Stereoselectivity of Addition of Organometallic Reagents to Pentodialdo-1,4-furanoses: Synthesis of L-Axenose and D-Evermicose from a Common Intermediate†

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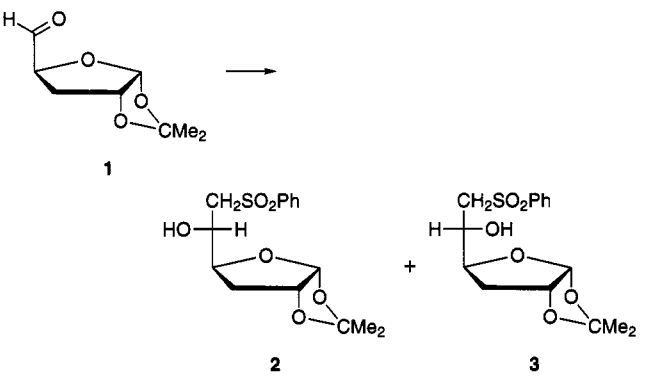
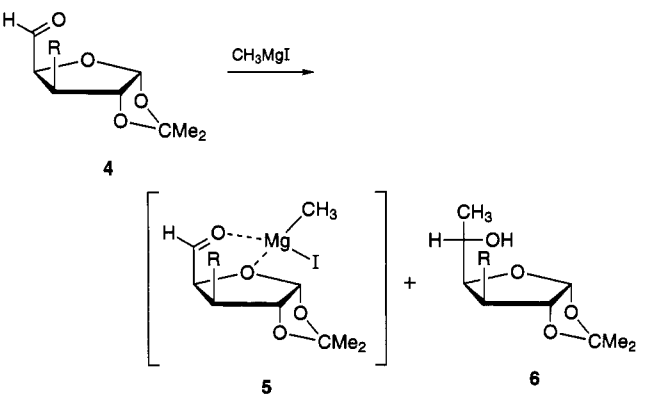
The additions of organometallic reagents to two pentodialdo-1,4-furanosides (methyl 3-*O*-benzyl-2-deoxy-α-D-*erythro*-pentofuranoside and its β-anomer) were carried out under a variety of experimental conditions. Methylmagnesium halides, methyllithium, methylcerium and the organotitanium reagent $MeTi(OiPr)_3$ were reacted with the pentodialdo-1,4-furanosides in an effort to determine if the stereoselectivity of addition to the formyl group is the result of chelation or nonchelation control and to determine the effect of anomeric configuration. The stereochemistry of the products was assigned by NMR methods and correlation with known compounds synthesized previously. The stereoselectivity of addition depends on the configuration at the anomeric center of the dialdose, with the β-anomer giving mainly the product of a non-chelation-controlled addition and the α-anomer giving the opposite stereoselectivity. The major product obtained from the β-anomer was utilized as a key intermediate in the synthesis of two branched-chain carbohydrates, axenose and evermicose, found in antibiotics. Methylcerium additions are the most efficient method for introducing the branching methyl group in a 2-deoxyfuranosid-3-ulose.

Introduction

Additions of organometallic reagents to aldehydo and keto sugars are critical steps for the synthesis of higher-carbon and branched-chain carbohydrates and for preparation of chiral subunits of macrolide antibiotics and polyethers.[1,2] Current models[3,4] of asymmetric induction can be used to predict the diastereofacial selectivity of these reactions in a wide variety of substrates. Carbohydrate-derived aldehydes and ketones, however, often exhibit a different level, or even direction, of stereoselectivity than that expected. For example, Kim and coworkers reported that the addition of phenylsulfonyl methide to carbohydrate aldehyde **1** gave **2** as the major product in four of six cases with Li^+, Mg^{2+}, and Zn^{2+} as counterion. This is contrary to predictions based on a transition state for addition that involves chelation of the carbonyl and ring oxygens with the metal, from which **3** would be obtained selectively.[5] The cyclic chelate model was proposed by Wolfrom and Hanessian in 1962 to account for the high diastereofacial selectivity of additions of organometallic reagents to dialdose **4a**.[6] They suggested that the formation of cyclic chelate **5** involving the aldehyde and ring oxygens occurred in the addition of methylmagnesium iodide to aldehyde **4a** in THF–ether. Attack of the nucleophile from the less hindered face of the carbonyl group gives **6a** selectively. Similar selectivity was reported in a recent study of methoxy derivative **4b**.[7]





a. R = OCH_2Ph; b. R = OCH_3

The control of facial selectivity of Grignard additions by the cyclic chelate mechanism, though widely postu-

† Taken from the Ph.D. thesis of Frank J. Villani, Jr.

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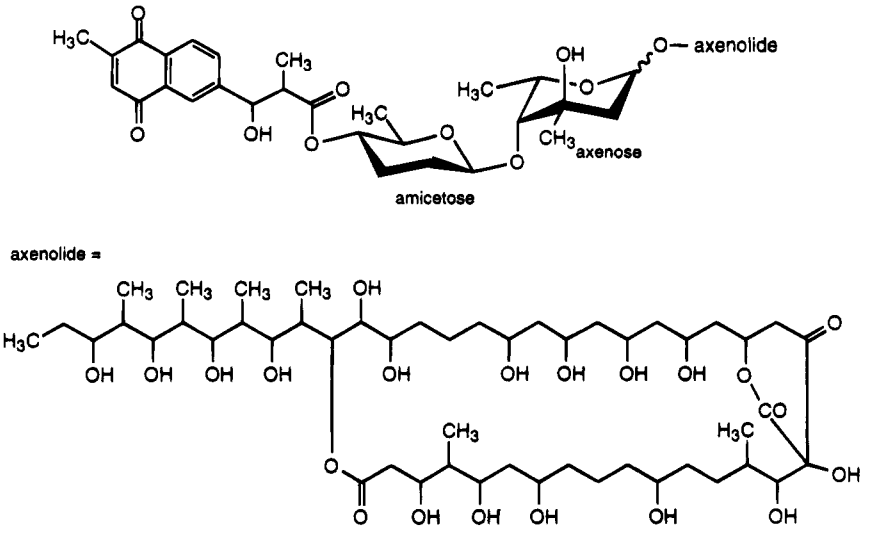
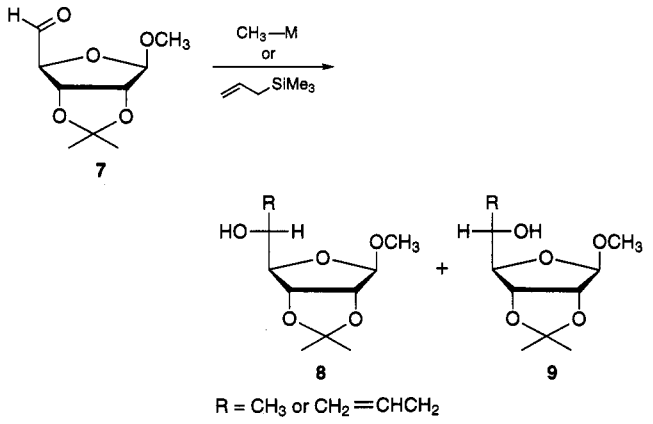


Figure 1. Axenomycin B.

lated, is not consistent in the additions of Grignard reagents to certain carbohydrate substrates. Low diastereoselectivity was observed by Boyd and Baker[8] and the Danishefsky group[9] for the additions of Grignard reagents to **7**, all of which gave **8** as the major product. Stereoselectivities for these reactions were typically in the range of 2–3:1 in favor of the non-chelation-controlled product **8**. The Kim group also observed low stereoselectivity for the additions of methylmagnesium halides to **1** and **4** except when carried out in the presence of Lewis acids.[5] In contrast, high stereoselectivity was reported for the addition of allyltrimethylsilane to **7** in the presence of $BF_3{\cdot}Et_2O$,which gave the D-*allo* isomer (**8**) selectively (>20:1), or $TiCl_4$, which gave the epimeric L-*talo* product (**9**), also in a ratio of >20:1.[9]



The examples cited above illustrate that conditions can be developed for highly selective additions of organometallic reagents to pentodialdo-1,4-furanosides. In order for improvements in the methodology to be realized, a better understanding of the factors that control the diastereoselectivity of addition to the carbonyl group of the sugar substrates is needed. Critical issues that need to be addressed include the involvement of cyclic chelates in the addition step and the effect of substitution at ring positions, in particular the C-3 and anomeric positions. The role of cyclic chelates in these reactions may not be important across a wide range of carbohydrate substrates which differ in substitution, nor for reagents having different counterions. While it is apparent that substituents at the 3-position of the furanose ring exert a dramatic effect on the diastereoselectivity, the effect of the anomeric substituent has not been determined in any of the reported studies.

Our long-standing interest in the synthesis of carbohydrate components of antibiotics led us to consider a systematic study of the reactions of pentodialdo-1,4-furanosides with different organometallic reagents. This study was undertaken in the context of a program directed at the synthesis of axenose, a branched-chain carbohydrate found in the antibiotic axenomycin B (Figure 1).[10,11] Our ultimate goal is to develop derivatives of axenose and related branched-chain carbohydrates for use in oligosaccharide synthesis. In a previous route to axenose, the addition of methylmagnesium iodide to a keto sugar in its *pyranose* form gave a mixture of epimers in which the desired product was the minor component.[12] We questioned whether stereocontrol parameters, in particular chelation control via the ring oxygen, would direct chain branching and extension in a pentodialdo-1,4-furanoside and enable us to develop a stereoselective route to axenose. Our approach is outlined retrosynthetically in Scheme 1.

