Self-assembly of [2]pseudorotaxanes based on pillar[5]arene and bis(imidazolium) cations†

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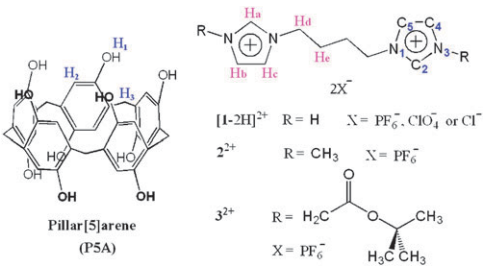
A simple bis(imidazolium) dication, 1,4-bis[*N*-(*N*′-hydroimidazolium)]butane, can act as a new template for formation of [2]pseudorotaxane with pillar[5]arene, in which the dethreading/rethreading process can be controlled by addition of base and acid. The effect on the association constant of both the solvent and counterion is also described.

Rotaxanes have been attracting considerable attention,[1] not only for their topological importance but also due to their potential applications in preparation of molecular devices and machines.[2] Pseudorotaxanes[3] are the supramolecular precursors of rotaxanes, and also viewed as prototypes of simple molecular machines. The ongoing search for new macrocyclic hosts (the 'wheels') and linear guest molecules (the 'axles') that template pseudorotaxane construction could increase the options available for the development of rotaxanes, catenanes, 'muscles',[4] switches,[2] and machines.[2] Pillar[5]arene (**P5A**), firstly synthesized by Ogoshi's group,[5] was a symmetrical calixarene analogue made up of five hydroquinone units linked by methylene (–CH_2–) bridges. Later, the family of pillar[*n*]arene hosts has been expanded to a larger-cavity homologue, pillar[6]arene, by Cao, Meier and co-workers.[6] More recently, Huang *et. al*[7] synthesized copillar[5]arene (**P5A** containing different repeating units). Being different from the conventional calixarene's "basket" structure, pillararene forms the symmetrical pillar architecture. Pillararenes' structural characteristics and π-rich cavities make the hosts suitable to develop pseudorotaxanes with linear cationic molecules. Searching new axles for the new supramolecular building blocks is thus very interesting. Our previous work[8] has reported the formation of a series of 1 : 1 [2]pseudorotaxanes and 2 : 1 host–guest complexes between **P5A** with dicationic 1,4-bis(pyridinium)butanes and alkyl-substituted paraquat derivatives. An essential contribution to the formation of these complexes is the cation–π-electron interactions.[8,9] We reasoned that by the substitution of the pyridinium on the 1,4-bis(pyridinium)butane dications for a similar sized imidazolium, to get 1,4-bis[*N*-(*N*′-hydroimidazolium)]butane ([**1**-2H]$^{2+}$, see Scheme 1), we could construct a new templating axle that would bind with the **P5A** host through cation–π interactions, and simultaneously, the resulting pseudorotaxane could be reversibly switched off (and back on) by deprotonation (and protonation) of the N_3 atoms on the axle (Scheme 1).



Scheme 1 Structure of pillar[5]arene (**P5A**) and bis(imidazolium) guests.

Herein, we report the self-assembly of [2]pseudorotaxanes based on **P5A** and 1,4-bis(imidazolium)butane cations ([**1**-2H]$^{2+}$–**3**$^{2+}$) that function as templating motifs, and the use of acid/base reaction to switch between complexed/uncomplexed states. Moreover, the solvent and counteranion effects have also been investigated to look at how they affect the association strength during the course of host–guest complexation.

Fig. 1 shows the ^{1}H NMR spectra of [**1**-2H]·2PF_6 in acetone-d_6 recorded in the absence and in the presence of about 1 equivalent (eq.) amount of the **P5A** host. The peaks for the methylene protons of [**1**-2H]·2PF_6 exhibit substantial upfield shifts and broadening effects compared to the free axle ($\Delta\delta$ = −0.96 and −1.25 ppm for H_d and H_e, respectively) as a consequence of inclusion-induced shielding effects.[10] At the same time, the signal corresponding to the α-protons of the imidazolium N_1 atom (H_a and H_c) exhibits a pronounced upfield shift, while no obvious changes were observed for the β-protons (H_b). In the control experiments, under identical conditions no NMR changes of [**1**-2H]·2PF_6 occurred upon

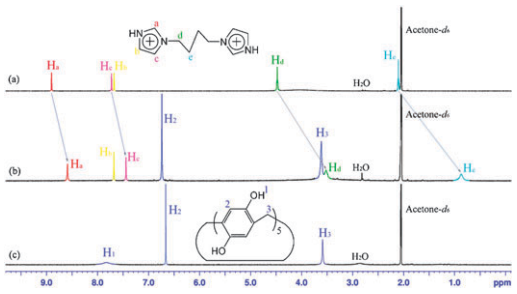


Fig. 1 ^{1}H NMR spectra (500 MHz) of (a) [**1**-2H]·2PF_6, (b) **P5A** + [**1**-2H]·2PF_6, and (c) **P5A** in acetone-d_6 at 5.0–5.3 mM.

