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# Cucurbit[7]uril: A Very Effective Host for Viologens and Their Cation Radicals

**Winston Ong, Marielle Gómez-Kaifer, and Angel E. Kaifer***

*Center for Supramolecular Science and Department of Chemistry, University of Miami,*
*Coral Gables, Florida 33124-0431*

*akaifer@miami.edu*

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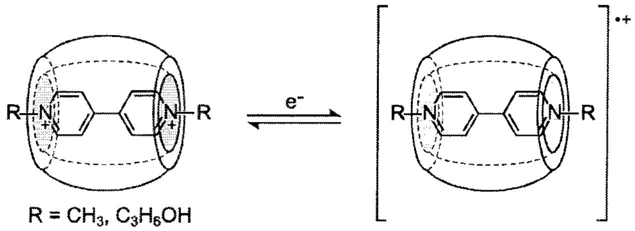
## ABSTRACT



**The host cucurbit[7]uril (CB7) forms very stable inclusion complexes with simple 4,4′-bipyridinium (viologen) dication guests in aqueous solution. The binding constants were measured by electronic absorption spectroscopy and found to be as high as $1 \times 10^5$ L/mol. One-electron reduction of the viologen guest results in a modest 2-fold decrease of the binding constant. The rate of the heterogeneous electron-transfer reaction between the complexed viologen dication and cation radical remained fast in the voltammetric time scale.**

The chemistry of cucurbituril hosts has been expanded by the work of Kim and co-workers,[1] who reported the preparation of cucurbit[*n*]urils (**CB*n***), where $n = 5$, 7, and 8, in addition to the well-known cucurbit[6]uril.[2] Day and co-workers have also recently reported the preparation of **CB9** and **CB10**.[3] These hosts are readily accessible by the acidic condensation of glycoluril and formaldehyde. **CB6** forms stable inclusion complexes with a number of amines and diamines through a combination of dipole−ion and hydrophobic interactions.[4] The higher analogues **CB7**−**CB10** form inclusion complexes with guests having cross-sections larger than that of an aliphatic chain.[5] In this work, we report the formation of inclusion complexes of high stability between the host **CB7** and 4,4′-bipyridinium (viologen) dications and their cation radicals. This system constitutes a rare example of tight binding in aqueous media between synthetic guests and hosts. Another interesting aspect of this system is that the electrochemical kinetics for the reversible one-electron reduction of the complexed viologen dication remains fast, with no kinetic effects due to the encapsulation of the electroactive guest.[6]

Hosts **CB6** and **CB7** were prepared as reported by Kim and co-workers,[1] methyl viologen dichloride (**MV**·$Cl_2$) is commercially available, and bis(3-hydroxypropyl)viologen dibromide (**HV**·$Br_2$) was synthesized by treatment of 4,4′-bipyridine with excess 3-bromo-1-propanol in DMF (Figure 1).[7]

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[1] Kim, J.; Jung, I.-S.; Kim, S. Y.; Lee, E.; Kang, J.-L.; Sakamoto, S.; Yamaguchi, K.; Kim, K. *J. Am. Chem. Soc.* **2000**, *122*, 540.

[2] Freeman, W. A.; Mock, W. L.; Shih, N.-Y. *J. Am. Chem. Soc.* **1981**, *103*, 7367.

[3] Day, A.; Arnold, A. P.; Blanch, R. J.; Snushall, B. *J. Org. Chem.* **2001**, *66*, 8094.

[4] (a) Cintas, P. *J. Incl. Phenom.* **1994**, *17*, 205. (b) Mock, W. L. In *Comprehensive Supramolecular Chemistry*; Vogtle, F., Ed.; Elsevier: Oxford, 1996; Vol. 2, p 467. (c) Marquez, C.; Nau, W. N. *Angew. Chem., Int. Ed.* **2001**, *40*, 3155.

