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New interlocked molecules generated from a podand containing urea units and imidazolium salts using an anion template

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Abstract—A podand containing urea units (**L**) was found to form interlocked structures with 2,5-dihexylamide imidazolium salts (**3·X**), 2,5-dihexyl imidazolium salts (**4·X**), and 2,5-dihexyl benzoimidazolium salts (**5·X**), where $X = Cl^-$, Br^-, and PF_6^- using anions as templates. The binding ability of **L** and guest molecules was evaluated by ^1H NMR titrations in $CDCl_3$. It was found that **L** could form complexes with guest molecules in the following order, **3·X** > **5·X** > **4·X**. Stabilities of the complexes also depended on shape of the templated anions: $Cl^- > Br^- \gg PF_6^-$. Hydrogen bonding and π–π stacking interactions played an important role in the self-assembling of these interlocked molecules.

Template synthesis has provided important advances in developing strategies for the synthesis of complex molecular architectures. Chemists employ cationic and neutral molecules as templates for synthesizing supramolecular species such as rotaxanes, catenanes, and other interlocked molecules.[1,2] Anions have recently been used as templates in synthetic chemistry.[3] Stoddart[4] and Vögtle[5] are pioneers in synthesizing rotaxanes and pseudorotaxanes using anions as templates. Recently, Beer and co-workers have reported the chloride-directed assembly of a [2]pseudorotaxane by organizing a macrocyclic ligand and an amide pyridinium molecule in an orthogonal fashion.[6,7]

Interestingly, the imidazolium cation has similar properties to the pyridinium cation such as holding a positive charge and possessing ionic liquid properties. Imidazolium units display main structural motifs for the formation of uncoventional $C–H\cdots Cl^-$ hydrogen bonding interactions.[8] Herein, we are interested in self-assembly recognition of azoaromatic onium compounds and a podand diurea compound. This receptor is able to organize itself in a cleft-like structure and assemble imidazolium compounds. In this paper we demonstrate that anion templating, hydrogen bonding, and π–π stacking interactions play an important role in producing new interlocked molecules. The podand containing a diurea receptor **L** was prepared in our group.[9] It contains two urea units as an anion binding site using hydrogen bonding interactions and a polyethyleneglycol unit as a cation binding site. The host and guests described herein are shown in Chart 1.

Compound **3** was synthesized by refluxing a chloroform solution of *N*-hexylchloroacetamide **1**[10] and hexylcarboxamide methyl imidazole **2**[11] prepared by generating the sodium imidazole salt from imidazole and NaH in dry THF and subsequently coupling it with the *N*-hexylchloroacetamide **1**. The reaction provided a white precipitate of **3·Cl**$^-$ in 61% yield.[12] In the case of **3·Br**$^-$ and **3·PF**$_6^-$, they were obtained by anion exchanges between **3·Cl**$^-$ in methanol and saturated NH_4Br and NH_4PF_6 in aqueous solution yielding white solids of **3·Br**$^-$ and **3·PF**$_6^-$ in 89% and 90% yields, respectively. The preparation of **3·X**, where $X = Cl^-$, Br^-, and PF_6^-, is shown in Scheme 1. All compounds were characterized by ^1H NMR and electrospray ionization mass spectrometry.[12,13] Compounds **3·Cl**$^-$, **3·Br**$^-$, and **3·PF**$_6^-$ show

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Keywords: Podand; Imidazolium salt; Anion template; Interlocked molecule.

