Self-stacking of naphthalene bis(dicarboximide)s probed by NMR †

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The self-stacking in water of a series of naphthalene-1,8 : 4,5-bis(dicarboximide)s (also known as naphthalene diimides, NDIs) bearing cationic side chains has been studied using NMR techniques. The position of the charge in the side chain has a strong effect on the propensity of the NDI to self-stack. Examples with a cationic center three atoms away from the NDI ring in general do not self-stack; those with cationic centers further out on the side chains are prone to self-stack at NMR concentrations. The size of the side chain *per se* does not appear to be a significant controlling factor; even a derivative with biotin side chains shows no evidence of self-stacking. Increasing the ionic strength of the solution can also induce stacking. Derivatives with aromatic side chains can show intramolecular self-stacking of the side chain with the central NDI ring. This is significant for side chains with isoquinoline and bipyridine groups but not significant for side chains with pyridine groups. An example of an NDI that undergoes both intramolecular and intermolecular stacking is the derivative bearing side chains ending in $Ru(bpy)_3^{2+}$ moieties. In methanol, the shift patterns of the aromatic resonances of the bipyridine rings are very close to those of a model compound. However, a more complicated chemical shift pattern is seen in water. This indicates that conformations with the $Ru(bpy)_3^{2+}$ moieties lying at least partly within the shielding cone of the aromatic NDI system are favored. Molecular modeling indicates that conformations in which the bipyridine ring interacts with the NDI ring are readily achievable. The temperature dependence of the chemical shifts for this molecule indicates that both intramolecular interactions of the bipyridine rings with the NDI ring and self-stacking of the NDI rings are significant.

Introduction

The excellent stability, redox and photophysical characteristics of the naphthalene-1,8 : 4,5-bis(dicarboximide) ring system have resulted in its widespread use. Naphthalene bis(dicarboximide)s (NDIs) are used in photoactive, high temperature and conductive polymers;[1,2] in molecules that self-assemble in solution;[3–5] in studies of π-stacking of anion radicals;[6–9] in donor–acceptor systems that undergo electron transfer;[10–22] as synthetic building blocks;[23,24] as probes that generate hydroxy radical upon irradiation;[25–34] and as DNA-binding molecules.[26,28,35–44]

π-Stacking,[45–51] either dimerization or formation of higher aggregates, plays a critical role in many uses of NDIs. Iverson and co-workers have used the aggregation properties of NDIs to form molecules that have a pleated form in solution.[4,40] Miller and co-workers have used the self-stacking properties of NDIs to create anion radical dimers with excellent photophysical signatures.[7–9] The intercalation of NDIs into duplex DNA has been the focus of a number of investigations;[35,36,38–43] in these studies the monomeric form is desired. In contrast, the stacking properties of related bis(dicarboximide)s have been used in a quantitative assay for small amounts of DNA by precipitating the DNA–bis(dicarboximide) complex.[37] The design of new NDIs for specific analytical and structural purposes demands an understanding of the extent to which they stack, as well as the structural features and solution conditions that promote self-stacking.

Herein we report a study of the self-stacking of a series of cationic NDIs in water as measured by NMR techniques. We find that the position of the cationic center in the side chain plays a role in determining self-stacking; derivatives with side chains bearing positive charges close to the NDI ring stack less at NMR concentrations than those with cationic centers further from the NDI moiety. Self-stacking can also be induced by increasing the ionic strength of the solution. Some derivatives with aromatic side chains show intramolecular self-stacking of the side chain with the central NDI ring.

This study complements other NMR studies of stacking of aromatic molecules in aqueous solution. Leading references include work on DNA binding molecules,[52–57] porphyrins and related molecules,[58–70] pharmaceutical agents,[71,72] dyes and pigments,[73,74] flavins,[75] diimine complexes,[76] carboxylic acids and amides,[77–79] and caffeine.[80–83] There have also been extensive studies of ATP and related molecules.[47,84–89]

Results and discussion

Synthesis

Naphthalene-1,8 : 4,5-bis(dicarboximide)s are readily synthesized *via* condensation of the appropriate amine with the commercially available naphthalenetetracarboxylic dianhydride using toluene or DMF as the solvent. The aliphatic derivatives **1** and **2** (Fig. 1) were synthesized from the commercially available amines $H_2NCH_2CH_2CH_2NR_2$, followed by alkylation with the appropriate alkyl iodide (R′I) to give the $CH_2CH_2CH_2N^+R_2R'$ side chain. NDI **3** was made *via* initial condensation of mono-Boc protected hexane-1,6-diamine with the dianhydride followed by deprotection. The small aromatic derivatives **4**–**7** were synthesized from the commercially available amino-

† The compounds in this study are at least dications. Thus, unless one takes specific precautions, one can end up with a mixture of counter ions. Some of the materials are hygroscopic. It is possible to get solids with all one counter ion which are not hygroscopic (*e.g.* the PF_6^- salt). However, the work involved is substantial in that these forms of the compounds are not useful; the more water soluble (and hygroscopic) forms are needed. Therefore, capillary electrophoresis and NMR were used to establish purity and HRMS to establish elemental composition in this study.

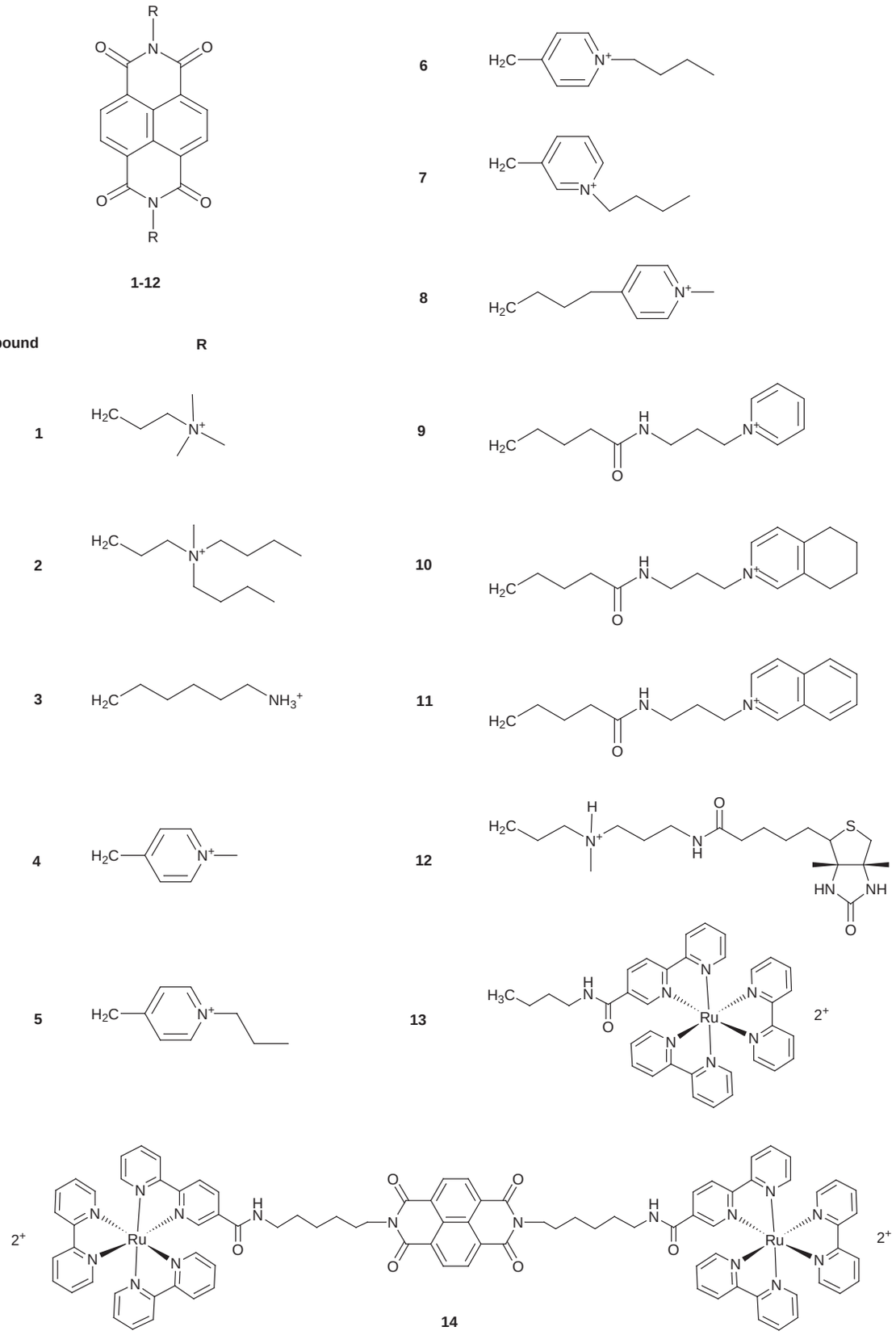

Fig. 1 Structures of naphthalene diimides used in this work.

pyridines, followed by alkylation with the appropriate alkyl iodide. Pyridinium derivative **8** was synthesized from the corresponding aminobutylpyridine. The pyridinium, tetrahydroisoquinolinium and isoquinolinium derivatives **9**, **10** and **11** used the diacid synthesized from naphthalene-1,4,5,8-tetracarboxylic dianhydride and 6-aminopentanoic acid as a starting material; condensation of the appropriate amine was effected with benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (BOP). A derivative with large aliphatic side chains, the biotin containing compound **12**, was constructed using the $H_2NCH_2CH_2CH_2N(Me)CH_2CH_2CH_2NH_2$ linker. The Boc-monoprotected diamine was allowed to condense with the naphthalene dianhydride. The product was deprotected and then condensed with biotin using BOP as a reagent. The largest derivative studied had side chains based on the ruthenium(II) polypyridine moiety, *i.e.* **13** as a side chain to

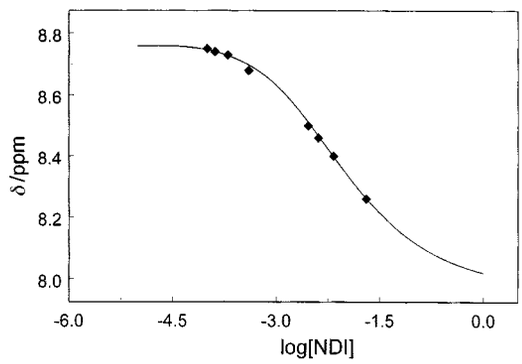

Fig. 2 Chemical shift of **3** as a function of its concentration in D_2O, 25 °C. The points are experimental. The line is the theoretical curve for a dimerization. Values for $\log(K_D) = 2.4 \times 10^2$ M^{-1}, $\delta_o = 8.73$ ppm and $\delta_i = 7.90$ ppm were calculated from a nonlinear least-squares fitting of the equation in the text.

give the NDI **14**. NDI **14** was made with a hexane-1,6-diamine-based linker. As above, the Boc-monoprotected hexane-1,6-diamine was allowed to condense with the naphthalene dianhydride. Deprotection followed by BOP-catalyzed amide formation with 2,2′-bipyridine-5-carboxylic acid led to the bipyridyl derivative, which was treated with *cis*-bis(2,2′-bipyridine)dichlororuthenium dihydrate to give **14**.

