Newman, P.; Lutkin, P.; Mislow, K. *J. Am. Chem. Soc.* **1958**, *80*, 465–473). b) Hydrogenation conditions: (*S*)-**3a** (2.4 mg, 2.6 μmol); **1a** (0.520 g, 5.20 mmol); S/C = 2000; 1-*tert*-butyl-4,4,4-tris(dimethylamikno)-2,2-bis[tris(dimethylamino)-phosphoranylidenamino]-2',4'-catenadi(phosphazene) (0.11 mL, 21.5 M solution in $(CH_3)_2CHOH$); C_2H_5OH (5.0 mL); P_{H_2} = 4 atm; T = 25 °C; t = 5 h. (*S*)-**2a** (100% yield, 97% ee). c) Hydrogenation conditions: (*S*)-**3b** (2.4 mg, 2.6 μmol); **1a** (0.520 g, 5.20 mmol); S/C = 2000; no base; C_2H_5OH (5.0 mL); P_{H_2} = 4 atm; T = 25 °C; t = 5 h. (*S*)-**2a** (100% yield, 97% ee). d) Hydrogenation conditions: (*S*)-**3a** (2.5 mg, 2.6 μmol); **1a** (0.520 g, 5.20 mmol); S/C = 2000; $KOC(CH_3)_3$ (14.5 mg, 0.13 mmol); CH_3OH (6.0 mL); P_{H_2} = 8 atm; T = 25 °C; t = 12 h. No conversion was detected. e) Hydrogenation conditions: (*S*)-**3a** (2.4 mg, 2.6 μmol); **1a** (0.521 g, 5.20 mmol); S/C = 2000; $KOC(CH_3)_3$ (14.5 mg, 0.13 mmol); $(CH_3)_2CHOH$ (6.0 mL); P_{H_2} = 9 atm; T = 25 °C; t = 12 h. (*S*)-**2a** (100% yield, 36% ee). f) Hydrogenation conditions: (*S*)-**3a** (2.5 mg, 2.6 μmol); **1a** (0.521 g, 5.20 mmol); S/C = 2000; $KOC(CH_3)_3$ (14.5 mg, 0.13 mmol); $(CH_3)_3COH$ (6.0 mL); P_{H_2} = 8 atm; T = 25 °C; t = 12 h. (*R*)-**2a** (100% yield, 68% ee). g) Hydrogenation conditions: (*S*)-**3a** (2.5 mg, 2.6 μmol); **1a** (0.520 g, 5.20 mmol); S/C = 2000; $KOC(CH_3)_3$ (14.5 mg, 0.13 mmol); a 2:3 mixture of CH_3OH and $(CH_3)_3COH$ (6.0 mL); P_{H_2} = 8 atm; T = 25 °C; t = 12 h. (*S*)-**2a** (100% yield, 99% ee). h) Hydrogenation conditions: (*S*)-**3a** (2.5 mg, 2.6 μmol); **1a** (0.520 g, 5.20 mmol); S/C = 2000; $KOC(CH_3)_3$ (15.9 mg, 0.15 mmol); (*R*)-1-phenylethanol (6.0 mL); P_{H_2} = 4 atm; T = 25 °C; t = 6 h. (*S*)-**2a** (100% yield, 76% ee). i) Hydrogenation conditions: (*S*)-**3a** (2.5 mg, 2.6 μmol); **1a** (0.520 g, 5.20 mmol); S/C = 2000; $KOC(CH_3)_3$ (15.9 mg, 0.15 mmol); (*S*)-1-phenylethanol (6.0 mL); P_{H_2} = 4 atm; T = 25 °C; t = 9 h. (*S*)-**2a** (100% yield, 39% ee). **2,2-Dimethyl-3-undecanone (1b).** 1-Nonanal (5.0 g, 35.3 mmol) was placed into a 100 mL three-necked, round bottomed flask and dissolved in freshly distilled ether (40 mL) under an argon atmosphere. This solution was cooled to –78 °C using a dry ice–acetone bath. *tert*-Butylmagnesium chloride (35.5 mL, 1.0 M solution in THF) was slowly added dropwise over a 15-min

period and the reaction mixture was stirred at the same temperature for 6 h. The solution was allowed to warm to RT and acidified with a dilute HCl solution. The crude product was extracted with ether (150 mL × 3), the organic layers were combined, washed with satd $NaHCO_3$ (40 mL × 2), water (40 mL × 2), and brine solution (40 mL × 2), and then dried over anhydrous Na_2SO_4. Removal of solvent under vacuum yielded a liquid product. Purification by chromatography (SiO_2, 100% hexane) gave racemic 2,2-dimethyl-3-undecanol (**2b**) as a colorless liquid in 92% yield (6.5 g). The oxidizing reagent was prepared by mixing $Na_2Cr_2O_7$ (5.25 g, 17.6 mmol) and conc H_2SO_4 (3.8 mL, 71.3 mmol) in acetic acid (40 mL) over a 30 min period with constant stirring, while maintaining the solution at 10 °C. 2,2-Dimethyl-3-undecanol (**2b**) (7.0 g, 35.0 mmol) was dissolved in glacial acetic acid (40 mL) in a 200 mL conical flask and the oxidizing reagent was slowly added while stirring. The color of the reaction mixture changed from orange to green over the following 2 h period. The resulting mixture was poured into brine solution (400 mL), extracted with CH_2Cl_2 (100 mL × 3), washed with saturated $NaHCO_3$ (50 mL × 2), water (50 mL × 3), and brine solution (40 mL × 2), and dried over anhydrous Na_2SO_4. The solvent was then removed under reduced pressure to obtain a mobile liquid. The required ketone **1b** was purified by vacuum distillation over CaH_2 (bp 76–78 °C/2 mmHg) in 91% yield (6.3 g). Caution! Decomposition of **1b** may occur during vacuum distillation. ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.87 (t, 3, J = 6.5 Hz, CH_2CH_3), 1.13 (s, 9, $C(CH_3)_3$), 1.2–1.3 (m, 10, $(CH_2)_5CH_3$), 1.5–1.6 (m, 2, CH_2CH_2CO), 2.46 (t, 2, J = 7.3 Hz, CH_2CO). $^{13}C\{^1H\}$ NMR (67.8 MHz, $CDCl_3$) δ 14.20 (CH_2CH_3), 22.74 (CH_2CH_3), 24.04 (CH_2CH_2CO), 26.49 ($C(CH_3)_3$), 29.26 (CH_2), 29.42 (CH_2), 29.55 (CH_2), 31.91 ($CH_2CH_2CH_3$), 36.51 (CH_2CO), 44.14 ($C(CH_3)_3$), 215.94 (C=O). Hydrogenation conditions: (*R*)-**3a** (0.4 mg, 0.4 μmol); **2b** (0.16 g, 0.8 mmol); S/C = 2300; $KOC(CH_3)_3$ (8.5 mg, 0.076 mmol); C_2H_5OH (3.0 mL); P_{H_2} = 5 atm; T = 25 °C; t = 5 h. The solvent was removed in vacuum and the product was purified by chromatography (SiO_2, ethyl acetate/hexane, 95:5), giving (*R*)-2,2-dimethyl-3-undecanol [(*R*)-**2b**] (0.15 g, 93% yield, 97% ee). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.86–0.89 (br s, 12, CH_2CH_3 and $C(CH_3)_3$), 1.28–1.35 (br m, 13, $(CH_2)_6$ and OH), 1.5–1.6 (br m, 2, CH_2CHOH), 3.15–3.20 (m, 1, $CHOH$). $^{13}C\{^1H\}$

NMR (67.8 MHz, $CDCl_3$) δ 14.19 (CH_2CH_3), 22.76 (CH_2CH_3), 25.77 ($C(CH_3)_3$), 27.20, (CH_2), 29.40 (CH_2), 29.72 (CH_2), 29.83 (CH_2), 31.60 (CH_2), 31.96 (CH_2), 34.97 ($C(CH_3)_3$), 79.97 (COH). GC conditions: CP-Chirasil-DEX CB column, P = 45 kPa, T = 125 °C, T(injection) = 200 °C, T(detector) = 200 °C, t_R of (*R*)-**2b** = 25.8 min, t_R of (*S*)-**2b** = 24.3 min, 97% ee. Absolute configuration: found $[\alpha]^{25}_D$ +29.1° (*c* 1.0, benzene), authentic sample made using (*R*)-MeCBS catalyst; $[\alpha]^{25}_D$ –27.3° (*c* 1.0, benzene) for (*S*)-**2b** (synthesis: Salunkhe, A. M.; Burkhardt, E. R. *Tetrahedron Lett*., **1997**, *38*, 1523–1526). **2,2-Dimethylpropiophenone (1d).** Hydrogenation conditions: (*S*)-**3a** (2.5 mg, 2.6 μmol); **1d** (0.85 g, 5.2 mmol); S/C = 2000; $KOC(CH_3)_3$ (15.0 mg, 0.13 mmol); C_2H_5OH (5.8 mL); P_{H_2} = 5 atm; T = 25 °C; t = 12 h. The solvent was removed under vacuum and the product was purified by chromatography (Al_2O_3, ethyl acetate/hexane, 5:95), giving (*R*)-2,2-dimethyl-1-phenyl-1-propanol [(*R*)-**2d**] (0.78 g, 96% yield, 97% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (s, 9, $3CH_3$), 1.82 (br s, 1, OH), 4.40 (br s, 1, CH), 7.2–7.4 (m, 5, aromatics). $^{13}C\{^1H\}$ NMR (67.8 MHz, $CDCl_3$) δ 25.92 (CH_3), 35.63 ($C(CH_3)_3$), 82.42 (COH), 127.28 (aromatic), 127.56 (aromatic), 127.60 (aromatic), 141.93 (aromatic-C1). GC conditions: CP-Chirasil-DEX CB column, P = 42 kPa, T = 125 °C, T(injection) = 200 °C, T(detector) = 200 °C, t_R of (*R*)-**2d** = 34.4 min, t_R of (*S*)-**2d** = 32.9 min, 97% ee. Absolute configuration: found $[\alpha]^{25}_D$ +24.3° (*c* 2.2, benzene), lit. $[\alpha]_D$ +25.9° (*c* 2.2, benzene) for (*R*)-**2d** (Vigneron, J. P.; Jacquet, I. *Tetrahedron* **1976**, *32*, 939–944). **2,2-Dimethyl-1-(2-furyl)-1-propanone (1e).** In a 100-mL three-necked, round-bottomed flask commercially available 2-formylfuran (2.32 g, 24.1 mmol) was dissolved in ether (20 mL) and the solution was cooled to –78 °C. *tert*-Butylmagnesium chloride (25.0 mL, 25 mmol, 1.0 M THF solution) was added dropwise with constant stirring within 45 min. The resulting mixture was brought to RT over a period of 6 h and then stirred at RT for 12 h. Following acidification with dilute HCl, the product was extracted with ether (100 mL × 2), washed with saturated $NaHCO_3$ (30 mL × 3), water (20 mL × 2), and brine solution (30 mL × 2), dried over anhydrous Na_2SO_4, concentrated under reduced pressure, and purified by chromatography (SiO_2, 100% hexane). The resulting 2,2-dimethyl-1-(2-furyl)-1-propanol (**2e**) (3.5 g, 25.4 mmol), *N*-methylmorpholine-*N*-oxide

(4.46 g, 36.0 mmol), 4A molecular sieves (12.0 g), CH_2Cl_2 (32 mL), and CH_3CN (15 mL) were placed in a 250-mL two-necked, round-bottomed flask under an argon atmosphere. TPAP (0.5 g, 1.42 mmol) was added to the reaction mixture in one lot. The resulting mixture was stirred at RT for 12 h. The product was filtered through a Celite® pad, concentrated under reduced pressure, and purified by vacumm distillation (bp. 25 °C/0.7 mmHg) to give **1e** in 52% yield (1.8 g, purity determined by GC was 93%). Caution! Sensitive to CaH_2 at higher temperature; polymerization may occur. ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.35 (s, 9, $3CH_3$), 6.49 (m, 1, aromatic-C4H), 7.22 (m, 1, aromatic), 7.54 (br s, 1, aromatic). $^{13}C\{^1H\}$ NMR (67.8 MHz, $CDCl_3$) δ 26.9 (CH_3), 43.0 ($C(CH_3)_3$), 111.6 (aromatic-C4), 117.9 (aromatic-C3), 144.8 (aromatic-C5), 152.3 (aromatic-C2), 194.6 (C=O). Hydrogenation conditions: (*S*)-**3a** (0.3 mg, 0.3 μmol); **1e** (0.11 g, 0.71 mmol); S/C = 2400; $KOC(CH_3)_3$ (9.5 mg, 0.085 mmol); C_2H_5OH (3.0 mL); P_{H_2} = 8 atm; T = 27 °C; t = 5 h. The solvent was removed under vacuum and the product was purified by chromatography (Al_2O_3, ethyl acetate/hexane, 5:95), giving (*R*)-2,2-dimethyl-1-(2-furyl)-1-propanol [(*R*)-**2e**] (0.10 g, 91% yield, 97% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (s, 9, $3CH_3$), 1.91 (d, 1, J = 3.9 Hz, OH), 4.38 (d, 1, J = 3.9 Hz, C*H*OH), 6.21 (d, 1, J = 3.2 Hz, aromatic-C3H), 6.34 (m, 1, aromatic-C4H), 7.36 (m, 1, aromatic-C5H). $^{13}C\{^1H\}$ NMR (100.4 MHz, $CDCl_3$) δ 25.71 (CH_3), 35.74 ($C(CH_3)_3$), 76.45 (COH), 106.94 (aromatic-C3), 109.9 (aromatic-C4), 141.31 (aromatic-C5), 155.68 (aromatic-C2). GC conditions: CP-Chirasil-DEX CB column, P = 40 kPa, T(column) = 110 °C, T(injection) = 200 °C, T(detector) = 200 °C, t_R of (*R*)-**2e** = 18.5 min, t_R of (*S*)-**2e** = 18.1 min, 97% ee. $[\alpha]^{25}_D$ +19.7° (c 2.2, benzene), The absolute configuration of (*R*)-**2e** was estimated by comparing ^{1}H-NMR signals of (*S*)-MTPA esters of this sample, racemic **2e**, (*S*)-**2d** (known configuration), and racemic **2d**. Chemical shifts (δ) of the (*S*)-MTPA esters at the methine protons: (*R*)-**2e** (hydrogenation product); 5.66, racemic **2e**; 5.66 and 5.72, (*S*)-**2d**; 5.72, racemic **2d**; 5.58 and 5.72. **2,2-Dimethyl-1-(2-thienyl)-1-propanone (1f).** A mixture of thiophene (5.0 g, 59.4 mmol), pivaloyl chloride (7.2 g, 59.7 mmol), and $AlCl_3$ (0.18 g, 1.3 mmol) was refluxed in a 100-mL round-bottomed flask for 8 h. The reaction mixture was then diluted with ether (50 mL) and filtered through a

Celite® pad. The product was separated by chromatography (SiO_2, 100 % hexane) and further purified by vacumm distillation (bp 50–52 °C/0.7 mmHg) to give 2,2-dimethyl-1-(2-thienyl)-1-propanone (**1f**) as a colorless liquid in 62% yield (6.2 g). ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.40 (s, 9, 3CH_3), 7.10 (dd, 1, *J* = 3.8, 4.9 Hz, aromatic-C4H), 7.56 (d, 1, *J* = 4.9 Hz, aromatic-C5H), 7.78 (d, 1, *J* = 3.8 Hz, aromatic-C3H). ^{13}C{^{1}H} NMR (67.8 MHz, $CDCl_3$) δ 28.22 (CH_3), 43.87 ($C(CH_3)_3$), 127.53 (aromatic-C4), 131.74 (aromatic-C3), 132.20 (aromatic-C5), 142.40 (aromatic-C2), 198.69 (C=O). Hydrogenation conditions: (*S*)-**3a** (0.6 mg, 0.6 μmol); **1f** (0.21 g, 1.2 mmol); S/C = 2100; $KOC(CH_3)_3$ (9.5 mg, 0.085 mmol); C_2H_5OH (3.0 mL); P_{H_2} = 8 atm; *T* = 27 °C; *t* = 5 h. The solvent was removed under vacuum and the product was purified by chromatography (Al_2O_3, ethyl acetate/hexane, 5:95), giving (*R*)-2,2-dimethyl-1-(2-thienyl)-1-propanol [(*R*)-**2f**] (0.20 g, 95% yield, 98% ee). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.98 (s, 9, 3CH_3), 2.02 (d, 1, *J* = 3.2 Hz, OH), 4.67 (d, 1, *J* = 3.2 Hz, C*H*OH), 6.9–7.0 (m, 2, aromatic-C3H and -C4H), 7.23 (d, 1, *J* = 5.1 Hz, aromatic-C5H). ^{13}C{^{1}H} NMR (67.8 MHz, $CDCl_3$) δ 25.96 (CH_3), 35.77 ($C(CH_3)_3$), 78.85 (COH), 124.07 (aromatic-C5), 125.01 (aromatic-C3), 125.81 (aromatic-C4), 145.76 (aromatic-C2). GC conditions: CP-Chirasil-DEX CB column, *P* = 40 kPa, *T*(column) = 120 °C, *T*(injection) = 200 °C, *T*(detector) = 200 °C, t_R of (*R*)-**2f** = 40.9 min, t_R of (*S*)-**2f** = 36.3 min, 98% ee. $[\alpha]^{25}_D$ +35.6° (*c* 0.32, benzene). The absolute configuration of (*R*)-**2f** was estimated by comparison of the sign of rotation and chiral GC behavior with those of (*R*)-**2d** and (*R*)-**2e**, which absolute configurations were determined as described above. All these alcohols, i.e., (*R*)-**2d**, **2e**, and **2f**, were dextrorotatory in benzene solutions, with shorter retention times than the *S* isomers in chiral GC analysis with a CP-Chirasil-DEX CB column. **(*E*)-4,4-Dimethyl-1-phenyl-1-penten-3-one (1g).** Synthesis as previously reported (Hill, G.A.; Bramann, G. M. *Org. Syn. Coll. Vol I*, 81–82). ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.23 (s, 9, 3CH_3), 7.13 (d, 1, *J* = 15.9 Hz, CHCO), 7.36–7.40 (m, 3, aromatics), 7.54–7.59 (m, 2, aromatics), 7.68 (d, 1, *J* = 15.9 Hz, C*H*C_6H_5). ^{13}C{^{1}H} NMR (67.8 MHz, $CDCl_3$) δ 26.35 (CH_3), 43.25 ($C(CH_3)_3$), 120.60 (*C*HCO), 128.13 (aromatic-CH), 128.70 (aromatic-CH), 130.04

