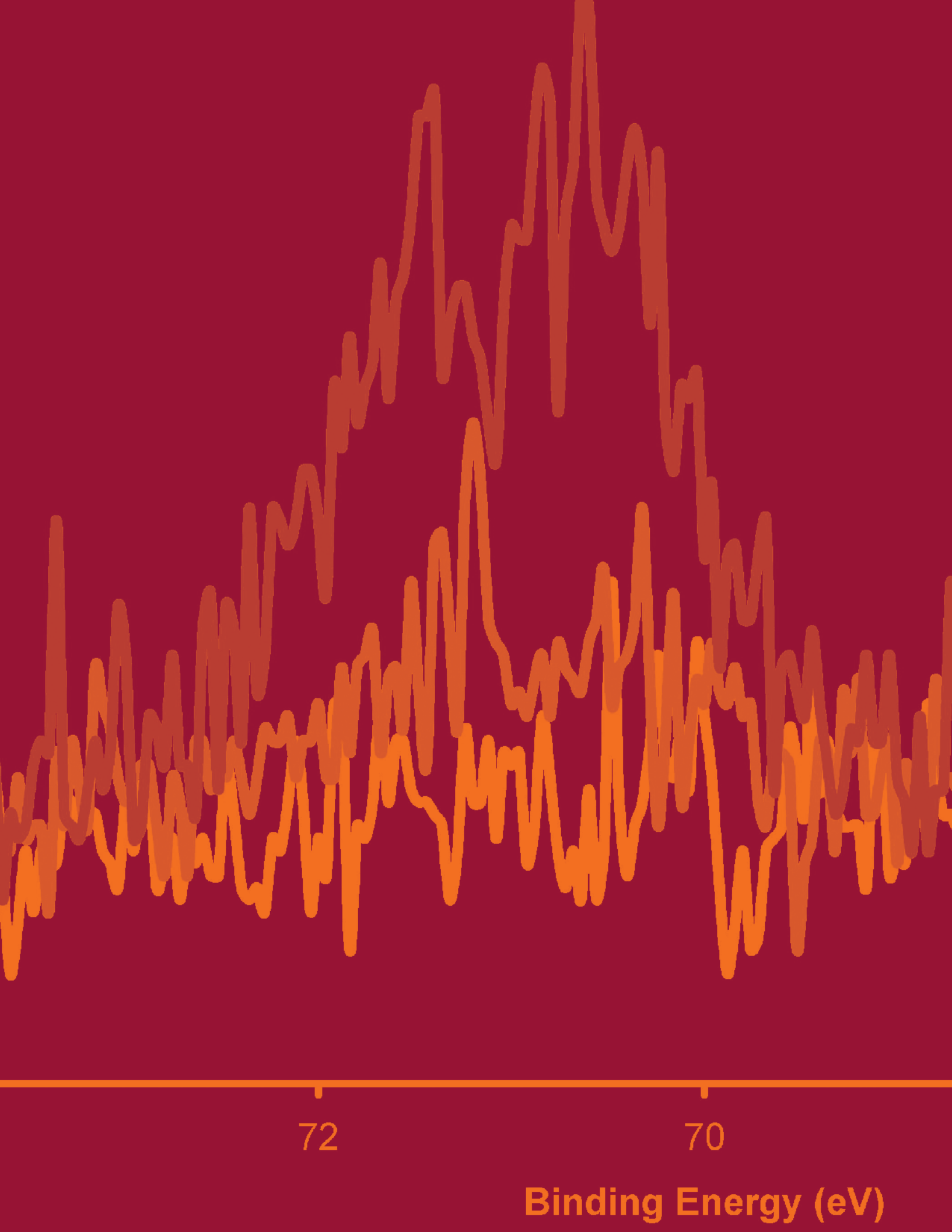
72
70
Binding Energy (eV)

Organic Monolayer Modification on a Silicon Surface Using Sonogashira Coupling: Working Towards the Development of Biological Sensors

Undergraduate Researcher
Amanda Boe
Washington University in St. Louis

Faculty Mentor
SonBinh T. Nguyen
Department of Chemistry
Northwestern University

Postdoctoral Mentor
Jun-Hyun Kim
Department of Chemistry
Northwestern University

Abstract

This research illustrates the modification of an iodostyrene layer on a Si(111) surface using a Sonogashira reaction. This was accomplished by applying UV irradiation (254 nm) to a hydrogen-passivated silicon surface in a solution of iodostyrene in benzene, followed by a Sonogashira coupling between the iodine group from iodostyrene and 4-bromophenylacetylene in a microwave condition at 40° C. Two precursor molecules — iodostyrene and 4-bromophenylacetylene — were successfully synthesized and characterized by nuclear magnetic resonance (NMR) spectroscopy and gas chromatography-mass spectrometry (GC-MS). X-ray photoelectron spectroscopy (XPS) was used to characterize both the iodostyrene-layered surface and the surface that was subjected to Sonogashira coupling. In addition, a Sonogashira coupling of these two molecules in solution via microwave was carried out prior to the solid phase reaction to ensure selective formation of product. The ability to modify the organic layers on a Si(111) wafer is a promising step toward developing reactive surfaces that can be used as scaffolds for more complex molecules and eventually as biological sensors.

