Abstract

This chapter deals with a brief introduction of the supramolecular chemistry, various methods used for synthesis of thiacalix[n]arenes (n = 4, 6, 8) and the functionalization of these thiacalix[n]arenes at wider rim, narrow rim and bridging sulfur atoms. The various derivatives of the thiacalix[4]arenes prepared by carrying out modifications at the wider rim, narrow rim and at the bridging sulphur atoms are also reviewed. The binding behaviour of these derivatives towards different types of cations and anions evaluated by solvent extraction method, UV-vis, fluorescence and $^1$H NMR spectroscopy and their metal complexes is also presented. In the last part of the chapter, the developments about the molecular switches, various molecular logic gates and devices based on different molecular scaffolds are reviewed.
1.1 Introduction and review of literature

The understanding of the structural and functional properties of living systems is a key challenge in chemical and biological sciences. In living systems, the non-covalent interactions are very significant in sustaining the two and three-dimensional structure of bio-molecules, such as proteins in which they bind specifically but transiently to one another. Supramolecular chemistry\(^1\) which is “chemistry beyond a molecule” provides one such platform to study the non-covalent interactions of biological systems. This is the chemistry where molecules are able to self-organize, self-assemble, and self-control into systems and the components are often analogues to biological molecules. During the last few decades, there have been significant developments in the areas of supramolecular chemistry which includes molecular recognition, catalysis, molecular devices, self-organization, ensembles and nanochemistry.\(^2\) Among these, molecular recognition chemistry aims at the design and synthesis of molecular receptors which are useful to understand and mimic nature’s specific interactions towards various guest molecules by non-covalent interactions. Since the origin of the concept of molecular recognition chemistry (host-guest chemistry), a wide variety of synthetic organic receptors like crown ethers,\(^3\) cryptands,\(^4\) spherands,\(^5\) porphyrins,\(^6\) calixarenes,\(^7\) thiocalixarenes,\(^8\) and cyclodextrins\(^9\) have been used as molecular receptors. For a molecular receptor to be an effective host, its basic molecular scaffold should be easily synthesized and should undergo chemical modification with designed recognition behaviour. Calix[4]arene\(^7,10\) is one of the most actively studied molecular scaffold among the various synthetic molecular scaffolds studied so far. Calixarenes are cyclic oligomer composed of phenolic units linked through methylene groups possessing well defined conformational properties and cavities of molecular dimensions which are able to encapsulate various guest species which is a subject of interest in biomimetic chemistry. The modified calixarene derivatives can be tuned to serve as efficient hosts towards different guest species either by controlling their conformations or by changing the nature and number of ligating sites. Several applications of chemically modified calix[4]arenes as ion-selective electrodes,\(^11\) supramolecular assemblies,\(^12\) chiral shift reagents for NMR and chiral catalysts,\(^13\) non-linear optical materials and liquid crystalline systems,\(^14\) for antibody labeling and biological mimics,\(^15\) mimics of enzyme\(^16\) and ion channels,\(^17\) as magnetic resonance imaging agents,\(^18\) for surface recognition of proteins,\(^19\) drug delivery systems,\(^20\) metal oxo surface mimics,\(^21\) molecular magnets,\(^22\) photochemical
and electron transfer devices,\textsuperscript{23} porous surfactants,\textsuperscript{24} and nanotechnology\textsuperscript{25} have recently been reported in the literature. Because of the above mentioned attractive features and applications as host compounds calixarenes have been actively studied and termed as ‘third generation’\textsuperscript{26} of the host molecules in addition to crown ethers\textsuperscript{27} and cyclodextrins.\textsuperscript{28}

Kumagai \textit{et al.}\textsuperscript{29} reported a second subclass of calixarene family i.e., the $p$-tert-butyliiithiacalix[4]arene, in which all four methylene bridges of conventional calix[4]arene are substituted by sulfide bonds. The presence of sulfur atoms makes them an attractive host for transition metal ions. In comparison with the structural characteristics of the conventional calix[4]arene moiety, thiacalix[4]arene is more attractive due to the following reasons: (i) the ring size of thiacalix[4]arene is 15\% larger\textsuperscript{30} than that of calix[4]arene because of the longer covalent bond length of C-S than C-C; (ii) ring linkages containing sulfurs may act cooperatively with phenolic oxygen upon the binding of metal ions, and (iii) easy modification (oxidation) of the bridging sulfur to form sulfoxide and sulfone which change the properties of the cavity formed by the calix benzene rings, which is superior to any other calixarenes. Thus, there is much more potential in investigating the chemistry of thiacalix[4]arenes as artificial receptors or enzyme mimics. However, the use of thiacalix[4]arene platform to immobilize different binding sites is still restricted because of either the lack of derivatization methods allowing regio- and/ or stereo-selective transformations or the unknown conformational preferences of these compounds.\textsuperscript{31}

Thus, keeping in view the significance of thiacalix[4]arene in molecular recognition chemistry, we have designed and synthesized a variety of thiacalix[4]arene derivatives having amide, sulphonamide and (thio)urea moieties and studied their recognition behaviour toward different cations, anions and various neutral molecules. Before proceeding to the results of our findings, a brief review of literature on thiacalixarenes is discussed below.

\textbf{1.2 Synthesis of thiacalix[4]arene}

Calixarene is a Greek word of which ‘\textit{calix}’ means ‘vase’ or ‘chalice’ and arene stands for aryl residue. Calixarenes\textsuperscript{32} are cyclic oligomers obtained from $p$-tert-butyliphenol and formaldehyde under basic conditions. The concentration of the base determines which oligomer is to be formed. A variety of derivatives can be prepared by carrying out modification at the phenolic hydroxyl group and at the \textit{para}-position
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by electrophilic substitution. Thiacalixarenes \(1_n\) \((n = 1, 3, 5)\), on the other hand, are cyclic oligomers obtained from \(p\)-\(t\)ert-butylphenol and elemental sulfur \((S_8)\) under basic conditions (Scheme 1.1) i.e the methylene bridges of conventional calixarene are replaced by sulfur atoms. The first synthesis of \(p\)-\(t\)ert-butylthiacalix[4]arene \(1_1\) was reported by Sone et al.\(^{33}\) This method involves tedious stepwise reaction of \(p\)-\(t\)ert-butylphenol and SCl\(_2\), affording \(p\)-\(t\)ert-butylthiacalix[4]arene \(1_1\) in poor yield (Scheme 1.2). However, Kumagai et al.\(^{29}\) reported synthesis of thiacalixarenes \(1_n\) \((n = 1, 3, 5)\) by one step and one pot procedure which involves reaction of \(p\)-\(t\)ert-butylphenol with elemental sulfur \((S_8)\) and NaOH in tetraethylene glycol dimethyl ether with concomitant removal of H\(_2\)S (Scheme 1.3). The major product of this reaction was thiacalix[4]arene \(1_1\) (54%) along with trace amounts of thiacalix[6]arene \(1_3\) and thiacalix[8]arene \(1_5\). Later on Kon et al.\(^{34}\) reported thiacalix[4]arenes \(1_1\) in higher yield by using convergent synthetic procedure involving two steps under alkaline conditions (Scheme 1.4). Kondo et al.\(^{35}\) reported the synthesis of thiacalixarenes \(1_n\) \((n = 1, 3, 5)\) by using acetic acid and terephthalic acid as a template in a combination with base catalyst such as NaOH and NaH. Recently, Patel et al.\(^{36}\) reported an alternative approach to synthesize higher heteracalixarenes, particular thiacalixarenes \(1_n\) \((n = 1, 3, 5)\), by using respective homologous calixarene \(2_n\) \((n = 1, 3, 5)\) templates (Scheme 1.5).

\[\text{Scheme 1.1: General method of synthesis of (thia)calixarenes.}\]

\[\text{Scheme 1.2: Four step synthesis of thiacalix[4]arene.}\]
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Scheme 1.3: Single step synthesis of thiacalixarenes.


Scheme 1.5: Calixarene templated synthesis of thiacalixarenes.

Thiacalix[4]arene scaffold like conventional calix[4]arene has two rims i.e. the narrow rim comprising of the phenolic groups, whereas the wider portion of the
scaffold comprising of the \textit{para}-substituent is known as the \textit{`Wider rim`} (Fig. 1A). Thiacalix[4]arene is capable of assuming four conformations depending upon the orientation of the phenolic units with respect to each other\textsuperscript{37} i.e. \textit{`Cone`} (uuuu), \textit{`Partial cone`}, (uuud), \textit{`1,2-Alternate`} (uudd) and \textit{`1,3-Alternate`} (udud) as shown in figure 1B. Thiacalix[4]arene like conventional calix[4]arene always exists in \textit{cone} conformation in the solution due to the favourable intramolecular circular hydrogen bonding between the adjacent phenolic groups. Akdas \textit{et al.}\textsuperscript{30} reported first X-ray crystal analysis of thiacalix[4]arene which showed its \textit{cone} conformation and the four hydroxyl groups form intramolecular cyclic hydrogen bonds in solid state with \textit{C}_4-symmetry. In the solution state, the \textit{^1}H NMR chemical shift for the OH group of thiacalixarenes 1\textsubscript{n} (n=1, 3, 5) in CDCl\textsubscript{3} suggested formation of intramolecular hydrogen bonding, the strength of which seems to be weaker than that of the corresponding calixarenes 2\textsubscript{n} (n=1, 3, 5), respectively.\textsuperscript{38} This may be ascribed to the enlarged skeleton of the thiacalixarene ring to separate OH groups further away from each other. The X-ray crystal analysis showed that thiacalix[4]arene have 15\% larger bond length between aromatic residue and bridging groups which indicates that thiacalix[4]arene cavity is larger than conventional calix[4]arene.

\textbf{Figure 1.} Various conformations of thiacalix[4]arene.

The versatility of thiacalix[4]arene 1\textsubscript{1} as host molecule is due to its chemical modifications at wider rim, narrow rim and on the bridging sulfide group. The
chemical modifications at narrow and wider rim of thiacalix[4]arene is intrinsic to phenols i.e. modification at the phenolic hydroxyl group and/ or the p-position. Therefore, a variety of thiacalix[4]arene derivatives can be prepared according to well known calix[4]arene chemistry. However presence of sulfide bonds brings steric and electronic effects into account of thiacalix[4]arene chemistry, particularly oxidation of sulfide bonds to sulfoxide and sulfone. Thus, reaction conditions used for the synthesis of a particular thiacalix[4]arene derivative by carrying out modification at the narrow rim, wider rim or bridging sulfur may considerably differ from those used for the methylene-bridged calix[4]arene counterpart. The different types of thiacalix[4]arene derivatives prepared by carrying out above modifications are as follows:

1.3 Modification at wider rim of thiacalix[4]arene
1.4 Modification at narrow rim of thiacalix[4]arene
1.5 Modification at bridging sulfur atoms of thiacalix[4]arene
1.6 Binding studies of thiacalix[4]arene based receptors

1.3 Modification at wider rim of thiacalix[4]arene

Much attention has been devoted to the introduction of functional groups onto wider rim of thiacalix[4]arene. The modification at the wider rim of thiacalix[4]arene was carried out mainly by two processes: (i) electrophilic aromatic substitution at the para-position of phenol residue, and (ii) direct ipso-substitution of tert-butyl groups by electrophilic agents. The Friedel-Crafts dealkylation of tert-butyl group at the wider rim is the first reaction of this approach. The tert-butyl groups of thiacalix[4]arene can be easily removed by a Friedel-Crafts dealkylation reaction using AlCl₃/phenol/toluene under reflux conditions to give fully de-tert-butylthiacalix[4]arene. Higuchi et al. have improved the dealkylation of tert-butyl groups of thiacalix[4]arene to large scale preparation of using 10.5 equiv of AlCl₃ at 80°C with phenol. The regioselective partial dealkylation of 1 was achieved using 7.1-7.4 equiv of AlCl₃ with shorter reaction time to mono, di and tri(p-tert-butylthiacalix[4]arene) 4-6 in 7%, 20% and 21% yield, respectively. The de-tert-butylated thiacalix[4]arene 3 also adopts a cone conformation in solution and in solid state like tert-butylthiacalix[4]arene 1. The X-ray structure analysis revealed that thiacalix[4]arenes 4-6 adopt cone conformations and dimeric self-inclusion units in such a way that phenol moieties are inserted into the cavity of each other molecules.
The *de-tert*-butylated thiacalix[4]arene 3 can be functionalized by different electrophilic aromatic substitution reactions. The bromination and nitration of thiacalix[4]arene by conventional methods leads to complex mixture of products due to concomitant oxidation of sulfide linkage.\textsuperscript{40} However Lhotak *et al.* successfully synthesized dibromo-derivative 7 and tetrabromo-derivative 8 of thiacalix[4]arene in high yield by bromination of 1,3-disubstituted thiacalix[4]arene.\textsuperscript{40a} Later, Kasyan *et al.* and Desroches *et al.* reported, independently, the synthesis of tetra-bromo derivative 9a by direct NBS bromination of *de-tert*-butylated thiacalix[4]arene 3.\textsuperscript{41} Further alkylation of 9a with propyl iodide in the presence of Cs$_2$CO$_3$ results in *tetra-o*-propylthiacalix[4]arene 9b. Desroches *et al.*\textsuperscript{41b} synthesized the trimethylsilylacetylene 10 and 4-pentylphenylacetylene 11 derivatives of *de-tert*-butylated thiacalix[4]arene 3 using dichlorobis(triphenylphoshane)palladium(II) as a catalyst and shown to have potential applications in nonlinear optical applications. The reaction of *tetra-o*-propylthiacalix[4]arene 9b with BuLi and N-formylpiperidine gave *p*-formyl thiacalix[4]arene 12 in good yield\textsuperscript{42} which could be used as useful starting material for various wider rim functionalizations.

