Chapter-1 | Introduction

This chapter provides an introduction to the silicon, alkoxy silanes and silatranes presented in this thesis. An overview of synthetic routes followed in the literature and its promising applications in the diverse field have been discussed. Further the last of the chapter is adorned with the aim of my research.

1. Introduction

1.1 Silicon

Silicon, the second most abundant element in the Earth’s crust (after oxygen)[1], the 3rd most abundant element after Fe and Zn in the human body [2] and the 8th most abundant element in the solar system [3]. It has perceived felicitous attention because of its availability, non toxicity, reactivity and appreciable bonding possibilities [4-5]. It is not surprising; therefore, that extensive research has been carried out on the chemistry of this element. In human body, it plays an important role in the development of bone and connective tissue, improves regeneration and increases mineral density of bones [2]. In addition, it is present as a source in some vegetables (spinach, root vegetables and beans), sea food, plant food, supplements [6]. With the growing interest in mobile phones, electric vehicles other electronic devices there is a need for energy storage devices and for that silicon serve as the promising anode material for Li-ion batteries [7-11]. Due to its relative efficiency, silicon is used as photovoltaic material for making solar cell [12-15]. Nowadays, nanostructured silicon thin films are used in antireflection coatings and hybrid silicon solar cells [16-22]. It plays an important role in providing resistance to diseases and pest thereby controlling environmental damage [23-26]. In human life silicon is incorporated in all forms as in textiles, healthcare, computer and electronics, automobiles, construction, architecture, agriculture and in food industry [27-28]. Although carbon and silicon belongs to the same group i.e. group 14 of periodic table and have identical reactivity pattern but they differ markedly in the fact that carbon forms the basis of life forms whereas silicon contributes to inorganic world forming higher coordinated silicon compounds. The inclusion of silicon onto carbon chemistry generates a new stem of chemistry termed as organosilicon chemistry that has wide range of applications in nearly all areas [29].
The few important parameters are counted for the study of silicon’s utility in the synthesis of organosilicon compounds. These are:

- Relative electronegativity,
- Bond strength,
- Coordination number,
- Bond energy
- Ability to form multiple bonds

The difference in the electronegativity between silicon (1.74) and carbon (2.50) suggests that Si is more electropositive that tends to create partial positive charge and negative charge on central Si atom and surrounding atom respectively that result in strong polarisation of C-Si bond. The electronic configuration of C: 1s\(^2\) 2s\(^2\) 2p\(^2\) and Si: 1s\(^2\) 2s\(^2\) 2p\(^6\) 3s\(^2\) 3p\(^2\) 3d\(^0\) suggests that silicon (1.06 Å) is larger in size than carbon (0.66 Å).

Due to the empty d orbitals Si can extends its coordination number by 4 while carbon have coordination number of 2,3,4. This imparts unique property to silicon by generating hypervalent bonds. Another important parameter is the bond energy, C-C > C-O while Si-O > Si-Si. Due to this, C can undergo catenation while Si-O forms chains of Si-O-Si in silicon polymers. Alkenes and alkynes are commonly formed by carbon while the analogous disilenes and disilynes are very rare [30-32].

1.2 Silanes

*Charles Friedel* and *James Crafts* first discovered the tetraethylsilane having direct C-Si covalent bond by reacting tetrachlorosilane with diethylzinc [33-35]. In 1900, Kipping used silicon tetrachloride and ethylmagnesium iodide to isolate the mixture of ethylchlorosilanes [36]. In 1950, Muller and Rochow developed the direct process for halo-organosilanes at large scale production [37].
Structure of Silanes

\[
\text{R - (CH}_2\text{)}_n\text{Si} - \text{X} - \text{X} - \text{X} = \text{Silicon functional group}
\]

\[
\text{R} = \text{Organo-functional group}
\]

\[
n = 0-3
\]

**Fig.1: General structure of Silanes**

The general structure of silane constitutes two components R and X (Fig 1). R is the organofunctional group attached through carbon chain or through silicon atom whereas X can be alkoxy component, commonly methoxy or ethoxy, halide functionality or an organic moiety. As the Si-C bond is hydrolytically stable, the non-hydrolysable/non polar R group attached to silicon molecule of silanes provides the organic compatibility to form hybrids while the X group that is prone to hydrolysis reacts with hydroxyl group to liberate alcohol forming covalent linkages. Therefore, alkoxy group play key role in chemical binding to many inorganic material [38-41].

Organosilanes act as a surface modifier and receives plenty of research interest due to various applications [42-43]. The functionalized surface stretch its interest in bioanalysis application, used as a material for ferrofluids [44], magnetic resonance imaging [45], high density information storage, labeling of cells [46], adsorption of heavy metal ion [47-50], adsorption of volatile organic compound [51], adsorption of organic pollutant [52-54], and chemical sensing [55]. Organosilanes based bioactive molecules have been designed for various applications that include antiviral activity against influenza A viruses, DNA chelators and protease inhibitors [56].

Different type of organosilanes having carboxyl, aldehyde, amine, and thiol groups have been used in the generation of organic–inorganic adsorbents that are used in the protein separation. The silane with the thiol group have greater efficiency for the separation of protein due to change in electrostatic interaction and conformational structure of protein [57].
organosilanes such as methyl/vinyl silane have been used in improving the mechanical strength and flow behaviour of cementous material [58].

Organotrialkoxysilanes undergo sol-gel hydrolysis condensation to form Polysilsesquioxane. These exist as random branched type, cage type and ladder-like structures. Polymethylsilsesquioxane (PMSQ) network provides transparent aerogels having great strength and flexibility with high thermal insulation property [59]. Alkoxy silanes rather than alkyl silanes were used in the formation of siloxane based nanomaterial because of its less reactivity and easy handling. The nanomaterial had a wide range of applications in biomedical science and in catalysis [60]. Alkoxy silanes have been used as fillers in the composite materials [61-62]. Aromatic alkoxy silanes have been used as a cross linking agent in the synthesis of hybrid poly(alkoxy silane) organogels[63]. Alkoxy siloxane oligomers have been synthesized by direct alkoxy silylation reaction [64].

The alkoxy silanes play a key role as adhesion promoters [65]. Organosilane coating can provide resistance to ultraviolet rays, chemicals, abrasion and moisture. They are also used in thermosetting and thermoplastic polymers [66]. Urethane methacrylate trimethoxysilane (UAMS) have been used as one of the coupling agent in hybrid coating that has the property of hardness and thermal stability. In the ordered mesostructure nanocomposites the monosilylated, bis-silyllated and multi-silylated organosilanes are used for hybrid coatings [67-68].

