Enantioselective synthesis of *erythro*-4-deoxyglycals as scaffolds for target- and diversity-oriented synthesis: New insights into glycal reactivity

Sirkka B. Moilanen and Derek S. Tan*

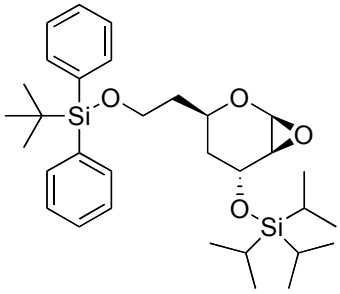
Tri-Institutional Training Program in Chemical Biology,
Tri-Institutional Research Program, and
Molecular Pharmacology & Chemistry Program

Memorial Sloan–Kettering Cancer Center
1275 York Ave., Box 422, New York, NY 10021 USA

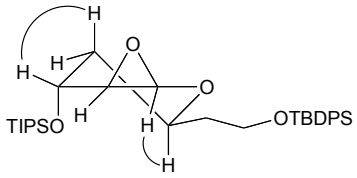
Supplementary Information

Reactions of *erythro*-4-deoxyglycal 23a

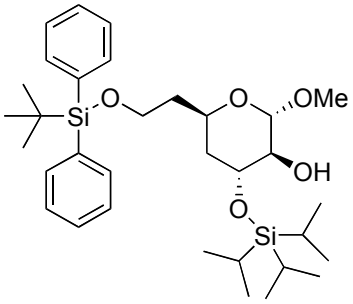
The following reactions were carried out with **(±)-23a**. Treatment of aldehyde **17** with allylmagnesium chloride provided **(±)-18**, which was converted to **(±)-23** as described in the Experimental section of the manuscript. Yields are non-optimized. Atom numbers shown in structures below correspond to standard carbohydrate nomenclature used in the text of the article and Supplementary Information and not to IUPAC nomenclature, which was used solely to name each compound.



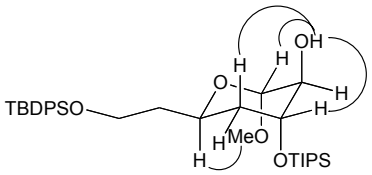
(2*R,4*R**,5*S**,6*S**)-2[2-(*tert*-Butyldiphenylsilyloxy)-ethyl]-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-5,6-oxide (25).** A solution of dimethyldioxirane (0.03 M in acetone, 1.9 mL, 0.056 mmol, 1.5 equiv) was added dropwise to a cooled (–78 ºC) solution of glycal **23a** (20.2 mg, 0.037 mmol, 1.0 equiv) in anhyd CH_2Cl_2 (1.9 mL). After 15 min the reaction was allowed to warm to rt and the solvent was removed with a stream of Ar. The crude glycal epoxide **25** was carried on without further purification, but was stable enough to characterize by NMR, which indicated a single diastereomer. The stereochemical configuration was assigned by multidimensional NMR analysis (COSY, NOESY). Diagnostic NOEs are shown below.



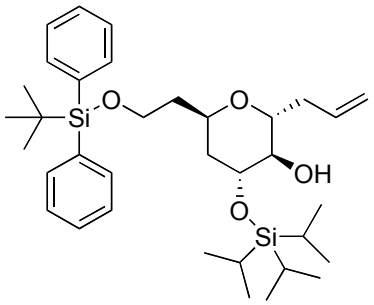
^{1}H-NMR (500 MHz, C_6D_6): δ 7.80 (m, 4H), 7.27 (m, 6H), 4.74 (d, 1H, *J* = 2.4), 4.41 (m, 2H), 3.98 (m, 1H), 3.78 (m, 1H), 2.95 (bs, 1H), 1.96 (m, 1H), 1.68-1.53 (m, 2H), 1.45 (d, 1H, *J* = 13.6), 1.16 (s, 9H), 1.02-0.95 (m, 21H). **^{13}C-NMR** (125 MHz, C_6D_6): δ136.0, 134.3, 134.2, 129.9, 77.8, 66.2, 64.9, 60.2, 54.6, 39.1, 36.7, 30.1, 27.1, 19.5, 18.2, 12.4.



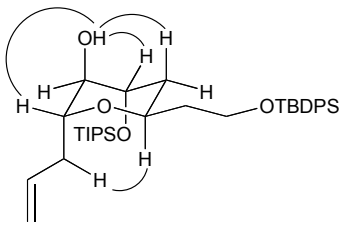
(2*S,3*R**,4*R**,6*R**)-6-[2-(*tert*-Butyldiphenylsilyloxy)-ethyl]-2-methoxy-4-(triisopropylsilyloxy)-tetrahydropyran-3-ol (26a).** Epoxide **25** formed from glycal **23a** (10 mg, 0.019 mmol, 1.0 equiv) was dissolved in anhyd MeOH (1.0 mL, sureseal bottle). After 10 min at rt the solvent was evaporated to yield methylglycoside **26a** as a clear oil (11.2 mg, 100%). NMR analysis indicated a single diastereomer. The stereochemical configuration was assigned by multidimensional NMR analysis (COSY, NOESY). Diagnostic NOEs are shown below.



