Catalytic Asymmetric Cyanosilylation of Ketones with Chiral Lewis Base

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Supporting Information

General Information. ^1H and ^{13}C NMR spectra were recorded on a Varian instrument (400 MHz and 100 MHz, respectively) and internally referenced to SiMe_4 signal. Exact mass spectra for all new compounds were recorded on a VG 7070 high resolution mass spectrometer. Infrared spectra were recorded on a Perkin Elmer FT-IR Spectrometer. Specific rotations were measured on a Jasco Digital Polarimeter.

Analytical gas-liquid chromatography (GC) was performed on a Hewlett-Packard 6890 Series instrument equipped with a split mode capillary injection system, a flame ionization detector, using a HP-5 GC column or a GC column with chiral stationary phase [Gamma cyclodextrin Trifluoroacetyl (30 m x 0.25 mm)]. All the GC analyses of chiral silylcyanohydrins were carried out with both a crude reaction mixture and a sample purified by silica gel chromatography. High pressure liquid chromatography (HPLC) analyses were performed on a Hewlett-Packard 1100 Series instrument equipped with an isostatic pump, using a Daicel Chiralpak AS (250 x 4.6 mm), AD (250 x 4.6 mm), OD (250 x 4.6 mm), OJ (250 x 4.6 mm), or/and Hypersil SI (200 x 4.6 mm) Column. UV detection was monitored at 254 nm or 220 nm.

Ketones (**4a-d**, **7a**), trimethylsilyl cyanide (TMSCN) were purchased from Aldrich and used without further purification. Ketone **7j** was prepared according to a literature procedure.¹ The yields of the acetal ketone were not optimized yet. The other ketones in Table 1 & 2 were prepared as described below. Chloroform was distilled over anhydrous K_2CO_3 before use, and commercial ethyl acetate (Aldrich) was used directly without further purification.

Catalyst (*DHQ*)₂-*AQN* purification: In most cases, commercially available modified cinchona alkaloids give reproducible results for the asymmetric cyanosilylation. Occasionally, modified cinchona alkaloids purchased from Aldrich Company did not give reproducible results for the asymmetric cyanosilylation. After purification following the extractive procedure described below, the modified cinchona alkaloids give reproducible results.

Commercial modified cinchona alkaloids (100 mg) was dissolved in aqueous HCl (0.2 M, 30 mL) by shaking the mixture at room temperature for 30 min. The resulting yellow solution was extracted with ether (3x15 mL). The aqueous solution was basified with K_2CO_3 (20 wt% aq.) to adjust the pH value of the mixture to 9-11. The resulting mixture was extracted with ether (3x25 mL), the combined ether solution was washed with distilled water (3x15 mL) and brine (3x10 mL), dried over anhydrous sodium

¹ Gupta, S. K. *J. Org. Chem.* **1976**, *41*, 2642.

sulfate, filtered and concentrated under vacuum. The yield of the resulting orange solid was obtained in greater than 98% and was applied in the asymmetric cyanosilylation to give reproducible results.

General procedure for the DABCO-catalyzed cyanosilylation of ketones

To a mixture of ketone (0.20 mmol) and trimethylsilyl cyanide (0.60 mmol) at room temperature (cooled with water bath) was slowly added DABCO (10 mol%). The mixture was stirred for 6-24 h and then purified by silica gel column chromatography (acetone:hexanes/1:100) to give the known silylcyanohydrin (**5a-d**).²

Preparation of the α,α -dialkoxymethyl phenyl ketones (**6b-c**)

1)

To a suspension of phenylglyoxal monohydrate (761 mg, 5.00 mmol) in toluene or benzene (20 mL) was added alcohol (50.0 mmol) and PTS (86 mg, 0.50 mmol). The resulting mixture was heated at reflux for 2h, then cooled to room temperature and then concentrated. The residue was purified by silica gel column chromatography (acetone:hexanes/1:100) to give the desired product.

The mixture of phenylglyoxal monohydrate and allyl alcohol was refluxed in benzene for 2 h. The product was obtained as a colorless oil in 55% yield. ¹H NMR (400 MHz, CDCl₃) δ 4.18 (dd, J = 12.8, 6.0 Hz, 2H), 4.24 (dd, J = 12.8, 5.2 Hz, 2H), 5.21 (d, J = 10.4 Hz, 2H), 5.31 (d, J = 17.6 Hz, 2H), 5.38 (s, 1H), 5.87-5.98 (m, 2H), 7.46 (t, J = 7.6 Hz, 2H), 7.57 (t, J = 7.4 Hz, 1H), 8.15 (d, J = 7.6 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 68.53, 101.19, 116.81, 118.15, 128.58,

² Selected references containing physical data, see: for **5a** and **5c**, Sigeru, T.; Tsutomu, I.; Sadahito, T.; Hirofumi, H.; Hideki, K.; Kenji, U. *Bull. Chem. Soc. Jpn.* **1987**, 60, 2173.; for **5b**, Billera, C. F.; Dunn, T. B.; Barry, D. A.; Engel, P. S. *J. Org. Chem.* **1998**, 63, 9763.; for **5d**, Choudary, B. M.; Narender, N.; Bhuma, V. *Synth. Commun.* **1995**, 25, 2829.

128.71, 129.94, 133.75, 193.68; IR (neat) ν 3071, 1688, 1600, 1584, 1453 cm^{-1} ; HRMS (EI) Calcd for $\text{C}_{14}\text{H}_{17}\text{O}_3$ (MH^+) 233.1178, found 233.1140.

The mixture of phenylglyoxal monohydrate and *n*-octyl alcohol was refluxed in toluene for 2 h. The product was obtained as a colorless oil in 100% yield. ^1H NMR (400 MHz, CDCl_3) δ 0.87 (t, $J = 7.2$ Hz, 6H), 1.18-1.29 (m, 20H), 1.55-1.65 (m, 4H), 3.53-3.60 (m, 2H), 3.65-3.72 (m, 2H), 5.23 (s, 1H), 7.42-7.47 (m, 2H), 7.51-7.57 (m, 1H), 8.16 (d, $J = 7.2$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.29, 22.85, 26.23, 29.42, 29.47, 29.84, 31.99, 68.05, 103.25, 128.49, 128.69, 130.13, 133.60, 194.39; IR (neat) ν 2923, 1691, 1599, 1467 cm^{-1} ; HRMS (EI) Calcd for $\text{C}_{24}\text{H}_{41}\text{O}_3$ (MH^+) 377.3056, found 377.3031.

2)

To a solution of 2,2-diethoxyacetophenone (**7a**) (1.04 g, 5.0 mmol) and cyclohexanol (10.0 g, 100 mmol) in toluene (30 mL) was added PTS (86 mg, 0.50 mmol). The mixture was refluxed for 2 h. The solvent was removed by distillation under normal pressure and the remaining cyclohexanol was removed under reduced pressure. The residue was purified by silica gel column chromatography (acetone:hexanes/1:100) to give the product (**6a**) as a colorless oil (1.52 g, 96%). ^1H NMR (400 MHz, CDCl_3) δ 1.13-1.38 (m, 8H), 1.39-1.54 (m, 4H), 1.59-1.83 (m, 6H), 1.87-1.97 (m, 2H), 3.59-3.67 (m, 2H), 5.26 (s, 1H), 7.39-7.46 (m, 2H), 7.54 (t, $J = 7.4$ Hz, 1H), 8.23 (d, $J = 7.6$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 24.05, 24.26, 25.72, 32.52, 33.20, 76.40, 102.06, 128.26, 130.50, 133.31, 133.74, 195.36; IR (neat) ν 2933, 1689, 1598, 1580, 1449 cm^{-1} ; HRMS (EI) Calcd for $\text{C}_{20}\text{H}_{29}\text{O}_3$ (MH^+) 317.2117, found 317.2098.

Preparation of the α,α -dialkoxymethyl aryl, alkenyl, alkynyl and alkyl ketones **7b-i**, **7k-m**.

1) Prepared from arylglyoxal monohydrate

To a suspension of arylglyoxal monohydrate (5.00 mmol) and PTS (43 mg, 0.25 mmol) in dichloromethane (20 mL) at room temperature was added dropwise triethyl orthoformate (10.0 mmol). The mixture was stirred for 30 min. Triethylamine (0.20 mL) was added and the mixture was concentrated. The residue was purified by silica gel

column chromatography (acetone:hexanes/1:100) to give an α,α -diethoxymethyl aryl ketone.

Ketone **7b** was obtained as a colorless oil in 95% yield. ^1H NMR (400 MHz, CDCl_3) δ 1.25 (t, $J = 7.0$ Hz, 6H), 3.60-3.72 (m, 2H), 3.73-3.80 (m, 2H), 3.86 (s, 3H), 5.24 (s, 1H), 6.93 (d, $J = 8.8$ Hz, 2H), 8.16 (d, $J = 8.8$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 15.35, 55.56, 63.23, 102.74, 113.70, 126.85, 132.28, 163.91, 192.79; IR (neat) ν 2977, 1683, 1601, 1574, 1511, 1460, 1422 cm^{-1} ; HRMS (EI) Calcd for $\text{C}_{13}\text{H}_{18}\text{O}_4$ (M^+) 238.1205, found 238.1179.

Ketone **7c** was obtained as a colorless oil in 96% yield.³ ^1H NMR (400 MHz, CDCl_3) δ 1.25 (t, $J = 7.0$ Hz, 6H), 3.60-3.68 (m, 2H), 3.75-3.82 (m, 2H), 5.18 (s, 1H), 7.42 (d, $J = 8.8$ Hz, 2H), 8.13 (d, $J = 8.8$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 15.34, 63.70, 103.26, 128.80, 131.49, 132.02, 140.04, 193.16.

