RZ 3914 (# ZUR1607-052) 07/25/2016
Physical Sciences 24 pages

Research Report

Generation, Manipulation and Characterization of Molecules by Atomic Force Microscopy

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This is the author-prepared version; the final version was published in *Nature Reviews Chemistry* **1,** article 0005 (2017): http://dx.doi.org/10.1038/s41570-016-0005 [© 2017 Macmillan Publishers Limited, part of Springer Nature.]

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Generation, Manipulation and Characterization of Molecules by Atomic Force Microscopy

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Atom manipulation can be used to dissociate, form, and rearrange bonds and to change the conformation or the charge state of molecules. Tip functionalization by atomic manipulation enabled atomic resolution on molecules with atomic force microscopy (AFM) revealing the molecular structure of initial reactants and final products after atomic manipulation with unprecedented resolution. Using atom manipulation in combination with AFM for molecular characterization we are approaching the type of molecule assembling that Richard P. Feynman did foresee in his famous talk "There is plenty of room at the bottom", where molecules and materials are formed by attaching and detaching individual atoms at will. Here, we review the recent progress and discuss prospects of molecule generation by atomic manipulation and molecular characterization with the AFM.

1. Introduction

In this paper we describe recent progress in the generation, manipulation and characterization of molecules on surfaces using scanning probe microscopy (SPM). In such microscopes atomically sharp tips are scanned across the surface to obtain an image, and moreover the tip can be used for atomic manipulation. There are different kinds of SPMs, on the one hand the scanning tunnelling microscope (STM), which was invented by G. Binnig and H. Rohrer in 1982 [1] and awarded with the Nobel Prize in Physics in 1986. The STM relies on the quantum mechanical effect of electron tunnelling to acquire images. Even more important for the focus of this article is atomic force microscopy (AFM) invented 1986 by G. Binnig, C. F. Quate and Ch. Gerber [2] awarded with the Kavli Prize in Nanoscience in 2016. In AFM the force acting between tip and sample is exploited to obtain images.

In 1990, D. Eigler and E. K. Schweizer pioneered atomic manipulation, demonstrating the possibility to place atoms with atomic precision [3] using the scanning tunnelling microscope (STM). Other milestones where achieved by Sugimoto and co-workers demonstrating atomic manipulation at room temperature creating atom inlays [4] and chemical sensitivity on atom inlays with the AFM [5].

However, only few examples of molecular chemical reactions activated by atomic manipulation have been reported until recently. Important works include the dissociation of molecular oxygen by Stipe et al. [6], an Ullmann reaction induced by atomic manipulation by Hla et al. [7] and polymerization by Y. Okawa and M. Aono [8], all performed and characterized using STM. A great challenge of these earlier works was the identification of the reaction products. Since a direct assignment of the molecular structure by atomic-resolution imaging was not possible, inventive methods were successfully developed and applied to determine the reaction products. For example, the generation of biphenyl from iodobenzene in the Ullmann reaction was proven by lateral manipulation, i.e. pulling of the product [7]. Molecular orbital imaging by STM [9] increased the insight into molecular reactions and allowed observation of metal complexation [10] and tautomerization reactions [11] triggered by atom manipulation.

Atomic resolution on molecules with the AFM was demonstrated in 2009 using atomic manipulation for tip functionalization [12]. This technique rendered it possible to identify even complex molecules by their image in real space [13] opening up the possibility to study more complex molecules and reactions by AFM.

At about the same time on-surface synthesis of covalently bonded molecules became an important topic of research [14]. Covalently bonded molecular wires and in particular graphene nanoribbons [15] are now grown by on-surface synthesis, that is, by thermal annealing of custom-made precursor molecules. Naturally, AFM with atomic resolution became an important tool to reveal the products and also intermediates of thermally-induced on-surface reactions [16, 17, 18, 19, 20, 21, 22]. One motivation for using AFM in this context is the identification of the products formed, another motivation is a better understanding of the reaction mechanisms, improving the control, the quality and the yield of the formed structures and finding novel structures.

Moreover, AFM can be used to study molecular reactions triggered by atom manipulation. In particular radicals can be created by dissociation and studied with the AFM [23, 24, 25, 26, 27]. Bonds can also be formed, attaching atoms to molecules or forming metal complexes [10, 28, 29, 25] or internal covalent bonds can be created and broken [26]. In these investigations the surface has an important role, for example an inert surface is required to isolate reactive molecules. One objective of molecular generation by atomic manipulation is the characterization of molecules that cannot be made or stabilized otherwise. Moreover, insight into on-surface reactions is obtained and the detailed characterization and testing of single-molecular switches becomes possible. An improved understanding and control of molecular generation by atomic manipulation holds the great promise of fabricating covalently bonded molecular or metal complex structures with custom-designed geometries using the probe tip.

Here we describe the technique and the developments that enabled molecular manipulation and characterization with the AFM, review the current status of research and discuss future goals and prospects.

2. Experimental setup

2.1. The Microscope

The atomic force microscope (AFM) just celebrated its 30st anniversary and nowadays is a widely used tool with many application areas. In general, most of the AFM tools work in ambient conditions and in so-called contact mode or tapping mode, where the sensor makes mechanical contact to the sample. For high-resolution imaging of single molecules it is advantageous to go to very stable and very clean conditions that can be obtained by working with cryogenic systems in ultra-high vacuum (UHV) conditions. For non-destructive imaging of the surface a mechanical contact between tip and sample should be avoided. In atomic imaging of molecules AFM is employed in the frequency modulated non-contact mode (NC-AFM) [30, 31]. In this mode a cantilever holding the tip is actively oscillated by a feedback circuit with constant amplitude at its resonance frequency. Due to the interaction of the tip at the cantilever with the sample surface, the resonance changes by the frequency shift Δf, the measurement signal in NC-AFM. In the limit of small amplitudes, the frequency shift Δf is proportional to the gradient of the interaction force between tip and sample F_{ts} (see Fig. 1). Using three-dimensional force spectroscopy [32] quantitative force maps can be extracted [33] and the interaction forces and energies can be measured.

