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Supporting Information

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Lewis Base Activation of Lewis Acids: Catalytic, Enantioselective Glycolate Aldol Reactions

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SUPPORTING INFORMATION

General Experimental

All reactions were performed in oven-dried (140 °C) or flame-dried glassware under an atmosphere of dry N_2. All reaction temperatures correspond to internal temperatures measured by Teflon-coated thermocouples unless otherwise noted. Reaction solvents including dichloromethane (Fisher, HPLC Grade), diethyl ether (Fisher, BHT stabilized HPLC Grade), and tetrahydrofuran (THF, Fisher, HPLC Grade) were dried by percolation through a column packed with neutral alumina and a column packed with Q5 reactant, a supported copper catalyst for scavenging oxygen, under a positive pressure of argon. Ethanol (AAPER) was freshly distilled from CaH_2. *n*-Butanethiol was freshly distilled from $CaCl_2$. Solvents for chromatography and filtration were: hexane (Fisher, ACS Grade), pentane (Fisher, ACS Grade), and ethyl acetate (Fisher, ACS Grade). Column chromatography was performed using EM Science 230-400-mesh silica gel. Benzaldehyde (Aldrich), 4-anisaldehyde (Aldrich), 4-trifluoromethylbenzaldehyde (Aldrich), 2-tolualdehyde, (*E*)-cinnamaldehyde (Aldrich), hydrocinnamaldehyde (Aldrich), and *tert*-butyldimethylsilyl chloride (TBSCl, Oakwood) were freshly distilled prior to use. 2-naphthaldehyde (Aldrich) was sublimed prior to use. Silicon tetrachloride (Aldrich) was heated at reflux for 24 h and then distilled prior to use. *N*-Methyl-*N*-nitroso-*p*-toluenesulfonamide (Diazald®, Aldrich), aluminum chloride (Fluka), potassium hydroxide (Fisher), and potassium hexamethyldisilazide (KHMDS, Aldrich) were used without further purification. Triethylamine (Aldrich), diisopropylethylamine (Aldrich), trimethylsilyl chloride (TMSCl, Aldrich) were freshly distilled from CaH_2 prior to use.

^{1}H NMR, ^{13}C NMR, ^{19}F NMR spectra were recorded on a Varian Unity 500 (500 MHz, ^{1}H; 126 MHz, ^{13}C; 376 MHz, ^{19}F) and Varian Unity Inova 500NB (500 MHz, ^{1}H) spectrometers. Spectra were referenced to residual chloroform (7.26 ppm, ^{1}H, 77.00 ppm, ^{13}C) and ^{19}F spectra were referenced to residual $CFCl_3$ (0.00 ppm). Chemical shifts are reported in ppm, multiplicities

are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet), bs (broad singlet), and bd (broad doublet). Coupling constants, *J*, are reported in Hertz. ^{1}H NMR and ^{13}C NMR assignments are corroborated by 2D experiments (COSY, HMQC, HMBC, and NOESY1D). Mass spectroscopy was performed by the University of Illinois Mass Spectrometer Center. EI mass spectra were performed on a 70-VSE spectrometer. ESI mass spectra were performed on a Q-Tof spectrometer. Data are reported in the form of (m/z). Infrared spectra (IR) were recorded on a Mattson Galaxy 5020 spectrophotometer in NaCl cells. Peaks are reported in cm^{-1} with indicated relative intensities: s (strong, 67-100%); m (medium, 34-66%); w (weak, 0-33%). Elemental analyses were performed by the University of Illinois Microanalytical Service Laboratory. Boiling points (bp) were head temperatures during distillations unless otherwise noted. Analytical thin-layer chromatography was performed on Merck silica gel plates with QF-254 indicator or silica gel 60 F_{254} TLC plates. Visualization was accomplished with UV(254), and potassium permanganate ($KMnO_4$) staining solutions. Optical rotation data was obtained on a JASCO DIP-360 digital polarimeter and are reported as follows: concentration (c = g/100 mL), and solvent. Analytical supercritical fluid chromatography (CSP-SFC) was performed on a Berger Instruments packed-column SFC with built-in photometric detector (220 nm) using Daicel Chiralcel OD and OJ, Daicel Chiralpak AD, and AS columns.

Literature Preparations

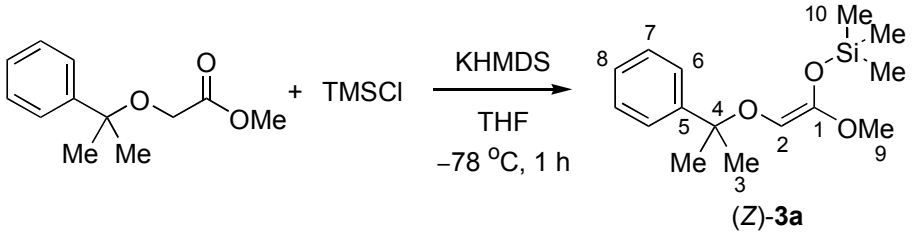
(*R*,*R*)-*N*,*N*'-bis[4,5-dihydro-3,5-dimethyl-4-(3Hdinaphtho[2,1-d:1',2'-f][1,3,2]-2-oxo-diazaphosphephepino)]-*N*,*N*'-dimethyl-1,5-pentanediamine ((*R*,*R*)-**1**) was prepared according to established procedures.[1]

Experimental Procedures

Preparations of Trimethylsilyl Ketene Acetals

General Procedure 1. Enolization of Glycolates to Trimethylsilyl Ketene Acetals.

Preparation of [[(*Z*)-1-Methoxy-2-(1-methyl-1-phenylethoxy)ethenyl]oxy]trimethylsilane ((*Z*)-3a)



(*Z*)-**3a**

To a flame-dried, 250-mL, 3-necked round-bottomed flask fitted with a magnetic stir bar, a thermocouple, a gas inlet tube, and a septum were added KHMDS (2.923 g, 14.653 mmol, 1.1 equiv) and THF (80 mL). The solution was cooled to −78 °C (internal temp.) in a dry ice-acetone bath and then a solution of 2-(1-methyl-1-phenylethoxy)acetic acid methyl ester (2.774 g, 13.321 mmol) in THF (10 mL) was added dropwise via syringe over 10 min. The internal temperature was kept below −70 °C during addition. After 20 min, TMSCl (1.860 mL, 14.653 mmol, 1.1 equiv) was added dropwise via syringe over 5 min while vigorous strring was maintained. After 1 h, the dry ice-acetone bath was removed and pentane (40 mL) was added. The reaction mixture was filtered through a glass frit at rt and was concentrated *in vacuo* (23 °C, 30 mmHg). The residue was distilled through a 8-cm Vigreux column under reduced pressure to give **3a** (3.059 g, 82%, >99/1, *Z*/*E*) as a colorless oil.

Data for (*Z*)-**3a**:

bp: 71-72 °C (0.4 mmHg)

^{1}H NMR: (500 MHz, $CDCl_3$)

7.44-7.42 (m, 2 H, HC(6)), 7.35-7.32 (m, 2 H, HC(7)), 7.26-7.23 (m, 1 H,

HC(8)), 5.07 (s, 1 H, HC(2)), 3.38 (s, 3 H, HC(9)), 1.58 (s, 6 H, HC(3)), 0.28 (s, 9 H, HC(10))

NOESY1D: (500 MHz, $CDCl_3$)

Irradiation at 5.07 ppm (HC(2)) enhanced signal at 3.38 ppm (HC(9)) in major isomer.

^{13}C NMR: (126 MHz, $CDCl_3$)

150.4 (C(1)), 146.1 (C(5)), 128.1 (C(7)), 126.8 (C(8)), 125.7 (C(6)), 105.4 (C(2)), 79.1 (C(4)), 56.0 (C(9)), 28.3 (C(3)), 0.4 (C(10))

IR: (neat)

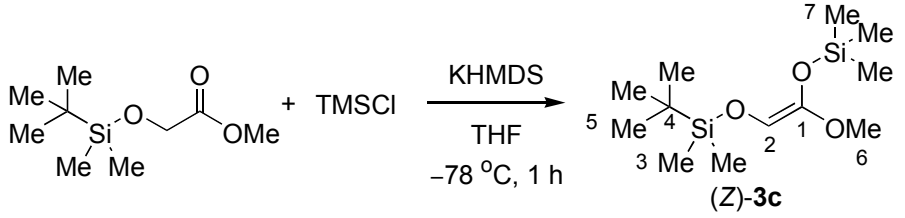
3089 (w), 3062 (w), 2980 (m), 2904 (w), 2837 (w), 1764 (w), 1742 (m), 1697 (m), 1496 (m), 1447 (m), 1380 (m), 1364 (m), 1328 (m), 1251 (s), 1233 (s), 1205 (s), 1170 (m), 1134 (s), 1102 (m), 1075 (m), 1047 (m), 971 (s), 848 (s), 764 (s), 700 (s)

MS: (ESI)

231.1 (100), 232.1 (6), 303.1 (M^++Na, 4)

HRMS: calcd for $C_{15}H_{24}O_3SiNa$: 303.1392, found 303.1393

Preparation of (4*Z*)-4-Methoxy-2,2,7,7,8,8-hexamethyl-3,6-dioxa-2,7-disilanon-4-ene[2] ((*Z*)-3c)



(*Z*)-**3c**

Following General Procedure 1, KHMDS (2.613 g, 13.097 mmol, 1.1 equiv) was

combined with [[(1,1-dimethylethyl)dimethylsilyl]oxy]acetic acid methyl ester[3] (2.433 g, 11.907 mmol) and TMSCl (1.662 mL, 13.097 mmol, 1.1 equiv) to yield, after distillation through a 5-cm Vigreux column under reduced pressure, **3c** (2.847 g, 86%, 99/1, *Z*/*E*) as a colorless oil.

Data for (*Z*)-**3c**:

bp: 51-52 °C (0.4 mmHg)

^{1}H NMR: (500 MHz, $CDCl_3$)

5.51 (s, 1 H, HC(2)), 3.47 (s, 3 H, HC(6)), 0.92 (s, 9 H, HC(5)), 0.22 (s, 9 H, HC(7)), 0.10 (s, 6 H, HC(3))

NOESY1D: (500 MHz, $CDCl_3$)

Irradiation at 5.51 ppm (HC(2)) enhanced signal at 3.47 ppm (HC(6)) in major isomer.

^{13}C NMR: (126 MHz, $CDCl_3$)

149.9 (C(1)), 106.2 (C(2)), 56.4 (C(6)), 25.8 (C(5)), 18.4 (C(4)), 0.3 (C(7)), –5.3 (C(3))

IR: (neat)

2959 (s), 2932 (s), 2899 (s), 2859 (s), 1765 (m), 1745 (m), 1701 (s), 1473 (s), 1464 (s), 1443 (s), 1407 (s), 1390 (m), 1370 (s), 1332 (m), 1253 (s), 1232 (s), 1158 (s), 1088 (m), 1043 (m), 1006 (m), 963 (s), 843 (s), 781 (s), 758 (s)

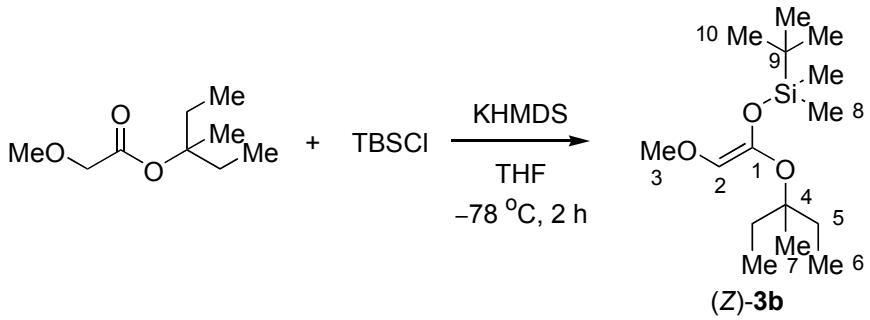
MS: (ESI)

227.1 (100), 228.1 (12), 299.1 (M^++Na, 2), 315.1 (24), 316.1 (3), 459.2 (2), 503.2 (4), 504.2 (2)

HRMS: calcd for $C_{12}H_{28}O_3Si_2Na$: 299.1475, found 299.1469

Preparations of *tert*-Butyldimethylsilyl Ketene Acetals

General Procedure 2. Enolization of Glycolates to *tert*-Butyldimethylsilyl Ketene Acetals. Preparation of (1,1-Dimethylethyl)[[(*Z*)-1-(1-ethyl-1-methylpropoxy)-2-methoxyethenyl] oxy]dimethylsilane ((*Z*)-3b)



(*Z*)-**3b**

To a flame-dried, 250-mL, 3-necked round-bottomed flask fitted with a magnetic stir bar, a thermocouple, a gas inlet tube, and a septum were added KHMDS (3.395 g, 17.020 mmol, 1.1 equiv) and THF (80 mL). The solution was cooled to –78 °C (internal temp.) in a dry ice-acetone bath and then a solution of 2-methoxyacetic acid 1-ethyl-1-methylpropyl ester (2.696 g, 15.473 mmol) in THF (10 mL) was added dropwise via syringe over 15 min. The internal temperature was kept below –70 °C during the addition of the ester. After 15 min, a solution of TBSCl (2.565 g, 17.020 mmol, 1.1 equiv) in THF (10 mL) was added dropwise via syringe over 15 min. After 2 h, the dry ice-acetone bath was removed and pentane (60 mL) was added. The reaction mixture was filtered through a glass frit at rt and concentrated *in vacuo* (23 °C, 30 mmHg). The residue was distilled through a 8-cm Vigreux column under reduced pressure to give **3b** (3.609 g, 81%, 96/4, *Z*/*E*) as a colorless oil.

