Surface Supported Supramolecular Pentamers

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Abstract: Chiral pentamers of all-*trans* retinoic acid molecules have been prepared on Au(111) surfaces and on a molecular monolayer. Over a range of coverages pentamers are the building blocks of larger arrays that become increasingly enantiopure. The stability of pentamers is analysed from experiments on an isomer and a more reactive substrate as well as from density functional theory. The linear shape of the molecule and suitable densities are crucial for the formation of pentamers, driven by cyclic hydrogen bonding between carboxylic acid moieties.

Supramolecular chemistry is of great interest in molecular recognition, catalysis, medicine, data storage and processing, and artificial photosynthetic devices.¹ Supramolecules are formed by directional and weak non-covalent interactions such as hydrogen bonding,² metal coordination,³ hydrophobic and van der Waals forces,⁴ $\pi - \pi$ and electrostatic interactions.⁵⁻⁷ Hydrogen bonding is particularly attractive for self-assembly for its directionality, specificity, and biological relevance.^{8,9}

On surfaces, supramolecular structures are affected by direct interactions with the substrate.¹⁰ In addition, substrate-mediated long-range molecule-molecule interactions occur, *e. g.*, via quantum interference of surface state electrons,¹¹ and lead to discrete supramolecules instead of closely packed molecular arrays. Supramolecular dimers, trimers, and tetramers of porphyrines and azobenzene derivatives have been self-assembled using these principles.¹² However, the fabrication of supramolecules with C_5 symmetry, which are mainly found in living organisms, has rarely been reported,¹³ most likely because a two-dimensional surface cannot be filled with a periodic arrangements of pentagons.¹⁴

Here we present the preparation of supramolecular pentamers from all-*trans* retinoic acid (ReA) on the Au(111) surface. Over a range of coverages these pentamers are the building blocks of larger arrays. While the ReA molecules, which become chiral upon adsorption, form a racemic mixture the pentamers become increasingly enantiopure as larger arrays form. Using a slightly different molecule, 13-*cis*-retinoic acid, or a more reactive substrate, Ag(111), we identify the forces driving the pentamer formation. Density functional theory calculations are used to further characterize the process.

ReA was sublimated onto Au(111) at room temperature in ultrahigh vacuum. Images were recorded with a 5-Kelvin

Figure 1. (a) Image of a ReA pentamer, observed close to a step on Au(111) at an average coverage $\Theta \sim 0.2$ ML.¹⁵ A scale bar indicates 1 nm in this and all other figures. (b) Optimized geometry of 5 ReA molecules, confined to a plane.

scanning tunneling microscope (STM) at low constant currents (10–60 pA) and low positive sample voltage (10–150 mV). Molecular double layers were imaged at 2.1 V. Images are displayed as an illuminated three-dimensional surface.

Electronic structure calculations were performed within density functional theory (DFT) using a plane wave basis set and the projector augmented wave method.¹⁶ The exchange and correlation energy was treated with the Perdew-Burke-Ernzerhof (PBE) form of the generalized gradient approximation.¹⁷ The importance of long-range van der Waals (vdW) interactions was studied using the DFT+D2 scheme of Grimme.¹⁸ Geometries were optimized until forces were smaller than 0.01 eV/Å.

All-*trans* retinoic acid (ReA) is one of the most active retinoids and essential for the control of epithelial cell growth

and cellular differentiation.^{19,20} The molecule has a quasilinear geometry with the carboxyl group ($-\text{COOH}$) at one end. Fig. 1a shows a STM image of a supramolecular pentamer that formed upon deposition of ReA on Au(111). As confirmed from DFT calculations the C_5 symmetric pentamer is stabilized by cyclic $\text{O} \cdots \text{H}-\text{O}$ hydrogen bonds at the center (Fig. 1b). The bulky 1,3,3-trimethyl-cyclohexen groups appear as protrusions (0.2 nm apparent height) at the periphery of the supramolecular cluster while the oligoene chains appear lower (0.14 nm).

Figure 2. (a) STM image of three pentamers comprising different enantiomers of ReA at $\Theta \sim 0.4$ ML. ρ and σ indicate examples. (b) Surface-induced enantiomeric forms ρ and σ of ReA. (c) STM image of a larger pentamer array. (d) Schematic geometry of two pentamers attracted by van der Waals interaction.

At low coverages, most ReA molecules arrange themselves into pentamers which interact to form larger agglomerates (Fig. 2). While the pentamers can still easily be identified the C_5 symmetry is usually lost. We attribute the reduced symmetry to the van der Waals interaction between pentamers and the flexibility of the oligoene chains on Au(111). In fact, no preference for a particular crystallographic direction of the Au substrate was discernible, in stark contrast to a Ag(111) substrate (see below).

