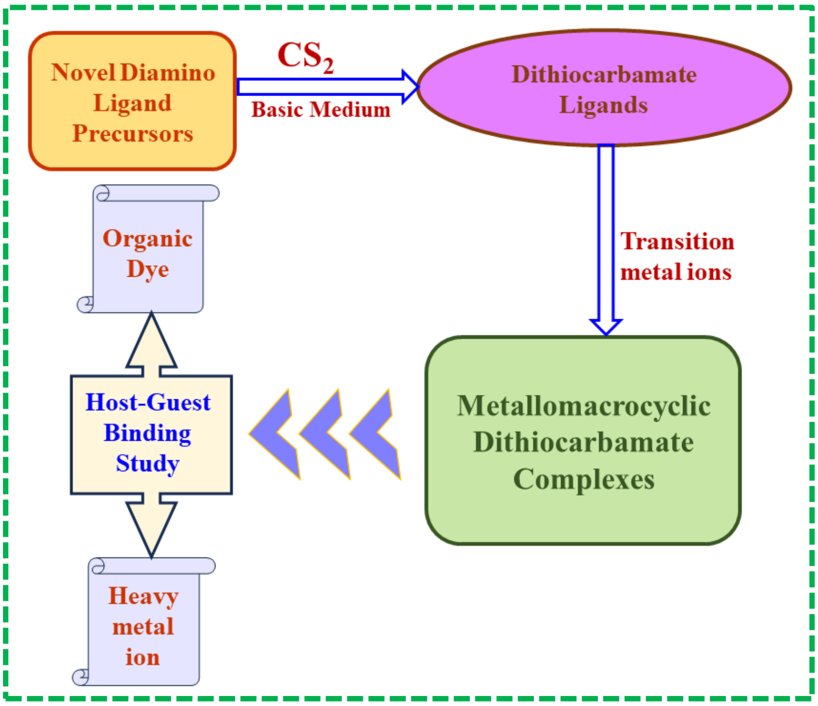
Introduction: Exploring Novel Metallomacrocyclic Dithiocarbamate Complexes: Applications and Insights into Host-Guest Binding Studies

Abstract



An overview of self-assembly, its wide array of applications in numerous aspects of material chemistry and specifically in host-guest binding Study along with the importance of the development of metal-directed self-assembled molecular architectures has been contained in this chapter. The exceptional stereoelectronic features of metal ions and Dithiocarbamate ligands in metal-directed self-assembly direct to the formation of distinct supramolecular frameworks with interesting physicochemical properties and their application in medicinal chemistry has also been highlighted in this section. The emphasized has been made on the coordination-driven self-assembly that has emerged as a dynamic research domain in chemistry during contemporary era. New strategies in ligand modifications and judicious selection of metal ions presenting opportunities for significant adjustments in the structural and electronic properties of the resulting self-assembled structures are also highlighted. The specific objectives of the present work are also mentioned at the end of this chapter.

1.1 Self-Assembly

One of the most effective methods available today for creating a wide variety of supramolecular architectures with cavities is coordination-driven self-assembly involving transition metal and organometallic building blocks with a variety of ligands.[1] These architectures can be used in various fields, including molecular and ion sensing,[2] host-guest chemistry,[3] catalysis,[4] separation, transport, and storage.[5] Systems that allow for the easy tuning of the structural and electrical characteristics of their cavities are needed to optimise and modify an aggregate's qualities to meet the requirements of the appropriate application. This can be accomplished in metallosupramolecular assemblies by changing the properties of the metal and the ligands.

However, owing to the labile nature of coordinative bonds, numerous systems formed through such interactions exhibit a dynamic nature, often linked to intra- or intermolecular rearrangements. Typically, these occurrences manifest in response to external stimuli like variations in temperature, concentration, pH levels, solvent properties, and, in specific instances, the presence of a guest.[6] Understanding the alterations induced by external disturbances offers insights into facets of self-assembly that can be utilized for the design and development of self-regulating materials, with potential applications in areas such as drug delivery, two-phase transport, biosensing, or systems chemistry.[7]

In a broader context, self-assembly occurs in biological systems and nature, from base pairing and protein folding to Rayleigh–Bernard convection and atmospheric storms.[8] The process from disorder to order, along with the variety and complexity of the functions produced from biological self-assembly, has promoted the design of non-living systems,[9] thus a series of artificial molecular aggregates with inspiring properties (such as micelles,[10] vesicles,[11] films,[12] fibres,[13] etc.) have been developed by the self-assembly of building blocks.

Literature evidences the existence of various noncovalent interactions such as hydrogen bonding, π–π stacking,[14] van der Waals interactions,[15] electrostatic interactions,[16] hydrophobic effects,[17] and host–guest interactions,[18] and dynamic covalent bonds [19] during the process of self-assembly. Using "bottom-up" methods, precisely modified precursor molecules form into required ensembles with specific physicochemical features.[20] Furthermore, the dynamics and reversibility of supramolecular architectures have led to new developments of several functional materials with fascinating stimuli response behaviours, for example, self-healing,[21] self-adjustment,[22] adaptivity,[23] shape memory,[24] and mechanochromic properties.[25] (Figure 1)

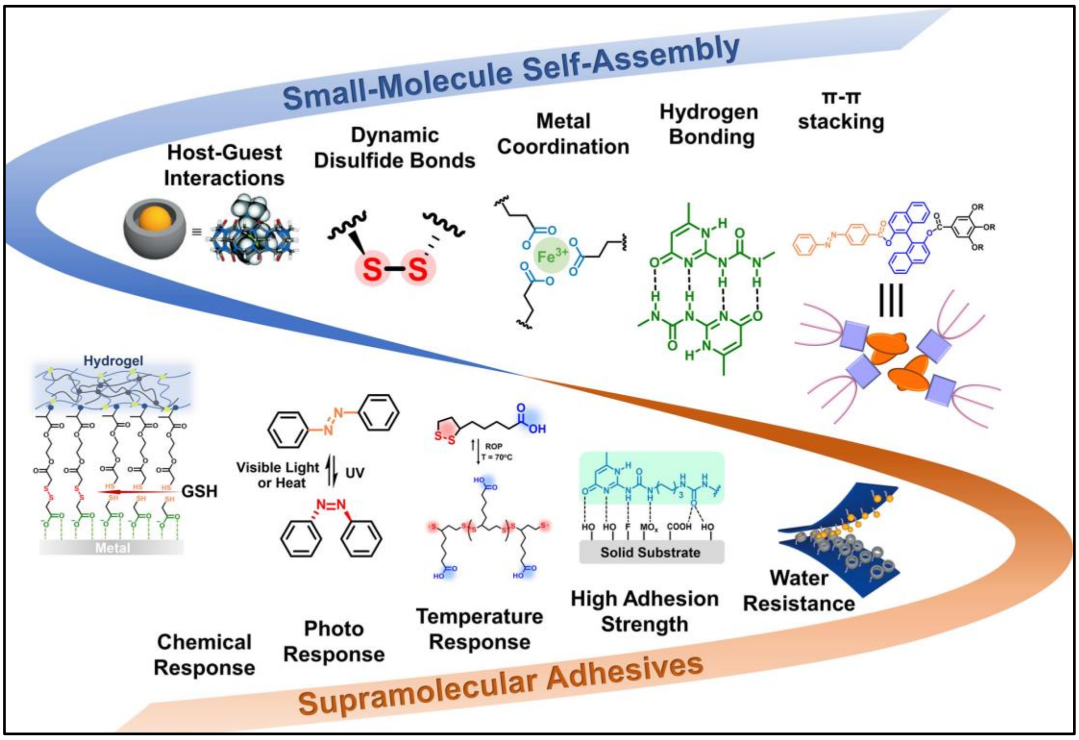


Figure 1. The schematic content of small-molecule supramolecular adhesive materials. (i) Small-molecule self-assembly through diverse supramolecular interactions. (ii) Versatile adhesion properties.