[5] See, for instance: (a) Kim, H.-J.; Heo, J.; Jeon, W. S.; Lee, E.; Kim, J.; Sakamoto, S.; Yamaguchi, K.; Kim, K. *Angew. Chem., Int. Ed.* **2001**, *40*, 1526. (b) Kim, S.-Y.; Jung, I.-N.; Lee, E.; Kim, J.; Sakamoto, S.; Yamaguchi, K.; Kim, K. *Angew. Chem., Int. Ed.* **2001**, *40*, 2119. (c) Marquez, C.; Nau, W. N. *Angew. Chem., Int. Ed.* **2001**, *40*, 4387. (d) Day, A. I.; Blanch, R. J.; Arnold, A. P.; Lorenzo, S.; Lewis, G. R.; Dance, I. *Angew. Chem., Int. Ed.* **2002**, *41*, 275.

[6] Cardona, C. M.; Mendoza, S.; Kaifer, A. E. *Chem. Soc. Rev.* **2000**, *29*, 37.

[7] **Experimental Procedure.** 4,4′-Bipyridine (620 mg, 4.0 mmol) and 3-bromo-1-propanol (8.3 g, 60 mmol) were stirred in DMF (30 mL) at 90 °C for 60 h. The mixture was poured into acetone (300 mL), and the precipitate was filtered and washed several times with acetone. The yellow solid was further washed with warm ethanol (20 mL) twice, filtered, rinsed

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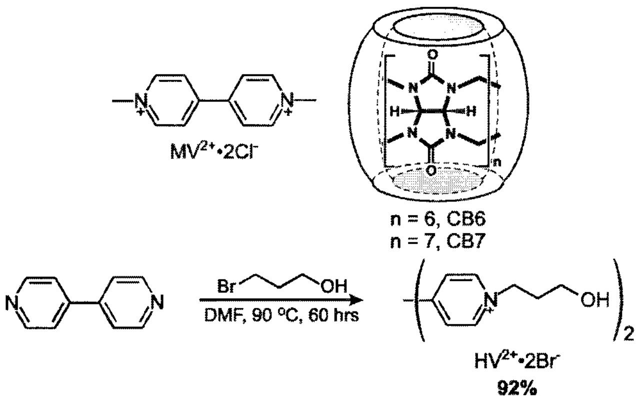


**Figure 1.** Structures of the compounds used in this work.

The formation of an inclusion complex between **MV**$^{2+}$ and **CB7** is clearly evident in $^1$H NMR spectroscopic experiments in 0.2 M NaCl−D$_2$O, as the $\beta$ aromatic protons of the viologen exhibit an upfield shift of more than 1.5 ppm in the presence of 1 equiv of the host (Figure 2). In addition to this large complexation-induced shift, irradiation of the methyne and methylene protons of **CB7** gives rise to nuclear Overhauser effects (NOEs) for the α and $\beta$ aromatic protons of **MV**$^{2+}$. These data can only be rationalized by the formation of a stable inclusion complex, in which the viologen guest is inserted in the cavity of the host (Scheme 1). At the mM concentrations required for the determination of binding constants by $^1$H NMR, the chemical shift changes linearly with the concentration of added host up to 1.0 equiv, where it levels off. The quantitative determination of binding constants is best accomplished by absorption spectrophotometric measurements, as the molar absorptivity coefficient corresponding to the intense UV absorption band of viologens is depressed in the presence of **CB7** (Figure 3). The absorbance vs host concentration data can be easily fitted to a 1:1 binding model to determine the equilibrium constant,[8] which was found to be $(1.03 \pm 0.03) \times 10^5$ L/mol for **CB7**•**MV**$^{2+}$ ($\lambda_{\max} = 253$ nm, $\epsilon = 1.12 \times 10^4$ M$^{-1}$ cm$^{-1}$) at 25 °C in 0.2 M NaCl. Similar experiments and data treatment with **HV**$^{2+}$ as the guest yielded values of $K = (8.98 \pm 0.4) \times 10^4$ L/mol, $\lambda_{\max} = 261$ nm and $\epsilon = 1.51 \times 10^4$ M$^{-1}$ cm$^{-1}$ for its **CB7** complex. These values are remarkably large for

