Light activated bioactive substrate release: Phototriggers for biology and chemistry

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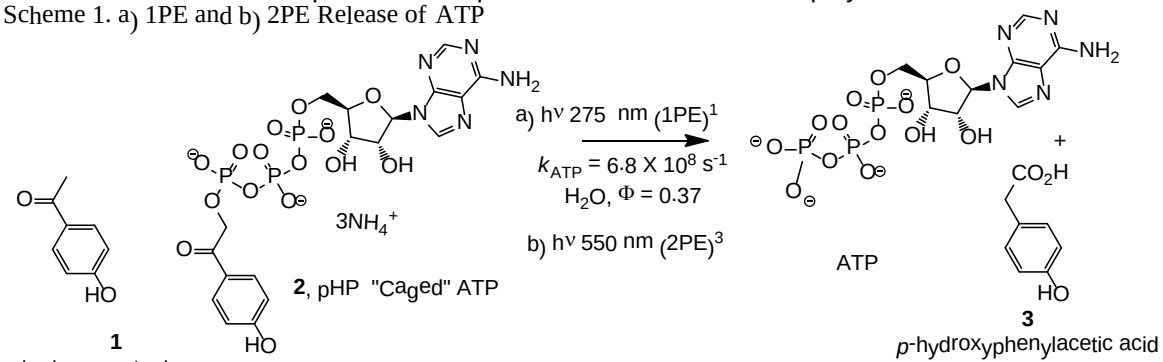
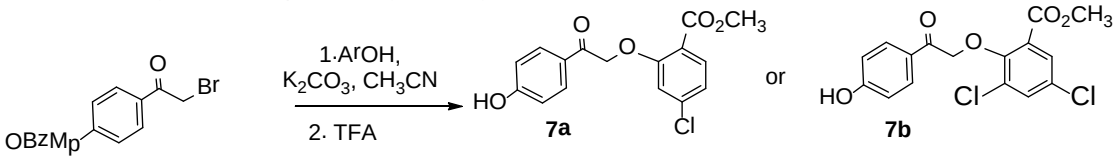
Our research objective is the synthesis and photochemistry of caged ATP, neurotransmitters and pharmaceutical agents.[1] Caged molecules are reagents that are rendered inactive by being coupled to a chromophore that is subsequently removed by irradiation with visible or UV light.[2] These inactive reagents are released through photolytic removal of the chromophore, a process that is extremely rapid (in nanoseconds), easy to control with respect to the amount released and its location. In our examples, the release is quantitative.[2] As an example, the photorelease of ATP from a caged ATP (**2**) is shown in Scheme 1 where both one-photon and 2-photon excitation can be employed.[3b]

Scheme 1. a) 1PE and b) 2PE Release of ATP



We collaborate with many research groups by providing them with caged reagents for release of glutamate, GABA, and ATP (as well as many other biological reagents). We build, test, and quantitate the cage reagents and provide the information necessary for others to use them in biological and physiological studies as phototrigger reagents.[4,5] Our collaborations might lead to mapping of nerve connectivity, to testing ATP activation of muscle action, or to blocking the activity of neurotransmission by spatially controlled release of pharmaceutical antagonists or inhibitors. Collaborative projects with Professor Chris Elles involves using lower energy 550 nm light to release ATP by 2-photon excitation (2PE) with a Ti:sapphire laser (Scheme 1). A second project with Professor Mike Johnson is to develop a caged antagonist for Dopamine release in brain tissue by using caged Raclopride, a phenolic D-2 dopamine receptor inhibitor to Dopamine release. The synthesis is outlined in Scheme 2.

Scheme 2; Synthesis of pHP salicylates agonists



We have also begun developing models for caged pro-drugs that will probe effects of agonists/antagonists for glutamate and dopamine release in tissue samples, opening new areas for phototrigger applications.

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