

Syntheses and functional studies of chiral metal-organic cages and supramolecular assemblies derived from imido and amido P(V) scaffolds

A

thesis

**Submitted in partial fulfillment of the requirements
for the degree of**

Doctor of Philosophy

By

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February 2020

Dedicated to
My Parents
&
Loved Ones...

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CERTIFICATE

Certified that the work incorporated in the thesis entitled “*Syntheses and functional studies of chiral metal-organic cages and supramolecular assemblies derived from imido and amido P(V) scaffolds*” submitted by **Mr. P. Rajasekar** was carried out by the candidate, under my supervision. The work presented here or any part of it has not been included in any other thesis submitted previously for the award of any degree or diploma from any other university or institution.

R. Boomi Shankar

Date: 3rd February-2020
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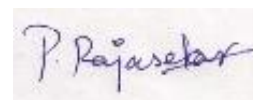
Dr. R. Boomi Shankar
(Research Supervisor)

DECLARATION

I declare that, this written submission represents my ideas in my own words and where other's ideas have been included; I have adequately cited and referenced the original sources. I also declare that I have adhered to all principles of academic honesty and integrity and have not misrepresented or fabricated or falsified any idea/data/fact/ source in my submission. I understand that violation of the above will be cause for disciplinary action by the Institute and can also evoke penal action from the sources which have thus not been properly cited or from whom proper permission has not been taken when needed.

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P. Rajasekar

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The thesis entitled “Syntheses and functional studies of chiral metal-organic cages and supramolecular assemblies derived from imido and amido P(V) scaffolds” is focused on the synthesis of chiral metal-organic cages derived from imido P(V) ligands and chiral amino phosphorus (V) ligands and the studies of their host-guest properties, chiral recognition and separation applications.

Chapter 1: Introduction

This chapter provides a brief introduction about the construction of chiral metal organic architectures. Various strategies to assemble chiral metal organic cages have been described in detail in this chapter with examples. Especially, the conversion of achiral tetrahedral metal organic cages into chiral tetrahedral metal organic cages has been described. In addition, this chapter gives an overview on the application of chiral metal-organic cages in enantioselective recognition, separation, sensing and in biological processes. Finally, it gives a brief outline on the working chapters pertaining to chiral imido P(V) ligands as supports for obtaining chiral tetrahedral cages for chiral separation applications and the use of chiral amino-phosphonium cations for chiral recognition.

Chapter 2: Synthesis and functional studies of chiral aminophosphonium salts

The research on chiral recognition and chiral selection is not only fundamental in deciding the mystery of homochirality, but also informative in enantiomers separation and asymmetric catalysis. In chapter 2 we report the first example of chiral recognition of mandelic acid and phenylglycinol guest enantiomers using novel chiral phosphonium salts. With these simple salts, an extremely high enantiomeric discrimination of phenylglycinol (PG) was achieved, with a binding selectivity of up to 7.96×10^6 for R-PG over S-PG with using the s-isomer of the aminophosphonium salt host. The high binding selectivity may be attributed to the presence of multiple interactions between the host and guest molecules. Also, we have synthesized novel chiral phosphonium anilates from chiral phosphonium salts with different anilate dianions (Figure 1).

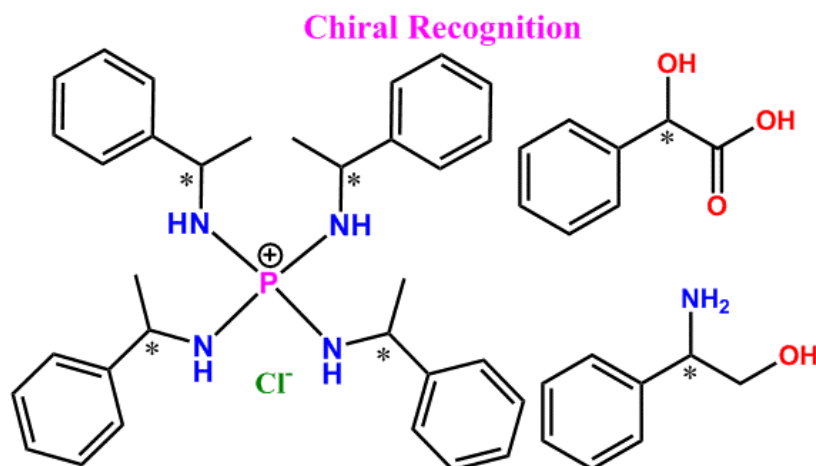


Figure 1: Chemical structure of chiral phosphonium salts and their chiral recognition of mandelic acid and phenylglycinol guest enantiomers.

Chapter 3: Imido-P(V) trianion supported enantiopure neutral tetrahedral Pd(II) cages

Charge-neutral chiral hosts are attractive due to their ability to recognize a wide range of guest functionalities and support enantioselective processes. However, reports on such charge-neutral cages are very scarce in the literature. In the second chapter, we report an enantiomeric pair of tetrahedral Pd(II) cages built from chiral tris(imido)phosphate trianions and oxalate linkers. The highly basic tris-imido phosphate ligand was generated in-situ by the deprotonation of the corresponding chiral phosphoric triamide ligand using soft Pd(II) ions. These cages were shown to exhibit enantioselective separation capabilities for the racemates epichlorohydrin, β -butyrolactone, and 3-methyl- and 3-ethyl cyclopentanone with epoxide, lactone and ketone functional groups (Figure 2).

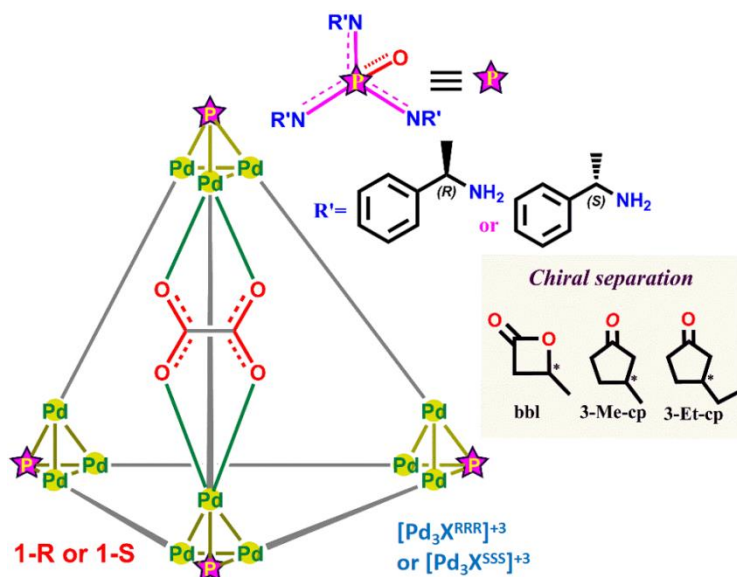


Figure 2: Schematic representation of neutral chiral tetrahedral cages and the racemic guest molecules employed in the chiral separation studies.

Chapter 4: Chiral Separation of Styrene Oxides Supported by Enantiomeric Tetrahedral Neutral Pd(II) Cages

The separation of enantiomers is of considerable importance in the preparation of the compounds of biological interests, catalysis, and drug development. An enantiomeric pair of imido Pd(II) derived tetrahedral cages built on chloranilate based linkers were synthesized and shown to exhibit high selectivity for the separation of racemic styrene epoxides. Chiral neutral cages of formula $[(\text{Pd}_3\text{X}^*)_4(\text{C}_6\text{O}_4\text{Cl}_2)_6]$ ($[\text{X}^*]^{3-} = \text{RRR- or SSS-}[\text{PO}(\text{N}^*\text{CH}(\text{CH}_3)\text{Ph})_3]^{3-}$) are constructed from Pd₃ building units supported by tris(imido)phosphate trianions and chloranilate linkers. These cages exhibit considerable enantioselective separation capabilities toward a series of styrene epoxides via a crystallization inclusion method. A highest enantiomeric excess (ee) value of up to 80% is achieved for the (R)-4-fluorostyrene oxide (Figure 3).

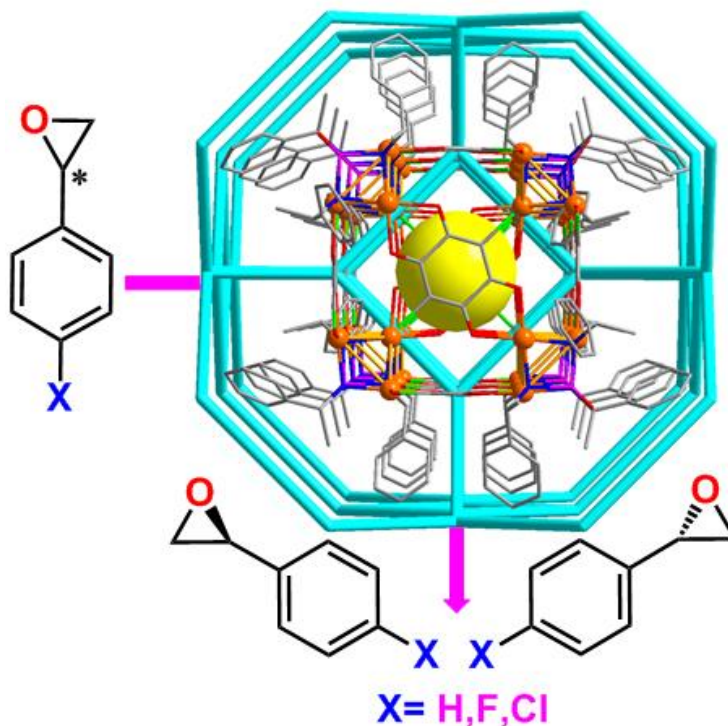


Figure 3: View of the chiral tetrahedral cages packing to resolve of 4-halostyrene oxides via crystallization inclusion.

Chapter 5: Enantiopure polyradical tetrahedral Pd_{12}L_6 cages

Synthesis of cages with polyradical framework remains a challenge. Here we report an enantiomeric pair of quinoid-bridged polyradical tetrahedral palladium (II) cages. These cages have been characterized by electron paramagnetic resonance, squid magnetometry and mass spectrometry. The EPR and magnetic measurements confirm the triplet and singlet nature of these cages depending on the substituents on the anilate backbone. Single crystal derived X-ray structural investigations of the iso-structural cages built on flouranilate linkers confirm the tetrahedral structure of the obtained radical cages. Theoretical spin density analysis reveal the presence of weak anti-ferromagnetic coupling of the adjacent radicals within the cage frameworks (Figure 4).

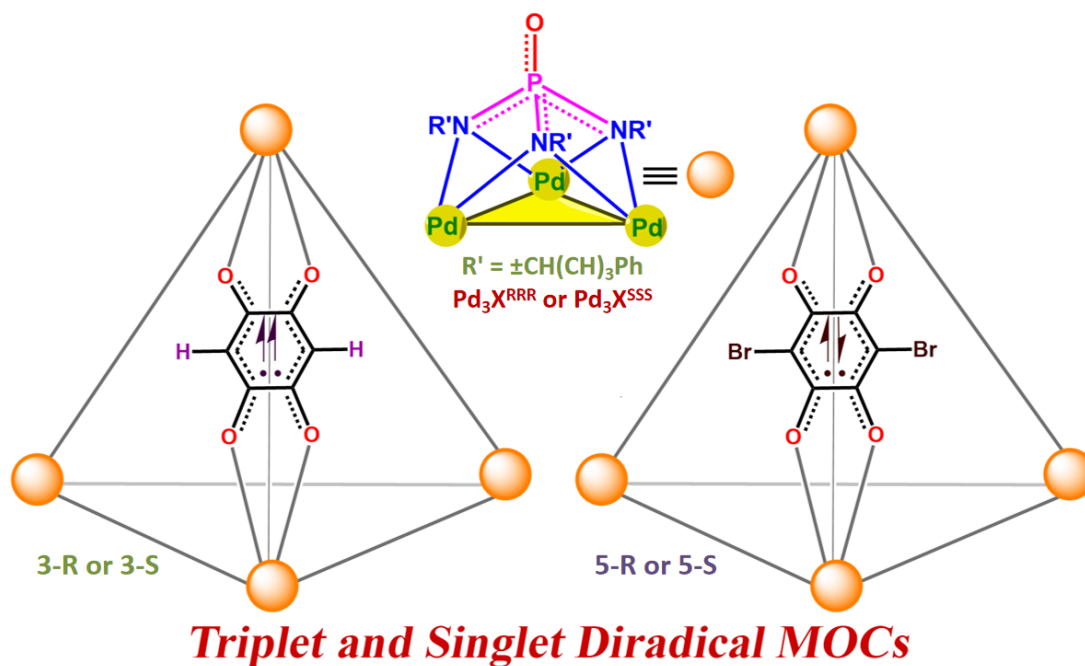


Figure 4: Schematic representation of triplet and singlet chiral tetrahedral metal organic cages.

Abbreviations

Anal.	Analysis
Calcd.	Calculated
CCDC	Cambridge Crystallographic Data Centre
DFT	Density Functional Theory
DMF	N, N-Dimethyl formamide
DMSO	Dimethyl sulphoxide
ESI	Electron Spray Ionization
FT-IR	Fourier Transform Infrared Spectroscopy
HRMS	High Resolution Mass Spectroscopy
MALDI-TOF	Matrix-Assisted Laser Desorption/Ionization – Time of Flight
MeOH	Methanol
MeCN	Acetonitrile
mg	Milligram
min	Minutes
μl	Microliter
ml	Millilitre
mm	Milimeter
mmol	Milimoles
MOF	Metal-Organic Framework
M.P.	Melting point
NMR	Nuclear Magnetic Resonance
RT	Room Temperature
Ph	Phenyl
PXRD	Powder X-ray Diffraction

Abbreviations

SCXRD	Single Crystal X-ray Diffraction
TGA	Thermogravimetric Analysis
EPR	Electron Paramagnetic Resonance
GC	Gas Chromatography
HPLC	High-performance Liquid Chromatography
ee	Enantiomeric excess
DCM	Dichloromethane



Chapter 3:

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Chapter 4:

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Contributions Included in the Thesis:

1. Imido-P(V) Trianion Supported Enantiopure Neutral Tetrahedral Pd(II) Cages
P. Rajasekar, S. Pandey, H. Paithankar, J. Chugh, A. Steiner and R. Boomishankar
Chem. Commun. **2018**, 54, 1873-1876.
2. Chiral Separation of Styrene oxides Supported by Enantiomeric Tetrahedral Neutral Pd(II) Cages
P. Rajasekar, S. Pandey, J. D. Ferrara, M. D. Campo, P. L. Magueres, R. Boomishankar.
Inorg. Chem. **2019**, 58, 15017-15020.
3. Chiral aminophosphonium salts as receptors for enantiodiscrimination of Mandelic acid and Phenylglycinol
P. Rajasekar, C. Jose, M. Sarkar, R. Boomishankar
(*Manuscript under preparation*)
4. Hydrogen bonded 1-D Chiral aminophosphonium anilates frameworks
P. Rajasekar, R. Boomishankar
(*Manuscript under preparation*)
5. Singlet and Triplet behaviour of polyradical chiral tetrahedral metal organic cages
P. Rajasekar, A. Swain, G. Rajaraman, R. Boomishankar
(*Manuscript under preparation*)

Contributions not included in the Thesis:

6. Chloro-Bridged Hexanuclear Pd(II) Clusters Supported by *cis*-Blocking Tris(imido)phosphate Trianions
A. K. Gupta, S. A. D. Reddy, **P. Rajasekar**, P. Prakash, R. Boomishankar
Chem. Select. **2017**, 2, 10636-10641.



Chapter 1



Introduction

1. 1 Introduction to chiral metal organic assemblies

Chirality is universal in nature and can be classified from subatomic and molecular to supramolecular, nanoscopic, macroscopic and galactic scales.¹ Molecular Level chirality has been used to make drugs and functional molecules, while the supramolecular level chirality in self-assembled systems represents one of the most striking and promising areas of research in supramolecular chemistry due to their ability to mimic the active sites of the enzymes.² The importance of supramolecular chirality is underscored by the fact that many of nature's intricate biochemical processes are related to the chiral receptors in the body. Chiral supramolecular assemblies have proved themselves as powerful tools to aid the understanding and exploration of chirality and their effect in chiral sensing, chiral molecular recognition and asymmetric catalysis.³ The supramolecular chirality in self-assembled systems was spawned from diverse non-covalent interactions such as hydrogen bonding, metal-ligand coordination, aromatic stacking, van der Waals interactions, etc.⁴ Among the various non-covalent interactions available, metal-ligand coordination has turned out to be one of the most successful and versatile methods because these coordination self-assemblies are well organized in manner and they allow exact control over the size, shape, and functionality.⁵ Metal-ligand interactions have so many advantages such as great diversity, stability and directionality; various coordination assemblies have been accessed with a view to both ligand- and metal-centered chiralities.⁶ Although the initial research in this area dates back to a few decades ago these systems have gained attention in recent years due to the feasibility to tailor their confined space with the potential for selective recognition of enantiomers (which are important building blocks for pharmaceuticals) and separation, and asymmetric catalysis.⁷

There exists number of ways to introduce chirality in metal-organic self-assemblies. In general, two basic methods are used to induce chirality in coordination architectures.⁸ Moreover, the inclusion of a suitable guest molecule within the coordination assemblies sometimes provides a strategy to perturb the symmetry of metallo-supramolecular architectures making them chiral. These aforementioned approaches are being employed in combination to construct chiral metallosupramolecular architectures.

1.2 Chiral architectures achieved by hard approach employing chiral building blocks

Usage of chiral building blocks is one of the successful methods for constructing enantioenriched metallosupramolecular architectures. The advantage of this method is that the chirality of the coordination species is predetermined by using optically pure ligands. Additionally, these ligands remain as chiral entities even after their dissociation from the metal center. Hence, from the viewpoint of their molecular symmetry, the chirality can be considered permanent or hard. In contrast to the achiral case, such a metallosupramolecular structure is unlikely to racemize.

In the hard approach optically pure chiral building blocks are used to yield assemblies with predetermined chirality, where the metal-free ligands are still chiral. The most appropriate method to produce chiral metallosupramolecular assemblies might be using enantiomerically pure starting materials via either chiral organic bridging ligands (Fig. 1a) or chiral metal auxiliaries (Fig. 1b). The enantiopure or racemic nature of the ligands determines the configuration of the overall complexes.

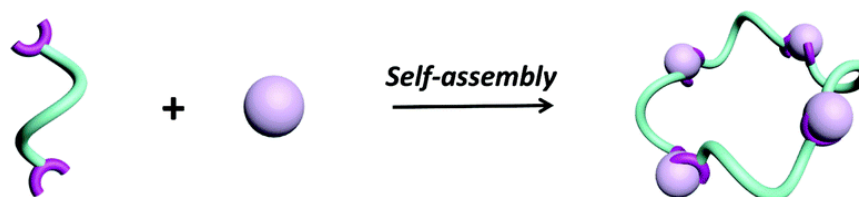
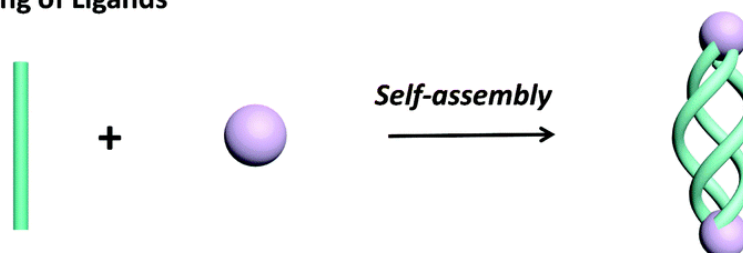
(i)**(a) Chiral Organic Bridging Units****(b) Chiral Auxiliaries****(ii)****(c) Metal Center****(d) Twisting of Ligands**

Figure 1.0: Two type of possible strategies for the construction of chiral metallasupramolecular architectures (i) hard approach (ii) soft approach.

1. 2.1 Chiral organic bridging ligands:

Lützen and coworkers have prepared enantiomerically pure hexa- and dodecanuclear metallosupramolecular spheres from two constitutionally isomeric bis(pyridine) ligands based on a chiral BINOL core with $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$, which exhibited extraordinary high molar circular dichroism depending on the substitution pattern of the BINOL core (Figure 1.1). Despite the relatively high rotational freedom around the central aryl–aryl bond of these BINOL based ligands, during the self-assembly process, these endo- and exo-functionalized chiral supramolecular spheres are formed selectively in a “narcissistic” self-recognition manner.

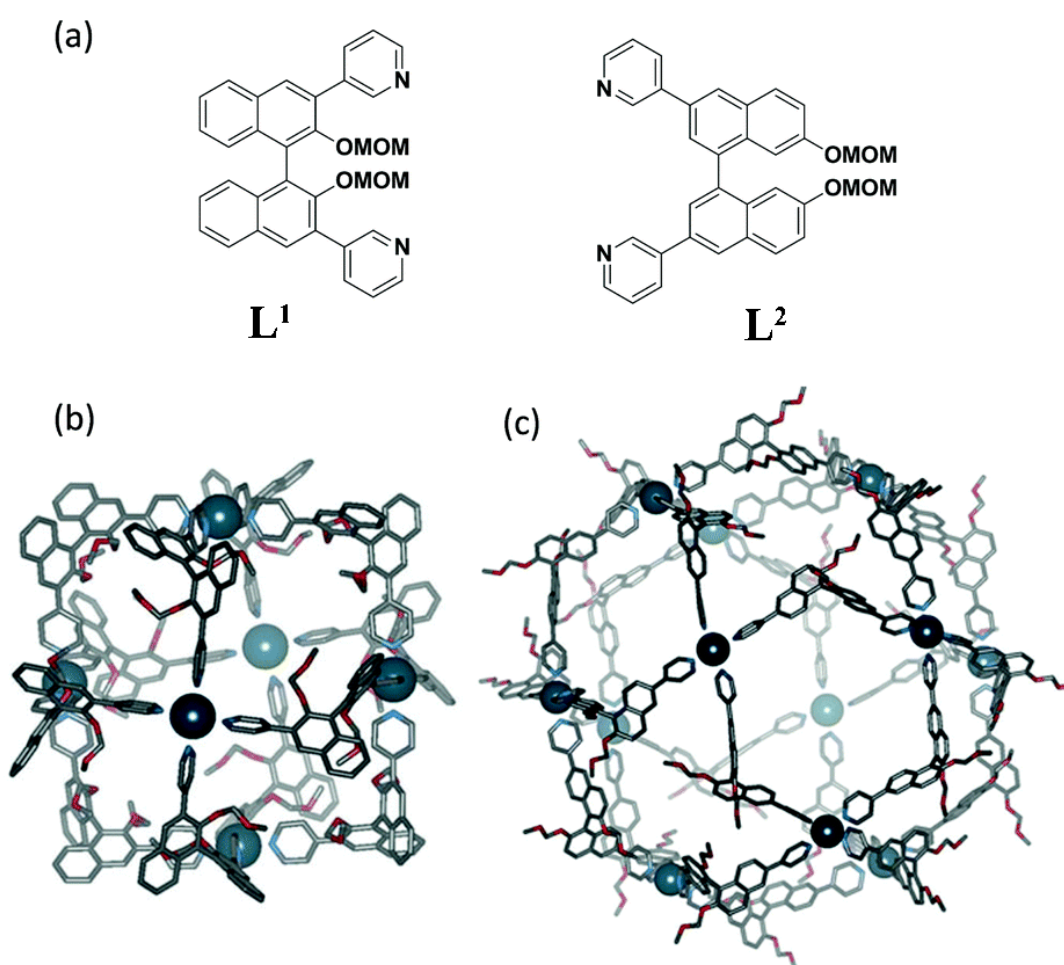


Figure 1.1: (a) The chemical structures of chiral BINOL ligands, L^1 and L^2 , (b) DFT-optimised structures of the O-symmetric complexes $[\text{Pd}_6\{(\text{M})\text{-}32\}_{12}]^{12+}$ and (c) $[\text{Pd}_{12}\{(\text{P})\text{-}33\}_{24}]^{24+}$ (top; petrol Pd, red O, blue N and gray C; hydrogen atoms are omitted for clarity). Reproduced with permission from ref. 1. Copyright © 2014, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

Hardie and coworkers synthesized a $[\text{Ag}_3(\text{L})_2]^{3+}$ species from tripyridyl-functionalised CTV ligands. Interestingly, it was not a simple metallo-cryptophane but rather an $\{[\text{Ag}_3(\text{L})_2]\}^{6+}$ triply interlocking [2]catenane in which two $[\text{Ag}_3(\text{L})_2]^{3+}$ cages (Figure 1.2) were independent of each other. It is interesting to note that catenane is chiral since all four ligands are of the same enantiomer. It is a highly unusual metallo-cryptophane that has formed in the absence of any template or strong-structure directing group.

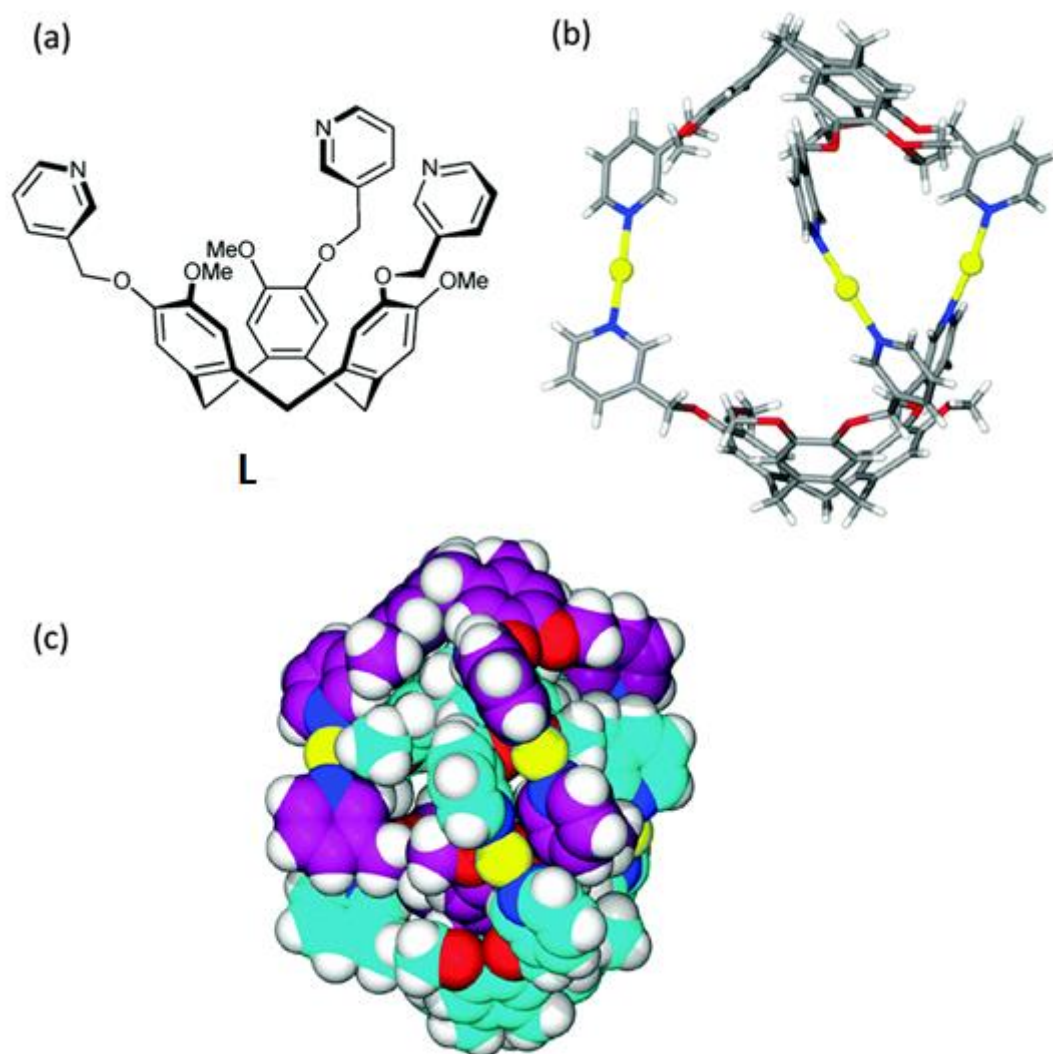


Figure 1.2: (a) The chemical structure of the trispyridyl-functionalised CTV ligand L, (b) crystal structure of a single $[\text{Ag}_3(\text{L})_2]^{3+}$ metallo-cryptophane and (c) a space-filling view of the crystal structure of two metallocryptophanes (shown in different colors) interlocking to form a [2]catenane. Reproduced with permission from ref. 2. Copyright © 2011, Royal Society of Chemistry.

1. 2.2 Chiral auxiliaries:

Fujita and co-workers have reported chiral M_6L_4 truncated tetrahedral cages which formed from achiral D_{2h} -symmetric pyridyl ligand and chiral (*R,R*)-diaminocyclohexane as an auxiliary attached to a Pd(II) center (Figure 1.3). The formation of two diastereomers confirmed by 1H NMR spectroscopy (ratio 1.3: 1) were driven by the template-effect of the aromatic guest molecule (e.g. *p*-dichlorobenzene, *p*-xylene) with a positive Cotton effect. The negative Cotton effect was however observed, when (*S,S*)-diaminocyclohexane auxiliary ligands were used.

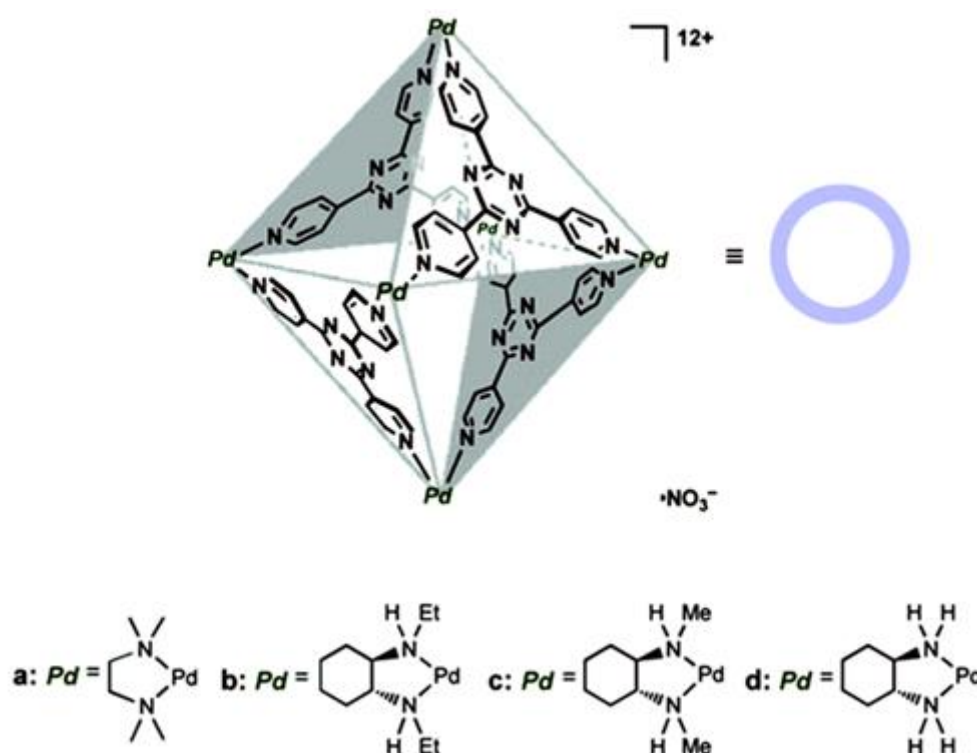


Figure 1.3: Chemical structures of octahedral Pd(II) cages with various chiral diamine auxiliary ligands. Reprinted with permission from ref .3. Copyright © 2002, The Chemical Society of Japan.