(aromatic-CH), 134.79 (aromatic-C1), 142.71 (CHC_6H_5), 203.90 (C=O). Hydrogenation conditions: (*S*)-**3a** (2.0 mg, 2.1 μmol); **1g** (0.80 g, 4.3 mmol); S/C = 2050; $KOC(CH_3)_3$ (11.5 mg, 0.102 mmol); C_2H_5OH (5.0 mL); P_{H_2} = 5 atm; T = 25 °C; t = 5 h. The solvent was removed under vacuum and the product was purified by chromatography (SiO_2, ethyl acetate/hexane, 98:2), giving (*S*)-(*E*)-4,4-dimethyl-1-phenyl-1-penten-3-ol [(*S*)-**2g**] (0.79 g, 97% yield, 97% ee). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.96 (s, 9, $3CH_3$), 1.73 (br s, 1, OH), 3.93 (br d, 1, J = 7.3 Hz, HOC*H*), 6.27 (dd, 1, J = 16.2 and 7.0 Hz, C*H*COH), 6.57 (d, 1, J = 16.2 Hz, CHC_6H_5), 7.20–7.41 (m, 5, aromatics). $^{13}C\{^1H\}$ NMR (67.8 MHz, $CDCl_3$) δ 25.85 (CH_3), 35.33 ($C(CH_3)_3$), 80.91 (CHOH), 126.31 (aromatic-C2 and -C6), 127.42 (*C*HCOH), 128.42 (aromatic-C3 and -C5), 129.45 (CHC_6H_5), 131.66 (aromatic-C4), 136.74 (aromatic-C1). GC conditions: CP-Chirasil-DEX CB column, P = 80 kPa, T(column) = 130 °C, T(injection) = 250 °C, T(detector) = 250 °C, t_R of (*R*)-**2g** = 29.9 min, t_R of (*S*)-**2g** = 28.3 min, 97% ee. $[\alpha]^{25}_D$ –15.3° (*c* 1.10, $CHCl_3$). The absolute configuration of (*S*)-**2g** was determined by the sign of rotation after conversion to (*S*)-2,2-dimethyl-5-phenyl-3-pentanol (2 atm H_2, 10% Pd/C, 23 °C, 12 h). $[\alpha]^{25}_D$ –48.9° (*c* 1.10, $CHCl_3$), lit. $[\alpha]^{20}_D$ +50.0° (*c* 1.15, $CHCl_3$) for the *R* alcohol in >95% ee (Beckmann, E.; Desai, V.; Hoppe, D. *Synlett* **2004**, 2275–2280). **(*E*)-2,2-Dimethyl-4-undecen-3-one (1h) (*E*/*Z* = 5:1).** Pinacolone (12.0 mL, 97.2 mmol) was dissolved in CH_3OH (50 mL) in a round-bottomed flask (200 mL) and the solution cooled in an ice bath. To this bromine was added (17.0 g, 106.4 mmol) in one portion quickly. It was stirred at the same temperature for 1 h and then at RT for 11 h. Water (10 mL) was added and the solution was stirred for 3 h, neutralized with $NaHCO_3$ (solid), and filtered through a filter paper. The solvent was removed under reduced pressure. The resulting mixture was extracted with ether and removal of the solvent gave a crude product mixture of 1-bromo-3,3-dimethyl-2-butanone (10.6 g, 60.9% yield) and 1,1-dibromo-3,3-dimethyl-2-butanone (2.99 g, 12% yield). Desired 1-bromo-3,3-dimethyl-2-butanone was obtained as a colorless liquid by fractional distillation (bp 73–75 °C/13 mmHg) in 49% yield (8.5 g). 1-Bromo-3,3-dimethyl-2-butanone (8.5 g, 47.2 mmol) and triphenylphosphine (12.4 g, 47.3 mmol) were placed in benzene (100 mL) and water (50 mL) and then a

solution of NaOH (1.81g in 10 mL water) was added over 15 min. The mixture was stirred at RT for 6 h. The organic layer was separated and washed with water (30 mL × 2), and removal of the solvent gave 14.0 g (86 %) of the expected ylide. This solid was subsequently used without further purification. The phosphorane (14.0 g, 38.8 mmol) and 1-heptanal (4.4 g, 38.5 mmol) were refluxed in benzene (50 mL) for 24 h. The solution was cooled, concentrated, extracted with hexane (100 mL × 2), and filtered. Removal of solvent resulted in an orange-colored liquid. It was purified by chromatography (SiO_2, hexane) followed by fractional distillation (bp 70–71 °C/1 mmHg) to give 5.5 g (73 %) of **2g** in a 5:1 *E*:*Z* ratio. ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85–0.90 (m, 3, CH_2CH_3), 1.15 (s, 9, $C(CH_3)_3$), 1.25–1.50 (br m, 8, $(CH_2)_4CH_3$), 2.15–2.25 (m, 2, CH=CHCH_2), 6.47 (d, 1, J = 15.1 Hz, CH=C*H*CO), 6.94 (dt, 1, J = 15.1 and 7.0 Hz, CH=C*H*CH_2). ^{13}C{^{1}H} NMR (67.8 MHz, $CDCl_3$) δ 14.07 (CH_2CH_3), 22.57 (CH_2CH_3), 26.23 ($C(CH_3)_3$), 28.19 (CH_2), 28.87 (CH_2), 31.60 (CH_2), 32.51 (CH_2), 40.34 ($C(CH_3)_3$), 123.96 (CH=*C*HCO), 147.45 (*C*H=CHCO), 204.01 (C=O). Hydrogenation conditions: (*R*)-**3a** (0.5 mg, 0.5 μmol); **1h** (210 mg, 1.1 mmol); S/C = 2040; $KOC(CH_3)_3$ (9.0 mg, 0.080 mmol); C_2H_5OH (3.0 mL); P_{H_2} = 8 atm; T = 27 °C; t = 5 h. The solvent was removed under vacuum, giving crude 2,2-dimethyl-4-undecene-3-ol (99.6 % yield) as a 5:1 mixture of *E*/*Z* isomers. The product was purified by chromatography (Al_2O_3, ethyl acetate/hexane, 95:5), yielding (*R*)-(*E*)-2,2-dimethyl-4-undecen-3-ol [(*R*)-**2h**] (152 mg, 72% yield, 98% ee). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85–0.93 (m, 3, CH_2CH_3), 0.89 (s, 9, $C(CH_3)_3$), 1.24–1.40 (br m, 9, $(CH_2)_4CH_3$ and OH), 2.05 (m, 2, CH=CHCH_2), 3.68 (d, 1, J = 7.6 Hz, C*H*OH), 5.50 (dd, 1, J = 7.6 and 15.4 Hz, CH=C*H*CHOH), 5.63 (dt, 1, J = 15.4 and 6.6 Hz, CH=C*H*CH_2). ^{13}C{^{1}H} NMR (67.8 MHz, $CDCl_3$) δ 14.07 (CH_2CH_3), 22.61 (CH_2CH_3), 25.70 ($C(CH_3)_3$), 28.82 (CH_2), 29.21 (CH_2), 31.68 (CH_2), 32.34 (CH_2), 34.73 ($C(CH_3)_3$), 81.14 (*C*HOH), 129.66 (CH=*C*HCHOH), 133.75 (*C*H=CHCHOH). GC conditions: CP-Chirasil-DEX CB column, P = 45 kPa, T(column) = 125 °C, T(injection) = 200 °C, T(detector) = 200 °C, t_R of (*R*)-**2h** = 24.1 min, t_R of (*S*)-**2h** = 23.3 min, 98% ee. The absolute configuration was determined by Pd/C hydrogenation of (*R*)-**2h** to give (*R*)-**2b** (83% ee) with some decrease in enantiomeric purity. The configuration of **2b** was

determined from product of hydrogenation with (*S*)-**1**: found $[\alpha]^{25}_{D}$ –28.5° (*c* 1.0, benzene), authentic sample made using (*R*)-MeCBS catalyst; $[\alpha]^{25}_{D}$ –27.3° (*c* 1.0, benzene) for (*S*)-**2b** (synthesis: Salunkhe, A. M.; Burkhardt, E. R. *Tetrahedron Lett*., **1997**, *38*, 1523–1526). **1-Adamantyl methyl ketone (4).** Hydrogenation conditions: (*S*)-**3a** (1.0 mg, 1.0 μmol); **4** (0.373 g, 2.1 mmol); S/C = 2000; $KOC(CH_3)_3$ (6.8 mg, 0.06 mmol); C_2H_5OH (3.0 mL); P_{H_2} = 5 atm; *T* = 25 °C; *t* = 5 h. The solvent was removed under vacuum and the product was extracted with hexane (5 mL) and filtered through a Celite® pad. Removal of the solvent under vacuum yielded solid (*S*)-1-(1-adamantyl)ethanol (0.86 g, 98% yield, 98% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (d, 3, *J* = 6.4 Hz, CH_3), 1.4–1.7 (u m, 13, adamantyl-CH_2 and OH), 1.98 (br s, 3, adamantyl-CH), 3.2–3.3 (m, 1, C*H*OH). ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$) δ 16.37 (CH_3), 28.25 (adamantyl-CH), 28.39 (adamantyl-CH), 36.47 (adamantly-C1), 37.18 (adamantyl-CH_2), 37.64 (adamantyl-CH_2), 75.82 (COH). The ee of the alcohol was determined by chiral HPLC analysis of the benzoyl derivative; column, CHIRALCEL AD, 4.6 mm i.d. x 250 mm, Daicel Chemical Industries; eluent, $(CH_3)_2CHOH$/hexane (2:98); temp, 30 °C; flow rate, 0.1 mL/min; detection, 254-nm light; t_R of (*R*)-1-(1-adamantyl)ethyl benzoate = 51.2 min, t_R of (*S*)-1-(1-adamantyl)ethyl benzoate = 57.7 min, 98% ee (Evans, D. A.; Michael, F. E.; Tedrow, J. S.; Campos, K. R. *Am. Chem. Soc.* **2003**, *125*, 3534–3543). Absolute configuration determined from the acetate derivative: found $[\alpha]^{25}_{D}$ –11.3° (*c* 3.77, CCl_4), literature $[\alpha]^{25}_{D}$ +18.1° (*c* 3.77, CCl_4) for (*R*)-1-(1-adamantyl)ethanol (Kuwano, R.; Sawamura, M.; Shirai, J.; Takahashi, M.; Ito, Y. *Bull. Chem. Soc. Jpn*. **2000**, *73*, 485–496). **2,2-Dimethylcyclohexanone (5).** The starting material was available in 92% purity. Hydrogenation conditions: (*S*)-**3a** (0.5 mg, 0.5 μmol); **5** (0.148 g, 1.17 mmol); S/C = 2250; $KOC(CH_3)_3$ (6.9 mg, 0.061 mmol); C_2H_5OH (3.0 mL); P_{H_2} = 8 atm; *T* = 25 °C; *t* = 5 h. The solvent was removed under vacuum and the product was purified by chromatography (SiO_2, ethyl acetate/hexane, 10:90), giving (*S*)-2,2-dimethylcyclohexanol (0.137 g, 91% yield, 84% ee). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85 (s, 3, CH_3), δ 0.97 (s, 3, CH_3), 1.2–1.5 (m, 7, $(CH_3)_2C(CH_2)_3$ and OH), 1.6–1.8 (m, 2, CH_2CHOH), 3.2–3.35 (m, 1,

