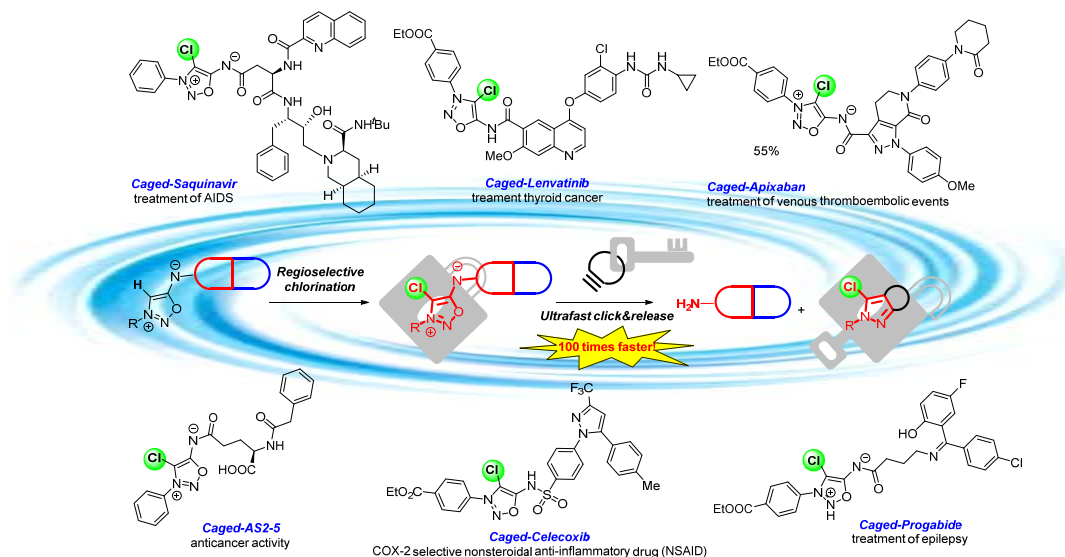


REGIOSELECTIVE CHLORINATION OF IMINOSYDNONE FOR ULTRAFAST CLICK AND RELEASE

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Exploring the chemistry of mesoionic compounds and its application in chemical biology is the focus of research work from our group. In 2017, we described a biorthogonal reaction between iminosydnone (ImSyd) and cycloalkynes, which is defined as a “click and release reaction”.^[1] This transformation has the particularity to allow simultaneous formation of a new compound and release of another one. However, the biological application of this reaction is limited due to low reaction speed. To achieve fast click and release reaction allowing the decaging of drugs, a regioselective chlorination at C4 position of ImSyd was developed to lower the LUMO of the mesoionic.^[2] Notably, this strategy can be applied to pharmaceutical molecules with complicated structures smoothly to produce different kinds of drugs caged with 4-Cl-ImSyd. Moreover, we observed an increase up to 100 times of the kinetic constant of the click and release process in aqueous media, which enable efficient “on demand” release of drugs. This strategy provides an alternative methodology which has the potential to be a powerful tool for drug delivery.



[1] S. Bernard *et al.* *Angew. Chem. Int. Ed.* **2017**, *56*, 15612–15616.

[2] a) H. Liu *et al.* *Angew. Chem. Int. Ed.* **2016**, *55*, 12073–12077 ; b) M. Riomet *et al.* *Chem. Eur. J.* **2018**, *24*, 8535 – 8541.