Molecular recognition of Anions by Novel functionalised Porphyrins,

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ABSTRACT

The design and syntheses of receptors for the molecular recognition of anion is a difficult area in Supramolecular chemistry. This field of research has been receiving increasing attention, considering the significant and indespensable role anions play in nature. Several hosts molecules have been designed, synthesized and anion recognition studies investigated over the years. These include protonated polyamines, quaternary ammonium derived receptors, Lewis acid receptors incorporating Sn, Si, Hg, B, Ca, Ag^+ Lewis acidic centers, positively charged cobalticinium amido, bipyridine amido, calixarenes amido, neutral ferrocenoyl amido, uranyl amido based receptors, calixarenes urea and thiourea hosts amongst others. However, anion recognition by porphyrins is even a more difficult area. Investigations have recently been started and the results obtained so far are very promising. This paper gives an account of the evolutionary trends in Anion recognition by novel functionalised porphyrins. [Nature and Science. 2008;6(3):22-42]. ISSN: 1545-0740.

Dr. Raymond C.Jagessar was born in Guyana, South America. He obtained his BSc degree from the University of Guyana with Honours and was awarded an Oxford scholarship to pursue his PhD in Supramolecular chemistry. At the University of Oxford, he worked on "Anion recognition by novel functionalized porphyrin". After completing his PhD in 1995 he was offered post doctoral research fellowships at Wichita State University and University of South Carolina. At Wichita State University he continued with the Design and syntheses of Porphyrin urea anion receptors for selective recognition and their applications. At the University of South Carolina, he worked on the design and synthesis of "Porphyin based molecular wires and their applications". He is currently a Senior lecturer in the Department of Chemistry, Faculty of Natural Sciences, University of Guyana, South America. Also, currently a member of the American Chemical Society, the Royal Society of Chemistry, the Caribbean Academy of Scientists and a chartered Chemist (CChem) of the Royal Society of Chemistry.

i. Introduction

Anion recognition is an important area of increasing research in Supramolecular chemistry[1]. This originate from many fundamental roles anion play in nature: biologically, chemically, biomedically and environmentally. Biologically, in enzymatic processes, many substrates are anionic in nature. For example, seventy percent of naturally occurring enzymes require an anion, either as a substrate or as a cofactor. The genetic DNA and RNA are polymeric anions. Chemically, anions act as nucleophiles (e.g CN^-, S^{2-}), redox active agents (e.g $S_2O_8^{2-}$), bases (e.g –OR) and as phase transfer agents and catalysts. Environmentally, anions such as nitrate and phosphate constitute a large proportion of current pollutants that cause "eutrophication" of rivers.Considering all these important roles anions fulfill, there is a need for the design and syntheses of anion receptors that can detect and exhibit a high degree of selectivity and strength of binding in highly competitive polar solvents such as DMSO and H_2O. An ideal situation would be a model system that can complex anion selectively in aqueous system considering anions in the environment are found dissolved in water. Medicinally, anions operate in an aqueous system in our body and not in organic solvents such as $CHCl_3$ or CH_3CN. Such receptor would be an excellent candidate to cleanse the aqueous

environment of anionic waste and useful in the field of medicine and biology. Thus, aqueous anion receptors are scarce in constrasts to organic based anion receptors.

The evolution of anion recognition started with the development of positively charged receptors, incorporating ammonium[2] and guanidinium[3] binding sites whose main motif of binding depended exclusively on coulombic or directional electrostatic attractions. Hydrogen bonding sites have also been incorporated to provide additional binding energy as encountered in the binding of Cl^-,F^-,Br^-, N^{3-}, Zwitterion, *w*-aminocarboxylate anions[4] etc. Guandinium[5] hydrogen bonding receptors have also been used for the complexation of carboxylate anions[6]. This was followed by the development of neutral receptors possessing neutral polar hydrogen bonding donor and acceptor groups such as –NHCO- or carboxyl groups that complex anion via anion hydrogen bonding interactions i.e anion----NHCO-.Subsequently, is the development of receptors incorporating Lewis acidic centers such as tin[8], silicon[9], boron, mercury[10] etc. In principle, the complexation is based on the interaction between the Lewis acidic centers and the anion. The binding strength can be further augmented by the incorporation of hydrogen bonding sites as is seen with uranyl amido salophen receptors selectively binding phosphate[11]. To improve the potency of the receptors, positively charged sites, acting cooperatively with hydrogen bond donor and acceptors groups were incorporated in the receptors. This include the syntheses of ferrocene, cobalticinium, bipyridine and calix(n)arene amido[12] and urea receptors[13] etc. Previously, there has been slow progress in the field of anion recognition and coordination. This has been due to the properties of anion. These include variable size, geometry, solvation energies, pH dependence and the charge of the anion[14],[15].

There are several organic host molecules, both acyclic and macrocyclic that have been used recently for anion recognition. These include ferrocene and cobalticinium amides, acyclic and macrocyclic bipyridine amides, calix(4) arene amido and urea macrocyclic receptors[12],[13]. However, there is no report of anion recognition by a naked porphyrin, such as a tetraphenylporphyrin.

Porphyrins are very attractive hosts to be used for anion recognition studies since they are spectrophotoelectroactive, allowing anion complexation to be monitored by a variety of physical methods. Also, porphyrin is an important ingredient of life in the oxygen binding haemoglobin of blood and the sunlight trapping chlorophyll of plant cell. Interestingly, anion recognition by porphyrins has received very little attention until recently [16-19]. The free neutral tetrapyrrolic ligand (1) has no anionic binding power on its own [20,21]. This is due to the small size of the porphyrin cavity which doesn't complex anions via convergent N-H---- anion hydrogen bonding interactions. Also, the rigidity of the porphyrin skeleton and cavity. Hence, this has given birth to the expansion of the porphyrin cavity via the insertion of one or more pyrrolic units in "expanded porphyrins", Fig 1.0. Amongst these are the sapphyrins(3) which complex anion only in its protonated state and exhibit modest anion selectivity due to non-directional coulombic interactions. For example, sapphyrin in its diprotonated state formed a very stable fluoride and phosphate complex in methanol ($K_{assn} = 1 \times 10^5\ M^{-1}$) [22].

It has been shown that a hexaprotonated porphyrin trimer system linked by butadiene linkages (4) complexes large anionic clusters such as $SiW_{12}O_4^{4-}$ and $Os_{10}C(CO)_{24}^{2}$-. However, this review is concerned primarily with Anion recognition by novel functionalised Porphyrins, mainly " Picket Fence" amido and " Picket Fence" urea porphyrins.

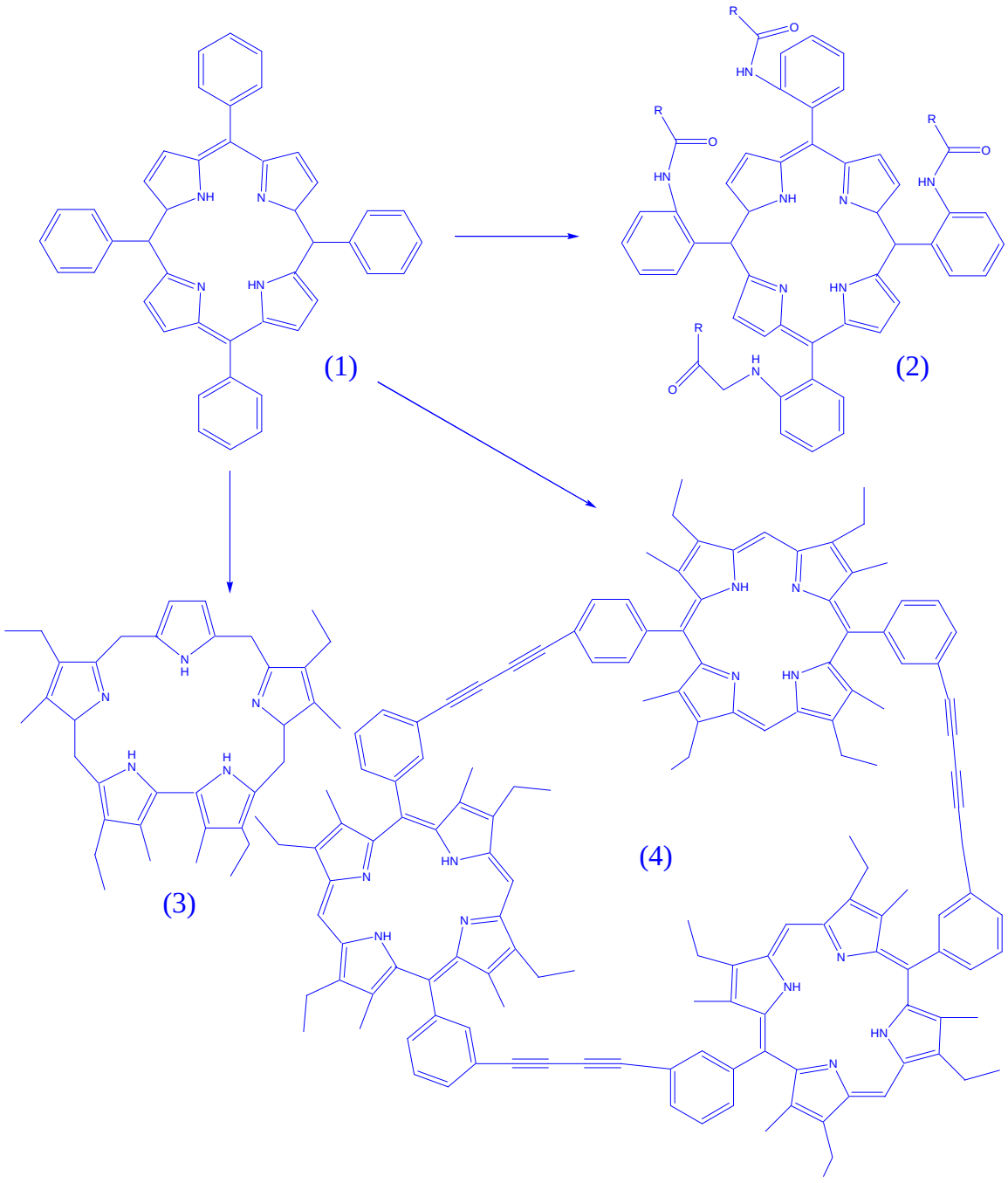


Fig: 1.0: Evolutionary trends in Anion recognition by porphyrins and porphyrinoid compounds.

