



## Remarkable effect of hydrogen bonding between ring and axle components on deslipping reactions of rotaxanes

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### ABSTRACT

A series of rotaxanes **1-5**, **2-5**, **3-5**, and **4-5** bearing a different substituent ( $X = \text{NO}_2$ , Br, H, and OMe, respectively) at *para* position on the phenol moiety of the ring component exhibit clear difference in deslipping behavior. The difference in the deslipping rates is consistent with the difference in intercomponent hydrogen bonding strength estimated from the O–H stretching vibration wavenumbers. The *para* substituent dictates the relative strength of the intra- and intermolecular hydrogen bonds. Thus the incorporation of an intramolecular hydrogen bond allows for tunability of the strength of the intercomponent interaction.

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Non-covalent interactions such as hydrogen bonding,<sup>1</sup> aromatic  $\pi$ -stacking,<sup>2</sup> hydrophobic interaction,<sup>3</sup> electrostatic interaction,<sup>4</sup> and metal coordination<sup>5</sup> are intentionally incorporated into most interlocked systems not only to allow template-directed syntheses but also to control intercomponent interactions.<sup>6</sup> Among the interactions mentioned above, hydrogen bonding interaction is one of the most important and attractive interactions, because its strength, selectivity, and directionality would allow creation of complex interlocked compounds with intriguing functions. There are many reports on the control of shuttling motions of rotaxanes by changing hydrogen bonding strength brought about by large structural changes induced by external stimuli.<sup>1</sup> However, there are no reports on rotaxanes whose motions are controlled by modulation of intercomponent hydrogen bonding strength without structural change. In this respect, it is interesting to see if the difference in hydrogen bonding strength would alter the relative thermodynamic stabilities of conformers of a rotaxane in which the ring component locates at different stations and/or affects the kinetic mobility of the rotaxane.

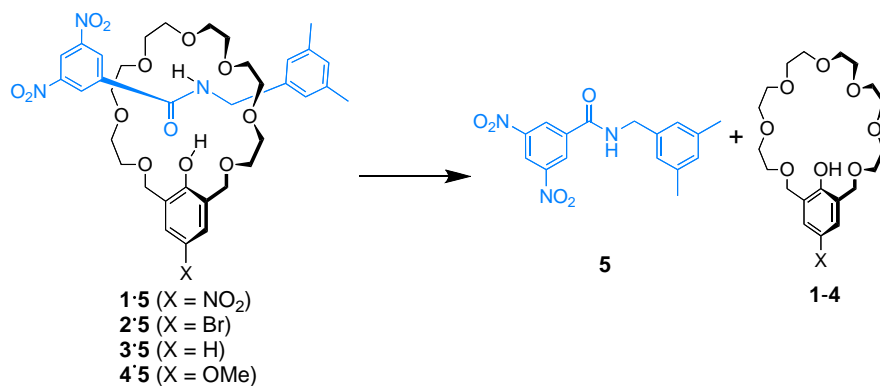
In the present study, kinetics of deslipping reactions of rotaxanes with different intercomponent hydrogen bonding abilities,<sup>7</sup> by which the ring and axle components are disconnected without breaking a covalent bond, were investigated. Deslipping reactions are suitable for this purpose because the factors governing the internal mobility of rotaxanes can be emphasized by the difference in the reaction rates.<sup>7e,f,i</sup> Toward this end, four rotaxanes **1-5**, **2-5**, **3-5**, and **4-5** were designed (Scheme 1).<sup>8</sup> The rotaxanes are composed of a common dumbbell component **5** and pseudo-crown ether type ring components **1-4** with different substituents

( $X = \text{NO}_2$ , Br, H, and OMe) at *para* position on the phenol unit. The inner phenolic hydroxy group of the ring component is expected to act as a hydrogen bond donor, forming intercomponent hydrogen bonding with the amide unit of the axle component. The acidity or hydrogen bonding ability of the hydroxy group should be highly sensitive to the electronic nature of the substituents due to the effective resonance between the substituents and the hydroxy group.

