Abstract

The dissertation entitled "Synthetic receptors for cations and carboxylate-based anions" embodies in detail the design and synthesis of molecular architectures that are capable of binding cations and anions of interest. In the present state of art, it has been possible to rationally design a series of compounds using the different hydrogen bonding groups as well as metal binder units for selective binding of anions and cations, respectively. The dissertation consists of two parts. Part-I describes cation binding and part-II deals with the recognition of carboxylate-based anions.

Cation plays many roles in biological processes. Concentration gradients of cations across cell membranes usually maintain potentials that are used to transport organic substrates into cell. They are associated with triggering of muscle contraction and also involved in the transmission of nerve impulses. Metal cations play vital roles in enzymes, stabilizing the polypeptide tertiary structure. Moreover, metal ions have serious effects in environment. Therefore, there has been a great deal of effort aimed at producing selective receptors for cationic guests.

Similarly, anions also play essential roles in many processes, both chemical and biological. Of the different anions, selective complexation of carboxylate anions by natural and synthetic hosts is a topic of interest in bioorganic and supramolecular chemistry as a large number of drugs like antibiotics, analgesics, anti-inflammatory agents contain carboxylic acid functionality. Enzymes, antibodies, amino acids and metabolic intermediates as well as the other natural products, contain a range of carboxylate functionalities that account for the characteristic biochemical behavior. It is worth noting the special role that carboxylate recognition plays in determining the biological activity of the vancomycin family of antibiotics. Di- and tri-carboxylates are the essential components of numerous metabolic processes, including for instance, the citric acid glyoxalate cycle. They are also involved in the formation of high energy phosphate bonds in our body.

The enantioselective recognition of chiral carboxylates is also an important goal, because several pharmaceutical compounds possess this functional group. Devise of efficient synthetic receptors for carboxylate anion recognition has thus been challenging. Among the different carboxylic acids, \( \alpha \)-hydroxycarboxylic and aminocarboxylic acids are considered to be important due to their biological
significance and also their use as useful synthon in synthetic organic chemistry. In the present case, the recognition of a particular enantiomer of either $\alpha$-hydroxy or $\alpha$-aminocarboxylic acid over their mirror image isomers draws attention. In order to be familiar with the recognition of such relevant species it was planned in the present research program to design and synthesize receptors of different topologies. Typically, receptors are of abiotic origin that are able to bind selectively and reversibly the analyte of interest with a concomitant change in one or more properties of the system, such as absorption or fluorescence spectra. In this aspect, the fluorescence-based receptors are of special attention both in terms of their cost effectiveness and high sensitivity and availability of wide number of opportunities for modulation of photophysical properties of a fluorophore (proton, energy and electron transfer, heavy atom effect and change of electron density etc.). With these in mind the content of the thesis has been divided into five chapters. Brief outlook of each chapter is described below.

Chapter-1: This chapter describes the introductory part in supramolecular chemistry / molecular recognition. Supramolecular chemistry refers to the domain of chemistry beyond that of molecules and focuses on the chemical systems made up of a discrete number of assembled molecular subunits or components. The forces responsible for the spatial organization may vary from weak to strong in nature. The study of non covalent interaction is crucial to understanding many biological processes from cell structure to vision that rely on these forces for structure and function. The multidisciplinary nature of this field has brought about wide-ranging collaborations between physicists, theorists and computational modelers, crystallographers, inorganic and solid-state chemists, synthetic organic chemists, biochemists and biologists. This fascinating and dynamic research area is now recognized worldwide as an important and technological frontier in chemistry. This introductory chapter thus highlights some general aspects of supramolecular chemistry or molecular recognition utilizing examples from the literature. At the end of this chapter organization of thesis and aim of the present research program have been cited.
Chapter-2: This chapter has been divided into two sections. Section A of this chapter introduces a review on tripodal shaped receptor modules that are critically important in cation recognition. Section B describes the present work, related to the design and synthesis of tripodal receptors derived from substituted morpholine lactone. The key aspect to the design of tripodal receptors is to exploit the fluorophore labeled morpholine lactone in synthesizing a series of molecules 2AB.1 – 2B.6 of different architectures. On subtle variation of molecular component in the designs led to selective recognition of different metal ions.

