Supporting Information

Lewis Acid Mediated Selective Chlorinations of Silyl Enolate

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General.

¹H NMR spectra were recorded on a Bruker Avance 400 (400 MHz) or 500 (500 MHz) spectrometer at ambient temperature. Chemical shift values (δ) are expressed in ppm downfield relative to internal standard (tetramethylsilane at 0 ppm). Multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). ¹³C NMR spectra were recorded on a Bruker Avance 400 (100 MHz) or 500 (125 MHz) spectrometer at ambient temperature, and are expressed in ppm using solvent as the internal standard (CDCl₃ at 77.0 ppm). Analytical gas-liquid chromatography (GLC) was performed on a Shimadzu GC-17A instrument equipped with a flame ionization detector and a capillary column of PEG (0.25 mm $\times$ 25 m) or γ -TA (0.25 mm $\times$ 25 m) using nitrogen as carrier gas. High-performance liquid chromatography (HPLC) was performed on a Varian ProStar Series equipped with a variable wavelength detector using chiral stationary columns (Chiracel OB-H or OD-H, 0.46 cm $\times$ 25 cm) from Daicel.

All reactions were carried out in oven-dried glassware with magnetic stirring under nitrogen atmosphere unless otherwise noted. Analytical thin layer chromatography (TLC) was performed on E. Merck precoated TLC plates (silica gel 60 GF254, 0.25 mm). Flash column chromatography was performed on silica gel 60 (E. Merck 230-400 mesh). Visualization was accomplished with UV light and phosphomolybdic acid solution in ethanol by heating. All solvents were freshly distilled. *N,N*-diisopropylamine and triethylamine were stored over KOH pellets. All other reagents and starting materials, unless otherwise noted, were purchased from commercial vendors and used without further purification.

Preparation of Substrates. Substrates **2a-c**, **3**, **4a-b** and **5** were prepared according to literature procedures.¹ Substrates **6a-d** and silyl enol ethers in Table 1 were prepared in the usual manner by treatment of the corresponding ketones with LDA in dry THF.

Preparation of 1a and 1b.²

Di-(-)-menthyl α,α-dichloromalonate(1a).

Malonyl dichloride (35.5 mmol, 3.45 mL) was slowly added to a stirred solution of Et₃N (70.9 mmol, 9.96 mL) and *l*-(-)-menthol (70.9 mmol, 11.08 g) in 100 mL CH₂Cl₂ at 0 °C under N₂, and the resulting solution was stirred for 1 h at rt. The reaction was quenched slowly with water (30 mL) and the aqueous layer was extracted with ether (3×50 mL). The combined organic phase was dried over sodium sulfate and the solvent was removed in vacuum. The pure di-(-)-menthyl malonate (6.33 g, 46.9% yield) was obtained from hexanes or methanol at low temperature as colorless needle crystals: $[\alpha]_D^{25} = -78.9^\circ$ ($c = 2.72$, acetone); ¹H NMR (400 MHz, CDCl₃) δ 4.76 (dt, 2H, $J = 4.4, 10.9$ Hz), 3.33 (s, 2H), 2.04-2.01 (m, 2H), 1.91-1.88 (m, 2H), 1.69-1.66 (m, 4H), 1.48-1.35 (m, 4H), 1.09-0.91 (m, 4H), 0.91-0.88 (m, 14H), 0.77 (d, 6H, $J = 6.9$ Hz). ¹³C NMR (125 MHz, CDCl₃) δ 20.83, 21.98, 23.29, 26.05, 31.37, 34.19, 40.68, 42.39, 46.88, 75.46, 166.24.

