Synthesis of Methylene-Expanded 2′,3′-Dideoxyribonucleosides

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A method for the preparation of methylene-expanded 2′,3′-dideoxyribonucleosides is reported. The very inexpensive starting material levoglucosenone **8** was converted into the known mixture of alcohols **12ab** which were converted into the required silyl ether alcohol **26** in six steps via either of two routes. The first involved a one-step acetylation and opening of the anhydro sugar bridge to give the triacetates **20ab** which were reduced with triethylsilane and silyl triflate to afford the diacetates **21ab**, both of which gave **26** after further functional group conversions. The second route entailed a simple acetylation of **12ab** followed by reduction with triethylsilane and silyl triflate to give the monoacetates **19ab**, both converted via straightforward chemistry into **26**. Mesylation of the alcohol of **26** furnished the mesylate **27**. Alkylation of adenine with the mesylate **27** afforded the silyl ether **28** which was deprotected to give the desired modified dideoxy nucleoside **7a**. Alkylation of 2,6-diaminopurine **38** with the mesylate gave the protected diaminopurine nucleoside **39.** Upon acetylation, it produced a mixture of di- and monoacetates **40**−**41**, the latter of which was transformed into the desired guanosine analogue **7e**. Thus, two new nucleoside analogues **7ae** were prepared from levoglucosenone **8**.

Introduction

The current global focus on the human immunodeficiency virus (HIV) and the discovery of selective nucleoside-based antiviral agents such as 3′-azido-3′-deoxythymidine (AZT, zidovudine), **1a**,[1] lamivudine (L-3-TC), **1b**,[2] 9-(2-hydroxyethoxymethyl)guanine (acyclovir, ACV), **1c**,[3] and oxetanocin A, **1d**,[4] have generated great interest in modified nucleoside analogues (Figure 1). Modifications among analogues with an altered sugar range from a simple exchange of azide or fluorine for the 3′-hydroxyl groups of ribose to the substitution of cyclopentene, cyclohexene, oxetane, or even acyclic ethers for the tetrahydrofuran core of the natural pentose carbohydrate. While only a handful of synthetic analogues have shown significant anti-HIV activity, the active agents demonstrate that the sugar moieties of the nucleosides can be altered considerably while still yielding compounds with important biological activity.

In 1992 Nair and Nuesca[5] reported on the synthesis and antiviral activity of a class of compounds called isonucleosides, where the base moiety of the nucleoside had been transposed from the natural 1′-position to the 2′-position while maintaining its cis relationship with the

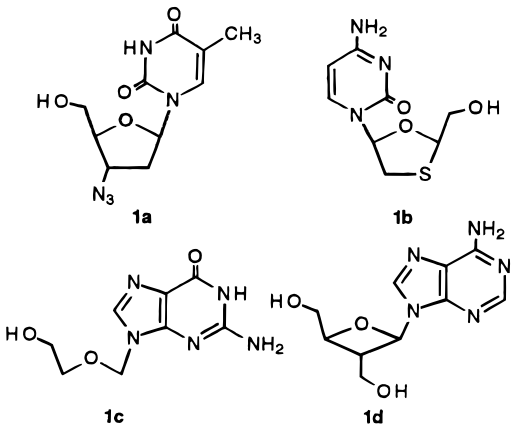

Figure 1.

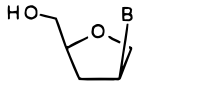

Figure 2.

hydroxymethyl group (Figure 2). Members of this conceptually new class of compounds were reported to be stable with respect to glycosidic bond cleavage and enzymatic deamination.

In 1994 Matsuda and co-workers[6] also described the synthesis and biological evaluations of what they named "ring-expanded oxetanocin analogues", compounds **3a**−**h** (Figure 3). It is noteworthy that several of the analogues **2** and **3** showed potent antiviral activity.[5,6]

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(2) (a) Chang, C.-N.; Doong, S.-L.; Zhou, J. H.; Beach, J. W.; Jeong, L. S.; Chu, C. K.; Tsai, C.-h.; Cheng, Y.-c. *J. Biol. Chem.* **1992**, *267*, 13938. (b) Chang, C.-N.; Skalski, V.; Zhou, J. H.; Cheng, Y.-c. *J. Biol. Chem.* **1992**, *267*, 22414. (c) Beach, J. W.; Jeong, L. S.; Alves, A. J.; Pohl, D.; Kim, H. O.; Chang, C.-N.; Coong, S.-L.; Schinazi, R. F.; Cheng, Y.-C.; Chu, C. K. *J. Org. Chem.* **1992**, *57*, 2217. (d) Coates, J. A. V.; Cammack, N.; Jenkinson, H. J.; Mutton, I. M.; Pearson, B. A.; Storer, R.; Cameron, J. M.; Penn, C. R. *Antimicrob. Agents Chemother.* **1992**, *36*, 202. (e) Schinazi, R. F.; Chu, C. K.; Peck, A.; McMillan, A.; Mathis, R.; Cannon, D.; Jeong, L.-S.; Beach, J. W.; Choi, W.-B.; Yeola, S.; Liotta, D. C. *Antimicrob. Agents Chemother.* **1992**, *36*, 672.

(3) Schaeffer, H. J.; Beauchamp, L.; de Miranda, P.; Elion, G. B.; Bauer, D. J.; Collins, P. *Nature* **1978**, *272*, 583.

(4) Hoshino, H.; Shimizu, N. *J. Antibiot.* **1987**, *40*, 1077.

(5) Nair, V.; Nuesca, Z. M. *J. Am. Chem. Soc.* **1992**, *114*, 7951.

(6) Kakefuda, A.; Shuto, S.; Nagahata, T.; Seki, J.; Sasaki, T.; Matsuda, A. *Tetrahedron* **1994**, *50*, 10167.

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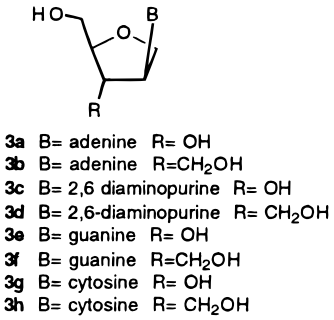


Figure 3.

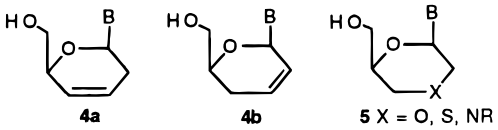


Figure 4.

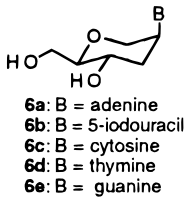
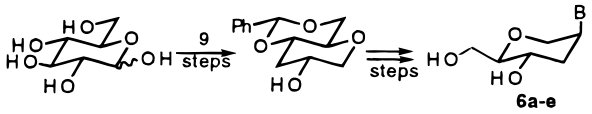


Figure 5.

Scheme 1



Herdewijn and co-workers (Figure 4)[7] reported that the 2,3,4-trideoxy-D-glycerohex-3-enopyranosyl nucleosides **4a**, the corresponding hex-2-enopyranosyl nucleosides **4b**, and analogues with 1,4-dioxane, 1,4-oxathiane, and 1,4-oxazine ring structures **5** did not exhibit any antiviral activity due to the compounds' poor intracellular phosphorylation. They later described the synthesis and antiviral activity of another example of hexose nucleosides **6** in which the base moiety was placed at the 2 position of the 1,5-anhydrohexitol structure (Figure 5).[8] Using a series of protections and deoxygenations, they converted D-glucose to the protected 3-deoxy-1,5-anhydro-D-hexitol which was coupled to the heterocyclic base either by direct nucleophilic displacement of a sulfonate or under Mitsunobu conditions (Scheme 1) to give the desired modified pyrimidines and purines. Several of these analogues **6a**−**e** also showed potent antiviral activity.[8]

Our objective was to devise an efficient and novel synthesis of 1,5-anhydrohexitol nucleosides (**7**) from levoglucosenone[9] that would allow for introduction of alternative substituents at the 4′-position of the sugar (Figure 6) and that would help determine the substituent

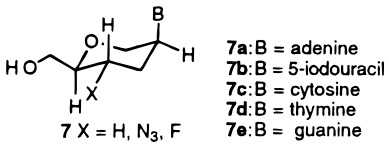


Figure 6.

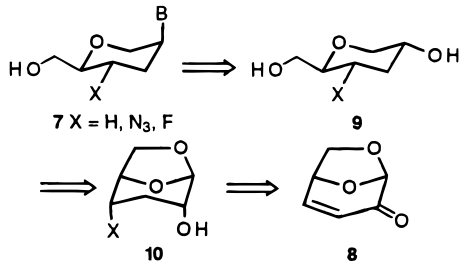


Figure 7.

effect on the antiviral activity of these compounds. Levoglucosenone, a highly functionalized chiral synthon containing six carbons and providing the correct stereochemistry at the 5 position, constituted an excellent starting material and building block for our synthetic plan (Figure 7).

Results and Discussion

Levoglucosenone (**8**) was the starting point for the synthesis of all of the compounds described.[9] Reduction of the olefin and the ketone functionalities of **8** was carried out chemoselectively by catalytic hydrogenation or hydride reducing agents, respectively. It is interesting to note that when the ketone of **8** was reduced first, the resulting allylic alcohol mixture **11ab** gave a 1:2 mixture of the fully reduced alcohols **12** and the ketone **13** on subsequent treatment with hydrogen and catalyst (Scheme 2). The unusual formation of the ketone **13** under these conditions is possibly due to the tautomerization of the unreacted allylic alcohol during chromatography. However when the olefin of **8** was hydrogenated to give **13** followed by reduction of the ketone with lithium aluminum hydride, the target diastereomeric alcohols **12ab** were produced more efficiently. At this stage the two diastereomers **12a** and **12b** were chromatographically inseparable and the ratio could only be determined from the integration of the peaks in the ^{1}H NMR spectra.

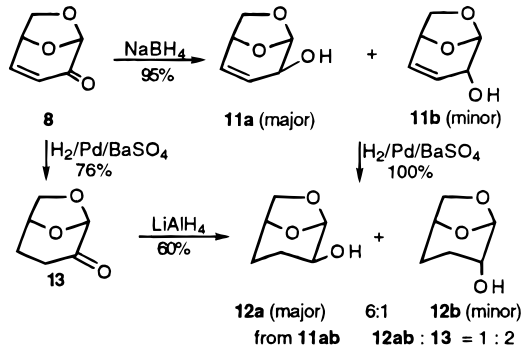
The mixture of alcohols **12a** and **12b** was transformed into the mixture of mesylates **14ab** and tosylates **15ab** by standard conditions. An unsuccessful attempt was

(7) (a) Herdewijn, P.; Van Aerschot, A. *Bull. Soc. Chim. Belg.* **1990**, *99*, 895. (b) Herdewijn, P.; Van Aerschot, A.; Balzarini, J.; De Clercq, E. *Nucleosides Nucleotides* **1991**, *10*, 119. (c) Van Aerschot, A.; Janssen, G.; Herdewijn, P. *Bull. Soc. Chim. Belg.* **1990**, *99*, 769.

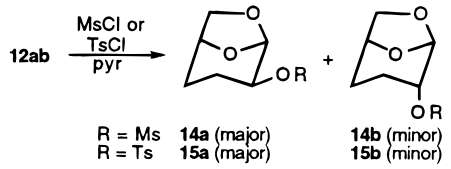
(8) Verheggen, I.; Van Aerschot, A.; Toppet, S.; Snoeck, R.; Janssen, G.; Balzarini, J.; De Clercq, E.; Herdewijn, P. *J. Med. Chem.* **1993**, *36*, 2033.

(9) (a) Shafizadeh, F.; Chin, P. S. *Carbohydr. Res.* **1977**, *58*, 79. (b) Shafizadeh, F.; Furneaux, R. H.; Stevenson, T. T. *Carbohydr. Res.* **1979**, *71*, 169. (c) *Levoglucosenone and Levoglucosans, Chemistry and Applications*, Proceedings from the Symposiom at the 203rd National Meeting of the American Chemical Society Washington, D.C.; Witczak, Z. J., Ed.; ATL Press: Illinois, 1993. (d) Ebata, T.; Matsumoto, K.; Yoshikoshi, H.; Koseki, K.; Kawakami, H.; Okano, K.; Matsushita H. *Heterocycles* **1993**, *36*, 1017. (e) Matsumoto, K.; Ebata, T.; Takashi, K.; Koshi, K.; Kawaki, H.; Matsushita, H. *Heterocycles* **1991**, *32*, 2225. (f) Isobe, M.; Fukuda, Y.; Nishikawa, T.; Chabert, P. *Tetrahedron Lett.* **1990**, *31*, 3327. (g) Laikhter, A. L.; Niyazymbetov, M. E.; Evans, D. H.; Samet, A. V.; Semenov, V. V. *Tetrahedron Lett.* **1993**, *34*, 4465. (h) Shafizadeh, F.; Ward, D. D.; Pang, D. *Carbohydr. Res.* **1982**, *102*, 217. (i) Forsyth, A.; Paton, R. M.; Watt, I. *Tetrahedron Lett.* **1989**, *30*, 993. (j) Furneaux, R. H.; Gainsford, G. I.; Stevenson, T. T. *Carbohydr. Res.* **1986**, *146*, 113. (k) Essig, M. *Carbohydr. Res.* **1986**, *156*, 225. (l) Although levoglucosenone is commercially available from Yuki Kogyo Co., Ltd., we conducted all our experiments on "self-made" material, prepared by pyrolysis of acid-treated newspaper or cellulose.

