Mechanically Regulated Rotation of a Guest in a Nanoscale Host

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The control of molecular motion drives much of the innovations for molecular devices showing functions reminiscent of macroscopic machinery.[1] The limited space available to encapsulated species may be useful in this regard: guest molecules, temporarily surrounded by self-assembled hosts,[2] give rise to new forms of isomerism as a result of their limited motions. We show here that guests of the host capsule **1·1**[3] are suitable subjects for regulated rotational freedom.

The application takes advantage of the shape of the space presented by the host and its ability to accommodate more than one guest. The cavity of **1·1** features two square prisms, rotated 45° with respect to each other at the center, and two square pyramids at each end, rotated at 45° with respect to the prisms (Figure 1A). The width of the square prism is 6.6 Å, (estimated by MM+ minimization[4]), which can just accommodate [2.2]-paracyclophane **2**, a guest of congruent shape and size (Figure 1B).

No apparent steric clashes exist between host and guest; rather, attractive forces between the electron-rich outer surfaces of the cyclophane's aromatic rings and the electron-deficient surfaces of the pyrazine imides are expected.[5] The rotation of the guest inside the host is described in Figure 1C. As the guest rotates, the energy of the complex rises up to a transition state at 45°; further rotation leads to the next degenerate minimum. Yet, compound **2** alone does not give any sign of complexation with **1** in mesitylene-d_{12} solution. The addition of certain coguests (G) to the solution causes nearly instantaneous[6] encapsulation of **2**. Figure 2A shows an aromatic region of the ^{1}H NMR spectrum (600 MHz) of the coencapsulated complex of **2** with CCl_4. A unique pattern of the NH and aromatic resonances of the capsule are observed; integration shows a ratio of 2:2:4, whereas other coencapsulation complexes based on **1·1** show a 4:4 integration in this region, a result of the different guests in the upper and lower halves of the capsule (see Supporting Information).

The 2:2:4 distribution is due to further disruption of the symmetry: The protons marked green and blue are in different magnetic environments only when the spinning rate of **2** along the axis of the capsule is slow on the NMR time scale. In contrast, protons at 45° to the guest planes (marked as red) are not affected by the spinning rate. These assignments were confirmed by NOE cross-peaks between the guest proton G and host protons D and E. Figure 2B shows proton resonances of the encapsulated guest **2**. The resonance observed at 1.66 ppm showed no chemical exchange with the proton G at −1.5 ppm: like other *p*-disubstituted aromatic guests, **2** is too long to tumble while inside the capsule. *Unlike any other guests previously observed in this capsule,[7] the spinning of **2** is slow on the NMR time scale.*

The spectra for the complex of **2** with CCl_4 taken at different temperatures are shown in Figure 3A. The gradual increase of the temperature from 300 K resulted in disappearance of resonances A, A′, C, and C′ and coalescence of resonances F and F′ as the spinning rate of **2** increased. At lower temperatures from 300K
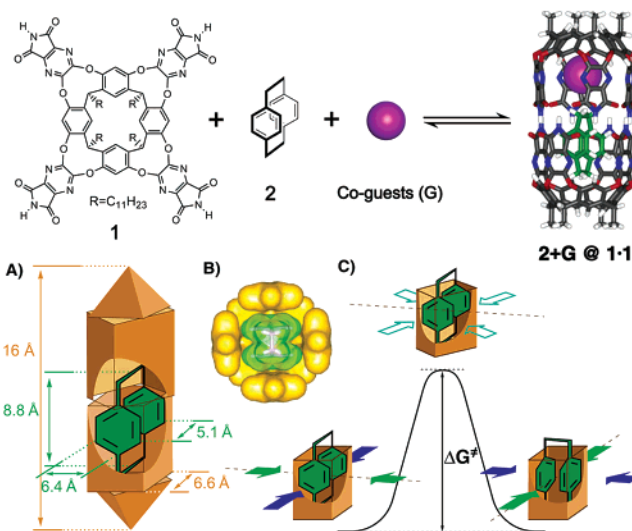

Figure 1. Line drawing of the synthetic receptor **1**, and energy-minimized dimeric structure of the capsule **1·1** (the $C_{11}H_{23}$ alkyl chains have been removed for clarity) and [2.2]-paracyclophane **2**. (A) Dimensions of capsule interior (orange) and the guest **2** (green). (B) Top view of the minimized (MM+) structure of the capsule containing **2** (showing only half of the capsule). (C) Energy profile for the restricted spinning of **2** within the capsule while coencapsulated with a coencapsulated guest G.
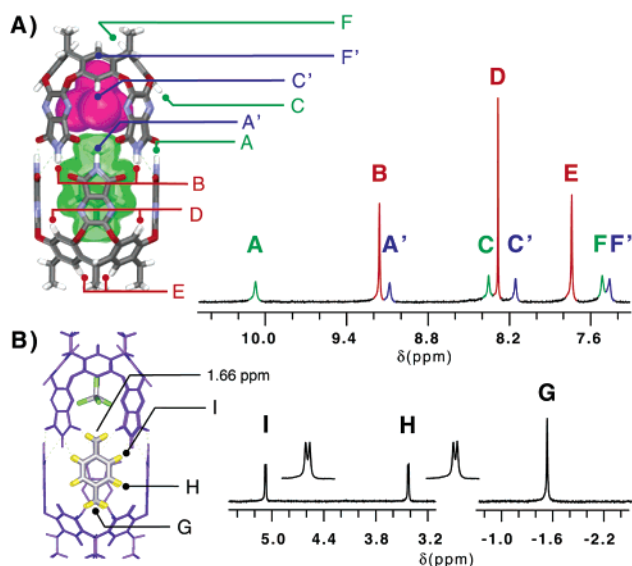