A chelation-controlled addition to pentodialdo-1,4-furanoside **10** would result in a product with the *S* configuration at C-5 required for axenose. Oxidation of the hydroxyl group at C-3, followed by a second addition of an organometallic reagent, would give **14**, with the required stereochemistry for axenose at each of its stereogenic centers. Alternatively, addition to **10** by a non-chelation, controlled reaction would produce the opposite, *R* configuration at C-5 in **12**. The product would then belong to the enantiomeric, D-series of branched-chain carbohydrates. An efficient synthesis of D-ever-

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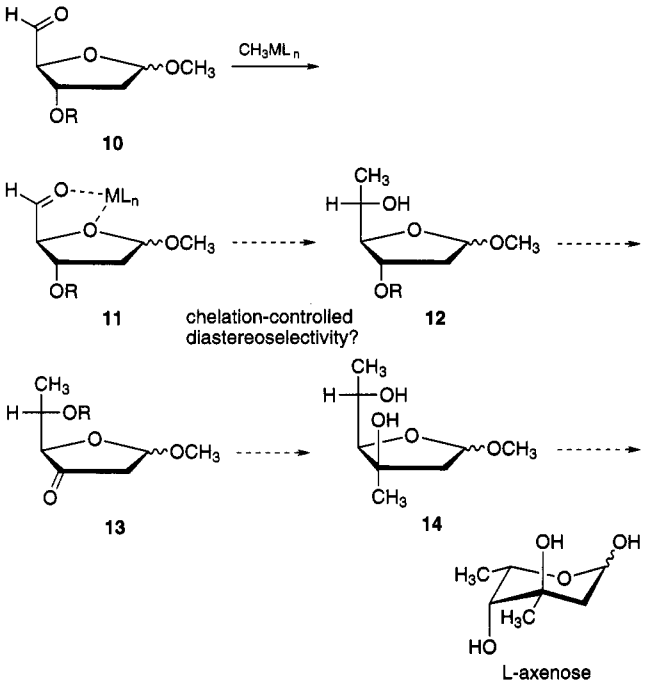
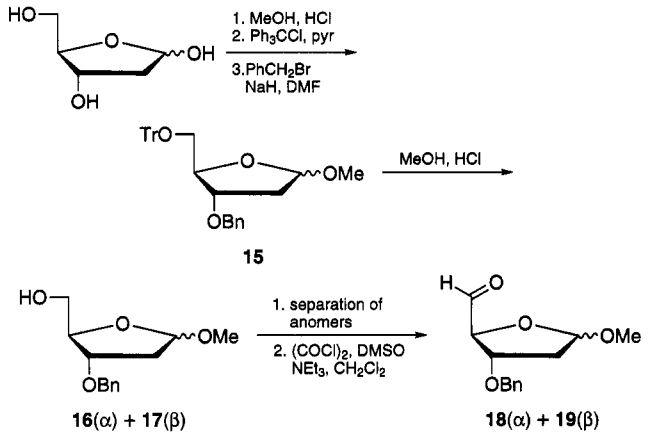
Scheme 1. Synthesis of Axenose from a Pento-1,4-dialdofuranoside



Scheme 2. Synthesis of Anomeric Pentodialdo-1,4-furanosides

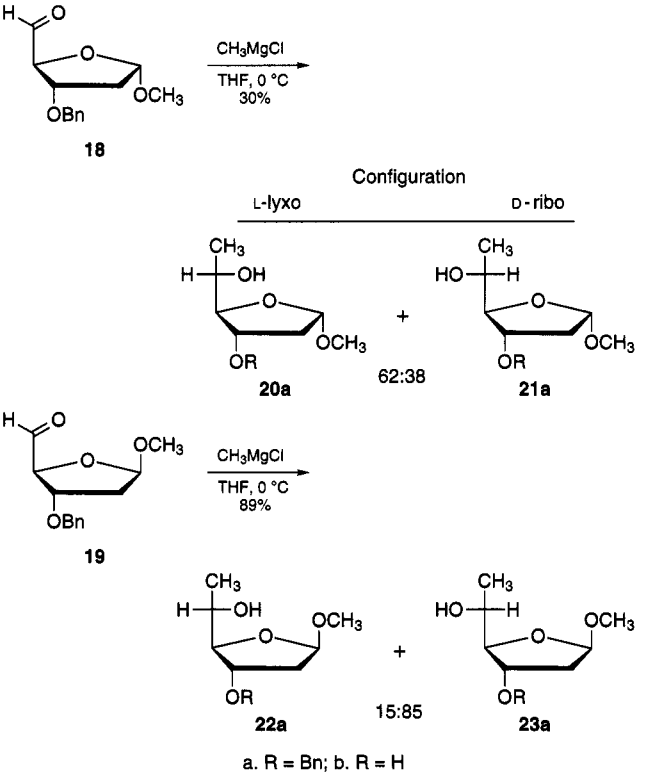


micose,[13] a component of the everninomicin antibiotics, could be developed from this alternate product. Ideally, we would be able to obtain either isomer at C-5 of **12** selectively, so that syntheses of both axenose and evermicose could be developed from a common intermediate. Critical to the success of this strategy is the ability to control the stereoselectivity of addition to **10**.

Results and Discussion

A mixture of anomers of 3-*O*-benzyl-2-deoxy-5-(triphenylmethyl)-D-*erythro*-pentofuranoside, **15**, was prepared from 2-deoxyribose in a ratio of approximately 1:1 by the methods of Hoffer and Suami (Scheme 2).[14,15] Cleavage of the trityl ether with methanolic HCl gave α- and β-anomers **16** and **17** which were separated by flash chromatography and characterized. Facile anomerization was observed for **16** and **17** in the presence of trace amounts of acid. Oxidation with chromium trioxide/pyridine complex proved less satisfactory in the case of the α-anomer, which gave a more labile aldehyde **18**; however, both aldehydes **18** and **19** were obtained in high isolated yields using the Swern method with oxalyl chloride.[16] Products of unique anomeric configuration were obtained and characterized by ^{1}H and ^{13}C NMR. Owing to their lability, the aldehydes were used without further purification.

Scheme 3. Addition of Methylmagnesium Chloride to 18 and 19



a. R = Bn; b. R = H

The aldehydes **18** and **19** were treated with methylmagnesium chloride under identical conditions (THF, 0 °C), and a mixture of two products was obtained from each as shown in Scheme 3. The major product obtained from the α-anomer was the L-lyxo isomer, **20a**, while the β-anomer gave the D-ribo isomer, **23a**, selectively. Products **22a** and **23a** were separated by flash chromatography. The ^{1}H-NMR spectrum of debenzylated **23b** was identical with that reported by Zeeck for methyl 2,6-dideoxy-β-D-*ribo*-hexofuranoside.[17] Products **20a** and **21a** could not be separated; however, the α-D-ribo isomer, **21a**,[17] was readily identified in the ^{1}H-NMR spectrum of the mixture, and the major product (**20a**) was assigned the L-lyxo configuration. It was possible to generate a mixture of all four diastereomers by debenzylation and anomerization of a product mixture obtained from **19**. All four H-3 proton resonances were resolved in the ^{1}H-NMR spectrum at 300 MHz (Figure 2). The chemical shifts of the H-3 peaks for each of the ribo isomers in the mixture matched those reported by Zeeck. The assignments of stereochemistry were confirmed by the completion of the synthesis of L-axenose and its C-5 epimer, D-evermicose, from **23a**.

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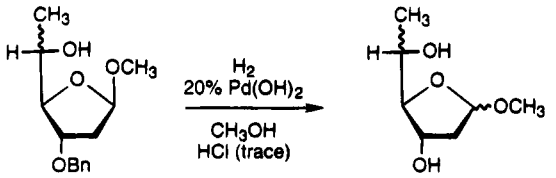


mixture of 22 + 23

20b, 21b, 22b, 23b

A Portion of the ^{1}HNMR Spectrum (5.7-3.0 ppm) of Mixture 20b, 21b, 22b and 23b.

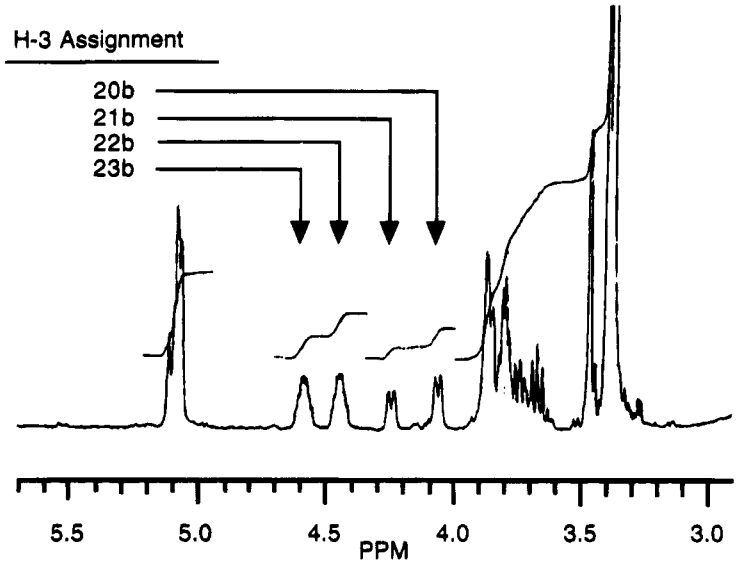


Figure 2. Structure assignment for the four diastereomers at C-1 and C-5.

