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Chiral Recognition

Direct Visualization of Enantiospecific Substitution of Chiral Guest Molecules into Heterochiral Molecular Assemblies at Surfaces[**]

*Ning Liu, Sam Haq, George R. Darling, and Rasmita Raval**

Chiral molecular recognition is a vital concept in many fields due to its fundamental importance in biological systems and its pivotal role in controlling key events in technological applications such as enantioselective chemistry, catalysis, chiral separation, and sensors.[1] However, chiral host–guest interactions are difficult to probe at the nanoscale with spatial tools, and attention has recently turned to supramolecular assemblies at solid surfaces as model systems to study the mechanisms driving molecular recognition. Surface assemblies offer the dual advantage of providing well-controlled lateral arrangements within which guest molecules can be captured, and also being amenable to interrogation by sophisticated spectroscopic and imaging techniques. This approach has allowed chiral recognition by homochiral assemblies to be captured at the molecular level, ranging from self-recognition processes that drive an enantiomeric mixture to undergo homochiral segregation,[2] to chiral recognition of dissimilar molecules.[3]

Herein we move beyond the recognition abilities of homochiral superstructures and present the first observation by scanning tunneling microscopy (STM) of chiral recognition in a two-dimensional heterochiral assembly, which leads to highly enantiospecific substitution of individual tartaric acid (TA) guest molecules in a racemate structure formed by succinic acid (SU) on Cu(110). This process is also an important stepping stone towards "symmetry breaking"[4] in intrinsically racemic architectures at solid surfaces, and detailed insights have been obtained by STM, low-energy electron diffraction (LEED), reflection absorption infrared spectroscopy (RAIRS), and periodic density functional theory (DFT).

Chirality can be created by adsorption of achiral molecules on achiral surfaces, due to the reduction of symmetry in two dimensions.[2–5] For example, the segregation of SU into two mirror-enantiomorphous chiral domains on Cu(110) at low coverage was resolved by both STM and LEED.[5] However, if SU is adsorbed on Cu(110) at a higher coverage of 0.25 monolayers, and the sample heated to 473 K, an achiral p(4×2) structure is detected by LEED (Figure 1A). The absence of spots at $\{\tfrac{1}{2}h+\tfrac{1}{4}, 0\}$ and $\{0, k+\tfrac{1}{2}\}$ (h, k are integers) positions in the diffraction pattern suggests the surface assembly has two glide planes, along the [1$\bar{1}$0] and [001] directions.[6]

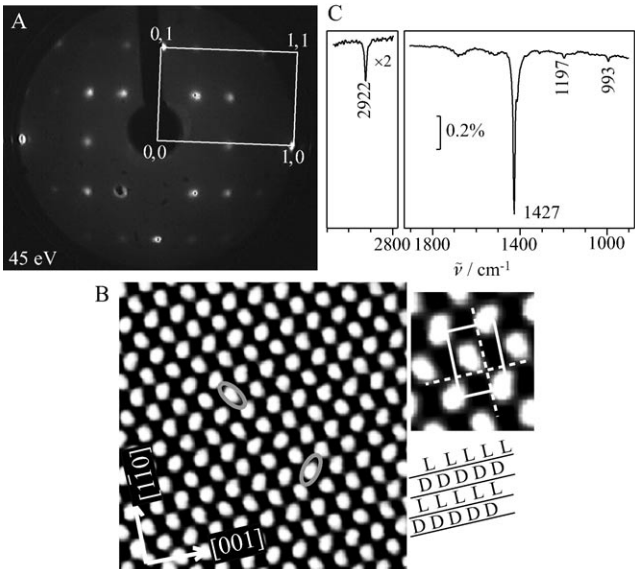

Figure 1. The p(4×2) overlayer of SU/Cu(110). A) p(4×2) LEED pattern at 45-eV beam energy showing missing diffraction spots. The white rectangle specifies the Cu(110) lattice. B) STM topography of the p(4×2) phase, 80×80 Å^2 ($I=0.35$ nA, $V=-0.88$ V). A close-up image, 17×20 Å^2, illustrates the unit cell and glide planes. Two ovals are used to highlight two molecular orientations. C) RAIR spectrum of the p(4×2) SU/Cu(110) structure.