Introduction

Although many investigators have examined the formation of organic monolayers on a silicon surface (e.g., Si(111)),[1–3] the effects of modifying the organic layers to further modify the silicon surface are not well-studied. The formation of organic layers is often limited because their size causes physisorption, and their functional groups can destroy the surface. To overcome these problems, the formation of simple organic overlayers on a silicon surface in this project was followed by their tunable modification, which provided a unique means of constructing multifunctional organic building blocks on a silicon surface. Studying this type of modification process can advance the development of devices in the areas of electronics, biotechnology, and sensors.[3] With a view to the eventual development of precursors for new biological sensors, the proposed research focused specifically on using a Sonogashira reaction on a Si(111) surface to modify iodine-functionalized styrene overlayers with acetylene-containing molecules.

Organohalide monolayers can provide excellent scaffolds for building complex molecules, and the halide moiety is readily detected by x-ray, which allows for the precise determination of the formation, orientation, and coverage of the layers.[2] The formation of halide-terminated monolayers on a silicon surface, however, may be difficult due to unwanted interactions between halide moieties and the silicon surface (e.g., Si-Br bond). A previous study showed the cleavage of Br-C bond from undec-10-enoic acid 2-bromoethyl ester on a Si(111) surface under UV irradiation.[3]

Given the radical mechanism used to synthesize monolayers on Si(111), the formation of Si-Br bond most likely occurred upon UV exposure because of the ability of silicon radicals (dangling bonds) to cleave the C-Br bond, and because Br is a strong cleaving group. In contrast, similar experiments carried out under the same reaction conditions demonstrated that 4-bromostyrene monolayers were solely formed on the Si(111) surface without any interaction between Br moiety and the silicon surface.[2] The inability to cleave the C-Br bond from bromostyrene was attributed to the lower stability of the phenyl radical compared to the stability of the alkyl radical formed in the undec-10-enoic acid 2-bromoethyl ester.

Based on these prior results, iodostyrene monolayers in this project were created on a Si(111) surface and subjected to a Sonogashira coupling reaction with 4-bromophenylacetylene. There were several reasons for using iodostyrene monolayers in place of bromostyrene monolayers. Iodine radicals are less likely to form than bromine radicals,[4] so given the lack of bromine-silicon bonds in the previous study, it was thought that no iodine-silicon interactions interfering with self-assembled monolayer (SAM) formation would occur. Furthermore, iodine is more reactive toward Sonogashira coupling than bromine,[2] which allows for shorter reaction times and lower microwave temperatures. These conditions precluded any damage to the silicon surface when the reaction was carried out on the solid phase media. In addition, UV was used as radical initiator for monolayer formation to avoid damaging the silicon wafer.

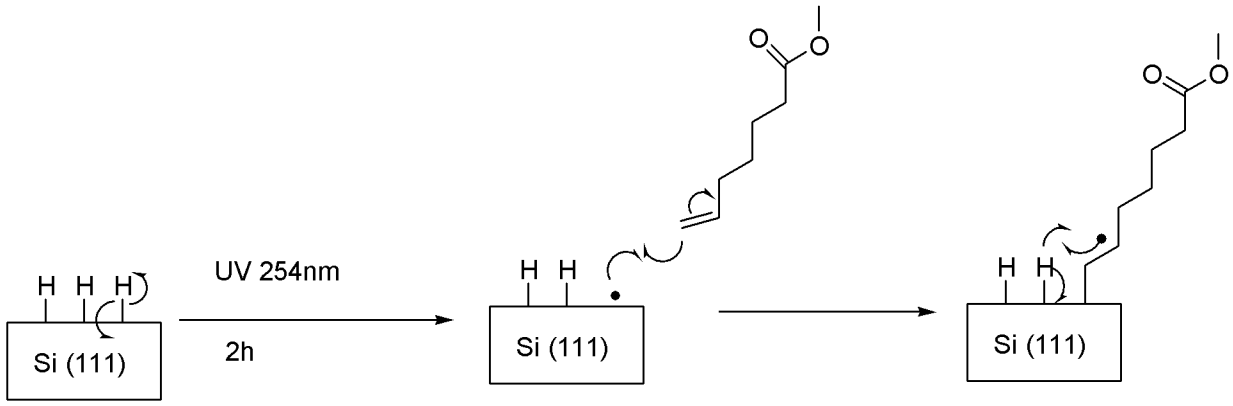

Figure 1: Radical mechanism used to create self-assembled monolayers.

The Sonogashira reaction was used to modify the organic monolayers on the Si(111) surface. This reaction can allow for the formation of a carbon-carbon bond and highly conjugated molecules that can attach new organic/biological compounds.[5] The reaction can be carried out under ambient reaction conditions that prevent the destruction of the Si(111) surface (via formation of an oxide layer). Additionally, the reaction is very practical because it generally affords high yields.

Modifying iodostyrene layers on Si(111) via Sonogashira coupling shows that a functionalized monolayer surface can react with molecules in solution. Inducing the same reaction with bigger and more complex molecules could be a step toward developing reactive surfaces on Si(111) that function as biological sensors.

