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Restricted Guest Tumbling in Phosphorylated Self-Assembled Capsules

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Abstract: AB*ii* diphosphonatocavitands self-assemble in chloroform solution to form dimeric molecular capsules. The molecular capsules can incarcerate an *N*-methylpyridinium or *N*-methylpicolinium guest. We have demonstrated that the supramolecular assembly acts as a molecular rotor as a result of the restricted motion of the guest inside the molecular cavity. In the solid state, X-ray diffraction analysis of the free host showed that two cavitands interact through strong hydrogen bonds to give the supramolecular self-assembled capsule. The solid-state structure of the *N*-methylpicolinium complex is comparable to that of the free host and indicates that the guest is not a prerequisite for the formation of the capsule. DOSY NMR studies provided a definitive argument for the formation of the free and complexed supramolecular capsule in $CDCl_3$ solution. In solution, the tumbling of the *N*-methylpyridinium and *N*-methylpicolinium guests about the equatorial axes of the host can be frozen and differs by the respective energy barriers, with the larger picolinium substrate having a larger value ($\Delta G^{\ddagger} = 69.7$ kJ mol^{-1}) than the shorter pyridinium guest ($\Delta G^{\ddagger} = 44.8$ kJ mol^{-1}). This behavior corresponds to the restricted rotation of a rotator in a supramolecular rotor.

Introduction

The cavitand structure is obtained by the bridging of a resorcarene molecule with various moieties, including methylene or higher alkyl groups, aromatic spacers, or silicium and phosphorus moieties.[1,2] Resorcarenes are known to self-assemble to form dimeric or hexameric molecular capsules with interesting complexation properties. For example, dicationic species were encapsulated within solvent (water)-driven resorcarene capsules.[3] On the other hand, (hemi)carcerands, made of two covalently bound cavitands, can encapsulate different guests. It has been shown that in the latter system, the tumbling of the guest in the molecular cavity is restricted and often is possible only along the polar axis of the cavity.[4] Thus, different dynamics of incarcerated guests are observed, depending on the size and shape of the guest. If the rotation of a molecular entity, either a molecule or part of it, can be monitored and controlled, it could act as a rotator, the mobile part of a molecular rotor or gyroscope. The trapped guest in the host cavity can play such a role. In these supramolecular systems, the stator and rotator are not covalently bound. Such features may present advantages and facilitate their syntheses. In this way, a wider variety of modular rotating subunits become more accessible without repeating synthetic efforts. Each part can suitably self-arrange during the thermodynamic equilibration process. In the design of new materials from such systems, it also offers the possibility to limit unfavorable interactions with surfaces in self-assembled systems, and the supramolecular encaging may prevent undesirable mechanical effects or electronic interactions between rotors.

The growing interest in the design of molecular receptors with nanometer-sized cavities based on self-assembly has resulted in very sophisticated molecular objects with potential interest in the design of chemical nanoreactors, containers, or delivery systems.[5] Undoubtedly, many properties of such systems are still unrevealed and will open new exciting fields of investigation, including mimicking biological processes and performing controllable functions at the molecular level. Self-assembled molecular capsules have been obtained by H-

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bonding,[6] coordination to metal atoms,[7] and ionic[8] or solvophobic interactions[9] when a suitable substitution was performed on the resorcarene structure. However, the driving forces for encapsulation of guests in these hosts are mainly due to rather weak CH−π and cation−π interactions or hydrophobic forces. The recent work of Kobayashi and co-workers[10] presents a self-assembled heterodimer capsule made of two cavitands that can encapsulate a 1,4-diacetoxybenzene derivative. In this example, the guest molecule can rotate along the north−south axis of the capsule and behaves as a supramolecular gyroscope. The energy barrier for the rotation depends on the substitution on the aromatic guest.

In this work, we considered the formation of molecular associations involving H-bonds and strong dipolar interactions between ammonium guests and phosphonate cavitands. Phosphonate cavitands represent an original family of molecular hosts that contain endohedral binding sites, giving them remarkable binding properties. For instance, the tetra-bridged 4*i*PO (*iiii*PO) cavitands **1** (Figure 1) are known to bind hard cationic species efficiently.[2,11] Partially phosphorylated cavitands can complex primary alcohols by means of CH−π interactions and H-bonds between the alcoholic OH and PO groups, indicating that increasing the number of PO groups enhances the stability of the complex.[12] We report herein the preparation and behavior of 2*i*PO (*ii*PO) phosphorylated cavitands that bear two phosphonate bridging moieties and can self-assemble in solution to form a molecular capsule. In the presence of a suitable pyridinium guest, which experiences restricted mobility, the newly designed capsular complexes act as molecular rotors.

In particular, we investigated the AB*ii* phosphorylated hosts formed by bridging only two (proximal) sites of the resorcarene scaffold (Figure 1), which thus still contains free OH functions that can arrange to form associations mediated by H-bonding. The cavities of these hosts are preorganized enough to provide novel self-assembled systems.

