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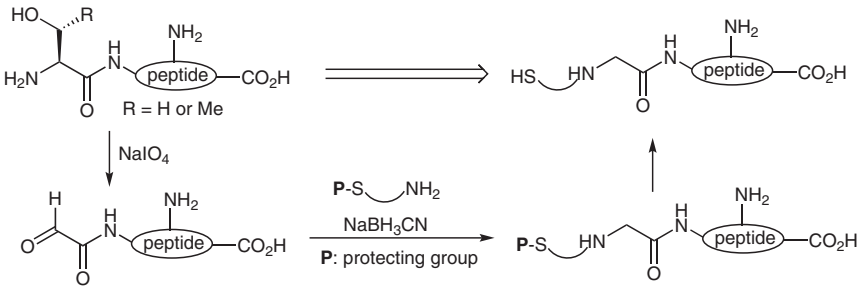
Peptide Bond Formation Mediated by 4,5-Dimethoxy-2-mercaptobenzylamine after Periodate Oxidation of the N-Terminal Serine Residue

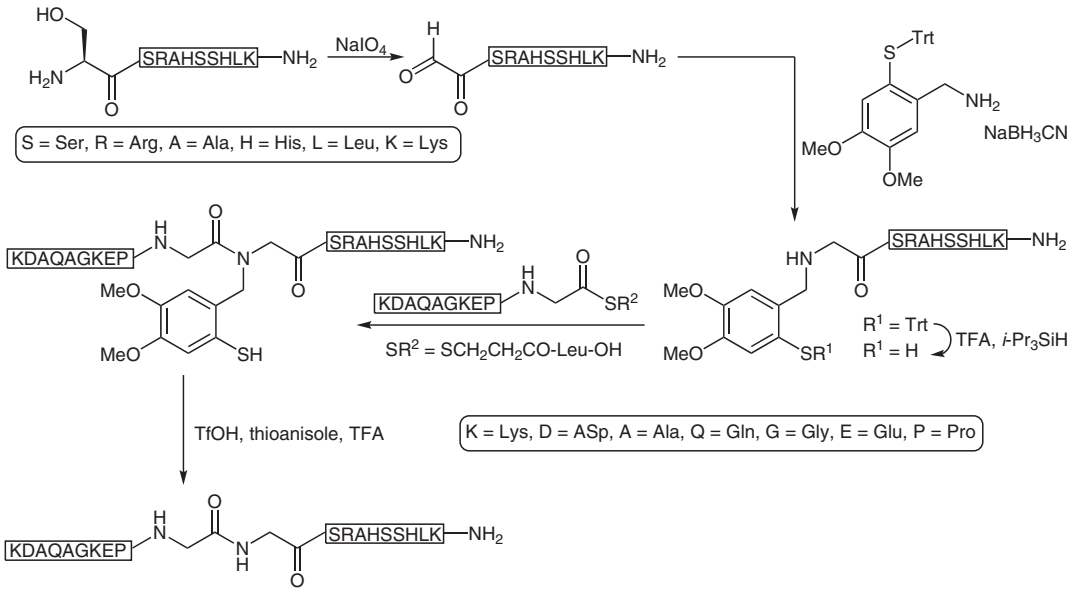
Org. Lett. **2001**, *3*, 1403–1405.

Synthesis of Peptides by Using Recombinant Proteins

Synthesis of thiol-linker-attached peptides as C-terminal building blocks from nonprotected peptides:



Peptide bond formation mediated by 4,5-dimethoxy-2-mercaptobenzylamine:



Significance: In 2001, Aimoto and co-workers reported an approach for the synthesis of polypeptides by using recombinant proteins in combination with peptide thioesters. A thiol-linker-attached peptide for condensation with the peptide thioester was successfully synthesized from a nonprotected peptide through periodate oxidation of an N-terminal serine residue, followed by reductive amination with 4,5-dimethoxy-2-mercaptobenzylamine (Dmmb-NH_2).

Comment: A *N*-2-mercaptobenzyl group on the backbone of a peptide is too stable under acidic conditions. The introduction of two methoxy groups on the benzene ring permitted the Dmmb group to be removed, after condensation, by treatment with 1 M TfOH in TFA. Instead of periodate oxidation of serine and threonine, transamination of N-terminal amino groups could also be used in principle, although the stereochemistry resulting from the reductive amination should be controlled.

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Category

Peptide Chemistry

Key words

nonprotected peptides

thiol linkers

selective oxidation

peptide thioesters

dimethoxymercapto-benzylamine