2) Prepared from α,α -dipropoxyacetone (**7j**)¹

To a mixture of α,α -dipropoxyacetone (**7j**) (348 mg, 2.0 mmol) and aryl aldehyde (2.5 mmol) was slowly added piperidine (2.00 mmol). The mixture was heated at 100 °C (the temperature of oil bath) until α,α -dipropoxyacetone was consumed completely (monitored with GC). The mixture was cooled to room temperature and purified by silica gel column chromatography (acetone:hexanes/1:100) to give an alkenyl ketone.

The reaction mixture was heated for 4 h in the presence of 10 mol% of benzoic acid and the product was obtained as a colorless oil in 70% yield. ^1H NMR (400 MHz, CDCl_3) δ 0.96 (t, $J = 7.2$ Hz, 6H), 1.62-1.71 (m, 4H), 3.49-3.55 (m, 2H), 3.61-3.68 (m, 2H), 4.81 (s, 1H), 7.12 (d, $J = 15.6$ Hz, 1H), 7.38-7.43 (m, 3H), 7.56-7.62 (m, 2H), 7.80 (d, $J = 15.6$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 10.72, 23.05, 69.37, 102.95, 120.94, 128.72, 129.01, 130.81, 134.77, 144.86, 194.46; IR (neat) ν 3060, 2964, 1698, 1611, 1576, 1494, 1450 cm^{-1} ; HRMS (EI) Calcd for $\text{C}_{16}\text{H}_{23}\text{O}_3$ (MH^+) 263.1647, found 263.1688.

The reaction mixture was heated for 7 h and the product was obtained as a colorless oil in 54% yield. ^1H NMR (400 MHz, CDCl_3) δ 0.96 (t, $J = 7.6$ Hz, 6H), 1.62-1.72 (m, 4H), 3.52 (dt, $J = 9.6, 6.4$ Hz, 2H), 3.64 (dt, $J = 9.6,$

³ Papillon-Jegou, D.; Bariou, B.; Soyer, N.; Kerfanto, M. *Bull. Soc. Chim. Fr.* **1977**, 977.

6.4 Hz, 2H), 3.84 (s, 3H), 4.80 (s, 1H), 6.91 (d, $J = 8.4$ Hz, 2H), 6.99 (d, $J = 16.0$ Hz, 1H), 7.55 (d, $J = 8.4$ Hz, 2H), 7.77 (d, $J = 16.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 10.74, 23.07, 55.52, 69.32, 102.99, 114.49, 118.67, 127.55, 130.54, 144.71, 161.93, 194.46; IR (neat) ν 2964, 1692, 1597, 1572, 1512, 1463, 1423 cm^{-1} ; HRMS (CH_4/CI) Calcd for $\text{C}_{17}\text{H}_{25}\text{O}_4$ (MH^+) 293.1753, found 293.1758.

The reaction mixture was heated for 5 h and the product was obtained as a colorless oil in 52% yield. ^1H NMR (400 MHz, CDCl_3) δ 0.96 (t, $J = 7.2$ Hz, 6H), 1.62-1.72 (m, 4H), 3.52 (dt, $J = 9.6, 6.4$ Hz, 2H), 3.64 (dt, $J = 9.6, 6.4$ Hz, 2H), 4.78 (s, 1H), 7.08 (d, $J = 16.0$ Hz, 1H), 7.37 (d, $J = 8.0$ Hz, 2H), 7.53 (d, $J = 8.0$ Hz, 2H), 7.73 (d, $J = 16.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 10.75, 23.08, 69.56, 103.07, 121.36, 129.34, 129.90, 133.32, 136.72, 143.38, 194.29; IR (neat) ν 2965, 1700, 1611, 1566, 1491, 1406 cm^{-1} ; HRMS (CH_4/CI) Calcd for $\text{C}_{16}\text{H}_{22}\text{O}_3\text{Cl}$ (MH^+) 297.1257, found 297.1254.

The reaction mixture was heated for 4 h and the product was obtained as a colorless oil in 35% yield. ^1H NMR (400 MHz, CDCl_3) δ 0.96 (t, $J = 7.2$ Hz, 6H), 1.63-1.72 (m, 4H), 3.52 (dt, $J = 9.2, 6.4$ Hz, 2H), 3.66 (dt, $J = 9.2, 6.4$ Hz, 2H), 4.79 (s, 1H), 7.18 (d, $J = 15.8$ Hz, 1H), 7.34 (dd, $J = 8.0, 4.8$ Hz, 1H), 7.78 (d, $J = 15.8$ Hz, 1H), 7.92 (d, $J = 8.0$ Hz, 1H), 8.61-8.63 (m, 1H), 8.80-8.81 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 10.74, 23.07, 69.69, 103.09, 122.77, 123.91, 130.61, 134.70, 141.06, 150.47, 151.43, 193.96; IR (neat) ν 2965, 1701, 1614, 1586, 1476, 1415 cm^{-1} ; HRMS (CH_4/CI) Calcd for $\text{C}_{15}\text{H}_{22}\text{O}_3\text{N}$ (MH^+) 264.1600, found 264.1597.

3) Prepared from diethoxyacetonitrile

To a solution of diethoxyacetonitrile (646 mg, 5.0 mmol) in ether (20 mL) at room temperature (cooled with water bath) was added dropwise a solution of RLi, RMgBr or RMgCl (1.0-1.5 eq.) in hexane or ether. The mixture was stirred for 0.5-18 h and then cooled with ice-water bath. Water (50 mL) was slowly added and the mixture was extracted with ether (2 x 20 mL). The combined organic layers were dried over anhydrous magnesium sulfate, and then concentrated. The residue was purified by silica gel column chromatography (acetone:hexanes/1:100) to give an α,α -dialkoxymethyl ketone.

The reaction mixture of diethoxyacetonitrile and $\text{PhC}\equiv\text{CMgBr}$ [1.0 eq., prepared *in situ* by adding EtMgBr (3.0 M in ether) to a solution of phenylacetylene in ether at room temperature under nitrogen] was stirred for 18 h and the product was obtained as a

colorless oil in 41% yield.⁴ ¹H NMR (400 MHz, CDCl₃) δ 1.31 (t, *J* = 7.2 Hz, 6H), 3.66-3.82 (m, 4H), 4.87 (s, 1H), 7.37-7.42 (m, 2H), 7.46-7.51 (m, 1H), 7.60-7.64 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 15.37, 63.23, 86.69, 94.89, 101.82, 128.82, 131.24, 132.14, 133.59, 183.30.

The reaction mixture of diethoxyacetonitrile and *n*-C₄H₉C≡CLi [1.0 eq., prepared *in situ* by adding BuLi (1.6 M in hexane) to a solution of 1-hexyne in ether at 0 °C under nitrogen] was stirred for 0.5 h and the product was obtained as a colorless oil in 49% yield.

¹H NMR (400 MHz, CDCl₃) δ 0.93 (t, *J* = 7.0 Hz, 3H), 1.27 (t, *J* = 7.0 Hz, 6H), 1.41-1.49 (m, 2H), 1.55-1.63 (m, 2H), 2.43 (t, *J* = 7.0 Hz, 2H), 3.59-3.67 (m, 2H), 3.68-3.76 (m, 2H), 4.73 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 13.61, 15.23, 19.11, 22.03, 29.69, 63.06, 79.28, 98.87, 101.75, 183.16; IR (neat) ν 2963, 2211, 1684, 1463 cm⁻¹; HRMS (CH₄/CI) Calcd for C₁₂H₂₁O₃ (MH⁺) 213.1491, found 213.1495.

The reaction mixture of diethoxyacetonitrile and BuLi (1.6 M in hexane, 1.0 eq.) was stirred for 0.5 h and the product was obtained as a colorless oil in 55% yield.⁵ ¹H NMR (400 MHz, CDCl₃) δ 0.91 (t, *J* = 7.2 Hz, 3H), 1.25 (t, *J* = 7.0 Hz, 6H), 1.28-1.36 (m, 2H), 1.52-

1.60 (m, 2H), 2.59 (t, *J* = 7.2 Hz, 2H), 3.52-3.61 (m, 2H), 3.66-3.74 (m, 2H), 4.56 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 14.01, 15.30, 22.44, 25.24, 36.65, 63.42, 102.85, 206.62.

The reaction mixture of diethoxyacetonitrile and *i*-PrMgCl (2.0 M in ether, 1.5 eq.) was stirred for 0.5 h and the product was obtained as a colorless oil in 94% yield.⁶ ¹H NMR (400 MHz, CDCl₃) δ 1.10 (d, *J* = 7.0 Hz, 6H), 1.25 (d, *J* = 7.2 Hz, 6H), 3.07 (sp, *J* = 7.0 Hz, 1H), 3.53-3.61 (m, 2H), 3.65-3.73 (m, 2H), 4.70 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 15.25, 18.54, 35.51, 63.13, 101.98, 209.76.

4) **7k** was prepared from the alkylation of enamine

To a flame-dried flask (250 mL) containing activated MS 4Å powder was added a solution of α,α-dipropoxyacetone (1.74 g, 10 mmol) in freshly distilled dichloromethane (12 mL) and cyclohexylamine (1.51 mL, 1.31 g, 13 mmol, 1.3 eq.) under N₂ at room

⁴ Somin, I. N.; Germanguz, E. A. *Zh. Org. Khim.* **1969**, 5, 1780.

⁵ Stambouli, A.; Hamed-Sangsari, F.; Amouroux, R.; Chastrette, F.; Blanc, A.; Mattioda, G. *Bull. Soc. Chim. Fr.* **1988**, 95.

⁶ Verhe, R. C.; de Kimpe, N.; de Buyck, L.; Schamp, N. *Synthesis*, **1982**, 667.

temperature. The mixture was stirred at rt for 3 h. The reaction was monitored by GC. The mixture was filtered through a short pad of Celite[®] and washed with dichloromethane. The combined filtrates were concentrated and dried in *vacuo*. The yellow oilish solid was obtained in quantitative yield which was subjected to alkylation without further purification. ¹H NMR (400 MHz, CDCl₃): δ 0.90-1.90 (m, 23 H, alkyl-H), 3.31-3.45 (m, 3 H, OCH₂, CHN=), 3.58-3.63 (m, 2 H, OCH₂), 4.54 (s, 1 H, CH).

