Synthesis of Methylene-Expanded Oxetanocin Isonucleosides in Both Enantiomeric Forms[1]

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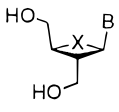
We report a novel route to isonucleosides of the 'methylene-expanded' oxetanocin class, in both the D- and L-enantiomeric forms, e.g., compounds L-(+)-**2a**, D-(−)-**2a**, and L-(−)-**2b**, beginning with the simple, known mono-*p*-bromobenzyl ether **3** of the very inexpensive 2-butene-1,4-diol. Sharpless asymmetric epoxidation of **3** gave either (−) or (+)-**4** depending on the chirality of the tartrate used. The *p*-bromobenzyl ether was used since the epoxide product is crystalline and can be recrystallized to high optical purity. Opening of the epoxide with vinylmagnesium bromide gave the 1,3-diol **5**, the primary alcohol of which was protected as the silyl ether **6**. Treatment of **6** with iodonium bis(*sym*-collidine) perchlorate afforded the desired 5-(iodomethyl)tetrahydrofuran-3-ol **8** with loss of the bromobenzyl cation in the key step in the synthetic scheme. This iodide **8** was then converted into the bis(silyloxy)-protected alcohol **15** by acetylation to give the acetate **10**, displacement of iodide with acetate, hydrolysis, and selective protection of the primary alcohols. The alcohol **6** could also be converted into **15** via initial acetylation and then iodocyclization to give **10**. The diol **5** could also be converted into **15** by a similar route involving bis-acetylation and iodocyclization followed by functional group transformations. The tosylate of **15** was displaced with the anion of adenine or thymidine to give, after final desilylation, the desired isonucleosides—the D-adenosine analogue (−)-**2a** and the L-adenosine and thymidine analogues (+)-**2a** and (−)-**2b**. All of the stereochemistry of the final products is derived from the first step of the synthesis, namely, the Sharpless asymmetric epoxidation of **3**. The biological activity of the new compounds L-(+)-**2a** and L-(−)-**2b** against HIV was determined in the anti-HIV drug-testing system of the National Cancer Institute. The adenosine analogue L-(+)-**2a** was inactive in this screen, while the thymidine analogue L-(−)-**2b** showed moderate anti-HIV activity ($IC_{50} > 2 \times 10^{-4}$ M, $EC_{50} = 8 \times 10^{-7}$ M, $TI_{50} > 250$).

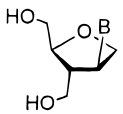
Introduction and Background

The continuing search for new antiviral compounds has recently led to the synthesis of a variety of natural and nonnatural nucleoside analogues, including oxetanocins A and G (**1a,b**),[4] its carbocyclic (**1c,d**)[5] and azetidine[6] analogues, and its methylene-expanded analogues such as the tetrahydrofurandimethanols (**2**).[7] These isonucleosides show good activity against a broad spectrum of viruses (HSV-1, HSV-2, HCMV, HBV, VZV, VV). The starting materials for the syntheses of these compounds are the natural sugars D-xylose[7a] and D-glucose.[7b]



1

a X = O B = A **c** X = CH_2 B = A
b X = O B = G **d** X = CH_2 B = G



2

a B=A **d** B=G
b B=T **e** B=5-bromovinylU
c B=C **f** B=5-iodoU

It has also been shown that a variety of L-enantiomers of known antiviral nucleosides, such as L-3TC,[8] L-FTC,[8a,9] L-ddC,[10] and L-FddC,[10b,c] have antiviral activity equal to or better than their D-enantiomers, in addition to having lower cytotoxicity. Presumably these compounds (or their triphosphate derivatives) interact with viral enzymes and inhibit viral DNA production without causing significant damage to normal human DNA. For this reason, many groups are working on ways to produce modified nucleosides in the unnatural L-configuration in order to test the antiviral activity and cytotoxicity in hopes of producing safer antiviral agents. In this paper

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(2) American Chemical Society Arthur C. Cope Scholar, 1995.

(3) (a) Natural Sciences and Engineering Research Council (NSERC) of Canada Scholar, 1992−1996. (b) Departmental Awardee for Excellence during the First Year of Graduate Study, UCLA, 1993. (c) Gregory Award Recipient for Excellence in Research, UCLA, 1995.

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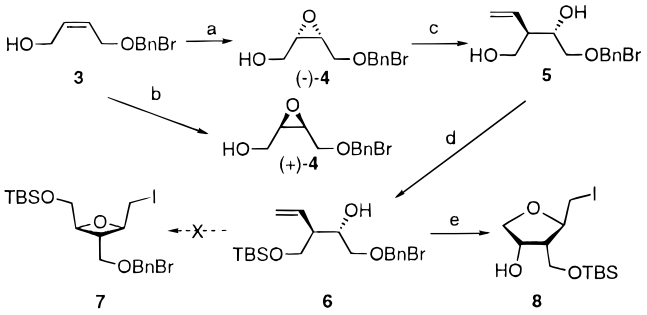
Scheme 1[a]

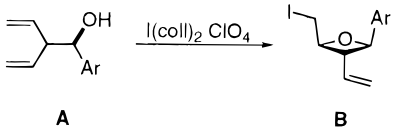


[a] Reagents and conditions (yields of enantiomeric series in parentheses): (a) L-(+)-DIPT, $Ti(OiPr)_4$, tBuOOH, CH_2Cl_2, mol sieves, −25 °C, 81%, 96% ee; (b) D-(+)-DIPT, $Ti(OiPr)_4$, tBuOOH, CH_2Cl_2, mol sieves, −25 °C, 70%, 100% ee; (c) CH_2=CHMgBr, CuI, THF, −78 °C → rt, 73% (71%); (d) TBSCl, Et_3N, DMAP, CH_2Cl_2, rt, 79% (85%); (e) $Ag(coll)_2ClO_4$, I_2, CH_2Cl_2, rt, 52% (50%).

we report the efficient total synthesis of both enantiomers of **2a** as well as that of L-**2b**. We anticipate that this work will help assess the viability of L-isonucleosides as antiviral agents.

Results and Discussion

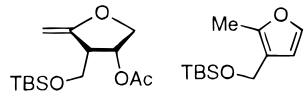
In the course of a synthesis of oxetanocins A and G (**1a,b**),[11] the known epoxide (−)-**4**[12] was made from the known monoprotected 2-butene-1,4-diol **3** (itself prepared by simple alkylation of butenediol in 88% yield) in 96% ee via a Sharpless epoxidation (Scheme 1). Addition of vinylmagnesium bromide[13] proceeded highly stereoselectively to give primarily the 1,3-diol **5**, with a small inseparable impurity (presumably the 1,2-diol). After selective protection of the primary alcohol to form the silyl ether **6**, we examined the course of an iodocyclization reaction using iodonium bis(*sym*-collidine) [$I(coll)_2^+$] perchlorate,[14] generated in situ from $Ag(coll)_2ClO_4$ and iodine, since we had shown earlier[11] that a vicinal dialkyl effect had allowed the formation of the all-trans-2,3,4-trisubstituted oxetanes from 2,3-disubstituted 3-butenols, e.g., **A** giving mainly **B** in good yield. In this case, it was



A **B**

interesting to see if this reaction would proceed via the alcohol to give the oxetane **7**, which has all the appropriate functionality necessary for its conversion to the oxetanocins **1a,b**, or whether it would cyclize to give the tetrahydrofuran **8**, which would result from cyclization through the benzyl ether oxygen and loss of a bromobenzyl cation.[15] In the event, cyclization of **6** under these conditions produced a good yield of the tetrahydrofuran **8** with none of the oxetane **7** being formed. This is an example of a 5-exo iodoetherification of an ether in preference to a 4-exo iodoetherification from an alcohol.[16] Examination of the structure of compound **8** indicates, however, that it should be easily converted to an L-isonucleoside, since it contains the basic carbon framework with the necessary functionality for attachment of the 5′-hydroxyl group and the base at C2′. Since all of the stereochemistry of the final isonucleosides is introduced in the very first step, the Sharpless epoxidation, we decided to prepare also the known D-isonucleosides by starting with the epoxide (+)-**4**. Therefore the same reaction sequence was carried out beginning with the reaction of **3** with D-(+)-tartrate to give (+)-**4** which was then converted into the enantiomer of **8** (Scheme 1, yields in parentheses).

Direct displacement of the iodide in the alcohol **8** with potassium acetate to install an oxygen functionality at C5 proved unsuccessful. We found it necessary to use the iodoacetate **10**, available by first protecting the alcohol **6** as the ester **9** and subsequent iodoetherification (Scheme 2). This iodo ester could have also been made by acetylation of **8** with acetyl chloride, and indeed, this reaction did work efficiently (81%) on the enantiomer of **8** to give the enantiomer of **10**. Nucleophilic substitution of the iodide **10** was quite difficult, presumably because of the reduced reactivity of the halide due to the presence of the inductively electron-withdrawing oxygen atom β to the iodide.[17] However, reaction of the iodide **10** with 10 equiv of potassium acetate in DMSO at 87 °C gave the diacetate **11** in 41% yield (the enantiomer of **11** was formed in 56% yield by this route). In some cases either the eliminated product **12** or the furan **13** was also isolated in small amounts (<10%). Deprotection of the



12 **13**

two acetates with ammonia in methanol gave the diol **14** in nearly quantitative yield. Reprotection of the primary alcohol of the diol **14** as the *tert*-butyldimethylsilyl (TBS) ether afforded the bis(silyl) ether **15** in 62% yield (enantiomer of **15** in 77% yield). Again the enan-

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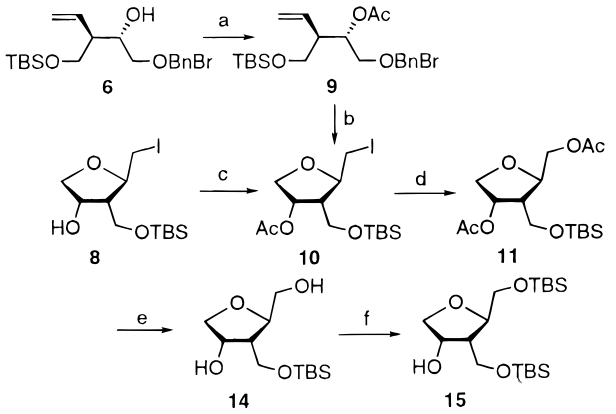
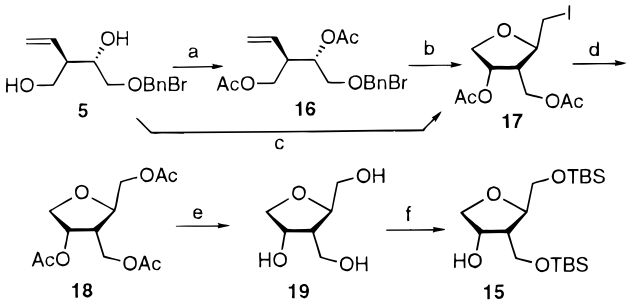
Scheme 2[a]



[a] Reagents and conditions (yields of enantiomeric series in parentheses): (a) AcCl, pyr, 0 °C, 90% (92%); (b) $Ag(coll)_2ClO_4$, I_2, rt, 52% (52%); (c) AcCl, pyr, 0 °C, (81%—ent-**10** only); (d) KOAc (10 equiv), DMSO, 87 °C, 41% (56%); (e) NH_3, MeOH, 0 °C → rt, 93% (98%); (f) TBSCl, Et_3N, DMAP, CH_2Cl_2, 62% (77%).

