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Two-Dimensional Nanoporous Networks Formed by Liquid-to-Solid Transfer of Hydrogen-Bonded Macrocycles Built from DNA Bases

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Abstract: We present an approach that makes use of DNA-base pairing to produce H-bonded macrocycles whose supramolecular structure can be transferred from solution to a solid substrate. A hierarchical assembly process ultimately leads to 2D nanostructured porous networks that are able to host size-complementary guests.

Self-assembly provides the guidelines to engineer two-dimensional (2D) molecular networks on flat surfaces.^[1] Those presenting void spaces, the so-called “2D porous networks”,^[2] are especially interesting since they offer the possibility of immobilizing, in a repetitive and ordered way, different functional guest units that are complementary in size and shape. Such networks can be produced from the deposition of persistent covalent macrocycles.^[3] Pore size and shape is in this way predefined during synthesis, but this approach can be tedious and time-consuming if tunable systems that allow for small pore modifications are to be produced. A more appealing alternative is the generation of lattices with regular cavities from small monomers that, once on the surface, interact *via* weaker noncovalent bonds.^[4] Upon physisorption, several degrees of translational, rotational and vibrational freedom are lost and, as a result, molecules that display very weak and ill-defined binding in solution can form well-ordered, yet dynamic assemblies held by multiple supramolecular interactions when confined in two dimensions. However, although much has been learned during the last years, this second approach has the limitation that the kind of network attained, which depends on a subtle interplay between molecule-molecule, molecule-solvent and molecule-substrate interactions, cannot be always reliably predicted.

An intermediate and ideal situation would be reached in the case of macrocycles that are assembled in solution from reversible noncovalent interactions,^[5] but robust enough to survive as well-defined, monodisperse species after the transfer process from solution to a substrate. These are indeed highly challenging requirements for self-assembled macrocycles, since the self-assembling rules change drastically when molecules are concentrated on a surface. On one hand, intra- and intermolecular binding events are compensated and chelate cooperativity, the

key factor promoting cycle formation in diluted solutions, is downgraded. On the other, the general tendency of physisorbed molecules is to maximize molecule-substrate interactions, so that networks with empty spaces are usually avoided if an alternative, more densely packed lattice can be accessed. All these issues ultimately result in a low-fidelity liquid-to-substrate transfer of supramolecular information. In other words, self-assembly in solution is typically not reproduced at the surface and *vice versa*.

Herein, we present a bioinspired approach that makes use of DNA-base^[19] pairing to produce tunable macrocycles (Figure 1) in solution whose supramolecular identity is reliably transferred to highly oriented pyrolytic graphite (HOPG), ultimately yielding ordered 2D porous networks *via* a hierarchical self-assembly process. This was accomplished by rational molecular structure tailoring. First, we reasoned that such cyclic systems should be endowed with high intermolecular association constants and effective molarities (thus leading to strong chelate effects), which must stem from an optimal monomer preorganization towards a specific cycle size.^[2c] Second, in order to produce robust, highly-ordered 2D networks, selective and directional inter-macrocycle interactions, of a secondary hierarchy level, should be promoted. Third, the generation of unique and uniform nanopores, whose dimensions would be precisely defined by the macrocycle cavity, must come from dense networks where any secondary unspecific pores are filled by a rational positioning of peripheral tails. In this way, additional stabilizing interactions with the substrate are also established, so that any other competing intermolecular arrangement is eluded. Furthermore, we demonstrate that the resulting 2D nanostructured porous lattices, studied by scanning tunnelling microscopy (STM) at the solvent-HOPG interface, are able to selectively host size-complementary guests in a controlled and reproducible fashion.

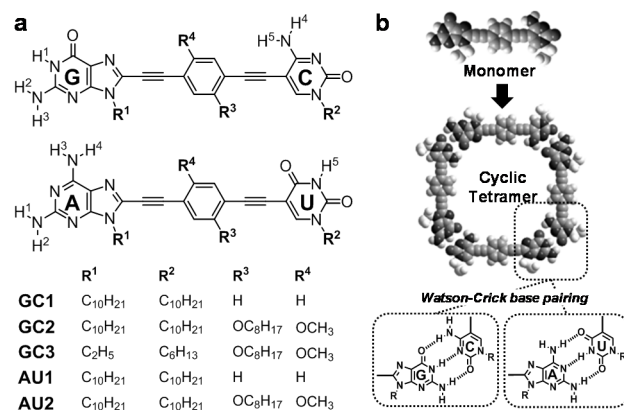


Figure 1. (a) Structure of monomers GC1-GC3 and AU1-AU2. (b) Square-shaped cyclic tetramers are assembled *via* Watson-Crick G-C / A-U H-bonding.

