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Electroactive Calixarenes. 1. Redox and Cation Binding Properties of Calixquinones

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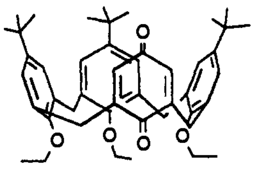
Abstract: The redox and cation binding properties of a series of four quinone-functionalized calix[4]arenes have been studied in acetonitrile. Di-, tri-, and tetraquinone calixarenes exhibit successive (separate) first electron transfers into each of the quinone units. Comparison with linear analogues cited in the literature suggests that the behavior is similar for both linear and cyclic systems. All four compounds when reduced to the monoanion state demonstrate interactions with Na$^+$ and Ag$^+$ to varying degrees. The neutral calix[4]arenemonoquinone binds Na$^+$ and shows a binding enhancement on the order of 10^6 when reduced to its monoanion state.

Introduction

Calixarenes have received much attention over the past decade as a fascinating class of cyclophanes possessing ionic and molecular-binding properties.[1] Their potential as enzyme mimics has been suggested,[2] and appropriate functionalization of the phenolic units could extend this comparison to redox-switching enzymes. Recently, interest in the synthesis of redox-active calixarenes has centered on the conversion of phenolic rings into quinone[3] and nitroaromatic[4] moieties. While considerable interest in these calixarenes derives from their redox-switching abilities, it is important to recognize the opportunity they afford as a means of addressing a number of questions related to the effects of electron transfer in spatially constrained systems with multiple redox units. The degree to which electrons may be localized or delocalized in such structures and the mechanism by which neighboring redox centers communicate may provide insight into similar processes that occur in redox-active proteins that possess multiple redox substituents either proximal to one another or directly linked to one another.

Electrochemical results for a series of quinone-functionalized calixarenes (**1–4**, see structures below) are presented in this paper. These calixarenes provide an opportunity for the elucidation of the effects of successive substitution of redox units into the constrained calix[4]arene framework. The ethoxy substituents on the rings may provide binding sites for ions such as Na$^+$. Complexation of this sort has been noted for calixarenes bearing methoxy tails.[5] Thus, these systems may afford enhanced metal cation binding when reduced to their corresponding anionic states, as has been described for redox-active crown ethers.[6]



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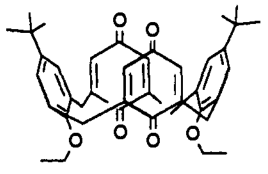

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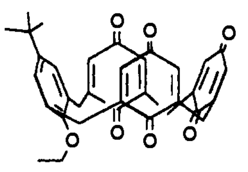

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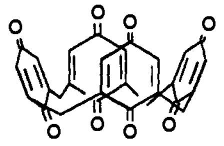

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Experimental Section

The quinone-functionalized calixarenes were synthesized according to published procedures.[7] 2,6-Dimethyl-*p*-benzoquinone (Aldrich, 99%) was dried overnight under reduced pressure (no heat) and used without further purification.

Tetrabutylammonium hexafluorophosphate, TBAPF$_6$ (Fluka, puriss grade), was recrystallized twice from ethanol (reagent grade) and dried overnight under reduced pressure at 100 °C. Electrochemistry in acetonitrile and dimethylformamide (DMF) was performed under an argon atmosphere or at the vapor pressure of the prevailing solvent. For argon atmosphere experiments, acetonitrile (Mallinckrodt or Aldrich, reagent, HPLC grade) was distilled over calcium hydride and transferred to volumetric flasks under N_2, while DMF (Aldrich, HPLC grade) was stirred with P_2O_5 under reduced pressure ("partial vacuum") for 20 min

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(1) (a) Gutsche, C. D. *Calixarenes*; The Royal Chemical Society: Cambridge, 1989. (b) Vicens, J. Böhmer, V., Eds. *Calixarenes*: *A Versatile Class of Macrocyclic Compounds*; Kluwer: Dordrecht, 1986.

(2) Gutsche, C. D. *Acc. Chem. Res.* **1983**, *97*, 332.

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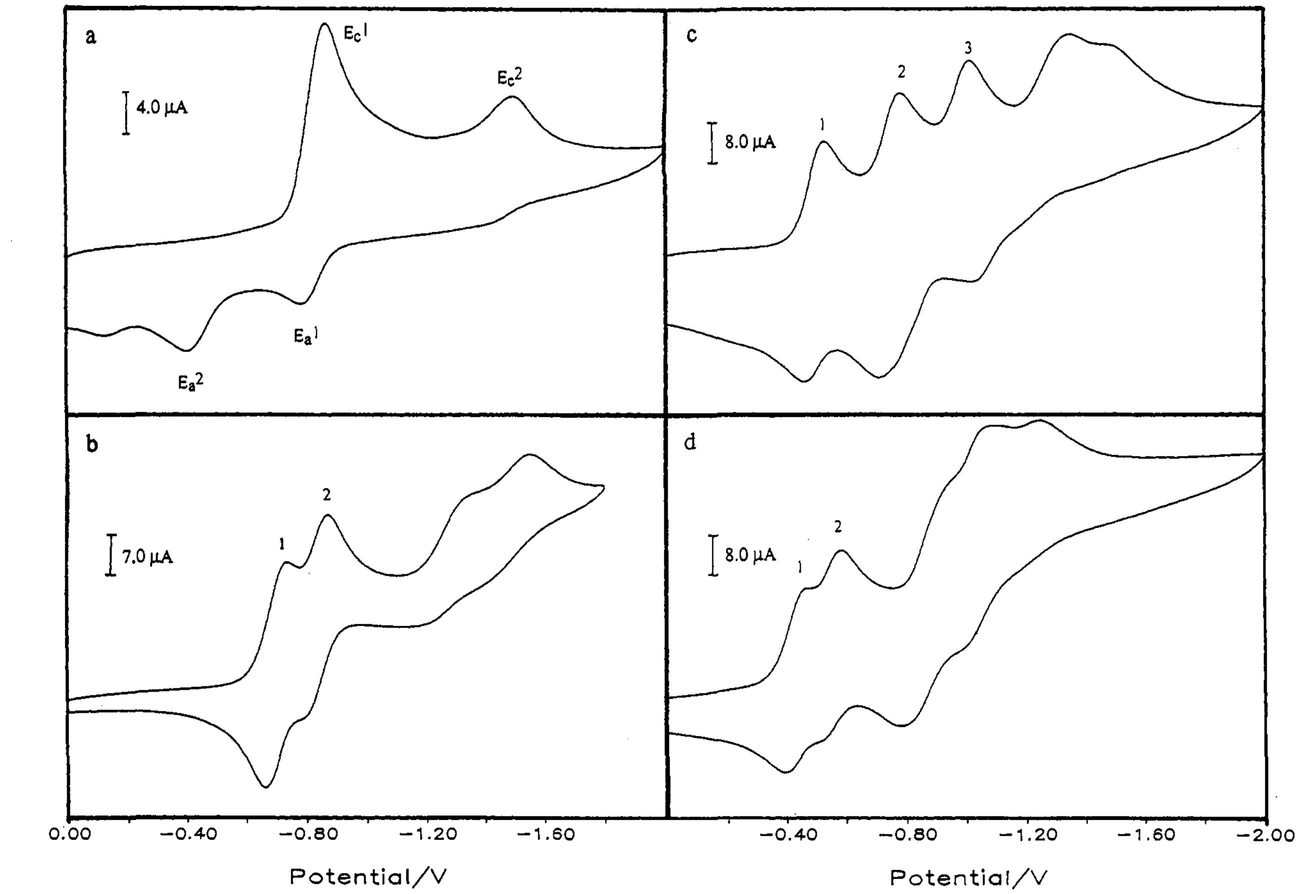