Scheme 3[a]



[a] Reagents and conditions (yields of enantiomeric series in parentheses): (a) AcCl, pyr, CH_2Cl_2, 0 °C, 89% (89%); (b) $Ag(coll)_2ClO4$, I_2, CH_2Cl_2, rt, 47% (43%), or I_2, CH_3CN, 0 °C → rt, 18 h (57%); (c) $Ag(coll)_2ClO_4$, I_2, CH_2Cl_2, rt, ii. AcCl, pyr, 0 °C, 26%; (d) KOAc (10 equiv), DMSO, 93 °C, 60% (60%); (e) NH_3, MeOH, 0 °C → rt; (f) TBSCl (3 equiv), Et_3N, DMAP, CH_2Cl_2, rt, 72% (71%) over two steps.

tiomer of **15** was also synthesized by exactly the same route (Scheme 2, yields in parentheses).

The alcohol **15** was also accessible through a slightly shorter route (Scheme 3). Protection of the original diol **5** with acetyl chloride gave the diacetate **16**, which could be cyclized with either $I(coll)_2^+ClO_4^-$ or I_2/CH_3CN[11] to form the iododiacetate **17**. The silylated compounds **6** and **9** could not be cyclized with I_2/CH_3CN due to desilylation,[18] presumably from traces of water in the solvent. Compound **17** could also be obtained in one pot in 26% yield from **5** by sequential treatment with $I(coll)_2^+ClO_4^-$, acetyl chloride, and pyridine. Displacement of the iodide **17** with acetate at 93 °C gave the triacetate **18** in 60% yield, which could be completely deprotected to the triol **19** with methanolic ammonia. Selective protection of the two primary alcohols produced the same bis-silylated alcohol **15** as before in 72% yield for the last two steps. Again the enantiomer of **15** was also synthesized by exactly the same route (Scheme 3, yields in parentheses).

Conversion of **15** to its tosylate **20** proceeded in good yield (Scheme 4). When **20** is treated with adenine under the conditions described by Tino et al.,[7a] the protected

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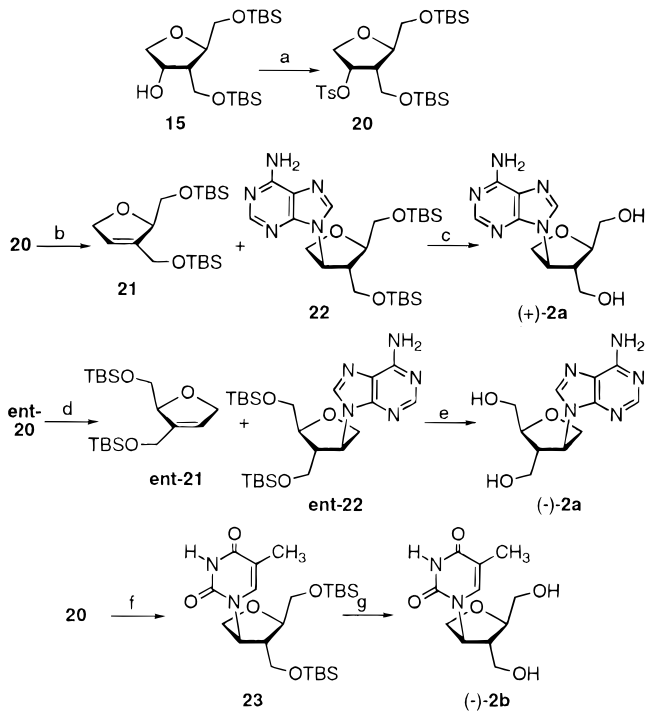
Scheme 4[a]



[a] Reagents and conditions: (a) TsCl, pyr, 0 °C → rt, 18 h, 68% (66%); (b) adenine, 18-crown-6, K_2CO_3, DMF, 90 °C, 18 h, 43% **22**, 26% **21**; (c) TBAF, THF, rt, 45 min, 80%; (d) same as step b, 44% ent-**22**, 29% ent-**21**; (e) same as step c, 83%; (f) thymine, 18-crown-6, K_2CO_3, DMSO, 90 °C, 18 h, 23%; (g) TBAF, THF, rt, 1 h, 94%.

L-adenosine analogue **22** was obtained in 43% yield, along with the product of E2 elimination, namely, the 2,5-dihydrofuran **21** in 26% yield. Deprotection of **22** with tetrabutylammonium fluoride proceeded in 80% yield to give the L-isonucleoside L-(+)-**2a**. Similarly, the enantiomer of **20** (ent-**20**) produced the enantiomer of **21** (ent-**21**) in 29% yield and the enantiomer of **22** (ent-**22**) in 44% yield. This latter compound (ent-**22**) was converted to the known isonucleoside[7] D-(−)-**2a** in 83% yield by desilylation. The thymidine L-isonucleoside was also made from the tosylate **20** by a similar route as follows. Reaction of the tosylate **20** with thymine, potassium carbonate, and 18-crown-6 in dimethyl sulfoxide gave the protected isonucleoside **23** in 21% yield. Deprotection of the silyl ethers with TBAF produced the product L-(−)-**2b**, which is the enantiomer of the known compound D-(+)-**2b**.

The biological activity of the new compounds L-(+)-**2a** and L-(−)-**2b** against HIV was determined in the anti-HIV drug-testing system of the National Cancer Institute. The adenosine analogue L-(+)-**2a** was inactive in this screen, while the thymidine analogue L-(−)-**2b** showed moderate anti-HIV activity ($IC_{50} > 2 \times 10^{-4}$ M, $EC_{50} = 8 \times 10^{-7}$ M, $TI_{50} > 250$).

Conclusion

We have developed a novel route to isonucleosides in both the D- and L-enantiomeric forms, e.g., compounds L-(+)-**2a**, D-(−)-**2a**, and L-(−)-**2b**, beginning with the simple, known monoether of the very inexpensive 2-butene-1,4-diol **3**. All of the stereochemistry of the final products is derived from the first step of the synthesis,

namely, the Sharpless asymmetric epoxidation of **3** to give the two enantiomeric epoxides (+)- and (−)-**4**. After regioselective opening of the epoxides and functional group conversions, the key step of the synthesis is the iodoetherification of the olefinic *p*-bromobenzyl ethers **5**, **6**, **9**, and **16** to give the corresponding tetrahydrofurans. Final protecting group interconversions and introduction of the bases afforded the desired isonucleosides. Further research on the synthesis of novel modified nucleosides and carbohydrates, especially those with the L-configuration, is underway in our laboratories.[19]

Experimental Section

General. All solvents were distilled prior to use: tetrahydrofuran (THF) from sodium/benzophenone; dichloromethane, triethylamine, pyridine, and DMSO from calcium hydride; and methanol from magnesium methoxide. Silver(I) bis(*sym*-collidine) perchlorate was prepared from silver nitrate, sodium perchlorate, and collidine as described.[14] (*Z*)-4-[(4-Bromophenyl)methoxy]-2-buten-1-ol (**3**) was prepared from 4-bromobenzyl bromide and *cis*-2-buten-1-ol as described.[12] All other reagents were used as provided except for L-(+)-diisopropyl tartrate, D-(−)-diisopropyl tartrate, titanium tetraisopropoxide, and acetyl chloride, which were distilled, and *p*-toluenesulfonyl chloride, which was recrystallized. All reactions were conducted under an inert atmosphere of argon. Enantiomeric excesses of (−)- and (+)-**4** were determined by the ^{31}P NMR method of Alexakis.[20]

(2*S*,3*R*)-3-[[(4-Bromophenyl)methoxy]methyl]oxiranemethanol ((−)-4). To a solution of L-(+)-diisopropyl tartrate (563 mg, 2.40 mmol) and oven-dried powdered 4-Å molecular sieves in dichloromethane (50 mL) cooled to −25 °C was added titanium tetraisopropoxide (0.57 mL, 1.93 mmol), and the mixture stirred for 15 min. With the temperature kept at −25 °C, a solution of *tert*-butyl hydroperoxide in *n*-decane (4.77 M, 4.1 mL, 19.6 mmol) was added, and the solution stirred for an additional 15 min. The monoprotected (*Z*)-2-butene-1,4-diol **3** (2.485 g, 9.66 mmol) in 5 mL of dichloromethane was then added; the reaction mixture stirred at −25 °C for 5 min and then was put into the freezer at −25 °C for 3 days. Water (10 mL) was added, and the mixture stirred for 1 h. A 30% solution of NaOH in brine (2 mL) was added, and the mixture stirred for 1 h. The layers were separated, and the aqueous layer was extracted twice with dichloromethane and dried over $MgSO_4$. The solution was filtered through Celite and the solvent removed in vacuo. The crude product was recrystallized from pentane/ether, giving 2.133 g of the pure epoxide (−)-**4** (7.81 mmol, 81%) as a colorless solid: mp 52 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.48 (2H, d, J = 8.4 Hz, Ar), 7.21 (2H, d, J = 8.6 Hz, Ar), 4.56 (1H, d, J = 12.0 Hz, CH_2Ar), 4.49 (1H, d, J = 12.0 Hz, CH_2Ar), 3.75 (2H, br t, J = 5.8 Hz, H_1), 3.688 (1H, dd, J = 11.1, 6.0 Hz, H_4), 3.686 (1H, dd, J = 11.1, 4.9 Hz, $H_{4'}$), 3.29 (1H, ddd, J = 5.4, 5.4, 4.5 Hz, H_2 or H_3), 3.23 (1H, ddd, J = 5.6, 5.6, 4.5 Hz, H_2 or H_3), 2.01 (1H, br t, J = 6.4 Hz, OH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 136.5, 131.7, 129.5, 121.9, 72.7, 68.3, 60.7, 55.6, 54.8. IR (KBr pellet): 3366 (br m), 3281 (br m), 1489 (m), 1399 (w), 1094 (s), 1049 (s), 1011 (s), 802 (m), 758 (m) cm^{-1}. $[\alpha]^{21}_D$ = −18.1 (c = 0.96, $CHCl_3$). ^{31}P NMR (10% C_6D_6 in C_6H_6, 162 MHz) δ: 140.5 (2.0%), 138.3 (98.0%), 96% ee.