Data for (*Z*)-**3b**:

bp: 59-60 °C (0.4 mmHg)

^{1}H NMR: (500 MHz, $CDCl_3$)

5.32 (s, 1 H, HC(2)), 3.46 (s, 3 H, HC(3)), 1.64-1.49 (m, 4 H, HC(5)), 1.17 (s, 3

H, HC(7)), 0.94 (s, 9 H, HC(10)), 0.86 (dd, J = 7.6, 7.6, 6 H, HC(6)), 0.16 (s, 6 H, HC(8))

NOESY1D: (500 MHz, $CDCl_3$)

Irradiation at 5.32 ppm (HC(2)) enhanced signal at 1.64-1.49 ppm (HC(5)), 1.17 ppm (HC(7)), and 0.86 ppm (HC(6)) in major isomer.

^{13}C NMR: (126 MHz, $CDCl_3$)

143.0 (C(1)), 121.6 (C(2)), 83.5 (C(4)), 59.5 (C(3)), 30.7 (C(5)), 25.7 (C(10)), 23.0 (C(7)), 18.2 (C(9)), 8.4 (C(6)), –4.5 (C(8))

IR: (neat)

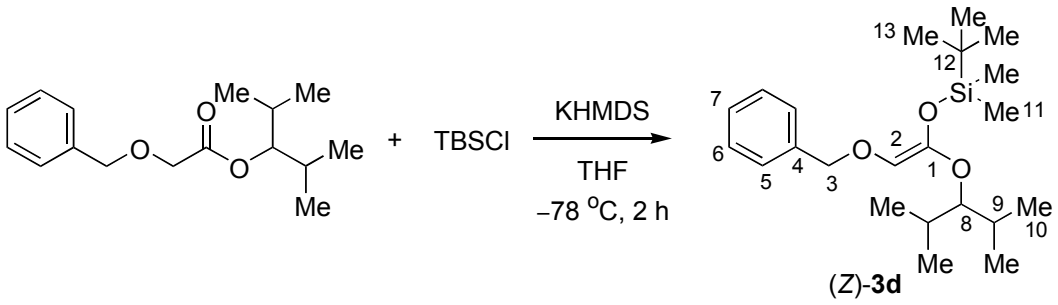
3062 (w), 2967 (s), 2932 (s), 2885 (m), 2859 (m), 2827 (m), 1746 (w), 1697 (m), 1463 (m), 1375 (m), 1362 (m), 1320 (s), 1251 (m), 1213 (s), 1130 (s), 1026 (m), 1000 (m), 971 (m), 854 (s), 840 (s), 828 (s), 813 (m), 784 (s), 735 (m), 694 (m)

MS: (ESI)

113.0 (9), 197.1 (100), 198.1 (5), 227.1 (5), 243.1 (7), 311.2 (M^++Na, 1), 327.2 (14), 337.1 (4)

HRMS: calcd for $C_{15}H_{32}O_3SiNa$: 311.2018, found 311.2021

Preparation of (1,1-Dimethylethyl)[[(*Z*)-1-[2-methyl-1-(1-methylethyl)propoxy]-2-(phenyl methoxy)ethenyl]oxy]dimethylsilane ((*Z*)-3d)



Following General Procedure 2, KHMDS (2.194 g, 11 mmol, 1.1 equiv) was combined with 2-(phenylmethoxy)acetic acid 2-methyl-1-(1-methylethyl)propyl ester (2.644 g, 10 mmol) and TBSCl (1.658 g, 11 mmol, 1.1 equiv) to yield, after bulb-to-bulb distillation under reduced pressure, **3d** (3.623 g, 96%, 89/11, *Z*/*E*) as a colorless oil.

Data for (*Z*)-**3d**:

bp: 200-210 °C (0.2 mmHg, ABT)

^{1}H NMR: (500 MHz, $CDCl_3$)

7.39-7.32 (m, 4 H, HC(5), HC(6)), 7.30-7.26 (m, 1 H, HC(7)), 5.42 (s, 1 H, HC(2)), 4.61 (s, 2 H, HC(3)), 3.40 (t, *J* = 5.4, 1 H, HC(8)), 1.86 (qqd, *J* = 6.8, 6.8, 5.4, 2 H, HC(9)), 0.96 (s, 9 H, HC(13)), 0.92 (d, *J* = 6.8, 6 H, HC(10)), 0.90 (d, *J* = 6.8, 6 H, HC(10))

NOESY1D: (500 MHz, $CDCl_3$)

Irradiation at 5.42 ppm (HC(2)) enhanced signal at 3.40 ppm (HC(8)), 1.86 ppm (HC(9)), 0.92 ppm (HC(10)), and 0.90 ppm (HC(10)) in major isomer.

^{13}C NMR: (126 MHz, $CDCl_3$)

150.5 (C(1)), 138.1 (C(4)), 128.2 (C(6)), 127.9 (C(5)), 127.5 (C(7)), 111.7 (C(2)), 87.3 (C(8)), 74.5 (C(3)), 30.1 (C(9)), 25.8 (C(13)), 19.8 (C(10)), 18.3

(C(12)), 18.0 (C(10)), –4.3 (C(11))

IR: (neat)

3066 (w), 3032 (w), 2960 (s), 2931 (s), 2858 (m), 1751 (w), 1700 (m), 1472 (m), 1386 (m), 1370 (m), 1324 I(m), 1252 (s), 1217 (s), 1150 (s), 1129 (s), 1046 (m), 1004 (m), 941 (m), 908 (m), 839 (s), 812 (m), 785 (s), 734 (m), 697 (m)

MS: (ESI)

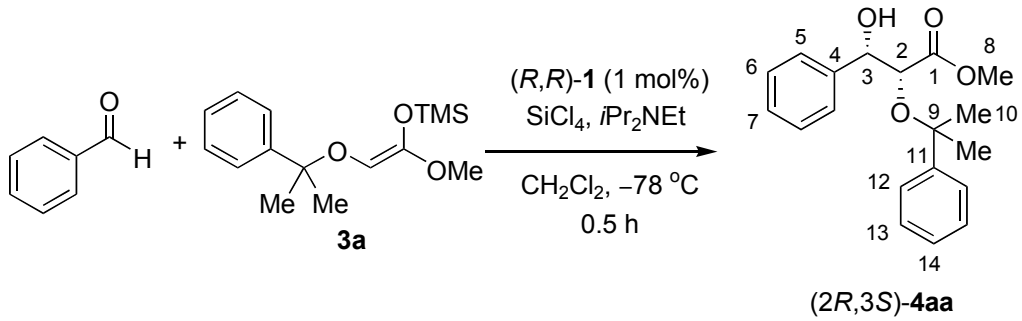
167.1 (5), 189.0 (52), 190.1 (7), 287.1 (100), 287.6 (92), 288.2 (56), 288.4 (20), 401.3 (M^++ Na, 22), 417.2 (42), 418.3 (15)

HRMS: calcd for $C_{22}H_{38}O_3SiNa$: 401.2488, found 401.2487

Aldol Additions of Silyl Ketene Acetals to Aromatic Aldehydes

General Procedure 3. Addition of Silyl Ketene Acetals to Aromatic Aldehydes

Preparation of (2*R*,3*S*)-3-Hydroxy-2-(1-methyl-1-phenylethoxy)-3-phenylpropanoic Acid Methyl Ester ((2*R*,3*S*)-4aa) (Table 1, entry 1)



To a flame-dried, 10-mL, Schlenk flask fitted with a magnetic stir bar, a thermocouple, a gas inlet tube, and a septum were added (*R*,*R*)-**1** (8.4 mg, 0.01 mmol, 0.01 equiv), CH_2Cl_2 (5 mL), and benzaldehyde (101.6 μL, 1.0 mmol). The solution was cooled to –78 °C (internal temp.) in a dry ice-acetone bath. After diisopropylethylamine (17.4 μL, 0.1 mmol, 0.1 equiv) and $SiCl_4$ (126 μL, 1.1 mmol, 1.1 equiv) were added to the flask via syringe, a solution of **3a** (336.5 mg, 1.2

mmol, 1.2 equiv) in CH_2Cl_2 (5 mL) was added dropwise via syringe over 15 min. The internal temperature was kept below −70 °C during the addition of **3a**. The reaction mixture was stirred for additional 15 min at −78 °C before a mixture of MeOH (1 mL), Et_3N (1 mL), and CH_2Cl_2 (5 mL) was added. The resulting solution was transferred into a 125-mL Erlenmeyer flask containing a sat. aq. $NaHCO_3$ solution (10 mL) and a sat. aq. KF solution (10 mL). The biphasic mixture was stirred vigorously for 2 h at room temperature. The mixture was filtered through a glass frit and the filtrate was transferred to a 125-mL separatory funnel where the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extracts were dried over Na_2SO_4 (15 g), filtered, and concentrated *in vacuo* (23 °C, 30 mmHg). The residue was purified by column chromatography (18 mm diam., hexane/EtOAc, 5/1 to 1/1) on silica gel (10 g) to give **4aa** (275 mg, 87%) as a colorless oil. The *syn*/*anti* ratio was determined to be 99/1 by ^{1}H NMR (500 MHz) analysis of the crude reaction mixture.

Data for (2*R*,3*S*)-**4aa**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.36-7.33 (m, 2 H, HC(12)), 7.31-7.22 (m, 8 H, HC(5), HC(6), HC(7), HC(13), HC(14)), 4.79 (d, *J* = 6.1, 1 H, HC(3)), 3.86 (d, *J* = 6.1, 1 H, HC(2)), 3.40 (s, 3 H, HC(8)), 2.98 (bs, 1 H, OH), 1.53 (s, 3 H, HC(10)), 1.52 (s, 3 H, HC(10))

^{13}C NMR: (126 MHz, $CDCl_3$)

172.3 (C(1)), 143.8 (C(11)), 138.8 (C(4)), 128.1 (C(6) or C(13)), 128.03 (C(6) or C(13)), 127.99 (C(7)), 127.4 (C(14)), 126.5 (C(5)), 126.1 (C(12)), 78.8 (C(9)), 77.4 (C(2)), 75.0 (C(3)), 51.5 (C(8)), 27.9 (C(10)), 27.1 (C(10))

IR: (neat)

3490 (br), 3062 (w), 3031 (w), 2981 (m), 2950 (w), 1745 (s), 1496 (m), 1451 (m), 1435 (m), 1385 (m), 1368 (m), 1264 (m), 1197 (m), 1170 (m), 1151 (m),

1086 (s), 1076 (s), 1059 (s), 1028 (m), 983 (m), 914 (m), 879 (m), 767 (s), 722 (m), 700 (s)

MS: (ESI)

119.1 (86), 120.1 (5), 136.1 (15), 179.1 (35), 214.1 (8), 332.2 (100), 337.1 (M^++Na, 58), 338.1 (6), 353.1 (23)

HRMS: calcd for $C_{19}H_{22}O_4Na$: 337.1416, found 337.1413

TLC: R_f 0.27 (hexane/EtOAc, 4/1) [UV(254)/$KMnO_4$]

SFC: (2*R*,3*S*)-**4aa**, t_R 7.61 min (96.6%); (2*S*,3*R*)-**4aa**, t_R 8.95 min (3.4%)

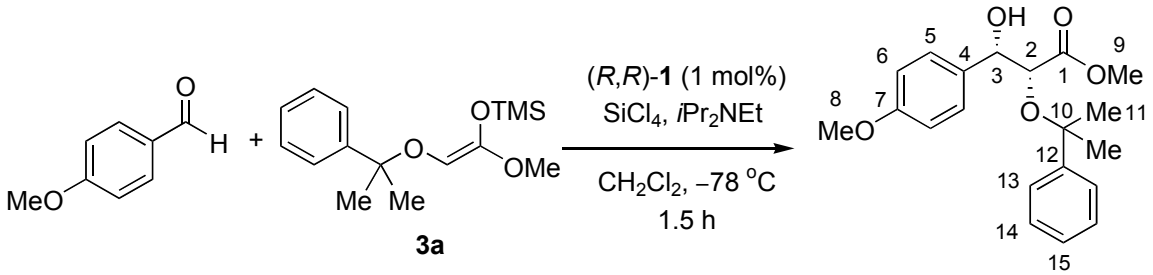
(Chiralpak AS, 125 bar, 40 °C, 1.6% MeOH in CO_2, 2.5 mL/min, 220 nm)

Opt. Rot.: $[\alpha]_D^{24}$ 42.2 (c = 1.0, EtOH)

Analysis: $C_{19}H_{22}O_4$ (314.38)

Calcd:	C, 72.59%;	H, 7.05%
Found:	C, 72.59%;	H, 7.08%

Preparation of (2*R*,3*S*)-3-Hydroxy-3-(4-methoxyphenyl)-2-(1-methyl-1-phenylethoxy) propanoic Acid Methyl Ester ((2*R*,3*S*)-4ab) (Table 1, entry 2)



(2*R*,3*S*)-**4ab**

Following General Procedure 3, (*R*,*R*)-**1** (8.4 mg, 0.01 mmol, 0.01 equiv) was combined with diisopropylethylamine (17.4 μL, 0.1 mmol, 0.1 equiv), 4-anisaldehyde (121.7 μL, 1.0 mmol), $SiCl_4$ (126 μL, 1.1 mmol, 1.1 equiv), and **3a** (336.5 mg, 1.2 mmol, 1.2 equiv) to yield,

after column chromatography (22 mm diam., hexane/EtOAc, 5/1 to 1/1) on silica gel (15 g), **4ab** (336 mg, 98%) as a colorless oil. The *syn*/*anti* ratio was determined to be 99/1 by ^{1}H NMR (500 MHz) analysis of the crude reaction mixture.

