Available online at www.sciencedirect.com
ScienceDirect
Carbohydrate Research 341 (2006) 2658–2668
Carbohydrate RESEARCH

Studies on enolization of *aldehydo*-aldose derivatives

Stephen J. Eitelman† and Derek Horton*

Department of Chemistry, American University, Washington, DC 20016, USA

Received 19 June 2006; received in revised form 1 August 2006; accepted 9 August 2006
Available online 18 September 2006

Abstract—Acetylation of the 2,3-*O*-isopropylidene derivative (**1**) of D-glyceraldehyde with hot acetic anhydride in the presence of sodium acetate give a mixture of (*Z*)- and (*E*)-enol acetates (**2** and **3**), together with the acetylated racemic aldehydrol (**4**) of **1**. Likewise, the acyclic *aldehydo* 2,3:4,5-diisopropylidene acetals of D- and L-arabinose, D-xylose, and D-ribose underwent conversion into enol acetates, with the (*Z*) isomers preponderating, and convertible photochemically into the corresponding (*E*) isomers. Under other conditions of acetylation, the *aldehydo* derivatives were converted into the corresponding aldehydrol diacetates.

Keywords: Enol acetates; *aldehydo*-Sugars; Aldehydrol diacetates; Photoisomerization; Aldehydrols

1. Introduction

The biochemically important interconversion of aldoses and ketoses, in particular the interconversion of D-glucose, D-mannose, and D-fructose, is presumed to take place via 1,2-enediol or 1,2-enediolate intermediates,[1,2] but such intermediates have never been isolated as stable entities.[3,4] The current work was undertaken in an attempt to capture such 1,2-enediol structures as stable derivatives and to study their properties.[5,6] While ketones may be converted without difficulty into enol esters or enol ethers, aldehydes do not react so readily to give stable enol derivatives.[7]

In this study, we have examined the behavior of substituted aldopentoses and an aldotriose, each having a free aldehyde group, under conditions of base-catalyzed acetylation, and show that under suitable conditions a pair of geometrically isomeric enol acetates can be isolated as stable products. Their identities have been established and conditions for their interconversion examined. Under different conditions of base-catalyzed acetylation, the *aldehydo* sugar derivatives undergo conversion into diacetates of the corresponding aldehydrol. The alkene functionality in these stable enolic sugar derivatives offers a wide range of useful potential for synthesis, as well as for studies on the ketose–enediol–aldose interconversion.

2. Results and discussion

Attempts to produce enol acetates from *aldehydo* sugars centered initially on the choice of acetylating reagents. When *aldehydo*-D-glucose pentaacetate was treated with pyridine–acetic anhydride, only modest yields of the acetylated aldehydrol were produced,[8] notwithstanding the fact that similar reagents have been commonly used for the preparation of enol acetates of keto sugar derivatives.[9–12]

Treatment of *aldehydo* sugar derivatives with alkaline acetylation reagents should, in principle, lead to the formation of two different enolate anions that may be captured by excess acetic anhydride. Provided that they do not revert to the original aldehyde under the reaction conditions, such species as aldehydrols, hemihydrates, and/or oligomers of aldehydes should become acetylated without other structural changes. Thus, a fully derivatized *aldehydo* sugar may yield mixtures containing various proportions of isomeric enol acetates, acetylated

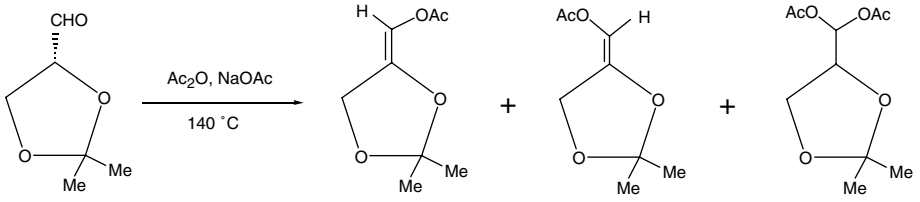
* Corresponding author. Tel.: +1 202 885 1767; fax: +1 202 885 1095; e-mail: carbchm@american.edu
† Present address: Center for Marine Science, University of North Carolina at Wilmington, Wilmington, NC 28407, USA.

0008-6215/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2006.08.009

aldehydrols, and hemihydrates, as well as possible oligomers (dimers and trimers of the aldehyde).

2.1. Acetylation of 2,3-*O*-isopropylidene-D-glyceraldehyde

The simple system 2,3-*O*-isopropylidene-D-glyceraldehyde (**1**) was chosen as a starting point both for its ease of synthesis and a clue to the expected behavior of the aldehyde from an earlier work from our laboratory.[13] When it was treated with excess ethynylmagnesium bromide and the subsequent chain extended, propargylic alcohol sugar derivatives were acetylated with acetic anhydride–sodium acetate, the expected acetates of the Grignard adducts were produced, together with a small proportion of a substance considered, from examination of its NMR spectrum, to be the acetylated aldehydrol of the starting aldehyde.



1 **2** **3** **4**

The chiral aldehyde **1** was prepared[14] from the 1,2:5,6-diisopropylidene acetal of D-mannitol by a 3,4-glycol cleavage with lead tetraacetate in benzene solution, and purified by distillation. It was boiled under reflux in acetic anhydride containing 1 equiv of anhydrous sodium acetate. Alternatively, the aldehyde was dissolved at room temperature in acetic anhydride, sodium acetate was then added, and the stirred suspension quickly heated to reflux. In each case, TLC analysis on Silica Gel G with 3:2 ether–benzene eluant showed the rapid (30 min) consumption of the starting material ($R_f = 0.38$) and the appearance of three new components, **2** (major), **3** (minor), and **4** (major) having R_f values equal to 0.89, 0.79, and 0.55, respectively, always in the same relative ratio. The isolated mixture was subjected to fractional high-vacuum distillation, which separated the higher-boiling, more-polar component **4** from the lower-boiling, less-polar mixture of **2** and **3**. The yield of **2** + **3** was approximately equal to that of **4**.

Component **4** crystallized spontaneously, mp 40–43 °C, was optically inactive, had the molecular formula $C_{10}H_{16}O_6$, and on the basis of NMR, IR, and mass spectrometry (see Section 3) was identified as the racemic aldehydrol 1,1-diacetate **4** of the starting aldehyde **1**. Its proton NMR data were in concordance with the data reported earlier[13] for a syrupy minor side product formed alongside Grignard addition products prepared from aldehyde **1**. It is noteworthy that the $J_{1,2}$ spin coupling for **4** (4.7 Hz) is significantly larger than that (1.7 Hz) for the precursor aldehyde **1**, indicating an important conformational contribution of the rotamer having H-1 antiparallel to H-2 in the aldehydrol derivative **4**.

The mixture of products **2** and **3** was resolved by column chromatography to afford the homogeneous major product **2** as an optically inactive oil, $C_8H_{12}O_4$, whose IR, NMR, and mass-spectral data (see Section 3) indicated it to be an enol acetate of the starting aldehyde, and it was considered (see later) to be the (*Z*) isomer. The minor component was not readily separable from the major one, but it was clearly the geometric isomer of the major component, as the oily 1:1 mixture of the two components showed an identical mass spectrum and elemental analysis as the isolated major component, and the mixture showed two sets of signals, one for the pure major component and a second set having slightly different chemical shifts that were attributed to the minor component, the (*E*) isomer.

2.1.1. Spectroscopic analysis. The NMR spectra of the major enol acetate showed a 3-proton singlet at δ 2.24 for the acetate methyl group and a 6-proton singlet at δ 1.56 for the isopropylidene methyl groups, along with a one-proton narrow triplet at δ 6.58 for the vinylic proton showing a $J_{1,3}$ coupling of 1.5 Hz to the methylene group that resonated as a doublet at δ 4.60. For the minor isomer these δ values were 2.18, 1.50, 7.00, and 4.70, respectively, while the vinyl proton signal appeared downfield at δ 7.0, and $J_{1,3}$ was 2.0 Hz. Assuming approximately planar geometry about the double bond for both **2** and **3**, the chemical-shift differences between the sets of vinyl or methylene protons may be rationalized by taking into account their proximity to O-2 and/or the carbonyl group. The vinyl and methylene signals of the *Z* enol acetate should be relatively upfield compared to those of the *E* isomer, whose H-1 resonance is influenced by the deshielding effects of O-2 and whose H-3,3′ protons are in proximity to the acetate group. These arguments based on relative chemical shift

allow assignment of (*Z*) stereochemistry to the major component **2** and the (*E*) geometry to the minor isomer **3**. These assignments have strong further support from similar chemical-shift differences in a related pair of geometric enol acetates (see later) where an X-ray crystallographic study provided unambiguous evidence for the (*Z*) and (*E*) assignments.