To an oven-dried three-necked flask (250 mL) bearing two addition funnels was added sequentially a solution of LDA (1.9 M in Hex/THF/benzene, 1.65 mL, 3.14 mmol, 1.1 eq.) and freshly distilled THF (5 mL) via a syringe under N₂ at room temperature. The flask was cooled to -78°C in the dry ice-acetone bath. A solution of the crude imine (700 mg, 2.75 mmol) in THF (5.0 mL) was added dropwise from one funnel in 1 h. The resulting brown mixture was stirred at -78°C for 1 h and then a solution of benzyl bromide (513 mg, 3.0 mmol) in THF (5 mL) was added dropwise from other funnel over 30 min. The mixture was stirred at this temperature for 30 min, after the mixture was warmed up to room temperature and stirred at this temperature for an additional 2 h. The reaction was quenched with aqueous HCl (3 N) and vigorously stirred at room temperature for 30 min. The pH value of the mixture was adjusted to 9 using aqueous potassium carbonate (20 wt%). Most of the solvent was removed under reduced pressure and the residue was extracted with ether (3×10 mL). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate and filtered concentrated. The residue was subjected to silica gel chromatography (Hex:EtOAc = 50:1) to give 3-benzyl-α,α-dipropoxyacetone (508 mg, 70% overall yield). ¹H NMR (400 MHz, CDCl₃) δ 0.92 (t, *J* = 7.2 Hz, 6H), 1.55-1.65 (m, 4H), 2.90-2.94 (m, 4H), 3.40 (dt, *J* = 9.2, 6.4 Hz, 2H), 3.56 (dt, *J* = 9.2, 6.4 Hz, 2H), 4.53 (s, 1H), 7.16-7.31 (m, 5H); ¹³C NMR (100 MHz, CDCl₃) δ 10.72, 23.07, 29.18, 38.62, 69.66, 103.18, 126.20, 128.58, 141.30, 205.64; IR (neat) ν 2965, 1730, 1604, 1496, 1454 cm⁻¹; HRMS (EI) Calcd. for C₁₆H₂₄O₃ (M⁺) 264.1725, found 264.1684.

Structures of commercially available modified cinchona alkaloids

General procedure for the preparation of racemic silylcyanohydrins

To a mixture of α,α -dialkoxy ketone (0.20 mmol) and trimethylsilyl cyanide (0.60 mmol) at room temperature (cooled with water bath) was slowly added DBU (10 mol%). The mixture was stirred for 1 h and then purified by silica gel column chromatography (acetone:hexanes/1:100) to give a racemic silylcyanohydrin in quantitative yield.

General procedure for the modified cinchona alkaloid-catalyzed asymmetric silylcyanation of α,α -dialkoxy-substituted ketones

To a solution of α,α -dialkoxy ketone (0.20 mmol) and modified cinchona alkaloid (2-20 mol% as indicated in Table 1 & 2) in chloroform or ethyl acetate (0.20 mL) at the temperature indicated in Table 1 & 2 was added trimethylsilyl cyanide (0.60 or 0.40 mmol). After being stirred for 7-94 h, methanol (50 μ L) was added to quench the reaction. The mixture was diluted with hexanes (5.0 mL) and then washed successively with 0.2 N aqueous HCl and water. The organic layer was dried over anhydrous sodium sulfate, and concentrated. The residue was purified by silica gel column chromatography (acetone:hexanes/1:400 to 1:100) to give the chiral silylcyanohydrin.

To the aqueous layer was added potassium carbonate to adjust the pH value of the solution to 9-11. The resulting mixture was extracted with ethyl acetate (10 mL), and the organic layer was washed with brine, dried over anhydrous sodium sulfate, concentrated to afford the recovered catalyst in quantitative yield. The catalyst is shown to be pure by ^1H NMR (400 MHz, CDCl_3).

1) Products of Table 1 (Entries 1-4)

3.60-3.68 (m, 1H), 4.62 (s, 1H), 7.31-7.37 (m, 3H), 7.54-7.58 9m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 1.11, 23.39, 23.73, 24.13, 24.17, 25.65, 25.78, 31.13, 32.30, 32.90, 33.02, 75.95, 76.83, 79.07, 102.19, 119.72, 127.05, 127.93, 128.78, 137.97; IR (neat) ν 2933, 1494, 1450 cm^{-1} ; HRMS (EI) Calcd for $\text{C}_{24}\text{H}_{37}\text{NO}_3\text{Si}$ (M-CN) 389.2512, found 389.2501.

The ee was determined by converting **6bP** to its corresponding β -aminoalcohol derivative **6bPD** (*vide infra*). ^1H NMR (400 MHz, CDCl_3) δ 0.15 (s, 9H), 3.87 (dd, J = 12.8, 6.0 Hz, 1H), 4.05 (dd, J = 11.8, 6.0 Hz, 1H), 4.22-4.27 (m, 2H), 5.04-5.09 (m, 2H), 5.19-5.23 (m, 1H), 5.29-5.34 (m, 1H), 5.57-5.68 (m, 1H), 5.87-5.96 (m, 1H), 7.35-7.39 (m, 3H), 7.56-7.59 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 1.16, 70.54, 70.98, 78.49, 104.73, 117.58, 117.64, 119.35, 126.90, 128.26, 129.14, 133.67, 134.08, 137.57; IR (neat) ν 2956, 1648, 1492, 1450 cm^{-1} ; HRMS (EI) Calcd for $\text{C}_{18}\text{H}_{26}\text{NO}_3\text{Si}$ (MH^+) 332.1682, found 332.1692.

The ee was determined by converting **6cP** to its corresponding β -aminoalcohol derivative **6cPD** (*vide infra*). ^1H NMR (400 MHz, CDCl_3) δ 0.16 (s, 9H), 0.86-0.91 (m, 6H), 1.08-1.42 (m, 20H), 1.56-1.66 (m, 4H), 3.38-3.65 (m, 4H), 4.38 (s, 1H), 7.33-7.37 (m, 3H), 7.54-7.57 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 1.18, 14.29, 22.85, 26.00, 26.23, 29.40, 29.58, 29.95, 30.27, 31.98, 32.03, 70.49, 70.73, 78.41, 106.73, 119.55, 126.90, 128.12, 128.93, 137.93; IR (neat) ν 2927, 1467 cm^{-1} ; HRMS (EI) Calcd for $\text{C}_{28}\text{H}_{50}\text{NO}_3\text{Si}$ (MH^+) 476.3560, found 476.3569.

2) Products of Table 2

(+)-8a was obtained as a colorless oil in 98% isolated yield and 90% ee [determined by converting this compound to its corresponding β -aminoalcohol derivative **8aD** (*vide infra*)] from a $(\text{DHQ})_2\text{AQN}$ (2 mol%)-catalyzed reaction which was run with 3.0 eq. of trimethylsilyl cyanide in chloroform at $-50\text{ }^\circ\text{C}$ for 19 h. $[\alpha]_{\text{D}}^{25} = 15.7$ (c 1.28, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 0.17 (s, 9H), 1.03 (t, J = 7.0 Hz, 3H), 1.25 (t, J = 7.2 Hz, 3H), 3.24-3.33 (m, 1H), 3.61-3.72 (m, 2H), 3.77-3.85 (m, 1H), 4.38 (s, 1H), 7.34-7.40 (m, 3H), 7.55-7.59 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 1.15, 14.99, 15.31, 66.01, 78.28, 106.42, 119.53, 126.86, 128.12, 128.97, 137.74; IR (neat) ν 2978, 1602, 1493, 1450 cm^{-1} ; HRMS (DCI/ NH_3) Calcd for $\text{C}_{16}\text{H}_{29}\text{N}_2\text{O}_3\text{Si}$ (MNH_4^+) 325.1947, found 325.1949.

(+)-8b was obtained as a colorless oil in 94% isolated yield and 97% ee [determined with chiral HPLC, Daicel Chiralpak AD, isopropanol:hexane/0.2:99.8, 0.20 mL/min, λ = 220 nm, t_{r} (major) = 29.9 min, t_{r} (minor) = 33.7 min] from a $(\text{DHQ})_2\text{AQN}$ (2 mol%)-catalyzed reaction which was run with 3.0 eq. of trimethylsilyl cyanide in chloroform at $-50\text{ }^\circ\text{C}$ for 18 h. $[\alpha]_{\text{D}}^{25} = 16.9$ (c 1.84, CHCl_3); ^1H NMR (400 MHz,

CDCl₃) δ 0.17 (s, 9H), 1.06 (t, J = 7.2 Hz, 3H), 1.25 (t, J = 7.2 Hz, 3H), 3.28-3.36 (m, 1H), 3.62-3.72 (m, 2H), 3.76-3.84 (m, 1H), 3.82 (s, 3H), 4.36 (s, 1H), 6.89 (d, J = 8.8 Hz, 2H), 7.48 (d, J = 8.8 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 1.16, 15.08, 15.29, 55.41, 65.94, 66.06, 77.88, 106.38, 113.42, 119.71, 128.15, 129.68, 160.03; IR (neat) ν 2977, 1611, 1512, 1464 cm⁻¹; HRMS (DCI/NH₃) Calcd for C₁₇H₃₁N₂O₄Si (MNH₄⁺) 355.2053, found 355.2049.

