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Synthesis and electrochemical switching of a dianthraquinone cryptand and related anthraquinone-diazacrown ether oligomers

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Abstract—Bis(diazacrown ether)-bisanthraquinones such as the cryptand represented in **5**, and related anthraquinone-diazacrown ether oligomers like **2**–**4** or **6** have been prepared and their potential for electrochemically-switched enhanced ion binding ability were evaluated. The presence of two or more quinone units close to the complexation site which act cooperatively in cation binding allows enhanced values for cation complexation. Thus, in compound **5** a binding enhancement ratio K_2/K_1 of 6×10^6 for sodium cation has been found upon electrochemical reduction.

1. Introduction

It is well known that redox changes can be used to enhance or diminish the binding affinity of ligands for guest ions. Such ligands can thus be viewed as redox switches. The topic of redox switching has been of considerable interest in supramolecular chemistry for over two decades.[1] Anthraquinone redox active moieties have been used as the switching antennae for enhanced cation binding.[2–4] This group undergoes two successive monoelectronic reductions, first to the anion radical and then to the dianion. We have previously described[5] a series of anthraquinones with pendant diazacrown ethers and bis(anthraquinone systems) with diazacrown ether spacers. Sodium binding enhancements obtained upon one-electron reduction in several of these systems were in the order of 10^5.

2. Results and discussion

Following our interest in studying the cooperation between several anthraquinone subunits in the complexation of alkaline metals,[6] we report here the design, synthesis and lithium and sodium binding enhancements of diazacrown ether compounds **2**–**6** substituted by two or more 9,10-anthraquinone moieties. Based on previous studies[3,5,6] we anticipated that bis(diazacrown ether)-bisanthraquinones, such as the cryptand represented by **5**, would result in larger binding enhancement values for cation complexation. The anthraquinone-diazacrown ether oligomers **3**, **4** and **6** were also attractive in this context. A characteristic feature of these systems is their relatively low conformational flexibility and the presence of two or more quinone units close to the complexation site, which can act cooperatively in cation binding.

Previously, we had prepared diazacrown ether- and cryptand-alkoxy anthraquinones, as well as lipophilic bis(diazacrown ether) anthraquinones from 1-fluoro- and 1,8-difluoro-9,10-anthraquinones.[5,6] A similar approach was used to prepare compounds **2**–**6**.

Compounds **2** and **3** were obtained in 80 and 9% yield, respectively by treatment of a slight excess of 1,7-diaza-4,10-dioxacyclododecane with 1,8-difluoro-9,10-anthraquinone (**1**) in butyronitrile as solvent (60°C, 96 h) (Scheme 1). In the same reaction compounds **4** and **5** were also obtained as minor components (yields <3%). The use of a base, like sodium carbonate or cesium carbonate increases the reaction rate, but higher oligomers, lower yields and intractable sodium complexes were obtained. In the above mentioned reaction only anthraquinone-'capped' oligomers **2**–**5** were isolated. The use of a higher ratio of diazacrown ether gave rise to increasing amounts of diazacrown ether-'capped' oligomers, which were difficult to isolate.

Cryptand **5** was prepared in 56% yield by reacting compound **2** with a deficient amount of 1,7-diaza-4,10-dioxacyclododecane in butyronitrile (100°C, 48 h) in order to avoid oligomer formation (Scheme 2). On the other, hand compound **6** was prepared in 48% yield by reacting compound **2** with the appropriate diazacrown ether using the same reaction conditions (Scheme 3).

