Preferred Conformation of C-Glycosides. 9. Conformational Analysis of 1,4-Linked Carbon Disaccharides[†,‡]

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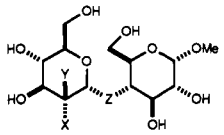
The preferred solution conformation of the 1,4-linked carbon disaccharides **3–10** has been determined based on vicinal coupling constants in the ^{1}H NMR spectrum. The conformation of these compounds can be predicted on the basis of the preference of the C-glycosidic bond for the "exo-anomeric" conformation and the diamond lattice analysis of 1,3-diaxial-like interactions around the C-aglyconic bond. The importance of 1,3-diaxial-like interactions has been demonstrated by showing that structural modifications which alter these interactions result in predictable and significant changes in the conformational behavior. The conformational similarity of carbon and oxygen disaccharides has been demonstrated experimentally by a comparison of NOE and T_1 data.

In previous publications,[1] it was shown that the carbon analogues of simple glycosides adopt a similar glycosidic conformation to that of the parent compounds. The preference of the carbon glycosides for the "exo-anomeric" conformation was used to predict the conformational behavior of the 1,6-linked carbon disaccharides *C*-isomaltoside and *C*-gentiobioside, and these predictions were confirmed experimentally. In order to gain insight into the conformational behavior of the more abundant 1,4-, 1,3-, and 1,2-linked oligosaccharides, the analysis was extended to the carbon analogues of methyl maltoside **1** and methyl cellobioside **2**.



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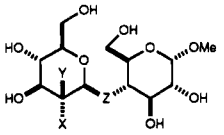

2: X=OH, Y=H, Z=O
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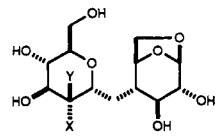

7: X=OH, Y=H
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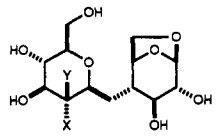

9: X=OH, Y=H
10: X=H, Y=OH

The conformational behavior of 1,6-linked carbon disaccharides was treated as two independent C-glycosidic bonds on tetrahydropyran rings. The conformational analysis of the 1,4-linked carbon analogues **3–10** requires consideration of one C-glycosidic bond and one C-aglyconic bond. No literature precedent was available for predicting the conformational behavior around the C-aglyconic bond. Furthermore, for the 1,6-linked disaccharides, it was not necessary to take into account nonbonded interactions between the two pyranose rings. The close proximity of the two pyranose rings in the 1,4-linked cases, however, make interactions between them likely. The conformational analysis of the 1,4-linked carbon disaccharides must therefore be based on the consideration of these interactions.

Three issues need to be addressed. First, we wish to determine whether the carbon analogues of the 1,4-linked disaccharides adopt the "exo-anomeric" conformation around the C-glycosidic bond. It has been shown that the parent compounds **1** and **2** adopt the exo-anomeric conformation in solution[2] and that steric hindrance results in distortion around the aglyconic bond predominantly.[3] It is important to determine whether these characteristics are reflected in the carbon analogues. Second, the steric factors responsible for the conformational behavior around the C-aglyconic bond must be analyzed. By virtue of the experimental nature of our approach, direct evidence of the effect of specific interactions can be provided. Finally, the issue of the conformational similarity between the carbon- and oxygen-linked disaccharides must be addressed experimentally. This comparison will determine whether the conclusions derived from the conformational analysis of carbon glycosides can be extended to natural oligosaccharides.

The synthesis of the 1,4-linked carbon disaccharides **3–10** and of their C.α-deuterated analogues has been described in a preceding paper.[4] The solution conformation of the carbon disaccharides can be determined experimentally on the basis of vicinal coupling constants in the ^{1}H NMR spectrum by relating the magnitude of the constant to the corresponding dihedral angle using the modified Karplus equation.[5] The 500-MHz ^{1}H NMR spectra of compounds **3–10** were recorded, and the data are presented in Table I. The resonances were assigned on the basis of homonuclear decoupling experiments. The coupling constants were determined by first-order analysis.

[†] Preliminary results of this work have been published: Babirad, S. A.; Wang, Y.; Goekjian, P. G.; Kishi, Y. *J. Org. Chem.* **1987**, *52*, 4825. Wang, Y.; Goekjian, P. G.; Ryckman, D. M.; Kishi, Y. *J. Org. Chem.* **1988**, *53*, 4151. Miller, W. H.; Ryckman, D. M.; Goekjian, P. G.; Wang, Y.; Kishi, Y. *J. Org. Chem.* **1988**, *53*, 5580. For Part 8 of this series, see: Wang, Y.; Babirad, S. A.; Kishi, Y. Previous paper in this issue.

[‡] Taken in part from Wang, Y. Ph.D. Dissertation, Harvard University, 1990.

(1) (a) Wu, T.-C.; Goekjian, P. G.; Kishi, Y. *J. Org. Chem.* **1987**, *52*, 4819. Wu, T.-C.; Goekjian, P. G.; Kishi, Y. *J. Org. Chem.* **1991**, *56*, 6412. (b) Goekjian, P. G.; Wu, T.-C.; Kang, H.-Y.; Kishi, Y. *J. Org. Chem.* **1987**, *52*, 4823. Goekjian, P. G.; Wu, T.-C.; Kang, H.-Y.; Kishi, Y. *J. Org. Chem.* **1991**, *56*, 6422.

(2) For the conformational analysis of cellobiose and maltose in solution, see, for example: (a) Shaskov, A. S.; Lipkind, G. M.; Kotchetkov, N. K. *Carbohydr. Res.* **1986**, *147*, 175 and references cited therein. (b) Nardin, R.; Saint-Germain, J.; Vincendon, M.; Taravel, F. R.; Vignon, M. R. *Nouv. J. Chim.* **1984**, *8*, 305 and references cited therein. (c) Lemieux, R. U.; Bock, K.; Delbaere, L. T. J.; Koto, S.; Rao, V. S. *Can. J. Chem.* **1980**, *58*, 631 and references cited therein. (d) St.-Jacques, M.; Sundararajan, P. R.; Taylor, K. J.; Marchessault, R. H. *J. Am. Chem. Soc.* **1976**, *98*, 4386 and references cited therein.

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(5) (a) Karplus, M. *J. Chem. Phys.* **1959**, *30*, 11. (b) Karplus, M. *J. Phys. Chem.* **1960**, *64*, 1793. (c) Karplus, M. *J. Am. Chem. Soc.* **1963**, *85*, 2870. (d) Haasnoot, C. A. G.; de Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783.

