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PAPER

Host–guest complexes of cucurbit[8]uril with some pentaerythritol derivative guests†

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A series of first generation dendritic guests from pentaerythritol derivatives have been designed and synthesized. Investigation of the complex structures of cucurbit[8]uril (Q[8]) and the guests based on the ^{1}H NMR technique have revealed that the host Q[8] selectively included different branch(es) of the first generation dendritic guests and formed inclusion complexes with different structural conformations. The experimental results obtained from electronic absorption spectroscopy showed that the 1 : 1 ratio of Q[8]-based host–guest inclusion complexes have moderate stability with an average formation constants of 10^4 L mol^{-1}. The single crystal structures of some of the guests (**g5** and **g6**) and Q[8]–guest complexes (Q[8]-**g4** and Q[8]-**g6**) further confirm but in some cases contradict the research results of the ^{1}H NMR technique and electronic absorption spectroscopy in aqueous solution.

Introduction

Derivatives of pentaerythritol, with an initial core from which reactive or functional branch units can be introduced at the periphery, can be used as starting materials for the synthesis of dendrimers[1–3] or organic ligands for synthesis of metal–organic frameworks (MOFs).[4–9] These show potential for applications in the nanoscale molecular devices and new material areas.[10–14] In particular, water soluble dendrimer guests can be used to study in host–guest chemistry or supramolecular self-assembly.[15]

A hydrophobic cavity and polar carbonyl groups surrounding the opening portals are common features of a relatively new host or receptor family—the cucurbit[*n*]uril (Q[*n*]) compounds. Of known examples, the structure of cucurbit-[6]uril (Q[6]) was first determined and reported by Mock and co-workers in 1981.[16] About two decades later, the homologous cucurbit[*n* = 5,7,8]urils (Q[5], Q[7], Q[8]) were synthesized and reported by two groups,[17,18] while cucurbit[10]uril (Q[10]), formed along with Q[5], was reported in 2002.[19] Since the structures of the Q[*n*]s were well known, the binding properties of Q[*n*]s have been extensively studied, and the related research has been reviewed during different periods in the development of cucurbit[*n*]uril chemistry.[20–26] However, little research on the binding interactions between Q[*n*] hosts and dendrimers has been reported[27–31] although this was summarized recently by Kaifer.[15]

In this work, we selected pentaerythritol as a starting material, designed and synthesized several of its first-generation or partial first-generation dendritic guests (referring to Scheme 1), and Q[8] as the host with a larger cavity. The guests are 1,1′-(2-phenyl-1,3-dioxane-5,5-diyl)bis(methylene)-dipyridinium(**g1**), 1,1′-(2-(thiophen-2-yl)-1,3-dioxane-5,5-diyl)-bis(methylene)dipyridinium(**g2**), 1,1′-(2-admintanyl-1,3-dioxane-5,5-diyl)bis(methylene)dipyridinium(**g3**), 1,1′-(2,2-dimethyl-1,3-dioxane-5,5-diyl)bis(methylene)dipyridinium(**g4**), 1,1′-(2,2-bis(hydroxymethyl)propane-1,3-diyl)dipyridinium(**g5**) and 1-(3-bromo-2,2-bis(bromomethyl)propyl)pyridinium bromide(**g6**), as shown in Scheme 1.

Generally, Q[8] can accommodate two molecules to form a 1 : 2 or 1 : 1 : 1 host–guest complex.[21] The capability of Q[8] provides a unique microenvironment or molecular container to study new forms of stereoisomerism,[32–39] molecular recognition,[40–45] and novel supramolecular assemblies.[46–49] On the other hand, the dendritic guests contain different short branches, which offer an opportunity to investigate the selective inclusion of Q[8] for these different branches. The investigation of the interaction between Q[8] and these water soluble dendritic guests has revealed that the inclusion complexes of Q[8]-**gn** (*n* = 1–6) have different conformations but with a fixed host : guest ratio of 1 : 1. The stability of the complexes has been estimated by using electronic absorption spectroscopy and the results of this study reported in this work.

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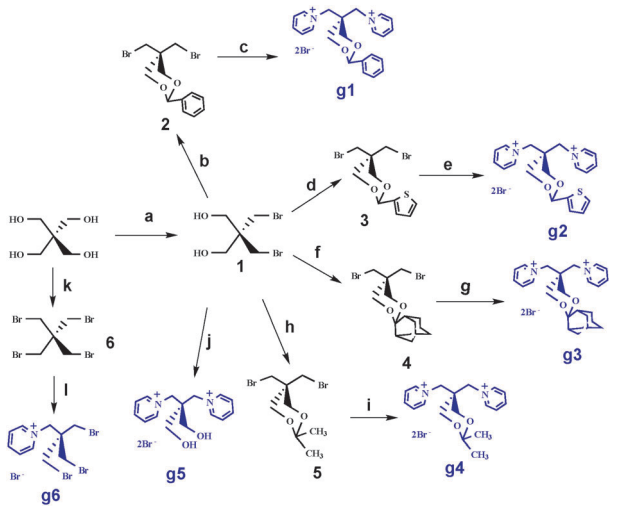

Scheme 1 Synthesis of guests **g1**, **g2**, **g3**, **g4**, **g5**, **g6**: Reagents and conditions: (a) $(CH_3CO)_2O$, gas HBr, EtOH/HCl; (b) toluene, *p*-toluenesulfonic acid, reflux; (c) DMF, pyridine, 120 °C; (d) toluene, *p*-toluenesulfonic acid, reflux; (e) DMF, pyridine, 120 °C; (f) toluene, *p*-toluenesulfonic acid, reflux; (g) DMF, pyridine, 120 °C; (h) acetone, *p*-toluenesulfonic acid, 30 °C; (i) DMF, pyridine, 120 °C; (j) pyridine, reflux, 48 h; (k) pyridine, TsCl, NaBr, PEG600; (l) dioxane, pyridine, reflux.