Background

In 1993, Linford and Chidsey were the first to demonstrate monolayer formation with hydrosilylation of Si(111) wafers.[6] The process involved inserting alkenes into the hydrogen-passivated surface by self-assembly under UV irradiation through the surface-confined radical reaction. This type of monolayer formation can also be accomplished under thermal conditions. Both methods for the formation of organic monolayers induce homolytic cleavage of the Si-H bond, so no radical initiator is needed.[1] Once the silicon radical is formed by the cleavage of the Si-H bond, the Si-C bond is likely to form next because silyl radicals are known for their rapid reactions with olefins (Figure 1). The reaction between silicon and carbon occurs all over the surface to produce SAMs. SAMs eliminate the need for attaching biomolecules directly to an inorganic substrate. Instead, SAMs are chemisorbed onto the silicon wafer and will bind to the silicon surface in an even and the most densely packed manner possible.[7] This is important for achieving complete control of the silicon surface, which is needed to eventually develop biological sensors.

Although there are no prior examples of modifying monolayers on a hydrogen-passivated Si(111) surface, many types of monolayer modification have been carried out on different surfaces.[8] Most commonly, modifications of organic monolayers have been performed on alkanethiol-based self-assembled monolayers (SAMs) on a gold surface — for example, nucleophilic substitution of a hydroxyl-terminated SAM[9] and

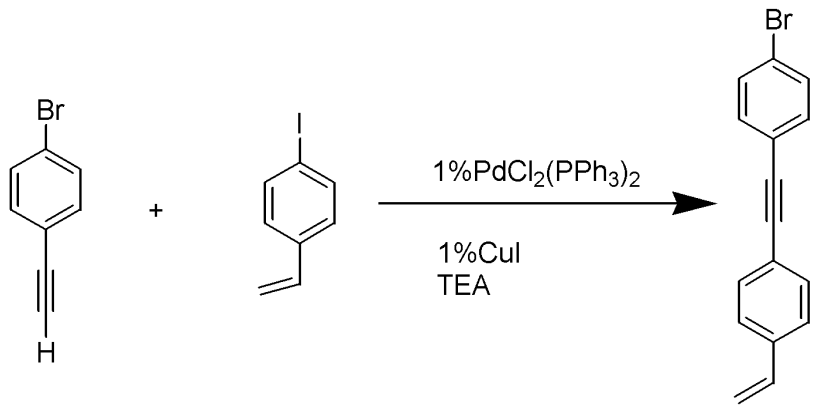

Figure 2: Synthetic scheme for wet chemical Sonogashira coupling.

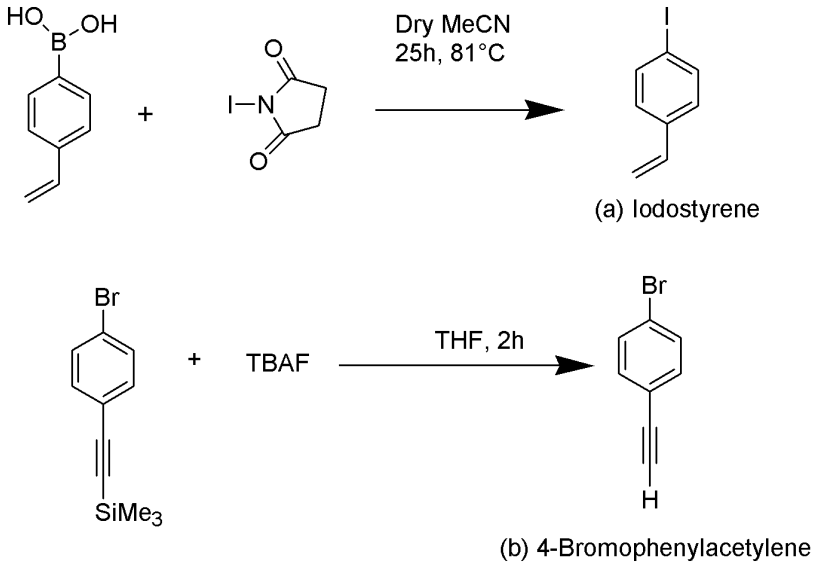

Figure 3: Synthetic schemes for (a) iodostyrene and (b) 4-bromophenylacetylene.

carboxylic acid–terminated monolayers undergoing esterfication[10] and amide bond formation.[11] In other cases, alkylsilane monolayers were used on Si/SiO_2 surfaces, such as coupling DNA fragments to aminopropylsilane SAMs,[12] alkene oxidation[13] and exchange reactions of alkyl chloride monolayers.[14] These modifications, however, were limited because silicon oxide surfaces have difficulty forming monolayers in a controlled manner and are nonconductive and produce no tunable electrical currents for sensing applications. However, monolayers formed on hydrogen-passivated silicon plates are electrically conductive[1] and thus have potential to be used in sensors.

The Sonogashira reaction (Figure 2) is used to couple a terminal alkyne with an aryl or vinyl halide. Even though the Sonogashira reaction has been successfully used for various solution phase reactions,[15] problems can occur when one of the substrates is in the solid phase. Reactions on silicon surfaces sometimes mirror their solution-phase counterparts, but generally the reaction pathway is changed by the presence of solid media.[1] Sonogashira reactions have been successfully carried out on solid media. For example, Erdélyi and Gogoll completed a Sonogashira reaction using 3-iodophenyl and 3-bromophenyl resins as the solid media.[16] Solid-phase Sonogashira reactions are also possible to carry out using polymer supports[17] and macrobeads with silyl linkers.[18] However, there has been no previous work testing this reaction on silicon, so it is unknown whether the Sonogashira reaction can work on a silicon surface.

