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Thermodynamics of Complexes between Dibenzo-24-crown-8 Derivatives and 1,2-Bis(pyridinium)ethanes

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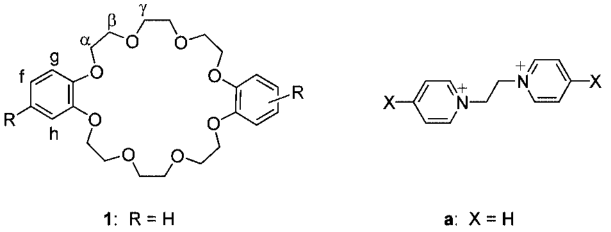
The binding behavior of *para*-substituted 1,2-bis(pyridinium)ethane derivatives (X-PyCH$_2$–CH$_2$Py-X, X = H, Me, Ph, and Py) **a**–**d** with dibenzo-24-crown-8 (DB24C8, **1**) and its derivatives, diformyldibenzo-24-crown-8 (**2**), dinitrodibenzo-24-crown-8 (**3**), dimethyldibenzo-24-crown-8 (**4**) and diaminodibenzo-24-crown-8 (**5**), has been comprehensively investigated by ^{1}H NMR and UV absorption spectroscopy and isothermal titration microcalorimetry in acetonitrile. The results obtained indicated that some of the complexes constructed from DB24C8 derivatives and 1,2-bis(pyridinium)ethane derivatives resulted in visible color changes. For example, upon the addition of equimolar proportions of **5**, the colorless CH$_3$CN solution of **d** changed to red. Furthermore, we investigated the thermodynamics of the complexation of crown ethers **1**–**5** with guests **a**–**d**, and found that the nature of the substituents attached to 1,2-bis(pyridinium)ethanes and the catechol rings on DB24C8 dramatically affects the molecular recognition behavior and the binding thermodynamics. Thermodynamically, the formation of these complexes is an enthalpy-driven process.

Introduction

In recent years much attention[1] has been focused on pseudorotaxanes, because they are the supramolecular precursors of rotaxanes and catenanes,[2] and also viewed as prototypes of simple molecular machines.[3,4] Among these pseudorotaxanes, the binding between [24]crown-8 ether wheels and various dibenzylammonium cations, *N*-benzylanilinium cations, paraquat derivatives as well as 1,2-bis(pyridinium)ethane derivatives has been investigated extensively for almost a decade.[5] The favorable hydrogen-bonding interactions and significant ion-dipole interactions result in the interpenetration of the axles into the cavity of the [24]crown-8 ether wheels to form a 1:1 pseudorotaxane complex. Stoddart et al.[5e] demonstrated that dibenzo-24-crown-8 (DB24C8) was interpenetrated by a wide range of disubstituted dibenzylammonium cations to generate [2]pseudorotaxane complexes by virtue of hydrogen bonds. ^{1}H NMR spectroscopic measurements indicated that the solution-phase binding strengths of the pseudorotaxane complexes can be controlled by judicious manipulation of the substituents attached to the dibenzylammonium cations' aryl rings. Loeb and co-workers' studies indicated that 1,2-bis(bipyridinium)ethane dications can act as axles for the efficient formation of [2]pseudorotaxanes when employing 24-membered crown ethers as the wheel component,[5a,5b,6] and the strength of the interaction was shown to be sensitive to the nature of the substituents on the pyridinium ring with electron-withdrawing groups resulting in increased binding. Recently, Chen et al.[7] reported a triptycene-based bis(crown ether) host which can complex with both paraquat derivatives and dibenzylammonium salts.

Although the binding behaviors have been investigated for a variety of pseudorotaxanes,[5e,8–11] most of them are determined by ^{1}H NMR or spectral titration. To the best of our knowledge, however, the binding thermodynamics for the resultant pseudorotaxanes has rarely been investigated,[5h,6] despite its importance in constructing interesting molecular machines and understanding the assembly mechanisms on the formation of pseudorotaxanes. In the present work, we wish to report the binding behavior of the resulting pseudorotaxane between DB24C8 derivatives **1**–**5** and 1,2-bis(pyridinium)ethane derivatives **a**–**d** (Scheme 1)



1: R = H
2: R = CHO
3: R = NO$_2$
4: R = CH$_3$
5: R = NH$_2$

a: X = H
b: X = CH$_3$
c: X = Phenyl
d: X = 4-Pyridyl

Scheme 1. Structural formulas of the DB24C8 derivatives **1**–**5** and *para*-substituted 1,2-bis(pyridinium)ethane hexafluorophosphate salts **a**–**d**.

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using ^{1}H NMR and UV absorption spectroscopy and isothermal titration microcalorimetry. Our special interest is to examine thermodynamically the electronic effects of substituted groups of both the guests and the hosts on the formation of pseudorotaxanes.

Results and Discussion

UV Spectra

As can be seen from Figure 1, when equivalent DB24C8 derivatives (**1**–**5**) were added to the CH_3CN solution of **d**, distinctly different photophysical behaviors were observed. While the resulting complexes **2·d** and **3·d** do not show obvious charge transfer (CT) bands, the complexes **1·d** and **4·d** give CT bands at 370 nm and 368 nm, respectively. On the contrary, the CT band of **5·d** appears at 438 nm which makes the pseudorotaxane appear red. In a related experiment, mixing phenylamine with **d** resulted in no color change or CT band being observed. One may reasonably deduce that the longer CT band comes from the stronger π-stacking interactions between the electron-rich aminocatechol and the electron-poor 4,4′-dipyridine aromatic rings of **d**. That is to say, the π-stacking interaction is an important factor in the complexation of crown ethers with 1,2-bis(pyridinium)ethane derivatives. Therefore, chromophoric sensors can be designed by changing substituted groups of both DB24C8 and 1,2-bis(pyridinium)ethane. The introduction of electron-donating groups to DB24C8 and electron-withdrawing groups and/or aryl groups to 1,2-bis(pyridinium)ethane would result in efficient chromophoric sensor behavior, and vice versa. Based on this deduction, we can understand easily that the color changes only for solutions of **1·d**, **4·c**, **5·a**, and **5·b** (from colorless to light yellow), **4·d** and **5·c** (from colorless to yellow), and **5·d** (from colorless to red).

