The occurrence of ansamers in the synthesis of cyclic peptides

G. Yao, S. Kosol, M. T. Wenz, E. Irran, B. G. Keller, O. Trapp, R. D. Süssmuth, *Nat Commun,* **2022***, 13,* 6488

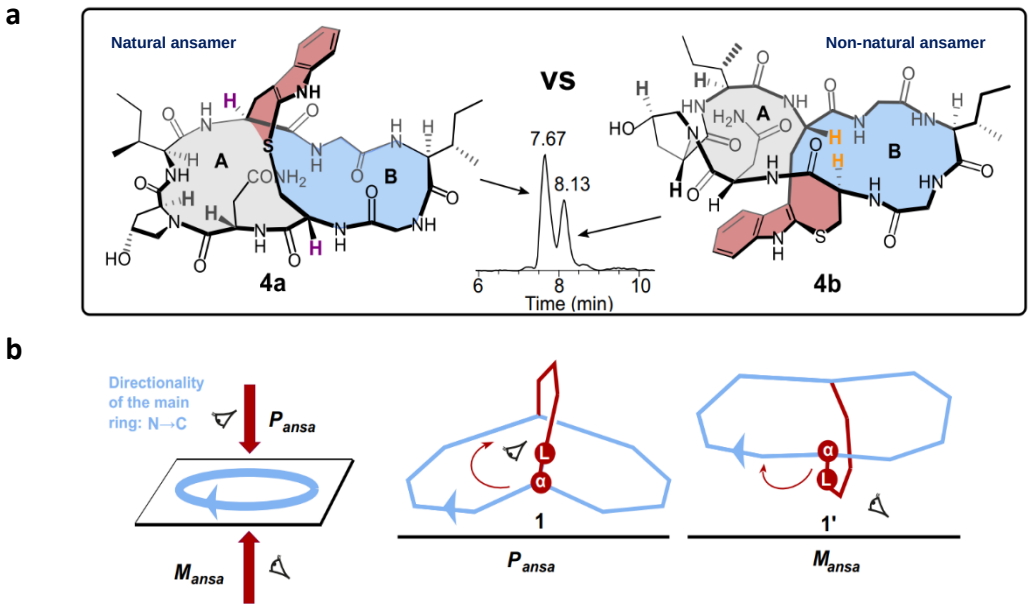

Fig 1: **a.** Proposed conformational isomers of α-amanitin. The A and B-rings are colored in gray and blue, respectively **b.** Determination of ansamer-configurations: (1) the main cycle and the directionality is identified (light blue): from N- to C-terminus. (2) Bridge-up/bridge-down cases in view of the priority order in the main cycle. Identification of the leading atom/group L of the bridge next to the bridgehead atom α is assigned. (3) The descriptor Pansa or Mansa is assigned according to the directionality (clockwise/counter-clockwise) from the position of the leading atom/group L.

Who are the corresponding authors and what are their research areas?

Roderich D. Süssmuth – *Professor of Chemistry at the Technical University of Berlin, Germany*
Roderich D. Süssmuth is a German biochemist and his research interest is mainly focused on the total synthesis of natural products and exploring the structure-activity relationship. For the past decade, he has been developing the synthesis of 'macrocyclic peptide' for medical applications.

What is the main claim of the article?

The authors unambiguously confirm the synthesis of two amatoxin-type isomers with their developed reaction conditions. The performed in-depth the spectroscopic, crystallographic and molecular dynamics studies were reported and used to clarify the isomerism of α-Amanitin. From the studies, the new terminology – ansamers was proposed and assigned to this isomerism

How is it demonstrated?

Authors proved the physicochemical differences of the amaninamide isomers based on UV-Vis, CD, Molecular dynamics simulations and the crystal structures. H-bond, showed in molecular dynamic simulations and found in crystal structure, is one of the main factors that used to indicate the differences in 3D structure of the two isomers.

What are the typical experimental conditions?

- NMR (Bruker Avance III 700 MHz spectrometer with a TXI 5 mm probe.; DMSO-d_6 (~10 mM))

- Molecular dynamics simulations (GROMACS. The force field parameters for the peptides were obtained with ACPYPE. The simulations were conducted at the *NpT* ensemble with p = 1 bar and T = 300 K with simulation time of 20 μs or T = 400 K with 0.1 μs)

Which are the key related papers?

1. G. Yao, C. H. Knittel, S. Kosol, M. T. Wenz, B. G. Keller, H. Gruß, A. C. Braun, C. Lutz, T. Hechler, A. Pahl, R. D. Süssmuth, *J. Am. Chem. Soc*. **2021**, *143*, 14322–14331.
2. R. Mannancherry, M. Devereux, D. Häussinger, M. Mayor, *J. Org. Chem.* **2019**, *84, 9*, 5271–5276.