Close inspection of Fig. 2a reveals that the surface induces a chirality of the achiral ReA molecule.^{21,22} The two enantiomers, denoted ρ and σ , are shown in Fig. 2b. While small islands of a few pentamers (Fig. 2a) comprise similar numbers of both enantiomers larger islands (Figs. 2c and 3) exhibit a significant ($\sim 10 : 1$) excess of one enantiomer. Most molecules with the minority chirality are found at the perimeter of islands. From an analysis of many islands we found that all pentamers that are surrounded by more than 4 neighboring pentamers are comprised of five identical enantiomers and thus are chiral themselves.²³ These observations indicate the importance of homochiral interactions. At coverages below 0.2 monolayers (ML¹⁵), $\sim 5\%$ of the pentamers are enantiopure as expected for random aggregation of σ and ρ enantiomers. This fraction increases to $\sim 80\%$ in pentamer islands at ~ 0.75 ML.

Although a planar surface cannot be completely filled with regular pentagons Figure 3 shows that ReA pentamers are capable of forming large ordered arrays. This is due to a degree of flexibility of the pentamers, which adapt themselves to form a rectangular unit cell with two different pairs of dis-

torted supermolecules. Moreover, the open structure of the periphery of the pentamers enables a degree of interlocking of the ReA molecules from neighboring pentamers. This is different from the case of rigid pentagonal molecules.²⁴

To address the role of the molecule-substrate interaction, we repeated the experiments on the more reactive Ag(111) surface, keeping all other parameters unchanged. On this surface, no pentamers were found over a wide range of coverages. Instead, rather densely packed islands were observed (Fig. S2). We attribute this striking difference between the Au and Ag substrates to the different strengths of the molecule-substrate interactions. Calculation shows that intermolecular hydrogen bonding favors pentamer formation. On Au(111) the interaction with the substrate is too small to change this preference. On Ag(111), the corrugation of the interaction potential is more significant and imposes an alignment of the molecules along $\langle 211 \rangle$ directions and effectively prevents the formation of pentamers. Moreover, the data suggest that the symmetry of Au(111) is not a key factor.

Figure 3. (a) Centered rectangular mesh of ReA on Au(111) observed at $\Theta \sim 0.6$ ML. The building blocks of the structure are hydrogen bonded ReA tetramers. The rectangular unit cell has dimensions of 3.2×3.1 nm². (b) STM image of a dense mesh on Au(111). Molecular dimers may be viewed as building blocks of the pattern. The dimensions of the oblique unit cell are 3.6×0.82 nm² with an angle of $54 \pm 1^\circ$ between the primitive vectors. (c) STM image of a hexagonal network formed by *cis*-ReA on Au(111). A virtually identical structure was observed on Ag(111) (supporting information S4). Optimized molecular superstructures are overlaid on the STM images in a, b and c. (d) STM image of a pentamer grown on top of an ReA dimer island on Au(111) with monolayer thickness. (e), (f) Optimized heterochiral pentamers for ReA and *cis*-ReA, respectively.

From the above results it appears likely that ReA pen-

tamers will form on other inert surfaces as well. As a first test of this idea, a small amount of ReA was deposited on a complete ReA monolayer on Au(111). The geometric and electronic structures of this layer deviate significantly from those of the metallic Au(111) substrate. Nevertheless, pentamers were found on top of the molecular layer (Fig. 4d) as expected.

Next, we experimentally address the role of shape of the ReA molecule. To this end the closely related molecule 13-*cis*-retinoic acid (*cis*-ReA, Fig. 4f) was deposited on Au(111) and Ag(111). On both substrates, hexagonal networks of H-bonded dimers were found (Fig. 4c) and pentamers were absent. This result highlights the relevance of the linear shape of the ReA molecule. In the case of *cis*-ReA, steric hindrance suppresses the formation of closed cycles of O...H-O hydrogen bonds. This is particularly important during the growth process when molecules with different chiralities try to attach to a ReA_n cluster ($n < 5$). Whereas ReA pentamers containing different enantiomers are stable owing to the linear shape of the constituents (Fig. 4e), closure of the cyclic hydrogen bond pattern is prevented in *cis*-ReA tetramers when a molecule with different chirality is added (Fig. 4f).

To characterize the driving force for pentamer formation the structure of ReA clusters was optimized using density functional theory. To keep the calculation tractable the interaction with the fairly inert Au(111) surface was neglected but the molecules were confined to two dimensions. This simplification is justified for the following reasons. First, the ReA molecules in pentamers were not observed to exhibit a clear preference for a particular crystallographic direction of the substrate. On the more reactive but structurally similar Ag(111) surface no pentamers were found and the ReA molecules are aligned with respect to the substrate. Second, at elevated coverages the pentamer islands extend over fcc and hcp areas as well as domain walls of the herringbone reconstruction without significant changes of the molecular arrangement. Clearly, the simplified model cannot reproduce the preferred nucleation of pentamers in fcc areas. Calculated binding energies $E(n)$ of cyclic clusters of $n = 2 - 6$ molecules are displayed in Table 1.

