Cycloaddition of Cyclopentadiene to 3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*erythro*-hex-3-enofuranose. Synthesis and Representative Chemistry of 1,6-Anhydro-2,3-dideoxy-*β*-D-*glycero*-hex-2-enopyran-4-ulose ("Isolevoglucosenone")

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Treatment of D-glucose-derived alkene **4** with cyclopentadiene in the presence of a Lewis acid results in the formation of cycloaddition products **8**−**11**. Evidence is presented to show that these 1,6-anhydro sugar−cyclopentadiene adducts do not arise from rearrangement of **4** to isolevoglucosenone (**5**) followed by cycloaddition but are the result of Lewis acid-catalyzed rearrangement of alkene **4** to acyclic dienophile **12** followed by addition of cyclopentadiene. Major cycloadduct **8** has been utilized as a source of the enantiomerically pure carbocycles **14**−**25** by manipulation of the alkene and ketone functions and cleavage of the 1,6-anhydro bridge. In the absence of diene, alkene **4** undergoes rearrangement to enone **5** in 32% yield. Reaction of **5** with several dienes results only in the formation of "bottom-face" adducts **10**, **11**, **28,** and **29**, and conjugate addition of either HN_3 or Me_3COOH is found to be completely stereoselective to afford **30** and **31**, respectively. Subsequent manipulation of azide **30** leads to precursors of several naturally occurring 2-amino-2,3-dideoxy sugars.

The use of natural monosaccharides for the synthesis of enantiomerically pure compounds has been of sustained interest[1] since many sugars are inexpensive, are available with a variety of relative and absolute stereochemistries, and are capable of undergoing a wide range of synthetic transformations.[2] Of recent interest has been the development of radical methodologies[3] and cycloaddition chemistry[4] in the carbohydrate field as routes to configurationally pure carbo- and heterocycles. Many examples of cycloaddition reactions of sugar-derived dienophiles to dienes, and conversely of sugar-derived dienes to dienophiles, have been reported in recent years.[5] We have shown[6] that [4 + 2] cycloaddition of cyclopentadiene to sugar-derived *acyclic* enoates is a predictable and useful method for the synthesis of configurationally well-defined cyclopentane derivatives.[7] In this paper, we detail the unusual rearrangement−cycloaddition chemistry of a D-glucose-derived dienophile with cyclopentadiene, which results in the formation of 1,6-anhydrohexopyranose−cyclopentadiene adducts, a practical preparation of "isolevoglucosenone", and several aspects of the chemistry of this versatile sugar enone.

Results and Discussion

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose (**1**) has enjoyed myriad applications in carbohydrate chemistry. Oxidation of the 3-hydroxyl group and reaction of the resultant 3-keto sugar with nucleophiles can lead to a wide variety of products having the D-*gluco* or D-*allo* configurations.[8] The 3-hydroxyl group is also readily converted into a potential leaving group through reaction

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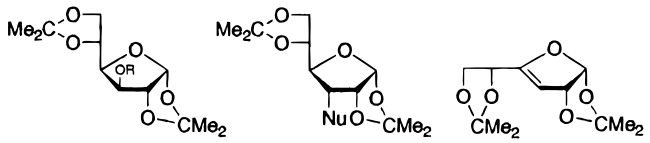
with, for example, triflic anhydride[9] or *p*-toluenesulfonyl chloride (see compound **2**);[10] however, displacement of these sulfonic esters with nucleophiles such as azide[11] or ammonia[12] is seldom a clean process.[13] On account of steric (and possibly electronic) interference from the adjacent 1,2-*O*-isopropylidene ring, bimolecular displacement at C-3 of such derivatives as **2** is retarded, and reactions with nucleophiles generally lead to varying amounts of displacement product **3** as well as the product of bimolecular elimination, namely, 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*erythro*-hex-3-enofuranose (**4**). We were intrigued by the possibility of inverse-demand Diels−Alder cycloaddition chemistry[14] involving **4** as a source of unusual carbocycles.



1 R = H
2 R = SO_2PhMe

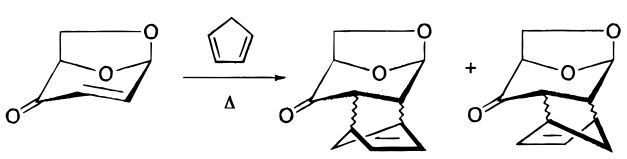
Several preparations of **4** from 3-sulfonate derivatives of **1** have been reported in the literature;[15] however, none of them proved amenable to large-scale preparation of the alkene, requiring either expensive or inconvenient reagents. The method of Srivastava et al.,[15c] in which tosylate **2** was dissolved in cold dimethyl sulfoxide and then treated with KO^{t}Bu, proved to be promising; however, preventing the solution from freezing was operationally difficult. A modification of this method, in which THF was used in place of dimethyl sulfoxide, was found to be convenient. Simply cooling a dilute THF solution of **4** to 0 °C, then adding the KO^{t}Bu in portions, and then refrigerating the resultant deep-red mixture overnight allowed the isolation of reasonably pure **4** in 80−90% yield. The major contaminant was 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**), the product of ester hydrolysis, but this could readily be removed by either flash chromatography[16] or Kugelrohr distillation of the crude reaction mixture. However, the crude product proved to be sufficiently pure for the subsequent cycloaddition chemistry described here, and compound **4** could be conveniently prepared in 25 g batches in three simple steps from D-glucose in 60−65% overall yield.

With convenient access to large amounts of **4**, we investigated the possiblity of cycloaddition chemistry with cyclopentadiene. Acceleration of inverse-demand Diels−Alder reactions has been shown to be possible by "radical-cation catalysis" [14] in which one of the reactants (presumably the dienophile) is oxidized by a reagent such as tris(*p*-bromophenyl)aminium hexachloroantimonate.[14a] Treatment of a dichloromethane solution of **4** and freshly distilled cyclopentadiene with a catalytic amount of this oxidant for 15 min indeed resulted in consumption of **4**; however, TLC analysis showed a complex mixture of products, along with much polymeric material near the base line. Such complexity suggested examination of the more common methods employed in Diels−Alder chemistry, namely, thermal and Lewis acid catalysis, to learn whether a simplification of the reaction outcome would be possible.

Thermal reaction of **4** with cyclopentadiene in refluxing toluene was slow, and TLC analysis revealed only extensive degradation and production of highly polar products. Reaction under Lewis acid catalysis was, however, more fruitful. Compound **4** was rapidly consumed in the presence of cyclopentadiene and $BF_3{\cdot}OEt_2$ catalyst at −20 °C to give, after extensive chromatography, two products. After much experimentation with various Lewis acids, the reaction of **4** with cyclopentadiene in the presence of $ZnCl_2$ in benzene at 47 °C was found to give optimal conversion and afforded, after chromatographic separation, three pure products, including the two isolated from the cycloaddition of **4** in the presence of $BF_3{\cdot}OEt_2$. It should be noted that the TLC profile from the $ZnCl_2$-catalyzed reaction was very similar to that of the "radical-cation catalyzed" reaction described earlier; however, the $ZnCl_2$-catalyzed reaction proved to be much cleaner and the products easier to separate.

The three compounds isolated, in 35, 16, and 3% yields, were isomeric, as judged by high-resolution mass-spectral analysis, with the molecular formula $C_{11}H_{12}O_3$. As 1:1 cycloadducts of **4** and cyclopentadiene should have the formula $C_{17}H_{25}O_5$, it was obvious that direct cycloaddition had not taken place. The ^{13}C spectra of the products gave key structural information on the molecular framework of these products. Thus, the major isomer showed 11 distinct ^{13}C signals, including a carbonyl singlet, an "anomeric region" doublet, two alkene doublets, a high-field methylene triplet, and a triplet for a CH_2O function. These signals, along with five additional doublets, could be accommodated into a molecular framework structure theoretically resulting from cycloaddition of cyclopentadiene with isolevoglucosenone (1,6-anhydro-2,3-dideoxy-β-D-*glycero*-hex-2-enopyran-4-ulose, **5**).[17] The ^{13}C spectra of the other two products were similar. All three products were optically active, and all showed carbonyl absorption in the infrared.

This reaction might be expected to yield up to four isomeric products, depicted generally as "exo" adducts **6** and "endo" adducts **7**. Stereochemical assignments were made possible by use of ^1H NMR spin-coupling and NOE data.



5 **6** **7**

The major isomer (the most polar of the three products) was isolated in ∼35% yield and identified as the "down-endo" derivative **8** (Scheme 1). That the annelated

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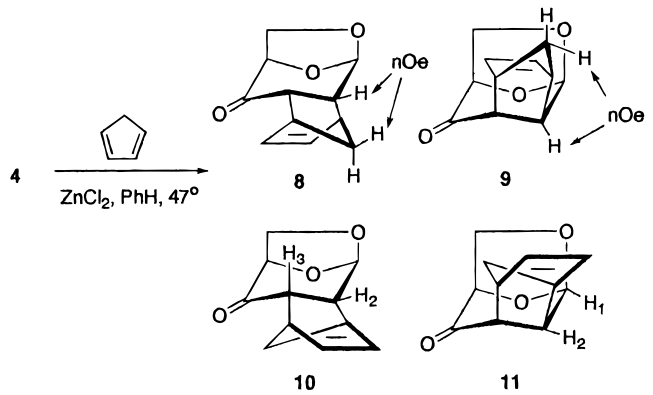
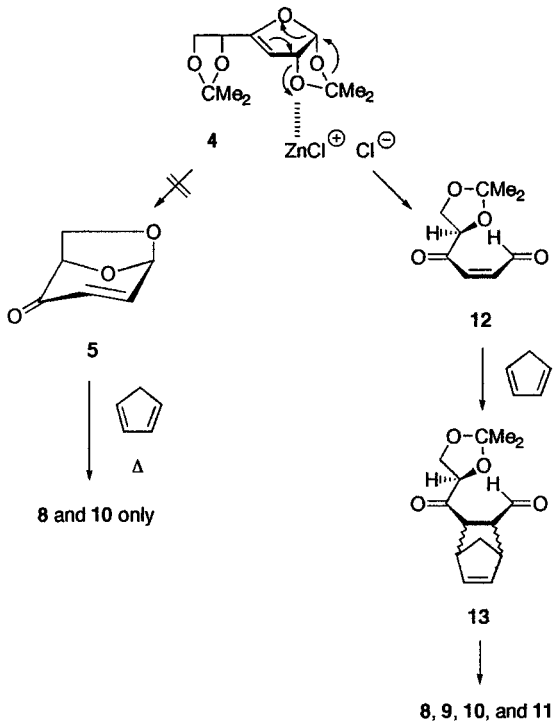
Scheme 1



Scheme 2



cyclopentene ring lies below the plane of the 1,6-anhydro sugar is indicated from the H-1−H-2 coupling constant of 0 Hz in the ^{1}H NMR spectrum, a conclusion that is reinforced by examination of models which clearly show a dihedral angle between H-1 and H-2 in such a structure as being ∼90°. The depiction of compound **8** as having the $^1C_4(_D)$ conformation stems from the large (∼9 Hz) coupling constant between H-2 and H-3 in the proton NMR. This value suggests a dihedral angle close to 0° and the eclipsing of H-2 and H-3, which is attributable to the pyranose ring being distorted by the annelated cyclopentene ring. The NOE enhancements shown in Scheme 2 support this structural assignment, and the remaining ^{1}H signals, as well as the ^{13}C absorbances, can be further reconciled with the structural assignment of **8**. These data are detailed in Tables 1 and 2, respectively.

