Supporting Information For:

Enantioselective Synthesis of α -Substituted Ketones by Asymmetric Addition of Chiral Zinc Enamides to 1-Alkenes

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General. All the reactions dealing with air or moisture sensitive compounds were carried out in a dry reaction vessel under nitrogen unless otherwise noted. Addition reaction was conducted in an autoclave (Hyper Glass Cylinder) purchased from Taiatsu Techno Co. Routine chromatographic purification was carried out with Kanto Silica gel 60 (spherical, neutral, 140-325 mesh). All ^1H NMR spectra (400 MHz) and ^{13}C NMR spectra (100 MHz) were measured on a JEOL AL-400 for a CDCl_3 solution in the presence of tetramethylsilane as an internal standard and reported in ppm (δ). Gas chromatographic analysis was performed on a Shimadzu GC-14B equipped with capillary column, CP-Chirasil-DEX CB (Chrompack, 25×0.25 mm, $0.25 \mu\text{m}$ film thickness), γ -DEX 225 (Spelco, $30 \text{ m} \times 0.25\text{mm}$, $0.25 \mu\text{m}$ film thickness) and CHIRALDEX G-TA (ASTEC, $20 \text{ m} \times 0.25$ mm, $0.125 \mu\text{m}$ film thickness). HPLC analysis was performed on a JASCO CD-1595. Chiral HPLC separations were accomplished using RU-1, RU-2 (Shiseido Fine Chemicals) and CHIRALPAK AS-H, CHIRALCEL OB-H (Daicel). IR spectra recorded on a FT/IR-420 (JASCO) or on a React IR 1000 Reaction Analysis System equipped with DuraSample IR (ASI Applied System) are reported in cm^{-1} . Mass spectra are taken with APCI (atmosphere pressure chemical ionization) or ESI (electron spray ionization) method with a Shimadzu LCMS-QP8000.

Solvent. Anhydrous diethyl ether (Et_2O) and hexane were purchased from Kanto Chemical Co. and degassed and dried over molecular sieves in a storage flask. The water content of the solvent was confirmed with a Karl-Fischer Moisture Titrator (MKC-210, Kyoto Electronics Company) to be less than 10 ppm. Anhydrous tetrahydrofuran (THF) was purchased from Kanto Chemical Co. and distilled from benzophenone ketyl under argon immediately before use.

Materials. Unless otherwise noted, materials were purchased from Tokyo Kasei Co., Aldrich Inc., and other commercial suppliers and were used either distilled or recrystallized before use. ZnCl_2 was purchased from Aldrich Inc. (*L*)-*tert*-Leucine and (*L*)-valine was purchased from Tokyo Kasei Co. Ethylene was purchased from Nippon Sanso Co. $\text{Pd}(\text{PPh}_3)_4$ and $\text{CuBr} \cdot \text{SMe}_2$ were prepared from PdCl_2 and CuBr according to literature.¹

Procedure for determination of *ee* of ketones (4, 6, 8, 10, 12, 14-20)

Table 1. Chiral GC assay of ketones (**4**, **6**, **8**, **10**, **12**, **14-16**)^a

ketone	column ^b	oven	<i>t_R</i> (R)	<i>t_R</i> (S)
2-ethylcyclohexanone, 4	A	80 °C	12.6 min	12.1 min
2-ethyl-4-methylcyclohexanone, 6	B	95 °C	17.9 min	17.1 min
7-ethyl-1,4-dioxaspiro[4.5]decan-8-one, 8	B	125 °C	31.9 min	31.1 min
2-ethylcycloheptanone, 10	C	82 °C	25.8 min	27.4 min
2-ethylcyclohept-4-en-1-one, 12	B	80 °C(40 min); +5 °C/min	19.0 min	17.0 min
4-methylhexan-3-one, 14	A	40 °C (10 min); +1 °C/min	12.2 min	12.8 min
2-isopropylcyclohexanone, 15	C	95 °C	10.9 min	11.9 min
2-(2-phenylethyl)cyclohexanone, 16	B	170 °C	25.7 min	26.4 min

^aCarrier gas, N₂ (75 mL/min); detector, FID at 250 °C; injection, 1 µL at 1-5 mg/mL, split ratio 30:1.

^bColumn A: CP-Chirasil-DEX CB (Chrompack, 25 m × 0.25 mm, 0.25 µm film).

Column B: γ-DEX 225 (Spelco, 30 m × 0.25mm, 0.25 µm film).

Column C: CHIRALDEX G-TA (ASTEC, 20 m × 0.25 mm, 0.125 µm film).

Table 2. Chiral HPLC assay of ketones (**17-20**)^a

ketone	column ^b	eluate	detection	<i>t_R</i> (R)	<i>t_R</i> (S)
	oven	flow rate			
4-methylene-2-(pent-4-enyl)cyclohexanone, 17	A	hexane	294 nm (CD)	14.2 min	17.9 min
	24 °C	0.8 mL/min			
4-methylene-2-(4-phenylbut-3-enyl)cyclohexanone, 18	B	MeOH	248 nm (UV)	114.5 min	126.2 min
	5 °C	0.08 mL/min			
4-methylene-2-(phenylethyl)cyclohexanone, 19	C	MeOH	286 nm (CD)	28.9 min	35.2 min
	15 °C	0.2 mL/min			
ethyl-2-[3-(5-methylene-2-oxocyclohexyl)propyl]acrylate, 20	D	hex/IPA=98/2	286 nm (CD)	19.0 min	17.0 min
	20 °C	0.5 mL/min			

^aDetector, CD/UV at room temperature; injection 5 µL at 1-5 mg/mL

^bColumn A: CHIRALCEL OB-H (Daicel). Column B: RU-1 (Shiseido Fine Chemicals). Column C: RU-2 (Shiseido Fine Chemicals). Column D: CHIRALCPAK AS-H (Daicel).