![Chemical structures](image)

Another significant reaction at the wider rim of *de-tert*-butylthiacalix[4]arene 3 is nitration. The nitration of *de-tert*-butylated thiacalix[4]arene 3 was achieved by reacting with KNO$_3$/AlCl$_3$ to give tetrinitrothiacalix[4]arene 13 in good yield without oxidation of sulfur.\textsuperscript{43} This reaction failed in most of the organic solvents like...
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Acetonitrile, tetrahydrofuran, toluene etc but surprisingly worked well in the presence of di-, tri- or tetraglyme. The tetraniitrothiacalix[4]arene 13 on reduction with SnCl₂ gave tetraamino derivative 14 almost quantitatively⁴³,⁴⁴ which can be useful starting point for wider rim derivatization. The selective nitration to dinitrothiacalix[4]arene 15⁴⁵ was achieved by Hu et al. by nitration of dibenzoyl derivative of 3 followed by debenzoylation in aqueous NaOH. Agarwal et al.⁴⁶ synthesized thiacalix[4]arene hydroxamic acids 16-18 by partial reduction of nitro-thiacalix[4]arenes with hydrazine hydrate, Raney-Ni, and their coupling with benzoyl chloride under the influence of microwave irradiation with excellent yields.

The de-tert-butylated thiacalix[4]arene 3 was functionalized⁴⁷ by Friedel-Craft alkylations at the wider rim with 1-adamantanol and 3-carboxy-1-adamantanol in trifluoroacetic acid with catalytic amount of LiClO₄ to give adamantylthiacalix[4]arenes 19 and 20. The diazotization of de-tert-butylated thiacalix[4]arene 3 with various diazonium salts results in various p-phenylazo derivatives 21a-f.⁴⁸ The reductive cleavage of 21b using Na₂S₂O₄ and NaOH in aqueous solution results in p-aminothiacalix[4]arene 14 which represents very useful intermediate for further functionalization.⁴⁸b A chloromethyl group was introduced at the wider rim of de-tert-butylated thiacalix[4]arene 3 by reacting it with excess amount of chloromethyl methyl ester to afford 22.⁴¹a The de-tert-butylated thiacalix[4]arene 3 undergoes ipso-sulfonation⁴⁹ by treatment with concentrated sulfuric acid followed by salting out with sodium chloride to give 4-sulfonic acid salt of thiacalix[4]arene 23 which is soluble in water and would expand its chemistry into aqueous solutions.
Kundrat et al.\textsuperscript{50} reported the formylation reactions (Gross and/or Duff conditions) at the wider rim of the tetrapropoxythiacalix[4]arene 33 (\textit{vide infra}) in the 1,3-\textit{alternate} conformation. Using an excess of the formylation agent, the unexpected regioselectivity of these reactions were noticed in which only two formyl groups were introduced exclusively into the \textit{meta}-positions of thiacalixarene skeleton 24a-c. The formation of \textit{meta} substituted aldehydes shows remarkably different reactivity of the thiacalix[4]arene system compared with that of a classical calix[4]arene analogue. The direct formylation of tetrapropoxythiacalix[4]arene 33 (\textit{vide infra}) in the \textit{cone} conformation results in unusual products compared to formylation in 1,3-\textit{alternate} conformation.\textsuperscript{51} The Duff reaction (urotropine/TFA) leads to unprecedented intramolecularly bridged compounds possessing two formyl groups on the opposite \textit{para}-positions or \textit{para-meta}-positions 25 or 26, respectively. The formylation results indicate that the electronic effect of sulfur bridges and conformation of the thiacalix[4]arene are the governing factors for the regioselectivity of electrophilic substitution in thiacalixarene series.
In comparison to Duff reaction, direct Gross formylation reaction (Cl₂CH-O-CH₃/SnCl₄/CH₂Cl₂) of tetrapropoxythiacalix[4]arene 33 (vide infra) in cone conformation results in introduction of only one formyl group into the meta-position of the thiacalixarene skeleton 27.⁵² The surprising regioselectivity indicates dramatically different reactivity of the thiacalix[4]arene system when compared with a calix[4]arene analogue, which yields exclusively para isomers. The introduction of functional groups into the meta-position represents an exceptional substitution pattern in thiacalixarene chemistry, which imparts an interesting conformational behaviour to these compounds.

1.4 Modification at narrow rim of thiacalix[4]arene

The narrow rim (phenolic hydroxyl group) of thiacalix[4]arene undergoes two types of reactions i.e. alkylation and esterification. The narrow rim functionalization of calix[4]arene is well established in literature but alkylations with simple alkyl halides under same conditions did not give the same conformational outcomes in thiacalixarene chemistry. The presence of four sulfur atoms in thiacalix[4]arene imparts many novel features that reflect significantly different behaviour and conformational preferences of thiacalix[4]arene upon functionalization.

tetraalkylated products in good yield.\textsuperscript{53} Lhotak \textit{et al.} prepared a series of tetra 28-35 and partially methylated 36-38 thiacalix[4]arene derivatives and studied their conformational preferences using NMR spectroscopy and X-ray crystallography. The conformer distribution of these alkylated products is different from that of calix[4]arene and found that 1,3-\textit{alternate} conformers are obtained in high yields while the \textit{cone} conformation forms only in low yields.

\textbf{Table 1.} Base catalyzed alkylated products of thiacalix[4]arene.

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The etherification of thiacalix[4]arene with ethylbromoacetate in the presence of alkali carbonates (M$_2$CO$_3$, M = Li$^+$, Na$^+$, K$^+$ and Cs$^+$) as base in acetone yields different acetate derivatives of thiacalix[4]arene i.e. \textit{cone} 39a-b, \textit{partial cone} 39c-d and 1,3-\textit{alternate} 39e-f.\textsuperscript{54} The conformational distribution of these isomers depends upon the type of metal carbonate which exhibits pronounced metal template effect and is the governing factor for these conformations. Lhotak \textit{et al.}\textsuperscript{55} synthesized lactone derivatives 40a-b and 41a-b from diacetate of thiacalix[4]arene by an unprecedented intramolecular cyclization. Compounds 40a and 40b showed an interesting $\pi$-$\pi$ and hydrogen bonding interactions as determined by the X-ray crystallography. These interactions make compounds 40a and 40b inherently chiral compounds which were demonstrated through their separation on a chiral HPLC column. The direct aminolysis of tetraacetate of \textit{cone} and 1,3-\textit{alternate} conformations with aliphatic diamines results in proximally bridged thiacalix[4]arenes 42a-c and 43a-b, respectively.\textsuperscript{56} Further, Stastny \textit{et al.}\textsuperscript{57} reported doubly bridged thiacalix[4]arenes 44a-c in the 1,3-\textit{alternate} conformation by direct aminolysis reaction of thiacalix[4]arene tetraacetates with $\omega$-$\omega$-diamines. Both sites of 1,3-\textit{alternate} conformer intramolecularly bridged to form the cagelike structures in high yields. The structural analysis of the novel cagelike molecules revealed a highly preorganized array of -C(O)-NH- bonds pointing to the interior of the cavity. Liu \textit{et al.}\textsuperscript{58} also synthesized bicyclic amides 45a-b and single crystal X-ray diffraction analysis
showed that these bicyclic amides of thiacalixarene exist mainly in 1,3-\textit{alternate} conformation.

Morohashi \textit{et al.} selectively synthesized conformational isomers of 46a in \textit{cone} and 1,3-\textit{alternate} conformations directly from tert-butylthiacalix[4]arene \textit{I}, using NaH and Cs$_2$CO$_3$ as base, respectively. However, three to four-steps were required for benzylation of \textit{p-}tert-butylthiacalix[4]arene \textit{I} to get \textit{partial cone} and 1,2-\textit{alternate} isomers, respectively. Similarly, Yamato \textit{et al.} synthesized tetra-
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kis(pyridylmethoxy)-thiacalix[4]arene 46b and 46c of cone and 1,2-alternate conformations by reaction of 1 with 2- and 4-(chloromethyl)pyridine in the presence of Cs₂CO₃ as base.

The intramolecularly bridged (1+1) or intermolecularly bridged (2+2) products 47a-d and 48a-d of calix[4]arene or thiacalix[4]arene have been reported by Xiong et al., using bis(tosyloxyethoxy)benzenes as bifunctional reagents. It was found that the bridging pattern strongly depended on the structure of bis(tosyloxyethoxy)benzene and the kind of calixarene moiety. For the ortho-isomer of bis(tosyloxyethoxy)benzene, intramolecularly bridged calix[4]arene and thiacalix[4]arene were the main products. For the para-isomer, the bridging reaction was in a (2+2) fashion.
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Bitter et al.\textsuperscript{62} carried out the regioselective distal alkylation of thiacalix[4]arene with alcohols using Mitsunobu protocol. By using this protocol only regioselective stable cone conformation was formed with distally substituted derivatives 49a-h and the reaction generally stopped at the disubstitution stage and tri- or tetraethers could not be isolated. This protocol has been proven to be one of the effective tools in functionalization of chiral/achiral thiacalix[4]arenes 50a-b in stable cone conformation with distally substituted derivatives. Csokai et al.\textsuperscript{63} reported intermolecular couplings versus intramolecular ring closures in the reaction of p-tert-butylthiacalix[4]arene 1\textsubscript{1} and diethylene glycols affording dimers 51a-b and/or the inherently chiral 1,2-thiacalix[4]crown-3 derivatives 52a-b and monocrowns 53a-e using the Mitsunobu protocol. Furthermore, Mitsunobu protocol was extended for cyclization of p-tert-butylthiacalix[4]arene 1\textsubscript{1} with glycols to oligoethylene glycol analogues composed of O, S, and N atoms in the chain to produce various monocrowns such as 54-57.

Thiacalix[4]arene 1\textsubscript{1} also undergoes regioselective O,O'-difunctionalization at the neighbouring phenol hydroxyl groups. The treatment of thiacalix[4]arene with
1,3-dichloro-1,1,3,3-tetraisopropylsiloxane provides the proximally-bridged compound which on reaction with alkyl halide in the presence of base gave 1,2-
alternate O”,O”’-dialkylated products 58a-d. The proximally-bridged compound is very useful synthetic intermediate for 1,2-disubstitution of thiacalix[4]arene, for example, both syn and anti-1,2-bis(O-2-aminoethyl)ethers of thiacalix[4]arene 59 and 60 were prepared stereoselectively by reaction of 58a with chloroacetonitrile followed by reduction. Narumi et al. synthesized 1,2-bridged monocrowns 61a-d by reaction of disiloxane-capped 58a with different oligoethylene glycol ditosylate using Cs$_2$CO$_3$ as the base which were desilylated using tetrabutylammonium fluoride. Serizawa et al. reported a dialkylation of the proximal OH groups of thiacalix[4]arene by protecting two proximal OH groups with tiflate moieties to give 62 by intramolecular rearrangement of 1,3-bistriflate ester to its 1,2-counterpart, followed by anti-selective dialkylation of the remaining OH groups with alkyl halides or using Mitsunobu conditions and subsequent removal of the triflate moieties.
The acylation of thiacalix[4]arene has been little explored compared to etherification. Hu et al.\textsuperscript{45} reported a dibenzoylated derivative \textbf{63} of \textit{de-tert}-butylated thiacalix[4]arene \textbf{3} by reacting with benzoyl chloride. The reaction of thiacalix[4]arene and \textit{de-tert}-butylated thiacalix[4]arene \textbf{3} with isonicotinoyl or nicotinoyl chloride afforded tetraacylated derivatives \textbf{64a-d} in all four conformations.\textsuperscript{68} Recently Simanova et al.\textsuperscript{69} reported the acylation of thiacalix[4]arenes with acetyl chloride or acetic anhydride which gave the corresponding narrow rim tetraacetoxy derivatives \textbf{65a-f} which are conformationally mobile in solution and represent a thermodynamical equilibrium of different conformers at room temperature. The conformational preferences of acetylated thiacalix[4]arenes mainly depend on the wider rim substitution. The tetraacetoxy derivatives of \textit{p-tert}-butylthiacalix[4]arene prefers 1,3-\textit{alternate} \textbf{65b} and 1,2-\textit{alternate} conformations \textbf{65f} (43 and 38\%, respectively), while the wider rim unsubstituted derivative adopts preferably the \textit{partial cone} conformation \textbf{65c} (70\%).

