

Ion-assisted synthesis of cyclic homopeptidesNikolina Vidović¹, Davide Riva¹, Gordana Horvat², Nikola Cindro², Vladislav Tomišić² and Giovanna Speranza¹¹Università degli Studi di Milano, Italy²University of Zagreb, Croatia

In the recent years, cyclic peptides have attracted attention since they find applications in many fields from drug discovery to nanomaterials. These compounds are difficult to prepare due to the fact that the activated peptide must adopt an entropically disfavoured conformation before forming the desired product. The most important factor for successful peptide macrocyclization is ring size. Peptides that contain less than seven aminoacids are troublesome to cyclize. In this work, we describe the synthesis of small cyclic homopeptides containing 4-6 aminoacids. Cyclic peptides are also known as versatile ion-binders but their binding affinities are often reduced by the inadequate orientation of amide functional groups. To overcome these problems, cyclopeptides will be conjugated to molecules with rigid geometry, such as calixarenes. Cyclic homolysine and cyclic homoserine will be bound to calixarenes exploiting functional groups on peptide's side chain. Influence of the length of side chains on affinities of these conjugates towards different anions will be investigated. Linear precursors were synthesized using standard solution phase peptide synthesis and HOBt, HBTU as coupling reagents. A three-dimensional orthogonal protection scheme was required to build the linear peptides, to deprotect the N- and C-termini and to cyclize them in a head-to-tail fashion. To promote the cyclization, different ions were used depending on the size of the desired cyclic peptide. These ions force the linear peptide to form a strong turn structure and to bring the N- and C-termini closer, allowing cyclization to occur.

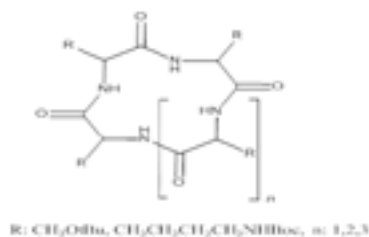


Figure: Structure of cyclic homopeptides.

Recent Publications

1. C. J. White, A. K. Yudin (2011) *Nature Chemistry* 3: 509-524.
2. U. Schmidt, J. Langner (1997) *J. Pept. Res.* 49: 67-73.
3. V. M. Mirsky, A. Yatsimirsky (2011) *Artificial Receptors for Chemical Sensors*, Wiley, Weinheim.
4. N. Bregovic, N. Cindro, L. Frkanec, V. Tomisic (2016) *Supramol. Chem.* 28: 608-615.
5. Y.-H. Ye, X.-M. Gao, M. Liu, Y.-C. Tang, G.-L. Tian (2003) *Letts. Pept. Sci.* 10: 571-579.

Biography

Nikolina Vidović completed her Master's in Chemistry in 2014 from the University of Zagreb, Croatia. Currently, she is a PhD student in Industrial Chemistry at the University of Milan, Italy. Her research activity is mainly focused on the preparation and characterization of cyclic peptides and study of their binding properties toward different ions.

nikolina.vidovic@unimi.it