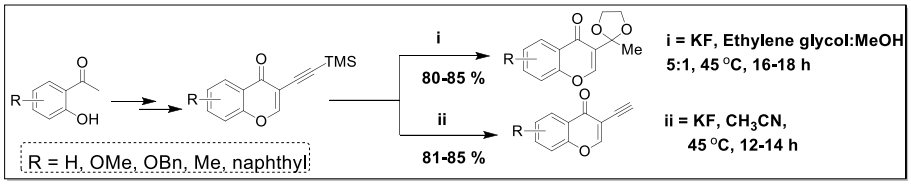
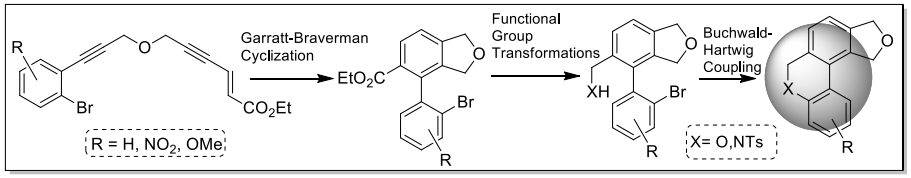
Abstract

Synthesis of Bio-Active Heterocycles from Alkenyl Propargyl Ethers and Sulfones

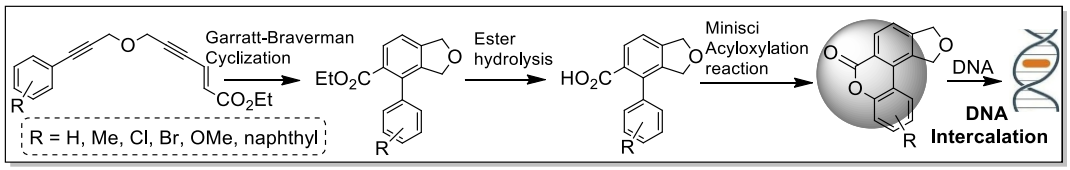
This thesis presents studies on the synthesis, reactivity and application of alkenyl propargyl ethers and sulfones for the synthesis of some privileged heterocyclic skeletons. The first chapter contains a brief review on the synthetic methodologies available in the literature for the synthesis of 4-chromenones, 6*H*-benzo[*c*]chromenes, 5,6-dihydrophenanthridines and 6*H*-benzo[*c*]chromen-6-ones. The second chapter contains synthetic studies on the desilylation of TMS-protected alkyne in chromone based systems. A series of cyclic ketals and terminal alkynes have been synthesized using the developed protocol (**Scheme 1**). A mechanistic rationalization of the path-selectivity of the reaction has been provided using reaction-progress NMR and HRMS studies. The third chapter comprises of an account on judicial use of Garratt-Braverman (GB) Cyclization and Buchwald Hartwig (BH) Coupling to synthesize a series of dihydroisofuran fused 6*H*-benzo[*c*]chromenes and 5,6-dihydrophenanthridines. Crystallographic studies established their helical motif. DNA binding studies revealed weak intercalation for the benzochromene derivatives (**Scheme 2**). In the fourth chapter, a strategic combination of Garratt-Braverman Cyclization and Minisci Acyloxylation reaction has been proposed to synthesize a series of dihydroisofuran fused 6*H*-benzo[*c*]chromen-6-ones. Their DNA-binding studies revealed intercalative mode of binding (**Scheme 3**). In the fifth chapter, an attempt towards the asymmetric synthesis of sulfolene fused biphenyl-amino acid hybrids, using Garratt-Braverman Cyclization, has been reported (**Scheme 4**).



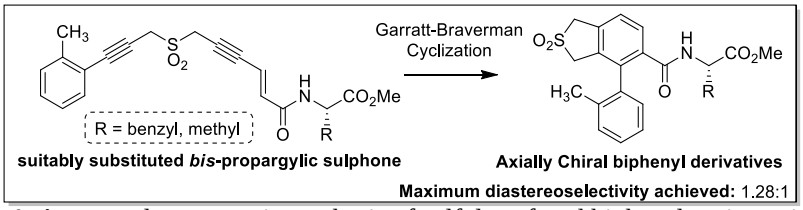
Scheme 1: Conversion of TMS-alkyne to protected ketones and terminal alkynes in 4-chromenone system.



Scheme 2: Synthesis of dihydroisofuran fused 6*H*-benzo[*c*]chromenes and 5,6-dihydrophenanthridines.



Scheme 3: Synthesis of dihydroisofuran fused 6*H*-benzo[*c*]chromen-6-ones.



Scheme 4: Attempted asymmetric synthesis of sulfolene fused biphenyl-amino acid hybrids.

Keywords: Desilylation, path-selectivity, Garratt-Braverman Cyclization, Buchwald Hartwig Coupling, Minisci Acyloxylation, Crystallographic studies, DNA-binding, Asymmetric synthesis, Diastereoselectivity.