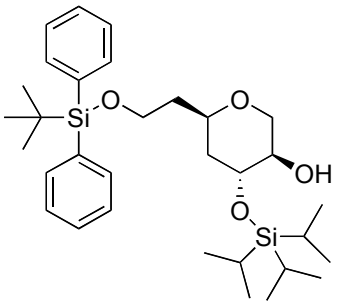
TLC: R_f: 0.61 (2:1 hexanes/EtOAc). **IR** (NaCl, film): 2943, 2864, 2345, 1462, 1428, 1101, 881, 700. **^{1}H-NMR** (400 MHz): δ 7.67 (m, 4H), 7.40 (m, 6H), 4.50 (d, 1H, *J* = 3.4), 4.39 (m, 1H), 4.00 (m, 1H), 3.82 (m, 1H), 3.71 (m, 1H), 3.50 (m, 1H),3.31 (s, 3H),2.00 (d, 1H, *J* = 5.7), 1.82-1.53 (m, 4H), 1.02 (m, 30H). **^{13}C-NMR** (125 MHz): δ135.5, 133.9, 129.5, 127.6, 101.5, 72.1, 69.0, 62.6, 60.2, 55.3, 3.7, 35.9, 26.8, 19.2, 18.0, 12.3. **ESI-MS** *m/z*: (pos) 609.3 $[M+Na]^+$; (neg) 585.3 $[M–H]^–$, 621.3 $[M+Cl]^–$.



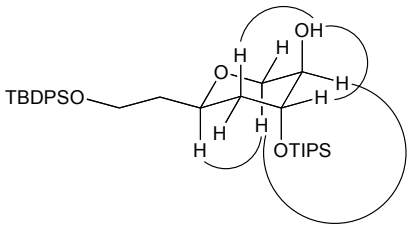
(2*R,3*R**,4*R**,6*R**)-2-Allyl-6-[2-(*tert*-butyldiphenylsilyloxy)-ethyl]-4-(triisopropylsilyloxy)-tetrahydropyran-3-ol (27).** Epoxide **25** formed from glycal **23a** (10 mg, 0.019 mmol, 1.0 equiv) was dissolved in anhyd THF (0.2 mL) and cooled to –78 ºC. Allylmagnesium chloride (2.0 M in THF, 18.6 μL, 0.037 mmol, 2.0 equiv) was added and the reaction mixture was stirred at –78 ºC for 20 min then warmed to 0 ºC. After 45 min at 0 ºC the reaction was quenched with sat'd aq NH_4Cl. The aqueous layer was extracted 3x with Et_2O and the combined organic layers were washed with H_2O and brine, dried ($MgSO_4$), filtered, and concentrated. The residue was purified by flash chromatography (elution with 9:1 hexanes/EtOAc) to yield **27** as a clear oil (8.9 mg, 80%). NMR analysis of the crude product indicated a single diastereomer. The stereochemical configuration was assigned by multidimensional NMR analysis (COSY, NOESY). Diagnostic NOEs are shown below.



TLC: R_f: 0.67 (2:1 hexanes/EtOAc). **IR** (NaCl, film): 3448, 2931, 2861, 2355, 1467, 1425, 1108, 873, 820, 738, 697. **^{1}H-NMR** (400 MHz): δ 7.65 (t, 4H, *J* = 7.8), 7.40 (m, 6H), 5.79 (m, 1H), 5.10-4.93 (m, 2H), 4.22 (m, 1H), 3.92 (m, 1H), 3.78 (m, 1H), 3.65 (m, 1H), 3.41 (td, 1H, *J* = 7.8, 3.6), 3.23 (td, 1H, *J* = 7.4, 3.4), 2.51 (m, 1H), 2.40 (m, 1H), 2.29 (d, 1H, *J* = 3.4), 1.99 (m, 1H), 1.80 (m, 2H), 1.61 (m, 1H), 1.05 (m, 30H). **^{13}C-NMR** (125 MHz): δ135.9, 135.6, 134.3, 130.0, 128.0, 117.0, 75.6, 73.8, 71.5, 66.2, 60.9, 37.2, 36.3, 35.2, 27.2, 19.6, 18.5, 15.7, 12.9. **ESI-MS** *m/z*: (pos) 619.4 $[M+Na]^+$; (neg) 595.4 $[M–H]^–$, 631.3 $[M+Cl]^–$.

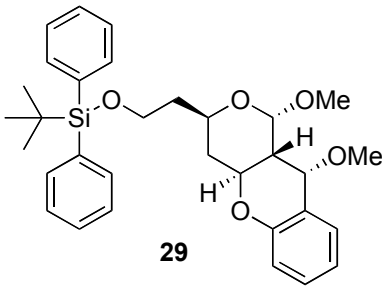


(3*R,4*R**,6*R**)-6-[2-(*tert*-Butyldiphenylsilyloxy)-ethyl]-4-(triisopropylsilyloxy)-tetrahydropyran-3-ol (28).** Thexylborane[†] (0.5 M in THF, 94 μL, 0.047 mmol, 2.0 equiv) was added dropwise to a cooled (0 ºC) solution of glycal **23a** (12.6 mg, 0.023 mmol, 1.0 equiv) in anhyd THF (0.3 mL). After 2 h at 0 ºC, aq NaOH (1.0 M, 0.15 mL, 0.15 mmol, 6.6 equiv) was added slowly, followed by H_2O_2 (30 wt % in H_2O, 18 μL, 0.15 mmol, 6.6 equiv). The reaction mixture was warmed to rt, stirred 1 h, then diluted with Et_2O. The aqueous layer was extracted 3x with Et_2O then the combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated. The residue was purified by flash chromatography (elution with 9:1 hexanes/EtOAc) to yield alcohol **28** as a clear oil (9.6 mg, 74%). NMR analysis of the crude product indicated a 11.7:1.0 diastereomeric ratio. The stereochemical configuration was assigned by multidimensional NMR analysis (COSY, NOESY). Diagnostic NOEs are shown below.

