

단 신

3차 암모늄염과 쿠커비튜릴을 이용한 유사로텍산의 형성에 대한 고찰

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[2]Pseudorotaxanes Containing the Tertiary Alkylammonium Salts as Strings and Cucurbit[6]uril as a Bead

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INTRODUCTION

One of the most significant challenges presently facing supramolecular chemists is to find ways of constructing nanometer-scale devices such as molecular machines and switches from molecular components. This challenge exists not only for designing and constructing of working devices, but also for developing new mechanically interlocked molecules using a self-assembling approach. One particularly interesting class of supramolecular aggregates (mechanically interlocked molecules) is the so-called pseudorotaxanes.¹ These supramolecular entities are comprised of one (or more) threadlike component(s) which is (are) encircled by one (or more) beadlike component(s). They are promising prototypes for a variety of nano-wired molecular machines,² such as switches³ and shuttles.⁴ Most pseudorotaxanes have been prepared by utilizing: (a) van der Waals interactions⁵ between cyclodextrin derivatives and hydrophobic guests, (b) metal-ligand interactions⁶ between metal ions, such as copper(I), and bipyridine-derived beads/threads, (c) attraction between π -electron-rich⁷ macrocyclic hosts

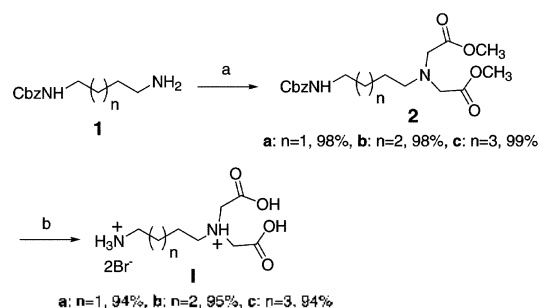
and π -electron-deficient threadlike guests or vice versa,⁸ and (d) association⁹ between secondary dialkylammonium ions, such as the linear threadlike cationic salts, and macrocyclic polyethers, such as dibenzo[24]crown-8 (DB24C8) and bis-*p*-phenylene[34]crown-10 (BPP34C10). In the past decade, Kim *et al.* have developed¹⁰ simple self-assembling systems capable of forming pseudorotaxanes, polyrotaxanes, molecular necklace, and so on. These supramolecular systems are based upon non-covalent interactions between diammoniumalkane derivatives as the linear threadlike cationic salts and cucurbit[6]uril.

Cucurbit[6]uril (CB[6]) is a large cage compound composed of six glycoluril units interconnected via twelve methylene bridges with relatively rigid structure which was prepared nearly 100 years ago.¹¹ Each of the two carbonyl-fringed portals at the upper and lower side of the molecule has a diameter of 4 Å. The internal cavity has a diameter of *ca.* 5.5 Å, while the distance between the portals is 6 Å. The interior of the molecule represents a hydrophobic region, whereas the two portals are hydrophilic. Consequently, the hydrophobic organic moiety of

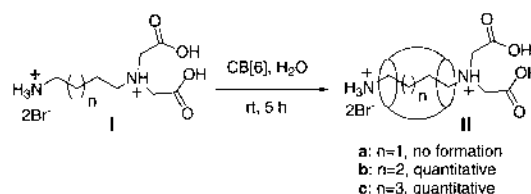
organic ammonium ions extends into the interior, and the ionic part coordinates to one of the planes spanned through the negatively polarized carbonyl groups. It is this potential for the formation of the supramolecular host-guest complexes which make this molecule interesting. A series of alkylammonium and alkyldiammonium ions formed host-guest complexes with CB[6] which was observed and analyzed by NMR spectroscopy.¹² Although CB[6] has now been demonstrated to have the ability to form host-guest complexes with primary and secondary alkyldiammonium salts, there have been relatively few studies with tertiary alkylammonium salts.^{12b, 13} We were thus intrigued to find out whether the tertiary alkylammonium salts, such as aminoalkyliminodiacetic acid salts as ligands, could be threaded with CB[6] to form pseudorotaxanes. Here, we report that pseudorotaxane complexes between the tertiary alkylammonium salts and CB[6] are indeed capable of being formed and characterized.

RESULTS AND DISCUSSION

Our interesting ligand structures are aminoalkyliminodiacetic acids **I** which their syntheses are outlined in *Scheme 1*. Cbz-protected aminoalkyl amines **1**¹⁴ were dialkylated with methyl bromoacetate to afford the tertiary amines **2** in excellent yields. Both Cbz group deprotection and ester group hydrolysis could be carried out simultaneously using HBr-H₂O to afford ammoniumalkyliminodiacetic acids **I** in 94-95% yields.