Tyuftin et al.\textsuperscript{70} synthesized \textit{ω}-bromoalkoxy derivatives \textbf{66a-e} (\(n = 2\)-6), thioacetates \textbf{67a-d} (\(n = 2\)-5). The hydrazinolysis of the thioacetates \textbf{67a-d} (\(n = 2\)-5) results in thiol derivatives \textbf{68a-d} (\(n = 2\)-5) which is the most efficient method for the synthesis of thiols. Stoikov et al.\textsuperscript{71} developed a regioselective synthesis of new thiacalix[4]arenes derivatives \textbf{69a-c}, \textbf{70} and \textbf{71} functionalised with amide groups at the narrow rim in \textit{cone}, \textit{partial cone} and 1,2-\textit{alternate} conformations by treating the thiacalix[4]arene with N-(\textit{p}-nitrophenyl)-\textit{α}-bromoacetamide in the presence of \(\text{M}_2\text{CO}_3\) (\(\text{M} = \text{Na}, \text{K} \text{ and Cs}\)). It was observed that the formation of two different disubstituted compounds i.e. distal disubstituted thiacalixarene in \textit{cone} conformation and \textit{proximal} disubstituted thiacalixarene in 1,2-\textit{alternate} conformation, is possible depending on
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the nature of the base. Polivkova et al.\textsuperscript{72} reported unexpected behaviour of monospirothiacalix[4]arene 72a under acidic conditions. The treatment of the monospirothiacalix[4]arene derivative 72a with various acidic agents (HCl or HBr) results in rearrangement of the thiacalixarene skeleton leading to the formation of a phenoxanthyli derivative 72b.

\begin{align*}
66a-e: & R = (\text{CH}_2)_n\text{Br} \\
67a-d: & R = (\text{CH}_2)_n\text{SC(O)}\text{CH}_2 \\
68a-d: & R = (\text{CH}_2)_n\text{SH} \\
& n = 2, 3, 4, 5, 6 \\
a, b, c, d, e
\end{align*}

\begin{align*}
69 & : R_1 = \text{H}_2\text{COCHN}-\text{NO}_2, R_2 = R_3 = R_4 = \text{H} \\
69a & : R_1 = R_2 = \text{H}_2\text{COCHN}-\text{NO}_2, R_3 = R_4 = \text{H} \\
69b & : R_1 = R_2 = \text{H}_2\text{COCHN}-\text{NO}_2, R_3 = \text{H} \\
\end{align*}

\begin{align*}
70 & : R_1 = R_2 = \text{H}_2\text{COCHN}-\text{NO}_2, R_3 = R_4 = \text{H} \\
71 & : R_1 = R_2 = \text{H}_2\text{COCHN}-\text{NO}_2, R_3 = \text{H}
\end{align*}

Antipin et al.\textsuperscript{73} reported first phosphorylated thiacalix[4]arene 73 by reaction of thiacalix[4]arene 1\textsubscript{1} with an excess of PCl\textsubscript{3}. The bis-chlorophosphate thiacalix[4]arene 73 adopts the 1,2-\textit{alternate} conformation. However, reaction of 1\textsubscript{1} with 2 equiv of PCl\textsubscript{3} in the presence of Et\textsubscript{3}N and subsequent condensation with
diethylamine led to isolation of the diester amide 74 without oxidation. Kasyan et al. synthesized a thiacalix[4]arene substituted by four carbamoylethylphosphine oxide groups at the wide rim forms hydrogen-bonded, dimeric capsules 75a-c with S8 symmetry in the crystalline state and in apolar solvents. The dimeric capsule was held together by intermolecular –N–H…O=P– hydrogen bonds. The structure was confirmed by single-crystal X-ray crystallography.

Thiacalix[4]arene can undergo complete replacement of phenolic OH groups by NH$_2$ and SH groups as in the calix[4]arene chemistry. Katagiri et al. used chelation–assisted $S_N$Ar methodology for the synthesis of tetraaminothiacalix[4]arenes 76 which is a useful molecular platform for synthesis of new functional materials. On the other hand, Rao et al. successfully synthesized p-tert-butyltetramercaptothiacalix[4]arene 77 by replacing OH groups by SH groups. This was achieved by a series of reactions i.e. acylation of 1 with $N,N$-dimethylthiocarbamoyl chloride producing $O$-thiocarbamoyl derivative which was thermally converted into $S$-carbamoyl derivative and then deprotection with hydrazine hydrate gave 77 in good yield. The X-ray crystallography revealed that mercapto
derivative 77 adopts the 1,3-alternate conformation in the solid state in contrast to thiacalix[4]arene 1. Katsyuba et al.\textsuperscript{78} demonstrated the role of different substituents at the narrow and wider rims and the type of interphenolic junctions in conformational behaviour and binding abilities of the thiacalix[4]arene molecules. Quantum-chemical computations in combination with IR and NMR spectroscopy prove that, in contrast to closely related calixarenes, the 1,3-alternate becomes a dominant conformer of $p$-tert-butyl-mercaptothiacalix[4]arene 77 not only in crystal, but also in solutions and in vacuum. The replacement of OH groups by SH groups in mercaptothiacalixarene 77 results in essential loss of cooperativity of the intramolecular H-bonding. The four SH groups are intramolecularly H bonded to the bridging S atoms solely as a result, the SH---S bonding almost equally stabilises all the conformations, and the energy gap between the cone and other conformations of 77 is much smaller than in the case of calixarenes. Further the replacement of OH group by SH group transform cone conformation to pinched-cone conformer. On the other hand, the introduction of four tert-butyl groups into wider rim of the molecule 77 increases destabilization of the cone, which, in turn, results in domination of the 1,3- alternate conformer where the repulsion of the tert-butyl groups is minimal.

1.5 Modification at bridging sulfur atoms of thiacalix[4]arene

One of the unique features of thiacalix[4]arene compared to classical calix[4]arene is the presence of sulfide group which can undergo oxidation to sulfinyl and sulfonyl function. Treatment of thiacalix[4]arene with an oxidant such as hydrogen peroxide/trifluoroacetic acid or sodium perborate in an organic acid solvent converted all four sulphide bonds to sulfone derivatives 78a-b and sulfoxide derivatives 79a-b.\textsuperscript{79} Structural analysis made by Mislin et al.\textsuperscript{79a} showed that sulfonyl derivatives 78a-b prefer 1,3-alternate conformation which is held together by 3D network of inter- and intra-molecular hydrogen bonds between phenolic groups and sulfonyl oxygens. The sulfoxide derivatives 79a-b, having free rotations of the phenol subunits, adopts four different stereoisomeric forms (rccc, rcct, rctt and rtct) due to disposition of the tetrahedral sulfoxide moiety. While attempting for ipso-nitrations of tetraacetate of 1, Lhotak et al.\textsuperscript{80} noticed no nitrated product but instead identified sulfoxide derivatives 80a-d. The regio- and stereocontrolled oxidation of sulphide to sulfoxide function was also reported using NaNO$_3$-CF$_3$CO$_2$H reagent.\textsuperscript{80}
1.6 Binding studies of thiacalix[4]arene based receptors

The presence of sulfur atoms (which possess lone pairs of electrons and vacant 3d orbitals) in thiacalix[4]arene results in many novel features, especially in the field of metal ion complexation. Compared to conventional calix[4]arene which itself has poor binding ability towards transition metal ions, thiacalix[4]arene has varying metal-recognition ability and this ability is improved by introducing different ligating functional groups. Thiacalix[4]arene $1_1$ was found to extract a wide range of transition metal ions from aqueous solutions. The complexation ability of sulfones $78a$-$b$ and sulfoxides $79a$-$b$ derivatives of thiacalix[4]arene $1_1$ was also systematically studied and found to have intrinsic participation in metal ion complexations. These results can be categorized as follows: (1) $1_1$ prefers to complex soft-to-intermediate metal ions (e.g. Ag$^+$, Zn$^{2+}$, Cd$^{2+}$, Cu$^{2+}$, Hg$^{2+}$); (2) sulfones $78a$-$b$ extracts hard metal ions (e.g. alkaline earth metals, lanthanoids), and (3) sulfoxides $79a$-$b$ represents a somewhat intermediate situation and extracts both the above mentioned groups of metals. These results enable us to speculate about the binding modes of thiacalix[4]arenes. The proposed binding modes of $1_1$, $78a$-$b$ and $79a$-$b$ are depicted schematically in figure 2 which shows the binding of $1_1$ towards soft metal ions, $78a$-$b$ toward hard metal ions and $79a$-$b$ toward soft and hard metal ions. The sulfoxide $79a$-$b$ can switch between an interaction involving the sulfoxide lone pair or its oxygen, depending on the coordinating metal. One more interesting feature of
thiacalix[4]arene $\text{1}_1$ is inclusion of organic molecules within their cavities formed by aromatic rings or in the crystal lattice. The inclusion behaviour was studied using NMR and X-ray structural analysis.$^{30, 38b, 82}$

Thus, the presence of sulfur atoms in thiacalix[4]arene moiety which is a soft donor leads to soft metal ion recognition and the incorporation of oxygens in functionalized thiacalix[4]arenes drifts the binding affinity from soft metal ions to hard metal ions. Therefore functionalization of thiacalix[4]arene with suitable ligating sites like N and S/ hydrogen bond donors in a specific design would lead to suitable receptors selective for sensing of soft metal ions and anions. Thiacalix[4]arene scaffolds, having vast possibilities of functionalization at the wider, narrow rim and at the sulfide groups, have been decorated in different ways to form different types of host molecules like thiacalix[4]podands, thiacalix[4]crowns and bisthiacalix[4]arenes. Further, the modification at the sulfide groups make its chemistry interesting in aqueous medium as well which is not seen in the case of conventional calix[4]arene chemistry.

In general, many efforts have been devoted for development of thiacalix[4]arene based derivatives for molecular recognition of various analytes (cations, anions and neutral molecules). The recent developments of recognition of cations, anions and neutral molecules based on thiacalix[4]arene derivatives have been discussed as follows:

1.6.1 (Thia)calix[4]arene based receptors for cations

Thiacalix[4]arene $\text{1}_1$ itself was found to have strong binding affinity towards transition metal ions. Ali et al. applied thiacalix[4]arene $\text{1}_1$ to a component of thin films for electrolyte-insulator-semiconductor (EIS), ion-sensitive field effect transistor.
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(ISFET), and gold microelectrodes, which allowed detection of Cu$^{2+}$ at a level of as low as $10^{-7}$ M. This affinity of metal ion recognition could be enhanced by introducing different ligating functional groups. Various thiacalix[4]arene based ligands have been prepared by introducing different functional groups such as ether, ester, ketones, amide, phosphine oxide, etc. Generally, the coordination ability of thiacalix[4]arene derivatives was investigated by solvent extraction of metal ions from aqueous phase to organic phase or by $^1$H NMR, UV and fluorescence spectroscopy. Lamartine et al. reported compound 81 containing amide groups which show significant complexation ability toward K$^+$, Rb$^+$ and Ag$^+$ cations. A series of 1,3-alt-thiacalix[4]arenes 82a-c containing different isomeric aminopyridyl pendant arms have been synthesized by Li et al. The crystal structure of meta-aminopyridyl derivative demonstrate intramolecular hydrogen bondings between the sp$^2$ nitrogen donors in the meta position of the aminopyridyl groups and the facing amide N–H of the adjacent aminopyridyl groups, and self-assembles via C–H...O weak hydrogen bondings and C–H...π interaction to generate a double stranded rectilineal networks. By contrast, the para-aminopyridyl derivative forms N–H...N strong hydrogen bonds between the individual molecules. Further it was found that meta-aminopyridyl derivative showed the best extraction capacity toward Ag$^+$ ion.

