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Original Research Article

Assembly and Dissociation of α-Cyclodextrin [2]Pseudorotaxanes with α,ω-Bis(*N*-(*N*,*N*′-dimethylethylenediamine)alkane Threads

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Abstract

A series of novel bischelate bridging ligands, $CH_3NH(CH_2)_2N(CH_3)(CH_2)_nN(CH_3)(CH_2)_2NHCH_3$ (n = 9, 10, 11, and 12) were synthesized as hydrochloride salts and characterized by elemental analyses, electrospray mass spectrometry, and ^1H and ^{13}C NMR spectroscopy. These ligands form [2]pseudorotaxanes with α-cyclodextrin (α-CD) and the stability constants have been determined from ^1H NMR titrations in D_2O. The kinetics and mechanism of the assembly and dissociation of a [2]pseudorotaxane in which α-CD has been threaded by the $CH_3NH_2(CH_2)_2N(CH_3)(CH_2)_{12}N(CH_3)(CH_2)_2NH_2CH_3^{2+}$ ligand were determined in aqueous solution using ^1H NMR spectroscopy. A weak inclusion of the dimethylethylenediamine end group precedes the passage of the α-CD onto the hydrophobic dodecamethylene chain.

Introduction

Pseudorotaxanes are supramolecular species in which a linear chain rapidly and reversibly threads through a cyclic molecular bead [1, 2]. If the linear chain has sufficiently bulky end groups, such that the complex is prevented from dissociating into the cyclic and linear components, the species is termed a rotaxane. At the boundary between these two groups are species in which the diameters of the end groups and the internal cavity of the cyclic bead are similar, such that the pseudorotaxane assembles and dissociates slowly. In some cases, the assembly of the pseudorotaxane occurs only at elevated temperatures by a process termed slippage [3–6]. When the assembled complex is returned to room temperature, it behaves as a rotaxane and is stable with respect to dissociation.

A cyclic molecular bead commonly employed in the assembly of pseudorotaxanes and rotaxanes is cyclodextrin (CD) [7–9]. Cyclodextrins are a group of cyclic oligosaccharides which most commonly contain six (α-CD), seven (β-CD), or eight (γ-CD) α-(1 → 4)-linked D-(+)-glucopyranose units [10–12]. The smallest α-CD, with a hydrophobic interior cavity of a 5.5 Å diameter, has been shown to have a strong affinity for linear polymethylene chains. The self-assembly of pseudorotaxanes and rotaxanes with cyclodextrins may proceed by a number of mechanisms depending on the nature of the threading molecule and in particular the size and shape of the terminal groups. We have observed, for example, that replacing one of the methyl groups one each end of the $(CH_3)_3N(CH_2)_{10}N(CH_3)_3^{2+}$ thread by ethyl groups reduces the rate of pseudorotaxane formation with α-cyclodextrin by a factor of 10 at 25 °C, while changing the thread to $(CH_3)_3P(CH_2)_{10}P(CH_3)_3^{2+}$ results in a decrease in the rate by about 10^6 at 75 °C with no assembly observed at room temperature [13]. With a series of $R(CH_2)_nR$ threads, where R is a *para*-substituted pyridinium end group and n = 10 or 12, the self-assembly of the pseudorotaxanes involves a weak binding of a 4-$Rpyr^+$ end group in the α-CD cavity, prior to threading [14, 15].

In this paper, a series of novel bischelate bridging ligands, $CH_3NH(CH_2)_2N(CH_3)(CH_2)_nN(CH_3)(CH_2)_2NHCH_3$ (n = 9–12) were synthesized as hydrochloride salts and combined with α-CD in aqueous solution to form [2]pseudorotaxanes. The stability constants for the $\{CH_3NH_2(CH_2)_2N(CH_3)(CH_2)_nN(CH_3)(CH_2)_2NH_2CH_3\bullet\alpha\text{-CD}\}^{2+}$ pseudorotaxanes were measured in D_2O at 25 °C by ^1H NMR titrations and are compared with the values for other $R(CH_2)_nR^{m+}$ threads. The kinetics and mechanism of the assembly and dissociation of the α-CD pseudorotaxane with the diprotonated $CH_3NH_2(CH_2)_2N(CH_3)(CH_2)_{12}N(CH_3)(CH_2)_2NH_2CH_3^{2+}$ ligand have been determined using variable temperature ^1H NMR spectroscopy.

Experimental

Materials

The α-cyclodextrin (Aldrich) was dried at 80 °C under reduced pressure for at least 10 hours prior to use.

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N,*N*′-Dimethylethylenediamine, 1,9-dibromononane, 1,10-dibromodecane, 1,11-dibromoundecane, and 1,12-dibromododecane (Aldrich) were used as received. The 1,12-bis(4,4′-bipyridyl)dodecane dibromide was prepared as reported previously [16].

