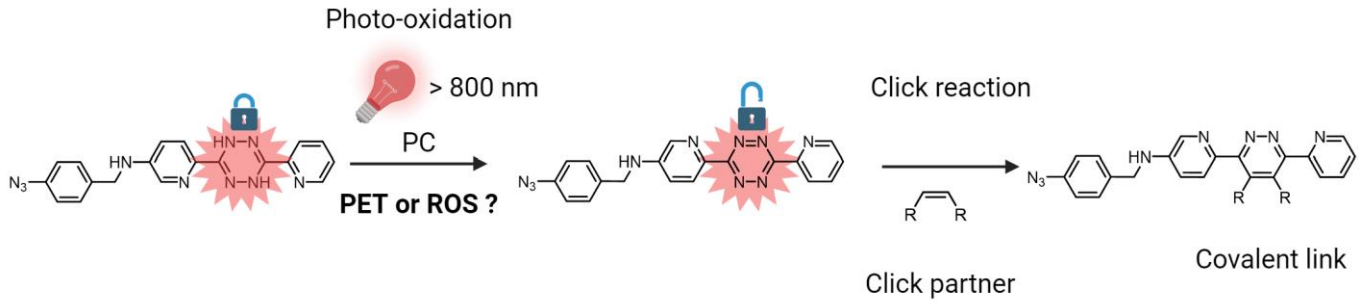
Near-Infrared Photooxidation of Dihydrotetrazine for Applications in Bioconjugate Chemistry: a radical pathway?

Margaux Walter, Murat Cihan, Mary-Lorène Goddard, Jean-Philippe Goddard*, Morgan Cormier*

Laboratoire d'Innovation Moléculaire et Applications (LIMA) UMR 7042, Université de Haute-Alsace, Université de Strasbourg, CNRS, 3bis Rue Alferd Werner, Mulhouse, FRANCE
margaux.walter@uha.fr

Synthetic chemists aspire to control each parameter involved in organic transformations, such as efficiency, selectivity (chemo-, regio-, enantio-selectivity), and kinetics. The next level of control needed for applications is the reaction's temporal and spatial trigger. This is particularly required for biological/pharmaceutical applications such as drug delivery or medical diagnostics.[1] Governing the reaction through a simple switcher is appealing, and the photo-click concept is a wonderful tool for achieving this goal.[1] In this case, the click reaction, which has many advantages (kinetic, selectivity…), is triggered by light. Until now, the photoclick concept has been developed from UV to visible light.[2] However, near-infrared light presents many advantages, such as light penetration, biocompatibility and low energy.[3]

Based on our previous works on NIR-photocatalysis driven by cyanines and squaraines[4,5], we tackle the challenge of NIR-Photoclick. Herein, the NIR-photooxidation of dihydrotetrazine to deliver the clickable tetrazine is presented. This study includes photocatalyst design, optimization, and mechanistic discussion. The last point is crucial to reach the best photocontrol. Does the reaction proceed through a photoinduced electron transfer, reactive species of O_2 or both?



Scheme 1 : Near-Infrared Light triggered click reaction

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