The compound of intermediate polarity, isolated in ∼16% yield, was identified as the isomeric "up-endo" cycloadduct **9**. A coupling constant of 4.3 Hz between H-1 and H-2 in the ^{1}H NMR spectrum of **9** corresponded well to that expected from models, and the NOE enhancements indicated in Scheme 2 established the proximity between the alkene portion of the cyclopentene ring and the endo proton at H-6 of the 1,6-anhydro bridge.

The third (least polar) of the three products proved to be the "down-exo" adduct **10**, isolated in ∼3% yield. Again, as with compound **8**, a coupling constant of 0 Hz between H-1 and H-2 suggested that the cyclopentene ring resides below the plane of the anhydro sugar skeleton in **10**. The NOE measurements on compound **10** were inconclusive for establishing the exo disposition of the cyclopentene ring, but the signals for H-2 and H-3 in the ^{1}H NMR spectra of **10** are significantly shifted upfield (relative to compound **8**), suggesting that these protons are affected by the anistropy of the nearby C=C bond. Such an effect would be less significant if the cyclopentene ring were in an endo orientation.

Traces of a fourth isomer were indictated in the 300 MHz ^{1}H NMR spectrum of the crude reaction mixture, with the most significant signal being a doublet at 5.86 ppm ($J_{1,2}$ = 4.3 Hz). This signal was tentatively assigned to the "up-exo" isomer **11**, although this compound could not be isolated in pure form. The two "down" isomers **8** and **10** were strongly dextrorotatory (+121° and +178°, respectively), whereas the "up" isomer **9** was strongly levorotatory (−200°).

The formation of compounds **8**−**11** is obviously the consequence of a rearrangement of alkene **4**. The timing of the cycloaddition step is not, however, immediately apparent, and two plausible mechanisms may be postulated. Since the products are those which might be expected to arise from the cycloaddition of isolevoglucosenone (**5**) with cyclopentadiene, it is conceivable that **5** is formed by Lewis acid-catalyzed rearrangement of alkene **4** and **5** which then undergoes cycloaddition. It is also possible that **4** could rearrange to some other reactive dienophile under the reaction conditions. Such a species could then react with cyclopentadiene and the subsequent Diels−Alder adduct rearrange to the observed products. To clarify this point, the behavior of isolevoglucosenone (**5**) on direct reaction with cyclopentadiene was investigated.

Isolevoglucosenone (**5**) is available in low to moderate yields by several multistep sequences,[17] and a sample was prepared by the method described by Shafizadeh and coworkers,[17b] beginning with "levoglucosenone" obtained by the pyrolysis of microcrystalline cellulose.[18] Enone **5** was found to react rapidly and essentially completely with cyclopentadiene in the presence of $ZnCl_2$ and also thermally without Lewis acid catalysis, and the reaction afforded two products only. Under both sets of reaction conditions, the sole products isolated were adducts **8** and **10**, the result of "bottom"-face addition to **5**. The 1,6-anhydro bridge appears to present a steric block to attack from the "top" face. In the case of $ZnCl_2$ catalysis, adducts **8** and **10** were formed in 83% combined yield, with the down-endo isomer **8** being favored by a factor of 4.5:1. Thermal conditions afforded **8** and **10** in 88% yield with **8** again being the major product, this time by a factor of ∼11:1. Under both thermal and Lewis acid conditions, enone **5** reacts much faster with cyclopentadiene than does alkene **4** and affords the cycloaddition products in higher yields.

These experiments show that cycloaddition to the top face of **5** does not occur, strongly suggesting that enone

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Table 1. ^{1}H NMR Chemical Shifts (δ) and Coupling Constants (J in Hz) for 1,6-Anhydro Sugar Derivatives (at 500 MHz in $CDCl_3$ relative to Me_4Si)

compd	H-1 $J_{1,2}$	H-2 $J_{2,3}$, $J_{2,7}$	H-3 $J_{3,4}$, $J_{3,10}$	H-4 $J_{4,5}$	H-5 $J_{5,6}$	H-6 $J_{6,6'}$	H-6′ $J_{5,6'}$	H-7 $J_{7,8}$	H-8 $J_{8,9}$	H-9 $J_{9,10}$	H-10 $J_{10,11}$	H-11′ $J_{10,11'}$, $J_{7,11'}$	H-11 $J_{11,11'}$, $J_{7,11}$
8	5.54 s	2.54dd	2.94 dd		4.20 d	3.85 dd	3.77 dd	3.01 bs	6.15 dd	6.06 dd	3.38 bs	1.31 d	1.49 ddd
	0.0	8.9, 3.3	—, 4.4		5.8	8.3	1.6	2.9	5.6	2.9	1.8	0.0, 0.0	8.5,1.8
9	5.73 d	2.86 m	2.91 m		4.31 dt	3.62 dd	3.32 dd	2.96 bs	5.96 dd	6.10 dd	3.26 bs	1.33 d	1.47 dd
	4.0	*a*	*a*		5.0	7.4	1.0	3.0	5.6	3.7	1.0	0.0, 0.0	8.0, 1.0
10	5.69 s	1.79 m	2.21 d		4.43 d	3.86 d	3.82 dd	2.83 d	6.27 dd	6.19 d	3.24 bs	1.21 ddd	1.79 m
	0.0	8.1, *a*	—, 0.0		6.0	8.2	1.3	3.1	5.6	3.0	*a*	1.5, 1.5	9.0, *a*
14	5.31 s	2.36 dd	2.26 ddd	3.62 m	4.17 td	3.62 m	3.91 dd	2.86 t	6.18 m	6.18 m	3.06 bs	1.33 d	1.44 dd
	0.0	10.0, 3.3	5.2, 4.8	6.0	6.0	7.9	1.9	*a*	*a*	*a*	1.8	0.0, 0.0	8.3, 1.8
15	5.29 s	2.21 dd	2.75 dt	3.84 m	4.18 dd	3.84 m	3.56 dd	2.90 bs	6.15 dd	6.36 dd	3.08 bs	1.25 d	1.40 dd
	0.0	9.9, 3.8	9.6, 3.8	0.0	8.0	8.0	2.9	3.0	5.6	3.0	1.8	0.0, 0.0	9.9, 1.8
16	5.36 s	2.38 dd	2.33 ddd	4.63 t	4.30 t	3.63 t	3.89 d	2.89 bs	6.22 m	6.31 m	3.09 bs	1.26 d	1.40 d
	0.0	9.6, 3.0	9.5, 4.5	5.3	5.3	7.8	2.0	*a*	*a*	*a*	*a*	0.0, 0.0	8.0, 0.0
17	5.32 s	2.19 dd	2.81 dd	4.93 d	4.21 dd	3.64 dd	3.81 t	2.88 bs	6,11 m	6.21 m	2.93 bs	1.23 d	1.36 d
	0.0	9.5, 3.7	9.6, 3.4	0.0	7.1	7.1	1.9	*a*	*a*	*a*	*a*	0.0, 0.0	8.2, 0.0
18	5.48 s	2.16 dd	2.08 dt	4.17 t	4.35 td	3.68 dd	4.00 dd	2.59 d	3.36 d	3.33 d	2.70 d	0.69 d	1.43 dt
	0.0	10.9, 3.7	4.7, 4.7	5.4	6.2	7.9	2.0	7.0	3.5	7.0	1.9	0.0, 0.0	9.9, 0.0
19	5.54 s	1.84 dd	2.47 dd	3.93 dd	4.49 m	3.73 m	3.73 m	2.15 s	4.49 m	4.10 d	2.77 t	1.38 dd	2.03 d
	0.0	9.9, 2.3	5.3, 5.3	2.6	*a*	*a*	*a*	*a*	0.0	4.9	0.0	1.2, 0.0	10.7, 0.0
20	5.24 d	3.01 dd	3.04 dd		3.94 t	4.26 dd	4.33 dd	2.99bs	3.37 bs	6.26 m	6.12m	1.33 d	1.44 d
	7.9	8.3, 3.7	—, 3.5		*a*	*a*	*a*	*a*	*a*	*a*	*a*	0.0 0.0	8.8, 0.0
21	5.62 s	2.23 dd	2.58 dd		4.47 dd	3.88 t	3.81 dd	2.49 bs	2.74 bs			1.26−1.47	
	0.0	10.8, 4.3	—, 4.8		8.3	8.3	1.0	*a*	*a*			a	
24	5.42 s	1.91 m	2.01 m	5.16 dd	4.56 m	3.96 dd	3.70 t	2.33 bs	2.40 bs			1.26−1.76	
	0.0	*a*	6.2, *a*	4.1	1.5	6.0	7.8	*a*	*a*			a	
25	5.43 s	1.83 m	1.95 m	4.91 d	4.44 dd	3.81 t	3.74 d	2.18 bs	2.39 bs			1.27−1.78	
	0.0	*a*	10.3, *a*	0.0	1.0	7.3	0.0	*a*	*a*			a	
20	5.24 d	3.01 dd	3.04 dd		3.94 t	4.26 dd	4.33 dd	2.99 bs	3.37 bs	6.26 m	6.12 m	1.33 d	1.44 d
	7.9	8.3, 3.7	—, 3.5		*a*	*a*	*a*	*a*	*a*	*a*	*a*	0.0, 0.0	8.8, 0.0
21	5.62 s	2.23 dd	2.58 dd		4.47 dd	3.88 t	3.81 dd	2.49 bs	2.74 bs			1.26−1.47	
	0.0	1.8, 4.3	—, 4.3		8.3	8.3	1.0	*a*	*a*			a	
24	5.42 s	1.91 m	2.01 m	5.16 dd	4.56 m	3.96 dd	3.70 t	2.33 bs	2.40 bs			1.26-1.76	
	0.0	*a*	6.2, *a*	4.1	1.5	6.0	7.8	*a*	*a*			a	
25	5.43 s	1.83 m	1.95 m	4.91 d	4.44 dd	3.81 t	3.74 d	2.18 bs	2.39 bs			1.27−1.78	
	0.0	*a*	10.3, *a*	0.0	1.0	7.3	0.0	*a*	*a*			a	

[a] Overlapping signals.

