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Is the *tert*-Butyl Group Bulky Enough to End-Cap a Pseudorotaxane with a 24-Crown-8-ether Wheel?

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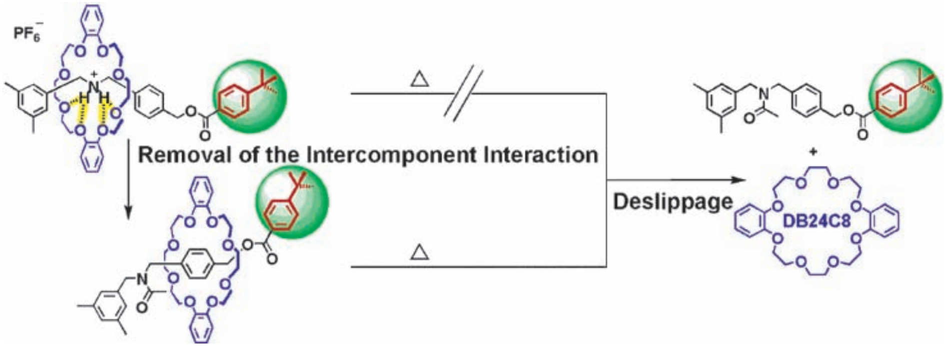
ABSTRACT



Although rotaxane chemists have long believed that the *tert*-butyl group is bulkier than the cavity of dibenzo-24-crown-8-ether (DB24C8), it is essentially smaller than the cavity of DB24C8. The *tert*-butyl (or 4-*tert*-butylphenyl) group can actually function as an end-cap of DB24C8-based rotaxanes when the intercomponent interaction is effectively operative. When such attractive interaction is removed, deslippage occurs.

Rotaxane chemists have long believed that the *tert*-butyl group is sterically large enough to end-cap pseudorotaxane consisting of dibenzo-24-crown-8-ether (DB24C8) and *sec*-ammonium salt to suppress the deslippage of DB24C8.[1] However, this view has recently been challenged.

Since Stoddart et al. established that DB24C8 forms stable threading complexes (pseudorotaxanes) with *sec*-ammonium salt,[2] a variety of rotaxanes have been prepared by researchers including our group.[1e−g,3] Basically, the end-cap group must be bulkier than the cyclohexyl group, which possesses a

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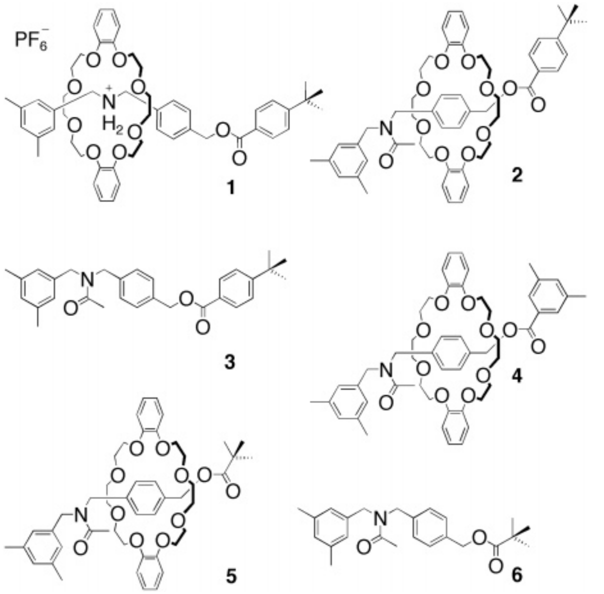

Figure 1. Rotaxanes with *tert*-butyl groups and their components.

borderline bulkiness toward DB24C8, to fix the rotaxane structure.[4] Rotaxanes with a 4-*tert*-butylphenyl group, which is one of the most frequently used end-caps,[5] are stable in various solvents, even in DMSO, and it has thereby been reported that the 4-*tert*-butylphenyl group is larger than the cavity of DB24C8.[4a,5b] Meanwhile, in our own CPK model studies, we noticed that the 4-*tert*-butylphenyl group is slightly smaller than the cavity of DB24C8. On the basis of these observations, it seemed logical to assume that the CPK model was unsuitable to estimate the bulkiness of the end-cap. Recently, we have experimentally found that the *tert*-butyl group is actually small enough to thread out from the wheel. Here, we wish to discuss the "actual and apparent bulkiness" of the *tert*-butyl end-cap along with the role of intercomponent interaction between wheel and axle. Our results reveal important aspects for the design of rotaxanes with a robust interlocked structure.

