



INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Thesis Title: Design and Synthesis of Fluorescent Unnatural Triazolyl Amino Acids and Constraints Molecular Scaffold and their Application in Peptidomimetics.

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SHORT ABSTRACT

In chapter I, describe the applications of unnatural amino acids and conformationally constrained small molecule scaffold: a review chapter.

In chapter II, We report herein the design and synthesis of microenvironment sensitive fluorescent triazolyl unnatural amino acids (UNAA) decorated with donor and/or acceptor aromatic chromophores via click chemistry. The synthesized fluorescent amino acids show interesting solvatochromic characteristic and/or intramolecular charge transfer (ICT) feature as is revealed from the UV-visible, fluorescence photophysical properties and DFT/TDDFT calculation. HOMO-LUMO distribution shows that the emissive states of some of the amino acids are characterized with more significant electron redistribution between the triazolyl moiety and the aromatic chromophores linked to it leading to modulated emission property.

In chapter III, The β -turn conformation and FRET process were established in the designed tripeptide containing fluorescent triazolyl donor and acceptor decorated unnatural amino acids separated by a natural alanine.

In chapter IV, Triazolo- β -aza- ϵ -amino acid and its aromatic analogue ($^{Al}TAA/^{Ar}TAA$) in the peptide backbone mark a novel class of conformationally constrained molecular scaffolds to induce β -turn conformations. This was demonstrated for ^{Al}TAA in a Leu-enkephalin analogue and in a designed pentapeptide wherein the FRET process was established. Restricted rotation induced chirality and turn conformation into the achiral aromatic amino acid scaffold, ^{Ar}TAA , which in a short tripeptide backbone acted as turn mimic as a β -sheet folding nucleator.

In chapter V, We are reporting two mechanisms for excimer emission in a designed trichromophoric pentapeptide wherein the triazolo aromatic amino acid scaffold (^{Ar}TAA) nucleates β -sheet conformation. The designed unnatural fluorescent pentapeptide shows an excimer emission either via FRET from the scaffold (^{Ar}TAA) acting as a donor or via direct excitation of an acceptor chromophore, ^{TPy}Ala^{D0}. Moreover, it serves as an effective fluorescence light-up probe for studying protein-peptide interactions.

In chapter VI, We report a unique fluorescence sensor based on an axially chiral unnatural triazolyl aromatic amino acid scaffold (^{Ar}TAA) for discrimination of methanol from ethanol via a switch on fluorescence response. All the three sensors, simple scaffold (^{Ar}TAA), mono- (PyAm-^{Ar}TAA) and bis-pyrenyl- (Py₂Am-^{Ar}TAA) amides, show similar sensitivity and detection limit of 2.2 v/v% of ethanol. The solid films of these sensors are also found to be effective in sensing ethanol vapour via generation of distinct and enhanced fluorescence signal. All our experimental results suggest the role of axial chirality of the hairpin-shaped scaffold in differential solvation guided H-bonding interaction and discriminating between ethanol and methanol with a switch-on fluorescence response