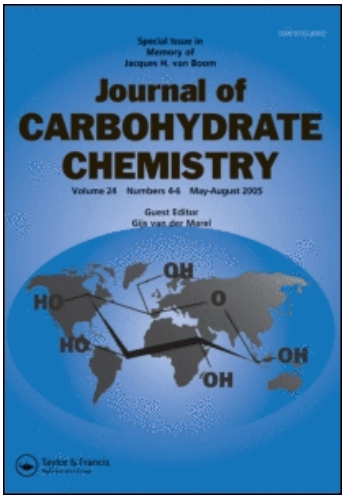

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SYNTHESIS OF A MEVINIC ACID LACTONE PRECURSOR

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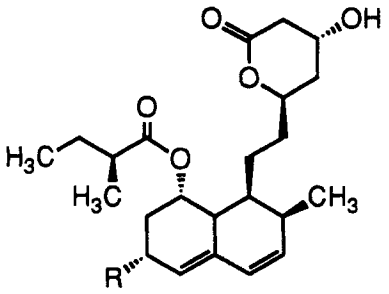
ABSTRACT

A synthesis of (*S*)-1-phenyl-2-(*tert*-butyldiphenylsilyloxy)ethyl (2*R*,4*R*,6*S*)-4-*tert*-butyldiphenylsilyloxy-6-hydroxymethyl-3,4,5,6-tetrahydro-2*H*-pyran-2-yl ether, a potentially valuable precursor to the mevinic acid lactone, is described. The synthesis begins with commercially available racemic sodio-3,4-dihydro-2*H*-pyran-2-carboxylate and utilizes a chromatographic resolution of diastereomeric (*S*)-methyl mandelyl pyranosides and a directed epoxidation. The overall yield, 21% over 10 steps, is competitive with routes from carbohydrates to comparable mevinic acid lactone precursors.

INTRODUCTION

The mevinic acids compactin (1) and mevinolin (2) are compounds of fungal origin[1-4] which possess remarkable inhibitory activity toward HMG CoA reductase, the enzyme which catalyzes the rate-limiting and committed step in the terpene biosynthetic pathway.[5] Studies subsequent to the isolation and characterization of 1 and 2 have demonstrated that certain analogues (e.g., 3 and 4) which possess the β-hydroxy-δ-lactone subunit can exhibit biological activities comparable to those of the natural mevinic acids.[6] Given the potential for therapeutic use in human medicine,[7] there continues to be much interest in the development of synthetic approaches to mevinic acid lactone precursors and related compounds.[8,9]



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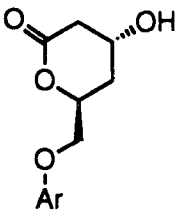
2 R = CH_3



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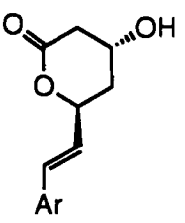

