plastic crystal nature of adamantane should introduce motion to give a narrowed peak. The doubly labeled cyclopolymer gives a single peak with a line width of 176 Hz.

The nutation experiment has been shown to determine bond lengths to an accuracy of ~1% for directly bonded ^{13}C nuclei. For this particular project, the question was not to determine bond lengths, but to find whether any directly bonded labeled positions existed. From rough estimates determined by spectral addition, the limit of detection appears to be at a directly bonded spin-pair concentration of less than 5% of the total ^{13}C concentration. Thus, few or no adjacent ^{13}C labels exist confirming predominant formation of the six-membered ring repeat unit during cyclopolymerization under the conditions used here.

Summary

Nutation NMR was used to confirm the structure of a ^{13}C doubly labeled cyclopolymer. A labeling experiment used to give information regarding the reaction mechanism for α-hydroxymethylacrylate formation and dimerization also provided a serendipitous synthesis of the labeled cyclopolymer.[4] The cyclopolymer was shown to be composed of primarily six-membered rings through the absence of spin-pair coupling. These results confirm the potential of the nutation NMR experiment for mechanism and structure elucidation in characterization of suitably labeled materials.

Acknowledgment. This research was supported in part by the Petroleum Research Foundation, administered by the American Chemical Society, and the Division of Materials Research of the National Science Foundation through Grant DMR-8620138. We also gratefully acknowledge the Department of Defense instrumentation grant through the Office of Naval Research, which was used to purchase the Bruker MSL-200 NMR spectrometer.

Registry No. $H_2C{=}CO_2CH_3$, 96-33-3; $^{13}CH_2O$, 3228-27-1; $H_2C{=}C(CO_2CH_3)^{13}CH_2OH$, 131237-17-7; $H_2{}^{13}C{=}C(CO_2CH_3)CH_2O^{13}CH_2C(CO_2CH_3){=}CH_2$, 131237-18-8; $H_2{}^{13}C{=}C(CO_2CH_3)CH_2O^{13}CH_2C(CO_2CH_3){=}CH_2$ (homopolymer), 131237-30-4; $H_2C{=}C(CO_2CH_3)CH_2OCH_2C(CO_2CH_3){=}CH_2$ (homopolymer), 109669-57-0.

Solvent Effect on the Anomeric Equilibrium in D-Glucose: A Free Energy Simulation Analysis

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Abstract: The equilibrium between the α and β anomers of D-glucopyranose in aqueous solution has been investigated by free energy simulations that permit a separation of the intramolecular and intermolecular contributions to the free energy difference. The simulations correctly predict that the free energy difference between the two forms in aqueous solution is small; the calculated free energy difference, $\Delta G(\beta \rightarrow \alpha)$, is -0.31 ± 0.43 kcal/mol, in comparison with the experimental value of 0.33 kcal/mol. The calculated free energy difference is the result of near cancelation of two larger, statistically significant contributions, i.e., an intramolecular electrostatic term favoring the α anomer and an intermolecular solute–solvent interaction term favoring the β anomer. This result supports the conjecture that solvation stabilizes the β anomer in water. There is a large difference in the intramolecular contribution to the anomeric equilibrium calculated in solution from the free energy simulation and the gas-phase minimum; this suggests that conformational averaging, modulated by the solvent, is significant even for the internal terms. An examination of the rotamer distribution in the hydroxymethyl side chain shows that the trans, gauche conformer is strongly disfavored in aqueous solution, in accord with experiment.

Introduction

The origin of the anomeric equilibrium between the α (axial) and β (equatorial) cyclic forms of simple sugars, such as glucose, is one of the most widely studied questions in carbohydrate chemistry.[1] The equilibrium concentrations for the various tautomers in aqueous solution have been measured, and empirical "stability factor" rules have been developed to rationalize these equilibria.[2] For D-glucose in aqueous solution at 293 K, the anomer distribution is 36% α-D-glucopyranose:64% β-D-glucopyranose, as measured by optical rotation and NMR experiments; only negligible amounts of the linear and furanoid tautomers are present under these conditions. The relative contributions of the gas-phase intramolecular potential and solvation effects to the observed α and β equilibrium distribution remain unclear.[3]