In recent times, Ignacio Insua et al[26] conducted a groundbreaking study on the first cyclic peptide with the unique ability to undergo sequential 1D-to-2D self-assembly in an aqueous medium, resulting in the formation of dynamic and expansive two-dimensional supramolecular structures on the mesoscale. The primary amino acid sequence of this cyclic peptide encodes all the essential chemical information necessary for the adoption of the secondary folded β-sheet motif. This motif, in turn, facilitates the formation of nanotubes, which were subsequently organized into crystalline yet dynamic two-dimensional nanosheets. The ultra-thin supramolecular assemblies described herein represent one of the most extensive fully organic two-dimensional structures ever synthesized in a solution, as illustrated in Figure 2.

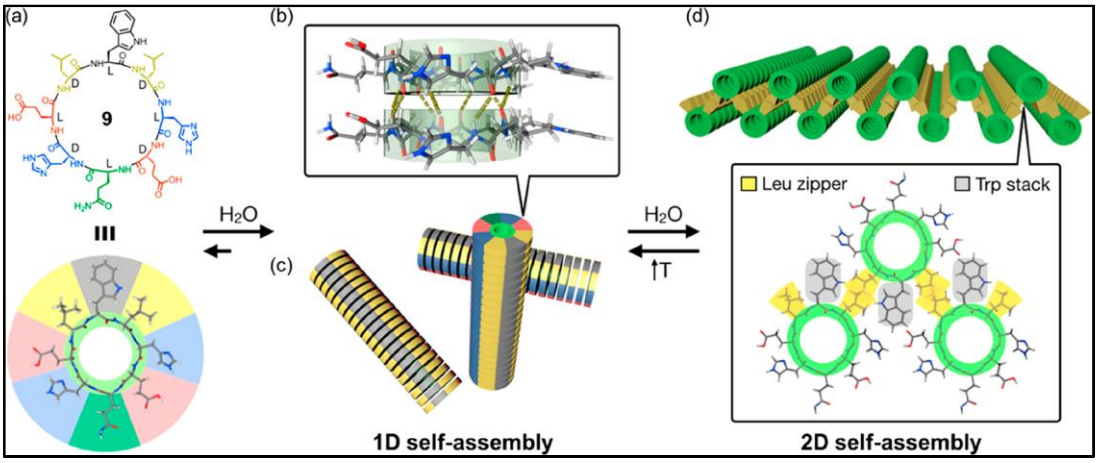
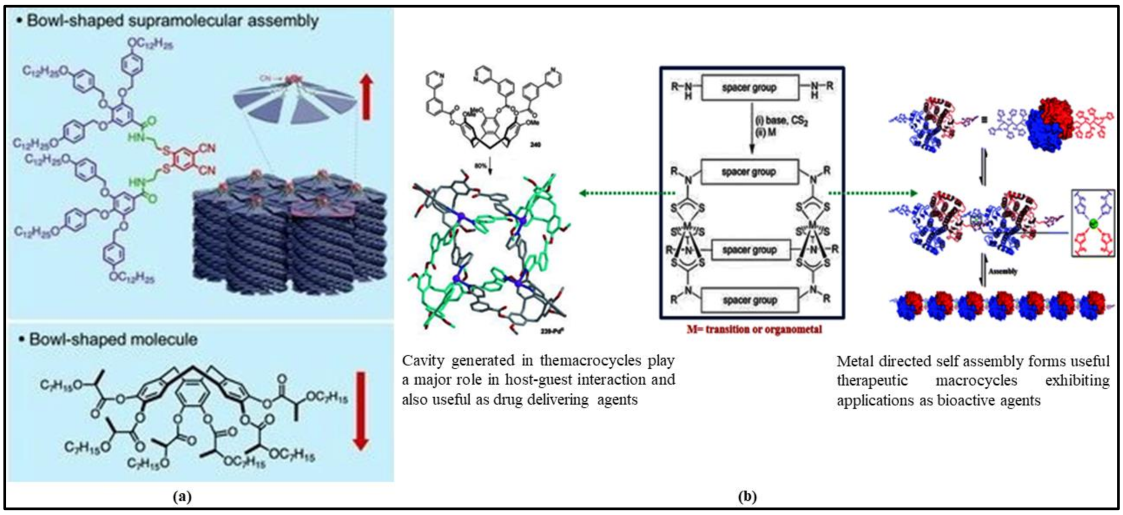


Figure 2. (a) Cyclic Peptide Structure (b) Amphiphilic Nanotube Formation (c) 2D Nanosheet Assembly (d) 2D self-assembly of Nanosheets with Bilayered Nanotubes

It is emphasized that the coordination-driven self-assembly has emerged as a dynamic research domain in chemistry during contemporary era.[27-36] In this connection, the novel strategies in ligand modifications and judicious selection of metal ions[37] present opportunities for significant adjustments in the structural and electronic properties of the resulting self-assembled structures, as depicted in Figure 3. As previously discussed, the application of metal-directed self-assembly principles leads to diverse supramolecular architectures, including 1D and 2D organic/inorganic hybrid frameworks such as molecular bowls, rods, filaments, racks, ladders, brick walls, cylinders, boxes, square grids, honeycombs, diamondoids, and helices.



Cavity generated in themacrocycles play a major role in host-guest interaction and also useful as drug delivering agents

Metal directed self assembly forms useful therapeutic macrocycles exhibiting applications as bioactive agents

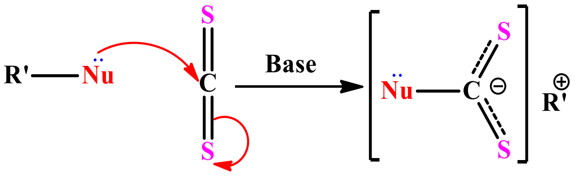
Figure 3. (a) Construction of diverse molecular architecture using Coordination chemistry **(b)** Application of metal directed self-assemblies in various fields of material and medicinal chemistry

Coordination chemistry so perfectly reveals unique structures with intriguing physicochemical features.[38-39] With the help of metal-directed self-assembly, metal ions with a variety of binding strengths, coordination geometries, and redox behaviors can be carefully chosen, all of which are essential for the assembly of self-assembly. Because metal-directed self-assembly only requires a few fundamental subunits to be assembled in a few stages of the synthetic process, it has several advantages over traditional approaches used to manufacture molecular supramolecular frameworks.[40-43] Ligands of the type, N, O-schiff base, azide, carboxylate, etc. are very well explored in the metal-directed self-assembly process, however, there are limited reports on such assembly process invading 1,1-dithio ligands.