To a solution of di-(-)-menthyl malonate (1 mmol, 0.38 g) in 15 mL CH₂Cl₂ at rt was added Et₃N (2 mmol, 0.28 mL) and CF₃SO₂Cl (2 mmol, 0.21 mL). After being stirred for 2 h, the reaction was quenched with water. The aqueous layer was washed with methylene chloride and the combined organic phases were dried over sodium sulfate and the solvent was removed in vacuum. The crude product was purified by column chromatography (Hexanes/CH₂Cl₂ 4:1) and the final product was colorless oil with 95.7% yield: $[\alpha]_D^{25} = -73.1^\circ$ ($c = 1.43$, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃) δ 4.84 (dt, 2H, $J = 4.4, 10.9$ Hz), 2.07-2.02 (m, 2H), 1.96-1.92 (m, 2H), 1.74-1.69 (m, 4H), 1.53-1.44 (m, 4H), 1.11-1.00 (m, 4H), 0.93-0.89 (m, 14H), 0.78 (d, 6H, $J = 6.9$ Hz). ¹³C NMR (100 MHz, CDCl₃) δ 16.01, 20.72, 21.93, 23.14, 25.92, 31.38, 33.99, 40.15, 46.95, 79.38, 162.51.

Di-(-)-2-phenylcyclohexyl α,α-dichloromalonate(1b). The title compound was prepared following the same procedure of di-(-)-

menthyl α,α -dichloromalonate. Di-(-)-2-phenylcyclohexyl malonate was isolated by column chromatography (Hexanes/Ether 5:1) as colorless crystals with 85% yield: ^1H NMR (400 MHz, CDCl_3) δ 7.27-7.11 (m, 10H), 4.96 (dt, 2H, $J = 4.4, 10.7$ Hz), 2.76 (s, 2H), 2.61-2.55 (m, 2H), 2.09-2.05 (m, 2H), 1.92-1.75 (m, 6H), 1.55-1.31 (m, 8H). And di-(-)-2-phenylcyclohexyl α,α -dichloromalonate was purified by column chromatography (Hexanes/ CH_2Cl_2 2:1) as colorless crystals with 94.7% yield: ^1H NMR (400 MHz, CDCl_3) δ 7.26-7.12 (m, 10H), 5.00 (dt, 2H, $J = 4.5, 10.7$ Hz), 2.68 (dt, 2H, $J = 3.6, 10.9$ Hz), 2.12-2.08 (m, 2H), 1.96-1.87 (m, 4H), 1.81-1.78 (m, 2H), 1.59-1.33 (m, 8H).

Preparation of 1c and 1d.²

The optically pure starting materials for these two compounds are not commercially available easily.

Trans-2-(1-naphthalyl)-cyclohexanol. To a stirred refluxing suspension of Mg (30 mmol, 0.73 g) in 20 mL ether was added 1-bromonaphthalene (25 mmol, 3.5 mL) dropwise. After refluxing for 1 h, 10 mL benzene was added to the solution without cooling. After cooling to rt., the solution was added to the cooled suspension of CuI (25 mol, 4.73 g) in 15 mL ether with stirring at -30°C . After 20 min, to this mixture was added cyclohexene oxide (28.3 mmol, 2.85 mL) in 10 mL ether dropwise at -30°C . After 30 min, the temperature was gradually raised to rt and the stirring was continued for 20 h at rt. The mixture was treated with saturated NH_4Cl and filtered through a celite pad. The organic layer was separated and dried over MgSO_4 . The solvent was removed in vacuo and the crude product was purified by column chromatography (Hexanes/Ethyl Acetate 8:1) to give products as white solids with 83% yield. ^1H NMR (400 MHz, CDCl_3) δ 8.20 (d, 1H, $J = 8.4$ Hz), 7.87-7.85 (m, 1H), 7.76-7.74 (m, 1H), 7.55-7.46 (m, 4H), 3.98 (m, 1H), 3.40 (m, 1H), 2.24-2.21 (m, 1H), 2.00-1.93 (m, 1H), 1.82-1.80 (m, 1H), 1.62-1.48 (m, 6H). HPLC (Chiralcel OD-H column, 10% *i*-PrOH/hexanes, 1 mL/min, 210 nm) analysis gave two isomers at $t_R = 8.1$ min and 13.2 min.

