Abstract:

Title: SYNTHESIS AND REACTIVITY OF AZOBENZENE, AMINO ACID AND PROPARGYL SULFONE HYBRIDS AND ASYMMETRIC CYCLOPROPANATION

Azobenzene-based bispropargyl bissulfone **1** containing stable *E*-azo moiety has been synthesized. Upon irradiation with long wavelength UV it isomerized to the *Z*-form **2**, which was thermally reisomerized to the *E*-isomer. Reactivity towards isomerization to the allenic system as well as DNA-cleaving efficiency under basic conditions was found to be significantly lower as compared to the previously synthesized cyclic sulfones. This lowering of reactivity has been explained in terms of low conversion to the allenic form and hence the lower extent of alkylation of DNA-bases.

C_2-symmetric *E*-azobenzene-amino acid linked bispropargyl sulfone **3** has been synthesized. Upon UV-irradiation these compounds isomerized to the *Z*-form **4,** whose thermal reisomerization to the *E* -isomer slowed down considerably. Under basic pH, the compounds showed DNA cleavage in μmolar concentrations with the *Z*-isomers showing better cleaving efficiency. The difference in cleaving efficiency between the *Z* and the *E* -isomer is more than the corresponding pair of sulfones without amino acid linker.

Another new class of azobenzene-amino acid/peptide hybrids with C_2-symmetry has been synthesized in both *E* and *Z* forms **5** and **6**. The *E*-isomers exhibited moderate to strong in vitro inhibition of mammalian cellular protease Subtilisin Kexin Isozyme-1 which plays vital roles in cholesterol synthesis, lipid metabolism, bone formation, and viral infections.

Finally, the asymmetric cyclopropanation of cinnamoyl amides **7** derived from amino acids with CH_2N_2 in the presence of catalytic $Pd(OAc)_2$ to produce **8** has been studied. The reaction proceeded with moderate to excellent diastereoselection. However, the selectivity depends upon the amino acid side chain as well as the electronic nature of the cinnamoyl moiety. A model based upon the formation of a palladocycle intermediate has been proposed to explain the diastereoselectivity.