Data for (2*R*,3*S*)-**4ab**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.39-7.37 (m, 2 H, HC(13)), 7.31-7.27 (m, 2 H, HC(14)), 7.26-7.23 (m, 1 H, HC(15)), 7.18-7.15 (m, 2 H, HC(5)), 6.84-6.81 (m, 2 H, HC(6)), 4.73 (d, J = 6.5, 1 H, HC(3)), 3.82 (d, J = 6.5, 1 H, HC(2)), 3.78 (s, 3 H, HC(8)), 3.38 (s, 3 H, HC(9)), 2.93 (bs, 1 H, OH), 1.55 (s, 3 H, HC(11)), 1.54 (s, 3 H, HC(11))

^{13}C NMR: (126 MHz, $CDCl_3$)

172.3 (C(1)), 159.4 (C(7)), 144.0 (C(12)), 130.7 (C(4)), 128.1 (C(14)), 127.9 (C(5)), 127.6 (C(15)), 126.2 (C(13)), 113.6 (C(6)), 78.9 (C(10)), 77.7 (C(2)), 74.7 (C(3)), 55.2 (C(8)), 51.6 (C(9)), 28.0 (C(11)), 27.3 (C(11))

IR: (neat)

3500 (br), 2981 (m), 2951 (m), 2250 (w), 1744 (s), 1614 (m), 1587 (w), 1515 (s), 1448 (m), 1385 (m), 1368 (m), 1304 (m), 1251 (s), 1198 (m), 1173 (s), 1111 (m), 1198 (m), 1067 (s), 1032 (s), 912 (m), 881 (w), 833 (m), 766 (m), 733 (m), 702 (s)

MS: (ESI)

119.1 (26), 136.1 (13), 209.1 (100), 210.1 (7), 362.2 (9), 367.2 (M^++Na, 78), 368.2 (8), 383.1 (15)

HRMS: calcd for $C_{20}H_{24}O_5Na$: 367.1521, found 367.1514

TLC: R_f 0.37 (hexane/EtOAc, 2/1) [UV(254)/$KMnO_4$]

SFC: (2*R*,3*S*)-**4ab**, t_R 9.09 min (97.7%); (2*S*,3*R*)-**4ab**, t_R 10.48 min (2.3%)

(Chiralpak AS, 125 bar, 40 °C, 2.5% MeOH in CO_2, 2.0 mL/min, 220 nm)

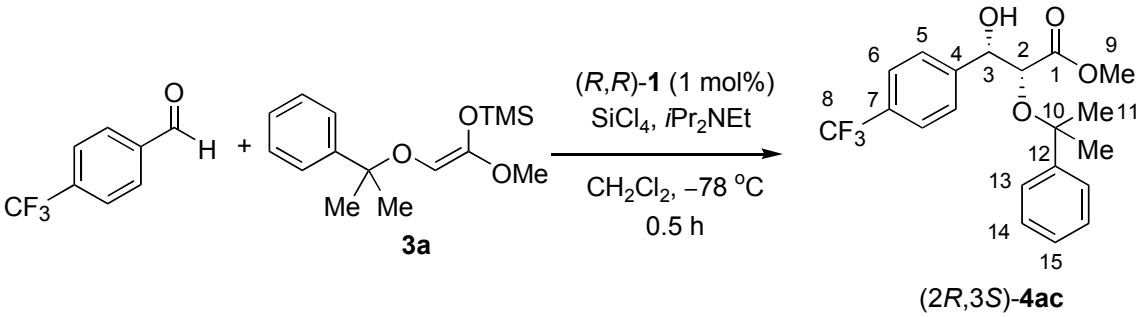
Opt. Rot.: $[\alpha]_D^{24}$ 32.4 (c = 3.0, EtOH)

Analysis: $C_{20}H_{24}O_5$ (344.40)

Calcd: C, 69.75%; H, 7.02%

Found: C, 69.51%; H, 7.07%

Preparation of (2*R*,3*S*)-3-Hydroxy-2-(1-methyl-1-phenylethoxy)-3-[4-(trifluoromethyl) phenyl]propanoic Acid Methyl Ester ((2*R*,3*S*)-4ac) (Table 1, entry 3)



Following General Procedure 3, (*R*,*R*)-**1** (8.4 mg, 0.01 mmol, 0.01 equiv) was combined with diisopropylethylamine (17.4 μL, 0.1 mmol, 0.1 equiv), 4-trifluoromethylbenzaldehyde (136.6 μL, 1.0 mmol), $SiCl_4$ (126 μL, 1.1 mmol, 1.1 equiv), and **3a** (336.5 mg, 1.2 mmol, 1.2 equiv) to yield, after column chromatography (22 mm diam., hexane/EtOAc, 5/1 to 2/1) on silica gel (15 g), **4ac** (380 mg, 99%) as a colorless oil. The *syn*/*anti* ratio was determined to be 99/1 by ^{1}H NMR (500 MHz) analysis of the crude reaction mixture.

Data for (2*R*,3*S*)-**4ac**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.55-7.54 (m, 2 H, HC(6)), 7.36-7.35 (m, 2 H, HC(5)), 7.27-7.21 (m, 5 H, HC(13), HC(14), HC(15)), 4.84 (dd, *J* = 5.4, 4.9, 1 H, HC(3)), 3.84 (d, *J* =

5.4, 1 H, HC(2)), 3.48 (s, 3 H, HC(9)), 3.07 (d, J = 4.9, 1 H, OH), 1.53 (s, 3 H, HC(11)), 1.51 (s, 3 H, HC(11))

^{13}C NMR: (126 MHz, $CDCl_3$)

172.1 (C(1)), 143.31 (C(4) or C(12)), 143.29 (C(4) or (C(12)), 130.1 (q, J = 32.5, C(7)), 128.1 (C(14)), 127.6 (C(15)), 126.8 (C(5)), 126.1 (C(13)), 125.1 (q, J = 3.6, C(6)), 124.1 (q, J =271.8, C(8)), 79.1 (C(10)), 76.9 (C(2)), 74.4 (C(3)), 51.9 (C(9)), 28.3 (C(11)), 26.7 (C(11))

^{19}F NMR: (376 MHz, $CDCl_3$)

−62.99 (FC(8))

IR: (neat)

3483 (br), 2983 (m), 2953 (w), 2251 (w), 1746 (s), 1621 (m), 1496 (m), 1449 (m), 1437 (m), 1418 (m), 1386 (m), 1369 (m), 1327 (s), 1265 (m), 1198 (m), 1166 (s), 1125 (s), 1068 (s), 1018 (s), 911 (m), 881 (m), 843 (m), 768 (m), 735 (m), 701 (s)

MS: (ESI)

119.1 (100), 136.1 (21), 282.1 (7), 400.2 (28), 405.1 (M^++Na, 46), 421.1 (8)

HRMS: calcd for $C_{20}H_{21}F_3O_4Na$: 405.1290, found 405.1284

TLC: R_f 0.22 (hexane/EtOAc, 4/1) [UV(254)/$KMnO_4$]

SFC: (2*R*,3*S*)-**4ac**, t_R 5.75 min (98.0%); (2*S*,3*R*)-**4ac**, t_R 6.62 min (2.0%)

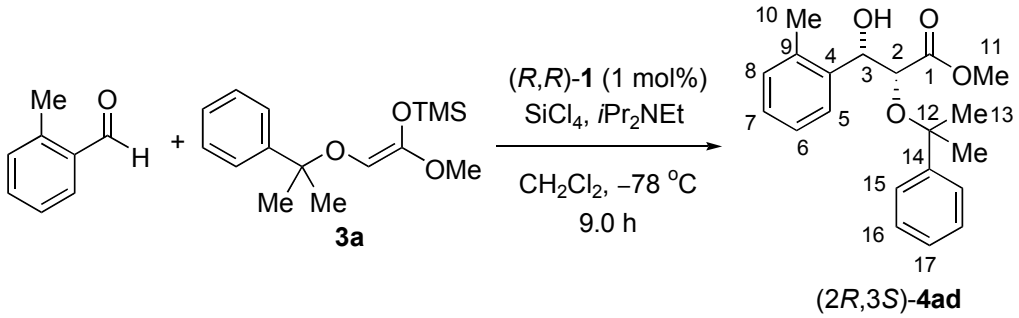
(Chiralpak AS, 125 bar, 40 °C, 1.6% MeOH in CO_2, 1.8 mL/min, 220 nm)

Opt. Rot.: $[\alpha]_D^{24}$ 34.3 (c = 8.3, EtOH)

Analysis: $C_{20}H_{21}F_3O_4$ (382.37)

Calcd:	C, 62.82%;	H, 5.54%
Found:	C, 62.50%;	H, 5.49%

Preparation of (2*R*,3*S*)-3-Hydroxy-3-(2-methylphenyl)-2-(1-methyl-1-phenylethoxy) propanoic Acid Methyl Ester ((2*R*,3*S*)-4ad) (Table 1, entry 4)



Following General Procedure 3, (*R*,*R*)-**1** (8.4 mg, 0.01 mmol, 0.01 equiv) was combined with diisopropylethylamine (17.4 μL, 0.1 mmol, 0.1 equiv), 2-tolualdehyde (116 μL, 1.0 mmol), $SiCl_4$ (126 μL, 1.1 mmol, 1.1 equiv), and **3a** (336.5 mg, 1.2 mmol, 1.2 equiv) to yield, after column chromatography (22 mm diam., hexane/EtOAc, 5/1 to 1/1) on silica gel (15 g), **4ad** (305 mg, 93%) as a colorless oil. The *syn*/*anti* ratio was determined to be 98/2 by ^{1}H NMR (500 MHz) analysis of the crude reaction mixture.

Data for (2*R*,3*S*)-**4ad**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.39-7.38 (m, 1 H, HC(5)), 7.26-7.16 (m, 7 H, HC(6), HC(7), HC(15), HC(16), HC(17)), 7.06-7.05 (m, 1 H, HC(8)), 5.04 (d, *J* = 5.3, 1 H, HC(3)), 3.91 (d, *J* = 5.3, 1 H, HC(2)), 3.47 (s, 3 H, HC(11)), 2.89 (bs, 1 H, OH), 2.16 (s, 3 H, HC(10)), 1.50 (s, 3 H, HC(13)), 1.47 (s, 3 H, HC(13))

^{13}C NMR: (126 MHz, $CDCl_3$)

172.5 (C(1)), 143.6 (C(14)), 137.1 (C(4)), 135.0 (C(9)), 130.4 (C(8)), 128.0 (C(16)), 127.8 (C(7)), 127.4 (C(17)), 127.1 (C(5)), 126.1 (C(15)), 125.8 (C(6)), 78.9 (C(12)), 75.4 (C(2)), 71.8 (C(3)), 51.7 (C(11)), 28.2 (C(13)), 26.8 (C(13)), 18.8 (C(10))

IR: (neat)

3492 (br), 3061 (w), 3027 (w), 2980 (m), 2951 (m), 1746 (s), 1495 (m), 1448 (m), 1436 (m), 1384 (m), 1368 (m), 1264 (s), 1197 (s), 1171 (s), 1151 (s), 1113 (s), 1100 (s), 1075 (s), 1057 (s), 1030 (m), 911 (m), 766 (s), 733 (s), 701 (s)

MS: (ESI)

119.1 (24), 193.1 (16), 346.2 (14), 351.1 (M^++Na, 100), 352.1 (12), 367.1 (5)

HRMS: calcd for $C_{20}H_{24}O_4Na$: 351.1572, found 351.1564

TLC: R_f 0.24 (hexane/EtOAc, 4/1) [UV(254)/$KMnO_4$]

SFC: (2*S*,3*R*)-**4ad**, t_R 4.46 min (3.2%); (2*R*,3*S*)-**4ad**, t_R 5.09 min (96.8%)