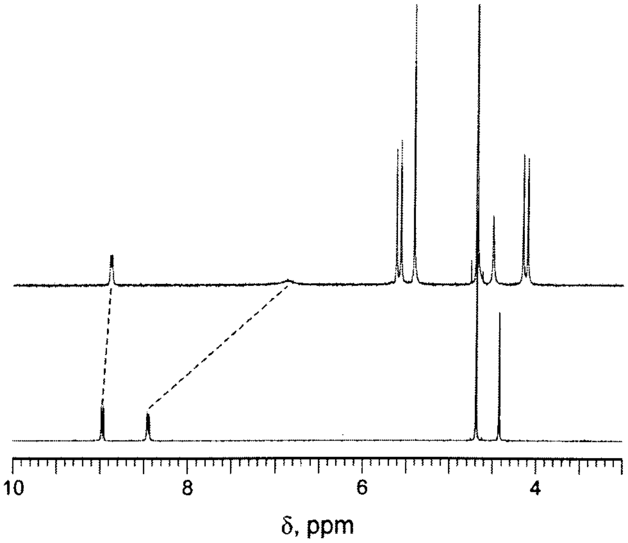
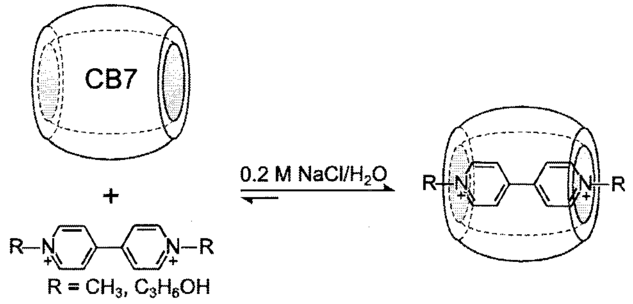


**Figure 2.** $^1$H NMR spectra (300 MHz, 0.2 M NaCl−D$_2$O) of **MV**$^{2+}$ in the absence (bottom) and in the presence (top) of 1 equiv **CB7**.

**Scheme 1.** Formation of Stable Inclusion Complexes between Viologens **MV**$^{2+}$ and **HV**$^{2+}$ with **CB7**



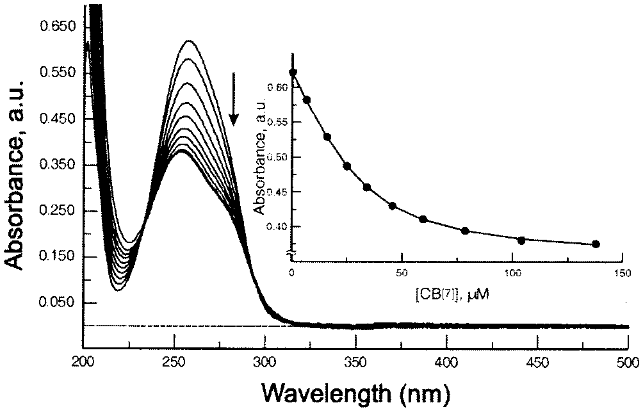


**Figure 3.** Electronic absorption spectrum of 30.5 $\mu$M **MV**•Cl$_2$ in the presence of increasing concentrations (6.38−138 $\mu$M, in the direction of the arrow) of **CB7**. Insert shows the best fit of the experimental data to the 1:1 binding model.

