Pressure Effects on the Dewetting Behaviors of Deep-Cavity Cavitands

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Introduction

Cavitands are supra-molecular host molecules with a bowl-shaped-like cavity that allows them to bind guests in 1:1, 2:1, 2:2 as seen in Figure 1. Cavitands can also form larger complexes such as hexamer and tetramer structures. The composition and conformation of the rim of the cavity greatly affects the behavior of the cavitand, particularly in its dewetting properties. The hydrophobicity of the pocket also causes the cavitand to behave as a molecular scale nonpolar surface. The effects of dewetting are important in the further development of cavitands for new separation techniques, nano-scale reactors, and as a probing tool in protein chromophores[1].

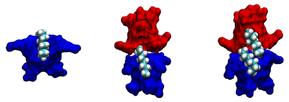

Fig.1: Shown here are a 1:1, 2:1, and 2:2 host-guest complex. The formation of the complexes primarily depends on the size of the guest.

The dewetting effect follows that if the contact angle- the angle formed by the tangent of the droplet with the surface- is larger than 90° then the surface is hydrophobic while if the contact angle is less than 90° then the surface is considered to be hydrophilic and is considered wetted.

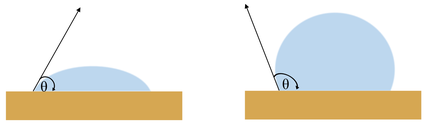

Fig.2: The water droplet on the left demonstrates water's response to a hydrophilic surface where the water droplet on the right has bubbled up or dewetted in response to a hydrophobic surface.

Simulation Methods

In the molecular simulations of the deep-cavity cavitands, the package GROMACS 5.1.3 was used. TIP4PEW model was used to simulate water and general amber force field (GAFF) was used to simulate the cavitands. In the simulations, the cavitands MEMOA, DEMOA, Tri-EMOA, TEMOA, TEXMOA, TEMOA-OH, and TEXMOA-OH were held at a constant temperature of 298.15 K. The system was simulated under a range of pressures from -500 bar to 2500 bar in 500 bar increments, and 1 bar was used in place of 0 bar. The simulation of the cavitand included 3000 water molecules. The net charge of each cavitand was set to be -6e due to six of the eight carboxylic groups being deprotonated to match the expected protonation state at pH 7. Six sodium ions were included in the simulation to neutralize the host charge.

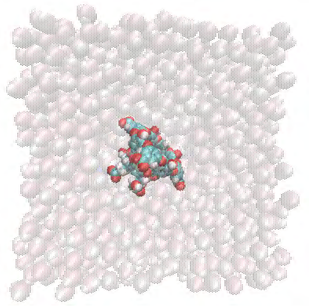

Fig.3: A snapshot of the simulation of the cavitand in water.

Cavitand Studies

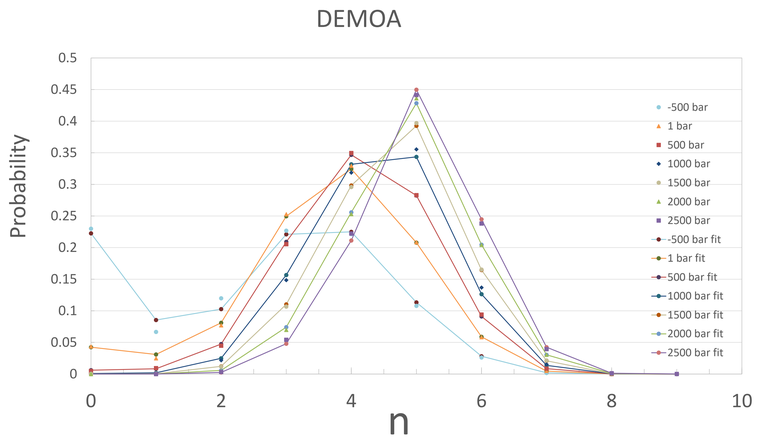

Fig.4: The probability distribution of water within the cavitand over different pressures.

