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EFFECTS OF SMALL STRUCTURAL CHANGING ON THE KINETIC AND THERMODYNAMIC STABILITIES OF PSEUDOROTAXANES

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Abstract – Pseudorotaxanes were synthesized in this study. They comprised secondary ammonium ions and 24-membered crown ethers possessing one–four benzene rings fusing macrocycles. Kinetic and thermodynamic stabilities of the complexes were dependent on their number of benzene rings.

The pseudorotaxane structure comprises a macrocyclic ring and an axle. It can tentatively be fixed by interaction of both components. Furthermore, the association-dissociation process between the two components is reversible,¹ and an important factor of the association-dissociation rate is the relationship between the sizes of the macrocycles and the axle ends.

Small structural changes can engender unexpectedly large effects on the association-dissociation reaction of pseudorotaxanes.² A particularly striking example has been reported: the replacement of CH₃ groups by CD₃ groups on stopper parts caused the rate constant value of deslipping of rotaxane to increase 10%.^{2a} We also demonstrated that isomerization of α -methylstilbene on the axle functioned effectively as a reversible end-closing and end-opening rotaxane process: (*Z*)- α -methylstilbene acted as a stopper, but (*E*)- α -methylstilbene was not sufficiently large to prevent deslipping of macrocycle.³ Stoddart also reported that the pseudorotaxanes' kinetic stability depends on the nature of the solvent and on the size of the axle ends.⁴

In all alkanes, carbon-carbon single bond lengths are all nearly constant at 1.54 Å, and the bonds are usually free to rotate. On the other hand, carbon-carbon bonds of benzene are 1.40 Å in length. Moreover, the bonds are rigid because of the cyclic structure and the conjugated π -bonds. Therefore, introduction of a C-C bond of benzene in replacement of a C-C single bond in a macrocycle produces a delicately smaller

cavity size, and it also produces a more rigid macrocycle.

In this communication, we describe the formation of pseudorotaxanes consisting of mono-, di-, tri-, and tetrabenzo[24]crown ethers with secondary ammonium salts. We show kinetic stability of pseudorotaxanes by a change in the number of benzene rings fusing the macrocycles, and also describe the thermodynamic stability of the pseudorotaxanes (Figure 1).

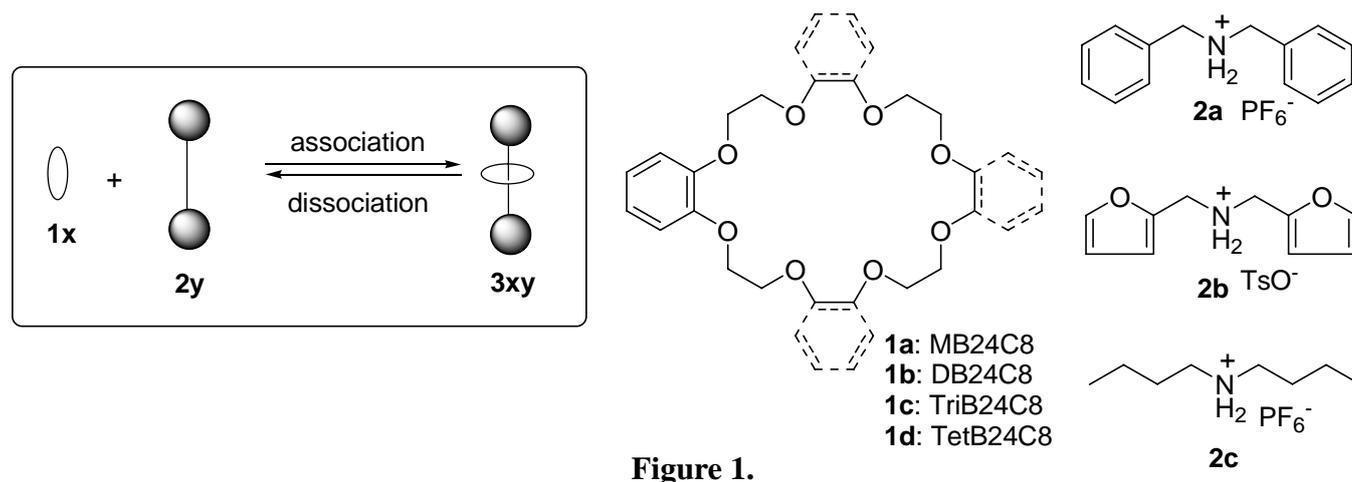


Figure 1.

