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Host–guest Complex of a Water-soluble Cucurbit[6]uril Derivative with the Hydrochloride Salt of 3-amino-5-phenylpyrazole

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Interaction between tetramethylcucurbit[6]uril and 3-amino-5-phenylpyrazole hydrochloride in aqueous solution has been investigated by using ^{1}H NMR spectroscopy, electronic absorption spectroscopy and fluorescence spectroscopy, as well as by a single crystal X-ray diffraction determination. The ^{1}H NMR spectra analysis established a basic interaction model in which an inclusion complex with a host:guest ratio of 1:1 forms, in which the host selectively binds the phenyl moiety of the guest. Absorption spectrophotometric and fluorescence spectroscopic analysis in aqueous solution defined the stability of the host–guest inclusion complexes quantitatively as $6.8 \times 10^5\,mol^{-1}\,L$ at pH 2.6; the interaction is pH dependent, decreasing as pH rises. The single crystal X-ray structure of the isolated inclusion complex shows the phenyl moiety of the guest inserted into the host cavity, which supports particularly the ^{1}H NMR spectroscopic study in solution. In the crystal structure of the inclusion complex, the host–guest interaction involves both inter- and intra-complex hydrogen bonding, forming 2:2 dimers that stack in one dimension as supramolecular tubes.

Keywords: Host–guest complex; *sym*-Tetramethyl-cucurbit[6]uril; 3-amino-5-phenylpyrazole; ^{1}H NMR spectroscopy; Binding constant; Single crystal X-ray structure

INTRODUCTION

A hydrophobic cavity and polar carbonyl groups surrounding the opening portals are common characteristic features for a relatively new receptor family—the cucurbit[n]uril (Q[n]) compounds. Amongst known examples, the structure of cucurbit[6]uril (Q[6]) was first determined and reported by Mock and co-workers in 1981 [1]. About two decades later, homologues cucurbit[n = 5, 7, 8]urils (Q[5], Q[7], Q[8]) were synthesized and reported by two groups in 2000 [2,3], while cucurbit[10]uril (Q[10]), formed along with Q[5], was reported in 2002 [4]. The varying cavity and portal sizes available in Q[n] molecules, and particularly their ability to form inclusion or exclusion complexes with organic species or inorganic ions, led to quite a few researchers focusing on this area and uncovering the remarkable molecular recognition properties that provide a building block for supramolecular chemistry [5–14].

Recently, a series of Q[n] derivatives such as fully substituted Q[5] and Q[6] [15,16] including a perhydroxycucurbit[6]uril ($(OH)_{12}$Q[6]) [17], as well as a diphenyl Q[6] [18], were synthesized and reported to overcome the poor solubility of the general Q[n] family in common solvents. Using the dimer of glycoluril synthesized in our laboratories and the diether of alkylglycoluril, we have been able to synthesize a series of new symmetrical and unsymmetrical substituted cucurbit[n]urils to augment those reported by others [19–27]. Some Q[n] molecules show surprising water solubility, which allows us to investigate host–guest chemistry in water.

In this work, we report a host–guest interaction system in which the host is a water soluble symmetrically-substituted tetramethylcucurbit[6]uril (Me_4Q[6]) [25] and the guest is the hydrochloride salt of 3-amino-5-phenylpyrazole (**app**) (Scheme 1),

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of some relevance to potential drug encapsulation given that a range of drugs have a similar moiety to that of the chosen guest. The guest **app** is composed of two unsaturated moieties—phenyl and pyrazole rings—both of which are sufficiently small that they could be included in the cavity of Q[6] or its substituted derivatives [28,29]. ^{1}H NMR spectroscopy and a single crystal X-ray diffraction determination reveal that the inclusion complex formed has an unsymmetrical configuration with a host:guest ratio of 1:1, with the phenyl moiety being the included moiety of the guest. The stability of this complex has been estimated by using electronic absorption spectroscopy and fluorescence spectroscopy methods. Results of this study are reported herein.

EXPERIMENTAL

Syntheses

$Me_4Q[6]$ was prepared and purified according to the method developed in our laboratories [25]. 3-amino-5-phenylpyrazole (**app**) was obtained from Aldrich and used without further purification. The corresponding HCl salt was prepared by dissolving **app** in 5M HCl followed by crystallization after ethanol addition, collecting the crystals by filtration and drying in air.

