

# **Self-Assembled Metal-Organic Cages and their Host-Guest studies**

*A Thesis*

*Submitted in partial fulfilment of requirements for the  
BS-MS Dual Degree Programme*

*by*

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*Under the guidance of*

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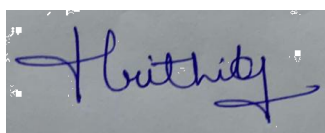
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**April, 2020**

# Certificate

This is to certify that this dissertation entitled “**Self-Assembled Metal-Organic Cages and their Host-Guest studies**” towards the partial fulfilment of the BS-MS dual degree programme at the Indian Institute of Science Education and Research, Pune represents study carried out by **Hrithik Gudapati (20141170)** at Indian Institute of Science Education and Research under the supervision of **Prof. R. Boomi Shankar**, Professor, Department of Chemistry, during the academic year 2019-2020.



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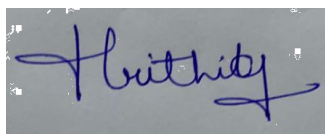
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## Declaration

I hereby declare that the matter embodied in the report entitled “**Self-Assembled Metal-Organic cages and their Host-Guest Studies**” are the results of the work carried out by me at Department of Chemistry, Indian Institute of Science Education and Research, Pune, under the supervision of **Prof. R. Boomi Shankar** and the same has not been submitted elsewhere for any other degree.



Hrithik Gudapati

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Prof. R. Boomi Shankar

Supervisor

**This thesis is dedicated to**  
**My Family & Friends**

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# Table of Contents

<b>Acknowledgements</b> .....	<b>6</b>
<b>Abstract</b> .....	<b>13</b>
<b>Chapter 1: Introduction</b> .....	<b>14</b>
1.1 Introduction to MOC.....	14
1.2.1 Cancer Therapeutics.....	15
1.2.2 Ion exchange.....	15
1.2.3 Carbon dioxide capture.....	16
1.2.4 Guest Trapping and Protection.....	17
1.3 Preparation Methods.....	18
1.3.1 Symmetric Interaction.....	18
1.3.2 Face-Directed Assembly.....	19
1.3.3 Weak-Link Approach.....	20
1.3.4 Directional Bonding and Reticular Chemistry.....	21
1.3.5 Molecular Library Model.....	22
<b>Chapter 2: Materials and Methods</b> .....	<b>23</b>
2.1 Experimental Material.....	23
2.2 Synthesis of Ligands.....	23
2.2.1 Ligand 1.....	23
2.2.2 Ligand 2.....	24
2.2.3 Ligand 3.....	24
2.2.4 Ligand 4.....	25
2.2.5 Ligand 5.....	26
2.2.6 Ligand 6.....	26
2.2.7 Preparation of (Zr-Nap Cage).....	27
2.2.8 Preparation of (Zr-Cycl hexyl Cage).....	27
2.2.9 Preparation of Zr-Isophthalic Cage.....	28
2.3 General Procedure for preparation of Guest-Host Assemblies.....	28

<b>Chapter 3: Results and Discussion</b> .....	<b>29</b>
3.1 Synthesis and structures of the self-assembled cages.....	29
3.2 Interaction studies for PX $\subset$ Zr-Nap MOC.....	29
<b>Chapter 4: Conclusion</b> .....	<b>39</b>
<b>Chapter 5: References</b> .....	<b>40-41</b>
<b><u>Supplementary Data</u></b> .....	<b>42-47</b>



## List of Figures

Figure No.	Title	Page No.
1	Ion Exchange between cages	16
2	Encapsulation of CO <sub>2</sub> by Ni <sub>14</sub> L <sub>24</sub> cage in methanol solution	17
3	Encapsulation of White phosphorus, an air-sensitive chemical warfare agent	18
4	Procedure for designing metal cages	19
5	Conversion of a truncated structure from a Platonic solid to Archimedean solid using Face-Directed Assembly	20
6	Strategy for development of the Weak-Link Approach (WLA)	21
7	Formation of Organometallic bonds	22
8	MALDI-TOF mass spectra for Zr-Nap MOC	30
9	View of the Zr <sub>3</sub> -core (top) and the SCXRD structure (bottom) for Zr-Nap MOC	32
10	MALDI-TOF mass spectrum of Zr-Cycl-Hexyl MOC	32
11	View of the Zr <sub>3</sub> -core (top) and the SCXRD structure (bottom) for Zr-Cycl Hexyl MOC	35
12	MALDI-TOF mass spectrum of PX ⊂ Zr-Nap MOC	35
13	UV-VIS titration data for PX ⊂ Zr-Nap MOC	36
14	PX ⊂ Zr-Nap MOC using UV-VIS spectroscopy	38

## List of Schemes

Scheme No.	Title	Page No.
1	Synthesis of Ligand 1	23
2	Synthesis of Ligand 2	24
3	Synthesis of Ligand 3	25
4	Synthesis of Ligand 4	25
5	Synthesis of Ligand 5	26
6	Synthesis of Ligand 6	27

## List of Tables

Table No.	Title	Page No.
1	Crystallographic Details for Zr-Nap cage	30
2	Crystallographic details of Zr-Cycl-Hexyl cage	33
3	Association constant for PX $\subset$ Zr-Nap MOC	37

## Abbreviations

MOC	Metal-Organic Cages
WLA	Weak Link Approach
TMS	Tetra-Methyl Silane
Zr	Zirconium
MALDI-TOF	Matrix-Assisted Laser Desorption/Ionization – Time of Flight
UV-VIS	Ultraviolet-Visible
HRMS	High Resolution Mass Spectrometry
MeoH	Methanol
mg	Milligram
mmol	millimolar
SCXRD	Single Crystal X-ray Diffraction
Nap	2,6-Napthelene di-carboxylic acid
Cycl Hexyl	1,1'-Bi(cyclohexyl)-4,4' dicarboxylic acid

## Abstract

Metal organic cages are a class of materials that are emerging as potential candidates for their excellent host guest binding abilities. These are essentially metal-based assemblies and have metal-organic (MOPs) frameworks and have inbuilt well-defined cavities with engineerable pores dimensions that make them so distinct. These well-built cavities for example in case of palladium derived cages have been used as catalyst for enantioselectivity. The applications of metal organic cages however are hindered due to their poor stability due to complex aqueous solution dynamics and short lived and unstable intermediates during their preparation. The work done in this project highlights the synthesis of ligands with the purpose of improving the synthesis of cages in solution state. The approach is based on hetero atom ligands containing phosphorus-nitrogen bonds due to their ease of bond formation and these form chemically stable bonds. Amongst various phosphorus nitrogen-based compounds the Amido and imido P(V) compounds, analogues to phosphorus oxo-groups, are very interesting molecules to work with, in the development of metal organic cages. The stout P- N bonds are capable of forming ligands used for the synthesis metal complexes. In my lab, amino P(V) backbones are employed as attractive platform for synthesis of multipurpose ligands. In polar solvents, soft transition metal ions such as Pd(II) are employed for development of P(V) bound poly imido species. In addition, we have also attempted to explore Zirconium carboxylate Cages, which to our knowledge has not been studied with respect to host-guest studies. These studies revealed that one of the cages, Zr-Nap cage, exhibits selective binding p-Xylene over its other ortho- and meta-isomers as indicated by mass spectral analysis and host-guest binding constants obtained from UV-VIS titrations.

# Chapter 1: Introduction

## 1.1 Introduction to Metal-Organic Cages

Metal–organic cages (MOCs) are distinctive metal-based assemblies of metal-organic polyhedra (MOPs) and are prepared from self-assembly of molecular structures having coordination bonded metal nodes and organic ligands<sup>[1]</sup>. Metal-organic cages (MOCs) represent an enticing class of metal based organic materials based on their host-guest binding ability and their excellent and well-defined cavities with engineerable pores dimensions <sup>[2]</sup>. Coordination-driven self-assembly is a prevailing method because unlike the other non-covalent interactions metal–ligand bonds are directional in nature as well as relatively robust. This method is one of the important methods because this leads to the formation of the rigid electron-deficient and electron-rich metal centres which leads to the wide variety of distinct stable supra-molecular structures which are thermodynamically stable. Studies from various laboratories have shown the synthesis of multifunctional MOPs and developed as molecular recognition materials exhibiting unique biological activity, confiscation of reactive species, catalysis and gas and ions adsorption and separation<sup>[3]</sup>. Self –assembly of MOPs have led to hierarchical coordination networks such as metal-organic squares and octahedrons with varying dimensionalities and topologies <sup>[4]</sup>. Despite their various applications, the development of the MOCs suffers with various challenges due to complex solution dynamics and the unstable nature of the intermediates during the preparation of such cages. Amongst many applications,

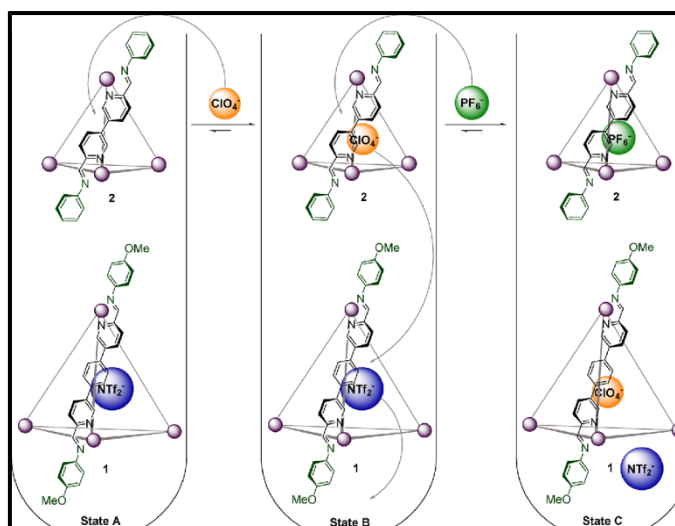
the host encapsulation of guests is very attractive. They are crucial in many aspects such as gas absorption, chiral molecules separation in medicines, biomedical devices etc. the present work emphasises on the synthesis of carboxylate ligand-based zirconium cages and their potential as host guest systems <sup>[5][6]</sup>.

### **1.2.1 Cancer Therapeutics:**

Therapeutics based on metal-organic cages have attracted a great deal of attention due to their potential application against cancerous cells. As a proof-of-concept Han et al have reported an octahedral Pt<sub>6</sub>L<sub>4</sub> Cage, developed from self-assembly of 1,10-phenanthroline-Pt(II) as centres and 2,4,6-tris(4-pyridyl)-1,3,5-triazine ligands, and have demonstrated enhanced bio-availability against chemo-resistant ovarian cancer cells<sup>[7][8]</sup>. They showed that the highly hydrophobic Pt<sub>6</sub>L<sub>4</sub> Cage could be stabilised and delivered in as high as 0.4 mM concentration to cells.

### **1.2.2 Ion Exchange:**

Ion exchange application has been demonstrated by metal organic cages forming groundwork for sequential multi step transformations. Shucong et al have shown metal-organic hosts and multiple guests where transfer of guest between hosts depends upon the differential binding affinities of hosts and guests whenever there is addition of a competing guest <sup>[9,10]</sup>. The schematic of the Ion exchange has been shown in Figure 1<sup>[10]</sup>.



