CHAPTER 7

Host-guest Chemistry: Influence of hydroxyethyl imidazolium group on host-guest interplay in building multi-component bilayers

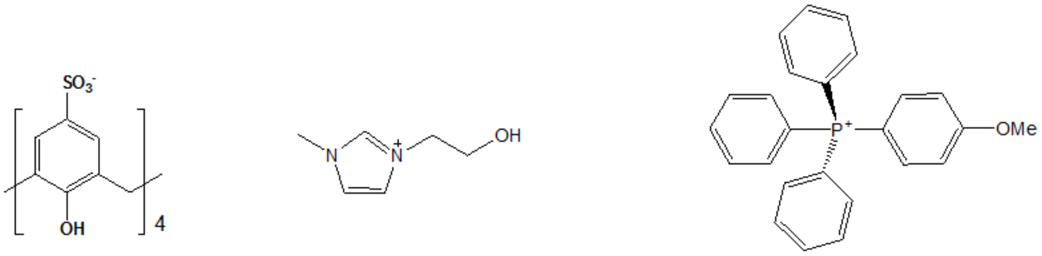
Functionalised 3-(2-hydroxyethyl)-1-methylimidazolium, p-sulfonatocalix[4]arene and phosphonium cation, in the presence of aquated gadolinium(III) ion, afforded self-assembled multi-component material where the imidazolium cation preferentially binds in the calixarene cavity, as supermolecules [3-(2-hydroxyethyl)-1-methylimidazolium∩p-sulfonatocalix[4]arene], which are organised into bilayers, with metal ions coordinated between the bilayers. The interplay of the components in the supermolecules has been mapped out using Hirshfeld surface analysis, with the same supermolecules also evident in aqueous solution, as determined using ^{1}H NMR spectroscopy.

7.1 Introduction

In supramolecular chemistry weak non-covalent interactions involving hydrogen bonding, metal coordination, van der Waals, π-π and cation-π interactions are important in understanding the nature of host-guest interactions [2]. Water-soluble calix[n]arenes show potential bio-activities for enzyme inhibition through anti-thrombotic activity and anti-viral activity.[84, 201, 202] These classes of calix[n]arenes can mimic the natural biological processes by binding apolar guests through the hydrophobic pockets [84, 118].

Water-soluble calix[n]arenes bearing sulfonate substituents at the *para*-positions have biological response activity, such as antimicrobial and anti-thrombotic activity.[84, 201, 202] Anionic *p*-sulfonatocalix[4]arene usually adopt a cone conformation with the upper rim being hydrophilic and the internal (*endo*-) and external (*exo*-) area of the cavity is hydrophobic. This class of calixarene assembles into bilayer arrangement as highlighted in Chapters 3 to 6, or more complicated supramolecular architectures such as spheroidal and tubular arrays [122-124]. Apart from its versatility in building various supramolecular architectures, *p*-sulfonatocalix[4]arene are of interest in forming *endo*-cavity inclusion complexes with different guest molecules of various sizes and shapes.

7.2 Structural features involving 3-(2-hydroxyethyl)-1-methylimidazolium



1
p-sulfonatocalix[4]arene

16
3-(2-hydroxyethyl)-1-methylimidazolium

11
[(3-methoxyphenyl) triphenylphosphonium

Figure 7.1. Components in synthesis of complex **XVIII**.

Slow evaporation of a water/tetrahydrofuran (THF) solution containing the components shown in Figure 7.1 afforded colourless prisms which crystallise in triclinic space group *P*-1 with the asymmetric unit comprised of one *p*-sulfonatocalix[4]arene anion, **1**, with an aquated gadolinium(III) cation, one 3-(2-hydroxyethyl)-1-methylimidazolium cation, **16**, and one phosphonium cation [(3-methoxyphenyl) triphenyl-phosphonium], **11**.

In the extended structure, the sulfonated calixarenes are assembled into bilayers with the phosphonium cations embedded in between the bilayers with a thickness of close to 13 Å, while the distance between bilayers is approximately 18 Å, Figure 7.2. This type of self-assembled construction is similar to structures as discussed in Chapter 4, involving *n*-octyl-imidazolium cation, having comparable bilayer and inter bilayer thicknesses. The building of the multi-component structure is assisted by the homoleptic gadolinium(III) metal ions which form secondary coordination sphere with eight water molecules and interact with the calixarene through hydrogen bonding, as indicated by the close proximity of the O-atom of the sulfonate group to the aquated gadolinium cations, closest O···O distances being 2.695(8) to 2.810(5) Å. The complex also contains included water molecules in the hydrophilic region which are involved in extended hydrogen bonding with calixarene sulfonate groups and also between themselves with O···O distances in the range 2.551(10) to 2.998(8) Å. The arrangement of the phosphonium cations in the bilayer is controlled by hydrogen bonding between H-atoms from the phosphonium to the O-atoms of calixarene (sulfonate and phenolic segments), with distances ranging from 2.36 to 2.79 Å.

