

SUPPORTING INFORMATION

New Stereoselective β -C-Glycosidation by Uncatalyzed 1,4-Addition of Organolithium Reagents to a Glycal-derived Vinyl Oxirane

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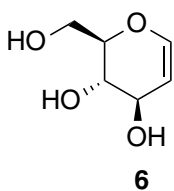
General Procedures. All reactions were performed in flame-dried modified Schlenk (Kjeldahl shape) flasks fitted with a glass stopper or rubber septa under a positive pressure of argon. Air/and moisture-sensitive liquids and solutions were transferred via a syringe. Organic solutions were dried on MgSO_4 and concentrated by a rotary evaporator below 40°C at *ca.* 25 Torr. Flash column chromatography was performed employing 230-400 mesh silica gel. Analytical TLC was performed on Alugram SIL G/UV254 silica gel sheets (Macherey-Nagel) with detection by 0.5% phosphomolybdic acid solution in 95% EtOH.

In the reactions carried out under *protocol A*, hydroxy mesylate **3** was pretreated with *t*-BuOK. In the reactions carried out under *protocol B*, hydroxy mesylate **3** was not pretreated with *t*-BuOK.

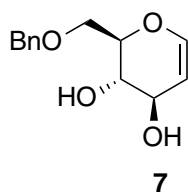
Materials. 1.0 M TBAF in THF, 3.0 M EtMgBr in Et_2O , 2.0 M PhMgCl in THF, 1.6 M MeLi in Et_2O , 1.6 M BuLi in hexane, 1.7 M *t*-BuLi in pentane, 0.7 M *i*-PrLi in pentane, 1.8 M PhLi in Et_2O , 3.0 M MeMgBr in Et_2O , and *tert*-BuOK were purchased from Aldrich and used without purification. Benzene, benzene- d_6 , Et_2O and tetrahydrofuran were distilled from sodium/benzophenone.

Instrumentation. Infrared (IR) spectra were obtained using a Mattson 3000 FTIR spectrophotometer. Data are presented as frequency of absorption (cm^{-1}). Proton and carbon-13 nuclear magnetic resonance (^1H NMR and ^{13}C NMR) spectra were recorded on a Bruker AC 200 (50 MHz) spectrometer; chemical shifts are expressed in parts per million (δ scale) downfield from tetramethylsilane and refer to residual protium in the NMR solvent (CHCl_3 : δ 7.26, CHD_2OD : 3.31, C_6HD_5 : δ 7.16). Data are presented as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, m=multiplet and/or multiple resonances),

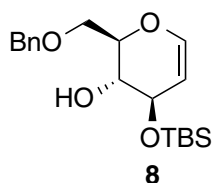
coupling constant (or $W_{1/2}$) in Hertz (Hz), integration. Melting points were recorded with a Kofler melting point apparatus and are uncorrected.



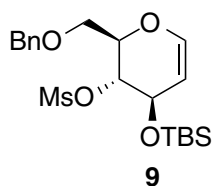
D-Glucal (6).¹ Sodium methoxide (0.10 g, 1.80 mmol) was added to a solution of tri-*O*-acetyl-D-glucal (**5**) (8.0 g, 29.4 mmol) in MeOH (80 mL) and the resulting reaction mixture was stirred at rt for 5 h. Evaporation of the organic solvent afforded a product (4.15 g, 97% yield) consisting of **6**, practically pure as a solid, mp 46-48°C: $R_f = 0.27$ (9:1 $\text{CH}_2\text{Cl}_2/\text{MeOH}$); $^1\text{H NMR}$ (CD_3OD) δ 6.26 (dd, $J = 6.0, 1.6$ Hz, 1H), 4.60 (dd, $J = 6.0, 2.2$ Hz, 1H), 4.04 (dt, $J = 7.0, 1.9$ Hz, 1H), 3.85-3.58 (m, 3H), 3.48 (dd, $J = 9.5, 7.0$ Hz, 1H). $^{13}\text{C NMR}$ (CD_3OD) δ 146.49, 106.09, 81.86, 72.53, 72.13, 63.84



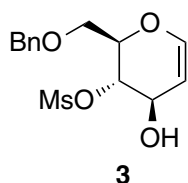
6-O-(benzyl)-D-glucal (7).² A 1M solution of LHMDS in THF (36.1 mL, 36.1 mmol) was added dropwise at -40°C to a stirred solution of D-glucal (**6**) (4.80 g, 32.9 mmol) in anhydrous DMF (97 mL). BrBn (3.91 mL 32.9 mmol) was added and the reaction mixture was stirred for 6 h allowing the temperature to rise to 0°C . Saturated aqueous NH_4Cl (25 mL) and AcOEt (100mL) were added to the reaction mixture. The organic layer was separated and the aqueous layer extracted with AcOEt (3x25 mL). Combined organic extracts were washed (saturated aqueous NaCl and water) and evaporated to afford a crude product which was subjected to flash chromatography. Elution with 1:1 hexane/AcOEt afforded the benzyl derivative **7** (2.45 g, 32% yield), pure as a solid, mp 38-40°C: $R_f = 0.19$ (1:1 hexane/AcOEt); FTIR (neat film) 3385, 1647, 1263, 1057 cm^{-1} . $^1\text{H NMR}$ (CDCl_3) δ 7.24-7.31 (m, 5H), 6.20 (dd, $J = 6.0, 1.5$ Hz, 1H), 4.57 (dd, $J = 6.0, 1.8$ Hz, 1H), 4.52 (d, $J = 12.0$ Hz, 1H), 4.46 (d, $J = 12.0$ Hz, 1H), 4.05-4.17 (m, 1H), 3.57-3.84 (m, 4H). $^{13}\text{C NMR}$ (CDCl_3) δ 143.89, 137.37, 128.15, 127.48, 102.53, 77.44, 73.40, 70.02, 69.50, 68.80.



