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Heterogeneous Catalysis of a Copper-Coated Atomic Force Microscopy Tip for Direct-Write Click Chemistry

Walter F. Paxton, Jason M. Spruell, and J. Fraser Stoddart*

Department of Chemistry, Northwestern University, 2145 Sheridan Road, Evanston, Illinois 60208

Received March 2, 2009; E-mail: stoddart@northwestern.edu

Spatial control over the chemical composition of surfaces with sub-100 nm precision has been demonstrated[1] with a range of scanning-probe lithographic (SPL) methods. These methods combine high resolution direct-write surface patterning with real-time imaging of patterned surfaces, offering, under certain circumstances, significant advantages over conventional top-down lithographic approaches. Nevertheless, the majority of these techniques are essentially destructive to the surface, involving the initial oxidation,[2,3] reduction,[4] or mechanical displacement[5] of surface materials, which are often incompatible with the direct deposition of delicate soft materials, such as biomolecules.

A particularly appealing SPL method is to use catalysis to attach soft materials directly to surfaces. Catalytic scanning probe tips capable of *destructive* chemical transformations have been used to hydrogenate surface-bound organic azides,[4,6] oxidize an organic dye photocatalytically,[3] and hydrolyze silyl ethers.[7] More importantly, some catalytic scanning probe tips are capable of *constructive* chemical transformations allowing the direct attachment of molecular compounds to surfaces. For example, atomic force microscopy (AFM) tips coated with palladium films and nanoparticles have been employed to couple organosilanes to alkene terminated surfaces[6] and to drive Suzuki[8] and Heck[8b] coupling reactions at surfaces under basic conditions. In some cases, the conditions required for such reactions may not be suitable for the coupling of delicate molecules. Thus, developing other versatile strategies for covalently attaching a wide range of molecules to surfaces would expand the toolkit of techniques afforded by scanning probe methods.

Copper-mediated azide−alkyne 1,3-dipolar cycloaddition[9] (CuAAC), "click" chemistry, is another promising candidate for coupling molecules to surfaces catalytically. This remarkable reaction proceeds in high yield under mild conditions with a demonstrated tolerance for a wide range of functional groups not exhibited by traditional coupling reactions. The procedure for carrying out these reactions homogeneously in solution has been adapted to functionalize either azide-[10] or alkyne-terminated[11] surfaces, involving relatively stable Cu(I) compounds or the *in situ* chemical[10] or electrochemical[12] reduction of Cu(II) to the catalytically active Cu(I) species. This reaction has also been applied toward scanning probe lithography. In a beautiful demonstration of catalytic scanning probe lithography, Frommer and Malkoch et al.[13] attached organoazides covalently to alkyne-terminated surfaces using dip-pen nanolithography (DPN).[14,15] In their approach, AFM tips inked with an acetonitrile solution containing (i) copper(I) iodide, (ii) diisopropylethylamine,[16] and (iii) azide-functionalized dendrons were used to *write* features (i.e., the dendrons) onto acetylide surfaces. Using this method of localized "click" chemistry, it was possible to prepare features with line widths as small as 300 nm.

In addition to the homogeneous Cu(I) catalysts, heterogeneous copper metal alone is known[17] to catalyze this reaction in solution, a procedure that can be generalized to surfaces as well. In fact, we have recently demonstrated[18] that heterogeneous copper metal stamps for microcontact printing, when inked with a terminal alkyne, are capable of catalyzing this reaction locally, i.e., where the stamp is in contact with a suitable substrate, and on the microscale. In this case, the reaction, believed to be catalyzed by Cu(I) that exists[19] in the native copper oxide layer, proceeds without the need for *in situ* reduction or additional reagents. We reasoned that, in an appropriate environment, a nanoscale heterogeneous copper surface would catalyze this reaction as well as a microscale one, even as it moves across a reactive surface.