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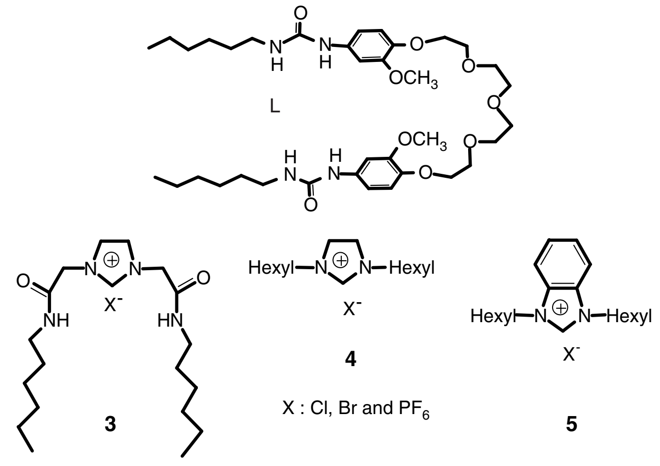
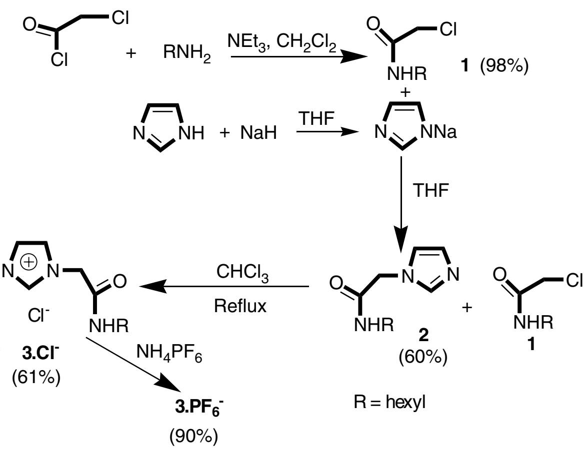


Chart 1.



Scheme 1. Synthesis of imidazolium guests.

the N*H* signal at ca. 8.4–8.5 ppm. The three ligands have similar NMR spectra as observed from the –NC*H*N– and –NC*H*C*H*N– signals at 9.08 and 7.65, 9.05 and 7.65 as well as at 9.03 and 7.64 ppm, for **3**·**Cl**$^-$, **3**·**Br**$^-$, and **3**·**PF**$_6^-$, respectively. However, the melting points of **3**·**Cl**$^-$, **3**·**Br**$^-$, and **3**·**PF**$_6^-$ were found to be distinguishable being 160, 132, and 139 °C, respectively. Compounds **4**·**Br**$^-$ and **5**·**Br**$^-$ were generated by coupling imidazole or benzoimidazole and excess hexylamine in the presence of excess K_2CO_3 in dried acetone.[14] Compounds **4**·**X** and **5**·**X**, where X = Cl$^-$ and PF$_6^-$, were obtained from anion exchanges using NH_4Cl and NH_4PF_6, respectively.[6]

Compounds **3**·**X**, **4**·**X**, and **5**·**X** are all ion-pairing guests, which possess positively charged imidazolium rings with the proton at the 2-position of the imidazolium ring able to hydrogen bond to anions. Only compound **3**·**X** incorporates an anion binding cleft due to the amide protons in addition to the ion pairing and the proton at the 2-position. This allows an anion to locate within its hydrogen bonding cleft in nonpolar solvents. All ligands and the guest molecules dissolve very well in $CDCl_3$, which is a noncompetitive solvent.

Upon addition of guest molecules **3**·**X**, **4**·**X**, and **5**·**X**, where X = Cl$^-$ and Br$^-$ and monitoring complexation processes by ^{1}H NMR spectroscopy, NMR spectra displayed significant shifts of signals of both **L** and guests. However, where X = PF$_6^-$, no change was observed in the NMR spectra of mixtures of **L** with **3**·**X**, **4**·**X**, and **5**·**X**. ^{1}H NMR spectra of **L**, **3**·**Br**$^-$ and a 1:1 mixture of the two compounds are illustrated in Figure 1. Proton labels are shown in Figure 2. Interestingly, all proton signals of the guest **3**·**Br**$^-$ (H_w, H_x, H_y, and H_z) shift upfield while those of the host **L** (aromatic and urea protons) shift downfield. Hydrogen bonding interactions between protons H_x and H_z with Br$^-$ was allocated to the urea protons (H_g and H_i) of **L** resulting in a decrease of hydrogen bonding interactions of protons H_x and H_z with the anion and upfield shifts of the signals. In contrast, the urea protons of **L** (H_g and H_i) display large downfield shifts because of the hydrogen bonding interactions with Br$^-$. Furthermore, the signal H_w of **3**·**X** displays an upfield shift upon addition of more guest species. It is probably due to the anisotropic deshielding effect of the aromatic ring belonging to **L**.[6] The effect of π–π stacking on the aryl protons of both the imidazole and benzene rings of **L** causes the upfield

