Supporting Information

Chlorodicyclohexylborane-Mediated Aldol Additions of α,α´-Dioxygenated Ketones

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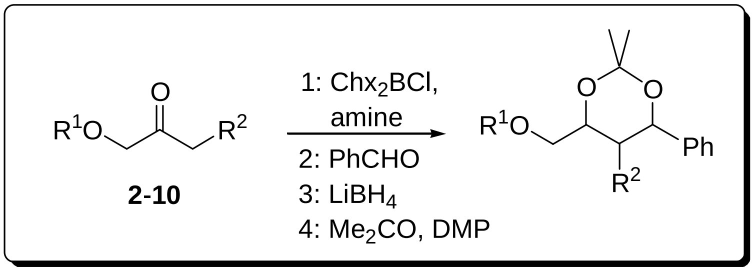
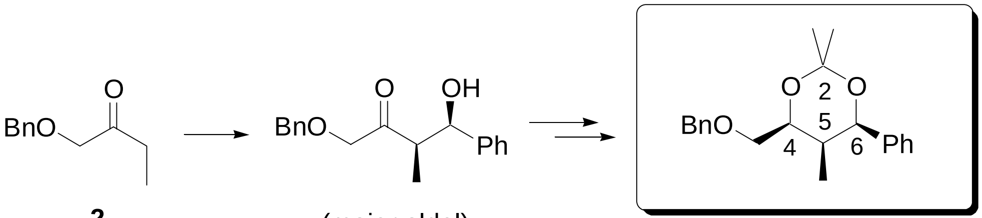
General Features. Column chromatography (CC) was performed on silica gel Süd-Chemie AG (60-200 μm. Experiments which required an inert atmosphere were carried out under dry argon (Ar) in a flame-dried glassware. Et_2O was freshly distilled from sodium/benzophenone ketyl and transferred via syringe. Commercially available reagents (Aldrich or Fluka) were used as received. The preparation of ketones **2-10** will be described in a future paper. Chx_2BCl (distilled neat liquid) was prepared according to the procedure described in: I. Paterson *et al.*, *J.Am.Chem.Soc*. **1994**, *116*, 11287.

^{1}H NMR spectra (400 or 500 MHz) and ^{13}C NMR spectra (100 or 125 MHz) were measured at 22 ºC. The signals of the deuterated solvent ($CDCl_3$) were taken as the reference (the singlet at δ 7.25 for ^{1}H NMR and the triplet centered at 77.00 ppm for ^{13}C NMR data). Unambiguous assignments of ^{1}H and ^{13}C NMR signals were made with a combination of spin decoupling, DEPT and HMQC experiments. Stereochemical assignments were made with the aid of NOE measurements. Mass spectra were run in a VG AutoSpec mass spectrometer using either the electron impact mode (EIMS, 70 eV) or the fast atom bombardment mode (FAB MS, *m*-nitrobenzyl alcohol matrix).

General experimental procedure for the aldolization-reduction-acetalization protocol: based on the general aldolization procedure described in: M. Carda, J. Murga, E. Falomir, F. González, J.A. Marco, *Tetrahedron* **2000**, *56*, 677-683. Neat Chx_2BCl was used here instead of a hexane solution.