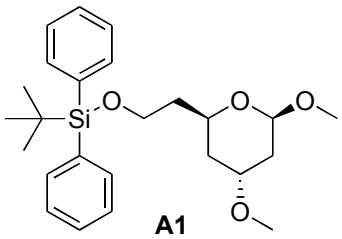


TLC: R_f: 0.38 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 3401, 2943, 2861, 2355, 1467, 1096, 885, 738, 703, 679. **^{1}H-NMR** (400 MHz): δ 7.68 (m, 4H), 7.40 (m, 6H), 4.00 (m, 3H), 3.81 (m, 1H), 3.70 (m, 2H), 3.48 (m, 1H), 2.20 (d, 1H, J = 8.8), 1.75 (m, 1H), 1.62 (m, 3H), 1.05 (m, 30H). **^{13}C-NMR** (125 MHz): δ135.6, 129.5, 127.6, 68.8, 67.99, 67.6, 59.9, 39.0, 35.4, 26.8, 18.1, 12.2. **ESI-MS** *m/z*: (pos) 579.2 $[M+Na]^+$; (neg) 555.3 $[M–H]^–$, 591.5 $[M+Cl]^–$.

[†] G. Zweifel and H.C. Brown, *J. Am. Chem. Soc.*, 1963, **85**, 2066-2072.

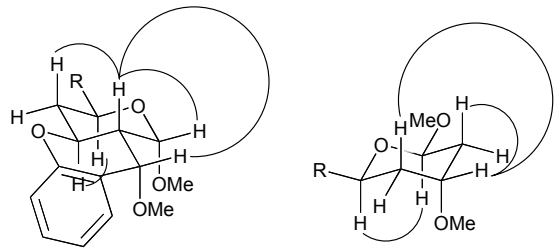


29

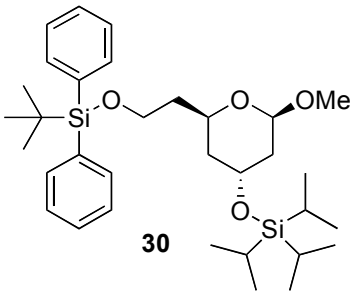


A1

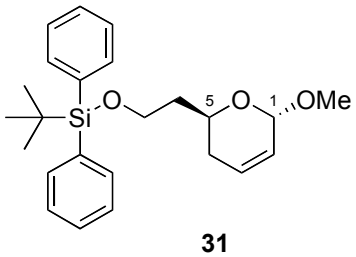
(1*S,3*R**,5*S**,6*S**,10*S**)-1,10-Dimethoxy-3-[2-(*tert*-butyldiphenylsilyloxy)-ethyl]-4,4a,10,10a-tetrahydro-1*H*,3*H*-pyrano[4,3-*b*]chromene (29)** and **(2*R**,4*R**,6*R**)-2,4-Dimethoxy-6-[2-(*tert*-butyldiphenylsilyloxy)-ethyl]-tetrahydropyran (A1).** A mixture of salicylaldehyde (23.3. µL, 0.22 mmol, 1.2 equiv), TMOF (24.4. µL, 0.22 mmol, 1.2 equiv), and $Sc(OTf)_3$ (2.7 mg, 5.6 µmol, 0.03 equiv) in anhyd CH_2Cl_2 (1.7 mL) was stirred at rt for 20 min. The reaction mixture was cooled to 0 ºC then treated with a solution of glycal **23a** (100 mg, 0.19 mmol, 1.0 equiv) in anhyd CH_2Cl_2 (1.0 mL). The reaction mixture was warmed to rt, stirred for 30 min, then quenched with H_2O. The aqueous layer was extracted 3x with CH_2Cl_2, dried ($MgSO_4$), filtered, and concentrated. NMR analysis of the crude product indicated a 1.0:3.5:1.3 ratio of **29**, **A1**, and Ferrier rearrangement product **31**. The crude material was purified by flash chromatography (4:1 hexanes/EtOAc) to yield a 2.5:1.0 mixture of **29** and **A1** (4.7 mg, 4% yield of **29**) as a clear oil. The stereochemical configurations were assigned by multidimensional NMR analysis (COSY, NOESY). Diagnostic NOEs are shown below.