A series of thiacalix[4]podands 83a-c and bisthiacalix[4]arenes 84a-b and 85a-d with imine units have been reported by Bhalla et al., and have shown that these thiacalix[4]arene derivatives quantitatively and selectively extracted Ag$^+$ ion from aqueous phase into organic ones. These extraction results were much better than those in the case of conventional biscalix[4]arene units.
Stoikov et al. synthesized morpholidine and pyrrolidine-appended thiacalix[4]arene derivatives of cone 86-87, partial cone 94-95, and 1,3-alternate 102-103 conformations (Table 2). The picrate extraction and dynamic light scattering (DLS) methods were used to evaluate recognition properties of 86-87, 94-95, and 102-103 for monocharged cations (Li⁺, Na⁺, K⁺, Cs⁺ and Ag⁺). It was shown that all derivatives of thiacalix[4]arene form nanoscale particles with silver cations. The pyrrolidine derivative in cone conformation showed both self-association and aggregation behaviour with lithium cations. The degree of extraction that formed nanoscale aggregates in the organic phase was more than 67% which offer opportunities for development of new materials with extended antibacterial properties, ‘smart’ materials in nanolithography and nanochip technologies (multiple analyte detection). Further, Stoikov et al. evaluated these receptors for cation recognition of p-(Al³⁺, Pb²⁺) and d-(Fe³⁺, Co³⁺, Ni²⁺, Cu²⁺, Cd²⁺, Hg²⁺) elements by the picrate extraction method, dynamic light scattering (DLS), and atomic force microscopy (AFM). It was observed that thiacalixarenes tetrasubstituted by the pyrrolidide group were effective extractants compared to morpholidine groups and were able to form dimers of about 1.0 nm with metal cations and nanoscale particles of 238 and 212 nm with Ni²⁺ and Pb²⁺ cations, respectively. The size of the particles consisting of metal cations and tetrasubstituted thiacalix[4]arenes depends on the configuration of macrocycles and the nature of the substrate and their binding centers.
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Further, Yushkova et al. synthesized thiacalix[4]arenes based receptors functionalized with secondary amide and hydrazide groups at the narrow rim in cone 88-93, partial cone 96-101, and 1,3-alternate 104-109 conformations and studied the self-assembly and recognition behaviour of metal ions of s-(Li⁺, Na⁺, K⁺, Cs⁺), p-(Al³⁺, Pb²⁺) and d-(Fe³⁺, Co³⁺, Ni²⁺, Cu²⁺, Ag⁺, Cd²⁺, Hg²⁺) block elements by picrate extraction method and dynamic light scattering (DLS). The DLS method was used for determination of the hydrodynamic diameter, polydispersity index, and molecular weight of nanoscale aggregate systems consisting of thiacalix[4]arene molecules and metal nitrates. It was seen that all these p-tert-butylihexa[4]arenes derivatives bind to alkaline metal cations with low efficiency. Silver ions were the only exception because of their complexation at “soft” sulfur atoms. A similar tendency was observed for p-tert-butylihexa[4]arenes 93, 101, 109 functionalized with hydrazide groups. This is due to insufficient electron donating ability of the substituents at carbamoyl groups as well as to the strong hydrogen bonding between the protons of NH groups and amide carbonyls which compete with the coordination of the cations with phenoxy oxygen atoms and amide carbonyls. The stereoisomers 93, 101, 109 showed...
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certain affinity not only toward silver cations but toward some cations of p- and d-elements. The increase in extraction ability of the compounds 93, 101, 109 toward “soft” cations can be explained by the introduction of an additional center for metal coordination i.e. lone electron pair of terminal nitrogen atoms of hydrazide groups. The DLS method showed that aggregates of stereoisomers 93, 101, 109 with nitrates of p- and d-metals are inclined to form nanosized aggregates but not to self-associate. All the investigated compounds form nanoscale aggregates with silver(I), copper(II), and iron(III) cations under experimental conditions but do not self associate. The binding properties of hydrazine derivative of thiacalix[4]arene of cone 93 and 1,3-alternate 109 conformations were evaluated by means of liquid–liquid extraction for a large variety of metal ions. The cone conformer of thiacalix[4]arene shows higher selectivity in a series of d-metal ions compared with its “classical” analogue. The extraction selectivity for Cu²⁺ and Hg²⁺ over another transition metals becomes very excellent when going from cone to 1,3-alternate conformation of thiacalix[4]arene.

Solovieva et al. reported the narrow rim thiacalix[4]arenes 110-127 (Table 3) of cone and 1,3-alternate conformations containing four carbonyl groups. The extraction studies showed that the removal of the tert-butyl groups decreases the extraction ability of the macrocycles and the selectivity can either increase or decrease depending on the nature of the stereoisomer. The compound 117 in the cone conformation is an efficient and selective extractant for the Li⁺ cation, and compounds 124 and 125 in the 1,3-alternate conformation are selective extractant of the Cs⁺ ions. An increase in the lipophilicity of compounds 118 and 127 in the absence of tert-butyl groups at the wider rim exerts no effect on the extraction of the alkaline metal cations. It was observed that the main factor of lower extraction ability of the unsubstituted thiacalixarenes at the wider rim was the absence of the preorganization effect of macrocyclic platform.
The (thia)calix[4]arene derivatives 128a-g\(^{100}\) bearing two to four thiophosphate substituents were found to be quantitatively selective for Ag\(^+\) (Extraction = 99). Extraction and complexation levels increase with the number of thiophosphates groups. The S atoms of thiacalix[4]arene moiety and thiophosphate may serve as a two-electron donor to a Ag\(^+\) ions. The results show that thiacalixarenes in general are better extractants than calixarenes suggesting the contribution of the bridging sulfur to the coordination.

<table>
<thead>
<tr>
<th>Cone</th>
<th>110</th>
<th>111</th>
<th>112</th>
<th>113</th>
<th>114</th>
<th>115</th>
<th>116</th>
<th>117</th>
<th>118</th>
</tr>
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<tbody>
<tr>
<td>1,3-alternate</td>
<td>119</td>
<td>120</td>
<td>121</td>
<td>122</td>
<td>123</td>
<td>124</td>
<td>125</td>
<td>126</td>
<td>127</td>
</tr>
<tr>
<td>R(_1)</td>
<td>Bu'</td>
<td>H</td>
<td>Bu'</td>
<td>Bu'</td>
<td>H</td>
<td>H</td>
<td>H</td>
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</tr>
<tr>
<td>R(_2)</td>
<td>H</td>
<td>H</td>
<td>OEt</td>
<td>Ph</td>
<td>NEt(_2)</td>
<td>OEt</td>
<td>Ph</td>
<td>NEt(_2)</td>
<td>NBu(_2)</td>
</tr>
</tbody>
</table>

The non-competitive and competitive extracting experiments showed that these novel hosts were good receptors for both metal cations and α-amino acids. Compounds 129a-d and 130a-d showed similar binding properties with high extraction percentage but low extracting selectivities. Bis(thia)calix[4]arene 131 exhibited not only high extracting abilities but also good extracting selectivities.

Lamare\textsuperscript{102} and Grun\textsuperscript{103} et al. reported thiacalix[4]crowns of 1,3-alternate conformations; thiacalix[4]bis(crown-5) 132a and -bis(crown-6) 132b and have shown to have remarkable selectivity towards K\textsuperscript{+} and Cs\textsuperscript{+} ions. The bicrown 132c showed high selectivity for Cs\textsuperscript{+} over K\textsuperscript{+}. van Leeuwen et al.\textsuperscript{104} studied in detail the reaction of thiacalix[4]arene with oligoethylene glycol ditosylate catalysed by alkali-metal carbonate to give thiacalix[4]crowns of cone, 1,3-alternate and 1,2-alternate conformatons and found that thiacalix[4]crowns 133a-c, 134a-b and 135a-b showed high extraction ability towards Ag\textsuperscript{+} ion over the alkali metal ions. The modified thiacalix[4]crowns 136a-b\textsuperscript{105} show high selectivity for Ra\textsuperscript{2+} even in the large excess of over other common alkali and alkaline-earth metal cations. The selective extraction of Ra\textsuperscript{2+} has attracted much interest because the ion is found in trace amount of naturally occurring radioactive materials in aqueous waste stream of non-nuclear industries.
The thiacalix[4]arene dimer $137^{106}$ of 1,3-\textit{alternate} conformation shows high affinity toward Cs$^+$ and K$^+$ ions. Encapsulation of Cs$^+$ by the internal cavity of the dimer strongly suggests that the size match factor drives the process. On the other hand, the K$^+$ is encapsulated by the thiacalix[4]arene units by supramolecular cation-$\pi$ interaction. Further Matthews et al. synthesized thiacalix[4]tube $138$ and found that it has poor binding ability toward K$^+$ ion compared to calix[4]tube. $107$ The asymmetric heterocalix[4]tube $139$ (calix[4]-thiacalix[4]tubes) was obtained by condensation of toslyoxyethoxycalix[4]arene with corresponding thiacalix[4]arene in the presence of K$_2$CO$_3$ in acetonitrile. $108$ The complexation of heterocalix[4]tube was controlled by wider rim substitution of thiacalixarene fragment. The molecular tube $139$ with an adamantine-containing thiacalixarene unit is capable of quantitatively binding potassium and rubidium cations. The 1,3-\textit{alternate} calix-thiacalix[4]crown trimers $140a-b$ bearing crown-5 and crown-6 encapsulate the Cs$^+$ and K$^+$ ions in the outer cavities, respectively and the Ag$^+$ ion was found to be entrapped in the central thiacalix spacer as 1:1 complex. The variable-temperature $^1$HNMR studies reveal that the encapsulated Ag$^+$ ion oscillate through the central thiacalix spacer with the aid of cation-$\pi$ interactions.
The thiacalix[4]podand 141 having pyridyl groups show high affinity for Ag$^+$ ion. The conformational changes of pyridine nitrogen atom from the original outward orientation against the cavity to the inside orientation toward the thiacalixarene cavity were observed in the process of Ag$^+$ complexation. Similarly compounds 142a and 142b having bithiazoyl and bipyridyl groups have best efficiency for Cu$^{2+}$ and Ag$^+$ ions.\(^{110}\)

Sykora \textit{et al.}\(^{111}\) synthesized self-assembled supramolecular networks of 143a-b formed by the interactions of thiacalix[4]arenes bearing simple alkyl groups on the narrow rim with silver triflate. The presence of four sulfur atoms enables the formation of S-Ag-S connections between the individual molecules. These systems form infinite 1-D coordination polymeric structures in the solid state. Interestingly, the linear coordination polymers were obtained using both the conformationaly immobilized and the conformationaly mobile thiacalix[4]arenes, which indicates the generality of this behaviour in thiacalix[4]arene series.

Csokai \textit{et al.}\(^{112}\) reported thiacalix[4]arene derivative 144 possessing dithiacrown ethers and allyloxy-substituted thiacalix[4]arene 145 and studied their complexation behaviour which shows that the 1,3-\textit{alternate} conformations are more effective silver binding agents than those which exist primarily in the \textit{cone} conformations. The ditopic receptor 146 possessing two complexation sites and bearing 1,3-\textit{alternate} conformation based on thiacalix[4]arene was prepared.\(^{113}\) The exclusive formation of mononuclear complexes of 1,3-\textit{alternate}-derivative with Na$^+$, K$^+$ and Ag$^+$ ions is of particular interest in regard to a negetive allosteric effect in the thiacalix[4]arene family. The decomplexation of K$^+$ from the ester sites to form the Ag$^+$ complex with 1,3-\textit{alternate}-derivative complex by addition of AgSO$_3$CF$_3$ is the first example of negative allosteric effect in the thiacalix[4]arene family.
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Appelhans et al. synthesized cone-type and spherical lysine dendrimers up to generation 3 based on thiacalix[4]arene core units and used them as molecular scaffolds for supramolecular host systems.\textsuperscript{114} The tetraacetate of thiacalix[4]arene \textsuperscript{148b} shows a high binding affinity for Fe\textsuperscript{3+} ions by the cone conformers at pH 5.5 compared to calix[4]arene derivative \textsuperscript{148a}. However interestingly the compound in 1,3-alternate conformation did not bind to any metal ion under similar conditions.\textsuperscript{115} Iki et al.\textsuperscript{116} reported chirally modified thiacalix[4]arene \textsuperscript{149} with R or S-phenylethylamine which showed a fair enantioseparation for various analytes including chiral alcohols, amino acids and amine derivatives.

Tu et al.\textsuperscript{117} developed a facile method to prepare size-controllable AuNPs in aqueous phase by using amphiphilic \textit{p-}tert\texttext{-}butyl thiacalix[4]arene \textsuperscript{150} grafted with poly(ethylene glycol) monomethyl ether (SCa-MPEG550) as stabilizer and reductant. During the preparation of AuNPs, the phenolic groups of SCa-MPEG550 \textsuperscript{150} without poly(ethylene glycol) chain are oxidized to benzoquinones (SCaQ-MPEG550) \textsuperscript{151a-c}, so SCa-MPEG550 acts as reductant of AuNPs. The particle sizes of AuNPs can be readily controlled by only adjusting the feeding ratio of Au/S. On the other hand,
Kozlova et al.\(^{118}\) reported a molecular tecton 152 with S4 symmetry and offering two sets of coordinating sites i.e. four sulfur atoms and four benzonitrile groups. The compound 152 in the presence of AgNO\(_3\) results in the formation \([152.(\text{AgNO}_3)_{10}]\) complex having 3-D coordination network in the crystalline phase resulting from the mutual interconnection of decanuclear silver nanoclusters and organic tectons. The important structural features for the organic tecton 152 are close to those observed for the free tecton.

Shamova et al.\(^{119}\) studied the complexation of methyl-glycine-amide functionalized thiacalix[4]arene 153 with K\(^+\) and Ag\(^+\) using density functional theory (DFT) in the gas phase. Hydrogen bonding of amide hydrogens of podand arms was found to take place predominantly with the ether oxygens of the same arm rather than the carbonyls of other arm. The silver cation favour coordination with S atom (for the cone conformer), N (for one of the 1,3-\textit{alternate} conformers); the S-coordination mode is clearly preferred. The stability order \textit{cone} > 1,3-\textit{alternate} > \textit{paco} was found for the Ag\(^+\) complexes. On the other hand, potassium cation favour interaction with the four carbonyl oxygens of the podand amide arms and the stability order of 1,3-\textit{alternate} > \textit{cone} > \textit{paco} was found for the K\(^+\) complex. For all obtained conformers, intramolecular hydrogen bonds disfavor complexation, increasing the pre-organizational energy to be paid.