0022-3263/92/1957-0482$03.00/0

Table I.[a] ^{1}H NMR Data for Glycosides 3–10

entry	proton	3 chemical shift (coupling pattern)	4 chemical shift (coupling pattern)
1	C.1	4.69 (d, 3.7)	4.69 (d, 3.7)
2	C.2	3.34 (dd, 9.5, 3.7)	3.35 (dd, 9.4, 3.7)
3	C.3	3.81 (dd, 10.6, 9.5)	3.69 (dd, 10.8, 9.4)
4	C.4	1.82 (dddd, 10.6, 8.8, 5.5, 2.9)	1.73 (dddd, 11.3, 10.8, 5.3, 3.3)
5	C.5	3.62 (ddd, 8.8, 4.9, 2.3)	3.57 (ddd, 11.3, 6.4, 2.4)
6	C.6	3.68 (dd, 12.0, 4.9)	3.73 (dd, 11.6, 2.4)
7	C.6	3.75 (dd, 12.0, 2.3)	3.79 (dd, 11.6, 6.4)
8	C.α *pro-S*	1.92 (ddd, 15.0, 10.3, 2.9)	1.82 (ddd, 14.4, 9.0, 3.3)
9	C.α *pro-R*	1.75 (ddd, 15.0, 5.5, 3.1)	1.67 (ddd, 14.4, 5.3, 4.6)
10	C.1′	4.23 (ddd, 10.3, 5.6, 3.1)	4.11 (ddd, 9.0, 4.6, 3.7)
11	C.2′	3.53 (dd, 9.2, 5.6)	3.71 (dd, 3.7, 2.5)
12	C.3′	3.49 (dd, 9.2, 8.2)	3.77 (dd, 9.8, 2.5)
13	C.4′	3.16 (dd, 9.0, 8.2)	3.58 (dd, 9.8, 7.6)
14	C.5′	3.60 (ddd, 9.0, 6.8, 2.7)	3.72 (ddd, 7.6, 7.0, 3.8)
15	C.6′	3.60 (dd, 14.3, 6.8)	3.57 (dd, 11.3, 7.0)
16	C.6′	3.81 (dd, 14.3, 2.7)	3.67 (dd, 11.3, 3.8)
		5	**6**
1	C.1	4.69 (d, 3.7)	4.68 (d, 3.7)
2	C.2	3.38 (dd, 9.3, 3.7)	3.37 (d, 9.3, 3.7)
3	C.3	3.58 (dd, 10.3, 9.3)	3.63 (dd, 10.3, 9.3)
4	C.4	1.72 (dddd, 10.9, 10.3, 4.7, 3.5)	1.67 (dddd, 10.3, 10.1, 5.2, 3.8)
5	C.5	3.70 (ddd, 10.9, 5.4, 1.7)	3.73 (ddd, 10.1, 5.4, 1.9)
6	C.6	3.60 (dd, 11.8, 5.4)	3.60 (dd, 11.8, 5.4)
7	C.6	3.82 (dd, 11.8, 1.7)	3.85 (dd, 11.8, 1.9)
8	C.α *pro-S*	2.08 (ddd, 15.3, 4.7, 1.7)	1.75 (ddd, 15.1, 3.8, 3.8)
9	C.α *pro-R*	1.59 (ddd, 15.3, 9.2, 3.5)	1.86 (ddd, 15.1, 9.1, 5.2)
10	C.1′	3.28 (ddd, 9.2, 9.2, 1.7)	3.63 (dd, 9.1, 3.8)
11	C.2′	3.05 (dd, 9.2, 9.1)	3.72 (d, 3.2)
12	C.3′	3.32 (dd, 9.1, 8.8)	3.43 (dd, 9.2, 3.2)
13	C.4′	3.19 (dd, 9.7, 8.8)	3.47 (dd, 9.2, 8.9)
14	C.5′	3.20 (ddd, 9.7, 6.8, 1.9)	3.16 (ddd, 8.9, 6.7, 2.3)[b]
15	C.6′	3.51 (dd, 11.9, 6.8)	3.60 (dd, 11.6, 6.7)[b]
16	C.6′	3.82 (dd, 11.9, 1.9)	3.83 (dd, 11.6, 2.3)
		7	**8**
1	C.1	5.28 (s)	5.28 (s)
2	C.2	3.62 (s)[d]	3.63 (s)
3	C.3	3.45 (s)	3.43 (s)
4	C.4	1.78 (dd, 8.4, 6.0)	1.79 (dd, 9.2, 4.5)
5	C.5	4.53 (d, 5.1)	4.50 (d, 5.0)
6	C.6	3.66 (dd, 6.7, 5.1)	3.66 (dd, 6.8, 5.0)
7	C.6	4.15 (d, 6.7)	4.14 (d, 6.8)
8	C.α *pro-S*	1.99 (ddd, ca. 14–15, 10.1, 6.0)	2.06 (ddd, 13.8, 11.2, 4.5)
9	C.α *pro-R*	2.01 (ddd, ca. 14–15, 8.4, 4.2)	1.83 (ddd, 13.8, 9.2, 3.0)[c]
10	C.1′	4.09 (ddd, 10.1, 5.6, 4.2)	4.03 (ddd, 11.2, 3.0, 2.4)
11	C.2′	3.61 (dd, 9.6, 5.6)	3.75 (dd, 3.0, 2.4)
12	C.3′	3.55 (dd, 9.6, 8.5)	3.71 (dd, 8.9, 3.0)
13	C.4′	3.22 (dd, 9.2, 8.5)	3.61 (dd, 9.0, 8.9)
14	C.5′	3.50 (ddd, 9.2, 6.4, 2.3)	3.50 (ddd, 9.0, 6.6, 2.5)
15	C.6′	3.63 (dd, 11.8, 6.4)	3.72 (dd, 11.8, 6.6)
16	C.6′	3.81 (dd, 11.8, 2.3)	3.81 (dd, 11.8, 2.5)
		9	**10**
1	C.1	5.28 (s)	5.29 (s)
2	C.2	3.52 (s)[d]	3.52 (s)
3	C.3	3.42 (s)	3.43 (s)
4	C.4	1.89 (dd, 9.8, 4.5)	1.83 (dd, 9.3, 1.4)
5	C.5	4.47 (d, 5.0)	4.46 (d, 5.2)
6	C.6	3.66 (dd, 6.7, 5.0)	3.66 (dd, 6.7, 5.2)
7	C.6	4.05 (d, 6.7)	4.10 (d, 6.7)
8	C.α *pro-S*	2.26 (ddd, 14.4, 9.8, 2.3)	1.85 (ddd, ca. 14–15, 9.3, 3.3)
9	C.α *pro-R*	1.66 (ddd, 14.4, 9.9, 4.5)	2.06 (ddd, ca. 14–15, 10.0, 1.4)[c]
10	C.1′	3.30 (ddd, 9.9, 8.7, 2.3)	3.61 (dd, 10.0, 3.3)[c]
11	C.2′	3.35 (dd, 8.7, 8.7)	3.72 (d, 2.7)
12	C.3′	3.24 (dd, 9.6, 8.7)	3.51 (dd, 9.4, 2.7)
13	C.4′	3.08 (dd, 9.6, 9.0)	3.54 (dd, 9.4, 9.1)
14	C.5′	3.22 (ddd, 9.0, 5.9, 1.7)	3.20 (ddd, 9.1, 6.2, 2.1)
15	C.6′	3.60 (dd, 12.1, 5.9)	3.65 (dd, 11.9, 6.2)
16	C.6′	3.85 (dd, 12.1, 1.7)	3.84 (dd, 11.9, 2.1)

[a] All spectra were recorded on a Bruker AM-500 (500-MHz) spectrometer. The chemical shifts are relative to the signal of CHD_2OD (3.30 ppm). The spin–spin coupling constants were obtained by first-order analysis. [b] Because of higher order effects, this vicinal coupling constant could not be obtained by first-order analysis. [c] Because of high-order spin–spin coupling patterns, these couplings were determined from the C.α-(s)-deuterated compound. [d] Assignment of the resonances of the C.2 and C.3 protons is based inconclusively on subtle changes in the 3.4 ppm resonance upon irradiation of the C.4 proton.

