A Practical Asymmetric Synthesis of β -Trichloromethyl- β -hydroxy Ketones by the Reaction of Chloral or Chloral Hydrate with Chiral Imines

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Graphical Table of Contents

(a) -78 °C to rt, overnight, toluene. (b) 10% HCl, rt, 1 h.

Supporting Information

Measurement. Optical rotations were measured in Uvasol grade CHCl_3 (Merck) on a HORIBA SEPA-300. High-performance liquid chromatography (HPLC) was achieved using DAICEL CHIRALCEL OD (0.46 cm ϕ $\times$ 25 cm) column on a SHIMADZU LC-4A. Melting points were obtained on a Yanagimoto MP-S2 micro melting point apparatus and are uncorrected. Infrared spectra (IR) were recorded on a SHIMADZU FT-IR 8100A spectrometer. ^1H NMR spectra were measured with a JEOL α -400 (400 MHz) FT-NMR spectrometers in deuteriochloroform (CDCl_3) solutions with tetramethylsilane (Me_4Si) as the internal standard. ^{13}C NMR spectra were obtained on a JEOL α -400 (100 MHz) FT-NMR spectrometers in CDCl_3 solutions Me_4Si as the internal standard. Mass spectra (MS) were taken on a Hitachi QP1000 mass spectrometer operating at an ionization potential of 70 eV. High resolution mass spectra (HRMS) were taken on a Hitachi-80B and/or JEOL JMS-700 mass spectrometer operating at an ionization potential of 70 eV. Elemental analyses were made on a Elementar Vario EL.

Materials. The isolation of pure products was carried out by column chromatography using silica gel (Wakogel C-200, 100-200 mesh, Wako Pure Chemical Ind., Ltd.). Analytical TLC was done on Merck precoated (0.25 mm) silica gel 60 F₂₅₄ plates. Diethyl ether were freshly distilled from sodium benzophenone ketyl. Hexane, benzene, toluene, and dichloromethane (CH_2Cl_2) were distilled over calcium hydride under argon. All chemicals were of reagent grade and, if necessary, were purified in the usual manner prior to use.

A Typical Procedure for the Synthesis of Chiral Imines. To the mixture of (*R*)-1-(1-naphthyl)ethylamine (2.128 g, 12.4 mmol) and acetophenone (2.240 g, 18.6 mmol) in benzene (15 ml) was added *p*-toluenesulfonic acid (0.036 g, 0.19 mmol) at room temperature under an inert atmosphere of argon. The reaction mixture was stirred at reflux temperature for 2 days using Dean-Stark apparatus. After being cooled to room temperature, the reaction mixture was quenched with a saturated NaHCO_3 (30 mL), followed by extraction with diethyl ether (30 ml $\times$ 3), drying over Na_2SO_4 , and concentration under vacuum. The residue was

distilled in vacuo to give (*R*)-*N*-(1-phenylethyliden)-1-naphthylethylamine (**2c**) (2.213 g, 69%).

(*R*)-*N*-(1-Phenylethyliden)-1-phenylethylamine (2a**):**

bp 142-143 °C (7 mmHg); $[\alpha]_D^{25} -72.8$ ($c = 1.0$, CHCl_3); IR (neat) 1634.1 (C=N) cm^{-1} ; *anti* : *syn* = 90 : 10; *anti*: ^1H NMR (CDCl_3) δ 1.54 (d, $J = 6.43$ Hz, 3H), 2.27 (s, 3H), 4.84 (q, $J = 6.43$ Hz, 1H), 7.06-7.85 (m, 10H); ^{13}C NMR (CDCl_3) δ 15.45 (s), 25.04 (s), 59.72 (s), 126.41 (s), 126.56 (s), 126.69 (s), 128.06 (s), 128.26 (s), 129.29 (s), 141.37 (s), 146.12 (s), 163.32 (s); *syn* : ^1H NMR (CDCl_3) δ 1.40 (d, $J = 6.43$ Hz, 3H), 2.32 (s, 3H), 4.42 (q, $J = 6.43$ Hz, 1H), 7.06-7.85 (m, 10H); ^{13}C NMR (CDCl_3) δ 24.53 (s), 29.33 (s), 60.79 (s), 125.56 (s), 125.69 (s), 128.39 (s), 132.96 (s), 139 (s), 145.65 (s), 167.19 (s); MS (EI) m/z (rel intensity) 223 (M^+ ; 48.4), 222 (85.1), 208 (45.9), 105 (100.0), 77 (87.1); HRMS (EI) Found: m/z 223.1355. Calcd for $\text{C}_{16}\text{H}_{17}\text{N}$: M, 223.1362.

