REVIEW OF LITERATURE

Chemosensors find wide applications in many disciplines such as environmental sciences, analytical chemistry, biochemistry, clinical, medical sciences and cell biology. These sensors specifically recognize a proper guest and are capable of producing a measurable signal. Optical signals based on change of absorbance or fluorescence are the most frequently exploited, because of their simple applications using relatively inexpensive instruments. Additionally, change of absorbance and wavelength of a characteristic band and consequent color immediately reveals the presence of a given analyte, on the other hand, assessment of fluorescence emission changes, wherever possible allow extreme sensitive determinations to be carried out with precision.

Owing to the thrust in coordination chemistry of metal ions, the cation recognition is now a well developed and mature area of chemistry. Anion recognition on the other hand received little attention in the early years due to problems inherent in binding of anions such as their large size (lower charge to radius ratio causing the less effective electrostatic binding interactions) than isoelectronic cations, pH sensitivity (protonation at low pH forcing the receptors to function within the pH window of their target anion), requirement of a higher degree of receptor design complementarity with an anion and the solvent effects which are to be competed by the receptors for the anions in certain solvents. Countering all these limitations, anion binding has now emerged as a mature field of research, and has been a subject of a number of excellent treatises, the presentation in this chapter has been restricted mainly to the reports that appeared in the last decade. However, the importance of investigated cations and anions will be highlighted in detail in the respective chapters of this thesis, wherever appropriate. In the following sections (2.1-2.3), different approaches used in the design of chemosensors outlined in chapter 1, are discussed along with suitable examples. A brief discussion on logic gates is presented in section 2.4.

2.1 Binding site-signalling subunit approach

For the development of anion chemosensors, the binding site-signalling subunit approach in which the binding site and signalling subunits are covalently attached (Figure 1), is the most widely used approach.
Figure 1. General representation of the binding site-signalling subunit approach.

In the chromogenic chemosensors, these two units are electronically bonded in such a way that the analyte upon binding to the receptor unit alters the electronic properties of the molecule as a whole, leading to the absorption, emission and/or related color changes emanating from different types of the interactions of the analytes with the receptors, such as electrostatic interactions, hydrogen bonding and/or deprotonation of the receptor and metal-ligand interactions. Among these, the receptors providing hydrogen bonding donor sites have widely been explored for the anion sensing and in most of the cases, the sensing event is performed in an organic solvent. As far as the interactions involving hydrogen bonding and deprotonation are concerned, the class of receptors which make use of urea and thiourea group(s) as receptors outweigh the others. In such receptors, bis-amide [-HN-C(=O/S)-NH-] moieties with two acidic NHs offer good hydrogen bonding sites for the anions. On the other hand, under suitable conditions, the presence of relatively basic anions can lead to the deprotonation of one or even both amidic NHs with concomitant spectroscopic and/or visual changes leading to colorimetric anion sensing.

Since the pioneering work of Wilcox and Hamilton\(^2\) reporting the urea moieties as appropriate binding sites for anions, a variety of urea/thiourea based receptors for sensing of anions have been developed. The report of Teramae \textit{et. al.}\(^3\) describes the colorimetric high selectivity of N,N-bis(p-nitrophenyl)thiourea \(1\) for acetate (AcO\(^-\)) ions over the other monovalent anions via formation of hydrogen bonded (1a) structure. Addition of the AcO\(^-\) ions to the solution of \(1\) in CH\(_3\)CN/H\(_2\)O (99:1, v/v), produced a significant bathochromic shift in the absorption band of \(1\) from 343 to 392 nm with simultaneous visual color change from colorless to yellow. Besides demonstrating that acetic acid in vinegar could be successfully determined by the complexation-induced chromogenic response of \(1\), the possibility of using \(1\) as anion transporter and/or electrochemical sensor owing to its very strong ability to form complexes with anions acting as hydrogen bond acceptors has also been suggested. Receptors \(2\) and \(3\)
containing urea/thiourea as binding sites, respectively and anthraquinone as signalling subunit detect\(^1\) fluoride (F\(^-\)) ions in CH\(_3\)CN/DMSO (9:1, v/v) selectively over other halides. Significant bathochromic shift in the main absorption bands of 2/3 was observed in the presence of F\(^-\) which has been attributed to the charge-transfer (CT) interaction between the electron rich urea/thiourea-bound F\(^-\) ions and the electron deficient anthraquinone moieties.

![Chemical structures](image)

Wu et. al.\(^5\) synthesized N-4-nitrophenyl-N\(^-\)-(anthraquinon-1-yl)thiourea 4 in which the hydrogen bond donor thiourea in combination with anthraquinone moiety serve as chromogenic signalling subunit.

![Chemical structures](image)

The interesting feature of this report is that the 4 detected F\(^-\) ions selectively in CH\(_3\)CN, over the other ions of the same basicity such as AcO\(^-\) and H\(_2\)PO\(_4\)\(^-\) showing the binding affinity in the order F\(^-\)>>AcO\(^-\)>H\(_2\)PO\(_4\)\(^-\), which is inconsistent with the anion basicity. This deviation has been explained on the basis of AM1 calculations which revealed the existence of intramolecular hydrogen bonded stable structure 4a which is less effective for oxygen anionic analytes. Upon addition of F\(^-\) ions, the absorption spectrum of 4 was bathochromically shifted with color change from colorless to yellow attributed to the formation of 4b. In contrast to this, thiourea-containing coumarin 5 synthesized by Ghosh and co-workers,\(^6\) lacks such intramolecular hydrogen bonding.
and show strong binding affinity to oxygen anionic analytes such as C_6H_5COO^- over F^- in CH_3CN in contrast to 4, thereby supporting the effect of the involvement of amidic NHs in intramolecular hydrogen bonding upon the selectivity. Upon the addition of F^- and C_6H_5COO^- ions to a solution of 5, the original absorption band showed remarkable bathochromic shift from 330 nm to 455 and 348 nm, which was also accompanied by a visual color change from colorless to yellowish-brown and light green, respectively.

Further by using the thiourea moiety as binding site and p-nitrophenylhydrazine as a signalling unit, Lin et. al.\(^7\) designed an efficient colorimetric sensor 6, which detected F^-, AcO^- and H_2PO_4^- in DMSO and DMSO/H_2O (95:5, v/v), over other anions via hydrogen bonding interactions, with binding affinity order: AcO^->F^-~H_2PO_4^-~Br^-~Cl^-~I^- The presence of F^-, AcO^- and H_2PO_4^- caused a significant bathochromic shift in the original absorption band of 6 accompanied by the color change from light to deep purple. In addition, 6 has been successfully employed for the detection of F^- in toothpaste also. However, another chemosensor 7 reported by the same group\(^8\) showed the almost equal affinity for F^-, AcO^- and H_2PO_4^- in DMSO/H_2O (95:5, v/v).

The detection of F^-, AcO^- and H_2PO_4^- has also been reported\(^9\) using 3-bis-N-(9,10-diaza-anthracen-1-yl)-N'-phenylurea 8 and 2,3-bis-N-(9,10-diaza-anthracen-1-yl)-N'-phenylthiourea 9. Upon addition of only F^- to the DMSO solutions of 8 and 9 showed the appearance of broad new bands centered at 512 and 516 nm, respectively, in the UV-vis spectra, along with color change from yellow to red. This suggested that F^- anion interacts with the receptors 8 and 9 more strongly due to its higher electronegativity and smaller size compared to the other halides. Moreover, the color change of receptor 9 was much more sensitive to F^- than that of receptor 8, also
suggested the formation of stronger hydrogen bonds between the acidic NH groups of receptor 9 and F⁻. Receptors 8 and 9 showed prominent orange color upon addition of \( \text{AcO}^- \) and \( \text{H}_2\text{PO}_4^- \), due to the formation of similar hydrogen bond interactions between the urea or thiourea groups and the corresponding anions.

\[
\begin{align*}
8 & \quad X = \text{O} \\
9 & \quad X = \text{S}
\end{align*}
\]

Vilar et al.\(^\text{10}\) utilized azo-phenylthiourea dyes 10 and 11 as colorimetric probes for \( \text{CN}^- \), \( \text{F}^- \), \( \text{AcO}^- \) and \( \text{H}_2\text{PO}_4^- \) ions. Interestingly, in CH\(_3\)OH these sensors detected only \( \text{CN}^- \) whereas in DMSO, all the four anions were detected. Each of these anions induced a different color change enabling the naked-eye detection. Further, the color changes were not due to hydrogen bonding interaction, but were attributed to deprotonation of thiourea NH groups. This study constituted the first report on the incorporation of the dye 10 in the nanostructured Al\(_2\)O\(_3\) films which were also used for sensing. In fact, the Al\(_2\)O\(_3\) film could detect \( \text{CN}^- \) at a much lower concentration (< 3 ppm) than in the solution state (8 ppm).

Johnson et al.\(^\text{11}\) synthesized an interesting hydrogen bonding receptor 12, based on arylacetylene core with the two urea moieties arranged to provide a binding cavity. As expected, 12 showed preferred binding with spherical halide anions. More interestingly, the pyridine N atom upon protonation also afforded an additional binding site as well as furnished enhanced binding constants by more than one order of magnitude over those of neutral 12 with an altered selectivity for larger halide ions.

Jiang et al.\(^\text{12}\) have reported the use of N-(acetamido)thiourea 13 as a sensor for \( \text{F}^- \), \( \text{AcO}^- \) and \( \text{H}_2\text{PO}_4^- \) anions in CH\(_3\)CN. The CT band of 13 at 331 nm showed a
bathochromic shift of the order of 56 nm with a concomitant color change from colorless to yellow. Likewise, [1-(naphthalen-2-yl)-3-(6-nitrobenzothiazol-2-yl)]-thiourea 14 detected\(^{13}\) \(\text{AcO}^-\) and \(\text{F}^-\) ions in DMSO along with naked-eye visible color changes attributed to two different mechanisms. For \(\text{AcO}^-\) ions hydrogen bonding interactions are proposed whereas for \(\text{F}^-\) ion hydrogen bonding interaction followed by deprotonation mechanism has been proposed as shown in the scheme 1. Such deprotonation of NHs by \(\text{F}^-\) in anion sensing chemistry was in fact first reported by Gunnlaugsson \textit{et. al.}\(^{14}\) and Gale \textit{et. al.}\(^{15}\) followed by Fabbrizzi \textit{et. al.}\(^{16}\) who had reported on the deprotonation of (thio)ureas in the presence of anions.

![Chemical structures and reactions](image)

**Scheme 1**

Among other aromatic molecules that have found utility in the design of chromophoric supramolecular materials, naphthalimide derivatives have attracted particular attention.\(^{17,14b}\) Their compact structures, rich spectroscopic and electrochemical properties render them as good chemosensors. A simple derivative 15 along with others was employed by Gunnlaugsson \textit{et. al.}\(^{14b}\) for the detection of anions in DMSO. In the presence of \(\text{F}^-\), the original absorption bands of 15 at 446 and 287 nm attributed to internal charge-transfer (ICT) and n-\(\pi^*\) transitions, respectively, exhibited significant bathochromic shifts accompanied by a visual color change. The cause of these perturbations was proposed to be the deprotonation of the amine group in the
presence of highly basic F− ions. Interestingly, when the solution of 15+\textit{F} was exposed to air for several hours, the color of the solution got reversed. The authors ascribed this reversal to the ability of deprotonated 15 to fix atmospheric CO₂ as HCO₃⁻.

![Chemical structures](image)

Further, chemosensor 16 derived by linking two naphthalimide groups via urea, could distinguish between the anions in the order of their basicities which was signaled by the development of vivid colors.\(^{18}\) It was observed that in the presence of less basic anions such as AcO⁻ and H₂PO₄⁻, the deprotonation of one of the NH fragments occurred whereas in the presence of more basic anions such as F⁻ and OH⁻, double deprotonation involving both the NH fragments took place and resulted in bathochromic shift in the absorption band and corresponding color changes.

