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COMMUNICATION

Progressive compression of 1, ω -diammonium-alkanes inside a rigid crystalline molecular cage

Cite this: DOI: 10.1039/x0xx00000x

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Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

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We present herein the compression mechanisms of linear of 1, ω -diammonium-alkanes, confined within a molecular cage self-assembled in water. The exact coiling behaviour is determined from atomic resolution X-ray diffraction and shows crenel-like conformations in the compressed states.

Self-assembled molecular cages and capsules, providing specific and confined nanospace, are extremely useful for catalysis and recognition applications.¹ Molecular encapsulation²⁻⁵ is a fascinating domain as the dynamic behaviors of encapsulated guests^{6,7} are generally different inside capsules and in the bulk solution. For example, the ability to encapsulate water-clusters offer possibilities to explore their dynamic behaviours which are very similar to pore-confined biological water.^{8,9} The question as to how the hydrophobic encapsulation occurs, has been previously answered: the formation of water-depleted interiors is correlated with dominating interactional dispersion forces and favourable enthalpy/entropy changes.¹⁰ Crossing the solution/capsule barrier, unexpected dynamic phenomena can be observed within a “compartmentalized” chemical space, that of “molecular flasks”,¹¹ opening the door for a new emergent area of chemistry under confined conditions.

Attempts to encapsulate alkane molecules in confined spaces have generally furnished very interesting details on their constitutional flexibility, inducing synergetic dynamic changes of the capsule/host system.¹²⁻¹⁹ Dynamic disordered conformations have been reported for alkyl chains confined into crystalline guanidinium-sulfonate networks.¹² Internal order can be reinforced by strong interactions between guests and host capsules.¹³ Dynamic covalent selection of congruent alkyl-ester hosts can be adaptively operated on guest encapsulation.¹⁴ Stabilization of the large alkanes, adapting their conformation in H-bonded molecular flasks, has been previously employed to show evidence of constrained conformations and give answers on how alkane compression occurs.^{15,16}

Another approach to get more information on compressed alkane architectures, using single-crystal X-ray diffraction, should be related to the appropriate design of a crystalline host-matrix optimally sequestering/immobilizing the host substrates within the confined space.⁵ The crystalline host matrix must have: a) an optimal design of the host interior volume and nature to the alkane sequestered molecules; b) specific anchoring groups to fix the host

confined molecule and finally c) a good quality diffraction data set. These considerations inspired us to design a crystalline superstructure “Pyrene box” from readily available commercial materials, containing the 1,3,5,8-pyrenetetrasulfonate anions, **PTS**, the guanidinium cations, **G** and 1, ω -diammonium-alkanes. The confinement of the 1,10-diammonium-decane (**1**), 1,11-diammonium-undecane, **2** and 1,12-diammonium-dodecane, **3** within the **PTSG** host-matrix have been readily realized in aqueous solutions of **G**⁺**Cl**⁻, **PTS**⁴⁻**Na**₄⁺ and **1**, **2** or **3** resulting in the formation of the inclusion single crystals of **PTSG**{**1**}, **PTSG**{**2**} and **PTSG**{**3**}, respectively.

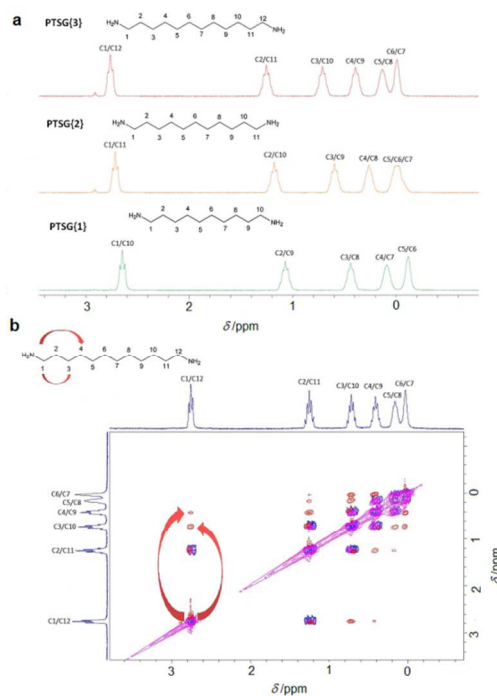


Fig. 1. ¹H-NMR analysis in aqueous solution. a. aliphatic region of the crystalline molecular flasks **PTSG**{**1**}, **PTSG**{**2**} and **PTSG**{**3**} respectively. b. Stack between the COSY (blue) and ROESY (red) spectra of **PTSG**{**3**}. Long range spatial interactions can be observed up to 4 carbon atoms away.

