Glycosidic linkage conformation of methyl-α-mannopyranoside

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We study the preferred conformation of the glycosidic linkage of methyl-α-mannopyranoside in the gas phase and in aqueous solution. Results obtained utilizing Car–Parrinello molecular dynamics (CPMD) simulations are compared to those obtained from classical molecular dynamics (MD) simulations. We describe classical simulations performed with various water potential functions to study the impact of the chosen water potential on the predicted conformational preference of the glycosidic linkage of the carbohydrate in aqueous solution. In agreement with our recent studies, we find that results obtained with CPMD simulations differ from those obtained from classical simulations. In particular, this study shows that the *trans* (t) orientation of the glycosidic linkage of methyl-α-mannopyranoside is preferred over its *gauche anticlockwise* ($g-$) orientation in aqueous solution. CPMD simulations indicate that this preference is due to intermolecular hydrogen bonding with surrounding water molecules, whereas no such information could be demonstrated by classical MD simulations. This study emphasizes the importance of *ab initio* MD simulations for studying the structural properties of carbohydrates in aqueous solution. © *2008 American Institute of Physics*. [DOI: 10.1063/1.2958916]

I. INTRODUCTION

Carbohydrates play an important role in many physiological processes such as energy storage, growth of cellular components, and control of water in cold- and drought-resistant organisms.[1] Adherence of bacteria by their surface lectins to host epithelial cells is considered an important event in bacterial pathogenesis;[1(b)] mannose-α-specific fimbriae are among the most commonly found lectins in enterobacteria. Important studies, such as the impact of α-mannopyranoside on the agglutination of various organisms, require a deep knowledge of the structure and conformation of the carbohydrate. High mannopyranoside precursors are found on the glycosylation sites of glycoproteins and the biosynthesis and insertion of vesicular virus G protein into membranes for probing the membrane assembly behavior of glycoproteins require knowledge of the carbohydrate conformation.[1(c)] Understanding the factors that influence a specific conformational stability of carbohydrates is challenging due to short time scales, small molecular distances, and the many torsional degrees of freedom present. Furthermore, the interaction mechanism between a carbohydrate and solvent medium that leads to the stabilization of certain conformations of the solvated biomolecule is not understood.[2–4]

Carbohydrate conformation is assumed to be determined by steric interactions and inter- and intramolecular hydrogen bonding. Understanding the impact of solvation on the conformational preference of methyl-α-mannopyranoside would be of general utility in studying various biological processes, such as the design of the biomembranes of secondary cell wall polymers of bacteria that have methyl-α-mannopyranoside as primary components or glycoproteins that have α-mannopyranoside as precursor active sites toward viruses.

The impact of intermolecular hydrogen bonding on the conformation of a solute in solution can be studied by numerous experimental techniques including extended x-ray absorption fine structure (EXAFS), x-ray, and neutron diffraction to obtain direct structural information and NMR, IR, and Raman spectroscopies to investigate dynamical information;[5] still, direct measurements of the local electronic environment are immensely challenging. X-ray analyses of liquids have provided some limited structural details that have been used to determine pair correlation functions; however, these functions have the disadvantage of being spherically averaged and thus it is very difficult to determine details of solvent structuring around carbohydrates, as most information involved with the asymmetric and anisotropic character is lost.[6,7]

Classical molecular dynamics (CMD) and Monte Carlo simulations have been proven to be powerful tools for studying the hydration structure of solutes.[8,9] However, their accuracy strongly depends on the quality of the interaction potential functions. Difficulties achieving accurate results for carbohydrates utilizing force field parameters have been reported, e.g., incorrect representation of the $\alpha(1\rightarrow6)$ linked oligosaccharides and misleading relative populations for some carbohydrates.[10,11] Recently, we studied the conforma-

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