Keywords: electrochemical switching; dianthraquinone; oligomers.
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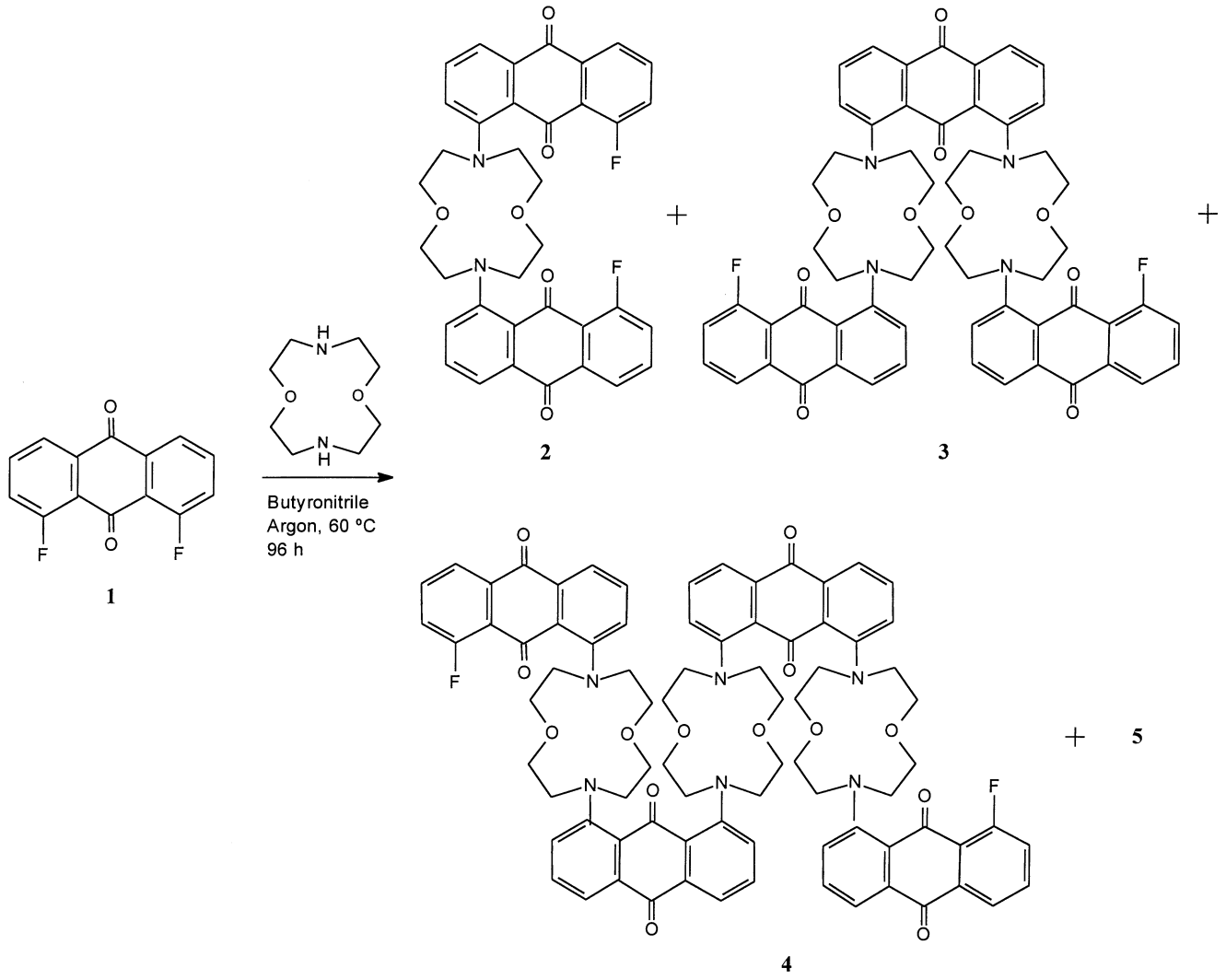
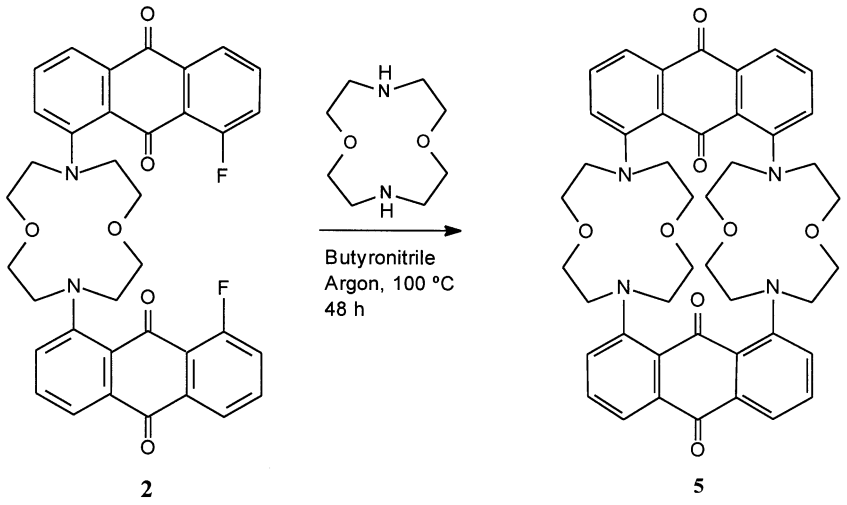
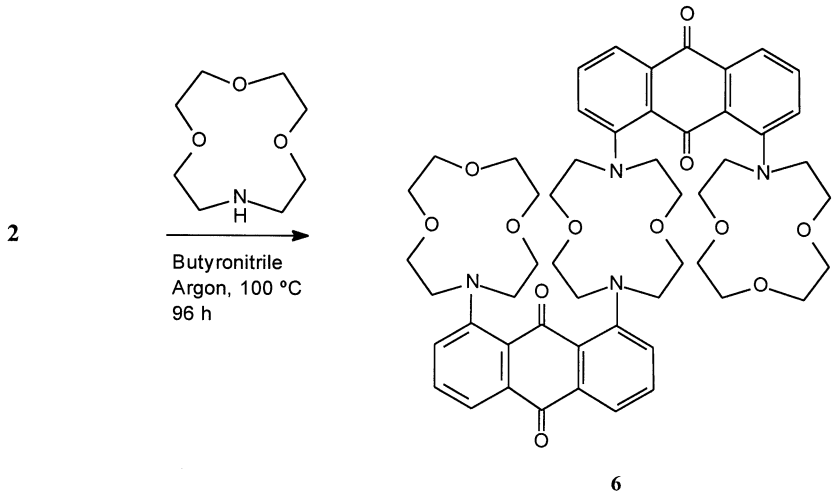


