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“Clicking” Polymer Brushes with Thiol-yne Chemistry: Indoors and Out

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Engineering the chemistry and topography of surfaces affords technological advancements for a variety of applications ranging from biosensors to microelectronics. This broad range of applications necessitates the development of a modular approach to surface engineering, ideally one that (1) enables the rapid generation of a diverse library of functional surfaces from a single substrate precursor, (2) utilizes a structurally diverse range of commercially available or easily attainable reagents, (3) proceeds rapidly to quantitative conversions under mild conditions, and (4) opens the door to orthogonal and site-selective functionalization. These criteria are, of course, similar to those that define a class of reactions commonly known as “click” chemistry.[1] Click chemistry, particularly Cu-catalyzed azide−alkyne cycloaddition (CuAAC), has proven a powerful approach toward meeting the aforementioned criteria for surface engineering.[2−4] However, the biotoxicity of Cu and the limited availability of cycloalkynes used in Cu-free AAC[5] reactions may limit utility in certain arenas. Modular surface reactions that circumvent these issues while retaining click-like characteristics are highly desirable. In this communication, we present thiol-yne chemistry as a modular approach toward surface engineering. Using this approach, we demonstrate the rapid generation of a library of highly functional, patterned, and multicomponent polymer brush surfaces under ambient conditions from a single substrate precursor. We also demonstrate the practicality of this approach by performing thiol-yne surface modifications using outdoor, ambient-air reactions with *sunlight* as the radiation source.

The recently highlighted utility and click-like characteristics of the radical-mediated thiol-yne reaction,[6−9] and the more thoroughly investigated thiol−ene reaction,[10,11] have been amply demonstrated in areas of macromolecular design,[12,13] postpolymerization modification[14−19] and even bioconjugation.[20] Thiol-ene reactions have also been demonstrated as a viable approach to surface modification by the Bowman[21,22] and Waldmann[23] groups; thiol-yne reactions, however, have yet to be explored for this purpose despite many common advantages. Notably, thiol-yne reactions proceed at room temperature with high efficiency and rapid kinetics, in the presence of oxygen/water, without expensive and potentially toxic catalysts, and are highly tolerant of a wide range of functional groups. Additionally, the thiol-yne reaction is orthogonal to a wide range of chemistries including the phosphine-catalyzed nucleophilic thiol-ene reaction.[7] The hydrothiolation reaction can also be photoinitiated in the UV−visible range (254−470 nm) affording both temporal and spatial control of the reaction site. The vast number of commercially available thiols is yet another advantage of this chemistry as a broadly applicable platform. Considering these attributes, we envisioned the fabrication of highly functional surfaces using thiol-yne reactions to modify the three-dimensional configuration of reactive “handles” expressed by densely tethered “yne”-containing polymer brushes. Similar postmodification of brush surfaces has been successfully demonstrated using pendant active esters[24] and azide modified nanoparticles.[25]

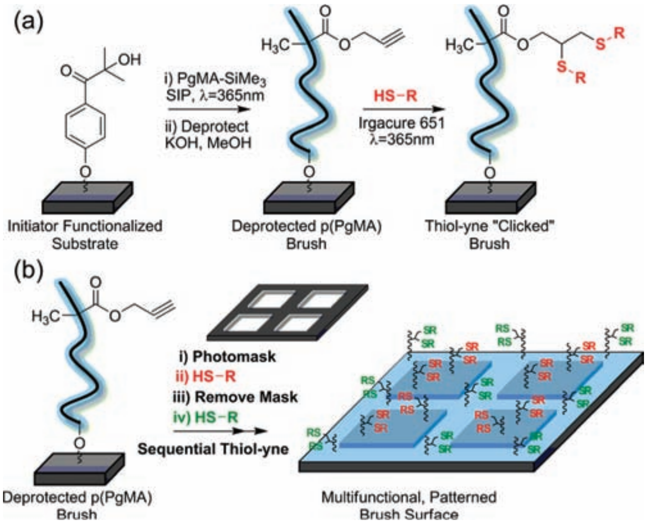

Figure 1. (a) Schematic procedure of surface-initiated photopolymerization of TMS-protected propargyl methacrylate, deprotection, and subsequent thiol-yne functionalization. (b) Schematic procedure for photopatterning “yne”-containing polymer brush surfaces with sequential thiol-yne reactions.