Preparation of (*S*)-2,2-dimethyl-1-(trimethylsilyloxymethyl)propylamine²

A 1-L three-neck round-bottom flask was fitted with a magnetic stir bar, a reflux condenser and an additional funnel. The flask was charged with sodium borohydride (8.63 g, 228 mmol) and THF (275 mL). To a resulting suspension, (*L*)-*tert*-leucine (12.46 g, 95 mmol) was added in one portion. A solution of iodine (24.13 g, 95 mmol) in THF (75 mL) was added dropwise through the additional funnel over 30 min at 0 °C. After evolution of hydrogen gas ceased, the reaction mixture was heated to reflux for 1 day and then cooled to 0 °C. Methanol was added cautiously until the

mixture become clear, then the solvent was removed with rotary evaporator to obtain a white paste, which was then dissolved to 20% aqueous KOH (200 mL). The solution was stirred for 4 h and extracted with methylene chloride (100 mL, five times). The organic extracts were dried over sodium sulfate and concentrated in vacuo to obtain a white solid (*S*-*tert*-leucinol, 100%). 1,1,1,3,3,3-Hexamethyldisilazane (20 mL, 95 mmol) was added to the solid. The reaction mixture was heated to reflux for 4 h. The reaction mixture was cooled to ambient temperature, then distilled to yield 15.8 g (88% yield, >99.5% ee) of the title compound as a colorless liquid: $[\alpha]_D^{23} +23.3$ (C = 4.0, MeOH); bp 80 °C/22 mm; IR(neat) 1589 (br), 1250, 1110, 1076, 883, 835, 746; ^1H NMR (400 MHz, CDCl_3) δ 0.12 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 0.90 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.35 (br, 2H, NH_2), 2.57 (dd, $J = 9.3, 2.9$ Hz, 1H, NCH), 3.28 (brt, $J = 9.5$ Hz, 1H, OCHH), 3.74 (dd, $J = 9.8, 2.9$ Hz, 1H, OCHH); ^{13}C NMR (100 MHz, CDCl_3) δ -0.5 (3C), 26.5 (3C), 32.9, 61.4, 64.3.

Methylation of (*S*)-valinol and (*S*)-*t*-leucionol

(*S*)-Valinol and (*S*)-*t*-leucionol were methylated with NaH/MeI.; see reference.³

Chiral imine 1d (A representative procedure for preparation of chiral imines)

Molecular sieves (4A, 5.0 g) was added to a 2-M hexane solution of cyclohexanone (2.51 g, 25.6 mmol) and 2,2-dimethyl-1-(trimethylsilyloxymethyl)propylamine (4.85 g, 25.6 mmol) at 0 °C. The reaction mixture was heated to 40 °C for 2 d. The reaction mixture was cooled to ambient temperature and then molecular sieves were filtered with a pad of celite and washed with dry Et_2O (20 mL, five times). The filtrate was evaporated *in vacuo* and distilled to yield 6.5 g (94% yield) of **1d** as a colorless liquid.

(*S*)-Cyclohexylidene-(1-methoxymethyl-2-methylpropyl)amine (**1a**)

Bp 25 °C/0.1 mm; IR(neat) 1663, ($\text{C}=\text{N}$), 1449 1199, 1114, 1079, 935; ^1H NMR (400 MHz, CDCl_3) δ 0.85 (d, $J = 6.4$ Hz, 3H, $\text{CH}(\text{CH}_3)\text{CH}_3$), 0.92 (d, $J = 6.8$ Hz, 3H, $\text{CH}(\text{CH}_3)\text{CH}_3$), 1.62-1.84 (m, 7H, $\text{CH}(\text{CH}_3)\text{CH}_3$, $\text{CH}_2(\text{CH}_2)_3\text{CH}_2$), 2.30-2.36 (m, 4H, $\text{CH}_2(\text{CH}_2)_3\text{CH}_2$), 3.30 (s, 3H, OCH_3), 3.35 (dd, $J = 9.0, 8.0$ Hz, 1H, OCHH), 3.40-3.45 (m, 1H, NCH), 3.55 (dd, $J = 9.0, 3.6$ Hz, 1H, OCHH); ^{13}C NMR (100 MHz, CDCl_3) δ 19.0, 19.6, 26.3, 27.3, 28.1, 29.4, 30.5, 40.5, 58.9, 63.8, 75.3, 172.4.

(S)-Cyclohexylidene-[2-methyl-1-(trimethylsilyloxymethyl)propyl]amine (1b)

Bp 100 °C/2.0 mm; IR(neat) 1664 (C=N), 1449, 1249 1101, 878, 834, 746; ^1H NMR (400 MHz, CDCl_3) δ 0.05 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 0.80 (d, $J = 6.4$ Hz, 3H, $\text{CH}(\text{CH}_3)\text{CH}_3$), 0.87 (d, $J = 6.8$ Hz, 3H, $\text{CH}(\text{CH}_3)\text{CH}_3$), 1.60-1.81 (m, 7H, $\text{CH}(\text{CH}_3)\text{CH}_3$, $\text{CH}_2(\text{CH}_2)_3\text{CH}_2$), 2.26-2.32 (m, 4H, $\text{CH}_2(\text{CH}_2)_3\text{CH}_2$), 3.30-3.34 (m, 1H, NCH), 3.43 (dd, $J = 9.6, 8.4$ Hz, 1H, OCHH), 3.76 (dd, $J = 9.6, 3.7$ Hz, 1H, OCHH); ^{13}C NMR (100 MHz, CDCl_3) δ -0.4 (3C), 19.1, 19.9, 26.3, 27.4, 28.1, 29.6, 30.0, 40.4, 64.9, 66.1, 172.3.

