J|A|C|S
COMMUNICATIONS

Spatially Resolved Suzuki Coupling Reaction Initiated and Controlled Using a Catalytic AFM Probe

Jason J. Davis,*,† Karl S. Coleman,*,‡ Katerina L. Busuttil,† and Claire B. Bagshaw†

Inorganic Chemistry Department, Central Research Laboratory, Oxford University, Mansfield Road, OX1 3TA, UK, and Department of Chemistry, University Science Laboratories, South Road, Durham University, DH1 3LE, UK

Received November 10, 2004; Revised Manuscript Received August 4, 2005; E-mail: jason.davis@chem.ox.ac.uk; k.s.coleman@durham.ac.uk

The two-dimensional control of molecular position and functionality enables one to establish flexible bottom-up approaches to the generation of dense, large capacity, interfaces of broad technological interest. Optical lithographic technologies, though powerful, are resolution limited and generally not chemically specific. Scanning probe lithographic methods are capable of creating nanometer-scale patterns under flexible, controllable environmental conditions.[1,2] Impressive results have been obtained through the utilization of either mechanical or electrochemical driving forces in AFM configurations, where the production of line widths as small as 15 nm is possible.[3−7] Despite much activity in this area, there are few examples of *reactions* being initiated by nonelectrochemical AFM in a controlled, site specific manner.[8−12] To our knowledge, the utilization of an AFM probe in mediating an organometallic coupling reaction with high spatial resolution has not been described. Herein we report a proximal probe mediated site-specific Suzuki coupling. Specifically, this organometallic catalysis was carried out by controlled force scanning of a palladium-functionalized AFM probe over a surface-assembled aryl bromide self-assembled monolayer (SAM) in a boronic acid reagent solution. We believe this to be the first reported instance of a catalytic coupling reaction controlled by AFM.

Though SAM mechanical nanolithography has been demonstrated on numerous occasions[13] such work highlights the relative ease with which a scanning probe operating in the repulsive regime can rupture substrate−adsorbate covalent interaction. To catalytically couple a solution-phase reagent to a reagent SAM, both tip scanning speed (and therefore the time frame available for reaction at each surface site) and imposed force must be controlled. If the probe itself plays an integral role in reaction then its physical interactions with the reagents must be sufficient for reaction to occur while simultaneously delicate enough to avoid removing the surface-bound reagent from the reaction area. In the first instance, the aryl bromide SAMs were assembled and characterized, and their tolerance to the forces imposed by a scanning tip was quantified (see Supporting Information).

The Suzuki cross-coupling reaction is a simple synthetic route to the fabrication of biaryls from aryl halides and aryl boronic acids.[14] A surface assembling, aryl bromide dialkyl sulfide (4-bromo-*N*-(3-(methylthio)propylbenzamide)) was synthesized through the coupling of 4-bromobenzoic acid to 3-(methylthio)propylamine. The reagent also possesses a central amide group, known to provide intramolecular hydrogen bonding which stabilizes subsequently formed adlayers.[15] Monolayers were typically prepared by immersing template stripped or annealed gold substrates[16] in a 1.3 mM methanolic solution of the compound overnight followed by repeated rinsing with methanol. They were subsequently characterized by AFM, XPS, and FTIR (see Supporting Information). Extensive force imaging analysis confirmed a maximum force tolerance of ~70 nN. At higher scan forces, the AFM probe can be utilized in the selective removal of patches of the SAM under solvent, a procedure which can be a useful characterization tool (see Supporting Informatio).

