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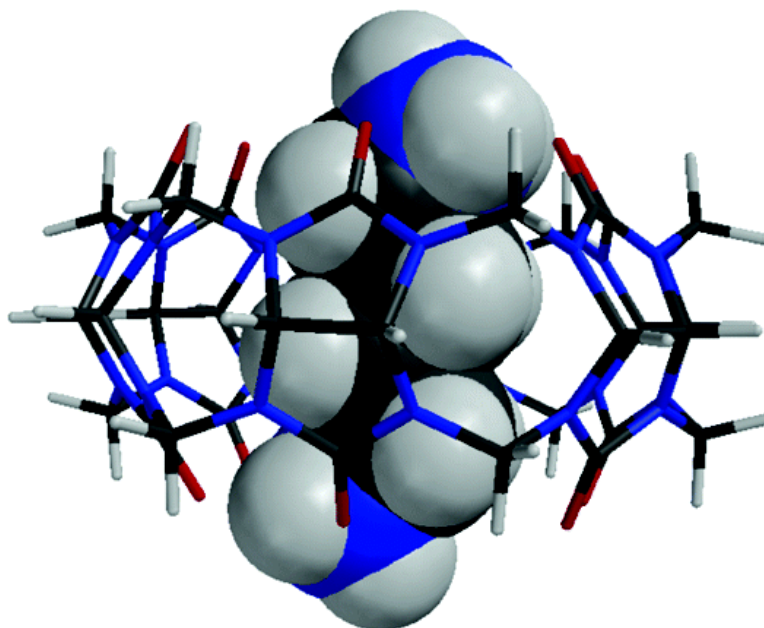
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Cucurbit[6]uril Pseudorotaxanes: Distinctive Gas-Phase Dissociation and Reactivity

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One of the prototypical supramolecular structures, rotaxane,[1] involves a wheel-and-axle architecture with a linear molecule (the "axle") threaded through another cyclic species (the "wheel"). Bulky groups at the ends of the axle prevent the wheel molecule from slipping off; pseudorotaxanes have a similar architecture but lack the bulky stopping groups. Mass spectrometry is increasingly being used to characterize such supramolecular structures,[2] but most studies do not go beyond establishment of the stoichiometry of the complex. Can pseudorotaxanes formed in solution survive the electrospray ionization process intact, and if so, will they exhibit characteristics that set them apart from conventional complexes that lack the pseudorotaxane architecture?

Cucurbit[6]uril[3] (Figure 1) has long been known to form pseudorotaxanes with diammonium cations[4] and other species[5,6] in condensed media. Recently, we have shown that electrospray ionization of a related molecule with a smaller central cavity, decamethylcucurbit[5]uril, results in the observation of cage complexes in the gas phase.[7] Here we report electrospray ionization mass spectrometric experiments that demonstrate cucurbit[6]uril pseudorotaxanes survive into the gas phase and exhibit dissociation and reactivity distinct from that of nonrotaxanes.
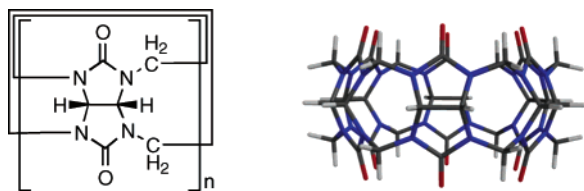

Figure 1. Structure of cucurbit[n]uril (left); cucurbit[6]uril model (gray = carbon, red = oxygen, blue = nitrogen, white = hydrogen).

