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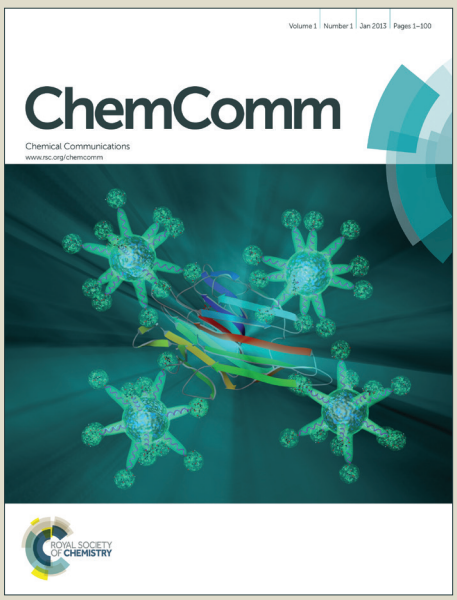

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A novel shell-like supramolecular assembly of 4,4'-bipyridyl derivatives and twisted cucurbit[14]uril molecule

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This work showed that the 4,4'-bipyridyl group and alkyl chain of 4,4'-bipyridyl derivatives are completely located in shell-like part cavity of the twisted cucurbit[14]uril molecule and formed novel shell-like 1:1 inclusion complexes. The complexation benefits from ion–dipole interactions for its enthalpy-driven.

Cucurbit[n]urils (Q[*n*]s) are a family of molecular container hosts generally bearing a rigid hydrophobic cavity and two identical carbonyl-fringed portals. The ability of Q[*n*]s to selectively encapsulate various guest molecules and to interact with reviewed by various works.[1-7] Q[*n*]s could be used in water remediation, and as components in artificial enzymes, molecular switches, supramolecular polymers, and so forth. Q[7], for example, effectively encapsulates and stabilizes a wide range of small molecules, such as fluorescent dyes,[8] It also controls aggregate formation by guest molecules,[9] and is thus applicable to light-harvesting systems.[10] Q[8] and Q[10] have large cavities, both can host two organic guests simultaneously. They can therefore function as molecular machines that respond to external stimuli.[11-15] Isaacs and his co-workers reported *nor-seco*-cucurbit[10]uril (*ns*-Q[10]) which they prepared by removal of two CH_2 bridges from Q[10] and by bond reorganization. The two cavities of *ns*-Q[10] are similar to those of Q[8], and the molecule forms ternary 1:2 complexes with various guests.[16,17]

Recently, our laboratory expanded the Q[*n*] family. We synthesized the largest, *t*Q[14], which contains 14 normal glycoluril units linked by 28 methylene bridges, the only one report on cucurbit[14]uril in the form of its coordination complex has been reported so far.[18] This molecule is formed from a chain containing 14 units of the –glycoluril-$(CH_2)_2$– moieties and is twisted by 180°. Consequently, it has two cavities and adopts a folded, figure of eight conformation (Fig. 1). Preliminary experiments revealed that the two cavities in *t*Q[14] are larger than those of Q[5] and Q[6], but are smaller than those of Q[7] and Q[8]. In this work, we investigated the host-guest interaction between *t*Q[14] and 4,4'-bipyridyl derivatives (PC*n*s) in aqueous solution by ^{1}H NMR spectroscopy, UV-vis spectrometry and isothermal titration calorimetry (ITC). The overall up-field shift of proton resonances of PC*n*s in the ^{1}H NMR spectra suggest that both the 4,4'-bipyridyl moieties and alkyl chains of PC*n*s were located in the portal and cavity of the *t*Q[14] molecule. UV-vis spectrometry and ITC experiments showed that the interaction between *t*Q[14] and PC*n*s result in 1:1 inclusion complexes. Additionally, complexation of PC*n* guests with *t*Q[14] is mainly enthalpy-driven, and thus could benefit from ion–dipole interactions. On the basis of the aforementioned results, we propose a complex model in which the alkyl chains of PC*n*s are situated in the two cavities and the 4,4'-bipyridyl moiety is in between the two portals of the *t*Q[14] molecule.