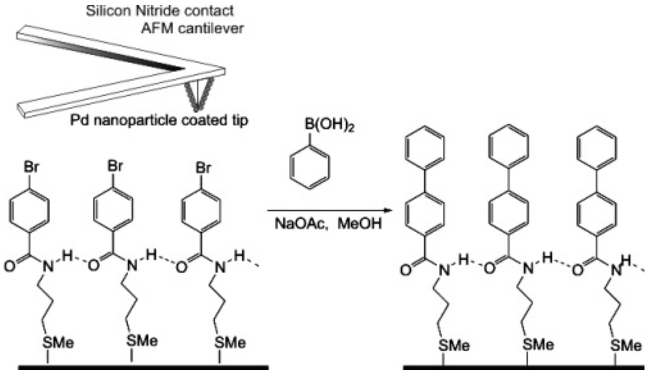

Figure 1. Schematic of the Suzuki reaction initiated on an aryl bromide monolayer by a Pd nanoparticle functionalized AFM probe in a methanolic solution of phenylboronic acid.

The large surface area/volume ratio associated with metallic nanoparticles can be conducive to high catalytic activity. Recently, palladium nanoparticles have been shown to be effective in catalyzing a variety of Heck and Suzuki carbon−carbon couplings.[17,18] PVP-Pd nanoparticles, previously used as catalysts in the Suzuki reaction,[19−22] were prepared according to a published method.[23] These nanoparticles are known to bind to silicon nitride,[24,25] and catalytically functional AFM probes were consequently generated by incubating precleaned silicon nitride probes (radius of curvature 10−40 nm) in an aqueous solution of PVP-Pd nanoparticles (palladium concentration of 1.4 M) for 5 min.

The aryl bromide dialkyl sulfide-modified gold surface was mounted onto an AFM sample plate and an area scanned with the catalytic probe at ~1 μm/s at a force of 20−25 nN. During scanning, a process carried out once over any one defined area, the probe and substrate were incubated in a reagent bath comprising a millimolar methanolic solution of phenylboronic acid and sodium acetate. A schematic representation of this reaction is shown in Figure 1. After reaction, the scan size was increased, the force was minimized (from a “reaction inducing” force of 20−25 nN to 1−5 nN), and the scan speed was increased to 40 μm/s in order to image the area with the same probe without causing further reaction.

No appreciable change in topography is expected in these coupling reactions as the increase in height resulting from the addition of the boronic acid is less than that reliably detectable by a finite radius AFM probe (bearing in mind the limitations of tip convolution and room temperature thermal noise). Reaction-induced changes in surface free energy can be mapped through the simultaneous acquisition of height and friction data. The latter, highly sensitive to the chemical identity of surface-bound species, can be reliably used to generate contrast produced by chemical

---

[†] Oxford University.
[‡] Durham University.

10.1021/ja043235+ CCC: $30.25

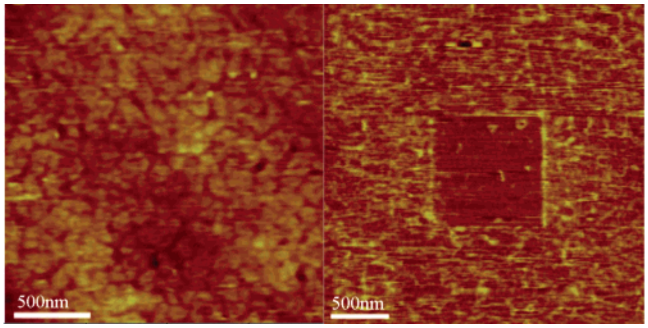

Figure 2. Height (left) and subtracted friction (right) AFM images of the spatially confined Suzuki reaction. Only on scanning an appropriately functionalized SAM with a catalytic probe at controlled force are localized changes in surface friction generated.

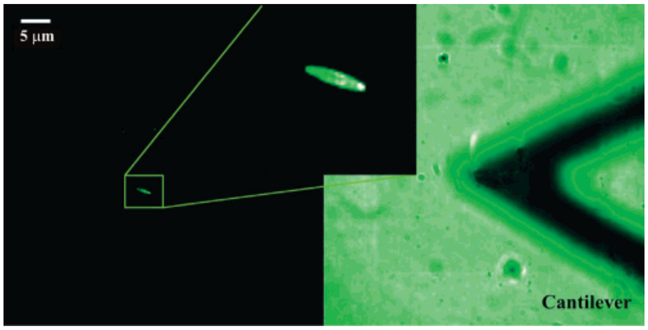

Figure 3. Fluorescence image (left and inset) showing a 5 µm line written on an otherwise blank sample. The bright field image (right), acquired before the fluorescence image, confirms that the reaction has proceeded only in the locality of the probe.