(*R*)-*N*-(1-Phenylethyliden)-1-cyclohexylethylamine (2b**):**

bp 159-160 °C (7 mmHg); $[\alpha]_D^{25} -84.5$ ($c = 1.1$, CHCl_3); IR (neat) 1636.1 (C=N) cm^{-1} ; *anti* : *syn* = 87 : 13; *anti*: ^1H NMR (CDCl_3) δ 0.87-1.87 (m, 11H), 1.12 (d, $J = 6.47$ Hz, 3H), 2.21 (s, 3H), 3.38 (quin., $J = 6.47$ Hz, 1H), 7.06-7.97 (m, 5H); ^{13}C NMR (CDCl_3) δ 15.94 (s), 18.44 (s), 26.26 (s), 26.35 (s), 26.83 (s), 29.71 (s), 29.86 (s), 44.45 (s), 60.78 (s), 126.53 (s), 128.01 (s), 128.90 (s), 141.90 (s), 161.86 (s); *syn*: ^1H NMR (CDCl_3) δ 0.87-1.87 (m, 11H), 1.03 (d, $J = 6.71$ Hz, 3H), 2.26 (s, 3H), 2.92 (quin., $J = 6.71$ Hz, 1H), 7.06-7.97 (m, 5H); ^{13}C NMR (CDCl_3) δ 26.60 (s), 19.41 (s), 28.76 (s), 28.94 (s), 29.18 (s), 29.37 (s), 43.19 (s), 30.12 (s), 60.78 (s), 125.71 (s), 128.42 (s), 132.94 (s), 139.92 (s), 166.20 (s); MS (EI) m/z (rel intensity) 229 (M^+ ; 1.0), 146 (100.0), 120 (42.4), 105 (82.3), 77 (35.5), 69 (20.5); HRMS (CI) Found: m/z 230.1910. Calcd for $\text{C}_{16}\text{H}_{24}\text{N}$: M+H, 230.1900.

(*R*)-*N*-(1-Phenylethyliden)-1-(1-naphthyl)ethylamine (2c**):**

bp 191-192 °C (3 mmHg); $[\alpha]_D^{25} -216.3$ ($c = 1.1$, CHCl_3); IR (neat) 1632.6 (C=N) cm^{-1} ; *anti* : *syn* = 91 : 9; *anti*: ^1H NMR (CDCl_3) δ 1.72 (d, $J = 6.43$ Hz, 3H), 2.25 (s, 3H), 5.51 (q, $J = 6.43$ Hz, 1H), 7.00-8.31 (m, 12H); ^{13}C NMR (CDCl_3) δ 15.94 (s), 24.64 (s), 56.48 (s), 123.47 (s), 123.96 (s), 125.21 (s), 125.69 (s), 125.77 (s), 126.77 (s), 126.96 (s), 128.17 (s), 128.96 (s), 129.42 (s), 130.62 (s), 133.95 (s), 141.45 (s), 142.31 (s), 164.21 (s); *syn*: ^1H NMR (CDCl_3) δ 1.53 (d, $J = 6.59$ Hz, 3H), 2.38 (s, 3H), 5.21 (q, $J = 6.59$ Hz, 1H), 7.00-8.31 (m, 12H); ^{13}C NMR (CDCl_3) δ 24.91 (s), 29.38 (s), 56.88 (s), 122.86 (s), 123.15 (s), 123.86 (s), 125.08 (s), 125.41 (s), 125.90 (s), 126.87 (s), 128.40 (s), 128.50 (s), 128.78 (s), 130.16 (s), 133.03 (s), 139.16 (s), 167.35 (s); MS (EI) m/z (rel intensity) 272 (M^+ ; 26.8), 258 (16.1), 155 (100.0), 128 (22.7), 115 (15.1), 103 (44.7), 77 (45.4); HRMS (EI) Found: m/z 273.1515. Calcd for $\text{C}_{20}\text{H}_{19}\text{N}$: M, 273.1519.

