Interaction of Methyl β-D-Xylopyranoside with Metal Ions: Density Functional Theory Study of Cationic and Neutral Bridging and Pendant Complexes

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Density functional theory calculations on complexes of $^4C_1$, $^1C_4$ and ^2S_O ring conformations of methyl β-D-xylopyranoside **1** with divalent metal cations, M = Mg^{2+}, Ca^{2+}, Zn^{2+}, and Cd^{2+}, are presented. Bridging and pendant cationic, $[M(H_2O)_4\mathbf{1}]^{2+}$ and $[M(H_2O)_5\mathbf{1}]^{2+}$, as well as neutral complexes, $[M(OH)_2(H_2O)_2\mathbf{1}]$ and $[M(OH)_2(H_2O)_3\mathbf{1}]$, and neutral complexes involving a doubly deprotonated sugar, $[M(H_2O)_4\mathbf{1}^{2-}]$, are considered. In aqueous and chloroform solution the stability of cationic and pendant neutral complexes is greatly diminished compared with gas-phase results. In contrast, bridging neutral complexes $[M(OH)_2(H_2O)_2\mathbf{1}]$ and those of type $[M(H_2O)_4\mathbf{1}^{2-}]$, are stabilized with increasing solvent polarity. Solvation also profoundly influences the preferred binding position and ring conformation. Compared with complexes of bare metal cations, additional ligands, *e.g.*, H_2O or OH^-, significantly reduce the stability of $^1C_4$ ring complexes. Irrespective of the cation, the most stable structure of bridging complexes $[M(H_2O)_4\mathbf{1}]^{2+}$ results from coordination of the metal to O3 and O4 of methyl β-D-xylopyranoside in its $^4C_1$ ring conformation.

Introduction

Metal-complexation induced conformational changes, *e.g.*, $^4C_1-^1C_4$ ring structure interconversions, of carbohydrates can be exploited for the construction of selective metal ion sensors.[1,2] In a previous publication, we have described a computational study (DFT and MP2) on the influence of metal cation complexation on the conformational properties of methyl β-D-xylopyranoside **1** as a simple model system for potential metal ion chemosensors.[3] Also addressed was the question of the preferred binding positions in this sugar. Triple coordination of the cation by two hydroxyl groups and the ring oxygen atom, possible in $^1C_4$ chairs and also ^2S_O skew forms, turned out to be a prominent stabilizing factor for the individual complexes. In $^4C_1$ chair xylose conformations at most two oxygens can be involved in metal coordination. Previous DFT calculations[4] also had indicated preferred triple coordination in, *e.g.*, *cis*-inositol. Depending on the ionic radii of the metals, binding occurred to the *ax*-O1−*ax*-O3−*ax*-O5 or *ax*-O1−*eq*-O2−*ax*-O3 oxygens. For β-D-glucose the most favorable binding position involved O1, O6, and the ring oxygen O5. For this type of binding no change of the more stable $^4C_1$ ring conformation[4] is required. In β-D-xylopyranose, which lacks the CH_2OH group, no such binding motif is possible. However, interconversion of glucose chairs ($^4C_1 \leftrightarrow {}^1C_4$) upon metal [Pt(IV)] complexation to O2, O4, and the ring oxygen O5 has been described as a new carbohydrate coordination mode.[5] In contrast, $(en)Pd^{II}$, en = ethylenediamine, forms binuclear $^4C_1$ complexes with two $(en)Pd^{II}$ moieties coordinated by O1,O2 and O3,O4, respectively.[6] Generally, thus, the structure and conformation of carbohydrate−metal complexes depend not only strongly on the particular sugar and metal but also on additional ligands coordinated to the metal. For instance, the complex-forming properties of chitosans[7] have been interpreted in terms of two models. In pendant complexes[8] only one group of the carbohydrate interacts with the metal whereas in bridging complexes several are involved.[9] Matters are further complicated by the existence of different binding positions.[3,4,10−12]

Despite the quite detailed computational study concerning metal cation binding by methyl β-D-xylopyranoside,[3] several open questions remained. Thus, a better understanding of the factors governing the stability of sugar−metal complexes is highly desirable as a prerequisite for the rational design of carbohydrate-based metal sensors. Furthermore, carbohydrate−metal interactions are of general importance in many areas of (bio)chemistry and technology.[5b,13] Thus, we found it worthwhile to extend previous computational studies[3,14] concerning the binding position and effect on sugar conformation of divalent metals in complexes with methyl β-D-xylopyranoside. As biologically and/or environmentally relevant species, Mg^{2+}, Ca^{2+}, Zn^{2+}, and Cd^{2+} have been chosen. Specific questions to be addressed in the following are (i) the effect of additional ligands on the stability of $^4C_1$, $^1C_4$, and ^2S_O ring conformations, (ii) stability of bridging vs pendant complexes, (iii) cationic vs neutral complexes, and (iv) preferred binding site (atoms of the sugar involved in coordinating the metal).

Computational Details

All computations have been performed with the Gaussian 03 suite of programs[15] with Becke's three-parameter hybrid Hartree−Fock density functional method[16] with the Lee−Yang−Parr correlation functional (B3LYP).[17] The LANL2DZ basis set[18] with polarization functions (d for oxygen, α = 0.8; p for hydrogen, α = 1.1) and diffuse functions taken from the 6-311++G(d,p) standard basis[19] set, added to oxygen (sp) and hydroxyl-hydrogen (s) atoms, thereafter denoted as basis I, was used. All structures were characterized by frequency calculations as true minima. Zero point energies (ZPE) and thermal corrections to Gibbs' free energies are obtained from the B3LYP/basis I calculations and are unscaled. For selected complexes of Mg^{2+}, Ca^{2+}, and Zn^{2+}, in addition B3LYP/6-311++G(d,p)[19]

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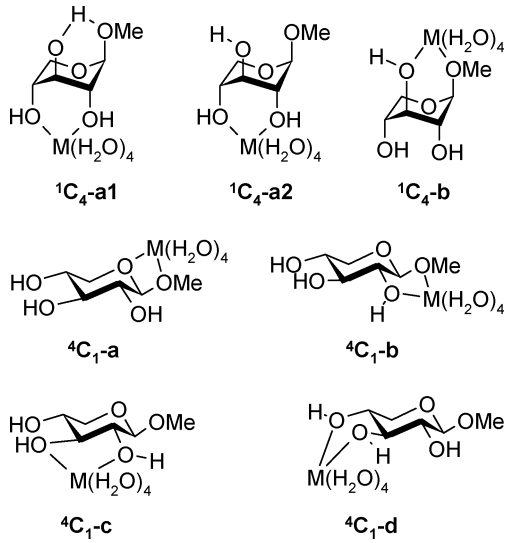
SCHEME 1: Structures of Cationic Bridging Complexes $[M(H_2O)_4\mathbf{1}]^{2+}$



