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Orthogonal reactivity of thiols toward chlorovinylsilanes: selective thiol-ene chemistry



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Introduction

The search for efficient orthogonal reactions continues to be active, particularly in regard to bioconjugate chemistry¹⁻³ and the synthesis of complex molecules such as dendrimers.⁴⁻⁶ The ability to discriminate between reactive groups allows for selective bond formation via different reaction mechanisms, and can result in highly functional molecules. Many orthogonal reactions fall into the category of 'click' chemistry, due to their selective nature and high efficiency.⁷ Over the last decade, the thiol-ene reaction has emerged as a well-accepted and versatile click reaction.^{8,9} This transformation generally proceeds under mild conditions and gives products in quantitative or near quantitative yields that require little to no purification.⁹ As such, the use of the thiol-ene reaction in synthetic chemistry and materials science has gained significant momentum and is shown to be useful for a growing number of applications.¹⁰⁻¹² Despite this, there is still need for new and innovative applications of this highly efficient reaction.

As part of our growing efforts to take advantage of this valuable synthetic tool in organosilicon chemistry,^{13–15} we now report a new and highly chemoselective reaction in which chlorovinylsilanes react exclusively with thiol-terminated molecules via the thiol-ene reaction. Previous reports in the literature have shown that thiol-terminated compounds, which are inherently nucleophilic, react with chlorosilanes by displacing the chloride atom;^{16,17} however, in the wide breadth of the current study, this

ABSTRACT

A variety of new chlorosilanes were synthesized by the selective thiol-ene reactions of various thiols (ethanethiol, 1,2-ethanedithiol, benzenethiol, and tetrakis(2-sulfanylethyl)silicate) with chlorovinylsilanes (chlorodimethylvinylsilane, dichloromethylvinylsilane, and trichlorovinylsilane). No silylthioester products were observed. All products were obtained in quantitative or near quantitative yields and were characterized using multinuclear NMR (¹H, ¹³C, ²⁹Si) spectroscopy. The products required no further purification. An example is presented which highlights the potential use of these compounds for future applications.

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was not the case. Additionally, the selective thiol-ene reaction of chlorovinylsilanes results in new thioether-substituted chlorosilanes, which may be very useful in organic synthesis as well as organometallic and materials chemistry. Some applications of chlorosilanes include functional group protection, functionalizing silica surfaces and polymers, and polymer synthesis.^{18–21} Moreover, this work further complements our previous efforts in exploiting selective reactions in organosilicon chemistry.²²

Results and discussion

The selective reactions of thiols with chlorovinylsilanes proceeded under mild conditions and simply involved stirring the thiol, photoinitiator (PI, benzophenone, 1 mol % with respect to C=C), and the chlorovinylsilane under a UV light source. It should be noted that due to the reactivity of chlorosilanes toward moisture, care must be taken to minimize exposure to air. To accomplish this, syringes that were previously purged with nitrogen were used to deliver the chlorovinylsilanes to the reaction flasks. Furthermore, all reactions were conducted under nitrogen. In most cases, the reactions yielded products in quantitative or near quantitative yields without the use of solvent or excess reagents. The versatility of this reaction is demonstrated by the diverse range of thiols employed in a series of reactions (Tables 1–4).

In Series 1, various chlorovinylsilanes were reacted with ethanethiol (Table 1). The reactions were also performed in the aprotic solvent, ether, and similar results were obtained.

In a similar fashion, Series 2 was obtained by reacting 1,2ethanedithiol with 2 equiv of the appropriate chlorovinylsilane







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Table 1 Results from Series 1, reactions with ethanethiol

/	SH + SiMe _{3-n} Cl _n + v, 4h, N ₂ 1 mol% PI	SiMe _{3-n} Cl _n
n	Compound	Yield (%)
1	1a	98 (99) ^a
2	1b	95 (94) ^a
3	1c	100 (99) ^a

^a Yields obtained in ether.

Table 2

Results from Series 2, reactions with 1,2-ethanedithiol



n	Compound	Yield (%)
1 2	2a 2b	97 (91) ^a 99 (87) ^a
3	2c	97 (91) ^a

^a Yields obtained in ether.

Table 3

Results from Series 3, reactions with benzenethiol

$SH = SiMe_{3-n}Cl_n + SiMe_{3-n}Cl_n + SiMe_{3-n}Cl_n$				
n	Compound	Reaction time (h)	Yield (%)	
1	3a	8	97	
2	3b	14	98	
3	3c	10	97	

Table 4

Results from Series 4, reactions with a multifunctional thiol



n	Compound	Yield (%)
1	4a	100
2	4b	100
3	4c	100

(Table 2). This set of reactions could also be performed in ether; however, the yields were slightly improved when bulk conditions were employed.

