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Preparation and Electrochemical Switching of Novel Bis(anthraquinone)diazacrown Ethers

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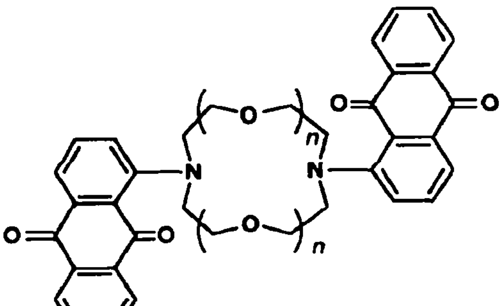
Abstract: *Novel bis (anthraquinone)diazacrown ethers 1 and 2 were prepared by nucleophilic displacement reactions on 1-fluoro-9,10-anthraquinone by diazacrown ethers. The electrochemically switched enhanced sodium binding capabilities of these compounds with Na^+ were evaluated. Both compounds exhibited enhanced sodium binding properties upon electrochemical reduction.*

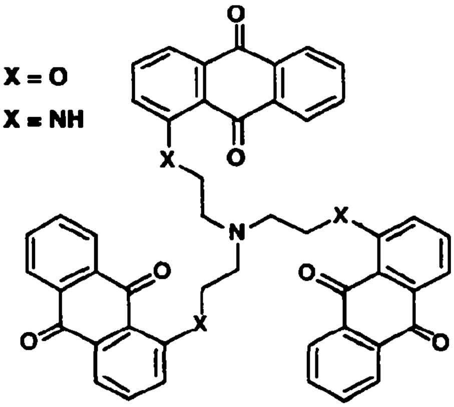
We are interested in the properties of electrochemically-switched systems based on anthraquinone-containing cation complexing subunits which are potentially useful in enhanced cation binding and transport across membranes.[1-5] In a previous report,[4] we described the preparation of azacrown ether- and criptand-alkoxy anthraquinones from 1-fluoro- and 1,8-difluoro-9,10-anthraquinones. More recently,[5] we reported the preparation of lipophilic bis(azacrown ether) anthraquinones. Anthraquinone-containing crown ethers continue to receive attention in various specialised fields. In a recent paper, Bachas et al.[6] have described the development of ion-sensitive electrodes based on anthraquinone-containing crown ethers.

In this paper, we report the synthesis and Na^+ binding enhancements of diazacrown ether systems **1** and **2** substituted by two 9,10-anthraquinone moieties. The most characteristic features of these systems are their relatively low conformational flexibility and the presence of two quinone units close to the complexation site which could act cooperatively in cation binding.