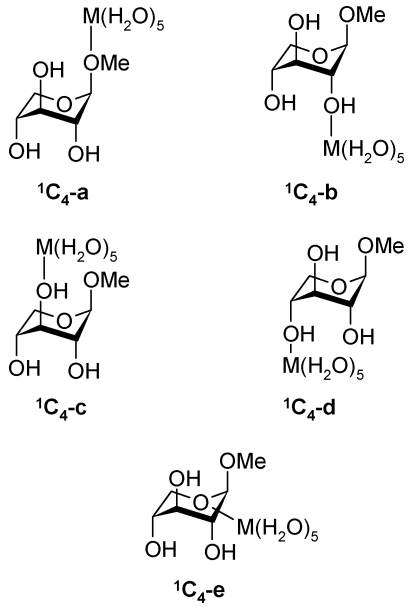
optimizations have been performed. In the Gaussian program suite, 6-311 indicate the basis sets of Blaudeau[19c] and Wachters and Hay,[19e,f] for Ca and Zn, respectively.[20] Solvent effects ($CHCl_3$, H_2O) were approximated by the IEF-PCM procedure.[21] Because no cavity parameters for the metal cations are available in the G03 implementation of the PCM model, only the electrostatic contribution to solvation of the complexes was taken into account. For neutral complexes $[M(OH)_2(H_2O)_x\mathbf{1}]$ and $[M(H_2O)_4\mathbf{1}^{2-}]$ UFF (universal force field) radii[22] with explicit hydrogen spheres instead of the usual united atom topological (UA0)[23] model had to be used. Visualization was done with MOLDEN.[24] Ring conformations are described by the relevant improper dihedrals[25] and Cremer−Pople puckering parameters[26,27] obtained by PLATON.[28]

Results and Discussion

To begin with, hexacoordination by H_2O as model ligand[11,29] of the metal cations M, M = Mg^{2+}, Ca^{2+}, Zn^{2+}, and Cd^{2+}, with octahedral geometry has been assumed. On the basis of crystal structures as well as calculations on $[M(H_2O)_n]^{2+}$ clusters, M = Be^{2+}, Mg^{2+}, Ca^{2+}, and Zn^{2+}, this coordination geometry has been found to be dominating in Mg^{2+}. For Zn^{2+} the coordination numbers range from 4 to 6 and in Ca^{2+} from 6 to 9.[29] Thus, in pendant complexes, one water molecule in $[M(H_2O)_6]^{2+}$ is replaced by a single sugar oxygen atom, anomeric methoxy O1, hydroxyl (O2, O3, O4) or ring oxygen O5. Two H_2O molecules are replaced in bridging complexes. Deviations from this behavior, which especially can be expected for the Ca^{2+} ion with its tendency to larger coordination numbers, will be pointed out accordingly. The naming convention for the bridging complexes is illustrated in Scheme 1.

The various species are characterized by their respective ring conformation, $^4C_1$, $^1C_4$, and ^2S_O, and binding position. Different conformations are indicated by additional numbers, *e.g.*, **$^1C_4$-a1** [*gauche*$^-$ conformation of the O3−H3a group, τ(C4−C3−O3−H3a) ∼ −60°] and **$^1C_4$-a2** [*trans* conformation of the O3−H3a group, τ(C4−C3−O3−H3a) ∼ 180°] in Scheme 1. No *gauche*$^+$ O3−H3a orientation, τ(C4−C3−O3−H3a) ∼ 60°, was found for **$^1C_4$** chelated complexes $[Mg(H_2O)_4\mathbf{1}]^{2+}$. For bridging ^2S_O complexes, the same nomenclature as for $^4C_1$ structures applies. The nomenclature of pendant complexes is illustrated in Scheme 2 for $^1C_4$ ring conformations. The same naming convention is used also for $^4C_1$ and ^2S_O structures.

SCHEME 2: Structures of Cationic Pendant Complexes $[M(H_2O)_5\mathbf{1}]^{2+}$



The metal−sugar interaction energy for cationic complexes can thus be evaluated from the following reaction (x = 4 and 5 for bridging and pendant complexes, respectively).[12]

$$[M(H_2O)_6]^{2+} + \mathbf{1} \rightarrow [M(H_2O)_x\mathbf{1}]^{2+} + (6 - x)H_2O \quad (1)$$

To model neutral complexes, first two H_2O molecules (x = 2 and 3 for bridging and pendant complexes, respectively) were replaced by OH^-, eq 2.[12] Alternatively, because frequently

$$[M(OH)_2(H_2O)_4] + \mathbf{1} \rightarrow [M(OH)_2(H_2O)_x\mathbf{1}] + (4 - x)H_2O \quad (2)$$

deprotonation of sugar OH groups in metal complexes is found,[6] reaction of hydrated metal cations with doubly ionized methyl β-D-xylopyranoside $\mathbf{1}^{2-}$ (eq 3) is used to assess complex stability.

$$[M^{2+}(OH^-)_2(H_2O)_4] + \mathbf{1} \rightarrow [M^{2+}(H_2O)_4\mathbf{1}^{2-}] + 2H_2O \quad (3)$$

To evaluate the above equations, the lowest calculated gas-phase geometries for methyl β-D-xylopyranoside **1** (*tttt*-$^4C_1$)[3] and the various metal complexes were used. A special feature arises for chelates with $^1C_4$ ring conformations.[3] Here, possible interaction with the ring oxygen O5 in addition to that with O2 and O4 would require replacement of a third H_2O molecule (x = 3 in eq 1). Similarly, in ^2S_O triple coordination involving O1, O3 and O5 is possible.

The outline of this paper is as follows: Carbohydrate modeling is computationally quite demanding.[30,31] Especially, selection of a proper basis set is crucial for the description of carbohydrate conformational properties.[30c−e,31] Thus, first a comparison of the chosen methods (section I) will be given. In section II, complex stabilities (interaction Gibbs free energies ΔG_{int}, evaluated according to eqs 1−3), are presented. Detailed descriptions of energetic and structural aspects of cationic and neutral complexes, respectively, are provided in sections III and IV.

I. Comparison of Methods. Before giving a detailed description of the results, two general remarks are in order. First, there is some dependence of the energetic ordering of the various

TABLE 1: Relative Enthalpies (ΔH) and Gibbs Free Energies[a] (ΔG, kcal mol^{-1}) for Mg^{2+} Complexes $[Mg(H_2O)_4\mathbf{1}]^{2+}$

	gas phase				H_2O ΔG		$CHCl_3$ ΔG	
	ΔH		ΔG					
$^1C_4$−a1	0.0	(0.0)	0.0	(0.0)	0.0	(0.0)	0.0	(0.0)
$^1C_4$−a2	1.7	(1.5)	0.9	(0.9)	−1.1	(−1.2)	−0.2	(−0.6)
$^4C_1$−c	4.3	(1.8)	2.1	(0.2)	−0.6	(−1.9)	1.4	(−0.7)
$^4C_1$−b	5.7	(4.7)	3.5	(3.0)	1.6	(1.8)	3.2	(2.8)
^2S_O−c	7.8	(7.2)	5.1	(4.8)	−0.2	(−0.2)	2.0	(1.9)
$^4C_1$−d	8.0	(5.0)	5.5	(3.1)	−1.2	(−2.2)	1.4	(−0.3)
^2S_O−d	8.1	(7.7)	5.6	(5.5)	1.5	(2.1)	3.3	(3.3)
^2S_O−b	10.7	(10.0)	8.0	(7.9)	5.5	(6.2)	7.3	(7.1)
^2S_O−a	12.7	(12.2)	8.6	(8.6)	8.7	(8.7)	9.8	(9.3)
$^4C_1$−a	13.3	(11.8)	9.5	(8.5)	4.4	(4.6)	6.9	(6.2)
$^1C_4$−b	15.2	(13.9)	14.1	(13.4)	5.8	(6.6)	9.2	(8.9)

[a] B3LYP/basis I values; B3LYP/ 6-311++G(d,p) results are given in parentheses.