Lusby and coworkers have reported first molecular capsule Ir_6L_4 based on an $[Ir(ppy)_2]^+$ unit (ppy = 2-phenylatopyridine) and tritopic 1,3,5-tricyanobenzene in both racemic and enantiopure form. The enantiopure form of Ir_6L_4 octahedra, prepared from Δ - $[(Ir(ppy)_2Cl)_2]$ and Δ - $[(Ir(ppy)_2Cl)_2]$ resolved the amino acid d- and l-serine, respectively (Figure 1.4). Upon addition of 1,3,5-tricyanobenzene to what was presumed to be Δ - and Δ - $[(Ir(ppy)_2OTf)_2]$, these Ir-based coordination capsules Δ - and Δ - featured orange luminescence and in some way inhibited the collisional O_2 quenching.

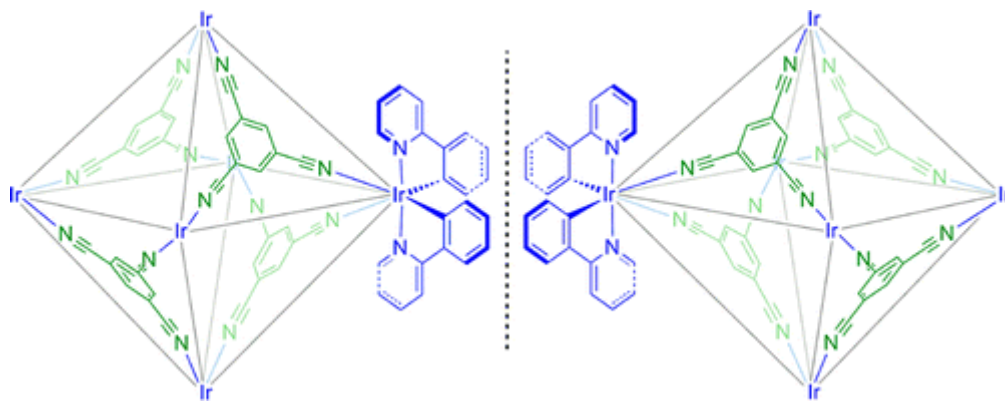


Figure 1.4: Schematic representation of enantiomers of M_6L_4 -MOCs from pre-resolved Ir(III) vertices. Reprinted with permission from ref .4. Copyright © 2012 ACS.

1.3 Chiral architectures achieved by soft approach employing achiral building blocks

In the soft approach achiral building blocks are used to yield chirality, where chirality disappears upon ligand dissociation from the metal center (Figure 1). Furthermore, in supramolecular chirality made up of achiral components, the chirality may arise from the spatial arrangements of achiral chelating ligands around a metal center (Figure. 1c), or as a result of the twisting of the ligands (Figure 1d). In these cases, chirality can be considered to be generated in-situ during the self-assembly process.

1.3.1 Metal center:

Raymond and co-workers resolved a $\Delta\Delta\Delta\Delta$ - $[Ga_4L^1_6]^{12-}$ tetrahedral assembly of labile metal ions and anionic ligand components without compromising its chiral tetrahedral structure. The $[Ga_4L^1_6]^{12-}$ tetrahedron, resulting from the C_2 symmetry of the six naphthyl-biscatecholamide ligands (L) and four octahedral gallium metal centers could be resolved into its $\Delta\Delta\Delta\Delta$ and $\Lambda\Lambda\Lambda\Lambda$ enantiomers by using chiral counter cations. Interestingly, upon subjecting the assembly to exchange of achiral cations as resolving agent, the tetrahedron ($\Delta\Delta\Delta\Delta$)- $[NEt_4^+Ga_4L^1_6]^{11-}$ retained the “chiral structural memory”. They have also shown the stepwise replacement of the naphthyl-biscatecholate ligands by the phenyl derivatives (L^2); these cages retain their original chirality (Figure 1.5). This is a noteworthy demonstration of structural and chiral memory in a single molecular species.

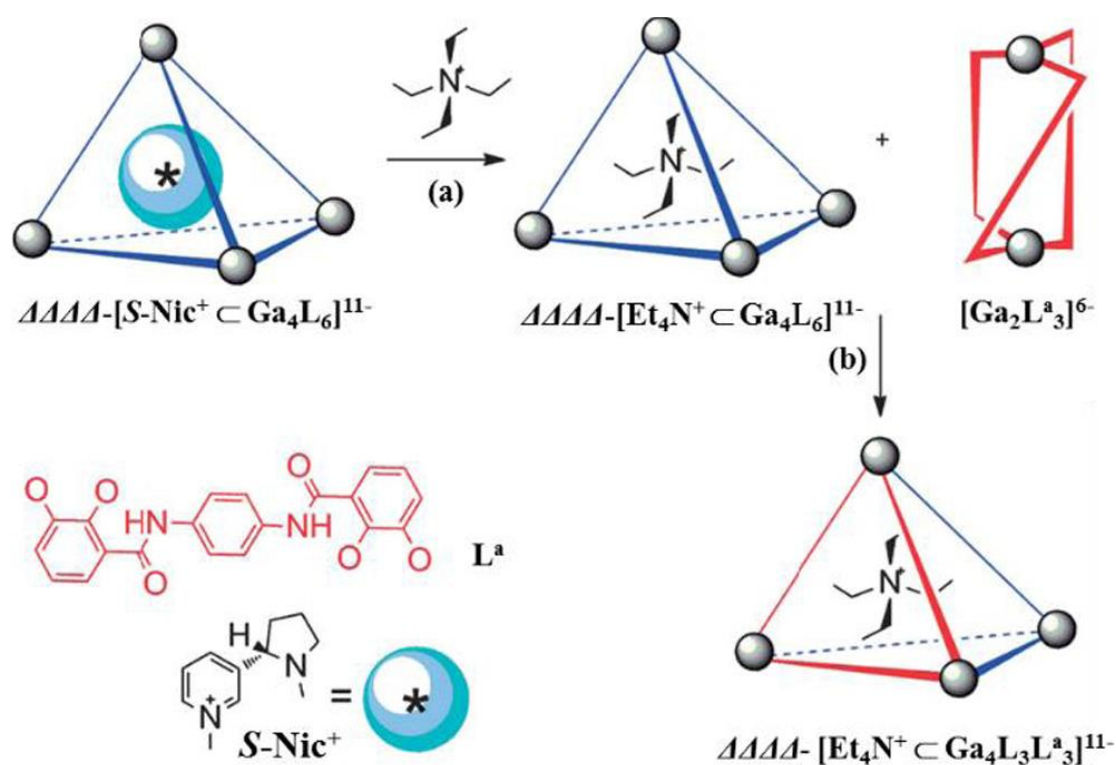


Figure 1.5: Schematic representation of chiral memory of $\Delta\Delta\Delta\Delta$ -[Ga₄L₆]¹²⁻ (a) ion exchange by achiral Et₄N⁺ and (b) substitution of three original L by L^a. Reprinted with permission from ref. 5. Copyright © 2003 WILEY.

Ward and coworkers described the diastereoselective formation of the tetrahedral cages $\{[X\subset\text{Zn}_4\text{L}_6][X]_7\}$ ($X = \text{BF}_4^-$, ClO_4^-) from the chiral bispyrazolyl pyridine ligand (Figure 1.6). Interestingly, chiral pinene group here decides the configurations of metal centers. After coordination, specific rotation value of these ligands increase by five-fold due to the consequence of chiral amplification.

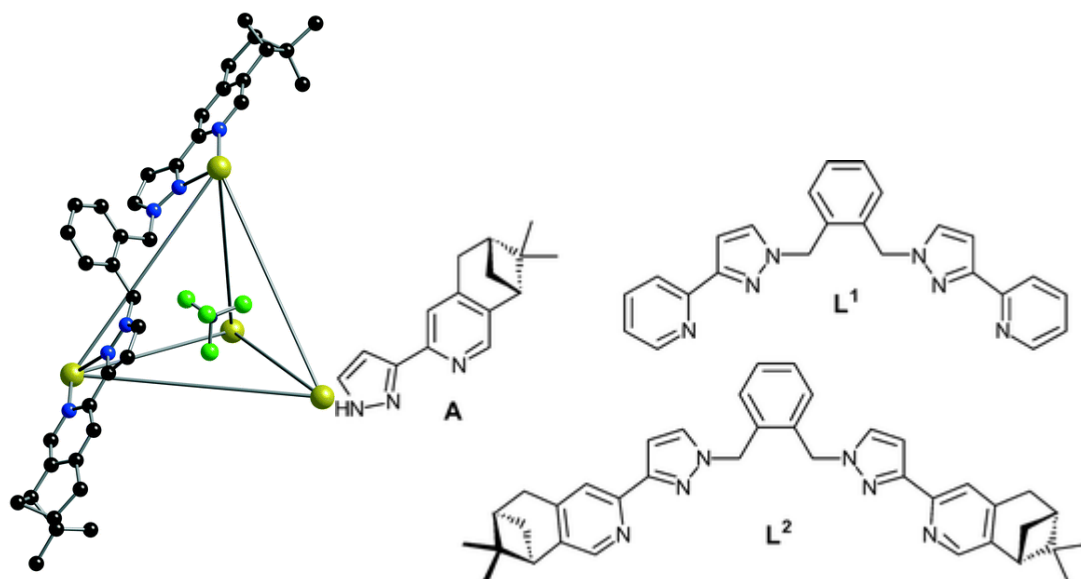


Figure 1.6: Structure of cage complex $[\text{Zn}_4(\text{L})_6(\text{BF}_8)]$ and the encapsulated anion: left, a view showing ligand chiral and achiral ligand were used for cage construction; right. Reprinted with permission from ref. 6. Copyright © 2005, Royal Society of Chemistry.

1.3.2 Twisting of ligands:

Hannon and co-workers have reported the self-assembly of an $\text{M}_{12}\text{L}_{12}$ chiral ball with T symmetry from bis-bidentate pyridylimine ligands and $\text{Cu}(\text{I})$ ions (Figure 1.7). Bowl-shaped triangular helicates were formed from the aggregation of the four bowl-shaped triangular units which assembled in a tetrahedral fashion through $\text{CH}\cdots\pi$ and $\text{CH}\cdots\text{F}$ interactions. Each triangle of the ball is of identical chirality due to the propeller-type twist arrangement of the pyridyl rings of each triangle.

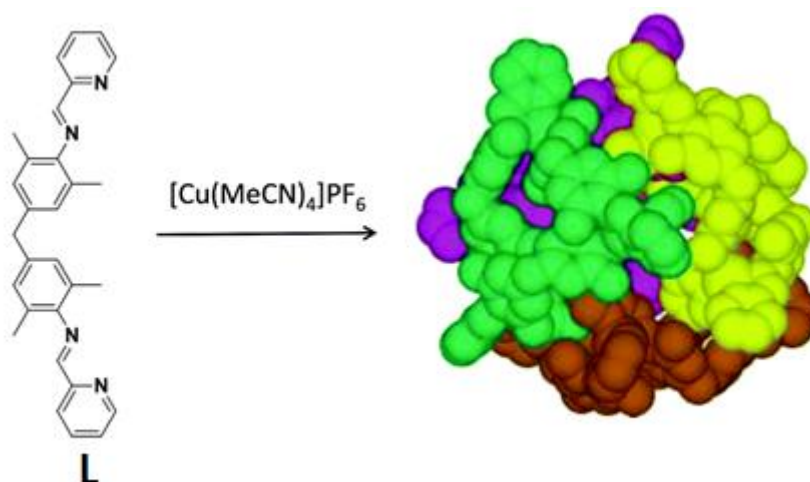


Figure 1.7: Formation of the $M_{12}L_{12}$ chiral ball $[\{Cu_3(L)_3\}_4]^{12+}$, (molecular structure of the ball shaped array resulting from the aggregation of four $[Cu_3(L)_3]^{3+}$ circular helicates; each circular helicate is shown in a different color. (Hydrogen atoms are omitted for clarity). Reproduced with permission from ref. 7. Copyright © 2002, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

Schalley and coworkers have described the self-assembly of chiral truncated tetrahedra M_6L_4 (Figure 1.8) derived from guanidine based ligands. Chirality arose from the ligands twisted in a screw-like orientation upon coordination to the metal centers at each face of the tetrahedron.

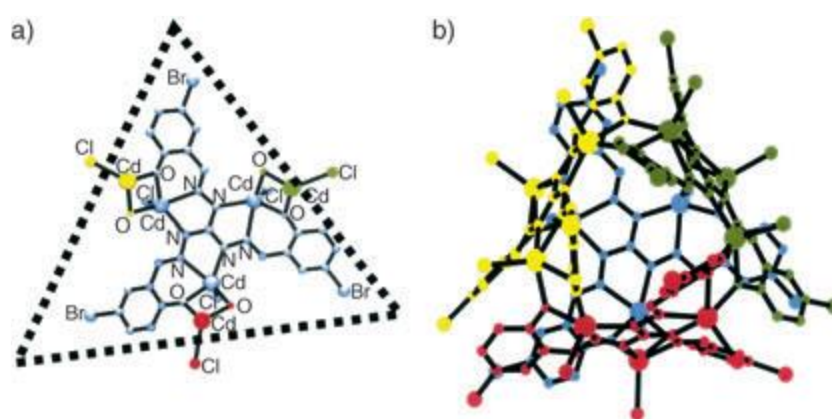


Figure 1.8: a) Connectivity of one $[(CdCl)_3Br_3L]$ unit. b) Crystal structure of $[\{[(CdCl)_3Br_3L]\}_4]^{8+}$, hydrogen atoms and counterions are omitted for clarity. Reproduced with permission from ref. 8. Copyright © 2005, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

1. 4 Synthesis of Chiral Tetrahedral Metal organic cages MOCs:

1. 4. 1 Vertice-directed assembly of chiral MOCs:

Mukherjee and coworkers have prepared chiral $M_{12}L_4$ molecular tetrahedron from the reaction of chiral *cis*- $[(1S,2S)\text{-}dch]Pt(NO_3)_2$ (**M**) [where $(1S,2S)\text{-}dch = (1S,2S)\text{-}1,2\text{-diaminocyclohexane}$] with a *exo*-hexadentate ligand tris(4-(pyrimidin-5-yl)phenyl)amine (**L**) in a 3 : 1 stoichiometric ratio via the vertice-directed method (Figure 1.9). It is shown that the cavity of these cages enable them to catalyze Michael addition reactions of a series of nitro styrene derivatives with indole in a 9:1 water: methanol mixture.

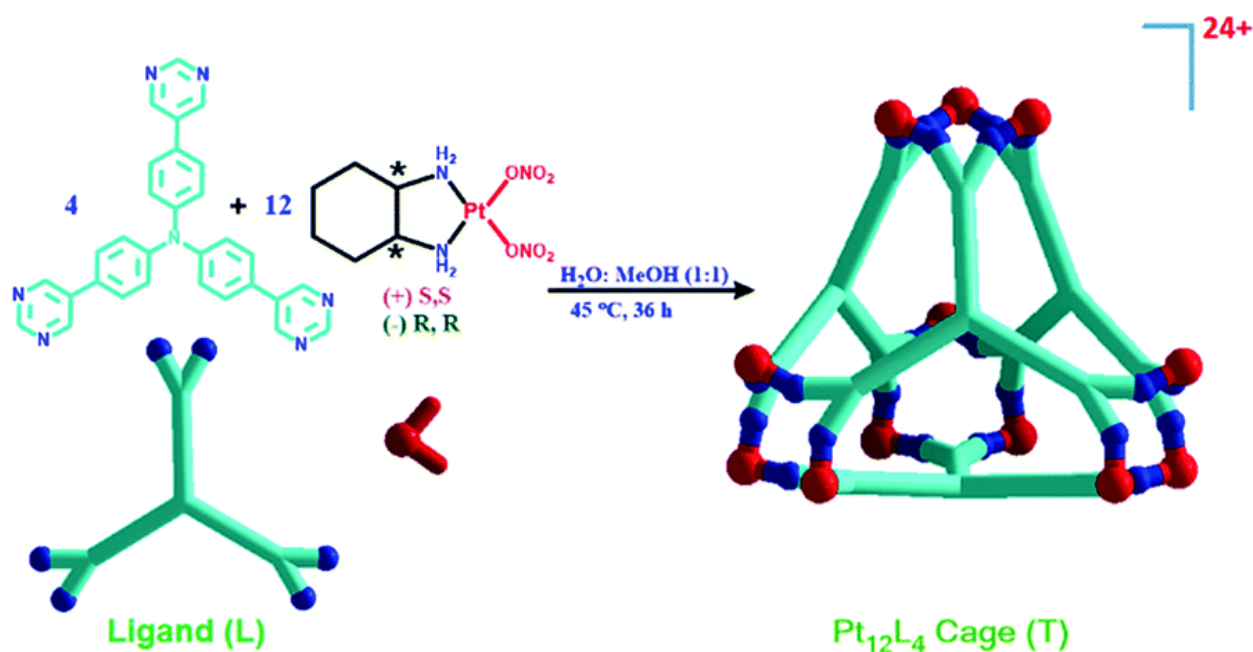


Figure 1.9: Schematic representation of the synthesis of tetrahedral cage (T) from Ligand (L). Reproduced with permission from ref. 9. Copyright © 2018, Royal Society of Chemistry.

1. 4. 2 Edge-directed assembly of chiral MOCs:

Nitschke and coworkers have reported subcomponent self-assembly of chiral cages $\Delta\Delta\Delta\Delta$ and $\Lambda\Lambda\Lambda\Lambda$ -Fe₄L₆ by using the edge-directed method (Figure 1.10). The chirality arises from the chiral glyceryl group attached to the organic ligands on six edges of the tetrahedron. The stereochemistry of the glyceryl groups also dictates the handedness of the apical Fe(II) centers regardless of remote distance, which resulted in [M₄L₆]⁸⁺ cages with all the metal centers having either Δ or Λ configuration. They have shown that the cage to be capable of encapsulating a variety of guest molecules and distinguish the enantiomers of R- and S-limonene guests. Also, it catalyzes the hydrolysis of the neurotoxic organophosphate dichlorvos.

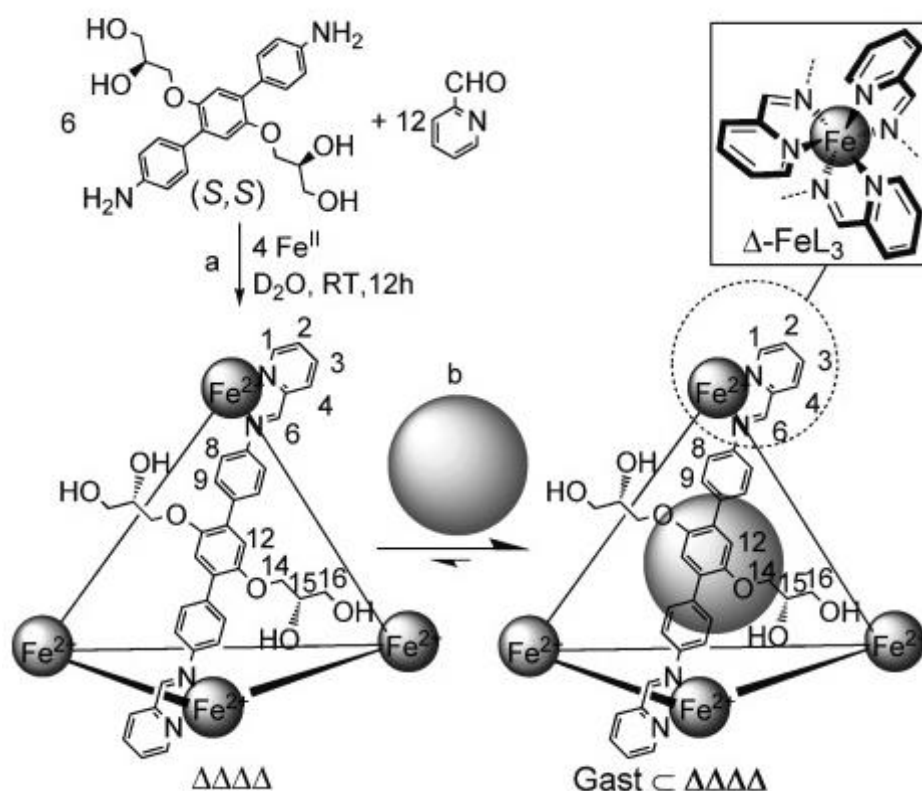


Figure 1.10: a) Enantioselective formation of $\Delta\Delta\Delta\Delta$ from (S,S), 2-formylpyridine, and $\text{Fe}^{\text{II}}\text{SO}_4$ by subcomponent self-assembly; b) Host-guest chemistry of cage $\Delta\Delta\Delta\Delta$. Top right: Δ - $[\text{FeL}_3]$ corner. Reprinted with permission from ref. 10. Copyright © 2013 WILEY.

1.4.3 Face-directed assembly of chiral MOCs:

Mukherjee and co-workers have described the synthesis of face and edge directed self-assembly of Pd_{12} tetrahedral nano-cages from *cis*-blocked $\text{Pd}(\text{II})$ 90° acceptor [*cis*-(tmeda) $\text{Pd}(\text{NO}_3)_2$] (**M**) with 1,4-di(1*H*-tetrazol-5-yl)benzene (L_A) and [1,3,5-tri(1*H*-tetrazol-5-yl)benzene] (L_B) in 1:1 and 3:2 molar ratios respectively, which yielded soft metallogels G1 and G2 [tmeda = *N,N,N',N'*-tetramethylethane-1,2-diamine]. The spatial arrangement of ligands L_A and L_B enable the final tetrahedron assemblies to adopt a specific geometry with a loss of symmetry in order to become square-planar $\text{Pd}(\text{II})$ based chiral cages using achiral building blocks (Figure 1.11).

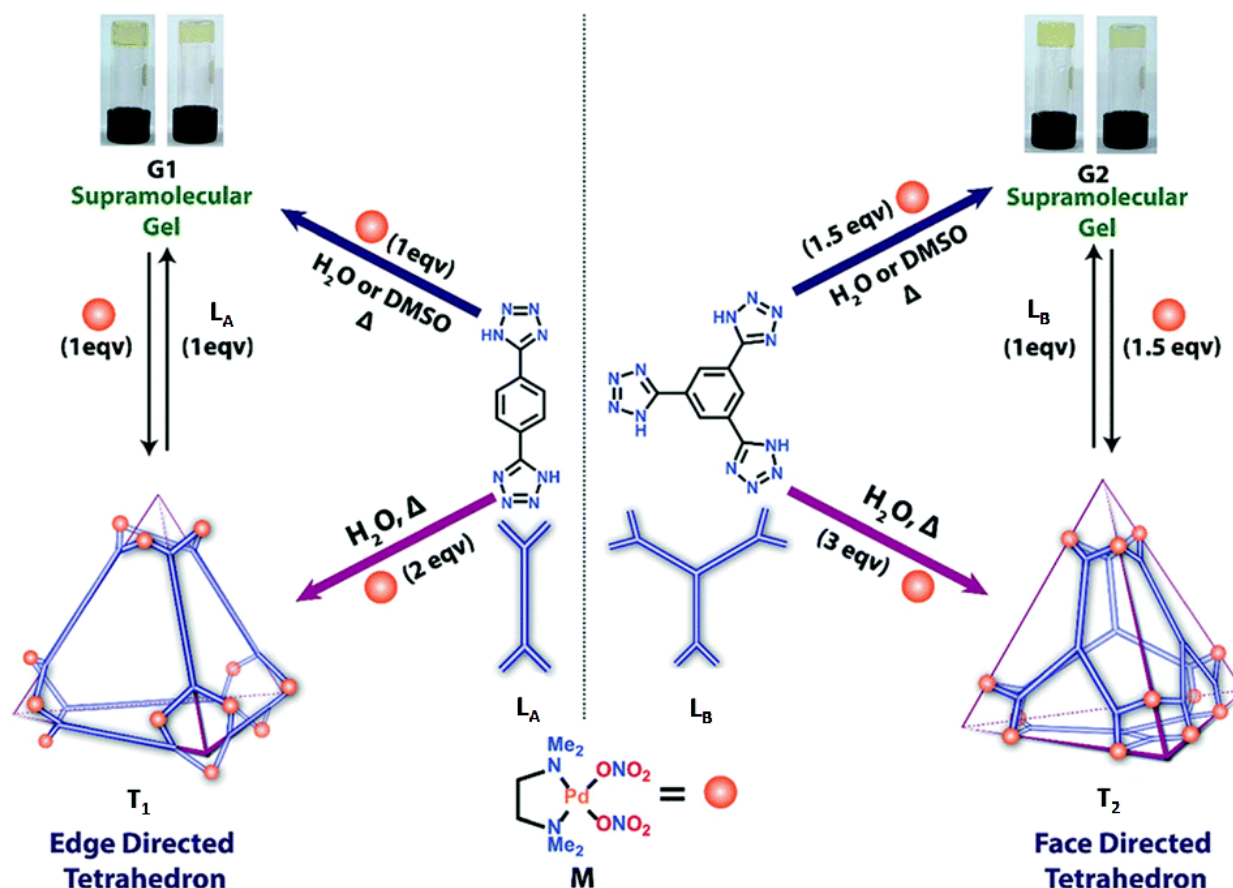


Figure 1.11: Schematic representation of the synthesis of metallogels and their facile conversion to 3D tetrahedral nano-cages L_A and L_B from ligands T₁ and T₂. Reproduced with permission from ref. 11. Copyright © 2016, Royal Society of Chemistry.

1.5 Applications of metal organic cages (MOCs):

1.5.1 Enantioselective recognition and separation:

Cui and co-workers reported a homochiral quadruple-stranded helicate cage [Zn₈L₄Cl₈] which was built from twisted metallosalen ligand (L) with ZnCl₂ (Figure 1.12). X-ray analysis revealed that this helicate cage is porous in nature and its porous binding pocket with chiral N-H functional groups and wide aperture is suitable for enantioselective recognition and separation. This helicate cage was able to distinguish enantiomers of amino acids such as alanine, phenylalanine and valine as detected by fluorescence measurements. Further, they have found that oxidation of this cage to an analogous salalen-based cage improved its fluorescent discriminating behavior and this was the first observation of enantioselective

luminescence sensing of saccharides in solution state and that of amines in the solid state by a coordination driven cage.

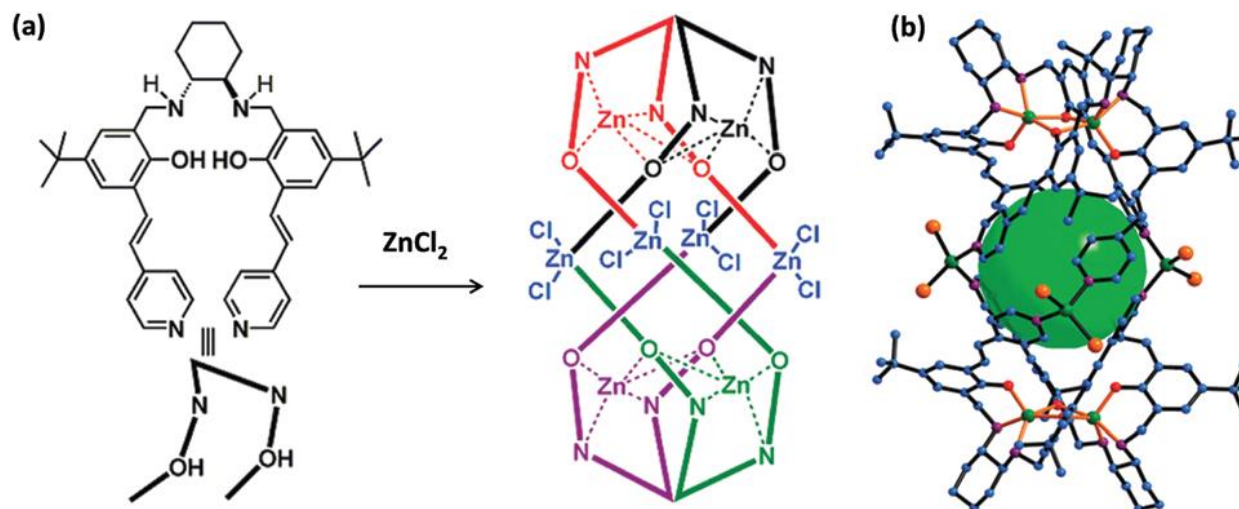


Figure 1.12: (a) Assembly of helicate cage from ligand chiral salen ligand and (b) view of the molecular structure of cage-(R) (dark-green, Zn; yellow, Cl; blue, C; red, O; purple, N). Reproduced with permission from ref. 12. Copyright © 2012, American Chemical Society.

1. 5. 2 Catalysis:

As discussed in the previous section, Fujita and co-workers have synthesized chiral M_6L_4 -type MOCs using *trans*-N, N'-diethyl-cyclohexanediamine attached to the Pd(II) as chiral auxiliaries. Asymmetric [2+2] olefin photoaddition of fluoranthene and N-cyclohexylmaleimide catalyzed by these cages yielded the adduct product with 50% *ee* value (Figure 1.13). Molecular dynamics calculation revealed that a steric hindrance on the chiral diamine auxiliaries forced the triazine ligand to tilt with different degree to create a chiral cavity, which effectively endorsed the stereo selectivity of the reaction. This was the first example of the asymmetric photo-addition reaction catalyzed by a M_6L_4 cage assisted by the presence of remote chiral auxiliaries. In this case there is no direct interaction between the reaction site of the cage and organic substrates with the chiral segments of the cage.

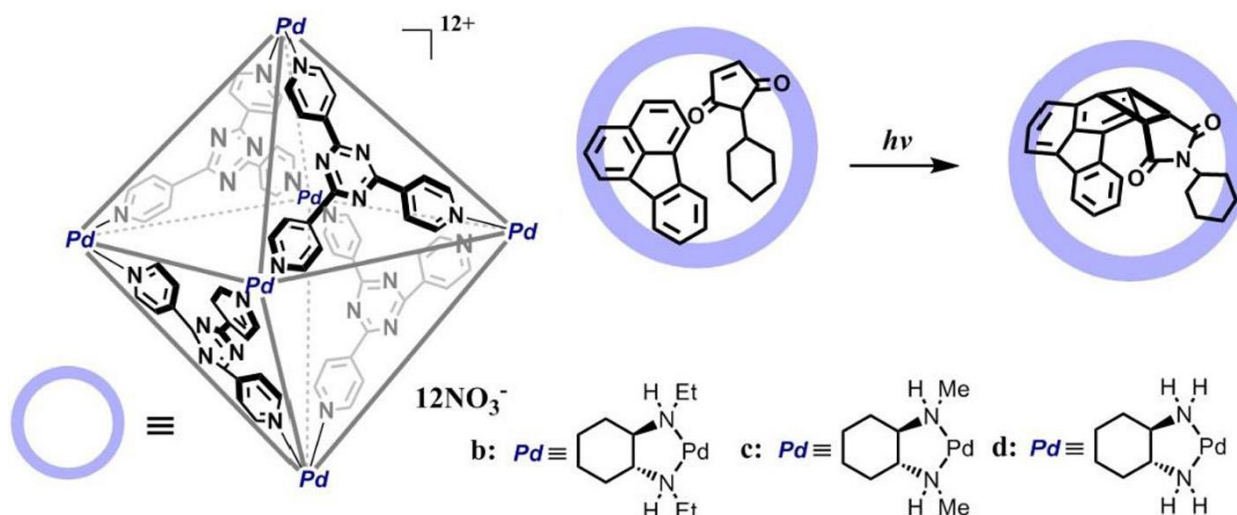


Figure 1.13: a) The chemical structure of octahedral cages with different chiral auxiliaries and (b) [2+2] photo addition reaction in the cage. Reproduced with permission from ref. 13. Copyright © 2008, American Chemical Society.