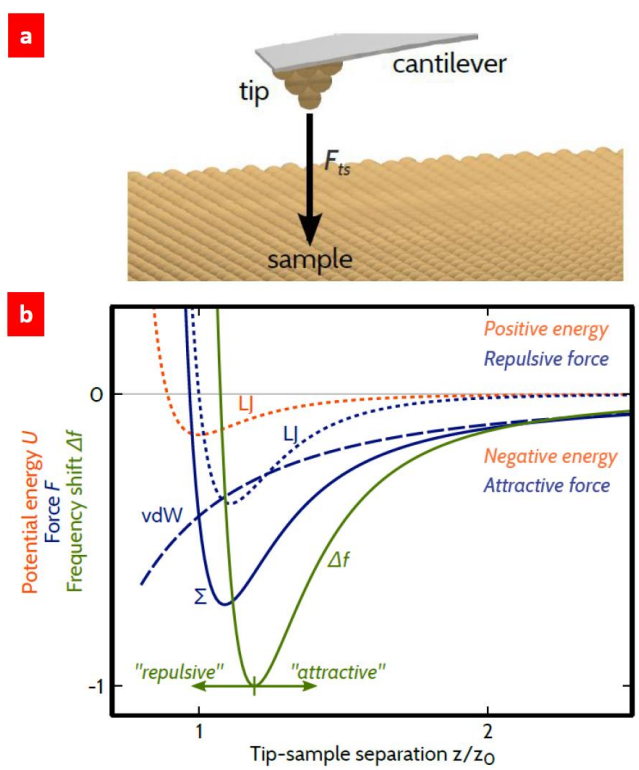

Figure 1: AFM Schematic. (a) Rendered model of an oscillating cantilever with a tip above a sample surface. (b) Short- and long-range contributions in AFM. Short-range contributions are modelled by Lennard-Jones pair potential (dotted orange line) and force (dotted blue). Adding an attractive background force due to van der Waals interactions (vdW, dashed blue) yields the total tip-sample force (Σ, solid blue). The resulting frequency shift Δf,

the measurement signal in AFM, is approximated as the force gradient, shown in green. The total force is only repulsive for tip-sample distances smaller than the equilibrium distance z_0. Nonetheless, it is common to distinguish between the "attractive" and "repulsive" branch based on the minimum in the frequency shift.

Typically (and for all experiments shown in this article), combined low-temperature STM/AFM systems are used and qPlus sensors are employed to achieve atomic resolution on molecules. The qPlus sensor was developed by Franz Giessibl [34, 35] based on quartz tuning forks used as time keeping elements in wrist watches. This sensor features piezoelectric detection and a comparably stiff force constant making it possible to operate AFM with oscillation amplitudes down to fractions of Ångström (1 Å = 10^{-10} m) and allowing simultaneous STM experiments with uncompromised performance. Working at small oscillation amplitudes is crucial to optimize the sensitivity with respect to short-range forces and thus for obtaining atomic resolution [36, 35]. Typically, peak-to-peak oscillation amplitudes of about 1 Å were used to obtain the atomic resolution AFM images presented in this article. However, atomic resolution on molecules was also demonstrated with Si cantilevers [37] using much larger oscillation amplitudes and even at room temperature [38].

Before we discuss molecular reactions performed by atomic manipulation it is instructive to review the capabilities of scanning probe microscopy for molecular imaging and analysis and the importance of atomic tip functionalization. Importantly, very complementary properties of molecules can be accessed using different scanning probe techniques, i.e. AFM, STM and Kelvin probe force microscopy (KPFM) as described in the following. As an illustrative example, data obtained on naphthalocyanine with different scanning probe microscopy modes and with different tip functionalizations are compiled in Fig. 2.

2.2. Atomic Force Microscopy

Most important for structure elucidation is non-contact atomic force microscopy as it gains atomic resolution on molecules [12] and its contrast mechanisms are well understood. The atomic contrast mechanism is based on Pauli repulsion: Bright features in the constant-height AFM images indicate repulsive force contributions and are often observed above atom positions and bonds. This repulsive atomic contrast arises from overlap of the electron distributions of the molecule imaged with that of the tip apex resulting in Pauli repulsion [39]. Van der Waals and electrostatic forces contribute only an overall attractive background with little corrugation on the atomic scale and give rise to the dark halo surrounding the molecules in AFM images. In a simplified picture the bright regions in the AFM images can be interpreted as regions of high electron density of the molecule imaged. Figure 3a shows a structural model of naphthalocyanine and Fig. 2b shows AFM data with a CO tip [40], reflecting the molecular structure. The faint contrast differences in the molecular centre even reveal the positions of the hydrogens, which are difficult to image by many techniques, including transmission electron microscopy (TEM).

