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Thiol−ene Click Reaction as a General Route to Functional Trialkoxysilanes for Surface Coating Applications

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S Supporting Information

ABSTRACT: Functionalized trialkoxysilanes are widely used to modify the surface properties of materials and devices. It will be shown that the photoinitiated radical-based thiol−ene "click" reaction provides a simple and efficient route to diverse trialkoxysilanes. A total of 15 trialkoxysilanes were synthesized by reacting either alkenes with 3-mercaptopropyltrialkoxysilane or thiols with allyltrialkoxysilanes in the presence of a photoinitiator. The functionalized trialkoxysilanes were obtained in quantitative to near-quantitative yields with high purity. The photochemical reactions can be run neat in standard borosilicate glassware using a low power 15-W blacklight. A wide range of functional groups is tolerated in this approach, and even complex alkenes click with the silane precursors. To demonstrate that these silanes can be used as surface coating agents, several were reacted with iron oxide superparamagnetic nanoparticles and the loadings quantified. The photoinitiated thiol−ene reaction thus offers a facile and efficient method for preparing surface-active functional trialkoxysilanes.

The ability to modify the physical and chemical properties of surfaces and interfaces is important in fundamental and applied materials science. One of the simplest and most common methods is to react trialkoxy- or trichlorosilanes with hydroxylated surfaces, such as metal oxides. Silanes form strong covalent oxane bonds to such surfaces, making them particularly useful for bridging the inorganic and organic components. Silanes have been used to prepare many important materials and devices, including catalyst-coated magnetic and mesoporous metal oxides,[1] superhydrophobic surfaces,[2] organic photovoltaics,[3] thin-film transistors,[4] and sensors,[5] to name a few.

In this communication, we demonstrate that the simple photoinitiated radical-based thiol−ene reaction can be used to synthesize tailored, functional trialkoxysilanes. The method is easily scaled up. The silanes synthesized by this method can be covalently bound to magnetite superparamagnetic nanoparticles (SPNs) and the loading quantified by elemental analysis.

The reactions most commonly used to produce mono-, di-, and trialkoxysilanes include hydrosilylation of alkenes and alkynes,[6−9] nucleophilic substitution reactions,[10−12] and reactions of amines and alcohols with isocyanate-containing trialkoxysilanes.[13−15] Of these methods, hydrosilylation is the most widely used because of the good to excellent product yields, ready availability of the metal catalysts, and low cost of the trialkoxysilane precursors. Hydrosilylation reactions can provide good product yields; the drawback is that they typically require expensive metal catalysts and/or chiral organic ligands, although ordinarily only low mol % catalysts and ligands are used. Hydrosilylation reactions also have only moderate functional group tolerance and product regioselectivities and require postsynthetic purification to remove metals and excess reactants from the moisture-sensitive products. The alternative methods have even more limited functional group tolerance, often have low-to-moderate product yields, and can require tedious product purification. The thiol−ene reaction has the potential to overcome many of these drawbacks.

The radical-based thiol−ene reaction has been widely used to synthesize dendrimers;[16−18] functionalize biomolecules, biomacromolecules, and surfaces; and synthesize new polymeric materials for applications ranging from soft lithography to porous microparticles.[19−24] This reaction, which involves the addition of one thiol across an alkene, is one member of the class of "click" reactions.[25] Thiol−ene reactions proceed under mild conditions in the presence of oxygen, are regioselective, tolerate many functional groups, can be run neat or in benign solvents such as water, and provide quantitative or near-quantitative yields with simple or no chromatographic separation required. The resulting thioether bond is a strong covalent linkage. These attributes led us to believe that the thiol−ene reaction would be well suited to synthesizing functionalized trialkoxysilanes for surface coating applications. Precedents for this approach include several syntheses of individual functional trimethoxysilanes for specific applications,[26−28] and the preparation of silicones and polymer-silane conjugates.[29−33]

Scheme 1 shows how the thiol−ene reaction can be used as a general approach to synthesizing functional silanes. Equimolar amounts of a 3-mercaptopropyltrialkoxysilane and an allyl/terminal alkene, or of a thiol and allyltrialkoxysilane, are mixed in the presence of 2 mol % photoinitiator. The mixture is irradiated at rt, typically for ∼24 h, under an argon or nitrogen blanket using a low power 15-W blacklight (λ_{max} = 368 nm with a total UV output of 2.2 W). Reactions are run neat or in the presence of a minimal amount of solvent (0.2−1 mL) and proceed smoothly in standard borosilicate glass containers.