Scheme 2



Scheme 3



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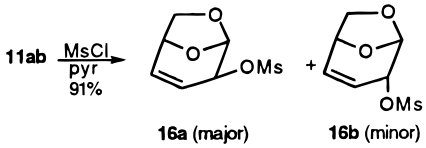
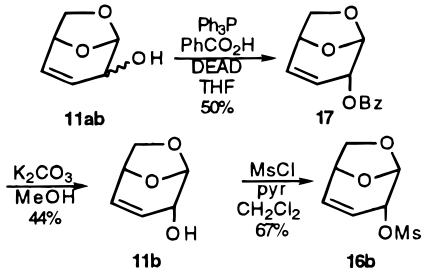


Scheme 5

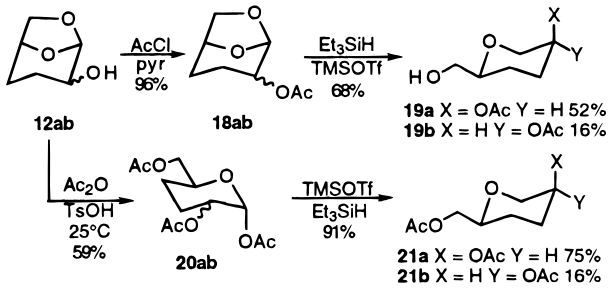


made to displace the leaving groups with heterocyclic bases (even though that would have given the desired β-oriented modified nucleosides as the minor isomers) (Scheme 3). Because allylic leaving groups are more reactive toward S_N2 reactions than nonallylic ones, the allylic mesylate mixture **16ab** was prepared from the corresponding alcohol mixture in 91% yield (Scheme 4). However displacement of the mesyl group of **16a** or **16b** did not occur, and no coupling products were observed.

Using Mitsunobu conditions[9e] (Scheme 5), the allylic alcohol **11** was inverted at C-2 in order to introduce the base on the β-face by an S_N2 process. The α-benzoate **17** was prepared from the predominantly β alcohol **11a** in 50% yield by treatment with triphenylphosphine, benzoic acid, and diethyl azodicarboxylate in tetrahydrofuran. Methanolysis of the benzoate **17** with potassium carbonate gave, in 44% yield, the desired α alcohol **11b** which was converted to the mesylate **16b** under normal conditions in 67% yield. However, none of the desired coupling product could be obtained from the reaction of the mesylate **16b** using various heterocyclic bases.

The resistance of the mesylate **16b** toward nucleophilic displacement was not altogether surprising given the fact that the 1,6-anhydro bridge exhibits effective steric hindrance on the top face of the molecule in levoglucosenone **8** and its dihydro analogue **13** and that approach of even smaller nucleophiles such as hydride and methyl Grignard is directed almost exclusively from the bottom face.[9] Thus cleavage of the acetal was necessary in order to achieve the desired coupling, which also would require protection of the primary alcohol at C-6. Because the anhydro bridge of levoglucosenone is a cyclic acetal, it should have been readily opened and/or reduced under existing literature conditions. However, the presence of the ketone group α to the acetal and the bicyclic structure of the molecule made the task less than trivial. After several unsuccessful attempts to open the acetals of **8** and **13** using several electrophilic reagents, it became apparent that the ketone had to be rendered less electrophilic. The free alcohols **12ab** were converted into the corresponding acetates **18ab** in 96% yield (Scheme 6). This mixture was reduced with triethylsilane and TMSOTf[10] to the desired monoacetates **19ab** in 52% and 16% yields, respectively. Alternatively the alcohol mixture could be opened directly by treatment with acetic anhydride and tosic acid giving a 59% yield of the triacetates **20ab**[11] which were then reduced with triethylsilane and TMSOTf to the diacetates **21ab** in 75% and 16% yields, respectively. Both the monoacetates **19ab** and the diacetates **21ab** were easily separable by column chromatography. The diacetates **21ab** could also be prepared directly from **12ab** without isolation of the triacetates **20ab** in 44% and 9% yields, respectively.

Scheme 6



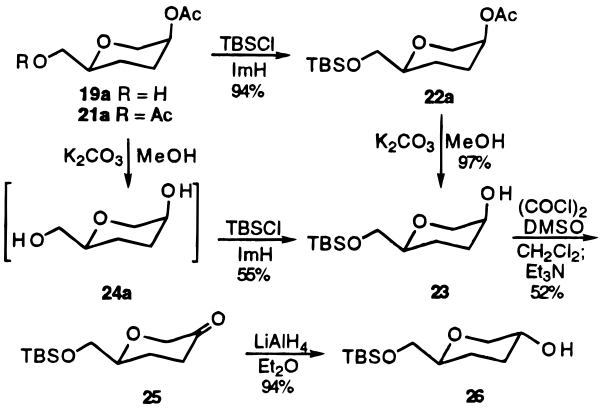
The minor isomers **19b** and **21b** could now be used directly in the synthesis while the major isomers **19a** or **21a** had to be inverted at C-2 to obtain the correct stereochemistry for use as precursors in a nucleophilic substitution reaction with heterocyclic bases. The inversion of both compounds was readily accomplished (Scheme 7). Silylation of the monoacetate **19a** gave in 94% yield the silyl ether **22a** which was hydrolyzed to the protected alcohol **23** in 97% yield. Hydrolysis of the diacetate **21a** (to give the diol **24a** which was not purified) and selective protection of the primary alcohol afforded the same protected alcohol **23** in 55% yield over two steps. Swern oxidation of **23** produced the desired ketone **25** in 52% yield. Reduction of the ketone with lithium aluminum hydride gave exclusively the desired equatorial alcohol **26** in 94% yield.

The minor isomers **19b** and **21b** were also converted into the same alcohol **26** as follows (Scheme 8). Silylation of **19b** afforded in 93% yield the silyl ether **22b** which was hydrolyzed to give the silyl ether alcohol **26** in 75% yield. Hydrolysis of the diacetate **21b** formed the diol

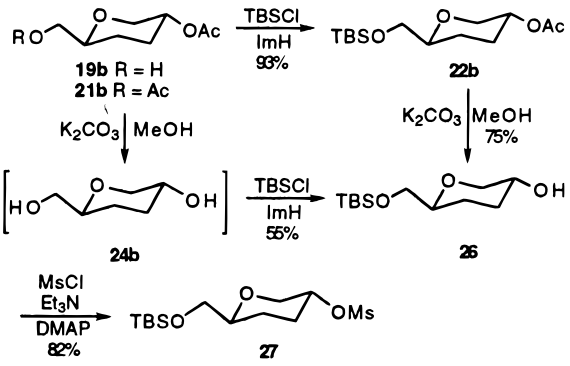
(10) Jeffery, A.; Nair, V. *Tetrahedron Lett.* **1995**, *36*, 3627.

(11) Acid-catalyzed acetolysis of the 1,6-anhydro bridge with acetic anhydride has been reported for levoglucosan derivatives. Zottola, M.; Venkateswara, R. B.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1991**, 969.

Scheme 7



Scheme 8

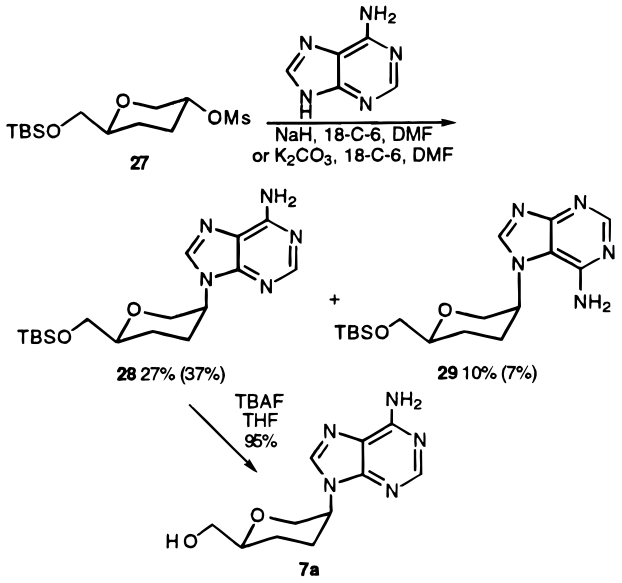


24b which was selectively silylated to produce **26** in 55% yield. Finally, mesylation of the alcohol under normal conditions gave the mesylate **27** in 82% yield.

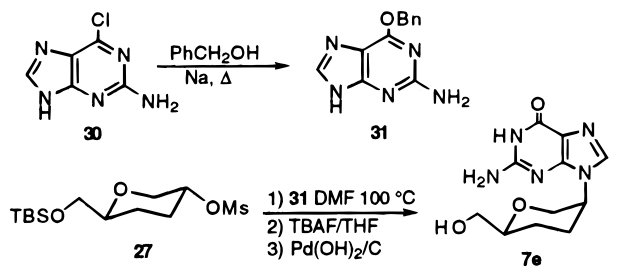
Two general procedures exist for adding base to sugar in preparing similar isonucleosides—direct nucleophilic displacement of a tosylate or mesylate[12] or coupling of the alcohol itself under Mitsunobu conditions.[13] The nature of the base usually determines the one chosen. Herdewijn reported using the sodium salt of 5-iodouracil as the active nucleophile for displacement of a tosylate to give the product of coupling at the 1-position of the iodouracil.[8] The anion initially formed at N-3 presumably equilibrates to the more nucleophilic anion at N-1 where alkylation occurs. Our attempts at alkylating this nucleophile with the carbohydrate mesylate **27** were unsuccessful, however, and in all cases the starting mesylate was cleanly recovered.

Reactions of the anions of 6-chloropurine (for adenine)[5] and of 2-amino-6-chloropurine (for guanine)[8] with the mesylate **27** were also unsuccessful, even varying conditions and changing base and solvent. Adenine, however, reacted with the mesylate **27** in the presence of either sodium hydride or potassium carbonate to give the desired adduct as a mixture of the regioisomers **28** and **29** (Scheme 9). The desired N-9 alkylated product **28** was produced in preference to the N-7 alkylated product **29** in modest yields. The structures were assigned by ^{1}H and ^{13}C NMR and by comparison of the spectra with those of similar compounds in the literature. Cleavage of the silyl ether of **28** with tetrabutylammonium fluoride

Scheme 9



Scheme 10



afforded the final target compound, 2-(6-amino-9*H*-purin-9-yl)-1,5-anhydro-2,3,4-trideoxy-D-*threo*-hexitol **7a**, in 95% yield.

Attempted condensation of **26** with 6-chloro- or 2-amino-6-chloropurine under normal Mitsunobu conditions or under Benner's modified conditions[14] failed. Treatment of the mesylate **27** with 2-amino-6-(phenylmethoxy)-purine **31** (prepared from 2-amino-6-chloropurine **30**)[15] in the presence of cesium carbonate gave an adduct that had some characteristics of the desired N-9 alkylated guanine derivative (Scheme 10). However the NMR spectrum of this compound did not allow for the unambiguous determination of the structure of this product. This route was abandoned after desilylation of the product followed by hydrogenolysis gave an inseparable mixture of the desired product **7e** and another higher molecular weight compound.

Since it can be converted to guanine by hydrolytic deamination,[16] the coupling of 2,6-diaminopurine **32** with the mesylate **27** was carried out to give the desired product **33** in 34% yield (Scheme 11). Enzymatic hydrolysis using enzyme adenosine deaminase is known to convert diaminopurine derivatives to guanine derivatives. However, given the literature evidence that adenosine

(12) Yu, K. L.; Bronson, J. J.; Yang, H.; Patrick, A.; Alam, M.; Brankovan, V.; Datema, R.; Hitchcock, M. J. M.; Martin, J. C. *J. Med. Chem.* **1992**, *35*, 2958.

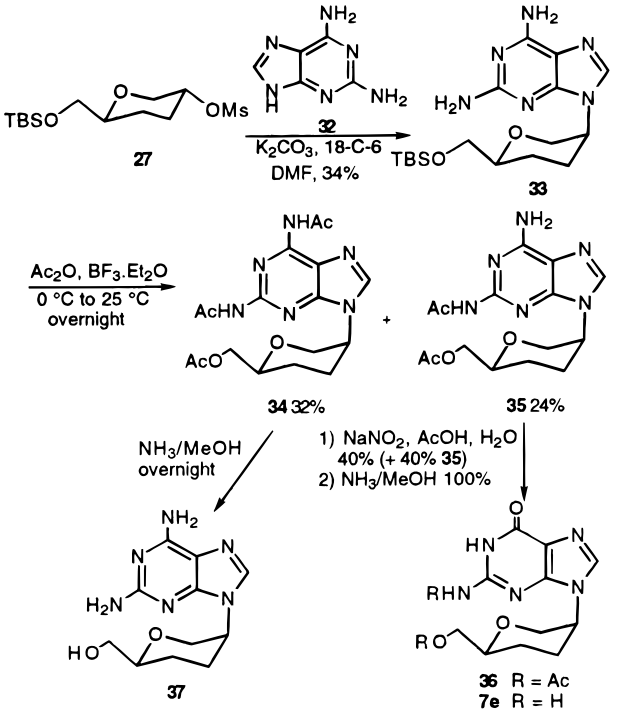
(13) Borthwick, A. D.; Crame, A. J.; Exall, A. M.; Weingarten, G. G.; Mahmoudian, M. *Tetrahedron Lett.* **1995**, *36*, 6929.