TLC: R_f: 0.11 (9:1 hexanes/EtOAc). **^{1}H-NMR** (400 MHz): **29**: δ 7.72-7.61 (m, 4H), 7.51 (d, 1H, J = 7.6), 7.40 (m, 6H), 7.18 (t, 1H, J = 7.6), 6.96 (t, 1H, J = 7.3), 6.78 (d, 1H, J = 7.3), 5.59 (d, 1H, J = 3.2), 4.71 (d, 1H, J = 4.7), 4.27 (m, 1H), 3.85 (m, 1H), 3.75 (m, 1H), 3.59 (s, 3H), 3.30 (m, 1H), 3.21 (s, 3H), 2.50 (m, 1H), 2.08 (ddd, 1H, J = 14.2. 5.0, 2.1), 1.82-1.70 (m, 2H), 1.25 (m, 1H), 1.07 (s, 9H). **A1**: 7.65 (m, 4H), 7.38 (m, 6H), 4.56 (dd, 1H, J = 9.8, 2.1), 3.99 (m, 1H), 3.89-3.70 (m, 2H), 3.69 (m, 1H), 3.40 (s, 3H), 3.31 (s, 3H), 2.01 (m, 1H), 1.84-1.68 (m, 3H), 1.44 (m, 1H), 1.34 (m, 1H), 1.04 (s, 9H). **ESI-MS** *m/z*: **29**: (pos) 555.2 $[M+Na]^+$; (neg) 531.2 $[M–H]^–$, 567.3 $[M+Cl]^–$. **A1**: 451.1 $[M+Na]^+$.

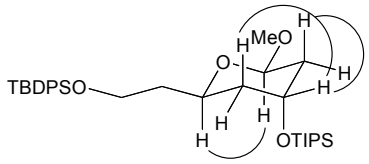


30

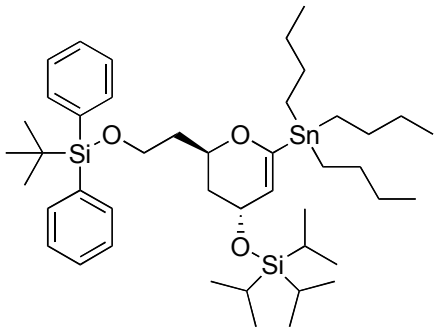


31

(2*R,4*R**,6*R**)-2-[2-(*tert*-Butyldiphenylsilyloxy)-ethyl]-6-methoxy-4-(triisopropylsilyloxy)-tetrahydropyran (30)** and **(2*R**,6*S**)-6-Methoxy-2-[2-(*tert*-butyldiphenylsilyloxy)-ethyl]-3,6-dihydro-2*H*-pyran (31).** Anhyd methanol (2.3 μL, 0.057 mmol, 3.0 equiv, sureseal bottle) then Ph_3P•HBr (0.3 mg, 0.95 μmol, 0.05 equiv) was added to a solution of **23a** (10 mg, 0.019 mmol, 1.0 equiv) in anhyd CH_2Cl_2 (0.2 mL). After 20 min at rt the reaction mixture was diluted with CH_2Cl_2, washed 2x with sat'd aq $NaHCO_3$, once with brine, dried ($MgSO_4$), filtered, and concentrated. NMR analysis of the crude product indicated a 3.0:1.0:3.3 ratio of **30**, its α-anomer, and **31**. Purification by flash chromatography (elution with 95:5 hexanes/EtOAc) yielded a 1.0:1.1 mixture of **30** and **31 (**4.5 mg, 24% yield of **30**, 27% yield of **31**) as a clear oil. The stereochemical configurations were assigned by multidimensional NMR analysis (COSY, NOESY). Diagnostic NOEs for **30** are shown below. The stereochemical configuration of **31** was assigned based on the absence of an NOE between the anomeric *C*1-H and *C*5-H.

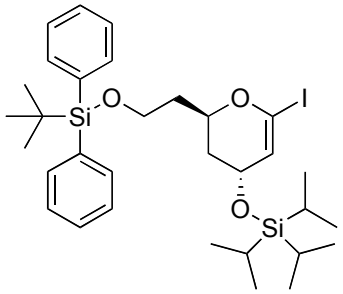


TLC: R_f: 0.31 (9:1 hexanes/EtOAc). **^{1}H-NMR** (400 MHz): **30**: δ 7.66 (m, 4H), 7.40 (m, 6H), 4.71 (dd, 1H, J = 1.9, 9.6), 4.38 (m, 1H), 4.22 (m, 1H), 3.93-3.69 (m, 2H), 3.42 (s, 3H), 1.90 (m, 1H), 1.76 (m, 2H), 1.63 (m, 1H), 1.54-1.39 (m, 2H). **31**: 7.65 (m, 4H), 7.38 (m, 6H), 6.00 (m, 1H), 5.72 (m, 1H), 4.80 (s, 1H), 4.11 (m, 1H), 3.92-3.72 (m, 2H), 3.32 (s, 3H), 1.96 (m, 2H), 1.78 (m, 2H), 1.02 (s, 9H). **ESI-MS** *m/z*: **30**: (pos) 593.4 $[M+Na]^+$; (neg) 605.2 $[M+Cl]^-$. **31**: (pos) 419.1 $[M+Na]^+$.



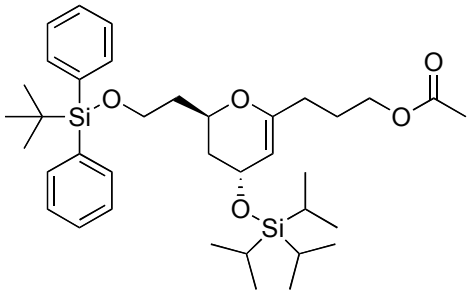
(2*R,4*R**)-2-[2-(*tert*-Butyldiphenylsilyloxy)-ethyl]-6-(tributylstannanyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran (A2).** *t*-BuLi (1.5 M in pentane, 2.1 mL, 3.20 mmol, 4.0 equiv) was added slowly to a cooled (–78 ºC) solution of glycal **23a** (431.5 mg, 0.80 mmol, 1.0 equiv) in anhyd THF (4.0 mL). After 15 min at –78 ºC, the reaction was warmed to 0 ºC, maintained at that temperature 1 h, then cooled to –78 ºC. Tributyltin chloride (540 µL, 2.00 mmol, 2.5 equiv) was added, the reaction was stirred at –78 ºC 30 min, then quenched with sat'd aq $NaHCO_3$. The aqueous layer was extracted 3x with Et_2O then the combined organic layers were washed with H_2O and brine, dried ($MgSO_4$), filtered, and concentrated. The crude material was purified by flash chromatography (elution with 7:1 hexanes/CH_2Cl_2+ 0.5% Et_3N) to yield glycal stannane **A2** as a clear oil (493.5 mg, 74 %).