Table 1 shows that a wide range of simple and complex alkenes can be quantitatively or near quantitatively clicked with 3-mercaptopropyltriethoxysilane (MPTES) to produce the functionalized triethoxysilane analogs. Only the synthesis of **9** required a longer irradiation time and additional initiator to reach high reactant conversion. This might be partly attributed to the increase in solution viscosity as the reaction proceeds, limiting mass

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Scheme 1. Methodology for Synthesis of Trialkoxysilanes

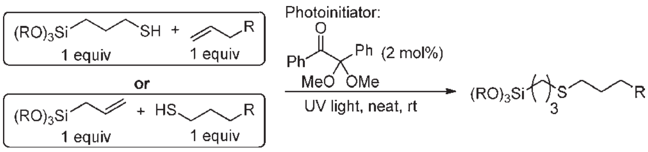
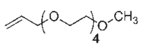
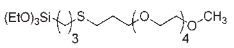
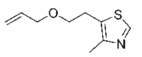
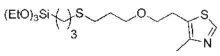
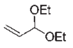
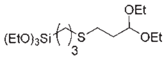
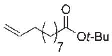
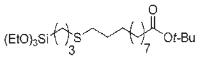
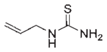
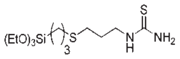
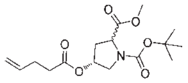
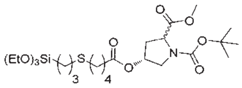
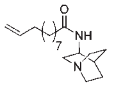
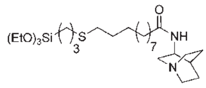
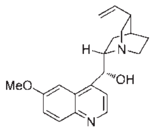
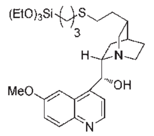
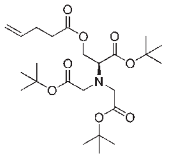
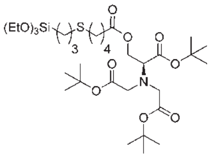
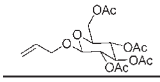
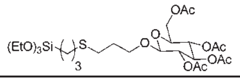


Table 1. Synthesis of Triethoxysilanes via Photoinitiated Thiol−ene Reactions between MPTES and Various Alkenes[a]

Alkene	Triethoxysilane		Conv. (%)[b]	Purity (%)[c]
		1	>99	96
		2	>99	95
		3	>99	96
		4	98	96
		5	>99[e]	95
		6	96	94
		7	98[d]	96
		8	98[d]	96
		9	94[f]	90
		10	>99[d]	97

[a] A dry 10 mL round-bottom was charged with 1 equiv of alkene (0.4−5.0 mmol), 1 equiv of MPTES (0.4−5.0 mmol), and 2 mol % Irgacure 651, backfilled with argon, and irradiated for 24 to 27 h with a 15 W blacklight (λ_{max} = 368 nm). [b] Quantified by ^{1}H NMR. [c] Determined by gas chromatography/mass spectrometry (GC/MS) or ^{1}H NMR. [d] Dry $CHCl_3$ (0.25−1.0 mL) added to solubilize alkene. [e] Dry MeOH (0.6 mL) added to solubilize alkene. [f] Reaction mixture irradiated 45 h with 3 mol % Irgacure 651, then an additional 22 h after addition of another 2 mol % Irgacure 651.

