Stabilities of cooperatively formed cyclic pseudorotaxane dimers

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Systematic analysis of the stabilities of cyclic pseudorotaxane dimers formed between complimentary homoditopic molecules demonstrates that cooperative cyclic dimerization can be minimized by increasing the length of one component *via* an aliphatic spacer.

Recently, we reported preparation of supramolecular linear polymer **5b** (Scheme 1) with up to 9.1 repeat units in which monomeric homoditopic molecules **1** and **2b** containing
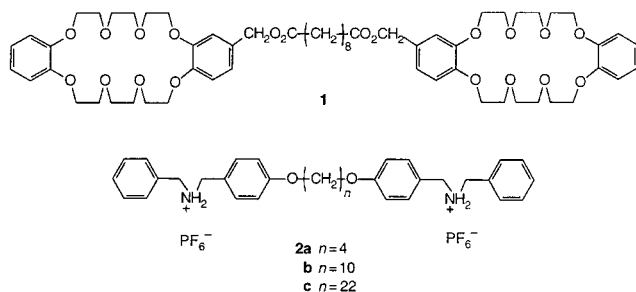
dibenzo-24-crown-8 (DB24C8) and dibenzylammonium hexafluorophosphate moieties, respectively, are linked non-covalently *via* pseudorotaxane complexes in equimolar concentrated solutions (>1.0 M in CD_3COCD_3–$CDCl_3$, 1 : 1 v/v at 295 K).[1]

Unsurprisingly, cyclic dimer **4b** (Scheme 1) was preferentially formed in equimolar dilute solutions ($<1.0 \times 10^{-3}$ M in CD_3COCD_3–$CDCl_3$, 1 : 1 v/v at 295 K) as observed in other cases.[2–6] In pursuit of more efficient construction of supramolecular polymers **5**, we speculated that by mismatching the
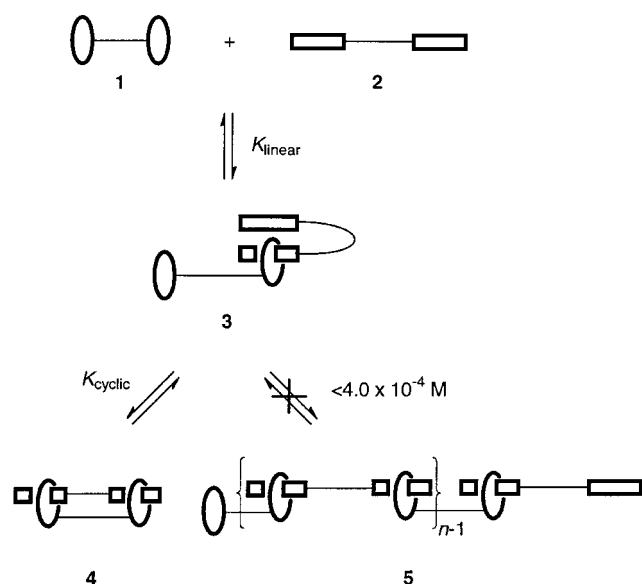
lengths of the aliphatic spacer units in the homoditopic molecules (*e.g.* **1** and **2**),† the equilibrium process may be reversed to favor linear extension (*e.g.* **3** and then to **5**) even in dilute conditions largely due to a greater steric penalty associated with the corresponding cyclic dimer complex (*e.g.* **4**).‡ Here, we investigate the stabilities of cyclic and linear dimer complexes based on complementary homoditopic molecules whose spacer segments were varied systematically.

The ^{1}H NMR spectra of dilute equimolar solutions of **1** and **2** [Fig. 1(*a*)–(*c*)] revealed four sets of N-CH$_2$ signals corresponding to (i) uncomplexed moieties of the ditopic guest molecule [H(**2**)$_u$], (ii) complexed moieties in cyclic dimer [H(**4**)], and (iii) complexed and (iv) uncomplexed moieties in the linear dimer [H(**3**)$_c$ and H(**3**)$_u$, respectively] on the basis of slow exchange on the NMR time scale.§ Integration of H(**3**)$_c$ and H(**3**)$_u$ gave a ratio of 1:1 for each solution,¶ indicating that the signals assigned to H(**3**)$_c$ and H(**3**)$_u$ arise from the same species.

The signal assignments were properly made based on our previous investigation[1] and the ^{1}H NMR spectrum [Fig. 1(*d*)] of a dilute solution of DB24C8 and **2b** which exhibited three sets of N-CH$_2$ signals corresponding to uncomplexed ammonium salt moieties of **2b** [H(**2b**)$_u$]‖ and complexed and uncomplexed ammonium salt moieties of **6b** [H(**6b**)$_c$ and H(**6b**)$_u$, respectively].** The signals for H(**6b**)$_c$ and H(**6b**)$_u$ were integrated to be 1 : 1; thus complex **6b** was exclusively formed, confirming that the two signals assigned to **6b** (and to **3**) arise from the same species. The considerable downfield chemical shift observed for H(**6b**)$_u$ with respect to H(**2b**)$_u$ in Fig.1(*d*) ($\Delta\delta$ = 0.17 ppm) is presumably a consequence of interaction(s) between the pseudorotaxane and free ammonium salt moieties in **6b** (and by analogy in **3**); *e.g.* 'intramolecular' π-stacking between a benzo ring of complexed DB24C8 and the terminal phenyl ring of the free ammonium salt moiety achieved by folding of the flexible aliphatic spacer, as illustrated in Scheme 2.†† These spectroscopic observations allowed us to conclude that the signals in the region of δ 4.35 to 4.45 in Fig. 1(*a*)–(*c*) correspond to H(**3**)$_u$, and that only **3** and **4** exist and cyclic or linear oligomers **5** are not present in detectable amounts in these dilute solutions.