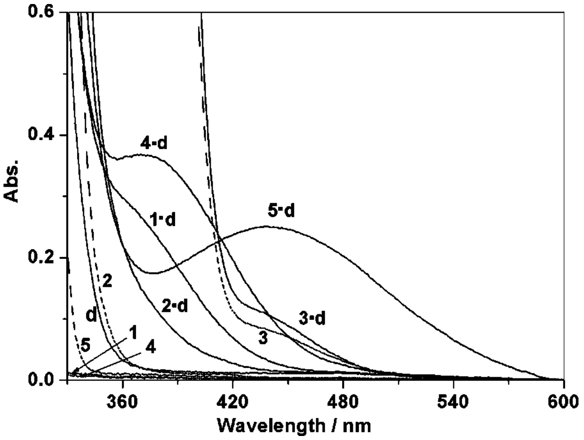

Figure 1. UV spectra of hosts **1**–**5** and **d** in the absence or presence of equimolar **1**–**5** in CH_3CN (1.0 mm) at 298 K.

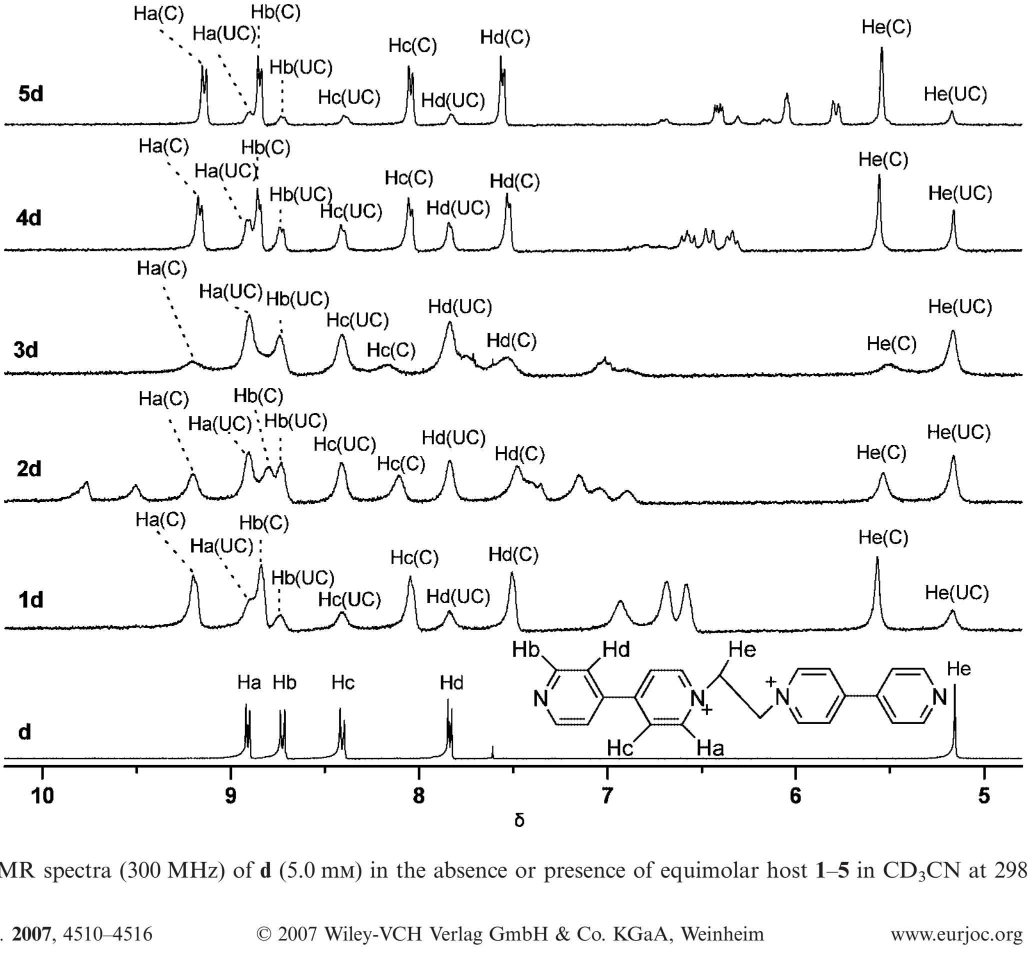

Figure 2. ^{1}H NMR spectra (300 MHz) of **d** (5.0 mm) in the absence or presence of equimolar host **1**–**5** in CD_3CN at 298 K.

Table 1. The chemical shift change [$\Delta\delta$ (ppm)] values of hosts **1**–**5** and guest **d** upon their complexations. See Scheme 1 and Figure 2 for position labels α–γ and a–h.[a]

Entry	Complex	Δδ [ppm]										
		DB24C8 derivative protons						Guest **d** protons				
		f	g	h	α	β	γ	a	b	c	d	e
1	**1·d**	–0.25	–0.36	–0.36	–0.08	0.21	0.31	0.29	0.11	–0.36	–0.33	0.41
2	**2·d**	[b]	–0.15	–0.21	–0.11	0.24	0.38	0.29	0.07	–0.30	–0.36	0.38
3	**3·d**	[b]	–0.15	[b]	–0.16	0.20	0.36	0.30	[b]	–0.24	–0.31	0.35
4	**4·d**	–0.37	–0.25	–0.33	–0.06	0.23	0.33	0.26	0.12	–0.36	–0.32	0.40
5	**5·d**	–0.37	–0.30	–0.28	–0.06	0.20	0.31	0.23	0.12	–0.36	–0.28	0.38

[a] $\Delta\delta = \delta$(complexed host or guest) – δ(free host or guest). Negative values indicate upfield shift. [b] The $\Delta\delta$ values could not be calculated due to the overlap of peaks.

