# Exclusion complexes of the HCl salts of benzidine and bis(4-aminophenyl) methane with two methyl-substituted cucurbiturils†

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The interaction between two partially methyl-substituted cucurbiturils, a *sym*-tetramethyl-substituted cucurbit[6]uril (TMeQ[6]) and a *meta*-hexamethyl-substituted cucurbituril (*m*-HMeQ[6]), with the hydrochloride salt of benzidine (g1·HCl) and the analogue bis(4-aminophenyl) methane (g2·HCl) was investigated by single crystal X-ray diffraction determination, $^1$H NMR spectroscopy, electronic absorption spectroscopy and fluorescence spectroscopy. Single crystal X-ray diffraction determination showed the two guest compounds were excluded at the portals of the partial methyl-substituted cucurbiturils in the solid state. The $^1$H NMR spectroscopic analysis in aqueous solution supported the crystallographic results in which an excluding or portal interaction occurs between the host and guest. Aqueous absorption spectrophotometric and fluorescence spectroscopic analysis defined the stability of the host–guest exclusion complex at pH 5.6 with a host : guest ratio of 1 : 1, which forms quantitatively as $\sim 10^5$ L mol$^{-1}$ for the TMeQ[6]–g1 system. The host : guest ratio of 2 : 1 forms quantitatively as $\sim 10^{10}$ L$^2$ mol$^{-2}$ for the *m*-HMeQ[6]–g2 system. The experimental results are in good agreement with HF and B3LYP computational approaches with a moderate-sized basis set.

## Introduction

Since the structure of the cucurbituril Q[6] was first determined and reported by Mock and Freeman in 1981,[1] a number of homologues and analogues of Q[6] have been reported in the last decade.[2] The hydrophobic cavity and the polar carbonyl group periphery surrounding the portals are characteristic features for all cucurbiturils. These functional groups can interact with various organic or inorganic species through a combination of different non-covalent interactions, such as dipole–ion interaction, hydrogen bonding, hydrophobic cavity interactions and so on, to form a series of self-assembled supramolecular entities with novel structures and properties. This has led to a dramatic development in Q[*n*] chemistry.[3] Based on the formation of inclusion complexes of cucurbit[*n*]urils, Kim and co-workers demonstrated elegant networks constructed of ''molecular necklace rings'' in which a number of Q[6] beads are threaded onto a large ring consisting of organic species and metal ions through coordination bonding.[4] Macromolecular encapsulation into Q[*n*] could improve drug stability, control the release of a potential drug, and increase drug activation or solubility in drug delivery applications.[5] A remarkable feature of Q[*n*]s is the ability to catalyze 1,3-dipolar cycloadditions in a regio-selective fashion.[6] More recently, Q[8] was used as a template for [2 + 2] and [4 + 4] photodimerizations in water.[7] The potential of cucurbit[*n*]urils for tuning the properties of fluorescent materials may lead to new applications, which include increased fluorescence intensity, brightness, enhanced photostability, protection towards fluorescence quenching, and the extension of fluorescence lifetimes of fluorescent materials.[3i,8] Most of the potential applications of cucurbit[*n*]urils are established on the basis of the inclusion of certain organic guests in cucurbit[*n*]urils. On the other hand, Fedin and co-workers demonstrated a series of supramolecular chains constructed of Q[6] and metal ions as well as their complexes and clusters formed through dipole–ion interaction and hydrogen bonding.[9] Recently, we first demonstrated the formation of some molecular bracelets in which alkyl-substituted Q[5]s are linked directly by coordinated metal ions.[10] The metal ions or their complexes are located at the portals of the cucubit[*n*]urils thereby forming exclusion complexes with the host Q[*n*]s. Only a few works have focused on exclusion complexes of Q[*n*]s and organic compounds such as mono- or di-ammonium ions.[11]

Benzidine (4,4′-diaminobiphenyl) and benzidine derivatives, which are potentially carcinogenic aromatic amines, have been widely used in the past as intermediates in the manufacture of dyes and pigments for cloth, paper, and leather. Benzidine and its derivatives are discharged by the dye industry and are often released in effluent waste water leading to their presence in lakes, rivers and soils.[12] Buschmann and Schollmeyer investigated the decolorization, or selective removal, of solutions containing different dyes with water-insoluble Q[6] precipitated on a carrier material or dissolved in formic acid in

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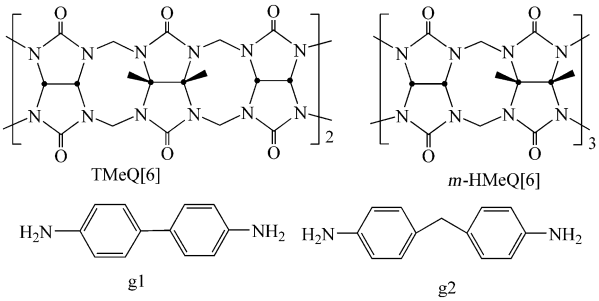


**Fig. 1** Structures of the host and the guests used in this work.

the 1990s, but few structural details of the Q[6]–dyes were reported due to the poor solubility of the normal Q[6].[13]

