

TOWARD BIOMEDICAL APPLICATIONS OF PHOTOREMOVABLE PROTECTING GROUPS.

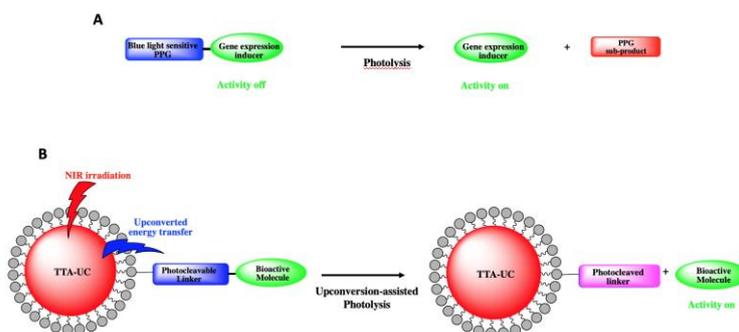


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The use of photolabile protecting groups (PPGs) has been growing in emphasis for decades, and they nowadays enable cutting-edge results in numerous fields ranging from organic synthesis to various field of biology.¹⁻² PPGs are chemical entities that can be conjugated to a biological effector to hide its biological activity, forming a stable so called “caged compound”. This conjugate can be simply cleaved by light and therefore, the functionality of the biological effector is restored with the formation of a PPG by-product. The use of UV irradiation (normally within power density between 10^{-1} and 10^{-3} W.cm⁻²) to manipulate the functions of biomolecules or mediate on-demand drug release in living systems *via* effective photoactivation with very high spatial and temporal control is a remarkable, well-developed and reviewed technique.² During the last two decades, the challenge was to overcome the difficulty that only high energy light (i.e. UV, the one damaging biological tissues) can induce photochemical reactions. One strategy to lower phototoxicity within the domain of one-photon excitation process is based on tailoring the caging groups with extended π -conjugation and introducing heteroatoms and functional groups in the ring system so that larger dipole change can be generated upon excitation. Therefore, blue light-sensitive photoremovable groups have been reported in the coumarin,³ *o*-nitrobenzyl,⁴ and *o*-nitrophenethyl series.⁵ This later strategies enable new biomedical applications in particular for the treatment of proliferative retinopathy. Therefore, the development of blue light sensitive caged small gene inducers⁶ will be presented in this context. (**Scheme 1A**).

For more general biomedical applications the development of Red to NIR sensitive systems is highly sought after. In this context, we will also present our recent development emissive upconversion nanoparticles systems using the TTA-UC strategy⁷ (for Red or NIR to blue light upconversion). And we will present how we have been able to further functionalize those nanoparticles with blue light-sensitive photocleavable linkers (**Scheme 1 B**) in order to trigger drugs releases using Red to NIR light.



References

1. R. Weinstein, et al. *Chem Rev*, **2020**, 120 (24), 13135-13272; C. Morville et al., *J Incl Phenom Macrocycl Chem*, **2021**, 101, 291-304.
2. A. Gautier, et al. *Nat Chem Biol*, 2014, **10**, 533-541 ; M. M. Lerch, et al. *Angew Chem Int Ed*, 2016, **55**, 10978-10999 ; P. Paoletti, G. C. R. Ellis-Davies and A. Mourou, *Nat Rev Neurosci*, **2019**, 20, 514-532.
3. L. Fournier, et al. *Chemistry*, **2013**, 19, 17494-17507 ; M. T. Richers, et al. *Angew Chem Int Ed*, **2017**, 56, 193-197 ; Q. Lin, et al. *Angew Chem Int Ed*, **2018**, 57, 3722-3726 ; J. Chaud et al., *Org. Lett*, **2021**, 23, 19, 7580-7585.
4. M. T. Richers, et al., *Angew Chem Int Ed*, **2019**, 58, 12086-12090.
5. A. Specht, et al. *Photochem Photobiol Sci*, **2012**, 11, 578-586.
6. B. Goegan, et al. *ChemBioChem*, **2018**, 19, 1341-1348.
7. D. K. K. Liu, *J Am Chem Soc* **1977**, 99 (14), 4594-4599; Y. Y. Cheng, et al., *J Phys Chem A* **2011**, 115 (6), 1047-1053, S.H.C. Askes, et al. *Angew Chem Int Ed* **2014**, **53** (4), 1029-1033.