Table 2. ^{13}C NMR Data for 1,6-Anhydro Sugar−Cyclopentadiene Adducts (125 MHz in $CDCl_3$ relative to Me_4Si)

	chemical shift (δ)												
compd	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C=O	CH_3
8	102.5	44.3	48.2	205.3	78.0	65.9	45.2	134.6	134.7	47.1	50.0		
9	101.9	42.8	48.5	210.8	76.8	66.0	44.5	131.6	136.4	46.0	49.5		
10	104.0	43.5	47.3	206.6	78.1	65.7	45.3	139.2	136.8	47.2	43.9		
14	101.7	45.8[a]	43.9[a]	61.4	73.2	68.4	46.5[a]	135.8	135.5	48.6[a]	50.6		
15	102.6	40.3[a]	44.3[a]	69.4	76.4	64.3	46.1[a]	133.0	137.4	46.8[a]	50.7		
16	102.4	41.7[a]	46.6[a]	71.0	71.1	62.9	47.2[a]	136.0	136.5	49.1[a]	50.9	170.6	21.8
17	103.0	38.1[a]	43.5[a]	71.5	74.3	65.9	46.6[a]	132.2	137.6	47.4[a]	50.2	170.9	21.9
18	100.9	45.9[a]	41.9[a]	65.0	73.0	61.4	40.1[a]	50.1	49.3	38.7[a]	27.1		
19	101.6	47.0[a]	42.8[a]	78.0	89.9	64.3	34.8[a]	75.3	42.3	33.4[a]	33.4		
20	95.6	43.6[a]	45.1[a]	209.0	79.8	63.9	50.7[a]	134.7	137.9	48.7[a]	50.7	169.1, 170.3	20.0, 21.2
21	103.1	42.0[a]	44.4[a]	207.8	79.2	65.8	40.0[a]	23.9	25.1	40.0[a]	48.2		
24	102.8	42.3[a]	44.9[a]	71.0	79.7	69.1	40.4[a]	23.0	24.1	41.0[a]	39.4	170.9	21.8
25	103.6	41.4[a]	41.5[a]	73.6	75.9	67.7	40.1[a]	24.7	25.1	40.3[a]	36.2	171.1	21.7

[a] Interchangeable.

5 is *not* an actual intermediate in the observed rearrangement−cycloaddition reaction of **4**. It is most likely that alkene **4** undergoes Lewis acid-catalyzed rearrangement before cycloaddition takes place. A possible course that would explain the reaction outcome is outlined in Scheme 2; thus, complexation of $ZnCl_2$ with alkene **4** could promote loss of the 1,2-*O*-isopropylidene group to create an enal (the acyclic dienophile **12**) which could then undergo cycloaddition to afford generalized adduct **13**. Loss of a second molecule of acetone from **13** would lead to 1,6-anhydro bridge formation and the production of all four isomeric products **8**−**11**.

Chemistry of Norbornene 8. The major cycloadduct **8** isolated in the rearrangement−Diels−Alder reaction was next studied in detail as a potential source of stereochemically defined norbornenes and norbornanes. We have previously shown such derivatives to be useful intermediates in the asymmetric synthesis of chirally substituted carbocycles related to such natural products as prostaglandins.[7] The potential for diastereoselective conversions of **8** relies mainly on the relative steric encumbrance of the 1,6-anhydro bridge above the plane of the sugar ring and that of the cyclopentene ring below.

Simple borohydride reduction of the 4-ketone in **8** led to approximately equal amounts of two diastereomeric alcohols (**14** and **15**). Isolation of **14** and **15** in 45.3 and 43% yields, respectively, suggested that the steric contributions of the 1,6-anhydro bridge and the annelated cyclopentene ring play an approximately equal role in deciding the reaction outcome. Separation of compounds **14** and **15** required MPLC due to their similar migrations on silica gel; however, conversion into their respective

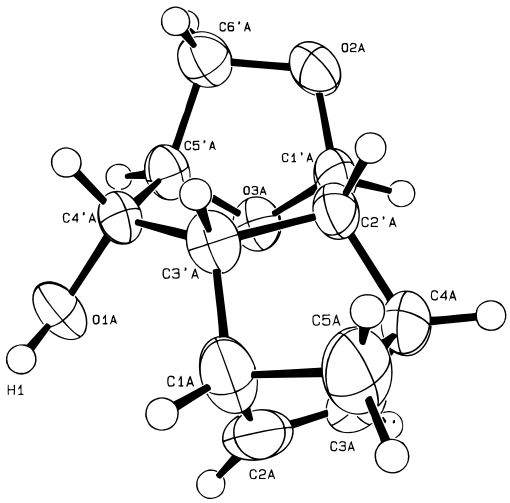
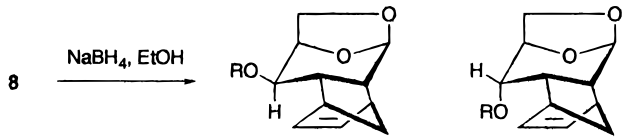


Figure 1. ORTEP representation of polycyclic alcohol **15**.

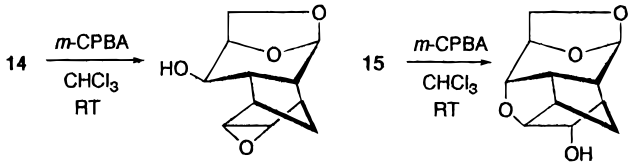
monoacetates (**16** and **17**) permitted facile separation by flash chromatography.



14 R = H **15** R = H
16 R = Ac **17** R = Ac

The formulation of **14** and **15** as products having the D-*gulo* and D-*allo* configurations, respectively, could not be made with confidence on the basis of ^{1}H NMR coupling constants alone. The distortion created in the $^1C_4$ pyranose ring by the attached cyclopentene ring causes enough perturbance around C-3, C-4, and C-5 of the sugar ring that little information regarding the stereochemistry at C-4 can be gathered from the values of $J_{3,4}$ and $J_{4,5}$. Firm assignments of **14** and **15** could, however, be made from subsequent chemical transformations on both of the epimeric alcohols and independently from the single-crystal X-ray structural analysis of **15**.[19,29] The ORTEP representation of alcohol **15** (Figure 1) clearly shows the OH group at C-4 occupying the axial position at C-4 of the sugar ring and provides independent verification of the structural assignments for **14** and **15** by chemical means.

The proximity of the alkene portion of the cyclopentene ring to the hydroxyl group in **14** and **15** suggested that chemical transformation of the double bond might be affected by the axial hydroxyl group in **15** but not by the equatorial hydroxyl considered to be present in **14**. Thus, treatment of either alcohol with *m*-CPBA led to consumption of starting material and the formation of different crystalline products. Alcohol **14** underwent smooth epoxidation to afford epoxy alcohol **18** in 88% yield after recrystallization. Alcohol **15** also gave a single product, formulated as the polycyclic alcohol **19**, in 95% yield. Compound **19** is clearly the product of double-bond epoxidation followed by intramolecular epoxide opening with the axial OH group acting as the nucleophile, and therefore alcohols **14** and **15** can be assigned as having the D-*gulo* and D-*allo* configurations, respectively. The two oxidation products **18** and **19** gave analytical and spectral data completely consistent with the proposed structures (for ^{1}H and ^{13}C NMR data see Tables 1 and 2, respectively).



18 **19**

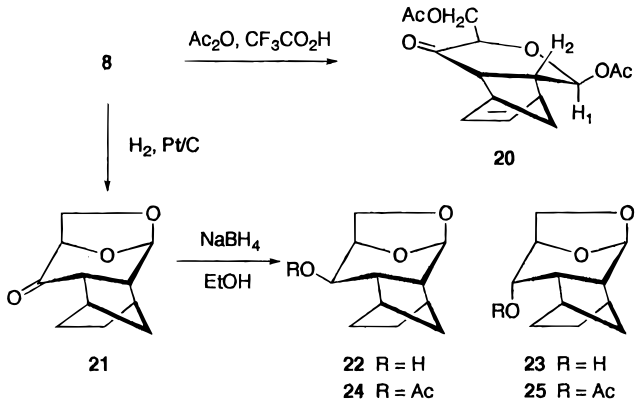
Hydrolysis of the 1,6-anhydro bridge in cycloadduct **8** proved to be somewhat more difficult than expected. It is known[20] that 1,6-anhydrohexopyranoses are generally hydrolyzed faster than simple glycosides, presumably through release of strain in the fused-ring system; however, 1,6-anhydropyranoses possessing electronegative or basic substituents at C-2 are hydrolyzed with more difficulty.[21] Initial attempts at hydrolysis utilizing either 90% aqueous trifluoroacetic acid at room temperature or standard acetolysis conditions (sulfuric acid−acetic acid−acetic anhydride mixture at room temperature) resulted only in the recovery of starting material. Success was met, however, when **8** was dissolved in trifluoroacetic acid and then treated with acetic anhydride. This afforded a single compound isolated in 63% yield after chromatography and identified as keto diacetate **20**. The ^{1}H NMR spectrum of **20** revealed a doublet at 5.23 ppm with a coupling constant $J_{1,2} = 8.3$ Hz. Such a large value for $J_{1,2}$ can only be explained by the formation of the β anomer **20**. The relief of strain after the 1,6-anhydro bridge is hydrolyzed allows for more flexibility in the pyranose ring and adoption of a flattened chairlike conformation.

