Click Chemistry on Surfaces: 1,3-Dipolar Cycloaddition Reactions of Azide-Terminated Monolayers on Silica

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Received: January 29, 2004

Monolayers of 11-azido-undecylsiloxane were prepared on powdered silica and on silicon wafers by the substitution of 11-bromo-undecylsiloxane and were subsequently coupled with three substituted acetylenes R−C≡C−R′ (R, R′ = C$_6$H$_{13}$, H (**1**); COOCH$_3$, H (**2**); COOC$_2$H$_5$, COOC$_2$H$_5$ (**3**)) to yield 1,2,3 triazoles via the Huisgen 1,3-dipolar cycloaddition reaction. The pathway and yield of the surface reactions were monitored by infrared spectroscopy and ellipsometry. No reaction was observed with **1**, whereas **2** and **3** react quantitatively both on powdered silica and on flat wafer surfaces at a temperature of 70 °C without catalytic activation. Thus, the unique properties of this reaction in solution (high selectivity, quantitative yields, no byproducts, simple reaction conditions) seem to be transferable to surface-bound reactants and might provide access to a range of novel, functionalized surfaces by analogy to the Sharpless click chemistry concept for solution-phase synthesis.

Introduction

Alkylsiloxane monolayers (CH$_3$−(CH$_2$)$_n$−SiO$_x$) on silica, absorbed from dilute solutions of alkyltrichlorosilane (R−SiCl$_3$) or alkyltrimethoxysilane (R−Si(OMe)$_3$) precursors onto either powdered SiO$_2$ or flat, native Si/SiO$_2$ wafer surfaces, form highly ordered, densely packed layers and have been extensively studied in the past.[1] One inherent limitation of this class of self-assembled monolayers is the high reactivity of the surface anchor group −SiX$_3$ (X = Cl or OCH$_3$), making it incompatible with many desired functionalities Y on the opposite end of bifunctional precursor molecules Y−(CH$_2$)$_n$SiX$_3$, which are needed to design monolayers with specific surface properties. As an alternative, in-situ surface modification of a suitable precursor monolayer Y$_1$−(CH$_2$)$_n$SiO$_x$ → Y$_2$−(CH$_2$)$_n$SiO$_x$ can be attempted, where the anchor groups are already bonded to the substrate and removed from the reaction scene. This strategy, however, often just trades one problem for another because the quantitative conversion Y$_1$− → Y$_2$− of a surface functionality in the rigid, densely packed environment of a surface-bound monolayer is anything but trivial and even the simplest quantitative textbook reactions often fail under these conditions. Although definitive predictions−which reactions will be most suitable for this purpose−are hardly possible, preselection can be based on the following criteria to be met under conventional, liquid-state reaction conditions: (i) quantitative conversion under mild conditions (atmospheric pressure and room temperature), (ii) compatibility with different functional groups, (iii) no catalytic activation required (because of potential problems in removing catalytic byproducts from the interface, and (iv) no reaction byproducts (which might accumulate at the interface and retard or stop the surface reaction). These criteria are closely related to the "click chemistry" concept introduced by Sharpless[2] as a modular approach for the synthesis of new compounds, which is based on a few highly selective and quantitative coupling reactions for the assembly of new molecules from individual "building blocks". We therefore attempted to test these reactions for their suitability to modify and functionalize solid-state surfaces.

The most perfect click reaction known to date is the Huisgen 1,3-dipolar cycloadditon[3,4] of azides and alkynes to form 1,2,3 triazoles. The present, preliminary report describes the first example of using this reaction to couple monolayer-covered, azide-terminated silica substrates with acetylenes.[5]