(+)-8c was obtained as a colorless oil in 96% isolated yield and 98% ee [determined with GC on a chiral support, Gamma cyclodextrin Trifluoroacetyl, 115 °C, 4.0 min, 0.05 °C/min to 122 °C, t_r (major) = 107.7 min, t_r (minor) = 110.4 min] from a (DHQ)₂AQN (2 mol%)-catalyzed reaction which was run with 3.0 eq. of trimethylsilyl cyanide in chloroform at -50 °C for 18 h. $[\alpha]_D^{25}$ = 15.3 (c 1.82, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 0.19 (s, 9H), 1.08 (t, J = 7.0 Hz, 3H), 1.25 (t, J = 7.0 Hz, 3H), 3.33-3.41 (m, 1H), 3.64-3.73 (m, 2H), 3.76-3.84 (m, 1H), 4.38 (s, 1H), 7.35 (d, J = 8.8 Hz, 2H), 7.51 (d, J = 8.8 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 1.13, 15.07, 15.25, 66.14, 66.24, 77.65, 106.12, 119.27, 128.29, 128.38, 134.98, 136.18; IR (neat) ν 2978, 1595, 1491, 1446, 1402 cm⁻¹; HRMS (DCI/NH₃) Calcd for C₁₆H₂₈N₂O₃ClSi (MNH₄⁺) 359.1558, found 359.1568.

(-)-8c was obtained as a colorless oil in 95% isolated yield and 94% ee from a (DHQD)₂PHAL (10 mol%)-catalyzed reaction which was run with 2.0 eq. of trimethylsilyl cyanide in chloroform at -50 °C for 40h.

(+)-8d was obtained as a colorless oil in 93% isolated yield and 91% ee [determined with chiral HPLC, Daicel Chiralpak AD, isopropanol:hexane/1:99, 0.10 mL/min, λ = 254 nm, t_r (major) = 37.7 min, t_r (minor) = 41.1 min] from a (DHQ)₂AQN (2 mol%)-catalyzed reaction which was run with 3.0 eq. of trimethylsilyl cyanide in chloroform at -50 °C for 16 h. $[\alpha]_D^{25}$ = 31.9 (c 2.03, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 0.24 (s, 9H), 0.94 (t, J = 7.2 Hz, 3H), 0.96 (t, J = 7.2 Hz, 3H), 1.60-1.70 (m, 4H), 3.53-3.62 (m, 2H), 3.70-3.77 (m, 2H), 4.45 (s, 1H), 6.25 (d, J = 16.0 Hz, 1H), 6.93 (d, J = 16.0 Hz, 1H), 7.28-7.45 (m, 5H); ¹³C NMR (100 MHz, CDCl₃) δ 1.59, 10.79, 10.86, 23.14, 23.25, 72.15, 72.49, 94.62, 105.91, 119.01, 124.83, 127.26, 128.72, 128.90, 133.90, 135.69; IR (neat) ν 2962, 1450 cm⁻¹; HRMS (DCI/NH₃) Calcd for C₂₀H₃₅N₂O₃Si (MNH₄⁺) 379.2417, found 379.2412.

(+)-8e was obtained as a colorless oil in 92% isolated yield and 90% ee [determined with chiral HPLC, Daicel Chiralpak AD, isopropanol:hexane/1:99, 0.20 mL/min, λ = 254 nm, t_r (major) = 22.6 min, t_r (minor) = 26.0 min] from a (DHQ)₂AQN (2 mol%)-catalyzed reaction which was run with 3.0 eq. of trimethylsilyl cyanide in chloroform at -50 °C for 18 h. $[\alpha]_D^{25}$ = 71.6 (c 1.52, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 0.24 (s, 9H), 0.94 (t, J = 7.6 Hz, 3H), 0.95 (t, J = 7.6 Hz, 3H), 1.59-1.70 (m, 4H), 3.52-3.62 (m, 2H), 3.71-3.78 (m, 2H), 3.81 (s, 3H), 4.45 (s, 1H), 6.11 (d, J = 16.0 Hz, 1H), 6.88 (d, J = 16.0 Hz, 1H), 6.88 (d, J = 8.8

Hz, 2H), 7.37 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 1.56, 10.74, 10.81, 23.09, 23.20, 55.46, 72.05, 72.44, 77.05, 105.88, 114.24, 119.08, 122.38, 128.37, 128.50, 133.40, 160.08; IR (neat) ν 2963, 1652, 1608, 1577, 1513, 1464 cm^{-1} ; HRMS (DCI/ NH_3) Calcd for $\text{C}_{21}\text{H}_{37}\text{N}_2\text{O}_4\text{Si}$ (MNH_4^+) 409.2523, found 409.2522.

(-)-**8e** was obtained as a colorless oil in 96% isolated yield and 92% ee as determined by chiral HPLC from a (DHQD) $_2$ PHAL (10 mol%)-catalyzed reaction which was run with 3.0 eq. of trimethylsilyl cyanide in ethyl acetate at -30 °C for 21 h.

(+)-**8f** was obtained as a colorless oil in 95% isolated yield and 92% ee [determined with chiral HPLC [Daicel Chiralpak AD, isopropanol:hexane/0.2:99.8, 1.0 mL/min, λ = 254 nm, t_r (major) = 16.8 min, t_r (minor) = 20.2 min] from a (DHQ) $_2$ AQN (2 mol%)-catalyzed reaction which was run with 3.0 eq. of trimethylsilyl cyanide in chloroform at -50 °C for 18 h. $[\alpha]_D^{25}$ = 47.0 (c 2.01, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 0.24 (s, 9H), 0.93 (t, J = 7.2 Hz, 3H), 0.95 (t, J = 7.2 Hz, 3H), 1.59-1.70 (m, 4H), 3.54-3.62 (m, 2H), 3.71-3.79 (m, 2H), 4.46 (s, 1H), 6.23 (d, J = 16.0 Hz, 1H), 6.88 (d, J = 16.0 Hz, 1H), 7.30-7.38 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 1.53, 10.74, 10.81, 23.10, 23.23, 72.17, 72.56, 76.78, 105.83, 118.83, 125.47, 128.42, 129.08, 132.62, 134.15, 134.44; IR (neat) ν 2964, 1612, 1594, 1492, 1464, 1406 cm^{-1} ; HRMS (DCI/ NH_3) Calcd for $\text{C}_{20}\text{H}_{34}\text{N}_2\text{O}_3\text{SiCl}$ (MNH_4^+) 413.2027, found 413.2022.

(+)-**8g** was obtained as a colorless oil in 97% isolated yield and 93% ee [determined with chiral HPLC, Daicel Chiralpak AD, isopropanol:hexane/1:99, 0.50 mL/min, λ = 254 nm, t_r (major) = 29.2 min, t_r (minor) = 33.6 min] from a (DHQ) $_2$ AQN (2 mol%)-catalyzed reaction which was run with 3.0 eq. of trimethylsilyl cyanide in chloroform at -50 °C for 18 h. $[\alpha]_D^{25}$ = 37.8 (c 1.60, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 0.25 (s, 9H), 0.94 (t, J = 7.2 Hz, 3H), 0.96 (t, J = 7.2 Hz, 3H), 1.59-1.71 (m, 4H), 3.54-3.63 (m, 2H), 3.72-3.79 (m, 2H), 4.48 (s, 1H), 6.34 (d, J = 16.0 Hz, 1H), 6.91 (d, J = 16.0 Hz, 1H), 7.27-7.32 (m, 1H), 7.73-7.77 (m, 1H), 8.52-8.54 (m, 1H), 8.65-8.67 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 1.54, 10.75, 10.82, 23.09, 23.23, 72.27, 72.65, 76.62, 105.81, 118.68, 123.80, 127.24, 130.27, 131.38, 133.77, 148.87, 149.64; IR (neat) ν 2963, 1613, 1478, 1416 cm^{-1} ; HRMS (DCI/ NH_3) Calcd for $\text{C}_{19}\text{H}_{31}\text{N}_2\text{O}_3\text{Si}$ (MH^+) 363.2104, found 363.2097.

(+)-**8h** was obtained as a colorless oil in 93% isolated yield and 96% ee [determined with chiral HPLC, Hypersil SI + Daicel Chiralpak AS, isopropanol:hexane/1:99, 0.20 mL/min, λ = 254 nm, t_r (major) = 35.3 min, t_r (minor) = 37.2 min] from a (DHQ) $_2$ AQN (2 mol%)-catalyzed reaction which was run with 3.0 eq. of trimethylsilyl cyanide in chloroform at -50 °C for 19 h. $[\alpha]_D^{25}$ = 12.9 (c 1.26, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 0.34 (s, 9H), 1.26-1.36 (m, 6H), 3.73-3.93 (m, 4H), 4.55 (s, 1H), 7.32-7.42 (m, 3H), 7.46-7.51 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 1.27, 15.37, 63.22, 66.03, 66.13, 83.38, 87.70, 105.03, 117.51, 128.60, 129.61, 132.06, 133.60; IR (neat) ν

2978, 2204, 1682, 1490, 1444 cm^{-1} ; HRMS (EI) Calcd for $\text{C}_{18}\text{H}_{26}\text{NO}_3\text{Si}$ (MH^+) 332.1682, found 332.1647.

(-)-8h was obtained as a colorless oil in 96% isolated yield and 93% ee as determined by chiral HPLC from a $(\text{DHQD})_2\text{PHAL}$ (10 mol%)-catalyzed reaction which was run with 3.0 eq. of trimethylsilyl cyanide in ethyl acetate at $-30\text{ }^\circ\text{C}$ for 21 h.

(+)-8i was obtained as a colorless oil in 94% isolated yield and 95% ee [determined by converting this compound to its corresponding β -aminoalcohol derivative **8iD** (*vide infra*)] from a $(\text{DHQ})_2\text{AQN}$ (2 mol%)-catalyzed reaction which was run with 3.0 eq. of trimethylsilyl cyanide in chloroform at $-50\text{ }^\circ\text{C}$ for 18 h. $[\alpha]_{\text{D}}^{25} = 1.9$ (c 1.56, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 0.29 (s, 9H), 0.92 (t, $J = 7.0$ Hz, 3H), 1.26 (t, $J = 7.0$ Hz, 3H), 1.27 (t, $J = 7.0$ Hz, 3H), 1.38-1.48 (m, 2H), 1.49-1.56 (m, 2H), 2.27 (t, $J = 7.0$ Hz, 3H), 3.68-3.77 (m, 2H), 3.81-3.89 (m, 2H), 4.42 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 1.21, 13.68, 15.28, 18.63, 22.11, 30.07, 65.97, 67.90, 74.61, 89.40, 104.97, 117.88; IR (neat) ν 2964, 2360, 1455 cm^{-1} ; HRMS (DCI/ NH_3) Calcd for $\text{C}_{16}\text{H}_{33}\text{N}_2\text{O}_3\text{Si}$ (MNH_4^+) 329.2260, found 329.2256.