Table II. Vicinal Coupling Constants across the C.4–C.α–C.1′ Bridge of Compounds 3–10

$^3J_{CH}$ (Hz)	3	4	5	6	7	8	9	10
$J(1',\alpha_R)$	3.1	4.6	9.2	9.1	4.2	3.0	9.9	10.0
$J(1',\alpha_S)$	10.3	9.0	1.7	3.8	10.1	11.2	2.3	3.3
$J(4,\alpha_R)$	5.5	5.3	3.5	5.2	8.4	9.2	4.5	1.4
$J(4,\alpha_S)$	2.9	3.3	4.7	3.8	6.0	4.5	9.8	9.3

The conformational analysis of these compounds requires the assignment of the absolute stereochemistry of the protons responsible for each of the C.α methylene resonances. Stereospecifically deuterated samples have been prepared,[4] and the absolute stereochemistry of the label was determined unambiguously. The assignment of the methylene resonances was made by comparison of the ^{1}H NMR spectra of **3–10** to those of the corresponding deuterated samples.

Results and Discussion

The observed coupling constants around the pyranose rings in compounds **3–10** show that they adopt the expected chair conformations. The left-hand ring adopts the chair conformer with the C.5′–C.6′ bond in the equatorial position (e.g., **5**, $J_{1',2'}$ = 9.2 Hz, $J_{2',3'}$ = 9.1 Hz, $J_{3',4'}$ = 8.8 Hz, $J_{4',5'}$ = 9.7 Hz; **6**, $J_{1',2'}$ = 0 Hz, $J_{2',3'}$ = 3.2 Hz, $J_{3',4'}$ = 9.2 Hz, $J_{4',5'}$ = 8.9 Hz). The right-hand ring of the methyl glycosides **3–6** also adopt the chair conformation with the C.2 through C.5 substituents in the equatorial position (e.g., **3**, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 10.6 Hz, $J_{4,5}$ = 8.8 Hz). Due to the presence of the 1,6-anhydro bridge, the right-hand rings of compounds **7–10** adopt the alternative chair with all substituents axial (e.g., **7**, $J_{1,2} = J_{2,3} = J_{3,4} = J_{4,5} = 0$ Hz).

The vicinal coupling constants across the interannular bridge for compounds **3–10** are listed in Table II. The conformation around the C-glycosidic bond can be determined from the vicinal coupling constants between the C.1′ and C.α protons; the conformational preference around the C-aglyconic bond can be established from the vicinal coupling constants between the C.α and C.4 protons.

The C-Glycosidic Conformation. On the basis of our results with the carbon monoglycosides and the 1,6-linked carbon disaccharides, we expect the 1,4-linked compounds to adopt preferentially the conformation with the C.α–C.4 bond antiperiplanar to the C.2′–C.1′ bond, i.e., the "exo-anomeric" conformation. The possible rotamers around the C.1′–C.α bond of α- (axial) and β-(equatorial) carbon disaccharides, and the corresponding coupling constants, are shown in Figure 1. The observed coupling constants for the axial disaccharides **3** (10.3, 3.1 Hz), **4** (9.0, 4.6 Hz), **7** (10.1, 4.2 Hz),[6] and **8** (11.2, 3.0 Hz) indicate a marked preference for the conformer I-A.[7] The coupling constants for the equatorial disaccharides **5** (9.2, 1.7 Hz), **6** (9.1, 3.8 Hz), **9** (9.9, 2.3 Hz), and **10** (10.0, 3.3 Hz) indicate that they exist predominantly in conformer II-A. The carbon analogues of the 1,4-linked disaccharides thus adopt preferentially the "exo-anomeric" conformer observed for the natural *O*-glycosides.

As was observed in the carbon monoglycosides, the C-glycosidic conformation of the 1,4-linked carbon disaccharides does not depend substantially on the substituent at the C.2′ position. The coupling constants observed for each of the C.2′ axial manno carbon disaccharides **4**, **6**, **8**, and **10** are similar to those observed for the corresponding gluco case. The conformational preference around the C-glycosidic bond can therefore be attributed primarily to steric interactions between the C.α–C.4 bond and the C.2′ carbon vs the O.5′ oxygen, rather than to 1,3-diaxial-like interactions between the C.α–C.4 and C.2′–O.2′ bonds.[1a]

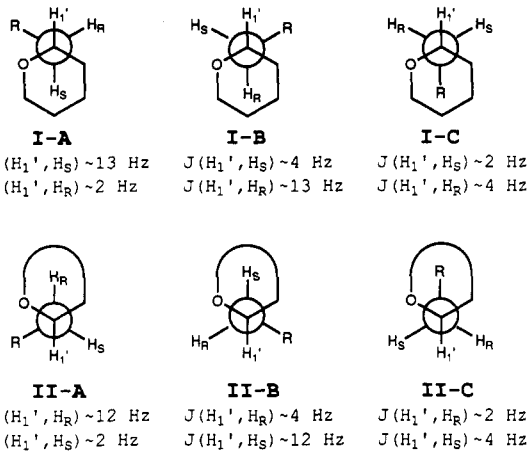


Figure 1. C-Glycosidic rotamers of axial and equatorial carbon glycosides.

Finally, the vicinal coupling constants across the interannular bridge of the carbon disaccharides (Table II) show that while the 1,6-anhydro compounds **7–10** exhibit a preference for one major conformation, the methyl glycosides **3–6** show considerable distortion (vide infra). It is important to note, however, that distortion in the methyl glycosides occurs predominantly around the C-aglyconic C.α–C.4 bond rather than around the C-glycosidic C.1′–C.α bond. This behavior is directly parallel to that observed for the natural oxygen-linked disaccharides.

Three important qualitative features of the glycosidic conformational behavior of natural glycosides are reproduced in the C-glycosidic conformation of the carbon analogues. The carbon analogues of the 1,4-linked disaccharides adopt predominantly the "exo-anomeric" conformation around the C-glycosidic bond, this preference is independent of the stereochemistry of the substituent at the C.2′ position, and steric repulsion results in distortion predominantly around the C-aglyconic bond rather than around the C-glycosidic bond. These observations indicate that the conformational properties of natural glycosidic linkages can be explained, as a first approximation, by steric effects alone.

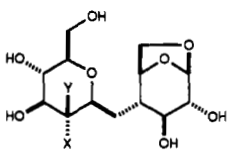
The C-Aglyconic Conformation. The ^{1}H NMR data have established that the C-glycosidic bond is conformationally more rigid than the C-aglyconic bond. Therefore, the conformational analysis of carbon glycosides can be performed, at least as a first approximation, by focusing on the steric effects around the C-aglyconic bond only. Steric destabilization (or stabilization) can be examined by rotating the C-aglyconic bond with the glycosidic bond fixed in the "exo-anomeric" conformation.