Experimental Details

Modification of Powdered SiO$_2$. To a flask containing 1 g of silica (Merck, specific surface area = 388 ± 2 m^2/g) suspended in 30 mL of toluene (Aldrich, 99.8%, HPLC grade), 250 µL of 11-bromoundecyltrichlorosilane (ABCR, 95%) was added. The mixture was stirred for 45 min at room temperature and was subsequently transferred to a centrifuge tube. After centrifuging and removing the supernatant solution, we washed the obtained silica powder three times with toluene and ethanol (Austria Hefe AG, p.a.) to remove excess bromoundecyltrichlorsilane; the powder was then dried under reduced pressure. Exchange of the bromine against the azide group was carried out following previous reports[6] by stirring 500 mg of the Br-terminated silica in 10 mL of a saturated solution of sodium azide (Aldrich, 99%) in *N,N*-dimethylformamide (DMF, Aldrich, 99.9+%, HPLC grade) for 48 h at room temperature. The supension was centrifuged, and the resulting powder was washed three times with distilled water, acetone, and ethanol and dried under reduced pressure. 1,3-Dipolar cycloaddition reactions with these azide-terminated silica substrates were carried out by adding 25 mg of modified SiO$_2$ to 200 µL of a 0.5 M ethanolic solution of one of the following alkynes: *n*-hexyl-acetylene (**1**, Aldrich, 97%), methoxycarbonyl acetylene (**2**, Aldrich, 99%) or bis-(ethoxycarbonyl) acetylene (**3**, Aldrich, 95%). The mixture was stirred for 24 h at the respective reaction temperature (20 or 70 °C), was centrifuged, and was washed three

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SCHEME 1

① (R)=(C₅H₁₃), (R')=(H)
② (R)=(COOMe), (R')=(H)
③ (R,R')=(COOEt)
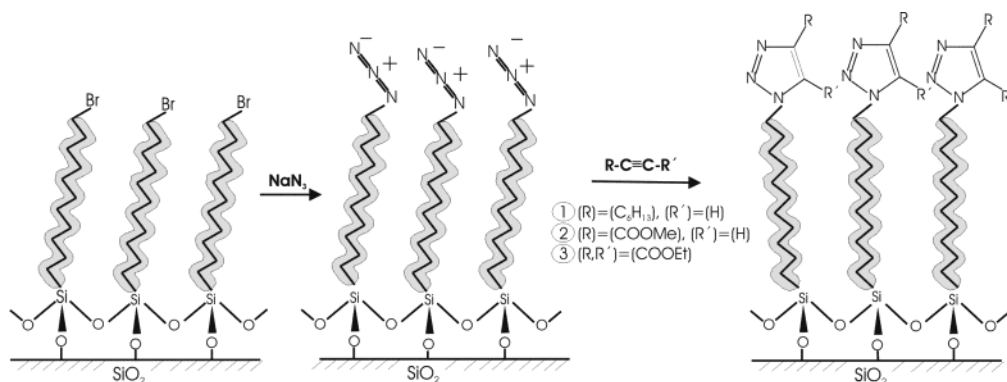
times with ethanol and three times with CH_2Cl_2. Finally, the powder was dried for 24 h at 40 °C.

Modification of Silicon Wafers. P-doped, (100)-oriented silicon wafers (Gritek, prime grade, 7–21 Ω cm specific resistivity, 0.5 mm thickness) were cut into 15 × 15 mm^2 pieces. Prior to adsorption, they were sonicated in ethanol, blow-dried in high-purity nitrogen, and exposed to a UV/ozone atmosphere in a commercial cleaning chamber (Boekel Industries, model UV-clean) for 20 min. This procedure removes hydrocarbon contaminants from the substrate surface and yields a (1.2 ± 0.2)-nm-thick native oxide layer as determined by ellipsometry. Monolayers were adsorbed by immersing the wafers in a 1 mmol solution of 11-bromoundecyltrichlorosilane in toluene for 45 min. After removal from the adsorbate solution, the wafers were sonicated in toluene, gently scrubbed with a toluene-soaked tissue to remove physisorbed multilayers, and rinsed with toluene, acetone, and ethanol. Finally, they were sonicated in ethanol, rinsed with ethanol, and blow-dried in high-purity nitrogen. The exchange of the bromine against the azide group was carried out by immersing the wafers in a saturated solution of sodium azide in DMF for 48 h at room temperature, followed by thorough rinsing with distilled water, ethanol, acetone, and toluene. Subsequently, the wafers were scrubbed with a toluene-soaked tissue, rinsed again with toluene, acetone, and ethanol, sonicated in ethanol, and blow-dried in nitrogen. Cycloaddition reactions with the azide-functionalized wafers were carried out in a manner similar to that for the powdered substrates by immersing the wafers for 24 h in 1 mL of the appropriate alkyne **1**, **2**, or **3** dissolved in ethanol (0.5 M) at the indicated reaction temperature. Afterward, the wafers were rinsed with ethanol, acetone, and toluene, wiped with a toluene-soaked tissue, and rinsed again with toluene, acetone, and ethanol. Finally, they were sonicated in ethanol and blow-dried in nitrogen.

