

## Silicon-containing amino acids and applications in bioactive peptides: an overview

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The need to replace natural amino acids in peptides with non-proteinogenic counterparts to obtain new medicinal agents, exhibiting better binding to specific receptors and more potent inhibition of target enzymes, has stimulated a great deal of innovation on synthetic methods. In this presentation, we will describe the synthesis of unnatural amino acids containing a silicon atom<sup>[1]</sup>, TMS-Ala<sup>[2]</sup>, Sip<sup>[3]</sup> and tetrasubstituted amino acids<sup>[4]</sup>. These new amino acids should increase the bioavailability of related peptides, considering their presumed resistance to proteolytic enzymatic degradation and the high lipophilicity of silyl groups.



**Figure 1.** Structure of silicon-containing amino acids

Here we report the incorporation of these new surrogates in biologically active peptides<sup>[5]</sup> and the evaluation of the activity of the resulting analogue peptides, with a focus on neurotensin<sup>[6]</sup>.

- [1] Reviews: (a) M. Mortensen, *Chem. Soc. Rev.*, **2009**, 38, 1002-1010. (b) E. Rémond, *Chem. Rev.*, **2016**, 116, 11654-11684. (c) F. Cavalier, *Topics in Heterocyclic Chemistry*, **2017**, 48 : pp 27-50.
- [2] (a) D. Marchand, *Eur. J. Org. Chem.* **2008**, 3107-3112. (b) A. René, *Amino Acids*, **2013**, 45 (2), 301-307.
- [3] (a) B. Vivet, *Eur. J. Org. Chem.*, **2000**, 807-811. (b) B. Vivet, *Acta Cryst.*, **2000**, C56, 1452-1454. (c) F. Cavalier, *J. Am. Chem. Soc.*, **2002**, 124 (12), 2917-2923. (d) V.I. Handmann, *Z Naturforsch, B: Chem Sci*, **2000**, 55, 133-138. (e) C. Martin, *Amino Acids*, **2012**, 43 (2), 649-655. (f) C. Martin, *Chem. Eur. J.*, **2014**, 20, 14240-14244.
- [4] (a) F. Cavalier, *Chem. Biodiv.* **2008**, 1279-1287. (b) R. Fanelli, *Org. Lett.*, **2015**, 17, 4498-4501. (c) R. Fanelli, *Org. Lett.*, **2017**, 2937-2940.
- [5] (a) F. Cavalier, *J. Pept. Res.* **2004**, 63, 290-296. (b) S. Pujals, *J. Am. Chem. Soc.* **2006**, 128, 8479-8483. (c) G. A. Dalkas, *J. Peptide Sci.* **2010**, 16 (2), 61-97.
- [6] (a) D. Hapău, *Eur. J. Org. Chem.*, **2016**, 1017-1024. (b) R. Fanelli, *J. Med. Chem.*, **2015**, 58, 7785-7795.