The deslipping reactions of **1-5**, **2-5**, **3-5**, and **4-5** were monitored by <sup>1</sup>H NMR spectroscopy in tetrachloroethane-*d*<sub>2</sub> (TCE-*d*<sub>2</sub>) and DMSO-*d*<sub>6</sub>. All deslipping reactions were confirmed to follow first-order kinetics. From the rate constants determined at several temperatures (Table S1 in Supplementary data), the kinetic parameters and *t*<sub>1/2</sub> (298 K) were estimated as summarized in Table 1. The deslipping of rotaxane **1-5** having a strong electron-withdrawing nitro group on the ring took place at 90 °C in TCE-*d*<sub>2</sub>, whereas the corresponding deslipping reactions of **2-5** and **3-5** were not observed under the same conditions. At higher temperature of 110 °C, thermal decomposition of **2-5** and **3-5** took place, giving complicated NMR signals. On the contrary, deslipping reactions of **1-5**, **2-5**, and **3-5** proceeded in DMSO-*d*<sub>6</sub> at around 100 °C. The half-lives of **2-5** and **3-5** were longer than that of **1-5** up to 5 times. On the other hand, rotaxane **4-5** having an electron-donating methoxy group on the ring component did not undergo deslipping reaction in both solvents.

Although half-life of **1-5** at 100 °C in TCE-*d*<sub>2</sub> is similar to that in DMSO-*d*<sub>6</sub>, the activation parameters are different from each other. The observed activation entropy in DMSO-*d*<sub>6</sub> was more negative than that in TCE-*d*<sub>2</sub>, while the activation enthalpy in DMSO-*d*<sub>6</sub> was smaller than that in TCE-*d*<sub>2</sub>. These results suggest that rotaxane **1-5** suffers from greater solvation in DMSO-*d*<sub>6</sub> than in TCE-*d*<sub>2</sub> at the transition state of deslipping. In the case of the reactions of **2-5** and **3-5**,

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Scheme 1. Deslipping reactions of rotaxanes 1-5-4.5.

**Table 1**  
 Kinetic parameters for deslipping reactions 1-5, 2-5, 4-5, and 4-5

| Solvent                     | Rotaxane | $\Delta H^\ddagger$ (kJ mol <sup>-1</sup> ) | $\Delta S^\ddagger$ (e.u.) | $\Delta G^\ddagger$ <sup>a</sup> (kJ mol <sup>-1</sup> ) | $t_{1/2}$ <sup>a</sup> (h) |
|-----------------------------|----------|---|----------------------------|--|----------------------------|
| TCE- <i>d</i> <sub>2</sub>  | 1-5      | 110   | -20                        | 118  | 0.97                       |
|                             | 2-5      | — <sup>b</sup>                              | — <sup>b</sup>             | — <sup>b</sup>   | — <sup>b</sup>             |
|                             | 3-5      | — <sup>b</sup>                              | — <sup>b</sup>             | — <sup>b</sup>   | — <sup>b</sup>             |
|                             | 4-5      | — <sup>b</sup>                              | — <sup>b</sup>             | — <sup>b</sup>   | — <sup>b</sup>             |
| DMSO- <i>d</i> <sub>6</sub> | 1-5      | 93  | -67                        | 118  | 0.96                       |
|                             | 2-5      | 71  | -142                       | 124  | 5.3                        |
|                             | 3-5      | 72  | -140                       | 124  | 6.4                        |
|                             | 4-5      | — <sup>b</sup>                              | — <sup>b</sup>             | — <sup>b</sup>   | — <sup>b</sup>             |

<sup>a</sup> At 373 K calculated from  $\Delta H^\ddagger$  and  $\Delta S^\ddagger$ .

<sup>b</sup> Deslipping not observed up to 100 °C.

the significantly negative activation entropies (greater than -140 e.u.) compared to 1-5 in DMSO-*d*<sub>6</sub> would originate from both the solvation in the transition state and the cleavage of the intercomponent hydrogen bonding present in the ground state.

To estimate the nature and strength of hydrogen bonding interactions of rotaxanes, IR spectra of rotaxanes 1-5-4.5, ring components 1-4, and *para*-substituted phenols 6-9 (Fig. 1) were measured at 25 mM in tetrachloromethane at room temperature. It is expected that the phenolic O-H group on the ring components of rotaxanes 1-5-4.5 would form both inter- and intracomponent hydrogen bonds with the amide group of the axle component and the ether oxygen on the ring component, respectively.<sup>9</sup> The deslipping rates would be affected mainly by anchoring of the ring component to the axle component by intercomponent hydrogen bonding. Therefore, it is important to estimate each strength of inter- and intracomponent hydrogen bondings of the O-H groups.<sup>10</sup> To extract these hydrogen bonding strengths, the shifts of the O-H stretching vibration wavenumber ( $\Delta\nu_{\text{O-H}}$ ) from the corresponding *para*-substituted phenols and difference of  $\Delta\nu_{\text{O-H}}$  between the

rotaxanes and the rings ( $\Delta\Delta\nu_{\text{O-H}} = \Delta\nu_{\text{O-H}}(\text{rotaxane}) - \Delta\nu_{\text{O-H}}(\text{ring})$ ) are also shown in Table 2.<sup>11</sup>