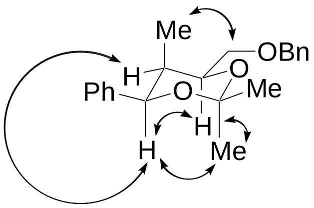
The appropriate ketone (1 mmol) dissolved in anhydrous ether (3 mL) was added at –78ºC to a stirred solution prepared by dissolving Chx_2BCl (neat, 394 μL, ca. 1.8 mmol) and Et_3N (278 μL, 2 mmol) in anhydrous Et_2O (6 mL). After stirring for 10 min., the temperature of the mixture was increased to 0°C and maintained at this value for 1 h. After re-cooling to -78ºC, a solution of benzaldehyde (4 mmol) in ether (6 mL) was added, and the reaction mixture was stirred at the same temperature for 5 h. After this time, a 2M solution of $LiBH_4$ in THF (1.5 mL, 3 mmol) was added via syringe and the stirring was continued for 2 h. The reaction was then quenched with pH 7 phosphate buffer (6 mL) and MeOH (6 mL), followed by a 30% aq H_2O_2 solution (3 mL). After stirring for 1 h at room temperature, the mixture was poured into satd. aq $NaHCO_3$ and extracted with Et_2O. The organic layer was washed with brine and dried on anhydrous Na_2SO_4. Solvent removal *in vacuo* afforded an oily residue which was dissolved in a mixture of acetone (8 mL) and 2,2-dimethoxypropane (2 mL). After adding *p*-toluenesulphonic acid (20 mg) and activated 3Å molecular sieves (300 mg), the mixture was stirred overnight under Ar at room temperature, filtered through a pad of silica gel, evaporated *in vacuo* and chromatographed on silica gel (hexane-Et_2O 19:1, then 9:1). This yielded the acetonides, which were then analysed by means of ^{1}H and ^{13}C NMR. The chemical yields of the aldolization step and (in parentheses) the overall yields of the aldolization-reduction-acetalization sequence were: **2**, 50 (58); **3**, 92 (65); **4**, 87 (-); **5**, 30 (35); **6a**, 85 (48); **6b**, 88 (55); **6c**, 89 (59); **7**, 63 (40); **8**, 85 (51); **9**, 87 (52); **10**, 90 (55). Aldols prepared from ketones **2**, **5** and **7** were unstable to chromatography on silica gel; this explains the low yields in the isolation of the aldols themselves. The diastereomeric ratios were estimated by $^{1}H/^{13}C$ NMR of the crude aldolization mixture, prior to chromatography. For ketones **3**, **5**, **6a-c** and **10**, no minor aldols were detected by NMR. At the signal/noise ratio of the measured spectra, this means more than 95% of the major isomer. The key spectral data of some selected acetonides are given hereafter.



2

(major aldol)

(±)-(4*R,5*S**,6*S**)-4-benzyloxymethyl-2,2,5-trimethyl-6-phenyl-1,3-dioxane**: oil; ^{1}H NMR (500 MHz) δ 7.45-7.25 (m, 10H, aromatic), 5.15 (d, 2.2 Hz, 1H, H-6), 4.64, 4.52 (AB system, 12 Hz, 2H, benzyl C$\underline{H}_2$), 4.42 (td, 6.3, 2.2 Hz, 1H, H-4), 3.60 (dd, 9.6, 6.3 Hz, 1H, BnOC$\underline{H}_2$), 3.49 (dd, 9.6, 6.3 Hz, 1H, BnOC$\underline{H}_2$), 1.90 (m, 1H, H-5), 1.60 (s, 6H, acetonide methyls), 0.66 (d, 7 Hz, 3H, $\underline{Me}$-C_5); ^{13}C NMR (125 MHz) δ 140.8, 138.1 (aromatic C_q), 128.3, 128.0, 127.7, 127.6, 127.5, 126.7, 125.5 (aromatic CH), 99.3 (C-2), 74.3 (C-6), 73.5 (benzyl $\underline{C}H_2$), 72.0 (C-4), 71.1 (BnO$\underline{C}H_2$), 35.2 (C-5), 29.9, 19.6 (acetonide methyls), 5.2 ($\underline{Me}$-C_5). FAB MS *m/z* 326.1885 [M^+]. Calcd. for $C_{21}H_{26}O_3$, M = 326.1882.



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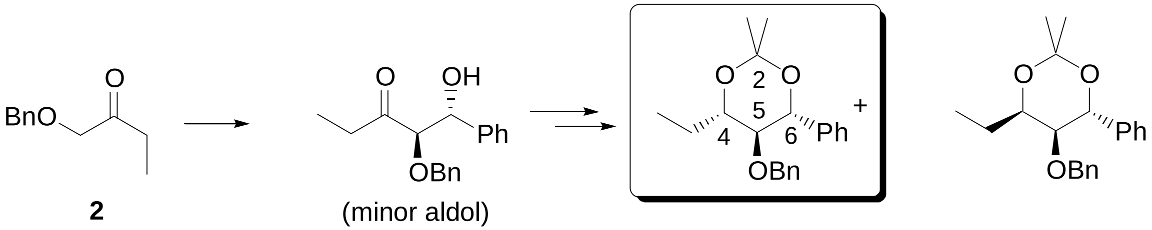
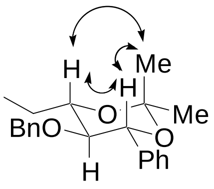


