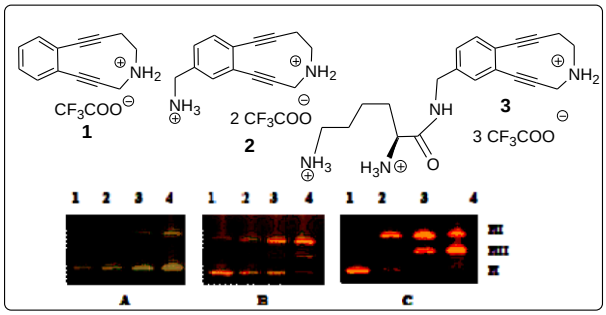
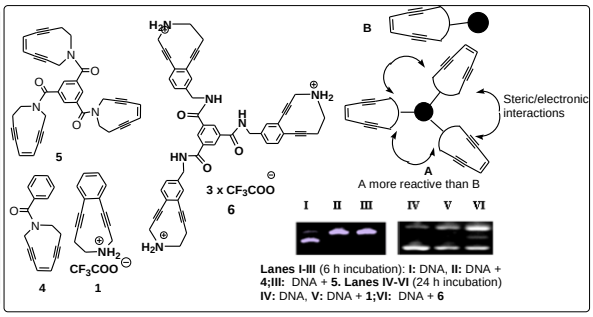
Abstract

Tuning the Reactivity of Enediynes, Eneynes and Silylated Alkynes

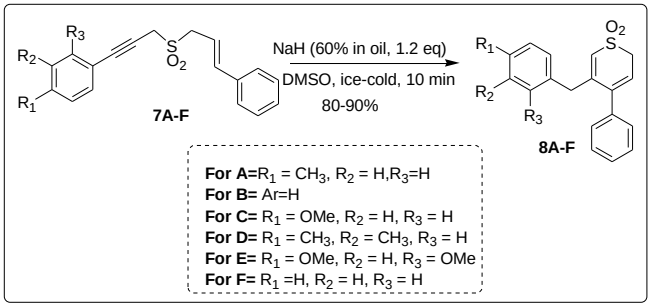
The enediynes and eneynes have garnered considerable attention in chemistry and biology due to their ability for spontaneous cyclization giving rise to a reactive diradicals (Bergman Cyclization, BC). These transient diradicals have been exploited mostly in two ways: to induce DNA strand scission and also in C-C bond forming reactions. To control the reactivity and selectivity in synthetic enediyne model compounds and cumulene-eneyne chromophores, we have adopted several strategies which are the topic of interest of the present thesis. In the first chapter, we have reported the synthesis of various *N*-substituted cyclic enediyne derivatives attached with diamine side chains (in the form of lysine) which under acidic pH, protonated and showed DNA cleaving activity by lowering the activation barrier of Bergman cyclization and inducing stronger DNA-binding (**Scheme 1**). The results have been further supported by molecular docking study which was in good agreement with our experimental findings that side chain of the enediyne plays an important role in DNA binding process. In the second chapter, we have developed a new design strategy which can be applied to lower the activation energy barrier for BC. Thus trimeric enediynes built on a dendritic 1,3,5-benzene core showed higher reactivity towards BC and hence faster DNA cleavage as compared to monoenediynes (**Scheme 2**). The results have been further supported by computational study. In the third chapter, we have reported the synthesis of various unsymmetrical *bis*-propargyl alkenyl sulfones with the arms attached to aromatic groups of different electronic character. Under basic condition, these underwent 6π-Electrocyclization (EC) generating substituted thiopyran derivative as sole product. Through this methodology, synthesis of a wide array of 4,5-disubstituted 2*H*-thiopyran derivative in high yields have been reported (**Scheme 3**). Lastly we have described a general route for the selective deprotection of alkynyl C-Si bond using Na_2S in MeOH. This methodology has been further extended to carry out simultaneous desilylation and sulfide formation in a single pot (**Scheme 4**).



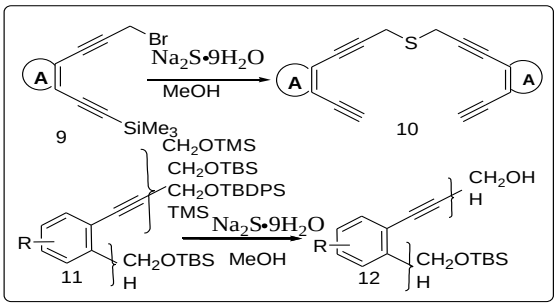
Scheme 1: Targeted DNA cleaving enediynes



Scheme 2: Reactivity of tri and mono enediynes



Scheme 3: Synthetic approach to thiopyran derivatives



Scheme 4: Silyl deprotection and sulfide formation

Keywords: Bergman, diradical, enediynes, eneynes, propargyl alkenyl, monomer, trimer, desilylation, sulfide.