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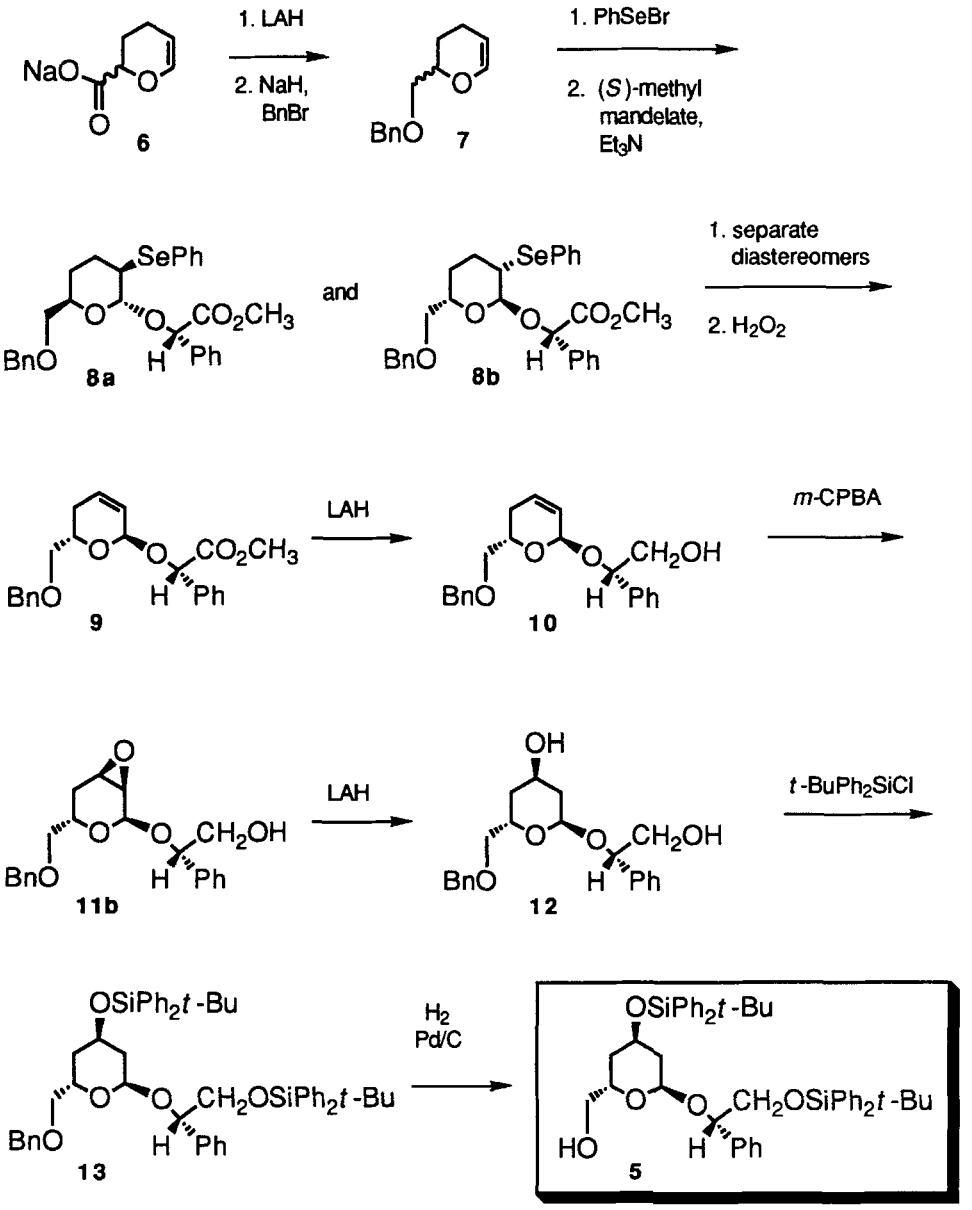
Recently we reported an enantioselective approach to carbohydrates and their derivatives via a general chromatographic resolution of diastereomeric furanoside and pyranoside acetals derived from α-hydroxy esters.[10,11] We herein describe a synthesis of mevinic acid lactone precursor **5** (Scheme I), which can be considered a 2,4-dideoxyhexopyranoside derivative.

RESULTS AND DISCUSSION

Reduction of the sodium salt of racemic 3,4-dihydro-2*H*-pyran-2-carboxylic acid (**6**)[12] using lithium aluminum hydride in tetrahydrofuran and subsequent *O*-benzylation provided the known[13] racemic 3,4-dihydro-2*H*-pyran **7** in 77% yield after vacuum distillation. Reaction of **7** with benzeneselenyl bromide in dichloromethane at -78 °C, followed by addition of a precooled solution of (*S*)-(+)-methyl mandelate and triethylamine in the same solvent, produced chromatographically separable (α = 1.54) diastereomers **8a** and **8b** in 34% and 39% yields, respectively. Structural assignments were based upon previous studies of alkoxyselenations of 3,4-dihydro-2*H*-pyrans[10,14] and upon conversion of the more polar diastereomer **8b** to **5** as described below.

