with fixed contributions ($B$ = 5.5 Å$^2$). Refinement of the non-hydrogen atoms with anisotropic temperature factors led to final values of $R$ = 0.053 and $R_w$ = 0.055. The final values of the positional parameters are given in the supplementary material.

**X-ray Crystallographic Analysis of 14.** A transparent single crystal of the title complex was mounted on a pin and transferred to a goniometer. The space group was determined to be the centric $P2_1/c$ from the systematic absences. A summary of data-collection parameters is given in Table III. Least-squares refinement with isotropic thermal parameters led to $R$ = 0.138. The geometrically constrained hydrogen atoms were placed in calculated positions 0.95 Å from the bonded carbon atom and allowed to ride on that atom with $B$ fixed at 5.5 Å$^2$. The methyl hydrogen atoms were located from a difference Fourier map and included with fixed contributions ($B$ = 5.5 Å$^2$). Refinement of the non-hydrogen atoms with anisotropic temperature factors led to final values of $R$ = 0.054 and $R_w$ = 0.057. The final values of the positional parameters are given in the supplementary material.

**X-ray Crystallographic Analysis of 17.** A transparent single crystal of the title complex was mounted on a pin and transferred to a goniometer. The space group was determined to be the centric $P2_1/c$ from the systematic absences. A summary of data-collection parameters is given in Table III. The geometrically constrained hydrogen atoms were placed in calculated positions 0.95 Å$^2$ from the bonded carbon atom and allowed to ride on that atom with $B$ fixed at 5.5 Å$^2$. Least-squares refinement with isotropic thermal parameters led to $R$ = 0.116. The methyl hydrogen atoms were located from a difference Fourier map and included with fixed contributions ($B$ = 5.5 Å$^2$). Refinement of non-hydrogen atoms with anisotropic temperature factors led to the final values of $R$ = 0.051 and $R_w$ = 0.060. The final values of the positional parameters are given in the supplementary material.

**Acknowledgment.** We thank the National Institutes of Health for financial support (Grant GM-28468), Professor A. L. Rheingold for his efforts in solving the structure of **29** by X-ray crystallography, and George Maynard for his generous assistance with the MODEL calculations.

**Supplementary Material Available:** Tables of bond distances and angles, final fractional coordinates, thermal parameters, and least-squares planes for **12**, **14**, **17**, and (in part) **29** (17 pages); tables of observed and calculated structure factors for **12**, **14**, and **17** (10 pages). Ordering information is given on any current masthead page.

# Dialdosides-(1,5) of Glucose and Galactose: Synthesis, Reactivity, and Conformation

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Methyl α-D-*gluco*-hexodialdoside-(1,5) 6-hydrate, **1a**, and the β-D-*gluco* (**4a**) and α-D-*galacto* (**6a**) isomers were prepared by oxidation of C6 by Moffatt, Swern, and photochemical oxidations. Dialdoside **1a** underwent dimer, hemiacetal, acetal, dithioacetal, and *gem*-diamine formation, exemplifying the facile transformations possible at C6, a strongly electrophilic aldehyde group. $NaBD_4$ reduction gave as predominant product the $S$ diastereomer from **1a** and the $R$ diastereomer from **6a**; reduction of **4a** gave almost equivalent amounts of $R$ and $S$ reduction product. These results were interpreted in terms of current theory of nucleophilic attack at chiral-substituted C=O groups. A combination of $^1$H NMR spectroscopy, optical rotation data, and calculations was used to deduce the major C5–C6 rotamers of the dimethyl acetal of **1a** (06-$R_{gg}$), and of **4a** (06-$R_{gg}$) and **6a** (06-$R_{gt}$). NOE experiments supported the rotamer structure assignment for the dimethyl acetal.

The α-1,6- and α-1,3-linked glucans synthesized from sucrose by the exocellular glucosyltransferase enzymes (GTF) of oral bacteria are constituents of cariogenic plaque and are a virulence factor in the formation of smooth surface dental caries.[1,2] Studies of GTF and the oral bacteria *Streptococcus sanguis* and *Streptococcus mutans* suggest that inhibition of glucan synthesis should have a prophylactic effect on the cariogenic process.[2] Also, studies of inhibitors should help in mapping the active site(s) of the GTF enzymes. A number of carbohydrate derivatives have been made that are competitive or uncompetitive inhibitors.[2,3] We targeted aldehyde derivatives of sucrose and glucose as potential GTF inhibitors.[4] Herein, we report on the synthesis and chemistry of dialdosides of glucose and galactose.

**Syntheses.** Our targets were the water-soluble methyl dialdopyranoside hydrates **1a**, **4a**, and **6a**.[5] Pettersson and

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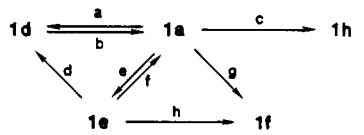
Theander prepared the α- and β-methyl dialdopyranosides of L-glucose and D-galactose (and of L-mannose and D-gulose) by periodate oxidation of the corresponding methyl heptopyranoside,[6] but we preferred more direct routes. Photolysis of primary azido derivatives of sugar glycosides has been successfully employed for synthesis of dialdose derivatives.[7] In addition, the mild Moffatt and Swern-type oxidations have been successfully applied to carbohydrates.[8] Accordingly, we explored photochemical and chemical oxidative routes to the dialdopyranosides. Starting with triacetate **2a**,[9] we found that the Swern reagents $(CH_3)_2SO$/trifluoroacetic anhydride/$(C_2H_5)_3N$ and $(CH_3)_2SO$/oxalyl chloride/$(C_2H_5)_3N$) gave mixtures of the desired aldehyde, trapped as **2b**, and the unsaturated aldehyde **3a**.[10] A similar result was obtained with a Moffatt reagent formulation using 1-ethyl-3-(3-(dimethylamino)propyl)carbiodiimide hydrochloride. However, use of diisopropylcarbodiimide with $(CH_3)_2SO$/pyridinium trifluoroacetate gave the desired aldehyde trapped as the imidazolidine **2b**, in nearly quantitative yield. Deacetylation afforded the stable derivatives **1e** in 91% yield. Dialdoside **1a** was liberated from **1e** in 70–80% yields by treatment of a suspension of **1e** in acetone/water with a sulfonic acid resin.

In a satisfactory alternate route to **1a**, we used the photolysis of water-soluble azido derivative **1g**[11] as the last step. In modifying the nonaqueous method of Horton and co-workers,[7] we found that the photolysis of unprotected azides in acidic water solution gave high yields of the corresponding dialdoside hydrates. Thus, **1a** could be prepared from **1g** in 90% yield. In a similar fashion, **4b**[11] afforded **4a**, and **6b**[12] afforded **6a**. Care had to be exercised to maintain an acidic pH during photolysis and to maintain neutral pH during evaporation of aqueous solutions to isolate the solid dialdosides. Basic photolysis solutions ($NH_3$ is produced) led to decomposition products—presumably from β-elimination—and acidic solutions during evaporation led to dimer formation (see below).

The benzyl group is a poorer leaving group than carboxylate, and with these as protecting groups in the case of β-glycoside **4d**, the Swern oxidation [$(CH_3)_2SO$/$(COCl)_2$/$(C_2H_5)_3N$] afforded aldehyde **4e** in high yield. Conversion of **4e** to **4f** and **4g** was straightforward.

**Characterization and Reactions.** The "free" dialdosides **1a**, **4a**, and **6a** were not successfully brought to analytical purity and, accordingly, were characterized through their derivatives. The distinguishing NMR spectral feature of the dialdosides was the $^{13}C$ resonance signal for the hydrated aldehyde carbon, C6, near δ 88 in $D_2O$ solution. No resonances for the dehydrated forms were evident in the $^{13}C$ NMR spectra. The H6 signal of **1a** appeared at δ 5.06 ($^3J_{H5,H6}$ = 1.8 Hz). For practical purposes, we considered **1a**, **4a**, and **6a** to be "completely" hydrated. Thus, the aldehyde groups of **1a**, **4a**, and **6a** are strongly electrophilic.

**Scheme I**[a]




[a] (a) $CH_3OH$, 4-Å molecular sieve, Amberlyst 15 ($H^+$), reflux, 6 h; 62%; (b) $H_2O$, pH ~2, 40–45 °C, $t_{1/2}$ ~30 min; (c) $CH_3OH$, $KHCO_3$, $NH_2OH$·HCl, reflux, 4 h; 90%; (d) $CH_3OH$, Amberlyst 15 ($H^+$), room temperature, 15 min; 65%; (e) $(C_6H_4NHCH_2)_2$, $CH_3OH$, pH 5–6, room temperature, 30 min; 95%; (f) acetone–$H_2O$ (1:1), Amberlyst 15 ($H^+$), room temperature, 30 min; 70%; (g) $(CH_2SH)_2$, $CH_3OH$, Amberlyst 15 ($H^+$), reflux, 6 h; 58%; (h) $CH_3OH$, $(CH_2SH)_2$, Amberlyst 15 ($H^+$), room temperature, 1.5 h; 90%.