Experimental

Materials

Unless otherwise indicated, all commercially available starting materials were used directly without further purification. DMF was dried by CaH_2. Silica gel Sorbent Technologies 200–300 mm were used for flash column chromatography.

Syntheses

1,1′-(2-Phenyl-1,3-dioxane-5,5-diyl)bis(methylene)dipyridinium (g1). Benzaldehyde (1.0 g, 9.4 mmol) was reacted by using procedures (b) and (c) as shown in Scheme 1 to give a yellow solid, which was recrystallized from ethanol–chloroform(4 : 1), and a white solid **g1** (1.1 g, 56%) was obtained. ^{1}H NMR (400 MHz, H_2O), δ (ppm): 8.85 (2H, d, Py–H, J = 11.2 Hz), 8.75 (2H, d, Py–H, J = 5.2 Hz), 8.62 (1H, t, Py–H, J = 15.6 Hz), 8.42 (1H, t, Py–H, J = 16.0 Hz), 8.11 (2H, t, Py–H, J = 14.8 Hz), 7.94 (2H, t, Py–H, J = 14.4 Hz), 7.25 (3H, m, Ar–H, J = 26.4 Hz), 6.89 (2H, d, Ar–H, J = 7.2 Hz), 5.379 (1H, s, Ar–CH), 5.04, 4.76 (4H, s, Py–CH_2), 4.42, 4.13 (4H, d, dioxane CH_2, J = 12.4 Hz). MS (m/z): calcd., 508.2; found, 508.2(M + Br)$^+$.

1,1′-(2-(Thiophen-2-yl)-1,3-dioxane-5,5-diyl)bis(methylene)-dipyridinium (g2). Thiophene-2-carbaldehyde (1.5 g, 13.4 mmol) was reacted by using procedures (d) and (e) as shown in Scheme 1 to give a brown solid which was recrystallized from methanol, a gray solid **g2** (2.5 g, 37%) was obtained. ^{1}H NMR (400 MHz, H_2O), δ (ppm): 8.84 (2H, d, Py–H, J = 5.6 Hz), 8.76 (2H, d, Py–H, J = 6.4 Hz), 8.62 (1H, t, Py–H, J = 15.6 Hz), 8.47 (1H, t, Py–H, J = 8.0 Hz), 8.10 (2H, t, Py–H, J = 8.0 Hz), 7.95 (2H, t, Py–H, J = 8.0 Hz), 7.29 (1H, d, thiophene-H, J = 6.4 Hz), 6.89 (2H, m, thiophene-H, J = 16.4 Hz), 5.65 (1H, s, thiophene–CH), 5.00, 4.75 (4H, s, Py–CH_2), 4.44, 4.16 (4H, d, dioxane CH_2, J = 12.8 Hz). MS (m/z): calcd., 514.3; found, 514.2(M + Br)$^+$.

1,1′-(2-Adamantanyl-1,3-dioxane-5,5-diyl)bis(methylene)-dipyridinium (g3). A solution of compound (**1**) in Scheme 1 (1.2 g, 4.6 mmol), 2-adamantanone (0.69 g, 4.6 mmol), and a catalytic amount of *p*-toluenesulfonic acid in toluene (100 mL) was heated to reflux with a Dean–Stark trap for 8 h. The mixture was filtered and the filtrate was evaporated under vacuum, to leave a brown solid. The resulting solid was washed with cold water (2 × 100 mL) and then recrystallized from EtOH to give a white solid (**4**), for use in the next reaction. The solid (**4**) was reacted by using procedure (g) as shown in Scheme 1 to give a gray solid **g3** (1.2 g, 55%). ^{1}H NMR (400 MHz, H_2O), δ (ppm): 8.77 (4H, d, Py–H, J = 5.6 Hz), 8.54 (2H, t, Py–H, J = 8.0 Hz), 8.00 (4H, t, Py–H, J = 6.8 Hz), 4.79 (4H, s, Py–CH_2), 3.98 (4H, s, dioxane CH_2), 1.39–1.63 (15H, m, adamantane). MS (m/z): calcd., 552.3; found, 552.1(M + Br)$^+$.

1,1′-(2,2-Dimethyl-1,3-dioxane-5,5-diyl)bis(methylene)dipyridinium (g4). A solution of 2,2-bis(bromomethyl) propane-1,3-diol, **1** in Scheme 1, (0.80 g, 3.1 mmol), and a catalytic amount of *p*-toluenesulfonic acid in 100 mL acetone was heated to 30 °C for 4 h, then concentrated to 10 mL. After cooling, the mixture was poured into saturated $NaHCO_3$ (100 mL). The resulting precipitate was filtered and washed with cold water (3 × 100 mL) then dried at 40 °C to give a white solid (**5**) in Scheme 1, to be used for the next reaction. To a stirred solution of pyridine (0.38 mL, 4.6 mmol) in DMF (50 mL) was added a solution of compound (**5**) (0.70 g, 2.3 mmol) in DMF (20 mL) at 120 °C and the resulting reaction mixture was refluxed for 48 h, then concentrated to 5 mL. Acetone (100 mL) was added to precipitate the product. The resulting gray precipitate was filtered and washed with acetone (3 × 100 mL) then dried at 80 °C to give **g4** (0.43 g, 40%) as a white solid. ^{1}H NMR (400 MHz, H_2O), δ (ppm): 8.81 (4H, d, Py–H, J = 6.0 Hz), 8.57 (2H, t, Py–H, J = 15.6 Hz), 8.05 (4H, t, Py–H, J = 14.0 Hz), 4.82 (4H, s, Py–CH_2), 4.51 (4H, s, dioxane CH_2), 1.00 (6H, s, –CH_3). MS (m/z): calcd., 460.2; found, 460.2(M + Br)$^+$.