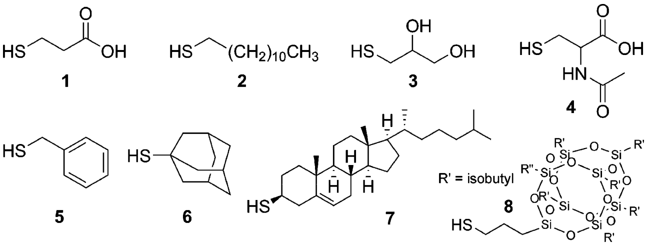

Figure 2. Commercially available thiols used for thiol-yne click reactions: mercaptopropionic acid (**1**), 1-dodecanthiol (**2**), thioglycerol (**3**), *N*-acetyl-L-cysteine (**4**), benzyl mercaptan (**5**), 1-adamantanethiol (**6**), thiochlolesterol (**7**), and 3-mercaptopropyl polyhedral oligomeric silsequioxane (POSS, **8**).

As shown in Figure 1a, silicon substrates were first functionalized with a chlorosilane derivative of commercially available 2-hydroxy-4′-(2-hydroxyethoxy)-2-methylpropiophenone (Irgacure 2959) photoinitiator.[26] These substrates were then inserted into a microchannel reactor (see Supporting Information) containing trimethylsilane-protected propargyl methacrylate (PgMA−SiMe$_3$, 1:1 in toluene) and surface-initiated by irradiating with UV$_{\lambda\max=365\text{ nm}}$ light (20 mW cm^{-1}, 45 min, ∼25 nm). Notably, the fabrication of a 14 mm × 65 mm substrate using our microchannel reactor requires only 400 μL of monomer solution (additional solution required depending on volume of connecting tubing), significantly reducing the cost of this approach. After Soxhlet extraction in toluene, the deprotection of the p(PgMA-SiMe$_3$) brush in KOH/MeOH was followed by ATR-FTIR. Quantitative deprotection was confirmed by the disap-

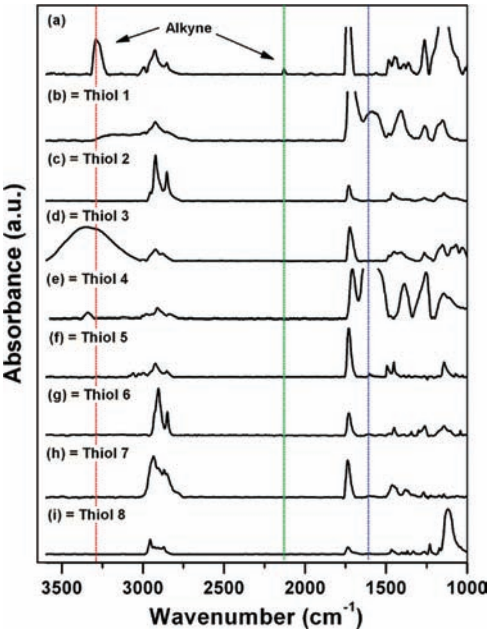

Figure 3. ATR-FTIR spectra of brushes on SiOx substrates (key peaks are identified): (a) poly(propargyl methacrylate) brush (3283 cm^{-1} C≡C—H (red), 2129 cm^{-1}, C≡C (green)) reacted with (b) 3-mercaptopropionic acid (3320−3000 cm^{-1}, COO—H) (c) 1-dodecanethiol (2955, 2922, 2852 cm^{-1}, C—H), (d) 1-thioglycerol (3600−3000 cm^{-1}), (e) *N*-acetyl-L-cysteine (3354 cm^{-1} CO—NH), (f) benzyl mercaptan (3061, 3028, 3000 cm^{-1}, =C—H; 1601 cm^{-1} C=C) (g) 1-adamantanethiol (2905, 2849 cm^{-1}, C—H), (h) thiocholesterol (2934, 2905, 2868, 2870 cm^{-1}, C—H), (i) 3-mercaptopropyl polyhedral oligomeric silsequioxane (1115 cm^{-1}, Si—O). The blue line indicates the position of the vinyl sulfide species (1609 cm^{-1}).

pearance of the protected alkyne C≡C stretch (~2185 cm^{-1}) and the appearance of the characteristic peaks of the unprotected alkyne (C—H 3288 cm^{-1}, C≡C 2131 cm^{-1}) (Figure SI.1).[27] The resulting "yne" functionalized polymer brush served as a "universal" reactive precursor for subsequent thiol-yne reactions eliminating the synthetic effort associated with the use of multiple functional monomers.