In order to clearly evaluate the present through-space steric interactions, such as 1,3-diaxial-like destabilization,[8] a diamond lattice analysis was introduced. For example, in Figure 2, 1,6-anhydro-*C*-cellobiose **9** is placed on a di-

(6) Some averaging of the vicinal coupling constants may be occuring due to higher-order effects. The difference in magnitude between the two real coupling constants is larger than between the coupling constants measured from the ^{1}H NMR spectrum. Bovey, F. A. *Nuclear Magnetic Resonance Spectroscopy*, 2nd ed., Academic Press: San Diego, 1988; Appendix B.

(7) It should be stressed that the ^{1}H NMR coupling constants provide information on the time-averaged conformation only. See ref 9.

(8) El Khadem, H. S.; Horton, D.; Page, Jr., T. F. *J. Org. Chem.* **1968**, *33*, 734.



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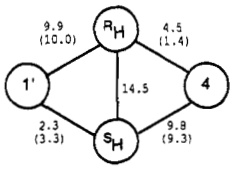
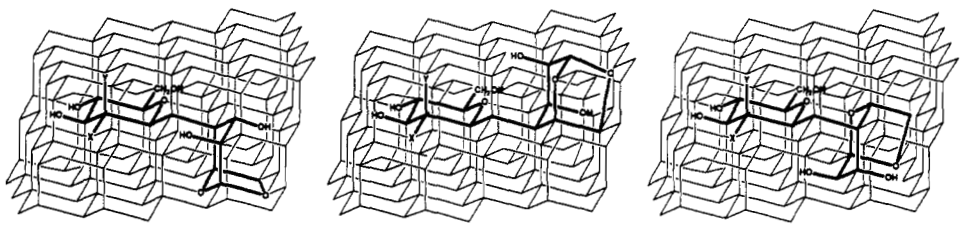
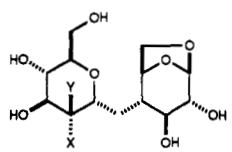


Coupling Constant Diagram for 9 (10)



9,10-A 9,10-B 9,10-C

Figure 2.



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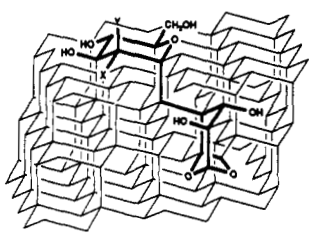
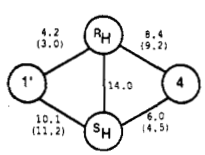


7,8-A



Coupling Constant Diagram for 7 (8)

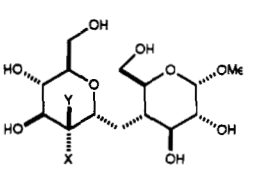
Figure 3.

amond lattice with the C-glycosidic bond fixed in the preferred conformation. Three ideal staggered conformers **9-A**, **9-B**, and **9-C** are shown with respect to the C-aglyconic bond. Conformer **9-C** is least favored because the C.1′–C.α bond is gauche to both the C.4–C.3 and C.4–C.5 bonds. Conformer **9-B** has a 1,3-diaxial-like interaction between the C.1′–O.5 and C.3–C.4 bonds. Conformer **9-A** is free of destabilizing 1,3-diaxial-like interactions. Thus, on the basis of nonbonded steric interactions, **9-A** is expected to be the preferred conformation. This prediction is supported by the vicinal coupling constants $J_{C4,\alpha(pro\text{-}S)}$ = 9.8 Hz and $J_{C4,\alpha(pro\text{-}R)}$ = 4.5 Hz. The disaccharide **9** exists predominantly in conformer **9-A**, which has an extended zigzag conformation from C.2′ to C.3. A similar conformational preference is observed for **10** based on the coupling constants $J_{C4,\alpha(pro\text{-}S)}$ = 9.3 Hz and $J_{C4,\alpha(pro\text{-}R)}$ = 1.4 Hz.

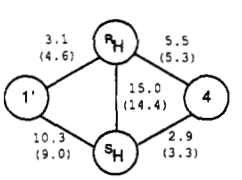
The analysis of the three ideal staggered conformers of the 1,6-anhydromaltose disaccharides **7** and **8** indicates that confomer **7,8-A** is free of 1,3-diaxial-like interactions and is expected to be preferred (Figure 3). The vicinal coupling constants **7**, $J_{C4,\alpha(pro\text{-}R)}$ = 8.4 Hz; $J_{C4,\alpha(pro\text{-}S)}$ = 6.0 Hz;[6] **8**, $J_{C4,\alpha(pro\text{-}R)}$ = 9.2 Hz; $J_{C4,\alpha(pro\text{-}S)}$ = 4.5 Hz, show that **7** and **8** also exist predominantly in an extended zigzag conformation from C.2′ to C.5.

The analysis of steric interactions adequately accounts for the conformational behavior of the 1,6-anhydro-*C*-disaccharides. Our attention therefore turned to the methyl *C*-disaccharides **3**–**6**. In the absence of the 1,6-anhydro bridge, the right-side pyranose ring exists in the alternative chair conformation. This substantially alters the pattern of steric interactions across the interannular bridge.

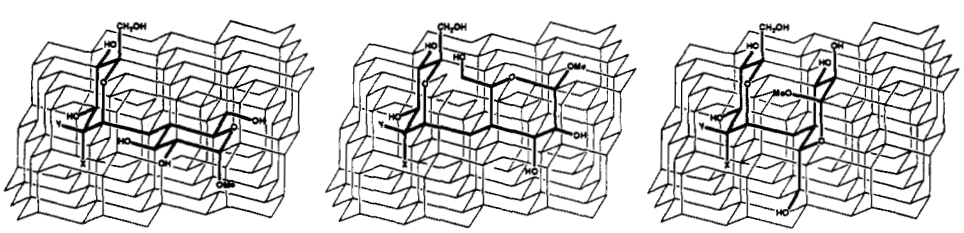
The vicinal coupling constants between C.α and C.4 measured from the ^{1}H NMR spectrum of *C*-maltoside **3** show that the C-aglyconic bond does not adopt an ideal extended conformation. The three staggered conformers around the C-aglyconic bond, **3-A**, **3-B**, and **3-C**, are considered in Figure 4. Conformer **3-C** suffers from steric



3: X=OH, Y=H
4: X=H, Y=OH



Coupling Constant Diagram for 3 (4)



3,4-A 3,4-B 3,4-C

Figure 4.

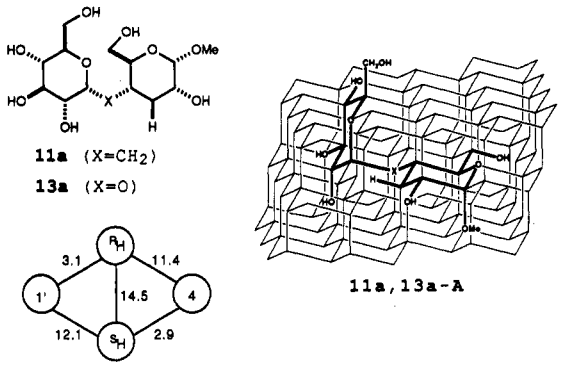


Figure 5.

