PREFACE

The porphyrinogens are hexahydroporphyrins in which the four pyrrole rings are linked together by methylene instead of the methine bridges of porphyrins. They are reduced porphyrins. Uroporphyrinogen III plays central role in the synthesis of vital compounds called as life pigments and is formed by condensation of four porphobilinogen (PBG) molecules catalysed by PBG deaminase (hydroxymethylbilane synthase) to hydroxy-methylbilane, followed by cyclisation of hydroxymethylbilane to uroporphyrinogen III catalyzed by uroporphyrinogen III synthase. Uroporphyrinogen III is the universal intermediate of all cellular tetrapyrroles, including haem, chlorophyll, corrin, cytochromes, sirohaem and vitamin B_{12}.

This thesis entitled “Synthesis of selected porphyrinogens and their non-covalent interactions” report the synthesis of a selected porphyrinogen and their applications in catalysis and non-covalent interactions. The thesis has been divided into five chapters. Each chapter has been subdivided into six sections: Introduction; Brief Review; Results and Discussion; Conclusion; Experimental and References.

Chapter I deals with synthesis of selected 3,4-disubstituted pyrrole and their use in the synthesis of porphyrinogen in different reaction conditions. It begins with an overview on the biosynthesis of porphobilinogen a natural 3,4-disubstituted pyrrole, structure, biosynthesis, biomimetic synthesis, theoretical and experimental detail for the mechanism of the synthesis of porphobilinogen. The symmetrical 3,4-disubstituted pyrrole core has special interest since the combination of these monomers with an aldehyde results in highly substituted porphyrins and with ketones results with an meso substituted porphyrinogens. These resulting 4-fold symmetric macrocycles are key molecules that are the basis for a large variety of synthetic and physiochemical studies. The synthesis of 3,4-disubstituted pyrroles have been carried out by the reaction of Tosylmethyl isocyanide and suitable alkenes in a stepwise manner and represented by appropriate schemes. Alkenes used for the synthesis of pyrroles were synthesized by the base catalyzed reaction of aldehyde with different ketones. The reaction of 5-aminolevulinic acid hydrochloride with different diketones under milder condition was
also examined and 3,4,5-trisubstituted pyroles were synthesized under milder condition taking water as a solvent. These trisubstituted pyroles were used in the synthesis of β-substituted porphyrinogen. The structures of the β-substituted porphyrinogens were characterized by different spectroscopic techniques for example UV-Visible, $^1$H NMR, ESI-MS, and IR spectroscopic methods. There non-covalent interaction behaviors were examined by concentration dependent studies and anion binding studies through UV-visible titration.

**Chapter II** describes anion templated synthesis of calix[4]pyrroles and N-confused calix[4]pyrroles and their non-covalent interaction with different anions. Calix[n]pyrroles, previously named as acetone-pyrrole and fully meso-substituted porphyrinogens, are oligopyrrolic macrocycles produced by the condensation of a pyrrole and ketones (n represents the number of pyrrole units in the molecule). Calixpyrrole, as the name implies, offer a cup-shaped skeleton, in which four pyrrole hydrogen bond donors are ideally pre-organized for anions and ion pair binding. Chapter presents the brief introduction on ion-pair receptors and role of calixpyrrole as an anion pair receptors based on their pyrrole units. Calix[4]pyrroles exist into four conformations: 1,3-alternate, 1,2-alternate, partial cone and cone. The 1,3-alternate is most stable and lowest energized wherein adjacent pyrrole rings are oriented in opposite directions to each other in unbound conditions. Whereas in the presence of anions, the molecule adopts a cone-like conformation with the anion sitting above the cone and forming four hydrogen bonds with the four pyrrole N-Hs and is calculated to be most stable. The octamethylcalix[4]pyrroles and N-confused octamethylcalix[4]pyrroles were synthesized by acid catalyzed reaction of acetone and pyrrole in presence of different anions in different reaction conditions.

Cyclocondensation reaction of pyrrole with acetone where examine in the presence of anion and without anion taking different acids and their comparative yield and time were measured. Further the reaction of pyrroles and acetone were also carried out in different solvents and the reaction yield was best observed in the case of dichloromethane as a solvent. The reaction of 2-hydroxymethyl pyrrole in the presence of tetrabutylammonium fluoride and acid gave meso-unsubstituted porphyrinogen and N-confused porphyrinogen. Their interaction with anion has been examined by the $^1$H
NMR spectroscopy. Anions templated synthesis of calixpyrroles and N-confused calixpyrroles were less time consuming with high yields of desired products. The reaction of pyrrole with different ketones were performed in presence of methane sulfonic acid in dichloromethane using different anions as template and best results were obtained when F\(^{-}\) anion was used as a template due to the smaller size and greater affinity to bind with calixpyrrole and N-confused calixpyrrole.