All experiments were performed using a Fourier transform ion cyclotron resonance mass spectrometer[8,9] (model APEX 47e, Bruker Daltonics; Billerica, MA) and a microelectrospray ionization source modified from an Analytica (Analytica of Branford; Branford, MA) design.[10] The instrument was controlled using a MIDAS data system[11] (National High Magnetic Field Ion Cyclotron Resonance Facility; Tallahassee, FL). Cucurbit[n]urils (hereafter abbreviated "cuc[n]," where n is the number of monomer units) were synthesized as has been described.[12] Samples were prepared for electrospray by first dissolving the cuc[n], at a concentration of 7.5 mM, in 88% formic acid. A 100 μL aliquot of this solution was mixed with 50 μL of aqueous amine, 7.5 mM, and the mixture was diluted to 1 mL. Electrospray (tip voltage, 1300 V; flow rate, 10 μL h^{-1}) resulted in strong signals for positive ions consistent with complexes of ammonium ions with cuc[n]. Sustained off-resonance irradiation-collision induced dissociation (SORI-CID)[13] was performed by using a stored waveform inverse Fourier transform (SWIFT)[14] pulse

to isolate the ions of interest, followed by a 6.5 ms pulse of air (at atmospheric backing pressure) and irradiation with a low amplitude, 3 s duration constant-frequency rf pulse 750 Hz below resonance with the ion to be excited. For reactivity studies, neutral amines were introduced into the trapping region of the instrument via controlled variable leak valves (Varian), typically to pressures around 1×10^{-7} mbar (as indicated by an uncorrected cold cathode gauge (Balzers)). Electrosprayed ions were injected into the trap and allowed to react with the neutral amines; reactant and product ions were monitored as a function of time.

We present evidence that cuc[6] and doubly protonated 1,4-butanediamine (DAB) cations form pseudorotaxanes that survive the electrospray process and exhibit distinctive behavior in the gas phase. This conclusion is based on the stoichiometries of observed doubly protonated cuc[n] complexes with DAB ions, on the collision-induced dissociation behavior of the complexes, and on the reactivities of the complexes with neutral amines. In each case we compare the behavior of the proposed pseudorotaxane with that of a complex that cannot adopt the pseudorotaxane architecture.

Electrospray of an acidic mixture of cuc[n] ($n = 5-6$) with DAB results in the mass spectrum shown in Figure 2. Only one complex is observed for cuc[5], a doubly charged ion corresponding to two singly protonated DAB ions attached to cuc[5] (a 2:1 complex). Almost all of the cuc[6] complexes, on the other hand, correspond to *one* doubly protonated DAB cation attached to the cucurbituril (1:1 complex), with only about 1% of the signal arising from a 2:1 complex analogous to that observed for cuc[5]. On the basis of the observed stoichiometry, we propose that the cuc[6] complex with doubly protonated DAB is a pseudorotaxane.
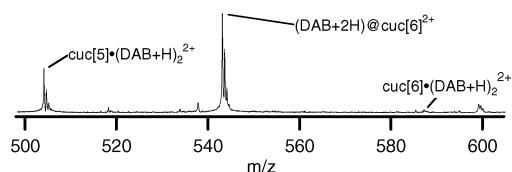

Figure 2. Electrospray Fourier transform mass spectrum of an acidic mixture of 1,4-diaminobutane with cucurbit[n]uril ("cuc[n]"), $n = 5-6$.

To test this conjecture, we performed SORI-CID on the proposed (DAB + 2H)@cuc[6]$^{2+}$ ion, m/z 543.2. A typical SORI-CID spectrum is shown in Figure 3a. Fragment ions were observed only at the highest SORI pulse amplitudes attempted, accompanied by severe attenuation of all the ion signal, suggesting that ejection of the parent ion from the trap is competitive with SORI-CID. The largest fragment peak, at m/z 997.3, corresponds to loss of singly protonated DAB from the complex, resulting in protonated cuc[6]. Other peaks, of similar intensity, are consistent with loss of protonated DAB coupled with fragmentation of the cuc[6] cage (m/z 694.2, 706.2, 759.2, 788.2, 800.2, 882.3, 911.3, and 925.3). The SORI-CID results therefore suggest the proposed (DAB +