The ditopic receptors 154 and 155 of thiacalix[4]arene of \textit{cone}- and 1,3-\textit{alternate} conformations, respectively, possessing four 2-pyridyl groups were synthesized by Yamato et al.\(^{120}\) The single crystal X-ray analysis of tetraamides in \textit{cone} conformation show strong intramolecular hydrogen bonding between sulfur atom on the bridge and NH proton (S---HN), and between the phenolic oxygen and the NH proton (ArO---HN). These receptors containing pyridine groups showed high
affinity toward Ag$^+$ ion complexation and poor affinity towards halide anions. Another thiacalix[4]arene based ditopic receptor 156\(^{121}\) forms mononuclear complexes with Li$^+$ and Ag$^+$ even though the formation of the heterogeneous dinuclear complexes was expected. Further, they have developed hydrogen-bonding self-assembly of heterodimeric systems of bis(4-pyridyl) and dicarboxylic acid derivatives 157 and 158 of thiacalix[4]arene of 1,3-\textit{alternate} conformation. Although the values of the dimerization constants are relatively small, the stability of the dimers is strong enough to overcome only small conformational changes upon complex formation.

Stoikov \textit{et al.}\(^{122}\) reported a series of new \textit{p-}\textit{tert}-butylthiacalix[4]arenes derivatives 159-175 of cone, partial cone, and 1,3-\textit{alternate} conformations (Table 4) with \textit{o-}, \textit{m-}, \textit{p-}amido and \textit{o-}, \textit{m-}, \textit{p-}(amidomethyl)pyridine substituents at the narrow rim. The binding ability of these derivatives was investigated by UV-vis spectroscopy and found to be selective to recognize the \textit{α}-hydroxy (glycolic, tartaric) and dicarboxylic (oxalic, malonic, succinic, fumaric, and maleic) acids.
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The chromogenic supramolecular vanadophiles $176a-f$ based on a 1,3-
alternate thiacalix[4]arene were found to show high affinity toward vanadate ions, attributed to the pre-organization of chelating sites on a stable molecular platform. These receptors simultaneously coordinate two vanadate ions giving a highly staggered geometry with almost $D_{2d}$ symmetry. Among various derivatives of $176a-f$, the superiority of $176f$ may be accredited to the high inductive and mesomeric effects of the nitro group, which make the N-OH protons more labile, thus facilitating complex formation. Kundrat et al.\textsuperscript{124} synthesized molecular tweezers based on calix[4]arene/thiacalix[4]arene-porphyrin conjugates $177a-b$ which form 1:1 complexes with $C_{60}$ and $C_{70}$ fullerenes in solution while possessing a high selectivity towards fullerene $C_{70}$.

Praveen et al.\textsuperscript{125} synthesized a thiacalix[4]arene derivative $178$ of 1,3-
alternate conformation bearing four quinolinoloxo groups which is highly selective for Hg$^{2+}$ ion showing “on-off” type fluorionophoric properties. The ligand attained unusual conformation of a tetra-mercury complex enclosing one Hg$^{2+}$ ion each in the four cavities of propyl arms containing quinolinoloxy groups. The fluorogenic receptor $179$ having dansyl moiety was used as effective chemosensor for Cd$^{2+}$ ions in aqueous medium.\textsuperscript{126} Further, various thiacalix[4]arene derivatives of mono to tetra-dansyl have also been synthesized and found to be selective for soft metal ions like Co$^{2+}$, Ni$^{2+}$ and Cd$^{2+}$. The ferrocene-based 1,3-
alternate thiacalix[4]arene ditopic receptor $180$ have been synthesized by Guo et al.\textsuperscript{127} that contains four identical polyether arms.

Table 4. Thiacalix[4]arenes based receptors 159-175.

<table>
<thead>
<tr>
<th>Cone</th>
<th>Partial cone</th>
<th>1,3-alternate</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>159</td>
<td>164</td>
<td>170</td>
<td>$o$-HNPy</td>
</tr>
<tr>
<td>160</td>
<td>165</td>
<td>171</td>
<td>$m$-HNPy</td>
</tr>
<tr>
<td>161</td>
<td>166</td>
<td>172</td>
<td>$p$-HNPy</td>
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<tr>
<td>162</td>
<td>167</td>
<td>173</td>
<td>$o$-HNCH$_2$Py</td>
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<td>163</td>
<td>168</td>
<td>174</td>
<td>$m$-HNCH$_2$Py</td>
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<tr>
<td>169</td>
<td>175</td>
<td>$p$-HNCH$_2$Py</td>
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Table 4. Thiacalix[4]arenes based receptors 159-175.
terminated with ferrocene amide moieties. This redox-active receptor can be used as an electrochemical sensor to recognize both Eu$^{3+}$ and dihydrogen phosphate (H$_2$PO$_4^-$) ions with a high selectivity.

Thus, from above review we observed that the binding studies of thiacalix[4]arenes derivatives have been evaluated by solvent extraction method, $^1$H NMR spectroscopy and X-ray crystallography. However, the fluorogenic and chromogenic chemosensors based on thiacalix[4]arene scaffold are much less explored. Compared to thiacalix[4]arene, the fluorogenic and chromogenic chemistry of calix[4]arene is much explored towards various analytes (cations, anions and neutral molecules). Kim et al.$^{128}$ synthesized a number of calix[4]arenes derivatives bearing different fluorogenic units.

A calix[4]arene derivative $^{181}$ with di(1-pyrenylmethyl)amide-dicarboxylic acid of 1,3-alternate conformation,$^{129}$ showed quenching of excimer emission upon complexation of Pb$^{2+}$ ions. However, addition of Ca$^{2+}$ ions to the solution of complex $^{181}$-Pb$^{2+}$ leads to the revival of the excimer fluorescence, leading to formation of an ‘On-Off-On’ molecular switch. The receptor $^{182}$ bearing one 2,3-naphthocrown-6
and two coumarin amide units at the narrow rim in *partial-cone* conformation of calix[4]arene showed colorimetric and fluorometric high selectivity for F⁻ and Cs⁺ ions. The high fluorescence selectivity toward F⁻ and Cs⁺ ions was due to intramolecular FRET from the naphthalene emission to the coumarin absorption. Kim *et al.*\(^{131}\) reported a pyrene-appended fluorescent chemosensor 183 having two different types of cation binding sites on the narrow rims of a 1,3-\*alternate* calix[4]arene forms a strong excimer in solution between two pyrene moieties. The excimer emission of 183 was quenched by Pb²⁺, but revived by addition of K⁺ to the Pb²⁺ ligand complex. The metal ion exchange produces an on-off switchable, fluorescent chemosensor. The computational results showed that the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbitals (LUMO) of the two pyrene moieties interact under UV irradiation of 183 and its K⁺ complex, while such HOMO-LUMO interactions are absent in the Pb²⁺ complex.

The calix[4]triazacrown 184 bearing primary alkylamine and two pyrene units reveal a quenched monomer emission because the pendent amine group (-CH₂CH₂NH₂) which takes part in a PET process: an electron transfer from a lone-pair electron of the nitrogen atom to two pyrene units.\(^{132}\) When Pb²⁺ is added to a solution of 184, the monomer emission increases with quenching in excimer emission due to conformational changes of the carbonyl bonds (flipping over) as well as to the participation of the primary amine. In contrast, the addition of Li⁺ to the ligand 184 causes both monomer and excimer emission to increase, which was attributed to the CHEF effect. In addition, compound 184 shows a high selectivity for F⁻ ions with decrease in fluorescence emission via hydrogen bonding between the amide NH of the triazacrown ring and F⁻ ions.
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The two photon-absorbing chemosensor 185 based on calix[4]arene of 1,3-
alternate conformation undergoes blue-shifted absorption and enhanced fluorescence
with the addition of an Al\(^{3+}\) or Pb\(^{2+}\).\(^{133}\) Addition of a Pb\(^{2+}\) ion to a solution of 185.K\(^{+}\)
enhanced the fluorescence emission due to the allosteric effect induced by the complexation of K\(^{+}\) with the crown loop. The two-photon processes provide a useful
design strategy for the synthesis of the two-photon sensors for biological applications.

Othman et al.\(^{134}\) reported a monobridged fluorogenic biscalix[4]arene 186
containing pyrene and rhodamine B moieties which was found to be selective for Hg\(^{2+}\)
and Al\(^{3+}\) ions. The addition of Hg\(^{2+}\) to a solution of compound 186 resulted in
significantly enhanced fluorescence at $\lambda_{em} = 575$ nm via FRET-ON from the pyrenyl
excimer to the ring opened rhodamine moiety with excitation at 343 nm. Whereas,
complexation of Al\(^{3+}\) results in strong emission of the pyrenyl excimer but weak
rhodamine emission, suggesting that Al\(^{3+}\) prefers the formation of a pyrenyl excimer
but not the ring-opening of the spirolactam of the rhodamine. Park et al.\(^{135}\) reported
calix[4]arene based fluorescent chemosensor 187 containing triazoles moieties which
showed high selectivity for Cd\(^{2+}\) and Zn\(^{2+}\) ions in a ratiometric manner through an
enhanced monomer and declining excimer emission.

Choi et al.\(^{136}\) reported the behaviour of PCT-based calix[4]crown fluorescent
chemosensors 188 towards transition metal ions (Pb\(^{2+}\) and Cu\(^{2+}\)) and an alkali metal
cation (K\(^{+}\)). For the transition metal ions, both monomer and excimer emissions were
quenched due to reverse PET and conformational changes. The addition of K\(^{+}\) ions
results in its encapsulation in the crown-5 ring which induces a more favourable
interaction between the HOMO and LUMO, resulting in stronger excimer formation.
The addition of K\(^{+}\) ions to the 188.Pb\(^{2+}\) complex, there was revival of fluorescence
emission indicating the metal ion exchange process between K\(^{+}\) and Pb\(^{2+}\) ion.
The fluorescent chemosensor 189 based on calix[4]arene bearing four iminoquinoline subunits on the wider rim showed a remarkable enhanced fluorescent intensity in the presence of Cu$^{2+}$ ion and a high selectivity toward Cu$^{2+}$ ion over a wide range of tested metal ions. Pathak et al.\textsuperscript{138} developed a fluorescence turn-on receptor 190 based on triazole linked calix[4]arene for selective recognition of Zn$^{2+}$ in aqueous-methanolic HEPES buffer. Further, the receptor 190 showed its utility for sensing Zn$^{2+}$ in blood serum milieu and in the presence of albumins.

Talanova et al. reported fluorogenic receptors 191 and 192 possessing sulphonamide moieties based on calix[4]arene of cone and partial-cone conformations. Receptor 191 showed fluorogenic detection of Hg$^{2+}$ ions in acidic aqueous solution even in the presence of 100-fold excess of various other metal ions,\textsuperscript{139} while receptor 192 of partial-cone conformation showed fluorescence enhancement in the presence of Pb$^{2+}$ ions with a lower detection limit of 2.5 ppb.\textsuperscript{140} The tetra-dansyl derivative of calix[4]arene 193 reported by Metivier et al.\textsuperscript{141} showed ratiometric selectivity towards Pb$^{2+}$ ions.\textsuperscript{142} Another tetra-dansyl appended calix[4]arene derivative 194 of 1,3-alternate conformation reported by Pandey et
al.\textsuperscript{143} showed high selectivity and adequate reversibility for Hg\textsuperscript{2+} ions. Compared to cone conformation of dansyl-appended calix[4]arenes, the derivative \textbf{194} of 1,3-alternate conformation showed high selectivity for Hg\textsuperscript{2+} ions. The disubstituted dansyl derivative \textbf{195} grafted on a large pore mesoporous silica material, showed an optical signaling of Hg\textsuperscript{2+} in aqueous solution, with reversible binding of the cation.\textsuperscript{144}

A triazole appended calix[4]crown derivative \textbf{196}\textsuperscript{145} of 1,3-alternate conformation synthesized using click chemistry shows a fluorescence quenching in presence of Pb\textsuperscript{2+}, Hg\textsuperscript{2+}, Cu\textsuperscript{2+} and Cr\textsuperscript{3+} ions. This fluorescence quenching is attributed to the reverse PET from anthracene unit to the triazole group. However, revival of fluorescence emission from the strongly quenched \textbf{196}-Pb\textsuperscript{2+} complex was observed on addition of K\textsuperscript{+} ions showing ‘On-Off’ switching phenomenon. Chen \textit{et al.}\textsuperscript{146} reported calix[4]arene based azacrown \textbf{197} substituted with a lariat arm carrying a dansylamide fluorophore. Receptor \textbf{197} showed a selective and sensitive sensing of Hg\textsuperscript{2+} ions based on a fluorescence quenching in presence of metal ion due to the excited state charge transfer from the dansyl moiety to the Hg\textsuperscript{2+} ions. Another azacrown modified derivative \textbf{198} reported by Kim \textit{et al.}\textsuperscript{147} showed selective quenching of pyrene fluorescence in presence of Hg\textsuperscript{2+} ions.