^{1}H NMR Spectra

As can be seen from Figure 2, the ^{1}H NMR spectra of equimolar mixtures of crown ethers **1**–**5** and guest **d** exhibit three sets of different resonances for: (a) the free crown ether, (b) the uncomplexed **d**, and (c) the 1:1 complex formed between both components. The corresponding chemical shift changes ($\Delta\delta$) of hosts **1**–**5** and guest **d** upon their complexation are listed in Table 1. As can be seen from Table 1, all the resulting complexes show significant downfield shifts for the *α* protons (H_a, $\Delta\delta$ = 0.23–0.30 ppm) and the NCH_2 protons (H_e, $\Delta\delta$ = 0.35–0.41 ppm) in **d** indicative of the formation of the C–H···O hydrogen bonds to the oxygens in the crown ethers, while upfield shifts were observed for the H_c ($\Delta\delta$ = –0.24 to –0.36 ppm), H_d ($\Delta\delta$ = –0.28 to –0.36 ppm) and crown ether aromatic protons H_f/H_g/H_h ($\Delta\delta$ = –0.15 to –0.37 ppm) indicating π-stacking between the two sets of aromatic rings. It is reasonable for **2** and **3** to show smaller $\Delta\delta$ values since they are substituted by electron-withdrawing groups, which lead to the weaker π-stacking interactions. Hence, weak C-H···O hydrogen bonds and π-stacking interactions are both important driving forces for complex formation,[1k,12] but the CT band resulting from π-stacking interactions provides the key diagnostic color test. In addition, the binding strength can also be monitored by the proportion of complexed species which increases in the following order: **3·d** < **2·d** < **1·d** < **4·d** < **5·d**.

Complexation Thermodynamics

In order to investigate quantitatively the thermodynamic origin of the complexation of DB24C8 derivatives with guests **a**–**d**, isothermal microcalorimetric titrations were performed at 298.15 K in CH_3CN, because the calorimetry measurement is the only method that directly measures the heat changes associated with intermolecular interactions. A representative titration curve is shown in Figure 3 and Figure 4, and the thermodynamic parameters obtained are listed in Table 2.

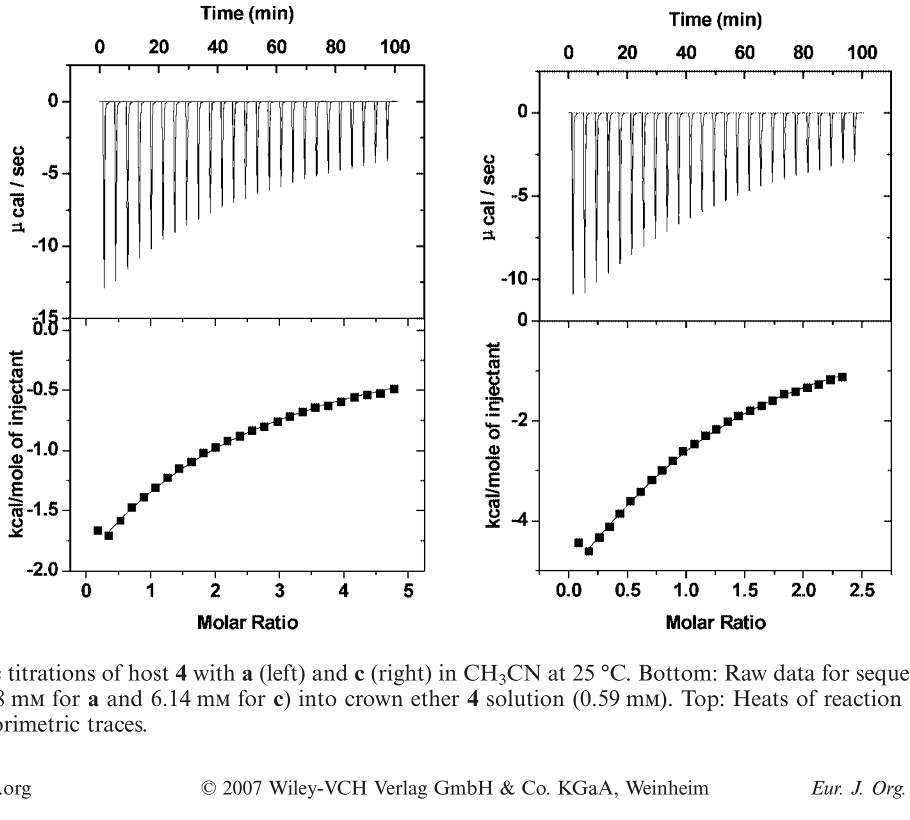

Figure 3. Calorimetric titrations of host **4** with **a** (left) and **c** (right) in CH_3CN at 25 °C. Bottom: Raw data for sequential 10 μL injections of guest solution (14.8 mM for **a** and 6.14 mM for **c**) into crown ether **4** solution (0.59 mM). Top: Heats of reaction as obtained from the integration of the calorimetric traces.

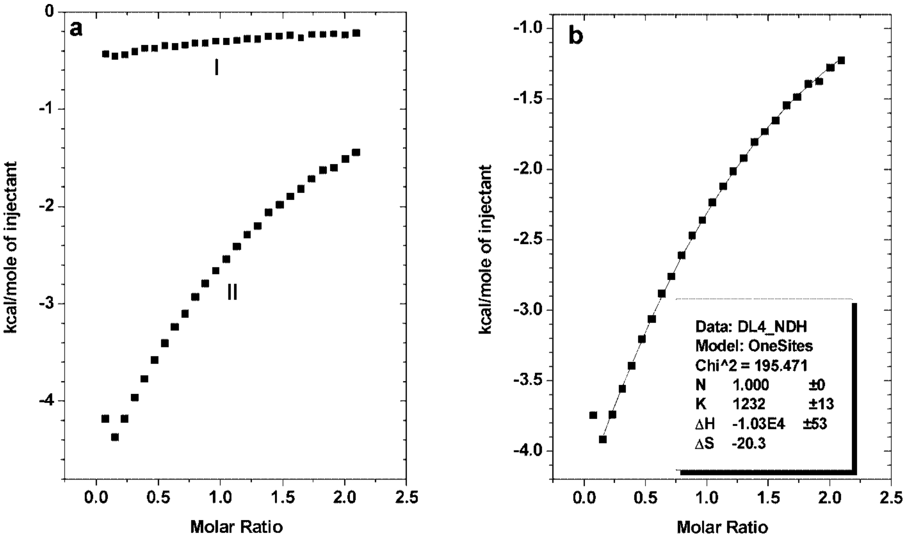

Figure 4. Calorimetric titration of host **5** with guest **c**. (a) Heat effects of dilution (I) and of complexation (II) of **5** with **c** for each injection during the titration microcalorimetric experiment. (b) Net heat effect obtained by subtracting the heat of dilution from the heat of reaction, which was analyzed by computer simulation using the “one set of binding sites” model.