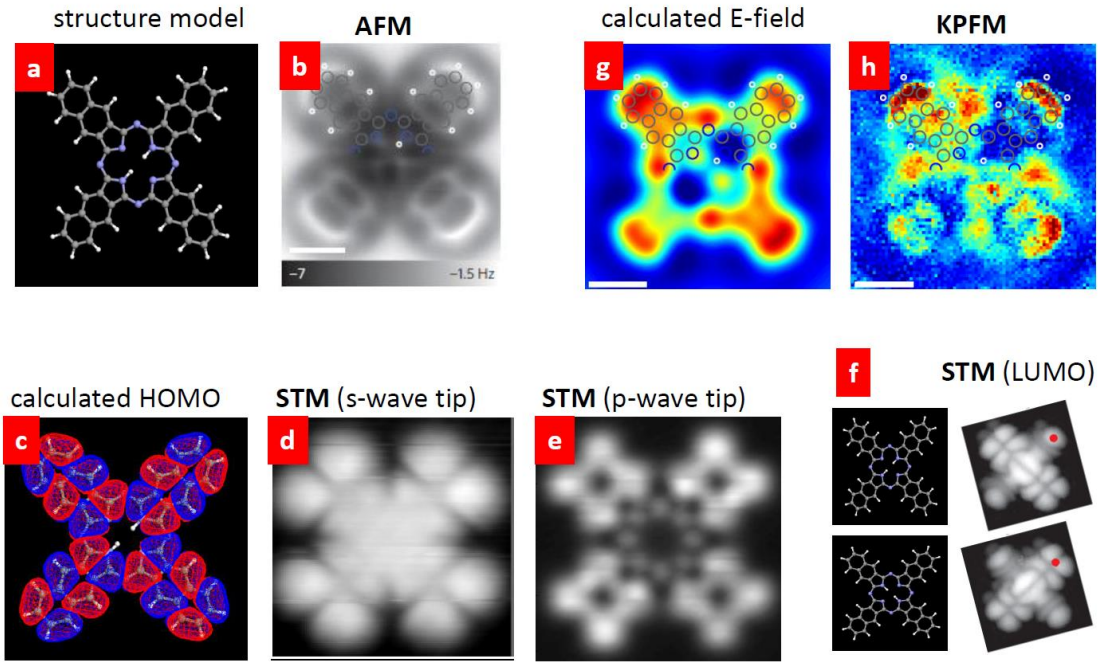

Figure 2: Molecule characterization by scanning probe microscopy. Naphthalocyanine on bilayer NaCl on Cu(111) imaged using different scanning probe techniques and different tip functionalizations. (a) Ball and stick model, (b) CO-tip AFM image [40], (c) calculated highest occupied molecular orbital (HOMO), (d,e) STM orbital image of the HOMO with (d) s-wave tip (Cu tip) and (e) p-wave tip (CO tip), respectively [41]. (f) Ball and stick model of the different tautomers (left) and corresponding STM images of the LUMO density (right) [11]. (g) Calculated electrostatic field and (h) local contact potential difference (LCPD) measured with KPFM [40].

The atomic tip-functionalization is of utmost importance for AFM imaging [12]. It is desirable to have small atoms/molecules as tip functionalization, as in general the lateral resolution limit scales with the tip radius. Secondly, the tip should be rather inert to prevent the imaged molecule from being picked up or displaced by the tip. For the latter reason metal tips are often not suited; due to their high reactivity they pick up the molecule before atomic contrast is obtained [12]. Other properties of the tip functionalizations that are important are relaxations of the tip and its charge distribution and the resulting electrostatic field.

Carbon monoxide (CO) has turned out to be an excellent tip functionalization for obtaining high resolution on molecules. The CO is picked up from the surface with a metallic tip and adsorbs on top of a metal atom of the tip (often Cu), with the carbon bonded to the metal atom and the oxygen protruding [42]. Thus it features a small atomic radius and even a high aspect ratio on the atomic scale. Additionally, tip relaxations, i.e., tilting of the CO, lead to apparent distortions and result in a sharpened appearance of bonds [43, 44] and facilitate bond-order analysis [43]. However, one has to be cautious as apparent bonds might arise as artifacts due to the CO tilting [45, 46]. These tip relaxation effects are well understood [43, 44, 46, 47, 48] and can also be corrected [49]. If less distorted images are desired,

other tip functionalizations like Xe [24], Cl [12], or CuO [50] can be employed. Depending on the properties to be measured, certain functionalizations are preferred, in particular Xe tips are suited for measuring the molecular adsorption geometry with high resolution [23] and also for Kelvin probe force microscopy [24]. For molecular structure elucidation by AFM the CO tips are most popular and all AFM data shown in this article have been acquired with CO functionalized tips.

2.3. Scanning Tunnelling Microscopy

With scanning tunnelling microscopy (STM) molecular orbital densities can be imaged [9]. The naphathalocyanine's LUMO, showing a two-fold symmetry was initially used to reveal the position of the inner hydrogen atoms that can be switched by a tautomerization reaction induced by electron attachment [11], see Fig. 2f. Typically, the frontier molecular orbitals, i.e. the lowest unoccupied molecular orbital (LUMO) and the highest occupied molecular orbital (HOMO) can be resolved using STM, as the accessible bias window for tunnelling is limited to a few volts around the Fermi level. For a neutral molecule the LUMO (HOMO) is imaged by applying a positive (negative) sample voltage to tunnel resonantly into the negative (positive) ion resonance. For orbital imaging it is beneficial to electronically decouple the molecule from the metallic substrate using a thin insulating film, e.g. a bilayer NaCl [9] or a monolayer of Xe atoms [51]. The calculated HOMO and the measured orbital density of the naphthalocyanine's HOMO using a metal (s-wave) tip are shown in Fig. 2c and Fig. 2d, respectively [9, 11, 41]. Fig. 2e shows the same orbital imaged with a CO tip. Note the increased lateral resolution because the CO tip exhibits a strong p-wave character (due to its π-molecular orbitals) leading to images of the gradient of the orbital density [41, 51].

In addition, STM imaging at voltages below resonance with functionalized tips, dubbed scanning tunnelling hydrogen microscopy (STHM) yields also intra-molecular/sub-molecular resolution on molecules [52]. In this case forces on the atomic scale lead to tip relaxations that modulate the measured tunnelling current with structural information. That is, tip functionalization acts like a force-to-current converter [53]. Vibrational spectroscopy by inelastic electron tunnelling spectroscopy (IETS) was pioneered in the group of W. Ho [54] and yields energies of vibrational molecular modes that can serve as molecular fingerprints and allow even isotope discrimination [54, 55, 56]. Because the chemical environment and the relaxation of the CO tip give rise to an energy shift of the frustrated translation vibrational mode of the CO at the tip, IETS maps acquired with CO tips also yield intra-molecular resolution on molecules [57].

2.4. Kelvin Probe Force Microscopy

Kelvin probe force microscopy (KPFM) is an offspring of non-contact AFM and is based on measuring the frequency shift as a function of applied voltage [58, 59, 60]. With KPFM one can measure the so called local contact potential difference (LCPD) which yields information about the charge state [61, 62, 63] and charge distribution of molecules [40].

