

RESEARCH ARTICLE

View Article Online
View Journal | View IssueCite this: *Org. Chem. Front.*, 2017, 4, 115

Dual-pH responsive host–guest complexation between a water-soluble pillar[9]arene and a 2,7-diazapyrenium salt†

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Received 26th September 2016.

Accepted 25th October 2016

DOI: 10.1039/c6qo00579a

rsc.li/frontiers-organic

The host–guest complexation between a water-soluble pillar[9]arene and a 2,7-diazapyrenium salt not only can be controlled by the sequential addition of an acid and a base (HCl and NaOH, respectively) but also can be switched through the sequential addition of a base and an acid (hexylamine and TFA, respectively).

In supramolecular chemistry, stimuli-responsive molecular recognition motifs have played an important role due to their topological importance and extensive application in the construction of various interesting supramolecular systems, such as molecular switches and machines,¹ supramolecular polymers,² and other functional materials.³ Up to now, light, metal ions, pH, redox, enzyme and other external stimuli have been widely employed in the construction of responsive host–guest systems on the basis of macrocyclic compounds (such as crown ethers,⁴ cyclodextrins,⁵ calixarenes⁶ and cucurbiturils⁷). As a new type of macrocyclic hosts, pillar[*n*]arenes⁸ have gained increasing attention since their first report in 2008.^{8a} Owing to their symmetrical pillar architecture and accessible functionalization, pillar[*n*]arenes have seen superior host–guest properties towards various guests and been further explored in the construction of numerous supramolecular systems, such as daisy chains,⁹ supramolecular polymers,¹⁰ drug-release systems,¹¹ transmembrane channels¹² and other advanced functional materials.¹³ By adopting different derivatization methods, anionic,¹⁴ cationic¹⁵ and neutral¹⁶ water-soluble pillararenes can be obtained according to previous reports. Among these water-soluble pillararenes, anionic ones decorated with carboxylate groups have an inherent advantage: they are responsive to acid/base reagent pairs (such as HCl and NaOH). Based on these pH-responsive pillararenes, plenty of molecular switches and corresponding supramolecular systems have been reported.^{11,17} However, these switches or systems can only be operated through a simple two-directional way: an acid turns them off/on and a base turns them on/off.

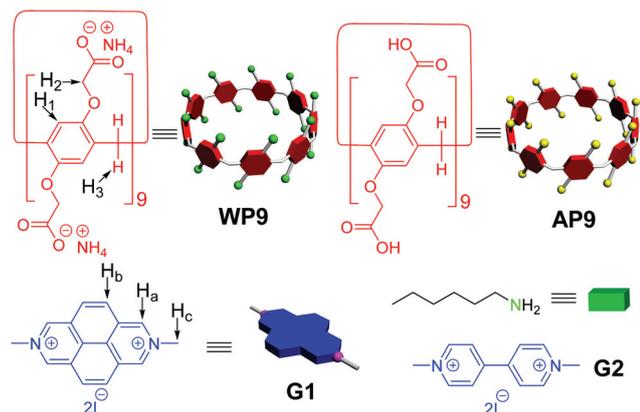
Due to the increasing need for logic gates that can provide different inputs and various functions, we now have a great urge in preparing a dual-pH responsive host–guest recognition motif which can be switched on and off not only through the action of a specific acid/base pair but also through the addition of another base/acid pair.

With the pH-responsive hosts in hand, we speculate that if one guest which also responds to pH can be found or designed, a dual-pH controlled host–guest complex may be obtained. Luckily enough, such guests were already found! 2,7-Diazapyrenium (DAP) dications, which unite the merits of π -electron-deficient character and extended π -surface, have been proved to exhibit excellent supramolecular associations with a number of π -electron-rich host partners and been applied successfully to establish various host–guest complexes and corresponding advanced mechanically interlocked architectures. It is worth noting that DAP dications can form stable adducts with aliphatic amines and be recovered to original states upon the addition of equivalent trifluoroacetic acid (TFA).¹⁸ That is to say, DAP dications are pH-responsive and they can be treated as desired counterparts to construct dual-pH responsive host–guest complexes with anionic water-soluble pillar[*n*]arenes. Recently, Xue *et al.* reported some studies about DAP-based host–guest complexes with pillar[10]arenes in water or organic solution.¹⁹ However, dual-pH responsive complexation between pillararenes and DAP dications has never been reported, presumably because of the difficulty in preparing suitable and complementary host/guest pairs which can respond to specific acid/base pairs and base/acid pairs, respectively. Herein, we describe a unique dual-action host–guest complex whose uncomplexed and complexed states can be controlled through the employment of not only an acid/base pair but also a base/acid pair in water. In this work, dimethyldiazapyrenium (DMDAP) dicationic salt **G1** served as the guest and anionic water-soluble pillar[9]arene

