Preferred Conformation of *C*-Glycosides. 13. A Comparison of the Conformational Behavior of Several *C*-, *N*-, and *O*-Furanosides

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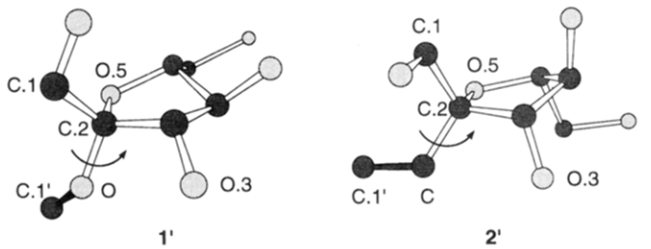
A qualitative comparison of *C*-furanosides, derived from arabinose and 2-deoxyribose, with the naturally occurring *O*- and *N*-furanosides was performed using solution ^{1}H NMR spectroscopy and X-ray crystallography. The ring conformations of β- and α-*C*-arabino- and β- and α-*C*-2-deoxyribofuranosides tend to possess equatorial anomeric C–C bonds, in contrast to the *O*-furanosides, which have ring conformations stabilized by axial anomeric C–O bonds due to a stereoelectronic effect. Installation of a quaternary anomeric center in *C*-furanosides introduces unfavorable 1,3-diaxial-like steric interactions, which can shift the ring conformational equilibrium in such a manner that the *C*-furanoside becomes more similar to the *O*-furanoside. The solid-state conformation of the *C*-nucleoside β-arabinosyl pseudouridine was shown to be virtually identical to *N*-nucleoside β-arabinosyluridine. In solution, however, the ring conformation of this *N*-furanoside, and its 2-deoxy analog, is intermediate to the corresponding oxygen- and carbon-derived entries. When compared to *C*-pyranosides, *C*-furanosides seem to have anomeric linkages prone to increased exo-anomeric conformational averaging. A quaternary furanosyl anomeric center such as in *O*-sucrose (**1**) and *C*-sucrose (**2**) appears to provide further flexibility at this anomeric linkage. Evidence is provided which suggests the flexible nature of sucrose arises at the fructofuranosyl linkage, as the glucopyranosyl linkage in this compound is conformationally well-defined in the exo-anomeric sense. The analysis of the preferred syn/anti base conformation in *C*-nucleosides can be complicated by a stronger equatorial base preference.

Introduction

Furanosides are ubiquitous in biological structures, and it is of general interest to understand conformational determinants in these systems. Understanding the impact of replacing the usual anomeric substituents (oxygen or nitrogen) with a carbon atom is of basic interest when considering the ground-state conformation of these flexible rings. For five-membered rings, multiple low-energy ring conformations are possible, and the spatial disposition of the substituents is dependent upon ring conformation.[1] Therefore, the ring and exo-anomeric conformational behavior are directly related to one another and both should be considered in conformational studies. For this reason, we have prepared a number of α- and β-*C*-furanosides for the purpose of comparing their structural features with naturally occurring oxygen- and nitrogen-derived furanosides. Our interest in the ring conformations of *C*-furanosides began with the synthesis and conformational analysis of *C*-sucrose and related derivatives.[2–4] Earlier studies from these laboratories have shown that the glycosidic bond in *C*-pyranosides preferentially adopts an exo-anomeric conformation similar to that found in *O*-glycosides.[5–7] We were interested in probing the behavior of *C*-furanosides in this regard as well. During the course of these investigations, Magnusson and Ellervik[8] reported their study of conformationally restricted *O*-, *C*-, *N*-, and *S*-furanosides embedded in a norbornane framework. They found strong axial anomeric preferences in *O*- and *S*-furanosides, equatorial anomeric preferences in *C*-furanoside model systems, and intermediate behavior for an *N*-furanoside. Our results indicate this behavior is generally true, but we show that these trends can be overcome in some cases with steric interactions resulting from the presence of a quaternary anomeric center.

A discussion of the conformational analysis of furanosides is challenged by the number of possible ring geometries. In this regard, it is useful to examine the solid-state structures of two closely related compounds, i.e., the furanoside portions of peracetylated *O*-sucrose (**1**) and peracetylated *C*-sucrose (**2**). X-ray studies are appealing because they provide a precise picture of ring conformation and substituent orientation in the solid state. The crystal structures are used here to facilitate discussion and will be referred to later in the text.



Structure **1′** is the fructofuranoside portion of *O*-sucrose octaacetate[9] using the X-ray coordinates—note that for clarity the acetates are removed but the glucosyl

[⊗] Abstract published in *Advance ACS Abstracts,* October 15, 1994.

(1) Jeffrey, G. A.; Saenger, W. *Hydrogen Bonding in Biological Structures*; Springer-Verlag: New York, 1991.

(2) O'Leary, D. J.; Kishi, Y. *Abstracts of Papers*; 33rd Experimental Nuclear Magnetic Resonance Conference, Pacific Grove, CA, March, 1992; M46.

(3) O'Leary, D. J.; Kishi, Y. *J. Org. Chem.* **1993**, *58*, 304–306.

(4) O'Leary, D. J.; Kishi, Y. *Tetrahedron Lett.* **1994**, *35*, 5591–5594.

(5) Wu, T.-C.; Goekjian, P. G.; Kishi, Y. *J. Org. Chem.* **1987**, *52*, 6412–6422.

(6) Haneda, T.; Goekjian, P. G.; Kim, S. H.; Kishi, Y. *J. Org. Chem.* **1992**, *57*, 490–498 and references cited therein.

(7) For part 12 of this series see: Wei, A.; Kishi, Y. *J. Org. Chem.* **1994**, *59*, 88–96.

(8) Ellervik, U.; Magnusson, U. *J. Am. Chem. Soc.* **1994**, *116*, 2340–2347.

0022-3263/94/1959-6629$04.50/0

C.1′ atom[10] and hydroxyl oxygen atoms are retained. This *O*-furanoside structure has several features thought to be stabilizing for five-membered rings. First, the substituents are largely equatorial, and there are no severe 1,3-diaxial-like steric interactions. Second, the vicinal trans-hydroxyl groups are gauche to each other. Perhaps the only unfavorable interaction is the eclipsed orientation of the anomeric substituent (C.2−O) and the C.3 hydroxyl group.

The exo-anomeric orientation of the anomeric substituent is indicated by the rotation about the anomeric bond in **1′**, defined by the dihedral angle C.1′−O−C.2−O.5. In sucrose octaacetate the pyranosyl C.1′ is gauche to the ring oxygen, with a dihedral angle of ca. 20°. Therefore, in the solid-state, an exo-anomeric conformation is preferred, although the orientation is not the optimal staggered value of ca. 60°.

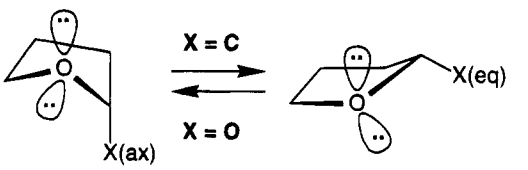
In the solution state, a description of the ring conformation must be inferred from spectroscopic information. ^{1}H NMR has proven useful in this regard, as the vicinal ring ^{1}H−^{1}H coupling constants are torsional angle-dependent.[11] Several detailed studies have recently appeared in which the observed ring coupling constants were iteratively fit to one or two conformations.[12,13] By their nature, these studies were quantitative, although the general conformational behavior of furanosides can be gleaned by a qualitative examination of ring coupling constants.