It has long been assumed that the anomeric equilibrium is related to other aspects of the anomeric effect.[4,5] This term refers to the observation that, for *substituted* sugars (such as the methyl pyranosides), the α anomer is more stable than the β anomer and that there are characteristic structural features that are configuration-dependent. For example, both C–O bond lengths involving the anomeric carbon atom C1 (see Figure 1) are shortened relative to more typical C–O bond lengths, with the C1–O1 bond longer than the C1–O5 bond for the preferred α anomer;[6] corresponding results are observed for the bond angles. In the most commonly accepted explanation, the anomeric effect is assumed to result from a back-donation of electrons from the lone-pair orbitals of the oxygen atom to the antibonding σ* orbital of the adjacent C–O bond, with this overlap being more pronounced for α configurations. Although some doubts have been expressed about this explanation,[7] it is generally consistent with the results of quantum

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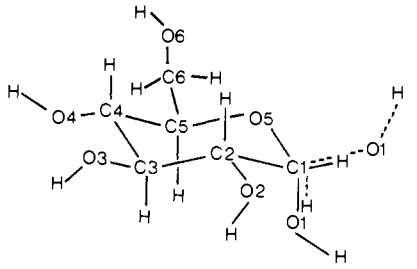

Figure 1. α-D-Glucopyranose in the $^4C_1$ conformation. The dashed bonds and associated atoms indicate the positions of the C1 ligands in the β anomer. In the MD simulations reported here, both α and β ligands at C1 were simultaneously present at both positions, with their energies scaled by either λ or 1 − λ as appropriate (see text).

mechanical studies of model systems.[8-10] A good general review of the anomeric effect is given by Tvaroška and Bleha.[10]

In the highest level ab initio studies of the anomeric effect published to date, Wiberg and Murcko[9] found an energy difference of 3.3 kcal/mol between the two conformers (+sc, +sc and +sc, 180°) of dimethoxymethane (DMM) that correspond to the spatial arrangements of the two anomers of a pyranoid carbohydrate.[8] By subtracting from this number the corresponding energy difference between the same conformations of the corresponding nonanomeric homologue (methyl propyl ether) in which one of the oxygen atoms is replaced by a carbon, they obtained an "anomeric stabilization" energy of the axial form of 4.7–5.4 kcal/mol. In the more realistic model compound 2-methoxytetrahydropyran, the anomeric preference for the axial form was approximately 2.1 kcal/mol. For methyl D-glucopyranoside, the experimentally measured anomeric ratio in aqueous solution is 67% in favor of the α anomer, corresponding to a free energy difference of 0.42 kcal/mol. Although the internal (gas-phase) contribution to the anomeric ratio is uncertain, these results indicate that the equatorial anomer is significantly favored by water, perhaps due to the hydrogen-bonding capacity of the anomeric group, as suggested by Praly and Lemieux.[11]

While the anomeric effect is readily apparent in substituted sugars, it is much less evident for *unsubstituted* sugars. Careful analysis of crystal data for the bond lengths of simple sugars[6] reveals that the structural signatures of the anomeric effect in carbohydrates are not found in these molecules, even though they are present in semiempirical calculations;[10] in the case of the O–C–O angle, there is a slight indication of an anomeric effect. Further, the anomeric preference for the α form is not always observed in aqueous solution; e.g., while D-mannose prefers the α configuration [$\Delta G(\alpha \rightarrow \beta)$ = 0.42 kcal/mol at 20 °C], D-glucose and D-galactose both prefer the β form [$\Delta G(\alpha \rightarrow \beta)$ = −0.33 kcal/mol for D-glucose and −0.40 kcal/mol for D-galactose, both at 20 °C].[1,2,10] Consequently, it has been suggested that the anomeric equilibrium in the simple sugars is determined primarily by interactions with the solvent;[3,12] i.e., there is a difference in the interactions of water molecules with the anomeric hydroxyl group in the two possible orientations. Most likely, both intramolecular and intermolecular factors contribute to the anomeric ratio in solution. It is possible, for example, that the intramolecular stabilization of the α form, whatever the explanation for its origin, might well be present in these systems, as suggested by the calculations for pyranoside analogues. If so, there would have to be a larger solvent shift stabilizing the β anomer of D-glucose in water.