Similar recognition of F⁻ via hydrogen bonding followed by deprotonation of the urea receptor connected to the naphthalimide 17 has recently been reported.\(^{19}\) The ICT from the NH of the urea donor to imide acceptor gets perturbed in the presence of F⁻ which is manifested in the form of bathochromic shift in the original absorption band and quenching of emission with related naked-eye color change. On the other hand, a core substituted naphthaleine diimide 18 bearing a bis-sulfonamide group exhibited an interesting solvent dependent behaviour towards binding with F⁻ over other anions.\(^{20}\) Unique selectivity and reactivity for F⁻ through a two stage deprotonation process was demonstrated in CHCl₃. However, when the experiment was performed in the more polar and competing DMSO, different spectroscopic and stoichiometric changes were observed which have been ascribed to the loss of basicity of F⁻ (through solvation) in the more polar DMSO.

![Chemical structures](image)
Kondo et al.\textsuperscript{21} have synthesized and studied the anion recognition properties of 2,2'-binaphthalene derivatives 19 and 20 bearing thiourea or urea moieties at the 8- and 8'-positions. The selectivity trends of association of anions were found to be F\textsuperscript{−}>AcO\textsuperscript{−}>H\textsubscript{2}PO\textsubscript{4}\textsuperscript{−}>Cl\textsuperscript{−}>HSO\textsubscript{4}\textsuperscript{−}>NO\textsubscript{3}\textsuperscript{−}>Br\textsuperscript{−} for 19, and F\textsuperscript{−}>AcO\textsuperscript{−}>Cl\textsuperscript{−}>H\textsubscript{2}PO\textsubscript{4}\textsuperscript{−}>Br\textsuperscript{−}>HSO\textsubscript{4}\textsuperscript{−}>I\textsuperscript{−} for 20. The remarkable selectivity for Cl\textsuperscript{−} shown by 20, has been attributed to its orientation suitable for effective hydrogen bond formation with Cl\textsuperscript{−}. It has also been suggested that a chemosensor with a near infrared (NIR) response could avoid interference from the endogenous chromophores and would be more useful in biological systems.\textsuperscript{22} Ghosh et al.\textsuperscript{23} reported thiourea/urea based indole conjugated receptors 21 and 22 that depicted huge red shifted (~600 nm) NIR signal at wavelength in excess of 900 nm, in the presence of F\textsuperscript{−} in CH\textsubscript{3}CN/DMF (9.6:0.4, v/v) solution. Upon adding F\textsuperscript{−} ions, the original absorption bands of 21 and 22 at 342 nm, attributed to Ar-CH=NH- conjugation got shifted to 936 and 904 nm in 21 and 22, respectively, accompanied by the appearance of multiple bands in the region of 500-600 nm as shown in figure 2.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{image}
\caption{Changes in the absorption spectrum of 21 (1 x 10\textsuperscript{−5} M) in CH\textsubscript{3}CN/DMF (9.6:0.4, v/v) solution upon addition of F\textsuperscript{−} ions. Inset: separated spectra from the titration plot. (Reproduced from reference 23)}
\end{figure}
The high energy bands are suggestive of the presence of deprotonated forms of the receptors in solution. The large shift observed in 21 ($\Delta \lambda = 594$ nm) has been attributed to the extended conjugation in planar 21 favouring the maximum distribution of the negative charge of the deprotonated form in the presence of $F^-$. The relatively small wavelength shift ($\Delta \lambda = 562$ nm) in case of 22 has been ascribed to the less acidic amidic proton of urea which led to the weaker binding with $F^-$. 

From the above reports, it has been concluded that most of the studies involving hydrogen bonding interactions have been carried out in either pure organic solvents or in organo-aqueous media containing very small volume of water to avoid the possible competition by the solvent for anions, although this shortcoming has been pointed out in many reports in the literature.\textsuperscript{b} Consistent with the interactions found in natural systems, and to mimic the biological recognition events, receptors capable of anion binding within highly competitive aqueous conditions, led\textsuperscript{24} to the colorimetric sensor 23, which could be used in highly competitive aqueous medium to detect $F^-$, AcO\textsuperscript{-} and H\textsubscript{2}PO\textsubscript{4}\textsuperscript{-}. The mechanism for the recognition event has been proposed to be mediated through bonding to a charge neutral receptor that causes concomitant changes in the ICT of 23. The discussion on the use of 23 as well as many more examples of urea/thiourea based derivatives employed for the recognition of anions and has been presented in the latest reviews by Jiang \textit{et. al.}\textsuperscript{25} and Fabrizzi \textit{et. al.}\textsuperscript{26}

\begin{center}
\includegraphics[width=0.3\textwidth]{23.png}
\end{center}

Despite the high acidity of the hydroxyl group, far less attention has been paid to the phenolic OH group as hydrogen bond donor binding sites for anions. Some studies on OH containing receptors have appeared in literature with specific reference to similar binding of anions by certain proteins employing hydroxylated residues as binding sites.\textsuperscript{27,28}
Azophenol derivatives are expected to have potential affinity for anions through hydrogen bonding and there are limited reports on their applications as anion sensors. Hong et al.\textsuperscript{29} explored the sensing behaviour of simple azophenols 24-26, which were claimed to be highly selective for $\text{F}^-$ over other anions in CHCl$_3$ solution. The same group subsequently reported\textsuperscript{30} azophenol-thiourea based anion sensor 27 which although recognized $\text{F}^-$, $\text{AcO}^-$ and $\text{H}_2\text{PO}_4^-$ but lacked selectivity. A structurally related azophenol 28, possessing $p$-nitrophenol moieties at the two thiourea residues, however detected these three anions as well as showed colorimetric differentiation.\textsuperscript{31}

![Chemical structures of azophenols and thiourea derivatives](image)

Hijji et al.\textsuperscript{32} synthesized $N$-(2-hydroxy-5-nitrophenyl)salicylidene 29 possessing two hydroxy groups which detected $\text{F}^-$, $\text{AcO}^-$ and $\text{H}_2\text{PO}_4^-$ via multiple hydrogen bondings as represented in 29a, 29b and 29c. Upon addition of these ions, the original absorption band of 29 showed a substantial bathochromic shift from 342 to 450 nm in CH$_3$CN. Interestingly, 29 could also distinguish $\text{AcO}^-$ from $\text{F}^-$ and $\text{H}_2\text{PO}_4^-$ in aqueous CH$_3$CN. The binding constant variation in the order of $\text{F}^-\approx\text{AcO}^-<\text{H}_2\text{PO}_4^-$ is roughly consistent with the basicity of the anions and is attributed to the double hydrogen bonding as shown in 29b.

![Chemical structures of azophenols and thiourea derivatives](image)
Recently, the binding property of curcumin 30, a compound containing two hydroxy groups was evaluated by Wu et al.\textsuperscript{33} The studies have shown that it is highly selective for F\textsuperscript{−} over AcO\textsuperscript{−}, H\textsubscript{2}PO\textsubscript{4}\textsuperscript{−} and Cl\textsuperscript{−} because of anionic complex formation via hydrogen bond formation/deprotonation of one of the hydroxyl groups (Eq. 1), due to which the absorption spectrum shifts bathochromically accompanied by visual color change. Also in the process emission got quenched.

\[
\text{LH}_2 + \text{F}^− \xrightleftharpoons{} [\text{LH}_2 \cdots \text{F}^−] \xrightarrow{} [\text{LH}]^− + \text{HF}
\]

(\text{Eq. 1})

The compounds bearing OH group in combination to NH group constitute another important class of sensors for the recognition of anions via either hydrogen bond or multiple hydrogen bond interactions. Kandhaswamy et al.\textsuperscript{34} synthesized novel colorimetric receptors 1-[(2-hydroxy-5-bromobenzylidene)amino]anthraquinone 31, 1-[(2-hydroxy-5-methylbenzylidene)amino]anthraquinone 32 and 1-[(2-hydroxy-5-nitrobenzylidene)amino]anthraquinone 33 which were highly selective for F\textsuperscript{−}. The solutions of receptors 31, 32 and 33 in DMSO showed dramatic color changes from light pink to dark pink, brown and golden yellow, respectively, accompanied by bathochromic shifts in their respective absorption bands. These modulations in visible and absorption changes have been proposed to be due to the hydrogen bond interactions between the OH groups and F\textsuperscript{−} ions. The higher selectivity for F\textsuperscript{−} ions was attributed to its higher electronegativity and smaller size compared to the other halides.

Related chromogenic receptors possessing phenolic OH and hydrazine NH groups as binding sites and nitro group as the signalling unit 34 and 35 have also been used\textsuperscript{35} for the detection of F\textsuperscript{−} ions via hydrogen bond or deprotonation events which affect the electronic properties of the chromophore, resulting in bathochromic shift in the absorption band as well as color change caused by a new CT interaction between the F\textsuperscript{−}-bound OH and NH and the electron deficient nitro group. Likewise, structurally similar phenol-hydrazone Schiff bases 36-38 reported by Lin et al.\textsuperscript{36-38} were found to
be sensitive to F⁻, AcO⁻ and H₂PO₄⁻. The sensing of these anions was achieved in DMSO or DMSO/H₂O (95:5, v/v) mixture, by virtue of forming multiple hydrogen bonding at charge neutral sites (36a, 37a, 38a). The perturbations in the visual as well as spectroscopic responses of 36, 37 and 38 have been ascribed to the CT processes as discussed for 31-35. Likewise, 39 was found to be highly selective for F⁻. The ICT within the molecule involving the electron rich -NH and the electron deficient -NO₂ groups³⁹ was interrupted through hydrogen bonding.

Simple cleft-shaped compounds 40 and 41 containing amidic NHs in combination with either benzimidazole (40) or hydroxyl groups (41) as recognition units were synthesized by Jang et. al.⁴⁰ and Bao et. al.,⁴¹ respectively, and used for the recognition of F⁻ and AcO⁻ in CH₃CN/DMSO (99:1, v/v) and DMSO, respectively,
selectively over other anions via multiple hydrogen bonding interactions involving amidic as well as benzimidazolic NHs in 40 and OH groups in 41. The ICT absorption band of both 40 and 41 got bathochromically shifted and showed concomitant color changes upon the addition of increasing amounts of the two anions.

A similar compound 42 utilised hydrazine NH as the binding site and allowed recognition of AcO− ions,42 through modulation of its ICT. By utilising the anthracene and nitrophenyl group as signalling unit, Kim and Kang et al.43 have developed 43 possessing two amidic hydrogens in combination with two amine hydrogens as binding sites for the anions. Thus, 43 bound anions with a selectivity order AcO−>H2PO4−>BzO−>HSO4−>ClO4−>NO3−. In addition, it also proved to be an efficient naked-eye sensor for F− and HP2O73−.

The pyrrole and indole moieties possess relatively acidic hydrogens44 and thus have marked tendency to form strong H-bonds with anions. A number of receptors bearing pyrrolic moieties have been described in recent years.45 Shao et al.46 have developed bis(indolyl)methene 44 containing an acidic hydrogen bond moiety as colorimetric chemosensor for anions in different media operating via deprotonation/protonation mechanism. It has been found to be highly selective for F− in CH3CN and HSO4− in CH3CN/H2O (4:1, v/v) solution, based on different proton transfer signalling modes. In CH3CN, 44 got deprotonated by F− and its original absorption band at 423 nm, attributed to the ICT of the conjugated bisindolyl skeleton showed a significant bathochromic shift accompanied by a dramatic color change. However, in aqueous medium, 44 got protonated by the strong acid, HSO4−, giving a selective yellow to pink color change accompanied by a bathochromic shift from 435 to 500 nm.
Sessler et al.\textsuperscript{47} have reported on the synthesis and anion binding properties of 2,3-diindol-3-yl quinoxalines 45 and 46. The molecules display greatest affinity for H$_2$PO$_4^-$ anion followed by F$^-$> BzO$^-$>Cl$^-$> HSO$_4^-$. Interestingly, 46 showed higher affinities for the anions studied as compared to 45, which has been attributed to the presence of electron withdrawing nitro group that enhanced the acidity of the pyrrolic NH. On the other hand, a simple indole-azadiene conjugate 47 was found to be highly selective for F$^-$ and the sensing event has been proposed\textsuperscript{48} to be driven by interaction between the indolic NH protons and F$^-$.  