For example, the solution conformation of the fructofuranoside in *O*-sucrose (**1**) has been described in terms of its ring coupling constants $^3J_{H.3-H.4}$ and $^3J_{H.4-H.5}$. Both values are large (8.0, 8.6 Hz, D_2O), which is consistent with ring conformations having anti-periplanar ring protons. Therefore, **1′** is an accurate representation of the five-membered ring solution conformation of *O*-sucrose (**1**).

Structure **2′** is the furanoside portion of *C*-sucrose octaacetate[3] (with the same atom display as for **1′**). Clearly, the solid-state conformation of **2′** is not similar to **1′**. Notably, the ring pucker is quite different, i.e., the C.3 and C.4 hydroxyl groups are anti instead of gauche. In solution, however, the furanoside ring of *C*-sucrose exhibits large ring coupling constants ($^3J_{H.3-H.4}$ = 7.2, $^3J_{H.4-H.5}$ = 8.0 Hz, D_2O), which indicates conformational similarity with **1**. Therefore, the ring solution conformation of **2** is better represented by solid-state conformation **1′** rather than **2′**, which would have small ring $^3J_{H-H}$ values. The fact that the five-membered ring conformations in derivatives of *C*-sucrose are different in solution vs the solid state is not unexpected. Here, we simply illustrate the spatial distribution of functional groups in these X-ray structures, while pointing out that solution NMR parameters can qualitatively distinguish between extremes of conformation.

Intrigued by the similar solution conformations of the five-membered rings in *C*-sucrose (**2**) and *O*-sucrose (**1**), we proceeded to compare both the ring and exo-anomeric conformational preferences in a number of β- and α-*C*-, *N*-, and *O*-arabino- and 2-deoxyribofuranosides. Considering the oxygen-derived systems as the parent compounds, it was hypothesized that replacing the electronegative carbon−oxygen anomeric bond with a carbon−carbon bond would shift the ring conformational equilibrium as shown in Scheme 1. In these systems, the anomeric effect is expected to contribute to an axial preference[14] for an electronegative substituent. With respect to our interest in exo-anomeric conformation in furanosides, we did not have a working hypothesis based upon any a prior expectations. Instead, we chemically modified several existing structures in order to gain unique insights into the role of specific functional groups.

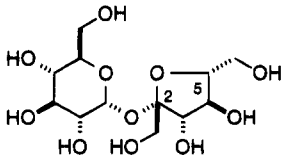
Scheme 1



In the following section, the results of our investigation are presented with an initial focus on the comparative ring structures of *C*-, *N*-, and *O*-arabino- and 2-deoxyfuranosides (both α and β anomers). These sections are followed by an examination of exo-anomeric conformational issues in *C*-furanosides, with particular emphasis on sucrose and *C*-nucleosides.

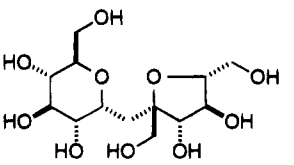
Results and Discussion

A Comparison of Ring Conformations: Arabinose Series. For this work, the ring ^{1}H−^{1}H NMR coupling constants are used as the principal means of conformational comparison in solution. In general, three coupling constants are available to assess ring conformation in arabinofuranosides. However, a direct comparison of $^3J_{H.1-H.2}$ among carbon, nitrogen, and oxygen derivatives is difficult due to electronegativity effects. It is important to note that the arabinose $^3J_{H.2-H.3}$ and $^3J_{H.3-H.4}$ are both trans couplings and therefore (i) have nondegenerate Karplus curves and (ii) should not be susceptible to Barfield "through-space" effects.[12]



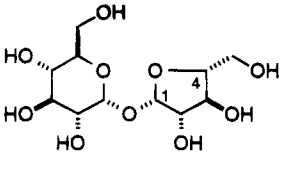
1

$^3J_{3-4}$ = 8.0 (Hz, D_2O)
$^3J_{4-5}$ = 8.6



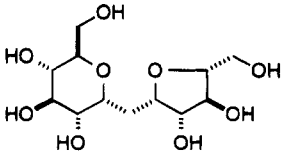
2

$^3J_{3-4}$ = 7.2 (D_2O)
$^3J_{4-5}$ = 8.0



3

$^3J_{1-2}$ = 4.7 (D_2O)
$^3J_{2-3}$ = 8.0
$^3J_{3-4}$ = 7.1

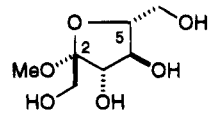


4

$^3J_{1-2}$ = 3.1 (CD_3OD)
$^3J_{2-3}$ = 0.9
$^3J_{3-4}$ = 2.4

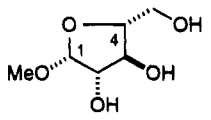
(9) Oliver, J. D.; Strickland, L. C. *Acta Crystallogr.* **1984**, *C40*, 820–824.
(10) Atom labels are provided with the chemical structures found throughout the text.
(11) Haasnoot, C. A. G.; de Leeuw, F. A. A. M.; de Leeuw, H. P. M.; Altona, C. *Org. Magn. Reson.* **1981**, *15*, 43–52.
(12) Raap, J.; Van Boom, J. H.; Van Lieshout, H. C.; Haasnoot, C. A. G. *J. Am. Chem. Soc.* **1988**, *110*, 2736–2743.
(13) de Leeuw, F. A. A. M.; Altona, C. *J. Comput. Chem.* **1983**, *4*, 428–437.

Earlier studies[15] have noted the similar five-membered ring conformations of the fructofuranoside in *O*-sucrose (**1**), *O*-methyl-β-D-fructofuranoside (**5**), and *O*-methyl-β-D-arabinofuranoside (**6**). Given this comparison of compounds, it would appear that the glucosyl residue in sucrose (**1**) does not influence the furanoside conformation. Additionally, the C.1 hydroxymethyl group can be removed from **5** to yield **6** without any substantial effect on conformation. To test whether these operations were mutually exclusive, the novel disaccharide 1-(deshydroxymethyl)-*O*-sucrose (**3**)[16] was prepared. Large ring coupling constants were observed for the furanoside in **3**, indicating conformational similarity among compounds **1**, **2**, **5**, and **6**.



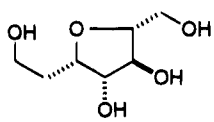
5

$^3J_{3\text{-}4}$ = 8.0 (Hz, D_2O)
$^3J_{4\text{-}5}$ = 8.0



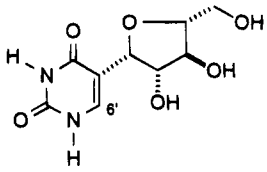
6

$^3J_{1\text{-}2}$ = 4.5 (D_2O)
$^3J_{2\text{-}3}$ = 8.0
$^3J_{3\text{-}4}$ = 8.0



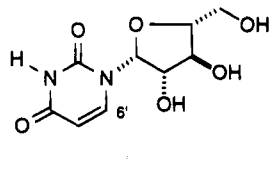
7

$^3J_{1\text{-}2}$ = 3.4 (CD_3OD)
$^3J_{2\text{-}3}$ = 1.5
$^3J_{3\text{-}4}$ = 2.7



8

$^3J_{1\text{-}2}$ = 3.4 (D_2O)
$^3J_{2\text{-}3}$ = 1.4
$^3J_{3\text{-}4}$ = 3.7



9

$^3J_{1\text{-}2}$ = 5.1 (D_2O)
$^3J_{2\text{-}3}$ = 4.5
$^3J_{3\text{-}4}$ = 5.5

β-*C*-Arabinofuranosides exhibit different ring conformations when compared to their oxygen counterparts and the corresponding *C*-fructofuranoside. Disaccharide **4**[17] and model compound **7** exhibit similar ring coupling constants, but are not similar to β-*O*-methyl arabinofuranoside (**6**). In particular, the very small $^3J_{H.2\text{-}H.3}$ coupling constant in **4** and **7** indicates that the anomeric C−C bond has a large impact on the preferred ring conformation. $^3J_{H.3\text{-}H.4}$ also diminishes measureably in **4** and **7** when compared to **6**. Based upon these ring coupling constants, the ground-state conformations of the carbon-derived **4** and **7** appear to have an equatorial anomeric substituent. In other words, the conformational equilibrium shown in Scheme 1 appears to hold for β-*C*-arabinofuranosides.

