#### Category

**Peptide Chemistry** 

### Key words

lanthionines

dehydroalanine phenylselenocysteine oxidative elimination



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# **Synthesis of Dehydroamino Acid Containing Peptides**

#### Chemoselective oxidation of peptides:

#### Synthesis of dehydropeptides:

$$\begin{array}{c} \text{Peptide-} \textcolor{red}{\textbf{U(Ph)-Peptide}} & \textcolor{red}{\color{blue}{\textbf{NaIO_4}}} \textcolor{blue}{(4 \; equiv)} \\ \hline \textcolor{red}{\color{blue}{\textbf{NaIO_4}}} \textcolor{blue}{(4 \; equiv)} \\ \hline \textcolor{red}{\color{blue}{\textbf{NeOH}}} \text{ or } \textcolor{blue}{\textbf{H}_2O-MeOH} \textcolor{blue}{(1-6 \; mM)} \end{array} \\ \begin{array}{rcl} \text{Peptide-Dha-Peptide} \\ \hline \textcolor{blue}{\color{blue}{\textbf{25}}} \circ \textbf{C} \\ \hline \\ \text{Fmoc-GLPDhaVIA} & \textbf{Fmoc-ISVDhaRSTS} & \textbf{Ac-GLPDhaVIA} & \textbf{Ac-ISVDhaRSTS} \\ \hline \textcolor{blue}{\textbf{72\%}} \text{ yield}^b & \textcolor{blue}{\textbf{82\%}} \text{ yield}^a & \textcolor{blue}{\textbf{82\%}} \text{ yield}^a \\ \hline \textcolor{blue}{\color{blue}{\textbf{*(H_2O_2} \; as \; oxidant)}} \\ \hline \textbf{Ac-GGC(S$_{\it f}$Bu)PDhaVIA} & \textbf{LDhaPGC(Trt)VG} & \textcolor{blue}{\color{blue}{\textbf{IDha}AECKI]_2}} & \textbf{RIADhaIALC(S$_{\it f}$Bu)K} \\ \hline \textbf{84\%} \text{ yield}^b & \textcolor{blue}{\color{blue}{\textbf{80\%}}} \text{ yield}^b & 33\%} \text{ yield}^b & 72\% \text{ yield}^b \\ \hline \end{array}$$

U(Ph)-(Se)-phenyl selenocysteine; Dha-dehydroalanine; G-Gly; L-Leu; P-Pro; V-Val; I-Ile; A- Ala; S-Ser; R-Arg, T-Thr; C- Cys; E-Glu; K-Lys; <sup>a</sup> MeOH; <sup>b</sup> H<sub>2</sub>O-MeOH

## Synthesis of lanthionines:

LeuDhaProGlyCys(Trt)ValGly

1. TFA
2. pH 8
56% yield for 2 steps

Pro
Gly
NH
NH
Leu
Gly
Val

[LeuDhaAlaAsnCysLysIle]<sub>2</sub>

1. TCEP
2. pH 8
75% yield for 2 steps

**Significance:** The  $\alpha$ , $\beta$ -unsaturated amino acids dehydroalanine and dehydrobutyrine are present in various natural products and polypeptides. The authors have developed a method for the chemoselective synthesis of dehydroalanine (dha) residues by oxidative elimination of nonnatural amino acids.

**Comment:** Chemoselective, site-specific incorporation of dha residues into peptides was achieved by the oxidative elimination of *Se*-phenylselenocysteine. Furthermore, cyclic lanthionines were synthesized by intramolecular Michael addition of cysteine onto the Dha residues.

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