TLC: R_f: 0.67 (9:1 hexanes/EtOAc). **IR** (NaCl, film): 2959, 2923, 2864, 1590, 1460, 1087, 1063, 998, 879, 737, 695. **^{1}H-NMR** (400 MHz): δ 7.63 (dt, 4H, J = 1.8, 7.7), 7.39 (m, 6H), 4.90 (d, 1H, J = 4.2), 4.09 (m, 2H), 3.81 (m, 2H), 1.82-1.71 (m, 3H), 1.60-1.40 (m, 7H), 1.23 (m, 6H), 1.02 (m, 30H), 0.82 (m, 15H). **^{13}C-NMR** (125 MHz): δ135.6, 134.1, 129.5, 127.6, 114.9, 68.2, 60.7, 60.6, 38.7, 38.6, 29.0, 27.2, 26.9, 19.2, 18.2, 13.7, 12.5, 9.6. **ESI-MS** *m/z*: (pos) 851.3 $[M+Na]^+$; (neg) 863.4 $[M+Cl]^-$.



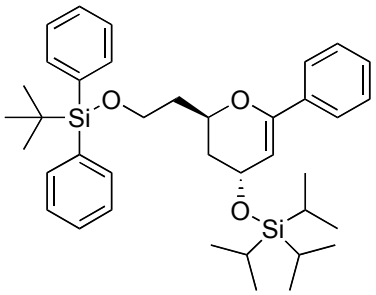
(2*R,4*R**)-2-[2-(*tert*-Butyldiphenylsilyloxy)-ethyl]-6-iodo-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran (A3).** A solution of iodine (0.2 M in CH_2Cl_2, 620 µL, 0.12 mmol, 1.0 equiv) was added dropwise to a solution of glycal stannane **A2** (101.7 mg, 0.12 mmol, 1.0 equiv) in anhyd CH_2Cl_2 (2.4 mL) in the dark. As soon as a purple color persisted in the reaction mixture, the reaction was quenched with 10% aq $Na_2S_2O_3$. The aqueous layer was extracted 3x with CH_2Cl_2, then the combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated. The crude material was purified by flash chromatography (elution with 4:1 hexanes/CH_2Cl_2 + 0.5% Et_3N) to yield glycal iodide **A3** as a clear oil (80.0 mg, 98%).

TLC: R_f: 0.70 (4:1 hexanes/EtOAc). **^{1}H-NMR** (400 MHz, C_6D_6): δ 7.77 (m, 4H), 7.40-7.22 (m, 6H), 5.58 (d, 1H, *J* = 4.0), 4.75 (m, 1H), 3.91 (m, 1H), 3.85 (m, 1H), 3.65 (m, 1H), 1.79-1.52 (m, 3H), 1.40 (m, 1H), 1.14 (s, 9H), 1.08-0.92 (m, 21H).



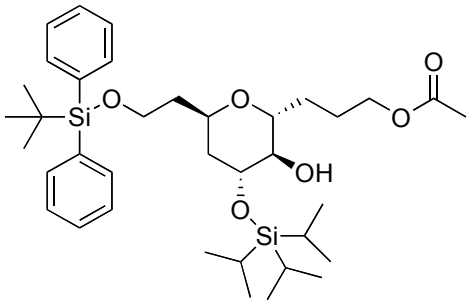
(2*R,4*R**)-2-[2-(*tert*-Butyldiphenylsilyloxy)-ethyl]-6-(3-acetoxypropyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran (32a).** 9-BBN (0.5 M in THF, 1.4 mL, 0.72 mmol, 3.0 equiv) was added dropwise to a cooled (0 ºC) solution of allyl acetate (39.2 µL, 0.36 mmol, 1.5 equiv) in anhyd THF (3.6 mL). The mixture was stirred at 0 ºC for 5 min then warmed to rt. After 4 h, aq NaOH (1 N, 725 µL, 0.72 mmol, 3.0 equiv) was added and the mixture was stirred an additional 30 min. The hydroboration reaction was then added to a mixture of glycal iodide **A3** (160 mg, 0.24 mmol, 1.0 equiv), $PdCl_2$(dppf) (19.7 mg, 0.024 mmol, 0.1 equiv), and H_2O (0.7 mL) in THF (2.4 mL, Optima grade). After 20 min at rt the reaction mixture was diluted with pentane and the solid was filtered off. The filtrate was washed with 1N NaOH, H_2O, and brine, dried ($MgSO_4$), filtered, and concentrated. The crude material was purified by flash chromatography (elution with 95:5 hexanes/EtOAc) to yield 1-alkylglycal **32a** as a clear oil (105.2 mg, 68%).