Results and Discussion

Synthesis. The strategy used to obtain the partially bridged phosphorus cavitands has been reported elsewhere.[13] The reaction of resorcarene **2a** or **2b** with $PhPCl_2$ followed by addition of sulfur gave a mixture of the corresponding AB*ii* derivative **3a** or **3b** and AC*ii* derivative **4a** or **4b**. Compounds **3a** and **4a** were obtained in 24 and 8% yield, respectively. A similar procedure was used to synthesize cavitands **3b** and **4b**, which were obtained with lower yields, probably because of their lower solubility. However, the phenethyl feet in the new derivatives **3b** and **4b** facilitated the formation of single crystals for X-ray analysis. The subsequent treatment of **3** and **4** with *m*-chloroperoxybenzoic acid (MCPBA) led to the derivatives **5** and **6**, respectively, in good yields. The NMR spectra of compounds **3**−**6** were in accord with a rigid cavity and an inward orientation of the P═X (X = S, O) bonds. The AC*ii* derivatives that were synthesized together with the AB*ii* isomers behave differently and were not considered in this study.

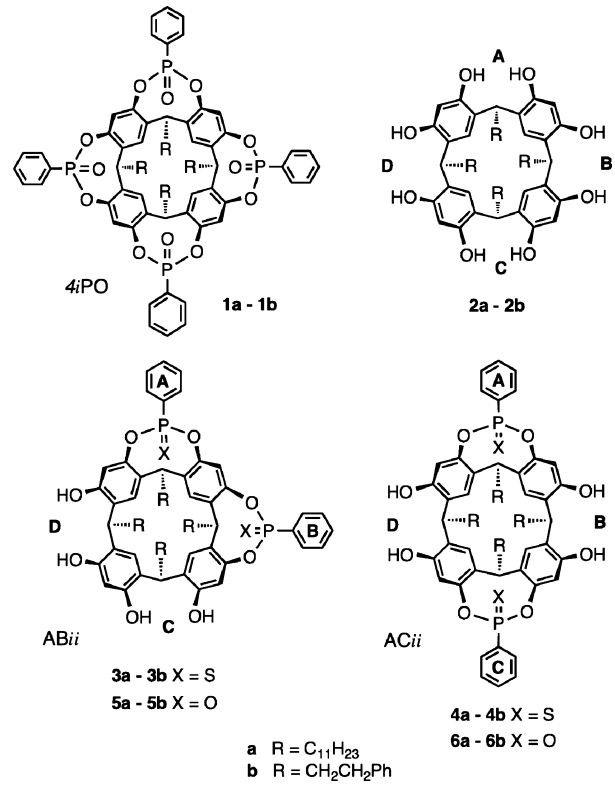

Figure 1. Structures of the 4*i*PO phosphorylated cavitands **1** and the 2*i*PO phosphorylated cavitands AB*ii* (**3** and **5**) and AC*ii* (**4** and **6**). The labels AB and AC indicate the proximal and distal positions of the two phosphorus groups in the 2*i* derivatives.

Binding of Pyridinium Guests. The encapsulation of pyridinium picrate and pyridinium iodide guests, namely, *N*-methylpyridinium picrate (PyrPic) and iodide (PyrIod) and *N*-methylpicolinium picrate (PicoPic) and iodide (PicoIod), by cavitand **5a** in CD_2Cl_2 was investigated using ^1H and ^{31}P NMR spectroscopy, which is a useful tool for studying the encapsulation process because of the strong anisotropic shifts due to ring-current effects from both the host and the pyridinium guest. Addition of PyrPic to a solution of **5a** in CD_2Cl_2 at 293 K resulted in the appearance of new signals for the host in the ^1H NMR spectrum that were unambiguously assigned on the basis of 2D NMR experiments, while the signals of the free host vanished as the concentration of the guest increased (Figure 2). After addition of 0.5 equiv of guest, only the signals of the new species were visible. After more than 0.5 equiv of guest was added, extra peaks from the free guest appeared, indicating that the host−guest exchange at room temperature is slow on

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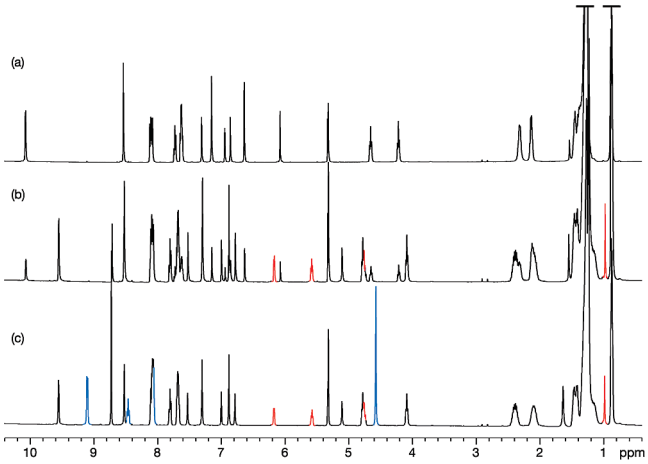


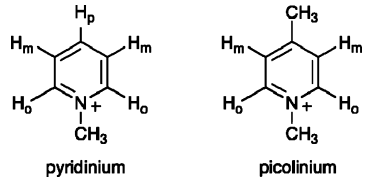
Figure 2. ^{1}H NMR spectra (500 MHz, CD_2Cl_2, 293 K) of (a) free host **5a**, (b) **5a** + 0.3 equiv of PyrPic, and (c) **5a** + 3.5 equiv of PyrPic. Colors: red, bound pyridinium; blue, free pyridinium.

