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Simultaneous Electron Transfer from Free and Intercalated 4-Benzoylpyridinium Cations in Cucurbit[7]uril

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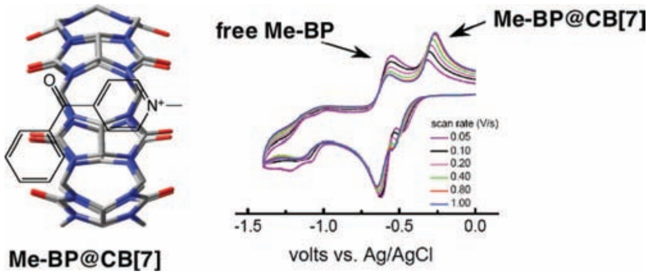
ABSTRACT



N-Substituted 4-benzoylpyridinium monocations form stable host−guest complexes with cucurbit[7]uril (CB[7]) in DMSO ($K_{eq} \approx 0.6-1.9 \times 10^3$ M^{-1}). Observation of simultaneous reversible and quasi-reversible e-transfer processes from the free and intercalated quests, respectively, is attributed to the pre-e-transfer host−guest equilibrium. The standard rate constant for Me-BP@CB[7] ($k_s = 1.0 \times 10^{-4}$ cm·s^{-1}) reflects e-transfer across 5.7 Å, corresponding to the distance of the intercalated guest from the outmost perimeter of CB[7] (5.3 Å).

The redox chemistry of host−guest complexes is studied for its relevance to biological electron transfer (e.g., in redox proteins) and also to applications based on molecular recognition (e.g., sensors).[1] The overwhelming majority of those studies report e-transfer exclusively from the free guests. Very few aberrations from this trend have been reported, e.g., when the guest is locked inside the host (case of hemicacerand/ferrocene)[2] or, when the host−guest equilibrium constant is very large like in the case of methylviologen (**MV**) in cucurbit[*x*]uril (**CB[x]**, $x = 7, 8$), where in both cases heterogeneous e-transfer takes place exclusively from the complex.[1,3] Simultaneous homogeneous e-transfer has been reported from free and **CB[7]**-intercalated (trimethylammonio)methylferrocene,[4] while here we provide evidence that guests based on the 4-benzoylpyridinium cation undergo *heterogeneous* e-transfer simultaneously from both their free state as well as their complexes with **CB[7]**.

CB[7], a water-soluble barrel-shaped host, consists of 7 glycoluril groups and 14 methylene bridges at both ends. The two rims are formed by the glycoluril carbonyl oxygens, thereby are negatively charged, and they develop ion−dipole

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(1) Kim, H.-J.; Jeon, W. S.; Ko, Y. H.; Kim, K. *Proc. Nat. Acad. Sci. U.S.A.* **2002**, *99*, 5007–5011.

(2) Mendoza, S.; Davidov, P. D.; Kaifer, A. E. *Chem.−Eur. J.* **1988**, *4*, 864–870.

(3) Jeon, W. S.; Kim, H.-J.; Lee, C.; Kim, K. *Chem. Commun.* **2002**, 1828–1829.

(4) Yuan, L.; Macartney, D. H. *J. Phys. Chem. B* **2007**, *111*, 6949–6954.

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interactions with cationic guests.[5] Since the portal diameter of **CB[7]** (5.4 Å) is wide enough for **MV** to enter the cavity easily, and also the length of the two species are comparable (9.1 and 7.3 Å, respectively), **MV@CB[7]** maximizes both the hydrophobic and the ion−dipole interactions between the two species resulting in a high complex formation constant ($K_{\mathrm{eq}} = 2 \times 10^5$ M^{-1}).[1]