2.1.2. Reactivity. The two enol acetates **2** and **3** began to decompose at room temperature after several hours, as evidenced by the detectable odor of acetic acid, but could be stored at −20 °C for several months without decomposition. When subjected to the conditions of their formation from aldehyde **1** (acetic anhydride–sodium acetate at 140 °C), compounds **2** and **3** did not undergo conversion into aldehydrol diacetate **4**, nor did **4** become transformed into **2** and **3**. It may be postulated that, in the reaction of aldehyde **1** with the acetylating reagents, the enol of **1** initially undergoes acetylation to give **2** and **3**, and the mole of acetic acid thus liberated allows conversion into acetylated aldehydrol **4**, resulting in the formation of approximately equal amounts of **4** and of **2** + **3**.

A re-examination of the literature procedure[8] for the acetylation of *aldehydo*-D-glucose pentaacetate with pyridine–acetic anhydride at room temperature, but with chromatographic monitoring, demonstrated that all the aldehyde had reacted after 2 h, and product isolation at this point afforded 45% of the crystalline aldehydrol heptaacetate, in contrast to the 25% yield reported after a 16-h reaction period. It may be supposed that, in the absence of added water, unstable enol acetates are concurrently formed in the reaction. In support of this hypothesis, it was shown that acetylation of the three-carbon aldehyde **1** with pyridine–acetic anhydride in the presence of water (to allow formation of the aldehydrol of **1**) afforded the crystalline aldehydrol diacetate **4** in an 80% yield.

2.2. Preparation of 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-pentoses and their conversion into enol acetates

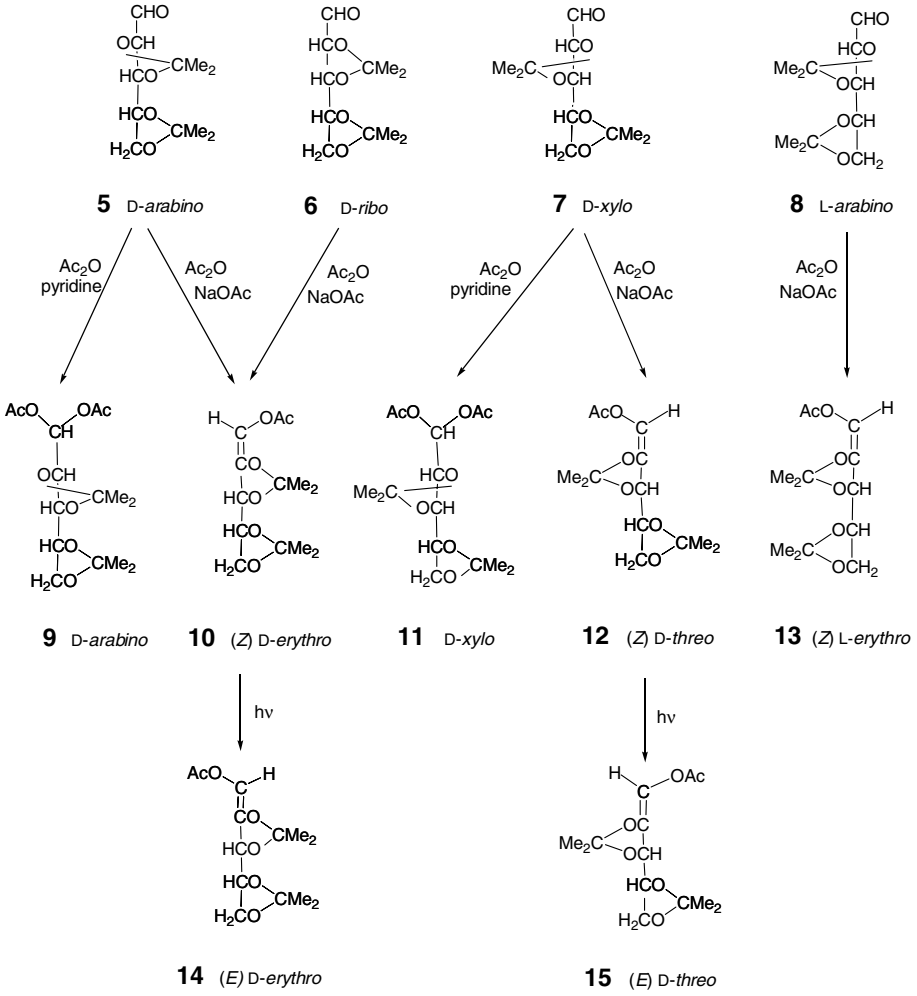
D- and L-Arabinose, D-ribose, and D-xylose were each converted successively into their diethyl dithioacetals, which were in turn transformed into the corresponding 2,3:4,5-diisopropylidene acetals, and these were then converted by the action of mercuric salts into the *aldehydo* derivatives, essentially by literature procedures. The thus obtained compounds were 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose (**5**) and its L enantiomer (**8**), 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose (**6**), and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-xylose (**7**). All four aldehydes were obtained as homogeneous syrups after purification by high-vacuum distillation and their NMR spectra (see Section 3) confirmed that they were single compounds free from any contaminants.

In the presence of water, each of the aldehydes **5**–**8** rapidly undergoes hydration to the aldehydrol as the major component of an aldehyde–aldehydrol equilibrium. This process was monitored by dissolving each aldehyde in a 3:1 mixture of acetone-d_6 and deuterium oxide and observing the NMR resonance for H-1, which was a narrow ($J_{1,2} \sim 2$ Hz) doublet near δ 9.7 for the aldehyde and a wider one ($J_{1,2} \sim 5$ Hz) near δ 5.0 for the aldehydrol. Equilibrium was established after ~20 min at room temperature, and integration of the H-1 signals indicated an aldehydrol–aldehyde ratio of 6:1 for the arabino derivative **5**, 3:1 for the ribo derivative **6**, and 4:1 for the xylo derivative **7**. As with the three-carbon aldehydrol derivative **4**, the larger $J_{1,2}$ values for the aldehydrols relative to the parent aldehydes reflects a larger proportion of the rotamers having H-1 antiparallel to H-2, avoiding eclipsing of bulky substituents along the C-1–C-2 bond. These results complement earlier results from this laboratory[15] on the aldehyde–aldehydrol equilibria of various acyclic acetylated *aldehydo*-hexoses and -pentoses in 7:3 tetrahydrofuran–deuterium oxide.

To establish favorable conditions for enol acetate formation in the pentose series, the reaction of arabino aldehyde **5** with the reagents used for conversion of triose **1** was investigated. A stirred mixture of aldehyde **5** in an excess of acetic anhydride containing 1 equiv of anhydrous sodium acetate was gradually heated and monitored using TLC. No reaction was evident below 110 °C, but the aldehyde ($R_f = 0.13$) was slowly consumed at this temperature and it reacted rapidly at 140 °C, the boiling point of the solvent, and was replaced by a less-polar product ($R_f = 0.7$) identified as the (*Z*)-enol acetate **10**, along with a minor, side product having $R_f = 0.31$. Isolation by the procedures used for enol acetates **2** and **3** afforded **10** as an oil that crystallized; recrystallization gave 51% of **10** as a sharp-melting single compound showing IR absorptions for C=O and vinyl C–H groups, and molecular formula $C_{13}H_{20}O_6$ by elemental analysis and mass spectrum. A solution of **10** decolorized bromine in carbon tetrachloride and it underwent conversion into arabinose upon deacetylation–acid hydrolysis. Borohydride reduction of **10** followed by acid hydrolysis and acetylation gave a 3:1 mixture of the peracetates of arabinitol and ribitol.