In this paper, we use a molecular mechanics potential and the free energy simulation method[13-15] to determine the solvent contribution to the anomeric ratio for D-glucose in aqueous solution. The simplicity of this system and the fact that the calculated equilibrium is directly comparable with the measured value (in contrast to other studies where thermodynamic cycles involving nonphysical changes must be introduced[16,17]) make this an ideal case for study. Because the free energy difference is very small (0.33 kcal/mol for $\beta \rightarrow \alpha$), the use of the thermodynamic integration method[18,19] to separate the sizable intramolecular and intermolecular contributions plays an essential role in the analysis. It permits us to conclude that solvation is a dominant factor favoring the β anomer of D-glucose in aqueous solution.

Method

By use of free energy simulation methods,[13,19] the free energy difference (ΔG) between some reference state (0) and a modified state (1) described by the potential energy functions V_0 and V_1, respectively, can be calculated from the relation[20]

$$\Delta G = -kT \ln \langle \exp[-\beta(V_1 - V_0)] \rangle_0 \qquad (1)$$

where $\beta = 1/kT$ and the ensemble average, indicated by the angle brackets, is carried out over the reference state (0). Molecular dynamics (MD) or Monte Carlo simulations can be used to evaluate this ensemble average. For this average to converge rapidly, the difference between the initial and final states used in eq 1 must be such that portions of the configuration space sampled by the two states overlap significantly. Since this condition may not be met for the transformation from α- to β-D-glucopyranose (that is, the solvent distribution surrounding α-D-glucopyranoside is a poor description of that surrounding the β form, and vice versa), a series of simulations with V_1 and V_0 replaced by intermediate values $V_{\lambda_{i+1}}$, V_{λ_i}, where

$$V_\lambda = \lambda V_0 + (1 - \lambda) V_1 \qquad 0 \le \lambda \le 1 \qquad (2)$$

must be performed to obtain adequate convergence. In this way, solvent and internal readjustments occur gradually and allow one to convert one system into another along a reversible path. Alternatively, it is possible to use thermodynamic integration[18,19,21] to obtain the free energy difference from the equation

$$\Delta G = G(1) - G(0) = \int_0^1 \langle V_1 - V_0 \rangle_\lambda \, d\lambda \cong \sum_i \langle \Delta V \rangle_{\lambda_i} \Delta\lambda_i \qquad (3)$$

Here, $\langle V_1 - V_0 \rangle_{\lambda_i}$ is obtained from a simulation with V_{λ_i} and $\Delta\lambda_i = \lambda_{i+1} - \lambda_i$. Both eqs 1 and 3 are exact, in principle, although only approximate results are obtained from simulations. It is not known which expression converges more rapidly though both have been used successfully.[19,22] Equation 3 has the advantage that it is a linear expression so that an additive decomposition of the calculated results into solvation and intramolecular contributions is possible.[19]

Since the free energy is a state function, there is no requirement that the actual path followed between the two forms 0 and 1 be a physical one; any convenient path can be used. The free energy difference being studied here is that between the α and β anomers of glucose. These two stereoisomers differ only in the configuration about the C1 carbon atom (see Figure 1); in the α anomer, the hydroxyl group is axial relative to the mean plane of the pyranoid ring, with the aliphatic hydrogen equatorial, and in the β anomer the positions of these two groups are reversed. Thus, the structural changes involved in the fictional "mutation" of α-D-glucopyranose into the β form are quite small (smaller, in fact, than

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many that have previously been considered[19,23]), and there is no change in the number of atoms between the initial and final structures, or in their charge or chemical character (e.g., polar to nonpolar). Although the actual reaction path from the α to β anomer could be used, a nonphysical path between these two forms was selected to simplify the simulation. The coupling parameter λ was chosen to gradually "mutate" the hydrogen atom on C1 into a hydroxyl group, while at the same time the hydroxyl group was mutated into a hydrogen atom. For intermediate values of λ, a potential energy function was used that included a term for both groups simultaneously present at both positions but scaled by either λ or $(1 - \lambda)$ as appropriate (see eq 2). An alternative nonphysical path would be to move the H and OH groups stepwise from the α and β positions; at the intermediate point, they would overlap.