Ellipsometric and Infrared Measurements. Ellipsometric thicknesses were measured with a PLASMOS SD 2300 ellipsometer as described in detail elsewhere.[7] Optical constants of $n = 3.865$ and $k = 0.020$ for Si, $n = 1.465$ and $k = 0$ for SiO$_2$, and $n = 1.50$ and $k = 0$ for the organic films were used. Infrared transmission spectra of modified silica powder were obtained from KBr pellets prepared from mixtures of 10 mg samples with 400 mg of KBr. Scans (128) at 4-cm^{-1} resolution were averaged from each pellet and were referenced against 128 scans of a pure KBr pellet. Infrared spectra of monolayers on silicon wafers were obtained using a surface-enhanced reflection technique described previously,[8] where the monolayer-covered wafer was pressed against a hemispherical germanium crystal and a p-polarized IR beam was directed through the Ge crystal onto the sample surface at 65° incidence. Owing to the large intensity enhancement of the vibrational components perpendicular to the substrate surface, "metal-like" reflection spectra

with a high signal-to-noise ratio are obtained with this method also on nonmetal, dielectric substrates.[8] Scans (256) at 4-cm^{-1} resolution were measured for each sample and were referenced to 256 scans of the Ge crystal in contact with air.

Results and Discussion

Azide-terminated monolayers were prepared in situ from 11-bromo-undecylsiloxane monolayers[6] and were subsequently reacted with three different acetylene compounds: *n*-hexyl-acetylene (**1**), methoxycarbonyl acetylene (**2**), and bis-(ethoxy-carbonyl) acetylene (**3**) according to Scheme 1. Powdered silica was used as the initial substrate. The exchange of the surface bromine of a 11-bromoundecylsiloxane monolayer against azide via nucleophilic substitution with sodium azide in DMF solution has been shown to proceed quantitatively[6] and is accompanied in the infrared spectra by the appearance of an intense $\nu_{as}(N_3)$ absorption at 2104 cm^{-1}. The integrated band intensities of the ν(CH) absorptions of adsorbed bromoundecylsiloxane show a strict linear relationship with the ν(N$_3$) stretching band after azide substitution over a surface coverage range from 10 to 100%, supporting the completeness of this substitution reaction also for densely packed, full monolayer films. The obtained, azide-terminated silica was suspended for 24 h in ethanolic solutions of acetylenes **1**–**3** at 20 °C. The infrared transmission spectra before and after these treatments are shown in Figure 1. Compound **1** shows no reaction at all (IR spectrum not shown), whereas both **2** and **3** cause distinct spectral changes, namely, a decrease of the $\nu_{as}(N_3)$ absorption and a growth of a ν(C=O) band at 1726 cm^{-1} (**2**) and 1732 cm^{-1} (**3**) and a ν(CH$_3$) absorption at 2984 cm^{-1} (the latter being barely visible for monosubstituted acetylene **2**). These spectral changes are clear indications of a reaction of the azide group with the acetylenes. The yields of this coupling reaction were derived from the $\nu_{as}(N_3)$ peak areas and give 37% for monosubstituted compound **2** and 82% for bisubstituted acetylene **3**, in agreement with the expected reactivity increase with an increasing number of electron-withdrawing substituents.[3] The same reactions were carried out at a temperature of 70 °C, and the corresponding IR spectra are shown in Figure 2. Nonactivated acetylene **1** again shows no reaction, whereas both **2** and **3** react quantitatively, as judged from the complete disappearance of the $\nu_{as}(N_3)$ absorption and the intensity gain of the ν(C=O) bands compared to the incomplete conversion in Figure 1.