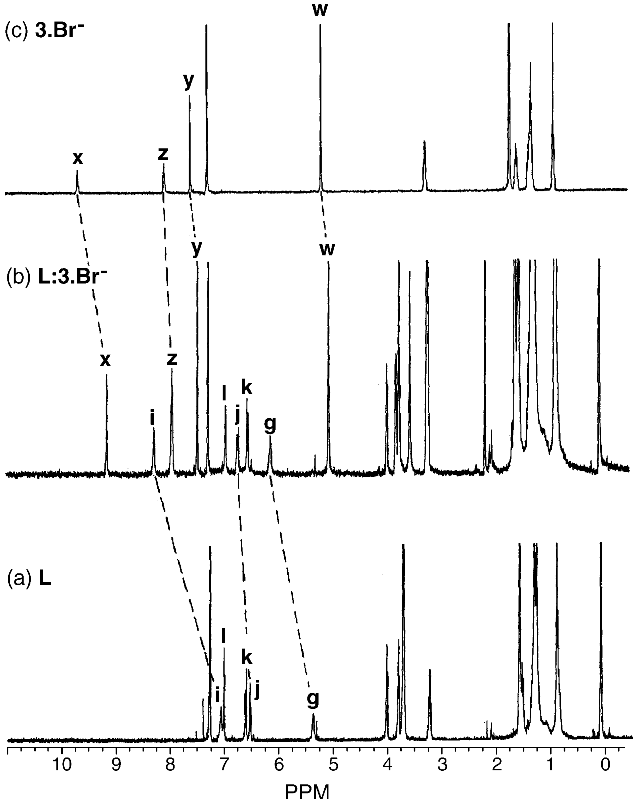
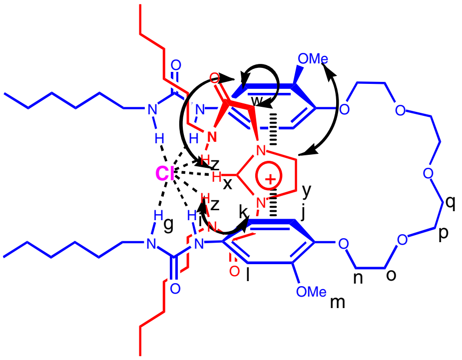


Figure 1. ^{1}H NMR spectra of (a) **L**, (b) a 1:1 mixture of **L** and **3·Br**$^-$, and (c) **3·Br**$^-$ in $CDCl_3$ at 400 MHz (298 K).



Δδ (ppm) of **3.Cl**$^-$; H_x: -1.07, H_y: -0.18 ppm, H_z: -0.49 ppm
Δδ (ppm) of **L**; H_i: +1.18 ppm, H_g: +0.68 ppm, H_j: +0.17 ppm,
H_k: +0.06 ppm, H_l: -0.14 ppm

Figure 2. The proposed structure of the complex between **L** and **3·Cl**$^-$, consistent with the cross relationship from ROSEY and the shifted signals of **L** and **3·Cl**$^-$.

shifts of protons H_y and H_w. The template effect is even more pronounced in the case of the Cl^- counter ion, which gives larger shifts of all proton signals.

In addition, interactions between the host and guests were supported by a ROSEY NMR spectrum of **L** and **3·Cl**$^-$ in $CDCl_3$. The cross relation peaks of H_y and OCH_3 protons, H_w and H_k, H_l and H_x as well as H_k and H_z signified weak interactions in the spectrum as shown in Figure 2. These interactions are indicative of the threading of the cations through the cavity of the podand.

In the case of **4·X** and **5·X**, interactions with **L** are similar to those of **3·X**. Considering ^{1}H NMR titration spectra of **L** and **4·Cl**$^-$, it was found that both NH protons of **L** shifted downfield corresponding to hydrogen bonding interactions with anions. Additionally, aromatic protons shifted significantly indicating the π–π stacking interactions between aromatic rings and the imidazolium ring belonging to **L** and **4·Cl**$^-$, respectively. In the case of the complex of **L** and **5·Cl**$^-$, the aromatic protons of the benzoimidazolium ring of **5·X** showed significant upfield shifts due to the anisotropic effect from the aromatic ring of **L**.