The α,ω-bis(*N*-(*N*,*N*′-dimethylethylenediamine) alkane tetrahydrochloride salts, (n = 9, 10, 11, and 12), were prepared by the general method of Miller [17], with the following modifications. To 5 mL of *N*,*N*′-dimethylethylenediamine, the appropriate α,ω-dibromoalkane was added slowly over 6 hours at 80 °C. The excess of *N*,*N*′-dimethylethylenediamine was removed under reduced pressure and the yellow residue was dissolved in chloroform. The solution was washed with 1 M NaOH and the chloroform evaporated. The amine was then dissolved in ethyl acetate and 10 mL of a 10% solution of HCl added. The separated HCl solution was neutralized with 1 M NaOH and evaporated to dryness. The solid was washed twice with ethyl acetate and once with diethyl ether.

1,9-bis(*N*-(*N*,*N*′-dimethylethylenediamine)nonane tetrahydrochloride. Yield 85%. Mp. 134–136 °C. Anal. Found C 44.96%; H 10.09%; N 11.34%. Calc. for $C_{17}N_4H_{40}$•4HCl•H_2O C 44.00%; N 9.91%; N 12.13%. ^{1}H NMR (D_2O) δ 3.31 (8H, d, $H_{1,2}$), 2.99 (2H, t, H_α), 2.72 (6H, d, N–CH_3), 2.70 (6H, d, N′-CH_3), 1.59 (2H, t, H_β), 1.23 (10H, m, $H_{\gamma\ \varepsilon}$) ppm. ^{13}C NMR (D_2O) δ 57.12 ($C_{N'}$), 50.64 (C_N), 42.68 (C_2), 39.96 (C_1), 33.25 (C_α), 28.10 (C_ε), 27.96 (C_β), 25.42 (C_δ), 23.43 (C_γ). ES$^+$-MS m/z = 301.3 $[M + H]^+$

1,10-bis(*N*-(*N*,*N*′-dimethylethylenediamine)decane tetrahydrochloride. Yield 86%. Mp. 166–168 °C. Anal. Found C 46.66%; H 10.02%; N 11.35%. Calc. for $C_{18}N_4H_{42}$•4.5HCl•0.5H_2O C 46.09%; N 10.02%; N 11.94%. ^{1}H NMR (D_2O) δ 3.40 (8H, d, $H_{1,2}$), 3.09 (2H, t, H_α), 2.80 (6H, d, N–CH_3), 2.71 (6H, d, N′-CH_3), 1.64 (2H, t, H_β), 1.26 (12H, m, $H_{\gamma-\varepsilon}$) ppm. ^{13}C NMR (D_2O) δ 56.99 ($C_{N'}$), 50.64 (C_N), 42.69 (C_2), 39.91 (C_1), 33.23 (C_α), 28.25 (C_ε), 28.06 (C_β), 25.36 (C_δ), 23.45 (C_γ). ES$^+$-MS m/z = 315.3 $[M + H]^+$

1,11-bis(*N*-(*N*,*N*′-dimethylethylenediamine)undecane tetrahydrochloride. Yield 81%. Mp. 144–146 °C. Anal. Found C 46.75%; H 9.93%; N 10.89%. Calc. for $C_{19}N_4H_{44}$•4.5HCl C 46.29%; N 9.84%; N 11.33%. ^{1}H NMR (D_2O) δ 3.40 (8H, d, $H_{1,2}$), 3.10 (2H, t, H_α), 2.81 (6H, d, N–CH_3), 2.68 (6H, d, N′-CH_3), 1.62 (2H, t, H_β), 1.16–1.21 (14H, m, $H_{\gamma-\xi}$) ppm. ^{13}C NMR (D_2O) δ 57.05 ($C_{N'}$), 50.65 (C_N), 42.69 (C_2), 39.94 (C_1), 33.28 (C_α), 28.41 (C_ξ), 28.40 (C_ε), 28.14 (C_β), 25.49 (C_δ), 23.47 (C_γ). ES$^+$-MS m/z = 329.6 $[M + H]^+$

