Bergman Cyclization: Effect of π-Stacking on the Reactivity of Enediyne-Nucleobase Conjugates, Synthesis of Artificial Peptide Cleaving Agents and Helicenes

In the first chapter of this dissertation, we have reported the synthesis of three distinct classes of enediyne-nucleobase hybrids with varying nature of the linker. Aromatic π-stacking interactions between the complementary as well as identical nucleobase components of these hybrids have been successfully exploited in lowering the activation barrier of Bergman Cyclization (BC).

Based on the reported susceptibility of amino acid and peptide to radical induced scission, different enediyne based peptides have been synthesized and described in the second chapter. Self decomposition study of these enediyne-peptide conjugates has shown the selective damage of the peptide strand from the third amino acid component starting from its carboxyl end by the 1,4-diradical intermediate, generated after the BC of enediyne moiety.

The next chapter has revealed the development of an unprecedented BC mediated tandem radical cyclization for the synthesis of differently substituted [4]helicenes in good yields starting from alkenyl cyclic enediynes. Significant perturbation effect was experienced by this radical process on varying the remote substituents as well as their orientations in the pendant aromatic ring of the cyclic enediyne substrates. Enediyne with sterically large *ortho* substituent exhibits the highest reactivity among all other differently substituted analogues. Activation energy calculation for the rate determining BC step using Density Functional Theory has explained that greater destabilization in the GS compared to that in the corresponding TS has increased the overall reaction kinetic for the enediyne possessing larger *ortho* substituent.

Last chapter of the thesis contains the synthesis of diastereomeric mixture of chiral amino acid tagged [4]helicenes using the similar tandem radical cyclization reaction triggered by BC. Due to the distant location of the chiral entity from the enediyne component, either a sterically bulky or a conformationally rigid amino acid component can't induce a good diastereoselection into the final product distribution.

Keywords: Bergman Cyclization, enediyne, nucleobase, peptide, helicenes, radical cyclization.