(S)-Cyclohexylidene-(1-methoxymethyl-2,2-dimethylpropyl)amine (1c)

Bp 50 °C/0.3 mm; IR(neat) 1665 (C=N), 1449, 1360, 1119, 1091, 922; ^1H NMR (400 MHz, CDCl_3) δ 0.89 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.54-1.77 (m, 6H, $\text{CH}_2(\text{CH}_2)_3\text{CH}_2$), 2.27-2.36 (m, 4H, $\text{CH}_2(\text{CH}_2)_3\text{CH}_2$), 3.27 (s, 3H, OCH₃), 3.32 (dd, $J = 8.8, 8.5$ Hz, 1H, OCHH), 3.39 (dd, $J = 8.5, 2.5$ Hz, 1H, NCH), 3.62 (dd, $J = 8.8, 2.5$ Hz, 1H, OCHH); ^{13}C NMR (100 MHz, CDCl_3) δ 26.4, 26.9 (3C), 27.3, 28.2, 29.3, 33.3, 40.6, 58.8, 66.6, 73.9, 171.9.

(S)-Cyclohexylidene-[2,2-dimethyl-1-(trimethylsilyloxymethyl)propyl]amine (1d)

Bp 70 °C/0.15 mm; IR(neat) 1666 (C=N), 1449, 1249, 1106, 1073, 874, 836, 746; ^1H NMR (400 MHz, CDCl_3) δ 0.06 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 0.88 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.48-1.84 (m, 6H, $\text{CH}_2(\text{CH}_2)_3\text{CH}_2$), 2.20-2.42 (m, 4H, $\text{CH}_2(\text{CH}_2)_3\text{CH}_2$), 3.31 (dd, $J = 8.7, 2.9$ Hz, 1H, NCH), 3.48 (dd, $J = 9.7, 8.7$ Hz, 1H, OCHH), 3.84 (dd, $J = 9.7, 2.9$ Hz, 1H, OCHH); ^{13}C NMR (100 MHz, CDCl_3) δ -0.4 (3C), 26.4, 27.0 (3C), 27.3, 28.2, 29.4, 33.3, 40.6, 63.3, 68.8, 171.6.

(S)-[1-(*tert*-Butyldimethylsilyloxymethyl)-2,2-dimethylpropyl]cyclohexylideneamine (1f)

Bp 150 °C/1.0 mm; IR(neat) 1666 (C=N), 1472, 1450, 1360, 1250, 1107, 1075, 1005, 848, 834, 773; ^1H NMR (400 MHz, CDCl_3) δ -0.2 (s, 3H, $\text{Si}(\text{CH}_3)\text{CH}_3$), 0.0 (s, 3H, $\text{Si}(\text{CH}_3)\text{CH}_3$), 0.85 (s, 9H, $\text{SiC}(\text{CH}_3)_3$), 0.87 (s, 9H, $\text{CHC}(\text{CH}_3)_3$), 1.52-1.78 (m, 6H, $\text{CH}_2(\text{CH}_2)_3\text{CH}_2$), 2.18-2.43 (m, 4H, $\text{CH}_2(\text{CH}_2)_3\text{CH}_2$), 3.30 (dd, $J = 8.5, 2.9$ Hz, 1H, NCH), 3.52 (dd, $J = 9.5, 8.5$ Hz, 1H, OCHH), 3.85 (dd, $J = 9.5, 2.9$ Hz, 1H, OCHH); ^{13}C NMR (100 MHz, CDCl_3) δ -5.4, -5.1, 18.3, 25.9 (3C), 26.4, 27.0 (3C), 27.2, 28.1, 29.4, 33.3, 40.5, 64.1, 68.9, 171.5.

(S)-Cyclohexylidene-[1-phenyl-2-(trimethylsilyloxy)ethyl]amine (1g)

Bp 110 °C/0.15 mm; IR(neat) 3086 and 3063 and 3028 (aromatic C=C), 1663 (vs, C=N), 1603 and 1493 (aromatic C-H), 1249, 1104, 1080, 877, 836, 745, 754 and 698 (aromatic C-H) ^1H NMR (400 MHz, CDCl_3) δ 0.05 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 1.51-1.79 (m, 6H, $\text{CH}_2(\text{CH}_2)_3\text{CH}_2$), 2.20-2.45 (m, 4H, $\text{CH}_2(\text{CH}_2)_3\text{CH}_2$), 3.83 (d, $J = 7.2$ Hz, 2H, OCH_2), 3.70 (t, $J = 7.2$ Hz, 1H, NCH), 7.32-7.40 (m, 5H, aromatic CH); ^{13}C NMR (100 MHz, CDCl_3) δ -0.5 (3C), 26.1 27.1, 27.9, 30.1, 40.3, 64.9, 68.6, 126.8, 127.6 (2C), 128.1 (2C), 142.3, 174.0.

(S)-(1-Methoxymethyl-2-methylpropyl)-(4-methylenecyclohexylidene)amine (21)⁴

Bp 130 °C/36 mm; IR(neat) 3073 (C=CH₂), 1663 (C=N), 1438, 1199, 1113, 950, 890; ¹H NMR (400 MHz, CDCl₃) δ 0.86 (d, 3H, *J* = 6.8 Hz, CH(CH₃)CH₃), 0.91 (d, 3H, *J* = 6.8 Hz, CH(CH₃)CH₃), 1.81 (oct, 1H, CH(CH₃)CH₃), 2.25-2.52 (m, 8H, N=C(CH₂CH₂)₂C), 3.30 (s, 3H, OCH₃), 3.35 (dd, *J* = 9.0, 8.0 Hz, 1H, OCHH), 3.41-3.46 (m, 1H, NCH), 3.56 (dd, *J* = 9.0, 3.6 Hz, 1H, OCHH), 4.76 (s, 2H, C=CH₂); ¹³C NMR (100 MHz, CDCl₃) δ 19.1, 19.6, 29.4, 30.6, 34.3, 35.0, 40.4, 58.9, 64.4, 75.2, 108.7, 147.1, 171.0.