To evaluate the ensemble averages in eqs 1 or 3, a series of molecular dynamics simulations with different values of λ were performed for a "glucose" molecule in a TIP3P[24] aqueous solution with use of the CHARMM program.[18,25] A stochastic-boundary molecular dynamics system consisting of a single glucose molecule surrounded by 371 water molecules was used.[18,26] The primary region included all water molecules within 12 Å of the center of the glucose molecule, while the water molecules between 12 and 14 Å were governed by a Langevin equation of motion with a boundary force that constrained all water molecules to remain within a 14-Å sphere centered on the solute.[26] Nonbonded interactions were truncated smoothly by the application of shifting functions that go to zero at 8 Å.[25] The equations of motion were integrated using a Verlet algorithm with a step size of 1 fs. The constraint algorithm SHAKE[27] was used to keep the geometry of the water molecules rigid and to fix the lengths of the solute chemical bonds that involve hydrogen atoms. One series of simulations was performed for the mutation of α-D-glucopyranose into β-D-glucopyranose and another series for the inverse process. For both transformations, five individual simulations were performed at values of λ equal to 0.1, 0.3, 0.5, 0.7, and 0.9; in addition, end point simulations were done to provide results for structural analysis. These simulations were equilibrated for at least 15 ps at each value of λ, followed by an additional 10-ps period of simulation for evaluation of $(\Delta V)_\lambda$. All the simulations had an average temperature in the range 297.7 ± 1.1 K. The behavior of the results for each λ value was monitored over the 10-ps interval, and convergence was achieved in all cases.

The carbohydrate potential energy function used in these studies was a standard CHARMM-type function[25] with a parameter set proposed for the study of carbohydrates in aqueous solution.[28] No provision is made in the potential to include the configuration-dependent geometric changes usually associated with the anomeric effect, since they apparently do not exist for unsubstituted monosaccharides (see above); there exist molecular mechanics potentials that do include such effects.[29,30] Although no special terms to mimic the anomeric effect are included, this energy function favors the α anomer in vacuum static-minimization studies by 0.7–0.9 kcal/mol, depending on the arrangement of the other hydroxyl groups, apparently due to unfavorable interaction of the C5–O5 and C1–O1 dipoles in the β anomer.

The starting glucose geometry used for both the α and β stereoisomers was the crystal geometry[31] except for the orientation of the exocyclic hydroxymethyl group. Defining the position of O6 by the two torsion angles O5–C5–C6–O6 and C4–C5–C6–O6 (see Figure 1), we used the so-called TG orientation,[32] which is the minimum-energy conformation in vacuum. This structure differs from the crystal conformation, where the exocyclic hydroxymethyl group is in the GT orientation, with the OH group making a hydrogen bond to a crystal neighbor. In the energy-minimized vacuum structure, the hydroxymethyl group makes an intramolecular hydrogen bond between the O6 and O4 hydroxyl groups, which is not possible in the GT conformation; the vacuum energy difference between these two conformers is 2.7 kcal/mol for the α anomer and 2.8 kcal/mol for the β form.

Table I. Free Energy Changes (kcal/mol) for the Transformation of an α-D-Glucopyranose into the β Anomer and for the Reverse Process in Aqueous Solution[a,b]

$\alpha \rightarrow \beta$				$\beta \rightarrow \alpha$			
λ_i	λ_j	$\Delta G(i \rightarrow j)$	ΔG^b	λ_i	λ_j	$\Delta G(i \rightarrow j)$	ΔG^b
0.1	0.0	−5.25	5.25	0.1	0.0	−6.32	6.32
0.1	0.2	2.62	7.87	0.1	0.2	3.03	9.36
0.3	0.2	−1.52	9.39	0.3	0.2	−1.41	10.77
0.3	0.4	0.80	10.19	0.3	0.4	0.71	11.49
0.5	0.4	−0.44	10.63	0.5	0.4	−0.25	11.74
0.5	0.6	0.02	10.64	0.5	0.6	−0.28	11.45
0.7	0.6	0.37	10.28	0.7	0.6	0.91	10.54
0.7	0.8	−0.98	9.30	0.7	0.8	−1.62	8.92
0.9	0.8	2.72	6.58	0.9	0.8	2.74	6.18
0.9	1.0	−6.07	0.50	0.9	1.0	−5.79	0.39

[a] Simulations were made at λ = 0.1, 0.3, 0.5, 0.7, and 0.9. This corresponds to λ_i (the reference state), and ΔG was calculated for the change to λ_j (the modified state) with eq 1. [b] The $\Delta G(i \rightarrow j)$ values correspond to those obtained in a single step, and ΔG is the cumulative value.