![Chemical Structures](image)

45 \( R=H \)  
46 \( R=\text{NO}_2 \)

Chow et al.\textsuperscript{49} designed receptors 48-50 that contain a maleimide unit as a signalling subunit and indoles (48 and 49) and pyrroles (50) as binding sites. Compounds 48 and 49 showed bathochromic shift in their absorption bands as well as change in color from yellow to orange in the presence of F$^-$ and H$_2$PO$_4^-$ ions. The two indolyl NH groups, chelating the anions through hydrogen bonding interactions have been held responsible for these changes. However, different behaviour was shown by 50 towards the anions, especially CN$^-$. The more basic nature of the CN$^-$ caused the deprotonation of one of the more acidic pyrrolic NH causing the perturbations in the electronic as well as visual properties of 50.

![Chemical Structures](image)

Further, employing indole based indolecarbazole-quinoxalines 51 and 52, Yan et al.\textsuperscript{50} reported efficient sensing of AcO$^-$ and F$^-$ ions. While both AcO$^-$ and F$^-$ caused
a bathochromic shift of the absorption band of 51 in DMSO, the absorption bands of 52 were shifted only by F⁻. The absorption band alterations are accompanied by visible color changes which could also help to distinguish these two ions by naked-eye. Recently, another indolecarbazole based chemosensor 53 has been prepared\(^{51}\) and evaluated for its behaviour towards anions. It has been found to be selective for F⁻ ions in CH₃CN/H₂O (4:1, v/v) mixture. The recognition mechanism has been proposed to proceed via deprotonation of phenolic OH as well as NH groups by F⁻ ions.

![Chemical structures](image)

The tetapyrrole calix[4]pyrroles have also been reported as anion\(^{52}\) and ion-pair receptors.\(^{53}\) The octamethylcalix[4]pyrrole has received considerable attention for the determination of anions,\(^{53,54}\) especially F⁻. It has been reported that calixpyrrole systems, in general, do not show good affinity for F⁻ in competitive solvents such as DMSO, but the structural modifications of the basic tetapyrrole scaffold led to much better affinity for F⁻ over other anions. Thus, the presence of strong electron withdrawing groups in 54-56 increased the spectral response as well as affinity (even > 10⁶ M⁻¹ in DMSO) and showed good selectivity for F⁻ over AcO⁻, H₂PO₄⁻ and HP₂O₇³⁻ ions.\(^ {55}\) The sensing event was accompanied by bathochromic shifts in the original absorption bands as well as prominent color changes in the presence of these anions. The spectroscopic perturbations and the visual color changes have been attributed to the CT resulting from the binding of the anion to the pyrrolic NH of the chromophore.
An interesting study on the use of calix[4]pyrrole derivative bearing dipyrrolylquinoxaline 57 was reported by Sessler et al. In this case, six pyrrolic NHs were available for binding to anions in the small macrocyclic cavity. However, in CH$_3$CN/DMSO (97:3, v/v) it showed a remarkable selectivity and affinity ($10^7$ M$^{-1}$) for F$^-$ over other anions such as Cl$^-$, AcO$^-$ and H$_2$PO$_4^-$ . A two-step binding process depending upon the concentration of F$^-$ ions has been suggested. It was proposed that at low anion concentration, all the six NHs were not involved in the binding, the two additional pyrrole moieties instead interacted via anion-π interactions and only at higher F$^-$ concentration, all the NH protons were directly involved in the binding process.

![Chemical structures](image)

Similar to calix[4]pyrroles, their intermediates dipyrrromethanes, have also been demonstrated as versatile anion receptors and sensors. The reports of Chauhan et al. and Jeon et al. have highlighted the use of dipyrrromethane derivatives 58-61 and 62-65, respectively as chemosensors. On the basis of the spectral and visual changes exhibited by 58-61 in the presence of different anions, the authors have proposed that the derivatives appended with electron withdrawing groups displayed enhanced affinity and selectivity for F$^-$, H$_2$PO$_4^-$ and AcO$^-$ than the ones with electron donating groups in different solvents, as the sensing event involves hydrogen bond interactions. In contrast to this, the derivatives 62-65 modulate their electronic properties only in the presence of F$^-$, thereby exhibiting high selectivity for F$^-$ over other anions in CH$_3$CN. During the
sensing event, establishment of an electrostatic interaction between pyrrole NH of dipyromethane and F⁻ anion has been suggested.

From the above examples, it is evident that in vast majority of the reported systems, anions are coordinated using hydrogen bonding interactions. The interaction between a metal centre and an anion (Lewis acid-base interaction) can also be a convenient route to achieve strong binding in comparison with the hydrogen bond, although the strength of this kind is qualitatively predicted by the Hard Soft Acid Base (HSAB) principle. A significant number of reports have appeared on such systems.⁶⁰

![Diagram of complexes 66 and 67](https://via.placeholder.com/512)

The group of Hong et. al. previously engaged in the synthesis of azophenol-based sensors for anions working via hydrogen bonding,²⁹-⁴¹ synthesized an azophenol-based compound 66 containing two Zn²⁺-bis(2-pyridylmethyl)amine (DPA) units, which could selectively recognize the biologically important P₂O₇⁴⁻ anion among other anions in water⁶¹ over a wide range of pH. In the recognition process, the original absorption band of 66 exhibited a bathochromic shift accompanied by the corresponding color change. The X-ray structure of 66-P₂O₇⁴⁻ complex revealed that the two sets of oxygen atoms on each P of P₂O₇⁴⁻ bound to the binuclear Zn complex by bridging the two metal ions to give rise to two hexacoordinated Zn²⁺ ions in 66-P₂O₇⁴⁻. Even though 66 showed high affinity and selectivity in aqueous solvent, in order to develop more effective sensor which could recognize P₂O₇⁴⁻ in biological systems where the concentration of P₂O₇⁴⁻ ions is very low, the same research group later on developed⁶² another sensor 67 which showed improved binding affinity, taking the advantage of synergistic effect of the metal coordination and hydrogen bonding. The
four amide hydrogen bond donors interact with the $P_2O_7^{4-}$ ion coordinated to the two $Zn^{2+}$ ions as shown in figure 3.

**Figure 3.** Single crystal X-ray structure of $67-P_2O_7^{4-}$. (Reproduced from reference 62)

Fabbrizzi *et al.*$^{63}$ have also explored the synergistic effect of metal coordination and hydrogen bonding/deprotonation. The versatility of metallo-azacyclam based systems 68 and 69 as anion receptors has been demonstrated and it has been shown that the proximate metal centre enhanced the intrinsically poor H-bond donor tendency of a single secondary amide group through two distinctive cooperative effects: i) multiple hydrogen binding with weakly basic $H_2PO_4^-$ ions, and ii) intramolecular binding mechanism involving carbonyl oxygen atom, thereby favoring the deprotonation of amidic group in the presence of more basic $AcO^-$ ions. Additionally, Fabbrizzi *et al.*$^{64}$ have also comprehensively reviewed the role of the transition metal ions in the signalling mechanism to support the anion recognition.

$$\text{68} \ R = NO_2$$

$$\text{69} \ R = CN$$

A neutral Pt(II) complex Pt-70 has been reported$^{65}$ in which the presence of Pt allowed preorganisation of 4,4'-di(1H-indol-7-yl)-2,2'-bipyridine-4,4'dicarboxamide 70 and enhanced its affinity for anions. The selectivity of the Pt complex for $H_2PO_4^-$, has been attributed to the higher degree of pre-organisation induced by the Pt(II) centre locking the rotation around the pyridine-pyridine bond as shown in scheme 2.
Scheme 2

That the alkaline earth metal ions could also serve as coordinative centres for anion recognition, was well demonstrated by the research group of Zhang and Wu et al.\textsuperscript{66} It has been shown that the Mg\textsuperscript{2+} and Ca\textsuperscript{2+} complexes of 71 recognize HSO\textsubscript{4}\textsuperscript{−} or H\textsubscript{2}PO\textsubscript{4}\textsuperscript{−} ions in CH\textsubscript{3}CN over the other anions, through the formation of a secondary complex between Mg\textsuperscript{2+}-71 and Ca\textsuperscript{2+}-71 and HSO\textsubscript{4}\textsuperscript{−} or H\textsubscript{2}PO\textsubscript{4}\textsuperscript{−} anion via center-metal-assisted hydrogen bonding. The tetrahedral structures of HSO\textsubscript{4}\textsuperscript{−} or H\textsubscript{2}PO\textsubscript{4}\textsuperscript{−} provided suitably conjugated oxygen atoms with negative charge for ligating to the metal center, which assisted the formation of hydrogen bonding between anion and carbonyl group of the complexes. The resulting electronic perturbations are manifested in the form of bathochromic shift in the original absorption bands of complexes Mg\textsuperscript{2+}-71 and Ca\textsuperscript{2+}-71.

Further, the effect of preorganisation and the resultant polarisation of the binding sites along with degree of steric and electrostatic repulsion by the peripheral substituents on the binding affinities of the receptors has been well demonstrated by Maeda et al.\textsuperscript{67} The authors have evaluated the binding behaviours of BF\textsubscript{2} complexes of β-tetraethyl-substituted dipyrrolyldiketones 72 and 73 with and without electron withdrawing groups, respectively, towards F\textsuperscript{−}, Cl\textsuperscript{−}, Br\textsuperscript{−}, AcO\textsuperscript{−}, H\textsubscript{2}PO\textsubscript{4}\textsuperscript{−} and HSO\textsubscript{4}\textsuperscript{−} and...
72 was shown to possess higher affinity than 73, ascribed to the electrostatic and steric repulsions provided by the latter to the anions. The substituents at the pyrrole rings not only control the polarisation of binding sites (NH and CH), but also stabilizes the preorganised conformations and degree of steric repulsion.

Recently, the BF$_2$ complexes 74 and 75 have been reported$^{68,69}$ as efficient anion sensors. While 74 exhibited high selectivity for F$^-$ in CH$_3$CN over other anions via hydrogen bonding interaction between the indolic NH proton and F$^-$, 75 exhibited selectivity for CN$^-$ in CH$_3$CN/H$_2$O (4:1, v/v) via the modulation of the ICT involving two o-cresol groups as donors conjugated to the difluoroboron enolate acceptor. The sensing event in 74 was accompanied by a bathochromic shift in the absorption band and emission quenching, whereas in 75, presence of electron withdrawing groups on the donor part of the 75 resulted in hypsochromic shift in both absorption and emission spectra while presence of electron donor groups resulted bathochromic shift in both absorption and emission spectra.

From the above examples, it was found that the metal centre and additional binding sites of the receptors work in conjunction during the sensing event. There are very limited reports on the receptors where the metal centre alone plays the detector’s function. One such example has been reported by Mandolini and Rissanen et. al.$^{70}$ where the neutral receptors 76 and 77 make use of an immobilised UO$_2^{2+}$ dication as the sole binding site for F$^-$. Additionally, both the complexes have almost equal affinity also for AcO$^-$ and CN$^-$ but differ with respect to affinity for H$_2$PO$_4^-$, which however is significantly recognized by 76. This is attributed to the presence of bulky tert-butyl groups in 77, which provide steric hindrance to the anion approaching the dication.

Another important class of receptors relying upon the binding site-signalling subunit approach is the charged receptors which employ electrostatic cation-anion interactions as the main driving force for binding. Despite the fact that these interactions are energetically very strong as compared to hydrogen bonding, these
Review of literature

Receptors have gained less importance because the cationic species are accompanied by unavoidable competing counter-anions. Consequently, there are limited reports in the literature on such systems. The doubly charged 78, a biphosphonium derivative of naphthalene has been found to be highly selective for \( F^- \) over other anions in DMSO which has been attributed to the acidity of the methylene protons and the small size of \( F^- \) ions.\(^{71}\) Similarly, the potential of protonated forms of merocyanine dyes 79-81 as anionic chemosensors was evaluated for different anions in CHCl₃ and CHCl₃-H₂O biphasic medium.\(^ {72}\) The different behaviour of these towards \( F^-, \) \( CN^- \) and \( H_2PO_4^- \) ions have been ascribed to their structural differences and the extent of stabilisation of the negative charge on the phenolate group. In addition to these, many more examples that appeared in literature have also been reviewed.\(^ {73}\) Here in, we present some systems that have been investigated recently and appeared to be good candidates for cation detection with special focus on transition elements.