Evidence for the presence of **1b** in solution was indicated, however, by the rapid formation of hemiacetal **1c** (stereochemistry not implied) and its epimer upon dissolution of **1a** in $CH_3OH$ or $CD_3OD$. This was evidenced by the disappearance of the 6C resonance of **1a** and the appearance of two signals, assigned as C6 of the **1c** epimers, at δ 97.1 and 97.6 when the $^{13}C$ NMR spectrum of **1a** was taken in $CD_3OD$. Also, when the $^1H$ NMR spectrum of **1a** was taken in $CD_3OD$ containing added $CH_3OH$, signals for three methoxyl groups were seen at δ 3.42, 3.41, and 3.40 (anomeric); the H6 doublet of **1a** was replaced with a new doublet at δ 4.75 ($^3J_{H5,H6}$ = 1.7 Hz). Because we failed to isolated pure hemiacetals **1c**, their characterization rests on NMR spectroscopy (see below for a discussion of structural data) and conversion to acetal **1d**. For example, when **1a** was dissolved in $CD_3OD$/$CH_3OH$ at pH 1.2, its conversion to **1d** (C6 at δ 105.1) by way of **1c** could be witnessed by $^{13}C$ NMR spectroscopy. Facile hemiacetal formation made isolation of the solid dialdosides difficult. Concentration of slightly acidic aqueous solutions of **1a**, **4a**, or **6a** resulted in loss of dialdosides presumably from dimerizing hemiacetal reactions as judged from the complex $^{13}C$ NMR spectra of the products. Drying **1a** over $P_2O_5$, for example, gave a mixture of two products, which, from their $^{13}C$ NMR spectra, we interpreted to be dimers of **1a**. The dialdoside of methyl β-D-galactopyranoside undergoes a hemiacetal-forming dimerization reaction as reported earlier by Perlin,[13,15a] and a similar process is operating in the case of **1a** (see below for a discussion of structural data). The reversibility of the dimerization of **1a**, **4a**, and **6a** under certain conditions also supported hemiacetal formation as a step in the dimerization process. For example, the $NaBH_4$ reduction of a sample of **4a** containing presumed dimeric products gave methyl β-D-glucopyranoside in high yield.

Scheme I outlines the conversion of **1a** to several derivatives. The optimum shelf storage compound for **1a** was the high-melting (240–241 °C), rapidly forming **1e**. The interconversions starting with **1a** served as models for reactions of **4a**, **6a**, and their derivatives (see Experimental Section). Interestingly, an attempted oximation/benzoylation of **6a** yielded, instead of oxime, the nitrile **8**.

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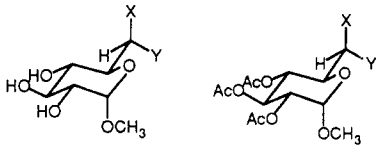
(15) The chemical shifts of the 6(*S*)- and 6(*R*)-hydrogens of D-glucose and D-galactose are derivative-dependent, but the $^3J$ values of H6(*S*) in these compounds, and of H5(*S*) in the D-pentofuranosides are, with the exception of peracetylated galactose derivatives, less than those of H5(*R*). (a) Ohrui, H.; Nishida, Y.; Huguchi, H.; Hori, H.; Meguro, H. *Can. J. Chem.* **1987**, *65*, 1145–53. (b) Nishida, Y.; Hiroshi, O.; Meguro, H. *Tetrahedron Lett.* **1984**, *25*, 1575–78. (c) Ohrui, H.; Nishida, Y.; Watanabe, M.; Hori, H.; Meguro, H. *Tetrahedron Lett.* **1985**, *26*, 3751–54. (d) Wu, G. D.; Serianni, A. S.; Barker, R. *J. Org. Chem.* **1983**, *48*, 1750–57. (e) Mackie, D. M.; Maradufu, A.; Perlin, A. S. *Carbohydr. Res.* **1986**, *150*, 23–33.

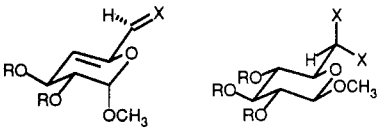


| | X | Y |
|---|---|---|
| 1a | OH | OH |
| b | =O | |
| c | OH | $OCH_3$ |
| d | $OCH_3$ | $OCH_3$ |
| e | DPED | |
| f | $(-SCH_2)_2$ | |
| g | H | $N_3$ |
| h | =NOH | |

DPED=$[-N(Ph)CH_2]_2$



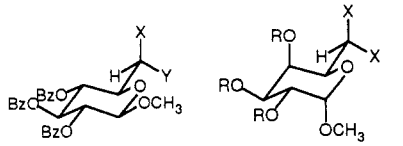
| | X | Y |
|---|---|---|
| 2a | H | OH |
| b | DPED | |
| c | D | OAc |
| d | OAc | D |
| e | H | OAc |



| | R | X |
|---|---|---|
| 3a | Ac | O |
| b | H | O |
| c | Ac | DPED |



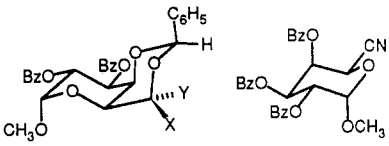
| | R | X |
|---|---|---|
| 4a | H | OH |
| b | H | H,$N_3$ |
| c | Bz | $OCH_3$ |
| d | Bn | H,OH |
| e | Bn | =O |
| f | Bn | DPED |
| g | H | DPED |



| | X | Y |
|---|---|---|
| 5a | H | OBz |
| b | D | OBz |
| c | OBz | D |



| | R | X |
|---|---|---|
| 6a | H | OH |
| b | H | H,$N_3$ |
| c | Bz | $OCH_3$ |
| d | H | $OCH_3$ |



| | X | Y |
|---|---|---|
| 7a | H | H |
| b | D | H(S) |
| c | H | D(R) |



8

**Stereochemistry of Reduction at C6.** We examined the $NaBD_4$ reduction of dialdosides **1a**, **4a**, and **6a** in water solution. We confirmed an earlier report of aqueous $NaBD_4$ reduction of **1a**[14] by $^1H$ NMR analysis of the corresponding tetraacetates, **2c** (*R*) and **2d** (*S*).[15] Table I summarizes our results with other aldehydes reduced with $NaBD_4$ in $H_2O$. To determine the stereochemistry of reduction of **4a**, we converted the reduced product to tetrabenzoates **5b** (*R*) and **5c** (*S*) for $^1H$ NMR analysis.[15] Stereochemistry of the reduction of galactodialdoside **6a** was determined after conversion of the reduction product to benzylidenes **7b** and **7c**. The H6 resonances of **7a** were well separated in $C_6D_6$. H6(*R*), which is axial, resonated at $\delta$ 3.40 ($^3J \leq 1$ Hz) and H6(*S*), equatorial, resonated downfield at $\delta$ 4.02 ($^3J \leq 1$ Hz). This assignment was confirmed by a difference NOE experiment, which showed that upon saturation of the benzylic H, the signal of H6(*R*) was enhanced 1.7 times that of H6(*S*).

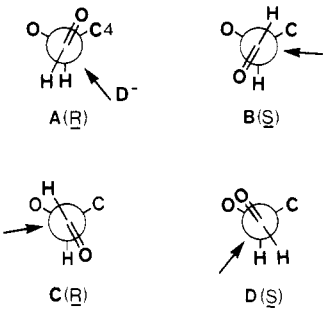
The conditions for reduction, which employed $Na^+$ as the $BH_4^-$ counterion and water as the solvent are not at all conducive to biasing the C5–C6 conformational population by intramolecular H-bonding or chelation effects.[16] Therefore, the stereochemical outcome of the $BD_4^-$ reductions should be rationalized by applying current theory of diastereofacial differentiation in nucleophilic addition to chiral aldehydes.[17] Qualitative consideration of the $\sigma^*$ orbital energies of the bonds to the C5 substituents (C–O < C–H < C–C) leads to a favoring of reaction pathways A and B for electronic reasons (Chart I). (With the C5–O5 bond having the lowest lying $\sigma^*$ orbital, O5 becomes the "large" group.) If C4 were to exert an unexpectedly large steric influence, then reaction pathways C and D could become important.[17] Given this, theory[17] and experimental results on a structural analogue[17a] lead to a prediction that reaction via pathway A should be the preferred pathway and than *R*-configured products should predominate. This occurred with the *galacto* dialdoside **4a** (Table I) and with the 6′ aldehyde group on sucrose. But, interestingly, the *S*-configured product was the major one in the *gluco* dialdoside cases (**1a** and 6-CH=O of sucrose, Table I).[18] Thus, reaction path A must be less favored in these instances. Perhaps this is due to a hindrance of the incoming nucleophile by a perilike interaction with the equatorial 4-OH group of glucose. If so, then *S*-producing reaction path B would appear to be still more disfavored. This leads to the conclusion that the major reaction pathway for reduction in the gluco series is D. This pathway, with

**Table I. Stereochemistry of $NaBD_4$ Reduction of Aldehyde Derivatives in $H_2O$**

| compound | % *S* | % *R* |
|---|---|---|
| Me α-D-Glc-6-CH=O, **1a** | 60 | 40 |
| Me β-D-Glc-6-CH=O, **4a** | 52 | 48 |
| Me α-D-Gal-6-CH=O, **6a** | 34 | 66 |
| sucrose 6-CH=O[a] | 55 | 45 |
| sucrose 6′-CH=O[a] | 34 | 66 |

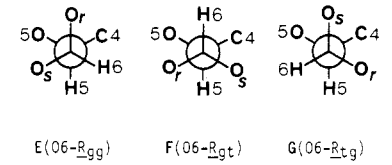
[a] Singh, S.; Doyle, R. J.; Taylor, K. G., to be published.