2H)@cuc[6]$^{2+}$ ion is strongly bound; loss of DAB and breakup of the cuc[6] cage occur at similar energies.
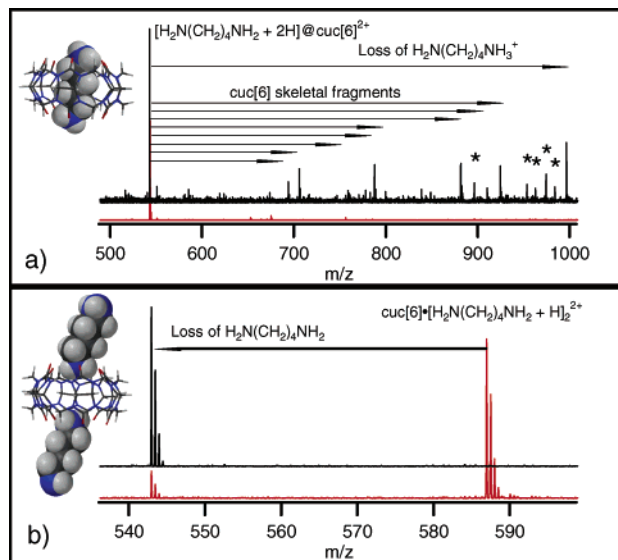
Figure 3. (a) SORI-CID of proposed (DAB+2H)@cuc[6]$^{2+}$ pseudorotaxane. The SORI excitation pulse is disabled in the lower (red) trace. The upper (black) trace, with SORI enabled, exhibits extensive fragmentation of the cuc[6] cage. Asterisks indicate noise peaks. (b) SORI-CID of the nonrotaxane cuc[6]·(DAB+H)$_2$$^{2+}$. Some loss of neutral DAB is observed even with the SORI pulse disabled, due to dissociation while isolating the parent ion (lower, red trace). SORI-CID results in facile loss of neutral DAB.

We examined SORI-CID of two other species as controls. When sprayed with an excess of DAB, the 2:1 DAB:cuc[6] complex is observed at nominal m/z 587.2. Using the same amplitude, duration, and frequency offset as was employed for the 1:1 complex, the SORI-CID spectrum shown in Figure 3b was obtained. Dissociation of the 2:1 complex via loss of neutral DAB, producing a doubly charged product ion with the same nominal m/z as the 1:1 complex, is facile and quantitative. It is difficult to isolate the 2:1 complex because dissociation to produce the 1:1 complex occurs during the isolation.

We also prepared complexes of ethylenediamine with cuc[6]. Electrospray of acidic mixtures of these two components results exclusively in doubly protonated 2:1 complexes with nominal m/z of 559.2, consistent with a cuc[6]·[H$_2$N(CH$_2$)$_2$NH$_2$ + H]$_2$$^{2+}$ complex. Molecular models suggest ethylenediamine is too short to simultaneously bind both rims of cuc[6]. Again, complete isolation of the parent complex ion is difficult because dissociation of protonated ethylenediamine occurs during the isolation event. SORI-CID of the 2:1 protonated ethylenediammonium:cuc[6] complex results in facile loss of protonated ethylenediammonium as well as loss of an additional neutral molecule of ethylenediamine. In summary, the 2:1 protonated diamine:cuc[6] complexes are easily dissociated via loss of the diamine (with or without the charge), whereas the 1:1 doubly protonated DAB:cuc[6] complex fragments primarily via breakup of the cuc[6] cage, consistent with a pseudorotaxane structure for the 1:1 complex.

The reactivity of the proposed pseudorotaxane in the gas phase is also distinctive and consistent with a pseudorotaxane structure.

Reaction of the proposed (DAB + 2H)@cuc[6]$^{2+}$ ion with neutral *tert*-butylamine in the gas-phase results in slow *addition* of the *tert*-butylamine to the complex, with kinetics that clearly do not show the expected simple pseudo-first-order behavior. Reasonable fits to the experimental reactant and product intensities as a function of time are obtained by assuming a model that involves slow conversion of the complex from an unreactive form to a reactive form, followed by addition of the amine. The addition reaction proceeds to equilibrium. Using this model, the rate of *tert*-butylamine addition is $1.3 \pm 0.2 \times 10^{-11}$ cm^3 molecule^{-1} s^{-1}.

