Polyfunctional clickable compounds as a useful tool for bioactive molecules labeling

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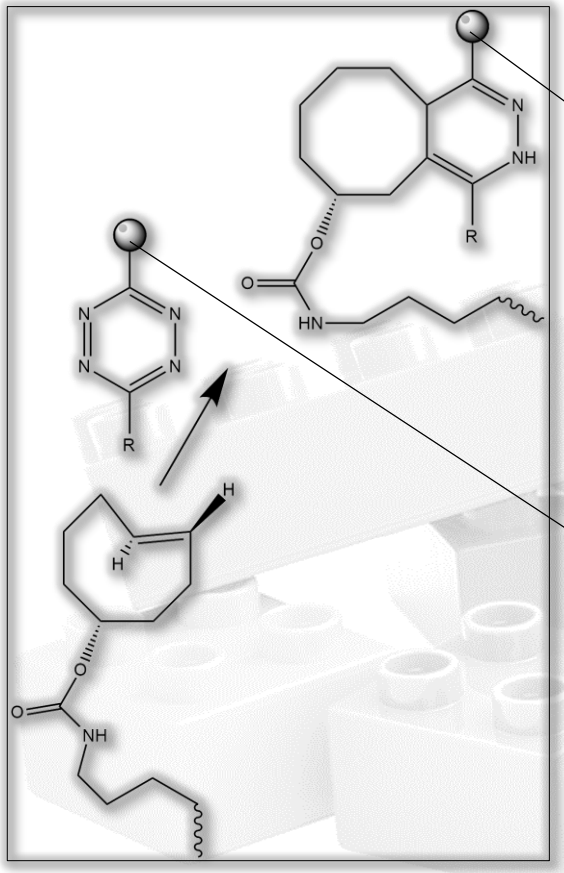
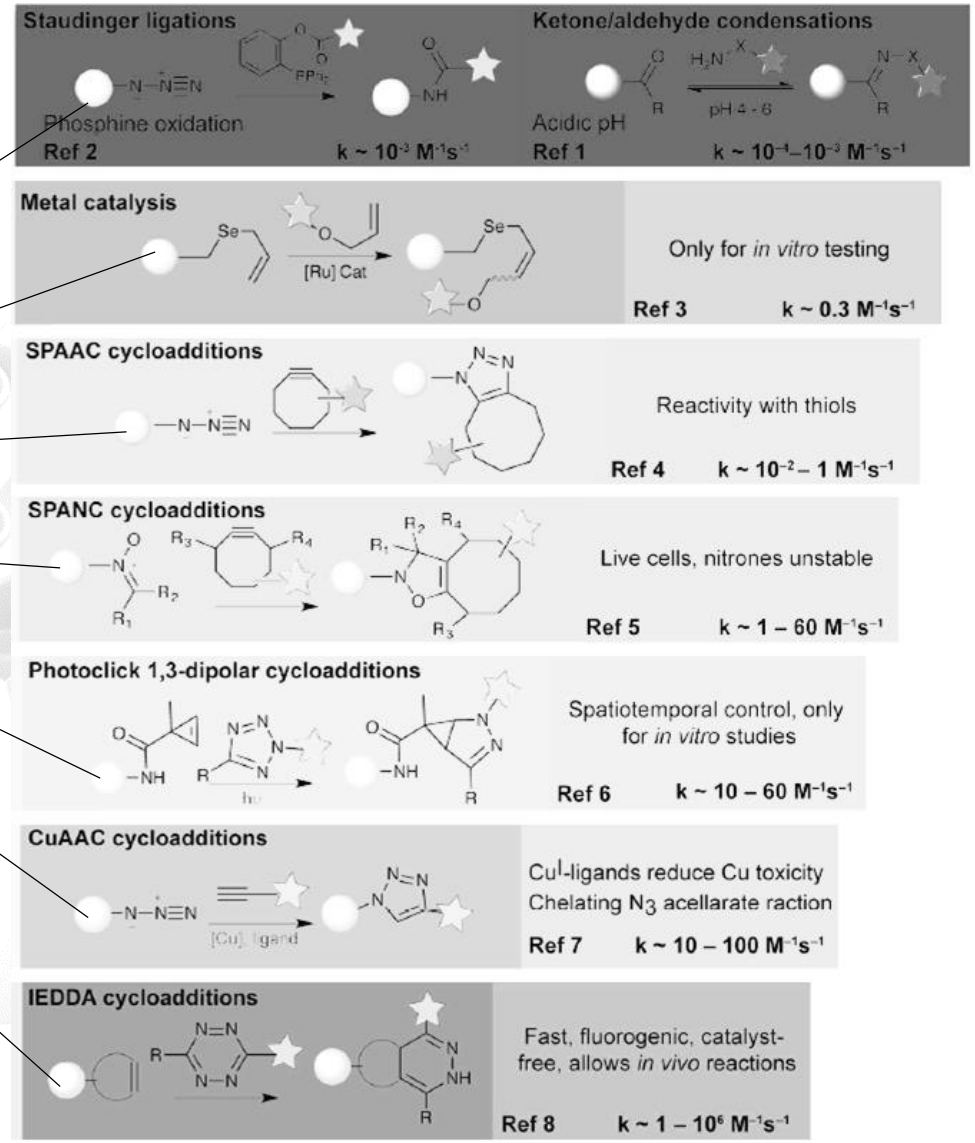
Abstract