(S)-[2,2-Dimethyl-1-(trimethylsilyloxymethyl)propyl]-(4-methylenecyclohexylidene)amine (22)

Bp 75 °C/0.15 mm; IR(neat) 3074 (C=CH₂), 1666 (C=N), 1250, 1108, 1070, 873, 837, 746; ¹H NMR (400 MHz, CDCl₃) δ 0.04 (s, 9H, Si(CH₃)₃), 0.89 (s, 9H, C(CH₃)₃), 2.25-2.52 (m, 8H, N=C(CH₂CH₂)₂C), 3.31 (dd, *J* = 8.8, 2.9 Hz, 1H, NCH), 3.48 (dd, *J* = 9.8, 8.8 Hz, 1H, OCHH), 3.84 (dd, *J* = 9.8, 2.9 Hz, 1H, OCHH), 4.75 (s, 1H, C=CHH), 4.75 (s, 1H, C=CHH); ¹³C NMR (100 MHz, CDCl₃) δ -0.4 (3C), 26.9 (3C), 29.4, 33.3, 34.4, 35.1, 40.5, 63.2, 69.4, 108.5, 147.5, 170.1.

(S)-[2,2-Dimethyl-1-(trimethylsilyloxymethyl)propyl]-(1,4-dioxaspiro[4.5]dec-8-ylidene)amine (23)

Bp 150 °C/1.0 mm; IR(neat) 1666 (C=N), 1250, 1124, 1099, 1071, 1034, 873, 836, 747; ¹H NMR (400 MHz, CDCl₃) δ 0.04 (s, 9H, Si(CH₃)₃), 0.86 (s, 9H, C(CH₃)₃), 1.76-1.91 (m, 4H, N=C(CH₂CH₂)₂C), 2.41-2.53 (m, 4H, N=C(CH₂CH₂)₂C), 3.26 (dd, *J* = 8.8, 2.9 Hz, 1H, NCH), 3.48 (dd, *J* = 9.7, 8.8 Hz, 1H, OCHH), 3.83 (dd, *J* = 9.7, 2.9 Hz, 1H, OCHH), 4.00 (s, 4H, OCH₂CH₂O); ¹³C NMR (100 MHz, CDCl₃) δ -0.4 (3C), 25.3, 26.9 (3C), 33.2, 34.8, 35.5, 36.7, 63.1, 64.4, 64.4, 69.7, 108.4, 169.4.

(S)-Cycloheptylidene-[2,2-dimethyl-1-(trimethylsilyloxymethyl)propyl]amine (24)

Bp 80 °C/0.15 mm; IR(neat) 1648 (C=N), 1249, 1113, 1072, 874, 836, 746; ¹H NMR (400 MHz, CDCl₃) δ 0.03 (s, 9H, Si(CH₃)₃), 0.86 (s, 9H, C(CH₃)₃), 1.43-1.75 (m, 8H, CH₂(CH₂)₄CH₂), 2.38-2.46 (m, 4H, CH₂(CH₂)₄CH₂), 3.29 (dd, *J* = 8.8, 2.9 Hz, 1H, NCH), 3.47 (dd, *J* = 9.7, 8.8 Hz, 1H, OCHH), 3.81 (dd, *J* = 9.7, 2.9 Hz, 1H, OCHH); ¹³C NMR (100 MHz, CDCl₃) δ -0.4 (3C), 25.2, 26.9 (3C), 27.2, 29.8, 30.1, 31.6, 33.5, 41.2, 63.6, 68.7, 174.4.

(S)-Cyclohept-4-enylidene-[2,2-dimethyl-1-(trimethylsilyloxymethyl)propyl]amine (25)⁵

Bp 100 °C/0.30 mm; IR(neat) 3020 (CH=CH), 1653 (C=N), 1250, 1111, 1073, 874, 837, 746; ¹H NMR (400 MHz, CDCl₃) δ 0.05 (s, 9H, Si(CH₃)₃), 0.88 (s, 9H, C(CH₃)₃), 2.17-2.34 (m, 4H, CH₂CH=CHCH₂), 2.54-2.68 (m, 4H, CH₂CCH₂), 3.31 (dd, *J* = 8.8, 2.7 Hz, 1H, NCH), 3.49 (dd, *J* = 9.7, 8.8 Hz, 1H, OCHH), 3.84 (dd, *J* = 9.7, 2.7 Hz, 1H, OCHH), 5.68-5.72 (m, 2H, CH=CH); ¹³C NMR (100 MHz, CDCl₃) δ -0.4 (3C), 24.7, 26.9 (3C), 28.0, 31.2, 33.4, 39.6, 63.4, 68.9, 129.4, 130.3, 173.3.

(S)-[2,2-Dimethyl-1-(trimethylsilyloxymethyl)propyl]-(1-ethylpropylidene)amine (26)

Bp 50 °C/0.30 mm; IR(neat) 1669 (C=N), 1250, 1106, 1072, 874, 837, 746; ¹H NMR (400 MHz, CDCl₃) δ 0.05 (s, 9H, Si(CH₃)₃), 0.88 (s, 9H, C(CH₃)₃), 1.03 (t, *J* = 7.8 Hz, 3H, CH₂CH₃), 1.08 (t, *J* = 7.8 Hz, 3H, CH₂CH₃), 2.13-2.32 (m, 4H, CH₂CH₃), 3.27 (dd, *J* = 8.5, 2.7 Hz, 1H, NCH), 3.46 (dd, *J* = 9.8, 8.5 Hz, 1H, OCHH), 3.84 (dd, *J* = 9.8, 2.7 Hz, 1H, OCHH); ¹³C NMR (100 MHz, CDCl₃) δ -0.5 (3C), 11.2, 11.5, 24.0, 26.9 (3C), 32.2, 33.4, 63.5, 68.9, 173.3.