In the present work, we used two water soluble partially methyl-substituted cucurbiturils, a *sym*-tetramethyl-substituted cucurbit[6]uril (TMeQ[6])[2i] and a *meta*-hexamethyl-substituted cucurbituril (*m*-HMeQ[6])[2h] (shorted as SQ[6]s), to investigate the interaction details of the hydrochloride salts of benzidine (g1·HCl) and its analogue, bis(4-aminophenyl) methane (g2·HCl) by using various methods, including X-ray crystal structure analysis, $^1$H NMR spectroscopy, electronic absorption spectroscopy and fluorescence spectroscopy (Fig. 1). The experimental results revealed that both TMeQ[6]–g1 and *m*-HMeQ[6]–g2 systems formed host–guest exclusion complexes. No host–guest inclusion complexes were observed despite the potential ability of the cavity to encapsulate the aromatic ring of the guest.[11]

## Experimental

### Materials

TMeQ[6] and *m*-HMeQ[6] were prepared and purified according to methods from the literature[2h] and our laboratory.[2i] The guests benzidine (g1) and bis(4-aminophenyl) methane (g2) were obtained from Shanghai Chongming Chemical Co., Ltd. and were of analytical grade and were used without further purification. The corresponding HCl salts of these guests were prepared by dissolving them in concentrated HCl followed by removal of excess HCl by using a rotary evaporator. The pure TMeQ[6] and *m*-HMeQ[6] were used in all processes in this work.

### X-Ray crystallography

**Preparation of 2(TMeQ[6]–g1)·Cl$_4$·25H$_2$O (1).** A single crystal of the TMeQ[6] adduct with g1 was obtained by dissolving TMeQ[6] (0.20 g, 0.19 mmol) in a solution of g1·HCl (0.051 g, 0.20 mmol) in water (5 mL). The final solution was mixed thoroughly and allowed to stand at room temperature. Crystals suitable for X-ray diffraction were formed after several days. Anal. Calcd. for $C_{104}H_{168}N_{52}O_{50}Cl_4$: C, 40.44; H, 5.48; N, 23.58. Found: C, 40.42; H, 5.36; N, 23.75%.

**Preparation of *m*-HMeQ[6]–g2·Cl$_2$·33H2O (2).** A single crystal of the *m*-HMeQ[6] adduct with g2 was obtained by dissolving *m*-HMeQ[6] (0.20 g, 0.19 mmol) in a solution of g2·HCl (0.054 g, 0.20 mmol) in water (5 mL). The final solution was mixed thoroughly and allowed to stand at room temperature. Crystals suitable for X-ray diffraction formed after several days. Anal. Calcd. for $C_{55}H_{64}N_{26}O_{12}Cl_2$: C, 33.93; H, 6.73; N, 18.71. Found: C, 33.55; H, 6.58; N, 18.88%.

The solvent molecules in the crystals of Q[*n*]s and their host–guest complexes are generally easily lost, which results in crystal deterioration. Although single crystals of the compounds **1** and **2** were of poor quality, they produced suitable X-ray reflection and allowed for orientation matrix determination in both cases. Experimental data were collected for the compounds **1** and **2** on a Bruker APEX2 CCD diffractometer [graphite monochromatized MoK$\alpha$-radiation, $\omega$ and $\phi$ scan mode, 10 s frame$^{-1}$].

Structures of the compounds **1** and **2** were solved and refined with anisotropic thermal parameters used for all non-hydrogen atoms. Hydrogen atoms of the host and guest were placed in calculated positions and further refined using the riding model.†

**Crystal data for the compound 1.** 2(TMeQ[6]–g1)·Cl$_4$·25H$_2$O, $M$ = 3086.29, monoclinic, $a$ = 23.9121(19) Å, $b$ = 17.6841(14) Å, $c$ = 16.8216(13) Å, $\beta$ = 99.475(2)°, $V$ = 7016.2(10) Å$^3$, $T$ = 223.0(2) K, space group $P2_1/c$ (no. 14), $Z$ = 2, $\lambda$(Mo-K$\alpha$) = 0.71073 Å, $\mu$(Mo-K$\alpha$) = 0.166 mm$^{-1}$, 12 318 reflections measured, 6528 unique ($R_{int}$ = 0.0639) which were used in all calculations. The final $R_1$ and w$R_2$ were 0.1170 and 0.3501 for $I > 2\sigma(I)$, 0.1602 and 0.3773 for all data.

**Crystal data for the compound 2.** *m*-HMeQ[6]–g2·Cl$_2$·33H$_2$O, $M$ = 1944.23, triclinic, $a$ = 16.897(9) Å, $b$ = 18.037(9) Å, $c$ = 18.475(10) Å, $\alpha$ = 68.835(8)°, $\beta$ = 69.689(7)°, $\gamma$ = 73.900(8)°, $V$ = 4849(4) Å$^3$, $T$ = 223.0(2) K, space group $P\bar{1}$ (no. 2), $Z$ = 2, $\lambda$(Mo-K$\alpha$) = 0.71073 Å, $\mu$(Mo-K$\alpha$) = 0.121 mm$^{-1}$, 15 535 reflections measured, 5499 unique ($R_{int}$ = 0.0833) which were used in all calculations. The final $R_1$ and w$R_2$ were 0.0966 and 0.2334 for $I > 2\sigma(I)$, 0.1706 and 0.2653 for all data.