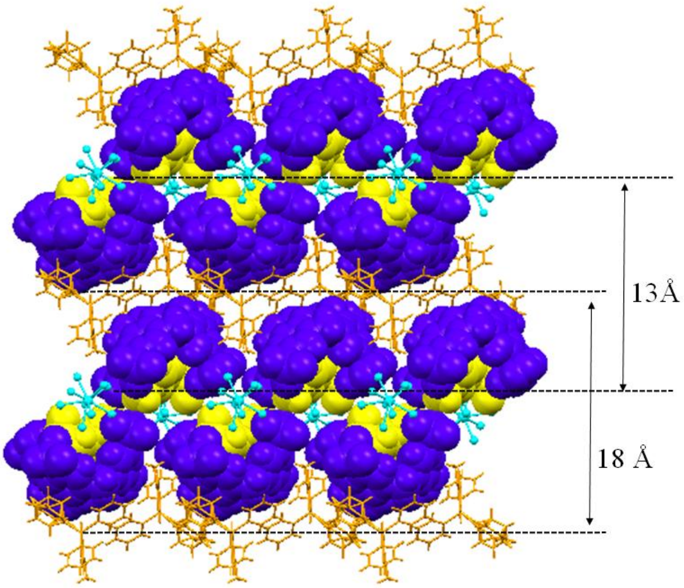


Figure 7.2. Projection down the *a*-axis with some space filling of calixarene (purple) and 3-(2-hydroxyethyl)-1-methylimidazolium cation (yellow), showing layers of phosphonium cations (orange).

The hydroxyethyl-methylimidazolium cation fits in the calixarene cavity, with two of the calixarene phenolic rings pinching around the imidazolium aromatic ring where the five-membered ring is positioned approximately parallel to one of the phenolic ring with the π···π centroid to centroid distance at 3.75 Å. The other two phenolic rings are splayed apart, with the corresponding sulfonate groups positioned close to the two terminis of the imidazolium cation, which are involved in C–H···O interactions at distances ranging from 2.31 to 2.60 Å (equivalent C···O distances from 3.22 to 3.60 Å). The C–H···O interaction is dominant and is evident from the fingerprint plot generated from the Hirshfeld surface analysis where the corresponding interaction has the largest contribution to the overall intermolecular interaction. The shortest C–H···O distance appeared as a spike (labelled **1**) and is apparent as a bright red spot on the d_{norm} visualization surface from the Hirshfeld surface. The weak C–H···π intermolecular interaction is also significant, involving the H-atoms of imidazolium aromatic ring and the methylene H-atom which point toward the calixarene phenyl rings, with distances ranging from 2.54 to 2.63 Å (equivalent C··· π distances from 3.28 to 3.60 Å). The wing at the upper left of the plot (circled in red), highlights the distinctive C–H···π donor interactions and the red regions on the d_{norm} surface designated as **2**, identify the associated C–H···π close contacts, Figure 7.3.

Interestingly, there is an included water molecule which is in close distance with the O-atom from the imidazolium hydroxy, with O···O distance at 2.7 Å, and is located above the imidazolium aromatic ring, having a close O···π contact at 3.1 Å, Figure 7.4. These intermolecular contacts are visible in the fingerprint plot (spikes labelled **3** and **4** respectively) and the corresponding contacts are noticeable at the d_{norm} surface as well. Shape index further clarifies the close contact between the molecules where a complementary hollow region (red) represents the two molecular surfaces touching one another. Interestingly, the O-H···π interaction was also noted for sulfonated calixarene between water and aromatic π electrons of the phenolic rings [86], as well as for the formation of inclusion complex between calixarene and adenine, where one water molecule is deeply embedded within the host cavity [96]. The water molecule also have a H-bond to one of the calixarene sulfonate groups with O···O distance at 2.68 Å.

