EXECUTIVE SUMMARY

of

UGC Major Research Project

entitled

L-Ascorbic Acid in Organic Synthesis: Asymmetric Synthesis of Bioactive Molecules. Studies Towards Synthesis of (-)-Cleistenolide, (+)-Goniotriol, (+)-Crassalactone A, (+)-Howiionol A, 2-C/3-C-alkyl Derivatives of L- Ascorbic Acid and Gulono-1,4-lactone Derivatives via The Paternò-Büchi Reaction.

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Executive Summary of the Research Project

Part-1: Studies towards synthesis of (−)-Cleistenolide

Simple methodology for construction of 5,6-dihydropyran-2-ones is developed from cheep starting material i.e. L-ascorbic acid. The key reactions involved in the above methodology include catalytic hydrogenation of L-ascorbic acid, Stille-Gennari olefination, One-pot deprotection followed by lactonisation sequence. This methodology is used in the total synthesis of (−)-Cleistenolide. The present protocol can be a good alternative to the reported methods for the synthesis of (−)-Cleistenolide. The catalytic hydrogenation of L-ascorbic directly induced two chiral centers. Thus L-ascorbic acid can also be used as a precursor for the synthesis of natural products having four chiral centers.

Part 2: One-pot synthesis and evaluation of novel 3-aryl-6-ethoxycarbonyl-4-hydroxy-2h-pyran-2-one as a potent cytotoxic agent.

We have synthesized a series of 3-aryl-6-ethoxycarbonyl-4-hydroxy-2H-pyran-2-one by one pot approach. Our method is metal free synthesis of α-pyrones, the synthetic procedure is straightforward, undemanding since it uses readily available starting materials and reagents, easily removable solvent and provides simple product isolation by non-chromatographic method like recrystallization. We have completed synthesis of seventeen compounds in overall good yields using this four step reaction procedure into a one-pot paradigm. Our methodology is highly regioselective and offers a number of advantages: firstly, it allows simple and highly efficient synthesis of multiple functionalized pyran ring structures which are of chemical and pharmaceutical interest and it is time efficient, more user-friendly and has wide scope.

These compounds are open-chain analogues of phelligridin J and evaluated as cytotoxic agents against human breast cancer (MCF-7) and normal fibroblast cells (NIH3T3). Compound 6-6thoxycarbonyl-4-hydroxy-3-phenyl-2H-pyran-2-one found to be two fold selective with IC_{50} values of 21.8 and 43.4 μM however, another compound 6-ethoxycarbonyl-4-hydroxy-3-(naphthalene-2-yl)-2H-pyran-2-one found to be the most potent with IC_{50} values of 12.39 and 13.76 μM against MCF-7 and NIH3T3 respectively.

Part 3: L-Ascorbic acid derived novel fused bicyclic Oxetanes via The Paterno Büchi reaction: Synthesis and biological evaluation as antiproliferative agents.

In this part we have developed a versatile strategy for preparation of diversely functionalized fused oxetane bicycles and oxetane derivatives, involving alkoxy, hydroxy methyl, alkyl, and aryl substituents. A wide variety of functional groups have been

introduced on the oxetane ring, accessing new chemical space. These compounds were tested for growth inhibition against MCF-7 breast cancer cell line, some of the compounds showed promising cytotoxic activity. We believe that these oxetane motifs will provide interesting new structural elements for medicinal chemistry programs as well as in organic synthesis.

Key words: Carbohydrates, (–)-Cleistenolide, α-pyrones, Oxetanes, cytotoxicity.