![Chemical structures](image)

The dye 82 containing aza-oxa binding site and nitrophenylazophenyl reporting group showed high selectivity for \( Hg^{2+} \) over the other metal ions.\(^ {74}\) The sensing event was manifested by a bathochromic shift in the CT band of 82 accompanied by a change in color. However, the addition of \( Fe^{3+} \) resulted in the complete disappearance of the CT band suggesting the result of either coordination of the \( Fe^{3+} \) with the azo group or a redox reaction. Likewise, Martínez-Máñez et. al.\(^ {75}\) synthesized a squaraine based receptor 83 with two dithia-dioxa-aza crown groups as the binding sites while the squaraine group as the signalling unit, towards the development of the colorimetric sensors for cations. The receptor 83 could discriminate \( Hg^{2+} \) from other thiophilic cations such as \( Ag^+ \) and \( Pb^{2+} \). Similarly, an unsymmetrical cationic squaraine dye 84 showed a significant shift in its absorption spectrum in the presence of \( Hg^{2+} \) as well as \( Pb^{2+} \) in DCM making it possible to visually detect these metal ions in the presence of other metal ions.\(^ {76}\)
The compounds containing azo groups constitute important colorimetric sensors for cations as their absorption band normally shifts to visible region of the electromagnetic spectrum in the presence of an analyte. Gunnlaugsson et. al.\textsuperscript{77} reported the first azobenzene-based highly selective and sensitive colorimetric sensor 85 for the detection of Cu\textsuperscript{2+}. The strong ICT band of 85, attributed to the push-pull effect of the electron donating amine and electron withdrawing nitro groups, got hypsochromically shifted in the presence of Cu\textsuperscript{2+} ions. The cause of this perturbation has been proposed to be the coordination of the Cu\textsuperscript{2+} to the two carboxylates, the amino moiety and the o-methoxy group which deconjugated the amino moiety from the aromatic receptor and inhibited the ICT. Similarly, the ICT bands of the compounds 86 and 87 functionalised with N\textsubscript{2}S\textsubscript{2}-donor macrocycle and p-nitroazobenzene and phenyltricyanovinyl acceptor groups exhibited the hypsochromic shifts of the order of 100 nm in the presence of Hg\textsuperscript{2+} accompanied by corresponding color changes, which has been attributed to the formation of a stable 1:1 complex involving the donor macrocyclic group and Hg\textsuperscript{2+} ions inhibiting the ICT.\textsuperscript{78}

A structurally similar dye 88 with p-nitroazobenzene as the acceptor and azathia-crown ether as electron donor providing coordinating atoms was also found to
be highly selective for Hg$^{2+}$ over other metal ions.$^{79}$ In this case, the sensing event has been proposed to involve the formation of a stable $^{88}$(Hg$^{2+}$)$_2$ complex involving binding of the Hg$^{2+}$ to S and N atoms within the macrocycle and the -N=N- site, thus perturbing the ICT in $^{88}$ causing a significant hypsochromic shift. A structurally simpler azo 8-hydroxy quinoline benzoate $^{89}$ has been reported to be selective for Hg$^{2+}$ and Cu$^{2+}$ in CH$_3$CN, however, with different spectral shifts for the two metal ions.$^{80}$ The bathochromic shift observed in case of Hg$^{2+}$ has been proposed to be due to binding of Hg$^{2+}$ with quinoline N together with carbonyl O facilitating the ICT process, while the hypsochromic shift observed in case of Cu$^{2+}$ has been ascribed to the complexation of Cu$^{2+}$ at –N=N–C$_6$H$_5$–N(Me)$_2$ unit, which diminished the degree of the ICT. The overall color change could be detected by ‘naked-eye’. Similar hypsochromic shifts in the absorption bands of azobenzene based compounds $^{90-93}$ accompanied by a visible color change from red to pale-yellow, have been observed in the presence of Cu$^{2+}$ in CH$_3$CN.$^{81}$ The silica gel plate immobilised with the compound $^{93}$ was also developed for the detection of Cu$^{2+}$ in low concentration, which could find applications in the medical diagnostics such as analysis of serum.

Further, simple mono azo compounds $^{94}$ and $^{95}$ have been reported$^{82}$ to possess high affinity for Hg$^{2+}$ in CH$_3$CN, as a result of which their original absorption bands got bathochromically shifted. The authors claimed that when these compounds were exposed to Hg$^{2+}$, one of the amine groups coordinated with the ion and the resultant strong metal-induced ICT caused a distinct change in the optical properties of the receptors.

Recently, bis-triazole appended azobenzene chromophore $^{96}$ has been found to be highly sensitive to Cu$^{2+}$ ions in CH$_3$CN/H$_2$O (4:1, v/v) solution.$^{83}$ The sensing event
has been manifested in terms of a hypsochromic shift in the original ICT band of 96 and was attributed to the coordination of Cu$^{2+}$ to the N,N-bis-triazolyl amine inhibiting the ICT. By combining the azo function with crown ether ring and carboxylic groups, Yan et al.$^{84}$ have recently developed a multifunctional compound 97, which exhibited well-defined Hg$^{2+}$-selective ratiometric colorimetric behaviour through bathochromic shift in its original absorption band. The authors have successfully applied this method for the detection of Hg$^{2+}$ in the environmental samples.

As is evident from the previous reports, the receptors containing urea groups have been widely adopted as anion sensors based on hydrogen bonding mechanism. However, the urea based receptors have rarely been employed for the detection of metal ions. Using anthraquinone as chromophore, urea 98-100 or thiourea 101 containing compounds have been synthesized and evaluated for affinity towards cations.$^{85,86}$ These compounds have been characterised by strong absorption bands attributed to the CT interaction between the electron rich urea/thiourea moieties and the electron deficient anthraquinone moiety.

The CT got perturbed in the presence of Hg$^{2+}$ ions, which has been proposed to be due to the interaction of Hg$^{2+}$ ions with the anthraquinone moiety and the NH fragment of the urea in 98-100. Though all three 98-100 were sensitive to Hg$^{2+}$ ions, 100 had higher affinity among these. The differential acidity of the NH fragments of the
urea moiety, caused by electron push-pull properties of the substituents on the para position of phenyl group, has been proposed to be the main reason for their different behaviours towards Hg$^{2+}$. However, compound 101 showed selectivity for both Hg$^{2+}$ as well as Ag$^+$ ions.

1,8-Naphthalimide group with an electron donating and an electron withdrawing group conjugated to the $\pi$-system, is a well known chromophore, exhibiting a strong ICT. The structural modulations in the basic scaffold could lead to the perturbations in the CT. Thus, 4-amino-1,8-naphthalimide linked to the macrocyclic dioxotetraamine 102 detected Cu$^{2+}$ as well as Hg$^{2+}$ in CH$_3$OH over other metal ions.$^{87}$ However, in the presence of Cu$^{2+}$, the absorption band of 102 got hypsochromically shifted, while in case of Hg$^{2+}$, it got bathochromically shifted. The possible reason for the blue shift in case of Cu$^{2+}$ has been proposed to be the coordination of the lone pair of electrons on the 4-amino group to the Cu$^{2+}$ bonded in the macrocyclic cavity, which raised the energy of the CT from amino group to the carbonyl fragment in the 1,8-naphthalimide group. In contrast to this, in case of detection of Hg$^{2+}$, it has been ascribed to the large radius that inhibited its entry in the macrocyclic cavity, but owing to enhanced polarization, compared to Cu$^{2+}$, it interacted with the chromophore via d-$\pi$ interaction and the consequent red shift. The presence of these two metal ions also quenched the fluorescence of 102 at 538 nm.

Further the 4,5-diamino-1,8-naphthalimide based chemosensor 103 recognized Cu$^{2+}$ ions in neutral aqueous solution.$^{88}$ It has been proposed that on capturing Cu$^{2+}$, secondary amine conjugated to the 1,8-naphthalimide chromophore deprotonated (Scheme 3) thereby enhanced the electron donation ability of N facilitating the CT, which led to the red shift in the absorption band as well as fluorescence quenching.
Scheme 3

Recently, 1,8-naphthalimide based perinone dye 104 has been reported to be highly selective for Cu$^{2+}$ over other heavy and transition metal ions. The sensing event has been proposed to be the result of efficient CT phenomenon caused by Cu$^{2+}$ chelation at the three potential binding sites comprising the nitrogen atoms and the carbonyl oxygen (Scheme 4), which resulted in a bathochromic shift in the original absorption band and remarkable enhancement of the fluorescence accompanied by a naked-eye color change.

Scheme 4

The ICT in the coumarin derivatives could be affected by the metal ions and consequently spectral as well as visual changes could be induced. Thus, these compounds were employed as molecular chemosensors for metal ions. Wang et al. synthesized coumarin 105 and was found to be quite sensitive to the presence of Hg$^{2+}$ ions in solution. The absorption band of 105 showed a significant bathochromic shift of 75 nm and the obvious color change could easily be observed by the naked-eye. Likewise, a coumarin Schiff-base 106 which recognized Cu$^{2+}$ selectively, over other metal ions was reported. The attendant visual and the spectral changes were attributed to the formation of push-pull Cu$^{2+}$ Schiff-base complex. They have also fabricated ‘test-strips’ for practical applicability.
Further, coumarin pyridyl ketone 107 was synthesized by Lin et al.\textsuperscript{92} as a chromogenic sensor for transition metal ions. The compound 107 was characterised by ICT induced by the electron push-pull system comprising of electron donating diethylamino group and electron withdrawing pyridyl ketone moiety. The compound 107 was not only able to detect Cu\textsuperscript{2+}, Ni\textsuperscript{2+} and Cd\textsuperscript{2+}, but was also able to discriminate these ions from each other as its absorption band showed bathochromic shift to varying extents in the order Cu\textsuperscript{2+} > Ni\textsuperscript{2+} > Cd\textsuperscript{2+}. The authors have proposed only pyridyl ketone moiety as the metal binding site.

By replacing the electron withdrawing pyridyl ketone moiety with the strong electron withdrawing thiazole ring, recently, Kim et al.\textsuperscript{93} have synthesized chemosensor 108 which has been found to be highly selective for Cu\textsuperscript{2+} in aqueous DMSO. The binding sites involved in binding to metal ions comprised the coumarin carbonyl oxygen, thiazole nitrogen and phenolic oxygen atoms. However, the thiazole based compounds 109 and 110 lacking the coumarin moiety, reported previously by the same research group,\textsuperscript{94,95} were found to be selective for Zn\textsuperscript{2+} in C\textsubscript{2}H\textsubscript{5}OH:H\textsubscript{2}O (9:1, v/v) and Cu\textsuperscript{2+}/Zn\textsuperscript{2+} in DMSO:H\textsubscript{2}O (1:9, v/v), respectively, utilizing the same binding sites for binding the metal ions, as receptor 108, except the coumarin carbonyl. The latter receptor has pyridine nitrogen as a replacement to coumarin.

From these studies, it has been found that most of the coumarin receptors showed selectivity for the transition elements. However, in contrast, coumarin derivative 111 reported by Das et al.\textsuperscript{96} exhibited significant selectivity for alkaline earth metals: Ca\textsuperscript{2+} and Mg\textsuperscript{2+}, over other metal ions including transition metal ions. The
preference of 111 for the alkaline metal ion has been attributed to the role of the ester groups which are known for their higher affinity towards these metal ions.

Application of NIR probes for the detection of metal cations of biological relevance has also surfaced. For that the cyanine (functionalised by two nitrogen atoms joined by polymethine groups) compounds have offered an important class of NIR active probes and have been widely used as chemosensors. Since these compounds have strong ICT, their sensing function involved the perturbations of ICT in the presence of analytes. Such perturbation in the presence of Hg$^{2+}$ ions has been reported$^{97}$ in the hemicyanine dye 112 composed of an electron donor N,N-dialkylaniline moiety and an electron acceptor benzothiazolium species which employed sulfur atom for coordinating Hg$^{2+}$. The authors have suggested that Hg$^{2+}$ formed a stable 1:1 complex with 112 involving the sulfur atom of the benzothiazolium group and oxygen atom of the phenolic group forcing 112 to adopt a cis-configuration in which both the chromophores were nonplanar. As a result of this, a hypsochromic shift in the ICT band of 112 was observed in the presence of Hg$^{2+}$. Besides, it showed fluorescence quenching also.