Reduction of the cyclopentene portion of norbornene **8** was achieved with hydrogen in the presence of a platinum catalyst and yielded norbornane **21**, isolated as an oil in 92% yield. The ^{1}H and ^{13}C NMR spectra of **21** (Tables 1 and 2, respectively) clearly showed the absence of alkene signals and an increase in the complexity of the aliphatic region between 1.2 and 2.8 ppm. The IR spectrum of **21** showed an absorption at 1725 cm^{-1}, revealing that the ketone function remained intact. Reduction of the ketone group in compound **21** with sodium borohydride, in a manner similar to that employed for norbornene **8**, again resulted in the formation of two epimeric alcohols. The infrared spectrum of the crude mixture of products showed a strong OH absorption at 3500 cm^{-1} but no ketone absorption at 1725 cm^{-1}. TLC analysis revealed two closely migrating products, and the 300 MHz ^{1}H NMR spectrum showed two resonances for anomeric signals at 5.40 and 5.43 ppm in approximately 1:2 ratio, arising from the epimeric alcohols **22** and **23**, respectively. The products again proved difficult to separate, and so the reaction mixture was immediately acetylated (acetic anhydride−pyridine) to afford the two epimeric monoacetates **24** and **25** in 21 and 47% yields, respectively, after flash chromatography. In the reduc-

(19) The crystal structure analysis of compound **15** was performed by Dr. Judith Gallucci of the Department of Chemistry at The Ohio State University using the following programs: TEXSAN, *TEXRAY Structural Analysis Package, version 2.1,* by Molecular Structure Corporation, College Station, Texas, 1987; MITHRIL, *A Computer Program for the Automatic Solution of Crystal Structures from X-ray Data,* by C. J. Gilmore, University of Glasgow, Scotland, 1983.

(20) Hall, H. K.; DeBlauwe, F. *J. Am. Chem. Soc.* **1975**, *97*, 655.
(21) Carlson, L. J. *J. Org. Chem.* **1965**, *30*, 3953.

tion of keto norbornene **8**, a 1/1 mixture of C-4 epimers was formed, and the preferential formation of D-*allo* isomer **25** from norbornane **21** is presumably caused by the more flexible cyclopentane ring in **21** blocking the bottom face of the carbonyl group.



Acid-Catalyzed Rearrangement of 4 in the absence of Diene: Facile Preparation of Isolevoglucosenone. Although the intermediacy of isolevoglucosenone (**5**) in the Lewis acid-catalyzed rearrangement–cycloaddition reaction of alkene **4** with cyclopentadiene had been discounted, it was considered possible that **5** might arise from rearrangement of compound **4** if a diene were not present to trap the presumed acyclic dieneophile intermediate **12** (Scheme 2). Accordingly, experiments were performed to study the possibility of converting alkene **4** into isolevoglucosenone (**5**).

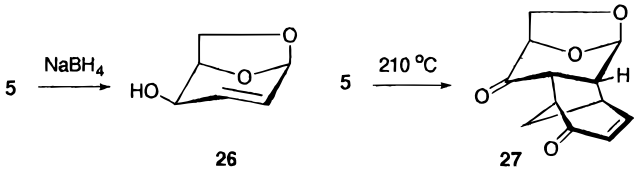
Treating a benzene solution of **4** with $ZnCl_2$, as described earlier for the preparation of norbornene adducts **8**–**11** but without the addition of cyclopentadiene, and monitoring the reaction by TLC over several hours against an authentic sample of **5** revealed the consumption of alkene **4** and the formation of numerous products, including one comparable in R_f and UV activity to **5**. However, a clean separation of compound **5** from this mixture could not be effected, and a detailed search was made to find reaction conditions that would permit facile isolation of **5** in good yield. Three general methods (A, B, and C) were examined.

Method A was related to the preparation of levoglucosenone from cellulose as employed by Brimacombe and co-workers:[18b] alkene **4** was treated with a variety of acid catalysts under high vacuum and compound **5** was collected as a pale-yellow distillate. By using the catalysts $KHSO_4$, $TsOH·H_2O$, and $ZnCl_2$ and a variety of reaction temperatures and catalyst concentrations, the maximum yield of reasonably pure **5** isolated was ~5%, with $TsOH·H_2O$ as catalyst.

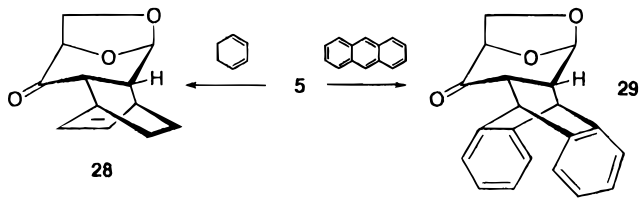
Method B employed a heterogeneous catalyst system in which the catalyst ($ZnCl_2$ or H_2SO_4) was adsorbed onto silica gel on the top of a flash chromatography column. By eluting a solution of alkene **4** through the column, the compound first came into contact with the catalyst, causing reaction, and the resultant products were separated on the bottom half of the column. Method B proved most efficient when H_2SO_4 was employed as catalyst, but the maximum yield of crude **5** attained in this study was only 10%.

Method C, in which a dilute solution of alkene **4** and catalyst was stirred and the reaction monitored by TLC, proved to be the most convenient procedure for one-step preparation of **5**. All three acid catalysts ($TsOH·H_2O$, $ZnCl_2$, or $AlCl_3$) led to **5** (TLC), but extensive experimentation revealed $AlCl_3$ to be the most efficient. A variety of solvents were examined (THF, toluene, CH_2Cl_2), and a pentane–Et_2O mixture gave the maximum yield. Isolation of **5** from the reaction mixture necessitated anhydrous conditions and rapid removal of catalyst to avoid extensive degradation of the sensitive enone. This was best achieved by complexing the catalyst with Et_3N and rapidly eluting the product through a short column of silica gel. This procedure gave a yellow syrup that contained **5** as the major component, and subsequent chromatography afforded **5** in 32% isolated yield. This convenient new access to substantial quantities of enone **5** in only four steps from D-glucose and in ~20% overall yield opened the possibility of a more extensive study of this potentially useful synthon.

Representative Chemistry of Isolevoglucosenone (5). Only two reactions of the previously inaccessible enone **5** have been reported: its stereospecific reduction with sodium borohydride[17a] to give allylic alcohol **26** and pyrolysis[17b] to afford cycloaddition product **27**. Both reactions take place as expected exclusively from the bottom face of the enone; the 1,6-anhydro bridge effectively blocks the top face of the enone. This selectivity augments the great potential of compound **5** as a versatile synthon. The chemistry detailed next shows a variety of reactions involving stereospecific addition of reagents to the bottom face of **5**, providing entry into a range of diastereomerically defined products.



As described earlier, compound **5** reacts efficiently with cyclopentadiene to afford two crystalline products identified as the down-endo adduct **8** and down-exo adduct **10** (Scheme 1), the 1,6-anhydro bridge blocking the top face of the dienophile and preventing the formation of "topside" adducts **9** and **11**. Similar reaction occurs in the presence of the symmetrical dienes cyclohexadiene and anthracene to afford crystalline cycloaddition products **28** and **29**, in 59 and 62% yields, respectively. In each case, only one product is formed because the symmetrical diene adds exclusively from the bottom face of the dienophile. The ^1H NMR resonances of H-1 in **28** and **29** both appear as singlets, indicating zero spin-coupling with H-2 as observed with the down-endo and down-exo adducts **9** and **11** formed from reaction of **5** with cyclopentadiene.



Enone **5** offers promise as a valuable synthon in the stereocontrolled synthesis of 2-amino-2,3-dideoxy sugars,

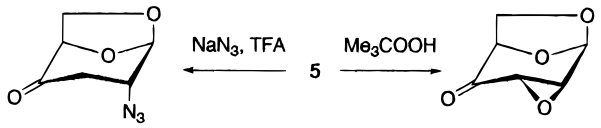
Table 3. ^{1}H NMR Chemical Shifts (ppm) and Multiplicities for Isolevoglucosenone (5) and Derivatives

	chemical shift (δ) and coupling constants (Hz)								
compd	H-1 $J_{1,2}$	H-2 $J_{2,3}$	H-3 $J_{2,3'}$	H-3′ $J_{3,3'}$	H-4 $J_{3,4}$, $J_{4,5}$	H-4′(OH) $J_{3',4}$	H-5 $J_{5,6exo}$	H-6$_{endo}$ $J_{5,6endo}$	H-6$_{exo}$ $J_{6exo,6endo}$
5	5.80 d	7.11 d	6.10 ddd				4.77 dt	3.64 dd	4.10 dd
	3.3	9.8			6.3	1.5	6.3	1.5	8.2
30	5.56 s	3.74 d	2.80 dd	2.56 ddd			4.54 d	3.96 d	3.87 d
	0.0	7.6	0.0	17.9			5.2	0.0	8.3
31	5.87 s	3.33 dd	3.46 dd				4.64 dt	3.96 dd	3.79 dd
	0.0	3.6					6.5	1.3	8.4
32	5.41 s	3.57 d	2.14 d	1.91 dt	3.62 dt	2.83 d	4.53 d	3.83 m	3.83 m
	0.0	4.8	1.7	15.6	4.8, 0.0	1.7	2.4	0.0	*a*
33	5.33 s	3.45 d	1.86 ddd	2.14 dddd	4.19 dd	2.06 bs	4.42 t	4.13 d	3.73 dd
	0.0	5.3	1.5	14.4	10.6, 0.0	6.1	4.0	0.0	*a*

[a] Overlapping signals.

common structural components of many important antibiotics.[22] Conjugate addition to the enone may be expected to be stereospecific to afford D-*erythro* analogs, with attack by the incoming nucleophile at the alkene face opposite the 1,6-anhydro bridge. Subsequent reduction of the ketone function should likewise be stereoselective. Treatment of **5** with an acidic solution of sodium azide (HOAc, NaN_3) by analogy with the procedure reported by Gero et al.[23] resulted only in degradation of the enone, but replacing HOAc with the less nucleophilic CF_3CO_2H resulted in almost complete conversion into the D-*erythro* azido sugar **30**. Rapid workup afforded an almost quantitative yield of crude **30**, which proved to be unstable and was therefore used without further purification for subsequent transformations. The ^{1}H NMR spectrum of this crude product did not show signals corresponding to the potential D-*threo* epimer of **30**, indicating that the stereochemistry of azide addition to compound **5** is completely governed by the steric bulk of the 1,6-anhydro bridge. Although complete characterization of compound **30** could not be made by elemental analysis and mass spectrometry, the IR spectrum showed a strong azide band at 2100 cm^{-1} and the ^{13}C NMR spectrum showed no alkene signals; the C-3 signal appeared upfield at 37.6 ppm. Proton−proton couplings in the ^{1}H NMR spectrum of **30** confirmed the D-*erythro* stereochemistry with $J_{1,2} = 0$ Hz. As with the cycloadducts described earlier, this coupling strongly suggests the substituent at C-2 to be axial with a quasiequatorial relationship between H-1 and H-2, as seen in compound **30**.

A second reaction of enone **5** considered to be synthetically important was that with reagents capable of epoxidizing the double bond. *tert*-Butyl hydroperoxide was chosen for this transformation, since its steric bulk would presumably contribute to stereodifferentiation upon addition to the enone double bond and the reagent can be used in nonaqueous medium. It was found that enone **5** reacted readily with *t*-BuOOH, in the presence of a catalytic amount of benzyltrimethylammonium hydroxide, to afford the crystalline epoxide **31** in 58% yield. The physical constants reported for **31** were in excellent agreement with those previously reported,[24] and none of the corresponding epoxide that would have resulted from top-face addition to compound **5** could be detected in the reaction mixture.