Organosilanes such as dimethoxybis(N-methylpyrrol-2-yl)silane (2), trimethoxy(N-methylpyrrol-2-yl)silane (1), tetrakis(N-methylpyrrol-2-yl)silane (7), methoxytris(N-methylpyrrol-2-yl)silane (3),N-methylpyrrolsilane(4), tris(Nmethylpyrrol-2-yl)silane (6) , bis(N-methylpyrrol-2-yl)silane (5), are synthesized . These silanes are used as potential hydrogenating agents due to its easy handing, easy accessibility and high thermal stability [69].

The alkoxy silanes such as 3-mercaptopropyl-trimethoxysilane (PropSSH), aminopropyltriethoxysilane (APS) and 3-mercaptopropyltriethoxysilane, are mainly used in organosilane coatings due to their protective nature towards the corrosion of alloys [70-72]. Alkoxy silane such as vinyl trimethoxysilane is used as an inorganic source in styrenated oil
based polyester films [73]. (3chloropropyl)trimethoxysilane have been used in the synthesis of nanocarrier for targeted gene delivery that serve as an application in cancer treatment [74]. 3-isocyanatopropyltriethoxysilane (ICTES) has been used in the synthesis of alkoxy silane dye for the formation of hybrid non-linear optical material [75]. Alkoxy silane have been used as additives for wood preservatives. Methyltrimethoxysilane (MTMOS) have been used as stabilizing agent for waterlogged wood. Moreover the leaching is also prevented by the chemical binding of alkoxy silanes with wood thereby protecting archaeological wood [76-77].

The basicity of alkylalkoxy silane decreases from the mono-functional alkylalkoxy silane to the tetrafunctional alkylalkoxy silane. The decrease in basicity is due to the functionality with the oxygen as there is increased contribution from delocalization of oxygen lone pair to the adjacent antibonding orbitals of silicon alkyl chain when methyl group is replaced with the electron negative methoxy oxygen on Si atom [78]. In the ordered mesostructure nanocomposites the monosilylated, bis-silylated and multi-silylated organosilanes are used for hybrid coatings [79-80]. Organotrimethoxysilanes have been used as coupling reagents in Hiyama coupling reaction with aryl bromide and chlorides [81].

Organosilanes are used as starting material for LED’s, used in producing novel catalysts, solar cells, In addition these are used in catalytic dehydrogenative silylation [82-83]. Organosilanes has a wide range of applications in organic synthetic chemistry. It may serve as silyl protecting and derivatisation reagents, act as reducing agents, used in cross coupling chemistry, most importantly in stabilizing α-Carbanions and β-Carbocations [84-85].

1.3 Silatranes

Silatranes having the general formula RSi (OCH₂CH₂)₃N are the cyclic organosilicon ethers of tris(2-oxyalkyl)amines. These constitute important class of pentacoordinate organosilicon compounds with distorted trigonal bipyramidal geometry [86]. The hypervalent silicon atom in silatranes forms transannular dative bond between silicon and the nitrogen atom thereby forming cage like structure that becomes the reason for higher stability of silatranes than their open chain
analogues. On the basis of heteroatom attached to silicon they may be further classified into groups. Fig2 represents the general structure of silatrane.

The three alkyl groups are connected with N atom on one end and O$_3$SiR group on other. The lone pair of nitrogen atom lies in such a direction that it becomes favourable to give its electron pair to silicon atom forming N-Si dative bond and exocyclic functionality Z just opposite to the transannular dative bond linked to silicon atom by an exocyclic bond.

The pentacoordinate silicon atom has much different characteristics from the tetra coordinate silicon complexes. The transannular interaction between the Si-N bond results in the formation of 3c-4e$^-$ bond as 2p orbitals of N donates its lone pair to unoccupied 3d orbital of silicon atom [87-90]. The idea was proposed by Pimentel and Rundle and also with efforts of Kutzelnigg and co-workers the concept of 3c-4e$^-$ bond is accepted. The bond length and strength of N-Si bond depends upon the exocyclic substituent, the electronic behaviour of carbon, oxygen, and nitrogen atom forming the equatorial plane, the steric effect and the atoms that are involved in bridging [91-92].

As the number of bridging units are increased the bond length of Si-N increases, indicates the inhibition of Si-N interactions with the successive chelate ring formation that might be due to the strain caused by five membered ring. The Si-N distance shortens on increase in Si-Z bond distance thereby supporting the three centre four electron type axial bonding in pentacoordinated

Figure 2: General Structure of silatrane
silicon compounds. It is concluded by some authors that Si and N are held together by crystal forces whereas in gas phase there is no actual Si-N bond.

In accordance with the hybridization theory, the pentacoordinate Si atom in the silatrane is sp$^3$d hybridized and the geometry is trigonal bipyramidal. The Si atom is located in the centre surrounded by three oxygen atoms and one atom from the substituent forms four covalent bonds and one N atom connected to the silicon form N-Si dative bond having lone pair on the nitrogen atom (act as a donor pair) is located in the corners of each trigonal pyramid. But the electron density of the three heterocyclic ring around the silicon atom is different from the substituent that are present on the other side. As a consequence, the silicon atom does not remain in the plane of three oxygen atoms and therefore the geometry is not perfect trigonal bipyramidal. The only drawback in the hybridisation theory is the involved d orbital, but the 3d orbital of silicon atom has high energy electrons and therefore is unable to hybridize. Thus 4s and 4p orbital participate in bonding giving sp$^3$4s hybridisation [93].

An X-ray crystal study confirms the tricyclic cage structure of silatranes having hypervalent silicon atom with distorted trigonal bipyramidal geometry. The silicon atom is equatorially surrounded by three endocyclic oxygens and axially it is surrounded by substituent group and the nitrogen is present just opposite to silicon in electrostatically favourable arrangement. The silatranes have N-Si bond distances in the range from 2.01 Å to 2.89 Å for chloro derivative and trans-dimethylphenylphosphino)platinum derivative which is shorter than the sum of van der Waal radius of both atoms, 3.8 Å and the typical Si-N bond length is 1.7-1.8 Å and alkyl chain is responsible for N→Si bond elongation. Due to this structural arrangement, silatranes become a great research interest to scientist worldwide as it possess many biological and chemical properties [94].