For the last few years, fluorescent imaging using various fluorescent probes provides a highly sensitive, efficient and temporal analysis of cells\textsuperscript{148} and is widely used in the field of biology and physiology. The development of optical fluorescent probes of a particular analyte for fluorescent imaging help to map the molecular details of biological processes like metal ion transport, homeostasis and participation in disease pathology.\textsuperscript{149} The optical detection of metal ions in living organisms offers great significance to study their site of action and physiological functions.\textsuperscript{150} The biological detection of particular analyte by fluorescent imaging can provide direct information on their spatiotemporal distributions in living systems.
Komatsu et al.\textsuperscript{151} reported the simultaneous imaging of intracellular Ca\textsuperscript{2+} and Mg\textsuperscript{2+} ions with a novel single-molecular multi-fluorescent probe 199 due to the different optical response patterns of the two selective binding sites. Upon complexation to Ca\textsuperscript{2+} ions, probe 199 shows a 45 nm blue shift in absorbance and a 5 nm blue shift in the fluorescence spectrum. For Mg\textsuperscript{2+} ions, a 21 nm red shift in absorbance and a 5 nm red shift in fluorescence occurred. The probe 199 was biologically evaluated by applying it into differentiated PC12 cells. Yang et al.\textsuperscript{152} reported a multi-signaling sensor 200 based on rhodamine B with a ferrocene substituent which shows extreme selectivity for Hg\textsuperscript{2+} ions over other metal ions. Multi-signaling changes were observed through UV/vis absorption, fluorescence emission, and electrochemical measurements. The confocal laser scanning microscopy experiments have shown that 200 can be used to detect Hg\textsuperscript{2+} ions in living cells and map its subcellular distration.

A rhodamine-based reversible chemosensor 201\textsuperscript{153} binds to Hg\textsuperscript{2+} and Cu\textsuperscript{2+} ions in aqueous methanol solution with detectable change in color and different fluorescence output signals. Further, this sensor 201 could detect the Hg\textsuperscript{2+} ion adsorbed on the cell surface of the microorganism such as Pseudomonas putida and thus could be useful for determining the amount of Hg\textsuperscript{2+} ions that could enter in the food chain affecting human beings along with phytoplanktons and zooplanktons. Another rhodamine based chemosensor 202\textsuperscript{154} possessing dansyl moiety has been utilized as ratiometric sensor for detection of Hg\textsuperscript{2+} ions in aqueous solution using resonance energy transfer mechanism. The receptor 202 could be used as staining agent for detection of Hg\textsuperscript{2+} ions uptake in bacteria living cells such as Pseudomonas putida.

The hypersensitive water-soluble fluorescent probe 203\textsuperscript{155} can selectively detect low levels of Hg\textsuperscript{2+} ions in buffered aqueous solution with high affinity and turn-on response. Further investigations in living cells demonstrated the potential
applications of this novel probe for the study of the toxicity or bioactivity of Hg$^{2+}$ ions in living cells. The quinoline-based fluorescent probes 204a-b displays high selectivity and sensitivity for Zn$^{2+}$ ions in a neutral buffer aqueous solution. The probes 204a-b exhibits 14-fold fluorescence enhancement in response to Zn$^{2+}$ ions which is favourable toward biological applications. The two-photon imaging of probes 204a-b showed good cell permeability and efficient detection of Zn$^{2+}$ ions in living cells. A rhodamine based thiosemicarbazide probe 205 which reacts irreversibly with methylmercury via a desulfurization reaction, can detect methylmercury with high sensitivity in aqueous media. The fluorescent imaging of HeLa cells and zebrafish demonstrated the detection and real-time monitoring of methylmercury in living cells and organisms.

Lalor et al.\textsuperscript{158} reported the cellular uptake processes and cellular fate for nitrobenzofurazan derivative of calix[4]arene 206. The fluorescent imaging of this calix[4]arene derivative showed accumulation of the probe within the cell cytoplasm. The rhodamine based fluorescent probe 207 possessing thiol and alkyne moieties have been synthesized by Lin et al.\textsuperscript{159} The probe exhibits large fluorescence enhancement, high selectivity and low detection limit for Hg$^{2+}$ ions based on the interactions of Hg$^{2+}$ to both thiol and alkyne moieties in a probe 207. Furthermore,
receptor 207 demonstrates its high utility for detection of Hg$^{2+}$ ions by fluorescent imaging in the living cells.

The cryptand–rhodamine conjugated chemodosimeter 208 reported by Jana et al.\textsuperscript{160} can detect Hg$^{2+}$ ions in aqueous medium selectively at ppb level in the presence of other biologically relevant metal ions. This system also shows a good viability in living cells imaging study (HEK 293 cell line) due to its greater extent of cell permeability that arises from its adjustable amphiphilic nature.

Wang et al.\textsuperscript{161} reported a nanoparticle conjugate of Fe$_3$O$_4$-Rh6G-LEDA 209 and demonstrates its high selectivity for detecting Fe$^{3+}$ ions among various metal ions in water with the detection limits reaching as low as 2 ppb. The sensitive detection of Fe$^{3+}$ ions by the NP conjugate is further demonstrated in HeLa cells indicating the potential applications of NP conjugate 209 in the biological monitoring and tracking of iron.

1.6.2 Thiacalix[4]arene based metal complexes

During the last few years, the high-nuclearity coordination clusters of transition metal cations have been receiving growing attention due to their interesting electronic and magnetic properties which contribute to their potential as nanoelectronic components, metalloenzyme models, nanoscale catalysts, and molecular magnets.\textsuperscript{162} Among various scaffold, calixarenes with hetero-atoms in the scaffold and on the rims are excellent candidates as ligands for making multinuclear metal complexes.\textsuperscript{163} Thiacalix[4]arene, possessing four phenoxyl groups and four bridging sulfur atoms, the sulfonyl and sulfinyl derivatives give polynuclear complexes with most transition metal ions. Further these have been proved to be good multidentate ligands in constructing polynuclear complexes.\textsuperscript{164} Such macrocyclic $\pi$-rich ligands may hold efficient energy-transfer properties for the luminescent materials and the proper orbitals for the construction of metal complexes.

The sulfonyl-based ligands 210a and 210b, synthesized by Horiuchi et al.\textsuperscript{165} form luminescent 1:1 complexes with Tb(III) ion having higher luminescent quantum yield ($\Phi = 0.29$ and 0.28, respectively) than 1:1 complexes of the corresponding thiacalix[4]arene-based di- and tetracarboxylate ligands ($\Phi = 0.04$ and 0.003, respectively), implying higher efficiency of sulfonyl ligands than those of thia ligands in the energy transfer process.
Mono- and dinuclear titanium complexes of \textit{p-}tert-butylthiacalix[4]arene $^{211}$ were applied as a catalyst for [2+2+2] cycloaddition of terminal alkynes and found to have high catalytic activity and regioselectivity toward 1,3,5-trisubstituted benzenes over 1,2,4-trisubstituted isomers. The regioselectivity was due to steric effect of the thiacalix[4]arene skeleton and the coordination of the bridging sulfur atom to the titanium centre.

The tetranuclear complexes of de-\textit{tert-}butylated thiacalix[4]arene $^{3}$ and \textit{p}-phenylthiacalix[4]arene $^{212}$ with lanthanide metals ($\text{Ln} = \text{Tb}^{III}$, Dy$^{III}$) demonstrated an efficient luminescent and magnetic properties.$^{167}$ All the frameworks obtained can be formulated as $[\text{Ln}^{III}_4(212/3)_2(\mu_4-\text{OH})\text{Cl}_3(\text{CH}_3\text{OH})_2(\text{H}_2\text{O})_3]$, and some methanol and water solvent molecules are occupied in the interstices. The compounds showed a sandwich like unit constructed by two tail-to-tail thiacalixarene molecules and a planar tetragonal ($\mu_4-\text{OH}$)$\text{Ln}_4$ cluster. There was an effective ligand-to-$\text{Ln}^{III}$ energy transfer for these compounds and $^{212}$ is a more efficient “antenna” than $^{3}$. The Dy$^{III}$ compounds exhibit slow magnetic relaxation behaviour of single-molecule magnet nature.

The replacement of the $t$-Bu group by a $p$-phenyl group at the wider rim of thiacalix[4]arene leads to different extended structures and a kind of multifunctional material with photoluminescence and small molecular magnet (SMM) like properties.

Bi \textit{et al.}$^{168}$ reported a novel complex of $\{\text{Co}_{32}\}$ cluster core capped by six $p$-\textit{tert-}butylthiacalix[4]arene $^{11}$ molecules and appear as a sodalite $\text{Co}^{II}_{24}$ cage encapsulating a $\text{Co}^{III}_8$ cube. The thiacalixarenes capping six faces of a hexahedron exhibit a unique arrangement for the thiacalixarenes. In two isomers, the thiacalixarene-capped $\{\text{Co}_{32}\}$ spherical units are arranged into a body-centered cubic lattice, while in the third isomer, they are assembled in a cubic closest packing pattern.

The single-crystal x-ray diffraction studies of $[\text{K}(11\cdot3\text{H})\cdot2\text{MeOH}]$ complex, obtained from the reaction of $p$-\textit{tert-}butylthiacalix[4]arene $^{11}$ with KH, shows the
formation of dimers.\textsuperscript{169} One of the dimers was formed by a hydrophobic interaction between each tert-Bu group of \textit{1}\textsubscript{1}-3H and the cavity of another \textit{1}\textsubscript{1}-3H in the crystal state. The other dimer made metal coordination S\cdots K\cdots(O,S,O) between neighbouring \textit{1}\textsubscript{1}-3H and potassium ions. In the overall structure, this complex indicates a nonporous structure and the adsorption capabilities toward gaseous organic molecules are studied.

Amirov \textit{et al.}\textsuperscript{170} reported the gadolinium (III) complexes possessing high relaxivity with various tetraacid stereoisomers based on \textit{p-}tert\textendash butylthiacalix[4]arene \textcolor{blue}{213-215} in micellar solutions of non-ionic surfactants (\textit{A-C}). The acid-base properties of individual isomers of the ligand were studied by pH-metric titration and UV spectroscopy and revealed the influence of the spatial arrangement of the functional groups in the \textit{p-}tert\textendash butylthiacalix[4]arene stereoisomers substituted by carboxy groups at the narrow rim on the ability to bind the Gd\textsuperscript{3+} ions to form water soluble complexes possessing high relaxivity. In addition, he evaluated the influence of type and concentration of the nonionic surfactant in solution on the degree of binding of the paramagnetic probe and relaxivity of gadolinium solutions containing calixarene-surfactant mixed aggregates.

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

\textbf{A B C}

Chen \textit{et al.}\textsuperscript{171} demonstrated the formation of a chiral Kagome network structure (A Kagome lattice,\textsuperscript{172} also known as trihexagonal tiling, represents a periodic arrangement of interlaced triangles such that each point where two triangles cross has four neighboring points) using thiacalix[4]arene tetrasulfonate (TCAS) \textcolor{blue}{216} as a building block at an aqueous/Au (111) interface with potential control. The
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interesting feature of the system was that the building block of the chiral Kagome network was a structure-complicated supramolecule calixarene rather than simple planar or near-planar organic molecules. It opens the possibility to construct a 2D nanoporous network by various functional supramolecules. Further, the TCAS can interact with guest molecules through hydrogen bonding as well as hydrophilic/hydrophobic and π-π stacking interaction, a plethora of host-guest complexes could be integrated into the Kagome network. The construction of a chiral cavity array in aqueous media would facilitate single molecular recognition with biological active chiral molecules. Liu et al evaluated the stability constants (K_a) and thermodynamic parameters (ΔG°, ΔH°, and TΔS°) for 1:1 complexation of water-soluble thiacalix[4]arene 216 / calix[4]arene 217 with pyridine and their methylated derivative by means of isothermal titrations calorimetry at pH 2.0 and 7.2 at 298.15K. The results obtained show that sulfonatocalixarenes afford stronger binding ability toward pyridine guests at pH 2.0, attributable to the positive electrostatic interactions and the more extensive desolvation effects, but present higher molecular selectivity at pH 7.2 owing to the strengthened C-H...π interactions.

The intercalation behaviour of water-soluble tetrasodium p-sulfonatothiacalix[4]-arene (TCAS) 216 was studied by intercalating it into layered double hydroxides (LDH). Utilizing the osmotic swelling of LDH in formamide, the bulky thiacalix[4]arene anion is introduced, leading to the recovery of LDH layers, and the hexagonal prism morphology. The osmotic swelling/restoration method could be a useful technique to prepare regularly stacked layered compounds with large bio- or organic molecules as guests in the interlayer. Further, Huang et al. intercalated water-soluble-tetrasodium p-sulfonatothiacalix[4]arene (TCAS) 216 into MgAl-LDH using an osmotic swelling/restoration reaction of the LDH in
formamide. The arrangement of TCAS in the interlayer can be controlled through adjusting the area per unit charge ($S_{\text{charge}}$) of TCAS. When $S_{\text{charge}}$ (TCAS)$<S_{\text{charge}}$ (LDH), monolayer (basal spacing, $d_{\text{basal}}$, 1.30 nm) and alternating “up-down” antiparallel ($d_{\text{basal}}$, 1.54 and 1.45 nm) arrangements were obtained. When $S_{\text{charge}}$ of TCAS was increased by forming an Ag$^+$ complex, bilayer arrangement ($d_{\text{basal}}$, 2.12 nm) of TCAS (Ag) was formed. This swelling/restoration reaction took place, and the composites retained the morphology of the LDH precursor. The thermal stability of TCAS in the composites was remarkably enhanced, and the “up-down” antiparallel arrangement of TCAS had the highest increase of thermal stability.

The photophysical properties of supramolecular complex of thiacalix[4]arene-$p$-sulfonate (TCAS) 218 with Tb(III), and Ag(I) ions in aqueous solution was found to exhibit energy-transfer luminescence with an exceptionally long lifetime (4.6 ms). The crystal structure of these complexes indicate that two TCAS ligands are linked by two S-Ag(I)-S linkages to adopt a double-cone supramolecular structure.