Corresponding [24]crown ethers (**1**) were prepared using standard procedures.⁵ As a first experiment, NMR spectrum monitored titrations were performed to demonstrate that pseudorotaxanes were formed by interaction between crown ethers (**1**) and the ammonium ion (**2a**). The ¹H NMR spectra of a 3 : 1 CDCl₃/CD₃CN solution containing equimolar quantities (5 mM) of monobenzo[24]crown8 (**1a**), or dibenzo[24]crown (**1b**) and ammonium salt (**2a**) revealed the formation of the expected pseudorotaxanes: typical signals of pseudorotaxanes were observed in the ¹H NMR spectra (e.g., δ 4.57 ppm in Figure 2a and δ 4.62 ppm in Figure 2b for benzylic protons).⁴ On the other hand, certain signals, assigned for pseudorotaxanes (**3ca** and **3da**), were not shown in ¹H NMR spectra of a mixture of **1c** or **1d** and **2a** at first. Nevertheless, new signals for pseudorotaxanes (**3ca** and **3da**) appeared as time progressed (for examples, δ 4.54 ppm in Figure 2c and δ 4.54 ppm in Figure 2d).⁶ As expected, introduction of benzene rings to the crown ethers (**1**) clearly reduced the association rate of pseudorotaxanes.

Next, difurfurylammonium ion (**2b**) was used as an axle, which has small furan rings at the both ends. Broad signals were observed in the ¹H NMR spectra of mixtures of **1a** and **2b** (Figure 3a), and **1b** and **2b** (Figure 3b), respectively, at room temperature. In contrast, new sets of signals attributed to the corresponding pseudorotaxanes (**3cb** and **3db**) appeared in ¹H NMR spectra of **1c** with **2b** and **1d** with **2b** at the same temperature, respectively (Figure 3c and d). Those results show that the [24]crowns were separable into two groups: large crowns (**1a** and **1b**) and small ones (**1c** and **1d**). The association-dissociation reaction of the former crowns and dibenzylammonium ion (**2a**) is fast, but slower than the