Scheme 1.

Solution electrochemistry of compounds **2**, **3**, **5** and **6** in acetonitrile (in dichloromethane for **5** due to its low solubility in the former solvent) was studied by cyclic voltammetry (CV) without and with cation salts (Li^+, Na^+) addition. Scheme 4 depicts the electrochemical processes that involve multiple equilibria, where processes 1 and 2 represent the reduction of the free ligand, and processes 3 and 4 the reduction of the ligand–cation complexes.



Scheme 2.

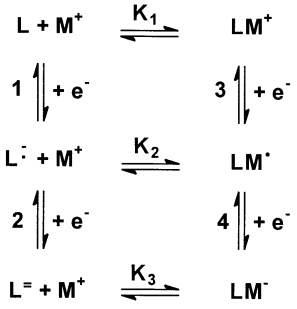


Scheme 3.

The electrochemical behaviour of compounds **2**, **3**, and **6** was quite similar to that of other previously studied anthraquinone derivatives **5**.[5,6] The voltammograms for **2** and **3** in acetonitrile as a function of added lithium or sodium cations are shown in Figs. 1–3.

Reduction of compound **2** shows a first reversible redox process around $E^1_{1/2}=-1.42$ V, and a second quasi-reversible process at $E^2_{1/2}=-1.85$ V, corresponding to steps 1 and 2 in Scheme 4. Upon addition of 0.5 equiv. of the Li^+ salt a new redox pair is observed at -1.23 V ($\Delta E_{pp}=0.19$ V) (Fig. 1). The observation of the oxidation of a complex even in the absence of added cation (Fig. 1a) is probably due to residual Na^+ coming from the glassware. On the basis of the individual measurement of all potentials for the resolved waves, it was possible to determine an apparent ratio $K_2/K_1=1.66\times10^3$. This value represents a cation binding enhancement due to electrochemical switching of the ligand to a more negatively charged state.[1,7] The enhancement observed is similar to that found for other related flexible dianthraquinone substituted systems.[6]

For compound **6**, bearing three crown ether moieties, two reduction waves were observed, the first quasi-reversible at $E^1_{1/2}=-1.70$ V and the second electrochemically irreversible at $E^2_{1/2}=-2.0$ V. Upon addition of 0.5 equiv. Li^+ salt a new redox pair was observed, at -1.40 V ($\Delta E_{pp}=0.3$ V), leading to an approximate binding enhancement of $K_2/K_1=1.2\times10^5$. This higher value, compared to that found for **2**, is in agreement with the presence of



Scheme 4.