Nuclear magnetic resonance

NMR is a useful tool to probe the stacking of aromatic rings.[45,46,50] The effect of stacking the rings is to place one ring in the shielding cone of the second, resulting in upfield shifts of the ^1H resonances for the stacked rings. Each of the derivatives in this study has identical side chains on the two sides of the NDI ring. Therefore, the ^1H NMR signal due to the NDI ring itself is a singlet for the four equivalent protons of the ring in each case.

Aliphatic side chains

NDIs with small aliphatic cationic side chains are generally unstacked at NMR concentrations, as indicated by the downfield position of their NDI protons. For example, **1,** with aliphatic $CH_2CH_2CH_2N^+(CH_3)_3$ side chains, has a singlet for the NDI ring protons at 8.70 ppm in D_2O (40 °C). The chemical shift is the same as that observed in DMSO-d_6 (8.72 ppm, 40 °C). The similarity of the chemical shifts in water and in DMSO-d_6, a solvent that does not favor stacking, indicates that **1** is not stacked in aqueous solution. Lack of stacking at NMR concentrations (1–10 mM) is also indicated by the observation that the chemical shift of **1** has essentially no temperature dependence.

The NDI derivative bearing hexyl side chains, **3**, showed a greater tendency to self-stack in solution. Fig. 2 shows the chemical shift of **3** as a function of concentration. A simple dimerization may be expressed by eqn. (1). Expressing all

$$M + M \rightleftharpoons D \quad (1)$$

concentrations in terms of the monomer, one can obtain a dimerization constant K_D [eqn. (2)]. For a system in fast

$$K_D = [D]/2[M]^2 \quad (2)$$

exchange on the NMR time scale, the mole fractions of monomer (f_M) and dimer (f_D) can be calculated from the chemical shifts using eqn. (3) and (4), where δ_o is the chemical shift of the

$$f_M = (\delta - \delta_i)/(\delta_o - \delta_i) \quad (3)$$

$$f_D = (\delta_o - \delta)/(\delta_o - \delta_i) \quad (4)$$

fully unstacked species, δ_i is the chemical shift of the fully stacked species (monomer or oligomer), and δ is the chemical shift under the experimental conditions. It was found that data fits were far more reliable when the difference in the chemical shift between the NDI protons and the α-CH_2 protons in the same molecule was used as the variable ($\Delta = \delta_{NDI} - \delta_{\alpha\text{-}CH_2}$) rather than the chemical shift with respect to an internal standard. Thus, the equilibrium constant for self-stacking was calculated at each concentration as $K_D = f_D/2f_M^2 = (\Delta_o - \Delta_i) \times (\Delta_o - \Delta)/\{(\Delta - \Delta_i)^2\, 2[C_t]\}$ where the Δ are defined analogously to the δ above and $[C_t]$ is the total concentration of NDI in solution. Non-linear least-squares fitting of the extent of stacking as a function of the concentration of **3** gave calculated values for δ_o, δ_i and K_D of 8.73 ppm, 7.90 ppm and 2.4×10^2 M^{-1}, respectively. The value for δ_o of 8.73 ppm is very similar to the chemical shift of **1** (above) and other unstacked NDIs (see below). The data herein have been treated in terms of a simple 1 : 1 dimerization. As pointed out in previous studies, mathematical analyses of self-stacking in terms of either simple dimerization or larger structures (the isodesmic model) are very similar; the equilibrium constants for the isodesmic model are a factor of two larger than the dimerization model if the chemical shift change due to stacking in the center of a stack is taken to be twice that of the chemical shift change in the dimer.[80,82]

The equilibrium was also probed by recording the NMR spectrum of **3** as a function of temperature. As the temperature increased, the NDI resonance moved smoothly upfield. Non-linear least-squares fitting of Δ as a function of temperature according to the van't Hoff equation (see the Experimental) gave values for δ_o, δ_i, ΔH and ΔS. When all four variables were fit, values of 8.75 ppm, 8.24 ppm, −7.4 kcal mol^{-1} and −10.5 e.u., respectively, were obtained. The value of 8.75 ppm for δ_o is in excellent agreement with that of 8.73 ppm from the concentration studies. The values for ΔH and ΔS allow calculation of an equilibrium constant of 1.4×10^3 M^{-1} at 25 °C. This equilibrium constant is a factor of approximately six higher than that calculated from the concentration data. The difference in the calculated values presumably arises because the chemical shifts are dependent not only on self-stacking but also on temperature. This is seen in the value of δ_i in the temperature study (8.24 ppm) which is different from that in the concentration study (7.90 ppm). It should also be noted that the temperature data encompass a narrower range of stacking (approximately 60–80%) than do the concentration data (approximately 40–100%).

The related derivative **2**, with $CH_2CH_2CH_2N^+Bu_2CH_3$ side chains, was also studied. This derivative has a cationic center three atoms away from the NDI ring, as does **1**, but has six more carbon atoms total in each side chain than **3** (twelve for **2** as opposed to six for **3**). The chemical shift of the NDI ring protons of **2**, 8.69 ppm (50 °C), is very similar to that of the NDI protons of **1**, 8.72 ppm, at the same temperature. The chemical shift of **2** is slightly temperature dependent, increasing from 8.64 ppm at 25 °C to 8.73 ppm at 90 °C. Both the value of the chemical shift itself and the small dependence of the chemical shift on temperature indicate only very slight stacking of the NDI ring at room temperature. This stacking is considerably less than that observed for the hexyl derivative **3**, arguing that the position of the cationic center in the side chain has a dominant effect on stacking in aqueous solution, with cationic centers closer to the NDI ring giving less self-stacking.

The largest derivative studied with aliphatic side chains was the bisbiotin derivative, **12**. This compound shows little stacking in D_2O at NMR concentrations as indicated by the chemical shift of the NDI ring at 8.75 ppm (30 °C). Thus, larger side chains *per se* do not necessarily promote self-stacking. The chemical shift for the NDI ring protons of unstacked aliphatic derivatives is approximately 8.7–8.8 ppm in D_2O. In this context it is worth noting that the chemical shift of the NDI ring protons for monomeric NDIs is independent of the placement of

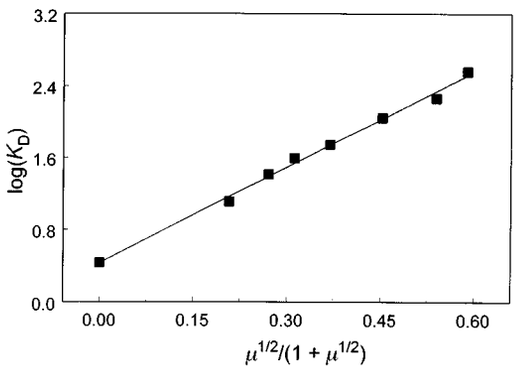

Fig. 3 Log(K_D) *vs.* $\mu^{1/2}/(1 + \mu^{1/2})$ for NDI **1** (8 mM **1**, added NaCl, D_2O, 25 °C). The points are experimental. The line is the theoretical curve for a dimerization. Values for $\log(K_{Do}) = 2.6$ M^{-1} and $\delta_o = 8.73$ ppm were calculated from a nonlinear least-squares fitting of the equation in the Experimental.

the cationic center in the side chain. For example, two derivatives with cationic centers three atoms away from the NDI ring, dibutylmethylammonium derivative **2** (8.78 ppm in CD_3OD) and the trimethylammonium derivative **1** (8.71 ppm in DMSO-d_6) have NDI chemical shifts that are almost the same as derivatives with neutral side chains. The NDIs with $[CH_2]_6$-NHBoc and $[CH_2]_5COOH$ side chains, as well as the tertiary amine precursor to **1**, all have chemical shifts of 8.7–8.8 ppm in DMSO-d_6.

Ionic strength dependence of stacking

Stacking can be induced by increasing the ionic strength of the solution. The chemical shift of the NDI protons for **1** decreased smoothly from 8.73 to 8.55 ppm as the salt concentration was increased from no added salt to 2.1 M NaCl (8 mM **1**, D_2O, 25 °C). In general, self-stacking of aromatic moieties as a function of salt concentration can be described by calculating the equilibrium constant for self-stacking as a function of the ionic strength. One approach is to treat self-stacking as a dimerization and plot the change in K_D as a function of ionic strength using the Debye–Hückel limiting law [69] [eqn. (5)], where K_{Do} is

$$\log(K_D) = \log(K_{Do}) + 2Az_Az_B\mu^{1/2}/(1 + \mu^{1/2}) \qquad (5)$$

the limiting value of K_D at zero ionic strength, μ is the ionic strength and z_A and z_B are the charges on the respective halves of the dimer (equal for self-stacking). For water, A is 0.509 at room temperature.[90] Non-linear least squares fitting of the chemical shift as a function of ionic strength (see Experimental) gave values for Δ_o, Δ_i and K_{Do} of 4.42 ppm, 4.20 ppm and 2.6 M^{-1}, respectively. The K_D were calculated from these chemical shifts as described above. Fig. 3 shows a plot of $\log(K_D)$ *vs.* $\mu^{1/2}/(1 + \mu^{1/2})$ for **1**. Data at low salt allowed calculation of a value of δ_o of 8.73, but the lack of a good number for the chemical shift of the α-CH_2 protons at infinite salt concentration makes estimation of δ_i speculative. The value of δ_o for the fully unstacked NDI for the salt concentration studies of **1** is the same as the value of 8.73 ppm from the concentration studies of **3**. It is also consistent with the general observation that NDI derivatives in solvents that disfavor stacking (*e.g.* DMSO-d_6) also have chemical shifts of 8.7–8.8 ppm. Values of K_{Do} calculated from the Debye–Hückel limiting law may have systematic errors because the assumptions on which the law is based are not valid at high ionic strengths.[69] Nevertheless, the approximate value of K_{Do} for **1** of 2.6 M^{-1} is lower than that of the more hydrophobic **3** and consistent with the observation that **1** itself does not self-stack in D_2O in the absence of salt.