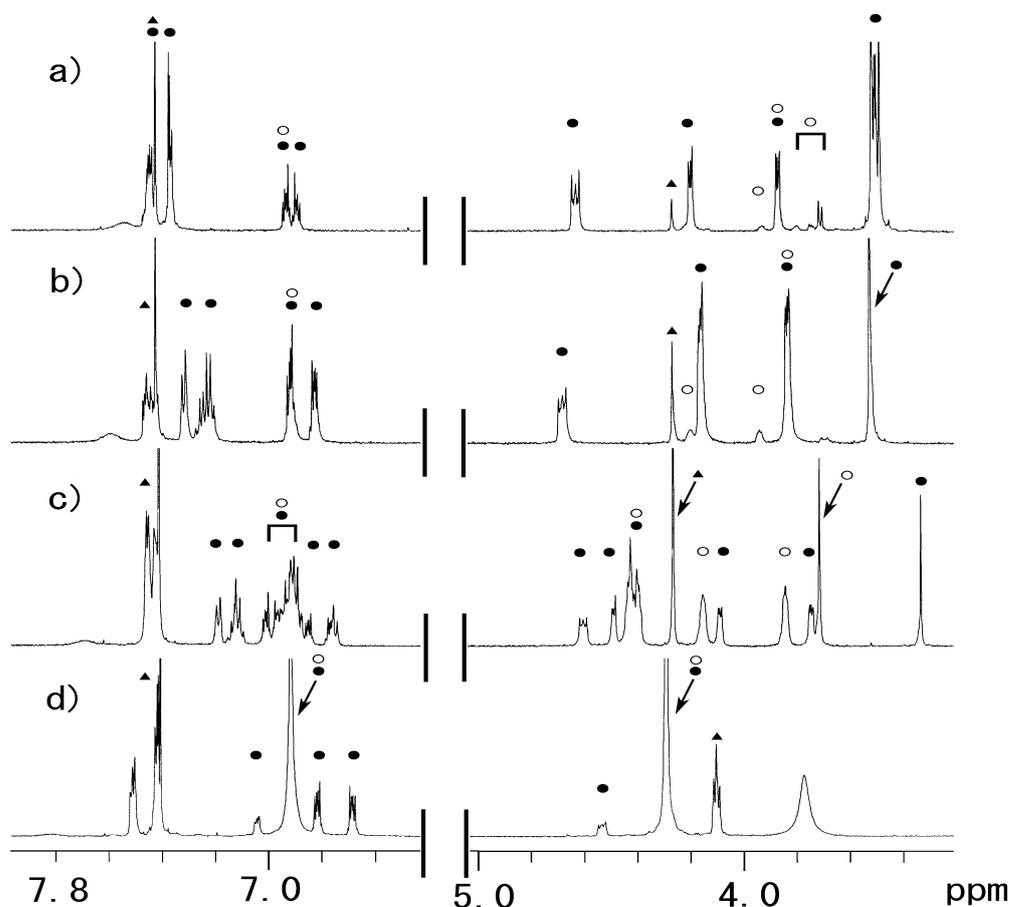


Figure 2. ¹H NMR (500 MHz, CDCl₃-CD₃CN (3 : 1)) spectra of a mixture of a) **1a** and **2a**, b) **1b** and **2a**, c) **1c** and **2a** after 1.5 h, and d) **1d** and **2a** after 17 days. ●: rotaxane, ○: crown ether, ▲: ammonium ion.

NMR time scale. In addition, the relationship between the later and difurfurylammonium ion (**2b**) is quite similar to that between the former and **2a**. The distances of the hydrogens on C-1 and C-4 of benzene and on C-2 and C-4 of furan are shown in Figure 3e. In consideration of the widths of the both aromatic rings and the lengths of C-C single bond and C-C bond of benzene, the cavity sizes and the rigidities of macrocycles are important to regulate the association-dissociation rate.

How different are these rates? VT NMR (500 MHz, CDCl₃ : CD₃CN (3 : 1), a 5 mM mixture of both species) experiments were performed to obtain the kinetic data of the association-dissociation, the temperature-dependent evolution of the spectra of **1a** and **2b** is shown in Figure 4a. At -50°C, two signals appeared independently: δ 4.53 ppm attributed to benzylic protons of pseudorotaxane (**3ab**) and δ 4.25 ppm for benzylic protons of ammonium ion (**2b**). In the range of -33 – 25°C, these signals broadened at elevated temperatures, eventually overlapping at 26°C. Similar VT NMR spectral experiments using a mixture of **1b** and **2b** were carried out (Figure 4b); the coalescence temperatures (*T_c*) of benzylic protons of **3ab** and **3bb** were estimated (Table 1, entries 1 and 2). Respective VT NMR spectra of mixtures of **1** and **2c** afforded *T_c* of benzylic protons, when dibutylammonium ion (**2c**), possessing smaller ends, was used as an axle in the same manner. The association-dissociation rates of pseudorotaxanes formation were

calculated from the T_c and the chemical shift difference of both species at low temperatures, respectively (Table 1). Results show that, with increasing the number of benzene rings fusing crown rings, coalescence temperatures rise (entries 1, 2 and entries 3–6), and the reaction rates tend to slow.⁷

