Notes

Stabilization of the (*E*)-1-Ferrocenyl-2-(1-methyl-4-pyridinium)ethylene Cation by Inclusion in Cucurbit[7]uril

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Summary: The (E)-1-ferrocenyl-2-(1-methyl-4-pyridinium)ethylene cation, (E)-FcMPE$^+$, forms a very stable guest−host complex (K_{CB7} = (1.3 ± 0.5) × 10^{12} M^{-1}) in aqueous solution with cucurbit[7]uril (CB[7]). The ^{1}H NMR, ES-MS, and UV−visible spectra are consistent with 1:1 {(E)-FcMPE·CB[7]}$^+$ species formation, in which the CB[7] encapsulates the ferrocenylethylene portion of the guest. The reduction potential of the (E)-FcMPE$^{2+/+}$ couple increases slightly (+0.03 V) in the presence of CB[7], while the rate constant for the oxidation of (E)-FcMPE$^+$ by Co(dipic)$_2^-$ (dipic^{2-} = 2,6-pyridinedicarboxylate) decreases significantly. UV−visible spectra of (E)-FcMPE$^+$ in the absence and in the presence of CB[7] during photoirradiation demonstrate that the photoisomerization to (Z)-FcMPE$^+$ is fully inhibited and photostabilization of (E)-FcMPE$^+$ is dramatically enhanced upon inclusion in CB[7].

Introduction

The cucurbiturils (CB[*n*], where *n* = 5−10) are a family of macrocyclic host molecules[1] comprised of methylene-bridged glycoluril units, whose remarkable binding behavior toward cationic guests has been of considerable recent interest. The cucurbiturils contain a hydrophobic cavity, with polar carbonyl groups surrounding the portals for inclusion of hydrophobic guest molecules. The cucurbit[7]uril (CB[7]) in particular has received considerable attention because of its relatively good water-solubility and a capacity to include aromatic molecules and mediate their chemical and photochemical reactivity.[2−9] Kim and co-workers have reported that CB[7] catalyzes the *trans*-to-*cis* photoisomerization of diaminostilbene and protects *cis*-diaminostilbene from isomerizing back to the *trans*-form.[3] Ramamurthy has investigated the ability of CB[7] to catalyze the *trans*-to-*cis* photoisomerization of 1,2-bis(4-pyridyl)ethylene and stilbazoles.[4] We have recently shown that CB[7] can mediate a stereoselective photodimerization of protonated 2-aminopyridine[5] and can facilitate a switching in the fluorescence behavior of protonated 2-aminoanthracene[6] upon inclusion in the cavity, through hydrogen bonding between the ammonium group and the portal carbonyl oxygens. Other applications of CB[7] have been as molecular drug carriers,[7] as hosts for polyaromatic cations[8a] and fullerenes,[8b] and the protection of organic dyes, such as rhodamine,[9] from photobleaching.

The cucurbit[7]uril has recently been shown to form very stable complexes (K_{CB} > 10^9 M^{-1}) with both oxidation states of ferrocene and its derivatives.[10] Our concurrent interests in inclusion complexes of substituted ferrocenes, with hosts such as the cyclodextrins[11−13] and calixarenes,[14] and the ability of CB[7] to catalyze photoisomerizations of stilbene and stilbazole derivatives[3,4] led us to investigate the complexation of the (*E*)-1-ferrocenyl-2-(1-methyl-4-pyridinium)ethylene cation, (*E*)-FcMPE$^+$ (Scheme 1), by CB[7] and the effects of inclusion on the photochemical and redox reactivity of the resulting {(*E*)-FcMPE·CB[7]}$^+$ inclusion complex.

A previous report[15] on photoreactivity of (*E*)-FcMPE$^+$ demonstrated that *trans*-to-*cis* photoisomerization of (*E*)-FcMPE$^+$ occurrs upon photoirradiation, similar to other stilbene or stilbazole derivatives. We herein report that the inclusion of the (*E*)-FcMPE$^+$ cation by CB[7] significantly enhances its stability with respect to photochemical isomerization and chemical oxidation in aqueous solution.