Anion complexation can be monitored by several means. Below is a description of various approaches used to monitor anion complexation or binding.

ii. Monitoring Anion Complexation

Anion complexation can be monitored using ^{1}H NMR titration studies, UV/Vis, Electrochemical and X-ray studies.

^{1}H nmr studies is conducted by the addition of tetrabutylammonium salts $Bu_4N^+X^-$ (X= Cl^-, Br^-, NO_3^- or HSO_4^-) to deuterated CD_2Cl_2, $CDCl_3$ or d_6-DMSO solutions of the receptor and monitoring the shifts in the host (porphyrin) protons. The concentration of the receptor is usually 0.01 $moldm^{-3}$. The initial ^{1}H nmr spectrum of the porphyrin receptor is recorded.This is followed by the addition of stoichiometric amount of anion. After each addition, the ^{1}H nmr profile is recorded and changes in the chemical shifts of diagnostic protons observed. Also, overall changes in the spectrum recorded. This include the appearance and disappearance of peaks. Host protons monitored are amide –NHCO-, aromatic ArH and substituent protons etc. The amide protons are labile and are the best to study since they are the most sensitive to the negatively charged electrostatic anion field via anion hydrogen bonding interactions viz anion----NHCO. From the ^{1}Hnmr titration studies, the displacement of chemical shifts in the host respective proton is plotted versus the number of equivalents of anion added to yield titration curves from which the receptor anion stoichiometry can be obtained i.e whether a 1:1 or 2:1 complexation via mole ratio method, EQNMR and Job's plot. From the shifts in the host protons, the computer program EQNMR can also be used to estimate the stability or association constants of binding.

The magnitude of the association constants gives an indication of the strength, degree and selectivity of anion binding. Also, it can indicate the mode of anion binding.

Anion complexation can also be monitored by UV/Vis spectral titration studies. This works well for hosts that posses strong and distinct UV/Visible spectroscopic bands or chromophore i.e richly photoactive resulting from the conjugated nature of the molecule. The porphyrin host molecule is a good UV/Visible host as it possess an intense Soret band of high extinction coefficient and four visible satellite bands of much lesser intensity (S_1,S_2,S_3 and S_4). In a metalloporphyrin, two of these are not evident as a result of a change in the symmetry of the porphyrin host from d_{4h} to d_{2h}. Also, the intensity of these bands will differ pending the type of "Picket fence".

UV/Vis spectroscopic complexation involve the addition of stoichiometric amounts of anions usually as their tetrabutyl ammonium salts: $Bu_4N^+X^-$, X= Cl^-, Br^-, NO_3^- or HSO_4^- to a dilute solution of the receptor of appropriate concentration in a cuvette. The initial spectrum is also recorded. This is followed by the addition of stoichiometric amount of anion and recording the spectrum. Changes in absorbance of diagnostic bands are observed. Titration curves are generated by a plot of change in absorbance versus the equivalents of anion added. The association constants are found using specific computer programs such as EQNMR[24].

The porphyrins is electro or redox active, having defined electrochemical redox waves, p/p^+, p^+/p^{2+} p/p^- and p^-/p^{2-}. The incorporation of redox active moieties further augments the redox properties of the porphyrins. As with other studies, the electrochemical nature of the free base porphyrin is recorded in a suitable solvent (CH_2Cl_2/CH_3CN) in the presence of conducting electrolyte. This is followed by the addition of stoichiometric amounts of anion. After each addition, the electrochemical nature of the host is recorded and compared with the initial electrochemical wave. Specific computer programs are then used to calculate the association constants of binding.

The uncomplexed functionalised porphyrin anion receptor is characterized by a spectral and electrochemical property, Spr and Epr. Upon complexation with substrate such as an anion, it emits a different spectral signal and electrochemical waves. This porphyrin superanionmolecule is characterized by a spectral and electrochemical property, Spr2 and Epr(2). If the binding is reversible, the porphyrin supramolecule can release the bound anion and return to its initial spectral and electrochemical state, Spr and Epr, Fig 2.0. Hence, performing the function of a spectral and electrochemical sensor and also as a transport mimic. Binding is not always reversible. The porphyrin supramolecule can retain the complex anion or if it does release it, its spectral and electrochemical properties changes. To investigate these hypotheses, the design and syntheses of ferrocene and cobalticinium atropisomeric " picket fence" porphyrins based anion receptors were initiated.

