



Understanding the interactions between hydrogen-bonded complexes of xylose and water: Quantum Chemical Investigation

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Abstract. Hydrogen-bonded complexes between xylose and water, modelled by xylofuranose...H₂O complexes were explored employing *ab initio* quantum chemical framework. The Møller–Plesset second-order perturbation theory (MP2) in conjugation with aug-cc-pVDZ basis set, is used for investigating the H-bonding interactions. The complete basis set limit interaction energies for α - and β -xylofuranose and xylopyranose water complexes were calculated at MP2 level. It is observed that the addition of water molecule does not change the conformational structure of xylose moieties. Further water is found to interact with xylose mainly through the O atom present in a ring and its neighboring OH group. Energy decomposition analysis by LMO-EDA approach indicates that the electrostatic and exchange interactions are the two largest contributing terms to the total interaction energy for bonding between Xylose and water.

Keywords. Xylofuranose; xylopyranose; EDA; frequency; critical point.

1. Introduction

Water being the universal solvent, its role in various processes has always attracted a great deal of research. One of the main research topics is the role of the water molecule in the vicinity of solute molecules, which has a wide range of applications in different disciplines such as environmental science, electrochemistry, surface science, biochemistry, drug designing and many more.^{1–3} Molecular hydration investigation provides valuable insights and information on various properties of molecules such as solubility, hydrophobicity, etc.^{1–9} The molecular hydration has special significance for biological molecules because the natural environment in for them is aqueous. Among many biological systems, carbohydrates are of particular interest because they are the prime source of energy and they form the main backbone of DNA and RNA. Further carbohydrates have significance in the recognition of N-linked glycans by carbohydrate-binding proteins.^{5–9} In particular, xylans, known as wood sugar, are of importance because xylose is the characteristic building block in N-linked glycans in plants and invertebrates. In nature, xylose is generally found in plants and also in mammalian cell surface

structures, such as proteoglycans.¹⁰ The xylopyranosides are found to initiate the biosynthesis of soluble GlycosAminoGlycan (GAG) chains and they are also found to function as inhibitors for enzymes in the biosynthesis of proteoglycans.¹⁰ These are some among many, are the reasons why xylose has attracted a great deal of research interest.

The following section represents some of the key studies on xylose-water interactions using experimental as well as computational techniques. Simon and co-workers,¹¹ performed infrared (IR) spectroscopy as well as density functional theory (DFT) investigations on mono-hydrates of α - and β -phenylxylopyranosides. According to this study, the water molecule occupies the position where it can replace existing interactions and generate stronger hydrogen bonds. They also observed that the xylose hydration retains the trans configuration of the molecule/s.¹¹ Extending the previous work, Simon and co-workers,¹² also investigated singly and doubly hydrated complexes of o-phenyl α - and β -anomers of glucose, galactose, fucose and xylose. In this work, they have generated the hydrated structures of carbohydrates in a cold molecular beam and probed them through infrared ultraviolet double resonance ion-dip (IRID) spectroscopy and quantum mechanical

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calculations.¹² It was found that the co-operative hydrogen bonding, bi-furcated and OH... π hydrogen bonding and dispersion interactions are the main governing effect associated with hydration of carbohydrates. Another work reports the investigation of conformation and structure of monohydrates of fucopyranosides by using resonant two-photon ionization (R2PI) spectroscopy and quantum chemical calculations within MP2 and DFT framework.¹³ In this work, they have also carried out the comparison of the spectra and structures of conformations of phenyl substituted α/β anomers of monosaccharides. They concluded that the conformational flexibility, complexity and nature of the interaction between water and the anomeric oxygen are the deciding factors conformational choice of the hydrates of monosaccharides.¹³

In a recent investigation Çarçabal *et. al.*,¹⁴ have studied the complexes between water molecule and O-phenyl substituted monosaccharide's by using UV-UV ionization and dissociation experimental methods. They have also calculated the binding energies of the monohydrates of monosaccharides at the RI-B97D+disp/TZVPP DFT framework. It was found that the binding energies of the fully cooperative structures are larger than those of the non-fully cooperative structures.¹⁴

All the above-mentioned works are focused on the structural aspects of the carbohydrate-water complexes and almost no study has commented on the nature of the interaction. In the present work, the xylose-water complexes have been studied by *ab initio* quantum chemical calculations. The complete basis set limit (CBS) interaction energies were calculated at Moller-Plesset Second Order (MP2) level. The contributions from various components to the total interaction energy were calculated by energy decomposition analysis. Further, the interactions have also been studied by frequency shift and molecular electron density critical points.