To probe the effect of salt on an NDI derivative with a greater tendency to stack, the NMR spectrum of **3** was recorded as a function of NaCl concentration. The chemical shift of the NDI resonances of a solution of **3** (8 mM) decreased from 8.37 to 8.30 ppm as the concentration of NaCl was increased from 0.0 to 0.27 M NaCl, consistent with increased self-stacking with increased NaCl concentration. At higher salt concentrations, **3** precipitated. This is again consistent with NDI derivatives with positive charges further from the central NDI ring stacking more readily, as observed above. Politi and co-workers have observed aggregation of the *N*,*N*′-dibutylnaphthalene-1,8:4,5-bis(dicarboximide) in aqueous solution with a critical concentration of less than 10^{-6} M.[15]

Pyridinium side chains

A series of NDI derivatives with pyridinium side chains was also studied. The first molecule, **4**, which has the small 1-methylpyridin-1-ium-4-yl aromatic side chain, has a chemical shift of 8.84 ppm in D_2O (25 °C). This chemical shift is slightly downfield of those of the aliphatic derivatives, presumably due to the ring current effects of the pyridinium ring on the NDI ring. The chemical shift of **4** is almost invariant with temperature from 25 to 90 °C, decreasing by only 0.03 ppm as the temperature is raised between these values (Table 1). This indicates that **4** is not stacked at NMR concentrations. NDI **6**, the *N*-butyl homolog of **4**, is very similar to **4**, with a chemical shift of 8.83 ppm at 20 °C. NDI **6** also showed almost no change in chemical shift as the temperature was raised. Other examples of pyridinium NDI derivatives that are unstacked at NMR concentrations include the 1-propylpyridin-1-ium-4-yl (**5**) and 1-butylpyridin-1-ium-3-yl (**7**) derivatives (Table 1). In all of these cases, the pyridinium ring is separated from the NDI ring by only one CH_2 group and thus the pyridinium ring cannot stack intramolecularly with the NDI ring.

Three pyridinium derivatives with longer side chains were studied: NDI **8**, with four atoms between the NDI and pyridinium rings; NDI **9**, with nine atoms between the NDI and pyridinium rings; and the tetrahydroisoquinolinium derivative **10**. For all three of these derivatives, molecular modeling shows that the side chains are long enough for the pyridinium rings to stack intramolecularly with the NDI ring. NMR evidence, however, indicates minimal intramolecular stacking of the pyridinium rings.

The chemical shift of the NDI protons of **9** is 8.42 ppm in D_2O (25 °C). There are two indications that the role of intramolecular stacking of the pyridinium ring with the NDI ring is minimal. First, the upfield chemical shifts of the pyridinium ring in **9** (2,6-H 8.90 ppm; 3,5-H 8.12 ppm) are very similar to those of the precursor for this side chain (2,6-H 8.88 ppm; 3,5-H 8.08 ppm, Table 1). Second, the chemical shifts of the pyridinium ring of **9** in D_2O are very similar to those in DMSO-d_6 (2,6-H 8.90 and 9.05 ppm; 3,5-H 8.12 and 8.13 ppm; 4-H 8.58 and 8.55 ppm in D_2O and DMSO-d_6, respectively). The upfield chemical shift of the NDI protons in water (8.42 ppm, 25 °C) compared to DMSO-d_6 (8.68 ppm, 25 °C) indicates that **9** undergoes intermolecular stacking at NMR concentrations in water.

The tetrahydroisoquinolinium NDI **10** may also be considered as a pyridinium derivative. The chemical shifts of the aromatic protons of the tetrahydroisoquinolinium ring are almost the same in the precursor tetrahydroisoquinoliniumylpropylamine as in NDI **10** (Table 1). This indicates that there is little intramolecular stacking of the tetrahydroisoquinolinium ring with the NDI ring. However, the upfield chemical shift of the NDI ring protons, 8.2 ppm at 25 °C, indicates substantial intermolecular stacking of this derivative at NMR concentrations.

Pyridinium derivative **8** is a structural isomer of **6** in which the pyridinium ring has been formally moved along the methylene chain away from the NDI ring to give the $CH_2CH_2CH_2$-CH_2–pyridinium–Me derivative. NDI **8** has a chemical shift for the NDI ring protons of 8.26 ppm (25 °C). In line with the

Table 1 Chemical shifts (ppm) of the aromatic protons of NDI derivatives in D_2O

Compound	*T*/°C	Chemical shifts (δ_H)			
Aliphatic derivatives		NDI			
1	40	8.70			
2	25	8.64			
3	90	8.73			
12	30	8.75			
Pyridine derivatives		NDI	2,6-H	3,5-H	
4	25	8.84	8.74	8.10	
	50	8.85	8.72	8.08	
	90	8.81	8.68	8.02	
5	80	8.76	8.69	8.02	
6	22	8.83	8.80	8.08	
	60	8.82	8.75	8.05	
7[a]	60	8.80	8.61 (6-H)	8.02 (5-H)	
8	22	8.26	8.59	7.89	
9[b]	25	8.42	8.90	8.12	
pyridiniumyl propylamine[c]	25		8.88	8.08	
Tetrahydroisoquinoline derivatives		NDI	1-H	3-H	4-H
10	30	8.2 (br)	8.51	8.42	7.70
tetrahydroisoquinoliniumyl propylamine	22		8.59	8.47	7.76
Isoquinoline derivatives		NDI	Ring protons		
11	30	8.4	9.54, 8.51, 8.32, 8.20, 8.12 (2H), 7.92		
isoquinoliniumyl propylamine	30		9.80, 8.56, 8.48 (2H), 8.28 (2H), 8.10		

[a] 2-H at 8.98 ppm, 4-H at 8.61 ppm. [b] 4-H at 8.58 ppm. [c] 4-H at 8.55 ppm.

observations for **9** and **10** above, we assign this upfield shift largely to intermolecular self-stacking of the NDI rings. The NDI chemical shift differences between **2** ($CH_2CH_2CH_2N^+Bu_2CH_3$) and **3** ($CH_2CH_2CH_2CH_2CH_2CH_2NH_3^+$) and between pyridinium derivatives **6** (CH_2–pyridinium–$CH_2CH_2CH_2CH_3$) and **8** ($CH_2CH_2CH_2CH_2$–pyridinium–CH_3) indicate that the NDI moiety has a greater tendency to self-stack as the positive charge is moved farther from the central NDI core.

An isoquinolinium derivative

Isoquinolinium derivative **11** has a chemical shift for the NDI ring protons of 8.4 ppm in D_2O (30 °C). The upfield shift of the NDI protons in this derivative can be due to both intermolecular stacking of the NDI itself and intramolecular interactions of the isoquinolinium group with the NDI moiety. The chemical shifts of the isoquinolinium group when attached to the NDI are upfield (range 7.92–9.54 ppm) of the chemical shifts of the parent isoquinoliniumylpropylamine (range 8.10–9.80 ppm) indicating that the isoquinoline is affected by the presence nearby of the NDI ring. Heating a sample of isoquinolinium derivative **11** from 25 to 80 °C resulted in the NDI peak moving from 8.37 to 8.50 ppm, indicating unstacking as the temperature was raised. The chemical shifts of the protons of the isoquinolinium ring also shifted downfield (*i.e.* toward the shifts of the parent isoquinoliniumylpropylamine) as the temperature was raised. The biggest change, observed for the doublet at 8.12 ppm, was 0.1 ppm. This is consistent with at least some intramolecular stacking of the isoquinolinium moiety.

The $[Ru(bpy)_3^{2+}]_2$ NDI derivative 14

Compound **14** can also stack both intramolecularly and intermolecularly. At 25 °C, the NDI protons of **14** are at 8.21 ppm (8 mM). This chemical shift compares with those for the same molecule of 8.48, 8.66 and 8.72 ppm in CD_3CN, CD_3OD and DMSO-d_6, respectively. The upfield shift in water, compared with the downfield shifts in CD_3OD and DMSO-d_6, solvents not expected to favor self-stacking, indicates substantial stacking of the NDI rings in water at room temperature. Even at a concentration of only 20 μM, the chemical shift of the NDI ring protons is still 8.48 ppm in water at 25 °C, indicating some interaction of the NDI ring with another aromatic moiety.

A detailed analysis of the bipyridine ring chemical shifts indicates interactions between the NDI and bipyridine moieties. In **14**, the protons of the bipyridine rings show complicated splitting patterns. To assess these, the spectrum of **14** in water was compared with the spectrum of the same molecule in methanol and with the spectrum in water of a model system bearing two unsubstituted bipyridine rings and one substituted bipyridine ring, **13** (Fig. 4). The $Ru(bpy)_3^{2+}$ moiety in **13** has 23 inequivalent bipyridine protons, eight each in the two unsubstituted rings and seven in the substituted ring. Table 2 gives the assignments of the ring protons, made through the COSY data set (see Fig. 4 for labels). The unique ring with the amide substituent at the 5-position is seen clearly, with the 3-H, 4-H and 6-H assigned as 8.54–8.65 (m), 8.31 (d) and 7.98 ppm (s), respectively. The remaining five bipyridine moieties have very similar chemical shifts, as would be expected because each of these rings is in a very similar chemical environment. However, sets of resonances can be distinguished for each different type of proton, with the 3-H, 4-H, 5-H and 6-H assigned as multiplets at 7.80–7.89, 7.40–7.48, 8.07–8.14 and 8.54–8.65 ppm, respectively. The net chemical shift spread for the bipyridine resonances in D_2O at 30 °C is 1.4 ppm (7.4–8.7).