1,1′-(2,2-Bis(hydroxymethyl)propane-1,3-diyl)dipyridinium (g5). A solution of **1** (1.0 g, 3.8 mmol) in pyridine (100 mL) was heated to reflux for 48 h, then cooled. A white solid which precipitated out was filtered off, washed with acetone (3 × 100 mL), and dried at 80 °C to give **g5** (0.67 g, 48%) as a white product. ^{1}H NMR (400MHz, H_2O), δ (ppm): 8.78 (4H, d, Py–H, J = 6.8 Hz), 8.50 (2H, t, Py–H, J = 14.4 Hz), 8.00 (4H, t, Py–H, J = 14.4 Hz), 4.75 (4H, s, Py–CH_2), 3.10 (4H, s, CH_2OH). MS (m/z): calcd., 420.1; found, 420.2(M + Br)$^+$.

1-(3-Bromo-2,2-bis(bromomethyl)propyl)pyridinium bromide (g6). A solution of pentaerythritol tetrabromide (**6**) (2.0 g, 5.2 mmol) and pyridine (0.41 mL, 5.2 mmol) in dioxane (100 mL) was refluxed for 24 h, then concentrated until the mass solid precipitated. The brown solid was filtered and washed with ether (3 × 60 mL). The needle product **g6** (0.48 g, 20%)was obtained after recrystallization from methanol.

Table 1 Crystallographic data for the compounds **g5**, **g6**, Q[8]-**g4**, Q[8]-**g6**

Compounds	**g5**	**g6**	Q[8]-**g4**	Q[8]-**g6**
Empirical formula	$C_{15}H_{23}N_2O_{3.5}Br_2$	$C_{10}H_{13}NBr_4$	$C_{66}H_{104}N_{34}O_{34}Br_2$	$C_{58}H_{110.5}N_{33}O_{40.5}Br_{3.5}Cl$
Formula weight	447.17	466.85	2077.67	2233.43
Crystal system	Orthorhombic	Monoclinic	Monoclinic	Orthorhombic
Space group	P b c n	P 21/c	P 21	P 21 21 2
a/Å	9.339(8)	13.284(3)	18.139(5)	25.514(4)
b/Å	15.689(14)	9.1181(18)	21.311(5)	27.351(4)
c/Å	12.461(11)	11.576(2)	22.340(6)	12.6917(18)
α (°)	90.00	90.00	90.00	90.00
β (°)	90.00	97.245(7)	90.915(3)	90.00
γ (°)	90.00	90.00	90.00	90.00
V/Å^3	1826(3)	1390.9(5)	8635(4)	8857(2)
Z	4	4	4	4
λ/Å	0.71073	0.71073	0.71073	0.71073
D calcd., g cm^{-3}	1.629	2.229	1.601	1.675
F 000	900	880	4336	4612
T/K	293	293	223	223
μ(Mo-Kα)/mm^{-1}	4.456	11.544	1.047	1.733
Unique reflns	1620	2719	27095	15516
Obsd reflns	1128	1999	21096	9360
Params	97	136	2199	987
R_{int}	0.0557	0.0772	0.0401	0.0923
$R[I > 2\sigma(I)]^a$	0.0327	0.0478	0.0599	0.0697
$wR[I > 2\sigma(I)]^b$	0.0772	0.1155	0.1571	0.1692
Flack value			0.034(2)	0.340(10)

^{a} Conventional R on Fhkl: $\Sigma||Fo| - |Fc||/\Sigma|Fo|$. ^{b} Weighted R on $|F hkl|^2$: $\Sigma[w(Fo^2 - Fc^2)^2]/\Sigma[w(Fo^2)^2]^{1/2}$.

^{1}H NMR (400 MHz, H_2O), δ (ppm): 8.78 (2H, d, Py–H, J = 6.8 Hz), 8.50 (H, t, Py–H, J = 14.4 Hz), 8.00 (2H, t, Py–H, J = 14.4 Hz), 4.75 (2H, s, Py–CH_2), 3.43 (6H, s, Br–CH_2).

Instrumentation and measurements

ESI MS spectra for the pentaerythritol derivatives were obtained on an HPLC-MSD-Trap-VL spectrometer without using the LC part. For the study of host–guest complexation of Q[8] and the title guests, samples of 1.0–2.0 mg of one of the guests in ~0.5 mL D_2O were prepared containing enough of the host Q[8] (note: the excess Q[8] is insoluble and precipitates in NMR tubes). The ^{1}H NMR spectra were recorded at 20 °C on a Varian INOVA-400 spectrometer. Absorption spectra of the host (Q[8])–guest (pentaerythritol derivatives) complexes were recorded on an Agilent 8453 spectrophotometer at room temperature. Aqueous solutions of the bromide salts of the pentaerythritol derivatives were prepared with a concentration of 1.0×10^{-3} mol L^{-1}. These stock solutions were combined to give solutions containing a fixed guest concentration of 6.0×10^{-5} mol L^{-1} in each solution with a Q[8] : guest ratio of 0, 0.2 : 1, 0.4 : 1, 0.6 : 1, 0.8 : 1, 1 : 1 *etc.*, and each solution was characterized by absorption spectroscopy. Determination of K values was performed and error analyses carried out as described by us elsewhere.[50]

Preparation of single crystals of compound g5 and g6

Single crystals of both compounds **g5** and **g6** can be obtained from an ethanol aqueous solution. The compound **g5** or **g6** (0.40 g) in ethanol aqueous solution (15 mL $V_{ethanol}/V_{water}$ = 1 : 1) was heated with stirring at 50 °C for 2 h. The solution was filtered and the filtrate was allowed to stand at room temperature for several days. Colorless X-ray quality crystals of the compound **g5** and **g6** were obtained from the solution. Anal. Calcd for $C_{15}H_{23}N_2O_{3.5}Br_2$ (**g5**): C, 42.88; H, 4.80; N, 6.67. Found: C, 42.76; H, 4.92; N, 6.58, and for $C_{10}H_{13}NBr_4$ (**g6**): C, 25.73; H, 2.81; N, 3.00. Found: C, 25.57; H, 2.87; N, 2.89.

