Photouncaging of Carboxylic Acids from Cyanine Dyes with Near-Infrared Light

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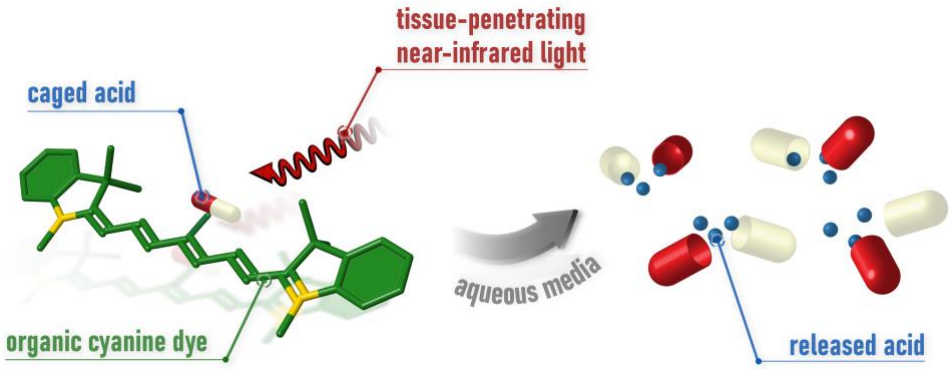
Photocages are light-sensitive groups that take advantage of biorthogonality as well as unparalleled spatial and temporal resolution of light as a stimulus to unmask and restore activity of a substrate.[1] However, extending their application towards therapeutic utility requires shifting their absorption into the near-infrared (NIR) phototherapeutic window (650–900 nm), a region of wavelengths applicable in the body. Although, NIR light offers unparalleled advantages as a biocompatible stimulus, the lack of molecules operating in such a region limits its use. The development of photocages that operate in this region represents a fundamental challenge due to the low energy of the excitation light.[2] Herein, we repurpose cyanine dyes into photocages that are available on a multigram scale in three steps and efficiently release carboxylic acids in aqueous media upon irradiation with NIR light up to 820 nm. The photouncaging process is examined using several techniques, providing evidence that it proceeds via photooxidative pathway. We demonstrate the practical utility in live HeLa cells by delivery and release of the carboxylic acid cargo, that was otherwise not uptaken by cells in its free form. In combination with modularity of the cyanine scaffold, the realization of these accessible photocages will fully unleash the potential of the emerging field of NIR-photoactivation and facilitate its widespread adoption outside the photochemistry community.



[1] P. Klán, T. Šolomek, C. G. Bochet, A. Blanc, R. Givens, M. Rubina, V. Popik, A. Kostikov, J. Wirz, *Chem. Rev.* **2013**, *113*, 119–191.
[2] R. Weissleder, *Nat. Biotechnol*. **2001**, *19*, 316–317.