(2*R*,3*S*)-3-[[(4-Bromophenyl)methoxy]methyl]oxiranemethanol ((+)-4). As in the preparation of (−)-**4**, D-(−)-diisopropyl tartrate (668 mg, 2.85 mmol), titanium tetraisopropoxide (0.700 mL, 2.37 mmol), *tert*-butyl hydroperoxide (4.77 M in *n*-decane, 5.0 mL, 23.8 mmol), and the monoprotected (*Z*)-2-butene-1,4-diol **3** (2.978 g, 11.58 mmol) yielded after column chromatography (SiO_2, 80% ether/20% pentane) and recrystallization 2.228 g of the epoxide (+)-**4** (8.16 mmol, 70%). ^{1}H NMR, ^{13}C NMR, and IR of (+)-**4** were identical with those of (−)-**4**. $[\alpha]^{21}_D$ = +16.5 (c = 0.93, $CHCl_3$). ^{31}P NMR (10% C_6D_6 in C_6H_6, 162 MHz) δ: 140.5, no peak at 138.3, 100% ee.

(2*R*,3*S*)-1-[(4-Bromophenyl)methoxy]-2-ethenyl-1,3-butenediol (5). To a slurry of copper(I) iodide (204 mg, 1.07 mmol) in THF (90 mL) cooled to −78 °C was added vinylmagnesium bromide (1.00 M in ether, 20 mL, 20 mmol), and the solution stirred for 10 min. The epoxide (−)-**4** (1.386 g, 5.07 mmol) was added at −78 °C and the solution allowed to warm to 21 °C overnight, which resulted in a deep-purple solution. This was quenched at 21 °C with aq HCl (1 M, 22 mL), and the mixture stirred for 20 min. Ether was added, and the layers were separated. The aqueous phase was extracted twice more with ether, the combined organic phase was washed with brine and dried over $MgSO_4$, and the solvent was removed in vacuo. Column chromatography (SiO_2, 50% ethyl acetate/50% hexane) yielded 1.122 g of the diol **5** (3.73 mmol, 73%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.47 (2H, d, J = 8.5 Hz, Ar), 7.19 (2H, d, J = 8.6 Hz, Ar), 5.88 (1H, ddd, J = 17.3, 10.4, 9.0 Hz, H_5), 5.23 (1H, dd, J = 10.4, 1.9 Hz, H_{4a}), 5.17 (1H, ddd, J = 17.3, 1.9, 0.9, H_{4b}), 4.50 (1H, d, J = 12.1 Hz, CH_2Ar), 4.49 (1H, d, J = 12.0 Hz, CH_2Ar), 4.04 (1H, ddd, J = 7.1, 4.1, 4.1 Hz, H_3), 3.77 (1H, dd, J = 10.8, 6.1 Hz, H_1), 3.75 (1H, dd, J = 10.8, 5.8 Hz, $H_{1'}$), 3.49 (1H, dd, J = 9.6, 4.4 Hz, H_4), 3.46 (1H, dd, J = 9.6, 7.3 Hz, $H_{4'}$), 2.39 (1H, dddd, J = 8.9, 5.8, 5.8, 3.9 Hz, H_2), 2.5−1.3 (2H, v br s, 2 OH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 136.8, 134.6, 131.6, 129.4, 121.8, 119.0, 72.9, 72.7, 71.1, 64.3, 48.6. IR (thin film): 3395 (br s), 2870 (m), 1640 (w), 1593 (w), 1489 (s), 1094 (s), 1071 (s), 1013 (s), 924 (m), 804 (s) cm^{-1}. High-resolution MS (EI, m/z): 302.0342, calcd for $C_{13}H_{17}O_3{}^{81}$Br 302.0341; 300.0356, calcd for $C_{13}H_{17}O_3{}^{79}$Br 300.0361. $[\alpha]^{21}_D$ = +2.9 (c = 0.84, $CHCl_3$).

(2*S*,3*R*)-1-[(4-Bromophenyl)methoxy]-2-ethenyl-1,3-butenediol (ent-5). As in the preparation of **5**, copper(I) iodide (181 mg, 0.95 mmol), vinylmagnesium bromide (1.00 M in ether, 19 mL, 19 mmol), and the epoxide (+)-**4** (1.289 g, 4.72 mmol) yielded after column chromatography 1.014 g of the diol ent-**5** (3.37 mmol, 71%). ^{1}H NMR, ^{13}C NMR, IR, and HRMS of ent-**5** were identical with those of **5**. $[\alpha]^{21}_D$ = −3.8 (c = 1.05, $CHCl_3$).

(2*S*,3*R*)-1-[(4-Bromophenyl)methoxy]-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl)-4-penten-2-ol (6). To a solution of the diol **5** (493.6 mg, 1.64 mmol) in dichloromethane (18 mL) at 21 °C were added sequentially triethylamine (300 μL, 2.15 mmol), (*N*,*N*-dimethylamino)pyridine(20 mg, 0.16 mmol), and *tert*-butyldimethylsilyl chloride (298 mg, 1.98 mmol), and the mixture was stirred at 21 °C for 16 h. Water was added, the layers were separated, and the aqueous layer was extracted with dichloromethane. The combined organic phase was washed with aq HCl (1 M), aq $NaHCO_3$ (10%), and brine and dried over $MgSO_4$. Removal of the solvent in vacuo and column chromatography (SiO_2, 20% ethyl acetate/80% hexane) yielded 540.8 mg of the silyl ether **6** (1.302 mmol, 79%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.46 (2H, d, J = 8.6 Hz, Ar), 7.20 (2H, d, J = 8.6 Hz, Ar), 5.91 (1H, ddd, J = 17.3, 10.4, 9.1 Hz, H_4), 5.16 (1H, dd, J = 10.4, 2.0 Hz, H_{5a}), 5.10 (1H, ddd, J = 17.3, 2.0, 0.9 Hz, H_{5b}), 4.51 (1H, d, J = 12.2 Hz, CH_2Ar), 4.48 (1H, d, J = 12.2 Hz, CH_2-Ar), 4.10 (1H, dddd, J = 5.9, 5.9, 3.0, 3.0 Hz, H_2), 3.78 (1H, dd, J = 9.9, 5.9 Hz, H_6), 3.75 (1H, dd, J = 9.9, 4.6 Hz, $H_{6'}$), 3.457 (1H, dd, J = 9.6, 5.3 Hz, H_1), 3.455 (1H, dd, J = 9.6, 6.6 Hz, overlapping with previous signal, $H_{1'}$), 2.97 (1H, d, J = 2.8 Hz, OH), 2.33 (1H, br dq, J = 9.1, 4.3 Hz, H_3), 0.88 (9H, s, *t*-Bu), 0.05 (6H, s, Me_2Si). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 137.2, 134.9, 131.5, 129.4, 121.5, 118.1, 72.9, 72.6, 71.2, 65.7, 48.0, 25.9, 18.2, −5.53, −5.57. IR (thin film): 3478 (br w), 2928 (s), 2859 (s), 1256 (m), 1096 (s), 1013 (m), 837 (s), 777 (m) cm^{-1}. High-resolution MS (EI, m/z): 417.1284, calcd for $C_{19}H_{32}O_3{}^{81}$BrSi 417.1284 (M + H)$^+$; 415.1304, calcd for $C_{19}H_{32}O_3{}^{79}$BrSi 415.1304 (M + H)$^+$. $[\alpha]^{21}_D$ = −9.2 (c = 1.11, $CHCl_3$).

(19) (a) For a novel synthesis of L-ribose and 2-deoxy-L-ribose from D-ribose and L-arabinose, see: Jung, M. E.; Xu, Y. *Tetrahedron Lett.* **1997**, *38*, 4199. (b) We have also developed a de novo synthesis of 2-deoxy-L-ribose: Jung, M. E.; Nichols, C. J. Manuscript in preparation.

(20) Alexakis, A.; Mutti, S.; Normant, J. F.; Mangeney, P. *Tetrahedron Asym.* **1990**, *1*, 437.

(2*R*,3*S*)-1-[(4-Bromophenyl)methoxy]-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-penten-2-ol (ent-6). As in the preparation of **6**, the diol ent-**5** (1.107 g, 3.68 mmol), triethylamine (0.65 mL, 4.66 mmol), (*N*,*N*-dimethylamino)-pyridine (47 mg, 0.38 mmol), and *tert*-butyldimethylsilyl chloride (669 mg, 4.44 mmol) yielded, after column chromatography on silica gel, 1.291 g (3.11 mmol, 85%) of the silyl ether ent-**6** as a colorless oil. ^{1}H NMR, ^{13}C NMR, IR, and HRMS of ent-**6** were identical with those of **6**. $[\alpha]^{21}_D = +9.7$ ($c = 1.12$, $CHCl_3$).

(3*S*,4*R*5*R*)-4-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-methyl]-5-(iodomethyl)tetrahydrofuran-3-ol (8). To a solution of silver(I) bis(*sym*-collidine) perchlorate (83.5 mg, 0.186 mmol) in dichloromethane (3 mL) at 21 °C was added iodine crystals (47.8 mg, 0.188 mmol), and the solution stirred in the dark for 20 min. A yellow precipitate (AgI) formed. The alcohol **6** was added in dichloromethane (2 mL), and the solution stirred for 18 h. The precipitate was filtered and the solution washed with aq $Na_2S_2O_3$ (10%), aq HCl (1 M), and brine and dried over $MgSO_4$. Removal of the solvent in vacuo and column chromatography (SiO_2, 15% ethyl acetate/85% hexane) gave 31.5 mg of the iodide **8** (0.085 mmol, 52%) as a slightly yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.53 (1H, dddd, $J = 5.7, 4.3, 4.3, 2.2$ Hz, H_3), 4.06 (1H, dd, $J = 9.7, 4.1$ Hz, H_2), 4.00 (1H, dd, $J = 10.6, 4.9$ Hz, H_7), 3.90 (1H, dd, $J = 10.6, 5.9$ Hz, $H_{7'}$), 3.88 (1H, dt, $J = 8.5, 4.8$ Hz, overlapping with previous signal, H_5), 3.79 (1H, dd, $J = 9.7, 2.2$ Hz, $H_{2'}$), 3.44 (1H, dd, $J = 10.5, 5.0$ Hz, H_6), 3.27 (1H, dd, $J = 10.5, 4.7$ Hz, $H_{6'}$), 3.10 (1H, d, $J = 4.5$ Hz, OH), 2.13 (1H, br dq, $J = 8.4, 5.5$ Hz, H_4), 0.91 (9H, s, *t*-Bu), 0.107 (3H, s, MeSi), 0.103 (3H, s, MeSi). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 77.8, 75.4, 74.6, 61.1, 51.0, 25.8, 18.1, 10.5, −5.50, −5.54. IR (thin film): 3428 (br w), 2930 (m), 1472 (w), 1256 (m), 1078 (s), 837 (s), 777 (s) cm^{-1}. High-resolution MS (EI, *m*/*z*): 373.0699, calcd for $C_{12}H_{26}IO_3Si$ 373.0696 $(M + H)^+$. $[\alpha]^{21}_D = -23.0$ ($c = 1.12$, $CHCl_3$).