(14) (a) Jenny, T. F.; Schneider, K. C.; Benner, S. A. *Nucleosides Nucleotides* **1992**, *11*, 1257. (b) Jenny, T. F.; Horlacher, J.; Previsani, N.; Benner, S. A. *Helv. Chim. Acta* **1992**, *75*, 1994.

(15) (a) Kjellberg, J.; Liljemberg, M. *Tetrahedron Lett.* **1986**, *27*, 877. (b) Bowles, W. A.; Schneider, F. H.; Lewis, L. R.; Robins, R. K. *J. Med. Chem.* **1963**, *6*, 471.

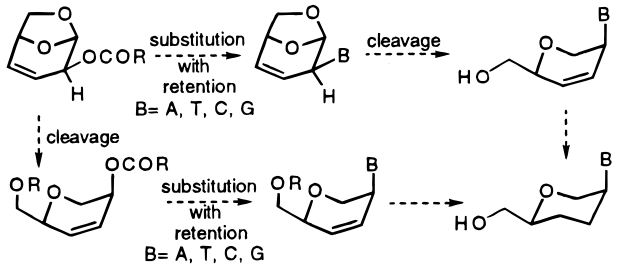
(16) Jones, M. F.; Meyers, P. L.; Robertson, C. A.; Storer, R.; Williamson, C. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2479.

Scheme 11

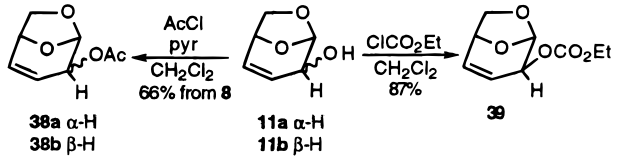


deaminase generally does not act on pyranosides,[17] a chemical method for this selective deamination was attempted instead. De Clercq's group had demonstrated a conversion of diaminopurine to guanine by using the different reactivities of the two amino groups in the starting purine.[18] After acetylation of both aromatic amines in the starting nucleoside, the more labile acetamide in the 6-position was cleaved with methanolic ammonia. The free amine was then deaminated with nitrous acid and the existing acetamide hydrolyzed to produce a guanine derivative. In a similar approach, Jones' group[16] reported selective acetylation of the amine at the C-2 position of 2,6-diaminopurine-bearing nucleosides using acetic anhydride in the presence of boron trifluoride etherate. Acetylation of the diaminopurine adduct **33** with acetic anhydride and catalytic boron trifluoride etherate produced a mixture of the diacetylated **34** and monoacetylated **35** products in 32% and 24% yields, respectively, with simultaneous exchange of the *tert*-butyldimethylsilyl protection for acetyl. Selective cleavage of the acetamide at C-6 was not possible, and treatment of **34** with methanolic ammonia hydrolyzed both acetamides cleanly to give the diaminopurine adduct **37**. However, when reacted with sodium nitrite and acetic acid in water, the monoacetamide **35** was successfully deaminated to give the protected guanine derivative **36.** Removal of the remaining protecting groups of **36** with methanolic ammonia gave the target guanine analogue 2-(2-amino-1,6-dihydro-6-oxo-9*H*-purin-9-yl)-1,5-anhydro-2,3,4-trideoxy-D-*threo*-hexitol **7e** in quantitative yield. Thus, we succeeded in preparing the two new nucleoside analogues **7a** and **7e** from levoglucosenone **8**.

Scheme 12



Scheme 13



Other Approaches

The major allylic alcohol formed from hydride reduction of levoglucosenone **11a** had the β configuration. If it were coupled to a base regioselectively at C-2 with retention of stereochemistry, the backbone structure of our target would be complete, requiring, in fewer steps and more efficiently, only reductive opening of the acetal and final reduction to produce the desired materials (Scheme 12). In a synthesis of carbovir,[19] Trost's group was the first to use palladium coupling reactions to add stereoselectively intact purines to activated allylic compounds. They later extended this technique to heterocycles in an asymmetric synthesis of an adenosine analogue.[20] We subsequently used this methodology to synthesize carbovir by a different route.[21]

Since this procedure had been successful in other systems, we attempted to couple both the allylic acetates (or carbonates) of the anhydro sugar and those of the ring-cleaved derivatives with purines. The allylic acetate **38a** was prepared from the corresponding alcohols **11ab** by treatment with acetyl chloride and pyridine in 66% yield from levoglucosenone **8** (Scheme 13). The carbonate **39** was also obtained as a pure diastereomer in 87% yield by the reaction of **11ab** with ethyl chloroformate. However, all attempts at coupling either the acetate **38** or the carbonate **39** with the anion of 2-amino-6-chloropurine **30** in the presence of Pd(0) were unsuccessful, the only products isolated being the alcohol **11a** resulting from the hydrolysis of the acetate or the carbonate and starting material. The fact that diethyl malonate was also ineffective as the nucleophile seems to imply that both the congested steric environment on the top face of the substrate, where nucleophilic attack is required, and poor overlap of the ester with the π system result in negligible formation of the π-allyl palladium complex.

Application of the same conditions that had reductively cleaved the acetal functionality in the saturated acetate **18** to the allylic compound **38** did not give clean results. However, acetolysis with acetic anhydride in the presence of catalytic triethylsilyl triflate gave the triacetates **40ab**

(17) Bloch, A.; Robins, M. J.; McCarthy, J. R., Jr. *J. Med. Chem.* **1967**, *10*, 908. Herdewijn has reported the use of adenosine deaminase to convert the 2-amino-6-chloro-9-pyranosylpurine into the guanosine system.[8]

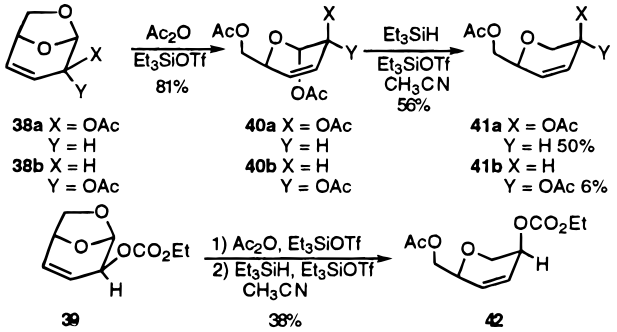
(18) Herdewijn, P.; Balzarini, J.; Baba, M.; Pauwels, R.; Van Aerschot, A.; Janssen, G.; De Clercq, E. *J. Med. Chem.* **1988**, *31*, 2040.

(19) Trost, B. M.; Li, L.; Guile, S. D. *J. Am. Chem. Soc.* **1992**, *114*, 8745.

(20) Trost, B. M,; Shi, Z. *J. Am. Chem. Soc.* **1996**, *118*, 3037. Ukai, T.; Kawazura, H.; Ishii, Y.; Bonnet, J. J.; Ibers, J. A. *J. Organomet. Chem.* **1974**, *65*, 253.

(21) Jung, M. E.; Rhee, H. *J. Org. Chem.* **1994**, *59*, 4719.

Scheme 14



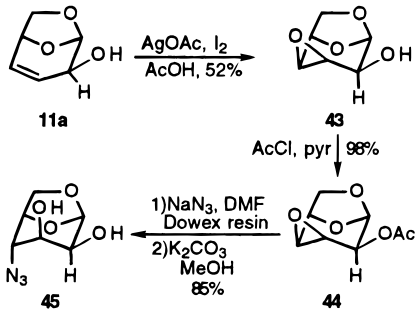
in good yield (Scheme 14). Further treatment with triethylsilane and catalytic triethylsilyl triflate removed the anomeric acetate, giving a diastereomeric mixture of the olefinic diacetates **41ab**, which was separated chromatographically. The allylic carbonate **39** was acetolyzed and reduced under the same conditions to give only the β diastereomeric carbonate **42** in 38% yield.

The allylic acetate **41a** was treated with the sodium salt of 2-amino-6-chloropurine **30** in the presence of either tetrakis(triphenylphosphine)palladium[22] or tetrakis[tri(isopropyl)phosphite]palladium, but only starting material was recovered. The more reactive allylic carbonate **42** was reacted with the sodium salt of 2-amino-6-chloropurine **30** and tetrakis[tri(isopropyl)phosphite]-palladium or dipalladium tris(benzylideneacetone),[23] but again only starting material was recovered. The simultaneous success of the first scheme and time constraints prevented us from addressing this problem further.

Since the enhanced biological activity of AZT **1a** as a chain terminator compared with that of deoxythymidine is apparently due to the presence of the azide substituent, it might be assumed that a similar substitution in these analogues would also have a beneficial effect on biological activity. Attempts at direct addition of an azide group via 1,4-addition to the enone of levoglucosenone were generally unproductive though as was treatment of the enone with trimethylsilyl azide and catalytic sodium azide. Using Horton's conditions,[24] only small amounts of any azide-containing product could be isolated.

In an alternate approach to introduce azide, the selective epoxidation of the olefin **11a** on the β face was carried out with iodine and silver acetate in acetic acid[25] to give the epoxide **43** in 52% yield (Scheme 15). Acetylation under normal conditions furnished the epoxy acetate **44** in 98% yield. Attack of azide anion on the oxirane ring of **44** occurred regioselectively at C-4, affording the azide with the desired regio- and stereochemistry.[26,27] Hydrolysis of the crude mixture with potassium carbonate gave the azidodiol **45** in 85% yield

Scheme 15



for the two steps. No further derivatization of this azidodiol **45** was attempted due to time constraints.[28]

Biological Activity

The biological activity of the new compounds **7a** and **7e** against HIV were determined in the anti-HIV drug testing system of the National Cancer Institute. Neither the adenosine analogue **7a** nor the guanosine analogue **7e** was active in this screen.

Conclusion

In summary, the methylene-expanded dideoxyribonucleoside analogues of adenosine **7a** and guanosine **7e** have been prepared from levoglucosenone **8** in 11 and 13 steps, respectively. The key synthetic steps are the reductive opening of the acetates **18ab** to give the monoacetates **19ab** and acid-catalyzed opening of the alcohols **12ab** to afford the triacetates **20ab** which were reduced to the diacetates **21ab** and the coupling of the mesylate **27** with the nucleobases to give, after deprotection, the desired modified nucleosides **7ae**. Further work in this area is underway.

Experimental Section

General Methods. All reactions were carried out under nitrogen with the exclusion of moisture. Reagents were purchased from commercial sources and used without further purification unless otherwise specified. The following solvents and reagents were distilled from the indicated agent under argon: tetrahydrofuran (THF) and diethyl ether from sodium benzophenone ketyl; dichloromethane, benzene and toluene from calcium hydride, and triethylamine from potassium hydroxide. Flash column chromatography was carried out in the indicated solvent system on 230−400 mesh silica gel.

The proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 200 and 400 MHz, and the carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded at 100 MHz. Spectra were taken in the indicated solvent at ambient temperature unless otherwise specified, and the chemical shifts are reported in parts per million relative to the solvent used.

The infrared (IR) spectra were recorded on a Fourier transform IR spectrometer. High-resolution mass spectra (HRMS) were recorded on a VG Autospec at the UCLA Mass Spectrometry Laboratory and are reported in *m*/*z* units for the most abundant peaks.

1,6-Anhydro-3,4-dideoxy-β-D-*glycero*-hex-3-enopyranos-2-ulose (Levoglucosenone, 8). This compound was prepared according to the procedure of Isobe and co-workers.[9c,f] Powdered cellulose (6 batches, 50 g each) was placed in a round-bottom flask and treated with methanolic phosphoric acid (20% v/v, 6 mL). The flask was heated in a Kugelrohr oven under reduced pressure (~25 mmHg) to 325 °C for 20 min. The caramel-colored tar collected in the condensor was combined

(22) Holzapfel, C. W.; Williams, D. B. G. *Tetrahedron* **1995**, *51*, 8555. Thomson, R.; von Itzein, M. *Carbohydr. Res.* **1995**, *274*, 29.

(23) Ukai, T.; Kawazura, H.; Ishii, Y.; Bonnet, J. J.; Ibers, J. A. *J. Organomet. Chem.* **1974**, *65*, 253.

(24) Horton, D.; Roski, J. P.; Norris, P. *J. Org. Chem.* **1996,** *61*, 3783.

(25) Matsumoto, K.; Ebata, T.; Koseki, K.; Okano, K.; Kawakami, H.; Matsushita, H. *Carbohydr. Res.* **1993**, *246*, 345.

(26) Thomson, R.; von Itzein, M. *Carbohydr. Res.* **1995**, *274*, 29.

(27) Some transfer of the acetate functionality from the 2- to the 3-hydroxyl occurred in this step as well as partial hydrolysis to the diol.