Table 1. Additions of Organometallic Reagents to Pentodialdo-1,4-furanoside 19

entry	reagent	condns: solvent	condns: T (°C)	ratio[a] **23a/22a**	yield[b] (%)
1	CH_3MgCl	THF	0	85/15	89
2	CH_3MgCl	THF	20	85/15	89
3	CH_3MgCl	THF	−45	85/15	93
4	CH_3MgBr	THF	0	82/18	91
5	CH_3MgBr	ether	0	60/40	80
6	CH_3Li	ether	−70	81/19	80
7	"CH_3CeCl_2·LiCl"	THF	−70	85/15	44
8	CH_3MgCl·2DMPU[c]	THF	0	86/14	83
9	CH_3MgBr·4DMPU[c]	THF	0	83/17	53
10	CH_3MgBr·$ZnCl_2$	THF	−70	75/25	30
11	CH_3MgBr·$TiCl_4$	THF	−70	86/14	43
12	CH_3MgCl "hi salt"	THF	−10	84/15	100
13	CH_3MgCl "low salt"	THF	0	83/17	85
14	$CH_3Ti(OiPr)_3$	CH_2Cl_2	−50	93/7	76

[a] Determined by integration of the ^{1}H NMR signals of the C-5-CH_3 in crude reaction mixtures. [b] Isolated yield of both diastereomers. [c] DMPU = dimethylpropyleneurea (1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone).

Table 2. Additions of Organometallic Reagents to Pentodialdo-1,4-furanoside 18

entry	reagent	condns: solvent	condns: T (°C)	ratio[a] **21a/20a**
1	CH_3MgCl	THF	0	38/62
2	CH_3MgCl	THF	−40	38/62
3	CH_3MgBr	THF	0	45/55
4	CH_3MgBr	ether	0	26/74
5	CH_3Li	ether	−70	50/50
6	"CH_3CeCl_2·LiCl"	THF	−70	45/55
7	CH_3MgBr·$ZnCl_2$	THF	−70	33/67
8	CH_3MgBr·$TiCl_4$	THF	−70	45/55
9	CH_3MgCl "hi salt"	THF	−10	45/55
10	CH_3MgCl "low salt"	THF	−10	45/55

[a] Determined by integration of the ^{1}H NMR signals of the C-5-CH_3 in crude reaction mixtures.

The addition of methylmagnesium halides, methyllithium, and other reagents were carried out for the aldehydes **18** and **19** under a variety of conditions. Methylmagnesium chloride and bromide were used in ether or THF, and in the presence of DMPU or Lewis acids. Methyllithium, methylcerium, and the organotitanium reagent $MeTi(OiPr)_3$ were also examined. The ratios of D-ribo and L-lyxo products obtained from these reactions were determined by ^{1}H-NMR spectroscopic integration and are shown in Tables 1 and 2. The data presented in Table 1 for the β-anomer reveal the following unanticipated results: (1) the diastereoselectivity of addition to the formyl group in **19** remains essentially invariant across a wide range of experimental conditions, and (2) the stereoselectivity of addition is opposite that predicted by the chelation model in every case.

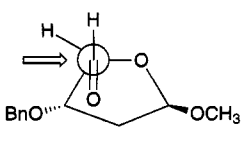
The reversal of diastereofacial selectivity with change in anomeric configuration was unprecedented to our knowledge and demonstrates that models for stereocontrol based solely on aldehyde conformation or chelation of aldehyde and ring oxygens are inadequate. A chelation-controlled addition to **19** would be expected to give **22a** as the major product, while the same selectivity would produce **20a** as the major product from **18**. The conditions in Table 1 were chosen to indicate any possible changes in the diastereoselectivity that would result from different levels of aggregation of the organomagnesium reagents, the presence of Lewis acids, salt concentration,

the presence of different metals as counterions, and the effect of temperature.

Organomagnesium reagents are more highly aggregated in diethyl ether than in THF, and alkylmagnesium chlorides are more aggregated than either the corresponding bromides or iodides.[18] It was considered that the addition of DMPU might further disrupt aggregate formation and lead to a change in the reactivity (and selectivity) of the Grignard reagent. The addition of a strong Lewis acid such as zinc chloride or titanium tetrachloride might be expected to favor the formation of chelation-controlled product **22a**, while the use of the titanium reagent, $MeTi(OiPr)_3$, which is known to possess very weak Lewis acidity,[3] should favor the formation of the Felkin–Anh[19,20] product, **23a**. The only two entries in Table 1 which show any significant changes in the diastereoselectivity are entries 5 and 14. The addition of methylmagnesium bromide in ether was attempted because these conditions had been shown by Still and Schneider to favor the formation of the product predicted by chelation control from acyclic α-alkoxy aldehydes.[21] Although an increase in the amount of **22a** relative to **23a** was observed, the product that would result from chelation control, **22a**, was still the minor one. The titanium reagent (entry 14) resulted in an increase in the amount of diastereomer **23a**. It is known that the Lewis acidity of organotitanium reagents can be decreased by substituting alkoxy ligands for halide. Coupled with the large steric bulk of the $MeTi(OiPr)_3$ reagent, its weak Lewis acidity would be expected to disfavor a chelation mechanism.

Additions to the α-anomer **18** are shown in Table 2. The instability of **18** resulted in lower yields throughout, and fewer experiments were conducted. In spite of these difficulties, sufficient data were obtained for comparison. The major product in every case except entry 4 was L-lyxo isomer **20a**, which would be predicted by a mechanism based on chelation control. The results of entries 2 and 7 are somewhat surprising since the use of Lewis acids would be expected to favor the formation of **20a** to an even greater extent, yet no effect was observed.

The most striking effect that emerges from the data shown in Tables 1 and 2 is the reversal in diastereoselectivity that results from a change in the anomeric configuration of the pentodialdo-1,4-furanoside. To our knowledge, this effect has not been described in the literature, and the results demonstrate that nucleophilic additions to such systems cannot be adequately described by the chelation model alone. In fact, the role of chelation in the attempted additions to **18** and **19** seems much less pronounced than one would have expected on the basis of the frequent citations of this model. The stereoselectivities observed for additions to the β-anomer **19** are consistent with preferred reaction via a Felkin–Anh transition state in which the furan ring oxygen would be antiperiplanar to the incoming nucleophile as shown in **24**, giving **23a** as the major product.



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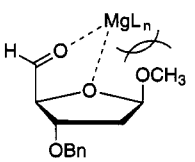

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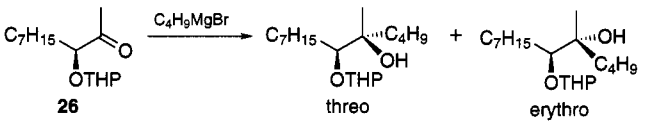
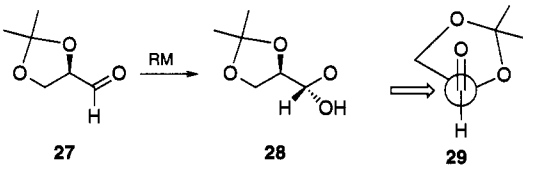
The minor product **22a** could result either from attack from the opposite face of **24** or from a chelation-controlled addition. The latter process would be less favorable in the β-anomer because of the disruption of the chelate by the methoxy group at the anomeric position as shown in **25**. In the α-anomer **18**, the formation of a cyclic chelate would be more favorable since the anomeric group occupies the opposite face. The loss of chelation-controlled diastereoselectivity due to unfavorable steric effects has precedent in studies of acyclic systems. A decrease in chelation-controlled addition products was observed by Still and McDonald for one of the diastereomers of α-alkoxy ketone **26**.[22] The authors postulate that the intermediate cyclic chelate is disfavored in one of the isomers, leading to a lower selectivity for the formation of the chelation-controlled addition product (threo isomer). A similar decrease in diastereoselectivity was also observed in the addition of Grignard reagents to the trityl ether of β-hydroxyisobutyraldehyde.[21] The decrease was ascribed to the large steric bulk of the trityl group which hinders the formation of a cyclic chelate.



26 threo erythro

The results for aldehydes **18** and **19** are consistent with the general trend observed for anti-addition to 2,3-*O*-isopropylidene-D-(or -L)-glyceraldehyde **27**, which has been interpreted in terms of a Felkin transition state, illustrated in structure **29**.[4] Anti addition to **27** results in products with the stereochemistry depicted in **28**.