Table 2. Complex stability constant [K_S (M^{-1})] and thermodynamic parameters (in kJ mol^{-1}) for complexation of DB24C8 derivatives **1**–**5** with 1,2-bis(pyridinium)ethane derivatives **a**–**d** in anhydrous acetonitrile at 298.15 K.

Entry	Host[a]	Guest[b]	N[c]	K_S	$-\Delta G°$	$-\Delta H°$	$T\Delta S°$
1	**1**	**a**	4	294 ± 4	14.09 ± 0.03	40.5 ± 1.3	–26.5 ± 1.1
2		**b**	3	391 ± 2	14.80 ± 0.01	49.0 ± 0.3	–34.1 ± 0.2
3		**c**	3	719 ± 19	16.30 ± 0.07	42.1 ± 0.5	–25.8 ± 0.6
4		**d**	5[e]	1659 ± 45	18.39 ± 0.07	48.7 ± 0.4	–30.2 ± 0.5
5	**2**	**a**	2	130 ± 1	12.06 ± 0.02	26.6 ± 0.7	–14.5 ± 0.7
6		**b**	2	125 ± 3	11.96 ± 0.05	40.5 ± 0.6	–28.5 ± 0.7
7		**c**	2	323 ± 15	14.32 ± 0.12	69.8 ± 2.3	–55.4 ± 2.4
8		**d**	2	524 ± 26	15.52 ± 0.12	68.9 ± 2.0	–53.4 ± 2.1
9	**3**	**a**	2	74 ± 5	10.67 ± 0.17	16.9 ± 0.1	–6.2 ± 0.3
10		**b**	2	63 ± 5	10.25 ± 0.21	31.4 ± 2.2	–21.1 ± 2.4
11		**c**	2	–[d]	–	–	–
12		**d**	2	–[d]	–	–	–
13	**4**	**a**	4	348 ± 10	14.50 ± 0.07	44.7 ± 1.8	–30.2 ± 1.8
14		**b**	3	496 ± 3	15.39 ± 0.02	54.5 ± 0.0	–39.1 ± 0.1
15		**c**	3	1911 ± 29	18.73 ± 0.04	42.5 ± 0.2	–23.7 ± 0.3
16		**d**	3	3760 ± 52	20.41 ± 0.04	55.7 ± 0.7	–35.2 ± 0.7
17	**5**	**a**	2	416 ± 1	14.95 ± 0.01	43.1 ± 0.3	–28.1 ± 0.3
18		**b**	2	648 ± 1	16.05 ± 0.01	48.0 ± 0.0	–31.9 ± 0.0
19		**c**	2	1226 ± 24	17.63 ± 0.05	43.3 ± 0.4	–25.7 ± 0.4
20		**d**	2[e]	4142 ± 147	20.65 ± 0.09	51.6 ± 1.5	–31.0 ± 1.6

[a] [host] = 0.12–0.60 mM except for the titration experiment of **1** with **d**. [b] [guest] = 6.14–30.80 mM except for the titration experiment of **1** with **d**. [c] Number of titration runs performed. [d] Reaction enthalpy is too small to be determined by titration microcalorimetry. [e] Ref.[13]

Complexation of 1,2-Bis(pyridinium)ethane Derivatives with the Parent DB24C8 (1)

As can be seen from Table 2, large differences in the K_S values were observed for the complexation of 1,2-bis(pyridinium)ethane derivatives **a**–**d** with **1**, suggesting that the substitution pattern on the 1,2-bis(pyridinium)ethane unit has a dramatic effect upon its molecular recognition behavior. The substitution of methyl for hydrogen in **a**, affording **b**, does not dramatically alter the original binding ability, but the introduction of phenyls and pyridinium rings increases the K_S value 2.4 times for **1·c** and 5.6 times for **1·d**, implying extra π-stacking interactions with the catechol rings in **1**.[5a] However, the sequence does not exist in the corresponding enthalpy changes and entropy changes. The enthalpy change for the complexation of **1** with **b** (49.0 kJ mol^{-1}) is the highest among the four pseudorotaxanes, while the entropy change (–34.1 kJ mol^{-1}) is the lowest, which is unexpected. For the “unexpected” observations, one reasonable explanation is that there is a C-H···π interaction between the methyl groups of **b** and the phenyls of **1** reducing the degree of freedom, because the largest enthalpic change for the resulting complex **1·b** could be ascribed to the unique extra interaction. We can also note that the enthalpy changes for the complexation of **1** with **b** (49.0 kJ mol^{-1})

and **1** with **d** (48.7 kJ mol^{-1}) are almost equal, but the higher entropy change for the latter (–30.2 kJ mol^{-1}) give the highest K_S value for **1·d**.

The Effect of Electron-Withdrawing Groups on the Catechol Rings in DB24C8s

Upon functionalizing **2** and **3** with electron-withdrawing groups, the electron-cloud density of the catechol rings decreases, which weakens not only the π-stacking interactions between the aromatic rings of the host and pyridinium groups of the guest, but also the ion-dipole interactions between the positive charge on the pyridinium nitrogens and the oxygens of the crown ether. As expected, the K_S values of **2** and **3** upon complexation with 1,2-bis(pyridinium)ethane derivatives are lower than those with parent DB24C8 **1** (Table 2). Especially of note is that the substitution of the stronger electron-withdrawing nitro group decreased the reaction enthalpy to unobservably low levels with host **3** and guests **c** and **d**.