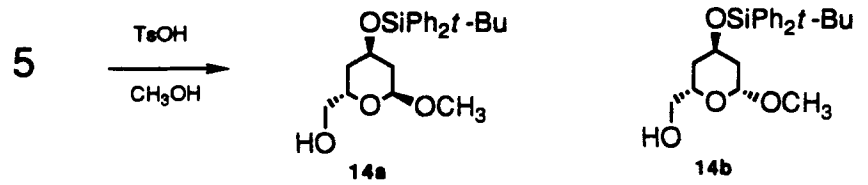
Oxidation of **8b** with hydrogen peroxide produced, via the corresponding selenoxide, the 5,6- dihydro-2*H*-pyranoside **9** in 89% yield (Scheme I). Reduction of this ester using $LiAlH_4$ in THF at 0 °C gave alcohol **10** in 95% yield. Treatment of **10** with *m*-chloroperoxybenzoic acid in dichloromethane at 0 °C provided separable (α = 1.24) diastereomeric epoxides **11a** and **11b** in 7% and 88% yields, respectively. Reductive opening of epoxide **11b** using $LiAlH_4$ in THF at 0 °C occurred regioselectively at C-2 to give diol **12** in 94% yield. Silylation with two equivalents of *t*-butyldiphenylchlorosilane gave in quantitative yield pyranoside acetal **13** having three differentially protected oxygen functionalities: benzyl ether, silyl ether, and acetal. Removal of the

Scheme I. Synthesis of Mevinic Acid Lactone Precursor **5**



benzyl ether using hydrogen and a palladium catalyst afforded the mevinic acid lactone precursor **5** in 99% yield.

The relative and absolute stereochemistries assigned to **5** were confirmed by acid-catalyzed methanolysis to a mixture of **14a** and **14b**, which have previously been prepared from D-glucose and have been utilized in syntheses of several mevinic acid analogues.[15]



The above synthesis demonstrates a potential for our diastereomer resolution/appendage-directed functionalization methodology[10,11] for syntheses of deoxy, branched, and/or heteroatom-containing hexopyranose derivatives. Further synthetic uses for the acetals made available by this methodology will be reported in future papers.

EXPERIMENTAL

Dichloromethane was distilled from calcium hydride. Diethyl ether and tetrahydrofuran were distilled from sodium benzophenone ketyl under an inert atmosphere. Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 250 and 62.9 MHz, respectively. Thin-layer chromatographic analyses were performed on Merck silica gel 60 plates (0.25mm, 70-230 mesh ASTM). Column chromatography was performed on Merck silica gel 60 (gravity driven, 70-230 mesh ASTM).

2-(Phenylmethoxy)methyl-3,4-dihydro-2H-pyran (7). To a suspension of $LiAlH_4$(1.90 g, 50 mmol) in dry THF (75 mL) at 0 °C was added sodium 3,4-dihydro-2*H*-pyran-2-carboxylate **6** (10.0 g, 66.6 mmol) in portions. The reaction was allowed to stir at ambient temperature for 2h and then quenched by successive additions of H_2O (1.9 mL), 10% NaOH (1.9 mL), and H_2O (5.7mL) while stirring vigorously. Filtration through Celite and removal of volatiles *in vacuo* gave a pale yellow oil (7.47 g, 65.4 mmol, 98%) that was used without further purification.

To a suspension of NaH (3.46 g, 74 mmol) in dry THF (75 mL) at 0 °C was added dropwise a solution of the above alcohol in THF (75 mL). The reaction was stirred for 1 h at room temperature, then benzyl bromide (7.8 mL, 65.4 mmol) was added and the mixture stirred for 2h. The reaction was quenched by careful addition of H_2O (100

mL), then extracted with ether (3 x 50 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. Anhydrous K_2CO_3 (1g) was added and the residue was distilled to afford the product 7 as a pale yellow oil, bp 2 mm 127-129 °C (9.56 g, 50.25 mmol, 77% yield over two steps). Spectral data for 7: IR ($CHCl_3$) cm^{-1} 1647, 1494, 1451, 1363, and 1240; ^1H NMR ($CDCl_3$) δ 1.59-2.17 (4, m), 3.48-3.63 (2, m) 3.97-4.07 (1, m), 4.58 (2, d,J=2.6 Hz), 4.63-4.70 (1, m), 6.39 (1, d,J=6.2Hz), and 7.23-7.40 (5, m); ^{13}C NMR ($CDCl_3$) δ 19.30(CH_2), 24.51 (CH_2), 72.39 (CH_2), 73.35 (CH_2), 74.00 (CH), 100.40 (CH), 127.58 (CH), 127.66 (CH), 128.32 (CH), 138.05 (C), and 143.54 (CH).

