Transition Metals in Peptide and Protein Synthesis

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Chemical Protein synthesis offers great opportunities to synthesize uniquely modified proteins with high homogeneity and workable quantities. The field relies on the synthesis of peptide fragments and the ligation of these peptides in their unprotected forms employing different ligation strategies such as native chemical ligation (NCL). We have recently reported that transition metals such as palladium and gold complexes can be used remove multiple Cys protecting groups within minutes in a fully aqueous medium, which could be coupled in-situ with NCL to provide excellent yields of the desired product. We have also demonstrated unprecedented gold mediated depropargylation from an amide bond to facilitate the synthesis of difficult peptides and proteins. We further showed the use of the propargyl group to mediate amide bond cleavage at different sites. This chemistry was further extended for the cyclization of a wide range of peptides bearing a propargyl group. Furthermore, we extend our chemistry for the removal of protecting groups from Cys residues for the rapid and one-pot disulfide bond formation in various bioactive peptides. Finally, using this chemistry we developed a strategy for the cellular delivery and on demand activation of synthetic proteins.

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