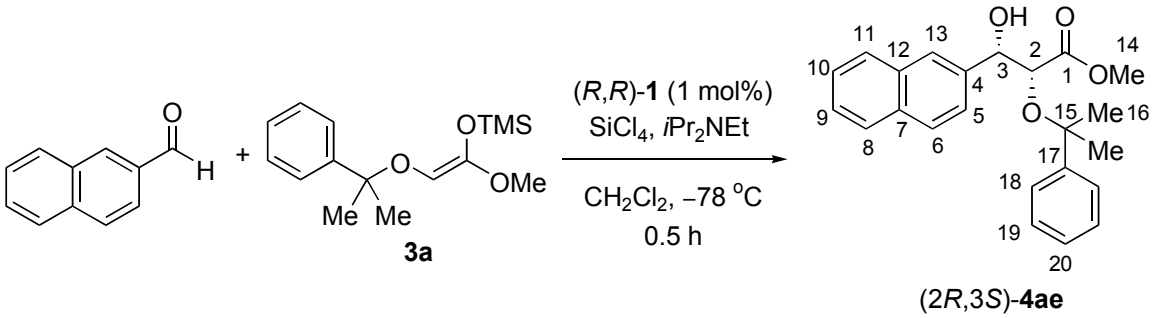
(Chiralcel OD, 125 bar, 40 °C, 5.0% MeOH in CO_2, 3.0 mL/min, 220 nm)

Opt. Rot.: $[\alpha]_D^{24}$ 68.5 (c = 2.0, EtOH)

Analysis: $C_{20}H_{24}O_4$ (328.40)

Calcd:	C, 73.15%;	H, 7.37%
Found:	C, 73.13%;	H, 7.33%

Preparation of (2*R*,3*S*)-3-Hydroxy-2-(1-methyl-1-phenylethoxy)-3-(2-naphthyl)propanoic Acid Methyl Ester ((2*R*,3*S*)-4ae) (Table 1, entry 5)



Following General Procedure 3, (*R*,*R*)-**1** (8.4 mg, 0.01 mmol, 0.01 equiv) was combined with diisopropylethylamine (17.4 μL, 0.1 mmol, 0.1 equiv), 2-naphthaldehyde (156 mg, 1.0

mmol), $SiCl_4$ (126 μL, 1.1 mmol, 1.1 equiv), and **3a** (336.5 mg, 1.2 mmol, 1.2 equiv) to yield, after column chromatography (22 mm diam., hexane/EtOAc, 5/1 to 2/1) on silica gel (15 g), **4ae** (342 mg, 94%) as a colorless oil. The *syn*/*anti* ratio was determined to be >99/1 by ^{1}H NMR (500 MHz) analysis of the crude reaction mixture.

Data for (2*R*,3*S*)-**4ae**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.83-7.79 (m, 2 H, HC(8), HC(11)), 7.77 (d, *J* = 8.3, 1 H, HC(6)), 7.72 (bs, 1 H, HC(13)), 7.49-7.45 (m, 2 H, HC(9), HC(10)), 7.36 (dd, *J* = 8.3, 1.7, 1 H, HC(5)), 7.32-7.30 (m, 2 H, HC(18)), 7.21-7.15 (m, 3 H, HC(19), HC(20)), 4.97 (dd, *J* = 5.7, 4.2, 1 H, HC(3)), 3.96 (d, *J* = 5.7, 1 H, HC(2)), 3.39 (s, 3 H, HC(14)), 3.15 (d, *J* = 4.2, 1 H, OH), 1.54 (s, 3 H, HC(16)), 1.521 (s, 3 H, HC(16))

^{13}C NMR: (126 MHz, $CDCl_3$)

172.4 (C(1)), 143.7 (C(17)), 136.4 (C(4)), 133.2 (C(7) or C(12)), 133.0 (C(7) or C(12)), 128.03 (C(19)), 128.00 (C(6), C(8), C(11), or C(20)), 127.96 (C(6), C(8), C(11), or C(20)), 127.6 (C(6), C(8), C(11), or C(20)), 127.5 (C(6), C(8), C(11), or C(20)), 126.1 (C(18)), 126.05 (C(9) or C(10)), 125.97 (C(9) or C(10)), 125.7 (C(13)), 124.2 (C(5)), 79.0 (C(15)), 77.3 (C(2)), 75.1 (C(3)), 51.7 (C(14)), 28.1 (C(16)), 27.0 (C(16))

IR: (neat)

3464 (br), 2984 (m), 2257 (m), 1741 (s), 1450 (m), 1439 (s), 1382 (m), 1368 (s), 1356 (m), 1315 (m), 1286 (m), 1200 (m), 1148 (s), 1113 (s), 1073 (s), 991 (m), 902 (s), 881 (m), 859 (s), 827 (s), 766 (s), 743 (m), 718 (s), 701 (s), 644 (m)

MS: (ESI)

119.1 (4), 229.1 (4), 287.2 (5), 387.1 (M^++Na, 100), 388.1 (26)

HRMS: calcd for $C_{23}H_{24}O_4Na$: 387.1572, found 387.1574

TLC: R_f 0.29 (hexane/EtOAc, 4/1) [UV(254)/$KMnO_4$]

SFC: (2*S*,3*R*)-**4ae**, t_R 5.60 min (1.5%); (2*R*,3*S*)-**4ae**, t_R 6.25 min (98.5%)

(Chiralcel OD, 125 bar, 40 °C, 10.0% MeOH in CO_2, 3.0 mL/min, 220 nm)

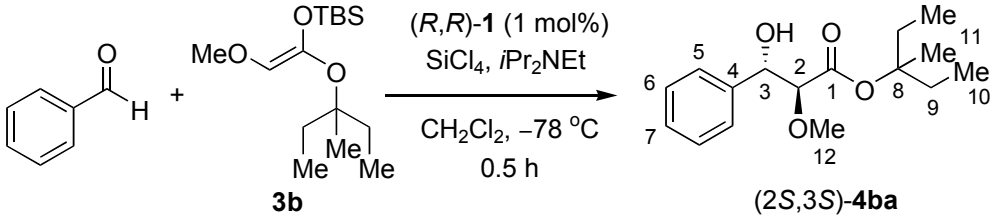
Opt. Rot.: $[\alpha]_D^{24}$ 30.7 (c = 2.0, EtOH)

Analysis: $C_{23}H_{24}O_4$ (364.43)

Calcd: C, 75.80%; H, 6.64%

Found: C, 75.67%; H, 6.37%

Preparation of (2*S*,3*S*)-3-Hydroxy-2-methoxy-3-phenylpropanoic Acid 1-Ethyl-1-methylpropyl Ester ((2*S*, 3*S*)-4ba) (Table 2, entry 1)



Following General Procedure 3, (*R*,*R*)-**1** (8.4 mg, 0.01 mmol, 0.01 equiv) was combined with diisopropylethylamine (17.4 μL, 0.1 mmol, 0.1 equiv), benzaldehyde (101.6 μL, 1.0 mmol), $SiCl_4$ (126 μL, 1.1 mmol, 1.1 equiv), and **3b** (346.2 mg, 1.2 mmol, 1.2 equiv) to yield, after column chromatography (30 mm diam., hexane/EtOAc, 5/1) on silica gel (30 g), **4ba** (255 mg, 91%) as a colorless oil. The *syn*/*anti* ratio was determined to be >1/99 by ^{1}H NMR (500 MHz) analysis of the crude reaction mixture.

Data for (2*S*,3*S*)-**4ba**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.41-7.40 (m, 2 H, HC(5)), 7.35-7.32 (m, 2 H, HC(6)), 7.29-7.26 (m, 1 H,

HC(7)), 4.96 (d, J = 5.6, 1 H, HC(3)), 3.89 (d, J = 5.6, 1 H, HC(2)), 3.40 (s, 3 H, HC(12)), 2.96 (bs, 1 H, OH), 1.81-1.73 (m, 3 H, HC(9)), 1.60 (dq, J = 13.9, 7.5, 1 H, HC(9)), 1.30 (s, 3 H, HC(11)), 0.77 (dd, J = 7.5, 7.5, 3 H, HC(10)), 0.74 (dd, J = 7.5, 7.5, 3 H, HC(10))

^{13}C NMR: (126 MHz, $CDCl_3$)

169.4 (C(1)), 139.6 (C(4)), 128.2 (C(6)), 127.9 (C(7)), 126.8 (C(5)), 87.7 (C(8)), 84.6 (C(2)), 74.0 (C(3)), 58.8 (C(12)), 30.3 (C(9)), 30.2 (C(9)), 22.6 (C(11)), 7.9 (C(10)), 7.8 (C(10))

IR: (neat)

3474 (br), 3064 (w), 3033 (w), 2976 (m), 2941 (m), 2884 (m), 2829 (w), 1734 (s), 1495 (w), 1456 (m), 1376 (m), 1266 (m), 1196 (s), 1151 (m), 1124 (s), 1065 (m), 980 (m), 846 (m), 752 (m), 700 (s), 613 (m)

MS: (ESI)

179.1 (100), 180.1 (3), 197.1 (18), 298.2 (36), 303.2 (M^++Na, 7)

HRMS: calcd for $C_{16}H_{24}O_4Na$: 303.1572, found 303.1559

TLC: R_f 0.27 (hexane/EtOAc, 5/1) [UV(254)/$KMnO_4$]

SFC: (2*S*,3*S*)-**4ba**, t_R 10.81 min (95.1%); (2*R*,3*R*)-**4ba**, t_R 11.40 min (4.9%)

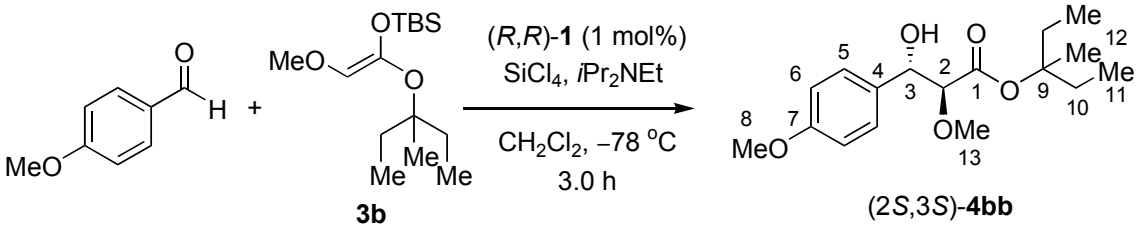
(Chiralpak AD, 125 bar, 40 ^oC, 2.0% MeOH in CO_2, 2.0 mL/min, 220 nm)

Opt. Rot.: $[\alpha]_D^{24}$ –5.6 (c = 4.0, EtOH)

Analysis: $C_{16}H_{24}O_4$ (280.36)

Calcd:	C, 68.54%;	H, 8.63%
Found:	C, 68.35%;	H, 8.72%

Preparation of (2*S*,3*S*)-3-Hydroxy-2-methoxy-3-(4-methoxyphenyl)propanoic Acid 1-Ethyl-1-methylpropyl Ester ((2*S*,3*S*)-4bb) (Table 2, entry 2)



Following General Procedure 3, (*R*,*R*)-**1** (8.4 mg, 0.01 mmol, 0.01 equiv) was combined with diisopropylethylamine (17.4 μL, 0.1 mmol, 0.1 equiv), 4-anisaldehyde (121.7 μL, 1.0 mmol), $SiCl_4$ (126 μL, 1.1 mmol, 1.1 equiv), and **3b** (346.2 mg, 1.2 mmol, 1.2 equiv) to yield, after column chromatography (22 mm diam., hexane/EtOAc, 5/1 to 1/1) on silica gel (15 g), **4bb** (289 mg, 93%) as a colorless oil. The *syn*/*anti* ratio was determined to be >1/99 by ^{1}H NMR (500 MHz) analysis of the crude reaction mixture.

Data for (2*S*,3*S*)-**4bb**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.35-7.32 (m, 2 H, HC(5)), 6.88-6.85 (m, 2 H, HC(6)), 4.89 (dd, *J* = 5.6, 5.6, 1 H, HC(3)), 3.86 (d, *J* = 5.8, 1 H, HC(2)), 3.80 (s, 3 H, HC(8)), 3.40 (s, 3 H, HC(13)), 2.86 (d, *J* = 5.4, 1 H, OH), 1.80 (dq, *J* = 14.1, 7.5, 1 H, HC(10)), 1.78 (m, 2 H, HC(10)), 1.63 (dq, *J* = 14.1, 7.5, 1 H, HC(10)), 1.32 (s, 3 H, HC(12)), 0.79 (dd, *J* = 7.5, 7.5, 3 H, HC(11)), 0.77 (dd, *J* = 7.5, 7.5, 3 H, HC(11))

^{13}C NMR: (126 MHz, $CDCl_3$)

169.6 (C(1)), 159.3 (C(7)), 131.9 (C(4)), 128.1 (C(5)), 113.5 (C(6)), 87.6 (C(9)), 84.7 (C(2)), 73.6 (C(3)), 58.8 (C(13)), 55.2 (C(8)), 30.3 (C(10)), 30.2 (C(10)), 22.6 (C(12)), 7.9 (C(11)), 7.8 (C(11))

IR: (neat)

3482 (br), 2975 (m), 2940 (m), 2884 (m), 2835 (w), 1733 (s), 1613 (m), 1587 (w), 1514 (s), 1462 (m), 1376 (m), 1355 (w), 1302 (m), 1250 (s), 1197 (m), 1180 (m), 1125 (s), 1071 (m), 1034 (m), 1010 (w), 981 (m), 899 (w), 835 (m), 767 (w), 734 (w)

MS: (ESI)

98.5 (4), 165.1 (5), 209.1 (100), 210.1 (6), 249.1 (20), 265.0 (3), 328.2 (4), 333.2 (M^++Na, 39), 349.1 (7)

