Energetics of Intercavity Diffusion in a Simple Model of a Low-Density p-tert-Butylcalix[4]arene Crystal

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Abstract: Potentials of mean force calculated for the diffusion of small guest molecules (CO_2 and CH_4) between adjacent host cavities in the β_0 p-tert-butylcalix[4]arene polymorph reveal sufficiently high barriers to diffusion to justify characterizing the lattice voids in this crystal as independent host cavities rather than as extended volumes. In addition, the calculated barrier heights are consistent with a "relay" model for gas diffusion in this ostensibly nonporous organic solid involving the lateral sliding of the host bilayers.

The unexpected sorption of small gas molecules by the β_0 p-tert-butylcalix[4]arene (TBC4) polymorph[1−5] has prompted several attempts to elucidate gas dynamics within these ostensibly nonporous organic crystals.[6−8] Recently, Liu and co-workers[9] reported molecular mechanics calculations associated with two plausible gas transport mechanisms: a "squeeze" mechanism, wherein gas molecules slip through gaps between adjacent TBC4 hosts, and a "relay" mechanism, wherein lateral motion of host bilayers facilitates host-to-host hopping. On the basis of their calculated diffusion paths alone, however, they could not distinguish clearly between these mechanisms. That work nonetheless raises questions about gas binding sites in TBC4. Are they indeed the 0.235 nm^3 lattice voids arising from the proximity of adjacent host cavities suggested by the initial work of Atwood et al.,[1] or do the individual host cavities provide independent binding sites?

In the present study, we have generated potentials of mean force[10] (PMFs; free energies for motion along a reaction coordinate) for the passage of guest molecules (CO_2 and CH_4) between the two host cavities comprising a TBC4 lattice void. These PMFs derive from molecular dynamics (MD) simulations[11,12] and subsequent WHAM analyses[13,14] carried out according to the prescription detailed in our previous work on guest binding to isolated hosts.[8] The structural integrity of the lattice void is ensured here by tethering the two hosts to their respective crystallographic sites. (See Figure 1. Specifically, we tether the eight methylene bridge carbons harmonically to their solid-state sites, a constraint strategy that minimally perturbs the vibrational dynamics of the hosts. Absent tethering, the dimer collapses to the expected self-inclusion structure characteristic of the high-density TBC4 polymorph.[15]) Here the PMF reaction coordinate is defined as the distance between the center of mass of the guest and the center of mass of the four lower-rim phenolic carbons of the host in which the guest is initially bound.

In Figure 2, we give PMFs generated for a CO_2 guest. The black curve (closed circles) is the result obtained for a system equilibrated at 298 K and tethered as described above with harmonic force constants of 8.368 kJ/(mol Å^2). Note that this roughly symmetric curve displays minima at distances of 2.9 and 9.4 Å along the reaction coordinate, the preferred binding positions of CO_2 in the
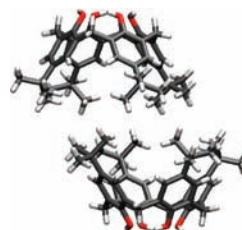

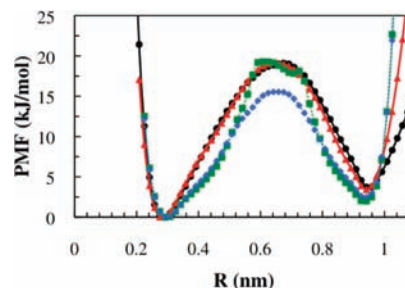**Figure 1.** TBC4 dimer (β_0 crystal relative orientations).

Figure 2. Potentials of mean force for a CO_2 guest interacting with a tethered TBC4 dimer: weak tether, 298 K (black); strong tether, 100 K (red); fixed hosts, 100 K (green); fixed hosts with *tert*-butyl rotations, 100 K (blue).

two host cavities. (The lack of perfect symmetry here reflects the choice of the reaction coordinate. Though at small distances the reaction coordinate lies along the 4-fold symmetry axis of a host cavity, such is not the case when the guest has crossed to the other host.) Separating these minima is a free energy barrier of 19.1 kJ/mol (7.7RT at this temperature), 5.0 kJ/mol higher than the barrier for loss of CO_2 from an isolated TBC4 monomer.[8]

We compare this room temperature, weakly tethered result with one obtained at 100 K using a 10-fold-stronger host tether. This second result, shown in red (triangles) in Figure 2, differs significantly only in the steepness of the rise of the PMF beyond the second minimum. The striking similarity between these two curves implies that the entropy change along the reaction coordinate is negligible and that the arbitrarily chosen tether strengths do not skew the estimation of the barrier height for passage between the host cavities. Note also that this barrier height is essentially identical with that found for loss of CO_2 from a TBC4 monomer at 100 K.[8]