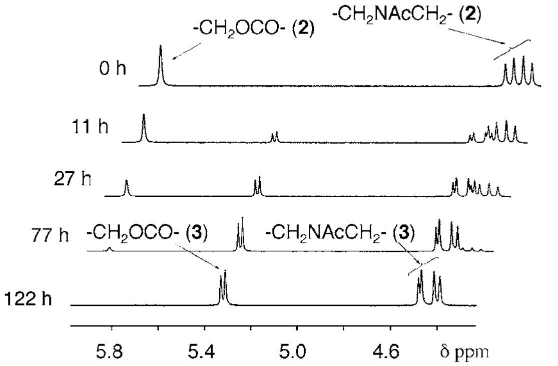

Figure 2. Partial ^{1}H NMR (500 MHz) spectral change during the deslippage of **2** to decompose to **3** and DB24C8 in DMSO-d_6 at 318 K.

Rotaxane **1** having a DB24C8 wheel and a 4-*tert*-butylphenyl end-cap on the axle was synthesized in 92% yield based on the tributylphosphine-catalyzed acylative end-capping protocol.[6] When **1** was allowed to stand at 100 °C in DMSO-d_6 for 31 days, no decomposition was observed (^{1}H NMR). The intercomponent hydrogen bonding interaction in **1** was then completely removed by acylative neutralization of the ammonium group[7] by treatment with acetic anhydride in the presence of triethylamine at 0 °C for 48 h to give nonionic rotaxane **2** in 76% yield.

Interestingly, **2** was isolated along with both DB24C8 and **3** (24% yield). Since no decomposition of the end-cap took place under N-acylation conditions, the fact that DB24C8 and **3** were isolated from the reaction mixture suggested the deslippage of the wheel DB24C8 over 4-*tert*-butylphenyl end-cap, which was caused by the removal of the intercomponent interaction.

In the ^{1}H NMR spectrum of **2**, the ester benzyl proton signal ($-CH_2OCO-$) was observed at 5.89 ppm, and the amide benzyl proton signals ($-CH_2NAcCH_2-$) were observed as four peaks around 4.3 ppm due to the presence of *s-cis* and *s-trans* conformers of the amide group. When a DMSO-d_6 solution of **2** was heated at 45 °C, new signals sluggishly appeared around 5.3 and 4.4 ppm in 10 h (Figure 2). These signals were identified as the benzyl protons of free axle **3**, which was actually isolated from the solution. After 5 days, the signals of **2** disappeared completely, and both DB24C8 and **3** were isolated quantitatively. In the same manner, the thermal stability of rotaxane **4**[7] with a 3,5-dimethylphenyl end-cap at both termini was examined. A DMSO-d_6 solution of **4** was heated at 100 °C for 30 days, but no decomposition product was detected in the ^{1}H NMR spectra. Therefore, it was found that the *tert*-butyl (i.e., 4-*tert*-butylphenyl) group is smaller than the cavity of DB24C8 and also smaller than the 3,5-dimethylphenyl group.

Since the decomposition of **2** followed first-order kinetics, the rate constant k_d, half-life time $\tau_{1/2}$, and thermodynamic

