

## PHOTOPATTERNED 'CLICK' FUNCTIONAL POLYMER SURFACES

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### Introduction

Soft surfaces are notoriously difficult to functionalize because of the wide variety of polymer surface properties. The literature on the functionalization of hard substrates (glass, silicon, gold, etc.) is extensive, and the toolbox of chemical anchors is well-known for hard surfaces: silanes for glass and silicon, thiols for gold, etc.<sup>1</sup> Comparable chemical anchors do not exist for polymer surfaces and as a result a number of alternate techniques have been developed to functionalize a polymer surface. Such techniques involve the incorporation of particular reactive groups during the synthesis of the polymer, the synthesis of surface-specific block copolymers<sup>2</sup>, or the degradation of the polymer via oxidation (ozonolysis) to provide functional groups on the surface. The focus of this work is to develop a methodology for surface functionalization that applies to nearly any polymer substrate without the need for unique polymer syntheses or indiscriminate degradation. Our aim is to use heterobifunctional small molecules comprised of a photoactive anchor tethered to a 'click' functional endgroup to pre-functionalize a surface with an orthogonally reactive moiety. This endgroup is then available for the subsequent attachment of a wide range of complementarily functionalized molecules.

### Experimental

**Materials.** All reagents were used without further purification. 6-bromohexanoyl chloride, propargyl alcohol, 3-(trimethylsilyl)propargyl alcohol, phthalimide potassium salt, sodium azide, and poly(acrylic acid) (35 wt% solution in water, avg.  $M_w = 100,000$ ) were purchased from Sigma Aldrich. Polystyrene ( $M_p = 1,056,000$ ,  $M_w/M_n = 1.03$ ) was purchased from Polymer Laboratories. *N,N*-bis(2-pyridinylmethyl)-1*H*-benzimidazole-2-methanamine (1Im2Py) and 3-azido-7-hydroxy-coumarin were generously received from S. Presolski in the lab of M.G. Finn at the Scripps Research Institute.

**Instrumentation.** <sup>1</sup>H NMR spectra were obtained using a Bruker 400 MHz spectrometer. ATR-IR spectra were obtained using a Nicolet Nexus 870 FT-IR with an Avatar Smart Multi-bounce HATR accessory. Water contact angles were obtained using deionized water (>18.2 MΩ cm, Millipore, Milli-Q) and measured at room temperature using a 100-00 contact angle goniometer (Rame-Hart, Inc.). Waveguide FTIR spectra were obtained using a homebuilt apparatus in transmission mode with a DTGS detector.<sup>3</sup>

**Synthesis of Prop-2-ynyl 6-bromohexanoate.** Propargyl alcohol (0.5 mL, 3.41 mmol, 1 eq.) was dissolved in 10 mL of dry pyridine and 10 mL of dry benzene under argon and this solution was cooled in an ice bath. 6-bromohexanoyl chloride (0.612 mL, 4.1 mmol, 1.2 eq.) dissolved in 10 mL of dry benzene under argon was then added dropwise to the propargyl alcohol solution and stirred overnight. The solution was acidified with 1M HCl, then extracted twice with CH<sub>2</sub>Cl<sub>2</sub>. The organic layers were twice washed with 1M NaOH, once washed with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed on a rotary evaporator to yield a light brown oil.

**Synthesis of 3-(trimethylsilyl)prop-2-ynyl 6-bromohexanoate.** As above using 3-(trimethylsilyl)propargyl alcohol in place of propargyl alcohol.

**Synthesis of Prop-2-ynyl 6-(phthalimido)hexanoate.** Prop-2-ynyl 6-bromohexanoate (0.606 g, 2 mmol, 1 eq.) was added to a solution of phthalimide potassium salt (0.441 g, 2.4 mmol, 1.2 eq.) in 50 mL of DMF and stirred overnight under argon. CHCl<sub>3</sub> was added to the solution flask and was transferred to a separatory funnel containing water. The aqueous layer was separated and twice extracted with CHCl<sub>3</sub>. The combined organic layers were twice extracted with water then the solvent was removed on a rotary

evaporator. Remaining solvent was removed under high vacuum overnight to yield a brown oil.

**Synthesis of 3-(trimethylsilyl)prop-2-ynyl 6-(phthalimido)hexanoate.** As above using 3-(trimethylsilyl)prop-2-ynyl 6-bromohexanoate in place of prop-2-ynyl 6-bromohexanoate.

**Synthesis of Azidoundecyl-functionalized Silica Nanopowder.** Azidoundecyl-functionalized silica nanoparticles were prepared according to literature procedures.<sup>4</sup>

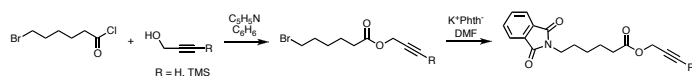
**Standard Preparation of Phthalimide-alkyne Coated Polystyrene Surface.** Glass microscope slides were cut in half, rinsed with water and ethanol, and dried in an oven. A 1% w/w solution of polystyrene in toluene was spin-coated (2500 rpm, 1 min) on the slide as a substrate for subsequent functionalization. Slides were then spin-coated (2500 rpm, 1 min) with a 1% w/w solution of a phthalimide-alkyne small molecule (prop-2-ynyl 6-(phthalimido)hexanoate or 3-(trimethylsilyl)prop-2-ynyl 6-(phthalimido)hexanoate) in ethanol. Films were then irradiated under a 300 nm lamp in air, and if a pattern was desired a chromium contact photomask was placed over the surface prior to irradiation. Adsorbed small molecules were removed by thrice rinsing with water and ethanol and drying with nitrogen.