Scheme 1. Synthesis of iminoacetic acids **I**. Reagents and conditions: (a) Methyl bromoacetate (2.2 eq.), DIEA, CH₂Cl₂, rt, 20 h; (b) HBr-H₂O, 80 °C, 5 h.



Scheme 2. Synthesis of CB[6]-pseudorotaxanes **II**.

Keeping in mind the host-guest chemistry with CB[6] and ammonium salts, we have tried to thread CB[6] with ammoniumalkyliminodiacetic acids **I** (*Scheme 2*). Ammoniumbutyliminodiacetic acid salt **Ia** ($n=1$; 4 methylene units between ammonium salts) and CB[6] in H₂O did not form the expected CB[6]-threaded complex. However, slight interaction between CB[6] and ammonium salt could be observed. This result is in contrast to the primary and secondary diammoniumalkyl salts having 4 methylene units between moiety which readily forms a CB[6]-threaded complex.¹² The diacetic acid in **Ia** might experience both steric hindrance and repulsion with carbonyl groups of CB[6] and disallow threading CB[6] with ligand **Ia**. Besides, this will make the 4 methylene units in ligand **Ia** nor long enough to coordinate a CB[6] molecule. On the other hand, ammoniumpentyliminodiacetic acid salt **Ib** ($n=2$; 5 methylene units between ammonium salts) and ammoniumhexyliminodiacetic acid salt **Ic** ($n=3$; 6 methylene units between ammonium salts) formed CB[6]-threaded complexes **IIb** and **IIc**, respectively, in quantitative yields. These CB[6]-threaded complexes were isolable and characterized by ¹H-NMR and ESI-mass spectroscopy.

In the ¹H-NMR spectrum, CB[6] positions in CB[6]-threaded complexes **IIb** and **IIc** can be distinguish from other peaks. In other words, the location of CB[6] leans to the primary ammonium salt in complexes **IIb** and **IIc**. As shown in *Fig. 1*, the ¹H-NMR shift of complex **IIb** exhibits five CH₂ peaks of which four methylene groups (*a*, *b*, *c*, and *d* in complex **IIb**) showing upfield shifts while one (*e* in complex **IIb**) showing a downfield shift.¹² These observations can be attributed as follows. First of all, the methylene unit *a* which is adjacent to primary ammonium group is included in the cav-

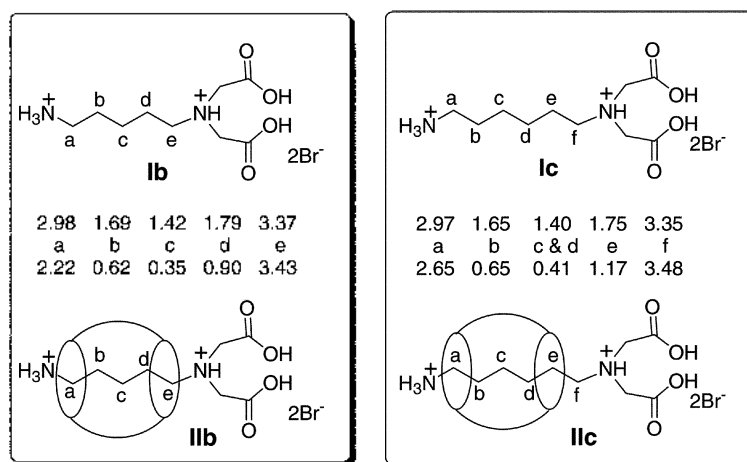


Fig. 1. Chemical shift of methylene peaks in $^1\text{H-NMR}$ (in D_2O) ligands **Ib** and **Ic** and complexes **IIb** and **IIc**.