Figure 1. Cyclic voltammograms over the full redox range for (a) **1** (the small anodic wave at −0.15 V vs Ag/AgCl is a decomposition product) (b) **2**, (c) **3**, and (d) **4** (initial scan). All voltammograms were obtained in approximately 1 mM solutions in CH_3CN, 0.10 M $TBAPF_6$ under an argon atmosphere at room temperature. All potentials are referenced to Ag/AgCl and the scan rate was 100 mV/s.

and then distilled at 10^{-5}–10^{-6} Torr into a Schlenk flask and stored under argon. Dimethyl sulfoxide, DMSO (Aldrich, HPLC grade), was used without further purification, under an argon atmosphere. Supporting electrolyte solutions were deoxygenated with purified argon, which had been passed through a solvent presaturation tube, for about 10 min prior to performing electrochemistry.

For several experiments extra care was taken to exclude residual water by rigorously drying the solvent and conducting the experiments at the vapor pressure of the prevailing solvent. For these experiments a double-manifold high-vacuum line, using a diffusion pump, was employed. CH_3CN or DMF were transferred from Aldrich "Sure-Seal" bottles into an argon-filled flask by using a double cannula. The solvent was stirred over P_2O_5 under reduced pressure for 1 h and then subjected to a freeze–pump–thaw routine[8] three times: the first time (20 min) at a pressure around 10^{-3} Torr, the second time for 10 min at 10^{-3} Torr followed by 10 min at 10^{-5}–10^{-6} Torr, and the third time for 20 min at 10^{-5}–10^{-6} Torr. The solvent was then distilled into the receiving bulb of a home-built electrochemical cell. The fully assembled cell containing the sample and supporting electrolyte was pumped overnight at a pressure around 10^{-3} Torr, and for 2 h at 10^{-5}–10^{-6} Torr, prior to distillation of the solvent.

Electrochemical experiments were performed on a Windows-driven BAS100B electrochemical analyzer (BAS100W) (Bioanalytical Systems, West Lafayette, IN) using positive feedback routines to compensate for resistance. The surface of the working electrode, a glassy carbon BAS minielectrode, was polished with 0.25-μm diamond paste and extender (Buehler, Lake Bluff, MN) and then rinsed successively with deionized water, acetone, and the appropriate solvent. A Pt wire counter electrode and a Ag/AgCl reference electrode (Bioanalytical Systems, West Lafayette, IN) were used for the voltammetric experiments in an argon atmosphere. The electrochemical experiments conducted at the vapor pressure of the solvent ("vacuum") employed two working electrodes (both BAS glassy carbon, prepared as above) while the counter electrode was a Pt mesh and the reference electrode a silver wire isolated from the main cell by a glass shroud. The electrical contact for the reference was made via a Pt wire in the base of the glass shroud, and supporting electrolyte solution was introduced, by agitation, into the shroud through an opening above the solution level of the cell. Ferrocene (sublimed three times under reduced pressure) was added at the end of the experiment as an internal standard by placing the cell under argon to deliver the solid and then rapidly evacuating the cell. The half-wave potentials obtained under these conditions could then be compared to those obtained under normal atmospheric conditions by examining the ferrocene half-wave potential in the same solvent at normal pressure, using the glassy carbon working and Ag/AgCl reference electrodes mentioned above. This is based on the assumption that the ferrocene half-wave potential is not significantly affected by the residual water that may be present in the solvent at normal atmospheric pressure.

Sodium ion was added as $NaClO_4$ (Aldrich, A.C.S. reagent grade, dried for 48 h under vacuum) or sodium tetraphenylborate, $NaB(Ph)_4$, (Aldrich, A.C.S. gold label, reagent grade, dried for 48 h under vacuum). Silver trifluoromethanesulfonate, silver triflate (Aldrich, 99+%), was used without further purification. All silver ion solutions were shielded from light with aluminum foil prior to use and the electrochemical experiments were conducted in semidarkness. Our preliminary binding studies employed cyclic voltammetry, Osteryoung square wave voltammetry, and differential pulse voltammetry. Fractional equivalents of Na^+ were added in the form of an CH_3CN or DMF solution to the (same solvent) sample solution by pipeting the desired volume using a Gilman pipet pump, stirring the solution while bubbling with purified argon, and allowing the system to reach equilibrium. Cryptand[2.2.1] (Aldrich) was used without further purification and was delivered with a Gilman pipet pump.

^1H-NMR spectra were acquired on a Varian VXR-400. The solvent was CD_3CN (Aldrich, 99%).

Results and Discussion

Voltammetry of the Calixquinones. Initial cyclic voltammograms of compounds **1–4** in CH_3CN, obtained under an argon atmosphere, are presented in Figure 1. Compound **1** exhibits a reversible first wave followed by a second wave, at a much more negative potential, that falls in the lower range of the quasire-

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[8] Shriver, D. E.; Drezdzon, M. A. In *Manipulation of Air-Sensitive Compounds*, 2nd ed.; John Wiley and Sons: New York, 1986; pp 104–105.