Table 1. ^{1}H NMR Chemical Shifts for the Protons of the Free and Bound *N*-Methylpyridinium and *N*-Methylpicolinium Guests in the Presence of **5a** in CD_2Cl_2 Solution at 293 K

guest[a]	$ArCH_3$	$^+NCH_3$	H_p	H_m	H_o
Pyr_{free}	–	4.58	8.46	8.06	9.10
Pyr_{bound}	–	0.98	4.74	5.58	6.17
$\Delta\delta_{free\text{-}bound}$	–	*3.60*	*3.72*	*2.48*	*2.93*
$Pico_{free}$	2.70	4.40	–	7.80	8.80
$Pico_{bound}$	−0.60	0.95	–	5.86	6.04
$\Delta\delta_{free\text{-}bound}$	*3.30*	*3.45*	–	*1.94*	*2.76*

[a] Picrate salt.

the ^{1}H NMR time scale. The 1:2 stoichiometry of the complex was determined from the integration of the host and guest signals. Each proton of the guest underwent a strong upfield shift (Table 1). This can be explained by the formation of a 1:2 PyrPic@(**5a**)$_2$ guest−host complex in which the encapsulated pyridinium is trapped between two cavitands. The two bound cavitands gave only one set of signals in the ^{1}H and ^{31}P NMR spectra, indicating that they are chemically equivalent. The behavior was similar with the iodide salt PyrIod (data not shown).



The same experiment was run with PicoPic as the guest. The addition of PicoPic to a solution of **5a** in CD_2Cl_2 led to the formation of the 1:2 PicoPic@(**5a**)$_2$ complex, which exhibited the typical upfield-shifted signals for the encapsulated guest (Figure 3 and Table 1). As for the pyridinium salt, the exchange between free and encapsulated guest at room temperature is slow on the ^{1}H NMR time scale. Addition of more than 0.5 equiv of guest showed the signals of the free guest. Moreover, in the complex, each of the host signals in the ^{1}H and ^{31}P NMR spectra were split into two resonances, indicating that the two cavitands in PicoPic@(**5a**)$_2$ are not chemically equivalent. *N*-Methylpicolinium picrate and iodide guests behaved similarly (see Figures S12−S14 in the Supporting Information).

These results show that pyridinium and picolinium cations combine with **5a** to form a 1:2 guest@(**5a**)$_2$ supramolecular

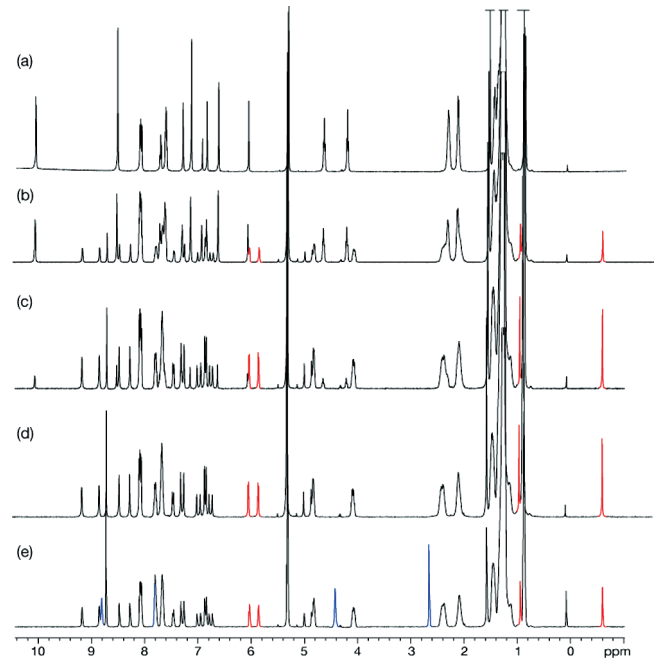


Figure 3. ^{1}H NMR spectra (500 MHz, CD_2Cl_2, 293 K) of (a) free host **5a**, (b) **5a** + 0.2 equiv of PicoPic, (c) **5a** + 0.4 equiv of PicoPic, (d) **5a** + 0.5 equiv of PicoPic, and (e) **5a** + 1.3 equiv of PicoPic. Colors: red, bound picolinium; blue, free picolinium.