30 **31**

Azide **30** offers potential in the synthesis of precursors of certain amino sugars.[22] Accessible in only five steps from D-glucose and formed in a completely stereospecific manner, azide **30** is potentially useful for syntheses of amino sugars having three chiral centers in the D-*ribo* configuration, such as nebrosamine, purpurosamine, and sisosamine.[23,25] Essential to this idea was the stereochemical course of the reduction of the C-4 ketone function in **30**. Unlike isolevoglucosenone (**5**), where the ketone reduction was predictably controlled by the 1,6-anhydro bridge, the analogous reduction in **30** was expected to be governed by the relative steric contributions of the axial β azide group at C-2 as well as the 1,6-anhydro bridge.

Reduction of **30** with sodium borohydride was expected to exhibit little face selectivity, and such reduction at −78 °C in 95% EtOH provided two major products identified as the epimeric azido alcohols **32** and **33** isolated in 24 and 46% yields, respectively, after chromatographic separation. The ^{1}H and ^{13}C NMR spectra (see Tables 3 and 4, respectively) of **32** and **33** firmly support their assignments as the D-*ribo* and D-*xylo* derivatives, respectively. The signal for the axial H-4 proton in compound **33** showed a diaxial coupling constant of 10.6 Hz through interaction with the neighboring axial H-3 proton whereas the corresponding H-4 proton in **32** showed a much smaller coupling because of its equatorial orientation. Also detected as a very minor component of the reaction mixture was allylic alcohol **34**. It is possible that this compound is formed by base-promoted loss of HN_3 between C-2 and C-3 to regenerate enone **5**, which is then reduced selectively to compound **34**.

It was thought that the bulkier reductants lithium trisamylborohydride (LS Selectride) or sodium bis(2-methoxyethoxy)aluminum hydride (Red Al) might provide greater stereodifferentiation.[26] However, treatment of azido ketone **30** with LS Selectride at −78 °C in THF solution gave a complex mixture from which axial alcohol **32** could be isolated with some difficulty and in only 11% yield. Similar reaction with Red Al also yielded numerous products, not including axial alcohol **32** but including

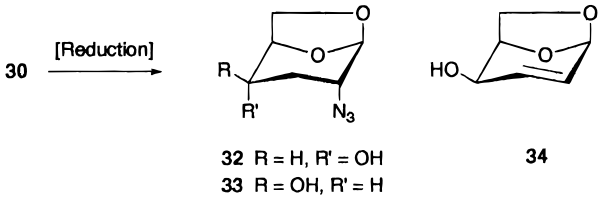
(22) Tanaka, N. in *Antibiotics*; Corcoran, J. W., Ed.; Springer-Verlag: Berlin, 1975; p 340.
(23) Jegou, E.; Cléophax, J.; Leboul, J.; Gero, S. D. *Carbohydr. Res.* **1975**, *45*, 323.
(24) Rolf, K. H.; Rennecke, W.; Köll, P. *Chem. Ber.* **1975**, *108*, 3645.
(25) Leboul, L.; Cléophax, J.; Gero, S. D.; Rolland, A.; Forchiune, A. *Tetrahedron* **1977**, *33*, 965.
(26) Krishnamurthy, S.; Brown, H. C. *J. Am. Chem. Soc.* **1976**, *98*, 3383.

Table 4. ^{13}C NMR Chemical Shifts (ppm) for Isolevoglucosenone Derivatives

	chemical shift (δ)					
compd	C-1	C-2	C-3	C-4	C-5	C-6
5	95.9	147.0	127.0	194.4	79.5	62.6
30	101.5	59.4	37.6t	201.5	79.1	66.9
31	99.7	49.2	52.7	198.6	79.1	66.5
32	99.9	59.0	30.0	63.2	75.7	63.4
33	99.9	59.1	30.0	63.2	75.7	63.4

equatorial alcohol **33** as only a minor component. The outcome of these reactions can probably be attributed to the relatively high basicities of these reagents,[27] which causes extensive degradation of the base-sensitive **30**.

Reaction with the electrophilic aluminum reagents diisobutylaluminum hydride (DIBAH) and triisobutylaluminum (TIBA) proved much more informative. When azido ketone **30** was treated with DIBAH in dichloromethane solution at −78 °C, both D-*ribo* and D-*xylo* epimers **32** and **33** were isolated in 42 and 34% yields, respectively. Raising the reaction temperature did not affect the isomer ratio, but at 25 °C increased amounts of side products were observed. This greater propensity for side-product formation was also noticed when the solvent was changed to pentane at −78 °C, although there was no noticeable change in the ratio of **32** and **33**. A dramatic change in the course of the DIBAH reduction was observed, however, when THF was employed as solvent. Analysis of the crude mixture by ^{1}H NMR showed it to contain mainly equatorial alcohol **33**, with axial alcohol **32** and allylic alcohol **34** being present in only trace amounts. Ultimately, compound **33** could be isolated in 46% yield after chromatography.



The change in stereospecificity upon changing from CH_2Cl_2 to THF was surprising, but may be explained by considering the nature of the reducing agent in the two solvents. Previous studies have shown[28] that DIBAH exists as a trimeric species (**35**, Figure 2) in such noncoordinating solvents as CH_2Cl_2; whereas, in solvents capable of donating lone pairs such as THF, the reducing agent forms reasonably stable 1:1 adducts (**36**, Figure 2). The difference in steric bulk between the trimeric species **35** and the 1:1 adduct **36** may well be the cause of the differing reaction outcome. In CH_2Cl_2 solution, the attack of species **35** from either the exo or endo face of the ketone would probably be hindered by both the axial α substituent (the 1,6-anhydro bridge) and the axial β substituent (the azide group), thereby leading to formation of both alcohols **32** and **33**. When THF is employed as solvent, the much smaller species **36** is probably able to differentiate better between the relative sizes of the 1,6-anhydro bridge and the azide substituent and thus attacks from the more accessible endo face of the ketone in compound **30** resulting in almost exclusive formation of D-*xylo* alcohol **33**.

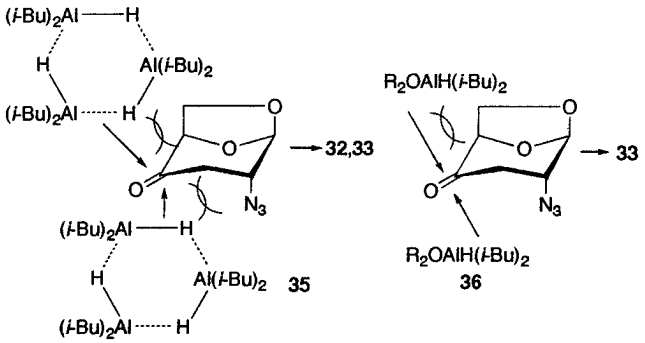
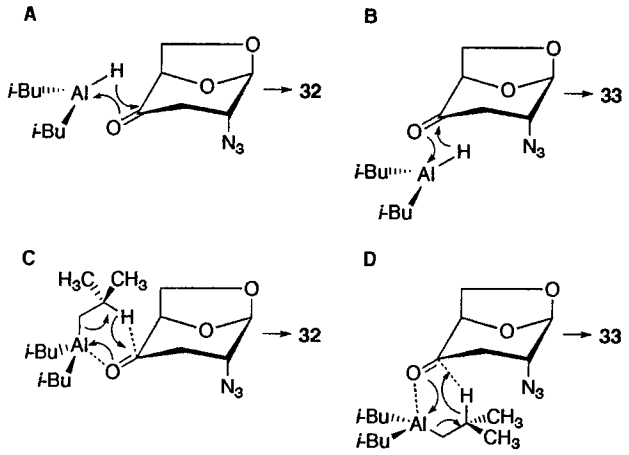


Figure 2. Possible steric interactions in the reduction of azido ketone **30** with DIBAH and TIBA.

Scheme 3



Reduction of **30** with TIBA also proved to be stereoselective when CH_2Cl_2 was employed as solvent at room temperature. Under these conditions, D-*xylo* alcohol **33** was again isolated as the major product in 56% yield, and epimeric alcohol **32** could not be detected upon ^{1}H NMR analysis of the crude mixture. The change in selectivity on moving from DIBAH in CH_2Cl_2 to TIBA in CH_2Cl_2 is probably a consequence of the different mechanisms operating with these two reductants. Although both reagents possess considerable steric bulk, the mode of hydride delivery is significantly different in each. As seen in Scheme 3, DIBAH can coordinate to the ketonic oxygen in either an exo (**A**) or endo (**B**) manner, with the bulk of the reducing agent residing away from the sugar skeleton and thereby allowing the formation of both epimeric alcohols **32** and **33**. When TIBA is employed, the hydride is transferred from an isobutyl group. In situation **C**, when the reducing agent has to align itself to deliver hydride to the exo face of **30**, an isobutyl group has to interfere with the axial 1,6-anhydro bridge, a situation that should be unfavorable. The alternative situation, where TIBA coordinates to the endo face of the ketone (**D**), is likely to be much more favorable with the azide group, creating less steric interference. The exclusive formation of alcohol **33** suggests that **D** is the favored reaction path in this reduction.

Synthetic conversion of axial alcohol **32** into several amino sugars has already been demonstrated,[23,25] and the convenient access to **32** in six steps from D-glucose will facilitate synthesis of this class of amino sugars.

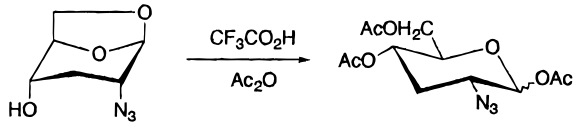
(27) Bazant, B.; Capka, M.; Cerny, M.; Chvalovsky, V.; Kochloefl, K.; Kraus, M.; Malek, J. *Tetrahedron Lett.* **1968**, 3303.

(28) Noyori, R.; Baba, Y.; Hayakawa, Y. *J. Am. Chem. Soc.* **1974**, *96*, 3336.

(29) The author has deposited atomic coordinates for compound **15** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

With the controlled reduction of azide **30** affording 1,6-anhydro-2-azido-2,3-dideoxy-β-D-*ribo*-hexopyranose (**32**), we examined the cleavage of the 1,6-anhydro bridge in **32** as a route to known precursors of 2-amino-2,3-dideoxy sugars. Treatment of compound **32** with dilute (2%) H_2SO_4 in refluxing methanol resulted in slow degradation and eventual recovery of most of the starting material. In contrast, acetolysis using trifluoroacetic acid and acetic anhydride afforded in high yield (97%) an anomeric mixture of the azido triacetates **37**. Separation of the anomers proved impossible because of their almost identical R_f values. However, the ^{1}H and ^{13}C NMR spectra, as well as IR and microanalytical data for the mixture, firmly established their identity.