Association constants of complexes between **L** and **3·X**, **4·X** and **5·X** where X = Cl^-, Br^-, and $PF_6{}^-$ were measured by ^{1}H NMR titrations monitoring the NH urea protons of **L**. Titration curves of **L** with **3·X**, **4·X**, and **5·X** are depicted in Figure 3. A Jobs plot indicated a stoichiometry of 1:1 for the host and guest molecules. Association constants of the self-assembly between two molecules can be calculated by the EQNMR program.[15]

The association constants of complexation for **L** with guest molecules are shown in Table 1. Both Cl^- and Br^- counter-ions have strong hydrogen-bonding interactions with the host **L** and act as templates for the formation of interlocked molecules. Among the guests, **3·X**, **4·X**, and **5·X**, where X = Cl^-, show higher binding constants with **L** than those where X = Br^-. Formation of these interlocked molecules thus prefers a spherical template to an octahedral template.

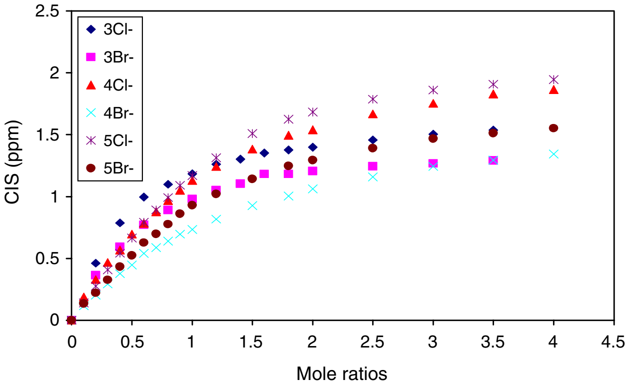


Figure 3. Titration curves of **L** and guest molecules in $CDCl_3$.

Table 1. The association constants (M^{-1}) in $CDCl_3$ at 298 K

	K_a (M^{-1})		
	Cl^-	Br^-	$PF_6{}^-$
L:**3·X**	3460.0	3157.0	[a]
L:**4·X**	892.4	545.0	[a]
L:**5·X**	1231.0	973.8	[a]

[a] No peak shifts were observed.

Additionally, the association constants of the complexes agree with the proposed structures corresponding to the highest K_a values of **L** with **3·X** because the anion encounters seven hydrogen bonding interactions from the host **L** and the imidazolium amide unit as well as the C–H—X interaction while the complexes of **L** and **4·X** and **5·X** were subjected to only five hydrogen bonding interactions.[16] Association constants of **L** and **5·X** are higher than those of **L** and **4·X** because of the enhancement of binding from π–π stacking interactions between the benzene rings of **L** and the benzoimidazolium ring of **5·X**.

In summary, self-assembly studies of the host **L** and guest molecules were carried out by ^{1}H NMR titrations in $CDCl_3$. The NH resonances of the urea unit of the ligand were monitored. Large downfield shifts attributed to hydrogen bonding interactions between NH protons of **L** and anionic species of guest molecules were observed. The results revealed that **L** selectively bound guest molecules in the following order, **3·X > 5·X > 4·X**. The binding ability also corresponded to the shape of the anion template ($Cl^- > Br^- \gg PF_6^-$), numbers of hydrogen bond donating sites and π–π stacking interactions. In addition, we have demonstrated that the anion recognition step has oriented the nonmacrocyclic ligand orthogonally to the cation to provide an interpenetrated geometry and produce interlocked architectures.