Monocationic *N*-methyl-4-benzoylpyridinium (**Me-BP**) is similar in length (7.7 Å) to **MV** and intercalates in **CB[7]** from water assuming an *endo*-orientation that places the benzoyl group inside the cavity.[6] Furthermore, in analogy to **MV**, **Me-BP** undergoes two sequential e-transfers.[7] However, unlike viologen, electrochemical studies with **Me-BP** cannot be conducted in water because its 2e reduced form develops hydrogen bonding with the solvent, shifting and merging the second reduction wave with the first, leading directly to the benzyl alcohol via a chemically irreversible 2e reduction process.[7d] Thus, e-transfer studies of the **Me-BP**/**CB[7]** system had to be conducted in organic aprotic media. **CB[7]** is not soluble in organic solvents; however, these studies became possible because the complexation itself increases the solubility of **CB[7]** in DMSO to the 10 mM range, in analogy to what has been observed with heptyl viologen.[8] Nevertheless, the orientation of the **Me-BP@CB[7]** complex in DMSO (*exo*- or *endo*-) is not obvious a priori, and it may have important implications in the electrochemical reduction of the guest; hence, the latter should be considered together with the former. For this, the relative orientation and electrochemistry of **Me-BP@CB[7]** were considered comparatively with two other control systems, **Bz-BP@CB[7]** and **Hex-BP@CB[7]** which, in analogy to corresponding viologens,[8,9] assume *exo*-orientations placing their most hydrophobic groups (benzyl and hexyl) inside the **CB[7]** cavity, leaving their benzoyl groups outside.

Synthesis of the three guests has been described before.[7b,c] **CB[7]** was prepared by modification of a literature procedure (see the Supporting Information).[10] The stoichiometry of the three **CB[7]** complexes is 1:1 (by ESI mass spectrometry in water and by Job's plots in DMSO; see the Supporting Information).[11] The possible orientations of the complexes was investigated with PM3 semiempirical calculations[12] using DFT-optimized structures (6-31G(d) basis set) for all three guests and **CB[7]**. All results (Figure 1) show two local minima very close in energy (e.g., −0.3501 vs −0.3647 au for **Me-BP@CB[7]** and −0.306 vs −0.315 au for **Bz-BP@CB[7]**) corresponding to the *endo*- and *exo*-orientations, respectively).

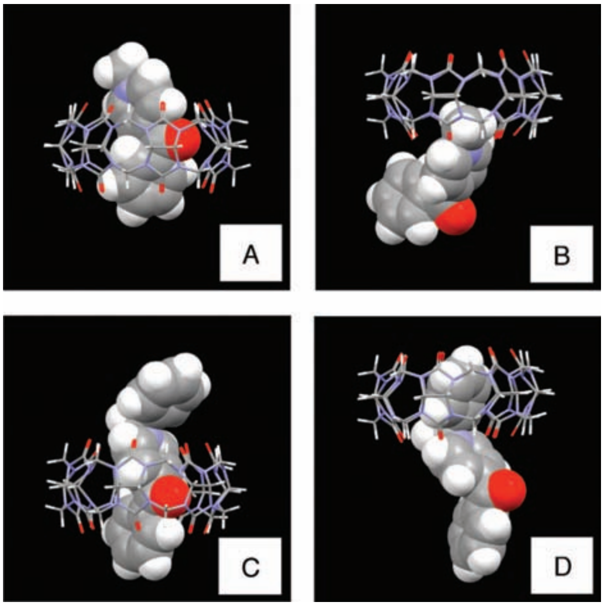
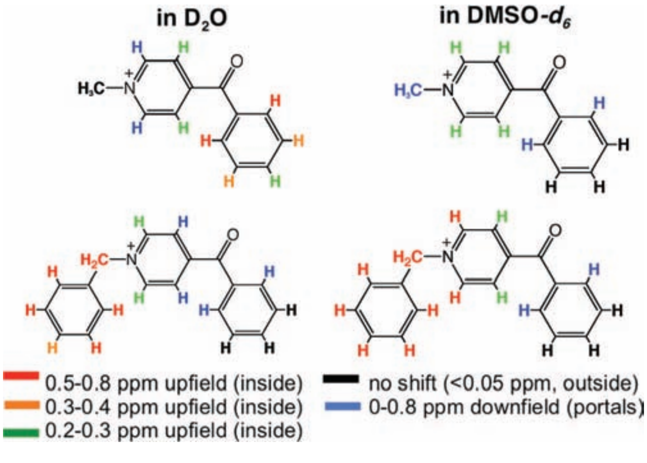


Figure 1. PM3 optimized structures for **Me-BP@CB[7]** (A, B) and **Bz-BP@CB[7]** (C, D) showing two minima: an *endo* (A, C) and an *exo* (B, D).