1.2 1,1-Dithio Ligands

The category of monoanionic 1,1-dithiolate ligands encompasses dithiocarbamate ($R_2NCS_2^-$ or $RNHCS_2^-$), xanthate ($ROCS_2^-$), carbamate ($R_2NCO_2^-$), dithiophosphate ($R_2PCS_2^-$), illustrated below. These ligands are frequently employed in the synthesis of high-value coordination compounds, contributing to advancements in the field.[44]

Additionally, owing to the fascinating stereoelectronic features of 1,1-dithio ligands, particularly their robust binding capability and diverse binding modes with various transition/non-transition metal ions in different oxidation states, this ligand class holds great promise for developing novel coordination-driven self-assembled molecular architectures.[45] Transition metal dithiocarbamate and xanthate complexes, in particular, have garnered significant attention due to their diverse applications in biology, agriculture, and industry.[46] Thus, this class of ligands has become a crucial factor in the design of diverse self-assembled novel supramolecular structures. A plethora of 1,1-dithio ligands is efficiently synthesized through the general reaction of carbon disulfide with various nucleophiles under diverse experimental conditions (Scheme 1).



Scheme 1. General synthetic strategy for 1,1-dithio ligands.

1.2.1 Dithiocarbamate

Dithiocarbamates ($R_2NCS_2^-$ or $RNHCS_2^-$) represent a specific instance within a broader category of monoanionic 1,1-dithiolate ligands. This general class encompasses other frequently employed ligands, including xanthates, carbamates, dithiophosphates (Figure 4), and numerous others.[47]

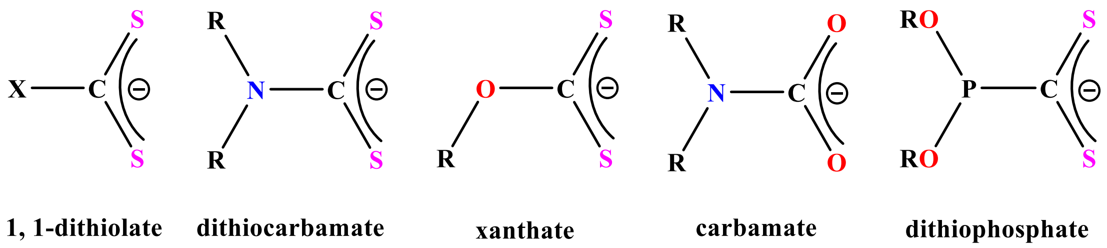


Figure 4. A diverse category of 1,1-dithiolates achieved through variations in heteroatoms.

The origin of dithiocarbamate chemistry can be traced back to the early twentieth century, with its formal inception in 1930.[48-49] Its commercial utilization began during World War II, where it was employed as a fungicide for the first time.[50] The extensive applications of dithiocarbamates span various fields, including accelerating vulcanization,[51] serving as flotation agents, playing a role in agriculture as fungicides,[52] pesticides,[53] contributing to biology,[54] materials science, medicine,[55] organic synthesis,[56] antioxidants[57] and performing functions such as photo-stabilizing polymers[58] and protecting radiators.[59-61] In the dominion of metal 1,1-dithiolate chemistry, considerable attention has been devoted to the exploration of dithiocarbamate complexes. This interest stems from their extensive structural diversity and their significance in a wide range of fields, including materials and analytical chemistry. Dithiocarbamate complexes serve as molecular precursors for the fabrication of thin film metal sulfides and find applications in industries such as rubber, agriculture, medicine, and biological processes.[62-65]

The synthesis of dithiocarbamates is typically straightforward and commonly entails a one-pot reaction where an amine reacts with carbon disulfide in the presence of a base. Alkali metal hydroxides, such as sodium hydroxide and potassium hydroxide, are frequently employed as bases, although tetraalkylammonium salts can also serve this purpose.[66]

In the realm of coordination chemistry, the employment of dithiocarbamate(DTC) ligands offers a convenient approach to stabilizing transition-metal and main-group elements, capitalizing on the chelate effect. Consequently, DTC ligands derived from secondary aliphatic amines exhibit a higher capacity to form stable metal complexes compared to those derived from primary aliphatic or aromatic amines. The distinctive presence of two sulfur atoms within a DTC group imparts an exceptional characteristic to these materials, enabling the stabilization of a broad spectrum of metal ions. Given their significant complexation ability, DTCs are recognized as bidentate ligands, and their efficient formation of complexes with various metals has been extensively documented, showcasing both high yields and diverse complex structures, some of the binding modes are shown below.

1.2.1.1 Binding Modes

Dithiocarbamates exhibit the ability to bind to metal centres in at least nine different coordination modes, although this discussion will focus on five of them (Figure 5), as the others are rare and lack apparent biological relevance.

Predominantly, dithiocarbamates function as chelate ligands (Figure 5 (binding mode a)) by forming two approximately equivalent metal-sulfur bonds. This chelation results in the formation of a small bite-angle (S-M-S), ranging from 65 to 80° and depending on the size of the metal ion in the ligand. In simple homoleptic complexes, $[M(S_2CNR_2)_n]$, the metal-sulfur bond lengths also vary with the size of the metal ion, falling within the range of 2.20 to 2.55 Å.[67] The adoption of the chelate binding mode is thermodynamically favoured due to the entropic gain, known as the chelate effect.

