Preface

The present thesis entitled “DESIGN, SYNTHESIS AND STUDIES ON THE ACTIVITIES OF BIOLOGICALLY RELEVANT MOIETIES” contains the research work carried out during the period of 2012-16. It has been divided into two parts: part I and part II. Each part is further subdivided into three chapters.

Part I

Chapter 1: A brief review on O- and N-formylation reactions

This chapter contains a brief literature review and the research problems on O- and N-formylation reaction that we intend to solve and the plans for solving these problems.

Chapter 2: Understanding the efficacy of N,N-dimethylformamide and oxalyl chloride combination as chemoselective O-formylating agent: An unified experimental and theoretical study

In this chapter we have reported a simple, general, and efficient method for selective O-formylation of a wide spectrum of aromatic hydroxyl groups in the presence of other sensitive functional groups using DMF and (COCl)₂ combination as a formylating agent. The method is free from addition of any metal catalysts and works well at ambient temperature, providing the desired O-formylated product with moderate to good yield. Again we have also performed DFT-based theoretical studies on the structural parameters of various reacting components involved in the present synthetic protocol. On the basis of theoretical results, we have proposed an explanation for the efficacy and chemoselectivity of DMF and (COCl)₂ combination as O-formylating agent for a wide range of phenolic substrates.

Chapter 3: Solvent- and catalyst-free N-formylations of amines at ambient condition: Exploring the usability of aromatic formates as N-formylating agents

In this chapter we have developed a solvent and catalyst free N-formylation protocol for amine type of compounds using aromatic formates as the N-formylating agents. The reaction condition is mild, easy to operate and it occurs smoothly under ambient conditions.
condition giving high yield of formamide derivatives of the corresponding amine substrate. This method is applicable to wide varieties of amine substrates ranging from aromatic amines (both primary and secondary) as well as aliphatic amine to a primary amide type of functionality.

Part II

Chapter 4: Review on the interaction of DNA with small molecules having chromophoric or fluorophoric behavior

This chapter contains a brief literature review on the binding interaction of small molecules having chromophoric/fluorophoric nature with bio-macromolecule like DNA.

Chapter 5: Fluorescent small molecules are BIG enough to sense biomacromolecule: Synthesis of aromatic thioesters and understanding their interactions with ctDNA

This chapter contains the development of easy and low cost synthetic methodologies for the syntheses of four structurally and photochromically different thiophenyl derivatives among which (1-3) are thiophenyl esters of p-hydroxycinnamic acid and (4) is a novel stilbene type compound substituted with dimethylamine and thiophenyl groups from p-hydroxycinnamic acid using (COCl)2/DMF and Ph-SH/Et3N in DCM medium at ambient temperature.

However, (1) and also (2) showed a drastic change in their intrinsic chromophoric/fluorophoric activities during their interactions with ctDNA. Spectroscopic (UV-Vis, fluorescence and CD) and viscometric measurements indicated the intercalation mode of binding between these thiophenyl esters (1/2) and ctDNA. However, results of a preliminary molecular docking study indicate the possibility of minor groove binding mode of (hydrogen bonding) interaction of 1 (or 2) with ctDNA. It is interesting to note that structurally these compounds satisfy both the characteristics of intercalator and groove binders for DNA. These two compounds have single bonded flexible parts for which torsional rotation of the molecule (1 or 2) is possible. This may help these molecules to be fit into the shallow minor groove of DNA. On the other hand, 1 or 2
planar parts (aromatic rings) which can allow them to interact with DNA through intercalation mode. So it is quite possible that these compounds are not perfect intercalator or perfect grooved binder of DNA.

Chapter 6: Understanding the interaction of ctDNA with an antioxidant flavone analogue: Exploring the utility of small molecules as fluorescent probe for biomacromolecule

In this chapter we have reported the interaction of 4′- N, N- dimethylamino-3- hydroxy flavone (DMAHF) with ctDNA by applying spectroscopic (UV-Vis, fluorescence and CD), viscometric measurements and molecular docking studies. DMAHF possibly binds the B-form of DNA at its minor groove through hydrogen bonding interaction. DMAHF is often considered as a prototype ESIPT fluorophore and we have seen that binding interaction between DMAHF and ctDNA has a pronounced effect on its ESIPT based dual emission behavior. This change of intrinsic fluorescence activity of DMAHF in the presence of biomacromolecules like ctDNA opens up the possibility for the application of this antioxidant small molecule as fluorescence probe for DNA based biomarkers.