HRMS: calcd for $C_{17}H_{26}O_5Na$: 333.1678, found 333.1669

TLC: R_f 0.36 (hexane/EtOAc, 3/1) [UV(254)/$KMnO_4$]

SFC: (2*S*,3*S*)-**4bb**, t_R 10.21 min (98.3%); (2*R*,3*R*)-**4bb**, t_R 11.65 min (1.7%)

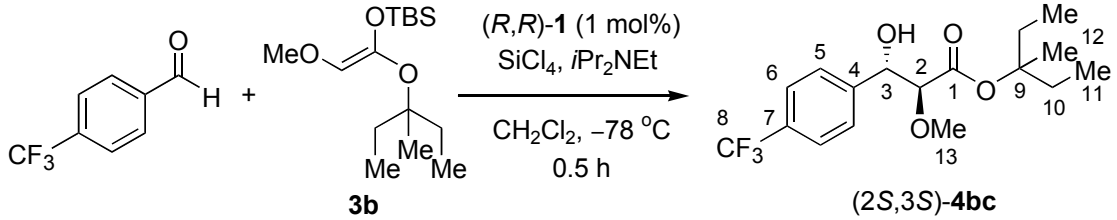
(Chiralcel OD, 125 bar, 40 °C, 2.0% MeOH in CO_2, 3.0 mL/min, 220 nm)

Opt. Rot.: $[\alpha]_D^{24}$ –2.8 (c = 8.4, EtOH)

Analysis: $C_{17}H_{26}O_5$ (310.39)

Calcd:	C, 65.78%;	H, 8.44%
Found:	C, 65.39%;	H, 8.55%

Preparation of (2*S*,3*S*)-3-Hydroxy-2-methoxy-3-[4-(trifluoromethyl)phenyl]propanoic Acid 1-Ethyl-1-methylpropyl Ester ((2*S*,3*S*)-4bc) (Table 2, entry 3)



3b (2*S*,3*S*)-**4bc**

Following General Procedure 3, (*R*,*R*)-**1** (8.4 mg, 0.01 mmol, 0.01 equiv) was combined

with diisopropylethylamine (17.4 μL, 0.1 mmol, 0.1 equiv), 4-trifluoromethylbenzaldehyde (136.6 μL, 1.0 mmol), $SiCl_4$ (126 μL, 1.1 mmol, 1.1 equiv), and **3b** (346.2 mg, 1.2 mmol, 1.2 equiv) to yield, after column chromatography (22 mm diam., hexane/EtOAc, 5/1) on silica gel (15 g), **4bc** (334 mg, 96%) as a colorless oil. The *syn*/*anti* ratio was determined to be >1/99 by ^{1}H NMR (500 MHz) analysis of the crude reaction mixture.

Data for (2*S*,3*S*)-**4bc**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.60 (m, 2 H, HC(7)), 7.54 (m, 2 H, HC(6)), 5.03 (d, *J* = 5.5, 1 H, HC(3)), 3.87 (d, *J* = 5.5, 1 H, HC(2)), 3.42 (s, 3 H, HC(13)), 3.10 (bs, 1 H, OH), 1.76 (dq, *J* = 14.0, 7.5, 1 H, HC(10)), 1.74 (q, *J* = 7.5, 2 H, HC(10)), 1.58 (dq, *J* = 14.0, 7.5, 1 H, HC(10)), 1.29 (s, 3 H, HC(12)), 0.75 (dd, *J* = 7.5, 7.5, 3 H, HC(11)), 0.72 (dd, *J* =7.5, 7.5, 3 H, HC(11))

^{13}C NMR: (126 MHz, $CDCl_3$)

169.0 (C(1)), 143.6 (C(4)), 130.0 (q, *J* = 32.2, C(7)), 127.1 (C(5)), 125.0 (q, *J* = 3.9, C(6)), 124.1 (q, *J* = 272.8, C(8)), 88.1 (C(9)), 84.3 (C(2)), 73.5 (C(3)), 58.8 (C(13)), 30.3 (C(10)), 30.2 (C(10)), 22.6 (C(12)), 7.8 (C(11)), 7.8 (C(11))

^{19}F NMR: (376 MHz, $CDCl_3$)

−63.06 (FC(8))

IR: (neat)

3461 (br), 2798 (m), 2944 (m), 2886 (m), 2883 (w), 1729 (s), 1621 (m), 1462 (m), 1417 (m), 1376 (m), 1327 (s), 1265 (m), 1196 (m), 1165 (s), 1126 (s), 1088 (m), 1068 (s), 1018 (m), 982 (m), 909 (w), 846 (m), 798 (w), 764 (w), 734 (m)

MS: (ESI)

119.1 (35), 131.1 (21), 149.0 (9), 163.1 (7), 191.0 (5), 247.1 (100), 248.1 (8),

265.1 (77), 266.1 (6), 282.1 (21), 287.0 (37), 365.0 (17), 371.1 (M^++Na, 52), 397.0 (5), 405.1 (5)

HRMS: calcd for $C_{17}H_{23}F_3O_4Na$: 371.1446, found 371.1437

TLC: R_f 0.30 (hexane/EtOAc, 4/1) [UV(254)/$KMnO_4$]

SFC: (2*S*,3*S*)-**4bc**, t_R 4.12 min (98.3%); (2*R*,3*R*)-**4bc**, t_R 4.68 min (1.7%)

(Chiralcel OD, 125 bar, 40 °C, 2.0% MeOH in CO_2, 3.0 mL/min, 220 nm)

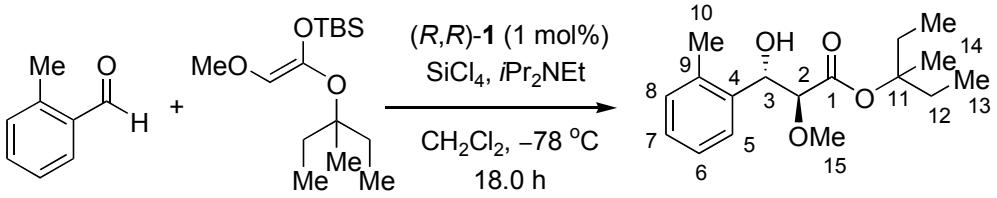
Opt. Rot.: $[\alpha]_D^{24}$ –1.4 (c = 0.75, EtOH)

Analysis: $C_{17}H_{23}F_3O_4$ (348.36)

Calcd: C, 58.61%; H, 6.65%

Found: C, 58.58%; H, 6.69%

Preparation of (2*S*,3*S*)-3-Hydroxy-2-methoxy-3-(2-methylphenyl)propanoic Acid 1-Ethyl-1-methylpropyl Ester ((2*S*,3*S*)-4bd) (Table 2, entry 4)



Following General Procedure 3, (*R*,*R*)-**1** (8.4 mg, 0.01 mmol, 0.01 equiv) was combined with diisopropylethylamine (17.4 μL, 0.1 mmol, 0.1 equiv), 2-tolualdehyde (116 μL, 1.0 mmol), $SiCl_4$ (126 μL, 1.1 mmol, 1.1 equiv), and **3b** (346.2 mg, 1.2 mmol, 1.2 equiv) to yield, after column chromatography (22 mm diam., hexane/EtOAc, 5/1 to 2/1) on silica gel (15 g), **4bd** (269 mg, 91%) as a colorless oil. The *syn*/*anti* ratio was determined to be 2/98 by ^{1}H NMR (500 MHz) analysis of the crude reaction mixture.

Data for (2*S*,3*S*)-**4bd**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.55-7.53 (m, 1 H, HC(5)), 7.22-7.16 (m, 2 H, HC(6), HC(7)), 7.14-7.12 (m, 1 H, HC(8)), 5.19 (d, *J* = 6.0, 1 H, HC(3)), 3.88 (d, *J* = 6.0, 1 H, HC(2)), 3.38 (s, 3 H, HC(15)), 2.78 (bs, 1 H, OH), 2.37 (s, 3 H, HC(10)), 1.78 (q, *J* = 7.5, 2 H, HC(12)), 1.77 (dq, *J* = 14.0, 7.5, 1 H, HC(12)), 1.59 (dq, *J* = 14.0, 7.5, 1 H, HC(12)), 1.32 (s, 3 H, HC(14)), 0.78 (dd, *J* = 7.5, 7.5, 3 H, HC(13)), 0.73 (dd, *J* = 7.5, 7.5, 3 H, HC(13))

^{13}C NMR: (126 MHz, $CDCl_3$)

169.7 (C(1)), 137.9 (C(4)), 135.7 (C(9)), 130.2 (C(8)), 127.7 (C(7)), 126.3 (C(5)), 126.0 (C(6)), 87.7 (C(11)), 84.0 (C(2)), 70.5 (C(3)), 58.7 (C(15)), 30.29 (C(12)), 30.27 (C(12)), 22.6 (C(14)), 19.3 (C(10)), 7.9 (C(13)), 7.8 (C(13))

IR: (neat)

3477 (br), 3024 (w), 2975 (s), 2941 (m), 2884 (m), 2829 (w), 1732 (s), 1491 (w), 1462 (m), 1377 (m), 1272 (m), 1199 (s), 1129 (s), 1109 (s), 1072 (m), 1048 (m), 1006 (m), 981 (m), 899 (w), 846 (m), 803 (w), 756 (m), 730 (m)

MS: (ESI)

233.1 (100), 234.1 (8), 317.2 (M^++Na, 81), 318.2 (8), 338.3 (12)

HRMS: calcd for $C_{17}H_{26}O_4Na$: 317.1729, found 317.1719

TLC: R_f 0.45 (hexane/EtOAc, 4/1) [UV(254)/$KMnO_4$]

SFC: (2*R*,3*R*)-**4bd**, t_R 6.09 min (6.9%); (2*S*,3*S*)-**4bd**, t_R 6.60 min (93.1%)

(Chiralpak AD, 125 bar, 40 ^{o}C, 2.0% MeOH in CO_2, 3.0 mL/min, 220 nm)

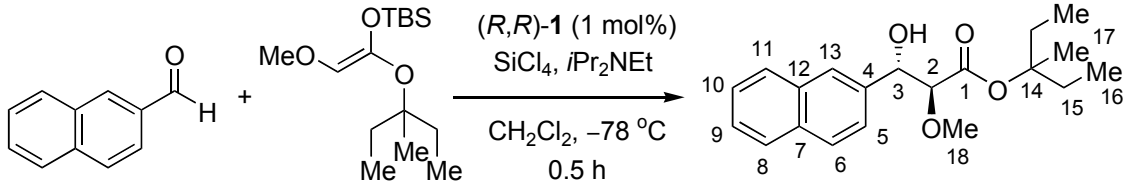
Opt. Rot.: $[\alpha]_D^{24}$ 4.9 (c = 2.2, EtOH)

Analysis: $C_{17}H_{26}O_4$ (294.39)

Calcd: C, 69.36%; H, 8.90%

Found: C, 69.59%; H, 9.07%

Preparation of (2*S*,3*S*)-3-Hydroxy-2-methoxy-3-(2-naphthyl)propanoic Acid 1-Ethyl-1-methylpropyl Ester ((2*S*,3*S*)-4be) (Table 2, entry 5)



3b (2*S*,3*S*)-**4be**

Following General Procedure 3, (*R*,*R*)-**1** (8.4 mg, 0.01 mmol, 0.01 equiv) was combined with diisopropylethylamine (17.4 μL, 0.1 mmol, 0.1 equiv), 2-naphthaldehyde (156.2 mg, 1.0 mmol), $SiCl_4$ (126 μL, 1.1 mmol, 1.1 equiv), and **3b** (346.2 mg, 1.2 mmol, 1.2 equiv) to yield, after column chromatography (22 mm diam., hexane/EtOAc, 5/1 to 2/1) on silica gel (15 g), **4be** (307 mg, 93%) as a colorless oil. The *syn*/*anti* ratio was determined to be >1/99 by ^{1}H NMR (500 MHz) analysis of the crude reaction mixture.