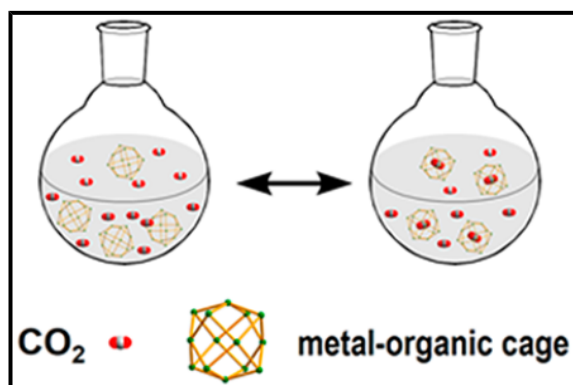
**Figure 1:** Two cages have been shown where both Cages 1 and 2 are cationic. It has been shown that the Cationic Tetrahedral cage retains a large cavity which allows the selective binding of Triflimide anion among a selection of anions. Furthermore, Interaction between the equimolar solution of larger cage and smaller cage with the anions has also been studied thoroughly. As a result, it demonstrates the role of binding affinities due to the anion exchange sequences between two cages in designing sequential reactions where guest passes from one host to another <sup>[10]</sup>

### 1.2.3. Carbon dioxide capture:

Metal organic cages also have found their use in capturing the gases such as CO<sub>2</sub>. For example, studies from the literature where Xiang group have studied controlled aperture for CO<sub>2</sub> encapsulation specifically and they have developed a series of Ni-Imidazolate cages which are basically rhombic dodecahedral and they provide tunable apertures to the cages assemblies via ligand decoration<sup>[11]</sup>. This was compared to the breathing function of lung alveoli. In methanol solution and under a pressure of 2.0–3.0 bar, CO<sub>2</sub> would be absorbed in the MOC and at lower pressures it is released thereby showing the versatile nature of breathing cages.



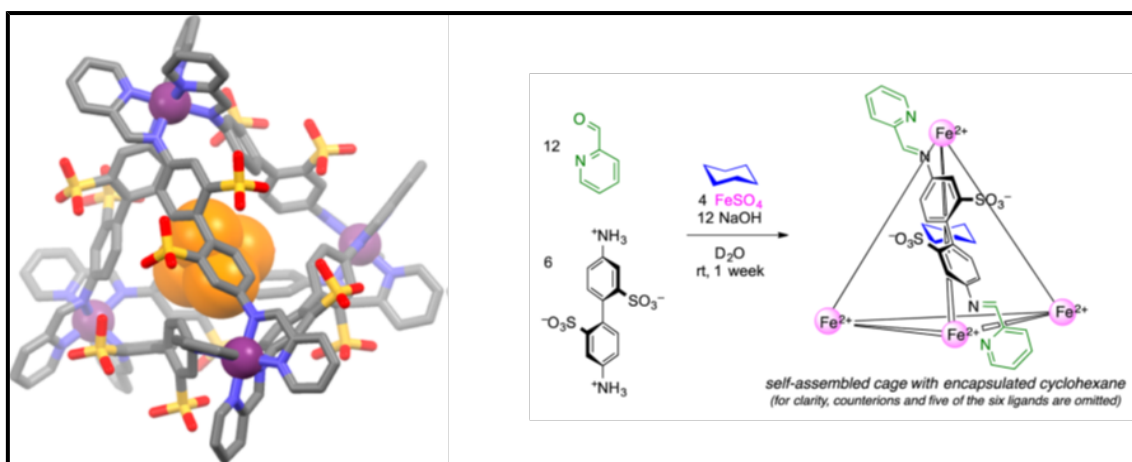
Even in the solid state at very high pressure of 15.0–30.0 bar CO<sub>2</sub> was found to be encapsulated in these cages (Fig.2)



**Figure 2:** Encapsulation of CO<sub>2</sub> by Ni<sub>14</sub>L<sub>24</sub> cage in methanol solution has been shown <sup>[16]</sup>.

#### **1.2.4. Guest Trapping and Protection:**<sup>[12]</sup>

Over the past decades, advancement in Host-Guest chemistry have led to many unique Metal-Organic Cages (MOCs) which have unambiguous shapes and cavities<sup>[12]</sup>. Eun Bin Go et al have demonstrated the self-assembling of an iron tetrahedral cage in D<sub>2</sub>O at room temperature capable of capturing small and neutral cyclohexane or tetra-hydro-furan molecules (Fig.3). Among all of the advantages, drug delivery is one of the significant advantages because there are a lot of drugs available which are insoluble and hence host-guest interactions provides one of the convenient ways regarding the delivery of the drug to the targeted molecule and hence plays a huge role in regulating therapeutic implications.



**Figure 3:** Encapsulation of White phosphorus, an air-sensitive chemical warfare agent has been shown. The figure also shows the development of iron cage development and encapsulation <sup>[4]</sup>.

### 1.3. Design Strategies for the preparation of MOCs:

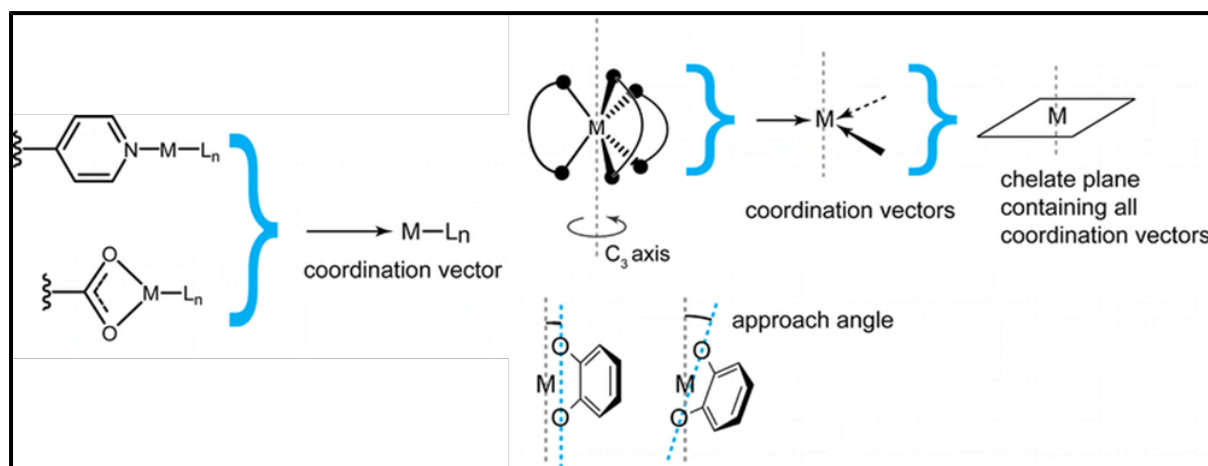
There are numerous methodologies to develop MOC. Amongst many methods, the most important methodologies for development of MOC have been explained briefly below.

#### 1.3.1. Symmetric Interaction:

The Symmetry-Interaction method engages tetrahedral metal centres as nodes which are uncapped. Discrete systems are developed successfully with no capping ligands, and the spacers imposed in a structural convergence manner. This can be attained by designing poly-topic chelating ligands such that these can occupy all accessible coordination sites. These coordination sites belong to the metal nodes and thus it strictly preserves directionality <sup>[13]</sup>.

This methodology is derived from Edge-directed Self Assembly which is very sensitive and depends on a very crucial parameter during the ligand designing for symmetry-interaction self-assembly<sup>[14]</sup>. This defines the angularity and the

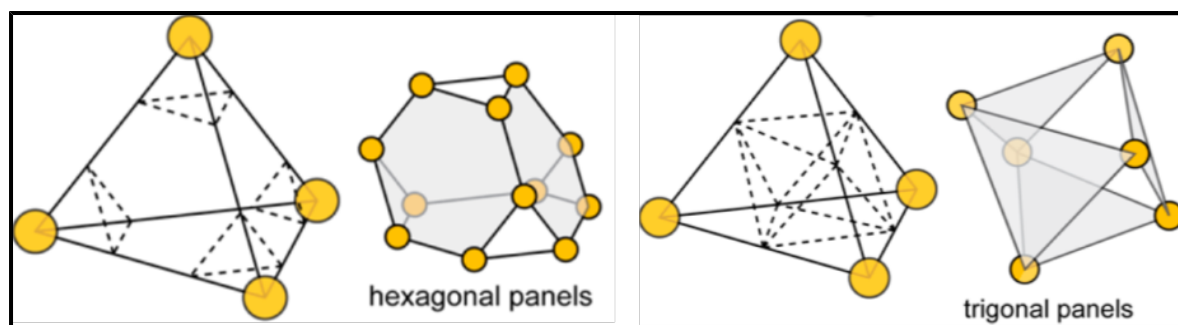
directionality of molecular binding blocks which are very critical during this process (Figure 4). One of the most eventually concluding parameter which is essential for stable and enlightened designing using the Symmetry-Interaction approach: “Approach Angle”. Approach Angle is basically defined as the angle formed between the principal rotation axis of the metal centre and the line defined by the two co-ordination atoms of the following chelating ligands (Fig.4)



**Figure 4:** The important principle and criteria has been shown in this figure to design metal organic cages. It has been shown that Co-ordination vectors play a crucial role in designing such Cages<sup>[13]</sup>.

### **1.3.2. Face-Directed Assembly:**

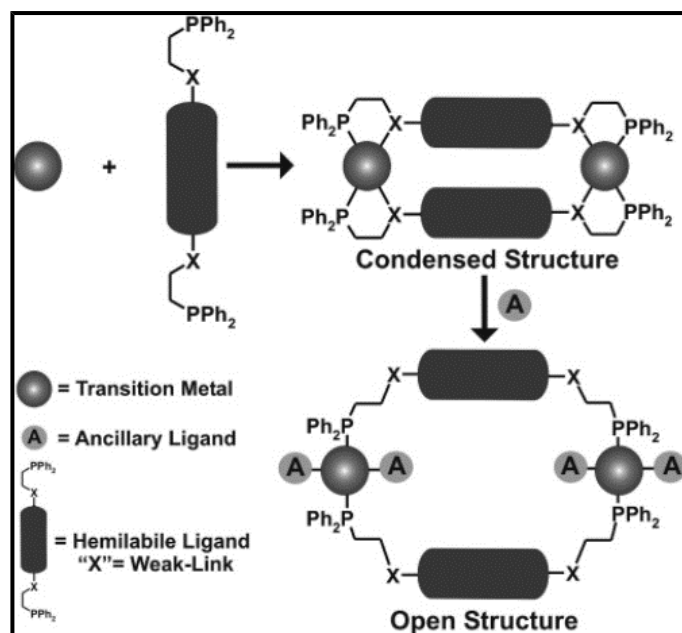
Face-Directed Assembly is one of the subsets of the directional bonding which allows us to interpret the 3D architecture of their faces including relatively smaller prisms and truncated tetrahedral structures to the larger sub octahedral structures which are comparatively and significantly larger <sup>[15]</sup>. The replacement of an n-connected node with a group of n nodes, a process that is known as augmentation <sup>[16]</sup>. A tetrahedron contains four vertices as three-connected nodes. Replacing three by three new nodes, an augmented structure is created. Archimedean solid is truncated from a Platonic solid in case of tetrahedron (Fig.5).



**Figure 5:** Conversion of a truncated structure: Archimedean solid using Face-Directed Assembly has been shown in this figure<sup>[13]</sup>

### **1.3.3. Weak-Link Approach:** <sup>[17]</sup>

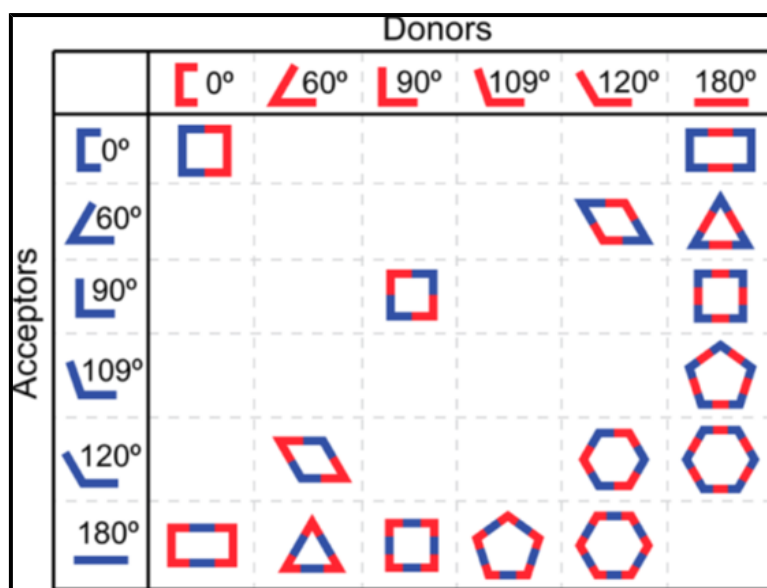
Weak-Link Approach (WLA) is one of the assembly processes which is based on co-ordination chemistry and this is essential for the formation of flexible architectures which have multi-domains and supra-molecular configuration. It utilizes the same metal which is involved in this approach for further available reactions without any disturbance to the supra-molecular structure which has been formed earlier. This approach hugely contributes towards the accessibility of a wide variety of flexible 2D and 3D supra-molecular structures because of the engagement of various thermodynamically and kinetically controlled elements with enormous tolerable properties. Interaction between these stable five membered chelate rings about the metal centres and various  $\delta$ - $\delta$  interaction leads to the formation of these supra-molecular structures <sup>[18,19]</sup>. In order to generate flexible macro-cyclic structures with high quantitative yield, small molecules or ions are delivered that have greater affinity towards the metal centre leading to the cleavage of the selective and specific weaker metal heteroatom bonds (Fig6).