**Chart I**



A(R) B(S) C(R) D(S)

**Chart II**



E(O6-Rgg) F(O6-Rgt) G(O6-Rtg)

(16) Boone, J. R.; Ashby, E. C. In *Topics in Stereochemistry*; Allinger, N. L., Eliel, E., Eds.; J. Wiley and Sons: New York, 1979; Vol. II, pp 53–95.

(17) (a) Lodge, E. P.; Heathcock, C. H. *J. Am. Chem. Soc.* **1987**, *109*, 3353–61. (b) Houk, K. N.; Wu, Y.-D. *J. Am. Chem. Soc.* **1987**, *109*, 908–10. (c) Houk, K. N. *Science* **1986**, *231*, 1108–17. References 17a and 17c also give succinct reviews of the theory of nucleophilic additions to chiral C=O systems.

(18) *R* is also favored in the $LiAlD_4$ reduction of a galactofurano configured case: 3-*O*-benzyl-1,2-*O*-isopropylidinexylofuranodialdose-(1,4). But intramolecular chelation may bias the C4–C5 conformation. Lemieux, R. U.; Howard, J. *Can. J. Chem.* **1963**, *41*, 308–16.

**Table II. C5-C6 Rotamer Populations of Hydrated Dialdosides and Acetals**

| compd | [M], deg | [M], deg, calcd[a] | $^3J_{H5,H6}$, Hz | rotamer, %[b] gg | gt | tg |
|---|---|---|---|---|---|---|
| Me α-D-Glcp | 308 | 297 | c | 56 | 42 | 2[c] |
| **1a** ($D_2O$) | 226 | | 1.8 | 23 | d | 77 |
| **1d** ($CD_3OD$) | 301 | | 4.0 | 77 | d | 23 |
| **1d** (pyridine) | 346 | | 2.1 | ~100 | d | |
| Me β-D-Glcp | −66 | −109[g] | c | 53 | 45 | 2[c] |
| **4a** ($D_2O$) | −71 | | 2.0 | ~100 | d | |
| Me α-D-Galp | 380 | 394 | e | 16 | 66 | 18[e] |
| **6a** ($D_2O$) | 335 | | 7.5 | f | 91 | 9 |
| **6d** ($CD_3OD$) | 311 | | 7.8 | f | 87 | 13 |

[a] Estimated using [M] as described in the text using the rotamer populations of ref 15a,b. [b] Estimated by weighting calculated [M] values; reference substituent is O6 or O6-*R* as appropriate. [c] See ref 15b. [d] Not considered because of low experimental $^3J_{H5,H6}$. [e] Averaged from ref 15a. [f] Not considered because of expected high contribution to [M] (395°) relative to rotamer tg (260°); see text. [g] Uncertainty about the $O_{ring}$–$CH_3$ contribution increases the difference in this case.

H5 in the "outside" position, is sterically favored over pathway C (H5 in "inside" position). An interesting result is that seen when the anomeric configuration of the glucodialdoside is changed from α to β, a change apparently enhancing reaction through pathway A. This must be an electronic effect. This configurational change is accompanied by a lengthening of the C5–O5 bond and a shortening of the C1–$OCH_3$ bond, and Kirby and co-workers have crystallographic evidence which indicates σ,σ* orbital interactions between these antiperiplanar C–O bonds.[19] Also, the downfield shift of the NMR signal of C5 attending this anomeric change suggests a lowering of the σ,σ* energy gap of the C5–O5 bond. This effect should strengthen the HOMO (nucleophile)–LUMO (C=O) interaction attending nucleophilic attack at C=O anti to the C5–O5 bond and facilitate reaction by pathway A. This is what is observed.

**Acetal Conformation.** We were precluded from using Davies' equations,[20] which are based on $^3J_{H5,H6}$ values of H6(*R*) and H6(*S*), for estimating the C5–C6 rotamer populations of the hydrated dialdosides and acetals. We resorted to using a combination of $^1H$ NMR spectroscopy, and molecular rotation data and calculations, to eliminate one rotamer as a major contributing conformation and then used the same data to estimate the proportion of the major rotamer. The method is illustrated below for **1d**. Table II summarizes the data for additional compounds. We used Lemieux's approach[21] to estimate the molecular rotations, [M], of the three C5–C6 rotamers of the hydrated aldehydes shown in Chart II. This was done by calculating the [M] for each rotamer of methyl α-D-glucopyranoside (gg, 275°; gt, 340°; tg, 240°) and then figuring the effect of a second OR group at C6 (interactions with C4 and O5): for F, 330°; for G, 195°; for E, 330°. As a check on the approach, we weighted the [M] of each rotamer of methyl glucoside according to the rotamer populations determined by Meguro and co-workers[15b] to arrive at the calculated [M] shown in Table II. The result was reasonable. We estimated the $^3J_{H5,H6}$ for each rotamer in Chart II by applying the calculational approach of Altona and co-workers[22] and by averaging the ranges used by Davies:[20] for F, 7.5–8.5 Hz; for G, 3.6–4.0 Hz; for E, 1.6–2.0 Hz. A major contribution from rotamer F to the structure of **1d** was deemed improbable because of the $^3J_{H5,H6}$ observed for **1d**: 4.0 Hz in $CD_3OD$ and 2.1 Hz in pyridine. We used the observed [M] value for **1d** in $CH_3OH$, 301°, and the calculated [M] for the remaining rotamers to apportion the mole fractions of the G and E rotamers as shown in Table II. The magnitude of $^3J_{H5,H6}$ would indicate, perhaps, a greater contribution of rotamer G (or F) than is calculated from the molecular rotation. In pyridine solvent, the molecular rotation was increased to 346° and $^3J_{H5,H6}$ was reduced to 2.1 Hz. Both measurements indicate an increase in the O6-$R_{gg}$ rotamer, E, to the point where it is certainly the major one in solution. If this is the case, and if we assume that the dimethyl acetal grouping assumes the conformation favored by steric considerations and the exo-anomeric effect,[19,23] the most favored structure of **1d** in pyridine should be represented by **9**. Support for this rotameric assignment for acetal **1d** was obtained from 2D NOE experiments. In dry pyridine-$d_5$ at room temperature and at −20 °C, **1d** displayed $^1H$ NMR signals for methoxyl groups at δ 3.47, 3.51, and 3.54. Positive NOE correlations were seen between the methoxyl at δ 3.54 and H1 and between the two methoxyls at δ 3.47 and 3.51 and H6. This differentiated the signals of the anomeric and C6 acetal methoxyl groups. Interestingly, the anomeric methoxyl as well as the acetal methoxyl groups displayed NOE correlations with H5. This result is consistent with the conformation of the anomeric methoxyl as shown in structure **9**. In a phase-sensitive 2D experiment the anomeric methoxyl was shown to give a positive NOE correlation with H5 and a weaker, but negative, correlation with H6. This result is consistent with the rotamer structure shown in **9** (rotamer E) and is inconsistent with a major contribution from rotamer G. The center methoxyl group (δ 3.51) is tentatively assigned as the *pro-S* methoxyl group since it would be further than the *R*-$OCH_3$ from any deshielding effect associated with pyridine solvent hydrogen bonded at OH-4.

In the galactodialdoside series the $^3J_{H5,H6}$ value of 7.5 Hz for **6a** and 7.8 Hz for **6d** indicated a major contribution from rotamer F. In light of our experimental values of [M], rotamer E was eliminated from consideration because of its expected high contribution to [M] of 395°.

The approach used to determine the rotamer populations has obvious limitations. But there is reasonable agreement, with the exception of **1a**, between the NMR and [M] results. The general picture that has emerged is

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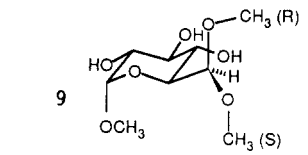
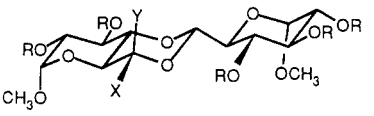
(21) (a) Lemieux, R. U.; Brewer, J. T. In *Carbohydrates in Solution*; Isbell, H. S., Ed.; American Chemical Society: Washington, DC, 1973; pp 121–46. (b) Shallenberger, R. S. *Advanced Sugar Chemistry*; AVI Publ. Co.: Westport, CN, 1982; pp 181–84. (c) We used the value of ±90° for the O6–$O_{ring}$ interactions. Use of the lower limit of ±55° gave a poorer agreement with NMR results.