**Standard (Unoptimized) Procedure for Copper-catalyzed Azide-alkyne Cycloaddition Reaction.** An azide (~approx. 4 μmol, 1 eq.), ligand (1Im2Py, 1 μmol, 1/4 eq.), and sodium ascorbate (100 μmol, 25 eq.) were dissolved in 20 mL of a 1:4 mixture of water and THF. Copper(II) sulfate pentahydrate (2 μmol, 1/2 eq.) was added and the solution was quickly poured over the slide. After sitting overnight the slide was removed from the reaction bath and repeatedly rinsed with water and DMF then ethanol, followed by drying in a stream of air.

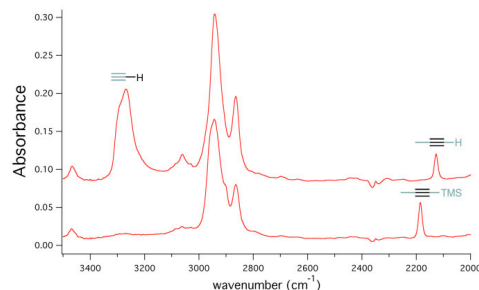
### Results and Discussion

**Synthesis of Phthalimide-alkyne Small Molecules.** The syntheses of both prop-2-ynyl 6-(phthalimido)hexanoate and 3-(trimethylsilyl)prop-2-ynyl 6-(phthalimido)hexanoate shown in **Figure 1** involved the condensation of an acid chloride with a terminal or 1-trimethylsilyl-protected 1-alkyn-3-ol followed by displacement of bromine by phthalimide. **Figure 2** shows the assigned IR spectra for both derivatives supporting the successful synthesis. The IR spectra are effectively identical in the region from 2000-3500 cm<sup>-1</sup> except for the stretches resulting from the different alkyne functionalities. The terminal alkyne exhibits both a C–H stretch at 3250 cm<sup>-1</sup> and a C≡C stretch at 2120 cm<sup>-1</sup> while the TMS-protected alkyne exhibits a C≡C stretch at the slightly higher frequency of 2190 cm<sup>-1</sup> and no terminal C–H stretch, as is expected. Additionally, the <sup>1</sup>H NMR spectra (not shown) for the two compounds are identical except for the terminal alkynyl proton (1H) which is shifted to 82.4ppm whereas the trimethylsilyl protons (9H's) are shifted to 80.15ppm. Mass spectra (FAB+) showed the appropriate M+1 molecular weight peaks at 300.45 for the terminal alkyne derivative and 372.2 for the TMS-alkyne derivative.

The design of the phthalimide-alkyne small molecules incorporates a



**Figure 1.** Syntheses of Prop-2-ynyl 6-(phthalimido)hexanoate and 3-(trimethylsilyl)prop-2-ynyl 6-(phthalimido)hexanoate.



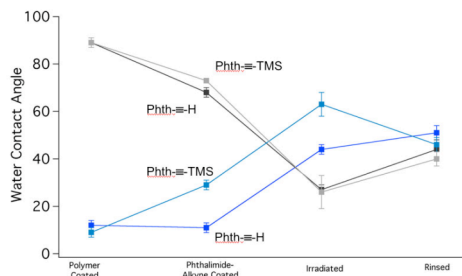
**Figure 2.** The FTIR Spectra of the Synthesized Prop-2-ynyl 6-(phthalimido)hexanoate (top) and 3-(trimethylsilyl)prop-2-ynyl 6-(phthalimido)hexanoate (bottom).

number of important characteristics that are necessary for the successful functionalization of polymer surfaces. Foremost, the photoactive anchor is a nearly universal anchoring moiety for polymer surfaces because of its well-known reaction with C–H bonds via the hydrogen abstraction mechanism. Excitation of the phthalimide carbonyl by ultraviolet light generates a biradical that abstracts a nearby hydrogen atom from the polymer to the carbonyl oxygen. The resultant radical on the polymer recombines with the remaining radical on the carbon of the phthalimide to generate a covalent bond between the phthalimide carbon and the polymer. Because the vast majority of polymers contain C–H bonds – which are not normally considered sites for reactive chemistry – such a photochemical method is ideally suited to the functionalization of numerous different types of polymers.