**Figure 6:** Strategy for development of the Weak-Link Approach (WLA) has been shown<sup>[20]</sup>

### 1.3.4. Directional Bonding and Reticular Chemistry:-

Starting with 2D architectures, a wide variety of macro-cycles of specific shapes have been developed by designing optimal Organic Ligands and Metal accommodating the edges and vertices of the target molecule. This approach is called “Edge-Directed Self-Assembly” rather than “Face-Directed Self-Assembly” as panels occupy the faces of a 3D structure <sup>[21,22]</sup>. It is possible to develop a regular convex polygon which requires internal angles of less than 180° and uniform length of all the sides <sup>[23]</sup>. Upon breaking this particular polygon along its edges leads to the formation of the fragments which has symmetry of 2-fold symmetry at a maximum scale (Fig.7).



**Figure 7:** Formation of Organometallic bonds has been shown in this figure.

### 1.3.5. Molecular Library Model:

Molecular Library model approach involves highly directional multi-branched and rigid mono-dentate ligands. Transition metal complexes via dative bond interactions. This includes a transition metal is highly possible to achieve using this technique by estimating the appropriate angles between the binding sites of the donor and acceptor subunit<sup>[24] [25]</sup>. These subunits can also be differentiated into two categories on the basis of the Binding angle value: 1) Linear Rod-like Subunits (L) which are opposite to each other (present at 180°) and 2) Angular Subunits (A) due to the enclosure of angles between 0° and 180°<sup>[17]</sup>. As a consequence, shapes of Mono-cyclic and poly-cyclic entities will resemble the structures of complex polygon and canonical polyhedral, respectively<sup>[18]</sup>.

In the present work I have utilised a cluster of three metals centre as a single trimeric centre for development of the MOC. These are transition elements and have been least explored. The two projects that I worked have been discussed in subsets which involves the attempt to synthesize Palladium and Zirconium based cages.

# Chapter 2: Materials and Methods

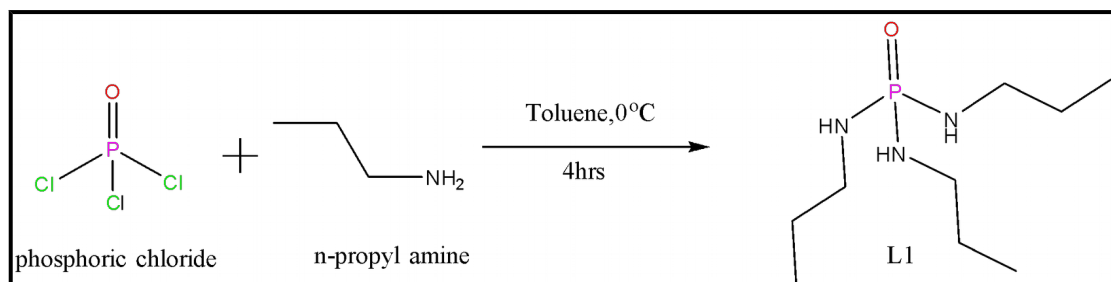
## 2.1 Experimental Material:

Manipulations have been done including phosphorus in the presence of dry nitrogen atmosphere in a standard Schlenk glassware. After the solvents were dried over potassium (thf, hexane) or sodium (toluene), <sup>1</sup>H NMR spectra were recorded on Bruker Advanced 400 MHz DPX spectrometer using 1,1,1,1-tetramethyl silane (TMS) as an internal standard.

## 2.2 Synthesis of Ligands:

### 2.2.1. Ligand 1

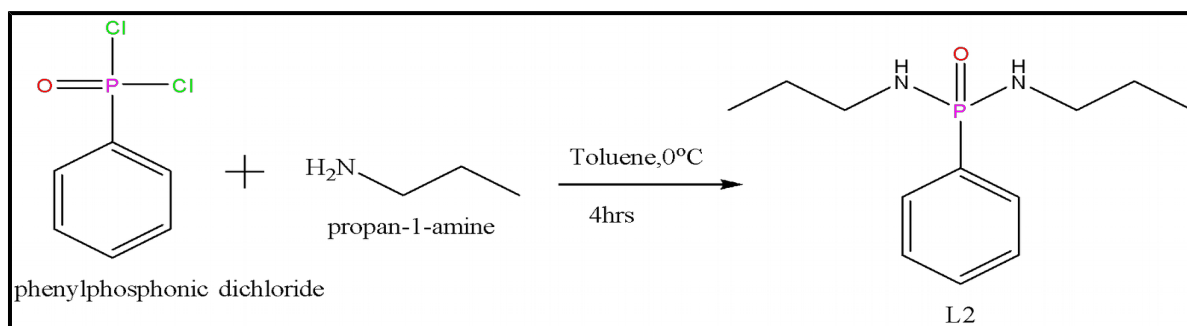
In excessive presence of n-propyl amine (9.58 mL, 7.583 g, 0.282 mol), POCl<sub>3</sub> (5 mL, 8.23 g, 0.0536 mol) was added drop wise in toluene (250 mL) at 0 °C. The solution which was prepared with the above reaction was brought down to the room temperature and stirred for 4hrs and the product was filtered and precipitate had been removed. The filtrate was reduced to 80ml and 50ml of hexane was added to it which was then kept at -15 °C for two days to yield a white impure solid of 63% which was purified to yeild 58%.



Scheme - 1

### 2.2.2. Ligand 2

For the preparation of following ligand,  $\text{PhPOCl}_2$  (2mL, 2.75 g, 0.0141 mol) was added dropwise in n-propyl amine (5.79 mL, 4.168 g, 0.0705 mol) which is present in excess in the solution and then the process had been followed by addition of toluene (100 mL) at 0 °C. Then the resulting mixture was brought to room temperature and stirred for 4 h which was followed by the filtration to remove the precipitate. The filtrate was reduced to 80 mL, and then hexane (50 mL) was added to it which led to the formation of the mixture. The mixture was kept at -15 °C for two days to yield a white impure solid of 72% which was then purified to yield 64%.



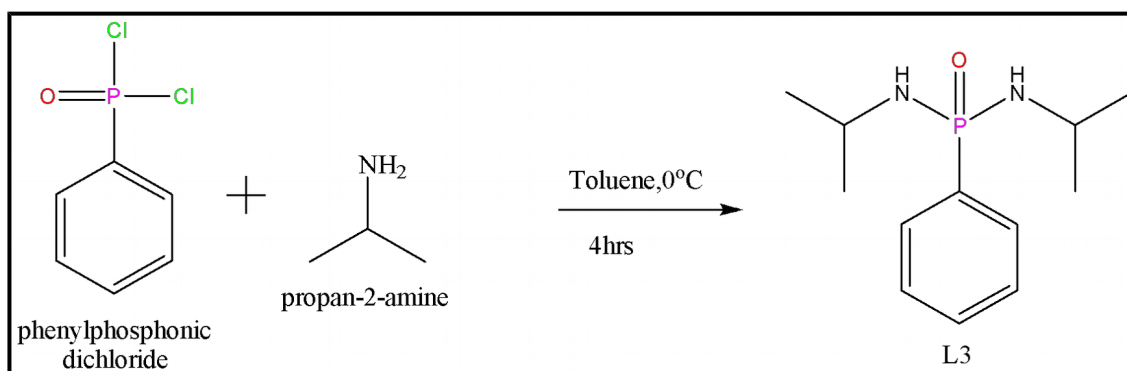
Scheme - 2

### 2.2.3. Ligand 3

For the preparation of particular ligand,  $\text{PhPOCl}_2$  (2mL, 2.75 g, 0.0141 mol) was added dropwise to an excess of iso-propyl amine (6.058 mL, 4.168 g, 0.0705 mol) and then toluene (100 mL) was added to it at 0 °C. The resulting mixture was slowly brought down to the room temperature and stirred for 4 h. After that, Filtration had been done to remove precipitate. The filtrate was reduced to 80 mL and then hexane (50 mL) was added to it to prepare the final mixture which



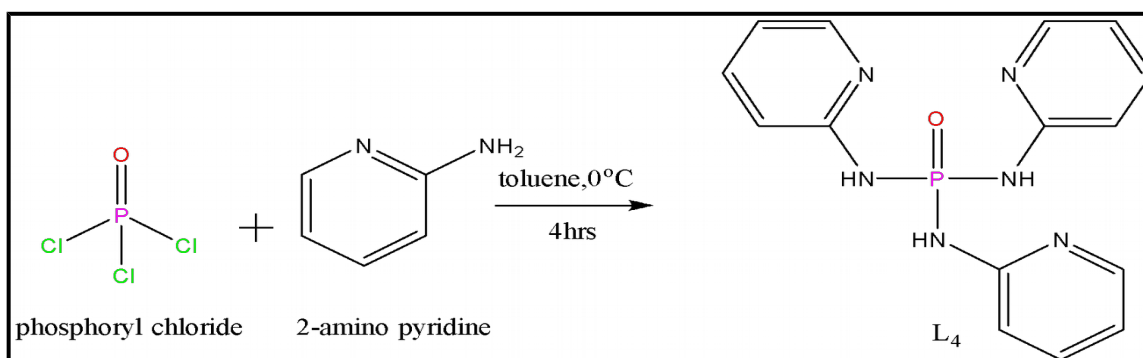
was kept at  $-15\text{ }^{\circ}\text{C}$  for two days to yield 56% white impure solid which was then purified to an yield of 49%.



**Scheme - 3**

### **2.2.4. Ligand 4**

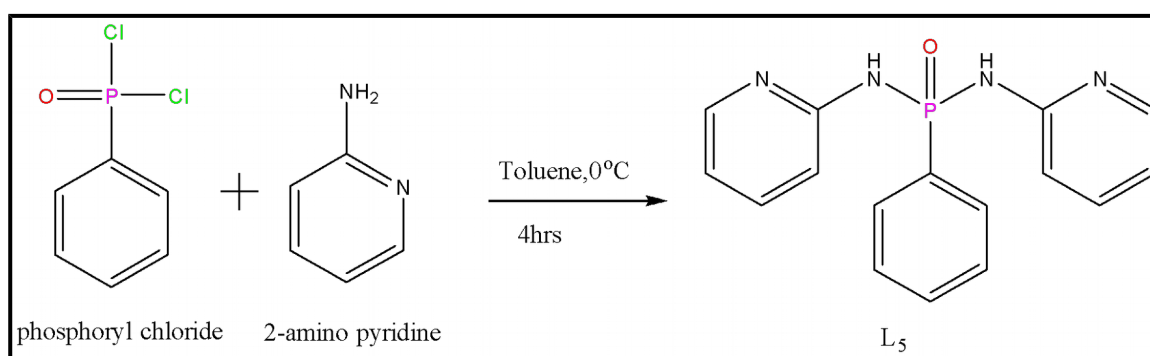
In order to prepare this compound,  $\text{POCl}_3$  (0.5 ml, 0.82 g, 0.00534 mol) was added slowly and drop wise to an excess solution of 2-amino pyridine (1.509 g, 0.01604 mol) in toluene (100 mL) at  $0\text{ }^{\circ}\text{C}$ . The resulting mixture was slowly brought down to the room temperature and stirred for 4 h. This procedure was followed by filtration in order to remove iso-propyl ammonium chloride which precipitated in the following reaction. The filtrate was then reduced to 80 mL, to which 50ml of hexane was added. The mixture was kept at  $-15\text{ }^{\circ}\text{C}$  for two days to yield a white impure solid of 75% which was purified to yield 69%.