(*R*)-*N*-[1-(4-Chlorophenyl)ethyliden]-1-(1-naphthyl)ethylamine (2d**):**

mp 91.5-92.5 °C (hexane); $[\alpha]_D^{25} -259.6$ ($c = 1.0$, CHCl_3); IR (KBr) 1632.0 (C=N) cm^{-1} ; *anti* : *syn* = 96 : 4; *anti*: ^1H NMR (CDCl_3) δ 1.71 (d, $J = 6.67$ Hz, 3H), 2.24 (s, 3H), 5.54 (q, $J = 6.67$ Hz, 1H), 7.26-8.30 (m, 11H); ^{13}C NMR (CDCl_3) δ 15.61 (s), 24.54 (s), 56.61 (s), 123.40 (s), 123.91 (s), 125.28 (s), 125.71 (s), 127.04 (s), 128.24 (s), 128.63 (s), 128.96 (s), 130.54 (s), 133.93 (s), 135.46 (s), 139.63 (s), 142.04 (s), 162.78 (s); *syn*: ^1H NMR (CDCl_3) δ 1.53 (d, J

= 6.67 Hz, 3H), 2.37 (s, 3H), 5.16 (q, J = 6.67 Hz, 1H), 7.26-8.30 (m, 11H); ^{13}C NMR (CDCl_3) δ 24.89 (s), 29.28 (s), 57.09 (s), 122.99 (s), 123.81 (s), 125.56 (s), 127.38 (s), 128.83 (s), 129.59 (s), 130.00 (s), 137.31 (s), 165.94 (s); MS (EI) m/z (rel intensity) 309 ($\text{M}^+ + 2$; 6.4), 307 (M^+ ; 17.6), 292 (20.6), 155 (100.0), 127 (11.9), 115 (8.7), 102 (6.1), 77 (8.9); Anal. Calcd for C, 78.04; H, 5.89; N, 4.55. Found: C, 77.96; H, 5.66; N, 4.50.

(R)-N-[1-(4-Methoxyphenyl)ethyliden]-1-(1-naphthyl)ethylamine (2e):

mp 118.0-119.0 °C (hexane); $[\alpha]_{\text{D}}^{25}$ -262.2 (c = 1.0, CHCl_3); IR (KBr) 1603.0 ($\text{C}=\text{N}$) cm^{-1} ; *anti* : *syn* = 95 : 5; *anti*: ^1H NMR (CDCl_3) δ 1.71 (d, J = 6.67 Hz, 3H), 2.22 (s, 3H), 3.84 (s, 3H), 5.53 (q, J = 6.67 Hz, 1H), 6.82-8.31 (m, 11H); ^{13}C NMR (CDCl_3) δ 15.66 (s), 24.74 (s), 55.20 (s), 56.32 (s), 113.41 (s), 123.22 (s), 123.78 (s), 125.19 (s), 125.66 (s), 125.79 (s), 126.89 (s), 128.27 (s), 128.95 (s), 130.64 (s), 133.95 (s), 134.18 (s), 142.55 (s), 160.75 (s), 163.32 (s); *syn*: ^1H NMR (CDCl_3) δ 1.53 (d, J = 6.51 Hz, 3H), 2.38 (s, 3H), 3.80 (s, 3H), 5.28 (q, J = 6.51 Hz, 1H), 6.82-8.31 (m, 11H); ^{13}C NMR (CDCl_3) δ 26.31 (s), 29.28 (s), 55.28 (s), 56.78 (s), 113.68 (s), 113.69 (s), 122.91 (s), 123.55 (s), 125.44 (s), 127.60 (s), 128.81 (s), 131.18 (s), 142.55 (s), 159.37 (s), 166.92 (s); MS (EI) m/z (rel intensity) 302 (M^+ ; 48.7), 288 (23.4), 155 (100.0), 128 (10.1), 115 (7.9), 91 (6.4), 77 (8.5); Anal. Calcd for C, 83.13; H, 6.98; N, 4.62. Found: C, 82.71; H, 7.34; N, 4.52.