R-(-)-8j was obtained as a colorless oil in 97% isolated yield and 92% ee [determined with GC on a chiral support, Gamma cyclodextrin Trifluoroacetyl, $95\text{ }^\circ\text{C}$, 4.0 min, $0.10\text{ }^\circ\text{C}/\text{min}$ to $98\text{ }^\circ\text{C}$, t_{r} (major) = 25.9 min, t_{r} (minor) = 25.2 min] from a $(\text{DHQ})_2\text{AQN}$ (2 mol%)-catalyzed reaction which was run with 3.0 eq. of trimethylsilyl cyanide in chloroform at $-50\text{ }^\circ\text{C}$ for 46 h. $[\alpha]_{\text{D}}^{25} = -16.8$ (c 2.16, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 0.25 (s, 9H), 0.92-0.98 (m, 6H), 1.56 (s, 3H), 1.60-1.69 (m, 4H), 3.50-3.58 (m, 2H), 3.68-3.75 (m, 2H), 4.33 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 1.48, 10.74, 10.79, 23.10, 23.14, 23.26, 72.04, 72.37, 72.72, 105.37, 120.98; IR (neat) ν 2964, 1463 cm^{-1} ; HRMS (DEI) Calcd for $\text{C}_{13}\text{H}_{28}\text{NO}_3\text{Si}$ (MH^+) 274.1838, found 274.1833.

S-(+)-8j was obtained as a colorless oil in 95% isolated yield and 96% ee from a $(\text{DHQD})_2\text{PHAL}$ (10 mol%)-catalyzed reaction which was run with 2.0 eq. of trimethylsilyl cyanide in ethyl acetate at $-50\text{ }^\circ\text{C}$ for 88 h.

(+)-8k was obtained as a colorless oil in 96% isolated yield and 97% ee [determined by converting this compound to its corresponding β -aminoalcohol derivative **8kD** (*vide infra*)] from a $(\text{DHQ})_2\text{AQN}$ (20 mol%)-catalyzed reaction which was run with 3.0 eq. of trimethylsilyl cyanide in chloroform at $-50\text{ }^\circ\text{C}$ for 24 h. $[\alpha]_{\text{D}}^{25} = 2.7$ (c 1.65, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 0.29 (s, 9H), 0.95 (t, $J = 7.2$ Hz, 3H), 0.96 (t, $J = 7.2$ Hz, 3H), 1.60-1.70 (m, 4H), 2.10-2.15 (m, 2H), 2.80-2.86 (m, 2H), 3.48-3.60 (m, 2H), 3.69-3.75 (m, 2H), 4.38 (s, 1H), 7.20-7.31 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) δ 1.62, 10.81, 10.88, 23.22, 23.28, 30.32, 38.32, 72.16, 72.25, 75.94, 105.01, 120.03, 126.29, 128.67, 128.70, 141.35; IR (neat) ν 2964, 1604, 1497, 1456 cm^{-1} ; HRMS (DCI/ NH_3) Calcd for $\text{C}_{20}\text{H}_{37}\text{N}_2\text{O}_3\text{Si}$ (MNH_4^+) 381.2573, found 381.2561.

(+)-8l was obtained as a colorless oil in 92% isolated yield and 90% ee [determined by converting this compound to its corresponding β -

aminoalcohol derivative **8ID** (*vide infra*)] from a (DHQ)₂AQN (5 mol%)-catalyzed reaction which was run with 3.0 eq. of trimethylsilyl cyanide in chloroform at -50 °C for 18 h. $[\alpha]_D^{25} = 0.20$ (c 1.50, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 0.25 (s, 9H), 0.94 (t, *J* = 7.0 Hz, 3H), 1.26 (t, *J* = 7.0 Hz, 3H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.33-1.41 (m, 2H), 1.45-1.52 (m, 2H), 1.76-1.83 (m, 2H), 3.60-3.69 (m, 2H), 3.78-3.87 (m, 2H), 4.33 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 1.52, 14.13, 15.32, 15.39, 22.78, 25.90, 36.01, 65.79, 66.00, 76.16, 104.87, 120.14; IR (neat) ν 2962, 1453 cm⁻¹; HRMS (DCI/NH₃) Calcd for C₁₄H₃₃N₂O₃Si (MNH₄⁺) 305.2260, found 305.2263.

(+)-8m was obtained as a colorless oil in 81% isolated yield and 94% ee [determined by converting this compound to its corresponding β-aminoalcohol derivative **8mD** (*vide infra*)] from a (DHQ)₂AQN (20 mol%)-catalyzed reaction which was run with 3.0 eq. of trimethylsilyl cyanide in chloroform at -40 °C for 94 h. $[\alpha]_D^{25} = 0.41$ (c 1.45, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 0.25 (s, 9H), 0.99 (d, *J* = 6.8 Hz, 3H), 1.07 (d, *J* = 6.8 Hz, 3H), 1.27 (t, *J* = 7.0 Hz, 6H), 2.15 (sp, *J* = 6.8 Hz, 1H), 3.60-3.70 (m, 2H), 3.76-3.89 (m, 2H), 4.42 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 1.65, 15.37, 15.38, 16.60, 18.09, 34.54, 65.35, 65.42, 79.64, 103.29, 119.49; IR (neat) ν 2977, 1447 cm⁻¹; HRMS (DCI/NH₃) Calcd for C₁₃H₃₁N₂O₃Si (MNH₄⁺) 291.2104, found 291.2114.

General procedure for the conversion of silylcyanohydrin to its corresponding β-aminoalcohol derivative and determination of ee

To a solution of silylcyanohydrin (0.10 mmol) in dry ether (15.0 mL) at room temperature was added LiAlH₄ (0.30 mmol). The mixture was stirred at that temperature for 1.0 h, and cooled with ice-water bath. Water (0.20 mL) was slowly added and the resulting mixture was filtered. The filtrate was dried over anhydrous potassium carbonate, and then filtered. To this filtrate was added triethyl amine (0.60 mmol) and benzoyl chloride (0.12 mmol). After being stirred at room temperature for 0.5 h, the mixture was filtered and concentrated. The residue was purified by silica gel column chromatography (acetone: hexanes/1:20 to 1:10) to give the amide.

1) β-aminoalcohol derivatives from the products of Table 1 (Entries 2-4)

¹H NMR (400 MHz, CDCl₃) δ 1.05-1.92 (m, 20H), 3.31-3.44 (m, 2H), 3.90 (dd, *J* = 14.0, 3.6 Hz, 1H), 4.24 (dd, *J* = 14.0, 7.4 Hz, 1H), 4.70 (s, 1H), 6.61-6.64 (m, 1H), 7.23-7.48 (m, 6H), 7.58-7.64 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 23.94, 24.23, 24.29, 24.44, 25.68, 25.72, 31.73, 32.76, 33.46, 33.59, 45.21, 76.24, 77.92, 103.33, 126.78, 127.09, 127.65, 128.13, 128.59, 129.29, 131.42, 134.99; IR (CHCl₃) ν 3372, 2932, 1640, 1578, 1537, 1488, 1449 cm⁻¹; HRMS

(EI) Calcd for $C_{28}H_{37}O_4N$ (MH^+) 451.2723, found 451.2733. HPLC conditions: Daicel Chiralpak OD, isopropanol : hexane (1 : 99), 1.0 mL/min, $\lambda = 254$ nm; for the derivative from the product of (DHQ)₂AQN-catalyzed reaction, t (major) = 30.3 min, t (minor) = 39.6 min.

¹H NMR (400 MHz, $CDCl_3$) δ 3.86-3.91 (m, 1H), 3.97-4.21 (m, 5H), 4.60 (s, 1H), 5.12-5.25 (m, 4H), 5.76-5.88 (m, 2H), 6.58-6.62 (m, 1H), 7.25-7.62 (m, 10H); ¹³C NMR (100 MHz, $CDCl_3$) δ 45.38, 71.01, 71.48, 78.19, 106.38, 117.78, 117.94, 126.61, 127.11, 127.80, 128.33, 128.62, 131.57, 133.91, 134.02, 134.64, 140.56, 168.60; IR (neat) ν 3421, 3061, 1713, 1644, 1603, 1578, 1538, 1489, 1450 cm^{-1} ; HRMS (EI) Calcd for $C_{22}H_{26}O_4N$ (MH^+) 368.1862, found 368.1832. HPLC conditions: Daicel Chiralpak OD, isopropanol : hexane (5 : 95), 1.0 mL/min, $\lambda = 254$ nm; for the derivative from the product of (DHQ)₂AQN-catalyzed reaction, t (major) = 33.3 min, t (minor) = 23.9 min.

¹H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, $J = 7.0$ Hz, 6H), 1.19-1.31 (m, 20H), 1.49-1.57 (m, 4H), 3.23-3.29 (m, 1H), 3.39-3.44 (m, 1H), 3.66-3.73 (m, 2H), 3.94 (dd, $J = 14.4, 3.8$ Hz, 1H), 4.21 (dd, $J = 14.4, 7.0$ Hz, 1H), 4.48 (s, 1H), 6.68-6.72 (m, 1H), 7.25-7.65 (m, 10H); ¹³C NMR (100 MHz, $CDCl_3$) δ 14.30, 22.85, 26.22, 26.25, 29.40, 29.54, 29.93, 30.10, 32.01, 45.39, 70.83, 71.38, 77.90, 107.90, 126.52, 127.12, 127.71, 128.28, 128.62, 131.56, 135.00, 140.67, 168.27; IR ($CHCl_3$) ν 2924, 1688, 1603, 1584, 1454 cm^{-1} ; HRMS (EI) Calcd for $C_{32}H_{49}NO_4$ (M^+) 511.3662, found 511.3720. HPLC conditions: Daicel Chiralpak OD, isopropanol : hexane (5 : 95), 1.0 mL/min, $\lambda = 254$ nm; for the derivative from the product of (DHQ)₂AQN-catalyzed reaction, t_r (major) = 7.1 min, t_r (minor) = 8.9 min.

