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COMMUNICATIONS

Published on Web 09/28/2004

Synthesis of [1]Rotaxane via Covalent Bond Formation and Its Unique Fluorescent Response by Energy Transfer in the Presence of Lithium Ion

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Many kinds of supramolecular systems such as rotaxanes and catenanes have been developed mainly by utilizing weak intermolecular interactions such as hydrogen bonding,[1] charge-transfer phenomena,[2] and intermolecular coordination with metal ions.[3] Much attention has been paid to the development of these systems from the viewpoint of topological interest and nanotechnology using supramolecular systems.[4] However, there are only a few reports so far on the synthesis and properties of stark [1]rotaxanes.[5]

Recently, we reported a new synthetic method for [2]rotaxanes via covalent bond formation.[6] They can be obtained in high yields by three steps starting from macrocyclic polyethers, i.e., tandem Claisen rearrangement, diesterification, and aminolysis. To apply covalent bond formation to the synthesis of a [1]rotaxane, we designed a macrocyclic compound (**1**) having the phenylene part substituted with an aldehyde group. Scheme 1 shows our strategy for the synthesis of our [1]rotaxane. The most important step might be the intramolecular bridging between the aldehyde part and one of the phenolic hydroxy groups of **2**.

According to the process, macrocyclic polyether (**1**) was prepared from the reaction of the bis(naphthol) derivative and the diiodide of oligoethylene glycol using a high-dilution method. The next step was a tandem Claisen rearrangement.[7] The rearranged product (**2**) was obtained in excellent yield. The *N*-benzylaminomethyl derivative (**3**) was obtained by the reaction of **2** with benzylamine followed by reduction of the imine with sodium boron hydride. We prepared di(acid chloride)s (**4**: R = $(CH_2)_{10}$) of dodecanoic acid. In the presence of potassium *tert*-butyloxide, the equimolar reaction of **3** with **4** gave bicyclic compound **5** (mixture of two isomers) in 24% yield. Then, without separation of isomers, **5** was used in aminolysis with 9-(3-(aminopropyl)aminocarbonyl)-anthracene (**6**), which was prepared by treating 9-chlorocarbonyl-anthracene with 1,3-propylenediamine. Treatment of mixed isomers of **5** with **6** in DMF at room temperature gave [1]rotaxane (**7**) and a macrocycle with a long tail (**8**).[8] These were separated by preparative gel permeation chromatography (GPC). Compound **8** was prepared by another method to confirm the structure, that is, the reaction of **3** with acid chloride having an anthryl end group (**9**), which was prepared in the reaction of di(acid chloride) **4** with **6**.[9]

Compounds **7** and **8** were confirmed to have the same parent peak by ESI mass spectroscopy but also exhibited quite different ^{1}H NMR spectra as shown in Figure 1. The NMR spectrum of **8** was the same as that of **8** prepared by the other reaction of **3** with **9** as described above. In the NMR of **7**, some protons of the oligomethylene moiety between anthryl and benzylamide moieties of the macrocycle were observed to shift upfield compared with that of **8**. This means that some part of the oligomethylene is close