All the refinements were performed using SHELXTL-Plus software.

**$^1$H NMR titrations.** The titration experiments were performed in D$_2$O solution at 25 °C. The concentration of the host was fixed about $\sim 1 \times 10^{-2}$ mol L$^{-1}$, and the guest concentration was increased, starting from $5.0 \times 10^{-3}$ mol L$^{-1}$. The highest guest/host concentration ratios investigated were ~7.0.

**Absorption and fluorescence studies.** UV-visible (UV-vis) absorption spectra of the host–guest complexes were recorded on an Agilent 8453 spectrophotometer at room temperature. Fluorescence spectra of the host–guest complexes were recorded on a Varian RF-540 fluorescence spectrophotometer. Aqueous solutions of HCl salts of the guests were prepared with a concentration of $1 \times 10^{-3}$ mol L$^{-1}$. Aqueous solutions of the hosts were prepared with a concentration of $2 \times 10^{-3}$ mol L$^{-1}$. These stock solutions were combined to give solutions with a guest : SQ[6] ratio of 0, 0.2 : 1, 0.4 : 1, 1 : 1, 1.5 : 1, 2 : 1... for both absorption spectra and fluorescence spectra determination. A model SA 720

(Aolilong) pH meter was used for accurate adjustment of the pH of the samples with HCl and NaOH.

### Computational methods

All calculations were processed on an Intel Pentium 3.0G PC with the Gaussian 03W (Revision C.02) software package.[14] The initial geometries of all structures were constructed with the aid of the Hyperchem package, release 7.52[15] and based on the corresponding crystal structures. Becke's three-parameter hybrid function with the correlation function of Lee, Yang, and Parr (B3LYP)[16] was used for energy calculations with a STO-3G basis set.[17]

## Results and discussion

### Crystal structures of the exclusion complexes TMeQ[6]–g1·HCl and *m*-HMeQ[6]–g2·HCl

The Q[*n*] hosts exhibit remarkably tight and selective inclusion binding of organic species, particularly organic ammonium ions in water.[18] During the last three decades, the inclusion binding characteristics of the Q[*n*] hosts were extensively studied in catalyzing special cycloadditions,[6,7] creating novel molecular shuttles or switches,[19] and constructing elegant supramolecular entities.[4] Little attention, however, has focused on the exclusion binding characteristics of the Q[*n*] hosts toward organic species and consequently the resultant novel supramolecular entities. Generally, the Q[6]s have a strong tendency to include five or six-membered aromatic rings, such as pyridyl, phenyl, and so on.[7b,20] Herein, we introduce two supramolecular entities constructed of two water soluble hosts, TMeQ[6] and *m*-HMeQ[6] with the guests g1 and g2, respectively. Although the guests contain both aromatic rings and protonated amines, which look the ideal moieties to be included by the host SQ[6]s, the resultant products were unexpectedly the exclusion complexes in which portal binding was observed.

The crystals obtained from an aqueous solution of TMeQ[6] and the hydrochloride salt of g1 had a stoichiometry of $2(TMeQ[6]–g1)\cdot Cl_4\cdot 25\cdot H_2O$ (**1**). In the crystal structure of the compound **1**, each host TMeQ[6] molecule was sandwiched by two guest dications. Each guest molecule was sandwiched by two host TMeQ[6] molecules through both of ion–dipole and hydrogen-bonding interactions. This resulted in the formation of a supramolecular chain consisting of alternating g1 dications and TMeQ[6] molecules (Fig. 2a). A close inspection of the structure reveals that the distances of the two terminal amine nitrogens, N25 and N26, of a guest to the two neighboring portals of the two neighboring TMeQ[6] molecules are different (Fig. 2b). The distance of N25 to the plane (O7, O8, O9, O10, O11, O12) is 1.730 Å, whereas the distance of N26 to the plane (O1, O2, O3, O4, O5, O6) is 0.866 Å. This means that the sandwiched guest g1 is not centrosymmetric, and the two phenyl rings in the guest are twisted away from each other by 26.03°. Each sandwiched TMeQ[6] molecule is centrosymmetric, and the same two end amine nitrogens N25 or N26 are excluded at both the portals of the TMeQ[6] molecule (Fig. 2a). Besides the ion–dipole interaction between the protonated amine nitrogens N25 or