2) β -aminoalcohol derivatives from the products of Table 2

8aD was obtained as a colorless oil in 81% isolated yield. ¹H NMR (400 MHz, $CDCl_3$) δ 1.13-1.21 (m, 6H), 3.28-3.37 (m, 1H), 3.43-3.51 (m, 1H), 3.68-3.81 (m, 2H), 3.93 (dd, $J = 14.2, 4.0$ Hz, 1H), 4.18 (dd, $J = 14.2, 6.6$ Hz, 1H), 4.47 (s, 1H), 6.62 (s, br., 1H), 7.24-7.45 (m, 6H), 7.58-7.62 (m, 4H); ¹³C NMR (100MHz, $CDCl_3$) δ 15.34, 15.52, 45.17, 66.25, 65.54, 77.75, 107.64, 126.53, 127.03, 127.67, 128.23, 128.58, 131.44, 134.80, 140.67, 168.27; IR (neat) ν 3356, 2976, 1714, 1643, 1535 cm^{-1} ; HRMS (EI) Calcd for $C_{20}H_{26}NO_4$ (MH^+) 344.1862, found 344.1839. HPLC conditions: Daicel Chiralpak OD, isopropanol:hexane/15:85, 1.0 mL/min, $\lambda = 254$ nm; for the derivative from the product of (DHQ)₂AQN-catalyzed reaction, t_r (major) = 6.1 min, t_r (minor) = 7.1 min].

8iD was obtained as a colorless oil in 59% isolated yield. ¹H NMR (400 MHz, $CDCl_3$) δ 0.84 (t, $J = 7.2$ Hz, 3H), 1.27 (t, $J = 7.0$ Hz, 6H), 1.32-1.49 (m, 4H), 2.21 (t, $J = 6.8$ Hz, 2H), 3.68-

3.76 (m, 2H), 3.80 (d, $J = 5.2$ Hz, 2H), 3.84-3.93 (m, 2H), 4.47 (s, 1H), 6.76-6.81 (m, 1H), 7.39-7.53 (m, 3H), 7.80 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.68, 15.51, 18.60, 22.04, 30.66, 45.78, 66.21, 66.35, 72.66, 78.71, 87.17, 105.85, 127.17, 128.66, 131.61, 134.78, 168.21; IR (neat) ν 3356, 2932, 2243, 1712, 1643, 1535 cm^{-1} ; HRMS (EI) Calcd for $\text{C}_{20}\text{H}_{30}\text{NO}_4$ (MH^+) 348.2175, found 348.2195. HPLC conditions: Daicel Chiralpak AD, isopropanol:hexane/5:95, 1.0 mL/min, $\lambda = 254$ nm; for the derivative from the product of (DHQ) $_2$ AQN-catalyzed reaction, t_r (major) = 12.7 min, t_r (minor) = 28.9 min].

8kD was obtained as a colorless oil in 41% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 0.95 (t, $J = 7.0$ Hz, 3H), 0.96 (t, $J = 7.0$ Hz, 3H), 1.59-1.71 (m, 4H), 1.88-1.93 (m, 2H), 2.76-2.82 (m, 2H), 3.45 (dt, $J = 8.4, 6.8$ Hz, 1H), 3.59 (dt, $J = 9.2, 6.8$ Hz, 1H), 3.72 (d, $J = 5.6$ Hz, 2H), 3.72-3.84 (m, 2H), 4.40 (s, 1H), 7.00 (s, br., 1H), 7.17-7.29 (m, 5H), 7.41-7.52 (m, 3H), 7.77-7.81 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 10.82, 10.88, 23.49, 23.60, 29.50, 36.83, 44.05, 72.81, 73.62, 75.29, 108.20, 125.96, 127.10, 128.59, 128.63, 128.71, 131.61, 134.83, 142.70, 168.01; IR (neat) ν 3393, 2962, 1712, 1642, 1534, 1489, 1452 cm^{-1} ; HRMS (EI) Calcd for $\text{C}_{24}\text{H}_{34}\text{NO}_4$ (MH^+) 400.2488, found 400.2495. HPLC conditions: Daicel Chiralpak AD, isopropanol:hexane/15:85, 1.0 mL/min, $\lambda = 254$ nm; for the derivative from the product of (DHQ) $_2$ AQN-catalyzed reaction, t_r (major) = 5.9 min, t_r (minor) = 8.7 min].

8lD was obtained as a colorless oil in 89% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 0.90 (t, $J = 7.2$ Hz, 3H), 1.27 (t, $J = 7.0$ Hz, 3H), 1.28 (t, $J = 7.0$ Hz, 3H), 1.25-1.35 (m, 2H), 1.36-1.46 (m, 2H), 1.53-1.63 (m, 2H), 2.54 (s, br., 1H), 3.57-3.70 (m, 4H), 3.85-3.93 (m, 2H), 4.37 (s, 1H), 6.96-7.03 (m, 1H), 7.39-7.51 (m, 3H), 7.76-7.81 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.17, 15.67, 15.73, 23.46, 24.99, 34.20, 43.99, 66.51, 67.00, 74.96, 107.98, 127.02, 128.60, 131.44, 134.89, 167.71; IR (neat) ν 3400, 2957, 1644, 1535 cm^{-1} ; HRMS (EI) Calcd for $\text{C}_{18}\text{H}_{30}\text{NO}_4$ (MH^+) 324.2175, found 324.2174. HPLC conditions: Daicel Chiralpak AD, isopropanol:hexane/5:95, 1.0 mL/min, $\lambda = 254$ nm; for the derivative from the product of (DHQ) $_2$ AQN-catalyzed reaction, t_r (major) = 10.4 min, t_r (minor) = 13.1 min].

8mD was obtained as a colorless oil in 86% isolated yield. ^1H NMR (400 MHz, CDCl_3) δ 1.00 (d, $J = 6.8$ Hz, 3H), 1.01 (d, $J = 6.8$ Hz, 3H), 1.27 (t, $J = 7.0$ Hz, 1H), 1.28 (p, $J = 7.0$ Hz, 3H), 2.01 (sp, $J = 6.8$ Hz, 1H), 3.54-3.75 (m, 4H), 3.85-3.96 (m, 2H), 4.51 (s, 1H), 7.14-7.19 (m, 1H), 7.38-7.51 (m, 3H), 7.76-7.81 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 15.65, 15.81, 17.04, 17.13, 42.47, 65.99, 67.58, 76.00, 107.32, 127.02, 128.57, 131.40, 134.90, 167.62; IR (neat) ν 3399, 2975, 1717, 1645, 1535 cm^{-1} ; HRMS (EI) Calcd for $\text{C}_{17}\text{H}_{28}\text{NO}_4$ (MH^+) 310.2018, found 310.1998. HPLC conditions: Daicel Chiralpak OD + Hypersil SI, isopropanol:hexane/2:98, 1.0 mL/min, $\lambda = 254$ nm; for the derivative from the product of (DHQ) $_2$ AQN-catalyzed reaction, t_r (major) = 22.9 min, t_r (minor) = 18.2 min].

Preparation of optically active tertiary silylcyanohydrin on a 100 mmol scale and the recovery of catalyst

To a solution of trimethylsilyl cyanide (29.7 g, 300 mmol) and (DHQ)₂AQN (1.71 g, 2.00 mmol) in chloroform (100 mL) at -50 °C was added dropwise α,α-dipropoxyacetone (17.4 g, 100 mmol). The mixture was stirred at that temperature for 72 h. Methanol (20 mL) was slowly added to the mixture, and after 5 min the mixture was diluted with hexanes (400 mL). The mixture was washed successively with aqueous HCl (0.2 N, 2 x 50 mL) and water (3 x 30 mL). The organic layer was dried over anhydrous sodium sulfate and concentrated to give the silylcyanohydrin (27.3 g, 100%, 92% ee) as a colorless oil.

To the aqueous layer was added K₂CO₃ to adjust the pH value of the solution to 9–11. The resulting mixture was extracted with ethyl acetate (150 mL), and the organic layer was washed with brine, dried over anhydrous sodium sulfate, concentrated to afford the recovered catalyst (DHQ)₂AQN in quantitative yield, which is shown to be pure by ¹H NMR (400 MHz, CDCl₃) (see more details in the **General Procedure**).

Conversion of (-)-9j to a chiral β-amino acid and the determination of its absolute configuration of (-)-8j

(-)-8j was obtained in 92% ee from a (DHQ)₂AQN-catalyzed reaction. (-)-8j (1.37 g, 5.00 mmol) was reduced to its corresponding β-aminoalcohol with LiAlH₄ using the same procedure as described above. To a solution of the crude β-aminoalcohol in ether (100 mL) at room temperature was added triethylamine (1.11 g, 11.0 mmol) and benzyl chloroformate (940 mg, 5.10 mmol). The mixture was stirred for 0.5 h. The

mixture was washed with brine, dried over magnesium sulfate and then concentrated. The residue was purified by silica gel column chromatography (acetone:hexanes/1:20 to 1:10) to give carbamate **9j** (1.47 g, 86% for two steps) as a colorless oil.⁷ The ee of **9j** was determined to be 92% [HPLC conditions: Daicel Chiralpak AD + Hypersil SI, isopropanol:hexane/1:99, 0.50 mL/min, t_r (major) = 113.3 min, t_r (minor) = 101.7 min]. $[\alpha]_D^{25} = 1.6$ (c 1.12, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 0.94 (t, J = 7.4 Hz, 6H), 1.17 (s, 3H), 1.58-1.68 (m, 4H), 2.45 (s, 1H), 3.30-3.36 (m, 2H), 3.43-3.50 (m, 2H), 3.71-3.79 (m, 2H), 4.24 (s, 1H), 5.11 (s, 2H), 5.25-5.30 (m, 1H), 7.39-7.39 (m, 5H); ¹³C NMR (100 MHz, CDCl₃) δ 10.79, 20.65, 23.43, 46.73, 66.84, 72.78, 72.82, 74.08, 107.77, 127.20, 128.22, 128.68, 136.91, 157.13.