Preparation of single crystal of compound {Q[8]-g4}

A solution containing Q[8] (0.15 g, 0.10 mmol) and **g4** (0.09 g, 0.20 mmol) in water (10 mL) was heated at 70 °C for 10 min, then filtered and the filtrate was allowed to stand at room temperature. Rock X-ray quality crystal formed after two weeks with a yield of 25%.

Preparation of single crystal of compound {Q[8]-g6}

A solution containing Q[8] (0.15 g, 0.10 mmol) and **g6** (0.09 g, 0.20 mmol) in water (10 mL) was heated at 70 °C for 10 min, then filtered and the filtrate was allowed to stand at room temperature. Rock X-ray quality crystal formed after two weeks with a yield of 23%.

X-Ray crystal structure determination of the related compounds

A suitable corresponding single crystal (~0.2 × 0.2 × 0.1 mm^3) was picked up with paratone oil and mounted on a Bruker Apex2 CCD diffractometer equipped with a graphite-monochromated Mo-Kα (λ = 0.71073 Å) radiation source and a nitrogen cold stream (−50 °C). The data were corrected for Lorentz and polarization effects (SAINT),[51] and semi-empirical absorption corrections based on equivalent reflections were applied (SADABS).[51] The structure was elucidated by direct methods and refined by the full-matrix least-squares method on F^2 (SHELXTL).[52] All the non-hydrogen atoms were refined anisotropically, and hydrogen atoms were added to their geometrically ideal positions. Water molecules in the compounds were omitted using the SQUEEZE option of the PLATON program. 33 and 24 water molecules were removed from the asymmetric units in Q[8]-g4 and Q[8]-g6 system

respectively. Details of the crystal parameters, data collection, and refinements for the guest **g5**, **g6** and the complexes Q[8]-**g4** and Q[8]-**g6** are summarized in Table 1. In addition, the crystallographic data for the reported structures were recorded in the Cambridge Crystallographic Data Centre as no. CCDC 791487 (**g5**), 791488 (**g6**), 791489 (Q[8]-**g4**) and 791490 (Q[8]-**g6**) seeing ESI† for details.

It should be noted that the compound **g5** has crystallographically imposed twofold symmetry on *b* axis. In the asymmetric unit of the compound Q[8]-**g4**, there are two independent Q[8]-**g4** complexes. In addition, the counter anion Br4 (Br4A, Br4B, Br4C, Br4D) is disordered over four positions with occupancies of 0.42495, 0.04718, 0.49496. 0.03556 (SHELXL SUMP) respectively, in particular, Br4C and Br4D are treated with EADP to ensure that these two atoms have common anisotropic displacement parameters. In the compound Q[8]-**g6**, The atoms C12, C31 and C40 of Q[8] are treated with commands EADP, DELU to modify anisotropic displacement parameters.

Results and discussion

Interaction of Q[8] with g1 and g2

It was surprising to discover that the guests **g1** and **g2** synthesized from aldehydes exhibit special stereo-rigidity so that the two methylenepyridyl branches and the 1,3-dioxane moiety in the molecules show different chemical shifts in the ^{1}H NMR spectra (Fig. 1a and 2a), and the guests **g1** and **g2** seem to be unsymmetrical.[53]

Fig. 1 shows the ^{1}H NMR spectra of the guests **g1** recorded in the absence and in the presence of enough equivalents of Q[8] (the excess Q[8] is insoluble and precipitates in the NMR tube). Compared to the free guest **g1**, the most noticeable effect observed upon Q[8] addition is the significant upfield displacement of one of the two pyridyls protons of the guest **g1**. The resonances of the pyridyl protons (positions 6, 7, 8) of the bound **g1** are shifted upfield by 1.0–1.4 ppm respectively in the presence of excess Q[8], and moreover, the resonances of the phenyl protons (position 10, 11, 12), methyl and methylene protons (positions 4′, 5, 5′ and 9) are also shifted upfield by 0.2–1.0 ppm, indicating a cavity inclusion. However, the resonances of another pyridyl protons (position 1, 2, 3) and the methyl protons (position 4) of the guest **g1** are shifted downfield by 0.1–0.4 ppm, indicating that these parts of the guest **g1** are near or just outside a portal of the host Q[8], and the consequent effect on the Q[8] proton resonances is that the

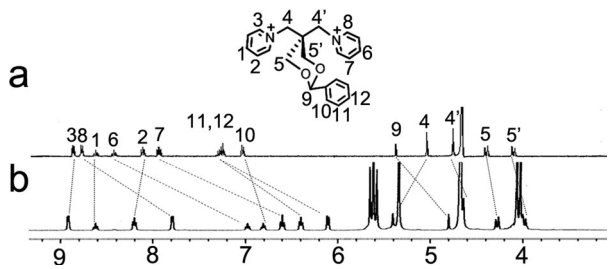

Fig. 1 ^{1}H NMR spectra of **g1** recorded in the absence (a) and in the presence of excess of Q[8] (b).

methylene resonances near the portal of the Q[8] molecule are magnetically not equivalent to those near the opposite portal. This is clearly evident from the split of the doublet of the methylene protons of the Q[8] host. A comparison of the integrals of the protons of the bound **g1** with the protons of Q[8] revealed the complex to be a 1 : 1 host : guest species.