Another cyanine based compound appended with dithia-dioxo-monoaza crown ether moiety 113 exhibited high selectivity for Hg$^{2+}$ in the NIR region.$^{98}$ The ICT band of 113 got blue shifted as compared to its starting heptacyanine dye which was attributed to an efficient excited state ICT from the donor nitrogen atom on the dithia-dioxo-monoaza macrocycle to the acceptor tricarbocyanine group inhibiting the ICT in the cyanine. However, on addition of Hg$^{2+}$, which got trapped in the macrocycle
through the donor nitrogen atoms, a red shift was observed in the absorption band of 113. A merocyanine compound 114 has been reported99 to be highly selective for Cu$^{2+}$, the presence of which shifted its ICT band hypsochromically. The authors have claimed this blue shift due to the coordination of Cu$^{2+}$ ions with the di-2-picolyamine, which decreased the electron donating ability of the nitrogen, thereby inhibiting the ICT process. This perturbation in the ICT also resulted in the fluorescence quenching in 114.

Similar coordination of Cu$^{2+}$ with the di-picolyamine appended on the dicyanomethylene indene alongwith quinoline also inhibited the ICT of the chromophore 115. The perturbation in the ICT was manifested in terms of a hypsochromic shift in the original absorption band and “turned on” the fluorescence of 115, attributed to the disrupted conjugation of amine and cyano groups.100 On the other hand, the chelation of the partially negatively charged oxygen atoms of the merocyanine 116 to Cu$^{2+}$, resulted in the bathochromic shift in its original longer wavelength band thus making it highly selective for Cu$^{2+}$ over other cations.101 Keeping in view the interesting applications of hemicyanine based dyes in various fields such as molecular probes to study the complex biological systems, photosensitisers in dye-sensitized solar cells etc., recently, Zeng et. al.102 have developed a hemicyanine chemosensor 117 for the detection of Hg$^{2+}$ ions over the other cations based on the mechanism of ICT. This chemosensor has additional advantage that being water soluble, it could detect Hg$^{2+}$ in water. Also, the pH stability of this compound in the absence and presence of Hg$^{2+}$, suggested that this sensor might be useful in practical applications.
Chapter 2

Calixarenes have also been found to be interesting platforms in supramolecular chemistry, especially for molecular recognition. The structural modifications of calixarenes give rise to a variety of derivatives such as esters, amides, carboxylic acids, crown ethers and azacrown ethers, with tunable binding properties and excellent selectivity towards various metal ions.\(^{103}\)

![Calixarene structures](image)

In order to make calixarenes selective for both cation and anion, Kim et al.\(^{104}\) have synthesized bis(indolyl)calix[4]crown-6, 118, by appending oxidised-bisindole groups known for anion binding via hydrogen bonding and crown-6 for cation complexation. Claimed to be a first example of its kind, compound 118 showed modulation of its ICT in the presence of Mg\(^{2+}\), Ca\(^{2+}\), Sr\(^{2+}\), Ba\(^{2+}\) and F\(^-\) in CH\(_3\)CN. Interestingly its binding affinity for Ca\(^{2+}\) was enhanced in the presence of F\(^-\). As a consequence of its spectral behaviour in the presence of Ca\(^{2+}\) and F\(^-\), the chemosensor 118 was capable of computing combinational three NOR logic gates and could find application in computational operations. In contrast to this, though the anthraquinone group has also been considered as the important chemosensor for metal ions and anions, 9,10-anthraquinone pendent calix[4]crown 119 detected only Cu\(^{2+}\) in CH\(_3\)CN.\(^{105}\) The addition of Cu\(^{2+}\) ion solution to a solution of 119 resulted in the formation of a new red shifted band which has been attributed to the enhanced ICT from the two oxygen atoms of 1- and 8- positions to the electron deficient carbonyl group, on coordination of Cu\(^{2+}\) to carbonyl oxygen atoms (Cu\(^{2+}\)--O=C) of 119. Keeping in view the sensitized luminescence of lanthanide complexes of calixarene derivatives, and their potential chemical and biological applications, Gao et al.\(^{106}\) have synthesized 120 by incorporating two imine linked p-cresol groups of the upper rim of calix[4]arene, which detected Dy\(^{3+}\) and Er\(^{3+}\) in DCM selectively, over other lanthanides. Unfortunately, the calix[4]arene derivatives bearing two spirobenzopyran moieties in the lower rim,
reported\textsuperscript{107} were found to recognize lanthanide ions without any selectivity. The reason for the selectivity of \textbf{120} for these two ions has been proposed to be the size-fit effect of the calix[4]arene cavity in addition to strengthened $\pi$-cation-interaction driven by the electron donating methoxy groups on the $p$-cresol imine unit. The new absorption band appeared at longer wavelength indicating that Dy$^{3+}$ or Er$^{3+}$ accept more charge from the Schiff base.

Further, a tripodal compound \textbf{121} equipped with three ligating azo groups to the cyclotriveratrylene platform has been utilised as a chemosensor for the determination of Hg$^{2+}$ ions.\textsuperscript{108} The wider pH range stability of this chemosensor made it more useful towards environmental samples. The authors have developed disposable strips by adsorbing it on a suitable support, for the rapid screening of Hg$^{2+}$ ions in aqueous environment.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{image.png}
\caption{Scheme 5 - Absorption and emission behaviour of chemosensors.}
\end{figure}

The quinoline based chemosensors \textbf{122} and \textbf{123} detect Zn$^{2+}$ and Al$^{3+}$ in THF/H$_2$O (9:1, v/v) and CH$_3$OH/H$_2$O (1:9, v/v), respectively.\textsuperscript{109,110} The sensing event in case of \textbf{122} involved the coordination of Zn$^{2+}$ to the N$_4$O$_2$ binding sites [1:2 (Zn$^{2+}$:\textbf{122}) complex] which interfered the intramolecular hydrogen bonding and increased the coplanarity of the conjugated system, resulting in the bathochromic shift in the original absorption band of \textbf{122}. Besides, fluorescence enhancement was also observed. On the other hand, the coordination of Al$^{3+}$ to NO sites [2:1 (Al$^{3+}$:\textbf{123}) complex] modulated the absorption as well as emission behaviour of \textbf{123}. The binding modes in both the cases are shown in scheme 5.
A series of benzooxadiazole skeleton based compounds 124-126 have been evaluated for their behaviour towards different metal ions. The chemosensor 124 was found to be selective for Hg$^{2+}$ and Cu$^{2+}$ ions in CH$_3$CN/H$_2$O (4:1, v/v)\textsuperscript{111} whereas the chemosensors 125 and 126 detected only Hg$^{2+}$ in C$_2$H$_5$OH/H$_2$O (9:1, v/v) and CH$_3$CN/H$_2$O (4:1, v/v), respectively.\textsuperscript{112,113} The sensing mechanism in case of 124 and 125 is based on the interaction of Hg$^{2+}$ and Cu$^{2+}$ ions with nitrogen and sulfur atoms while 126 has triazole group as the additional binding site for Hg$^{2+}$ ions. The hypsochromic shift observed in the original band of 124 in the presence of Cu$^{2+}$ and Hg$^{2+}$ ions was attributed to the diminished degree of CT in the presence of these metal ions.

On the other hand, a bathochromic shift observed in case of 125 in the presence of Hg$^{2+}$ ions was attributed to the formation of stable Hg$^{2+}$-125 complex in the ground state involving nitrogen atoms of the benzooxadiazole group, thereby reducing the charge separation and facilitating the ICT. The bathochromic shift observed in case of 126 has interestingly been explained on the basis of involvement of both the triazole and amino acid moiety in 126 upon complexation with Hg$^{2+}$ ions and the resulting more polar environment induced the related spectral change.
2.2 Displacement approach

Since the pioneering work of Anslyn et. al.\textsuperscript{114} and Fabbrizzi et. al.,\textsuperscript{115} the displacement assays have been extensively used for the development of chromogenic sensors as outlined in figure 4.

![Figure 4. General representation of the displacement approach.](image)

The sensing protocol is based upon two main approaches: (i) the two or more units comprising of organic-organic, organic-indicator or organic-metal-indicator combinations, form an inclusion complex and upon addition of the analyte a displacement reaction occurs i.e. the interaction of analyte with one of the former two cases and organic-metal unit in the later case, releases the other in solution with a concomitant change in their optical characteristics and, (ii) the receptor binds with the metal and the signalling protocol is based upon the demetallation. The first approach is most commonly employed perhaps the interesting feature of this approach is the non-covalent interaction between the groups which allows much better tuning of the sensing systems.

Guo et. al.\textsuperscript{116-118} have developed the non-covalent CT assemblies as chemosensors for selective sensing of anions using this approach. The assemblies, 127-129 were formed from the combination of pyrrole based electron rich species and electron deficient species such as 7,7’,8,8’-tetracyanoquinodimethane (TCNQ) and tetrachlorobenzoquinone (TCBQ, \textit{p}-chloranil). The molecular complex 127 was characterised by an absorption band at 622 nm attributed to the CT interaction between calix[4]pyrrole and \textit{p}-chloranil which got perturbed in the presence of \textit{F}⁻ and \textit{H}_2\text{PO}_4⁻ resulting in the appearance of a new band in the region of 400-500 nm accompanied blue to orange-yellow color change. The authors have claimed that the involvement of
hydrogen bond interactions of NH protons of calix[4]pyrrole with these anions was not the only cause of this CT perturbation, but also the interaction of these anions with \( p \)-chloranil part played an important role.\(^{118}\)

The same group later reported\(^{117}\) another non-covalent CT assembly \( 128 \) comprised of the TCBQ as acceptor and dihydroxymethyl di-(2-pyrrolyl) methane as a donor and evaluated its behaviour towards different anions. This assembly was found to be sensitive to the presence of \( \text{PO}_4^{3-} \) and \( \text{HPO}_4^{2-} \) ions over other inorganic anions, depicting a change in color from blue to orange-yellow in the presence of \( \text{PO}_4^{3-} \) and to yellow-green in the presence of \( \text{HPO}_4^{2-} \) anions and the sensing event has been proposed to involve the same mechanism as described for \( 127 \). In continuation, they have reported\(^{116}\) another CT assembly \( 129 \), using TCNQ as acceptor and keeping the donor same as in \( 128 \). It recognized \( \text{PO}_4^{3-} \) and \( \text{CO}_3^{2-} \) ions in CH\(_3\)CN/H\(_2\)O (1:1, \( \nu/\nu \)) over the other anions.\(^{116a}\) However, when the experiments were performed in CH\(_3\)CN/H\(_2\)O (1:1, \( \nu/\nu \)) at pH 7 using HEPES buffer, it recognized \( \text{SO}_4^{2-} \) ions over the other anions.\(^{116b}\) This variation in the behaviour of \( 129 \) has been correlated with the basicity of the anions. The original blue color of the solution attributed to the \( \pi-\pi \) CT interactions between the donor pyrrole unit and the acceptor TCNQ turned colorless indicating the breakage of the CT interactions. It has been proposed that the presence of \( \text{SO}_4^{2-} \) established a n-\( \pi \) CT interaction with the TCNQ as shown in scheme 6 and released the donor unit. However, such interaction has not been proposed for the behaviour of \( 129 \) towards \( \text{PO}_4^{3-} \) and \( \text{CO}_3^{2-} \). Interestingly, the sensing events were reversible in all the above discussed examples.

![Scheme 6](image)

The examples of the organic-indicator type ensembles are the non-covalent compounds \( 130 \) and \( 131 \) in which the dyes are anchored non-covalently to the calix[4]pyrrole and calix[4]arene receptors, respectively. The dye in the ensemble \( 130 \) got displaced\(^{119}\) by \( \text{F}^- \) and to a lesser extent by \( \text{Cl}^- \) and \( \text{H}_2\text{PO}_4^- \) in CH\(_3\)CN solution,
while in 131, the dye was equally displaced by both the $F^-$ and $H_2PO_4^-$, in DMSO/H$_2$O (1:1, v/v). These displacements resulted in the absorption as well as visual changes.

