

[3]Rotaxane synthesized *via* covalent bond formation can recognize cations forming a sandwich structure†

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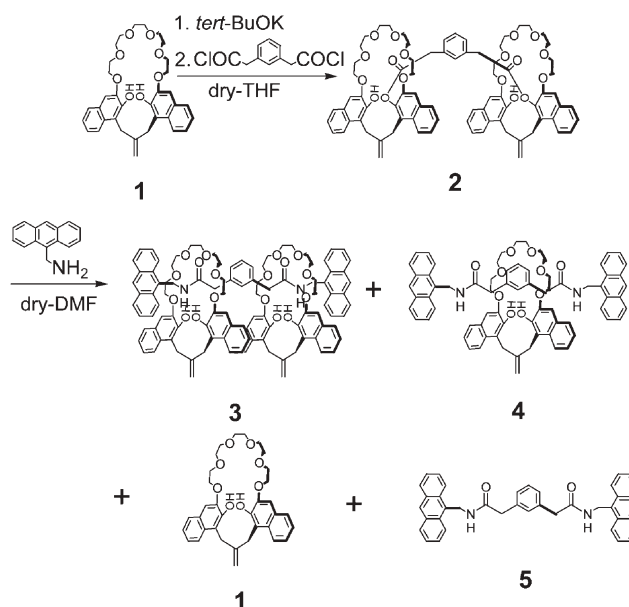
A novel [3]rotaxane composed of two 25-membered crownphanes and one axle molecule having two anthryl end groups was successfully synthesized *via* covalent bond formation followed by aminolysis, and can incorporate caesium ion into the space between the two macrocycles as a 1 : 1 sandwich-type complex, whereas it makes a 1 : 2 complex with lithium ion.

Much attention has been paid to the development of rotaxanes and catenanes from the viewpoint of topological interest and nanotechnology using supramolecular systems.^{1–4} Although many kinds of rotaxanes have been reported so far, reports on the synthesis and properties of [3]rotaxanes are far fewer than for [2]rotaxanes.^{5–10} In addition, there has been no report on the synthesis *via* covalent bond formation so far.

Recently, we reported a new synthetic method for [2]rotaxanes *via* covalent bond formation.^{11,12} They can be obtained in high yields in three steps starting from macrocyclic polyethers, *i.e.*, tandem Claisen rearrangement, diesterification, and aminolysis. To apply covalent bond formation to the synthesis of a [3]rotaxane, we used a macrocyclic compound, the so called crownophane (**1**) having two hydroxy groups as a rotor. Scheme 1 shows our synthetic strategy for the reaction processes for [3]rotaxane. The most important step is the aminolysis because two amine compounds must attack from the outside of the bridged crownophane **2**.

According to the processes, the reaction of two molar equivalent of the previously-reported¹³ crownophane **1** with one molar equivalent 1,3-phenylenediacetic acid dichloride gave bridged crownophane **2** as a main product in 35% yield. The reaction of **2** with an excess amount of 9-aminomethylantracene resulted in the formation of a mixture of [3]rotaxane **3**, [2]rotaxane **4**, crownophane **1** recovered, and an axle molecule **5**. They can be separated by gel permeation chromatography (GPC) completely. The yields of [3]rotaxane **3** and [2]rotaxane **4** were 20% and 32%, respectively. Thus, we succeeded in synthesizing a [3]rotaxane *via* covalent bond formation for the first time in moderate yields.†

The features of [3]rotaxanes were investigated by NMR. The ¹H NMR spectrum of **3** at room temperature is shown in Fig. 1a. Assignments of the spectrum were performed from several two-dimensional NMR spectra such as DQF-COSY, NOESY, HMQC, and HMBC. Five kinds of signals for each of the



Scheme 1 Synthesis of [3]rotaxane *via* covalent bond formation.

anthracene rings and the naphthalene rings were observed in the ¹H NMR spectrum. It reflects the symmetrical structure of the axle and the rotors of **3**.

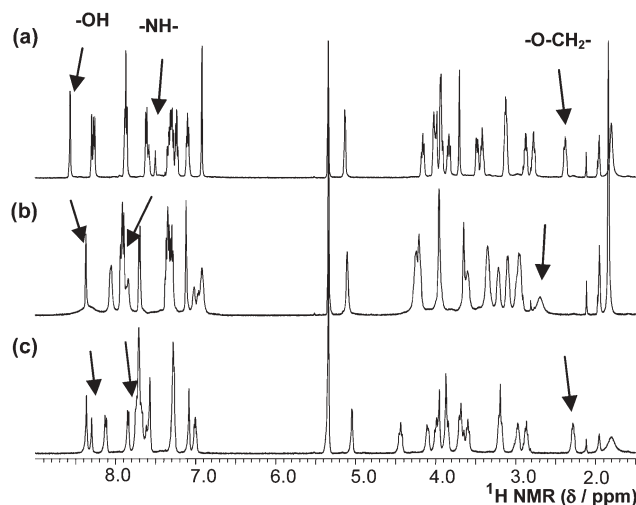


Fig. 1 ¹H NMR spectra of **3** (a), **3** + Li⁺ (b), and **3** + Cs⁺ (c) in CD₂Cl₂/CD₃CN (9 : 1).