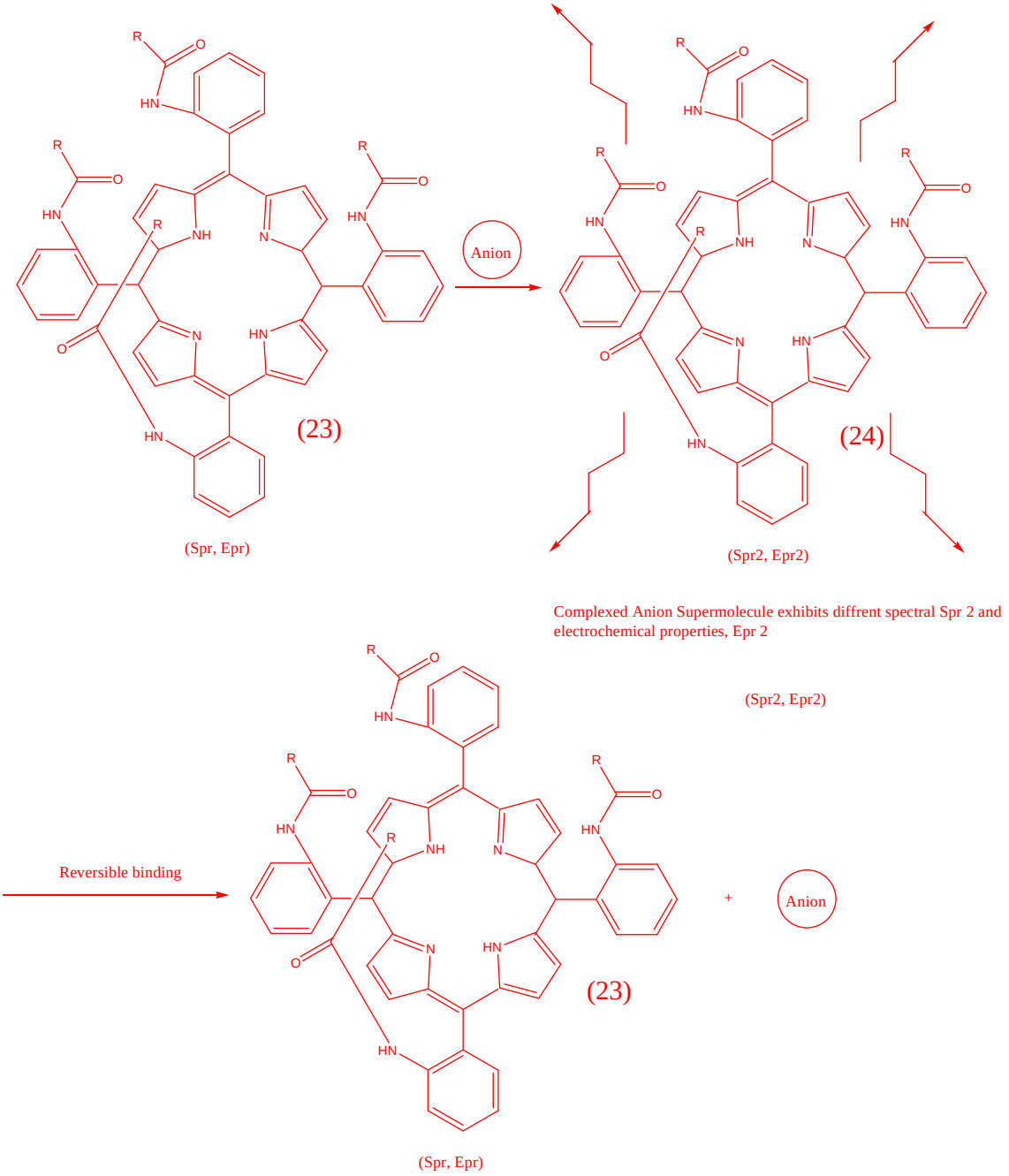
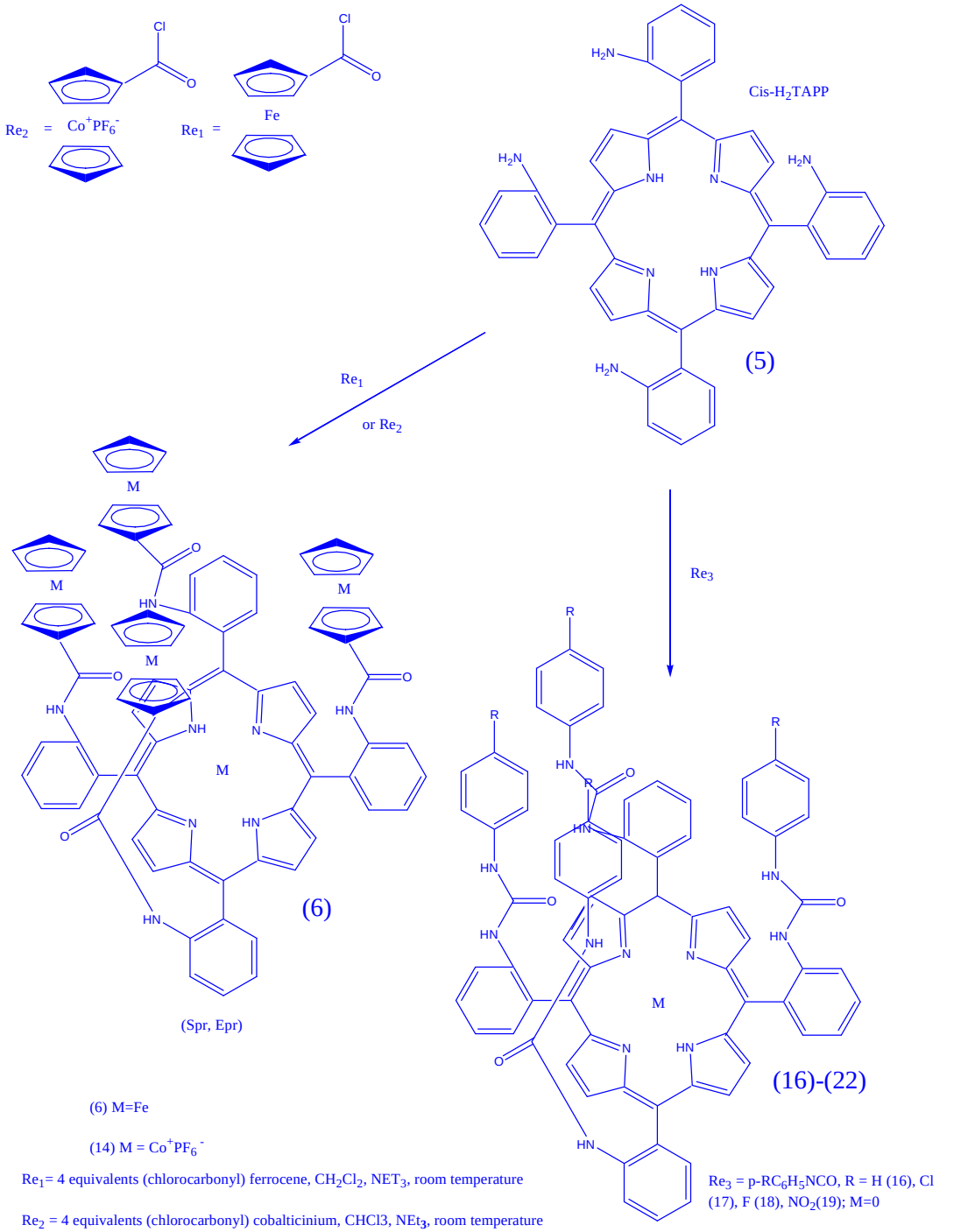


Fig 2.0

iii. <u>Porphyrin Syntheses</u>

Before further discussion can be made, the syntheses of these novel porphyrins anion receptors need to be discussed. The syntheses of these porphyrin have already been mentioned [26,27,28]. The porphyrins were synthesized under a dry and inert atmosphere of N_2 for 24 hours. For receptor (6)-(9), this involves the condensation of the respective atropisomer of 5, 10, 15, 20-*meso* tetrakis(2-amino) phenyl porphyrin, H_2TAPP(5) with an excess amount of four equivalents of chlorocarbonyl ferrocene in dry dichloromethane, using triethylamine as the base. For receptor (14) and (15), this is achieved by the condensation of four and two equivalents of cobalticinium acid chloride respectively with *cis*-H_2TAPP in CH_3CN and subsequent purification via sephadex LH-20. For receptor (16)-(19), this involves the addition of four equivalents of the requisite isocyanate to the *cis*- isomer of H_2TAPP in $CHCl_3$. Receptors (16)-(19) and (20)-(22) were purified via silica gel chromatography using dichloromethane-ethylacetate (4:1, v/v) and dichloromethane-ethylacetate (8:1, v/v) respectively. This yielded purple microcrystalline solids in yields of 70-85% for receptor (16)-(19). The Zn complexes (20)-(22) were synthesized by stirring the free base porphyrins with excess $Zn(OAc)_2.2H_2O$ in CH_2Cl_2/MeOH (2:1, v/v) and were obtained in 90-95% yield following purification by silica gel chromatography using dichloromethane/ethylacetate (8:1, v/v) respectively.



(6) M=Fe

(14) M = $Co^{+}PF_6^{-}$

Re_1= 4 equivalents (chlorocarbonyl) ferrocene, CH_2Cl_2, NET_3, room temperature

Re_2 = 4 equivalents (chlorocarbonyl) cobalticinium, CHCl3, NEt_3, room temperature

Re_3 = 4 equivalents, p-RC_6H_4NCO, $CHCl_3$, room temperature

Re_3 = p-RC_6H_5NCO, R = H (16), Cl (17), F (18), NO_2(19); M=0

M = Zn, R=H (20), R=Cl (21), R=F (22)

Scheme 1.0

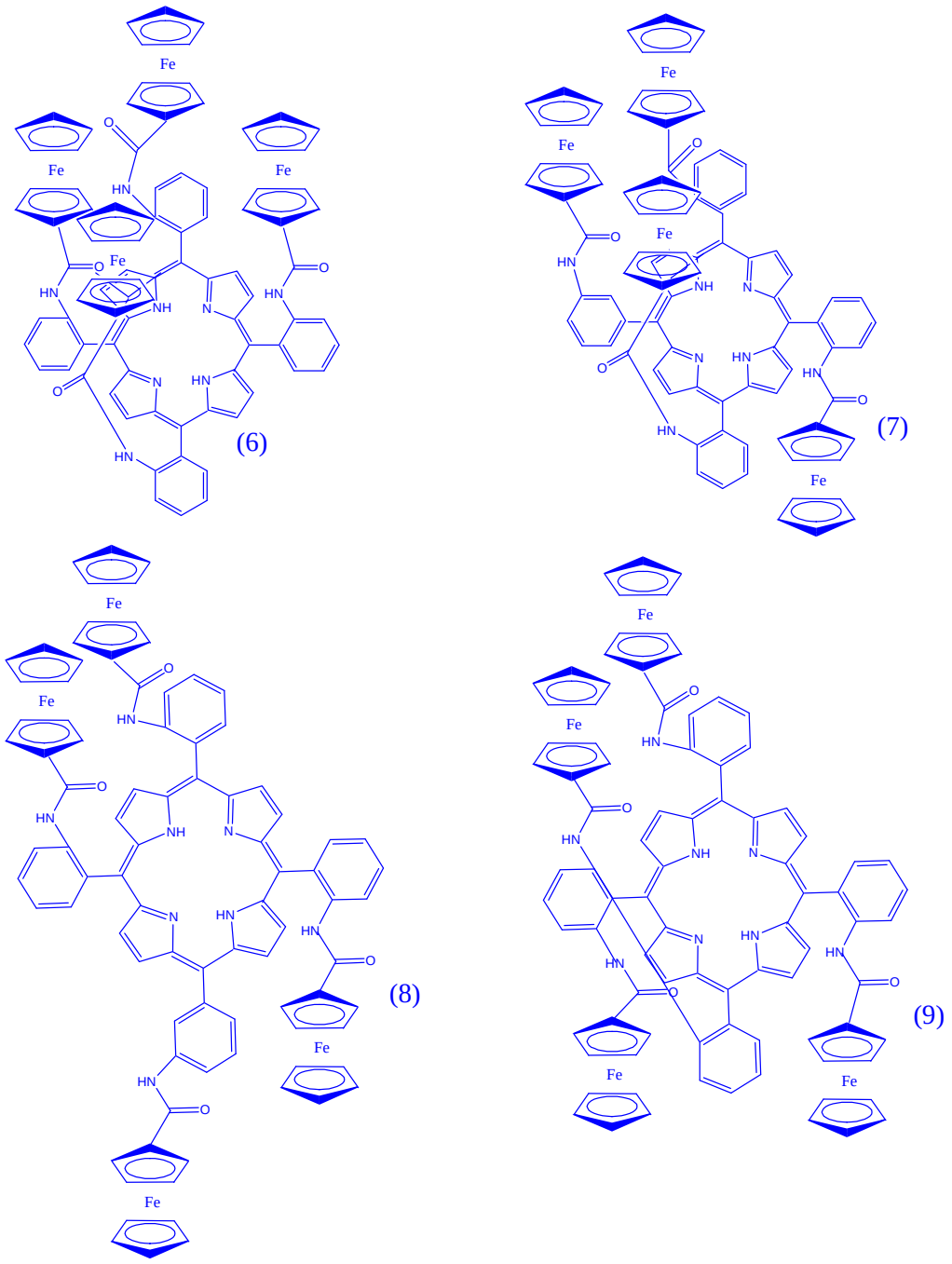
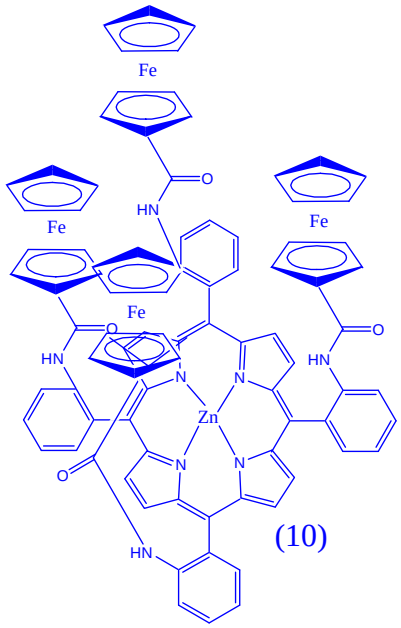
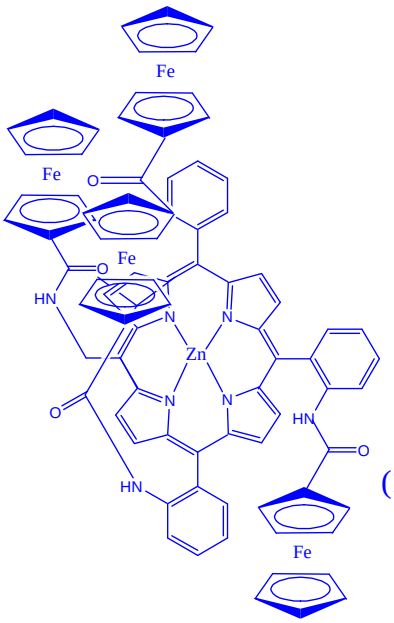