assembly under slow-exchange conditions on the NMR time scale at room temperature. The upfield chemical shifts of all of the protons of the encapsulated guests suggest the formation in solution of a molecular capsule made of two cavitands that totally entrap the guests. From the NMR titration experiments, it was not possible to extract accurate association constant values. Such values could only be estimated to be $>10^5$ M^{-1}, emphasizing the high stability of the complexes.[14]

X-ray Analysis of Host and Host−Guest Supramolecular Assemblies. The presence of the dimeric capsule was further supported by the X-ray diffraction molecular structures of the parent derivatives **5b** (Figure 4) and PicoIod@(**5b**)$_2$ (Figure 5). A set of NMR experiments in solution analogous to those performed with **5a** showed similar behavior for **5b** with the *N*-methylpicolinium salt (Figure S11 in the Supporting Information). In the solid, the free host **5b** and its picolinium complex have very comparable structures. Both exist as a molecular capsule made of two cavitands **5b** facing each other at their wide rims and assembled by means of four strong H-bonds between the PO groups of one cavitand and the OH groups of the other. In the free capsule, the average PO···OH distances is 2.64 Å, and the main axes of the two cavitands are 3.55 Å apart,[15] leading to a shift of one cavitand relative to the other (Figure 4). Two methanol molecules from the crystallization solution (CH_2Cl_2/MeOH) are present in the cavity but do not participate in the formation of the capsule.

(14) Under slow exchange conditions on the NMR time scale, the addition of aliquots of a millimolar solution of guest to a millimolar solution of host revealed only the host−guest complex and the free host. The free guest was undetectable in the NMR spectra because of an expectedly large association constant K_{assoc}. Thus, the concentration of the undetectable species could be estimated only to ≤2−5% of the starting concentration. In this case, only a lower value of K_{assoc} could be estimated.

(15) The main axis chosen for the cavitand corresponds to the C_4 pseudoaxis of the resorcarene structure.

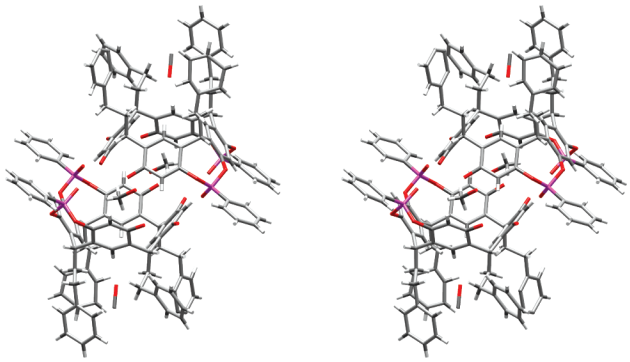


Figure 4. Stereoview of the X-ray structure of the capsular dimeric assembly [**5b**·CH_3OH]$_2$.

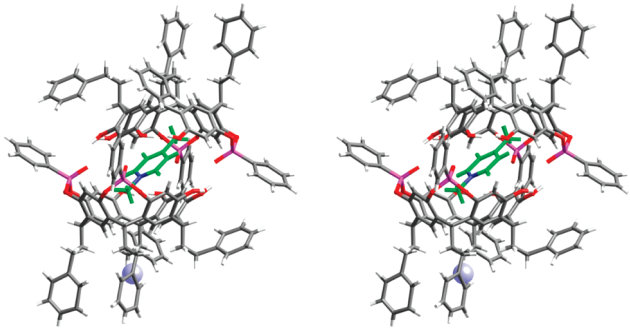


Figure 5. Stereoview of the X-ray structure of the supramolecular complex PicoIod@(**5b**)$_2$.

A question arises concerning the structure of the complexes and the driving forces for the encapsulation. It is known that the CH_3N^+ group is strongly bound to the cavity of phosphorylated cavitands by efficient PO···N^+ interactions and van der Waals interactions between the CH_3N^+ methyl group and the aromatic cavity.[11,16] Examination of the X-ray structure of PicoIod@(**5b**)$_2$ showed that the N^+ atom of the guest is tightly bound to two PO oxygen atoms (average PO···N distance = 3.85 Å). The two cavitands are assembled by means of four strong H-bonds with an average PO···OH distance of 2.63 Å between the PO group of one cavity and the OH of the other. In comparison, the free capsule discussed above has a distance of 2.64 Å. Interestingly, the iodide anion is located in the pseudocavity formed by the phenethyl groups at the narrow rim of the cavitand, as previously observed with phosphonatocavitand complexes (Figure S18 in the Supporting Information).[17] As in the free capsule (**5b**)$_2$, the two cavitands roughly face each other at their wide rims but have their respective main axes shifted by 3.44 Å. This results from an inclination of the guest relative to the main axes of the cavitands (46° with respect to the picolinium CH_3-CH_3 axis). Consequently, the CH_3 heads point toward the aromatic rings bearing the two phosphonate groups in their respective cavities (Figure 5). Moreover, the