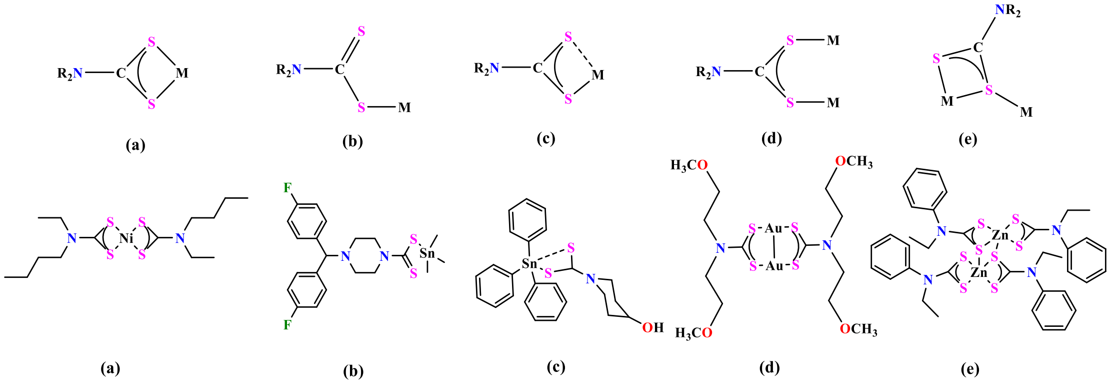


Figure 5. Five different coordination modes of dithiocarbamates

Masnovi et al. reported the synthesis of homoleptic mixed-organic bis-dithiocarbamates, specifically $[Ni(S_2CN(ethyl)(n\text{-}butyl))]_2$ and $[Ni(S_2CN(phenyl)\text{-}(benzyl))]_2$. According to structural analyses, both complexes exhibit a slightly distorted square planar coordination environment, illustrated in Figure 5 (binding mode a). N. Singh *et. al.* reported the one-pot synthesis of bimetallic complexes with the formula $M[UO_2(DED)_2]$ [M = Co(II), Ni(II), Cu(I1). Zn(II), Pd(I1). Pb(I1) or 2Tl(I); DED = l,l-dicarboethoxy-2,2-ethylenedithiolate dianion] have been prepared by the reaction of $K_2[UO_2(DED)_2]$ and the corresponding metal salts. $K_2[UO_2(DED)_2]$ prepared in situ and used in the synthesis of the above bimetallic complexes was precipitated as $(Bu_4N)_2[UO_2(DED)_2]$ for the first time. [47] In this arrangement, the nickel ion is situated at the centre, coordinated with two dithiocarbamate ligands positioned on opposite sides of the metal. The Ni–S bond lengths in these complexes ranged from 2.2020 to 2.2084 Å.[68] The monodentate coordination mode Figure 5 (binding mode b) is another relatively common arrangement, typically adopted when the steric and electronic demands of other metal-bound ligands make second sulfur coordination impractical, or when the loss of a ligand prerequisite for such coordination faces a high activation barrier.[48] In the context of a specific example,[69] the tin atom is four-coordinated, chelated by three methyl groups, and one sulfur atom of the dithiocarbamate ligand. In this case, the dithiocarbamate ligand coordinates the tin center in the monodentate coordination mode. (Figure 5 (binding mode b))

As discussed, earlier metal primarily forms a monodentate bond with a dithiocarbamate ligand. Various known organotin compounds, featuring one or more dithiocarbamates, highlight the infrequency of symmetrical binding of these ligands to tin. In the present case, Sn1-S1 forms a conventional covalent bond with a distance of 2.4757(7) Å, while the Sn1-S2 distance is notably long (3.0336(7) Å).[70] However, the latter is significantly smaller than the total van der Waals radius of the two atoms (3.97 Å), suggesting the potential existence of a weak bonding interaction between them. The Sn-C bonds exhibit a range between 2.120 and 2.166 Å, falling well within the typically observed Sn-C distances in organotin compounds.[71] (Figure 5 (binding mode c))

When discussing an alternative binding mode of dithiocarbamate, a notable example is found in $[Au_2\{S_2CN(C_2H_4OMe)_2\}_2]$. The supramolecular array is characterized by an almost linear, polymeric backbone of gold atoms, featuring alternate gold–gold contacts of 2.7902(6) Å (intramolecular) and 3.1572(7) Å (intermolecular). The crystal structure of gold complex reveals two gold(I) atoms forming a slightly puckered eight-membered ring composed of two gold, four sulfur, and two carbon atoms which is shown in Figure 5 (binding mode d). Each gold atom coordinates with two sulfur atoms [Au(1)]S(2) 2.289(2), [Au(1)]S(4) 2.292(2), [Au(2)]S(3) 2.296(2), [Au(2)]S(1) 2.300(2) Å], one from each bridging ligand, achieving almost linear coordination with [S(2)]Au(1)]S(4) 174.58(9)8 and [S(1)]Au(2)]S(3) 173.58(9)8.[72] In addition to a short intramolecular gold–gold separation of 2.7902(6) Å, molecules are linked by longer intermolecular gold–gold interactions [3.1572(7) Å], generating a supramolecular array dominated by a polymeric backbone of gold atoms (Figure 6).[73] Similar structural features have been observed in $[Au_2(S_2CNPr_2)_2]$ and $[Au_2(S_2CNBu_2)_2]$, although the latter exhibits a much longer gold–gold intermolecular interaction of 3.40 Å in the former complex.[74]

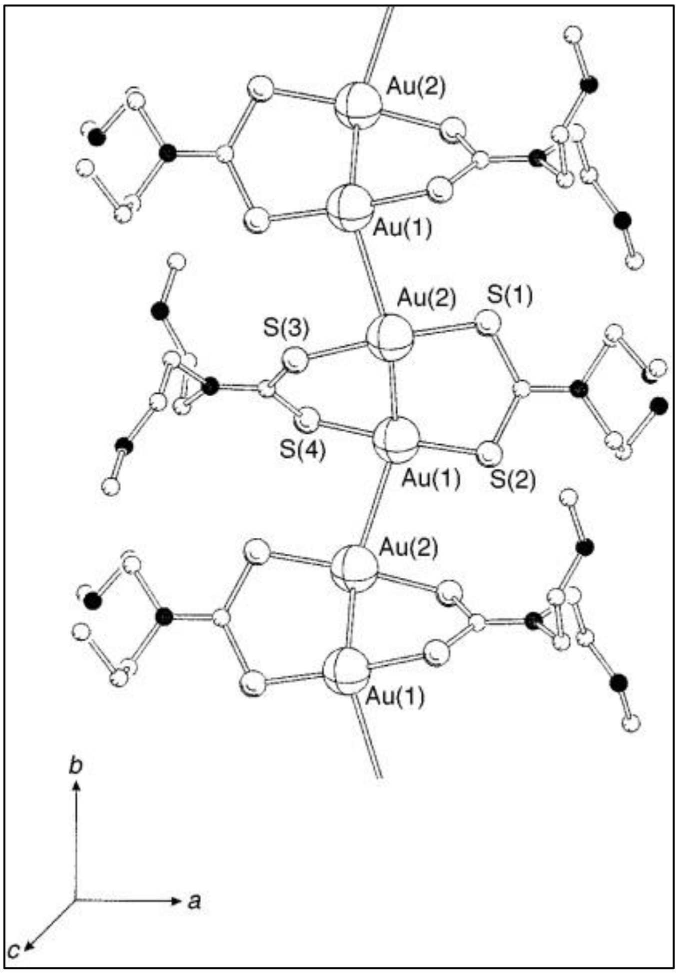


Figure 6. The crystal packing diagram of compound [$Au_2(S_2CNPr_2)_2$], observed along the c-axis of the unit cell, illustrates the polymeric backbone of gold atoms aligned in the direction of the b-axis.

The final coordination mode is infrequent and lacks known biological relevance. The structure of Zn(II) bis(N-alkyl-N-phenyldithiocarbamate) exhibits a distinctive geometry, featuring a bridging bond between Zn and an adjacent S atom, forming a bridged dimeric complex as depicted in Figure 5 (binding mode e).[75] In this instance, a centrosymmetric dimeric structure surrounds the central Zn atom. The dithiocarbamates are chelated in a bidentate manner to the metal centre and non-symmetrically coordinated to the other dithiocarbamate anion.[76]

1.2.2 Application of Dithiocarbamates

Dithiocarbamates (DTCs) represent a class of small organic molecules renowned for their robust chelating capabilities towards inorganic species, finding extensive utility in the agricultural industry for over eight decades.[77] Recent years have witnessed a broadening spectrum of their applications, evolving beyond conventional roles as pesticides and fungicides.[78-79] Notably, DTCs have emerged as pivotal vulcanization accelerators within the rubber industry. Beyond their industrial significance, DTCs exhibit notable biological importance, showcasing antibacterial, antituberculosis, and antifungal properties, as illustrated in Figure 7. Their intrinsic antioxidant attributes[80] further enhance their value. Noteworthy examples include disodium ethylenebisdithiocarbamate, commercially known as Nabam, alongside its zinc and manganese complexes (Zineb and Maneb), as well as the zinc and iron complexes of dimethyldithiocarbamic acid (Ziram and Ferbam), all demonstrating considerable promise. Thiram, functioning as a fungicide, ectoparasiticide, and animal repellent, plays a vital role in preventing fungal diseases in both seeds and crops, while also safeguarding fruit trees and ornamentals from damage by rabbits, rodents, and deer.[81] Ziram, or Zinc Dimethyldithiocarbamate, serves as a carbamate fungicide,[78] applied through leaf spray to control fungal infections or as a seed treatment to enhance germination. Mancozeb,[82] a non-systemic agricultural fungicide within the DTC category, operates with multi-site, protective action upon contact. It comprises a combination of two other dithiocarbamates, namely maneb and zineb. The extensive use of this class of compounds as superior ligands is primarily attributed to the insolubility of metal salts (excluding sodium and other alkali and alkaline earth metals) and the DTCs' ability to form stable metal complexes.