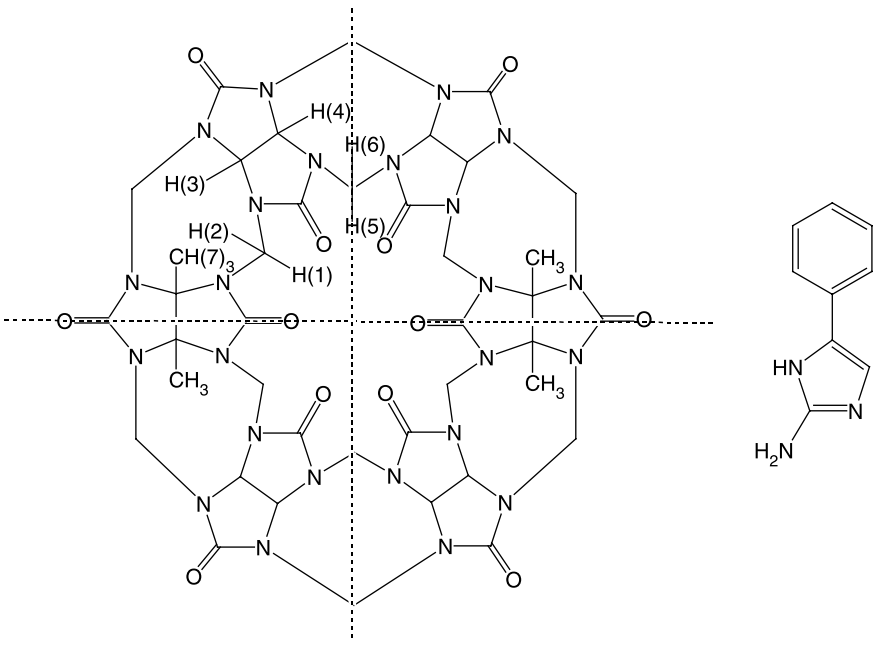
The single crystals of $Me_4Q[6]$ adduct with **app**·HCl were obtained by dissolving $Me_4Q[6]$ (0.50 g, 0.47 mmol) in a solution of **app**·HCl (0.12 g, 0.61 mmol) in water (5 mL). The final solution was mixed thoroughly and allowed to stand at room temperature; crystals formed after several days, and were collected.

Host–guest Complexation

For the study of host–guest complexation of $Me_4Q[6]$ and the **app** guest, $2.0–2.5 \times 10^{-3}$ mmol samples of $Me_4Q[6]$ in 0.5–0.7 g D_2O with guest:$Me_4Q[6]$ ratios ranging between 1 and 100 were prepared. The ^{1}H NMR spectra were recorded at 20°C on a Varian INOVA-400 spectrometer; pD was adjusted by NaOD addition. Absorption spectra of the host–guest complex were recorded on a HP8453 UV–visible spectrophotometer and fluorescence spectra of the host–guest complexes were recorded on a Varian RF-540 fluorescence spectrophotometer at room temperature. For absorption and fluorescence studies, aqueous solutions of **app**·HCl were prepared with a fixed concentration of 3.20×10^{-5} mol L^{-1}, and the samples of these solutions were combined with $Me_4Q[6]$ to give solutions with a guest:$Me_4Q[6]$ ratio of 0:10, 1:9, 2:8, ⋯, 9:1, 10:0.

X-ray Crystallography

A Bruker SMART ApexII CCD diffractometer employing graphite monochromated MoKα radiation was used for the data collection. A suitable crystal of $Me_4Q[6]$–**app**·HCl was selected and mounted at the end of a glass fiber. Cell constants were obtained from a least squares refinement against 964 reflections located between 3.4 and 53.6° 2θ. Data were collected at 223(2) Kelvin with φ scans. No crystal decay was observed.



$Me_4Q[6]$ app

SCHEME 1

Data integration and reduction and subsequent computations were carried out with the Bruker ApexII package, including Lorentz polarization and absorption correction. The structure was solved by direct methods with SHELXS-97, and extended and refined with SHELEL-97 [30]. Hydrogen atoms were added at calculated positions and refined using a riding model; solvent H-atoms were not usually located. Anisotropic displacement parameters were used for all non-H atoms; H-atoms were given isotropic displacement parameters equal to 1.2 (or 1.5 for methyl hydrogen atoms) times the equivalent isotropic displacement parameter of the atom to which the H-atom is attached. Residuals are defined as $R1 = \sum||F_o| - |F_c||/\sum|F_o|$ for $F_o > 2\sigma(F_o)$ and $wR2 = (\sum w(F_o^2 - F_c^2)^2/\sum(wF_c^2)^2)^{1/2}$ for all reflections, with $w = 1/[\sigma^2(F_o^2) + (AP)^2 + BP]$ where $P = (F_o^2 + 2F_c^2)/3$ and A and B are given below.

$Me_4Q[6]$–app·HCl. Formula $C_{49}H_{82}ClN_{27}O_{26}$, $M = 1500.87$, triclinic, space group *P-1*. $a = 12.036(2)$, $b = 12.903(2)$, $c = 22.467(4)$ Å, $\alpha = 76.327(2)$, $\beta = 89.287(2)$, $\gamma = 85.571(2)°$, $V = 3379.9(10)$ Å^3, $D_c = 1.475\,g\,cm^{-3}$, $Z = 2$, crystal size 0.18 by 0.21 by 0.28 mm, colourless, prism, temperature 223(2) Kelvin, λ(MoKα) 0.71073 Å, μ(MoKα) 0.158 mm^{-1}, $F(000)$ 1580, $T_{min,max}$ 0.9571; 0.9722. Range of θ 1.68–26.79°. *hkl* range −13 14, −15 15, −27 28, N 24289, N_{ind} 12681(R_{int} 0.0364), restraints 0, parameters 949, N_{obs} 8388 ($I > 2\sigma(I)$). Residuals *R1(F)* [for 8388 reflections with $I > 2\sigma(I)$] 0.1114, *wR2(F^2)* 0.3339 for A = 0.2000 and B = 0.0000. GoF(all) 1.352, $\Delta\rho_{min,max}$ −1.637, 1.148 e$^-$ Å^{-3}.