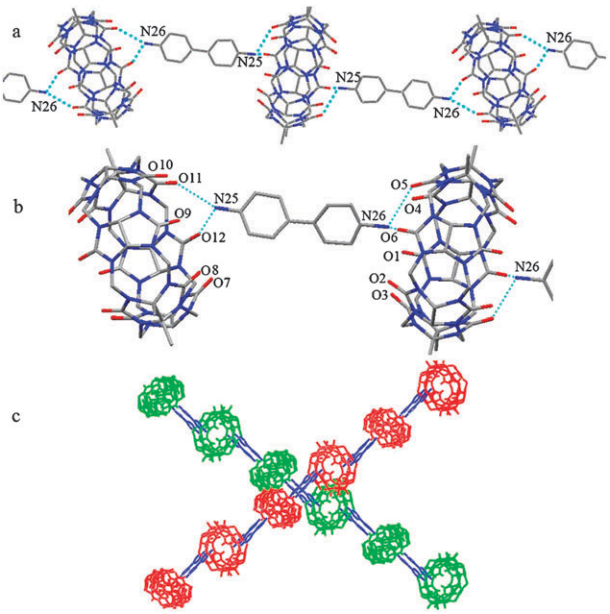


**Fig. 2** Crystal structure of (a) a 1D supramolecular chain constructed of alternating TMeQ[6] and g1, (b) the interaction between the neighboring TMeQ[6] and g1, (c) the crossed supramolecular chains in the compound **1**.

N26 of the guests and the portal carbonyl oxygens of the hosts (with an average distance of 4.036 Å for N25, and 3.602 Å for N26), hydrogen bonding between N25–H···O11 (3.003 Å), N25–H···O12 (2.770 Å), N26–H···O5 (2.835 Å), and N26–H···O6 (2.553 Å) is an additional force in the formation of the 1D supramolecular chain. Fig. 2c shows that the 1D supramolecular chains cross each other in the crystal structure of the compound **1**.

In contrast, the crystal structure obtained from *m*-HMeQ[6] and the hydrochloride salt of g2 also presents supramolecular chains consisting of alternating g2 dications and *m*-HMeQ[6] molecules through both ion–dipole and hydrogen bonding interactions. Other ion–dipole and hydrogen bonding interactions link two 1D supramolecular chains in pairs (Fig. 3a). Unlike the case in **1**, each sandwiched *m*-HMeQ[6] molecule is not centrosymmetric, two end amine nitrogens N25 and N26 belonging to the two neighboring guest g2 are excluded at the two portals of the *m*-HMeQ[6] molecule or an excluded guest g2 and a *m*-HMeQ[6] are a repeated unit in the 1D supramolecular chain (Fig. 3a). A close inspection of the 1D supramolecular chain reveals that a g2 guest is excluded at the portal of a host *m*-HMeQ[6], and sandwiched by two *m*-HMeQ[6] molecules. The distance of N25 to the plane (O1, O2, O3, O4, O5, O6) is 0.230 Å, whereas the distance of N26 to the plane (O7, O8, O9, O10, O11, O12) is 1.961 Å. The formation of a 1D supramolecular chain is attributed to a combination of the ion–dipole interaction between the protonated amine nitrogens N25 or N26 of guests with the portal carbonyl oxygens of the hosts and the hydrogen bonding between N25–H···O2 (2.960 Å), N25–H···O3 (3.029 Å), N25–H···O4 (2.894 Å), N26–H···O10 (2.816 Å), and N26–H···O11 (2.955 Å). The formation of the 1D supramolecular chain pair is attributed to a combination of spare ion–dipole and hydrogen bonding interactions between the

 

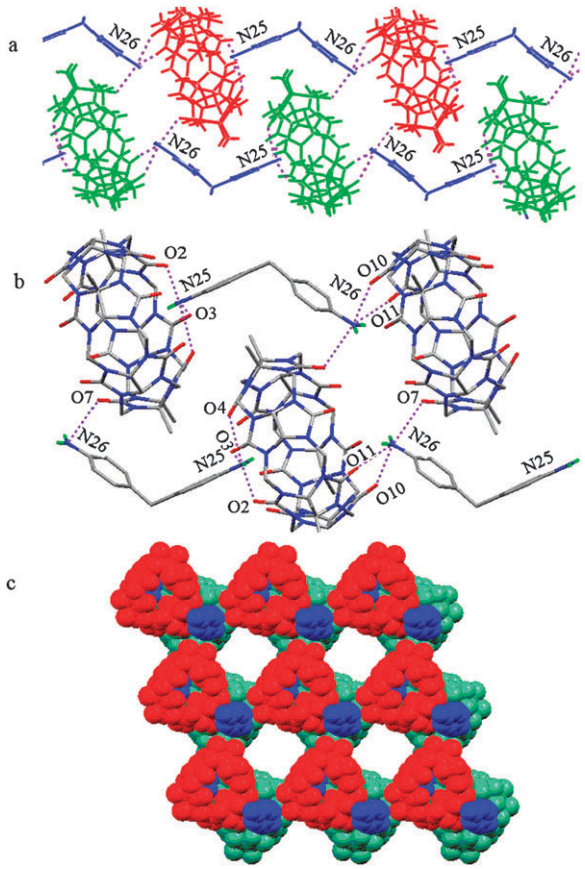


**Fig. 3** Crystal structure of (a) a 1D supramolecular chain pair constructed of alternating *m*-HMeQ[6] and g2, (b) the interaction between the neighboring *m*-HMeQ[6] and g2, (c) the arrangement of the supramolecular chain pairs in the compound **2**.

protonated amine nitrogens in a chain pair with the portal carbonyl oxygens of *m*-HMeQ[6] in a chain pair, such as the interaction between the atoms N26 and O7 (2.936 Å) (Fig. 3b). Fig. 3c shows that the supramolecular chain pairs in **2** are arranged in such a way as to produce a structure with linear, tetragonal channels extending along the *b* axis. The supramolecular chain pairs are surrounded by four neighboring chains. The mean diameter of the channels is about 10 Å, and the channels are filled with water molecules that form a complicated hydrogen bonding network. No organic molecules are found in the channels.