(22) (a) Haasnoot, C. A. G.; DeLeeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783–92. (b) A shorter method is found in Altona, C.; Haasnoot, C. A. G. *Org. Magn. Reson.* **1980**, *13*, 417–29.

(23) (a) *Anomeric Effect*; Szarek, W. A., Horton, D., Eds.; American Chemical Society: Washington, DC, 1979. (b) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer-Verlag: New York, 1983.



9



| | X | Y | R |
|---|---|---|---|
| 10a | OH | H | H |
| b | H | OH | H |
| c | OAc | H | Ac |
| d | H | OAc | Ac |

that the introduction of a second large group at C6 results in an increase in preference for one rotamer, and this is what would be expected.

**Hemiacetal Configuration.** As noted above, the dissolution of **1a** in $CD_3OD$ rapidly gave epimeric hemiacetals, **1c**. As judged from the integration of the $^{13}C$ signals of C6 at $\delta$ 97.1 and 97.6, the epimer having the lower field signal predominated by a ratio of 1.8:1. A $^1H$ NMR spectrum in $CD_3OD/CH_3OH$ corroborated this finding. The methoxyl signals at $\delta$ 3.41 and 3.42, assigned as the hemiacetal methoxyls, were in the approximate ratio of 1.7:1. On the basis of the results with acetal **1d** we assign the higher field (and more intense) methoxyl signal to the hemiacetal having the *S* configuration at C6. The rapid formation of **1c** and the apparent lack of exchange of methoxyl groups under neutral conditions indicates that the hemiacetals are kinetic products. The predominance of *S*-configured hemiacetal is consistent with what was observed in the reduction of **1a** with $NaBD_4$.

**Dimer Structure.** As noted above, evaporation of aqueous solutions of **1a** often produced dimeric products, to which we've assigned structures **10a,b**. This assignment is based on the proof of structure of the dimer of methyl $\beta$-D-*galacto*-hexodialdoside-(1,5) by Perlin[13] and the confirmation of that structure by Nishida and co-workers.[15a] Acetylation of **10a,b** gave a mixture of hexacetates, **10c,d**, which gave crystalline **10c** after chromatography. The telltale $^1H$ NMR resonances of **10c** and **10d** are those for H6 at $\delta$ 5.85 (d, $^3J_{5,6}$ = 7.8 Hz) and 6.34 (d, $^3J_{5,6}$ = 3.1 Hz), respectively. Correlation NMR spectroscopy of **10c** fully corroborated the proposed structure, and signal assignments are listed in the Experimental Section.

## Experimental Section

Melting points were determined with a Thomas-Hoover melting point apparatus and are uncorrected. TLC was performed at room temperature on silica gel GF-254 (Merck) with detection by charring with sulfuric acid. Optical rotations were determined with a Perkin-Elmer Model 141 polarimeter. Column chromatography was carried out with Baker (60–300 mesh) silica gel at room temperature. Photolyses were done with a Hanovia 450-W medium-pressure lamp with a quartz imersion well. NMR spectra were recorded with a Varian XL-300 spectrometer. Some NOE experiments were run on a Varian XR-400 spectrometer. Proton and carbon signal assignments were done with use of INDOR, APT, and heteronuclear 2D experiments, unless noted otherwise. 1D difference NOE experiments employed a truncated selective inversion recovery sequence[24] with a constant cycle time of 1 s and mixing times of 0.1–0.5 s. Two-dimensional NOE experiments used the standard three-pulse sequence[25] with phase-sensitive detection.[26] One experiment was carried out at 300 MHz with a mixing time of 2 s, and a second experiment was carried out at 400 MHz with a mixing time of 1 s.

**Methyl 2,3,4-Tri-*O*-acetyl-(*R*)-5-*C*-(1,3-diphenyl-2-imidazolidinyl)-$\alpha$-D-xylopyranoside (2b).** A solution of 1.60 g (5.0 mmol) of **2a**,[9] dry DMSO (15 mL), benzene (30 mL) (**Caution**: carcinogen), diisopropylcarbodiimide (1.89 g, 15.0 mmol), pyridine (0.4 mL, 5 mmol), and trifluoroacetic acid (0.19 mL, 2.4 mmol) was stirred overnight at room temperature. The mixture was cooled to 0 °C, and a solution of oxalic acid (1.35 g, 15.0 mmol) in 20 mL of $CH_3OH$ was added to destroy diisopropylcarbodiimide. After 30 min, $N^1$,$N^2$-diphenylethane-1,2-diamine (2.12 g, 10.0 mmol) was added, and the mixture was stored overnight at room temperature. The mixture was diluted with ice water (150 mL), and the product was extracted with ethyl acetate (2 × 150 mL). The organic layer was washed with aqueous, saturated $NaHCO_3$. After drying over anhydrous $MgSO_4$, the solvents were distilled in vacuo, the residue was dissolved in ether, and on addition of petroleum ether, diisopropyl urea crystallized and was removed by filtration. The concentrated filtrate was chromatographed, eluting with ether–petroleum ether (1:1). Fractions having $R_f$ = 0.5 (TLC, ether) were combined and concentrated to give a foam (2.5 g, 100%): mp 76–80 °C; $[\alpha]^{20}_D$ 21.5° ($c$ = 1.068, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.71, 2.02, 2.03 (3 s, 9 H, $OCOCH_3$), 3.16 (s, 3 H, $OCH_3$), 3.51–3.74 (m, 4 H, $CH_2CH_2$), 4.32 (d, 1 H, H5, $J_{4,5}$ = 10.2), 4.76 (dd, 1 H, H2, $J_{2,3}$ = 6.8), 4.96 (d, 1 H, H1, $J_{1,2}$ = 3.6), 5.06 (t, 1 H, H4, $J_{3,4}$ = 9.0), 5.34 (t, 1 H, H3), 5.57 (s, 1 H, H6), 6.70–7.30 (m, 10 H, $C_6H_5$). Anal. Calcd for $C_{27}H_{32}N_2O_8$: C, 63.28; H, 6.25; N, 5.46. Found: C, 62.92; H, 6.39; N, 5.26.

**Methyl (*R*)-5-*C*-(1,3-Diphenyl-2-imidazolidinyl)-$\alpha$-D-xylopyranoside (1e).** A solution of **2b** (1.5 g, 2.9 mmol) in 25 mL of dry $CH_3OH$ containing a trace of sodium methoxide (wet pH paper indicated pH ≈9–10) was stirred at room temperature for 2 h. A white solid, which precipitated after 10 min of stirring, was separated by filtration, washed with methanol (2 × 10 mL), and dried in a vacuum desicator over $P_2O_5$ to give 1.02 g (91%): mp 240–241 °C; $[\alpha]^{21}_D$ 24.1° ($c$ = 1.33, DMF); $^1H$ NMR (DMSO-$d_6$) $\delta$ 4.72 (d, 1 H, OH2, $J$ = 6.5), 4.85 (d, 1 H, OH3, $J$ = 4.8), 5.39 (d, 1 H, OH4, $J$ = 5.3), 3.40 (s, 3 H, $OCH_3$), 5.76 (s, 1 H, H6), 4.52 (d, 1 H, H1, $J_{1,2}$ = 3.52), 3.90 (d, 1 H, H5, $J_{4,5}$ = 9.8), 3.3–3.39 (m, 1 H, H3), 3.0–3.2 (m, 2 H, H2,4), 3.53–3.76 (m, 4 H, $CH_2CH_2$), 6.55–7.24 (m, 10 H, $C_6H_5$). Anal. Calcd for $C_{21}H_{26}N_2O_5$: C, 65.28; H, 6.76; N, 7.25. Found: C, 64.99; H, 6.79; N, 7.08.

**Methyl 2,3-Di-*O*-acetyl-5-*C*-(1,3-diphenyl-2-imidazolidinyl)-4-deoxy-$\beta$-L-*threo*-pent-4-enopyranoside (3c).** A solution of 4.14 g (12.9 mmol) of **2a**[9] in 25 mL of DMSO and 50 mL of $C_6H_6$ was cooled to 0 °C, and 7.40 g (38.8 mmol) of 1-ethyl-3-(3-(dimethylamino)propyl)carbodiimide hydrochloride, 1.02 g (12.9 mmol) of pyridine, and 0.730 g (6.45 mmol) of trifluoroacetic acid were added. This mixture was stirred at room temperature for 24 h. After the mixture was cooled to 0 °C, 3.75 g of oxalic acid in 25 mL of $CH_3OH$ was added. After 30 min of stirring, 4.11 g (19.4 mmol) of $N^1$,$N^2$-diphenyl-1,2-ethanediamine was added, and this solution was stirred for 12 h. Cold water (50 mL) was added, and the organic products were extracted with ethyl acetate (4 × 100 mL). After drying ($MgSO_4$) and evaporation of the solvent, the addition of ether produced 5.0 g (84.7%) of a white solid, mp 159–160 °C (lit.[10] mp 159–160 °C).