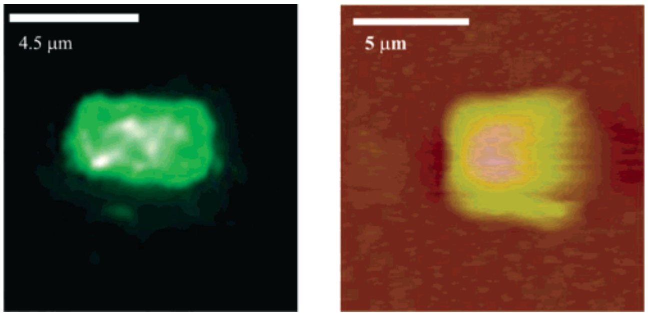

Figure 4. Fluorescence image (left) of a 4.5 × 2.25 μm^2 Suzuki patterned rectangle tagged with an amine-specific fluorophore. AFM-height image (right) of a 5 µm square Suzuki coupled SAM patch tagged with 100 nm aldehyde functionalized nanospheres.

inhomogeneities in the sample.[26] Friction trace and retrace data sets were subtracted from each other to produce an image, the contrast within which is generated by frictional contributions alone (Figure 2).[27] Importantly, such surface free energy changes are not observed in scanning carried out with "normal" (uncatalytic) AFM probes or with palladium functionalized probes in the absence of either solution phase reagent. Although the catalytic nanoparticles can be delivered to substrates by dip-pen nanolithography,[28] there was no evidence of such delivery during this work.

To further verify the coupling reaction proceeds as described, it was repeated using a boronic acid subsequently amenable to chemically-specific tagging (namely 3-aminophenylboronic acid). After reaction initiation the surface was incubated with NHS-fluorescein, an amine-specific fluorophore. The sample was then imaged by epifluorescence microscopy (using an inverted Nikon Eclipse TE2000-U microscope equipped with an Andor Ixon iCCD camera), with resultant fluorescence observed to emanate only from the surface region defined by the reaction-inducing scan parameters. A fluorescent rectangle with a 4:1 aspect ratio, approximately 5 µm across and typical of a number obtained, is shown in Figure 3. In addition, a 4.5 µm 2:1 aspect ratio rectangle is shown in Figure 4.

Though frictional contrast can be introduced to an SAM by tip-induced mechanical perturbation alone,[9] the (reagent dependent) site-specific fluorescent tagging is confirmatory of the presence of spatially confined surface amine groups and, by inference, successful Suzuki coupling.

In addition to fluorescent tagging, the presence of localized amine moieties was further confirmed by chemical labeling with aldehyde-functionalized nanospheres (Figure 4). These bind to the amine group, but not the unreacted aryl bromide.

In summary, catalyst modified AFM probes can be utilized in the spatially resolved chemical coupling of surface-bound and solution phase reagents. The surface chemical, environmental, and force/pressure flexibility available to such experiments is of broad potential application.

Acknowledgment. The authors acknowledge financial support from the Engineering and Physical Sciences Research Council (EPSRC) and Dr. G. Beamson of the Surface and Nuclear Division, Daresbury Laboratory, UK for help with XPS.