The study of β-*C*-arabinofuranosides **4** and **7** provides some insight into the conformationally similar five-membered rings of *C*-sucrose (**2**) and *O*-sucrose (**1**). Using *O*-sucrose as a reference compound, the following comparison of compounds **1**−**4** can be made: in sucrose, the C.1 hydroxymethyl group can be replaced with a proton without significantly altering the five-membered ring conformation, i.e., **1** vs **3**. Alternatively, retaining the sucrose C.1 hydroxymethyl group and replacing the anomeric C−O bond with a C−C bond can also be accomplished without a large impact on the furanoside conformation, i.e., **1** vs **2**. However, if both operations are done simultaneously, e.g., **4**, then the five-membered ring reorganizes. The gauche C.2−C.3 hydroxyl interaction becomes anti, a consequence of the anomeric substituent taking an equatorial position. This type of conformation is represented by the furanoside in structure **2′** (note the atom labels have changed). In solution, such a reorganization in *C*-sucrose would create an unfavorable 1,3-diaxial-like steric interaction between the C.1 hydroxymethyl group and the C.4 hydroxyl group, which can be visualized by comparing structures **1′** and **2′**. If this is the case, then such a destabilizing 1,3 interaction might be responsible for the conformational similarity of the furanosides in *C*- and *O*-sucrose. The quaternary anomeric center in *C*-sucrose (**2**) shifts the equilibrium shown in Scheme 1, causing its ring conformation to be more like the oxygen derivative.

Table 1. Selected NOE Values[a] Observed in Nitrogen and Carbon Nucleosides

		enhancement (%)			
compd	irradiation	H_1	H_2	H_3	H_4
8	$H_{6'}$	2.0		0.5	
9	$H_{6'}$	1.6		4.3	
8	H_2	13.5		4.5	0.5
9	H_2	13.5		3.4	2.2
16	$H_{6'}$	6.8	1.7	0.22	
17	$H_{6'}$	3.8	3.0	1.7	

[a] 500 MHz 1D NOE difference data (see supplementary material) obtained under identical conditions (4 s irradiation, 2 s recycle delay, 1.5 s acquisition time) for all compounds.

Ring ^3J values for β-arabinosylpseudouridine[18] (**8**) are comparable to those measured for β-*C*-arabinofuranosides **4** and **7**. This observation suggests that the degree of carbon hybridization (i.e., sp^3 vs sp^2) does not influence the ring conformational behavior in this series of compounds. In the β-*C*-arabinofuranoside, one would expect a fairly strong equatorial preference for the pseudouracil group.

The ring coupling constants for nitrogen-derived β-arabinosyl uridine (**9**) are intermediate to those for the carbon and oxygen entries. The ring ^3J values of β-arabinosyluridine (**9**) have been analyzed[19] to show a slight excess (ca. 60%) of a conformer possessing an axial C−N bond. Further differences in the ring conformations of the *C*-nucleoside **8** and *N*-nucleoside **9** were detected with transannular NOE measurements (Table 1). Irradiation of H.2 in the nitrogen analog produces a strong NOE (2.2%) at H.4, whereas in the carbon nucleoside this enhancement (0.5%) diminishes. Inspection of molecular models reveals that this NOE behavior is consistent with the respective coupling constant data. In solution, therefore, the ring conformation of the *C*-furanoside appears qualitatively different when compared to the *N*-furanoside.

(14) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: Oxford, 1983.
(15) Stevens, E. S.; Duda, C. A. *J. Am. Chem. Soc.* **1991**, *113*, 8622−8627.
(16) Note that the ring position atom labels have changed: the anomeric carbon is C.2 in the fructofuranoside and C.1 for the arabinofuranoside.
(17) The details of the synthesis of **4** and **13** will be published in due course.
(18) Reichman, U.; Chu, C. K.; Wempen, I.; Watanabe, K. A.; Fox, J. J. *J. Heterocycl. Chem.* **1976**, *13*, 933−937. We prepared this compound from pseudouridine using a protection/oxidation scheme described for the preparation of arabinosyl uracil, see: Hansske, F.; Madej, D.; Robins, M. J. *Tetrahedron* **1984**, *40*, 125−135.
(19) de Leeuw, F. A. A. M.; Altona, C. *J. Chem. Soc., Perkin Trans. 2* **1982**, 375−384.

Table 2. Comparison of Solid-State Geometries of β-Arabinosylpseudouridine (8) and β-Arabinosyluridine (9)[21a]

parameter	8	9
Furanose Bond Lengths, Angles,[a] and Torsional Angles		
C1−C2	1.537 101.0	1.536 100.4
C2−C3	1.509 103.5	1.518 103.6
C3−C4	1.529 105.6	1.536 105.6
C4−O4	1.446 109.9	1.463 109.3
O4−C1	1.443 104.3	1.403 105.8
C1−C2−C3−C4	−37.5	−34.9
C2−C3−C4−O4	24.8	20.8
C3−C4−O4−C1	−0.8	3.8
C4−O4−C1−C2	−23.0	−26.8
O4−C1−C2−C3	37.5	38.5
pucker	C_2 endo	C_2 endo
Base Orientation		
r(C1−X), Å	1.519 (X = C)	1.470 (X = N)
∠(O4−C1−X−C6), deg	23.5	33.9
base orientation	*anti*	*anti*
Unit Cell Comparison		
space group	$P2_1$	$P2_12_12_1$
unit cell dimensions:		
a, *b*, *c* (Å)	6.0, 6.8, 12.4	6.8, 6.9, 21.0

[a] Three-atom bond angles follow each internuclear distance (Å), with third atom of next highest increment; e.g., the bond angle for entry C1−C2 is for ∠C1−C2−C3.