**Scheme - 4**

### 2.2.5. Ligand 5

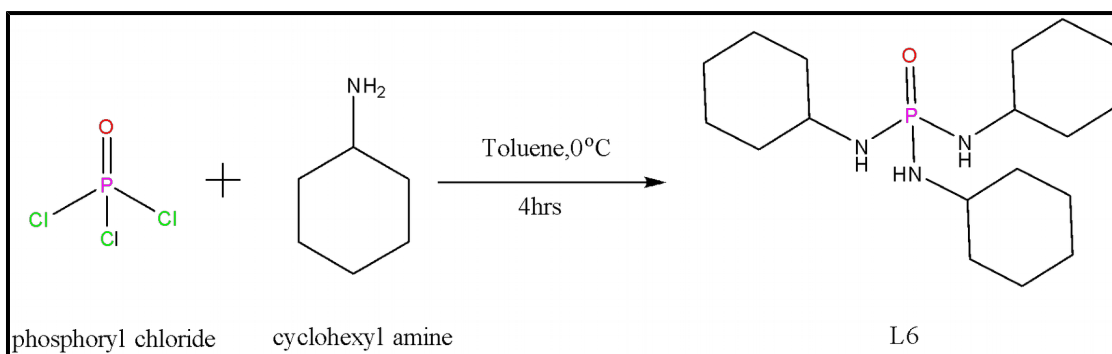
For the preparation of this ligand,  $\text{PhPOCl}_2$  (0.5 ml, 0.687 g, 0.00384 mol) was added drop wise to an excess amount of 2-amino pyridine (0.723 g, 0.00768 mol) in toluene (100 mL) at 0 °C. The resulting mixture was slowly brought down and cooled down to room temperature and stirred for 4 h and Then precipitate was filtered using filtration method. The filtrate was reduced to 80 mL, and hexane (50 mL) was also added to it. The resulting mixture was kept at  $-15$  °C for two days to yield a white impure solid of 55% which was purified to an yeild of 69%.



**Scheme - 5**

### 2.2.6. Ligand 6

For the preparation of the ligand,  $\text{POCl}_3$  (0.5 ml, 0.82 g, 0.00534 mol) was added dropwise to an excess amount of cyclohexyl amine (1.839 ml, 1.59106 g, 0.01643 mol) in toluene (100 mL) at 0 °C. The resulting mixture was slowly brought to room temperature and stirred for 4 h. The precipitate was removed by filtration. The filtrate was reduced to 80 mL, and hexane (50 mL) was added to it. The mixture was kept at  $-15$  °C for two days to yield a white impure solid of 67% and then purified to yield 62%.



**Scheme - 6**

### **2.2.7. Preparation of (Zr-Nap Cage):**

For the preparation of Zr-Nap MOC, reaction between zirconocene dichloride (Cp<sub>2</sub>ZrCl<sub>2</sub>) (0.03 g, 0.102 mmol) and 2,6-Naphthalene di-Carboxylic acid (0.0072 g, 0.03 mmol) has been done in 0.5 ml THF, 1.0 ml DMF and then 6 drops of distilled water was added. The resultant mixture was heated at 65°C for 4 hours which led to the formation of small, white and square shaped crystals after a span of 5 days. In order to confirm the Zr-Nap cage, we have performed MALDI-TOF mass spectrum and single crystal XRD (SCXRD) data which gave us detailed confirmations for the cage formation.

### **2.2.8. Preparation of (Zr-Cycl hexyl Cage):**

We have prepared Zr-Cycl hexyl MOC where zirconocene dichloride (Cp<sub>2</sub>ZrCl<sub>2</sub>) (0.03 g, 0.102mmol) and 1,1'-Bi (Cyclo-hexyl)-4,4'-dicarboxylic acid (0.0052 g, 0.02mmol) reacted with each other in presence of 0.5 ml THF , 1.0 ml DMF and 6 drops of distilled water. After that the resulting mixture was heated at 65°C for 4 hours where the reaction led to the formation of the thin, white and needle-shaped crystals which appeared after 5 days confirming that reaction has been worked successfully. For further confirmations, we have performed MALDI-TOF mass spectrum and single crystal XRD (SCXRD) data for confirming the formation of cages.

### 2.2.9. Preparation of Zr-Isophthalic Cage

We have also tried preparing Zr-Isophthalic MOC where we added zirconocene dichloride ( $\text{Cp}_2\text{ZrCl}_2$ ) (0.03 g , 0.102 mmol) and Isophthalic acid (0.005 g, 0.03 mmol) in 0.5 ml THF , 1.0 ml DMF and 6 drops of distilled water and allowed them to react and then followed by the heating of the mixture 60°C for 8 hours. We were successful in preparing it for the first time but unfortunately, we were not able to reproduce the same data in further attempts due to which we have excluded it from further studies.

### 2.3. General Procedure for preparation of Guest-Host Assemblies:

We have prepared Guest-Host assemblies, where we have stirred solution of cage assemblies a stirred solution of cage assemblies (5 mg) in MeOH (2.5 ml) followed by the addition of the guest solvent (Para-Xylene, Meta-Xylene, Ortho-Xylene) (10ul). The resulting solution was stirred further for 30mins. Furthermore, the obtained mixture was diluted in MeOH and in order to analyse and confirm the structure, MALDI-TOF mass spectroscopy and UV-VIS spectral studies has been performed which confirmed the formation of host-guest complexes and later on, UV-VIS titration has been also been done in order to determine the binding affinities of these prepared Guest-Host Assemblies.

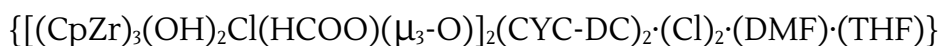
## Chapter 3: Results and Discussion

### 3.1. Synthesis and structures of the self-assembled cages:

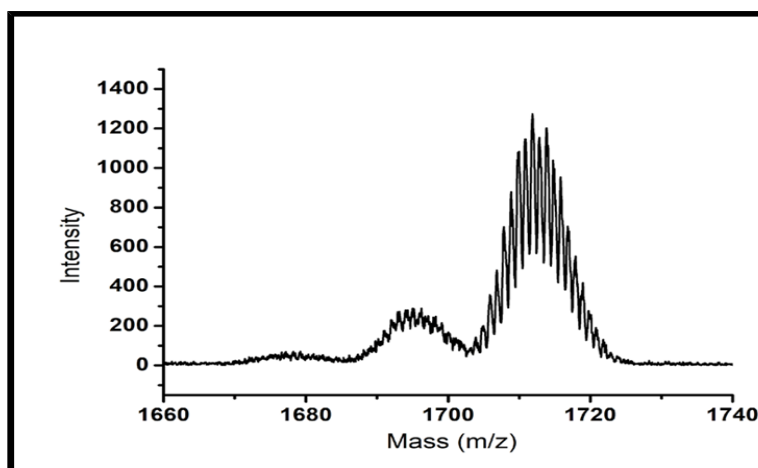
The phosphoramidate ligands were synthesized from the earlier reported procedures. Attempts to synthesize metal-ligand cages utilizing these ligands were unsuccessful. For example, treatment of the ligand OP(NH<sup>i</sup>Pr)<sub>3</sub> with oxalic acid (C<sub>2</sub>O<sub>4</sub>H<sub>2</sub>) yields the tetrahedral cage of formula [Pd<sub>12</sub>(OP(NiPr)<sub>3</sub>)]<sub>4</sub>(C<sub>2</sub>O<sub>4</sub>)<sub>6</sub>. However, no such cages were observed for the structurally similar ligands L1 and L6 in reaction with palladium (II) acetate oxalic acid (C<sub>2</sub>O<sub>4</sub>H<sub>2</sub>) presumably due to some inherent variations in the steric and electronic effects of these ligands. Attempts to synthesize cages and cluster using the other phosphoramidate ligands were also unsuccessful. Hence, we adopted a different procedure where well known trinuclear (CpZr)<sub>3</sub> core was utilized for cage forming reactions. Thus, we treated the precursor Cp<sub>2</sub>ZrCl<sub>2</sub> with various carboxylic acids that can potentially form cages and macrocycles. The reaction of Naphthalene dicarboxylic acid with Cp<sub>2</sub>ZrCl<sub>2</sub> in DMF and THF mixtures under solvothermal conditions yield the crystals of hexanuclear cage of formula as shown below



Where, NAP-DC is Naphthalene-2,6-dicarboxylate acid [C<sub>10</sub>H<sub>6</sub>(COO<sup>-</sup>)<sub>2</sub>]. A similar reaction with cyclohexane dicarboxylic acid gave the tub shaped open cage assembly of formula



Where, CYC-DC is Cyclohexyl-1,4-dicarboxylate [C<sub>6</sub>H<sub>10</sub>(COO<sup>-</sup>)<sub>2</sub>]. The formation of the formate ligation may be tracked to the cleavage of the DMF molecules under hydrothermal conditions and the presence of oxo and hydroxyl groups in both these cages are due to the deportation of the adventitious amount of water molecules in the added solvents.

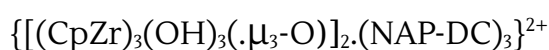


**Figure 8:** MALDI-TOF mass spectrum of Zr-Nap cage

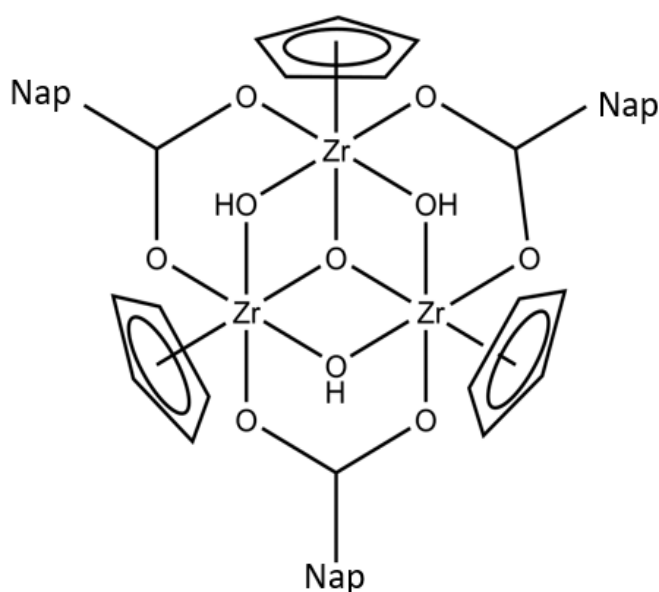
Chemical formula	$C_{66}H_{48}N_2O_{23}Zr_6Cl_2$
Formula weight	1717.16
Crystal system, space group	Monoclinic, P2(1)/n
Temperature (K)	100
a (Å); $\alpha$ (°)	10.7493(16); 90
b (Å); $\beta$ (°)	24.785(4); 93.206(4)
c (Å); $\gamma$ (°)	37.245(6); 90
V (Å <sup>3</sup> )	9907.4
Z	4
Density (gcm <sup>-3</sup> )	1.337
Radiation type	Mo K $\alpha$
2 $\theta$ max (°)	56.73
R1	0.1166
wR2	0.433