In methanol, the shift patterns of the aromatic resonances of **14** are very similar to those of the model compound **13**. This indicates that **14** is unfolded in this solution, *i.e.* that the bipyridine rings do not spend a substantial amount of time over the NDI ring. In water, the complexity of the shift patterns in **14** is greater than that in methanol and greater than that of model compound **13** in water, as can be seen in Fig. 4. However,

Table 2 Chemical shifts of bipyridine ring protons in **13** and **14** (D_2O, 50 °C, 500 MHz)[a]

Compound		δ_H 3-H	4-H	5-H	6-H
13	ring				
	1	8.54–8.65[b]	8.31[b] (d)	—	7.98 (s)
	2–6	7.80–7.89	7.4–7.48	8.07–8.14	8.54–8.65
14	ring				
	1	8.62–8.67	8.27 (dd)	—	[c]
	2	7.73 (d)	7.36–7.43	8.03–8.15	8.52–8.58
	3	7.80 (d)	7.31–7.35	7.91–7.95 (t)	8.49 (d)
	4	7.85–7.89	7.44–7.49	8.03–8.15	8.62–8.67
	5	7.80 (d)	7.36–7.43	8.03–8.15	8.52–8.58
	6	7.86–7.89	7.44–7.49	8.03–8.15	8.52–8.58

[a] All peaks appear as multiplets unless otherwise indicated. The appearance as a multiplet is often due to overlap of the resonances from more than one ring. [b] Assumes the 3-H to be the farther downfield of the 3-H, 4-H coupled pair. [c] Probably in the 7.91–7.95 ppm region from the integrated intensities.

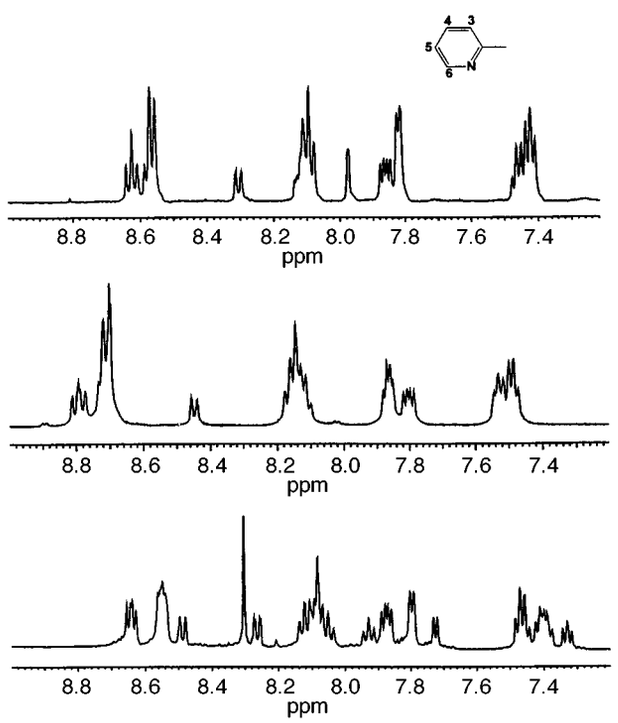

Fig. 4 Aromatic region (500 MHz) of the 1D spectra of **13** in D_2O (top, 50 °C), **14** in CD_3OD (center, 25 °C) and **14** in D_2O (bottom, 50 °C).

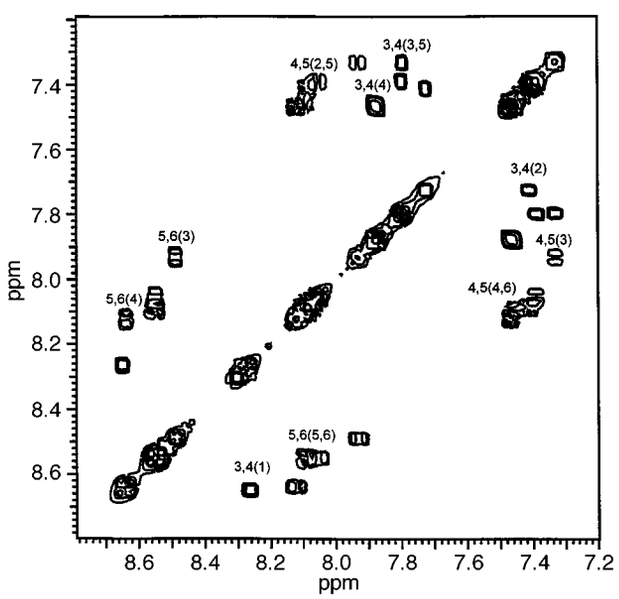

Fig. 5 COSY spectrum of the aromatic region of **14** in D_2O (50 °C, 8 mM, 500 MHz). The substituted ring is labeled 1; the unsubstituted bipyridine rings are arbitrarily labeled 2–6. Labels on the COSY data set refer to the position of the protons on the ring and the number of the ring, *e.g.* 4,5(2,5) are the 4 and 5 protons on rings 2 and 5.

the net chemical shift spread of **14**, 1.5 ppm (7.2–8.7 ppm) is not much larger than that of the model compound **13** in D_2O. The increased complexity of the chemical shift pattern of **14** implies that the different protons in the bipyridine rings feel slightly different magnetic fields. This is consistent with favored conformations in which the $Ru(bpy)_3^{2+}$ moiety lies, at least in part, in the shielding cone over the aromatic NDI ring system. This results in each of the bipyridine protons experiencing a different magnetic environment, leading to spreads of the multiplets of the bipyridine ring protons. Slight differences in the effective magnetic field experienced by the different bipyridine rings is seen most clearly in the COSY of **14** (Fig. 5), which shows one of the unsubstituted bipyridine rings to be shifted upfield (Table 2). The upfield-shifted ring has resonances for the 3-H, 4-H, 5-H and 6-H of 7.8 (d), 7.31–7.35 (m), 7.91–7.95 (t) and 8.49 ppm (d). The unique 5-substituted ring shows chemical shifts very similar to the unique 5-substituted ring of model compound **13**, with the 3-H, 4-H and 6-H assigned in the regions 8.6, 8.3 and 7.95 ppm, respectively. This indicates that the unique 5-substituted ring lies beyond the effect of the NDI ring current.

Fig. 6 shows two different minimized geometries for **14**. In the top conformation, one of the unsubstituted bipyridine rings partially overlaps the NDI ring. In the bottom conformation, neither of the bipyridine rings is stacked over the NDI ring; in this conformation both unsubstituted bipyridine rings adopt similar geometries in which they are approximately at 45° to the NDI ring. Both structures have comparable energies and are also similar in energy to the fully extended conformation. Many other, less symmetrical, structures are also possible (large set of structures within 10 kcal mol^{-1} of one another). Different conformations of **14** have very different Ru–Ru distances. Both structures in Fig. 6 have Ru–Ru distances of approximately 13 Å while the fully extended structure has a Ru–Ru distance of 37 Å. Calculations were done without explicit solvent, and thus can be used to obtain a picture of the conformations that this structure can achieve but should not be interpreted as indicative of specific geometric interactions between the aromatic rings.

It should be noted that the complexity of the spectrum of **14** is not due to the presence of isomers. Each $Ru(bpy)_3^{2+}$ is intrinsically chiral, giving rise to Δ,Λ (*meso*) as well as Λ,Λ and Δ,Δ pairs (*dl*) of isomers. The *meso, dl* isomers of joined Δ and Λ $Ru(bpy)_3^{2+}$ entities have been observed by ^1H NMR when the two $Ru(bpy)_3^{2+}$ groups are near one another.[91,92] In the present case, however, the two ruthenium centers are expected to be

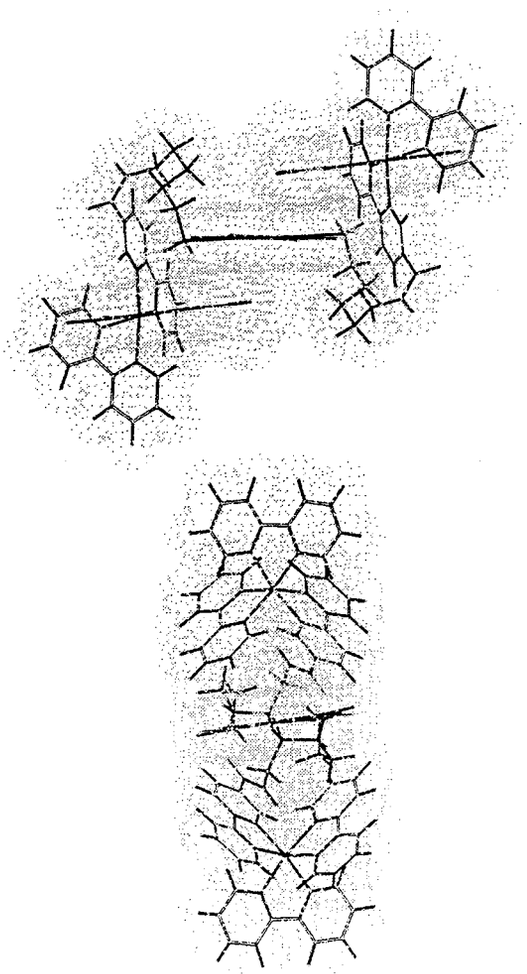

Fig. 6 Molecular models of two conformations of **14**; the energies of the minimized structures differ by only approximately 1 kcal mol^{-1}.

too far apart to have a measurable magnetic effect upon one another. In addition, had the intrinsic existence of *dl* isomers had a significant effect on the NMR spectrum, one also might have expected the spectra in methanol and water to have been of similar complexity.

Fig. 7 shows the aromatic region of the NMR spectrum of **14** as a function of temperature at intervals from 20 to 90 °C. The NDI singlet moves downfield as the temperature is increased (0.26 ppm from 20 to 90 °C), as would be expected for destacking of the aromatic rings with increasing temperature. Non-linear least-squares analyses of the chemical shifts to both intramolecular (open $\rightleftharpoons$ closed) and intermolecular (2 M $\rightleftharpoons$ D) models gave similar fits, and thus did not allow a choice between these two models.