The formation of this anomeric mixture of 1,4,6-tri-*O*-acetyl-2-azido-2,3-dideoxy-D-*ribo*-pyranose in eight steps from D-glucose documents the promising synthetic utility of isolevoglucosenone for the preparation of amino sugars, as well as non-carbohydrate targets.



32 **37**

Experimental Section

General Procedures. Melting points are uncorrected. Optical rotations were measured at ~25 °C. Mass spectra were obtained either in EI mode at 70 eV or using CI (NH_3). ^{1}H NMR spectra were recorded at either 500 or 300 MHz and ^{13}C NMR spectra at either 125 or 75 MHz. All NMR spectra were recorded for solutions in $CDCl_3$. All *J* values are reported in hertz. Column chromatography was performed on silica gel 60 (230−400 mesh, E. Merck) and thin layer chromatography (TLC) on aluminum-backed plates of silica gel 60 F_{254} (E. Merck). Zones were detected by spraying plates with 5% H_2SO_4 in aqueous ethanol and subsequent heating. Elemental analyses were performed by Atlantic Microlabs, Inc., Norcross, GA.

1,2:5,6-Di-*O*-isopropylidene-3-deoxy-α-D-*erythro*-hex-3-enofuranose (4). To an ice-cold solution of 1,2:5,6-di-*O*-isopropylidene-3-*O*-tosyl-α-D-glucofuranoses[10] (10.0 g, 24.2 mmol) in dry THF (400 mL) was added KO^{t}Bu (8.14 g, 72.4 mmol) in four portions over 10 min. After stirring for 2 h at 0 °C, the solution was partitioned between hexane (300 mL) and water (300 mL). The aqueous layer was extracted with hexane (200 mL), and the combined organic layers were washed with 5% H_2SO_4, saturated $NaHCO_3$, and saturated NaCl and then dried. Evaporation afforded **4** as a yellow solid (5.96 g) which proved sufficiently pure for the next step; however, chromatography (3:1 hexane−EtOAc) yielded the pure alkene as a colorless solid (4.9 g, 84%): mp 48−49 °C, lit.[15] mp 48−50 °C; $[\alpha]_D$ +25.4° (*c* 1.5, $CHCl_3$), lit.[15] $[\alpha]_D$ +21.2° (*c* 1, $CHCl_3$). Anal. Calcd for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49. Found: C, 59.53; H, 7.49.

Cycloaddition of 4 with Cyclopentadiene. Preparation of Norbornene Derivatives 8, 9, and 10. A. BF_3-Catalyzed. To a solution of **4** (7.0 g, 28.9 mmol) in dry toluene (15 mL) kept at −20 °C under an argon atmosphere was added freshly distilled cyclopentadiene (6.8 mL, 28.7 mmol), and BF_3·OEt_2 (3.54 mL, 28.7 mmol) was added slowly. The mixture was stirred at −20 °C for 3 h. After being warmed to rt, the solution was washed twice with saturated $NaHCO_3$, once with water, and then dried and evaporated to afford a yellow syrup. Two separations on silica gel (6:1 hexane−EtOAc) gave **8** [549 mg, 9.9%; mp 94−95 °C, recrystallized from EtOAc−hexane; R_f 0.47 (3:1 hexane−EtOAc); $[\alpha]_D$ +121° (*c* 1.1, $CHCl_3$); IR ($CHCl_3$) 1725 cm^{-1}; *m*/*z* 192 (M^+)] and **9** [67 mg, 1.2%; mp 107−108 °C, recrystallized from EtOAc−hexane; R_f 0.53 (3:1 hexane−EtOAc); $[\alpha]_D$ −198.9° (*c* 1.6, $CHCl_3$); IR ($CHCl_3$) 1725 cm^{-1}; *m*/*z* 192 (M^+)]. For ^{1}H and ^{13}C NMR, see Tables 1 and 2, respectively. Anal. Calcd for $C_{11}H_{12}O_3$ (**8**): C, 68.73; H, 6.30. Found: C, 69.24; H, 6.53. Anal. Calcd for $C_{11}H_{12}O_3$ (**9**): C, 68.73; H, 6.30. Found: C, 68.70; H, 6.33.

B. $ZnCl_2$-Catalyzed. A solution of **4** (0.99 g, 0.409 mmol) in benzene (5 mL) was warmed to 47 °C, and then freshly distilled cyclopentadiene (0.07 mL, 0.84 mmol) and $ZnCl_2$ (1 M in ether, 0.20 mL, 0.84 mmol) were added successively. After 30 min of stirring, Et_3N (0.10 mL, 0.72 mmol) was added and the mixture immediately passed, with pressure, through a short plug of silica gel which was washed through with additional benzene (10 mL). Evaporation afforded a yellow syrup which was initially purified by flash chromatography (3:1 hexane−EtOAc). Fractions that contained a mixture of isomers were further purified by MPLC (9:1 hexane−EtOAc). Combination of pure fractions gave 1,6-anhydro-2,3-*C*-[(3*S*,5*R*)-1-cyclopentene-3,5-diyl]-2,3-dideoxy-β-D-*ribo*-hexopyranos-4-ulose (**8**, 274 mg, 34.8%), 1,6-anhydro-2,3-*C*-[(3*R*,5*S*)-1-cyclopentene-3,5-diyl]-2,3-dideoxy-β-D-*lyxo*-hexopyranos-4-ulose (**9**, 12.5 mg, 15.9%), and 1,6-anhydro-2,3-*C*-[(3*R*,5*S*)-1-cyclopentene-3,5-diyl]-2,3-dideoxy-β-D-*ribo*-hexopyranos-4-ulose [**10**, 2.6 mg, 3.3%, mp 107−108 °C, recrystallized from ether−pentane; R_f 0.58 (3:1 hexane−EtOAc); $[\alpha]_D$ +177.8° (*c* 0.6, $CHCl_3$); IR ($CHCl_3$) 1725 cm^{-1}; *m*/*z* 192 (M^+)]. Anal. Calcd for $C_{11}H_{12}O_3$ (**10**): C, 68.73; H, 6.30. Found: C, 68.74; H, 6.33. For ^{1}H and ^{13}C NMR data, see Tables 1 and 2, respectively.

1,6-Anhydro-2,3-*C*-[(3*S*,5*R*)-1-cyclopentene-3,5-diyl]-2,3-dideoxy-β-D-gulopyranose (14) and 1,6-Anhydro-2,3-*C*-[(3*S*,5*R*)-1-cyclopentene-3,5-diyl]-2,3-dideoxy-β-D-allopyranose (15). Cycloadduct **8** (1.50 g, 7.81 mmol) was dissolved in 95% EtOH at rt, and $NaBH_4$ (0.39 g, 24.0 mmol) was added in four portions over 10 min. After 1 h, acetone (2 mL) was added to decompose excess borohydride and the solution made neutral by stirring for 30 min with Dowex-50W H^+ resin (1.35 g). The solids were filtered off, and the filtrate evaporated to afford a pale-yellow syrup (1.55 g). A portion of this mixture (1.07 g) was separated by MPLC on silica gel (6:1 hexane−EtOAc) to afford the epimeric alcohols **14** and **15**. Compound **14** was isolated as colorless solid [474 mg, 45.3% corrected; mp 111−113 °C, recrystallized from hexane−EtOAc; R_f 0.26 (2:1 hexane−EtOAc); $[\alpha]_D$ +18.8° (*c* 1.4, $CHCl_3$); IR (KBr) 3484 cm^{-1}; *m*/*z* 194 (M^+)]. Compound **15** was also a colorless solid [450 mg, 43.0% corrected; mp 90−92 °C, recrystallized from hexane−EtOAc; R_f 0.23 (2:1 hexane−EtOAc); $[\alpha]_D$ −61.1° (*c* 1.2, $CHCl_3$); IR (KBr) 3446 cm^{-1}; *m*/*z* 194 (M^+)]. Anal. Calcd for $C_{11}H_{14}O_3$ (**14**): C, 68.00; H, 7.27. Found: C, 67.86; H, 7.31. Anal. Calcd for $C_{11}H_{14}O_3$ (**15**): C, 68.00; H, 7.27. Found: C, 67.90; H, 7.30. The ^{1}H and ^{13}C NMR data for **14** and **15** are detailed in Tables 1 and 2, respectively.

The separation of **14** and **15** could be greatly facilitated by derivatization to the monoacetates **16** and **17**. Reduction of compound **8** was carried out as above and after neutralization and evaporation of the reaction mixture, the residue was dissolved in pyridine, acetic anhydride was added, and the mixture was stirred at rt overnight. After standard aqueous workup, the residue was separated by flash chromatography to afford the two monoacetates. Compound **16** was a colorless oil [R_f 0.31 (6:1 hexane−EtOAc); $[\alpha]_D$ +6.5° (*c* 0.89, $CHCl_3$); IR (neat) 1730 cm^{-1}; *m*/*z* 237 (M^+ + 1)]. Anal. Calcd for $C_{13}H_{16}O_3$: C, 66.10; H, 6.78. Found: C, 65.80; H, 6.92.

Compound **17** was a colorless solid [mp 79−80 °C, recrystallized from EtOAc−hexane; R_f 0.27 (6:1 hexane−EtOAc); $[\alpha]_D$ +16.2° (*c* 0.91, $CHCl_3$); IR ($CHCl_3$) 1735 cm^{-1}; *m*/*z* 237 (M^+ + 1)]. Anal. Calcd for $C_{13}H_{16}O_3$: C, 66.10; H, 6.78. Found: C, 66.0; H, 6.85. For ^{1}H and ^{13}C NMR data, see Tables 1 and 2, respectively.

1,6-Anhydro-2,3-*C*-[(1*R*,3*S*,4*S*,5*R*)-4,5-epoxycyclopentan-1,3-diyl]-2,3-dideoxy-β-D-allopyranose (18). *m*-Chloroperoxybenzoic acid (80% purity, 159 mg, 0.737 mmol) dissolved in $CHCl_3$ (5 mL) was added dropwise to a solution of **14** (136 mg, 0.702 mmol) in $CHCl_3$ (10 mL). After the solution was stirred for 2h at rt, saturated $NaHCO_3$ (15 mL) was added and the biphasic mixture stirred an additional 0.5 h. The aqueous layer was extracted with additional $CHCl_3$ (3 × 10

mL), and the organic layers were dried and evaporated to yield **18** as a white solid [131 mg, 88.6%; mp 154−156 °C, recrystallized from hexane−ether; R_f 0.40 (3:1 hexane−EtOAc); $[\alpha]_D$ +11.2° (*c* 0.8, $CHCl_3$); IR (KBr) 3472 cm^{-1}; *m*/*z* 210 (M^+)]. Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.81; H, 6.71. Found: C, 62.69; H, 6.77. The ^1H and ^{13}C NMR spectra of **18** are listed in Tables 1 and 2, respectively.