The coming age of personalized medicine needs reactions and reagents with fast kinetics, excellent orthogonality and biocompatibility. Click-chemistry processes such as inverse-electron demand Diels–Alder (IEDDA) reaction – have become extremely popular with promises to revolutionize chemical biology, radiochemistry and materials science. The exceptional fast kinetics of this catalyst-free reaction, using low concentrations of highly strained unsaturated dienophiles and 1,2,4,5-tetrazines coupling agents, make it appropriate for in vivo radiolabelling using pretargeting methodologies. The IEDDA reaction can be tuned to reach rate constants from 1 up to 10^6 M^{-1} s^{-1} by changing the electron deficiency of the 1,2,4,5-tetrazine precursors (Tz), or by manipulating the ring strain and electronic effects on the dienophiles (TCO). Significant efforts have focused on accelerating the reaction rate by synthesizing new derivatives of TCO and Tz. The present study is aimed to the synthesis of new TCO and Tz moieties appropriate for further bioconjugation via oxime or hydrazone formation.



Biomolecules (proteins, antibodies, nucleic acids, glycans, lipids, small bioactive molecules); Radiolabeled molecules; Fluorescent molecules etc.



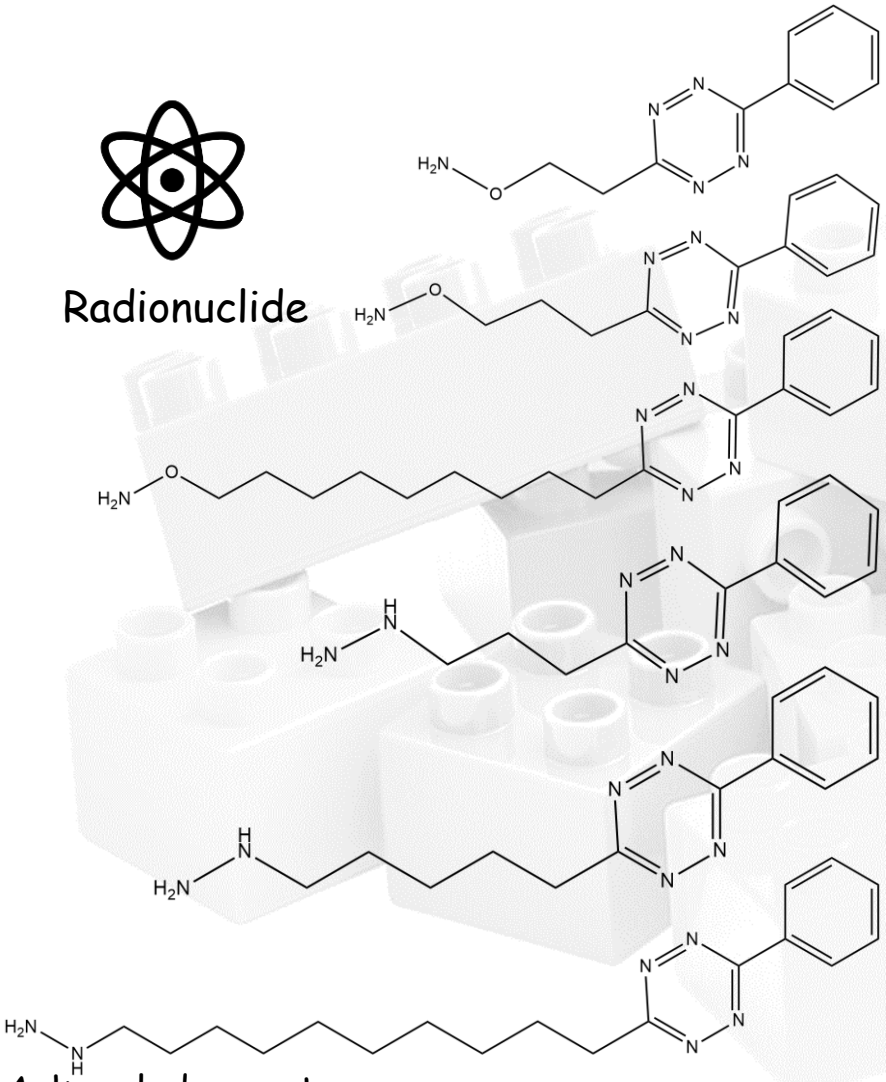
Inverse-electron demand Diels-Alder reaction - "Click reaction"