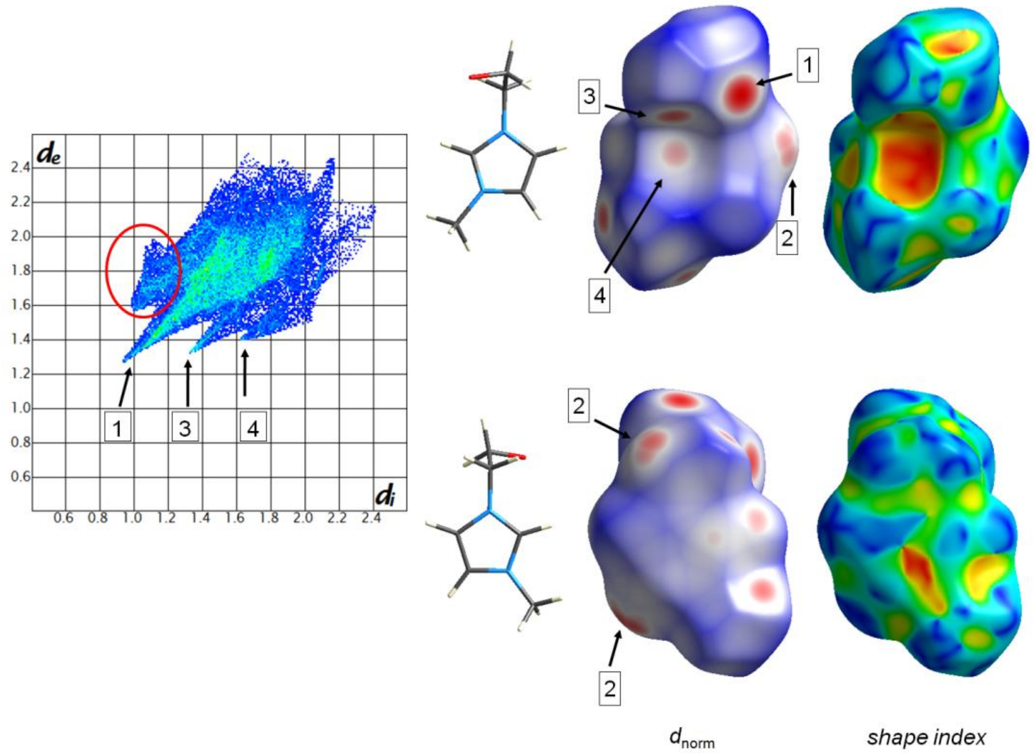


Figure 7.3. Fingerprint plot, and front and back views of the Hirshfeld surface for 3-(2-hydroxyethyl)-1-methylimidazolium, mapped with d_{norm} and shape index.

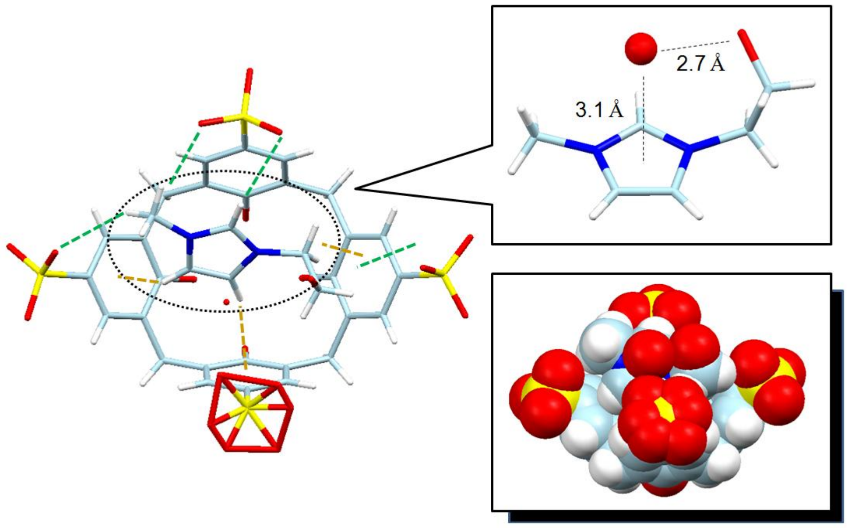


Figure 7.4. Stick representation showing close contacts between 3-(2-hydroxyethyl)-1-methylimidazolium and calixarene (H-bonds and C–H···π are shown as green and brown dashed lines respectively). Water molecule in close distance with the cation (inset top) and space filling showing the upper surface of the supermolecule is essentially hydrophilic (inset bottom).