### $^1$H NMR spectra analysis of the interaction between the SQ[*n*]s with g·HCl

Above, we demonstrated the two exclusion complexes of two partially methyl-substituted SQ[6]s with two guests, containing both phenyl groups and protonated amines, in the solid state where the guests did not move into the cavity of the host SQ[6]s. Fig. 4 and Fig. 5 show the $^1$H NMR titration spectra of the HCl salts of the guest recorded in the absence, and in the presence of various equivalents, of the host SQ[6]s in aqueous solution. One can see that the spectra are unexpectedly simple without obvious chemical shifts of the proton resonances for either the guest or the host at the different host/guest ratios for the TMeQ[6]–g1 system. For

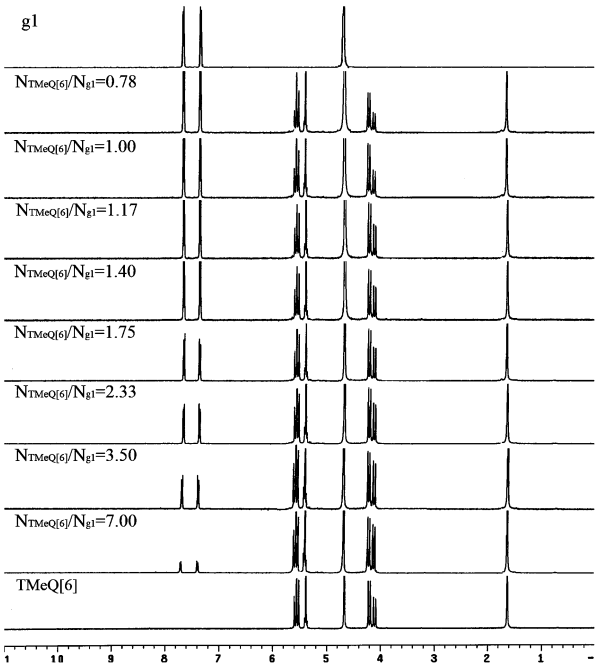


**Fig. 4** Variation in the $^1$H NMR spectra of TMeQ[6]–g1·HCl system with increasing concentration of TMeQ[6].

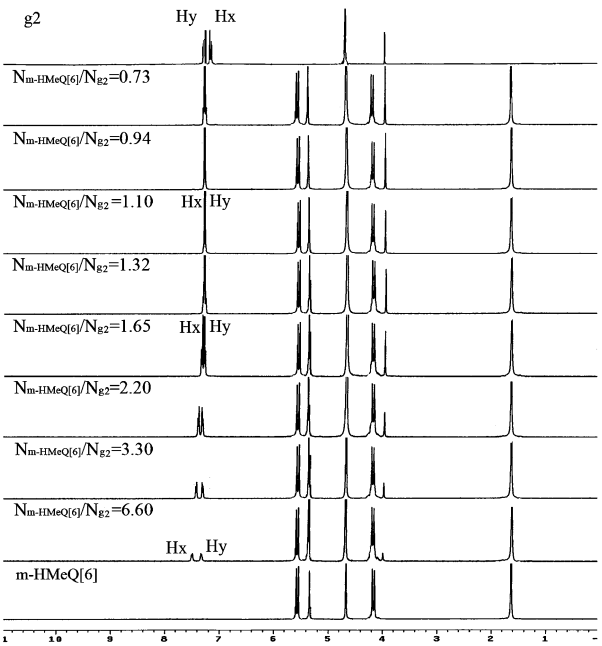


**Fig. 5** Variation in the $^1$H NMR spectra of *m*-HMeQ[6]–g2·HCl system with increasing concentration of *m*-HMeQ[6].

the *m*-HMeQ[6]–g2 system, resonances of the protons on the aromatic ring experience different chemical environment, and experience different deshielding extents by the carbonyl portal of *m*-HMeQ[6]. The resonance of the proton Hx experiences a downfield shift of 0.24 ppm, while the resonance of the proton Hy experiences a downfield shift of only 0.05 ppm when the ratio of $N_{m\text{-}HMeQ[6]}/N_{g2}$ is up to 6.6. Therefore, one can see that the two separated resonances of the protons Hx and Hy overlap together and then separate again with an increase in

the ratio of $N_{m\text{-HMeQ[6]}}/N_{g2}$, but the positions of Hx and Hy are swapped. All the above information suggests that the guest is not included by the host in solution and an exclusion interaction could be occurring between the host and the guest. However, the detailed interaction between the host and the guest is still unclear in solution.