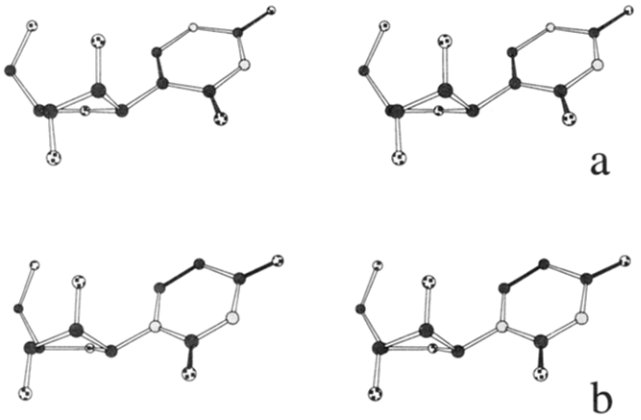
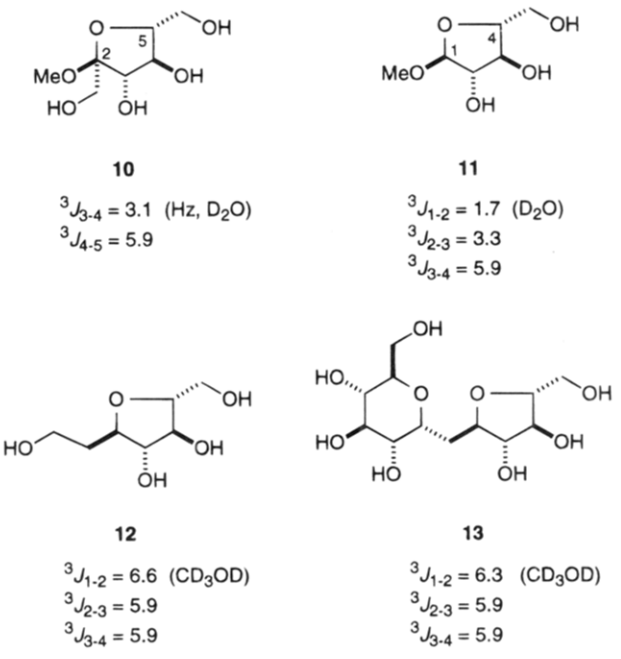


Figure 1. (a) Stereoview of **8** as determined by X-ray diffraction. (b) Stereoview of **9** using atomic coordinates reported in ref 21a.

In the solid state, however, **8**[20] and **9**[21] are nearly superimposable at the molecular level, in spite of long-range crystal lattice differences (Table 2, Figure 1). In both crystal structures, the pucker of the five-membered ring is C.2 endo. Both structures also possess intramolecular hydrogen bonds between the 5- and 2- hydroxyl groups. The C.1−O.4 bond length in **9** is perceptively shorter than that in *C*-nucleoside **8**, attributable to a stereoelectronic effect in the former. The solid-state conformation of **8** (Figure 1) has features consistent with the observed solution NMR parameters: a nearly orthogonal arrangement of the H.2 and H.3 protons (small ^3J), a distal H.2−H.4 relationship, and the equatorially displaced anomeric substituent.

To complete the arabinose series, α-*C*-arabinofuranosides **12** and **13** were compared with the corresponding parent substances, α-methyl *O*-fructofuranoside (**10**) and α-methyl *O*-arabinofuranoside (**11**). A recent analysis[22] of several α-*O*-arabinofuranosides revealed an interchange between conformers which both possessed a relatively fixed O.1−C.1−O.4−C.4 segment with a pseudoaxial O.1 orientation. As for the oxygen-derived β-fructo- and β-arabinofuranosides **5** and **6**, a conformational similarity was observed for **10** and **11**, suggesting stereoelectronic stabilization irrespective of the quaternary anomeric center in **10**. It is worth noting that in **11** $^3J_{H.1-H.2}$ is quite small (1.7 Hz) when compared to the larger values (6.6, 6.3 Hz) in the carbon derivatives **12** and **13**, suggesting that the oxygen and carbon entries are indeed different with respect to the orientation of the respective anomeric substituents. Although it is orientation dependent,[23] $^3J_{H.1-H.2}$ should maximally decrease by only ca. 2 Hz due to oxygen substitution. In **11**, the small $^3J_{H.1-H.2}$ suggests a nearly axial anomeric methoxy group, which is optimal for the endo-anomeric effect. As was seen for *C*-sucrose, replacing the α-anomeric center with a C−C bond shifts the equilibrium as shown in Scheme 1.



A Comparison of Ring Conformations: 2-Deoxyribose Series. The solution ring conformations of several *C*-β-2-deoxyribofuranosides were examined and compared with methyl 2-deoxy-β-D-ribofuranoside (**14**). A recent analysis[12] of the five-membered ring in **14** found an equally populated two conformer equilibrium of the type $^4E \rightleftharpoons {}_2E$. The $_2E$ (envelope) conformation is stabilized by an axial methoxy group whereas a favorable gauche effect (O.4 is gauche to O.3) is present in the ^4E conformation.

C-β-2-Deoxyribofuranoside (**15**) and the *C*-nucleoside 2-deoxy-β-D-ribofuranosylpseudouracil (**16**)[24] are similar

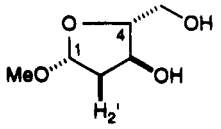
(20) Crystals of **8** were grown by slow evaporation of an aqueous solution. Crystallographic data for compound **8**: $a = 5.989(4)$ Å, $b = 6.819(5)$ Å, $c = 12.419(4)$ Å, $T = 233$ K, space group $P2_1$, $Z = 2$, $2\theta_{min/max} = 3-45°$, unique data ($F_o2 > 3\sigma F_o^2$) 729, $R = 5.33\%$, $R_w = 5.72\%$. Data were collected with MoKα radiation. The structure was solved by standard procedures, and all atoms were refined isotropically. The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

(21) (a) Tollin, P.; Wilson, H. R.; Young, D. W. *Acta Crystallogr.* **1973**, *B29*, 1641−1647. (b) Sherfinski, J. S.; Marsh, R. E. *Acta Crystallogr.* **1974**, *B30*, 873−878.

(22) Hoffmann, R. A.; van Wijk, J.; Leeflang, B. R.; Kamaling, J. P.; Altona, C.; Vliegenthart, J. F. G. *J. Am. Chem. Soc.* **1992**, *114*, 3710−3714.

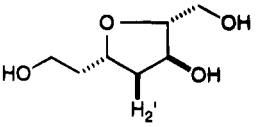
(23) Booth, H. *Tetrahdron Lett.* **1965**, *7*, 411.

to one another yet have markedly different ring ^3J values when compared to **14**. The large (10.0 Hz) $^3J_{H.1-H.2}$ value in **15** and **16** is consistent with an equatorial anomeric substituent. The ring conformation of the nitrogen-containing 2-deoxyuridine **17** appears to be intermediate to the carbon- and oxygen-derived entries.



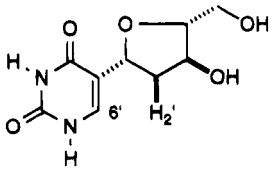
14

$^3J_{1-2}$ = 2.7 $^3J_{2-3}$ = 6.7
$^3J_{1-2'}$ = 5.5 $^3J_{2'-3}$ = 5.9
$^3J_{3-4}$ = 4.2 (Hz, D_2O)



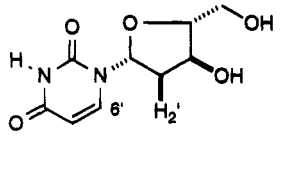
15

$^3J_{1-2}$ = 10.0 $^3J_{2-3}$ = 6.3
$^3J_{1-2'}$ = 5.4 $^3J_{2'-3}$ = 1.8
$^3J_{3-4}$ = 2.9 (CD_3OD)



16

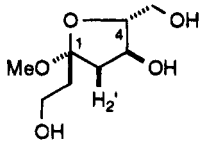
$^3J_{1-2}$ = 10.0 $^3J_{2-3}$ = 5.8
$^3J_{1-2'}$ = 6.0 $^3J_{2'-3}$ = 2.1
$^3J_{3-4}$ = 2.5 (D_2O)



17

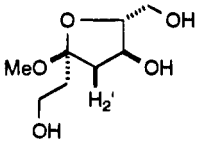
$^3J_{1-2}$ = 7.5 $^3J_{2-3}$ = 6.5
$^3J_{1-2'}$ = 6.5 $^3J_{2'-3}$ = 3.0
$^3J_{3-4}$ = 4.0 (D_2O)

Compounds **18**–**20** were prepared to examine the effect of quaternizing the anomeric center in the β-2-deoxyribose system. As was seen in the β-arabinose series, there is general agreement between quaternary and nonquaternary *O*-2-deoxyribofuranosides, cf. **18** with **14** and **19** with **22**.



