

Seminar

Highly water-soluble thiol catalysts for Native Chemical Ligation

Vishal Malik

TIFR, Hyderabad

Native chemical ligation involves a reaction between two unprotected peptide segments, an α -thioester and another N-terminal cysteine residue containing peptide, which eventually leads to the formation of a native amide bond between the two peptides. It has been known that adding exogenous thiol additives increases the rate of ligation by many folds. This thiol-thioester exchange leads to the formation of a more reactive thioester and hence, increases the rate of transthioesterification process. Thiol additives that are commonly used are a mixture of thiophenol/benzyl mercaptan, mercaptoethane sulfonate sodium salt (MESNa), or (4-carboxymethyl)thiophenol (MPAA). Out of all these, MPAA has been found to be the most effective catalyst because of its moderate nucleophilicity and good leaving ability. But, because of the high cost and lack of availability of this reagent in selected countries, including India, there is an urgent need for an alternative reagent, which is economical, readily available, highly water soluble, and equally or more reactive than MPAA.

In this talk, I will discuss the synthesis, ligation kinetics, and solubility study of six potential thiol additives designed to function as catalysts that are either comparable to or more effective than the existing ones.

Monday, Mar 11th 2024

14:30 Hrs (Tea / Coffee 14:15 Hrs)

Auditorium, TIFR-H