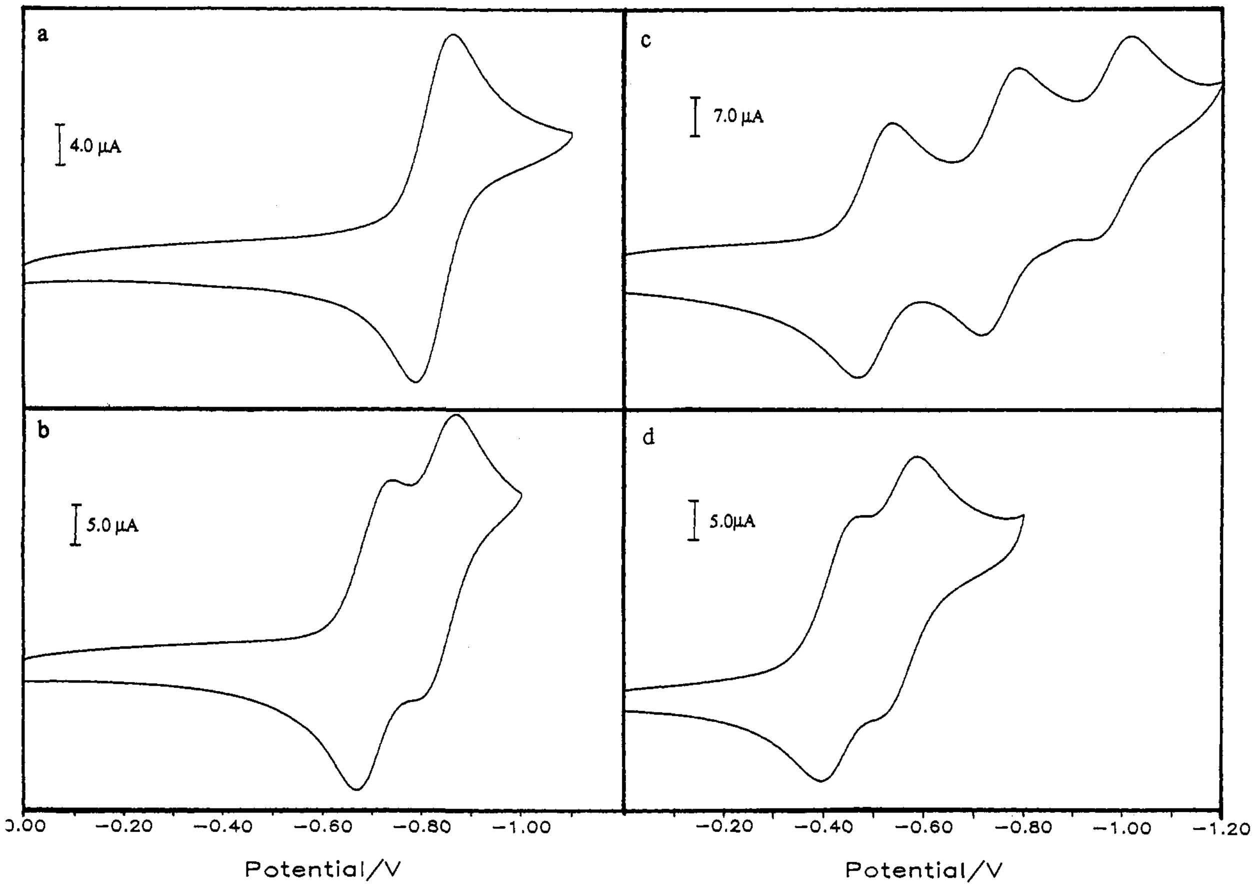

Figure 2. Cyclic voltammograms over the redox range for the first electrons uptake for (a) **1**, (b) **2**, and (c) **3**. (d) The first two redox waves (initial scan) for **4**. All voltammograms were obtained in approximately 1 mM solutions in CH_3CN, 0.10 M $TBAPF_6$ under an argon atmosphere at room temperature. All potentials are referenced to Ag/AgCl and the scan rate was 100 mV/s.

versible regime. In the voltammogram shown in Figure 1a the respective peak potentials E_c^1/E_a^1 and E_c^2/E_a^2 are labeled, where E_c and E_a are the cathodic and anodic peak potentials, respectively. Note that the anodic wave corresponding to the second reduction wave of **1** is, in fact, the more positive anodic wave, a point confirmed by scan rate studies. The small anodic wave around −0.15 V appeared to be linked to slow decomposition of a reduced intermediate species. This wave was observed *only* when the full potential range was scanned, and the peak current intensity increased when the potential was cycled. We have not attempted to assign these waves to specific structures in the present work. When the potential is scanned just beyond the first reduction (see Figure 2a) this wave is not observed, even after repeatedly cycling the potential. In the voltammogram for **2**, Figure 1b, the two waves labeled 1 and 2 are separated by 140 mV, while in **3** the waves labeled 1, 2, and 3 are separated by over 200 mV, in both cases. For **1**–**3** these waves were assigned to the first electron transfers into each of the available quinone units, hereafter referred to as the first electron uptake. The corresponding electrochemical processes involved for **1**–**3** are

$$\mathbf{1} \overset{e^-}{\rightleftharpoons} \mathbf{1}^-$$

$$\mathbf{2} \overset{e^-}{\rightleftharpoons} \mathbf{2}^- \overset{e^-}{\rightleftharpoons} \mathbf{2}^{2-}$$

$$\mathbf{3} \overset{e^-}{\rightleftharpoons} \mathbf{3}^- \overset{e^-}{\rightleftharpoons} \mathbf{3}^{2-} \overset{e^-}{\rightleftharpoons} \mathbf{3}^{3-}$$

where an electron is placed on one of each of the quinone units, as in Scheme 1. For the triquinone system, the first electron is assigned to the middle quinone on the basis of electron-withdrawing effects (*vide infra*). Delivery of a second electron is assumed to impose a redistribution of electron density onto opposing quinone units, while the third electron would then be centered between the first two units. The foregoing assignments are based on considerations of simple Coulombic repulsion.

Voltammograms a–c in Figure 2 were obtained when only the potential range corresponding to the first electron uptake is scanned. On the basis of ΔE_p (the separation between E_c and E_a) values, the redox waves for the first electron uptake of **1**, **2**, and **3** are reversible. The initial and steady state voltammograms were identical for these three systems. Figure 2d shows the initial cyclic voltammogram corresponding to the first two reductions for **4** (two *single* electron transfer waves). The initial and steady state voltammograms were not the same for **4** even over this limited potential range. Steady state voltammograms suggest chemical irreversibility in this solvent, as will be discussed below. The half-wave potentials, $E_{1/2}$ (the midpoint of E_c and E_a), and ΔE_p values obtained by cyclic voltammetry for **1**–**4** are given in Table 1. The second electron transfers (second electron uptake) in several of these systems appear to be irreversible electrochemically and will not be discussed. The currents for the second electron uptake were always considerably smaller than those obtained for the first electron uptake. This point is readily visible in the voltammograms seen for **2** where four well-resolved redox waves for the reduction of both quinone units are observed, each to its corresponding dianion state. The reasons for this behavior are not presently understood.

Electrochemical studies of comparable linear analogues, **5** and **6** (see structures below), were published in 1962 by Lindsey et al.[9] An important finding in their elegant work is the fact that *well-separated, successive first electron transfers* into the quinone units were noted for the linear systems. This is in contrast to the result expected for non-interacting redox-active sites, where the separation in redox potentials is typically on the order of tens of

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[9] Lindsey, A. S.; Peover, M. E.; Savill, N. G. *J. Chem. Soc.* **1962**, 4558. Lindsey, A. S. In *Polymeric Quinones, The Chemistry of the Quinoid Compounds*; Patai, S., Ed.; John Wiley and Sons: New York, 1974; Chapter 15, pp 793–855.

