Host–Guest Chemistry

Cucurbit[8]uril-Mediated Redox-Controlled Self-Assembly of Viologen-Containing Dendrimers**

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Dendrimer self-assembly is a research topic of great current interest as it targets the preparation of relatively large three-dimensional structures with defined shapes and sizes which start from dendritic building blocks that already fall within the nanometer range. The self-assembly of dendrimers has been investigated by a number of groups who have taken advantage of π–π stacking,[1] fluorophobic,[2] solvophobic,[3] hydrogen bonding,[4] ion–dipole,[5] metal coordination,[6] and other intermolecular interactions[7] to drive the aggregation of appropriately functionalized dendrimers. The type and location of functional recognition groups in the dendrimers determines the "program" for self-assembly. An attractive goal in this research area is to externally control the self-assembly process by dictating the assembly or dissociation conditions to the system through the application of appropriate stimuli.

Both the group of Kim and our own group have actively investigated the binding interactions between 4,4′-bipyridinium (viologen) derivatives and the host cucurbit[7]uril (CB7).[8] Recently, we reported that CB7 also forms stable inclusion complexes with a series of water-soluble dendrimers that contain a viologen residue covalently attached to the focal point of Newkome-type dendrons.[9] Kim and co-workers reported that the larger host, cucurbit[8]uril (CB8), effectively enhances the dimerization of methyl viologen radical cations—the one-electron-reduced form of methyl viologen.[10] Their report intrigued us and led us to investigate the binding interactions between our water-soluble, viologen-containing dendrimers and CB8. As this host favors the dimerization of methyl viologen radical cations, our expectation was that its presence would lead to extensive dimerization of viologen dendrimers upon their one-electron reduction. Thus, the presence of CB8 may afford a convenient, simple, and *reversible* mechanism to drive the self-assembly of dendrimer dimers under redox control. Herein, we report the results of this investigation.

The viologen-containing dendrimers **1**—**3** were prepared following reported methods.[11] Dendrimer **4** was prepared by exhaustive esterification of **3** with methanol and fully characterized by NMR spectroscopy, MALDI-TOF mass spectrometry, and electrochemical techniques. The complexation of the viologen residue in dendrimers **1**, **2**, and **4** by the host CB8 was monitored by using electronic absorption spectroscopy. The molar absorptivity coefficient of the characteristic UV absorption of the viologen moiety at ≈ 260 nm was suppressed upon exposure to the CB8 host, although the magnitude of this effect is less pronounced than that observed with the CB7 host.[8a] Analysis of the UV/Vis data obtained in titration experiments of the dendrimers with CB8 yielded the equilibrium association constants $K = 2.8\times10^4$, 1.4×10^4, and $2.9\times10^3\,\mathrm{L\,mol^{-1}}$ for the dendrimer guests **1**, **2**, and **4**, respectively. The gradual decrease in the binding constant with increasing dendrimer size is consistent with previous observations by our group.[9,12] The values of K are smaller but comparable to the value reported by Kim and co-workers for the 1:1 complexation of methyl viologen by the host CB8.[10]

The electrochemical behavior of dendrimer **1** exhibits the two consecutive one-electron reductions anticipated for any viologen compound (Figure 1). The first wave corresponds to the reversible reduction from the viologen dication (v^{2+}) to the radical-cation form ($v^{+\bullet}$), whereas the second wave reflects the reversible reduction from the cation ($v^{+\bullet}$) to the neutral form (v). In the presence of 0.5 equivalents of CB8, the half-wave potential ($E_{1/2}$) associated with the first wave

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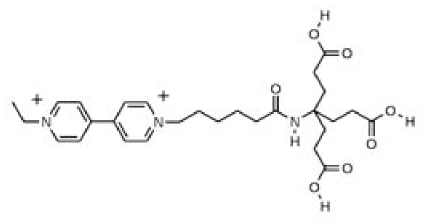