Supporting Information Available: Synthesis of monolayer, XPS and FTIR spectra of reagent monolayer, procedures and schematics for amine tagging and control reactions. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Decossas, S.; Mazen, F.; Baron, T.; Bremond, G.; Souifi, A. *Nanotechnology* **2003**, *14*, 1272−1278.
(2) Decossas, S.; Patrone, L.; Bonnot, A. M.; Comin, F.; Derivaz, M.; Barski, A.; Chevrier, J. *Surf. Sci.* **2003**, *543*, 57−62.
(3) Fuierer, R. R.; Carroll, R. L.; Feldheim, D. L.; Gorman, C. B. *Adv. Mater.* **2002**, *14*, 154−157.
(4) Gorman, C. B.; Carroll, R. L.; He, Y.; Tian, F.; Fuierer, R. *Langmuir* **2000,** *16*, 6312−6316.
(5) Kleineberg, U.; Brechling, A.; Sundermann, M.; Heinzmann, U. *Adv. Funct. Mater.* **2001**, *11*, 208−212.
(6) Kramer, S.; Fuierer Ryan, R.; Gorman Christopher, B. *Chem. Rev.* **2003**, *103*, 4367−4418.
(7) Ginger, D. S.; Zhang, H.; Mirkin, C. A. *Ang. Chem., Int. Ed.* **2004**, *43*, 30−35.
(8) Blasdel, L. K.; Banerjee, S.; Wong, S. S. *Langmuir* **2002**, *18*, 5055−5057.
(9) Peter, M.; Li, X.-M.; Huskens, J.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **2004**, *126*, 11684−11690.
(10) Matsubara, S.; Yamamoto, H.; Oshima, K.; Mouri, E.; Matsuoka, H. *Chem. Lett.* **2002**, 886−887.
(11) Blackledge, C.; Engebretson, D. A.; McDonald, J. D. *Langmuir* **2000**, *16*, 8317−8323.
(12) Mueller, W. T.; Klein, D. L.; Lee, T.; Clarke, J.; McEuen, P. L.; Schultz, P. G. *Science* **1995**, *268*, 272−273.
(13) Xu, S.; Miller, S.; Laibinis, P. E.; Liu, G.-y. *Langmuir* **1999**, *15*, 7244−7251.
(14) Li, Y.; Boone, E.; El-Sayed, M. A. *Langmuir* **2002**, *18*, 4921−4925.
(15) Valiokas, R.; Oestblom, M.; Svedhem, S.; Svensson, S. C. T.; Liedberg, B. *J. Phys. Chem. B* **2002**, *106*, 10401−10409.
(16) Wagner, P.; Hegner, M.; Guentherodt, H.-J.; Semenza, G. *Langmuir* **1995**, *11*, 3867−3875.
(17) Reetz, M. T.; Westermann, E. *Ang. Chem., Int. Ed.* **2000**, *39*, 165−168.
(18) Reetz, M. T.; Breinbauer, R.; Wanninger, K. *Tetrahedron Lett.* **1996**, *37*, 4499−4502.
(19) Li, Y.; Hong, X. M.; Collard, D. M.; El-Sayed, M. A. *Org. Lett.* **2000**, *2*, 2385−2388.
(20) Li, Y.; El-Sayed, M. A. *J. Phys. Chem. B* **2001**, *105*, 8938−8943.
(21) Narayanan, R.; El-Sayed, M. A. *J. Am. Chem. Soc.* **2003**, *125*, 8340−8347.
(22) Narayanan, R.; El-Sayed, M. A. *J. Phys. Chem. B* **2004**, *108*, 8572−8580.
(23) Teranishi, T.; Miyake, M. *Chem. Mater.* **1998**, *10*, 594−600.
(24) Boonekamp, E. P.; Kelly, J. J.; Fokkink, L. G. J. *Langmuir* **1994**, *10*, 4089−4094.
(25) Boonekamp, E. P.; Kelly, J. J.; Fokkink, L. G. J.; Vandenhoudt, D. W. E. *J. Electrochem. Soc* **1995**, *142*, 519−524.
(26) Carpick, R. W.; Salmeron, M. *Chem. Rev.* **1997**, *97*, 1163−1194.
(27) Leggett, G. J. *Anal. Chim. Act.* **2003**, *479*, 17−38.
(28) Thomas, P. J.; Kulkarni, G. U.; Rao, C. N. R. *J. Mater. Chem.* **2004**, *14*, 625−628.

JA043235+