Data for (2*S*,3*S*)-**4be**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.88 (d, *J* = 1.7, 1 H, HC(13)), 7.83-7.81 (m, 3 H, HC(6), HC(8), HC(11)), 7.52 (dd, *J* = 8.6, 1.7, 1 H, HC(5)), 7.48-7.45 (m, 2 H, HC(9), HC(10)), 5.13 (d, *J* = 5.6, 1 H, HC(3)), 3.97 (d, *J* = 5.6, 1 H, HC(2)), 3.41 (s, 3 H, HC(18)), 3.08 (bs, 1 H, OH), 1.74 (dq, *J* = 14.0, 7.5, 1 H, HC(15)), 1.73 (q, *J* = 7.5, 2 H, HC(15)), 1.55 (dq, *J* = 14.0, 7.5, 1 H, HC(15)), 1.27 (s, 3 H, HC(17)), 0.72 (dd, *J* = 7.5, 7.5, 3 H, HC(16)), 0.67 (dd, *J* = 7.5, 7.5, 3 H, HC(16))

^{13}C NMR: (126 MHz, $CDCl_3$)

169.5 (C(1)), 137.1 (C(4)), 133.11 (C(7) or C(12)), 133.10 (C(7) or C(12)), 128.0 (C(6), C(8), or C(11)), 127.8 (C(6), C(8), or C(11)), 127.6 (C(6), C(8), or C(11)), 126.0 (C(9), C(10), or C(13)), 125.88 (C(9), C(10), or C(13)), 125.86 (C(9), C(10), or C(13)), 124.6 (C(5)), 87.8 (C(14)), 84.7 (C(2)), 74.2 (C(3)), 58.8 (C(18)), 30.3 (C(15)), 30.2 (C(15)) 22.5 (C(17)), 7.8 (C(16)), 7.7 (C(16))

IR: (neat)

3464 (br), 3057 (m), 2976 (s), 2941 (s), 2883 (m), 2830 (m), 2249 (w), 1731 (s), 1603 (w), 1509 (m), 1461 (s), 1376 (s), 1359 (s), 1270 (s), 1202 (s), 1151 (s), 1126 (s), 1072 (s), 1007 (m), 982 (m), 910 (s), 857 (s), 821 (s), 774 (m), 734 (s)

MS: (ESI)

169.1 (5), 185.1 (3), 229.1 (28), 269.1 (100), 270.1 (8), 348.2 (7), 353.1 (M^++Na, 85), 354.2 (9)

HRMS: calcd for $C_{20}H_{26}O_4Na$: 353.1729, found 353.1723

TLC: R_f 0.26 (hexane/EtOAc, 5/1) [UV(254)/$KMnO_4$]

SFC: (2*R*,3*R*)-**4be**, t_R 8.84 min (2.6%); (2*S*,3*S*)-**4be**, t_R 9.76 min (97.4%)

(Chiralcel OJ, 125 bar, 40 ^oC, 3.0% MeOH in CO_2, 3.0 mL/min, 220 nm)

Opt. Rot.: $[\alpha]_D^{24}$ 7.3 (c = 3.8, EtOH)

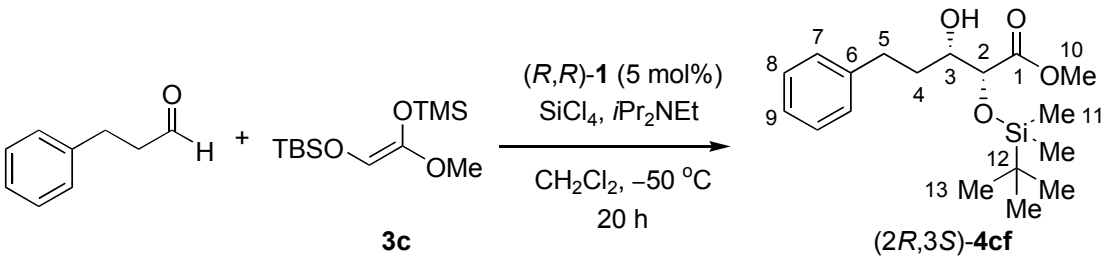
Analysis: $C_{20}H_{26}O_4$ (330.42)

Calcd:	C, 72.70%;	H, 7.93%
Found:	C, 72.63%;	H, 8.01%

Aldol Additions of Silyl Ketene Acetals to Aliphatic Aldehydes

General Procedure 4. Addition of Silyl Ketene Acetals to Aliphatic Aldehydes

Preparation of (2*R*,3*S*)-2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-3-hydroxy-5-phenyl pentanoic Acid Methyl Ester ((2*R*,3*S*)-4cf) (Scheme 2)



To a flame-dried, 10-mL, Schlenk flask fitted with a magnetic stir bar, a thermocouple, a gas inlet tube, and a septum were added (*R*,*R*)-**1** (42 mg, 0.05 mmol, 0.05 equiv), CH_2Cl_2 (1.5 mL), and hydrocinnamaldehyde (132 μL, 1.0 mmol). The solution was cooled to –50 °C (bath temp.) in an acetone bath of Cryocooler®. After diisopropylethylamine (17.4 μL, 0.1 mmol, 0.1 equiv) and $SiCl_4$ (126 μL, 1.1 mmol, 1.1 equiv) were added to the flask via syringe, a solution of **3c** (331.8 mg, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 (1 mL) was added dropwise via syringe over 10 min. The reaction mixture was stirred for 20 h at –50 °C before a mixture of MeOH (1 mL), Et_3N (1 mL), and CH_2Cl_2 (5 mL) was added. The resulting solution was transferred into a 125-mL Erlenmeyer flask containing a sat. aq. $NaHCO_3$ solution (10 mL) and a sat. aq. KF solution (10 mL). The biphasic mixture was stirred vigorously for 2 h at room temperature. The mixture was filtered through a glass frit and the filtrate was transferred to a 125-mL separatory funnel where the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extracts were dried over Na_2SO_4 (15 g), filtered, and concentrated *in vacuo* (23 °C, 30 mmHg). The residue was purified by column chromatography (22 mm diam., hexane/EtOAc, 10/1 to 5/1) on silica gel (20 g) to give **4cf** (165 mg, 49%) as a colorless oil. The *syn*/*anti* ratio was determined to be 90/10 by ^{1}H NMR (500 MHz) analysis of the crude reaction

mixture.

Data for (2*R*,3*S*)-**4cf**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.30-7.27 (m, 2 H, HC(8)), 7.21-7.18 (m, 3 H, HC(7), HC(9)), 4.14 (d, *J* = 3.4, 1 H, HC(2)), 3.84-3.81 (m, 1 H, HC(3)), 3.74 (s, 3 H, HC(10)), 2.86 (ddd, *J* = 13.9, 9.4, 5.6, 1 H, HC(5)), 2.69 (ddd, *J* = 13.9, 9.2, 7.5, 1 H, HC(5)), 2.25 (bs, 1 H, OH), 1.88-1.76 (m, 2 H, HC(4)), 0.93 (s, 9 H, HC(13)), 0.11 (s, 3 H, HC(11)), 0.07 (s, 3 H, HC(11))

^{13}C NMR: (126 MHz, $CDCl_3$)

172.5 (C(1)), 141.6 (C(6)), 128.42 (C(7)), 128.38 (C(8)), 125.9 (C(9)), 74.8 (C(2)), 72.5 (C(3)), 52.0 (C(10)), 35.3 (C(4)), 31.8 (C(5)), 25.6 (C(13)), 18.2 (C(12)), −5.0 (C(11)), −5.5 (C(11))

IR: (neat)

3490 (br), 3063 (w), 3028 (m), 2953 (s), 2930 (s), 2896 (m), 2858 (s), 1759 (s), 1604 (m), 1497 (m), 1472 (m), 1456 (m), 1438 (m), 1390 (m), 1362 (m), 1255 (s), 1206 (m), 1137 (s), 1053 (m), 1008 (m), 859 (s), 838 (s), 780 (s), 748 (m), 700 (s)

MS: (ESI)

129.1 (7), 189.1 (7), 339.2 (8), 361.2 (M^++Na, 100), 362.2 (17)

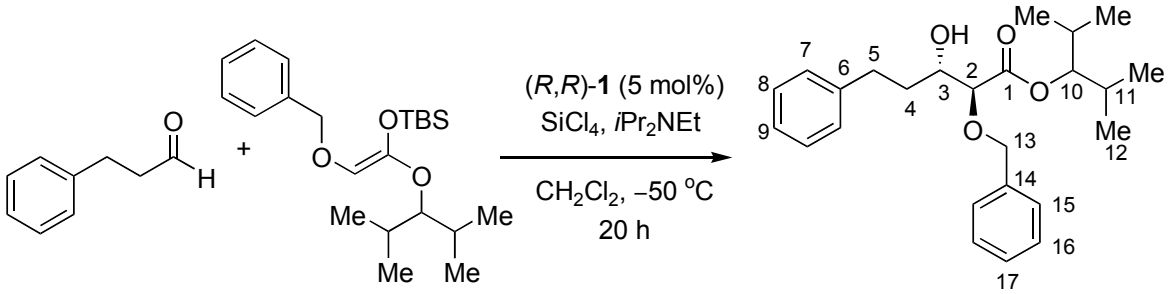
HRMS: calcd for $C_{18}H_{30}O_4SiNa$: 361.1811, found 361.1811

TLC: R_f 0.42 (hexane/EtOAc, 5/1) [UV(254)/$KMnO_4$]

SFC: (2*S*,3*R*)-**4cf**, t_R 8.04 min (12.7%); (2*R*,3*S*)-**4cf**, t_R 8.69 min (87.3%)

(Chiralpak AD, 125 bar, 40 ^oC, 2.5% MeOH in CO_2, 1.0 mL/min, 220 nm)

Preparation of (2*S*,3*S*)-3-Hydroxy-5-phenyl-2-(phenylmethoxy)pentanoic Acid 2-Methyl-1-(1-methylethyl)propyl Ester ((2*S*,3*S*)-4df) (Scheme 3)



3d (2*S*,3*S*)-**4df**

Following General Procedure 4, (*R*,*R*)-**1** (42 mg, 0.05 mmol, 0.05 equiv) was combined with hydrocinnamaldehyde (132 μL, 1.0 mmol), diisopropylethylamine (17.4 μL, 0.1 mmol, 0.1 equiv), $SiCl_4$ (126 μL, 1.1 mmol, 1.1 equiv), and **3d** (454 mg, 1.2 mmol, 1.2 equiv) to yield, after column chromatography (22 mm diam., hexane/EtOAc, 10/1 to 5/1) on silica gel (20 g), **4df** (325 mg, 82%) as a colorless oil. The *syn*/*anti* ratio was determined to be 2/98 by ^{1}H NMR (500 MHz) analysis of the crude reaction mixture.

Data for (2*S*,3*S*)-**4df**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.38-7.37 (m, 4 H, HC(15), HC(16)), 7.36-7.31 (m, 1 H, HC(17)), 7.29-7.27 (m, 2 H, HC(8)), 7.20-7.17 (m, 3 H, HC(7), HC(9)), 4.85 (d, *J* = 11.4, 1 H, HC(13)), 4.75 (dd, *J* = 6.1, 6.1, 1 H, HC(10)), 4.45 (d, *J* = 11.4, 1 H, HC(13)), 4.06 (d, *J* = 4.7, 1 H, HC(2)), 3.99-3.95 (m, 1 H, HC(3)), 2.87 (ddd, *J* = 13.7, 9.3, 5.5, 1 H, HC(5)), 2.69 (ddd, *J* = 13.7, 9.0, 7.6, 1 H, HC(5)), 2.28 (bs, 1 H, OH), 1.98-1.85 (m, 4 H, HC(4), HC(11)), 0.93 (d, *J* = 6.9, 3 H, HC(12)), 0.903 (d, *J* = 6.8, 3 H, HC(12)), 0.901 (d, *J* = 6.8, 3 H, HC(12)), 0.86 (d, *J* = 6.8, 3 H, HC(12))

^{13}C NMR: (126 MHz, $CDCl_3$)

170.7 (C(1)), 141.7 (C(6)), 137.2 (C(14)), 128.52 (Aryl), 128.49 (Aryl), 128.3

(Aryl), 128.2 (Aryl), 128.1 (C(17)), 125.8 (C(9)), 84.1 (C(10)), 81.4 (C(2)), 72.9 (C(13)), 71.5 (C(3)), 33.9 (C(4)), 31.8 (C(5)), 29.4 (C(11)), 29.2 (C(11)), 19.7 (C(12)), 19.5 (C(12)), 17.4 (C(12)), 17.2 (C(12))

IR: (neat)

3484 (br), 3063 (w), 3028 (m), 2966 (s), 2935 (s), 2876 (m), 1743 (s), 1603 (w), 1497 (m), 1455 (s), 1389 (m), 1371 (m), 1271 (m), 1200 (s), 1128 (s), 1095 (s), 1045 (m), 1029 (m), 1000 (m), 967 (m), 949 (m), 897 (m), 748 (s), 699 (s)

MS: (ESI)

91.1 (7), 219.1 (10), 237.1 (55), 238.1 (7), 287.2 (18), 301.1 (23), 399.2 (11), 421.2 (M^++Na, 100), 422.2 (22)

HRMS: calcd for $C_{25}H_{34}O_4Na$: 421.2355, found 421.2361

TLC: R_f 0.30 (hexane/EtOAc, 10/1) [UV(254)/$KMnO_4$]

SFC: (2*R*,3*R*)-**4df**, t_R 6.63 min (3.6%); (2*S*,3*S*)-**4df**, t_R 8.46 min (96.4%)

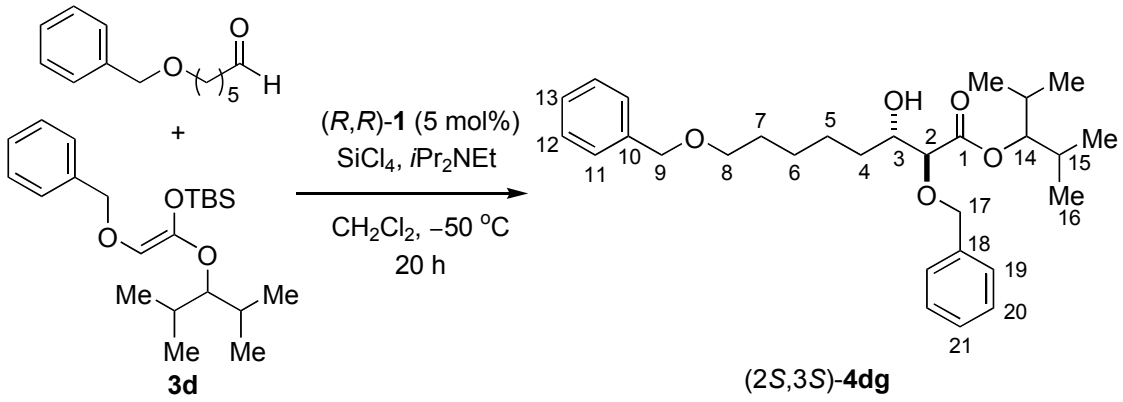
(Chiralcel OD, 125 bar, 40 °C, 5.0% MeOH in CO_2, 3.0 mL/min, 220 nm)

Opt. Rot.: $[\alpha]_D^{24}$ –47.6 (c = 5.0, EtOH)

Analysis: $C_{25}H_{34}O_4$ (398.54)

Calcd:	C, 75.34%;	H, 8.60%
Found:	C, 75.26%;	H, 8.57%

Preparation of (2*S*,3*S*)-2,8-Di(phenylmethoxy)-3-hydroxyoctanoic Acid 2-Methyl-1-(1-methylethyl)propyl Ester ((2*S*,3*S*) -4dg) (Scheme 3)



Following General Procedure 4, (*R*,*R*)-**1** (42 mg, 0.05 mmol, 0.05 equiv) was combined with 6-benzyloxyhexanal (206 mg, 1.0 mmol), diisopropylethylamine (17.4 μL, 0.1 mmol, 0.1 equiv), $SiCl_4$ (126 μL, 1.1 mmol, 1.1 equiv), and **3d** (454 mg, 1.2 mmol, 1.2 equiv) to yield, after column chromatography (22 mm diam., hexane/EtOAc, 10/1 to 5/1) on silica gel (20 g), **4dg** (420 mg, 89%) as a colorless oil. The *syn*/*anti* ratio was determined to be 2/98 by ^{1}H NMR (500 MHz) analysis of the crude reaction mixture.