Scheme 1. Color-Coded ^{1}H-NMR Data for **Me-BP** and **Bz-BP** in the Presence of 1 Molar Equiv of **CB[7]**



The actual orientation in DMSO was investigated by ^{1}H NMR in comparison to water. All chemical shifts have been color-coded and are summarized in Scheme 1. In D_2O, *all* aromatic protons move upfield in the presence of **CB[7]** (compare parts A−D of Figure 2), consistent with the *endo*-orientation where the entire benzoylpyridinium system is inside the cavity (Figure 1A).[13] In DMSO-d_6 some protons move upfield, some downfield, while others hardly move (Scheme 1), consistent with an intermediate state between *endo*- and *exo*- (compare Scheme 1 with parts A and B of

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(5) Lee, J. W.; Samal, S.; Selvapalam, N.; Kim, H.-J.; Kim, K. *Acc. Chem. Res.* **2003**, *36*, 621–630.

(6) Rawashdeh, A.-M. M.; Thangavel, A.; Sotiriou-Leventis, C.; Leventis, N. *Org. Lett.* **2008**, *10*, 1131–1134.

(7) (a) Leventis, N.; Yang, J.; Fabrizio, E. F.; Rawashdeh, A.-M. M.; Oh, W. S.; Sotiriou-Leventis, C. *J. Am. Chem. Soc.* **2004**, *126*, 4094–4095. (b) Leventis, N.; Meador, M. A. B.; Zhang, G.; Dass, A.; Sotiriou-Leventis, C. *J. Phys. Chem. B* **2004**, *108*, 11228–11235. (c) Leventis, N.; Rawaswdeh, A.-M. M.; Zhang, G.; Elder, I. A.; Sotiriou-Leventis, C. *J. Org. Chem.* **2002**, *67*, 7501–7510. (d) Leventis, N.; Elder, I. A.; Gao, X.; Bohannan, E. W.; Sotiriou-Leventis, C.; Rawashdeh, A.-M. M.; Overschmidt, T. J.; Gaston, K. R. *J. Phys. Chem. B* **2001**, *105*, 3663–3674. (e) Leventis, N.; Gao, X. *J. Electroanal. Chem.* **2001**, *500*, 78–94.

(8) Moon, K.; Kaifer, A. E. *Org. Lett.* **2004**, *6*, 185–188.

(9) Sindelar, V.; Moon, K.; Kaifer, A. E. *Org. Lett.* **2004**, *6*, 2665–2668.

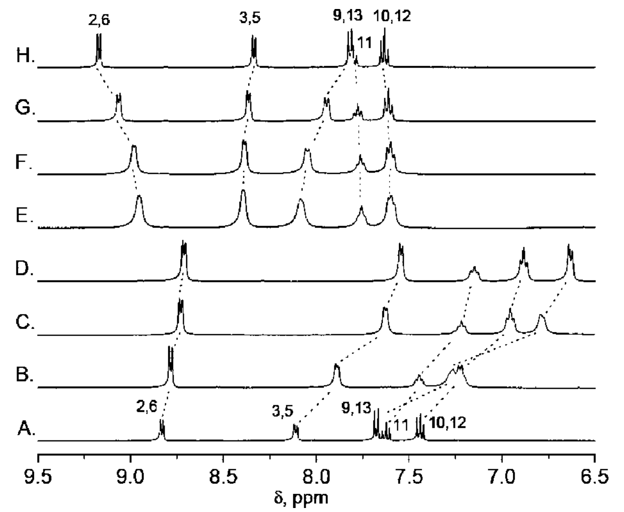

Figure 2. ^{1}H NMR at 23 °C of the aromatic protons of **Me-BP** in D_2O (A−D; 21.1 mM) and DMSO-d_6 (E−H; 9.1 mM). A,H: no **CB[7]**. B, G: 0.5 molar equiv of **CB[7]**. C, F: 1.0 molar equiv of **CB[7]**. D, E: 1.25 molar equiv of **CB[7]**.