(S)-MethylMandelyl6-(Phenylmethoxy)methyl-3-phenylselenyl-3,4,5,6-tetrahydro-2H-pyran-2-yl Ethers 8a and 8b. Bromine (0.22 mL, 0.68 g, 4.25 mmol) was added dropwise to a solution of diphenyl diselenide (1.325 g, 4.245 mmol) in dry CH_2Cl_2 (10 mL) and the resulting mixture was then added dropwise via cannula to a solution of 6-benzyloxymethyl-3,4-dihydro-2*H*-pyran 7 (1.617 g, 8.50 mmol) in CH_2Cl_2 (10 mL) at -78 °C. Decolorization occurred instantly. The mixture was stirred for 0.5 h, then a precooled (-78°C) solution of (*S*)-(+)-methyl mandelate (1.41 g, 8.50 mmol) and triethylamine (1.30 mL, 0.94 g, 9.35 mmol) in CH_2Cl_2 (10 mL) was added rapidly. The mixture was allowed to warm to room temperature and was stirred for 24 h. The reaction mixture was washed with H_2O, saturated aq. $NaHCO_3$, saturated aq. NaCl, dried (Na_2SO_4), filtered, and volatiles removed *in vacuo*. The residue was chromatographed on silica gel 60 (300 g) eluted with 10% ethyl acetate/hexanes, affording 1.525 g (2.90 mmol, 34%) of the less polar diastereomer **8a** (R_f 0.17, 10% EtOAc/hexanes), and 1.756 g (3.34 mmol, 39%) of the more polar diastereomer **8b** (R_f 0.11).

Spectral data for **8a**: an oil, $[\alpha]_D$-29.8° (*c* 0.7, $CHCl_3$); IR ($CHCl_3$) cm^{-1} 1744; ^1H NMR ($CDCl_3$) δ 1.25-1.98 (3, m), 2.41 (1, tt, J=13, 4Hz), 3.38 (1, dd, J=10, 4Hz), 3.50 (1, dd, J=10, 6Hz), 3.62-3.70 (1, m), 3.63 (3, s), 3.84 (1, m), 4.53 (2, d, J=2Hz), 5.26 (1, s), 5.33 (1, s), and 7.24-7.61 (15, m); ^{13}C NMR ($CDCl_3$), δ 23.51 (CH_2), 23.80 (CH_2), 43.30 (CH), 52.18 (CH_3), 68.97 (CH), 73.03 (CH_2), 73.19 (CH_2), 75.59 (CH), 98.67 (CH), 127.29 (CH), 127.38 (CH), 127.46 (CH), 128.28 (CH), 129.11 (CH), 129.84 (C), 133.43 (CH), 136.34 (C), 138.35 (C), and 171.31 (C).

Spectral data for **8b:** an oil, $[\alpha]_D$+83.8° (*c* 0.7, $CHCl_3$); IR ($CHCl_3$) cm^{-1} 1749; ^1H NMR ($CDCl_3$) δ 1.60-2.10 (3, m), 2.62 (1, tt, J=13, 4Hz), 3.50-3.67 (3, m), 3.71 (3, s), 4.26 (1, m), 4.67 (2, s), 5.03 (1, s) 5.28 (1, s), 5.28 (1, s), and 7.19-7.48 (15, m); ^{13}C NMR ($CDCl_3$) δ 23.62 (CH_2), 23.94 (CH_2), 29.63 (CH), 43.39 (CH), 52.21 (CH_3), 68.93 (CH), 73.09 (CH_2), 73.21 (CH_2), 76.73 (CH), 97.91 (CH), 127.24 (CH), 127.46 (CH), 128.27 (CH), 128.58 (CH), 128.70 (CH), 129.02 (CH), 129.61 (C), 133.33 (CH), 135.69 (C), 138.40 (C), and 170.77 (C).