The atomic numbering scheme, selected bond lengths and angles are listed in supplementary material. Views of the complex appear in Figs. 6 and 7. Crystallographic data (excluding structure factors) for the structure reported have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-634615. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat. +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

RESULTS AND DISCUSSION

The interaction of a host and guest to form an inclusion complex commonly causes a change in the environment of the guest that is sufficient to be monitored by spectroscopic methods. Often, water solubility of one or both species is problematical, and a range of studies have been reported only in non-aqueous environments. In the present study, water solubility is sufficient to permit determination of the form and strength of interaction in aqueous solution.

^{1}H NMR Spectra Analysis of the Interaction Between $Me_4Q[6]$ with app·HCl

Figure 1 shows the ^{1}H NMR spectra of **app**·HCl recorded in the absence and in the presence of up to 2.1 equivalents of $Me_4Q[6]$, as well as that of neat $Me_4Q[6]$. Signals corresponding to the unbound and bound **app**·HCl are present after addition of 0.6 equivalents of $Me_4Q[6]$ (Fig. 1a and b), with the signals of the unbound guest almost disappearing when the concentration of $Me_4Q[6]$ reaches 1.4 equivalents (Fig. 1c). Three phenyl ring resonances are shifted significantly upfield by 1.01 (for H^3), 0.76 (for H^4) and 0.77 ppm (for H^2). This suggests that the phenyl ring of

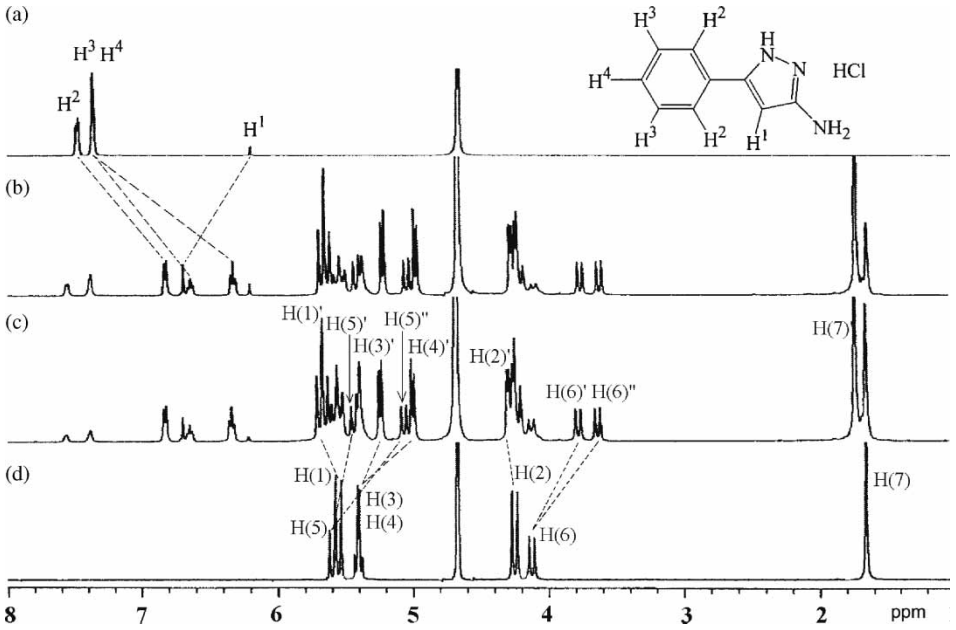


FIGURE 1 ^{1}H NMR spectra of the $Me_4Q[6]$–**app**·HCl system. The spectra of **app**·HCl recorded in the absence (a) and in the presence of 0.6 (b) and 1.4 (c) equivalents of $Me_4Q[6]$, as well as neat $Me_4Q[6]$ (d).

the guest is in the shielding zone in the cavity of the host. The sharp peaks of the bound **app**·HCl indicate that exchange between the included and excluded guest is slow on the NMR time scale.

For the $Me_4Q[6]$ host, the resonances of the protons H(1), H(2) and H(7) in the inclusion complex experience a downfield shift by ~0.1 ppm (marked H(1)′, H(2)′ and H(7)′ in Fig. 1), whereas the resonances of the protons H(3), H(4), H(5), and H(6) experience not only an upfield shift, but also split into two sets compared to the free $Me_4Q[6]$ (Fig. 1c and d). The overlapped resonances of the protons H(3), H(4) are displaced by an upfield shift by ~0.2 ppm (marked H(3)′) and ~0.4 ppm (marked H(4)′), respectively, and both H(5) and H(6) are shifted upfield with splitting by 0.2 ~ 0.3 ppm (marked H(5)′ and H(6)′), and ~0.5 ppm (marked H(5)″ and H(6)″) for each pair.