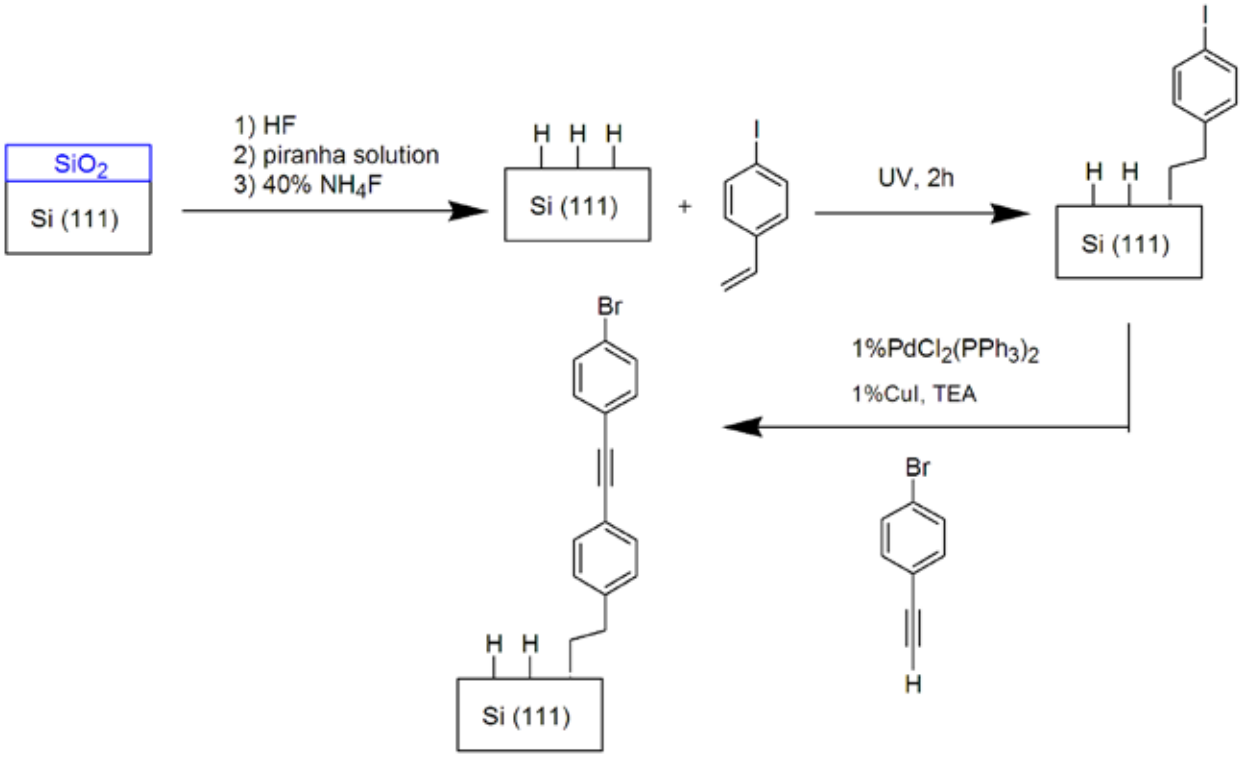

Figure 4: Synthetic scheme for solid phase Sonogashira coupling.

Approach

Modification of organic monolayers on Si(111) surfaces was carried out by: (1) synthesizing organic monomers (iodostyrene and 4-bromophenylacetylene); (2) conducting a control experiment based on Sonogashira coupling using the two monomers via a wet chemical method; (3) preparing hydrogen-passivated Si(111) wafers, followed by the formation of iodostyrene monolayers on Si(111) surfaces using UV light; (4) performing a solid-phase Sonogashira coupling between iodostyrene monolayers on Si(111) surfaces with 4-bromophenylacetylene; and (5) characterizing the purity of monomers and monolayers on the Si(111) surface. Unless otherwise noted, all reactions were carried out either under a N_2-filled glovebox or in an air-free environment.

Synthesis of Iodostyrene and 4-bromophenylacetylene

Iodostyrene was synthesized by a previously reported procedure (Figure 3).[19] Then, 4-vinylboronic acid was dissolved in 50 mL of dry acetonitrile in a 100 mL Schlenk flask with a stir bar, followed by the addition of 1.5 equivalents of N-iodosuccinimide. The reaction mixture was taken out from the glovebox, equipped with condenser, and stirred for 25 hr at 81° C under an N_2 environment.

The mixture was cooled to room temperature, extracted with 3 x 50 mL of pentane. Then it was washed with 150 mL of deionized water, 150 mL of 1M $NaHSO_3$ (aq), 150 mL of 1M $NaHCO_3$ (aq) and another 150 mL of deionized water. The final solution was dried with $MgSO_4$ and filtered through a silica column using pentane. The filtrate was collected and evaporated off to yield 31% of a shiny white solid. NMR and GC-MS were used to determine the formation and purity of the compound.