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† Electronic supplementary information (ESI) available: Determination of the association constant, UV-vis data, mass spectrometric data and other materials. See DOI: 10.1039/c6qo00579a



Scheme 1 Chemical structures of compounds used here.

WP9 acted as the macrocyclic host. The larger cavity^{17a} of **WP9** compared with those of pillar[5,6]arenes should be more suitable for this guest to thread into (Scheme 1).

WP9^{17a} and **G1**^{18d} were synthesized according to previously reported procedures. Firstly, the host-guest complexation between **WP9** and **G1** was investigated by ¹H NMR spectroscopy. Fig. 1 shows the ¹H NMR spectra of **G1** in D₂O recorded in the absence and presence of approximately 1.0 equiv. of the host. Fast exchange on the NMR time scale was observed for this complex. After complexation with **WP9**, the peaks corresponding to the protons on complexed **G1** became broad and shifted upfield significantly compared with those on free **G1** (Fig. 1a). The reason was that the protons on **G1** located within the cavity of **WP9**, thereby generating a shielding effect. On the other hand, the signals related to **WP9** also exhibited slight chemical shift changes. Then, a 2D NOESY NMR experiment was conducted as it's a powerful tool for exploring the conformations of host-guest complexes. As

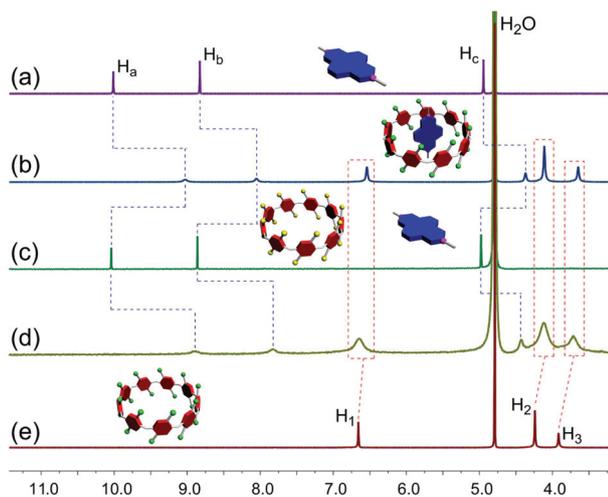


Fig. 1 Partial ¹H NMR spectra (500 MHz, D₂O, 293 K): (a) **G1** (2.00 mM); (b) **WP9** (2.00 mM) and **G1** (2.00 mM); (c) after addition of DCl to b; (d) after addition of NaOD to c; (e) **WP9** (2.00 mM).

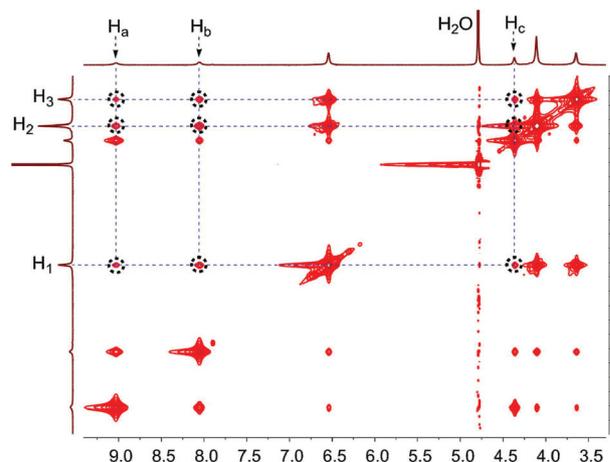


Fig. 2 2D NOESY NMR (500 MHz, D₂O, 293 K) spectrum of a solution of **WP9** (2.00 mM) and **G1** (2.00 mM).