By comparison, the relative chemical shifts observed for the proton resonances of the guest **g2** bound in Q[8] (Fig. 2) are similar in direction and vary only slightly in magnitude. One of two pyridyl protons (positions 6, 7, 8), the thiophene protons (position 10, 11, 12), and the methyl and methylene protons (positions 4′, 5, 5′ and 9) of the guest **g2** are shifted upfield by 0.2–1.4 ppm, while the resonances of the remaining pyridyl protons (position 1, 2, 3) and the methyl protons (position 4) of the guest **g2** are shifted downfield by 0.1–0.4 ppm. The largest difference (0.3 ppm further upfield) is found for the thiophene ring protons (position 11) when the guest **g2** is bound in the cavity of Q[8], compared to the guest **g1**. The reason for this difference could be the size of the aromatic ring. Obviously, the phenyl ring is larger than the thiophene ring, so the proton at position 11 on the guest **g2** is deeper than that at position 11 on the guest **g1** in the cavity of the host Q[8]. The integrals of the protons of the bound **g2** and Q[8] revealed the complex also to be a 1 : 1 host : guest species.

Thus, it became clear from the ^{1}H NMR spectra of Q[8] and the guest **g1** or **g2** interactions that the host Q[8] includes all branches of the guest **g1** or **g2** except one of the methyl-pyridyl branches due to the limit of cavity capacity. Although Q[8] proved to have a strong preference for inclusion of two aromatic rings,[40–45,54] the repulsion of the two positively charged pyridyl rings on the guest would prevent the existence of two pyridyl rings in the same cavity of the host Q[8]. Thus, the ^{1}H NMR study implies that the host Q[8] exhibits a preference towards including one of the methyl-pyridyl branches and the 1,3-dioxane with an aromatic tail, and excluding the rest of the methyl-pyridyl branch for the host–guest complexes of Q[8]-**g1** and Q[8]-**g2**.

To quantify the interaction between Q[8] and **g1** or **g2**, a ratio-dependent study was pursued by electronic absorption spectroscopy. Usually, the free host Q[8] shows no absorbance at $\lambda > 210$ nm. Fig. 3(a) and (b) show the variation in the UV spectra obtained from aqueous solutions containing a fixed concentration of the guest **g1** or **g2** (6.0×10^{-5} mol L^{-1}) and variable concentrations of Q[8]. Both absorption bands of the guests **g1** and **g2** exhibit a progressively lower absorbance as the ratio of $N_{Q[8]}/N_{\mathbf{g1}\text{ or }\mathbf{g2}}$ is increased, and the sharp isosbestic points at 244 and 269 nm for the Q[8]-**g1** system and at 270 nm for the Q[8]-**g2** system are consistent with a simple interaction between Q[8] and the guest **g1** or **g2**. The absorbance (A) *vs.* ratio of moles of the host Q[8] and the guest **g1** or **g2** ($N_{Q[8]}/N_{\mathbf{g1}\text{ or }\mathbf{g2}}$) data can be fitted to a 1 : 1 binding model for both of the Q[8]-**g1** and Q[8]-**g2** systems at λ_{max} 260 nm [the insert in the Fig. 3(a) and (b)]. This behavior is consistent with the results from the ^{1}H NMR study.

The data from the absorption spectra for both host–guest systems fitted to a simple 1 : 1 host : guest complexation,[50] and yielded a calculated binding constant (K) of 2.88×10^3 L mol^{-1} for the Q[8]-**g1** system and 1.24×10^4 L mol^{-1} for the Q[8]-**g2** system.

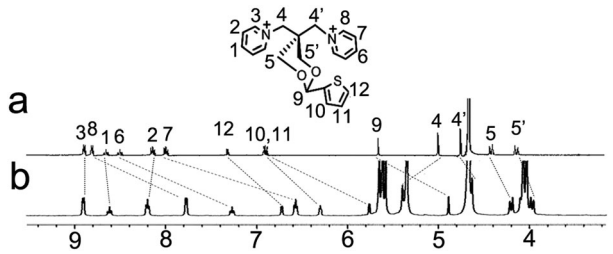

Fig. 2 ^{1}H NMR spectra of **g2** recorded in the absence (a) and in the presence of excess of Q[8] (b).

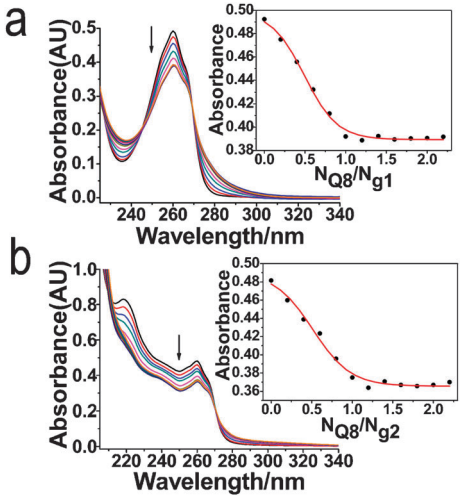

Fig. 3 Electronic absorption spectra of **g1** (a) and **g2** (b) in the presence of increasing concentrations of Q[8] and corresponding absorbance *vs.* $N_{[Q8]}/N_{\mathbf{g1}}$ curve [insert in (a)] and $N_{[Q8]}/N_{\mathbf{g2}}$ curve [insert in (b)] at λ_{max} = 260 nm.