1,12-bis(*N*-(*N*,*N*′-dimethylethylenediamine)dodecane tetrahydrochloride. Yield 88%. Mp. 176–178 °C. Anal. Found C 47.85%; H 9.69%; N 10.87%. Calc. for $C_{20}N_4H_{46}$•4.5HCl C 47.45%; N 9.98%; N 11.12%. ^{1}H NMR (D_2O) δ 3.35 (8H, d, $H_{1,2}$), 3.05 (2H, t, H_α), 2.75 (6H, d, N–CH_3), 2.66 (6H, d, N′-CH_3), 1.58 (2H, t, H_β), 1.15-1.20 (16H, m, $H_{\gamma-\xi}$) ppm. ^{13}C NMR (D_2O) δ 57.09 ($C_{N'}$), 50.63 (C_N), 42.66 (C_2), 39.96 (C_1), 33.24 (C_α), 28.58 (C_ξ), 28.45 (C_ε), 28.16 (C_β), 25.50 (C_δ), 23.46 (C_γ). ES$^+$-MS m/z = 343.4 $[M + H]^+$

Methods

The ^{1}H NMR spectra, titrations, and kinetic measurements were recorded on a Bruker Avance 400 instrument and the ^{13}C NMR spectra were recorded on a Bruker Avance 500 instrument in D_2O. The α-cyclodextrin inclusion stability constants for the guest compounds in this study were determined by ^{1}H NMR titrations of the compounds with α-CD. Typically, a 0.50 mL solution of 2.0 mM guest, at a constant ionic strength of 0.050 M (NaCl), was titrated with consecutive additions (5–100 μL, using a 250 μL graduated Hamilton gas-tight syringe) of a concentrated α-CD solutions, also containing 2.0 mM guest species. The solutions were thoroughly mixed and allowed to equilibrate in the probe (298.0 ± 0.1 K) prior to obtaining a spectrum. The stability constant was determined as described previously [18].

In the kinetics experiments for the formation of the pseudorotaxane, a weighed amount of dried α-CD (10–40 mg) was directly added to a 5 mm NMR tube with a thermostatted solution of the 1,12-bis(*N*-(*N*,*N*′-dimethylethenediamine))dodecane (5.0 mM) in D_2O containing 0.05 M NaCl (pH ∼ 5). Spectra were collected at fixed intervals for at least four half-lives and again after 10–15 half-lives until the equilibrium was reached. The concentration of L•CD formed from the guest (L) and host (CD) threaded molecules was determined by integrating the H_β resonance of the guest. The plots of $\ln\{([L\bullet CD]_e-[L\bullet CD]_0)/([L\bullet CD]_e-[L\bullet CD]_t)\}$ against time were linear for at least 3 half-lives, with the slopes yielding rate constants with error limits in the range of 3–7% from linear regressions. For the kinetics of the dissociation of the [2]pseudorotaxane, a weighed amount (20 mM, 0.50 mL) of a competing guest, 1,12-bis(4,4′-bipyridinyl)dodecane dibromide, was added to the solution of the [2]pseudorotaxane prepared by equilibrating a 0.50 mL mixture of 2.0 mM ligand (L) and 6.0 mM α-CD.

The mass spectrometry measurements were obtained on a VG Quattro quadrupole mass spectrometer, with an atmospheric pressure electrospray source. Samples, as solutions in distilled water with α-CD, were introduced into the source at a flow rate of 5 mL min^{-1}. Elemental analyses were preformed by Canadian Microanalytical Services Ltd. (Delta, BC).

Results and discussion

Pseudorotaxane stability constants

The bischelating ligands $CH_3NH(CH_2)_2N(CH_3)(CH_2)_n$ $N(CH_3)(CH_2)_2NHCH_3$ (n = 9, 10, 11, and 12) were synthesized by the reaction of N,N′-dimethylethylenediamine with the appropriate α,ω-dibromoalkane and

were isolated as hydrochloride salts. In solution at neutral pH, the ligands exist as dications, with the protonation of the secondary nitrogen atoms. By comparison with other alkyl ethylenediamine ligands, such as $CH_3NH(CH_2)_2N(CH_3)(CH_2)_2NHCH_3$, the p$K_a$ values for the conjugate acids of the tertiary amine nitrogens are about 3, while the pK_a values for the conjugate acids of the secondary amine nitrogens are 9–10 [19]. At a pH of about 5, the conditions under which the measurements in this study were carried out, the ligands would be protonated on the secondary amine nitrogens, and thus the ligands would be dications, $CH_3NH_2(CH_2)_2N(CH_3)(CH_2)_nN(CH_3)(CH_2)_2NH_2CH_3^{2+}$.