All of the foregoing evidence supports the assigned enol acetate structure for **10**, and its NMR spectrum confirmed that it was a single geometrical isomer in manifesting a single vinyl proton signal for H-1 as a narrow doublet ($J_{1,3}$ 1.5 Hz) at δ 6.75 in acetone-d_6. A definitive proof that **10** is the (*Z*) isomer was afforded by a single-crystal X-ray structure analysis,[5] which showed an O-1–O-2 interatomic distance of 2.7 Å.

The yield of **10** in the acetylation reaction decreased upon prolongation of the reaction time beyond that for the disappearance of the precursor aldehyde **5**, and



was diminished when less-fresh samples of aldehyde **5** were used. Compound **10** was not stable on storage and decomposed after 2 weeks at room temperature. Data for the purpose of permanent reference for crystalline **10** and other unstable compounds in this study are recorded in X-ray powder diffraction data on the crystals.

The L enantiomer **8** of aldehyde **5** underwent a similar conversion by acetic anhydride–sodium acetate into the L-(*Z*) enol acetate **13**, having identical physical constants as **10** except for the sign of optical rotation, and a mixed melting point of the enantiomers was not depressed. The D-ribo aldehyde **6**, the epimer of D-arabino aldehyde **5**, subjected to the same acetylation conditions, predictably gave the identical (*Z*)-enol acetate **10** as was obtained from **5**.

2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-D-xylose (**7**), when subjected to the action of acetic anhydride–sodium acetate at 140 °C as already described gave a single product, isolated initially as an oil and subsequently as crystals in 60% yield, which was characterized as (*Z*)-D-*threo* enol acetate **12**. It was isomeric with enol acetate **10**, showed a similar low stability on storage, had the same mass spectrum and a similar IR spectrum as **10**, and was a single geometrical isomer, as evidenced by a single narrow doublet ($J_{1,3}$ 1.5 Hz) at δ 6.68 in its NMR spectrum (acetone-d_6). In contrast to enol acetate **10**, whose NMR spectrum showed a significant signal overlap and second-order character for the H-4,5,5′ protons, the spectrum of **12** was readily amenable to first-order analysis. Degradation of **12** by successive reduction, hydrolysis, and acetylation as performed for **10** gave a 3:1 mixture of the peracetates of xylitol and lyxitol. A single-crystal X-ray structure determination[5] of crystals grown from ethanol solution established definitively that compound **12** was the (*Z*) isomer; the O-1–O-2 interatomic distance was 2.8 Å.

Although enol acetates **10** and **12** were the principal products when carefully purified aldehydes **5** and **7** were subjected to the acetylation conditions, the minor side products migrating somewhat faster than the precursor aldehydes became more prominent when pyridine–acetic anhydride was used for the acetylation, and addition of water to the reaction medium caused them to be the principal products. From D-arabino aldehyde **5** the product was obtained in a crystalline form and identified

as aldehydrol diacetate **9**, and D-xylo aldehyde **7** likewise gave the corresponding aldehydrol diacetate **11**, obtained as an oil. The proton NMR spectra of **9** and **11** showed typical low-field doublets ($J_{1,2} \sim 4.5$ Hz) near δ 7 ppm for the strongly deshielded H-1 proton, and their mass spectra exhibited typical M^+-15 (*m/z* 317) and other fragments characteristic of acetate and isopropylidene acetal derivatives.

2.2.1. (*Z*) to (*E*) Isomerization of enol acetates. As the acetylation of the aldehyde derivatives **5**–**8** led in each case to the isolation of only one of two possible geometrically isomeric enol acetates, the possibility of interconversion with the other geometric isomer was examined. Heating the (*Z*) enol acetate **10** in pyridine–acetic anhydride at 67 °C for 24 h with NMR monitoring failed to effect isomerization, and prolongation of the reaction time in the conversion of aldehyde **5** into **10** merely decreased the yield of **10**. The use of acidic reagents to effect isomerization[16,17] was not considered on account of the acid-labile substituents in **10** and **12**, and a photochemical approach was investigated.

A photoexcited alkene may, in principle undergo various modes of decay, including such chemical reactions as cis–trans isomerization or photodimerization.[18] To favor intramolecular isomerization over intermolecular dimerization, dilute (0.1 M) solutions of **10** in three different nitrogen-purged solvent systems were irradiated for 1 h with unfiltered radiation from a high-pressure mercury lamp and the reaction was monitored by TLC and GLC. In 4:1 benzene–acetone, **10** was converted into a 1:1 mixture of **10** and a second compound having a slightly lower TLC mobility and clearly faster elution time on GLC; it was subsequently identified as the (*E*) isomer (**14**) of **10**. Further irradiation did not change the ratio of the two compounds, but led progressively to conversion into products that were more polar. If the solvent was not purged with nitrogen the time required for maximum conversion into the 1:1 mixture increased to 4 h. The use of acetone alone as a solvent gave only ~10% conversion of **10** into the second compound, and none of the latter was detected when benzene alone was used as the solvent.

The photoisomerization procedure was repeated on a preparative scale with the (*Z*)-D-*erythro* enol acetate **10** and also the (*Z*)-D-*threo* enol acetate **12**, and in each instance the resultant 1:1 mixture of products was separated by preparative TLC. From compound **10** there was recovered unchanged starting material, along with a product identified as its (*E*) isomer **14**, isolated as an analytically pure oil, and from compound **12** there was recovered approximately equal amounts of **12** and its (*E*) isomer **15**, isolated crystalline. The two new compounds, $C_{13}H_{20}O_6$, showed characteristic IR absorptions, and their mass spectra were identical to those of the (*Z*) isomers. When the pure (*E*) isomers **14** and **15** were irradiated under the conditions used for their preparation they underwent conversion into ~1:1 mixtures of the respective (*Z*) and (*E*) isomers, as determined by GLC.

The proton NMR spectra of all four enol acetates **10**, **14**, **12**, and **15** in acetone-d_6 all showed broad similarities, with the vinyl (H-1) proton resonating near δ 7 ppm as a narrow doublet and the allylic (H-3) proton signal being separated to low field ($\delta \sim 5$ ppm) of the resonances for H-4, 5, and 5′. The relative chemical shifts of the H-1 signals between the (*Z*) and (*E*) isomers may be considered stereochemically diagnostic, with the (*E*) isomers showing the H-1 resonance ~0.25 ppm to a lower field than that of the (*Z*) isomers (6.75 ppm for **10** vs 7.04 ppm for **14**, and 6.68 ppm for **12** vs 6.89 ppm for **15**). The closer proximity of H-1 to O-2 in the (*E*) isomers would account for the additional deshielding in the latter. The allylic ($J_{1,3}$) coupling is also larger (2.0 Hz) for the (*E*) isomers than that (1.5 Hz) for the (*Z*) isomers. Interestingly, the (*Z*) isomers showed very small specific rotations, whereas values for the (*E*) isomers were large (+122 for **14** and −198 for **15**). As with the (*Z*) isomers, the (*E*) isomers decomposed after several days at room temperature.

From this rationale based on the H-1 chemical shifts, and the definitive X-ray structural attribution for compounds **10** and **12**, the structural assignments made for the glyceraldehye-derived enol acetates **2** and **3** are confirmed.