Scheme 1. Synthetic Strategy for [1]Rotaxane via Covalent Bond Formation

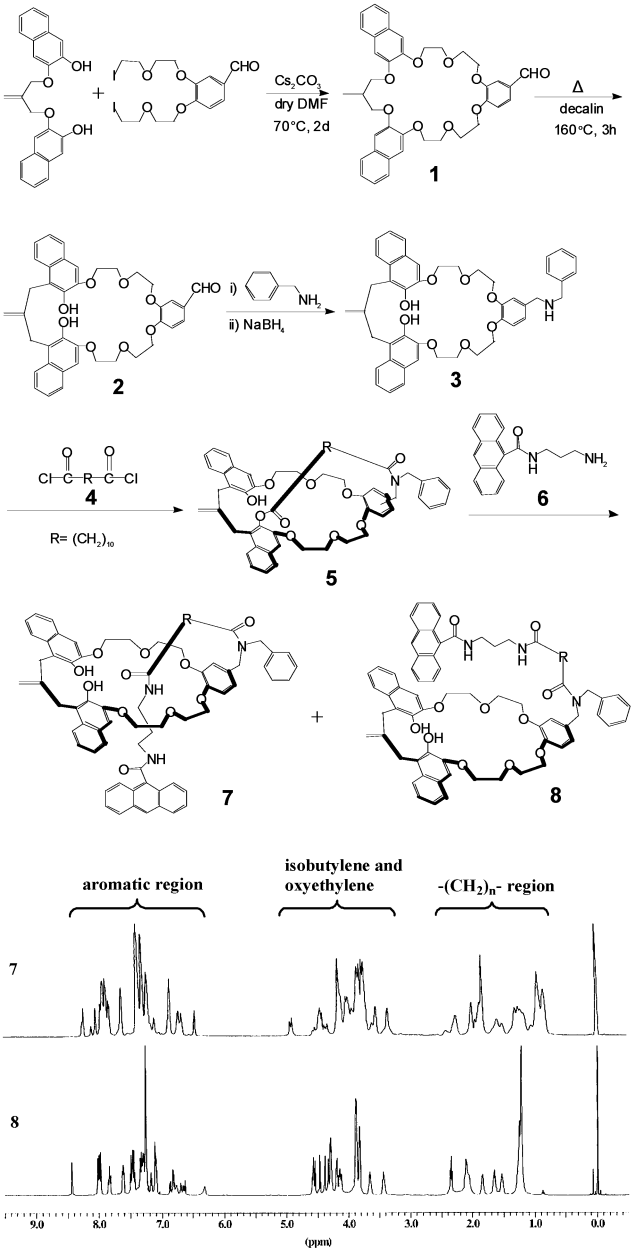

Figure 1. ^{1}H NMR (500 MHz) spectra of **7** and **8** in $CDCl_3$ at 25 °C.

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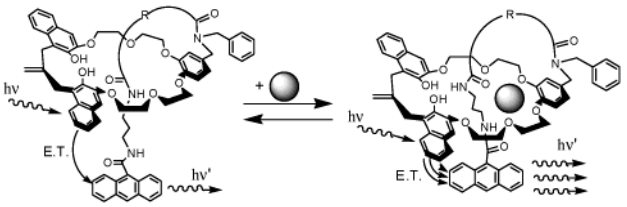
10.1021/ja046929r CCC: $27.50

Scheme 2. Behavior of Energy Transfer of [1]Rotaxane Due to Schematic Host−Guest Interaction



to the aromatic rings and affected by the ring current. On the other hand, the NMR spectrum of **8** shows usual chemical shifts compared to those of **3** as the macrocycle part and **9** as the long chain part. In addition, the GPC peak due to compound **8** was observed to flow faster than that of compound **7**, although both parent peaks in the ESI mass are the same. This means that the molecular volume of **7** is apparently smaller than that of **8** in GPC. From these results it is presumed that **7** is a macrocycle through which a long chain threads, whereas **8** is a macrocycle having a long and unthreaded molecular chain as shown in Scheme 1. In addition, thermal isomerization of **7** to form **8** did not occur. Heating **7** in dimethyl sulfoxide at 160 °C for 0.5 h and at 100 °C for 5 h gave no new product, and both NMR spectra were the same as that for starting compound **7**. This means that [1]rotaxane **7** is not isomerized to **8** under those conditions.

[1]Rotaxane (**7**) might have a three-dimensionally small cavity constructed by both the ring and the chain connected with the macrocycle. The inside of the cavity, which is surrounded by several ether-oxygens and amide groups, is expected to catch a small cation among electron-deficient species such as metal ions and onium ions as shown in Scheme 2.