Three lines of evidence indicate that both intramolecular and intermolecular stacking are taking place. First, as seen in Fig. 7, the chemical shift patterns of the bipyridine resonances are quite temperature sensitive. This indicates intramolecular stacking. The bipyridine rings are six methylene units removed from the NDI center; intermolecular stacking of the NDI alone would not be expected to produce such major temperature-induced changes in the bipyridine rings. Second, the chemical shift changes of the methylene groups in the side chain as a function of temperature are larger in **14** (both intra- and intermolecular stacking possibilities) than those in **3** (only intermolecular stacking possible). The data are shown in Fig. 8. For **14**, the chemical shift of the CH_2 group adjacent to the dicarboximide ring is the most sensitive to temperature; it increases by 0.28 ppm as the temperature is raised from 20 to 90 °C. As one moves along the chain away from the diimide nucleus, the effect diminishes; the methylene group adjacent to

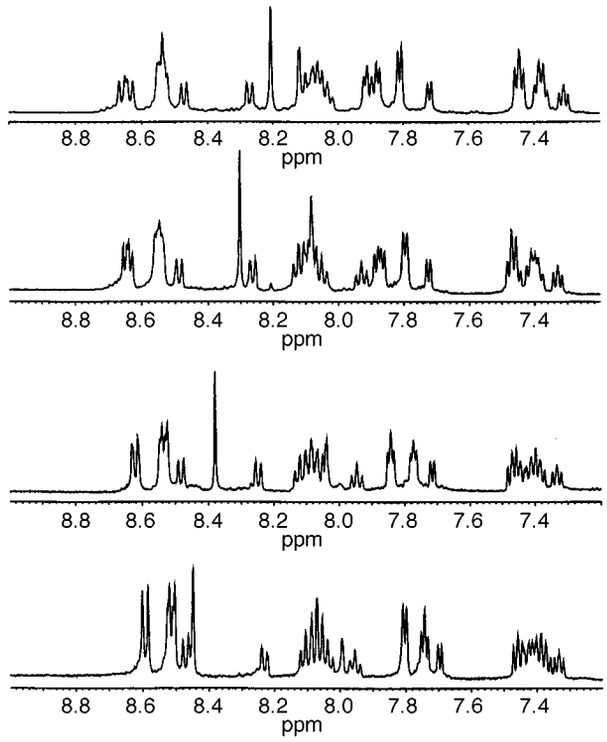

Fig. 7 Aromatic region of the ^1H NMR of **14** (8 mM) as a function of temperature in D_2O. Temperature increases from top to bottom: 20, 50, 70, 90 °C. Chemical shifts were measured from the HOD line.

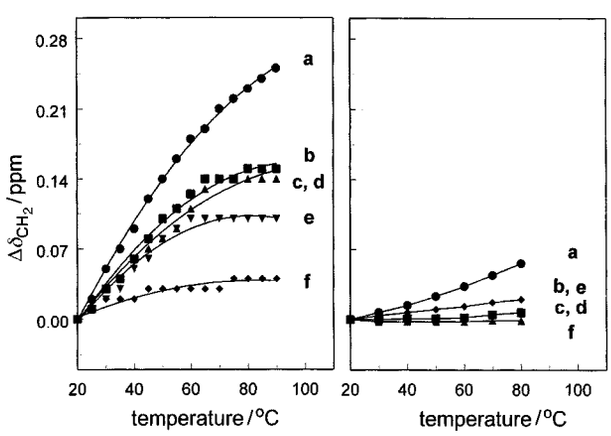

Fig. 8 Chemical shift $\Delta\delta_{CH_2} = \delta_{CH_2}(T) - \delta_{CH_2}(25\,°C)$ of the side chain protons of **14** (8 mM, left hand panel) and **3** (8 mM, right hand panel) as a function of temperature in D_2O. Methylene units are labeled a–f in increasing distance from the imide nitrogen.

the $Ru(bpy)_3^{2+}$ moiety shows almost no change in chemical shift with increasing temperature (<0.04 ppm). For **3**, the chemical shift of the CH_2 group adjacent to the dicarboximide ring is also the most sensitive to temperature, but the changes for all of the side chain protons with temperature are much smaller than for **14**. Because **3** can undergo only intermolecular stacking, the greater chemical shift changes as a function of temperature for **14** indicate that this derivative undergoes both intramolecular and intermolecular stacking. The third line of evidence for both intra- and intermolecular stacking is the difference between the chemical shifts of the NDI and α-CH_2 protons as a function of temperature. For **3** at a concentration of 8 mM, this difference increases monotonically as the temperature increases (Fig. 9). For **14** at low concentration (20 μM), the difference also increases monotonically as the temperature increases but the change is somewhat smaller than that seen for **3**. For **14** at 8 mM, however, the difference first decreases and then increases (Fig. 9). Taken together, these data indicate that at least two

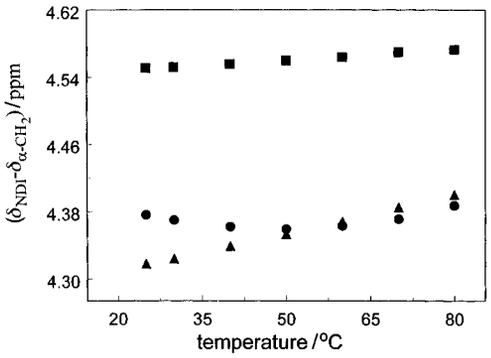

Fig. 9 Chemical shifts ($\delta_{NDI} - \delta_{\alpha\text{-}CH_2}$) of **3** and **14** as a function of temperature in D_2O: (▲) **3**, 8 mM; (●) **14**, 8 mM; (■) **14**, 20 μM.

processes are taking place as a function of temperature for **14** at 8 mM (intramolecular and intermolecular stacking), while only one process is taking place as a function of temperature at 20 μM (intramolecular stacking).

Conclusions

Naphthalene-1,8:4,5-bis(dicarboximide)s can self-stack in solution. The tendency to aggregate is a function of the side chains on the molecule. Examples with cationic centers near the NDI ring, *e.g.* $CH_2CH_2CH_2N^+R_3$ or CH_2–pyridinium–R derivatives, do not generally self-stack significantly at NMR concentrations. Even a large side chain, as found in the bis-biotin derivative, does not cause the NDI rings to self-stack. However, moving the charge further away from the central NDI ring results in a significant tendency to self-stack. Examples of NDIs that are substantially self-stacked in water at NMR concentrations include those bearing side chains with the groups: $(CH_2)_4$–pyridinium–Me, $(CH_2)_6NH_3^+$, $[CH_2]_6NHCO$-$Ru(bpy)_3^{2+}$ and $(CH_2)_4CONH(CH_2)_3R$. NDI derivatives with aromatic moieties in the side chain can also undergo intramolecular stacking. Examples include side chains terminating in isoquinolinium and $Ru(bpy)_3^{2+}$ moieties; side chains ending in pyridinium groups do not appear to undergo significant intramolecular self-stacking with the NDI core. The chemical shift data and dependence of the NMR spectrum on temperature for **14** are interpreted in terms of both intramolecular interactions of the $Ru(bpy)_3^{2+}$ groups with the NDI ring and intermolecular self-stacking of the NDI rings. Overall, the propensity of a naphthalene-1,8:4,5-bis(dicarboximide) to self-stack can be controlled to a significant extent by the design of the molecule, most effectively by the placement of the cationic centers in the side chain.

Experimental

NMR experiments

These were performed on Varian Unity+ 500 and 600 MHz spectrometers. Data were collected and processed using the Varian library of pulse programs and Varian software packages. NMR samples were prepared in D_2O (Aldrich) in 5 mm NMR tubes. Chemical shifts were measured from the HOD line (4.7718 ppm at 25 °C) corrected for temperature changes with a correction factor of −0.01037 ppm per degree or internal dioxane (3.743 ppm, assumed to be temperature independent). ^1H–^1H correlation COSY (absolute value) spectra were recorded at 500 MHz, 50 °C, using the same spectral width in *F*1 and *F*2, 4296.9 Hz and 2592.5 Hz for **14** and **13** respectively. For **14**, the HDO signal was reduced by selective irradiation during the delay time; 2048 complex points were recorded for each of 516 t_1 increments. For **13**, 1024 complex points were recorded for each of 256 t_1 increments. Data workup used the unshifted sine-bell squared function for apodization. The data were Fourier-transformed in both dimensions and symmetrized about the diagonal. Molecular modeling was done using Sybyl 6.1, Tripos Associates, St. Louis, MO.

Non-linear least-squares fitting was performed using KaleidaGraph (Synergy Software). Best results were usually obtained on data sets using chemical shift differences between two peaks in the compound, *e.g.* ($\Delta = \delta_{NDI} - \delta_{\alpha\text{-}CH_2}$) rather than the chemical shift with respect to an internal standard. In all cases a simple dimerization (1:1 complex) was assumed. Concentration data were fitted as described in the text. Temperature data were fitted to the van't Hoff equation for the open $\rightleftharpoons$ closed model: $T = \Delta H/\{\Delta S - R\ln[(\Delta_{closed} - \Delta)/(\Delta - \Delta_{open})]\}$ and 2 M $\rightleftharpoons$ D model: $T = \Delta H/(\Delta S - R\ln\{(\Delta_o - \Delta_i)\text{-}(\Delta_o - \Delta)/(\Delta - \Delta_i)^2 2[C_t]\})$.[93] Data as a function of ionic strength were fitted to the Debye–Hückel limiting law as $\mu^{1/2}/(1 + \mu^{1/2}) = [\log\{((\Delta_o - \Delta_i)(\Delta_o - \Delta))/(\Delta - \Delta_i)^2 2[C_t]\} - \log(K_{Do})]/\text{slope}$. Compound **1** was approximately 5–70% stacked from 0–2.1 M NaCl.

Capillary electrophoresis

Experiments were performed using a Beckman PACE 5510 instrument equipped with a fused-silica capillary (57 cm × 75 μm i.d.) and P/ACE diode array detector. Electrophoresis was performed at a voltage of 13 kV. The sample was introduced into the capillary by high pressure injection for 5 s. A solution of 50 mM sodium phosphate, pH 2.06 was used as the buffer electrolyte.

Mass spectra

FAB mass spectra were run on a VG Instruments 70SE mass spectrometer with a primary xenon beam (8 kV) using *m*-nitrobenzyl alcohol as the carrier. Electron impact mass spectra were run on a VG Instruments 70SE mass spectrometer. Electrospray mass spectra were run on a Micromass Platform II spectrometer.

Syntheses

N-*tert*-Butoxycarbonylhexane-1,6-diamine hydrochloride was purchased from Fluka; *cis*-bis(2,2′-bipyridine)dichlororuthenium was purchased from ALFA. All other reagents were obtained from Aldrich. Dry *N*,*N*-dimethylformamide (DMF) was used as received from Aldrich. Neutral alumina (150 mesh, Brockman I, Aldrich) was deactivated by adding 6% water before use in chromatography of the metal complexes. 2,2′-Bipyridine-5-carboxylic acid was prepared according to the literature.[94] Ether refers to diethyl ether.

N,*N*′-Bis(3-*N*,*N*-dimethylaminopropyl)naphthalene-1,8:4,5-bis(dicarboximide) 15[7,35]

A mixture of naphthalene-1,4,5,8-tetracarboxylic dianhydride (1.3 g, 5.0 mmol) and *N*,*N*-dimethylpropane-1,3-diamine (1.0 g, 10 mmol) in toluene (150 mL) was stirred and refluxed with a Dean–Stark receiver for 3 h. The product was filtered, washed with hot toluene, ethanol and ether and dried (1.8 g, 83%). ^1H NMR (DMSO-d_6, 70 °C): δ 1.81 [m, 4H, $CH_2CH_2N(CH_3)_2$], 2.13 (s, 12H, CH_3), 2.35 [t, 4H, $CH_2N(CH_3)_2$], 4.13 [t, 4H, $CH_2(CH_2)_2N(CH_3)_2$], 8.68 (s, 4H, Ar); FAB-MS *m*/*z* 437.2273 (M + H^+, calc. 437.2189 for $C_{24}H_{28}N_4O_4$).