1. 5. 3 Biological Studies:

Guo gu and co-workers have facilely synthesized four pairs of enantiomers of water-stable tetrahedral cages with the formula [Ni₄L₆]⁸⁺ (Figure 1.14). The high positive charge of these tetrahedral cage and its suitable size efficiently stabilized antiparallel G-quadruplex DNA with moderate enantioselectivity. Also, they exhibited promising cytotoxicity against the human cancer cell lines HCT116, HepG2 and MCF-7. These findings pave the way for the metal–organic cages as attractive candidates for telomerase inhibitors and design of chiral G-quadruplex-based anticancer agents.

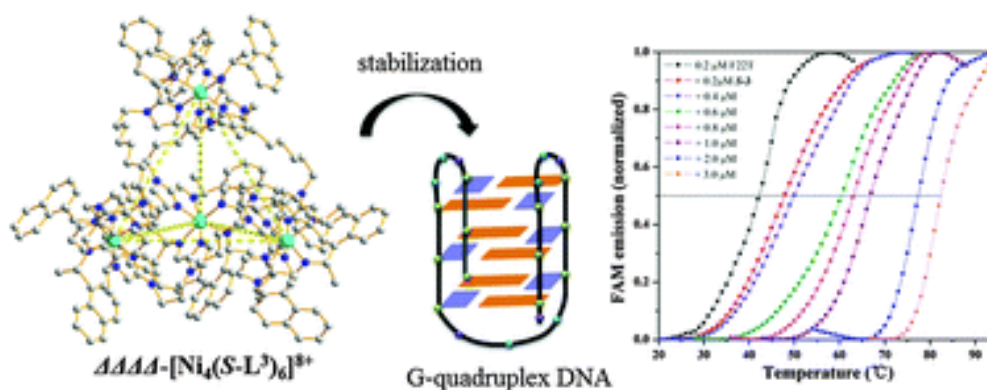


Figure 1.14: Representative illustration of a chiral tetrahedral cage bound to G-quadruplex DNA in the end-stacking mode. Reproduced with permission from ref. 14. Copyright © 2016, Royal Society of Chemistry.

The same group has synthesized four pairs of chiral tetrahedral nickel (II) coordination cages, which act as high-performance inhibitors against amyloid- β (A β) aggregation with a high inhibition rate of 0.64–0.86 (Figure 1.15). The reasons such as electrostatic interaction, π – π stacking and van der Waal forces are responsible for the inhibition of A β aggregation by these cages. Atomic force microscopy and fluorescence assay were used to examine the effect of chiral nickel cages on the fibrillation of A β peptide. These outcomes offer new visions into the size, charge, functional groups and stereo selectivity of supramolecular complexes for the design of chiral A β inhibitors.

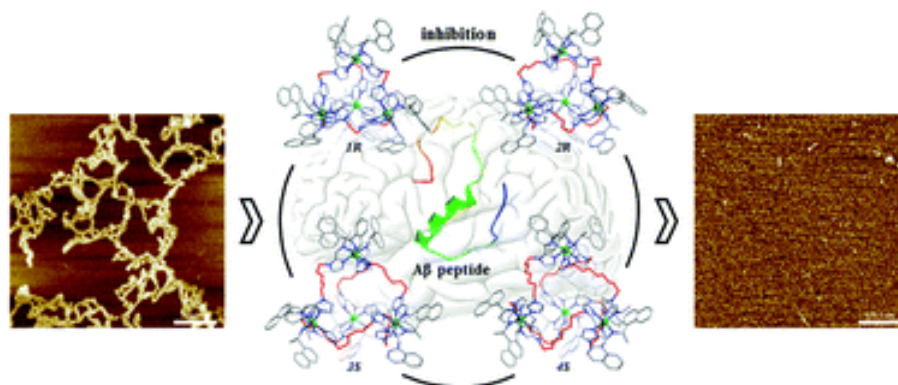


Figure 1.15: Schematic representation of chiral supramolecular coordination cages as high-performance inhibitors against amyloid- β aggregation. Reproduced with permission from ref. 14. Copyright © 2018, Royal Society of Chemistry.

1. 6 Outline of the Thesis

An overview of the developments in the chemistry of chiral metal-ligand cages indicates that most of these assemblies are either cationic or anionic, except a few examples as shown in Figure 1.12. Hence, the present thesis aims to build the chemistry of chiral neutral cages by extending the chemistry of neutral tetrahedral cages based on imido-P(V) ligands that are developed earlier in our laboratory.

Thus, this thesis established the development chiral metal-organic cages utilizing chiral phosphorus (V) ligands that acts as chiral auxiliaries. The next four chapters will discuss about synthesize a library of P-N scaffolds, such as, neutral phosphoramidate ligands or cationic phosphonium salts, which support in acquiring enantioselective metal-organic or organic self-assemblies and promote to assess their chiral recognition and separation properties. The chapter 2 will discuss the synthesis of the chiral phosphonium salts based on α -methylbenzylamino groups in the presence of halide and carboxylate containing anions, their supramolecular structures and their ability to recognize small chiral molecules as indicated by NMR analysis.

The chapter 3 describes the synthesis of a pair of enantiomeric phosphoramidate ligands and their reactions leading to a pair of chiral neutral tetrahedral cages built by oxalate bridges. These cages were further shown to exhibit the enantio-separation capabilities of certain small racemate molecules. The chapters 4 will discuss the synthesis of chloranilate tethered chiral tetrahedral cages and their ability to resolve series of 4-halostyrene oxides. Finally, the chapter 5 will deal with the synthesis of chiral radical metal organic cages based dihydroxybenzoquinonate (DHBQ) and Bromanilate anion linkers.

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End of Chapter 1



Chapter 2



**Synthesis and functional studies of
chiral aminophosphonium salts**

2.1 Introduction

Chirality plays a substantial role in various fields ranging from chemical, pharmacological, biological and materials science.¹ Most of the living systems like DNA, RNA, peptides, and enzymes are chiral in nature. Chiral recognition is defined as the ability of a chiral host molecule to selectively bind one guest enantiomer over the other. Chiral recognition can be sensed via techniques such as X-ray crystallography and nuclear magnetic resonance (NMR) and by chemical derivatization. NMR is a powerful technique to detect recognition of analytes in solution without derivatization and gives information about the interaction between chiral host and guest.²⁻³ The non-covalent driving forces such as ion-pairing, hydrogen bonding, π - π interaction, etc. play an important role in chiral recognition mechanisms and can be sensed by NMR techniques. Several synthetic receptors such as crown ethers,⁴ cryptands,⁵ spherands,⁶ cyclodextrins,⁷ cryptophanes,⁸ cyclophanes,⁹ carcerands,¹⁰ hemicarcerands,¹¹ cucurbiturils¹² are used for chiral guest recognition apart from their well-known anion recognition and complexation studies. These receptors are highly complex in nature and can be incorporated with specific targeting groups to attain selectivity. Other novel examples of synthetic receptors include metal-organic¹³ and covalent organic frameworks,¹⁴ self-assembled cages,¹⁵ rotaxanes, catenanes,¹⁶ paraphenylenes¹⁷ and pillararenes.¹⁸ Typically, the receptor molecules exhibit certain enantiomeric functionalities that have been premeditated to sense and distinguish suitable substrates. For example, receptors with chiral NH groups are suitable for recognizing biological substrates such as carbohydrates, amino acids, amines, and other important drug compounds that contains complementary sites for hydrogen bonding.¹⁹ Despite these advancements, there is a constant need to develop novel chiral hosts with multiple driving forces that can assist in strengthening the host and guest interactions that favours the chiral discrimination of enantiomers with various functionalities. Chiral amino-phosphonium salts have been utilized in enantioselective catalytic transformations, for example, the Mannich reaction, the Henry reaction, and the hydrophosphonylation of aldehydes. Inspired by the simple protocols involved in the synthesis of tetra-functionalized chiral amino-phosphonium salts, we set out to employ the aminophosphonium salts in the selective recognition of chiral organic guest substrates supported by various supramolecular interactions such as H-bonding, dipole-dipole and ion-dipole interactions, etc. In this chapter, we describe the synthesis of new examples of chiral aminophosphonium salts containing R- or S- α -methyl benzyl substituents on the amino group and utilized them for the enantioselective discrimination of various two

enantiomeric pair of guest molecules and anion exchange studies. In the first part of this chapter, the enantiomeric pair of chiral phosphonium salts was employed for the recognition of R- and S-mandelic acid and R- and S-phenyl glycinol. The recognition of these guest molecules were believed to take place via multiple driving forces consisting of hydrogen bonding, ion pair formation and π - π interactions. In the second part of this chapter, we subjected these phosphonium chloride salts to anion exchange studies with certain carboxylic acids. Particularly, using anilic acids, these salts form enantiomeric pairs of crystals in 2:1 stoichiometry.

2.2 EXPERIMENTAL SECTION

2.2.1 General remarks

All manipulations involving phosphorus pentachloride were performed under dry nitrogen atmosphere in standard Schlenk glassware. Solvents were purchased locally. PCl_5 and chiral amines were purchased from Aldrich and used as received. The chiral (R and S) mandelic acid, (R and S) phenyl glycinol were locally procured (AVRA, India) and used as received. NMR spectra were recorded on a 400 MHz Varian FT spectrometer (^1H NMR 400.13 MHz, ^{13}C { ^1H } NMR 100.62 MHz, ^{31}P { ^1H } NMR 161.97 MHz, ^{19}F NMR 377.10 MHz) at room temperature using SiMe_4 (^1H , ^{13}C), 85% H_3PO_4 (^{31}P), CCl_3F (^{19}F) as external standards. The mass spectra were obtained on an Applied Bio system matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF)/TOF spectrometer. Thermal analysis (TGA) data have been obtained from a PerkinElmer STA-6000 thermo gravimetric analyzer. Elemental analyses were performed on a Vario-EL cube elemental analyzer.

2.2.2 Synthesis

2.2.2.1 Synthesis of chiral phosphonium ligands P-R₄ and P-S₄

Phosphorous pentachloride (0.675 gm, 0.0032 mmol) placed in a schlenk round bottom flask under inert atmosphere and dissolved in 15ml of dichloromethane. The chiral R or S α -methyl benzyl amine (2 ml, 0.0129 mmol) and triethylamine (2.28 ml, 0.016 mmol) were introduced drop wise slowly at 0 °C. The resultant mixture stirred for 24 hrs. The precipitated triethylamine hydrochloride salt was filtered and the solution was evaporated to acquire the crude phosphonium salt as an oily substance. This was further purified by washing with water and diethyl ether to obtain a pure white solid. P-R₄: Yield: 84% (1.15 gm, based on P). ^1H NMR

(400 MHz, CDCl₃): δ 1.33 (d, 12H, CH₃), 3.99-4.09(m, 4H, CH), δ 6.13-6.19 (t, 4H, NH), 7.11-7.22 (m, 20H, aromatic). ¹³C NMR (100 MHz, CDCl₃): δ 26.2, 50.7, 105.6, 126.2, 127.0, 128.4, 145.3, 172.4. ³¹P NMR (161 MHz, CDCl₃): δ 22.81. MALDI-TOF/TOF: 511 (M⁺). P-S₄: Yield: 80% (1.05 gm, based on P). ¹H NMR (400 MHz, CDCl₃): δ 1.33 (d, 12H, CH₃), 3.99-4.09(m, 4H, CH), δ 6.13 (t, 4H, NH), 7.11-7.22 (m, 20H, aromatic). ¹³C NMR (100 MHz, CDCl₃): δ 26.2, 50.7, 105.6, 126.2, 127.0, 128.4, 145.3, 172.4. ³¹P NMR (161 MHz, CDCl₃): δ 22.81. MALDI-TOF/TOF: 511 (M⁺).

2.2.2.2 Typical procedure for enantio-discrimination of chiral guests using P-R₄ and P-S₄:

The samples of chiral hosts P-R₄ and P-S₄ (10mg, 0.6ml) and guest (30eq in 0.3 ml) were prepared separately in DMSO-d₆ and then subjected to ¹H NMR titrations to understand their binding behavior.

The ¹H-NMR titrations were performed for all the host-guest systems. A 10⁻³ M solution of the phosphonium salt was prepared in DMSO-d₆. To this, subsequent equivalents of the guest molecules in DMSO-d₆ were added from their stock solutions. Chemical shift changes (either upfield or downfield) were observed for the guest and/or the host protons. The titration experiment was continued until the peak shifts finally became constant indicating completion of the chiral-recognition process. The data were then analysed and fitted in 2:1 and 1:2 host-guest binding model using the Bindfit^{4,5} online tool which gave the final association constant values.

2.2.2.3 Synthesis of chiral phosphonium anilates from P-R₄ and P-S₄

Typical procedures used for the synthesis of chiral phosphonium anilates has been described with one example as given below for the synthesis of phosphonium chloranilates. A similar procedure has been adopted for the synthesis of other phosphonium anilates as well.

To a well stirred solution of P-R₄ or P-S₄ (100 mg, 0.18 mmol) in methanol (~5ml), a solution of sodium salts of chloranilate (25 mg, 0.091 mmol) in water (3 ml) was slowly added to the solution with continuous stirring. Further, the reaction mixture refluxed with stirring 24 hrs. The precipitate was filtered and washed with water to remove the NaCl salt and dried at oven. The obtained precipitate was dissolved in methanol and kept for crystallization to get pure product. This gave colored crystals suitable for single crystal X-ray diffraction (SCXRD) analysis (Table 2.2).

PD-**R** (Phosphonium dihydroxy beznoquinat dianion): Yield: 79.7% (90 mg, based on P). ^1H NMR (400 MHz, DMSO- d_6): δ 1.34 (d, 24H, CH_3), 3.99-4.09(m, 8H, CH), δ 6.57-6.62 (t, 8H, NH), 7.09-7.19 (m, 40H, aromatic). ^{13}C NMR (100 MHz, DMSO- d_6): δ 26.4, 50.5, 101.6, 126.1, 126.9, 128.4, 145.5, 180.5. ^{31}P NMR (161 MHz, DMSO- d_6): δ 23.6. MALDI-TOF/TOF: 511 (M^+).

PD-**S** (Phosphonium dihydroxy beznoquinat dianion): Yield: 86.7% (98 mg, based on P). ^1H NMR (400 MHz, DMSO- d_6): δ 1.34 (d, 24H, CH_3), 3.99-4.09(m, 8H, CH), δ 6.57-6.62 (t, 8H, NH), 7.09-7.19 (m, 40H, aromatic). ^{13}C NMR (100 MHz, DMSO- d_6): δ 26.4, 50.5, 101.6, 126.1, 126.9, 128.4, 145.5, 180.5. ^{31}P NMR (161 MHz, DMSO- d_6): δ 23.6. MALDI-TOF/TOF: 511 (M^+).

PF-**R** (Phosphonium Fluoranilate): Yield: 73.42% (80 mg, based on P). ^1H NMR (400 MHz, DMSO- d_6): δ 1.34 (d, 24H, CH_3), 3.99-4.09(m, 8H, CH), δ 6.23-6.29 (t, 8H, NH), 7.09-7.21 (m, 40H, aromatic). ^{13}C NMR (100 MHz, DMSO- d_6): δ 26.4, 50.5, 101.6, 126.1, 126.9, 128.4, 145.5, 180.5. ^{31}P NMR (161 MHz, DMSO- d_6): δ 22.7. ^{19}F NMR (377 MHz, DMSO- d_6): δ -177.9. MALDI-TOF/TOF: 511 (M^+).

PF-**S** (Phosphonium Fluoranilate): Yield: 76.1% (83 mg, based on P). ^1H NMR (400 MHz, DMSO- d_6): δ 1.34 (d, 24H, CH_3), 3.99-4.09(m, 8H, CH), δ 6.23-6.29 (t, 8H, NH), 7.09-7.21 (m, 40H, aromatic). ^{13}C NMR (100 MHz, DMSO- d_6): δ 26.4, 50.5, 101.6, 126.1, 126.9, 128.4, 145.5, 180.5. ^{31}P NMR (161 MHz, DMSO- d_6): δ 22.7. ^{19}F NMR (377 MHz, DMSO- d_6): δ -177.9. MALDI-TOF/TOF: 511 (M^+).

PC-**R** (Phosphonium Chloranilate): Yield: 80% (90 mg, based on P). ^1H NMR (400 MHz, DMSO- d_6): δ 1.33 (d, 24H, CH_3), 3.99-4.09(m, 8H, CH), δ 6.13-6.19 (t, 8H, NH), 7.11-7.22 (m, 40H, aromatic). ^{13}C NMR (100 MHz, DMSO- d_6): δ 26.2, 50.7, 105.6, 126.2, 126.9, 127.0, 128.4, 145.3, 172.4. ^{31}P NMR (161 MHz, DMSO- d_6): δ 21.97. MALDI-TOF/TOF: 511 (M^+).

PC-**S** (Phosphonium Chloranilate): Yield: 83% (93 mg, based on P). ^1H NMR (400 MHz, DMSO- d_6): δ 1.33 (d, 24H, CH_3), 3.99-4.09(m, 8H, CH), δ 6.13-6.19 (t, 8H, NH), 7.11-7.22 (m, 40H, aromatic). ^{13}C NMR (100 MHz, DMSO- d_6): δ 26.2, 50.7, 105.6, 126.2, 126.9, 127.0, 128.4, 145.3, 172.4. ^{31}P NMR (161 MHz, DMSO- d_6): δ 21.97. MALDI-TOF/TOF: 511 (M^+).

PB-**R** (Phosphonium Bromanilate): Yield: 75% (90 mg, based on P). ^1H NMR (400 MHz, DMSO- d_6): δ 1.34 (d, 24H, CH_3), 3.99-4.09(m, 8H, CH), δ 6.14-6.19 (t, 8H, NH), 7.12-7.20

(m, 40H, aromatic). ^{13}C NMR (100 MHz, DMSO- d_6): δ 26.2, 50.7, 98.0, 126.2, 127.0, 128.4, 145.3, 172.6. ^{31}P NMR (161 MHz, DMSO- d_6): δ 20.8. MALDI-TOF/TOF: 511 (M^+).

PB-S (Phosphonium Bromanilate): Yield: 79% (95 mg, based on P). PB-R: Yield: 84% (1.15 gm, based on P). ^1H NMR (400 MHz, DMSO- d_6): δ 1.34 (d, 24H, CH_3), 3.99-4.09(m, 8H, CH), δ 6.14-6.19 (t, 8H, NH), 7.12-7.20 (m, 40H, aromatic). ^{13}C NMR (100 MHz, DMSO- d_6): δ 26.2, 50.7, 98.0, 126.2, 127.0, 128.4, 145.3, 172.6. ^{31}P NMR (161 MHz, DMSO- d_6): δ 20.8. MALDI-TOF/TOF: 511 (M^+).

2.2.3 Crystallography

Reflections were collected on a Bruker Smart Apex Duo diffractometer at 100 K using Mo $\text{K}\alpha$ radiation ($\lambda = 0.71073 \text{ \AA}$) for chiral phosphonium salts P-R₄ and P-S₄, Chiral phosphonium anilates PD-R, PD-S, PF-R, PF-S, PC-R, PC-S, PB-R, and PB-S. All structures were solved using intrinsic phasing method, and refined by full-matrix least-squares on F^2 (G. M. Sheldrick, SHELXle, program for crystal structure refinement, University of Gottingen, Germany, 2015).¹¹ Crystallographic data for all these compounds are listed in Table 2.1 and 2.2. All non-hydrogen atoms were refined anisotropically if not stated otherwise. Hydrogen atoms were constrained in geometric positions to their parent atoms. All the phenyl rings are constrained to ideal six membered rings. The disordered benzene rings were treated with SIMU and DELU restraints and refined isotropically.

Table 2.1 Crystallographic Data for chiral phosphonium salts P-R₄ and P-S₄.

Compound	P-R ₄	P-S ₄
Chemical formula	C ₃₂ H ₄₀ Cl N ₄ P	C ₃₂ H ₄₀ Cl N ₄ P
Formula weight	547.10	547.10
Temperature	100(2)K	100(2)K

Crystal system	Orthorhombic	Orthorhombic
Space group	F 2 2 2	F 2 2 2
a (Å); α (°)	16.008(13); 90	16.026(13);90
b (Å); β (°)	25.35(2); 90	25.33(2);90
c (Å); γ (°)	30.42(3); 90	30.46(3);90
V (Å ³); Z	12344(18)	12366(18)
ρ (calc.) mg m ⁻³	1.212	1.764
μ (Mo K α) mm ⁻¹	0.206	1.118
2 $\theta_{\max}$ (°)	58.158	57.046
R(int)	0.3699	0.1443
Data / param.	8156/349	7490/349
GOF	0.978	1.199
R1 [F>4 σ (F)]	0.1283	0.1078
wR2 (all data)	0.2870	0.2573
Flack parameter	-0.10(18)	0.01(8)
Max. peak/ hole (e.Å ⁻³)	0.948/-0.722	1.102/-0.855

Table 2.2 Crystallographic Data for Chiral Phosphonium anilates PD-**R**, PD-**S**, PF-**R**, PF-**S**, PC-**R**, PC-**S**, PB-**R**, and PB-**S**.

Compound	PD- R	PD- S	PF- R	PF- S
Chemical formula	C ₇₂ H ₉₀ N ₈ O ₇ P ₂	C ₇₂ H ₉₀ N ₈ O ₇ P ₂	C ₇₀ H ₈₀ F ₂ N ₈ O ₄ P ₂	C ₇₀ H ₈₀ F ₂ N ₈ O ₄ P ₂
Formula weight	1241.45	1241.45	1197.36	1197.36
Temperature	100(2)K	100(2)K	100(2)K	100(2)K
Crystal system	Orthorhombic	Orthorhombic	Orthorhombic	Orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁	P2 ₁ 2 ₁ 2 ₁	P2 ₁ 2 ₁ 2 ₁	P2 ₁ 2 ₁ 2 ₁
a (Å); α (°)	13.153(3); 90	13.1872(17);90	12.600(3);90	12.653(5);90
b (Å); β (°)	21.442(5); 90	21.536(3);90	21.151(5);90	21.282(9);90
c (Å); γ (°)	24.139(6); 90	24.231(3);90	23.605(5);90	23.720(10);90
V (Å ³); Z	6808(3)	6881.4(15)	6291(3)	6387(5)
ρ (calc.) mg m ⁻³	1.211	1.198	1.264	1.245
μ (Mo K α) mm ⁻¹	0.123	0.121	0.131	0.129
2 $\theta_{\max}$ (°)	56.992	50.484	56.904	57.576
R1 [F>4 σ (F)]	0.0674	0.0795	0.0481	0.0247
Data / param.	17079/803	17120/814	15692/783	16336/783
		1.253	0.982	0.958

GOF	1.019	0.1147	0.0481	0.0824
R(int)	0.1236	0.1933	0.1369	0.1739
wR2 (all data)	0.1594	0.05(5)	0.00(4)	0.07(9)
Flack parameter	-0.02(5)	1.102/-1.078	0.409/-0.485	0.507/-0.463
Max. peak/ hole (e.Å ⁻³)	1.234/-0.477			

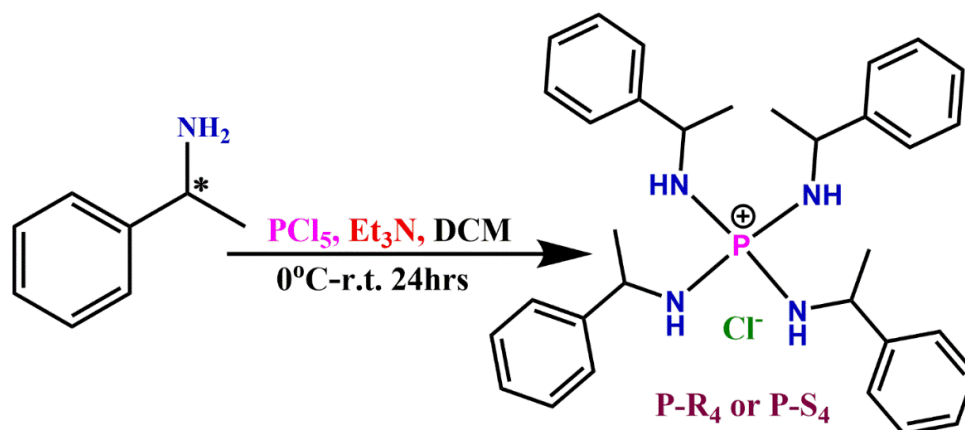
Compound	PC-R	PC-S	PB-R	PB-S
Chemical formula	C ₇₀ H ₈₁ Cl ₂ N ₈ O ₄ P ₂	C ₇₀ H ₈₀ N ₈ O ₄ P ₂	C ₇₀ H ₈₀ Br ₂ N ₈ O ₄ P ₂	C ₇₀ H ₈₀ Br ₂ N ₈ O ₄ P ₂
Formula weight	1231.26	1230.26	1319.18	1319.18
Temperature	100(2)K	100(2)K	100(2)K	100(2)K
Crystal system	Orthorhombic	Orthorhombic	Orthorhombic	Orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁	P2 ₁ 2 ₁ 2 ₁	P2 ₁ 2 ₁ 2 ₁	P2 ₁ 2 ₁ 2 ₁
a (Å); α (°)	12.550(3); 90	12.557(2);90	12.531(5);90	12.498(5);90
b (Å); β (°)	21.580(6); 90	21.589(4);90	21.718(8);90	21.714(8);90
c (Å); γ (°)	24.405(6); 90	24.385(4);90	24.413(9);90	24.448(9);90
V (Å ³); Z	6610(3)	6610.6(19)	6644(4)	6635(4)
ρ (calc.) mg m ⁻³	1.237	1.236	1.319	1.321
μ(Mo K _α) mm ⁻¹	0.201	0.201	1.322	1.324
2θ _{max} (°)	56.874	56.632	56.856	56.660
R1 [F>4σ(F)]	0.0689	0.0647	0.0491	0.0650
Data / param.	16507/783	16460/771	16598/783	16449/784
GOF	1.052	0.929	0.967	0.907
R(int)	0.1059	0.0795	0.0673	0.1462
wR2 (all data)	0.1782	0.2072	0.1342	0.1909
Flack parameter	0.03(3)	0.006(15)	0.011(3)	0.016(6)
Max. peak/ hole (e.Å ⁻³)	1.597/-0.562	1.576/-0.697	1.419/-1.360	1.416/-0.805

2.3 RESULTS AND DISCUSSION

PART A: Chiral aminophosphonium chlorides and their chiral recognition studies

2.3A.1 Synthesis

Scheme 2.1: Synthetic scheme for chiral phosphonium salts P-R₄ and P-S₄.



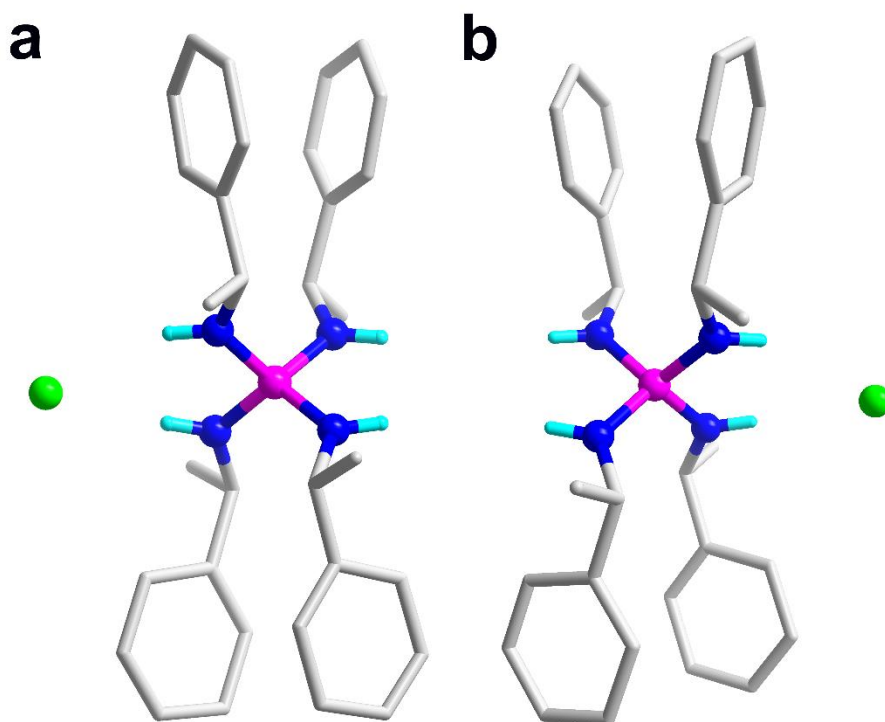
Chiral phosphonium salts **P-R₄** and **P-S₄** were obtained from the reaction of R or S α -methyl benzyl amine with PCl_5 in the presence of the triethylamine (Scheme 2.1). The MALDI-TOF mass spectrum of both **P-R₄** and **P-S₄** in chloroform gave a peak at $m/z = 511$ corresponding to cationic phosphonium species (Figure A2.1-2.2, Appendix). The ^{31}P NMR spectra of both **P-R₄** and **P-S₄** displayed a singlet at 22.81 ppm, while ^1H NMR spectra gave well resolved signals at the aliphatic and the aromatic regions for the α -methyl benzyl amino group attached to the phosphonium **P-R₄** and **P-S₄** (Figure A2.3-2.6, Appendix). The ^{13}C NMR gave six signals for the six different types of carbon atoms present in the α -methyl benzyl amino group of the phosphonium salts (Figure A2.7-2.8, Appendix). In TGA, these compounds showed a weight loss at 211 °C due to loss of chloride ion from the **P-R₄** and **P-S₄** salts (Figure A2.9, Appendix).

2.3A.2 Crystal Structures:

The molecular structures of all the phosphonium salts **P-R₄** or **P-S₄** were solved in the orthorhombic chiral space group $F222$. The asymmetric units of **P-R₄** or **P-S₄** consist of one phosphonium cation and one chloride anion. In **P-R₄** or **P-S₄**, benzene rings adopt a staggered conformation relative to each other. The P–N distances of the four chiral methyl benzyl amino group directly bound to the phosphorus atom are in the range of 1.597(5)–1.62(7) Å and N–P–N bond angles ranges in 113.50–114.53°. The SCXRD analyses reveal strong hydrogen bonding interactions between chloride ion and N–H of the chiral phosphonium cations. In return, chloride ions are involved in a direct H-bonding with phosphonium cations forming 1D framework structures (Figure 2.1-2.3 and Table 2.3).

Table. 2.3: Hydrogen bond data for chiral phosphonium salts P-**R**₄ and P-**S**₄.

