ABSTRACT

The doctoral thesis titled "**Asymmetric Synthesis of Non-Biaryl C-C Atropisomers and Spiro-Oxindoles**" encompasses five chapters focused on the advancement of organocatalytic enantioselective C-C and C-O bond formation. Chapter 1 is introductory and briefly explains the terminology and importance of asymmetric catalysis. In chapters 2 and 3, the concept of VQM has been elaborated and axially chiral styrenes containing barbiturates are synthesized in chapter 2 while axially chiral styrenes bearing multiple stereogenic elements are constructed in chapter 3. In chapters 4 and 5, oxindole fused spiro [furo[2,3-d]pyrimidines] and spirodihydrobezofuran are synthesized enantioselectively using organocascade approach.

Chapter 1: provides a concise overview of the importance of chirality and its practical aspects with intriguing examples. It covers methods of asymmetric induction, with special emphasis on organocatalysis, followed by its brief history and modes of activation including covalent and non-covalent organocatalysis. Then, a brief introduction to atropisomerism, axially chiral styrenes, spirocycles and spiro-oxindoles is provided, followed by various challenges and strategies for synthesising them.

Chapter 2: describes the inaugural enantioselective method for axially chiral barbiturate-substituted styrenes from vinylidene *ortho*-quinone methide (VQM) derived from 1-alkynylnaphthalen-2-ols, facilitated by quinidine-derived bifunctional catalyst *via* C-5 functionalization of barbituric acids. This mild and straightforward protocol offers tolerance to a broad range of substrates bearing electronically diverse functional groups to afford axially chiral barbiturate bearing styrenes in excellent yield (up to 99%), diastereo- and enantioselectivities (up to 99%). The scale-up synthesis, post synthetic transformations and stereodivergent synthesis demonstrate its synthetic potential.

Chapter 3: In this chapter, an enantioselective methodology is demonstrated for synthesizing highly functionalized styrenes bearing multiple stereogenic elements. This methodology involves the nucleophilic addition of nucleophile generated from β-keto esters in presence of quinine-derived bifunctional squaramide catalyst on *in situ* generated vinylidene ortho-quinone methide

(VQM) from 1-alkynylnaphthalen-2-ols. A series of axially chiral styrenes bearing axial and central chirality has been synthesized successfully with excellent yield (up to 90%) and stereoselectivity (dr up to 98:2, er up to 96:4) at room temperature.

Chapter 4: Here, we have developed an unparalleled enantioselective methodology to access oxindole-fused spiro [furo[2,3-*d*]pyrimidines] with high bond efficiency, involving the formation of two new C-C bonds and one C-O bond with two contiguous stereocenters. A library of chiral spiro[furo[2,3-d]pyrimidines] with various substitutions has been synthesised with high yields (up to 90%) and exceptional stereoselectivity (dr up to 99:1, er up to 97:3) at room temperature. The scale-up synthesis, while maintaining reactivity and selectivity, showcases its synthetic potential. The reaction mechanism involving ammonium ylide and the subsequent synthesis of spirocyclopropylbarbiturate has been investigated using ^{1}H NMR and HRMS titrations.

Chapter 5: illustrates the unprecedended protocol to access chiral oxindole fused spirodihydrobezofuran *via* organocascade approach, applicable to *N*-unprotected as well as protected 3-chlorooxindoles and the spiro product formed with high bond efficiency (1 new C-C and 1 C-O bond) with two contiguous stereocenters. A series of chiral oxindole fused spirobezofuran has been synthesized successfully with high yield (up to 82%) and excellent stereoselectivity (dr and er up to 99:1) at room temperature. Further, the potential practicality of the protocol is shown by gram scale and stereodivergent synthesis without compromising the reaction outcome. Dynamic HRMS titrations have been conducted to propose the reaction pathway.