The  $\Delta\nu_{\text{O-H}}$  value of the ring component 1 (260 cm<sup>-1</sup>) having nitro group was apparently larger than those of 2 (224 cm<sup>-1</sup>), 3 (218 cm<sup>-1</sup>), and 4 (206 cm<sup>-1</sup>), indicating that the intracomponent hydrogen bonding interaction of the hydroxy group with ether oxygen of the polyoxyethylene moiety of 1 is stronger than those of 2-4. It has been demonstrated that the hydrogen donating ability of a hydroxy group correlates with the electronic nature of a substituent on phenol.<sup>12</sup> In the case of 1-4 too, a linear correlation between  $\Delta\nu_{\text{O-H}}$  versus  $\sigma_p$  was observed (Fig. 2): the electron-withdrawing nitro group reduces the electron density of the hydroxy oxygen leading to the greater hydrogen donating ability.

Contrary to the intracomponent hydrogen bonding, the  $\Delta\nu_{\text{O-H}}$  values of rotaxanes 1-5-4.5 are similar to each other (234, 239, 235, and 242 cm<sup>-1</sup>, respectively). This indicates that the hydrogen bonding abilities of the hydroxy group of 1-5-4.5 are similar to each other in spite of the different hydrogen bonding strengths between the corresponding free ring components 1-4. In other words, the hydrogen bonding strengths of the hydroxy group in the rotaxane systems do not depend directly on the acidity of the corresponding phenols, which is affected by the electronic nature of the substituent on the phenol moiety.

Although there seems to be no relationship between the ease of deslipping and the hydrogen bonding strengths of the rotaxanes, the deslipping behavior should be understood by taking into account the intra- and intercomponent hydrogen bonding separately. For this purpose, we compare  $\Delta\nu_{\text{O-H}}$  of rotaxanes and those of ring components ( $\Delta\Delta\nu_{\text{O-H}}$ ). The values of  $\Delta\nu_{\text{O-H}}$  for 2-5, 3-5, and 4-5

**Table 2**  
 O-H stretching vibration bands for phenols 6-9, ring components 1-4, and rotaxanes 1-5-4.5 in tetrachloromethane

| Compound | X               | $\nu_{\text{O-H}}$ (cm <sup>-1</sup> ) | $\Delta\nu_{\text{O-H}}$ <sup>a</sup> (cm <sup>-1</sup> ) | $\Delta\Delta\nu_{\text{O-H}}$ <sup>b</sup> (cm <sup>-1</sup> ) |
|----------|-----------------|--|---|---|
| 6        | NO <sub>2</sub> | 3595                                   |   |   |
| 1        |                 | 3335                                   | 260   |   |
| 1-5      |                 | 3361                                   | 234   | -26   |
| 7        |                 | 3608                                   |   |   |
| 2        | Br              | 3384                                   | 224   |   |
| 2-5      |                 | 3369                                   | 239   | 15  |
| 8        | H               | 3611                                   |   |   |
| 3        |                 | 3393                                   | 218   |   |
| 3-5      |                 | 3376                                   | 235   | 17  |
| 9        | OMe             | 3617                                   |   |   |
| 4        |                 | 3411                                   | 206   |   |
| 4-5      |                 | 3375                                   | 242   | 36  |

<sup>a</sup> The difference between  $\nu_{\text{O-H}}$  of the ring components or rotaxanes and that of the corresponding *p*-substituted phenol.

<sup>b</sup>  $\Delta\Delta\nu_{\text{O-H}} = \Delta\nu_{\text{O-H}}(\text{rotaxane}) - \Delta\nu_{\text{O-H}}(\text{ring})$ .