3-*O*-(*t*-Butyldimethylsilyl)-6-*O*-(benzyl)-D-glucal (8). A solution of diol **7** (2.40 g, 10.2 mmol) in anhydrous DMF (24 mL) containing imidazole (1.34 g, 20.4 mmol) was treated at 0°C with TBDMS-Cl (1.54 g, 10.2 mmol) and the reaction mixture was stirred 18 h at rt. Dilution with Et₂O (80 mL) and evaporation of the washed (saturated aqueous NaCl and water) organic solution afforded a crude product (3.47 g) which was subjected to flash chromatography. Elution with 9:1 hexane/AcOEt afforded alcohol **8** (3.0 g, 84% yield), as a liquid: *R*_f = 0.33 (9:1 hexane/AcOEt); FTIR (neat film) 3393, 1647, 1447, 1248, 1095 cm⁻¹. ¹H NMR (CDCl₃) δ 7.24-7.32 (m, 5H), 6.28 (d, *J* = 6.0 Hz, 1H), 4.58-4.63 (m, 3H), 4.19 (d, *J* = 6.0 Hz, 1H), 3.92-3.99 (m, 1H), 3.71-3.79 (m, 3H), 0.87 (s, 9H), 0.084 (s, 6H). ¹³C NMR (CDCl₃) δ 143.52, 138.06, 128.56, 127.90, 103.70, 77.1, 73.81, 70.95, 70.03, 69.42, 25.96, 18.22, -4.27. Anal.Calcd for C₁₉H₃₀O₄Si: C, 65.10; H, 8.63. Found: C, 64.97; H, 8.51.

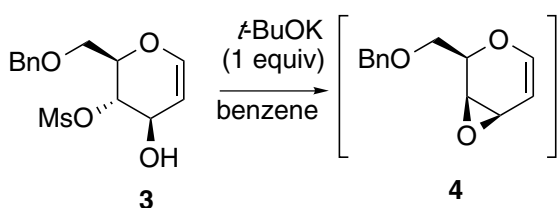


3-*O*-(*t*-Butyldimethylsilyl)-4-*O*-mesyl-6-*O*-(benzyl)-D-glucal (9). A solution of alcohol **8** (1.20 g, 3.42 mmol) in anhydrous pyridine (15 mL) was treated at 0°C with MsCl (0.53 mL, 6.84 mmol). The reaction mixture was stirred 18 h at rt, then diluted with Et₂O. Evaporation of the washed (water) organic layer afforded a residue which was subjected to flash chromatography. Elution with 9:1 hexane/AcOEt yielded mesylate **9** (1.07 g, 72% yield), pure as a liquid, *R*_f = 0.11 (9:1 hexane/AcOEt); FTIR (neat film) 1647, 1361, 1253, 1176, 1072 cm⁻¹. ¹H NMR (CDCl₃) δ 7.24-7.32 (m, 5H), 6.37 (d, *J* = 6.4 Hz, 1H), 4.71-4.81 (m, 2H) 4.61 (d, *J*=12.3 Hz, 1H), 4.52 (d, *J*= 12.3 Hz, 1H), 4.22-4.42 (m, 2H), 3.81 (dd, *J* = 11.0, 7.0 Hz, 1H), 3.69 (dd, *J* = 11.0, 3.5 Hz, 1H), 3.05 (s, 3H), 0.86 (s, 9H), 0.09 (s, 6H). ¹³C NMR (CDCl₃) δ 143.48, 137.65, 128.41, 127.86, 127.74, 101.49, 77.35, 75.48, 73.66, 67.97, 64.79, 38.97, 25.86, 18.04, -4.48. Anal.Calcd for C₂₀H₃₂O₆SSi: C, 56.05; H, 7.52. Found: C, 54.72; H, 7.18.



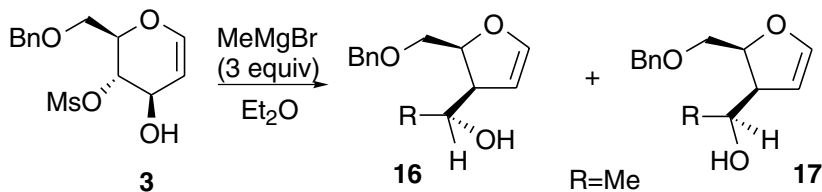
6-O-(Benzyloxy)-4-O-Mesyloxy D-glucal (3). A solution of mesylate **9** (0.50 g, 1.17 mmol) in anhydrous THF (40 mL) was treated dropwise at 0°C with 1M TBAF in THF (1.17 mL, 1.17 mmol) and the reaction mixture was stirred for 20 min at the same temperature, then diluted with water (15 mL) and extracted with Et₂O (2 x 50 mL). Evaporation of the combined ether extracts afforded a residue (0.33 g) which was subjected to flash chromatography. Elution with 1: 1 hexane/AcOEt afforded hydroxy mesylate **3** (0.27 g, 74% yield), pure as a solid, mp 39-41°C: R_f = 0.29 (1:1 hexane/AcOEt); FTIR (neat film) 3447, 1649, 1348, 1182 cm⁻¹. ¹H NMR (CDCl₃) δ 7.28-7.39 (m, 5H), 6.43 (dd, *J* = 6.0, 1.5 Hz, 1H), 4.78-4.90 (m, 2H), 4.61 (s, 2H), 4.42-4.51 (m, 1H), 4.11 (dt, *J* = 9.3, 3.4 Hz, 1H), 3.81-3.85 (m, 2H), 3.14 (s, 3H). ¹³C NMR (CDCl₃) δ 144.43, 137.47, 128.43, 127.97, 127.85, 102.03, 79.06, 75.13, 73.74, 68.11, 67.19, 38.63. Anal. Calcd for C₁₄H₁₈O₆S: C, 53.49; H, 5.77. Found: C, 53.17; H, 5.54.