Odo et al.177 reported a new water-insoluble Fe$^{3+}$-TCAS (216)/TMPyP (219) complex of tetraanionic Fe(III)-thiacalix[4]arenetetrasulfonate (Fe$^{3+}$-TCAS) with tetracationic tetrakis(1-methylpyridinium-4-yl)porphine (TMPyP) 219 via ionic interaction. The peroxidase-like catalytic activity of the Fe$^{3+}$-TCAS/TMPyP complex was investigated based on the dye formation reaction by oxidation of 4-aminoantipyrine and phenol with H$_2$O$_2$ catalyzed by peroxidase. This Fe$^{3+}$-TCAS/TMPyP complex showed the highest activity at pH 5.5 acetate buffer solutions, and it was applied to the photometric determination of trace amounts of H$_2$O$_2$. Moreover, the method using glucose oxidase and the Fe$^{3+}$-TCAS/TMPyP complex was applied to the determination of glucose. The Fe$^{3+}$-TCAS/TMPyP complex can be applied to a practical sample, such as blood or urine, as an analytical reagent for the photometric determination of H$_2$O$_2$ in place of peroxidase.

A heterogeneous one-step self-assembly of Ag$^+$, Tb$^{3+}$, and tetrasodium $p$-sulfonatothiacalix[4]arene (TCAS) 216 was reported by Tanaka et al.178 of which the donor atoms S and O showed high selectivity toward Ag$^+$ and Tb$^{3+}$ ions, respectively. The cage structure of ternary complex, [Ag$_4$Tb(tcass)${}_2$dmf$_2$]$^9$ was formed by the one-step heterogeneous self-assembly of Ag$^+$ and Tb$^{3+}$ ions with the TCAS ligands. The Tb$^{3+}$ ion was encapsulated in an octa-oxygen cube, it was shielded from solvent molecules such as water and DMF, which has advantage of construction of a highly luminescent environment for a lanthanide (III).
The mononuclear \textbf{220} and dinuclear complexes \textbf{221} of \textit{p}-sulfonatothiacalix[4]arene (TCAS) \textbf{216} with Ce(IV) was synthesized by Matsumiya \textit{et al.}\textsuperscript{179} The dinuclear Ce(IV) complex \textbf{221} promoted the hydrolysis of \textit{p}-nitrophenyl phosphate with a turnover frequency of 6.8 h\textsuperscript{-1} at 50 °C, showing fourfold higher activity than the mononuclear complex. The dinuclear complex was readily immobilized onto an antibody by simply mixing them in water, and its phosphatase-like activity was applied to the color-developing reaction in immunoassay. The model assay using an antibody labelled with the dinuclear complex allowed the detection of as little as 10 ng mL\textsuperscript{-1} of a tumor marker, Bence-Jones protein, in a 96-well microtiter plate format.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{complexes}
\caption{Mononuclear and Dinuclear Complexes}
\end{figure}

Iki \textit{et al.}\textsuperscript{180} reported an assembled supramolecular structure \textbf{222} consisting of multidentate and photon-absorbing \textit{p}-sulfonatothiacalix[4]arene (TCAS) \textbf{216}, luminescent Tb\textsuperscript{III} and analyte Ag\textsuperscript{I}, with linear coordination geometry that is capable of sensing Ag\textsuperscript{I} ions at nanomolar concentrations. Two thiacalix[4]arene ligands are linked by analyte Ag\textsuperscript{I} ions and then coordinate to Tb\textsuperscript{III} ions to form a luminescent ternary complex, Ag\textsuperscript{I}\textsubscript{2}.Tb\textsuperscript{III}\textsubscript{2}.TCAS\textsubscript{2}, enabling the nanomolar detection of Ag\textsuperscript{I}. The sensing function of assembled structure originates from the supramolecular nature of complex \textbf{222}, and not from TCAS and Tb\textsuperscript{III} individually. Thus, the complex \textbf{222} truly demonstrates the “supramolecular strategy.”

Two isomorphous complexes of \textit{p}-sulfonatothiacalix[4]arene (TCAS) \textbf{216}, cobalt(II) nitrate or zinc(II) nitrate and methylviologen dihexafluorophosphate (MV(PF\textsubscript{6})\textsubscript{2}) , \{[M(H\textsubscript{2}O)\textsubscript{6}]\textsuperscript{2+} [MV]\textsuperscript{2+}[(MV)\textsubscript{2}M\textsubscript{2}(H\textsubscript{2}O)\textsubscript{4}(\textbf{216})\textsubscript{2}]\textsuperscript{4+}\}\cdot 14H\textsubscript{2}O (M= Co; Zn) form a dimer with \textit{C}_{i} symmetry through the coordination of sulfonate groups.\textsuperscript{181} The
dimers further extend their structures through second-sphere coordination and π-π stacking interactions into three-dimension nets.

Buccella et al.\textsuperscript{182} reported the mononuclear Mo and W complexes \textbf{223a-b, 224} and \textbf{225a-b} of \textit{p-}tert-butylthiacalix[4]arene \textbf{1}, and \textit{p-}tert-butyltetrasulfonylcalix[4]arene (TCAS) \textbf{216}. The comparison with the related calix[4]arene complexes indicates that the chemistry of the system is strongly influenced by the nature of the calixarene linker, i.e., CH\textsubscript{2}, S, and SO\textsubscript{2}. For example, in contrast to the methylene-bridged calixarene system, the thiacalixarene and sulfonylcalixarene systems readily coordinate a second metal center to form homo- and heterodinuclear complexes \textbf{223-225}. Of most interest, incorporation of Ni into complex \textbf{223a} using Ni(PMe\textsubscript{3})\textsubscript{4} results in cleavage of a C-S bond to give \textbf{226}, an observation that is of relevance to the role that Ni plays in hydrodesulfurization catalysis.

1.6.3 (Thia)calix[4]arene based receptors for anions

Anion recognition chemistry has emerged as an exciting research field in supramolecular chemistry in recent years owing to the biological and environmental relevance of anions.\textsuperscript{183} The anion recognition has been a great challenge since anion complexation with the receptor is quite different from that for metal cations because of their varying size, shape and charge, and pH-dependent species. However, significant progress has been made in the development of anion receptors using
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different molecular scaffolds. The recognition of anion has been achieved using different artificial receptors such as neutral anion receptors (amide, urea/thiourea, benzimidazole, pyrrole, alcohol and phenol) containing different hydrogen bond donors and positively charged anion receptors (comprising of functional moieties like ammonium, guanidinium, phosphonium, metal-complexes and pyridinium). Various anions such as fluoride, cyanide, sulphate and phosphate play many key roles in biological systems. Therefore selective recognition of particular anions is of considerable interest. Among various scaffolds, (thia)calix[4]arene scaffold has also been utilized for the design and synthesis of anion receptors bearing different binding moieties such as amide, (thio)urea and various other neutral/electrostatic groups. A brief review of anion receptors based on (thia)calix[4]arene scaffold is reviewed below.

Xu et al. reported a F- ion selective calix[4]arene based fluorogenic receptor which binds through NH groups of napthalimide moiety. Liu et al. have appended various anion sensing moieties with chromogenic and fluorogenic reporters to calix[4]arene-1,3-diamide derivatives with a chiral amino acids in some cases providing chiral recognition features. One such derivative shows chromogenic sensing towards enantiomers of α-phenylglycinate anion and is found to form a 1:1 hydrogen bonded complex with a chiral discrimination of both the enantiomers.

Quinlan et al. reported calix[4]arene derivatives possessing amido-urea and p-nitrophenyl group for chromogenic recognition of anions such as
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pyrophosphate and fluoride. Chawla et al.\textsuperscript{191} reported 2,4-dinitrophenylsemicarbazone derivative 230 of calix[4]arene for chromogenic recognition of fluoride ions.

Kim et al.\textsuperscript{192} synthesized various calix[4]arene based derivatives containing pyrene moieties 231-233 for colorimetric and fluorometric sensing of anions. The binding site of 231 and 232 for anions could be differentiated based on the acidity of the compounds and the H-bonding patterns. The fluoride anion bound to the amide groups (-NHs) of 231 and to the hydroxyl protons (-OHs) of 232. The addition of F\(^{-}\) to the solution of 231 changes the characteristic excimer emission peak at 480 nm and forms a new emission peak at 460 nm (static excimer). Contrary to 231, the addition of F\(^{-}\) to the solution of 232 changes the characteristic absorption spectrum. On the other hand, the addition of F\(^{-}\) to the solution of 233 causes a red shift of its absorption band to 400 nm (\(\Delta\lambda = 54\) nm) and a blue shift of the excimer emission to 470 nm (\(\Delta\lambda = 12\) nm) together with enhanced fluorescence intensity. The blue-shifted excimer emission is attributed to a static excimer formed in the ground state between two pyrene units.

Lang et al.\textsuperscript{193} reported a chromogenic receptor 234 based on calix[4]arene possessing ureido moieties for detection of spherical and non-spherical anions such as NO\(_3^-\) and BzO\(^-\). The stoichiometry of complexation depends on the substitution pattern (distal vs proximal) and anion concentration. While the distally substituted receptor forms 1:1 complexes with anions, the corresponding proximal derivative prefers the 2:1 stoichiometry (calixarene:anion) under identical conditions. Miao et al.\textsuperscript{194} reported a bridged fluorescent calix[4]arene 235 with 1,8-diaminoanthracene and glycine at the wider rim. The compound 235 showed good selectivity for recognition for AcO\(^-\) over other anions via a PET process due to the formation of hydrogen bonds between CONH, 9-H (of anthracene) and anions.
Schazmann et al.\textsuperscript{195} reported a pyrene-appended tetra-substituted compound 236 based on calix[4]arene of 1,3-\textit{alternate} conformation bearing neutral two-site urea functional groups for chloride recognition. The addition of chloride to receptor 236 leads to ratiometric response with quenching of excimer emission and simultaneous increase in the monomer emission. The receptor 236 has suitability and advantages of ratiometric optical response for chloride ions even in the aqueous media. Chawla et al.\textsuperscript{196} synthesized many neutral calix[4]arene receptors 237a-d (Table 5) with hydrazone functions at their narrow rim which exhibit a prominent ‘naked-eye’ colour change with significant bathochromic shifts when interacted with fluoride ions. Among these receptors, 237b exhibits a selective binding with fluoride ions via H-bond interactions in preference to other ions and elicits a distinct colour change from yellow to dark purple through efficient deprotonation.

Zlatuskova et al.\textsuperscript{197} reported the first example of anion receptors 238a-b in the thiacalixarene series possessing mixed amido-urea/thiourea functionalities which exhibited a competitive anion/ cation complexation of Cl\textsuperscript{−} and K\textsuperscript{+} ions. Further, they reported\textsuperscript{198} regioselective ipso-nitration of \textit{tert}-butylthiacalix[4]arene-tetrasulfone for the construction of thiacalix[4]arene derivatives 239 and 240a-c bearing arylureido functions on the wider rim of \textit{cone} and 1,3-\textit{alternate} conformation. The pre-organization of ureido units leads to anion receptors with good complexation ability toward selected anions of various geometries. The thiacalix[4]arene derivative showed better complexation ability compared to calix[4]arene for these anions even in highly polar solvent, such as DMSO.
1.6.4 Development of molecular switches and logic devices

Another significant application of supramolecular chemistry is its use in molecular computing\(^{199}\) based on chemical reactions performed either in solution or at functionalised interfaces. Currently used computers and other electronic digital devices are based on monolithic semiconductor structures fabricated on the surface of silicon wafers.\(^{200}\) All these devices use binary logic for information transmission, processing, and storage, and utilize electric signals as information carriers. All the information is encoded in series of zeros and ones, represented as low and high potential values. Various logic gates such as OR, AND, XOR, INH, NOR, NAND and XNOR gates\(^{201}\) (Table 6 & 7) are the basic elements for processing information whose output (0 or 1) depends on input conditions. The data introduced into a computer are elaborated through a sequential integration of logic operations and converted into a specific output. The dimensions of these communicating components of logic circuits continue to be reduced to miniaturization which permits the assembly of integrated circuits and faster processors.\(^{202}\) The conventional silicon based devices have limitation of their miniaturization down to the nanoscale.\(^{202}\) Therefore, the development of materials for information storage and retrieval at the molecular level is promising choice for this limitation.\(^{203}\) The idea of computation at the molecular level was first mentioned by Richard Feynman in 1959.\(^{204}\) Vincenzo Balzani was the first to report the molecular machines based on molecular recognition and self-assembly in 1992.\(^{205}\) After one year, the first molecular logic gate was reported by A. Prasanna de Silva based on molecular recognition of target molecules using fluorescent probes and introduced Binary information processing in the chemical
system. The molecular logic gates and other devices were controlled exclusively by chemical inputs, while the output was observed as changes in fluorescence and absorption spectra. Thereafter, the scientists have developed keen interest in molecular computing which is an attractive research subarea of unconventional computing, involving integration of molecular information processes using various Boolean logic operations (OR, AND, XOR, INH, NOR, NAND and XNOR gates) at the molecular level. The molecular information processes are related to the integration and processing of binary data of microprocessor systems. The optical sensing of specific analyte and its integration into molecular level devices such as logic gates and molecular switches have stimulated interest in the development of molecular electronic and photonic devices for information processing, sensing and computation.