It has also been reported that the covalently bonded dye to the receptor may also be displaced by the analyte. The example of this is provided by the research group of Machado et al. where the dye in the compound 132 got displaced significantly by the $F^-$ and to a lesser extent by the AcO$^-$ in CH$_3$CN solution, attributed to the nucleophilic strength of the anions. In addition to these CT interactions, the metal ligand interactions have also been considered as highly favourable in assembling the sensor as: (i) the metal ion can present some geometrical preferences, thus imparting selective binding tendencies towards anions of a given shape and, (ii) systems involving the metal ligand interactions could be employed in polar media and find applications in various biological and environmental assays to counter the competing solvation effect. Thus, the approach relying on the use of an indicator bound to the organic-metal complex by means of non-covalent interactions has also been introduced as an important chemosensing ensemble paradigm and has proven to be a useful method in biological assays.

Kim et al. have explored the complex 133 for the detection of HPO$_4^{2-}$ ions. In the complex, the sulphonated pyrocatechol dye (indicator) was bonded to the two Zn$^{2+}$ centres and this binding imparted blue color to the otherwise yellow complex solution in the absence of the dye. The blue color of the aqueous solution of 133 turned yellow on the addition of HPO$_4^{2-}$ ions, accompanied by a hypsochromic shift in the original absorption band at 624 to 444 nm indicating the displacement of the dye by the HPO$_4^{2-}$ ions. The binding to the Zn$^{2+}$ centres in the complex has been found to be two fold stronger than with the dye as revealed by isothermal titration calorimetry method.
The molecular ensemble 134 when anchored with the fluorescent coumarin dye 135 recognized $\text{P}_2\text{O}_7^{4-}$ ions through the displacement of the dye from the complex\(^{123}\) in a manner similar to 133. This displacement restored the fluorescence of the dye which was quenched on binding of 135 with the Cu\(^{2+}\) centres.

The indicator-displacement assay comprised of the metallo-host 136 and the indicator 5(6)-carboxyfluorescein dye 137 has also been employed by Anslyn et al.\(^{124}\) to detect the PO\(_4^{3-}\) ions. Like the previous examples, the introduction of the PO\(_4^{3-}\) ion solution to the host-dye complex solution displaced the dye from the host cavity, thereby creating a sensing ensemble for PO\(_4^{3-}\). Interestingly, when this ensemble was employed for the detection of the PO\(_4^{3-}\) ions in both horse serum and human saliva, gave the results comparable to the clinical results, thereby highlighting the usefulness of this synthetic receptor in real life practical applications.

The indicator-displacement approach has also been employed for the detection of biologically important F\(^-\) ion also. Owing to its high electronegativity, F\(^-\) is known to form stable binary and ternary complexes with many trivalent and tetravalent metal ions, and even with their complexes. Pyrocatechol violet dye-Zr(IV)-EDTA ensemble
138 has been employed\textsuperscript{125} for the detection of F\textsuperscript{−}, which changes its color from blue to orange red accompanied by the corresponding absorption changes in the presence of F\textsuperscript{−} ions.

\begin{center}
\includegraphics[width=0.8\textwidth]{image.png}
\end{center}

Similarly, the oxine-Zr(IV)-EDTA complex 139 and hemicyanine-Zr(IV)-EDTA complex 140 have been successfully employed for F\textsuperscript{−} detection in C\textsubscript{2}H\textsubscript{5}OH/H\textsubscript{2}O (2:8, v/v) and DMSO/H\textsubscript{2}O (3:7, v/v), respectively, following the dye displacement process by F\textsuperscript{−} ions.\textsuperscript{126,127} Moreover, receptor 140 was also employed in determining F\textsuperscript{−} ions in toothpastes. Many similar examples have been reviewed by Martínez-Máñez \textit{et al.} in their latest review.\textsuperscript{1a}

However, this traditional displacement assay has been modified by introducing a coordination metal complex as the signalling system and the signalling protocol is based on an anion-induced demetallation (ligand exchange mechanism). Mainly the copper complexes have been employed in this approach except one report on the use of aluminium complex. The success of this approach was based on the assumption that the competing anion-metal ion should have higher binding affinity than the metal ion-ligand complex from where metal ion has to be removed.

In a similar approach discussed above,\textsuperscript{126} a metal complex 141 has been employed to detect F\textsuperscript{−} via ligand displacement protocol.\textsuperscript{128} The metal:ligand (1:2) complex 141 detected F\textsuperscript{−} ions in aqueous medium at pH 4.38 using acetate buffer without interference from other common ions. The high affinity of Al\textsuperscript{3+} to F\textsuperscript{−} ions caused the release of both the ligand molecules accompanied by a rapid change in the absorption and fluorescence intensity. In a related approach, the copper complex 142 constituted highly sensitive and selective chemosensor for CN\textsuperscript{−} ions with the detection limit 0.13 ppm.\textsuperscript{129} It also detected F\textsuperscript{−} ions but with lesser efficiency and different mechanism. Since CN\textsuperscript{−} is one of the most toxic anions, the detection limit remains an important parameter to be considered for the development of chemosensors able to
detect even the trace amounts of CN\textsuperscript{−}. The US Environmental Protection Agency (EPA) has set the Maximum Contamination Level (MCL) for CN\textsuperscript{−} in drinking water to be 0.2 ppm. In an attempt to develop efficient sensors, Li \textit{et al.}\textsuperscript{130} evaluated the recognition behaviour of Cu\textsuperscript{2+} complex of 143 towards various anions including CN\textsuperscript{−} in water. Though it responded to CN\textsuperscript{−} ion selectively, the detection limit (about 3 ppm) was a bit on higher side and this low sensitivity has been attributed to high stability constant of the 143-Cu\textsuperscript{2+} complex. Keeping this factor in mind, the same group\textsuperscript{131} employed Cu\textsuperscript{2+} complex of Rhodamine based dye 144 for the detection of anions. Interestingly, it was found to be highly selective and sensitive to CN\textsuperscript{−} over other anions like the previous chemo sensors, and the detection limit was as low as 0.013 ppm, conforming to the limit set by the EPA in drinking water. Similarly, the Cu\textsuperscript{2+} complex of 2,2\textprime\textendash;dihydroxyazobenzene 145 demonstrated high sensitivity and selectivity towards CN\textsuperscript{−} manifested in terms of enhanced fluorescence intensity by about 45-fold and visible red-to-reddish orange color change.\textsuperscript{132}

![Chemical Structures](images)

Further the Cu\textsuperscript{2+} complexes of 1,8-naphthalimide derivatives 146 and 147 allowed ratiometric determination of CN\textsuperscript{−} over other anions via fluorescent and colorimetric changes.\textsuperscript{133} Moreover, these chemo sensors work in a 100\% aqueous medium which can find applications in environmental CN\textsuperscript{−} detection assays. Interestingly, the sensing event involved in all the above examples employing the Cu\textsuperscript{2+}
complexes, rely on the formation of stable CuCN complex resulting from the ligand displacement reactions.

In addition to the ligand displacement, the ligand replacement (not involving the demetallation) protocol has also been employed to detect anions. For example, the substitution of Co\textsuperscript{III}-bound water in \textbf{148}-\textbf{150} allowed the colorimetric detection of trace amounts of CN\textsuperscript{−} over other anions.\textsuperscript{134} However, under the same experimental conditions, whereas \textbf{148} and \textbf{150} showed a high tolerance towards SCN\textsuperscript{−}, \textbf{149} showed a slight, almost negligible, hypsochromic shift. On the basis of the results obtained for the binding affinity studies of all the three complexes with CN\textsuperscript{−} at almost neutral and higher pH values, it has been concluded that while the CN\textsuperscript{−} affinities of \textbf{148} and \textbf{150} at higher pH are almost in the same order as their values at lower pH, the value of \textbf{149} is approximately five times higher at lower pH, which is attributed to the effect of the side chains at the periphery of these metal complexes affecting the electronic properties at the cobalt centre. The mechanism of the sensing event was proposed as the replacement of water molecule at the cobalt centre by CN\textsuperscript{−} ions.

In contrast to this, the dinuclear cyclopalladated complexes of methyl orange \textbf{151} and \textbf{152} have been reported\textsuperscript{135} to exhibit binding preference for SCN\textsuperscript{−} over CN\textsuperscript{−}. The sensing event has been proposed to involve the ligand exchange of bridge bonds as shown in scheme 7 for SCN\textsuperscript{−}. In addition to this, \textbf{152} also showed sensitivity towards S\textsuperscript{2−} and SO\textsubscript{3}\textsuperscript{2−} ions and importantly was able to discriminate S\textsuperscript{2−}, SO\textsubscript{3}\textsuperscript{2−} and SCN\textsuperscript{−} from each other on the basis of color changes it showed in the presence of these ions. This
difference in behaviour of 151 and 152 has been attributed to their metalloaromaticity, tuned by the substituents of the azobenzene groups.

\[
\begin{align*}
\text{Scheme 7} \\
151 & R^1 = \text{SO}_2\text{H}, R^2 = \text{N(Me)}_2 \\
152 & R^1 = R^2 = \text{OH}
\end{align*}
\]

2.3 Chemodosimeter approach

Alternatively known as the reaction based approach, chemodosimeter approach (Figure 5) is based upon a reversible/irreversible reaction where the equilibrium is shifted to the product and the product is isolable. Since this process involves the rupture and formation of several covalent bonds, and thus is associated with remarkable spectroscopic and visual modulations.

![Figure 5](image.png)

**Figure 5.** General representation of the chemodosimeter approach.

The key requirements of a good design of the chemodosimeters include (i) operation with high selectivity, (ii) operation preferably in water or mixed organic-aqueous solutions, and (iii) quick response. Though this approach has received relatively little attention as compared to the other two approaches (Section 2.1 and 2.2), it is merited by high selectivity towards the analytes. Most of the assays where chemodosimeter approach has enjoyed great success are the sensing of CN\(^-\) and F\(^-\) ions, where the sensing event is realized through the nucleophilic attack of these anions to the
electron deficient atoms or functional groups of the chemodosimeter that result in the modulation of the electron density in the whole molecule leading to color changes.

Martínez-Mañez et al.\textsuperscript{136} have explored the nucleophilic character of CN\textsuperscript{−} and have reported a squaraine based selective probe 153 for CN\textsuperscript{−} determination in water. The authors have observed the decoloration selectivity upon nucleophilic attack of CN\textsuperscript{−} to a functionalised squaraine. The receptor 153 is characterised by a CT band at 641 nm responsible for its color. When CN\textsuperscript{−} attacks on the four-membered squaraine ring, both the loss of acceptor character of the ring as well as the rupture of the electronic delocalisation result in the disappearance of the CT band. Similar complete bleaching of the color has also been observed during the reaction of calix[4]pyrrole based compound 154 with CN\textsuperscript{−} in DMSO/CH\textsubscript{3}CN (97:3, v/v) even in the co-presence of excess of other anions.\textsuperscript{137} It has been proposed that the nucleophilic attack of CN\textsuperscript{−} at the α-position of the dicyano-vinyl group reduces the extent of conjugation which is responsible for the hypsochromic shift.

The croconium based dyes are expected to exhibit higher sensitivity and rapid response towards the nucleophiles due to the stronger electron withdrawing ability of the croconic acid as compared to squaric acid. In order to probe this, when the behaviour of croconium and squaraine based dyes 155 and 156 respectively,\textsuperscript{138} was compared in probing nucleophilic species, 155 was found to be a better chemodosimeter for cysteine, homocysteine and cysteine-glycine at pH 5.7 and CN\textsuperscript{−} at pH 9.0.

N-acyl triazenes 157 and 158 have been reported\textsuperscript{139} to show selectivity towards CN\textsuperscript{−} as well as F\textsuperscript{−} over other anions via the nucleophilic displacement of the acyl group.
in triazine as shown in scheme 8. The former has equal affinity for both the anions whereas the later showed higher affinity for CN\(^-\) as compared to F\(^-\) in CH\(_3\)CN. Interestingly, when the experiment was performed in CH\(_3\)CN/H\(_2\)O mixture both of them showed sensitivity towards CN\(^-\) only. The authors have ascribed this behaviour to the strong nucleophilicity of CN\(^-\) towards the acyl group and weak hydrogen bonding ability as compared to other anions.