(28) We believe that the less hindered hydroxyl group at C-2 could be selectively protected to allow deoxygenation at C-3 and then an application of the synthesis described for **7a** to the resulting azido alcohol would afford the ring-expanded AZT analogue.

and neutralized with solid sodium bicarbonate followed by a saturated solution of sodium bicarbonate (200 mL). This aqueous layer was extracted with dichloromethane (3 × 75 mL) and dried over $MgSO_4$, and the solvent was evaporated. Vacuum distillation (bp 108−113 °C, 3 mmHg) gave the desired enone acetal **8** as a fragrant yellow oil (9.83 g, 3.7 wt % from cellulose). The spectral data for this compound are consistent with the literature data.[9a,b] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.27 (1H, dd, J = 10.0, 4.7 Hz, H4), 6.11 (1H, dd, J = 10.0, 1.7 Hz, H3), 5.34 (1H, d, J = 1.6 Hz, H1), 5.00 (1H, dd, J = 4.7, 4.7 Hz, H5), 3.89 (1H, dd, J = 6.8, 4.7 Hz, H6), 3.76 (1H, d, J = 6.8 Hz, H6′). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 188.85, 148.05, 126.95, 101.70, 71.80, 66.62. $[\alpha]^{25}_D = -192.2$ (c = 0.4, EtOAc).

1,6-Anhydro-3,4-dideoxy-*β*-D-*threo*-hex-3-enopyranose (11a) and 1,6-Anhydro-3,4-dideoxy-*β*-D-*erythro*-hex-3-enopyranose (11b). Levoglucosenone **8** (374 mg, 2.97 mmol) was dissolved in water (5 mL) and treated with a solution of sodium borohydride (179 mg, 4.75 mmol) in water (2 mL). The reaction was mildly exothermic and was complete in 10 min. Acetone (3 mL) was added, and heat evolution was observed. The aqueous solution was extracted with ethyl acetate (4 × 5 mL), and the combined organic extracts were dried over $MgSO_4$. Upon evaporation of the solvent, the products **11ab** were obtained as a clear oil (363 mg, 95%) which crystallized on standing. This crude material was carried on without further purification. The spectral data for this compound were consistent with literature data.[29] Although the ^{1}H NMR shows only one set of peaks for **11a**, the diastereomer **11b** must be present in small amounts since a product derived from it is observed in later steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.11 (1H, ddd, J = 9.8, 4.2, 0.6 Hz, Ha), 5.71 (1H, dt, J = 9.8, 2.3 Hz, Hb), 5.32 (1H, dd, J = 2.4, 2.3 Hz, Hc), 4.66 (1H, dd, J = 4.2, 4.2 Hz, Hd), 4.33 (1H, br d, J = 11.8 Hz, He), 3.84 (1H, d, J = 6.5 Hz, Hf), 3.75 (1H, dd, J = 6.5, 4.2 Hz, Hg), 2.08 (1H, d, J = 11.9 Hz, Hh).

1,6-Anhydro-3,4-dideoxy-*β*-D-*glycero*-hexopyranos-2-ulose (13). Levoglucosenone **8** (470 mg, 3.73 mmol) was dissolved in ethyl acetate (25 mL) and treated with 5% palladium on barium sulfate (920 mg). The suspension was hydrogenated at atmospheric pressure for 1 h. The catalyst was filtered off, and excess solvent was evaporated. The residue was subjected to flash chromatography (hexane/ether 1:3) to give the desired ketone **13** as a colorless oil (365 mg, 76%). The spectral data for this compound are consistent with the literature data.[9a,b] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.11 (1H, br s), 4.70 (1H, m), 4.05 (1H, dd, J = 7.4, 0.9 Hz), 3.96 (1H, ddd, J = 7.4, 5.1, 1.2 Hz), 2.64 (1H, ddd, J = 16.5, 11.5, 8.3 Hz), 2.32−2.42 (2H, m), 1.99−2.04 (1H, br dd, J = 13.8, 8.8 Hz).

1,6-Anhydro-3,4-dideoxy-*β*-D-*threo*-hexopyranose (12a) and 1,6-Anhydro-3,4-dideoxy-*β*-D-*erythro*-hexopyranose (12b). To a solution of the ketone **13** (200 mg, 1.59 mmol) in dry ether (10 mL) was added lithium aluminum hydride (60.3 mg, 1.59 mmol) in portions. The suspension was stirred at room temperature until all starting material was consumed (TLC). The reaction was then quenched with water (10 mL), and the resulting emulsion was treated with a small amount of 1 N HCl (2 mL). This aqueous layer was extracted several times with ethyl acetate (5 × 10 mL). The aqueous layer was then saturated with sodium chloride and further extracted with ethyl acetate (5 × 10 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was evaporated. The 6:1 mixture of diastereomeric alcohols **12a** and **12b** thus obtained (122 mg, 60%) was used without purification. The spectral data for these compound were consistent with the literature data.[9a] The spectral data reported here are those of the major isomer; the minor isomer was formed in a small amount and its spectrum was not completely distinguishable from that of the major isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.31 (1H, br s), 4.49 (1H, br s), 3.79−3.92 (2H, m), 3.59 (1H, br s), 2.01−2.07 (1H, m), 1.85−1.90 (1H, m), 1.76 (1H, br s), 1.41−1.66 (2H, m).

2-*O*-(Methanesulfonyl)-1,6-anhydro-3,4-dideoxy-*β*-D-*threo*-hexopyranose (14a) and 2-*O*-(methanesulfonyl)-1,6-anhydro-3,4-dideoxy-*β*-D-*erythro*-hexopyranose (14b). The alcohols **12ab** (316 mg, 2.43 mmol) were dissolved in dichloromethane (10 mL) and treated with pyridine (384 mg, 4.86 mmol) and methanesulfonyl chloride (556 mg, 4.86 mmol). The solution was stirred at room temperature overnight, and then water (10 mL) was added. The organic layer was separated, and the aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined organic extracts were washed successively with saturated sodium bicarbonate solution and brine (10 mL each) and dried over $MgSO_4$. Evaporation of the solvent afforded the desired mesylate **14a** (348 mg, 69%) along with the diastereomer **14b** (6:1 mixture) as a white solid that was used without further purification. The spectral data reported here are those of the major isomer **14a**; the minor isomer **14b** was formed in a small amount and its spectrum was not completely distinguishable from the spectrum of the major isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.45 (1H, br s), 4.58 (1H, m), 4.50 (1H, m), 3.90 (1H, br d, J = 7.3 Hz), 3.80−3.82 (1H, m), 3.02 (3H, s), 2.06−2.13 (1H, m), 1.87−1.99 (2H, m), 1.65−1.71 (1H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 100.15, 76.85, 72.93, 68.59, 38.73, 27.99, 22.98. FT-IR (neat): 2961.1, 2903.2, 1356.1, 1174.8, 1134.3 cm^{-1}. MS (EI) m/z (rel intensity) 209.0 ([M + H]$^+$,10), 129.0 (100), 113.1 (70). High-resolution EI MS (m/z): 209.0483, calcd for $C_7H_{12}O_5S$ ([M + H]$^+$) 209.0484.

2-*O*-[(4-Methyl)phenylsulfonyl]-1,6-anhydro-3,4-dideoxy-*β*-D-*threo*-hexopyranose (15a) and 2-*O*-[(4-Methyl)phenylsulfonyl]-1,6-anhydro-3,4-dideoxy-*β*-D-*erythro*-hexopyranose (15b). The alcohols **12ab** (237 mg, 1.82 mmol) were dissolved in pyridine and treated with *p*-toluenesulfonyl chloride (520 mg, 2.73 mmol). The solution was stirred at room temperature for 24 h, and then water (5 mL) was added. The aqueous layer was extracted with ethyl acetate (3 × 5 mL), and the combined organic extracts were dried over $MgSO_4$. After evaporation of the solvent, the residue was flash chromatographed on silica gel (hexane/ethyl acetate 1:1) to give the desired tosylate **15a** as a white solid (75 mg, 19%). The product was mixed with a small amount of the diastereomer **15b**. The spectral data reported here are those of the major isomer, **15a**; the minor isomer **15b** was formed in a small amount and its spectrum was not completely distinguishable from the spectrum of the major isomer Mp: 77−84 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (2H, d, J = 8.3 Hz), 7.33 (2H, d, J = 8.3 Hz), 5.25 (1H, br s), 4.46 (1H, br s), 4.39−4.43 (1H, m), 3.87 (1H, br d, J = 7.3 Hz), 3.79 (1H, br dd, J = 6.8, 5.3 Hz), 2.44 (3H, s), 1.83−1.91 (3H, m), 1.58−1.62 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.96, 133.94, 129.93, 127.77, 100.06, 77.60, 72.91, 68.55, 28.03, 22.76, 21.66. FT-IR (neat): 2961.1, 2899.4, 1361.9, 1176.7, 954.9, 844.9, 669.4 cm^{-1}. MS (EI) m/z (rel intensity) 285.1 ([M + H]$^+$, 7), 129.1 (83), 113.1 (100), 91.1 (39). High-resolution EI MS (m/z): 285.0797, calcd for $C_{13}H_{17}O_5S$ ([M + H]$^+$) 285.0797.

2-*O*-(Methanesulfonyl)-1,6-anhydro-3,4-dideoxy-*β*-D-*threo*-hex-3-enopyranose (16a). The mixture of allylic alcohols **11ab** (72.4 mg, 0.56 mmol) was dissolved in dichloromethane (5 mL) and treated with methanesulfonyl chloride (128 mg, 1.12 mmol) and pyridine (88.5 mg, 1.12 mmol). The solution was stirred at room temperature overnight, and then water (5 mL) was added. The organic layer was separated, and the aqueous layer was extracted with dichloromethane (3 × 5 mL). The combined organic extracts were washed with saturated sodium bicarbonate solution and brine (10 mL each) and dried over $MgSO_4$. Evaporation of the solvent gave the mesylate **16a** as a colorless oil (115 mg, 91%). The crude material was carried on without further purification. The spectral data for this compound are consistent with the literature data.[11b] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.29 (1H, ddd, J = 10.3, 4.3, 1.4 Hz), 5.66−5.69 (2H, m), 5.40 (1H, dd, J = 2.4, 1.2 Hz), 4.70 (1H, dd, J = 4.2, 4.2 Hz), 3.96 (1H, d, J = 6.7 Hz), 3.79−3.82 (1H, m), 3.10 (3H, s).

(29) Matsumoto, K.; Ebata, T.; Matsushita, H. *Carbohydr. Res.* **1995**, *267*, 187.

2-*O*-(Benzoyl)-1,6-anhydro-3,4-dideoxy-*β*-D-*erythro*-hex-3-enopyranose (17). To a solution of a mixture of the allylic alcohols **11ab** (148 mg, 1.15 mmol) in tetrahydrofuran (5 mL) were added triphenylphosphine (603 mg, 2.3 mol) and benzoic acid (281 mg, 2.3 mmol). The mixture was cooled to 0 °C and treated with a solution of diethyl azodicarboxylate (338 mg, 2.3 mmol) in THF (4 mL). The solution was stirred at room temperature for 2 d. Upon evaporation of the solvent, the crude material was adsorbed on silica gel and flash chromatographed (hexane/ether 2:1) to give the desired product **17** (133 mg, 50%). The spectral data for this compound are consistent with the literature data.[11b] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.07−8.11 (2H, m), 7.55−7.60 (1H, m), 7.41−7.47 (2H, m), 6.36 (1H, ddd, J = 9.8, 4.5, 1.1 Hz, H4), 5.90 (1H, ddd, J = 9.8, 3.8, 1.9 Hz, H3), 5.68 (1H, s, H1), 5.01 (1H, d, J = 3.8 Hz, H2), 4.80 (1H, dd, J = 4.5, 4.5 Hz, H5), 3.72−3.78 (2H, m, H6, H6′).

1,6-Anhydro-3,4-dideoxy-*β*-D-*erythro*-hex-3-enopyranose (11b). A solution of the benzoate **17** (57.3 mg, 0.25 mmol) in methanol (40 mL) was treated with potassium carbonate (170 mg, 1.23 mmol) and stirred at room temperature for 2 h until reaction was complete (TLC). The solvent was evaporated, and the precipitate was filtered, washing thoroughly with dichloromethane. Evaporation of the solvent and flash chromatography (hexane/ether 1:1) gave the desired alcohol **11b** as a clear oil (13.8 mg, 44%). The spectral data for this compound were consistent with the literature data.[10b] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.17 (1H, ddd, J = 9.8, 4.7, 0.7 Hz), 5.80 (1H, ddd, J = 9.8, 3.9, 1.9 Hz), 5.51 (1H, br s), 4.66−4.68 (1H, m), 3.60−3.69 (3H, m), 2.21 (1H, d, J = 10.6 Hz).

2-*O*-(Methanesulfonyl)-1,6-anhydro-3,4-dideoxy-*β*-D-*erythro*-hex-3-enopyranose (16b). The alcohol **11b** (14 mg, 0.11 mmol) was taken up in dichloromethane (2 mL) and treated with methanesulfonyl chloride (25 mg, 0.21 mmol) and pyridine (17 mg, 0.22 mmol). The reaction was allowed to proceed at room temperature for 1 d. Water (2 mL) was then added, the two layers were separated, and the aqueous layer was extracted with chloroform (3 × 2 mL). The combined organic extracts were washed with saturated sodium bicarbonate solution and brine (3 mL each). After drying over $MgSO_4$ the solvent was evaporated to give the crude product **16b** as a white solid (15 mg, 67%). This compound was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.39 (1H, ddd, J = 9.8, 3.8, 0.9 Hz), 5.84 (1H, ddd, J = 9.8, 3.9, 2.0 Hz), 5.69 (1H, br s), 4.79 (1H, m), 4.60 (1H, d, J = 3.9 Hz), 3.69−3.73 (2H, m), 3.08 (3H, s).

