

Chemical Reactions on Self-Assembled Monolayers

Self-assembled monolayers (SAMs) produce uniform homogeneous surfaces. The chemical groups presented to the outer surface can be controlled by simply choosing an alkanethiol with the appropriate head group for the assembly. Once formed, these surfaces provide unique substrates for further chemical reactions. By selecting an alkanethiol with a reactive head group one can use the resulting SAMs as substrates to generate any desired chemistry. Though surface reactions can often be different than their solution counterparts, most reaction chemistries can be done on SAMs. Table 1 shows a summary of several chemical reactions that can be carried out on SAMs. For a review of reactions on SAMs, refer to the article "Reactions on Monolayers: Organic Synthesis in Two Dimensions" by Sullivan and Huck.¹

Reactions on SAMs should be successful as long as the reaction conditions do not destroy the underlying monolayer and the functional groups are not sterically hindered. Steric hindrance may be alleviated by using a mixed monolayer with the reactive group placed on a longer chain thiol that spaces it above the underlying layer. Mixed monolayers may also be advantageous since they can be used to space out the reactive groups laterally and thereby reduce steric problems for further reactions or molecular immobilizations.

Using SAMs as substrates for chemical modification creates endless possibilities for surface modifications. For example, SAMs can be designed and modified to bind DNA, proteins, cells, and polymers. These modified SAM surfaces can then be used for applications limited only by the imagination.

Reactions/ Head groups	Generalized Reaction
	For more information about these and other reactions please see references 2 and 3 below.
Addition Alkene	$\text{S}-(\text{CH}_2)_n-\text{CH}=\text{CH}_2 \xrightarrow{\text{R}-\text{SH}} \begin{array}{l} \text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{CH}_2-\text{S}-\text{R} \\ \text{S}-(\text{CH}_2)_n-\text{CH}(\text{S}-\text{R})-\text{CH}_3 \end{array}$
Nucleophilic substitution Alkyl halides	$\text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{Br} \xrightarrow{\begin{array}{l} \text{a) R}-\text{OH} \\ \text{b) R}_1-\text{SH} \\ \text{c) R}_2-\text{NH}_2 \end{array}} \begin{array}{l} \text{a) } \text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{O}-\text{R} \\ \text{b) } \text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{S}-\text{R}_1 \\ \text{c) } \text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{NH}-\text{R}_2 \end{array}$
Disulfide formation Thiol	$\text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{SH} \xrightarrow{\text{HS}-\text{R}} \text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{S}-\text{S}-\text{R}$

Reactions/ Head groups	<p style="text-align: center;">Generalized Reaction</p> <p style="text-align: center;">For more information about these and other reactions please see references 2 and 3 below</p>
Condensation Hydroxide Sulfide Amine	<div style="display: flex; justify-content: space-around;"> <div style="text-align: center;"> <p>a) $\text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{OH}$</p> <p>b) $\text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{SH}$</p> <p>c) $\text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{NH}_2$</p> </div> <div style="text-align: center;"> $\xrightarrow[\text{Carbodiimide}]{\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{OH}}$ </div> <div style="text-align: center;"> <p>a) $\text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{O}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}$</p> <p>b) $\text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{S}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}$</p> <p>c) $\text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{NH}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}$</p> </div> </div>
Condensation Hydroxide Sulfide Amine	<div style="display: flex; justify-content: space-around;"> <div style="text-align: center;"> <p>a) $\text{R}-\text{OH}$</p> <p>b) R_1-SH</p> <p>c) R_2-NH_2</p> </div> <div style="text-align: center;"> $\xrightarrow[\text{Carbodiimide}]{\text{S}-(\text{CH}_2)_n-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{OH}}$ </div> <div style="text-align: center;"> <p>a) $\text{S}-(\text{CH}_2)_n-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\text{R}$</p> <p>b) $\text{S}-(\text{CH}_2)_n-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{S}-\text{R}_1$</p> <p>c) $\text{S}-(\text{CH}_2)_n-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}-\text{R}_2$</p> </div> </div>
CDI Coupling	<div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;"> <p>$\text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{NH}_2$</p> </div> <div style="text-align: center;"> $\xrightarrow{\text{CDI}}$ </div> <div style="text-align: center;"> <p>$\text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{NH}-\overset{\text{O}}{\parallel}{\text{C}}-\text{N}(\text{CH}_2)_2\text{CH}$</p> </div> </div> <div style="display: flex; justify-content: space-around; align-items: center; margin-top: 10px;"> <div style="text-align: center;"> <p>$\text{S}-(\text{CH}_2)_n-\text{CH}_2-\text{NH}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}-\text{R}$</p> </div> <div style="text-align: center;"> $\xleftarrow{\text{R}-\text{NH}_2}$ </div> </div>
Anhydride formation/ Carboxylic acids	<p>Step 1:</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;"> <p>$\text{S}-(\text{CH}_2)_n-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{OH}$</p> </div> <div style="text-align: center;"> \longrightarrow </div> <div style="text-align: center;"> <p>$\text{S}-(\text{CH}_2)_n-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2-(\text{CH}_2)_n-\text{S}$</p> </div> </div> <p>Step 2:</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;"> <p>$\text{S}-(\text{CH}_2)_n-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2-(\text{CH}_2)_n-\text{S}$</p> </div> <div style="text-align: center;"> $\xrightarrow{\text{R}_1-\text{NH}_2}$ </div> <div style="text-align: center;"> <p>$\text{S}-(\text{CH}_2)_n-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{OH}$</p> <p>$\text{S}-(\text{CH}_2)_n-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}-\text{R}_1$</p> </div> </div>

References:

- Sullivan, T. P.; Huck, W. T. S., *Eur. J. Org. Chem.* **2003**, 17-29.
- Hermanson, G. T., *Bioconjugate Techniques*. Academic Press: San Diego, 1996.
- Larock, R. C., *Comprehensive Organic Transformations A Guide to Functional Group Preparations Second Edition*. Wiley-VCH: New York, 1999.