structures of the individual complexes on whether relative enthalpies, ΔH_{rel}, or Gibbs free energies, ΔG_{rel}, are used. In bridging complexes $[Mg(H_2O)_4\mathbf{1}]^{2+}$ (Table 1) entropic contributions lead to a decreased stability of the **$^1C_4$-a1** structure compared with all other conformations. In pendant complexes $[Mg(H_2O)_5\mathbf{1}]^{2+}$ (Table S5) there is essentially no difference between ΔH_{rel} and ΔG_{rel} values. The same also holds for Ca^{2+}, Zn^{2+}, and Cd^{2+} complexes (Tables S1−S3 and S6 and S7 in the Supporting Information). Thus, the following discussions will be based on Gibbs free energies. Second, the suitability of the chosen computational procedures needs to be established. The energetic ordering of methyl β-D-xylopyranoside conformations (ring structures and O−H(CH_3) torsions) obtained by B3LYP/basis I calculations showed close correspondence[3] with those resulting from a composite energy approach [MP2/cc-pVTZ//MP2/cc-pVDZ + CCSD/6-31G(d)].[30d] Similarly, B3LYP/basis I results for methyl 2,4-diacetyl-β-D-xylopyranoside also were in agreement with the composite energy approach.[14d] Thus, despite the known deficiencies of B3LYP in correctly treating electron correlation and weak interactions,[32] it appears to be adequate for the present systems. To further elaborate on the reliability of the B3LYP/basis I procedure, in the following we compare it with B3LYP/6-311++G(d,p) results for Mg^{2+}, Ca^{2+}, and selected Zn^{2+} complexes.[33]

In analogy to the energetic ordering of α- and β-D-allopyranose structures found by B3LYP/6-31+G(d) vs B3LYP/6-311++G(d,p) calculations,[31b] here, too, both basis sets give quite similar results.[33] Notable exceptions are the **$^4C_1$-c** and **$^4C_1$-d** structures of $[Mg(H_2O)_4\mathbf{1}]^{2+}$ complexes (Table 1).[34] For these a somewhat greater stability compared with **$^1C_4$-a1** is calculated with B3LYP/6-311++G(d,p) than B3LYP/basis I. Completely analogous results are also obtained for Ca^{2+} and Zn^{2+} complexes. Smaller relative enthalpy (or Gibbs free energy) differences between the two basis sets result for pendant complexes $[Mg(H_2O)_5\mathbf{1}]^{2+}$ (Table S5) and $[Ca(H_2O)_5\mathbf{1}]^{2+}$ (Table S6) than for bridging complexes.

Calculated interaction Gibbs free energies (eq 1) for **$^1C_4$-a1** and **$^4C_1$-b1** structures of $[M(H_2O)_4\mathbf{1}]^{2+}$ and $[M(H_2O)_5\mathbf{1}]^{2+}$ complexes, respectively, are summarized in Table 2.

Interaction energies calculated with the 6-311++G(d,p) basis set are slightly less negative or more positive (diminished stability of the sugar−metal complex) than those obtained with basis I, especially in the gas phase. Differences are smaller for pendant complexes. Thus, we are confident that B3LYP/basis I results for Cd^{2+} - complexes will be sufficiently reliable [the 6-311++G(d,p) basis set is not available for Cd].

TABLE 2: Calculated Interaction Gibbs Free Energies ΔG_{int} (eq 1, kcal mol^{-1}) with Respect to the $^1C_4$-a1 and $^4C_1$-b1 Conformations of $[M(H_2O)_4\mathbf{1}]^{2+}$ and $[M(H_2O)_5\mathbf{1}]^{2+}$ Complexes, Respectively[a]

	gas phase		H_2O		$CHCl_3$	
			$[M(H_2O)_4\mathbf{1}]^{2+}$			
Mg	−15.5	(−12.6)	−0.1	(1.5)	−1.7	(0.7)
Ca	−13.6	(−10.6)	1.5	(1.8)	0.6	(1.0)
Zn	−15.8	(−13.3)	−0.9	(0.8)	−2.0	(−0.2)
Cd	−13.8		−0.7		−1.8	
			$[M(H_2O)_5\mathbf{1}]^{2+}$			
Mg	−21.0	(−18.5)	10.7	(11.9)	6.0	(7.5)
Ca	−17.2	(−16.0)	9.6	(10.8)	6.3	(7.5)
Zn	−21.1		9.8		5.6	
Cd	−19.2		9.0		5.4	

[a] B3LYP/basis I values; B3LYP/ 6-311++G(d,p) results are given in parentheses.

Despite some problems associated with the calculation of entropy and, thus, Gibbs free energies, especially for molecules with many low-frequency motions,[35] the following discussion will be mainly based on Gibbs free energy differences ΔG.

II. Complex Stability. ***Interaction Energies for Cationic Complexes.*** The stability of cationic methyl β-D-xylopyranoside metal complexes was evaluated according to eq 1. Resulting interaction Gibbs free energies, ΔG_{int}, for both $[M(H_2O)_4\mathbf{1}]^{2+}$ and $[M(H_2O)_5\mathbf{1}]^{2+}$ complexes, M = Mg^{2+}, Ca^{2+}, Zn^{2+}, and Cd^{2+}, are summarized in Table 2. Data refer to the *tttt*-$^4C_1$ strucuture of methyl β-D-xylopyranoside **1** and the **$^1C_4$-a1** and **$^4C_1$-b1** ring conformation in chelated and pendant complexes, respectively. Both types of isolated complexes, $[M(H_2O)_4\mathbf{1}]^{2+}$ and even more so $[M(H_2O)_5\mathbf{1}]^{2+}$, are significantly stabilized with respect to the free sugar and $[M(H_2O)_6]^{2+}$, $\Delta G_{int} < 0$. Slightly more negative values, *i.e.*, greater complex stability, are calculated for the smaller[36] cations Mg^{2+} and Zn^{2+}. Inclusion of solvent effects leads also to a substantial reduction of the binding affinities of these cations. Generally, **$^4C_1$-d** conformations are more stable in aqueous solution and **$^4C_1$-c** or **$^1C_4$-a2** in $CHCl_3$ (Tables 1 and S1−S3). Thus, taking into account this change in the preferred $[M(H_2O)_4\mathbf{1}]^{2+}$ complex conformation upon solvation, interaction Gibbs free energies are in the range $\Delta G_{int} = -1.1$ to -2.9 kcal mol^{-1} (B3LYP/basis I) and $\Delta G_{int} = -0.7$ to -1.7 kcal mol^{-1} [B3LYP/6-311++G(d,p)] for aqueous solution. In $CHCl_3$, $\Delta G_{int} = -1.9$ to -2.7 kcal mol^{-1} (B3LYP/basis I) and $\Delta G_{int} = +0.1$ to -1.3 kcal mol^{-1} [B3LYP/6-311++G(d,p)] is obtained. A significantly stronger metal−sugar interaction is computed for isolated pendant complexes $[M(H_2O)_5\mathbf{1}]^{2+}$. However, the solvent effect is even larger here, leading to $\Delta G_{int} > 0$ for each metal cation considered; thus in solution cationic pendant complexes are unstable.

Interaction Energies for Neutral Complexes. Complex stabilities for **$^4C_1$-d1** and **$^1C_4$-b1** structures of "chelate" and pendant neutral complexes (eq 2), $[M(OH)_2(H_2O)_2\mathbf{1}]$ and $[M(OH)_2(H_2O)_3\mathbf{1}]$, and $[M^{2+}(H_2O)_4\mathbf{1}^{2-}]$ (eq 3) are summarized in Table 3.

With the exception of Ca^{2+} in $CHCl_3$, formation of pendant neutral complexes is highly unlikely, especially in aqueous solution. In contrast, replacement of two water molecules by methyl β-D-xylopyranoside generally leads to stable complexes in solution, $\Delta G_{int} < 0$. This is mainly attributable to the solvation energy of H_2O. However, these stable complexes generally are not true chelates: only one sugar oxygen atom is coordinated to the metal cation.