To a solution of **9j** (495 mg, 1.46 mmol) in acetone (20 mL) at room temperature was added 3 N aqueous HCl (4.0 mL). The mixture was stirred for 3 h. After being quenched with aqueous potassium carbonate (828 mg in 4 mL of water), acetone was removed under reduced pressure. The mixture was extracted with ethyl acetate (2 x 20 mL), and the organic layer was dried over anhydrous magnesium sulfate, concentrated. The residue was dissolved in methanol (50 mL) and cooled to 0 °C. To this mixture was added KOH (212 mg, 3.79 mmol) and then I₂ (480 mg, 1.90 mmol).⁸ The mixture was stirred for 30 min, and added dropwise 1 N aqueous HCl (4.5 mL). Saturated aqueous sodium thiosulfate was added until the mixture turned colorless. Methanol was removed under reduced pressure and the mixture was extracted with ethyl acetate (3x20 mL). The organic layer was dried over anhydrous sodium sulfate, concentrated. The residue was purified by silica gel column chromatography (acetone:hexanes/1:10 to 1:5) to give **10j-Me** (238 mg, 61% for two steps) as a colorless oil. The ee of **10j-Me** was determined to be 92% [HPLC conditions: Daicel Chiralpak OD, isopropanol:hexane/10:90, 1.0 mL/min, t_r (major) = 13.3 min, t_r (minor) = 15.3 min]. $[\alpha]_D^{25} = -18.9$ (c 1.95, CHCl₃); ¹H NMR (400 MHz, CDCl₃, 3.5:1 mixture of rotamers) δ 1.39 (s, 3H), 3.26 (dd, J = 14.0, 5.2 Hz, 1H), 3.65 (dd, J = 14.0, 7.6 Hz, 1H), 3.72 (s, 3H), 5.07 (s, 2H), 5.36-5.41 (m, 1H), 7.27-7.38 (m, 5H); ¹H NMR (400 MHz, CDCl₃, minor rotamer, partial) δ 3.78 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 23.32, 48.96, 53.16, 66.98, 74.74, 128.18, 128.24, 128.61, 136.48, 156.74, 176.01; IR (neat) ν 3390, 2953, 1732, 1538, 1454 cm⁻¹; HRMS (DCI/NH₃) Calcd for C₁₃H₁₈NO₅ (MH⁺) 268.1185, found 268.1195.

To a solution of **10j-Me** (123 mg, 0.46 mmol) in methanol (15 mL) at room temperature was added 5% aqueous KOH (7.5 mL). The mixture was stirred for 30 min and methanol was removed under reduced pressure. The mixture was extracted with ether (10 mL) and the aqueous layer was acidified with 3 N aqueous HCl to PH = 2. The mixture was extracted with ethyl acetate (3 x 20 mL). The organic layer was dried over anhydrous sodium sulfate, and then concentrated to give **10j** (82.6 mg, 71%) as a white solid. $[\alpha]_D^{25} = -9.7$ (c 1.2, DMSO), literature value for (**S**)-**10j**: $[\alpha]_D^{25} = 9.1$ (c 1.0, DMSO);⁹ ¹H NMR (400 MHz, DMSO, 3.5:1 mixture of rotamers) δ 1.20 (s, 3H), 3.18 (dd, J = 13.2, 5.6 Hz, 1H), 3.29 (dd, J = 13.2, 6.8 Hz, 1H), 5.00 (s, 2H), 7.05-7.09 (m, 1H), 7.26-7.38 (m, 5H); ¹H NMR (400 MHz, DMSO, minor rotamer, partial) δ 1.51 (s, 3H), 3.34 (d, J = 9.0 Hz, 1H), 3.63 (d, J = 9.0 Hz, 1H), 7.68 (s, br., 1H); ¹³C NMR (100

⁷ Tian, S.-K.; Deng, L. *J. Am. Chem. Soc.* **2001**, 123, 6195.

⁸ Yamamoto, K.; Shimizu, M.; Yamada, S. *J. Org. Chem.* **1992**, 57, 33.

⁹ Pires, R.; Burger, K. *Synthesis* **1996**, 1277.

MHz, DMSO, mixture of rotamers) δ 23.16, 48.81, 65.32, 73.57, 127.66, 127.78, 128.37, 137.16, 156.43, 176.13; ^{13}C NMR (400 MHz, DMSO, minor rotamer, partial) δ 22.99, 49.31, 79.48, 157.67, 172.82.

By comparing the specific rotation of **10j** with known (*S*)-**10j**, the absolute configuration of (*-*)-**8j** was assigned to be *R*.

Conversion of (+)-**9j** to (*-*)-**11j**

9j (225 mg, 0.66 mmol) was hydrolyzed with 3.0 N aqueous HCl (4.0 mL) as described above. The residue was dissolved in methanol (7 mL) and cooled to 0 °C. To this solution was added portionwise NaBH₄ (100 mg, 2.6 mmol). The resulting mixture was warmed to room temperature and stirred for 2 h. Aqueous HCl (3N, 2 mL) was slowly added. The methanol was removed under reduced pressure and the residue was extracted with ethyl acetate (2 × 10 mL). The organic layer was dried over anhydrous sodium sulfate, concentrated. The residue was purified by silica gel column chromatography (acetone:hexanes/1:4) to give **11j** (101 mg, 64% for two steps) as a colorless oil. The ee of **11j** was determined to be 92% [HPLC conditions: Daicel Chiralpak OJ, isopropanol:hexane/10:90, 1.0 mL/min, *t_r* (major) = 18.7 min, *t_r* (minor) = 16.5 min]. $[\alpha]_{\text{D}}^{25} = -6.9$ (c 1.69, CHCl₃); ^1H NMR (400 MHz, CDCl₃) δ 1.12 (s, 3H), 2.91 (s, 1H), 3.17 (dd, *J* = 14.4, 6.4 Hz, 1H), 3.24 (dd, *J* = 14.4, 6.8 Hz, 1H), 3.33-3.48 (m, 3H), 5.11 (s, 2H), 5.35-5.40 (m, 1H), 7.31-7.39 (m, 5H); ^{13}C NMR (100 MHz, CDCl₃) δ 22.16, 47.63, 67.36, 67.48, 72.97, 128.34, 128.53, 128.79, 136.26, 158.26; IR (neat) ν 3407, 2936, 1693, 1537, 1454 cm⁻¹; HRMS (DCI/NH₃) Calcd for C₁₂H₁₈NO₄ (MH⁺) 240.1236, found 240.1241.

Conversion of (+)-**9j** to (+)-**12j**

9j (225 mg, 0.66 mmol) was hydrolyzed with 3.0 N aqueous HCl (4.0 mL) as described above. The residue was dissolved in benzene (10 mL) and Ph₃P=CHCO₂Et (453 mg, 1.3 mmol) was added. The mixture was stirred for 2 h and concentrated to about 1 mL. The residue was purified by silica gel column chromatography (ethyl acetate:hexanes/1:4) to give **12j** (129 mg, 63% for two steps) as a colorless oil. The ee of

12j was determined to be 91% [HPLC conditions: Daicel Chiralpak OJ, isopropanol:hexane/10:90, 1.0 mL/min, t_r (major) = 28.5 min, t_r (minor) = 38.4 min]. $[\alpha]_D^{25} = 22.2$ (c 1.95, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 1.29 (t, $J = 7.0$ Hz, 3H), 1.33 (s, 3H), 2.96 (s, 1H), 3.24 (dd, $J = 14.0, 6.0$ Hz, 1H), 3.40 (dd, $J = 14.0, 6.8$ Hz, 1H), 4.19 (q, $J = 7.0$ Hz, 2H), 5.10 (s, 2H), 5.11-5.16 (m, 1H), 6.13 (d, $J = 15.6$ Hz, 1H), 6.88 (d, $J = 15.6$ Hz, 1H), 7.31-7.39 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.42, 25.69, 50.51, 60.78, 67.42, 73.73, 121.14, 128.32, 128.47, 128.78, 136.34, 151.21, 157.87, 166.65; IR (neat) ν 3371, 2962, 1713, 1644, 1537, 1455 cm^{-1} ; HRMS (DCI/ NH_3) Calcd for $\text{C}_{16}\text{H}_{22}\text{NO}_5$ (MH^+) 308.1498, found 308.1485.

Preparation of β -hydroxylamine **12d** from silylcyanohydrin **8d**:

To a suspension of LiAlH_4 (13 mg, 0.346 mmol, 5.0 eq.) in dry THF (0.5 mL) was added dry diethyl ether (2.5 mL). The mixture was stirred at room temperature for 30 min, and then to this mixture was added dropwise a solution of **8d** (25 mg, 0.87 mmol) in dry ether (2.0 mL) under N_2 at room temperature. The mixture was stirred for 30 min, and then water (0.5 mL) was added dropwise to the mixture at 0°C via a syringe. The resulting mixture was stirred at room temperature for an additional 30 min. Then anhydrous sodium sulfate (300 mg) was added in one portion to this mixture. The mixture was vigorously stirred at room temperature for 1 h, then filtered and washed with ether. The combined ether solution was concentrated and used without further purification.