(R)-N-[1-(2-Thienyl)ethyliden]-1-(1-naphthyl)ethylamine (2f):

mp 68.5-69.5 °C (hexane); $[\alpha]_{\text{D}}^{25}$ -363.3 (c = 1.1, CHCl_3); IR (KBr) 1647.4 ($\text{C}=\text{N}$) cm^{-1} ; *anti* : *syn* = 98 : 2; *anti*: ^1H NMR (CDCl_3) δ 1.68 (d, J = 6.67 Hz, 3H), 2.22 (s, 3H), 5.49 (q, J = 6.67 Hz, 1H), 7.00-8.31 (m, 10H); ^{13}C NMR (CDCl_3) δ 15.48 (s), 24.73 (s), 56.25 (s), 123.58 (s), 124.03 (s), 125.15 (s), 125.61 (s), 125.74 (s), 126.43 (s), 126.92 (s), 127.05 (s), 128.55 (s), 128.86 (s), 130.44 (s), 133.90 (s), 142.14 (s), 148.25 (s), 158.55 (s); *syn*: ^1H NMR (CDCl_3) δ 1.55 (d, J = 6.83 Hz, 3H), 2.26 (s, 3H), 4.95 (q, J = 6.83 Hz, 1H), 7.00-8.31 (m, 10H); ^{13}C NMR (CDCl_3) δ 26.75 (s), 29.43 (s), 56.33 (s), 121.26 (s), 122.79 (s), 125.29 (s), 125.82 (s), 126.81 (s), 127.94 (s), 132.34 (s), 133.62 (s), 143.23 (s), 159.49 (s); MS (EI) m/z (rel intensity) 278 (M^+ ; 8.4), 264 (54.8), 155 (100.0), 127 (19.4), 115 (13.1), 110 (15.5), 77 (11.8); Anal. Calcd for C, 77.38; H, 6.13; N, 5.01. Found: C, 77.29; H, 6.32; N, 4.93.

(R)-N-(1-Cyclohexylethyliden)-1-(1-naphthyl)ethylamine (2g):

bp 214-215 °C (7 mmHg); $[\alpha]_{\text{D}}^{23}$ -56.3 (c = 1.0, CHCl_3); IR (KBr) 1655.1 ($\text{C}=\text{N}$) cm^{-1} ; *anti* : *syn* = 90 : 10; *anti*: ^1H NMR (CDCl_3) δ 1.17-1.85 (m, 11H), 1.59 (d, J = 6.67 Hz, 3H), 1.74 (s, 3H), 5.28 (q, J = 6.67 Hz, 1H), 7.42-8.21 (m, 7H); ^{13}C NMR (CDCl_3) δ 15.43 (s), 24.53 (s), 26.03 (s), 26.09 (s), 30.04 (s), 30.19 (s), 50.64 (s), 54.97 (s), 123.42 (s), 123.55 (s), 125.06 (s), 125.48 (s), 125.69 (s), 126.66 (s), 128.83 (s), 130.61 (s), 133.82 (s), 142.59 (s), 172.75 (s); *syn*: ^1H NMR (CDCl_3) δ 1.17-1.85 (m, 11H), 1.55 (d, J = 6.42 Hz, 3H), 2.01 (s, 3H), 4.96 (q, J = 6.42 Hz, 1H), 7.42-8.21 (m, 7H); ^{13}C NMR (CDCl_3) δ 24.74 (s), 25.63 (s), 25.83 (s), 28.33 (s), 29.27 (s), 41.48 (s), 46.40 (s), 51.32 (s), 53.55 (s), 121.26 (s), 122.81 (s), 123.15 (s), 123.83 (s), 125.29 (s), 125.82 (s), 127.10 (s), 128.72 (s), 130.38 (s), 130.38 (s), 143.25 (s), 173.73 (s); MS (EI) m/z (rel intensity) 278 (M^+ ; 2.3), 224 (8.8), 155 (100.0), 127 (10.5), 115 (7.5), 77 (3.6), 70 (8.6); HRMS (EI) Found: m/z 279.1986. Calcd for $\text{C}_{20}\text{H}_{25}\text{N}$: M, 279.1989.