Fingerprint plot for calixarene exhibits three “spikes” that are evident with the outermost spikes represent hydrogen bonding interactions (with the lower spike being the acceptor spike while the upper spike being the donor spike), Figure 7.5 (a). The acceptor spike is more intense than the donor spike, making up 27% of the Hirshfeld surface (compared to 5% for the donor spike), which can be understood by the -5 charge on the calixarene where only 3 O-atoms are protonated. The third spike with red streaking, which bisects the acceptor and donor spikes, corresponds to close O···O contact, principally from the O-atom of the calixarene sulfonate group to the closest water molecule bound in close proximity to the calixarene and imidazolium cation.

Figure 7.5 (b) displays the fingerprint plot for phosphonium cation at close proximity around calixarene molecule. The H···H bonding network is dominant in the overall intermolecular interaction, comprises 50% of the surface for both structures, with closest contacts for $d_e + d_i$ at 2.10 Å. The O···H donor spike in the finger print plot show close contacts corresponding to H-bonding between phosphonium H-atoms and methoxy group to O-atoms of calixarene sulfonate and hydroxy groups.

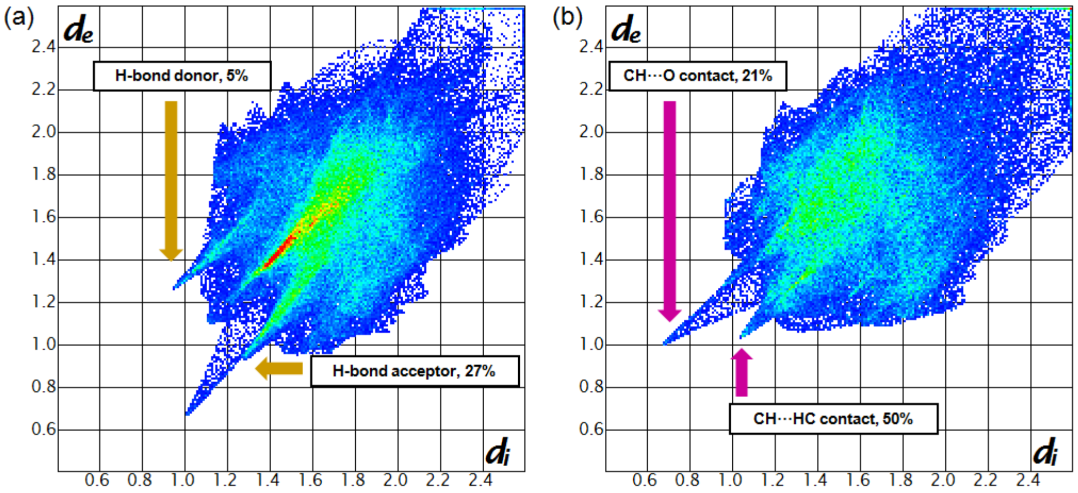


Figure 7.5. Fingerprint plots for (a) *p*-sulfonatocalix[4]arene and (b) [(3-methoxyphenyl) triphenyl-phosphonium.

7.3 Solution studies

The persistence of [3-(2-hydroxyethyl)-1-methylimidazolium∩*p*-sulfonatocalix[4]arene] supermolecule formation in solution was examined using ^{1}H NMR at 25^{o}C (D_2O) for a 1:1 mixture of the two species, Figure 7.6. The findings from the solution study are comparable to other host-guest system involving other imidazolium cations and calixarene. The interplay of the two components, in solution is consistent with the crystal packing in the solid state. Upfield chemical shifts experienced by all the protons of the hydroxyethyl-methylimidazolium cation are consistent with the shielding effect of the calixarene when the imidazolium cation resides in the cavity. Also noteworthy is that is that the calixarene is conformationally rigid, with a well resolved AB spin system for the methylene protons (*). This is different to our previous solution studies involving other imidazolium cations where the conformation mobility for calixarene was present. This presumably relates to the structure of the supermolecule in solid state which has the imidazolium cation embedded in the cavity with the associated water molecule then hydrogen bonding with sulfonate groups, at the same time making the upper surface of the supermolecule hydrophilic, Figure 7.4.