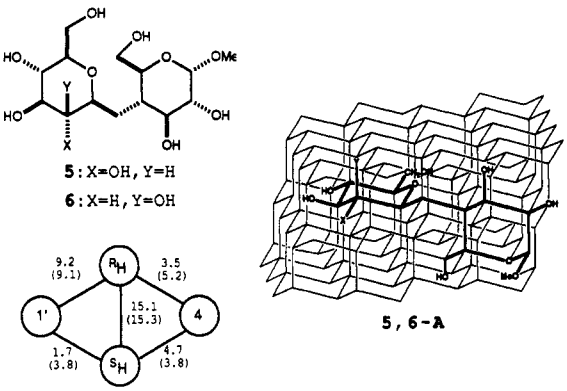


Figure 6.

congestion because the C.1′–C.α bond is gauche to both the C.3 and C.5 pyranose carbons. Conformer **3-B** has two 1,3-diaxial-like interactions (C.5–C.6/C.1′–C.α and C.1′–O.5′/C.4–C.5). Conformer **3-A** has one 1,3-diaxial-like interaction between the C.3–O.3 and C.1′–C.α bonds. None of the three conformers is free of unfavorable steric interactions, although conformer **3-A** seems to be the least destabilized.

This analysis is reflected nicely in the experimental vicinal coupling constants in the ^{1}H NMR spectrum of **3**, i.e., $J_{C4,\alpha(pro\text{-}R)}$ = 5.5 Hz; $J_{C4,\alpha(pro\text{-}S)}$ = 2.9 Hz. These data suggest that the preferred conformation of the C-aglyconic bond is a mixture of conformers or one conformer deviating slightly from the ideal staggered conformation **3-A**.[9]

This analysis suggests an experiment to establish the importance of 1,3-diaxial-like interactions directly. Altering the 1,3-diaxial-like interactions in the molecule would be expected to substantially affect its conformational behavior. For example, examining the three ideal staggered conformers of **3** on a diamond lattice, removal of the C.3 hydroxyl group, or inversion of its configuration should eliminate the only destabilizing 1,3-diaxial-like steric interaction in conformer **3-A**. This conformer is consequently expected to become dominant. To test this hypothesis, we have synthesized methyl 3-deoxy-*C*-maltoside (**11a**).[4] The vicinal coupling constants around

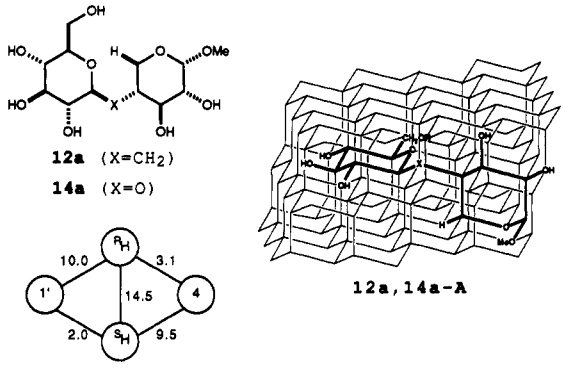


Figure 7.

Table III. Vicinal Coupling Constants across the C.4–C.α–C.1′ Bridge of the Protected Forms[a] of Compounds 3–12 in $CDCl_3$

$^3J_{CH}$ (Hz)	3b	4b	5b	6b	7b	8b	9b	10b	11b	12b
$J(1',\alpha_R)$	2.9	*b*	9.2	9.9	2.5	3.0	9.8	10.5	3.1	10.3
$J(1',\alpha_S)$	10.8	*b*	3.5	2.7	10.7	11.1	2.3	3.8	12.1	3.5
$J(4,\alpha_R)$	7.1	*b*	*b*	3.6	7.8	9.2	5.6	4.9	11.5	1.0
$J(4,\alpha_S)$	2.3	*b*	*b*	4.1	5.4	5.0	8.9	10.5	2.7	8.9

[a] **3b, 4b, 5b, 6b**: peracetyl-*C*-disaccharide; **7b, 8b, 9b**: 1,6-anhydro-2,3,3′,4′-tetra-*O*-benzyl-6′-*O*-benzoyl-*C*-disaccharide; **10b**: 1,6-anhydro-2,3,3′,4′-tetra-*O*-benzyl-6′-*O*-acetyl-*C*-disaccharide; **11b, 12b**: perbenzyl-*C*-disaccharide. [b] These values are not available due to higher order effects in the ^{1}H NMR spectra.

the C-aglyconic bond show its conformational behavior to be exactly as predicted, $J_{C4,\alpha(pro\text{-}S)}$ = 2.9 Hz; $J_{C4,\alpha(pro\text{-}R)}$ = 11.4 Hz (Figure 5).

The conformational analysis of the cellobiose *C*-disaccharides **5** and **6** can be performed in the same manner. None of the conformers is free of unfavorable interactions, although conformer **5,6-A** is least destabilized, having only one 1,3-diaxial-like interaction between C.5–C.6 and C.1′–C.α (Figure 6). The ^{1}H NMR data again provide experimental support for this analysis. The vicinal coupling constants, **5**, $J_{C4,\alpha(pro\text{-}R)}$ = 3.5 Hz; $J_{C4,\alpha(pro\text{-}S)}$ = 4.7 Hz; **6**, $J_{C4,\alpha(pro\text{-}R)}$ = 5.2 Hz; $J_{C4,\alpha(pro\text{-}S)}$ = 3.8 Hz, indicate that the C-aglyconic bond does not exist in any of the ideal extended conformations, but exists either as a mixture of conformers or as a single conformer deviating from the least destabilized conformer. In addition, the structural modification indicated by the diamond lattice analysis works nicely. Removal of the C.5–hydroxymethyl moiety or inversion of the stereochemistry at C.5 should eliminate the destabilization in conformer **5-A**. Compound **12a**,[4] the 5-deshydroxymethyl analogue of **5**, is thus expected to exist predominantly in conformer **12a–A** (Figure 7). Indeed, the ^{1}H NMR data of **12a** confirm this hypothesis: $J_{C1',\alpha(pro\text{-}R)}$ = 10.0 Hz; $J_{C1',\alpha(pro\text{-}S)}$ = 2.0 Hz; $J_{C4,\alpha(pro\text{-}R)}$ = 3.1 Hz; $J_{C4,\alpha(pro\text{-}S)}$ = 9.5 Hz.

In conclusion, the conformational behavior of carbon disaccharides can be analyzed and predicted based principally on steric interactions. The conformational preference of the C-glycosidic bond is so overwhelming that primarily the C-aglyconic bond deviates from the extended conformation to avoid 1,3-diaxial-like interactions. The importance of 1,3-diaxial-like interactions in controlling the conformation around the C-aglyconic bond has been demonstrated experimentally. In addition, as was shown in the case of the carbon monoglycosides and the 1,6-linked disaccharides, the vicinal coupling constants observed for the protected disaccharides in $CDCl_3$ are similar to those observed for the polyols in CD_3OD (Table III). Hydrogen

(9) A small temperature effect on the vicinal coupling constants in the ^{1}H NMR spectrum was observed. For instance, $J_{4,\alpha(pro\text{-}R)}$ and $J_{4,\alpha(pro\text{-}S)}$ for compound **4** were 3.7 and 4.7 Hz at 40 °C, 3.5 and 4.7 Hz at 25 °C, 3.1 and 4.9 Hz at 0 °C, 2.9 and 5.1 Hz at −20 °C, and 2.8 and 5.2 Hz at −40 °C. Although the temperature effects are too small to distinguish unambiguously between a mixture of staggered conformers and a single distorted conformation, temperature studies on the carbon monoglycosides[1a] point to a mixture of conformers.

bonding and electrostatic interactions do not seem to play a major role in the overall conformational behavior of these substrates.