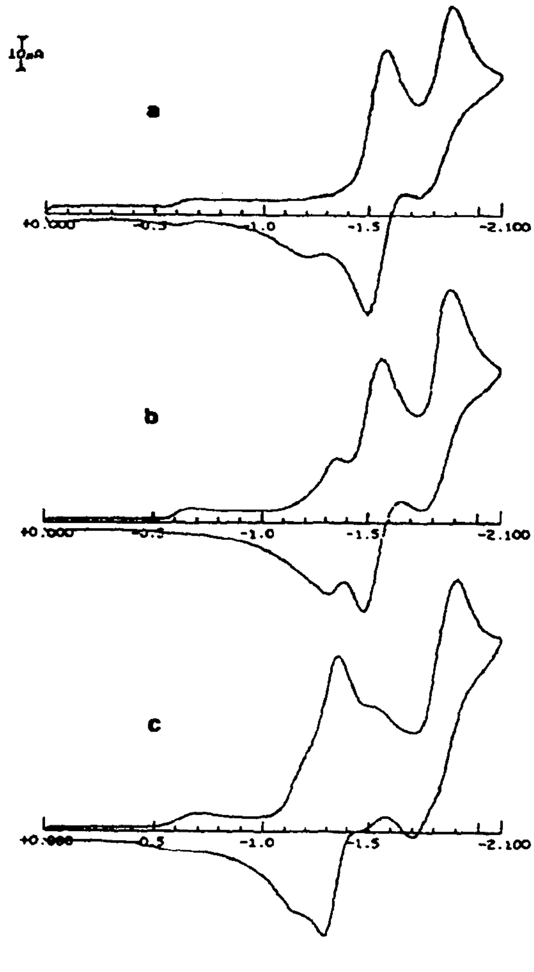
1 $n = 1$
2 $n = 2$

3 X = O
4 X = NH



Compounds **1** and **2** were obtained in good yield by treatment of equimolar amounts of 1-fluoro-9,10-anthraquinone[4] with the corresponding diazacrown ether in DMF as solvent (50°, 48h).[7] Substitution of fluoride by simple amines[8,9] and monoazacrown ethers[4] in haloanthraquinones have been described.

The electrochemical behavior of compounds 1 and 2 was quite similar to that of other previously studied anthraquinone derivatives.[4] The voltammograms for 1 and 2 in dichloromethane as a function of added Na^+ are shown in Figures 1 and 2 respectively.[10]



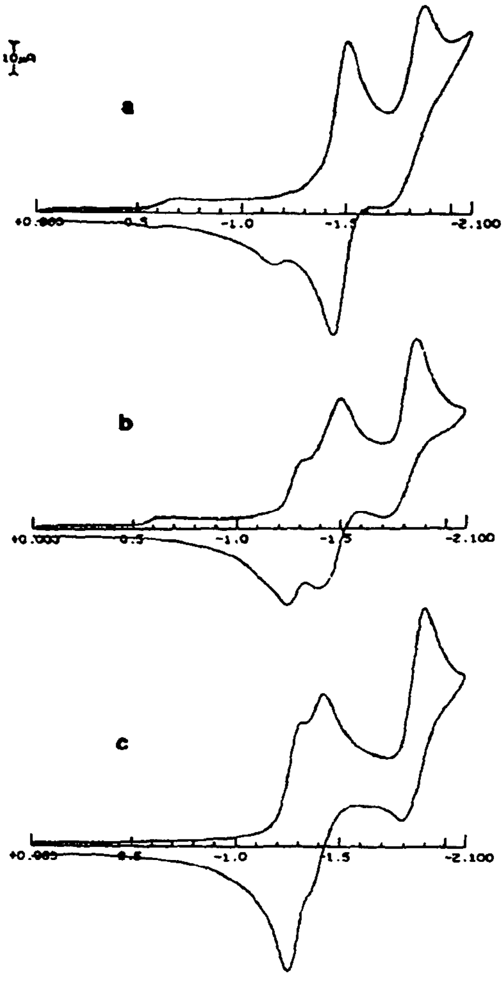
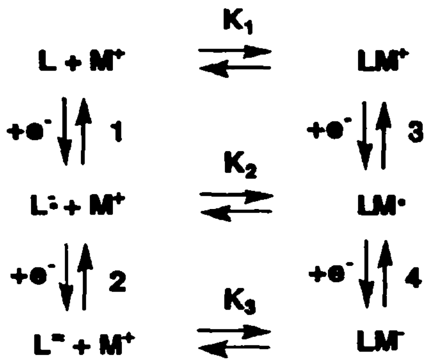


Figure 1. Cyclic voltammograms for 1 in dichloromethane containing 0.1 M $TBAPF_6$. (a) in the absence of Na^+, (b) in the presence of 0.5 equiv. of Na^+ and (c) in the presence of 2.0 equiv. of Na^+. Scan rate = 0.1 V/s.

Figure 2. Cyclic voltammograms for 2 in dichloromethane containing 0.1 M $TBAPF_6$. (a) (b) and (c) as in Figure 1.