Figure 2. ^{1}H NMR spectrum (600 MHz) of the complex **2** + CCl_4 in **1·1** at 300 K with the assignments of the proton resonances of (A) the host **1·1** and (B) the encapsulated guest **2**. Insets are the aromatic signals expanded. The $C_{11}H_{23}$ alkyl chains and some atoms from the walls have been removed for clarity.

sharper resonances for these protons were observed. A series of two-dimensional EXSY experiments were performed to determine
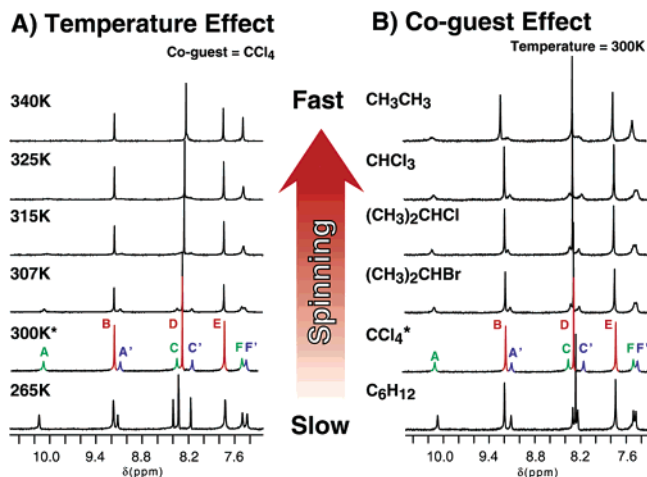
A) Temperature Effect

Co-guest = CCl₄

B) Co-guest Effect

Figure 3. (A) ¹H NMR spectra (600 MHz) for the complex **2** + CCl₄ in **1·1** at different temperature. (B) ¹H NMR spectra (600 MHz) at 300 K for the complexes of **2** with different coguests (G) in **1·1**. The two spectra marked with an asterisk (*) are identical to the spectrum shown in Figure 2 (**2** + CCl₄ in **1·1** at 300 K).

Table 1. Effects of (A) Temperature and (B) Coguest on the Rotational Motion of **2** in **1·1** ($\Delta\delta$ Ethylene Proton G of Figure 2A).

(A) temperature effect

coguest (G)	temp (K)	k (min⁻¹)
CCl₄	300	238
(91 Å³)	275	161
	263	65
	249	12
(CH₃)₂CHCl	275	257
(76 Å³)	263	76
C₆H₁₂	300	255
(97 Å³)	263	23

(B) coguest effect (measured temp = 263 K)

	volume (Å³)	PC (%)	k (min⁻¹)	$\Delta G^{\ddagger}$ (kcal/mol)	$\Delta\delta$ (ppm)
CH₃CH₃	42	62	178	14.8	4.43
(CH₂)₃	52	64	257	14.6	4.45
(CH₃)₂CO	60	66	297	14.5	4.44
CHCl₃	75	69	127	15.0	4.48
(CH₃)₂CHCl	76	70	76	15.2	4.49
(CH₃)₂CHBr	84	72	75	15.2	4.47
CCl₄	91	73	65	15.3	4.49
CHBr₃	99	75	36	15.6	4.52
C₆H₁₂	97	75	23	15.9	4.57
CCl₃Br	114	79	46	15.5	4.51

the energy barrier to spinning.[8] The rate of exchange was estimated on the basis of the integration of the cross-peaks between two adjacent NH protons (e.g., protons A and A′ in Figure 2A), and the Eyring equation was used to calculate the free energy of activation ($\Delta G^{\ddagger}$).

Similar spectra were observed when the coguest (G) was varied (Figure 3B). Coguests ranged from ethane (42 Å³) to CCl₃Br (114 Å³). All of the coguests lead to remarkably high packing coefficients

(PCs). This is far above the usual value for solution complexes (ca. 55%)[9] and some of the higher values are comparable to those of the solid state.[10] The trends shown by the spectra indicated that a larger coguest slows the spinning of **2**. Coguests smaller than CHCl₃ showed negligible effects on the spinning of **2** effectively.

Table 1 summarizes the effect of temperature and the size of the coguests (G). Table 1B also shows the correlation between guest size and the upfield shifts experienced by the resonances of the ethylene near the capsule's end (e.g., protons G in Figure 2B). Increasing the size of G forces **2** further into the shielding zone at the tapered ends where spinning involves more steric clashes; the resorcinarene subunits at the ends of the capsule are covalently bound and rigidly held in place. The hydrogen-bonding seam at the middle is deformable and allows breathing motions of the walls during the guest's spin. Although the data is limited, it appears that dimensions rather than volumes determine the "size" of the coguest (compare the wider, disc-shaped cyclohexane with the more compact CCl₃Br).[11] The larger coguests apply brakes to the spinning rate. Conversely, attractive forces between coguests could accelerate spinning by pulling **2** closer to the center of the capsule. We are working on these notions to refine control of motion at the molecular level.

Supporting Information Available: Complete assignment of ¹H NMR spectrum of **2** + CCl₄ in **1·1** and ¹H NMR spectra of the complex **2** + all tested coguests in **1·1**, as well as the calculation procedure for the estimation of k and $\Delta G^{\ddagger}$ (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) For both the aromatic hydrogens of **2** (H and I), a general increase of the $\Delta\delta$($\Delta\Delta\delta$ −0.05, −0.15 ppm, respectively) was observed by increasing the size of the guest from CH₃CH₃ to CCl₃Br. This behavior is consistent with the effect of the coguest that forces **2** deeper into the tapered ends of the cavity.

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