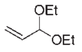
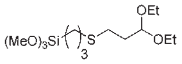
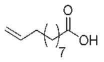
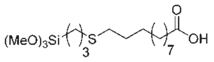
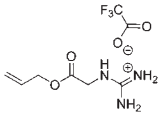
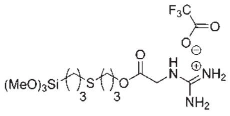
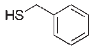
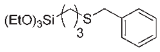
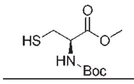
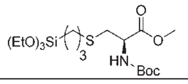
transport.[21] A second factor might be that product **9** absorbs at the same wavelength as the initiator, diminishing the rate of initiation as the reaction proceeds (see Supporting Information). A variety of common functional groups were found to be well-tolerated under these reaction conditions. Because the reactions were essentially quantitative and contained only small amounts of unreacted MPTES, alkene, and decomposed photoinitiator, no chromatographic purification of the products was conducted. Importantly, the remaining non-silane impurities do not affect the ability of the triethoxysilanes to couple with surfaces, and they can be washed away after the surface modification process is complete.

The alkenes in Table 1 were selected because they form silanes that are potentially useful for a variety of applications. Tetraethylene glycol-functionalized silane **1** is similar to most graftable oligoethylenoxides that are used to minimize protein adsorption in biomedical and biosensor applications.[6] Thiazole- terminated silane **2** is a precursor for preparing surface-bound ionic liquids or thiazolium carbenes that are useful organocatalysts and strong metal coordinating ligands.[10] Silanes **3** and **4** contain masked distal aldehyde and carboxylic acid groups that can be deprotected by mild acid hydrolysis and could be very effective to pattern aldehydes and carboxylic acids on planar substrates using photolithography and photoacids.[34] Silane **5**, while not a catalyst itself, was made to demonstrate the compatibility of this methodology with thioureas, an important class of coordinating organocatalysts.[35] Silanes **6**, 7, and **8** can be coated on surfaces and then deprotected to form valuable heterogeneous catalysts.[1] NTA silane **9** contains a ligand that is used to bind histidine-tagged proteins once the *tert*-butyl esters have been cleaved; it has been utilized for protein purification and as an intracellular pH-sensitive peptide delivery agent.[36,37] Finally, tetra-acylated glycopyranoside silane **10** can be used after acyl deprotection to binding lectins and has the potential to be used in cancer diagnostic tools.[38]

MPTES was selected as the silane precursor for the initial reactions shown in Table 1 because of its low moisture sensitivity; however, as shown by the first three entries in Table 2, it can be replaced with 3-mercaptopropyltrimethoxysilane (MPTMS) to make the more reactive trimethoxysilane coating agents. For example, MPTES coupled smoothly to 11-undecenoic acid, with no evidence of hydrolysis of the trimethoxysilane. An alkene containing a guanidinum salt was also successfully coupled with MPTMS; in this example, some silane co-condensed to form silane dimers due to incomplete removal of water from the salt. The last two entries in Table 2 illustrate that the mercaptosilane precursors can be replaced with allyltriethoxysilane (ATES) to cleanly couple thiol-containing compounds such as cysteine.

A major advantage of synthesizing silanes using the thiol−ene methodology is that the reactants MPTES, MPTMS, APTES, and many different alkenes and thiols are commercially available at low cost. Because of this, we explored the ease and feasibility of scaling up the thiol−ene reaction by resynthesizing diethyl acetal triethoxysilane **3** on a >100 mmol scale. The reaction of acrolein diethyl acetal with MPTES was selected because of the low cost of the reactants and the similarity of product **3** to one of the few commercially available acetal-terminated trialkoxysilanes.[39] Following irradiation of the reactants for 24 h using two 15 W blacklights, the reaction reached >98% conversion, which is similar to that obtained for the 2-mmol scale reaction (Table 1). The product purity was 93%, slightly lower than that in the small scale reaction. Most likely this is due either to misweighing the reactants or to some loss of the alkene while purging the reaction vessel. A rough estimate indicates that preparing **3** by this method costs \$0.63/mmol **3**. This is roughly ~1/13 the price at which a similar commercially available terminal acetal-containing triethoxysilane[39] is sold. (See Supporting Information for cost analysis.) This finding suggests that the thiol−ene reaction methodology could be a low cost way to synthesize silanes on a commercial or industrial scale.