(+)-2-(1-naphthalyl)-cyclohexanol. A suspension of above compound (21.5 mmol, 4.86 g), vinyl acetate (215 mmol, 20 mL) and Lipase PS (4.3 g) in *t*-BuOMe (175 mL) was stirred at rt for several weeks by using HPLC to monitor the process. After filtration through a

celite pad, the filtrate was evaporated in vacuum and chromatographed in silica gel (Hexanes/Ethyl Acetate 8:1). The second compound was the title compound as light yellow crystals with 48.5% yield and 97.3% ee.

(-)-2-(1-naphthyl)-cyclohexanol. The first compound from above was (+)-2-(1-naphthyl)-cyclohexyl acetate with 95.6% ee: ^1H NMR (500 MHz, CDCl_3) δ 8.17 (d, 1H, J = 8.5 Hz), 7.85 (d, 1H, J = 7.8 Hz), 7.71 (d, 1H, J = 7.9 Hz), 7.54-7.36 (m, 4H), 5.25 (m, 1H), 3.60 (m, 1H), 2.25-2.23 (m, 1H), 2.10-2.07 (m, 1H), 1.94-1.93 (m, 1H), 1.85-1.83 (m, 1H), 1.59 (s, 3H), 1.58-1.45 (m, 4H). A solution of this ester (11.6 mmol, 3.11 g) and K_2CO_3 in 50 mL MeOH was stirred at rt for 24 h and after removing the solvent in vacuo, the residue was treated with water and extracted with ethyl acetate. The extract was washed with brine, dried over MgSO_4 , evaporated under reduced pressure and chromatographed on silica gel (Hexanes/Ethyl Acetate 5:1) to give title compound as light yellow crystals with 57.3% yield and 96% ee.

Di-(+)-2-(1-naphthyl)-cyclohexyl

α,α -

dichloromalonate (1c). The initial malonate ester was prepared following the same procedure of dimethyl malonate and isolated by column chromatography

(Hexanes/Ethyl acetate 10:1) as light yellow crystals with 71% yield: ^1H NMR (400 MHz, CDCl_3) δ 7.99-7.97 (m, 2H), 7.79-7.77 (m, 2H), 7.65 (d, 2H, J = 8.1 Hz), 7.41-7.36 (m, 8H), 5.16-5.11 (m, 2H), 3.48-3.44 (m, 2H), 2.40 (s, 2H), 2.10-1.92 (m, 4H), 1.82-1.68 (m, 4H), 1.63-1.31 (m, 8H). Then the title compound was synthesized by the same procedure of dimethyl dichloromalonate and isolated by column chromatography (Hexanes/Ethyl acetate 20:1) as white solids with 99% yield: $[\alpha]_{\text{D}}^{25} = +7.4^\circ$ (c = 1.03, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3) δ 7.99-7.95 (m, 2H), 7.80-7.77 (m, 2H), 7.65 (d, 2H, J = 8.1 Hz), 7.43-7.25 (m, 8H), 5.20-5.19 (m, 2H), 3.58-3.53 (m, 2H), 2.09-1.99 (m, 4H), 1.88-1.82 (m, 4H), 1.53-1.46 (m, 8H). ^{13}C NMR (100 MHz, CDCl_3) δ 24.65, 25.83, 31.71, 34.10, 43.05, 80.20, 122.62, 122.87, 125.26, 125.43, 125.74, 126.91, 128.81, 131.84, 133.86, 137.89, 161.93.

Trans-2-(9-phenanthryl)-cyclohexanol. n-BuLi (80 mmol) was added over a 20 min period to a solution of 9-Bromophenanthrene (40 mmol,