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addition of hydroquinone, *i.e.*, the monomeric unit of the **P5A** host. Hence, the **P5A**-induced upfield shifts and broadening effects on the imidazolium H_a and H_c protons and methylene (H_d and H_e) protons reveal that the **P5A** wheel is fully threaded by the axle and the main binding site for the host is the methylene linker. Meanwhile, part of the imidazolium ring (N_1^+, C_2 and C_5) is also included in the host cavity. From 2D NOESY analysis (Fig. S18, ESI†), NOE correlations were observed between H_a, H_c, H_d and H_e of the axle and aromatic protons (H_2) of **P5A**. While no correlations between H_2 and H_b were observed. These results also confirm the threading binding mode. This inclusion complex can be considered to have a 1 : 1 [2]pseudorotaxane structure.

For comparison purpose, we also selected for our study two substituted bis(imidazolium) cations where the H proton in $[\mathbf{1}\text{-}2H]^{2+}$ was replaced by $-CH_3$ and $-CH_2COO$*t*Bu ($\mathbf{2}^{2+}$ and $\mathbf{3}^{2+}$) (Scheme 1, for synthesis, see ESI†). Although **2**·2PF_6 has good solubility in acetone-d_6, precipitation occurred immediately when mixed with **P5A**, which itself signals an interaction between the host and guest. Therefore, we chose 3 : 2 (v : v) acetone-d_6 and DMSO-d_6 as solvent for the ^{1}H NMR experiments (Fig. S13, ESI†). Upon addition of the **P5A** host, the NMR response of **2**·2PF_6 in this mixed solvent was fast and the signal changes were similar to that of [**1**-2H]·2PF_6 (Fig. 1b and 3b). In contrast, no obvious signal changes were observed for **3**·2PF_6 in acetone-d_6. Since the bulky *t*Bu unit was unable to thread the cavity of **P5A**, the **P5A**–**3**·2PF_6 inclusion complex did not form.

Further evidence of 1 : 1 host–guest complex was obtained by the ESI mass experiments. For example, in the ESI mass spectrum of an eq. mixture of **2**·2PF_6 and **P5A** (Fig. S23, ESI†), only two intense peaks for a 1 : 1 complex were observed, one for $[\mathbf{2}\text{–}\mathbf{P5A}]^{2+}$ (m/z 415.8), and one for $[\mathbf{2}\cdot PF_6\text{–}\mathbf{P5A}]^+$ (m/z 975.4). On the other hand, job plots based on proton NMR data also demonstrated that the complexes between [**1**-2H]·2PF_6 and **2**·2PF_6 with **P5A** were of 1 : 1 stoichiometry (Fig. S24, ESI†). Combined with the ^{1}H NMR experiments, we can unambiguously conclude the formation of [2]pseudorotaxane-type complex, as shown in Fig. 2.

We have also explored the effect on the association constants of the solvent and counterion. It can be seen from Table 1 that the solvent effects are very pronounced on the formation of **P5A**–[**1**-2H]·2PF_6 and **P5A**–**2**·2PF_6 inclusion complexes since the K_a values significantly increased when the solvent polarity was reduced. For example, the **P5A**–[**1**-2H]·2PF_6 K_a values in 3 : 7 acetone-d_6 : DMSO-d_6 (1.2×10^2 M^{-1}), 3 : 2 acetone-d_6 : DMSO-d_6 (2.7×10^2 M^{-1}), pure acetone-d_6 (4.6×10^2 M^{-1}) and 1 : 1 acetone-d_6 : $CDCl_3$ (3.1×10^3 M^{-1}) are enhanced by factors of 2.2, 4.9, 8.4 and 56.4 compared with that of pure DMSO-d_6. It is reasonable that cation–π-electron interactions

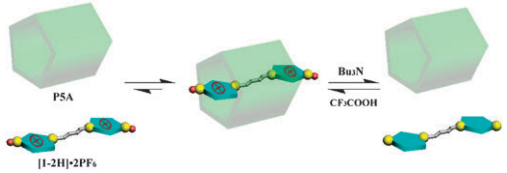

Fig. 2 Formation of [2]pseudorotaxanes between [**1**-2H]·2PF_6 and **P5A** and the base–acid controlled dethreading/rethreading movements.