The addition of α-cyclodextrin to aqueous solutions of the ligands results in the formation of pseudorotaxane complexes. The inclusion of the ligand in the asymmetric α-CD cavity results in a splitting of the majority of the resonances of the symmetry-related protons (Figure 1) into pairs of peaks, as depicted in Figure 2 for the α, β, γ and N–CH_3 protons for the $CH_3NH_2(CH_2)_2N(CH_3)(CH_2)_{12}N(CH_3)(CH_2)_2NH_2CH_3^{2+}$ ligand. The N′-CH_3 protons did not separate into pairs of peaks for this ligand, but splittings were observed for $n = 9$, 10, and 11. The separations of the peaks are presented in Table 1 (the separations in the δ, ε, and ξ protons are difficult to resolve). The upfield peaks of the pairs have been shown to correspond to the protons on the half of the thread nearest to the narrower end of the thread [13]. As observed in other pseudorotaxanes of α-CD with symmetrical $R(CH_2)_nR^{m+}$ threads (such as those listed in Table 2) the peak separations generally decrease with the polymethylene chain length n and increase from the outsides of the thread towards the center [13–16, 18, 20–25]. The similarities in the separations for the $CH_3NH_2(CH_2)_2N(CH_3)(CH_2)_nN(CH_3)(CH_2)_2NH_2CH_3^{2+}$ ligands where $n = 9$ and 10, despite the change in chain length, is likely due to the orientation effects of the odd/even chain lengths. There are also complexation induced shifts (CIS) in the resonances for the α-CD, the H-3 and H-5 in the interior of the cavity, in particular. Because of the overlaps of the resonances of the bound and unbound cyclodextrin, they are not useful in determining the inclusion stability constants.

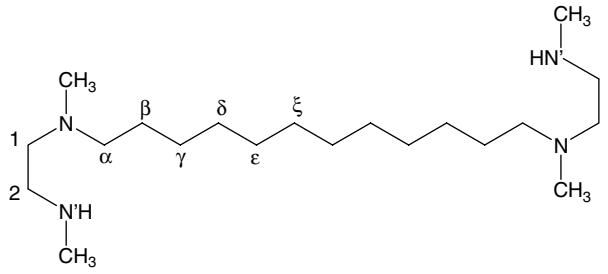

Figure 1. Structure of $CH_3NH(CH)_2N(CH_3)(CH_2)_{12}N(CH_3)(CH_2)_2NHCH_3$ with the proton and carbon numbering scheme for the ^1H and ^{13}C NMR assignments.

The α-cyclodextrin inclusion stability constants (K_L) were determined by means of ^1H NMR titrations of the ligand with α-CD in D_2O containing 0.05 M NaCl (pH ~ 5).

$$2^+ + \alpha - CD \overset{K_L}{\rightleftharpoons} \{L \bullet \alpha - CD\}^{2+} \qquad (1)$$

The aliphatic ligand proton resonances are upfield from the CD signals (3.4–3.9 ppm) and upon addition of α-CD the changes of the ligand peaks are clearly evident. Therefore, the binding constants may be determined from the integrations of the bound and unbound H_α and H_β at various concentrations of α-CD. The inclusion stability constants K_L are presented in Table 2, along with corresponding values for other $R(CH_2)_nR^{m+}$ threads.

The stability constants measured in this study increase with an increase in the methylene chain length n, as observed for other thread systems (Table 2). This trend is because with the shorter methylene chain lengths the more hydrophilic R groups are placed closer to the hydrophobic cavity of the α-cyclodextrin. There is less dependence of the stability constants on the nature of the end group. For the decamethylene threads, for example, the values of K_L range primarily from 600 to 1500 M^{-1}. The exceptions to this are observed for $R = NH_3^+$ and OH, where hydrogen bonding of the end groups with the hydroxyl groups on the rims of the cyclodextrin enhances the pseudorotaxane stability constants. Harada has also demonstrated that in addition to the steric bulk of the end groups of the threading ligands, positive charges generated by protonation or alkylation of nitrogen centers may be used to "stopper" the threads and increase the stability of the rotaxanes [26]. While [3]pseudorotaxanes have been observed for some $R(CH_2)_{12}R$ and $R(CH_2)_{12}R'$ threads (R,R′ = NH_2 and COOH) [21], complexed by two α-CD molecules, there is no evidence in the ^1H NMR or electrospray mass spectra for such complexes with the ligands in the present study.

A ^1H NMR variable temperature study was performed to determine the coalescence temperature at which the assembly/dissociation process becomes rapid on the NMR timescale. Although the peaks began to broaden above 60 °C, coalescence of the H_α and H_β peaks as not observed below 90 °C.