Scheme 8

Taking the advantage of the strong affinity of CN\(^-\) towards the acyl carbonyl carbon, a series of N-nitrophenyl benzamide derivatives 159-163 have been employed for the detection of CN\(^-\) in aqueous medium.\(^{140}\) Among these, the sensitivity of 159 was greater than the others. It has been proposed that during the sensing event, the nucleophilic attack of CN\(^-\) at the activated amide carbonyl function followed by fast proton transfer of the acidic amide hydrogen pushes the nitro aniline group into its active anionic form (Scheme 9) leading to bathochromic shift in the ICT band.

Scheme 9
Kim et. al.\textsuperscript{141} have utilised the intramolecular hydrogen bond of the phenolic OH with carbonyl oxygen in salicylaldehyde based azo compound \textbf{164} for CN\textsuperscript{−} sensing. The authors have proposed that such hydrogen bonding helps in stabilising the anionic character of the intermediate during the nucleophilic attack of the CN\textsuperscript{−}. The original absorption band of \textbf{164} showed a significant bathochromic shift of 160 nm in DMSO accompanied by a visual color change in the presence of CN\textsuperscript{−}.

A cyanide-specific Benzil-cyanide reaction/rearrangement (Scheme 10), has also been exploited to produce a colorimetric chemosensor for CN\textsuperscript{−}. Sessler et al.\textsuperscript{142,143} have employed π-extended benzil derivatives \textbf{165} and \textbf{166} as highly selective reaction based chemosensors for CN\textsuperscript{−} which gave rise to dramatic changes in color, absorption as well as fluorescence properties when their extended π-conjugation pathway got interrupted after reaction with CN\textsuperscript{−}.

Further, the nucleophilic nature of CN\textsuperscript{−} has also been utilised to develop a highly sensitive and effective chemosensor which could even recognize trace amounts of CN\textsuperscript{−} in aqueous environment.\textsuperscript{144} The anthraquinone and azoaniline based derivative
containing trifluoroacetyl groups as electrophiles 167 and 168 respectively, modulated their electronic properties on recognizing CN⁻ ions in CH₃CN/H₂O solvent system which are highlighted in terms of color and absorption changes. These changes are ascribed to the stabilisation of intermediate cyanohydrin by the NH as shown in scheme 11 for 167.

![Scheme 11](image)

Probes 169 and its polymeric analogue 170 containing the trifluoroacetyl group as electrophile detected CN⁻ among other competing anions through reversible covalent bonding, proposed to be the result of unique binding mode of the o-(trifluoroacetyl)carboxanilide group toward the anions.

The molecular probes 171-173 behave as chemodosimeters for CN⁻, wherein the CN⁻ ion added at C-2 of the benzimidazolium carbon to form the adduct restoring the lone pair of electrons on the nitroaniline groups and shifting the absorption bands from 270 to 376 nm, accompanied by visual color changes.

Cheng and co-workers have developed a cyanine dye-based chromofluorescent probe 174 for the detection of CN⁻ in water by making use of strong nucleophilic character of CN⁻ to the positively charged imine moiety of the cyanine dye.
(Scheme 12). This probe has the added advantage of being a NIR sensor with considerably lower detection limit.

![Scheme 12]

The colorimetric and fluorometric changes exhibited by a coumarin derivative 175 having α,β-unsaturated nitro group as activating acceptor unit, in the presence of CN⁻ has been explored by Kim et. al.¹⁴⁹ Nucleophilic aromatic substitution of CN⁻ modulated properties of this chemodosimeter in CH₃CN.

![Scheme 13]

Oxazines are subject to a ring opening equilibrium and the addition of nucleophiles can suppress the ring closing reaction. Based on this, oxazine derivative 176 was employed¹⁵⁰ for the colorimetric determination of CN⁻ in CH₃CN.¹⁵¹ In the presence of CN⁻, the 1,3-oxazine ring of 176 opened to form a 4-nitrophenylazophenolate chromophore as shown in scheme 13. This transformation led to drastic changes in absorbance as well as color visible to naked-eye.

Similar oxazine ring opening of 177 and 178 via the nucleophilic attack of CN⁻ has been reported by Tian’s group.¹⁵² Since the specific reaction accompanied by color change and bathochromic shift in the absorbance occurred only in the presence of CN⁻
over other anions, the authors have labelled these chromophores as highly selective chemodosimeters for CN⁻.

The spiropyran derivative 179 reported by the Shiraishi’s group, also behaved as a chemodosimeter for CN⁻ in aqueous media under the influence of UV irradiation. 179 got converted to a highly colored 180 (Scheme 14), characterised by an intense absorption band at 519 nm. Nucleophilic addition of CN⁻ to 180 induced hypsochromic absorption change through localisation of the π-electron density on the p-nitrophenolate moiety in 179-CN⁻ complex, otherwise delocalised over the whole molecule.

![Scheme 14](image)

Although in the yesteryears, the chemistry of reaction-based sensors for F⁻ ions remained far less developed than CN⁻, recently it has attracted a lot of attraction like CN⁻, through specific reactions induced by F⁻ ions, such as the cleavage reaction of Si-C/O bond, lewis acid-base reactions between electron deficient atom and F⁻ ions, and the intramolecular hydrogen transfer leading mostly to the cyclisation reactions. Among these, the lewis acid-base reaction between boron and F⁻ has taken the lead.

![181-184](image)

In one such approach, the intense absorption bands of a series of trianthrylborane derivatives 181-184, exhibiting extended π-conjugation through vacant p-orbital of the boron atom, upon interaction with F⁻ got interrupted as shown in
figure 6, causing a dramatic color change and hypsochromic shift in the absorption band.

![Diagram](image)

**Figure 6.** Schematic representation of the switching of π-conjugation in the LUMO of boron-based π-electron systems. (Reproduced from reference 157c)

Axially substituted subphthalocyanine* 185 has also been reported\textsuperscript{158} as a colorimetric and fluorescent chemodosimeter via coordination of F\textsuperscript{-} to the boron centre. This coordination has been highlighted in the form of decrease in the intensity of the main absorption band at 565 nm as well as that of the emission band at 578 nm accompanied by naked-eye color change from magenta to colorless.

![Image of 185](image)

It has been reported\textsuperscript{159} that arylboronic acids may also be considered as sensors for F\textsuperscript{-} as the formation of corresponding trifluoroborate species may switch on the ICT involving boron moiety as donor and electron deficient aryl group as acceptor causing the turn-on colorimetric response.

Using this approach, Gabbai and co-workers\textsuperscript{160} have employed cationic boranes with electron deficient pyridinium moieties 186 and 187 (Scheme 15) as turn on colorimetric sensors for F\textsuperscript{-} ions in organic as well as organic/aqueous media on the basis of on-set of ICT which also imparted dark yellow color to the solution.

The silyl-containing 188 also acted as a chromogenic and fluorescent chemodosimeter\textsuperscript{161} for F\textsuperscript{-} taking the advantage of silyl ether deprotection reaction.

---

* a term used for a lower homologue of phthalocyanine consisting of three isoindole units and boron as the central atom.
releasing resorufin in CH$_3$CN/H$_2$O (1:1, v/v). This dosimeter displayed selective drastic changes in absorption and fluorescence emission intensities in the presence of F$^-$ over other anions through F$^-$-triggered Si-O bond cleavage as shown in scheme 16.

![Scheme 15](image)

**Scheme 15**

The compounds 189 and 190 reported$^{162,163}$ recently have also been employed as selective colorimetric and fluorescent chemodosimeters for F$^-$ ion, taking advantage of F$^-$ ion induced cleavage of the trimethylsilyl group. Their interactions with F$^-$ caused drastic changes in their absorption as well as emission behaviour accompanied by corresponding color changes.

![Scheme 16](image)
In addition to these, there are some reports in literature on the detection of \( \text{F}^- \) ions based on intra-molecular cyclization triggered by \( \text{F}^- \) ions. Recently, terphenyl derivatives 191 and 192 having \textit{tert}-butyldimethylsilyl (OTBS) group were employed\textsuperscript{156a} as chemodosimeter for \( \text{F}^- \) ions. Addition of \( \text{F}^- \) ions caused desilylation followed by cyclization via phenolate anion accompanied by naked-eye color change from colorless to violet (Scheme 17).

![Scheme 17](image)

Likewise, pentacenequinone derivatives 193-195 led to the formation of higher quinone derivatives promoted by \( \text{F}^- \) ions-induced desilylation followed by cyclization\textsuperscript{164}. Gong \textit{et. al.} synthesized a pyridinium derivative 196 upon efficient intramolecular cyclization promoted by the addition of \( \text{F}^- \) ions led to its use as a chemodosimeter for \( \text{F}^- \) ions\textsuperscript{165}

![Scheme 17](image)

The chemodosimeter approach has also been employed for the detection of other anions but with few reports in comparison to \( \text{CN}^- \) and \( \text{F}^- \) ions. The aniline-pyrylium derivative 197\textit{a} reported by Martínez-Máñez \textit{et. al.}\textsuperscript{166} showed a significant bathochromic shift in its CT band upon conversion to thiopyrylium derivative 197\textit{b}.

51
The authors proposed that this conversion accompanied by color change from magenta to blue could potentially be applied for the development of selective chemodosimeter for \(S^{2-}\) ion detection in aqueous environment.

\[
\begin{align*}
\text{197a} & \quad X = O \\
\text{197b} & \quad X = S
\end{align*}
\]

Similarly, a facile conversion of 2-arylethynyl aniline 198 on reaction with nitrite ions to form 4(1H)-cinnolones (Scheme 18) displayed a yellow color and led to chemodosimetric approach to detect \(NO_2^-\) ion.\(^{167}\) The change in electronic properties during the conversion has been monitored by visual color, absorbance and emission changes.

\[
\begin{align*}
\text{198} \quad & \xrightarrow{\text{NaNO}_2, \text{HCl (2 N)}} \\
& \quad \text{0-5°C, 5 min.}
\end{align*}
\]

**Scheme 18**

As is evident from the vast literature, although cation recognition parallels anion binding as a major interest in supramolecular chemistry, but in most of the structural motifs the cation selectivity is known to be highly dependent on the structure which has posed tremendous difficulty to detect certain cations using typical metal binding motifs. In order to overcome this problem, a protocol involving use of thiocarbonyl compounds which upon detecting thiophilic \(\text{Hg}^{2+}\) ion, ensue desulfurisation, has gained importance. Czarnik group\(^{168}\) was the first to use this desulfurisation reaction to develop a reaction-based indicator 199 for the detection of \(\text{Hg}^{2+}\). Later on, Zhang *et. al.*\(^{169}\) reported a desulfurisation reaction in which \(\text{Hg}^{2+}\) converted a poorly fluorescent 200 to highly fluorescent 201, thus labelling 200 as a dosimeter for \(\text{Hg}^{2+}\).
Relying on desulphurization reaction, Martinez-Máñez et al.\textsuperscript{170} have also developed a chromofluorogenic chemodosimeter 202 which forms a squaraine dye upon interaction with Hg\textsuperscript{2+} (Scheme 19) which is highlighted by fluorescence enhancement, and a very large shift in absorption with the development of a blue color from colorless solutions.

![Scheme 19](image)

Further, the Hg\textsuperscript{2+} chemodosimeter 203 relied\textsuperscript{171} on the formation of a guanidinium moiety 204 from thiourea involving desulfurization followed by cyclization (Scheme 20). The resultant change in the \( \pi \)-conjugation pathway led to a change in the absorption and the emission spectral patterns.

![Scheme 20](image)

Similarly a series of benzoylthiourea derivatives 205-207 undergo Hg\textsuperscript{2+} ion induced desulfurization which involves a cyclization leading to irreversible unique color changes, along with distinctive blue shifts in absorption spectra in aqueous medium.\textsuperscript{172} Similar blue shifts, driven by desulfurization reaction between Nile blue 208 and Hg\textsuperscript{2+}, in the absorption and emission spectra has been reported by Kim and his co-workers.\textsuperscript{173} They have also employed it for the detection of Hg\textsuperscript{2+} in blood plasma and albumin.
Further, the Hg\(^{2+}\) induced desulfurization of the thiourea moiety in fluorescent benzoxadiazole-thiourea conjugate 209 resulted in the fluorescence quenching\(^{174}\) which has been attributed to the formation of imidazoline moiety by the reaction of 209 with Hg\(^{2+}\) (Scheme 21). As a consequence of this reaction, a photoinduced electron transfer takes place from the aniline moiety to the excited state benzoxadiazole moiety and results in the fluorescence quenching. The original absorption band of 209 also gets hypsochromically shifted as a result of this conversion.