Table 1 Association constants[15] (K_a/M^{-1}) for 1 : 1 complexation of **P5A** and [**1**-2H]·2PF_6 and **2**·2PF_6 in different solvents at 25 °C

Solvent (v : v)	[**1**-2H]·2PF_6	**2**·2PF_6
DMSO	$(5.5 \pm 0.2) \times 10$	$(1.4 \pm 0.2) \times 10^2$
3 : 7 $(CD_3)_2CO$: DMSO	$(1.2 \pm 0.4) \times 10^2$	$(3.3 \pm 0.4) \times 10^2$
3 : 2 $(CD_3)_2CO$: DMSO	$(2.7 \pm 0.3) \times 10^2$	$(1.0 \pm 0.2) \times 10^3$
$(CD_3)_2CO$	$(4.6 \pm 0.6) \times 10^2$	—[a]
1 : 1 $(CD_3)_2CO$: $CDCl_3$	$(3.1 \pm 0.5) \times 10^3$	—[a]

[a] Could not be determined due to the poor solubility of the **P5A**–**2**·2PF_6 complex in these solvents.

should be the important driving forces[8,9,11] during the course of complexation of **P5A** with these positively charged guests and they are dramatically affected by the solvent polarity. In order to assess counterion effects for the new synthetic receptor **P5A**, the $[\mathbf{1}\text{-}2H]^{2+}$ guest was synthesized with a noncoordinating counterion, [**1**-2H]·2ClO_4, and a coordinating counterion, [**1**-2H]·2Cl, and the dependence of the association constants of $[\mathbf{1}\text{-}2H]^{2+}$ with **P5A** on the anion type in acetone-d_6 and 3 : 2 acetone-d_6 : DMSO-d_6 was determined (Table 2). It's well known that ion-pairing effects hamper the complexation of charged species by neutral receptors.[12] In a lower polarity acetone-d_6 solvent, when the counterion of $[\mathbf{1}\text{-}2H]^{2+}$ changed from PF_6^- to a little strongly coordinating anion, ClO_4^-, the K_a value decreases from 4.6×10^2 to 3.6×10^2 M^{-1}. The counterion effects of pseudorotaxane formation between **P5A** and $[\mathbf{1}\text{-}2H]^{2+}$ in acetone-d_6 were similar to those of crown ether complexes in lower polarity solvent systems.[13] On the other hand, no counterion effects were found in 3 : 2 acetone-d_6 : DMSO-d_6, since the K_a values between **P5A** and $[\mathbf{1}\text{-}2H]^{2+}$ with different counterions (PF_6^-, ClO_4^- and Cl^-) were almost the same (Table 2). This is reasonable because the counterion effects were overruled by the relatively high polarity of DMSO and the threads would be expected to be nearly completely ionized in the 3 : 2 acetone-d_6 : DMSO-d_6 solvent. That is to say, **P5A** can form pseudorotaxane complexes with bis(imidazolium) threads containing strongly coordinating anions (such as Cl^-) in high polarity solvents (such as 3 : 2 acetone-d_6 : DMSO-d_6), which is very rare in the calix[*n*]arene and large crown ether series.[14]

With the aim of investigating the ability of the new [2]pseudorotaxane to perform dethreading/rethreading movement by pH control, we chose 3 : 2 (v : v) acetone-d_6 : DMSO-d_6 as solvent due to the lower solubility of the deprotonated [**1**-2H]·2PF_6 (**1**) in pure acetone-d_6. [**1**-2H]·2PF_6 and **P5A** form a [2]pseudorotaxane with $K_a = 2.7 \times 10^2$ M^{-1} in the mixed solvent, while the neutral compound **1** is unable to associate with **P5A**. ^{1}H NMR spectra of a solution of **P5A** and [**1**-2H]·2PF_6 following the addition of ~2.2 eq. of *n*-Bu_3N,

Table 2 Association constants[15] (K_a/M^{-1}) for 1 : 1 complexation of **P5A** and $[\mathbf{1}\text{-}2H]^{2+}$ with different counterions at 25 °C

X^-	Acetone-d_6	3 : 2 (v : v) acetone-d_6 : DMSO-d_6
PF_6^-	$(4.6 \pm 0.6) \times 10^2$	$(2.7 \pm 0.3) \times 10^2$
ClO_4^-	$(3.6 \pm 0.3) \times 10^2$	$(2.5 \pm 0.4) \times 10^2$
Cl^-	—[a]	$(2.6 \pm 0.4) \times 10^2$

[a] Could not be determined due to the poor solubility of the salt.