The nanoscale organization of SU at this coverage was probed by STM and, at first sight, the molecules seem to be arranged in a simple c(4×2) structure (Figure 1B). On closer examination, however, two distinct molecular orientations, aligned along asymmetric directions of the substrate, can be identified from the high-resolution STM image. These two orientations are highlighted by ovals in the main image and can be seen clearly in the close-up image. The angle between the long axis of the oval-shaped SU and the [001] direction is approximately +65° for one adsorbate and −65° for the other, that is, they correspond to two distinguishable local chiral motifs, each the mirror form of the other. We call them D- and L-SU.

Thus, the true unit cell of this structure is p(4×2) and is heterochiral with two mirror orientations of SU in a 1:1 ratio. This arrangement naturally creates the glide reflection planes

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[*] Dr. N. Liu, Dr. S. Haq, Dr. G. R. Darling, Prof. R. Raval
Surface Science Research Centre and
Dept. of Chemistry
The University of Liverpool
Liverpool L69 3BX (UK)
Fax: (+44) 151-794-3896
E-mail: r.raval@liverpool.ac.uk

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in the [001] and [1$\bar{1}$0] directions, delineated in the close-up STM image of Figure 1B. Our STM observations are thus consistent with the LEED pattern. In addition, STM data reveal that all molecules in the same row along the [001] direction adopt the same adsorbate orientation, whereby adjacent rows have the opposite orientation.

For further detail, we utilized RAIRS to identify the chemical nature of the adsorbed SU species, and periodic DFT calculations to ascertain the adsorption site and packing arrangement. The RAIR spectrum of this system (Figure 1C) is remarkably similar to that of the dehydrogenated bisuccinate species on Cu(110),[5] where O–H cleavage creates COO groups which have a prominent ν_s(OCO) band at 1427 cm^{-1}. The RAIRS selection rules suggest that the presence of the ν_s(OCO) band but absence of the equally strong ν_{as}(OCO) band is consistent with both oxygen atoms in each COO group being located at approximately the same distance above the surface. Previous experiments and calculations on bitartrate, formate, and acetate molecules on Cu(110)[7,8] indicate that the oxygen atoms of the COO group are adsorbed atop adjacent Cu atoms along the [1$\bar{1}$0] direction, and thus suggest that SU is anchored on the surface by four Cu–O bonds.

Therefore, two possible adsorption geometries consistent with the STM and RAIRS data are proposed (Figures 2A and B). In Figure 2A, the molecule bridges straight across the two Cu rows, as suggested for a different phase of SU on Cu(110);[7] in Figure 2B, the Cu atoms bonded to the two COO groups are offset by one Cu lattice constant in the [1$\bar{1}$0] direction, giving rise to a diagonal adsorption site. Periodic DFT calculations[9] yielded the optimized structures (Figures 2C and D) for the models in Figures 2A and B, respectively. Interestingly, the overlayer structure in Figure 2D is 15.9 kJ mol^{-1} lower in energy than that in Figure 2C.