4-bromophenylacetylene was synthesized by dissolving (4-bromophenylethynyl) trimethylsilane in tetrahydrofuran in a 100 mL round-bottom flask with a stir bar and adding excess tetra-*n*-butylammonium fluoride (TBAF) (Figure 3).[20] The reaction mixture was stirred for at least 2 hr to completely deprotect the trimethylsilane groups, which was followed by the evaporation of the solvent. The mixture was dissolved in 15 mL of methylene chloride, extracted with 3 x 15 mL washes of deionized water, dried with NaSO4 and filtered through a silica column using a 9:1 ratio of hexane:methylene chloride. The solvent was evaporated off to give a 47% yield of a light orange-yellow solid. NMR and GC-MS were again used to confirm the formation and purity of the monomer.

Wet Chemical Sonogashira Coupling
A solution-phase Sonogashira coupling between iodostyrene and 4-bromophenylacetylene was carried out as a control experiment for the solid-phase coupling.[21] 5 mL of triethylamine (TEA), 1% $PdCl_2(PPh_3)_2$ catalyst, 1% CuI co-catalyst and 1 equivalent of iodostyrene was added to a 5 mL microwave vial with a stir bar . The mixture was stirred for 1 min, and 1 equivalent of 4-bromophenylacetylene was added to the mixture. The microwave vial was immediately capped, removed from the glovebox, placed in the microwave (Biotage Initiator, SW Version) and allowed to react for 45 min at 40° C. The compound was purified with silica column chromatography using a 9:1 ratio of hexane:methylene chloride as the eluent. The final solvent was evaporated off to yield 71% of a slightly yellow-tinted solid. NMR and GC-MS confirmed the formation and purity of the product.

Formation of the Iodostyrene Monolayer on the Silicon Wafer (Figure 4)
Prior to the formation of iodostyrene monolayers on the hydrogen-passivated Si(111) surface, Si(111) wafers were treated to remove any native oxide layer. All solvents and water used in this process were sparged with N_2 gas for 30 min before use. The wafers were immersed in 1% HF for 45 sec and rinsed with Milli-Q water. Then they were placed in a piranha solution (70% H_2SO_4:30% H_2O_2) for 10 min and rinsed again with pure water for 5–10 sec. The wafers were then immersed in 40% NH_4F for 30 min, followed by the final rinse with pure water for 30 sec. The hydrogen-passivated wafers were dried with N2 gas and stored in the glovebox before use.

For monolayer formation, 3 mL of a 0.2 M solution of iodostyrene in benzene was pipetted onto the Si(111) wafer. A UV lamp (wavelength = 254 nm) was adjusted the distance ~1 cm away from the wafer. The setup was covered with aluminum foil, which allowed for the surface-confined reaction to occur for 2 hr in a dark environment. The wafer was rinsed in methylene chloride and sonicated (Fisher Ultrasonic Cleaners, Sonic Cleaner, Model FS6) for 2x 2 min, and then another 1 min. The leftover reaction liquid after the UV treatment was collected to test the purity and/or possible side products. The wafers were placed back in the glovebox until needed for the solid-phase Sonogashira reaction.

Solid-Phase Sonogashira Coupling
Figure 4 shows the solid-phase Sonogashira coupling, which was similar to the wet chemical reaction except for the lack of a stir bar. In a 5 mL microwave vial was placed 5 mL of TEA, 1% $PdCl_2(PPh_3)_2$ catalyst, and 1% CuI catalyst. The Si(111) wafer with the iodostyrene monolayer was immersed in this mixture, followed by the addition of 4-bromophenylacetylene. The microwave vial was sonicated 1 min before being placed in the microwave reactor at 40° C. 4-bromophenylacetylene starting concentration (.05 M and .16 M) and overall reaction time (45 min and 120 min) were controlled to find optimum reaction conditions. The leftover liquid after the microwave reaction was collected to confirm the purity of the monomers and/or side reactions. The final wafer was rinsed with methylene chloride, sonicated for 2x 2 min and then for another 1 min, dried with N_2 gas, and stored in the glove box before analysis.

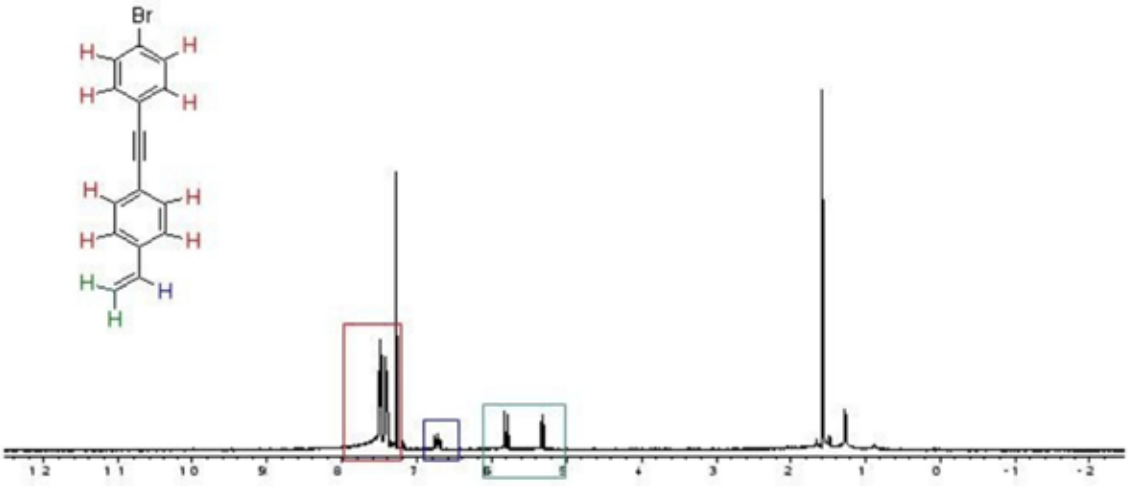

Figure 5: NMR spectrum of 4-(4-Bromophenethynyl)styrene prepared by a wet chemical Sonogashira reaction.

