

Pseudoproline Dipeptides for Smart Peptide Synthesis

Novabiochem® is the leading provider of state-of-the-art and innovative building blocks, resins and solid-supported reagents for peptide-, protein- and high-throughput chemical synthesis. A special focus is given on derivatives for the synthesis of long or difficult peptides. Therefore Merck offers for example Novabiochem isoacyl dipeptides, Hmb/Dmb dipeptides and pseudoproline dipeptides!

According to one of our key customers, pseudoproline dipeptides are undoubtedly the most powerful tools described to date for enhancing synthetic efficiency in Fmoc solid phase peptide synthesis.

The routine use of pseudoproline dipeptides has been found to:

- help avoid costly and unnecessary repeat syntheses of failed sequences;
- increase purity of crude products;
- simplify HPLC purification;
- increase yield of crude and purified products;
- enable synthesis to be carried out on a lower scale.

Pseudoproline dipeptides consist of a dipeptide in which the Ser or Thr residue has been reversibly protected as proline-like TFA-labile oxazolidine. The insertion of a pseudoproline dipeptide into a sequence disrupts the formation of the secondary structures thought responsible for problems during peptide assembly. This leads to better and more predictable acylation and deprotection kinetics.

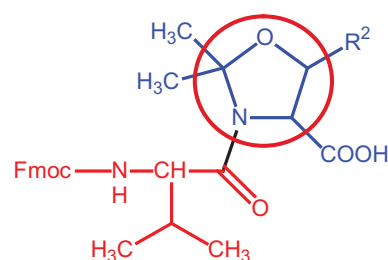


Fig. 1: General structure of pseudoproline dipeptide; showing the example of Fmoc-Val-Ser/Thr($\Psi^{\text{Me,Me}}\text{pro}$)-OH; Ser: $\text{R}^2=\text{H}$; Thr: $\text{R}^2=\text{CH}_3$

The most dramatic results are seen in the preparation of highly aggregated sequences, where 10-fold increases in product yield have been achieved from insertion of a single pseudoproline. However, the enhanced and more uniform reaction rates also benefit routine synthesis, providing improved yields, purities and solubilities of crude products, and easier HPLC purification with higher product return. For longer peptides, the incorporation of several pseudoprolines at regular intervals throughout the sequence has been found to be particularly effective. Pseudoproline dipeptides are extremely simple to use. They are introduced into the peptide sequence using standard coupling methods, substituting any Aaa-Ser or Aaa-Thr dipeptide.

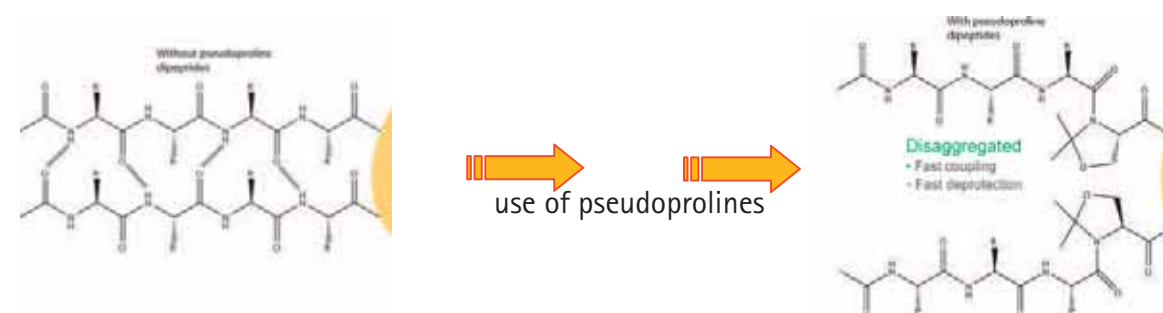


Figure 2: Mode of action of pseudoproline dipeptides during Fmoc-SPPS.

In a model study to explore how the presence of pseudoproline dipeptides can influence the outcome of Fmoc SPPS, a model peptide 1 was prepared under 12 different sets of conditions, varying the coupling method, solid support and position of the pseudoproline dipeptide.



Figure 2: Sequence of peptide 1, highlighting the possible insertion point for pseudoproline dipeptide.

In this particular sequence, only the use of a pseudoproline dipeptide had a marked influence on the purity of the final product. The exact position of the pseudoproline dipeptide had little effect on the outcome of the synthesis, provided it was no more than six residues before the onset of coupling and deprotection difficulties [Novabiochem Innovations 4/04].

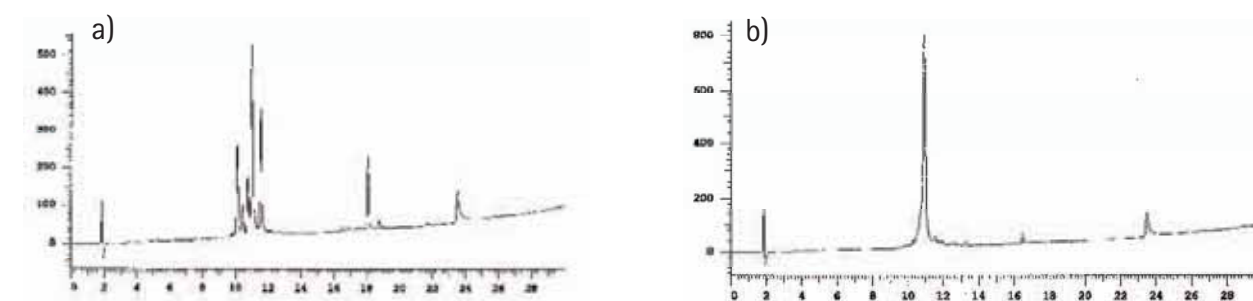


Figure 3: Crude HPLC profiles of peptide 1 obtained from a) the synthesis using standard Fmoc-amino acid derivatives and b) using one pseudoproline-dipeptide. Coupling conditions: Wang resin, using 3.3 eq. using HCTU/DIPEA (1:1.5), Coupling time: 30 min

Merck Biosciences offers more than 20 Novabiochem pseudoproline dipeptides for smart peptide synthesis. We also offer synthesis notes for tips and tricks to use these products and all you need for peptide synthesis from resins to reagents.

Novabiochem®

Novabiochem offers solutions for peptide and oligonucleotide synthesis.

- Amino acid building blocks
- Pseudoproline dipeptides
- Dmb-/Hmb dipeptides
- Isoacyl dipeptides
- Phosphoamino acids
- Labeling reagents
- Ligation reagents
- Pre-filled cartridges
- Condensation reagents and linkers
- Resins for solid phase synthesis
- Synthesis notes
- Reagents for oligonucleotide synthesis

For further information on products and applications and for ordering:
www.novabiochem.com

Orders
service@novabiochem.com

Technical Support
technical@novabiochem.com

Novabiochem®
your number one provider for really smart peptide synthesis tools!