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Slow-exchange C_3-symmetric cryptand/trispyridinium inclusion complexes containing non-linear guests: a new type of threaded structure

Feihe Huang,[a,†] Frank R. Fronczek,[b] Mehdi Ashraf-Khorassani[a] and Harry W. Gibson[a,*]

[a]*Department of Chemistry, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061-0212, USA*
[b]*Department of Chemistry, Louisiana State University, Baton Rouge, LA 70803, USA*

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Abstract—Slow-exchange C_3-symmetric inclusion complexes were successfully prepared based on a new cryptand/trispyridinium recognition motif as confirmed by proton NMR spectroscopy, electrospray ionization mass spectrometry, and molecular modeling. These inclusion complexes are the first examples of a new type of threaded structure with non-linear guests.

Interlocked molecular structures, usually prepared by threading linear guests through the cavities of cyclic hosts, are attractive not only because of their topological importance but also due to their potential applications in preparation of nanoscale devices.[1,2] They mainly include pseudorotaxanes, rotaxanes, catenanes, polypseudorotaxanes, polyrotaxanes, and polycatenanes. Cryptands and supramolecular cryptands have been studied for binding organic guests, such as paraquat derivatives,[3] diquat,[4] bis(secondary ammonium) ions,[5] and bisparaquat.[6] Previous host–guest studies using 1,3,5-tris(*N*-pyridiniummethyl)benzene salts were mainly focused on anion binding.[7] Up to now, almost all slow-exchange host–guest complexation systems have been based on the dibenzo-24-crown-8/secondary ammonium recognition motif.[1,8] Here, we report three slow-exchange C_3-symmetric inclusion complexes based on a new cryptand/trispyridinium recognition motif, in which 1,3,5-tris(*N*-pyridiniummethyl)benzene salts act as guests for the first time. These inclusion complexes belong to a new type of threaded structure because the guests are non-linear.

The preparation of cryptand host **1** was reported before.[3a] Trispyridinium salts **2** were made by the reaction of excess pyridine or pyridine derivative with 1,3,5-tris(bromomethyl)-2,4,6-trimethylbenzene followed by ion exchange with NH_4PF_6 and purified by recrystallization in deionized water. The X-ray structure[9] (Fig. 1) shows that all three pyridinium arms of **2a** are at one side of the benzene ring to form a concave cavity, which can envelop a phenylene ring of **1**.

Partial proton NMR spectra of **1**, **2a**, and an equimolar solution of **1** and **2a** are shown in Figure 2. Two sets of peaks were found in the spectrum of the solution of **1** and **2a**, indicating slow-exchange complexation on the proton NMR time scale.[10] After complexation, peaks corresponding to aromatic (H_1), β-ethyleneoxy (H_5), γ-ethyleneoxy (H_3), and δ-ethyleneoxy protons (H_4) on **1** and α-pyridinium (H_8), benzylic (H_7), and methyl protons (H_6) of **1** moved upfield, while α-ethyleneoxy protons (H_2) of **1** and β-pyridinium (H_9) and γ-pyridinium protons (H_{10}) of **2a** moved downfield. The fact that only one set of complexed signals was found for protons on **1** and **2a** indicated that all three pyridinium arms of complexed **2a** are threaded and rapidly flipping up and down in solution.[11] Otherwise, the presence of the two isomers of the complex shown in Figure 1 would result in a more complicated (non-C_3 symmetric) spectrum; the top isomer would render the two aromatic rings of the host **1** non-equivalent and the bottom isomer would render the pyridinium units non-equivalent.

Keywords: Host–guest systems; Self-assembly; Inclusion complex; Cryptand; Pyridinium.

[*] Corresponding author. Tel.: +1 540 231 5902; fax: +1 540 231 8517; e-mail: hwgibson@vt.edu

[†] Present address: Department of Chemistry, University of Utah, 315 South 1400 East, Salt Lake City, UT 84112-0850, USA.