Hence, Dithiocarbamates (DTCs) manifest robust binding affinities with various transition metal ions, forming stable and distinctly colored complexes. Spectroscopy serves as a predominant method for the quantitative determination of these complexes, although alternative techniques such as gravimetry, fluorimetry, titrimetry, neutron activation analysis (NAA), turbidimetry, voltammetry, and chromatography, while less prevalent, are also employed.[83] Melanoma acknowledged as the most severe form of skin cancer, poses a formidable challenge due to its resistance to chemotherapy, rendering it one of the deadliest cancer types. DTCs emerge as promising candidates for melanoma treatment, particularly the metal complexes of pDTC (pyrrolidine dithiocarbamate), which are widely explored and commonly utilized as antioxidants in cell toxicity studies. The distinctive properties of these DTC complexes open avenues for potential therapeutic applications in the context of melanoma. Complexes of dithiocarbamate ligands also have various applications in vulcanization accelerators, analysis, radiation protectors and as precursors for the preparation of metal sulfide and metal oxide nanoparticles.[84-85]

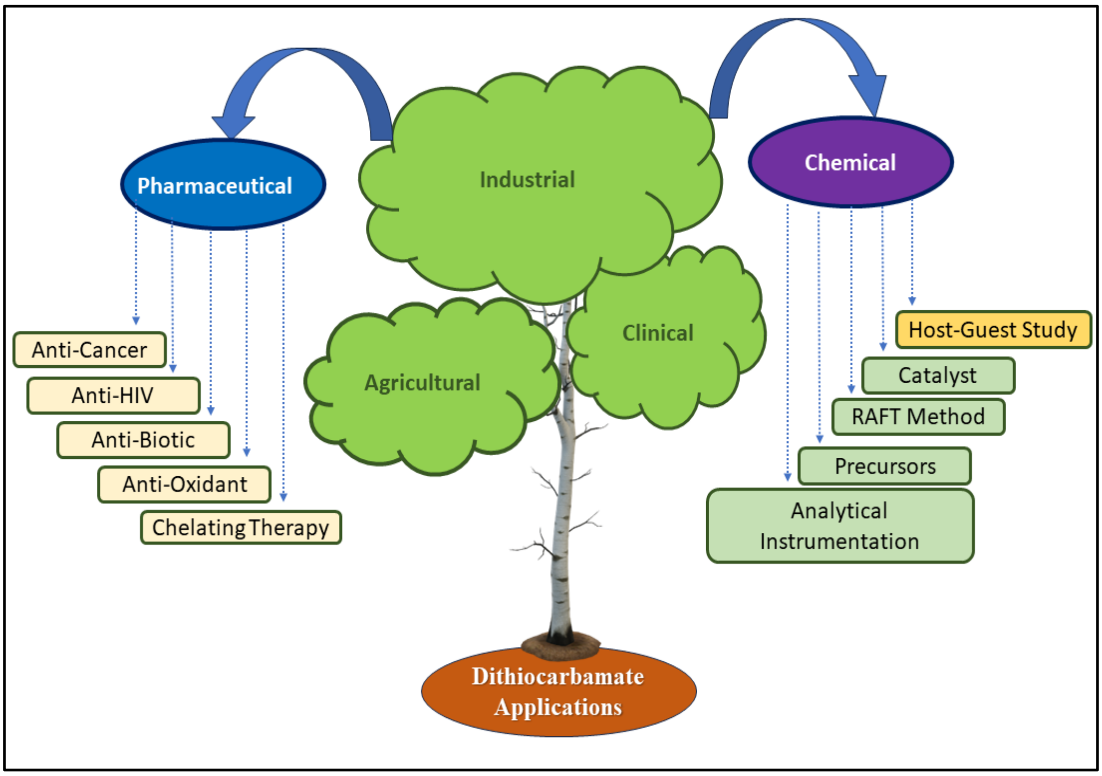


Figure 7. Various Applications of the Complexes of dithiocarbamate ligands

Moreover, Hendrickons *et. al.*, have conducted research on the electrochemical behaviours exhibited by dithiocarbamates involving Cu(I), Cu(II), Cu(III), and Co(III) metal ions.[86] Recently, there has been a noteworthy emphasis on the recognition of potassium ions through a straightforward assembly of benzo-15-crown-5–gold nanoparticles utilizing dithiocarbamates.[87] Jayashree Nath *et al.* have reported a convenient one-pot synthesis of cyanamide from dithiocarbamate employing molecular iodine.[88] The exploration of multiple nitrene insertions into copper–sulfur bonds of dithiocarbamate ligands, along with the synthesis and molecular structure elucidation of the tetraamido complex $[Cu\{\eta^2\text{-}RNSC(NMe_2)SNR\}_2]$ (R = $SO_2C_6H_4Me$-p), has been documented by Hogarth and collaborators.[89]

Hence, among the diverse array of organic-inorganic chemical species, dithiocarbamates stand out as one of the most remarkable groups.[90] Numerous dithiocarbamates (DTCs) have been identified for their wide-ranging pharmacological activities. In a study by Cao et al.[91] the antiproliferative properties of specific DTC-containing compounds were explored against various human cancer cell lines, including A549 (lung cancer), MCF-7 (breast adenocarcinoma), HeLa (cervical carcinoma), HT29, and HCT-116 (colorectal cancer). Substantial research has successfully demonstrated their diverse biological effects, encompassing efficacy as antimycobacterial agents Substantial research has successfully demonstrated their diverse biological effects, as depicted in Figure 8, encompassing efficacy as antimycobacterial agents,[92] anti-HIV activity,[93] and spermicidal properties.[94] The presence of sulfur atoms in molecules is noted to play a significant role in biological processes, exhibiting proficient interactions with biomolecules.[95] Notably, the inclusion of 1,1-dithio moieties in organic compounds imparts crucial biological effects, including antioxidant activity[96] and the inhibition of cardiac hypertrophy.[97]