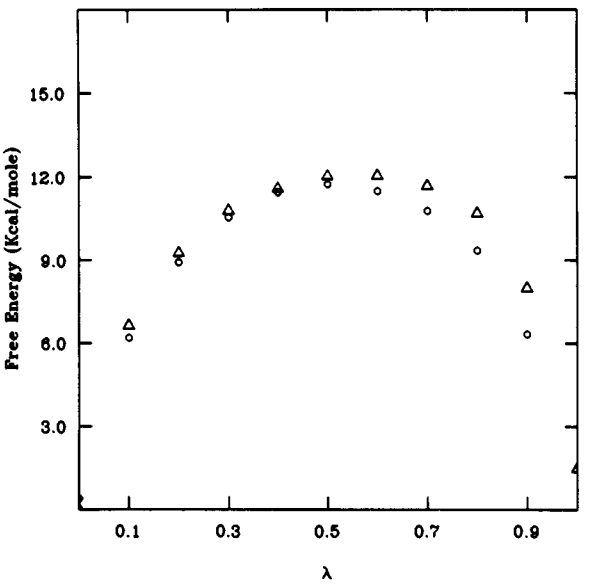

Figure 2. Free energy changes in the "mutation" of an α-D-glucopyranose into the β anomer in aqueous solution, and vice versa. The values calculated in the simulation on going from α to β are indicated by triangles, and those calculated from β to α are indicated by circles.

Results and Discussion

The free energy changes for the various λ "steps" along the mutation pathway from β to α and from α to β are summarized in Table I; the calculated free energy changes are plotted as a function of λ in Figure 2. As can be seen from the figure, the free energy of the system changes in a smooth fashion on going from one form to the other and the calculations are nearly reversible; the differences give an estimate of the statistical error. The free energy of the system increases rapidly with λ at small or large values of λ and becomes approximately 12 kcal/mol less favorable at λ = 0.5 than at the end points. At this intermediate value of λ, both groups are present equally in both positions around the C1 carbon. This effectively destroys the capacity of the C1 hydroxyl(s) to form hydrogen bonds, and the anomeric center behaves essentially like a large nonpolar group. Figure 3 displays a stereopair of the water molecules in the neighborhood of the anomeric center; shown are the mean positions of the nearby water molecules, averaged over a typical 200-fs segment to give a so-called "V structure"[33] at λ = 0.5, along with the positions of the

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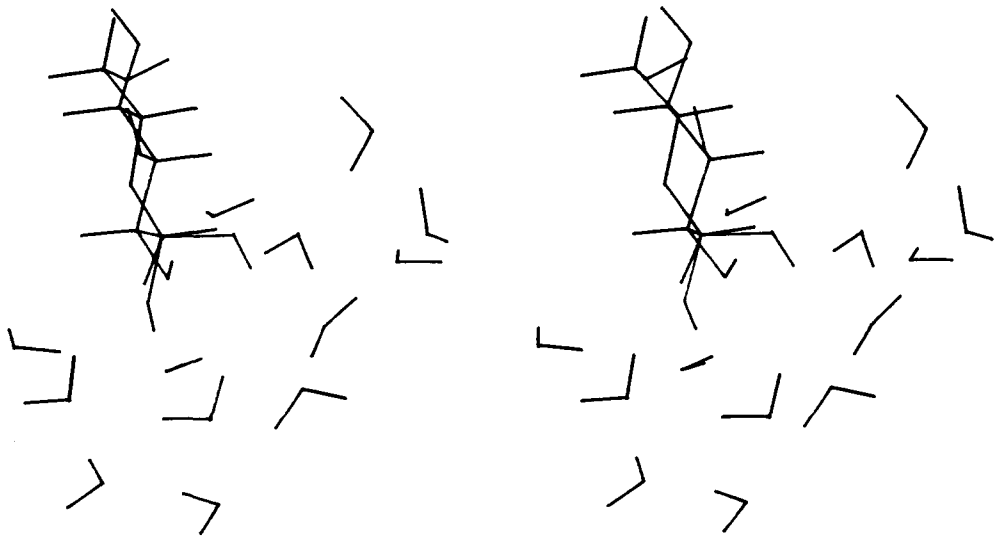

Figure 3. Stereoview of the glucose molecule and water molecules in the immediate vicinity of the anomeric center from an MD simulation with $\lambda = 0.5$. These coordinates represent a "V structure" (see ref 33) for this system and are obtained by averaging over 200 fs of dynamics.