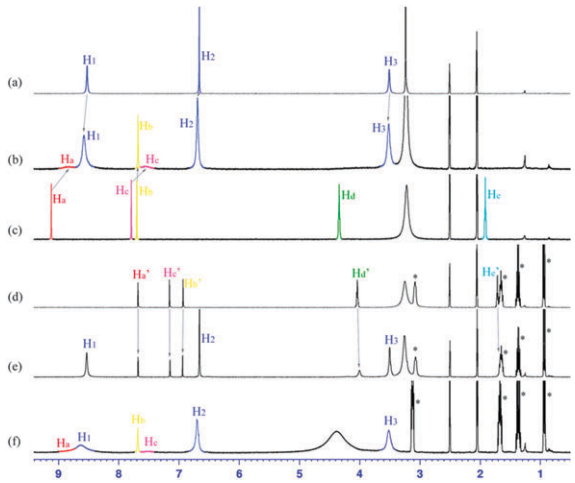

Fig. 3 ^{1}H NMR spectra (500 MHz) of (a) **P5A**, (b) **P5A** + [**1**-2H]·2PF_6, (c) [**1**-2H]·2PF_6, (d) [**1**-2H]·2PF_6 + *n*-Bu_3N, (e) **P5A** + [**1**-2H]·2PF_6 + *n*-Bu_3N, (f) **P5A** + [**1**-2H]·2PF_6 + *n*-Bu_3N + CF_3COOH, in 3 : 2 acetone-d_6 : DMSO-d_6. The concentrations of **P5A** and [**1**-2H]·2PF_6 were 5.9–6.4 mM; the concentrations of *n*-Bu_3N and CF_3COOH were 12.6–13.8 mM.

together with only [**1**-2H]·2PF_6 in the absence and the presence of *n*-Bu_3N, are shown in Fig. 3. In this acetone-d_6 and DMSO-d_6 mixed solvent, the changes of proton resonance bands of [**1**-2H]·2PF_6 observed upon **P5A** addition are similar to those when using acetone-d_6 as solvent (Fig. 3a–c), indicating the formation of [2]pseudorotaxane. Among the protons in $[\mathbf{1}\text{-}2H]^{2+}$, methylenes H_d and H_e exhibit the most remarkable complexation-induced broadening effects because their signals can't be observed in the ^{1}H NMR spectrum (Fig. 3c). After the addition of ~2.2 eq. of *n*-Bu_3N, the resonances associated with **P5A**–[**1**-2H]·2PF_6 completely disappears, and only the resonances of **P5A** and the deprotonated $[\mathbf{1}\text{-}2H]^{2+}$ are observed (Fig. 3d and e). This is an unambiguous confirmation of the dethreading process. The rethreading process can be reversed quantitatively by the addition of ~2.2 eq. of CF_3COOH (Fig. 3f), which is attributed to the protonation of **1** restoring the original equilibrium between $[\mathbf{1}\text{-}2H]^{2+}$ and **P5A**. DOSY results further confirm the pH-controllable dethreading/rethreading process definitely (Fig. S19, ESI†). The diffusion coefficient of $[\mathbf{1}\text{-}2H]^{2+}$ (D_{guest}) decreases from 6.61×10^{-10} to 5.81×10^{-10} m^2 s^{-1} upon addition of **P5A**, indicating the host–guest complexation. The D_{guest} value increases to 9.77×10^{-10} m^2 s^{-1} (resembling the value of free guest) upon addition of *n*-Bu_3N, showing that guest **1** has been released from the cavity of **P5A**. Upon addition of CF_3COOH again, the D_{guest} value (5.84×10^{-10} m^2 s^{-1}) restores the original value, indicating the rethreading process. To the best of our knowledge, the present pH-controlled assembly–disassembly system is the first pillararene-based molecular switch (Fig. 2).

In summary, we have presented that a simple bis(imidazolium) dication, 1,4-bis[*N*-(*N*′-hydroimidazolium)]butane, is able to thread through the cavity of pillar[5]arene to construct stable [2]pseudorotaxane, and the dethreading/rethreading process can be reversibly controlled by acid–base stimulus. We have explored the effect of both the solvent and counterion on the binding interaction, indicating that **P5A** can form a [2]pseudorotaxane-type complex with bis(imidazolium) thread containing strongly coordinating anions (such as Cl^-) in high polarity solvents (such as 3 : 2 acetone-d_6 : DMSO-d_6).

The availability of the simple components, the controllable assembly and disassembly, the ability to easily tune the association strength, and the generality of the solvent and the type of counterion imply potential applications of this motif in the fabrication of interlocked structures and molecular devices.

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15 The K_a values in acetone-d_6 or 1 : 1 acetone-d_6 : $CDCl_3$ should be taken as approximate because they do not take into account the extent of ion pair dissociation on the observed binding interaction with **P5A**. For a detailed discussion, see ref. 12*c*.