2-*O*-Acetyl-1,6-anhydro-3,4-dideoxy-*β*-D-*threo*-hexopyranose (18a) and 2-*O*-Acetyl-1,6-anhydro-3,4-dideoxy-*β*-D-*erythro*-hexopyranose (18b). The mixture of alcohols **12ab** (136 mg, 1.05 mmol) was taken up in dichloromethane (5 mL) and treated with pyridine (0.17 mL, 2.1 mmol) and acetyl chloride (0.15 mL, 2.1 mmol). The solution was stirred under argon overnight, and then saturated sodium bicarbonate solution (5 mL) was added. The aqueous layer was extracted with dichloromethane (3 × 5 mL), and the combined organic extracts were washed with brine. The organic layer was dried over $MgSO_4$, and the solvent was evaporated. The residue was flash chromatographed (hexane/ether 1:1) to give an inseparable 5:1 mixture of diastereomeric acetates **18a** and **18b** as a clear oil (173 mg, 96%). Major isomer **18a**. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.38 (1H, br s), 4.74 (1H, ddd, J = 10.2, 5.8, 1.2 Hz), 4.53 (1H, br s), 3.92 (1H, d, J = 7.1 Hz), 3.84 (1H, br t, J = 6.5 Hz), 2.07 (3H, s), 1.93−2.03 (2H, m), 1.62−1.67 (1H, m), 1.72−1.80 (1H, m).^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.94, 101.61, 76.11, 74.45, 71.79, 33.82, 28.26, 27.59. Minor isomer **18b**. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.40 (1H, br s), 4.63 (1H, br s), 4.55 (1H, br s), 3.92 (1H, d, J = 7.1 Hz), 3.80 (1H, br t, J = 6.5 Hz), 2.11 (3H, s), 1.43−1.46 (1H, m) (some peaks overlapping with those of the major isomer not resolved). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.94, 100.83, 76.06, 71.46, 70.30, 31.28, 27.67, 27.31. Mixture: FT-IR (neat): 2961.1, 2897.4, 1743.9, 1732.3, 1371.6, 1244.2, 1134.3, 1039.8 cm^{-1}. High-resolution EI MS (m/z): 172.0734, calcd for $C_8H_{12}O_4$.

2-*O*-Acetyl-1,5-anhydro-3,4-dideoxy-D-*threo*-hexitol (19a) and 2-*O*-Acetyl-1,5-anhydro-3,4-dideoxy-D-*erythro*-hexitol (19b). The mixture of diastereomeric acetates **18ab** was dissolved in acetonitrile (0.5 mL). Triethylsilane (53 μL, 0.33 mmol) and trimethylsilyl trifluoromethanesulfonate (42 μL, 0.22 mmol) were added under argon. The clear solution was stirred overnight, and then saturated sodium bicarbonate solution (1.0 mL) was added. The volatiles were evaporated under reduced pressure, and the resulting aqueous solution was extracted with ethyl acetate (3 × 1 mL). The combined organic extracts were dried over $MgSO_4$ and evaporated. Flash chromatography on silica gel (ether) yielded two products. The anti acetoxy alcohol **19b** was isolated as a film (3 mg, 16%), and the more polar syn acetoxy alcohol **19a** was obtained as a colorless oil (10 mg, 52%). Major product **19a**. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.83 (1H, br s), 4.05 (1H, dt, J = 12.8, 1.5 Hz), 3.63 (1H, dd, J = 12.8, 1.5 Hz), 3.58−3.62 (2H, m), 3.48−3.52 (1H, m), 2.11 (3H, s), 2.00−2.06 (2H, m), 1.78 (1H, dddd, J = 14.1, 14.1, 4.2, 3.0 Hz), 1.63−1.72 (1H, m), 1.40−1.44 (1H, m).^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.61, 77.67, 69.39, 67.13, 65.86, 26.66, 22.09, 21.22. FT-IR (neat): 3435.7, 2951.5, 2856.9, 1736.2, 1377.3, 1248.1 cm^{-1}. MS (EI) m/z (rel intensity) 175.1 ([M + H]$^+$, 95), 143.0 (100), 115.1 (42), 97.1 (40). High-resolution EI MS (m/z): 175.0971, calcd for $C_8H_{15}O_4$ ([M + H]$^+$) 175.0970. $[\alpha]^{25}_D$ = −15.7 (c = 3.1, CH_2Cl_2). Minor product **19b**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.76 (1H, ddd, J = 15.8, 10.4, 4.8 Hz), 4.07 (1H, ddd, J = 10.6, 5.0, 2.2 Hz), 3.39−3.45 (1H, m), 3.49−3.55 (1H, m), 3.59−3.63 (1H, m), 3.24 (1H, dd, J = 10.5, 10.4 Hz), 2.17−2.20 (1H, m), 2.04 (3H, s), 1.96−1.98 (1H, m), 1.44−1.69 (3H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.27, 77.26, 69.02, 68.11, 65.52, 28.67, 25.95, 21.10. FT-IR (neat): 3435.7, 2951.5, 2864.7, 1736.2, 1371.6, 1244.2, 1103.4, 1043.6 cm^{-1}. MS (EI) m/z (rel intensity) 175.1 ([M + H]$^+$, 100). High-resolution EI MS (m/z): 175.0967, calcd for $C_{18}H_{15}O_4$ ([M + H]$^+$) 175.0970. $[\alpha]^{25}_D$ = +5.64 (c = 0.4, CH_2Cl_2).

2,6-Di-*O*-acetyl-1,5-anhydro-3,4-dideoxy-D-*erythro*-hexitol (21b) and 2,6-Di-*O*-acetyl-1,5-anhydro-3,4-dideoxy-D-*threo*-hexitol (21a). A solution of the alcohols **12ab** (180 mg, 1.38 mmol) in acetic anhydride (5 mL) was treated with tosic acid monohydrate (catalytic) and stirred at room temperature overnight. Water (5 mL) was added, and the mixture was extracted with dichloromethane (3 × 5 mL). The combined organic extracts were washed with saturated sodium bicarbonate solution (2 × 5 mL) and brine (5 mL) and dried over $MgSO_4$. Evaporation gave the triacetate **20ab** as a pale yellow oil (59% crude yield) which was taken up in acetonitrile (2 mL) and treated with triethylsilane (481 mg, 4.14 mmol). Trimethylsilyl triflate (613 mg, 2.76 mmol) was added dropwise to this solution. After stirring at room temperature for 14 h, the reaction was quenched with a saturated sodium bicarbonate solution (2 mL) and the mixture extracted with ethyl acetate (2 × 2 mL). The combined organic extracts were washed with brine and dried over $MgSO_4$. After evaporation the residue was flash chromatographed on silica gel (hexane/ether 1:1) to give the anti diacetate **21b** (22 mg, 9%) as the minor product and the more polar syn diacetate (105 mg, 44%) **21a** as the major product. The total yield was 53% for two steps. Crude triacetates **20ab**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.01 (1H, br s), 4.74 (1H, br s), 2.08 (3H, s), 1.50−2.10 (3H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.85, 169.98. 168.62, 90.69, 68.66, 66.32, 66.10, 22.49, 21.40, 21.02, 20.95, 20.80. Minor product **21b**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.75 (1H, ddd, J = 15.4, 10.2, 4.8 Hz, H3), 4.10 (1H, dd, J = 11.7, 3.4 Hz, H6), 4.04 (1H, ddd, J = 10.7, 4.9, 2.2 Hz, $H1_{eq}$), 3.99 (1H, dd, J = 11.7, 6.8 Hz, H6′), 3.52 (1H, ddd, J = 13.8, 6.8, 3.4 Hz, H5), 3.21 (1H, dd, J = 10.5, 10.5 Hz, $H1_{ax}$), 2.16−2.21 (1H, m), 2.07 (3H, s), 2.01 (3H, s), 1.71−1.74 (1H, m), 1.49−1.51 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.00, 170.23, 74.96, 69.08, 67.77, 66.42, 28.62, 26.40, 21.07, 20.89. FT-IR (neat): 2955.3, 2855.0, 1740.0, 1369.6, 1236.5, 1043.6 cm^{-1}. MS (EI) m/z (rel intensity) 217.1 ([M + H]$^+$, 45), 143.1 (47), 96.1 (100). High-resolution EI MS (m/z): 217.1077, calcd for $C_{10}H_{17}O_5$ ([M + H]$^+$) 217.1076. $[\alpha]^{25}_D$ = +11.5 (c = 0.9, CH_2Cl_2). Major product **21a**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.81 (1H, br s), 4.12 (1H, dd, J = 11.7, 3.4 Hz), 4.05 (2H, m), 3.61 (1H, dd, J = 12.8, 1.3 Hz), 3.59−3.64 (1H, m), 2.10 (3H, s), 2.09 (3H, s), 2.00−2.06 (1H, m), 1.62−1.82 (2H, m), 1.46−1.50 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.07, 170.78, 75.04, 69.52, 67.00,

66.89, 26.79, 22.64, 21.31, 20.92. FT-IR (neat): 2924.5, 2851.1, 1736.2, 1373.5, 1240.4 cm^{-1}. MS (EI) *m/z* (rel intensity) 217.1 ($[M + H]^+$, 27), 143.1 (53), 96.1 (100). High-resolution EI MS (*m/z*): 217.1079, calcd for $C_{10}H_{17}O_5$ ($[M + H]^+$) 217.1076. $[\alpha]^{25}_D$ = +126.5 (*c* = 0.6, CH_2Cl_2).

2-*O*-Acetyl-1,5-anhydro-3,4-dideoxy-6-*O*-[(1,1-dimethyl)ethyldimethyl]silyl-D-*threo*-hexitol (22a). In a procedure identical to the one described for compound **22b** below, the syn acetoxy alcohol **19a** (135 mg, 0.77 mmol) was reacted with *tert*-butyldimethylsilyl chloride (173 mg, 1.15 mmol) in the presence of imidazole (131 mg, 1.92 mmol) to give the silyl ether **22a** (209 mg, 94%). This material was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.80 (1H, br s), 4.00−4.03 (1H, dt, *J* = 12.8, 1.7 Hz), 3.70 (1H, dd, *J* = 10.4, 5.3 Hz), 3.59 (1H, dd, *J* = 12.8, 1.5 Hz), 3.53 (1H, dd, *J* = 10.4, 5.8 Hz), 3.38−3.43 (1H, m), 2.09 (3H, s), 1.96−2.03 (1H, m), 1.71−1.78 (1H, m), 1.57−1.65 (2H, m), 0.89 (9H, s), 0.07 (3H, s), 0.06 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.77, 77.82, 69.53, 67.27, 65.97, 26.80, 25.95, 25.66, 22.23, 21.35, −3.57. FT-IR (neat): 2951.5, 2856.9, 1736.2, 1244.2, 1064.8 cm^{-1}. MS (EI) *m/z* (rel intensity) 289.2 ($[M + H]^+$, 47), 231.1 (68), 171.1 (96), 117.0 (100). High-resolution EI MS (*m/z*): 289.1836, calcd for $C_{14}H_{29}O_4Si$ ($[M + H]^+$) 289.1835. $[\alpha]^{25}_D$ = −20.0 (*c* = 0.1, CH_2Cl_2).

2-*O*-Acetyl-1,5-anhydro-3,4-dideoxy-6-*O*-[(1,1-dimethyl)ethyldimethyl]silyl-D-*erythro*-hexitol (22b). The anti acetoxy alcohol **21b** (30.4 mg, 0.17 mmol) was dissolved in *N*,*N*-dimethylformamide (0.5 mL) and treated with *tert*-butyldimethylsilyl chloride (38 mg, 0.25 mmol) and imidazole (29 mg, 0.42 mmol). The clear solution was stirred at room temperature overnight, and then water (0.5 mL) was added. The aqueous phase was extracted with dichloromethane (3 × 1 mL), and the combined organic extracts were dried over $MgSO_4$. The yellow oil obtained on evaporation of the solvents, compound **22b** (45 mg, 93%), was used in the subsequent step without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.75 (1H, ddd, *J* = 15.6, 10.4, 4.8 Hz, H2), 4.03 (1H, ddd, *J* = 10.6, 5.0, 2.1 Hz, $H1_{eq}$), 3.66 (1H, dd, *J* = 10.5, 5.5 Hz, H6), 3.51 (1H, dd, *J* = 10.5, 5.5 Hz, H6′), 3.33 (1H, dddd, *J* = 10.9, 5.5, 5.5, 2.2 Hz, H5), 3.21 (1H, dd, *J* = 10.4, 10.4 Hz, $H1_{ax}$), 2.16−2.20 (1H, m), 2.03 (3H, s), 1.79−1.83 (1H, m), 1.37−1.54 (2H, m), 0.88 (9H, s), 0.06 (6H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.27, 77.63, 69.03, 68.11, 65.54, 28.68, 25.96, 25.66, 21.11, −3.57 (one upfield carbon not resolved). FT-IR (neat): 2951.5, 2856.9, 1736.2, 1371.6, 1242.3, 1103.4, 1043.6 cm^{-1}. MS (EI) *m/z* (rel intensity) 289.2 ($[M + H]^+$, 44), 231.1 (77), 171.1 (75), 117.0 (100). High-resolution EI MS (*m/z*): 289.1834, calcd for $C_{14}H_{29}O_4Si$ ($[M + H]^+$) 289.1835. $[\alpha]^{25}_D$ = −35.4 (*c* = 0.1, CH_2Cl_2).