four "pseudo groups" on the C1 carbon atom. As can be seen, the water molecules in this region do not have typical hydrogen-bonding orientations, in which either a hydrogen atom or a lone-pair position is pointing at a hydroxyl moiety. Instead, the waters are "straddling" these substituents as they would a nonpolar group.[34]

The total free energy difference obtained from eq 1 on going from β to α was found to be 0.39 kcal/mol and 0.50 kcal/mol from α to β; the corresponding values calculated from eq 3 are −0.01 and 1.10 kcal/mol. Averaging these results and computing the standard error from them lead to a free energy difference $\Delta G(\beta \rightarrow \alpha) = -0.31 \pm 0.43$ kcal/mol, which is to be compared with the experimental value of 0.33 kcal/mol. It should be noted that, in addition to the statistical uncertainty of the simulations that is estimated here, there could also be a systematic error due to the approximate nature of the potential function. The error due to the use of stochastic boundary conditions in this system with a constant number of particles is expected to be negligible.[18]

Although the simulation results presented here are well converged when compared with other free energy calculations,[35] they are still not sufficiently precise to distinguish between the two stereoisomers because the free energy difference of interest is so small.[36] What is important and meaningful is that the simulations correctly predict a very small free energy difference between the anomers in solution, with a statistical error that brackets the experimental result. Use of thermodynamic integration (eq 3) makes it possible to determine the effects of solvation by separating the intramolecular and intermolecular contributions to the total free energy difference (see Table II). For both calculations (α to β and β to α), the overall free energy difference is a result of the approximate cancelation of intramolecular and intermolecular contributions of comparable magnitudes and opposite signs. In accord with other models,[10] there is a substantial intramolecular free energy of 3.6 kcal/mol, mainly electrostatic, favoring the α stereoisomer. This can be compared with the potential energy difference in vacuum of less than 1 kcal/mol (see above). In one of the simulations ($\beta \rightarrow \alpha$), there is also an angle-bending contribution favoring the β form; since this contribution is smaller in the other simulation, its significance is not clear. Most important, there is a sizable solute–solvent free energy contribution favoring the β form. The magnitude of the solvent effect is sufficiently large (3.03 kcal/mol), in comparison with the statistical error of the simulations (±0.5 kcal/mol, see above), that it should be meaningful.

Table II. Component Analysis and Total Free Energy Changes for the Transformation in Aqueous Solution of an α-D-Glucopyranose to the β Anomer and for the Reverse Process[a]

	total	vdw	elec	angle	dihed
		$\alpha \rightarrow \beta$			
total	1.10	−0.16	1.50	−0.27	0.03
solute	4.31	−0.37	4.92	−0.27	0.03
solute–water	−3.21	0.21	−3.42		
		$\beta \rightarrow \alpha$			
total	−0.01	0.16	−1.66	1.51	−0.02
solute	−2.86	0.29	−4.64	1.51	−0.02
solute–water	2.85	−0.13	2.98		
		$[(\alpha \rightarrow \beta) - (\beta \rightarrow \alpha)]/2$			
total	0.56	−0.16	1.58	−0.89	0.03
solute	3.59	−0.33	4.78	−0.89	0.03
solute–water	−3.03	0.17	−3.20		

[a] Values (kcal/mol) are obtained by thermodynamic integration (eq 3).

In accord with a previous MD simulation of α-D-glucopyranose[37] in SPC water,[38] the degree of hydrogen bonding of the various hydroxyl groups is not the same in α-D-glucopyranose ($\lambda = 0$) and β-D-glucopyranose ($\lambda = 1$). The orientational ordering found here for the water molecules hydrogen bonding to O2 is greater (more typically hydrogen bond like) for β-D-glucopyranose than for α-D-glucopyranose, in agreement with the earlier simulation results.[37] However, it should be noted that, with the TIP3P water model, all of the hyroxyl groups impose somewhat less orientational ordering (structuring) on their hydrogen-bonded neighbors than in the SPC study. The previous simulation indicates that the orientational-structuring results are sensitive to the hydroxyl rotamer states and may require longer simulations for full convergence. One other difference between the TIP3P and SPC water model simulations is that the SPC simulation was initiated with the exocyclic hydroxymethyl group in the crystallographic GT