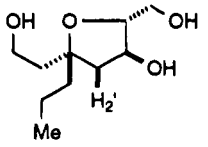
18

$^3J_{2-3}$ = 7.2
$^3J_{2'-3}$ = 7.9
$^3J_{3-4}$ = 5.8
(Hz, CD_3OD)



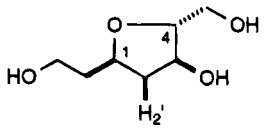
19

$^3J_{2-3}$ = 8.1
$^3J_{2'-3}$ = 3.2
$^3J_{3-4}$ = 4.9
(CD_3OD)



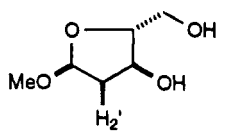
20

$^3J_{2-3}$ = 6.7
$^3J_{2'-3}$ = 7.8
$^3J_{3-4}$ = 6.6
(CD_3OD)



21

$^3J_{1-2}$ = 5.8 $^3J_{2-3}$ = 6.4
$^3J_{1-2'}$ = 6.7 $^3J_{2'-3}$ = 6.4
$^3J_{3-4}$ = 4.8 (CD_3OD)



22

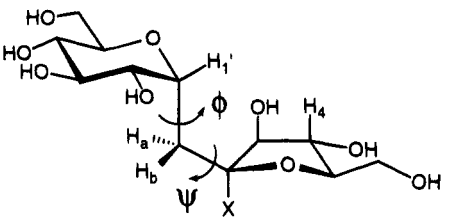
$^3J_{1-2}$ = 5.3 $^3J_{2-3}$ = 7.3
$^3J_{1-2'}$ = 1.0 $^3J_{2'-3}$ = 2.3
$^3J_{3-4}$ = 3.4 (D_2O)

Like the arabinose series, quaternization of the anomeric center with 2 C–C bonds resulted in a compound which was conformationally distinct from the monosubstituted β-*C*-furanoside **15** and more similar to the β-oxygen derived compounds **18** and **14**. Again, quaternization of the anomeric center in a *C*-furanoside produces a shift in ring conformation (Scheme 1) such that the carbon analog becomes more similar to the parent *O*-furanoside.

Methyl α-*O*-2-deoxyribofuranoside (**22**) has been described[12] as possessing an $_1E$ conformation which places the anomeric C–O bond in a favorable axial orientation (H.1 and H.2 nearly orthogonal with a small ^3J). This anomeric stabilization is thought to occur in concert with a favorable gauche effect involving the C.3 and C.4 substituents. The ^3J values for α-*C*-2-deoxyribofuranoside **21** do not possess the same qualitative features as seen for **22**. As with the other compounds, replacing the C.1 methoxy group with a carbon atom produces a shift toward conformations with an equatorial anomeric substituent.

The Exo-Anomeric Effect in *C*-Furanosides: Implications for *O*-Sucrose. The exo-anomeric effect[25] in pyranosides is well established.[14] This effect is used to explain the gauche (to the ring oxygen) preference of anomeric substituents. Experimental studies from these laboratories have found this preference (structure I, Figure 2a) is retained in simple *C*-pyranosides[5,26] and in *C*-di- and -trisaccharides.[6] Most *O*-furanosides retain the exo-anomeric geometry in the solid state.[27,28]

Our studies indicate that, in general, *C*-furanosides do not have the same strong exo-anomeric conformational preferences seen in the α- and β-*C*-pyranosides. This is illustrated with compound **4**, an analog of *C*-sucrose lacking the C.1 hydroxymethyl group. In **4**, it is feasible to make a direct comparison of the pyranosidic and furanosidic anomeric behavior using proton spin–spin coupling constants. The pyranoside linkage (ϕ) was found to adopt a more well-defined, exo-anomeric conformation as evidenced by the large (10.7 Hz) and small (2.7 Hz) coupling constants (Table 3). On the other hand, the furanoside linkage (ψ) is less well-defined, as evidenced by equivalent ^3J values (7.4, 7.4 Hz). Structures consistent with the experimental data for **4** are shown in Figure 2b. In these structures, ϕ stays fixed in the exo-anomeric conformation and ψ pivots between two staggered forms, one of which is exo-anomeric. Alternatively, a single staggered conformer at the ψ linkage cannot be ruled out.

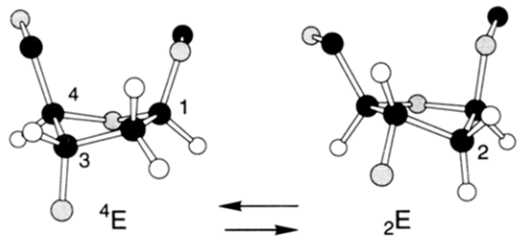


4: X = H.1
13: epi-1-4
2-^{13}C: X = $^{13}CH_2OH$

Compound **13**, the C.1 epimer of **4**, exhibits a different behavior at the furanosidic linkage. In this compound, both ϕ and ψ possess exo-anomeric conformations. A single conformation consistent with the NMR data is shown in Figure 2c. Unlike compound **4**, the furanosyl exo-anomeric conformation of **13** is free of any unfavor-

(24) A sample of **16** was prepared by Dr. S. C. Ahn of this laboratory.

Scheme 2



able 1,3-diaxial-like steric interactions with the neighboring pyranoside.

The quaternary fructofuranosyl anomeric center in *C*-sucrose (**2**) precludes the use of $^3J_{HH}$ as a means of assessing ψ conformational preferences. In order to conveniently monitor ψ using $^3J_{CH}$, **2** was prepared[29] with a ^{13}C label at C.1 (**2**-^{13}C, Table 3). In methanolic solution, the pyranoside linkage shows the usual exo-anomeric preference, whereas the $^3J_{CH}$ values[30] are nearly equal, indicative of no such preference (Table 3). The similar intraresidue conformational behavior of both **1** and **2** was evident by a small H.1′−H.4 NOE in both substances. This NOE is consistent with a well-defined exo-anomeric pyranosyl ϕ linkage and a more flexible fructofuranosyl ψ linkage (Figure 3). Taken together, these experimental results lend further support to the proposal of differential flexibility about the ϕ and ψ linkage in both *C*-sucrose[3] and *O*-sucrose.[31−34]

The differential ϕ/ψ flexibility in *O*-sucrose (**1**) could arise from the presence of the fructofuranosyl C.2 quaternary center. To test this hypothesis, the glucosyl H.1 in 1-(deshydroxymethyl)-*O*-sucrose (**3**) was irradiated. A H.1$_g$−H.3 interaction could not be detected in this substance—note the atom numbering change. A similar