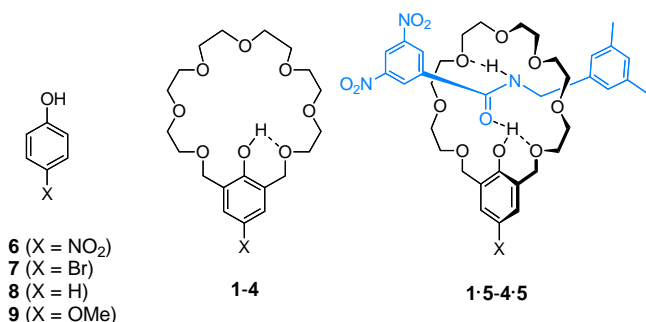
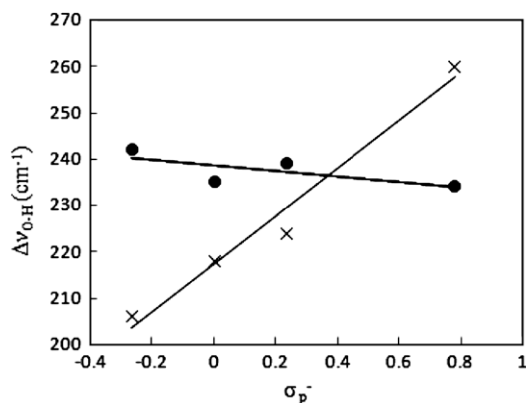


Figure 1.



**Figure 2.** Plots of  $\sigma_p^-$  versus  $\Delta\nu_{\text{O-H}}$ : ●, rotaxanes **1-5-4-5**; ×, ring components **1-4**:  $\sigma_p^-$  ( $\text{NO}_2$ ) = 0.81,  $\sigma_p^-$  ( $\text{Br}$ ) = 0.23,  $\sigma_p^-$  ( $\text{H}$ ) = 0,  $\sigma_p^-$  ( $\text{OMe}$ ) = -0.27.

are larger than those of the corresponding ring components ( $\Delta\Delta\nu_{\text{O-H}} > 0$ ), indicating that the hydroxy group simultaneously interacts with not only the polyoxyethylene oxygen of the ring but also the amide group in the dumbbell. However, in the case of **1-5**, the  $\Delta\nu_{\text{O-H}}$  value is much smaller than that of the free ring **1** ( $\Delta\Delta\nu_{\text{O-H}} < 0$ ), indicating that the insertion of the axle component into the cavity of the ring disturbs the intracomponent hydrogen bonding rather than to enforce it by the additional intercomponent interaction. Therefore, the intercomponent hydrogen bonding of **1-5** should be weaker than those of **2-5-4-5**. The difference in the hydrogen bonding strength between **1-5**, **2-5**, **3-5**, and **4-5** estimated from  $\Delta\Delta\nu_{\text{O-H}}$  is consistent with the difference in the deslipping rates. Namely, the deslipping reaction of **1-5** took place more easily than those of **2-5-4-5** because of the weaker intercomponent hydrogen bonding. Regarding the solvent effect, the deslipping reactions of **2-5** and **3-5** having stronger intercomponent hydrogen bonding in TCE- $d_2$  are accelerated in DMSO- $d_6$  because solvation by DMSO- $d_6$  breaks the hydrogen bonds in the transition state of deslipping, being consistent with the large negative activation entropy.

In conclusion, we revealed that rotaxanes **1-5**, **2-5**, **3-5**, and **4-5** bearing a different substituent at the *para* position on the phenol unit of the ring component exhibit clear difference in deslipping facility. The deslipping reaction of **1-5** easily occurs compared to those of **2-5** and **3-5**. The reason for the low thermostability of interlocked structure of **1-5** is ascribed to the weaker hydrogen bonding between the phenolic hydroxy group on the ring component and the amide group in the dumbbell component than those of **2-5** and **3-5**, as indicated by the O-H stretching vibration wavenumber of these rotaxanes and corresponding free ring components in the IR spectra. These results clearly demonstrate the tunability of intermolecular interactions dictated by intra- and intercomponent hydrogen bonds. These results could be exploited in the rational design of molecular machines based upon hydrogen bonding interactions.

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## Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.02.179.

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- The phenolic OH/ether hydrogen bond (O–O 2.78 Å), phenolic OH/carbonyl hydrogen bond (O–O 2.78 Å), and the amide/ether hydrogen bond (O–N length 3.02 Å) of rotaxane **2-5** were confirmed as shown in Figure 1 by X-ray structural analysis in our previous work.<sup>8</sup>
- In the cases of rotaxanes **1-5-4-5**, the stretching vibration frequencies ( $\nu_{\text{C=O}}$ ) of amide carbonyl groups of the axles in tetrachloroethane do not provide clear difference (1667–1669  $\text{cm}^{-1}$ ). The frequency can be affected by intercomponent hydrogen bond between the amide NH group and ether oxygen of the ring component in addition to the intercomponent hydrogen bonding between the carbonyl oxygen and the hydroxyl group. The effect could not be clearly estimated. Therefore, the stretching vibration frequency of the carbonyl group cannot be used for the estimation of hydrogen bonding strengths of rotaxanes **1-5-4-5**.
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