Communication

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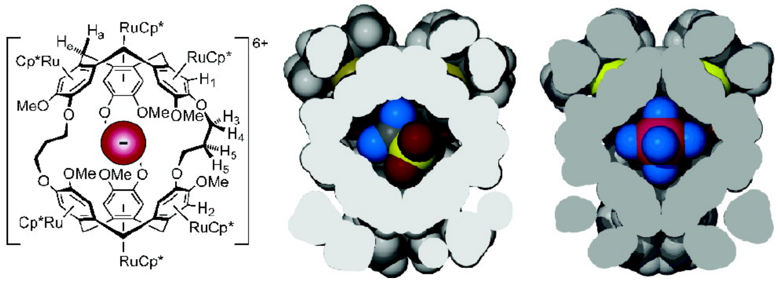

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Selective Anion Encapsulation by a Metalated Cryptophane with a π-Acidic Interior

Robert M. Fairchild and K. Travis Holman*

Department of Chemistry, Georgetown University, Washington, D.C. 20057

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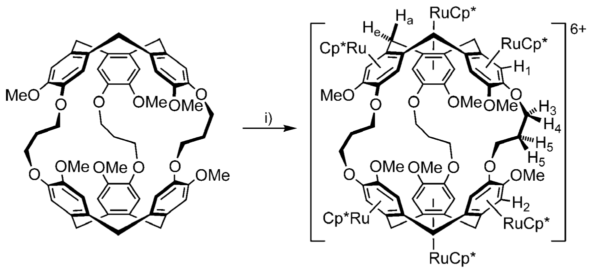
The design of artificial receptors for the selective binding or sensing of anions has been a subject of sustained interest in light of the ubiquity and general importance of anionic species in biochemistry, the environment, etc.[1] Anion binding sites provided by synthetic receptors most commonly employ positive charge,[2] neutral[3] or cationic[4] hydrogen bond donors and/or Lewis acidic metal centers.[5] Recently, however, there is growing evidence to suggest that certain anion−π or, more specifically, anion−arene interactions might be successfully exploited in the design of artificial receptors for anions. The gas-phase interaction between anions and ostensibly π-acidic arenes, such as hexafluorobenzene, 1,3,5-trinitrobenzene, and 1,3,5-triazene, for instance, appears to be attractive.[6] Experimentally, close chloride−arene contacts have recently been observed in a copper(II)−triazine complex.[7] Moreover, recognizing that the electrophilicities of aryl carbon atoms are greatly enhanced upon η^6-metalation by certain electron-withdrawing transition metal moieties (e.g., $[(\text{arene})Ru]^{2+}$), Atwood and co-workers have reported several metalated cavitands that bind anions within their cup-shaped, aryl-lined cavities.[8] Related organometallic species have also been used extensively by Beer and co-workers to provide sensory features to a variety of H-bonding anion receptors.[9] We herein report the synthesis of a $[Cp^*Ru]^+$-functionalized "molecular container",[10] namely, Collet's well-known cryptophane-E ((±)-**E**),[11] and the selective encapsulation of anions within its apparently π-acidic interior. The volume of the cryptophane cavity is effectively enlarged upon metalation, and the barrier to guest complexation increased, resulting in kinetically stable complexes of relatively large anions.

Collet's elegant cryptophanes are fascinating examples of so-called molecular containers,[10] displaying an impressive ability to selectively encapsulate guests of appropriate size, shape, and chemical identity within their rigidly ellipsoidal cavities. π-Basic (±)-**E**, for example (Scheme 1), is well-suited for the binding of small organic cations (e.g., Me_4N^+) and neutral molecules (e.g., $CHCl_3$), but shows no propensity toward anion encapsulation. Permetalation of all six arene faces with transition metal moieties was expected to transform the π-basic aryl-lined cavity into one more amenable to anion binding and better described as mildly π-acidic. As the $[Cp^*Ru(CH_3CN)_3]^+$ moiety ($\mathbf{1}^+$) is highly areneophilic,[12] $\mathbf{1}[CF_3SO_3]$ and $\mathbf{1}[SbF_6]$ were separately reacted with (±)-**E** in CH_2Cl_2 at 55 °C (sealed vessel) to give the hexametalated capsule $[(\pm)\text{-}\mathbf{2}]^{6+}$ as highly air/water stable $[CF_3SO_3]^-$ and $[SbF_6]^-$ salts.[13]

Scheme 1. Synthesis of the Permetalated Cryptophane $(\pm)\text{-}[(Cp^*Ru)_6(\mathbf{E})]^{6+}$ ($[(\pm)\text{-}\mathbf{2}]^{6+}$) [(i): $\mathbf{1}[X]$ ($X = [CF_3SO_3]^-$, $[SbF_6]^-$), CH_2Cl_2, 55°, 24 h]



(+/-)-cryptophane-E, (+/-)-**E**

$[(+/-)\text{-}\mathbf{2}][CF_3SO_3]_6$ (76%)
$[(+/-)\text{-}\mathbf{2}][SbF_6]_6$ (65%)