¹H NMR confirmation of the formation of epoxide **4**.



A solution of hydroxy mesylate **3** (0.020 g, 0.064 mmol) in C₆D₆ (0.7 mL) was treated in the NMR tube with *t*-BuOK (0.007 g, 0.064 mmol). After 15 min at rt, the ¹H NMR analysis showed pure epoxide **4**: ¹H NMR δ 7.24-7.07 (m, 5H), 6.07 (dd, *J* = 6.0, 1.5 Hz, 1H), 4.74 (dd, *J* = 6.0, 4.0 Hz, 1H), 4.26 (s, 2H), 4.02 (td, *J* = 6.5, 1.0 Hz, 1H), 3.62 (unresolved d, *J* = 6.6 Hz, 2H), 3.20 (dd, *J* = 4.6, 1.0 Hz, 1H), 2.78 (td, *J* = 4.2, 1.5 Hz, 1H).

Reaction of Hydroxy Mesylate **3** with MeMgBr (*Protocol B*)



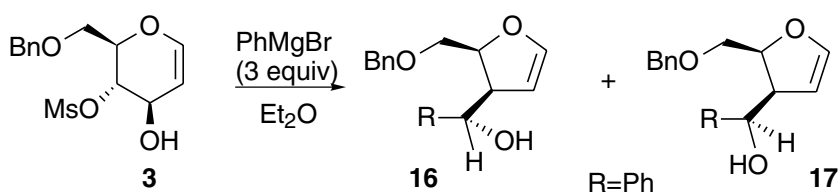
Typical procedure. A solution of hydroxy mesylate **3** (0.050 g, 0.16 mmol) in anhydrous Et₂O (2 mL) was treated at 0°C with 3 M MeMgBr in Et₂O (0.16 mL, 0.48 mmol) and the

resulting reaction mixture was stirred at rt for 18 h. Dilution with Et₂O and evaporation of the washed (saturated aqueous NaCl) organic solution afforded a crude product consisting of a 1:1 mixture of alcohols **16** and **17** (R=Me) (¹H NMR) (0.036 g, 95% yield) which was subjected to flash chromatography. Elution with 1:1 hexane/AcOEt afforded pure alcohols **16** (or **17**, R=Me) (0.016 g) and **17** (or **16**, R=Me) (0.012 g).

(4S,5S)-5-(Benzyloxymethyl)-4-[(R or S)-1-hydroxyethyl]-4,5-dihydrofuran (**16** or **17**, R=Me), a liquid: R_f = 0.44 (6:4 hexane/AcOEt); FTIR (neat film) 3435, 1643, 1446, 1375, 1284, 1071 cm⁻¹. ¹H NMR (CDCl₃) δ 7.27-7.38 (m, 5H), 6.38 (t, *J* = 2.5 Hz, 1H), 4.77 (t, *J* = 2.5 Hz, 1H), 4.57-4.69 (m, 1H), 4.61 (s, 2H), 3.58-3.74 (m, 1H), 3.64 (dd, *J* = 9.8, 6.1 Hz, 1H), 3.49 (dd, *J* = 9.8, 5.5 Hz, 1H) 2.72 (tt, *J* = 6.4, 2.3 Hz, 1H), 1.17 (d, *J* = 6.4 Hz, 1H). ¹³C NMR (CDCl₃) δ 146.99, 137.98, 128.65, 127.96, 100.36, 82.42, 73.68, 72.35, 70.07, 53.93, 20.98. Anal.Calcd for C₁₄H₁₈O₃: C 71.77; H, 7.74. Found: C, 71.79; H, 7.92.

(4S,5S)-5-(Benzyloxymethyl)-4-[(S or R)-1-hydroxyethyl]-4,5-dihydrofuran (**17** or **16**, R=Me), a liquid: R_f = 0.38 (6:4 hexane/AcOEt); FTIR (neat film) 3416, 1639, 1460, 1371, 1074 cm⁻¹. ¹H NMR (CDCl₃) δ 7.27-7.39 (m, 5H), 6.42(t, *J* = 2.3 Hz, 1H), 4.86 (t, *J* = 2.5 Hz, 1H), 4.54-4.65 (m, 1H), 4.63 (d, *J* = 12.2 Hz, 1H), 4.57 (d, *J* = 12.2 Hz, 1H), 3.66-3.78 (m, 1H), 3.60 (dd, *J* = 10.2, 6.5 Hz, 1H), 3.46 (dd, *J* = 10.2, 4.9 Hz, 1H), 2.78-2.89 (m, 1H), 1.15 (d, *J* = 6.4 Hz, 3H). ¹³C NMR (CDCl₃) δ 147.53, 138.29, 128.64, 127.92, 98.58, 82.15, 73.69, 72.27, 69.24, 52.78, 20.87. Anal.Calcd for C₁₄H₁₈O₃: C, 71.77; H, 7.74. Found: C, 71.49; H, 7.43.

Reaction of Hydroxy Mesylate **3** with PhMgBr (*Protocol B*)



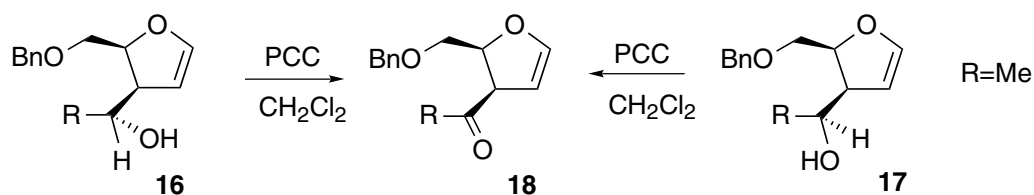
Proceeding as previously described for the corresponding reaction with MeMgBr, the reaction of hydroxy mesylate **3** (0.050 g, 0.16 mmol) in anhydrous Et₂O (2 mL) with 1 M PhMgBr in Et₂O (prepared from PhBr and Mg) (0.48 mL, 0.48 mmol) afforded a crude product consisting of a 1:1 mixture of alcohols **16** and **17** (R=Ph) (¹H NMR) (0.040 g, 84% yield) which was subjected to flash chromatography. Elution with 6:4 hexane/AcOEt afforded pure alcohols **16** (or **17**, R=Ph) (0.018 g) and **17** (or **16**, R=Ph) (0.015 g).