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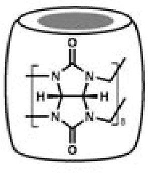
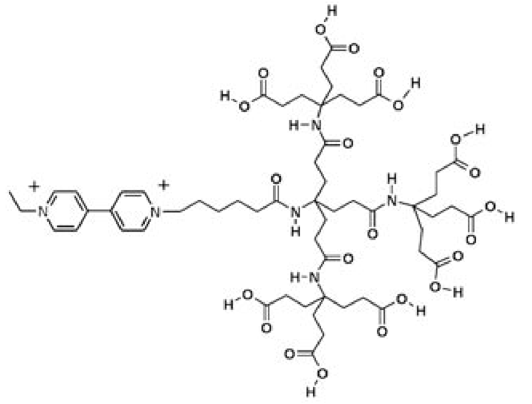


CB8



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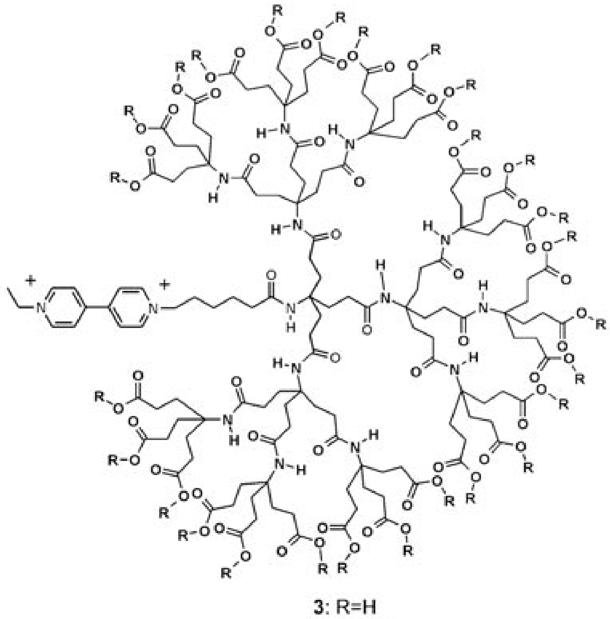

3: R=H
4: R= Me

shifts to a more-positive value (Figure 1). Since the dication form of the viologen is stabilized by inclusion into CB8, the observed anodic shift of the $E_{1/2}$ value implies that the $v^{+\bullet}$ form is even more strongly stabilized by CB8 than the dicationic form itself. By analogy to the behavior reported for the radical cation of methyl viologen by Kim and coworkers,[10] this finding strongly suggests that two dendrimers associate through dimerization of their viologen radical cations inside the cavity of CB8.

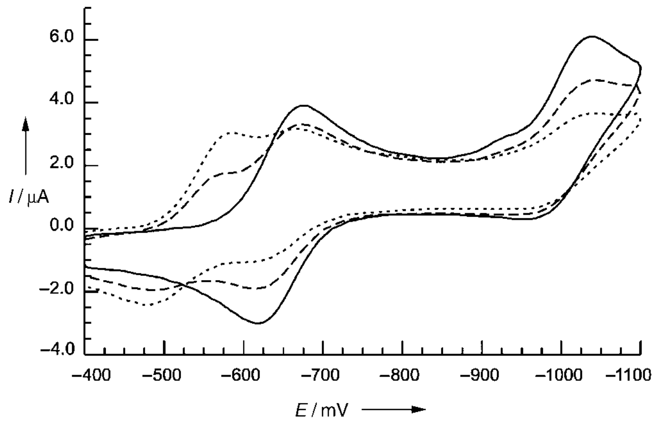

Figure 1. Cyclic voltammograms of dendrimer **1** (0.5 mm) in a phosphate buffer solution (pH 7, I = 0.1 m) in the presence of 0.00 (——), 0.25 (– – –), and 0.50 equivalents (-----) of CB8. Potentials measured versus Ag/AgCl; scan rate = 0.100 V s^{-1}.