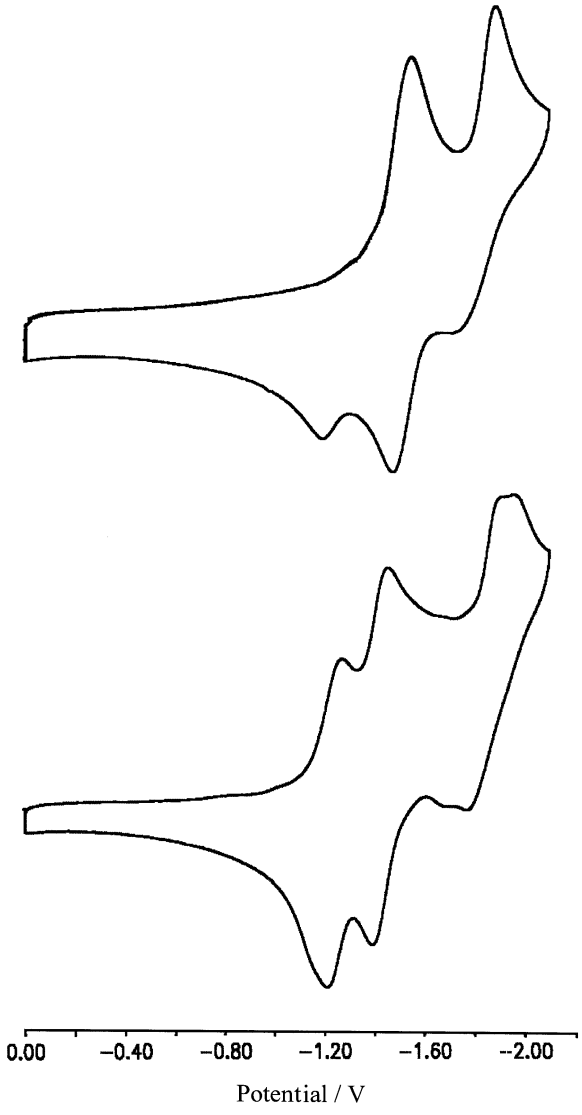


Figure 1. Cyclic voltammograms for **2** in acetonitrile. (a) In the absence of Li^+, (b) in the presence of 0.5 equiv. of $LiClO_4$.