(3*R*,4*S*,5*S*)-4-[[[(1,1-Dimethylethyl)dimethylsilyl]-oxy]methyl]-5-(iodomethyl)tetrahydrofuran-3-ol (ent-8). As in the preparation of **8**, silver(I) bis(*sym*-collidine) perchlorate (115 mg, 0.256 mmol), iodine (72.5 mg, 0.286 mmol), and the alcohol ent-**6** (93.3 mg, 0.225 mmol) gave after chromatography on silica gel 41.7 mg of the iodide ent-**8** (0.112 mmol, 50%) as a yellow oil. ^{1}H NMR, ^{13}C NMR, IR, and HRMS of ent-**8** were identical with those of **8**. $[\alpha]^{21}_D = +26.1$ ($c = 0.90$, $CHCl_3$).

(3*R*,4*S*)-4-(Acetyloxy)-5-[(4-bromophenyl)methoxy]-3-[[[(1,1-dimethylethyl)dimethylsilyloxy]methyl]-1-pentene (9). To a solution of the alcohol **6** (417.2 mg, 1.004 mmol) in dichloromethane (12 mL) cooled to 0 °C were added pyridine (0.50 mL, 6.18 mmol) and acetyl chloride (0.22 mL, 3.09 mmol). The solution was stirred for 18 h, with slow warming to 21 °C. Water and dichloromethane were added to the resulting orange solution, the layers were separated, and the aqueous layer was extracted once with dichloromethane. The combined organic phase was washed with aq HCl (1 M) and the aqueous layer again extracted with dichloromethane. The combined organic phase was washed with brine and dried over $MgSO_4$, and the solvent was removed in vacuo. Column chromatography (SiO_2, 10% ethyl acetate/90% hexane) yielded 413.9 mg of the acetate **9** (0.905 mmol, 90%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.45 (2H, d, $J = 8.5$ Hz, Ar), 7.18 (2H, d, $J = 8.6$ Hz, Ar), 5.72 (1H, ddd, $J = 16.6, 11.0, 9.1$ Hz, H_2), 5.32 (1H, ddd, $J = 6.2, 4.9, 4.9$ Hz, H_4), 5.15−5.10 (2H, m, H_1, $H_{1'}$), 4.48 (1H, d, $J = 12.3$ Hz, CH_2Ar), 4.43 (1H, d, $J = 12.3$ Hz, CH_2Ar), 3.569 (1H, d, $J = 6.6$ Hz, H_6), 3.567 (1H, d, $J = 5.0$ Hz, overlappingwith previous signal, $H_{6'}$), 3.566 (1H, dd, $J = 10.5, 6.2$ Hz, overlapping with previous two signals, H_5), 3.52 (1H, dd, $J = 10.5, 4.9$ Hz, $H_{5'}$), 2.55 (1H, br dq, $J = 9.1, 5.7$ Hz, H_3), 2.04 (3H, s, OAc), 0.87 (9H, s, *t*-Bu), 0.01 (3H, s, MeSi), 0.00 (3H, s, MeSi). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.4, 137.2, 134.9, 131.5, 129.3, 121.5, 118.5, 72.2, 71.1, 69.8, 63.1, 47.4, 25.8, 21.1, 18.2, −5.5. IR (thin film): 2930 (m), 2859 (m), 1744 (s), 1372 (w), 1237 (s), 1105 (s), 839 (m) cm^{-1}. High-resolution MS (EI, *m*/*z*): 459.1386, calcd for $C_{21}H_{34}{}^{81}BrO_4Si$ 459.1389 $(M + H)^+$; 457.1408, calcd for $C_{21}H_{34}{}^{79}BrO_4Si$ 457.1410 $(M + H)^+$. $[\alpha]^{21}_D = +2.2$ ($c = 1.21$, $CHCl_3$).

(3*S*,4*R*)-4-(Acetyloxy)-5-[(4-bromophenyl)methoxy]-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1-pentene (ent-9). As in the preparation of **9**, the alcohol ent-**6** (1.173 g, 2.83 mmol), pyridine (1.35 mL, 16.7 mmol), and acetyl chloride (0.60 mL, 8.44 mmol) yielded after chromatography on silica gel 1.192 g of the acetate ent-**9** (2.60 mmol, 92%) as a colorless oil. ^{1}H NMR, ^{13}C NMR, IR, and HRMS of ent-**9** were identical with those of **9**. $[\alpha]^{21}_D = -3.2$ ($c = 0.88$, $CHCl_3$).

(2*R*,3*R*,4*S*)-4-(Acetyloxy)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-2-(iodomethyl)tetrahydrofuran (10). To a solution of silver(I) bis(*sym*-collidine) perchlorate (360 mg, 0.800 mmol) in dichloromethane (30 mL) at 21 °C was added iodine (202 mg, 0.796 mmol), and the solution stirred in the dark for 20 min. A solution of the acetate **9** (333.9 mg, 0.730 mmol) in dichloromethane (5 mL) was then added, and the mixture stirred for 18 h. The precipitate was filtered and washed with dichloromethane, and the filtrate and washings were combined, washed with aq $Na_2S_2O_3$ (10%), aq HCl (1 M), and brine, and dried over $MgSO_4$. Column chromatography (SiO_2, 5% ethyl acetate/95% hexane → 8% ethyl acetate/92% hexane) yielded 158.1 mg of the iodide **10** (0.382 mmol, 52%) as a colorless oil, as well as 61.3 mg of the recovered acetate **9** (0.134 mmol, 18%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.38 (1H, ddd, $J = 5.4, 4.0, 1.4$ Hz, H_4), 4.15 (1H, dd, $J = 10.5, 3.9$ Hz, H_5), 3.839 (1H, dd, $J = 10.1, 6.4$ Hz, H_7), 3.838 (1H, dd, $J = 10.6, 1.5$ Hz, overlapping with previous signal, $H_{5'}$), 3.77 (1H, ddd, $J = 9.2, 5.3, 4.0$ Hz, H_2), 3.68 (1H, dd, $J = 10.1, 7.8$ Hz, $H_{7'}$), 3.58 (1H, dd, $J = 10.5, 3.6$ Hz, H_6), 3.34 (1H, dd, $J = 10.6, 5.1$ Hz, $H_{6'}$), 2.33 (1H, dddd, $J = 8.9, 7.8, 6.4, 5.4$ Hz, H_3), 2.06 (3H, s, OAc), 0.88 (9H, s, *t*-Bu), 0.058 (3H, s, MeSi), 0.055 (3H, s, MeSi). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.4, 80.2, 75.6, 73.3, 60.0, 50.4, 25.8, 21.0, 18.2, 11.5, −5.50, −5.52. IR (thin film): 2930 (m), 1744 (s), 1235 (s), 1090 (m), 837 (s), 777 (m) cm^{-1}. High-resolution MS (EI, *m*/*z*): 415.0802, calcd for $C_{14}H_{28}IO_4Si$ 415.0802 $(M + H)^+$. $[\alpha]^{21}_D = -42.5$ ($c = 1.12$, $CHCl_3$).

(2*S*,3*S*,4*R*)-4-(Acetyloxy)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-2-(iodomethyl)tetrahydrofuran (ent-10). From ent-8: To a solution of the alcohol ent-**8** (56.8 mg, 0.153 mmol) in dichloromethane (2 mL) cooled to 0 °C were added pyridine (75 μL, 0.93 mmol) and acetyl chloride (33 μL, 0.46 mmol), and the solution stirred for 1 h at 0 °C. Water and dichloromethane were added, the layers were separated, and the aqueous layer was extracted with dichloromethane. The combined organic phase was washed with aq HCl (1 M) and the aqueous layer extracted with dichloromethane. The combined organic layers were washed with brine and dried over $MgSO_4$. Column chromatography (SiO_2, 10% ethyl acetate/90% hexane) yielded 51.4 mg of the acetate ent-**10** (0.124 mmol, 81%) as a colorless oil.

From ent-9: As in the preparation of **10** from **9**, silver(I) bis(*sym*-collidine) perchlorate (542 mg, 1.21 mmol), iodine (282 mg, 1.11 mmol), and the acetate ent-**9** (518.1 mg, 1.13 mmol) yielded after chromatography on silica gel 243.2 mg of the acetate ent-**10** (0.590 mmol, 52%) as well as 80.3 mg of the recovered acetate ent-**9** (0.178 mmol, 15%). ^{1}H NMR, ^{13}C NMR, IR, and HRMS of ent-**10** were identical with those of **10**. $[\alpha]^{21}_D = +49.8$ ($c = 0.82$, $CHCl_3$).

(2*R*,3*S*,4*S*)-4-(Acetyloxy)-2-[(acetyloxy)methyl]-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]tetrahydrofuran (11). To a solution of the iodide **10** (141.5 mg, 0.341 mmol) in DMSO (3 mL) was added potassium acetate (315 mg, 3.21 mmol). The solution was heated at 87 °C for 16 h and then cooled to 21 °C. Ether and water were added, the layers were separated, and the aqueous layer was extracted twice more with ether. The combined organic phase was washed with brine and dried over $MgSO_4$, and the solvent was removed in vacuo. Column chromatography (SiO_2, 10% ethyl acetate/90% hexane → 20% ethyl acetate/80% hexane) yielded 48.4 mg of the diacetate **11** (0.140 mmol, 41%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.37 (1H, ddd, $J = 5.4, 4.0, 1.4$ Hz, H_4), 4.38 (1H, dd, $J = 11.3, 2.1$ Hz, H_6), 4.09 (1H, ddd, $J = 9.1, 6.8, 2.3$ Hz, H_2), 4.07 (1H, dd, $J = 10.7, 3.9$ Hz,

overlapping with previous signal, H_5), 4.03 (1H, dd, J = 11.3, 6.5 Hz, overlapping with previous two signals, $H_{6'}$), 3.85 (1H, dd, J = 10.7, 1.4 Hz, $H_{5'}$), 3.84 (1H, dd, J = 10.0, 7.0 Hz, overlapping with previous signal, H_7), 3.66 (1H, dd, J = 10.0, 7.3 Hz, $H_{7'}$), 2.33 (1H, dddd, J = 9.0, 7.1, 7.1, 5.3 Hz, H_3), 2.10 (3H, s, OAc), 2.07 (3H, s, OAc), 0.88 (9H, s, *t*-Bu), 0.052 (3H, s, MeSi), 0.047 (3H, s, MeSi). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.9, 170.5, 79.1, 74.9, 73.3, 66.1, 59.7, 46.9, 25.8, 20.99, 20.90, 18.2, −5.51, −5.58. IR (thin film): 2955 (m), 1744 (s), 1373 (m), 1233 (s), 1094 (s), 839 (s), 777 (m) cm^{-1}. High-resolution MS (EI, *m*/*z*): 347.1890, calcd for $C_{16}H_{31}O_6Si$ 347.1890 (M + H)$^+$. $[\alpha]^{21}_D$ = −67.4 (c = 0.80, $CHCl_3$).