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with acetone, and dried under vacuum to afford **HV**$^{2+}$ (1.59 g, 92%) as the dibromide salt. $^1$H NMR (300 MHz, D$_2$O): $\delta$ 2.21 (m, 4 H, $J$ = 6.3 Hz), 3.61 (t, 4H, $J$ = 6.0 Hz), 4.74 (t, 4H, $J$ = 7.2 Hz), 8.45 (d, 4H), 9.05 (d, 4H). $^{13}$C NMR (75 MHz, D$_2$O): $\delta$ 33.2, 58.3, 60.0, 127.6, 146.3, 150.7. FAB-MS: 274 (M − 2Br)$^+$, 215 (M − C$_3$H$_6$OH − 2Br)$^+$, 157 (M − 2C$_3$H$_6$-OH − 2Br + H)$^+$. UV−vis: ($\lambda_{\max}$, 263 nm, $\epsilon$ = 22700 M$^-$cm$^-$).

(8) Connors, K. A. *Binding Constants*; Wiley: New York, 1987; Ch. 4.

binding in aqueous media and reflect the good fit between the cavity of the host and the cross section of the 4,4′-bipyridinium moiety, as well as the similarity between the N−N′ distance in the viologen guest (~7 Å) and the distance between the two carbonyl portals on the host (~6 Å), which maximizes the overall ion−dipole interactions in the inclusion complex.

The smaller host **CB6** also binds $\mathbf{MV^{2+}}$, but the corresponding binding constant, which in this case can be easily determined by $^1$H NMR spectroscopy, was found to be 21 ± 2 L/mol (Figure 4). The large difference in complex stability clearly suggests that $\mathbf{CB7{\cdot}MV^{2+}}$ and $\mathbf{CB7{\cdot}HV^{2+}}$ are true inclusion complexes, as supported by the NMR and UV−vis data, whereas the interaction of the viologens with host **CB6** can be better described as partial inclusion. Kim and co-workers have also reported the formation of an inclusion complex between $\mathbf{MV^{2+}}$ and the larger host **CB8**, but they did not report any binding constant values.[5a]

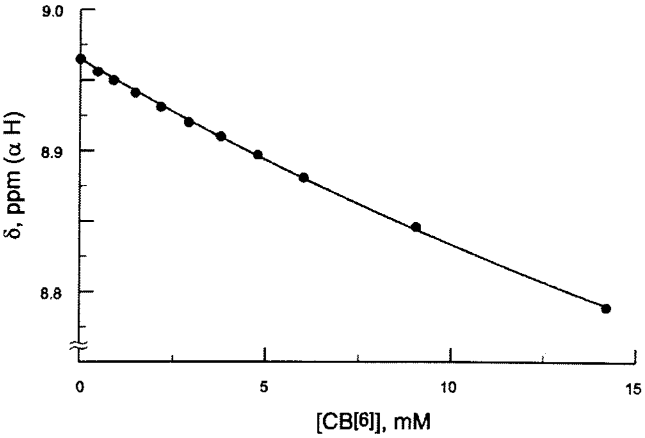

**Figure 4.** $^1$H NMR (300 MHz) titration curve of $\mathbf{MV^{2+}}$ with **CB6** in 0.2 M NaCl−$D_2O$. Line shows best fit of the experimental data to the 1:1 binding model.

Cyclic voltammetry of 1 mM viologen solutions shows that the half-wave potential ($E_{1/2}$) of the first one-electron reduction of the guest ($V^{2+} \rightarrow V^{+\bullet}$) is shifted slightly to more negative values in the presence of **CB7**, whereas the second reduction process ($V^{+\bullet} \rightarrow V$) is affected in a more pronounced fashion. The diminished currents observed in the presence of **CB7** confirm the binding interactions between this host and both viologens, that is, the complex has a smaller diffusion coefficient than the free viologen guest. The current−potential curves for $\mathbf{MV^{2+}}$ in the absence of **CB7** are slightly affected by precipitation on the electrode surface of the fully reduced species **MV**, but the voltammetric data for the more water-soluble viologen $\mathbf{HV^{2+}}$ are free from any precipitation effects (Figure 5). The shift in the $E_{1/2}$ value for the first reduction of both guests levels off upon the addition of 1 equiv of **CB7**, thus yielding the corresponding half-wave potential for the viologen−**CB7** complex. It is thus possible to use eq 1 to determine the