Table 1. Calculated binding energies, in eV, of enantiopure ReA clusters. For the hexamer, the first value was found for a cyclic arrangement that is obtained by inserting a sixth molecule into a pentamer. The second, higher binding energy corresponds to a different structure (see Supporting Information) that would require a drastic rearrangement of the pre-existing pentamer. The quantity in the right column shows the relative stability (details in the text) of respective clusters.

n	E^{PBE}	$E^{PBE+vdW}$	$\Delta_{2,n}^{PBE+vdW}$
2	0.76	0.85	0.69
3	0.88	1.01	-0.05
4	0.96	1.23	-0.01
5	1.00	1.45	0.84 / 0.53
6	0.22 / 0.68	0.83 / 1.15	—

With increasing cluster size, the binding energy E^{PBE} calculated with the PBE functional continuously grows up to a magic size $n = 5$. Most of the binding of the clusters is due to O...H-O bonds. The energy per O...H-O bond is higher for the dimer (0.43 eV), which can be tracked to an angle closer to 180° and a shorter distance. When adding more molecules, additional H-bonds are formed, but they are weaker because of the spatial restrictions of accommodating the consecutive molecules. That leads to a less open bond

Figure 4. STM image of ReA pentamers in a rectangular two-dimensional mesh at $\Theta \sim 0.75$ ML. Dotted lines indicate some unit cells with dimensions 5.7×5.2 nm². The unit cell comprises two different pairs of pentamers indicated by red and blue pentagons. Defects in the interior of the pentamer array are marked with yellow circles.

(farther from 180°) with bigger distances. Finally, the addition of the sixth molecule lowers the energy per dangling bond so much that there is an overall reduction in energy, inhibiting the formation of the hexamer and stopping the process at the pentamer. At lower coverages the process is governed by kinetics and pentamers are formed, but at higher coverages the most stable structures per H-bond are formed, i.e., dimer networks (see below). Van der Waals interactions ($E^{PBE+vdW}$) further increase the binding energy and do not change the overall trend. These results show that the attachment of single ReA molecules to existing clusters is favorable until a pentamer is formed. While fission of pentamers into smaller clusters would lead to a gain of energy, the abundance of pentamers in the experiments shows that this process is inefficient. This indicates that the barrier for fission is significant.

The formation of pentamer arrays as the one shown in Fig. 3 was also found to be energetically favorable. We have checked several packing configurations of pentamers, finding that the binding energy per pentamer increases due to the pentamer-pentamer interactions, going up to 1.85 eV in the best of the tested cases.

Finally, we compare the binding of heterochiral and homochiral ReA pentamers. The respective calculated binding energies of 1.42 eV and 1.45 eV are similar although homochirality is slightly favored. This is consistent with the observation of coexisting homo- and heterochiral pentamers.

The effects of molecular coverage, supporting substrates, and molecular structure on the formation mechanism of pentamers have been systematically investigated in the experiments. Pentamers were the most abundant structural motif in the range $0.01 \text{ ML} < \Theta < 0.4 \text{ ML}$ although decreasing percentages of pentamers were observed up to $\Theta \sim 1 \text{ ML}$. At very low coverages $\Theta \lesssim 0.01 \text{ ML}$ we observed dimers, possibly because the aggregation into larger clusters was too slow. At densities exceeding half a monolayer, ordered islands form. They may be viewed as being comprised of supramolecular tetramers (Fig. 4a) or dimers (Fig. 4b). Optimized geometries of these building blocks are overlaid on the respective STM images. Close to 1 ML, the Au(111) substrate is mostly covered with the dimer pattern of Fig. 4b. This is consistent with the results of Table 1, which show that the binding energy per ReA molecule is maximal in dimers. To account for the interaction between dimers a monolayer formed by dimers in the configuration of the is-

land of Fig. 4b was considered, finding a binding energy of 1.51 eV per dimer, considerably larger than the binding energy of an isolated dimer.

At $\Theta \lesssim 0.01$ ML, we occasionally observed trimers. This may be understood from their low stability compared to dimers and tetramers. In Table 1 the relative stability is indicated by the quantity $\Delta_{2,n} = 2E(n) - E(n+1) - E(n-1)$.²⁵ The larger negative value of the trimers shows their instability. Again, dimers and pentamers are the more stable formations.

In conclusion, pentamers of all-*trans* retinoic acid molecules have been prepared on the pristine Au(111) surface and a molecular monolayer. Cycles of hydrogen bonds between carboxylic acid moieties stabilize the pentamers. The linear shape of ReA and suitable molecular densities are crucial for pentamer formation. We speculate that related self-assembly of pentamers may be achieved on other weakly interacting surfaces.

Supporting Information Available

Two optimized planar geometries of 6 all-*trans* retinoic acid (ReA) molecules.

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