TABLE 3: Calculated[a] Interaction Gibbs Free Energies ΔG_{int} (kcal mol^{-1}) for $^4C_1$-d1 and $^1C_4$-b Structures of Neutral Complexes [M(OH)$_2$(H$_2$O)$_2$1] and [M(OH)$_2$(H$_2$O)$_3$1] (eq 2), and $^1C_4$-a1 Conformations of [M^{2+}(H$_2$O)$_4$1^{2-}] Complexes (eq 3)

	[M(OH)$_2$(H$_2$O)$_2$**1**]			[M(OH)$_2$(H$_2$O)$_3$**1**]			[M(H$_2$O)$_4$**1**$^{2-}$]		
	gas	H$_2$O	CHCl$_3$	gas	H$_2$O	CHCl$_3$	gas	H$_2$O	CHCl$_3$
Mg	3.3	−3.4	−0.5	9.1	11.3	10.2	3.6	−1.6	−0.7
Ca	0.3	−0.9	−1.7	−10.1	4.9	−3.1	*b*	*b*	*b*
Zn	2.9	−5.1	−0.9	2.9	6.2	5.1	3.1	0.5	0.0
Cd	3.2	−9.3	−6.9	2.7	5.5	4.3	4.3	−1.4	−0.1

[a] B3LYP/basis I; Radii=UFF in IEF−PCM calculations. [b] No [Ca(H$_2$O)$_4$**1**$^{2-}$] complexes could be found.

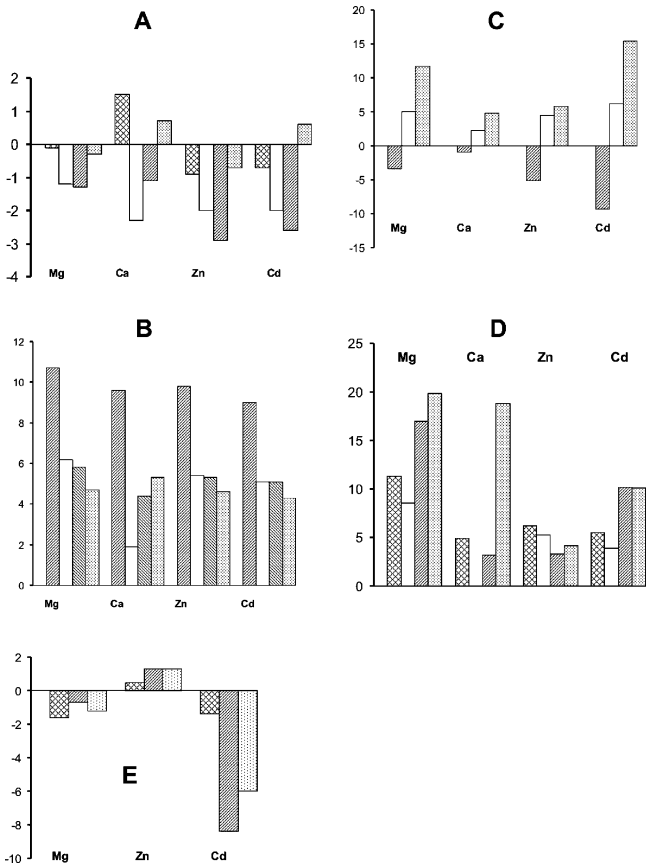


Figure 1. Calculated (B3LYP/basis I) interaction Gibbs free energies for $^1C_4$ (empty and cross-hatched bars), $^4C_1$ (hatched bars) and ^2S_O (dotted bars) ring conformations of chelated and pendant cationic complexes, (A) [M(H$_2$O)$_4$**1**]$^{2+}$ and (B) [M(H$_2$O)$_5$**1**]$^{2+}$, as well as neutral complexes, (C) [M(OH)$_2$(H$_2$O)$_2$**1**], (D) [M(OH)$_2$(H$_2$O)$_3$**1**], and (E) [M^{2+}(H$_2$O)$_4$**1**$^{2-}$].

Interaction energies of divalent cations Mg^{2+}, Zn^{2+}, and Cd^{2+} with **1**$^{2-}$, evaluated by eq 3, are also listed in Table 3. In the gas phase no complexes of this type should be formed. Increasing solvent polarity, $CHCl_3$ vs H_2O, generally leads to increased complex stability. Whereas in aqueous solution neutral complexes [M(H$_2$O)$_4$**1**$^{2-}$] are predicted to be fairly stable for M = Mg^{2+} and Cd^{2+}, those of Zn^{2+} barely should be formed, $\Delta G_{int} > 0$. Despite several attempts, no stable structures for Ca^{2+} complexes of this type could be found. In the case of cadmium complexes, the lowest energy structure in both H_2O and $CHCl_3$ solution is the $^4C_1$ ring conformation **^{4}C$_1$-d** (Table S11) resulting in quite strong binding, $\Delta G_{int} = -8.4$ (H_2O, Figure 1E) and −1.7 kcal mol^{-1} ($CHCl_3$), respectively. The influence of the cations on the stability of $^1C_4$, $^4C_1$, and ^2S_O ring conformations of cationic and neutral chelated and pendant methyl β-D-xylopyranoside **1** complexes in aqueous solution is illustrated in Figure 1. Clearly, in aqueous solution neither cationic nor neutral pendant complexes are stable (**B** and **D** in Figure 1). A greater stability of $^1C_4$ structures can possibly be expected only for cationic Ca^{2+} complexes, [Ca(H$_2$O)$_4$**1**]$^{2+}$, and neutral Mg^{2+} complexes with the doubly deprotonated xylopyranoside, [Mg^{2+}(H$_2$O)$_4$**1**$^{2-}$] (**A** and **E** in Figure 1).

III. Cationic Complexes. Because none of the pendant cationic complexes [M(H$_2$O)$_5$**1**]$^{2+}$ is stable in solution, $\Delta G_{int} > 0$, Table 2, the discussion of energetic and structural features will be restricted to chelated complexes, [M(H$_2$O)$_4$**1**]$^{2+}$. For the sake of completeness, relative enthalpies and Gibbs free energies for pendant cationic complexes are given in Tables S5−S7 of the Supporting Information.

Chelated Cationic Complexes [M(H$_2$O)$_4$1]$^{2+}$. Relative enthalpies and Gibbs free energies for [Mg(H$_2$O)$_4$**1**]$^{2+}$ are collected in Table 1, those for complexes of Ca^{2+}, Zn^{2+}, and Cd^{2+} in Tables S1−S3 in the Supporting Information.