Kinetics of pseudorotaxane assembly and dissociation

The addition of an excess of α-CD to the $CH_3NH_2(CH_2)_2N(CH_3)(CH_2)_{12}N(CH_3)(CH_2)_2NH_2CH_3^{2+}$ thread resulted in the slow, spontaneous threading of the host by the guest molecule, as illustrated in Figure 2. The observed first-order kinetic rate constants for the formation of the pseudorotaxane may be calculated using the integrated

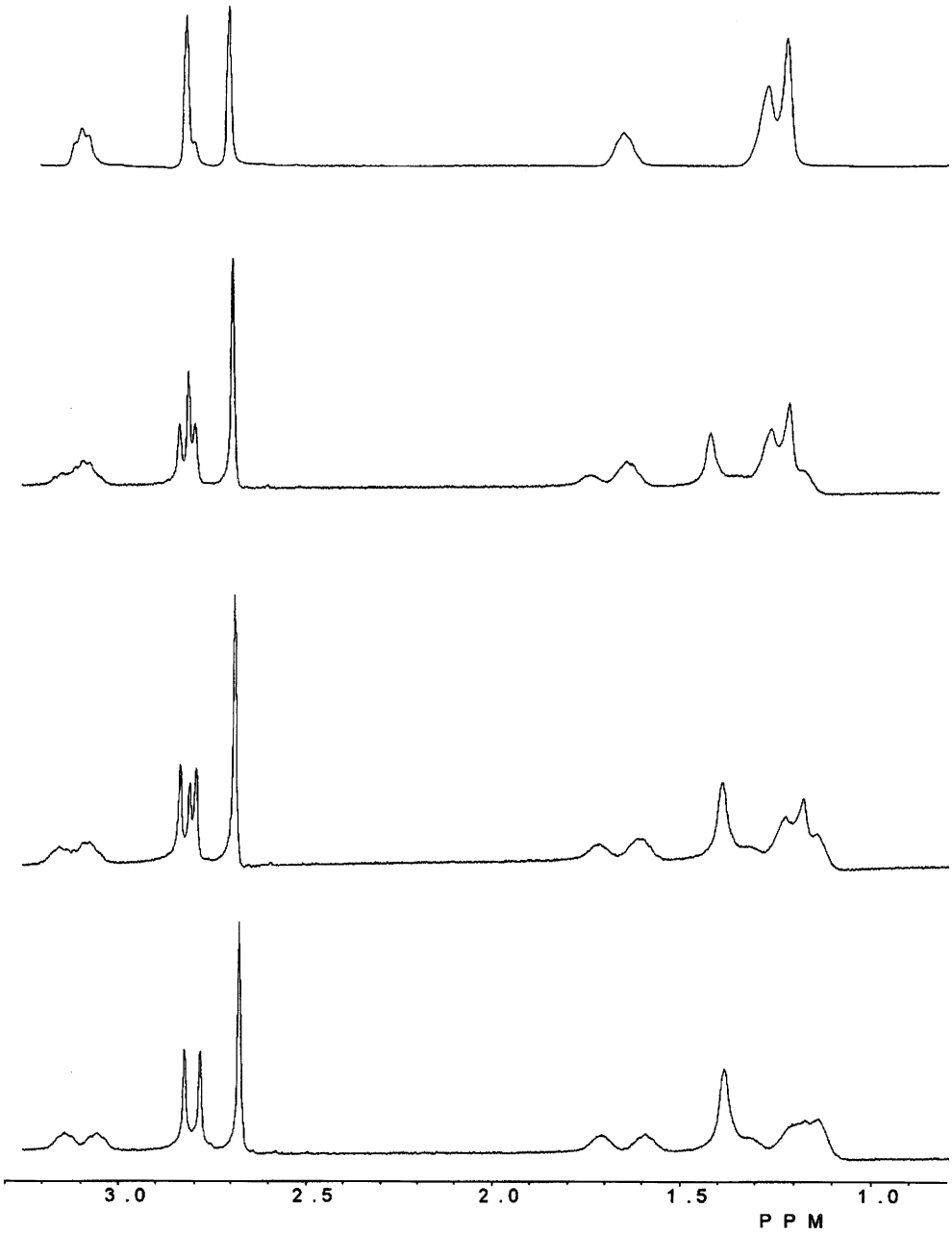

Figure 2. ^{1}H NMR spectra of a mixture of α-CD (6.0 mM) with $CH_3NH_2(CH)_2N(CH_3)(CH_2)_{12}N(CH_3)(CH_2)_2NH_2CH_3^{2+}$ (2.0 mM) in D_2O (0.05 M NaCl, pH ~ 5) at 25 °C as a function of time, from top to bottom: immediately after mixing, after 3.5 min, after 14.6 min, and after 34.8 min.

areas of the resonances of the included thread. With this particular pesudorotaxane, the concentration of [LCD] formed from the guest (L) and host (CD) was determined by integrating the H_β resonance of the guest. The plots of ln $\{([LCD]_e\text{-}[LCD]_0)/([LCD]_e\text{-}[LCD]_t)\}$ against time (where $[LCD]_0$, $[LCD]_t$, and $[LCD]_e$ are the pseudorotaxane concentrations initially, at time t, and at equilibrium, respectively) were linear for at least three half-lives, with the observed rate constant obtained from the slope.