3. Experimental

3.1. General methods

Solvent evaporation was performed under diminished pressure (~20 torr). Melting points were determined by using a Thomas–Hoover Unimelt apparatus and are uncorrected. IR spectra were recorded with a Perkin–Elmer infrared spectrophotometer. Optical rotations were measured with a Perkin–Elmer Model 141 recording polarimeter. NMR spectra were recorded at 90 MHz with a Bruker HX-90 spectrometer and at 100 MHz with either a Jeol MH-100 or a Varian HA-100 spectrometer. The 220 MHz spectra were recorded on a Varian HR-200 instrument. Chemical shifts are measured relative to an internal standard of Me_4Si (δ 0.0). Proton assignments were established by spin-decoupling experiments. Electron impact mass spectra were recorded by Mr. C. R. Weisenberger with an AEI MS-902 double-focusing, high-resolution, mass spectrometer at an inlet temperature of 150 °C, an ionizing potential of 70 eV and an accelerating potential of 8 kV. Mass numbers were calibrated by the addition of tris(nonafluorobutyl)amine as an internal standard. TLC was performed with 0.25 mm layers of Silica Gel G

(E, Merck, Darmstadt, Germany). Plates were activated at 120 °C. Developments were accomplished using solvent A [60:40 (v/v), Et_2O–benzene], solvent B (1:9, Et_2O–benzene), or solvent C (3:1 Et_2O–$CHCl_3$). Spots were detected by spraying the plates with 5% (v/v) H_2SO_4 in EtOH and heating. Preparative TLC was performed on chromatoplates (200 × 200 × 15 mm) of Silica Gel G containing 1% Lumilux Green 25. Column chromatography was conducted with Merck Silica Gel To4. GLC analyses were undertaken using a Beckman GC-5 gas chromatograph dual-column instrument equipped with 2 mm × 1.98 m stainless-steel columns, packed with either A (3% SE 30 on Chromosorb 0) or B (3% OV 225 on Chromosorb W). Paper chromatography was performed on Whatman No. 1 chromatography paper in the descending mode using 4:1:1 1-BuOH–AcOH–water. Spots were indicated by treating the dried chromatogram with ethanolic $AgNO_3$ solution followed by spraying with 10% (w/v) NaOH solution. X-ray powder diffraction data give interplanar spacings in Å for Cu Kα radiation (camera diameter = 114.59 mm). The strongest lines are numbered in order of decreasing intensity (1, strongest). Relative intensities were visually estimated: m, medium; s, strong; v, very; w, weak.

3.2. Preparation of 2,3-*O*-isopropylidene-*aldehydo*-D-glyceraldehyde (1)

1,2:5,6-Di-*O*-isopropylidene-D-mannitol (50 g, 190 mmol), prepared in 48% yield by acetonation of D-mannitol by the literature procedure[14] was treated with freshly supplied lead tetraacetate (G. F. Smith Chemical Co., Columbus, OH) (90 g, 200 mmol) in dry benzene (600 mL) by the procedure of Baer and Fischer[14] to give aldehyde **1**, which was distilled at 35 °C/10 torr; yield 27 g (54%), ν_{max}^{NaCl} 2780 (CHO), 1740 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) showed chemical shifts and coupling constants in agreement to those reported by Horton et al.[13]

3.3. Conversion of aldehyde 1 into (*Z* and *E*)-1-*O*-acetyl-2,3-*O*-isopropylidene-tri-l-enitols (2 and 3) and 1,1-di-*O*-acetyl-2,3-*O*-isopropylidene-D,L-g1yceraldehyde aldehydrol (4)

Freshly distilled 2,3-*O*-isopropylidene-*aldehydo*-D-glyceraldehyde (**1**, 5.9 g, 45 mmol) was dissolved in freshly distilled Ac_2O (60 mL), anhydrous NaOAc (4.1 g, 49 mmol) was added, and the mixture was heated to 140 °C. After 45 min TLC (solvent A) showed that the starting material ($R_f = 0.38$) had been replaced by products giving three spots (A, B, and C) having R_f values of 0.89, 0.79, and 0.55, respectively. The solution was then evaporated at 40 °C/10 torr to afford a dark-brown mixture. Ether was added and the mixture was filtered to remove NaOAc. The filtrate was evaporated at 10 torr and the residual oil was fractionally distilled through a 6 in. Vigreux column to give four fractions: (a) bp 63–67 °C at 0.75 torr, yield 0.70 g; (b) bp 69–79 °C at 0.75 torr, yield 2.25 g; (c) bp 79–83 °C at 0.50 torr, yield 2.25 g; and (d) bp 83 °C at 0.50 torr, yield 0.54 g. TLC showed fractions a and b to contain only spots A and B, whereas fraction c showed some contamination of spot C with spot B; fraction d showed only spot C. Upon refrigeration fractions c and d crystallized, affording the crude aldehydrol derivative **4** having mp 34–38 °C. An analytically pure sample was obtained by recrystallization from 1:1 ether–pentane; mp 40–43 °C (further recrystallizations failed to increase the melting point): $[\alpha]_D^{23}$ 0, $[\alpha]_{578,546,436,365}^{23}$ 0 (*c* 1.0, $CHCl_3$); ν_{max}^{KBr} 1770 (C=O), 1380 cm^{-1} (CMe_2); ^1H NMR ($CDCl_3$): δ 6.75 (d, 1H, $J_{1,2} = 5.0$ Hz, H-1), 4.4–3.7 (m, 3H, H-2,3,3′), 2.03 (s, 6H, OAc), 1.39, 1.30 (s, 3H, CMe_2); *m*/*z*: 218 (3), 217 (29), 175 (5), 172 (2), 131 (2), 130 (3), 116 (6), 115 (94), 102 (4), 101 (72), 85 (5), 73 (5), 72 (10), 61 (9), 60 (8), 59 (20), 43 (100); X-ray powder diffraction data: 10.45 m, 7.79 vs (1), 6.34 s (3), 5.94 s, 5.40 m, 4.75 s (2), 4.23 m, 3.99 m. Anal. Calcd for $C_{10}H_{16}O_6$: C, 51.72; H, 6.94. Found: C, 51.47; H, 6.92.

TLC (solvent B) of fractions *a* and *b* showed two main spots having $R_f = 0.57$ and 0.48, together with some contamination at $R_f = 0.98$–0.90. Column chromatography on Silica Gel G with solvent B gave 0.3 g of a 1:1 mixture of the two main components (**2** and **3** as an oil), and 2.1 g of the major component (**2**) as a chromatographically homogeneous second spot; it was also an oil: ν_{max}^{NaCl} 3175 (vinyl C–H), 1750 (C=O), 1370 cm^{-1} (CMe_2); ^1H NMR ($CDCl_3$): δ 6.58 (t, 1H, $J_{1,3} =$ 1.5 Hz, H-1), 4.60 (d, 2H, H-3,3′), 2.24 (s, 3H, OAc), 1.56 (s, 6H, CMe_2).

The mixture displayed the signals of the major component together with the following: δ 7.00 (t, 1H, $J_{1,3} = 2.0$ Hz, H-1), 4.70 (d, 2H, H-3,3′), 2.18 (s, 3H, OAc), 1.50 (s, 6H, CMe_2).

Mass-spectral data of either the mixture or the major component were identical: *m*/*z* 173 (1.1), 172 (10), 157 (0.5), 130 (17), 101 (4), 59 (47), 43 (100). Anal. Calcd for $C_8H_{12}O_4$: C, 55.83; H, 6.97. Found: C, 55.47; H, 6.99.

These enol acetates were found to be unstable; neat liquids that quickly acquired the odor of acetic acid when kept for 30 min at room temperature, but samples could be stored without decomposition for two months at −20 °C.

3.4. Attempted interconversion of enol acetates (2,3) and acetylated aldehydrol (4)

A mixture of **2** and **3** (100 mg, 0.6 mmol) in Ac_2O (1 mL) containing NaOAc (50 mg, 0.6 mmol) was heated for 30 min at 140 °C. TLC showed no spots of

R_f value comparable to that of acetylated aldehydrol **4**. New spots having very high R_f values (0.98) gradually replaced those of the starting materials. Similarly, acetylated aldehydrol **4** (0.1 g, 0.4 mmol) was not converted into enol acetates **2** and **3** upon exposure to NaOAc (50 mg, 0.6 mmol) in Ac_2O (1 mL) at 140 °C. Some spots of lower R_f values slowly appeared.

3.5. Reaction of 2,3-*O*-isopropylidene-*aldehydo*-D-glyceraldehyde with pyridine–Ac_2O–water. General procedure for preparing acetylated aldehydrols

Freshly distilled aldehyde **1** (0.542 g, 4 mmol) was dissolved in Ac_2O (4 mL) and pyridine (4 mL) was added, followed by distilled water (0.4 mL, 22 mmol). The mixture was kept for 16 h at room temperature, after which time it was heated for 10 h at 60 °C. TLC (solvent B) showed one new spot ($R_f = 0.55$) and none of the starting aldehyde ($R_f = 0.25$). The crude mixture was evaporated, purified by loose-layer chromatography using 1:1 benzene–EtOAc and the resulting yellow oil crystallized; yield 0.77 g (80%). The IR and NMR spectra were identical to the already described aldehydrol acetate **4**.