(4S,5S)-5-(Benzyloxymethyl)-4-[(S or R)-phenylhydroxymethyl]-4,5-dihydrofuran (**16** or **17**, R=Ph), a liquid: R_f = 0.44 (6:4 hexane/AcOEt); FTIR (neat film) 3406, 1616,

1452, 1263, 1074, 1028 cm^{-1} . ^1H NMR (CDCl_3) δ 7.21-7.45 (m, 10H), 6.36 (t, J = 2.3 Hz, 1H), 4.74 (dd, J = 11.5, 6.3 Hz, 1H), 4.48-4.63 (m, 2H), 4.56 (s, 2H), 3.52 (dd, J = 10.0, 6.3 Hz, 1H), 3.40 (dd, J = 10.0, 5.0 Hz, 1H), 3.08 (tt, J = 6.9, 2.0 Hz, 1H). ^{13}C NMR (CDCl_3) δ 147.12, 142.33, 137.97, 128.58, 127.86, 127.63, 126.39, 125.55, 100.31, 82.76, 76.38, 73.52, 72.16, 54.12. Anal.Calcd for $\text{C}_{19}\text{H}_{20}\text{O}_3$: C, 77.00; H, 6.80. Found: C, 77.19; H, 6.54.

(4*S*,5*S*)-5-(Benzyloxymethyl)-4-[(*R* or *S*)-phenylhydroxymethyl]-4,5-dihydrofuran (17 or 16, R=Ph), a liquid: R_f = 0.38 (6:4 hexane/AcOEt); FTIR (neat film) 3448, 1616, 1283, 1028 cm^{-1} . ^1H NMR (CDCl_3) δ 7.15-7.32 (m, 10H), 6.35 (t, J = 2.3 Hz, 1H), 4.82 (t, J = 2.3 Hz, 1H), 4.35-4.56 (m, 2H), 4.43 (s, 2H), 3.35 (dd, J = 10.3, 6.4 Hz, 1H), 3.20 (dd, J = 10.3, 4.5 Hz, 1H), 3.10 (tt, J = 6.1, 2.0 Hz, 1H). ^{13}C NMR (CDCl_3) δ 147.61, 142.21, 138.11, 128.64, 128.58, 127.95, 127.84, 126.33, 99.19, 82.25, 76.22, 73.44, 71.71, 53.12. Anal.Calcd for $\text{C}_{19}\text{H}_{20}\text{O}_3$: C 77.00; H, 6.80. Found: C, 76.69; H, 6.61.

PCC Oxidation of Alcohols 16 and 17 (R=Me)

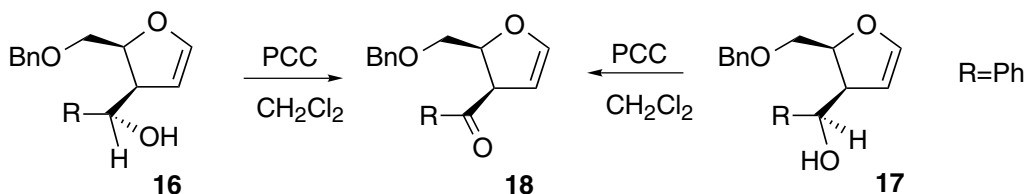


(4*R*,5*S*)-5-(Benzyloxymethyl)-4-acetyl-4,5-dihydrofuran (18, R=Me). A solution of alcohol **16** (R=Me) (0.025 g, 0.11 mmol) in CH_2Cl_2 (0.3 mL) was added at 0°C to a stirred solution of PCC (0.018 g, 0.11 mmol) in anhydrous CH_2Cl_2 (0.48 mL) containing 4 Å molecular sieves (0.030 g) and AcONa (0.009 g, 0.11 mmol) and the reaction mixture was stirred for 18 h at rt. After dilution with Et_2O (100 mL), stirring was prolonged for 30 min. The resulting reaction mixture was filtered through a pad of Celite and the organic solution was evaporated to afford a crude product (0.023 g) consisting of ketone **18** (R=Me) which was subjected to preparative TLC with 8:2 hexane/AcOEt as the eluant. Extraction of the most intense band afforded pure ketone **18** (R=Me) (0.019 g, 75% yield), as a liquid: R_f = 0.29 (8:2 hexane/AcOEt); FTIR (neat film) 1715, 1616, 1259, 1093 cm^{-1} . ^1H NMR (CDCl_3) δ 7.23-7.42 (m, 5H), 6.40 (t, J = 2.4 Hz, 1H), 5.09-5.00 (m, 2H), 4.59 (s, 2H), 3.60-3.68 (m, 2H), 3.56 (unresolved d, J = 5.2 Hz, 1H), 2.19 (s, 3H). ^{13}C NMR (CDCl_3) δ 206.19, 147.57, 138.10, 128.60, 127.88, 98.34, 80.79, 73.63, 71.37, 57.95, 29.88. Anal.Calcd for $\text{C}_{14}\text{H}_{16}\text{O}_3$: C 72.39; H, 6.94. Found: C, 72.08; H, 7.01.

Application of the same procedure to diastereoisomeric alcohol **17** (R=Me) (0.025 g, 0.11 mmol) afforded a crude reaction product which was subjected to preparative TLC with 8:2

hexane/AcOEt as the eluant. Extraction of the most intense band afforded pure ketone **18** (R=Me) (0.021 g, 82% yield).

