Synthesis and Electrochemical Complexation Studies of 1,8-Bis(azacrown ether)anthraquinones

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Received February 2, 1994®

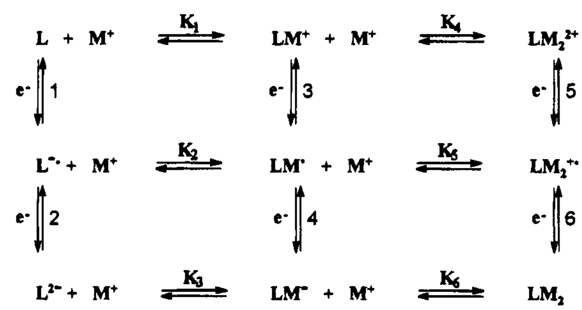
Treatment of 1,8-difluoroanthraquinone with aza-12-crown-4 and aza-15-crown-5 in DMF at 50 °C affords the disubstituted anthraquinones **6** and **7** in good yields. A similar methodology has been used to prepare the lipophilic diaza-12-crown-4 anthraquinone systems **12−14**. Compounds **6** and **7** exhibit enhanced sodium and lithium binding upon electrochemical reduction to the corresponding mono- and dianions. Both **6** and **7** form 1:1 complexes with Na^+. However, with the smaller Li^+ cation, both compounds form 1:2 ligand:Li^+ complexes. Cation binding enhancements for Li^+ and Na^+ are very large with K_2/K_1 values as high as 10^5.

Introduction

Electrochemical switching with redox-active groups such as anthraquinone-substituted ligands is of great interest to the electrochemist. This is because these systems have the unique capability of enhancing cation binding and transport across membranes.[1−3] These enhancements result from the direct coupling of the redox processes of the quinones with the cation binding equilibria.[2,3] Scheme 1 is a representation of these multiple equilibria. Several electrochemical processes can be seen in this scheme. Processes 1 and 2 represent the reduction of the free ligand while 3 and 4 represent the reduction of the ligand−cation complex. These processes are coupled to the cation binding equilibria of the ligand. K_1 and K_2 represent the equilibria for the neutral complex and the anion radical, respectively, while K_3 represents that for the dianion. Typical values $<10^3$ [2,3] have been obtained for binding enhancements K_2/K_1 and K_3/K_2.

The lack of convenient and effective synthetic methods for the preparation of the required substituted anthraquinones has been a major drawback in these studies. Access to 1,8-disubstituted anthraquinone derivatives, especially with alkoxy or bulky amino substituents is not a trivial matter.[1,4] Gokel *et al.* have demonstrated that direct nucleophilic aromatic substitution of 1-chloroanthraquinone derivatives is successful with oligoethyleneoxy and alkynyl nucleophiles although alkanols fail in this approach.[4−6] Recently we have reported a highly efficient double nucleophilic displacement of fluoride atoms in 1,8-difluroranthraquinone (**1**) by alkoxides derived from alkanols and lariat ether macrocycles to afford 1,8-dialkoxyanthraquinones.[1] Addition of amino side chains to anthraquinones has often involved displacements of chlorine by amines.[7] This method is ineffective when a monoazacrown ether is used as the amine.[4] On the other hand, substitution of nitro groups[8] and fluoride[7,9] is effective for simple amines. In this paper we describe the synthesis of several new lipophilic diaza-12-crown-4 anthraquinone systems and related compounds starting from fluoroanthraquinones. Complexation studies of the anions and dianions of **6** and **7** with some alkali metal cations using cyclic voltammery is also reported.

Scheme 1



Results and Discussion

1,8-Dimorpholino- and 1-morpholinoanthraquinones (**5** and **8**) were prepared in almost quantitative yield by the reaction of an excess of morpholine with the correspond-

® Abstract published in *Advance ACS Abstracts*, June 15, 1994.

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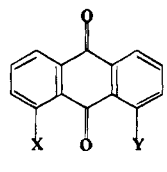
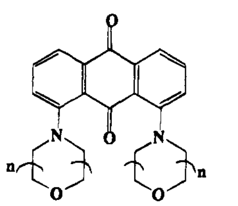
0022-3263/94/1959-3814$04.50/0

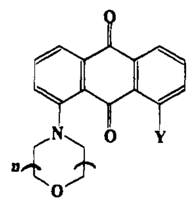
ing fluoroanthraquinones **1** and **3**[1] in the absence of solvent. Previously,[4] compounds **5** and **8** had been prepared in low yields (34% and 30%, respectively) starting from the corresponding chloroanthraquinones **2** and **4** in acetonitrile in the presence of potassium carbonate. On the other hand, we have reacted 3 equiv of aza-12-crown-4 and aza-15-crown-5 with 1,8-difluoroanthraquinone (**1**) in DMF at 50 °C to afford the disubstituted anthraquinones **6** and **7** in 82% and 60% yields, respectively. In both cases monosubstituted anthraquinones **9** and **10** were isolated by chromatography as minor products (5% and 25%). Compound **7** has previously been prepared by Gokel *et al.* from 1,8-dichloroanthraquinone (**2**) in 7% yield using a mixture of benzene–diethyl ether as solvent and *n*-butyllithium as base. In this reaction the monosubstituted derivative **11** was also obtained in 19% yield.[4] A similar methodology



1 X = Y = F
2 X = Y = Cl
3 X = F Y = H
4 X = Cl Y = H

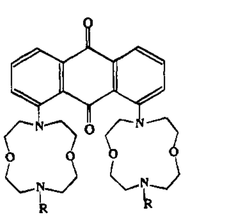


5 n = 1
6 n = 3
7 n = 4

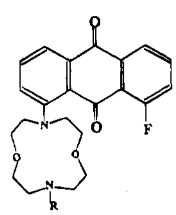


8 Y = H n = 1
9 Y = F n = 3
10 Y = F n = 4
11 Y = Cl n = 4

has been used to prepare the new lipophilic diaza-12-crown-4 anthraquinone systems **12–14**. Thus the reaction of 1,8-difluoroanthraquinone (**1**) with the corresponding monosubstituted aza-12-crown-4 **22–24** in DMF affords anthraquinones **12–14** in 48%, 53%, and 56% yields, respectively. In all three cases, the corresponding monosubstituted compounds **15–17** were also obtained in lower yields (25%, 16% and 18%, respectively).