3.6. Preparation of 1,1,2,3,4,5,6-hepta-*O*-acetyl-*aldehydo*-D-glucose aldehydrol

The following procedure is an improvement over the literature procedure.[8] Penta-*O*-acetyl-*aldehydo*-D-glucose[19] (0.5 g, 1.3 mmol) was dissolved in pyridine (2.5 mL) and Ac_2O (6.25 mL), and the mixture was kept at room temperature. TLC (solvent A) showed that after 2 h the starting material ($R_f = 0.17$) had been replaced by a new major ($R_f = 0.51$) and minor ($R_f = 0.57$) product. The mixture was poured onto ice (50 g) and then extracted twice with CH_2Cl_2 (25 mL). The dried ($MgSO_4$) extract was evaporated to a black residue, which crystallized on refrigeration. Recrystallization from EtOH gave the title compound as white needles; yield 287 mg (45%) (lit.[8] 25%), mp 119–120 °C (lit.[8] mp 118.5–119.5 °C); mixed mp with an authentic sample, 117–119 °C; ^{1}H NMR ($CDCl_3$): δ 6.80 (d, 1H, $J_{1,2} = 4.5$ Hz, H-1), 5.55–5.30 (m, 3H, H-2,3,4), 5.00 (br q, 1H, $J_{4,5} = 5.5$ Hz, H-5), 4.28 (dd, 1H, $J_{5,6} = 4.0$, $J_{6,6'} = 12.5$ Hz, H-6), 4.10 (dd, 1H, $J_{5,6} = 5.5$ Hz, H-6′), 2.00 (21H, OAc); *m*/*z*: 433 (2.0), 419 (1.5), 347 (30), 331 (4.0), 330 (1.0), 317 (2.0), 289 (5.0), 275 (3.0), 259 (2.0), 245 (6.0), 242 (29), 228 (2.5), 217 (9.0), 215 (8.0), 200 (9.0), 187 (9.0), 173 (5.0), 169 (8.0), 168 (4.0), 158 (7.0), 157 (39), 145 (35), 144 (4), 143 (5), 140 (10), 139 (6.0), 128 (3.0), 127 (5.0), 126 (3.0), 115 (31), 103 (23), 102 (5.0), 98 (16), 97 (5), 43 (100). Anal. Calcd for $C_{20}H_{28}O_{14}$: C, 48.78; H, 5.73. Found: C, 48.79; H, 5.50.

3.7. Preparation of 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose (5)

Using a slight modification of the method of Fischer,[20] D-arabinose (250 g, 1.66 mol) was dissolved in 37% HCl (250 mL) and cooled to 0 °C. Technical-grade EtSH (250 mL) was added and the two layers were vigorously shaken. Copious crystallization occurred after about 15 min. After 30 min, the crude D-arabinose diethyl dithioacetal was recovered by filtration and then recrystallized from water; yield 380 g (91%), mp 124–125 °C, lit.[20] mp 125–126 °C.

To the vacuum-dried dithioacetal (20 g, 78 mmol) in dry acetone (200 mL) was added 0.5 mL of concentrated H_2SO_4. The mixture was stirred overnight at room temperature, neutralized with aqueous ammonia, filtered, and the filtrate evaporated to dryness. The residue was extracted with CH_2Cl_2 (150 mL), which was washed with water (40 mL), dried ($MgSO_4$), filtered, and then evaporated to a light-brown syrup that was purified by vacuum distillation to afford 2,3:4,5-di-*O*-isopropylidene-D-arabinose diethyl dithioacetal as a syrup;[21] $[\alpha]_D^{24}$ +82 (MeOH), lit.[22] $[\alpha]_D$ +83; ν_{max}^{KBr} 1380 cm^{-1} (CMe_2); ^{1}H NMR (benzene-d_6): δ 4.67–3.90 (m, 6H, H-1,2,3,4,5,5′), 2.74 (dq, 4H, SCH_2), 1.40, 1.33, 1.25, 1.20 (s, 3H, CMe_2), 1.15 (dt, 6H, SCH_2–CH_3); *m*/*z* 338 (4), 337 (6), 336 (35), 321 (5), 263 (3.0), 261 (1.0), 217 (33), 203 (9.0), 201 (2.0), 177 (3.5), 159 (15), 143 (96), 135 (90), 101 (22), 87 (18), 85 (15), 75 (18), 59 (55), 43 (100). Anal. Calcd for $C_{15}H_{28}O_4S_2$: C, 53.39; H, 8.32; S, 19.05. Found: C, 53.30; H, 8.21; S, 18.99.

In an adaptation of the method of Zinner and coworkers[22] the di-*O*-isopropylidene-D-arabinose diethyl dithioacetal (3.36 g, 10.0 mmol) was dissolved in acetone (60 mL) and then to the stirred mixture HgO (yellow, 6.0 g, 28 mmol), $HgCl_2$ (6.0 g, 22 mmol), and water (6 mL) were added in succession. After heating for 2 h at 56 °C the mixture was filtered into a receiver containing HgO (3 g). The resultant mixture was evaporated to dryness, extracted with CH_2Cl_2 (100 mL), washed with 5% KI solution (30 mL), and then twice with water (30 mL). Evaporation gave the crude aldehyde; yield 1.4 g (60%), whose IR spectrum showed both OH and C=O absorptions. Distillation at 80 °C and 30 mtorr gave the pure aldehyde **5**; yield 1.1 g (47%); ^{1}H NMR (acetone-d_6): δ 9.71 (d, 1H, $J_{1,2} = 2.0$ Hz, H-1), 4.37 (dd, 1H, $J_{2,3} = 5.0$ Hz, H-2), 4.20–3.80 (m, 4H, H-3,4,5 and 5′), 1.41, 1.32 and 1.29 (12H, CMe_2).

3.8. Hydration of the *arabino* aldehyde (5)

To the foregoing aldehyde (80 mg) in acetone-d_6 (0.3 mL) was added deuterium oxide (0.1 mL). Analysis by ^{1}H NMR showed a decrease in the intensity of the H-1 signal (δ 9.71) and the appearance of a new doublet at δ 5.01 ($J_{12} = 5.0$ Hz) attributable to the hydrated form

of the aldehyde. The ratio of aldehydrol to free aldehyde gradually leveled off at 6:1 (20 min).

3.9. 1,1-Di-*O*-acetyl-2,3:4,5-di-*O*-isopropylidene-D-arabinose aldehydrol (9)

Freshly distilled aldehyde **5** (0.876 g, 5.8 mmol) was dissolved in Ac_2O (2 mL), and pyridine (4 mL) and distilled water (9.4 mL, 22 mmol) was added. The mixture was kept for 16 h at an ambient temperature and then heated to 64 °C. After 3 h, the aldehyde, having $R_f = 0.13$ (solvent B), had disappeared, and was replaced by a major component ($R_f = 0.31$) and a very minor one having $R_f = 0.7$. GLC also revealed two components (column A at 150 °C, $t_R = 1.0$ min (7%) and 4.7 min (93%)), the first peak matching the retention time (and TLC R_f value) of a sample of compound **5**. Evaporation of the mixture at 40 °C/0.2 torr yielded 1.0 g of a black oil, and this crude product was quickly passed through a column (1 × 6 in.) of silica gel with 9:1 benzene–ether as eluant. The effluent was then evaporated to afford a colorless oil that crystallized on being kept; yield 0.621 g (64%); mp 44–46 °C. Recrystallization from EtOH–pentane did not change the melting point. An analytically pure sample was obtained by sublimation at 45 °C/20 torr; $[\alpha]_D^{25}$ −5.2 (*c* 0.5, $CHCl_3$); ν_{max}^{KBr} 1770 (C=O), 1375 cm^{-1} (CMe_2); ^1H NMR (C_6D_6): δ 7.30 (d, 1H, $J_{1,2} =$ 4.9 Hz, H-1), 4.36 (dd, H-2), 4.30–3.90 (H-3,4,5,5′), 1.70 (s, 6H, OAc), 1.36, 1.29 (s, 3H, CMe_2); *m*/*z* 317 (40), 231 (15), 215 (13), 173 (17), 143 (42), 139 (20), 43 (100); X-ray powder diffraction data: 9.35 m, 8.38 m, 7.62 s (2), 7.13 vw, 6.10 vw, 5.19 m, 4.70 m, 4.36 vs (1), 4.23 w, 4.04 w, 3.89 m (3). Anal. Calcd for $C_{15}H_{24}O_8$: C, 54.24; H, 7.22. Found: C, 54.32; H, 7.17.