Scheme 1

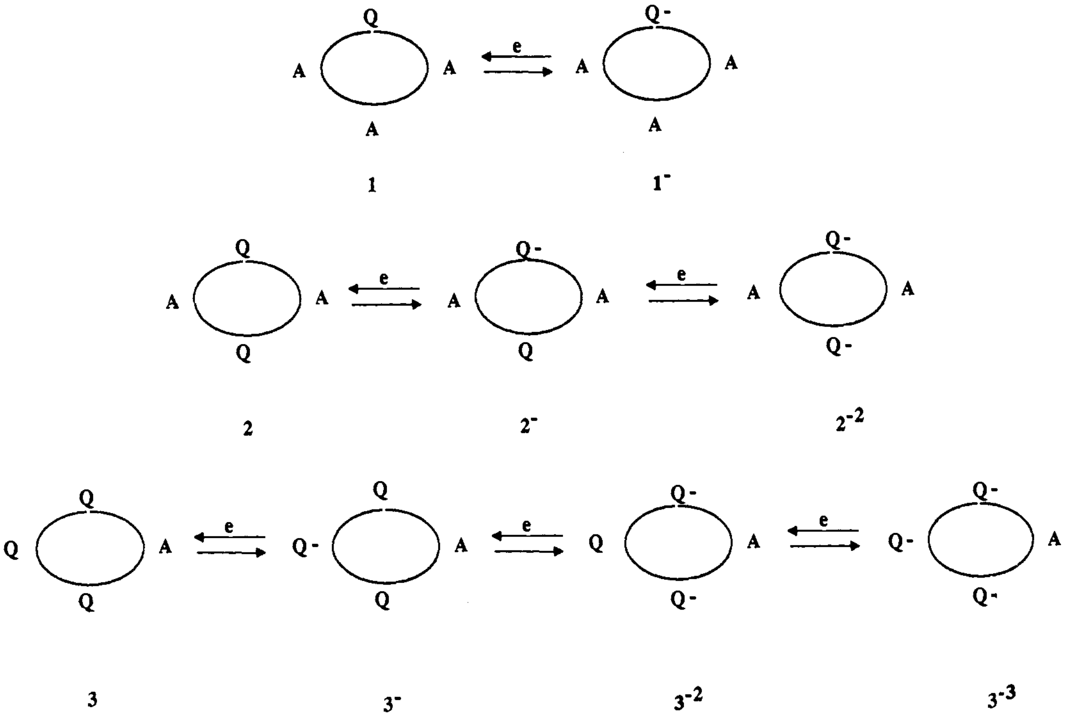
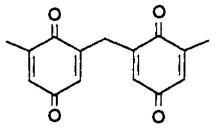


Table 1. $E_{1/2}$ and ΔEp Values for Calixquinones in CH_3CN[a]

compd	$E_{1/2}{}^1$, V	$\Delta E_p{}^1$, mV	$E_{1/1}{}^2$, V	$\Delta E_p{}^2$, mV	$E_{1/2}{}^3$, V	$\Delta E_p{}^3$, mV	$E_{1/2}{}^4$, V	$\Delta E_p{}^4$, mV	$E_c{}^5$, V	$E_6{}^6$, V
1	–0.823	76	–1.447[b]	1088						
2	–0.699	74	–0.840	81	–1.225	134	–1.436	130		
3	–0.501	65	–0.752	67	–0.982[c]	68[c]	(–1.346)[d]		–1.483	
4	–0.429	67	–0.552	61	(–0.934)[d]		(–1.071)[d]		–1.122	–1.240
5[e]	–0.60		–0.77							
6[e]	–0.54		–0.72							
2,6-DMQ	–0.607	70	–1.242	82						

[a] All potentials vs a Ag/AgCl reference, all scan rates at 100 mV/s unless otherwise noted. [b] Value obtained by differential pulse voltammetry (at a scan rate of 20 mV/s). [c] Value obtained when only the first three waves are scanned. [d] Values in parentheses are *cathodic peak potentials* not half-wave potentials. [e] Values from reference 9, corrected to potentials vs Ag/AgCl.



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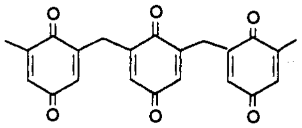

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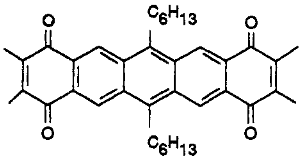
millivolts,[10,11] thus giving the appearance of "simultaneous" multiple electron transfers. The values obtained in these systems were on the order of hundreds of millivolts. Assuming the absence of significant molecular reorganization or solvation changes, the total difference between the half-wave potentials ($\Delta E_{1/2}$) in a molecule bearing two identical non-interacting redox substituents is governed by statistics. On the basis of symmetry considerations this results in a theoretical separation of (RT/F) ln 4 mV, at 25 °C.[12]

Redox groups, particularly aromatic ones, may interact by delocalization of electrons. The correlation between the separation of half-wave potentials and the extent to which a first electron is delocalized over a molecule with multiple redox sites has been discussed by several authors.[13] Miller et al. have presented electrochemical results for fused bisquinone systems where the half-wave potential separations ($\Delta E_{1/2}$) values for the quinone reductions vary from 120 mV to more than 400 mV.[14] Some of the structures studied by the authors include **7** and **8**.



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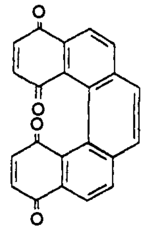

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Typical values of $\Delta E_{1/2}$ in the delocalized bisquinone systems are on the order of 400 mV.[15] It is important to note that for both the cyclic (**1**–**4**) and linear systems (**5**,**6**) the separation between successive first electron transfers is larger than that expected for a structure bearing multiple non-interacting redox sites but is not as large as the separation anticipated if all of the electrons are delocalized over the entire structure.[16] This clearly indicates

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(10) Flanagan, J. B.; Margel, S.; Bard, A. J.; Anson, F. C. *J. Am. Chem. Soc.* **1978**, *100*, 4248. Bard, A. J. *Pure Appl. Chem.* **1971**, *25*, 379.

(11) El-Kasmi, A.; Lexa, D.; Maillard, P.; Momenteau, M.; Savéant, J. M. *J. Phys. Chem.* **1993**, *97*, 6090 and references cited therein.

(12) Ammar, F.; Savéant, J. M. *J. Electroanal. Chem.* **1973**, *47*, 115.

(13) For example: Weaver, M. J.; Gao, X. *J. Phys. Chem.* **1993**, *97*, 332. Liberko, C. A.; Miller, L. L.; Katz, T. J.; Liu, L. *J. Am. Chem. Soc.* **1993**, *115*, 2478 and references cited therein.

(14) Liberko, C. A.; Miller, L. L.; Katz, T. J.; Liu, L. *J. Am. Chem. Soc.* **1993**, *115*, 2478. Rak, S. F. *J. Am. Chem. Soc.* **1992**, *114*, 1388. Yang, B.; Liu, L.; Katz, T. J.; Liberko, C. A.; Miller, L. L. *J. Am. Chem. Soc.* **1991**, *113*, 8993. Almlöf, J. E.; Feyereisen, M. W.; Jozefiak, T. H.; Miller, L. L. *J. Am. Chem. Soc.* **1990**, *112*, 1206. Jozefiak, T. H.; Almlöf, J. E.; Feyereisen, M. W.; Miller, L. L. *J. Am. Chem. Soc.* **1989**, *111*, 4105. Jozefiak, T. H.; Miller, L. L. *J. Am. Chem. Soc.* **1987**, *109*, 6560.

(15) Liberko, C. A.; Miller, L. L.; Katz, T. J.; Liu, L. *J. Am. Chem. Soc.* **1993**, *115*, 2478.

(16) Weaver, M. J.; Gao, X. *J. Phys. Chem.* **1993**, *97*, 332.

that structures **1**–**4** exhibit behavior intermediate between these extremes. We are currently pursuing ESR studies of the calixquinones to examine the extent to which the electron in the anionic calixarenes is localized, or delocalized, on the quinone units. Preliminary results on **1** clearly demonstrate that spin density is localized only on the quinone and on its connecting methylene protons, i.e. no delocalization throughout the calixarene framework is observed. We anticipate that electron hopping may be significant in **2** and **3**, as noted for the helicene bisquinone systems (such as **8**) where the quinone units are proximal to one another.