1,5-Anhydro-3,4-dideoxy-6-*O*-[(1,1-dimethyl)ethyldimethyl]silyl-D-*threo*-hexopyranose (23). The syn acetoxy silyl ether **22a** (209 mg, 0.72 mmol) was hydrolyzed in a procedure identical to the one described below for compound **22b** to give the desired alcohol **23** (172 mg, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.90 (1H, dt, *J* = 12.0, 2.2 Hz, $H1_{eq}$), 3.76 (1H, br s, H2), 3.67 (1H, dd, *J* = 10.5, 5.5 Hz, H6), 3.58 (1H, dd, *J* = 12.0, 1.2 Hz, $H1_{ax}$), 3.54 (1H, dd, *J* = 10.5, 5.2 Hz, H6′), 3.38−3.43 (1H, m, H5), 1.92−1,96 (1H, m), 1.54−1.71 (3H, m), 0.89 (9H, s), 0.07 (6H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 78.46, 72.46, 66.49, 64.80, 29.43, 25.96, 22.51, 18.43, −5.24, −5.29. FT-IR (neat): 3402.9, 2930.2, 2856.9, 1255.8, 1109.2, 839.1 cm^{-1}. MS (EI) *m/z* (rel intensity) 247.2 ($[M + H]^+$, 22), 189.1 (100), 171.1 (66). High-resolution EI MS (*m/z*): 247.1725, calcd for $C_{17}H_{27}O_3Si$ ($[M + H]^+$) 247.1729. $[\alpha]^{25}_D$ = −22.1 (*c* = 1, CH_2Cl_2).

1,5-Anhydro-3,4-dideoxy-6-*O*-[(1,1-dimethyl)ethyldimethyl]silyl-D-*glycero*-hexitolulose (25). A solution of oxalyl chloride (0.12 mL, 1.40 mmol) in dichloromethane (5 mL) was cooled to −78 °C and treated with a solution of dimethyl sulfoxide (0.20 mL, 2.8 mmol) in dichloromethane (0.2 mL). After the solution stirred for 30 min at this temperature, a solution of the alcohol **23** (172 mg, 0.70 mmol) in dichloromethane (2 mL) was added dropwise. After the reaction stirred for 2 h, it was treated with triethylamine (0.78 mL, 5.6 mmol) and was allowed to warm to room temperature. A solution of saturated sodium bicarbonate (5 mL) was then added. The organic layer was separated, and the aqueous layer was extracted with ether (3 × 5 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was evaporated. The residue was flash chromatographed (hexane/ether 3:1) to afford the pure ketone **25** as a colorless oil (89 mg, 52%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.17 (1H, dd, *J* = 16.5, 1.3 Hz, $H1_{eq}$), 3.97 (1H, d, *J* = 16.5 Hz, $H1_{ax}$), 3.76 (2H, m, Hc, H6, H6′), 3.64 (1H, m, H5), 2.62 (1H, dt, *J* = 16.7, 5.1 Hz, $H3_{eq}$), 2.46 (1H, ddd, *J* = 16.7, 10.9, 6.7 Hz, $H3_{ax}$), 2.10 (1H, m), 1.93 (1H, m), 0.90 (9H, s), 0.08 (6H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 208.74, 75.79, 73.84, 65.66, 36.58, 25.91, 18.39, −5.30, −5.34 (one upfield carbon not resolved). FT-IR (neat): 2930.2, 2858.9, 2359.2, 2341.8, 1730.4, 1111.1, 839.1 cm^{-1}. MS (EI) *m/z* (rel intensity) 244.1 ($[M]^+$, 2), 187.1 (68), 173.1 (100), 131.1 (42), 99.0 (52). High-resolution EI MS (*m/z*): 244.1482, calcd for $C_{12}H_{24}O_3Si$ 244.1497. $[\alpha]^{25}_D$ = −17.0 (*c* = 0.5, CH_2Cl_2).

1,5-Anhydro-3,4-dideoxy-6-*O*-[(1,1-dimethyl)ethyldimethyl]silyl-D-*erythro*-hexitol (26). Method A. The acetate **22b** (45 mg, 0.16 mmol) was dissolved in methanol (2 mL) and treated with potassium carbonate (26 mg, 0.19 mmol). The reaction proceeded overnight at room temperature. Excess methanol was removed by rotary evaporation, and the residue was partitioned between water and ether (2 mL). The water layer was extracted with ether (2 × 2 mL), and the combined organic extracts were dried over $MgSO_4$. Evaporation of the solvent gave **26** as a colorless oil (29 mg, 75%) which was pure enough to be used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.99 (1H, ddd, *J* = 10.7, 4.9, 2.3 Hz, $H1_{eq}$), 3.64−3.72 (1H, m, H2), 3.66 (1H, dd, *J* = 10.4, 5.4 Hz, H6), 3.50 (1H, dd, *J* = 10.4, 5.5 Hz, H6′), 3.31 (1H, m, H5), 3.11 (1H, dd, *J* = 10.4, 10.4 Hz, $H1_{ax}$), 2.13−2.17 (1H, m), 1.78−1.82 (1H, m), 1.29−1.45 (3H, m), 0.89 (9H, s), 0.06 (6H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 77.69, 77.58, 66.17, 66.12, 32.37, 27.10, 25.94, 18.40, −5.27, −5.34. FT-IR (neat): 3379.7, 2930.2, 2856.9, 1464.9, 1255.8, 1103.4, 839.1 cm^{-1}. MS (EI) *m/z* (rel intensity) 247.2 ($[M + H]^+$, 68), 229.2 (55), 189.1 (100), 171.1 (95). High-resolution EI MS (*m/z*): 247.1733, calcd for $C_{17}H_{27}O_3Si$ ($[M + H]^+$) 247.1729. $[\alpha]^{25}_D$ = −5.6 (*c* = 0.5, CH_2Cl_2).

Method B. The ketone **25** (128 mg, 0.52 mmol) was dissolved in ether (5 mL) and treated with lithium aluminum hydride (23.5 mg, 0.62 mmol). The reaction was complete (TLC) after 10 min, and water (5 mL) was then added. The two layers were separated, and the aqueous layer was extracted with ether (3 × 5 mL). The combined ether extracts were dried over $MgSO_4$, and the solvent was evaporated. The crude oil obtained **26** (120 mg, 94%) was not further purified and had an identical proton NMR spectrum to that prepared by method A.

Method C. In a procedure similar to that described for the acetate **22b,** the anti diacetate **21b** (105 mg, 0.49 mmol) was hydrolyzed to give the crude 2,6-diol **24b** which was in turn silylated selectively at C-6 (as described for **19b**) to give the title compound **26** (67 mg, 0.27 mmol, 55%), the spectral data for which were identical to those of **26** prepared by method A.

1,5-Anhydro-3,4-dideoxy-6-*O*-[(1,1-dimethyl)ethyldimethyl]silyl-2-*O*-(methanesulfonyl)-1,3,4-trideoxy-D-*erythro*-hexitol (27). To the solution of alcohol **26** (132 mg, 0.54 mmol) in dichloromethane (8 mL) were added triethylamine (0.19 mL, 1.35 mmol), 4-(dimethylamino)pyridine (6.6 mg, 0.054 mmol), and methanesulfonyl chloride (0.083 mL, 1.08 mmol). The clear solution was stirred at room temperature overnight, and then water (10 mL) was added. The two layers were separated, and the aqueous phase was extracted with dichloromethane (3 × 8 mL). The combined organic extracts were washed successively with saturated sodium bicarbonate solution and brine (10 mL each). After drying over $MgSO_4$ and evaporation of the solvent, the residue was flash chromatographed (hexane/ethyl acetate 1:1) to give the desired product **27** as a pale yellow oil (144 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.61 (1H, ddd, *J* = 16.0, 10.1, 4.9 Hz, H2), 4.13 (1H, ddd, *J* = 10.8, 5.0, 2.2 Hz, $H1_{eq}$), 3.64 (1H, dd, *J* = 10.6, 5.4 Hz, H6), 3.50 (1H, dd, *J* = 10.6, 5.2 Hz, H6′), 3.33 (1H, tm, *J*

= 10.8 Hz, H5), 3.32 (1H, dd, J = 10.6, 10.4 Hz, $H1_{ax}$), 3.01 (3H, s), 2.30 (1H, br dm, J = 15.6 Hz), 1.84 (1H, br dm, J = 13.7 Hz), 1.65−1.76 (1H, m), 1.38−1.50 (1H, m), 0.87 (9H, s), 0.04 (6H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 77.67, 75.06, 69.35, 65.72, 38.52, 29.97, 26.95, 25.92, 18.40, −5.29, −5.34. FT-IR (neat): 2955.3, 2930.2, 2856.9, 1356.0, 1176.7, 1108.4 cm^{-1}. MS (EI) m/z (rel intensity) 325.2 ([M + H]$^+$, 2), 229.2 (37), 171.1 (100). High-resolution EI MS (m/z): 325.1505, calcd for $C_{13}H_{29}O_5SSi$ ([M + H]$^+$) 325.1505. $[\alpha]^{25}_D$ = −9.6 (c = 0.4, CH_2Cl_2).

1,5-Anhydro-3,4-dideoxy-6-*O*-[(1,1-dimethyl)ethyldimethyl]silyl-D-*threo*-hexitol (23). Applying the above procedure to the syn diacetate **21a** (413 mg, 1.91 mmol) resulted in the title silyl ether **23** (260 mg, 55%). Spectral data for this compound are identical to those obtained for the same compound prepared by hydrolysis of the acetate **22a**. The intermediate syn diol **24a** was never completely characterized.

2-(6-Amino-9*H*-purin-9-yl)-6-*O*-[(1,1-dimethyl)ethyldimethyl]silyl-1,5-anhydro-2,3,4-trideoxy-D-*threo*-hexitol (28) and 2-(6-Amino-7*H*-purin-7-yl)-6-*O*-[(1,1-dimethyl)ethyldimethyl]silyl-1,5-anhydro-2,3,4-trideoxy-D-*threo*-hexitol (29). Method A. A mixture of the mesylate **27** (28.5 mg, 0.088 mmol), adenine (23.8 mg, 0.18 mmol), potassium carbonate (24.3 mg, 0.18 mmol), and 18-crown-6 (23.2 mg, 0.088 mmol) was taken up in *N*,*N*-dimethylformamide (2.5 mL) and heated to 100 °C for 24 h. The solution was cooled, and the solvent was evaporated on the rotary with heating. The resulting solid was dissolved in methanol and adsorbed on silica gel. Flash chromatography (10% MeOH in $CHCl_3$) gave the desired N-9 adduct **28** (11.7 mg, 37%) as well as the more polar N-7 adduct **29** (2.3 mg, 7%) as pale yellow solids. Major product **28**. Mp: 122−124 °C. ^{1}H NMR (500 MHz, CD_3OD) δ: 8.62 (1H, s), 8.23 (1H, s), 4.71 (1H, br s), 4.37 (1H, d, J = 12.8 Hz), 4.12 (1H, dd, J = 12.8, 1.8 Hz), 3.79 (1H, dd, J = 10.9, 3.6 Hz), 3.73 (1H, dd, J = 10.9, 4.2 Hz), 3.65−3.68 (1H, m), 2.19−2.24 (2H, m), 1.55−1.70 (2H, m), 0.95 (9H, s), 0.14 (3H, s), 0.12 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.31, 153.62, 150.53, 142.40, 79.32, 70.41, 67.20, 50.39, 28.41, 26.44, 22.88, 19.27, −5.18, −5.22 (one low-field carbon not resolved). FT-IR (neat): 3296.8, 3138.6, 2926.4, 2855.0, 1676.3, 1605.0, 1304.0, 1126.6, 835.3 cm^{-1}. MS (EI) m/z (rel intensity) 364.2 ([M + H]$^+$, 2), 306.1 (100). High-resolution EI MS (m/z): 364.2166, calcd for $C_{17}H_{30}N_5O_2Si$ ([M + H]$^+$) 364.2169. $[\alpha]^{25}_D$ = +9.6 (c = 5, CH_2Cl_2). Minor product **29**. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.02 (1H, s), 8.08 (1H, s), 5.03 (1H, s), 4.51 (1H, d, J = 13.6 Hz), 4.12 (1H, dd, J = 13.6, 2.9 Hz), 3.70 (3H, m), 2.39 (1H, dm, J = 14.7 Hz), 2.23 (1H, dt, J = 14.1, 4.5 Hz), 1.64 (1H, dm, J = 14.3 Hz), 1.52−1.58 (1H, m), 0.90 (9H, s), 0.09 (6H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.90, 150.35, 143.95 (2C's), 77.91, 68.00, 65.74, 53.30, 26.39, 24.99, 21.31, 17.82, −6.60, −6.66 (one low-field carbon not resolved). FT-IR (neat): 2953.4, 2926.4, 2856.9, 1684.1, 1651.3, 1412.1, 1169.0 cm^{-1}. MS (EI) m/z (rel intensity) 364.2 ([M + H]$^+$, 7), 306.1 (100). High-resolution EI MS (m/z): 364.2170, calcd for $C_{17}H_{30}N_5O_2Si$ ([M + H]$^+$) 364.2169. $[\alpha]^{25}_D$ = +20 (c = 0.5, MeOH).