### Spectrophotometric analysis on the interaction between SQ[6]s and g·HCl

To further quantify the interaction between the methyl substituted SQ[6]s and g1–2·2HCl in solution, a ratio-dependent study was pursued by monitoring electronic absorption and fluorescence spectra at pH 5.6. Usually, the two hosts SQ[6]s show no absorbance at $\lambda > 210$ nm, and the free HCl salt of the two guest shows a maximum absorption at $\lambda_{max}$ 281 nm for g1·HCl and 242 nm for g2·HCl, respectively. Fig. 6(a) and (c) show the variation in the UV spectra obtained with aqueous solutions containing a fixed concentration of g1·HCl or g2·HCl (32 mM) and variable concentrations of SQ[6]s, respectively. The absorption band of the guests exhibits a progressively lower absorbance with a slight blue shift as the ratio $N_{SQ[6]}/N_{g\cdot HCl}$ is increased. The absorbance change ($\Delta A$) *vs.* ratio of moles of $[N_{g1\cdot HCl}/(N_{TMeQ[6]} + N_{g1\cdot HCl})]$ data can be fitted to a 1 : 1 binding model for the TMeQ[6]–g1·HCl system at $\lambda_{max}$ (Fig. 6b). Interestingly, the absorbance change ($\Delta A$) *vs.* ratio of moles of $[N_{g2\cdot HCl}/(N_{m-HMeQ[6]} + N_{g2\cdot HCl})]$ data can be fitted to a 2 : 1 binding model for the *m*-HMeQ[6]–g2·HCl system at $\lambda_{max}$ (Fig. 6d).

Using fluorescence spectroscopy, similar experiments were performed. The two free host SQ[6]s are non-fluorescent compounds and the maximum fluorescence emission wavelengths of the guests g1·HCl and g2·HCl are 411 nm and 353 nm, respectively. Fig. 6e, g show the variation in the emission spectra obtained with aqueous solutions containing a fixed concentration of g1–2·HCl (32 mM) and variable concentrations of SQ[6]s, respectively. The emission spectra of the guest g1·HCl exhibit a progressive increase in fluorescence intensity with a slightly blue shift as the ratio $N_{TMeQ[6]}/N_{g1\cdot HCl}$ is increased. The fluorescence intensity change ($\Delta I_f$) *vs.* ratio of moles of $[N_{g1\cdot HCl}/(N_{TMeQ[6]} + N_{g1\cdot HCl})]$ data can be fitted to a 1 : 1 binding model for the TMeQ[6]–g1HCl system (Fig. 6f), while the emission spectra of the guest g2·HCl exhibit a progressive decrease in fluorescence intensity as the ratio $N_{m\text{-HMeQ[6]}}/N_{g2\cdot HCl}$ is increased. The fluorescence intensity change ($\Delta I_f$) *vs.* ratio of moles of $[N_{g2\cdot HCl}/(N_{m\text{-HMeQ[6]}} + N_{g2\cdot HCl})]$ data are also fitted to a 2 : 1 binding model for the *m*-HMeQ[6]–g2·HCl system (Fig. 6h). This behavior is consistent with the results from the absorption spectrophotometric analysis.

Generally, the binding constants can be calculated based on the absorbance or fluorescence intensity *vs.* ratio of moles of the host SQ[6] and guest ($N_{SQ[6]}/N_{guest}$) data. However, for these two typical host–guest interaction systems, both the absorbance and fluorescence intensity data are almost linear as the ratio $N_{SQ[6]}/N_{guest}$ is increased and are not suitable for calculating the related binding constants (see the figures in the ESI†). Based on the corresponding Job plots (Fig. 6b,d,f,h), the binding constants ($K$) can be estimated for the two exclusion host–guest systems. They are $7.59 \times 10^5$ L mol$^{-1}$ and $7.16 \times 10^5$ L mol$^{-1}$ for the TMeQ[6]–g1 system, $4.43 \times 10^{10}$ L$^2$ mol$^{-2}$ and $5.43 \times 10^{10}$ L$^2$ mol$^{-2}$ fot the *m*-HMeQ[6]–g2 system, respectively.

### Molecular mechanics calculations

Above, we have demonstrated two host–guest systems which exhibit unexpected behaviors and properties. Although the guests have protonated aniline moieties, which are typical species to form inclusion host–guest complexes with the SQ[6]s,[20] the exclusion host–guest complexes of the SQ[6]s with g1 or g2·HCl were observed. When compared to a number of known inclusion host complex systems,[3d,18] the quantification of the interaction between the methyl