Fig 3.0



(10)



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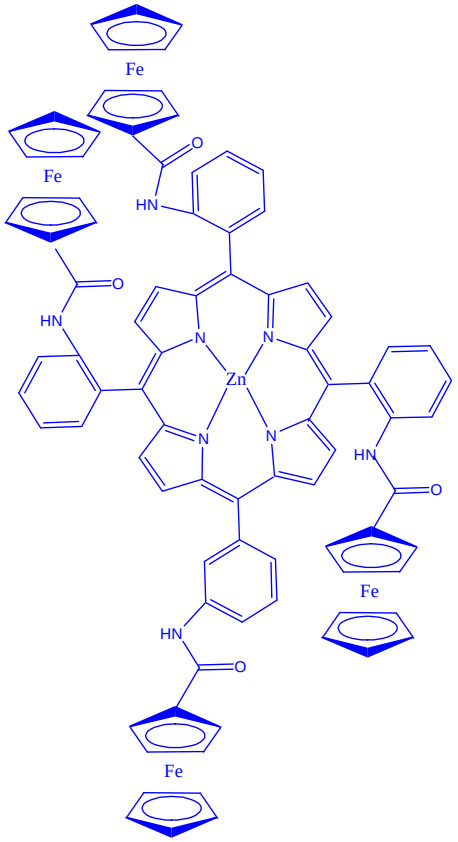
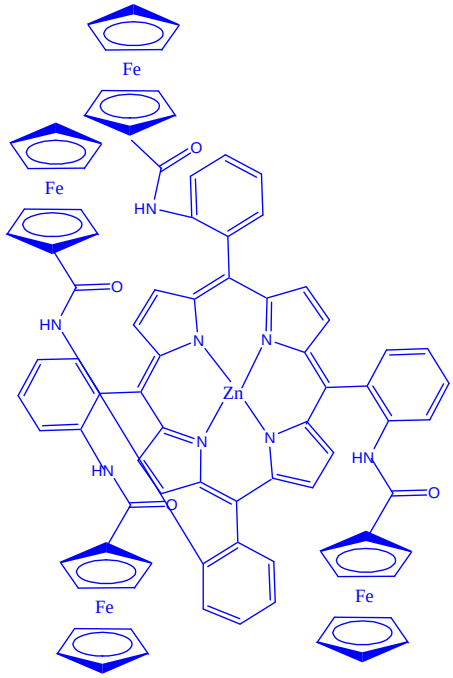


(12)



(13)

Fig 4.0:

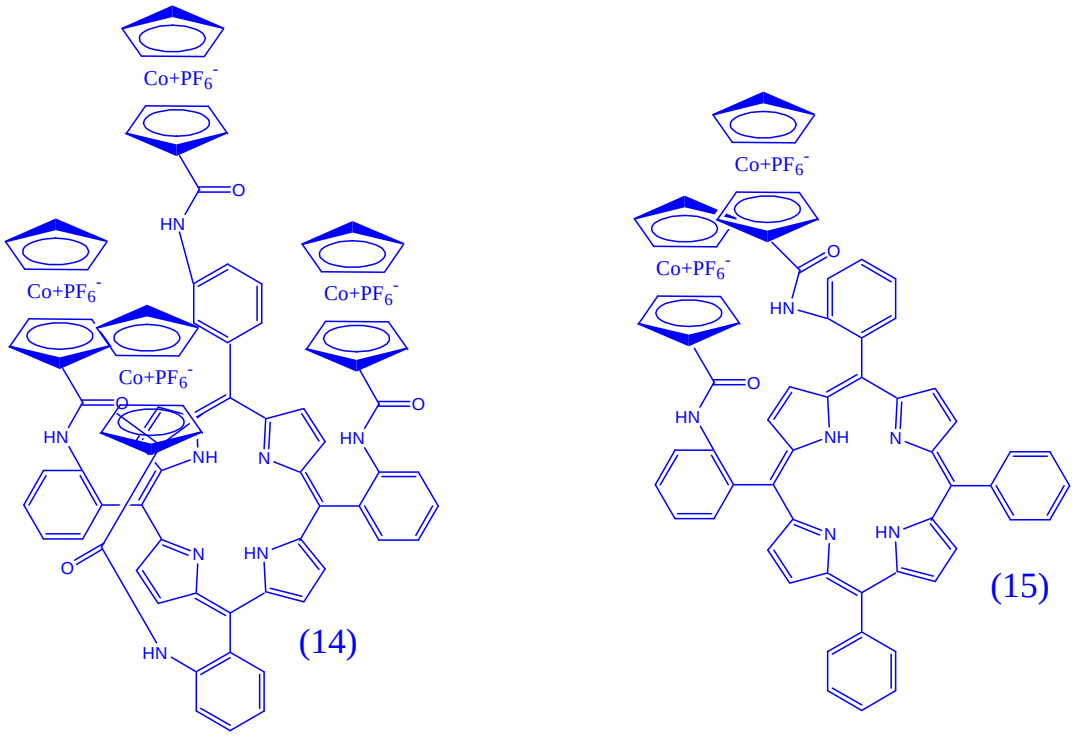


Fig 5.0: 5,10,15,20-*meso tetrakis* atropisomeric cobalticinium porphyrin receptors

iv: Design of Porphyrin Anion Receptors:

Following the work on expanded porphyrins, is the development of functionalised porphyrin based anion receptors. It was envisaged that neutral functionalised amido porphyrin receptors and those that have a positively charged binding sites in close proximity to amide hydrogen bonding environment should complex anion via virtue of an electrostatic interaction of the anion sphere and the positively charge center and favourable anion----NHCO---- hydrogen bonding interactions. In addition, amides are thermodynamically stable, pH insensitive and hydrolysis resistant.

Before an anion receptor can be synthesized, its design is necessary and of utmost importance. The design must make the compound synthetically accessible in large yields so that extensive physical studies can be carried out and also for application in technological science studies.

In the design, the porphyrin basal template used are the atropisomers of 5,10,15,20 – *meso tetrakis* tetraphenylporphyrins.Attached to the planar porphyrins are the "Picket fence" amide or urea arms which delineate a spherical cavity. The purpose of the cavity or pocket is to shield the bound anion or guest from the solvation forces of the environment i.e to act as an hydrophobic cavaity. There will be competition between the solvent molecule and anion guest for the host binding site. Thus, complexation to neutral host may involve solvent desolvation. Also, the host must be preorganised for substrate binding. It is anticipated that the four amide or eight urea NHs groups are pointing in the cavity, a position that allows them to converge on the anion. Also, another factor to take into consideration is the accumulation of H-bond donor sites in close vicinity to each other. This allows for a maximum number of hydrogen bonding contacts for the anionic guests, resulting in improve binding. Also, the urea –NHCONH- binding units must be placed at such a distance that there is no intermolecular hydrogen bonding. What about the ring current effect of the porphyrins? The porphyrin's internal β-pyrrole protons resonate far upfield at negative ppm as a result of the diamagnetic shielding effect of the ring current, whereas the outer *meso* proton deshielded by the aromatic ring current resonate far downfield resulting from the paramagnetic effect of the ring current, Fig 7.0. It is expected that the bound anion would in one region of the porphyrin augments the ring current and in another region depreciate it. Thus, the ring current can affect the association constants. It is left to the imaginative Supramolecular chemist to design a porphyrin receptor whose ring current should increase the overall association constant.

