Towards a computational protocol for VCD spectra of cyclic peptides

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Vibrational Circular Dichroism (VCD) is a type of spectroscopy that can be used to investigate chirality and to obtain information about conformers of flexible molecules. The experimentally measured VCD spectra rely heavily on calculated spectra to extract this kind of information. In our work, we are developing a computational protocol that together with experiments can determine the absolute configuration of cyclic peptides. This type of spectroscopy is very sensitive to minor structural changes and a common way to find the relevant conformations is to use Molecular Dynamics simulations. In our work we are testing a different approach for the conformational search; CREST developed by Grimme *et. al*. which uses a semi-empirical quantum chemistry method (GFN2-xTB) in combination with meta-dynamics.[1] The method has been tested for NMR spectroscopy and we are exploring its use for VCD.

When the protocol is found reliable, it will be used as a tool to determine the absolute configuration of cyclic peptides that are shown to be promising antibiotic candidates by the DigiBiotics project.[2]

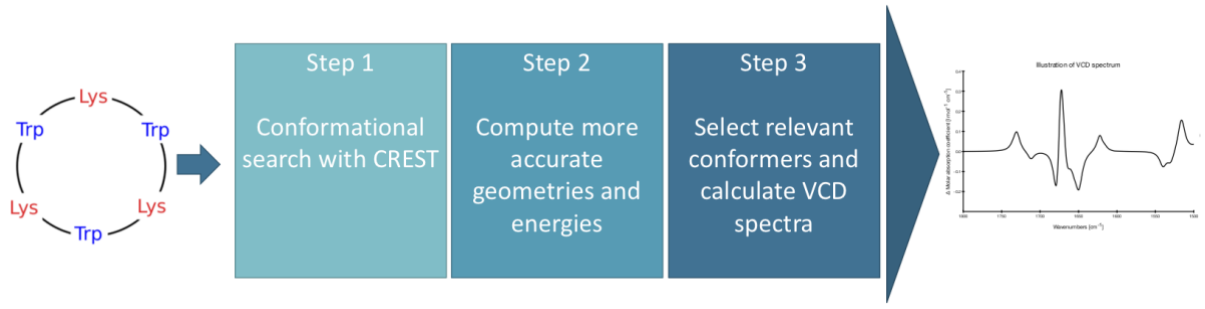

Figure: Overview of the protocol - An example of an interesting cyclic peptide consisting of the two amino acids Lysine (Lys) and Tryptophan (Trp), a summary of the three steps of the protocol and an illustration of how a VCD spectrum can look.

References

1. Grimme, S; Bannwarth, C; Dohm, S; Hansen, A; Pisarek, J; Pracht, P; Seibert, J; Neese, F. *Angew. Chem. Int. Ed.* **2017**, *56*, 14763-14769.
2. Web page: http://site.uit.no/antibiotics/