Comparison of the Conformational Behavior of *C*- and *O*-Disaccharides. The major features of the glycosidic conformation of natural *O*-glycosides are duplicated by the carbon analogues. If the overall conformational behavior of the two classes of compounds is similar, two important ramifications emerge. First, the specific conformation of an oligosaccharide can be estimated from the experimentally determined conformation of its carbon analogue. Second, the conformational analysis of natural oligosaccharides can be performed based on the principles developed for the carbon disaccharides. The conformational similarity of the carbon and oxygen linked disaccharides must therefore be demonstrated experimentally. A reliable comparative experimental method is required.

Many experimental techniques have been applied to the conformational study of carbohydrates. These include X-ray crystallography,[10] circular dichroism (CD),[11] optical rotation,[12] and NMR techniques.[13-15] The presence of macromolecular hydrogen bond lattices makes the application of X-ray crystallography to solution conformation studies ambiguous.[16] Some solution conformational studies using CD and optical rotation have been published. However, these methods are used infrequently because of difficulties in data interpretation. NMR spectroscopic methods have been widely employed. Among them, nuclear Overhauser effect (NOE),[13,15] spin-lattice relaxation time (T_1),[13] and heteronuclear three-bond coupling ($J_{^{13}C-^1H}$)[14] methods are the most common.

It is often difficult to translate NOE and T_1 data into unambiguous relative distances.[17] However, if the carbon- and oxygen-linked disaccharides adopt similar conformations, a proton in one series should have a similar spin-spin interaction and dipole environment to that of the corresponding proton in the other series. NOE and T_1 measurements should therefore be in relatively good agreement. A comparison of NOE and T_1 data between the *C*-glycosides and the corresponding *O*-glycosides will thus establish unambiguously the extent of conformational similarity between these two systems.

Table IV. Nuclear Overhauser Effect (NOE) Data at Room Temperature of 11a,b, 11a,b-d_2, and 13a,b

	enhancement[a] (%)		
	1′,3(eq)[b]	1′,4	3(eq).1′
13a	6.9	7.2	8.7
11a	5.1	0.0	6.1
11a-d_2	5.2	3.1	9.1
13b	4.6	5.3	8.0
11b	3.2	0.0	5.1
11b-d_2	5.1	5.1	6.3

[a] NOE experiments were performed in CD_3OD for **13a**, **11a**, and **11a-d_2** and in CD_3Cl for **13b**, **11b**, and **11b-d_2**. [b] This notation indicates the NOE enhancement of H-3 (equatorial) observed on irradiation of H-1′.

Table V. Proton Spin-Lattice Relaxation Time (T_1, s) at Room Temperature for 11a,b, 11a,b-d_2, and 13a,b[a,b]

	H-C1′	H-C3	H-C4
13a	0.94	0.36	0.79
11a	0.72	0.36	0.36[c]
11a-d_2	0.71	0.37	0.81
13d	0.65	0.29	*d*
11b	0.50	0.25	0.50
11b-d_2	0.65	0.29	0.65

[a] T_1 measurements were performed in CD_3OD for **13a**, **11a**, and **11a-d_2** and CD_3Cl for **13b**, **11b**, and **11b-d_2**. [b] T_1 values were obtained from a plot for all compounds except **11a-d_2**, for which a curve-fitting method was employed. [c] H-4 and H-α overlap. The T_1 value for H-4 might not be exact but is larger than 0.36. [d] H-4, H-3′, and H-5′ overlap.

There are obvious differences between the two series. For example, the C–C and C–O bond lengths, angles, and polarities are different.[18] More importantly, the *C*-disaccharides have two protons at C.α which are not present in the parent *O*-glycosides and can participate via relaxation in the NOE and T_1 experiments. The effect of the additional protons is expected to be substantial and must be addressed in order for the comparison to be meaningful.

A set of *C*-disaccharides, **11a,b** and **12a,b** and their parent *O*-disaccharides, **13a,b** and **14a,b**, were chosen for comparison, where the **a** series corresponds to the polyols and the **b** series corresponds to their perbenzyl ethers. These compounds were selected because the carbon cases have been shown to exist in one dominant conformation in the ground state, i.e., **11a-A** and **12a-A**.

In the preferred conformation of methyl 3-deoxy-*C*-maltosides **11a,b**, the proton at C.1′ is in close proximity to the equatorial proton at C.3 (Figure 5). Therefore, a relatively large NOE is expected between H.3 (equatorial) and H.1′. Similar enhancements are anticipated in the oxygen counterpart. The T_1 values of these two series should also display a certain degree of similarity. As expected, upon irradiation of H.1′ of methyl 3-deoxy-*O*-maltoside **13a**, a 6.9% enhancement of H.3 (equatorial) was observed (Table IV). In the opposite direction, irradiation of H.3 (equatorial) showed an 8.7% enhancement of H.1′. The corresponding experiments with methyl 3-deoxy-*C*-maltoside **11a** gave a 5.1% enhancement of H.3

(10) For X-ray structures of cellobiose and maltose see: (a) Fries, D. C.; Rao, S. T.; Sundaralingam, M. *Acta Crystallogr. B* **1971**, *27*, 994. (b) Quigley, G. J.; Sarko, A.; Marchessault, R. H. *J. Am. Chem. Soc.* **1970**, *92*, 5834. (c) Ham, J. T.; Williams, D. G. *Acta. Crystallogr. B* **1970**, *26*, 1373. (d) Chu, S. S. C.; Jeffrey, J. *Acta. Crystallogr. B* **1968**, *24*, 830. (e) Chu, S. S. C.; Jeffrey, J. *Acta. Crystallogr.* **1967**, *23*, 1038. (f) Brown, C. J. *J. Chem. Soc. Inorg. Phys. Theor. A* **1966**, 927. (g) Jocobson, R. A.; Wunderlich, J. A.; Lipscomb, W. N. *Acta. Crystallogr.* **1961**, *14*, 598. (h) Jocobson, R. A.; Wunderlich, J. A.; Lipscomb, W. N. *Nature (London)* **1959**, *184*, 1719.

(11) Wiesler, W. T.; Nakanishi, K. *J. Am. Chem. Soc.* **1989**, *111*, 3446 and references cited therein.

(12) Stevens, E. S.; Sathyanarayana, B. K. *J. Am. Chem. Soc.* **1989**, *111*, 4150 and references cited therein.

(13) For reviews of NMR in the study of carbohydrate conformation see: (a) Carver, J. P.; Brisson, J.-R. The Three-Dimensional Structure of N-Linked Oligosaccharides. In *Biology of Carbohydrates*; Ginsburg, V., Robbins, P. W., Eds.; Wiley: New York, 1984; Vol. II. (b) Kotowycz, G.; Lemieux, R. U. *Chem. Rev.* **1973**, *73*, 699.