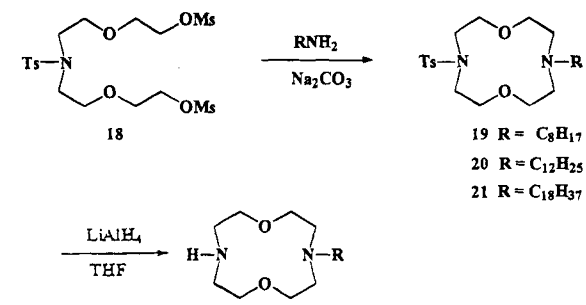
12 R = C_8H_{17}
13 R = $C_{12}H_{25}$
14 R = $C_{18}H_{37}$



15 R = C_8H_{17}
16 R = $C_{12}H_{25}$
17 R = $C_{18}H_{37}$

The *N*-alkyl diaza-12-crown-4 systems **22–24** were prepared according to the method depicted in Scheme 2. Treatment of *p*-toluenesulfonamide with 2-(2-chloroethoxy)ethanol in basic media affords the corresponding dialkylated derivative, which is dimesylated *in situ* to give **18**.[10] Compound **18** is reacted with the corresponding long-chain alkylamine in acetonitrile in the presence

Scheme 2



18; 19 R = C_8H_{17}; 20 R = $C_{12}H_{25}$; 21 R = $C_{18}H_{37}$; 22 R = C_8H_{17}; 23 R = $C_{12}H_{25}$; 24 R = $C_{18}H_{37}$

of anhydrous sodium carbonate to yield **19–21**, which are detosylated with lithium aluminum hydride[11] to yield **22–24**.

The electrochemical behavior of compounds **6** and **7** is somewhat similar to that of other previously studied substituted anthraquinones.[2,3] The voltammograms for **6** and **7** in acetonitrile are shown in Figures 1 and 2 as a function of added Na^+. In the absence of any added cation, the voltammograms exhibited the usual quasi-reversible waves corresponding to the one- and two-electron-transfer processes resulting in the formation of the dianionic anthraquinone, processes 1 and 2 in Scheme 1. Addition of 0.5 equiv of Na^+ to both **6** and **7** results in the appearance of a new redox couple corresponding to process 3. In addition to process 3, process 4 is also observed for **6**. As the concentration of the cation is increased, beyond 2.0 equiv, the voltammograms of **6** show waves corresponding exclusively to processes 3 and 4 while those of **7** show waves corresponding to processes 3 and 2. Figures 3 and 4 show the voltammograms of **6** and **7** as a function of added $LiClO_4$. As expected, before the addition of the Li^+ salt, only two quasi-reversible redox pairs are observed in each case. Upon addition of 0.5 equiv of Li^+, two additional redox couples are observed simultaneously. These correspond to processes 3 and 4 in Scheme 1. As the concentration of Li^+ is increased, a new redox couple (at 1.06 V for **6** and at 1.10 V for **7**) corresponding to process 5 can be seen, which corresponds to the redox process for the 1:2 complex. This is an interesting observation which was not seen with the larger Na^+ cation. Precedent for this type of behavior has been previously found for anthraquinone–podand systems using ESR spectroscopy.[12] It was found that the two equivalent Li^+ ions interacted with the corresponding anthraquinone ligand anion radical. This work led to postulation that the two pendant arms of the anthraquinone moiety each enveloped a Li^+ cation, which were coordinated to one of the anthraquinone carbonyls. After this structure was postulated, additional evidence for such 1:2 complexation with Li^+ was found during ESR and electrochemical studies of an anthraquinone cryptand.[13] Interestingly, the latter molecule posseses a

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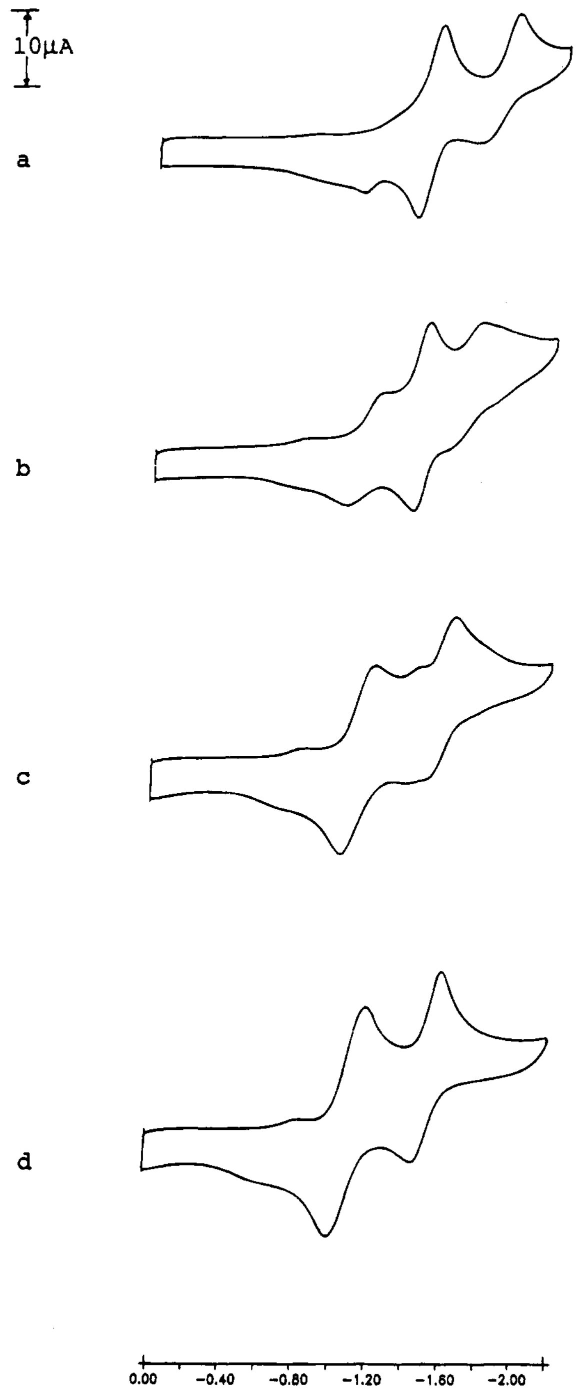

Figure 1. Cyclic voltammograms of **6** in acetonitrile as a function of added Na^+: (a) no added Na^+; (b) 0.5 equiv of Na^+ added per equiv of **6**; (c) 1.5 equiv of Na^+ added; and (d) 3.0 equiv of Na^+ added. Scan rate is 0.1 V/s.