It is well known that the electron-cloud density of benzene is bigger than that of pyridine, and methyl is the smallest among pyridine, benzene and methyl. Upon substituting the hydrogen in **a** with the methyl and phenyl group, the enthalpy changes for the complexation of **2** with these 1,2-bis(pyridinium)ethane derivatives gradually increased from 26.6 kJ mol^{-1} for **2·a** to 69.8 kJ mol^{-1} for **2·c**, while the corresponding entropy changes ($T\Delta S$) decreased from –14.5 kJ mol^{-1} to –55.4 kJ mol^{-1}. That is to say, both of the thermodynamic parameters correlate with the electron-cloud density of the substituent on 1,2-bis(pyridinium)ethane; the lower the electron-cloud density of the substituent, the smaller the enthalpy changes, the larger the entropy changes, and vice versa. It is reasonable because the decrease of the ion-dipole interactions between the pyridinium nitrogens and the oxygens of the crown ether makes the π-stacking interactions between the catechol rings and the aromatic rings of the guest become the major driving force for the complexation of **2** with 1,2-bis(pyridinium)ethane derivatives. Despite that, larger entropy losses for the complexation of **2** with **c** or **d** were obtained, which might be attributed to forming contact-ion pairs between the complexes (**2** with **c** or **d**) and counteranion PF_6^-, and therefore, the lower solvation of the complexes reduces the entropic contributions to the complex stabilities.

The Effect of Electron-Donating Groups on the Catechol Rings in DB24C8s

In contrast with **2** and **3**, the electron-cloud density of the catechol rings on modified DB24C8 **4** or **5** increases because of the electron-donating behavior of methyl and amino groups, which enhances not only the π-stacking interactions between the aromatic rings of **4/5** and the pyridinium groups of guests, but also the ion-dipole interactions between the positive charge on the pyridinium nitrogens and the oxygens of the crown ether. Thus, the binding constants of **4** and **5** upon complexation with 1,2-bis(pyridinium)ethane derivatives are larger than those with **1**–**3**. As shown in Table 2, hosts **4** and **5** showed lower binding abilities to **a** and **b** as compared with **c** and **d**, which is similar to the trend observed with hosts **1** and **2**. The universal decreased binding ability toward **a** and **b** results from the structural differences between **a/b** and **c/d**. The introduction of aryl or pyridinium groups to 1,2-bis(pyridinium)ethane (**a**), affording **c** or **d**, respectively, can result in stronger π-stacking interactions. In addition, we note that the K_S values of **d** with **1**–**5** are larger than that of **c**, which could be attributed to the electron-withdrawing nature of the pyridine groups on **d**, which increase the positive charge on the central nitrogens on bis(pyridinium)ethane.

As can be seen from Table 2, while the enthalpy changes for the complexation of **4/5** with **b/d** obviously increase compared with **4·a** and **5·a**, those for the complexation of **4/5** with **c**, possessing the biggest electron-cloud density among the three guests, decrease to some extent (the enthalpy changes of **5·a** and **5·c** are almost equal). This is distinctly different from the case of hosts **2** and **3**. Namely, the bigger the electron-cloud density of the substituent, the smaller the enthalpy changes and the larger the entropy changes.

Molecular Binding Ability and Molecular Selectivity

It is also interesting to compare the “host selectivity” sequence obtained for each guest. The binding constant for the complexation of each guest by DB24C8 (**1**) and the substituted DB24C8 **2**–**5** increases in the following order:

a: **3** < **2** < **1** < **4** < **5**

b: **3** < **2** < **1** < **4** < **5**

c: **2** < **1** < **5** < **4**

d: **2** < **1** < **4** < **5**

Guests **a**, **b** and **d** give the same host selectivity and **c** reverses the binding selectivity for **4** and **5**, showing larger binding constants for **4** than **5**. The K_S values for **2**, **1**, **4** and **5** with **b** are enhanced by factors of 2.0, 6.2, 7.9, and 10.3, respectively, compared with that of **3·b**. The differential reaction enthalpy and entropy changes calculated by using the data presented in Table 2 reveal that all the enthalpy changes ($-9.1\ \text{kJ mol}^{-1} < \Delta H^\circ_{\text{host }\mathbf{1,2,4,5}} - \Delta H^\circ_{\text{host }\mathbf{3}} < -23.1\ \text{kJ mol}^{-1}$) are more remarkable than the entropy changes ($-7.4\ \text{kJ mol}^{-1} < T\Delta S^\circ_{\text{host }\mathbf{1,2,4,5}} - T\Delta S^\circ_{\text{host }\mathbf{3}} < -18.0\ \text{kJ mol}^{-1}$). Therefore, the enthalpy changes apparently control the enhanced binding ability.

On the other hand, we also note that the difference of the Gibbs free energy changes for the complexation of **4** with **d** or **a** ($\Delta\Delta G^\circ = \Delta G^\circ_{\mathbf{d}} - \Delta G^\circ_{\mathbf{a}}$) is the largest at 5.91 kJ mol^{-1}, which corresponds with the largest guest selectivity for **d** vs. **a** of 10.8 ($K_{S(\mathbf{4\cdot d})}/K_{S(\mathbf{4\cdot a})}$). For host **5**, the guest selectivity for **d** vs. **a** is 10.0 times. While hosts **1**, **4** and **5** show larger K_S values for complexation with **b** than that with **a**, hosts **2** and **3** reverse this binding sequence, showing a little larger binding constants for complexation with **a**. Thermodynamically, the complexation of **2** with **a** gives ΔH° and $T\Delta S^\circ$ values comparable to those for complexation with **b**, and the enthalpic gain ($\Delta H^\circ_{\mathbf{b}} - \Delta H^\circ_{\mathbf{a}} = -13.9\ \mathrm{kJ\,mol^{-1}}$) is well compensated for by the equally increased entropic loss ($T\Delta S^\circ_{\mathbf{b}} - T\Delta S^\circ_{\mathbf{a}} = -14.0\ \mathrm{kJ\,mol^{-1}}$). In contrast, although the complexation of **5** with **b** gives a smaller enthalpic gain than that for complexation with **a** ($\Delta H^\circ_{\mathbf{b}} - \Delta H^\circ_{\mathbf{a}} = -4.9\ \mathrm{kJ\,mol^{-1}}$), it is not as completely compensated by the relatively small entropic loss ($T\Delta S^\circ_{\mathbf{b}} - T\Delta S^\circ_{\mathbf{a}} = -3.8\ \mathrm{kJ\,mol^{-1}}$).