3.10. Preparation of 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-L-arabinose (8)

This compound was obtained from L-arabinose by an identical procedure used for the D-enantiomer.

3.11. Preparation of 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose (6)

D-Ribose (50 g, 300 mmol) was dissolved in 37% aqueous HCl (50 mL) and the solution was cooled to 0 °C. Ethanethiol (50 mL) was added and the two-layer system was shaken vigorously for 1 h at 0 °C. The resultant purple solution was added in portions to a stirred suspension of lead carbonate (90 g) in MeOH (100 mL). After completion of the addition and a further 16 h of stirring, decolorizing carbon was added. The mixture was filtered and the colorless filtrate evaporated to a syrup. The crude syrupy product upon refrigeration precipitated out traces of solids, but did not crystallize. Addition of 95% EtOH (250 mL) followed by filtration then evaporation of the filtrate produced a light-yellow syrup that crystallized upon refrigeration. Recrystallization from 1-butanol gave pure dithioacetal; yield 25 g (35%), mp 80–82 °C, lit.[23] mp 83–84 °C.

The D-ribose diethyl dithioacetal (20 g, 0.78 mmol) was then acetonated exactly as described for the arabino analogue, yielding 5 g (58%) of 2,3:4,5-di-*O*-isopropylidene-D-ribose diethyl dithioacetal as a light-yellow syrup. This product was treated with mercuric chloride and mercuric oxide as described for the D-*arabino* analogue, to yield the *aldehydo* derivative **6**; ^1H NMR (acetone-d_6): δ 9.68 (d, 1H, $J_{1,2} = 2.0$ Hz, H-1). Addition of 25% D_2O to the NMR sample led to the appearance of a new H-1 doublet at δ 4.95 ($J_{1,2} = 5.0$ Hz) for the aldehydrol of **6**; the ratio of aldehydrol to aldehyde was 3:1.

3.12. Preparation of *aldehydo*-2,3:4,5-di-*O*-isopropylidene-D-xylose (7)

D-Xylose (50 g, 300 mmol) was converted into its diethyl dithioacetal by the same procedure used for D-ribose. Addition of Et_2O (150 mL) together with MeOH (10 mL) to the syrup obtained caused crystallization, and the product was recovered by filtration; yield 30.4 g (42%); mp 61–63 °C, lit.[24] mp 63–65 °C. The obtained D-xylose diethyl dithioacetal (20 g, 78 mmol) was treated with acetone (200 mL) and H_2SO_4 as catalyst (0.3 mL). Processing as described for the arabinose analogue **5** gave the crude 2,3:4,5-diisopropylidene acetal; yield 18 g (75%), which upon distillation yielded pure product; yield 17.0 g (70%); bp 118–124 °C at 40 mtorr; $[\alpha]_D^{24}$ −50 (*c* 1.0, benzene) (lit.[25] bp 100–105 °C at 1 mtorr, $[\alpha]_D^{23}$ −51.25 in benzene).

In the same manner as described for the D-arabinose derivative, 2,3:4,5-di-*O*-isopropylidene-D-xylose diethyl dithioacetal was converted into aldehyde **7** in 50–60% yield after distillation; bp 80–85 °C at 20 mtorr; ^1H NMR (acetone-d_6): δ 9.75 (d, 1H, $J_{1,2} = 2.0$ Hz, H-1), 4.55–3.70 (m, 5H, H-2,3,4,5,5′), 1.45, 1.38, and 1.32 (12H, CMe_2).

3.13. Hydration of aldehyde 7 with deuterium oxide

Under the same conditions used for **5**, aldehyde **7** showed a new doublet resonating at δ 4.95, $J_{1,2} = 5.0$ Hz, and the final ratio of aldehydrol to aldehyde was 4:1.

3.14. (*Z*)-1-*O*-Acetyl-2,3:4,5-di-*O*-isopropylidene-D-*erythro*-pent-l-enitol (10)

Freshly distilled 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose (**5**, 5.0 g, 21 mmol) was treated, as previously described, with NaOAc (1.5 g, 20 mmol) in Ac_2O

(25 mL). TLC (solvent B) showed that, after 30 min the starting aldehyde ($R_f = 0.15$) had been replaced by a major component having $R_f = 0.7$, and a very minor component with $R_f = 0,3$. The mixture was then evaporated at 40 °C/0.2 torr, ether was added, and filtration from the NaOAc followed by evaporation of the ether solution afforded the crude product as a light-yellow oil that crystallized on being kept; yield 5.1 g, mp 95–100 °C. Recrystallization from either absolute EtOH or 1:1 ether–pentane gave 3.0 g (51%) of **10** as a white solid; mp 100–100.5 °C; $R_f = 0.7$ (solvent B); $[\alpha]_D^{23}$ +1.85 (*c* 1.0, $CHCl_3$); ν_{max}^{KBr} 3125 (vinyl C–H), 1760 (C=O), 1380 cm^{-1} (CMe_2); ^1H NMR (220 MHz, acetone-d_6): δ 6.75 (d, 1H, $J_{1,3} = 1.5$ Hz, H-1), 4.70 (dm, 1H, $J_{3,4} \sim 4.4$ Hz, H-3), 4.13–4.00 (m, 2H, H-4,5), 3.90 (m, 1H, H-5′), 2.10 (s, 3H, OAc), 1.55, 1.45, 1.40, 1.30 (s, 3H, CMe_2). The ^1H NMR spectra at 100 MHz in acetone-d_6, benzene-d_6, $CDCl_3$, CCl_4, pyridine-d_5, and Me_2SO-d_6 all failed to minimize the high degree of second-order character of the signals for H-3, H-4, H-5, and H-5′. MS: *m*/*z* 272 (10), 257 (10), 214 (20), 142 (12), 129 (31), 101 (58), 43 (100); X-ray powder diffraction data: 9.50 w, 7.86 vs (2), 7.45 w, 5.77 w, 5.01 s (3), 4.57 m, 4.07 vs (1), 4.01 s, 3.83 w, 3.63 w-m, 3.42 vw, 3.19 w, 3.09 w, 2.59 w, 2.42 w, 2.04 w. Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.19; H, 7.32.

Compound **10** rapidly decolorized a solution of Br_2 in CCl_4, and reacted with NaOMe–MeOH at room temperature to give a product that was detectable by Schiff's reagent on TLC plates.

Compound **10** was very soluble in $CHCl_3$, EtOAc, and Et_2O, soluble to a moderate degree in acetone and absolute EtOH, and insoluble in pentane. On being kept for 2 weeks at room temperature, the crystals became oily and smelled of acetic acid. For the purposes of single-crystal X-ray study the compound was recrystallized three times from Et_2O–pentane, and then vacuum-dried for 24 h at room temperature.

3.15. Preparation of 10 from the ribo aldehyde 6

Fresh 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-ribose (**6**, 2.40 g, 10 mmol) was treated with NaOAc (1.47 g, 20 mmol) in Ac_2O at reflux (7 mL). Recrystallization of the product gave 1.14 g of white solid, mp 100–100.5 °C. The optical rotation, IR, and ^1H NMR spectra were identical to that of compound **10**, and a mixture of the two compounds had mp 99–100.5 °C.

The mother liquors from these recrystallizations contained more enol acetates, together with two other components suspected of being the acetylated aldehydrols, and a diisopropylidene acetal of the pentose (GLC MS). However, insufficient quantities of these could be isolated for complete characterization.

3.16. (*Z*)-1-*O*-Acetyl-2,3:4,5-di-*O*-isopropylidene-L-*erythro*-pent-1-enitol (13)

2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-L-arabinose (**8**, 1.75 g, 7.6 mol) was treated with NaOAc (0.66 g, 8 mmol) in boiling Ac_2O (8 mL), and processing as for compound **5** gave 1.17 g (85%) of **13** as a white solid; mp 96–100 °C. Recrystallization from Et_2O–pentane gave 0.6 g (60%), mp 100–100.5 °C; $[\alpha]_D^{23}$ −1.9 (*c* 1.0, $CHCl_3$). The IR and ^1H NMR spectra of this compound were identical to those of the already mentioned *Z* enitol **10**. A mixed melting point of a well ground 1:1 mixture of the D and L compounds showed mp 99–100 °C.