(S)-Methyl Mandelyl (2R,6S)-6(Phenylmethoxy)methyl-5,6-dihydro-2H-pyran-2-yl Ether (9). To a solution of the more polar selenide **8b** (1.449 g, 2.757 mmol) and pyridine (400 μL, 391 mg, 5 mmol) in CH_2Cl_2 (10 mL) was added dropwise 30% H_2O_2 (680 μL, 755 mg, 6.62 mmol) diluted with additional H_2O (680 μL). The resulting mixture was stirred at ambient temperature for 48 h, then diluted with CH_2Cl_2 (100 mL), washed with saturated $NaHCO_3$, saturated NaCl, dried (Na_2SO_4), filtered, and volatiles removed *in vacuo*. The residue was chromatographed on silica gel 60 (200 g) eluted with 20% ethyl acetate/hexanes, affording 905 mg (2.456 mmol, 89%) of **9** (R_f 0.24, 20% EtOAc/hexanes), mp 57-58 °C.

Spectral data for **9**: $[\alpha]_D$+63.2°(*c* 1.3, $CHCl_3$); IR ($CHCl_3$) cm^{-1} 1747;^{1}H NMR ($CDCl_3$) δ 1.92-2.06 (1, m), 2.16-2.34 (1, m) 3.54 (2,d,J=4Hz), 3.61 (3, s), 4.27 (1, m), 4.60 (2,d,J=4Hz), 5.04 (1, bs), 5.27 (1, s), 5.75 (1, dm,J=10Hz), 6.07 (1,dd,J=10, 6Hz), and 7.23-7.50 (10, m); ^{13}C NMR ($CDCl_3$) δ 26.59 (CH_2), 52.07 (CH_3), 66.11 (CH), 71.97 (CH_2), 73.18 (CH_2) 77.68 (CH), 94.02 (CH), 124.52 (CH), 127.29 (CH), 127.49 (CH), 128.26 (CH), 128.53 (CH), 128.66 (CH), 129.39 (CH), 136.22 (C), 138.19 (C), and 171.28 (C).

Anal. Calcd for $C_{22}H_{24}O_5$: C, 71.72; H, 6.57. Found: C, 72.10; H, 6.61.

(S)-1-Phenyl-1-hydroxyethyl (2R, 6S)-6-(Phenylmethoxy)methyl-5,6-dihydro-2H-pyran-2-yl Ether (10). To a suspension of $LiAlH_4$ (92 mg, 2.4 mmol) in dry THF (5 mL) at 0 °C was added a solution of **9** in THF (5 mL) dropwise via cannula. The reaction was stirred for 0.5 h, then quenched by successive additions of H_2O (92μL), 10% NaOH (92μL), and H_2O (276μL) while stirring vigorously. The mixture was filtered through Celite using EtOAc (100 mL) and volatiles removed in vacuo. The residue was chromatographed on silica gel 60 (100 g) eluted with 30% ethyl acetate/hexanes to afford 747 mg (2.194 mmol, 95%) of **10** (R_f 0.22, 30% EtOAc/hexanes).

Spectral data for **10**: an oil, $[\alpha]_D$+58.8°(*c* 1.1, $CHCl_3$); IR ($CHCl_3$) cm^{-1} 3580, 3472; ^{1}H NMR ($CDCl_3$) δ 1.88-2.18 (2, m), 2.96 (1, bs), 3.58 (2,d,J=5Hz), 3.68-3.80 (2, m), 4.32 (1, m), 4.63 (2, s), 4.91 (1,dd,J=7, 4Hz), 5.01 (1, bs), 5.72 (1, dm,J=10Hz), 6.03 (1,dd, J=10, 5Hz) and 7.22-7.45 (10, m); ^{13}C NMR ($CDCl_3$) δ 26.63 (CH_2), 66.44 (CH), 67.57 (CH_2), 72.18 (CH_2), 73.32 (CH_2), 80.99 (CH), 93.20 (CH), 125.52 (CH), 126.79 (CH), 127.66 (CH), 127.87 (CH), 128.35 (CH), 128.40 (CH), 128.58 (CH), 137.95 (C), and 138.89 (C).