Table 2. Synthesis of Trimethoxysilanes and Triethoxysilanes via Photoinitiated Thiol−ene Reaction between MPTMS/Alkenes or ATES/Thiols

Alkene	Trialkoxysilane		Conv. (%)[c]	Purity (%)[d]
		**11**	>99[a]	96
		**12**	>99[a,e]	96
		**13**	>99[a,f]	95[g]
		**14**	>99[b]	97
		**15**	>99[b]	97

[a] A dry 10 mL round-bottom was charged with 1 equiv of alkene (1.0−2.5 mmol), 1 equiv of MPTMS (1.0−2.5 mmol), and 2 mol % Irgacure 651, backfilled with argon, and irradiated for 24 h with a 15 W blacklight (λ_{max} = 368 nm). [b] A dry 10 mL round-bottom was charged with 1 equiv of thiol (2.0−2.5 mmol), 1 equiv of 3-mercaptopropyltriethoxysilane (2.0−2.5 mmol), and 2 mol % Irgacure 651, backfilled with argon, and irradiated for 24 h with a 15 W blacklight (λ_{max} = 368 nm) [c] Quantified by ^{1}H NMR. [d] Determined by gas chromatography/mass spectrometry (GC/MS) or ^{1}H NMR. [e] Dry $CHCl_3$ (0.5 mL) added to solubilize alkene. [f] Dry MeCN (0.7 mL) added to solubilize alkene. [g] Silane partly co-condensed to form some silane dimers due to water trapped in guanidinium salt.

Scheme 2. Functionalizing Magnetite SPNs with Thiol−ene Clicked Triethoxysilanes

When silanes are used as surface coating agents, it is often desirable to quantify the amount of silane that is bound to the surface. Doing so can be challenging, especially when the silanes lack a distinctive atom or functional group that can be identified spectroscopically. An advantage of the thiol−ene approach is that the product silanes have at least one sulfur atom in their structure, which facilitates their quantification by elemental analysis. To verify that all of the trialkoxysilanes in Table 1 could be used as surface coating agents, they were immobilized on magnetite superparamagnetic nanoparticles (SPNs) as shown in Scheme 2. Oleic acid coated SPNs were heated at 75 °C in toluene or dioxane for 24 h with 0.4 to 1 mmol of the silane. After particle isolation using a hand-held rare earth magnet and rinsing, the resulting constructs were characterized by sulfur elemental analysis and FT-IR spectroscopy. The silane ligand loadings determined by sulfur elemental analysis varied from 0.15 to 0.79 mmol silane/g particles (see Supporting Information). This loading variability is thought to be a consequence of differences in the silane solubilities, the varying degrees of intermolecular interactions between silanes and oleic acid coatings on SPNs, the sterics of the silane tail, and small differences in the amount of water in the solvents, as water catalyzes the silane coating process. All particles retained their superparamagnetic properties after surface modification (see Supporting Information).

In summary, we have shown that the thiol−ene reaction is a simple and efficient way to synthesize functional triethoxy- and trimethoxysilane surface coating agents. The methodology uses inexpensive MPTES, MPTMS, or ATES silane precursors, alkenes or silanes that are commercially available or easily prepared in one to two steps, a low mol % of photoinitiator, and a low power blacklight. The reactions proceed smoothly neat or with minimal solvent in standard borosilicate glassware to provide silanes in quantitative or near-quantitative yields and high purity. The reactions tolerate a good range of chemical functionalities, and a preliminary study shows that the reactions can be scaled-up easily without sacrificing product yield or purity. Our findings suggest that the thiol−ene methodology could be used to produce silanes at low costs on a pilot or even an industrial scale. The synthesized silanes were found to be active surface coating agents and were successfully immobilized on magnetite SPNs. This synthetic methodology will aid in the future development of new materials, interfaces, and devices by allowing easier access to complex and unique silane coating agents.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. Contains: a detailed materials list; experimental methods for silane and nanoparticle synthesis; cost estimates for silane syntheses; nanoparticle magnetic, elemental, and spectral information; and spectroscopic data for synthesized alkenes and silanes. This material is available free of charge via the Internet at http://pubs.acs.org.

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