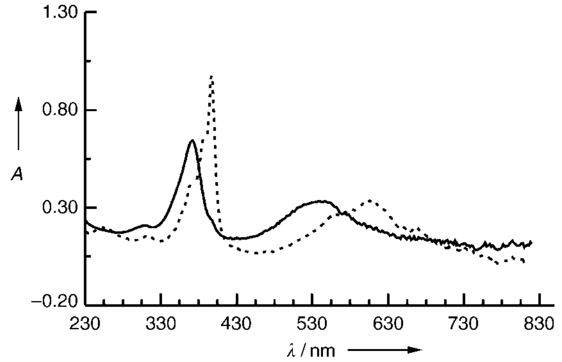

Figure 2. Electronic absorption spectra of a solution of dendrimer **2** (0.3 mm in phosphate buffer) after exhaustive one-electron reduction, in the absence (-----) and in the presence (——) of CB8 (0.8 equiv); optical path = 0.1 cm.

The dimerization of viologen radical cations gives rise to considerable changes in their electronic absorption spectra.[13] As viologen radical cations are oxygen sensitive, we investigated the spectral changes observed upon reduction of our viologen-containing dendrimer solutions in an evacuated, sealed cell. For instance, reduction of the second-generation dendrimer **2** with activated Zn powder gives rise to the UV/Vis spectrum shown in Figure 2. The observed spectral pattern reveals that (1) the viologen units (v) are exhaustively reduced to their $v^{+\bullet}$ form owing to the complete disappearance of the intense absorption of the v^{2+} form (at 260 nm), and that (2) most of the viologen radical-cation residues exist as monomers from the absorption maxima observed at 396 and 602 nm. On the other hand, reduction of **2** in the presence of CB8 gives rise to a completely different absorption spectrum with maxima at 370 and 546 nm, which are characteristic of the viologen radical-cation dimer. This spectroscopic evidence strongly indicates that the presence of CB8 greatly enhances dimerization of the one-electron-reduced (radical-cation) forms of the viologen-containing dendrimers relative to the low levels of dimerization observed in the absence of CB8.

These spectroscopic data reveal that the first-generation dendrimer **1** also dimerizes extensively in the presence of CB8 upon one-electron reduction, whereas dimerization is not detected at all in the absence of this host. In a control experiment, the one-electron-reduced (radical cation) form of **1** was generated in the presence of host CB7. The spectroscopic results showed that CB7 is completely ineffective at fostering dimerization of the radical-cation forms of dendrimer **1** (Figure 3). This reflects the smaller cavity size of CB7 compared to CB8 which prevents the former host from including two viologen radical-cation subunits simultaneously. The reversible character of the dimerization process in the presence of CB8 was verified by exposing the solution of the one-electron-reduced viologen dendrimer to air. Oxidation quickly leads to a colorless solution, which shows an absorbance spectrum indistinguishable from the spectrum obtained before reduction.

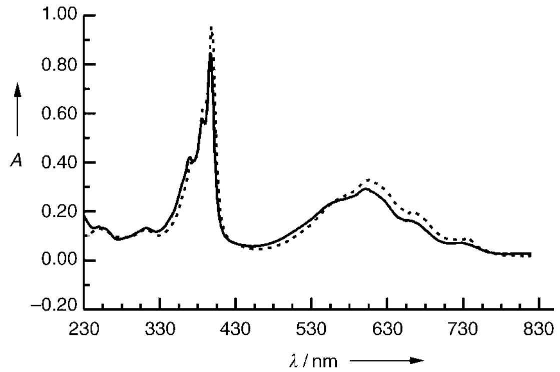

Figure 3. Electronic absorption spectra of a solution of dendrimer **1** (0.3 mM in phosphate buffer) after exhaustive one-electron reduction in the absence (-----) and in the presence (——) of CB7 (0.3 mM); optical path = 0.1 cm.

Some years ago, our group showed that the ratio of the absorbances at 364 and 394 nm (A_{364}/A_{394}) in the electronic spectrum of one-electron-reduced methyl viologen increases linearly with the ratio of the concentrations of dimer to monomer ([d]/[m]) in the solution.[14] Although the viologen compounds used in this work are structurally more complex, it is reasonable to assume that the corresponding absorbance ratios should also correlate with the ratios of the concentrations ([d]/[m]) present in solutions of the viologen-containing dendrimers upon extensive one-electron reduction. The collected data are given in Table 1.