Scheme 1. Synthesis of the CH_2-Bridged AB*ii* Cavitands **7a** and **7b**

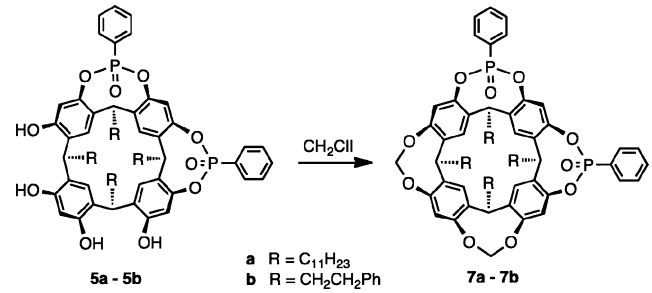


Table 2. Diffusion Coefficients for **1**, **5**, Guest + **5**, and **7** and the Corresponding Hydrodynamic Volume Ratios As Determined by DOSY NMR Spectroscopy in $CDCl_3$ (T = 298 K)

compound **x**	D(**x**) (m^2 s^{-1})	V_H(**x**)/V_H(**1**)	V_H(**x**)/V_H(**7**)
5a	3.29×10^{-10}	2.2	2.9
Pico + **5a**	3.14×10^{-10}	2.5	3.3
1a	4.27×10^{-10}	1	1.3
7a	4.67×10^{-10}	0.8	1
5b	3.91×10^{-10}	1.9	2.0
Pico + **5b**	3.96×10^{-10}	1.9	1.9
1b	4.87×10^{-10}	1	1.1
7b	4.95×10^{-10}	0.9	1

π-electron-deficient picolinium ring is sandwiched between the 1,3-dihydroxy aromatic rings of the two cavitands with a separation of 3.56 Å. It is noteworthy that the picolinium guest encapsulation does not dramatically change the structure of the capsule, which is almost superimposable with that observed in the free host.

Is the Capsular Structure Maintained in Solution? DOSY and ROESY NMR Experiments. In order to determine whether the free capsule exists in solution, we performed diffusion-ordered NMR spectroscopy (DOSY) experiments.[18] It was convenient to compare the self-diffusion constants D of **5a** and its complex with those of cavitands **1a** and **7a** as external references. We chose these two reference molecules because of their very similar structures and the absence of phenol OH groups at the wide rim, which excludes dimeric or higher self-association. Compound **7a** was previously synthesized by Dalcanale and co-workers[12b] through the introduction of the two phosphonate moieties on the doubly methylene-bridged resorcarene precursor. In the present case, the addition of an excess of CH_2ClI to cavitand **5a** afforded **7a** in 33% yield (Scheme 1). Cavitand **1a** has been described previously.[19]

The results reported in Table 2 indicate two different behaviors for **5a** alone and **5a** in presence of the picolinium guest on one hand and for **1a** and **7a** on the other hand. The diffusion coefficients of **5a** and **5a** in the presence of picolinium salt are almost identical (i.e., the ratio of the diffusion coefficient for host **5a** to that for its picolinium complex is $D_{host}/D_{cplx} \approx 1.0$), but they are smaller than those of **1a** and **7a** in the same solvent. The ratio of the diffusion coefficients, which are related to the hydrodynamic radii r_H of the species by the Stokes−Einstein equation ($D = k_BT/6\pi\eta r_H$), was used to obtain an estimate of

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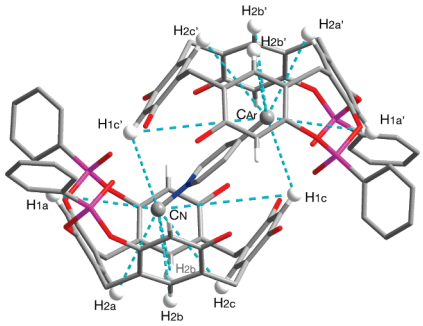

Figure 6. Main ROESY correlations observed between the bound guest and the capsular host.

the hydrodynamic volume ratio (Table 2).[20] We see that V_H(**5a**) $\approx$ V_H(Pico + **5a**) $\approx$ 2.3V_H(**1a**) $\approx$ 3.0V_H(**7a**), supporting the formation of the (**5a**)$_2$ capsule both for the free host and the complex. This was not foreseeable from the ^{1}H NMR spectra of **5a**. Furthermore, we showed by ^{1}H NMR spectroscopy that in a 2:1 mixture of **5a** and picolinium salt, only the Pico@(**5a**)$_2$ complex was observed. The DOSY data argue that free **5a** in solution exists as a dimeric assembly and that the guest is not a prerequisite for formation of the capsular structure. We similarly examined the behavior of **5b** alone and **5b** in the presence of the picolinium guest and compared their self-diffusion coefficients with those of **1b** and **7b**. Compounds **1b** and **7b** were synthesized following the procedures used for **1a** and **7a**. The results reported in Table 2 led to the same conclusion as drawn for the $C_{11}H_{23}$-substituted compounds, with V_H(**5b**) $\approx$ V_H(Pico + **5b**) $\approx$ 1.9V_H(**1b**) $\approx$ 2.0V_H(**7b**). The structure of the free host in $CDCl_3$ solution corresponds to the (**5b**)$_2$ self-assembled molecular capsule and is thus closely related to the one observed in the solid state by X-ray diffraction. It is noteworthy that the long-chain substituents in **5a**, a prolate ellipsoid assembly, probably lead to an overestimated molecular volume. The overestimation is minimized with the shorter phenethyl groups in **5b**, which results in a more spherical assembly.[20] This can explain why V_H(**5a**) is slightly greater than 2V_H(**1a**) and 2V_H(**7a**) whereas the value of V_H(**5b**) is almost equal to 2V_H(**1b**) and 2V_H(**7b**).