The electrochemistry of the calix[4]arenediquinone (**2**) and calix[4]arenetetraquinone (**4**) has recently been examined by other authors in CH_2Cl_2[17] and DMF,[18] respectively. Although the behavior of the former in CH_2Cl_2 is quite similar to that observed in our own studies of **2** in CH_3CN, we were suprised to note that **4** gives a very different behavior in CH_3CN compared to that described by Suga et al. in DMF. In our studies, reduction of **4** in CH_3CN resulted in the formation of brown films at the electrode surface. The first two redox waves, seemingly electrochemically reversible based on ΔE_p values, are complicated by a slow chemical process. When the working electrode was cycled several times over the potential range shown in Figure 2d, slow film formation on the electrode surface was noted. When the potential was cycled over the range shown in Figure 1d the electrode was passivated quite rapidly—as little as three or four cycles results in formation of a thick non-conducting film on the electrode surface. In contrast, the results obtained by Suga et al. showed that the electrochemistry of **4** in DMF results in four well-separated redox couples, appearing to follow the same trend noted for **2** and **3** in CH_3CN. We examined the voltammetric behavior of **4** in DMF under an argon atmosphere and found results that were similar to those of Suga et al. However, when the potential of the electrode was cycled 15–20 times in this solvent (over the full reduction range), formation of a film on the working electrode surface was again observed. Furthermore, the position of the cathodic waves appeared to shift after the first scan, i.e. the steady-state voltammetry differed in appearance from that of the initial cyclic voltammogram. (We should note that these authors did use a slightly different supporting electrolyte, tetraethylammonium perchlorate.)

Residual water is notorious for complicating quinone electrochemistry and, as such, experiments were also conducted at the vapor pressure of the solvent after a rigorous drying procedure (see Experimental Section). The cyclic voltammetry of **4**, at the vapor pressure of the dry solvent, is shown in Figures 3 and 4 for CH_3CN and DMF, respectively. In Figure 3, the voltammogram represented with the dashed line corresponds to that in CH_3CN under an argon atmosphere, and the one represented with the solid line corresponds to that at the vapor pressure of the solvent. The potentials have been converted to those of the Ag/AgCl reference electrode, using the method described in the Experimental Section. Comparing the two it is clearly evident that the behavior in this solvent is not significantly complicated by aqueous impurities. The positions of the first, second, and third cathodic waves are virtually identical, although the behavior beyond the third wave differs somewhat. Differing amounts of residual water under the two sets of conditions is most likely to affect these subsequent waves, since the basicity of the higher anionic (tri-, tetraanions, etc.) states is increased. Passivation of the electrode surface was just as rapid under the very dry conditions as it was for the same system under argon.

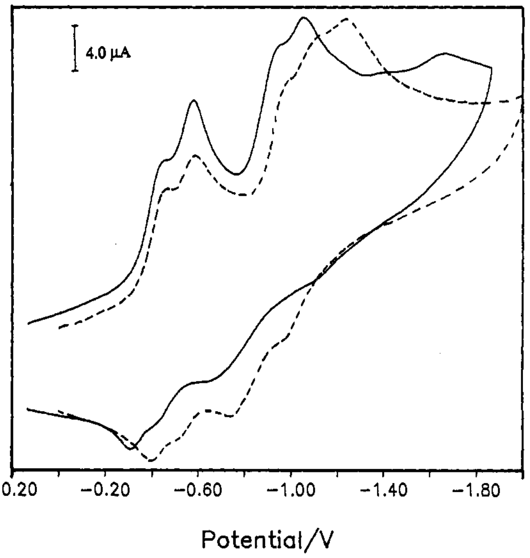

Figure 3. Cyclic voltammograms (initial scans) for **4** in CH_3CN under vacuum (solid line) with potentials corrected to Ag/AgCl, and argon atmosphere (dashed line), at atmospheric pressure. The scan rate was 100 mV/s for both voltammograms.

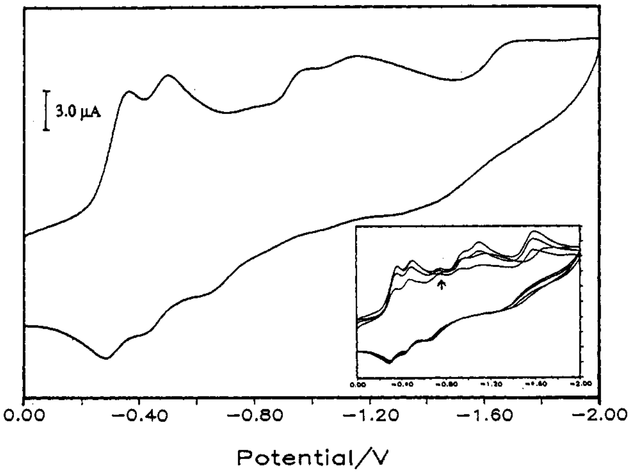

Figure 4. Cyclic voltammograms (initial scans) for **4** in DMF under high vacuum, with inset showing the behavior obtained after multiple scans, where the arrow indicates the formation of the new third wave in the region of the potential gap for the initial scan. The scan rate was 100 mV/s. The solution was 0.50 mM and 0.10 M $TBAPF_6$.

The results obtained in DMF (Figure 4) were different, however. Here the initial voltammogram shows a substantial potential gap between the second and third electron transfers. A slight peak in the valley between these waves grows as the potential is cycled 4 or 5 times and decreases when the electrode is held at positive potentials (0.5 V vs the Ag wire) (see the inset in Figure 4). We attribute this finding to formation of thin films of **4** adsorbed onto the electrode surface, a point confirmed by double potential step chronocoulometry (DPSCC) and by the fact that a thin film was visible upon opening the cell. The results of the DPSCC experiments clearly suggest adsorption, since the absolute value of the intercept for the backward step is greater than that of the forward step. (The amount of **4** adsorbed cannot be quantified since we do not know the number of electrons transferred in the process and this number cannot be obtained by standard coulometry due to fouling of the working electrode surface.)

The initial voltammogram obtained in DMF, displaying well-separated second and third electron transfer processes, is similar to that obtained in CH_3CN and suggests that *the potential gap observed between the second and third electron transfers in this system is intrinsic*. The fact that the working electrode does not become passivated in DMF, as it does in CH_3CN, probably reflects the greater solvating ability of this solvent. Thus, on the basis of the above results, the appearance of four successive and equally spaced redox waves for reduction of each of the quinones in **4** to

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(18) Suga, K.; Fujihira, M.; Morita, Y.; Agawa, T. *J. Chem. Soc., Faraday Trans.* **1991**, *87*, 1575.