KPFM maps on molecules qualitatively resemble the vertical electrostatic field above the molecule [64]. Naphthalocyanine exhibits an electrostatic quadrupole moment that is also switched in the tautomerization reaction. The electrostatic field of naphtalocyanine was measured by KPFM and its

electric quadrupole moment could be revealed [40], see Fig. 2g,h. Furthermore, KPFM can be used to infer about the charge distribution and electrostatic field of the tip [59, 65, 48], important for the interpretation of AFM results.

2.5. The manipulation toolbox

In general, to perform chemical reactions using atomic manipulation different mechanisms can be employed. First, the force between tip and adsorbate can be used. This tip-adsorbate force can be varied by different parameters, for example the tip-adsorbate distance, the applied voltage which changes the electric field and, consequentially, the electrostatic forces within the junction, or by switching the charge state and/or the conformation of an adsorbate. Second, the tunnelling current can trigger reactions, e.g. by means of electronic excitations (electron or hole attachment) or inelastic energy transfer from tunnelling electrons to the adsorbate (inelastic electron tunnelling, IET), or *via* hot carriers in surface states. Finally, annealing the sample to elevated temperatures can induce or assist processes.

Atoms and molecules can be moved laterally and vertically, i.e., being picked up and dropped from the tip [3]. Lateral manipulation can be further divided into pulling, pushing and sliding modes [66] and detailed information about the manipulation process can be extracted during lateral molecular manipulation [66, 67]. Using AFM the forces needed to pull an atom on a surface can even be quantified [68]. Also larger molecules with many internal degrees of freedom can be laterally manipulated [69]. For molecular generation by atomic manipulation, lateral manipulation can be important for arranging the products on the surface and it might also be used to prove successful bond formation, e.g. by pulling the fused product [7]. Furthermore, intramolecular degrees of freedom, like their conformations can be switched, most often by means of tunnelling electrons [70, 71, 72, 73]. Recently, intramolecular tautomerization reactions were induced by force [74].

The most important mechanism for bond dissociation and bond formation seems to be inelastic electron tunnelling (IET). Energy, typically up to few eV, can be transferred from the tunnelling electrons (or holes) to the molecule on the surface. Depending on the actual system, different processes can occur. One way is that part of the tunnelling electrons' energy is directly transferred to vibrational modes of the molecule [6, 75]. Alternatively, electrons might be temporarily injected into a vibronic state of the molecule and part of their energy may then be deposited in the molecule as vibrational energy [76]. Whereas in the former case the threshold voltage corresponds to the energy of a vibrational mode, in the latter case the threshold corresponds to the energy of an electronic resonance (molecular orbital). In some cases, different mechanisms of energy transfer, i.e., electronic excitation of an antibonding orbital and vibrational excitation can be distinguished [77, 78]. Other processes are also possible, e.g., energy transfer via hot carriers in surface states [79, 80].

Molecule reactions can occur if the transferred energy exceeds the reaction barrier. Depending on the energy transfer per electron, one or several electrons (vibrational heating [75]) might be needed to trigger the reaction. Already early on, pioneering studies with the STM provided insight into the reactions, measuring yields as a function of voltage and current, gaining information about the energy

and the number of electrons needed for the reaction [6, 75]. Using IET, controlled bond dissociation [6, 7, 75, 10, 81] and formation [55, 7, 10] were demonstrated. Also hydrogen tautomerization reactions within individual molecules could be induced using inelastic tunnelling [11, 81, 82] (see Fig. 2f).

However, because STM probes merely electronic properties it is not always straightforward to infer the chemical structure of complex reaction products. Only recent progress in sub-molecular resolution made it possible to go further and tackle the generation of more complex molecules by atomic manipulation.

2.6. Sample Preparation

The sample preparation is typically performed under UHV conditions. Several ingredients of the prepared sample are important and have to be considered: A clean substrate has to be prepared on which the molecules to be investigated or their precursors, and, additionally, atoms or molecules for tip functionalization have to be deposited (see Fig. 3).

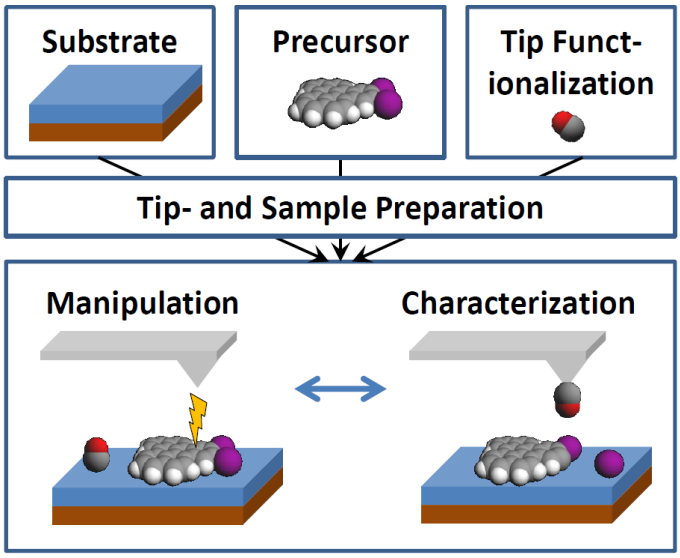

Figure 3: Schematic illustration of the prepared samples and AFM measurements. A clean substrate is prepared; often surfaces of noble metal single crystals are used. Thin insulating layers, e.g. NaCl or Xe, can be grown on top. Molecules, precursors and atoms/molecules intended for tip functionalization are deposited.

The sample surface is important for several different reasons. It anchors the molecules when they are imaged, and it can influence their adsorption geometry. It is often desirable for the surface-adsorbate coupling to be weak, in order to both preserve the reactivity, geometry and molecular structure of a species, as well as to allow charge state manipulation. For these reasons ultrathin insulating films can be employed, e.g. bilayer (100)-oriented NaCl grown on Cu(111) [83]. The surface is also important to prepare the tip: Often the tip is indented in a metal substrate to form a stable, yet atomically sharp, conductive tip and the substrate also has to allow the pick-up of atoms or molecules for tip functionalization. Moreover, the substrate might have an important role as catalyst in on-surface

reactions. Finally, surface structures or defects can be important as reaction sites or guiding structure for manipulation experiments [7].