(R)-N-(1-tert-Butylethyliden)-1-(1-naphthyl)ethylamine (2h):

mp 71.5-72.5 °C (hexane); $[\alpha]_D^{25} -35.4$ ($c = 1.0$, CHCl_3); IR (KBr) 1653.2 (C=N) cm^{-1} ; *anti* : *syn* = 88 : 12; **anti**: ^1H NMR (CDCl_3) δ 1.15 (s, 9H), 1.53 (d, $J = 6.67$ Hz, 3H), 1.74 (s, 3H), 5.28 (q, $J = 6.67$ Hz, 1H), 7.42-8.21 (m, 7H); ^{13}C NMR (CDCl_3) δ 12.89 (s), 24.61 (s), 27.80 (s), 55.41 (s), 123.76 (s), 123.91 (s), 125.06 (s), 125.39 (s), 125.75 (s), 126.64 (s), 128.85 (s), 130.71 (s), 133.93 (s), 142.97 (s), 173.01 (s); **anti**: ^1H NMR (CDCl_3) δ 1.14 (s, 9H), 1.50 (d, $J = 6.53$ Hz, 3H), 1.95 (s, 3H), 4.95 (q, $J = 6.53$ Hz, 1H), 7.42-8.21 (m, 7H); ^{13}C NMR (CDCl_3) δ 26.32 (s), 28.07 (s), 40.65 (s), 46.44 (s), 121.33 (s), 122.87 (s), 125.59 (s), 125.89 (s), 127.19 (s), 175.25 (s); MS (EI) m/z (rel intensity) 253 (M^+ ; 8.3), 196 (3.9), 155 (100.0), 127 (6.9), 115 (4.5), 102 (1.1), 77 (2.4); HRMS (EI) Found: m/z 253.1829. Calcd for $\text{C}_{18}\text{H}_{23}\text{N}$: M, 253.1832.

A Typical Procedure for the Synthesis of β -Trichloromethyl- β -hydroxy Ketones. To a solution of (*R*)-*N*-(1-phenylethylidene)-1-(1-naphthyl)ethylamine (**2c**) (0.273 g, 1.0 mmol) in toluene (4 mL) was added chloral **1a** (0.147 g, 1.0 mmol) at -78 °C under an argon atmosphere. After being stirred overnight at -78 °C to room temperature, the reaction mixture was hydrolyzed with 10% HCl aq. (4 mL) for 1 h, followed by extraction with diethyl ether (30 mL $\times$ 3), drying over Na_2SO_4 , and concentration under vacuum. The residue was chromatographed on silica gel using hexane-AcOEt, giving 4,4,4-trichloro-3-hydroxy-1-phenyl-1-butanone (**3a**) (0.206 g, 77%, 92.2% *ee* (*S*), Table 2, entry 1). The enantiomeric excess of the product was determined by chiral HPLC analysis (DAICEL, CHIRALCEL OD, hexane:*i*-PrOH = 95:5, 0.8 mL/min, 254 nm). On the other hand, the aqueous layer and the precipitate from the hydrolysis were made with alkaline solid NaOH, followed by extraction with diethyl ether (30 mL $\times$ 3), drying over Na_2SO_4 , and concentration under vacuum. (*R*)-1-(1-Naphthyl)ethylamine was recovered in 74% (0.127 g).