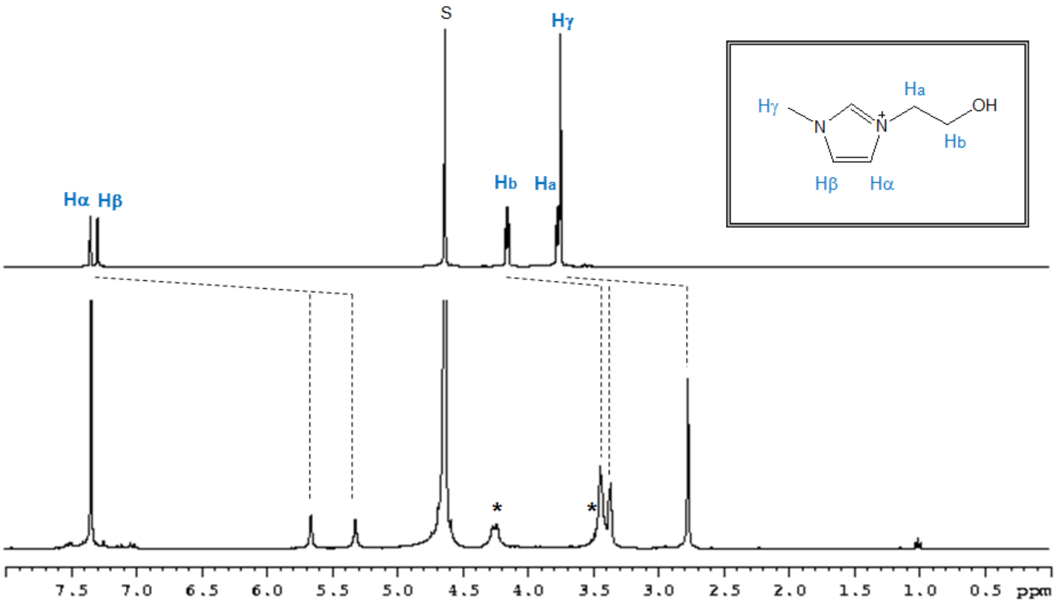


Figure 7.6. ^{1}H NMR spectrum for (top) 3-(2-hydroxyethyl)-1-methylimidazolium, and (bottom) 3-(2-hydroxyethyl)-1-methylimidazolium in *p*-sulfonatocalix[4]arene (1:1), measured in D_2O (**S**).

7.4 Conclusions

This host-guest interplay of the hydroxyethyl-methylimidazolium cations with the calixarenes is similar to other findings for imidazolium cations bearing different alkyl chains in Chapters 3 to 6, which also reside in calixarene cavities in the solid state and in solution. The thickness of the bilayers with phosphonium cations embedded within them is also similar with other calixarene-imidazolium systems. The hydroxy group from the imidazolium cation which resides in the calixarene cavity effectively restricts the conformation of calixarene as compared to previous findings in Chapters 4 to 6.

7.5 Experimental Section

A. General remarks on crystal growth

p-Sulfonatocalix[4]arene sodium salt, was synthesised as described in Section 3.4. (3-methoxyphenyl) triphenylphosphonium iodide, **11** and 3-(2-hydroxyethyl)-1-methylimidazolium dicyanamide **16** were purchased from Sigma Aldrich. A hot solution of three fold excess of $GdCl_3{\cdot}6H_2O$ in water (0.5 mL) was added to a hot solution of mixture containing one equimolar of each component; phosphonium, hydroxyethyl-methylimidazolium and *p*-sulfonatocalix[4]arene, in a mixture of THF/water (1:1, 2 mL). The prepared solutions were left to cool and allowed to slowly evaporate, with crystals forming over several days. Several suitable crystals were selected for X-ray diffraction studies. ^{1}H NMR spectra were collected on a Varian 400 MHz spectrometer using D_2O at 25°C.

B. Crystallography details

X-ray Crystallography

All data were measured as described in Section 3.4.

Crystal/refinement details for Complex XVIII:

$C_{28}H_{20}O_{16}S_4^{5-}$, $C_{25}H_{22}OP^+$, $C_6H_{11}N_2O^+$, $Gd(H_2O)_9^{3+}$, 4.5(H_2O), $C_{59}H_{79}GdN_2O_{31.50}PS_4$, M = 1636.70, colorless plate, 0.37 x 0.18 x 0.11 mm^3, a = 12.4592(18), b = 13.347(2), c = 20.678(3) Å, α = 91.837(12), β = 101.514(12), γ = 92.699(12)°, V = 3362.5(9) Å^3, Z = 2, D_c = 1.617 g/cm^3, μ = 1.227 mm^{-1}, F_{000} = 1684, $2\theta_{max}$ = 58.6°, 32176 reflections collected, 15649 unique (R_{int} = 0.0735). Final *GooF* = 0.936, $|\Delta\rho_{max}|$ = 1.576 e Å^{-3}, *R1* = 0.0599, *wR2* = 0.1186, *R* indices based on 15649 reflections with I >2σ(I), 904 parameters, 25 restraints. CCDC number: 760928.