Data for (2*S*,3*S*)-**4dg**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.38-7.26 (m, 10 H, Aryl), 4.84 (d, *J* = 11.5, 1 H, HC(17)), 4.75 (dd, *J* = 6.1, 6.1, 1 H, HC(14)), 4.49 (s, 2 H, HC(9)), 4.45 (d, *J* = 11.5, 1 H, HC(17)), 4.01 (d. *J* = 4.3, 1 H, HC(2)), 3.94-3.91 (m, 1 H, HC(3)), 3.45 (dd, *J* = 6.7, 6.7, 2 H, HC(8)), 2.19 (bs, 1 H, OH), 1.96 (qqd, *J* = 6.8, 6.8, 6.1, 1 H, HC(15)), 1.95 (qqd, *J* = 6.6, 6.6, 6.1, 1 H, HC(15)), 1.64-1.31 (m, 8 H, HC(4), HC(5), HC(6), HC(7)), 0.93 (d, *J* = 6.8, 6 H, HC(16)), 0.90 (d, *J* = 6.6, 6 H, HC(16))

^{13}C NMR: (126 MHz, $CDCl_3$)

170.8 (C(1)), 138.6 (C(10)), 137.2 (C(18)), 128.4 (Aryl), 128.3 (Aryl), 128.1 (Aryl), 128.0 (C(21)), 127.6 (C(11)), 127.4 (C(13)), 84.0 (C(14)), 81.5 (C(2)), 72.85 (C(9) or C(17)), 72.79 (C(9) or C(17)), 72.3 (C(3)), 70.3 (C(8)), 32.2 (C(4)), 29.6 (C(7)), 29.4 (C(15)), 29.3 (C(15)), 26.1 (C(6)), 25.5 (C(5)), 19.7 (C(16)), 19.6 (C(16)), 17.4 (C(16)), 17.3 (C(16))

IR: (neat)

3475 (br), 3064 (m), 3031 (m), 2965 (s), 2937 (s), 2874 (s), 2247 (w), 1743 (s), 1605 (w), 1587 (w), 1496 (m), 1455 (s), 1389 (m), 1370 (s), 1270 (s), 1199 (s), 1099 (s), 1028 (s), 1000 (m), 968 (m), 898 (m), 735 (s), 698 (s), 611 (m)

MS: (ESI)

181.1 (7), 193.1 (8), 373.2 (8), 493.3 (M^++Na, 100), 494.3 (15)

HRMS: calcd for $C_{29}H_{42}O_5Na$: 493.2930, found 493.2934

TLC: R_f 0.35 (hexane/EtOAc, 5/1) [UV(254)/$KMnO_4$]

SFC: (2*S*,3*S*)-**4dg**, t_R 7.23 min (98.5%); (2*R*,3*R*)-**4dg**, t_R 8.29 min (1.5%)

(Chiralcel OJ, 125 bar, 40 ^oC, 5.0% MeOH in CO_2, 3.0 mL/min, 220 nm)

Opt. Rot.: $[\alpha]_D^{24}$ –41.0 (c = 2.5, EtOH)

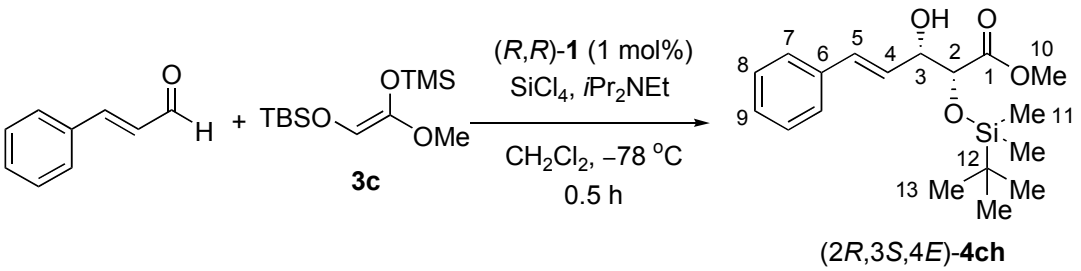
Analysis: $C_{29}H_{42}O_5$ (470.64)

Calcd:	C, 74.01%;	H, 8.99%
Found:	C, 73.93%;	H, 8.93%

Aldol Additions of Silyl Ketene Acetals to Alkenyl Aldehydes

General Procedure 5. Addition of Silyl Ketene Acetals to Alkenyl Aldehydes

Preparation of (2*R*,3*S*,4*E*)-2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-3-hydroxy-5-phenyl-4-pentenoic Acid Methyl Ester ((2*R*,3*S*,4*E*)-4ch) (Scheme 4)



To a flame-dried, 10-mL, Schlenk flask fitted with a magnetic stir bar, a thermocouple, a gas inlet tube, and a septum were added (*R*,*R*)-**1** (8.4 mg, 0.01 mmol, 0.01 equiv), CH_2Cl_2 (5 mL), and (*E*)-cinnamaldehyde (126 μL, 1.0 mmol). The solution was cooled to −78 °C (internal temp.) in a dry ice-acetone bath. After diisopropylethylamine (17.4 μL, 0.1 mmol, 0.1 equiv) and $SiCl_4$ (126 μL, 1.1 mmol, 1.1 equiv) were added to the flask via syringe, a solution of **3c** (332 mg, 1.2 mmol, 1.2 equiv) in CH_2Cl_2 (5 mL) was added dropwise via syringe over 15 min. The internal temperature was kept below −70 °C during the addition of **3c**. The reaction mixture was stirred for additional 15 min at −78 °C before a mixture of MeOH (1 mL), Et_3N (1 mL), and CH_2Cl_2 (5 mL) was added. The resulting solution was transferred into a 125-mL Erlenmeyer flask containing a sat. aq. $NaHCO_3$ solution (10 mL) and a sat. aq. KF solution (10 mL). The biphasic mixture was stirred vigorously for 2 h at room temperature. The mixture was filtered through a glass frit and the filtrate was transferred to a 125-mL separatory funnel where the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extracts were dried over Na_2SO_4 (15 g), filtered, and concentrated *in vacuo* (23 °C, 30 mmHg). The residue was purified by column chromatography (22 mm diam., hexane/EtOAc, 5/1) on silica gel (20 g) to give **4ch** (302 mg, 90%) as a colorless oil. The *syn*/*anti* ratio of **4ch**

was determined to be 99/1 by ^{1}H NMR (500 MHz) analysis of the crude reaction mixture.

Data for (2*R*,3*S*,4*E*)-**4ch**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.37-7.36 (m, 2 H, HC(7)), 7.33-7.30 (m, 2 H, HC(8)), 7.26-7.23 (m, 1 H, HC(9)), 6.68 (dd, *J* = 15.9, 1.2, 1 H, HC(5)), 6.22 (dd, *J* = 15.9, 5.9, 1 H, HC(4)), 4.56 (ddd, *J* = 5.9, 3.4, 1.2, 1 H, HC(3)), 4.28 (d, *J* = 3.4, 1 H, HC(2)), 3.76 (s, 3 H, HC(10)), 2.64 (bs, 1 H, OH), 0.92 (s, 9 H, HC(13)), 0.12 (s, 3 H, HC(11)), 0.06 (s, 3 H, HC(11))

^{13}C NMR: (126 MHz, $CDCl_3$)

171.9 (C(1)), 136.4 (C(6)), 131.8 (C(5)), 128.6 (C(8)), 128.0 (C(4) or C(9)), 127.8 (C(4) or C(9)), 126.5 (C(7)), 75.4 (C(2)), 74.1 (C(3)), 52.1 (C(10)), 25.6 (C(13)), 18.3 (C(12)), −5.0 (C(11)), −5.4 (C(11))

IR: (neat)

3505 (br), 3027 (w), 2953 (m), 2930 (m), 2887 (m), 2857 (m), 1759 (s), 1496 (m), 1472 (m), 1463 (m), 1449 (m), 1437 (m), 1389 (m), 1362 (m), 1257 (s), 1203 (m), 1143 (s), 1044 (m), 1007 (m), 968 (m), 864 (s), 837 (s), 781 (s), 746 (m), 694 (m)

MS: (ESI)

177.1 (10), 187.1 (8), 319.2 (100), 320.2 (9), 354.2 (19), 359.2 (M^++Na, 19)

HRMS: calcd for $C_{18}H_{28}O_4SiNa$: 359.1655, found 359.1646

TLC: R_f 0.28 (hexane/EtOAc, 5/1) [UV(254)/$KMnO_4$]

SFC: (2*R*,3*S*,4*E*)-**4ch**, t_R 4.29 min (97.4%); (2*S*,3*R*,4*E*)-**4ch**, t_R 5.46 min (2.6%) (Chiralpak AS, 125 bar, 40 °C, 1.0% MeOH in CO_2, 2.5 mL/min, 220 nm)

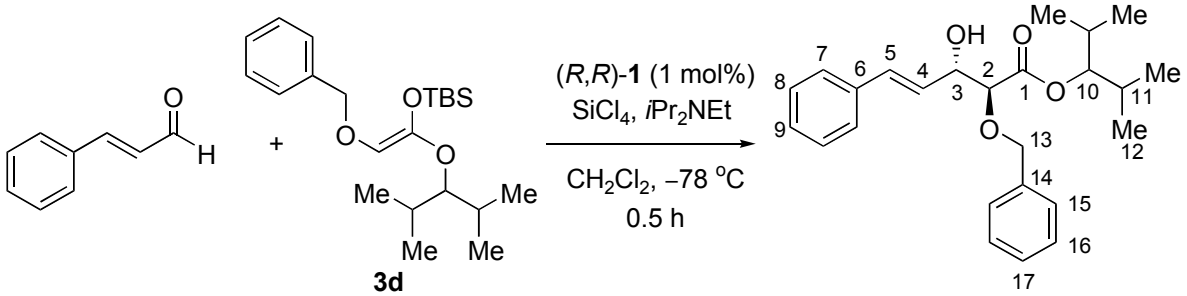
Opt. Rot.: $[\alpha]_D^{24}$ 5.7 (c = 4.5, EtOH)

Analysis: $C_{18}H_{28}O_4Si$ (336.50)

Calcd: C, 64.25%; H, 8.39%

Found: C, 64.31%; H, 8.52%

Preparation of (2*S*,3*S*,4*E*)-3-Hydroxy-5-phenyl-2-(phenylmethoxy)-4-pentenoic Acid 2-Methyl-1-(1-methylethyl)propyl Ester ((2*S*,3*S*,4*E*)-4dh) (Scheme 4)



Following General Procedure 5, (*R*,*R*)-**1** (8.4 mg, 0.01 mmol, 0.01 equiv) was combined with (*E*)-cinnamaldehyde (126 μL, 1.0 mmol), diisopropylethylamine (17.4 μL, 0.1 mmol, 0.1 equiv), $SiCl_4$ (126 μL, 1.1 mmol, 1.1 equiv), and **3d** (454 mg, 1.2 mmol, 1.2 equiv) to yield, after column chromatography (22 mm diam., hexane/EtOAc, 10/1 to 5/1) on silica gel (20 g), **4dh** (358 mg, 90%) as a colorless oil. The *syn*/*anti* ratio of **4dh** was determined to be 1/99 by ^{1}H NMR (500 MHz) analysis of the crude reaction mixture.

