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Molecular Imaging

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Single-Molecule Chemical Reactions Tracked at the Atomic-Bond Level

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The imaging of atomic bonds of individual molecules has been the ultimate goal of molecular imaging for a long time.[1] These bonds determine chemical reactivity, and their visualization would allow chemists to understand how atoms or molecules bond at a most fundamental level. Even after the invention of scanning probe microscopy in 1981, the imaging of chemical bonds during molecular reactions at the atomic level remained elusive until a recent breakthrough by Fischer, Crommie, and co-workers: The imaging of the atomic bonds in a single molecule before and after its cyclization reaction was achieved by using noncontact atomic force microscopy (nc-AFM).[1d] The prospect to depict how atoms bond in chemical reactions at the molecular level is exciting, as it may lead to an enhanced understanding of catalytic processes, more precise drug design, and the bottom-up assembly of molecules for molecular devices. Their results clearly herald a new era, in which the atomic imaging of chemical bonds will constitute a new method for examining chemical structures and reaction mechanisms.

Scanning tunneling microscopy (STM) has been an important technique in nanoscience since its invention by Binning and Rohrer.[2] Its ability to image a molecule relies on quantum mechanical tunneling effects and depends on the probability with which the electronic states localized in the molecule contribute to the tunneling current. In most cases, the imaged electron densities associated with the molecular orbitals appear as convoluted electron clouds, which render the observation of the atoms within the molecule difficult.[3] New possibilities for directly imaging chemical bonds of molecules that are deposited on insulating and conducting surfaces recently emerged with the development of quartz tuning fork-based nc-AFM (qPlus nc-AFM).[4] While the tip scans back and forth over the sample surface at a constant height, the spatial variation in the extremely small force between tip and sample creates a minuscule frequency shift in the qPlus resonator, which is then converted into a microscopic contrast in nc-AFM imaging. An ingenious way to achieve sub-nanometer resolution when imaging a molecule involves decorating the apex of the atomically sharp tip with a closed-shell carbon monoxide (CO) molecule (Figure 1a).[1c] The CO molecule orients itself with its carbon atom bonded to the metal tip and the oxygen atom pointing towards the surface. The atomic contrast arises from a short-range (<1 nm) Pauli repulsion force between the CO molecule at the tip and the imaged molecule on the surface.[1a] The chemical inertness and the minuscule p orbital of the oxygen atom render this molecule particularly suitable for sensing the regions with the highest electron density (C≡C and C=C bonds; Figure 1b). Long-range attractive van der Waals and electrostatic interactions only add a diffuse attractive background to the image (a dark halo observed along the periphery of the molecule). Astoundingly, the imaged atomic structure resembles the "skeleton" of the individual molecule, and it allows the discrimination of chemical bonds and bond orders (Figure 1).[1b]

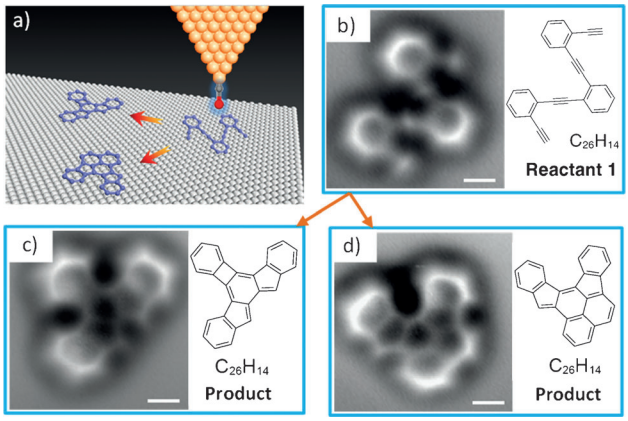

Figure 1. a) The tip apex was functionalized with a CO molecule for imaging of the reactant and the final products on the metal surface. b) AFM image of the reactant 1,2-bis[(2-ethynylphenyl)ethynyl]benzene. c, d) Two representative products that were observed after the sample had been heated to 90 °C.[1d] Scale bars: 0.3 nm.

