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Electronic Supplementary Information for

What causes tumbling of *altro-α*-CD derivatives? Insight from computer simulations

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Physical origins of the free-energy barriers. There are several common factors contributing to the free-energy barriers in water and in DMSO, including (1) the inevitable isomerization of the altropyranose unit and of its two neighboring glucopyranose units, (2) the deformation of the CD, (3) the desolvation of the side chain, (4) breaking hydrogen bonds at the secondary side of the CD, and (5) the unfavorable interaction of the hydroxyl groups of the altropyranose unit with the hydrophobic cavity. The latter two factors also constitute the main barrier in the tumbling of the altropyranose unit of a mono-*altro*-α-CD, as was reported previously.[1] Fig. 5 shows the conformational transition of the altropyranose unit of the alkyl *altro*-α-CD during tumbling. The free-energy barrier for the interconversion between the chair and the boat conformers is an integral part of the activation free energy. The deformation of the CD during tumbling was estimated by monitoring the distance root mean square deviation (RMSD) over the six glycosidic oxygen atoms of the CD with respect to their initial positions, as shown in Fig. S1. The deformation of the CD leads to the increase of its structural energy, and, thus, contributes to the free-energy barrier.

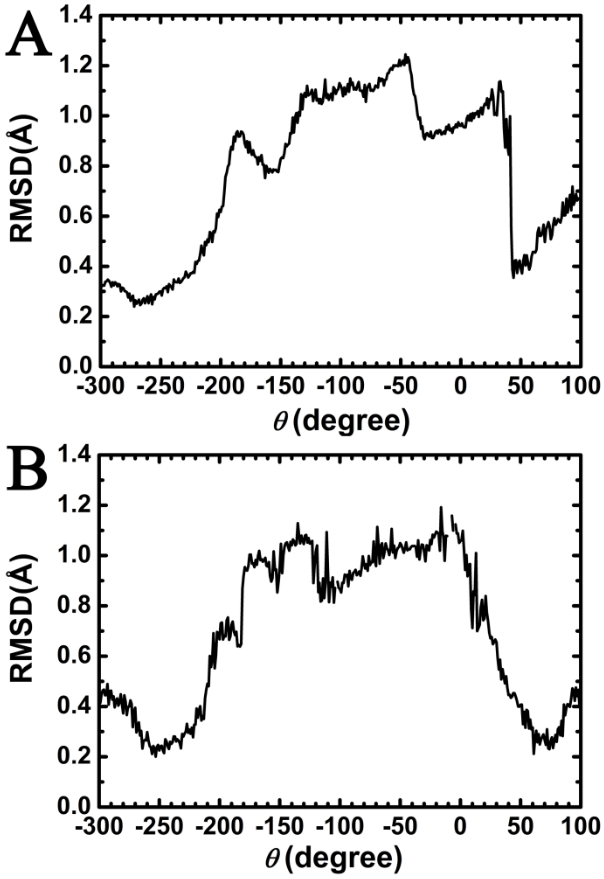

Fig. S1 Evolution of the distance root mean square deviation (RMSD) over the six glycosidic oxygen atoms of CD with respect to their equilibrium position in (A) water, and in (B) DMSO.

Steric constraints of the polyvinyl alcohol chain. In order to evaluate the steric hindrance of the polyvinyl alcohol chain, the chain−CD interaction was computed and further decomposed into van der Waals and electrostatics contributions. As shown in Fig. S2, the slight rise of the chain−CD (vdw) component stems from steric hindrances rooted in the inclusion of the polyvinyl alcohol chain into CD cavity. However, the chain−CD (vdw) term is compensated by the chain−CD (elec) term, resulting in the overall favorable chain−CD interaction. The steric constraints of the hydroxyl groups of the polyvinyl alcohol chain, therefore, have little bearing on the stability of the self-included polyvinyl alcohol *altro*-*α*-CD.