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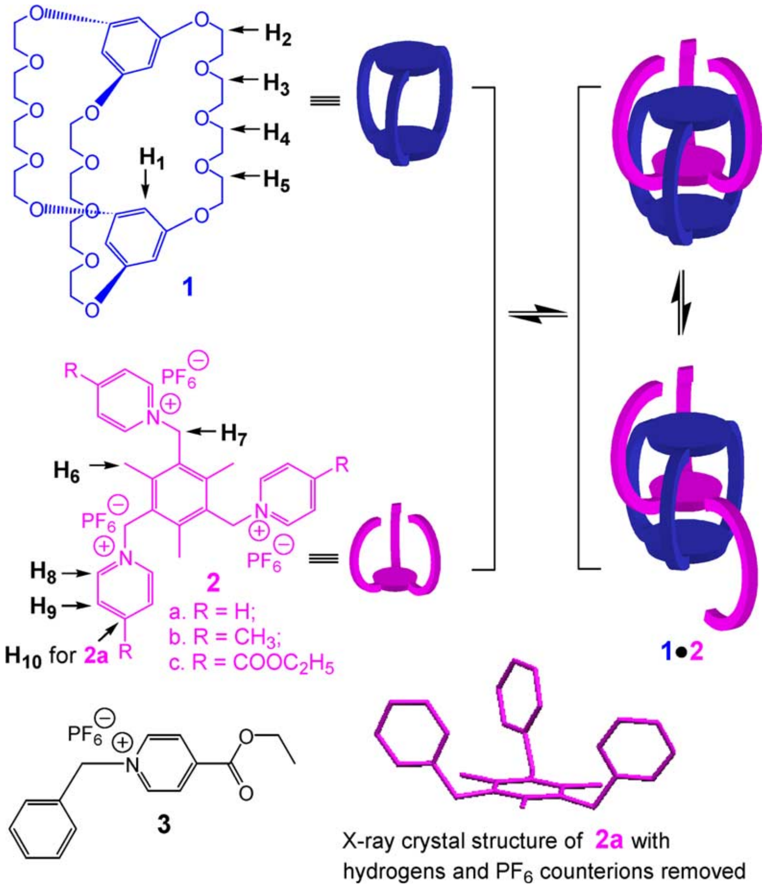

Figure 1. Compounds used in this study and X-ray crystal structure of **2a**.

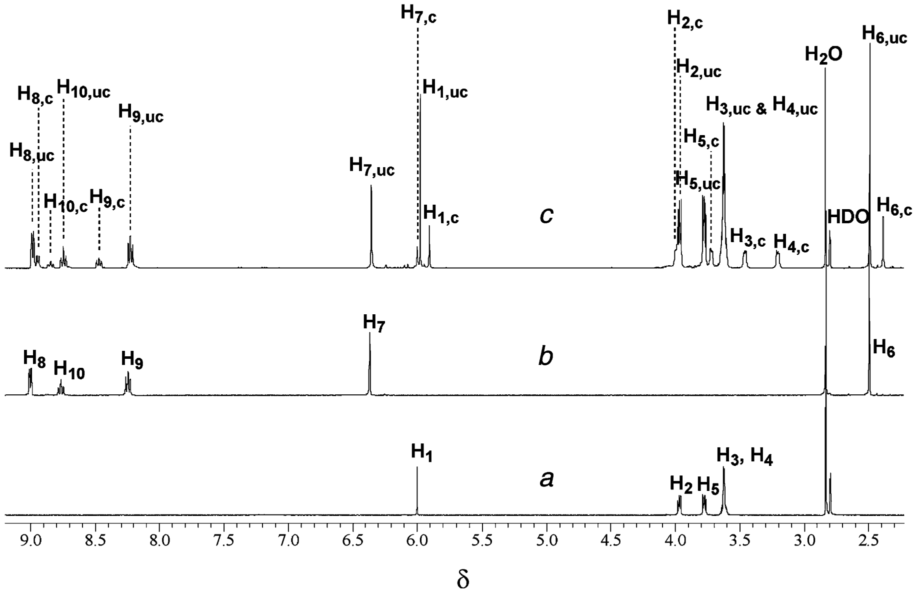

Figure 2. Partial proton NMR spectra (400 MHz, CD_3COCD_3, 22 °C) of cryptand **1** (a, bottom), trispyridinium **2a** (b, middle), and 10.0 mM each of **1** and **2a** (c, top). Complexed and uncomplexed species are denoted by 'c' and 'uc', respectively.

From integrations of all peaks, the stoichiometry of the complexation between **1** and **2** was determined to be 1:1.

The complex is presumably held together by a combination of H-bonding interactions between all of the α-pyridinium protons H_8 and the oxygen atoms of the ethyleneoxy units, as observed by X-ray crystallography with a model complex of monopyridinium salt **3** with bis(*m*-phenylene)-32-crown-10,[12] coupled with π-stacking of the central aromatic ring of the guest with the two phenylene units of the host.[13] A pyridinium ring probably enters the cavity first[11] and the rest of the guest then slides in to maximize H-bonding interactions between the host and the guest.

