A DETAILED KINETIC STUDY OF THE THIOL-MICHAEL ADDITION REACTION: AN EFFICIENT TOOL FOR THE ASSEMBLY OF SEQUENCE-DEFINED POLYMERS

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The thiol-Michael addition reaction is a highly efficient reaction and is widely referred to as a "click" reaction because of its simplicity and atom efficiency. It has found use in a wide variety of applications, ranging from small molecule synthesis to functionalization of biological systems.[1] The Alabi lab recently developed orthogonal N-allylacrylamide building blocks that employ the thiol-Michael addition for the de novo assembly of sequence-defined oligomers.[2,3] These novel oligomers are being used as membrane disruptive agents, protease resistant linkages, antibacterial agents and drug delivery scaffolds.

As a result of the widespread use of the thiol-Michael addition, there is broad interest in understanding the reaction mechanism as it pertains to specific applications. Several in-depth studies examining the base and nucleophile catalyzed thiol-Michael reaction have been performed and an accepted reaction mechanism has been developed.[4-7] In this project, we will adopt this mechanism and develop a robust assay that will be used to measure the kinetics of the thiol-Michael addition under the conditions used to assemble our sequence-defined oligomers. Specifically, we will probe the effect of reaction temperature, catalyst type, catalyst concentration, solvent and substrate on the reaction rate and use this information to appropriately design and improve the conditions used for the assembly of sequence-defined oligomers.

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