Table 1. Separations (Hz) of pairs of ^{1}H NMR (400 MHz in D_2O) resonances for symmetry-related protons for the guest molecule in the $CH_3NH_2(CH_2)_2N(CH_3)(CH_2)_nN(CH_3)(CH)_2NH_2CH_3$•α-$CD^{2+}$ pseudorotaxane

n	H_α	H_β	H_γ	N–CH_3	N′–CH_3
9	48	69	79	34	5
10	56	69	79	36	6
11	45	58	93	26	3
12	34	48	98	18	< 1

The observed first-order rate constants increase with an increase of the α-CD concentration, with plots of k_{obs} against [α-CD] displaying curvature towards rate saturation at high [α-CD]. Assuming that k_{-1} is negligible with respect to k_1 the observed first-order rate constant may be fit to equation 2.

Table 2. Inclusion stability constants (K_L, M^{-1}) for the [2]pseudorotaxanes of α-cyclodextrin with $R(CH_2)_nR$ threads in aqueous solution at 25.0 °C

R	*n*			
	9	10	11	12
$N(CH_3)CH_2CH_2NH_2(CH_3)^{+a}$	257 ± 20	628 ± 20	880 ± 30	1088 ± 50
NH_3^{+b}		13500		7100
$N(CH_3)_3^{+c}$	240 ± 50	1360 ± 290	3170 ± 970	6760 ± 850
pyr^{+d}	410	1300		2700
bpy^{+e}	440 ± 34	1500 ± 100	3100 ± 400	3700 ± 540
pyz^{+f}	310 ± 70	1100 ± 100	2700 ± 300	3200 ± 740
R = bpy^+, R′ = pyz^{+f}	220 ± 30	1400 ± 130	2800 ± 330	4200 ± 300
COO^{-g}	690	1500	1700	6100
OH^h	3500 ± 400	7100 ± 800		

[a]This work, I = 0.05 M.
[b]Ref. 20, 21, I = 0.10 M.
[c]Ref.13, I = 0.10 M.
[d]Ref. 22. Ionic strength not stated; measured at T = 5 °C and calculated for T = 25 °C using $\Delta G°$ values.
[e]Ref. 18.
[f]Ref. 23.
[g]Ref. 24. I = 0.10 M, calculated for T = 25 °C using $\Delta G°$ values.
[h]Ref. 25.

Table 3. Kinetic and thermodynamic parameters for the assembly and dissociation of the α-cyclodextrin [2]pseudorotaxane $CH_3NH(CH_2)_2N(CH_3)(CH_2)_{12}N(CH_3)(CH)_2NHCH_3$·α-CD] in D_2O, *I = 0.05 M (NaCl)*

T (°C)	$10^3\ k_1$ (s^{-1})	K_{CD} (M^{-1})	$10^4\ k_{-1}$ (s^{-1})	K_1 (M^{-1})
20.0	2.03 ± 0.10	39 ± 3	1.02 ± 0.20	967 ± 20
22.5	4.02 ± 0.20	33 ± 3	1.31 ± 0.20	981 ± 30
25.0	5.83 ± 0.20	33 ± 2	2.14 ± 0.30	899 ± 20
27.5	7.90 ± 0.30	32 ± 4	2.77 ± 0.50	913 ± 30
$\Delta H^‡$ (kJ mol^{-1})	128 ± 17		99 ± 9	
$\Delta S^‡$ (J K^{-1} mol^{-1})	141 ± 50		29 ± 19	
$\Delta H°$ (kJ mol^{-1})		−20 ± 7		−10 ± 4
$\Delta S°$ (J K^{-1} mol^{-1})		−282 ± 22		−222 ± 12

Table 4. Rate constants (25 °C) and activation parameters for the self-assembly of α-CD pseudorotaxanes with $R(CH_2)_nR^{2+}$ threads

R	*n*	$10^2\ k_{in}$ ($M^{-1}\ s^{-1}$)[a]	$\Delta^‡$ (kJ mol^{-1})	$\Delta S^‡$ (J K^{-1} mol^{-1})
$–N(CH_3)(CH_2)_2NH_2CH_3^{+b}$	2	19.2 ± 2.8	111 ± 17	112 ± 50
$–N(CH_3)_3^{+c}$	10	16.4 ± 2.2	117 ± 2	134 ± 6
$–N(CH_3)_2CH_2CH_3^{+c}$	10	0.58 ± 0.04	120 ± 6	114 ± 16
-bpy-$(CH_2)_2CH_3^{2+d}$	10	83 ± 13	49.8 ± 0.4	−79.5 ± 8.0
4-*tert*-butylpyridinium^{+e}	10	0.76 ± 0.14	102 ± 10	58 ± 32
4-(α-ethyl-α-methyl-methanol)pyridinium^{+f}	12	17.1 ± 0.9	138 ± 8	165 ± 24
4-(α-propyl-α-methyl-methanol)pyridinium^{+f}	12	10.0 ± 0.5	109 ± 8	64 ± 24
$–COO^{-g}$	12	400,000	47.4	−17.0