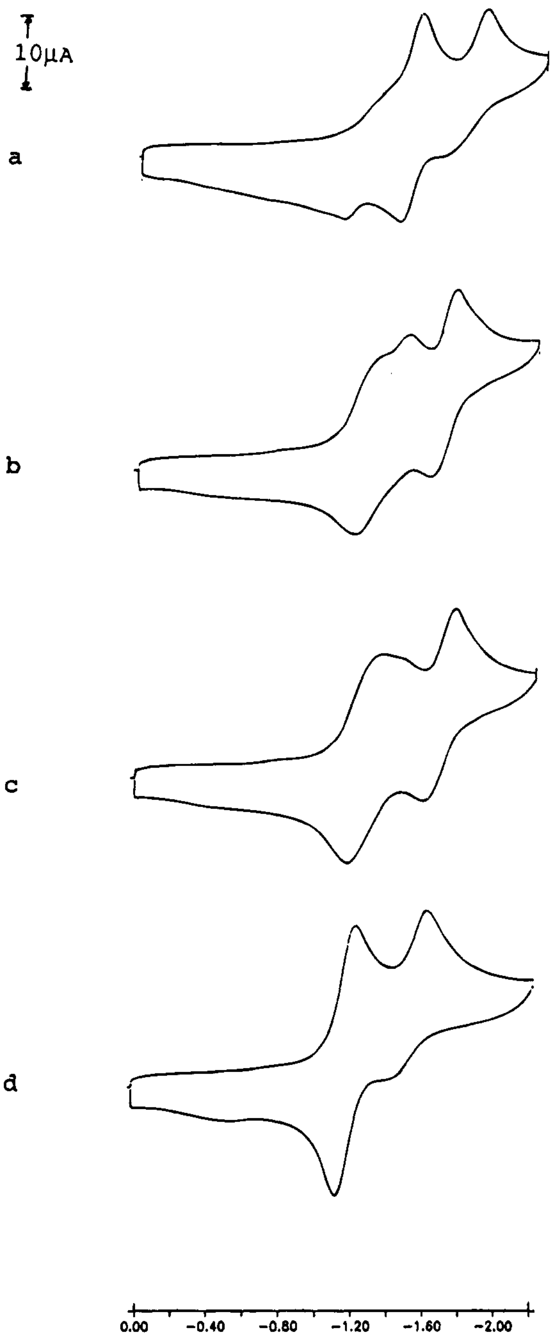

Figure 2. Cyclic voltammograms of **7** in acetonitrile as a function of added Na^+: (a) no added Na^+; (b) 1.0 equiv of Na^+ added; (c) 1.5 equiv of Na^+ added; and (d) 3.0 equiv of Na^+ added. Scan rate is 0.1 V/s.

structural motif which is very similar to that postulated for the podand−Li^+ complex. In the cryptand, the poly(ethyleneoxy) chains are covalently linked at both ends to the anthraquinone. In the podand, only one end of the chain is connected covalently to the anthraquinone moiety. Due to the small size of Li^+, it is able to form a 1:2 complex with both **6** and **7**. The distortion of the cathodic waves at low potentials in the voltammograms of **6** and **7** in the absence of added metal cations is probably due to binding of the neutral ligands with residual Na^+ present in laboratory glassware. The well-resolved anodic waves at low potentials in the voltammograms of **6** and **7** in the absence of cations is probably due to some decomposition of the dianions.

Procedures for the determination of the apparent ratios K_2/K_1, K_3/K_2, and K_5/K_4 have been reported elsewhere.[2] These values represent cation binding enhancements due to electrochemical switching of the ligand to more negatively charged states. The electrochemical results and the cation binding enhancements are shown in Tables 1−4. The above-described results show the convenience of using flourine as a leaving group in the double nucleophilic aromatic substitution reaction by bulky substituted azacrowns in 1,8-anthraquinone derivatives. The K_2/K_1 values obtained for these systems are significantly high. For instance, the Na^+ and Li^+ binding

