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Synthesis of cyclophane carrying poly(acrylic acid) chains and its complexation behavior

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Summary

Poly(*tert*-butyl acrylate)-coupled cyclophane was obtained by coupling 1,6,20,25-tetraaza[6.1.6.1]paracyclophane with carboxyl-terminated poly(*tert*-butyl acrylate) . The poly(*tert*-butyl acrylate) was quantitatively hydrolyzed to poly(acrylic acid). The cyclophane carrying poly(acrylic acid) was soluble in alkaline water and formed an inclusion complex with trimethyl-2-naphthylmethylammonium bromide as a guest.

Introduction

Water-soluble cyclophanes (bridged aromatic compounds) having a large hydrophobic cavity of definite shape and size are able to accommodate organic compounds as guests in the cavity through hydrophobic interaction to form an inclusion complex in aqueous solution. Such cyclophanes are of great interest as artificial inclusion hosts, since host-guest complex formation in water is a fundamental process in many biological reactions. A strategy for a water-soluble cyclophane was an introduction of water-solubility-providing ionic group onto the cyclophane molecule. For example, cyclophanes having an ammonium[1,2] or sulfonium[3] functionality are soluble in neutral water. Considerable studies have been reported on the preparation of water-soluble cyclophanes and their complexation behavior.[4]

We present an alternative approach for a water-soluble cyclophane. We prepared a water-soluble cyclophane by coupling the water-soluble polymer, poly(acrylic acid), with cyclophane. Poly(acrylic acid) bounded cyclophane is considered to be a new separation material for a guest compound. In a basic solution poly(acrylic acid) polymer chain assumes an extended form by electrostatic repulsion between carboxylate anions on the polymer chain. The core cyclophane can easily complex with the guest molecule (Fig. 1a). On the other hand, the polymer chain starts to collapse on addition of acid to this system. Finally, the host molecule precipitates holding the guest in the cavity (Fig. 1b).

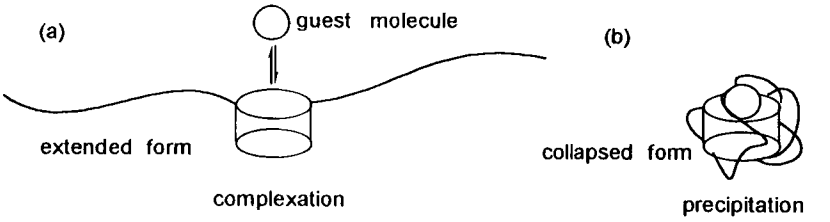

Fig. 1. Schematic illustration of host-guest complexation in (a) alkaline solution and (b) acidic solution.

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In this work we report the synthesis of cyclophane carrying poly(acrylic acid) chain and its complexation behavior with some aromatic compounds in alkaline aqueous solution.

Experimental

1,6,20,25-Tetraaza[6.1.6.1]paracyclophane (1). Cyclophane **1** was prepared according to the literature[5] by the direct 2:2 cyclization between *N,N'*-ditosyl-4,4'-diaminodiphenylmethane[6] and 1,4-dibromobutane followed by the detosylation: mp 182 °C dec (lit.[5] 182.5-184 °C dec); IR (KBr) $\nu_{N\text{-}H}$ 3294 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.92 (d, J = 8.6 Hz, 8H), 6.44 (d, J = 8.6 Hz, 8H), 3.73 (s, 4H), 3.55 (t, J = 5.8 Hz, 4H), 3.1 (m, 8H), 1.7 (m, 8H).

Carboxyl-terminated Poly(tert-butyl acrylate) (2). Carboxyl-terminated poly(*tert*-butyl acrylate) was prepared as described in the literature.[7] To dry tetrahydrofuran (THF) (100 mL) containing 0.7 g of LiCl was added *sec*-butyllithium (1.05 M in hexane, 2.2 mmol) using an air-tight syringe. 1,1-Diphenylethylene (0.44 g, 2.4 mmol) was added dropwise using an air-tight syringe, resulting in a deep red color. After the reaction mixture was cooled to -78 °C, *tert*-butyl acrylate (2.9 g, 22.4 mmol) in 20 mL of THF was added dropwise using an air-tight syringe. The color of the reaction mixture changed from deep red to light yellow during the addition of the monomer. After stirring for 15 min, succinic anhydride (0.37 g, 3.6 mmol) in 10 mL of THF was added to the living poly(*tert*-butyl acrylate) solution, and the reaction mixture was allowed to warm to room temperature, poured into aqueous hydrochloric acid (150 mL) and extracted with 150 mL of hexane. The organic layer was dried with anhydrous magnesium sulfate and placed under reduced pressure to yield a colorless viscous material. It was charged on a silicagel column using carbon tetrachloride as an eluent. After the first band was collected to remove the excess 1,1-diphenylethylene, the eluent was changed to ethyl acetate and the second band was collected to give 3.47 g (96%) of **2** as a colorless sticky material: ^1H NMR ($CDCl_3$,δ) 7.3-7.1 (m, phenyls), 2.7, 2.6, 2.3-1.8 (broad, CH and CH_2), 1.4 (s, *tert*-butyl), 0.8-0.6 (m, CH_3). M_n (pSt) = 1685. M_w/M_n = 1.09.