shown in Fig. 2, nuclear overhauser effect (NOE) correlation signals were clearly observed between protons H_{1,2,3} on the pillar[9]arene unit and protons H_{a,b,c} on the guest unit, indicating that guest **G1** penetrated into the cavity of **WP9**, in good agreement with the results from ¹H NMR study.

UV-vis absorption spectroscopy gives further evidence for the existence of host-guest complexation between **WP9** and **G1**. When **WP9** was mixed with equimolar **G1** in water, the colour of the resulting solution turned to yellow (Fig. S6a, ESI[†]) and the UV-vis spectrum of the solution exhibited a clear charge-transfer band above 450 nm (Fig. S5, ESI[†]), indicating the charge-transfer interaction existed between electron-rich **WP9** and electron-deficient **G1**.

Fluorescence titration experiments (Fig. S2–S4, ESI[†]) were carried out to estimate the association constant (K_a) of the complexation between **WP9** and **G1** at room temperature in aqueous solution. Fluorescence intensity of **G1** decreased significantly upon gradual addition of **WP9** (Fig. S2, ESI[†]). A mole ratio plot (Fig. S3, ESI[†]) showed the 1 : 1 stoichiometry of the complex between **WP9** and **G1**, which was in good agreement with the result obtained from ESI mass spectrometry (Fig. S7, ESI[†]). An ion peak at m/z 1188.9 for $[\text{WP9} \supset \text{G1} - 2\text{I} - 18\text{NH}_3]^{2+}$ was observed to reveal the formation of the complex **WP9** \supset **G1**. By means of non-linear curve-fitting, the K_a value for **WP9** \supset **G1** was estimated to be $(9.42 \pm 1.33) \times 10^8 \text{ M}^{-1}$ (Fig. S4, ESI[†]), which is much higher than the corresponding K_a value for the complex between **WP9** and the paraquat guest **G2** ($2.27 \times 10^6 \text{ M}^{-1}$) reported previously by us.^{17a} We assumed that **WP9** had only one cavity when it was dissolved in water because of the repulsive electrostatic force resulting from the eighteen anionic carboxylate groups on both rims of the host molecule. So, we speculated that the architecture of DMDAP guest **G1** was more suitable than that of **G2** to locate in the cavity of **WP9** due to the size selectivity. The reason for the remarkably high binding affinity of this host-guest complex may be ascribed to the cooperative interactions of electrostatic

interaction, hydrophobic interaction and π - π interaction between **WP9** and **G1**.

Additionally, the assembly and disassembly of the inclusion complex between **WP9** and **G1** can be reversibly controlled by sequential addition of HCl and NaOH aqueous solutions. Proton NMR spectroscopy was conducted to confirm this reversible process (Fig. 1). When DCl (20.0 equiv.) was added to the equimolar solution of **WP9** and **G1**, the signals for the protons on **WP9** disappeared (Fig. 1c) due to the precipitation of the resulted carboxylic acid pillar[9]arene (**AP9**) from the solution (Fig. S6b, ESI†). Meanwhile, the peaks of H_{a-c} on **G1** migrated back to their free original values, suggesting that the guest dethreaded from the cavity of **AP9** (Fig. 1c). On the other hand, after the addition of NaOD (20.0 equiv.) to the mixed solution, the system returned to the original complexed state and significant upfield shifts corresponding to protons on **G1** were observed again (Fig. 1d), indicating the reformation of the inclusion complex between **WP9** and **G1**. Thus, the sequential addition of HCl and NaOH to the solution of **WP9** and **G1** can be employed to switch the two components from unthreaded to rethreaded states, *i.e.*, this host-guest complex can behave as an acid/base-controlled molecular switch.