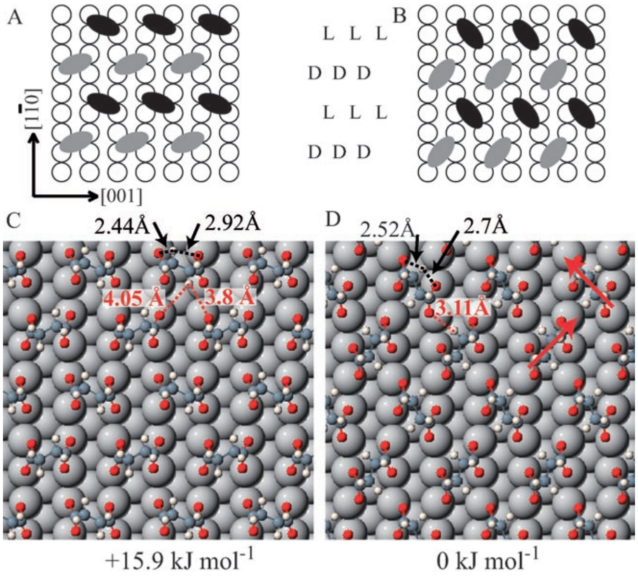

Figure 2. A, B) Schematics of two possible adsorption geometries for the p(4×2) SU/Cu(110) overlayer. L and D indicate the different surface enantiomers of bisuccinate. C, D) The DFT-optimized structures of (A) and (B). The COO oxygen atoms are all located in atop sites, but do not occupy identical positions. Intramolecular (black) and intermolecular (red) H···O distances are indicated.

The Cu–O distances of the molecule–metal bonds in both configurations are essentially the same (av 1.95 Å for Figure 2C and 1.96 Å for Figure 2D). We find appreciable intramolecular H-bonding interactions between the horizontally oriented hydrogen atoms of the methylene groups and the COO oxygen atoms, with H···O distances of 2.44 and 2.92 Å for the structure in Figure 2C, and 2.52 and 2.7 Å for that in Figure 2D. In addition, weak intermolecular H-bonding between heterochiral species is possible in the structure of Figure 2D, with a distance of 3.11 Å between the CH_2 group of SU and a COO oxygen atom of the neighboring SU. However, these differences in H-bonding interactions contribute only slightly to the relative stability of the two structures. Instead, the energy difference is mainly attributed to the different degrees of deformation suffered by the molecular skeleton; the configuration in Figure 2D is closer to the gas-phase geometry, and thus the energy penalty of molecular distortion in Figure 2D is less than that in Figure 2C.[10]

The optimized structure in Figure 2D shows how local chirality is created from an achiral system: the diagonal adsorption site and the distortion of the molecular skeleton destroy both the molecular and local surface mirror planes.[7] Furthermore, the structure is optimized when molecules of the same chirality align along the [001] direction, but with each row alternating in chirality. This generates an interesting overlayer that is truly racemic but contains homochiral chains. Finally, the strong intensity of the partial charge density (integrated from −0.9 eV to the Fermi level) along the diagonal connecting the vertically aligned hydrogen atoms of the CH_2 groups (indicated by the red arrows in Figure 2D) rationalizes the 65° angle between the long axis of the molecule and the [001] direction, as imaged by STM.

To evaluate the recognition response of this racemate structure to chiral guests, (*R*,*R*)-tartaric acid (TA) was coadsorbed with SU and the system heated to 473 K to create the structurally analogous dehydrogenated bitartrate species at the surface.[11] The STM image of this mixed system is displayed in Figure 3A. Interestingly, the introduction of TA molecules does not change the organization of the SU racemic structure, nor is TA expelled from the system. Instead, (*R*,*R*)-TA is incorporated within the structure, resides in a similar site to the SU molecules, and thus a local quasiracemic structure is created. In contrast to the oval shape imaged for SU, the TA molecules are resolved as much thinner "slots", which allow us to pinpoint their exact locations from the STM image.