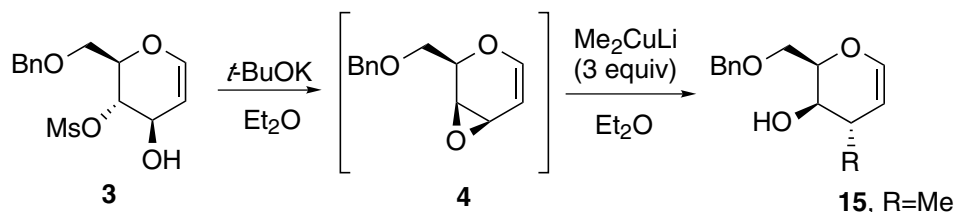
PCC Oxidation of Alcohols **16** and **17** (R=Ph)



(4R,5S)-5-(Benzyloxymethyl)-4-benzoyl-4,5-dihydrofuran (18, R=Ph). Application to alcohol **16** (R=Ph) (0.018 g, 0.061 mmol) of the procedure previously used for the corresponding reaction of alcohol **16** (R=Me) afforded a crude reaction product (0.017 g) which was subjected to preparative TLC with 8:2 hexane/AcOEt as the eluant. Extraction of the most intense band afforded pure ketone **18** (R=Ph) (0.013 g, 72% yield), as a liquid: $R_f = 0.29$ (8:2 hexane/AcOEt); FTIR (neat film) 1685, 1450, 1259, 1095, 1006 cm^{-1} . ^1H NMR (CDCl_3) δ 7.95-8.04 (m, 2H), 7.29-7.68 (m, 8H), 6.41 (t, $J = 2.5$ Hz, 1H), 5.38 (dd, $J = 11.4, 5.0$ Hz, 1H), 4.99 (t, $J = 2.6$ Hz, 1H), 4.63 (s, 2H), 4.51-4.68 (m, 1H), 3.66 (unresolved d, $J = 5.0$ Hz, 2H). ^{13}C NMR (CDCl_3) δ 197.17, 147.25, 133.56, 128.88, 128.62, 127.96, 99.63, 81.10, 73.68, 71.11, 52.80. Anal. Calcd for $\text{C}_{19}\text{H}_{18}\text{O}_3$: C, 77.53; H, 6.16. Found: C, 77.21; H, 5.98.

Application of the same procedure to diastereoisomeric alcohol **17** (R=Ph) (0.015 g, 0.051 mmol) afforded a crude reaction product which was subjected to preparative TLC with 8:2 hexane/AcOEt as the eluant. Extraction of the most intense band afforded pure ketone **18** (R=Ph) (0.012 g, 80% yield).

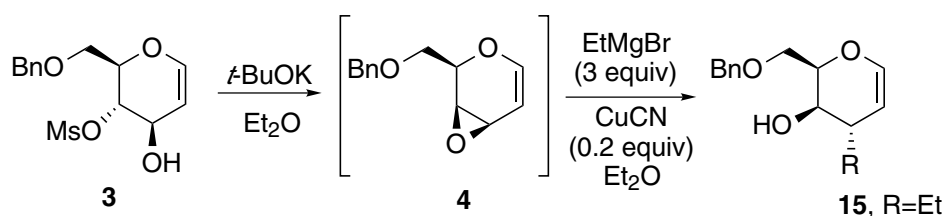
Reaction of Hydroxy Mesylate **3** with Me_2CuLi (Protocol A)



6-O-(Benzyl)-3-deoxy-3-methyl-D-gulal (15, R=Me). A solution of hydroxy mesylate **3** (0.040 g, 0.13 mmol) in anhydrous Et_2O (2 mL) was treated with *t*-BuOK (0.015 g, 0.13 mmol). After 15 min stirring at rt, the reaction mixture was cooled at 0°C and treated with a 1

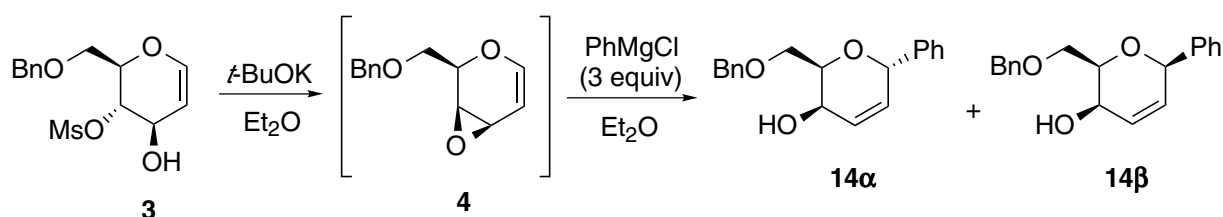
M solution of Me_2CuLi in anhydrous Et_2O (0.39 mL, 0.39 mmol) (prepared from 1.6 M MeLi in Et_2O and CuI) and stirring was prolonged for 30 min at rt. Dilution with Et_2O (20 mL) and evaporation of the washed (saturated aqueous NH_4Cl and saturated aqueous NaCl) organic solution afforded a crude product mostly consisting of glycal **15**, $\text{R}=\text{Me}$ (^1H NMR) (0.025 g) which was subjected to flash chromatography. Elution with 7:3 hexane/ AcOEt afforded pure alcohol **15** ($\text{R}=\text{Me}$) (0.018 g, 59% yield), as a liquid: $R_f=0.30$ (7:3 hexane/ AcOEt); FTIR (neat film) 3439, 1645, 1457, 1379, 1083 cm^{-1} ; ^1H NMR δ 7.23-7.40 (m, 5H), 6.41 (d, $J=6.2$ Hz, 1H), 4.68-4.76 (m, 1H), 4.63 (d, $J=12.2$ Hz, 1H), 4.57 (d, $J=12.2$ Hz, 1H), 3.66-3.89 (m, 3H), 3.70 (d, $J=6.4$ Hz, 1H), 2.06-2.25 (m, 1H), 1.02 (d, $J=7.2$ Hz, 3H). ^{13}C NMR δ 142.65, 137.75, 128.69, 128.05, 104.74, 74.08, 71.97, 71.13, 70.80, 33.79, 21.26. Anal.Calcd for $\text{C}_{14}\text{H}_{18}\text{O}_3$: C, 71.77; H, 7.74. Found: C, 72.06; H, 7.65.