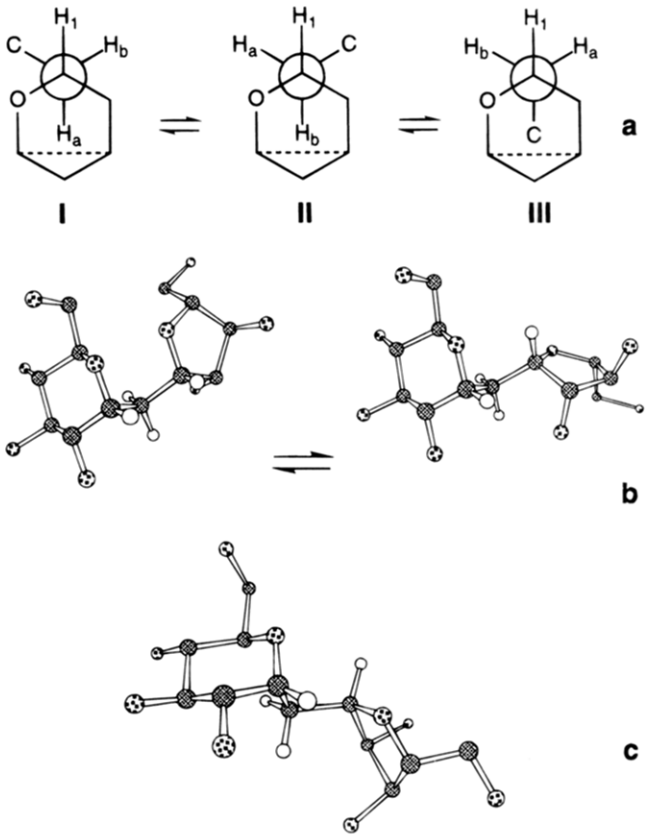


Figure 2. (a) Definition of staggered rotamers at the *C*-glycosidic linkage. Rotamer I possesses the exo-anomeric conformation. (b) Two staggered conformers of compound **4** consistent with the observed time-averaged NMR data. (c) Single staggered conformation of compound **13** consistent with the NMR data. Structures shown in b and c are shown for illustrative purposes only and do not represent energy-minimized structures.

Table 3. *C*-Glycosidic ^3J Values (Hz)

compd	solvent	$^3J_{H.1'-H.a}$	$^3J_{H.1'-H.b}$	$^3J_{C.1-H.a}$	$^3J_{C.1-H.b}$
2-^{13}C	CD_3OD	9.3	2.5	4.1	3.3
				$^3J_{H.1-H.a}$	$^3J_{H.1-H.b}$
4	CD_3OD	10.7	2.7	7.4	7.4
13	CD_3OD	11.5	2.4	3.0	9.5
7	CD_3OD			6.0	7.4
12	CD_3OD			4.5	8.5
15	CD_3OD			5.2	7.3
21	D_2O			5.5	7.7

observation was made in comparing *C*-sucrose (**2**) with its 1-(deshydroxymethyl) derivative **4**.

In sucrose analogs lacking the C.1 hydroxymethyl group, the reduced flexibility about ψ results in a fairly "extended" geometry (Figure 3) in which the glucosyl H.1 is distant from H.4 (H.3 in the arabinose series). This picture is consistent with the spin coupling data and the NOE result. When the anomeric center is quaternized, as in both *O*-sucrose and *C*-sucrose, the degree of freedom about ψ appears to increase sufficiently such that conformations in which H.1$_g$ and H.4 are in close proximity are significantly populated. This is perhaps an expected result based upon a simple steric analysis of the quaternary center in *O*-sucrose (**1**) and *C*-sucrose (**2**). However, the result obtained from 1-(deshydroxymethyl)-*O*-sucrose (**3**) provides direct experimental support for this picture. The five-membered ring conformation in **3** is very similar

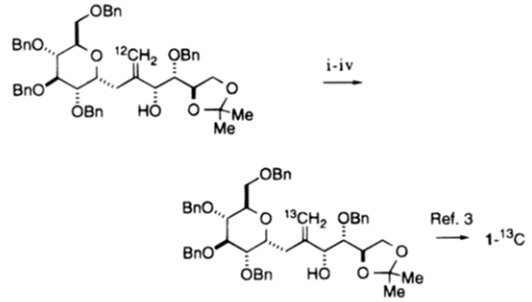
(25) Lemieux, R. U.; Chu, N. J. *Abstracts of Papers*, 133rd National Meeting of the American Chemical Society, San Francisco, April, 1958; American Chemical Society: Washington, DC, 1958; 31N.

(26) For a recent theoretical treatment of this phenomenon in pyranosides, see: Houk, K. N.; Eksterowitcz, J. E.; Wu, Y.-D.; Fuglesang, C. D.; Mitchell, D. B. *J. Am. Chem. Soc.* **1993**, *115*, 4170−4177.

(27) Raap, J. van Boom, J. H.; Bruinslot, H. J.; Beurkens, P. T.; van Wietmarschen, J. A. C.; Smits, J. M. M.; Haasnoot, C. A. G. *Acta Crystallogr.* **1987**, *B43*, 219−223.

(28) Kopf, J.; Koll, P. *Carbohydr. Res.* **1984**, *135*, 29−46.

(29) The allylic alcohol *C*-sucrose precursor was elaborated as shown: ((i) TES-Cl/DMAP/py/rt, (ii) O_3, DMS/CH_2Cl_2−MeOH (1:1)/−78 → 0 °C, (iii) $Ph_3P^{13}CH_2$/Tol-THF (4:1)/55 °C, (iv) TBAF/THF/rt).



(30) Marshall, J. L. *Carbon−Carbon and Carbon−Proton NMR Couplings: Applications to Organic Stereochemistry and Conformational Analysis*; Verlag Chemie: Deerfield Beach, FL, 1983.

(31) du Penhoat, C. H.; Imberty, I.; Roques, N.; Michon, V.; Mentech, J.; Descotes, G.; Perez, S. *J. Am. Chem. Soc.* **1991**, *113*, 3720−3727.

(32) Poppe, L.; van Halbeek, H. *J. Am. Chem. Soc.* **1992**, *114*, 1092−1094.

(33) Duker, J. M.; Serianni, A. S. *Carbohydr. Res.* **1993**, *249*, 281−303.

(34) For purely theoretical investigations, see: (a) French, A. D.; Schafer, L.; Newton, S. Q. *Carbohydr. Res.* **1993**, *239*, 51−60. (b) Tran, V. H.; Brady, J. W. Biopolymers **1990**, *29*, 967−997 and references cited therein.

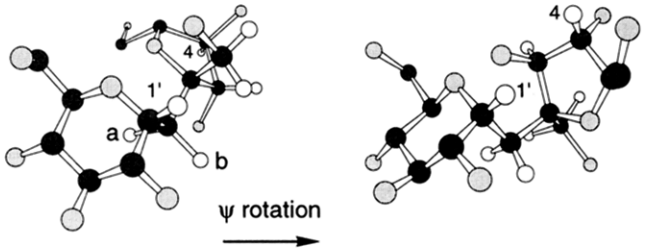


Figure 3. Models showing the H.1′−H.4 distance in sucrose and *C*-sucrose (shown) mediated by displacement about ψ. In both representations, the pyranosyl linkage ϕ remains in the exo-anomeric conformation.

to that in *O*-sucrose (**1**), so any differences in intraresidue NOE behavior reflect a difference in exo-anomeric conformation.