Optimized geometries [B3LYP/6-311++G(d,p] of pertinent cationic [Mg(H$_2$O)$_4$**1**]$^{2+}$ complexes are depicted in Figure 2. Similar structures are obtained for the analogous Ca^{2+}, Zn^{2+}, and Cd^{2+} complexes. In magnesium complexes, M = Mg^{2+} (Table 1), with $^1C_4$ ring conformation (**^{1}C$_4$-a1** in Figure 2) coordination of the cation by four water molecules, prevents interaction of Mg^{2+} with the ring oxygen O5. This third sugar coordination site presumably contributes to the increased $^1C_4$ stability calculated for Mg^{2+} - complexes lacking additional ligands (gas phase: $\Delta G \geq 30$ kcal mol^{-1}, B3LYP/basis I[3]). The water ligands block formation of this third metal−carbohydrate "bond". Consequently, one would expect a significantly reduced stability of $^1C_4$ compared with $^4C_1$ structures. Indeed, a considerably diminished stability of $^1C_4$ complexes results. For instance, ΔG(**^{1}C$_4$-a1**−**^{4}C$_1$-c**) = −2.1, kcal mol^{-1} and −0.2 kcal mol^{-1}, with B3LYP/basis I and B3LYP/6-311++G(d,p), respectively, in the gas phase. Larger **^{1}C$_4$-a1**−**^{4}C$_1$-c** differences are obtained for relative enthalpies instead of Gibbs free energies (see Table 1). According to B3LYP/basis I calculations,[3] uncomplexed methyl β-D-xylopyranoside preferentially adopts the $^4C_1$ chair conformation, $\Delta G(^4C_1 - {}^1C_4) = -2.5$ kcal mol^{-1}. Thus, despite the lack of a third coordinating site in $^1C_4$ structures of [Mg(H$_2$O)$_4$**1**]$^{2+}$ complexes, there is—at least in the gas phase—still a tendency for a shift of the $^4C_1 \rightarrow {}^1C_4$ equilibrium toward $^1C_4$ structures upon metal binding. Contrary to binding of the "naked" metal cation,[3] there is apparently no correlation with the metals' ionic radii. Instead, the **^{1}C$_4$-a1**−**^{4}C$_1$-c** gas-phase Gibbs free energy difference slightly decreases in the series $Mg^{2+} > Ca^{2+} > Zn^{2+} > Cd^{2+}$ (B3LYP/basis I; with B3LYP/6-311++G(d,p) one obtains $Ca^{2+} > Zn^{2+} \approx Mg^{2+}$). However, the **^{1}C$_4$-a1** structures of Ca-complexes differ from those of the other cations; see below. Inclusion of solvation has a profound effect on relative stabilities. First, the **^{1}C$_4$-a1** ring structure, characterized by a g^- conformation of O3−H3a, τ(C4−C3−O3−H3a) = −81°, becomes less stable than the *trans* conformation, τ(C4−C3−O3−H3a) = 178°, **^{1}C$_4$-a2**, especially in aqueous solution. The former one is characterized by a stabilizing intramolecular O3−H3a···O1 hydrogen bond.[37,38] In contrast, the **^{1}C$_4$-a2** rotamer which lacks this feature, should be capable of acting as H-bond donor in intermolecular hydrogen bonds with the solvent H_2O. Second, with increasing solvent polarity, $CHCl_3$ vs H_2O, the stability of $^4C_1$ compared with $^1C_4$ chairs increases. With respect to different binding positions, complexes involving interaction with the anomeric oxygen O1 and/or the ring oxygen O5 (**^{1}C$_4$-b**, **^{4}C$_1$-a**, **^{2}S$_O$-a**, **^{2}S$_O$-b**; and, to a lesser extent, **^{4}C$_1$-b**) are the

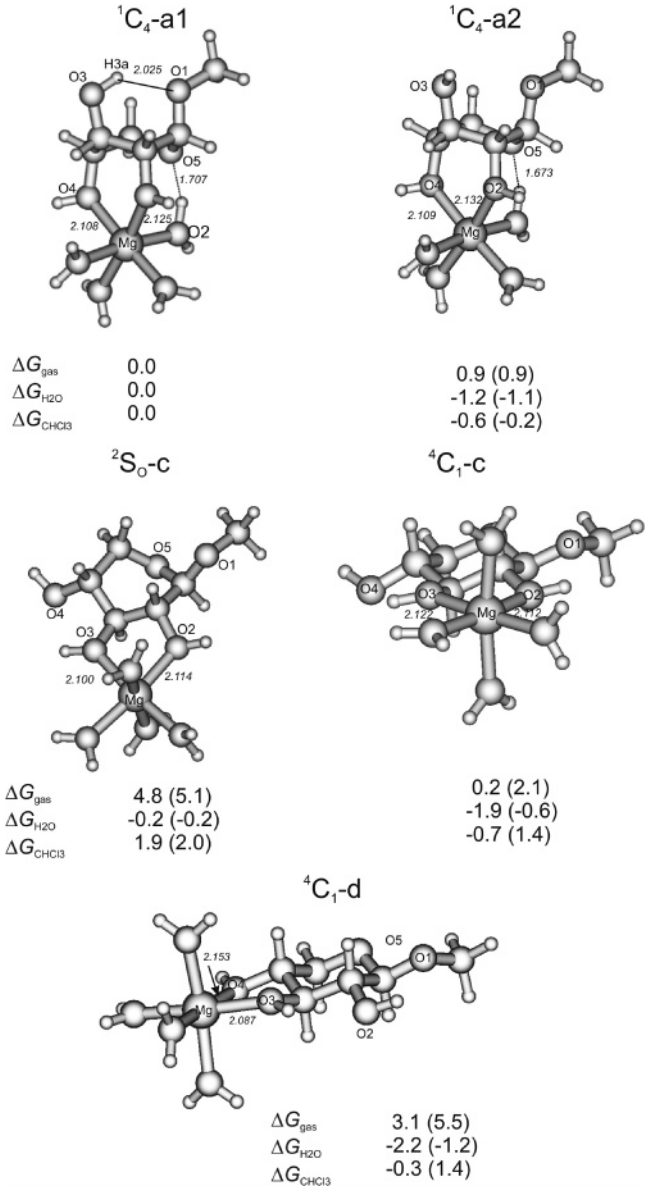


Figure 2. Calculated B3LYP/6-311++G(d,p) structures and relative Gibbs free energies ΔG (B3LYP/basis I ΔG values in parentheses) of representative conformations of cationic bridging complexes $[Mg(H_2O)_4\mathbf{1}]^{2+}$.

least stable ones. This holds for all phases (gas phase, $CHCl_3$, or H_2O solution) as well as all cations, Mg^{2+}, Ca^{2+}, Zn^{2+}, or Cd^{2+} (Tables 1 and Tables S1−S3 of the Supporting Information). Interestingly, in aqueous solution the relatively high-energy gas-phase structure **$^4C_1$-d**, becomes the most stable $[Mg(H_2O)_4\mathbf{1}]^{2+}$ species. In chloroform, however, binding of Mg^{2+} by O2 and O3 (**$^4C_1$-c**) is predicted to be competitive if not preferred, Table 1. Largely analogous results are found for the other cations. Skew conformations ^2S_O are predicted to be of minor importance in $[Mg(H_2O)_4\mathbf{1}]^{2+}$ complexes. Irrespective of the phase, the most favorable binding position in ^2S_O ring conformations is by O2 and O3 (**^2S_O-c**). On the basis of Gibbs free energies the same also holds for complexes of Ca^{2+}, Zn^{2+} as well as Cd^{2+} (Tables 1 and Tables S1−S3). Thus, there is little difference in the binding properties of methyl β-D-xylopyranoside toward the closed-shell divalent cations Mg^{2+}, Ca^{2+}, Zn^{2+}, and Cd^{2+}.