Reaction of Hydroxy Mesylate **3** with $\text{EtMgBr}/\text{CuCN}$ (Protocol A)



6-O-(Benzyl)-3-deoxy-3-ethyl-D-gulal (15, R=Et). A 3 M solution of EtMgBr in Et_2O (0.16 mL, 0.48 mmol) was added at -40°C to a suspension of CuCN (0.003 g, 0.032 mmol) in anhydrous Et_2O (0.5 mL) and the resulting reaction mixture was stirred for 30 min at the same temperature. This mixture was supplemented, via a syringe at -40°C , with a solution of hydroxy mesylate **3** (0.050 g, 0.16 mmol) in anhydrous Et_2O (2 mL), previously left in contact with $t\text{-BuOK}$ (0.021 g, 0.19 mmol) for 15 min under stirring at rt. After the addition was completed, the temperature was allowed to rise to rt and stirring was prolonged 1.5 h at this temperature. Dilution with Et_2O (20 mL) and evaporation of the washed (saturated aqueous NaCl) organic solution afforded a crude reaction product (0.028 g) which was subjected to flash chromatography. Elution with 6:4 hexane/ AcOEt afforded alcohol **15** ($\text{R}=\text{Et}$), pure as a liquid (0.022 g, 55% yield^d): $R_f=0.38$ (6:4 hexane/ AcOEt); FTIR (neat film) 3421, 1645, 1454, 1240, 1058 cm^{-1} . ^1H NMR (CDCl_3) δ 7.24-7.42 (m, 5H), 6.44 (dd, $J=6.1, 1.3$ Hz, 1H), 4.74-4.84 (m, 1H), 4.64 (d, $J=12.2$ Hz, 1H), 4.59 (d, $J=12.2$ Hz, 1H), 3.69-3.89 (m, 4H), 1.85-2.03 (m, 1H), 1.15-1.50 (m, 2H), 0.96 (t, $J=7.3$ Hz, 3H). ^{13}C NMR δ 142.78, 137.78, 128.68, 128.02, 102.98, 74.05, 72.54, 71.16, 69.22, 40.90, 29.11, 11.41. Anal.Calcd for $\text{C}_{15}\text{H}_{20}\text{O}_3$: C, 72.55; H, 8.12. Found: C, 72.37; H, 7.92.

Reaction of Hydroxy Mesylate **3** with PhMgCl (*Protocol A*)

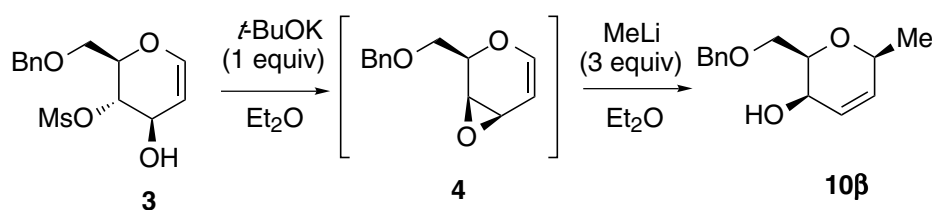


A solution of hydroxy mesylate **3** (0.077 g, 0.24 mmol) in anhydrous Et₂O (4 mL), was treated with *t*-BuOK (0.030 g, 0.24 mmol). After 15 min stirring at rt, the reaction mixture was cooled at 0°C, treated with 2M PhMgCl in THF (0.36 mL, 0.72 mmol) and stirred 30 min at rt. Dilution with Et₂O (20 mL) and evaporation of the washed (saturated aqueous NaCl) organic solution afforded a crude product (0.060 g) consisting of a 3:7 mixture (¹H NMR) of the two diastereomeric C-glycosides **14α** and **14β** (¹H NMR) which was subjected to preparative TLC with 6:4 hexane/AcOEt. Extraction of the two most intense bands afforded pure **14α** (0.014 g, 64% yield) and **14β** (0.035 g, 70% yield).

(2R,5R,6R)-6-(benzyloxymethyl)-5-hydroxy-2-phenyl-2H-5,6-dihydropyran (14β), a liquid: R_f = 0.44 (6:4 hexane/AcOEt); FTIR (neat film) 3421, 1645, 1454, 1068 cm⁻¹; ¹H NMR (CDCl₃) δ 7.27-7.40 (m, 10H), 6.15 (ddd, *J* = 10.2, 5.4, 2.2 Hz, 1H), 5.98 (dd, *J* = 10.2, 1.3 Hz, 1H), 5.13-5.19 (m, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 3.89-4.09 (m, 2H), 3.80 (dd, *J* = 10.1, 5.3 Hz, 1H), 3.74 (dd, *J* = 10.1, 6.5 Hz, 1H). ¹³C NMR (CDCl₃) δ 140.19, 138.29, 134.04, 128.73, 128.56, 128.30, 127.95, 127.83, 127.29, 126.94, 78.09, 77.80, 73.78, 70.09, 62.75. Anal. Calcd for C₁₉H₂₀O₃: C, 77.00; H, 6.80. Found: C, 77.12; H, 6.60.