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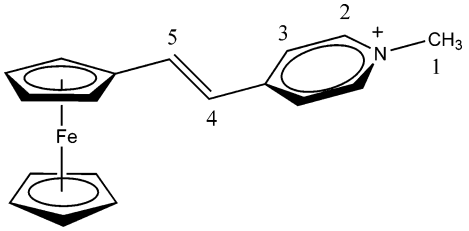
Scheme 1. Structure of (*E*)-FcMPE$^+$ and Proton-Numbering Scheme



Experimental Section

Materials. (*E*)-1-Ferrocenyl-2-(1-methyl-4-pyridinium)ethylene iodide, [(*E*)-FcMPE]I, and 1-aminoadamantane were purchased from Aldrich. Cucurbit[7]uril[16] and $NH_4[Co(dipic)_2]$ ($dipic^- = 2,6$-pyridinedicarboxylate)[17] were synthesized according to literature methods. The (*E*)-FcMPE$^+$ solutions used for cyclic voltammetry and kinetics experiments were prepared by anion exchange (Dowex (1-X8)) of the I^- ion by Cl^-. The $\{(E)\text{-FcMPE}\cdot\text{CB[7]}\}^+$ inclusion complex was prepared in aqueous solution by mixing equimolar amounts of (*E*)-FcMPE$^+$ and CB[7] with stirring for 20 min.

Methods. The UV−visible absorption spectra were measured by using a Hewlett-Packard 8452A diode array spectrophotometer. The photoirradiation light source was a hand-held Spectroline UV lamp (365 nm). ^{1}H NMR spectra were recorded on a Bruker AV-400M NMR spectrometer, and the ESI-MS spectrum was acquired on a Waters 2Q Single Quad MS spectrometer equipped with an ESI/APcI multiprobe. Cyclic voltammograms were collected using a Bioanalytical Systems CV-1B cyclic voltammeter, with a glassy carbon working electrode, a platinum auxiliary electrode, and a Ag/AgCl reference electrode. The kinetic experiments were performed on an Applied Photophysics SV-MX17 stopped-flow spectrophotometer. The electron-transfer reactions between (*E*)-FcMPE$^+$ (1.0×10^{-4} M) and $Co(dipic)_2^-$ (1.0×10^{-3} M) were carried out in aqueous solution containing 0.10 M NaCl at 25.0 ± 0.1 °C. The second-order rate constants were determined from five to six replicate traces. The energy-minimized structure of the $\{(E)\text{-FcMPE}\cdot\text{CB[7]}\}^+$ inclusion complex was determined from ab initio calculations using Gaussian 03 software and HF/3-21**G basis sets.[18] Details of the energy-minimization calculations are provided in the Supporting Information.

Results and Discussion

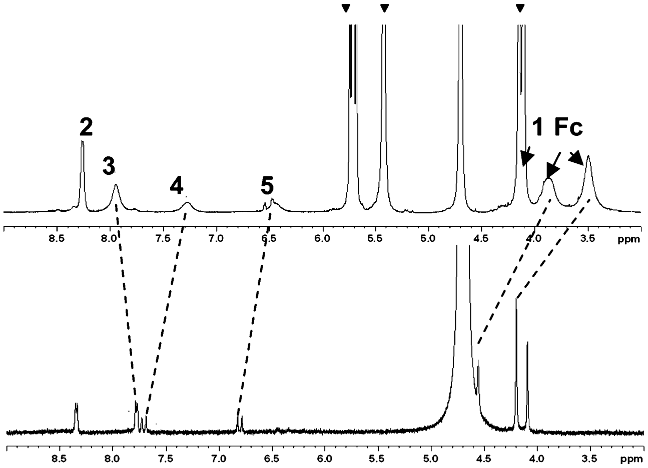


Figure 1. ^{1}H NMR spectra (400 MHz, D_2O) of (*E*)-FcMPE$^+$ in the absence (bottom) and the presence (top) of 1 equiv of CB[7]. Resonances labeled with black inverted triangles correspond to protons of the CB[7] host.

The encapsulation of (*E*)-FcMPE$^+$ inside the cavity of CB-[7] to form a $\{(E)\text{-FcMPE}\cdot\text{CB[7]}\}^+$ inclusion complex in aqueous solution has been established by ^{1}H NMR and UV−visible spectroscopy, ESI-MS spectrometry, and cyclic voltammetry, as well as from kinetic measurements of an outer-sphere electron-transfer reaction. In the presence of 1 equiv of CB[7], the resonances for the ethylene protons (H_4 and H_5) and the protons of the two cyclopentadienyl rings in the ^{1}H NMR spectrum of its inclusion complex (Figure 1) have moved upfield from those of the free guest, indicative of their positioning within the cavity of CB[7]. The resonance of one of two pyridine proton resonances (H_3) moved downfield, while the other pyridine proton resonance (H_2), along with the methyl proton (H_1) resonance, exhibited no chemical shift change. This behavior indicates that the *N*-methylpyridinium group is situated outside of the cavity of CB[7], as the downfield shift of one pyridine proton resonance may be attributed to the deshielding effect of the carbonyl-rimmed portal of CB[7]. Therefore, on the basis of the ^{1}H NMR characterization, the ferrocenylethylene portion of (*E*)-FcMPE$^+$ is encapsulated in the cavity of CB[7]. The exchange rate between bound and free (*E*)-FcMPE$^+$ is slow on the ^{1}H NMR time scale (400 MHz) at room temperature, as the resonances of free and bound ligands were distinguishable in the ^{1}H NMR spectra when less than 1 equiv of CB[7] was added. The asymmetry of the orientation of the guest inclusion in the CB[7] cavity is also reflected in the separation of the two resonances for the symmetry-related methylene protons, on the exterior of the CB[7], into pairs of doublets.