**Methyl $\alpha$-D-*gluco*-Hexodialdoside-(1,5) 6-Hydrate (1a).** Compound **1e** (0.500 g, 1.29 mmol) was suspended in 80 mL of acetone–water (1:1). Amberlyst 15 $H^+$ resin (3.5 g) was added, and the mixture was stirred at room temperature for 0.5 h. The mixture was filtered, and the filtrate was neutralized with Rexyn 201 (OH) resin. After filtration through Celite and concentration in vacuo (temperature ≤30 °C), **1a** was obtained as an amorphous solid, 0.19 g (~70%): $[\alpha]^{21}_D$ = 107.6° ($c$ = 2.09, $H_2O$) [lit.[6] $[\alpha]_D$ −120° for L enantiomer ($H_2O$)]; we took care to insure that samples for rotation were monomeric and had not been exposed to alcohols; this may account for differences between ours and published

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rotation data for **1a**, **4a**, and **6a**; $^{13}C$ NMR ($D_2O$) $\delta$ 56.04 ($OCH_3$), 100.34 (C1), 89.02 (C6), 74.06, 73.46, 72.20, 71.39; $^1H$ NMR ($D_2O$) $\delta$ 5.06 (d, 1 H, H6, $J_{5,6}$ = 1.8), 4.64 (d, 1 H, H1, $J_{1,2}$ = 3.6), 3.23 (s, 3 H, $OCH_3$). Anal. Calcd for $C_7H_{14}O_7$: C, 40.00; H, 6.66. Found: C, 40.40; H, 6.14.

**Methyl α-D-*gluco*-Hexodialdoside-(1,5) 6-Hydrate (1a) by Photolysis of 1g.** To a solution of 3.00 g (13.6 mmol) of **1g**[11] in 250 mL of deionized water was added 1 equiv of glacial acetic acid. The solution was photolyzed under $N_2$ with stirring for 4 h. The temperature was maintained below room temperature by circulating cold water in the jacketed reaction vessel. After the completion of reaction (monitored by TLC), the solution was concentrated to 50 mL in vacuo at a temperature below 20 °C. Dowex MR-3 mixed resin (3 g) was added, and the mixture was stirred for 1 h. After filtration, the filtrate was stirred with neutral charcoal for 2 h and processed conventionally. The last traces of water were removed in vacuum desicator over $P_2O_5$ to give 2.00 g (70%) of amorphous white solid. Dialdoside **1a** prepared this way was chemically and spectroscopically identical with that prepared from **1e**.

**Dimer of Methyl α-D-*gluco*-Hexodialdoside-(1,5) (10).** A 3.50-g (16.6-mmol) sample of **1a** prepared by photolysis of **1g** at pH 2–3 was evaporated to dryness below 30 °C without neutralization by resin. The amorphous solid was dried over $P_2O_5$ to yield **10a,b** ($^{13}C$ NMR evidence) containing some **1a**. Trituration with hot $CH_3CN$ left a residue of purified, amorphous **10a,b**: $^{13}C$ NMR ($D_2O$) $\delta$ 101.17, 100.93 (C6′ of **10a** and **10b**), 100.51, 100.42, 97.78, 96.68 (C1 and C1′), 92.01 (C6 of **10a**), 91.13 (C6 of **10b**), 79.19 (C4 of **10a**), 75.12 (C4 of **10b**), 73.89–68.6 (12 signals), 65.89 (C5′ of **10a** and/or **10b**), all assignments are tentative.

A solution of 1.0 g (2.4 mmol) of **10a,b** in pyridine was treated with excess acetic anhydride overnight at room temperature. The usual workup followed by chromatography (ethyl acetate–hexane, 3:4) gave 1.54 g (93%) of a solid residue. Crystallization from ether yielded 0.08 g of pure **10c**, mp 179–181 °C: $^{13}C$ NMR ($CDCl_3$) $\delta$ 170.2–168.9 (six signals, C=O), 97.75 (C6′), 97.07 and 96.51 (C1, C1′), 92.44 (C6), 77.08 (C4), 70.94 and 70.39 (C2, C2′), 70.02 (C3), 68.81 (C3′), 67.52 (C4′ and C5′), 64.93 (C5), 55.42, 55.09 ($OCH_3$), 20.8–20.6 (acetyl $CH_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 5.85 (d, H6, $J$ = 7.8), 5.4 (2 t, 2 H, H3,3′), 5.23 (t, H4′, $J$ = 8.0), 4.9–4.8 (m, 5 H, H1,2,1′,2′,6′), 3.89 (b d, H5′, $J$ = 8.0), 3.63 (t, H5, $J$ = 7.9), 3.43 (t, H4, $J \sim 8$), 3.36 (s, 2 $OCH_3$). Anal. Calcd for $C_{26}H_{36}O_{18}$: C, 49.05; H, 5.65. Found: C, 49.23; H, 5.60.

The ether filtrate was evaporated to yield 1.4 g of a solid identified by NMR spectroscopy[13,15a] as a mixture of **10c** and **10d**. Key $^1H$ NMR signal: $\delta$ 6.34 (d, H6 of **10d**, $J$ = 3.1).

**Methyl α-D-*gluco*-Hexodialdoside-(1,5) Methyl Hemiacetals (1c).** Dissolution of **1a** in $CD_3OD$ or $CD_3OD/CH_3OH$ gave the following spectral results: $^{13}C$ NMR ($CD_3OD$) **1c-*S*** $\delta$ 101.13 (C1), 97.58 (C6), 74.83, 73.32, 73.04, 71.94, 55.60 ($OCH_3$); **1c-*R*** $\delta$ 101.06 (C1), 97.09 (C6), 74.83, 73.83, 73.15, 71.94, 55.60 ($OCH_3$); $^1H$ NMR ($CD_3OD$, $CH_3OH$) $\delta$ 4.75 (d, H6, $J_{5,6}$ = 1.7), 4.71 (d, H1, $J_{1,2}$ = 3.6), 3.44 (s, 6(*R*)-$OCH_3$), 3.41 (s, 6(*S*)-$OCH_3$), 3.40 (s, 1-$OCH_3$), 3.35 ($CH_3OH$).

**Methyl-α-D-*gluco*-Hexodialdoside-(1,5) Dimethyl Acetal (1d).** Compound **1e** (0.560 g, 1.45 mmol) was mixed with 40 mL of $CH_3OH$ (dry) and 2.85 g of Amberlyst $H^+$ resin and stirred for 15 min. During this time, **1e** dissolved completely. Solid material was filtered, and the filtrate was concentrated. The residue was chromatographed, eluting with ethyl acetate/methanol (9:1). Fractions having material with $R_f$ = 0.17 were combined and concentrated to give **1d**, 0.22 g (65%) as a thick oil: $[\alpha]^{22.5}_D$ 126.3° ($c$ = 0.520, $CH_3OH$); $^{13}C$ NMR ($CD_3COCD_3$) $\delta$ 104.76 (C6, $^1J_{C,H}$ = 162), 100.33 (C1, $^1J_{C,H}$ = 169), 74.28 (C5), 72.40, 71.53 (2 C), 55.68, 55.60, 55.38; $^1H$ NMR ($CD_3COCD_3$) $\delta$ 4.62 (d, 1 H, H1, $J_{1,2}$ = 3.7), 4.54 (d, 1 H, H6, $J_{5,6}$ = 3.4), 4.26 (d, 1 H, OH3, $J$ = 3.7), 4.02 (d, 1 H, OH4, $J$ = 3.4), 3.83 (d, 1 H, OH2, $J$ = 7.5), 3.58 (m, 1 H, H3, $J$ = 9.0, 3.7), 3.55 (m, 1 H, H5), 3.41 (s, 3 H, 6(*R*)-$OCH_3$), 3.4 (m, H4), 3.40 (s, 3 H, 6(*S*)-$OCH_3$), 3.33 (s, 3 H, 1-$OCH_3$); $^1H$ NMR ($C_5D_5N$, −20 °C) $\delta$ 5.16 (d, 1 H, H1, $J_{1,2}$ = 3.7), 5.10 (d, 1 H, H6, $J_{5,6}$ = 2.1), 5.0 (br s, OH), 4.53 (td, 1 H, H3, $J_{2,3} \sim J_{3,4} \sim 9.5$), 4.25 (m, 2 H, H4,5), 4.13 (q, 1 H, H2, $J_{1,2}$ = 3.7, $J_{2,3}$ = 9.5), 3.54 (s, 3 H, 6(*R*)-$OCH_3$), 3.51 (s, 3 H, 6(*S*)-$OCH_3$), 3.47 (s, 3 H, 1-$OCH_3$); $^3J_{5,6}$ (Hz) 2.1 ($C_5D_5N$), 2.4 (DMSO-$d_6$), 3.6 ($CD_3CN$), 4.0 ($CD_3OD$). Anal. Calcd for $C_9H_{18}O_7$: C, 45.38; H, 7.56. Found: C, 45.57; H, 7.51.