(2S,5R,6R)-6-(benzyloxymethyl)-5-hydroxy-2-phenyl-2H-5,6-dihydropyran (14α), a liquid: R_f = 0.31 (6:4 hexane/AcOEt); FTIR (neat film) 3356, 1655, 1595, 1471, 1236, 1080 cm⁻¹; ¹H NMR (CDCl₃) δ 7.20-7.45 (m, 10H), 6.19-6.33 (m, 2H), 5.35 (s, 1H), 4.50 (s, 2H), 3.89-3.99 (m, 1H), 3.59-3.86 (m, 3H). ¹³C NMR (CDCl₃) δ 139.02, 138.30, 131.39, 128.59, 128.55, 128.13, 128.05, 127.93, 127.80, 74.37, 73.58, 70.87, 70.03, 62.87. Anal. Calcd for C₁₉H₂₀O₃: C, 77.00; H, 6.80. Found: C, 76.69; H, 6.65.

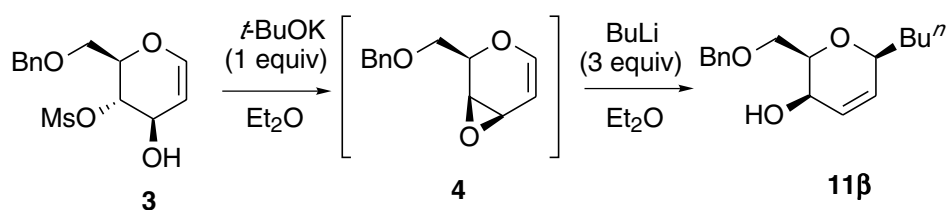
Reaction of Hydroxy Mesylate **3** with MeLi (*Protocol A*)



(2*S*,5*R*,6*R*)-6-(Benzyloxymethyl)-5-hydroxy-2-methyl-2*H*-5,6-dihydropyran (**10 β**).

Typical procedure. A solution of hydroxy mesylate **3** (0.044 g, 0.14 mmol) in anhydrous Et₂O (2 mL), was treated with *t*-BuOK (0.019 g, 0.17 mmol). After 15 min stirring at rt, the reaction mixture was cooled at 0°C, treated with 1.6 M MeLi in Et₂O (0.26 mL, 0.42 mmol) and stirred at the same temperature for 30 min. Dilution with Et₂O (20 mL) and evaporation of the washed (saturated aqueous NaCl) organic solution afforded a crude product (0.038 g) consisting of practically pure β -C-glycoside **10 β** (¹H NMR) which was subjected to flash chromatography. Elution with 6:4 hexane/AcOEt afforded pure **10 β** (0.032 g, 80% yield), as a liquid: *R*_f = 0.22 (7:3 hexane/AcOEt); FTIR (neat film) 3427, 1643, 1446, 1375, 1091 cm⁻¹; ¹H NMR (CDCl₃) δ 7.21-7.34 (m, 5H), 5.99 (ddd, *J* = 10.2, 5.4, 2.1 Hz, 1H), 5.85 (d, *J* = 10.2 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.32-4.15 (m, 1H), 3.88 (broad singlet, *W*_{1/2} = 15.4 Hz, 1H), 3.74-3.67 (m, 3H), 1.28 (d, *J* = 6.8 Hz, 3H). ¹³C NMR (CDCl₃) δ 138.36, 135.67, 128.58, 128.01, 127.85, 126.52, 73.79, 71.74, 70.26, 63.10, 21.19. Anal. Calcd for C₁₄H₁₈O₃: C 71.77; H, 7.74. Found: C, 71.97; H, 7.45.

Reaction of Hydroxy Mesylate **3** with BuLi (*Protocol A*)

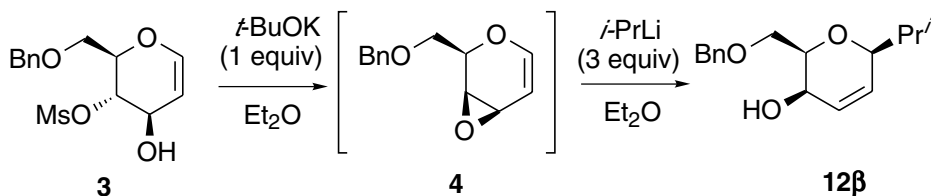


(2*S*,5*R*,6*R*)-6-(Benzyloxymethyl)-5-hydroxy-2-butyl-2*H*-5,6-dihydropyran (**11 β**).

Proceeding as previously described for the corresponding reaction with MeLi, the treatment of hydroxy mesylate **3** (0.050 g, 0.16 mmol) in anhydrous Et₂O (2 mL) with *t*-BuOK (0.021 g, 0.19 mmol) and 1.6 M BuLi in hexane (0.30 mL, 0.48 mmol) afforded a crude liquid product (0.036 g, 81% yield) consisting of practically pure β -C-glycoside **11 β** (¹H NMR) which was subjected to preparative TLC with 8:2 hexane/AcOEt. Extraction of the most intense band afforded pure **11 β** (0.014 g, 32% yield), as a liquid: *R*_f = 0.27 (hexane/AcOEt 8:2); FTIR (neat film) 3431, 1645, 1091 cm⁻¹. ¹H NMR (CDCl₃) δ 7.24-

7.41 (m, 5H), 6.02 (ddd, $J = 10.2, 5.3, 2.1$ Hz, 1H), 5.85 (d, $J = 10.2$ Hz, 1H), 4.65 (d, $J = 12.2$ Hz, 1H), 4.58 (d, $J = 12.2$ Hz, 1H), 4.05-4.15 (m, 1H), 3.84-3.95 (m, 1H), 3.65-3.82 (m, 3H), 1.20-1.71 (m, 6H), 0.91 (t, $J = 6.8$ Hz, 3H). ^{13}C NMR (CDCl_3) δ 138.47, 134.72, 128.57, 127.94, 127.82, 126.90, 77.43, 75.56, 73.74, 70.25, 63.32, 34.99, 27.34, 22.89, 14.23. Anal. Calcd for $\text{C}_{17}\text{H}_{24}\text{O}_3$: C, 73.88; H, 8.75. Found: C, 73.95; H, 8.61.