The ion-pairing proxy interactions between 1, ω -diammonium cations **1-3** and PTS anions can be detected in aqueous solution. The formation of $\text{PTS}\{\mathbf{1-3}\}_2$ and $\text{PTSG}\{\mathbf{1-3}\}$ complexes can be observed by the upfield shift (~ 0.8 ppm) of the protons of C3-C6/10 of **1-3** (Figs. 1a and Supplementary S2-S4). The broad upfield protons signals, showing $-\text{C-H}/\pi(\text{PTS})$ interactions are reminiscent of important dynamic behaviour of alkane chains within the ion-pairing system $\text{PTS}\{\mathbf{1-3}\}_2$. (Supporting Information) This conformational motion is largely reduced in the presence of **G** cations, as shown by the presence of sharp peaks (Supplementary Figs. S2-S4). This means that the presence of the **G** counter ion is required for the stabilization of the “Pyrene box” formation, in which the motion of alkane chains is restricted. The slight upfield shift decrease with increasing length of alkane chains of **2** to **3** can be explained only if the alkane chains adopt coiled conformations within the **PTSG** capsule, spatially allowing the folding within the confined space, as previously observed.¹⁵⁻¹⁹ The compression of the alkane chains is confirmed by COSY/ROESY experiments. In the case of $\text{PTSG}\{\mathbf{1}\}$, the alkyl chain appears to have a elongated zig-zag conformation, with no correlation observed on a distance larger than 2 carbons (H_1 to H_2) (Supplementary Fig. S5). In the case of $\text{PTSG}\{\mathbf{2}\}$ (Supplementary Fig. S6) and $\text{PTSG}\{\mathbf{3}\}$ (Fig.1b) spatial correlations are visible up to 4 carbon atoms away (H_1 to H_4). The DOSY spectroscopy showed that only one dimensionally constant capsule is present in solution for the **1-3** 1, ω -diammonium-alkanes series (Supplementary Figs. S7-S9, Table S1).

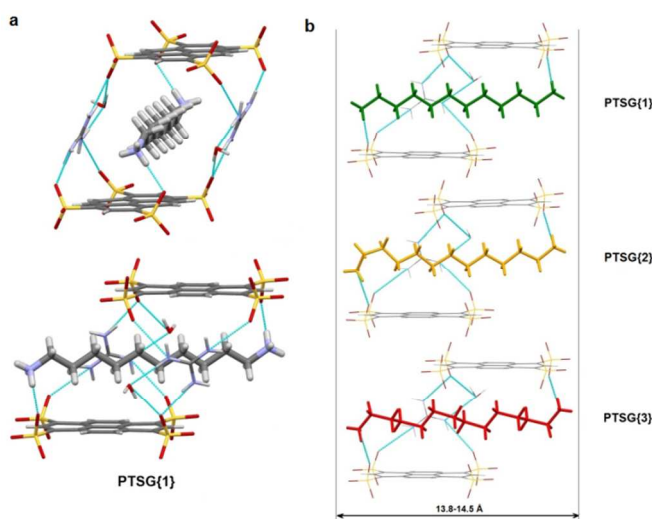


Fig. 2. X-ray structures of $\text{PTSG}\{\mathbf{1-3}\}$. a. Front (top) and side (bottom) view of the $\text{PTSG}\{\mathbf{1}\}$ inclusion complex; b. 1, ω -diammonium guests inside the $\text{PTSG}\{\mathbf{1-3}\}$ (H bonds - blue lines): uncompressed **1**, slightly- **2** and highly compressed **3**, respectively (see also Fig. 4b), (front **G** have been removed for clarity).