To further demonstrate the scope of this newly discovered selectivity, an aromatic thiol was employed in Series 3 (Table 3).

During the studies conducted with benzenethiol, it was determined that significantly longer reaction times were required; however, this was not an unexpected result. The thiol-ene reaction proceeds by a free-radical mechanism, the rate of which is dependent on a number of factors including the chemical nature of the –ene and thiol as well as the stability of the resulting radical.^{9,10} The decreased rate for this set of reactions is attributed to

formation of a resonance stabilized benzenethiyl radical, which would be less reactive than its alkyl counterparts. Despite this, excellent yields were still obtained by simply increasing the reaction times. Performing the reactions shown in Table 3 in ether significantly increased the reaction times. For example, when the synthesis of **3a** was attempted in ether, the reaction was incomplete even after 8 h of stirring under the UV light source (see Fig. S48, Supporting information).

In the fourth and final study, this novel selectivity was applied to a multifunctional thiol that was previously synthesized in our laboratory (Table 4).²² The reactions with the multifunctional thiol were performed in ether. When attempted under bulk conditions, the reactions were incomplete after 4 h (see Fig. S49, Supporting information). The multifunctional thiol that was employed is more viscous than the thiols used in Series 1–3. Thus, it was necessary to use a solvent to improve the reagents' miscibility in order to obtain completely reacted products after 4 h.

The compounds shown in Tables 1-4 were characterized using multi-nuclear NMR spectroscopy (¹H, ¹³C, ²⁹Si) and all analyses demonstrated no need for further purification (see Figs. S3-38, Supporting information). In some cases, trace amounts of benzophenone can be seen in the ¹H and ¹³C NMR spectra, but the signals are easily distinguishable from the product peaks (see Figs. S1 and S2, Supporting information). Additionally, when performing the thiol-ene reaction there is a small percentage of thiol that adds to the interior carbon atom of the -ene, yielding what is known as the alpha product. The formation of the alpha product can easily be distinguished by a characteristic upfield doublet in the ¹H NMR spectrum, which corresponds to the methyl protons coupled to the methine proton. As previously mentioned, chlorosilanes are very reactive toward moisture so the products should be stored in a glove box. Attempts to obtain combustion analysis data on the products from Series 1-4 were unsuccessful, and were attributed to the reactive nature of chlorosilanes under normal atmospheric conditions.

To demonstrate that the compounds synthesized in Tables 1–4 could be used for further chemical transformations, compounds **2a–2c** were reacted with the appropriate amount of 2-mercaptoethanol (2, 4, or 6 equiv), producing Series 5, branched compounds **5a–5c**, through an orthogonal reaction we reported earlier.²² Table 5 summarizes these results.

Compounds **5a–5c** were obtained in good yield and characterized by multi-nuclear NMR spectroscopy (¹H, ¹³C, ²⁹Si) and combustion (C, H, N) analysis (see Figs. S39–S47, Supporting

information). Compounds **5b** and **5c** could serve as cores for hydrolytically sensitive dendrimers.

In all cases, the orthogonality of the reactions was evident. The chlorovinylsilanes reacted with the thiols exclusively via thiol-ene

Table 5Results from the synthesis of Series 5



n	Compound	Reaction conditions	Yield (%)
1	5a	THF, RT, 30 min, 55 °C, overnt.	99
2	5b	THF, RT, 30 min, 55 °C, overnt.	92
3	5c	THF/Et ₂ O (1:1), RT, 30 min, 55 °C, 60 h	83

reactions, and nucleophilic substitution of the chloride with thiol was not observed. This is likely due to the low rate of substitution in the absence of an acid acceptor, which is normally required for the formation of silyl thioethers from chlorosilanes and thiols.^{16,17}

Conclusion

In conclusion, the orthogonal reaction of chlorovinylsilanes with a variety of thiols via the thiol-ene reaction was demonstrated. The reactions proceeded under mild conditions and gave products in quantitative or near quantitative yields. In all cases, the Si-Cl bonds were preserved and could be used for further functionalization. Future efforts will focus on utilizing this selective reaction to obtain dendritic and hyperbranched molecules.

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Supplementary data

Supplementary data (experimental procedures, characterization data, and copies of ¹H, ¹³C, ²⁹Si NMR spectra) associated with this article can be found, in the online version, at http://dx.doi.org/ 10.1016/j.tetlet.2014.09.113.

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