3.17. Degradative structure proof of compound 10

Compound **10** (100 mg) was dissolved in absolute EtOH (3 mL), $NaBH_4$ (10 mg) was then added, and the mixture was stirred for 30 min at room temperature. TLC (solvent B) showed the disappearance of the starting material ($R_f = 0.7$) and appearance of a new, elongated spot ($R_f = 0.1$). The mixture was poured into 50 mL of CH_2Cl_2, washed successively with aqueous NH_4Cl and water, dried ($MgSO_4$), and then evaporated to a syrup. MeOH (5 mL), followed by concentrated H_2SO_4 (two drops), were added to the syrup, and the mixture was stirred for 24 h at room temperature. After neutralization with aqueous ammonia and evaporation to dryness, pyridine (1 mL) followed by Ac_2O (0.5 mL) were added, and the resulting solution was kept for 24 h at room temperature. GLC (column B at 200 °C and 100 mL/min flow rate of gas) revealed the presence of two 'acetylated' products [$t_R = 3.8$ min (20%), and $t_R = 4.1$ min (80%)] whose retention times exactly matched those of per-*O*-acetyl-D-ribitol and D-arabinitol. The GLC data and mass spectra confirmed the gross identities of these peaks: product of $t_R = 3.8$ min: *m*/*z* 304 (0.5), 303 (3), 289 (2), 261 (0.5), 260 (0.5), 242 (1), 219 (1), 218 (5), 217 (26), 202 (1), 201 (2), 200 (7), 199 (1), 188 (2), 187 (18,5), 182 (1), 176 (1), 175 (11), 171 (0.5), 170 (5.5), 159 (2), 158 (21), 157 (9), 147 (1), 146 (4), 145 (72), 142 (1), 141 (7), 140 (9), 133 (1), 129 (1), 128 (10.5), 127 (21.5), 117 (2), 116 (27), 115 (86), 112 (1.5), 104 (2), 103 (46), 102 (2,5), 101 (2), 100 (1), 99 (5), 98 (13), 97 (2), 87 (1), 86 (7), 85 (16), 82 (1), 81 (6), 74 (1), 73 (7), 71 (1), 70 (1.5), 69 (2), 68 (1.5), 61 (2.5), 60 (1.5), 57 (1), 56 (1.5), 55 (1), 44 (3), 43 (100). The product having $t_R = 4.1$ min, and authentic samples of the peracetylated pentitols themselves all had identical spectra, except for minor differences in relative intensities.

3.18. Transesterification and deacetonation of compound 10

The *Z* enitol **10** (10 mg) was dissolved in MeOH (10 mL) in which a small lump (2 mg) of sodium had been

dissolved. After 48 h at 25 °C the solution was neutralized with solid CO_2 and evaporated to dryness. Water (10 mL) was added, followed by a few beads of Amberlite IR-120 H^+ ion-exchange resin, and after 30 min at 90 °C the resin was filtered off. The solution was spotted directly onto Whatman No., 1 chromatography paper. Analysis of the developed chromatogram (solvent C) revealed only one spot present corresponding to a pentose. Authentic samples of D-ribose and D-arabinose had R_{ribose} 1.0 and 0.64, respectively. The product from the *Z* enitol showed only 0.64.

3.19. Photochemical reactions of compound 10

Three samples of compound **10** were prepared for photolysis as follows: (a) a solution of **10** (31 mg) in nitrogen-purged benzene (1 mL), and acetone (10 drops) in a closed NMR tube; (b) a solution of **10** (27 mg) in nitrogen-purged benzene (1 mL) in a stoppered, quartz UV cell; and (c) a solution of **10** (27 mg) in nitrogen-purged acetone (1 mL) in a stoppered NMR tube. These three samples were suspended immediately next to an ACE Hanovia high-pressure mercury lamp (450 W), and simultaneously irradiated. After 1 h, the samples were examined by both TLC (solvent B, two developments) and GLC (column A at 118 °C). Sample a revealed the presence of the starting material ($R_f = 0.8$), and a new component of a slightly lower R_f (0.72). Sample b showed mainly starting material and traces of components having significantly lower R_f values (0.5, 0.35), and sample c contained mainly starting material and a minor component having $R_f = 0.72$. GLC analysis of sample a indicated occurrence of a reaction; there were two main components, namely, starting material ($t_R = 5.7$ min) and a new component ($t_R = 4.9$ min) in the ratio of ~1:1. Sample c revealed the same two components, but the percentage of the new component was only ~10%. Continued irradiation of sample a did not change the ratio of the starting material to the new component; however, peaks of a greater retention time became progressively more significant. It was later found that the deletion of the nitrogen purging of the solvents increased to 4 h the time required for reaching 'equilibrium'.

3.20. (*E*)-1-*O*-Acetyl-2,3:4,5-di-*O*-isopropylidene-D-*erythro*-pent-l-enitol (14)

Compound **10** (60 mg) was weighed into each of four soft glass tubes, and nitrogen-purged benzene (2 mL) and acetone (20 drops) were added. The tubes were closed and hung adjacent to a high-pressure mercury lamp. After 1 h of irradiation the contents of the tubes were combined, evaporated, redissolved in ether (2 mL), applied to twelve 20 × 20 × 0.125 cm preparative TLC plates, which were eluted once with 7:3 benzene–ether. Two spots were observed (UV) having R_f values of 0.56 and 0.63, the faster-migrating one yielding 115 mg of white solid identical to **10**, and the slower one affording 67 mg of **14** as a colorless oil. Compound **14** had $[\alpha]_D^{24}$ +122 (c 1.0, $CHCl_3$); ν_{max}^{NaCl} 3200 (vinyl C–H), 1760 (C=O), 1370 cm^{-1} (CMe_2); ^1H NMR (acetone-d_6): δ 7.04 (d, 1H, $J_{1,3} = 2.0$ Hz, H-1), 5.02 (dd, 1H, $J_{3,4} = 4.5$ Hz), 4.44 (o, 1H, $J_{4,5} = 6.5$ Hz, H-4), 4.02 (dd, 1H, $J_{4,5'} = 7.0$ Hz, H-5), 3.94 (dd, 1H, $J_{5,5'} = 9.0$ Hz, H-5′), 2.09 (s, 3H, OAc), 1.55, 1.45, 1.40, 1.30 (s, 12H, CMe_2); MS same main peaks as **10** with minor intensity variations. Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.37; H, 7.34.

3.21. (Z)-1-*O*-Acetyl-2,3:4,5-di-*O*-isopropylidene-D-*threo*-pent-l-enitol (12)

Freshly distilled 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-xylose (**7**, 2.44 g, 10 mmol) was dissolved in Ac_2O (7 mL), NaOAc (1.47 g, 20 mmol) was added, and the solution was gradually heated to 140 °C. TLC analysis (solvent B) showed that the starting aldehyde ($R_f = 0.29$) had disappeared by the time the solution had reached 140° (30 min), being replaced by two new spots ($R_f = 0.63$ major, 0.47 very minor). Processing as described for compound **10** afforded 2.55 g of a yellow oil. Chromatography on a 70 × 5 cm column (silica gel, 9:1 benzene–ether) yielded 1.5 g of a white solid, mp 59–60 °C. Recrystallization from 1:1 ether–pentane, or absolute EtOH gave pure **12**; mp 61–62 °C, $[\alpha]_D^{22}$ +8.4 (*c* 0.8, $CHCl_3$); ν_{max}^{KBr} 3145 (vinyl C–H), 1750 (C=O), 1380 cm^{-1} (CMe_2); ^1H NMR (acetone-d_6): δ 6.68 (d, 1H, $J_{1,3} = 1.5$ Hz, H-1), 4.85 (dd, 1H, $J_{3,4} = 3.5$ Hz, H-3), 4.29 (o, 1H, $J_{4,5} = 6.4$ Hz, H-4), 4.02 (dd, $J_{4,5'} = 7.2$ Hz, H-5), 3.72 (dd, 1H, $J_{5,5'} = 8.2$ Hz, H-5′), 2.05 (s, 3H, OAc), 1.47, 1.35, 1.26 (12H, CMe_2); MS similar to that of **10** and **14**, except for minor intensity variations; X-ray powder diffraction data: 8.11 vs (2), 6.58 w, 5.81 w, 5.29 w, 4.95 w, 4.54 vs (1), 4.23 s (5), 4.05 w, 5.54 m, 3.26 m, 3.04 vw. Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.37; H, 7.48.