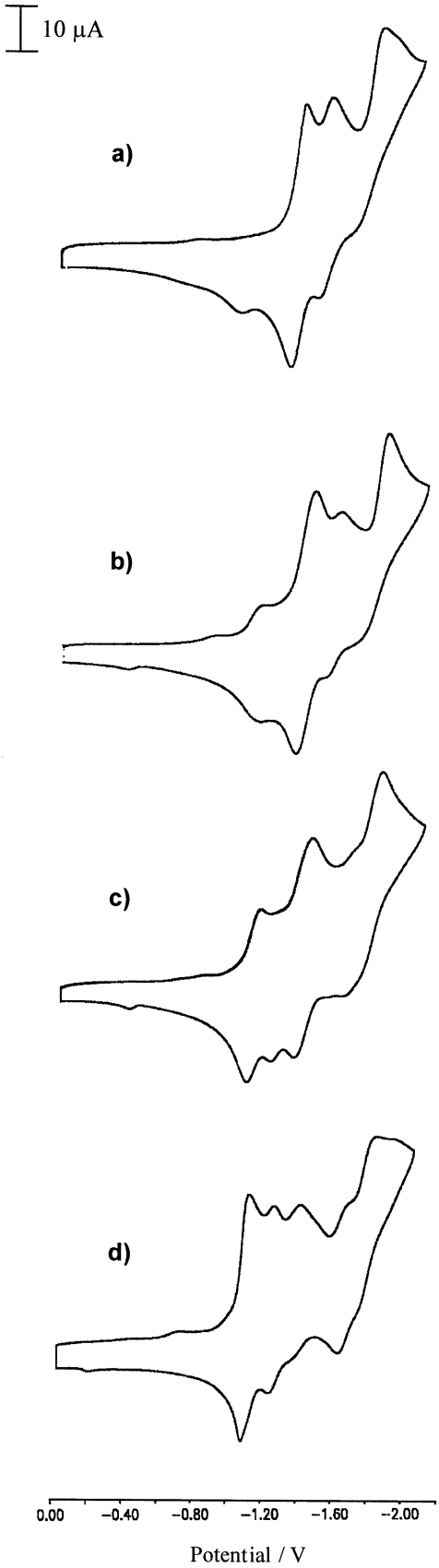


Figure 2. Cyclic voltammograms for **3** in acetonitrile. (a) In the absence of Li^+, (b)–(d) in the presence of 0.5, 1.0 and 1.5 equiv., respectively of $LiClO_4$.

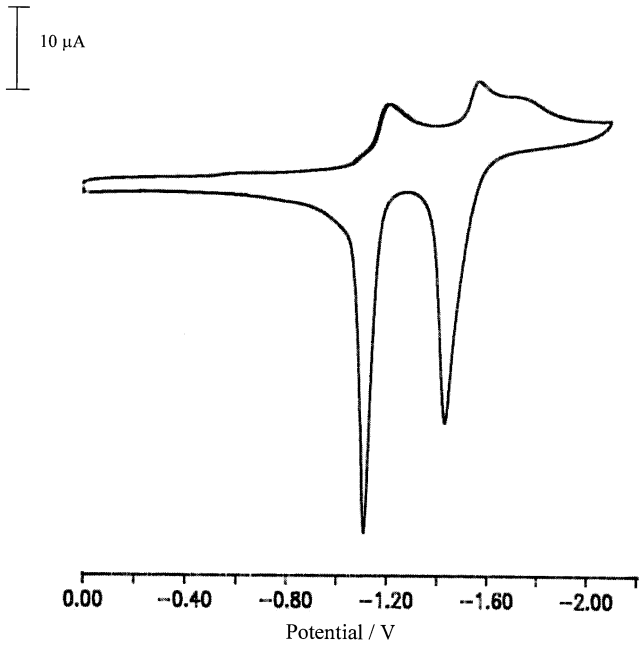


Figure 3. Cyclic voltammogram for **2** in acetonitrile in the presence of 0.5 equiv. of Na^+.

cooperative binding of three crown ether subunits with the cation.[8] This value is similar to that observed for other anthraquinone-diazacrown ethers systems reported by us. When 1.0 equiv. of Li^+ salt was added to solutions of **2** and **6**, adsorption was observed on the electrode surface.

Compound **3**, possessing three anthraquinone subunits, exhibits three redox pairs at $E^1_{1/2}=-1.4$ V, $E^2_{1/2}=-1.57$ V and $E^3_{1/2}=-1.81$ V, respectively, and the first two are reversible while the third is chemically irreversible. The first one is assigned to the monosubstituted anthraquinone subunits, and the second to the disubstituted anthraquinone moiety while the third process probably corresponds to the second reduction of the monosubstituted quinone, based on comparison with the values found for compounds **2** and **6**. Upon addition of aliquots of Li^+ salt until a 1.5 equiv. ratio, new redox pairs are observed at −1.10, −1.25 and −1.66 V, respectively, with the gradual disappearance of the waves at −1.40 and −1.57 V, as shown in Fig. 2. The cation binding enhancement values calculated were $K_2/K_1=1.2\times10^5$ ($\Delta E_{pp}=0.3$ V) based on the shift measured for the monosubstituted anthraquinone group, and $K_2/K_1=2.6\times10^5$ ($\Delta E_{pp}=0.32$ V) based on the disubstituted quinone shift. The addition of 2.0 equiv. of Li^+ salt leads to deposition on the electron surface.