It is interesting to compare the results of rotating-frame Overhauser effect spectroscopy (ROESY) experiments run in CD_2Cl_2 solution for the PicoIod@(**5a**)$_2$ complex with the solid-state structure of the parent PicoIod@(**5b**)$_2$. This allows for the determination of the spatial proximity of the protons involved in the host−guest association in solution. The main cross-peaks were measured between the CH_3 groups of the *N*-methylpicolinium guest and the H_{1c} proton at the wide rim of the opposite cavity (C−C distance in the crystal is 3.91 Å) and the H_{1a} and H_2 protons of its own cavity (C−C distances in the crystal are 3.62 and 3.23−3.84 Å, respectively). No other significant correlations between host and guest were measured in the ROESY spectra (Figure 6 and Figure S9 in the Supporting Information). The agreement between the data from the solution and those from the solid state suggests that on the NMR time scale, the preferred average orientation of the guest inside the capsule in solution is similar to that observed in the crystal.

Guest Tumbling Dynamics: NMR Characterization of the Guest@(5a)$_2$ Supramolecular Rotor. The dimeric capsules (**5a**)$_2$ and (**5b**)$_2$ exist preferentially in solution, as evidenced by the

(20) Macchioni, A.; Ciancaleoni, G.; Zuccaccia, C.; Zuccaccia, D. *Chem. Soc. Rev.* **2008**, *37*, 479.

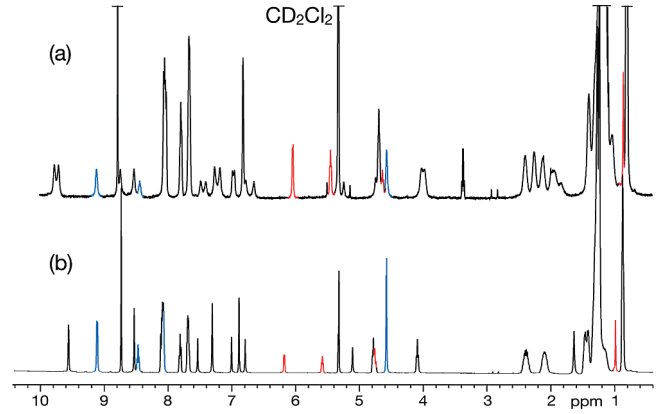

Figure 7. ^{1}H NMR spectra (500 MHz, CD_2Cl_2) of **5a** + 3.5 equiv of PyrPic at (a) 203 and (b) 293 K (red, bound guest; blue, free guest).

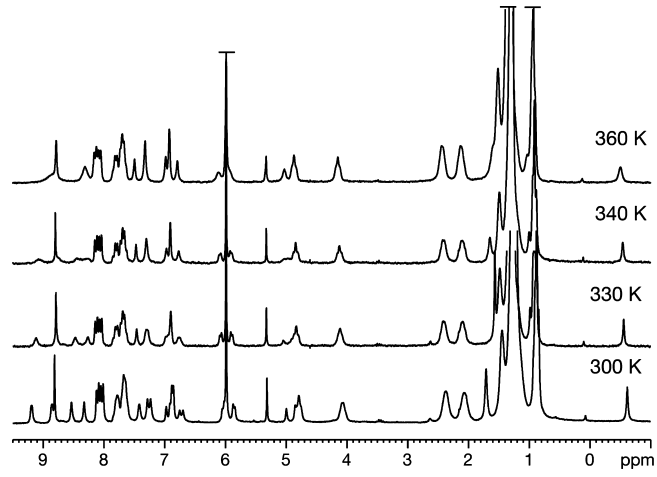

Figure 8. VT ^{1}H NMR spectra (200 MHz, $C_2D_2Cl_4$) of **5a** + 0.5 equiv of PicoPic.