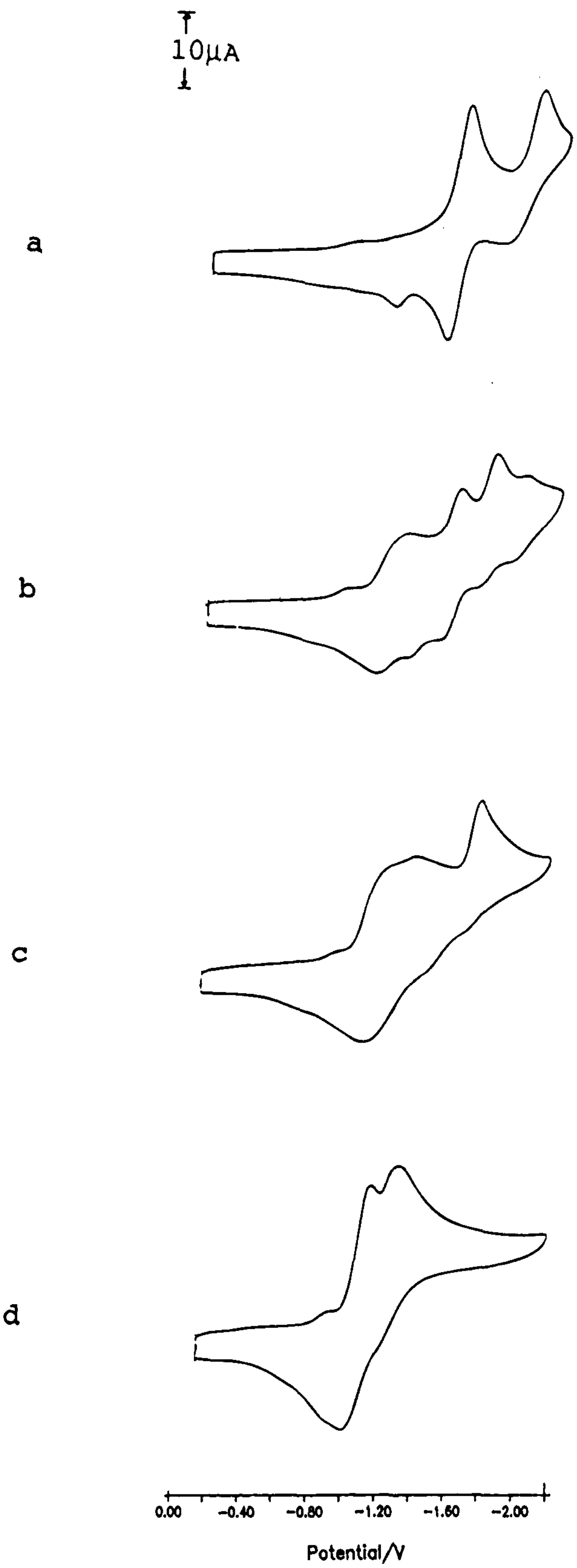

Figure 3. Cyclic voltammograms of **6** in acetonitrile as a function of added Li^+: (a) no added Li^+; (b) 0.5 equiv of Li^+ added per equiv of **6**; (c) 1.0 equiv of Li^+ added; and (d) 2.0 equiv of Li^+ added. Scan rate is 0.1 V/s.

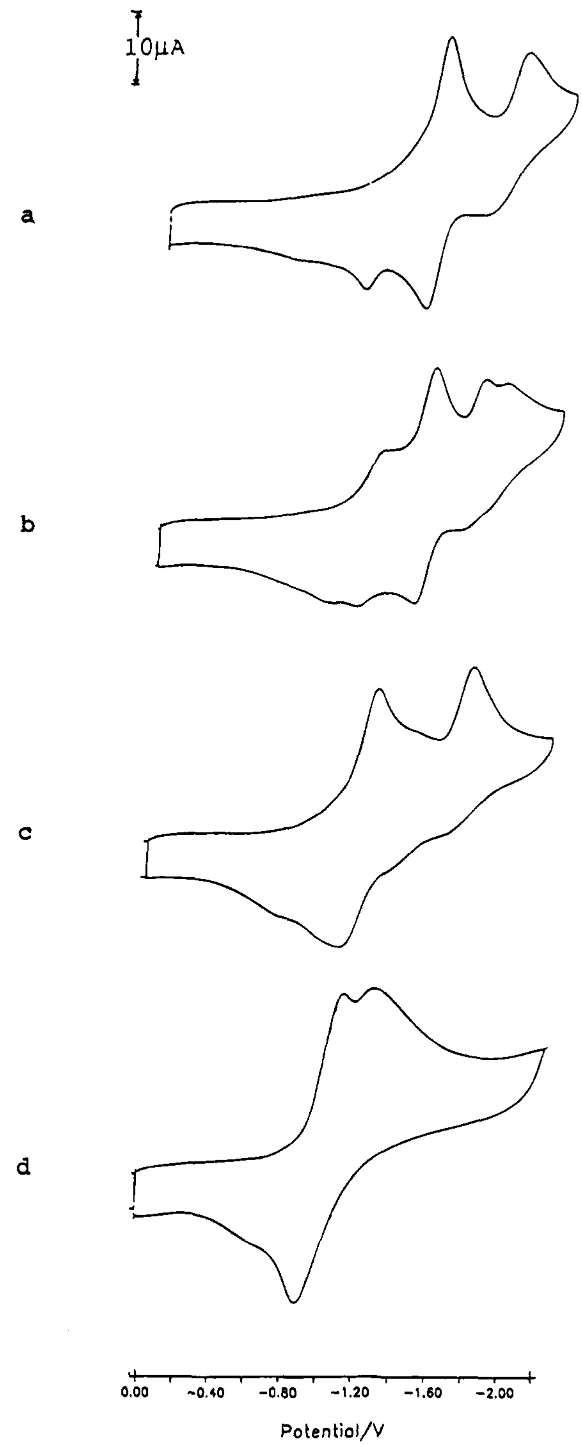

Figure 4. Cyclic voltammograms of **7** in acetonitrile as a function of added Li^+: (a) no added Li^+; (b) 0.5 equiv of Li^+ added per equiv of **7**; (c) 1.5 equiv of added Li^+; and (d) 3.0 equiv of Li^+ added. Scan rate is 0.1 V/s.

enhancements for **6** are 1.05×10^5 and 2.19×10^5, respectively, while **7** exhibits corresponding values of 1.32×10^6 and 1.89×10^4 for Li^+ and Na^+ binding enhancements. Variable scan rates between 100 and 1000 mV/s were analyzed. No shifts in peak potential positions were observed, implying electrochemical reversibility in all cases. The preparation of other lipophilic azacrown ether anthraquinone systems and their electrochemical studies is in progress. If the new lipophilic systems exhibit similar binding enhancements, they could be very useful for cation pumping across lipophilic environments using a redox gradient. The electrochemical results for one of the highly lipophilic derivatives, **14**, proved to be chemically and electrochemically irreversible. This is probably

Table 1. Electrochemical Results for 6 in the Presence of Different Cations

cation	equiv	E_c^1	E_a^1	E_c^2	E_a^2	E_c^3	E_a^3	E_c^4	E_a^4	E_c^5	E_a^5
Li^+	0	−1.498	−1.424	−1.929	−1.758						
	0.5	−1.490	−1.416	−1.888	−1.840			−1.693	−1.612		
	1.0							−1.677	−1.595		
	1.5					−1.286	−1.190			−1.058	−0.920
	2.0					−1.197	−1.131			−1.042	−0.895
Na^+	0	−1.483	−1.431	−1.910	−1.754						
	0.5					−1.226	−1.042	−1.776	−1.615		
	1.0	−1.483	−1.410			−1.218	−1.072	−1.703	−1.556		
	1.5	−1.439	−1.402			−1.211	−1.064	−1.644	−1.519		
	2.0					−1.204	−1.057	−1.615	−1.498		
	2.5					−1.196	−1.050	−1.600	−1.490		
	3.0					−1.174	−1.042	−1.578	−1.483		