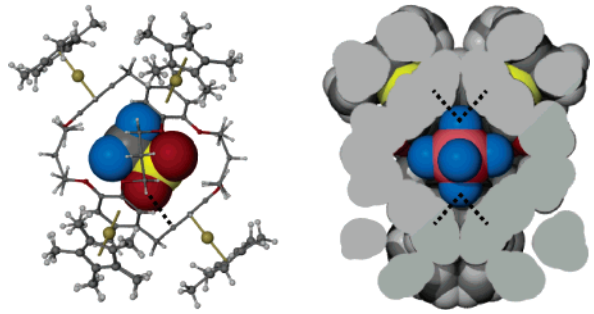


Figure 1. The $[(\pm)\text{-}\mathbf{2}\cdot CF_3SO_3]^{5+}$ (left) and $[(\pm)\text{-}\mathbf{2}\cdot SbF_6]^{5+}$ (right) species as observed in the X-ray crystal structures of their salts. The image on the right illustrates a vertically sliced view of the capsule. Dashed lines indicate close contacts.

X-ray single-crystal structures of $[(\pm)\text{-}\mathbf{2}][CF_3SO_3]_6$ and $[(\pm)\text{-}\mathbf{2}][SbF_6]_6$ were obtained, and although the data are of modest quality, both structures clearly establish the encapsulation of the anions by the host (Figure 1). Interestingly, the cryptophane moieties of $[(\pm)\text{-}\mathbf{2}]^{6+}$ in both structures are nearly indistinguishable from that of (±)-**E** as observed in the crystal structure of its complex with $CHCl_3$ (V_{vdW} = 72 Å^3), its optimal neutral guest.[11a] Thus, while the cryptophane structure of $[(\pm)\text{-}\mathbf{2}]^{6+}$ is virtually identical to that of (±)-**E**, its cavity appears to be larger, accommodating anionic guests that are clearly greater in volume than the neutral molecules bound by (±)-**E**.[13] This behavior is reminiscent, albeit a role reversal, of the observation that π-basic (±)-**E** binds comparatively larger organic cations than neutral molecules.[11a] The snug fit of the comparatively large anions within the cavity of $[(\pm)\text{-}\mathbf{2}]^{6+}$ is manifested in the form of unusually short anion−arene contacts. For example, in the $[(\pm)\text{-}\mathbf{2}\cdot SbF_6]^{5+}$ complex, the C_4 axis of the octahedral $[SbF_6]^-$ ion coincides with the C_3 axis of the cation and the "axial" fluorines are in close contact with all six basal arene carbon atoms (F⋯C = 2.97(1) Å, F⋯centroid = 3.08 Å). The reliable determination of interatomic distances is precluded by significant disorder of the anion in the $[(\pm)\text{-}\mathbf{2}\cdot CF_3SO_3]^{5+}$ complex. Nonetheless, the triflate ion clearly lies centrally within the cavity and is tilted by ca. 60° from the C_3 axis such that one of the triflate oxygen atoms lies within van der Waals contact of the two basal carbon atoms of one arene ring. Notably, the host−guest interactions in these structures (anion−π) differ markedly from those observed in the calixarene-based capsule reported by Dalcanale, wherein the anions adopt positions adjacent to the Pd(II) cations.[14]

NMR studies reveal the binding of anions by $[(\pm)\text{-}\mathbf{2}]^{6+}$ in

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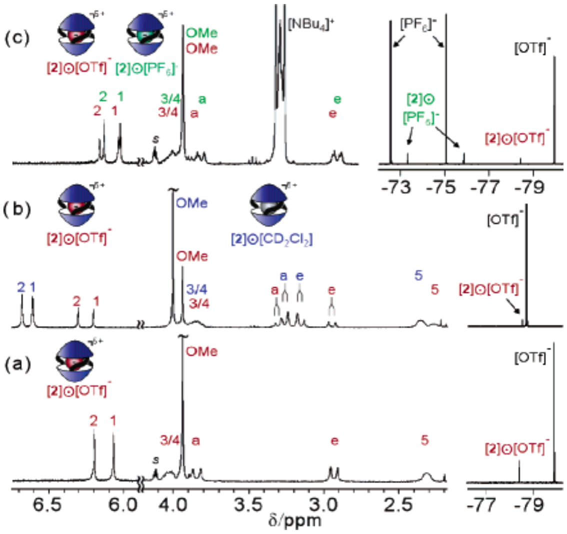

Figure 2. ^{1}H (left) and ^{19}F (right) NMR spectra of $[(\pm)\text{-}\mathbf{2}][CF_3SO_3]_6$ (0.9 mM, 300 MHz, 298 K): (a) at equilibrium in CD_3NO_2; (b) near equilibrium, after 3 weeks, in CD_2Cl_2; (c) at equilibrium (3 weeks) in the presence of ~6 equiv of $[NBu_4][PF_6]$. See Scheme 1 for spectral assignments.