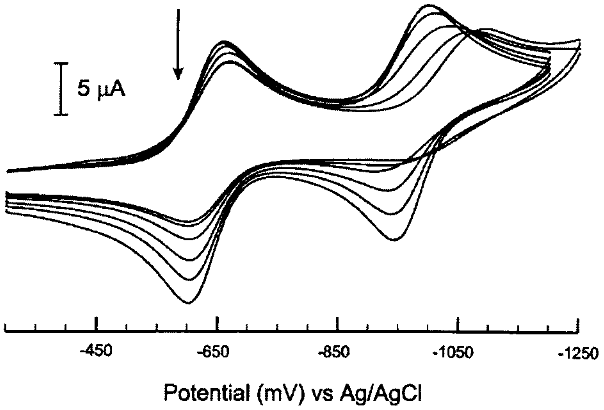

**Figure 5.** Cyclic voltammetric response on a glassy carbon electrode (0.071 cm$^2$) for solutions containing 0.81 mM $\mathbf{HV^{2+}}$ in the presence of increasing concentrations of **CB7** (0, 0.18, 0.36, 0.60, 0.95, and 1.4 mM, in the direction of the arrow). Medium: 0.2 M NaCl. Scan rate: 0.1 V sec$^{-1}$.

$$K'/K = \exp(F\Delta E^{\circ\prime}/RT) \qquad (1)$$

binding constant ($K'$) between the one-electron reduced viologen and **CB7** from the previously determined $K$ values (binding constants between **CB7** and the unreduced viologens), where $\Delta E^{\circ\prime}$ can be estimated from the difference between the half-wave potentials of the complexed and free viologen, i.e., $E_{1/2}{}^{c} - E_{1/2}{}^{f}$. We obtained $K'$ values of 5.0 × $10^4$ and 4.5 × $10^4$ L/mol for binding of $\mathbf{MV^{+\bullet}}$ and $\mathbf{HV^{+\bullet}}$, respectively. These values reveal a *rather moderate stability drop* upon the loss of one positive charge in the guest structure. The remarkable stability of the complex between viologen cation radicals and **CB7** was also evident in FAB mass spectrometric experiments, where intense peaks corresponding to the *m/z* ratio of the $\mathbf{CB7{\cdot}MV^{+\bullet}}$ and $\mathbf{CB7{\cdot}HV^{+\bullet}}$ complexes were readily detected (Figure 6).

Redox conversions on the guest or the host usually result in large changes in the stability of the host−guest complex.[9] For instance, inclusion complexes between ferrocene derivatives and $\beta$-cyclodextrin ($\beta$-CD) are disrupted upon oxidation of the ferrocene guests.[10] The same phenomena are observed on fully reduced viologen−$\beta$-CD complexes upon oxidation of the viologen guests.[11] Charge transfer complexes are also strongly affected by oxidation of the donor or reduction of the acceptor components.[12] In contrast to these, the complex between **CB7** and viologen guests only exhibits a decrease in its stability of ~0.4 kcal/mol upon one-electron reduction, as both viologen species (2+ and +•) are strongly bound

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[9] Kaifer, A. E. *Acc. Chem. Res.* **1999**, *32*, 62.

[10] (a) Matsue, T.; Evans, D. H.; Osa, T.; Kobayashi, N. *J. Am. Chem. Soc.* **1985**, *107*, 3411. (b) Isnin, R.; Salam, C.; Kaifer, A. E. *J. Org. Chem.* **1991**, *56*, 35.

[11] Mirzoian, A.; Kaifer, A. E. *Chem. Eur. J.* **1997**, *3*, 1052.

[12] Balzani, V.; Credi, A.; Raymo, F. M.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2000**, *39*, 3348.