(2*S*,3*R*,4*R*)-4-(Acetyloxy)-2-[(acetyloxy)methyl]-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]tetrahydrofuran (ent-11). As in the preparation of **11**, the iodide ent-**10** (56.6 mg, 0.137 mmol) and potassium acetate (134 mg, 1.37 mmol) yielded after treatment at 80 °C and chromatography on silica gel (20% ethyl acetate/80% hexane) 26.4 mg of the diacetate ent-**11** (0.076 mmol, 56%) as a colorless oil. ^{1}H NMR, ^{13}C NMR, IR, and HRMS of ent-**11** were identical with those of **11**. $[\alpha]^{21}_D$ = +65.3 (c = 1.22, $CHCl_3$).

When performed on a larger scale and at 93 °C, the acetate **11** was isolated (31%) as well as the olefin **12** (8%). Another experiment produced a 53% yield of **11** and a 4% yield of the furan **13**, which was isolated from the column as the dihydrofuran **12** but subsequently eliminated acetic acid and rearranged to **13**.

12: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.42 (1H, dd, J = 5.2, 3.0 Hz, H_4), 4.33 (1H, ddd, J = 2.5, 2.2, 1.0 Hz, H_{6b}), 4.15 (1H, dd, J = 10.7, 3.0 Hz, H_5), 4.12 (1H, dd, J = 10.7, 1.1 Hz, $H_{5'}$), 3.84 (1H, br dd, J = 2.3, 2.3 Hz, H_{6a}), 3.810 (1H, dd, J = 9.8, 8.3 Hz, overlapping with previous signal, H_7), 3.805 (1H, dd, J = 9.8, 6.3 Hz, $H_{7'}$), 3.06 (1H, ddddd, J = 8.4, 6.3, 5.2, 2.3, 2.3 Hz, H_3), 2.07 (3H, s, OAc), 0.88 (9H, s, *t*-Bu), 0.07 (3H, s, MeSi), 0.04 (3H, s, MeSi); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 161.1, 80.5, 74.0, 73.0, 59.5, 46.7, 25.7, 21.0, 18.1, −5.5, −5.6; IR (thin film) 2957 (m), 2930 (m), 1746 (s), 1676 (m), 1237 (s), 1117 (m), 1082 (s), 837 (s), 777 (m) cm^{-1}; high-resolution MS (EI, *m*/*z*) 287.1679, calcd for $C_{14}H_{27}O_4Si$ 287.1679 (M + H)$^+$.

13: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.23 (1H, d, J = 1.8 Hz, H_5), 6.32 (1H, d, J = 1.7 Hz, H_4), 4.51 (2H, s, H_7), 2.26 (3H, s, CH_3), 0.91 (9H, s, *t*-Bu), 0.08 (6H, s, Me_2Si); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 162.4, 147.9, 140.0, 110.9, 57.1, 25.8, 18.3, 11.6, −5.3; IR (thin film) 2928 (s), 2859 (s), 1472 (m), 1256 (m), 1077 (s), 837 (s), 775 (m) cm^{-1}; high-resolution MS (EI, *m*/*z*) 226.1391, calcd for $C_{12}H_{22}OSi$ 226.1389.

(3*S*,4*R*,5*R*)-4-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-methyl]-5-(hydroxymethyl)-3-tetrahydrofuranol (14). To a solution of the diacetate **11** (36.8 mg, 0.106 mmol) in methanol (10 mL) cooled to 0 °C was added vigorously a stream of ammonia gas for 5 min. The solution was stirred for 18 h and allowed to warm to 21 °C. Removal of the solvent in vacuo followed by column chromatography (SiO_2, 60% ethyl acetate/40% hexane) yielded 25.8 mg of the diol **14** (0.098 mmol, 93%) as a white solid: mp 47 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.51 (1H, m, H_3), 4.06 (1H, dt, J = 9.2, 4.2 Hz, H_5), 3.98 (1H, dd, J = 9.6, 4.1 Hz, H_2), 3.96 (1H, dd, J = 11.0, 5.3 Hz, overlapping with previous signal, H_7), 3.90 (1H, dd, J = 10.6, 5.5 Hz, $H_{7'}$), 3.79 (1H, dd, J = 9.6, 2.1 Hz, H_2), 3.77 (1H, br ddd, J = 11.8, 4.0, 4.0 Hz, overlapping with previous signal, H_6), 3.57 (1H, br ddd, J = 11.6, 7.1, 4.5 Hz, $H_{6'}$), 3.13 (1H, d, J = 4.5 Hz, 3-OH), 2.27 (1H, br t, J = 5.7 Hz, 6-OH), 2.20 (1H, br dq, J = 9.3, 5.4 Hz, H_4), 0.90 (9H, s, *t*-Bu), 0.10 (3H, s, MeSi), 0.09 (3H, s, MeSi). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 79.9, 75.5, 74.5, 63.5, 60.8, 46.5, 25.8, 18.1, −5.57, −5.63. IR (thin film): 3409 (br s), 2930 (m), 1092 (m), 1049 (m), 839 (m), 779 (m). High-resolution MS (EI, *m*/*z*): 263.1683, calcd for $C_{12}H_{27}O_4Si$ 263.1679 (M + H)$^+$. $[\alpha]^{21}_D$ = −36.7 (c = 1.25, $CHCl_3$).

(3*R*,4*S*,5*S*)-4-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-methyl]-5-(hydroxymethyl)-3- tetrahydrofuranol (ent-14). As in the preparation of **14**, the diacetate ent-**11** (18.4 mg, 0.053 mmol) yielded, after column chromatography on silica gel, 13.6 mg of the diol ent-**14** (0.052 mmol, 98%) as a white solid: mp 50−51 °C. ^{1}H NMR, ^{13}C NMR, IR, and HRMS of ent-**14** were identical with those of **14**. $[\alpha]^{21}_D$ = +28.5 (c = 1.25, $CHCl_3$).

(3*R*,4*S*)-4-(Acetyloxy)-3-[(acetyloxy]methyl]-5-[(4-bromophenyl)methoxy]-1-pentene (16). To a solution of the diol **5** (2.038 g, 6.77 mmol) in dichloromethane (50 mL) cooled to 0 °C were added pyridine (4.0 mL, 47 mmol) and acetyl chloride (1.9 mL, 27 mmol). The solution was stirred for 18 h, allowing to warm to 21 °C. Dichloromethane and water were added, the layers were separated, and the aqueous layer was extracted with dichloromethane. The combined organic phase was washed with aq HCl (1 M) and brine and dried over $MgSO_4$. Removal of the solvent in vacuo and column chromatography (SiO_2, 20% ethyl acetate/80% hexane) yielded 2.309 g of the diacetate **16** (5.99 mmol, 89%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.46 (2H, d, J = 8.5 Hz, Ar), 7.18 (2H, d, J = 8.6 Hz, Ar), 5.69 (1H, ddd, J = 17.1, 10.4, 9.1 Hz, H_2), 5.24 (1H, ddd, J = 6.0, 5.2, 4.2 Hz, H_4), 5.21 (1H, dd, J = 10.5, 1.9 Hz, H_{1a}), 5.18 (1H, ddd, J = 17.1, 1.7, 0.9 Hz, H_{1b}), 4.47 (1H, d, J = 11.9 Hz, CH_2Ar), 4.44 (1H, d, J = 12.2 Hz, CH_2Ar), 4.10 (1H, dd, J = 11.1, 7.2 Hz, H_6), 4.03 (1H, dd, J = 11.1, 6.6 Hz, $H_{6'}$), 3.53 (1H, dd, J = 10.2, 6.2 Hz, H_5), 3.47 (1H, dd, J = 10.2, 5.3 Hz, $H_{5'}$), 2.79 (1H, dddd, J = 9.0, 7.0, 7.0, 4.2 Hz, H_3), 2.06 (3H, s, OAc), 2.04 (3H, s, OAc). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.9, 170.4, 136.9, 133.2, 131.5, 129.2, 121.6, 119.7, 72.4, 70.5, 69.5, 63.7, 44.2, 21.0, 20.9. IR (thin film): 1744 (s), 1489 (w), 1372 (m), 1233 (s), 1101 (m), 1037 (m) cm^{-1}. High-resolution MS (EI, *m*/*z*): 387.0632, calcd for $C_{17}H_{22}{}^{81}BrO_5$ 387.0630 (M + H)$^+$; 385.0652, calcd for $C_{17}H_{22}{}^{79}BrO_5$ 385.0651 (M + H)$^+$; 384.0580, calcd for $C_{17}H_{21}{}^{79}BrO_5$ 384.0572. $[\alpha]^{21}_D$ = +3.9 (c = 0.67, $CHCl_3$).

(3*S*,4*R*)-4-(Acetyloxy)-3-[(acetyloxy)methyl]-5-[(4-bromophenyl)methoxy]-1-pentene (ent-16). As in the preparation of **16**, the diol ent-**5** (639.1 mg, 2.122 mmol), pyridine (1.20 mL, 14.8 mmol), and acetyl chloride (0.67 mL, 9.4 mmol) yielded, after chromatography on silica gel, 726 mg of the diacetate ent-**16** (1.88 mmol, 89%) as a colorless oil. ^{1}H NMR, ^{13}C NMR, IR, and HRMS of ent-**16** were identical with those of **16**. $[\alpha]^{21}_D$ = −3.8 (c = 1.44, $CHCl_3$).