^{1}H NMR and DOSY experiments, and their structures are closely related to that in the solid state described above. Thus, the formation of the capsule is not a consequence of the encapsulation of the charged guest but rather the stabilizing effect of the self-assembly of two cavitands through strong H-bonding. Here we underline an important point that concerns the dynamics of the encapsulated guest and the behavior of the two complexes, which differ as a function of the temperature. At 293 K in CD_2Cl_2 solution, the two cavitands in PyrPic@(**5a**)$_2$ were indistinguishable by NMR analysis (one set of signals for both cavitands; Figure 2), whereas they were distinguishable in PicoPic@(**5a**)$_2$ (two sets of signals; Figure 3). When the PyrPic@(**5a**)$_2$ sample was cooled to 203 K, each of the host signals split into two resonances, and the two cavitands were thus differentiated, leading to a situation similar to that observed with PicoPic@(**5a**)$_2$ at room temperature (Figure 7). On the other hand, when a solution of PicoPic@(**5a**)$_2$ in $C_2D_2Cl_4$ was heated to 360 K, we observed a change in the ^{1}H NMR spectra leading to the average of the signals of the two cavitands, a situation analogous to that observed with PyrPic@(**5a**)$_2$ at room temperature (Figure 8).

This behavior was also observed using variable-temperature (VT) ^{31}P NMR spectroscopy. At room temperature, only one resonance for the phosphorus nuclei in PyrPic@(**5a**)$_2$ was detected. When the temperature was lowered to 220 K, two 1:1 signals corresponding to each cavitand were detected (Figure 9a). Similarly, the 1:1 signals observed at room temperature

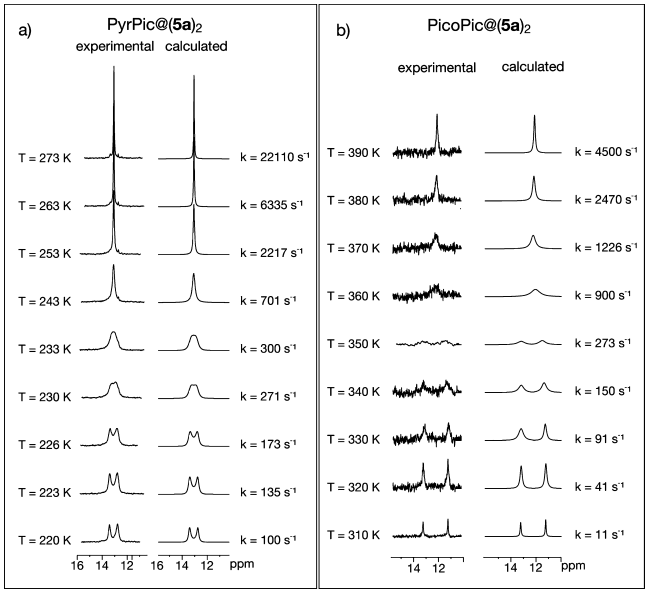

Figure 9. Experimental and calculated ^{31}P NMR spectra at different temperatures for (a) **5a** + 1 equiv of PyrPic in CD_2Cl_2 and (b) **5a** + 1 equiv of PicoPic in $C_2D_2Cl_4$.

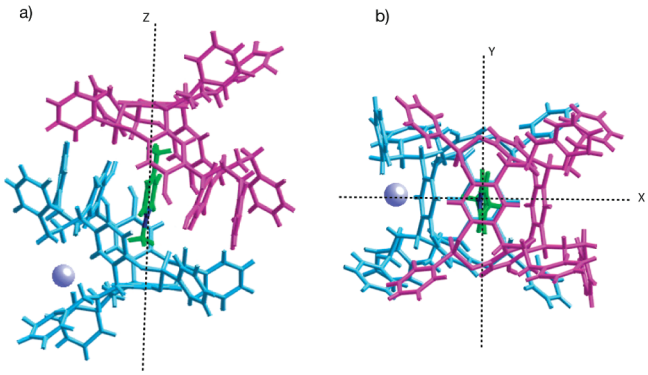

Figure 10. (a) Side and (b) top views of the X-ray structure of PicoIod@(**5b**)$_2$ that emphasize the formation of the supramolecular rotor.

for the complex PicoPic@(**5a**)$_2$ vanished at 353 K and above to give one averaged ^{31}P NMR signal (Figure 9b). VT experiments performed with the free host **5a**, which forms a (**5a**)$_2$ capsule in solution, did not detect changes in the ^1H NMR spectra. This means that the temperature dependence observed with the complexes is inherent to the host−guest association and also demonstrates the high stability of the dimeric capsule.