Molecules to be investigated or precursor molecules that serve as the initial product for a manipulation experiment are deposited, typically by thermal sublimation, onto the sample surface. Moreover, small molecules or atoms to be used for tip functionalization are dosed into the chamber and adsorbed onto the surface. Alternatively, atoms for tip functionalization can be picked out of the substrate (e.g. Cl from NaCl) [12, 50] or dissociated from precursor molecules (e.g. Br from dibromo-anthracene) [24].

3. Applications

3.1. Molecule identification

A directly emerging technique for atomic resolution AFM, which does not necessarily include atomic manipulation, is the identification of molecules. Molecular elucidation with AFM was already used for the identification of *a priori* unknown natural products [13, 84], synthesized products [85] and characterization of complex molecular mixtures [86]. Figure 4a shows breitfussin A, which could only be assigned combining nuclear magnetic resonance (NMR), mass spectrometry, and density functional theory (DFT) calculations with AFM, revealing a previously unknown molecule and a novel class of molecular structures. In this study AFM revealed all the connection positions of the cyclic systems as well as those of the substituents (methoxy group, Br and I heteroatoms) [84]. Furthermore, AFM was used to identify the products of on-surface synthesis using heating [16, 17, 18] and it confirmed the atomic structure of zig-zag graphene nanoribbons (GNR) [21], fused GNR [87, 88] and boron doped GNR [19]. Also it revealed how molecules were covalently coupled to graphene edges [22].

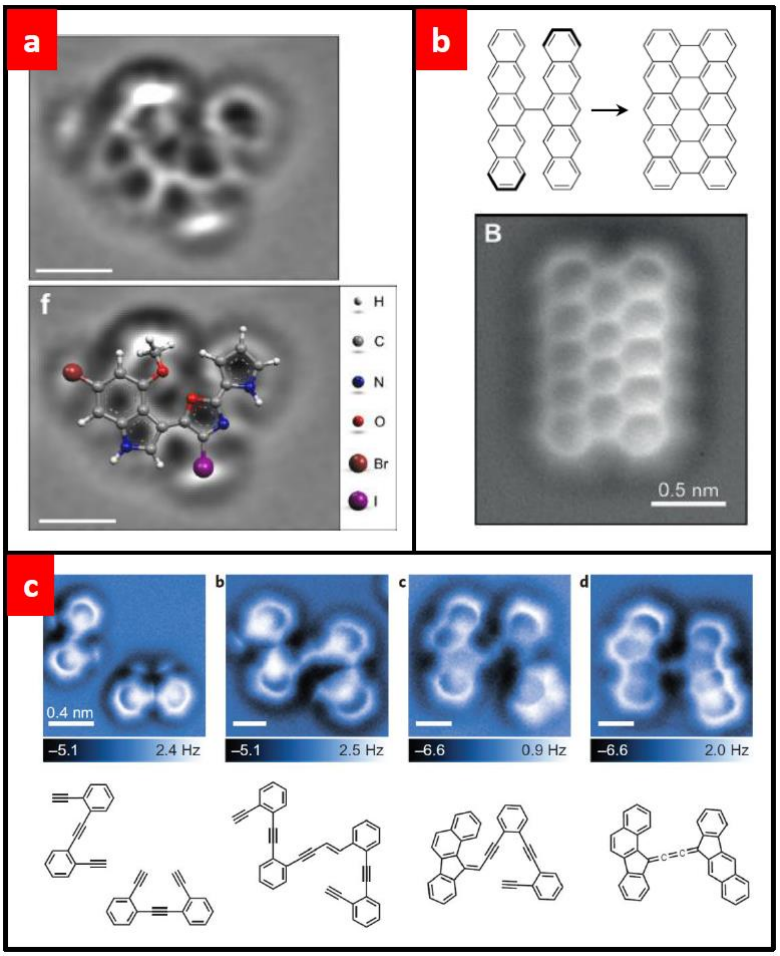

Figure 4: Molecule identification by AFM. All measurements are AFM data with CO functionalized tips, (a) the natural compound Breifussin A, which could only be identified with the help of AFM [84], (b) peripentacene, formed by thermally induced cyclodehydrogenation reaction of 6,6'-bipentacene precursors on Au(111) [18], (c) transient intermediates in a stepwise bimolecular enediyne coupling and cyclization cascade [20].

AFM was also applied to reveal novel molecules generated by on-surface synthesis. For example the thermally induced cyclodehydrogenation reaction of 6,6'-bipentacene precursors on Au(111) was found to yield peripentacene (Fig. 4b) [18]. Also different intermediates of on-surface reactions could be imaged, shown in Fig. 4c, and their abundance as a function of annealing temperature was quantified yielding unprecedented insight into the reaction pathway of such catalytic reactions on surfaces [20].

3.2. Molecule-metal complexes generated by atomic manipulation

Molecule-metal complexes could be formed using tip-induced manipulation and AFM was employed to reveal the resulting structures revealing the possibility of AFM to follow reactions induced by atomic manipulation.

AFM could reveal the different products upon reversible bond formation in a metal-molecule complex formed by a Au atom and a PTCDA (perylene-3,4,9,10-tetracarboxylic acid dianhydride) molecule. In this case electron/hole attachment was employed to charge and discharge the products, which were adsorbed on a bilayer NaCl film on Cu(111). Charging and discharging are among the possible mechanisms to form and break bonds as demonstrated for this complex. Upon electron attachment the PTCDA-Au complex gets doubly negatively charged and the bond between metal atom and PTCDA molecule is broken, resulting in an isolated negatively charged PTCDA molecule and a Au anion that repel each other due to Coulomb repulsion (Fig. 5a,b). If a hole is attached, the Au will bond again to the PTCDA and a singly negatively charged Au-PTCDA complex is formed as revealed by AFM, see Fig. 5c,d. This process of bond formation and annihilation in the Au-PTCDA complex is reversible, repeatable, reliable and directed (as electrons and holes are attached at opposite voltages) and therefore interesting for possible applications as a single-molecule switch [28].