Method B. A suspension of adenine (32.4 mg, 0.24 mmol), sodium hydride (9.6 mg, 0.24 mmol), and 18-C-6 (12.7 mg, 0.05 mmol) in anhydrous DMF (1 mL) was heated at 85 °C for 0.5 h. A solution of mesylate **27** (40 mg, 0.12 mmol) in anhydrous DMF (1 mL) was added to this suspension, and the resulting mixture was heated at 100 °C overnight. The mixture was then cooled and evaporated under reduced pressure with heating. Water and ethyl acetate (3 mL each) were added to the evaporation residue. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 2 mL). The combined organic extracts were dried over $MgSO_4$, and the solvent was evaporated. The residue was flash chromatographed on silica gel (chloroform/methanol 9:1) to give the adducts **28** and **29** in 27% and 10% yields, respectively. The spectroscopic data for these two compounds are identical to those of the compounds obtained under different conditions above.

2-(6-Amino-9*H*-purin-9-yl)-1,5-anhydro-2,3,4-trideoxy-D-*threo*-hexitol (7a). To the solution of the silyl ether **28** (11.8 mg, 0.032 mmol) in tetrahydrofuran (1.5 mL) was added tetrabutylammonium fluoride (38 mg, 0.038 mmol) on silica gel. The suspension was stirred at room temperature for 24 h. The mixture was filtered through a plug of cotton and flash chromatographed (10% methanol in $CHCl_3$) to give the desired alcohol **7a** as a white film (7.6 mg, 95%). ^{1}H NMR (400 MHz, CD_3OD) δ: 8.57 (1H, s), 8.18 (1H, s), 4.65 (1H, br s), 4.38 (1H, d, J = 12.8 Hz), 4.07 (1H, dd, J = 12.8, 2.6 Hz), 3.55−3.63 (3H, m), 2.16−2.19 (2H, m), 1.37−1.54 (2H, m), 1.26 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.76, 152.05, 148.99, 140.77, 78.07, 68.73, 64.46, 48.98, 26.83, 21.45 (one low-field carbon not resolved). FT-IR (neat): 3283.3, 3140.5, 2926.4, 2855.0, 1606.9, 1462.2, 1306.0, 1055.2 cm^{-1}. MS (EI) m/z (rel intensity) 250.1 ([M + H]$^+$, 41), 143.2 (93), 136.1 (100). High-resolution EI MS (m/z): 249.1225, calcd for $C_{11}H_{15}N_5O_2$ 249.1226. $[\alpha]^{25}_D$ = −61.4 (c = 0.3, CH_3OH). Mp: 222−226 °C.

2-Amino-6-(phenylmethoxy)purine (31). This purine derivative was prepared from benzyl alcohol, sodium, and 2-amino-6-chloropurine **30** according to known literature procedures.[15]

2-(2,6-Diamino-9*H*-purin-9-yl)-6-*O*-[(1,1-dimethyl)ethyldimethyl]silyl-1,5-anhydro-2,3,4-trideoxy-D-*threo*-hexitol (33). To a solution of the mesylate **27** (21.1 mg, 0.065 mmol) in *N*,*N*-dimethylformamide (1.5 mL) were added potassium carbonate (18.0 mg, 0.13 mmol), 2,6-diaminopurine **32** (17.5 mg, 0.13 mmol), and 18-crown-6 (17.1 mg, 0.065 mmol). The solution was heated to 110 °C for 16 h. The solvent was evaporated under reduced pressure with heating, and the residue was redissolved in methanol and adsorbed on silica gel. Flash chromatography (7% MeOH in chloroform) gave the desired N-9 adduct **33** as a film (8.4 mg, 34%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.21 (1H, s), 5.56 (2H, br s), 4.76 (2H, br s), 4.50 (1H, br s), 4.30 (1H, d, J = 13.1 Hz), 3.97 (1H, dd, J = 12.7, 2.6 Hz), 3.72 (1H, dd, J = 10.7, 5.2 Hz), 3.64 (1H, dd, J = 10.7, 4.5 Hz), 3.54−3.60 (1H, m), 2.16−2.21 (1H, m), 1.98−2.07 (1H, m), 1.49−1.59 (2H, m), 0.90 (9H, s), 0.09 (3H, s), 0.08 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.58, 155.73, 138.60, 78.38, 69.68, 66.33, 48.09, 27.57, 25.97, 22.41, 18.45, −5.27 (two low-field carbons not resolved). FT-IR (neat): 3329.6, 3188.7, 2955.3, 2856.9, 1633.9, 1597.3, 1406.3, 1103.4, 839.1 cm^{-1}. MS (EI) m/z (rel intensity) 378.2 ([M]$^+$, 17), 321.1 (100), 150.1 (31). High-resolution EI MS (m/z): 378.2201, calcd for $C_{17}H_{30}N_6O_2Si$ 378.2199. $[\alpha]^{25}_D$ = +38.3 (c = 0.2, CH_2Cl_2).

2-(2-Acetylamino-6-amino-9*H*-purin-9-yl)-6-*O*-acetyl-1,5-anhydro-2,3,4-trideoxy-D-*threo*-hexitol (35) and 2-(2,6-Di(acetylamino)-9*H*-purin-9-yl)-6-*O*-acetyl-1,5-anhydro-2,3,4-trideoxy-D-*threo*-hexitol (34). The diaminopurine derivative **33** (125 mg, 0.33 mmol) was dissolved in acetic anhydride (4 mL) and cooled to 0 °C. The solution was treated with boron trifluoride etherate (0.15 mL, 1.25 mmol) and stirred at 0 °C for 10 min and at room temperature for another 2 h. Saturated sodium bicarbonate solution (4 mL) was added carefully to the reaction mixture. The mixture was extracted with ethyl acetate (5 × 4 mL) and washed with brine. The combined organic extracts were dried over $MgSO_4$, and the solvent was evaporated (with final coevaporation with toluene). Flash column chromatography on silica gel (3% methanol in chloroform) gave the diacetamide **34** (41 mg, 32%) as well as the more polar monoacetamide **35** (28 mg, 24%). Diacetamide **34**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.99 (1H, s), 9.41 (1H, s), 8.56 (1H, s), 4.66 (1H, s), 4.41 (1H, d, J = 13.0 Hz), 4.18 (1H, d, J = 12.0, 3.4 Hz), 4.06 (1H, dd, J = 11.8, 6.3 Hz), 4.03 (1H, dd, J = 12.9, 2.4 Hz), 3.77−3.81 (1H, m), 2.51 (3H, s), 2.44 (3H, s), 2.27 (1H, b dm, J = 13.9 Hz), 2.07−2.14 (1H, m), 2.07 (3H, s), 1.41−1.57 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.91 (2 C's), 166.23, 148.56, 148.46, 145.95, 138.57, 114.46, 71.56, 65.24, 62.53, 44.77, 23.15, 21.28, 21.22, 18.21, 16.88. MS (EI) m/z (rel intensity) 391.2 ([M + H]$^+$, 51), 235.1 (38), 192.1 (96), 150.1 (100). High-resolution EI MS (m/z): 391.1729, calcd for $C_{17}H_{23}N_6O_5$ ([M + H]$^+$) 391.1730. $[\alpha]^{25}_D$ = +82.1 (c = 0.9, CH_2Cl_2). Monoacetamide **35**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.27 (1H, br s), 8.34 (1H, s), 4.58 (1H, br s), 4.43 (1H, d, J = 13.2 Hz), 4.22 (1H, dd, J = 11.8, 3.2 Hz), 4.08 (1H, dd, J = 11.8, 6.3 Hz), 4.05 (1H,dd, J = 12.9, 2.5 Hz), 3.80 (1H,

ddd, J = 13.9, 6.2, 3.1 Hz), 2.61 (3H, s), 2.28 (1H, dm, J = 14.0 Hz), 2.12 (3H, s), 2.08−2.12 (2H, m), 1.51−1.55 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.90 (2C's), 156.93, 153.29, 139.74, 115.84, 75.55, 69.40, 66.58, 48.43, 27.25, 25.56, 22.13, 20.89 (one low-field carbon not resolved). FT-IR (neat): 3445.3, 3329.6, 2949.5, 1743.9, 1660.9, 1641.6, 1597.3, 1471.9, 1383.1, 1319.5, 1226.9 cm^{-1}. High-resolution EI MS (m/z): 348.1551, calcd for $C_{15}H_{20}N_6O_4$ 348.1546. $[\alpha]^{25}_D$ = 147.7 (c = 0.1, CH_2Cl_2).

2-(2-Acetylamino-1,6-dihydro-6-oxo-9*H*-purin-9-yl)-6-*O*-acetyl-1,5-anhydro-2,3,4-trideoxy-D-*threo*-hexitol (36). The purine derivative **35** (25 mg, 0.072 mmol) was dissolved in water (3 mL) and glacial acetic acid (1 mL). Sodium nitrite (84 mg, 1.22 mmol) was added to this solution, and the reaction was allowed to proceed overnight at room temperature. Additional sodium nitrite was added to consume residual starting material. The reaction mixture was neutralized to pH 7 with a 2 N sodium hydroxide solution. Evaporation and gradient flash column chromatography on silica gel (5−15% methanol in chloroform) yielded the desired product **36** as a white film (10 mg, 40%), as well as recovered starting material **35** (10 mg, 40%). The yield of **36** was 67% based on recovered starting material. ^{1}H NMR (400 MHz, CD_3OD) δ: 8.32 (1H, s), 4.55 (1H, br s), 4.36 (1H, d, J = 13.0 Hz), 4.13 (2H, m), 4.04 (1H, dd, J = 13.0, 2.4 Hz), 3.77−3.83 (1H, m), 2.06−2.23 (2H, m), 2.19 (3H, s), 2.06 (3H, s), 1.27−1.31 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.45, 171.18 (2C's), 75.10, 68.64, 66.20, 49.12, 26.70, 22.42, 21.64, 19.26 (purine carbons not resolved).

2-(2-Amino-1,6-dihydro-6-oxo-9*H*-purin-9-yl)-1,5-anhydro-2,3,4-trideoxy-D-*threo*-hexitol (7e). Methanol (3 mL) was saturated with ammonia at 0 °C. The acetylated purine derivative **36** (10 mg, 0.029 mmol) was treated with the methanolic ammonia, and the reaction was allowed to proceed at room temperature overnight. Volatiles were evaporated to give the crude guanine derivative **7e** (8 mg, 100%).^{1}H NMR (400 MHz, d_6-DMSO) δ: 10.48 (1H, br s), 7.94 (1H, s), 6.44 (2H, br s), 4.72 (1H, t, J = 5.6 Hz), 4.33 (1H, br s), 4.16 (1H, d, J = 12.6 Hz), 3.86 (1H, dd, J = 12.6, 2.6 Hz), 3.41−3.49 (3H, m), 1.96−2.00 (2H, m), 1.36−1.48 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.31, 153.89, 151.43, 137.03, 116.50, 78.15, 69.04, 64.48, 48.19, 27.20, 22.40.

2-*O*-Acetyl-1,6-anhydro-3,4-dideoxy-*β*-D-*threo*-hex-3-enopyranose (38a) and 2-*O*-Acetyl-1,6-anhydro-3,4-dideoxy-*β*-D-*erythro*-hex-3-enopyranose (38b). To a solution of the mixture of crude allylic alcohols **11a** and **11b** (138 mg, 1.08 mmol) in dichloromethane (5 mL) were added acetyl chloride (0.15 mL, 2.16 mmol) and pyridine (0.17 mL, 2.16 mmol). The solution was stirred at room temperature overnight. Water (5 mL) was then added, and the two layers were separated. The aqueous phase was extracted with dichloromethane (2 × 5 mL), and the combined organic extracts were washed with brine. After drying over $MgSO_4$ and evaporation of the solvent, the residue was flash chromatographed (hexane/ether 1:1) to give the desired acetate **38a** as a clear oil (122 mg, 66% from levoglucosenone). The spectral data for this compound were consistent with the known compound.[29] Although the ^{1}H NMR shows only one set of peaks, the diastereomer **38b** must be present in small amounts since a product derived from it is observed in later steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.19 (1H, ddd, J = 10.4, 4.3, 1.4 Hz), 5.60−5.63 (2H, m), 5.49−5.50 (1H, br s), 4.68 (1H, dd, J = 4.1, 4.2 Hz), 3.96 (1H, d, J = 6.6 Hz), 3.79 (1H, ddd, J = 6.6, 4.1, 1.2 Hz), 2.12 (3H, s).