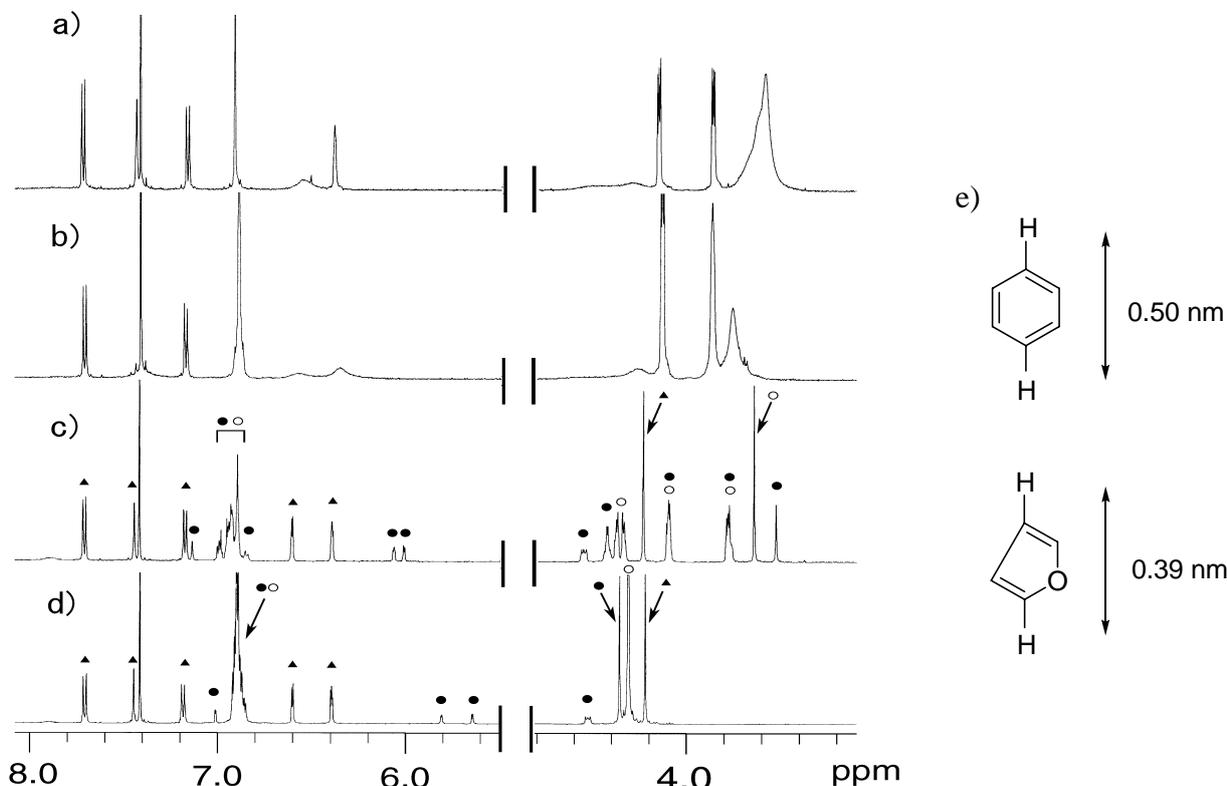


Figure 3. ^1H NMR (500 MHz, CDCl_3 : CD_3CN (3 : 1), 25°C) spectra of mixtures of a) **1a** and **2b**, b) **1b** and **2b**, c) **1c** and **2b**, and d) **1d** and **2b**. ●: rotaxane, ○: crown ether, ▲: ammonium ion. e) The distances of the hydrogens on C-1 and C-4 of benzene and on C-2 and C-4 of furan.

