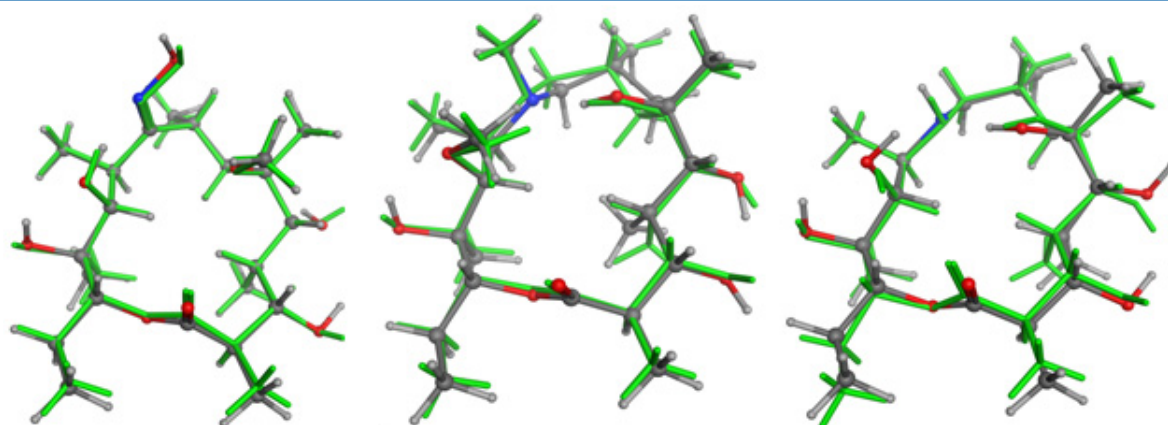


3D Structure (Conformation) of Macrocycles

Objectives

- The goal of this study was to gain insight in the 3D structures and behaviour of the macrolactone ring found in natural products (macrolides)
- The conformational study of selected macrolide aglycones was performed using single crystal X-ray crystallography to gain information about the solid state, while a combination of NMR spectroscopy and molecular modelling was employed to study the solution structures



Superposition of 3D solution and solid state structures of aglycones

- Macrolide 3D shape is very important for positioning the molecule within the active site of the ribosome; conformational analysis can be the source of valuable information in the rational design of new molecules with improved antibacterial activity
- Comparison of the obtained crystal structures with their solution counterparts showed no significant differences between them, confirming the relative rigidity of the macrocyclic ring
- In all three examples aglycones adopt energetically more favoured folded-out conformation
- The highest value of obtained compounds is in their building block potential – they are an excellent starting point for transformations at the C3 and C5 positions

References:

1. I. Čaleta et al., *Struct. Chem*, **23** (2012) 1785-1796.