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Table 1. Kinetic Data for the Decomposition of Rotaxanes **2** and **5**

$$\text{(i) } \mathbf{2} \xrightarrow[\text{solvent}]{} \mathbf{3} + \text{DB24C8} \qquad \text{(ii) } \mathbf{5} \xrightarrow[\text{solvent}]{} \mathbf{6} + \text{DB24C8}$$

rotaxane	solvent	$k_{\mathrm{d},\,313\,\mathrm{K}}$ (sec^{-1})	$t_{1/2,\,313\,\mathrm{K}}$ (h)	$\Delta G_{313\,\mathrm{K}}^{\ddagger}$(kJ mol^{-1})	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J mol^{-1} K^{-1})
2	DMSO-d_6	$(4.6 \pm 0.2) \times 10^{-6}$	42	108.8 ± 0.1	84.1 ± 1.6	-79 ± 5
	chloroform-d_1	$(2.0 \pm 0.1) \times 10^{-6}$	97	111.2 ± 0.1	86.8 ± 1.1	-77 ± 3
	benzene-d_6	$(1.4 \pm 0.2) \times 10^{-6}$	143	112.0 ± 0.1	84.6 ± 1.0	-75 ± 8
5	DMSO-d_6	$(4.1 \pm 0.2) \times 10^{-5}$	4.7	103.1 ± 0.1	100.3 ± 0.3	-9 ± 1
	chloroform-d_1	$(5.2 \pm 0.1) \times 10^{-5}$	3.7	102.5 ± 0.1	96.7 ± 0.4	-19 ± 1
	benzene-d_6	$(3.1 \pm 0.2) \times 10^{-5}$	7.0	103.8 ± 0.1	99.3 ± 0.6	-15 ± 2

parameters were calculated.[5b] The results are summarized in Table 1.

The large $\Delta H^{\ddagger}$ indicates that the disadvantageous conformation change is necessary for the deslippage of DB24C8 over the 4-*tert*-butylphenyl group. The decomposition rate is dependent on the solvent, although the reasons behind the solvent effect are not clear at the present time.

The bulkiness of the 4-*tert*-butylphenyl group can be attributed to the *tert*-butyl group. The van der Waals diameter of the *tert*-butyl group is larger than that of the phenyl group, and DB24C8 can actually freely slip over the benzene ring. The thermal stability of rotaxane **5** with a *tert*-butyl end-cap was then investigated. Although **5** could be prepared similarly to **2** and **4**, **5** was always obtained as a mixture with a small amount of axle **6** and DB24C8 even by repeated purifications, suggesting the decomposition of **5** via deslippage. **5** with a purity of ca. 90% was used for the decomposition experiment, in which the kinetic parameters were determined by taking purity into consideration. The results are summarized in Table 1.

Although the decomposition of **5** was faster than that of **2**, $\Delta H^{\ddagger}$ of **5** was larger than that of **2** in all solvents tested, probably because of the dipole−dipole repulsion between the crown ether and the carbonyl group. The total decrease of $\Delta G^{\ddagger}$ in **5** was attributed to the extremely large $\Delta S^{\ddagger}$ of **5**. This result indicates a more suppressed molecular freedom at the transition state of **2** than that of **5**, due to the introduction of a *p*-phenylene moiety. The bulkiness in this case may include not only bulkiness but also flexibility, both of which are considered important factors for the end-cap group of rotaxane.

In conclusion, the present study demonstrated that the *tert*-butyl group is not large enough to act as an end-cap group of rotaxane consisting of DB24C8 as a wheel. The introduction of a phenylene group changing to a 4-*tert*-butylphenyl group suppresses the activation entropy of the deslippage due to the decrease of freedom of the *tert*-butyl group by the adjacent rigid benzene ring, eventually leading to more effective end-capping. Furthermore, it was confirmed that any group can only be declared as a true end-cap of rotaxane after the complete removal of the intercomponent interaction. The intercomponent hydrogen-bonding in **1**, which did not completely disappear even in DMSO, made the end-cap look more bulky. N-Acylative neutralization of **1** to **2** to eliminate the intercomponent interaction made the bulkiness of the end-cap obvious.

In summary, the following points are deemed important: (1) the *tert*-butyl group is not large enough to function as an end-cap group of DB24C8-based rotaxanes, (2) the attractive interaction between the rotaxane components enhances the apparent bulkiness of the end-cap group, and (3) end-capping ability depends on both the bulkiness and the structural rigidity of the end-cap group.[8]

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Supporting Information Available: Experimental procedures, spectroscopic data of all compounds, and ^{1}H NMR spectral changes of the decomposition of **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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