[a]$k_{in} = k_{-1}K_{CD}$
[b]This work.
[c]Ref. 13.
[d]Ref. 27. Asymmetric $[R(CH_2)_{10}R']^{2+}$ thread, where R is the viologen shown and R′ is a bulky carbazole group that cannot thread through α-CD.
[e]Ref. 14.
[f]Ref. 15.
[g]Ref. 24.

$$k_{obs} = k_1K_{CD}[\alpha - CD]\ 1 + K_{CD}[\alpha - CD] \quad (2)$$

A double reciprocal plot of k_{obs}^{-1} against $[\alpha\text{-CD}]^{-1}$ at 25 °C (Figure 3) yields a value of k_1 = (5.83 ± 0.20) × 10^{-3} s^{-1} from the intercept and K_{CD} = 33 ± 2 M^{-1} from the ratio of the intercept to the slope. From rate constant determinations at several temperatures between 20 and 28 °C, the activation

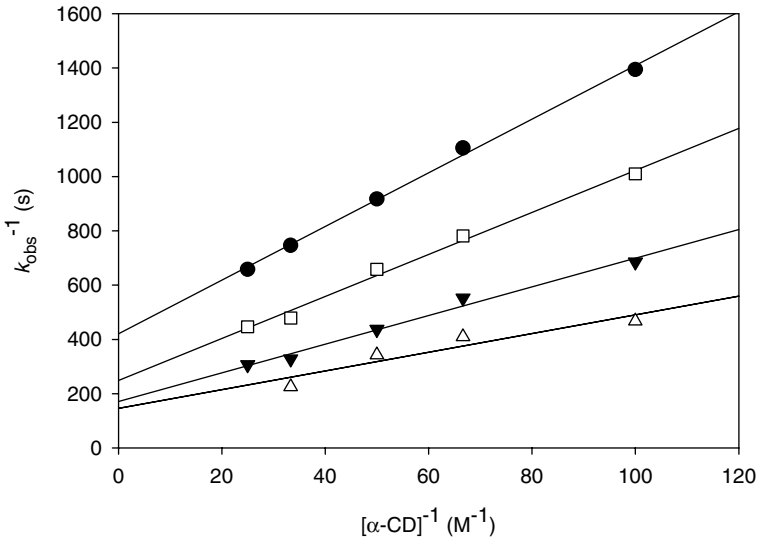

Figure 3. Plots of k_{obs}^{-1} against $[\alpha\text{-CD}]^{-1}$ for the formation of the pseudorotaxane $\{CH_3NH_2(CH)_2N(CH_3)(CH_2)_{12}N(CH_3)(CH_2)_2NH_2CH_3\bullet\alpha\text{-CD}\}^{2+}$ at (•) 20.0 °C, (□) 22.5 °C, (▲) 25.0 °C, and (△) 27.5 °C.