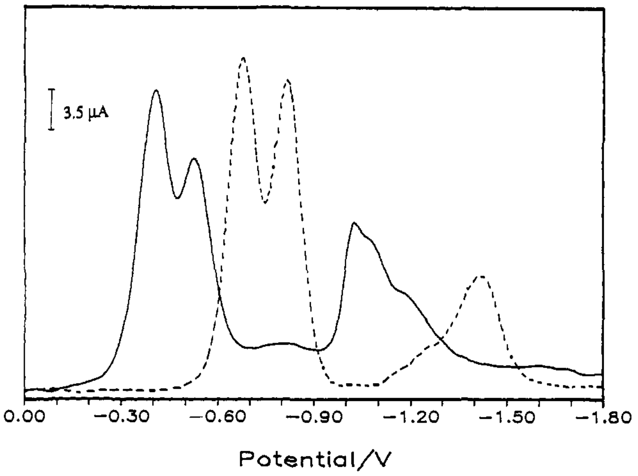


Figure 5. Differential pulse voltammograms comparing the voltammetric behavior of 1 mM solutions of **2** (dashed line) and **4** (solid line) in CH_3CN, 0.10 M $TBAPF_6$, under an argon atmosphere. The scan rate for both voltammograms was 20 mV/s.

the monoanion state is observed for films of **4**, not for the freely diffusing compound whose representative electrochemistry is the initial voltammogram shown by the solid line in Figure 3. The electrochemistry of **4** in DMSO (under argon) was also examined and was found to exhibit a behavior that was intermediate between that obtained in CH_3CN and in DMF under argon.

The reason for the potential gap between the second and third redox waves in this system remains obscure. The tendency of **4** to form films and the lack of a clearly defined first electron uptake in CH_3CN implies that this compound behaves differently from the other members of this group. Nonetheless, in some respects the voltammetric behavior of **4** obtained with pulsed techniques resembles that of the diquinone system **2**, see Figure 5. In examining the differential pulse voltammograms in Figure 5, it is important to note that the solution concentrations were nearly identical (1 mM). On the basis of current intensities, the first two waves in both systems correspond to *single* electron transfers. (Again, coulometry with **4** is not possible because of its tendency to passivate the electrode surface.) The striking similarity of the differential pulse voltammograms for **2** and **4** suggests that symmetry may be an important clue as to the origin of the differences between **1**–**3** and this system.

Careful examination of Table 1 shows that successive quinone substitutions into the calix system cause the *first* half-wave potential to shift to more positive values. This is demonstrated in Figure 6. The first electron uptake for **1** and **2** occurs at more negative potentials than that observed for a model compound, 2,6-dimethyl-*p*-benzoquinone (2,6-DMQ in Table 1). In fact, the first half-wave potential of **1** is shifted about 210 mV more negative than that observed for 2,6-DMQ. It seems reasonable to attribute this to the more electron donating effect of the surrounding aromatic groups in the calixarene as compared with the methyl substituents. The mono- and diquinone systems are equivalent to having replaced one of the hydrogens on each of the methyl groups of 2,6-DMQ with a *p*-(*tert*-butyl)ethoxyarene unit. The overall trend in the $E_{1/2}$ values of **1**–**4** may reflect the electron withdrawing nature of the quinone units versus that of the more electron donating arene units in the calixarene framework. These results are similar to those obtained with the linear systems[9] as shown in Table 1, although the second and third electron transfer potentials for the cyclic systems **2** and **3** are more negative. Nonetheless, the fact that **5**, quinone next to quinone, shows a first redox potential that is more positive than that of **2**, quinone next to arene, suggests that the electron donating effects of the neighboring substituents are significant.

The potential gap between successive quinone reductions is also of interest. Although the difference between the first and second $E_{1/2}$ values for **2** is about 140 mV, the potential difference for the same process in **3** is close to 250 mV, suggesting that additional energy is required for redistribution of electron density to occur in the system, as mentioned above and shown in Scheme 1. The first electron delivered to **3** is most likely localized on the middle quinone (based on electron-withdrawing effects), but a second electron will favor localization on opposing units. This interpretation is verified to some extent by results we have recently obtained with a 1,2-diquinone calix[4]arene analogue of **2**, which shows a $\Delta E_{1/2}$ of 300 mV between the first and second redox waves. This system does not possess the ability to redistribute electron density to opposing units and the negatively charged quinones reside side by side. These effects are not observed to the same extent in **5** and **6**, where the smaller values of $\Delta E_{1/2}$ may reflect the fact that these systems can still undergo free rotation about the methylenes and thus minimize the Coulombic repulsion between neighboring units.

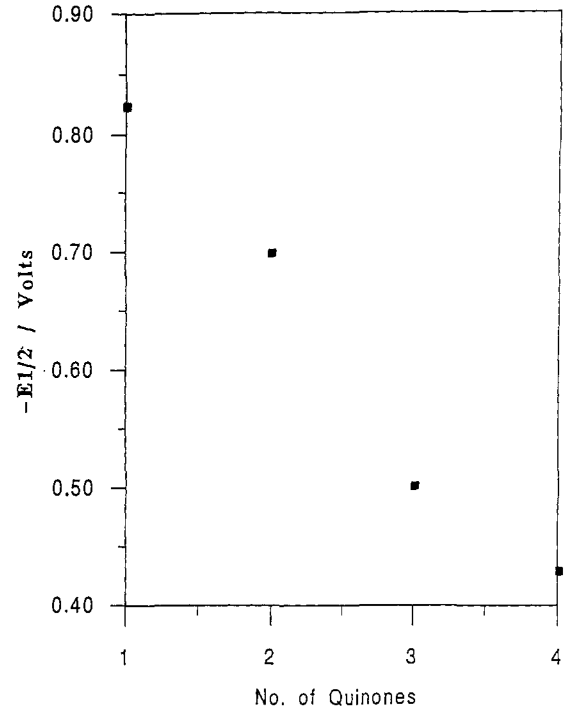


Figure 6. Plot of the effect of quinone substitution on the first $E_{1/2}$ in the calix[4]quinones.

Electrochemistry of the Calixquinones in the Presence of Na^+ and Ag^+. Calix[4]arenes with *p*-(*tert*-butyl)methoxy substituents have been reported[5] to bind Na^+, so we were interested in the possibility of obtaining enhanced binding with the reduced calixquinones, due to added electrostatic forces. Proton NMR studies of the four calixquinones indicated that *only* **1**, the monoquinone, demonstrates significant binding of Na^+ in the neutral state, as evidenced by the broadening of peaks in the $ArCH_2Ar$ and CH_3CH_2O ethoxy region of the ^1H-NMR spectrum CD_3CN (see Figure 7a,b). This calixarene has been reported to have a partial cone conformation, with respect to the arene units, in solution when at room temperature (two sets of pairs of doublets in the methylene region), although the quinone can rotate freely on the NMR time scale.[7] Conformational interchange of the arene units is prevented by the presence of the bulky ethoxy tails on the arene units. Evidence of binding Na^+ in the neutral state, as detected by broadening in the ^1H-NMR spectra, was not observed for any of the other calixquinones, which may imply that the binding constant is low. ^1H-NMR spectra have often been used to assess the solution conformations of calix[4]arenes.[1a] It is important to note that the rotation of the quinones in these systems is probably too fast to be detected on the NMR time scale. The methylene protons (QCH_2Ar) in the calixquinones are diastereotopic, and thus always lead to a pair of doublets, regardless of the quinone orientation. Such factors prevent a firm assignment of the solution conformation, although the NMR