10.7 g) in 300 mL ether under nitrogen. The resulting milky yellow solution was stirred for 2 h, and cyclohexene oxide (80 mmol, 8.25 mL) in 60 mL ether was added dropwise. The mixture was stirred overnight and 150 mL water was added. The separated ether layer was washed successively with water and brine and dried over Na₂SO₄. The solvent was removed in vacuo and crude viscous residue was purified by column chromatography (Hexanes/Ethyl acetate 9:1) to give title compounds as light yellow crystals with 90% yield: ¹H NMR (400 MHz, CDCl₃) δ 8.70-8.63 (m, 1H), 8.58-8.56 (m, 1H), 8.21-8.18 (m, 1H), 7.83-7.76 (m, 1H), 7.64 (s, 1H), 7.59-7.51 (m, 4H), 4.04-3.97 (m, 1H), 3.42-3.32 (m, 1H), 2.27-2.24 (m, 1H), 2.15-2.12 (m, 1H), 1.93-1.92 (m, 1H), 1.85-1.84 (m, 1H), 1.72 (bs, 1H), 1.51-1.41 (m, 4H). HPLC (Chiralcel OD column, 30% *i*-PrOH/hexanes, 1 mL/min, 210 nm) analysis gave two isomers at *t*_R = 35.3 min and 82.2 min.

Kinetic resolution. The procedure was same as 2-(1-naphthyl)-cyclohexanol. After being stirred at rt for 36 days by using HPLC to monitor the process, (+)-2-(9-phenanthryl)-cyclohexyl acetate as white crystals with 45.3% yield and 96% ee was obtained: ¹H NMR (400 MHz, CDCl₃) δ 8.76-8.73 (m, 1H), 8.65-8.63 (m, 1H), 8.24-8.22 (m, 1H), 7.85-7.83 (m, 1H), 7.64 (s, 1H), 7.66-7.56 (m, 4H), 5.39-5.34 (m, 1H), 3.65-3.60 (m, 1H), 2.30-2.27 (m, 1H), 2.18-2.15 (m, 1H), 1.96-1.94 (m, 1H), 1.86-1.83 (m, 1H), 1.61 (s, 3H), 1.64-1.55 (m, 4H), as well as (+)-2-(9-phenanthryl)-cyclohexanol as white crystals with 48.7% yield and 98.5% ee. (-)-2-(9-phenanthryl)-cyclohexanol was obtained from (+)-2-(9-phenanthryl)-cyclohexyl acetate following the same procedure as above with 98% yield and 99% ee.

Di-(+)-2-(9-phenanthryl)-cyclohexyl α,α-dichloromalonate (1d). The initial malonate ester was prepared following the same procedure of dimethyl malonate and isolated by column chromatography (Hexanes/Ethyl acetate 20:1) as white solids with 65%

yield: ¹H NMR (400 MHz, CDCl₃) δ 8.69 (d, 2H, *J* = 8.0 Hz), 8.63-8.61 (m, 2H), 7.95 (d, 2H, *J* = 8.3 Hz), 7.82-7.80 (m, 2H), 7.61-7.53 (m, 8H), 7.48-7.44 (m, 2H), 5.22-5.21 (m, 2H), 3.37 (m, 2H), 2.44 (s, 2H), 2.08-2.05 (m, 2H), 1.97-1.94 (m, 2H), 1.77-1.75 (m, 4H), 1.55-1.39 (m, 6H), 1.26-1.24 (m, 2H). Then the title compound was synthesized by the

same procedure of dimethyl dichloromalonate and isolated by column chromatography (Hexanes/CH₂Cl₂ 2:1) as white solids with 78% yield: $[\alpha]_D^{25} = +62.1^\circ$ ($c = 1.30$, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃) δ 8.68 (d, 2H, $J = 8.0$ Hz), 8.60 (d, 2H, $J = 7.7$ Hz), 7.93 (d, 2H, $J = 8.2$ Hz), 7.79 (d, 2H, $J = 7.1$ Hz), 7.59-7.46 (m, 10H), 5.23 (m, 2H), 3.47 (m, 2H), 2.11-2.08 (m, 2H), 1.97-1.95 (m, 2H), 1.80-1.76 (m, 4H), 1.50-1.26 (m, 8H). ¹³C NMR (100 MHz, CDCl₃) δ 24.63, 25.74, 31.56, 34.03, 42.88, 80.02, 122.26, 123.17, 123.48, 126.02, 126.22, 126.44, 126.55, 128.57, 129.43, 130.66, 130.87, 131.51, 136.09, 162.08.