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Monomer design (**GC1-GC3** and **AU1-AU2**;^[6,7] Figure 1a) is based on a π -conjugated *p*-diethynylbenzene unit substituted with complementary nucleobases at the edges: guanine (G) and cytosine (C), or 2-aminoadenine (A) and uracil (U). This rigid and linear structure, together with the 90° angle provided by Watson-Crick pairing, results in the quantitative formation of unstrained square-shaped tetrameric assemblies (Figure 1b) over a broad concentration, temperature and solvent polarity range, as previously demonstrated by us in solution experiments (see also Figure S1).^[8] Such exceptional stability, specially evident for the G-C couple, was ascribed to the strong chelate effect measured upon cyclotetramerization, which originate mainly from the optimally preorganized monomer structure.

We initiated our studies with monomers **GC1** and **AU1**, both equipped with long decyl tails at both bases. Despite our efforts, no ordered network could be imaged with these monomers onto HOPG in a variety of solvents within the 10^{-4} – 10^{-6} M concentration regime. The only exception was **GC1** in a 1,2,4-trichlorobenzene (TCB):octanoic acid (OA) (1:1) mixture. When a 5.0×10^{-6} M solution of **GC1** was dropcasted onto freshly cleaved HOPG, large organized domains of non-cyclic oligomers were obtained (Figure 2a). Instead of establishing the expected Watson-Crick interactions, the models suggested that the ditopic π -conjugated monomers were arranged in parallel rows comprising packed pairs of molecules^[9] that are associated via H-bonding interactions between the G-carbonyl group and the amino C-H⁴ proton (Figure 2b). At the same time, the rows grow by additional H-bonding between the C-carbonyl group and the G-H¹ and G-H² protons. Although not clearly observed in the images, such double-chain pattern leaves all the peripheral long alkyl tails lying flat on the surface and arranged orthogonally with respect to the rows, so that they can establish multiple van der Waals interactions to stabilize the network. Furthermore, we believe that OA solvent molecules might also participate in the network by establishing H-bonding interactions with the nucleobases and van der Waals interactions with the alkyl tails between rows (see Figure S2). As a matter of fact, the use of this solvent was essential to properly solubilize the samples and to reproduce such pattern and in its absence no ordered networks were imaged. **GC1** is an interesting sample because, despite it forms macrocyclic assemblies in solution (Figure S1), it is then reorganized onto HOPG to yield a more densely packed network, calculated as 228.0 g/mol·nm². Cyclic **GC1** or **AU1** assemblies are probably not preserved on the surface because they leave large void spaces, 2.2 nm² in diameter, that would lead to lower-density network, estimated as 180.3 g/mol·nm².^[6] Hence, we reasoned that partial filling of the cavity with alkyl tails, introduced at the central benzene block (as in **GC2** and **AU2**), might be a strategy to increase surface density and favor the formation of cyclic tetramer networks.