Conclusions

In summary, we have demonstrated the binding behavior of DB24C8 derivatives with 1,2-bis(pyridinium)ethane derivatives. The results obtained indicate that the nature of the substituents attached to the catechol rings in DB24C8 dramatically affects the molecular recognition behavior and the binding thermodynamics. For the electron-withdrawing groups, not only is the binding ability reduced, but also the smaller the electron-cloud density of the substituent on the guest, the smaller the enthalpy changes, the larger the entropy changes, and vice versa. For the electron-donating groups, the binding ability is enhanced, and the bigger the electron-cloud density of the substituent on the guest, the smaller the enthalpy changes and the larger the entropy changes. As a result, only the [2]pseudorotaxanes **1·d**, **4·c**, **4·d**, **5·a**, **5·b**, **5·c**, and **5·d** are colored from light yellow to red. Thermodynamically, the negative values of ΔH° and ΔS° in each case suggest that these complexation events are enthalpy-driven processes, and hence, these thermodynamic parameters of the interaction between DB24C8 derivatives and 1,2-bis(pyridinium)ethanes are significant for understanding the assembly mechanisms on the formation progress of [2]pseudorotaxanes.

Experimental Section

Materials: Starting materials were commercially available unless noted otherwise. Analytical-grade CH_3CN was dried with calcium hydride and then distilled fractionally to give the anhydrous solvent for calorimetry. Of the macrocyclic hosts in Scheme 1, dibenzo-24-crown-8 (**1**),[14] diformyl-dibenzo-24-crown-8 (**2**),[15] dinitro-dibenzo-24-crown-8 (**3**),[16] dimethyl-dibenzo-24-crown-8 (**4**),[17] and diamino-dibenzo-24-crown-8 (**5**)[16] were prepared according to the literature procedures. No efforts were made to separate the *cis*/*trans* isomers. All pyridinium bromide salts were prepared by the literature method.[18] The hexafluorophosphate salts were precipitated from water by the addition of saturated aqueous NH_4PF_6 and recrystallized before use.

Isothermal Microcalorimetric Titration: The microcalorimetric titrations were performed at atmospheric pressure and 25 °C in anhydrous CH_3CN by using a Microcal VP-ITC titration microcalorimeter, which allowed us to determine simultaneously the enthalpy and equilibrium constant from a single titration curve. Each solution was degassed and thermostatted using a ThermoVac accessory before titration. In each run, a CH_3CN solution of 1,2-bis(pyridinium)ethane derivative guest (or crown ether host) in a 0.250 mL syringe was sequentially injected with stirring at 300 rpm into the calorimeter sample cell containing a CH_3CN solution of crown ether host (or guest). The sample cell volume was 1.4227 mL in all experiments. Each titration experiment was composed of 25 successive injections (10 μL per injection). Typical titration curves are shown in Figure 3. Each titration of guest into the sample cell gave rise to a heat of reaction, caused by the formation of inclusion complexes between guests and crown ether hosts. The heat of reaction decreased after each injection because less and less crown ether molecules were available to form inclusion complexes. A control experiment to determine the heat of dilution was carried out with each run by performing the same number of injections with the same concentration of guest (or host) compound as used in the titration experiments into a pure CH_3CN solution without the host crown ether (or guest). The dilution enthalpies determined in control experiments were subtracted from the enthalpies measured in the titration experiments to obtain the net reaction heat. The ORIGIN software (Microcal Inc.), which was used to simultaneously compute the equilibrium constant (K_S) and standard molar enthalpy of reaction (ΔH°) from a single titration curve, gave a standard deviation based on the scatter of the data points in the titration curve. The net reaction heat in each run was calculated by the "one set of binding sites" model. Additionally, the first point was removed from the titration curve acknowledging that the concentration of host (or guest) in the cell far exceeded the concentration of the guest (or host). A typical titration curve and the fitted results for the complexation of **c** with host **5** are shown in Figure 4. The knowledge of the binding constant (K_S) and molar reaction enthalpy (ΔH°) enabled The calculation of the standard free energy of binding (ΔG°) and entropy changes (ΔS°), according to the equation

$$\Delta G^\circ = -RT \ln K_S = \Delta H^\circ - T\Delta S^\circ$$

where R is the gas constant and T is the absolute temperature. Multiple independent titration runs ($N = 2$–3) were performed to afford self-consistent thermodynamic parameters, and the averaged values are reported in Table 2. The uncertainties in the thermodynamic parameters reported for host-guest complexation are two standard deviations from the mean value unless stated otherwise. It should be mentioned that the status of guests **a**–**d** is rather similar before and after complexation which had been confirmed unambiguously by conductivity experiments. For example, the molar conductivity of guest **d** in anhydrous CH_3CN was 280 $\mathrm{S\,cm^2\,mol^{-1}}$. After the addition of excess (10.4 equiv.) host **1**, the molar conductivity decreased to 272 $\mathrm{S\,cm^2\,mol^{-1}}$, which suggests the similar status between guest **d** and complex **1·d**.[19]

Supporting Information (see footnote on the first page of this article): Color changes of **d** in CH_3CN solution in the absence and presence of hosts **1**–**5**.