Chapter III deals with the synthesis calix[4]pyrroles and calix[6]pyrroles and their non-covalent interactions with different ionic liquids. Ionic liquids (ILs) are potential environmentally benign solvent for a variety of reactions. Apart from their use as solvents, ILs are also used as catalyst, scavengers and reagents. Various biodegradable and advance ILs have been prepared for many organic transformations. The task-specific ionic liquids are prepared by introducing desired functional groups to either organic cations or anions part of the ILs to catalyzing specific reactions. The improved, economical, eco-friendly syntheses of calix[n]pyrroles have been achieved under milder conditions using task-specific ionic liquids. The products were purified by column chromatography and the structures were confirmed by IR, \(^1\)H NMR, \(^{13}\)C NMR and ESI-MS spectroscopy. Effect of catalyst, cationic and anionic counterparts of ILs, solvent and concentration were examined in the formation of products. The non-covalent interactions of 5,5,15,15 meso-tetramethyl-10,10,20,20-tetraethyl-calix[4]pyrrole and 5,5,15,15,25,25-hexamethyl-10,10,20,20,30,30-hexaethyl calix[6]pyrrole with different ionic liquids have been studied by \(^1\)H NMR and UV-visible spectroscopic technique in acetonitrile at room temperature. The acidic ILs having trihalogenated anionic group shows dominant product as calix[6]pyrrole, this shows that acidic ILs with trihalogenated anionic group act as catalyst as well as template for the synthesis of calix[6]pyrrole.

Chapter IV deals with the synthesis of carbaporphyrinogen and heterocarbaporphyrinoids by the reactions of azulene and their non-covalent interactions. Core modified novel carbaporphyrinogen 5,5,10,10,15,15,20,20-octamethyl-22,24-dithiadiazuli porphyrinogen have been synthesized by the reaction of 2,5-bis(1-dimethyl-hydroxymethyl)-thiophene with azulene which was synthesized by the reaction of 2,7-dimethyl-octa-3,5-diyne-2,7-diol with NaSH in methanol under nitrogen atmosphere.
followed by reaction of silver acetate under nitrogen atmosphere at room temperature. The structure of the compound was characterized by $^1$H NMR, $^{13}$C NMR and ESI-MS spectroscopy. The non-covalent interactions of 5,5,10,15,16,20,21,26-octamethyl-22,23-dithiadiazuli porphyrinogen and 5,10,15,20-tetra-(4-tert-butyl-phenyl)-22,23-dithia/dioxo diazuliporphyrinogen with mercury (II) perchlorate have been studied by UV-visible spectroscopic technique in DMSO at room temperature.

5,10,15,20-tetrakis(6-azulenyl)porphyrin was synthesized by the reaction of tetra-(4-pyridyl)porphyrin,1-chloro-2,4-dinitrobenzene and 2M THF solution sodium cyclopentadienide. Their comparative spectroscopic and emission properties were studied with 5,10,15,20-tetra-anthrylporphyrin and 5,10,15,20-tetra-2-naphthylporphyrin to understand the properties of 5,10,15,20-tetrakis(6-azulenyl)porphyrin.

**Chapter V** describe the organocatalytic synthesis of different 5,5'-disubstituted dipyrromethane and calix[4]pyrroles and their use in organocatalysis. Organocatalysis is a purely organic and metal-free small molecule catalyzed chemical reaction. Hydrogen bonding acts as a ubiquitous glue to sustain the intricate architecture and functionality of proteins, nucleic acids and many supramolecular assemblies in nature. In addition to its primacy as a structural determinant, hydrogen bonding also plays a crucial role in catalysis. Calix[4]pyrroles are conformationally flexible macrocycles of significant importance due to their binding under different conditions with anions, neutral substrates and metal ions. These are macrocyclic compounds are capable of binding anions and neutral molecules by means of multiple hydrogen bonds with their pyrrolic NH units. As hydrogen bond donors, calixpyrroles act as hydrogen bond donors in the organocatalytic reactions reported for taddols, binols, urea and thiourea derivatives.

The reaction of the pyrrole with different ketones in the presence of 10 mol% solution of piperidinium, pyrrolidinium and prolinium tetrafluoroborate in aqueous THF was performed and the better yields of dipyrromethane and calix[4]pyrrole were obtained. Reactions of epoxides with elemental iodine and bromine have been examined using calix[4]pyrrole as catalyst. The solution of iodine, iodine monochloride and iodine monobromide in dichloromethane was added to a stirred solution of catalyst and styrene.
oxide in dichloromethane at room temperature. The product obtained from the reaction shows regioselectivity and selectively 2-halo-1-phenylethanol was formed, which appears to be opposite to that observed in the ring opening of the same epoxides with aqueous hydrohalogenic acids, under classic conditions. The regioselective halohydrin formation may be explained the use of calix[4]pyrrole as a organocatalyst in the ring opening of epoxide. The reactivity of the halide anion in the reaction is governed by solvent polarity, non-covalent reaction of calixpyrroles and temperature of the reaction mixture.