2-*O*-Ethoxycarbonyl-1,6-anhydro-3,4-dideoxy-*β*-D-*threo*-hex-3-enopyranose (39). A solution of the mixture of allylic alcohols **11ab** (184 mg, 1.44 mmol) in dichloromethane (5 mL) was cooled to 0 °C, and ethyl chloroformate (0.27 mL, 2.88 mmol) was added dropwise. After the solution stirred for 1 h at 0 °C, a solution of saturated ammonium chloride (5 mL) was added. The organic layer was separated, and the aqueous layer was extracted with dichloromethane (3 × 4 mL). The combined organic extracts were dried over $MgSO_4$, and the solvent was evaporated to give the desired allylic carbonate **39** as a pale yellow oil (250 mg, 87%) which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.22 (1H, ddd, J = 9.8, 4.2, 0.9 Hz), 5.66−5.71 (2H, m), 5.35−5.36 (1H, m), 4.69 (1H, dd, J = 4.2, 4.2 Hz), 4.21 (2H, q, J = 7.1 Hz), 3.96 (1H, d, J = 6.6 Hz), 3.80 (1H, ddd, J = 6.6, 4.2, 0.9 Hz), 1.32 (3H, t, J = 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.76, 132.99, 124.26, 98.90, 74.38, 71.32, 71.29, 64.39, 14.19. FT-IR (neat): 2982.3, 1743.9, 1257.7, 1024.3 cm^{-1}. MS (EI) m/z (rel intensity) 201.1 ([M + H]$^+$, 51), 111.0 (70). High-resolution EI MS (m/z): 201.0765, calcd for $C_9H_{13}O_5$ ([M + H]$^+$) 201.0763.

1,2,6-Tri-*O*-acetyl-3,4-dideoxy-α-D-*erythro*-hex-3-enopyranose (40b) and 1,2,6-Tri-*O*-acetyl-3,4-dideoxy-α-D-*threo*-hex-3-enopyranose (40a). The allylic acetates **38ab** (100 mg, 0.59 mL) were dissolved in acetic anhydride (3 mL) and cooled in an ice bath. Triethylsilyl triflate (3 drops) was added to the chilled solution. After 30 min the reaction was complete (TLC) and a solution of saturated sodium bicarbonate (3 mL) was added. This mixture was extracted with ethyl acetate (3 × 5 mL), and the combined organic extracts were washed with saturated bicarbonate solution (10 mL) and brine (10 mL). Drying over $MgSO_4$ and evaporation of the solvent gave a residue which was flash chromatographed on silica gel (hexane/ether 1:1) to give a 9:1 mixture of desired diastereomeric triacetates **40a** and **40b** as a clear oil (130 mg, 81%). These compounds could not be separated and were used as the mixture. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.18 (1H, s), 6.03 (2H, m), 4.93 (1H, m), 4.51 (1H, m), 4.22 (1H, m), 4.21 (1H, m), 2.094 (6H, s), 2.090 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.80, 170.12, 168.87, 130.65, 121.94, 90.85, 67.81, 65.03, 64.18, 20.93, 20.88, 20.82. FT-IR (neat): 1743.9, 1371.6, 1224.9, 1028.2 cm^{-1}. MS (EI) m/z (rel intensity) 271.1 ([M − H]$^+$, 32), 213.1 (100), 153, (26). High-resolution EI MS (m/z): 271.0818, calcd for $C_{12}H_{15}O_7$ ([M − H]$^+$) 271.0818.

2,6-Di-*O*-acetyl-3,4-dideoxy-D-*erythro*-hex-3-enopyranose (41b) and 2,6-Di-*O*-acetyl-3,4-dideoxy-D-*threo*-hex-3-enopyranose (41a). To a solution of the mixture of the triacetates **40a** and **40b** (199 mg, 0.73 mmol) in acetonitrile (2 mL) cooled to 0 °C were added triethylsilyl triflate (4 drops) and triethylsilane (0.35 mL, 2.19 mmol). The ice bath was removed, and the solution stirred at room temperature overnight. A saturated sodium bicarbonate solution (2 mL) was then added, and the mixture was extracted with ethyl acetate (3 × 2 mL). The combined organic extracts were washed with brine and dried over $MgSO_4$. Evaporation of the solvent followed by flash chromatography on silica gel (hexane/ether 2:1) gave the anti diacetate **41b** as the minor product (9.4 mg, 6%) and the more polar syn diacetate **41a** as the major product (78 mg, 50%). Diacetate **41b.** ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.98 (1H, dd, J = 10.4, 2.7 Hz), 5.87 (1H, ddd, J = 10.4, 2.1, 1.4 Hz), 5.21−5.27 (1H, m), 4.36−4.41 (1H, m), 4.08−4.21 (3H, m), 3.60 (1H, dd, J = 11.6, 4.8 Hz), 2.09 (3H, s), 2.08 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.87, 170.52, 129.53, 126.71, 71.78, 64.89, 64.56, 64.40, 21.05, 20.89. FT-IR (neat): 2920.6, 2851.1, 1736.2, 1369.6, 1230.7 cm^{-1}. MS (EI) m/z (rel intensity) 215.1 ([M + H]$^+$,47), 155.1 (39), 141.1 (47), 95.1 (100). High-resolution EI MS (m/z): 215.0915, calcd for $C_{10}H_{15}O_5$ (([M + H]$^+$) 215.0919. $[\alpha]^{25}_D$ = −141.5 (c = 0.2, CH_2Cl_2). Diacetate **41a:** ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.03 (1H, dddd, J = 10.2, 5.0, 2.1, 1.3 Hz, Ha), 5.93 (1H, br m, J = 10.2 Hz, Hb), 5.01 (1H, m, Hc), 4.25−4.28 (1H, m, Hd), 4.19 (1H, dd, J = 11.6, 3.7 Hz, He), 4.13 (1H, dd, J = 11.6, 7.1 Hz, Hf), 4.06 (1H, dt, J = 12.9, 1.3 Hz, Hg), 3.77 (1H, dd, J = 12.9, 2.8 Hz Hh), 2.08 (3H, s), 2.06 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.83, 170.76, 131.58, 124.72, 72.16, 67.41, 65.56, 64.24, 21.14, 20.83. FT-IR (neat): 2957.2, 2855.0, 1743.9, 1732.3, 1441.0, 1371.6, 1234.6, 1101.5, 1041.7, 962.6 cm^{-1}. MS (EI) m/z (rel intensity) 213.0 ([M − H]$^+$, 48), 156.0 (78), 95.0 (100). High-resolution EI MS (m/z): 213.0763, calcd for $C_{10}H_{13}O_5$ ([M − H]$^+$) 213.0763. $[\alpha]^{25}_D$ = +99.5 (c = 1.5, CH_2Cl_2).

6-*O*-Acetyl-2-*O*-ethoxycarbonyl-3,4-dideoxy-D-*threo*-hex-3-enopyranose (42). Triethylsilyl triflate (2 drops) was added to a solution of the carbonate **39** (170 mg, 0.85 mmol) in acetic anhydride (2 mL) cooled to 0 °C. The reaction was complete in 10 min (TLC), and a saturated sodium bicarbonate solution (5 mL) was then added. The solution was stirred at room temperature for 30 min until all gas evolution stopped. The aqueous solution was extracted with ethyl acetate (3 × 3

mL), and the combined organic extracts were washed successively with saturated bicarbonate solution and brine (5 mL each). The organic phase was dried over $MgSO_4$, and the solvent was evaporated at reduced pressure (2 mmHg) to give a yellow oil as crude product (221 mg). This crude material was dissolved in acetonitrile (2 mL) and treated with triethylsilane (0.35 mL, 2.19 mmol) and catalytic triethylsilyl triflate (2 drops). The solution was stirred at room temperature overnight. A saturated sodium bicarbonate solution (3 mL) was then added, and the mixture was extracted with ethyl acetate (3 × 3 mL). The combined organic extracts were washed succesively with brine and water (5 mL each) and dried over $MgSO_4$. Evaporation of the solvent followed by flash chromatography on silica gel (hexane/ether 2:1) gave the desired product **42** as a clear oil (79 mg, 38% for two steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.06−6.09 (1H, m), 5.97 (1H, ddd, J = 10.3, 1.5, 0.6 Hz), 4.88 (1H, dd, J = 4.6, 2.2 Hz), 4.26−4.28 (1H, m), 4.11−4.22 (3H, m), 4.18 (2H, q, J = 7.1 Hz), 3.79 (1H, dd, J = 12.9, 2.7 Hz), 2.08 (3H, s), 1.29 (3H, t, J = 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.88, 154.82, 132.16, 124.16, 72.16, 67.38, 66.97, 65.47, 64.14, 20.86, 14.24. FT-IR (neat): 2924.5, 2853.1, 1740.0, 1258.7 cm^{-1}. MS (EI) *m*/*z* (rel intensity) 245.1 ([M + H]$^+$, 40), 171.1 (32), 155.1 (47), 95.0 (81). High resolution EI MS (*m*/*z*): 245.1019, calcd for $C_{11}H_{17}O_6$ ([M + H]$^+$) 245.1025. $[\alpha]^{25}_D$ = +80.3 (*c* = 0.35, CH_2Cl_2).

1,6:3,4-Dianhydro-β-D-talopyranose (43). To a solution of the crude allylic alcohol **11a** (128 mg, 1 mmol) in acetic acid (4.6 mL) was added silver acetate (334 mg, 2 mmol). Iodine (267 mg, 1.05 mmol) was added slowly to this mixture, and the resulting light yellow paste was stirred at room temperature for 5 h. Then ammonium hydroxide (40 mL, 28%) and methanol (40 mL) were added, and the mixture was allowed to stir at room temperature overnight. The precipitate was filtered and washed with water, and the filtrate was evaporated. The residue was flash chromatographed on silica (hexane/ethyl acetate 1:2) to give the epoxide **43** (75 mg, 52%) as a clear liquid which crystallized on standing. The spectral data for this compound are consistent with literature data.[25] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.27 (1H, d, J = 3.6 Hz), 4.79 (1H, dd, J = 4.7, 4.7 Hz), 3.93 (1H, d, J = 6.6 Hz), 3.75−3.77 (2H, m), 3.53 (1H, dd, J = 6.6, 4.8 Hz), 3.30−3.32 (1H, ddd, J = 3.9, 3.9, 1.0 Hz), 3.10−3.25 (1H, br s).

2-*O*-Acetyl-1,6:3,4-dianhydro-β-D-talopyranose (44). A solution of the epoxide **43** (68 mg, 0.47 mmol) in dichloromethane (2 mL) was treated with pyridine (83 μL, 1.03 mmol) and acetyl chloride (37 μL, 0.52 mmol). The solution was stirred at room temperature overnight, and then a solution of saturated sodium bicarbonate (2 mL) was added. The organic layer was separated, and the aqueous layer was extracted with dichloromethane (2 × 2 mL). The combined organic extracts were washed with brine and dried over $MgSO_4$. On evaporation of the solvent, the desired epoxy acetate **44** was obtained as a light yellow oil (86 mg, 98%) which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.42 (1H, dd, J = 3.5, 1.0 Hz, H_1), 4.94 (1H, dd, J = 3.5, 3.5 Hz, H_2), 4.83 (1H, dd, J = 4.6, 4.6 Hz, H_5), 4.09 (1H, d, J = 6.6 Hz, H_6), 3.76 (1H, dd, J = 4.5, 4.5 Hz, H_4), 3.61 (1H, dd, J = 6.6, 4.7 Hz, $H_{6'}$), 3.41 (1H, ddd, J = 4.3, 3.5, 1.2 Hz, H_3), 2.20 (3H, s).

1,6-Anhydro-4-azido-β-D-mannopyranose (45). To the solution of the epoxy acetate **44** (48 mg, 0.26 mmol) in *N*,*N*-dimethylformamide were added Dowex resin (24 mg, 50W-X8 acidic) and sodium azide (34 mg, 0.52 mmol). The resulting suspension was heated at 95 °C for 20 h. The mixture was then cooled and filtered through Celite. The filtrate was evaporated and redissolved in methanol (2 mL). A catalytic amount of potassium carbonate was added, and the suspension was stirred overnight. After evaporation of the solvent the residue was flash chromatographed on silica gel (ethyl acetate) to give the azido diol **45** as a clear oil (23 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.42 (1H, s), 4.61 (1H, dd, J = 4.9, 0.7 Hz), 4.25 (1H, dd, J = 7.5, 0.7 Hz), 4.05 (1H, br s), 3.81 (1H, dd, J = 7.4, 5.7 Hz), 3.76 (1H, br s), 3.66 (1H, br s), 3.26 (1H, br s), 3.10 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 101.69, 74.34, 69.40, 66.59, 65.76, 62.99. FT-IR (neat): 3408.6, 2965.0, 2910.9, 2106.5, 1084.1, 1034.0 cm^{-1}. MS (EI) *m*/*z* (rel intensity) 188.1 ([M + H]$^+$, 58), 141.0 (100). High-resolution EI MS (*m*/*z*): 188.0673, calcd for $C_6H_{10}N_3O_4$ ([M + H]$^+$) 188.0671. $[\alpha]^{25}_D$ = −468.7 (*c* = 0.5, CH_2Cl_2).

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra and IR spectra of all new compounds (91 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 information.

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