Silatranes exist in two cage conformations with respect to nitrogen atom i.e exo and endo as shown in figure 3. In endo form, nitrogen lone pair points towards the silicon atom whereas in exo form lone pair is directed out of the cage. The N-Si transannular interactions results in 3c-4e- bond in endo form. The endo form is more stable due to dipole-dipole, conformational, and covalent interactions [95].
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Figure 3: Silatranes with endo and exo geometries at the nitrogen atom

The shortening of Si-N distance in endo-exo transition in silatrane (Fig 4) is associated with increase in degree of nitrogen pyramidalization and decrease in X-Si-O valence angle.

Figure 4: Endo-exo transition in silatrane

When the theoretical calculations are performed on 1-methylsilatrane, the unstable exo form transforms to the more stable endo form. The frontier molecular orbitals supports the stability of endo configuration: LUMO i.e the lowest unoccupied molecular orbital lie higher and the HOMO i.e the highest occupied molecular orbital lower than the corresponding orbitals in exo configuration. Therefore endo form depicts the structural representation of the silatrane [96-97].

Recently Gilbert et al. identified many computational ways for the synthesis of exo-silatranes. They undertook four chemical features that might allow the formation of these silatranes. The first approach is to reduce the size of cage ring, second is employing highly constrained rings to
stiffen the cage backbones and third is the less crowded geometry around exo nitrogen and the last is to modify the lewis basicity and acidity around nitrogen and silicon [95]

1.4 Click Chemistry

Click chemistry, the Dynamic combinatorial chemistry or the linking chemistry defined by Sharpless and associates constitute a fast growing promising field with numerous applications [98]. The aim of click reaction is to synthesize number of products with high yield from easily available reagents with wide scope and high selectivity. A click reaction is easy to perform, involves fast procedures, insensitive to water and oxygen with simple isolation procedures. The click chemistry provides simple solution to the researchers because of its flexibility. It has found ample of applications in drug development, polymer chemistry, nanoscience, biomedical research, chemical biology, gene delivery, lead discovery, bio-labelling, radiochemistry and many more [99-102].

The click chemistry reactions are of four types:

i) Cycloaddition reactions

ii) Non-aldol carbonylation reactions

iii) Nucleophilic ring-opening reactions

iv) Carbon-carbon multiple bond addition reactions

Of all the reactions, one particular powerful reaction that has remarkably useful in innumerable applications is the 1,3- dipolar cycloaddition between the azide and the terminal alkyne called the ‘cream of crop’ that was first reported in 1893 by Mechael [103] and then in 1960s it was studied in detail by Rolf Huisgen [104] (Scheme 1). Later on Sharpless and Meldal groups in 2002 introduced the advanced method of formation of 1,2,3 triazole using Cu(I) salts. The copper catalyzed azide alkyne cycloaddition reaction is the advanced version of Huisgen 1, 3 cycloaddition reaction and is termed as click reaction. The reaction uses the suitable conditions to generate plethora of complex molecules from olefins and heteroatom linkers. In addition, the bond formation in the product is highly stable [105-106].
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It is considered to be the fast and modular approach to join smaller unit together that can work on small as well as large industrial scale. The product generated in Cu(I) catalyzed cycloaddition is highly regiospecific i.e 1,4 product of 1,2,3 triazole is obtained exclusively on reacting azide and alkyne.

![Scheme 1: Huisgen 1,3-dipolar cycloaddition reaction and modified azide–alkyne cycloaddition reaction](image)

Moreover the complete conversion of reactants to specific product requires no purification technique, no protecting groups. So, this methodology filled the gap of many researchers and practitioners whose work is focused on chemical biology, cell biology, carbohydrate chemistry that accelerate the development of life science [107-108]. The stitching together of azide and alkyne in the presence of Cu (I) as a catalyst follows the proposed mechanistic cycle represented in Scheme 2

1,2,3- triazole possess aromatic character and can form stable hydrogen bond . Moreover, they possess the tendency to bind with various heavy metal ions and thus can act as efficient binding unit for the detection of cations and anions[99,109-111].

Due to its high reliability, selectivity and specificity the reactions involving click universe have increasingly in demand in all aspect of life forms. These triazole can act as great
pharmacophores and are non-classical isosters of amide moiety. The aromatic triazole unit are involved in \( \pi-\pi \) stalking interactions with the side chains of aromatic amino acids, the nitrogen present in the triazole (N2,N3) can act as hydrogen bond acceptor and the C-H bond act as hydrogen bond donor. The triazole core has excellent metabolic stability and is inert to hydrolytic, reducing and oxidizing agents even at high temperature, these properties favours their use in medicinal chemistry [112-113]. In addition, due to the relative planarity, H-bond forming capacity and strong dipole moment these triazole have strong physicochemical resemblance to amide bond thereby finding application in peptide chemistry [114-115].

Scheme 2: Proposed mechanistic cycle of Cu(I) assisted azide–alkyne cycloaddition reaction

CuAAC show numerous biological activities, such as antifungal, anticancer, antibacterial, antiviral, antileishmanial, antitrypanosomal, antimicrobial, antiinflammatory and antitubercular
activity [116-118]. The ongoing interest in click chemistry covers all aspects of research in lead discovery and optimization, drug discovery, such as target-template invitro chemistry, bioconjugated reactions and proteome chemistry [119]. Furthermore, click chemistry is highly useful in generating polymeric biomaterials that serve a great application in tissue engineering and gene therapy. It is highly successful in generating self-assembled monolayer on various surfaces. It is used in the synthesis of forming non-linear optical (NLO) materials [120-121]. Moreover it aimed for the synthesis of nano engineered materials that have found numerous application in field of biomedical science [122].