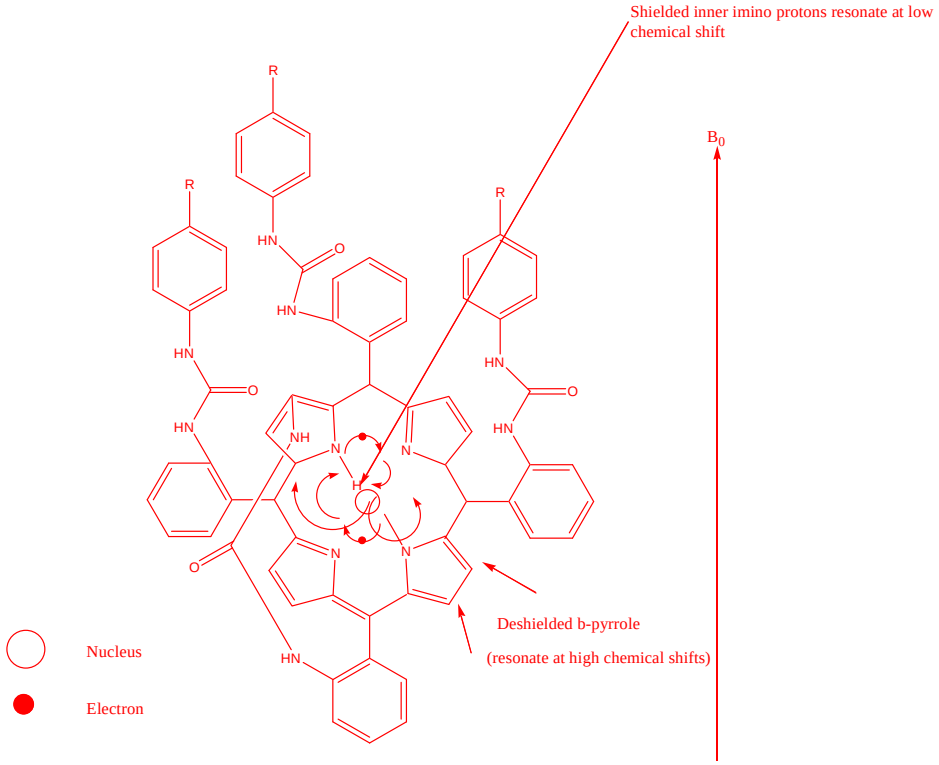


Fig 6.0: Ring current effect of Porphyrin

Recently, several types of porphyrin based anion receptors have been synthesized. These are as follows:

(v) Novel Ferrocene, Cobalticinium functionalized amido and Urea porphyrins anion Receptors.

(a) Novel Ferrocene Amido Porphyrins Receptors

The first set of receptors synthesized, characterized and anion binding studies investigated are a series of neutral ferrocenoyl amido atropisomeric porphyrins receptors as shown in Fig 3.0. In nature, the selective binding for anion is dependent on the positional alignment of the anion binding sites. These receptors are design so that the positional alignment of the hydrogen bond groups and cavity dimensions varies.

It was found that all neutral ferrocene atropisomeric receptors don't complex anions. This is shown by negligible shifts in the host protons $\Delta < 0.05$ ppm, unperturbed Soret and Q bands and unperturbed electrochemical diagnostic redox waves. This was surprising, considering neutral acyclic and macrocyclic ferrocene amides complex anions[30]. Maybe, the ferrocene amide protons in the "Picket fence" arrangements are not acidic enough for anion complexation. It was thought that a combination of a Lewis acidic site in close proximity to amido linkages should do so. Thus, in the presence of a Lewis acidic centre, Zn^{2+} incorporated in the porphyrin core for (10)-(13) and the rich surrounding convergent amido linkages "switch" on anion binding, both spectrally and electrochemically for (10)-(13). For example, the addition of tetrabutylammonium salts: $Bu_4N^+X^-$ (X = Cl^-, Br^-, NO_3^- and HSO_4^-) to deuterated CD_2Cl_2 solutions of compounds (10)-(13) resulted in pertinent significant shifts in the host protons. Porphyrin amide proton perturbation of δ = 0.40 ppm and 0.64 ppm were observed for (10) and (13) after the addition of one equivalent of nitrate[26] and bromide.

(b) Novel Ferrocenoyl Amido Zinc Porphyrins Receptors

It was envisaged that all metallated amido porphyrins should complex anions using the metal Lewis acidic center as the primary recognition element and the surrounding amido linkages as the secondary recognition element, Fig 7.0, the second hypothetical mode of anion binding. It is anticipated that these atropisomeric zinc metallated porphyrins should be selective for anion binding, since in nature, the selective binding for anion is achieved by the positional alignment or directive hydrogen bonding[31]. For example, sulphate and phosphate binding proteins complex anions exclusively via directive hydrogen bonds.

Association constant (K/dm^3mol^{-1}) for receptors (10)-(13) in dichloromethane at room temperature.

Anions	Receptor (10)	Receptor (11)	Receptor (12)	Receptor (13)
Br^-	6200	3200	5600	5800
NO_3^-	2300	5000	1600	1300
HSO_4-	2100	2000	900	600
Cl^-	-----	------	1000	------

Errors were typically <5 to 10%.

[1] H nmr titration studies revealed that receptor (10) displayed a preference or selectivity for the complexation of spherical anions (Cl^-,Br^-) over non spherical anions (HSO_4^- and NO_3^-), indicating that a complementary spherical host hydrogen bonding amide environment exists for the complexation of anion with all four or two hydrogen bonds acting cooperatively in complexation for the spherical anion. This may also be reflective of the higher charge to radius ratio polarisabilities of the anion. Also, receptor (10) showed the highest for halide as compared with the $\alpha,\alpha,\beta,\beta$ or $\alpha,\beta,\alpha,\beta$ atropisomer, since four cooperative convergent –NHCO- hydrogen sites are involved in the anion receognition process as compared with two for (12) and (13). Also,

the magnitude of the halide association constant is greater for the α,β,α,β atropisomer as compared with the α,α,β,β atropisomer. This may be due to the cooperative amide hydrogen bonding functionality converging in an anti manner for (13) as opposed to (12). Receptor (13) may be described as a cleft type receptor. Interestingly, the α,α,α,β isomer showed a preference of binding for NO_3^- over halides (Cl^-, Br^-) and hydrogen sulphate i.e the selectivity trend of $NO_3^- > Cl^- > Br^- > HSO_4^-$. This indicates that a trigonal shaped hydrogen bonding environment is prevalent for the complementary NO_3^-ions.

In all cases, the mode of anion complexation involves an electronic interaction of the anion electrostatic coordination sites with the primary recognition zinc lewis acid centre and a secondary interaction with the amide hydrogen bonding environments as shown in Fig 7.0.

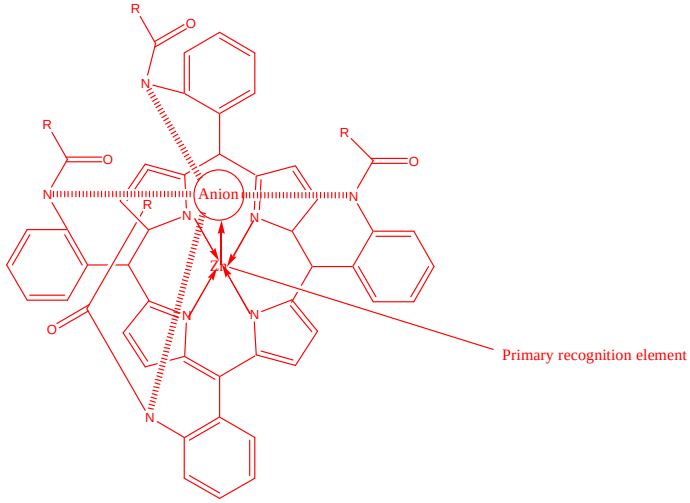


Fig 7.0: Illustration of mode of anion binding for compound (10).

(b) **Novel Cobalticinium Amido Porphyrin Receptors**:

To investigate the third hypothetical mode of anion binding, a *cis meso tetrakis* cobalticinium amido porphyrin has been synthesized and characterized. Here, the combination of a positively charge cobalticinium centre in close proximity to the amide hydrogen bonding should complex and switch on anion binding for this porphyrin amide system. This has been found to be so, spectrally and electrochemically. Unlike a zinc metallated " Picket fence porphyrins, a *cis meso tetrakis* cobalticinium amido porphyrin has been shown to complex anions with small anion selectivity between halides, nitrate and sulphate in CD_3CN. The selectivity been: $Cl^- > Br^- >> NO_3^- > HSO_4^-$. A high degree of selectivity for spherical chloride anions suggests that anion binding recognition site delineates a spherical cavity and all four amide hydrogen bonds act cooperatively in complexing the anion. The association constants for compound (14) are shown in Table 2.0

Table 2.0: The association constants in CD_3CN for compound (14).