(S)-1-Phenyl-2-hydroxyethyl(2R,3R,4R,6S)-3,4-Epoxy-6-(phenylmethoxy)methyl-3,4,5,6- tetrahydro-2H-pyran-2-yl Ether (11b). To a solution of **10** (675 mg, 1.98 mmol) in dry CH_2Cl_2 (40 mL) at 0 °C was added 50% *m*CPBA (821 mg, 2.38 mmol active) in portions. The reaction was maintained at 0-5 °C for 8 days, then washed with 10% aq.Na_2CO_3 (50 mL), the aqueous layer extracted with CH_2Cl_2 (3 x 25 mL), the combined organic extracts dried (Na_2SO_4), filtered, and volatiles removed *in vacuo*. The residue was chromatographed on silica gel 60 (200 g) eluted with 50% ethyl acetate/hexanes to

afford 53 mg (0.15 mmol, 7%) of the less polar diastereomer **11a** (R_f 0.21, 50% EtOAc/hexanes) and 624 mg (1.751 mmol, 88%) of the more polar diastereomer **11b** (R_f 0.17).

Spectral data for the less polar epoxide **11a**; an oil, $[\alpha]_D$+99.8°(*c* 2.4,$CHCl_3$); IR ($CHCl_3$) cm^{-1} 3477; ^1H NMR ($CDCl_3$) δ 1.72-1.98 (2, m) 2.90 (1, bs), 3.01 (1,d,J=4Hz), 3.32-3.50 (3, m), 3.66-3.78 (2, m), 4.27 (1, sextet, J=5Hz), 4.58 (2,d,J=3Hz), 4.89 (1,dd,J=7, 4Hz), 5.02 (1, s) and 7.24-7.40 (10, m); ^{13}C NMR ($CDCl_3$) δ 25.16 (CH_2), 49.15 (CH), 49.86 (CH), 63.89 (CH), 67.15 (CH_2), 71.84 (CH_2), 73.29 (CH_2), 80.94 (CH), 93.41 (CH), 126.86 (CH), 127.49 (CH), 127.64 (CH), 128.11 (CH), 128.34 (CH), 128.47 (CH), 137.72 (C), and 138.02 (C).

Spectral data for the more polar epoxide **11b**; an oil,$[\alpha]_D$+121.5°(*c* 0.5,$CHCl_3$); IR ($CHCl_3$) cm^{-1} 3488, 1492, 1452;^1H NMR ($CDCl_3$) δ 1.76-2.05 (2,m), 2.98 (1, bs), 3.26 (1,t,J=4Hz), 3.38-3.85 (5, m), 4.19 (1, m), 4.59 (2,d,J=2Hz), 4.91 (1.dd,J=8, 3Hz), 5.03 (1,d,J=3Hz), and 7.24-7.42 (10, m); ^{13}C NMR ($CDCl_3$) δ 26.78 (CH_2), 50.67 (CH), 51.32 (CH), 64.26 (CH), 67.26 (CH_2), 71.91 (CH_2), 73.19 (CH_2), 80.14 (CH), 92.29 (CH), 126.96 (CH), 127.61 (CH), 128.04 (CH), 128.34 (CH), 128.44 (CH), 137.87 (C), and 138.34 (C).

Anal. Calcd for $C_{21}H_{24}O_5$: C, 70.77; H, 6.79. Found: C, 70.47; H, 6.91.

(S)-1-Phenyl-2-hydroxyethyl (2R,4R,6S)-4-Hydroxy-6-(phenylmethoxy)methyl-3,4,5,6-tetrahydro-2H-pyran-2-yl Ether (12). To a suspension of $LiAlH_4$ (75 mg, 1.97 mmol) in dry THF (3 mL) at 0 °C was added a solution of **11b** (600 mg, 1.683 mmol) in THF (3 mL) dropwise via cannula. The reaction was stirred 4 h at this temperature and then quenched by successive additions of H_2O (75 μL), 10% NaOH (75 μL), and water (225 μL) while stirring vigorously. The mixture was filtered through Celite using EtOAc (100 mL) and volatiles removed *in vacuo*. The residue was chromatographed on silica gel 60 (100 g) eluted with 75% ethyl acetate/hexanes to afford 566 mg (1.579 mmol, 94%) of **12** (R_f 0.38, EtOAc).