C*H*OH). $^{13}C\{^1H\}$ NMR (67.8 MHz, $CDCl_3$) δ 19.42 (CH_2), 21.66 (CH_3), 24.45 (CH_2), 28.46 (CH_2), 30.60 (CH_3), 35.41 ($C(CH_3)_2$), 38.36 (CH_2), 77.32 (CHOH). GC conditions: Chiramix column, flow rate = 0.7 mL/min, *T*(column) = 40–160 °C (0.7 °C/min), *T*(injection) = 230 °C, *T*(detector) = 250 °C, t_R of (*R*)-2,2-dimethylcyclohexanol = 63.9 min, t_R of (*S*)-2,2-dimethylcyclohexanol = 65.7 min, 84% ee. Absolute configuration determined from the 3,5-dinitrobenzoate derivative: found $[\alpha]_D$ –35.6° (c 1.73, $CHCl_3$), lit. $[\alpha]^{20}_D$ –42.5° (*c* 1.73, $CHCl_3$) for (*S*)-2,2-dimethylcyclohexanol (Yamamoto, H.; Oritani, T.; Koga, H.; Horiuchi, T.; Yamashita, K. *Agric. Biol. Chem.* **1990**, *54*, 1915–1920). **2,2-Dimethyl-1-indanone (6a).** This compound was prepared according to literature (Jaonen, G.; Meyer, A. *J. Am. Chem. Soc.* **1975**, *97*, 4667–4672). Sodium *tert*-amylate (9.5 g, 86.4 mmol) was added to a THF (50 mL) solution of 2-methyl-1-indanone (5.0 g, 37.8 mmol) in a two-necked, round-bottomed flask, and the mixture was stirred at RT for 15 min. The resulting slurry was cooled in an ice bath and CH_3I was added (8.0 mL, 128 mmol). The reaction mixture was stirred at the same temperature for 6 h and then at RT for 12 h. The solid was filtered through a filter-paper and washed with ethyl acetate (3 × 50 mL). The filtrates were combined and the solvent was removed under vacuum to give a viscous liquid. Following distillation from CaH_2 (bp 61–62 °C/1 mmHg), **6a** was obtained as a white crystalline solid in 88% yield (5.3 g). ^1H NMR (500 MHz, $CDCl_3$) δ 1.24 (s, 6, $2CH_3$), 3.00 (s, 2, CH_2), 7.37 (dd, 1, *J* = 7.6 and 7.8 Hz, aromatic-C6), 7.42 (d, 1, *J* = 7.6 Hz, aromatic-C4), 7.59 (dd, 1, *J* = 7.6 and 7.6 Hz, aromatic-C5), 7.77 (d, 1, *J* = 7.8 Hz, aromatic-C7). $^{13}C\{^1H\}$ NMR (125.65 MHz, $CDCl_3$) δ 25.2 ($2CH_3$), 42.8 (CH_2), 45.4 ($C(CH_3)_2$), 124.4 (aromatic-CH), 126.5 (aromatic-CH), 127.3 (aromatic-CH), 134.7 (aromatic-CH), 135.3 (aromatic-C), 152.1 (aromatic-C), 211.2 (C=O). Hydrogenation conditions: (*R*)-**3a** (0.6 mg, 0.6 μmol); **6a** (0.205 g, 1.3 mmol); S/C = 2050; $KOC(CH_3)_3$ (7.5 mg, 0.067 mmol); C_2H_5OH (3.0 mL); P_{H_2} = 8 atm; *T* = 27 °C; *t* = 20 h. The solvent was removed under vacuum and the product was purified by chromatography (SiO_2, ethyl acetate/hexane, 10:90), giving (*S*)-2,2-dimethyl-1-indanol [(S)-**7a**] (0.20 g, 99% yield, 90% ee). ^1H NMR (270 MHz, $CDCl_3$) δ 1.03 (s, 3, CH_3), δ 1.18 (s, 3, CH_3), 1.62 (d, 1, *J* = 7.9 Hz, OH), 2.65 (d, 1, *J* = 15.8 Hz, CH*H*), 2.78 (d, 1, *J* = 15.8 Hz, C*H*H), 4.68

(d, 1, J = 7.9 Hz, C*H*OH), 7.1–7.25 (m, 3, aromatics), 7.3–7.4 (m, 1, aromatic). $^{13}C\{^1H\}$ NMR (67.8 MHz, $CDCl_3$) δ 21.49 (CH_3), 26.80 (CH_3), 44.64 ($C(CH_3)_2$), 44.92 (CH_2), 83.56 (CHOH), 124.29 (aromatic-CH), 124.96 (aromatic-CH), 126.48 (aromatic-CH), 127.95 (aromatic-CH), 141.75 (aromatic-C), 144.35 (aromatic-C). GC conditions: CP-Chirasil-DEX CB column, P = 70 kPa, T(column) = 110 °C, T(injection) = 200 °C, T(detector) = 200 °C, t_R of (*R*)-**7a** = 26.1 min, t_R of (*S*)-**7a** = 27.4 min, 90% ee. Absolute configuration: found $[\alpha]^{20}_D$ +24.4° (*c* 1.31, $CHCl_3$), lit. $[\alpha]^{22}_D$ +29.0° (*c* 1.31, $CHCl_3$) for (*S*)-**7a** (Jaonen, G.; Meyer, A. *J. Am. Chem. Soc.* **1975**, *97*, 4667–4672). **2,2-Dimethyl-1-tetralone (6b).** This compound was prepared according to literature (Jaonen, G.; Meyer, A. *J. Am. Chem. Soc.* **1975**, *97*, 4667–4672). Sodium *tert*-amylate (3.50 g, 31.81 mmol) was added to a THF solution (75 mL) of 2-methyl-1-tetralone (5.0 g, 31.25 mmol) in a two-necked, round-bottomed flask, and the mixture was stirred at RT for 15 min. The resulting slurry was cooled in an ice bath and CH_3I was added (2.0 mL, 32.1 mmol). The reaction mixture was stirred at the same temperature for 6 h and then at RT for 12 h. The solid was filtered through a filter-paper and washed with ethyl acetate (3 × 50 mL). The filtrates were combined and the solvent was removed under vacuum to give a viscous product. Subsequent distillation over CaH_2 (bp 94–96 °C/2 mmHg), **6b** was obtained as a colorless liquid in 90% yield (4.90 g). ^1H NMR (270 MHz, $CDCl_3$) δ 1.21 (s, 6, $2CH_3$), 1.98 (t, 2, J = 6.0 Hz, $CH_2C(CH_3)_2$), 2.98 (t, 2, J = 6.0 Hz, $ArCH_2$), 7.22 (d, 1, J = 7.8 Hz, aromatic-C5), 7.29 (dd, 1, J = 7.8 and 8.1 Hz, aromatic-C7), 