What clearly emerges from the STM image in Figure 3A is that (*R*,*R*)-TA only substitutes sites originally occupied by L-SU. The (*R*,*R*)-TA in this site images as a "slot" aligned −20° from the symmetric [001] direction, (see close-up inset in Figure 3A). To confirm this enantiospecific substitution behavior, we repeated the experiment with the opposite enantiomer (*S*,*S*)-TA. As shown in Figure 3B, (*S*,*S*)-TA now only substitutes at the D-SU sites, and images as a "slot"

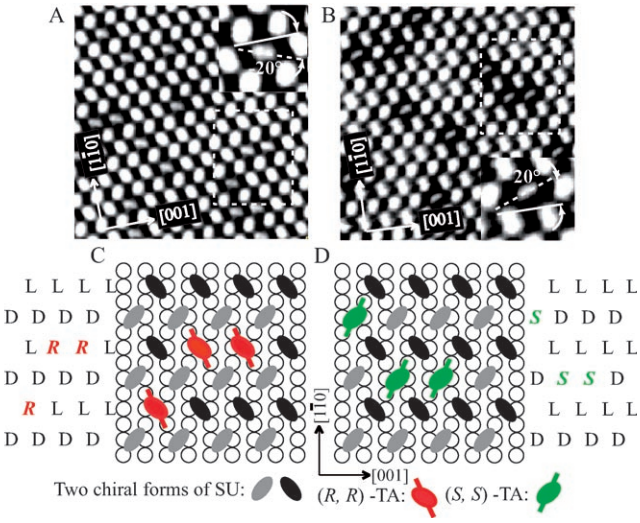

Figure 3. A, B) STM topographic images of (*R*,*R*)- and (*S*,*S*)-TA substitution in the p(4×2) SU/Cu(110) structure (80×80 Å^2, $I = 0.35$ nA, $V = -0.88$ V). The angle of the long axis of TA with respect to the [001] direction is indicated in the close-up images, 16×16 Å^2 for (*R*,*R*)-TA and 18×16 Å^2 for (*S*,*S*)-TA. C) Schematic of the adsorption sites occupied by (*R*,*R*)-TA (*R* in the figure) in the area defined by the dashed rectangle in (A). D) Schematic of the adsorption sites occupied by (*S*,*S*)-TA (*S* in the figure) in the area defined by the dashed rectangle in (B).

aligned +20° to the [001] direction. The proposed mixed overlayer structures are shown in Figures 3C and D. We note that the enantiospecific insertion of dissimilar enantiopure guest molecules into the homochiral chains essentially breaks the racemic state of the adlayer, and the random substitution within a particular chain leads to stochastic symmetry breaking and creation of a range of diastereomers across the surface.[4]

To gain insight into this highly enantiospecific behavior, DFT calculations were performed for each enantiomer of TA substituted at an L-SU site in a (4×4) unit cell, with each TA molecule surrounded by six SU molecules, as in Figure 4. The optimized structures for the two substitutions show that the TA molecule is now adsorbed in the diagonal site vacated by the SU molecules, that is, TA adopts an adsorption geometry within the SU lattice that is different from its preferred straight-across bridge geometry on a bare Cu(110) surface.[7] Significantly, we find that the adlayer in which (*S*,*S*)-TA is substituted into an L-SU site has an energy that is 48 kJ mol^{-1} higher than that obtained for (*R*,*R*)-TA substitution in the same site. This is a substantial energy difference and reveals a strong enantiospecific preference within the heterochiral p(4×2) structure.

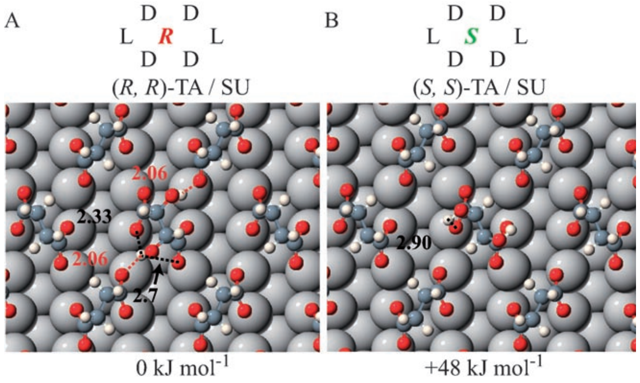

Figure 4. Optimized DFT structures of A) (*R*,*R*)- and B) (*S*,*S*)-TA substituting a single L-SU adsorption site within the heterochiral SU structure. Intra- and intermolecular H–O distances are indicated. Note that the intramolecular bonds are only shown for one side of the molecule.