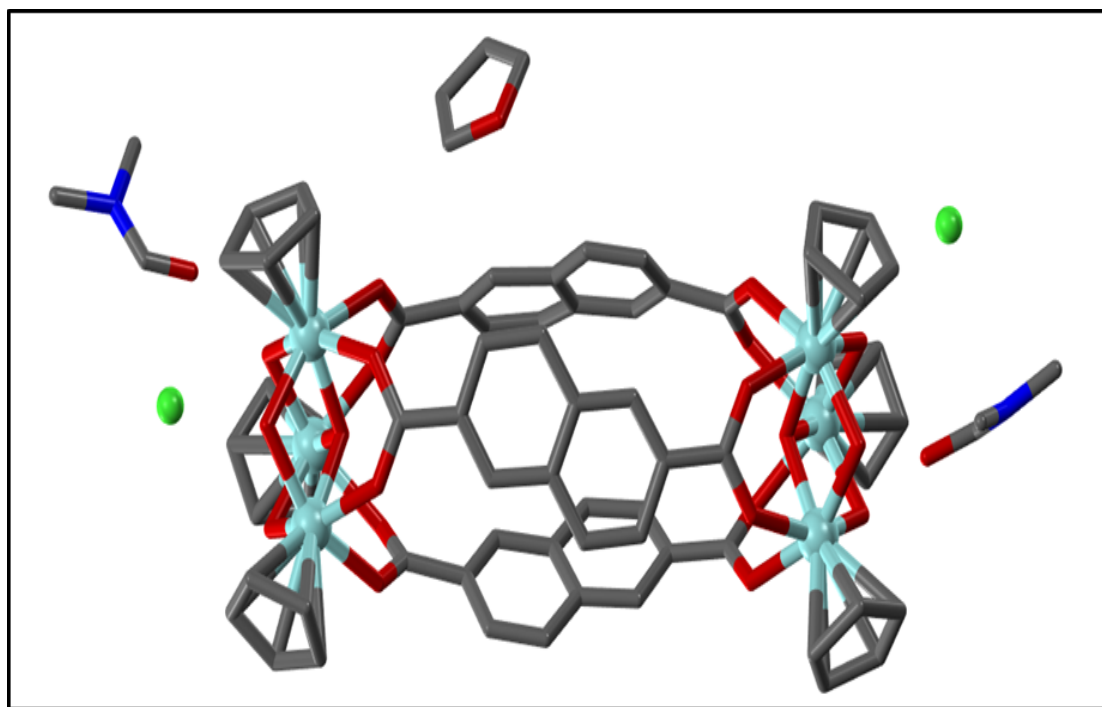
**Table 1 :** Crystallographic Details for Zr-Nap cage

The MALDI-TOF mass spectrum of the crystals of Zr-Nap cage gave an isotopic distribution of peaks centred around  $m/z = 1710-1720$ . This experimental mass value coincides with the theoretically computed value of based on the formula suggesting the formation of the Zr-Nap cage. For further confirmations, we also performed SCXRD for these crystals where we observed the molecular structure of Zr-Nap cage. The molecular structure of Zr-Nap cage has been shown in the Figure 9. It shows that the presence of two  $[(\text{CpZr})_3\text{O}(\text{OH})_3]^{4+}$  clusters that are bridged by three bis-bidentate naphthalene dicarboxylate ligands (Figure 16, top). Each hydroxo group connects two adjacent Zr centers by a  $\mu_2$ -bridging mode and the central oxo group connect the three Zr centres by  $\mu_3$ -bridging interactions. The cage molecule is cationic as represented by the formula

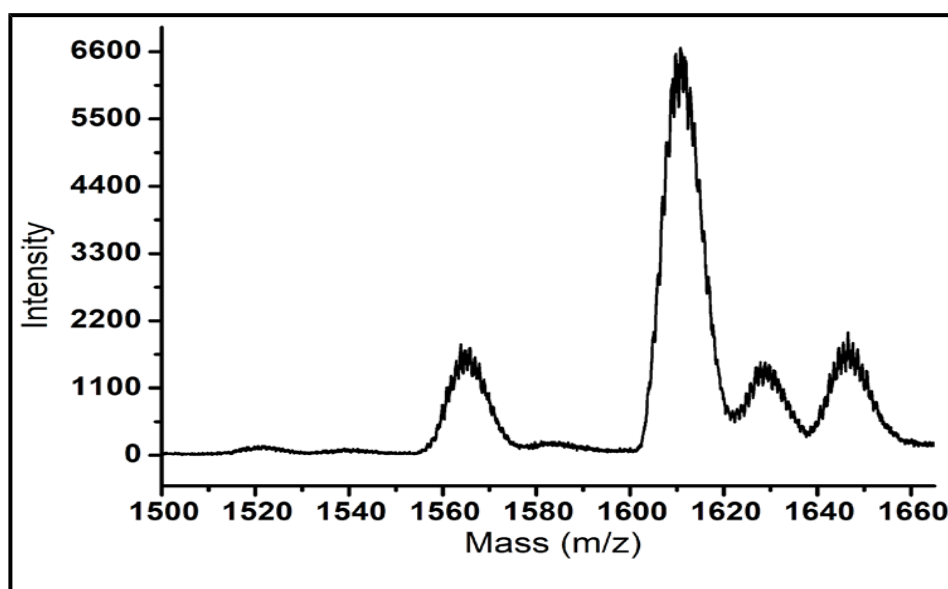


The charge balance in the molecule is restored by two chloride ions. One molecule of THF and two of DMF molecules have been found to be crystallised along with the cage in its asymmetric unit. These confirmations successfully led us to use these cages to perform further studies.





**Figure 9:** View of the  $Zr_3$ -core (top) and the SCXRD structure (bottom) for Zr-Nap MOC. Colour codes: C- grey; N- blue; O- red; Cl- green; Zr- light blue



**Figure 10 :** MALDI-TOF mass spectrum of Zr-Cycl-Hexyl MOC



Chemical formula	$C_{48}H_{52}NO_{20}Zr_6Cl_4$
Formula weight	1652.08
Crystal system, space group	Monoclinic C2/c
Temperature (K)	100
a (Å); $\alpha$ (°)	34.166(5); 90
b (Å); $\beta$ (°)	13.6521(19); 122.040(3)
c (Å); $\gamma$ (°)	20.170; 90
V (Å <sup>3</sup> )	7974.99
Z	4
Density (gcm <sup>-3</sup> )	1.609
Radiation type	Mo K $\alpha$
2 $\theta$ max (°)	56.76
R1 [F>4 $\sigma$ (F)]	0.0863
wR2	0.2873

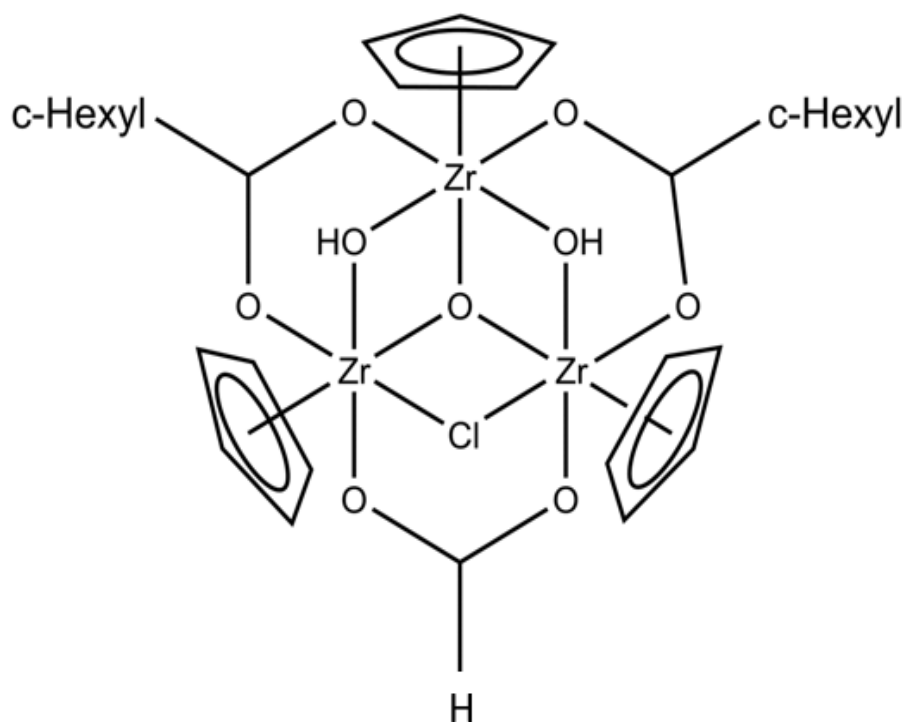
**Table 2** : Crystallographic details of Zr-Cycl-Hexyl cage

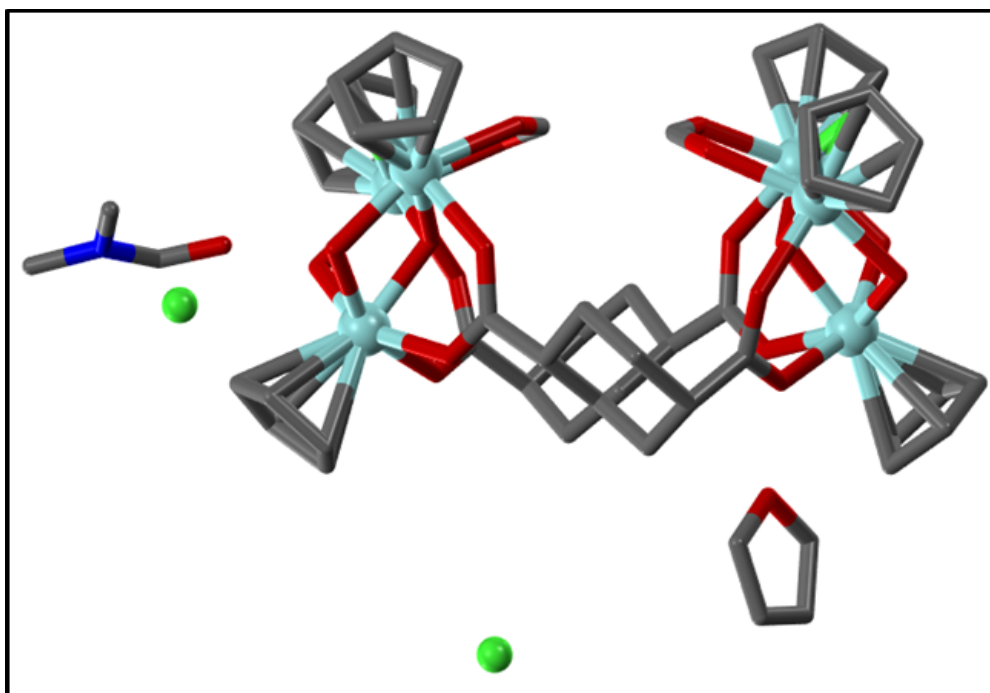
The MALDI-TOF mass spectrum of the crystals of Zr-Cycl-Hexyl cage gave a prominent peak centred around  $m/z = 1652$  for the cationic cage. The SCXRD analysis of the needle-shaped crystals of Zr-Cycl-Hexyl MOC confirmed the molecular structure of the cage as shown in the Figure 11. It has been observed that the Zr-Cycl-Hexyl cage exhibits a slight difference in molecular structure than that of the Zr-Nap cage which has been discussed previously. It shows that the two  $(CpZr)_3$  clusters are bridged by only bis-bidentate cyclohexane

dicarboxylate ligands. The hydrothermal reaction cleaved the DMF solvent and hence two in-situ generated formate ligands take up the coordination sites that are expected to be bound by the third cyclohexane dicarboxylate ligands. In addition, the cluster core is slightly different than that of the previous cage with one bridging chloride ion instead of one hydroxyl group as shown in Figure 19 (top) represented by the core formula  $[(\text{CpZr})_3\text{O}(\text{OH})_2\text{Cl}]^{4+}$ . Again, the whole cage is cationic as represented by the formula



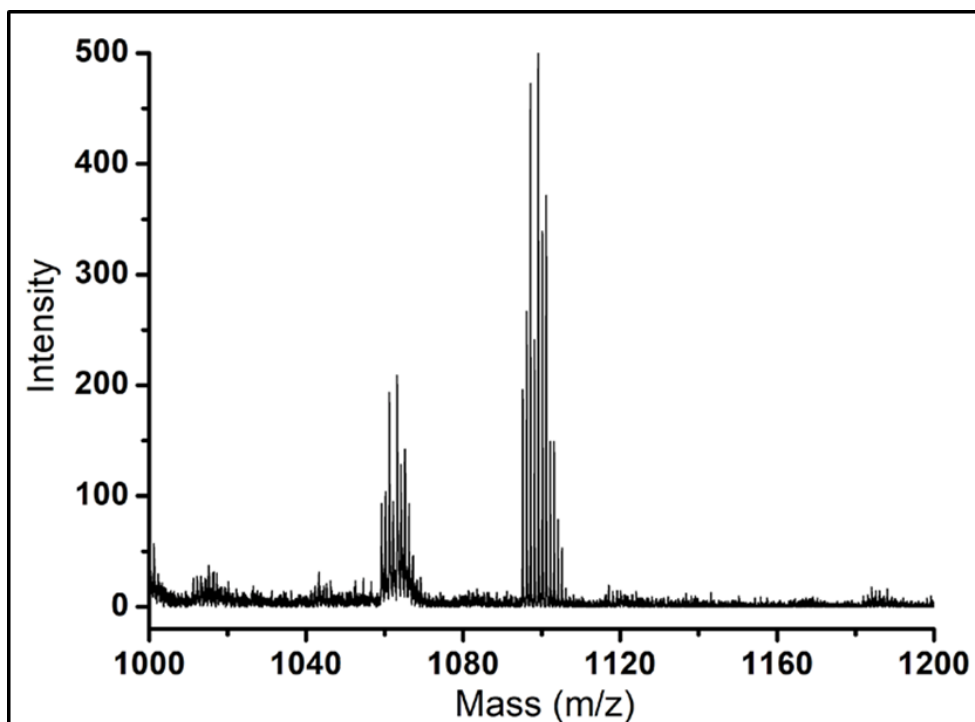
Finally, the charge balance in the molecule is restored by two diffuse chlorides ions. Two molecules of THF and DMF have been found to be crystallised along with the cage. This cage is not closed from one side by a third cyclohexyl linker due to the non-rigid confirmation of the cyclohexyl diacid linker giving it an open cage bowl-like structure.