ity of CB[6]. The methylene unit *e* is outside the cavity due to steric hindrance offered by the substituents attached to the tertiary ammonium nitrogen adjacent to *e*. Secondly, the methylene units *b* and *d* in complex **IIb** stay at different shielding zones within CB[6]; the unit *b* is located at strong shielding zone due to strong interaction of the primary ammonium salt and the unit *d* is located at weak shielding zone resulting from weak interaction of the tertiary ammonium salt. The methylene unit *c*, however, remains at strong shielding zone. The $^1\text{H-NMR}$ spectrum of complex **IIc** exhibits six CH_2 peaks where five methylene groups (*a*, *b*, *c*, *d*, and *e* in complex **IIc**) show upfield shifts and one methylene group (*f* in complex **IIc**) shows a downfield shift (Figure 1). The location of CB[6] in complexes **IIc** leans to the primary ammonium salt as in case of complexes **IIb**. The chemical environment of methylene units *a*, *b*, *e*, and *f* in complexes **IIc** correspond similar to that of methylene units *a*, *b*, *d*, and *e* in complex **IIb**, respectively, even though they show different magnitude of chemical shifts due to different alkane chain lengths. We can assume that complex **IIb** is stronger compared to complex **IIc** considering the lengths of methylene chain and the different strengths of interactions of the tertiary ammonium part. For ligand substrates **I**, pentylammonium salt **Ib** forms the most stable complex **IIb** (five

methylene units) and the order of affinities for CB[6] follows the trend; *number of methylene unit* - $4 \ll 6 < 5$. The plausible explanation is that the pentyl substituent optimally fills the cavity, the butyl chain is short to form a stable complex, while the hexyl substituent is obliged to protrude into the second occlus of CB[6].

In summary, we have demonstrated the host-guest chemistry using tertiary ammonium salts such as aminoalkyliminodiacetic acids as ligands with cucurbit[6]uril. From the formation of pseudorotaxane complex between aminoalkyliminodiacetic acids salt and CB[6], it was proven that five methylenes are best to form stable complex but four methylenes unit is short to form complex **II**, and the location of CB[6] leans to the primary ammonium salt in complexes **II**.

EXPERIMENTAL SECTION

General Methods. Materials were obtained from commercial supplier and used without further purification. Thin-layer chromatography (TLC) was carried out on glass coated with silica-gel 60 (Merck 5554). Column chromatography was performed on silica-gel 60 (Merck 9385, 230-400 mesh). Electrospray ionization (ESI) mass spectra were measured on a VG Prospec mass spectrometer. $^1\text{H-}$

NMR spectra were recorded on a Bruker AC300 (300 MHz) or a Bruker AMX500 (500 MHz) spectrometer using deturated solvent. ^{13}C -NMR spectra were recorded on a Bruker AC300 (75 MHz) spectrometer. All chemical shifts are quoted on the δ scale, and all coupling constants are expressed in Hertz (Hz).

General Procedure for dialkylation of primary amine. To a solution of primary amine (4 mmol) and diisopropylethylamine (8.1 mmol) in CH_3CN (40 mL) was added methyl bromoacetate (8.8 mmol) under ice bath and then the resulting solution was stirred for 20 h at room temperature. The reaction solution was concentrated and dissolved with methylene chloride (80 mL). The resulting solution was washed with NaHCO_3 aqueous solution, dried, and evaporated to give crude which was purified by column chromatography using EtOAc/n -hexane system as an eluent.

N-Cbz-aminobutyliminodiacetic ester 2a. Amine 1a gave 2a (98 %): ^1H NMR (CDCl_3) δ 1.51 (m, 4H), 2.70 (t, $J = 6.8$ Hz, 2H), 3.19 (distorted t, 2H), 3.52 (s, 4H), 3.68 (s, 6H), 4.91 (br s, 1H), 5.08 (s, 2H), 7.32 (m, 5H).

N-Cbz-aminopentyliminodiacetic ester 2b. Amine 1b gave 2b (98 %): ^1H NMR (CDCl_3) δ 1.32 (m, 2H), 1.48 (m, 4H), 2.68 (t, $J = 7.2$ Hz, 2H), 3.18 (distorted t, 2H), 3.53 (s, 4H), 3.69 (s, 6H), 4.92 (br s, 1H), 5.08 (s, 2H), 7.34 (m, 5H); ^{13}C NMR (CDCl_3) δ 24.5, 27.8, 30.1, 41.3, 51.9, 54.5, 55.2, 66.9, 128.4, 128.9, 137.1, 156.8, 172.1.

N-Cbz-aminohexyliminodiacetic ester 2c. Amine 1c gave 2c (99%): ^1H NMR (CDCl_3) δ 1.31 (m, 4H), 1.47 (m, 4H), 2.67 (t, $J = 7.2$ Hz, 2H), 3.18 (distorted t, 2H), 3.53 (s, 4H), 3.70 (s, 6H), 4.90 (br s, 1H), 5.08 (s, 2H), 7.33 (m, 5H); ^{13}C NMR (CDCl_3) δ 26.8, 27.0, 28.1, 30.2, 41.3, 51.9, 54.5, 55.2, 66.9, 128.4, 128.5, 128.9, 137.1, 156.8, 172.1.