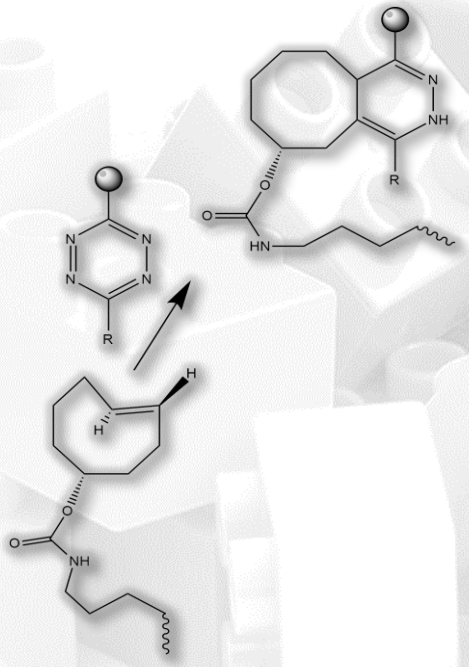
Useful biorthogonal reactions for bioconjugation and their rate constants

Results and discussion

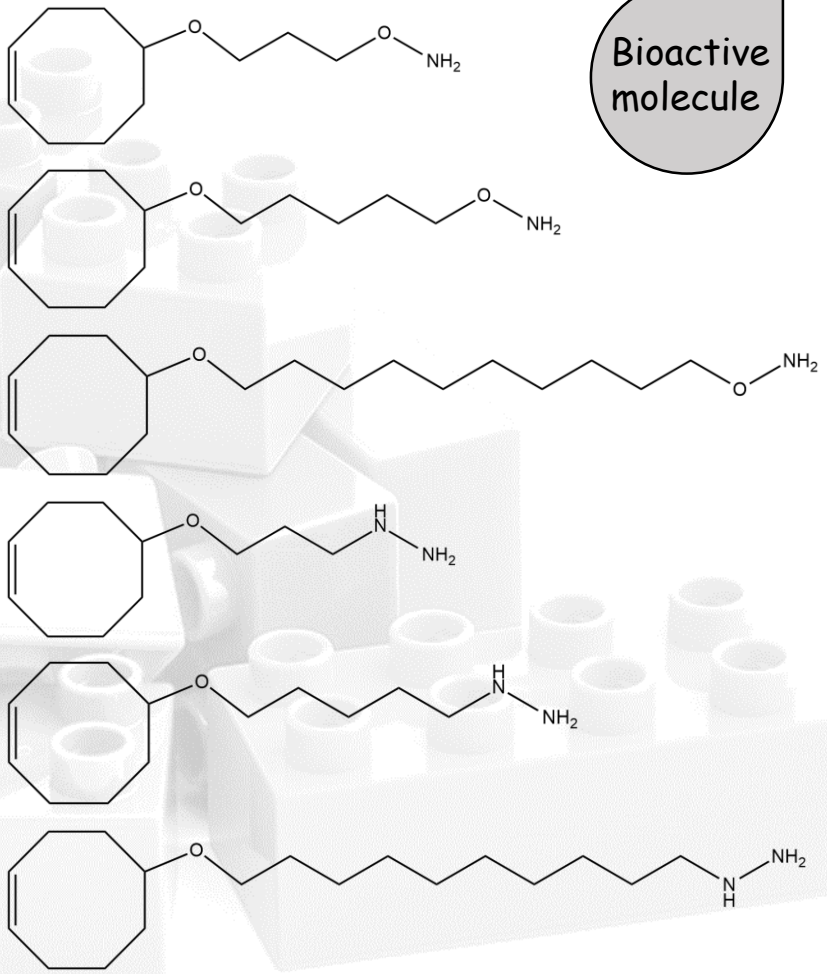
Newly synthetized "Click" molecules

Radionuclide





Bioactive molecule



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