Compound	D-H...A	d(D-H) Å	d(H...A) Å	d(D...A) Å	<(DHA) ^o
P- R ₄	N(1)-H(1)...Cl(1)	0.861(2)	2.436(2)	3.297(2)	157.96(2)
P- S ₄	N(2)-H(2)...Cl(1)	0.860(5)	2.469(5)	3.329(5)	156.22(1)

**Figure 2.1:** SCXRD structures of chiral phosphonium salt a) P-**R**₄ and b) P-**S**₄.

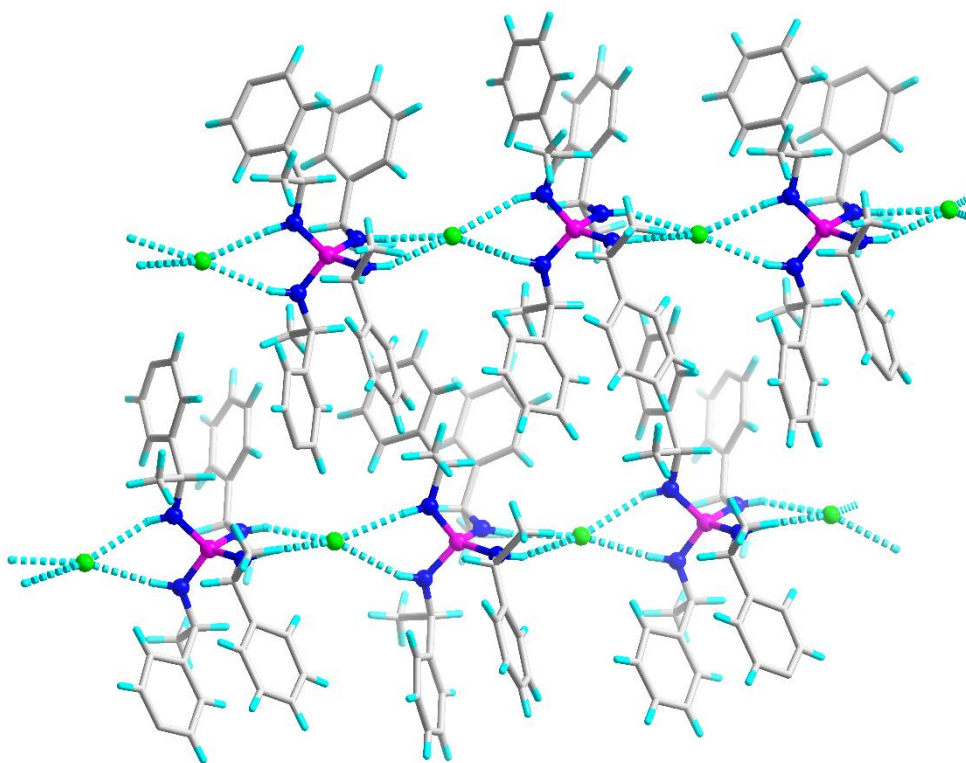


Figure 2.2: 1-D hydrogen bonded structure of the chiral phosphonium salt P-R₄.

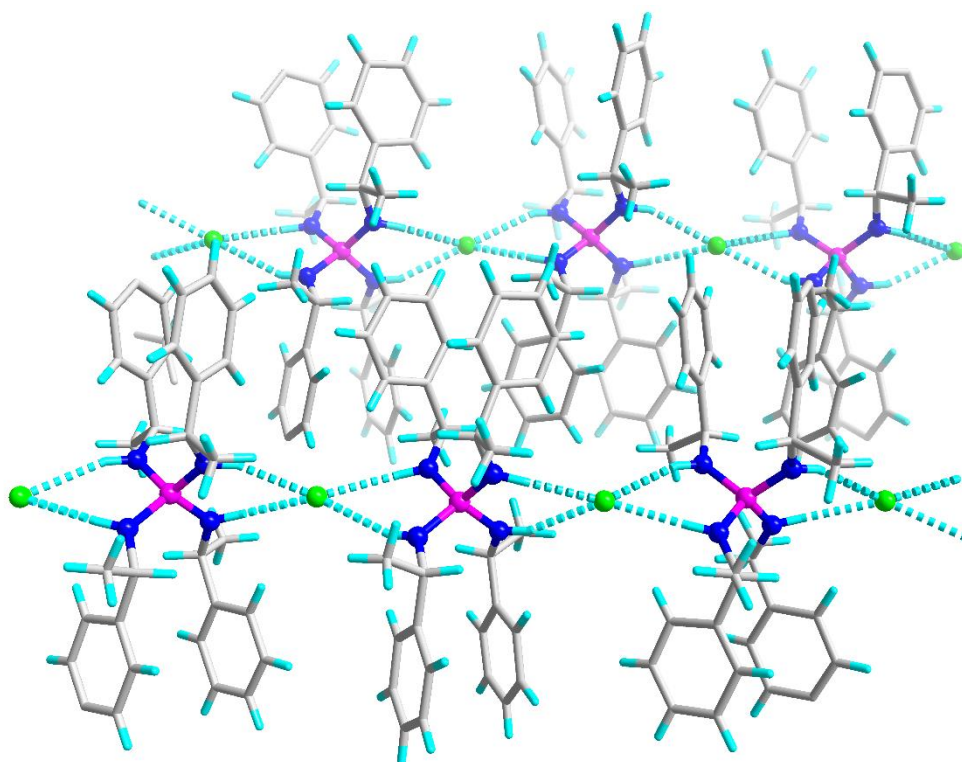


Figure 2.3: 1-D hydrogen bonded structures of the Phosphonium salt P-S₄.

2.3A.3 Chiral recognition studies:

The enantio-recognition capability of the phosphonium salts P-**R**₄ and P-**S**₄ were evaluated for the R- and S-isomers of mandelic acid (MA) and phenyl glycinol (PG) using ¹H-NMR titrations (Figure A2.10-A2.17, Appendix).. The change in chemical shift values for the host N-H protons or the α-hydrogen of the guest molecules were monitored during the titration experiments. Association constants of P-**R**₄ with R-MA and S-MA were obtained by fitting the corresponding ¹H NMR titration data to a 2: 1 binding model. A similar 2: 1 binding model was again adopted for the P-**S**₄ with R-MA and S-MA as well (Figure 2.5-2.6).

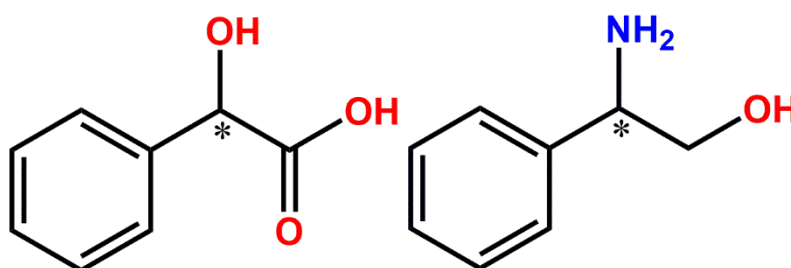


Figure 2.4: Enantiomeric guest molecules used in the chiral recognition studies.

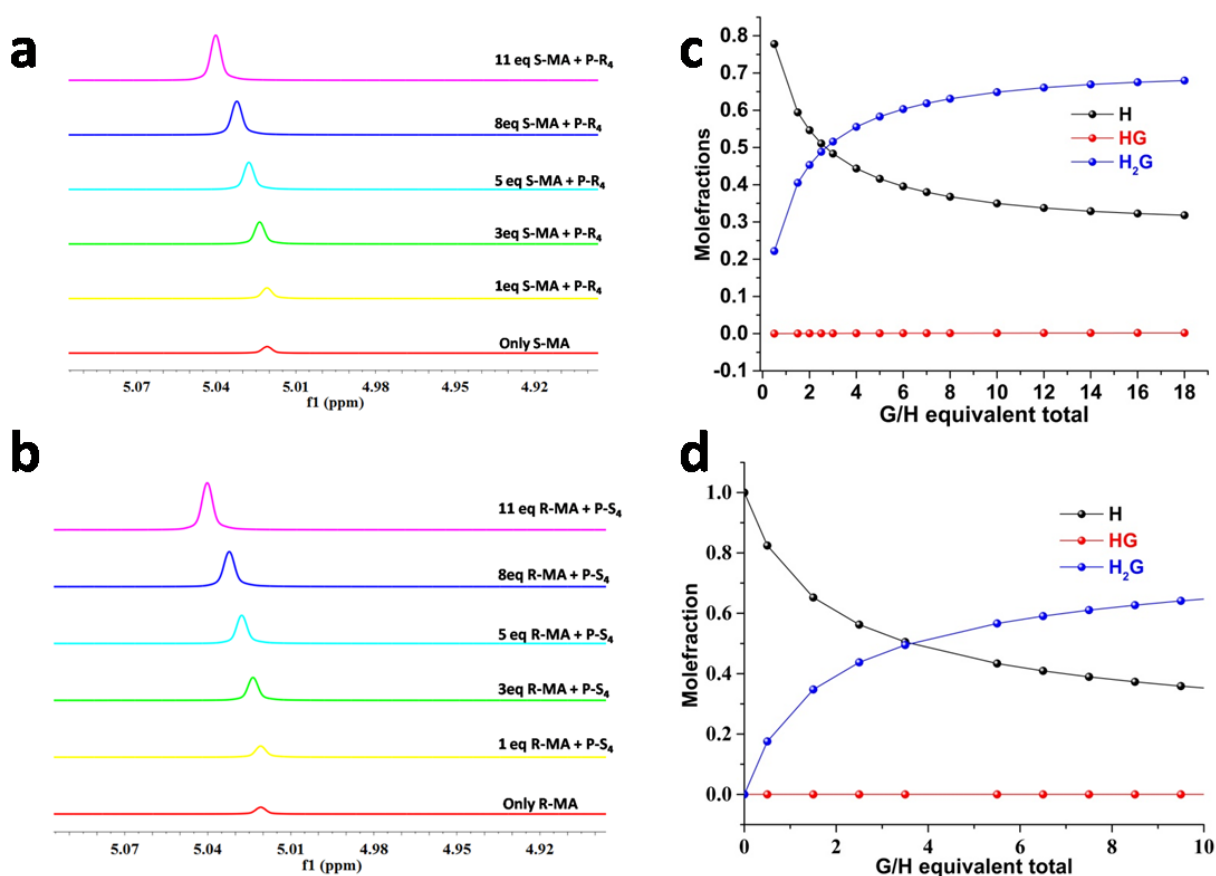


Figure 2.5: Stacked ¹H NMR plot for (a) α-H of S-MA (b) R-MA upon addition to the P-**R**₄, P-**S**₄ and (c) Bind fit plot for P-**R**₄ with S-MA (d) P-**S**₄ with R-MA.

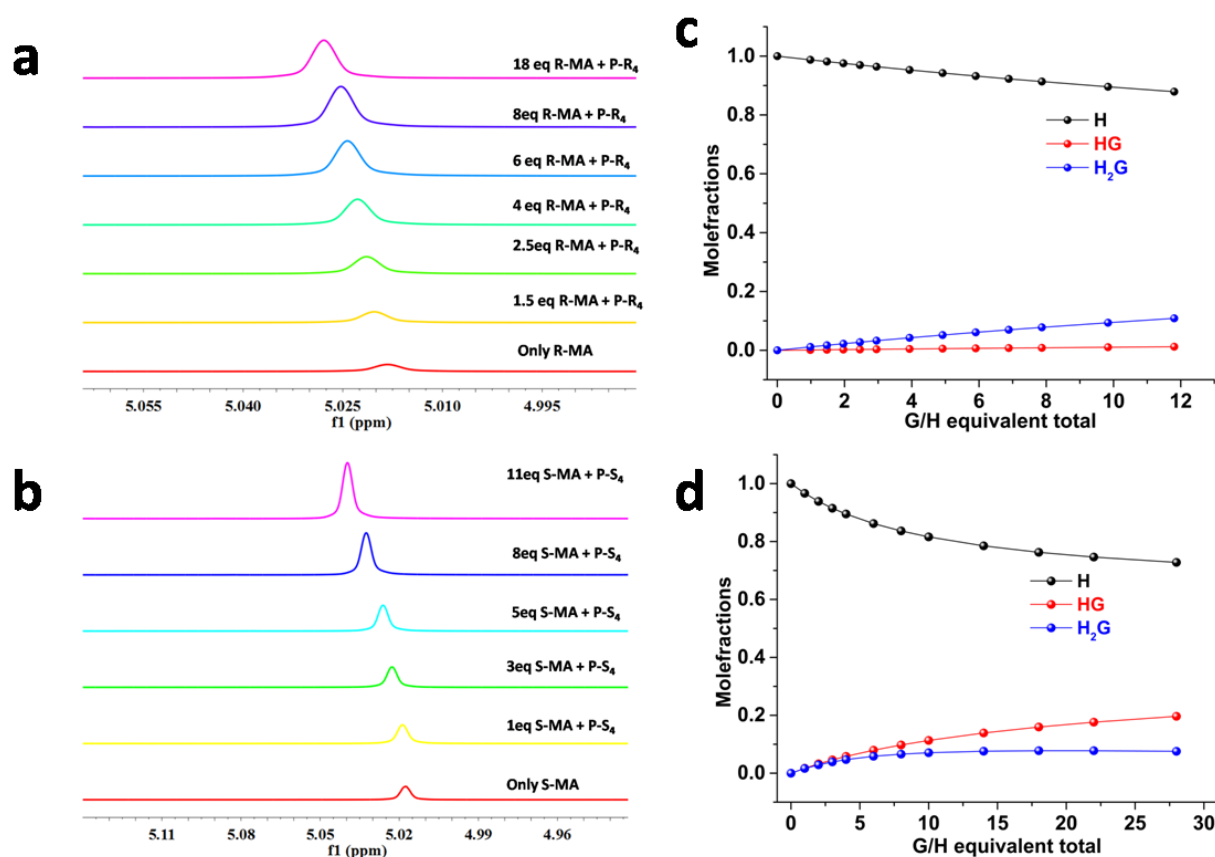


Figure 2.6: Stacked ^1H NMR plot for (a) α -H proton of R-MA (b) S-MA upon addition to the P-R₄, P-S₄ and (c) Bind fit plot for P-R₄ with R-MA (d) P-S₄ with S-MA.

The titration of P-R₄ with S-MA shows a characteristic strong and enantioselective 2:1 binding with an association constant of $27,232 \text{ M}^{-1}$. Similarly, P-S₄ forms a 2:1 complex with R-MA with a much higher K_a value of $4,60,420 \text{ M}^{-1}$ (Figure 2.5). The highest association constant values in this instance can be attributed to multiple interactions of the guest molecules with the host phosphonium salt P-S₄. Much lower association constant (K_a) value of 165 M^{-1} and 16.75 M^{-1} were obtained for the P-R₄ with R-MA, P-S₄ with S-MA (Figure 2.6) indicating the poor association of the guest molecules with the phosphonium salts of the same chirality. During the titrations, the change in chemical shift values for the α -H of R-MA was found to be more up-field shifted than that of S-MA. From the obtained association constants, the P-R₄ forms stronger 2:1 complex with S-MA than R-MA. Similarly P-S₄ forms stronger complex with R-MA than S-MA as seen from the obtained association constant values. The higher association constants observed in these 2:1 host-guest complexes can be attributed to the deshielding effect of the aromatic ring of the benzyl groups of the phosphonium salts on the α -Hs of the MA.

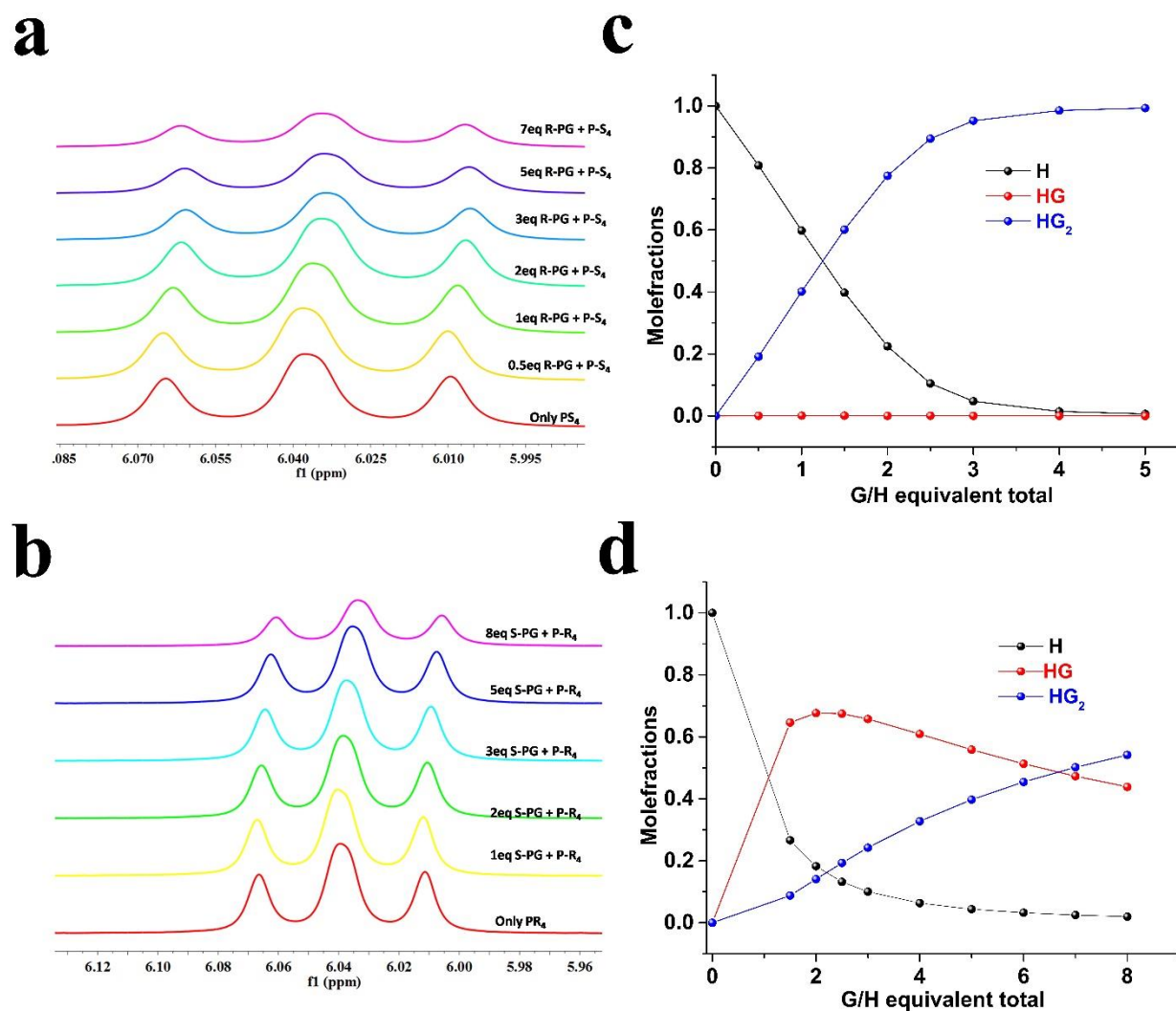


Figure 2.7: Stacked ^1H NMR plot for (a) N-H proton of P-S_4 in the presence of R-PG and (b) P-R_4 with S-PG guest and (c) Bind fit plot for P-S_4 with R-PG (d) P-R_4 with S-PG .

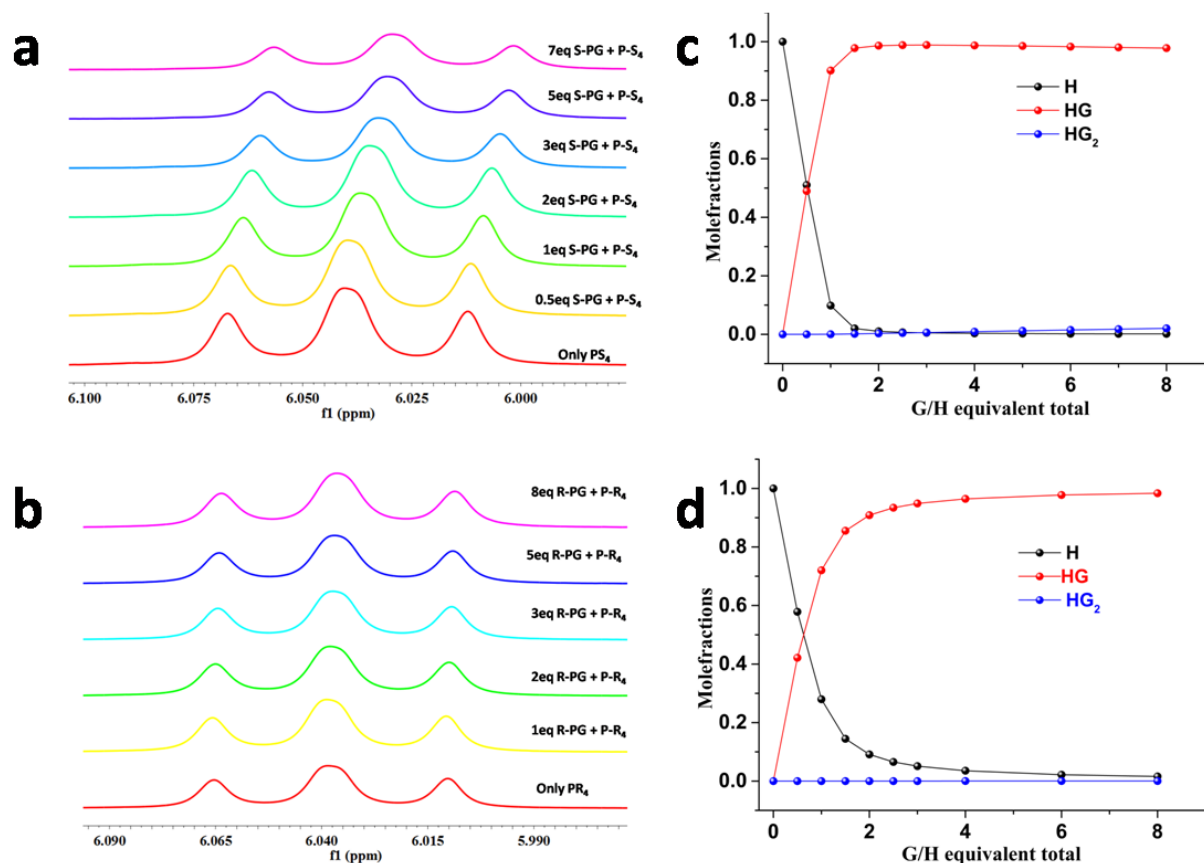


Figure 2.8: Stacked ^1H NMR plot for the (a) N-H proton of P-S_4 in the presence of S-PG and (b) P-R_4 with R-PG guest and (c) Bind fit plot for P-S_4 with S-PG (d) P-R_4 with R-PG .

Furthermore, NMR titrations were performed for the chiral guest R and S -phenyl glycinol with the enantiopure hosts of P-R_4 and P-S_4 which gave better fits for the 1:2 binding model for host-guest assemblies. The association constant values of 184 M^{-1} and 0.10 M^{-1} were obtained for the P-R_4 and P-S_4 with R and S phenyl glycinol (R-PG , S-PG), respectively (Figure 2.8). A highest K_a value of $79,655 \text{ M}^{-1}$ is obtained for P-S_4 with R-PG , while a K_a value of 6.6 M^{-1} is seen for P-R_4 with R-PG (Figure 2.7). The lower values indicate that weaker binding affinity of guest molecules with the chiral hosts (P-R_4 or P-S_4). Also, the shielding of the host N-H proton is found to be higher for the complementary host-guest pairs of P-R_4 with S-PG and P-S_4 with R-PG , in comparison with the host-guest pairs of same chirality, P-R_4 with R-PG and P-S_4 with S-PG (Figure 2.7-2.8).

Table 2.4. Association constants (K/M^{-1}) of receptors **P-R₄**, **P-S₄** with chiral guests R-MA, S-MA, R-PG, S-PG.

Chiral guests	P-R₄	P-S₄
R-Mandelic acid(R-MA) ^a	$K_{21} = 165 (0.5)^d$	$K_{21} = 460420 (53)$
S-Mandelic acid (S-MA)	$K_{21} = 27232 (4)$	$K_{21} = 16.75 (1.3)$
R-Phenyl glycinol (R-PG) ^b	$K_{12} = 0.002 (0.6)$	$K_{12} = 79655 (28)$
S-Phenyl glycinol (S-PG)	$K_{12} = 6.6 (31)$	$K_{12} = 0.1 (0.1)$

Guest proton (H_α) was monitored for Mandelic acid^a and the data fits well to a 2:1 host-guest complex model. For phenylglycinol^b the N-H protons of the amino group is monitored and the data fits well into a 1:2 host-guest complex model. All the K_a values have been derived from the binding model provided by the Bind Fit online tool^c. The standard deviations ($\pm$)^d are given in the parentheses; [host] = 10mg in 0.6ml, d_6 -DMSO, $T = 298\text{ K}$.

The Guest (G) selectivity ($\xi = K_a (\text{larger}) / K_a (\text{smaller})$) values for all examined chiral guests was obtained by taking the ratio between the larger and smaller K_a values within the given host guest systems, as given in the Table 2.5. The chiral discrimination efficiency was largely dependent on the chemical structure of chiral hosts and guests. For example, the complexation of **P-R₄** with mandelic acid, which bears no amino group, not only shows the lowest binding affinity but also the lowest ξ value of 165, demonstrating the importance of guest molecules in the selective complexation. The ξ value for **P-S₄** (27,487) is significantly higher than that for **P-R₄** (165) with mandelic enantiomers, which indicates the chiral discrimination behaviour of host **P-S₄** is far better than **P-R₄**. Interestingly, a ξ value as high as 7,96,550 was observed with phenylglycinol enantiomers when **P-S₄** was used as the host, which is much higher than those obtained with mandelic acid enantiomers with **P-R₄** and **P-S₄** host. The lower ξ value of 165 obtained in the case of **P-R₄** with R-MA and S-MA was due to low binding behavior of host **P-R₄**.

Table 2.5. Binding selectivities (ξ) of the chiral hosts **P-R₄** and **P-S₄** for the enantiomers of mandelic acid and phenylglycinol.

Chiral guests	Guest (G) Selectivity (ξ) (K_a (larger)/ K_a (smaller))	
	P- R ₄ ($K_a(S_G)/K_a(R_G)$)	P- S ₄ ($K_a(R_G)/K_a(S_G)$)
R-Mandelic acid(R-MA) S-Mandelic acid (S-MA)	$K_{21} = 165$	$K_{21} = 27,487$
R-Phenyl glycinol (R-PG) S-Phenyl glycinol (S-PG)	$K_{12} = 3300$	$K_{12} = 7,96,550$

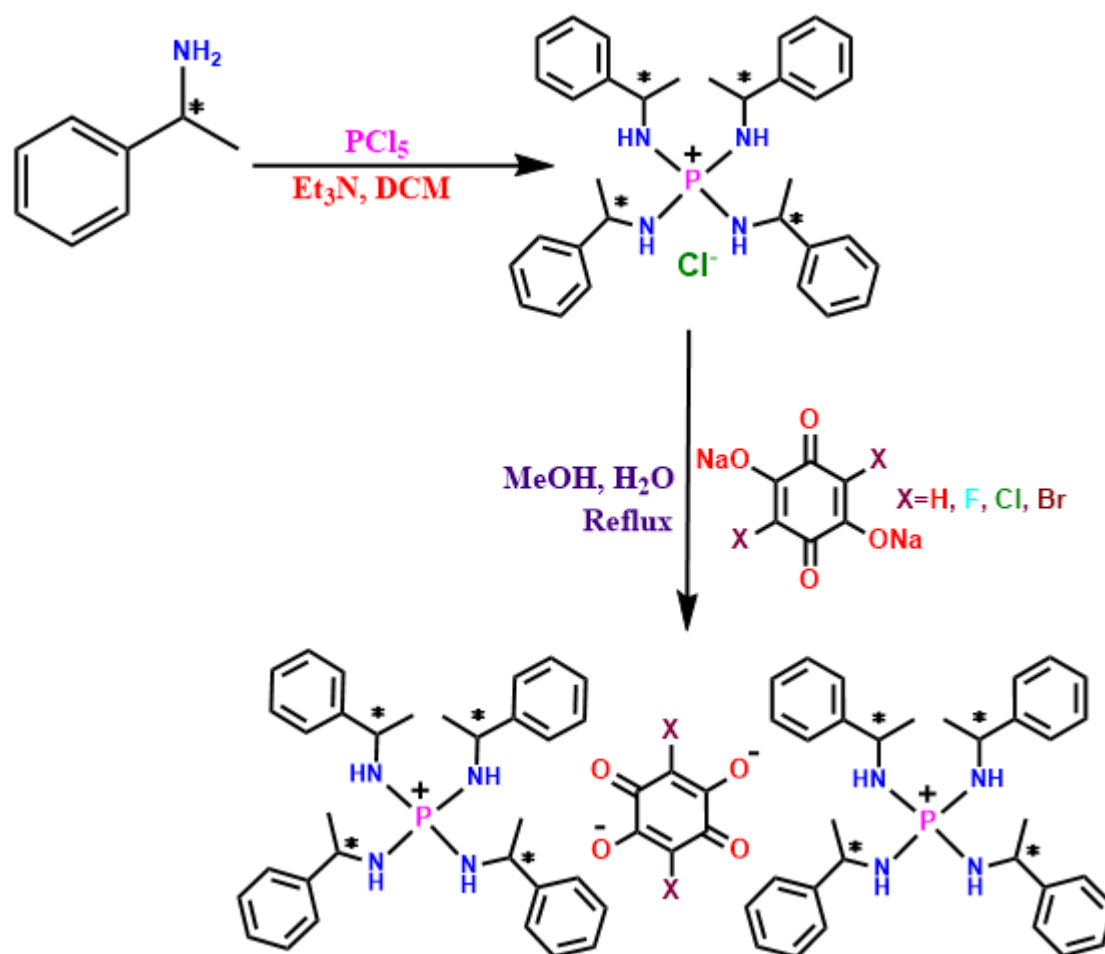
PART B: Syntheses and structures of chiral aminophosphonium anilates

2.3B.1 Synthesis

Chiral phosphonium anilates [(P-**R**₄)₂C₆O₄X₂] and [(P-**S**₄)₂C₆O₄X₂] for X=H, F, Cl, Br were synthesized from the P-**R**₄, P-**S**₄ and sodium salts of the corresponding anilates in methanol water mixture (Scheme 2.2). Though other carboxylate salts of these phosphonium salts have been prepared for terephthalic and isophthalic acids, they did not yield the enantiomeric pairs of crystals for R- and S-aminophosphonium and hence have not been discussed in this part.

All these chiral phosphonium anilates were characterized by ¹H, ¹³C and ³¹P NMR spectroscopy (Figure A2.18-2.41, Appendix). The phosphonium moieties in the chiral phosphonium anilates showed a single peak at proton decoupled ³¹P NMR spectra. The observed chemical shifts for these compounds are very close to their precursor chiral phosphonium chlorides in *d*₆-DMSO. The ESI-mass spectra recorded in the positive ion mode for these chiral phosphonium anilates gave a peak at *m/z* = 511 due to the phosphonium motifs in them.

Scheme 2.2: Synthetic scheme for chiral phosphonium anilates from chiral phosphonium salts P-**R**₄ and P-**S**₄.



2.3B.2 Crystal structures

The molecular structures of all the phosphonium anilates were solved in the orthorhombic enantiomorphic space group $P2_12_12_1$. The asymmetric unit of all phosphonium anilates consists of an anilate dianion, two P-**R**₄ or P-**S**₄ cations. In the case of unsubstituted anilates (PD), the asymmetric unit consists of solvent molecules of methanol. The general formula of phosphonium anilates is given by $[(\text{P-}\mathbf{R}_4)_2 (\text{C}_6\text{O}_4\text{X}_2)^{2-}]$ or $[(\text{P-}\mathbf{S}_4)_2 (\text{C}_6\text{O}_4\text{X}_2)^{2-}]$ ($\text{X} = \text{H}, \text{F}, \text{Cl}, \text{Br}$) (Figure 2.9-2.11). All four benzene rings of P-**R**₄ or P-**S**₄ adopt a staggered conformation in all the phosphonium anilates. The P–N distances in all of them were found to range from 1.570 (5) to 1.60(5) Å and the N–P–N bond angles were in the range of 113.32–115.33 °. The SCXRD analyses reveal hydrogen bonding interactions between oxygen of the anilate dianion and N–H of the chiral phosphonium cations. In return, anilate anion is involved in a direct H-bonding with two phosphonium cations forming 2D framework structures (Figure 2.3, and

Figure A2.42-2.44, Appendix). Selected bond length and angles for the all phosphonium anilates are listed in table 2.6.