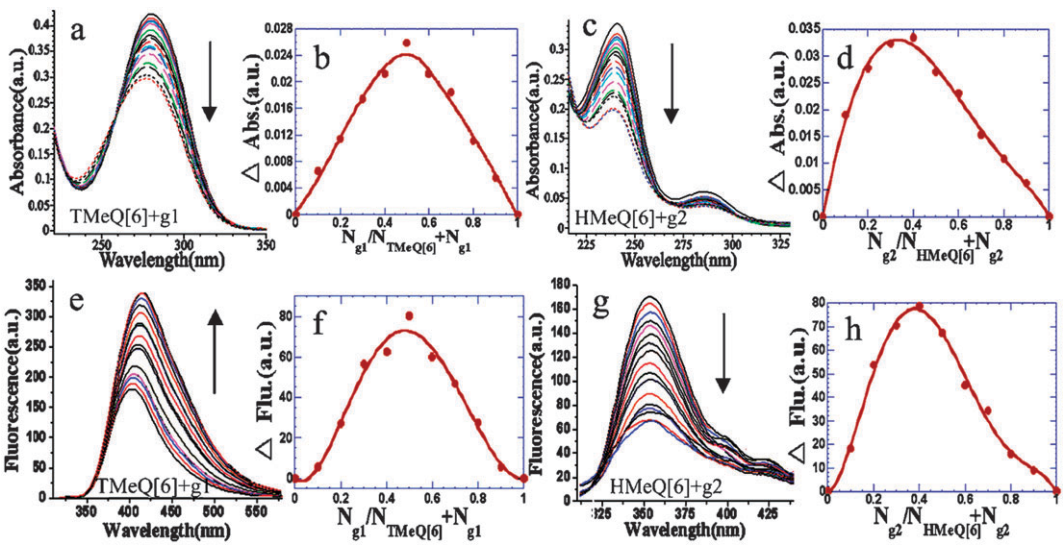


**Fig. 6** (a, c) Electronic absorption spectrum for the TMeQ[6]–g1·HCl and *m*-HMeQ[6]–g2·HCl systems, (b, d) the corresponding $\Delta A$–$N_{g\cdot HCl}/(N_{SQ[6]} + N_{g\cdot HCl})$ curves. (*e.g.*) Fluorescence emission spectra for the TMeQ[6]–g1·HCl and *m*-HMeQ[6]–g2·HCl systems, (f, h) the corresponding $\Delta I_f$–$N_{g\cdot HCl}/(N_{SQ[6]} + N_{g\cdot HCl})$ curves.

 

substituted SQ[6]s and g1–2·2HCl in solution revealed that the formed exclusion host–guest complexes presented unexpected stability. Although the two guests used in this work have similar structures, the absorption spectrophotometric and fluorescence spectroscopic analysis in aqueous solution indicated the formation of the host–guest exclusion complex with a host : guest ratio of 1 : 1 for the TMeQ[6]–g1 system, and a host : guest ratio of 2 : 1 for the *m*-HMeQ[6]–g2 system. In addition, a novel 1D supramolecular construction based on the exclusion host–guest complexes was observed in the solid state.

To understand these unexpected behaviors and properties, we have selected the B3LYP/STO-3G method implemented in Gaussian 03. All simulations were done in the gas phase in the presence of host and guest only. We assumed that the pathways for ingression and egression are the same (microscopic reversibility) and have therefore only modeled the process of guest egression. The activation energies for guest egression from the inner cavity of Q[6] were calculated by defining a complexation coordinate coinciding with the Q[6] rotational symmetry axis, along which the guest could be forced in 0.5 Å increments from the center of the cavity (0 Å) through the portals (*ca.* 3 Å) into free space (10 Å). To achieve this, the position of a dummy atom was fixed at the center of cavity of the cucurbiturils.[21] The distance between host and guest was then varied and calculations provided the potential energy at each step.

Fig. 7 shows the profile of the relative potential energy to the point of the lowest potential energy at $d_{min}$ 8.0 Å (*E*, a.u.) *vs.* the distance between the geometric center of the guest g1 and the dummy atom (*d*, Å) and the structures corresponding to the energy maxima. Overall, the energy of TMeQ[6]–g1·2H$^+$ appears to increase with increasing distance. A close inspection of the profile reveals a wave-like curve in the distance range 0–8.0 Å. There are two wave minima (B and D) and two maxima (A and C) (Fig. 7, inset). It is understandable that only one of the aromatic rings of guest g1 is included in the cavity of the host TMeQ[6], as shown in Fig. 7B. In addition, the protonated amine group on the aromatic ring just inside a portal of the TMeQ[6] host could interact with the carbonyl groups of the portal through ion–dipole interactions and hydrogen bonding at the calculated minimum B. A combination of the hydrophobic cavity interaction, ion–dipole interaction and hydrogen bonding could lead to the formation of such a partial inclusion host–guest complex. However, the structure corresponding to the lowest minimum (D) shows that the guest moves out of the cavity of the host completely at a distance of about 8.0 Å which is consistent with the structural parameters presented in the crystal structure of the compound **1**. In the presence of ion–dipole interactions and hydrogen bonding, the exclusion host–guest complex formed shows unexpected stability, which is confirmed by the calculations, absorption spectrophotometry, and fluorescence spectroscopy. As for the two maxima A and C in Fig. 7, the corresponding structures have the common feature that the aromatic ring(s) is (are) included in the portal(s), but not the cavity of the host. This causes high strain on the portal(s) and consequently the inclusion host–guest complexes have higher potential energies. In general, the cavity of a Q[6] favors inclusion of a single aromatic ring, such as phenyl or pyridyl and so on which can fit comfortably in the cavity. In our previous work, the demonstration of interaction between Q[6]s with 2,2′-dipyridyl and its derivatives revealed that one pyridyl ring of the guest was contained within the cavity of Q[6] and that the other pyridyl ring of the guest protruded from one portal of the host Q[6], and a 1 : 1 unsymmetrical host–guest complex was formed, where the protonated N atom on the pyridyl further strengthened the interaction of the host (Q[6]) and 2,2′-dipyridyl through hydrogen bonding and ion–dipole interactions between the protonated N atom and the portal carbonyl oxygens.[22] However, in this case, no such extra interaction exists between the host and guest, and in addition, the neighboring phenyl ring sits at the portal area, and increases the geometric strain.