Electrospray ionization mass spectra of solutions of **1** and **2** in 4:1 CH_3CN:$CHCl_3$ confirmed the formation of the 1:1 complexes. Four peaks were found for **1**·**2a** (Fig. 3): *m*/*z* 1412.52 (3%) [**1**·**2a**−PF_6]$^+$, 1360.63 (5%) [**1**·**2a**−PF_6−C_6H_7N+Na+H_2O]$^+$, 633.89 (100%) [**1**·**2a**−2PF_6]$^{2+}$, and 374.26 (80%) [**1**·**2a**−3PF_6]$^{3+}$. Three peaks were found for **1**·**2b**: *m*/*z* 1454.85 (3%) [**1**·**2b**−PF_6]$^+$, 654.89 (99%) [**1**·**2b**−2PF_6]$^{2+}$, and 388.26 (41%) [**1**·**2b**−3PF_6]$^{3+}$; the base peak was at *m*/*z* 727.34, corresponding to [**1**+H]$^+$. Five peaks were found for **1**·**2c**: *m*/*z* 1468.99 (5%) [**1**·**2c**−2PF_6−CH_3]$^+$, 834.4 (15%) [**1**·**2c** PF_6+K+H]$^{2+}$, 741.97 (36%) [**1**·**2c**−2PF_6]$^{2+}$, 688.49 (36%) [**1**·**2c**−3PF_6+K]$^{2+}$, and 446.29 (56%) [**1**·**2c**−3PF_6]$^{3+}$; the base peak was at *m*/*z* 471.21, corresponding to a fragment from cryptand **1** (see Supplementary data). No peaks related to other stoichiometries were found.

The ^1H NMR chemical shift changes of **1** upon complexation are consistent with the calculated minimized-energy structure[14] (Fig. 4). Protons H_1, H_3, and H_4 are in shielding regions of the central phenylene and three terminal pyridinium rings of **2a** so they moved upfield after complexation. H_2 and H_5 reside in the deshielding environment of the central phenylene ring, but the shielding environment of the three terminal pyridinium rings of **2a** so their chemical shift changes are small. What is more important is that γ- and δ-ethyleneoxy protons (H_3 and H_4) on **1** are divided into two peaks after complexation (Fig. 2) due to the difference in shielding by the terminal pyridinium rings of the guest **2a** (H_3 is closer to the deshielding regions of terminal pyridinium rings than H_4, see Fig. 4). The downfield shifts of H_9 and H_{10} of **2a** are consistent with their positions in the deshielding regions of the aromatic moieties of **1**, while the upfield shifts of H_6 and H_7 of the guest **2a** are consistent with their positions in the shielding regions of the aromatic moieties of **1**.

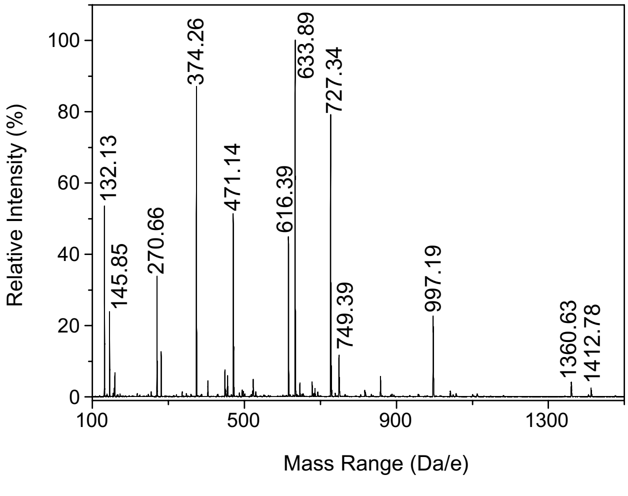

Figure 3. Electrospray ionization mass spectrum of a solution of **1** and **2a** (1.5:1 molar ratio) in acetonitrile–chloroform (4:1). For details on the assignment of main peaks, see Supplementary data.