Since the concentrations of each species (**1**, **2**, **3** and **4**) at equilibrium are readily known, one can estimate the association
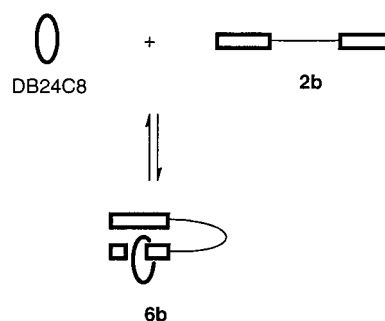

Scheme 1 Cartoon illustrations of formation of the linear dimer complex **3** and cyclic dimer complex **4** from homoditopic molecules **1** and **2** in substantially dilute conditions.

Scheme 2 Cartoon illustrations of formation of the 1 : 1 dimer complex **6b** from DB24C8 and homoditopic molecule **2b** in substantially dilute conditions.

Table 1 Association constants (K_{linear}) at 295 K and enthalpy and entropy for linear dimerization in CD_3COCD_3–$CDCl_3$ (1 : 1, v/v)[a]

Complex	K_{linear}/M^{-1}	ΔH_1/kcal mol^{-1}	ΔS_1/cal mol^{-1} K^{-1}
3a	$(1.3 \pm 0.3) \times 10^3$	-8.0 ± 0.6	-13 ± 1
3b	$(3.7 \pm 0.7) \times 10^3$	-11 ± 2	-20 ± 3
3c	$(5.2 \pm 0.6) \times 10^3$	-10 ± 3	-23 ± 7

[a] $\pm$ values represent standard deviations.

Table 2 Association constants (K_{cyclic}) at 295 K and enthalpy and entropy for cyclic dimerization in CD_3COCD_3–$CDCl_3$ (1 : 1, v/v)[a]

Complex	K_{cyclic}/M^{-1}	ΔH_c/kcal mol^{-1}	ΔS_c/cal mol^{-1} K^{-1}
4a	2.5 ± 0.4	-8.6 ± 1.0	-27 ± 2
4b	1.7 ± 0.3	-3.7 ± 0.1	-12 ± 1
4c	0.62 ± 0.03	-2.1 ± 0.6	-8.1 ± 0.4

[a] $\pm$ values represent standard deviations.

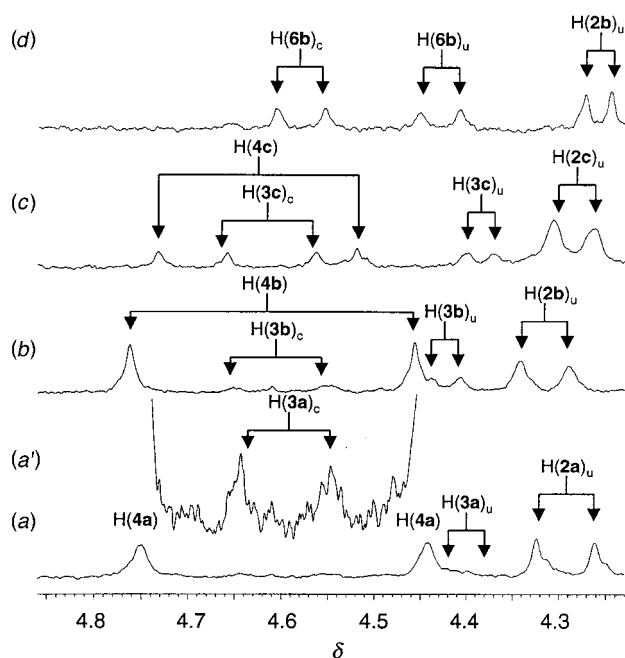**Fig. 1** The stacked ^1H NMR spectra of equimolar solutions of (*a*) **1** and **2a**, (*b*) **1** and **2b**, and (*c*) **1** and **2c** (4.0×10^{-4} M each) and (*d*) a solution of DB24C8 and **2b** ($8.0 \times 10^{-4}/4.0 \times 10^{-4}$ M) at 295 K (400 MHz, CD_3COCD_3–$CDCl_3$, 1 : 1, v/v). A vertically enlarged version of the spectrum in Fig. 1(*a*) (δ 4.45-4.75) is shown in Fig. 1(*a'*). In Fig. 1(*a*)–(*c*) the four sets of signals are assigned for the benzylic protons of the ammonium salt units in **2** (uncomplexed, u), **3** (complexed end, c, and uncomplexed end, u) and **4**. In Fig. 1(*d*) the three sets of signals are assigned for the benzylic protons of the ammonium salt units in **2b** (uncomplexed, u) and **6b** (complexed end, c, and uncomplexed end, u).