The same experiments were carried out on native silicon (Si/SiO$_2$) wafers, where the reactions were monitored by surface-enhanced infrared reflection spectroscopy[8] and by ellipsometry. For the precursor monolayer of 11-bromo-undecylsiloxane, a film thickness of 1.45 ± 0.1 nm was measured, which remained essentially constant (1.35 ± 0.1 nm) after the substitution of
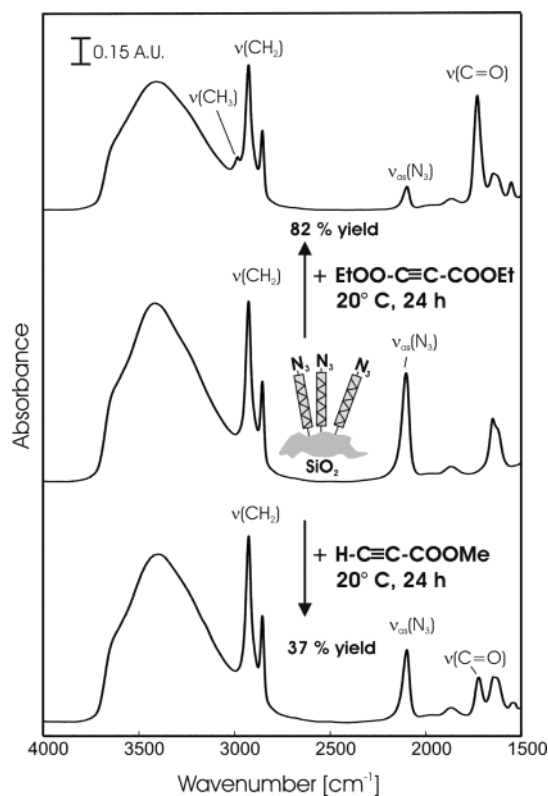
Figure 1. IR transmission spectra of powdered silica coated with a monolayer of 11-azido-undecylsiloxane ($N_3-(CH_2)_{11}-SiO_x$, middle spectrum) and of the coupling products of this monolayer with methoxycarbonyl acetylene (lower spectrum) and bis-(ethoxycarbonyl) acetylene (upper spectrum) after 24 h of reaction at 20 °C.
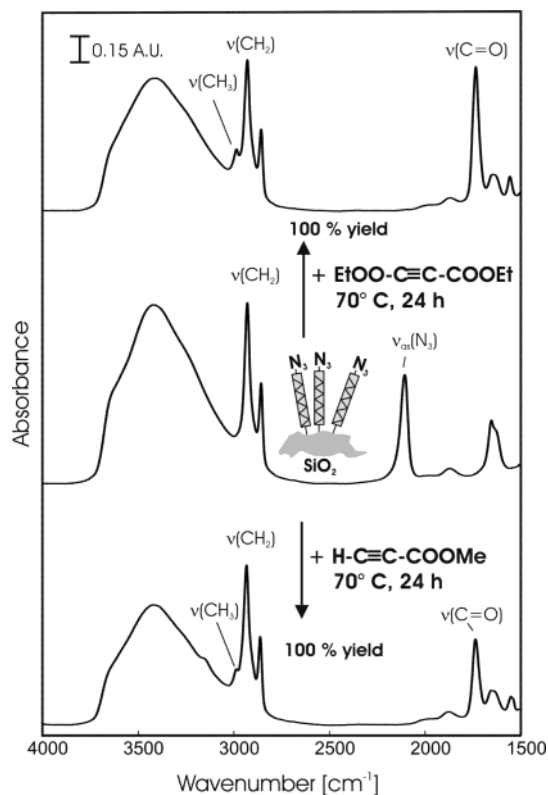