2

(minor aldol)

~ 2:1 mixture formed after an only partially
stereoselective $LiBH_4$ reduction step
(NMR analysis performed on the mixture)

(±)-(4*R,5*R**,6*R**)-5-benzyloxy-4-ethyl-2,2-dimethyl-6-phenyl-1,3-dioxane** (major acetonide): oil; ^1H NMR (500 MHz) δ 7.50-7.20 (m, 10H, aromatic), 4.68 (d, 9.5 Hz, 1H, H-6), 4.02, 3.72 (AB system, 10.2 Hz, 2H, benzyl $C\underline{H}_2$), 3.80-3.70 (m, 2H, H-4), 3.12 (t, 1H, 9.5, H-5), 1.90-1.70 (m, 2H, $C\underline{H}_2CH_3$), 1.57, 1.50 (2 x s, 2 x 3H, acetonide methyls), 0.98 (t, 7 Hz, 3H, $CH_2C\underline{H}_3$); ^{13}C NMR (125 MHz) δ 140.1, 137.5 (aromatic C_q), 128.6, 128.5, 128.3, 127.7, 127.6, 127.5, 127.2 (aromatic CH), 99.0 (C-2), 80.6 (C-5), 76.2 (C-6), 74.4 (benzyl $\underline{C}H_2$), 74.3 (C-4), 29.7, 19.6 (acetonide methyls), 25.2 ($\underline{C}H_2CH_3$), 9.6 ($CH_2\underline{C}H_3$). FAB MS *m/z* 326.1884 [M^+]. Calcd. for $C_{21}H_{26}O_3$, M = 326.1882.



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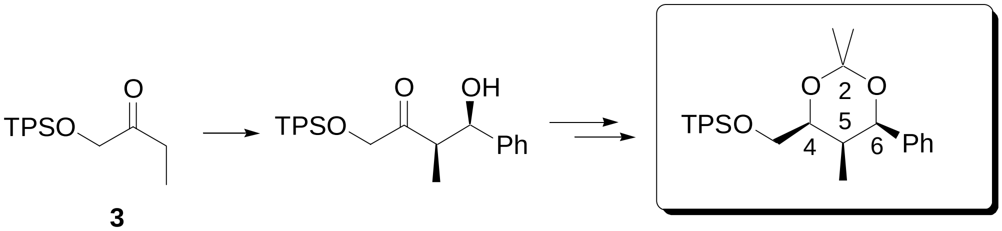
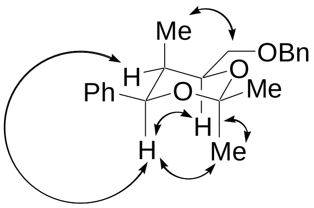


3

(±)-(4*R,5*S**,6*S**)-4-(*t*-butyldiphenylsilyloxymethyl)-2,2,5-trimethyl-6-phenyl-1,3-dioxane**: oil; ^{1}H NMR (400 MHz) δ 7.70-7.60 (m, 4H, aromatic), 7.50-7.20 (m, 11H, aromatic), 5.12 (d, 2.5 Hz, 1H, H-6), 4.29 (td, 6.5, 2.2 Hz, 1H, H-4), 3.79 (dd, 10.2, 6.5 Hz, 1H, TPSOC$\underline{\mathit{H}}_2$), 3.67 (dd, 10.2, 6.5 Hz, 1H, TPSOC$\underline{\mathit{H}}_2$), 1.92 (m, 1H, H-5), 1.53 (s, 6H, acetonide methyls), 1.11 (s, 9H, $\underline{t\mathrm{Bu}}$Si), 0.62 (d, 7 Hz, 3H, $\underline{\mathit{Me}}$-C$_5$); ^{13}C NMR (100 MHz) δ 141.0, 135.6, 133.7 (aromatic C$_q$), 135.7, 129.7, 129.6, 128.0, 127.7, 127.6, 127.5, 126.8, 125.6 (aromatic CH), 99.2 (C-2), 74.6 (C-6), 73.5 (C-4), 64.5 (TPSO$\underline{\mathit{C}}$H$_2$), 34.8 (C-5), 29.9, 19.6 (acetonide methyls), 26.9 (SiC$\underline{\mathit{Me}_3}$), 19.3 (Si$\underline{\mathit{C}}Me_3$), 5.0 ($\underline{\mathit{Me}}$-C$_5$); FAB MS *m/z* 475.2682 [M+H$^+$]. Calcd. for $C_{30}H_{39}O_3Si$, M = 475.2668.