Furthermore, we explored the reverse strategy: base/acid-controlled mode. The addition of hexylamine to an equimolar solution of **WP9** and **G1** caused a colour change from yellow to dark green because the more stable adduct between **G1** and the aliphatic amines formed^{18a} while the complex **WP9** \supset **G1** dissociated. Subsequently, it can be recovered again when enough TFA was used to neutralize hexylamine accompanied with the reappearance of the yellow colour associated with the host-guest complex (Fig. S6c, ESI†). Proton NMR studies were performed to testify this reversible process (Fig. 3). When hexylamine (40.0 equiv.) was added to the mixture solution of **WP9** and **G1**, the peaks corresponding to the protons on **G1**

disappeared substantially while the signals of **WP9** returned to the original positions as the free host (Fig. 3c). On the other hand, when TFA (40.0 equiv.) was added to the mixed solution of **WP9**, **G1**, and hexylamine, an ¹H NMR spectrum similar to that of the original solution of **WP9** and **G1** was obtained (Fig. 3d),²⁰ indicating the regeneration of the complex between the host and the guest in this solution. Therefore, the host-guest complex **WP9** \supset **G1** can be controlled reversibly from its complexed state to its uncomplexed state upon the sequential addition of a base and an acid, and this complex can also act as a base/acid-controllable molecular switch.

In summary, we reported a novel dual-pH responsive molecular recognition motif between water-soluble pillar[9]arene **WP9** and DMDAP **G1**. It was demonstrated that **WP9** and **G1** formed a stable 1:1 inclusion complex in water with an extraordinarily high association constant of $9.42 \times 10^8 \text{ M}^{-1}$. Furthermore, this host-guest complex can behave as a molecular switch that not only can be operated between its complexed and decomplexed states through the sequential addition of an acid and a base (HCl and NaOH, respectively) but also can be controlled upon the continual addition of a base and an acid (hexylamine and TFA, respectively). Future work will be focused on the fabrication of advanced controlled-release systems and other smart materials on the basis of this novel dual-pH responsive recognition motif.

This work was supported by the Fundamental Research Funds for the Central Universities.

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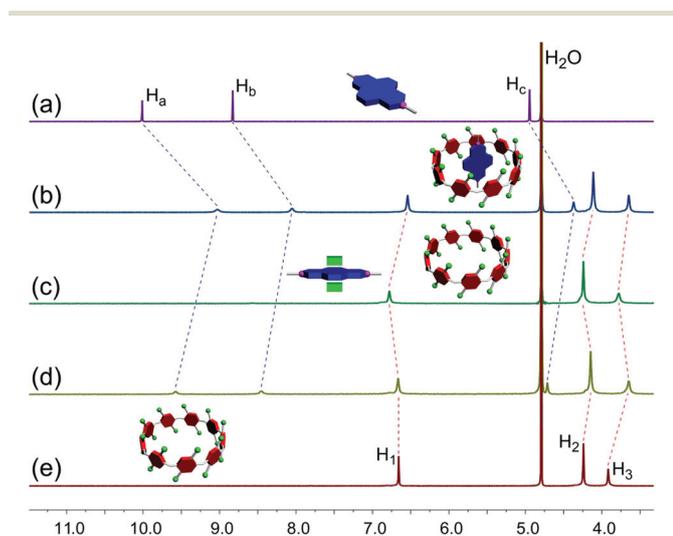


Fig. 3 Partial ¹H NMR spectra (500 MHz, D₂O, 293 K): (a) **G1** (2.00 mM); (b) **WP9** (2.00 mM) and **G1** (2.00 mM); (c) after addition of hexylamine to b; (d) after addition of TFA to c; (e) **WP9** (2.00 mM).

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- 20 Chemical shifts corresponding to H_a, H_b, and H_c in the original solution of **WP9** and **G1** were not fully recovered (spectra b and d in Fig. 3). Two possible reasons are: (1) the solution was diluted because of the additions of trifluoroacetic acid and hexylamine; (2) the ionic strength of the solution increased because of the production of C₆H₁₃NH₃⁺TFA⁻ salt. Both reasons could change the chemical shifts and/or decrease the complexation percentage.