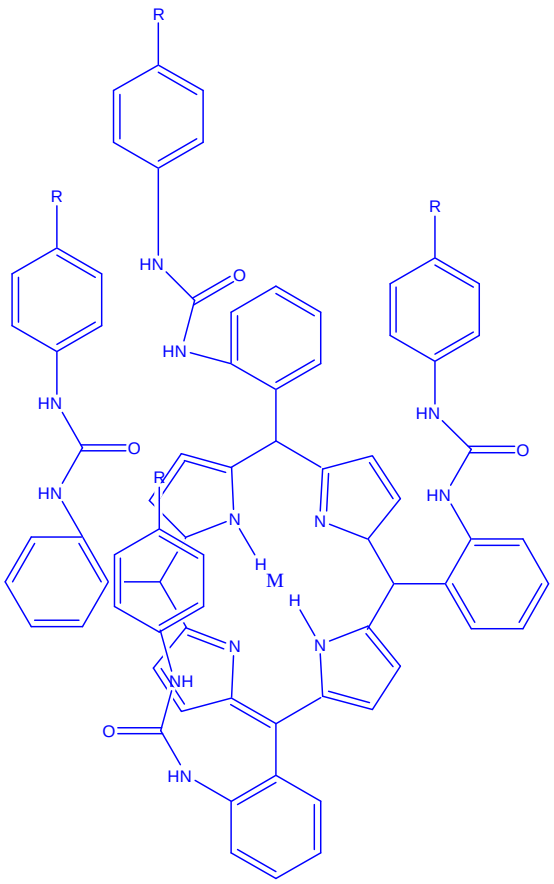
Receptor (14)	Anion	K/dm^3mol^{-1}
	Cl-	1000
	Br-	824
	NO_3-	450
	HSO_4-	420

By varying the geometrical arrangement of binding sites, different selectivity can be sought. For example, the *bis* amido *α,α,ββ-meso tetrakis* cobalticinium amido porphyrins have shown a high degree of selectivity for nitrate anions over chloride, thus exhibiting the rare selectivity trends: NO_3- > Br^- > Cl^-. This indicates that a complementary trigonal host cavity exists for nitrate[30].

(c) Novel Urea Functionalised Porphyrin Anion receptor:

So far it has been shown that neutral porphyrin ferrocene amides don't complex anion. Also, even though cobalticinium amides are good anion binders, the preparation of cobalticinium amide porphyrin receptors are arduous. Besides, cobalticinium amide porphyrin receptors are virtually chromatographically immobile on silica gel, making them difficult to purify and hence relatively scare. Hence, this has provided the impetus for the search of other porphyrin anion receptors with a high affinity for anion.

To broaden the scope of porphyrin based anion recognition, it would be interesting to prepare neutral porphyrin urea based anion receptors. Neutral receptors have certain advantages. They are more selective in comparison to positively charged hosts. Neutral receptors are scare relative to positively charged ones. Also, in nature the selective binding for anion is achieved by the positional alignment of hydrogen bond donor groups. For example, sulfate and phosphate binding proteins complex anion exclusively via hydrogen bonding with a selectivity factor of 10^5 [31]. In positively charged host, selectivity is modest due to non directional coulombic interactions. Neutral Lewis acidic host have limited synthetic flexibility for optimizing binding selectivity. In addition, Lewis acidic hosts suffers from the problem of solvent competition with the guest species. Most organic solvents are Lewis bases and exceed molar concentration of a guest anion by several orders of magnitude. Solvation design is more difficult, the smaller and more Lewis basic the solvent molecules are. The syntheses of neutral anion receptors that are highly selective and exhibits a strong degree of binding is also relatively scarce. Neutral receptors use hydrogen bonding motif exclusively to complex anion guest species. They are electroneutral. In addition, several hydrogen bonding sites can be incorporated in the host in different geometrical arrangements. Also, the molecular framework can be be further elaborated. There can be self assembly of neutral receptors. A further advantage is that electroneutrality is important in the application of membrane transport or potentiometric ion sensing. Neutral receptors reported to date bind strongly to phosphate and carboxylate anion. There is a need to broaden the scope of neutral receptors selectivity and applicability. Thus, a series of neutral urea appended free base porphyrin receptors were prepared [27,28] , Fig. 9.0.



R = H, (16)

R = Cl, (17)

R = F, (18)

R = NO_2 (19)

M = Zn

R =H (20), R=Cl (21), R = F (22)

Fig 9.0: Urea Appended Free base Porphyrins

These receptors bind exceptionally strong to Cl^- (K ass > 10^5 dm^{-3} mol^{-1}) in $(CD_3)_2SO$ and in DMSO/H_2O, highly competitive solvent medium and exhibit significant selectivity for Cl^- over NO_3^- and $H_2PO_4^-$ since they complex with Cl^- to a much greater extent 1000:1 compared with the trigonal NO_3^- and 280: 1, compared with the tetrahedral $H_2PO_4^-$ anions in DMSO. They displayed a higher degree of selectivity and strength of binding for anions as compared with protonated expanded porphyrins such as (3), positively charged functionalized cobalticinium amido porphyrins (14) and (15) and metallated zinc ferrocene atropisomeric porphyrin receptors (10)-(13). Neutral ferrocenoyl atropisomeric receptors don't complex anions unless metallated. Both cobalticium and metallated zinc ferrocene atropisomeric receptor systems showed little anion selectivity (a 4:1 binding selectivity between halides, nitrate and sulfate ions in acetonitrile and dichloromethane respectively.

Expanded porphyrin receptors can complex anions only in the mono or diprotonated state and selectivity is modest. For example, sapphyrin in its diprotonated state complexes $H_2PO_4^-$ and F^- ions with similar association constants in methanol. (K assn = 1 x 10^5 M^{-1}). Unlike, expanded porphyrins these receptors don't need to be protonated. Receptors (16)-(18) are indeed the first examples of a neutral class of free base functionalized porphyrins anion receptors that are remarkably selective and binds exceptionally strong for Cl^- in a highly competitive solvent solvent system such as DMSO and DMSO/H_2O. Table 3.0 gives the association constants for receptors (16)-(21) with various anionic substrates.

Association constants (K/dm^{-3} mol^{-1}) for receptor porphyrins (16)-(21) with anions: Cl^-, Br^-, NO_3^- and $H_2PO_4^-$ in $(CD_3)_2SO$.

Table 3.0

Receptor Porphyrin	Cl^-	Br^-	NO_3^-	HSO_4^-	$H_2PO_4^-$
(16)	> 10^5	1.01 x 10^4	90	115	400
(17)	> 10^5	1.0 x 10^4	60	137	300
(18)	> 10^5	9.99 x 10^3	55	147	1400
(19)	> 10^5	1.00 x 10^4	163	226	9.6 x 10^3
(20)	9.5 x 10^3	1.51 x 10^3	23	d	49
(22)	9.82 x 10^3	1.1 x 10^3	d	d	489

Association constants were determined using EQNMR and the errors were in the range: 5 to 10%.

d: impossible to determine the association constant due to broadness in the host proton.

These receptors display a high affinity and selectivity for Cl^-. This is due to the complementary nature of the urea binding site for the spherically shaped anion and the strength of the urea anion binding interaction. Infact, the association constants for the binding of Cl^- are very much larger than those reported for urea and non urea functionalized anion receptors [1,32].

It is anticipated that the attachment of electronegative substituents such as F, Cl and Br to the phenyl ring would intensify the acidity of the urea NH protons via an inductive effect and thus strengthen their hydrogen bonding propensity for anions, leading to a stronger degree of complexation. Electronic tuning via the attachment of electronegative substituents resulted in a small degree of selectivity between the p-fluorophenylurea porphyrin and other porphyrin receptors (16)-(22) in their affinity for $H_2PO_4^-$. However, modification of the phenyl ring with the NO_2 substituent resulted in the anion binding selectivity changing dramatically with the association constants increasing by a factor of 24 i.e from 400 for (16) to 9600 for (19). Infact, the *para* substituted nitro porphyrins exhibits the largest binding constants for anions and the same order of selectivity as for the other receptors. With nitrate and sulphate, there is apparently not much degree of selectivity.

To investigate selectivity for Cl^-, anion complexation was done in a more competitive solvent system such as DMSO/H_2O (88:12%, v/v). The results revealed that the p-fluorophenyl (18), 9.73 x 10^3 is more selective than (16), 1.36 x 10^3 for the Cl^-. The higher affinity for Cl^- is due to the complementary nature of the urea binding cavity and hydrogen bonding sites for the spherically shaped anion. The selectivity trend: Cl^- > Br^->$H_2PO_4^{2-}$->HSO_4^->NO_3^- displayed by these receptors is novel for any urea anion binding receptors.

The zinc complexes showed a smaller degree of binding and selectivity for the various anions in DMSO. This is due to an increase in rigidity or decrease in flexibility of the porphyrin core as a result of the insertion of the zinc. This is shown in Table 3.0. In order to complex a substrate, there must be a balance between rigidity and flexibility of the receptor active site. However, for those receptors (20)-(22), the selectivity trend of Cl^- > Br^- > $H_2PO_4^{2-}$-> NO_3^- was the same.The stoichiometry of anion binding was found to be 1:1 for all urea porphyrins receptors using Job's method of continous variation and EQNMR. In all cases, where anion binding was evident, shifts in the porphyrin protons were observed. For example, shifts were observed for the receptor porphyrin, β- pyrroles, porphyrin NH, urea NHs, urea phenyl protons and *meso*-phenyl. Also, diagnostic shifts were observed. For example, upfield shifts were

always observed for the β-pyrrole whereas downfield shifts were observed for the amide and urea NH protons, indicating NH----anion and urea NH----anion hydrogen bonding interactions.