Table 2. Electrochemical Results for 7 in the Presence of Different Cations

cation	equiv	E_c^1	E_a^1	E_c^2	E_a^2	E_c^3	E_a^3	E_c^4	E_a^4	E_c^5	E_a^5
Li^+	0	−1.493	−1.434	−1.917	−1.756						
	0.5	−1.485	−1.420	−1.873	−1.815	−1.230	−0.951	−1.756	−1.683		
	1.0	−1.485	−1.420	−1.866	−1.844	−1.229	−0.907	−1.734	−1.654		
	1.5	−1.449	−1.405			−1.229	−1.100	−1.734	−1.654		
	2.0					−1.222	−1.140	−1.800	−1.726	−1.100	−0.980
	2.5									−1.127	−0.966
	3.0									−1.100	−0.922
Na^+	0	−1.493	−1.434	−1.851	−1.668						
	0.5	−1.493	−1.398	−1.749	−1.632	−1.244	−1.141				
	1.0			−1.734	−1.610	−1.302	−1.185				
	1.5			−1.727	−1.580	−1.324	−1.171				
	2.0			−1.727	−1.588	−1.324	−1.171				
	2.5			−1.602	−1.427	−1.215	−1.127				
	3.0			−1.589	−1.434	−1.207	−1.127				

Table 3. Cation Binding Enhancements Resulting from Electrochemical Reductions of 6

cation	K_2/K_1	K_3/K_2	K_5/K_4
Li^+	1.05×10^5	3.690×10^3	1.980×10^3
Na^+	2.194×10^5	1.990×10^2	

Table 4. Cation Binding Enhancements Resulting from Electrochemical Reductions of 7

cation	K_2/K_1	K_3/K_2	K_5/K_4
Li^+	1.315×10^6	1.250×10^2	2.420×10^2
Na^+	1.890×10^4		

due to slow diffusion and/or deposition on the electrode surface.

Experimental Section

Electrochemical experiments were performed using a Bioanalytical Systems 100B analyzer equipped with IR compensation and recorded on a Hewlett-Packard Color Pro plotter. The working electrode was glassy carbon and the counter electrode a platinum wire. The reference electrode consisted of a silver wire immersed in a 0.1 M tetra-*n*-butylammonium hexafluorophosphate solution containing 5 mM $AgNO_3$ in acetonitrile.

All experiments were run at room temperature under a dry argon atmosphere with the electroactive species present in ~1 mM concentrations. The cation-containing salt was added in half-equivalent increments of the perchlorate and tetraphenylborate salts. Na^+ was added as the tetraphenylborate salt while Li^+ was added as the corresponding perchlorate salt. After each successive addition, the voltammograms were recorded at a scan rate of 100 mV/S. Melting point measurements are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Bruker WP 200 SY instrument. Mass spectra were recorded on VG Autospec and Varian MAT 312 spectrometers and IR spectra on a Perkin-Elmer 257. Aldrich neutral alumina, Brockmann I, 150 mesh, was used for chromatographic purifications. Except in the cases indicated, solvents were purified and dried by standard procedures. Reagents (Aldrich) were used as received without further purification. Tetrabutylammonium hexafluorophosphate (Fluka) was recrystallized twice from ethyl alcohol and dried in a vacuum oven at 100 °C for 15 h. Sodium tetraphenylborate (Aldrich) was used without further purification. MeCN (Aldrich) was dried over CaH_2 for 36 h and distilled under dry nitrogen gas prior to use.

1,8-Bis(1′-aza-4′,7′,10′-trioxacyclododecan-1′-yl)-9,10-anthraquinone (6). A mixture of 1,8-difluoroanthraquinone (**1**) (60 mg, 0.25 mmol) and monoaza-12-crown-4 (0.26 g, 1.5 mmol) in dry DMF (3 mL) under argon was stirred and heated at 50 °C for 48 h. After the solution was cooled to room temperature, the solvent was removed and the residue was chromatographed on alumina using a mixture of ethyl acetate−dichloromethane (5:1) as eluent. The first eluted minor component was identified as the monosubstituted derivative 1-(1′-aza-4′,7′,10′-trioxacyclododecan-1′-yl)-8-fluoro-9,10-anthraquinone (**9**): yield 5%; dark-red crystals, mp 137−139 °C (ethyl acetate−hexane); ^1H NMR ($CDCl_3$) δ 8.15 (dd, 2H, H-4, H-5), 7.73 (t, 1H, H-3), 7.6 (ddd, 2H, H-6), 7.52 (dd, 1H, H-2), 7.48 (ddd, 1H, H-7), 3.8 (t, 4H, H-6′, H-8′), 3.7 (t, 8H, H-3′, H-5′, H-9′, H-11′), 3.50 (t, 4H, H-2′, H-12′); MS-EI (high resolution) *m/z* calcd for $C_{22}H_{22}FNO_5$ 399.1482 (M^+), found 399.1473. The second eluted compound was identified as **6**: yield 82%; red crystals, mp 115−117 °C (ethyl acetate−hexane); ^1H NMR ($CDCl_3$) δ 7.82 (dd, 2H, H-4, H-5), 7.65 (dd, 2H, H-2, H-7), 7.51 (t, 2H, H-3, H-6), 3.8 (t, 8H, H-6′, H-8′), 3.6 (m, 16H, H-3′, H-5′, H-9′, H-11′), 3.51 (t, 8H, H-2′, H-12′); MS-EI *m/z* (relative intensity) 554 (M^+, 100), 408 (10), 263-(12). Anal. Calcd for $C_{30}H_{38}N_2O_8$: C, 64.97; H, 6.91; N, 5.05. Found: C, 64.86; H, 6.88; N, 5.30.