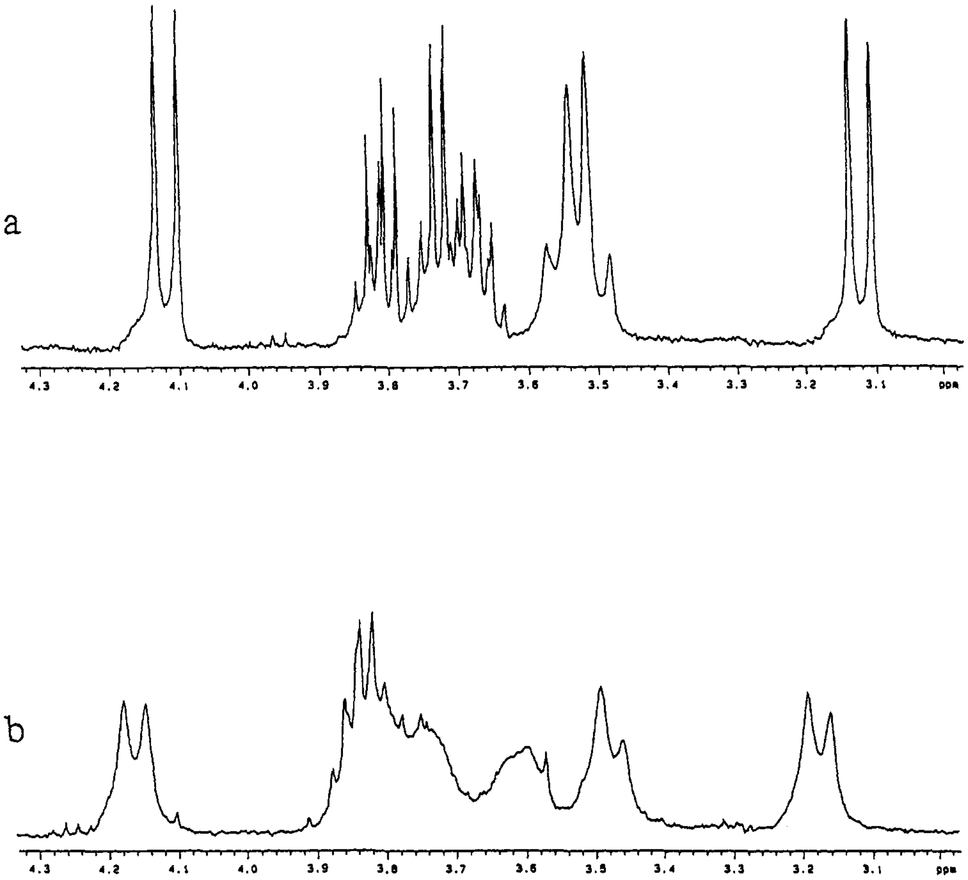


Figure 7. 400-MHz ^{1}H-NMR spectra of the methylene region of **1** in the (a) absence and (b) presence of 2 equiv of Na^+. Spectra were obtained in CD_3CN at room temperature. Changes were also noted in the aromatic region (not shown).

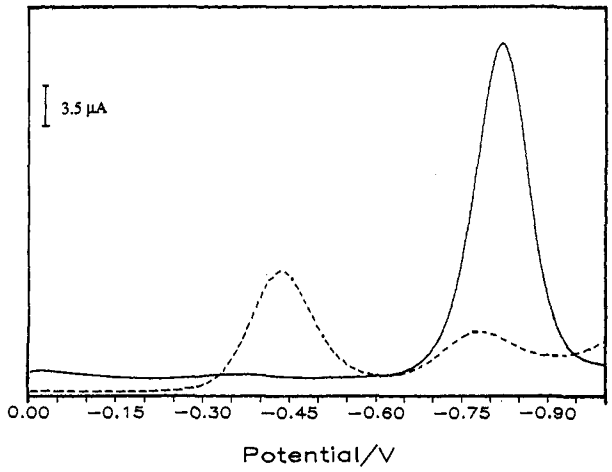
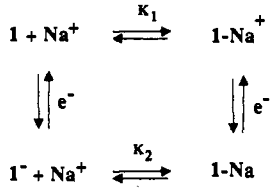


Figure 8. Osteryoung square wave voltammogram of **1** in the absence (solid line) and presence (dashed line) of 1 equiv of Na^+. The solution concentration was 0.5 mM in CH_3CN, 0.10 M $TBAPF_6$ under an argon atmosphere, at room temperature. Two equivalents of Na^+ resulted in formation of a single wave at the more positive potential. The scan rate was 375 mV/s.

spectrum of **2** is compatible with a full cone conformation.[7] The conformations of the remaining compounds are more difficult to assign.

With the addition of <1 equiv of Na^+, the voltammetry for **1** displayed an additional wave at a far more positive potential than that of the free calixarene. As the stoichiometric ratio of Na^+:**1** approached 1.0, the wave at the more positive potential dominated, Figure 8. When the full potential range (0.0 → −2.0 V) was examined, both the first and second redox couples of **1** were shifted to more positive potentials, and the reversibility of the second couple was somewhat improved. The potential of the new wave corresponding to the complex does not change after addition of 2 equiv of Na^+. Addition of cryptand[2.2.1] resulted in complete reversal of this behavior, i.e., the normal redox potentials were recovered for both the first and second waves.

Scheme 2. A Square Scheme for Binding Enhancement



Redox switching in the electroactive calixarenes can be described by the processes shown in Scheme 2. The binding constant in the neutral state has not been measured but can be reasonably estimated[19] to be on the order of 10^3 M^{-1}. The binding constant in the reduced state can be estimated by use of the cation binding enhancement. Binding enhancement, the increase in K_S in the reduced versus the neutral state, may be calculated by considering the shift in the $E_{1/2}$ for the bound and free calixquinones using the relation $K_2/K_1 = \exp\{-(nF/RT)\Delta E_{1/2}\}$ where $\Delta E_{1/2}$ is equal to $(E^1{}_{1/2} - E^2{}_{1/2})$.[20] For **1**, a shift 0.371 V positive of the $E_{1/2}$ for the neutral calixquinone is equivalent to an estimated binding enhancement of $K_2/K_1 = 1.9\ (\pm 0.50) \times 10^6$. However, the actual enhancement may be higher, if the true K_1 value is 10^4 M^{-1} or less.[21] Table 2 shows the effect of the Na^+ binding on the $E_{1/2}{}^1$ for all four calixquinones in CH_3CN, at a ratio of 2:1 for Na^+ to ligand. We are presently investigating the ESR spectra of **1** in the presence of Na^+ and [2.2.1]-bound Na^+.

While the results for the other calixquinones show less spectacular binding enhancement than does compound **1**, the

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[19] Izatt, R. M.; Lamb, J. D.; Hawkins, P. R.; Izatt, S. R.; Christensen, J. J. *J. Am. Chem. Soc.* **1983**, *105*, 1782. McKervey, M. A.; Seward, E. M.; Ferguson, G.; Ruhl, B.; Harris, S. *J. Chem. Soc., Chem. Commun.* **1985**, 388.

[20] See ref 6a, pp 377–380.

[21] Miller, S. R.; Gustowski, D. A.; Chen, Z.; Gokel, G. W.; Echegoyen, L.; Kaifer, A. E. *Anal. Chem.* **1988**, *60*, 2021.