The UV−visible spectrum of the (*E*)-FcMPE$^+$ cation (Figure 2) has peaks with λ_{max} values of 356 nm (an intraligand charge transfer (ILCT) from the cyclopentadienyl ring to the pyridinium group) and 546 nm (a Fe(II) to pyridinium MLCT transition).[15,19] Upon addition of CB[7], there are bathochromic shifts in both peaks to 372 and 554 nm, respectively, with the shorter wavelength peak decreasing in intensity and the longer wavelength peak increasing in intensity.

These bathochromic shifts and intensity changes upon inclusion of the ferrocenyl portion of the cation in the CB[7] are consistent with the solvatochromism observed previously for this complex.[15] While only the ferrocenyl portion of the cation is included in the CB[7] cavity, this portion contains the donor sites for both the ILCT (Cp^- ring) and MLCT (Fe(II)) transitions.

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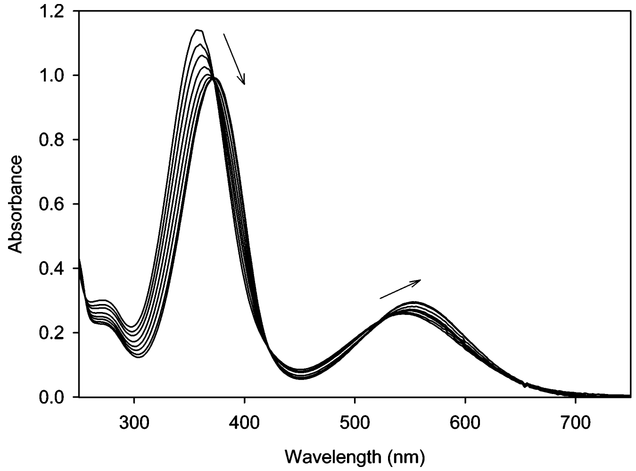

Figure 2. UV−visible spectra of aqueous (*E*)-FcMPE$^+$ (50 μM) in the presence of various concentrations of CB[7] (from 0 to 70 μM) in the arrow direction.

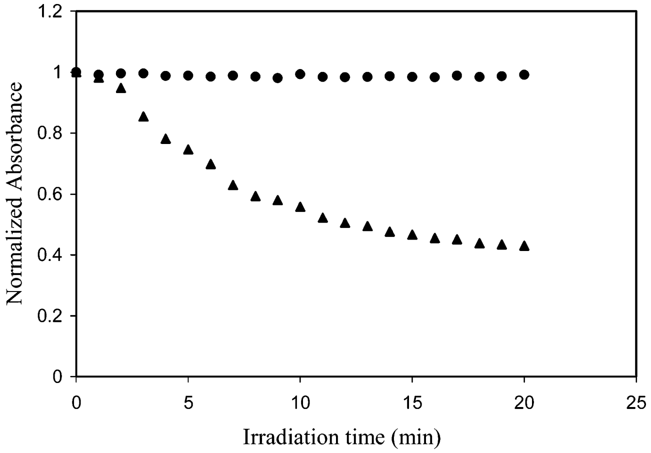

Figure 3. Absorbance changes for (*E*)-FcMPE$^+$ in the absence (triangles, normalized absorbance at 358 nm) and presence of CB[7] (dots, normalized absorbance at 372 nm), recorded after 365 nm irradiation for various time intervals.

The 1:1 stoichiometry of the $\{(E)\text{-FcMPE}\cdot\text{CB}[7]\}^+$ inclusion complex was also established by a Job's plot (based on the continuous variation method) employing UV−visible spectroscopy[11] and by the ESI-MS spectrum, which showed the singly charged peak at m/z = 1466 for the $\{(E)\text{-FcMPE}\cdot\text{CB}[7]\}^+$ inclusion complex (Supporting Information). It was not possible to calculate the binding constant directly from UV−visible spectrophotometric titrations of $[(E)\text{-FcMPE}]^+$ with CB[7] because of the very high value of the binding constant. Instead, a ^{1}H NMR competition experiment of the $\{(E)\text{-FcMPE}\cdot\text{CB}[7]\}^+$ complex with 1-aminoadamantane, whose binding constant with CB[7] has been reported as $(4.23 \pm 1.00) \times 10^{12}$ M^{-1},[10b] was carried out. Using a limiting amount of CB[7], a binding constant of $(1.3 \pm 0.5) \times 10^{12}$ M^{-1} was determined for $\{(E)\text{-FcMPE}\cdot\text{CB}[7]\}^+$.