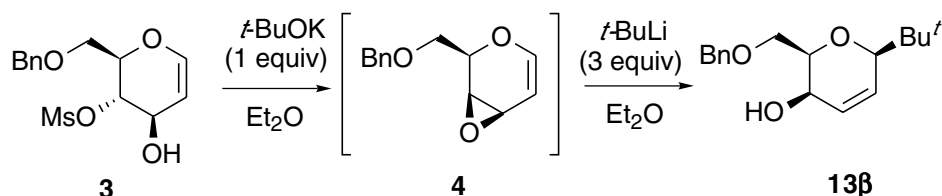
Reaction of Hydroxy Mesylate **3** with *i*-PrLi (Protocol A)



(2*S*,5*R*,6*R*)-6-(Benzyloxymethyl)-5-hydroxy-2-(1-methylethyl)-2*H*-5,6-

dihydropyran (12β). Proceeding as previously described for the corresponding reaction with MeLi, the treatment of hydroxy mesylate **3** (0.070 g, 0.22 mmol) in anhydrous Et₂O (2 mL) with *t*-BuOK (0.030 g, 0.26 mmol) and 0.7 M *i*-PrLi in pentane (0.94 mL, 0.66 mmol) afforded a crude product (0.050 g) consisting of practically pure **12β** which was subjected to flash chromatography. Elution with 8:2 hexane/AcOEt afforded pure **12β** (0.045 g, 78% yield), as a liquid: $R_f = 0.44$ (8:2 hexane/AcOEt); FTIR (neat film) 3452, 1647, 1261, 1095 cm^{-1} . ^1H NMR (CDCl_3) δ 7.24-7.42 (m, 5H), 6.07 (ddd, $J = 10.1, 5.4, 2.0$ Hz, 1H), 5.86 (d, $J = 10.1$ Hz, 1H), 4.63 (d, $J = 12.2$ Hz, 1H), 4.58 (d, $J = 12.2$ Hz, 1H), 3.63-4.01 (m, 5H), 1.75-1.97 (m, 1H), 0.95 (d, $J = 2.5$ Hz, 3H), 0.92 (d, $J = 2.5$ Hz, 3H). ^{13}C NMR (CDCl_3) δ 138.63, 132.85, 128.66, 128.00, 127.88, 80.10, 76.66, 73.83, 70.37, 63.47, 32.40, 18.25, 17.88. Anal. Calcd for $\text{C}_{16}\text{H}_{22}\text{O}_3$: C, 73.25; H, 8.45. Found: C, 73.59; H, 8.17.

Reaction of Hydroxy Mesylate **3** with *t*-BuLi (Protocol A)

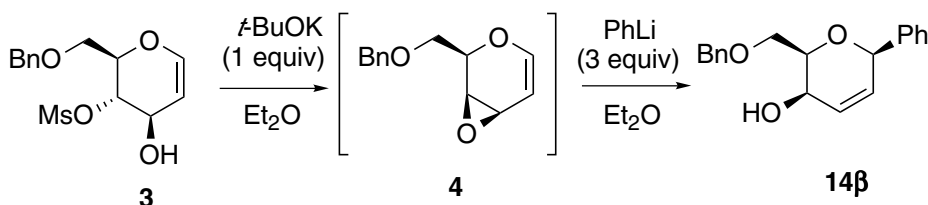


(2*R*,5*R*,6*R*)-6-(Benzyloxymethyl)-5-hydroxy-2-(1,1-dimethylethyl)-2*H*-5,6-

dihydropyran (13β). Proceeding as previously described for the corresponding reaction with MeLi, the treatment of hydroxy mesylate **3** (0.045 g, 0.14 mmol) in anhydrous Et₂O (2

mL) with *t*-BuOK (0.019 g, 0.17 mmol) and 1.7 M *t*-BuLi in pentane (0.25 mL, 0.42 mmol) afforded a crude product (0.038 g) mostly consisting of **13 β** which was purified by flash chromatography. Elution with a 8:2 hexane/AcOEt afforded pure **13 β** (0.031 g, 80% yield), as a liquid: $R_f = 0.32$ (8:2 hexane/AcOEt); FTIR (neat film) 3448, 1645, 1462, 1365, 1093 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.25-7.40 (m, 5H), 6.11 (ddd, $J = 10.4, 5.6, 2.2$ Hz, 1H), 5.97 (d, $J = 10.3$ Hz, 1H), 4.62 (s, 2H), 3.82-3.95 (m, 1H), 3.61-3.81 (m, 4H), 0.95 (s, 9H). ^{13}C NMR (CDCl_3) δ 138.67, 134.71, 131.80, 128.55, 128.39, 127.79, 83.14, 77.02, 73.70, 70.34, 63.20, 34.48, 25.97. Anal.Calcd for $\text{C}_{17}\text{H}_{24}\text{O}_3$: C, 73.88; H, 8.75. Found: C, 74.08. H, 8.55.

Reaction of Hydroxy Mesylate **3** with PhLi (*Protocol A*)



Proceeding as previously described for the corresponding reaction with MeLi, the treatment of hydroxy mesylate **3** (0.062 g, 0.20 mmol) in anhydrous Et_2O (2 mL) with *t*-BuOK (0.027 g, 0.24 mmol) and 1.8 M PhLi in Et_2O (0.33 mL, 0.60 mmol) afforded a crude liquid product (0.055 g, 93% yield) consisting of β -C-glycoside **14 β** (^1H NMR), practically pure as a liquid.

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- 1) Brimacombe, J.S.; Da'Aboul, J.; Tucker, L.C.N. *Carbohydr. Res.* **1971**, *19*, 276.
- 2) Deshpande, P.P.; Kim, H.M.; Zatorski, A.; Park, T.-K.; Ragupathi, G.; Livingston, P.O.; Live, D.; Danishefsky, S.J. *J. Am. Chem. Soc.* **1998**, *120*, 1600.