The two sets of split doublet resonances of H(5) and H(6) show that the two protons on the portal methylenes of the $Me_4Q[6]$ lie in different magnetic environments, caused by a preferential orientation of the protruding pyrazole of the guest **app**·HCl towards one portal of $Me_4Q[6]$. A comparison of the integrals of the shifted protons of the bound **app**·HCl with the shifted protons of $Me_4Q[6]$ revealed the complex to be a 1:1 host:guest species. Thus, the ^{1}H NMR study strongly implies that $Me_4Q[6]$ exhibits a pronounced preference towards including the phenyl moiety rather than the pyrazole moiety of **app**·HCl [28], with the structure of the inclusion complex being unsymmetrical.

It is noticeable that unbound host and guest can be observed in the ^{1}H NMR spectra of the included $Me_4Q[6]$–**app**·HCl system even when the guest or host is in excess (Fig. 1b and c), which suggests that the inclusion complex of $Me_4Q[6]$–**app**·HCl is not fully formed, *i.e.* the title complex is not very stable under the determining condition (pD = 5.7). Since the pK_a of the guest (estimated as 4–5, from data for analogues) is such that protonation–deprotonation will be a feature of its behaviour in aqueous solution, and it is anticipated that the strength of the inclusion complex will be compromised by deprotonation, it is expected that the inclusion complex stability will be pH dependent.

Influence of pH on Interaction of $Me_4Q[6]$ and app·HCl

Generally, increasing the pH of the medium of an interacting system can significantly influence the combination of a host and a guest, as a result of breakdown of strong hydrogen bonds involving the ionic form when deprotonation occurs [31]. Supporting this contention in the present case, the variation in the ^{1}H NMR spectrum with pH from 5.6 to 8.0 (Fig. 2) shows a clear diminution in complex formation as the pH rises, to the point where it is insignificant at pH ~8. The interaction and stability of the $Me_4Q[6]$–**app**·HCl complex were further investigated by using electronic absorption spectroscopy and fluorescence spectroscopy at different pH values.

A plot of absorbance at λ_{max} (250 nm) vs. pH is shown in Fig. 3(a) for **app**·HCl alone (curve A) and for the inclusion complex with a 1:1 host:guest ratio (curve B). Likewise, Fig. 3(b) shows the fluorescence

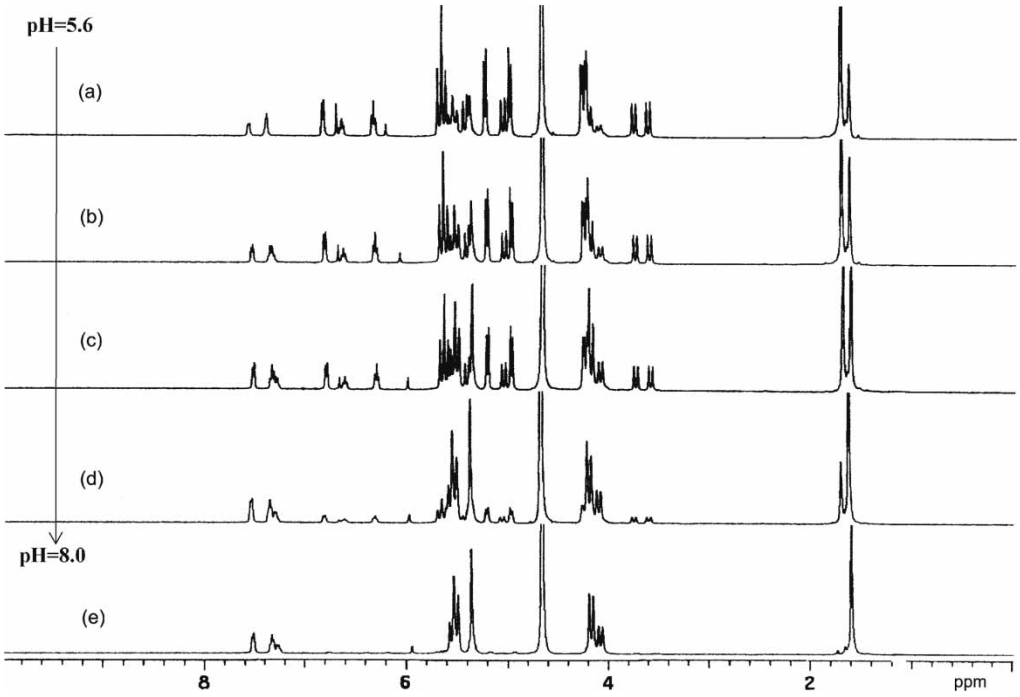


FIGURE 2 Variation in the ^{1}H NMR spectra of the $Me_4Q[6]$–**app**·HCl system with increasing pH.