4,4,4-Trichloro-3-hydroxy-1-phenyl-1-butanone (**3a**):

Rf 0.18 (benzene); mp 65.0-66.0 °C (>99.9% *ee* (*S*), hexane); $[\alpha]_D^{20} -31.9$ (>99.9% *ee* (*S*), $c = 1.0$, CHCl_3); Chiral HPLC (DAICEL, CHIRALCEL OD, hexane:*i*-PrOH = 95:5, 0.8 mL/min, 254 nm, $t_R = 16.0$ min (*S*), 20.0 (*R*)); IR (KBr) 1684.1 (C=O), 3447.2 (OH) cm^{-1} ; ^1H NMR (CDCl_3) δ 3.51 (dd, $J = 17.45$, 9.03 Hz, 1H), 3.65 (dd, $J = 17.45$, 2.08 Hz, 1H), 3.87 (br s, 1H), 4.89 (dd, $J = 9.03$, 2.08 Hz, 1H), 7.48-7.52 (m, 2H), 7.60-7.64 (m, 1H), 7.99-8.01 (m, 2H); ^{13}C NMR (CDCl_3) δ 40.95 (s), 78.97 (s), 102.54 (s), 128.27 (s), 128.80 (s), 133.90 (s), 136.30 (s), 197.12 (s); MS m/z (rel intensity) 252 ($\text{M}^+ - \text{H}_2\text{O} + 4$; 0.5), 250 ($\text{M}^+ - \text{H}_2\text{O} + 2$; 1.0), 248 ($\text{M}^+ - \text{H}_2\text{O}$; 1.1), 151 (10.1), 150 (11.5), 132 (5.4), 121 (11.0), 112 (4.8), 106 (100.0), 91 (8.5), 77 (100.0), 63 (9.2); Anal. Calcd for: C, 44.89; H, 3.39. Found: C, 44.89; H, 3.38.

4,4,4-Trichloro-3-hydroxy-1-(4-chlorophenyl)-1-butanone (**3b**):

Rf 0.25 (benzene); mp 97.3-98.5 °C (98.2% *ee* (*S*), hexane-AcOEt); $[\alpha]_D^{22} -20.5$ (98.2% *ee* (*S*), $c = 1.0$, CHCl_3); Chiral HPLC (DAICEL, CHIRALCEL OD, hexane:*i*-PrOH = 95:5, 0.4 mL/min, 254 nm, $t_R = 41.0$ min (*S*), 42.5 (*R*)); IR (KBr) 1684.1 (C=O), 3447.2 (OH) cm^{-1} ; ^1H NMR (CDCl_3) δ 3.48 (dd, $J = 17.44$, 8.78 Hz, 1H), 3.59 (dd, $J = 17.44$, 2.08 Hz, 1H), 3.90 (br s, 1H), 4.88 (dd, $J = 8.79$, 2.08 Hz, 1H), 7.47 and 7.97 (AB quartet, $J = 8.79$ Hz, 4H); ^{13}C NMR (CDCl_3) δ 40.74 (s), 78.84 (s), 102.49 (s), 129.09 (s), 129.65 (s), 134.59 (s), 140.40 (s), 195.75 (s); MS m/z (rel intensity) 286 ($\text{M}^+ - \text{H}_2\text{O} + 4$; 1.0), 284 ($\text{M}^+ - \text{H}_2\text{O} + 2$; 1.7), 282 ($\text{M}^+ - \text{H}_2\text{O}$; 1.4), 154 (9.5), 149 (7.7), 139 (100.0), 113 (16.3), 111 (42.4), 105 (7.5), 84 (13.1), 82 (14.5), 75 (27.4), 69 (9.6); Anal. Calcd for: C, 39.77; H, 2.67. Found: C, 39.81; H, 2.31.