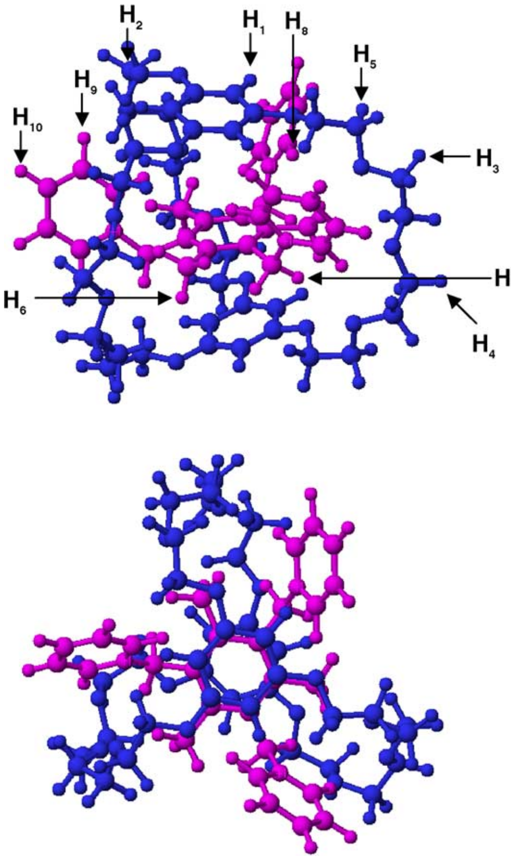

Figure 4. Two views of the minimized-energy structure of **1**·**2a** at the AM1 level with three PF_6 counterions removed. **1** is blue and **2a** is magenta.

The minimized-energy structure of **1**·**2a** also agrees with the results from the NOESY spectrum (see Supplementary data) of a solution of **1** and **2a**. The aromatic (H_1) and ethyleneoxy protons (H_2, H_3, H_4, and H_5) of **1** strongly interact through space with the α-pyridinium (H_8), β-pyridinium (H_9), and methyl protons (H_6), but not with the benzylic (H_7) and γ-pyridinium protons (H_{10}) of **2a**. This is consistent with the fact that the α-pyridinium (H_8), β-pyridinium (H_9), and methyl protons (H_6) of trispyridinium guest **2a** reside inside the cavity of cryptand host **1**, but the benzylic (H_7) and γ-pyridinium protons (H_{10}) of **2a** stay outside the cryptand cavity as shown in Figure 4.

It is noteworthy that in the energy-minimized structure the pyridinium moieties' nitrogen atoms are sterically prevented from ion pairing with the PF_6^- counterions. As we have previously demonstrated,[15] when non-ion paired complexes form from guest salts in relatively low polarity organic media, application of the usual equation K_a = [complex]/{[host]$_0$ − [complex]}{[guest]$_0$ − [complex]} leads to concentration dependent values, showing that this is not a valid treatment; a pre-equilibrium ionization of the salt must be taken into account along with the equilibrium constant for binding the resultant free ion by the host. That situation exists in the present case (more than an order of magnitude change in K_a from 1 to 10 mM). In contrast, the complexation of host **1** and monopyridinium salts such as **3** are fast-exchange processes whose K_a values calculated by the above equation are not concentration dependent. The slow-exchange and concentration dependence in the present case are, therefore, further evidence of the formation of inclusion complexes like that shown in Figure 4.

The present situation is complicated by the fact that the guest salt is trivalent, making mathematical treatment of the equilibria involving ion pair dissociation very challenging or requiring simplifying assumptions, since three counterions are released by the complexation process. Therefore, we have simply chosen to measure the extent of complex formation under a standard set of conditions, namely 1.00 mM in each component, in order to make quantitative comparisons. The following are the percentages of each component included in complexes in acetone-d_6 at 22 °C: **1**·**2a**, 12.0±0.6%; **1**·**2b**, 13.7±0.7%; and **1**·**2c**, 13.9±0.7%.[16] The changes reflect differences in two parameters: ion pair dissociation of the salts and binding of the free cations by the host. For comparison, at 1.00 mM in both components, 8.0% of each component in a solution of bis(*m*-phenylene)-32-crown-10 and pyridinium salt **3** is complexed in the less polar solvent, 1:1 chloroform-*d*–acetone-d_6.[12] This increase in binding with **1**·**2** is due to hydrogen bonding between all three pyridinium moieties of **2** and the ether oxygen atoms of **1**, even though π-stacking interactions of the electron-poor pyridinium ring with the two phenylene units of the host are lost.

In summary, slow-exchange C_3-symmetric inclusion complexes were successfully prepared based on the new cryptand/trispyridinium recognition motif. They belong to a new type of threaded structure because they have non-linear guests. Once appropriate stoppers are introduced at the terminal pyridinium rings, a new type of mechanically interlocked structure can be made. It has the potential to be reduced to a neutral interlocked structure.[17]

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Supplementary data

Syntheses of trispyridinium salts **2**, the NOESY spectrum of a solution of **1** and **2a**, and electrospray ionization mass spectra of cryptand/trispyridinium complexes. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2005.07.094.

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