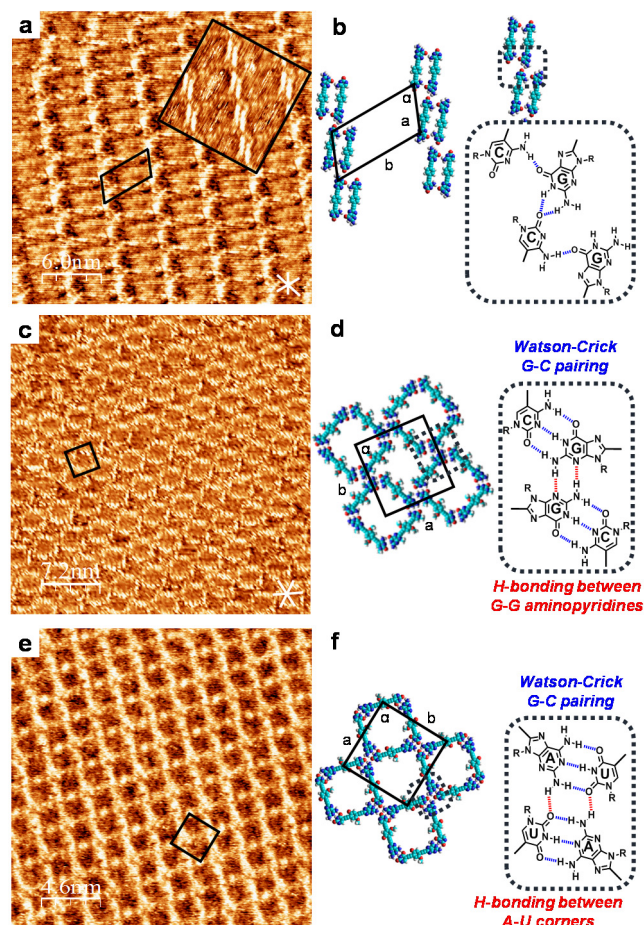


Figure 2. (a) High-Resolution STM image of **GC1** on HOPG from a solution 5.0×10^{-6} M in TCB:OA 1:1 (tunneling parameters: $I_{\text{set}} = 50$ pA, $V_{\text{bias}} = -350$ mV). The inset, showing the arrangement in monomer pairs, corresponds to another STM image on HOPG from a **GC1** 6.0×10^{-6} M solution in TCB:OA 1:1 ($I_{\text{set}} = 50$ pA, $V_{\text{bias}} = -350$ mV). (b) Model for **GC1**. The unit cell is indicated by black lines: $a = 2.7 \pm 0.1$ nm; $b = 4.5 \pm 0.1$ nm; $\alpha = 68 \pm 1^\circ$. (c) High-Resolution STM image of **GC2** on HOPG from a solution 7.1×10^{-6} M in OA ($I_{\text{set}} = 280$ pA, $V_{\text{bias}} = -180$ mV). (d) Model for **GC2**: $a = 3.4 \pm 0.1$ nm; $b = 3.6 \pm 0.1$ nm; $\alpha = 92 \pm 2^\circ$. (e) High-Resolution STM image of **AU2** on HOPG from a solution 7.9×10^{-5} M in TCB:OA 1:1 ($I_{\text{set}} = 100$ pA, $V_{\text{bias}} = -350$ mV). (f) Proposed model for **AU2**: $a = 3.5 \pm 0.1$ nm; $b = 3.5 \pm 0.1$ nm; $\alpha = 91 \pm 1^\circ$. White lines indicate the normal axes of graphite.

When applying TCB-OA (0:1 or 1:1) 10^{-5} – 10^{-6} M solutions of **GC2** or **AU2** onto HOPG, large domains of cyclic tetrameric species were now successfully imaged (Figures 2c, 2e, and S3). Interestingly, STM reveals that these networks are mainly stabilized by two sets of H-bonding motifs of different hierarchy. First, strong G-C/A-U Watson-Crick triple H-bonding, leading to the observed square-shaped motifs, is conserved on the surface. These discrete tetramers then pack in 2D by establishing secondary interactions between H-bonding donor and acceptor groups that do not participate in Watson-Crick pairing. However, these interactions are different for **GC2** and **AU2** and thus lead to distinct network arrangements, as evidenced before in other H-bonded systems.^[1h] In the first case, G-G double H-bonding interactions between aminopyridine-type fragments (Figure 2d) are established, leading to regular lattices in which the rings interact through their G-edges. For **AU2**, on the contrary, the

squared-shaped cycles bind through their corners by establishing H-bonding interactions between the A-H² proton and the external U-carbonyl lone pair (Figure 2f), so the resulting network appears as a continuous grid. It should be remarked that **GC2** or **AU2** could in principle establish any of these two secondary H-bonding configurations (see Figure S4), but these distinct centrosymmetric lattice arrangements were always observed for each molecule under different concentration conditions and annealing or time-dependent studies (Figure S5) did not show any network reorganization, suggesting that they constitute equilibrium states. Both **GC2/AU2** networks leave secondary pores between cyclic tetramers, having a comparable size than the ones defined by the macrocycle cavity, where the external alkyl tails placed at the nucleobases are forced to group. However, the proposed models show that the C₁₀ alkyl chains in each **GC2/AU2** base do not fit properly in the space left between 4 cyclic tetramers. Despite their high affinity for the HOPG substrate, some of these chains must necessarily desorb and backfold toward the supernatant solution. This is an energetically unfavorable situation that indicates that secondary H-bonding interactions between tetramers dominate over van der Waals interactions in the stabilization of the networks. The interaction between corners leaves secondary pores that are significantly larger (5.6 nm²) than those generated by interaction between purine edges (3.4 nm²), where the long peripheral tails should fit better and establish stronger interactions with the substrate. As a matter of fact, larger and better-ordered domains were observed for **AU2**, for which the surface density was calculated as 232.1 g/mol·nm², than for **GC2** (see Figure S5).^[10]