**Acetal 1d from 1a.** Compound **1a** (1.5 g, 7.19 mmol) was mixed with 50 mL of $CH_3OH$ (dry) and 5.50 g of 4-Å molecular sieve and stirred for 6 h. After filtration, the filtrate was mixed with 3.5 g of Amberlyst $H^+$ resin and refluxed for 6 h. After cooling, the mixture was filtered through Celite. The filtrate was treated with charcoal for 2 h and again filtered through Celite. After concentration, the residue was chromatographed, eluting with ethyl acetate/methanol (9:1). Fractions having material with $R_f$ = 0.17 were combined and concentrated to give **1d**, 1.05 g (62%) as a thick oil, chemically and spectrally identical with that prepared from **1e**.

**Methyl 2,3,4,6-*O*-Tetraacetyl-[6-$^2$H]-(*R*)- and -[6-$^2$H]-(*S*)-α-D-glucopyranosides (2c and 2d).** Compound **1a** (0.938 g, 4.45 mmol) was dissolved in 15 mL of $D_2O$. To the solution was added 0.280 g of $NaBD_4$ in small portions over a period of 5 min. The reaction mixture was stirred at room temperature for 3 h and then brought to pH 6–7 with DCl. The solvent was evaporated in vacuo; the solid residue was treated with $CH_3OH$ (20 mL) and concentrated. After being dried in vacuum dessicator over $P_2O_5$, the residue was acetylated with acetic anhydride and pyridine. After the usual workup the residue was chromatographed, eluting with ether–petroleum ether (2:3). Fractions having material with $R_f$ = 0.3 (TLC, ether/petroleum ether, 1:1) were combined and concentrated to give 0.90 g (68%) of a white solid: mp 100–101.5 °C [lit.[14] mp 101–101.5 °C]; $^1H$ NMR ($C_6D_6$) $\delta$ 5.79 (t, 1 H, H3, $J_{3,4} \sim J_{3,2} \sim 9.9$), 5.28 (t, 1 H, H4, $J_{4,3} \sim 10.1$, $J_{4,5} \sim 9.5$), 5.02 (dd, 1 H, H2, $J_{1,2}$ = 3.6, $J_{2,3}$ = 10.2), 4.88 (d, 1 H, H1, $J_{1,2}$ = 3.8), 4.23 (d, 0.60 H, H6(*R*), $J_{6R,5}$ = 4.5), 4.03 (d, 0.40 H, H6(*S*), $J_{6S,5}$ = 1.9), 3.80 (dd, 1 H, H5, $J_{5,4}$ = 9.9), 2.97 (s, 3 H, $OCH_3$), 2.97, 1.72, 1.70 (3 s, 9 H, $OCOCH_3$); $^{13}C$ NMR ($C_6D_6$) $\delta$ 97.03 (C1), 71.30 (C2), 70.58 (C3), 68.97 (C4), 67.55 (C5), 61.23 (t, C6), 54.91 ($OCH_3$).

**Methyl α-D-*gluco*-Hexodialdoside-(1,5) Cyclic Ethylene Mercaptal (1f).** Compound **1e** (0.540 g, 1.39 mmol) was suspended in 40 mL of $CH_3OH$, and to this were added 3.5 g of Amberlyst 15$H^+$ resin and 2 equiv of 1,2-ethanedithiol. The mixture was stirred at room temperature for 1.5 h and then filtered, and the filtrate was concentrated in vacuo. The residue was chromatographed, eluting with chloroform–methanol (3:1). Fractions containing material having $R_f$ = 0.36 were combined and concentrated to give 0.32 g (85.5%) of **1f** as a thick, air-sensitive oil: $[\alpha]^{22}_D$ +112.7° ($c$ = 0.308, $CH_3OH$); $^{13}C$ NMR (DMSO-$d_6$) $\delta$ 99.75 (C1), 75.76 (C5), 73.37 (C4), 73.22 (C3), 71.90 (C2), 54.26 ($OCH_3$), 52.96 (C6), 38.39 and 38.24 ($CH_2$); $^1H$ NMR (DMSO-$d_6$) $\delta$ 4.85 (d, H1, $J$ = 3.7), 4.55 (d, H6, $J$ = 5.1), 3.48 (q, H2, $J$ = 3.7, 8.0), 3.3 (m, 4 H, H3 and $OCH_3$), 3.2 (m, H5), 3.05 (t, H4, $J$ = 8), 2.51 ($CH_2$). Anal. Calcd for $C_9H_{16}S_2O_5$: C, 40.29; H, 5.97; Found: C, 40.89; H, 6.21.

**Preparation of 1f from 1a.** Compound **1a** (0.750 g, 3.57 mmol) was dissolved in 50 mL of dry $CH_3OH$, and the solution was dried over 3 g of 4-Å molecular sieve overnight. The molecular sieve was removed by filtration, and the filtrate was mixed with 4 g of Amberlyst 15$H^+$ resin and 2.5 equiv of 1,2-ethanedithiol. The reaction mixture was refluxed gently for 6 h. After filtration, the filtrate was concentrated, and the residue was chromatographed, eluting with $CHCl_3$–$CH_3OH$ (3:1). Fractions with material having $R_f$ = 0.36 were combined with concentrated to give **1f**, 0.55 g (58%) as a thick oil. Its $^{13}C$ NMR spectrum was identical with that prepared from **1f**.

**Methyl α-D-*gluco*-Hexodialdoside-(1,5) 6-Oxime (1h).** A mixture of 1.00 g (4.76 mmol) of **1a**, 2.0 g of anhydrous $KHCO_3$, and 1.0 g of hydroxylamine hydrochloride in 50 mL anhydrous methanol was refluxed with stirring for 4 h. After cooling, the solution was filtered through Celite and concentrated. This material was chromatographed, eluting with $CHCl_3$–$CH_3OH$ (3:1) to yield 0.88 g (90%) of **1h** as a hygroscopic, amorphous solid: $[\alpha]^{22}_D$ 118.2° ($c$ = 0.85, $CH_3OH$); $^{13}C$ NMR (DMSO-$d_6$) $\delta$ 55.76 ($OCH_3$), 70.81 (C5), 73.26 (C2), 73.64 (C4), 74.50 (C3), 101.39 (C1), 149.38 (C6); $^1H$ NMR (DMSO-$d_6$) $\delta$ 10.96 (s, 1 H, =NOH), 7.31 (d, 1 H, H6, $J_{5,6}$ = 7.7), 4.67 (d, 1 H, H1, $J_{1,2}$ = 3.4), 3.82 (q, 1 H, H5, $J_{5,6}$ = 7.7, $J_{4,5}$ = 9.8), 3.25 (s, $OCH_3$), 3.1–3.42 (m, 6 H, $OCH_3$, $H_2$, $H_3$, $H_4$). Anal. Calcd for $C_7H_{13}NO_6$: C, 40.57; H, 6.28; N, 6.76. Found: C, 40.59; H, 6.48; N, 7.04.

**Methyl β-D-*gluco*-Hexodialdoside-(1,5) 6-Hydrate (4a).** Typically, a solution of 0.5–1.5 g (2.3–6.8 mmol) of **4b** in about 200 mL of deionized water was acidified to pH 3 with concentrated

HCl and then introduced into a photolytic chamber [Ace Glass, quartz photochemical reaction vessel 7844B]. The solution was stirred magnetically and maintained under an inert atmosphere during the course of its irradiation. Cooling water was circulated during the reaction. After 0.5 h, the reaction mixture was reacidified, and photolysis was continued for up to 2 h. The course of the reaction was monitored by TLC. After the completion of the reaction the solution was neutralized, and the reaction mixture was concentrated in vacuo (bath temperature < 35 °C) to yield, in most cases, a syrup containing ammonium chloride. Yields obtained were in the range 75–80% (theoretical yield of $NH_4Cl$ assumed): $[\alpha]^{22}_D = -71°$ (*c* = 0.5, $H_2O$, corrected for $NH_4Cl$) [lit.[6] $[\alpha]_D$ +40° for L enantiomer ($H_2O$)]; $^{13}C$ NMR ($D_2O$) δ 100.0 (C1), 84.5 (C6), 54.0 ($OCH_3$), 73.08, 72.22, 69.62, 66.80 constitute the shifts for the other carbon atoms.

**Methyl 6-Azido-6-deoxy-β-D-glucopyranoside (4b).** Compound **4b** was obtained as a syrup via the "single-pot" procedure of Hannessian et al.[11] and was converted into methyl 6-azido-6-deoxy-2,3,4-tri-*O*-benzoyl-β-D-glucopyranoside for characterization: mp 61–62 °C; $^1H$ NMR ($C_6D_6$) δ 4.45 (d, 1 H, H1, $J_{1,2}$ = 7.9), 5.88 (m, 1 H, H2, $J_{2,3}$ = 9.8), 6.05 (m, 1 H, H3), 5.50 (m, 1 H, H4, $J_{4,5}$ = 9.8), 3.56 (m, 1 H, H5), 2.95 (m, 1 H, H6), 3.15 (m, 1 H, H6'), 6.85 (m, 12 H, aromatic), 8.05 (m, 3 H, aromatic), 3.25 (s, 3 H, $OCH_3$). Anal. Calcd for $C_{28}H_{25}O_8N_3$: C, 63.27; H, 4.74. Found: C, 63.27; H, 4.95.