Compounds 1 and 2 exhibited additional and time-resolved redox pairs upon addition of aliquots of sodium tetraphenylborate. Prior to addition of the Na^+ salt, only two quasireversible redox pairs were obtained corresponding to steps 1 and 2 in Scheme 1 (see Figure 1a). These two waves correspond to two-electron processes each, for a total of four electrons. After addition of the Na^+ salt, an additional redox couple was observed for each of compounds 1 and 2 ($E_{1/2}$ = 1.33 for 1 and $E_{1/2}$ = 1.27 for 2) (see Figures 1 and 2). These additional redox couples correspond to step 3 in Scheme 1. All redox couples were resolved.



Scheme 1

On the basis of the individual measurement of all potentials for the resolved waves, it was possible to determine the apparent ratio K_2/K_1 as previously described.[1,3] For 1 $K_2/K_1 = 1.39 \times 10^3$ while for 2, $K_2/K_1 = 9.8 \times 10^2$. These values represent cation binding enhancements[11] due to electrochemical switching of the ligand to more negatively charged states. The enhancements observed are similar to those found for more flexible dianthraquinone substituted systems.[4] However, the values found are lower than the ones reported previously by us for bis (azacrown ether) anthraquinones ($K_2/K_1 \sim 10^5$).[5] On the other hand, in a previous paper[4] we studied the electrochemistry of compound 3 which has three quinone units. This compound showed large Na^+ binding enhancements which was surprising, since without crown ether subunits, it was not expected to have a substantial binding affinity for Na^+. In order to study the behavior of a related more rigid receptor, the diaza-analogue 4[12] was prepared by reaction of 1-fluoroanthraquinone with tris(2-aminoethyl)amine in similar reaction conditions to those described above for 1 and 2. This compound has three intramolecular hydrogen bonds.

The cyclic voltammogram of 4 in dichloromethane exhibits two quasireversible redox pairs that correspond to the one- and two-electron redution of each of the essentially independent and uncoupled quinone groups to its corresponding anion and dianion radicals, respectively (Scheme 1). Both reductions correspond to a three-electron wave as explained before. However, in this case no changes were observed in the voltammogram upon addition of increasing amounts of Na^+. This behavior can be attributed to conformational constraints of the three quinone groups to cooperate in sodium complexation due to the presence of three hydrogen bonds. Further work is required to clarify this point.

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(7) Compounds **1** and **2** were purified by flash chromatography on alumina (ethyl acetate-hexane, 1:1). **1**: Yield 68%, m.p. 250-251 °C (ethyl acetate); ^{1}H-NMR ($CDCl_3$): δ 8,21 (dd, 4H, H-5',H-8'), 7.9 (dd, 2H, H-4'), 7.7 (m, 6H, H-3',H-6',H-7'), 7.53 (dd, 2H, H-2'), 3.62 (t, 8H, C$\underline{H}_2$OC$\underline{H}_2$), 3.58 (t, 8H, C$\underline{H}_2$NC$\underline{H}_2$) ppm. ^{13}C-NMR ($CDCl_3$): δ 184.1 (C-9'), 181.8 (C-10'), 151.0 (C-1'), 135.6 (C-3'), 134.0 (C-6'), 133.6 (C-7'), 132.8 (C-8'), 132.5 (C-11', C-12'), 129.1 (C-14'), 126.9 (C-5'), 126.5 (C-2'), 122.1 (C-13'), 119.8 (C-4'), 68.7 (CH_2O), 53.4 (CH_2N) ppm. FAB-MS (*m*-NBA): *m/z* 587 [$M+H^+$]. Elemental analysis for $C_{36}H_{30}N_2O_6$: Calc.: C, 73.70; H, 5.15; N, 4.77. Found: C, 73.63; H, 4.99; N, 4.78.