We also considered two strongly constrained model systems at 100 K: one in which all host atoms were held fixed and a second in which all but the upper-rim methyl-group atoms were held fixed, thus allowing the normal rotation of the *tert*-butyl groups. The first of these systems yielded the green curve (squares) shown in Figure 2. Absent the low-frequency breathing of the hosts, this PMF does not rise as steeply beyond the first minimum, a difference attributable to a reduction in the energy associated with a 90° rotation of CO_2. (Periodic cavity constrictions inhibit this reorienta-
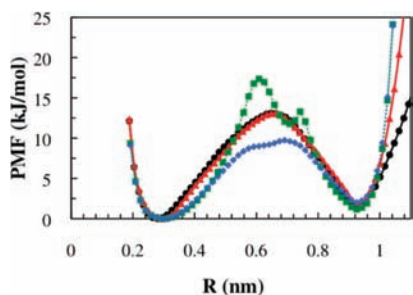
Figure 3. Potentials of mean force for a CH₄ guest interacting with a tethered TBC4 dimer, all at 100 K: weak tether (black); strong tether (red); fixed hosts (green); fixed hosts with *tert*-butyl rotations (blue).

tion in the full-dynamics systems.) As this guest departs its initial host and comes into close contact with a (now fixed) *tert*-butyl group of the second host, it slips laterally along a relatively flat potential barrier until it reaches the entrance to the other host cavity. It finally rotates again, aligning its major axis with the C_4 axis of that host, as it passes into the cavity. The key observation here is that constraints on the motion of the hosts alter the topology of the intercavity potential barrier.

This observation is corroborated by the fourth result shown in Figure 2, corresponding to a system in which all but the upper-rim methyl group atoms are held fixed (blue diamonds). Although this PMF closely tracks the result obtained in the fully constrained case, the intercavity barrier is now lower than that found in the full-dynamics cases by 4.5 kJ/mol (roughly, 25%). Clearly, the ability of a *tert*-butyl group to rotate away from a mobile guest facilitates cavity-to-cavity transfer; but, nonetheless, the environment in which the CO_2 guest moves is better described as two distinct host cavities rather than one extended cavity.

To assess the generality of the behavior noted above, we also investigated a CH₄ guest under similar conditions. (Here the weakly tethered, full-dynamics case corresponds to a temperature of 100 K; at 298 K, methane is lost from the system during sampling along the reaction coordinate.) The results of these calculations are shown in Figure 3. As for CO_2, a 10-fold increase in the strength of the tethers binding the methylene bridge carbons to their crystal-lographic sites has a negligible influence on the PMF except for increasing the steepness of the curve beyond the second minimum. The intercavity barrier height here is found to be 13.1 kJ/mol (15.6RT at 100 K), a value greater than the free energy barrier to loss of CH₄ from an isolated TBC4 host (9.9 kJ/mol).[8]

Here, too, holding the host cavities fixed alters the topology of the energy barrier for intercavity gas transfer. In contrast with the CO_2 case, this dynamical constraint significantly increases the height of the barrier; entanglement of the methane guest with a fixed terminal methyl group increases the barrier height by 4.3 kJ/mol (32%). Effectively, we find more friction associated with passage of the nearly spherical methane molecule between the TBC4 bilayers than we do for CO_2 moving with its major axis parallel to those bilayers. Releasing the *tert*-butyl group rotation constraints

again lowers the intercavity energy barrier, here by 3.4 and 7.7 kJ/mol compared with the full-dynamics and fully constrained cases, respectively.

The PMF calculations described here strongly suggest a need to modify the initial characterization of the β_0 TBC4 guest cavity,[1] to view it not as a continuous 0.235 nm³ cavity but rather as a pair of distinct TBC4 host cavities separated by an appreciable energy barrier for passage of a small guest molecule between them. This barrier is nonetheless lower than those reported by Liu and co-workers[9] for bilayer translation and "squeeze" diffusion. Thus, our results attest to the plausibility of the "relay" model of gas transport in TBC4. Given that the intercavity barrier derives in part from interactions of the guest with a *tert*-butyl group of the second host molecule, lateral motion of the TBC4 crystal bilayers that eliminates the "offset" of the adjacent host cavities will lower the barrier and facilitate gas movement through the crystal. Of course, guest−guest attractions comparable to the 10−20 kJ/mol intercavity barrier also should enhance gas transport. Investigations are underway exploring whether guests interacting through hydrogen bonds, which are of just this magnitude, "pull" one another from cavity to cavity.

Finally, that rotation of the *tert*-butyl groups significantly lowers but does not eliminate the barrier to gas transport is also intriguing because it prompts a different way of thinking about the participation of these groups in the gas diffusion process. Instead of viewing them as turnstiles that gate the passage of gas into the host cavities,[3] we suggest that they are better viewed as "ball bearings" that, by lessening the effective friction, facilitate the lateral sliding of the TBC4 bilayers. Entanglement of the terminal methyl groups inhibits this sliding in the absence of *tert*-butyl group rotation.

Supporting Information Available: Complete ref 11. This material is available free of charge via the Internet at http://pubs.acs.org.

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