The radical-mediated reaction of a thiol with an alkyne generates a dithioether adduct as shown in Figure 1a. The reaction occurs in a two-step process involving the addition of the thiyl radical to the C≡C bond yielding an intermediate vinyl sulfide species that subsequently undergoes a second, formally thiol-ene reaction, yielding the 1,2-dithioether adduct.[6] To explore the efficacy of the thiol-yne reaction at surfaces, we selected a library of commercially available thiols (Figure 2), including 3-mercaptopropionic acid (MPA, **1**), of interest for pH responsive surfaces, *N*-acetyl-L-cysteine (**4**) as a model for the attachment of peptide fragments to brush surfaces, and thiocholesterol (**7**) as a ubiquitous component of biomembrane structures.[28] Thiol-yne reactions were carried out in the presence of α,α-dimethoxy-α-phenylacetophenone (Irgacure 651, 2 wt % I:thiol) at 365 nm under ambient air, temperature, and humidity conditions to afford the functional brushes. Reactions were performed solvent-free when possible, but in some cases, solvent was required to solubilize the thiol and/or solvate the brush. After the thiol-yne reaction, substrates were washed extensively with multiple solvents to remove any physisorbed species and then characterized by water contact angle and ATR-FTIR. Static water contact angles confirmed the expected changes in wettability associated with each functional moiety conjugated to the surface (Figure SI.2). ATR-FTIR was used to follow the thiol-yne functionalization of the brushes. Under these conditions, quantitative conversion of the tethered alkynes was observed within *minutes* (compared with hours typically required for CuAAC surface reactions) as indicated by the disappearance of the peaks assigned to the alkyne (C—H 3288 cm^{-1}, C≡C 2131 cm^{-1}) for the entire series of functional brushes (Figure 3). Further, the spectra clearly show peaks that are indicative of the incorporated thiols (see Table SI.1 for additional spectra/peak assignments). For small MW thiols, we see little evidence for the vinyl sulfide species (~1609 cm^{-1}, position shown by blue marker in Figure 3)[6] that would result from monosubstitution of the alkyne indicating full conversion to the 1,2-dithioether adduct. However, full conversion to the disubstituted adduct may be more difficult to achieve as the MW (or steric bulk) of the thiol increases. As shown in Figure 3g,h, there exists a very weak band at ~1609 cm^{-1} that could be assigned to the vinyl sulfide, but quantitative analysis is potentially complicated by weak absorbance and spectral overlap. Further to this point, we observe an increase in brush thickness (Table SI.2), which is attributed to the increase in molar mass of the monomer repeat unit and, consequently, an increase in MW of the brush after functionalization.[24] We note that other factors may also contribute to the changes in film thickness observed, including molecular stacking, hydrophobicity effects, etc. From cursory analysis of the film thickness increase relative to the MW of the thiol derivatives (where the MW of the thiol would dictate a one or two times increase in the molar mass of the monomer repeat depending on whether mono- or disubstitution occurs), it is apparent that larger MW thiols are not fully substituted to the 1,2-dithioether adduct. For example, the brush thickness increases by a factor of ~4.5 after functionalization with 1-dodecanethiol (DDT) and only by ~2.7 for thiocholesterol, despite DDT being half the molecular weight of the latter (202.4 and 402.72 g/mol, respectively). A similar dependence of substitution efficiency on the increasing MW of amines was observed with *N*-hydroxysuccinimide brushes.[24] In our case, the effect is exacerbated by the steric hindrance of adding a second bulky thiol per alkyne within the densely grafted polymer brush. Model studies using time-resolved reactions and application of the relationships reported by Murata et al.[24] to calculate the predicted film thickness at full 1,2-adduct conversion are ongoing to better understand the efficacy of the thiol-yne reaction within the confinements of the brush surface. Ultimately, we believe this observation does little to affect the potential of the thiol-yne reaction as a platform for surface engineering.