Interaction of Q[8] with g3–5

Unlike the guests **g1** and **g2**, the guests **g3** and **g4** which are synthesized from ketones exhibit a symmetrical configuration, and the two methylenepyridyl moieties and the 1,3-dioxane ring in the guest molecules show the same chemical shifts in the ^{1}H NMR spectra [Fig. 4(a, c, e)]. Fig. 4 shows the ^{1}H NMR spectra of the three guests **g3–5** recorded in the absence and in the presence of enough equivalents of Q[8] (the excess Q[8] is insoluble and precipitates in the NMR tube). Compared to the first two Q[8]-**g1** and Q[8]-**g2** host–guest interaction systems, there are no significant upfield displacement for any protons in these three guests **g3–5** upon Q[8] addition. For the guest **g3**, one can see the obvious upfield displacement for the protons of the 1,3-dioxane branch and the adamantanyl tail, indicating a cavity inclusion. However, the protons of the two methylenepyridyl branches in the guest molecule are shifted slightly upfield by 0–0.4 ppm in the presence of excess Q[8] indicating that the two methylpyridyl branches of the guest molecule are included at a portal zone of the host Q[8]. The split of the doublet resonances of the methylene proton of the host further supports this conclusion [Fig. 4(b)]. For the guests **g4** and **g5**, all proton resonances in the molecule are shifted upfield by 0.15–0.8 ppm in the presence of excess Q[8], indicating that the whole guest molecule is in the shielding area of the host Q[8]. That is, the whole guest molecule is included in the cavity of the host Q[8] [Fig. 4(d) and (f)]. The integrals of the protons of the three bound guests and Q[8] revealed the inclusion complexes to be also 1 : 1 host : guest species.

Fig. 5 shows the variation in the UV spectra obtained from aqueous solutions containing a fixed concentration of the guest **g3** or **g4** or **g5** (6.0×10^{-5} mol L^{-1}) and variable concentrations of Q[8]. The absorption bands of the guest **g3** exhibit a progressively higher absorbance, with a blue shift, as the ratio of $N_{Q[8]}/N_{\mathbf{g3}}$ is increased. While the absorption bands of the guests **g4** and **g5** exhibit a progressively lower absorbance as the ratio of $N_{Q[8]}/N_{\mathbf{g4\,or\,g5}}$ is increased. One can also see the sharp isosbestic points at 245 and 268 nm for the Q[8]-**g4** system and at 225, 246 and 268 nm for Q[8]-**g5**. The absorbance (A) *vs.* mole ratio of the host Q[8] and the guest **g3** or **g4** or **g5** ($N_{Q[8]}/N_{\mathbf{g3\,or\,g4\,or\,g5}}$) data can be fitted to a 1 : 1 binding model for these three host–guest inclusion systems at λ_{max} 258 nm for the Q[8]-**g3** system [the insert in Fig. 5(a)] and λ_{max} 260 nm for both Q[8]-**g4** and Q[8]-**g5** systems [the inserts in Fig. 5(b) and (c)], respectively.

The data from the absorption spectra of these three host–guest systems, fitted to a simple 1 : 1 host : guest complexation, yielded a calculated binding constant (K) of 2.43×10^4 L mol^{-1} for the Q[8]-**g3** system, 1.00×10^4 L mol^{-1} for the Q[8]-**g4** system and 2.68×10^4 L mol^{-1} for the Q[8]-**g5** system, respectively.

Based on the results from spectrophotometric analysis, one can see the absorption bands of all guests exhibiting similar trends and showing sharp isosbestic points, except those of the guest **g3**, which gives progressively higher absorbance bands without an obvious isosbestic point. A comparison of the absorption bands of the mentioned five guests with the corresponding ^{1}H NMR spectra, in the presence of the host Q[8], indicates that all five host–guest complexes are with a 1 : 1 host : guest ratio and the preference for inclusion of the host Q[8] for the different branches of the guests can lead to different absorbance properties. For example, the guest(s), for which the methylpyridyl branch is included in the cavity of the host Q[8] exhibit a progressively lower absorbance and sharp isosbestic points as the ratio of $N_{Q[8]}/N_{\mathbf{g}}$ is increased. In contrast, Q[8]-**g3** system, in which the branches other than the methylpyridyl branch(es) are included in the cavity of Q[8], exhibit a progressively higher absorbance and no obvious isosbestic point as the ratio of $N_{Q[8]}/N_{\mathbf{g}}$ is increased.

Interaction of Q[8] with g6

In this work, the guest **g6** is the only one containing one substituted pyridyl. Unexpectedly, the ^{1}H NMR spectra of the guest **g6** recorded in the absence and presence of sufficient Q[8] reveal that the host Q[8] prefer to include the three brominemethyl branches but the aromatic ring[54] (Fig. 6). Compared to the free guest **g6**, the proton resonances of the brominemethyl branches of the bound guest **g6** are shifted upfield by 0.5 ppm indicating a cavity inclusion. However, the proton resonances of the aromatic ring in the guest **g6** are partially shifted upfield (for the protons at positions 3 by 0.4 ppm) and partially shifted downfield (for the protons at

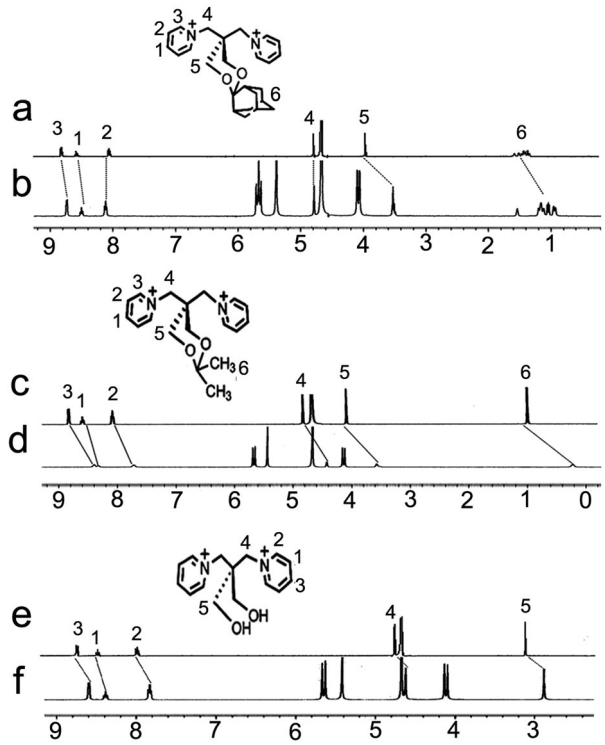

Fig. 4 ^{1}H NMR spectra (400 MHz, D_2O, rt) recorded for the free guest (a) **g3**, (c) **g4**, (e) **g5** and in the presence of excess of Q[8] (b) Q[8]-**g3**, (d) Q[8]-**g4**, (f) Q[8]-**g5**.