(2*R*,3*R*,4*S*)-4-(Acetyloxy)-3-[(acetyloxy)methyl]-2-(iodomethyl)tetrahydrofuran (17). From 16: To a solution of silver(I) bis(*sym*-collidine) perchlorate (821 mg, 1.83 mmol) in dichloromethane (35 mL) at 21 °C was added iodine crystals (435 mg, 1.71 mmol), and the solution stirred for 20 min in the dark. A solution of the diacetate **16** (500.2 mg, 1.298 mmol) in dichloromethane (5 mL) was added, and the mixture stirred for 18 h. The precipitate was filtered and rinsed with dichloromethane, and the filtrate and washings the combined and washed with aq sodium thiosulfate (10%). The aqueous layer was extracted once with dichloromethane, and the combined organic phase was washed with aq HCl (1 M) and brine and dried over $MgSO_4$. Removal of the solvent in vacuo and column chromatography (SiO_2, 10% ethyl acetate/90% hexane → 20% ethyl acetate/80% hexane) yielded 209.4 mg of the iodide **17** (0.612 mmol, 47%) as a slightly yellow oil.

From 5: To a solution of silver(I) bis(*sym*-collidine) perchlorate (103 mg, 0.229 mmol) in dichloromethane (5 mL) at 21 °C was added iodine crystals (52 mg, 0.23 mmol), and the solution stirred for 20 min. A solution of the diol **5** (67.6 mg, 0.224 mmol) in dichloromethane (2 mL) was added, and the mixture stirred for 18 h. This mixture was then cooled to 0 °C, and pyridine (180 μL, 2.23 mmol) and acetyl chloride (160 μL, 2.25 mmol) were added. After stirring for 6 h, the solution was allowed to warm to 21 °C, then aq sodium thiosulfate (10%) was added, the layers were separated, and the aqueous layer was extracted once with dichloromethane. The combined organic phase was washed with aq HCl (1 M) and the aqueous layer again extracted with dichloromethane. The combined organic phase was washed with brine and dried over $MgSO_4$. Removal of the solvent in vacuo and column chromatography (SiO_2, 25% ethyl acetate/75% hexane) yielded 20.3 mg of the iodide **17** (0.059 mmol, 26%) as a slightly yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.49 (1H, ddd, J = 5.4, 4.0, 1.4 Hz, H_4), 4.34 (1H, dd, J = 11.3, 7.2 Hz, H_7), 4.19 (1H, dd, J = 10.7, 4.0 Hz, H_5), 4.10 (1H, dd, J = 11.3, 7.1 Hz, $H_{7'}$), 3.86 (1H, dd, J = 10.7, 1.5 Hz, $H_{5'}$), 3.74 (1H, ddd, J = 9.0, 4.3, 4.3 Hz, H_2), 3.54

(1H, dd, J = 10.8, 3.9 Hz, H_6), 3.31 (1H, dd, J = 10.8, 4.7 Hz, $H_{6'}$), 2.48 (1H, dddd, J = 9.0, 7.2, 7.2, 5.5 Hz, H_3), 2.08 (3H, s, OAc), 2.07 (3H, s, OAc). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.6, 170.3, 79.3, 75.1, 73.4, 60.7, 47.4, 20.9, 20.8, 9.9. IR (thin film): 1740 (s), 1370 (m), 1235 (s), 1040 (m) cm^{-1}. High-resolution MS (EI, *m*/*z*): 343.0049, calcd for $C_{10}H_{16}IO_5$ 343.0043 $(M + H)^+$. $[\alpha]^{21}_D = -52.4$ (c = 1.16, $CHCl_3$).

(2*S*,3*S*,4*R*)-4-(Acetyloxy)-3-[(acetyloxy)methyl]-2-(iodomethyl)tetrahydrofuran (ent-17). To a solution of the diacetate ent-**16** (25.9 mg, 0.067 mmol) in acetonitrile (1 mL) at 0 °C was added iodine crystals (57.7 mg, 0.227 mmol), and the solution stirred for 18 h, allowing to warm to 21 °C. Ether was added, the solution was washed with aq sodium thiosulfate (10%), and the aqueous layer was extracted with ether. The organic layer was washed successively with aq HCl (1 M) and water, each time extracting the aqueous layer once more with ether. The combined organic phase was washed with brine and dried over $MgSO_4$, followed by removal of the solvent in vacuo. Column chromatography (SiO_2, 20% ethyl acetate/80% hexane) yielded 13.0 mg of the iodide ent-**17** (0.038 mmol, 57%) as a slightly yellow oil.

On a larger scale, as in the preparation of **17** from **16**, the diacetate ent-**16** (710.5 mg, 1.84 mmol), silver(I) bis(*sym*-collidine) perchlorate (925 mg, 2.06 mmol), and iodine (525 mg, 2.07 mmol) afforded 269.8 mg (0.789 mmol, 43%) of the iodide ent-**17**. In each case, ^{1}H NMR, ^{13}C NMR, IR, and HRMS of ent-**17** were identical with those of **17**. $[\alpha]^{21}_D = +47.9$ (c = 0.86, $CHCl_3$).

(2*R*,3*S*,4*S*)-4-(Acetyloxy)-2,3-bis[(acetyloxy)methyl]tetrahydrofuran (18). To a solution of the iodide **17** (183.0 mg, 0.535 mmol) in DMSO (4 mL) at 21 °C was added potassium acetate (510 mg, 5.20 mmol), and the solution was heated at 93 °C for 18 h. The solution was allowed to cool to 21 °C, water and ether were added, and the layers were separated. The aqueous layer was extracted three times with ether, and the combined organic phase was washed with brine and dried over $MgSO_4$. Removal of the solvent in vacuo followed by column chromatography (SiO_2, 25% ethyl acetate/75% hexane → 50% ethyl acetate/50% hexane) yielded 87.4 mg (0.319 mmol, 60%) of the triacetate **18** as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.40 (1H, ddd, J = 5.4, 4.1, 1.5 Hz, H_4), 4.32 (1H, dd, J = 11.1, 7.4 Hz, H_6), 4.31 (1H, br q, J = 6.6 Hz, H_2), 4.13−4.07 (4H, m, H_5, $H_{6'}$, H_7, $H_{7'}$), 3.86 (1H, dd, J = 10.7, 1.5 Hz, H_2), 2.48 (1H, br quin, J = 7.2 Hz, H_3), 2.10 (3H, s, OAc), 2.08 (3H, s, OAc), 2.05 (3H, s, OAc). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.8, 170.7, 170.3, 78.8, 74.5, 73.4, 65.2, 60.7, 43.5, 20.91, 20.85, 20.79. IR (thin film): 1740 (s), 1372 (m), 1233 (s), 1040 (m) cm^{-1}. High-resolution MS (EI, *m*/*z*): 275.1135, calcd for $C_{12}H_{19}O_7$ 275.1131 $(M + H)^+$. $[\alpha]^{21}_D = -74.8$ (c = 0.97, $CHCl_3$).

(2*S*,3*R*,4*R*)-4-(Acetyloxy)-2,3-bis[(acetyloxy)methyl]tetrahydrofuran (ent-18). As in the preparation of **18**, the iodide ent-**17** (252.3 mg, 0.737 mmol) and potassium iodide (719 mg, 7.33 mmol) were heated in DMSO (10 mL) at 97 °C for 30 h and yielded after workup 120.5 mg of the triacetate ent-**18** (0.439 mmol, 60%) as a colorless oil. ^{1}H NMR, ^{13}C NMR, IR, and HRMS of ent-**18** were identical with those of **18**. $[\alpha]^{21}_D = +68.7$ (c = 0.42, $CHCl_3$).

(3*S*,4*R*,5*R*)-4,5-Bis(hydroxymethyl)-3-tetrahydrofuranol (19). To a solution of the triacetate **18** (76.4 mg, 0.279 mmol) in methanol (15 mL) cooled to 0 °C was added a vigorous stream of ammonia for 7.5 min. The solution was stirred overnight and allowed to warm to 21 °C. The solvent was removed in vacuo, chloroform was added, and the solution stirred. The chloroform was decanted, leaving behind a precipitate which was dissolved in methanol. The methanol was removed in vacuo, yielding 41.5 mg of the crude triol **19** as a white solid, which was used directly in the synthesis of **15**. ^{1}H NMR (MeOH-d_4, 400 MHz) δ: 4.38 (1H, ddd, J = 5.0, 3.6, 1.3 Hz, H_3), 3.91 (1H, dd, J = 9.5, 3.6 Hz, H_2), 3.856 (1H, ddd, J = 9.1, 5.0, 4.1 Hz, H_5), 3.848 (1H, dd, J = 10.9, 6.8 Hz, overlapping with previous signal, H_7), 3.71 (1H, dd, J = 9.5, 1.4 Hz, $H_{2'}$), 3.650 (1H, dd, J = 11.7, 3.8 Hz, H_6), 3.649 (1H, dd, J = 10.8, 6.4 Hz, overlapping with previous signal, $H_{7'}$), 3.53 (1H, dd, J = 11.7, 5.1, $H_{6'}$), 2.13 (1H, dddd, J = 9.3, 6.8, 6.8, 5.1 Hz, H_4). ^{13}C NMR (MeOH-d_4, 100 MHz) δ: 81.1, 74.9, 72.5, 63.4, 59.0 (C-4 signal obscured by residual MeOH-d_4). IR (thin film): 3366 (br s), 2932 (m), 1233 (s) cm^{-1}. High-resolution MS (EI, *m*/*z*): 149.0815, calcd for $C_6H_{13}O_4$ 149.0814 $(M + H)^+$. $[\alpha]^{21}_D = -67.7$ (c = 0.47, MeOH).

(3*R*,4*S*,5*S*)-4,5-Bis(hydroxymethyl)-3-tetrahydrofuranol (ent-19). As in the preparation of **19**, the triacetate ent-**18** (114.3 mg, 0.417 mmol) was converted to 67.7 mg of the crude triol ent-**19** as a white solid, which was directly used in the preparation of ent-**15**. ^{1}H NMR, ^{13}C NMR, IR, and HRMS of ent-**19** were identical with those of **19**. $[\alpha]^{21}_D = +41.4$ (c = 1.02, MeOH).

(3*S*,4*R*,5*R*)-4,5-Bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-tetrahydrofuranol (15). From 19: To a suspension of the crude triol **19** (41.5 mg) in dichloromethane (3 mL) at 21 °C weres added triethylamine (135 μL, 0.969 mmol), (*N*,*N*-dimethylamino)pyridine (12 mg, 0.099 mmol), and *tert*-butyldimethylsilyl chloride (130 mg, 0.863 mmol), and the mixture stirred for 18 h. The solution was decanted from some residual solid, and the solid was rinsed with dichloromethane. The combined organic phase was washed with aq HCl (1 M) and the aqueous layer extracted with dichloromethane. The combined organic layers were washed with aq sodium bicarbonate (10%) and brine and dried over $MgSO_4$. Removal of the solvent in vacuo and column chromatography (SiO_2, 20% ethyl acetate/80% hexane) yielded 75.2 mg of **15** (0.200 mmol, 72% from **18**) as a colorless oil.