Solution electrochemistry of cryptand **5**, insoluble in acetonitrile, was performed in dichloromethane. The insolubility of $LiClO_4$ in dichloromethane, where compound **5** is slightly soluble, precludes the performance of studies with lithium cation. Cryptand **5**, in dichlorometane, in the absence of any added cation, exhibits two reduction waves at $E^1_{1/2}=-1.72$ V and $E^2_{1/2}=-2.20$ V, being the second one chemically irreversible. Upon addition of 0.5 equiv. of Na^+ salt, two new waves were observed at −1.32 V ($\Delta E_{pp}=$ 0.4 V) and −1.95 V ($\Delta E_{pp}=0.25$ V) with binding enhancement ratios $K_2/K_1=6\times10^6$ and $K_3/K_2=1.7\times10^4$. The

cryptand structure of **5** must be responsible for the large enhancement ratio found.[2] Unfortunately the addition of 1.0 equiv. of Na^+ salt led to deposition on the electrode surface. The same phenomenon of deposition on the electrode surface was observed for compounds **2**, **3** and **6** upon addition of only 0.5 equiv. of Na^+ (Fig. 3).

In summary, relatively large binding enhancement ratios upon reduction, when compared with those of structurally related anthraquinone systems, have been found for lithium and sodium complexation of anthraquinone-diazacrown ether oligomeric ligands **3** and **6**, and the cryptand **5** studied. The preparation of more soluble ligands would facilitate the complexation processes, thus probably allowing a more effective electrochemical switching.

3. Experimental

3.1. General

Melting points were determined on a Büchi 504392 (S) apparatus and are uncorrected. ^1H and ^{13}C spectra were recorded on a Bruker WP 200 SY and AMX 30 instruments at 200 or 300 MHz and 50 or 75 MHz in $CDCl_3$ as the solvent. MS spectra were recorded on a VG Autospec spectrometer, and IR spectra were obtained on a Bruker IFS 66V spectrophotometer. Solvents were purified and dried by standard procedures, and reagents (Aldrich) were used as received without further purification.

3.2. Cyclic voltammetry measurements

Electrochemical experiments were performed using a Bioanalytical Systems 100 analyser, equipped with IR compensation. A glassy carbon electrode was used as the working electrode and a platinum wire was used as a counter electrode. The reference electrode was a piece of silver immersed in a 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 a 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 lithium perchlorate or sodium tetraphenylborate salt. Voltammograms were recorded after each successive addition. The potential was scanned at a rate of 100 mV s^{-1} unless otherwise specified.

3.3. Synthesis

3.3.1. Reaction of 1,8-difluoroanthraquinone (1) with 1,7-diaza-4,10-dioxacyclododecane. A solution of 1,7-diaza-4,10-dioxacyclododecane (0.3 g, 1.71 mmol) and 1,8-difluoroanthraquinone (**1**) (0.357 g, 1.46 mmol) in butyronitrile (50 mL) under argon was stirred and heated at 60°C for 96 h. The reaction mixture was cooled to room temperature and the solvent was removed under reduced pressure to afford a residue, which was chromatographed on silica gel, using the eluents indicated in each case. Low polarity impurities were removed using a mixture of chloroform–ethyl acetate (10:1) and then the polarity of the eluent was increased (same mixture, 3:1), and the first eluted red band afforded the major component, *1,7-bis(8′-fluoro-9′,10′-anthraquinon-1′-yl)-1,7-diaza-4,10-dioxacyclododecane* (**2**). The compound was washed with absolute EtOH (2×50 mL) and dried under vacuum (10^{-2} Torr) at 100°C for 72 h, giving a red black powder **2**; yield 0.363 g, 80%; mp 170–172°C (dec); IR (KBr) 1668, 1652, 1582, 1307, 1250, 1126 cm^{-1}; ^1H NMR δ 8.06 (dd, 2H, J=7.6, 1.6 Hz, H-5′), 7.83 (dd, 2H, J=7.6, 1.6 Hz, H-4′), 7.7–7.6 (m, 2H, H-6′), 7.55–7.4 (m, 6H, H-2′, H-3′, H-7′), 3.59 (s br, 16H, N–CH_2CH_2–O); ^{13}C NMR δ 182.9 (C-9′), 181.3 (C-10′), 163.1 and 157.8 (C-8′), 150.3 (C-1′), 134.6 (C-4′a, C-10′a), 134.4 (C-8′a), 133.9 and 133.7 (C-6′), 133.4 (C-3′), 129.0 (C-2′), 123.3 (C-9′a), 122.8 (C-5′), 122.4 (C-4′), 119.2 (C-7′), 68.3 (CH_2O), 53.4 (CH_2N); FAB-MS *m/z* 623 $[M+H]^+$ (100), 624 $[M+2H]^+$ (54). Anal. Calcd for $C_{36}H_{28}N_2O_6F_2$: C, 69.45; H, 4.53; N, 4.50; F, 6.10. Found: C, 69.62; H, 4.42; N, 4.58; F, 6.40.