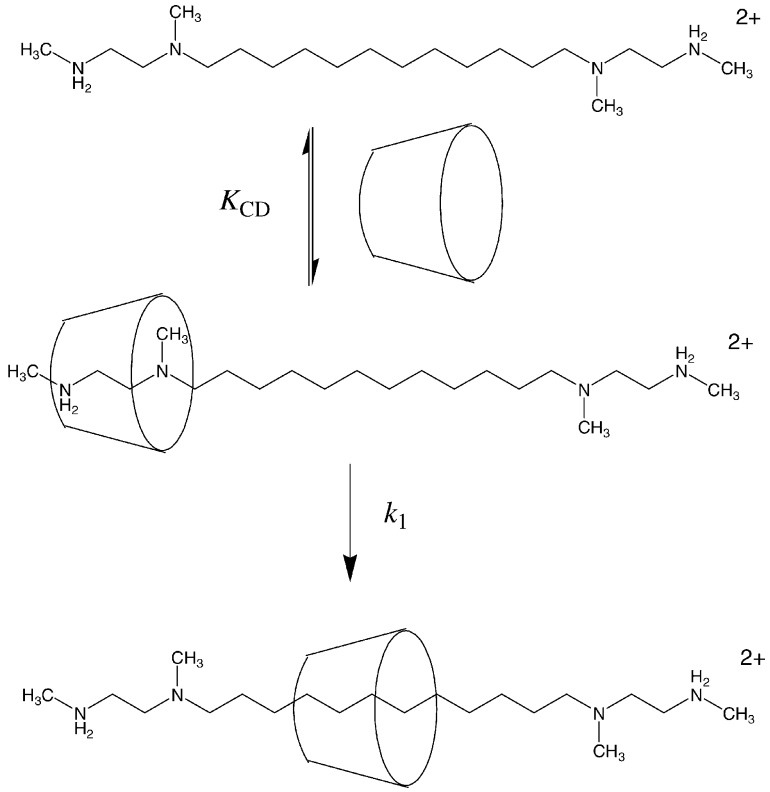

Figure 4. Mechanism of the self-assembly of the [2]pseudorotaxane $\{CH_3NH_2(CH_2)_2N(CH_3)(CH_2)_{12}N(CH_3)(CH_2)_2NH_2CH_3\bullet\alpha\text{-CD}\}^{2+}$.

parameters associated with k_1 were determined to be $\Delta H^{\ddagger} = 128 \pm 17$ kJ mol^{-1} and $\Delta S^{\ddagger} = 141 \pm 50$ k^{-1}J mol^{-1}.

The kinetic behavior is consistent with a mechanism in which the α-cyclodextrin initially forms a weak inclusion complex with the *N*,*N*′-dimethylethylenediamine end group, prior to passing over tertiary amine center to end up including the hydrophobic polymethylene chain, as depicted in Figure 4.

The kinetics of the dissociation of the $\{CH_3NH_2(CH_2)_2N(CH_3)(CH_2)_{12}N(CH_3)(CH_2)_2NH_2CH_3\bullet\alpha\text{-CD}\}^{2+}$ pseudorotaxane were investigated (using ^{1}H NMR), in the presence of a 10-fold excess of a competing guest, 1,12-bis(4,4′-bipyridinyl)dodecane, $[bpy(CH_2)_{12}bpy]^{2+}$. The $[bpy(CH_2)_{12}$- $bpy]^{2+}$ guest rapidly forms a very stable pseudorotaxane with α-CD [16, 18] (see Table 2), as a result of the hydrophobic dodecamethylene chain, and therefore should efficiently capture the α-CD upon the dissociation of the $\{CH_3NH_2(CH_2)_2N(CH_2)_{12}N(CH_2)_2NH_2CH_3\bullet\alpha\text{-CD}\}^{2+}$ pseudorotaxane. The process most likely involves the initial dissociation of the dication guest followed by the

rapid inclusion of the α-CD [16, 18] by the $[bpy(CH_2)_{12}bpy]^{2+}$ dication. An associative process involving inclusion of both the dication guest and the $[bpy(CH_2)_{12}bpy]^{2+}$ dication is highly unlikely due to the limited size of the α-CD cavity and the electrostatic repulsion that would be created between the two dication guests. The first-order rate constants were determined by monitoring the disappearance of the pair of H_β resonances of the guest. At 25 °C ($I = 0.10$ (NaCl), pH∼5), k_{-1} was determined to be $(2.14 \pm 0.30) \times 10^{-4} s^{-1}$, with $\Delta H^{\ddagger}_{-1} = 99 \pm 10$ kJ mol^{-1} and $\Delta S^{\ddagger}_{-1} = 29 \pm 19$ k^{-1} mol^{-1}, from rate constant measurements between 20 and 28 °C (Table 2). The stability constant K_1 for the [2]pseudorotaxane, with respect to the dissociated linear and cyclic components may be calculated from $K_1 = k_{in}/k_{out} = k_1 K_{CD}/k_{-1}$ The value of K_1 at 25 °C is about 900 ± 30 M^{-1}, in good agreement with the value of 1088 ± 50 M^{-1} determined from the ^{1}H NMR titration. Previous kinetic studies with other $R(CH_2)_nR^{m+}$ threads, such as $R = N(CH_3)_3^{+}$, have shown that the assembly rate constant k_{in} decreased very slightly with an increase in the polymethylene chain length n, while the dissociation rate constant $k_{out} = k_{-1}$ decreased much more rapidly with an increase in n, such that the observed trend in the stability constants (Table 2) is primarily a function of the effect of chain length on the dissociation rate constant.

The *N*,*N*′-dimethylethylenediamine end groups on the threading ligand are capable of chelating transition metals, as demonstrated by the use of *N*,*N*′-dimethylethylenediamine chelating ligands in the Cu(I) catalysis of *N*-amidation of aryl halides [28]. Investigations into the effect of metal coordination on the kinetics of the assembly and dissociation of the rotaxanes formed in this study are in progress.

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