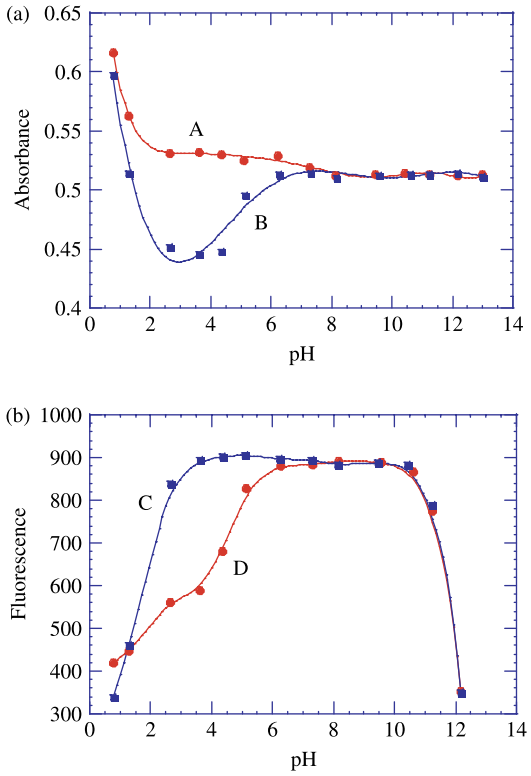


FIGURE 3 Absorbance—pH (a) and fluorescence—pH (b) curves for the $Me_4Q[6]$–**app**·HCl system (determined at 250 nm and 424 nm, respectively). Data are shown for **app**·HCl alone (curves A, C) and for the inclusion complex with a 1:1 host:guest ratio (curves B,D).

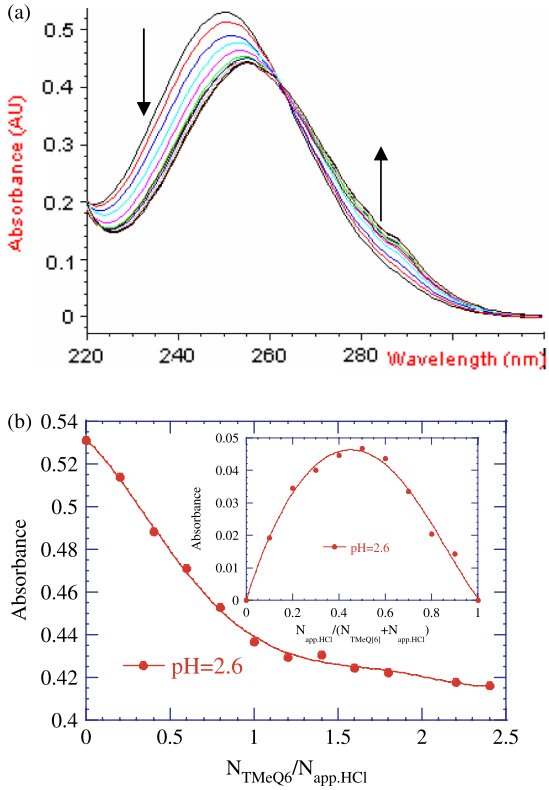


FIGURE 4 Electronic absorption spectra of **app**·HCl in the presence of increasing concentrations of $Me_4Q[6]$ (a) and corresponding absorbance vs $N_{Me4Q[6]}/N_{\mathbf{app}\cdot HCl}$ curve and absorbance (ΔA) vs $[N_{Me4Q[6]}/(N_{Me4Q[6]} + N_{\mathbf{app}\cdot HCl})]$ (inset) at $\lambda_{max} = 250$ nm (b).

intensity at λ_{Ifmax} (424 nm) vs. pH for **app**·HCl (curve C) and the inclusion complex with a ratio of 1:1 host:guest ratio (curve D). One can see an obvious absorbance or fluorescence intensity difference between the free guest and the bound guest in the pH range 1–6, where the curve B or D is clearly differentiated from the curve A or C, respectively. Moreover, there is no strong evidence of binding at pH $>$ 7. This is consistent with ^{1}H NMR spectra of the inclusion complex above pD 5.7, where behaviour suggests that the encapsulated **app**·HCl has a greater tendency to leave the host $Me_4Q[6]$ than at lower pH.

Spectrophotometric Analysis on the Interaction Between $Me_4Q[6]$ and app·HCl

As mentioned above, the pH of the medium will affect the formation of the inclusion complex. Therefore, to quantify the interaction between $Me_4Q[6]$ and **app**·HCl, a ratio-dependent study was pursued by electronic absorption and fluorescence spectra at pH 2.60, the pH of maximum absorbance change. Usually, the free host $Me_4Q[6]$ shows no absorbance at $\lambda > 210$ nm. Figure 4(a) shows the variation in the UV spectra obtained with aqueous solutions containing a fixed concentration of **app**·HCl (32 mM) and variable concentrations of $Me_4Q[6]$. The absorption band of the guest **app**·HCl exhibits a progressively lower absorbance with a red shift as the ratio of $N_{Me4Q[6]}/N_{\mathbf{app}\cdot HCl}$ is increased, and a sharp isosbestic point at 262 nm is consistent with a simple interaction between $Me_4Q[6]$ and **app**·HCl. The absorbance (A) vs ratio of moles of the host $Me_4Q[6]$ and guest **app**·HCl ($N_{Me4Q[6]}/N_{\mathbf{app}\cdot HCl}$) data can be fitted to a 1:1 binding model for the $Me_4Q[6]$–**app**·HCl system at λ_{max} 250 nm (Fig. 4(b)). The insert shows the absorbance change (ΔA) vs ratio of $[N_{Me4Q[6]}/(N_{Me4Q[6]} + N_{\mathbf{app}\cdot HCl})]$ data which can also be fitted to a 1:1 binding model. This behaviour is consistent with the results from the ^{1}H NMR study.