The second minor component *1,8-bis[7′(8″-fluoro-9″,10″-anthraquinon-1″-yl)-1′,7′-diaza-4′,10′-dioxacyclo-dodecanyl]-9,10-anthraquinone* (**3**) was separated using chloroform–ethyl acetate (2:1) as eluent. The compound was washed with a mixture of ethyl ether–ethanol (1:1) (2×20 mL) and dried under vacuum (10^{-2} Torr) at 70°C for 72 h, giving a red black powder **3**; yield 0.045 g, 9%; mp 120–121°C (dec); IR (KBr) 1667, 1583, 1306, 1249, 1126 cm^{-1}; ^1H NMR δ 8.06 (dd, 2H, J=7.6, 1.6 Hz, H-5″), 7.85 (m, 4H, H-4, H-4″, H-5), 7.7–7.65 (m, 4H, H-3″, H-6″), 7.55–7.45 (m, 8H, H-2, H-2″, H-3, H-6, H-7, H-7″), 3.65 (s br, 16H, CH_2OCH_2), 3.55 (m, 16H, CH_2NCH_2); ^{13}C NMR δ 183.2 (C-9, C-9″), 181.6 (C-10, C-10″), 165.5 and 163.3 (C-8″), 150.4 (C-1, C-1″), 134.7 (C-4″a, C-10″a), 134.1 (C-4a), 134.0 (C-6″), 133.4 (C-3, C-3″), 131.7 (C-8″a), 128.9 (C-2, C-2″), 122.8 (C-4, C-4″, C-9a), 122.4 (C-5″, C-9″a), 119.3 (C-7″), 69.4 and 68.1 (CH_2O), 54.5 and 53.5 (CH_2N); FAB-MS *m/z* 1001 $[M+H]^+$ (96), 1002 $[M+2H]^+$ (100), 1003 $[M+3H]^+$ (56). Anal. Calcd for $C_{58}H_{50}N_4O_{10}F_2$: C, 69.59; H, 5.03; N, 5.60; F, 3.80. Found: C, 69.34; H, 5.04; N, 5.64; F, 4.03.

Finally, using ethyl acetate as eluent a mixture of compounds *1,7-bis {8′[7″ (8‴-fluoro-9‴,10‴-anthraquinon-1‴-yl)-1″,7″-diaza-4″,10″-dioxacyclododecan-1″-yl]-9′,10′-anthraquinon-1′-yl}-1,7-diaza-4,10-dioxacyclododecane* (**4**) and *1,8-bis[7′,7′-(9,10-anthraquinon-1,8-diyl)-1′,7′-diaza-4′,10′-dioxacyclododecan-1′-yl]-9,10-anthraquinone* (**5**) was obtained, 0.021 g (estimated yields 3 and 1%, respectively). The data of **3** are taken from the mixture of both components. ^1H NMR δ 8.06 (dd, 2H, H-5‴), 7.85 (m, 6H, H-4′, H-4‴, H-5′), 7.7–7.4 (m, 16H, H-2′, H-2‴, H-3′, H-3‴, H-6′, H-6‴, H-7′, H-7‴), 3.65 (m, 24H, CH_2OCH_2), 3.55 (m, 24H, CH_2NCH_2); FAB-MS *m/z* 1379 $[M+H]^+$ (64), 1380 $[M+2H]^+$ (100), 1381 $[M+3H]^+$ (77).