The crude β -amino alcohol was dissolved in dry ether (4.0 mL). Benzyl chloroformate (12 μL , 14 mg, 0.084 mmol, 1.2 eq.). Triethylamine (15 μL , 11 mg, 0.108 mmol, 1.5 eq.) were added dropwise at room temperature via a pipette. The resulting white suspension was stirred at room temperature for 1 h, then filtered through a short pad of silica gel. The silica gel pad was washed with ether (3×10 mL). The combined ether solution was concentrated and the residue was subjected to silica gel chromatography (Hexanes: $\text{EtOAc} = 3 : 1$) to afford the desired product **13d** (27 mg, 90% yield). The ee of **13d** was determined to be 90%. $[\alpha]_D^{25} = -33.4$ (c 0.70, CHCl_3). HPLC analysis conditions: Chiralcel OJ, isopropanol:hexanes/15:85, 0.5 mL/min, $\lambda = 254$ nm. t_r (minor) = 1.6 min, t_r (major) = 16.2 min. ^1H NMR (400 MHz, CDCl_3): δ 0.95, 0.94 (each t, $J = 7.2$ Hz, CH_3), 1.57-1.70 (m, 4 H, $2 \times \text{CH}_2$), 2.81 (s, 1H, OH), 3.42-3.55 (m, 4 H, $2 \times \text{CH}_2\text{O}$), 3.75 (M, 2 H, $\text{CH}_2\text{-NH}$), 4.34 (s, 1 H, $-\text{CH}$), 5.06 (s, 2H, OCH_2Ph), 5.16 (brs, 1 H, NH), 6.29 (d, $J = 16$ Hz, 1 H, $-\text{CH}=\text{}$), 6.78 (d, $J = 16$ Hz, 1 H, $\text{PhCH}=\text{}$), 7.25-7.39 (m, 10 H, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ 10.60, 23.14, 23.21, 45.58, 66.65, 72.20, 72.69, 77.20, 106.97, 126.61, 127.53, 127.92, 127.95, 128.41, 128.49, 128.53, 130.87, 136.74, 157.11. FT-IR (neat) ν 1721 cm^{-1} . HRMS: Calcd. for $\text{C}_{25}\text{H}_{33}\text{NO}_5\text{Na}$: 450.2256; Found: 450.2268.

To a flask charged with a solution of **13d** (15 mg, 0.035 mmol) in acetone (3.0 mL) was added HCl (3.0N, 1.0 mL) at room temperature. The flask was sealed by a septum. The mixture was stirred at room temperature for 30h, and then aqueous potassium carbonate (20 wt%) was added to the mixture to adjust the pH value to 9-11. The resulting mixture was extracted with diethyl ether (3×5 mL). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, and concentrated in *vacuo*. The crude aldehyde was subjected to the next step without further purification.

An oven-dried Schlenk tube (5.0 mL) was charged under nitrogen with a stir bar, sodium hydride (4.2 mg, 0.105 mmol, 3 eq.) and distilled THF (1.0 mL). Triethyl phosphonoacetate (28 μ L, 31 mg, 0.14 mmol, 4 eq.) was added dropwise via a pipette. The mixture was stirred at room temperature for 30 min until no gas was emitted. A solution of the crude aldehyde in THF (1.0 mL) was added dropwise via a syringe at 0°C. The mixture turned to red immediately upon the addition of the aldehyde. The color faded to yellow after the mixture was stirred for 30 min. The mixture was stirred at room temperature for an additional 30 min and then concentrated. The residue was subjected to preparative TLC plate ($\text{CH}_2\text{Cl}_2/\text{MeOH} = 50/1$) to give the desired (*E*)-isomer **12d** in (10 mg, 73% yield). The ee of **12d** was determined to be 90%. $[\alpha]_{\text{D}}^{25} = 7.8$ (c 0.50, CHCl_3). HPLC analysis conditions: Chiralcel OD, isopropanol:hexanes/10:90, 1.0 mL/min, $\lambda = 254$ nm. t_{r} (major) = 41.8 min, t_{r} (minor) = 48.1 min. ^1H NMR (400 MHz, CDCl_3): δ 1.29 (t, $J = 6.8$ Hz, CH_3), 3.35 (s, 1H, OH), 3.42 (dd, $J = 6, 14$ Hz, 1 H, AB, $-\text{CH}_2\text{-NH}$), 3.51 (dd, $J = 6, 14$ Hz, 1 H, AB, $-\text{CH}_2\text{-NH}$), 4.20 (q, $J = 6.8$ Hz, 2 H, $-\text{O}-\text{CH}_2\text{-CH}_3$), 5.09 (s, 2H, OCH_2Ph), 5.16 (t, $J = 6$ Hz, 1 H, NH), 6.19 (d, $J = 16$ Hz, $=\text{CH}-$), 6.22 (d, $J = 16$ Hz, 1 H, $=\text{CHCO}$), 6.74 (d, $J = 16$ Hz, 1 H, $-\text{CH}=\text{}$), 6.98 (d, $J = 15.2$ Hz, 1 H, $\text{PhCH}=\text{}$), 7.25-7.37 (m, 10 H, Ar-H). ^{13}C NMR (100 MHz, CDCl_3): δ 14.44, 49.86, 60.88, 67.50, 76.74, 121.59, 126.03, 126.91, 128.30, 128.33, 128.46, 128.77, 128.87, 129.52, 131.32, 136.28, 148.74, 158.05, 166.57. FT-IR (neat) ν 1712 cm^{-1} . HRMS: Calcd. for $\text{C}_{23}\text{H}_{29}\text{N}_2\text{O}_5$: 413.2076; found: 413.2079.

HPLC conditions: Daicel Chiralpak OD, isopropanol:hexane/15:85, 1.0 mL/min, λ = 254 nm

Racemic (±)-**8aD**

Derivative of the product (+)-**8a** of (DHQ)₂AQN-catalyzed reaction

HPLC conditions: Daicel Chiralpak AD, isopropanol:hexane/0.2:99.8, 0.20 mL/min, λ = 220 nm

Racemic ($\pm$)-**8b**

Product (+)-**8b** of (DHQ)₂AQN-catalyzed reaction

GC conditions: Gamma cyclodextrin Trifluoroacetyl, 115 °C, 4.0 min, 0.05 °C/min to 122 °C

Racemic (±)-**8c**

Product (+)-**8c** of (DHQ)₂AQN-catalyzed reaction

Product (-)-**8c** of (DHQD)₂PHAL-catalyzed reaction

HPLC conditions: Daicel Chiralpak AD, isopropanol:hexane/1:99, 0.10 mL/min, λ = 254 nm

Racemic (±)-**8d**

Product (+)-**8d** of (DHQ)₂AQN-catalyzed reaction

HPLC conditions: Daicel Chiralpak AD, isopropanol:hexane/1:99, 0.20 mL/min, λ = 254 nm

Racemic ($\pm$)-**8e**

Product (+)-**8e** of (DHQ)₂AQN-catalyzed reaction

Product (-)-**8e** of (DHQD)₂PHAL-catalyzed reaction

HPLC conditions: Daicel Chiralpak AD, isopropanol:hexane/0.2:99.8, 1.0 mL/min, λ = 254 nm

Racemic ($\pm$)-**8f**

Product (+)-**8f** of (DHQ)₂AQN-catalyzed reaction

HPLC conditions: Daicel Chiralpak AD, isopropanol:hexane/1:99, 0.5 mL/min, λ = 254 nm

Racemic (±)-**8g**

Product (+)-**8g** of (DHQ)₂AQN-catalyzed reaction

HPLC conditions: Hypersil SI + Daicel Chiralpak AS, isopropanol:hexane/1:99, 0.20 mL/min, $\lambda = 254$ nm

Racemic ($\pm$)-**8h**

Product (+)-**8h** of (DHQ)₂AQN-catalyzed reaction

Product (-)-**8h** of (DHQD)₂PHAL-catalyzed reaction

HPLC conditions: Daicel Chiralpak AD, isopropanol:hexane/5:95, 1.0 mL/min, $\lambda = 254$ nm

Racemic ($\pm$)-**8iD**

Derivative (+)-**8i** of the product of
 (DHQ)₂AQN-catalyzed reaction

GC conditions: Gamma cyclodextrin Trifluoroacetyl, 95 °C, 4.0 min, 0.10 °C/min to 98 °C

Product reaction of (DHQ)₂AQN-catalyzed

Product reaction of (DHQD)₂PHAL-catalyzed

HPLC conditions: Daicel Chiralpak AD, isopropanol:hexane/15:85, 1.0 mL/min, λ = 254 nm

Racemic ($\pm$)-**8kD**

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AREA%	RT	AREA	TYPE	WIDTH	AREA%
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8.549	10115728	PB	.468	49.74170	

TOTAL AREA=2.0337E+07
 MUL FACTOR=1.0000E+00

Derivative of the product (+)-**8k** of
 (DHQ)₂AQN-catalyzed reaction

Error storing signal to M:SIGNAL .BNA
 DIRECTORY FULL
 Storing processed peaks to M:SIGNAL .PRA

RUN# 2170 DEC 22, 2001 06:22:03

PEAK FILE : M:SIGNAL.PRA

AREA%	RT	AREA	TYPE	WIDTH	AREA%
5.960	10935152	SBB	.321	98.27312	
8.656	192153	PB	.459	1.72686	

TOTAL AREA=1.1127E+07
 MUL FACTOR=1.0000E+00

HPLC conditions: Daicel Chiralpak AD, isopropanol:hexane/5:95, 1.0 mL/min, $\lambda = 254$ nm

Racemic ($\pm$)-**8ID**

Derivative of the product (+)-**8I** of (DHQ)₂AQN-catalyzed reaction

HPLC conditions: Daicel Chiralpak OD + Hypersil SI, isopropanol:hexane/2:98, 1.0 mL/min, $\lambda = 254$ nm

Racemic ($\pm$)-**8mD**

Derivative of the product (+)-**8m** of (DHQ)₂AQN-catalyzed reaction

HPLC conditions: Daicel Chiralcel OJ, isopropanol:hexane/15:85, 0.5 mL/min, $\lambda = 254$ nm

HPLC conditions: Daicel Chiralcel OD, isopropanol:hexane/10:90, 1.0 mL/min, λ = 254 nm