Figure 2. Same as Figure 1 but for a reaction temperature of 70 °C.
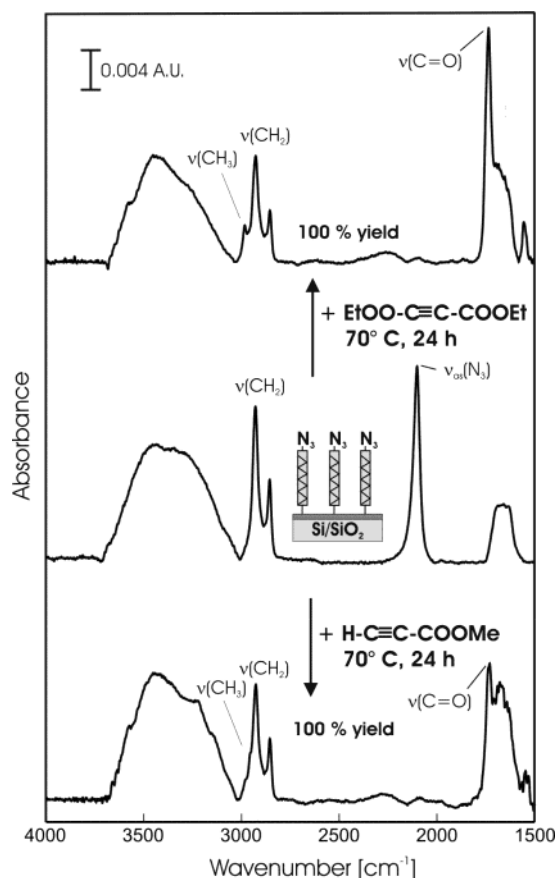

Figure 3. Surface-enhanced IR reflection spectra of a monolayer of 11-azido-undecylsiloxane on a native silicon wafer (middle spectrum) and of the coupling products of this monolayer with methoxycarbonyl acetylene (lower spectrum) and bis-(ethoxycarbonyl) acetylene (upper spectrum) after 24 h of immersion in the reactant solutions at 70 °C.

the terminal bromine with the azide functionality. The IR spectrum of the azide-terminated monolayer (Figure 3, middle spectrum) shows a strong absorption at 2102 cm^{-1} ($\nu_{as}(N_3)$)

and CH stretching bands at 2929 cm^{-1} (ν_{as} (CH$_2$)) and 2956 cm^{-1} (ν_s(CH$_2$)). In consideration of the strict surface selection rule of this surface-enhanced reflection technique,[8] which allows only vibrational components perpendicular to the substrate surface to be detected, the large intensities of the CH absorptions indicate a largely disordered structure of the hydrocarbon chains in this monolayer. This is also supported by their relatively high peak frequencies, which are essentially identical to the spectra on powdered silica (Figures 1 and 2). Immersion of the azide-covered wafers in ethanolic solutions of **2** and **3** for 24 h at 70 °C gives the same spectral changes as on the powdered substrates (Figure 3): The essentially quantitative addition of both acetylenes **2** and **3** with the azide groups is again evidenced by the complete disappearance of the $\nu_{as}(N_3)$ peak, the growth of a $\nu(C=O)$ peak (1732 cm^{-1} for **2**, 1736 cm^{-1} for **3**), and a small $\nu(CH_3)$ absorption at 2984 cm^{-1}. The ellipsometric thicknesses were determined to be 1.83 nm after reaction with **2** and 1.95 nm after reaction with **3**, corresponding to a thickness increase of about 0.5 nm for **2** and 0.6 nm for **3**. Regarding the regioselectivity of this reaction, two isomers can form upon the addition of **2**; these have the methoxycarbonyl substituent either in the 4 or in 5 position of the 1,2,3 triazole ring. In solution, it has been shown that a 1:1 mixture of these two isomers is usually formed,[9] whereby the application of a copper(I) catalyst exclusively yields the 4-substituted product. We currently have no information about the regioselectivity of this reaction either on the silica powder or on the wafer surfaces, although for steric

reasons the 4-substituted product, where the substituent points away from the surface, might be more favorable than the 5 isomer.

In summary, we have shown that 1,3-dipolar cycloaddition reactions of azide-terminated surfaces with activated acetylenes provide a simple and convenient way for surface derivatization via a quantitative fusion reaction devoid of side products and without the need for catalytic activation. Given the large variety of oxidic substrates modifiable by organosilane monolayers[10] in combination with the tolerance of this coupling reaction for different reaction conditions and for the presence of other substituents,[9] this process might provide access to a large number of novel, chemically modified surfaces. Moreover, the quantitative coupling under relatively mild reaction conditions makes this reaction a promising candidate for solid-state fusion processes, for example, for creating a strong, covalent linkage between two silicon wafers upon contacting two activated surfaces ("wafer bonding"[11]). Related experiments are currently underway in our laboratory.

References and Notes

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