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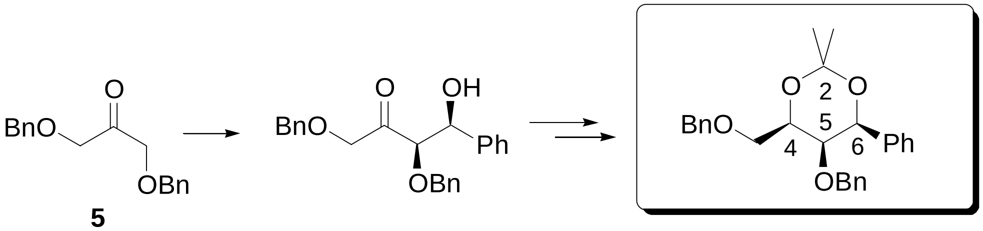
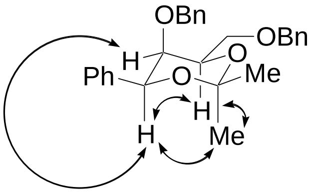


5

(±)-(4*R,5*R**,6*S**)-5-benzyloxy-4-benzyloxymethyl-2,2-dimethyl-6-phenyl-1,3-dioxane**: oil; ^{1}H NMR (500 MHz) δ 7.50-7.20 (m, 15H, aromatic), 5.03 (br s, 1H, H-6), 4.52, 4.46 (AB system, 11.8 Hz, 2H, benzyl C$\underline{H}_2$), 4.29 (br t, 6.5 Hz, 1H, H-4), 3.88, 3.82 (AB system, 11.2 Hz, 2H, benzyl C$\underline{H}_2$), 3.60 (m, 2H, BnOC$\underline{H}_2$), 3.50 (br s, 1H, H-5), 1.60, 1.57 (2 x s, 2 x 3H, acetonide methyls); ^{13}C NMR (125 MHz) δ 139.0, 138.0 (aromatic C$_q$), 128.4, 128.3, 128.1, 127.9, 127.8, 127.6, 127.5, 126.7 (aromatic CH), 99.1 (C-2), 74.3 (C-6 + benzyl$\underline{C}$H$_2$), 73.6 (benzyl$\underline{C}$H$_2$), 73.4 (C-4), 71.6 (C-5), 69.7 (BnO$\underline{C}$H$_2$), 29.7, 19.1 (acetonide methyls). FAB MS *m/z* 419.2234 [M+H$^+$]. Calcd. for $C_{27}H_{31}O_4$, M = 419.2222.



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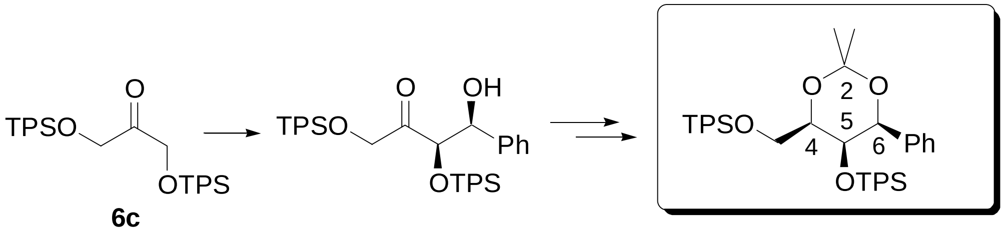
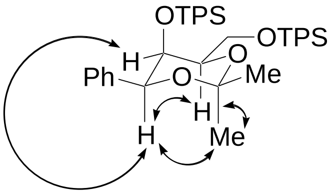