Preparation of α,α -dichloro-1,3-dicarbonyl compounds with achiral end groups.

Di-*t*-butyl α,α -dichloro-1,3-diketone. To a solution of di-*t*-butyl 1,3-diketone (60 mmol, 12.6 mL) in 750 mL CH₂Cl₂ at rt was added DBU (132 mmol, 20.1 mL) and CF₃SO₂Cl (132 mmol, 14.2 mL) at room temperature under N₂. After being stirred for 5 h, the reaction was quenched with water. The aqueous layer was washed with methylene chloride and the combined organic phases were dried over sodium sulfate and the solvent was removed in vacuum. The crude product was purified by column chromatography (Hexanes/CH₂Cl₂ 4:1) and the final product was colorless crystals with 72% yield: ¹H NMR (400 MHz, CDCl₃) δ 1.41 (s, 18H). ¹³C NMR (100 MHz, CDCl₃) δ 28.93, 45.24, 166.62, 200.24.

Diethyl α,α -dichloromalonate. To a solution of diethyl malonate (10 mmol, 1.53 mL) in 150 mL CH₂Cl₂ at rt was added Et₃N (20 mmol, 2.85 mL) and CF₃SO₂Cl (20 mmol, 2.15 mL) at room temperature under N₂. After being stirred overnight, the reaction was quenched with water. The aqueous layer was washed with methylene chloride and the combined organic phases were dried over sodium sulfate and the solvent was removed in vacuum. The pure product was isolated by column chromatography (Hexanes/EtOAc 10:1) as pale yellow oil with 85% yield: ¹H NMR (400 MHz, CDCl₃) δ 4.38 (q, 4H, $J = 7.1$ Hz), 1.35 (t, 6H, $J = 7.1$ Hz). ¹³C NMR (100 MHz, CDCl₃) δ 13.77, 64.67, 77.07, 162.84.

Di-*t*-butyl α,α -dichloromalonate. The title compound was prepared following the same procedure as above, starting from di-*t*-butyl malonate. The pure product was isolated by column chromatography (Hexanes/EtOAc 20:1) as colorless crystals with 80% yield: ^1H NMR (500 MHz, CDCl_3) δ 1.53 (s, 18H). ^{13}C NMR (125 MHz, CDCl_3) δ 27.51, 78.96, 85.68, 161.56.

Di-*t*-butylmethyl α,α -dichloromalonate. The title compound was prepared following the same procedure as above, starting from di-*t*-butylmethanol which was synthesized from ethyl formate and *t*-Butyllithium. The pure product was isolated by column chromatography (Hexanes/ CH_2Cl_2 8:1) as colorless crystals with 52% yield: ^1H NMR (400 MHz, CDCl_3) δ 4.74 (s, 2H), 1.08 (s, 36H). ^{13}C NMR (100 MHz, CDCl_3) δ 28.49, 37.70, 91.75, 162.87.

α -Chlorinated products.

2-Chloro-1-tetralone (9). The title compound was obtained according to the general procedure for chlorination of silyl enol ether and isolated by column chromatography (Hexanes/ CHCl_3 1:1) as colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 8.09 (d, 1H, $J = 7.8$ Hz), 7.54-7.50 (m, 1H), 7.37-7.33 (m, 1H), 7.28-7.26 (m, 1H), 4.65 (dd, 1H, $J = 7.7, 3.8$ Hz), 3.28-3.25 (m, 1H), 3.03-2.96 (m, 1H), 2.61-2.43 (m, 2H). Enantiomeric excess was determined by HPLC (Chiralcel OD-H column, 0.5% *i*-PrOH/hexanes, 1 mL/min, 210 nm).