Figure 1). In both solvents, the evolution of the chemical shifts from 0 to 1.25 molar equiv of **CB[7]** is consistent with fast exchange of **Me-BP** between its free and complexed states. The line-broadening observed in DMSO-d_6, taken together with the position of **Me-BP** in the cavity might originate from the equilibrium between the *endo*- and *exo*-forms. The more effective retreat of **Me-BP** inside **CB[7]** in water is attributed exclusively to the solvent polarity.[8]

By ^{1}H NMR again, the mode of intercalation of **Hex-BP** and **Bz-BP** with **CB[7]** is the same in both water and DMSO, and analogous to the interaction of **Me-BP** with **CB[7]** in DMSO in the sense that some protons move strongly upfield, some downfield and some protons hardly move at all. Figure 3 demonstrates those patterns for **Bz-BP** and the results have been color-coded in Scheme 1. (Results for **Hex-BP** are given in the Supporting Information). Clearly **Bz-BP@CB[7]** assumes the *exo*-orientation (compare parts C and D of Figures 1 and Scheme 1), signifying the importance of placing the most hydrophobic group inside the cavity.

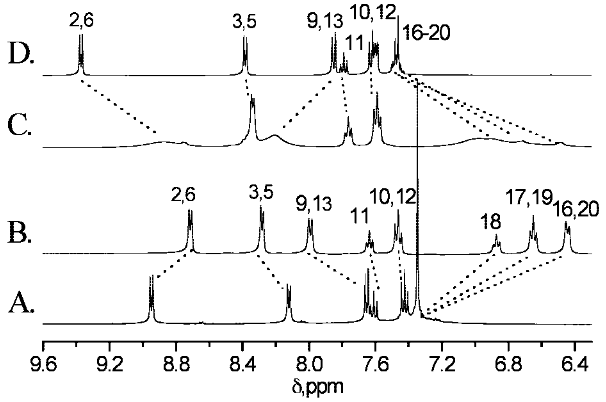

Figure 3. ^{1}H NMR at 23 °C of the aromatic region of **Bz-BP**. A, D: no **CB[7]**, in D_2O (9.4 mM) and DMSO-d_6 (18.8 mM), respectively. B, C: plus 1.0 molar equiv of **CB[7]** in D_2O and DMSO-d_6, respectively.

All equilibrium constants, K_{eq}, of the guest−host complex formation reactions were determined from spectrophotometric titration data (e.g., Figure 4 for **Me-BP**) using the Benesi−Hildebrand double-reciprocal method (see the inset in Figure 4; K_{eq} = slope/intercept), and the results are summarized in Table 1.[14]

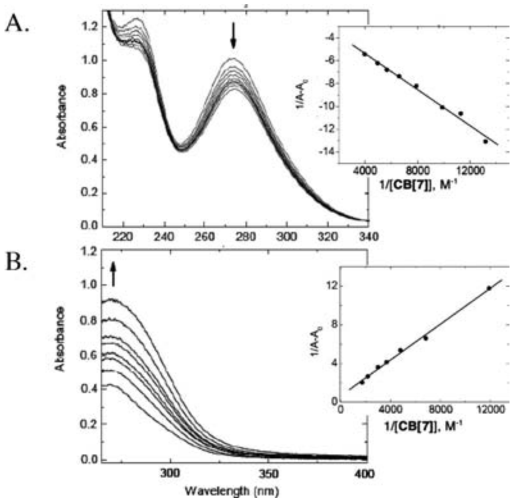

Figure 4. Titration at 23 °C of **Me-BP** with **CB[7]** in H_2O/0.1 M KCl (A, [**Me-BP**] = 1.01×10^{-4} M, λ_{max} = 274 nm) and in DMSO/0.1 M $NaClO_4$ (B, [**Me-BP**] = 2.03×10^{-4} M, λ_{max} = 270 nm). (Insets: double-reciprocal plots for the determination of K_{eq}.[13] [**CB[7]**] refers to free **CB[7]**. **CB[7]** does not absorb at the two λ_{max} (see the Job's plot data in the Supporting Information), so no correction was applied.