Fig.1 Structure of *t*Q[14] and PC*n*.

First, we describe the binding of the N,N'-dimethyl-4,4'-bipyridyl chloride salt (PC*1*) to the *t*Q[14] host in aqueous solution. Fig. 2 shows titration ^{1}H NMR spectra obtained by using a fixed equivalent of *t*Q[14] and various equivalents of PC*1*. As only one set of proton signals of the PC*1* guest show a gradual downfield shift with increasing number of equivalents of PC*1* (Fig. 2a to Fig. 2h), the guest is entirely located in a shielding environment. The signals are averaged signals of the free and bound guest molecules, which have a high exchange ratio for binding and unbinding on the NMR time

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scale. Notably, the pyridyl protons Ha and Hb of bound PC*1* swap resonance positions with increasing equivalents of PC*1* compared with the Ha and Hb of free PC*1*, the protons signals of Ha and Hb overlap as the *t*Q[14]/guest molecule ratio reached 1:0.8. Resonance positions of Ha and Hb shifted from 8.48 and 9.02 ppm to 8.24 and 8.11 ppm, respectively as the composition changed from 1: 0.5 *t*Q[14]/ PC*1* ratio to neat PC*1*. Similarly, the resonance position of methyl protons (Hc) shifted from 4.48 to 3.92 ppm during this change.

The titration ^{1}H NMR spectra also reveal that interaction of *t*Q[14] with PC*2* is a phenomenon that is similar to the interaction of *t*Q[14] with PC*1* (Fig. S1, ESI†). This result suggests that both the bipyridyl moieties and alkyl chains of PC*1* and PC*2* experience shielding effects by the host or that entire molecules of PC*1* and PC*2* are in the shielding area. Averaged signals of the free and bound guests reveal a higher exchange ratio for binding and unbinding on the NMR time scale.

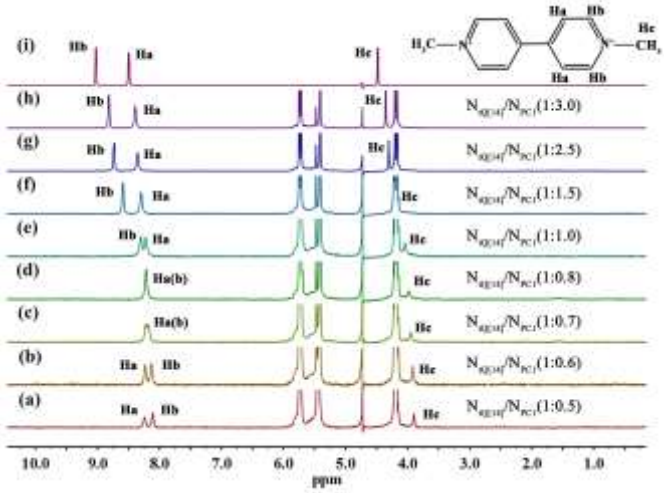

Fig. 2 Titration ^{1}H NMR spectra (400 MHz , D_2O) for *t*Q[14] in the presence of various equivalents of PC*1*(a-h)and for neat PC*1* (i).

Unlike those resulting from the interaction with PC*1* and PC*2*, ^{1}H NMR spectra for interaction of *t*Q[14] with PC*n* guest molecules(n = 4, 6, 8), show two sets of proton signals, one of which belongs to bound PC*n*s and the other to free PC*n*s. For example, Fig. 3 shows the ^{1}H NMR spectra for the titration *t*Q[14] with PC*6*. Only one set of proton signals for PC*6* are observable when the *t*Q[14]/PC*6* ratio reached 1:0.8 (Fig. 3a), whereas two sets signals for bound and unbound protons of PC*6* are present in the ^{1}H NMR spectrum (in Fig. 3b and Fig. 3c). The resonance positions of Ha and Hb of the pyridyl moiety of PC*6* shifted to 7.44 and 8.70 ppm, relative to those of the Ha and Hb protons of free PC*6* (8.51 and 9.09 ppm, respectively; Fig. 3d). Meanwhile, the proton resonances of the alkyl moiety of PC*6* broadened and were slightly shifted upfield.