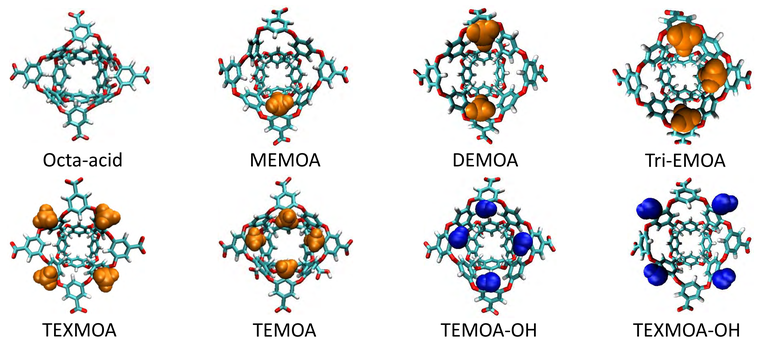

Fig.5: Starting from the top-left, Octa-acid (OA) has no functional groups around the rim. MEMOA (mono-endo-methyl octa-acid), DEMOA (di-endo-methyl octa-acid), Tri-EMOA (tri-endo-methyl octa-acid), and TEMOA (tetra-endo-methyl octa-acid) have 1, 2, 3 ,and 4 methyl groups respectively around the rim in the endo position. TEXMOA (tetra-exo-methyl octa-acid) also has four methyl groups but they are in the exo position along the rim. Conversely, TEMOA-OH and TEXMOA-OH have the same respective positions as TEMOA and TEXMOA but have hydroxyl groups in place of methyl groups.

Thermodynamic Models

The change in free energy, ΔG, can be calculated according to the following formula $\Delta G(n) = -kTln\frac{P(n)}{P(4)}$ where k is the Boltzmann constant, T is the temperature, P(n) is the probability of n water molecules occupying the cavitand, and P(4) is the chosen reference state for this experiment and the probability of 4 molecules occupying the cavitand. P(n) can be calculated using the following partition function: $P(n) = \frac{\exp(-\frac{G(n)}{RT})}{\sum_i \exp(-\frac{G(i)}{RT})}$. The free energy can also be modeled as a function of the incompressible volume V(n) as: $G(n) = a(n) + V(n) * P$,where a(n) is a constant and P is pressure. At constant temperature, and the differential of this equation is modeled as: $\frac{\partial G(n)}{\partial P}|_T = V(n)$.

The Methyl Effect

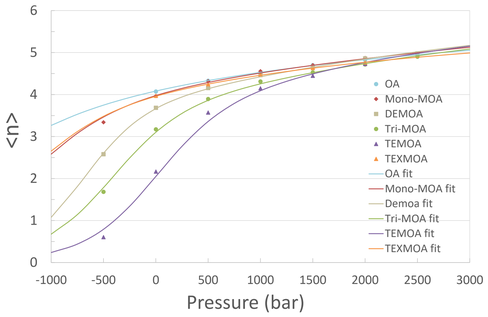

Fig.6: The average number of water molecules present in the cavitand as a function of pressure. The data points were collected in simulations; the lines are the data points fitted to a curve.

Increasing the methylation of the rim increases the hydrophobicity of the cavitand and decreases the likelihood that water will be found in the cavitand at any given moment. As methyl groups are added around the rim of the cavitand in place of hydrogen, the relative bulkiness of the methyl group narrows the mouth of the cavitand creating a smaller gateway for the water molecules in addition to the hydrophobic effect of the interactions between water and the methyl group.

The Hydroxyl effect

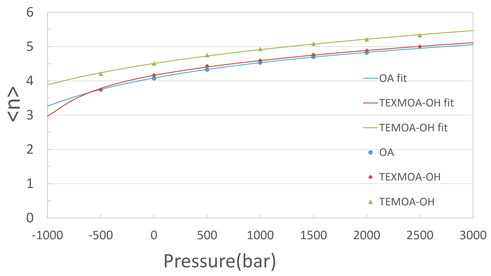

Fig.7: The average number of water molecules present in the cavitand as a function of pressure over the whole course of the simulation. The data points were collected in simulations; the lines are the data points fitted to a curve.

The addition of hydroxyl groups to the rim of the cavitand increases the likelihood that water will be found in the cavitand. The hydrophilicity of the hydroxyl groups attracts water to the mouth of the cavitand and thus increases the likelihood that water will find its way into the belly of the cavitand.

Conclusions

By varying the functional groups located on the rim of deep-cavity cavitand OA, we were able to determine that the methylation of the rim increases the hydrophobicity of the cavitand while also decreasing the average number of water molecules present and the likelihood that water will enter the cavitand. We also concluded that the addition of hydroxyl groups to the rim of the cavitand will increase the number of water molecules present while increasing the likelihood water will enter the cavitand.

References

[1]Jordan, J. H.; Gibb, B. C. *Chem. Soc. Rev.*2015, *44*(2), 547–585.

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