2. Computational methodology

The xylose-water complexes have been studied at MP2 by using Dunning's¹⁵ augmented correlated consistent basis set *viz.*, aug-cc-pvdz. The alpha and beta anomers of five and six-membered forms of xylose were chosen for this purpose. Initially, all the four isomers of xylose were optimized at MP2/aug-cc-pvdz level of theory. From these structures, various starting structures of complexes with water were generated for each isomer. These structures were generated by using the lock and key model based on

the molecular electrostatic potential (MESP) guidelines.^{16–18} The structures thus generated were subjected for geometry optimization using Gaussian 16 suite of programs.¹⁹ The lowest energy structures of each isomer were chosen for analysis. In order to confirm their minimal nature, vibrational frequency calculation was carried out.

Further, the localized molecular orbital energy decomposition analysis (LMOEDA), was carried out for each lowest energy complex, as available in GAMESS Package.^{20,21} The molecular electron density (MED) critical points corresponding to H-bonding between water and xylose have also been calculated by DAMQT software.²² The results thus obtained are discussed in the following section.

3. Results and Discussion

As mentioned above the interactions present in xylofuranose- and xylopyranose-water complexes were investigated at the MP2/aug-cc-pvdz level of theory. The MP2 level optimized geometries of all complexes are displayed in Figure 1.

It may be seen from Figure 1 that, in all complexes (except β -xylofuranose), the water molecule is H-bonded to 'O' atom present in xylose ring and OH group attached to its neighboring carbon atom. In the case of β -xylofuranose-water complex the water molecule interacts with the two OH groups (Figure 1). One of the OH groups is attached to -CH₂ and other is attached to the ring carbon atom (Figure 1). In case of both isomers of xylopyranose also, the water molecule interacts through the O atom in ring and its neighboring OH group. It is found that both in furanose and pyranose rings, added water molecule incorporates the co-operativity by the formation of a sequence of hydrogen bonds. Here the hydrogen bonds are formed due to rotation of one of the OH groups which are attached to the ring (both furanose and pyranose) carbon atoms. It is worth to note here that the addition of water molecule to xylose doesn't change the conformational structure of isolated xylose ring.

In the literature, there is no work which investigates hydration of five-membered ring *viz.*, Xylofuranose. Investigations on water-pyranose complexes have been reported in the literature.^{11,13} Simon and co-workers have reported that for phenyl-substituted xylopyranose, where water interact through two OH groups and forms co-operative sequence of hydrogen bonds. However, in the current work, it is seen that the water molecule binds to xylopyranose ring through 'O' atom in a ring and forms a co-operative sequence of