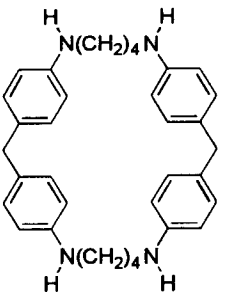
Poly(tert-butyl acrylate)-Coupled Cyclophane (3). A mixture of cyclophane **1** (0.28 g, 0.6 mmol), carboxyl-terminated poly(*tert*-butyl acrylate) **2** (1.9 g, 1.2 mmol), 2-chloro-1-methylpyridinium iodide (0.40 g, 1.6 mmol), and tributylamine (0.49 g, 2.6 mmol) in 30 mL of dichloromethane was heated under reflux for 20 h. The mixture was washed with hydrochloric acid solution, dried with anhydrous magnesium sulfate, and placed under reduced pressure to remove the solvent. The residue was charged on an alumina column using ethyl acetate as an eluent to remove the unreacted carboxyl-terminated poly(acrylic acid). The first band was collected and charged on a silicagel column using ethyl acetate as an eluent to remove the unreacted cyclophane **1**. The first band was collected to give **3** (1.1 g, 51%) as a colorless viscous material. M_n(pSt) = 3010. M_w/M_n = 1.12.

Poly(acrylic acid)-Coupled Cyclophane (4). Poly(*tert*-butyl acrylate)-coupled cyclophane **3** (0.61 g, 0.16 mmol) was dissolved in 20 mL of formic acid (90%), and the solution was stirred at 40 °C for 20 h. The reaction mixture was placed under reduced pressure to remove the volatile materials. The residue was dissolved in a small amount of THF and poured into excess isopropyl ether (IPE) to precipitate 0.35 g (85%) of **4** as a white powder.

Complexation Experiments. A mixture of **4** (0.008 mmol) and guest compound **5-8** (0.008 mmol) was dissolved in 0.4 mL of D_2O containing KOH (0.4 mol/L). The ^1H NMR spectrum of the resulting solution was measured at room temperature.

Results and discussion

(a) Molecular Design and Synthetic Strategy. The cyclophane of our choice is 1,6,20,25-tetraaza-[6.1.6.1]paracyclophane (**1**), which was reported to form an inclusion complex with various aromatic compounds such as 2,7-dihydroxynaphthalene and 1-naphthalene sulfonic acid in acidic aqueous solution.[8] Moreover, cyclophane **1** has amine functionality which is considered to be an useful binding site for the polymer chain.



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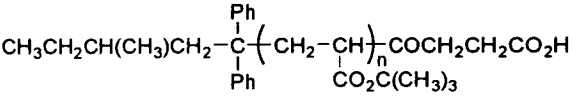
The following is the synthetic route for the cyclophane carrying poly(acrylic acid) chain. The living anionic polymerization of *tert*-butyl acrylate was carried out by the LiCl-modified organolithium-initiated polymerization according to the literature.[9] The living anion was terminated with succinic anhydride to give a carboxyl-terminated poly(*tert*-butyl acrylate) (**2**).[7] The degree of polymerization of the poly(*tert*-butyl acrylate) was designed to be 10. The short polymer chain should be sufficient to control the solubility of the cyclophane attached, and the low molecular weight of the polymer chain will simplify the ^{1}H NMR analysis for the resulting structure. The carboxyl-terminated poly(*tert*-butyl acrylate) was coupled to cyclophane **1** using 2-chloro-1-methylpyridinium iodide[10] as a coupling agent to give a cyclophane carrying poly(*tert*-butyl acrylate) chain (**3**). Finally, the *tert*-butyl esters of poly(*tert*-butyl acrylate) chain were hydrolyzed to obtain the cyclophane carrying poly(acrylic acid) (**4**).