Table. 2.6: Selected bond lengths and bond angles for chiral Phosphonium anilates PF-**R**, PF-**S**, PC-**R**, PC-**S**, PB-**R**, and PB-**S**, PD-**R**, PD-**S**.

Compound	Bond length	Bond angles
PF- R	P(1)-N(2): 1.616(3) P(1)-N(3): 1.627(6) P(1)-N(1): 1.632(3)	N(2)-P(1)-N(1): 97.95(14) N(3)-P(1)-N(1): 118.02(14) C(33)-N(5)-P(2): 123.7(2)
PF- S	P(1)-N(2): 1.645(6) P(1)-N(3): 1.622(3) P(1)-N(1): 1.615(6)	N(8)-P(2)-N(7): 111.2(3) N(5)-P(2)-N(7): 117.8(3) C(1)-N(1)-P(1): 124.5(4)
PC- R	P(1)-N(2): 1.609(5) P(1)-N(3): 1.624(4) P(1)-N(1): 1.620(4)	N(2)-P(1)-N(1): 116.8(2) N(2)-P(1)-N(3): 108.9(2) C(17)-N(3)-P(1): 125.0(3)
PC- S	P(1)-N(2): 1.631(4) P(1)-N(3): 1.630(4) P(1)-N(1): 1.623(4)	N(1)-P(1)-N(2): 108.6(2) N(3)-P(1)-N(2): 119.4(2) C(57)-N(8)-P(2): 122.9(3)
PB- R	P(1)-N(2): 1.627(4) P(1)-N(3): 1.631(4) P(1)-N(1): 1.618(4)	N(4)-P(1)-N(3): 117.1(2) N(2)-P(1)-N(3): 108.8(2) C(33)-N(5)-P(2): 122.9(3)
PB- S	P(1)-N(2): 1.629(7) P(1)-N(3): 1.618(7) P(1)-N(1): 1.605(7)	N(1)-P(1)-N(4): 117.8(4) N(1)-P(1)-N(3): 103.2(4) C(57)-N(8)-P(2): 122.5(5)
PD- R	P(1)-N(2): 1.622(4) P(1)-N(3): 1.627(4) P(1)-N(1): 1.612(4)	N(7)-P(2)-N(5): 101.0(2) N(7)-P(2)-N(8): 108.4(2) C(18)-N(3)-P(1): 121.6(3)
PD- S	P(1)-N(2): 1.628(5) P(1)-N(3): 1.624(5) P(1)-N(1): 1.618(5)	N(8)-P(2)-N(5): 116.1(2) N(8)-P(2)-N(7): 108.6(2) C(9)-N(2)-P(1): 122.6(4)

Table. 2.7: Hydrogen bond data for chiral Phosphonium anilates PF-R, PF-S, PC-R, PC-S, PB-R, and PB-S, PD-R, PD-S.

Compound	D-H...A	d(D-H) Å	d(H...A) Å	d(D...A) Å	<(DHA) ^o
PF-R	N(1)-H(1)...O(1)	0.859(5)	2.228(2)	3.087(2)	152.90(1)
PF-S	N(2)-H(2)...O(1)	0.861(5)	2.227(5)	3.088(1)	153.270(1)
PC-R	N(1)-H(1)...O(1)	0.859(5)	2.088(2)	2.947(2)	159.42(2)
PC-S	N(2)-H(2)...O(1)	0.859(5)	2.082(3)	3.088(1)	150.31(2)
PB-R	N(1)-H(1)...O(1)	0.860(5)	2.071(2)	2.931(2)	154.21(5)
PB-S	N(2)-H(2)...O(1)	0.860(5)	1.965(2)	2.825(1)	154.36(1)
PD-R	N(1)-H(1)...O(1)	0.859(5)	2.088 (2)	2.947(2)	163.48(9)
PD-S	N(2)-H(2)...O(1)	0.858(5)	2.146(5)	3.004(1)	148.99(1)

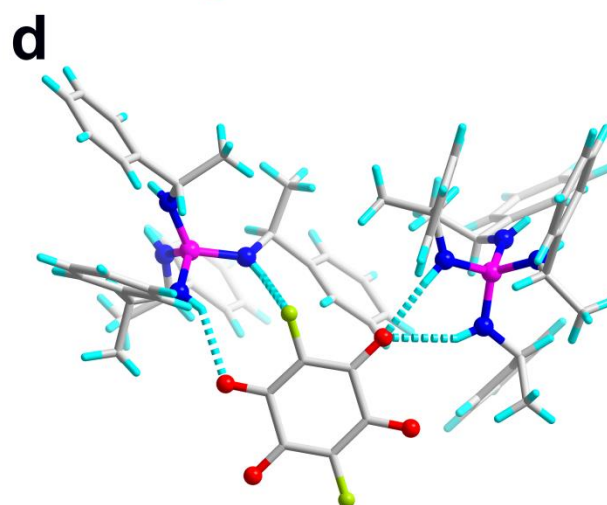
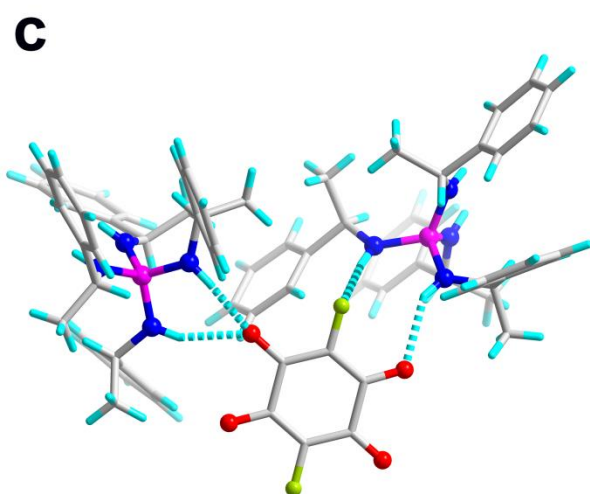
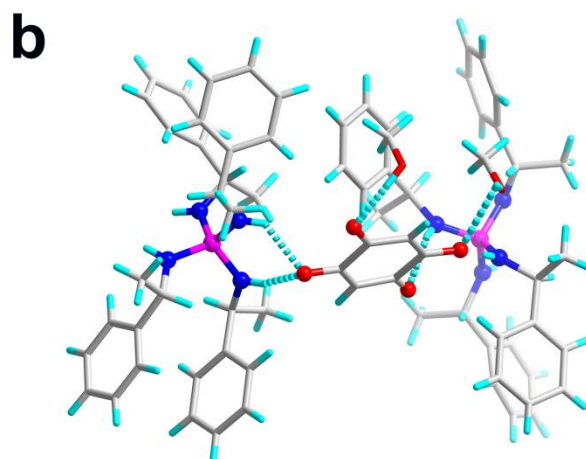
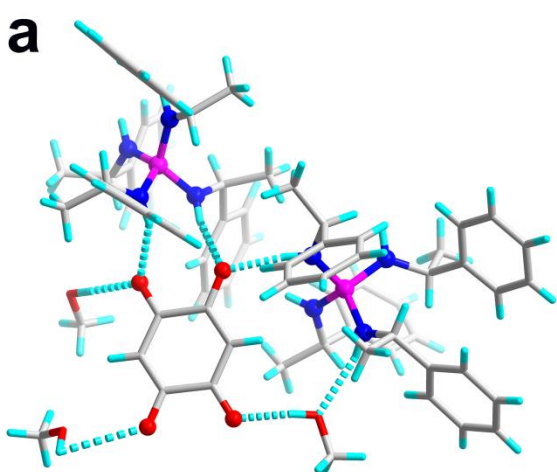


Figure 2.9: SCXRD structures of (a) PD-**R**, (b) PD-**S** (c) PF-**R** and (d) PF-**S** (hydrogen bonds shown in dotted lines).

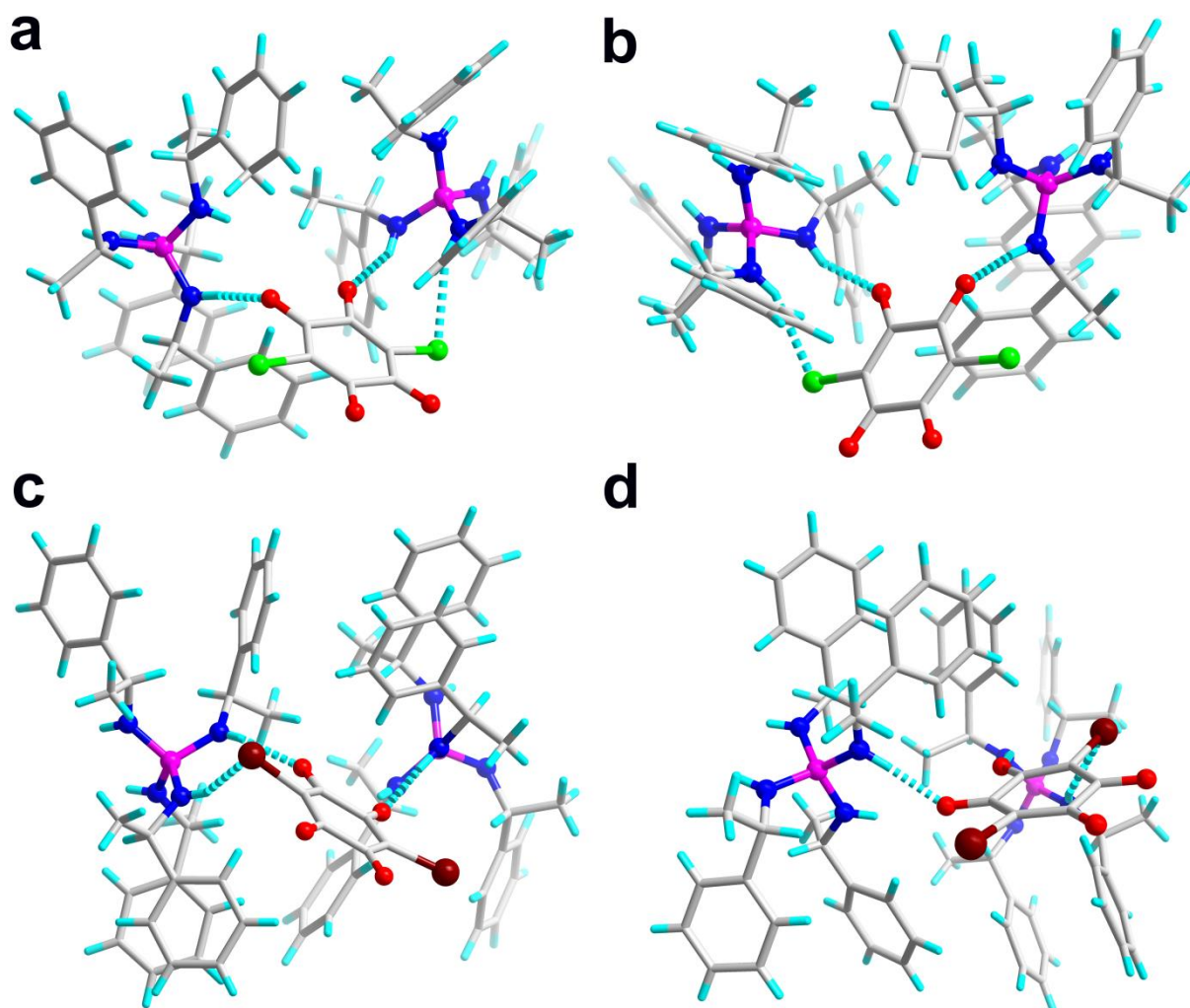


Figure 2.10: SCXRD structures (a) PC-**R**, (b) PC-**S** (c) PB-**R** and (d) PB-**S** ((hydrogen bonds shown in dotted lines).

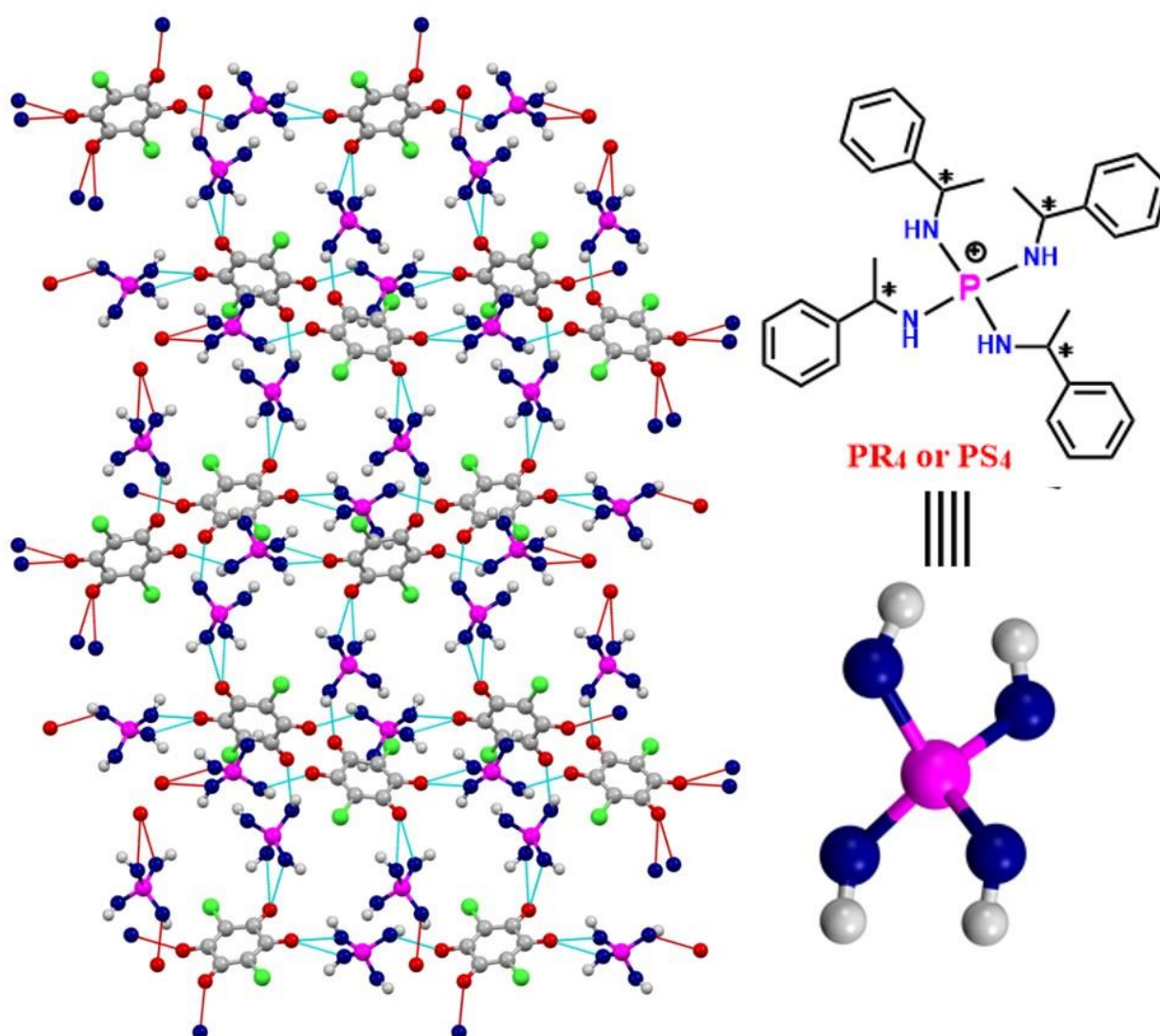


Figure 2.11: The 2*2*2 packing structure of phosphonium chloranilate PC-**R** or PC-**S** (chiral α -methyl benzyl groups are omitted for clarity).

Furthermore, all these phosphonium anilates were probed for the presence of any persistent radicals due to the presence of the quinanoid structures of these anilate anions. However, all of these compounds were found to be diamagnetic in nature as indicated by EPR.

2.4 Conclusion

In conclusion, in the first part of this chapter, a novel pair of chiral phosphonium salts P-**R**₄ and P-**S**₄ was synthesized efficaciously used in the chiral recognition of chiral guest molecules such as Mandelic acid and phenylglycinol using ¹H-NMR titration studies. In particular, an extremely high binding selectivity for (*R*)-Mandelic acid over the corresponding *S* isomer was achieved for P-**S**₄ and vice versa for P-**R**₄. Similarly, *R*-phenylglycinol is selectively recognized over *S*-isomer by using P-**S**₄ and vice versa for P-**R**₄. Hydrogen bonding, ion-dipole, π - π interactions between the phosphonium salts and the guest are presumed to play a crucial role in the enantioselective guest recognition process. In the second part, we have new examples of chiral phosphonium anilates which will be utilized for chiral recognition and separation of organic guest molecules. We have also described the synthesis of a series of enantiomeric pairs of chiral aminophosphonium salts supported by anilate anions. All these salts were found to possess 2:1 stoichiometry. The single crystal X-ray diffraction analysis of these anilate salts shows the formation of 2D-hydrogen bonded structures mediated by N-H $\cdots$ O interactions between the phosphonium amino groups and the carboxylate groups of the anilates. Further utilization of these phosphonium anilates in the enantiomeric recognition studies are currently underway.

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End of Chapter 2



Chapter 3



**Imido-P(V) Trianion Supported
Enantiopure Neutral Tetrahedral
Pd(II) Cages**

3.1 Introduction

Chiral recognition is a fundamental phenomenon in nature which plays a vital role in many chemical and biological functions.¹ Current efforts in this area have been devoted towards the synthesis of artificial chiral architectures and utilize them in a manner akin to natural systems.² Over the years, several synthetic receptors such as capsules, cages, porous materials and supramolecular polymers are pursued for this purpose.³ In this regard, discrete and well defined coordination-driven self-assemblies or metal-organic cages (MOCs) exhibiting chirotopic spaces offer great potential for enantioselective recognition, sensing, separation as well as asymmetric catalysis.⁴⁻⁵ The uniqueness of these cage assemblies stems from their ready synthesis and the presence of their cavities that can exhibit exceptional recognition and discrimination of guest molecules from the bulk solution. Chirality in MOCs is typically achieved (a) by the use of organic stereocenters at the ligand backbone, (b) by the presence of stereogenic transition metal ions and (c) by employing achiral ligands that favour axial or helical chirality.⁶ Most of the known chiral MOCs are charge-separated (anionic or cationic) moieties derived from the self-assembly of geometrically prefixed metal-nodes and directional bridging ligands and take-up the topologies of a regular polyhedron.⁷ Anionic M_4L_6 cages have been used for chiral recognition and catalytic reactions such as aza-cope rearrangement and terpene-cyclization reactions,⁸ while cationic M_6L_4 cages performed asymmetric thermal and photochemical reactions.⁹ Examples of certain axially chiral Fe_4L_6 and Fe_4L_4 assemblies have also been employed for recognition of chiral organic molecules. Recently, a few examples of neutral tetrahedral cages with axial chirality supported by bis-diketonate linker ligands were shown to resolve small racemic alcohols through co-crystallization.¹⁰ Charge-neutral cages that are soluble in organic solvents, with chiral pockets are particularly desirable as they can recognize a wide range of functional groups and support the enantioselective processes in a continuous and recyclable manner. However, owing to the challenges associated with the large-scale synthesis of the chiral cages in optically pure form, there are only a limited number of MOCs (cationic, anionic or neutral) that can support enantioselectivity based studies.^{4-5,8-10}

3.2 EXPERIMENTAL SECTION

3.2.1 General remarks

All manipulations involving phosphorus halides were performed under dry nitrogen atmosphere in standard Schlenk glassware. Dry Solvents were purchased from local vendors and used without further purification. The Chiral amines, oxalic acid, palladium acetate were purchased from Aldrich and used as received. POCl_3 was purchased locally and was distilled prior to use. The ligand $\text{X}^{\text{RRR}}\text{H}_3$ and $\text{X}^{\text{SSS}}\text{H}_3$ was synthesized according to the modified reported procedure.¹ NMR spectra were recorded on a Jeol 400 MHz spectrometer (^1H NMR: 400.13 MHz, ^{13}C { ^1H } NMR: 100.62 MHz, ^{31}P { ^1H } NMR: 161.97 MHz) or on a Bruker 400 MHz (^1H NMR: 500.00 MHz, ^{13}C { ^1H } NMR: 125.725 MHz, ^{31}P { ^1H } NMR: 202.404 MHz) spectrometer at room temperature using TMS (^1H , ^{13}C) and 85% H_3PO_4 (^{31}P). The mass spectra were obtained on an Applied Bio system matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF)/TOF spectrometer. Thermal analysis (TGA) data have been obtained from a PerkinElmer STA-6000 thermo gravimetric analyzer. CD spectra were measured in JASCO J815 spectrometer from 400 nm – 190 nm. Elemental analyses were performed on a Vario-EL cube elemental analyzer. GC was performed on Agilent 7890B GC system using Supelco β -dex 225 (30 m* 0.25 mm * 0.25 μm) and Supelco γ -dex (30 m* 0.25 mm * 0.25 μm) columns, Split ratio 30:1, FID temperature 300 $^\circ\text{C}$.

3.2.2 Synthesis

3.2.2.1 Synthesis of phosphoramidate ligands $\text{X}^{\text{RRR}}\text{H}_3$ and $\text{X}^{\text{SSS}}\text{H}_3$

To a stirred solution of R or S alpha-methyl benzyl amine (1.25 ml, 9.72 mmol) and triethylamine (1.35 ml, 9.72 mmol) in dichloromethane (15 ml) at 0 $^\circ\text{C}$ was added POCl_3 (0.3 ml, 3.24 mmol) drop wise. The resultant mixture was slowly brought to room temperature and stirred for an over-night period. The precipitated triethylamine hydrochloride salt was filtered and the solution was evaporated to obtain the crude phosphoramidate as an oily substance. This was further purified on a silica gel column using dichloromethane and methanol as an elutant to obtain a colorless solid. $\text{X}^{\text{RRR}}\text{H}_3$: Yield: 84% (1.15 gm, based on P). ^1H NMR (400 MHz, CDCl_3): δ 1.35 (d, 9H, CH_3), 4.3-4.40(m, 3H, CH), δ 2.45 (t, 3H, NH), 7.15-7.30 (m, 15H, aromatic). ^{13}C NMR (100 MHz, CDCl_3): δ 25.6, 51.0, 125.7, 126.9, 128.5, 145.7. ^{31}P NMR (161 MHz, CDCl_3): δ 11.07. MALDI-TOF/TOF: 446 ($\text{M}+\text{K}$)⁺. $\text{X}^{\text{SSS}}\text{H}_3$: Yield: 80% (1.05 gm, based on P). ^1H NMR (400 MHz, CDCl_3): δ 1.35 (d, 9H, CH_3), 4.3-4.40(m, 3H, CH), δ 2.45 (t,

3H, NH), 7.15-7.30 (m, 15H, aromatic). ^{13}C NMR (100 MHz, CDCl_3): δ 25.6, 51.0, 125.7, 126.9, 128.5, 145.7. ^{31}P NMR (161 MHz, CDCl_3): δ 11.07. MALDI-TOF/TOF: 446 (M+K) $^+$.

3.2.2.2 Preparation of Enantiopure chiral Tetrahedral Cages (1-R) or (1-S):

The Ligand $\text{X}^{\text{RRR}}\text{H}_3$ or $\text{X}^{\text{SSS}}\text{H}_3$ (20 mg, 0.049 mmol) and Palladium acetate (33 mg, 0.147 mmol) and oxalic acid (9 mg, 0.073 mmol) in DMSO (2 ml) were heated to 60 °C for 1 hr to yielded an orange colored precipitate. The precipitated compound was recovered by filtration, washed with methanol 2-3 times and dried under vacuum. The cage assemblies **1-R** or **1-S** were crystallised from slow evaporation of its dichloromethane solution in 2 days. **1-R**: Yield: 83% (based on P). MALDI-TOF/TOF: 3462 (M+K) $^+$. ^{31}P NMR (161 MHz, CD_2Cl_2): δ 71.30. ^1H NMR (400 MHz, CD_2Cl_2): δ 1.55 (d, 3H, CH_3), 3.70-3.86 (m, 3H, CH), 7.73-7.80(d, 2H, aromatic), 7.44-7.54 (m, 3H, aromatic). ^{13}C NMR (100 MHz, CD_2Cl_2): δ 25.7, 63.3, 130.5, 130.5, 131.1, 142.9, 175.6. Elemental Analysis (%): Calcd for $\text{C}_{108}\text{H}_{108}\text{N}_{12}\text{O}_{28}\text{P}_4\text{Pd}_{12}$: C, 37.90; H, 3.18; N, 4.91. Found: C, 37.80; H, 3.05; N, 4.82; **1-S**: Yield: 81% (based on P). MALDI-TOF/TOF: 3462 (M+K) $^+$. ^{31}P NMR (161 MHz, CD_2Cl_2): δ 71.30. ^1H NMR (400 MHz, CD_2Cl_2): δ 1.55 (d, 3H, CH_3), 3.70-3.86 (m, 3H, CH), 7.73-7.80(d, 2H, aromatic), 7.44-7.54(m, 3H, aromatic). ^{13}C NMR (100 MHz, CD_2Cl_2): δ 25.7, 63.3, 130.5, 130.5, 131.1, 142.9, 175.6. Elemental Analysis (%): Calcd for $\text{C}_{108}\text{H}_{108}\text{N}_{12}\text{O}_{28}\text{P}_4\text{Pd}_{12}$: C, 37.90; H, 3.18; N, 4.91. Found: C, 37.80; H, 3.05; N, 4.83.

3.2.2.3 General procedure for encapsulation-separation experiment and resolved results for racemic substrates by 1-R and 1-S.

In a typical encapsulation-separation experiment, excess of racemic guests were separately added to **1-R** and **1-S** in dry DCM (10 ml). For rac-epichlorohydrin (epi) and β -butyrolactone (BBL) the reaction mixture was stirred for 1 hour and left for slow evaporation for up to one week. For 3-Methyl cyclopentanone (3-Me-Cp) and 3-Ethyl cyclopentanone (3-Et-Cp), the solutions were heated to 50 °C for 2-3 days in tightly screw-capped pressure vials and the resulting DCM solutions were left stranded for evaporation to yield the crystalline solids of the host-guest complexes. The excess of guest molecules were removed from the surface of the complexes by repeated washing with diethyl ether (3-5 times). The adsorbed guest molecules were subsequently removed from the complexes by soaking in MeOH and analyzed by gas chromatography. The GC methods employed in the study along with the GC chromatogram and analysis plots are given in the appendix (Figures A3.21- A3.32, Appendix).

3.2.3 Crystallography

Reflections were collected on a Bruker Smart Apex Duo diffractometer at 100 K using Mo K α radiation ($\lambda = 0.710\ 73\ \text{\AA}$) for ligand X^{SS}H₃, **1-R**, **1-S**, $\pm\text{bbl}\subset\pm\mathbf{1}$. All structures were solved using intrinsic phasing method, and refined by full-matrix least-squares on F² (G. M. Sheldrick, SHELXL, program for crystal structure refinement, University of Gottingen, Germany, 2015).¹¹ Crystallographic data for all these compounds are listed in Table S1. All non-hydrogen atoms were refined anisotropically if not stated otherwise. Hydrogen atoms were constrained in geometric positions to their parent atoms. The diffuse solvent molecules in **1-R** and **1-S** could not be modeled appropriately. Hence, these were treated as diffuse contributions to the overall scattering and removed by the SQUEEZE/PLATON for a better refinement data.¹² All the phenyl rings are constrained to ideal six membered rings. The disordered $\pm\text{bbl}$ guests in $\pm\text{bbl}\subset\pm\mathbf{1}$ were treated with same/sadi restraints and refined isotropically.

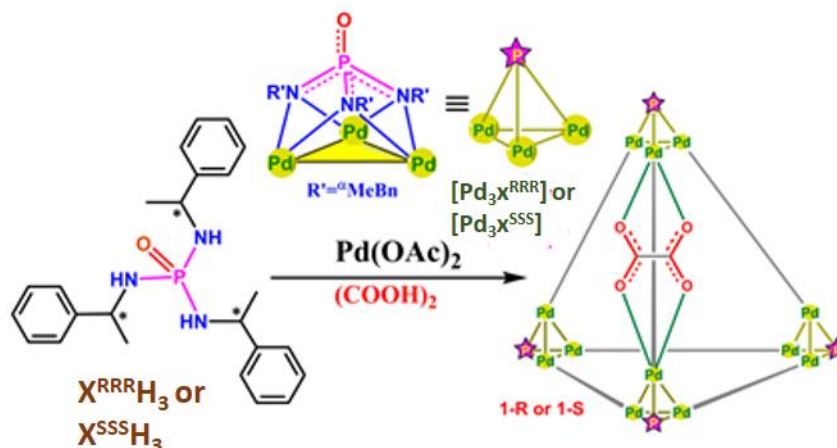
Table 3.1 Crystallographic Data for X^{SS}H₃, Cages **1-R**, **1-S** and $\pm\text{bbl}\subset\pm\mathbf{1}$.

Compound	1-R	1-S	$\pm\text{bbl}\subset\pm\mathbf{1}$
Chemical formula	C ₁₀₈ H ₁₀₈ N ₁₂ O ₂₈ P ₄ Pd ₁₂	C ₁₀₈ H ₁₀₈ N ₁₂ O ₂₈ P ₄ Pd ₁₂	C ₂₉₂ H ₃₃₀ N ₂₄ O ₉₅ P ₈ Pd ₂₄
Formula weight	3422.74	3422.74	8497.14
Temperature	100(2)K	100(2)K	100(2)K
Crystal system	Cubic	Cubic	Monoclinic
Space group	F 23	F 23	Cc
a (Å); α (°)	28.28800; 90	28.04600; 90	20.679(2); 90
b (Å); β (°)	28.28800; 90	28.04600; 90	25.531(2); 94.48
c (Å); γ (°)	28.28800; 90	28.04600; 90	31.458(3); 90
V (Å ³); Z	22636(67)	22060	16557(3)
ρ (calc.) mg m ⁻³	1.004	1.031	1.704
μ (Mo K α) mm ⁻¹	0.997	1.023	1.39
2 θ_{max} (°)	50.006	56.668	56.86
Flack parameter	0.01(4)	-0.023(18)	0.03(5)
R(int)	0.152	0.066	0.053
Data / param.	4782/113	4648/113	40598/1831
GOF	1.015	1.05	1.133
R1 [F > 4 σ (F)]	0.072	0.042	0.068
wR2 (all data)	0.0917(3343)	0.1316(4648)	0.1837
Max. peak/hole(e.Å ⁻³)	2.66/−0.73	0.40/−0.76	1.77/ −1.74

3.3 RESULTS AND DISCUSSION

3.3.1 Synthesis

Scheme 3. 1: Synthesis of enantiopure cages **1-R** or **1-S** from the chiral ligand $X^{RRR}H_3$ or $X^{SSS}H_3$.