Table 1. Equilibrium Constants (K_{eq}) of the Host−guest Complex Formation in Water and DMSO at 23 °C[a]

	K_{eq}	(M^{-1})
guest	in water	in DMSO
Me-BP	$(3.1 \pm 0.3) \times 10^{3}$[b]	$(0.59 \pm 0.13) \times 10^{3}$
Hex-BP	$(9.1 \pm 0.1) \times 10^{3}$	$(1.3 \pm 0.5) \times 10^{3}$
Bz-BP	$(3.4 \pm 0.1) \times 10^{3}$	$(1.9 \pm 0.0_4) \times 10^{3}$

[a] Experiments conducted twice; errors are spreads. [b] Value reported before ($(6.2 \pm 2.1) \times 10^3$ M^{-1}) was obtained through nonlinear fit of titration results at low **CB[7]** concentrations.[5]

Qualitatively, the evolution of the absorption spectra by adding **CB[7]** supports the modes of inclusion identified by ^{1}H NMR. For **Me-BP**, for example, the different mode of inclusion in the two solvents causes an absorbance decrease in water (Figure 4A) and an increase in DMSO (Figure 4B), matching the relative polarity of the environment around the benzoyl chromophore: in water (*endo*-orientation) the chromophore is inside the hydrophobic cavity, while in DMSO it also interacts with the portal carbonyl dipoles. Since in both solvents **Bz-BP@CB[7]** and **Hex-BP@CB[7]** are *exo*-oriented, the benzoyl groups are near the portal dipoles and the absorbance increases by adding **CB[7]** (see Supporting Information). Overall, K_{eq} values are higher in water than in DMSO. **Hex-BP**, with the longest hydrophobic group, has the highest tendency to avoid water, while in less polar DMSO its K_{eq} is similar to that of **Bz-BP**.

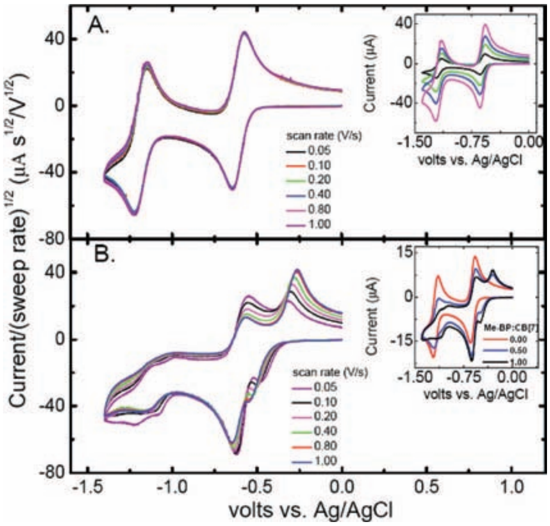

Figure 5. Normalized voltammetry of **Me-BP** (3.2 mM) in Ar-degassed DMSO/0.1 M $NaClO_4$ using a Au-disk (0.0201 cm^2) working electrode. (A) No **CB[7]**. Inset: raw data. (B) After addition of 1 molar equiv of **CB[7]**. Inset: voltammetry by adding **CB[7]** (raw data).