Results and Discussion

NMR (Varian Mercury, 400MHz, H1, $CDCl_3$) spectroscopy was used to confirm the formation and purity of the organic molecules. From NMR analysis, the iodostyrene monomer showed distinctive peaks for the benzyl protons (δ7.15-7.67) and vinyl protons (δ5.27-5.79 and δ6.61-6.65). The extra peak observed at 1.56 ppm was probably due to a water moiety from the NMR solvent. In addition, GC-MS (Agilient Technologies) confirmed the purity of the monomer by presenting only a single trace with a molecular weight of 230 g/mol. The reaction yielded 31% of a shiny white solid; the yield was 78% in previous literature. The difficulty in obtaining a higher yield might have arisen from the inability to get complete dissolution of 4-vinylboronic acid compound in the acetonitrile solvent. For 4-bromophenylacetylene, NMR showed multiple peaks from phenyl groups at δ7.21-7.48 and a single peak from acetylene at δ3.13. GC-MS confirmed the purity of the monomer by showing a single trace and 1:1 mass ratio at 180 g/mol and 182 g/mol, implying the presence of bromine group. The product was a light orange-yellow and the yield was 47%.

NMR and GC-MS were also used to investigate the formation and purity of 4-(4 bromophenethynyl)styrene after Sonogashira coupling between iodostyrene and 4-bromophenylacetylene in solution under microwave via a wet chemical reaction. Given the nature of the Sonogashira reaction, it was possible to form dimers of 4-bromophenylacetylene instead of the desired product, so the solution-phase reaction was run to ensure there was no dimerization and/or polymerization under microwave conditions. NMR presented the phenyl protons (δ7.26-7.50) and the vinyl protons (δ5.31-5.82 and 6.68-6.76) from 4-(4 bromophenethynyl)styrene synthesis (Figure 5). GC-MS additionally confirmed product formation by showing a single GC trace, and two peaks in the MS data in a 1:1 ratio at 282 g/mol and 284 g/mol (Figure 6) illustrated the presence of bromine in the molecule. The reaction yielded 71% of a light yellow solid.

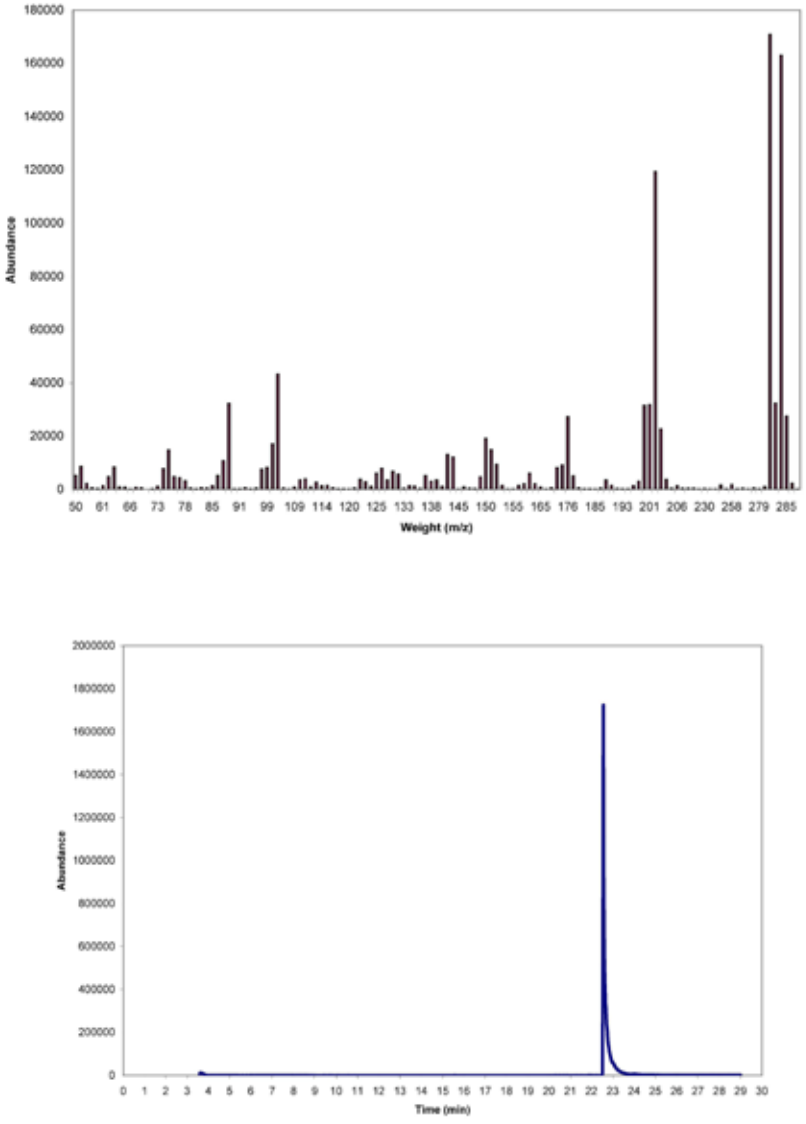

Figure 6: GC-MS data for the solution phase Sonogashira coupling confirming synthesis of 4-(4 bromophenethynyl)styrene.