Using fluorescence spectroscopy, similar experiments were performed. Figure 5(a) shows emission spectra of the guest **app**·HCl obtained with aqueous solutions containing a fixed concentration of **app**·HCl (32 mM) and variable concentrations of $Me_4Q[6]$. The emission spectra of the guest **app**·HCl exhibit a progressive change in fluorescence intensity with a violet shift as the ratio of $N_{Me4Q[6]}/N_{\mathbf{app}\cdot HCl}$ is increased. Both the curves of fluorescence intensity (I_f) vs $N_{Me4Q[6]}/N_{\mathbf{app}\cdot HCl}$ and ΔI_f vs $[N_{Me4Q[6]}/(N_{Me4Q[6]} + N_{\mathbf{app}\cdot HCl})]$ can also be fitted to a 1:1 binding model for the $Me_4Q[6]$–**app**·HCl system at λ_{max} 424 nm (Fig. 5(b)).

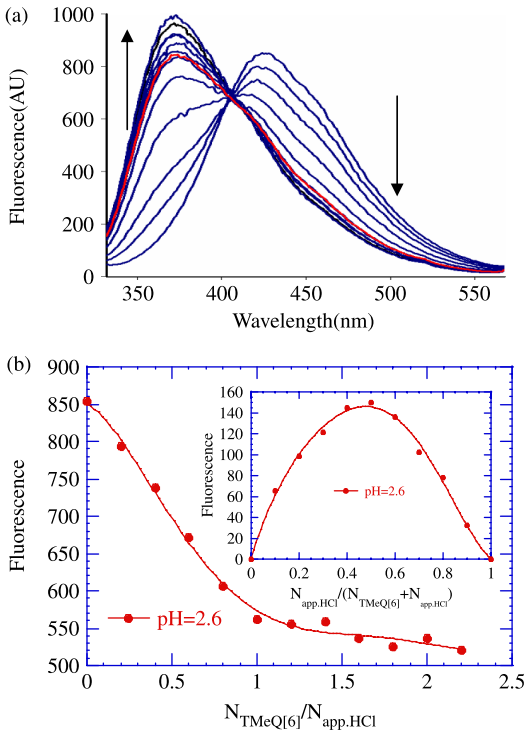


FIGURE 5 Fluorescence emission (I_f) spectra of **app**·HCl in the presence of increasing concentrations of $Me_4Q[6]$ (a) and corresponding I_f vs $N_{Me4Q[6]}/N_{\mathbf{app}\cdot HCl}$ curve and ΔI_f vs $[N_{Me4Q[6]}/(N_{Me4Q[6]} + N_{\mathbf{app}\cdot HCl})]$ (inset) at $\lambda_{max} = 424$ nm (b).

The measured data from both absorption spectrophotometric and fluorescence spectroscopy analysis fitted to a simple 1:1 host:guest complexation [32], yielded a calculated binding constant (*K*) of 6.67×10^5 L/mol based on the absorption spectrophotometric analysis and 7.01×10^5 L/mol based on the fluorescence spectroscopy analysis. The values of *K* are reasonably consistent, with an average value of $6.8(\pm 0.2) \times 10^5$ L/mol.

Subsequently, we tested the interaction between $Me_4Q[6]$ and **app**·HCl at different pH values. The experimental results showed that the absorbance change decreased with increasing pH, although a similar red shift of the absorption bands can be observed. The determined stability constants also decreased with an increase of the pH. This suggests that the inclusion complex $Me_4Q[6]$–**app**·HCl is not favoured in a neutral or basic environment, implying that deprotonation of the guest limits complexation. The ^{1}H NMR spectra of $Me_4Q[6]$–**app**·HCl at different pD values (Fig. 2) further supports this observation.

Crystal Structure Determination of the Inclusion Complex $Me_4Q[6]$–app·HCl

Based on the solution studies, one can conclude that the host $Me_4Q[6]$ prefers to include the phenyl moiety rather than the pyrazole moiety of the guest **app**·HCl. Although the stability of the inclusion complex is affected by the pH of the solution, there is no spectroscopic evidence for a changeover in the included group. The crystal structure of the inclusion complex was determined in order to give more details on the interaction between $Me_4Q[6]$ and **app**·HCl. Figure 6 shows two views of the $Me_4Q[6]$–**app**·HCl adduct. In the solid state, the phenyl moiety of the guest has clearly intruded into the cavity center of the host, whereas the pyrazole moiety lies in a portal zone of the host. Thus, the phenyl ring in the cavity will undergo a shielding effect, and the corresponding proton resonances will experience a significant upfield shift (as observed in the ^{1}H NMR spectra discussed above). Moreover, the protonated pyrazole moiety at the portal hydrogen bonds with the rimmed carbonyls of $Me_4Q[6]$, increasing the stability of the title inclusion complex (although it is unclear which N of the pyrazole moiety is protonated in solution). It is notable that a preferential orientation of **app** protruding from the

