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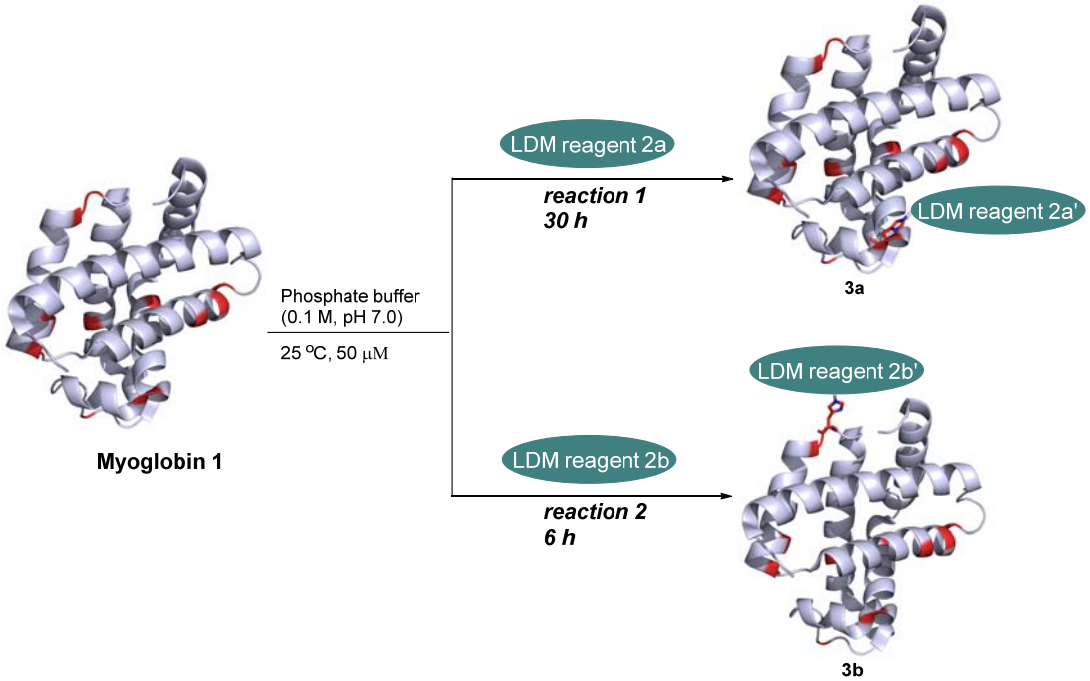
Site-selective histidine modification of native proteins

S. R. Adusumalli, D. Rawale, V. Rai*

Organic and Bioconjugate Chemistry Laboratory (OBCL), Department of Chemistry
Indian Institute of Science Education and Research Bhopal
Email: vrai@iiserb.ac.in

Abstract: The interest in site-selective labeling of protein has emerged from the necessity to understand and regulate their structure and function. Initially, the site-selectivity was driven by incorporation of unnatural amino acid, a fragment recognized by enzymes and semi-synthetic methods.[1] However, these methods don't extend to the native or endogenous proteins.[2] The site-selective identification of a backbone residue on natural proteins are achieved with few restricted methodologies.[3] In this perspective, our group has developed a chemical technology that enables site-selective labeling of native proteins and antibodies.[4] The success of the technology involves three consecutive steps. The first step of the reaction sequence places the reversible "chemical linchpins" globally on multiple accessible residues. These linchpins have the capability to drive single-site labeling of proteins. Next, the linchpin detaches within physiological conditions and capacitates the installation of various tags, protein stapling, and protein-protein conjugation. The site of modification is regulated with the modular reagent where discrete labels are attached at distinct sites.



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