The chiral phosphoramidate precursors, (R,R,R)-(+)-*N,N',N''*- and (S,S,S)-(-)-*N,N',N''*-PO(NH(*CH(CH₃)Ph)₃, denoted as $X^{RRR}H_3$ and $X^{SSS}H_3$, were prepared from the corresponding R- and S- α -methylbenzylamine (α MeBnNH₂) and POCl₃.¹⁷ The optical purity of the ligands has been confirmed by circular dichroism (CD) in DCM and X-ray structure analysis (Figure A3.1-A3.5, Appendix). Treatment of Pd(OAc)₂ with the respective phosphoramidate ($X^{RRR}H_3$ or $X^{SSS}H_3$) in the presence of oxalic acid (LH₂) in DMSO gave the neutral cages R-[(Pd₃X^{RRR})₄L₆] (**1-R**)all and S-[(Pd₃X^{SSS})₄L₆] (**1-S**)all (shortly referred as **1-R** and **1-S**) in good yields (Scheme 3.1). The MALDI-TOF mass spectrum of both **1-R** and **1-S** in DCM gave an isotopic distribution of peaks centred at $m/z = 3462$ corresponding to their $[M+K]^+$ ions (Figure 3.1).

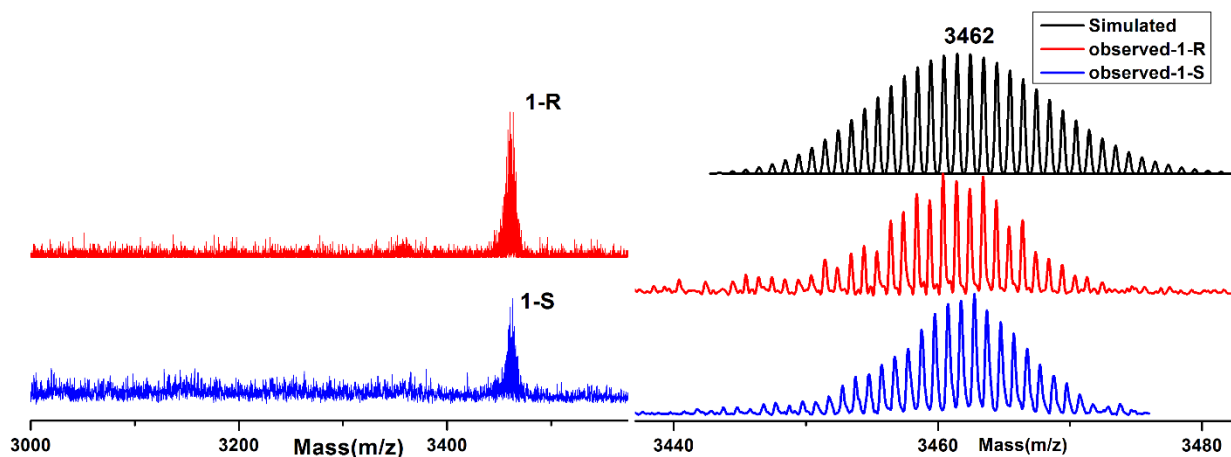


Figure 3.1: MALDI-TOF mass spectra of **1-R** and **1-S** and their isotopic distribution of peaks.

The ^{31}P NMR spectra of cages **1-R** and **1-S** show a singlet at 71.3 ppm, while ^1H NMR spectra gave well resolved signals for the ligand environments at both the aliphatic and the aromatic regions which are marginally shifted downfield with respect to the free ligands. Their ^{13}C NMR showed a single peak at 173.7 ppm suggestive of a symmetric environment of the oxalate ligands (Figures A3.6- A3.8, Appendix). Both cage compounds decompose above 250 °C (Figure A3.9, Appendix).

The enantiomeric purity of **1-R** and **1-S** was confirmed by CD spectra in DCM which gave mirror image signals due to both enantiomers. For each enantiomeric cage, bisignate bands at 264 ($\pi\text{-}\pi^*$), 302 (MLCT), 332 (MLCT) nm were observed (Figure 3.2). Interestingly, the self-assembly reaction leading to these cages is also accompanied by chiral amplification. Thus, the observed absolute configuration (α_D) values of +666° and -684° for **1-R** and **1-S**, respectively were substantially much higher in comparison with the corresponding phosphoramides, +23°, $\text{X}^{\text{RRR}}\text{H}_3$ and -25°, $\text{X}^{\text{SSS}}\text{H}_3$.

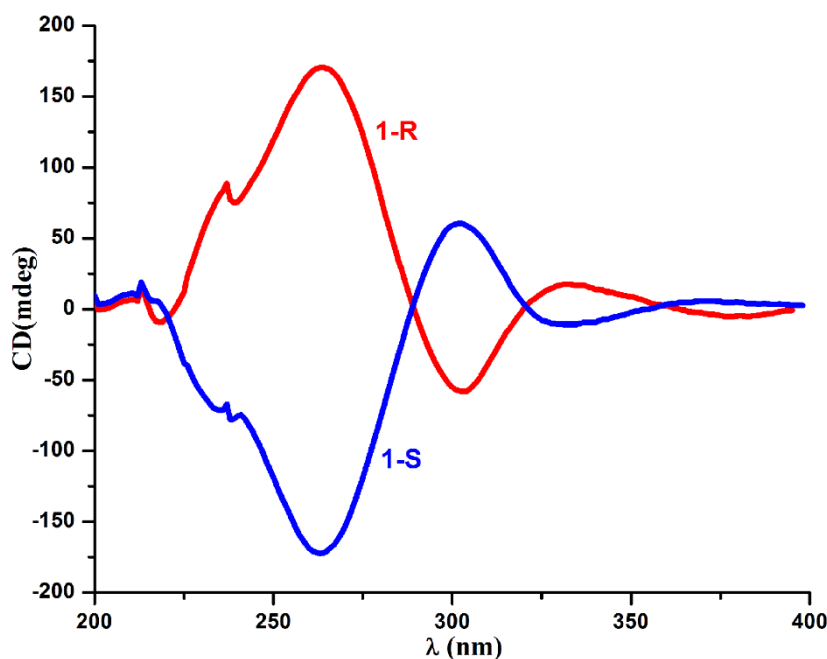


Figure 3.2: Circular Dichroism spectra of **1-R** and **1-S**.

3.3.2 Crystal Structures

Crystals of **1-R** and **1-S** suitable for single crystal X-ray diffraction (SCXRD) analysis were obtained by slow evaporation of their DCM solutions. The structural determination of these crystals confirmed the absolute configurations of **1-R** and **1-S**. They crystallized in the cubic chiral space group $F 23$ (Figure 3.3) mirroring the symmetry of the chiral tetrahedral cages (T). The Pd_3X^* -units constitute the corners of the tetrahedron, while the oxalate ligands link them across its edges. The wide angle chelation of the oxalate ligands offers perfect coordination for the 90° cisoidal sites at the Pd_3 units. The Pd_3X^* -units exhibit trigonal symmetry; their α -Me groups attached to the stereo genic carbon centers are oriented either clockwise (in **1-R**) or anticlockwise (in **1-S**).

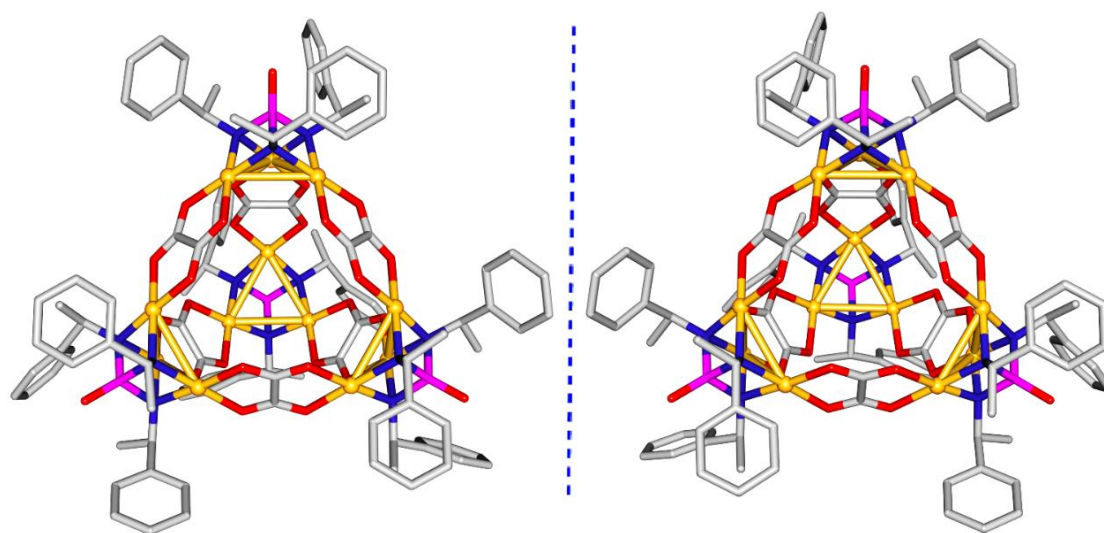


Figure 3.3: SCXRD derived structures of **1-R** (top left) and **1-S** (top right); Color code: Pd, orange; C, gray; N, blue; O, red; P, magenta.

The crystal structures showed the presence of large solvent accessible voids both inside and outside of the cages, which amount to 51%, which is $13051 \text{ \AA}^3$ of the total unit-cell volume (Figures A3.10-A3.12, Appendix). MSROLL¹³ calculations gave $86 \text{ \AA}^3$ as the intrinsic volume of the cavity which is comparable to that of the isostructural achiral $[(\text{Pd}_3\text{X})_4\text{L}_6]$ cage (Figure 3.4, Table 3.2 and Figures A3.13, Appendix).¹⁴

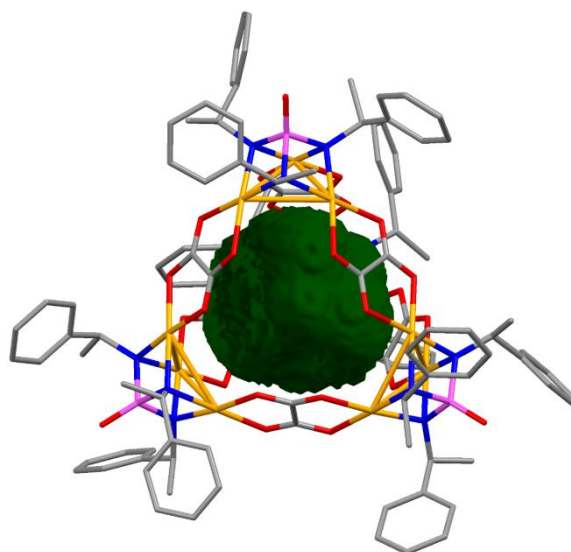


Figure 3.4: View of the intrinsic cavity surface present in **1-S**.

Table 3.2: Molecular volume and area calculated for **1-R** from MSROLL calculations⁴

Probe Radius (Å)	Surface Area (Å ²)	Volume (Å ³)
1.3	100.801	86.45
1.4	96.225	83.420
1.5	95.20	79.73

The void structure of the crystals of **1-R** and **1-S** is remarkable in that it consists of an open 3D-network of diamondoid channels that runs externally of the cages, while the internal voids of the cages are linked to this external network (Figure 3.5). This loose packing is only supported by hydrophobic interactions between peripheral α -methyl benzyl groups. It is reminiscent to that of nanoporous crystals of awkwardly shaped molecules.^{12, 13} However, these crystals are not stable and will disintegrate into a denser, amorphous form upon desolvation. Nevertheless, the denser form still shows some porosity: CO₂ adsorption data at 195 K reveal a moderate uptake of 2.7 mmol g⁻¹. The BET surface area amounts to 450 m² g⁻¹ and DFT derived pore size analysis suggests a pore diameter of 3.5 Å (Figures A3.14- A3.16, Appendix).

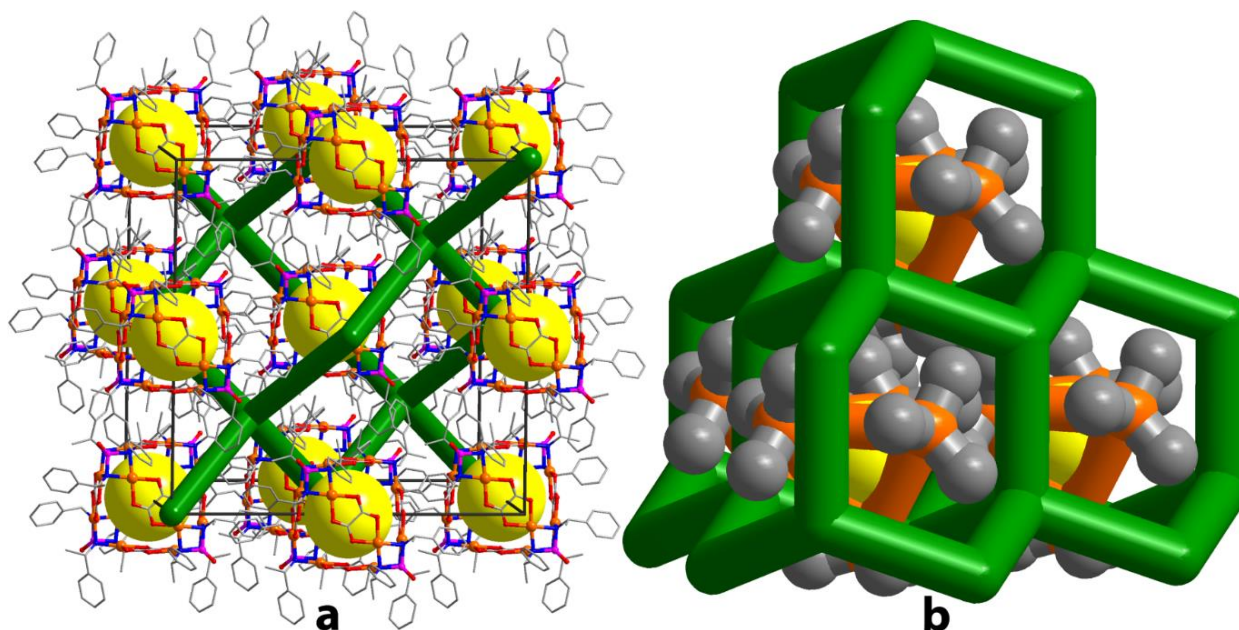


Figure 3.5: (a) The packing diagram of **1-S** showing the 3D-network of channels as green links. The yellow spheres represent the intrinsic cavity. (b) View of the diamondoid network formed by the external channels; the frameworks of the cages are represented as orange tetrahedral frames and the chiral R-groups as grey spheres.

3.3.3 Guest-Encapsulation studies of cage **1-R** and **1-S**

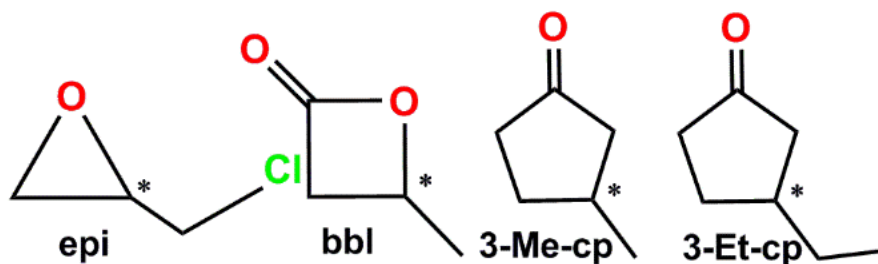


Figure 3.6: Guest molecules used in the chiral recognition studies.

The dichloromethane solutions of **1-R** and **1-S**, respectively, were treated with racemates of epichlorohydrin (epi), b-butyrolactone (bbl), 3-methyl cyclopentanone (3-Me-cp) and 3-ethyl cyclopentanone (3-Et-cp) (Figure 3.6) yielding the corresponding host-guest assemblies as opaque crystalline solids. The MALDI-TOF mass spectral analysis recorded in DCM solutions of all these solids gave an isotopic distribution of peaks at 3538, 3538, 3533, and 3533 corresponding to $\pm\text{epi}\subset\mathbf{1-R}$, $\pm\text{epi}\subset\mathbf{1-S}$, $\pm\text{bbl}\subset\mathbf{1-R}$ and $\pm\text{bbl}\subset\mathbf{1-S}$ respectively. Also, broad peaks centred at 3522, 3522, 3535 and 3535 have been observed for $\pm\text{3-Me-cp}\subset\mathbf{1-R}$, $\pm\text{3-Me-cp}\subset\mathbf{1-S}$,

$\pm 3\text{-Et-cp}\text{-}\mathbf{1}\text{-R}$ and $\pm 3\text{-Et-cp}\text{-}\mathbf{1}\text{-S}$ assemblies (Figures A3.17- A3.22, Appendix). The $^1\text{H-NMR}$ spectra of $\pm\text{epi}\text{-}\mathbf{1}\text{-R}$ and $\pm\text{bbl}\text{-}\mathbf{1}\text{-R}$ in CD_2Cl_2 showed prominent chemical shifts for the guest protons (Figures A3.23- A3.24, Appendix) indicating the formation of host-guest assemblies upon crystallization. The $^1\text{H-2D-diffusion}$ ordered spectroscopy¹⁵ (DOSY) studies suggest that the guest molecules are not firmly bound to the hosts at their intrinsic cavities but are loosely associated with the exterior of the cage (Figures A3.25- A3.26, Appendix). Unfortunately, the crystals of the host-guest complexes were not of sufficient quality for X-ray structure analysis.

Since the structural analysis of the denser chiral material and the host-guest complexes remained unsuccessful, we attempted to crystallise the corresponding racemates ($\mathbf{1}\text{-R} + \mathbf{1}\text{-S}$) to probe if they exist in a similarly dense form and, thus, may provide some insights into the host-guest interactions. We were able to obtain crystals from the $\pm\text{bbl}\text{-}\pm\mathbf{1}$ system that were suitable for X-ray analysis (Figure 3.7). They crystallised in space group *Cc* exhibiting the composition $[(\text{Pd}_3\text{X})_4\text{L}_6].(\text{bbl})_{9.5}.(\text{H}_2\text{O})$. The structural analysis revealed that it contains a 1 : 1 mixture of $\mathbf{1}\text{-R}$ and $\mathbf{1}\text{-S}$ cages which form packings that are about 1.37 times denser (via *Z/V*) than in the enantiopure cubic crystals. Although one has to accept the limitations of a direct comparison between the packing of the enantiopure and the racemic materials, the racemic structure shows some interesting properties that may shed some light on the structure of the chiral host-guest complexes. The crystal structure of the racemic host-guest compound still contains a significant external void space of 32% which amounts to $5002 \text{ \AA}^3$ of the unit cell volume and the computed intrinsic void was again found to be $88 \text{ \AA}^3$ per cage molecule. The bbl guests were found at both the intrinsic and extrinsic cavities of the cages exhibiting both ordered and disordered arrangements. The majority of the ordered guest molecules were located in the external cavities at pockets formed by the optically active α -methyl benzyl groups and the oxalate ligands indicating potential interactions for chiral recognition (Figures A3.27- A3.29, Appendix).

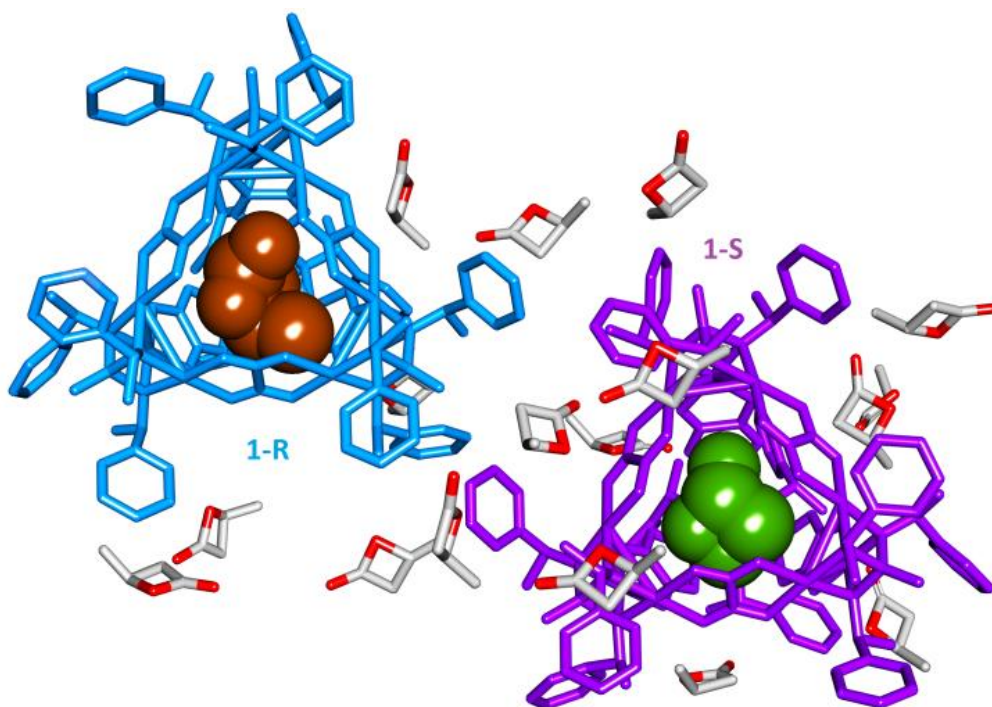


Figure 3.7: View of the location of bbl guests in the structure of $\pm\text{bbl} \subset \pm\mathbf{1}$. Only the ordered bbl molecules located close to the chiral centers are shown here. The bbl molecules at the intrinsic voids are depicted as space filling models.

3.3.4 Chiral separation studies of cage **1-R** and **1-S**

The enantioselective separation capabilities of **1-R** and **1-S** for the above mentioned racemic substrates were evaluated by gas chromatography (GC) analysis. For the GC experiments, the guest molecules were first mixed with the DCM solutions of apohosts and allowed to evaporate at room temperature. The obtained inclusion solids were washed with diethyl ether and the guest molecules were subsequently desorbed by treatment with methanol. The chiral GC analyses of $\pm\text{epi}$, $\pm\text{bbl}$, $\pm 3\text{-Me-cp}$ and $\pm 3\text{-Et-cp}$ desorbed from **1-R** upon washing with methanol yielded the respective enantiomeric excess (*ee*) values of 6, 34, 14 and 12%, with the R enantiomers being in excess (Table 3.3 and Figures A3.30-A3.41, Appendix). Similar experiments with the **1-S** cage yielded *ee* values of 10, 14, 16, and 14% for the respective excess S-enantiomers (Table 3.3 and Figures A3.30-A3.41, Appendix). A change in size did not seem to affect the enantioselectivities observed for the two ketone guests probed in this study irrespective of the chirality of the host cage. The lower *ee* values obtained for other

assemblies might be attributed to the poor binding of the guest molecules to the host cages as some amounts of the bound guests could also be lost during the initial diethyl ether washing. Control experiments showed that the ligands $X^{RRR}H_3$ and $X^{SSS}H_3$, alone could not resolve the enantiomers of the examined substrates under identical conditions, indicating that the more open structure of the chiral cage assembly plays a role in the enantioselective recognition and separation. Notably, the cage assemblies of **1-R** and **1-S** can be regenerated after each separation experiment either by heating to 100 °C or drying under vacuum overnight followed by recrystallization from DCM at room temperature. The recrystallized cages can then be directly used for subsequent separation runs which resulted in similar *ee* values. This indicates that the cage assemblies are very robust as the apohosts can be regenerated after guest desorption and reused without any apparent performance loss. The structural and optical robustness of these cages were further confirmed by CD spectra, optical rotation and single-crystal X-ray diffraction analysis performed on recrystallized samples of **1-R** and **1-S** (Figures A3.42 and Table A3.1-3.2, Appendix). The separation efficiencies of these chiral cages are comparable with those of some of the previously reported best performing metal–ligand discrete assemblies.⁴ Previously reported methods described the separation of epoxides via hydrolytic kinetic resolution.¹⁶ In contrast, our cage assemblies have been shown to resolve $\pm$ epi in a more direct fashion.

Table 3.3: Summary of GC-separation results for the racemic guest molecules by **1-R** and **1-S**

Guest Substrate	Resolved <i>ee</i> by 1-R (%)	Resolved <i>ee</i> by 1-S (%)
Epichlorohydrin	6	10
β -butyrolactone	34	14
3-Me-cyclopentanone	14	16
3-Et-cyclopentanone	12	14

3.4 Conclusion

In conclusion, we have synthesized enantiopure tetrahedral cages **1-R** and **1-S**. These were found to promote the enantioselective separation of small racemic molecules having varied functionalities such as epoxide, lactone and ketone via crystallization inclusion. Single crystal X-ray analysis of $\pm\text{bbl} \subset \pm\mathbf{1}$ showed that guest recognition predominantly takes place at the extrinsic cavities of the cage. Currently, we are focusing on generating new examples of chiral cages with varied polyhedral shapes and cavity sizes for chiral separation of larger substrates in solution and in the solid state as well as performing asymmetric transformations in their chiral pockets.

3.5 References

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End of Chapter 3



Chapter 4



**Chiral Separation of Styrene Oxides
Supported by Enantiomeric
Tetrahedral Neutral Pd(II) Cages**

4.1 Introduction

Chiral separation is defined as the process of separating the individual enantiomers from their racemic pairs. Separation of enantiomers is essential owing to their unique biochemical activities as living systems are chiral in nature.¹ Chiral epoxides are important synthons in synthetic and pharmaceutical chemistry as the epoxy rings are very reactive towards nucleophiles and yield various chiral organic functionalities. Especially, styrene oxides act as excellent precursors for various biologically relevant compounds. (*S*)-styrene oxide (phenyl oxirane) is an important intermediate for the synthesis of nematocide,² Levamisole (anticancer agent),³ and (–) hyperolactone C (anti-HIV agent).⁴ The (*S*)-4-fluorostyrene oxide (2-(4-Fluorophenyl) oxirane) is a useful starting material for the synthesis of several potential bioactive compounds.^{5–6} A number of antiviral agents have been prepared from (*S*)-4-chlorostyrene oxide (2-(4-Chlorophenyl) oxirane).⁷ Among the methods available, a well-known protocol for the separation of epoxides is the hydrolytic or aminolytic kinetic resolution procedure (HKR) that was first shown to be assisted by Jacobsen's Co^{III}-(salen) type complexes, in which one of the enantiomer is converted into a chiral diol while the other one is retained as the epoxide.^{8,9} Such HKR reactions have also been shown to be catalyzed by enzymes such as lipases and hydrolases.¹⁰ However, for incorporating a variety of functional groups on the chiral backbone, it is highly desired that the epoxides are separated by other methods without altering them to diols. Hence, benign methods based on supramolecular systems like capsules, cavitands, metal-organic cages and frameworks as host materials for the chiral recognition and separation of epoxides have been investigated.^{11, 12} Recently, our group has reported the synthesis of an oxalate tethered enantiomeric pair of neutral tetrahedral cages **1-R** and **1-S** of formula [(Pd₃X*)₄(C₂O₄)₆] ([X*]^{3–} = RRR- or SSS-[PO(N(*CH(CH₃)Ph)₃)₃]^{3–}) that showed a direct separation of small organic compounds and epoxide such as (±)epichlorohydrin via the crystallization inclusion method, albeit with low enantiomeric excess (*ee*) values.¹³ Spurred by this, we set out to investigate the separation of biochemically important styrene oxides by utilizing tailor-made Pd(II) cages built on anilate bound tetrahedral cages. The cage assemblies **2-(R)_{all}** and **2-(S)_{all}** of formula [(Pd₃X^{RRR})₄(C₆O₄Cl₂)₆] and [(Pd₃X^{SSS})₄(C₆O₄Cl₂)₆] were formally formed via the self-assembly of four chiral Pd₃X^{RRR} or Pd₃X^{SSS} units and six bis-bidentate chloranilate linkers. Further, we demonstrate the ability of these larger chiral cages for the efficient separation of racemic styrene derived epoxides by crystallization inclusion method. A highest *ee* value of 80% was obtained for the R-4-fluorostyrene oxide (+F-SO) and reasonably good *ee* values as estimated by gas

chromatography (GC) or high-pressure liquid chromatography (HPLC), were obtained for all the other investigated styrene epoxides.

4.2 EXPERIMENTAL SECTION

4.2.1 General remarks

All manipulations involving phosphorus halides were performed under a dry nitrogen atmosphere in standard Schlenk glassware. POCl_3 purchased locally and was distilled before use. Dry Solvents were purchased from local vendors and used without further purification. The Chiral amines, Chloranilic acid, palladium acetate, were purchased from Sigma-Aldrich and used without further purifications. 2-(4-Fluorophenyl)oxirane, 2-(4-Chlorophenyl)oxirane, 2-(4-Bromophenyl)oxirane were purchased from Sigma-Aldrich and used after purifications. NMR spectra were recorded on a Jeol or a Bruker 400.13 (^1H), 100.62 ($^{13}\text{C}\{^1\text{H}\}$), 161.97 ($^{31}\text{P}\{^1\text{H}\}$) MHz spectrometer at room temperature using TMS (^1H , ^{13}C) and 85% H_3PO_4 (^{31}P). The mass spectra were obtained on an Applied Biosystem matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF)/TOF spectrometer. Thermal analysis (TGA) data have been obtained from a PerkinElmer STA-6000 thermogravimetric analyzer. CD spectra were measured in JASCO J815 spectrometer from 400 nm-190 nm. Elemental analyses were performed on a Vario-EL cube elemental analyzer. The gas chromatogram (GC) was performed on Agilent 7890B GC system using Supelco β -dex 225 (30 m* 0.25 mm * 0.25 μm) and Supelco γ -dex (30 m* 0.25 mm * 0.25 μm) columns, Split ratio 30:1, FID temperature 300°C. HPLC analysis was performed on Agilent Technologies 1260 Infinity equipment fitted with a UV detector. The ChiralCel OD-H column with a flow rate of 0.5 and 1 mL/min was employed for the chiral HPLC analysis using 99:1 of hexane: isopropanol as eluent.

4.2.2 Synthesis

4.2.2.1 Synthesis of Enantiopure Tetrahedral Cages (2-R and 2-S):

The Ligand $\text{X}^{\text{RRR}}\text{H}_3$ or $\text{X}^{\text{SSS}}\text{H}_3$ (20 mg, 0.049 mmol) and Palladium acetate (33 mg, 0.147 mmol) and chloranilic acid (15.36 mg, 0.073 mmol) in methanol were heated at 90 °C in a 15 ml closed cap vial for 24hrs to yield an reddish brown colored precipitate. The precipitated compound was collected by filtration, washed with methanol 2-3 times and dried under vacuum. The cage assemblies 2-R or 2-S were crystallized from slow evaporation of their corresponding dichloromethane solution in two days.

2-R: Yield: 83% (based on P). ^1H NMR (400 MHz, CDCl_3): δ 1.53 (d, 9H, CH_3), 4.05-4.19 (dq, 3H, CH), 7.41-7.76 (m, 15H, aromatic). ^{13}C NMR (100 MHz, CDCl_3): δ 23.79, 62.08, 128.67, 128.91, 129.31, 141.46, 180.59, 181.03. ^{31}P NMR (161 MHz, CDCl_3): δ 69.39. MALDI-TOF/TOF (Linear): 4159 ($\text{M}+\text{Na}$) $^+$. Elemental Analysis (%): Calcd for $\text{C}_{132}\text{H}_{108}\text{N}_{12}\text{O}_{28}\text{P}_4\text{Cl}_{12}\text{Pd}_{12}$: C, 38.33; H, 2.63; N, 4.06. Found: C, 37.80; H, 3.05; N, 4.82.