(14) (a) Lemieux, R. U.; Nagabhushan, T. L.; Paul, B. *Can. J. Chem.* **1972**, *50*, 773. (b) Schwarcz, J. A.; Perlin, A. S. *Can. J. Chem.* **1972**, *50*, 3667. (c) Gagnaire, D. Y.; Nardin, R.; Taravel, F. R.; Vignon, M. R. *Nouv. J. Chim.* **1977**, *1*, 423. (d) Hamer, G. K.; Balza, F.; Cyr, N.; Perlin, A. S. *Can. J. Chem.* **1978**, *56*, 3109. (e) For a review of ^{13}C NMR in the study of carbohydrate conformation see: Gorin, P. J. *Adv. Carbohydr. Chem. Biochem.* **1981**, *38*, 13 and references cited therein.

(15) Schirmer, R. E.; Noggle, J. H.; Davis, J. P.; Hart, P. A. *J. Am. Chem. Soc.* **1970**, *92*, 3266. For 2D NOE see: (a) Bax, A.; Davis, D. G. *J. Magnet. Res.* **1985**, *63*, 207. (b) Jansson, P.-E.; Kenne, L.; Wehler, T. *Carbohydr. Res.* **1987**, *166*, 271.

(16) In many cases, differences in the hydrogen bonding network were observed in different crystal structures. For an example, see refs 11a and 11f.

(17) Schirmer, R. E.; Noggle, J. H.; Davis, J. P.; Hart, P. A. *J. Am. Chem. Soc.* **1970**, *92*, 3266. Lemieux, R. U. in ref 3: "It is to be noted, first of all, that the magnitude of a given NOE can be importantly influenced by the experimental conditions and on its own provides little information as to conformational preference. Also the magnitude of the enhancement is weighted by an inverse sixth power distance relationship and it is possible that an enhancement was provided by conformers that do not dominate the equilibrium".

(18) Concerning the bond length at the glycosidic linkage, see: Jones, P. G.; Kirby, A. J. *J. Am. Chem. Soc.* **1984**, *106*, 6207 and references cited therein.

Table VI. Nuclear Overhauser Effect (NOE) Data at Room Temperature of 12a,b, 12a,b-d_2, and 14a,b

	enhancement[a] (%)					
	1',5	1',4	5(eq),1'	4,1'	4,2'	2',4
14a	4.8	12.1[b]	11.7[c]	*d*	*d*	3.4[b]
12a	5.1	4.3	4.8	1.9	1.6	*d*
12a-d_2	5.7	5.9	5.9	3.4	3.8	4.8
14b	NOE[e]	5.2	*d*	5.3	*d*	*d*
12b	*d*	*d*	4.6[f]	4.2[f]	*d*	*d*
12b-d_2	*d*	*d*	2.9[f]	2.3[f]	*d*	*d*

[a] NOE experiments were performed in CD_3OD for **14a**, **12a**, and **12a-d_2**, in CD_3Cl for **14b**, and in C_6D_6 for **12b** and **12b-d_2**. [b] H-3, H-4, and H-6' overlap. [c] Partial irradiation of H-4 may contribute to the magnitude of the observed NOE. [d] These data are not available. [e] H-5(eq), H-3', H-4', H-6'a, and H-6'b overlap. A 5.4% enhancement within this multiplet was observed and was assigned to H-3' and H-5(eq). NOE enhancement of H-4', H-6'a, and H-6'b could not be excluded. [f] H-1', H-2', H-5', and H-OMe overlap. NOE enhancement of H-2', H-5', and H-OMe could not be excluded.

and a 6.1% enhancement of H.1'. The NOE enhancements between H.1' and H.3 show reasonable correlation between the carbon and oxygen series.

However, a 7.2% enhancement at H.4 of methyl 3-deoxy-*O*-maltoside **13a** was also observed when H.1' was irradiated. No corresponding enhancement was observed in experiments in the carbon series. In addition, the T_1 values (Table V) of H.1' and H.4 are 0.94 and 0.79 s, respectively, in **13a**. The T_1 values in **11a** are 0.72 s for H.1' and 0.36 s for H.4. These differences are consistent with the anticipated effect of the two protons at C.α in **11a,b** which provide additional channels for spin–spin interactions and relaxations at H.1' and H.4.

In order to compare the NOE and T_1 data directly, it is necessary to have the same arrangement of protons in the two series. This can best be achieved by replacing the two C.α protons with deuterium. The dideuterated compounds **11a,b-d_2** were therefore prepared.[19] Indeed, the T_1 values of H.4 increased from 0.36 s for **11a** to 0.81 s for **11a-d_2** (Table V). Upon irradiation H.1' of **11a-d_2**, a 3.1% enhancement of H.4 was observed, while none had been detected in **11a**. The NOE enhancement of H.1' on irradiation of H.3 (equatorial) of **11a-d_2** increased to 9.1%, compared to 6.1% with **11a**. The NOE and T_1 data (Tables IV and V) for **11a,b-d_2** are in far better agreement with those of the oxygen counterparts **13a,b**. Some differences are expected to remain due to the shorter C–O bond in **13a–b**. Indeed, observed NOE enhancements across the interannular linkage are consistently larger in the oxygen cases. The direct comparison of the NOE and T_1 data for the oxygen-linked disaccharides **13a,b** and the carbon-linked disaccharide **11a,b-d_2** having the same arrangement of protons therefore shows that there can be only minor differences between the conformational behavior of the carbon- and oxygen-linked disaccharides.

The same trends were observed in the NOE and T_1 data of the perbenzyl compounds **11b**, **11b-d_2** and **13b**. The NOE and T_1 data for the perbenzylated oxygen linked disaccharide **13b** is in excellent agreement with that of the bisdeuterated perbenzyl carbon disaccharide **11b-d_2**. The conformation of polyol **11a** and the perbenzyl **11b** have been shown to be identical by the vicinal coupling constants in the ^1H NMR spectra. A comparison of the NOE and T_1 data between **11b-d_2** and **13b**, and between the polyol **13a** and the perbenzyl **13b**, shows that the conformational similarity between the polyol and its protected form also holds for the oxygen-linked disaccharides. The conclusion that hydrogen bonding and electrostatic interactions do not play a major role in defining the overall conformational behavior of the glycosides can therefore be extended to a first approximation to the oxygen cases as well.

In the preferred conformation of methyl 5-(deshydroxymethyl)-*C*-cellobiosides **12a,b** (Figure 7), the proton at C.1' is in close proximity to the proton (equatorial) at C.5. On irradiation of H.1' of methyl 5-(deshydroxymethyl)-*O*-cellobiose **14a**, 4.8% enhancement of H.5 (equatorial) was observed along with a 12% enhancement of H.4 (Table VI). Upon irradiation of H.5 (equatorial), an 11.7% enhancement[20] of H.1' was observed. In the corresponding carbon series **12a-d_2**, 5.7% and 5.9% enhancements of H.5 (equatorial) and H.4 were observed when H.1' was irradiated. A 5.9% enhancement of H.1' was obtained when H.5 (equatorial) was irradiated. The T_1 values of H.1' and H.4 increased to 0.87 and 1.01 s, respectively, in the deuterated compound **12a-d_2** relative to the nondeuterated

Table VII. Proton Spin–Lattice Relaxation Time (T_1, s) at Room Temperature for 12a,b, 12a,b-d_2, and 14a,b[a,b]

	H-1'	H-4	H-5(eq)
14a	0.79	0.79	0.50
12a	0.58	0.58	0.36
12a-d_2	0.87	1.01	0.43
14b	0.58	0.72	*c*
12b	0.65	0.58	0.36
12b-d_2	0.89	1.0	0.38

[a] T_1 measurements were performed in CD_3OD for **14a**, **12a**, and **12a-d_2**, in CD_3Cl for **14b**, and in C_6D_6 for **12b** and **12b-d_2**. [b] T_1 values were obtained from a plot for all compounds except **12a-d_2**, for which a curve-fitting method was employed. [c] H-5(eq), H-3, H-4', H-6a', and H-6b' overlap.