Data for (2*S*,3*S*,4*E*)-**4dh**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.38-7.29 (m, 9 H, HC(7), HC(8), HC(15), HC(16), HC(17)), 7.25-7.22 (m, 1 H, HC(9)), 6.69 (dd, *J* = 15.9, 1.2, 1 H, HC(5)), 6.30 (dd, *J* = 15.9, 6.6, 1 H, HC(4)), 4.89 (d, *J* = 11.6, 1 H, HC(13)), 4.74 (dd, *J* = 6.2, 6.2, 1 H, HC(10)), 4.65 (ddd, *J* = 6.6, 4.8, 1.2, 1 H, HC(3)), 4.51 (d, *J* = 11.6, 1 H, HC(13)), 4.14 (d, *J* = 4.8, 1

H, HC(2)), 2.59 (bs, 1 H, OH), 1.98-1.89 (m, 2 H, HC(11)), 0.90 (d, J = 6.8, 6 H, HC(12)), 0.88 (d, J = 6.8, 6 H, HC(12))

^{13}C NMR: (126 MHz, $CDCl_3$)

170.3 (C(1)), 137.1 (C(14)), 136.5 (C(6)), 132.9 (C(5)), 128.5 (C(8), C(15), or C(16)), 128.4 (C(8), C(15), or C(16)), 128.2 (C(8), C(15), or C(16)), 128.1 (C(9) or C(17)), 127.7 (C(9) or C(17)), 126.7 (C(4)), 126.6 (C(7)), 84.3 (C(10)), 81.1 (C(2)), 73.03 (C(3) or C(13)), 73.00 (C(3) or C(13)), 29.4 (C(11)), 29.3 (C(11)), 19.6 (C(12)), 19.5 (C(12)), 17.4 (C(12)), 17.3 (C(12))

IR: (neat)

3447 (br), 3027 (m), 2965 (s), 2935 (s), 2875 (m), 1734 (s), 1496 (m), 1453 (m), 1338 (m), 1371 (m), 1272 (m), 1202 (s), 1129 (s), 1097 (s), 1028 (m), 1000 (m), 967 (s), 893 (m), 749 (s), 695 (s)

MS: (ESI)

281.1 (17), 419.2 (M^++Na, 100), 420.2 (27), 498.3 (15)

HRMS: calcd for $C_{25}H_{32}O_4Na$: 419.2198, found 419.2192

TLC: R_f 0.32 (hexane/EtOAc, 5/1) [UV(254)/$KMnO_4$]

SFC: (2*S*,3*S*,4*E*)-**4dh**, t_R 4.21 min (98.0%); (2*R*,3*R*,4*E*)-**4dh**, t_R 4.89 min (2.0%) (Chiralcel OD, 125 bar, 40 ^oC, 10.0% MeOH in CO_2, 3.0 mL/min, 220 nm)

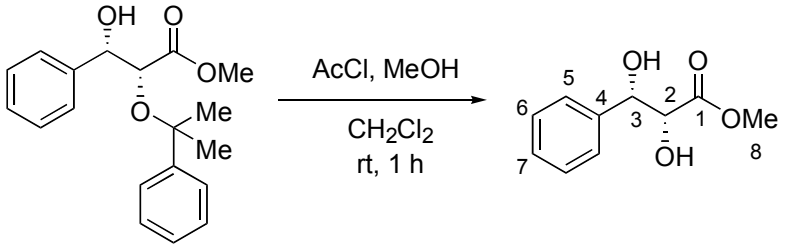
Opt. Rot.: $[\alpha]_D^{24}$ –9.9 (c = 2.0 , EtOH)

Analysis: $C_{25}H_{32}O_4$ (396.52)

Calcd:	C, 75.73%;	H, 8.13%
Found:	C, 75.74%;	H, 8.03%

Determination of Absolute Configurations

Preparation of (2*R*,3*S*)-1,2-Dihydroxy-3-phenylpropanoic Acid Methyl Ester[4] ((2*R*,3*S*)-5)



4aa (2*R*,3*S*)-**5**

To a flame-dried, 5-mL, 2-necked round-bottomed flask fitted with a magnetic stir bar, a gas inlet tube, and a septum were added CH_2Cl_2 (1 mL), acetyl chloride (69 μL, 0.966 mmol, 1.1 equiv), and MeOH (39 mL, 0.966 mmol 1.1 equiv). The resulting solution was transferred via cannula to a stirred solution of **4aa** (276 mg, 0.878 mmol) in CH_2Cl_2 (3 mL) in 10-mL 2-necked round-bottomed flask fitted with a magnetic stir bar, a gas inlet tube, and a septum at rt. After 1h, the reaction mixture was transferred to a 125-mL separatory funnel where the reaction was quenched with sat. aq. $NaHCO_3$ solution (20 mL). The organic layer was separaed. The aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were dried over Na_2SO_4 (5 g), filtered, and concentrated *in vacuo* (23 °C, 30 mmHg). The residue was purified by column chromatography (22 mm diam., hexane/EtOAc, 1/1) on silica gel (15 g) to give **5** (161 mg, 93%) as white crystals.

Data for (2*R*,3*S*)-**5**:

^{1}H NMR: (500 MHz, $CDCl_3$)

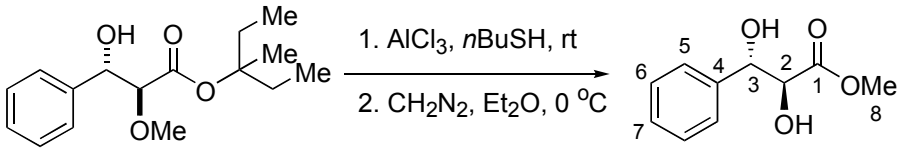
7.42-7.36 (m, 4 H, HC(5), HC(6)), 7.34-7.30 (m, 1 H, HC(7)), 5.03 (d, J = 2.9, 1 H, HC(3)), 4.38 (d, J = 2.9, 1 H, HC(2)), 3.82 (s, 3 H, HC(8)), 3.08 (bs, 1 H, OH), 2.70 (bs, 1 H, OH)

TLC: R_f 0.31 (hexane/EtOAc,1/1) [UV(254)/$KMnO_4$]

Opt. Rot.: $[\alpha]_D^{24}$ 7.9 (c = 1.0, EtOH)

lit. $[\alpha]_D^{24}$ 8.2 (c = 1.1, EtOH) for (2*R*,3*S*)-**5**[4]

Preparation of (2*S*,3*S*)-1,2-Dihydroxy-3-phenylpropanoic Acid Methyl Ester[5] ((2*S*,3*S*)-6)



4ab (2*S*,3*S*)-**6**

To a flame-dried, 5-mL, 2-necked round-bottomed flask fitted with a magnetic stir bar, a gas inlet tube, and a septum were added $AlCl_3$ (309 mg, 2.318 mmol, 5.0 equiv) and *n*BuSH (1 mL, 9.336 mmol, 20 equiv). To the solution was added a solution of **4ab** (130 mg, 0.464 mmol) in *n*BuSH (1 mL, 9.336 mmol, 20 equiv) via syringe at rt. After 24 h, the reaction mixture was transferred to a 50-mL separatory funnel and was diluted with CH_2Cl_2 (10 mL) and 1*N* aq. HCl solution (10 mL). The organic layer was separaed. The aqueous layer was extracted with EtOAc (8 × 10 mL). The combined organic extracts were dried over Na_2SO_4 (3 g), filtered, and concentrated *in vacuo* (23 °C, 30 mmHg). The residue dissolved in Et_2O (1 mL) and placed in the receiving flask of Aldrich mini diazald® apparatus. The solution was cooled to 0 °C in an ice-water bath. CH_2N_2 (ca. 23.4 mg, 0.557 mmol, 1.2 equiv), which was generated according to Aldrich tech note AL-180 (70% yield was assumed), was distilled to the receiving flask over 10 min. The excess CH_2N_2 was quenched by acetic acid (1*N* in Et_2O, 0.5 mL). The resulting solution was transferred to a 50-mL separatory funnel and was washed with sat. aq. $NaHCO_3$ solution (3 × 5 mL), dried over Na_2SO_4 (2 g), filtered, and concentrated *in vacuo* (23 °C, 30 mmHg). The residue was purified by column chromatography (18 mm diam., hexane/EtOAc, 2/1 to 1/1) on silica gel (10 g) to give **6** (48 mg, 53% for two steps) as white crystals.

Data for (2*S*,3*S*)-**6**:

^{1}H NMR: (500 MHz, $CDCl_3$)

7.37-7.34 (m, 2 H, HC(5)), 7.32-7.29 (m, 3 H, HC(6), HC(7)), 5.01 (d, J = 4.3, 1 H, HC(3)), 4.50 (d, J = 4.3, 1 H, HC(2)), 3.69 (s, 3 H, HC(8)), 2.94 (bs, 2 H, OH)

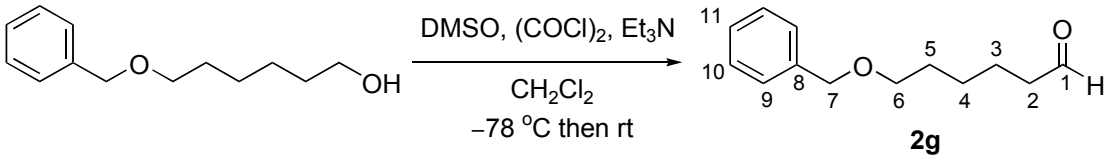
TLC: R_f 0.27 (hexane/EtOAc, 1/1) [UV(254)/$KMnO_4$]

Opt. Rot.: $[\alpha]_D^{24}$ 51.0 (c = 1.0, $CHCl_3$)

lit. $[\alpha]_D^{24}$ 36.1 (c = 0.72, $CHCl_3$) for (2*S*,3*S*)-**6**[5]

Miscellaneous

Preparation of 6-(Phenylmethoxy)hexanal[6] (2g)



2g

To a flame-dried, 500-mL, 3-necked round-bottomed flask fitted with a magnetic stir bar, a thermocouple, a gas inlet tube, and a septum was added CH_2Cl_2 (100 mL). The solution was cooled to –78 °C (internal temp.) in a dry ice-acetone bath prior to addition of $(COCl)_2$ (2.058 mL, 24 mmol, 1.2 equiv). While the internal temperature was maintained below –65 °C, DMSO (3.409 mL, 48 mmol, 2.4 equiv) was added dropwise via syringe over 10 min. To the resulting solution was added 6-(phenylmethoxy)hexanol (4.166 g, 20 mmol) dropwise via syringe over 5 min while the internal temperature was maintained below –70 °C. After 30 min, Et_3N (11.15 mL, 80 mmol, 4.0 equiv) was added dropwise via syringe over 5 min while the internal temperature was maintained below -68 °C. The dry ice-acetone bath was removed and the reaction mixture was allowed to warm to rt over 15 min. The reaction mixture was diluted with Et_2O (100 mL),

filtered through $MgSO_4$ (10 g), and concentrated *in vacuo* (23 °C, 30 mmHg). The resulting material was diluted with Et_2O (10 mL), filtered, and concentrated *in vacuo* (23 °C, 30 mmHg). The residue was purified by column chromatography (55 mm diam., hexane/EtOAc, 10/1 to 5/1) on silica gel (100 g) and distillation through a 5-cm Vigreux column under reduced pressure to give **2g** (3.345 g, 81%) as a colorless oil.

Data for **2g**:

bp: 95-96 °C (0.2 mmHg)

^{1}H NMR: (500 MHz, $CDCl_3$)

9.75 (t, *J* = 1.7, 1 H, HC(1)), 7.37-7.32 (m, 4 H, HC(9), HC(10)), 7.31-7.27 (m, 1 H, HC(11)), 4.50 (s, 2 H, HC(7)), 3.47 (t, *J* = 6.5, 2 H, HC(6)), 2.43 (td, *J* = 7.3, 1.7, 2 H, HC(2)), 1.68-1.61 (m, 4 H, HC(3), HC(5)), 1.45-1.39 (m, 2 H, HC(4))

^{13}C NMR: (126 MHz, $CDCl_3$)

202.7 (C(1)), 138.5 (C(8)), 128.3 (C(10)), 127.6 (C(9)), 127.5 (C(11)), 72.8 (C(7)), 69.9 (C(6)), 43.7 (C(2)), 29.4 (C(5)), 25.7 (C(4)), 21.8 (C(3))

IR: (neat)

3426 (w), 3064 (m), 3031 (m), 2938 (s), 2860 (s), 2721 (m), 1724 (s), 1496 (m), 1479 (m), 1454 (s), 1410 (m), 1391 (m), 1364 (m), 1310 (m), 1250 (m), 1205 (m), 1175 (m), 1100 (s), 1028 (m), 1001 (m), 909 (m), 819 (m), 737 (s), 699 (s), 611 (m)

MS: (EI, 70 eV)

55.0 (7), 57.0 (3), 65.0 (9), 67.1 (2), 69.1 (7), 77.0 (4), 79.0 (9), 81.0 (3), 82.0 (3), 91.0 (100), 92.1 (27), 97.1 (5), 99.1 (3), 100.1 (4), 105.1 (2), 107.1 (41), 108.1 (7), 115.1 (4), 206.1 (M^+, 2)

HRMS: calcd for $C_{13}H_{18}O_2$: 206.1307, found 206.1297

TLC: R_f 0.27 (hexane/EtOAc, 10/1) [UV(254)/$KMnO_4$]

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