2: Yield 58%; m.p. 223-225 °C; ^{1}H-NMR ($CDCl_3$): δ 8.23 (dd, 4H, H-5', H-8'), 7.88 (dd, 2H, H-4'), 7.7 (m, 6H, H-3', H-6', H-7'), 7.64 (dd, 2H, H-2'), 3.7 (broad, 16H, CH_2O), 3.58 (s, 8H, CH_2N) ppm. ^{13}C-NMR ($CDCl_3$): δ 184.2 (C-9'), 181.7 (C-10'), 152.3 (C-1'), 136.3 (C-3'), 135.5 (C-6'), 134.1 (C-7'), 133.6 (C-8'), 132.9 (C-11', C-12'), 132.5 (C-14'), 127.3 (C-5'), 127.1 (C-2'), 126.5 (C-13'), 120.1 (C-4'), 79.7 (CH_2OCH_2), 69.7 ($\underline{C}H_2OCH_2N$), 53.4 (N$\underline{C}H_2CH_2O$) ppm. FAB-MS (*m*-NBA): *m/z* 675 [$M+H^+$]. Elemental analysis for $C_{40}H_{38}N_2O_8$): Calc.: C, 71.20; H, 5.67; N, 4.15; Found: C, 71.16; H, 5.63; N, 4.20.

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(10) Electrochemical experiments were performed using a Bioanalytical Systems 100 analyser, equipped with IR compensation, and recorded on a Houston DMP-40 plotter. Glassy carbon electrode was used as the working electrode and a platinum wire as counter electrode. The reference electrode was a piece of silver wire immersed in 0.1 M tetra-*n*-butyl-ammonium hexafluorophosphate solution containing 5 mM $AgNO_3$ in dichloromethane-acetonitrile (9:1). The experiments were run at room temperature under dry nitrogen atmosphere. The electroactive species was present in ~1 mM concentrations. All voltammograms were recorded using full IR compensation. The cation-containing salt was added in half-equivalent increments as the tetraphenylborate salt. Voltammograms were recorded after each successive addition. The potential was scanned at a rate of 0.1 V/s. Acetonitrile (Aldrich) and dichloromethane (Aldrich) were dried over CaH_2 for three days and distilled under dry nitrogen gas. Tetrabutylammonium hexafluorophosphate (Fluka) was recrystallised from ethyl alcohol two times and dried at 100 °C for ~15 hours in a vacuum oven. Sodium tetraphenylborate (Aldrich) was used as received.

(11) The enhancements were calculated from the corresponding $E_{1/2}$ values for each of the waves which in turn, were determined from the average of the cathodic and anodic peak potentials [$(Ep^a+Ep^c)/2$].

(12) Compound **4** was purified by flash chromatography on silica gel (dichloromethane-ethyl acetate, 10:1) Yield: 52%. M.p. 233-235 °C. ^{1}H-NMR ($CDCl_3$): δ 9.86 (t, 3H, NH), 8.07 (dd, 6H, H-5', H-8'), 7.83 (dd, 3H,H-4'), 7.9-7.4 (m, 9H, H-3',H-6',H-7'), 7.03 (dd, 3H, H-2'), 3.53 (t,6H, $NCH_2C\underline{H}_2N$-quinone), 3.06 (t, 6H, $NC\underline{H}_2CH_2N$-quinone) ppm. ^{13}C-NMR ($CDCl_3$): δ 184.3 (C-9'), 183.5 (C-10'), 151.3 (C-1'), 135.3 (C-3'), 134.9 (C-6',C-7') 134.7 (C-8'), 133.6 (C-11',C-12'), 132.6 (C-14'), 126.8 (C-5'), 126.4 (C-2'), 123.3 (C-13'), 117.7 (C-4'), 54.2 (CH_2N-quinone), 41.7 (CH_2N) ppm. FAB-MS (*m*-NBA): *m/z* 765 [$M+H^+$], 528 [$M-C_{14}H_7O_2NHCH_3{}^+$], 305 [$528-C_{14}H_7O_2NH_2{}^+$]. Elemental analysis for $C_{48}H_{36}N_4O_6$: Calc.: C,75.38; H, 4.74; N, 7.32; Found: C, 74.46; H, 4.79; N, 7.25.

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