(vi) **X-ray crystallography**

X-ray crystallography both in solid and solution states is also a useful tool to study anion complexation. An X-ray crystal structure of the zinc complex of (10) was isolated. Here a bound methanol solvent is coordinated to the zinc atom. The zinc atom is 0.27Å above the plane of the four nitrogen atom and is towards the coordinated methanol oxygen atom. An important feature is the positioning of one carbonyl oxygen atom in the cavity and the other three outside of the cavity.

A step was taken further to isolate the first coordination complex of an anion (chloride, bromide) bound by a neutral free base porphyrins, α,α,α,α-5,10,15,20-*meso-tetrakis* (2-(4-chlorophenylurea) phenyl porphyrin[28], a great achievment!!. For compounds (16)-(22), crystal structures obtained are (21).5DMSO, (17) + TBABr.5DMSO, (17) + TBABr.3DMSO and (17) + TBACl.5DMSO.

X-ray crystallography of free base porphyrin (17) + TBABr.5DMSO shows that the single bound anion is deeply buried in the pocket of the porphyrin and is positioned over one pyrrole. The anion is kept intact via four NH hydrogen bonds resulting from two adjacent urea groups. In addition, in (17) + TBABr.5DMSO, a DMSO molecule is positioned in the center of the cavity and provides further stabilization via a coulombic interaction between the electron deficient sulfur and the chloride or bromide anion. The crystal structure supports the 1:1 stoichiometry of binding. The high selectivity for the halides is due to the complementary nature of spherical cavity created by four urea groups together with the inclusion of the ordered solvent DMSO between the two arms of the "urea pickets". There is also no self association of urea groups.

The urea free base porphyrins exhibit a high degree of binding for the halides at a factor of 10^5. It is also interesting to note that sulfate binding protein exhibit a $K_{assn}=10^6M^{-1}$ with discrimination against hydrogen phosphate by a factor of 10^5 and *vice versa*. Thus, the "Picket fence" urea *meso tetrakis* porphyrin design and synthesized above have indeed been able to match the selectivity of binding, reminiscent of nature's sulphate and phosphate binding proteins. Also, X-ray crystallography shows that the anion is deeply buried in the interior of the protein with the help of seven hydrogen bonds in contact with the guest. In addition, there is no functional groups present in the binding cavity that would perform the role of an hydrogen bond acceptor as is required for the complexation of the $H_2PO_4^2$-. In the above mentioned, X-ray crystallography also shows that the anion is deeply buried in the pocket of the porphyrin urea receptor and is positioned over one pyrrole and is bound to four hydrogen bonds.

(vii) **UV/Vis Spectral Anion Recognition Studies:**

The porphyrin is highly spectrophotoactive. Its an 18 π electron conjugated systems resulting in a longer wavelength of the absorption maximum. The chromophore is characterized by an intense Soret band around 420-425 nm and four visible satellite Q bands in the range 450-700 nm. These transitions are π-π*. It is anticipated that the complexed anion should perturb these π-π* bands. This was found to be so.

UV/Visible spectral anion studies revealed perturbation of the Soret and the visible (Q) bands of receptors (16)-(22) following the addition of anions Cl^-, NO_3^-, HSO_4^- and $H_2PO_4^-$ as their NBu_4^+ salts. Each anion induced almost specific or diagnostic changes in the spectrum, indicating selective behaviour. The fact that these anions produced diagnostic shifts in the Soret and Q bands with specific anions means that these receptor can act as a good UV/Vis sensors or spectral probe. A comparison can be drawn for receptors (14) and (16)-(19) for illustrative purposes.

Anions	Ligand (14)	Ligand (16)-(19)
Cl^-	Hypsochromatic shift of the Soret	Hypsochromic shift with concomitant decrease in intensity of the Soret band
Br^-	Decrease in intensity, Hypochrome effect	Hypsochromic shift with concomitant decrease in intensity of the Soret band

NO_3^-	Decrease in intensity, Hypochrome effect	Decrease in absorbance, Hypochromic effect
HSO_4^-	Broadening and a split Soret Band	Hypochromic effect, gradual broadening and splitting of the Soret
$H_2PO_4^-$	Bathochromatic shift of Soret and Q bands	Hypsochromic followed by bathochromic shift and an increase in absorbance of Soret and Q bands. For (17) and (18), a broadened Soret band with a shoulder was observed.

The fact that these changes are distinct meant that the anions are bound within the "Picket fence" cavity or anion binding cavity of the porphyrin.

(viii). Electrochemical Studies:

Electrochemistry is used as a means of characterizing and studying the anion binding properties of porphyrins receptors. First, the electrochemical nature of the host had to be characterized. The electrochemical nature of receptor (6)-(9) and (10)-(13) were investigated by Cyclic and Square wave voltammetry. Receptors (6)-(13) exhibited the typical "Picket Fence" porphyrin redox properties. A single two one electron porphyrin oxidation wave at positive potential range 0.67 to 0.93V and two one electron reduction waves at negative potential range –1.08 to -1.79V. It is interesting to note that the four ferrocene moieties of (6), (8), (9) and (10), (12) and (13) display a single four electron oxidation wave, indicating that the ferrocene redox centers are electronically equivalent and undergo independent reversible one electron transfer at the same potential. However, receptor (7) and (11) exhibit two oxidation waves for the ferrocene moieties. Receptor (14) displayed a reversible reduction wave for the cobalticinium/cobaltocene redox wave in the region –1.25 to –1.75V. The p/p^{2+} occurred at 0.75V whereas the reversible p/p^- and p/p^{2-} occurred in the region –1.2 to –1.27 V respectively.

Cyclic voltammograms were then recorded after the progressive addition of stoichiometric equivalents of anion guests to the electrochemical solutions of receptor (6)-(9), (10)-(13), (14) and the results are shown in Table 4.0. It is seen that significant one wave cathodic shifts of the respective porphyrin oxidation waves and the ferrocene redox couples were observed for the porphyrin oxidation and cobalticinium/cobaltocene redox waves for receptors (14). This results from the complexed anion in close proximity effectively stabilizing the respective oxidized redox couple of (10)-(13) and the porphyrin p/p^{2+} cation radical making each harder to reduce. The magnitude of the anion cathodic perturbation of the porphyrin oxidation wave is larger than those of the ferrocene or cobalticinum redox couple, indicating that the bound anion is closer to the porphyrin skeleton than the ferrocene or cobalticinium redox centers.

The magnitude of the cathodic shift is dictated by the polarizing power i.e the charge to radius ratio of the anionic guest species and follows the sequence: $HSO_4^- > Cl^->Br^->NO_3^-$ for receptor (10)-(13) and $HPO_4^- > HSO_4^- > Cl^->Br^- > NO_3^-$ for receptor (14). It is interesting to note that in all cases negligible shifts of $\Delta E < 5$ mV were observed for the p/p^{2-} redox couple with all anionic guest species.

Table 4.0: Eletrochemical behaviour of receptor **(10)-(13)** in the presence of anions.

Receptor	(10)	(10)	(11)	(11)
ΔE, Anion, mV	Porphyrin Oxidation	Ferrocene Oxidation	Porphyrin Oxidation	Ferrocene Oxidation
Cl-	115	30	90	25
Br-	85	20	75	20
NO_3^-	110	25	100	20
HSO_4^-	100	60	125	50

Receptor	(12)	(12)	(13)	(13)
ΔE, Anion, mV	Porphyrin Oxidation	Ferrocene Oxidation	Porphyrin Oxidation	Ferrocene Oxidation
Cl-	70	20	90	20
Br-	65	20	75	20
NO_3^-	60	60	100	15
HSO_4^-	150	105	125	105

The above data were obtained in dichloromethane/acetonitrile solution (3:2, v/v) containing 0.2 moldm^{-3} NBu_4BF_4 as supporting electrolyte. Solutions were 5 x 10^{-4} moldm-^{3} and compound potentials were referenced with respect to Ag/Ag$^+$ electrode.
H

Electrochemical behaviour of receptor (14) in the presence of anions.

ΔE, Anion, mV	ΔEpa(p/p^{2+})	$E_{1/2}$(Co/Co$^+$)	ΔEpa(p/p^2-)
$H_2PO_4^-$	75	225	40
HSO_4^-	50	75	30
Cl^-	15	40	25
Br^-	10	35	10
NO_3^-	5	5	5

Obtained in acetonitrile solution containing 0.1 moldm^{-3}($NBu^n{}_4BF_4$) as the supporting electrolyte.Solutions were 1.0 x 10^{-4}M in compound and potentials were determined with reference to a Ag/AgCl electrode at 21 + 1C, 50 mVs-1 scan rate, E_{pa} and E_{pc} represent the anodic and cathodic current peak potentials of the cobaltocene/cobaltocenium redox couple of the free ligand.