![Scheme 21](image)

The Hg\(^{2+}\) chemodosimeters 210-212 and 213, reported by Yen\(^{175}\) and Chang\(^{176}\) groups, respectively, also relied on the desulfurization reactions converting thiourea moieties to the urea groups. In case of 210-212, the conversion was accompanied by red shifts in the absorption band, as well as fluorescence emission, while in case of 213, a blue shift in the absorption and increased emission intensity were observed.

![Chemodosimeters](image)

Like sulfur, Hg\(^{2+}\) has a high affinity for selenium also. Consequently, Yoon \textit{et al.}\(^{177}\) have developed rhodamine B selenolactone 214 for detection of Hg\(^{2+}\) and CH\(_3\)Hg\(^{+}\). It displayed absorption as well as fluorescence enhancement accompanied by
a visual color change from colorless to pink in the presence of Hg$^{2+}$. The authors have proposed that the Hg$^{2+}$-induced spiro ring opening of rhodamine followed by deselenation (Scheme 22), is likely to be responsible for these spectral changes. The authors further demonstrated the usefulness of their probe in the detection of Hg$^{2+}$ and CH$_3$Hg$^+$ in the HeLa* cells.

Scheme 22

Further, Chang et al.$^{178}$ reported a chemodosimeter behaviour of dichlorofluorescein derivative 215 towards Hg$^{2+}$ which relied on the direct mercuration to the ortho-position of the phenol subunit of the 215 (Scheme 23).

Scheme 23

Consequently, the original absorption bands at 475 and 505 nm of 215 in DMSO/H$_2$O (1:9, v/v) gradually decreased in intensity and red-shifted to 483 and 533 nm accompanied by a visual color change from yellowish green to orange. Also, the characteristic fluorescence emission band of 215 got effectively quenched in the presence of Hg$^{2+}$ ions. By utilizing the similar reaction-based approach, recently Costa et al.$^{179}$ have developed a squaramide-based chemodosimeter 216, for Cu$^{2+}$, which

* The term "HeLa" has been derived from Henrietta Lacks.
upon selective chelation to Cu$^{2+}$ formed a highly colored zwitterionic radical. The initially colorless solution of 216 in CH$_3$CN/H$_2$O (1:1, v/v) turned deep purple with obvious absorption shift, when treated with Cu$^{2+}$ ion solution.

![Image of 216](attachment:image.png)

Rhodamine dyes have been used extensively to construct chemosensors because of their excellent spectroscopic properties such as long absorption and emission wavelengths accompanied by large extinction coefficients and high fluorescence quantum yields. Moreover, rhodamine undergoes an equilibrium between the spirocyclic (closed-ring) and ring-opened amide forms which showed completely different properties e.g. the spirocyclic form was colorless and non-fluorescent, while ring-opened form was characterised by strong absorption and fluorescence emission (Scheme 24).

![Scheme 24](attachment:scheme.png)

Based on this mechanism, Czarnik and his co-workers employed rhodamine-B hydrazide 217 for detection of Cu$^{2+}$ ions and following this, replacing the oxygen atom in 217 with sulfur, Xu et. al. prepared chemodosimeter 218. Switching oxygen to sulfur also led to the alteration of selectivity from Cu$^{2+}$ to Hg$^{2+}$. The high thiophilicity of Hg$^{2+}$ ions and strong nucleophilicity of sulfur atom played significant role in selective recognition of Hg$^{2+}$ ions.
Various structural variants of rhodamine, capable of sensing Hg$^{2+}$ ions e.g. carbohydrazone 219, thiospirolactones 220, ferrocenium derivative 221, 8-hydroxyquinoline derivative 222 have been reported. Similarly, rhodamine based chemodosimeters bearing salicylaldehyde-hydrazone 223, thiosemicarbazide 224, furan unit 225, sulfonyl hydrazide 226, quinaldine unit 227 as chelating moieties were employed for the selective detection of Cu$^{2+}$ ions over other cations in organic-aqueous medium. The sensing mechanism in all these systems was mainly based on ring-opening triggered by the metal ions.

![Chemodosimeters](image)

### 2.4 Molecular logic gates

The logic gates are the devices used to perform basic logic operations. In the fields of supramolecular chemistry and nanotechnology, great interest has been shown in the construction of simple electronic and photonic systems and networks that function as molecular devices incorporating logic gates. Molecular logic gates can be realized in several ways, but the most common are based on the optical properties of the molecular switches, encoding the guest molecules as inputs and the absorption and/or fluorescent signals as the outputs. The inputs and the outputs are encoded as 0 (low) and 1 (high) (off and on, respectively). Although the first proposal to execute logic operations at molecular level was made in 1988, but it was actually adopted when analogy between molecular switches and logic gates was experimentally demonstrated.
by de Silva. Since then a number of logic gates depending upon the number of inputs and outputs have been reported (Tables 1 and 2) and consequently molecular logic gates and their integrated operations have become an important focus of chemistry which is evident from the development of basic (YES, NOT, AND and OR) as well as rather complicated two-integrated logic functions (NAND, NOR, XOR and INHIBIT). In most of the cases, the building of logic gates is achieved when the chemically encoded information is converted into fluorescent (enhancement or quenching) outputs. Here in this part of this chapter, we have limited our discussion to some representative molecular logic gates reported recently.

**Table 1.** Truth tables for single input logic gates.

<table>
<thead>
<tr>
<th>input</th>
<th>YES</th>
<th>NOT</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

**Table 2.** Truth tables for two input logic gates.

<table>
<thead>
<tr>
<th>input</th>
<th>OR</th>
<th>AND</th>
<th>XOR</th>
<th>INH</th>
<th>NOR</th>
<th>NAND</th>
<th>XNOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

The pyrene appended calix[4]crown 228 undergoes fluorescence quenching in the presence of Pb$^{2+}$. The reason for this quenching has been ascribed to the photo-induced electron transfer from pyrene to the electron deficient amide oxygen atoms. Also the addition of, either HClO$_4$ or Et$_3$N, to the solution of 228, quenched fluorescence. On the basis of the fluorescence behaviour shown by 228 in the presence of Pb$^{2+}$, HClO$_4$ and Et$_3$N, the logic gates NOR, XNOR and INHIBIT were generated. Jang *et al.* have applied the fluorescence emission behaviour of benzimidazole-based fluorescent receptor 229 in the presence of Cu$^{2+}$ and Fe$^{3+}$, to develop a molecular ‘OR’ gate. The receptor 229 exhibited dual emissions at 320 and 420 nm in aqueous CH$_3$CN, which got quenched and showed a new emission band at 490 nm upon addition of Cu$^{2+}$ and Fe$^{3+}$. Thus, with Cu$^{2+}$ and Fe$^{3+}$ as two inputs and fluorescence emission as output, the receptor 229 offered an interesting ‘OR’ molecular logic gate. A chemosensor consisting of an L-histidine covalently linked to an anthracene unit 230 showed its sensing behaviour with metal ions at different pH values as evaluated by fluorescence.
and absorption changes.\(^{198}\) As a result of metal coordination at different pH, the change in spectral properties led to the use of 230 as logic gates with multiple configurable outputs, by selecting the initial chemical inputs. Three logic gates (XNOR, OR, NOR), a logic circuit composed of ‘OR’ and ‘INHIBIT’ gates and a half-subtractor at the molecular level were realized.

Jiang et al.\(^{199}\) have reported a Schiff-base chemosensor 231 for Cu\(^{2+}\) and Zn\(^{2+}\) that exhibited absorption and fluorescence changes in the presence of these ions in THF and has been utilized to derive a tuneable system integrated with one ‘OR’ logic gate as well as one ‘INHIBIT’ logic gate with Zn\(^{2+}\) and Cu\(^{2+}\) as chemical inputs and absorbance and fluorescence as output signals. In addition to this, ‘IMPLICATION’ gate operating in fluorescence mode with Cu\(^{2+}\) and EDTA as chemical inputs has also been derived. The azobenzene containing 232 and 233 have been shown\(^{200}\) to exhibit interesting sensing characteristics towards metal ions at various pH levels. The authors have claimed that the compound 232 acted as a fluorescent ‘INHIBIT’ logic gate driven by Zn\(^{2+}\) ions and pH (OH\(^{-}\)) as chemical inputs while 233 operated as fluorescent ‘OR’ logic gate utilizing OH\(^{-}\) and Cu\(^{2+}\) as chemical inputs.

A pyrene linked triazole modified homooxacalix[3]arene 234 has shown a potential application in sensing, detection and recognition of Zn\(^{2+}\) and H\(_2\)PO\(_4\)\(^{-}\) ions with different optical signals.\(^{201}\) However, its fluorescence emission behaviour in the
presence of Zn$^{2+}$ and H$_2$PO$_4^-$ ions as chemical inputs, has been utilised to construct a simple but efficient logic circuit for a molecular traffic signal with the help of binary logic based on ‘INHIBIT’ and ‘OR’ gates. A fluorescent bischromophoric dyad \textbf{235} derived by combining anthracene and naphthalene anhydride units showed emission changes upon interaction with F$^-$, AcO$^-$ and Hg$^{2+}$ ions accompanied by naked-eye color change.\textsuperscript{202} The output fluorescence signals exhibited by \textbf{235} on chemical inputs of F$^-$, AcO$^-$ and Hg$^{2+}$ ions mimicked ‘OR’, ‘XNOR’ and ‘INHIBIT’ logic functions. The compound \textbf{236} decorated with two metal cation receptors showed changes in its fluorescent behaviour (driven by photoinduced electron transfer, PET and ICT process) as a result of selective binding of Zn$^{2+}$ and Cu$^{2+}$ with two cation receptors with different affinities, and thus performed ‘OR’, ‘NOR’ and ‘INHIBIT’ logic functions using Zn$^{2+}$ and Cu$^{2+}$ inputs.\textsuperscript{203}

Similarly rhodamine derivative \textbf{237} mimicked a molecular level keypad lock in the presence of Cu$^{2+}$ ions which could be opened only by a password resulting in the strong fluorescence emission at particular wavelength. Thus, this molecular keypad lock showed the potential for protecting information at the molecular scale.\textsuperscript{204} The metal ion sensors based on the metal-ligand coordination or chemical reactions have also been employed for the detection of analytes, especially the heavy metal ions. For example, iridium (III) complex with N-O donor ligand \textbf{238} has been developed as an ‘AND’ and ‘INHIBIT’ logic gate with Hg$^{2+}$ and histidine as chemical inputs and phosphorescence signal as output.\textsuperscript{205} The fluorescent Zn(II) complex \textbf{239} exhibiting “on-off-on” switching by Cu$^{2+}$ and Ag$^+$ ions, also mimicked the molecular level keypad lock that
followed a correct chemical input order \((\text{Cu}^{2+}\rightarrow\text{Zn}^{2+}\rightarrow\text{Ag}^+)\) because of reversible ‘switch-off’ and ‘switch-on’ signalling in the presence of \(\text{Cu}^{2+}\) and \(\text{Ag}^+\) ions, respectively.\(^{206}\)

2.5 Conclusions

This brief overview on the recent developments in the field of chemosensors delineates the diversity thus far explored and an insight into the different approaches adopted for the development of these chemosensors. Wherever possible, applications of these chemosensors in various fields such as chemical and biological analyses and electronics in the form of development of logic gates etc. have been realized. It is evident that most of the sensors reported so far involve complex synthetic and operational methods which sometimes limit their use for practical applications. Thus, the need for the development of the readily available sensors possessing inherent capacity for determination of analytes prompted us to develop simple-to-use and cost-effective chemosensors for various analytes. The chapters 3 and 4 of this thesis report rational designs and synthesis of different chemosensors as well as their implementation in detection of different analytes as well as applications in various areas including live cell imaging and logic gates etc.

2.6 References


Chapter 2


Review of literature


113. Ruan, Y. -B.; Maisonneuve, S.; Xie, J. Dyes Pigm. 2011, 90, 239-244.