1,8-Bis-(1′-aza-4′,7′,10′,13′-tetraoxacyclopentadecan-1′-yl)-9,10-anthraquinone (7). Following the same procedure described above for the preparation of **6**, from **1** (0.25 mmol) and monoaza-15-crown-5 (1.5 mmol) a mixture of compounds **7** and **10** was obtained. **7**: yield 60%; viscous red oil; ^1H NMR ($CDCl_3$) δ 7.79 (dd, 2H, H-4, H-5), 7.59 (dd, 2H, H-2, H-7), 7.51 (dd, 2H, H-3, H-6), 3.7 (t, 32H, CH_2O), 3.6 (t, 8H, CH_2N); MS-EI *m/z* (relative intensity) 642 (M^+, 100), 452 (12), 263(14). Anal. Calcd for $C_{34}H_{46}N_2O_{10}$: C, 63.54; H, 7.21; N, 4.36. Found: C, 63.60; H, 7.36; N, 4.21. 1-(1′-Aza-4′,7′,10′,13′-tetraoxacyclopentadecan-1′-yl)-8-fluoro-9,10-anthraquinone (**10**): yield 25%; purple crystals, mp 103−104 °C (ethyl acetate−hexane); ^1H NMR ($CDCl_3$) δ 8.2 (dd, 2H, H-4, H-5), 7.72 (t, 1H, H-3), 7.6 (ddd, 2H, H-6), 7.57 (dd, 1H, H-2), 7.49 (ddd, 1H, H-7), 3.67 (br signal, 16H, H-3′, H-5′, H-6′, H-8′, H-9′, H-11′, H-12′, H-14′), 3.61 (t, 4H, H-2′, H-15′); MS-EI (high resolution) m/z calcd for $C_{24}H_{26}FNO_6$ 443.1744 (M^+), found 443.1740.

General Procedure for the Preparation of Lipophilic 1,8-Bis(diazacrown ether)-9,10-anthraquinones 12–14. A mixture of 1,8-difluoroanthraquinone (**1**) (0.12 g, 0.5 mmol) and the corresponding diazacrown ether (**22–24**) (4 mmol) in dry DMF (4 mL) under argon was stirred and heated at 50 °C for 48 h. After the solution was cooled to room temperature, the solvent was removed and the residue was chromatographed on alumina using successively ethyl acetate–hexane (1:1), ethyl acetate, and finally ethyl acetate–methanol (20:1). The first eluted compound was identified as the corresponding reaction product intermediate **15–17**. The second one was identified as the corresponding anthraquinone **12–14**.

1,8-Bis(7′-octyl-1′,7′-diaza-4′,10′-dioxacyclopentadecan-1′-yl)-9,10-anthraquinone (12): yield 48%; viscous red oil; ^{1}H NMR ($CDCl_3$) δ 7.81 (dd, 2H, H-4, H-5), 7.68 (dd, 2H, H-2, H-7), 7.51 (t, 2H, H-3, H-6), 3.74 (t, 8H, OCH_2CH_2NAr), 3.57 (t, 16H, $CH_2OCH_2CH_2NAr$), 2,69 (br t, 8H, $CH_2NC_8H_{17}$), 2.49 (t, 4H, $NCH_2C_7H_{15}$), 1.5 (q, 4H, $NCH_2CH_2C_6H_{13}$), 1.3 (br signal, 20H, CH_2), 0.88 (t, 6H, CH_3); FAB-MS (mNBA) m/z 777 (M + H^+). Anal. Calcd for $C_{46}H_{72}N_4O_6$: C, 71.10; H, 9.34; N, 7.21. Found: C, 71.00; H, 9,21; N, 7.33. In this reaction the minor compound 1-fluoro-8-(7′-octyl-1′,7′-diaza-4′,10′-dioxacyclododecan-1′-yl)-9,10-anthraquinone (**15**) was also isolated: yield 25%; ^{1}H NMR ($CDCl_3$) δ 8.15 (dd, 2H, H-4, H-5), 7.72 (t, 1H, H-3), 7.61 (ddd, 1H, H-6), 7.52 (dd, 1H, H-2), 7.42 (ddd, 1H, H-7), 3.7 (t, 4H, H-3′, H-11′), 3.63 (t, 4H, H-5′, H-9′), 3.49 (t, 4H, H-2′, H-12′) , 2.62 (t, 4H, H-6′, H-8′), 2.41 (t, 2H, $NCH_2C_7H_{15}$), 1,5 (m, 2H, $CH_2CH_2C_6H_{13}$), 1.3 (br signal, H-10′, CH_2), 0.87 (t, 3H, CH_3); FAB-MS (mNBA) (high resolution) m/z calcd for $C_{30}H_{40}FN_2O_4$ 511.2972 (M + H^+), found 511.2960.

1,8-Bis(7′-dodecyl-1′,7′-diaza-4′,10′-dioxacyclododecan-1′-yl)-9,10-anthraquinone (13): yield 53%; viscous red oil; ^{1}H NMR ($CDCl_3$) δ 7.81 (dd, 2H, H-4, H-5), 7.67 (dd, 2H,H-2, H-7), 7.51 (t, 2H, H-3, H-6), 3.76 (t, 8H, OCH_2CH_2NAr), 3.58 (t, 16H, $CH_2OCH_2CH_2NAr$), 2.70 (br t, 8H, $CH_2NC_{12}H_{25}$), 2.49 (t, 4H, $NCH_2C_{11}H_{23}$), 1.5 (q, 4H, $NCH_2CH_2C_{10}H_{21}$), 1.3 (br signal, 36H, CH_2), 0.88 (t, 6H, CH_3); FAB-MS (mNBA) m/z 889 (M + H^+). Anal. Calcd for $C_{54}H_{88}N_4O_6$: C, 72.93; H, 9.97; N, 6.30. Found: C, 72.84; H, 9.77; N, 6.35. In this reaction the minor compound (1-(7′-dodecyl-1′,7′-diaza-4′,10′-dioxacyclododecan-1′-yl)-8-fluoro-9,10-anthraquinone (**16**)) was also isolated: yield 16%; ^{1}H NMR ($CDCl_3$) δ 8.15 (dd, 2H, H-4, H-5), 7.73 (t, 1H, H-3), 7.63 (ddd, 2H, H-6), 7.53 (dd, 1H, H-2), 7.43 (ddd, 1H, H-7), 3.69 (t, 4H, H-3′, H-11′), 3.64 (t, 4H, H-5′, H-9′), 3.49 (t, 4H, H-2′, H-12′), 2.63 (t, 4H, H-6′,H-8′, CH_2), 2.4 (t, 2H, $NCH_2C_{11}H_{23}$), 1.5 (m, 2H, $CH_2CH_2C_{10}H_{21}$) 1.3 (br signal, 18H, CH_2), 0.87 (t, 3H, CH_3); FAB-MS (mNBA) (high resolution) m/z calcd for $C_{34}H_{48}FN_2O_4$ 567.3598 (M + H^+), found 567.3579.