In the crystal, the “Pyrene box” results from the self-assembly of two **PTS** anions and of two **G** cations *via* H-bonding ($d_{\text{O}\cdots\text{H-N}}$ of 2.003 Å). This network is reinforced by two bridging water molecules, which are simultaneously H-bonded to **G** ($d_{\text{O}\cdots\text{H-N}}$ of 2.006 Å) and to **PTS** ($d_{\text{O}\cdots\text{H-N}}$ of 1.986 Å), playing a critical role in organizing the partners *via* three sulfonate moieties on the faces of the “Pyrene box”. The 1, ω -diammonium-alkanes, **1-3** are confined within the parallelepiped inner space defined between two **G** and two **PTS** molecules, while the ammonium moieties form two anchoring H-bonds ($d_{\text{N}\cdots\text{O}}$ =1.934 Å) with two other sulfonate moieties themselves non bonded to **G** cations (Fig. 2a). It results that the 1, ω -diammonium-alkane, **1-3** molecules have well-defined electron density sites in the Fourier maps. All combined host-guest

interactions are vital for the encapsulation and insulation as well as for the low mobility of the guest molecules in the “Pyrene Box”. 1,10-Diammonium-decane, **1** fits perfectly the length of the “Pyrene box”, with each ammonium moiety bonding to an **PTS**-sulfonate moiety. The chain adopts a classical ‘zig-zag’ elongated conformation, with an average sp^3 carbon- sp^3 carbon length of 1.522 Å in the expected range.¹⁹ By increasing the alkane chain length by one only carbon atom, the 1,11-diammonium-undecane chain becomes longer than the length of the box and adopts an asymmetrical conformation, **2** having one *gauche* conformation. Another incremental increase to 1,12-diammonium-dodecane leads to an even more compressed alkane chain. (Fig. 2) Careful crystallographic modelling allowed us to identify two co-existing conformers **3a** and **3b** of the chain in a 2 : 1 ratio. Both cases show high compression, with conformer **3a** having 6 *gauche* conformations and **3b** having 4 *gauche*, respectively (Supplementary Fig. S11). X-ray structure determinations at variable temperature were performed in order to better understand the dynamic behaviour of the compressed chains. No change was observed in the case of **1** and **3**, even at temperatures as high as 340 K. This is consistent with the expected stability of the complexes both for the extended decamethylene chain of **1** fitting perfectly inside the “Pyrene box” and the two similarly disordered dodecane chains of **3**, probably too constrained to move. On the other hand, the undecamethylene chain in $\text{PTSG}\{\mathbf{2}\}$ becomes disordered and symmetrical at room temperature. We interpreted this change as the rapid movement of the *gauche* conformation at room temperature from one end of the chain to the other. By plotting the mole fraction $2\mathbf{a}/2\mathbf{b}$ the occupancy of the two conformers against temperature, it is observed that the alkyl chain show dynamic behaviours at temperatures higher than 140 K (Fig. 3).

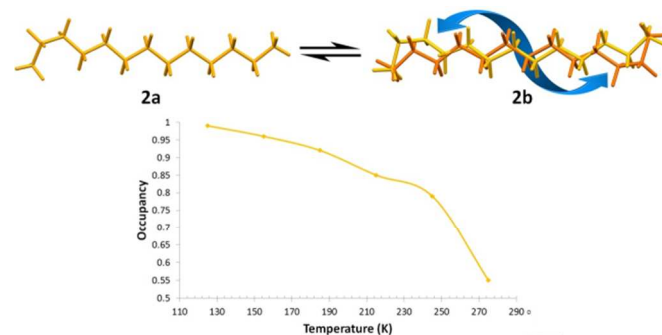


Fig.3. Reversible flipping of the 1,11-diammonium-undecane chain from one yellow to orange conformations in $\text{PTSG}\{\mathbf{2}\}$. Site occupancy factor of **2a** as a function of temperature: the asymmetry of the undecane chain disappears at higher temperatures and the *gauche* conformation moves along the chain.