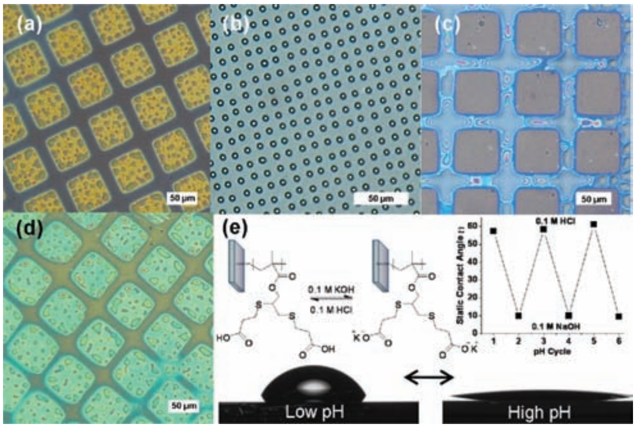

Figure 4. Condensation images of sequential thiol-yne micropatterned brushes showing water droplets selectively nucleating on the hydrophilic MPA areas: (a) MPA/DDT (square/bars), 300 mesh; (b) MPA/DDT (squares/bars), 2000 mesh; (c) inverse DDT/MPA (squares/bars), 300 mesh; (d) Sunlight MPA/DDT (squares/bars); (e) static water contact angle measurements showing pH responsive reversible wettability of MPA surfaces prepared outdoors in sunlight. Note: Color variations result from thin film interference under humid conditions.

To illustrate both the modularity and the versatility of our approach, we conducted sequential and area-selective thiol-yne/thiol-yne brush modifications using a simple photopatterning technique. The process is schematically shown in Figure 1b. Copper grids (300 mesh, 58 μm holes/25 μm bars and 2000 mesh, 7.5 μm holes/5 μm bars) were used as photomasks. The grids were placed in direct contact with the brush surface, immersed in MPA containing 2 wt % Irgacure 651, and irradiated with $\mathrm{UV}_{\lambda\mathrm{max}=365\ \mathrm{nm}}$ light (8 min) yielding a patterned MPA/"yne" surface. After removing the grid and washing with THF, the unexposed and unreacted "yne" was then subjected to a second thiol-yne reaction with DDT (8 min) affording the micropatterned, multicomponent surface. Figure 4a−b show the optical condensation images for the MPA/DDT patterned surface. As shown, the hydrophilic MPA regions (deprotonated with 0.01 M KOH) preferentially nucleate condensation of water permitting facile visualization of the chemically patterned surface.[29] The inverse pattern DDT/MPA was also demonstrated (Figure 4c). Well-defined edges and droplet confinement indicate a sharp interface between the hydrophilic MPA and hydrophobic DDT regions.

Since thiyl radicals can be generated close to visible wavelengths,[16] we further demonstrate the practicality of the thiol-yne approach for surface modification by performing homogeneous and patterned thiol-yne surface reactions outdoors using *sunlight* as a radiation source. Reactions were carried out in Petri dishes with nonpurged thiol solutions. For consistency, we again used 2 wt % Irgacure 651 although photoinitiators that absorb further into the visible are readily available. Quantitative conversion of the tethered alkynes was observed within 1 h of sunlight exposure (Figure SI.3). Figure 4d shows the condensation image of the resulting sunlight patterned MPA/DDT brush. The results are analogous to those obtained in the lab suggesting the possibility of large scale surface modifications using renewable energy resources. As a final point, we show that homogeneous, pH responsive MPA functionalized brushes can easily be synthesized in sunlight. These surfaces exhibit reversible wettability upon protonation and deprotonation of the carboxylic acid functionalities as shown in Figure 4e.

In summary, we have demonstrated thiol-yne chemistry as a modular platform for rapid and practical fabrication of highly functional, multicomponent surfaces. Although demonstrated here on polymer brushes, this approach is certainly extendable to a broad range of surfaces, including biorelated substrates. Considering the mild reaction conditions, rapid throughput, and compatibility with orthogonal chemistries, we expect this platform to find widespread use among the materials science community.

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Supporting Information Available: Details of synthesis procedures, water contact angle measurements, and additional FTIR characterization and assignments. This material is available free of charge via the Internet at http://pubs.acs.org.

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