General Procedure for the preparation of substituted-iminodiacetic acids by Cbz deprotection and simultaneous hydrolysis. A solution of Cbz-protected aminoester (1 mmol) in $\text{HBr-H}_2\text{O}$ (10 mL) was stirred for 5 h at 80 °C. The resulting solution was concentrated and solidified from EtOAc which the generated solid was filtered to collect and

washed with ether extensively.

Aminobutyliminodiacetic acid Ia. Compound 2a gave Ia (94 %): ^1H NMR (D_2O) δ 1.72 (m, 2H), 1.84 (m, 2H), 3.03 (t, $J = 7.5$ Hz, 2H), 3.41 (t, $J = 7.7$ Hz, 2H), 4.19 (s, 4H); ^{13}C NMR (D_2O) δ 21.2, 24.1, 39.1, 55.5, 56.3, 168.9.

Aminopentyliminodiacetic acid Ib. Compound 2b gave Ib (95 %): ^1H NMR (D_2O) δ 1.42 (m, 2H), 1.69 (m, 2H), 1.79 (m, 2H), 2.98 (t, $J = 7.4$ Hz, 2H), 3.37 (t, $J = 8.2$ Hz, 2H), 4.20 (s, 4H); ^{13}C NMR (D_2O) δ 23.0, 23.4, 26.5, 39.5, 55.2, 56.8, 168.8.

Aminohexyliminodiacetic acid Ic. Compound 2c gave Ic (94 %): ^1H NMR (D_2O) δ 1.40 (m, 4H), 1.65 (m, 2H), 1.75 (m, 2H), 2.97 (t, $J = 7.5$ Hz, 2H), 3.35 (t, $J = 8.3$ Hz, 2H), 4.18 (s, 4H); ^{13}C NMR (D_2O) δ 23.5, 25.4, 26.8, 39.7, 55.2, 57.0, 168.9.

General Procedure for the Preparation of CB-threaded Complexes. To a solution of polyamine ligand (0.3 mmol) in 30 mL of H_2O was added cucurbit[6]uril (0.4 mmol) in a small portions and stirred for 2~5 h at room temperature. Excess cucurbit[6]uril was filtered out to provide clear solution which was evaporated to leave ca. 1 mL. 30 mL of EtOH was added to the resulting solution to make the precipitate which was isolated by the filtration to afford the desired CB-threaded complex quantitatively.

CB-threaded complex IIb. Ligand Ib gave IIb: ^1H NMR (D_2O) δ 0.35 (m, 2H), 0.62 (m, 2H), 0.90 (m, 2H), 2.22 (t, $J = 9.0$ Hz, 2H), 3.43 (t, $J = 8.5$ Hz, 2H), 4.33 (d, $J = 8.5$ Hz, 6H), 4.38 (d, $J = 8.6$ Hz, 6H), 4.80 (dd, $J = 25.9$ Hz and 17.7 Hz, 4H), 5.61 (s, 12H), 5.75 (d, $J = 15.8$ Hz, 6H), 5.81 (d, $J = 15.6$ Hz, 6H); ESI-MS: m/z 608.3 ($[\text{M} + 2\text{H}]^{2+}$), 1215.5 ($[\text{M} + \text{H}]^+$).

CB-threaded complex IIc. Ligand Ic gave IIc: ^1H NMR (D_2O) δ 0.41 (m, 4H), 0.65 (m, 2H), 0.17 (m, 2H), 2.65 (m, 2H), 3.48 (t, $J = 8.1$ Hz, 2H), 4.30 (d, $J = 9.1$ Hz, 6H), 4.35 (d, $J = 9.2$ Hz, 6H), 4.61 (dd, $J = 25.3$ Hz and 17.6 Hz, 4H), 5.58 (s, 12H), 5.76 (d, $J = 15.1$ Hz, 6H), 5.81 (d, $J = 14.9$ Hz, 6H); ESI-MS: m/z 615.3 ($[\text{M} + 2\text{H}]^{2+}$), 626.2 ($[\text{M} + \text{H} + \text{Na}]^{2+}$), 1229.4 ($[\text{M} + \text{H}]^+$).

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