From 14: To a solution of the diol **14** (23.7 mg, 0.090 mmol) in dichloromethane (1.5 mL) at 21 °C were added triethylamine (26 μL, 0.187 mmol), a small amount of (*N*,*N*-dimethylamino)pyridine, and *tert*-butyldimethylsilyl chloride (20.3 mg, 0.135 mmol), and the solution stirred for 18 h. Dichloromethane and water were added to the mixture, the layers were separated, and the aqueous layer was extracted with dichloromethane. The combined aqueous phase was washed with aq HCl (1 M), aq sodium bicarbonate (10%), and brine and dried over $MgSO_4$. Removal of the solvent in vacuo and column chromatography (SiO_2, 20% ethyl acetate/80% hexane → 60% ethyl acetate/40% hexane) yielded 21.2 mg of the alcohol **15** (0.056 mmol, 62%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.49 (1H, dddd, J = 5.7, 4.2, 4.2, 2.2 Hz, H_3), 3.99 (1H, dd, J = 10.5, 4.6 Hz, H_7), 3.96 (1H, ddd, J = 8.8, 4.5, 4.5 Hz, H_5), 3.94 (1H, dd, J = 9.8, 4.1 Hz, H_2), 3.88 (1H, dd, J = 10.5, 6.6 Hz, $H_{7'}$), 3.76 (1H, dd, J = 9.5, 2.3 Hz, $H_{2'}$), 3.69 (1H, dd, J = 10.6, 4.3 Hz, H_6), 3.67 (1H, dd, J = 10.6, 4.9 Hz, $H_{6'}$), 3.24 (1H, d, J = 4.3 Hz, OH), 2.26 (1H, dddd, J = 8.5, 6.5, 5.7, 4.7 Hz, H_4), 0.90 (9H, s, *t*-Bu), 0.89 (9H, s, *t*-Bu), 0.09 (3H, s, MeSi), 0.08 (3H, s, MeSi), 0.06 (6H, s, Me_2-Si). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 79.4, 75.4, 74.6, 64.5, 61.2, 47.2, 25.9, 25.8, 18.3, 18.1, −5.37, −5.41, −5.52, −5.57. IR (thin film): 3433 (br m), 2930 (s), 1472 (m), 1256 (s), 1088 (s), 837 (s) cm^{-1}. High-resolution MS (EI, *m*/*z*): 377.2551, calcd for $C_{18}H_{41}O_4{}^{28}Si_2$ 377.2543 $(M + H)^+$. $[\alpha]^{21}_D = -26.0$ (c = 0.90, $CHCl_3$).

(3*R*,4*S*,5*S*)-4,5-Bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-tetrahydrofuranol (ent-15). From ent-**19**: As in the preparation of **15** from **19**, the crude triol ent-**19** (67.7 mg), triethylamine (210 μL, 1.51 mmol), (*N*,*N*-dimethylamino)pyridine (26 mg, 0.21 mmol), and *tert*-butyldimethylsilyl chloride (190 mg, 1.26 mmol) yielded after chromatography on silica gel 111.2 mg of ent-**15** (0.295 mmol, 71% from ent-**18**) as a colorless oil.

From ent-14: To a solution of the diol ent-**14** (37.8 mg, 0.144 mmol) in dichloromethane (2 mL) were added triethylamine (40 μL, 0.29 mmol), (*N*,*N*-dimethylamino)pyridine (3.7 mg, 0.030 mmol), and *tert*-butyldimethylsilyl chloride (25.6 mg, 0.170 mmol), and the solution stirred for 18 h. TLC control (50% ethyl acetate/50% hexane) showed an incomplete reaction so more triethylamine (30 μL, 0.22 mmol) and *tert*-butyldimethylsilyl chloride (25 mg, 0.166 mmol) were added, and the mixture stirred for an additional 24 h. Workup as in the preparation of **15** from **14** and column chromatography (SiO_2, 20% ethyl acetate/80% hexane → 60% ethyl acetate/40% hexane) yielded 41.8 mg of the alcohol ent-**15** (0.110 mmol, 77%) as a colorless oil, as well as 3.4 mg of the unreacted diol ent-**14** (0.013 mmol, 9%). In either case, ^{1}H NMR, ^{13}C NMR,

IR, and HRMS of ent-**15** were identical with those of **15**. $[\alpha]^{21}_D = +16.5$ ($c = 0.55$, $CHCl_3$).

(2*R*,3*S*,4*S*)-2,3-Bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-[(4-methylphenyl)sulfonyl]oxy]tetrahydrofuran (20). To a solution of the alcohol **15** (16.2 mg, 0.043 mmol) in pyridine (0.5 mL) cooled to 0 °C was added *p*-toluenesulfonyl chloride (82 mg, 0.43 mmol), and the solution stirred for 18 h, allowing to warm to 21 °C. The solution was diluted with ethyl acetate, washed with aq sodium bicarbonate (10%), aq HCl (1 M), and brine, and dried over $MgSO_4$. Removal of the solvent in vacuo and column chromatography (SiO_2, 10% ethyl acetate/90% hexane → 25% ethyl acetate/75% hexane) yielded 15.5 mg of the tosylate **20** (0.029 mmol, 68%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.79 (2H, m, OTs), 7.34 (2H, m, OTs), 5.14 (1H, ddd, J = 5.5, 2.6, 2.6 Hz, H_4), 3.90 (1H, ddd, J = 8.4, 3.4, 3.4 Hz, H_2), 3.85 (2H, d, J = 2.7 Hz, H_5, $H_{5'}$), 3.79 (1H, dd, J = 10.9, 3.2 Hz, H_6), 3.70 (1H, dd, J = 10.2, 6.6 Hz, H_7), 3.64 (1H, dd, J = 10.2, 7.5 Hz, $H_{7'}$), 3.59 (1H, dd, J = 10.9, 3.6 Hz, $H_{6'}$), 2.48 (1H, dddd, J = 8.3, 7.4, 6.8, 5.5 Hz, H_3), 2.45 (3H, s, MeAr), 0.87 (9H, s, *t*-Bu), 0.86 (9H, s, *t*-Bu), 0.03 (6H, s, Me_2Si), 0.01 (6H, s, Me_2Si). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 144.8, 134.0, 129.9, 127.8, 82.8, 81.7, 72.6, 64.9, 60.0, 46.4, 25.9, 25.8, 21.6, 18.3, 18.2, −5.36, −5.47, −5.51, −5.55. IR (thin film): 2955 (m), 2930 (m), 2859 (m), 1372 (m), 1256 (m), 1179 (s), 1094 (s), 897 (m), 839 (s) cm^{-1}. High-resolution MS (EI, *m*/*z*): 531.2634, calcd for $C_{25}H_{47}O_6S^{28}Si_2$ 531.2632 $(M + H)^+$. $[\alpha]^{21}_D = -32.4$ ($c = 0.52$, $CHCl_3$).

(2*S*,3*S*,4R)-2,3-Bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-[[(4-methylphenyl)sulfonyl]oxy]tetrahydrofuran (ent-20). As in the preparation of **20**, the alcohol ent-**15** (37.5 mg, 0.100 mmol) and *p*-toluenesulfonyl chloride (50.2 mg, 0.262 mmol) yielded after chromatography on silica gel 35.0 mg of the tosylate ent-**20** (0.066 mmol, 66%) as a colorless oil, as well as 11.8 mg of the unreacted alcohol ent-**15** (0.031 mmol, 31%). ^{1}H NMR, ^{13}C NMR, IR, and HRMS of ent-**20** were identical with those of **20**. $[\alpha]^{21}_D = +36.3$ (c = 0.90, $CHCl_3$).

9-[(3*R*,4*R*,5*R*)-Tetrahydro-4,5-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-furanyl]-9*H*-purin-6-amine (22) and (2*R*)-2,5-Dihydro-2,3-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]furan (21). To a solution of the tosylate **20** (96.3 mg, 0.181 mmol) in *N*,*N*-dimethylformamide (2.5 mL) at 21 °C were added adenine (79.3 mg, 0.587 mmol), 18-crown-6 (60.7 mg, 0.230 mmol), and potassium carbonate (99.7 mg, 0.721 mmol), and the solution heated to 90 °C for 18 h. After the mixture cooled to 21 °C, the *N*,*N*-dimethylformamide was removed by Kugelrohr distillation at reduced pressure and the residue purified by column chromatography (SiO_2, 100% dichloromethane → 5% isopropyl alcohol/95% dichloromethane) which yielded 38.7 mg of the purine **22** (0.078 mmol, 43%) as a white solid, as well as 16.7 mg of the dihydrofuran **21** (0.047 mmol, 26%) as a colorless oil.

22: mp = 142 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.34 (1H, s, adenine), 8.20 (1H, s, adenine), 5.70 (2H, br s, NH_2), 5.13 (1H, ddd, J = 5.5, 3.6, 3.6 Hz, H_3), 4.09 (1H, dd, J = 10.0, 3.4 Hz, H_2), 4.06 (1H, dd, J = 9.8, 5.4 Hz, $H_{2'}$), 4.00 (1H, dd, J = 10.8, 3.5 Hz, H_6), 3.94 (1H, ddd, J = 7.4, 3.5, 3.5 Hz, H_5), 3.86 (1H, dd, J = 10.1, 5.4 Hz, H_7), 3.84 (1H, dd, J = 10.8, 3.7 Hz, overlapping with previous signal, $H_{6'}$), 3.78 (1H, dd, J = 10.1, 4.6 Hz, $H_{7'}$), 2.66 (1H, m, H_4), 0.91 (9H, s, *t*-Bu), 0.87 (9H, s, *t*-Bu), 0.12 (3H, s, MeSi), 0.10 (3H, s, MeSi), 0.06 (3H, s, MeSi), 0.05 (3H, s, MeSi); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.2, 152.7, 149.9, 139.6, 119.3, 82.5, 73.1, 64.0, 62.6, 57.5, 50.2, 26.0, 25.8, 18.6, 18.2, −5.26, −5.36, −5.52 (2C); IR (thin film) 3366 (w), 3281 (w), 3244 (w), 3129 (m), 2928 (m), 1682 (s), 1603 (s), 1306 (m), 1252 (s), 1117 (m), 835 (s), 779 (m) cm^{-1}; high-resolution MS (EI, *m*/*z*) 494.2981, calcd for $C_{23}H_{44}H_5O_3{}^{28}Si_2$ 494.2983 $(M + H)^+$; $[\alpha]^{21}_D = +36.3$ ($c = 0.50$, $CHCl_3$).