Our experimental efforts directed toward conformational issues in *O*-sucrose have revealed the important role of the quaternary fructofuranosyl anomeric center in terms of exo-anomeric flexibility. In this regard, we tend to view the α-pyranosyl linkage (ϕ) as conformationally well-defined in an exo-anomeric sense. In other words, the flexibility of *O*-sucrose and *C*-sucrose arises largely from a lack of an exo-anomeric preference at the β-fructofuranosyl linkage (ψ). Interestingly, the ψ linkage of *C*-sucrose does adopt an exo-anomeric conformation in methanolic solutions of divalent cations such as Ca^{2+}, whereas the parent *O*-sucrose does not.[4]

The monofuranosides were also examined for their exo-anomeric behavior (Table 3). The model arabinofuranosides **7** and **12** behaved in a manner similar to their disaccharide counterparts **4** and **13**. The β- and α-*C*-2-deoxyribose entries **15** and **21** have values similar to the β-arabinose case. In contrast to *C*-pyranosides, strong exo-anomeric conformational preferences do not appear to be a general feature of *C*-furanosides.

The Exo-Anomeric Effect in *C*-Furanosides: Base Orientation in *C*-Nucleosides. In connection with our interest in exo-anomeric conformational preferences in *C*-glycosides, we compared compounds **8** and **9** with respect to the preferred syn/anti base orientation in the solution state. In the crystalline state, both compounds possess the anti conformation (Table 2, Figure 1). In solution, the base orientation is probed by nuclear Overhauser interactions between the base H.6′ and the sugar H.1 and H.3. For an anti arrangement (Figure 1), one expects an H.6′−H.3 interaction while for a syn arrangement H.6′ is spatially close to H.1, as visualized by a 180° rotation of either base in Figure 1. The NOE values (Table 1) appear to indicate a stronger anti orientation for nitrogen-derived **9** (H.6′−H3 NOE > H.6′−H.1 NOE) when compared to **8** (H.6′−H.1 NOE > H.6′−H.3 NOE). Do these data reflect a different preferred base orientation, or is it simply a consequence of differences in ring pucker? The latter makes a reasonable contribution, on the basis of the ring coupling constants and trans-annular NOE measurements discussed earlier in the context of ring conformation. Based upon these criteria, the H.6′−H.3 internuclear distance, for an anti orientation, is most likely greater in **8** than in **9** because of a stronger equatorial preference in the *C*-nucleoside.

The NOE behavior for compounds **16** and **17** under the conditions of H.6′ irradiation were also compared (Table 1). 2-Deoxyuridine (**17**) has been reported[35] to exist mainly in the anti conformation. Under the conditions of our study, irradiation of H.6′ in **17** produced enhancements of 3.8 and 1.7% at H.1 and H.3, respectively. In the carbon analog **16**, this irradiation resulted in a larger H.1 enhancement (6.8%) and a barely detectable H.3 enhancement (0.22%). As for the arabinonucleosides, these observations can be rationalized either in terms of preferred base orientation or ring pucker. Again, differences in ring conformation, as evidenced by the scalar coupling constant data, makes the case for a contribution from the latter.

In this context, it is interesting to note that a similar syn preference has been reported[36] for the ribose-derived pseudouridine, in contrast to an anti preference in uridine. In this system, the differences have been ascribed solely to differences in the base orientation.

Conclusions

The ring conformations of β- and α-*C*-arabino- and β- and α-*C*-2-deoxyribofuranosides are not similar to their naturally occurring oxygen-derived counterparts. The anomeric C−C bond tends to adopt an equatorial position in contrast to the known axial preference of the anomeric C−O bond. In the solution state, ring conformations of *N*-furanosides appear to have intermediate behavior when compared with *C*- and *O*-furanosides. In the solid state, however, the molecular conformation of the *C*-nucleoside β-arabinosyl pseudouridine was shown to be nearly superimposable with the *N*-nucleoside β-arabinosyluridine. Indeed, crystal lattice requirements can sometimes mask conformational preferences observed in the solution state.

For the carbon furanosides, installation of an anomeric quaternary center can sterically influence the ring conformation so that it becomes more similar to the β-*O*-furanoside. Our results indicate that quaternizing the anomeric center with two C−C bonds can expand the available number of ground-state *C*-furanoside conformations, a feature that is not found for quaternary, oxygen-derived furanosides. In principle, this property of quaternary *C*-furanosides could be used to one's advantage as an element of conformational control when considering *C*-furanosides as surrogates for natural products.

Whereas *C*-pyranosides exhibit strong exo-anomeric conformational preferences, the same degree of conformational bias was only observed for the α-*C*-arabino-furanosides. In *O*-sucrose and related disaccharides, the experimental evidence is in favor of differential flexibility at the respective ϕ and ψ linkages. The quaternary fructofuranosyl anomeric center appears to increase the exo-anomeric motional degrees of freedom in *O*-sucrose. Removal of the C.1 hydroxymethyl group in *O*-sucrose or *C*-sucrose produced substances with qualitatively different intraresidue NOE behavior. Thus, the flexible nature of *O*-sucrose appears to arise largely at the quaternary fructofuranosyl ψ linkage, whereas the pyranosyl ϕ linkage is conformationally more well-defined in the exo-anomeric geometry.

Finally, the base orientation in *C*-nucleosides derived from arabinose and 2-deoxyribose appears to be quite different in comparison with the analogous *N*-nucleo-

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(36) Neumann, J. M.; Bernassu, J. M.; Gueron, M.; Tran-Dinh, S. *Eur. J. Biochem.* **1980**, *108*, 457−463.

sides. In particular, stronger syn conformational preferences were observed in the *C*-nucleosides, using base–sugar NOE's as the sole criterion. The stronger equatorial preference of the *C*-nucleoside base precludes any direct comparison of the base–sugar NOE's between the carbon and nitrogen-derived nucleosides.

Experimental Section

1-(Deshydroxymethyl)-*O*-sucrose (3). Prepared by adopting the known procedure[37] for the synthesis of *cis*-1,2 arabinofuranosides, condensing tetra-*O*-benzylglucose with 2,3,5-tri-*O*-benzyl-α-arabinosyl fluoride ($SnCl_2/Et_2O$/0 °C), followed by benzyl deprotection ($H_2/Pd(OH)_2$ on C/MeOH): ^{1}H NMR (500 MHz, CD_3OD) δ 5.1 (d, J = 4.7 Hz, 1 H), 4.99 (d, J = 3.8, 1 H), 4.00 (dd, J = 4.7, 8.0, 1 H), 3.90 (t, J = 7.0, 1 H), 3.85 (m, 1 H), 3.79 (dd, J = 2.3, 11.84, 1 H), 3.75–3.58 (m, 5 H), 3.38 (dd, J = 3.8, 9.8, 1 H), 3.31 (dd, J = 9.1, 10.0, 1 H); $[\alpha]_D$ +35.5° (*c* 1.3, CH_3OH); HRMS (FAB, NaI) $[M + Na]^+$, calcd for $C_{25}H_{34}O_{17}$ (M + Na, heptaacetate, mp 114–116 °C) 629.1694, found 629.1702.