N,*N*′-Bis(3-*N*,*N*,*N*-trimethylammoniopropyl)naphthalene-1,8:4,5-bis(dicarboximide) diiodide 1[7]

A mixture of *N*,*N*′-bis(*N*,*N*-dimethylaminopropyl)naphthalene-1,8:4,5-bis(dicarboximide) (0.44 g, 1.0 mmol) and iodomethane (1 mL) in ethanol (10 mL) was stirred and heated at a bath temperature of 60 °C for 1 day. The mixture was evaporated and the residue recrystallized from water to give 0.45 g (63%) of a yellow solid. ^1H NMR (DMSO-d_6, 40 °C): δ 2.16

[m, 4H, $CH_2CH_2N^+(CH_3)_3$], 3.03 (s, 18H, CH_3), 3.48 [t, 4H, $CH_2N^+(CH_3)_3$], 4.18 [t, 4H, $CH_2(CH_2)_2N^+(CH_3)_3$], 8.72 (s, 4H Ar); FAB-MS *m/z* 466.2576 (M^+, calc. 466.2580 for $C_{26}H_{34}N_4O_4$).

N,*N*′-Bis(3-*N*,*N*-dibutylaminopropyl)naphthalene-1,8:4,5-bis(dicarboximide)[95]

A mixture of naphthalene-1,4,5,8-tetracarboxylic dianhydride (1.3 g, 5.0 mmol) and *N*,*N*-dibutylpropane-1,3-diamine (1.9 g, 10 mmol) in toluene (150 mL) was stirred and refluxed with a Dean–Stark receiver for 3 h. The reaction mixture was cooled and evaporated. The product was recrystallized from MeOH to give 2.3 g (76%) of a light brown solid. ^{1}H NMR ($CDCl_3$, 25 °C): δ 0.88 (t, 12H, CH_3), 1.28 (m, 8H, CH_2CH_3), 1.37 (m, 8H, $CH_2CH_2CH_3$), 1.88 (m, 4H, $CH_2CH_2NBu_2$), 2.38 [m, 8H, $CH_2(CH_2)_2CH_3$], 2.57 (t, 4H, CH_2NBu_2), 4.21 [t, 4H, $CH_2(CH_2)_2NBu_2$], 8.77 (s, 4H, Ar); FAB-MS *m/z* 605.4067 ($M + H^+$, calc. 605.4083 for $C_{36}H_{52}N_4O_4$).

N,*N*′-Bis(3-*N*,*N*-dibutyl-*N*-methylammoniopropyl)naphthalene-1,8:4,5-bis(dicarboximide) diiodide 2

A mixture of *N*,*N*′-bis(3-*N*,*N*-dibutylaminopropyl)naphthalene-1,8:4,5-bis(dicarboximide) (0.61 g, 1.0 mmol) and iodomethane (0.30 g, 2.1 mmol) in toluene (10 mL) was stirred and heated at a bath temperature of 60 °C for 1 day. The product was filtered and recrystallized from EtOH to give 0.75 g (84%) product. ^{1}H NMR (CD_3OD, 22 °C): δ 1.0 (t, 12H, CH_2CH_3), 1.41 (m, 8H, CH_2CH_3), 1.72 (m, 8H, $CH_2CH_2CH_3$), 2.23 (m, 4H, $CH_2CH_2CH_2N^+Bu_2CH_3$), 3.05 [br s, 14H, CH_3, $CH_2(CH_2)_2CH_3$], 3.5 (t, 4H, $CH_2CH_2CH_2N^+CH_3Bu_2$), 4.3 (t, 4H, $CH_2CH_2CH_2N^+Bu_2CH_3$), 8.79 (s, 4H, Ar); FAB-MS *m/z* 634.4399 (M^+, calc. 634.4458 for $C_{38}H_{58}N_4O_4$).

N,*N*′-Bis(6-aminohexyl)naphthalene-1,8:4,5-bis(dicarboximide) 16[95]

N-*tert*-Butoxycarbonylhexane-1,6-diamine hydrochloride (0.51 g, 2.0 mmol) and sodium bicarbonate (0.17 g, 2.0 mmol) were mixed in water, evaporated and redissolved in toluene. Naphthalene-1,4,5,8-tetracarboxylic dianhydride (0.27 g, 1.0 mmol) was added to the solution. The mixture was stirred and refluxed with a Dean–Stark receiver for 5 h. The reaction mixture was evaporated, washed with water, ethanol and ether and dried to give 0.56 g (84%) of product. A portion of the resulting brown powder (0.10 g) was dissolved in trifluoroacetic acid and left for three hours at room temperature for deprotection. The solution was evaporated, dissolved in water and washed with chloroform (3 × 20 mL). The water solution was evaporated and dried to give the desired product which NMR and capillary electrophoresis showed to be pure (62 mg, 60%). ^{1}H NMR (D_2O, 30 °C): δ 1.48 [m, 8H, $(CH_2)_2(CH_2)_2N$], 1.72 (m, 8H, $CH_2CH_2NH_2$, CH_2CH_2Ar), 3.03 (t, 4H, CH_2NH_2), 3.96 (t, 4H, CH_2Ar), 8.25 (s, 4H, Ar); FAB-MS *m/z* 465.2508 ($M + H^+$, 465.2502, calc. for $C_{26}H_{33}N_4O_4$).

N,*N*′-Bis(4-pyridylmethyl)naphthalene-1,8:4,5-bis(dicarboximide) 17[8,95]

A mixture of 4-(aminomethyl)pyridine (1.1 g, 10 mmol) and naphthalene-1,4,5,8-tetracarboxylic dianhydride (1.3 g, 5.0 mmol) in toluene (80 mL) was stirred and refluxed with a Dean–Stark receiver for 3 h. The reaction mixture was filtered. The product was dissolved in hot water (pH 2). The pH of the resulting solution was adjusted carefully to neutrality with saturated $NaHCO_3$. The resulting precipitate was filtered, washed with water and dried (1.4 g, 60% yield). ^{1}H NMR (DMSO-d_6, 60 °C): δ 5.32 (s, 4H, CH_2), 7.4 (d, 4H, Py), 8.5 (d, 4H, Py), 8.74 (s, 4H, Ar).

N,*N*′-Bis(1-methylpyridin-1-ium-4-ylmethyl)naphthalene-1,8:4,5-bis(dicarboximide) diiodide 4[8,95]

A mixture of *N*,*N*′-bis(4-pyridylmethyl)naphthalene-1,8:4,5-bis(dicarboximide) (45 mg, 0.10 mmol) and iodomethane (2 mL) was allowed to stand overnight at room temperature, and evaporated to dryness. The residue was dissolved in hot water (100 mL), washed with $CHCl_3$ (3 × 20 mL) and evaporated. The product was recrystallized from H_2O to give a red–purple powder (41 mg, 56% yield). ^{1}H NMR (DMSO-d_6, 25 °C): δ 4.30 (s, 6H, CH_3), 5.53 (s, 4H, CH_2Py), 8.23 (d, 4H, Py), 8.76 (s, 4H, Ar), 8.91 (d, 4H, Py); FAB-MS *m/z* 478.1710 (M^+, calc. 478.1641 for $C_{28}H_{22}N_4O_4$).

N,*N*′-Bis(1-*n*-propylpyridin-1-ium-4-ylmethyl)naphthalene-1,8:4,5-bis(dicarboximide) dibromide 5

A mixture of *N*,*N*′-bis(4-pyridylmethyl)naphthalene-1,8:4,5-bis(dicarboximide) (45 mg, 0.10 mmol) and 1-bromopropane (1.2 g, 10 mmol) was refluxed with stirring for 5 h in DMF, allowed to stand overnight at room temperature, and evaporated to dryness. The residue was dissolved in hot water (100 mL), washed with $CHCl_3$ (3 × 20 mL), and evaporated. The product was recrystallized from methanol (20 mg, 29% yield). ^{1}H NMR (D_2O, 80 °C): δ 0.87 (t, 6H, CH_3), 1.95 (m, 4H, CH_2CH_3), 4.45 (t, 4H, $CH_2CH_2CH_3$), 5.59 (s, 4H, NCH_2Py), 8.02 (d, 4H, Py), 8.69 (d, 4H, Py), 8.76 (s, 4H, Ar); FAB-MS *m/z* 534.2296 (M^+, calc. 534.2267 for $C_{32}H_{30}N_4O_4$).

N,*N*′-Bis(1-*n*-butylpyridin-1-ium-4-ylmethyl)naphthalene-1,8:4,5-bis(dicarboximide) dibromide 6

Following the procedure for **5**, *N*,*N*′-bis(4-pyridylmethyl)-naphthalene-1,8:4,5-bis(dicarboximide) (45 mg, 0.10 mmol) and 1-bromobutane (1.4 g, 10 mmol) in DMF gave **6**. The product was recrystallized from methanol (32 mg, 44% yield). ^{1}H NMR (D_2O, 30 °C): δ 0.9 (t, 6H, CH_3), 1.32 (m, 4H, CH_2CH_3), 1.95 (m, 4H, $CH_2CH_2CH_3$), 5.63 (s, 16H, CH_3Py), 8.02 (d, 4H, Py), 8.73 (d, 4H, Py), 8.81 (s, 4H, Ar).

N,*N*′-Bis(3-pyridylmethyl)naphthalene-1,8:4,5-bis(dicarboximide)[95]

Following the procedure for **16**, naphthalene-1,4,5,8-tetracarboxylic dianhydride (1.3 g, 5.0 mmol) and 3-(aminomethyl)-pyridine (1.1 g, 10 mmol) gave 1.9 g (81%) of product. ^{1}H NMR (DMSO-d_6, 60 °C): δ 5.3 (s, 4H, CH_2Py), 7.32 (t, 2H, Py), 7.81 (d, 2H, Py), 8.46 (d, 2H, Py), 8.68 (s, 2H, Py), 8.73 (s, 4H, Ar).