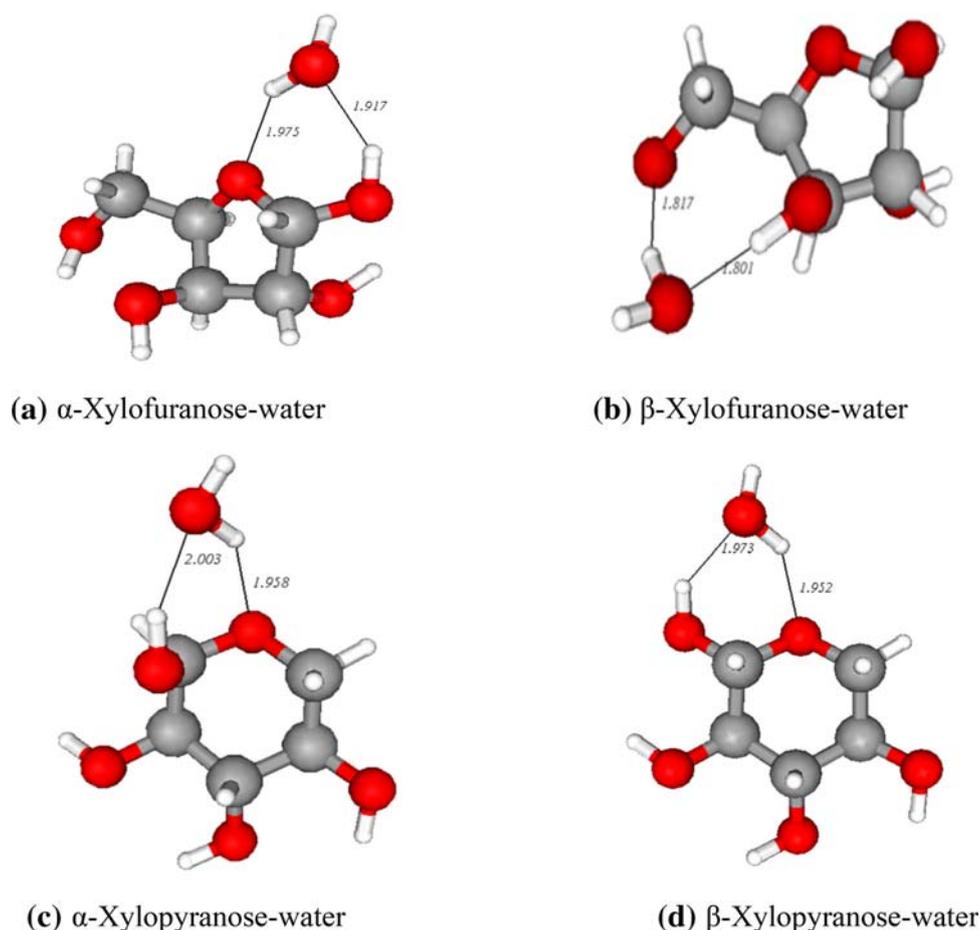


Figure 1. Optimized structures of α & β -Xylofuranose-water complex and α & β -Xylopyranose-water complex at MP2/aug-cc-pVDZ level of theory.

hydrogen bonds. This difference in the way of bonding with water is because in the work by Simon and co-worker, they use Phenyl-substituted xylose and the bulky phenyl group have almost blocked the side from ring O atom. However, the observations in current work are in agreement with the literature^{11,13} that addition of water incorporates co-operative effects (sequence of hydrogen bonds) in the complex which is responsible for stabilization the complex.

The complete basis set limit interaction energies for these complexes have been obtained by Helgakare's two-point method²³ and the energies thus obtained are

Table 1. Complete basis set limit interaction energies (kcal/mol) of a xylose-water complex at MP2 Level.

Complex	ΔE
α -Xylofuranose	-19.73
β -Xylofuranose	-12.19
α -Xylopyranose	-9.16
β -Xylopyranose	-9.49

reported in Table 1. It was observed that the xylofuranose-water complexes are energetically favorable than xylopyranose-water complexes. This shows that xylofuranose form has more affinity towards water than the six-membered xylopyranose. It may be seen from Table 1 that the α -xylofuranose-water complex is energetically favorable over β -anomer complex by 7.6 kcal/mol. This, in turn, suggests that the incoming water molecule favors the single directed (at 'O' atom) than the two bifurcated H bonds as in β -anomer complex (Figure 1). Further in α -xylofuranose-water complex two hydrogen bonds are formed by rotation of two OH groups. On the other hand, in case of β -anomer, only one bond is formed due to the rotation of one OH bond. The lower interaction of α -xylofuranose-water complex is because of this extra hydrogen bond formed due to co-operativity. In the case of six-membered xylopyranose both the, α and β complexes interaction energies are found to be comparable (within 0.33 kcal/mol in case of MP2). Hence also the 'O' in water has formed the single directed H-bond with the H atom in OH group.

Table 2. Energy decomposition analysis of the xylose-water complex at MP2/aug-cc-pvdz level of theory.

	α -Xylofuranose	β -Xylofuranose	α -Xylopyranose	β -Xylopyranose
ΔE_{Es}	-17.27	-23.10	-15.77	-16.59
ΔE_{Ex}	-20.70	-28.64	-18.98	-19.89
ΔE_{Rep}	37.68	52.49	34.25	36.08
ΔE_{Pol}	-5.68	-8.94	-4.78	-5.11
Dispersion Energy	-2.86	-11.65	-2.98	-2.95