The prevailing gas-phase stability of $^1C_4$ chairs in the Mg^{2+} complexes upon saturation of the metal's coordination number by water molecules can be rationalized in terms of the calculated structures, Figure 2 and Table S4 in the Supporting Information. Magnesium−oxygen distances r(Mg−O) are in the range 2.09−2.15 Å [B3LYP/6-311++G(d.p); B3LYP/basis I distances are shorter by ≤0.015 Å], somewhat longer than those in "naked" Mg^{2+} complexes (1.88−2.01 Å, B3LYP/basis I).[3] In contrast, r(Mg−O5) > 3.4 Å in **$^1C_4$-a1** and **$^1C_4$-a2** compared with r(Mg−O5) = 2.0 Å in the triply coordinated complexes.[3] This rules out any Mg−O5 interaction. However, **$^1C_4$-a1** and **$^1C_4$-a2** are unique among the various $[Mg(H_2O)_4\mathbf{1}]^{2+}$ structures (Figure 2). Here, one of the water ligands coordinated to Mg^{2+} forms a hydrogen bond to the ring oxygen O5. No H-bond of this type is calculated for the other ring conformations. Apparently this hydrogen bond stabilizes the $^1C_4$ ring conformations of the Mg^{2+} complexes. Because a shorter H−O5 distance is calculated by B3LYP/basis I than by B3LYP/6-311++G(d,p), a more pronounced $^4C_1 \rightarrow {}^1C_4$ conformation interconversion upon metal binding is predicted by the former basis set (see Table S4). To put these numbers in context, we find r(O1−H3a) = 2.03 Å with both basis sets for the intramolecular O1··· H3a hydrogen bond. This H-bond has been suggested to be a key factor in stabilizing $^1C_4$ chairs of acylated xylose derivatives.[37] It is interesting to note that the hydrogen bond between a ligand water and O5 in $^1C_4$ structures also persists in three-water complexes $[Mg(H_2O)_3\mathbf{1}]^{2+}$; only if a further H_2O is removed, the Mg−O5 interaction can be observed in the calculated structures. Similar structures are also calculated for **$^1C_4$-a1** and **$^1C_4$-a2** ring conformations of Zn^{2+} and Cd^{2+} complexes. In contrast, for Ca^{2+} with its propensity to higher coordination numbers, a triply coordinated structure similar to that obtained without additional ligands, is calculated. This might explain the quite low energy of the **$^1C_4$-a2** structure for $[Ca(H_2O)_4\mathbf{1}]^{2+}$, Table S1. Note that in contrast to the other metal complexes—at least with basis I—this structure is also more stable in aqueous solution than **$^4C_1$-d**.

The increased **$^1C_4$-a2** stability in solution likely is due to interaction of the solvent with the "outward-pointing" O3−H3a group [torsion angle τ(C4−C3−O3−H3a) = 180°]. This interaction is not possible in **$^1C_4$-a1** where O3−H3a is oriented toward the anomeric oxygen O1 [τ(C4−C3−O3−H3a) = −85°]. Among all complexes, **$^4C_1$-d** has the highest calculated dipole moment. Thus, preferential stabilization of this species by polar solvents is expected. Accordingly, in aqueous solution, chelation of M^{2+}, M = Mg^{2+}, Ca^{2+}, Zn^{2+}, and Cd^{2+}, by the sugar's O3 and O4 oxygen atoms in the $^4C_1$ chair conformation, is predicted to be the preferred binding mode. Complexation of the cation by the anomeric and ring oxygen atoms, O1 and O5, in **$^4C_1$-a** or **^2S_O-a** requires the methoxy group to adopt the unfavorable *gauche*$^+$ instead of the preferred *trans* conformation[3,14d] resulting in quite high-energy structures. The structure of a α-D-xylose−$CaCl_2$·$3H_2O$ complex has been determined by X−ray crystallography.[39,40] α-D-xylose adopts the $^4C_1$ chair and Ca^{2+} is coordinated to O1 and O2 of one xylose molecule as well as O3 and O4 of a symmetry-related second xylose.[40] The calculated structure for the $CaCl_2$·$3H_2O$ complex with two molecules of α-D-xylose is presented in Figure 3. Also shown there is a section of the corresponding X-ray structure displaying the nearest neighbors around the Ca^{2+} cation (hydrogens are not given in the X−ray data).

Finally, it should be noted that in the course of geometry optimization some of the ring structures change their original starting conformation. For instance, pendant complexes of all four cations labeled as **^2S_O-e** and **$^1C_4$-a** actually are more properly characterized as boat conformations $B_{3,O}$ or skews $^3S_1$. Improper dihedrals[25] $\alpha_1 - \alpha_3$ and Cremer-Pople ring puckering

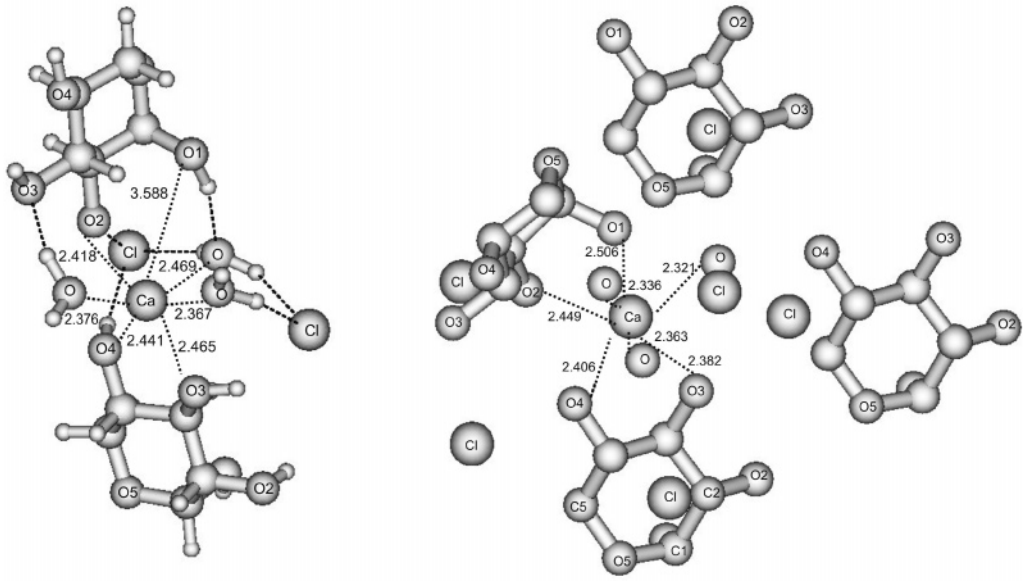


Figure 3. Comparison of the calculated (B3LYP/basis I, left) with the X−ray structure (right) of the α-D-xylose $CaCl_2$·3 H_2O complex.

parameters,[26] q, ϕ, and θ, used to describe the respective ring conformation[27] are presented in Table S12 for some representative structures.[28]

IV. Neutral Complexes. The initial structures of the neutral complexes $[M(OH)_2(H_2O)_x\mathbf{1}]$, $x = 2$ or 3, were generated by replacing two water molecules in the respective cationic complexes $[M(H_2O)_x\mathbf{1}]^{2+}$, $x = 4$ or 5, with two hydroxide anions. Consequently, the various isomers/conformers are designated in analogy to the original cationic complexes. However, in most if not all instances upon geometry optimization substantial reorientation of the $M(OH)_2(H_2O)_x$ moiety occurred. This led to calculated structures often bearing little resemblance to those of the parent cationic complexes. Representative structures are displayed in Figure 4. For comparability, however, we keep the notation used above for the $[M(H_2O)_x\mathbf{1}]^{2+}$ derivatives. In chloroform solution apparently only Ca^{2+} forms a stable complex $[Ca(OH)_2(H_2O)_3\mathbf{1}]$. No stable neutral pendant complexes at all are obtained in water (Table 3). Thus, the following discussion will be restricted to complexes of type $[M(OH)_2(H_2O)_2\mathbf{1}]$ and $[M^{2+}(H_2O)_4\mathbf{1}^{2-}]$.