solution. The ^{1}H NMR spectrum of $[(\pm)\text{-}\mathbf{2}][CF_3SO_3]_6$ in CD_3NO_2 (at equilibrium, Figure 2a) is remarkably simple, highlighting the D_3 point group symmetry of the cationic host. The corresponding ^{19}F spectrum gives two triflate signals with an integral ratio of exactly 1:5, suggesting that essentially all of the capsules exist as $[(\pm)\text{-}\mathbf{2}{\cdot}CF_3SO_3]^{5+}$ species at equilibrium in CD_3NO_2. In CD_2Cl_2, however, an additional set of host peaks grows in over time at the expense of the original set such that, after approximately 3 weeks, the system approaches equilibrium and the new host peaks predominate (Figure 2b). During this time frame, the ^{19}F NMR spectrum shows that the signal assigned to the encapsulated triflate anion diminishes as the free triflate signal grows. Correlation between the ^{1}H and ^{19}F integral intensities confirms that the new signals in the ^{1}H spectrum are due to the "free" (likely CD_2Cl_2 occupied) cation. Quickly drying the sample and redissolving in CD_3NO_2 results in ^{1}H and ^{19}F spectra that initially show two species ($[(\pm)\text{-}\mathbf{2}{\cdot}CF_3SO_3]^{5+}$ and $[(\pm)\text{-}\mathbf{2}{\cdot}\text{solvent}]^{6+}$), but, over time, revert to spectra similar to that of Figure 2a, indicating the slow uptake of triflate by the host. As the decomplexation process occurs at a comparatively negligible rate, the kinetics of triflate complexation could readily be fit to a simple second-order expression. Eyring analysis yields an activation barrier for triflate encapsulation (the "constrictive binding" energy)[10] of $\Delta G^{\ddagger}_{298K} = 18.0(8)$ kcal·mol^{-1} ($\Delta H^{\ddagger} = 17.5(4)$ kcal·mol^{-1} and $\Delta S^{\ddagger} = 2(1)$ cal·mol^{-1}·K^{-1}). Notably, this value is considerably larger than that for the encapsulation of $CHCl_3$ by $(\pm)\text{-}\mathbf{E}$ in $(CDCl_2)_2$ ($\Delta G^{\ddagger}_{298K} = 13.3$ kcal·mol^{-1})[11a] and is likely a reflection of either the larger guest size or an increase in the rigidity of the cryptophane upon metalation.

Addition of other anions, as their $[NBu_4]^{+}$ salts, to CD_3NO_2 solutions of $[(\pm)\text{-}\mathbf{2}{\cdot}CF_3SO_3][CF_3SO_3]_5$ reveals interesting competitive behavior. $[PF_6]^{-}$ and $[SbF_6]^{-}$ ions, for instance, compete directly with triflate for the cavity, but take weeks to establish equilibrium. The association constants for these anions can be determined relative to that for triflate (K_{X^-}/K_{OTf^-}), measuring 1.18 and 0.30, respectively (Figure 2c). The addition of $[BF_4]^{-}$ has no effect on the spectra. Thus, these results follow the familiar pattern for guest complexation by cryptophanes: those too large for the cavity, or too small to fill it, are bound less effectively than some optimally sized guest, in this case $[PF_6]^{-}$. The binding of other anions, however, is more complicated and reveals interesting allosteric effects. Reversible anion binding at cationic sites exterior to the cavity appears to switch off binding within the host's interior due to electrostatic repulsion between exterior and encapsulated anions. Some anions ($[CF_3CO_2]^{-}$, $[CH_3SO_3]^{-}$, $[CH_3CH_2SO_3]^{-}$) appear to simultaneously compete with triflate for the cavity while diminishing overall cavity binding, whereas others (halides, $[NO_3]^{-}$, $[HCO_2]^{-}$) seem to only turn off cavity binding. The allosteric behavior additionally provides rationale for the counterintuitive observation that the K_a for triflate complexation is apparently very large in CD_3NO_2 ($K_a > 3 \times 10^{4}$ M^{-1}, by dilution), but very small in the less polar CD_2Cl_2 ($K_a \approx 10$ M^{-1}). As CD_2Cl_2 less effectively solvates the anions, they more effectively ion pair (in fast exchange) with sites exterior to the cryptophane cavity, and thereby turn off cavity binding. Vastly different chemical shifts for H_a/H_e protons in CD_2Cl_2 versus CD_3NO_2 serve as spectral indicators for fast-exchange anion binding at the exterior sites (Figure 2b).

In summary, metalation of the exterior arene faces of cryptophane-E with $[Cp^{*}Ru]^{+}$ moieties results in a π-acidic cavity capable of size-selective encapsulation of relatively large anions. This work is currently being extended to metalated cryptophanes that are zwitterionic, water soluble, and/or homochiral.

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Supporting Information Available: Detailed experimental procedures, spectroscopic, kinetic, and crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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