**Methyl 2,3,4-Tri-*O*-benzoyl-β-D-*gluco*-hexodialdoside-(1,5) Dimethyl Acetal (4c).** Compound **4a** (0.50 g, 2.4 mmol) was mixed with 25 mL of dry $CH_3OH$ and 0.5 g of 3-Å molecular sieve and cooled in an ice bath. Three drops of concentrated sulfuric acid were added, and the solution was allowed to attain ambient temperature. After the reaction mixture was stirred for 4–5 h, it was neutralized with saturated $NaHCO_3$ and extracted with ethyl acetate. Purification by column chromatography (ethyl acetate–$CH_3OH$, 10:1) followed by benzoylation (benzoyl chloride, pyridine), the usual workup, and crystallization from methanol yielded **4c**, 0.6 g (52%), as a white solid: mp 147–148 °C; $^1H$ NMR ($CDCl_3$) δ 4.70 (d, 1 H, H1, $J_{1,2}$ = 7.8), 5.55 (m, 1 H, H2, $J_{2,3}$ = 9.6), 5.85 (m, 1 H, H3, $J_{3,4}$ = 9.5), 5.62 (m, 1 H, H4, $J_{4,5}$ = 9.4), 3.85 (m, 1 H, H5, $J_{5,6}$ = 5.3), 4.55 (d, 1 H, H6), 3.65 (s, 3 H, 6(*R*)-$OCH_3$), 3.45 (s, 3 H, 6(*S*)-$OCH_3$), 3.55 (s, 3 H, 1-$OCH_3$). Anal. Calcd for $C_{30}H_{30}O_{10}$: C, 65.45; H, 5.49. Found: C, 65.26; H, 5.39.

**Methyl 2,3,4-Tri-*O*-benzyl-(*R*)-5-*C*-(1,3-diphenyl-2-imidazolidinyl)-β-D-xylopyranoside (4f).** Compound **4d**[27] was prepared by the method of Liptak et al.[28] and was subjected to Swern oxidation to yield **4e** as follows. To a solution of 0.093 mL (0.73 mmol) of oxalyl chloride in 2.30 mL of $CH_2Cl_2$ at −60 °C was added a solution of 0.160 mL (1.07 mmol) of DMSO in 1.13 mL of $CH_2Cl_2$. A solution of **4d** (0.50 g, 1.07 mmol) in 1.13 mL of $CH_2Cl_2$ was then added. After the reaction mixture was stirred for 45 min at −60 °C, 0.640 mL (6.33 mmol) of triethylamine was added; the reaction mixture was maintained at −60 °C for an additional 20 min and then warmed to room temperature. The mixture was diluted with 2.20 mL of $H_2O$, and the organic layer was given two aqueous washings, dried, and concentrated to give syrupy **4e**, 0.48 g (96%): $^{13}C$ NMR ($CDCl_3$) key resonances δ 196.78 (C6), 104.28 (C1), 57.09 ($OCH_3$); the δ 83–74 region of the spectrum showed six carbon resonances and was not analyzed further. Compound **4e** was further characterized by converting it into **4f** as follows.

A solution of 0.100 g (0.216 mmol) of **4e** and 0.050 g (0.235 mmol) of $N^1$,$N^2$-diphenylethanediamine in dry $CH_3OH$ was acidified with a few drops of trifluoroacetic acid and stirred in the dark for 24 h. Partial concentration and cooling of the reaction mixture precipitated **4f**, 0.095 g (67%): mp 91–92 °C. Anal. Calcd for $C_{42}H_{44}N_2O_5$: C, 76.80; H, 6.75. Found: C, 76.54; H, 6.95.

**Methyl 2,3,4,6-Tetra-*O*-benzoyl-[6-$^2$H]-(*R*)- and -[6-$^2$H]-(*S*)-β-D-glucopyranoside (5b,c).** To a solution of **4a** (1.00 g) (5.20 mmol) in 10 mL of deionized water was added a solution of 0.3 g (1.5 equiv) of $NaBD_4$ in 10 mL of deionized water, and the mixture was kept overnight. The reaction mixture was neutralized with 5% HCl; methanol (10 mL) was then added, and after stirring at room temperature for 1 h, the mixture was concentrated. Benzoylation was performed as usual to yield 3 g (95%) of **5b,c**. A portion of the product was crystallized from methanol to give **5b,c**, mp 161–162 °C, which was characterized spectroscopically. The $^1H$ NMR spectrum of the mixture **5b,c** was identical with that of **5a**[29] except for the effects arising from deuterium incorporation at C-6: δ 4.75 (d, 1 H, H6(*S*), $J_{5,6}$ = 3.1), 4.61 (d, 1 H, H6(*R*), $J_{5,6}$ = 5.5). The sum of the integrals of H6(*R*) and H6(*S*) was equal to 1 proton while the ratio of the integrals (H6(*R*)/H6(*S*) = 0.92.

**Methyl α-D-*galacto*-Hexodialdoside-(1,5) 6-Hydrate (6a).** A solution of **6b**[12] (0.500 g, 2.28 mmol) in 250 mL of deionized water was acidified to pH 2.0 with 20% HCl and photolyzed at room temperature under a $N_2$ atmosphere for 3 h. During the photolysis reaction progress was monitored by TLC ($CHCl_3$–$CH_3OH$, 3:1), and it was reacidified to maintain pH = 4–6. The solution was concentrated in vacuo to yield a light yellow oil (~100%): $[\alpha]^{25}_D$ = 160.3° (*c* 0.75, $H_2O$) [lit.[6] $[\alpha]_D$ 132° ($H_2O$)]; $^{13}C$ NMR ($D_2O$) δ 100.00 (C1), 89.12 (C6), 72.99 (C5), 70.00, 68.45 (C2, C3), 69.32 (C4), 55.86 ($OCH_3$); $^1H$ NMR ($D_2O$, 40 °C) δ 5.14 (d, 1 H, H6, $J_{6,5}$ = 7.5), 4.85 (b s, 1 H, H1, $J_{1,2}$ ~ 1.0), 4.16 (b s, 1 H, H4), 3.84 (b m, 2 H, H2,3), 3.60 (d, 1 H, H5, $J_{5,6}$ = 7.5), 3.42 (s, 3 H, $OCH_3$).

**Methyl 2,3,4-Tri-*O*-benzoyl-α-D-*galacto*-hexodialdoside-(1,5) Dimethyl Acetal (6c).** The hydrated aldehyde **6a** (0.500 g, 2.38 mmol) was dissolved in a 0.4 M solution of $CeCl_3 \cdot 7H_2O$ (850 mg) in $CH_3OH$ containing 1.8 mL (16 mmol) of trimethyl orthoformate.[30] The reaction, monitored by TLC ($CHCl_3$–MeOH, 3:1), was stirred at room temperature for 24 h, 5 mL of pyridine was added, and the solution was concentrated in vacuo. Then, a 4:1 pyridine–benzoyl chloride (6 equiv) mixture was added. The reaction was stirred overnight at room temperature and processed conventionally. The residuum was chromatographed, eluting with ethyl acetate–hexane (1:1). This was followed by preparative TLC ($CH_2Cl_2$), which yielded **6c** as a white foam: $^{13}C$ NMR ($CD_3COCD_3$) δ 103.32 (C6), 98.27 (C1), 70.33 (C4), 69.97 (C2), 69.63 (C5), 69.53 (C3), 55.85 (C1-$OCH_3$), 55.40, 54.39(C6-$OCH_3$'s); $^1H$ NMR ($CD_3COCD_3$) δ 6.17 (m, 1 H, H4, $J_{4,5}$ ~ 1.0), 6.05 (dd, 1 H, H3, $J_{2,3}$ = 10.8, $J_{3,4}$ = 3.4), 5.82 (dd, 1 H, H2, $J_{2,3}$ = 10.8, $J_{1,2}$ = 3.6), 5.50 (d, 1 H, H1, $J_{1,2}$ = 3.6), 4.72 (d, 1 H, H6, $J_{6,5}$ = 7.2), 4.44 (d, 1 H, H5, $J_{5,6}$ = 6.7), 3.69 (s, 3 H, C1-$OCH_3$), 3.62 (s, 3 H, C6-$OCH_3$), 3.43 (s, 3 H, C6-$OCH_3$). Anal. Calcd for $C_{30}H_{30}O_{10}$: C, 65.45; H, 5.46. Found: C, 65.26; H, 5.60.