27 **28** **29**

While the same product would also be favored by a mechanism involving chelation to the β-oxygen of the isopropylidene group, the analogous process involving chelation by the C-3 β-oxygen in **18** and **19** would not be expected to affect the diastereoselectivity of addition since the C-3 substituent occupies the opposite face of the ring. A mechanism involving β-chelation of magnesium has been proposed to explain the stereoselectivity of additions of Grignard reagents to **4**.[5]

The most suitable precursor for axenose and evermicose is β-D-ribo product **23a**, which can be obtained in high yield by the addition of the methyltitanium reagent or a Grignard reagent to dialdose **19**. Either reaction can be carried out on a multigram scale, and the minor product, **22a**, can be separated by a straightforward chromatographic step. Compound **23a** possesses the opposite configuration at C-5 from axenose; hence, an epimerization is required in addition to chain branching at C-3 for the completion of the synthesis. These steps are shown in Scheme 4. The inversion of configuration at C-5 was carried out efficiently by the Martin-modified

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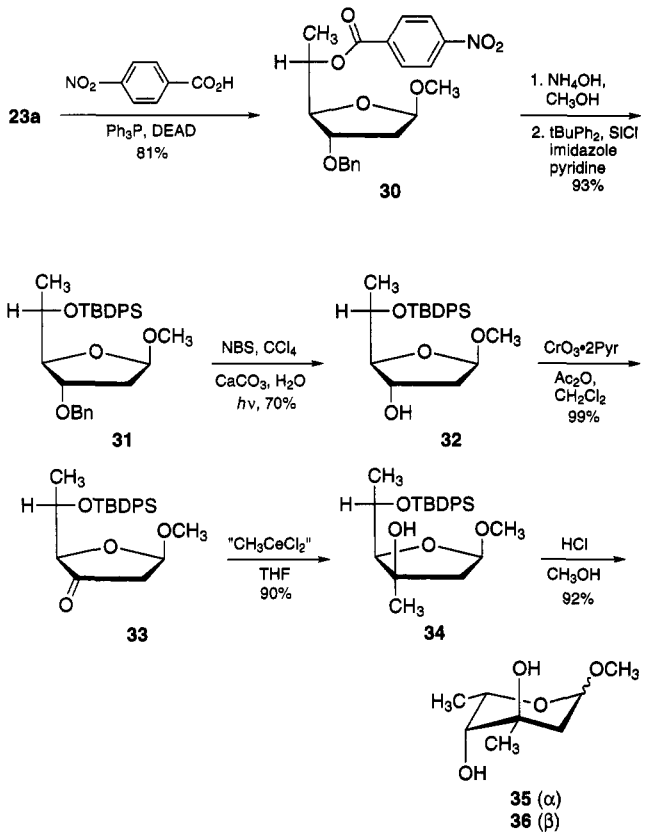
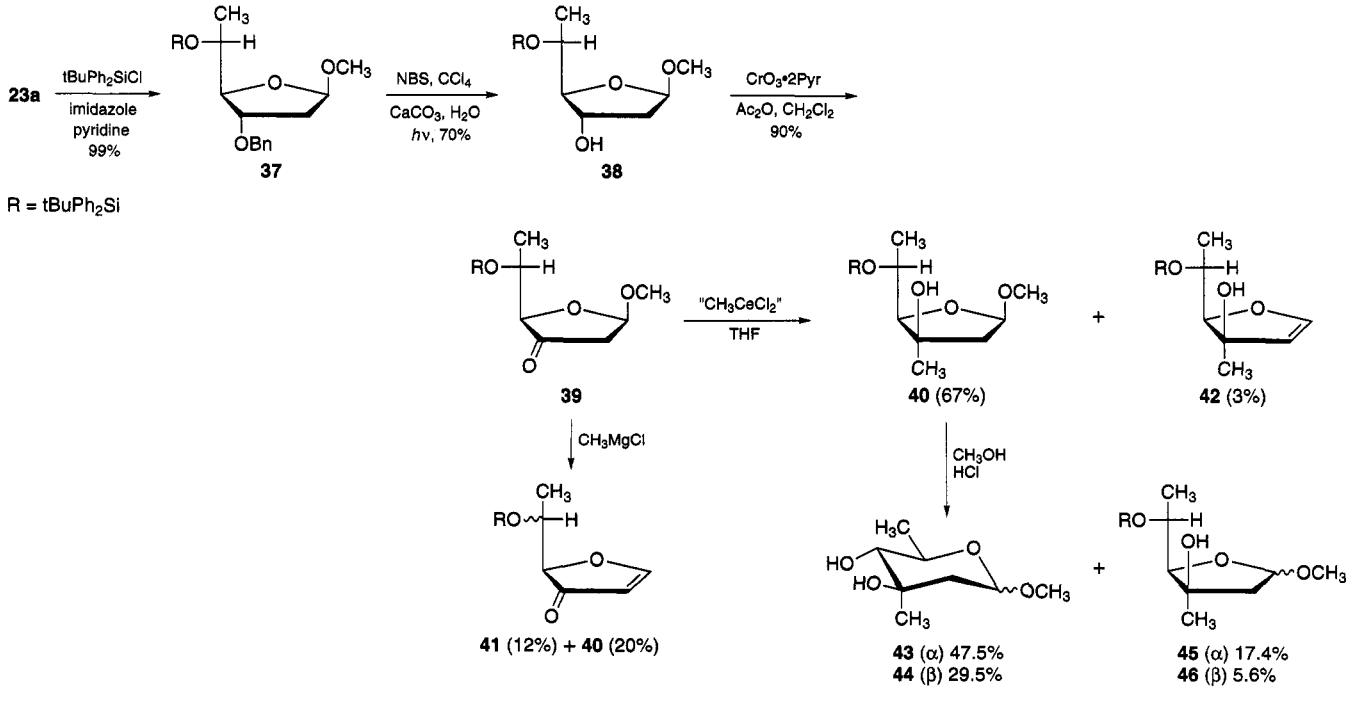
Scheme 4. Synthesis of Methyl Glycosides of Axenose



Mitsunobo reaction.[23] Treatment of **23a** with *p*-nitrobenzoic acid, triphenylphosphine, and DEAD gave ester **30** in 81% yield. Exchange of the ester group for a silyl ether was accomplished in two steps in high overall yield to give **31**. Debenzylation of **32** proved to be more dificult than expected; however, the photochemical procedure of Binkley and Hehemann[24] was found to be suitable. Competitive overoxidation of the benzyl ether to a benzoate ester was observed on scale-up; however, the desired alcohol could be obtained from the ester by hydrolysis with methanolic KOH. Oxidation of **32** to the 3-ulose **33** was then carried out with chromium trioxide/pyridine complex in the presence of acetic anhydride[25] in quantitative yield. Additions of either methylmagnesium halides or methyllithium to **33** occurred in low yield, and products resulting from elimination were observed. In the completion of the synthesis of D-evermicose (vide infra), products derived from elimination and elimination–enolization were isolated and characterized. We discovered that formation of these products could be avoided through the use of methylcerium in the addition step. The addition of methylcerium to **33** gave methyl-branched sugar **34** as a single diastereomer in 76% yield after purification by column chromatography. Desilylation and conversion to a mixture of α and β-methyl glycosides were accomplished in a single step by treatment of **34** with methanolic HCl. The ^{1}H-NMR spectra and melting points of the separated anomers matched those reported for 2,6-dideoxy-3-*C*-methyl-α-L-xylohexopyranoside and its β-anomer.[10,12]

The synthesis of methyl D-evermicoside was carried out similarly as shown in Scheme 5. Protection of **23a** as the silyl ether followed by debenzylation by the Binkley method and oxidation gave ulose **39**. The attempted addition of methylmagnesium chloride to **39** gave the desired methyl-branched product **40** in only 20% yield. A diastereomeric mixture of enones **41** was also obtained in 12% yield and characterized. The addition of methylcerium gave a 67% yield of **40** accompanied by 3% of allylic alcohol **42**. Treatment of **40** with methanolic HCl gave a mixture of furanose and pyranose α- and β-glycosides of evermicose which could be separated. The ^{1}H-NMR spectrum of the α-pyranoside matched that reported by Carey and Frank[26] for methyl 2,6-dideoxy-3-*C*-methyl-α-D-arabinohexopyranoside, while the ^{1}H-NMR data for the β-pyranoside matched that reported for the

Scheme 5. Synthesis of Methyl Glycosides of Evermicose



enantiomeric methyl glycoside of olivomycose.[27] Complete ^1H and ^{13}C-NMR data are given for the methyl glycosides of both axenose and evermicose in the experimental section. NMR data for the α- and β-furanosides of evermicose have not been published previously.

In conclusion, we have developed efficient and stereoselective syntheses of two branched-chain carbohydrates, L-axenose and D-evermicose, found in antibiotics of the axenomycin and everninomicin classes. Our approach differs from those reported previously in that it is based on the addition of organometallic reagents to pentodialdo-1,4-furanosides. A survey of the addition of organometallic reagents to the α- and β-anomers of a pentodialdo-1,4-furanoside was conducted in order to evaluate the factors which control the stereoselectivity of addition to the formyl group. Evidence for a mechanism involving a cyclic chelate was not observed in the case of the β-anomer, which gave as major products those diastereomers favored by the Felkin model. Selectivity for the product favored by chelation control was low in the α-anomer. These results were contrary to expectations based on the cyclic chelate model which is widely cited to rationalize the high asymmetric induction that is observed in addition reactions of this class of carbohydrate substrate. The stereoselectivity of addition to the formyl group of the dialdose was found to depend strongly on anomeric configuration. The major diastereomer proved to be a valuable intermediate for the synthesis of both axenose and evermicose, two components of antibiotics belonging to different enantiomeric series. The use of methylcerium to incorporate the branching methyl group at C-3 was found to be superior to either Grignard reagents or methyllithium, both of which gave side products resulting from elimination. The preparation of axenose on a gram-scale will facilitate studies of the synthesis of oligosaccharides that contain this branched-chain carbohydrate.

Experimental Section

General Methods. The ^1H NMR spectra were recorded at 300 or 400 MHz in $CDCl_3$ unless specified otherwise. J values are given in Hz. The ^{13}C NMR spectra were recorded at 75.4 or 100.6 MHz in $CDCl_3$ unless specified otherwise. Melting points were determined in an open capillary tube and are uncorrected. Elemental analysis were performed by the Analytical Research and Development Department of the R. W. Johnson Pharmaceutical Research Institute. TLC analysis was conducted on silica gel plates visualized with UV at 254 nm and/or treatment with 20% phosphomolybdic acid in C_2H_5OH and heat (180 °C). Preparative chromatographic separations were performed by flash chromatography on silica gel (230–300 mesh). Polarimetry were conducted with a 10-cm cell. Following extractive workup, organic solvents were dried with anhydrous $MgSO_4$ unless specified otherwise. Solvents were removed by rotary evaporation with bath temperature ≤50 °C. Title compounds were isolated as syrups unless specified otherwise.