**Table 6. Truth table 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 7. Truth table for two inputs 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>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
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<td>0</td>
<td>1</td>
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<td>1</td>
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<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 first molecular logic gate formulated was AND logic gate by de Silva et al. based on receptor comprised of cyanoanthryl fluorophore, azacrown cation receptor, and the tertiary amino group (proton acceptor). The binding of sodium ions within the azacrown does not influence the luminescence of the compound as PET
from amine can efficiently quench the fluorescence. Only simultaneous binding of sodium ions and protons prohibits PET and switches the fluorescence on. The receptor 242 showed same behaviour of independent binding of protons and alkali metal cation which results in operation of AND gate. This is the first reported computational chemical system confined to the nanometer scale objects.\textsuperscript{209}

The pyrene based receptor 243 containing nitroxide group conjugated on imidazole ring showed 100-fold increase of fluorescence intensity with the addition of trifluoroacetic acid and cysteine which result in the formulation of AND gate.\textsuperscript{210} The receptor 244\textsuperscript{211} containing three carboxylate groups bind to magnesium and calcium ions. This non-selectivity constitutes the basis of OR operation based on the PET phenomenon. The binding with metal ions results in rearrangement of electronic structure of compound 244 and fluorescence of the receptor gets switched on. The receptor 245 also undergoes cation-induced rearrangement upon binding of sodium ions which bound to the polyether chains, while Hg\textsuperscript{2+} binds to the bipyridine unit. Irrespective of the cation, the molecule undergoes the same guest-enforced rearrangement, which greatly reduces the distance between two anthryl units and allows photoinduced dimerization.\textsuperscript{212} The ditopic binding leads to formulation of OR gate.

The compounds 246 and 247 show pH-controlled PET processes which form the basis of XOR gates.\textsuperscript{213} The XOR gate requires a chemical system that responds to two different stimuli in such a way that one of these two stimuli should switch on the
gate, while concomitant presence of both triggering molecules should leave the system in the OFF state. First protonation of compounds 246 and 247, which occurs at more basic aliphatic amine group, switches the fluorescence on due to inhibition of the PET process, while the second protonation at pyridine moiety switches the fluorescence off by enabling the second PET process involving the pyridinium cation.

A ditopic receptor 248 based on isoquinoline N-oxide with an attached benzo-15-crown-5 receptor perform the operation of INHIBIT gate (INH) which is a concatenation of AND and NOT gates.\textsuperscript{214} Molecules based on this framework show dual fluorescence from locally excited and charge transfer states involving the benzocrown moiety. Charge-transfer fluorescence is observed only in the case of the protonated N-oxide moiety. Binding of cations by crown ether results in a decrease of HOMO energy of the donor, and CT fluorescence is not observed.

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

de Sousa \textit{et al.}\textsuperscript{215} reported 1,8-naphthalimide derivative 249 which shows very weak fluorescence because of efficient PET quenching. The interaction of compound 249 with Eu\textsuperscript{3+} ions results in stronger luminescence of the naphthalimide due to inhibition of PET. However, in the presence of oxygen, no red europium luminescence was observed. Therefore, compound 249 regarded as chemically driven INH gate with Eu\textsuperscript{3+} and O\textsubscript{2} inputs and red luminescence as output. The receptor 250 and 251 perform NOR logic operations using protonation and complexesation with Hg\textsuperscript{2+} and Zn\textsuperscript{2+}, respectively.\textsuperscript{216}

Zong \textit{et al.}\textsuperscript{217} used supramolecular interactions of compound 252 as the basis for NAND gate. In the presence of ATP and H\textsuperscript{+} ions, intermolecular interactions of 252 become much stronger (\pi-\pi stacking + electrostatic interaction + hydrogen bonding), which result in significant quenching of the fluorescence due to PET from the adenosyl moiety. Margulies \textit{et al.}\textsuperscript{218} reported first complex molecular arithmetic system 253 based on fluorescent indicator fluorescein, integrating full adder and full subtractor within the same molecular system. They have used acids and bases as input
signals, while changes in absorbance, transmittance, and fluorescence are used as outputs. Protonation and deprotonation of fluorescein changes its absorption spectrum. The neutral form of fluorescein shows only weak absorption at both analytical wavelengths. In order to achieve full adder based on fluorescein, the transmittance at 447 nm is assigned to the sum output, while absorbance at 474 nm as carry output.

The calix[4]arene based fluorescent probe 254 was activated by protons to detect cesium in an acidic environment and potassium ions in an alkaline environment. Furthermore, the fluorescence behaviour of 254 mimics the functions of a logic gate. The fluorescent chemosensor 255 based on calixarene possessing imine linkage can effectively recognize Cu^{2+} ions. The off–on–off fluorescent switching is realized by the irradiation of compound 255 with ultraviolet and visible light. Based on off–on–off switching, the corresponding INHIBIT (INH) logic gate was constructed using ultraviolet and visible light.

Yuan et al.\textsuperscript{221} reported a fluorescent probe 256 possessing both BODIPY and Rhodamine moieties in which chemical inputs of Hg^{2+} and Ba^{2+} ions have been used to construct a combinational logic circuit using INHIBIT and YES logic operations at the molecular level. Lee et al.\textsuperscript{222} reported a fluorogenic calix[4]arene-18-crown-6 derivative 257 whose fluorescence is quenched in the presence of Pb^{2+} ions, acid or base. The combination of three inputs formulate logic functions such as NOR and XNOR. The NOR logic gate operates at 395 nm in which the strong fluorescence signal appears, only when neither of triethylamine nor Pb(ClO\textsubscript{4})\textsubscript{2} is added. Further, XNOR gate operates only when both the inputs are added (triethylamine and HClO\textsubscript{4})
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or when neither of the two inputs is added. A new INHIBIT gate system was designed using these combinational inputs (HClO₄, Pb(ClO₄)₂ and triethylamine).

Joseph et al. reported a calix[4]arene derivatives 258 and 259 bearing four pyridyl moieties and hydroxymethyl salicylyl imine, respectively. An INHIBIT (INH) logic gate has been generated by choosing Ag⁺ and Cys as input and by monitoring the output signal at 445 nm that originates from the excimer emission of 258 in the presence of Ag⁺. On the other hand, compound 259 mimics the behaviour of an INHIBIT logic gate in the presence of Zn²⁺ and HPO₄²⁻ ions.

Shiraishi et al. reported two output channel based on design 260 containing two anthryl fluorophores linked with the diethylenetriamine chain. The interaction of compound 260 with different transition metal in the presence of varying pH results in formulation of various logic gates through dual channel emission. The fluorescent sensor 261 responds to several heavy metals such as Zn²⁺ (In1), Cd²⁺ (In2), and Pb²⁺ (In3) with high intensity fluorescence (output). This strong fluorescence is observed only in the absence of strong acids (In4). The integration of these four inputs results in complex logic device containing one three-input OR, two input AND, and NOT gates.

Zhou et al. reported pyridine based chemosensor 262 possessing two pyrene units. The application of three inputs of trifluoroacetic acid (In1), Zn²⁺ (In2), and TETA (In3) results complex logic device through two output channels (excimer; out1) and (monomer; out 2).

Another simple molecular design 263 also acquires acid and base as inputs, and the outputs are both in fluorescence channels at different wavelengths. The luminescence of the BDPY central unit of compound 263 is controlled by two
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processes: PET from the phenol moiety and ICT involving the dimethylaniline moiety. Deprotonation of the phenol moiety results in complete quenching of the fluorescence. However, protonation of the amino group results in a strong hypsochromic shift (from 660 to 565 nm). Emission at 565 nm due to protonation of amino group regarded as an output of the INH gate, while emission at 660 nm corresponds to XNOR function. Application of positive logic to the INH output and negative logic to the XNOR output results in binary half-subtractor.

Liu et al.\textsuperscript{229} reported molecular device 264 operated with acid and base inputs and integrates three devices within one molecule: half-adder, half-subtractor, and comparator. Furthermore, due to the presence of four spectrally different forms (anion, neutral, cation dication) of compound 264, it is possible to implement binary full adder and full subtractor within this molecule. This device is the only known example of a molecular binary comparator. Andreasson et al.\textsuperscript{230} reported a molecule device 265 which acts as both an AND and an XOR Boolean logic gate that share the same two photonic inputs and comprises a half-adder, adding two binary digits with only light as inputs and outputs. The AND function is based on the absorption properties of the molecule, whereas the XOR function is based on an off-on-off response of the fluorescence to the inputs that results from inter chromophore excited-state quenching interactions.

Magri et al.\textsuperscript{231} reported fluorescent chemosensor 266 which illustrate the AND gate in response to the three electrolyte inputs Na\textsuperscript{+}, H\textsuperscript{+}, and Zn\textsuperscript{2+} in water with an enhanced fluorescence signal. The compound 266 is a “lab-on-a-molecule” prototype since a clinically relevant result would emerge from on-board information processing of several sensory channels simultaneously in targeted cases.

The three-state molecular switch 267 based on spiropyran derivative was synthesized by Raymo et al.\textsuperscript{232} The light and chemical stimulations induce the switching of spiropyran derivative (SP) to the merocyanine forms ME and MEH.
This molecular system transduces the light and chemical inputs into optical outputs through a complex sequence of logic operations. Further, Raymo et al.\textsuperscript{233} used SP, ME and MEH forms of spiropyran derivative \textsuperscript{267} to develop ultraminiaturized processors which communicate intermolecular signals to a fluorescent probe at the molecular level. The intermolecular communication is responsible for the transduction of three input signals into a single optical output. The behaviour of these communicating ensembles of molecules corresponds to that of a logic circuit incorporating seven gates. The molecular switching of SP, ME and MEH forms of spiropyran derivative \textsuperscript{267} were further used to gate optical signals in response to optical signals\textsuperscript{234} in which data are communicated optically but processed electronically.

The covalent immobilization of compound \textsuperscript{268} on silicon nanowires (SiNWs) was used to formulate the YES and INH logic operations with three chemical inputs (pH, Hg\textsuperscript{2+} and Cl\textsuperscript{-} or Br\textsuperscript{-} ions).\textsuperscript{235} The SiNW-based fluorescent logic gate is compatible with silicon-based semiconductor technology, thus providing a good approach to build various logic gates to integrate more logic operations.

Applying the principles of molecular Boolean logic, Margulies et al.\textsuperscript{236} used a molecular system \textsuperscript{269} based on fluorescein conjugated with pyrene to develop a reconfigurable molecular keypad lock that “opens” by inserting the right sequences of three keys: EDTA (E), base (B), and UV light (U). Only keys E, B, and U hold the correct inputs and can initiate a strong fluorescence at 525 nm that activates the green channel, whereas keys E and U are enough for generating high emission at 390 nm that triggers the blue channel. The other keys can hold a high concentration of fluorescence quenchers, so if pressed, the password entry will fail. Suresh et al.\textsuperscript{237} synthesized a chemosensor \textsuperscript{270} which can detect Hg\textsuperscript{2+} in water and Hg\textsuperscript{2+}/Cu\textsuperscript{2+} in
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acetonitrile. The compound 270 was mimicked as a molecular keypad lock using particular sequence of Cu$^{2+}$ and F$^{-}$ as ionic inputs with strong fluorescence at 422 nm.

Another molecular device “molecular automaton” was developed by Ozlem et al.\textsuperscript{238} The compound 271 works as a photodynamic therapy agent which release singlet oxygen at a much larger rate when two cancer related cellular parameters (Na$^{+}$ and H$^{+}$) are above a threshold value within the same spatiotemporal coordinates. The proposed logic gate would be actually an AND logic gate, the output would be singlet oxygen. The molecular system 271 is an automaton which seek higher concentration of both hydrogen and sodium ions for the release the cytotoxic agent (singlet oxygen).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{molecular_device.png}
\caption{Molecular devices used in the study.}
\end{figure}

Li et al.\textsuperscript{239} reported the fabrication a small organic molecule 272 based device that has unexpected ternary memory device with I-V performance under a constant reading voltage. This prototype device consumes less power and is easier to scale than traditional devices. The molecule exhibits promising ternary behaviour under an electric field, increasing the data-storage capacity of the device from $2n$ to $3n$. This device exhibits typical write once read-many-times (WORM) behaviour. The results are promising for the development of an ideal ternary memory system and will open the door to the development of next-generation HDDS devices.

Thus, from the above review of literature, it is clear that thiacalix[4]arene scaffold is a unique host with vast possibilities of functionalization not only at the wider and narrow rim but also at the bridging sulfide groups. The following conclusion can be drawn from the above review of literature:
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3. The modifications at the sulfide groups make its chemistry interesting in aqueous medium.
4. Thiacalix[4]arenes can be functionalized with different functional moieties like amines, imines, crown ethers, amides, ureas/thioureas, etc. for binding of different types of analytes (cations, anion and neutral molecules).

Thus, keeping in view of these observations, in the present investigation we have designed and synthesized various thiacalix[4]arene derivatives possessing amides, sulphonamides and (thio)ureas moieties. The results of our findings have been discussed in following three chapters.

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