The redox chemistry of the three host−guest complexes was studied by cyclic voltammetry in DMSO/0.1 M $NaClO_4$. All free guests show two chemically reversible 1e reductions ($i_{p,c} \approx i_{p,a}$) of the pyridinium and the benzoyl group, respectively.[7] Data for **Me-BP** are shown in Figure 5; for **Bz-BP** and **Hex-BP**, see the Supporting Information. In the absence of **CB[7]**, voltammograms normalized by dividing the faradaic current by the square root of the sweep rate coincide (Figure 5A), showing fast interfacial e-transfer kinetics (electrochemical reversibility). Upon addition of **CB[7]**, we note two new waves (in addition to the old ones) at more positive potentials relative to those of free **Me-BP** (Figure 5B). Normalized voltammograms no longer coincide, implying quasi-reversible (slow) interfacial e-transfer. The positive shift of the first new wave is consistent with complexation that stabilizes the LUMO of the free guest;[15] based on $nF\Delta E^o = RT \ln K_{eq}$ and $\Delta E_{1/2} \approx \Delta E^o$, the wave of **Me-BP@CB[7]** should be 0.162 V more positive than the wave of free **Me-BP**, in agreement with the experiment (0.201 V). Based on $K_{eq} = 590$ M^{-1} (Table 1), an equimolar solution (3.2 mM) of **Me-BP** and **CB[7]** contains 1.6 mM of each free guest and **Me-BP@CB[7]**, in agreement with the relative sizes of the voltammetric waves (taking into consideration the significantly lower diffusion coefficient expected for **Me-BP@CB[7]**). The peak-to-peak separation ($\Delta E_{p\text{-}p}$) of the wave assigned to **Me-BP@CB[7]** increases with the sweep rate (as expected from a quasi-reversible e-transfer). **Bz-BP@CB[7]** and **Hex-BP@CB[7]** behave similarly (see the Supporting Information), supporting the theory that the rate of e-transfer is low irrespective of the guest position in the cavity. $\Delta E_{p\text{-}p}$ in the case of **Me-BP@CB[7]** is measured easily, and it was analyzed according to Kochi's method (see the Supporting Information),[16] yielding a standard rate constant $k_s = 1.0 \times 10^{-4}$ cm s^{-1} (comparable to the one reported for **MV**).[1] With a reversibility limit for k_s at about 0.03 cm s^{-1} (this value yields $\Delta E_{p\text{-}p} = 65$ mV at 0.1 V s^{-1} for $D = 10^{-5}$ cm^2•s^{-1}) and a distance attenuation factor for long-range electron transfer of 10 nm^{-1},[17] it is calculated that in **Me-BP@CB[7]** e-transfer takes place from a distance of 5.7 Å, which is about equal to the vertical distance (5.3 Å) between the edge of the rim and the outer perimeter of **CB[7]**. Spectroelectrochemically (see the Supporting Information), the neutral 1e reduced form of **Me-BP** (**Me-BP$^\bullet$**) remains intercalated in **CB[7]**, and from the positive shift (~0.12 V) of its reduction wave from the second wave of free **Me-BP** it is calculated that its formation equilibrium constant from free **Me-BP$^\bullet$** and **CB[7]** is ≈110 M^{-1}.

Clearly, the ability to observe electrochemically both of the free and the complexed guest in the **Me-BP**/**CB[7]** systems is determined by the pre-e-transfer K_{eq}.[18] In the **MV**/**CB[7]** system, where $K_{eq} = 2 \times 10^5$ M^{-1}, the equilibrium concentration of free **MV** is very small, and consequently, it is not observed electrochemically.[1] These results have definite implications in the design of molecular devices, while the aptitude of the most hydrophobic groups for the cavity is further explored for supramolecular protection in fundamental organic reactions such as the Hoffmann elimination and the Sandmeyer reaction.

Acknowledgment. We thank the University of Missouri Research Board for financial support.

Supporting Information Available: Preparation of **CB[7]**; ESI mass spectra and Job's plot data; additional ^{1}H NMR, absorption, and electrochemical data for all three complexes; e-transfer kinetic data analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) Halterman, R. L.; Moore, J. L.; Mannel, L. M. *J. Org. Chem.* **2008**, *73* (8), 3266–3269.

(11) Cartwright, H. M. *Microchem. J.* **1986**, *34*, 313–318.

(12) (a) Marques, C.; Hudgins, R. R.; Nau, M. W. *J. Am. Chem. Soc.* **2004**, *126*, 5806–5816. (b) Buschmann, H.-J.; Wego, A.; Zielesny, A.; Schollmeyer, E. *J. Inclusion Phenom. Macrocycl. Chem.* **2006**, *54*, 85–88.

(13) Choi, S.; Park, H. S.; Ziganishina, A. Y.; Ko, Y. H.; Lee, J. W.; Kim, K. *Chem. Commun.* **2003**, 2176–2177.

(14) Connors, K. A. *Binding Constants, The Measurement of Molecular Complex Stability*; John Wiley and Sons, Inc.: New York, 1987.

(15) It is noted that since the absorbance λ_{max} does not change, both the HOMO and the LUMO of **Me-BP** are stabilized by the same energy.

(16) Klingler, R. J.; Kochi, J. K. *J. Phys. Chem.* **1981**, *85*, 1731–1541.

(17) Amatore, C.; Bouret, Y.; Maisinhaute, E.; Abruña, H. D.; Goldsmith, J. I. C. R. *Chimie* **2003**, *6*, 99–115.

(18) Bard, A. J.; Faulkner, L. J. *Electrochemical Methods, Fundamentals and Applications*, 2nd ed.; Wiley: New York, 2000.