Methyl 3-*O*-Benzyl-2-deoxy-α-D-*erythro*-pentofuranoside (16) and Methyl 3-*O*-Benzyl-2-deoxy-β-D-*erythro*-pentofuranoside (17). A solution of **15**[14,15] (26.7 g, 55.6 mmol) in CH_3OH (500 mL) was treated with HCl (15 mL of 3% anhydrous HCl/CH_3OH) and the reaction stirred at 20 °C for 3.5 h. The reaction mixture was treated with Ag_2CO_3 (2.5 g, 9.0 mmol), stirred an additional 15 min, filtered (filter aid), and evaporated. The crude product was chromatographed, eluting first with 25% ethyl acetate–hexane followed by 50% ethyl acetate–hexane, to afford the β-anomer (3.9 g, elutes first) and the α-anomer (3.5 g) for a combined yield of 56%.

Methyl 3-*O*-Benzyl-2-deoxy-α-D-*erythro*-pentofuranoside (16): ^1H NMR (400 MHz) δ 2.02 (d, 1H, J = 13.2), 2.20 (ddd, 1H, J = 13.2, 8.0, 5.0), 2.28 (br s, 1H), 3.38 (s, 3H), 3.55 (dd, 1H, J = 11.8, 3.8), 3.75 (dd, 1H, J = 11.8, 3.1), 3.98 (m, 1H), 4.13 (dd, 1H, J = 7.7, 3.8), 4.53 (AB q, 2H, $\Delta\nu$ 35.7, J_{ab} = 12.2), 5.12 (d, 1H, J = 5.0) 7.2–7.4 (m, 5H): ^{13}C NMR (100 MHz) δ 39.1, 55.0, 62.5, 71.7, 79.0, 83.0, 105.0, 127.6, 127.7, 128.1, 137.9; $[\alpha]^{22}_D$ +132.9° (*c* 1.00, CH_3OH). Anal. Calcd for $C_{14}H_{20}O_4$: C, 65.53; H, 7.61. Found: C, 65.31, H, 7.78.

Methyl 3-*O*-Benzyl-2-deoxy-β-D-*erythro*-pentofuranoside (17): ^1H NMR (400 MHz) δ 2.1–2.3 (m, 2H), 2.81 (br s, 1H), 3.37 (s, 3H), 3.58 (br s, 1H), 3.71 (d, 1H, J = 11.8), 4.2–4.3 (m, 2H), 4.48 (AB q, 2H, $\Delta\nu$ < 1, J_{ab} = 12.2), 5.12 (dd, 1H, J = 3.9, 1.3) 7.2–7.4 (m, 5H); ^{13}C NMR (100 MHz) δ 40.0, 55.3, 68.0, 71.6, 79.0, 85.5, 105.7, 127.6, 127.7, 128.4, 137.8; $[\alpha]^{22}_D$ −69.0° (*c* 1.00, CH_3OH). Anal. Calcd for $C_{14}H_{20}O_4$: C, 65.53; H, 7.61. Found: C, 65.48, H, 7.74.

Methyl 3-*O*-Benzyl-2-deoxy-5-β-D-*erythro*-pentodialdo-1,4-furanoside (19). Method A. To a solution of pyridine (8.00 g, 101 mmol) in CH_2Cl_2 (100 mL) was added chromium trioxide (5.00 g, 50.0 mmol) and the mixture stirred for 15 min at 20 °C. To the resulting dark red solution was added a solution of **17** (1.00 g, 4.20 mmol) in CH_2Cl_2 (20 mL). After being stirred for 15 min the reaction mixture was poured into saturated $NaHCO_3$, the layers were separated, the aqueous layer extracted with CH_2Cl_2 (1 × 50 mL), and the combined organic layers dried and evaporated. Two dilutions and evaporations with toluene (25 mL) afforded the title compound (0.75 g, 76%). The crude labile dialdose was used without further purification: ^1H NMR (400 MHz) δ 2.13 (dt, 1H, J = 13.6, 5.4), 2.22 (dd, 1H, J = 13.6, 7.0), 3.41 (s, 3H), 4.1–4.44 (m, 2H), 4.54 (AB q, 2H, $\Delta\nu$ = 27.4, J_{ab} = 11.8), 5.21 (d, 1H, J = 4.8), 7.2–7.5 (m, 5H), 9.65 (s, 7H); ^{13}C NMR (100 MHz) δ 39.8, 55.4, 71.9, 79.5, 88.2, 106.3, 127.7, 127.8, 128.4, 137.3, 202.5; $[\alpha]^{22}_D$ −96.4° (*c* 1.00, $CHCl_3$); IR ($CHCl_3$) ν 1730 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_4 \cdot 0.35H_2O$: C, 64.37; H, 6.94. Found: C, 64.32; H, 6.96.

Method B. A solution of oxalyl chloride (2.93 g, 23.1 mmol) in CH_2Cl_2 (50 mL) was cooled to −70 °C under argon, and a solution of dimethyl sulfoxide (3.61 g, 46.2 mmol) in CH_2Cl_2 (20 mL) was added at a rate so the temperature was ≤−50 °C. After the mixture was stirred for 2 min, a solution of **17** (5.00 g, 21.0 mmol) in CH_2Cl_2 (10 mL) was added at ≤−50 °C. After the mixture was stirred for an additional 15 min, triethylamine (14 mL) was added and the reaction was allowed to warm to 20 °C. The reaction was poured into H_2O (50 mL) and diethyl ether (150 mL), and the layers were separated. The organic layer was washed with H_2O (50 mL) and saturated NaCl and then dried. Evaporation afforded the title compound (4.90 g, 98%) with ^1H and ^{13}C NMR spectra identical to material prepared by method A. The crude labile dialdose was used without further purification.

Methyl 3-*O*-Benzyl-2-deoxy-5-α-D-*erythro*-pentodialdo-1,4-furanoside (18). Using the procedure to prepare **19** (method A) with pyridine (16.0 g, 0.202 mol) in CH_2Cl_2 (150 mL), chromium trioxide (10.0 g, 0.100 mol) and **16** (2.00 g, 8.40 mmol) in CH_2Cl_2 (20 mL) afforded the title compound (0.78 g, 39%). The crude labile dialdose was used without further purification: ^1H NMR (400 MHz) δ 2.1–2.2 (m, 2H), 3.44 (s, 3H), 4.13 (dd, 1H, J = 9.3, 3.8), 4.54 (d, 1H, J = 3.8), 4.48 (AB q, 2H, $\Delta\nu$ = 16.9, J_{ab} = 12.4), 5.19 (dd, 1H, J = 3.1, <1) 7.2–7.4 (m, 5H), 9.65 (s, 1H); ^{13}C NMR (100 MHz) δ 39.0, 55.6, 71.7, 78.2, 88.0, 105.9, 127.9, 128.0, 129.0, 137.8, 200.0.

Using the procedure to prepare **19** (method B) with oxalyl chloride (0.35 g, 2.8 mmol) in CH_2Cl_2 (5 mL), dimethyl sulfoxide (0.43 g, 5.5 mmol) in CH_2Cl_2 (2 mL), **16** (0.60 g, 2.5 mmol) in CH_2Cl_2 (2 mL) and triethylamine (1.7 mL) afforded the title compound (0.45 g, 76%) with ^1H and ^{13}C NMR spectra identical to material prepared by method A. The crude labile dialdose was used without further purification.

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(26) Carey, F. A.; Frank, W. C. *J. Org. Chem.* **1982**, *47*, 3548–3550.
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Methyl 3-*O*-Benzyl-2,6-dideoxy-β-D-*ribo*-hexofuranoside (23a). A solution of methylmagnesium chloride (45.0 mmol) in THF (45 mL) was chilled to −45 °C, and a solution of **19** (7.57 g, 32.0 mmol) in THF (25 mL) added while the temperature was maintained at −50 to −40 °C. After the mixture was stirred for 5 min, the temperature was allowed to rise to −20 °C, and the reaction was quenched (cautiously) with saturated NH_4Cl (15 mL). Diethyl ether (100 mL) and H_2O (25 mL) were added and the layers separated. The aqueous layer was extracted with diethyl ether (1 × 50 mL), and the combined organic layers were washed with H_2O (25 mL) and saturated NaCl and dried. Evaporation afforded the product and its C-5 epimer as an 85:15 mixture, total yield 93%. The major diastereomer was purified by chromatography using 33% ethyl acetate−hexane; the major D-*ribo* diastereomer (23a) elutes first, 4.98 g (62%): ^{1}H NMR (300 MHz) δ 1.18 (d, 3H, J = 6.6), 2.1−2.3 (m, 2H), 3.20 (br s, 1H), 3.38 (s, 3H), 3.85−3.95 (m, 1H), 4.04 (t, 1H, J = 3.0), 4.3−4.4 (m, 1H), 4.47 (s, 2H), 5.11 (dd, 1H, J = 5.0, 2.8), 7.31 (s, 5H); ^{13}C NMR (75 MHz) δ 18.4, 40.4, 55.4, 68.0, 71.4, 77.5, 89.6, 105.9, 127.6, 127.7, 128.5, 137.9; $[\alpha]^{22}_D$ −72.9° (*c* 1.00, CH_3OH). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.47, H, 8.03.