7.45 (dd, 1, J = 7.8 and 8.1 Hz, aromatic-C6), 8.04 (d, 1, J = 7.8 Hz, aromatic-C8). $^{13}C\{^1H\}$ NMR (67.8 MHz, $CDCl_3$) δ 24.4 ($2CH_3$), 25.7 (CH_2Ar), 36.6 ($CH_2C(CH_3)_2$), 41.6 ($C(CH_3)_2$), 126.4 (aromatic-CH), 127.8 (aromatic-CH), 128.5 (aromatic-CH), 131.2 (aromatic-C), 132.8 (aromatic-CH), 143.2 (aromatic-C), 202.6 (C=O). Hydrogenation conditions: (*R*)-**3a** (0.5 mg, 0.5 μmol); **6b** (0.217 g, 1.25 mmol); S/C = 2400; $KOC(CH_3)_3$ (8.0 mg, 0.071 mmol); C_2H_5OH (3.0 mL); P_{H_2} = 8 atm; T = 27 °C; t = 5 h. The solvent was removed under vacuum and the product was separated by passing solution through a Celite® pad and silica gel, giving (*S*)-2,2-dimethyl-1-tetranol [(*S*)-**7b**] (0.215 g, 99% yield, 98% ee). ^1H NMR (500 MHz, $CDCl_3$) δ 0.98 (s, 3, CH_3), δ 1.00 (s, 3, CH_3), 1.53 (ddd, 1, J = 6.6, 6.7, and 13.5 Hz,

C*H*HC(CH_3)$_2$), 1.55–1.65 (m, 1, OH), 1.81 (ddd, 1, *J* = 6.6, 7.0, and 13.5 Hz, CH*H*C(CH_3)$_2$), 2.75 (ddd, 1, *J* = 6.7, 7.0, and 17.1 Hz, C*H*HAr), 2.83 (ddd, 1, *J* = 6.6, 6.6, and 17.1 Hz, CH*H*Ar), 4.25 (d, 1, *J* = 6.9 Hz, C*H*OH), 7.07–7.12 (m, 1, aromatic), 7.16–7.22 (m, 2, aromatics), 7.41–7.45 (m, 1, aromatic). $^{13}C\{^1H\}$ NMR (67.8 MHz, $CDCl_3$) δ 22.5 (CH_3), 25.6 (CH_3), 25.9 (CH_2Ar), 32.0 (*C*H_2C(CH_3)$_2$), 33.8 (*C*(CH_3)$_2$), 76.6 (CHOH), 126.1 (aromatic-CH), 127.3 (aromatic-CH), 128.7 (aromatic-CH), 128.8 (aromatic-CH), 135.9 (aromatic-C), 138.5 (aromatic-C). GC conditions: CP-Chirasil-DEX CB column, *P* = 70 kPa, *T*(column) = 120 °C, *T*(injection) = 200 °C, *T*(detector) = 200 °C, t_R of (*R*)-**7b** = 33.7 min, t_R of (*S*)-**7b** = 34.4 min, 98% ee. Absolute configuration: found $[\alpha]^{24}_D$ +18.7° (*c* 3.37, $CHCl_3$), lit. $[\alpha]^{22}_D$ –23.5° (*c* 3.37, $CHCl_3$) for (*R*)-**7b** (Jaonen, G.; Meyer, A. *J. Am. Chem. Soc.* **1975**, *97*, 4667–4672). **Ethyl 2,2-dimethyl-3-oxobutanoate (8a).** This compound was prepared according to literature (Brown, H. C.; Chandrasekharan, J.; Ramachandran, P. V. *J. Am. Chem. Soc.* **1988**, *110*, 1539–1546). Ethyl 2-methyl-3-oxobutanoate (5.01 g, 34.8 mmol) was added dropwise, with stirring, to a 200-mL round-bottomed flask containing a suspension of NaH (1.06 g, 44.0 mmol) in THF (40 mL) at 0 °C. The mixture was stirred at RT for 1 h. The resulting near homogeneous mixture was cooled with an ice bath and mixed with CH_3I (8.20 g, 57.0 mmol). The resulting mixture was stirred at RT for 16 h. The solvent was removed under vacuum, and the mixture was extracted with hexane and purified by chromatography (SiO_2, ethyl acetate/hexane, 1:7). Distillation (bp 73–75 °C/14 mmHg) yielded 3.90 g (71% yield) of **8a**. ^1H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, 3, *J* = 7.2 Hz, CH_2CH_3), 1.36 (s, 6, (CH_3)$_2$CO), 2.16 (s, 3, CH_3CO), 4.20 (q, 2, *J* = 7.2 Hz, CH_2CH_3). Hydrogenation conditions: (*S*)-**3a** (2.0 mg, 2.1 μmol); **8a** (0.670 g, 4.2 mmol); S/C = 2000; KOC(CH_3)$_3$ (12.3 mg, 0.11 mmol); C_2H_5OH (4.8 mL); P_{H_2} = 5 atm; *T* = 25 °C; *t* = 5 h. The solvent was removed under vacuum and the product was purified by bulb-to-bulb distillation, giving (*S*)-ethyl 2,2-dimethyl-3-hydroxybutanoate [(*S*)-**9a**] (0.77 g, 98% yield, 97% ee). ^1H NMR (270 MHz, $CDCl_3$) δ 1.14 (d, 3, *J* = 6.6 Hz, CH_3CHOH), 1.17 (s, 3, CH_3CCO), 1.18 (s, 3, CH_3CCO), 1.27 (t, 3, *J* = 7.3 Hz, CH_2CH_3), 2.81 (br d, 1, *J* = 6.3 Hz, OH), 3.86 (dq, 1, *J* = 6.3 and 6.6 Hz, C*H*OH), 4.16 (q, 2, *J* = 7.3 Hz, CH_2). $^{13}C\{^1H\}$ NMR (67.8 MHz, $CDCl_3$) δ

14.16 (CH_2CH_3), 17.72 ($COCCH_3$), 19.81 ($COCCH_3$), 22.32 (CH_3CHOH), 46.96 ($C(CH_3)_2$), 60.60(CH_2CH_3), 72.33 (CHOH), 177.57 (C=O). GC conditions: CP-Chirasil-DEX CB column, P = 35 kPa, T(column) = 100 °C, T(injection) = 250 °C, T(detector) = 250 °C, t_R of (R)-**9a** = 14.7 min, t_R of (S)-**9a** = 14.0 min, 97% ee. Absolute configuration: found $[\alpha]^{25}_D$ +9.8° (c 1.32, $CHCl_3$), lit. $[\alpha]_D$ +6.98° (c 1.26, $CHCl_3$) Kuwano, R.; Sawamura, M.; Shirai, J.; Takahashi, M.; Ito, Y. Bull. Chem. Soc. Jpn., **2000**, *73*, 485–496) for (S)-**9a**. **Ethyl 2,2-dimethyl-3-oxo-3-phenylpropanoate (8b).