Acknowledgements

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10. A solution of chloroacetyl chloride (0.67 g, 5.9 mmol) in dichloromethane (30 mL) was added dropwise over 30 min into the mixed solution of hexylamine (1.50 g, 4.9 mmol) and freshly distilled triethylamine (0.5 g, 4.5 mmol) in dichloromethane (45 mL) at 0 °C. The mixture was kept stirring at 0 °C under N_2 for 2 h. The reaction mixture was allowed to warm to room temperature. The solution was then washed with aq 2 M HCl (4×50 mL). The organic layers were combined and dried with $MgSO_4$. The solvent was subsequently evaporated to give a white solid **1** (1.47 g, 98%). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 6.45 (s, br, –N*H*–, 1H), 3.97 (s, $ClCH_2CO$, 2H), 3.26–3.19 (q, *J* = 6.9 Hz, $–NHCH_2CH_2–$, 2H), 1.47 (m, $–NHCH_2CH_2CH_2–$, 2H), 1.23 (m, $–CH_2CH_2CH_2–$, 6H), 0.82 (m, $–CH_3$, 3H); ESI-TOF *m/z* 178.21 [M+H$^+$].
11. A solution of imidazole (0.5 g, 7.4 mmol) in THF (20 mL) was added dropwise into a solution of NaH (0.18 g, 7.4 mmol) in THF (20 mL) under N_2 at 0 °C. The reaction mixture was stirred until gas production stopped. A solution of *N*-hexylchloroacetamide **1** (0.79 g, 6.70 mmol) in THF (20 mL) was added into the solution of sodium imidazole and the mixture was stirred at room temperature under N_2 overnight. Precipitated NaCl was then filtered off. The solution was partitioned with CH_2Cl_2 and water. The organic phase was extracted with water several times and then dried with $MgSO_4$. The solvent was removed by a rotary evaporator to afford yellow solid **2** (0.47 g, 60%). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.43 (s, –NC*H*N–, 1H), 7.06 (s, –NCHC*H*NCH–, 1H), 6.88 (s, $–NCHCHNCH_2–$, 1H), 5.54 (s, br, –N*H*–, 1H), 4.57 (s, $–NCH_2CO–$, 2H) 3.18–3.11 (m, $–NHCH_2CH_2–$, 2H), 1.38–1.33 (m, $–NHCH_2CH_2CH_2–$, 2H), 1.21–1.13 (m, $–CH_2CH_2CH_2–$, 6H), 0.82–0.77 (m, $–CH_3$, 3H); ESI-TOF *m/z* 210.25 [M+H$^+$].
12. A solution of chloromethylhexyl carboxamide (**1**) (2.70 g, 15.1 mmol) in $CHCl_3$ (20 mL) was added dropwise into a solution of hexylcarboxamide methylimidazole (**2**) (0.79 g, 3.77 mmol) in $CHCl_3$ (20 mL) and stirred under N_2 atmosphere. The reaction mixture was heated at reflux under N_2 atmosphere for 3 days. A white solid precipitated during that time. The reaction was allowed to cool to room temperature. The white solid (**3·Cl**$^-$) was filtered and dried (2.30 g, 61%). ^{1}H NMR (300 MHz, DMSO-d_6, TMS):δ 9.08 (s, –NC*H*N–, 1H), 8.51 (t, *J* = 5.4 Hz, –N*H*–, 2H), 7.65 (s, –NC*H*C*H*N–, 2H), 5.00 (s, $–NCH_2CO–$, 4H), 3.08 (q, *J* = 6.6 Hz, $NHCH_2CH_2–$, 4H), 1.41 (m, $–NHCH_2CH_2CH_2–$, 4H), 1.25 (m, $–CH_2CH_2CH_2–$, 12H), 0.86 (m, $–CH_3$6H); ESI-TOF MS (*m/z*): 351.51 [M+H$^+$]. Mp: 160 °C.
13. Characterization for **3·Br**$^-$: ^{1}H NMR (300 MHz, DMSO-d_6, TMS): δ 9.05 (s, –NC*H*N–, 1H), 8.38 (t, *J* = 5.4 Hz, –N*H*–, 2H), 7.65 (s, –NC*H*C*H*N–, 2H), 4.90 (s, $–NCH_2CO–$, 4H), 3.11 (q, *J* = 6.3 Hz, $–NHCH_2CH_2–$, 4H), 1.42 (m, $–NHCH_2CH_2CH_2–$, 4H), 1.26 (m, $CH_2CH_2CH_2–$, 12H), 0.87 (m, $–CH_3$, 6H). ESI-TOF MS (*m/z*): 351.51 [M+H$^+$]. Melting point: 132.0 °C. Characterization for **3·PF**$_6^-$: ^{1}H NMR (300 MHz, DMSO-d_6, TMS): δ 9.03 (s, –NC*H*N–, 1H), 8.36 (t, *J* = 5.4 Hz, –N*H*–, 2H), 7.64 (s, –NC*H*C*H*N–, 2H), 4.97 (s, $–NCH_2CO–$, 4H), 3.10 (q, *J* = 6.6 Hz, $–NHCH_2CH_2–$, 4H), 1.39 (m, $–NHCH_2CH_2CH_2–$, 4H), 1.25 (m, $–CH_2CH_2CH_2–$,12H), 0.86 (m, $–CH_3$, 6H). ESI-TOF MS (*m/z*): 351.51 [M+H$^+$]. Mp: 139.3 °C.
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