In conclusion, a series of neutral and metallated 5, 10, 15, 20- *meso tetrakis*(*ortho* metallocene) amido phenyl porphyrins and 5, 10, 15, 20- *meso tetrakis(ortho* urea phenyl porphyrins anion receptors were synthesized, characterized and anion binding studies investigated in polar solvents. The 5,10,15,20- *meso tetrakis*(*ortho* ferrocenoylcarbonylamidophenyl porphyrin receptors do not complex anion whereas the corresponding zinc metallated 5,10,15,20- *meso tetrakis*(*ortho*-ferrocenoylcarbonylamidophenyl-substituted) atropisomeric *meso tetrakis* zinc metalloporphyrin have been shown to do so with very good association constants. In constrasts, both neutral and zinc metallated *meso tetrakis*(*ortho* urea phenyl porphyrins receptors complex anions with excellent selectivity in highly competitive solvents such as DMSO and DMSO/H_2O(88:12, v/v). Some of these receptors have found direct application as ion selective electrodes. For examples, receptors (16)-(19) have been tested and incorporated in ion selective electrode for acetate and is thus a good probe to measure the acetic acid content in Vinegar. This is the first example of a porphyrin ionophore without a metal center been used for an anion selective electrode.

References:

(1) For reviews, see (a) Izatt R.M, Pawlak K, Bradshaw J.S., *Chem. Rev*., 1995; 95, 2529 (b) Dietrich B, *Pure Appl.Chem*., 1993; 65, 1457. (c) K. Kavallieratos K, de Gala S.R., Austin. D.J., Crabtree R.H.,

J.Am.Chem.Soc., 1997; 119, 2325 (d) Davis A.P, Perry J.J., Williams R.P., *J. Am.Chem.Soc*., 1997; 119, 1793 (e) Berger M, Schmidtchen F.P., *J.Am.Chem.Soc*., 1996; 118, 8947 (f) Kral V, Furuta. H, Schreder. K., Lynch V, Sessler J.L., *J.Am.Chem.Soc*., 1996; 118, 1595 (g) Gale P.A., Sessler J.L., Kral V., Lynch V., *J.Am.Chem.Soc*., 1996; 118, 5140.

(2) (a) Dietrich B. ; Guilhem J., Lehn J.M., Pascard C.,Somveaux E. *Helv.Chim.Acta* 1984; 67, 91. (b) Schmidtchen F.P. *J.Org. Chem*. 1986; 51, 5161. (c) Hosseini M.W.; Blacker, A.J.; Lehn, J.M. *J.Am.Chem.Soc*. 1990; 112, 3896. (d) Sessler, J.L.; Cyr, M.; Furuta H.; Kral V.; Mody T.; Morishima T.; Shionoya M.; Weghorn S.*Pure Appl.Chem*. 1993; 65, 393.

(3) (a) Deslongchamps G.Galan A; de Mendoza J.; Rebek J., Jr. *Angew.Chem.Int.Ed.Engl*.1992; 31,61.(b) Echavarren A; Galan A.; Lehn, J.M.;de Mendoza, *J.Am.Chem.Soc*.1989; 111,4994. (c) Schiessl P.; Schmidtchen F.P. *Tetrahedron Lett*. 1993; 34, 2449. (d) Muller G.; Riede J.; Schmidtchen F.P. *Angew.Chem*.1988; 27, 1574.

(4) (a) Dietrich B.; Guilhem J.; Lehn J.M.; Pascard, C.; Sonveaux, *E.Helv.Chim.Acta*.1984; 67, 91. (b) Sessler J.L.; Cyr M.; Furuta H.; Kral V.Mody, T.; Morishima T.; Shionoya M.; Weghorn S.*Pure.Appl.Chem*.1993; 65,393.

(5) Schmidtchen, F.P. *J.Org.Chem*.1986; 51, 5161.

(6) Echavarren, A.; Galan, A.; Lehn, J.M, de Mendoza, *J.Am.Chem.Soc*.; 1989; 111, 4994.

(7) Valigaveetgil S., Engbersen. J.F.J., Veerboom W, Reinhoudth, D.N., *Angew.Chem; Int.Ed.Engl*.; 1993; 32, 900.

(8) Blanda, M.T.; Horner, J.N.; Newcombs, M. *J.Org.Chem*.1989; 54,4626.

(9) (a) Yang, X.; Knobler, C.B.; Hawthorne, M.F.; *Angew. Chem.Int.Ed.Engl*.1991; 30, 1507. (b) Zheng, Z.; Yang, X.; Knobler, C.B.; Hawthorne, M.F. *J.Am.Chem.Soc.;* 1993; 115, 5320. (c) Hawthrone, M.F.; Yang, X.; Zheng, Z.*Pure. Appl.Chem*.1994; 66, 245. (d) Wuest, J.D.; Zacharie, B. *J.Am.Chem.Soc*.; 1987; 109, 4715.

(10) Jung, M.E.; Xia, H. *Tetrahedron Lett*. 1998; 29, 297. (b) Katz, H.E. *J.Am.Chem.Soc*., 1986; 108, 7640. (b) Katz, H.E.*J.Org.Chem*.1989; 54, 2179. (c) Katz, H.E.Ibid. 1995; 50, 5027.

(11) Rudkevich D.M, W.P.R.V. Stauthamer, W.Verboom, J.F.J.Engbersen, Harkema. S., Reinhoudth. D.N., *J.Am.Chem.Soc*.; 1992; 114, 9671.

(12) Beer, P.D.; Hesek, D.; Hodacova, J.; Stokes, S.E.*J.Chem.Soc*.; *Chem.Commun*. 1992; 270. (b) Beer, P.D.; Hazlewood, C.; Hesek, D.; Hodacova J.; Stokes S.E.*J.Chem.Soc.; Dalton Trans*. 1993; 1327. (c) Beer, P.D.; Drew, M.G.B.; Hazlewood C.;Hesek D.; Hodacova J.; Stokes S.E.*J.Chem.Soc., Chem.Commun*. 1993; 229. (d) Beer P.D.; Dickson, C.A.D.; Fletcher, N.; Goulden, A.J.; Grieve, A.; Hodacova, J.; Wear, T. *J.Chem.Soc.; Chem.Commun*.1993; 828.

(13) Scheerder J., Fochi M., Engbersen J.F.J., Reinhoudth. D.N., *J.Org.Chem*., 1994; 59, 7815-7820.

(14) Purcell K.F., Kotz. J.C., *Inorganic Chemistry*, W.B.Sanders, 1977.

(15) Phillips C.S.G., Williams. R.J.P., *Inorganic Chemistry*, Oxford University Press; 1965; 2, 159.

(16) Lindoy. L.F.; "The Chemistry of Macrocyclic Ligands, Cambridge University Press, Cambridge, 1989; Chapter 5.

(17) Lehn J.M., *Angew.Chem*. ; *Angew.Chem.Int.Ed.Engl*.; 1988; 27,89.

(18) Vogtle F., Sieger H., Muller W.M., *Top.Curr.Chem*.; 1981; 98, 107.

(19) Schmidtchen F.P., *Top.Curr.Chem*.; 1986; 132, 101.

(20) Sessler J.L.; Cyr M.; Furuta H.; Kral V.; Mody T.; Morishima T.; Shionoya M.; Weghorn, S.*Pure Appl.Chem*.1993; 65, 393.

(21) Sessler J.L.; Burrell A.K.*Top.Curr.Chem*.1991; 161, 177.

(22) Shionoya M.; Furuta H.; Lynch V.; Harriman A.; Sessler,

J.L.*J.Am.Chem.Soc*.1992; 114, 5714.

(23) Anderson H.L., Sanders J.K.; *J.Chem.Soc.; Chem.Commun*.; 1992; 946.

(24) The computer program EQNMR was used to calculate the binding constants: M.J.Hynes, *J.Chem.Soc.; Dalton Trans*., 1993; 311.

(25) Lipskier J.F.; Trans-Thi, T.H.*Inorg.Chem*.; 1993; 32, 722-731.

(26) Beer P.D., M.G.B., Jagessar. R., *J.Chem.Soc.; Dalton trans*.; 1997; 881-886.

(27) Jagessar R.C., Burns D.H., *J.Chem.Soc.; Chem Commun*.; 1997; 1685.

(28) Jagessar R.C., Shang M., Scheidt W.R., Burns D.H., *J.Amer.Chem.Soc*. 1998; 11684-11692.

(29) Beer P.D., Drew M.G.B., Hesek. D., .Jagessar. R., *J.Chem.Soc.; Chem Commun*., 1995; 1187.

(30) Beer, P.D. *Chem Commun*, 1996; 689.

(31) Luecke H., Quiocho F.A., Nature (London), **1990**; 347, 402; Plugrath, J.W. Quiocho F.A., *J.Biol.Chem*.**1998**; 200, 163.

(32) Hughes M.P., Smith B.D., *J.Org.Chem*.1997; **62**, 4492; Hamann, B.C; Branda, N.R; Rebek, J. *Tetrahedron Lett*.1993; 34, 6834; E.Fan; S.A Van Arman; S.Kincaid; A.D.Hamilton. *J.Am.Chem.Soc*. 1993; 115, 369.

(33) Amemiya S., Buhlmann P., Umezawa Y., R.C.Jagessar, D.H.Burns, *Anal. Chem*.1999; 71, 1049-1054.