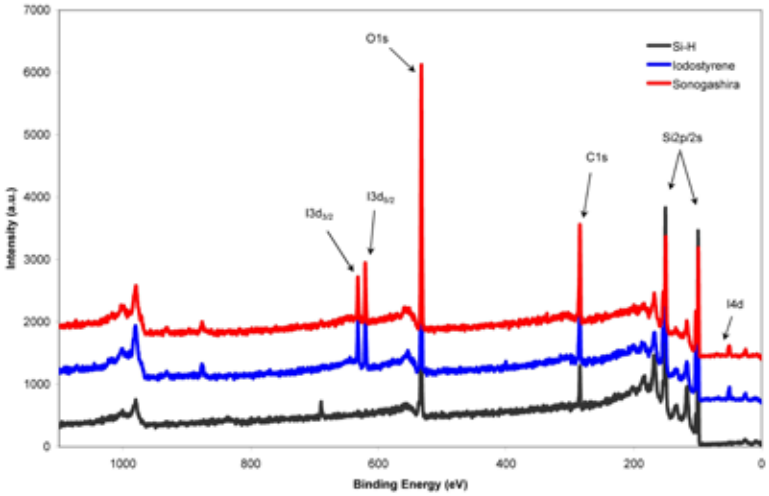

Figure 7: XPS general scans showing a hydrogen-passivated silicon wafer (black), a HPS wafer that had been UV-irradiated in the presence of iodostyrene (blue), and an HPS wafer that was UV-irradiated in the presence of iodostyrene and then subjected to a Sonogashira coupling reaction with 4-bromophenylacetylene (red).

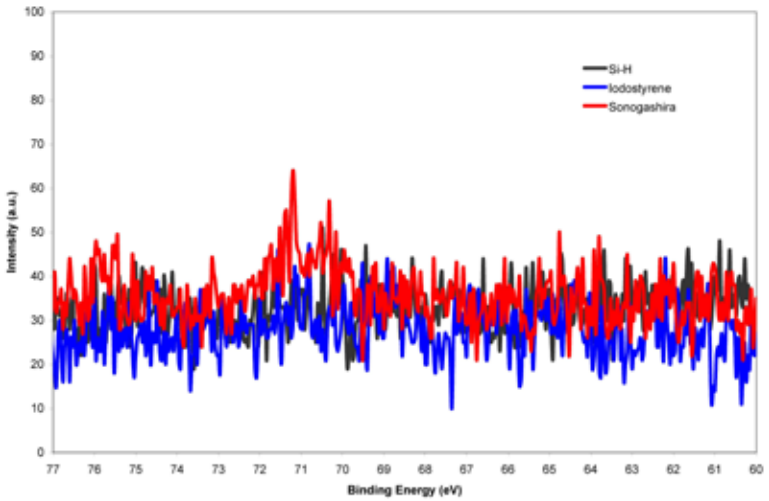

Figure 8: XPS detailed scans of Br3d binding energy.

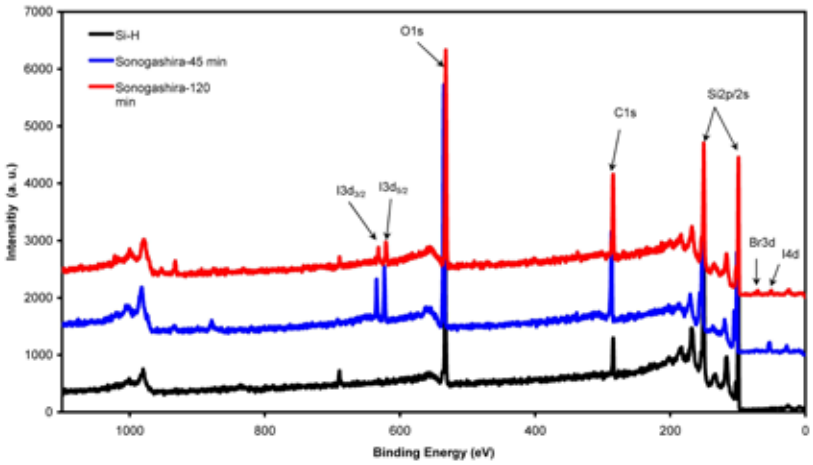

Figure 9: XPS general scans comparing a Si-H wafer (black), a wafer that underwent UV irradiation in the presence of iodostyrene and then 45min of Sonogashira coupling (blue), and a wafer that underwent UV irradiation in the presence of iodostyrene and then 120min of Sonogashira coupling(red).

