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[2]Pseudorotaxanes Based on Naphtho-21-crown-7 and Secondary Dialkylammonium Salts: Remarkably Improved Association Constants Among Four Threaded Structures

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This research article is focused on the recognition interaction of a new host naphtho-21-crown-7 and four secondary dialkylammonium salts. In acetone, they can form 1∶1 host-guest complexes which belong to slow-exchange systems. We also found the differences of binding affinity and binding selectivity between the host and its complementary guest moieties, which could be ascribed to the aromatic π-π stacking effect and the acidity increase of *N*-methylene and ammonium hydrogens due to the increasing electron withdrawing ability from butyl to methoxyphenyl to phenyl to *p*-cyanophenyl substituents in the recognition motif.

Keywords crown ethers, host-guest systems, pseudorotaxanes, secondary ammonium salts

Introduction

Pseudorotaxanes, known as mechanically interlocked molecular architectures which were fabricated from linear molecular components surrounded by macrocyclic components, have attracted great interest and widely have been studied throughout the world.

Pseudorotaxanes as synthetic templates were widely used to construct rotaxanes,[1-11] catenanes[12-17] and supramolecular polymers,[18-30] which have potential application in intelligent material such as molecular device,[31] artificial molecular machine,[32] molecular electronic device[33] and new functional materials,[34-37] *etc*.

Pseudorataxanes as threaded structures attracted much interest from supramolecuar scientist because of their topological importance but also due to their many potential applications. Recently, Gibson reported [2]pseudorotaxane and pseudocryptand-type poly[2]-pseudorotaxane based on bis(*meta*-phenylene)-32-crown-10 and paraquat derivatives,[38] pseudocryptand-type [2]pseudorotaxanes based on bis(*meta*-phenylene)-32-crown-10 derivatives and paraquats,[39] and pseudocryptand-type [3]pseudorotaxane based on a bis(*meta*-phenylene)-32-crown-10 derivative and bisparaquat derivatives.[40] Ganguly *et al.* demonstrated folding and unfolding movements in a [2]pseudorotaxane.[41] Schalley has found [4]pseudorotaxanes with remarkable self-sorting selectivities.[42] Philp developed a method of low temperature capture of pseudorotaxanes.[43]

Crown ethers have been widely used in fabricating threaded structures as host molecules for organic salts, such as paraquat derivatives[38-40] and secondary dialkylammonium salts.[42]

A rotaxane had been synthesized in 74% yield from benzo-21-crown-7 containing 21 atoms in the macrocycle and a secondary dialkylammonium salt different from the previously widely accepted point that a macrocycle needs at least 24 C, N, O, or S atoms for the well-threading of an alkyl group into its cavity.[4]

We want to improve host-guest interactions in order to construct more stable threaded structures.

In this paper, we synthesized a new host naphtho-21-crown-7 and studied the recognition interaction of naphtho-21-crown-7 and four secondary dialkylammonium salts.

Experimental

Compounds **1**, **G1**, **G3** and **G4** were prepared according to the previously reported method.[5] ^{1}H NMR was run on Varian Unity INOVA 400 MHz spectrometer with TMS as internal standard. ^{13}C NMR was measured on Bruker AVANCE DMX 500 MHz spectrometer.

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Synthesis of naphtho-21-crown-7 (H1)

A suspension of 2,3-dihydroxynaphthalene (2.70 g, 16.9 mmol), compound **1** (10.00 g, 16.9 mmol), potassium carbonate (7.00 g, 50.7 mmol) and potassium hexafluorophosphate (4.66 g, 25.3 mmol) in acetonitrile (350 mL) was stirred at reflux under nitrogen atmosphere for 72 h. The reaction mixture was cooled to room temperature. Then, the reaction mixture was filtered. After the organic solvent in organic phase was evaporated, dichloromethane (50 mL) was used to dissolve this residue. The organic phase was washed with sodium hydroxide (50 mL, 2 mol/L). Then, the separated organic phase was dried over sodium sulfate. The organic solution was concentrated. The crude product thus obtained was subjected to column chromatography over silica gel column and elution done with mobile phase of dichloromethane/acetonitrile (10∶1, *V*∶*V*), the desired fraction thus eluted was evaporated under vacuum to afford a white solid (2.3 g, 33%)