1,6-Anhydro-5′,4-epoxy-2,3-*C*-[(1*R*,3*S*,4*R*,5*R*)-4-hydroxycyclopentan-1,3-diyl]-2,3-dideoxy-*β*-D-allopyranose (19). A solution of *m*-CPBA (80% purity, 113 mg, 0.534 mmol) in $CHCl_3$ (5 mL) was added dropwise to **15** (96.6 mg, 0.498 mmol) in $CHCl_3$ (10 mL). After 4 h, additional *m*-CPBA (20 mg, 0.116 mmol) was added and the mixture stirred an additional 3 h at rt. Saturated $NaHCO_3$ (15 mL) was added, the mixture was stirred for 0.5 h, and the layers were separated. Workup was then performed exactly as for compound **18** to yield, after evaporation, **19** as a white solid [99.5 mg, 95.2%; mp 143−145 °C, recrystallized from hexane−ether; R_f 0.24 (3:1 hexane−EtOAc); $[\alpha]_D$ −104.0° (*c* 1.0, $CHCl_3$); IR (KBr) 3456 cm^{-1}; *m*/*z* 210 (M^+)]. Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.81; H, 6.71. Found: C, 62.73; H, 6.73. The ^1H and ^{13}C NMR spectra for **19** are detailed in Tables 1 and 2, respectively.

1,6-Di-*O*-acetyl-2,3-*C*-[(3*S*,5*R*)-1-cyclopentene-3,5-diyl]-2,3-dideoxy-*β*-D-*ribo*-hexopyranos-4-ulose (20). Compound **8** (50.0 mg, 0.260 mmol) was dissolved in a mixture of trifluoroacetic acid (0.1 mL) and acetic anhydride (1.5 mL). The mixture was stirred at rt for 3 h and then evaporated to a pale-brown syrup. Chromatography on silica gel (6:1 hexane−EtOAc) provided **20** as a colorless oil [48 mg, 63%; R_f 0.25 (6:1 hexane−EtOAc); $[\alpha]_D$ +99.4° (*c* 0.79, $CHCl_3$); IR (neat) 1750 cm^{-1}; *m*/*z* 294 (M^+)]. Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.22; H, 6.12. Found: C, 61.12; H, 6.20. ^1H and ^{13}C NMR spectra are detailed in Tables 1 and 2, respectively.

1,6-Anhydro-2,3-*C*-[(3*S*,5*R*)-1-cyclopentane-3,5-diyl]-2,3-dideoxy-*β*-D-*ribo*-hexopyranos-4-ulose (21). Compound **8** (1.15 g, 5.99 mmol) was dissolved in EtOAc (30 mL) and hydrogenated under 42 psi in the presence of 10% Pt/C (600 mg) for 2 h. After removal of catalyst, the solution was evaporated to afford **21** as a chromatographically homogenous syrup [1.07 g, 92%; R_f 0.41 (6:1 hexane−EtOAc); $[\alpha]_D$ +58.2° (*c* 0.68, $CHCl_3$); IR (neat) 1720 cm^{-1}; *m*/*z* 194]. Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.04; H, 7.22. Found: C, 67.99; H, 7.35. ^1H and ^{13}C NMR data can be found in Tables 1 and 2, respectively.

1,6-Anhydro-2,3-*C*-[(3*S*,5*R*)-1-cyclopentane-3,5-diyl]-2,3,-dideoxy-*β*-D-gulopyranose (22), 1,6-Anhydro-2,3-*C*-[(3*S*,5*R*)-1-cyclopentane-3,5-diyl]-2,3-dideoxy-*β*-D-allopyranose (23), and Their Respective Monoacetates (24 and 25). To a solution of norbornane **21** (1.297 g, 6.69 mmol) in 95% EtOH (20 mL) was added $NaBH_4$ (0.40 g, 10.5 mmol) in four portions over 10 min. After the reaction was stirred at rt for 2 h, acetone (3 mL) was added to decompose the excess of $NaBH_4$ and then the solution was made neutral by stirring with Dowex-50W H^+ resin (1.6 g) for 0.5 h. After filtration, the solids were washed with ethanol (10 mL) and the filtrate was evaporated to afford a colorless syrup (1.14 g) that contained two products by ^1H NMR and TLC (R_f 0.35 and 0.40, 6:1 hexane−EtOAc). The crude mixture (1.14 g) was dissolved in pyridine (15 mL) and acetic anhydride (10 mL), and the mixture was stirred at rt overnight. After evaporation, the residue was chromatographed (10:1 hexane−EtOAc) to afford **24** as a colorless solid [0.27 g, 17% yield; mp 85−87 °C, recrystallized from EtOAc−hexane; R_f 0.42, 6:1 hexane−EtOAc; $[\alpha]_D$ −3.4° (*c* 1.77, $CHCl_3$); IR (CH_2Cl_2) 1730 cm^{-1}; *m*/*z* 238]. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.55; H, 7.56. Found: C, 65.63; H, 7.62.

Compound **25** was a colorless oil [0.61 g, 38% yield; R_f 0.33, 6:1 hexane−EtOAc; $[\alpha]_D$ +24.2° (*c* 1.95, $CHCl_3$); IR (neat) 1728 cm^{-1}; *m*/*z* 238]. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.55; H, 7.56. Found: C, 65.44; H, 7.66. See Tables 1 and 2, respectively, for ^1H and ^{13}C NMR data.

Preparation of 1,6-Anhydro-2,3-dideoxy-*β*-D-*glycero*-hex-2-enopyran-4-ulose (Isolevoglucosenone, 5). Method A. Alkene **4** (500 mg, 2.07 mmol) and $TsOH{\cdot}H_2O$ (8.0 mg, 0.042 mmol) were dissolved in CH_2Cl_2 (5 mL) in a 50 mL round bottom flask which was then connected to a trap held at −78 °C in an acetone−dry ice bath. The system was placed under high vacuum (0.03 mmHg), and after the solvent had been removed, the resultant solid was heated to 80 °C for 1 h. The vacuum was released, and the distillate, warmed to rt, was then evaporated (12 mm) to afford a brown syrup. Chromatography (3:1 hexane−EtOAc) gave a yellow syrup (12.0 mg, 4.6% yield) which contained **5** as the major component, as judged by ^1H NMR analysis.

Method B. A glass chromatography column (12 mm i.d.) was filled with silica gel to a depth of 12.5 mm and then equilibrated with 2:1 hexane−EtOAc. The solvent layer was lowered to that of the silica gel, a 10% solution of H_2SO_4 in acetone (0.5 mL) was added, and the level was again lowered to the top of the silica gel. Compound **4** (50 mg, 2.1 mmol) was adsorbed onto silica gel (0.5 g). This was added to the top of the column and then hexane−EtOAc was passed through the silica gel at rt at a rate of ∼12 mL/min. After 200 mL of eluent had been collected, no further UV-active material could be detected by TLC. The solvent was evaporated to afford a yellow syrup (2.6 mg, 10%), which again contained **5** as the major component by ^1H NMR.

Method C (Preparative Method). Anhydrous aluminum chloride (260 mg, 1.95 mmol) was added to an efficiently stirred mixture of dry Et_2O (30 mL) and pentane (22 mL) which had been cooled to 0 °C under an argon atmosphere. A solution of alkene **4** (1.07 g, 4.42 mmol) in Et_2O (6 mL) was added dropwise over a 2 min period. The resultant solution was stirred for an additional 7 min at 0 °C and then quickly transferred to a flash chromatography column (25 mm i.d.) containing silica gel (4 cm depth). The solution was rapidly passed through the silica gel with air pressure, followed by a 1:1 mixture of Et_2O−pentane until no more UV-active material could be detected by TLC (∼300 mL). Evaporation afforded a brown syrup which was flash chromatographed using 5:1 pentane−Et_2O to give **5** as a pale-yellow syrup (179 mg, 32.1%). Compound **5** could be obtained as an analytically pure colorless syrup after a second chromatographic purification using 5:1 pentane−Et_2O ($[\alpha]_D$ +412° (*c* 0.9, $CHCl_3$), lit.[17] $[\alpha]_D$ +331°; IR (neat) 1725 cm^{-1}; *m*/*z* 126 (M^+)). Anal. Calcd for $C_6H_6O_3$: C, 57.14; H, 4.80. Found: C, 57.41; H, 4.88.

Reaction of Isolevoglucosenone (5) with Cyclopentadiene. A. Thermal Conditions. A mixture of freshly distilled cyclopentadiene (0.20 mL, 2.3 mmol) and compound **5** (30.0 mg, 0.238 mmol) in benzene (3 mL) was boiled under reflux for 1.5 h, additional cyclopentadiene (0.20 mL, 2.3 mL) was added, and refluxing was continued an additional 4.5 h. Evaporation of solvent afforded a yellow syrup which was chromatographed to remove the most and least polar impurities. The middle fractions afforded a white solid (40.4 mg, 88.4%) which was found by ^1H NMR to contain norbornene adducts **8** and **10** in a 11.1:1.0 ratio.

B. Lewis Acid Catalysis. Compound **5** (53.0 mg, 0.421 mmol) was dissolved in benzene (5 mL) kept at 48 °C, freshly distilled cyclopentadiene (0.07 mL, 0.85 mmol) and 1 M $ZnCl_2$ in Et_2O (0.20 mL, 0.20 mmol) were added, and the mixture was stirred for 45 min. The mixture was cooled to rt, Et_3N (0.10 mL) was added, and the mixture was passed through a plug of silica gel. Evaporation of the solvent afforded a white solid (66.8 mg, 82.7%) which contained compounds **8** and **10** in a 4.5:1 ratio by ^1H NMR.

