

Curcumin and Cyclocurcumin-based Derivatives as Potential Candidates for Photocontrolled Treatment

Raúl Losantos^{1,2*}, Andreea Pasc², Antonio Monari^{1,3}

¹ Université de Lorraine and CNRS, LPCT UMR 7019, Bvd des Aiguillettes, F-54506 Vandoeuvre-lès-Nancy, France.

² Université de Lorraine and CNRS, L2CM UMR 7053, Bvd des Aiguillettes, F-54506 Vandoeuvre-lès-Nancy, France.

³ Université de Paris and CNRS, ITODYS, F-75006 Paris, France.

* email: raul.losantos-cabello@univ-lorraine.fr

Cyclocurcumin is a natural compound extracted from turmeric and showing an interesting solvent-dependent photoswitching ability. The solvent-dependent photochemistry of cyclocurcumin has been rationalized on the basis of a competition between $\pi\text{-}\pi^*$ and $n\text{-}\pi^*$ states.¹ Furthermore, we have reported the synthesis of a biomimetic analogue showing enhanced photochemical properties and in particular presenting photoswitching capacity in various media.² In addition, molecular modeling and simulation, including density functional and wavefunction based methods were used to explore the excited states potential energy surface landscape. We realize that with cyclocurcumin, the addition of a carbon-carbon double bond to the core of the natural compound favors the population of the $\pi\text{-}\pi^*$ state, whatever the choice of the solvent, and hence leads to photoisomerization, with fluorescence reduced to only a minor channel comparing with natural derivative.³ In addition, the two-photon absorption (TPA) cross section is also strongly increased compared to the parent compound, paving the way to the use in biologically oriented applications. Apart of that, we are also interested in the interaction between these systems and lipidic membranes as a potential photocontrolled way to destabilize it, which can yield in cellular apoptosis or vesicle drug delivery. Likewise, natural curcumin was studied as a potential photodynamic therapy candidate taking advantage of its larger TPA comparing with other used drugs.

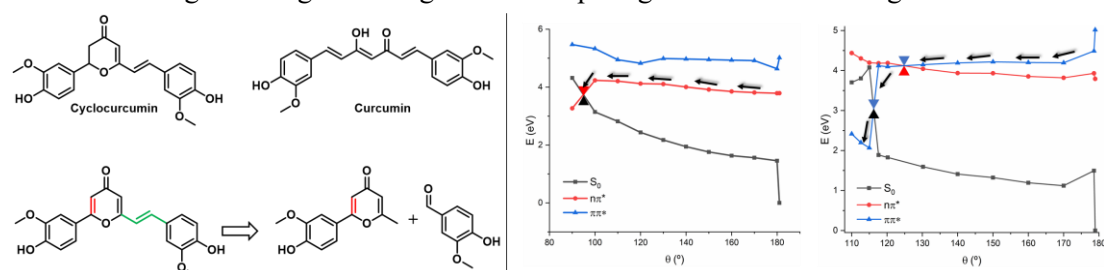


Figure. Molecular formula and retrosynthetic design of cyclocurcumin derivatives (left). PES of the rotation scan following $n\text{-}\pi^*$ and $\pi\text{-}\pi^*$ states, respectively (right).

References

- [1] M. Marazzi, A. Francés-Monerris, M. Mourer, A. Pasc and A. Monari *Phys. Chem. Chem. Phys.* **2020**, *22*, 4749–4757.
- [2] J. Pecourneau, R. Losantos, A. Monari, S. Parant, A. Pasc, M. Mourer *J. Org. Chem.* **2021**, *86*, 12, 8112–8126.
- [3] R. Losantos, J. Pecourneau, M. Mourer, S. Parant, A. Pasc, A. Monari *Phys. Chem. Chem. Phys.* **2021**, *23*, 22, 12842–12849.