Another molecular-metal complex was created fusing two isolated phenazine molecules with a Au anion on bilayer NaCl on Cu(111) by electron tunnelling at a sample bias of -2.5 V. AFM helped assigning the geometric structure of the resulting molecule-metal-molecule bridge, shown in Fig. 5e,f. In addition, STM was employed to characterize the electronic structure, revealing covalent bonding of the complex formed [29].

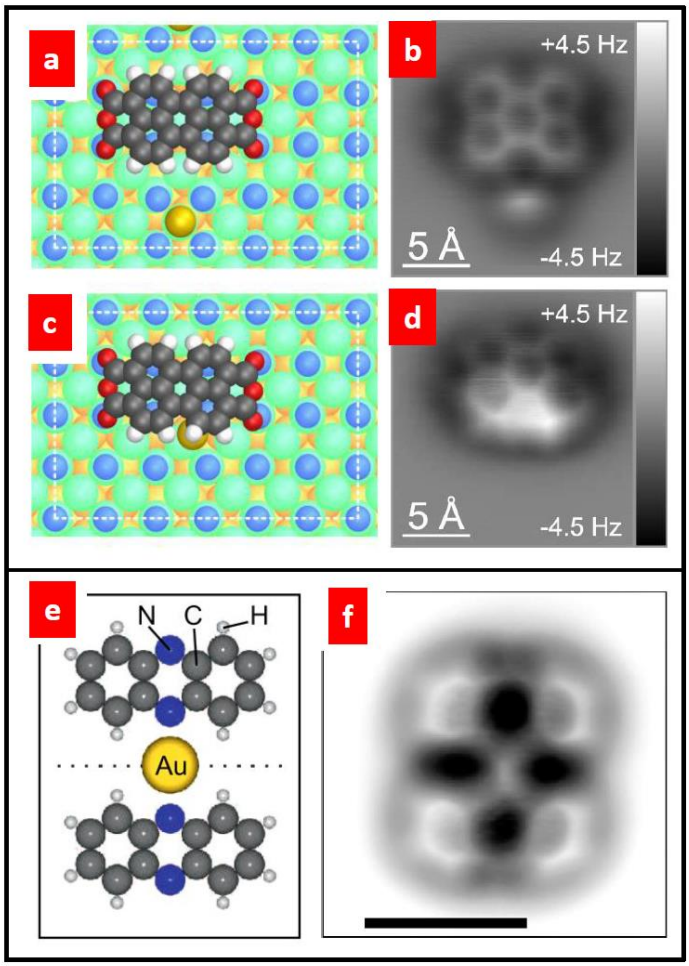

Figure 5: Molecule-Metal complexes. (a-d) Switching a metal-molecule complex formed by a Au atom and a PTCDA molecule. (a) Model and (b) AFM measurement of non-bonded complex; (c) and (d) model and AFM measurement of bonded complex, respectively. The bond formation is directed, reproducible and reversible [28]. (e,f) Molecule-metal-molecule bridge formed by two phenazine molecules and a Au anion [29]. All complexes were formed and investigated on bilayer NaCl on Cu(111).

3.3. Radicals generated by atomic manipulation

Bond dissociation is one of the best studied chemical reactions by atomic manipulation. Typically, bond dissociation is achieved by inelastic electron tunnelling breaking the weakest bonds in a molecule if sufficient energy is provided. With this method halogen or hydrogen atoms can be dissociated [7, 75]. Dehydrogenation of aromatic hydrocarbons can lead to radicals, which often results in chemisorption and the formation of covalent bonds to a metallic substrate [89, 23, 90]. It is important to distinguish σ- and π-radicals. While the molecular structure of a π-radical may mostly preserve its planarity [23], σ-radicals often deviate strongly from planarity, in particular on metallic surfaces where they form bonds to the substrate [89, 90, 25, 26]. To preserve the radical character and prevent the

radical from forming a covalent bond to the substrate one has to employ inert surfaces, e.g. ultrathin insulating layers [25, 26].

Carbon bonds to iodine and bromine are weaker than those to hydrogen. In a phenyl group the bond enthalpies of C-H, C-Br, and C-I bonds are 4.9 eV, 3.6 eV, and 2.9 eV, respectively [91]. Hence halogen atoms in the precursor molecules can predefine the positions at which atoms will be dissociated and radical centres will be created. Often dissociation occurs by temporary electron attachment and often the minimal electron energy (applied voltage times elementary charge) needed to dissociate the bond matches within a few 100 meV the respective bond enthalpy. Using this method, specific radicals can be created by atomic manipulation, and they might be stabilized and characterized at low temperature on inert substrates.