In order to investigate the nature of the interaction between xylose and water molecule, the localized molecular orbital energy decomposition analysis (LMO-EDA) has been carried out for the lowest energy structures of all the four complexes at MP2/aug-cc-pvdz level. In the LMO-EDA method by Su and Li,²⁰ the total interaction energy is decomposed into electrostatic, exchange, repulsion, polarization, and dispersion terms. The contributions towards the total interaction energy due to different components are reported in Table 2. The EDA analysis shows that in all the xylose-water complexes electrostatic (E_{Es}) and exchange (E_{Ex}) terms contribute more towards the stabilization of water-xylose complexes. On the other hand, the repulsion term is seen to destabilize the total interaction with a much higher contribution. However, the destabilization caused by the repulsion term is compensated by electrostatic (E_{Es}) and exchange (E_{Ex}) terms collectively. For example, in the α -xylofuranose complex, E_{Es} and E_{Ex} contributions are -17.27 kcal/mol and -20.70 kcal/mol. Adding these contribution yield higher value (with opposite sign) than the E_{Rep} term which is 37.68 kcal/mol. It is worth noting that the polarization contribution (less than or equal to -9.22 kcal/mol) to total interaction energy is low in all cases. This shows that in this interaction, there may be a very small overlap between the orbitals of participating atoms and hence the interaction is far from forming a covalent bond. This may be due to the large distance between the interacting atoms (between 1.8 and 2.0 Å in all cases). Thus, the more contribution from E_{Es} and E_{Ex} while low E_{Pol} suggest that the interaction is mainly a long-range non-covalent governed by coulombic (electrostatic) attraction.

Vibrational frequencies of isolated and monohydrated α - and β - xylofuranose and xylopyranose were calculated at MP2/aug-cc-pvdz level of theory. The stretching frequency of neighboring OH to the O atom in a Xylose ring was monitored for the formation of H bond between Xylose and water and the frequencies thus calculated are listed in Table 3. In all the cases the stretching frequency of O—H bond shows redshift after complexation. As discuss above

Table 3. Vibrational frequencies of OH stretching Xylose ring before and after forming a complex with water at MP2/aug-cc-pvdz level of theory.

Complex	Frequency (cm^{-1})	
	Isolated	Complex
α -Xylofuranose	3815	3616
β -Xylofuranose	3714	3701
α -Xylopyranose	3799	3683
β -Xylopyranose	3807	3669

structure of complexes, in the α -anomer of both the form of xylose the OH bond is nearer to the water molecule and hence may be taking part actively in H bonding. This could be the reason for a larger shift in frequency after forming complex than that of β -anomer.

In isolated α -xylofuranose molecule, the OH frequency is observed to be 3815 cm^{-1} which is found to reduce by 200 cm^{-1} after forming complex (*cf.* Table 3). However, in the case of β -xylofuranose-water complex the water molecule is not forming interaction with the said OH. Hence the shift in frequency is only 13 cm^{-1} much smaller than that of α -anomer. In this case, the shift (of 13 cm^{-1}) may be due to the participation of OH group in the intramolecular H-bonding. In the case of an isolated α -xylopyranose molecule, the OH stretch frequency is found to be 3799 cm^{-1} which is red-shifted to 3683 cm^{-1} after forming a complex with water. On the other hand, in the case of the β -anomer complex, the OH frequency is smaller by 138 cm^{-1} than that of the isolated molecule (*cf.* Table 3).

The scalar field of molecular electron density (MED) has been widely used scalar field over the past four decades by Bader and co-workers²⁴ through their fundamental and exhaustive investigation, which has culminated into the celebrated atoms in molecules (AIM) theory. These studies have revealed that a chemical bond is represented by (3,-1) CP.^{24,25} The interaction between water and xylose is further

investigated by calculating the MED critical points (CPs) employing DAMQT software.²² The structures showing CPs obtained for water-xylose interactions are displayed in Figure 2. As these figures indicate, in α -xylofuranose, α - and β -xylopyranose complexes, (3,−1) bond CP is obtained for the interaction between ‘H’ atom of OH in xylose and ‘O’ atom in the water molecule. This supports our earlier discussion that the interaction in the aforementioned three complexes is through ‘O’ atom present in xylose ring and OH group attached to its neighboring carbon atom. However, in the case of β -xylofuranose, there is no interaction between water and O atom in a ring. But the water is interacting through two OH groups.

It is worth noting that the electron density value (0.051 a.u.) at the OH...O hydrogen-bond CP in α -xylofuranose is higher than both the CP values (0.032 a.u. and 0.034 a.u.) for OH...O interaction in β -xylofuranose (Figure 2). In the case of α -xylopyranose, the OH...O hydrogen-bond CP exhibits density value as 0.043 a.u. whereas in the β -isomer complex it is 0.023 a.u. This again shows that the OH...O interaction is stronger in the case of α -isomer, revealing that the OH of α -isomer is taking part actively in the interaction than the β -isomer.