6c

(±)-(4*R,5*R**,6*S**)-5-(*t*-butyldiphenylsilyloxy)-4-(*t*-butyldiphenylsilyloxymethyl)-2,2-dimethyl-6-phenyl-1,3-dioxane**: oil; ^{1}H NMR (400 MHz) δ 7.50-7.20 (m, 25H, aromatic), 4.83 (br s, 1H, H-6), 3.84 (br dd, 7.7, 3 Hz, 1H, H-4), 3.78 (br s, 1H, H-5), 3.55 (dd, 11, 7.7 Hz, 1H, TPSOC$\underline{H_2}$), 2.98 (dd, 11, 3 Hz, 1H, TPSOC$\underline{H_2}$), 1.72, 1.46 (2 x s, 2 x 3H, acetonide methyls), 0.94 (s, 9H, $\underline{tBu}$Si), 0.50 (s, 9H, $\underline{tBu}$Si); ^{13}C NMR (100 MHz) δ 139.4, 133.7, 133.5, 132.6 (aromatic C_q), 136.0, 135.9, 135.5, 129.3, 129.0, 128.0, 128.1, 127.5, 127.4, 127.3, 127.2, 127.1, 127.0, 126.2 (aromatic CH), 99.2 (C-2), 75.3 (C-6), 69.4 (C-5), 65.5 (TPSO$\underline{C}$H$_2$), 29.8, 19.1 (acetonide methyls), 26.8, 26.1 (2 x SiC$\underline{Me_3}$), 19.5, 19.0 (2 x Si$\underline{C}$Me$_3$). EIMS *m/z* (rel.int.) 657.2875 [M–*t*Bu]$^+$ (14), 241 (100). Calcd. for $C_{45}H_{54}O_4Si_2$–*t*Bu, M = 657.2856.



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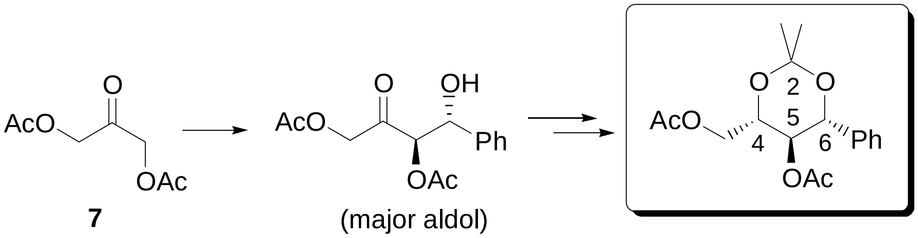
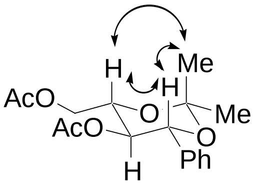


7

(major aldol)

(±)-(4*R,5*S**,6*R**)-5-acetoxy-4-acetoxymethyl-2,2-dimethyl-6-phenyl-1,3-dioxane**: oil; ^{1}H NMR (500 MHz) δ 7.40-7.20 (m, 5H, aromatic), 4.84 (t, 9.5 Hz, 1H, H-5), 4.73 (d, 9.5 Hz, 1H, H-6), 4.20-4.10 (m, 3H, H-4 + AcOC$\underline{\mathit{H}_2}$), 2.08, 1.84 (2 x s, 2 x 3H, 2 x OAc), 1.63, 1.54 (2 x s, 2 x 3H, acetonide methyls); ^{13}C NMR (125 MHz) δ 170.9, 169.0 (acetate C=O), 137.7 (aromatic C$_q$), 128.6, 128.4, 127.3 (aromatic CH), 99.7 (C-2), 74.3 (C-6), 70.6 (C-4), 68.7 (C-5), 63.6 (AcO$\underline{\mathit{C}}$H$_2$), 29.4, 19.3 (acetonide methyls), 20.9, 20.5 (acetate Me). FAB MS *m/z* 323.1493 [M+H$^+$]. Calcd. for C$_{17}$H$_{23}$O$_6$, M = 323.1494.