β- and α-*C*-Arabinofuranosides 7 and 12. Prepared in five steps ((1) allyl TMS/BF_3–OEt_2/TMSOTf/CH_3CN, (2) O_3/DMS/$NaBH_4$/MeOH/CH_2Cl_2, (3) $H_2/Pd(OH)_2$ on C/MeOH/rt, (4) 2,2-dimethoxypropane/CSA, (5) 80% aqueous HOAc) from methyl tri-*O*-benzyl-D-arabinofuranoside. β-**7:** ^{1}H NMR (500 MHz, CD_3OD) δ 4.08 (m 1 H), 3.94 (dd, J = 1.3, 2.8 Hz, 1 H), 3.83 (dd, J = 1.3, 3.4, 1 H), 3.73–3.58 (m, 5 H), 1.86 (m, 2 H); $[\alpha]_D$ + 24.2° (*c* 1.3, CH_3OH); HRMS $(M - H)^-$ calcd for $C_7H_{14}O_5$ 179.0919, found 179.0921. α-**12:** ^{1}H NMR (500 MHz, CD_3OD) δ 3.94 (t, J = 6.0, 1 H), 3.83 (ddd, J = 4.5, 6.7, 8.4, 1 H), 3.78–3.62 (m, 5 H), 3.60 (dd, J = 5.5, 11.8, 1 H), 1.91–1.75 (m, 2 H); $[\alpha]_D$ +65.6° (*c* 0.92, CH_3OH); HRMS (FAB) calcd for $C_7H_{14}O_5$ $(M - H)^-$ 179.0919, found 179.0921.

5-(β-D-Arabinofuranosyl)uracil (8). Prepared from pseudouridine employing, in part, a known procedure[13] ((1) TIPDS-Cl/Py, (2) Dess–Martin periodinane/CH_2Cl_2/rt, followed by reduction and deprotection, (3) DIBAL/CH_2Cl_2/0 °C, (4) TBAF/THF/rt): ^{1}H NMR (500 MHz, D_2O) δ 7.48 (s, 1H), 4.89 (d, J = 3.4 Hz, 1H), 4.15 (dd, J = 3.4, 1.4, 1H), 3.97 (dd, J = 1.4, 3.7, 1H), 3.82 (m, 1H), 3.68 (dd, J = 3.9, 12.0, 1H), 3.63 (dd, J = 6.5, 12.0); $[\alpha]_D$ +34° (*c* 0.6, CH_3OH); HRMS (FAB) calcd for $C_{15}H_{18}N_2O_9$ (M + Na, triacetate) 393.0910, found 393.0914.

β-*C*-2-Deoxyribofuranoside 15. Prepared in four steps ((1) $LiCH_2COOEt$/THF/–50 °C, (2) Et_3SiH/BF_3–OEt_2/CH_3CN/0 °C, (3) DIBAL/CH_2Cl_2/0 °C, (4) $H_2/Pd(OH)_2$ on C/MeOH/rt, from 3,5-bis-*O*-benzyl-2-deoxyribonolactone): ^{1}H NMR (500 MHz, CD_3OD) δ 4.22 (m, 1H), 4.17 (m, 1H), 3.73 (dt, J = 2.9, 5.0, 1 H), 3.66 (t, J = 6.6, 2 H), 3.52 (m, 2 H), 1.92 (ddd, J = 1.9, 5.4, 7.2, 1 H), 1.83–1.68 (m, 3 H); $[\alpha]_D$ +10.2° (*c* 0.41, CH_3OH); FAB HRMS $[M + Na]^+$ calcd for $C_{13}H_{20}O_7$ (triacetate) 311.1107, found 311.1114.

α-*C*-2-Deoxyribofuranoside 21. Prepared in three steps ((1) allyl TMS/BF_3–OEt_2/CH_3CN/0 °C, (2) O_3/DMS/$NaBH_4$/MeOH:CH_2Cl_2(2:1)/–78 to 0 °C, (3) $H_2/Pd(OH)_2$ on C/MeOH/rt, from methyl tri-*O*-benzyl 2-deoxyribofuranoside): ^{1}H NMR (500 MHz, CD_3OD) δ 4.14 (m, 1 H), 4.07 (m, 1 H), 3.74 (m, 1 H), 3.55 (t, J = 6.7, 2 H), 3.53 (dd, J = 3.7, 12.1, 1 H), 3.47 (dd, J = 6.3, 12.1, 1 H), 2.32 (m, 1 H), 1.80 (m, 1 H), 1.70 (m, 1 H), 1.55 (m, 1 H); $[\alpha]_D$ +53.2° (*c* 0.89, CH_3OH); HRMS (FAB) calcd for $C_{13}H_{20}O_7$ (M + H, triacetate) 289.1287, found 289.1284.

β- and α-2-Deoxy-*O*-methylfructofuranosides (18) and (19). Prepared as a 1:1 α/β mixture in four steps ((1) $LiCH_2$-COOEt/THF/–50 °C, (2) cat. H_2SO_4/MeOH/rt, (3) $LiEt_3BH$/THF/0 °C, (4) $H_2/Pd(OH)_2$ on C/MeOH/rt) from 3,5-bis-*O*-benzyl-2-deoxyribonolactone. β-**18:** ^{1}H NMR (500 MHz, CD_3OD) δ 4.22 (m, 1H), 3.8 (m, 1H), 3.66 (dd, J = 4.1, 11.6 Hz, 1H), 3.6 (m, 1H), 3.55 (dd, J = 11.6, 7.1, 1H), 3.2 (s, 3H), 2.3 (dd), 2.13 (m, 1H), 1.95–1.85 (m, 2H); $[\alpha]_D$ –14° (*c* 0.17, CH_3OH); HRMS (FAB) calcd for $C_{14}H_{22}O_8$ (M + Na, triacetate) 341.1212, found 341.1206. α-**19:** ^{1}H NMR (500 MHz, CD_3OD) δ 4.12 (m, 1 H), 3.85 (m, 1H), 3.67 (dd, J = 3.6, 11.9, 1 H), 3.63–3.55 (m, 3 H), 3.24 (s, 3 H), 2.22 (dd, J = 8.1, 13.5, 1 H), 2.09 (m, 1 H), 1.95 (dd, J = 3.1, 13.5, 1 H), 1.85 (m, 1 H); $[\alpha]_D$ +89° (*c* 0.89, CH_3OH); HRMS (FAB) calcd for $C_{14}H_{22}O_8$ (M + Na, triacetate) 341.1212, found 341.1227.

β-*C*-2-Deoxyfructofuranoside 20. Prepared in four steps ((1) TBDPSCl/imidazole/CH_2Cl_2/rt, (2) allyl TMS/BF_3–OEt_2/CH_3CN/0 °C, (3) TBAF/THF/rt, (4) $H_2/Pd(OH)_2$ on C/MeOH/rt) from the $LiEt_3BH$ reduction product used in the preparation of **18**): ^{1}H NMR (500 MHz, CD_3OD) δ 4.21 (m, 1H), 4.17 (m, 1H), 3.73 (m, 1H), 3.66 (t, J = 7.3 Hz, 2H), 3.51 (m, 2H), 1.92 (ddd, J = 1.8, 6.3, 12.0), 1.81–1.68 (m, 3H); $[\alpha]_D$ +34° (*c* 0.18, CH_3OH); HRMS (FAB) calcd for $C_{18}H_{20}O_{24}$ (M + Na, triacetate) 353.1576, found 353.1588.

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Supplementary Material Available: ^{1}H NMR spectra, including NOE data for compounds discussed in the text (20 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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