Abstract

This Ph.D. thesis entitled "**Stereoselective 1,4- and 1,6-addition to Quinone Methides**" deals with the development of protocols for the stereoselective reactions that are divided into five chapters. The first chapter is introduction briefly describes about chiral induction and homologation approaches. Next two chapters 2 and 3 of this dissertation deal with the enantioselective [4+2] annulation reaction and vinylogous 1,6-addition reactions respectively. Chapter 4 involves the umpolung process to generate a-phosphonyloxy anion *via* [1,2]-phospha-Brook rearrangement and its subsequent addition to afford phosphate-bearing adducts. Chapter 5 is sub-divided into 5a, 5b, and 5c that involve a sequential transformation in one-pot, herein, the first step $P(NMe_2)_3$ mediates *in situ* generation of dispiro-cyclopropane adduct which in presence of Lewis acid undergoes homologation or intramolecular cyclization to furnish the corresponding products.

Chapter 1 briefly describes the Brook rearrangement and [1,2]-phosha-Brook rearrangements. The importance of chirality with various interesting examples of compounds having stereoisomers has been demonstrated. An introduction to asymmetric catalysis with an emphasis on organocatalysis has been elaborated. The homologation approaches are also described that involve the ring expansion.

Chapter 2 describes a chiral base-catalyzed cascade reaction involving *o*-quinone methides and *N*-Boc oxindoles is explored with excellent selectivities. Here, *o*-quinone methides react with *N*-Boc oxindole in presence of a chiral cinchona alkaloid-derived base that induces the chirality in the molecule and afforded substituted coumarins in good yield and selectivities.

Chapter 3 deals with the vinylogous 1,6-addition of 4-methyl-3-cyano coumarin to *p*-QMs. Here, an environmentally benign reaction condition has been achieved. The 1,6-adducts are obtained in excellent yields in milder conditions. Broad substrate scopes are shown. Also, an enantioselective version of this reaction is attempted.

In chapter 4 addition of α-ketoamide to *p*-quinone methide initiated by dialkylphosphite in presence of organic base 1,8-Diazabicyclo(5.4.0)undec-7-ene (DBU) is explored. The coupling of dialkylphosphite to α-ketoamide in presence of a base follows [1,2]-phospha-Brook rearrangement, generating corresponding α-phosphonyloxy enolates that are subsequently seized by *p*-quinone methides (*p*-QMs). The two-step one-pot 1,6-conjugate addition provides effective access to a series of isatin incorporated phosphate-bearing 1,6-adducts having two vicinal tertiary carbons with good yields and selectivities.

The chapter 5a describes Lewis acid-mediated one-carbon homologation approach involving 1,2-aryl migration of dispiro-cyclopropane intermediate aids in installing *para*-quinone methide embedded 2-quinolinone cores with high yields and regioselectivity. Also, the synthetic modifications of obtained adduct were further derivatized by C-P, C-S, and C-C bond formation. Further, cyclopropanation of 2-quinolinone embedded *p*-QMs is also demonstrated affording a contiguous quarternary spiro centre.

In chapter 5b a diastereoselective protocol for synthesis of oxindole-containing spiro-substituted phenanthrenes has been established. The dispiro-cyclopropane intermediates were generated by the coupling of isatins and 2-aryl *p*-QMs *via* [1,2]-phospha-Brook rearrangement. Subsequently, the ring opening of cyclopropane in presence of Lewis acids leads to the formation of an *ortho*-aza-xylylene intermediate that undergoes intramolecular nucleophilic attack affording desired spiro adducts in good yield and diastereoselectivities.

The chapter 5c describes an efficient protocol for synthesis of 2,3-disubstituted phenalenone frameworks has been demonstrated through one-pot procedure. Here, the sequential addition of $P(NMe_2)_3$ and Lewis acid lead the installation of phenalenone core. Firstly, $P(NMe_2)_3$ mediates the *in situ* generation of dispiro-cyclopropane ring by the coupling of acenaphthoquinone to *p*-QMs *via* [1,2]-phospha-Brook rearrangement followed by intramolecular cyclization, then Lewis acid mediate the homologation of dispiro-cyclopropane adduct to 2,3-disubstituted phenalenones. This methodology demonstrates the use of unconventional 1,2-carbonyl migration in the ring expansion affording substituted phenalenones with very broad substrate scope.