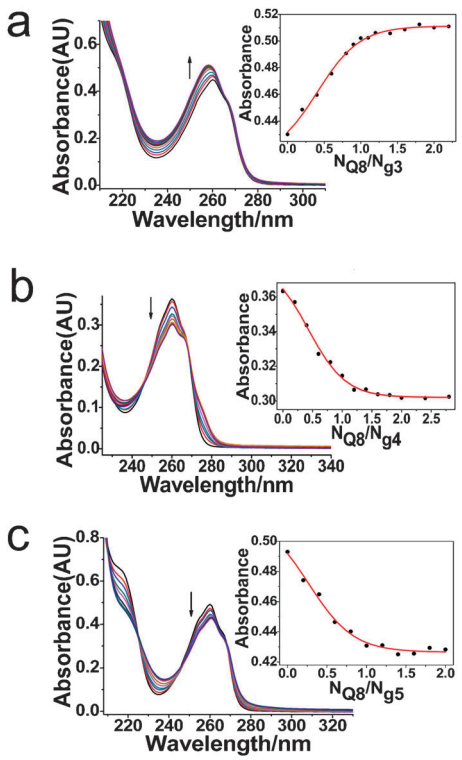

Fig. 5 Electronic absorption spectra of **g3** (a), **g4** (b) and **g5** (c) in the presence of increasing concentrations of Q[8] and absorbance *vs.* $N_{[Q8]}/N_{\mathbf{g3}}$ curve [insert in (a)] at λ_{max} = 258 nm, and absorbance *vs.* $N_{[Q8]}/N_{\mathbf{g4}\text{ or }\mathbf{g5}}$ curves [insert in (b) and (c)] at λ_{max} = 260 nm.

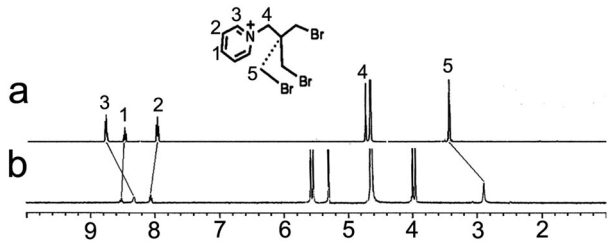

Fig. 6 ^{1}H NMR spectra of **g6** recorded in the absence (a) and in the presence of excess of Q[8] (b).

position 1, 2 by ~0.1 ppm) suggesting that the pyridyl moiety is at the portal zone of the Q[8] cavity. This is confirmed by the crystal structure of Q[8]-**g6**, which we will describe later. Unfortunately, the guest **g6** shows no obvious absorption property, so we cannot use spectrophotometric analysis to quantify the interaction between Q[8] and **g6**. However, we can obtain some structural information from other methods, such as crystal structure determination.

Although we have not obtained crystal structures of all species, the crystal structures obtained can provide additional information for related species, and further confirm or contradict the structural information obtained under aqueous conditions. Fig. 7 shows the structure of the guest **g5**, in which the two methylpyridyl branches are located far apart so the molecule has a ~6.0 Å width and ~11.8 Å length. Compared to the portal size of the host Q[8] (showing a variation from ~8.6 to ~11.8 Å in the crystal structures in this work), the guest **g5** can easily thread through the cavity of the host Q[8] lengthways with a fast exchange. It should be noted that the cavity of Q[8] can not contain the whole guest **g5**, and the formation of a symmetrical inclusion host–guest complex just results in the fast exchange of the guest **g5** in the cavity of Q[8]. This explains well why the doublet methylene resonances of the host Q[8] do not split in the ^{1}H NMR spectra [Fig. 4(f)]. Similarly, the guest **g4** can thread through the cavity of the host Q[8] lengthways, and seems to form a symmetrical inclusion host–guest complex in aqueous solution, One can also see that the doublet methylene resonances of the host Q[8] do not split in the ^{1}H NMR spectra [Fig. 4(d)].

It is interesting that the observation of an asymmetrical structural conformation of Q[8]-**g4** in the solid state seems to present a controversy in that the crystal structure is not consistent with the solution structure. The single crystal structure of Q[8]-**g4** reveals that a pyridylmethylene branch and the 1,3-dioxane branch are included in the cavity of the

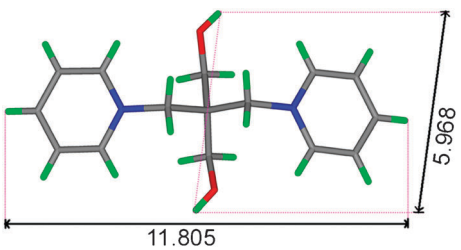

Fig. 7 Crystal structure of the free guest **g5**.

