

On-Surface Synthesis of Adenine Oligomers via Ullmann Reaction

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Despite the fact that DNA bases have been well-studied on surface, the on-surface synthesis of one-dimensional DNA analogs through in situ reactions is still an interesting topic to be investigated. Herein, from the interplay of high-resolution scanning tunneling microscopy (STM) imaging and density functional theory (DFT) calculations, we have delicately designed a halogenated derivative of adenine as precursor to realize the combination of DNA bases and Ullmann reaction, and then successfully synthesized adenine oligomers on Au(111) via Ullmann coupling. This model system provides a possible bottom-up strategy of fabricating adenine oligomers on surface, which may further give access to man-made DNA strands with multiple bases.

DNA, as the carrier of genetic information, is significant for all living organisms. Due to the numerous fascinating characteristics, DNA strands have been introduced to the surface science community and explored by various means over the past several decades.^[1-12] Among others, scanning tunneling microscope (STM) has been widely employed due to its capability of real-space imaging as well as manipulating at the atomic scale.^[4,7-10] Previously, self-assembly of DNA bases and derivatives have been widely studied on different surfaces where non-covalent interactions are mostly considered.[13-27] Meanwhile, DNA macromolecules have also been introduced onto surfaces by using pulse-injection deposition method to alleviate the difficulties in vacuum sublimation method.^[4,8-10,28,29] Although advanced deposition strategies have been successfully employed, it is nevertheless of general interest to explore comparatively simple routes toward in situ synthesis of DNA macromolecules on surfaces. Considering the rapidly developing field of on-surface synthesis,[30-34] it would be highly intriguing to combine DNA bases and on-surface synthesis strategy with the aim of synthesis of man-made quasi DNA oligomers on the surface. Ullmann reaction has been extensively studied on sur-

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to building up covalently linked nanostructures by well-designed halogenated precursors.^[30,31,34] In this work, we have designed and synthesized a halogenated derivative of adenine molecule, i.e., 9-[3,5-dibromophenyl]-9H-purin-6-amine (shortened as DBPA, as shown in Scheme 1), in which the dibromophenyl group is modified on the N9 site (normally connected with the sugar moiety in DNA) to simply mimic the naturally occurring nucleotides and also give access to the formation of backbones via Ullmann reaction. We choose the Au(111) surface as the template because the interactions between DNA bases and Au(111) substrate are relatively weak and the intermolecular interactions are thus dominant.^[15, 16, 18, 24] It is also known that the adenine moiety adopts a flat-lying configuration on Au(111) and is resolved as a triangle in STM images.^[15,18] Herein, from the interplay of high-resolution STM imaging and DFT calculations, we have demonstrated that adenine oligomers, that is, a kind of DNA analogue in linear structure with adenine, can be successfully synthesized from the DBPA monomers via Ullmann reaction on the Au(111) surface (as depicted in Scheme 1), where the polyphenyl backbone is artificially designed within such an oligomer. These results thus provide a bottom-up strategy to synthesize adenine oligomers on the surface, which may hold great potentials in further single-molecule-scale exploration of such man-made quasi DNA strands.

faces and considered as one of the most versatile approaches

After deposition of DBPA molecules on Au(111) held at room temperature (RT), we find the coexistence of two kinds of selfassembled nanostructures, as shown in Figure S1a of the Supporting Information (SI). The large-scale STM images of the corresponding two phases are shown in Figure 1a and 1d. From the close-up STM images (Figures 1b and 1e), we can clearly identify that the individual DBPA molecule is resolved as a dark triangle linked with a V-shaped protrusion (as depicted by the white contours in both phases). According to the literatures,^[30,31,35,36] halogen atoms usually appear as bright protrusions in STM images, and the dibromophenyl group is symmetrical in morphology, [37] we thus assign the symmetrical Vshaped protrusion to the dibromophenyl group. Further with the previous studies of adenine and its derivatives on surface, ^[15,18] the remaining dark triangle is naturally attributed to the adenine moiety (denoted as A in Figures 1b and 1e). In Phase 1, all of the adenine moieties adopt an alternating zipper-like arrangement (Figure 1 b) which is similar to the adenine ribbon structure as reported previously.[18] While, in Phase 2, the adenine moieties interact with the neighboring ones in both head-to-head and side-to-side modes, as can be

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Scheme 1. Schematic illustration of the formation of an adenine oligomer from the DBPA molecule via Ullmann reaction.



Figure 1. The two self-assembled structures of DBPA on Au(111): a, d) STM images showing the formation of self-assembled Phase 1 and Phase 2 after deposition of DBPA molecules on Au(111) held at RT, respectively. b, e) Close-up STM images showing more details where the individual DBPA molecules are highlighted by white contours (adenine moieties are denoted as A). c, f) STM images of Phase 1 and Phase 2 superimposed with corresponding DFT-optimized structural models, respectively, where the possible halogen bonds and hydrogen bonds are depicted by black and blue dash lines, respectively. H: white; C: gray; N: blue; Br: orange. Scanning conditions: I = 0.90 nA, V = 1200 mV.

observed from the highlighted ones in Figure 1 e. To further unravel such structures, DFT calculations have been performed

on the basis of the high-resolution STM images. The energetically most favorable structural models in gas phase are super-



imposed on the corresponding STM images (Figures 1 c and 1 f), respectively, where good agreements in both dimension and morphology are achieved. From the DFT-optimized models, it can be seen that the adenine moieties in Phase 1 interact with each other via double NH···N hydrogen bonds forming adenine ribbon structure and the dibromophenyl groups gather together via Br···Br halogen interaction and CH···Br hydrogen bonds.^[35–40] In the case of Phase 2, the opposite two adenine moieties interact via double NH···N hydrogen bonds forming a head-to-head arrangement, and the dibromophenyl groups gather together via Br···Br halogen interaction and CH···Br hydrogen bonds at the same time.^[35–40] Note that such two structures have very similar stabilities based on the DFT calculations.