In view of these results, we decided to further optimize the GC cyclic tetramer network and synthesize a third-generation monomer (**GC3**), which is now equipped with shorter C₂ and C₆ chains at the G and C bases, respectively. The length of these alkyl groups was precisely tailored at each base in order to completely fill the secondary unspecific pores generated between 4 cyclic tetramers and, at the same time, to allow the chains to physisorb onto HOPG, thus promoting additional interactions to stabilize the network. When **GC3** solutions in 1:1 TCB-OA were dropcasted onto HOPG, large domains of cyclic tetrameric species were again observed by STM (Figures 3a and S5). The macrocycle network, whose density was calculated now as 247.7 g/mol·nm², showed in this case a higher stability at the solid-liquid interface and, as a result, excellent coverage and a superior monolayer resolution was attained (Figure 3b). In some images with higher resolution, ill-defined features of bright contrast (though darker than the π -conjugated skeleton) were observed within and between the pores (Figure 3c), which we assigned to the inner and outer alkyl tails, as depicted in the model in Figure 3d. The growth of the domains, driven by thermodynamics, could be observed with time along consecutive scans until large, single domains, whose size may extend well beyond 100 x 100 nm² (Figure S5), were reached. The **GC3** (and also **GC2**) domains were constituted by cyclic tetramers with the same surface chirality (Figures 3e and S6).^[11] This chirality is originated by the side of the macrocycle that is in contact with the substrate. Assuming an arbitrary cycle sense taking the Watson-Crick H-bonding interaction from G to C, we could define a clockwise (CW) and a counter-clockwise (CCW) tetramer configurations on the surface (Figures 3f and S6).

