Supramolecular Guided Site Selective Functionalization of Peptides and Proteins

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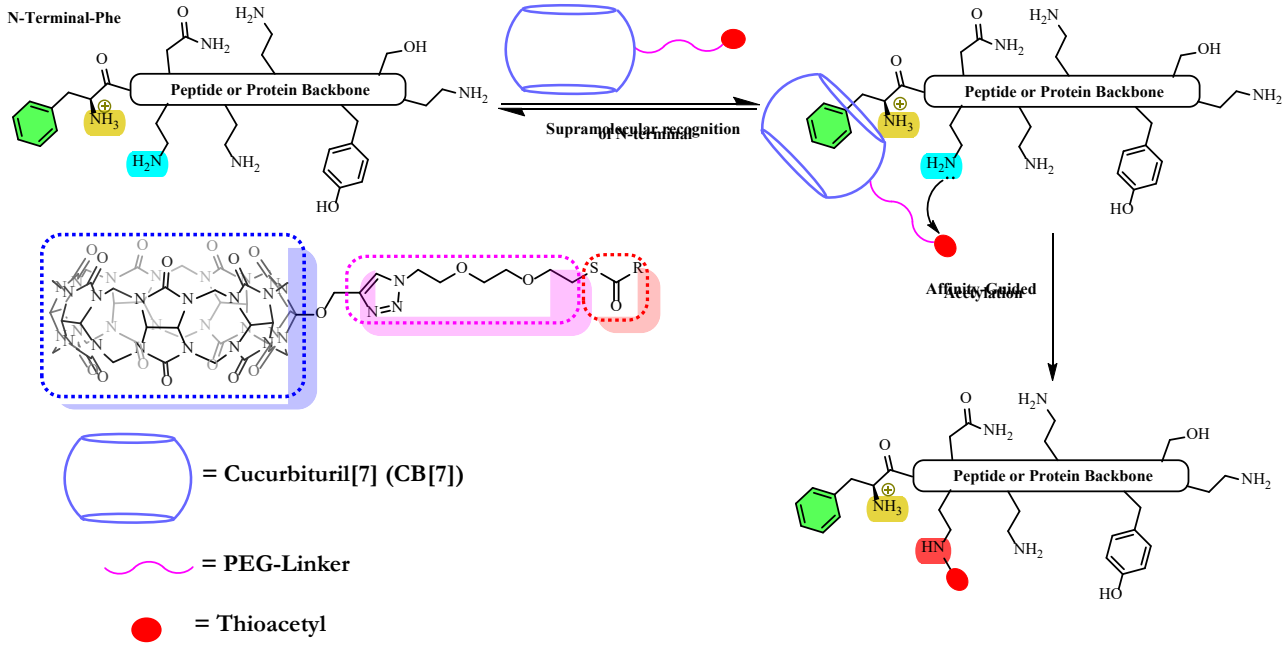
Achieving site selective functionalization on peptides and proteins is a fundamental difficult challenge, due to the presence of multiple reactive sites. In this study, we propose a supramolecular approach to overcome this challenge. Cucurbituril[7] (CB[7]) is known to selectively bind peptides and proteins containing N-terminal phenyl alanine. By covalently attaching thioacetal motifs to CB[7], we envision to direct the functionalization of lysine residues in proximity of the N-terminal and thereby obtain site selective functionalization. Synthesis of monofunctionalized CB[7] covalently attached to thioacetal motifs was achieved. Acetylation experiments on model peptides revealed the optimal pH range for the site selective acetylation. Under the optimal conditions, selectivity towards lysine closest to the N-terminal was observed indication utility of our supramolecular approach.



1. A. Urbach, *J. Am. Chem. Soc.* **2011**, 133, 23, 8810-8813.