TLC: R_f: 0.32 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 2935, 2864, 1739, 1661, 1460, 1241, 1093, 695. **^{1}H-NMR** (500 MHz): δ 7.68 (d, 4H, *J* = 7.3), 7.40 (m, 6H), 4.69 (d, 1H, *J* = 5.0), 4.29-4.19 (m, 2H), 4.02 (t, 2H, *J* = 6.6), 3.90-3.70 (m, 2H), 2.05 (t, 2H, *J* = 7.3), 2.02 (s, 3H), 1.82-1.71 (m, 5H), 1.51 (m, 1H), 1.03 (m, 30H). **^{13}C NMR** (125 MHz): δ155.3, 135.6, 133.9, 129.5, 127.6, 99.5, 68.4, 63.9, 61.2, 60.1, 38.2, 38.1, 30.6, 26.8, 25.9, 21.0, 19.2, 18.2, 12.4. **ESI-MS** *m/z*: (pos) 661.3 $[M+Na]^+$.

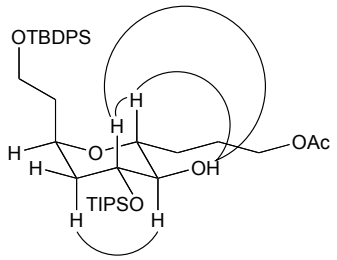


(2*R,4*R**)-2-[2-(*tert*-Butyldiphenylsilyloxy)-ethyl]-6-phenyl-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran (32b).** A mixture of glycal stannane **A2** (80.2 mg, 0.097 mmol, 1.0 equiv), bromobenzene (15.3 μL, 0.15 mmol, 1.5 equiv), and $Pd(PPh_3)_4$ (5.6 mg, 4.9 μmol, 0.05 equiv) in anhyd THF (1.9 mL) was refluxed 7 h. The solvent was evaporated and the residue was purified by flash chromatography (elution with 98:2 hexanes/EtOAc) to yield 1-phenylglycal **32b** as a clear oil (57.5 mg, 96%).

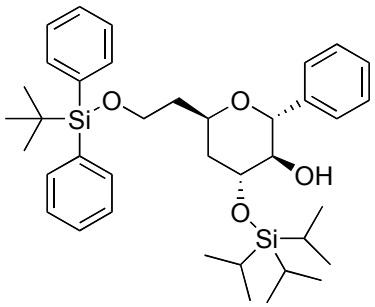
TLC: R_f: 0.54 (9:1 hexanes/EtOAc). **IR** (NaCl, film): 2935, 2864, 1644, 1466, 1424, 1282, 1093, 1004, 873, 737, 701. **^{1}H-NMR** (400 MHz): δ 7.69 (m, 4H), 7.51 (m, 2H), 7.42-7.27 (m, 9H), 5.49 (d, 1H, J = 4.8), 4.45 (m, 2H), 4.02 (m, 1H), 3.90 (m, 1H), 2.00-1.86 (m, 3H), 1.69 (m, 1H), 1.06 (m, 30H). **^{13}C-NMR** (125 MHz): δ135.6, 129.5, 128.3, 128.1, 127.6, 125.1, 99.7, 68.7, 61.6, 60.2, 38.4, 38.2, 26.8, 19.2, 18.2, 12.4. **ESI-MS** *m/z*: (pos) 615.5 $[M+H]^+$, 637.2 $[M+Na]^+$; (neg) 649.2 $[M+Cl]^-$.



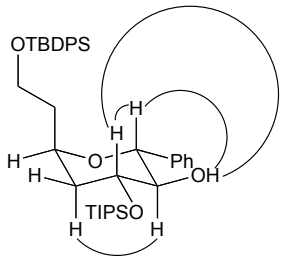
(2*R,3*R**,4*R**,6*R**)-2-(3-Acetoxypropyl)-6-[2-(*tert*-butyldiphenylsilyloxy)-ethyl]-4-(triisopropylsilyloxy)-tetrahydropyran-3-ol (33a).** Thexylborane† (0.5 M in THF, 65 μL, 0.033 mmol, 2.0 equiv) was added dropwise to a cooled (0 ºC) solution of 1-alkylglycal **32a** (10.4 mg, 0.016 mmol, 1.0 equiv) in anhyd THF (0.2 mL). The reaction mixture was stirred for 1.5 h at 0 ºC then warmed to rt. After 1.5 h at rt, aq NaOH (1.0 M, 0.11 mL, 0.11 mmol, 6.6 equiv) was added slowly, followed by H_2O_2 (30 wt % in H_2O, 12 μL, 0.11 mmol, 6.6 equiv). The reaction mixture was stirred for 1 h then diluted with Et_2O. The organic layer was washed with sat'd aq NH_4Cl, H_2O, and brine, dried ($MgSO_4$), filtered, and concentrated. The residue was purified by flash chromatography (elution with 4:1 hexanes/EtOAc) to yield alcohol **33a** as a clear oil (8.1 mg, 76%). NMR analysis of the crude product indicated a single diastereomer. The stereochemical configuration was assigned by multidimensional NMR analysis (COSY, NOESY). Diagnostic NOEs are shown below.