To extend the scope of click chemistry, the CuAAC reactions are performed with the reactants that are highly moisture sensitive. For this approach, Moietra et al in 2010 carried out the reaction between 3-azidopropyltriethoxysilane and functional alkynes (Scheme 3) under moisture free, microwave and thermal conditions giving hybrid silica precursors with high purity and good yield that overcome the limitations of conventional methods that give the mixture of products [123-124]. The revolutionized methodology have boost the use of CuAAC reaction using Cu (I) as a catalyst under term “click–silylation” [125-129]. The incorporation of triethoxysilanes with triazole moiety can broaden its physical, chemical and mechanical properties and endowed innumerable application in polymer chemistry, biomedical science and material chemistry [130-132].
1.5 Molecular Sensing

The heavy metal ions such as Hg$^{2+}$, Cu$^{2+}$, Zn$^{2+}$, Fe$^{2+}$, Cd$^{2+}$, Pb$^{2+}$ and many more are hazardous to human beings when their level exceeds above the threshold unit. These metal ions play an important role in various biological systems so their detection becomes the immense research interest to many research analysts. The HTM such as Hg$^{2+}$ cause damage to brain, kidney, central nervous system, and its accumulation in the human body cause neurodegenerative disorders [133-135]. Cu$^{2+}$ is an essential element and has a role in synaptic transmission, neurite outgrowth, axonal targeting, and thereby play a key role in the development of nervous system. It involves in the iron absorption and transport into the human body. It is required for the development of connective tissue, peptide amidation and pigment formation. It acts as a cofactor for many proteins and enzymes. It plays a role in ATP biosynthesis and helps in melanin production. But when taken in excess or below level it can be destructive to human beings. It can cause many diseases such as Wilson’s disease, Alzheimer’s diseases, Parkin diseases etc [136-137]. On the other hand Pb$^{2+}$ cause lead poisioning when its level got increased in the human body. It also affects central nervous, immune, and reproductive system. Similar effects are encountered by other metal ions [138].

The toxic effects of these entire ions create an urgent need for the detection of heavy metal ions. To date, many sophisticated techniques such as inductively coupled plasma mass spectrometry (ICPMS), atomic absorption spectrometry (AAS), atomic fluorescence spectrometry (AFS), voltammetry, cold vapor atomic absorption spectrometry, electrothermal atomic absorption spectrometry, X-ray fluorescence spectrometry and high performance liquid chromatography are used for the detection of heavy metal ions [139-143].

But these techniques have certain limitations that includes expensive and complicated instruments, are more time consuming, need highly controlled experimental conditions. Hence for the detection of these ions, viable and economic methods are needed. So with the aim of developing chemical sensor technology, and inspired by the nature’s biological processes that involve receptor-ghost and enzyme substrate interactions, considerable attention has focused on generating abiotic host molecules that contain signalling unit or responsive functional groups as shown in Figure 5.
For the sensing of ion the recognition process requires synthetic or natural receptors termed as ionophores. In accordance with the Pearson concept of hard and soft acid and bases (HSAB) the ionophores take high advantage of nitrogen, sulphur and oxygen atoms towards these ions. \(\text{Cu}^+, \text{Cd}^{2+}, \text{Hg}^{2+}, \text{Ag}^+, \text{and Pb}^{2+}\) being classified as soft acids binds to sulphur containing ligands; while the border line acids such as \(\text{Cu}^{2+}, \text{Ni}^{2+}, \text{Zn}^{2+}\) and \(\text{Co}^{2+}\) preferably bind with nitrogen [144-148].

J.M. Lehn in 1987 was awarded with the Nobel Prize for his pioneering work in the field of supramolecular chemistry that becomes the interdisciplinary field of biology, chemistry and material science along with incredible impact on analytical chemistry.

The concept of chemosensor was first introduced by Czarnick in 1923, who defined chemosensor as “a portable miniaturized analytical device, which can deliver real-time and on-line information in presence of specific compounds or ions in complex sample” [149]. A sensor consists of recognition element for the identification and specific interaction of analyte, the transducer element that converts recognition process into notifying optical signal, an optical device, and the detector that detects and then amplifies the primary signal into readout unit. The optical properties studied can be absorbance, photoluminescence, light polarization and reflectance [150-154]. Efficient sensors acquire adequate sensitivity, selectivity and dynamic detection range towards recognition of species. The enviable functions of sensor include:

i)  Good signal-to-noise ratio
ii) Fast response time
iii) Long term stability
An ideal sensor must be simple, robust, reliable and economic in terms of design, size and activity. But there are many sensors that suffer from certain limitations in terms of long term stability, detection limit, and interference of other ions rather than the target ions. The sensor found innumerable applications in diverse field that include environmental study, biomedicine, and clinical study. They can act as powerful analytical tool for the constant monitoring and real time information [155-157].

This thesis is primarily focused on the development of fluorescent sensors via click silylation to improve the application of synthesized compounds. The ionophore forms complex with the metal ion in two possible ways, first is the enhancement in the fluorescence of probe called chelation enhanced fluorescence (CHEF) or decrease in the fluorescence of probe called chelation enhanced quenching (CHEQ). The sensor which provides irreversible response termed as ‘probe’. The signal recognition of fluorionophore includes charge transfer (CT) and photoinduced electron transfer (PET) process. The intramolecular charge transfer probes involve the direct interaction of analyte with ligand which is the part of fluorophore system. The charge transfer occurs via excitation by light where electron donating group conjugates with an electron withdrawing group and from this fluorescence and absorbance intensity got fluctuated and simultaneous shift in absorbance and fluorescence spectra are observed. The probes that are based on photoinduced electron transfer mechanism involve the interaction with the analyte that is electronically isolated from the fluorophore system. The electron density of free binding site quenches the fluorescence of covalently linked fluorophores. The electron density got reduced in the bound state by bound species thereby releasing the quenching effect [158-160].

2. Literature review

2.1 Synthetic aspects of silanes

Silicon halides SiX₄ (X =Cl, Br, I), especially SiCl₄ (1) is widely used as starting material for the preapartion of different silanes (2-7) as depicted in (Scheme4) [161]. Among the silanes, halosilanes and alkoxy silanes occupies the greater importance in silicon chemistry because of the ability to modify the physical and chemical properties of surfaces and interfaces [162-163]
Scheme 4: Derivatization of silicon tetrachloride

Anderson reported variety of pseudo halides of silicon (8-13) and studied their reactivity towards ethanol and water [164] (Scheme 5)

Scheme 5: Synthesis of pseudohalosilanes

Mehring *et al.* synthesized trimethoxy(N-methylpyrrol-2-yl)silane (15), dimethoxybis(N-methylpyrrol-2-yl)silane (16), methoxytris(N-methylpyrrol-2-yl)silane (17) by lithiation of N-methylpyrrole (14) with n-BuLi/TMEDA. (n-butyl lithium /tetramethylethylene diamine). The organosilanes showed high thermal stability and hence widely used in many applications (Scheme 6) [165].
Scheme 6: Synthesis of N-methyl pyrrole silanes

Welker et al. have reported 2-silicon substituted 1,3-diene triethoxysilanes (19) from 1,3 diene(18) which are further used for Diels-Alder/cross-coupling reactions and ligand exchange reactions and as described in Scheme 7 [166-167].