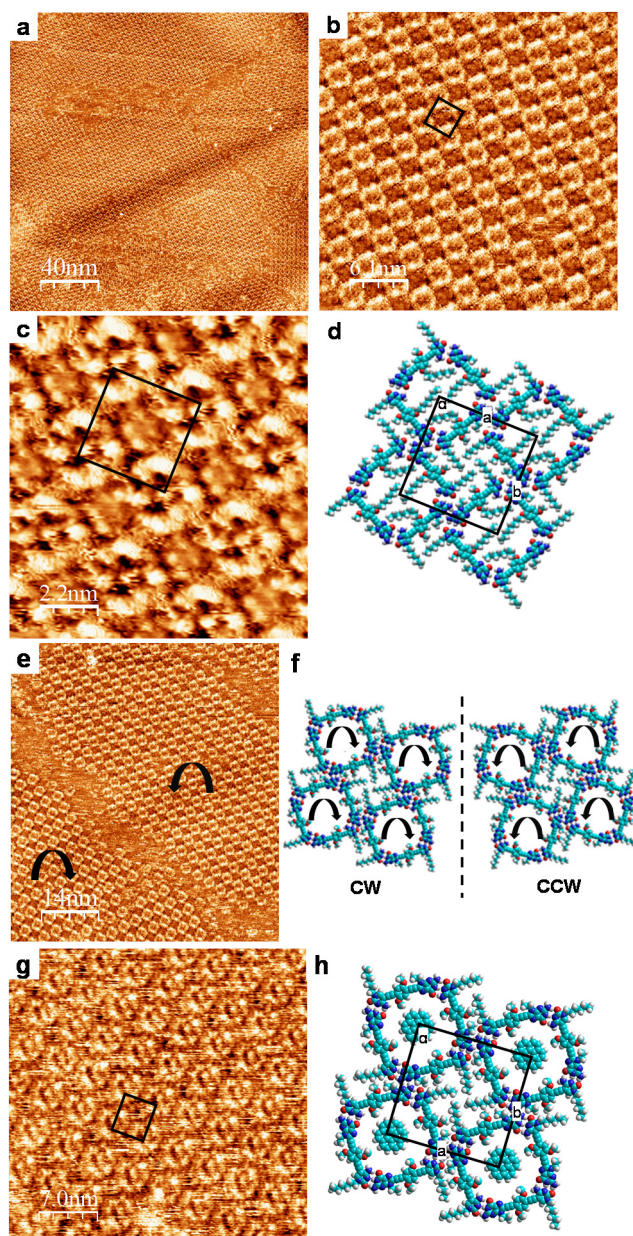


Figure 3. (a,b) STM images of **GC3** on HOPG from a solution 8.2×10^{-6} M in TCB:OA 1:1 ($I_{\text{set}} = 200$ pA, $V_{\text{bias}} = -300$ mV). (c) High-Resolution STM image of **GC3** on HOPG from a solution 8.2×10^{-6} M in TCB:OA 1:1 ($I_{\text{set}} = 200$ pA, $V_{\text{bias}} = -300$ mV). (d) Model for **GC3**: $a = b = 3.6 \pm 0.1$ nm; $\alpha = 89 \pm 1^\circ$. (e) STM images of **GC3** showing (f) two domains with different pore chiralities. (g) STM image of **GC3-cor** bicomponent system at the HOPG/TCB:OA 1:1 interface ($I_{\text{set}} = 80$ pA, $V_{\text{bias}} = -350$ mV). (h) Model for this host-guest system: $a = 3.6 \pm 0.1$ nm; $b = 3.5 \pm 0.2$ nm; $\alpha = 89 \pm 1^\circ$.

To prove the ability of our nanostructured porous surface to host size-complementary molecules, mixtures of **GC1-GC3** and matching π -conjugated planar guests, namely coronene (**cor**), were codeposited and imaged by STM at the solid-liquid interface. Premixed solutions of the monomer with an excess of guest were prepared in TCB-OA (1:1) and dropcasted onto HOPG.^[6] The mixtures led consistently to surface networks that appear very different under STM imaging to those in the absence of guests (please compare Figures 3b and 3g). Medium-sized domains

covering large areas were observed and bright features are now localized inside the cavities that are strong evidence for the coadsorption of **cor** molecules (see also Figures S7 and S8). According to the models, this smaller host fits properly within the cyclic tetramer cavity, but it must compete for the pore with the C₈H₁₇ chains at the central block. We propose that these inner chains are back-folded in the supernatant solution in order to leave room for the guest molecule, which can then establish strong interactions with HOPG. At the domain borders fuzzy areas were observed that may be an evidence of this adsorption/desorption equilibrium between the C₈H₁₇ chains and **cor** (Figure S8B), which is faster than scanning. We believe **cor** inclusion results from an energy minimized packing to achieve maximum density. It is interesting to note that independent **cor** islands were never observed, even using a high excess of guest, and that these high-contrast central features were only observed when both host and guest are transferred together from solution onto HOPG, and never when an excess of **cor** was added to a preformed **GC3** cyclic tetramer network. This indicates that the **GC3** porous network, having adsorbed C₈H₁₇ chains, is kinetically stable enough to impede **cor** physisorption.

In summary, we have described a novel strategy based on molecular self-assembly towards unconventional 2D nanoporous systems. Our approach differs to previous H-bonded lattices where the porous network is built on the surface from weak interactions between di- or tritopic molecules, the phthalic or trimesic acids being representative examples. Here, a robust macrocycle is assembled via Watson-Crick interactions between DNA bases whose supramolecular structure can be preserved upon surface transfer by rational molecular tailoring. Chiral domains are then assembled by the establishment of multiple and distinct H-bonding interactions, of a second-order hierarchy, between tetrameric macrocycles. The ability of the nanoporous network to host size-complementary guests was preliminary demonstrated and stable bimolecular assemblies with coronene were reproducibly obtained. A wide number of possibilities for modular surface nanostructuring opens now.

Acknowledgements

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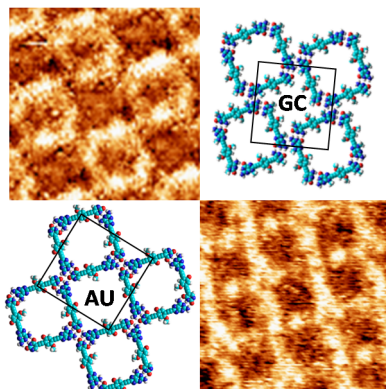
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Entry for the Table of Contents

COMMUNICATION

2D Nanoporous networks, able to recognize shape-complementary guests, are structured onto graphite substrates *via* a hierarchical self-assembly process from ditopic monomers with complementary nucleobase pairs.



Nerea Bilbao, Iris Destoop, Steven De Feyter and David González-Rodríguez**

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Tailoring 2D Nanoporous Networks by Liquid-to-Solid Transfer of DNA-base Hydrogen-bonded Macrocycles
