



Traceless Staudinger Ligation for the Synthesis of Peptides and Proteins in Water

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WARF: P08350US02

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing methods and reagents for the formation of an amide bond in an aqueous solution, which is useful in the synthesis of peptides and proteins in biological systems.

Overview

UW–Madison researchers previously developed a method of using traceless Staudinger ligation to chemically synthesize proteins (see WARF reference number P00315US). This method is based on the Staudinger reduction, in which a phosphine reduces an azide via an iminophosphorane intermediate. It has been used in the assembly of proteins and for site-specific immobilization of peptides and proteins to a surface.

The phosphinomethanethiol reagents used for this reaction allow high yields but are not soluble in water, limiting their use in biological environments. All traceless Staudinger ligations have been performed in organic solvents or organic/aqueous mixtures. The ability to perform traceless Staudinger ligation in water could expand the utility of the reaction.

The Invention

UW–Madison researchers have discovered that the traceless Staudinger ligation can be achieved in water with a water-soluble reagent such as bis(*p*-dimethylaminoethylphenyl)phosphinomethanethiol. This discovery enables the formation of an amide bond in a physiological setting. It integrates traceless Staudinger ligation with expressed protein ligation, thus extending the reach of modern protein chemistry.

Applications

- Provides a series of water-soluble phosphinothiol reagents for the Staudinger ligation
- Allows protein synthesis in a biological system
- Also useful for immobilizing a molecule on a surface in an aqueous system

Key Benefits

- Enables the formation of an amide bond in a physiological setting
- Capable of mediating the ligation of equimolar substrates in water with yields greater than 90 percent
- Does not require a cysteine residue, in contrast to the native chemical ligation method of preparing proteins
- Traceless—leaves no residual atoms in the ligated peptide product

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Related Technologies

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- [WARF reference number P00315US describes a method of using traceless Staudinger ligation for the total chemical synthesis of proteins.](#)

Publications

- Tam A., Soellner M.B. and Raines R.T. 2007. Water-Soluble Phosphinothiols for Traceless Staudinger Ligation and Integration with Expressed Protein Ligation. J. Am. Chem. Soc. 129, 11421–11430.
- Tam A. and Raines R.T. 2009. Coulombic Effects on the Traceless Staudinger Ligation in Water. Bioorg. Med. Chem. 17, 1055-1063.

Tech Fields

- [Materials & Chemicals : Synthesis](#)
- [Research Tools : Synthesis & purification](#)

For current licensing status, please contact Jennifer Gottwald at jennifer@warf.org or 608-960-9854

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