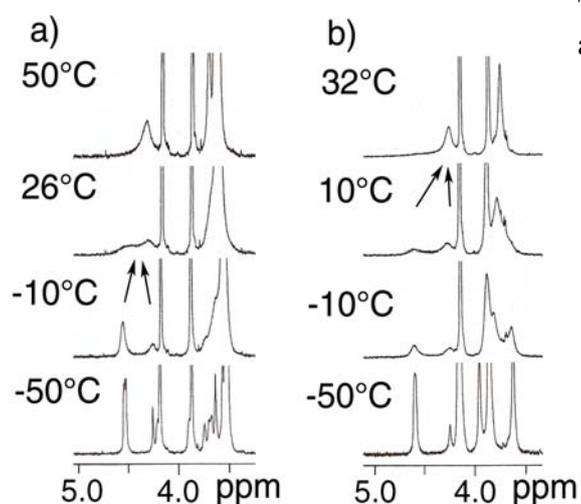


Figure 4. Partial VT NMR spectra of equimolar (5 mM) mixtures of a) **1a** and **2b** and b) **1b** and **2b**.

Table 1. Association-dissociation rate of pseudorotaxanes **3** at coalescence temperatures in CD_3CN - CDCl_3 (Hz).^{a,b}

		T_c ($^\circ\text{C}$)	-21	-10	26	31	32
entry	compounds						
1	1a + 2b				302 ^c		
2	1b + 2b						380 ^c
3	1a + 2c	285 ^c					
4	1b + 2c		358 ^d				
5	1c + 2c				196 ^e		
6	1d + 2c					179 ^e	

^a All NMR spectral experiments were performed at 5 mM of crown ethers (**1**) and ammonium ions (**2**). ^b Estimated using the coalescence method. ^c Association-dissociation rates (ν_c) at the coalescence temperatures (T_c) were evaluated by employing the approximate expression $\nu_c = \pi(\Delta\nu)^{1/2}$, where $\Delta\nu$ is the chemical shift difference between coalescing signals in the absence of any exchange. The values were measured ^c at -60°C , ^d at -40°C , and ^e at -30°C .

During these NMR spectral experiments, we obtained association constants K of the pseudorotaxanes

(**3aa**, **3ba**, **3cb**, and **3db**) from integration of the three species. Salient observations are that the K values increase with decreasing number of benzene rings.⁹ Dramatic changes of association constants were found during the experiments; we could not explain the reason using only the difference of rigidity and ring size of the crown ethers. One would expect that dialkyl ether, more basic than alkyl aryl ones, would form stronger hydrogen bonds.¹⁰ Basicity seems to be the major factor determining the rotaxanes' relative stabilities.

Table 2. Association constants and ΔG° values of pseudorotaxanes (**3**).

entry	compounds	K (M^{-1}) ^a	ΔG° (kJ/mol) ^a
1	1a + 2a	12300 ± 1600	-23.3 ± 0.3
2	1b + 2a	4500 ± 460	-20.9 ± 0.2
3	1c + 2b	210 ± 10	-13.3 ± 0.0
4	1d + 2b	49 ± 1	-9.7 ± 0.1

^a at 25 °C.

In conclusion, we constructed pseudorotaxanes consisting of ammonium ions and mono-, di-, tri-, and tetrabenzocrowns. Increasing the number of benzene rings fusing the 24-membered macrocycles increases the kinetic stability of the pseudorotaxanes and decreases the thermodynamic stability.

ACKNOWLEDGEMENTS

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 7. Since the difference of the association-dissociation rates of the pseudorotaxanes (**3ab** and **3bb** or **3ac** and **3bc**) was not clearly observed, the association rates of the pseudorotaxanes were investigated. Reaction, using equimolar mixtures (15 mM) of **1a** and bis(cyclohexylmethyl)ammonium ion in CDCl₃-CD₃CN (3 : 1) was carried out at 30 °C. The plots of 1/[**1a**] vs. time at low conversion were linear and gave rise to second order rate constants ($k_{1a} = 3.0 \times 10^{-4} \text{ M}^{-1}\text{h}^{-1}$). In the same manner, monitoring of a mixture of **1b** and the ammonium was examined, reaction constant, $k_{1b} = 3.0 \times 10^{-5} \text{ M}^{-1}\text{h}^{-1}$, was obtained.
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