Axis 4

Structural chemistry and biology

Lasso Peptides

Lasso peptides are bioactive peptides produced by bacteria that present a mechanically interlocked structure where the C-terminal tail of the peptide is threaded through and trapped within an N-terminal macrocycle. They exhibit different biological activities (enzyme inhibition, receptor antagonism, antibacterial and/or anti-HIV activities), and the lasso topology is a pre-requisite for the activities reported. Therefore, discovering new lasso peptides and using these peptides in drug design require to unambiguously characterize the lasso topology and differentiate the lasso from the molecules named branched-cyclic where the C-terminal tail is unthreaded.

We have shown that lasso peptides and their branched-cyclic topoisomers have different profiles in ion mobility mass spectrometry when observed as highly charged protonated molecules (**Figure 1**).

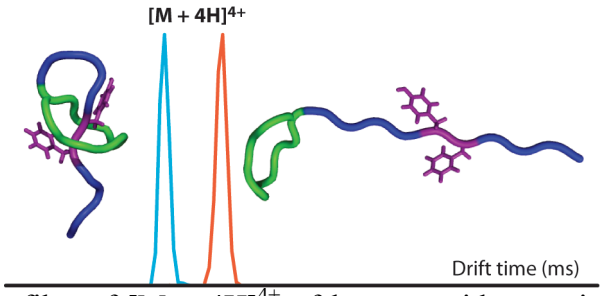

Figure 1. Drift time profiles of $[M + 4H]^{4+}$ of lasso peptide astexin-1 (blue) and its cyclic branched topoisomer (red) Jeanne Dit Fouque, K.; Afonso, C.; Zirah, S.; Hegemann, J. D.; Zimmermann, M.; Marahiel, M. A.; Rebuffat, S.; Lavanant, H. Anal. Chem. **2015** 87 (2), 1166–1172.

Real time monitoring of organic synthesis reactions

Real-time monitoring of reactions can be studied by ESI-IM-MS: transient intermediates can be evidenced. Their structures can be elucidated by accurate mass measurements and tandem mass spectrometry (MS/MS). Comparison and matching of experimental and calculated CCS help structural elucidation of intermediates and rationalize experimental data.

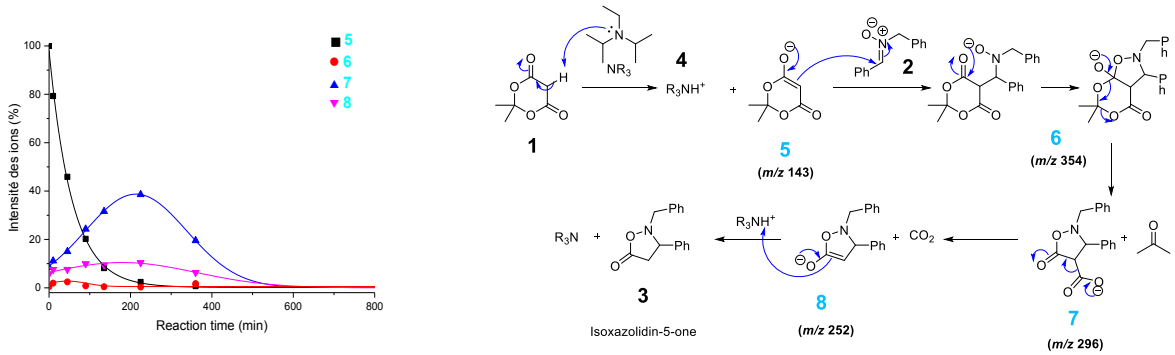

Figure 2. ESI-MS monitoring of isoxazolidinone organocatalytic synthesis and associated mechanism