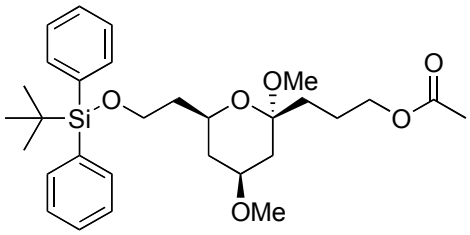
TLC: R_f: 0.40 (9:1 DCM/Et_2O). **IR** (NaCl, film): 3460, 2943, 2861, 1731, 1425, 1361, 1243, 1108, 703. **^{1}H-NMR** (400 MHz): δ 7.64 (m, 4H), 7.39 (m, 6H), 4.22 (m, 1H), 4.01 (m, 2H), 3.90 (m, 1H), 3.75 (m, 1H), 3.65 (m, 1H), 3.32 (m, 1H), 3.19 (td, 1H, J = 3.3, 7.3), 2.29 (d, 1H, J = 3.3), 2.01 (s, 3H), 1.95 (m, 1H), 1.81-1.48 (m, 7H), 1.03 (m, 30H). **^{13}C NMR** (125 MHz): δ135.5, 129.6, 127.6, 73.2, 71.1, 64.6, 41.0, 36.8, 34.8, 26.8, 24.9, 18.1, 12.4. **ESI-MS** *m/z*: (pos) 679.5 $[M+Na]^+$; (neg) 655.4 $[M+H]^-$, 691.3 $[M+Cl]^-$.



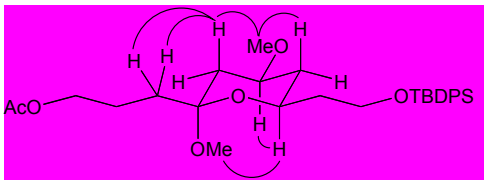
(2*R,3*R**,4*R**,6*R**)-2-Phenyl-6-[2-(*tert*-butyldiphenylsilyloxy)-ethyl]-4-(triisopropylsilyloxy)-tetrahydropyran-3-ol (33b).** Thexylborane† (0.5 M in THF, 140 µL, 68 µmol, 10 equiv) was added dropwise to a cooled (0 ºC) solution of 1-phenylglycal **32b** (4.2 mg, 6.8 µmol, 1.0 equiv) in anhyd THF (0.2 mL). The reaction mixture was stirred for 1 h at 0 ºC then warmed to rt and stirred for 20 h. At this time, the reaction was approximately 50% complete (TLC). Additional freshly prepared thexylborane (0.5 M in THF, 140 µL, 68 µmol, 10 equiv) was added and the reaction mixture was stirred an additional 4 h at rt. Aq NaOH (1.0 M, 0.45 mL, 0.45 mmol, 66 equiv) was added slowly, followed by H_2O_2 (30 wt % in H_2O, 51 µL, 0.45 mmol, 66 equiv). The reaction mixture was stirred 2 h then diluted with Et_2O. The organic layer was washed with sat'd aq NH_4Cl, brine, dried ($MgSO_4$), filtered, and concentrated. The residue was purified by flash chromatography (elution with 9:1 hexanes/EtOAc) to yield alcohol **33b** as a clear oil (3.1 mg, 72%). NMR analysis of the crude product indicated a single diastereomer. The stereochemical configuration was assigned by multidimensional NMR analysis (COSY, NOESY). Diagnostic NOEs are shown below.



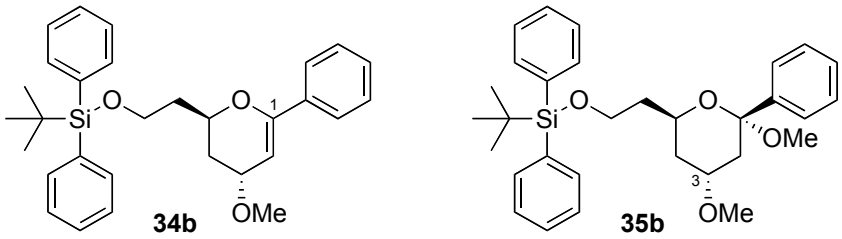
TLC: R_f: 0.21 (9:1 hexanes/EtOAc). **IR** (NaCl, film): 2931, 2861, 1462, 1428, 1111, 882, 738, 700. **^{1}H-NMR** (400 MHz): δ 7.62 (m, 4H), 7.40-7.21 (m, 11H), 4.40 (m, 1H), 4.22 (d, 1H, J = 9.2), 4.05 (m, 1H), 3.80 (m, 1H), 3.69 (m, 1H), 3.49 (m, 1H), 2.18 (m, 2H), 1.98 (m, 2H), 1.75 (m, 1H), 1.02 (m, 30H). **^{13}C-NMR** (125 MHz): δ139.5, 135.5, 129.6, 129.5, 128.3, 128.0, 127.6, 127.5, 77.7, 75.3, 71.2, 70.0, 60.7, 37.3, 33.8, 26.8, 19.2, 18.1, 18.0, 12.5, 12.3. **ESI-MS** *m/z*: (pos) 655.4 $[M+Na]^+$; (neg) 631.4 $[M–H]^–$, 667.4 $[M+Cl]^–$.



