Abstract

This thesis is divided into four chapters:

Chapter 1  One pot oxidative cleavage of 1,2-arylalkenes into arylketones under microwave in aqueous conditions

Chapter 2  Domino C-C bond formation approaches for the synthesis of α,β-unsaturated carbonyl functionalized stilbenoids and unsymmetrical hydroxy distyrylbenzenes

Chapter 3  Synthesis and structure-activity relationship of some phenolic derivatives for antimalarial activity

Chapter 4  Design and synthesis of bioactive hybrid molecules possessing phenyl ethanoid and propanoid scaffolds

Chapter 1: One pot oxidative cleavage of 1,2-arylalkenes into arylketones under microwave in aqueous conditions.

The oxidative scission of C=C double bonds is a fundamental synthetic transformation and has wide spread applications in organic synthesis including total synthesis of natural products. The major utility of such cleavage reactions is due to their ability to truncate large compounds with simultaneous introduction of carbonyl function. In this chapter, a new approach has been developed for a one-pot and selective oxidative cleavage of 1,2 aryl and diaryl alkenes into one carbon shorter aryl ketones instead of arylaldehydes, thereby, providing a complementary approach to classical ozonolysis. The protocol was also extended towards a useful one-pot oxidative cleavage-condensation sequence for synthesis of α,β-unsaturated carbonyl scaffolds having aromatic as well as heteroaromatic rings.

Chapter 2: Domino C-C bond formation approaches for the synthesis of α,β-unsaturated carbonyl functionalized stilbenoids and unsymmetrical hydroxy distyrylbenzenes.

One of the central goal of contemporary organic synthesis is the realization of new strategies for sequential formation of multiple C=C bonds in one-pot. The condensation and transition metal catalyzed coupling reactions constitute two of the most fundamental C=C bond forming strategies. It would be a significant advantage if these two classical approaches can also be combined orthogonally. The present chapter describes some novel tandem reactions involving chemoselective Knoevenagel/Perkin condensation-decarboxylation-Heck or Aldol-Heck sequences. These enabled the first concise and efficient synthesis of several important hydroxy
functionalized compound classes such as stilbene-cinnamoyl hybrids a class of potent PTP1B inhibitor (antidiabetic) besides the synthesis of cinnamoyl-cinnamic acid hybrids and unsymmetrical distyrylbenzenes in one or two steps in comparison to earlier seven or eight step approaches.

Chapter 3: Synthesis and structure-activity relationship of some phenolic derivatives for antimalarial activity.

The compounds belonging to the phenolics family have found widespread applications in pharmaceuticals since the beginning of human history. Stilbenoids, a class of phenolics, exhibit a wide range of biological activities including hypolipidemic, antioxidant and anticarcinogenic. However, their antimalarial potential has not been much explored. In the present chapter, a wide range of hydroxylated stilbenoids (stilbenes, symmetrical and unsymmetrical distyrylbenzenes and octupolar molecules) have been explored for antimalarial activity against *Plasmodium falciparum*. Significantly, for the first time, \((E,E,E)-1,3,5\)-Tris(4-hydroxy-3,5-dimethoxystyryl)benzene, a trimeric stibenoid was found to be the most potent lead candidate with an IC\(_{50}\) upto 0.5 µM and proved to be non-cytotoxic against HeLa cell line.

Chapter 4: Design and synthesis of bioactive hybrid molecules possessing phenyl ethanoid and propanoid scaffolds.

The concept of hybrid molecules (i.e. a covalent combination of two or more than two pharmacophores) has attracted widespread interest for development of future generation of drugs to combat the development of resistance against the various existing drugs including antimalarial drugs. In this chapter, some novel compounds comprising natural and nature identical phenylethanoids/phenylpropanoid scaffolds i.e. stilbene-chalcone (S-C) hybrids were synthesized via a sequential Claisen-Schmidt-Knoevenagel-Heck approach and evaluated for antiplasmodial activity. The most potent hybrid \((2E)-1\{4\{[(E)-2-(4-hydroxy-3,5-dimethoxyphenyl)ethe-nyl]phenyl\}-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one showed IC\(_{50}\) (µM) of 2.2, 1.4 and 6.4 against 3D7, Indo and Dd2 strains of *Plasmodium falciparum* respectively. Interestingly, stilbene, chalcone, equimolar mixture of stilbene and chalcone, distyrylbenzene and bis-chalcone were less potent than the S-C hybrid. Further the lead compound showed good selectivity indices for HeLa (42.3) and L929 Fibroblast (45.5) cell lines.