Table VIII. Nuclear Overhauser Effect (NOE) Data for 15a,b and 19a,b

	enhancement[a] (%)		
	1',3[b]	1',4	4,1'
19a	4.0	3.5	4.8
15a	1.7	3.2	5.5
19b	5.7	2.9	3.1
15b	1.2	2.5	2.7

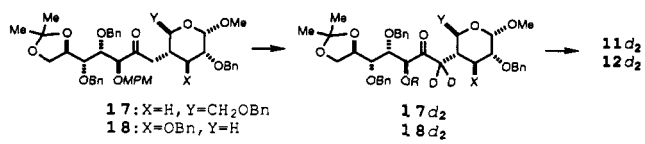
[a] NOE experiments were performed in D_2O containing 13% pyridine for **19a** and **15a** and in C_6D_6 for **19b** and **15b**. [b] This notation indicates that an NOE enhancement of H-3 was observed on irradiation of H-1'.

Table IX. Proton Spin–Lattice Relaxation Time (T_1, s) for 15a,b and 19a,b

	T_1[a] (s)		
	H.1'	H.3	H.4
19a	0.79	0.79	0.69
15a	0.58	0.50	0.54
19b	0.69	0.65	0.54
15b	0.43	0.58	0.45

[a] Experiments were performed in D_2O containing 13% pyridine for **19a** and **15a** and in C_6D_6 for **19b** and **15b**.

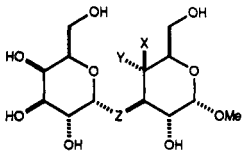
(19) Deuterium incorporation was performed by treatment of **17** and **18** with potassium carbonate in methanol-d_4. Compounds **17-d_2** and **18-d_2** were converted into the dideuterated *C*-disaccharides **11-d_2** and **12-d_2** by the same procedures as the parent compounds (ref 4).



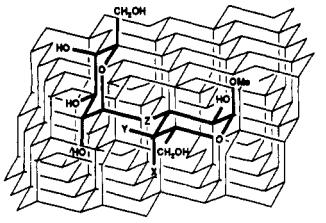
17: X=H, Y=CH_2OBn
18: X=OBn, Y=H

17-d_2
18-d_2

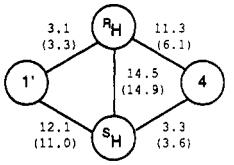
(20) The large enhancement of H.1' (11.7%) may be due to partial irradiation of H.4.



15: X=OH, Y=H, Z=CH_2
16: X=H, Y=OH, Z=CH_2
19: X=OH, Y=H, Z=O



15,16,19-A



Coupling Constant Diagram for 15 (16)

Figure 8.

compound and are in good agreement with the oxygen case **14a** (Table VII). Again, the fact that NOE's of the same magnitude are observed for the two series indicates that the conformation of methyl 5-(deshydroxymethyl)-*O*-cellobioside **14** is similar to that of the corresponding *C*-glycoside **12**.

In all experiments, substantial NOE enhancements of H.4 were observed upon irradiation of H.1′ which were not readily predicted on the basis of the known conformational behavior of these compounds. As was pointed out earlier, the translation of NOE data into relative distance is not straightforward.[17] A significant advantage of our study is that spectroscopic measurements can be compared directly, without interpreting the meaning of the NOE and T_1 data or comparing a translation of the NOE measurements to a postulated conformational behavior. Regardless of the possible interpretations of the NOE and T_1 data, the conformational similarity of *C*-glycosides and their oxygen counterparts is established unambiguously by the comparison of the experimental NOE and T_1 data.

Conclusions

The conformational preference of the carbon analogues of 1,4-linked disaccharides has been determined experimentally using vicinal coupling constants. It has been shown that the conformation can be predicted solely on the basis of (a) the preference of the *C*-glycosidic bond for the "exo-anomeric" conformation and (b) the consideration of 1,3-diaxial-like interactions as revealed by diamond lattice analysis. Experimental support for the importance of 1,3-diaxial-like interactions on the conformation around the C-aglyconic bond has been presented by demonstrating that altering the 1,3-diaxial-like interactions has a significant and predictable effect on the conformational behavior of these compounds.

Direct comparison of the experimental NOE and T_1 data of the carbon disaccharides with those of the parent O-linked disaccharides demonstrates that the conformational behavior of the two classes of compounds are very similar. The conformational analysis of carbon disaccharides is therefore directly applicable to natural oligosaccharides. Carbon glycosides provide effective experimental models for the conformational study of carbohydrates.

This conformational analysis is also applicable to systems with other linkages. The $\alpha(1,3)$-linked carbon disaccharides **15** and **16** have been prepared by adapting the routes developed for the 1,4-linked cases. Diamond lattice analysis predicts that compound **15** will adopt predominantly conformer **15,16-A**, which is free of 1,3-diaxial-like interactions. Changing the stereochemistry at C.4 as in **16** will introduce a 1,3-diaxial interaction, and this compound is expected to exist either as a conformer deviating from **15,16-A** or as a mixture of conformers. These predictions were borne out by the experimental coupling constants (Figure 8). Again, distortion occurs around the C-aglyconic bond in preference to the C-glycosidic bond. In addition, the NOE data for compound **15** show a reasonable correlation to the parent oxygen compound **19**.[21] The application of this analysis to carbon trisaccharides will be discussed in a subsequent publication.

Experimental Section

NOE Experiments. All experiments were carried out on a Bruker AM 500-MHz instrument using the program NOEDIFF.AUR with D1 = 3 s, D2 = 3 s, D3 = 0.1 s, NE = 16 or 32, decoupler power = 40–50 L, NS = 4, and PW = 13.8 ($\pi/2$). CD_3OD was used for all polyols, and $CDCl_3$ was used for all perbenzyl compounds. All samples were degassed by argon sparge. The concentration of the samples was ca. 0.01 M. The measurement of the C and O series were performed on the same instrument in direct succession.

All T_1 measurements were carried out on a Bruker AM 500 MHz instrument using the program INVREC.AUR.

The *O*-disaccharides **13**, **14**, and **19** were synthesized using the Schmidt imidate glycosidation method (Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212). Spectroscopic data and copies of ^1H NMR spectra for these compounds are included in the supplementary material.

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Supplementary Material Available: Spectroscopic data for the oxygen disaccharides **13**, **14**, and **19** and the NOE measurement spectra (47 pages). This material is contained in many 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.

(21) Nuclear Overhauser effect (NOE) data at room temperature for **15a,b** and **19a,b** are given in Table VIII.