Neutral Complexes [M(OH)₂(H₂O)₂1]. A previous computational study already had strongly indicated a change in the coordination number of magnesium ions upon replacing H_2O by hydroxide.[29a] We obtain a completely analogous result for $[M(OH)_2(H_2O)_4]$ not only in the case of $M = Mg^{2+}$ but also for $M = Ca^{2+}$, Zn^{2+}, and Cd^{2+}. Hydrated tetracoordinated metal hydroxides $[M(OH)_2(H_2O)_2]$·$2H_2O$ are calculated (B3LYP/basis I, aqueous solution) to be more stable than the corresponding hexa-coordinated structures $[M(OH)_2(H_2O)_4]$ by $\Delta G = 18$, 12, 20, and 21 kcal mol^{-1} for $M = Mg^{2+}$, Ca^{2+}, Zn^{2+}, and Cd^{2+}, respectively. The structures of all hydroxides $[M(OH)_2(H_2O)_2]$·$2H_2O$ correspond to that obtained by B3LYP/aug-cc-pVTZ calculations[29a] for $M = Mg^{2+}$. Consequently, the data discussed below have to be taken *cum grano salis*, especially because several of these "rearrangements" obviously are specific for coordinated water and might not occur for other ligands. Calculated relative Gibbs free energies for magnesium complexes $[Mg(OH)_2(H_2O)_2\mathbf{1}]$ are summarized in Table 4, those for the other metal ions in Table S8.

The lowest energy species, $^4\mathbf{C_1}$**-d1**, of $[Mg(OH)_2(H_2O)_2\mathbf{1}]$ complexes does not correspond to a chelated but rather to a pendant structure, Figure 4. It is characterized by interaction of Mg with O3 [r(O3−Mg) = 2.09 Å] and a hydrogen bond of

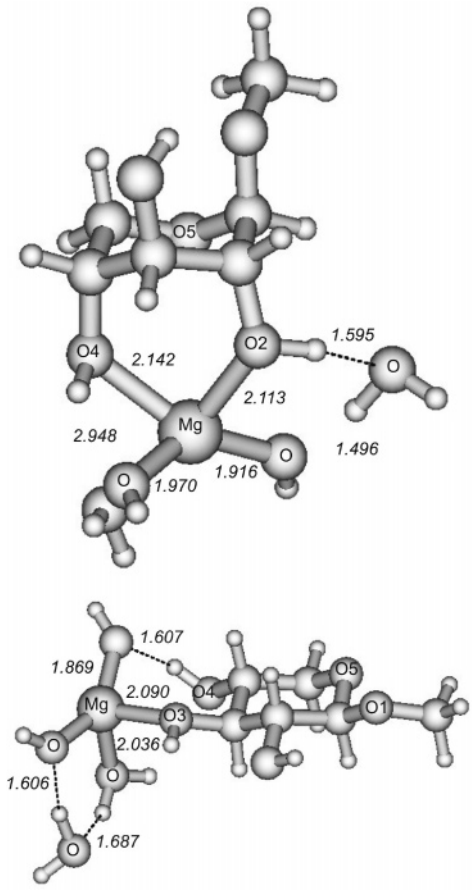


Figure 4. Calculated (B3LYP/basis I) structures of $^1\mathbf{C_4}$**-a1** and $^4\mathbf{C_1}$**-d1** conformations of neutral "bridging" complexes $[Mg(OH)_2(H_2O)_2\mathbf{1}]$.

O4-H and a hydroxide in $Mg(OH)_2(H_2O)_2$ [r(H4−O) = 1.61 Å]. Apparently there is no Mg−O4 interaction present [r(O4−Mg) = 3.04 Å]. A similar result is also obtained for the $^4\mathbf{C_1}$**-c** complex. In contrast, all $^1C_4$ and ^2S_O structures involve double coordination of the cation. The lowest energy *chelate* $^4C_1$ complex, $^4\mathbf{C_1}$**-d2**, is not only significantly less stable than $^4\mathbf{C_1}$**-d1** but also less stable than any of the $^1C_4$ structures. Magnesium and zinc $^2\mathbf{S_O}$**-d** structures are more properly designated as $B_{3,O}$ or $^1S_3$ (Table S12). The lowest energy $[Ca(OH)_2(H_2O)_2\mathbf{1}]$

TABLE 4: Relative Enthalpies (Δ*H*) and Gibbs Free Energies (Δ*G*, B3LYP/basis I, kcal mol^{-1}) for Neutral Mg^{2+} Complexes $[Mg(OH)_2\ (H_2O)_2\mathbf{1}]$[a]

	gas phase		H_2O	$CHCl_3$
	Δ*H*	Δ*G*	Δ*G*	Δ*G*
$^4C_1$−**d1**	0.0	0.0	0.0	0.0
$^1C_4$−**a1**	2.8	4.4	8.4	5.7
$^1C_4$−**b**	5.7	6.7	8.5	6.4
$^1C_4$−**a3**	7.4	8.6	10.4	8.7
$^4C_1$−**d2**	9.0	9.8	14.1	10.9
$^4C_1$−**c**	9.2	9.9	14.1	11.0
^2S_O−**c**	12.4	12.4	15.1	12.6
^2S_O−**d**	12.7	14.1	17.9	14.9
$^4C_1$−**b**	16.2	16.2	16.9	15.1
$^4C_1$−**a**	18.1	17.5	19.6	17.3
^2S_O−**b**	21.7	21.6	22.2	20.4
^2S_O−**a**	22.2	21.6	22.7	20.7

[a] B3LYP/basis I; Radii=UFF in IEF−PCM calculations.

TABLE 5: Relative Enthalpies (Δ*H*) and Gibbs Free Energies (Δ*G*, B3LYP/basis I, kcal mol^{-1})[a] for Neutral Mg^{2+} Complexes $[Mg(H_2O)_4\mathbf{1}^{2-}]$

	gas phase		H_2O	$CHCl_3$
	Δ*H*	Δ*G*	Δ*G*	Δ*G*
$^1C_4$-**a1**	0.0	0.0	0.0	0.0
$^1C_4$-**a2**	3.8	3.6	2.3	3.3
$^4C_1$-**d**	6.7	6.2	0.9	3.5
$^4C_1$-**d**	7.3	6.5	0.7	3.4
^2S_O-**c**	8.2	7.0	0.4	3.7
$^4C_1$-**c**	10.4	8.8	1.1	4.8
^2S_O-**c**	11.2	8.1	5.3	6.2
^2S_O-**d**[b]	13.4	11.6	4.6	7.7

[a] Radii=UFF in IEF−PCM calculations. [b] Better designated as $^1S_3$.

complex ($^1C_4$-**a1a**, Table S8) actually is a sugar−OH^- complex of type $[Ca(OH)(H_2O)_2\mathbf{1}(OH)]$ with a triply coordinated Ca^{2+} and one OH^- hydrogen bonded to O3-H and O4-H. No such structure is found for the other metal complexes, M = Mg^{2+}, Zn^{2+}, and Cd^{2+}. The corresponding $^1C_4$-**a1** calcium chelate complex is considerably less stable than $^1C_4$-**a1a** in the gas phase, $\Delta G = +6.9$ kcal mol^{-1}, Table S8. In solution this energy difference is greatly reduced, $\Delta G(CHCl_3) = +1.2$ kcal mol^{-1}, or even reversed, $\Delta G(H_2O) = -2.4$ kcal mol^{-1}. Single coordination of the metal cation to O3, *i.e.*, $^4C_1$-**d1**, is also obtained as the lowest energy structure for complexes of Zn^{2+}, and Cd^{2+}. Like the analogous Mg-complex, for Zn^{2+} the $^4C_1$-**c** conformation is characterized by sole interaction of the cation with O2, but with significantly lower energy (Table S8). In contrast, all $[Ca(OH)_2(H_2O)_2\mathbf{1}]$ complexes are chelates. Here, the various structures $^4C_1$−d1, $^4C_1$-**d2**, and $^4C_1$-**d3** differ only in the position/orientation of the OH^- groups. For *chelate* $[M(OH)_2(H_2O)_2\mathbf{1}]$ complexes, binding of Mg^{2+} and Cd^{2+} leads to a greater stability of $^1C_4$ ring structures, $^1C_4$-**a1** and/or $^1C_4$-**b**, Tables 4 and S8. $^4C_1$ structures are preferred for Ca^{2+} (especially in solution $^4C_1$-**d1**) and Zn^{2+} complexes ($^4C_1$-**b**), Table S8.