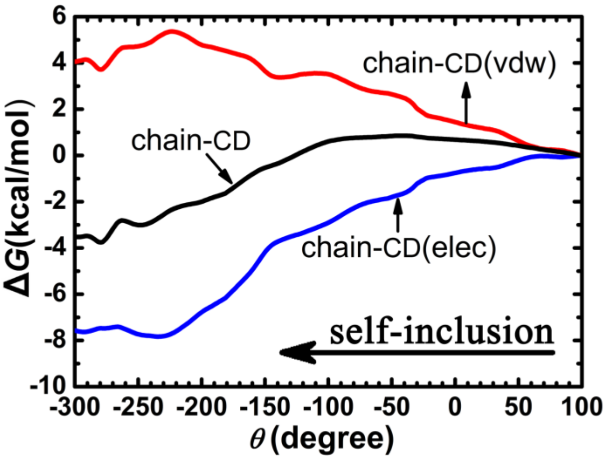

Fig. S2 Interaction of the polyvinyl alcohol chain with the *altro*-*α*-CD.

Stable binding of DMSO molecules to the CD. To estimate the binding affinity of DMSO molecules to the CD, the free-energy profiles characterizing the reversible unbinding of a DMSO molecule from each rim of an *altro*-*α*-CD were determined and are depicted in Fig. S3. The transition coordinate, ξ, was defined as the projection onto the z-axis of the distance between the center of mass of a DMSO molecule and that of the CD glycosidic oxygen atoms. As can be observed, the minima at +2.6 Å (see Fig. S3A) and −2.8 Å (see Fig. S3B) suggest that each rim of the *altro*-*α*-CD can bind a DMSO molecule. The stable binding of DMSO molecules to the CD entails a lower mobility of the former, hindering the tumbling of the altropyranose unit and penetration of the chain into the cavity.

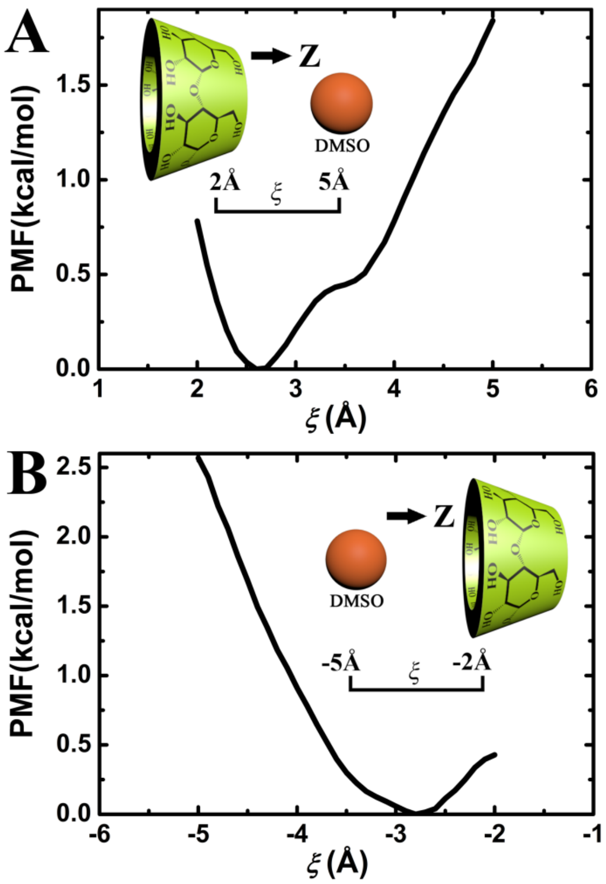

Fig. S3 Free-energy profiles characterizing the reversible unbinding of a DMSO molecule from (A) the primary rim and (B) the secondary rim of an *altro*-*α*-CD.

References:

1 Y. Liu, C. Chipot, X. G. Shao and W. S. Cai, J. Phys. Chem. C, 2014, 118, 19380–19386.