The ratios of the absorbances measured in the absence of CB8 are all within the 0.43–0.50 range, which indicates minimal dimerization (< 5 %) of the viologen radical-cation residues. The ratios of the absorbances increased substantially in the presence of the host CB8 and reveal extensive dimerization (> 80 %). The only exception to this trend was provided by dendrimer **3**, which dimerizes to a very low extent (≈ 20 %) as indicated by its relatively low A_{370}/A_{396} ratio. This finding may be a result of electrostatic repulsion between two approaching molecules of **3**, each one bearing a large number of negative charges at the neutral pH value at which these experiments were conducted. The existence of considerable electrostatic effects is further supported by the extensive dimerization observed with the methyl ester form of the third-generation dendrimer, **4**. Thus, although the increase in size of the dendrimers may be a factor that hinders their dimerization, electrostatic interactions play a much more important role.

Table 1: Spectroscopic data obtained with solutions of viologen-containing dendrimers (≈ 0.3 mM) upon exhaustive one-electron reduction in buffered aqueous solution (pH 7).

Dendrimer	Added Host	A_{370}	A_{396}	A_{370}/A_{396}	% Dimer
1	None	0.504	1.017	0.495	< 5
1	CB8	0.634	0.179	3.540	> 80
1	None	0.396	0.869	0.455	< 5
1	CB7	0.420	0.849	0.495	< 5
2	None	0.422	0.955	0.441	< 5
2	CB8	0.638	0.242	2.636	> 80
3	None	0.435	1.011	0.430	< 5
3	CB8	0.750	1.260	0.595	~ 20
4	None	0.554	1.271	0.436	< 5
4	CB8	0.525	0.454	1.200	~ 50
1+**2**	None	0.417	0.856	0.487	< 5
1+**2**	CB8	0.699	0.252	2.780	> 80
1+**4**	None	0.438	0.931	0.471	< 5
1+**4**	CB8	0.655	0.303	2.160	> 80
2+**4**	None	0.475	1.069	0.444	< 5
2+**4**	CB8	0.591	0.254	2.340	> 80

Table 1 also contains data which confirm that dimerization takes place between reduced dendrimers of different sizes. For instance, reduction of a solution that contains an equimolar mixture of dendrimers **1** and **2** in the presence of CB8 leads to extensive dimerization. The spectroscopic data do not permit the assessment of the relative abundances of homo- and heterodimers, but dimerization is nonetheless as predominant upon one-electron reduction as in the cases of the individually reduced dendrimers.

To obtain independent confirmation of these results we carried out Pulse Gradient Stimulated Echo (PGSE) NMR spectroscopic experiments to determine the diffusion coefficients (D_o) of these dendrimers under different experimental conditions. The paramagnetic character of the one-electron-reduced form of viologens introduces some complications in these experiments, but in spite of the broadening of the proton signals of the viologen residue, NMR spectroscopic and PGSE D_o measurements were possible. Relevant values are given in Table 2. The results are consistent with the UV/Vis spectroscopic data and lead to similar conclusions. Note that the D_o values suffer a considerable decrease upon one-electron reduction of the viologen residue in the presence of CB8. The decrease in the D_o values reflects the larger effective size of the aggregates formed upon reduction, presumably owing to the enhanced dimerization fostered by the CB8 host. Control experiments with dendrimer **1** in the presence of the smaller host CB7 did not reveal any decrease in D_o values upon one-electron reduction of the viologen unit. In fact, in this case we observed an increase in D_o values (from 3.1×10^{-6} to 3.5×10^{-6}) which may correlate to the lower relative affinity of the reduced viologen for the CB7 host.

Table 2: Diffusion coefficients (D_o [$cm^2 s^{-1}$]) determined from PGSE NMR experiments with dendrimers **1**–**4** in D_2O solution (pH 7).

Conditions	1	2	3	4
Oxidized, in the absence of CB8	3.8×10^{-6}	2.5×10^{-6}	1.5×10^{-6}	–[a]
Oxidized, in the presence of CB8	3.1×10^{-6}	2.3×10^{-6}	–[a]	1.7×10^{-6}
Reduced (1 e^-), in the presence of CB8	2.3×10^{-6}	1.7×10^{-6}	–[a]	1.4×10^{-6}

[a] not measured.