These experiments reveal that the two cavitands in PyrPic@(**5a**)$_2$ at low temperature and in PicoPic@(**5a**)$_2$ at room temperature experience different chemical environments. The "north" and "south" hemispheres of the capsule can be differentiated only if tumbling is restrained inside the cavity on the NMR time scale. This can be explained by considering the slowing of the tumbling of the guest in the restrictive environment of the inner cavity of the capsule. The interaction of the CH_3N^+ group of the guest with one cavitand and of the group in the para position on the guest aromatic ring with the other cavitand results in the upfield shielding of the respective protons of the encapsulated guest. The tumbling of the guest can be roughly decomposed into two main rotations (Figure 10): (i) rotation about the N−C_{para} direction of the guest (i.e., about the *Z* axis), which exchanges the two protons in the ortho positions and the two protons in the meta positions without exchanging the CH_3N^+ and Pyr-H_p (or Pico-CCH_3) positions, and (ii) rotation about the transverse direction (i.e., about any axis in the *XY* plane), which exchanges the CH_3N^+ and Pyr-H_p (or Pico-CCH_3) positions. If the tumbling occurs only via the *Z* axis, the two cavitands constituting the capsule should look different in the NMR spectra, as observed with the picolinium guest at room temperature and below and with the pyridinium guest at low temperature. Tumbling in the *XY* plane would average the NMR spectra of the two cavitands and make their signals indistinguishable, as observed with the pyridinium guest at room temperature and above and with the picolinium guest at high temperature.

Table 3. Kinetic Parameters for the Guest Tumbling in PyrIod@(**5a**)$_2$ and PicoIod@(**5a**)$_2$ Complexes

complex	$\Delta G^{\ddagger}$ (kJ mol^{-1})[a]	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J K^{-1} mol^{-1})
PyrIod@(**5a**)$_2$	44.8	46.8	6.8
PicoIod@(**5a**)$_2$	69.7	72.6	9.7

[a] T = 300 K.

The energy barriers for guest tumbling in PyrIod@(**5a**)$_2$ and PicoIod@(**5a**)$_2$ were estimated from the VT ^{31}P NMR experiments. Bandwidth analysis afforded $\Delta G^{\ddagger}$, $\Delta H^{\ddagger}$, and $\Delta S^{\ddagger}$ values (Table 3). ^1H VT NMR experiments gave similar results, although these had lower confidence because of the difficulties resulting from the simulation of the experimental spectra, which were less well resolved, and because of overlapping signals (data not shown). It is interesting to compare these data with those reported previously for the rotational movement of guests in the cavity of carceplexes. For instance, the movement of dimethylacetamide, dimethylformamide, or *N*-methylpyrrolidinone guests in carceplexes can be highly constrained, with energy barriers ranging from 40 to 65 kJ mol^{-1}.[21] A limiting case was shown in the recent work of Kobayashi and coworkers[10] on a self-assembled capsule involving boronic ester bonds within which the encapsulated aromatic guest rotated only along the long axis of the cage. In our case, the energy barriers are in the range 45−70 kJ mol^{-1}, which is an unexpected result considering the noncovalent character of the cage. Moreover, these results demonstrate the restricted tumbling of the guest that acts as a molecular rotator inside the capsule.[22]

Conclusion

In summary, we have described the self-assembly of AB*ii* diphosphonatocavitands that form dimeric capsular structures by means of strong H-bonds between OH phenol groups and PO H-bond acceptors. The capsules are stable in $CDCl_3$ and CD_2Cl_2 solutions and can encapsulate an *N*-methylpyridinium or *N*-methylpicolinium guest. We have demonstrated that guest encapsulation is not a prerequisite for the formation of the capsule. The supramolecular capsules are stable over a wide range of temperature, and the encapsulated guest experiences a restricted tumbling movement inside the capsular cavity. Free rotation of the guest was observed only about the long axis of the host, while rotation about the short equatorial axes of the host can be frozen for both guests. The longer *N*-methylpicolinium substrate was more tightly encapsulated inside the capsular cavity than was the N-methylpyridinium guest and had

(21) (a) Sherman, J. C.; Knobler, C. B.; Cram, D. J. *J. Am. Chem. Soc.* **1991**, *113*, 2194. (b) Peak, K.; Ihm, H.; Lee, H. C.; No, K. T. *J. Org. Chem.* **2001**, *66*, 5736.
(22) Jose, D.; Datta, A. *J. Phys. Chem. Lett.* **2010**, *1*, 1363.

a higher energy barrier for the tumbling process (69.7 vs 44.8 kJ mol^{-1}, respectively). Thus, the tumbling of *N*-methylpicolinium is slow on the NMR time scale at room temperature, as the signals corresponding to the two cavitands can be differentiated in their ^{1}H and ^{31}P NMR spectra. These supramolecular architectures possess endohedral functionalities, a feature representing a new step in the area of nanoscale engineering that associates the simplicity of self-assembly with the incorporation of functionalities, which could lead to artificial enzyme mimetics, molecular magnets, sensors, or delivery systems. The present system can provide insights into the design of new molecular rotors. Current work to further exploit these results in order to conceive novel functional materials is underway.

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Supporting Information Available: Synthetic details; ^{1}H and ^{13}C NMR spectra of **7a** and **3b**−**7b**; VT NMR spectra; ROESY and DOSY experimental details; and X-ray crystallographic data (CIF) and additional molecular structure views for $(\mathbf{5b})_2$ (CCDC 775618) and PicoIod@$(\mathbf{5b})_2$ (CCDC 775619). This material is available free of charge via the Internet at http://pubs.acs.org.

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