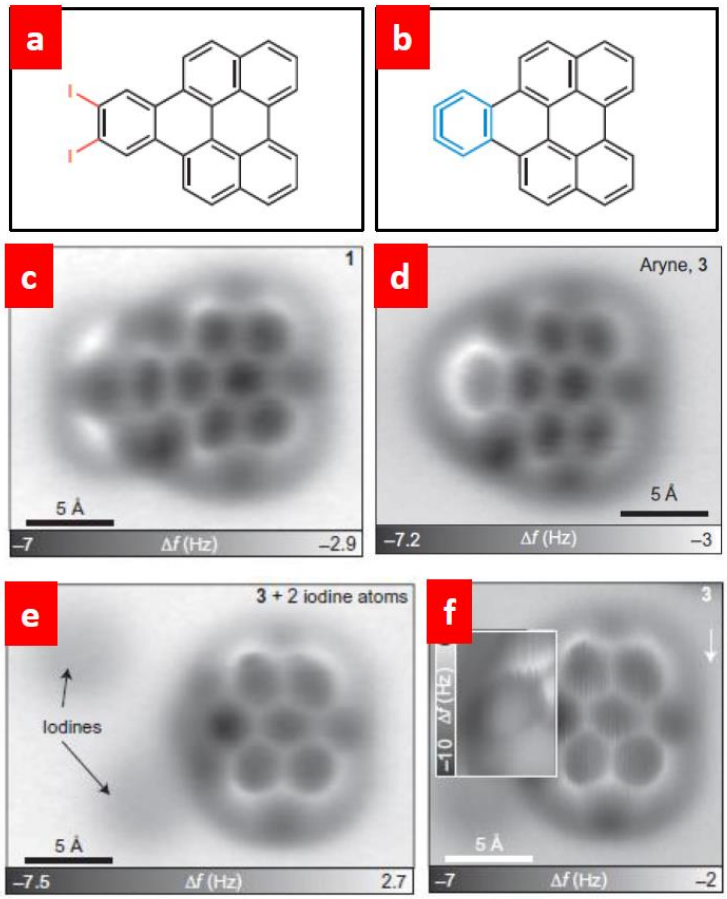

Figure 6: Aryne generation and characterization. (a) Precursor molecule (b) aryne product, formed by iodine dissociation. (c,d) AFM of (c) precursor and (d) aryne product on bilayer NaCl on Cu(111), respectively. (e,f) AFM of product on Cu(111). In the highlighted region in (f) the tip height has been decreased, revealing the left-hand side ring of the molecule, which formed bonds to the Cu substrate [25].

Arynes are prominent reactive intermediates that only live for a very short time under ambient conditions rendering their characterization extremely difficult. We intended to create and study an aryne using atomic manipulation. To that end we deposited diiodonaphthoperylene (DINP, see Fig. 6a for the chemical structure and Fig. 6c for the AFM image) on bilayer NaCl on Cu(111). We created an aryne (Fig. 6b) by dissociating the two iodine atoms located at ortho-positions of the outermost hexagon using electron attachment to the lowest unoccupied molecular orbital (LUMO) of DINP at sample voltages above 1.6 V, indicating bond cleavage by electronic excitation [77, 78, 25]. The resulting aryne is shown in Fig. 6d. The extended planar aromatic hydrocarbon core of the molecule (the perylene backbone) permitted us to perform a bond-order analysis by AFM [43]. We could resolve the cumulenic representation as the dominant resonance structure for the aryne molecule generated. It was also possible to re-establish the initial DINP molecule from an aryne and two nearby lying iodine atoms using a voltage pulse, indicating that the reactivity of the aryne is preserved [25]. The latter result is promising for the use of such radicals for the generation of larger, more complex molecules using bond formation by atomic manipulation.

Note that on a copper surface the formed aryne immediately reacts with the surface. The iodines can also be dissociated on Cu(111) and show up as faint depressions in Fig. 6e. But the complete right hand side carbon ring of the molecule can no longer be seen in the constant height AFM image in Fig. 6e. In Fig. 6f, which uses a decreased tip height in the region of this ring, it is revealed that the adsorption height of this ring is lowered due to bonds formed to the Cu(111) substrate [25]. A similar reaction had been previously for dehydrogenated benzene on Cu(110) [78].

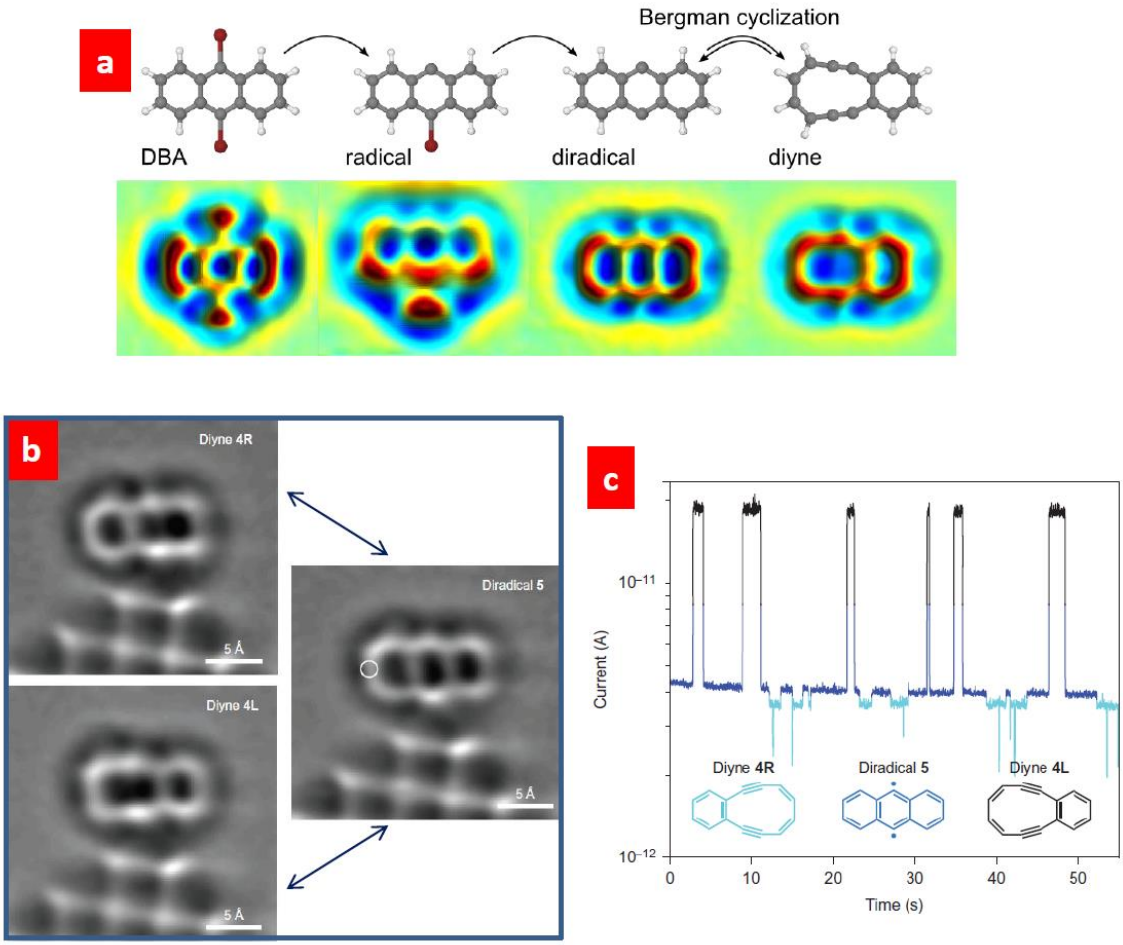

Figure 7: Reversible Bergman cyclization. The Br atoms from dibromoanthracene (DBA) are dissociated to form a diradical. The diradical can be reversible switched between diyne and diradical by tunnelling electrons at above 1.6 V (see text). All measurements on bilayer NaCl on Cu(111) [26].