1,8-Bis(7′-octadecyl-1′,7′-diaza-4′,10′-dioxacyclododecan-1′-yl)-9,10-anthraquinone (14): yield 56%; viscous red oil; ^{1}H NMR ($CDCl_3$) δ 7.82 (dd, 2H, H-4, H-5), 7.68 (dd, 2H, H-2, H-7), 7.5 (t, 2H, H-3, H-6), 3.72 (t, 8H, OCH_2OCH_2NAr), 3.56 (t, 16H, $CH_2OCH_2CH_2NAr$), 2.71 (br t, 8H, $CH_2NC_{18}H_{37}$), 2.5 (t, 4H, $NCH_2C_{17}H_{35}$), 1.5 (m, 4H, $NCH_2CH_2C_{16}H_{33}$), 1.25 (br signal, 60H, CH_2), 0.88 (t, 6H, CH_3); FAB-MS (mNBA) m/z 1057 (M + H^+). Anal. Calcd for $C_{66}H_{112}N_4O_6$: C, 74.95; H, 10.67; N, 5.30. Found: C, 74.91; H, 10.50; N, 5.42. In this reaction the minor compound 1-fluoro-8-(7′-octadecyl-1′,7′-diaza-4′,10′-dioxacyclododecan-1′-yl)-9,10-anthraquinone (**17**) was also isolated: yield 18%; ^{1}H NMR ($CDCl_3$) δ 8.16 (dd, 2H, H-4, H-5), 7.75 (t, 1H, H-3), 7.64 (ddd, 2H, H-6), 7.53 (dd, 1H, H-2), 7.45 (ddd, 1H, H-7), 3.72 (t, 4H, H-3′, H-11′), 3.64 (t, 4H, H-5′, H-9′), 3.49 (t, 4H, H-2′, H-12′), 2.65 (t, 4H, H-6′, H-8′, CH_2), 2.4 (t, 2H, $NCH_2C_{17}H_{34}$), 1.4 (m, 2H, $CH_2CH_2C_{16}H_{33}$), 1.3 (br signal, 30H, CH_2), 0.88 (t, 3H, CH_3); FAB-MS (mNBA) (high resolution) m/z calcd for $C_{40}H_{60}FN_2O_4$ 651.4537 (M + H^+), found 651.4512.

General Procedure for the Preparation of 4-Alkyl-10-(4′-methylbenzenesulfonyl)-4,10-diaza-1,7-dioxacyclododecane (19–21). A mixture of *N,N*-bis(5′-hydroxy-3′-oxapent-1′-yl)-4-methylbenzenesulfonamide (**18**) (1.1 g, 2.21 mmol), the corresponding alkylamine (2.37 mmol), and anhydrous sodium carbonate (1.17 g, 11.1 mmol) in dry acetonitrile (50 mL) under argon was heated to reflux for 48 h. After the solution was cooled to room temperature, the mixture was filtered and the inorganic salt was successively washed with acetonitrile (25 mL) and dichloromethane (25 mL). The collected filtrates were evaporated and the residue was chromatographed on alumina using successively ethyl acetate–hexane (1:1) and ethyl acetate as eluent. Analytical samples were obtained by recrystallization from acetonitrile.

4-Octyl-10-(4′-methylbenzenesulfonyl)-4,10-diaza-1,7 dioxacyclododecane (19): yield 43%; white solid, mp 46–48 °C; ^{1}H NMR ($CDCl_3$) δ 7.71 (dd, 2H, H-2′, H-6′), 7.30 (dd, 2H, H-3′, H-5′), 3.82 (t, 4H, CH_2OCH_2NTs), 3.56 (t, 4H, CH_2OCH_2NR), 3.27 (t, 4H, CH_2NTs), 2.68 (t, 4H, CH_2OCH_2N), 2.5 (t, 2H, $CH_2NCH_2CH_2$), 2.43 (s, 3H, CH_3), 1.5 (q, 2H, NCH_2CH_2), 1,25 (br signal, 10H, CH_2), 0.88 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 143.2 (C-1′), 136.5 (C-4′), 129.9 (C-2′), 127.4 (C-3′), 70.3 (C-8,12), 69.2 (C-2,6), 57.3 (C-9,11), 55.5 (C-3,5), 50.6 ($CH_2NC_7H_{15}$), 31.6, 29.2, 27.4, 26.9, 23.4 (CH_2), 21.5 (CH_3), 14.2 (CH_3); MS-EI m/z (relative intensity) 440 (M^+, 10), 341 (100). Anal. Calcd for $C_{23}H_{40}N_2O_4S$: C, 62.69; H, 9.15; N, 6.36; S, 7.28. Found: C, 62.53; H, 9.10; N, 6.45; S, 7.15.

4-Dodecyl-10-(4′-methylbenzenesulfonyl)-4,10-diaza-1,7-dioxacyclododecane (20): yield 49%; white solid, mp 64–65 °C; ^{1}H NMR ($CDCl_3$) δ 7.72 (dd, 2H, H-2′, H-6′), 7.30 (dd, 2H, H-3′, H-5′), 3.81 (t, 4H, CH_2OCH_2NTs), 3.55 (t, 4H, CH_2OCH_2NR), 3.28 (t, 4H, CH_2NTs), 2.65 (t, 4H, CH_2OCH_2N), 2.5 (t, 2H, $CH_2NCH_2CH_2$), 2.40 (s, 3H, CH_3), 1.5 (q, 2H, NCH_2CH_2), 1.26 (br signal, 18H, CH_2), 0.88 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 143.3 (C-1′), 136.2 (C-4′), 129.9 (C-2′), 127.5 (C-3′), 70.4 (C-8,12), 69.1 (C-2,6), 57.5 (C-9,11), 55.8 (C-3,5), 50.8 ($NCH_2C_{11}H_{23}$), 32.5, 30.0, 27.3, 26.7, 23.3 (CH_2), 21.7 (CH_3), 14.2 (CH_3); MS-EI m/z (relative intensity) 496 (M^+, 5), 341 (100). Anal. Calcd for $C_{27}H_{48}N_2O_4S$: C, 65.28; H, 9.73; N, 5.64; S, 6.46. Found: C, 65.12; H, 9.69; N, 5.76; S, 6.23.