(S)-(1-Ethylpropylidene)-(1-methoxymethyl-2,2-dimethylpropyl)amine (27)

Bp 60 °C/0.60 mm; IR(neat) 1668 (C=N), 1178, 1119, 1089, 941, 893; ^1H NMR (400 MHz, CDCl_3) δ 0.89 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.04 (t, $J = 7.8$ Hz, 3H, CH_2CH_3), 1.09 (t, $J = 7.8$ Hz, 3H, CH_2CH_3), 2.20-2.30 (m, 4H, CH_2CH_3), 3.27-3.35 (m, 5H, OCH_3 , OCHH , NCH), 3.84 (dd, $J = 9.8$, 2.7 Hz, 1H, OCHH); ^{13}C NMR (100 MHz, CDCl_3) δ 11.3, 11.5, 23.8, 26.8 (3C), 32.3, 33.5, 58.9, 66.9, 74.2, 173.8.

Asymmetric synthesis of (*R*)-2-ethylcyclohexanone (**4**)³ (general procedure of asymmetric ethylation [A])

To a solution of mesityl bromide (0.153 mL, 1.0 mmol) in Et_2O (1.0 mL) was added *t*-BuLi (1.40 M in pentane, 1.43 mL, 2.0 mmol) at -78°C , and the mixture was warmed to 0°C . After 1 h, imine **1d** (0.307 mL, 1.0 mmol) was slowly added to a white suspension of mesityllithium at 0°C and rinsed with Et_2O (1.0 mL). After 12 h, the reaction mixture changed to a colorless solution, then ZnCl_2 (0.5 M in Et_2O , 2.0 mL, 1.0 mmol) was added at 0°C . After 50 min, methyllithium (1.2 M in Et_2O , 0.833 mL, 1.0 mmol) was added at -78°C and the reaction mixture was warmed to 0°C . After 30 min, hexane (2.0 mL) was added and the reaction mixture was stirred at 45°C for 30 min to remove Et_2O under dry nitrogen stream. The reaction mixture was pressurized with ethylene (20 atm) and heated to 40°C . After 24 h, the reaction mixture was cooled to room temperature and excess ethylene was released. The reaction mixture was poured into saturated tartaric acid (3.0 mL) via a cannula with vigorous stirring at 0°C and rinsed with hexane (three times, 2.0 mL). After 3 min, saturated sodium potassium tartrate (1.5 mL) and acetic acid buffer [7.5 mL, prepared from AcOH (37.5 mL), water (37.5 mL) and of AcONa (16.5 g)] were added at 0°C and the reaction mixture was warmed to room temperature. Decane (39.0 μL , 0.2 mmol) was added as an internal standard.

GC analyses were carried out after 5 min (29% yield, 99.3% *ee*) and after 50 min (91% yield, 95.0% *ee*). After 50 min, the organic layer was removed and the aqueous layer was extracted three times with pentane at 0 °C. The combined organic extracts were washed with saturated sodium bicarbonate, 0.5-N aq.HCl, saturated sodium bicarbonate and dried over sodium sulfate at 0 °C, then chromatographed on silica gel (4 g, pentane and then 5% Et₂O in pentane) to obtain ketone **4** (0.088g, 70% yield). $[\alpha]^{31}_{\text{D}} -24.5$ (C = 4.0, MeOH, 95.0% *ee*).

(R)-2-Ethyl-4-methylenecyclohexanone (6)

Conditions: imine **22** (0.318 mL, 1.0 mmol), 60 °C, 24 h, 30 atm of ethylene. 91% yield on GC analysis. Ketone **6** (0.117 g, 85% yield) was obtained after silica gel column chromatography. $[\alpha]^{23}_{\text{D}} -34.1$ (C = 2.4, MeOH, 97.7% *ee*); $R_f = 0.45$, 10% EtOAc in hexane; IR(neat) 3076 (C=CH₂), 1711 (vs, C=O), 1651 (C=C), 894 (C=CH₂); ¹H NMR (400 MHz, CDCl₃) δ 0.9 (t, *J* = 7.4 Hz, 3H, CH₃), 1.28-1.39 (m, 1H, CHH CH₃), 1.72-1.83 (m, 1H, CHHCH₃), 2.17 (dd, 1H, *J* = 13.4, 10.3 Hz, CHCHHC=CH₂), 2.36 (m, 1H, CH), 2.37-2.59 (m, 4H, CH₂CH₂C=CH₂), 2.65 (dd, 1H, *J* = 13.4, 5.6 Hz, CHCHHC=CH₂), 4.87 (s, 1H, C=CHH), 4.89 (s, 1H, C=CHH); ¹³C NMR (100 MHz, CDCl₃) δ 11.4, 22.8, 34.0, 39.4, 40.9, 52.0, 111.0, 144.0, 212.5; APCI-MS (positive): *m/z* 139[M+H]⁺.

(R)-7-Ethyl-1,4-dioxaspiro[4.5]decan-8-one (8)⁶

Conditions: imine **23** (0.328 g, 1.0 mmol), 60 °C, 24 h, 25 atm of ethylene. Ketone **8** (0.164 g, 89% yield) was obtained after silica gel column chromatography. $[\alpha]^{31}_{\text{D}} -16.1$ (C = 4.0, MeOH, 90% *ee*).