In summary, both the experimental results and the theoretical analysis suggest that the guest g1 with two neighboring aromatic rings does not favor the formation of a stable inclusion host–guest complex due to the geometric strain caused by two neighboring aromatic rings in the cavity of a Q[6].

Fig. 8 shows the profile of the relative potential energy (to the point of the lowest potential energy at $d_{min}$ 8.0 Å) *vs.* the distance (*d*) between the geometric center of the guest g2

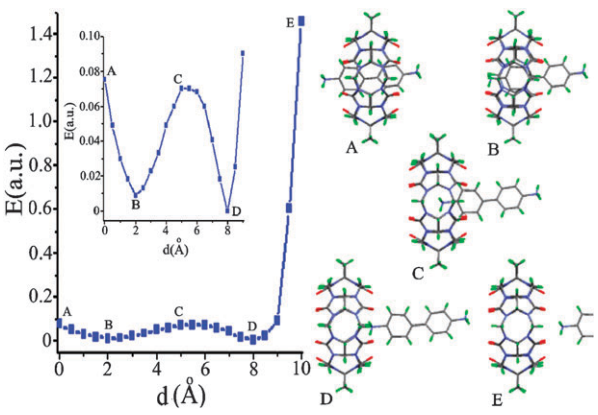


**Fig. 7** The profile of potential energy (*E*, a.u.) *vs.* distance (*d*, Å), and the corresponding structures at the peaks for the TMeQ[6]–g1 system

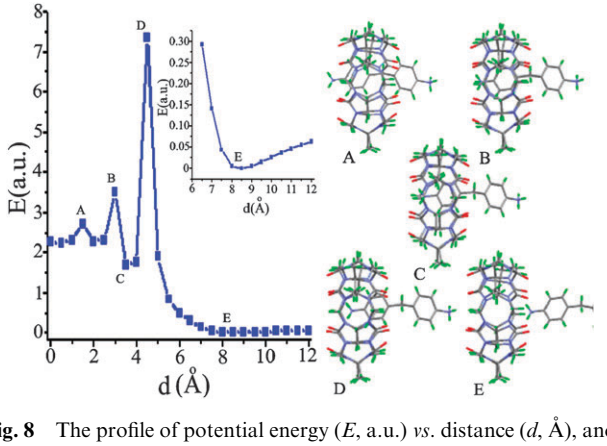


**Fig. 8** The profile of potential energy (*E*, a.u.) *vs.* distance (*d*, Å), and the corresponding structures at the peaks for the *m*-HMeQ[6]–g2 system.

and the dummy atom. Typical structures corresponding to the peak points in the profile are included. The calculated results revealed that the potential energies of the inclusion models are always higher than those of the exclusion models. The profile also shows a minimum at $d_{min}$ 8.0 Å (Fig. 8, inset), and the corresponding structure is consistent with the crystal structure in the compound **2**. Looking into the structure of the guest g2, a bridged methylene orients the two neighboring phenyl rings at 113.76° (see the CIF file of compound **2**†), which causes a more strained geometry when the guest moves into the cavity of the host Q[6] and consequently leads to the higher potential energy of the inclusion model.

## Conclusion

The single crystal X-ray diffraction determination of the interaction complexes obtained from methyl-substituted cucurbiturils (TMeQ[6] and *m*-HMeQ[6]) and guests containing protonated aniline groups (hydrochloride salts of benzidine hydrochloride and bis(4-aminophenyl) methane) showed the formation of two host–guest exclusion complexes in which the guest molecules were excluded at the portals of the host cucurbiturils. In the solid state, each guest or host was sandwiched between neighboring hosts or guests leading to the formation of 1D supramolecular chains. Analysis of the $^1$H NMR spectra showed no obvious change in the proton chemical shifts of either the host or guest molecules thereby suggesting that an inclusion interaction was not present between TMeQ[6] with g1·HCl in the solution state, while a downfield shift of the resonances of the aromatic protons of g2 clearly suggested the formation of the exclusion complex for the *m*-HMeQ[6]–g2 system. Spectroscopic analysis not only revealed unexpectedly high formation constants $\sim 10^5$ L mol$^{-1}$ for the TMeQ[6]–g1 system and $\sim 10^{10}$ L$^2$ mol$^{-2}$ for the *m*-HMeQ[6]–g2 system in aqueous solution at pH 5.6, but also revealed that the interaction ratio of the host : guest was 1 : 1 for the TMeQ[6]–g1 system and 2 : 1 for the TMeQ[6]–g1 system. For the systems studied here, the experiments are in good agreement with HF and B3LYP computational approaches using moderately-sized basis sets. Overall, guests with neighboring aromatic rings favor formation of the exclusion host–guest complexes due to the geometric strain in the Q[6] cavity.

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