4,4,4-Trichloro-3-hydroxy-1-(4-methoxyphenyl)-1-butanone (3c):

R_f 0.09 (benzene); mp 93.0-94.0 °C (98.6% *ee* (*S*), hexane-AcOEt); $[\alpha]_D^{20}$ -27.1 (98.6 % *ee* (*S*), *c* = 1.0, CHCl₃); Chiral HPLC (DAICEL, CHIRALCEL OD, hexane:*i*-PrOH = 95:5, 0.8 mL/min, 254 nm, *t_R* = 36.0 min (*S*), 27.0 (*R*)); IR (KBr) 1674.4 (C=O), 3447.2 (OH) cm⁻¹; ¹H NMR (CDCl₃) δ 3.44 (dd, *J* = 17.17, 9.15 Hz, 1H), 3.59 (dd, *J* = 17.17, 2.20 Hz, 1H), 3.88 (s, 3H), 4.24 (br s, 1H), 4.86 (dd, *J* = 9.15, 2.20 Hz, 1H), 6.95 and 7.97 (AB quartet, *J* = 8.79 Hz, 4H); ¹³C NMR (CDCl₃) δ 40.22 (s), 55.53 (s), 79.09 (s), 102.62 (s), 113.91 (s), 129.34 (s), 130.64 (s), 164.09 (s), 195.72 (s); MS *m/z* (rel intensity) 300 (*M*⁺+4; 0.8), 298 (*M*⁺+2; 2.7), 296 (*M*⁺; 2.8), 150 (3.7), 135 (100.0), 107 (7.2), 92 (8.8), 82 (2.9), 77 (13.7), 69 (4.4), 64 (5.7); Anal. Calcd for: C, 44.40; H, 3.73. Found: C, 44.72; H, 3.60.

4,4,4-Trichloro-3-hydroxy-1-(2-thienyl)-1-butanone (3d):

R_f 0.10 (benzene); mp 64.5-66.0 °C (95.4% *ee* (*S*), hexane-AcOEt); $[\alpha]_D^{21}$ -20.8 (95.4% *ee* (*S*), *c* = 1.0, CHCl₃); Chiral HPLC (DAICEL, CHIRALCEL OD, hexane:*i*-PrOH = 95:5, 0.8 mL/min, 254 nm, *t_R* = 23.5 min (*S*), 31.5 (*R*)); IR (KBr) 1645.2 (C=O), 3447.2 (OH) cm⁻¹; ¹H NMR (CDCl₃) δ 3.44 (dd, *J* = 16.78, 8.91 Hz, 1H), 3.58 (dd, *J* = 16.78, 2.14 Hz, 1H), 3.97 (brs, 1H), 4.85 (dd, *J* = 8.91, 2.14 Hz, 1H), 7.17 (dd, *J* = 4.94, 3.85 Hz, 1H), 7.72 (dd, *J* = 4.94, 0.98 Hz, 1H), 7.81 (dd, *J* = 3.85, 0.98 Hz, 1H); ¹³C NMR (CDCl₃) δ 41.21 (s), 78.99 (s), 102.39 (s), 128.37 (s), 133.03 (s), 134.92 (s), 143.43 (s), 189.66 (s); MS *m/z* (rel intensity) 274 (*M*⁺+2; 0.8), 272 (*M*⁺; 0.8), 237 (3.1), 157 (3.5), 150 (5.1), 127 (5.5), 112 (100.0), 106 (7.0), 105 (6.4), 83 (8.4), 77 (3.2).

1-Cyclohexyl-4,4,4-trichloro-3-hydroxy-1-butanone (3e):