3.3.2. 1,8-Bis[7′,7′-(9,10-anthraquinon-1,8-diyl)-1′,7′-diaza-4′,10′-dioxacyclododecan-1′-yl]-9,10-anthraquinone (5). A solution of **2** (0.128 g, 0.2 mmol) and 1,7-diaza-4,10-dioxacyclododecane (0.076 g, 0.43 mmol) in butyronitrile (10 mL) was stirred and heated at 100°C for 48 h under argon. The reaction mixture was cooled and the precipitate filtered, washed with a mixture of hexane–dichloromethane (1:1) (3×50 mL) and dried under vacuum (10^{-2} Torr) at

120°C for 72 h to afford 68 mg of **5** as a red powder. By concentration of the mother liquor an additional amount of **5** (16 mg) was collected. Total yield 56%; mp 263–265°C (dec); IR (KBr) 1665, 1582, 1303, 1233, 1128, 1057 cm^{-1}; ^1H NMR δ 7.82 (dd, 4H, J=7.6, 1.6 Hz, H-4), 7.54 (dd, 4H, J=7.6, 7.6 Hz, H-3), 7.45 (dd, 4H, J=7.6, 1.6 Hz, H-2), 3.99, 3.88 (2×m, 16H, CH_2OCH_2), 3.6 (m, 16H, CH_2NCH_2), 1.55 (s, H_2O); ^{13}C NMR δ 184.7 (C-9), 183.9 (C-10), 153.1 (C-1, C-8), 134.8 (C-4a, C-10a), 132.5 (C-3, C-6), 129.0 (C-8a, C-9a), 128.2 (C-2, C-7), 120.3 (C-4, C-5), 68.4 (CH_2O), 53.8 (CH_2N); FAB-MS m/z 757 $[M+H]^+$ (51), 758 $[M+2H]^+$ (100), 759 $[M+3H]^+$ (60). Anal. Calcd for $C_{44}H_{44}N_4O_8$: C, 69.83; H, 5.86; N, 7.40: Found: C, 70.02; H, 5.87; N, 7.48.

3.3.3. 1,7-Bis[8′-(1″-aza-4″,7″,10″-trioxacyclododecan-1″-yl)-9′,10′-anthraquinon-1′-yl]-1,7-diaza-4,10-dioxacyclododecane (6). A solution of **2** (0.1 g, 0.16 mmol) and 1-aza-4,7,10-trioxacyclododecane (0.227 g, 1.3 mmol) in butyronitrile (10 mL) was stirred and heated at 100°C under argon. The reaction was monitored by TLC (dichloromethane–methanol (20:1)). The monosubtituted compound, initially formed, evolved to the disubstituted **6** after 96 h. The reaction mixture was cooled at room temperature, the solvent was removed and the residue was chromatographed on silica gel using dichloromethane–methanol (100:1)–(20:1) as eluent to afford **6**. The compound was disolved in toluene, precipitated with hexane, filtered and dried under vacuum (10^{-2} Torr) at 50°C for 96 h to give **5** as dark red powder; yield 0.072 g, 48%: mp: 70–72°C; IR (KBr) 1662, 1618, 1583, 1306, 1215, 1129 cm^{-1}; ^1H NMR δ 7.86 (m, 4H, H-4′, H-5′), 7.75–7.4 (m, 8H, H-2′, H-3′, H-6′, H-7′), 3.9–3.4 (m, 48H, CH_2OCH_2, CH_2NCH_2); ^{13}C NMR δ 184.6 (C-9′), 183.7 (C-10′), 151.6 (C-1′), 134.9 and 134.6 (C-3′), 132.6 (C-4′a), 130.6 (C-2′), 120.7 (C-9′a), 120.1 (C-4′), 71.4, 70.4 and 69.0 (CH_2O), 54.9 and 54.3 (CH_2N); FAB-MS m/z 933 $[M+H]^+$ (73), 934 $[M+2H]^+$ (100), 935 $[M+3H]^+$ (60). Anal. Calcd for $C_{52}H_{60}N_4O_{12}$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.66; H, 6.42; N, 6.03.

Acknowledgements

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