Scheme 7: Synthesis of substituted 1,3-dienes triethoxysilanes

Voronkov and his co-workers have synthesized numerous alkoxy silanes (22) using different routes. In general route, for the synthesis of heterylsilanes the sodium salt (20) of heterocyclic moiety is reacted with 1-chloromethyltriethoxysilane (21) as depicted in Scheme 8 [169-170].
Scheme 8: Synthesis of N-derivative trialkoxysilanes

Rinaldi et al. have reported the synthesis of (2-Trimethoxysilyl)ethyl(trimethoxysilyl)-Cyclohexane (24) by reacting 4-vinyl-1-cyclohexene, (23) trichlorosilane, and platinum-divinyltetramethylsiloxane complex (Scheme9) [171]

Scheme 9: Synthesis of silane derived from vinyl cyclohexane

Maegawa et al. have reported the well efficient approach for the synthesis of organic-bridged alkoxy silane (26) from ene (25). The silanes with triisopropoxysilyl group showed a good tolerance for various organic transformations and hence widely used in cross-coupling reactions (Scheme10) [172].
Murata *et al.* have reported trialkoxysilanes (29) synthesized from “Hiyama coupling” that involves the Pd(0) catalysed cross-coupling of organic halides (28) with organosilane (27) This method becomes the powerful and atom-economical method for synthesis of organosilanes [173].as it requires cheap starting materials having low toxicity (Scheme11)

Angelome *et al.* synthesized organosilanes(31) that involves clicking of mercaptosuccinic or mercaptoacetic thioacids with vinyltrimethoxysilane (30), using benzophenone as the photoradical initiator. This reaction allowed the formation of COOH-modified silica thin films in one step, without the need of hard reaction conditions or deprotection steps(Scheme12) [174]
Grignard’s reagents can be treated with suitable silicon electrophiles to yield trialkoxysilanes (32) (Scheme 13). The reaction results in lower yields and provides hindrance due to different electrophilic functional groups such as ketones, esters etc [175-176]

Schwartz et al. have reported various functionalized trialkoxysilanes (37) by reacting thiols (36) with allyltialkoxy silanes (35) or alkenes (34) with 3-mercaptopropyltrialkoxy silanes (33) using simple photoinitiated radical based thio-ene reaction as shown in Scheme 14 [177]
Singh et al. have synthesized chalcone holding triazole capped organotriethoxysilanes (OTES) (41) in good yield. The click methodology is followed for the functionalisation of acetylinic chalcones (39) with 3-azidopropyltriethoxysilane (40). The acetylinic chalcones formed from the o-alkylation (38) of commercially available hydroxyacetophenones. The synthesized compounds are well characterized by different spectroscopic techniques and are screened for photophysical studies (Scheme 15) [178].
Scheme 15: Synthesis of triazole encapped chalconyl substituted organotriethoxysilanes (OTES)
Singh et al have used one-pot, three component protocol for the synthesis of thioester allied organosilanes (43). The reaction proceeds via the 1,10-carbonyldiimidazole (CDI) mediated thioesterification of carboxylic acid (42) with mercaptopropyltrimethoxysilane (MPTMS). The product obtain have been characterized with elemental analysis, infrared and NMR spectroscopic techniques and further the different substituent effect analyzed by UV-spectra analysis (Scheme16) [179].
Jian et al have reported alkoxysilyl-functionalized poly(phthalazinone ether ketone) (PPEK) (46) from PPEK (44) followed by the ring-opening reaction of 3-glycidoxypropyltrimethoxysilane (GPTMS) (45). The product obtained showed wide application in micro-electro-mechanical system (MEMS). (Scheme 17) [180].

![Scheme 17: Synthesis of alkoxysilyl-functionalized poly(phthalazinone ether ketone)](image)

Singh et al. have synthesized polyfunctional triethoxysilanes (48) by click silylation via the chemical modification of 3-azidopropyltriethoxysilane (40) with a wide range of terminal alkynes (47) as depicted in Scheme 18. N-heterocycle, aniline, ether, acrylate, acetate, azomethine, aldehyde and ketone have been used as terminal alkyne functionalities [181].
Scheme 18: Synthesis of polyfunctional triethoxysilanes
Dey et al have synthesized layered inorganic–organic magnesium silicate (Mg-GTPS-TU) (51) using silylating agent GTPS-TU (50) derived from 3-glycidoxypropyltrimethoxysilane (GTPS) (49) and thiourea (TU) (Scheme 19) [182].

Scheme 19: Synthesis of layered inorganic – organic magnesium silicate (Mg-GTPS-TU)
Singh et al. have synthesized indole linked triazole silanes (54) from acetylenic indole Schiff bases (53). The reaction of indolecarboxaldehyde with the propargyl bromide gives the intermediate acetylinic indolecarboxaldehyde (52). The microwave and conventional method are used for the methodology. The synthesized products are further studied for the sensing applications (Scheme 20) [183]
Singh et al. have synthesized benzothiazole linked triazole-silane (56) from benzothiole based silane (55) and AzPTES (40) via Click chemistry approach. The products obtained are further studied for the biological evaluation and molecular docking approach (Scheme 21) [184].

Scheme 21: Synthesis of benzothiazole linked triazole-silane

2.2 Synthesis aspect of Silatranes

A.B. Finestone first prepared silatrane by azeotropic distillation of triethanolamine (58) and organotrialkoxysilanes (57) in benzene but he failed to isolate the pure 1-ethoxysilatrane (59) as depicted from its low melting point (35-37 °C) [185]. Then in 1961 Frye et al isolated first silatrane using similar methodology (Scheme 22) [186]
Vranken et al. have synthesized silatrane derivatives (61) from trisisopropanolamine (60) and phenyl and methyltrichlorosilanes by this route (Scheme 23) [187]. They have reported steric congestion among methyl groups leading to the reduction of the transannular Si-N interaction with increase in Si-N bond length to 2.32 Å than unsubstituted 1-methylsilatrane i.e. 2.17Å.