21: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.77 (1H, br sextet, J = 1.7 Hz, H_4), 4.71−4.60 (3H, m), 4.33 (1H, br d, J = 14.8 Hz, H_7), 4.19 (1H, br d, J = 14.9 Hz, $H_{7'}$), 3.69 (1H, dd, J = 10.5, 4.5 Hz, H_6), 3.67 (1H, dd, J = 10.5, 5.0 Hz, $H_{6'}$), 0.91 (9H, s, *t*-Bu), 0.88 (9H, s, *t*-Bu), 0.08 (6H, s, Me_2Si), 0.052 (3H, s, MeSi), 0.050 (3H, s, MeSi); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.6, 121.3, 86.1, 75.0, 65.3, 59.7, 25.88, 25.85, 18.35, 18.24, −5.40, −5.42, −5.45 (2C); IR (thin film) 2955 (s), 2930 (s), 2856 (s), 1472 (m), 1256 (s), 1090 (s), 1007 (m), 839 (s), 777 (s) cm^{-1}; high-resolution MS (EI, *m*/*z*) 357.2282, calcd for $C_{18}H_{37}O_3{}^{28}Si_2$ 357.2281 $(M - H)^+$.

9-[(3*S*,4*S*,5*S*)-Tetrahydro-4,5-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-furanyl]-9*H*-purin-6-amine (ent-22) and (2*S*)-2,5-Dihydro-2,3-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]furan (ent-21). As in the preparation of **22**, the tosylate ent-**20** (10.2 mg, 0.019 mmol), adenine (7.6 mg, 0.056 mmol), 18-crown-6 (6.6 mg, 0.025 mmol), and potassium carbonate (12.1 mg, 0.087 mmol) yielded after chromatography on silica gel 4.2 mg of the purine ent-**22** (0.0085 mmol, 44%) as a white solid, as well as 2.0 mg of the dihydrofuran ent-**21** (0.0056 mmol, 29%) as a colorless oil. The ^{1}H NMR, ^{13}C NMR, IR, and HRMS of ent-**22** were identical with those of **22**, and those of ent-**21** were identical with those of **21**. For ent-**22**: $[\alpha]^{21}_D = -35.8$ ($c = 0.46$, $CHCl_3$).

9-[(3*R*,4*R*,5*R*)-Tetrahydro-4,5-bis(hydroxymethyl)-3-furanyl]-9*H*-purin-6-amine ((+)-2a). To a solution of the bis(silyl) ether **22** (43.9 mg, 0.089 mmol) in THF (3 mL) at 21 °C was added a solution of tetrabutylammonium fluoride in THF (1 M, 0.35 mL, 0.35 mmol), and the mixture stirred for 45 min. Removal of the solvent in vacuo and column chromatography (SiO_2, 15% methanol/85% dichloromethane) followed by recrystallization by adding methanol and allowing it to evaporate slowly gave 18.9 mg (0.071 mmol, 80%) of the isonucleoside (+)-**2a** as a white solid. ^{1}H and ^{13}C NMR matched that of (−)-**2a** previously prepared:[7] mp = 172 °C. ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 8.28 (1H, s, adenine), 8.14 (1H, s, adenine), 7.22 (2H, br s, NH_2), 5.01 (1H, m), 5.00 (1H, t, J = 5.6 Hz, OH), 4.94 (1H, t, J = 5.0 Hz, OH), 4.00 (1H, dd, J = 9.5, 4.2 Hz), 3.97 (1H, dd, J = 9.5, 6.0 Hz), 3.78 (1H, ddd, J = 7.6, 4.5, 3.6 Hz), 3.71 (1H, ddd, J = 11.8, 5.2, 3.2 Hz), 3.63−3.53 (3H, m), 2.52 (1H, dddd, J = 7.5, 5.5, 5.5, 5.0 Hz). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 156.4, 152.8, 149.7, 139.6, 119.1, 82.9, 71.9, 62.4, 60.9, 57.4, 49.6. IR (KBr pellet): 3402 (w), 3326 (w), 3206 (m), 1649 (s), 1613 (m), 1020 (m) cm^{-1}. High-resolution MS (EI, *m*/*z*): 265.1171, calcd for $C_{11}H_{15}N_5O_3$ 265.1175. $[\alpha]^{21}_D = +22.9$ (c = 0.51, 1:1 MeOH/H_2O).

(3*S*,4*S*,5*S*)-9-[Tetrahydro-4,5-bis(hydroxymethyl)-3-furanyl]-9*H*-purin-6-amine ((−)-2a). As in the preparation of (+)-**2a**, the bis(silyl) ether ent-**22** (36.5 mg, 0.074 mmol) and tetrabutylammonium fluoride (1 M in THF, 0.30 mL, 0.30 mmol) yielded after two purifications by column chromatography (SiO_2, 15% methanol/85% dichloromethane; SiO_2, 100% dichloromethane → 15% methanol/85% dichloromethane) 16.2 mg of (−)-**2a** (0.061 mmol, 83%) as a white solid. ^{1}H NMR, ^{13}C NMR, IR, and HRMS were identical with those of (+)-**2a** and matched those of (−)-**2a** previously prepared:[7] mp = 174 °C (lit.[7] mp = 185−195 °C dec). $[\alpha]^{21}_D = -26.4$ (c = 0.52, 1:1 MeOH/H_2O).

5-Methyl-1-[(3*R*,4*R*,5*R*)-tetrahydro-4,5-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-furanyl]-2,4(1*H*,3*H*)-pyrimidinedione (23). To a solution of the tosylate **20** (100.9 mg, 0.190 mmol) in DMSO (1 mL) were added potassium carbonate (108.7 mg, 0.786 mmol), thymine (46.9 mg, 0.372 mmol), and 18-crown-6 (50.5 mg, 0.191 mmol), and the solution was heated to 90 °C for 18 h. Cooling of the solution to 21 °C followed by two successive purifications by column chromatography (SiO_2, 50% ethyl acetate/50% hexane → 100% ethyl acetate; SiO_2, 10% ethyl acetate/90% hexane → 25% ethyl acetate/75% hexane) yielded 21.1 mg of **23** (0.044 mmol, 23%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.69 (1H, br s, thymine), 7.43 (1H, q, J = 1.2 Hz, thymine), 5.11 (1H, ddd, J = 6.3, 3.9, 2.2 Hz, H_3), 3.97 (1H, dd, J = 11.1, 2.9 Hz, H_6), 3.94 (1H, dd, J = 10.6, 2.1 Hz, overlapping with previous signal, H_2), 3.88 (1H, dd, J = 10.6, 6.4 Hz, $H_{2'}$), 3.843 (1H, ddd, J = 7.9, 3.3, 3.3 Hz, overlapping with previous signal, H_5), 3.840 (1H, dd, J = 10.0, 5.5 Hz, overlapping with previous two signals, H_7), 3.77 (1H, dd, J = 11.1, 3.6 Hz, $H_{6'}$), 3.74 (1H, dd, J = 10.1, 3.8 Hz, overlapping with previous signal, $H_{7'}$), 2.34 (1H, ddtdd, J = 8.1, 5.4, 4.0, 4.0 Hz, H_4), 1.92 (3H, d, J = 1.2 Hz, thymine), 0.90 (9H, s, *t*-Bu), 0.89 (9H, s, *t*-Bu), 0.084 (3H, s, MeSi), 0.082 (3H, s, MeSi), 0.07 (3H, s, MeSi), 0.05 (3H,

s, MeSi). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 163.6, 150.9, 137.3, 111.6, 82.7, 72.2, 63.4, 62.2, 58.2, 49.6, 26.0, 25.8, 18.6, 18.2, 12.7, −5.3, −5.4, −5.5, −5.6. IR (thin film): 3195 (w), 3065 (w), 1692 (s), 1472 (w), 1256 (m), 837 (s), 777 (m) cm^{-1}. High-resolution MS (EI, *m*/*z*): 485.2871, calcd for $C_{23}H_{45}N_2O_5{}^{28}Si_2$ 485.2867 $(M + H)^+$. $[\alpha]^{21}_D = +4.1$ (*c* = 1.04, $CHCl_3$).

5-Methyl-1-[(3*R*,4*R*,5*R*)-tetrahydro-4,5-bis(hydroxymethyl)-3-furanyl]-2,4(1*H*,3*H*)-pyrimidinedione ((−)-2b). To a solution of the bis(silyl) ether **23** (20.7 mg, 0.043 mmol) in THF (2 mL) at 21 °C was added a solution of tetrabutylammonium fluoride (1 M in THF, 170 μL, 0.17 mmol), and the mixture stirred for 60 min. Removal of the solvent in vacuo and two successive purifications with column chromatography (SiO_2, 10% methanol/90% dichloromethane; SiO_2, 100% dichloromethane → 10% methanol/90% dichloromethane) followed by recrystallization by dissolving in methanol and letting it slowly evaporate yielded 10.3 mg of the isonucleoside (−)-**2b** (0.040 mmol, 94%) as a white solid. ^{1}H and ^{13}C NMR matched that of (+)-**2b** previously prepared:[7] mp = 86 °C (lit.[7] mp = 93−96 °C for (+)-**2b**). ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 11.23 (1H, s, thymine), 7.67 (1H, q, *J* = 1.0 Hz, thymine), 4.99 (1H, t, *J* = 5.6 Hz, OH), 4.94 (1H, ddd, *J* = 6.5, 4.5, 3.0 Hz), 4.85 (1H, t, *J* = 4.9 Hz, OH), 3.85 (1H, dd, *J* = 10.0, 2.9 Hz), 3.77 (1H, dd, *J* = 10.1, 6.6 Hz), 3.72 (1H, ddd, *J* = 11.9, 5.1, 2.8 Hz), 3.66 (1H, br ddd, *J* = 8.0, 3.1, 3.1 Hz), 3.57−3.49 (3H, m), 2.26 (1H, m, H_4), 1.77 (3H, d, *J* = 0.9 Hz, thymine). ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 164.0, 151.3, 138.3, 109.6, 82.9, 71.5, 61.8, 60.8, 57.9, 48.9, 12.6. IR (KBr pellet): 3389 (br m), 3179 (br m), 3036 (br w), 1698 (s). High-resolution MS (EI, *m*/*z*): 256.1060, calcd for $C_{11}H_{16}N_2O_5$ 256.1059. $[\alpha]^{21}_D = -11.6$ (*c* = 0.30, MeOH).

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Supporting Information Available: Copies of the ^{1}H and ^{13}C NMR spectra for all compounds described in the article (76 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering instructions.

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