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(36) The small error in the free energy simulation method can be compared with attempts to calculate the individual solvation energies of the two conformers. Two separate simulations of α- and β-glucose (with use of the SPC water model) led to a difference in the solvation energy of 24 kcal/mol in favor of the α anomer (J. W. Brady, unpublished results). This very large error results from the fact that the energy difference is dominated by change in the energy of the solvent in the two calculations. The free energy simulation avoids this problem because only the difference between solute and solute–solvent energies enters directly into the calculation (see eqs 1 and 3) and because a single simulation on going from α to β or the reverse is done so that the system is sampling the same portion of phase space.
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conformation, instead of the TG conformation used here. In that study there was a transition in the orientation of this group at 6 ps to the TG conformation; this conformation persisted for the remaining 36 ps of the simulation. In the present simulations, the hydroxymethyl group went from the starting TG conformation to either GT or GG early in the simulation; in one case ($\lambda = 0.7$ for β and α), this group oscillated three times from GT to GG and back again during the 10 ps of data collection. No transitions back to TG were observed in any of the simulations. During the total analysis time of 100 ps, the hydroxymethyl group spent approximately 15.5 ps in the GG form and 83 ps in the GT conformation, with very few transitions. This rotamer distribution, with no observed TG population, is in agreement with experimental data.[39-41] The source of this difference in exocyclic rotational behavior between the two MD simulations could be incomplete sampling of rare events,[42] differences between the SPC[38] and TIP3P[24] water models, and/or differences in the truncation method. In any case, the C6-O6H group is on the opposite side of the molecule from the anomeric group and so is unlikely to have a significant effect on the calculated free energy difference, which is of primary interest here.

Conclusions

Free energy simulations with an empirical force field show that a substantial interaction (3.03 ± 0.5 kcal/mol), mainly electrostatic, between the sugar and the solvent favors the β anomer of D-glucose, which predominates in aqueous solution at room temperature. There is a counterbalancing internal free energy of nearly the same magnitude, also mainly electrostatic, that favors the α form. Although the exact quantitative results of the simulations are expected to depend on the choice of potential function and parameters, the qualitative features of the analysis should be correct. The essential result is that the preference of D-glucose for the β anomer is primarily a solvation effect, as has been suggested from experimental studies.[3,43]

The results from the present study are not directly comparable to the intramolecular anomeric stabilization energy obtained in ab initio calculations, since the corresponding energy difference for the cyclohexane polyalcohols is not available. The simulation suggests that there is a significant intramolecular term favoring the α form. From the difference between the intramolecular contribution to the free energy in solution and the energy minimum in vacuum, it is clear that a dynamic average (in the presence of solvent) is required to obtain a meaningful result.

The anomeric preference found here does not result from any chemically distinct properties of the anomeric group, since it was treated the same as the other hydroxyl groups and had the same parameters whether axial or equatorial. Thus, the difference in solvation found in the present simulations arises from the structural and dynamic properties of the two glucose anomers rather than from a difference in hydrogen-bonding characteristics resulting from a configuration-dependent redistribution of charge.[11]

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Registry No. α-D-Glucopyranose, 492-62-6; β-D-glucopyranose, 492-61-5.

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trans-Dimethyldisilyne ($Si_2(CH_3)_2$): An Achievable Synthetic Target

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Abstract: The trans, twist, and dimethyldisilavinylidene isomers of dimethyldisilyne have been studied at the configuration interaction level of theory, and the trans and dimethyldisilavinylidene are found to be minima. The relative energy of these two minima are evaluated with larger basis sets. Our final prediction of this energy difference is 12.0 kcal/mol with the *trans*-$H_3CSiSiCH_3$ being higher in energy. To aid in the prospective observation of the first potential silicon-silicon triple bond, the vibrational frequencies and infrared intensities are reported.

1. Introduction

In 1986 Sekiguchi, Zigler, and West[1] proposed dimethyldisilyne as an intermediate in the thermolysis of bis(7-silanorbornadiene) leading to the production of an anthracene adduct. In addition, they speculated that the anthracene product itself could decompose to yield dimethyldisilyne, citing mass spectral data yielding a peak with m/e 86 and having the correct isotopic ratios to implicate a composition of $C_2H_6Si_2^+$. Subsequent studies[2,3] provided evidence for the reaction of bis(7-silanorbornadiene) with disubstituted acetylene to yield 1,4-disilabarrelenes via a similar mechanism. These studies presented the first evidence for the possibility of a species containing a Si-Si triple bond. The parent

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