This reactivity contrasts with that exhibited by cuc[6]·(NH$_3$ + H)$_2$$^{2+}$ with *tert*-butylamine in the gas phase. The *tert*-butylamine reacts with this nonrotaxane ion by *displacing* neutral ammonia from the complex, in two sequential steps. Excellent fits to the experimental data are obtained, assuming simple pseudo-first-order kinetics, yielding rate constants of $2.2 \pm 0.1 \times 10^{-10}$ and $1.4 \pm 0.1 \times 10^{-10}$ cm^3 molecule^{-1} s^{-1} for the first and second displacements, respectively.

These results are consistent with (DAB + 2H)@cuc[6]$^{2+}$ having a pseudorotaxane structure in the gas phase; the pseudorotaxane ion cannot react via amine displacement because the ammonium ion is attached to the cucbituril at both ends. Externally bound ammonium, on the other hand, is easily displaced by another amine.

In summary, all available evidence indicates (DAB + 2H)@cuc[6]$^{2+}$ is a pseudorotaxane in the gas phase. Molecular mechanics modeling suggests an appropriate size relationship between the two molecules for pseudorotaxane formation. The 1:1 stoichiometry of the observed complexes is consistent with this interpretation, and the SORI-CID experiments strongly support a pseudorotaxane structure. Finally, the complex exhibits reactivity consistent with a pseudorotaxane structure. These results suggest that SORI-CID and reactivity tests can be used to identify such structures for gas-phase ions.

Supporting Information Available: Kinetic plots for reactions of *tert*-butylamine with (DAB + 2H)@cuc[6]$^{2+}$ and cuc[6]·(NH$_3$ + H)$_2$$^{2+}$ (PDF). This material is available free of charge at http://pubs.acs.org.

References

(1) Sauvage, J.-P.; Dietrich-Buchecker, C., Eds. *Molecular Catenanes, Rotaxanes, and Knots*; Wiley-VCH: Weinheim, Germany, 1999.
(2) Schalley, C. A. *Int. J. Mass Spectrom.* **2000**, *194*, 11−39.
(3) Mock, W. L. In *Comprehensive Supramolecular Chemistry*; Vögtle, F., Ed.; Elsevier: New York, 1996; Vol. 2, pp 477−493.
(4) Mock, W. L.; Shih, N.-Y. *J. Org. Chem.* **1986**, *51*, 4440−4446.
(5) Kim, K. *Chem. Soc. Rev.* **2002**, *31*, 96−107.
(6) Buschmann, H.-J.; Wego, A.; Schollmeyer, E.; Döpp, D. *Supramol. Chem.* **2000**, *11*, 225−231.
(7) Kellersberger, K. A.; Anderson, J. D.; Ward, S. M.; Krakowiak, K. E.; Dearden, D. V. *J. Am. Chem. Soc.* **2001**, *123*, 11316−11317.
(8) Dearden, D. V.; Dejsupa, C.; Liang, Y.; Bradshaw, J. S.; Izatt, R. M. *J. Am. Chem. Soc.* **1997**, *119*, 353−359.
(9) Pope, R. M.; Shen, N.; Nicoll, J.; Tarnawiecki, B.; Dejsupa, C.; Dearden, D. V. *Int. J. Mass Spectrom. Ion Processes* **1997**, *162*, 107−119.
(10) Wigger, M.; Nawrocki, J. P.; Watson, C. H.; Eyler, J. R.; Benner, S. A. *Rapid Commun. Mass Spectrom.* **1997**, *11*, 1749−1752.
(11) Senko, M. W.; Canterbury, J. D.; Guan, S.; Marshall, A. G. *Rapid Commun. Mass Spectrom.* **1996**, *10*, 1839−1844.
(12) Day, A. I.; Arnold, A. P. Cucurbiturils and Method for Synthesis. World Intellectual Property Organization Patent WO 00/68232, Nov. 16, 2000.
(13) Gauthier, J. W.; Trautman, T. R.; Jacobson, D. B. *Anal. Chim. Acta* **1991**, *246*, 211−225.
(14) Chen, L.; Wang, T.-C. L.; Ricca, T. L.; Marshall, A. G. *Anal. Chem.* **1987**, *59*, 449−454.

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