Methyl 3-*O*-Benzyl-2,6-dideoxy-5-*O*-(4-nitrobenzoyl)-α-L-*lyxo*-hexofuranoside (30). A mixture of **23a** (5.50 g, 21.8 mmol), triphenylphosphine (11.4 g, 43.6 mmol), 4-nitrobenzoic acid (7.28 g, 43.6 mmol), and benzene (300 mL) was stirred at 20 °C while diethyl diazodicarboxylate (7.59 g, 43.6 mmol) was added over 10 min. During the addition the reaction became homogeneous. After being stirred at 20 °C for 2 h, the reaction mixture was evaporated. The residue was chromatographed, eluting with 25% ethyl acetate−hexane, to give the title compound (7.06 g, 81%): ^{1}H NMR (300 MHz) δ 1.41 (d, 3H, J = 6.5), 2.00−2.15 (m, 1H), 2.32 (dd, 1H, J = 12.2, 6.6), 3.33 (s, 3H), 4.11 (dd, 1H, J = 7.0, 6.5), 4.20 (dd, 1H, J = 7.0, 6.6), 4.50 (AB q, Δν 20.3, J_{ab} = 11.6), 5.08 (d, 1H, J = 4.4), 5.24 (dq, 1H, J = 7.0, 6.5), 7.2−7.4 (m, 5H), 8.1−8.3 (m, 4H); ^{13}C NMR (75 MHz) δ 16.5, 39.3, 54.9, 72.0, 73.0, 78.5, 85.3, 105.1, 123.5, 127.8, 127.9, 128.5, 130.8, 135.9, 137.5, 150.5, 164.1. Anal. Calcd for $C_{21}H_{23}NO_7$: C, 62.84; H, 5.78; N, 3.49; $[\alpha]^{22}_D$ −18.7° (*c* 1.00, CH_3OH). Found: C, 62.76, H, 5.77; N, 3.31.

Methyl 5-*O*-(*tert*-Butyldiphenylsilyl)-3-*O*-benzyl-2,6-dideoxy-α-L-*lyxo*-hexofuranoside (31). A solution of **30** (6.90 g, 17.2 mmol) in CH_3OH (100 mL) was treated with concd NH_4OH (12 mL) and the mixture stirred for 72 h. After evaporation, the residue was chromatographed, eluting with 35% ethyl acetate−hexane, to afford 4.03 g (93%) of methyl 3-*O*-benzyl-2,6-dideoxy-α-L-*lyxo*-hexofuranoside: ^{1}H NMR (300 MHz) δ 1.20 (d, 3H, J = 6.4), 2.1−2.3 (m, 2H), 2.86 (d, 1H, J = 7.5), 3.38 (s, 3H), 3.6−3.75 (m, 1H), 3.99 (t, 1H, J = 3.7), 4.1−4.3 (m, 1H), 4.47 (AB q, 2H, Δν = 15.6, J_{ab} = 11.7), 5.11 (dd, 1H, J = 5.5, 2.2) 7.2−7.4 (m, 5H); ^{13}C NMR (75 MHz) δ 19.6, 39.8, 55.4, 68.6, 71.6, 79.8, 89.0, 105.8, 127.7, 127.8, 128.4, 137.8; $[\alpha]^{22}_D$ −35.5° (*c* 1.00, CH_3OH). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.64, H, 7.92.

A solution of methyl 3-*O*-benzyl-2,6-dideoxy-α-L-*lyxo*-hexofuranoside (7.61 g, 30.16 mmol), *tert*-butyldiphenylsilyl chloride (8.70 g, 31.7 mmol), and imidazole (4.31 g, 63.3 mmol) in dry pyridine (60 mL) was allowed to stir at 20 °C for 17 h. The reaction was evaporated and the residue partitioned between diethyl ether (200 mL) and H_2O (100 mL). The separated organic layer was washed with H_2O (2 × 100 mL) and saturated NaCl (1 × 50 mL) and dried. Evaporation afforded the product (14.8 g, 100%): ^{1}H NMR δ 1.05 (d 3H), 1.06 (s, 9H), 2.0−2.2 (m, 2H), 3.27 (s, 3H), 3.9−4.0 (m, 2H, H-4), 4.24 (q, 1H, J = 5.9), 4.34 (AB q, Δν 14.8, J_{ab} = 11.8), 5.0−5.1 (m, 1H) 7.2−7.4 (m, 10H), 7.6 −7.8 (m, 5H); ^{13}C NMR (75 MHz) δ 19.1, 19.3, 27.0, 39.5, 55.1, 70.4, 71.8, 78.3, 87.9, 105.0, 127.4, 127.6, 127.7, 127.7, 128.4, 129.5, 129.6, 134.6, 134.9, 136.0, 136.2, 138.1; $[\alpha]^{22}_D$ −17.9° (*c* 1.00, CH_3OH). Anal. Calcd for $C_{30}H_{38}O_4Si$: C, 73.43; H, 7.81. Found: C, 73.40; H, 7.88.

Methyl 5-*O*-(*tert*-Butyldiphenylsilyl)-2,6-dideoxy-α-L-*lyxo*-hexofuranoside (32). A mixture of **31** (15.3 g, 31.3 mmol), *N*-bromosuccinimide (7.79 g, 43.8 mmol), calcium carbonate (13.8 g, 137 mmol), H_2O (30 mL), and carbon tetrachloride (400 mL) was sparged with N_2 for 30 min and then the reaction irradiated with visible light (2 × 150 W floodlamps) for 30 min at 20−25 °C (water bath). The reaction mixture was filtered, the layers were separated, and the organic layer was dried (Na_2SO_4) and evaporated in vacuo. The residue was dissolved in a solution of KOH (2.0 g) in CH_3OH (150 mL) and the resulting mixture stirred for 18 h at room temperature. Following the addition of solid NH_4Cl (2.0 g) and evaporation, the product was isolated by chromatography eluting with 20% ethyl acetate−hexane to give 8.90 g (70%) of **32**: ^{1}H NMR (300 MHz) δ 1.07 (s, 9H), 1.08 (d, 3H), 1.88 (d, 1H, J = 3.1), 1.88−2.08 (m, 1H), 2.17−2.24 (m, 1H), 3.26 (s, 3H), 3.79 (dd, 1H, J = 6.5, 5.0), 4.10 (dq, 1H, J = 6.3, 2.0), 4.52−4.60 (m, 1H), 4.96 (dd, 1H, J = 5.2, 1.1) 7.3−7.5 (m, 6H), 7.6−7.8 (m, 4H); ^{13}C NMR (75 MHz) δ 17.9, 19.3, 27.0, 40.9), 54.9, 69.9, 70.0, 87.3, 104.2, 127.6, 127.7, 129.7, 129.8, 133.5, 134.0, 135.8, 135.9; $[\alpha]^{22}_D$ −19.7° (*c* 1.00, CH_3OH). Anal. Calcd for $C_{23}H_{32}O_4Si$: C, 68.96; H, 8.05. Found: C, 68.55; H, 8.25.

Methyl 5-*O*-(*tert*-Butyldiphenylsilyl)-2,6-dideoxy-α-L-*threo*-hexofuranosid-3-ulose (33). To a mixture of chromium trioxide (2.03 g, 20.3 mmol) in CH_2Cl_2 (60 mL) was added pyridine (3.21 g, 40.6 mmol) and the mixture stirred under argon at 20 °C for 15 min. To the resulting dark red solution was added a solution of **32** (2.03 g, 5.08 mmol) in CH_2Cl_2 (80 mL) followed immediately by acetic anhydride (2.07 g, 20.3 mmol). After being stirred for 15 min, the reaction mixture was filtered through a plug of silica gel and the plug washed with ethyl acetate (150 mL). The combined colorless filtrate and washings were evaporated with toluene to afford the title compound (2.00 g, 99%): ^{1}H NMR (300 MHz) δ 1.00 (s, 9H), 1.08 (d, 3H, J = 6.5), 2.54 (ddd, 1H, J = 18.6, 2.3, 1), 2.76 (dd, 1H, J = 18.6, 6.0), 3.50 (s, 3H), 3.85 (d, 1H, J = 3.1), 4.12 (dq, 1H, J = 6.0, 3.1), 5.38 (dd, 1H, J = 6.5, 2.3), 7.3−7.5 (m, 6H), 7.7−7.9 (m, 4H); ^{13}C NMR (75 MHz) δ 19.3, 19.7, 26.7, 43.8, 55.0, 69.8, 84.6, 101.9, 127.3, 127.5, 129.4, 129.6, 133.1, 134.5, 135.9, 136.0, 212.1; $[\alpha]^{22}_D$ +9.6° (*c* 1.00, CH_3OH); IR ($CHCl_3$) ν 1760 cm^{-1}. Anal. Calcd for $C_{23}H_{30}O_4Si$: C, 69.31; H, 7.59. Found: C, 69.24; H, 7.58.