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(b) Characterization. Fig. 2 shows the GPC traces of poly(*tert*-butyl acrylate)-coupled cyclophane **3** together with that of the parent carboxyl-terminated poly(*tert*-butyl acrylate) **2**. The molecular weight of **3** was about twice of that of **2**, indicating that two poly(*tert*-butyl acrylate) chains were coupled to the cyclophane **1**. The ^{1}H NMR spectrum of **3** along with the peak assignments is shown in Fig. 3. The methylene protons of diphenylmethane skeleton exhibited a single peak at 3.8 ppm (peak H_d). In addition, the coupling reaction of **1** with four equivalent of **2** also gave **3** in which two amine moieties remained unreacted. These experimental results suggested 1,20-disubstitution of the polyacrylic chains. Conversion of poly(*tert*-butyl acrylate) into poly(acrylic acid) was confirmed by ^{1}H NMR as shown in Figure 4. The *tert*-butyl peak at 1.4 ppm disappeared completely and the peaks due to cyclophane remained unchanged.

(c) Solubility. The solubilities of **1**, **3**, and **4** are summarized in Table 1. The poly(acrylic acid)-coupled cyclophane **4** was not soluble in chloroform but was completely soluble in methanol, dimethylsulfoxide (DMSO), and alkaline water. It was concluded that the poly(acrylic

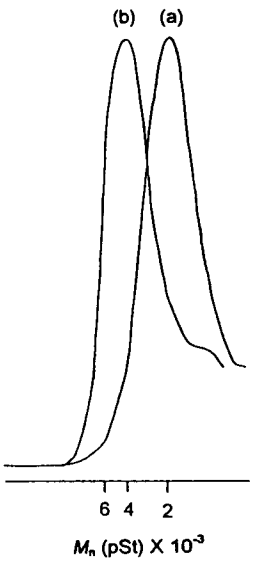


Fig. 2. GPC curves of (a) **2** and (b) **3**.

acid) chain was sufficient to control the solubility of the attached cyclophane.

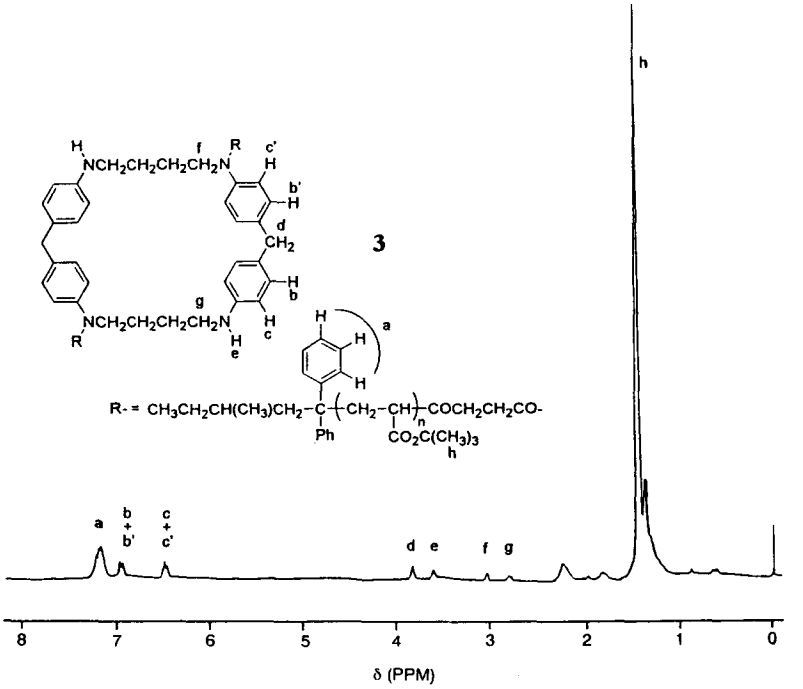


Fig. 3. ^{1}H NMR spectrum of **3** in $CDCl_3$.