In summary, this work has clearly established that CB8 strongly favors the dimerization of the viologen-containing dendrimers upon their one-electron reduction (Figure 4). The CB8-mediated dimerization is extremely efficient in most of the cases investigated here and constitutes a rather unique example of redox-switchable dendrimer self-assembly, in which the noncovalent interactions between the host CB8 and the viologen residues of the dendrimers can be manipulated to select different host–guest assemblies as a function of the oxidation state of the viologen unit.

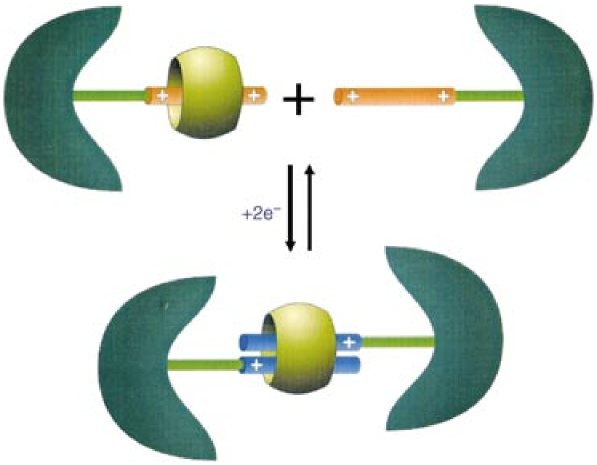

Figure 4. Redox control of the CB8-induced dimerization of viologen-containing dendrimers.

Experimental Section

Dendrimers **1**–**3** were prepared as previously reported.[9] The host CB8 was obtained from Sigma–Aldrich. For the electrochemical and spectroscopic experiments, the dendrimers were dissolved in phosphate buffer solution (pH 7, 0.1-M ionic strength). The electrochemical experiments were run in a single-compartment cell fitted with a glassy carbon working electrode (0.071 cm^2), a Pt counter electrode, and a Ag/AgCl reference electrode. The solutions were exhaustively purged and kept under an atmosphere of purified nitrogen during the electrochemical experiments. For the spectroscopic experiments, the dendrimer solutions were placed inside a glass cell assembly, which was sealed under vacuum. The dendrimer was reduced by exposure to activated Zn powder and transferred for spectroscopic analysis to a quartz cell (0.1-cm optical path), which was fitted to the end of a sidearm of the evacuated glass-cell assembly.

Viologen dendrimer **4**: The hydrolyzed form of dendrimer **3** and acetyl chloride (81.0 equiv) were stirred in dry MeOH (7 mL) for 12 h under N_2. The solution was then concentrated in vacuo. Acetone was added to the residue followed by a saturated solution of NH_4PF_6 in acetone/H_2O (2:1). The solution was stirred for 15 mins, and then acetone was gently removed in vacuo. The remaining suspension was extracted with EtOAc (2 × 10 mL), and the combined extracts were evaporated to afford the viologen dendrimer **4** (96 %). ^{1}H NMR (400 MHz, [D$_3$]MeCN): $\delta = 9.15$ (d, 2H), 9.05 (d, 2H), 8.62 (d, 4H), 6.70 (s, 1H), 6.30 (t, 3H), 6.23 (t, 9H), 4.72 (m, 4H), 3.60 (s, 81H), 2.25 (m, 78H), 2.08 (m, 4H), 1.94 (m, 78H), 1.85 (m, 2H), 1.69 (t, 3H), 1.27 ppm (m, 2H); ^{13}C NMR (100 MHz, [D$_3$]MeCN): $\delta = 176.5$, 175.2, 151.2, 147.3, 146.8, 128.6, 63.3, 59.5, 59.0, 52.7, 50.3, 32.1, 30.5, 29.3, 17.0 ppm; MALDI-TOF MS: m/z: 3801 $[M-PF_6]^+$, 3658 $[M-2PF_6]^{+\cdot}$, 3400 $[M-2PF_6-\text{viologen}]$.

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