^{1}H NMR (400 MHz, CD_3COCD_3) δ: 7.67—7.73 (m, 2H), 7.25—7.32 (m, 4H), 4.24 (t, J=4.8 Hz, 4H), 3.92 (t, J=4.8 Hz, 4H), 3.75 (t, J=4.8 Hz, 4H), 3.66 (t, J=4.8 Hz, 4H), 3.55—3.62 (m, 8H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ: 149.4, 129.5, 126.3, 123.9, 108.0, 71.0, 70.8, 70.4, 69.3, 68.9; ESI-MS *m*/*z*: 424.2 $[M+NH_4]^+$, 429.1 $[M+Na]^+$. HRMS-EI calcd for $C_{22}H_{30}O_7$: 406.1992, found 406.1994.

Synthesis of G2

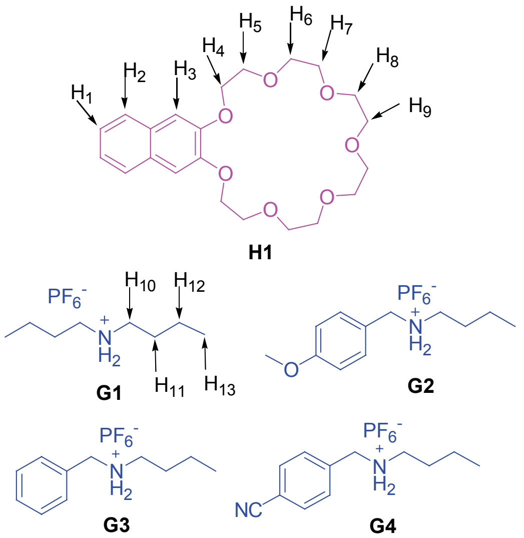
A solution of *p*-methoxybenzaldehyde (10.27 g, 75.4 mmol) and *n*-butylamine (5.50 g, 75.2 mmol) in methanol (150 mL) was stirred at reflux overnight. When the reaction mixture was cooled to room temperature, sodium borohydride (4.00 g, 105.3 mmol) was added into the mixture in several portions. Then the mixture was stirred at room temperature for 24 h. After completion of the reaction, water (50 mL) was used to quench the reaction. The mixture was filtered and methanol was distilled off. The residue was extracted with dichloromethane and the extract was concentrated to get a yellow oil. After the oil was added to a hydrochloric acid solution and stirred for a moment, a white precipitate formed. The mixture was filtered and the solid was dissolved in water to get a saturated solution. The solution was added to a saturated ammonium hexafluorophosphate solution to produce a precipitate. It was collected by suction filtration and recrystallized from deionized water three times to afford **G2** (3.31 g, 23.3%) as a white solid.

^{1}H NMR (400 MHz, CD_3COCD_3) δ: 7.49 (d, J=8.8 Hz, 2H), 7.00 (d, J=8.8 Hz, 2H), 4.50 (s, 2H), 3.80 (s, 3H), 3.38 (t, J=8.0 Hz, 2H), 1.77—1.88 (m, 2H), 1.37—1.50 (m, 2H), 0.92 (t, J=7.6 Hz, 3H); ESI-MS *m*/*z*: 194.1 $[M-PF_6]^+$, 121.1 $[M-PF_6-C_4H_{11}N]^+$. HREIMS *m*/*z* calcd for $[M-HPF_6]^+C_{12}H_{19}NO$: 193.1467, found 193.1473.

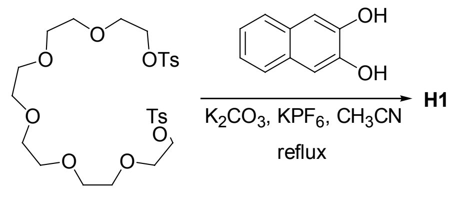
Results and Discussion

The structures of naphtho-21-crown-7 and four secondary dialkylammonium salts were showcased in Scheme 1.