Non-Covalent Interactions (NCI) plots^{20,21} of the alkane chains inside the “Pyrene box” showed that the compressed states might present dihydrogen contacts reminiscent of weak interactions inside the *gauche* conformations (Fig. 3b). A closer examination of these ‘crenel’ conformations **3a** and **3b** revealed a distance of only 2.246 Å between the hydrogens inside (ie. the hydrogens in positions 1 and 4, 3 and 6 etc.), shorter than the sum of their van der Waals radius (approx. 2.5 Å).²²⁻²⁴ Future more elaborated theoretical calculations will establish if such dihydrogen contacts,²² induced *via* geometrical constraints under confinement, would contribute to an extra degree of stabilization of the compressed chains.²²⁻²⁸ This compression under confinement results in a decrease of the overall length of the uncompressed ‘zig-zag’ alkandiyl 1,12-diammonium-dodecane, **3** and 1,11-diammonium-undecane **2** chains: from 16.534 Å to 14.465 Å (**3a,b**) and from 15.036 Å to 14.239 Å (**2a,b**), respectively.

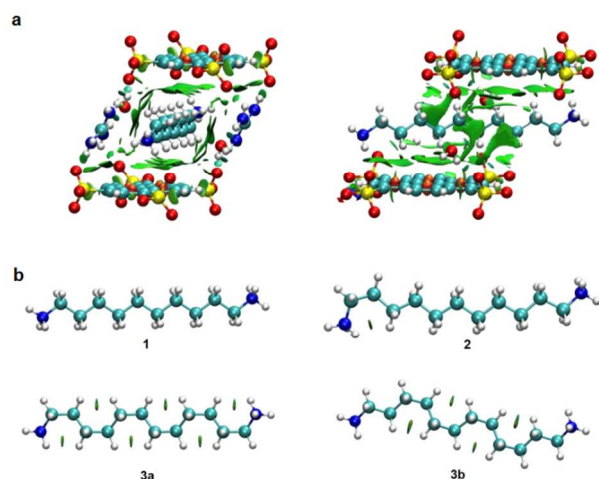


Fig.4. Non-Covalent Interactions calculations. a. Front (left) and side (right) views of the NCI plots of PTSG{1}. Green surfaces represent weak van der Waals interactions, blue surfaces indicate H-bonding and red surfaces steric repulsion, respectively. b. NCI plots of the compressed alkane chains (Pyrene box has been omitted for clarity). In the case of **1** no intramolecular interactions are observed. The compression in the case of **2** leads to the appearance of a faint stabilizing dihydrogen contacts (green surfaces). By increasing the length of the chain even further, six dihydrogen contacts are present in the case of **3a** and four in the case of **3b**. All isosurfaces are drawn at 0.4 au.

The progressive compression of 1, ω -diammonium-alkanes inside molecular flasks previously predicted by modelling and confirmed by spectroscopic studies^{15,16} is supported by the crystal structures of 1, ω -diammonium-alkanes confined in H-bonded crystalline “Pyrene boxes” PTSG{1-3} determined here. We observed three distinct geometries: the thermodynamic elongated zig-zag geometry of 1,10-diammonium-decane, **1** perfectly fitting the length of the box, the asymmetrical conformation of 1,11-diammonium-undecane **2** having one *gauche* conformation and two co-existing conformers **3a** (6 *gauche*) and **3b** (4 *gauche*) in a 2 : 1 ratio of 1,12-diammonium-dodecane. The constrained conformations of the compressed aliphatic chains present homopolar dihydrogen contacts. The undecane chain in PTSG{2} shows an interesting movement of the *gauche* conformation from one end of the chain to the other, while the decane chain of PTSG{1} and the compressed dodecane chain of PTSG{3}, are stable in an elongated zig-zag and crenel-type conformations, respectively. Alkane chains have been successfully constrained inside a unique rigid molecular flask, at different levels of compression. These results not only shows that chemists are able to tune, from inside, physical properties (pressure) at the molecular scale, but also provides hints for, so far, not fully understood conformations of long alkane chains.

This work was conducted within the framework of DYNANO, PITN-GA-2011-289033 (www.dynano.eu) and ANR “LABEX Chemisyst” (D.D.) “Pole Balard” Montpellier.

Notes and references

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†Electronic Supplementary Information (ESI) available: [NMR and X-ray details, supplementary figures]. CCDC 986088-986092. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c000000x/

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