

Supramolecular Chirogenesis in a Sterically Hindered Porphyrin: A Critical Theoretical Analysis



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Invited for the cover of this issue are the groups of Irina Osadchuk at Tallinn University of Technology and Mathias Senge at Trinity College Dublin. The image depicts how a porphyrin with two guest molecules (*R*)-camphor sulfonic acid is irradiated with UV-visible light to measure and simulate ECD and UV-Vis spectra. Read the full text of the article at [10.1002/chem.202301408](https://doi.org/10.1002/chem.202301408).

How would you describe to the layperson the most significant result of this study?

The most significant result of this study is the development of the correct theoretical analysis of chirogenic phenomena in supramolecular systems. To determine chirality and spatial structure unambiguously, several methods should be used to minimize the likelihood of accidental coincidences, even if computational simulations are in good agreement with the experimental results. For example, in our case, using two solvents and repeating the simulation in both solvents was very helpful, as the electronic circular dichroism (ECD) spectra theoretically obtained in dichloromethane alone were in excellent agreement with the measured spectra; however, the simulations in chloroform gave a large discrepancy. As a result, another structure of the host–guest complex was discovered, the spectra of which are in good agreement with the experimental data in both solvents.

What is the most interesting result of this study?

We studied different factors influencing the ECD spectra of porphyrin-based host–guest complexes, because porphyrins find broad applications as optical, chemical, and chirality sensors. Interestingly, during this study it was found that a change in the ethyl substituents in the porphyrin structure can also influence the ECD spectra of the host–guest complex. Although the orbitals participating in the electron transfer are not localized on the ethyl groups of porphyrin chromophores, a change in the ethyl positions resulted in a change of the entire cavity size formed by the nonplanar porphyrin; hence, forcing a structural shift of guest molecules in the host–guest complex. As a result, surprisingly not only intensities of the ECD bands were altered, but the signs of corresponding bands were changed as well.

What was the biggest challenge (on the way to the results presented in this paper)?

From a computational chemist's point of view, the most difficult part of this work was performing the conformational search. First, we tried to find the lowest-energy conformer by creating structures manually, but this had no success. As our supramolecule is rather large (200 atoms) and has many flexible substituents, a systematic conformational search was also not suitable. A molecular mechanics approach was not appropriate either, because the supramolecule contains phenol rings, and noncovalent interactions determine the lowest energy conformer. This is because the computational programs for conformational search, which use molecular mechanics, optimize phenol rings incorrectly and are not accurate in describing noncovalent interactions. Thus, we were limited to semi-empirical conformational searches. Moreover, we had to use only semi-empirical methods, which were parametrized on benchmarks that included hydrogen bonds, which further limited us. Therefore, we were very happy when we found the conformer–rotamer ensemble sampling tool (CREST), which met all the structural requirements.