Reaction of Isolevoglucosenone (5) with Cyclohexadiene: Formation of Cycloadduct 28. To a solution of **5** (71 mg, 0.57 mmol) in benzene (1 mL) were added $ZnCl_2$ (0.57 mL, 0.57 mmol, 1M in Et_2O) and cyclohexadiene (0.15 mL, 2.8 mmol). After 4 h at rt, additional cyclohexadiene (0.15 mL, 2.8 mmol) was added and stirring continued a further 20 h. Et_3N (0.56 mL, 1.1 mmol) was added, and the mixture was passed through a short plug of silica gel with pressure. Evaporation of solvent afforded a colorless syrup which was chromatographed (3:1 hexane−EtOAc) to give 1,6-anhydro-2,3-*C*-[3*S*,5*R*)-1-cyclohexene-3,6-diyl]-2,3-dideoxy-*β*-D-*ribo*-hexopyranos-4-ulose (**28**) as a colorless solid [69.7 mg, 59% yield; mp 78−79 °C; R_f 0.56 (3:1 hexane−EtOAc); $[\alpha]_D$ +67.2° (*c* 0.5, $CHCl_3$); IR (KBr) 1708 cm^{-1}; *m*/*z* 206 (M^+)]. For **28**: ^1H NMR (500 MHz, $CDCl_3$) δ 1.25 (dt, J = 11.8, 1 H), 1.30 (dt, J = 2.0, 11.3, 1 H), 1.35 (dt, J = 11.8, 3.3, 1 H), 1.60 (dt, J = 11.8, 1 H), 2.23 (d, J = 9.2, 1 H), 2.61 (m, J = 7.4, 3.0, 2.8, 2 H), 3.19

(bd, J = 3.3, 2.9, 1 H), 3.79 (m, 2 H), 4.24 (t, J = 3.5, 1 H), 5.44 (s, 1 H), 6.12 (t, J = 7.1, 1 H), 6.30 (dt, J = 7.4, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.9, 26.6, 32.6, 33.1, 44.5, 48.4, 66.5, 78.0, 104.7, 131.6, 133.9, 206.4. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 70.33; H, 6.88.

Reaction of Isolevoglucosenone (5) with 9,10-Dimethylanthracene: Formation of Cycloadduct 29. A solution of **5** (100 mg, 0.794 mmol) and 9,10-dimethylanthracene (233 mg, 1.13 mmol) in benzene (10 mL) was refluxed for 72 h. The solvent was evaporated and the pale-yellow solid dissolved in hot ether and then cooled to crystallize excess 9,10-dimethylanthracene, which was removed by filtration. Chromatography of the filtrate (3:1 hexane−EtOAc) gave 1,6-anhydro-2,3-*C*-[9,10-dimethyl-9,10-dihydroanthracene-9,10-diyl]-2,3-dideoxy-β-D-*ribo*-hexopyranos-4-ulose (**29**) as a white solid [170 mg, 62% yield; mp 149.5−150.5 °C, recrystallized from pentane−Et_2O; R_f 0.53 (3:1 hexane−EtOAc); $[\alpha]_D$ +61.7° (c 1.7, $CHCl_3$); IR (KBr) 1725 cm^{-1}; m/z 332 (M^+)]. For **29**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.10 (s, 3 H), 2.17 (s, 3 H), 2.18 (d, J = 9.4, 1 H), 2.57 (dd, 1 H), 3.52 (dd, J = 7.6, 1 H), 3.71 (d, J = 7.6, 1 H), 3.97 (d, J = 5.3, 1 H), 5.70 (d, 1 H), 7.15−7.35 (m, 8 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.9, 16.9, 42.7, 45.0, 49.5, 54.7, 68.3, 78.7, 101.6, 120.6−146.1, 207.4. Anal. Calcd for $C_{28}H_{26}O_3$: C, 79.49; H, 6.07. Found: C, 79.43; H, 6.08.

1,6-Anhydro-2-azido-2,3-dideoxy-α-D-*erythro*-hexopyranos-4-ulose (30). A solution of compound **5** (760 mg, 6.03 mmol), sodium azide (1.18 g, 18.15 mmol), and trifluoroacetic acid (0.466 mL, 6.05 mmol) in dry THF (46 mL) was stirred at rt for 10 h. The solvent was evaporated at rt to a thick paste which was then extracted with successive portions (2 × 50 mL) of pentane. After filtration, the organic extracts were evaporated under reduced pressure at rt to afford crude **30** as an unstable syrup [IR (neat) 2100, 1740 cm^{-1}] which was used without further purification.

1,6:2,3-Dianhydro-β-D-*ribo*-hexopyranos-4-ulose (31). A solution of compound **5** (169 mg, 1.34 mmol) and 3 M *tert*-butyl hydroperoxide in isooctane (0.671 mL, 20.1 mmol) in benzene (1 mL) was cooled to 0 °C, and then 3 M benzyltrimethylammonium hydroxide (Triton B) in MeOH (0.01 mL, 0.03 mmol) was added. After the solution was stirred for 1 h at 0 °C, the solvent was evaporated and the resultant syrup purified twice by chromatography (1:2 hexane−EtOAc) to afford **31** as a colorless solid [110 mg, 58%; mp 63−64 °C, lit.[24] mp 64.5−65.5 °C; $[\alpha]_D$ −7.4° (c 1.3, dioxane), lit.[24] $[\alpha]_D$ −4.5° (c 1.0, dioxane); m/z 142 (M^+)]. The ^{1}H and ^{13}C NMR data (Tables 3 and 4, respectively) were in excellent agreement with those previously reported.[24]

Reduction of Azido Ketone 30: Formation of Azido Alcohols 32 and 33. A. With Sodium Borohydride. A solution of freshly prepared **30** (85.5 mg, 0.506 mmol) in 95% EtOH (5 mL) was cooled to −78 °C, and $NaBH_4$ (38 mg, 1.0 mmol) in EtOH (2 mL) was added dropwise. After being warmed to rt and stirred overnight, the solution was treated with Dowex-50W H^+ resin (0.20 g) for 15 min, the resin filtered off, and the filtrate evaporated to afford a colorless syrup which, by ^{1}H NMR analysis, contained **32** and **33** in a ratio of 0.64:1.00 and a trace of allylic alcohol **34**. Separation on silica gel (1:2 hexane−EtOAc) afforded two products. 1,6-Anhydro-2-azido-2,3-dideoxy-α-D-*xylo*-hexopyranose (**33**) was a syrup [40.4 mg, 46% yield; R_f 0.37 (1:1 hexane−EtOAc); $[\alpha]_D$ −15.4° (c 3.4, $CHCl_3$); IR (neat) 3400, 2100 cm^{-1}; m/z 101 ($M^+ - C_2H_3N_3$, H)]. ^{1}H and ^{13}C NMR data are given in Tables 3 and 4, respectively. Anal. Calcd for $C_6H_9N_3O_3$: C, 42.10; H, 5.30; N, 24.56. Found: C, 42.97; H, 5.24; N, 24.27.

1,6-Anhydro-2-azido-2,3-dideoxy-α-D-*ribo*-hexopyranose (**32**) was a colorless syrup [21.0 mg, 24% yield; R_f 0.18 (1:1 hexane−EtOAc); $[\alpha]_D$ −75° (c 3.1, $CHCl_3$); IR ($CHCl_3$) 3500, 2100 cm^{-1}; m/z 101 ($M^+ - C_2H_3N$, H)]. The ^{1}H and ^{13}C NMR constants for compound **32** are given in Tables 3 and 4, respectively. Anal. Calcd for $C_6H_9N_3O_3$: C, 42.10; H, 5.30; N, 24.56. Found: C, 42.31; H, 5.34; N, 24.56.

B. With LS Selectride. Reduction of **30** (167 mg, 0.998 mmol) in THF (3 mL) with 1 M LS Selectride in THF (1.0 mL, 1.0 mmol) at −78 °C for 3 h afforded, after aqueous workup, a yellow syrup (77 mg) which contained **32** as the major component by ^{1}H NMR. Crystallization from 1:1 Et_2O−pentane afforded **32** as a pale-yellow solid (18.6 mg, 11%).

C. With Diisobutylaluminum Hydride in CH_2Cl_2. A solution of **30** (1.11 g, 6.58 mmol) in dry CH_2Cl_2 (75 mL) under an Ar atmosphere was cooled to −78 °C, and then a 1.5 M solution of DIBAH in toluene (5.20 mL, 7.80 mmol) was added slowly. After 3 h of stirring at −78 °C, the mixture was brought to rt and then water (1.20 mL, 66.0 mmol) was added cautiously. After the solution was stirred for 10 min, $MgSO_4$ was added, the resultant paste filtered, and the solid extracted with EtOAc (2 × 10 mL). The combined filtrate and extracts were evaporated, and the crude syrup chromatographed (3:2 hexane−EtOAc) to afford alcohol **33** (475 mg, 42%) as a colorless syrup and alcohol **32** (336 mg, 30%) as a colorless solid.

D. With Diisobutylaluminum Hydride in THF. A solution of **30** (59.4 mg, 0.351 mmol) in dry THF (3 mL) was cooled to −78 °C under Ar, a solution of 1.5 M DIBAH in toluene (0.47 mL, 0.71 mmol) was added slowly, and the resultant mixture stirred at −78 °C for 20 h. After the solution was warmed to rt and stirred for 1.5 h, water (0.84 mL) was added carefully and the mixture worked up as described in the previous experiment to afford, after flash chromatography, alcohol **33** as a colorless syrup (27.5 mg, 45.7%).

E. With Triisobutylaluminum Hydride in CH_2Cl_2. A solution of freshly prepared **30** (99.7 mg, 0.59 mmol) in dry CH_2Cl_2 (7.5 mL) under Ar was treated with 1 M TIBA in toluene (1.18 mL, 1.18 mmol). After the solution was stirred for 1 h, water (0.10 mL) was added carefully, and the mixture was stirred for 2 h, and then worked up as described in the previous experiments to afford, after chromatography, alcohol **33** as a colorless syrup (56.5 mg, 56%).

Acetolysis of 32 To Give 1,4,6-Tri-*O*-acetyl-2-azido-2,3-dideoxy-α,β-D-*ribo*-hexopyranosides 37. Azido alcohol **32** (361 mg, 2.11 mmol) was dissolved in Ac_2O (7.46 mL) and CF_3CO_2H (5.1 mL), and the mixture was stirred at rt for 8 h. After the solvent was evaporated, the resultant brown syrup (741 mg) was chromatographed (2:1 hexane−EtOAc) to afford anomeric triacetates **37** as a colorless syrup (640 mg, 97%); R_f 0.30 (3:1 hexane−EtOAc); $[\alpha]_D$ +84° (c 2.2, $CHCl_3$); IR (neat) 2100, 1750 cm^{-1}; m/z 256 ($M^+ - CH_3CO_2$). Anal. Calcd for $C_{12}H_{17}N_3O_7$: C, 45.71; H, 5.44; N, 13.33. Found: C, 45.61; H, 5.45; N, 13.23.

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