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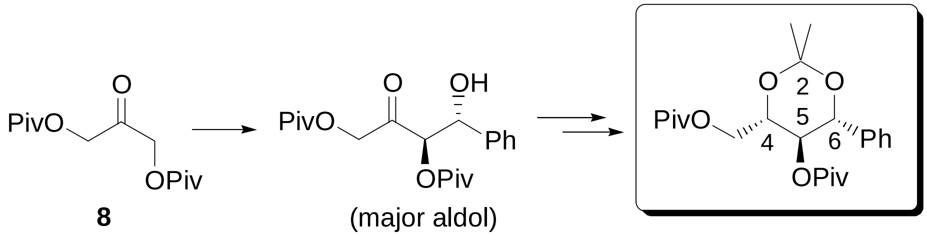
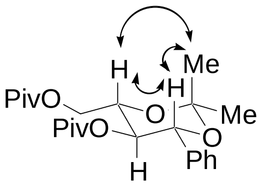


(±)-(4*R,5*S**,6*R**)-5-pivaloyloxy-4-pivaloyloxymethyl-2,2-dimethyl-6-phenyl-1,3-dioxane**: oil; ^{1}H NMR (400 MHz) δ 7.40-7.20 (m, 5H, aromatic), 4.91 (t, 9.8 Hz, 1H, H-5), 4.72 (d, 9.8 Hz, 1H, H-6), 4.20 (dd, 12, 2 Hz, 1H, PivOC$\underline{H_2}$), 4.13 (ddd, 9.8, 5.5, 2 Hz, 1H, H-4), 4.00 (dd, 12, 5.5 Hz, 1H, PivOC$\underline{H_2}$), 1.62, 1.52 (2 x s, 2 x 3H, acetonide methyls), 1.22, 0.98 (2 x s, 2 x 9H, 2 x $\underline{Me_3}$CCOO); ^{13}C NMR (100 MHz) δ 178.2, 176.3 (pivaloate C=O), 137.4 (aromatic C$_q$), 128.3, 127.9, 127.7 (aromatic CH), 99.6 (C-2), 74.8 (C-6), 71.0 (C-4), 67.7 (C-5), 62.7 (PivO$\underline{C}$H$_2$), 38.9, 38.6 (Me$_3\underline{C}$COO), 29.4, 19.3 (acetonide methyls), 27.1, 27.0 ($\underline{Me_3}$CCOO). FAB MS *m/z* 429.2261 [M+Na$^+$]. Calcd. for $C_{23}H_{34}O_6Na$, M = 429.2253.



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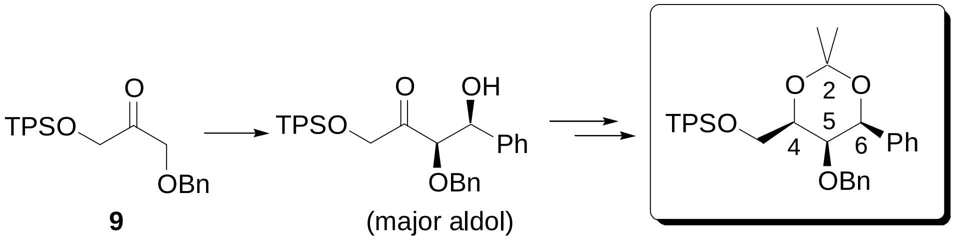
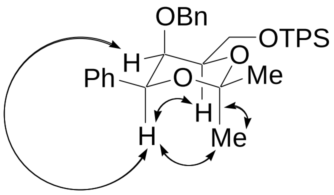


9

(major aldol)