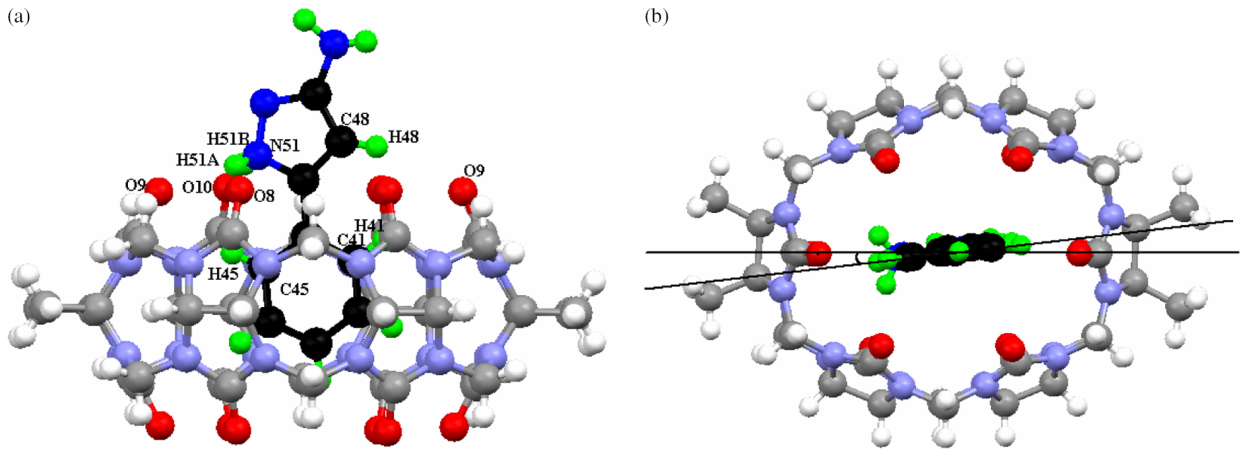


FIGURE 6 Views of the crystal structure of the inclusion complex $Me_4Q[6]$–**app**·HCl: (a) side view; (b) top view (with the small twist of the guest highlighted by inserted lines).

portal of $Me_4Q[6]$ will cause a significant chemical shift difference for the protons H(5)/H(6) and H(1)/H(2). This preferential orientation favours C—H···π interaction between the phenyl ring and the protons H(5)/H(6) [25,33–36], which leads to an obvious upfield shift of the H(5) and H(6) signals. In addition, the location of the bound **app**·HCl favours C—H···π interaction between not only the phenyl ring but also the pyrazole ring and the protons H(5)″ or H(6)″ (upper fringe of the $Me_4Q[6]$), while the H(5)′ or H(6)′ (lower fringe of the TMeQ[6]) experience interaction with the phenyl ring only. Consequently, the H(5) and H(6) signals are further split into two sets (H(5)′/H(5)″ and H(6)′/H(6)″) due to their experiencing different shielding effects. In the solid state, the guest is inserted to the extent that the aromatic ring sits essentially in line with opposite sets of oxygen donors, but is twisted away from symmetrical alignment by 8.0°. The phenyl and pyrazole rings are exactly coplanar. The closest contacts are between the protonated secondary amine of the pyrazole ring (N51) and carbonyl atoms (O8, O9, O10) of the cucurbituril, with N51…O8, N51…O9 and N51…O10 of 3.153, 2.720 and 2.912 Å, respectively, differing as a result of the twist of the guest in the cavity. The NH51B…O10 and NH51A…O8, NH51A…O9 distances are 2.431 Å, 2.023 Å and 2.153 Å, respectively, for example, indicative of the strong hydrogen bonding assisting to locate the guest in the host. Presumably, the orientation of the guest in the cavity is directed mainly by this set of hydrogen bonds, although an increase in electron density on the carbonyl group of the substituted glycouril moiety (O9) in particular, arising from the influence of the substituents, may play a role. There are some close contacts between hydrogen atoms on the benzene ring and carbonyls also (e.g., C41—H41…O12 of 2.410 Å and C45—H45…O9 of 2.478 Å). Carbon atoms of the benzene ring lie between 3.40 Å and 5.21 Å from nearest-neighbour atoms in the host ring, with space filling models showing that the ring fits reasonably tightly in the cavity. Thus, a combination of a hydrophobic interaction between the cavity of the $Me_4Q[6]$ and the phenyl moiety of **app**·HCl together with the hydrophilic interactions between a polar carbonyl portal group of $Me_4Q[6]$ and the positively charged pyrazole of **app**·HCl was observed in this inclusion complex.