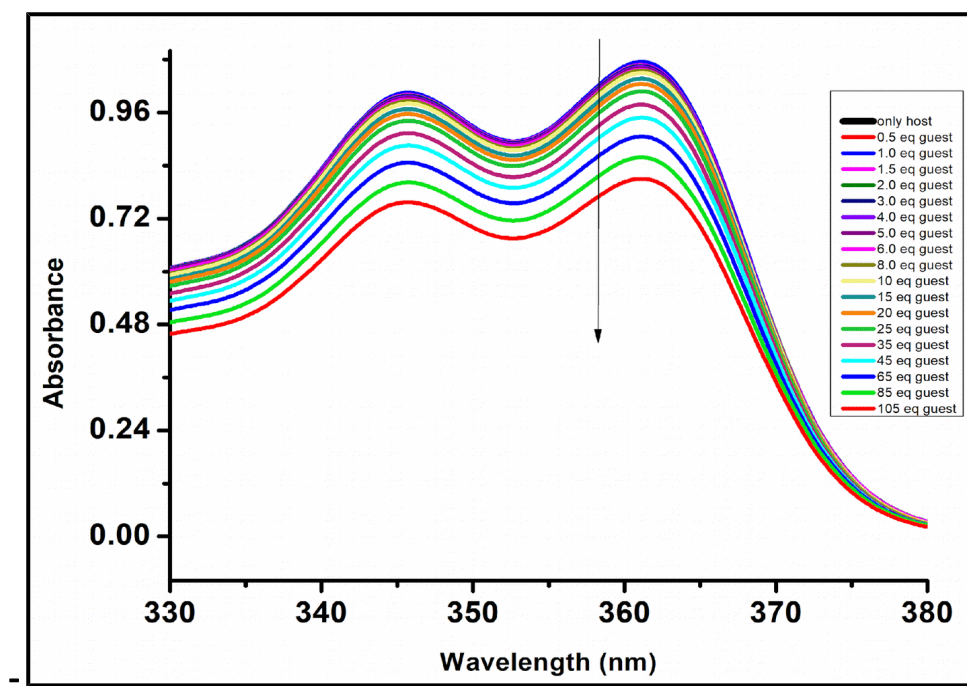
**Figure 11:** View of the Zr<sub>3</sub>-core (top) and the SCXRD structure (bottom) for Zr-Cycl Hexyl MOC: Colour codes: C- grey; N- blue; O- red; Cl- green; Zr- light blue

### 3.2: Interaction studies for PX $\subset$ Zr-Nap MOC



**Figure 12:** MALDI-TOF mass spectrum of PX  $\subset$  Zr-Nap MOC

In order to study Host-Guest interaction in our case, we have tried the interaction between Zr-Nap cage. Owing to the presence of naphthyl linkers and narrow portals, we investigated its host-guest interactions with xylene isomers. To determine the Guest-Host interaction, we performed MALDI-TOF mass spectral analysis where we have observed that the Zr-Nap cage is capable of interacting with only one of the three isomeric form of the xylene (p-xylene). The Figure 12 shows that the mass spectrum of the p-xylene treated Zr-Nap cage showing peaks due to both free and p-xylene bound cages.



**Figure 13:** UV-VIS titration data for PX c Zr-Nap MOC

Furthermore, UV-VIS titration has been performed to determine the interaction between the prepared Zr-Nap cage and all the three xylenes. Figure 13 shows that the treatment of p-Xylene (PX) with Zr-Nap cage where here it has been observed that the absorbance value was found to be gradually decreasing with subsequent guest addition. The decrease in the Host (only) concentration and

increasing Host-Guest concentration indicates that Cage Zr-Nap is capable of interacting with guest molecules and that interaction is very selective. We have confirmed this selective behaviour of this particular cage by calculating association constant and plotting the graphs for Host-Guest interactions.

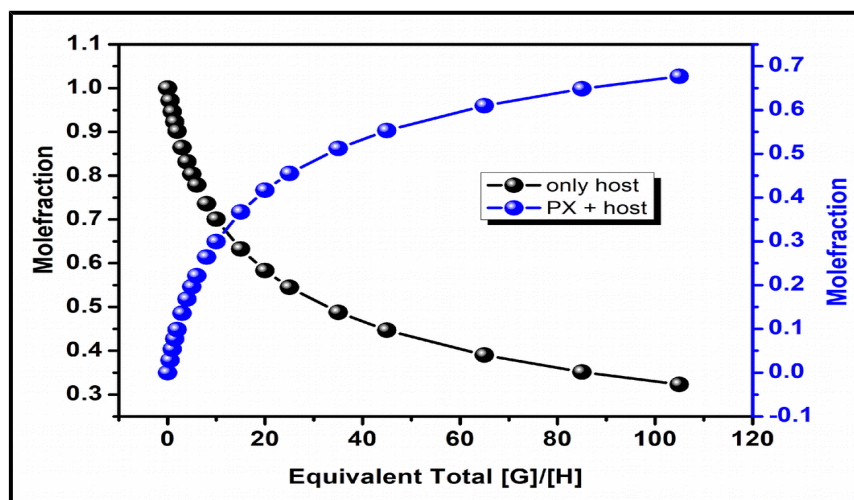
The reason for the decrease in absorption intensity is due to naphthyl conjugated rings present in the host as it absorbs UV radiations. Initially, host has high UV absorption. After adding guest molecules, they enter into the host cavity and get stabilized by  $\pi$ - $\pi$  stacking of naphthyl conjugated rings. Therefore, the  $\pi$  system in naphthyl ring is getting busy in the  $\pi$  stacking with guest. So, by increasing the guest concentration, more and more naphthyl walls get engaged in  $\pi$  stacking and hence there will be a decrease in UV absorption as shown in figure 13.

Details			
Time to fit	0.2190 s		
SSR	3.3942e-3		
Fitted datapoints	19		
Fitted params	2		
Parameters			
Parameter (bounds)	Optimised	Error	Initial
K ( 0 $\rightarrow$ $\infty$ )	2.52 M <sup>-1</sup>	$\pm$ 9.9319 %	10.00 M <sup>-1</sup>

**Table 3 :** Association constant for PX  $\subset$  Zr-Nap MOC

The binding constants have also been calculated using an online calculator: Bindfit online calculator (<http://app.supramolecular.org/bindfit/>) and revealed that among the three of the isomeric forms of Xylenes, 1:1 Host-Guest fitting was visible only in the case of PX  $\subset$  Zr-Nap cage whereas for the ortho and meta-

xylene guest added systems fitting failed which suggests that there is no Host-Guest interaction taking place. These observations suggest that, the prepared cage has very good capability of being selective in the recognition of only one isomer of xylenes.



**Figure 14:** PX c Zr-Nap MOC using UV-VIS spectroscopy

In summary, host-guest interactions have been established for the Zr-Nap and PX assembly as evident from the Figure 14 which shows a decrease in the concentration of the host and increase in the concentration of the host-guest complex for the PX c Zr-Nap system. We also observed that the value for the association constant is  $K = 2.52 \text{ M}^{-1}$  which is very small but it can be speculated that this could be attributed to the weaker interactions such as Van Der-waals interaction and pi-pi stacking occurring between these two molecules which is actually bringing them together in the assembly process.

## Chapter 4: Conclusion

In this thesis, we have successfully synthesized both open and closed multi-centered MOCs from the subunit assembly of a trimeric  $Zr_3$  clusters bound by carboxylic acid units. Furthermore, synthesis has also been supported by MALDI-TOF and UV-VIS spectroscopy where we characterised the molecular weight and the molecular structure of the following cages which will allow us to speculate the properties of these cages, for example, nature of the molecule, selectivity etc. Competitive experiments have been performed which have shown that these cages are selective, where we have checked the interactions between cage and guest molecules. In our case, we have used Zr-Nap cage as “HOST” and Xylene as a “GUEST” and this data has also been supported by MALDI-TOF mass spectrometry and UV-VIS spectroscopy. Interestingly, it has been observed that the cage is capable of recognising and encapsulating a single isomer guest from a mixture of three isomers which is Para-Xylene and being selective reveals one of the advantageous characteristics of the Cage. These cages also exhibit good solubility in aqueous media and this can further be used to fish out important organic and bio-organic molecules and act as a carrier for them in a polar/aq media. Furthermore, these cages have great potential in the field of guest separation and molecular recognition.

## Chapter 5: References

- [1] Stang.P.J, Cao.D.H, *J. Am. Chem. Soc.*, **1994**, *116*, *11*, 4981-4982.
- [2] Zhang.X, Dong.X, Lu.W, Luo.D, Zhu.X.W, Li.X, Zhou.X.P, Li., *J. Am. Chem. Soc.*, **2019**, *141*, *29*, 11621-11627.
- [3] Aoyama.Y, Tanaka.Y, Toi.H, Ogoshi.H, *J. Am. Chem. Soc.*, **1988**, *988*, *110*, *2*, 634-635.
- [4] Go.E.Bin, Srisuknimit.V, Cheng.S.L, Vosburg.D.A, *J. Chem. Educ*, **2016**, *93*, *2*, 368-371.
- [5] Zhang.J, Sun.H, Ma.P.X, *ACS Nano*, **2010**, *4*, *2*, 1049-1059.
- [6] Xiong.Q, Cui.M, Bai.Y, Liu.Y, Liu.D, Song.T, *Colloids Surf. B*, **2017**, *155*, 93-103.
- [7] Wang.L, Li.L.L, Fan.Y.S , Wang.H , *Adv. Mater*, **2013**, *25*, 3888-3898.
- [8] Chan-A-K-W, Lam-W-H, Tanaka.Y, Wong.K.M.C, Yam.V.W.W, *Proc. Natl. Acad. Sci.*, **2015**, *112*, 690-695.
- [9] Amouri.H, Mimassi.L, Rager.M.N, Mann.B.E, Guyard-Duhayon.C, Raehm. L ,*Angew. Chemie*, *July 18*, **2005**,*117* Pages 4619-4622.
- [10] Ma.S, Smulders.M.M.J, Hristova.Y.R, Clegg.J.K, Ronson.T.K, Zarra.S, Nitschke.J.R, *J. Am. Chem. Soc.*, **2013**, *135*, 5678–84.
- [11] Schoedel.A, Ji.Z, Yaghi.O.M, *Nat Energy*, **2016**, *1*, 16034.
- [12] Li.K, Zhang.L.Y, Yan.C, Wei.S.C, Pan.M, Zhang.L, Su.C.Y, *J. Am. Chem. Soc.*, **2014**, *136*, 4456–9.
- [13] Cook.T.R, Zheng.Y.R, Stang.P.J, *Chem. Rev.*, **2013**, *113*, *1*, 734–77.
- [14] Jin.J, Cai.L, Jia.Y.G, Liu.S, Chen.Y, Ren.L, *J. Mater. Chem.*, **2019**, *7*, 1637–51.
- [15] Howlader.P, Mukherjee.P.S, *Chem. Sci.*, **2016**, *9*, 5893–5899.
- [16] Mitchell.S.G, Streb.C, Miras.H.N, Boyd.T, Long.D.L, Cronin.L, *Nature*



