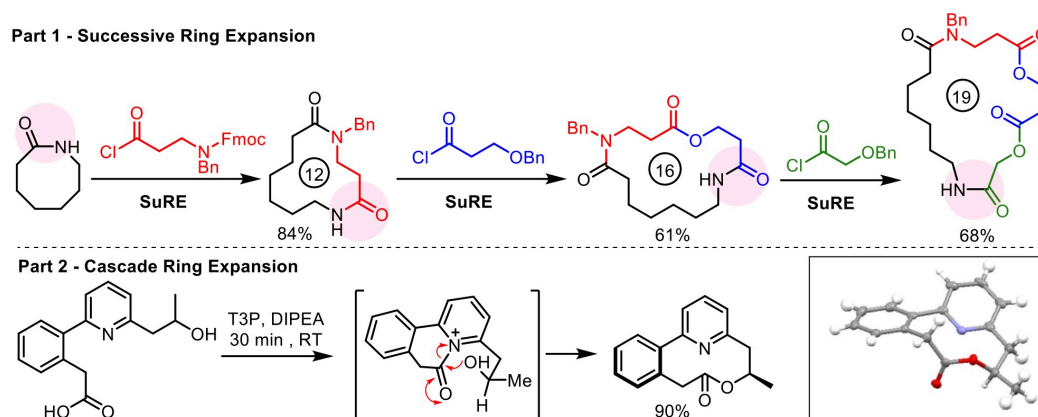


Ring Expansion Approaches for the Synthesis of Functionalised Macrocycles

W. P. Unsworth¹

¹University of York, York, YO10 5DD (UK), e-mail: william.unsworth@york.ac.uk

This talk concerns the development of two ring enlargement new way to construct functionalised macrocycles (12+ membered rings) and medium-sized rings (8–11-membered). These ring systems are usually difficult to make, with one of the key challenges being the effective control of intra- and intermolecular reaction during end-to-end cyclisation.^[1,2] Both approaches I will discuss in this talk are based on strategies by which the difficult end-to-end cyclisation step can be completely avoided. First, I will describe an iterative ring enlargement approach known as ‘Successive Ring Expansion’ (SuRE).^[3–6] SuRE works by enabling the controlled insertion of amino acid and hydroxy acid fragments into ring enlarged products via a telescoped acylation/rearrangement reaction sequence. Background, methods development, substrate scope/limitations, the synthesis of compound libraries for biological evaluation^[4] and DFT calculations^[7] will all be covered. Second, a new ring expansion cascade strategy^[8,9] will be introduced, that enables the atroposelective synthesis of medium sized rings directly from linear precursors.^[10]



[1] Ring Enlargement in Organic Chemistry, M. Hesse, **1991**, VCH

[2] W. P. Unsworth, J. R. Donald, *Chem. Eur. J.* **2017**, *23*, 8780–8799.

[3] C. Kitsiou, J. J. Hindes, P. l’Anson, P. Jackson, T. C. Wilson, E. K. Daly, H. R. Felstead, P. Hearnshaw, W. P. Unsworth, *Angew. Chem. Int. Ed.* **2015**, *54*, 15794–15798.

[4] L. G. Baud, M. A. Manning, H. L. Arkless, T. C. Stephens, W. P. Unsworth, *Chem. Eur. J.* **2017**, *23*, 2225–2230.

[5] T. C. Stephens, M. Lodi, A. Steer, Y. Lin, M. Gill, W. P. Unsworth, *Chem. Eur. J.* **2017**, *23*, 13314–13318.

[6] T. C. Stephens, A. Lawer, T. French, W. P. Unsworth, *Chem. Eur. J.* **2018**, *24*, 13947–13953.

[7] A. Lawer, R. G. Epton, T. C. Stephens, K. Y. Palate, M. Lodi, E. Marotte, K. J. Lamb, J. K. Sangha, J. Lynam, W. P. Unsworth, *Chem. Eur. J.* **2020**, doi: 10.1002/chem.202002164.

[8] T. C. Stephens, W. P. Unsworth, *Synlett* **2020**, *31*, 133–146.

[9] A. K. Clarke, W. P. Unsworth, *Chem. Sci.*, **2020**, *11*, 2876–2881.

[10] A. Lawer, J. A. Rossi-Ashton, T. C. Stephens, B. J. Challis, R. G. Epton, J. M. Lynam, W. P. Unsworth, *Angew. Chem., Int. Ed.* **2019**, *58*, 13942–13947.