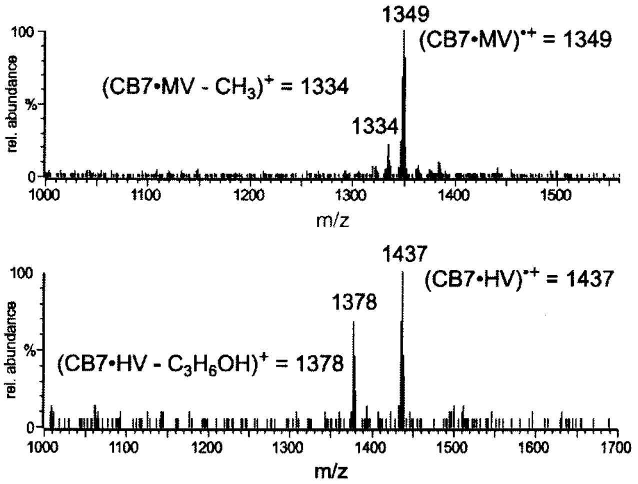
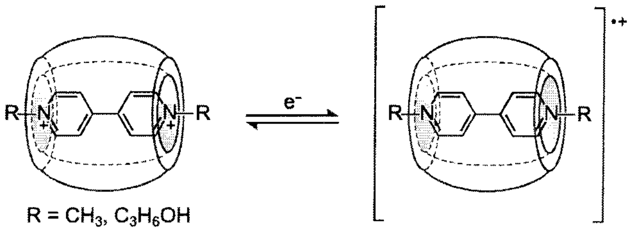


**Figure 6.** FAB-MS spectra of **CB7·MV**$^{\bullet+}$ and **CB7·HV**$^{\bullet+}$ complexes in glycerol matrixes. In both cases, the molecular ion peaks are also the parent ion peaks.

by the **CB7** host. The stability of the cation radical complexes reflects the importance of hydrophobic interactions among the intermolecular forces responsible for the formation of these host−guest complexes.

In the presence of **CB7** the shape of the first voltammetric wave ($V^{2+} \rightarrow V^{+\bullet}$) did not change with the scan rate in the range 0.1−1 V s$^{-1}$. Usually, chemical reactions coupled to the electron-transfer step, such as complex dissociation or association, lead to distortions in the wave shape as the time scale of the voltammetric experiment and the complex lifetime become similar.[9] We did not observe any of these effects in this host−guest system. In addition to this, most viologen dication/cation radical couples exhibit extremely fast heterogeneous electron-transfer kinetics.[13] This property facilitates the electron-transfer process between the dication and cation radical complexes of **CB7** investigated in this work. The peak-to-peak potential splittings ($\Delta E_p$) for the first reduction wave remained constant at ~60 mV in the surveyed scan rate range. Therefore, any kinetic slowdowns due to molecular encapsulation effects[6] are rendered undetectable in the time scale of our electrochemical experiments (Scheme 2). To the best of our knowledge this is an unprecedented finding.

**Scheme 2.** Electron Transfer between **CB7·V**$^{2+}$ and **CB7·V**$^{+\bullet}$



In contrast to the first wave, the second voltammetric wave ($V^{+\bullet} \rightarrow V$) exhibits considerably more complicated behavior in the presence of **CB7**, as is clearly apparent in Figure 5. For instance, the peak potentials and $\Delta E_p$ values depend strongly on the scan rates. These observations must be related to a considerably smaller binding constant between the fully reduced (and uncharged) viologen and the **CB7** host, as well as to the slower kinetics of heterogeneous electron-transfer associated with the $V^{+\bullet/0}$ redox couple. We are currently investigating these electrochemical processes using digital simulations.

We thus conclude from our data that simple viologen dications and cation radicals form highly stable inclusion complexes in aqueous solution with the host **CB7**. This is an important finding because of the widespread use of viologens in many electron-transfer processes.[13] Furthermore, **CB7** should largely prevent the dimerization/oligomerization of viologen cation radicals, a side reaction that has hindered the use of viologens in electrochromic displays and other applications.[13]

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