Using a similar methodology another diradical could be created by dissociating bromine from dibromoanthracene (DBA), see Fig. 7a. Again, bilayer NaCl on Cu(111) was used as substrate to stabilize the radical product. In contrast to the ortho-aryne discussed above, the dissociation of the Br atoms in para-positions occurred in two steps [92]. While the voltage threshold for dissociation of the first Br corresponded to resonant tunnelling into the molecule at above 1.6 V, appreciably higher electron energies (V > 3.3 V) were required for the second Br. On the diradical a further reaction could be induced by atomic manipulation. Electron attachment to the diradical resulted in a ring-opening reaction, forming a diyne structure featuring a ten-membered ring. Moreover, this process is reversible; the ten-membered ring can be reconverted to the diradical triggering a Bergman reaction. Both Bergman and retro-Bergman reactions occur upon electron attachment, i.e. at above a threshold of 1.6 V to tunnel resonantly into the molecule.

Often the induced reactions are accompanied by a lateral displacement of the molecule. This displacement can be suppressed by anchoring the molecule at a defect, e.g. a step edge. Applying

electrons with energy above the switching threshold to an anchored molecule resulted in continuous switching between three different tunnel current plateaus (see Fig. 7c). The three plateaus correspond to the diradical and the two diyne molecules with ten-membered rings on either side of the molecule. The reaction can be stopped at any of these three molecular conformations by reducing the voltage below its threshold value. At lower voltage the molecule remains stable and can be imaged using AFM revealing the product formed (Fig. 7b). This reversible molecular switch is interesting as also the spin-multiplicity is switched between diyne, which features a singlet ground state, and the diradical, which is in a triplet ground state with unpaired electrons localized at the radical centres [26]. Note that besides the optical and magnetic properties also the reactivity of the diradical is switched in this reaction which could be important for future molecular generation by atomic manipulation.

4. Outlook

We foresee some important goals for molecular identification by AFM and molecule generation by atomic manipulation, which seem feasible to be reached in the next decade. For identification this is on the one hand chemical sensitivity and on the other hand the extension to more complex molecules, that is, larger and non-planar molecules. For molecular generation by manipulation the most important goal is the controlled fusion of molecular segments and, connected, an improved understanding of the underlying mechanisms of molecular generation by atomic manipulation.

Elemental sensitivity is extremely challenging within molecules. This is mainly due to the huge effect of the bonding environment. For example, a carbon atom will appear very differently if it is sp, sp^2 or sp^3 hybridized and even minute differences in the bond order lead to different contrast. Furthermore, the non-planarity of molecules, i.e. the topography, which is not easily separated from the chemical contrast, and the relatively small atom distances within molecules render a direct elemental sensitivity extremely difficult. We foresee that chemical sensitivity could be established using fingerprinting of molecular subgroups by AFM. For this a database of AFM contrast of such measured (and/or calculated) molecular moieties, using different well defined tip functionalizations could be established, providing an identification scheme.

To extend molecular identification by AFM to more complex and larger molecules there are two main obstacles. The first is to prepare such molecules in the clean environment needed. To this end, deposition by electrospray ionization can be employed, already demonstrated to be feasible yielding large molecules on the order of 10,000 Da on atomically clean surfaces [93, 94, 95]. On the other hand, there is a severe limitation of AFM given by its extreme surface sensitivity. Methods to image the surface of non-planar molecules by atomic resolution AFM have been successfully developed [96, 17, 37]. However, the atoms of a molecule that are below the top atomic layer exposed to the tip are much more challenging to resolve. Smaller three-dimensional molecules might be possible to assign after planarization by atomic manipulation [27] or by using manipulation to reveal the different facets of a molecule towards the tip. Still, imaging the surface of a large molecule by atomic resolution might lead

to important insights. Moreover, large numbers of known and unknown planar molecules or molecules with planar moieties exist; on which AFM in its current form can be applied [97].

In terms of manipulation, the fusion of molecules by atomic manipulation, although achieved in some cases [7] still is a great challenge. Bond formation by atomic manipulation seems much more challenging than bond dissociation. For bond dissociation it is often enough to provide the energy needed, typically by an IET process. Whereas, for bond formation not only the energy must be provided, but also other conditions have to be fulfilled. Importantly, the products to be fused have to be placed at a certain spacing and orientation with respect to each other [7]. Possibly the tip functionalization could be important in bond formation, e.g. providing a catalyst for the reaction. So far the role of the tip functionalization for molecule generation by atomic manipulation has not been studied in detail. However, in several cases of atom manipulation on surfaces it is known that only special tips can be employed for the desired manipulations, highlighting the role of the tip also for manipulation.

What can be expected from molecular generation by manipulation in the future? As already demonstrated for a few examples, molecules that are unstable otherwise can be generated, stabilized and characterized. Especially radicals have already been generated successfully by dissociation and AFM will improve the understanding of radical generation, radical stabilization, adsorption and reactions of radicals (internal ones and with other reaction partners). Moreover, molecules that were never created before could be generated. Manipulation experiments can also yield insights in reaction pathways and mechanisms for on-surface synthesis and catalysis. Thus novel reaction schemes might be explored and novel catalysts might be found. Finally, atom manipulation will be used to build custom designed molecular or molecule-metal-complex networks and molecular machines.

Acknowledgements

We thank B. Schuler, N. Moll, Z. Majzik, S. Fatayer, G. Meyer, D. Peña, and R. Allenspach for discussions. We acknowledge financial support from the European Research Council Consolidator Grant AMSEL (agreement no. 682144), the European Research Council Advanced Grant CEMAS (agreement no. 291194), the European Union project PAMS (agreement no. 610446) and the Initial Training Network QTea (agreement no. 317485).

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