Two factors account for this energy difference. First, H-bonding interactions play an important role. In the optimized structures of Figure 4, four intramolecular H···O bonds between the hydroxy and COO groups of (*R*,*R*)-TA can be formed (2.33 and 2.7 Å), while (*S*,*S*)-TA can only sustain two such bonds (2.90 Å). Also, when (*R*,*R*)-TA resides in the L-SU site, two strong intermolecular H-bonding interactions are also formed with adjacent D-SU molecules, each with a H···O distance of 2.06 Å (Figure 4), which stabilize the structure. In contrast, no intermolecular H-bonding is possible for (*S*,*S*)-TA. Finally, the diagonal adsorption site causes both enantiomers of TA to distort from their most favored geometries on Cu(110), where adsorption straight across the bridge site is accompanied by a chiral distortion of the molecular backbone.[7] Within the SU assembly, the backbone distortion of (*R*,*R*)-TA is in the same direction as its preferred geometry on Cu(110), whereas (*S*,*S*)-TA is forced to deform its C–C backbone into the opposite orientation from its optimized configuration in order to occupy the L-SU site. This unfavorable distortion, accompanied by weaker intra- and intermolecular H-bonding interactions, creates the large energy penalty that eliminates the possibility of (*S*,*S*)-TA residing in the L-SU site.

To summarize, we reported herein the first STM observation of site-specific chiral recognition within a two-dimensional heterochiral structure leading to highly enantiospecific substitution of a dissimilar chiral guest. Theoretical modeling shows that the enantiospecificity of site substitution is dictated by the architecture of the vacancy created within the heterochiral structure, which leads to significant enantiospecific differences in inter- and intramolecular H-bonding interactions and penalties for distortion of the molecular backbone. This work provides nanoscale insights into the nature of chiral recognition in complex 2D heterochiral systems and also into related phenomena, for example, tailored chiral growth through occlusion of inhibitor or modifier molecules at crystal surfaces.[12] Significantly, it shows that ordered heterochiral assemblies at solid surfaces can be efficiently desymmetrized by enantiospecific insertion of enantiopure guests within homochiral chains in the structure with stochastic creation of a range of diastereomers. Such processes leading to departures from the racemic state have been suggested[4] as important steppingstones in the creation of biological homochirality, where subsequent lattice-controlled polymerization can generate nonracemic libraries of oligomers. If such processes can be realized at solid surfaces, powerful new avenues for chiral technologies would be opened up.

Experimental Section

STM data were collected with an Aarhus 150 SPECS STM. RAIRS data (4-cm^{-1} resolution, 256 scans) were recorded with a Mattson 6020 FTIR spectrometer. All experiments were conducted in ultra-high-vacuum chambers ($P < 2\times10^{-10}$ mbar). Succinic acid (99% Sigma Aldrich) was sublimed onto a clean Cu(110) surface, held at room temperature. DFT calculations were performed with the VASP code with standard ultrasoft pseudopotentials for all atoms and PW91 GGA corrections. The bisuccinate and bitartrate species on Cu(110) arise from O–H cleavage of the COOH groups. The hydrogen atoms recombine and are desorbed as molecular hydrogen,[13] and the resulting charge-neutral OOCCHRCHRCOO/Cu(110) system was modeled (see the Supporting Information).

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[10] We also compared the energy difference at half coverage of Figures 2C and D with only one molecule in the (4×2) unit cell to ensure that no intermolecular H-bonds are formed in the structure. The diagonal adsorption configuration is still 14 kJ mol^{-1} lower in energy than the straight-across one, that is, the molecular deformation energy is the direct cause of this energy difference.

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