

BIO-ORTHOGONAL SULFO-CLICK REACTION BETWEEN SULFONYLAZIDES AND IN SITU GENERATED THIOACIDS AND IT'S USE IN KINETIC TARGET-GUIDED SYNTHESIS

Niranjan K Namelikonda and Roman Manetsch*

Department of Chemistry, University of South Florida, 4202 E. Fowler Ave, Tampa, FL 33620.

Compounds consisting of *N*-acyl sulfonamide functionality have emerged as interesting scaffolds for medicinal and pharmacological applications. Though the synthesis of compounds with *N*-acyl sulfonamide moiety has been lately done by sulfo-click reaction efficiently, it suffers from the availability of unstable thioacids. A protocol has been developed, in which the thioacids were generated rapidly from the corresponding 9-fluorenylmethyl thioesters by treating with 3.5% DBU in DMF and reacted *in situ* with sulfonylazides to reveal the *N*-acyl sulfonamides in two minutes. In this reaction a variety of functional groups were tolerated and has been successfully applied for the synthesis of natural product derivatives. This method has also been applied in kinetic target guided synthesis, which enables the rapid identification of small molecule protein-protein interaction modulators by incubating reactive fragments decorated with a sulfonylazide and a thioacid functional group with target protein. This reaction has vast potential for conjugation and ligation applications.