oil (88.0% *ee* (*S*)); $[\alpha]_D^{23}$ -20.4 (88.0% *ee* (*S*), *c* = 1.0, CHCl₃); IR (KBr) 1707.2 (C=O), 3503.2 (OH) cm⁻¹; ¹H NMR (CDCl₃) δ 1.04-1.38 (m, 6H), 1.68-1.85 (m, 4H), 2.35 (tt, *J* = 10.90, 3.42 Hz, 1H), 2.90 (dd, *J* = 17.14, 8.79 Hz, 1H), 3.03 (dd, *J* = 17.14, 1.83 Hz, 1H), 4.16 (br s, 1H), 4.60 (dd, *J* = 8.79, 1.83 Hz, 1H); ¹³C NMR (CDCl₃) δ 25.41 (d, *J* = 4.86 Hz), 25.65 (s), 28.01 (d, *J* = 11.58 Hz), 42.45 (s), 51.41 (s), 78.70 (s), 102.65 (s), 211.20 (s); MS *m/z* (rel intensity) 276 (*M*⁺+4; 0.6), 274 (*M*⁺+2; 1.6), 272 (*M*⁺; 2.4), 218 (4.6), 157 (18.1), 156 (18.3), 154 (11.0), 120 (3.5), 112 (40.2), 111 (32.7), 83 (100.0), 79 (3.7), 71 (5.3), 67 (9.4).

6,6,6-Trichloro-5-hydroxy-2-dimethyl-3-hexanone (3f):

mp 101.5-102.5 °C (80.8% *ee* (*S*), hexane-AcOEt); $[\alpha]_D^{22}$ -31.0 (80.8% *ee* (*S*), *c* = 1.0, CHCl₃); IR (KBr) 1697.6 (C=O), 3481.9 (OH) cm⁻¹; ¹H NMR (CDCl₃) δ 1.19 (s, 9H), 3.01 (dd, *J* = 17.44, 8.79 Hz, 1H), 3.12 (dd, *J* = 17.44, 2.08 Hz, 1H), 3.60 (br s, 1H), 4.66 (dd, *J* = 8.79, 2.08 Hz, 1H); ¹³C NMR (CDCl₃) δ 26.07 (s), 38.76 (s), 44.62 (s), 79.07 (s), 102.57 (s), 213.26 (s); MS *m/z* (rel intensity) 193 (22.4), 192 (29.9), 191 (25.3), 190 (28.7), 157 (39.0), 156 (38.4), 155 (61.9), 154 (62.7), 112 (24.7), 111 (22.2), 85 (100.0), 69 (23.5).

Methyl 1-Hydroxy-3-oxo-4-phenylpropanate (7b):

R_f 0.05 (benzene); Chiral HPLC (DAICEL, CHIRALCEL OD, hexane:*i*-PrOH = 95:5, 0.3 mL/min, 254 nm, *t_R* = 137.5 min (*S*), 134.0 (*R*)); IR (KBr) 1743.9 (C=O), 1684.1 (C=O), 3503.2 (OH) cm⁻¹; ¹H

NMR (CDCl₃) δ 3.47 (dd, J = 17.81, 5.93 Hz, 1H), 3.48 (d, J = 6.83 Hz, 1H), 3.56 (dd, J = 17.81, 3.78 Hz, 1H), 3.80 (s, 3H), 4.69 (dd, J = 5.93, 3.78 Hz, 1H), 7.44-7.51 (m, 2H), 7.57-7.61 (m, 1H), 7.93-7.97 (m, 2H); ¹³C NMR (CDCl₃) δ 42.10 (s), 52.63 (s), 67.11 (s), 128.11 (s), 128.65 (s), 133.62 (s), 136.25 (s), 174.13 (s), 197.54 (s); MS m/z (rel intensity) 208 (1.0), 190 (2.9), 176 (3.1), 149 (10.9), 105 (100.0), 77 (54.4), 74 (2.3), 71 (2.3), 60 (4.0).

Typical Procedure for the Recrystallization of 4,4,4-Trichloro-3-hydroxy-1-phenyl-1-butanone (3a).

4,4,4-Trichloro-3-hydroxy-1-phenyl-1-butanone (**3a**) (0.124 g, 91.6% *ee*) was dissolved in hot hexane (7.44 ml, 60 ml/g), and left at room temperature for 3 h. After storage in a refrigerator overnight, the crystal was separated from the solution by filtration. Concentration of the mother liquor under vacuum gave **3a** in 15% yield (0.018 g, 66.8 % *ee*), and crystals of **3a** were obtained in 61% yield (0.075 g, >99.9% *ee*).