Lazareva et al. reported that trans-silylation of silatranes (62) by trialkoxysilanes (63) is a reversible and highly chemoselective process under MeONa catalysis and the results demonstrate a regular shift of equilibrium towards the formation of silatrane with shorter trans-annular N→Si bond [188] (Scheme 24).
Scheme 24: Synthesis of silatranes by trans-silylation.

‘Wongkasemjit’s method’ used in the synthesis of silatranes (65) from silica involves the reaction of fuming silica with trialkoxyamine (64) using triethylenetetramine as catalyst, and ethylene glycol as solvent medium. The water formed during the reaction is constantly removed and reaction mixture is refluxed at 200°C. The drawback of this methodology is the difficulty in separation of silatrane which is accompanied by silica (5%) (Scheme 25) [189,190].

Scheme 25: Wongkasemjit’s method’ of silatrane synthesis

Singh et al. have synthesized 1-Isothiocyanato-3,7,10-trimethyl-5-aza-2,8,9-trioxa-1-silabicyclo[3.3.3.0]undecane (67), by the transesterification reaction of trisisopropanolamine (60) and triethoxyisothiocyanato silane (66). The compound formation further confirmed by the Single crystal X-ray study [191] (Scheme 26).

Scheme 26: Synthesis of 1-isothiocyanatosilatrane
1-Chlorosilatranes (70) can be prepared by the reaction of the corresponding tris(2-hydroxyalkyl)amine hydrochlorides (69) with (2-chloroethyl)trichlorosilane (68) followed by β-elimination [192] (Scheme 27).

Scheme 27: Synthesis of 1-Chlorosilatranes

Singh et al. have reported series of functionalized phenyl unsymmetrical urea and thiourea possessing silatranes (72) in good yields by the rearrangement reaction of electrophiles 1-isocyanato-4-nitrobenzene, 1-isothiocyanato-4-nitrobenzene, 1-isocyanato-4-methoxybenzene, 1-isothiocyanato-4-methoxybenzene, 1-isothiocyanatobenzene with primary amines (71) [193] (Scheme 28).

Scheme 28: Synthesis of phenyl unsymmetrical urea and thiourea possessing silatranes
Singh et al. have synthesized unsubstituted and 3,7,10-trimethyl substituted organopropylsilatranes (74) by transesterification reaction of N-(3-trioethoxysilylpropyl)benzimidazole, and N-(3-trioethoxysilylpropyl)-2-isopropylimidazole (73) with triethaolamine and trisisopropanolamine (58,60) (Scheme 29) [194].

Scheme 29: Synthesis of unsymmetrical silatranes

Singh et al. synthesized series of substituted aniline derivatized bis(1,2,3-triazolyl-c-propylsilatranes(77). The reaction proceeds via the formation of substituted acetylinic aniline (75) and silane (76) The silatranes are explored for their thermal stability by thermogravimetric analysis (TGA)/differential thermal analysis (DTA)/differential scanning calorimetry (DSC) study and electronic properties by UV–vis spectroscopy and fluorescence study (Scheme 30) [127].
Scheme 30: Synthesis of substituted aniline derivatized bis(1,2,3-triazolyl-c-propylsilatranes

Singh et al have reported phthalimide linked trimethoxysilyl derivative (82) by transimidization reaction of phthalic anhydride (78) and (3-aminopropyl)triethoxysilane (80) using 2-(3-methylpyridin-2-yl)isoindoline-1,3-dione as intermediate (79) (Scheme31). Further transesterification reaction of produced silane (81) with triethanolamine and trisisopropanolamine gives the desired product. The products have been characterized by all spectroscopic, thermogravimetric and X-ray diffraction analysis (Scheme31) [195].
Singh et al have synthesized Schiff base silatrane by the transesterification reaction of triethoxysilanes with triethanolamine. The aromatic Schiff base (83) underwent o-alkylation with propargyl bromide (84) followed by the formation of Schiff base derived silane (85). Further transesterification with triethanolamine gives the desired silatrane (86). The synthesized compounds are well characterized by IR, NMR (1H, 13C), mass spectroscopy, elemental analysis and complete structure elucidation by X ray diffraction studies (Scheme 32) [196].

Scheme 31: Synthesis of phthalimide linked trimethoxysilyl derivative
Scheme 32: Synthesis of modified Schiff base silatranes
Singh et al have reported new unsymmetrically Substituted Urea enclosed Silatranes (87-90) in good yield by nucleophilic attack of N-methylbenzenamine, piperidine, 3-methylpyridine-2-amine and pyrrolidine containing active hydrogen on 3-isocyanatopropylsilatrane. The synthesized compounds are characterized by elemental analysis, IR, multinuclear (1H and 13C) NMR and mass spectrometry (Scheme 33) [197].

Scheme 33: Synthesis of new unsymmetrically Substituted Urea enclosed Silatranes
Recently Singh et al., have reported pyrene–functionalized silatrane (93,94). The 1-pyrenecarboxaldehyde (91) and aminopropylsilane (80) under refluxing conditions give pyrene functionalized silane (92) which on further transesterification with triethanolamine (58) and trisisopropanolamine (60) gives desired silatrane. The silatranes obtained high potential towards anti-oxidant, anti-giardiasis, and anti-trichomoniasis activity (Scheme 34) [198].

Scheme 34: Synthesis of pyrene –functionalized silatrane

Other Reactions:

- 1-fluorosilatrane (97) can be synthesized by the reaction of silatrane (96) with iodon trifluoromethane (95) in the presence of triethylamine in chloroform as solvent at 80°C [192] (Scheme 35).

Scheme 35: Synthesis of Fluorosilatrane
1-Allylsilatrane (98) can be modified into 1-iodosilatrane (99) by reaction with iodine. (Scheme 36) [192].

\[
\begin{align*}
\text{I}_2 + \text{H}_2\text{C} \equiv \text{CHCH}_2\text{Si(OCH}_2\text{CH}_2)_3\text{N} & \rightarrow \text{I}_2 \left(\text{CH}_2\text{Cl}_2\right) \rightarrow \text{H}_2\text{C} \equiv \text{CH}\text{I}
\end{align*}
\]

Scheme 36: Synthesis of 1-iodosilatrane from 1-allylsilatrane

Silatranes react with trimethylhalosilanes (100) in presence of various catalysts as morpholine, pyridine, quinoline, and N-cyanopiperidine to yield halosilatranes (101) (Scheme 37).