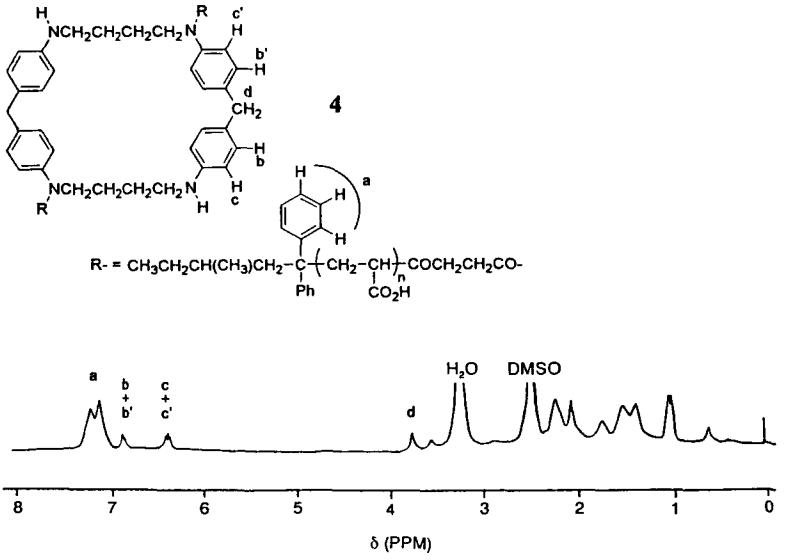


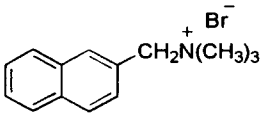
Fig. 4. ^{1}H NMR spectrum of **4** in DMSO-d_6.

Table 1. Solubilities[a] of **1**, **3**, and **4**

	solvent					
				water		
compound	$CHCl_3$	methanol	DMSO	acidic	neutral	alkaline
1	+	+	+	+	-	-
3	+	+	+	-	-	-
4	-	+	+	-	±	+

[a] +, soluble; ±, partially soluble; -, insoluble.

(d) Complexation. The complexations of **1** with various aromatic guests were examined by ^1H NMR in KOH-D_2O solution at the KOH concentration of 0.4 mol/L. The guest compounds examined are trimethyl-(1-naphthylmethyl)ammonium bromide (**5**), 2,7-dihydroxynaphthalene (**6**), and quinoxaline (**7**), which are soluble in alkaline water. It is reported that the cyclophane **1** prefers the naphthalene to the benzene nucleus in complexation.[11]



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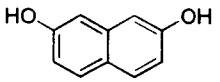

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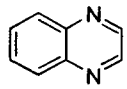

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The ^1H NMR spectra of (a) **4**, (b) **5**, and (c) the equimolar mixture of **4** and **5** are shown in Fig. 5. The equimolar mixture of **4** and **5** in KOH/D_2O gave marked upfield shifts of the aromatic protons of the guest as shown in Figure 5c. These upfield shifts can be ascribed to a strong shielding effect of the aromatic ring of the cyclophane, indicating a formation of inclusion complex. The ^1H NMR spectrum of the equimolar mixture of **5** and carboxyl-terminated poly(acrylic acid) which was prepared by the hydrolysis of **2** did not exhibit such an upfield shift. Odashima et al. measured dissociation constant in the complexation of cyclophane **1** with 1-anilinonaphthalene-8-sulfonate (ANS) by the fluorescence method.[1] Since our host molecule **4** did not complex with ANS, it was not possible to compare the complexation

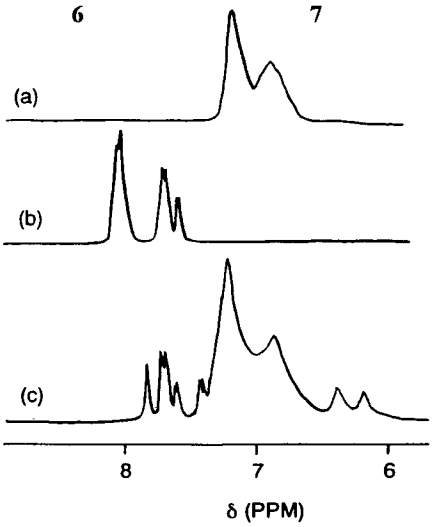

Fig. 5. ^1H NMR spectra of (a) 2.0×10^{-2} M of **4**, (b) 2.0×10^{-2} M of **5**, and (c) the mixture of 2.0×10^{-2} M of **4** and 2.0×10^{-2} M of **5** in D_2O/KOH solution at 25 °C.

ability. However, it is conceivable that the complex formation is weakened due to the steric hindrance of polymer chain or the conformational change of the cyclophane unit. Soga et al. found that introduction of side group onto nitrogen of **1** resulted in a weaker host-guest complexation.[12]

When compounds **6** or **7** were employed as guest molecules, such upfield shifts were not observed. It was concluded that our host molecule **4** showed a selective molecular recognition for **5**. Although Odashima et al. reported that cyclophane **1** formed inclusion complex with **6** in acidic water, our host molecule **4** which has the same cyclophane unit did not complex with **6**, indicating that poly(acrylic acid) chains on the cyclophane **1** effected the complexation selectivity. We explain this in terms of the electrostatic repulsion between carboxylate anion on the poly(acrylic acid) chain and the phenoxide anion of **6** or the lone pair of **7** in alkaline solution. Complex formation was observed for **5** with a positive charge.

Acknowledgment.

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