With a knowledge of the large stability constant for the $\{(E)\text{-FcMPE}\cdot\text{CB}[7]\}^+$ inclusion complex, we examined the effect of CB[7] complexation on photoreactivity of the (*E*)-FcMPE$^+$ cation in aqueous solution. The *trans*-to-*cis* photoisomerization of (*E*)-FcMPE$^+$, which is known to occur upon irradiation at 365 nm,[15] may be monitored by UV−visible spectroscopy (Figure 3). The changes in the spectrum of (*E*)-FcMPE$^+$ upon photoirradiation in the absence of CB[7] are very similar to those previously reported, with the band at 356 nm (ILCT) shifting to 386 nm and a disappearance of the band at 546 nm (MLCT). The reduced intensities of these bands arise from the reduction in conjugation in the *Z* isomer.[9,12] In contrast, the UV−visible absorbance spectrum of the $\{(E)\text{-FcMPE}\cdot\text{CB}[7]\}^+$ inclusion complex (1.2 equiv of CB[7] added), during the same period of photoirradiation, showed no changes (Figure 3). The photoreactivity of aqueous (*E*)-FcMPE$^+$ is thus dramatically inhibited by CB[7] complexation.

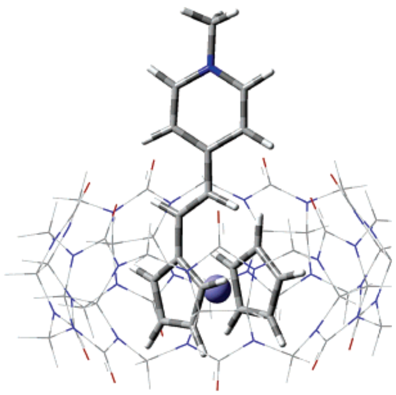

Figure 4. Energy-minimized structure of the $\{(E)\text{-FcMPE}\cdot\text{CB}[7]\}^+$ inclusion complex.

The photostability enhancement in $[(E)\text{-FcMPE}]^+$ may be explained by the inclusion orientation of $[(E)\text{-FcMPE}]^+$ in the cavity of CB[7], demonstrated by ab initio energy-minimized calculations on the structure of the inclusion complex (Figure 4).

The relatively large ferrocene portion of this molecule fits inside the cavity with the neighboring vinyl group positioned close to the portal of the cavity. This orientation is such that only the *trans* isomer can reside in the cavity with only a small steric hindrance between carbonyl portals of CB[7] and the guest pyridine group. In contrast, the *cis* isomer would likely experience a significant steric hindrance between carbonyl groups of CB[7] and the guest pyridine group if the ferrocenylethylene portion were to be included in the CB[7] cavity. The inclusion of a vinyl group in the cavity of CB[7] also serves to protect it from any other chemical attack, such as photoaddition of water. The overall photoreactivity of $[(E)\text{-FcMPE}]^+$, therefore, is highly inhibited, and solutions of the $\{(E)\text{-FcMPE}\cdot\text{CB}[7]\}^+$ inclusion complex appear to remain unchanged indefinitely on the benchtop under normal light conditions.

Cyclic voltammetry (CV) was employed to study the redox behavior of (*E*)-FcMPE$^+$ in the absence and presence of CB-[7]. The presence of 1.2 equiv of CB[7] resulted in a modest anodic shift (∼30 mV) in the position of the corresponding $E_{1/2}$ value for (*E*)-FcMPE$^{2+/+}$ couple (0.53 V vs NHE). Larger anodic shifts of >100 mV have been reported for other cationic ferrocenes, such as the (trimethylammonio)methylferrocene, where the positive charge on the substituent would be located close to the carbonyl portals of CB[7]. Neutral hydroxymethylferrocene[10b] and ferrocene[10a] itself exhibit much smaller changes of 10 and −22 mV, respectively, upon inclusion in CB[7]. The anodic and cathodic peak currents and reversibility of the waves for $\{(E)\text{-FcMPE}\cdot\text{CB}[7]\}^+$ also decreased as a result of the host−guest complexation.[10] The modest anodic shift indicates that the binding constant for the reduced state of ferrocene is only slightly higher than that of the oxidized state of ferrocene. Using $\Delta E_{1/2}$ = 30 mV and the stability constant for the reduced $\{(E)\text{-FcMPE}\cdot\text{CB}[7]\}^+$ inclusion complex, a value of $K_{\text{CB}}{}^{\text{ox}} = 4 \times 10^{11}$ M^{-1} can be estimated ($\Delta E_{1/2} = -(RT/F)\ln(K_{\text{CB}}{}^{\text{ox}}/$