**Methyl α-D-*galacto*-Hexodialdoside-(1,5) Dimethyl Acetal (6d).** To a solution of **6c** (0.208 g, 0.378 mmol) in 10 mL of anhydrous $CH_3OH$ was added 0.123 g of KCN (0.189 mmol).[31] The reaction, monitored by TLC ($CHCl_3$–MeOH, 5:1), was stirred at room temperature for 24 h. Then, mixed resin (Dowex MR-3) was added. The mixture was stirred for 1 h, filtered through Celite, and concentrated in vacuo. The residuum was dissolved in water, and washed three times with ether. Concentration of the aqueous layer in vacuo yielded 0.0784 g (87%) of an off-white foam: $[\alpha]^{25}_D$ = 130.7° (*c* 0.29, $D_2O$); $^{13}C$ NMR ($D_2O$) δ 105.23 (C6), 102.34 (C1), 72.00 (C5), 71.90 (C3), 71.21 (C2), 70.61 (C4), 58.43, 58.16 (C6-$OCH_3$'s), 56.49 (C1-$OCH_3$) [assignments are based on data published for methyl α-D-galactopyranoside];[32] $^1H$ NMR ($D_2O$) δ 4.75 (d, 1 H, H6, $J_{6,5}$ = 7.8), 4.67, 3.84 (b s, 1 H, H5, $J_{5,4}$ ~ 1.0), 3.64–3.62 (b m, 3 H, H2,3,4), 3.33, 3.28, 3.24 (each is s, 3 H, $OCH_3$); $^1H$ NMR ($CD_3OD$) δ (H1, $J_{1,2}$= 3.6 Hz), (H6, $J_{6,5}$ = 7.8 Hz).

**Methyl 4,6-*O*-Benzylidene-[6-$^2$H]-(*R*)- and -[6-$^2$H]-(*S*)-2,3-di-*O*-benzoyl-α-D-galactopyranosides (7b,c).** Compound **6a** (0.500 g, 2.604 mmol) was dissolved in 5 mL of deionized water and added dropwise, with constant stirring, at room temperature to a solution of 0.167 g (1.5 equiv) of $NaBD_4$ in 3 mL of deionized water. After 5 h the reaction mixture, which was monitored by using the Benedict's test, was neutralized with 2 N HCl and concentrated in vacuo. The residuum was dissolved in methanol and evaporated in vacuo three times to remove trimethyl borate. The resulting mixture was combined with 1.9 g of similarly reduced and used directly in the next reaction. The deuterated galactoside

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was treated with 2.07 g (15.2 mmol) of fused $ZnCl_2$ in 20 mL (0.20 mol) of anhydrous benzeldehyde at room temperature for 36 h. After the usual workup procedure, the crude product was benzoylated in pyridine at room temperature. The residuum obtained after the workup was chromatographed, eluting with ethyl acetate–hexane (3:1); decolorization with charcoal (Norit A) was followed by crystallization from hot methanol to give white crystals: mp 189–90 °C (mp **7a**, 196–197 °C; lit.[33] mp 202–203 °C); $^{13}C$ NMR ($CD_3COCD_3$) of **7a** $\delta$ 166.26 (benzoyl C=O), 101.08 (benzylidene acetal), 98.74 (C1), 75.19 (C4), 69.84, 69.72, 69.55 (C3, C6, C2), 63.33 (C5), 55.66 ($OCH_3$); $^1H$ NMR ($C_6D_6$) $\delta$ 6.25 (dd, 1 H, H3, $J_{3,4}$ = 3.0, $J_{3,2}$ = 10.5), 6.15 (dd, 1 H, H2, $J_{2,3}$ = 10.5, $J_{2,1}$ = 3.0), 5.33 (d, 1 H, H1, $J_{1,2} \sim 3$) 5.27 (s, 1 H, benzylidene H), 4.29 (d, 1 H, H4, $H_{4,5} \sim 0$, $J_{4,3} \sim 3$), 4.02 (d, 1 H, $H6_{eq}$, $J_{gem}$ = 12.5), 3.39 (d, 1 H, $H6_{ax}$, $J_{gem}$ = 12.4), 3.15 (s, 1 H, H5, $J_{5,4} \sim 0$), 2.99 (s, 3 H, $OCH_3$); $^1H$ NMR of **7b,c** ($C_6D_6$) $\delta$ 4.02 (s, 0.66 H, H6(*S*), 3.41 (s, 0.34 H, H6(*R*)).

**Methyl 2,3,4-Tri-*O*-benzoyl-α-D-galactopyranosiduronic Acid Nitrile (8).** To a stirred solution of **6a** (0.480 g, 2.28 mmol) in 10 mL of pyridine over 5-Å molecular sieve was added 0.240 g of hydroxylamine hydrochloride (1.5 equiv). The reaction, monitored by TLC ($CHCl_3$–$CH_3OH$, 3:1), was heated to 65 °C for 24 h. Then 6 mL of pyridine and 1.6 mL of benzoyl chloride (2 equiv) were added, and the reaction mixture was stirred at room temperature for 20 h. The reaction was quenched with water, worked up conventionally, and chromatographed, eluting with ethyl acetate–hexane (1:1). This was followed by preparative TLC (benzene) and crystallization from ether to give white needles: mp 157–158 °C; $^{13}C$ NMR ($CD_3COCD_3$) $\delta$ 166.00, 165.79, 165.54 (carbonyls on the benzoates), 115.83 (C6), 99.16 (C1), 70.14 (C4), 69.01 (C2), 67.86 (C3), 61.17 (C5), 56.88 ($OCH_3$); $^1H$ NMR ($C-D_3OCD_3$) $\delta$ 6.23 (m, 1 H, H4, $J_{4,5} \sim 1.0$), 6.02 (dd, 1 H, H3, $J_{3,2}$ = 10.7, $J_{3,4}$ = 3.4), 5.76 (dd, 1 H, H2, $J_{2,1}$ = 3.4, $J_{2,3}$ = 10.7), 5.66 (b s, 1 H, H5), 5.52 (d, 1 H, H1, $J_{1,2}$ = 3.5), 3.63 (s, 3 H, $OCH_3$). Anal. Calcd for $C_{28}H_{23}NO_8$: C, 67.06; H, 4.62; O, 25.52. Found: C, 66.84; H, 4.64; O, 25.76.

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# Highly Selective Metal–Graphite-Induced Reductions of Deoxy Halo Sugars

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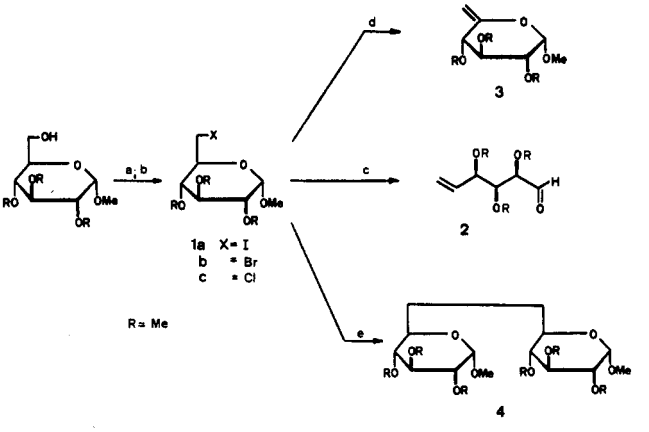
To explore the applicability of highly active metal–graphite reducing agents to polyfunctional compounds a variety of suitably protected chloro-, bromodeoxy-, and deoxyiodohexopyranosides and hexofuranoses were each treated with potassium–graphite laminate ($C_8K$) and zinc/silver–graphite, respectively, invariably leading to the efficient formation of olefinic products. However, while $C_8K$ in all cases causes dehydrohalogenation, zinc/silver–graphite reductions proceed by dealkoxyhalogenation, results quite opposite to the formation of glycals by each of the reagents. In contrast, magnesium on graphite readily dimerizes methyl 6-deoxy-6-iodo-α-D-glucopyranoside (**1a**) by a Wurtz reaction.

## Introduction

In recent years numerous kinds of metal–graphite combinations[1] containing metals such as zinc,[2] zinc/silver,[3,4] magnesium,[5] titanium,[5,6] tin,[7] iron,[8] nickel,[9] palladium,[10] and platinum,[11] generally prepared by the reduction of metal salts by $C_8K$,[1,12] proved to be highly effective one- or two-electron donors widely applicable in various kinds of reduction. Among these the highly efficient formation of furanoid and pyranoid glycals by $C_8K$[13] or zinc/silver–graphite[4] reduction of *O*-alkyl-, *O*-alkylidene-, or *O*-acylglycosyl halides are particularly noteworthy. The new glycal syntheses[4,13] favorably complement each other. They not only allow aprotic Fischer–Zach type reductions

**Scheme I**[a]




[a] (a) $CH_3SO_2Cl$, pyridine, $CH_2Cl_2$, 89%; (b) TBAX, acetonitrile, reflux, 78–84%; (c) zinc/silver–graphite, THF; (d) $C_8K$, THF; (e) magnesium–graphite, THF.

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