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Theoretical study on conformations of glucose and trehalose in the gas phase and in aqueous solution

Taiki Yoshikawa,[1,2] Dai Akase,[1,2] Misako Aida[1,2]

[1] Department of Chemistry, Graduate School of Science, Hiroshima University
[2] Center for Quantum Life Sciences, Hiroshima University

Introduction

Trehalose is a non-reducing disaccharide composed of two D-glucose units linked by a 1,1-glycosidic linkage. There are three possible isomers of trehalose, generally "trehalose" indicates α,α-trehalose composed of two α-D-glucose units (Fig.1). It has been known that trehalose may induce extraordinary stabilization of biological materials. Trehalose has a number of conformers because it has 12 rotatable bonds, including 8 OH groups, the glycosidic linkage, and CH_2OH groups. In this work, we investigate several conformations of glucose and trehalose in the gas phase and in aqueous solution.

Mothods

In the gas phase, comprehensive conformational search of glucose and trehalose was performed using ab initio MO theory (glucose: MP2/aug-cc-pVDZ, trehalose: MP2/6-31G*). All conformations of glucose and trehalose were fully optimized, confirming that no imaginary frequencies were found in the vibrational calculations. Twenty-two optimized conformers of glucose and 104 optimized conformers of trehalose were obtained.

In aqueous solution, QM/MM-MD simulations for glucose and trehalose molecules were performed using a droplet model. In QM/MM calculations, a sugar molecule (QM) and *m* TIP3P water molecules (MM) were treated. As an initial structure of the QM part, one of the optimized conformers of glucose or trehalose in the gas phase was used. After simulated annealing processes, QM/MM-MD simulations were performed with the NVT ensemble at 300 K and 1 g/cm^3.

Results and Discussion

In the gas phase, α-anomer of a conformer of glucose is more stable than its β-anomer. For trehalose, the most stable conformer is the one that is composed of the most stable conformer of glucose. In some conformers of trehalose, inter-residue hydrogen bonds are formed. The relative stabilities of trehalose conformers can not be estimated straightforwardly from the stabilities of the constituting glucose units.

In aqueous solution, the stabilities of conformers of glucose or trehalose mainly depend on intermolecular hydrogen bonds between a solute and solvent. In glucose aqueous solution, around 30 water molecules are found in 3.5 Å from glucose molecule. In trehalose aqueous solution, around 45 water molecules are found in 3.5 Å from the trehalose molecule. Various intra- and inter-residue hydrogen bond networks are formed in trehalose aqueous solution. The characteristic inter-residue hydrogen bond network from O2 to O4' in trehalose is formed. (Fig. 2)

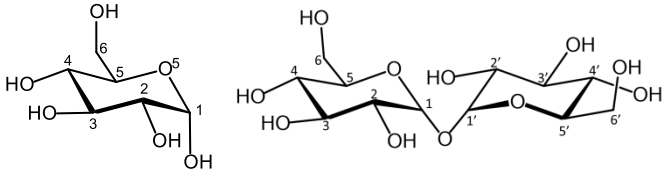

Fig. 1 Chemical structures of α-glucose molecule and α, α -trehalose molecule with atom labelings.

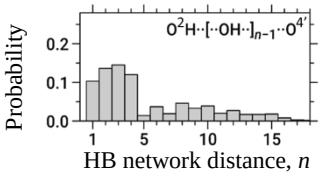

Fig. 2 The distribution of the inter-residue hydrogen bond network distance *n* in trehalose.