Alkali metal ions as guest species were investigated for this experiment. Among them, only lithium ion can change the chemical shifts of **7** in the NMR spectrum in $CDCl_3$. On the other hand, compound **8** has no response (no change of the spectrum) when adding alkali metal ions. This means that [1]rotaxane (**7**) can work as a host molecule toward lithium guest ions. The fluorescence spectrum was measured in $CH_2Cl_2 + CH_3CN$ (9:1) in both the presence and absence of alkali metal ions. The energy transfer from naphthalene to anthryl groups was observed in both cases when irradiated at 285 nm in $CHCl_3$;[10] that is, the emittance from 400 to 500 nm based on the anthryl group was observed. Figure 2 shows the fluorescence spectrum of **7** with and without alkali ion. Only lithium ion drastically enhanced the fluorescence intensity, while the other cations did not change the spectrum. The association constant was estimated by changing the concentration ratio of the cation toward [1]rotaxane (**7**). The association constant (Ka) of **7** toward lithium ion is $8.4 \pm 0.3 \times 10^3$, with a ratio of complexation of 1:1. Surprisingly, there is no detectable value of K_a for any other cations.

The three-dimensionally small cavity formed seems to recognize lithium ion with the smallest ion radius among alkali metal ions. The NMR study of the complex of **7** with lithium ions supports the interaction of lithium ion with the polyether and amide-carbonyl oxygen atoms. Complexation with lithium ion is presumed to result in the uptake of a lithium ion into the cavity with high selectivity. The uptake might restrain the movement of the threaded chain moiety and the anthryl group and approximate the distance between naphthyl and anthryl groups eventually to suppress the quenching phenomenon.

Thus, we synthesized novel [1]rotaxanes via covalent bond formation in three steps starting with crownophane **2** having two hydroxy groups. Compound **7** exhibited a fluorescence intensity

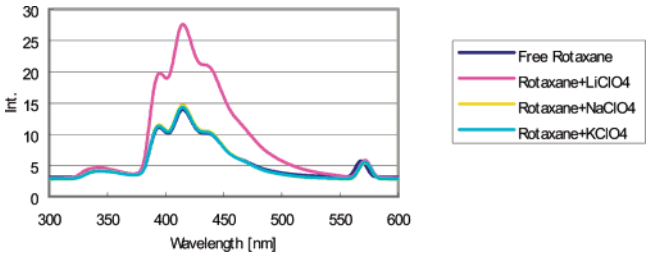


Figure 2. Fluorescence spectra of **7** (5.0×10^{-6} M) in CH_2Cl_2/CH_3CN (9/1); excitation wavelength = 285 nm, which originally excited naphthalene ring (see ref 10).

increase only in the presence of lithium ions, which might make it a candidate for a lithium ion-sensing agent.

Acknowledgment. K.H. would like to thank the Ministry of Education, Culture, Sports, Science and Technology (MEST) for partial support through a Grant-in-Aid for Scientific Research (No. 14540526).

Supporting Information Available: Electronic supplementary information (ESI): ^1H and ^{13}C NMR spectra and ESI-mass data for [1]rotaxane **7**, crownophane **8**, and the complex of **7** with lithium ion (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) Synthesis of **7** and **8**: Compound **5** (80 mg, 0.086 mmol) was dissolved in 10 mL of anhydrous DMF, and then amine **6** (95 mg, 0.34 mmol) was added. The solution was stirred at room temperature under an argon atmosphere for 5 days. After removal of DMF under vacuum, the residue was submitted to gel permeation chromatography. Mainly, three peaks in GPC were collected. The first elute (21 mg; 20% yield) and the second elute (45 mg; 45% yield) have the same molecular weight (found: 1214.7 ($+H^+$); calcd: 1213.60). The third one was excess amine **6**. The NMR, IR, and ESI-mass spectra of the first and second elutes by GPC were measured.

(9) NMR spectra of the first elute (**8**) and the second elute (**7**) are shown in Figure 1.

(10) Synthesis of **8** by another method: To diacid dichloride **4** (47 mg, 0.18 mmol) in 80 mL of anhydrous THF were added compound **3** (0.13 g, 0.18 mmol) and triethylamine (18 mg, 0.18 mmol). The solution was stirred at ice−water temperature for 2 h. Then, to the solution were added amine **6** (73 mg, 0.26 mmol) and triethylamine (18 mg, 0.18 mmol) at room temperature for 2 h. After removal of THF, the residue was submitted to column chromatography with chloroform and then GPC for isolation of **8** (30 mg; 14% yield). The ^1H NMR spectrum of the product was identified to the second elute described above (see ref 8).

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JA046929R