** Synthesis adapted from a previous literature procedure (Best, W. M.; Cook, A. P. F.; Russell, J. J.; Widdowson, D. A. *J. Chem. Soc., Perkin Trans. I* **1986**, 1139–1143). A mixture of commercially available ethyl 3-oxo-3-phenylpropanoate (5.09 g, 26.4 mmol) and K_2CO_3 (5 g) in DMSO/$CHCl_3$ (30/40 mL) was cooled to 0 °C. CH_3I (4.97 g, 35.0 mmol) was added and the mixture was stirred at RT for 24 h. Solvent was removed under vacuum, and the product was extracted with 80 mL of ether, filtered through a filter-paper, and washed with 45 mL of water containing 5 mL of acetic acid. The ether solution was dried with $MgSO_4$ and solvent was removed under vacuum giving ethyl 2-methyl-3-oxo-3-phenylpropanoate in 94% yield (5.02 g). This crude mixture (4.88 g, 23.2 mmol) was added to a suspension of NaH (0.678 g, 28.4 mmol) in DMSO (30 mL). The mixture was stirred to become a homogeneous phase and then CH_3I (6.53, 46.3 mmol) was added. The resulting mixture was stirred for 16 h, extracted with hexane, and purified by chromatography (SiO_2, ethyl acetate/hexane, 1:7). Distillation (bp 84–87 °C/0.5 mmHg) yielded 2.09 g (39 % yield) of **8b**. ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.05 (t, 3, J = 7.3 Hz, CH_2CH_3), 1.54 (s, 6, CH_3), 4.11 (q, 2, J = 7.3 Hz, CH_2), 7.4–7.6 (m, 3, aromatics), 7.84 (d, 2, J = 7.3 Hz, aromatic-C2H and -C6H). $^{13}C\{^1H\}$ NMR (67.8 MHz, $CDCl_3$) δ 13.79 (CH_2CH_3), 23.94 ($(CH_3)_2CCO$), 53.25 ($C(CH_3)_2$), 61.29 (CH_2), 128.28 (aromatic-C3 and -C5), 128.45 (aromatic-C2 and -C6), 132.48 (aromatic-C4), 135.07 (aromatic-C1), 174.74 ($COOCH_2CH_3$), 197.49 (COC_6H_5). Hydrogenation conditions: (S)-**3a** (2.0 mg, 2.1 μmol); **8b** (0.92 g, 4.2 mmol); S/C = 2000; $KOC(CH_3)_3$ (11.0 mg, 0.098 mmol); C_2H_5OH (4.0 mL); P_{H_2} = 5 atm; T = 25 °C; t = 5 h. The solvent was removed in vacuum and the product was purified by bulb-to-bulb distillation, giving (S)-ethyl 2,2-dimethyl-3-hydroxy-3-

phenylpropanoate [(*S*)-**9b**] (0.86 g, 93% yield, 82% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (s, 3, $COCCH_3$), 1.13 (s, 3, $COCCH_3$), 1.26 (t, 3, J = 7.3 Hz, CH_2CH_3), 3.26 (d, 1, J = 4.3 Hz, OH), 4.17 (q, 2, J = 7.3 Hz, CH_2CH_3), 4.88 (d, 1, J = 4.3 Hz, C*H*OH), 7.2–7.4 (m, 5, aromatics). $^{13}C\{^1H\}$ NMR (67.8 MHz, $CDCl_3$) δ 14.15 (CH_2CH_3), 19.12 ($COCCH_3$), 23.08 ($COCCH_3$), 47.55 ($C(CH_3)_2$), 60.87 (CH_2CH_3), 78.60 (CHOH), 127.53 (aromatic-C4), 127.54 (aromatic-CH), 127.57 (aromatic-CH), 139.88 (aromatic-C1), 177.56 (C=O). GC conditions: CP-Chirasil-DEX CB column, P = 50 kPa, T(column) = 150 °C, T(injection) = 250 °C, T(detector) = 250 °C, t_R of (*R*)-**9b** = 20.5 min, t_R of (*S*)-**9b** = 22.1 min, 82% ee. Chiral HPLC: column, CHIRALCEL OD, 4.6 mm i.d. x 250 mm, Daicel Chemical Industries; eluent, $(CH_3)_2CHOH$/hexane (5:95); temp, 30 °C; flow rate, 0.5 mL/min; detection, 254-nm light; t_R of (*R*)-**9b** = 54.8 min, t_R of (*S*)-**9b** = 50.6 min, 82% ee. Absolute configuration determined for 2,2-dimethyl-3-hydroxy-3-phenylpropanoic acid: found $[\alpha]^{25}_D$ +6.2° (*c* 0.45, CH_3OH), lit. $[\alpha]^{25}_D$ –4.7° (*c* 0.96, CH_3OH) for (*R*)-**9b** (Kinugasa, M.; Harada, T.; Egusa, T.; Fujita, K.; Oku, A. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 3639–3650). **Acetophenone.** a) Hydrogenation conditions: (*S*)-**3a** (2.5 mg, 2.6 μmol); acetophenone (0.62 g, 5.2 mmol); S/C = 2000; $KOC(CH_3)_3$ (15.0 mg, 0.13 mmol); C_2H_5OH (5.8 mL); P_{H_2} = 5 atm; T = 25 °C; t = 12 h. The conversion and the ee of (*R*)-1-phenylethanol determined by chiral GC analysis were 100% and 54%, respectively. GC conditions: CP-Chirasil-DEX CB column, P = 41 kPa, T = 105 °C, T(injection) = 200 °C, T(detector) = 200 °C, t_R of (*R*)-1-phenylethanol = 18.7 min, t_R of (*S*)-1-phenylethanol = 21.2 min (Ohkuma, T.; Koizumi, M.; Muñiz, K.; Hilt, G.; Kabuto, C.; Noyori, R. *J. Am. Chem. Soc*. **2002**, *124*, 6508–6509). b) Hydrogenation conditions: (*S*)-**3a** (2.5 mg, 2.6 μmol); acetophenone (0.62 g, 5.2 mmol); S/C = 2000; $KOC(CH_3)_3$ (15.0 mg, 0.13 mmol); $(CH_3)_2CHOH$ (5.8 mL); P_{H_2} = 5 atm; T = 25 °C; t = 12 h. (*R*)-1-phenylethanol (100% yield, 14% ee).

6. Acknowledgment

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