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[1] a) H. W. Gibson, H. Marand, *Adv. Mater.* **1993**, *5*, 11–21; b) M. C. T. Fyfe, J. F. Stoddart, *Acc. Chem. Res.* **1997**, *30*, 393–401; c) F. M. Raymo, J. F. Stoddart, *Chem. Rev.* **1999**, *99*, 1643–1663; d) G. A. Breault, C. A. Hunter, P. C. Mayers, *Tetrahedron* **1999**, *55*, 5265–5293; e) K. Kim, *Chem. Soc. Rev.* **2002**, *31*, 96–107; f) F. Huang, L. N. Zakharov, A. L. Rheingold, J. W. Jones,

H. W. Gibson, *Chem. Commun.* **2003**, 2122–2123; g) F. Huang, H. W. Gibson, *J. Am. Chem. Soc.* **2004**, *126*, 14738–14739; h) M. Venturi, S. Dumas, V. Balzani, J. Cao, J. F. Stoddart, *New J. Chem.* **2004**, *28*, 1032–1037; i) F. Huang, L. N. Zakharov, A. L. Rheingold, M. Ashraf-Khorassani, H. W. Gibson, *J. Org. Chem.* **2005**, *70*, 809–813; j) P. R. Ashton, D. Philp, N. Spencer, J. F. Stoddart, *J. Chem. Soc. Chem. Commun.* **1991**, 1677–1679; k) G. Kaiser, T. Jarrosson, S. Otto, Y.-F. Ng, A. D. Bond, J. K. M. Sanders, *Angew. Chem. Int. Ed.* **2004**, *43*, 1959–1962; l) B. A. Blight, K. A. Van Noortwyk, J. A. Wisner, M. C. Jennings, *Angew. Chem. Int. Ed.* **2005**, *44*, 1499–1504; m) P. D. Beer, M. R. Sambrook, D. Curiel, *Chem. Commun.* **2006**, 2105–2117; n) W. Abraham, L. Grubert, S. Schmidt-Schäffer, K. Buck, *Eur. J. Org. Chem.* **2005**, *2*, 374–386.

[2] a) D. H. Busch, N. A. Stephenson, *Coord. Chem. Rev.* **1990**, *100*, 119–154; b) S. Anderson, H. L. Anderson, J. K. M. Sanders, *Acc. Chem. Res.* **1993**, *26*, 469–475; c) R. Cacciapaglia, L. Mandolini, *Chem. Soc. Rev.* **1993**, *22*, 221–231; d) R. Hoss, F. Vögtle, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 375–384; e) J. P. Schneider, J. W. Kelly, *Chem. Rev.* **1995**, *95*, 2169–2187; f) F. M. Raymo, J. F. Stoddart, *Pure Appl. Chem.* **1996**, *68*, 313–322; g) T. J. Hubin, A. G. Kolchinski, A. L. Vance, D. H. Busch, *Adv. Supramol. Chem.* **1999**, *6*, 237–357; h) S. A. Nepogodiev, J. F. Stoddart, *Chem. Rev.* **1998**, *98*, 1959–1976; i) S. J. Cantrill, K. S. Chichak, A. J. Peters, J. F. Stoddart, *Acc. Chem. Res.* **2005**, *38*, 1–9; j) G. Wenz, B.-H. Han, A. Muller, *Chem. Rev.* **2006**, *106*, 782–817.

[3] a) V. Balzani, A. Credi, F. M. Raymo, J. F. Stoddart, *Angew. Chem. Int. Ed.* **2000**, *39*, 3348–3391; b) special issue of *Acc. Chem. Res.* **2001**, *34*, 409–522; c) *Molecular Machines and Motors* (Ed.: J.-P. Sauvage), Springer-Verlag, Berlin, **2001**, vol. 99 in the series Structure and Bonding; d) V. Balzani, A. Credi, M. Venturi, *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 4814–4817; e) V. Balzani, A. Credi, M. Venturi, *Molecular Devices and Machines – A Journey into the Nano World*, Wiley-VCH, Weinheim, **2003**; f) V. Balzani, M. Gomez-Lopez, J. F. Stoddart, *Acc. Chem. Res.* **1998**, *31*, 405–414; g) J.-P. Sauvage, *Acc. Chem. Res.* **1998**, *31*, 611–619.

[4] For some literature on molecular machines, see: a) J. D. Badjic, V. Balzani, A. Credi, S. Silvi, J. F. Stoddart, *Science* **2004**, *303*, 1845–1849; b) C. P. Collier, E. W. Wong, M. Belohradsky, F. M. Raymo, J. F. Stoddart, P. J. Kuekes, R. S. Williams, J. R. Heath, *Science* **1999**, *285*, 391–394; c) C. P. Collier, G. Matterstei, E. W. Wong, Y. Luo, K. Beverly, J. Sampaio, F. M. Raymo, J. F. Stoddart, J. R. Heath, *Science* **2000**, *289*, 1172–1175; d) N. Koumura, R. W. J. Zijlstra, R. A. Van Delden, N. Harada, B. L. Feringa, *Nature (London)* **1999**, *401*, 152–155; e) T. R. Kelly, H. D. Silva, R. A. Silva, *Nature (London)* **1999**, *401*, 150–152; f) L. Raehm, J.-M. Kern, J.-P. Sauvage, *Chem. Eur. J.* **1999**, *5*, 3310–3317; g) V. Balzani, A. Credi, S. J. Langford, F. M. Raymo, J. F. Stoddart, M. Venturi, *J. Am. Chem. Soc.* **2000**, *122*, 3542–3543; h) V. Bermudez, N. Capron, T. Gase, F. G. Gatti, F. Kajzar, D. A. Leigh, F. Zerbetto, S. Zhang, *Nature (London)* **2000**, *406*, 608–611; i) P. R. Ashton, R. Ballardini, V. Balzani, A. Credi, K. R. Dress, E. Ishow, C. J. Kleverlaan, O. Kocian, J. A. Preece, N. Spencer, J. F. Stoddart, M. Venturi, S. Wenger, *Chem. Eur. J.* **2000**, *6*, 3558–3574; j) B. Armaroli, V. Balzani, J.-P. Collin, P. Gavina, J.-P. Sauvage, B. Ventura, *J. Am. Chem. Soc.* **1999**, *121*, 4397–4408; k) F. G. Gatti, S. Leon, J. K. Y. Wong, G. Bottari, A. Allieri, M. A. F. Morales, S. J. Teat, C. Frochet, D. A. Leigh, A. M. Brouwer, F. Zerbetto, *Proc. Natl. Acad. Sci. USA.* **2003**, *100*, 10–14; l) P.-N. Cheng, P.-T. Chiang, S.-H. Chiu, *Chem. Commun.* **2005**, 1285–1287; m) F. Huang, K. A. Switek, H. W. Gibson, *Chem. Commun.* **2005**, 3655–3657; n) D. A. Leigh, J. K. Y. Wong, F. Dehez, F. Zerbetto, *Nature (London)* **2003**, *424*, 174–179.