constants (K_{linear} and K_{cyclic}); the results at 295 K are summarized in Tables 1 and 2 with ΔH and ΔS values.‡‡

K_{linear} (Table 1) varies systematically, increasing as the length of the aliphatic spacer increases (from **3a** to **3c**). Note that ΔH_1 and ΔS_1 become more negative from **3a** to **3b**, but the values for **3b** and **3c** are essentially identical. This observation is consistent with more effective stabilization of **3b** and **3c** relative to **3a** by 'intracomplex' interaction between the threaded crown ether and the non-threaded ammonium salt moiety; as shown by CPK models the longer spacers in the latter two species allow more effective interaction.

Similarly, K_{cyclic} (Table 2) varies systematically, decreasing as the length of the aliphatic spacer increases (from **4a** to **4c**).

ΔH_c and ΔS_c also become less negative as the spacer length increases, the most dramatic change taking place from **4a** to **4b**. These observations are consistent with two factors: (i) limited stabilization of precursor **3a** by intracomplex interaction and (ii) the increasing end-to-end distance of the linear precursors **3**.

As we anticipated, K_{cyclic} for **4c** was reduced, almost three-fold, compared to that for **4b**. Most importantly, the K_{linear}/K_{cyclic} value, which should be regarded as a critical parameter for the efficiency of linear extension to **5**, obtained for **3c/4c** (8.4×10^3 M^{-1}) clearly stands out, showing nearly a 16-fold improvement with respect to that of **3a/4a** (5.2×10^2 M^{-1}).

Our present results, contrary to our initial speculation, indicate that the steric penalty associated with **4** may not be as important as the end-to-end distance of **3** in terms of shifting the equilibrium over to the linear dimer complex. Nevertheless, purposely increasing the length of the spacer in one component successfully reversed the equilibrium of **3** and **4** toward **3**. Our preliminary investigation of construction of a supramolecular polymer using **1** and **2c** as building components has revealed an improved linear extension in **5c** at lower concentrations relative to using **1** and **2b**. We will report these results in detail in a forthcoming publication.

Footnotes and references

† All compounds were characterized by ^1H NMR spectroscopy, FAB mass spectrometry, and elemental analysis.

‡ Similar observations, though qualitative in nature, were reported for complexation of ditopic aromatic guests with biscyclophanes in water (ref. 6).

§ Slow exchange was also reported for the complexation of Bn-NH$_2^+$–Bn·PF$_6^-$ and DB24C8 in solution (ref. 7).

¶ The ^1H NMR spectra of three sets of each solution were recorded with at least 50 min of acquisition time for determination of ratios of the H(**3**)$_c$ and H(**3**)$_u$ signals. Each spectrum was enlarged vertically (thus the signals of interest were detectable from the baselines; *e.g.* Fig. 1(*a'*) shows a vertically enlarged version of the spectrum in Fig. 1(*a*) from δ 4.45 to 4.75) and the signals were integrated using a deconvolution technique. Ratios of the H(**3**)$_c$ and H(**3**)$_u$ signals were determined within experimental errors (*ca.* 5%).

‖ The downfield chemical shift ($\Delta\delta$ = 0.05 ppm) observed for H(**2b**)$_u$ in Fig. 1(*b*) compared to that in Fig. 1(*d*) is attributed to the increased ratio of PF$_6^-$ relative to uncomplexed ammonium salt moieties of **2b**. To demonstrate this phenomenon experimentally, a solution of DB24C8 and **2b** ($8.0 \times 10^{-4}/4.0 \times 10^{-4}$ M in CD_3COCD_3–$CDCl_3$, 1 : 1 v/v) was mixed with solutions of Bu$_4$N$^+$PF$_6^-$ (from 4.0×10^{-4} to 16×10^{-4} M in the same solvent system) and the ^1H NMR spectra were taken at 295 K. A gradual downfield chemical shift for H(**2b**)$_u$ was observed as the PF$_6^-$ concentration was increased, validating the hypothesis.

** Many different conformations existing at the pseudorotaxane complexation site of **6b** contribute to the broadening of the H(**6b**)$_c$ and H(**6b**)$_u$ signals since the signals are time averaged.

†† In the crystal structure of the pseudorotaxane from DB24C8 and Bn–NH$_2^+$–Bn·PF$_6^-$ (ref. 7) one of the benzo rings π-stacks with one of the phenyl rings. The other electron rich benzo ring is uncomplexed.

‡‡ Variable-temperature ^1H NMR spectroscopy was performed in the range 285–313 K. Plots of $R\ln K_{linear}$ and $R\ln K_{cyclic}$ *versus* $1/T$ yielded straight lines ($R > 0.97$) from which ΔH and ΔS values for linear and cyclic dimerization were obtained.

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