Methyl 5-*O*-(*tert*-Butyldiphenylsilyl)-2,6-dideoxy-3-*C*-methyl-α-L-*xylo*-hexofuranoside (34). Cerium trichloride (2.46 g, 10.0 mmol) was dried in a 100 mL round bottom flask in vacuo at 140 °C (silicone oil bath) for 2 h. After the cerium chloride was cooled under argon to 0 °C, THF (30 mL) was added and the mixture sonicated[28] for 1 h. The suspension was cooled to −75 °C, and methyllithium (7.2 mL of 1.4 M methyllithium in diethyl ether, 10 mmol) was added dropwise (temp ≤−70 °C). After the mixture was stirred for an additional 1 h at −75 °C, a solution of **33** (1.98 g, 4.97 mmol) in THF (10 mL) was added and the reaction stirred for 10 min. Saturated NH_4Cl (5 mL) was added and the reaction allowed to warm to 20 °C. Additional water (20 mL) was added, the layers were separated, the aqueous layer was extracted with diethyl ether (2 × 25 mL), and the combined organic layers were washed with water, saturated NaCl, and dried (Na_2SO_4). Evaporation afforded the crude product (1.90 g, 92%) which was further purified by chromatography eluting with 10% ethyl acetate−hexane to give 1.57 g (76%) of **34**: ^{1}H NMR (300 MHz) δ 1.07 (s, 9H), 1.15 (d, 3H, J = 6.3), 1.35 (s, 3H), 2.05 (d, 2H, J = 2.4), 3.20 (s, 3H), 3.46 (s, 1H), 3.67 (d, 1H, J = 6.9), 4.01 (dq, 1H, J = 6.9, 6.3) 4.96 (dd, 1H, J = 2.4, 2.4) 7.3−7.5 (m, 6H), 7.7−7.8 (m, 4H); ^{13}C NMR (75 MHz) δ 19.3, 20.4, 24.6, 26.9, 48.4, 54.7, 71.6, 77.0, 91.43, 103.7, 127.3, 127.4, 129.4, 129.4, 134.0, 135.0, 136.0, 136.1; $[\alpha]^{22}_D$ −22.8° (*c* 1.00, CH_3OH). Anal. Calcd for $C_{24}H_{34}O_4Si$: C, 69.53; H, 8.27. Found: C, 69.85; H,8.28.

Methyl Glycosides of Axenose (35/36). A solution of **34** (1.40 g, 3.38 mmol) in CH_3OH (50 mL) was treated with HCl (5.7 mL of 0.68 M HCl in CH_3OH (3.7 mmol, 1.1 equiv)) and the reaction stirred for 3 h at 50 °C. The reaction was quenched with Ag_2CO_3 (1.5 g, 5.4 mmol) and, after being stirred for 30 min at 20 °C, was filtered (filter aid) and the filtrate evaporated. The resulting mixture of methyl α,β-

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pyranosides with small amounts of the methyl α,β- furanosides (total yield 0.545 g, 91%) was separated by chromatography (30% ethyl acetate–hexane) to give the title compounds.

First eluting product (0.150 g; 27%), methyl 2,6-dideoxy-3-*C*-methyl-α-L-*xylo*-hexopyranoside (**35**): ^{1}H NMR (300 MHz) δ 1.25 (s, 3H), 1.26 (d, 3H, J = 6.6), 1.67 (d, 1H, J = 14.6), 1.84 (d, 1H, J = 8.1), 1.92 (dd, 1H, J = 14.6, 3.8), 3.14 (d, 1H, J = 8.1), 3.38 (s, 3H), 4.04 (s, 1H), 4.30 (q, 1H, J = 6.6), 4.80 (d, 1H, J = 3.8); ^{13}C NMR (75 MHz) δ 16.7, 26.0, 35.4, 55.2, 62.5, 70.2, 74.5, 99.0; mp 103–104 °C; $[\alpha]^{22}_D$ −148° (*c* 0.100, $CHCl_3$) (lit.[10] mp 101–103 °C; $[\alpha]^{20}_D$ −140° ($CHCl_3$)).

Second eluting product (0.310 g, 57%), methyl 2,6-dideoxy-3-*C*-methyl-β-L-*xylo*-hexopyranoside (**36**): ^{1}H NMR (300 MHz) δ 1.28 (d, 3H, J = 6.6), 1.34 (s, 3H), 1.47 (s, 1H), 1.55–1.75 (m, 2H), 2.10 (d, 1H, J = 10.2), 2.98 (dd, 1H, J = 10.2, 0.7), 3.50 (s, 3H), 4.13 (dq, 1H, J = 6.6, 0.7), 4.62 (dd, 1H, J = 9.2); ^{13}C NMR (75 MHz) δ 16.6, 27.8, 39.0, 56.5, 68.9, 72.5, 74.4, 100.4; mp 117–119 °C; $[\alpha]^{22}_D$ +40.0° (*c* 0.100, $CHCl_3$) (lit.[10] mp 122–123 °C; $[\alpha]^{20}_D$ +38° ($CHCl_3$)).

Methyl 5-*O*-(*tert*-Butyldiphenylsilyl)-3-*O*-benzyl-2,6-dideoxy-β-D-*ribo*-hexofuranoside (37). A mixture of **23a** (4.06 g, 16.1 mmol), imidazole (2.41 g, 35.4 mmol), *tert*-butyldiphenylsilyl chloride (4.42 g, 16.1 mmol), and pyridine (20 mL) was warmed to 40 °C and then allowed to stir for 17 h at 20 °C. The reaction mixture was evaporated and then partitioned between H_2O (25 mL) and diethyl ether (50 mL). The separated organic layer was washed with H_2O and brine, dried, and evaporated to afford **37** (7.83 g, 99%): ^{1}H NMR (300 MHz) δ 1.05 (s, 9H), 1.10 (d, J = 6.1, 3H), 1.85 (dq, 1H, J = 3.7, 6.4, 13.9), 2.10 (dq, 1H, J = 3.5, 5.5, 13.9), 3.28 (s, 3H), 3.84 (dq, 1H, J = 7.5, 6.1), 4.10 (dd, 1H, J = 7.5, 2.2), 4.20–4.30 (m, 1H), 4.44 (AB q, Δν 20.2, J_{ab} = 11.2), 5.08 (dd, 1H, J = 5.5, 3.7) 7.2–7.8 (m, 15H); ^{13}C NMR (75 MHz) δ 19.3, 20.4, 27.0, 38.7, 55.5, 70.2, 71.0, 79.9, 88.8, 105.8, 127.4, 127.4, 127.5, 127.5, 127.6, 127.6, 128.2, 128.3, 129.6, 129.6, 136.0, 136.1; $[\alpha]^{22}_D$ −24.9° (*c* 1.00, CH_3OH). Anal. Calcd for $C_{30}H_{38}O_4Si$: C, 73.43; H, 7.81. Found: C, 73.12; H, 7.83.

Methyl 5-*O*-(*tert*-Butyldiphenylsilyl)-2,6-dideoxy-β-D-*ribo*-hexofuranoside (38). Using the procedure for **32** with **37** (1.51 g, 3.08 mmol), *N*-bromosuccinimide (0.77 g, 4.3 mmol), calcium carbonate (0.43 g, 4.3 mmol), H_2O (3 mL), carbon tetrachloride (30 mL), KOH (0.30 g) in CH_3OH (50 mL), and NH_4Cl (0.5 g) gave 1.00 g (62%) of the title compound: ^{1}H NMR (300 MHz) δ 1.06 (s, 9H), 1.11 (d, 3H, J = 6.0), 1.90 (br s, 1H), 1.98–2.03 (m, 2H) 3.22 (s, 3H), 3.64 (dd, 1H, J = 8.3, 4), 3.78 (dq, 1H, J = 6.0, 4), 4.46 (m, 1H), 4.98 (dd, 1H, J = 4.0. 3.5), 7.3–7.5 (m, 6H), 7.7–7.9 (m, 4H); ^{13}C NMR (75 MHz) δ 19.2, 20.9, 27.0, 40.9, 55.0, 71.8, 73.2, 90.3, 104.9, 127.5, 127.6, 129.6, 129.7, 133.6, 134.2, 135.7, 135.8; $[\alpha]^{22}_D$ −32.7° (*c* 1.00, CH_3OH). Anal. Calcd for $C_{23}H_{32}O_4Si$: C, 68.96; H, 8.05. Found: C, 68.79; H, 8.10.

Methyl 5-*O*-(*tert*-Butyldiphenylsilyl)-2,6-dideoxy-β-D-*erythro*-hexofuranosid-3-ulose (39). Using the procedure for **33** with chromium trioxide (1.00 g, 10.0 mmol) in CH_2Cl_2 (40 mL), pyridine (1.58 g, 20.0 mmol), **38** (1.00 g, 2.50 mmol) in CH_2Cl_2 (40 mL), acetic anhydride (1.02 g, 10.0 mmol) afforded **39** (0.90 g, 90%): ^{1}H NMR (300 MHz) δ 1.04 (d, 3H, J = 6.5), 1.07 (s, 9H), 2.37 (dd, 1H, J = 18.4, 3), 2.67 (dd, 1H, J = 18.4, 5.8), 3.48 (s, 3H), 3.96 (d, 1H, J = 3.7), 4.19 (dq, 1H, J = 6.0, 3.7), 5.27 (dd, 1H, J = 5.8, 3), 7.3–7.5 (m, 6H), 7.7–7.9 (m, 4H); ^{13}C NMR (75 MHz) δ 18.9, 19.1, 26.7, 43.5, 55.3, 70.0, 84.1, 101.6, 127.4, 127.4, 129.5, 129.5, 133.6, 134.2, 135.8, 135.8, 211.0; $[\alpha]^{22}_D$ −33.4° (*c* 1.00, $CHCl_3$); IR ($CHCl_3$) ν 1760 cm^{-1}. Anal. Calcd for $C_{23}H_{30}O_4Si$: C, 69.31; H, 7.59. Found: C, 69.32; H, 7.59.