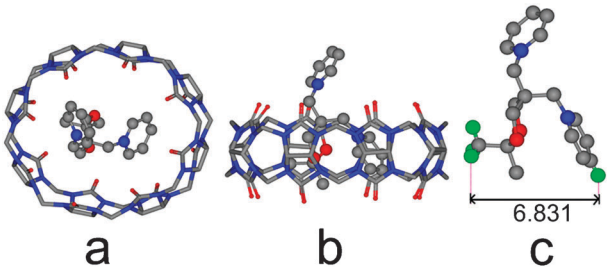

Fig. 8 Crystal structures of the inclusion complex Q[8]-**g4** top view (a), side view (b) and the bound guest **g4** (c).

host Q[8], while the remaining pyridylmethylene branch is included in a portal zone of the host Q[8] as shown in Fig. 8(a) and (b), the bound guest presents an unsymmetrical conformation as shown in Fig. 8(c). The formation of an asymmetrical host–guest complex is a direct consequence of inclusion of the asymmetrical guest. However, based on the solution studies, we suggest that the host Q[8] prefers to include the whole guest molecule in a symmetrical arrangement to form a symmetrical inclusion host–guest complex. To explain this contradiction, it should be noted that the broadening of the guest proton resonances indicates host–guest binding with fast exchange in the solution, the two identical pyridyl can go alternately into the cavity of Q[8] so that the signals for pyridyl (7.7–8.5 ppm) might be the average signals for two pyridyl due to fast exchange. Moreover, if the guest rearranges itself into the conformation as shown in Fig. 8(c), the size of the two branches of pyridylmethylene and the 1,3-dioxane with two methyl tails can be as large as ~6.8 Å which is more suitable for the stable inclusion in the cavity of the host Q[8]. This could be the reason for the formation of an asymmetrical host–guest complex in the solid state.

Fig. 9 shows the crystal structures of the free guest **g6** and the inclusion complex of Q[8]-**g6**. Compared with the crystal structure of the free guest **g6** to that of the bound guest **g6** [Fig. 9(a), (b)], one can see that one C–Br bond is almost vertical to other two C–Br bonds in three brominemethylene branches in both cases.The pyridyl is *trans* to this C–Br bond in the free guest, while the pyridyl is *cis* to the this C–Br bond in the bound guest, and the orientation of the pyridyl in the bound guest facilitates the guest entering the cavity of the host Q[8]. Although the size of the guest **g6** could be entirely included in the cavity of Q[8], the ion–dipole interaction of the positive nitrogen in the pyridyl moiety with the carbonyl oxygens lead the pyridyl to stay at the portal [Fig. 9(c) and (d)]. Thus, the brominemethylene branches in the cavity will undergo a shielding effect, and the corresponding proton resonances will experience an upfield shift (as observed in the ^{1}H NMR spectra discussed above). Whereas the methylene-pyridyl branch at the portal zone will undergo a deshielding effect, and most proton resonances will experience a downfield shift, as observed in the ^{1}H NMR spectra of Fig. 6.

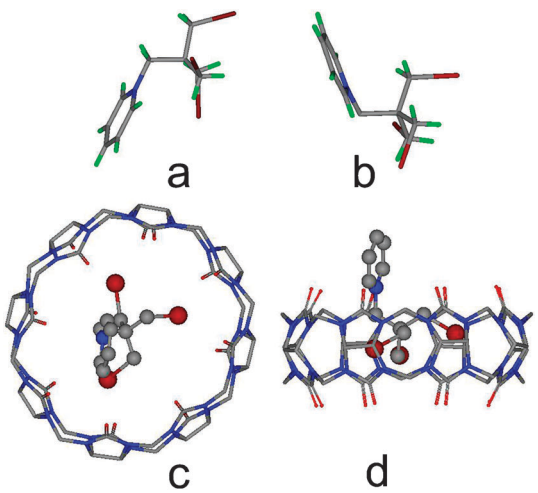

Fig. 9 Crystal structures of the free guest **g6** (a), the bound guest **g6** (b), the inclusion complex Q[8]-**g6**, top view (c), side view (d).

Conclusions

We present a discussion of six Q[8]-based host–guest inclusion complexes. Based on information obtained from ^{1}H NMR, electronic absorption spectroscopy and single crystal X-ray diffraction determinations, the possible interaction models are summarised in Fig. 10. The ^{1}H NMR spectral analysis of the interaction between Q[8] and the named six pentaerythritol derivative guests has established the basic interaction models in aqueous solution. The host Q[8] selectively binds the different branch(es) of the first generation dendritic guests forming different inclusion complexes with a host : guest ratio of 1 : 1. The formation constants in aqueous solution are ~10^4 L mol^{-1} and are determined through electronic absorption spectroscopic analysis. The single crystal structures of two guests and the two Q[8]-**g*n*** complexes are useful for understanding the solution structures of the Q[8]-**g*n*** complexes analyzed using the ^{1}H NMR technique and electronic absorption spectroscopy. In particular, a contradiction in that the crystal structure shows an asymmetrical structural conformation of Q[8]-**g4**, while ^{1}H NMR spectra seem to present a symmetrical solution structure is explained by using fast exchange of the guest in the solution.

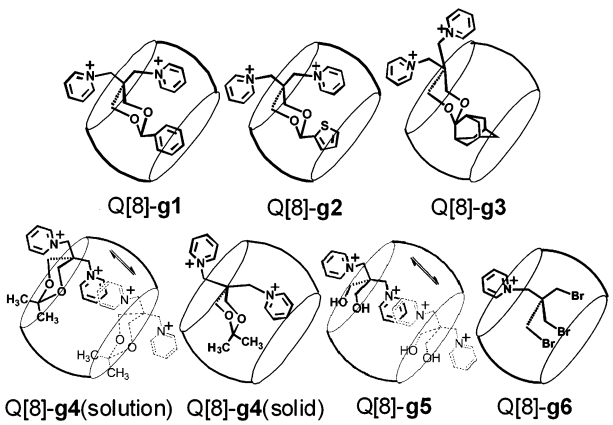

Fig. 10 Possible host–guest complex structures of Q[8]-**g*n*** (***n*** = **1–6**).

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