Compound **12** showed solubility and stability behavior similar to that of compound **10**. Crystals for the single-crystal X-ray analysis were grown slowly from absolute EtOH.

3.22. Degradative structure proof for compound 12

By using the methods described for the degradation of compound **10**, the D-*threo* enitol **12** (100 mg) was successively reduced, hydrolyzed, deacetonated, acetylated, and then analyzed by GLC–MS. The chromatogram (identical conditions as used for **10**) revealed two peaks $t_R = 5.8$ min and $t_R = 4.9$ min in relative abundance of 26% and 74%, respectively. The retention times

corresponded exactly to those of authentic samples of lyxitol and xylitol peracetates, thus confirming the identities of these compounds. The fragmentation patterns matched those of the authentic peracetates and were superposable except for minor differences in relative intensities to the fragmentations listed for the degradative studies of compound **10**.

3.23. (*E*)-1-*O*-Acetyl-2,3:4,5-di-*O*-isopropylidene-D-*threo*-pent-l-enitol (15)

Compound **12** (104 mg) in nitrogen-purged benzene (4 mL) and acetone (40 drops), was irradiated for 1 h with a Hanovia high-pressure lamp at an ambient temperature. TLC (silica gel, 9:1 benzene–ether, two developments) showed the starting material ($R_f = 0.67$) and a new compound ($R_f = 0.59$) in the ratio of ~1:1. Analysis by GLC (column A) confirmed the presence of a two-component mixture consisting of the starting material, $t_R = 6.2$ min and a new compound having $t_R = 5.7$ min, in the ratio of ~11:9. Preparative TLC in 9:1 benzene–ether (two developments; UV indication) yielded 30 mg (29%) of starting material and 31.6 mg (30%) of **15**; mp 68–70 °C, after recrystallization from 1:1 ether–pentane; $[\alpha]_D^{24}$ −198 (*c* 0.2, $CHCl_3$); ν_{max}^{KBr} 3095 (vinyl C–H), 1740 (C=O), 1380 cm^{-1} (CMe_2); ^1H NMR (acetone-d_6): δ 6.89 (d, 1H, $J_{1,3} = 2.0$ Hz, H-1); 4.82 (t, 1H, $J_{3,4} = 3.0$ Hz, H-3), 4.39 (o, 1H, $J_{4,5} = 6.8$ Hz, H-4), 3.96 (dd, 1H, $J_{4,5'} = 8.3$ Hz, H-5), 3.83 (dd, 1H, $J_{5,5'} = 8.3$ Hz, H-5′), 2.02 (s, 3H, OAc), 1,41, 1,26, 1.23, 1.17 (s, 12H, CMe_2); MS similar to **10**, **12**, and **14**, except for minor signal intensities; X-ray powder diffraction data: 11.1 w, 8.66 s, 7.40 s, 6.75 vs (1), 5.45 w, 5.14 w, 4.90 vs (2), 4.64 m, 4.42 vs (3), 4.23 s. Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.51; H, 7.31.

3.24. 1,1-Di-*O*-acetyl-2,3:4,5-di-*O*-isopropylidene-D-xylose aldehydrol (11)

Freshly distilled aldehyde **7** (241 mg, 1 mmol) was dissolved in Ac_2O (1 mL), and pyridine (2 mL) was added, followed by distilled water (0.1 mL, 5 mol). The solution was kept for 16 h at 27 °C and then heated for 4 h to 60 °C. GLC (column A at 150 °C) showed that the starting material, $t_R = 0.4$ min, had been replaced by a new compound, $t_R = 2.7$ min. The dark-brown solution was evaporated at 40 °C/0.2 torr to a syrup that was redissolved in ether. The solution was quickly passed through a short (1 × 6 in.) column of silica gel with the same solvent, and evaporated to give **11** as a colorless oil that resisted crystallization; yield 271 mg (77%) $[\alpha]_D^{24}$ +2.6 (*c* 0.5, $CHCl_3$); ν_{max}^{NaCl} 1770 (C=O), 1370 cm^{-1} (CMe_2); ^1H NMR (C_6D_6): δ 7.30 (d, 1H, H-1), 4.36 (dd, 1H, H-2), 4.30–3.90 (m, 4H, H-3,4,5,5′), 1.70 (s, 6H, OAc), 1.36, 1.30, 1.24 (12H, CMe_2); MS similar to that of compound **9** except for minor intensity variations. Anal. Calcd for $C_{15}H_{24}O_8$: C, 54.24; H, 7.22. Found: C, 54.19; H, 7.42.

Acknowledgements

Supported in part by NIH grant GM-11976.

References

1. Lobry de Bruyn, C. A.; Alberda van Ekenstein, W. *Recl. Trav. Chim. Pays-Bas* **1897**, *16*, 262.
2. Isbell, H. S.; Frush, H. L.; Wade, C. W. R.; Hunter, C. E. *Carbohydr. Res.* **1969**, *9*, 163–175.
3. Yaylayan, V. A.; Ismail, A. A. *Carbohydr. Res.* **1995**, *276*, 253–265.
4. Anderson, L.; Liegel, J. J.; Painter, C. J. *Abstr. Pap. Am. Chem. Soc.* **2004**, *277*, CARB-072.
5. For a preliminary report, see: Ducruix, A.; Pascard-Billy, C.; Eitelman, S. J.; Horton, D. *J. Org. Chem.* **1976**, *41*, 2652–2653.
6. (a) Eitelman, S. J. Ph.D. Dissertation, Ohio State University, Columbus, OH, 1975; (b) Eitelman, S. J. *Dissertation Abstr. Int.* **1976**, *356*, 5687–5688.
7. De Graaf, S. A. G.; Oosterhoff, P. E. R.; van der Gen, A. *Tetrahedron Lett.* **1974**, 1653–1656.
8. Wolfrom, M. L. *J. Am. Chem. Soc.* **1935**, *57*, 2498–2500.
9. Tronchet, J. M. J.; Tronchet, J. *Compt. Rend.* **1968**, *267*, 626–629.
10. Horton, D.; Just, E. *Carbohydr. Res.* **1969**, *9*, 129–137.
11. Meyer zu Reckendorf, W. *Chem. Ber.* **1969**, *102*, 1071–1075.
12. Baker, D. C.; Defaye, J.; Gadelle, A.; Horton, D. *J. Org. Chem.* **1976**, *41*, 3834–3840.
13. Horton, D.; Hughes, J. B.; Thomson, J. K. *J. Org. Chem.* **1968**, *33*, 728–734.
14. Baer, E.; Fischer, H. O. L. *J. Biol. Chem.* **1939**, *128*, 463–473.
15. Horton, D.; Wander, J. D. *Carbohydr. Res.* **1971**, *16*, 477–479.
16. House, H. O.; Kramar, V. *J. Org. Chem.* **1963**, *28*, 3362–3379.
17. House, H. O.; Trost, B. *J. Org. Chem.* **1965**, *30*, 1341–1348.
18. Swenton, J. S. *J. Chem. Educ.* **1969**, *46*, 7–11.
19. Wolfrom, M. L. *J. Am. Chem. Soc.* **1929**, *51*, 2188–2193.
20. Fischer, E. *Ber.* **1894**, *27*, 673–679.
21. Horton, D.; Varela, O. *Carbohydr. Res.* **1984**, *134*, 205–214.
22. Zinner, H.; Wittenburg, E.; Rembarz, G. *Chem. Ber.* **1959**, *92*, 1614–1617.
23. Zinner, H. *Chem. Ber.* **1953**, *86*, 495–496.
24. Wolfrom, M. L.; Newlin, M. R.; Stahly, E. E. *J. Am. Chem. Soc.* **1931**, *53*, 4379–4383.
25. Kochetkov, N. K.; Dimitriev, B. A. *Tetrahedron* **1965**, *21*, 803–815.