4. Conclusions

The study of biological molecules in the vicinity of water has a special significance because the natural environment for them is aqueous. Further, carbohydrates are known to play a crucial role in the recognition of N-linked glycans by carbohydrate-binding proteins, and this process occurs in the presence of water. In view of this, it is important to study the behavior of carbohydrate in the presence of water molecules.

In the present work, the nature of the interaction between α and β xylofuranose and xylopyranose-water complexes were investigated at MP2/aug-cc-VDZ and MP2/CBS levels of theory. The calculated CBS limit interaction energies of xylofuranose complexes are found to be lower than the xylopyranose complexes. It was found that the added water molecule incorporates the co-operativity effects in both five and six-membered xylose ring by forming the sequence of hydrogen bonds. This shows that the five-membered ring of xylose has more affinity towards water than the six-membered xylose form. It is observed that the addition of water molecule doesn't seem to change the conformational structure of xylose moieties. Further water is

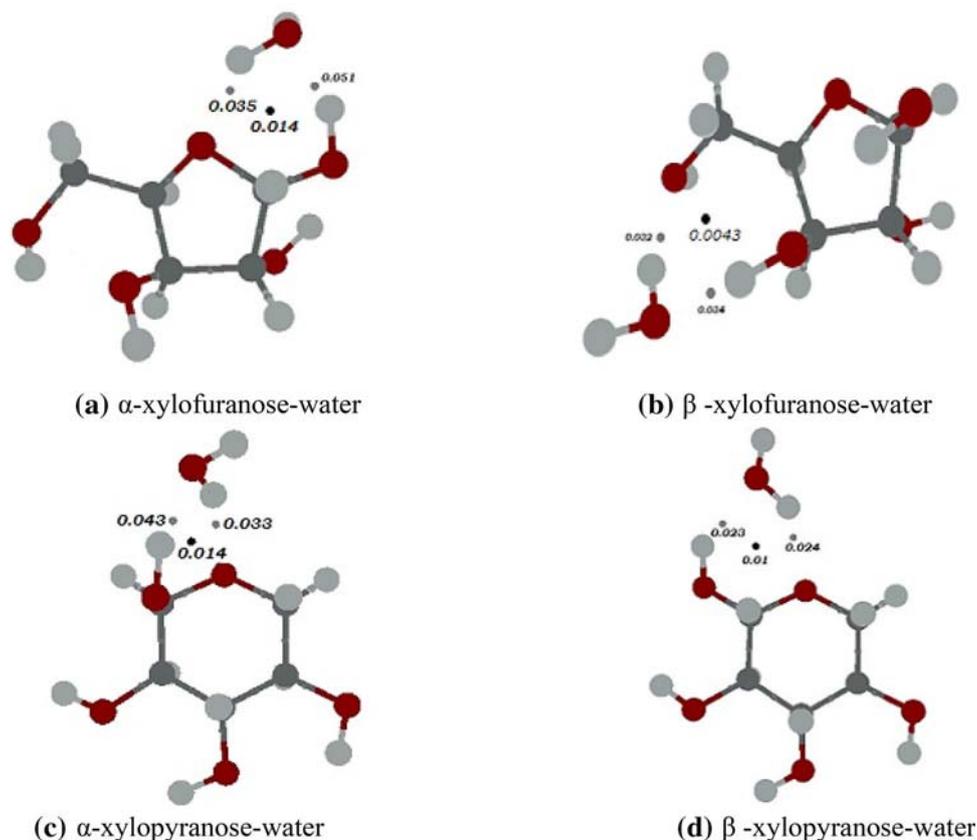


Figure 2. Molecular Electron Density (3,−1) critical points calculated at MP2/aug-cc-pvdz level of theory.

found to interact with Xylose moiety mainly through the 'O' atom present in a ring and its neighboring OH group. This observation is further supported by vibrational frequency analysis and electron density critical point calculation. Energy decomposition analysis shows that interaction between xylose-water complex have more Es and Ex contribution and these may be responsible for the stabilization of interaction between water and xylose. Further, the EDA analysis suggests that the water-xylose interaction is electrostatic governed long-range non-covalent interaction. It is hoped that this work is useful and may act as an impetus for further investigation in this field. It is also hoped that further investigation in this direction would help shed light on the role of water during protein-carbohydrate interaction.

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