Spectral data for **12**: an oil, $[\alpha]_D$+140.2°(*c* 1.2, $CHCl_3$); IR ($CHCl_3$) cm^{-1} 3472; ^1H NMR ($CDCl_3$) δ 1.62-2.04 (4, m), 3.45-3.82 (5, m), 4.00 (1, bs), 4.13 (1, bs), 4.52-4.66 (3,m), 4.85 (1,dd,J=8, 3Hz), 4.93 (1, bs), and 7.22-7.37 (10, m); ^{13}C NMR ($CDCl_3$) δ 34.08 (CH_2), 63.09 (CH), 63.81 (CH), 66.88 (CH_2), 72.94 (CH_2), 73.19 (CH_2), 79.15 (CH), 95.08 (CH), 126.91 (CH), 127.05 (CH), 127.52 (CH), 128.07 (CH), 128.27 (CH), 128.43 (CH), 137.74 (C), and 138.10 (C).

(S)-1-Phenyl-2(tert-butyldiphenylsilyloxy)ethyl (2R,4R,6S)-4-tert-Butyldiphenylsilyloxy-6-(phenylmethoxy)methyl-3,4,5,6-tetrahydro-2H-pyran-2-yl Ether (13). To a solution of **12** (565 mg, 1.576 mmol) and imidazole (452 mg, 6.636 mmol) in dry DMF (3 mL) was added *t*-butyldiphenylchlorosilane (822 μL, 869 mg, 3.161 mmol) dropwise. The reaction was stirred at ambient temperature for 72 h, then diluted with ether (100 mL),

washed with H_2O, brine, dried (Na_2SO_4), filtered, and volatiles removed *in vacuo*. The residue was chromatographed on silica gel 60 (100 g) eluted with 10% ethyl acetate/hexanes to afford 1.316 g (1.576 mmol, 100%) of **13** (R_f 0.48, 20% EtOAc/hexanes).

Spectral data for **13**: an oil, $[\alpha]_D$+57.4°(*c* 1.1,$CHCl_3$); IR ($CHCl_3$) cm^{-1} 1470, 1426, 1111; ^1H NMR ($CDCl_3$) δ 0.96 (8, s), 1.03 (8, s), 1.07 (2, s), 1.52-1.78 (4, m), 3.39 (1,dd,J=10, 5 Hz), 3.49 (1,dd,J=10, 4Hz), 3.69 (1,dd,J=10, 7Hz), 4.05-4.16 (2, m), 4.54 (2,dd,J=20, 12Hz), 4.63 (1, m), 4.74 (1,d,J=4Hz), 4.89 (1,t,J=6Hz), and 7.22-7.78 (30, m); ^{13}C NMR ($CDCl_3$) δ 19.10 (C), 26.53 (CH_3), 26.78 (CH_3), 26.86 (CH_3), 34.89 (CH_2), 35.88 (CH_2), 63.30 (CH), 64.60 (CH), 68.21 (CH_2), 73.10 (CH_2), 73.23 (CH_2), 78.32 (CH), 94.55 (CH), 127.41 (CH), 127.52 (CH), 127.69 (CH), 127.75 (CH), 128.00 (CH), 128.26 (CH), 129.38 (CH), 129.46 (CH), 129.61 (CH), 133.46 (C), 133.60 (C), 134.13 (C), 134.49 (C), 134.76 (CH), 135.46 (CH), 135.58 (CH), 135.73 (CH), 135.94 (CH), 138.46 (C), and 140.30 (C).