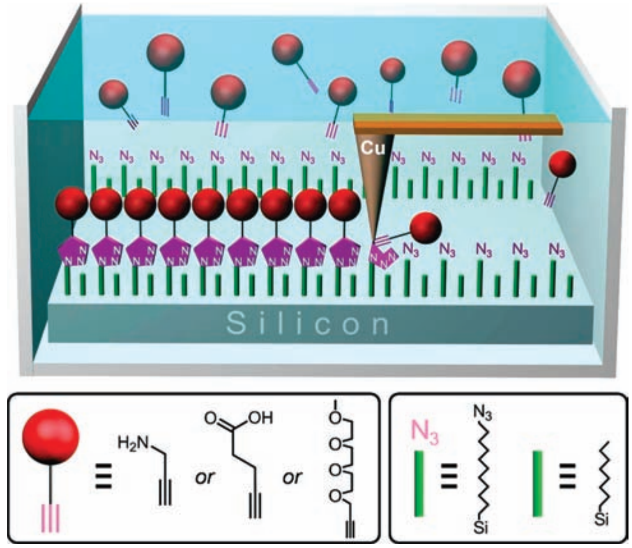

Figure 1. A schematic representation of a scanning probe lithography approach to copper-catalyzed azide−alkyne cycloaddition (CuAAC) on surfaces, illustrating the three critical elements required for direct-write "click" chemistry: (1) a surface-anchored azide-terminated species that can be functionalized selectively with (2) a solvated terminal alkyne in the presence of (3) a copper catalyst. Terminal alkynes (including propargylamine, 4-pentynoic acid, and 2,5,8,11-tetraoxatetradec-13-yne) dissolved in EtOH are "clicked" to a reactive surface, a mixed monolayer of 11-azido-undecyltrichlorosilane and octytrichlorosilane (1:1) on a silicon wafer, as the copper-coated AFM tip is moved across the surface with the spatial resolution comparable to the tip dimensions.

In this communication, we report an alternative approach (Figure 1) toward direct-write coupling of molecules to surfaces via CuAAC using a movable heterogeneous copper surface, in the form of a thin layer of copper deposited onto an AFM tip. This method is capable of catalyzing CuAAC on a suitable surface locally without the need for auxiliary reagents. Using this approach, we observed a significantly higher degree of spatial control than previously reported.[13] In contrast to DPN experiments, this work was carried out under EtOH because of its ability to solvate a variety of alkynes and its chemical compatibility with the liquid cell. For each experiment, a silicon wafer with an azide-terminated self-assembled

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monolayer (SAM) was fixed into a polystyrene Petri dish which was then filled with a 50 mM ethanolic solution of a compound bearing a terminal alkyne.

Catalytically active tips were produced by thermal evaporation of a 4 nm adhesion layer of titanium, followed by a 10 nm layer of copper onto commercially available silicon nitride AFM tips (DNP-S from Veeco Instruments, Woodbury, NY). These copper-coated tips were then aged in air for at least 24 h to facilitate the formation of the catalytically active oxide layer.[20] Azide-terminated silicon wafers were prepared using an adaptation[21] of a previously described[22] procedure. Briefly, mixed monolayers of 11-bromoundecyltrichlorosilane and octyl-trichlorosilane (1:1) were formed on piranha-cleaned silicon wafer pieces. The terminal bromide was then displaced from the SAM-coated silicon by soaking wafers in a 0.1 M solution of NaN_3 in DMF.

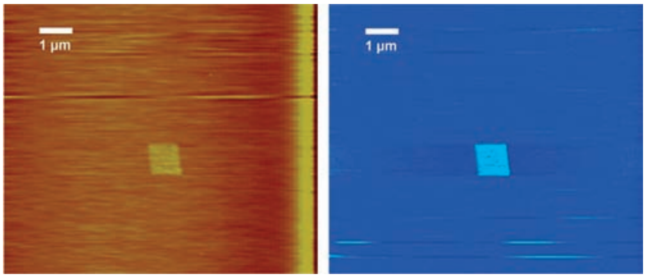

Figure 2. Contact mode AFM images in an ethanolic solution of 4-pentynoic acid (50 mM) using a copper-coated AFM tip. Topography (left) and tip−substrate friction (right) of a 9 μm × 10 μm region at low force (30 nN) and high speed (40 μm/s) after *writing* a 1 μm × 1 μm square (center) at high force (200 nN) and low speed (1 μm/s).