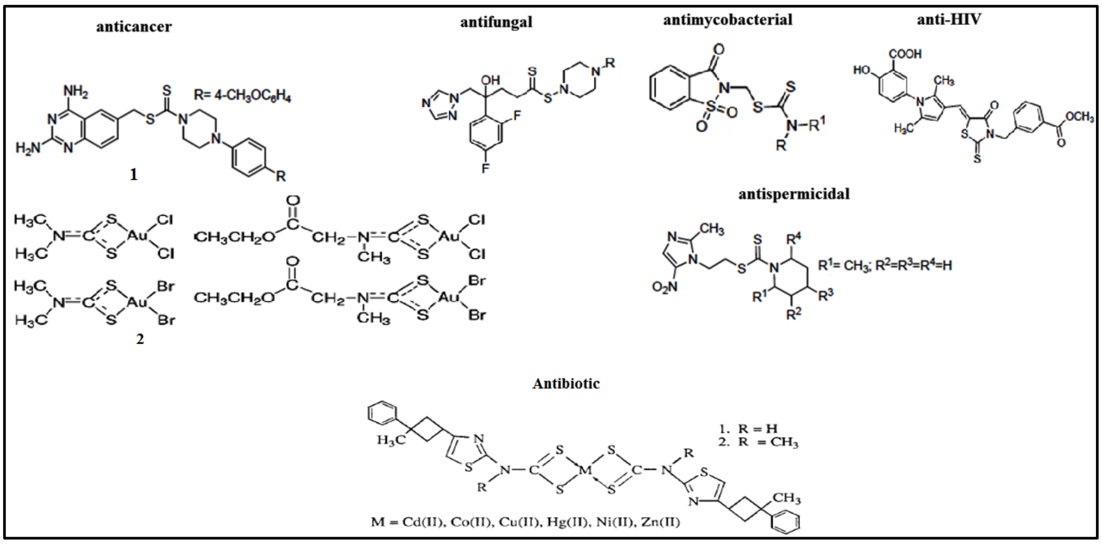


Figure 8. Examples of dithiocarbamates depicting medicinal significance

Notably, P. D. Beer and collaborators have detailed various dinuclear dithiocarbamate macrocycle complexes and their efficacy as ditopic receptors for diverse guest molecules in recent investigations.[98]

1.2.2.1 Host-Guest Binding Study

The adaptability of the architecture and the comprehensive weak interactions inherent in macrocyclic self-assembly render the system highly responsive to external disturbances. This quality enhances the potential applicability of macrocycles in supramolecular chemistry, particularly in the investigation of 'host-guest reactivity' concerning various guest species such as cationic, anionic, neutral guests, and ion-pair recognition.[99] In host-guest reactivity, the binding stoichiometry (1:1 or 2:1) of host-guest complexes is primarily determined by the size compatibility of the hosts and guests, as well as electronic factors (Figure 9). Notably, the small size of the macrocyclic cavity results in the formation of exclusively 2:1 host-guest complexes, while larger macrocycles lead to 1:1 complex, indicating the formation of intramolecular inclusion complexes (Figure 9).[100-101]

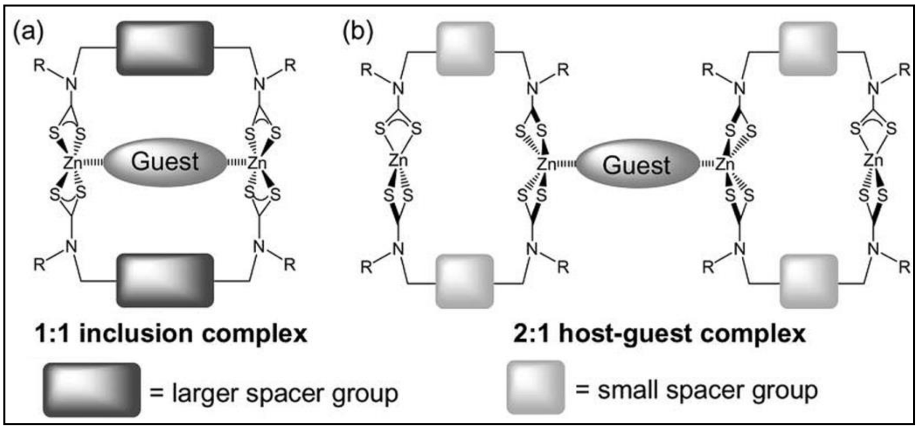


Figure 9. Host-guest complex formation in 1:1 or 2:1 ratio based on the size compatibility of the hosts-guest species.

However, when the macrocyclic cavity is suitable, ditopic hosts preferentially form intramolecular inclusion complexes with ditopic guests. These materials demonstrate promising applications as purifiers at the ppm level, effectively capturing a diverse range of molecules owing to the presence of their cavities. Motivated by this, our exploration extends to investigating the host-guest binding capabilities of selected macrocyclic complexes towards various guest species, including 1,4-dioxane, 4,4’-bipyridine, piperazine, and triethylamine. Within our research group, it has been observed that different binding stoichiometries (1:1, 1:2, and 2:1) of host-guest complexes emerge. This variation is primarily influenced by the size of the guests and the size of the cavity, as determined through the Jobs plot experiment employing UV-visible absorption spectroscopy techniques. (Figure 10)[102]

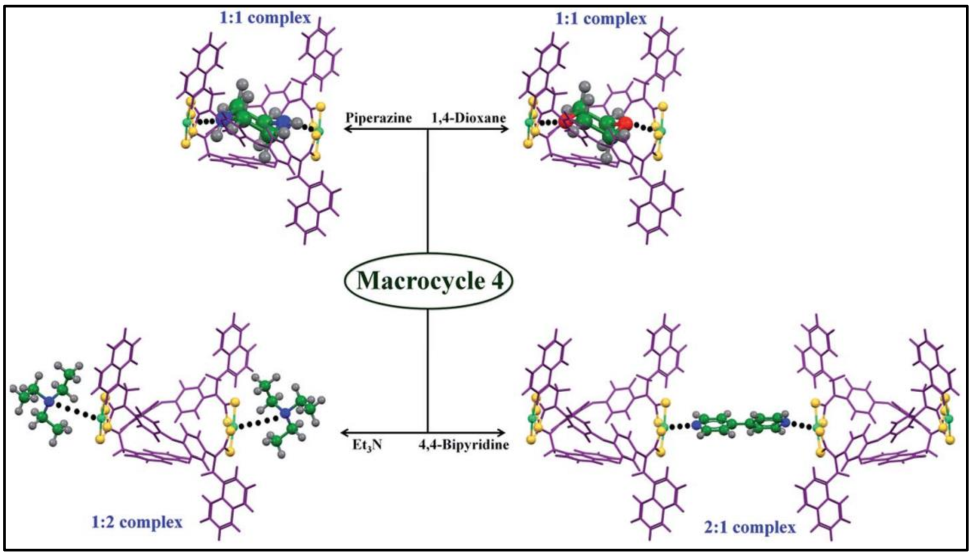


Figure 10. A representation of the interacting modes between macrocycles and diverse guests, as derived from Job's plot experiment.

Observing the example of dimers created by N-alkylated cyclic α, γ-peptides reveals cavities with customizable properties, positioning them as promising contenders for molecular capsules designed to ensnare guest molecules. For instance, a hydrogen-bonded dimer involving a cyclic hexapeptide with three pyridyl moieties connected to its backbone has been documented for encapsulating a single xenon atom (Figure 11).[103] In single-crystal X-ray diffraction, the drum-shaped dimer reveals an approximate van der Waals internal equatorial diameter of 5.4 Å and a height suitable for accommodating a sphere with a maximum diameter of 4.5 Å. This dimension aligns well with the size of a single xenon atom (4.3 Å).