The titration ^{1}H NMR spectra also reveals that the interaction between *t*Q[14] and PC*4* and PC*8* was similar to that between *t*Q[14] and PC*6* (Fig. S2 and Fig.S3, ESI†). Both bipyridyl moieties and alkyl chains of PC*4* and PC*8* experienced shielding effects of the *t*Q[14] host. Although the averaged signals of guests suggest different exchange ratios for binding and unbinding on the NMR time scale with increasing substitution of the alkyl chain, entire guests molecules appeared to be localized with in the shielding area of the *t*Q[14] host.

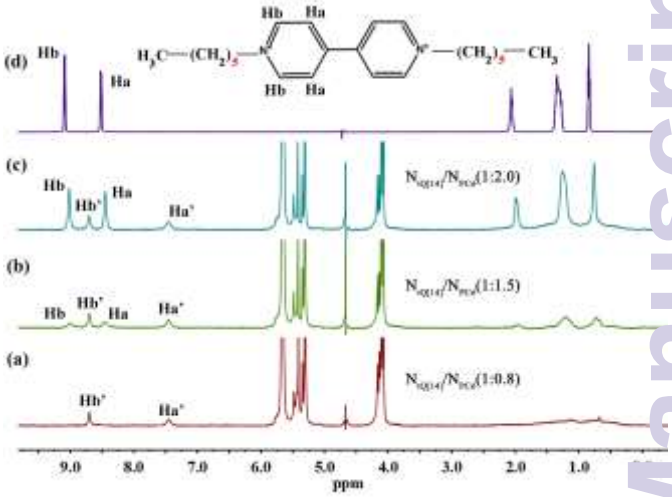

Fig. 3 Titration ^{1}H NMR spectra (400 MHz, D_2O) for *t*Q[14] in the presence of various equivalents of PC*6* (a-c) and for neat PC*6* (d).

To understand better the binding of PC*n*s to *t*Q[14], we also investigated by UV–vis spectrophotometry and ITC the interactions between *t*Q[14] and PC*n*s. Fig. 4 shows the exclusive formation of a 1:1 complex which was confirmed by UV–visible spectroscopy. With the gradual increase in *t*Q[14] concentration in the PC*1* solution, the absorption band initially weakened and shifted from 257 to 272 nm, resulting in well-defined isosbestic points at 230 and 279 nm. These points also suggest that PC*1* and *t*Q[14] formed a 1:1 complex exclusively. The formation constant for the 1:1 PC*1*–*t*Q[14] complex, as determined by photometric titration is (5.90 ± 0.02) × 10^6 L·mol^{-1}.[19] The PC*2*-PC*4* complex exhibited absorption changes similar to those of the PC*1*–*t*Q[14] complex upon addition of *t*Q[14] (Fig. S4 and Table S1, ESI†). The strong binding of *t*Q[14] to PC*1* is presumably due to the favorable ion–dipole interaction between the positively charged of the guest and the portal oxygen atoms of *t*Q[14] in addition to the hydrophobic effects.

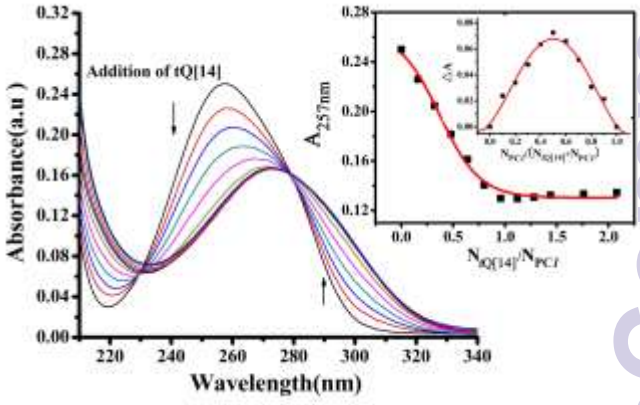

Fig. 4 Absorption spectra of aqueous solutions of PC*1* (10 μM) with various *t*Q[14] concentrations and the corresponding plot of A_{257nm} *vs* $N_{tQ[14]}/N_{PC1}$ (inset).