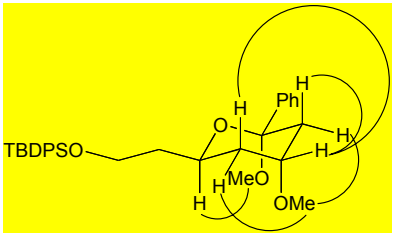
(2*R,3*R**,4*R**,6*R**)-2-(3-Acetoxypropyl)-6-[2-(*tert*-butyldiphenylsilyloxy)-ethyl]-2,4-dimethoxytetrahydropyran (35a).** Anhyd MeOH (2.3 μL, 0.058 mmol, 3.0 equiv, sureseal bottle) then Ph_3P•HBr (0.3 mg, 0.96 μmol, 0.05 equiv) were added to a solution of 1-alkylglycal **32a** (12.3 mg, 0.019 mmol, 1.0 equiv) in anhyd CH_2Cl_2 (0.2 mL). The reaction was stirred at rt for 1 h then diluted with CH_2Cl_2, washed with sat'd aq $NaHCO_3$, brine, dried ($MgSO_4$), filtered, and concentrated. The residue was purified by flash chromatography (elution with 4:1 hexanes/EtOAc) to yield methyl glycoside **35a** as a clear oil (5.1 mg, 50%). The stereochemical configuration was assigned by multidimensional NMR analysis (COSY, NOESY). Diagnostic NOEs are shown below.



TLC: R_f: 0.14 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 2935, 2864, 1739, 1466, 1424, 1359, 1235, 1093, 701. **^{1}H-NMR** (500 MHz): δ 7.65 (m, 4H), 7.42 (m, 6H), 4.06 (t, 2H, J = 6.4), 3.87-3.79 (m, 2H), 3.75 (m, 1H), 3.60 (m, 1H), 3.32 (s, 3H), 3.08 (s, 3H), 2.15 (dd, 1H, J = 3.5, 12.1), 2.04 (s, 3H), 1.98 (dt, 1H, J = 12.3, 2.1), 1.77-1.53 (m, 6H), 1.17 (t, 1H, J = 12.1), 1.05 (s, 10H). **^{13}C NMR** (125 MHz): δ135.5, 129.6, 127.6, 100.7, 73.5, 65.6, 64.4, 60.2, 55.5, 47.2, 38.8, 37.2, 32.5, 26.9, 22.9, 21.0. **ESI-MS** *m/z*: (pos) 551.2 $[M+Na]^+$; (neg) 563.3 $[M+Cl]^–$.



(2*R,4*R**)-2-[2-(*tert*-Butyldiphenylsilyloxy)-ethyl]-4-methoxy-6-phenyl-3,4-dihydro-2*H*-pyran (34b)** and **(2*R**,3*R**,4*R**,6*R**)-2-Phenyl-6-[2-(*tert*-butyldiphenylsilyloxy)-ethyl]-2,4-dimethoxytetrahydropyran (35b).** Anhyd MeOH (3.4 µL, 0.084 mmol, 3.0 equiv, sureseal bottle) then Ph_3P•HBr (0.5 mg, 1.4 µmol, 0.05 equiv) were added to a solution of 1-phenylglycal **32b** (15 mg, 0.028 mmol, 1.0 equiv) in anhyd CH_2Cl_2 (0.3 mL). The reaction was stirred at rt for 1 h then diluted with CH_2Cl_2, washed 2x with sat'd aq $NaHCO_3$, once with brine, dried ($MgSO_4$), filtered, and concentrated to afford a 3.4:1 mixture of **34b** and **35b**. The residue was purified by flash chromatography (elution with 98:2 hexanes/EtOAc then 9:1 hexanes/EtOAc) to yield methyl ether **34b** (2.8 mg, 24%) and methyl glycoside **35b** (1.0 mg, 8%) as clear oils. The stereochemical configuration of **34b** was tentatively assigned based on comparison of chemical shifts with other *C*1-substituted glycals. The stereochemical configuration of **35b** was assigned by multidimensional NMR analysis (COSY, NOESY). Formation of the axially oriented *C*3-OMe (in contrast to the equatorial orientation in **35a**) may result from stereoelectronic effects of the *C*1-phenyl substituent. Diagnostic NOEs are shown below.



34b: TLC: R_f: 0.18 (9:1 hexanes/EtOAc). **^{1}H-NMR** (400 MHz): δ 7.68 (m, 4H), 7.52 (m, 2H), 7.41-7.22 (m, 9H), 5.59 (dd, 1H, J = 1.2, 5.2), 4.28 (m, 1H), 3.94 (m, 2H), 3.82 (m, 1H), 3.40 (s, 3H), 2.04-1.89 (m, 3H), 1.61 (m, 1H), 1.02 (s, 9H). **ESI-MS** *m/z*: (pos) 495.3 $[M+Na]^+$; (neg) 507.2 $[M+Cl^-]$.

35b: TLC: R_f: 0.17 (9:1 hexanes/EtOAc). **IR** (NaCl, film): 2926, 2863, 1427, 1109, 1087, 742, 700. **^{1}H-NMR** (500 MHz): δ 7.68 (m, 4H), 7.46-7.26 (m, 11H), 4.30 (m, 1H), 3.90 (m, 2H), 3.57 (m, 1H), 3.38 (s, 3H), 2.92.(s, 3H), 2.28 (dt, 1H, J = 2.1, 14.9), 1.93-1.74 (m, 3H), 1.58 (obs, 1H), 1.45 (m, 1H), 1.05 (s, 9H). **ESI-MS** *m/z*: (pos) 527.2 $[M+Na]^+$.