- Chem*, **2010**, *2*, 308–312.
- [17] Gianneschi.N.C, Masar.M.S, Mirkin.C.A, *Acc. Chem. Res.*, **2005**, *38*, 825–37.
- [18] Kuehl.C.J, Mayne.C.L, Arif.A.M, Stang.P.J, *Org. Lett.* **2000**, *2*, 23, 3727-3729.
- [19] Fujita.M, Nagao.S, Ogura.K, *Angew. Chem.*, 1995, **117**, 1649–50.
- [20] Ghosh.A, *Acc. Chem. Res.*, **2005**, *38*, 12, 943-954.
- [21] Thi.Thanh.D, Mai An.P, Thi Thuy Trang.G, Thi Minh Thuy.N, Huu Kien.P, *J. Sci. Nat. Sci. Technol.*[S.l.],**2019**, *35*, 3.
- [22] Homan.R.A, Hendricks.D.S, Rayder.T.M, Thein.U.S, Fossum.K.J, Claudio Vázquez.A.P, Yan.J, Grimm.R.L, Burdette.S.C, MacDonald.J.C, *Cryst. Growth Des.*, **2019**, *19*, 11, 6331-6338.
- [23] Pan.M, Wu.K, Zhang.J.H, Su.C.Y, *Coord. Chem. Rev.*, **2019**, *378*, 333-349.
- [24] Sun.S., Lees.A.J, *J. Am. Chem. Soc.*, **2000**, *122*, 8956-8967.
- [25] Mendez-Arroyo.J, D'Aquino.A.I, Chinen.A.B, Manraj.Y.D, Mirkin.C.A, *J. Am. Chem. Soc.*, **2017**, *139*, 1368–71.

# Supplementary Data

## 3.1. HRMS Data

### 3.1.1 High-resolution Mass spectrometry studies of L1

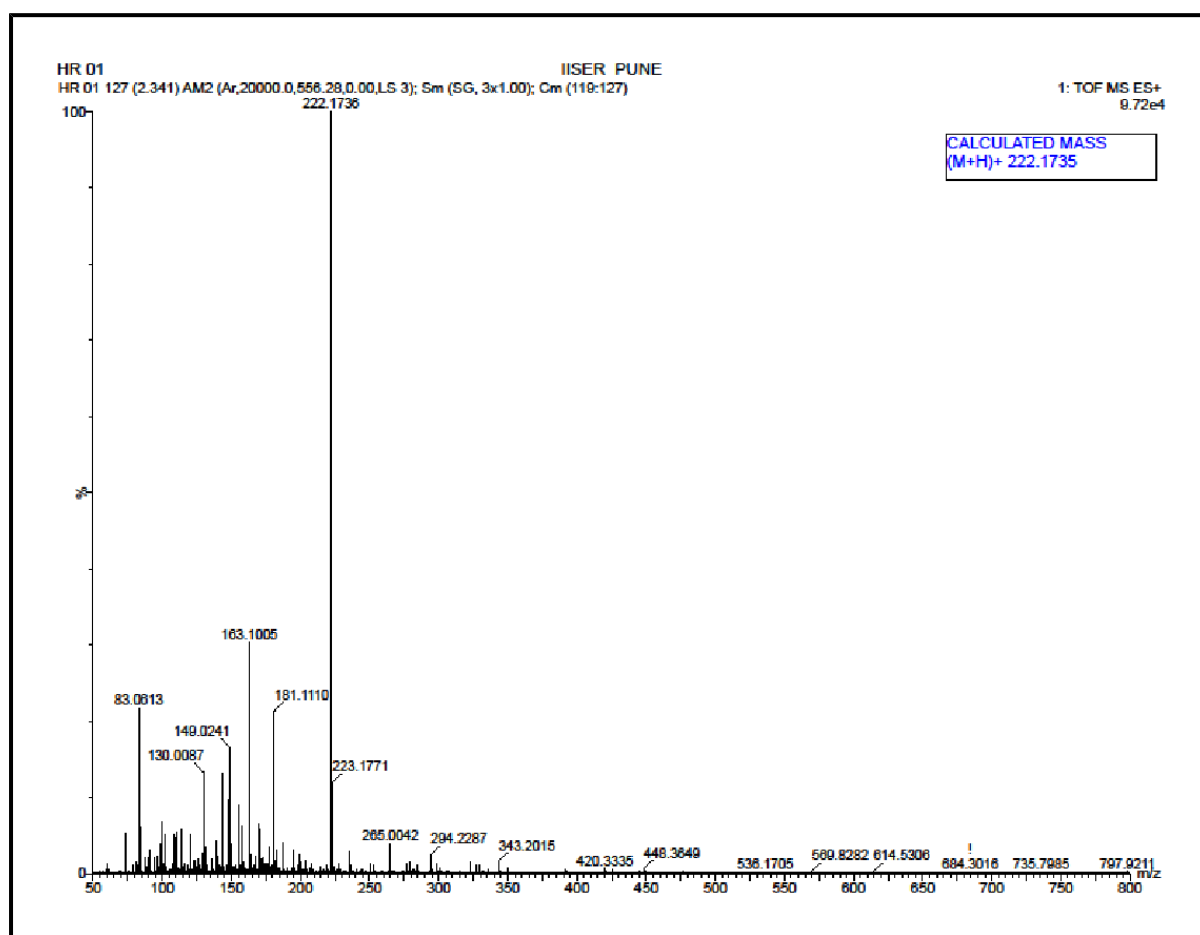
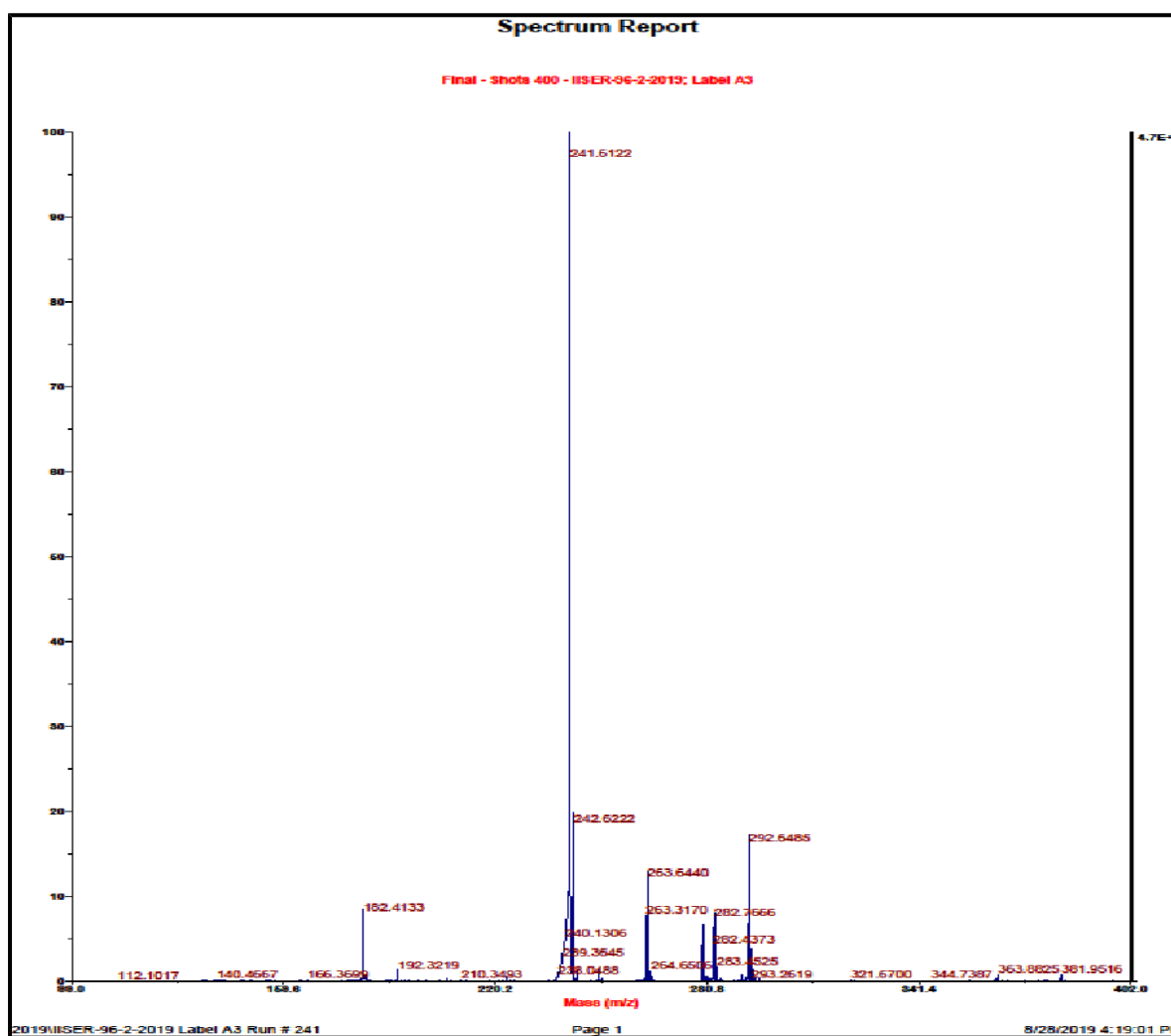