Chelated Neutral Complexes [M(H$_2$O)$_4$1]. Relative energies of different conformations and binding positions for neutral complexes between Mg^{2+} and doubly deprotonated methyl β-D-xylopyranoside $\mathbf{1}^{2-}$ are summarized in Table 5, those for Zn^{2+} and Cd^{2+} in Table S11. Despite several attempts, no stable Ca^{2+} complexes of this type could be found. In each case $^1C_4$-**a1** structures of the complexes are the most stable ones in the gas phase. In aqueous solution, $^4C_1$-**d** (Mg^{2+}, Cd^{2+}) and/or $^4C_1$-**c** (Zn^{2+}) as well as ^2S_O-**c** structures are preferentially stabilized. Despite this stabilization, for Mg^{2+} and Zn^{2+}, $^1C_4$ structures are still lower in energy than $^4C_1$ conformations. However, Zn^{2+} complexes of this type are not stable in solution, $\Delta G_{int} > 0$, Table 3. For Cd^{2+} complexes in both aqueous and chloroform solution the $^4C_1$-**d** structure is more stable than $^1C_4$-**a1** (Table S11). Thus, if at all, only for complexation of Mg^{2+} by doubly deprotonated methyl β-D-xylopyranoside $\mathbf{1}^{2-}$ a shift of the $^4C_1 \leftrightarrow {}^1C_4$ equilibrium could be possible.

Conclusions

Density functional calculations (B3LYP) using the LANL2DZ basis set augmented by polarization and diffuse functions on oxygen and hydroxyl hydrogen atoms (basis I), and the standard 6-311++G(d,p) basis have been performed on complexes of biologically and environmentally relevant divalent metal cations, M = Mg^{2+}, Ca^{2+}, Zn^{2+}, and Cd^{2+}, with $^4C_1$, $^1C_4$, and ^2S_O ring conformations of methyl β-D-xylopyranoside **1**. The influence of additional metal coordination (6-fold coordination) was assessed by using H_2O as a model ligand. Bridging and pendant cationic, $[M(H_2O)_4\mathbf{1}]^{2+}$, $[M(H_2O)_5\mathbf{1}]^{2+}$ as well as neutral complexes, $[M(OH)_2(H_2O)_2\mathbf{1}]$ and $[M(OH)_2(H_2O)_3\mathbf{1}]$, as likely species in weakly acidic and basic solution, respectively, were considered. In addition, neutral complexes resulting from binding to the doubly deprotonated sugar, $[M(H_2O)_4\mathbf{1}^{2-}]$, were treated. The main focus is on the effect of metal complexation on the stability of the various sugar ring conformations, $^4C_1$, $^1C_4$, and ^2S_O. No attempt has been made to study the mechanism of a possible metal complexation induced ring interconversion.[41] Results obtained by the two basis sets used, basis I and 6-311++G(d,p), closely agree with each other. The B3LYP/6-311++G(d,p) procedure generally leads to a larger stability of the $^4C_1$ ring conformation and smaller tendency to complex formation. In contrast to complexation of bare metal cations,[3] relevant to gas-phase reactions, *e.g.*, in mass spectrometric oligosaccharide analysis,[4,10,42] additional ligands greatly diminishes the sugar−metal interaction energy (eq 1−3). In addition, the propensity to a metal-binding induced shift of the $^4C_1 \leftrightarrow {}^1C_4$ conformation equilibrium is greatly reduced. Blocking of the interaction between the cation and O5 of the sugar likely is the main reason for this effect. Apparently, the stabilizing hydrogen-bonding between a water ligand and O5 in $^1C_4$ structures cannot overcome the "blocking" effect of the ligand. Inclusion of solvent effects ($CHCl_3$ and H_2O) further decreases the stability of cationic complexes. With the possible exception of Ca^{2+} in $CHCl_3$, actually none of the cationic pendant complexes $[M(H_2O)_5\mathbf{1}]^{2+}$ is predicted to be stable in solution ($\Delta G_{int} > 0$). Bridging cationic complexes $[M(H_2O)_4\mathbf{1}]^{2+}$ were found to be stable in solution, $\Delta G_{int} < 0$, especially in water. The tendency to a $^4C_1 \leftrightarrow {}^1C_4$ shift decreases with solvent polarity. In aqueous solution $^4C_1$ complexes with binding of the metal by O3 and O4 are the lowest energy structures. Similarly, neutral pendant complexes $[M(OH)_2(H_2O)_3\mathbf{1}]$ appear to be unstable both in the gas phase and in solution with the possible exception of Ca^{2+} complexes in $CHCl_3$. Neutral complexes of type $[M(OH)_2(H_2O)_2\mathbf{1}]$ result to be stable in solution, especially in H_2O. Irrespective of the phase, $[M(OH)_2(H_2O)_2\mathbf{1}]$ adopt the $^4C_1$ ring structure $^4C_1$-**d**. Although formally of bridging complex stoichiometry, actually only one oxygen atom of the sugar (O3) is coordinated to the cation; the hydrogen atom of the second sugar−OH group (O4) is hydrogen-bonded to the OH^- ligand. Thus, these complexes more closely resemble pendant structures. No neutral Ca^{2+} complexes resulting from doubly protonated methyl β-D-xylopyranoside $\mathbf{1}^{2-}$ could be found. Zinc complexes are barely stable, $\Delta G_{int} > 0$. In contrast, both Mg^{2+} and Cd^{2+} cations form stable complexes $[M(H_2O)_4\mathbf{1}^{2-}]$

in solution, especially in H_2O. Whereas binding of Cd^{2+} results in **$^4C_1$-d** as the most stable complex structure, interaction of methyl β-D-xylopyranoside with Mg^{2+} to form $[Mg(H_2O)_4\mathbf{1}^{2-}]$ possibly could result in $^1C_4$ complex structures. Finally, it should be reiterated that H_2O has been used as a ligand model and not to describe the first solvation shell.[43] Therefore, some of the structural aspects important for relative ring conformation stability will be specific for this ligand.

Acknowledgment. S.K. thanks the Higher Education Commission of Pakistan for a scholarship.

Supporting Information Available: Tables of relative enthalpies and Gibbs free energies for cationic bridging complexes $[M(H_2O)_4\mathbf{1}]^{2+}$ (Tables S1−S3), and pendant complexes, $[M(H_2O)_3\mathbf{1}]^{2+}$ (Tables S5−S7), neutral bridging $[M(OH)_2(H_2O)_2\mathbf{1}]$ (Table S8) and pendant complexes $[M(OH)_2(H_2O)_3\mathbf{1}]$ (Tables S9−S10), and neutral complexes $[M(H_2O)_4\mathbf{1}]$, M = Ca^{2+}, Zn^{2+}, and Cd^{2+} (Table S11). Selected distances and ring puckering parameters are given in Table S4 and S12. Basis set effects on calculated relative conformer Gibbs free energies are illustrated in Figure S1. This material is available free of charge via the World Wide Web at http://pubs.acs.org.

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