After examining a plausible binding model and establishing the stoichiometry of the complex formed between *t*Q[14] and PC*n*s, we proceeded to determine the binding constant (*K*) and relevant

thermodynamic parameters for PC*n*s binding to *t*Q[14] by ITC (Fig. S5, ESI†). Results are shown in Table 1. PC*n*s showed high binding affinity (~10^6 M^{-1}) to *t*Q[14]. Formation of the five inclusion complexes form *t*Q[14] and PC*n*s was almost exclusively enthalpy-driven(|⊿H|>|T⊿S|). The high enthalpy gain for the formation of these complexes may be attributed to the strong ion–dipole interactions between the ammonium and carbonyl groups of the host portal.

Table 1 Binding constants (*K*) and relevant thermodynamic parameters for *t*Q[14]-PC*n* complex formation obtained from isothermal titration calorimetry experiments at 298.15 K

Guest	K (M^{-1})	⍰⊿H(kJ·mol^{-1})	T⊿S (kJ·mol^{-1})
PC*1*	(6.12±0.50)×10^6	-42.3±0.24	-3.54
PC*2*	(9.79±0.53)×10^6	-51.6±0.36	-11.6
PC*4*	(5.85±0.48)×10^6	-53.5±0.29	-14.8
PC*6*	(1.22±0.08)×10^6	-43.2±0.20	-8.51
PC*8*	(4.63±0.43)×10^6	-53.4±0.34	-21.1

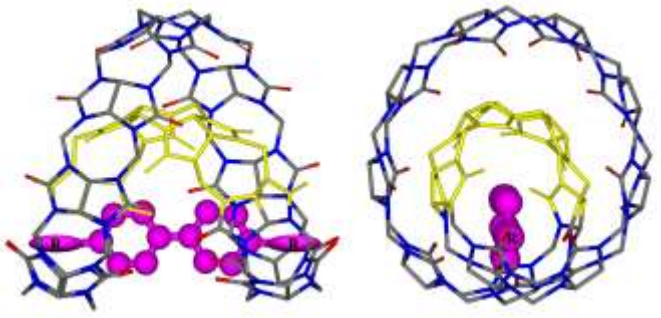

Fig. 5 Possible model of the host-guest interaction in the *t*Q[14]-PC*n* system

Initially, we hypothesized that the alkyl chains of a PC*n* guest threads to a 'shell' of two neighboring *t*Q[14] molecules to form one-dimensional supramolecular polymers. Unexpectedly, the ^{1}H NMR data suggest that the *t*Q[14] host shields both the bipyridyl moiety and alkyl chains of the PC*n* guest, the UV–vis spectra and ITC data shows that 1:1 complex inform between PC*n*s and *t*Q[14]. The *t*Q[14] molecule is very flexible and has a shell-like feature when it is in aqueous solution. Thus, it is reasonable to presume that each *t*Q[14] molecule encapsulates a PC*n* guest molecule. The two alkyl chains at the ends of the bipyridyl group can move back and forth between the two *t*Q[14] cavities, and the 4,4'-bipyridyl moiety of PC*n*s inserts into the shell-like crevice of *t*Q[14]. The long alkyl chains are known to take unusual conformations, such as a folded conformation, U-shaped conformation and helical conformation when bound to the cucurbit[*n*]urils.[20] So the long aliphatic chains (PC*4*-PC*8*) could be bent in the "shells" of the *t*Q[14] host. Fig. 4 shows front and top views of the models for the *t*Q[14]-PC*n* complex.

In summary, we investigated the binding of PC*n*s to the novel, twisted Q[*n*] molecule, *t*Q[14]. The resulting supramolecular assembly had a shell-like structure. This is the first time that a shell-like supramolecular assembly of Q[*n*]s is prepared from *t*Q[14]. We discovered that PC*n* guests form stable 1:1 inclusion complexes with the *t*Q[14] host, as the complexation was mainly enthalpy-driven, it could be enhanced by ion-dipole interactions. Our results provide first insight into the design and construction of novel molecular machines and switches based on twist space capsules.

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