PYRROC as an alternative to Copper catalysts in strain promoted azide-alkyne cycloaddition reactions

The talk will provide an introduction to CuAAC and SPAAC, their current usage and future potential applications. The alternative PYRROC will then be discussed with details provided on its synthesis and kinetic properties. A comparison of PYRROC with CuAAC and SPAAC will be made to highlight the advantages of this new material and approach with respect to reaction rate and selectivity.

In more detail the application of SPAAC at the moment is primarily related to the labelling of biomolecules localized inside the cell or at the cell membrane. Such molecules are for example proteins, RNAs or glycans. It is also possible to use PYRROC as a part of a sequential bioconjugation or for the antibody-free western blot analysis. The advantage of PYRROC over other commonly used cycloalkynes is that the reaction rate in aqueous media with up to 930 $M^{-1}s^{-1}$ is to our knowledge the highest reported to date. Therefore reactions of substrates in very low concentrations as they are used in the biochemistryfield will be finished in less time. Furthermore, PYRROC has two ester and one hydroxyl group and can therefore be functionalized to fit special needs in solubility or size.

The application of CuAAC is in material and surface science to produce large molecules and polymers. Considering the field of research, CuAAC is among other things used in drug discovery as a neat way to synthesize big screening libraries. Usually the screening hits thereof will be structurally optimized and further used as potential drug candidates. These molecules are typically very big and might not fit Lipinski's rule of five leading to an unfavourably oral bioavailability. Using SPAAC instead of CuAAC to synthesize screening libraries would offer the possibility to not only gain new hits but also to make it possible to administer two separate small molecules as prodrugs instead of a big one. The reaction will then take place inside the cell at their target location. PYRROC does only form one single product upon click reaction, therefore it is also advantageous over other cycloalkynes which lead to at least two isomers.

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