Scheme 1 The structures of naphtho-21-crown-7 and four secondary dialkylammonium salts



The synthesis of naphtho-21-crown-7 was illustrated in Eq. 1. Compound **1** reacted with 2,3-dihydroxynaphthalene in the presence of K_2CO_3 and KPF_6 in CH_3CN to afford naphtho-21-crown-7 in 33% yield.



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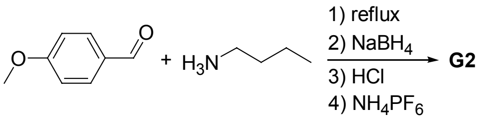
(1)

The synthesis of **G2** was shown in Eq. 2. *p*-Methoxybenzaldehyde reacted with *n*-butylamine to give a reaction mixture, followed by reduction with $NaBH_4$. After completion of the reaction, water was used to quench the reaction. Then, the residue was treated with a hydrochloric acid solution then with a saturated NH_4PF_6 solution to produce **G2** (23.3%) as a white solid.



(2)

The ^{1}H NMR spectrum (Figure 1) of an equimolar solution of naphtho-21-crown-7 (**H1**) and **G1** in acetone-d_6 showcases three sets of resonances for uncomplexed **H1**, uncomplexed **G1**, and the complex between **H1** and **G1**, indicating slow-exchange complexation on the ^{1}H NMR time scale.[44] Proton NMR of H_4, H_5, H_6, H_{10}, H_{11}, H_{12} and H_{13} split into two parts after complexation. This implied the threading of **G1** through the

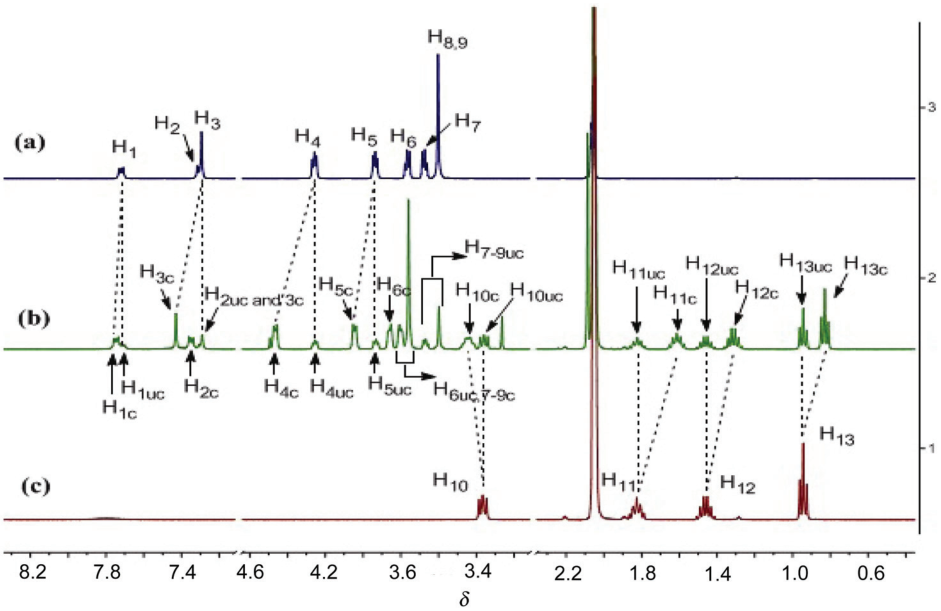


Figure 1 Partial ^{1}H NMR spectra (400 MHz, CD_3COCD_3, room temperature) of 16.00 mmol/L **H1** (a), 16.00 mmol/L **H1** and **G1** (b), and 16.00 mmol/L secondary dialkylammnium salt **G1** (c).

cavity of **H1** to form a pseudorotaxane. In the same way, complexations of **H1** with secondary ammonium salts **G2** and **G3** and **G4** were also found to be slow-exchange systems.

The stoichiometry of the complexes between **H1•G1**, was determined to be 1∶1 and confirmed by an electrospray ionization mass spectrum (ESI-MS) *m*/*z*: 536.1 [**H1•G1**–PF_6]$^+$ (Figure 2).