4-Octadecyl-10-(4′-methylbenzenesulfonyl)-4,10-diaza-1,7 dioxacyclododecane (21): yield 59%; white solid, mp 75–76 °C; ^{1}H NMR ($CDCl_3$) δ 7.70 (dd, 4H, H-2′, H-6′), 7.3 (dd, 2H, H-3′, H-5′), 3.83 (t, 4H, CH_2OCH_2NTs), 3.57 (t, 4H, CH_2OCH_2NR), 3.27 (t, 4H, CH_2NTs), 2.70 (t, 4H, CH_2OCH_2N), 2.5 (t, 2H, $CH_2NCH_2CH_2$), 2.42 (s, 3H, CH_3), 1.5 (q, 2H, NCH_2CH_2), 1.25 (br signal, 30H, CH_2), 0.88 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 143.5 (C-1′), 135.8 (C-4′), 129.6 (C-3′), 127.2 (C-2′), 70.1 (C-8,12), 68.8 (C-2,6), 57.0 (C-9,11), 55.2 (C-3,5), 50.5 ($NCH_2NC_{17}H_{35}$), 31.8 ($NCH_2CH_2C_{16}H_{33}$), 29.6, 29.3, 27.3, 27.0, 22.6 (CH_2), 21.4 (CH_3), 14.0 (CH_3); MS-EI m/z (relative intensity) 580 (M^+, 7), 425 (100). Anal. Calcd for $C_{33}H_{60}N_2O_4S$: C, 68.23; H, 10.41; N, 4.82; S, 5.52. Found: C, 68.00; H, 10.28; N, 4.89; S, 5.14.

General Procedure for the Preparation of 1-Alkyl-1,7-diaza-4,10-dioxacyclododecanes (22–24). A solution of the corresponding tosylate (**19–21**) (1.13 mmol) in dry THF (10 mL) was added dropwise over a well-stirred suspension of lithium aluminum hydride (0.30 g, 7.78 mmol) in dry THF (10 mL) under argon, and the mixture was heated to reflux for 48 h. After the solution was cooled to room temperature, ethyl acetate (25 mL) and then ice water (5 mL) were added. The suspension was filtered through Celite, which was washed with dichloromethane (50 mL). The collected filtrates were evaporated and the residue extracted with dichloromethane (2 × 35 mL) and the solution was dried over anhydrous sodium sulfate. The solvent was removed and the residue was chromatographed on alumina using successively hexane–ethyl acetate (5:1), hexane–ethyl acetate (1:1), ethyl acetate, and finally ethyl acetate–methanol (10:1) as eluent.

1-Octyl-1,7-diaza-4,10-dioxacyclododecane (20): yield 73%; colorless oil; mp 46–48 °C; ^{1}H NMR ($CDCl_3$) δ 3.70 (t, 4H, $HNCH_2O$), 3.57 (t, 4H, OCH_2NR), 2.86 (t, 4H, CH_2NH), 2.71 (t, 4H, CH_2NR), 2.57 (t, 2H, $CH_2NCH_2CH_2$), 1.4 (q, 2H, NCH_2CH_2), 1.3 (br signal, 10H, CH_2), 0.88 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 66.2, 65.3 (C-3,5,9,11); 50.6, 49.0 (C-2,6,8,12), 47.6 (CH_2N), 31.8, 29.5, 29.1, 27.3, 22.6 (CH_2), 14.0 (CH_3); MS-EI m/z (relative intensity) 286 (M^+, 15), 200 (76); 168 (100). Anal. Calcd for $C_{16}H_{34}N_2O_2$: C, 67.09; H, 11.96; N, 9.80. Found: C, 67.07; H, 12.09; N, 9.70.

1-Dodecyl-1,7-diaza-4,10-dioxacyclododecane (23): yield 69%; colorless oil; ^{1}H NMR ($CDCl_3$) δ 3.71 (t, 4H, HNCH_2O), 3.59 (t, 4H, OCH_2NR), 2.84 (t, 4H, CH_2NH), 2.70 (t, 4H, CH_2-NR), 2.56 (t, 2H, CH_2NC$H_2$$CH_2$), 1.4 (q, 2H, N$CH_2CH_2$), 1.3 (br signal, 18H, CH_2), 0.88 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 66.3, 65.4 (C-3,5,9,11); 50.7, 48.7 (C-2,6,8,12), 47.5 (CH_2N), 31.7, 29.5, 29.0, 27.3, 22.6 (CH_2), 14.0 (CH_3); MS-EI m/z (relative intensity) 342 (M^+, 12), 256 (66); 224 (100). Anal. Calcd for $C_{20}H_{42}N_2O_2$: C, 70.12; H, 12.36; N, 8.18. Found: C, 69.85; H, 12.03; N, 8.32.

1-Octadecyl-1,7-diaza-4,10-dioxacyclododecane (24): yield 53%; white solid, mp 51–53 °C; ^{1}H NMR ($CDCl_3$) δ 3.72 (t, 4H, HNCH_2O), 3.58 (t, 4H, OCH_2NR), 2.87 (t, 4H, CH_2NH), 2.71 (t, 4H, CH_2NR), 2.58 (t, 2H, NC$H_2$$CH_2$), 1.4 (q, 2H, N$CH_2CH_2$), 1.3 (br signal, 30H, CH_2), 0.88 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 66.3, 65.4 (C-3,5,9,11); 50.6, 48.8 (C-2,6,8,12), 47.5 (CH_2N), 31.7, 29.4, 29.0, 27.3, 22.6 (CH_2), 14.0 (CH_3); MS-EI m/z (relative intensity) 426 (M^+, 20), 340 (100). Anal. Calcd for $C_{26}H_{54}N_2O_2$: C, 73.18; H, 12.76; N, 6.56. Found: C, 73.40; H, 12.62; N, 6.30.

Acknowledgment. R. Lawson, C. Lopez, and L. Echegoyen wish to thank the National Science Foundation (Grants DMR-9119986 and CHE-9313018) and the donors of the Petroleum Research Fund (ACS-PRF#27827-AC1) for generous financial support of this work.