With the nc-AFM technique, the chemical transformation of an individual molecule could be tracked at the atomic-bond level. M-shaped oligo(1,2-diethynylbenzene) (Figure 1b) was deposited on a Ag(100) surface, and then heated to induce a cyclization reaction. Imaging of the molecule by nc-AFM was performed immediately before and after the reaction at

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very low temperatures (ca. 4 K). The striking nc-AFM image obtained (Figure 1c,d) unambiguously shows the chemical structures of three abundant final products. It may be deduced that the reactants undergo a series of bond rearrangements before eventually transforming into polycyclic aromatic compounds. In combination with ab initio density functional theory (DFT) calculations, this technique thus offers unparalleled insights into the chemistry involved in the complex enediyne cyclization cascade on a Ag(100) surface.

This was the first time that bond-resolved images of individual molecules were obtained before and after a complex organic reaction. The ability to visualize intramolecular structural changes at the atomic-bond level allows an in-depth understanding of the mechanism of chemical reactions. Reaction intermediates can be trapped on a surface at cryogenic temperatures; the new technique thus allows the visualization of the chemical structures of these non-equilibrium products, and offers an unprecedented opportunity to determine the kinetic and thermodynamic properties of the system. This information may prove useful in the development of bond-specific reactions for tailor-made products. The on-surface cyclization reaction explored by Crommie, Fischer, and co-workers is only the tip of the iceberg. Their approach should enable the observation of Heck couplings and C–H bond activations on surfaces,[5] thus clarifying their heavily debated reaction mechanisms. The ability to directly visualize chemical structures will allow the clear identification of unknown or only partially explored natural molecules, because the resulting images resemble textbook-type structural formulas.[1c] It should be pointed out that the possibilities of the new nc-AFM technique extend beyond thermally induced reactions, and photochemical or electrochemical transformations may also be studied. For example, insights into photoinduced conformational changes of molecular switches[6] and phototriggered catalytic processes, such as water splitting, could also be provided. The technique thus entails potentially far-reaching implications for synthetic chemistry.

Insights into defect formation at the atomic level are crucial for defect engineering in materials science. However, imaging by transmission electron microscopy requires elaborate sample preparation. Dynamically imaging the defect formation process is also challenging in most cases. At the same time, STM images of defects are dominated by convoluted electronic effects, which often obscure the atomic structure. The nc-AFM technique, however, is capable of imaging the chemical bonds in defects, such as the four-, five-, and seven-membered rings in a honeycomb lattice, which is anticipated to result in new insights and strategies for defect engineering and two-dimensional crystal growth.[7]

One of the drawbacks of imaging molecules on a metallic surface is that the metal substrate generally alters the reaction kinetics, and consequently the reaction pathways may differ from those of homogeneous solution-phase reactions. Nevertheless, the use of frequency-modulated AFM to visualize molecular reactions on an insulating surface is alluring. The imaging of molecular reactions on these surfaces, such as quartz or sodium chloride, at the single-molecule level provides an opportunity to unveil intrinsic molecular reactivity.

Although the results summarized herein are exciting, the nc-AFM technique is still at an early stage of its development. It works best at a low degree of molecular coverage, and for high-resolution images, the molecules must lie flat on a smooth surface. To date, the majority of high-resolution nc-AFM imaging has been applied to covalent bonds with high local electron density (such as C=C and C≡C bonds). Weak intermolecular bonds, such as hydrogen bonds or other long-range dipole–dipole interactions, are central to the assembly of biological molecules. Owing to their low local electronic density, the direct visualization of weak bonds requires additional charge accumulation to generate a noticeable repulsion force.[8]

The presented nc-AFM technique has an STM counterpart. Inserting H_2 (or D_2) at the tunneling junction between the measuring tip and the molecules on the surface enhances the imaging resolution of the molecular layers to a remarkable extent.[9] The single H_2 molecule confined to the tunneling junction changes its position because of Pauli repulsion forces, which results in a change in the tunneling current.[1c,9] This technique, scanning tunneling hydrogen microscopy, has allowed the imaging of the internal honeycomb structure of perylene tetracarboxylic dianhydride.[9b]

In summary, the attachment of a sensor molecule to the tip appears to be a viable way of enhancing atomic resolution in both AFM and STM. However, the imaging of weak, non-covalent interactions in molecular networks remains elusive. If spin-polarized atoms could be attached to the tip, these techniques might even become suitable for the imaging of spin electron densities in a molecule.

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