The stoichiometries of the complexes between **H1** and **G2**, between **H1** and **G3**, and between **H1** and **G4** were also determined to be 1∶1 and confirmed by an electrospray ionization mass spectrum (ESI-MS) *m*/*z*: 600.1 [**H1•G2**–PF_6]$^+$, 570.1 [**H1•G3**–PF_6]$^+$, and 595.1 [**H1•G4**–PF_6]$^+$ (see Supporting Information).

Since the stoichiometries of all four complexation systems were determined to be 1∶1, then the association constants (K_a) of 1∶1 complexes[4,42] of **H1•G1** were determined to be 467 (±51) L•mol^{-1} (Figure 3).

The association constants (K_a) of 1∶1 complexes of **H1•G2**, **H1•G3** and **H1•G4** in acetone-d_6 were determined to be 775 (±77) L•mol^{-1}, 930 (±91) L•mol^{-1} and 1473 (±102) L•mol^{-1}, respectively (Supporting Information).

Some observed values are higher than the corresponding K_a values of 615 (±36) L•mol^{-1} (**B21C7•G2**), and 1062(±102) L•mol^{-1} (**B21C7•G4**) for **B21C7**-based complexes,[4] indicating that the aromatic π-π stacking effect in naphtho-21-crown-7/secondary dialkylammonium salts system is larger than **B21C7**/secondary dialkylammonium salts system. The K_a increase from **H1•G1** to **H1•G2**, **H1•G3** and **H1•G4** is a result of the acidity increase of *N*-methylene and ammonium hydrogens due to the increasing electron withdrawing ability from butyl to methoxyphenyl to phenyl to *p*-cyanophenyl substituents.

The proposed host-guest interaction model was explained in Scheme 2 according to previous literatures.[4,45-49] There exist host-guest interaction between

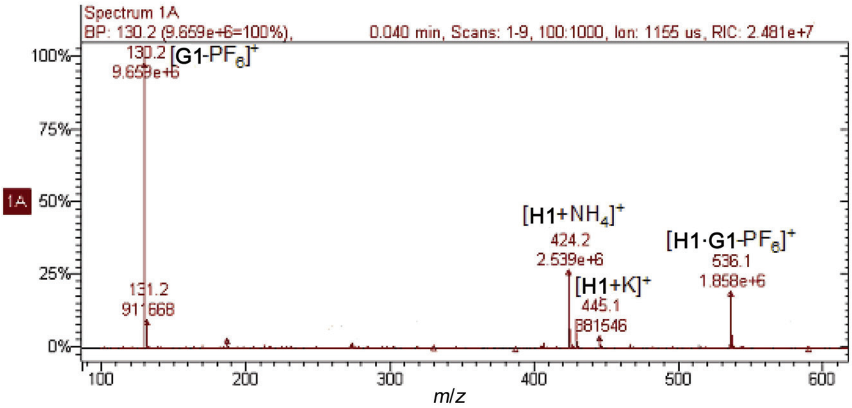


Figure 2 Electrospray ionization mass spectrum of a solution of **H1** and **G1**. *m*/*z*: 130.2 [**G1**–PF_6]$^+$, 424.2 [**H1**+NH_4]$^+$, 445.1 [**H1**+K]$^+$, 536.1 [**H1•G1**–PF_6]$^+$.