2-S: Yield: 80% (based on P). ^1H NMR (400 MHz, CDCl_3): δ 1.53 (d, 9H, CH_3), 4.05-4.19 (dq, 3H, CH), 7.41-7.76 (m, 15H, aromatic). ^{13}C NMR (100 MHz, CDCl_3): δ 23.79, 62.08, 128.67, 128.91, 129.31, 141.46, 180.59, 181.03. ^{31}P NMR (161 MHz, CDCl_3): δ 69.39. MALDI-TOF/TOF (Linear): 4159 ($\text{M}+\text{Na}$) $^+$. Elemental Analysis (%): Calcd for $\text{C}_{132}\text{H}_{108}\text{N}_{12}\text{O}_{28}\text{P}_4\text{Cl}_{12}\text{Pd}_{12}$: C, 38.33; H, 2.63; N, 4.06. Found: C, 37.60; H, 3.0; N, 4.09.

4.2.2.2 General procedure for chiral resolution by using 2-R and 2-S:

Resolution of $\pm\text{SO}$ with 2-S: The cage 2-S (50 mg, 0.0120 mmol) and large excess $\pm\text{SO}$ (75 μl) were dissolved in 10 ml of dry chloroform and the resultant mixture is kept for evaporation for period of seven days. The obtained crystalline solid was washed with ice-cold n-pentane for three times to remove excess racemic guest molecules monitored by GC or HPLC. The enantio-enriched guest molecules of these inclusion solids were recovered by soaked the solid in n-hexane for 2 h. Yield of the isolated $\pm\text{SO}$ was found to be 1.08 mg, 75 %. The enantiomeric excess (*ee*) values of these isolated styrene oxides were determined from chiral HPLC analysis as described in page numbers (A4.20-A4.27, Appendix).

Similar procedure has been followed for the chiral resolution of all the other oxirane guests with 2-R and 2-S.

Resolution of $\pm\text{SO}$ with 2-R: Yield of the isolated $\pm\text{SO}$ 1.11 mg, 77 %.

Resolution of $\pm\text{F-SO}$ with 2-S: Yield of the isolated $\pm\text{F-SO}$ 1.25 mg, 75 %

Resolution of $\pm\text{F-SO}$ with 2-R: Yield of the isolated $\pm\text{F-SO}$ 1.32 mg, 80%

Resolution of $\pm\text{Cl-SO}$ with 2-S: Yield of the isolated $\pm\text{Cl-SO}$ 1.39 mg, 75 %

Resolution of $\pm\text{Cl-SO}$ with 2-R: Yield of the isolated $\pm\text{Cl-SO}$ 1.45 mg, 78 %

4.2.3 Crystallography

Reflections were collected on a Bruker Smart Apex Duo diffractometer at 100 K using Mo $\text{K}\alpha$ radiation ($\lambda = 0.71073 \text{ \AA}$) for 2-R, 2-S. All structures were solved using intrinsic phasing method and refined by full-matrix least-squares on F^2 (G. M. Sheldrick, SHELXL program for crystal structure refinement, University of Gottingen, Germany, 2015). The multi-scan absorption correction was applied for both compounds by using the SADABS program.¹⁴

Crystallographic data for all these compounds are listed in Table 4.1. All non-hydrogen atoms were refined anisotropically if not stated otherwise. Hydrogen atoms were constrained in geometric positions to their parent atoms. The diffuse solvent molecules in 2-R and 2-S could not be modelled appropriately. Hence, these were treated as diffuse contributions to the overall scattering and removed by the SQUEEZE/PLATON for better refinement data. All the phenyl rings are constrained to ideal six-membered rings. The Disordered phenyl rings were treated with similar distances and with similar U-restraints using SAME/SADI commands.

4.2.3.1 Crystallography of guest treated cage assemblies:

Crystals were selected and mounted using Paratone-n on a nylon fiber loop then flash cooled at 100K. Data were collected on a Rigaku MicroMax-007HF rotating anode generator equipped with an Osmic VariMax-VHF optic, 4-circle kappa goniometer and Dectris Pilatus 200K hybrid pixel array detector. Screening, indexing, data collection and processing were completed with CrysAlis^{Pro}.¹⁵ The reduced data were input to Olex2,¹⁶ solved using SHELXT¹⁷ and refined with SHELXL.¹⁸ The phenyl rings of the capping ligands were all restrained to be idealized phenyl rings. All temperature factors were restrained with the RIGU command. Attempts were made to locate guest molecules in the host cavity but the guest molecules could not be modelled satisfactorily and hence one model solution for each of the R- and S-cages in R3 phase has been obtained and given in the table 4.1.

Table 4.1: Crystallographic Data for Chiral Cages 2-R and 2-S

Compound	2-R (I23)	2-S (I23)	2-R-(R3)	2-S (R3)
Chemical formula	C ₁₃₂ H ₁₀₈ N ₁₂ O ₂₈ P ₄ Pd ₁₂ Cl ₁₂	C ₁₃₂ H ₁₀₈ N ₁₂ O ₂₈ P ₄ Pd ₁₂ Cl ₁₂	C ₅₂₈ H ₄₂₉ Cl ₄₈ N ₄₈ O ₁₁₂ P ₁₆ Pd ₄₈	C ₅₂₈ H ₄₂₉ Cl ₄₈ N ₄₈ O ₁₁₂ P ₁₆ Pd ₄₈
Formula weight	4136.38	4136.38	16542.49	16542.49
Temperature	100(2)K	100(2)K	100(2)K	100(2)K
Crystal system	Cubic	Cubic	Trigonal	Trigonal
Space group	I 2 3	I 2 3	R 3	R 3
a (Å); α (°)	21.100 (2); 90	21.094(4);90	53.2572(4);90	53.2892(2);90
b (Å); β (°)	21.100(2); 90	21.094(4);90	53.2572(4);90	53.2892(2);90
c (Å); γ (°)	21.100(2); 90	21.094(4);90	26.2713(2);120	26.3182(10);120
V (Å ³); Z	9394 (67)	9386(5)	64531.0(11)	64723.9(5)
ρ (calc.) mg m ⁻³	1.462	1.464	1.277	1.273
μ(Mo Kα) mm ⁻¹	1.380	1.381	9.955	9.925
2θ _{max} (°)	56.668	56.526	66.595	66.587
R(int)	0.1246	0.0712	0.0331	0.0208
Data / param.	3944 / 140	3884 / 141	46066/2238	44409/2237
GOF	1.039	1.073	0.982	1.066

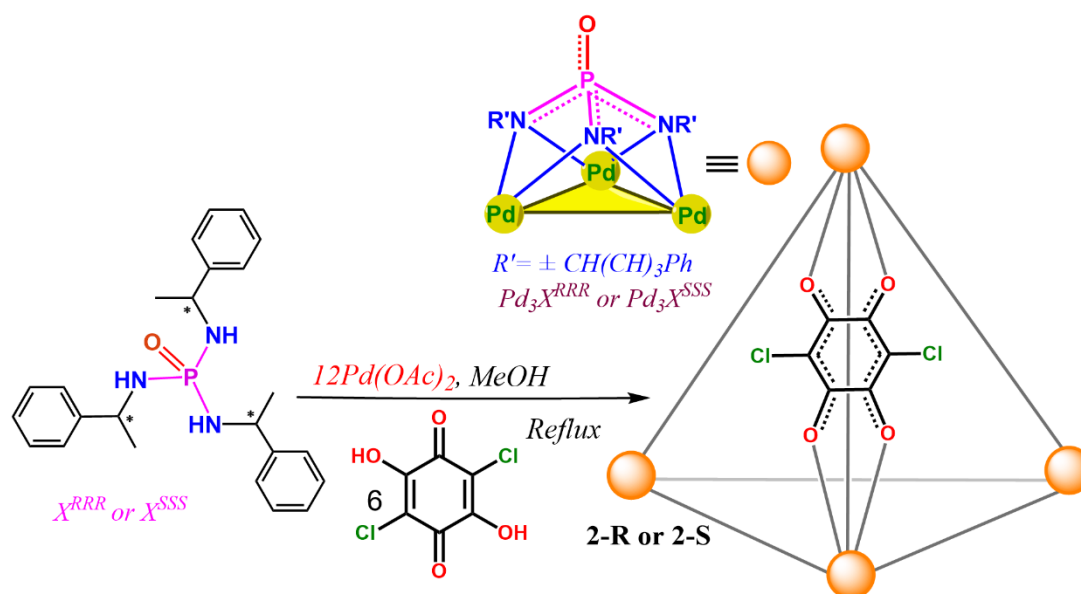
R1 [F>4 σ (F)]	0.06	0.0492	0.0411	0.0247
wR2 (all data)	0.1306	0.1324	0.1121	0.0670
Flack parameter	-0.02(3)	0.00(2)	0.024	-0.016(3)
Max. peak/ hole (e. $\text{\AA}^{-3}$)	0.359/ -0.497	0.414/ -0.504	0.731/ -0.317	0.530/-0.222
CCDC Number ¹⁸	1898032	1898033	1957460	1957461

4.3 RESULTS AND DISCUSSION

4.3.1 Synthesis

The chiral tetrahedral cages, **2**-(R)_{all} and **2**-(S)_{all} (henceforth shortly referred as **2**-R and **2**-S)¹⁸ were isolated as brownish red solids from the reaction of the respective chiral phosphoramides, X^{RRR}H₃ and X^{SSS}H₃, with Pd(OAc)₂ in the presence of chloranilic acid (LH₂) in methanol (Scheme 1). The MALDI-TOF mass spectrum of both **2**-R and **2**-S in chloroform gave peaks centered at 4159 and 4278 corresponding to the [M+Na]⁺ and [M+CHCl₃+Na]⁺ species, respectively (Figure A4.1, Appendix). The ¹H-NMR spectrum gave well resolved signals due to the peripheral imido-P(V) trianions, presenting chemical shifts due to the α -methyl benzyl amino group. The ¹³C-NMR gave peaks corresponding to the chloranilate linkers at 141.46, 180.59 and 181.03 ppm, in addition to the peaks due to the imido-ligands (Figures A4.2-A4.6, Appendix). The thermogravimetric analysis (TGA) data revealed that the cages were stable up to 250 °C (Figure A4.7, Appendix).

Scheme 4.1: Synthesis of chiral neutral cages **2**-R or **2**-S from the enantiopure X^{RRR}H₃ or X^{SSS}H₃ ligands.



Only one out of the six chloranilate linkers along the edges of the tetrahedron is shown for clarity.

The circular dichroism (CD) spectra confirm the enantio-enrichment of **2-R** and **2-S** in solution. Thus, both **2-R** and **2-S** gave mirror image peaks at 249, 341 and 396 nm, with the respective positive and negative cotton effects. While the first peak is due the ligand centric $\pi-\pi^*$ transitions, the second and third ones are due to metal to ligand charge transfer (MLCT) transitions (Figure 4.1). The absolute configurations ($[\alpha]^2\text{D}$) of **2-R** and **2-S** were determined by optical rotation measurements in 0.1 M solution of CHCl_3 . The observed $[\alpha]^2\text{D}$ values of **2-R** (1322°) and **2-S** (-1340°) were higher than the corresponding phosphoramidate ligands $X^{\text{R}}\text{H}_3$ ($+23^\circ$) and $X^{\text{S}}\text{H}_3$ (-25°).

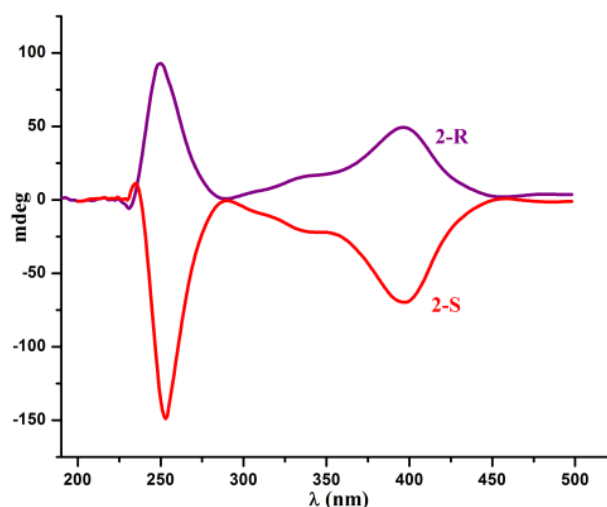


Figure 4.1: Circular dichroism spectra of the chiral cages **2-R** and **2-S**.

4.3.2 Crystal Structures

Further, the enantiopure structures of these cages were confirmed by their structural determination. Crystals of **2-R** and **2-S** suitable for single crystal X-ray diffraction (SCXRD) analysis were grown from slow evaporation of their corresponding DCM solutions. Both the cages were crystallized in chiral cubic space group $I23$ signifying the T-symmetry of these cages (Figure 4.2). The asymmetric unit consists of one-twelfth of cage molecule.

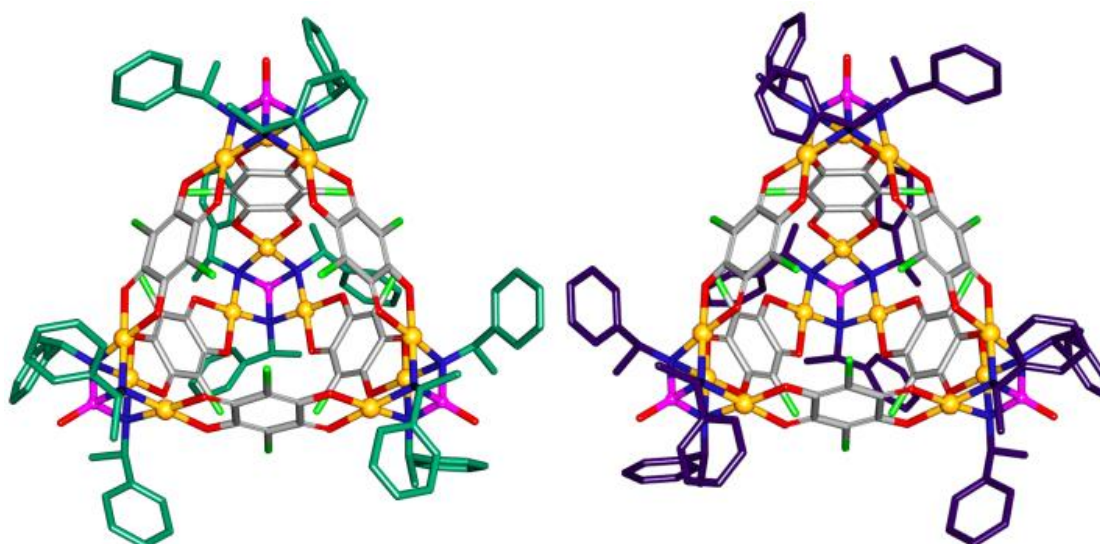


Figure 4.2: SCXRD structures of **2-R** (left) and **2-S** (right). Color code: Pd, Orange; $C_{anilate}$, gray; N, blue; O, red; Cl, chlorine; P, magenta. The carbon atoms of the chiral substituents are represented as dark green and violet colored atoms.

Each corner of the tetrahedron consists of the trigonal Pd_3X^* chiral units that are built via the *cis*-coordination of the tridentate tris(imido)phosphate trianions. The edges of the tetrahedron consist of chloranilate linkers which offer a pair of wide-angle O,O- chelation to the 90° cisoidal sites at each Pd(II) center. The cages exhibit additional rotational chirality as observed by the clockwise (in **2-R**) or anticlockwise (in **2-S**) orientation of the methyl groups attached to the stereogenic carbon centers. Their packing structures indicate solvent accessible voids of volume $3000 \text{ \AA}^3$ which amounts to 33% of the total unit cell volume (Figures A4.8-4.10, Appendix). Notably, both **2-R** and **2-S** exhibit a tighter packing than the previously reported **1-R** and **1-S** ($13051 \text{ \AA}^3$; 51% of the unit cell volume), though, the intrinsic void volumes of these new cages are higher at $224 \text{ \AA}^3$ per cage. A closer analysis of the void structures in **2-R** and **2-S** indicates that they exhibit a remarkable 3D-net of Sodalite topology for channels running along the exterior cavities of the cages which are in turn connected to the intrinsic cavities of the individual cages (Figure 4.3).

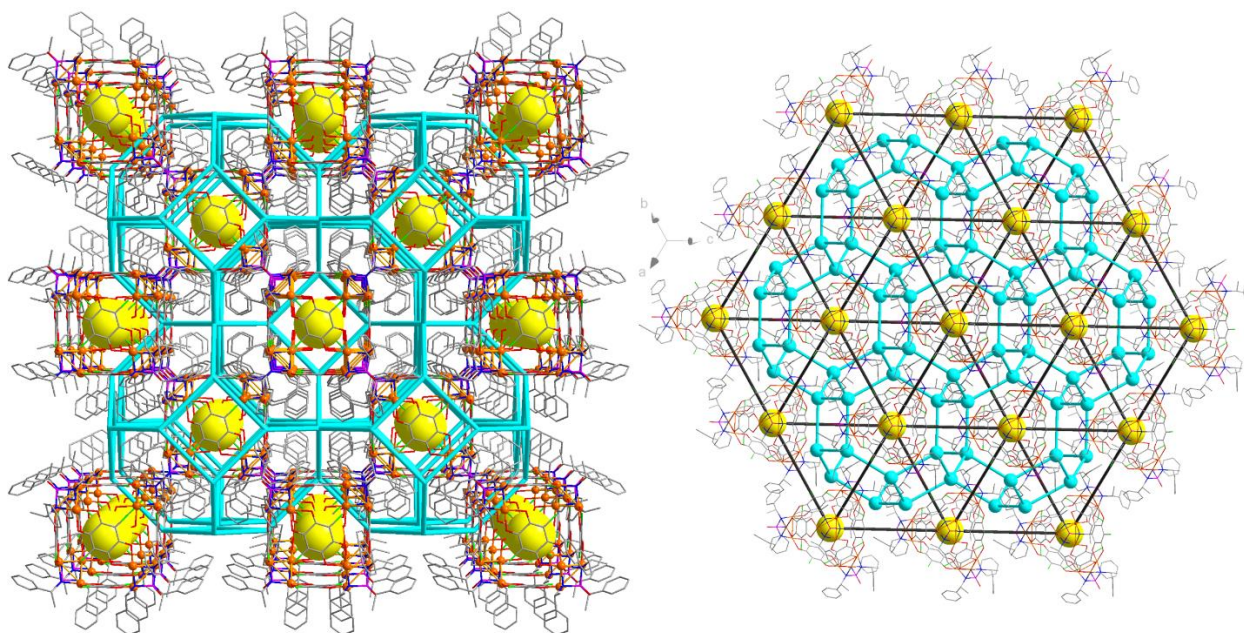


Figure 4.3: (a) Packing Structure of **2-S** (left) in $I23$ showing the 3-D net of Sodalite topology. The yellow spheres depict the intrinsic voids of the individual cages. b) View of the Sodalite network along the offset axes. On the other hand, **1-R** and **1-S** were shown to form a more open diamondoid network in a face-centered cubic lattice.

On the other hand, **1-R** and **1-S** were shown to form a more open diamondoid network in a face-centered cubic lattice. In the absence of any strong H-bonding interactions, the loose association of these cages, **2-R** and **2-S**, has been supported by only hydrophobic interaction of the methyl benzyl groups attached to the imido nitrogen. Upon drying, these crystals collapse into a denser, amorphous form which does not contain any porosity as revealed by gas adsorption analysis.

4.3.3 Guest-Encapsulation studies of cage **2-R** and **2-S**

Inspired by the host-guest capabilities of the earlier reported cages based on such imido-Pd₃ motifs, we examined the preliminary guest encapsulation studies of these chiral cages for CCl₄ and toluene. Thus, the CCl₄ and toluene treated samples of **2-S** gave the respective peaks at $m/z = 4310$ and 4256 corresponding to the $[\text{CCl}_4\text{C-2-S}]^+$ and $[\text{C}_7\text{H}_8\text{C-2-S}]^+$ ions (Figures A4.11 and A4.12, Appendix). A similar set of experiments yielded the same results for **2-R** as well. To track the nature of interaction of these racemic styrene oxides with the chiral cages, ¹H-NMR and MALDI-TOF mass spectral analysis were performed on the host-guest mixtures in solution. Since, the size of $\pm\text{SO}$ is similar as that of toluene, we presumed that it might exhibit

encapsulation within the intrinsic cavities of the cage. However, the MALDI-TOF mass spectrometry of the $\pm$ SO treated cages showed the peaks due to only CHCl_3 encapsulated cages (Figures A4.13 and A4.14, Appendix). Similarly, the ^1H NMR of these host-guest solids in CDCl_3 did not show any change in the chemical shifts for the $\pm$ SO protons indicating that the observed signals are due to the residual $\pm$ SO molecules adsorbed at the surface of the cages (Figure A4.15-A4.16, Appendix). This observation is further confirmed by the ^1H -2D-DOSY NMR experiments where no separate diffusion coefficients for the bound and free $\pm$ SO molecules could be observed (Figure A4.17-A4.18, Appendix). Also, no encapsulation was detected at the intrinsic cavities of the cages for the other styrene oxide derivatives as well.

Furthermore, we obtained crystals of both 2-R and 2-S when treated with either $\pm$ SO or $\pm$ F-SO. However, higher quality data sets from these crystals did not show the presence of these guest molecules in their structures, albeit the fact that these cages were found to crystallize in the rhombohedral space group of $R3$. Formation of these new polymorphs could presumably be driven by the template effects of the guest molecules which resulted in the efficient packing of the cages in the $R3$ phase than in the $I23$ phase. These observations suggests that the guest molecules would seemingly be recognized at the chiral centers located at the exteriors of the cages via any one of the possible $\text{C-H}\dots\text{N}_{\text{imido}}$, $\text{C-H}\dots\text{O}_{\text{epoxide}}$ and $\pi_{\text{ligand}}\dots\pi_{\text{epoxide}}$ interactions. This inference is in line with our earlier report where the X-ray derived structure of an iso-structural cage exhibiting prominent encapsulation of the guest molecules at their external cavities.¹³

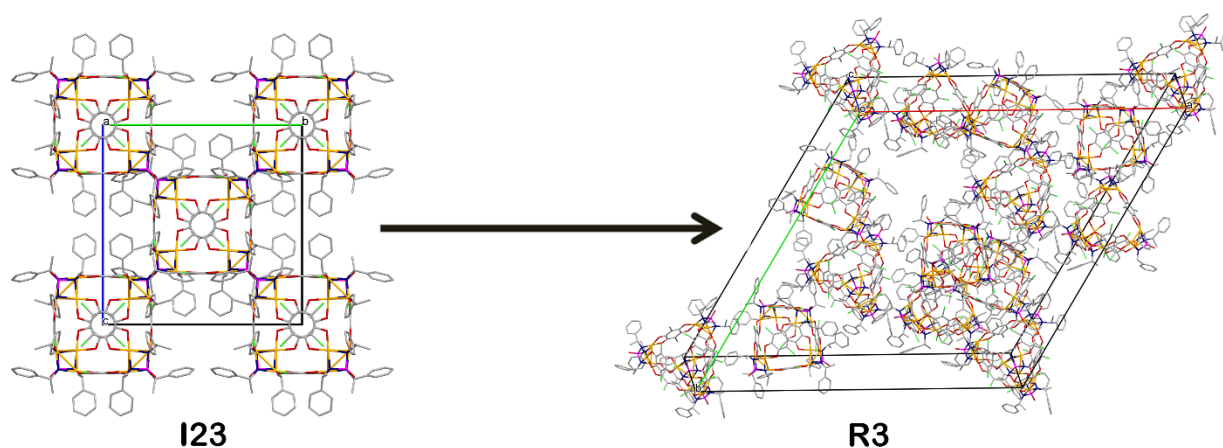


Figure 4.4: Comparative unit cell packing diagrams of 2-R in $I23$ and $R3$ space groups.

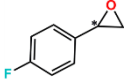
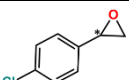
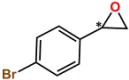
Similar transformations have been observed in the family of chiral tetrahedral cages reported by Cooper and co-workers.²⁰ In the case of Cooper's cage, the transformation of cubic *P*23 phase to cubic *F*23 phase was obtained via heating of the single crystals to 383 K which further gave rhombohedral *R*3 phase upon cooling to 100 K. In our cages, we observed a transformation of cubic body-centered *I*23 to rhombohedral *R*3 presumably via guest triggered or template driven effects (Figure 4.4). Moreover, the packing structures of the *R*3 polymorphs of 2-R and 2-S showed a much lower solvent-accessible channel volume of 16.8% (10860 Å) of the total unit cell in comparison with those observed for the *I*23 polymorphs (33%, 3000 Å³). This reduction in the void volume could be due to the efficient packing of the cages in the *R*3 polymorph than in the *I*23 polymorph. However in the Cooper's cages, the high symmetry phases are metastable which gave an effective packing of the cages in the *R*3 space group via tilting of the aliphatic exo-cage substituents (Figure A4.19, Appendix).

4.3.4 Chiral separation studies of cage 2-R and 2-S

A family of styrene oxides, phenyl oxirane (SO), 2-(4-Fluorophenyl)oxirane (F-SO), 2-(4-Chlorophenyl)oxirane (Cl-SO), 2-(4-Bromophenyl)oxirane (Br-SO) were probed for the enantioselective adsorption experiments with 2-R and 2-S. For the separation experiments, the chloroform solutions of the host cages were mixed with the racemic mixture of the styrene oxides in excess and left for evaporation at 298 K. The obtained solids were washed with cold n-pentane in order to remove the remaining guest molecules. The resultant solids were soaked in n-hexane to remove the enantio-enriched styrene oxides and the filtrates were subsequently injected for the HPLC analysis. The highest *ee* value of 80% is recorded for the R-isomer of F-SO resolved by cage 2-R. A similarly high *ee* value of 78% is again obtained for the +F-SO desorbed from 2-S as well. For SO, the *ee* values of 7 and 39% for the R-isomer as resolved by 2-R and 2-S, respectively, were obtained from HPLC analysis. The HPLC resolved *ee* values were found to be intermediate at 57 and 56% for the R-isomer of Cl-SO using the cages 2-R and 2-S, respectively (Table 4.2). The obtained *ee* values were consistently reproducible for three independent separation experiments (Tables A4.2 and Figure A4.20-A4.27, Appendix). Remarkably, the host cages can be regenerated after each separation cycle by crystallizing them from DCM. From the above observations, the obtained enantioselectivities fall in the order of F-SO > Cl-SO > SO with respect to the cages 2-R and 2-S. The Br-SO did not show any selectivity at all, probably due to its larger size being incompatible with the guest binding sites at the external cavities of the cages. Control experiments showed that the ligands X^{RRR}H₃,

$X^{SS}H_3$ alone could not resolve the above said styrene oxides under identical conditions. The previously reported cages **1-R** and **1-S** did not show any selectivity as well. This indicates that the tight association of the present cages, containing planar metal-coordinated electron deficient chloranilate dianion surfaces, with the oxirane guests plays a vital role in their enantioselective separation.

Table 4.2: Racemic epoxides employed in the chiral separation studies resolved by **2-R** and **2-S** along with their HPLC-determined separation results.

Compound	% <i>ee</i> resolved by 2-R (excess enantiomer)	% <i>ee</i> resolved by 2-S (excess enantiomer)
	7 (R)	39 (R)
	80 (R)	78 (R)
	57 (R)	56 (R)
	cannot resolve	cannot resolve

We screened a range of racemic guest molecules such as 2-butanol, 1-phenyl ethanol, and *p*-cyano and *p*-nitro styrene oxides. However, none of them showed any expected selectivity. Furthermore, due to the charge neutral nature of these chiral cages as well as due to the presence of quinoid linkers, we investigated the suitability of these cages for the chiral separation of racemic styrene oxides (SOs).

4.4 Conclusion

In summary, this work illustrates a reasonably-good enantio-separation of styrene epoxides by crystallization inclusion method using supramolecular ensembles. The tetrahedral cages **2-R** and **2-S** were built in a facile strategy by using trinuclear Pd(II) clusters containing chiral tris(imido)phosphate trianions and chloranilate linkers. A highest enantioseparation of 80% has been observed for the +F-SO compound using the **2-R** cage. For the other SOs, the *ee* values were found to range from 7 to 78% indicating the variations in the non-covalent interactions between the host- and guest molecules play a crucial role in the enantioseparation process.

These findings pave the way for the search of novel supramolecular systems that can facilitate the efficient separation of epoxides and other sensitive organic racemates.

4.5 References

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End of Chapter 4



Chapter 5



**Enantiopure polyradical tetrahedral
 Pd_{12}L_6 cages**

5.1 Introduction

Metal-organic polyhedral assemblies are an interesting class of coordination compounds due to their capabilities for host-guest chemistry, guest recognition and separation, as molecular reaction vessels and also as support platforms for certain biologically relevant transformations.¹ Over the years, a large number of cages have been shown to be synthesized with cationic, anionic and neutral framework structures. Interestingly, there are few reports pertaining to the preparation of polyhedral cages and supramolecular capsules with polyradical framework.²⁻³ Molecules possessing polyradical sites are attractive for their redox activities, charge-transfer characteristics and long-range electronic communications that make them as potential candidates for electrical conductors, optoelectronic materials and molecular magnets.⁴ The simple bis-chelating 2, 5-Dihydroxy benzoquinone (dhbq-2H) is an interesting redox reagent and resembles transition metal ions due to similarities in the energetics of their frontier orbitals.⁵ It can undergo either one electron oxidation or two one electron reductions to yield species of charges from -1 to -4 in which the species with -1 and -3 charges yield the persistent radicals. Notably, the radical form of (C₆H₂O₄)^{•3-} (abbreviated as dhbq^{•3-}) that are found in several mixed-valent metal organic frameworks show enhanced electrical conductivities and strong magnetic coupling and exhibit inter-valance charge-transfer bands in their electronic spectra.⁶ However, such polyradical frameworks are found to be very rare for discrete and polyhedral cage assemblies, although there are a few reports based on stable verdazyl radicals² or highly reactive TTF-based radicals.³ In fact, the nonradical dhbq²⁻ form prevails most often for heavier divalent transition metal ions to yield diamagnetic discrete self-assemblies possibly due to the presence of additional redox innocent co-ligands in them.⁷⁻⁸ Recently, our group has shown the formation of neutral chiral tetrahedral cages from trinuclear Pd(II) clusters *cis*-protected by tris(imido)phosphate trianions and *bis*-chelating oxalate linkers.⁹ Thus, we postulated that the polyradical character can be incorporated in this framework via the replacement of the oxalate linkers with the similarly coordinating dhbqⁿ⁻ linkers. Herein, we report an enantiomeric pair of polyradical tetrahedral cages (**3-R**)_{all} and (**3-S**)_{all} (shortly referred as **3-R** and **3-S**) of formula [(Pd₃X^{RRR})₄(C₆O₄H₂)₆] and [(Pd₃X^{SSS})₄(C₆O₄H₂)₆] based on chiral imido-Pd₃ motifs and anilate linkers with hitherto unknown [dhbq²⁻]^{••} diradical backbone. The formation of these tetrahedral cages have been confirmed by MALDI-TOF spectrometry and by the X-ray structural analyses of the enantiomeric pair of neutral-spin model cages (**4-R**)_{all} and (**4-S**)_{all} containing flouranilate (C₆F₂O₄)²⁻ linkers. The EPR and magnetic susceptibility measurements reveal that these cages, **3-R** and **3-S**, exhibit twelve identical spin centers. The

theoretical spin density analyses reveal that the cages 3-R and 3-S exhibit weak anti-ferromagnetic interactions between the two adjacent [dhbq²⁻]^{••} linkers. Interestingly, the enantiomeric cages 5-R and 5-S derived from the bromanilate linkers are found to exhibit singlet structure for the [C₆Br₂O₄²⁻]^{••} diradical dianion.