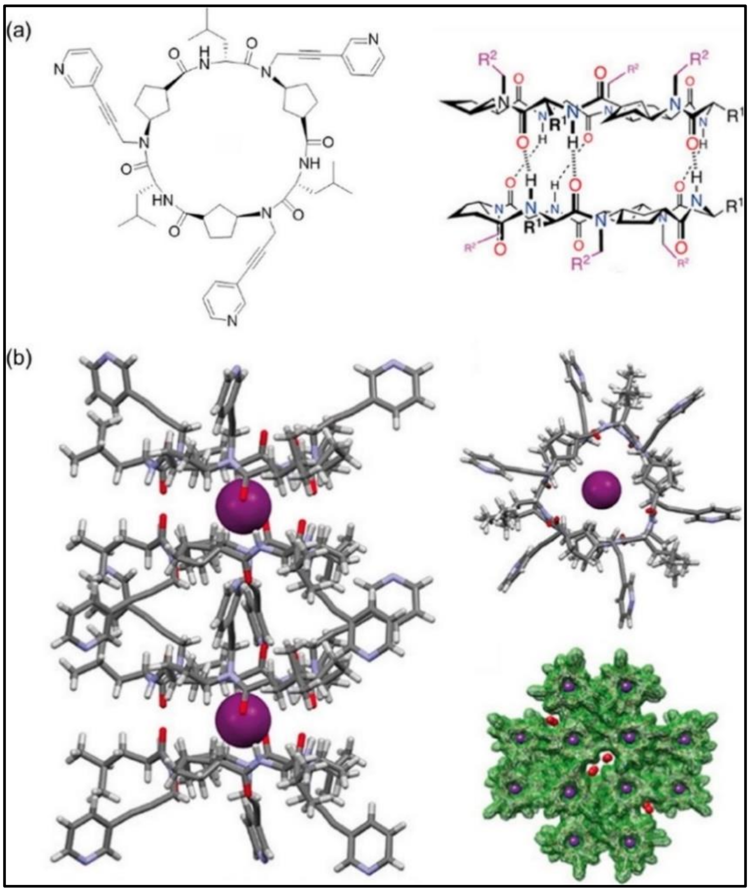


Figure 11. (a) The chemical configurations of the cyclic hexapeptide and its associated dimer (b) The crystalline arrangements of the dimeric assembly featuring a xenon (Xe) atom within the intradimer cavity

The strategic design of N-alkylated cyclic α,γ-peptides is anticipated to produce dimeric motifs with customized cavity properties, acting as supramolecular hosts capable of binding with high affinity and selectivity to guest molecules.[104] Nevertheless, the widespread application of 40–70% of recently developed anticancer drugs/probes in clinical cancer treatment is hindered by poor solubility and stability. To address these challenges, an effective strategy involves encapsulating therapeutic agents within macrocyclic hosts. This section delves into four primary categories of macrocyclic hosts employed to create supramolecular therapeutic agents, including calixarenes, cucurbiturils, cyclodextrins and pillar(n)arene shown in Figure 12[105-106] Other than these organic macrocyclic hosts some organic macrocycles have specific capability to bind with the Group IA and IIA metals only. Some of them are Cryptands, Hemispherands, and Spherands as these organic macrocyclic hosts have the ability to only bind with K^+, Na^+ and Li^+ respectively.

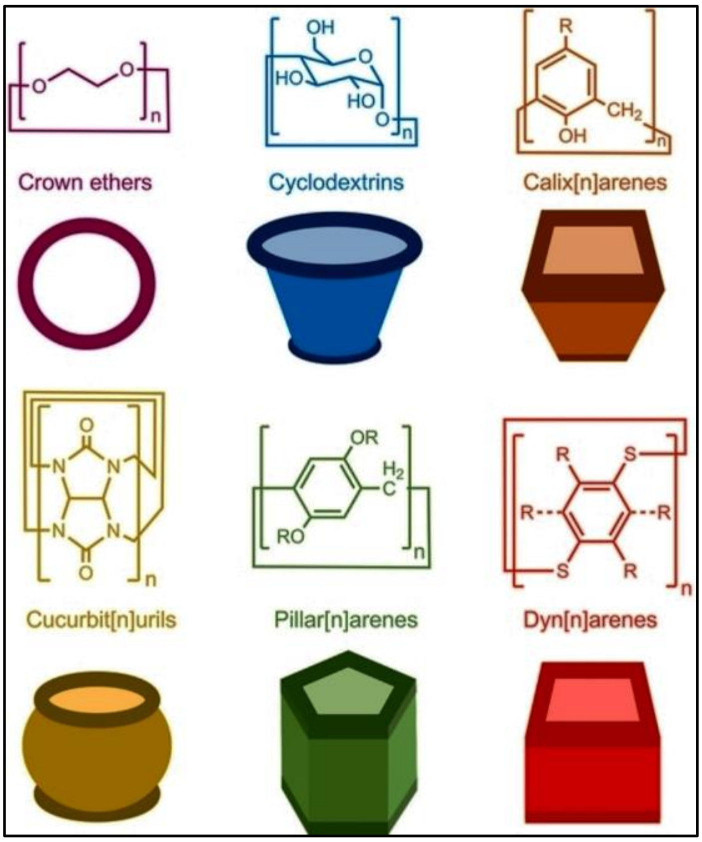


Figure 12. The structure of major organic macrocyclic host molecules and their shape.

Extensive research has been conducted on organic macrocyclic hosts, whereas the study of inorganic macrocyclic hosts remains comparatively limited, despite their comparable capabilities to their organic counterparts. Notably, inorganic macrocyclic hosts have demonstrated significant potential in sensing environmentally hazardous heavy metal ions and facilitating their separation through host-guest binding studies.

As shown in Figure 13,[107-108] the macrocycles (a), (b) and (c) exhibit highly effective anticancer activity, with alterations limited to the spacer groups and variations in the metal ions. Notably, a consistent observation reveals that optimal anticancer activity is associated with spacer groups containing more than a phenyl ring. Figure 13(d)[109] presents an inorganic macrocycle featuring piperazine as a spacer on one side and biphenyl as a spacer on the other side. This configuration significantly enlarges the cavity, incorporating two silicon atoms, two tin atoms, two nitrogen atoms, and four sulfur atoms, thereby expanding the potential for host-guest chemistry interactions. In Figure 13, macrocycle (e)[110] deviates from the presence of a phenyl ring as the spacer, opting instead for an alkyl chain combined with the xanthate-incorporated nickel complex. This configuration comprises two nitrogen atoms, four oxygen atoms, eight sulfur atoms, and two nickel atoms. Notably, this particular inorganic macrocyclic structure has not been examined for host-guest binding studies; rather, its focus lies in the investigation of thermochromism. Contrary to the previous information, Figure 13 macrocycle (f)[111] indeed possesses the same number of nitrogen, oxygen, and sulfur atoms as well as two metals. Unlike earlier indications, this inorganic macrocyclic structure has been systematically studied for host-guest binding, yielding highly favorable results. The sufficient cavity of this inorganic macrocyclic host enables effective binding with guests such as 1,4-dioxane, 4,4'-bipyridine, piperazine, and triethylamine in DMSO solution.