(S)-1-Phenyl-2-(tert-butyldiphenylsilyloxy)ethyl(2R,4R,6S)-4-tert-Butyldiphenylsilyloxy-6-hydroxymethyl-3,4,5,6-tetrahydro-2H-pyran-2-yl Ether (5). A mixture of **13** (195 mg, 0.233 mmol) and 10% Pd/C catalyst (50 mg) in absolute ethanol (5 mL) was stirred at ambient temperature under 1 atm H_2 for 72 h. Filtration through a plug of silica, removal of volatiles *in vacuo*, and chromatography of the residue on silica gel 60 (25 g) eluted with 20% EtOAc/hexanes afforded 173 mg (0.232 mmol, 99%) of **5** (R_f 0.18, 20% EtOAc/hexanes).

Spectral data for **5**: a tacky semi-solid, $[\alpha]_D$+64.0°(*c* 0.5,$CHCl_3$);IR ($CHCl_3$) cm^{-1} 3590, 1470, 1426;^1H NMR ($CDCl_3$) δ 0.98 (8, s), 1.04 (8, s), 1.07 (2, s), 1.52-1.60 (3, m), 1.68-1.80 (2, m), 3.37-3.50 (1,m), 3.58-3.66 (1, m), 3.70 (1,dd,J=10, 7Hz), 4.04-4.13 (2, m), 4.56 (1, m), 4.72 (1,d,J=4Hz), 4.81 (1,t,J=6Hz), and 7.24-7.80 (25, m);^{13}C NMR ($CDCl_3$) δ 19.13 (C), 26.81 (CH_3), 26.86 (CH_3), 34.20 (CH_2), 35.84 (CH_2), 64.35 (2xCH), 65.97 (CH_2), 68.21 (CH_2), 78.54 (CH), 94.36 (CH), 127.43 (CH), 127.49 (CH), 127.55 (CH), 127.64 (CH), 128.10 (CH), 129.49 (CH), 129.55 (CH), 133.49 (C), 133.55 (C), 134.08 (C), 134.46 (C), 135.62 (CH), 135.72 (CH), 135.96 (CH), and 140.08 (C).

Anal. Calcd for $C_{46}H_{56}O_5Si_2$: C, 74.15; H, 7.57. Found: C, 74.72; H, 7.70.

Methyl (2R, 4R, 6S)-4-tert-Butyldiphenylsilyloxy-6-hydroxymethyl-3,4,5,6-tetrahydro-2H-pyran-2-yl Ether (14b).[15] To a solution of **5** (62 mg, 83 μmol) in dry methanol (2 mL) was added *p*-TsOH monohydrate (10 mg). The mixture was stirred at ambient temperature for 6 h, then diluted with sat. $NaHCO_3$ (20 mL), extracted with ether (3 x 20 mL), the extracts dried (Na_2SO_4), filtered and volatiles removed *in vacuo*. The residue was chromatographed on silica gel 60 (100 g) eluted with 50% ether/hexanes, affording 3 mg (7.5 μmol, 9%) of the less polar anomer **14a** (R_f 0.25, 50% ether/hexanes), and 25 mg (62.4 μmol, 76%) of the more polar anomer **14b** (R_f 0.22).

Spectral data for **14b**: mp 96-97 °C,$[\alpha]_D$-15.9°(*c* 0.7, $CHCl_3$), Lit.[15]mp 97-98 °C, $[\alpha]_D$-11.2°(*c* 4.03, $CHCl_3$); IR ($CHCl_3$)cm^{-1} 3593, 3440; ^1H NMR ($CDCl_3$) δ 1.09 (9, s), 1.30-2.20 (5, m), 3.53 (3,s), 3.45-3.70 (2,m), 4.16 (1, m), 4.31 (1, m), 4.90 (1,dd,J=10,2Hz), 7.27-7.46 (6, m), and 7.60-7.70 (4, m);^{13}C NMR ($CDCl_3$) δ 19.13 (C), 26.86 (CH_3), 34.18 (CH_2), 35.80 (CH_2), 64.35 (CH_3), 65.94 (CH_2), 68.21 (CH_2), 78.52 (CH), 94.35 (CH), 127.44 (CH), 127.49 (CH), 127.55 (CH), 127.64 (CH), 128.10 (CH), 129.50 (CH), 129.55 (CH), 133.47 (C), 133.52 (C), 134.06 (C), 134.44 (C), 135.61 (CH), 135.73 (CH), 135.96 (CH), and 140.08 (C).

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