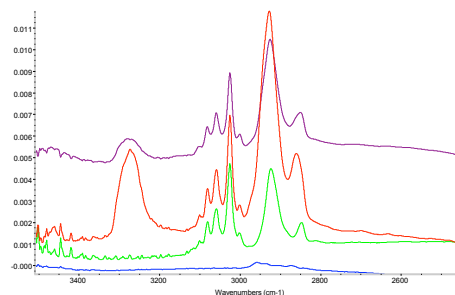
At the other end of the molecule, the alkyne and the TMS-protected alkyne offer a dual function for the appropriate functionalization of the surface. Most obviously they are both capable of reaction with azides via the Huisgen 1,3-dipolar cycloaddition which is often catalyzed by a trace amount of copper(I). Though inert to the reaction in its protected form, the TMS-alkyne is facily deprotected using a solution of potassium carbonate in  $\text{CH}_2\text{Cl}_2$  and methanol. In addition to its orthogonal reactivity with azides, the alkyne group has a very low surface energy that aids in the orientation of the molecule in the preferred manner; the phthalimide end is oriented toward the polymer-film interface and the alkyne end is oriented to the air-film interface. Previous research has most often functionalized a surface with an azide because its IR signature is more pronounced than that of the alkyne. For this application, however, the azide is ill-suited to functionalization on the surface because of its well-known photochemistry. After excitation of the azide and loss of molecular nitrogen to generate a nitrene, a hydrogen shift generally inactivates the nitrene forming an imine. Since we aim to photochemically bind the small molecule to the surface, we should not simultaneously inactivate the click-functional end.

**Surface Preparation and Characterization.** In addition to simply functionalizing polymer surfaces, a secondary requirement of this research is to do so without the need for expensive apparatuses or inaccessible techniques. Therefore we rely on the standard photolithographic techniques of spin-coating and irradiation through a contact mask for generating surfaces and patterns. Initial experiments irradiated the phthalimide-alkyne coated polymer surfaces for an unoptimized two hours to ensure reaction of the phthalimide anchor. Surfaces were then washed with ethanol and water and characterized by water contact angle analysis as shown in **Figure 3**. Two polymers – polystyrene and poly(acrylic acid) – were chosen as model polymers because of their very different initial water contact angles. By tracking the contact angle through each of the various processing steps, it was found that the water contact angles for both the phthalimide-alkyne and the TMS-protected phthalimide-alkyne approach the same range of surface energies after irradiation and rinsing. We interpret this to indicate that the water drop interacts with a similar alkyne surface despite the underlying hydrophobic polystyrene or hydrophilic poly(acrylic acid) films. Furthermore, in each case a drastic change in the contact angle was observed following irradiation that may be indicative of small molecule reordering as a result of H-abstraction-induced covalent bonding of the phthalimide to the polymer surface. It should be noted that TMS-protection of the alkyne does not have a significant effect on the final surface energy as evidenced by the comparable water contact angles.

Although characterization by water contact angle was encouraging, we were unable to spectroscopically visualize the alkyne on the polymer surface



**Figure 3.** Water Contact Angle Analysis Following the Unoptimized Generation of Alkyne-Functionalized Surfaces on Polystyrene (navy, blue) and Poly(Acrylic Acid) (black, gray).



**Figure 4.** Waveguide FTIR Spectra of Bare Glass Slide (blue, bottom), Polystyrene Film (green), Phthalimide-Alkyne Mixed into Polystyrene Film (red), and Phthalimide-Alkyne Film Deposited onto Polystyrene Film (purple, top). None of these samples were irradiated.

using conventional IR techniques; this is a key hurdle when using the alkyne-functional surface instead of the azide-functional surface. We therefore turned to waveguide FTIR spectroscopy to both verify and optimize the irradiation procedures for the click-functional polymer surfaces. Fortunately, waveguide FTIR spectroscopy employs a film with a high index of refraction (e.g. polystyrene) to internally reflect a beam of light in order to simultaneously collect multiple passes for the detection of a surface bound analyte. Preliminary data from the waveguide FTIR shown in **Figure 4** was used to determine the specific spectroscopic features resulting from the presence of the phthalimide-alkyne. The large peak at  $3260\text{ cm}^{-1}$  is assigned to the terminal alkyne C–H stretch and will act as an indicator of the phthalimide-alkyne in future experiments. These preliminary experiments have also indicated that the unoptimized irradiation time of two hours was ablating the polystyrene film. As a result, we have varied the amount of irradiation time from 0 to 30 minutes to optimize the attachment of the phthalimide-alkyne without ablating the polystyrene substrate.

Future work will continue to focus on the visualization of the patterned alkyne surfaces. One technique will involve the selective attachment of azide-functionalized silica nanoparticles<sup>4</sup> while another relies on a non-fluorescent coumarin azide<sup>5</sup> that fluoresces upon 1,3-cycloaddition with an alkyne. The covalent attachment of an azide-functional analyte to a pre-patterned polymer surface will find a wide array of applications from DNA microarray technology to antimicrobial surfaces, from selectively adhesive surfaces to micro- and nanoelectronics.

## Conclusions

Heterobifunctional small molecules have been synthesized that combine a photoactive anchor with a ‘click’ functional, low surface energy end group. When these molecules are applied to different polymer surfaces using common spin coating and irradiation techniques, the surfaces have been shown to approach a common surface energy, which it is argued is a result of the presence of the alkyne functional group. Ongoing work aims to characterize functionalized surfaces using both waveguide FTIR spectroscopy and the judicious reaction of azide functional molecules with the patterned alkyne surface.

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