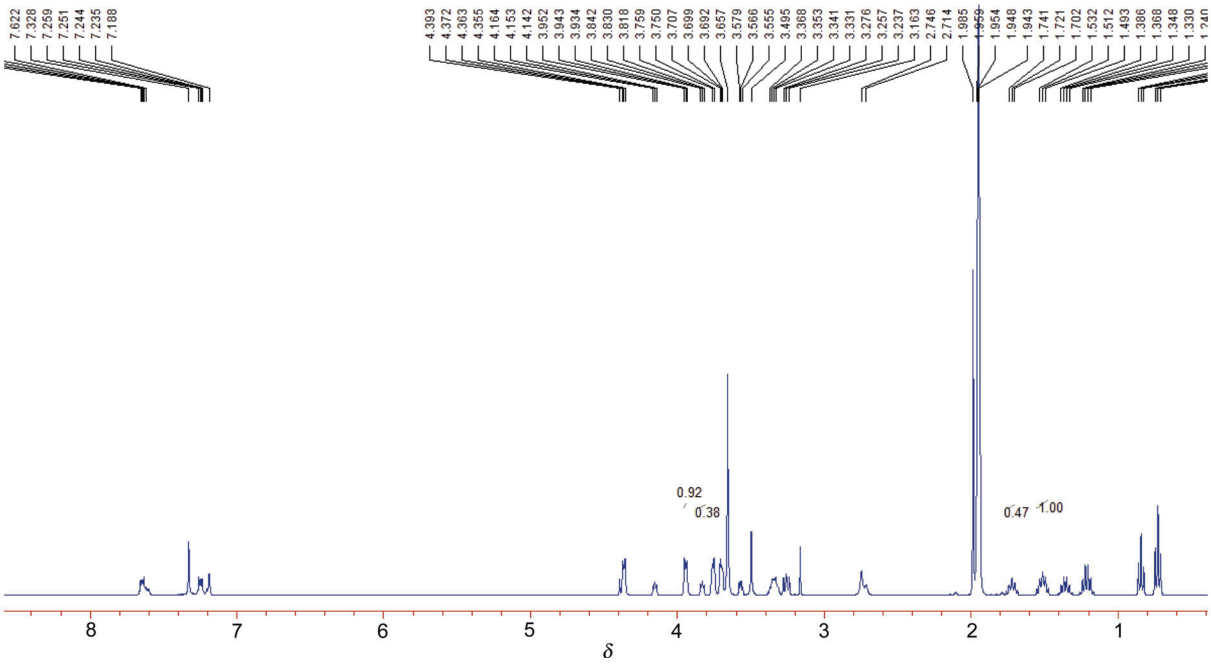
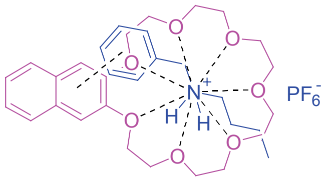


Figure 3 ^{1}H NMR spectrum (400 MHz, CD_3COCD_3, room temperature) of 16.00 mmol/L **H1** and **G1**. The association constant $K_{a,\ \mathbf{H1•G1}}$ value calculated from integrations of complexed and uncomplexed peaks of H_5 of **H1** is $[(0.92/1.30)\times 16.00\times 10^{-3}]/[(1-0.92/1.30)\times 16.00\times 10^{-3}]^2=518$ L•mol^{-1}. The association constant $K_{a,\ \mathbf{H1•G1}}$ value calculated from integrations of complexed and uncomplexed peaks of H_{11} of **G1** is $[(1.00/1.47)\times 16.00\times 10^{-3}]/[(1-1.00/1.47)\times 16.00\times 10^{-3}]^2=416$ L•mol^{-1}. Therefore, $K_{a,\ \mathbf{H1•G1}}=(518+416)/2=467(\pm 51)$ L•mol^{-1}.

Scheme 2 Proposed host-guest interaction model (for example **H1•G3**)



crown ether and dialkylammonium salts, and π-π stacking interaction.[4,45-49]

Conclusions

In conclusion, the successful preparation of naphtho-21-crown-7-based [2]pseudorotaxane threaded structures again proved that macrocycles consisting of less than 24 atoms can be threaded by alkyl groups. Furthermore, we have found that naphtho-21-crown-7 can bind secondary dialkylammonium salts more strongly than **B21C7**, because the aromatic π-π stacking effect in naphtho-21-crown-7/secondary dialkylammonium salts system is larger than **B21C7**/secondary dialkylammonium salts system. Considering the easy availability of naphtho-21-crown-7 derivatives and secondary dialkylammonium salts and the efficient binding between them, we believe that the work advanced here will promote further studies on threaded structures based on the naphtho-21-crown-7/secondary dialkylammonium salt recognition motif. The researches on the pseudorotaxane, rotaxane, catenane and supromolecular polymer based on naphtho-21-crown-7/secondary dialkylammonium salt system are on the progress.

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