Methyl 5-*O*-(*tert*-Butyldiphenylsilyl)-2,6-dideoxy-3-*C*-methyl-β-D-*arabino*-hexofuranoside (40). Method A: Grignard Method. To a chilled solution of methyl magnesium chloride (3.60 mmol) in THF (6.2 mL) at −20 °C was added **39** (1.26 g, 3.16 mmol) in THF (5 mL). After the mixture was stirred for 10 min, saturated NH_4Cl (5 mL) and diethyl ether (10 mL) were added. After the layers were separated and the aqueous layer was extracted with diethyl ether (10 mL), the combined organics were washed with H_2O and brine and dried and the solvents evaporated. The residue was chromatographed eluting with 15% ethyl acetate–hexane to afford **40** (0.26 g, 20%) and a mixture of diastereomers **41** (0.14 g (12%), see NMR data below): ^{1}H NMR (300 MHz) δ 1.04 (s, 9H), 1.11 (d, 3H, J = 6.2), 1.30 (s, 3H), 2.02 (d, 1H, J = 3.8), 2.03 (s, 1H), 3.31 (s, 3H), 3.38 (br s, 1H), 3.71 (d, 1H, J = 5.4), 4.22 (dq, 1H, J = 6.2, 5.4), 4.95 (dd, 1H, J = 3.9, 1.4) 7.3–7.5 (m, 6H), 7.7–7.8 (m, 4H); ^{13}C NMR (75 MHz) δ 19.3, 20.6, 24.6, 27.0, 47.6, 55.0, 69.8, 77.2, 91.3, 104.1, 127.4, 127.6, 129.5, 129.6, 134.8, 135.9; $[\alpha]^{22}_D$ −45.2° (*c* 1.00, CH_3OH). Anal. Calcd for $C_{24}H_{34}O_4Si$: C, 69.53; H, 8.27. Found: C, 69.36; H, 8.31.

Method B. Using the procedure for **34** with cerium trichloride (1.11 g, 4.52 mmol), methyllithium (3.20 mL of 1.40 M methyllithium in diethyl ether, 4.48 mmol), and **39** (0.80 g, 2.0 mmol) in THF (4 mL) afforded 0.56 g (67%) of **40** identical to that prepared using method A by ^{1}H and ^{13}C NMR and 23 mg (3%) of **42** (see NMR data below).

2(*R,S*)-[2(*R*)-[(Diphenyl-*tert*-butylsilyl)oxy]ethyl]-3*H*-4,5-dihydrofuran-3-one (41): ^{1}H NMR (300 MHz) δ 0.96 (s, 9H), 1.05 (s, 9H), 4.18 (d, 1H, J = 2.9), 4.32 (d, 1H, J = 1.9), 4.3–4.4 (m, 2H) 5.64 (d, 1H, J = 2.5), 5.70 (d, 1H, J = 2.5), 7.3–7.5 (m, 12H), 7.6–7.8 (m, 8H), 8.22 (d, 1H, J = 2.5), 8.26 (d, 1H, J = 2.5); ^{13}C NMR (75 MHz) δ 16.5, 19.2, 19.4, 19.94, 26.7, 26.8, 68.8, 69.3, 87.7, 88.1, 108.1, 108.1, 127.4, 127.6, 127.6, 127.7, 129.5, 129.7, 129.8, 129.8, 132.6, 133.3, 133.6, 134.3, 135.8, 136.0, 178.6, 178.7, 202.4, 203.0.

(2*R*,3*R*)-2-[(*R*)-[(Diphenyl-*tert*-butylsilyl)oxy]ethyl]-3-hydroxy-3-methyl-4,5-dihydro-furan (42): ^{1}H NMR (300 MHz) δ 1.05 (s, 9H), 1.27 (d, 3H, J = 6.7, 1.53 (s, 3H), 3.85 (d, 1H, J = 3.2), 4.31 (s, 1H, 4.35 (dq, 1H, J = 6.7, 3.2), 5.10 (d, 1H, J = 2.7), 6.40 (d, 1H, J = 2.7), 7.3–7.5 (m, 6H), 7.6–7.8 (m, 4H); ^{13}C NMR (75 MHz) δ 19.3, 26.9, 29.2, 71.2, 81.3, 89.1, 110.3, 127.6, 129.8, 129.9, 132.4, 133.7, 135.9, 136.2,146.8.

Methyl Glycosides of Evermicose (43–46). A solution of **40** (0.55 g, 1.3 mmol) in CH_3OH (20 mL) was treated with 2 mL of 3% HCl in CH_3OH (1.6 mmol of HCl) and the reaction stirred for 2 h at 50 °C. The reaction was treated with silver carbonate (0.50 g, 1.8 mmol), filtered, and evaporated. The resulting crude mixture of α,β-methyl furanosides and α,β-methyl pyranosides was separated by chromatography (eluting with 30% hexane–ethyl acetate) to give samples of each diastereomer and some overlapping fractions, total yield 0.216 g (92%).

First eluting product (20 mg, comprising 5.6% of crude mixture by NMR), methyl 2,6-dideoxy-3-*C*-methyl-β-D-*arabino*-hexofuranoside (**46**): ^{1}H NMR (300 MHz) δ 1.35 (d, 3H, J = 6.3), 1.47 (s, 3H), 2.05 (dd, 1H, J = 13.6, 4.1), 2.13 (d, 1H, J = 13.6), 2.96 (d, 1H, J = 3.0), 3.35 (s, 3H), 3.52 (d, 1H, J = 8.7), 3.65 (s, 1H), 3.91 (m, 1H), 4.94 (d, 1H, J = 4.1); ^{13}C NMR (75 MHz) δ 20.3, 26.4, 48.0, 54.7, 69.2, 78.4, 90.2, 104.6.

Second eluting product (35 mg, comprising 17.4% of crude mixture by NMR), methyl 2,6-dideoxy-3-*C*-methyl-α-D-*arabino*-hexofuranoside (**45**): ^{1}H NMR (300 MHz) δ 1.38 (d, 3H, J = 6.6), 1.51 (s, 3H), 1.98 (dd, 1H, J = 14.0, 3.5), 2.30 (dd, 1H, J = 14.0, 5.7), 2.70 (br s, 1H), 3.35 (s, 4H), 3.52 (d, 1H, J = 6.1), 4.11 (dq, 1H, J = 6.6, 6.1), 5.07 (dd, 1H, J = 5.7, 3.5); ^{13}C NMR (75 MHz) δ 19.9, 28.1, 50.2, 55.0, 68.2, 79.3, 85.9, 103.6; $[\alpha]^{22}_D$ +65.7° (*c* 3.21, $CHCl_3$).

Third eluting product (17.7 mg, comprising 47.5% of crude mixture by NMR), methyl 2,6-dideoxy-3-*C*-methyl-α-D-*arabino*-hexopyranoside (**43**): ^{1}H NMR (300 MHz) δ 1.30 (d, 3H, J = 6.2), 1.40 (s, 3H), 1.86 (dd, 1H, J = 13.6, 4.3), 2.00 (dd, 1H, J = 13.6, 1), 2.5 (vbr s, 2H), 3.27 (d, 1H, J = 9.6), 3.35 (s, 3H), 3.61 (m, 1H), 4.71 (dd, 1H, J = 4.3, 1); ^{13}C NMR (75 MHz) δ 18.2, 22.1, 43.2, 54.8, 66.6, 72.0, 79.5, 98.3; $[\alpha]^{22}_D$ +132.0° (*c* 1.00, C_2H_5OH).

Fourth eluting product (13.4 mg, comprising 29.5% of crude mixture by NMR), methyl 2,6-dideoxy-3-*C*-methyl-β-D-*arabino*-hexopyranoside (**44**): ^{1}H NMR (300 MHz) δ 1.30 (s, 3H), 1.35 (d, 3H, J = 6.1), 1.72 (dd, 1H, J = 12.9, 9.6), 1.80 (br s, 1H), 2.00 (d, 1H, J = 3.2) overlapping 2.02 (dd, 2H, J = 12.9, 2.1), 3.36 (dd, 1H, J = 9.4,3.2), 3.41 (m, 1H), 3.49 (s, 3H), 4.44 (dd, 1H, J = 9.6, 2.1); ^{13}C NMR (75 MHz) δ 18.4, 20.4, 45.0, 56.5, 71.1, 72.2, 79.3, 100.4.

2,6-Dideoxy-3-*C*-methyl-β-D-*arabino*-hexose (Evermicose). A mixture of **43/44** (130 mg, 0.74 mmol) and 0.1 M H_2SO_4 (10 mL) was stirred at 40 °C for 2 h. The reaction was

treated with $BaCO_3$ (1 g) and, after being stired for an additional 15 min, was filtered (filter aid) and evaporated in vacuo. The residue was crystallized from acetone (0.5 mL) to afford evermicose (77 mg, 64%): mp 101–103 °C; ^1H NMR (D_2O, 300 MHz) δ 1.19 (s, 3H), 1.20 (d, 3H, J = 6), 1.07 (dd, 1H, J = 12.5, 10.0), 1.99 (dd, 1H, J = 12.5, 1.9), 3.13 (d, 1H, J = 10.2), 3.43 (m, 1H), 4.88 (dd, 1H, J = 10.0, 1.9); ^{13}C NMR (D_2O, 75 MHz) δ 19.1, 20.6, 44.5, 72.6, 73.1, 79.9, 94.3; $[\alpha]^{22}_D$ +20.5° (c 1.00, H_2O, 24 h) (lit.[13] mp 108–112 °C; $[\alpha]_D$ +20.7° (H_2O, 24 h).

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Supplementary Material Available: Copies of ^1H NMR spectra of **18, 19, 41,** and **42** (4 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.