(±)-(4*R,5*R**,6*S**)-5-(benzyloxy)-4-(*t*-butyldiphenylsilyloxymethyl)-2,2-dimethyl-6-phenyl-1,3-dioxane**: colorless oil; ^{1}H NMR (400 MHz) δ 7.70-7.25 (m, 20H, aromatic), 4.98 (d, 1.6 Hz, 1H, H-6), 4.10 (ddd, 7.7, 5.7, 1.6 Hz, 1H, H-4), 4.04, 3.74 (AB system, 11 Hz, 2H, benzyl C$\underline{H_2}$), 3.83 (dd, 10.2, 7.7 Hz, 1H, TPSOC$\underline{H_2}$), 3.75 (dd, 10.2, 5.7 Hz, 1H, TPSOC$\underline{H_2}$), 3.51 (t, 1.6 Hz, 1H, H-5), 1.52, 1.49 (2 x s, 2 x 3H, acetonide methyls), 1.07 (s, 9H, $\underline{t\mathrm{Bu}}$Si); ^{13}C NMR (100 MHz) δ 139.1, 138.1, 133.6, 133.4 (aromatic C$_q$), 135.6, 135.5, 129.7, 129.6, 128.2, 128.1, 127.9, 127.7, 127.5, 127.3, 126.8 (aromatic CH), 100.0 (C-2), 74.4 (C-6), 74.3 (benzyl $\underline{C}$H$_2$), 73.3 (C-5), 73.1 (C-4), 63.3 (TPSO$\underline{C}$H$_2$), 29.6, 19.1 (acetonide methyls), 27.0 (SiC$\underline{Me_3}$), 19.2 (Si$\underline{C}$Me$_3$). FAB MS *m/z* 589.2741 [M+Na$^+$]. Calcd. for $C_{36}H_{42}O_4NaSi$, M = 589.2750.



NOEs detected
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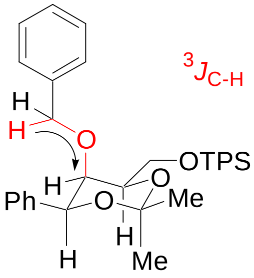
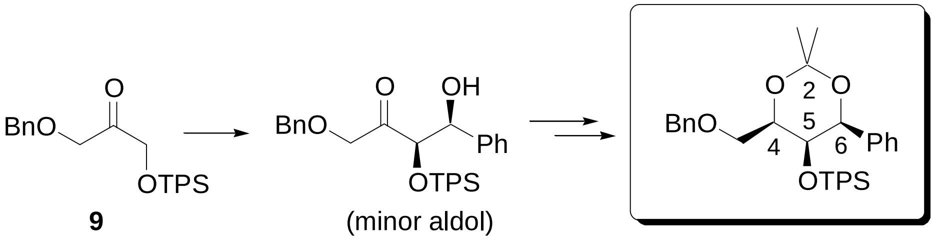
The position of the protecting groups (Bn on 5-OH, TPS on the primary OH) was deduced from long-range heteronuclear 2D correlation experiments (HMBC). The relevant correlation is indicated below.

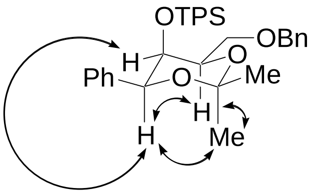




9

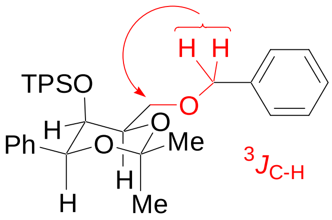
(minor aldol)