† Electronic supplementary information (ESI) available: synthesis of compounds **2–4**, their ¹H NMR, IR, and ESI mass spectral data, and fluorescence spectra of **3** with caesium ion. See <http://www.rsc.org/suppdata/cc/b413715a/>

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On the other hand, 10 kinds of signals were observed for the methylene protons of the oligooxyethylene chain. According to the HMQC spectrum (Fig. 2), the signals of two methylene protons in the same carbon of the chain are magnetically non-equivalent. This indicates that these two rotors having exactly the same structure cannot be replaced with each other, which shows the character of [3]rotaxane.

The signals of the methylene protons of the oligooxyethylene chain at the farthest position from the naphthalene ring are significantly shifted upfield (*ca.* 0.5–0.6 ppm) compared with those of the protons of the 25-membered crownophane itself. As in the case of [2]rotaxanes having the crownophane,⁴ the anthracene ring of the axle is located near these protons and the magnetic shielding of the anthracene ring is quite effective. The NOESY spectrum of **1a** also suggests such a conformation. NOE cross peaks were observed between the protons of the anthracene ring and those at the farthest position from the naphthalene ring in the oligooxyethylene chain. The hydroxy protons are quite low field at 8.59 ppm, which suggests that the hydroxy groups form strong hydrogen bonds. The carboxy group of the axle may form the hydrogen bonds to the hydroxy group.

Besides, the line shape of the ¹H NMR spectrum changed distinctly, when metal ion was added into the solution of **3** (Figs. 1b and 1c). Adding lithium ion into the solution of **3**, the *exo*-methylene proton was shifted to low field by 0.29 ppm in the ¹H NMR spectrum. In the case of adding caesium ion to it, however, the signal of the proton moved to high field by 0.06 ppm.

Using a titration method of fluorescence spectra in CD₂Cl₂/CD₃CN (9 : 1), binding ratios of the complex between **3** with lithium ion and **3** with caesium ion are 1 : 2 and 1 : 1, respectively. The binding constants of the complex with lithium ions for the first step and the second step are 1.0 × 10⁴ M⁻¹ and 5.0 × 10⁷ M⁻¹, respectively. In the case of caesium ion, the binding constant of the complex is 6.3 × 10⁵ M⁻¹. Two lithium ions are incorporated into the cavities of two rotors of **3**, however, a caesium ion is sandwiched between two rotors as shown in Fig. 3. Mass spectra of **3** also suggest the stoichiometry of the complexes. The ESI-MS spectrum of a dilute CH₃CN–CH₂Cl₂ solution of the complex of **3** with lithium ion showed a peak at *m/z* 869, corresponding to

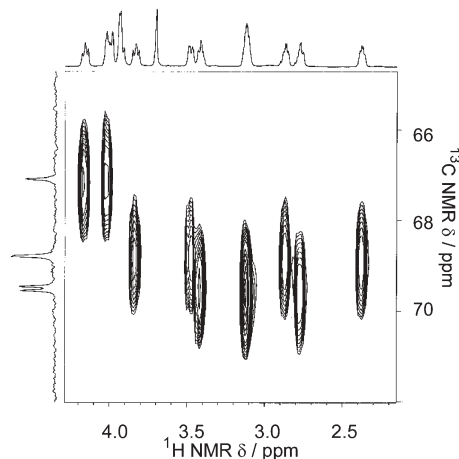


Fig. 2 Partial HMQC spectrum of **3** (oligooxyethylene region) in CD₂Cl₂/CD₃CN (9 : 1).

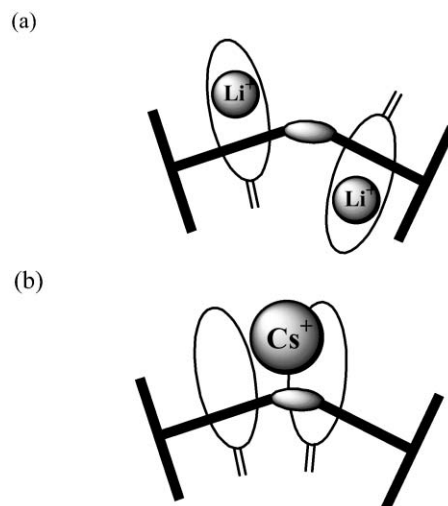


Fig. 3 Proposed schematic structures of [3]rotaxane with Li⁺ ion (a) and Cs⁺ ion (b).

[**3** + 2Li]²⁺. The complex of **3** with caesium ion showed a peak at 1855, corresponding to [**3** + Cs]⁺ in the ESI-MS spectrum.

As the structures of the complex of lithium ion and caesium ion are quite different, the chemical shifts of these complexes appear differently as stated above. Indeed, the cross peaks in the NOESY spectrum became quite different between the complexes of lithium ion and caesium ion. In the case of the complex of **3** and lithium ion, NOE cross peaks were observed between the protons of the anthracene ring and those at the closest position of the naphthalene ring in the oligooxyethylene chain. In contrast, NOE cross peaks were observed between the oligooxyethylene protons at the farthest position from the naphthalene ring and those of the anthracene ring in the complex of **3** and caesium ion.

Thus, we succeeded in the synthesis of a novel [3]rotaxane *via* covalent bond formation in three steps starting from a crownophane having two hydroxy groups. It was found that the fluorescence intensity of the [3]rotaxane increased in the presence of caesium ion, suggesting it might be a candidate for a caesium ion sensing agent.

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