\[
\begin{align*}
\text{HSi(OCH}_2\text{CH}_2)_3\text{N} + \text{Me}_3\text{SiX} & \rightarrow \text{XSi(OCH}_2\text{CH}_2)_3\text{N} + \text{Me}_3\text{SiH}
\end{align*}
\]

Scheme 37: Trans-silylation using hydrosilatrane

Lazareva et al [199] synthesized 1-[(N-methyl-N-tritylamino)methyl]silatrane (103) from 1-(methylaminomethyl)silatrane (102) with Ph\(_3\)CCl in the presence of base (Scheme 38).

\[
\begin{align*}
\text{MeNHCH}_2\text{Si(OCH}_2\text{CH}_2)_3\text{N} + \text{TrCl,Base} & \rightarrow \text{MeNCH}_2\text{Si(OCH}_2\text{CH}_2)_3\text{N} \quad \text{Tr} = \text{Ph}_3\text{C}
\end{align*}
\]

Scheme 38: Synthesis of 1-[(N-methyl-N-tritylamino)methyl]silatrane

Sztorch et al [200] synthesized (E)–substituted alkenyl silatranes (106) using vinylsilatrane (104) and substituted styrenes (105) in the presence of ruthenium as an active catalyst (Scheme 39).

\[
\begin{align*}
\text{Ruc(O)(PCy}_3)_2 \quad \text{Toluene,120°C,85%} & \rightarrow \text{MeNHCH}_2\text{Si(OCH}_2\text{CH}_2)_3\text{N} \quad \text{RuHCl(CO)(PCy}_3)_2
\end{align*}
\]

Scheme 39: Synthesis of (E)–substituted alkenyl silatranes
3. Applications of Silanes and Silatranes:

3.1 Silanes:

Alkoxysilanes are key component for a variety of organosilicon compounds [201]. The polycondensation and hydrolysis of alkoxysilanes generates silsesquioxanes cage like structure. These silsesquioxanes act as a building block for the plethora of compounds that has numerous applications in area of material science, catalysis and coordination chemistry [202]. They are used in the formation of cross linked structures of hybrid polymers. The trialkoxysilane attached to the backbone of polymer when they reacts with the organic polymers. The silane reacts with the moisture to cross-link the silane into a 3D siloxane structure. The polyethylene and organic resins like urethanes and acrylics can be crosslinked using this mechanism [203-204]. Organosilanes are efficient adhesion promoters for inks, paints, coatings, adhesives and sealants. These are the strong aspirants for the adhesive bonding of aluminium and act as adhesion promoters between metal and paints such as polyureethanes [205]. Glycidoxypropyltrimethoxysilano (glymo) acta as an adhesion promoter between water based epoxy paint and sandblasted steel [206]. Azidopropyltriethoxysilane is used for the modification of silica surfaces to enhance the adhesion in fibre glass epoxy composites. The films of APTES are used in the adhesion of protein and metal nanoparticles adhesion to silica substrates by strong interactions between metal particles and amines. In addition, methacryloxypropyl trimethoxysilane is used in the formulation of dental adhesives. The organosilanes are widely used for the synthesis of various inorganic-organic hybrid materials. The alkoxysilane coupling agents improves the insulating, mechanical and thermal properties of organosilicon polymer [207-208]. It increases the resistance to moisture. The most common coupling agent is the 3-aminopropyltriethoxysilane (APTES). It also produces photoresponsive films on silica. 2-
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[acetoxy (polyethyleneoxy) propyl] triethoxysilane (SIA0078.0) is used is generating super hydrophilic coating material. It increases the antidust and self cleaning property of photovoltaic cells. They have been used as filler modifying agents that enhanced the filler dispersion state in polyolefin and polyurethane matrices thereby improving its composite properties. They have been used in the preparation of flame retardant composites. Methyltrimethoxy silane is also used as a silane coupling agent. Some hybrid material derived from sol-gel processes are most promising NLO materials because of its high thermal stability, low optical propagation loss and ease of device fabrication. NLO active dye 4-nitro-4-hydroxy-azobenzene and 3-isocyanatopropyltriethoxysilane are used in the synthesis of alkoxy silane dye which shows the excellent NLO activity in which the –NO$_2$ group acts as acceptor and –OH group as donor [209]. The alkoxy silanes are used as external donor in Ziegler-Natta catalyzed polymerization. It helps to control the stereochemistry of resulting polypropylene by using specific organosilanes [210]. The alkoxy silanes are used for the hydrophobicity of various materials used in chemical, construction, and textile industry [211]. These hydrophobic cross-linked networks of alkoxy silanes have strong tendency to absorb oils. In addition, they are used as additives for wood preservatives [212]. The silanes form stable Si-O-C and Si-O-Si bonds with the wood surface, reducing its hydrophilicity. Methyltrimethoxysilane (MTMOS) is used as a potential stabilization agent for waterlogged wood treatment. The aromatic alkoxy silanes are used in achieving hydrophobic structure [213-214]. The amino trimethoxysilanes are used in organic coating to improve the corrosion protection properties of steel by generating a protective barrier layer between the steel substrate and corrosive environment [215]. Ramezanzadeh et al found that the mixture of silanes i.e the mixture of tetraethylorthosilicate (TEOS) and (3-Aminopropyl) triethoxysilane (APTS) results in the more compact film formation giving better anti-corrosion properties than that when used separately. The silanes contain hydrolysable ethoxy or methoxy groups which on hydrolysis with water converts to hydrophilic silanol groups (Si-OH). The silanol groups interact with metal hydroxide i.e Me-OH groups through H-bonding. In the next step i.e curing the condensation reaction results in the formation of metallo-siloxane covalent bonds (Me-O-Si) which increases the adhesion of silanes to substrates. The alkoxy silanes are used as a key component in high performance paints and coatings because of its tendency to react with inorganic substrates such as minerals, glass, and organic materials. The alkoxy silane coating can provide resistance to chemicals, UV-radiations and moisture [216]. APTES is used
for the surface modification of glass substrates via silanization process. The grafting and co-condensation are employed for the further functionalization. The use of silane coupling agents to attach various polymers and biomolecules to glass surfaces becomes the area of prime importance. In addition, these silanes are important precursors for the fabrication of attractive luminescent materials. 3-aminopropyltriethoxysilane (APTES) and vinyltrimethoxysilane (VTMS) are used in the preparation of polypropylene clay nanocomposites that are used as nanofillers for PP at different concentration [217-218].

