Cyclodextrin crosslinked polymers as versatile reaction vessels to implement flow photochemistry in water

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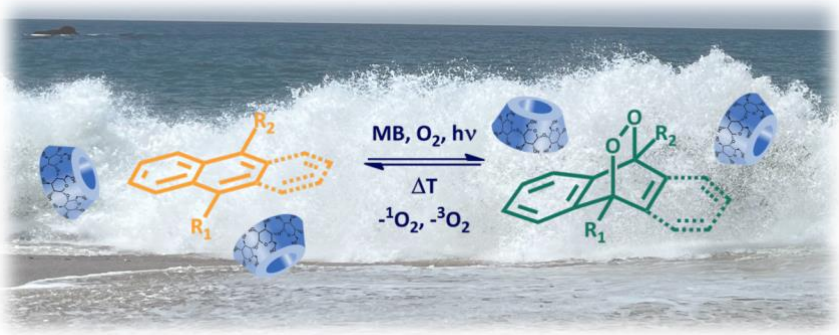
Cyclodextrin (CyD) crosslinked polymers[1] were explored to implement photochemical synthesis of endoperoxides in water exploiting the inclusion of aromatic guests in the CyD cavity. There's wide interest in the design of Oxygen releasing agents (ORA) as molecular systems able to supply O_2 in tissues. They are promising for various therapeutic applications, such as the relieve of low O_2 levels in tumor tissues inducing resistance to chemotherapy, the improvement of the efficacy of Photodynamic Therapy (PDT) in conditions of hypoxia, etc. On basis of computational calculations we selected some new Anthracenes and Naphthalenes for transformation in Endoperoxides as ORA candidates. They were solubilized in water by means of CyD crosslinked polymers. Visible light photocatalyzed conversion of the aromatic substrates in endoperoxides has been achieved in the presence of methylene blue in homogeneous aqueous environment thanks to the use of CyD polymers as inert reaction matrix solubilizing the aromatics.[2] In a first approach, few ml of the CyD polymer solution of the aromatic compound and MB were irradiated with Hg lamp for endoperoxide production, next flow photochemistry with red emissive leds was exploited to optimize the reaction time and product amount. Some of the endoperoxides obtained indeed act as ORA and release O_2 thermally either in its triplet state to feed the photosensitizer or as singlet oxygen ($^1O_2$). Next, co-encapsulation of the ORA and PS in the CyD polymeric carrier has been achieved in dosage-consistent amounts for the implementation of PDT under hypoxia. Our results forecast the use of these CyD polymers as interesting, scalable vessel for the green production of new molecules and the delivery of a combination of therapeutic agents.



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References

M. Agnes, E. Pancani, M. Malanga, E. Fenyvesi, and I. Manet, *Macromol. Biosci*. **2022**, 22, 2200090 DOI: 10.1002/mabi.202200090

M. Agnes, A. Mazza, E. Kalydi, S. Béni, M. Malanga, and I. Manet, *Chem. Eur. J.* **2023**, e202300511 DOI: 10.1002/chem.202300511