Table 2. $\Delta E_{1/2}$ Observed for Calixquinones upon Addition of Na^+ and Ag^+ [a]

compd	$E_{1/2}$	$E_{1/2}^{Na^+}$ (ratio Na^+:ligand)	$E_{1/2}^{Ag^+}$ (ratio Ag^+:ligand)
1	–0.828	–0.457 (2:1)	–0.733 (2:1)
2	–0.703	–0.613 (2:1)	–0.675 (3:1)
3	–0.507	–0.443 (2:1)	–0.505 (3:1)[b]
4	–0.412	–0.408 (2:1)	–0.433 (3:1)[c]
2,6-DMQ	–0.619	–0.593 (2:1)	–0.608 (2:1)

[a] Values obtained by differential pulse voltammetry (at a scan rate of 20 mV/s). All potentials are vs a Ag/AgCl reference. Na^+ was added as $NaClO_4$ and Ag^+ was added as $AgCF_3SO_3$. [b] The second wave is affected, rather than the first. [c] Silver plating onto the electrode surface makes determining the accuracy of this value difficult.

actual electrochemical behavior of these systems is intriguing. Addition of 2 equiv of Na^+ to 1 equiv of **2** results in the formation of a new wave corresponding to approximately two electrons transferred at a potential 90 mV more positive than that of the first reduction potential of **2**. That is, *the interaction of* **2** *with* Na^+ *appears to nullify the electrostatic communication between the quinone units* that results in their reduction at differing $E_{1/2}$ values. This effect is already quite evident at a 1:1 ratio and is completely reversed by addition of an excess of cryptand[2.2.1], which efficiently sequesters the Na^+ ions. The potentials continue to change slightly as an increasing number of equivalents of Na^+ are added, although the changes are on the order of millivolts. Since the binding constant for the neutral system is probably well below 10^3 M^{-1} and a facile voltammetric estimation of the binding enhancements diminishes sharply in this range, calculation of these values was not attempted.[21] Similar results are seen with **3**, where the most prominent change in peak current intensity occurs in the second and third redox waves at substoichiometric ratios of Na^+ to **3**. These two redox waves are moved to more positive potentials. At a final ratio of 2:1 for Na^+ to calix **3**, the new wave is some 60 mV more positive that the first $E_{1/2}$ of the free calixquinone, and the peak current is more than that associated with a single electron transfer but less than that of a three electron transfer process. A residual wave in the region of the first and second $E_{1/2}$ range for the free calixarene is noted. Interestingly, addition of Na^+ ions to this system seems to result in formation of thin brown films much like those noted with **4**. It is possible that the triquinone is subject to the same chemical process that consumes **4**, but at a slower rate.

The effect of Na^+ on **4** is difficult to assess because of the tendency of **4** to form films at the electrode surface. We can qualitatively say that the addition of Na^+ appears to actually accelerate film formation, a finding in agreement with the result noted for **3**. When the electrode is removed and polished after each addition, the differential pulse voltammogram obtained at a final ratio of 2:1 Na^+ to **4** yields two waves, the first of which is only about 40 mV more positive than that of the first $E_{1/2}$ of free **4**, while the second wave, at about –1.05 V, shows a substantially higher current than the first wave, a reversal of the scenario seen in the free calixquinones where the waves associated with the second electron transfers are always smaller than the first electron waves. These observations are not presently well understood, and we cannot attribute this second wave to second electron transfers into the quinone units. In fact, it may correspond to reduction of a new product.

Interaction of the calixquinones with silver ion was first noted serendipitously with **4**. A 2 mM solution of this compound stripped a layer of AgBr off the surface of a reference electrode, resulting in a "whittled" appearance for the electrode and a change in the color of the solution of **4** from the typical pale, clear yellow to a deep rusty orange. On the basis of this finding, all of the calixquinones were examined for their Ag^+ binding properties, and all four were found to interact to varying degrees.

Compound **1** binds Ag^+, albeit not as strongly as it does Na^+. Our results were obtained using differential pulse voltammetry (DPV) exclusively, as the addition of the triflate anion along with the Ag^+ ion was found to adversely affect the capacitive current recorded for the working electrode. Figure 9 shows the DPVs obtained for **1** in the presence of various equivalents of Ag^+. Interestingly, only with a substantial excess of Ag^+ is Ag° plated onto the surface of the electrode. On the basis of the number of equivalents of Ag^+ necessary to drive the binding to completion (i.e. complete disappearance of the peak corresponding to free **1**) we postulate that the mode of interaction differs from that seen in the Na^+ binding. Although it would seem that the most likely interaction is a π-bonded interaction between Ag^+ and the arene units and/or the quinone units in these systems, this has not been borne out by ^{1}H-NMR studies performed using a 5:1 excess of Ag^+.

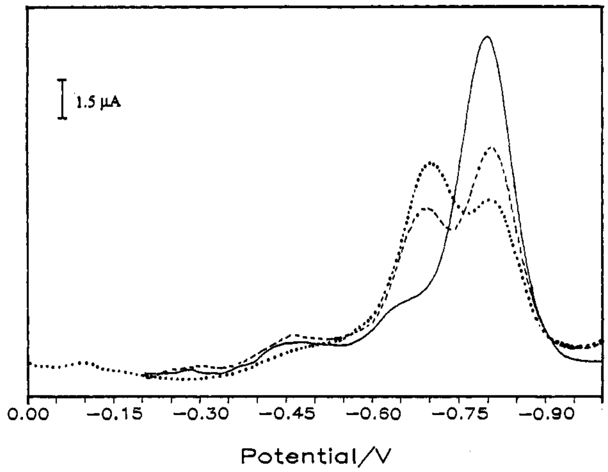

Figure 9. Differential pulse voltammograms of **1** in the absence (solid line) and presence of 1 (dashed line) and 2 (dotted line) equiv of Ag^+. The solution concentration was 1 mM in CH_3CN, 0.10 M $TBAPF_6$ under an argon atmosphere, at room temperature. Thus equivalents of Ag^+ resulted in formation of a single wave at the more positive potential. The scan rate for the voltammograms was 20 mV/s.

Addition of Ag^+ was found to affect the voltammetry of the remaining calixquinones as well, but to a lesser extent. The shift in the $E_{1/2}$ for **2** was less than 30 mV for the first wave, while for **3** and **4** it is the second wave that appears to be affected the most by the presence of Ag^+. Surprisingly, little charge in the voltammetry of **4** is noted, although solutions of this compound undergo the most noticeable visible change in the presence of Ag^+: the solution color changes from yellow to orange.

We should note that the model compound, 2,6-DMQ, did not demonstrate shifts in $E_{1/2}$ of more than 30 mV in the presence of a 10-fold excess of either Na^+ or Ag^+.

Conclusions

The voltammetric studies presented herein support the case for electronic communication in these quinone systems. The present electrochemical study shows that these systems undergo reversible first electron transfers for the quinone units, with the exception of **4**, which undergoes a competing chemical process. Na^+ binding enhancement on the order of 10^6 was noted for **1**, while more modest values were obtained for the other calixquinones. Compound **1** was also found to interact with Ag^+, while the remaining calixquinones did not provide voltammetric evidence of strong interactions. The mode of cation binding probably differs for Na^+ and Ag^+.

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