Figure 15

### 3.1.2. High-resolution Mass Spectrometry studies of L2



**Figure 16**

### 3.1.3 High-Resolution Mass Spectrometry studies of L3

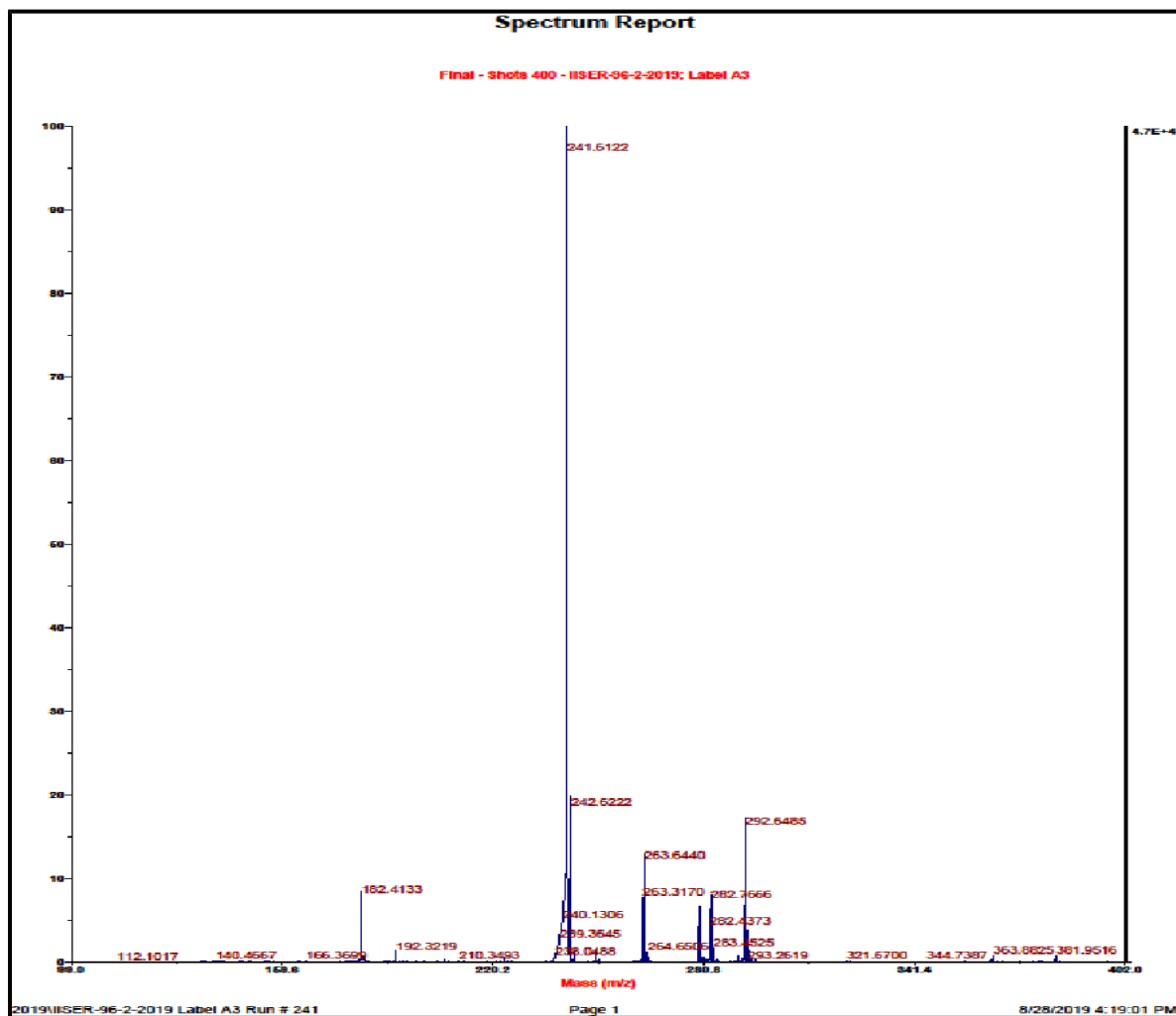
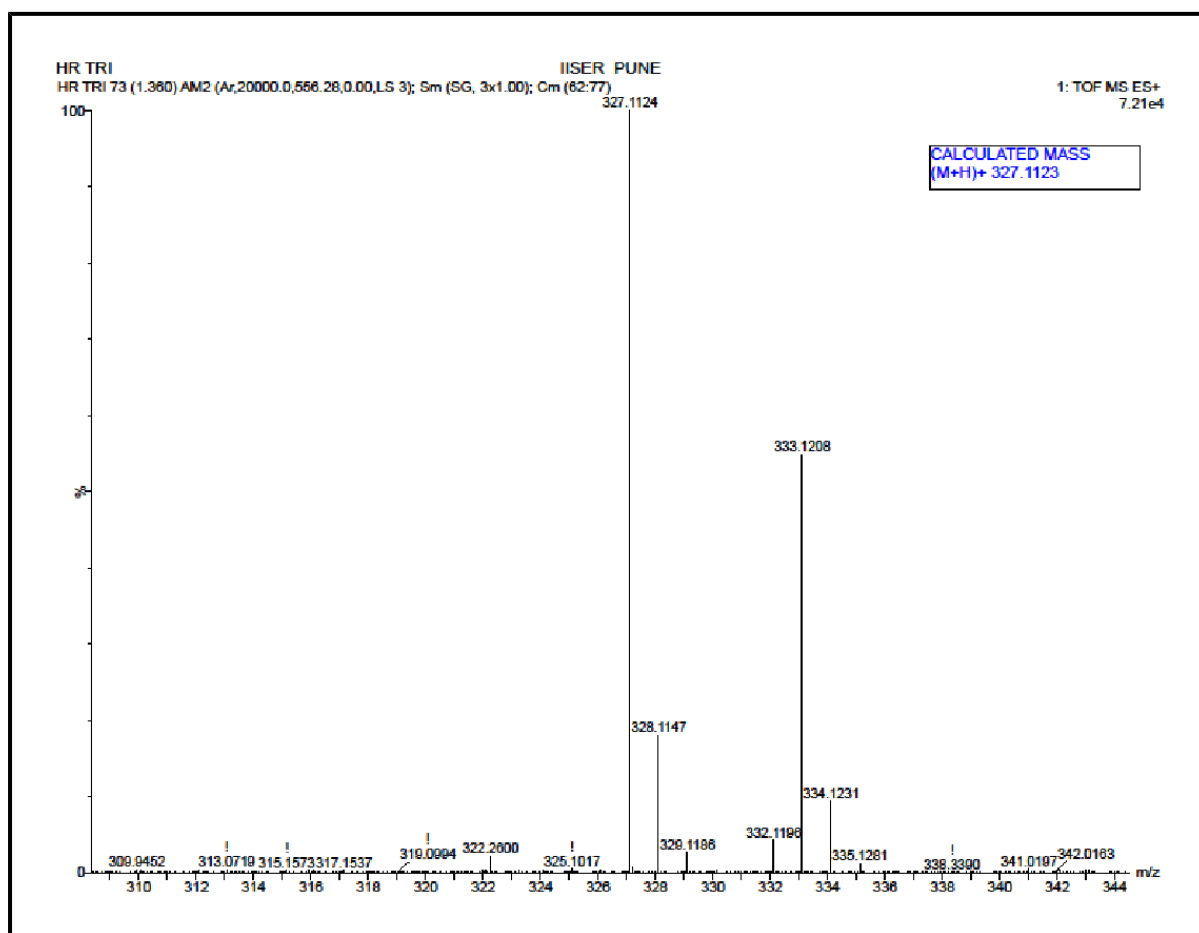


Figure 17

### 3.1.4. High-Resolution Mass Spectrometry studies of L4



**Figure 18**

### 3.1.5. High Resolution Mass Spectrometry studies of L5

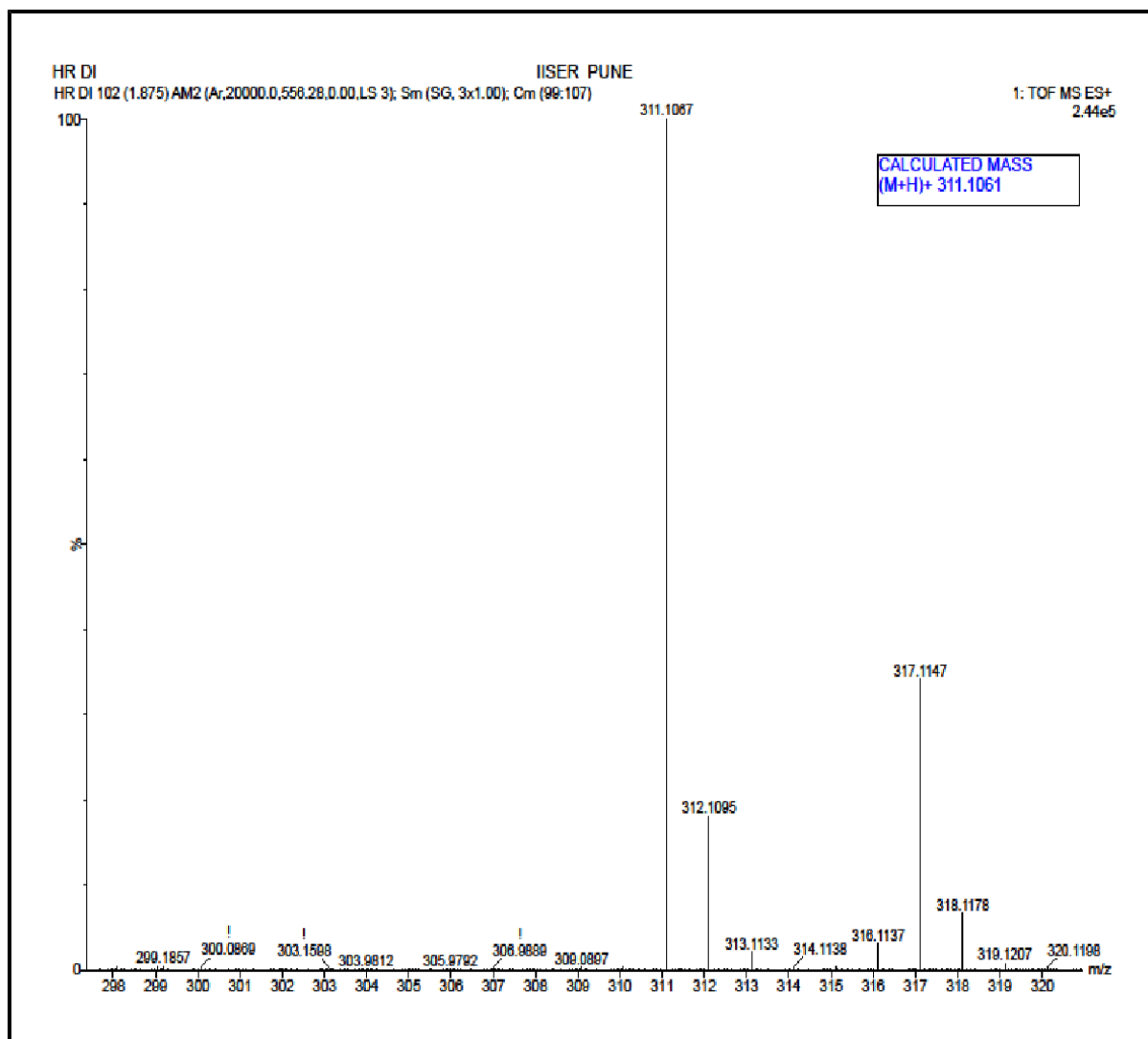
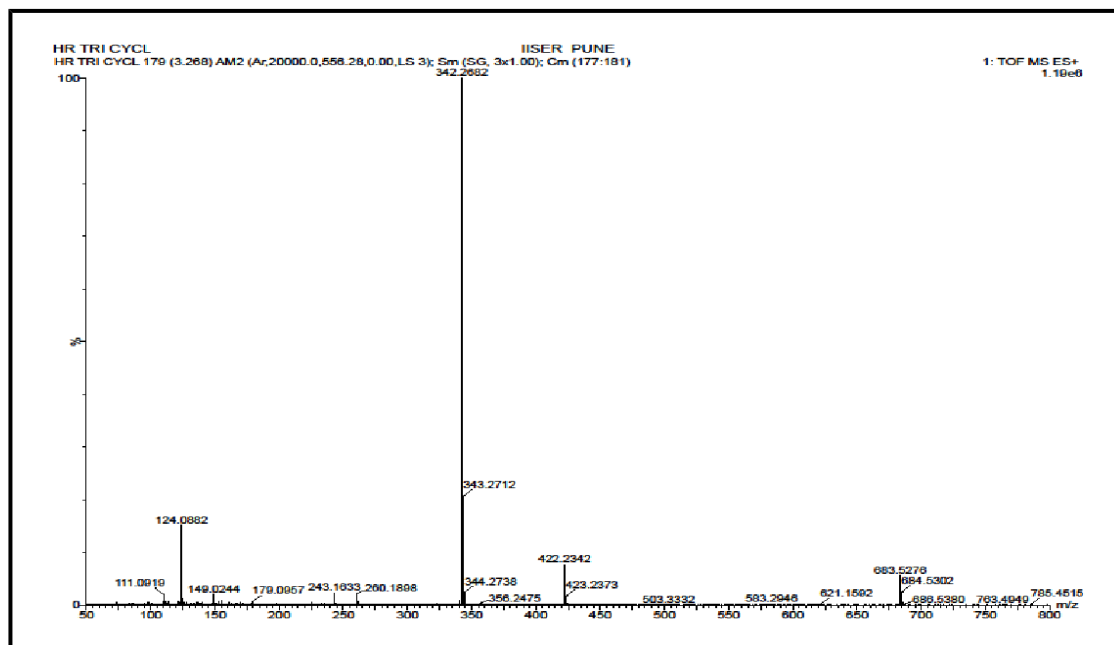


Figure 19

### 3.1.6. High Resolution Mass Spectrometry studies of L6:



**Figure 20**