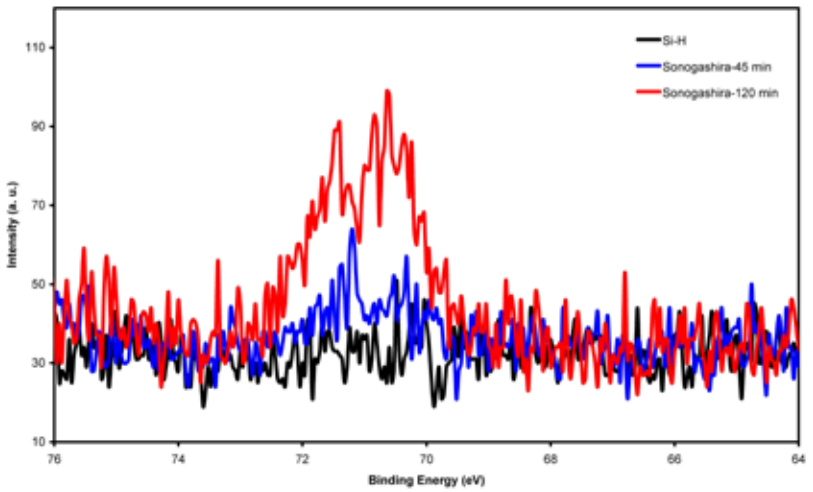

Figure 10: XPS detailed scans of Br3d binding energy.

For the solid-phase Sonogashira reaction, iodostyrene monolayers on a Si(111) wafer, which were formed under UV irradiation, were coupled with a 0.050 M solution of 4-bromophenylacetylene in triethylamine in the microwave for 45 min at 40° C. XPS was used to determine the molecular composition of the surface by measuring the intensity and energy of electrons freed from the surface to determine the element they came from. This resulting wafer, along with the hydrogen-passivated Si(111) wafer, and the Si(111) wafer with iodostyrene monolayers, were scanned using XPS (Figure 7). The Si-H wafer showed the presence of C1s (284.5 eV), O1s (532.5 eV), Si2s (150.5 eV) and Si2p (99.5 eV), which indicated a clean surface. An extra peak at 690.5 eV was caused by fluorine ions that were the remnants of improper washing during the hydrogen-passiavation steps. Iodostyrene monolayers on a Si(111) wafer showed distinctive doublet peaks at 620.7 eV and 632.5 eV for $I3d_{5/2}$ and $I3d_{3/2}$, which indicated the I-C bond. The Sonogashira wafer also had doublet peaks at 620.7 eV and 632.3 eV for $I3d_{5/2}$ and $I3d_{3/2}$, but these were at a lesser intensity, which was believed to be the result of successful Sonogashira coupling. Figure 8 shows the expanded Br3d region. Signals at $Br3d_{5/2}$ at 70.3 eV and $Br3d_{3/2}$ at 71.2 eV indicated the presence of a C-Br bond. Because the solid-phase Sonogashira reaction conditions mimicked those for the solution reaction, only a small amount of coupling was observed.

To optimize the coupling reaction, a 0.16 M solution (3x concentrated) of 4-bromophenylacetylene in triethylamine was allowed for the solid-phase Sonogashira coupling in the microwave for 2 hr. Figure 9 shows the comparison of XPS survey scans for monolayer modification via Sonogashira coupling on a Si(111) surface under different conditions. Both $Br3d_{5/2}$ and $Br3d_{3/2}$ intensified due to more coupling with surface-bound iodostyrene groups. The integration of detail scans of the whole Br3d region were estimated to show five times more coupling, as seen in Figure 10.

In the meantime, as iodine containing compounds are known to be light-sensitive, the activity of iodostyrene monomer toward UV irradiation during the monolayer formation on hydrogen-passivated Si(111) wafers was verified by collecting the final compound from the remaining solvent after UV treatment. Analysis of the final compound by NMR and GC-MS did not show any UV-induced side reactions or polymerizations of iodostyrene monomers, but presented only pure compound. In addition, the remaining solution after the solid-phase Sonogashira coupling was collected and analyzed to ensure the reaction. Initial findings showed a mixture of pure 4-bromophenylacetylene and its dimerized form. However, major product was not the dimerized molecule from GC-MS trace.

Conclusion

Iodostyrene and 4-bromophenylacetylene were successfully synthesized, and a selective solution-phase Sonogashira coupling between these two molecules was carried out. Iodostyrene was used to form organic layers on hydrogen-passivated Si(111) wafers, and these wafers underwent Sonogashira coupling with 4-bromophenylacetylene. XPS showed the formation of the iodostyrene layers on H-passivated Si(111) surface under UV exposure and demonstrated partial coupling of the iodine group with 4-bromophenylacetylene depending upon the concentration and/or reaction time. The increase observed in both the $Br3d_{5/2}$ and $Br3d_{3/2}$ regions in the second trial showed that a stronger amount of coupling can be achieved under the right conditions.

Further investigation will be required to find out the optimum condition for the complete reaction depending upon the concentration, reaction time and reaction temperature. Further tests, such as atomic force microscopy (AFM), x-ray fluorescence spectroscopy (XRF) and x-ray reflectivity (XRR), can confirm the formation, coverage and orientation of the monolayers on an H-passivated Si(111) surface. In addition, monolayers composed of 4-iodophenylacetylene would be an ideal future experiment, because it would create a fully conjugated system — an important factor when forming sensors that use electrical conductance to detect molecules attached to the surface.

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