Chapter-3: This chapter has also been divided into two sections. Section A deals with the review on the cation sensors built on rhodamine motif. Rhodamine - labeled chemosensors are considered to be productive towards metal ions due to switching in between the spirocyclic form (which is colorless and non fluorescent) and the ring-opened amide form which is colored and strongly fluorescent.
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Section B of the chapter reports the present work on rhodamine-based molecular receptors 3B.1 – 3B.7. It is mentionable that we took initiative towards the development of new systems that are simple, easy-to-make and reusable. In this regard, a simple, general and effective strategy to immobilize rhodamine-labeled receptor onto the Merrifield resin to yield sensor bead which are reusable and reports the presence of a particular metal ion in water by exhibiting change in emission and color has been undertaken.

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**Chapter-4:** This chapter has two sections. Section A describes the survey on the synthetic receptors that are capable of recognizing and sensing of amino acids and small peptides. The development of
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synthetic receptors for peptides and amino acid derivatives is of considerable interest because the intermolecular interactions involved in small molecule-peptide complexes are of direct relevance to many biological peptide-protein interactions, and may also lead to new bio-sensors, therapeutics and catalysis for peptide hydrolysis.

Peptides as a substrate are interesting for two reasons - their biological significance and their chemical structure. First, there are many biochemical or medicinal processes, for example enzymatic activity, bacterial infections, or neurodegenerative diseases, in which a selective molecular interaction of a peptide with another molecule or with itself (self-association) plays a decisive role. Hence study of artificial receptor systems capable of selective binding to a specific peptide may help to understand the peptide-molecule or peptide-peptide interactions on a detailed molecular basis. Second, beside this biological significance, peptides have a large variety of different potential binding sites for a receptor molecule to bind to - an amide backbone with hydrogen bond donors and acceptors and side-chains with polar and non-polar groups. In addition to the hydrogen bond network to the peptide backbone, salt bridges to ionic amino acid residues (as in arginine, lysine, aspartic acid, etc.) or at the termini of the peptide (carboxylate or ammonium) and hydrophobic interactions with apolar side-chains (as in phenylalanine, valine, leucine) can further stabilize the receptor-substrate complex. These are introduced in brief in the review. Based on the review of the literature, the framed objectives were fulfilled in sections B and C of this chapter.

Section B addresses the present work on the design and synthesis of some pyridinium and naphthyridine - based molecular receptors (4B.1-4B.4) that are capable of recognizing N-protected α-aminocarboxylates. In the designs, urea, amide functional groups cooperatively act as H-bond donors with the charged pyridinium and neutral naphthyridine motifs to complex the guests. In addition to this, the design and synthesis of anthracene-labeled pyridinium -based molecular receptors 4B.5 and 4B.6 are documented in this chapter. In the designs, the small peptide side chains are derived from L-amino acids. The fluorometric binding properties of these optical sensors 4B.5 and 4B.6 for N-protected small peptides with a carboxylate terminus have been cited.
Chapter- 5: This chapter contains two sections.

Section A describes the progress on the artificial chiral receptors in the literature for enantioselective sensing of α-hydroxy and aminocarboxylic acids or their derivatives. The development of chiral artificial receptors, which have the properties of chiral recognition and chiral catalysis, has attracted considerable attention, because recognition and catalysis are fundamental characteristics of biochemical systems and could contribute to the development of pharmaceuticals, enantioselective sensors, catalysts, enzyme models and other molecular devices.
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Section B represents the present work on the optical sensors 5B.1 - 5B.5, linked with enantioselective sensing of α-hydroxycarboxylates (mono-/dicarboxylates). The sensors are urea, benzimidazole and pyridinium-based. L-Valine has been taken as the chiral source of the sensors. Sensors exhibit good response towards the enantioselection of tartrates.