N,*N*′-Bis(1-*n*-butylpyridin-1-ium-3-ylmethyl)naphthalene-1,8:4,5-bis(dicarboximide) dibromide 7

Following the procedure for **5,** *N*,*N*′-bis(3-pyridylmethyl)-naphthalene-1,8:4,5-bis(dicarboximide) (45 mg, 0.10 mmol) and 1-bromobutane (1.4 g, 10 mmol) in DMF gave **7.** The product was recrystallized from methanol (25 mg, 35% yield). ^{1}H NMR (D_2O, 30 °C): δ 0.91 (t, 6H, CH_3), 1.32 (m, 4H, CH_2CH_3), 1.98 (m, 4H, $CH_2CH_2CH_3$), 5.64 (s, 4H, CH_2Py), 8.02 (t, 2H, Py), 8.6 (d, 2H, Py), 8.72 (d, 2H, Py), 8.78 (s, 4H, Ar), 8.99 (s, 2H, Py).

N,*N*′-Bis[4-(4-pyridyl)butyl]naphthalene-1,8:4,5-bis(dicarboximide)

Following the procedure for **16**, naphthalene-1,4,5,8-tetracarboxylic dianhydride (1.3 g, 5.0 mmol) and 4-(4-aminobutyl)-pyridine[97] (1.5 g, 10 mmol) gave 1.9 g (71%) product. ^{1}H NMR (DMSO-d_6, 22 °C): δ 1.69 (m, 8H, CH_2CH_2Py, $CH_2CH_2CH_2Py$), 2.67 (t, 4H, CH_2Py), 4.07 (t, 4H, $CH_2CH_2CH_2CH_2Py$), 7.25 (d, 4H, Py), 8.42 (d, 4H, Py), 8.65 (s, 4H, Ar).

N,N′-Bis[4-(1-methylpyridin-1-ium-4-yl)butyl]naphthalene-1,8:4,5-bis(dicarboximide) diiodide 8

Following the procedure for **4**, *N*,*N*′-bis[4-(4-pyridyl)butyl]-naphthalene-1,8:4,5-bis(dicarboximide) (53 mg, 0.10 mmol) and iodomethane (2 mL) gave **8** (31 mg, 38% yield). ^{1}H NMR (D_2O, 22 °C): δ 1.71 (m, 4H, CH_2CH$_2$Py), 1.84 (m, 4H, CH_2CH$_2$CH$_2$Py), 3.01 (t, 4H, CH_2Py), 4.02 (t, 4H, CH_2CH$_2$-CH$_2$CH$_2$Py), 4.28 (s, 6H, CH_3), 7.89 (d, 4H, Py), 8.26 (s, 4H, Ar), 8.59 (d, 4H, Py).

N,N′-Bis(4-carboxybutyl)naphthalene-1,8:4,5-bis(dicarboximide)

Following the procedure for **15**, naphthalene-1,4,5,8-tetracarboxylic dianhydride (1.3 g, 5.0 mmol) and 5-aminocaproic acid (1.2 g, 10 mmol) gave 2.0 g (86%) product. ^{1}H NMR (DMSO-d_6, 30 °C): δ 1.60 (m, 4H, CH_2CH$_2$COOH), 1.68 (m, 4H, CH_2CH$_2$CH$_2$COOH), 2.27 (t, 4H, CH_2COOH), 4.06 (t, 4H, CH_2CH$_2$CH$_2$CH$_2$COOH), 8.66 (s, 4H, Ar); EI-MS *m*/*z* 466.1388 (M^+, calc. 466.1376 for $C_{24}H_{22}N_2O_8$).

1-(3-Ammoniopropyl)pyridinium dibromide 18[96]

An excess of anhydrous pyridine and 3-bromopropylammonium bromide (0.44 g, 2.0 mmol) were refluxed in dry acetonitrile (30 mL) for 5 h. The reaction mixture was cooled and filtered to give pure product (0.31 g, 50% yield). ^{1}H NMR (D_2O, 22 °C): δ 2.41 (m, 2H, CH_2CH$_2$Py), 3.12 (t, 2H, CH_2CH$_2$CH$_2$Py), 4.72 (t, 2H, CH_2Py), 8.08 (t, 2H, Py), 8.55 (t, 1H, Py), 8.88 (d, 2H, Py).

N,N′-Bis{4-[*N*-(3-pyridiniopropyl)carbamoyl]butyl}naphthalene-1,8:4,5-bis(dicarboximide) dibromide 9

1-(3-Ammoniopropyl)pyridinium dibromide (0.13 g, 0.40 mmol), *N*,*N*′-bis(4-carboxybutyl)naphthalene-1,8:4,5-bis-(dicarboximide) (93 mg, 0.20 mmol), BOP (0.18 g, 0.40 mmol) and triethylamine (0.12 g, 1.2 mmol) were mixed in dry DMF (10 mL). The mixture was allowed to stir for one day at room temperature. The residue was filtered and recrystallized from methanol to give **9** (78 mg, 46% yield).^{1}H NMR (D_2O, 25 °C): δ 1.75 (br s, 8H, CH_2CH$_2$CONH, CH_2CH$_2$CH$_2$CONH), 2.30 (m, 4H, CH_2CH$_2$Py), 2.38 (br t, 4H, CH_2CONH), 3.30 (t, 4H, CH_2CH$_2$CH$_2$Py), 4.10 (br t, 4H, CH_2CH$_2$CH$_2$CH$_2$CONH), 4.68 (t, 4H, CH_2Py), 8.12 (t, 4H, Py), 8.42 (s, 4H, Ar), 8.58 (t, 2H, Py), 8.90 (d, 4H, Py); FAB-MS *m*/*z* 704.3554 (M^+, calc. 704.3322 for $C_{40}H_{44}N_6O_6$).

2-(3-Ammoniopropyl)-5,6,7,8-tetrahydroisoquinolinium dibromide

Following the procedure for **18**, 5,6,7,8-tetrahydroisoquinoline (0.67 g, 5.0 mmol) and 3-bromopropylammonium bromide (1.1 g, 5.0 mmol) were refluxed in dry acetonitrile (30 mL) for 5 h. The reaction mixture was cooled, decanted and washed with acetonitrile to give pure product (1.2 g, 68% yield). ^{1}H NMR (D_2O, 22 °C): δ 1.88 (m, 4H, CH_2CH$_2$CH), 2.38 (m, 2H, CH_2CH$_2$Py), 2.90 (br s, 2H, CH_2CH), 3.01 (br s, 2H, CH_2CH), 3.13 (t, 2H, CH_2CH$_2$CH$_2$Py), 4.60 (t, 2H, CH_2Py), 7.72 (d, 1H, Py), 8.43 (d, 1H, Py), 8.55 (s, 1H, Py).

N,N′-Bis(4-{*N*-[3-(5,6,7,8-tetrahydroisoquinolinio)propyl]-carbamoyl}butyl)naphthalene-1,8:4,5-bis(dicarboximide) dibromide 10

Following the procedure for **9**, 2-(3-ammoniopropyl)-5,6,7,8-tetrahydroisoquinolinium dibromide (0.18 g, 0.50 mmol), *N*,*N*′-bis(4-carboxybutyl)naphthalene-1,8:4,5-bis(dicarboximide) (0.12 g, 0.25 mmol), BOP (0.23 g, 0.52 mmol) and triethylamine (0.15 mg, 1.5 mmol) were mixed in dry DMF (10 mL). The mixture was allowed to stir for one day at room temperature. The residue was precipitated with ether, dissolved in methanol and applied to a Sephadex LH-20 column (eluent methanol). The first band from the column was pure **10** (0.15 g, 60% yield). ^{1}H NMR (DMSO-d_6, 30 °C): δ 1.62 (m, 8H, CH_2-CH$_2$CONH, CH_2CH$_2$CH$_2$CONH), 1.78 (m, 8H, ArCH$_2$CH_2), 2.03 (m, 4H, CH_2CH$_2$Py), 2.12 (t, 4H, CH_2CONH), 2.82 (br t, 4H, CCH_2CH$_2$), 2.95 (br t, 4H, CCH_2CH$_2$), 3.05 (m, 4H, CH_2CH$_2$CH$_2$Py), 4.05 (t, 4H, CH_2CH$_2$CH$_2$CH$_2$CONH), 4.44 (t, 4H, CH_2Py), 7.8 (d, 2H, Py), 7.91 (t, 2H, NH), 8.63 (s, 4H, Ar), 8.66 (d, 2H, Py), 8.8 (s, 2H, Py).

2-(3-Ammoniopropyl)isoquinolinium dibromide[98]

Following the procedure for **18**, isoquinoline (0.65 g, 5.0 mmol) and 3-bromopropylammonium bromide (1.1 g, 5.0 mmol) were refluxed in dry acetonitrile (30 mL) for 5 h. The reaction mixture was cooled, filtered and washed with acetonitrile to give pure product (0.59 g, 34% yield). ^{1}H NMR (D_2O, 30 °C): δ 2.55 (m, 2H, CH_2CH$_2$Py), 3.21 (t, 2H, CH_2CH$_2$CH$_2$Py), 4.9 (t, 2H, CH_2Py), 8.10 (br d, 1H, Py), 8.28 (br m, 2H, Ar), 8.48 (br m, 2H, Ar), 8.56 (d, 1H, Py), 9.80 (br s, 1H, Py).

N,N′-Bis{4-[*N*-(3-isoquinoliniopropyl)carbamoyl]butyl}naphthalene-1,8:4,5-bis(dicarboximide) dibromide 11

Following the procedure for **9**, 2-(3-ammoniopropyl)isoquinolinium dibromide (0.11 g, 0.30 mmol), *N*,*N*′-bis(4-carboxybutyl)naphthalene-1,8:4,5-bis(dicarboximide) (70 mg, 0.15 mmol), BOP (0.14 g, 0.31 mmol) and triethylamine (0.10 g, 1.0 mmol) were mixed in dry DMF (10 mL). The mixture was allowed to stir for one day at room temperature. The residue was precipitated with ether and recrystallized twice from ether–methanol to give an oil **11** (39 mg, 27% yield). ^{1}H NMR (D_2O, 30 °C): δ 1.65 (br m, 8H, CH_2CH$_2$CONH, CH_2CH$_2$CH$_2$-CONH), 2.28 (m, 8H, CH_2CH$_2$Py, CH_2CONH), 3.34 [t, 4H, CH_2(CH$_2$)$_2$Py], 4.02 (br t, 4H, CH_2CH$_2$CH$_2$CH$_2$CONH), 4.66 (m, 4H, CH_2Py), 7.83 (m, 2H, Ar), 8.03 (m, 6H, Py, Ar), 8.26 (m, 6H, Ar), 8.41 (d, 2H, Py), 9.51 (s, 2H, Py); FAB-MS *m*/*z* 804.3641 (M^+, calc. 804.3635 for $C_{48}H_{48}N_6O_6$).