(R)-2-Ethylcycloheptanone (10)⁷

Conditions: imine **24** (0.318 mL, 1.0 mmol), 60 °C, 24 h, 30 atm of ethylene. Ketone **10** (0.115 g, 82% yield) was obtained after silica gel column chromatography. $[\alpha]^{31}_{\text{D}} -77.5$ (C = 0.5, MeOH, 95.6% *ee*).

(R)-2-Ethylcyclohept-4-en-1-one (12)

Conditions: imine **25** (0.311 mL, 1.0 mmol), 60 °C, 24 h, 25 atm of ethylene. 93% yield on GC analysis. Ketone **12** (0.109 g, 79% yield) was obtained after silica gel column chromatography. $[\alpha]^{22}_{\text{D}} -112.9$ (C = 2.0, MeOH, 96.4% *ee*); $R_f = 0.41$, 10% EtOAc in hexane; IR(neat) 3020 (CH=CH), 1703 (vs, C=O), 1656 (C=C), 659 (CH=CH); ^1H NMR (400 MHz, CDCl_3) δ 0.9 (t, $J = 7.4$ Hz, 3H, CH_3), 1.33-1.43 (m, 1H, CHH CH_3), 1.70-1.80 (m, 1H, CHHCH_3), 2.09-2.16 (m, 1H, CHCHHCH=CH), 2.21-2.25 (m, 1H, $\text{CH}_2\text{CHHCH=CH}$), 2.30-2.35 (m, 1H, CHCHHCH=CH), 2.47-2.53 (m, 2H, CHHCHHCH=CH), 2.68-2.78 (m, 2H, $\text{CHHCH}_2\text{CH=CH}$, COCH), 5.72-5.80 (m, 2H, CH=CH); ^{13}C NMR (100 MHz, CDCl_3) δ 11.7, 24.0, 24.1, 30.4, 42.1, 52.6, 128.8, 129.4, 214.8; APCI-MS (positive): m/z 139 $[\text{M}+\text{H}]^+$.

(S)-4-Methylhexan-3-one (14)⁸

Conditions: imine **26** (0.232 mL, 1.0 mmol), 40 °C, 24 h, 20 atm of ethylene. 81% yield on GC analysis. Ketone **14** (0.051 g, 45% yield) was obtained after silica gel column chromatography. $[\alpha]^{22}_{\text{D}} +19.1$ (C = 1.0, Et_2O , 58% *ee*).

(S)-2-Isopropylcyclohexanone (15)⁹

Zinc enamide **2d** was prepared from imine **1d** (0.307 mL, 1.0 mmol) according to the procedure **A**. Hexane (0.5 mL) was added and the reaction mixture was stirred at 45 °C for 30 min to remove Et₂O under dry nitrogen stream. The reaction mixture was pressurized with propene (8 atm) and heated to 60 °C. After 36 h, the reaction mixture was cooled to room temperature and excess propene was released. The reaction mixture was poured into saturated tartaric acid (2.5 mL) via a cannula with vigorous stirring at 0 °C and rinsed with hexane (three times, 2.0 mL). After 3 min, acetic acid buffer (7.5 mL) was added at 0 °C and the reaction mixture was warmed to room temperature. Tridecane (24.4 μL, 0.1 mmol) was added as an internal standard. GC analyses were carried out after 1 h (15% yield, 98.0 % *ee*) and after 6 h (47% yield, 93.3% *ee*). After 6 h, organic layer was removed and the aqueous layer was extracted three times with pentane at 0 °C. The combined organic extracts were washed with saturated sodium bicarbonate, 0.5-N aq.HCl, saturated sodium bicarbonate and dried over sodium sulfate at 0 °C. Silica gel chromatography (2 g pentane and then 5% Et₂O in pentane) gave ketone **15** (0.046 g, 35% yield). $[\alpha]_D^{24}$ -73.6 (C = 0.5, CHCl₃, 93.3% *ee*).

(S)-2-(2-Phenylethyl)-cyclohexanone (16)¹⁰

Zinc enamide **2c** was prepared from imine **1c** (0.235 mL, 1.0 mmol) according to procedure **A**. Hexane (0.5 mL) was added and the reaction mixture was heated to 45 °C for 30 min to remove Et₂O under dry nitrogen stream. Styrene (0.172 mL, 1.5 mmol) was added and the reaction mixture was heated to 70 °C in the dark. After 48 h, the reaction mixture was poured into saturated tartaric acid (3.0 mL) via a cannula with vigorous stirring at 0 °C and rinsed with hexane (three times, 2.0 mL). After 3 min, saturated sodium potassium tartrate (1.5 mL) and acetic acid buffer (7.5 mL) were added at 0 °C and the reaction mixture was warmed to room temperature. After 1 h, organic layer was removed and the aqueous layer was extracted three times with hexane at 0 °C. The combined organic extracts were washed with saturated sodium bicarbonate, 0.5-N aq.HCl and saturated

sodium bicarbonate, and dried over sodium sulfate at 0 °C. Silica gel chromatography (4 g, hexane and then 3% AcOEt in hexane) gave ketone **16** (0.143g, 71% yield). $[\alpha]_D^{24} -5.0$ (C = 2.0, CHCl₃, 77.6% ee).