Because the reaction proceeds at some finite rate and requires good contact between the reacting surface and the catalyst, we presumed that, as with other AFM-based direct-write methods, it would be possible to switch between *read* and *write* modes by changing the applied force and the scanning speed of the copper AFM tip. Figure 2 shows the topography and friction contact mode AFM images (*reading*) of a 9 μm × 10 μm region acquired using a relatively low scan force (30 nN) and fast scan speed (40 μm/s) after scanning (*writing*) a 1 μm × 1 μm area at a higher force (300 nN) and slower scan speed (2 μm/s) in a 50 mM ethanolic solution of 4-pentynoic acid. The written feature is evident in both the topography and friction images, indicating the deposition of a material (increase in topography) that exhibits higher friction compared with the surrounding areas. These changes in topography and friction are consistent with "clicked" monolayers of 4-pentynoic acid on azide surfaces formed by microcontact printing. Writing of alkynes onto azide surfaces was also possible with propargylamine and 2,5,8,11-tetraoxatetradec-13-yne (see Supporting Information).

Control experiments attempting to reproduce this same effect with an unmodified silicon-nitride AFM tip on the same surface in 50 mM 4-pentynoic acid failed, as did experiments using a copper-modified tip on an azide surface in EtOH that did not contain a terminal alkyne (see Supporting Information). In each of these cases, no pattern was evident in either the topography or the friction image at scanning forces below 400 nN. Above 400 nN, deformation of the SAM was evident, resulting in topographical depressions (rather than raised features) and regions of lower (rather than higher) friction, presumably as a result of mechanical deformation of the SAMs at high scanning forces. These control experiments indicate that copper metal and a molecule bearing a terminal alkyne group are both required to produce features.

We explored the effect (Table 1) of *writing* at different scan forces and at different scan speeds. In each case, the written surfaces were *read* using a scan force of 53 nN and a scan speed of 40 μm/s. Scanning at a force in excess of 200 nN was required to cause any changes in surface topography. Thereafter, the degree of surface modification scales to some extent with increased forces up to at least 350 nN. Despite the lack of topographical changes at forces below 200 nN, we observed changes in the friction image even at forces as low as 31 nN with these tips. This relatively low force is on the order of that used previously[8] in surface Suzuki and Heck couplings.

Table 1. Effect of Varying *Writing* Scan Speed and Contact Force on Observed Height and Friction of 0.25 μm² 4-Pentynoic Acid Features Written via Direct-Write Click Chemistry[a]

speed (μm/s)	force (nN)	height (nm)	max. friction (arb. units)
2	350	1.1	12
2	300	1.4	12
2	260	1.3	13
2	200	0.4	15
2	200	0	15
2	31	0	7
2	53	0	10
4	53	0	9
8	53	0	11
16	53	0	5
32	53	0	5
64	53	0	2

[a] Imaging (*reading*) in all cases was performed over a 25 μm² area using scan force and speed of 53 nN and 40 μm/s, respectively.

We also adjusted the scan speed and found that these changes in tip−surface friction were still evident, but to a lesser degree, at *writing* speeds as high as 64 μm/s! This surprising observation indicates that, although *reading* at scan speeds up to 64 μm/s cannot completely prevent reaction, the scan speed can be adjusted to decrease the extent of the surface functionalization. More importantly, the ability to pattern surfaces with this method using these significantly higher scan speeds amounts to an important advantage over typical DPN methods[23] and should facilitate higher throughput SPL patterning of nanoscale features.

In addition to *writing* relatively simple patterns, we have successfully produced more elaborate features as well. The outline of the letter "N," written by a copper AFM tip on an azide-terminated surface in a 50 mM ethanolic solution of 4-pentynoic acid and shown in Figure 3, demonstrates the spatial control possible with this method. The enlarged region (Figure 3, right) shows minimum line widths on the order of 50 nm, in contrast with the 300 nm line widths reported previously.[13] These line widths are comparable with the nominal unmodified AFM tip diameter (20 nm) and could presumably be reduced by using sharper AFM tips.