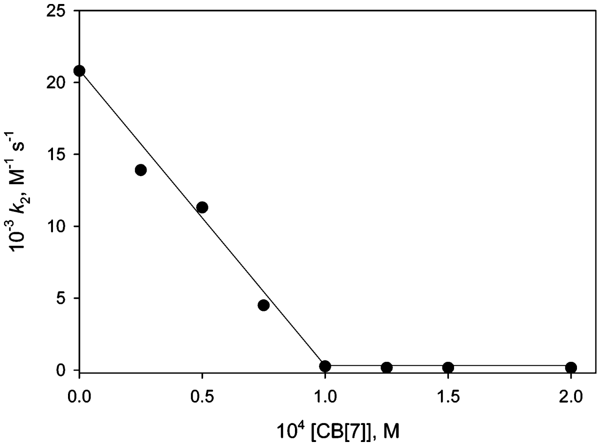

Figure 5. Plot of k_2 against [CB[7]] for the reaction of (*E*)-FcMPE$^+$ (1.0×10^{-4} M) with Co(dipic)$_2^-$ (1.0×10^{-3} M) at 25.0 °C ($I = 0.10$ M (NaCl)).

K_{CB}^{red})) for the oxidized {(*E*)-FcMPE·CB[7]}$^{2+}$ form of the inclusion complex.

The effect of CB[7] inclusion on the rate constant for the chemical oxidation of (*E*)-FcMPE$^+$ was investigated employing Co(dipic)$_2^-$ (dipic$^-$ = 2,6-pyridinedicarboxylate) as the oxidant, as it does not form an inclusion complex with CB[7]. Using Co(dipic)$_2^-$ in a pseudo-first-order excess (1.0×10^{-3} M) over (*E*)-FcMPE$^+$ (1.0×10^{-4} M), the [CB[7]] was varied up to 2.0×10^{-4} M at 25.0 °C and $I = 0.10$ M. The second-order rate constant, k_2, decreased linearly with increasing [CB[7]] until a 1:1 ratio of (*E*)-FcMPE$^+$ and CB[7] was present (Figure 5), at which point a limiting rate constant was established.

The rate constants for the oxidation of (*E*)-FcMPE$^+$ and {(*E*)-FcMPE·CB[7]}$^+$ by Co(dipic)$_2^-$ were determined to be $k_0 = (2.1 \pm 0.1) \times 10^4$ M^{-1} s^{-1} and $k_{CB} = (1.6 \pm 0.1) \times 10^2$ M^{-1} s^{-1}, respectively. The decrease in the rate constant for the oxidation of (*E*)-FcMPE$^+$ upon its inclusion in CB[7] may be attributed to (a) the slight increase in the (*E*)-FcMPE$^{2+/+}$ reduction potential and (b) a steric hindrance of the close approach of the reactants by CB[7] inclusion of the reductant. Similar diminutions in the rate constants for the oxidations of cationic ferrocenes by Co(dipic)$_2^-$ upon their inclusion in cyclodextrins[11−13] and calixarenes[14] have been reported and attributed to these thermodynamic and steric factors.

In conclusion, cucurbit[7]uril has been demonstrated to have the ability to eliminate the photoinstability of (*E*)-FcMPE$^+$ in aqueous solution by supramolecular encapsulation of the ferrocenylethylene portion of the included guest. In addition, the inclusion of the ferrocene in the CB[7] cavity significantly reduces the complex's electron-transfer reactivity. In the same fashion, CB[7] might be able to regulate the reactivity and stability of other ferrocene derivatives through the strong complexation between CB[7] and the ferrocene moiety and/or reactive substituent groups. We are currently investigating the effect of CB[7] inclusion on the kinetics of the outer-sphere electron exchange and electron-transfer reactions of other substituted monomeric and dimeric ferrocenes.

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Supporting Information Available: Cyclic voltammograms, ES-MS and UV−visible spectra, and details of energy-minimized structure calculations for the {(*E*)-FcMPE·CB[7]}$^+$ inclusion complex. This material is available free of charge via the Internet at http://pubs.acs.org.

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