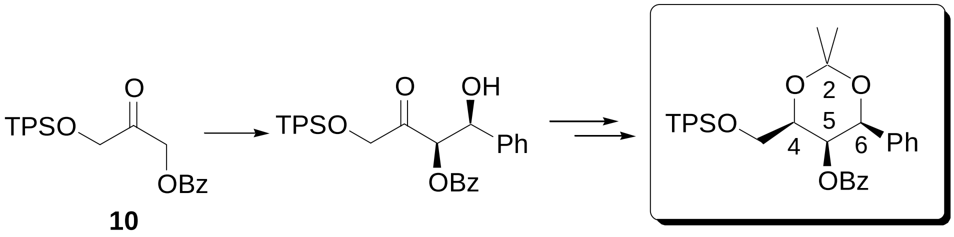
(±)-(4*R,5*R**,6*S**)-5-(*t*-butyldiphenylsilyloxy)-4-(benzyloxymethyl)-2,2-dimethyl-6-phenyl-1,3-dioxane**: colorless oil; ^{1}H NMR (400 MHz) δ 7.70-7.25 (m, 20H, aromatic), 4.93 (br s, 1H, H-6), 4.15, 3.92 (AB system, 11.8 Hz, 2H, benzyl C$\underline{\mathit{H}_2}$), 4.05 (br dd, 6.8, 4.8 Hz, 1H, H-4), 4.00 (br s, 1H, H-5), 3.27 (dd, 10, 6.8 Hz, 1H, BnOC$\underline{\mathit{H}_2}$), 2.97 (dd, 10, 4.8 Hz, 1H, BnOC$\underline{\mathit{H}_2}$), 1.72, 1.52 (2 x s, 2 x 3H, acetonide methyls), 0.57 (s, 9H, $\underline{t\mathrm{Bu}}$Si); ^{13}C NMR (100 MHz) δ 139.2, 138.1, 134.3, 132.7 (aromatic C$_q$), 136.3, 136.0, 129.4, 129.2, 128.2, 128.0, 127.8, 127.4, 127.3, 127.2, 127.0, 126.1 (aromatic CH), 99.4 (C-2), 75.0 (C-6), 74.0 (C-4), 73.0 (benzyl $\underline{C}$H$_2$), 71.0 (BnO$\underline{C}$H$_2$), 69.3 (C-5), 29.8, 19.3 (acetonide methyls), 26.2 (SiC$\underline{\mathit{Me}_3}$), 19.6 (Si$\underline{C}Me_3$). FAB MS *m/z* 589.2763 [M+Na$^+$]. Calcd. for $C_{36}H_{42}O_4NaSi$, M = 589.2750.



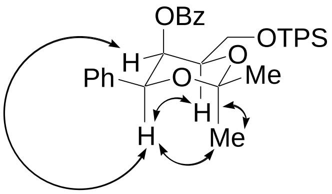
NOEs detected
(> 5% intensity)

The position of the protecting groups (TPS on 5-OH, Bn on the primary OH) was deduced from long-range heteronuclear 2D correlation experiments (HMBC). The relevant correlation is indicated below.





(±)-(4*R,5*R**,6*S**)-5-(benzoyloxy)-4-(*t*-butyldiphenylsilyloxymethyl)-2,2-dimethyl-6-phenyl-1,3-dioxane**: colorless oil; ^{1}H NMR (400 MHz) δ 7.85 (m, 2H, aromatic), 7.65-7.10 (m, 18H, aromatic), 5.44 (br s, 1H, H-5), 5.18 (br s, 1H, H-6), 4.36 (br dd, 7.5, 5.8 Hz, 1H, H-4), 3.70 (dd, 10.2, 7.5 Hz, 1H, TPSOC$\underline{\mathit{H}_2}$), 3.67 (dd, 10.2, 5.8 Hz, 1H, TPSOC$\underline{\mathit{H}_2}$), 1.58 (s, 6H, acetonide methyls), 0.98 (s, 9H, $\underline{t\mathrm{Bu}}$Si); ^{13}C NMR (100 MHz) δ 164.8 (benzoate C=O), 137.5, 133.3, 132.7, 130.0 (aromatic C_q), 135.6, 135.5, 133.0, 129.7, 129.5, 128.2, 128.1, 127.8, 127.7, 127.5, 127.3, 126.6 (aromatic CH), 99.3 (C-2), 73.6 (C-5), 71.7 (C-6), 66.7 (C-4), 62.7 (TPSO$\underline{\mathit{C}}$H$_2$), 29.7, 19.2 (acetonide methyls), 26.7 (SiC$\underline{\mathit{Me}_3}$), 19.1 (Si$\underline{\mathit{C}}Me_3$). FAB MS *m/z* 603.2561 [M+Na$^+$]. Calcd. for $C_{36}H_{40}O_5NaSi$, M = 603.2543.



NOEs detected
(> 5% intensity)

The position of the protecting groups (Bz on 5-OH, TPS on the primary OH) was deduced from long-range heteronuclear 2D correlation experiments (HMBC). The relevant correlation is indicated below.