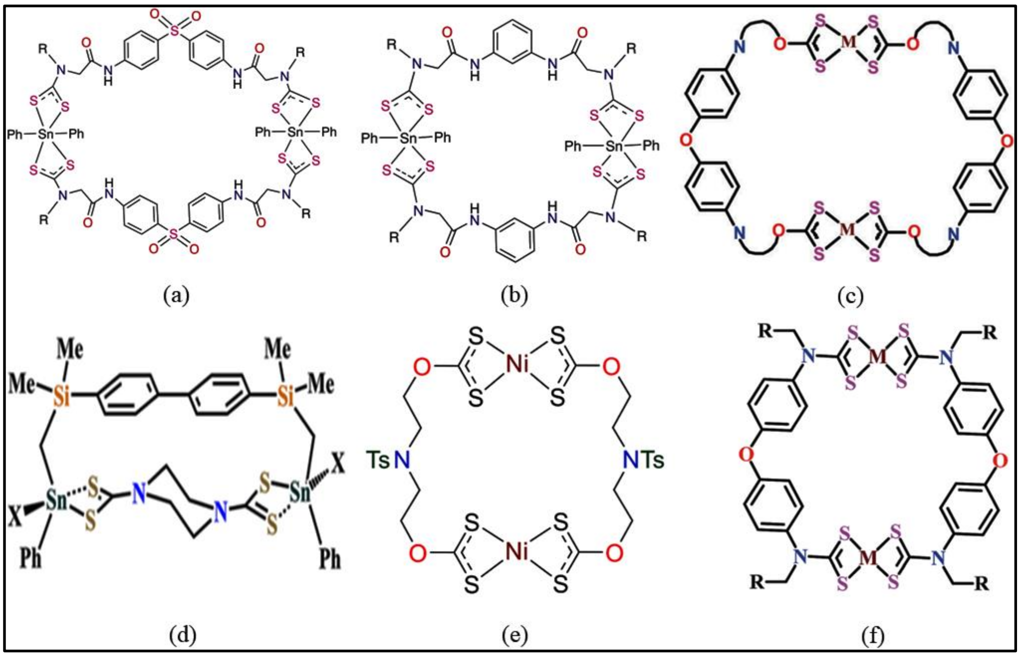


Figure 13. The structure of inorganic macrocyclic complexes.

1.2.2.2 Heavy metal ion sensing study

The sensing and isolation of environmentally hazardous heavy metal ions, such as Cd^{2+}, Hg^{2+}, and Pb^{2+}, which pose significant health risks, have become focal points in current research efforts.[112] Studies indicate that even at very low concentrations (15 ppb), Pb^{2+} is directly absorbed by cells from the environment, leading to interference with various biological processes and subsequent adverse effects on neurological, cardiovascular, reproductive, and developmental aspects in humans.[113] Pb^{2+} is recognized for its interactions with proteins, either mimicking or antagonizing the physiological effects of divalent metals like Ca^{2+} and Zn^{2+}. Similar to Pb^{2+}, Cd^{2+} is toxic to cells as it disrupts Ca^{2+} and Zn^{2+} dependent processes. However, a notable challenge in advancing Cd^{2+} probes arise from the closely similar binding properties of Cd^{2+} and Zn^{2+}, making it challenging to develop selective probes for Cd^{2+} that do not interfere with Zn^{2+} under physiological conditions.[114-1115] Additionally, the detection of Hg^{2+} is crucial due to its high toxicity, widespread distribution in the environment, and its tendency to accumulate in organisms through the food chain.[116]

High-performance liquid chromatography (HPLC),[117] capillary electrophoresis,[118] potentiometric,[119] conductometric/electrochemical,[120] colourimetry,[121] chromogenic stain, dyes,[122] and fluorescence [112-116] techniques have traditionally been employed for visualizing metals of interest, with a focus on their application in the complex context of multiple metals. While instrumental methods offer direct and quantitative insights into metal ions, they prove less suitable for rapid field detection or in vivo studies related to heavy metal ion biology and toxicology. Addressing these challenges, synthetic chemists have endeavoured to design and synthesize small-molecule metal ion sensors. Professor Pandey et al. have reported several chemosensors for selectively detecting free Hg^{2+} and Pb^{2+} ions, extensively reviewed elsewhere.[123] Due to the enhanced thiophilicity of Hg^{2+} and Pb^{2+} ions compared to oxophilicity, numerous sulphur-rich chemosensors have been developed for imaging HeLa cells and zebrafish.[124-125] Specifically, histidine residues attached to a bipodal thiocarbamate scaffold (Hatai Hg-1) contribute sulphur atoms as donors, thereby increasing selectivity for Hg^{2+}.[126] Despite the existence of sensitive and selective chemosensors for Pb^{2+}, Cd^{2+}, and Hg^{2+}, the field actively pursues improved sensors to address escalating environmental pollution concerns. For example, substituted organic macrocyclic compounds containing azacrown ethers, calix[127] arene, diazatetrathia-crown ether, cyclam, dipyrrolylquinoxaline-bridged organic macrocycles, and various other organic macrocyclic chelates exhibit fluorescence turn-off and turn-on activity[128-132] However, many of these probes lack sufficient selectivity for d^{10} metal ions compared to other divalent metal ions such as Ni^{2+}, Cu^{2+}, and Zn^{2+}.

Notably, numerous dinuclear/mononuclear dithiocarbamates macrocycles have been reported by various authors, including ourselves, primarily for in vitro-biological studies, molecular recognition, anion receptors, ion-pair recognition in gas storage sensing, and metal-sulphide nanoparticle synthesis[133, 134] The exploration of metallomacrocyclic dithiocarbamate transition metal complexes as chemosensor probes for detecting Pb^{2+}, Cd^{2+}, and Hg^{2+} is still in its early stages. Surprisingly, despite their sulphur-rich nature, these complexes have not been thoroughly studied in the context of sensing and isolating heavy metal ions Pb^{2+}, Cd^{2+}, and Hg^{2+}, except for Li^+, Na^+, K^+, Cs^+, neutral organic, or anionic guest species such as halides, $H_2PO_4^-$, CH_3COO^-, and $C_6H_5COO^-$.[135]

1.3 Objectives of the present work

Taking into consideration of all these features of metal directed self-assembly, versatile properties and the exceptional host-guest study of dithiocarbamate moiety, the entire focus of the work has been directed towards the development of number of metal-directed self-assembled macrocyclic structures using exclusively dithiocarbamate ligands. The objectives of the current study are briefly stated below.

- To design and synthesize novel organic secondary diamine precursors appropriate for developing macrocyclic bimetallic bis-dithiocarbamate macrocyclic complexes.
- To synthesize bis-dithiocarbamate ligands *in situ* from secondary diamines and carbon disulphide in the presence of a base.
- To explore the possible reactivity of 1,1-dithio ligands (prepared *in situ*) towards transition metal ions, Ni^{II}, Cu^{II}, Zn^{II} in the development of novel binuclear dithiocarbamate macrocyclic complexes.
- To characterize newly synthesized compounds by relevant spectroscopic techniques such as ESI-MS, IR, NMR, UV visible and thermogravimetric analysis.
- To execute DFT calculations to reinforce the experimental outcomes.
- The binding study of hazardous organic dyes with these synthesized binuclear dithiocarbamate macrocyclic complexes have been explored.
- Heavy metal ion sensing study with the environmentally hazardous Cd^{2+}, Hg^{2+}, and Pb^{2+} metal ions.

1.4 References

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