Asymmetric synthesis of (R)-Ethyl-2-[3-(5-methylene-2-oxocyclohexyl)propyl]acrylate (20**)**
(General procedure of three-component coupling [B])

To a solution of mesityl bromide (0.765 mL, 5.0 mmol) in Et₂O (5.0 mL) was added *t*-BuLi (1.40 M in pentane, 7.14 mL, 10.0 mmol) at –78 °C, and the mixture was warmed to 0 °C. After 1 h, imine **22** (1.59 mL, 5.0 mmol) was slowly added to a white suspension of mesityllithium at 0 °C, and rinsed with Et₂O (5.0 mL). After 12 h, the reaction mixture changed to a colorless solution, then ZnCl₂ (0.5 M in Et₂O, 10 mL, 5.0 mmol) was added at 0 °C. After 1 h, methyllithium (1.2 M in Et₂O, 4.17 mL, 1.0 mmol) was added at –78 °C and the reaction mixture was warmed to 0 °C. After 30 min, hexane (10 mL) was added and the reaction mixture was stirred at 45 °C for 30 min to remove Et₂O under dry nitrogen stream. The reaction mixture was pressurized with ethylene (30 atm). The reaction mixture was heated to 60 °C and stirred for 1 d, then cooled to room temperature and excess ethylene was released. The solvent was removed *in vacuo* and in THF (10 mL) was added. The reaction mixture was poured into CuBr·SMe₂ (1.03 g, 5.0 mmol) at –78 °C and ethyl-2-(bromomethyl)acrylate (1.21 mL, 10.0 mmol) was added at –78 °C. After 50 min, the reaction mixture was warmed to 0 °C and stirred for 3 h. The solvent was removed *in vacuo* and added hexane (25 mL) and acetic acid buffer (10 mL) at 0 °C. The reaction mixture was warmed to room temperature. After 50 min, the organic layer was removed and the aqueous layer was extracted three times with hexane at 0 °C. The combined organic extracts were washed with saturated sodium bicarbonate, 0.5-N aq.HCl, saturated sodium bicarbonate and dried over sodium

sulfate at 0 °C, then evaporated and chromatographed on silica gel (40 g, hexane and then 5%, 10% AcOEt in hexane) to obtain ketone **20** (1.05 g, 84% yield). $[\alpha]_D^{23} -12.8$ (C = 2.0, MeOH, 96.8% *ee*); $R_f = 0.28$, 10% EtOAc in hexane; IR(neat) 3076 (C=CH₂), 1709 (vs, C=O), 1654 and 1631 (C=C), 1181 and 1147 (C-O), 897 (C=CH₂); ¹H NMR (400 MHz, CDCl₃) δ 1.29-1.35 (m, 4H, CHCHHCH₂, CH₃), 1.41-1.52 (m, 2H, CHCH₂CH₂), 1.76-1.82 (m, 1H, CHCHHCH₂), 2.19 (dd, 1H, *J* = 13.5, 12.2 Hz, CHCHHC=CH₂), 2.28-2.61 (m, 7H, COCH₂CH₂, CHCH₂CH₂CH₂), 2.67 (dd, 1H, *J* = 13.5, 5.6 Hz, CHCHHC=CH₂), 4.20 (q, 2H, CH₂CH₃), 4.87 (s, 1H, CHCH₂C=CHH), 4.89 (s, 1H, CHCH₂C=CHH), 5.53 (d, 1H, CHH=CCO₂Et), 6.14 (d, 1H, CHH=CCO₂Et); ¹³C NMR (100 MHz, CDCl₃) δ ; 14.2, 25.7, 29.3, 31.8, 34.1, 39.9, 41.0, 50.2, 60.6, 111.2, 124.6, 140.5, 144.0, 167.2, 212.3; Anal. Calcd for C₁₅H₂₂O: C, 71.97; H, 8.86. Found: C, 71.68; H, 8.99.

(*R*)-4-Methylene-2-(pent-4-enyl)cyclohexanone (**17**)

Addition reaction was conducted as the procedure **B** by using **22** (0.318 mL, 1.0 mmol). After releasing excess ethylene, the solvent was changed to THF (2.0 mL). The reaction mixture was poured into CuBr·SMe₂ (41 mg, 0.20 mmol) and allyl bromide (0.173 mL, 2.0 mmol) was added at -78 °C. The reaction mixture was warmed to 0 °C and stirred for 3 h. The solvent was changed to hexane (5.0 mL) and acetic acid buffer (2.0 mL) at 0 °C. The reaction mixture was warmed to room temperature. After 50 min, the organic layer was removed and the aqueous layer was extracted three times with hexane at 0 °C. The combined organic extracts were washed with saturated sodium bicarbonate, 0.5-N aq.HCl, saturated sodium bicarbonate and dried over sodium sulfate at 0 °C, then evaporated and chromatographed on silica gel (6 g, hexane and then 3%, 5% AcOEt in hexane) to obtain ketone **17** (0.158 g, 89% yield). $[\alpha]_D^{23} -21.8$ (C = 2.0, MeOH, 96.9% *ee*); $R_f = 0.43$, 10% EtOAc in hexane; IR(neat) 3076 (C=CH₂), 1711 (vs, C=O), 1654 and 1651 (C=C), 897 (C=CH₂); ¹H NMR (400 MHz, CDCl₃) δ 1.24-1.39 (m, 3H, CHCHHCH₂), 1.72-1.89 (m, 1H, CHCHHCH₂), 2.04-2.08 (m, 2H, CH₂CH=CH₂), 2.16 (dd, 1H, *J* = 13.4, 12.2 Hz, CHCHHC=CH₂), 2.35-2.58 (m, 5H, CH₂CH₂C=CH₂, CHCO), 2.64 (dd, 1H, *J* = 13.4, 5.6 Hz, CHCHHC=CH₂), 4.87 (s, 1H, C=CHH), 4.89 (s, 1H, C=CHH), 4.94 (d, 1H, *J* = 10.0 Hz, CH=CHH), 5.00 (d, 1H, *J* = 17.1 Hz, CH=CHH), 5.74-5.84 (s, 1H, CH=CH₂); ¹³C NMR (100

MHz, CDCl₃) δ ; 26.2, 29.2, 33.6, 34.0, 39.8, 40.9, 50.3, 111.0, 114.5, 138.4, 143.9, 212.2; Anal. Calcd for C₁₂H₁₈O: C, 80.85; H, 10.18. Found: C, 80.80; H, 10.26.