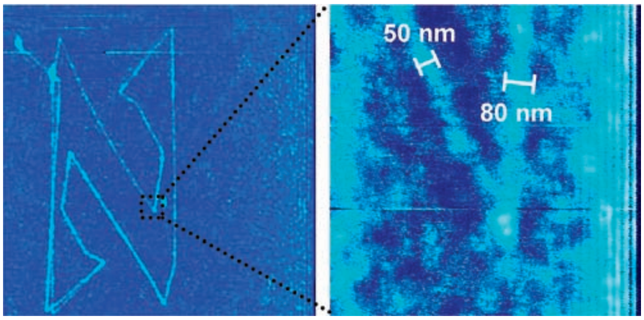

Figure 3. Friction image (left) of a 4 μm tall "N" catalytically *written* in 4-pentynoic acid onto an azide-terminated surface using a copper-coated AFM tip, and a 0.8 μm × 0.8 μm close-up (right) of features indicating resolution of copper-catalyzed direct-write "click" chemistry.

In summary, we have demonstrated an alternative approach toward the constructive patterning of surfaces using azide−alkyne cycloadditions in which the coupling reaction is catalyzed by a copper-coated AFM tip. This method builds upon previous work by using spatially controlled heterogeneous (rather than homogeneous) catalysis to attach molecules covalently to an appropriate surface under relatively mild conditions, without the need for additional reagents, and with dramatically improved spatial resolution. All that is required is (1) an azide surface, (2) a solution of a terminal alkyne, and (3) a copper-coated AFM tip. The CuAAC reaction can be carried out under liquid which becomes essentially an infinite reservoir of molecular "ink." Surprisingly, substantial patterning of alkynes onto azide surfaces is possible at *writing* speeds as high as 64 μm/s, a marked improvement over those required for patterning with conventional DPN. Because our method uses the same platform as many AFM-based methods, it is amenable to other advantageous modifications, such as massive parallelization.[24] These advantages open the door for the direct covalent attachment of a potentially limitless library of molecules that bear terminal alkyne functionality, including biomolecules, under relatively mild conditions, with sub-100 nm spatial resolution.

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Supporting Information Available: Control experiments, preparation and AFM analysis of microcontact printed substrates, and results of direct-writing of propargylamine and 2,5,8,11-tetraoxa-tetradec-13-yne. This material is available free of charge via the Internet at http://pubs.acs.org.

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(20) We observed previously (ref 18) that the performance of catalytically active copper-coated PDMS stamps, used to attach terminal alkynes onto azide-terminated surfaces, was sensitive to the elapsed time between (i) copper evaporation onto the stamps and (ii) the use of those stamps for catalytic microcontact printing. Copper stamps that had been aged in air for 24 h were at least 5 times more active than those that were used immediately after copper evaporation.

(21) Silicon wafers cut into 1.5 × 1.5 cm^2 square pieces were soaked in freshly prepared piranha solution, i.e., 1:4 mixture of 30% H_2O_2 and concentrated H_2SO_4 (CAUTION: piranha is extremely corrosive and liberates oxygen gas and large amounts of heat) for 20 min and then liberally rinsed with deionized H_2O and dried under a stream of N_2 gas. Cleaned wafers were further dried under vacuum at 20 °C for 1 h. These wafers were placed in a solution of 0.5% octyltrichlorosilane and 0.5% 11-bromo-undecyltrichlorosilane in dry CH_2Cl_2 at 20 °C for 1 h and then transferred directly to dry CH_2Cl_2. The wafers were then soaked for >5 min and sonicated for >1 min in each of the following: CH_2Cl_2, and then EtOH, and finally deionized H_2O. (The wafers emerged from the H_2O autophobic.) The bromo-terminated wafers were placed in 0.12 M NaN_3 in wet (∼1% H_2O) DMF at 60 °C for 48 h. Wafers were rinsed liberally with DMF and then H_2O and dried under a stream of N_2. The wafers were stored in individual fluoroware containers and protected from heat and light until used or for up to 1 month.

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