2-Chloro-2-methyl-1-tetralone (10). The title compound was obtained according to the general procedure: ^1H NMR (400 MHz, CDCl_3) δ 8.10 (dd, 1H, $J = 7.9, 1.0$ Hz), 7.50 (dt, 1H, $J = 7.5, 1.3$ Hz), 7.34 (t, 1H, $J = 7.6$ Hz), 7.25 (d, 1H, $J = 7.3$ Hz), 3.43-3.35 (m, 1H), 2.89 (td, 1H, $J = 17.2, 3.8$ Hz), 2.52-2.47 (m, 1H), 2.37-2.29 (m, 1H), 1.83 (s, 3H). Enantiomeric excess was determined by HPLC (Chiralcel OD-H column, 0.2% *i*-PrOH/hexanes, 1 mL/min, 210 nm).

2-Chloro-2-methyl-1-indanone (11). The title compound was obtained according to the general procedure: ^1H NMR (400 MHz, CDCl_3) δ 7.84 (d, 1H, $J = 8.0$ Hz), 7.67 (dt, 1H, $J = 7.5, 1.1$ Hz), 7.46-7.42 (m, 2H), 3.65 (d, 1H, $J = 17.8$ Hz), 3.45 (d, 1H, $J = 17.8$ Hz), 1.80 (s, 3H). Enantiomeric excess was determined by HPLC (Chiralcel OD-H column, 0.2% *i*-PrOH/hexanes, 1 mL/min, 210 nm).

2-Chloro-1-benzosuberone (12). The title compound was obtained according to the general procedure: ^1H NMR (400 MHz, CDCl_3) δ 7.65 (dd, 1H, $J = 7.7, 1.3$ Hz), 7.42 (dt, 1H, $J = 7.5, 1.4$ Hz), 7.31 (t, 1H, $J = 7.2$ Hz), 7.21 (d, 1H, $J = 7.6$ Hz), 4.81 (dd, 1H, $J = 8.7, 4.7$ Hz), 3.06-2.93 (m, 2H), 2.42-2.36 (m, 1H), 2.24-2.19 (m, 1H), 2.07-1.98 (m, 2H). Enantiomeric excess was determined by HPLC (Chiralcel OB-H column, 0.2% *i*-PrOH/hexanes, 1 mL/min, 210 nm).

2-Chloro-2-phenylcyclohexanone(13). The title compound was obtained according to the general procedure as colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.44-7.33 (m, 5H), 3.03-2.94 (m, 2H), 2.64-2.60 (m, 1H), 2.52-2.45 (m, 1H), 1.97-1.82 (m, 4H). Enantiomeric excess was determined by HPLC (Chiralcel OD-H column, 0.5% *i*-PrOH/hexanes, 1 mL/min, 210 nm).

2-Chloroheptanophenone (14). The title compound was obtained according to the general procedure as colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 8.01-7.99 (m, 2H), 7.62-7.58 (m, 1H), 7.51-7.47 (m, 2H), 5.11 (dd, 1H, $J = 8.1, 5.7$ Hz), 2.15-1.98 (m, 2H), 1.56-1.32 (m, 6H), 0.90-0.87 (m, 3H). Enantiomeric excess was determined by HPLC (Chiralcel OD-H column, 0.5% *i*-PrOH/hexanes, 1 mL/min, 210 nm).

4-Chloro-2,2-dimethyl-3-hexanone (15). The title compound was obtained according to the general procedure as colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 4.54 (dd, 1H, $J = 7.7, 6.4$ Hz), 1.98-1.83 (m, 2H), 1.22 (s, 9H), 0.98 (t, 3H, $J = 7.4$ Hz). Enantiomeric excess was determined by GLC (γ -TA, 80 $^\circ\text{C}$, 100 kPa), $t_R = 3.69, 6.91$ min.

2-Chloro-4-*t*-butylcyclohexanone. The title compound was obtained according to the general procedure. Diastereoselectivity was determined by GLC (PEG, 115 °C, 100 kPa), t_{trans} = 7.6 min, t_{cis} = 30.8 min.

References

- (1) Cazeau, P.; Duboundin, F.; Moulines, F.; Babot, O.; Dunogues, J. *Tetrahedron* **1987**, *43*, 2075.
- (2) Simply changing the configuration of starting material can give the final product with opposite configuration.