3.2: Silatranes:

Silatranes have been used in rubber composition to improve adhesion properties. Aminopropylsilatrane (APS) provides nonaggregated adhesive layer and reproducibly high quality film for anchoring nanoparticles strongly to silica substrates [219]. The silatrane based polymers are designed which are being used as adhesion promoters, catalyst support and molding material. The silatranyl moiety in the polymers helps in forming electric insulating coating films having good dielectric constant with uniform thickness [220].

Voronkov studied the specific biological activity of 1-arylsilatrane which led to discovery of other biological aspects of silatranes due to the interactions of silatrane structure with biological membranes:

(i) Voronkov et al. have discovered specific biological activity of 1-Chloromethylsilatrane (CMS). It prevents the loss of calcium from the bones of skeleton [221]. CMS owns immunotrophic properties and helps restoring the eye tissue without cicatrix and wound suture and prevent leukoma formation. CMS significantly increases the collagen level providing the confirmation of its anti-inflammatory activity. 1-Chloromethyl-3,7,10-trimethylsilatrane inhibits growth of some transferred and carcinogen-induced tumors. Silatranes display biological activity against k562 oncocytes of erythroleukemia [222].

(ii) 1-ethoxysilatrane is involved in the development of connective tissue resulting in accelerated healing of wounds, ulcers and burns. 1-Ethoxy- and 1-methoxy-silatrane markedly inhibit the growth of a range of tumors in animals and improves productivity of farm animals, birds and beneficial insects [223].

(iii) Hypervalent silicon complexes produced by incorporating a 5-fluorouracil moiety are also active for treating cancer [224].
(iv) 3’-O-(trimethyl)silatranylthymidine, incorporated within a nucleoside, possess antiviral activity due to transition-state analogs for phosphoryl transfer reactions. These silatranes have also been found to be active for treating cancers of breast, central nervous system and lung [225].

Singh et al. have synthesized a series of chalconyl blended triazole linked silatranes in good yields using click silylation pathway. The unification of three different pharmacologically active moieties into a single molecular scaffold resulted into synergistic effect in their bioactivity. Various substitutions were also tried to study the structure activity relationship (SAR) of the synthesized compounds. These compounds when screened for their physico-chemical properties using Molinspiration software depicted good oral bioavailability. The antiparasitic activity of the newly synthesized compounds was evaluated against unicellular parasites (G. lamblia and T. vaginalis) in comparison to standard drug (metronidazole) by 3-(4,5-dimethylthiazolyl)-diphenyl tetrazolium bromide (MTT) assay. All the compounds displayed considerable activity against G.lamblia and T.vaginalis with comparable IC$_{50}$ values [226]. Silatranes are widely used in DNA imaging. The reliable imaging of DNA is obtained by modifying the surface of mica using aminopropyl silatranse. The silatrynyl unit consist of Si-N transannular bond , due to its donor acceptor properties these silatranes play a key role in Atomic Force Microscopy [227-228]. Singh et al studied the role of alkyl silatranes as plant growth regulators in root and shoot development of wheat and maize [229]. The new silatranes are derived from the aminopropylsilatranes by the derivatization of amino groups. The silatranyl component found many applications in various organic reactions such as ring opening reactions, palladium-catalyzed cross-coupling reactions, as reducing agent in organic, organometallic chemistry and aldol reaction. They are being used as coupling agents for silatran containing polymers. They are used as catalytic support, molding material and in non-linear optics. They form complexes with the transition metal ion when properly derivatized [230-231]

Siliceous materials such as silica shells, silica nanospheres and molecular sieves act as inorganic solid support for inorganic–organic hybrid materials because of its high thermal and mechanical stability, high surface area and surface modification flexibility, biocompatibility and connection feasibility with other functional group. For the incorporation of organic moiety over the silica surface the organosilanes are used as the precursors. However the organosilanes have the property of agglomeration and polymerization resulting in irregular surface morphology. So the
silatranes are used as precursors as they are more stable than their open chain analogues. The triethanolamine-capped trialkoxysilanes, i.e silatranes having silicon atom locked into a caged position, have more hydrolytic and environmental stability, purification ease and less polymerization chances. The number of hybrid material has been synthesized using silatranyl group. The whole process occurs via nucleophilic attack by the surface hydroxyl groups on the silicon site forming siloxyl bonds on the surface. The hybrid materials have found promising application in diverse fields including, solar photovoltaic cells, DNA imaging, heterogeneous catalysis and chemosensing [232-233].

4. Aim of the Thesis:

The aim of the thesis is to develop a new class of organosilanes and silatranes ligated with various flexible ligands that are ideal for the detection of heavy metal ions. These heavy metal ions are the major environmental pollutants when exceeds above threshold level proved to be dangerous to human beings. Some heavy metal ions regulate certain pathway mechanism in the human body. So the determination of HTM’s without the need of expensive technology becomes the area of urgent concern. The prime aim of chemist is to design more efficient methodologies and chemical reactions that can overrule the more time consuming purification steps in the conventional total synthesis and developed the future chemical and biological research in this field.

An investigation towards the synthesis of organosilicon compounds mainly trialkoxysilanes and silatranes is still a great challenge that is hooked with numerous applications. Several methodologies have been used for the synthesis of substituted trialkoxysilanes but they require tedious purification steps. So new synthetic approach has been developed named ‘Click Chemistry’ approach. It involves the cyclization of various functional alkynes with azidopropyltriethoxysilanes (AzPTES) to give active chemosensors. The copper catalysed azide alkyne cycloaddition (CuAAC) reaction show wide range of applications due to its 1,2,3-triazole core. In order to found the efficacy of these 1,2,3-triazole based trialkoxysilanes, we used it as a precursor moieties for the synthesis of silatranes linked with heterocyclic moiety through propyl chain. The instigation of capping agent onto silanes results into compounds that found number of application in the diverse field of biomaterial science,
nanoscience, catalysis, immobilization and polymer chemistry. With this perspective, the silatranes are generated using click reaction with functional alkynes. In addition, the organosilicon derivatives have the tendency to be moved onto silica based inorganic-organic hybrid nanocomposite. Therefore, a new protocol is proposed that involves the anchoring of organosilatrane onto magnetic silica surface for the construction of organic-inorganic hybrid nanoparticles (HNPs). So the thesis aims for the development of sensing strategies for the recognition of heavy metal ions without any need of expensive technology and generating H-NPs that serve as a large application in the diverse field of science.

5. References:

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