(R)-4-Methylene-2-(4-phenylbut-3-enyl)cyclohexanone (18)

Addition reaction was conducted as the procedure **B** by using **22** (0.127 mL, 0.4 mmol). After releasing excess ethylene, the solvent was changed to THF (1.0 mL). Pd(PPh₃)₄ (23 mg, 0.02 mmol) and β -bromo styrene¹¹ (0.103 mL, 0.8 mmol, >99.9% *E*) were added at 0 °C, then the reaction mixture was warmed to room temperature and stirred for 12 h. The solvent was changed to hexane (2.5 mL) and acetic acid buffer (1.0 mL) at 0 °C. The reaction mixture was warmed to room temperature. After 50 min, the organic layer was removed and the aqueous layer was extracted three times with hexane at 0 °C. The combined organic extracts were washed with saturated sodium bicarbonate, 0.5-N aq.HCl, saturated sodium bicarbonate and dried over sodium sulfate at 0 °C, then evaporated and chromatographed on silica gel (4 g, hexane and then 3%, 5% AcOEt in hexane) to obtain ketone **18** (0.086 g, 90% yield). [α]_D²³ -14.2 (C = 2.0, MeOH, 97.4% *ee*); *R_f* = 0.37, 10% EtOAc in hexane; IR(neat) 3076 (C=CH₂), 3025 (aromatic C=C), 1708 (vs, C=O), 1653 (C=C), 1598 and 1493 (aromatic C-H), 965 (CH=CH), 896 (C=CH₂), 743 and 692 (aromatic C-H); ¹H NMR (400 MHz, CDCl₃) δ 1.39-1.48 (m, 1H, CHCHHCH₂), 1.95-2.02 (m, 1H, CHCHHCH₂), 2.16-2.26 (m, 3H, CH₂CH=CH, CHCHHC=CH₂), 2.38-2.61 (m, 5H, CHCH₂C=CH₂, COCH₂CH₂), 2.68 (dd, 1H, *J* = 13.5, 5.6 Hz, CHCHHC=CH₂), 4.87 (s, 1H, C=CHH), 4.89 (s, 1H, C=CHH), 6.18 (dt, 1H, *J* = 15.9, 6.8 Hz, CH=CHPh), 6.38 (d, 1H, *J* = 15.9 Hz, CH=CHPh), 7.18-7.35 (m, 5H, aromatic CH); ¹³C NMR (100 MHz, CDCl₃) δ ; 29.3, 33.3, 34.1, 39.9, 41.1, 49.6, 111.2, 125.9 (2C), 126.9, 128.5 (2C), 130.0, 130.4 137.6, 143.9, 212.2; Anal. Calcd for C₁₇H₂₀O: C, 84.96; H, 8.39. Found: C, 85.08; H, 8.63.

(R)-4-Methylene-2-(2-phenylethyl)cyclohexanone (19)

Addition reaction was conducted as the procedure **B** by using **22** (0.127 mL, 0.4 mmol). After releasing excess ethylene, the solvent was changed to THF (1.0 mL). Pd(PPh₃)₄ (23 mg, 0.02 mmol) and β-bromo styrene (0.103 mL, 0.8 mmol) were added at 0 °C, then the reaction mixture was warmed to 50 °C and stirred for 12 h. The solvent was changed to hexane (2.5 mL) and acetic acid buffer (1.0 mL) at 0 °C. The reaction mixture was warmed to room temperature. After 50 min, the organic layer was removed and the aqueous layer was extracted three times with hexane at 0 °C. The combined organic extracts were washed with saturated sodium bicarbonate, 0.5-N aq.HCl, saturated sodium bicarbonate and dried over sodium sulfate at 0 °C, then evaporated and chromatographed on silica gel (4 g, hexane and then 3%, 5% AcOEt in hexane) to obtain ketone **18** (0.071 g, 83% yield). $[\alpha]_D^{23} -12.3$ (C = 2.0, MeOH, 97.4% ee); $R_f = 0.40$, 10% EtOAc in hexane; IR(neat) 3074 (C=CH₂), 3027 (aromatic C=C), 1708 (vs, C=O), 1653 (C=C), 1603 and 1496 (aromatic C-H), 896 (C=CH₂), 749 and 698 (aromatic C-H); ¹H NMR (400 MHz, CDCl₃) δ 1.54-1.63 (m, 1H, CHCHHCH₂), 2.07-2.16 (m, 1H, CHCHHCH₂), 2.20 (dd, 1H, *J* = 12.2, 13.2 Hz, CHCHHC=CH₂), 2.38-2.70 (m, 8H, CHCHHC=CH₂, COCH₂CH₂, CH₂Ph), 4.87 (s, 1H, C=CHH), 4.89 (s, 1H, C=CHH), 7.17-7.30 (m, 5H, aromatic CH); ¹³C NMR (100 MHz, CDCl₃) δ ; 31.6, 33.1, 34.1, 40.0, 41.1, 49.7, 111.2, 125.9, 128.4 (2C), 128.4 (2C), 141.9, 143.8, 212.2; Anal. Calcd for C₁₅H₁₈O: C, 84.07; H, 8.47. Found: C, 84.08; H, 8.68.

Recovery of *O*-methylated aminoalcohol

See reference.³

Recovery of *O*-silylated aminoalcohol

The acetic acid buffer and 0.5-N aq.HCl (used on hydrolysis) was combined and neutralized with solid KOH to pH14. The reaction mixture was saturated with sodium chloride. This aqueous solution was extracted five times with CH₂Cl₂. Combined CH₂Cl₂ layer was dried with sodium sulfate and concentrated carefully to afford colorless liquid (*S*-*tert*-leucinol), which was silylated with 1,1,1,3,3,3-hexamethyldisilazane and distilled. The silylated aminoalcohol was recovered in >70% yield.

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