[5] a) S. J. Loeb, J. A. Wisner, *Angew. Chem. Int. Ed.* **1998**, *37*, 2838–2840; b) S. J. Loeb, *Chem. Commun.* **2005**, 1511; c) S. J. Loeb, J. Tiburcio, S. J. Vella, *Org. Lett.* **2005**, *7*, 4923–4926; d) S. J. Cantrill, A. R. Pease, J. F. Stoddart, *J. Chem. Soc. Dalton Trans.* **2000**, 3715–3734; e) P. R. Ashton, M. C. T. Fyfe, S. K. Hickingbottom, J. F. Stoddart, A. J. P. White, D. J. Williams, *J. Chem. Soc. Perkin Trans. 2* **1998**, 2117–2128; f) A. R. Williams, B. H. Northrop, K. N. Houk, J. F. Stoddart, D. J. Williams, *Chem. Eur. J.* **2004**, *10*, 5406–5421; g) H. W. Gibson, N. Yamaguchi, J. W. Jones, *J. Am. Chem. Soc.* **2003**, *125*, 3522–3533; h) S.-H. Chiu, K.-S. Liao, J.-K. Su, *Tetrahedron Lett.* **2004**, *45*, 213–216; i) P.-N. Cheng, C.-F. Lin, Y.-H. Liu, C.-C. Lai, S.-M. Peng, S.-H. Chiu, *Org. Lett.* **2006**, *8*, 435–438; j) D. B. Amabilino, J. F. Stoddart, *Chem. Rev.* **1995**, *95*, 2725–2828; k) R. Jäger, F. Vögtle, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 930–944.

[6] S. J. Loeb, J. Tiburcio, S. J. Vella, J. A. Wisner, *Org. Biomol. Chem.* **2006**, *4*, 667–680.

[7] a) T. Han, C.-F. Chen, *Org. Lett.* **2006**; *8*, 1069–1072; b) Q. S. Zong, C. F. Chen, *Org. Lett.* **2006**, *8*, 211–214; c) X. Z. Zhu, C. F. Chen, *J. Am. Chem. Soc.* **2005**, *127*, 13158–13159.

[8] a) R. Castro, K. R. Nixon, J. D. Evanseck, A. E. Kaifer, *J. Org. Chem.* **1996**, *61*, 7298–7303; b) M. Asakawa, W. Dehaen, G. L′abbe, S. Menzer, J. Nouwen, F. M. Raymo, J. F. Stoddart, D. J. Williams, *J. Org. Chem.* **1996**, *61*, 9591–9595.

[9] a) P.-L. Anelli, P. R. Ashton, R. Ballardini, V. Balzani, M. Delgado, M. T. Gandolfi, T. T. Goodnow, A. E. Kaifer, D. Philp, M. Pietraszkiewicz, L. Prodi, M. V. Reddington, A. M. Z. Slawin, N. Spencer, J. F. Stoddart, C. Vicent, D. J. Williams, *J. Am. Chem. Soc.* **1992**, *114*, 193–218; b) M. Asakawa, P. R. Ashton, S. E. Boyd, C. L. Brown, R. E. Gillard, O. Kocian, F. M. Raymo, J. F. Stoddart, M. S. Tolley, A. J. P. White, D. J. Williams, *J. Org. Chem.* **1997**, *62*, 26–37.

[10] a) H. W. Gibson, H. Wang, K. Bonrad, J. W. Jones, C. Slebodnick, L. N. Zackharov, A. L. Rheingold, B. Habenicht, P. Lobue, A. E. Ratliff, *Org. Biomol. Chem.* **2005**, *3*, 2114–2121; b) P. R. Ashton, P. J. Campbell, E. J. T. Chrystal, P. T. Glinke, S. Menzer, D. Philp, N. Spencer, J. F. Stoddart, P. A. Tasker, D. J. Williams, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1865–1869; c) T. Clifford, A. Abushamleh, D. H. Busch, *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 4830–4836.

[11] A. Credi, S. Dumas, S. Silvi, M. Venturi, A. Arduini, A. Pochini, A. Secchi, *J. Org. Chem.* **2004**, *69*, 5881–5887.

[12] a) F. M. Raymo, M. D. Bartberger, K. N. Houk, J. F. Stoddart, *J. Am. Chem. Soc.* **2001**, *123*, 9264–9267; b) J. G. Hansen, N. Feeder, D. G. Hamilton, M. J. Gunter, J. Becher, J. K. M. Sanders, *Org. Lett.* **2000**, *2*, 449–452; c) K. N. Houk, S. Menzer, S. P. Newton, F. M. Raymo, J. F. Stoddart, D. J. Williams, *J. Am. Chem. Soc.* **1999**, *121*, 1479–1487.

[13] Y. Liu, C.-J. Li, H.-Y. Zhang, L.-H. Wang, Q. Luo, G. Wang, *J. Chem. Phys.* **2007**, *126*, 064705 (6 pages).

[14] C. J. Pedersen, *J. Am. Chem. Soc.* **1967**, *89*, 7017–7036.

[15] H.-Q. Wang, D.-S. Liu, X.-G. Wang, *Acta Polym. Sin.* **2001**, *4*, 433–436.

[16] I. Smukste, D. B. Smithrud, *J. Org. Chem.* **2003**, *68*, 2547–2558.

[17] O. Ryba, E. Knizakova, J. Petranek, *Collect. Czech. Chem. Commun.* **1973**, *38*, 497.

[18] M. I. Attalla, N. S. McAlpine, L. A. Summers, *Z. Naturforsch., Teil B* **1984**, *39*, 74–78.

[19] W. J. Geary, *Coord. Chem. Rev.* **1971**, *7*, 81–122.

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