

22.05.2020

+++ News Ticker Science #40 +++ Cyclic peptides +++

Organic & Biomolecular Chemistry

COMMUNICATION

Check for updates

Insights into the secondary structures of lactam *N*-substituted stapled peptides†

Adrian V. Vasco,¹ C. G. Moya,² Sören Gröger,³ Wolfgang Brandt,⁴ Jochen Balbach,⁵ Carlos S. Pérez,¹ Ludwig A. Wessjohann,¹ and D. G. Rivera¹

Received 10th April 2020
Accepted 10th April 2020
DOI: 10.1039/D0OB00767F

The Royal Society of Chemistry

View Article Online

† Stapled peptides derived from the Ugi macrocyclization comprise a special class of cyclopeptides with an *N*-substituted lactam bridge cross-linking two amino acid side chains. Herein we report a comprehensive analysis of the structural factors influencing the secondary structure of these cyclic peptides in solution. We focus on the *s-cis/s-trans* isomerism and the effect of *N*-functionalization on the conformation.

† Stapled peptides in which the amino acid side-chains have been esterified using methoxycarbonyl (MOC) have recently emerged as a unique class of functionalized cyclic peptides. With such as the *N*-methyl-*s-cis* and *s-trans* isomers have proven to be interesting in understanding conformational isomerism by reflecting amino acid side-chains, while at the same time incorporating additional non-covalent fragments. Other side-chains have been also employed to macrocyclize peptides by their termini, leading to increasing conformational diversity.

† Ugi-stapled peptides are compounds in which amino (Zn) and carboxylic acid (Zn) and the corresponding side chains are linked by the Ugi reaction, with the subsequent formation of a lactam bridge. This method has enabled the rapid preparation of stapled peptides with hydroxyl, methyl, and thiol at the lactam bridge.† Compared with traditional lactam-bridged stapled peptides, as those reported by Hübner and co-workers,† the *N*-substituted Ugi-derived lactam bridge is a source of functional and conformational diversity. This latter diversity originates from the influence of the

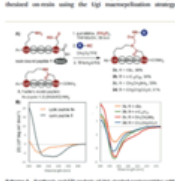


Figure 1 Chemical structures of stapled peptides and their corresponding NMR spectra. The top part shows the chemical structures of various stapled peptides with different side chains (R1, R2) and their corresponding NMR spectra. The bottom part shows two graphs: one for the *s-cis/s-trans* isomerism and another for the effect of *N*-functionalization on the conformation.

Insights into the secondary structures of lactam *N*-substituted stapled peptides

IPB chemists together with collaborators from the MLU Halle and the University of Havana have taken a closer look at features of a special class of cyclopeptides. Their results were recently published in *Organic & Biomolecular Chemistry*. This special class of cyclopeptides forms when generating stapled peptides through Ugi macrocyclization. They exhibit an *N*-substituted lactam bridge cross-linking two amino acid side chains. The researchers report a comprehensive analysis of the structural factors influencing the secondary structure of these cyclic peptides in solution. Furthermore, the authors reveal novel insights into the *s-cis/s-trans* isomerism and the effect of *N*-functionalization on the conformation.

Publication:

A. V. Vasco, C. G. Moya, S. Gröger, W. Brandt, J. Balbach, C. S. Pérez, L. A. Wessjohann and D. G. Rivera. Insights into the secondary structures of lactam *N*-substituted stapled peptides, *Org Biomol Chem*, 2020, Advance Article, DOI: 10.1039/D0OB00767F