It is worth noting that such self-assembled DBPA nanostructures can maintain further thermal treatments to \approx 460 K. Further annealing at \approx 480 K for 3 hours results in the formation of only some covalently bonded dimers^[41] and desorption of most of the DBPA molecules from the surface (as shown in Figure S2). This may be explained by the narrow window between the activation temperature of Ullmann reaction for DBPA molecule on Au(111) and the desorption temperature. Therefore, it is not easy to achieve the expected covalently linked adenine oligomers by direct thermal treatments.

As previously shown in the literature,^[41] the strategy of hightemperature deposition can lead to the formation of an extended network in the Ullmann reaction. Thus, we then try to deposit DBPA molecules on hot surfaces with different sample temperatures. After deposition of DBPA molecules on Au(111) held at \approx 500 K, we interestingly find the formation of some oligomers^[42,43]. From the typical STM images (Figure 2a), also in comparison with the self-assembled structures, we observe that the oligomers are composed of adenine moieties(the triangular parts) that are alternatingly linked together by the polyphenyl backbones (zig-zag backbones) as highlighted in Figure 2a, which should be the products of Ullmann reaction.^[42,43] The DFT-optimized gas-phase structural model of the oligomer is superimposed on the STM image (Figure 2b). Such oligomers can further endure thermal treatments at \approx 400 K for 10 minutes (Figure S3).

The neighboring oligomers can further laterally bind together via the interactions between adenine moieties through double NH···N hydrogen bonds, and the DFT-optimized structural model of such a network is shown in Figure 2c. A small quantity of dispersed oligomers are scattered on the surface mixed with unreacted molecules and Br atoms as shown in Figure S4. With this strategy, the quasi DNA strand with different bases can be easily achieved by introducing alternative precursors with other bases. The results demonstrate the potential that such man-made DNA oligomers could be served as templates to explore the complementary base pairing and further more sequencing at the single-molecule-scale.

In conclusion, by designing a halogenated precursor based on the adenine molecule, we have developed a model system for bottom-up synthesis of adenine oligomers on the surface via Ullmann reaction. Undoubtedly, DNA strands should be composed of different bases and much more complicated backbones. Despite the simplification of our system, more sophisticated man-made quasi DNA strands with multiple bases and different backbones would be expected by modifying and introducing various precursors and on-surface reactions.

Experimental Section

All STM experiments were performed in a UHV chamber (base pressure 1×10^{-10} mbar) equipped with a variable-temperature, fast-scanning "Aarhus-type" STM using electrochemically etched W tips purchased from SPECS,^[44,45] a molecular evaporator and an e-



Figure 2. The adenine oligomers formed on Au(111): a) STM image showing the formation of oligomers after deposition of DBPA molecules on Au(111) held at \approx 500 K, with one of them highlighted by blue shadow (adenine moieties are denoted as A). b) STM image of the oligomer structure superimposed with the corresponding DFT-optimized gas-phase model. c) DFT-optimized gas-phase structural model of the network where the hydrogen bonds are highlighted by dashed lines. Scanning conditions: *I* = 0.90 nA, *V* = 1200 mV.



beam evaporator, and other standard instrumentation for sample preparation. The Au(111) substrate was prepared by several cycles of 1.5 keV Ar⁺ sputtering followed by annealing to 800 K for 15 min, resulting in clean and flat terraces separated by monatomic steps. The detailed synthetic routes and procedures of DBPA molecule are shown in the supporting information. After a thorough degassing, the DBPA molecules were deposited onto the Au(111) surface from a Knudsen cell by thermal sublimation at 440 K for 1 minutes (≈ 0.8 monolayer). The sample was thereafter transferred within the UHV chamber to the STM, where measure-

The calculations were performed in the framework of DFT using the Vienna ab initio simulation package (VASP).^[46,47] The projectoraugmented wave method was used to describe the interaction between ions and electrons.^[48,49] We employed the Perdew-Burke-Ernzerhof generalized gradient approximation exchange-correlation functional,^[50] and van der Waals interactions were included using the dispersion-corrected DFT-D3 method of Grimme.^[51] The atomic structures were relaxed using the conjugate gradient algorithm Scheme as implemented in VASP until the forces on all unconstrained atoms were $\leq 0.03 \text{ eV} \text{ Å}^{-1}$ for geometry optimization.

ments were carried out at \approx 150 K. All the STM images were fur-

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ther smoothed to eliminate noises.

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Conflict of interest

The authors declare no conflict of interest.

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COMMUNICATIONS



From the interplay of high-resolution scanning tunneling microscopy imaging, density functional theory calculations, we have successfully synthesized

adenine oligomers on Au(111) through Ullmann coupling of a halogenated adenine derivative. Y. Zhang, Y. Ding, L. Xie, H. Ma, X. Yao, C. Zhang, C. Yuan,* W. Xu*



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