3-[3-(*tert*-Butoxycarboxamido)propyl(methyl)amino]propylamine[99]

According to the literature protocol for related diamines,[100] *N*,*N*-bis(3-aminopropyl)methylamine (2.90 g, 19.97 mmol) and 2-(*tert*-butoxycarbonyloxyimino)-2-phenylacetonitrile (1.25 g, 5.07 mmol) in dioxane gave 3-[3-(*tert*-butoxycarboxamido)-propyl(methyl)amino]propylamine. The product was purified by evaporating the reaction mixture, dissolving it in water and extracting with CH_2Cl_2. The methylene chloride solution was washed with water, dried over magnesium sulfate and evaporated to give pure product (998 mg, 75%). ^{1}H NMR ($CDCl_3$, 25 °C): δ 1.49 (s, 9H, Boc), 1.71 (m, 4H, CH_2CH$_2$N), 2.36 (s, 3H, CH_3), 2.43 (m, 4H, CH_2N), 2.86 (t, 2H, CH_2NBoc), 3.21 (m, 2H, CH_2NH$_2$).

N,N′-Bis{3-[3-aminopropyl(methyl)ammonio]propyl}naphthalene-1,8:4,5-bis(dicarboximide) ditrifluoroacetate

3-[3-(*tert*-butoxycarboxamido)propyl(methyl)aminopropylamine (245 mg, 1.00 mmol) and naphthalene-1,4,5,8-tetracarboxylic dianhydride (135 mg, 0.50 mmol) were stirred and refluxed in 100 mL of toluene with a Dean–Stark receiver for 5 h. The reaction mixture was filtered and evaporated. The residue was dissolved in trifluoroacetic acid and left for three hours at room temperature for deprotection. The solution was evaporated, dissolved in water and washed with chloroform (3 × 20 mL). The water solution was evaporated; the residue was recrystallized from MeOH and dried to give product which NMR showed to be pure (200 mg, 53%). ^{1}H NMR (D_2O, 22 °C): δ 2.12 (m, 8H, CH_2CH$_2$N), 2.85 (s, 6H, CH_3), 3.02 (t, 4H, CH_2NH$_2$), 3.23 (m, 8H, CH_2N), 4.20 (t, 4H, CH_2Ar), 8.71 (s, 4H, Ar).

N,*N*′-Bis{3-[3-biotinamidopropyl(methyl)ammonio]propyl}-naphthalene-1,8:4,5-bis(dicarboximide) diacetate 12

N,*N*′-Bis{3-[3-aminopropyl(methyl)ammonio]propyl}naphthalene-1,8:4,5-bis(dicarboximide) ditrifluoroacetate (200 mg, 0.27 mmol), biotin (270 mg, 1.1 mmol), BOP (442 mg, 1.0 mmol) and triethylamine (303 mg, 3 mmol) were mixed in dry DMF (10 mL). The mixture was allowed to stir for one day at room temperature. The residue was evaporated, dissolved in MeOH and purified by alumina column with use of gradient elution (from CH_3CN with 1% CH_3COOH to CH_3CN–MeOH (1:1) with 1% CH_3COOH). The last band was collected and evaporated to give product, presumably the diacetate, which NMR showed to be pure (84 mg, 32%). ^{1}H NMR (D_2O, 20 °C): δ 1.21 (m, 4H, C*H*$_2$CH$_2$Bi), 1.52 (m, 8H, C*H*$_2$CH$_2$CO, C*H*$_2$Bi), 2.01 (t, 4H, C*H*$_2$CO), 2.22 (t, 8H, C*H*$_2$CH$_2$N), 2.61 (d, 2H, C*H*$_2$S), 2.86 (dd, 2H, C*H*$_2$S), 2.97 (s, 6H, C*H*$_3$), 3.12 (m, 2H, C*H*S), 3.24 (t, 4H, C*H*$_2$NHCO), 3.33 (t, 4H, C*H*$_2$NCH$_3$), 3.38 (t, 4H,C*H*$_2$-NCH$_3$), 4.28 (m, 6H, C*H*$_2$Ar, Bi), 4.51 (m, 2H, Bi), 8.69 (s, 4H, Ar). NMR assignments are based on those in the literature;[101] capillary electrophoresis: 7 min retention time; FAB-MS *m*/*z* 975.4526 ($M^+ - H$, calc. 975.4585 for $C_{48}H_{67}N_{10}O_8S_2$).

N-Butyl-2,2′-bipyridine-5-carboxamide

1-Aminobutane (15 mg, 0.20 mmol), 2,2′-bipyridine-5-carboxylic acid (20 mg, 0.10 mmol), BOP (60 mg, 0.15 mmol) and triethylamine (40.4 mg, 0.40 mmol) were mixed in dry DMF (5 mL). The mixture was allowed to stir for one day at room temperature. The solution was evaporated, dissolved in water and extracted with chloroform (3 × 20 mL). The chloroform solution was washed with water, evaporated and dried to give the desired product which NMR showed to be pure (22 mg, 86%). ^{1}H NMR ($CDCl_3$, 22 °C): δ 0.80–0.97 (m, 5H, C*H*$_3$C*H*$_2$-(CH$_2$)$_2$N), 1.42 (t, 2H, C*H*$_2$CH$_2$Ar), 3.50 (t, 2H, C*H*$_2$Ar), 7.35 (t, 1H, Py), 7.83 (t, 1H, Py), 8.21 (d, 1H, Py), 8.45 (dd, 2 H, Py), 8.70 (d, 1H, Ar), 9.05 (d, 1H, Py).

(*N*-Butyl-2,2′-bipyridine-5-carboxamide)bis(2,2′-bipyridine)-ruthenium dichloride 13

Following the procedure for **14**, *N*-butyl-2,2′-bipyridine-5-carboxamide (25.5 mg, 0.10 mmol) and *cis*-bis(2,2′-bipyridine)-dichlororuthenium dihydrate (50 mg, 0.096 mmol) gave **13** (19 mg, 26%). ^{1}H NMR (D_2O, 50 °C): δ 0.87 [t, 3H, C*H*$_3$CH$_2$-(CH$_2$)$_2$N], 1.23 [m, 2H, CH$_3$C*H*$_2$(CH$_2$)$_2$N], 1.50 (t, 2H, C*H*$_2$CH$_2$Ar), 3.30 (t, 2H, C*H*$_2$Ar), 7.4–7.48 (m, 5H, Py), 7.80–7.89 (m, 5H, Py), 7.98 (s, 1H, Py), 8.07–8.14 (m, 5H, Py), 8.31 (d, 1H, Py), 8.54–8.65 (m, 6H, Py); FAB-MS *m*/*z* 669.1835 (M^+, calc. 669.1790 for $C_{35}H_{33}N_7ORu$).

N,*N*′-Bis[6-(2,2′-bipyridine-5-carboxamido)hexyl]naphthalene-1,8:4,5-bis(dicarboximide)

N,*N*′-Bis(6-aminohexyl)naphthalene-1,8:4,5-bis(dicarboximide) (0.16 g, 0.23 mmol), **16**, 2,2′-bipyridine-5-carboxylic acid (0.11 mg, 0.55 mmol), BOP (0.26 mg, 0.59 mmol) and triethylamine (0.20 mg, 2.0 mmol) were mixed in dry DMF (10 mL). The mixture was allowed to stir for one day at room temperature. The solution was filtered, washed with DMF and dried to give the desired product, which NMR showed to be pure (0.11 g, 58%). ^{1}H NMR (DMSO-d_6, 60 °C): δ 1.42 [m, 8H, (C*H*$_2$)$_2$(CH$_2$)$_2$N], 1.59 (t, 4H, C*H*$_2$CH$_2$NH$_2$), 1.72 (t, 4H, C*H*$_2$CH$_2$Ar), 3.31 (t, 4H, C*H*$_2$NH), 4.08 (t, 4H, C*H*$_2$Ar), 7.69 (t, 2H, Py), 8.22 (t, 2H, Py), 8.42 (d, 2H, Py), 8.52 (m, 4H, Py), 8.67 (s, 4H, Ar), 8.79 (d, 2H, Py), 9.12 (s, 2H, Py).

{*N*,*N*′-Bis[6-(2,2′-bipyridine-5-carboxamido)hexyl]naphthalene-1,8:4,5-bis(dicarboximide)}bis[bis(2,2′-bipyridine)ruthenium] tetrachloride 14

N,*N*′-Bis[6-(2,2′-bipyridine-5-carboxamido)hexyl]naphthalene-1,8:4,5-bis(dicarboximide) (45 mg, 0.054 mmol) dissolved in 15 mL of DMF was added to *cis*-bis(2,2′-bipyridine)dichlororuthenium dihydrate (50 mg, 0.096 mmol) dissolved in 15 mL of hot water. The solution was deaerated with nitrogen for 20 min and then heated and refluxed for 3 h under nitrogen. The reaction mixture was evaporated, the residue was dissolved in acetonitrile and purified by alumina column twice with use of gradient elution (CH_3CN to 7% H_2O–CH_3CN). The second orange band was collected and evaporated to give the desired product, which NMR showed to be pure (29 mg, 37%). ^{1}H NMR (CD_3OD, 25 °C): δ 1.42 [m, 8H, (C*H*$_2$)$_2$(CH$_2$)$_2$N], 1.56 (t, 4H, C*H*$_2$CH$_2$NH$_2$), 1.73 (t, 4H, C*H*$_2$CH$_2$Ar), 4.15 (t, 4H, C*H*$_2$Ar), 7.42–7.52 (m, 10H, Py), 7.79 (m, 4H, Py), 7.88 (m, 6H, Py), 8.14 (m, 12H, Py), 8.44 (d, 2H, Py), 8.71 (m, 12H, Py, Ar), 8.78 (t, 4H, Py). The COSY data are described in detail in the Results section. A NOESY spectrum (D_2O, mixing time of 0.5 s) showed no cross-peaks between the bipyridine and NDI ring protons; capillary electrophoresis: 8.59 min retention time; ESI *m*/*z* 414.1 (50:50 MeOH–H_2O; 5 μL min^{-1} infusion; calc. 1656.421 for $[C_{88}H_{76}N_{16}O_6Ru_2]^{4+}$).

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