Cucurbit[n]urils and their derivatives have been studied extensively as the building blocks for supramolecular chemistry, summarized in an extensive series of reviews [5–11]. A number of supramolecular compounds formed from molybdenum and tungsten chalcogenide cluster aqua complexes [7,37–39] with metal ions or their complexes [40,41] or organic guests [42–44] within the macrocyclic cavity have been reported. Drawing

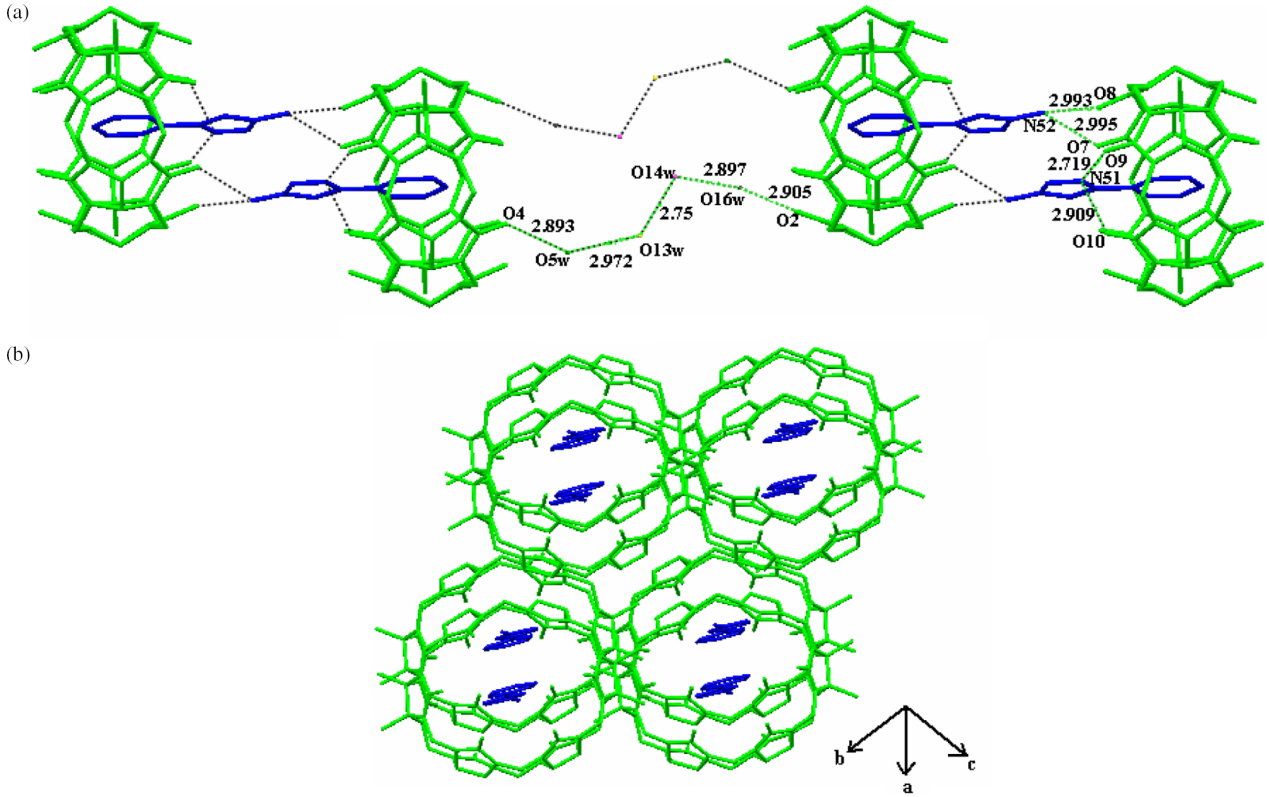


FIGURE 7 Dimer units of the inclusion complex $Me_4Q[6]$–**app**·HCl shown assembled through hydrogen-bonding in a single supramolecular tube (a), with stacking of the tubes in the crystal structure also shown (b).

on these investigations to inform the $Me_4Q[6]$–**app**·HCl inclusion complex system, one might expect a one dimensional supramolecular structure in which the inclusion complexes combine through simply dipole interaction and hydrogen bonds in a head-to-tail manner. However, the $Me_4Q[6]$–**app**·HCl inclusion complexes actually combine in a head-to-head manner in the solid state, with pairs of inclusion complexes forming dimers that are held together through strong hydrogen bonds between the protonated amine of **app** and the portal carbonyl oxygens of the host $Me_4Q[6]$ and between the terminal amine of one guest and carbonyl oxygens in the opposite host (Fig. 7(a)). Two hydrogen-bonded chains, each involving four water molecules and carbonyl groups on different hosts (O…O range 2.75–2.97 Å), then connect dimer assemblies via their tails, leading to a supramolecular tube. These tubes stack in the crystal structure to yield the final three-dimensional framework (Fig. 7(b)).

CONCLUSION

The ^{1}H NMR spectra analysis of the interaction between tetramethylcucurbit[6]uril and 3-amino-5-phenylpyrazole hydrochloride established a basic interaction model in which the host selectively binds the phenyl moiety of the title guests, forming an inclusion complex with a host:guest ratio of 1:1. A relatively high formation constant in aqueous solution at pH 2.6 of 6.8×10^5 was determined through absorption and fluorescence spectroscopic analysis. The stability of the host–guest inclusion complexes is pH dependent, with complexation only observed for pH < 7, this behaviour being consistent with deprotonation of the guest at higher pH. The single crystal structure of the inclusion complex supports the solution studies, the inclusion complex assembled as identified in the solution NMR studies and existing as stacked one-dimensional supramolecular tubes. The strength of the interaction determined here reflects the ability of cucurbit[n]urils to act as a host for suitably-shaped guests, even in aqueous solution.

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