5.2 EXPERIMENTAL SECTION

5.2.1 General remarks

All manipulations involving phosphorus halides were performed under dry nitrogen atmosphere in standard Schlenk glassware. Dry Solvents were purchased from local vendors and used without further purification. Chemicals, reagents and metal salts were purchased from Aldrich without purifications. ¹H NMR, ¹³C {¹H} NMR, ³¹P {¹H} NMR, ¹⁹F NMR spectra were recorded on a Bruker and JEOL 400 MHz spectrometer. The mass spectra were obtained on an Applied Bio system matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF)/TOF spectrometer in linear mode. The Thermal analysis (TGA) data was carried out from a PerkinElmer STA-6000 thermo gravimetric analyzer under N₂ atmosphere with a heating rate 10°C min⁻¹. CD spectra were measured in JASCO J815 spectrometer from 800 nm – 190 nm. Elemental analyses were performed on a Vario-EL cube elemental analyzer. Electron paramagnetic resonance spectra were recorded with a Bruker EMX-plus X-band spectrometer (ν = 9.35 GHz). High-resolution solid-state NMR spectrum was recorded at ambient pressure on a Bruker AVANCE III spectrometer using a standard CP-TOSS pulse sequence (cross polarization with total suppression of sidebands) probe with 4 mm (outside diameter) zirconia rotors. Cross-polarization with TOSS was used to acquire ¹³C data at 100.37 MHz. The ¹³C ninety-degree pulse widths were 4 μs. The decoupling frequency corresponded to 72 kHz. The TOSS sample-spinning rate was 5 kHz. Recycle delays was 2s. Polycrystalline powder samples were characterized by recording magnetic response on a SQUID vibrating sample magnetometer (Quantum Design).

5.2.2 Synthesis

The ligand X^{RRR}H₃ and X^{SSS}H₃ was synthesized according to the earlier reported procedure.¹

5.2.2.1 Synthesis of Enantiopure radical tetrahedral Cages 3-R and 3-S:

Cages 3-R and 3-S: To a mixture of X^{RRR}H₃ or X^{SSS}H₃ (20 mg, 0.049 mmol) and Palladium acetate (33 mg, 0.147 mmol) in methanol (5 mL), a solution of Dihydroxy benzoquinone (15.36mg, 0.073 mmol) in methanol (2 mL) was added drop wise and the obtained reaction

mixture was stirred at 90 °C for 24 hrs to yielded a brown precipitate. The precipitate was purified by washing them with methanol several (2-3) times to yield the cages **3-R** or **3-S**.

Cages 3-R: Yield: 78% (based on P): ¹H NMR (400 MHz, CDCl₃): δ 1.53 (d, 9H, CH₃), 4.05-4.19 (dq, 3H, CH), 7.41-7.76 (m, 15H, aromatic). ³¹P NMR (161 MHz, CDCl₃): δ 70.1. MALDI-TOF/TOF (Linear): 3762 (M+K)⁺. ¹³C NMR (100 MHz): δ 23.79, 62.08, 128.67, 128.91, 129.31, 141.46, 180.59, 181.03. Elemental Analysis (%): Calcd for C₁₃₂ H₁₂₀ N₁₂ O₂₈ P₄ Pd₁₂: C, 42.58; H, 3.25; N, 4.51. Found: C, 42.50; H, 3.15; N, 4.53;

Cages 3-S: Yield: 83% (based on P): ¹H NMR (400 MHz, CDCl₃): δ 1.53 (d, 9H, CH₃), 4.05-4.19 (dq, 3H, CH), 7.41-7.76 (m, 15H, aromatic). ³¹P NMR (161 MHz, CDCl₃): δ 70.1. ¹³C NMR (100 MHz): δ 23.79, 62.08, 128.67, 128.91, 129.31, 141.46, 180.59, 181.03. MALDI-TOF/TOF (Linear): 3762 (M+K)⁺. Elemental Analysis (%): Calcd for C₁₃₂ H₁₂₀ N₁₂ O₂₈ P₄ Pd₁₂: C, 42.58; H, 3.25; N, 4.51. Found: C, 42.50; H, 3.15; N, 4.53;

5.2.2.2 Synthesis of chiral tetrahedral Cages 4-R and 4-S:

Cages 4-R and 4-S: To a mixture of X^{RRR}H₃ or X^{SSS}H₃ (20 mg, 0.049 mmol) and Palladium acetate (33 mg, 0.147 mmol) in methanol (5 ml), a solution of fluoranilic acid (12.84 mg, 0.073 mmol) in methanol (2 ml) was added drop wise and the obtained reaction mixture was stirred at 90 °C for 12 hrs to yielded a red precipitate. The precipitate was purified by washing them with methanol several (2-3) times to yield the cages **4-R** or **4-S**.

4-R: Yield: 83% (based on P). ¹H NMR (400 MHz, CDCl₃): δ 1.43 (d, 36H, CH₃), 3.98-4.10 (dq, 12H, CH), 7.38-7.76 (m, 60H, aromatic). ¹⁹F NMR (377 MHz, CDCl₃): δ -171.41. ³¹P NMR (161 MHz, CDCl₃): δ 70.34. MALDI-TOF/TOF (Linear): 3978 (M+K)⁺. Elemental Analysis (%): Calcd for C₁₃₂ H₁₀₈ N₁₂ O₂₈ P₄ F₁₂ Pd₁₂: C, 40.25; H, 2.76; N, 4.27. Found: C, 39.80; H, 2.56; N, 4.20.

4-S: Yield: 80% (based on P). ¹H NMR (400 MHz, CDCl₃): δ 1.43 (d, 36H, CH₃), 3.98-4.10 (dq, 12H, CH), 7.38-7.76 (m, 60H, aromatic). ¹⁹F NMR (377 MHz, CDCl₃): δ -171.41. ³¹P NMR (161 MHz, CDCl₃): δ 70.34. MALDI-TOF/TOF (Linear): 3978 (M+K)⁺. Elemental Analysis (%): Calcd for C₁₃₂ H₁₀₈ N₁₂ O₂₈ P₄ F₁₂ Pd₁₂: C, 40.25; H, 2.76; N, 4.27. Found: C, 40.22; H, 2.73; N, 4.25.

5.2.2.1 Synthesis of chiral radical tetrahedral Cages 5-R and 5-S:

Cages 5-R and 5-S: To a mixture of X^{RRR}H₃ or X^{SSS}H₃ (20 mg, 0.049 mmol) and Palladium acetate (33 mg, 0.147 mmol) in methanol (5 mL), a solution of bromanilic acid (21.74 mg, 0.073 mmol) in methanol (2 mL) was added drop wise and the obtained reaction mixture was stirred at 90 °C for 24 hrs to yielded a red precipitate. The precipitate was purified by washing them with methanol several (2-3) times to yield the cages 5-R or 5-S.

5-R: Yield: 80% (based on P). ¹³C NMR (100 MHz): δ 24.13, 63.80, 127.59, 140.66, 129.31, 141.46, 180.0, 191.0. MALDI-TOF/TOF (Linear): 4709 (M+K)⁺. Elemental Analysis (%): Calcd for C₁₃₂ H₁₀₈ N₁₂ O₂₈ P₄ Br₁₂ Pd₁₂: C, 33.95; H, 2.33; N, 3.60. Found: C, 33.88; H, 2.30; N, 3.50.

5-S: Yield: 85% (based on P). ¹³C NMR (100 MHz): δ 24.13, 63.80, 127.59, 140.66, 129.31, 141.46, 180.0, 191.0. MALDI-TOF/TOF (Linear): 4709 (M+K)⁺. Elemental Analysis (%): Calcd for C₁₃₂ H₁₀₈ N₁₂ O₂₈ P₄ Br₁₂ Pd₁₂: C, 33.95; H, 2.33; N, 3.60. Found: C, 33.80; H, 2.33; N, 3.62.

5.2.3 Crystallography

Reflections were collected on a Bruker Smart Apex Duo diffractometer at 100 K using Mo K α radiation ($\lambda = 0.710\ 73\ \text{\AA}$) for **4-R** and **4-S**. All structures were solved using intrinsic phasing method, and refined by full-matrix least-squares on F² (G. M. Sheldrick, SHELXL, program for crystal structure refinement, University of Gottingen, Germany, 2015).² The multi-scan absorption correction was applied by using the SADABS program.³ Crystallographic data for all these compounds are listed in Table S1. All non-hydrogen atoms were refined anisotropically if not stated otherwise. Hydrogen atoms were constrained in geometric positions to their parent atoms. The diffuse solvent molecules in **4-R** and **4-S** could not be modeled appropriately. Hence, these were treated as diffuse contributions to the overall scattering and removed by the SQUEEZE/PLATON for a better refinement data. All the phenyl rings are constrained to ideal six membered rings.

Table. 5.1: Crystallographic data for Isostructural Fluoranilate bridged chiral cages.

Compound	4-R	4-S
Chemical formula	C ₁₃₂ H ₁₀₈ F ₁₂ N ₁₂ O ₂₈ P ₄ Pd ₁₂	C ₁₃₂ H ₁₀₈ F ₁₂ N ₁₂ O ₂₈ P ₄ Pd ₁₂
Formula weight	3938.98	3938.98
Temperature	100(2)K	100(2)K
Crystal system	Orthorhombic	Orthorhombic
Space group	P 2 ₁ 2 ₁ 2	P 2 ₁ 2 ₁ 2
a (Å); α (°)	17.958(5); 90	18.032(5);90
b (Å); β (°)	31.190(8); 90	31.105(9);90
c (Å); γ (°)	17.495(5); 90	17.518(5);90
V (Å ³); Z	9799(8)	9826(5)
ρ (calc.) mg m ⁻³	1.334	1.331
μ(Mo K _α) mm ⁻¹	1.170	1.166
2θ _{max} (°)	57.38	56.58
R(int)	0.1033	0.0472
Data / param.	25015/846	24340/ 859
GOF	1.013	1.214
R1 [F>4σ(F)]	0.0755	0.0481
wR2 (all data)	0.1884	0.1491
Flack parameter	0.10(6)	0.011(8)
Max. peak/ hole (e.Å ⁻³)	1.23/-0.927	0.918/ -1.237

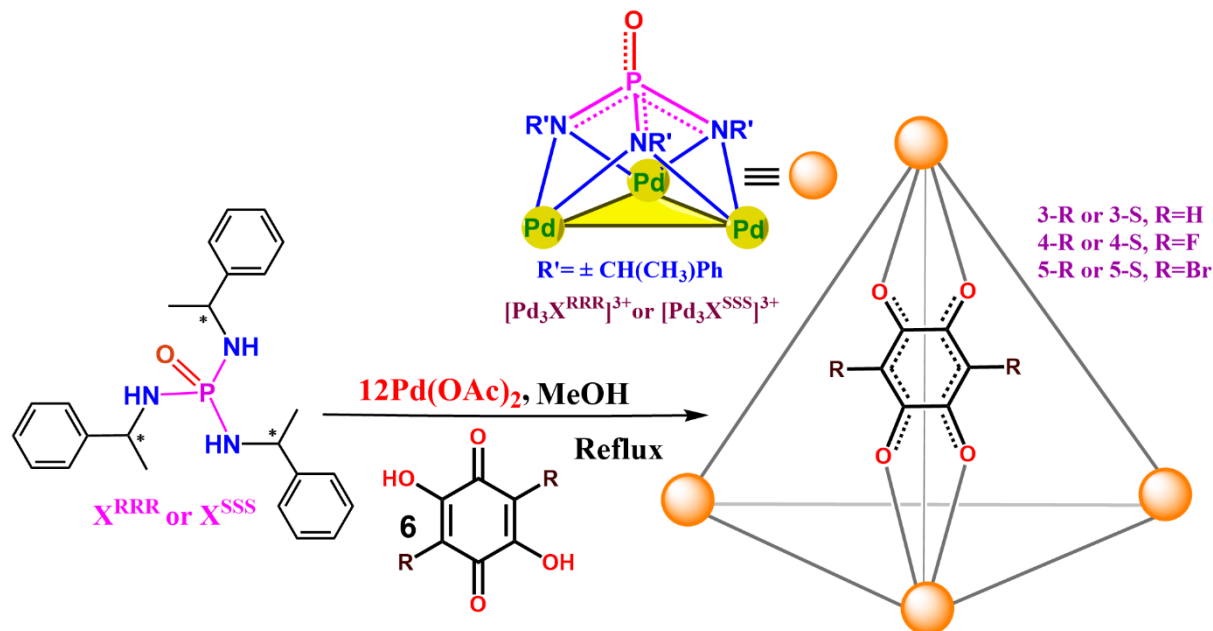
5.2.4 Computational Details:

The exchange between the radical-radical (quinone based radical) is described by the given spin Hamiltonian, $H = -JS_{\text{rad1}}S_{\text{rad2}}$, where J is the coupling constant and S_{rad1} and S_{rad2} are the spin of the radical one and radical two ($S_{\text{rad1}}=3/2$, $S_{\text{rad2}}=3/2$), respectively. DFT methods with broken symmetry approach were used for calculating the J values ($J = \text{EBS-EHS}/2S_1S_2 + S_2$) which has been well established for exchange calculations. All the calculations were performed by Gaussian 09 suit programme. Hybrid B3LYP functional were employed with triple zeta valanced quality basis set for all the atoms except for Pd; for Pd, TZp level basis sets were used. A very tight SCF convergence has been implemented throughout the calculations.

5.3 RESULTS AND DISCUSSION

5.3.1 Syntheses

Scheme 5.1: Synthetic scheme for anilate tethered chiral tetrahedral cages.



The spin-cages **3-R** and **3-S** were synthesized in a direct reaction involving the corresponding chiral ligands $X^{RRR}\text{H}_3$ and $X^{SSS}\text{H}_3$, palladium (II) acetate and dnbq-2H in methanol. The formation of the cage assemblies **3-R** and **3-S** were confirmed by the MALDI-TOF (Linear mode) spectrometry which unveiled a single peak at $m/z = 3762$ corresponding to their molecular $[\text{M}+\text{K}]^+$ ion (Figure A5.1-A5.2, Appendix). The ^{31}P NMR of **3-R** and **3-S** in CDCl_3 displayed a singlet at 70.14 ppm which confirms the presence of the pure cage (Figure A5.3, Appendix). The ^1H NMR analysis of **3-R** and **3-S** revealed broad signals for the protons of the α -methyl benzyl groups attached to the tris(imido) phosphate ligand at the Pd_3 PBUs. The signal broadening is ascribed to the presence of paramagnetic species in the cage framework (Figure 5.1).

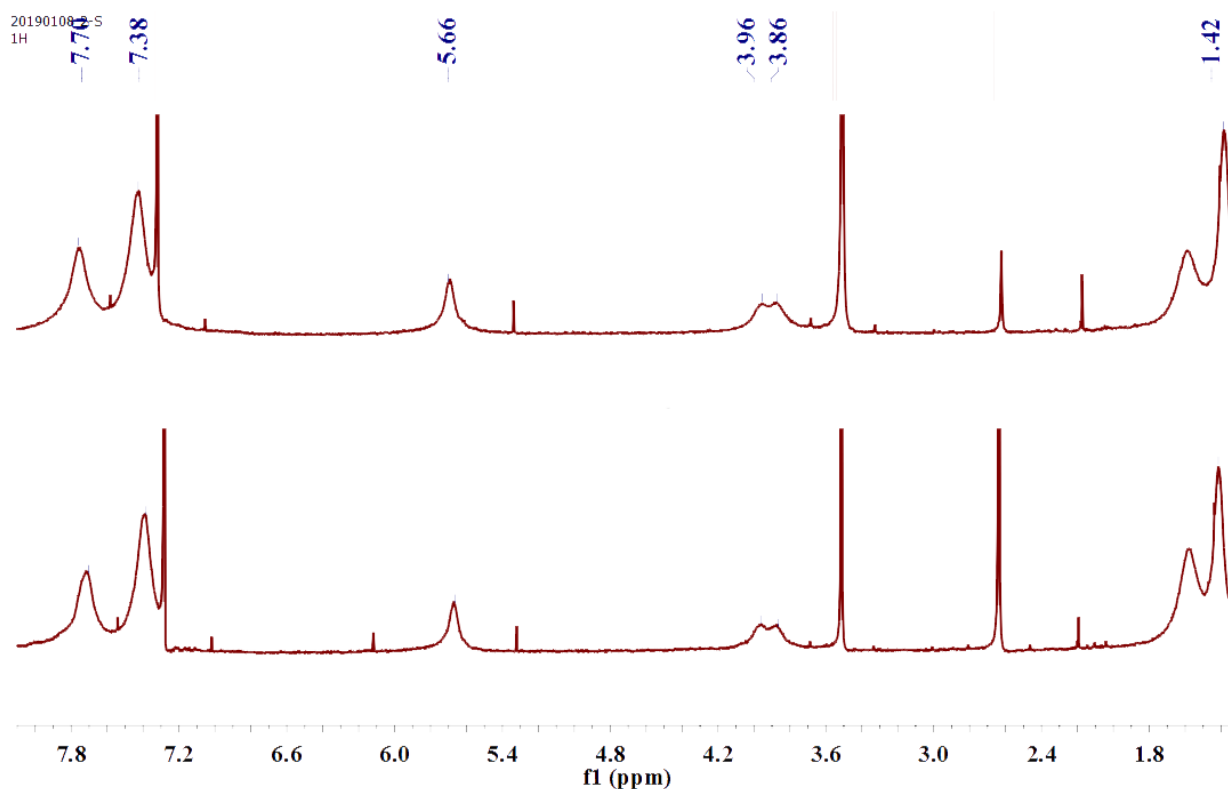


Figure 5.1: ¹H NMR of spin cages **3-R** and **3-S**.

The poor solubility of the radical cages in CDCl₃ hampered the solution-phase ¹³C NMR analysis. The solid-state ¹³C NMR spectrum showed the presence of carbonyl carbon ($\delta = 187$, 192 ppm) and C-H carbon ($\delta = 100$ ppm) of the dmbq linkers in addition to the carbon atoms of the imido-phosphate ligands in the cage framework (Figure A5.4-5.5, Appendix). Thermogravimetric analysis (TGA) reveals the absence of solvate molecules inside the cage cavities and shows a thermal stability of up to 200 °C for both **3-R** and **3-S** (Figure A5.6, Appendix). The solid state CD spectra of **3-R** and **3-S** gave mirror image signals at 260nm and 353nm due to the respective ligand-centred and ligand to metal charge transfer transitions showing the enantio-enriched nature of the radical cages (Figure 5.2a). The absolute configurations ($[\alpha]^{2D}$) of **3-R** and **3-S** were found to be 1322° and -1340° in 0.1 M solution of CHCl₃ as determined by the optical rotation measurements. The iso-structural spin-neutral cages were synthesized from the reaction of fluoranilic acid, chiral phosphoramidate ligands and Pd(OAc)₂. Formation of the tetrahedral cages of formula **4-R** and **4-S** (C₁₃₂ H₁₀₈ N₁₂ O₂₈ P₄ F₁₂ Pd₁₂) has been confirmed by NMR and mass spectral analysis (Figure A5.7-5.8, Appendix). Unlike **3-R** and **3-S**, **4-R** and **4-S** were found to be diamagnetic as revealed by its ¹H-NMR analysis which gave clear resonances for the α -methyl benzyl groups (Figure A5.9-5.10, Appendix). The ¹⁹F NMR and ³¹P NMR of these cages are shown in figure (Figure A5.11-5.12, Appendix). Cages **4-R**

and **4-S** exhibited singlet at -171.41ppm and 70.34ppm corresponding to ¹⁹F NMR and ³¹P NMR spectra, respectively. The enantiomeric nature of the cages **4-R** and **4-S** were confirmed by Circular dichroism measurements (Figure 5.2b) and the four bisignate bands are 262(π - π^*), 356(π - π^*), 428(LMCT) and 503 nm (LMCT).

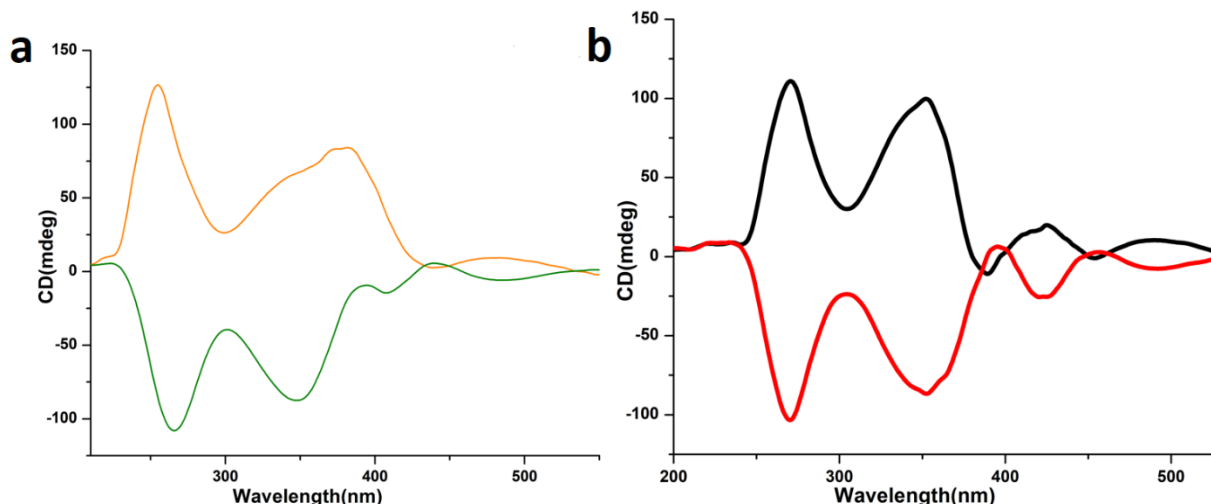


Figure 5.2: a) Solid state Circular dichroism spectra of radical cages **3-R** (orange) and **3-S** (green). b) Circular dichroism spectra of isostructural cages of **4-R** (black) and **4-S** (red) in Chloroform solution.

Cages **5-R** and **5-S** were synthesized by using Bromanilic acid, X^{RRR}H₃ and X^{SSS}H₃ and Pd(OAc)₂. The formation of **5-R** and **5-S** characterized by solid state ¹³C NMR and MALDI-TOF mass spectrometry (Figure A5.17-5.20, Appendix). The poor solubility of the **5-R** and **5-S** in CDCl₃ hindered the solution ¹H, ³¹P and ¹³C NMR analysis. In ¹³C NMR analysis gave peaks at 24.1, 63.8, 127.5, 140.6, 180.0, and 191 ppm. The CD spectrum of **5-R** and **5-S** exhibits mirror image spectra at 245 and 347 nm, indicating their enantiomeric nature (Figure A5.21, Appendix). The optical rotation measurements of **5-R** and **5-S** gave values are +2050° and -1950°, respectively.

5.3.2 Crystal structures:

Several attempts to crystallize the polyradical cages **3-R** and **3-S** went unsuccessful. Thus, we employed a similar ligand motif based on fluoranilic acid in combination with the corresponding chiral phosphoramidate ligands in reaction with Pd(OAc)₂ to build iso-structural cages. Crystals of **4-R** and **4-S**, suitable for single-crystal X-ray diffraction analysis was obtained from their corresponding dichloromethane solutions. Again, cages **5-R** and **5-S** based on bromanilic acid could not be crystallized due to their radical nature. Both **4-R** and **4-S** crystallized in the chiral orthorhombic space group *P2₁2₁2*. The asymmetric units of **4-R** and

4-S possess one fourth of the cage molecule. The structural analysis confirmed the enantiopure nature of these cages. The tetrahedral cages in **4-R** and **4-S** are build-up of trigonal Pd₃X* chiral units at each of its four corners. The *bis*-bidentate fluoranilate dianions tether them across the six edges of the tetrahedron via the wide-angle O, O- chelation to the 90° cisoidal sites at each Pd(II) centers. Each Pd₃ unit is *cis*-protected by the hexadentate coordination of tris(amino)phosphate trianion at the exteriors of the cage. These cages further exhibit a rotational chirality as observed by the clockwise (in **4-R**) or anticlockwise (in **4-S**) orientation of the α -Me groups attached to the stereogenic carbon centers. The intrinsic void volumes of these new cages were found to be 224 Å³ as indicated by MSROLL calculations. The packing structure of these cages exhibit solvent accessible voids of volume 651 Å³ which amounts to 6.6% of the total unit cell volume.

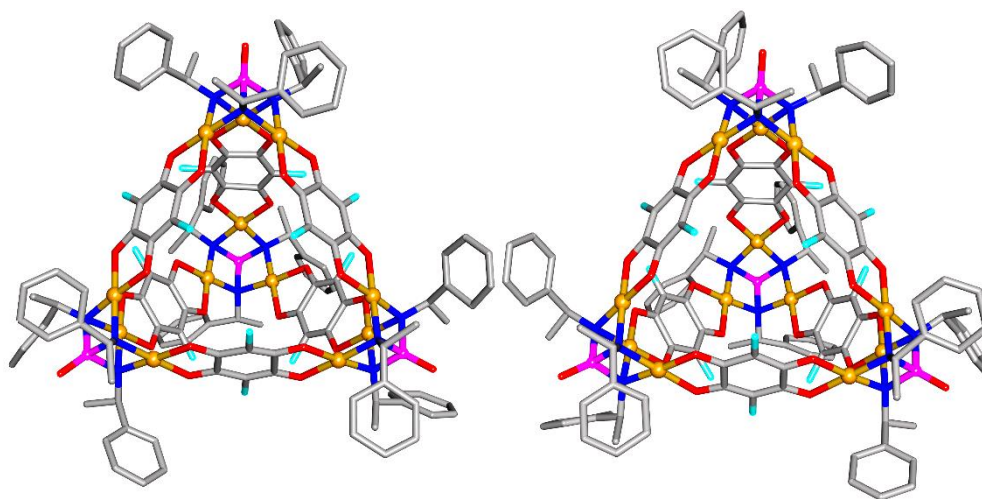


Figure 5.3: SCXRD Structures of chiral cages **4-R** (left) and **4-S** (right).

5.3.3 Electron Paramagnetic Resonance and Magnetism:

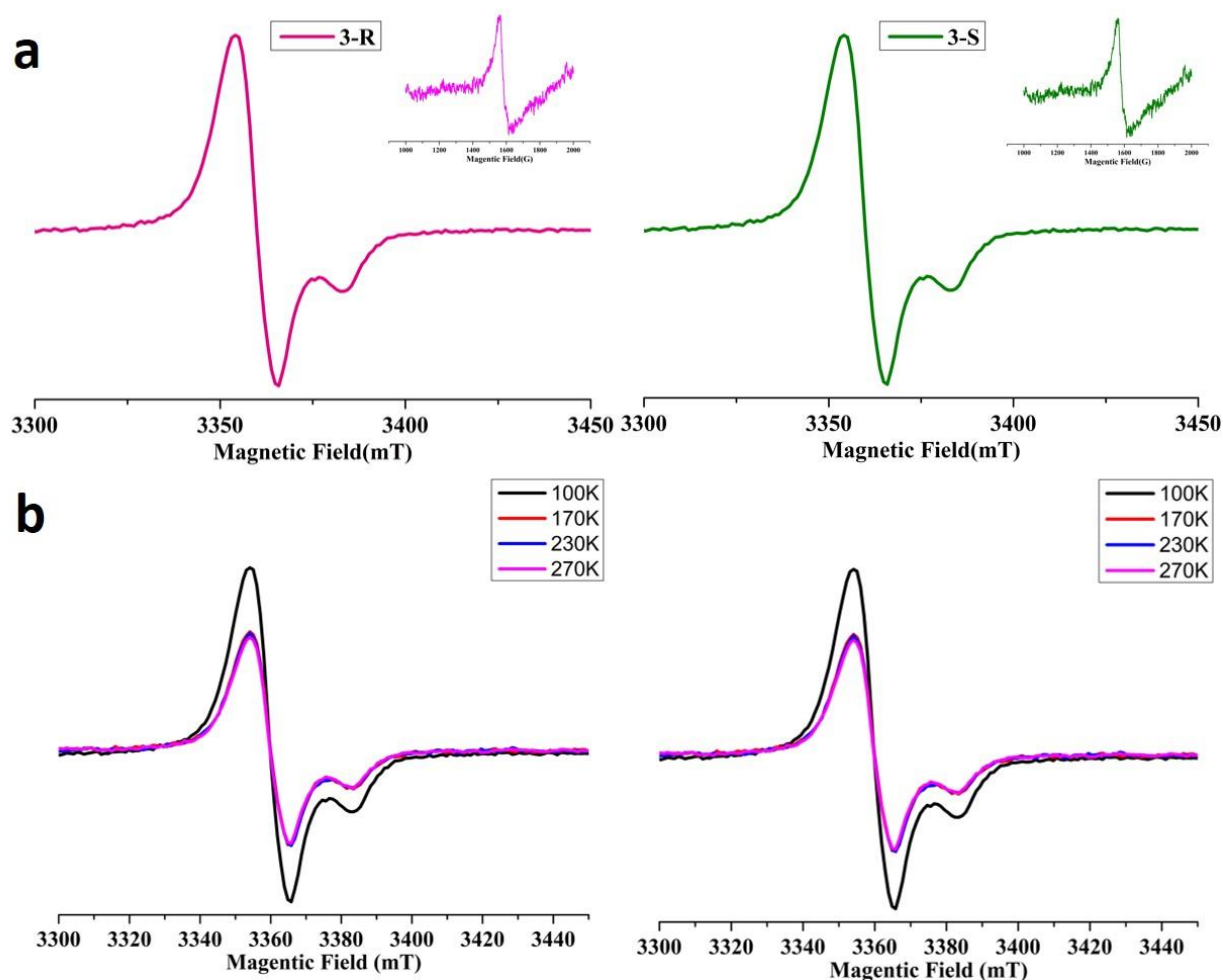


Figure 5.4: a) EPR spectra of triplet diradical cages **3-R** and **3-S** and Inset (Forbidden transition at 1600 T). b) Variable Temperature of EPR spectra of cage **3-R** and **3-S**.

The electron paramagnetic resonance (EPR) spectroscopy was recorded on the samples of **3-R**, **3-S**, **5-R** and **5-S** to understand the nature of radicals present in these cage molecules. The room temperature EPR spectrum of **3-R** or **3-S** in the solid state displays a single sharp signal at $g = 2.002$ corresponding to an unpaired electron (Figure 5.4a). This indicates the presence of a unique d_hb_q radical species within the polyradical cage framework. The variable temperature EPR spectrum recorded in the range of 270 to 100 K on both **3-R** and **3-S** shows an increase in intensity for the signal suggesting the population of their triplet states at low temperature (Figure 5.4b). The existence of the triplet state in them is further confirmed by the observation of the forbidden transition ($\Delta m_s = 2$) at half the field (1600 mT) of the main signal (~ 3200 mT) at 100 K.

The variable temperature DC magnetic susceptibility measurements on **3-S** gave a room temperature (293 K) $\chi_{\text{m}}T$ product of 5.8 emu K mol⁻¹ at 1000 Oe which indicates presence of triplet radicals at each of the six [d_hbq²⁻]⁻ motifs in the cage (Figure 5.5). The obtained magnetic moment (μ_{eff}) value of 12.50 μ_{B} is consistent with the computed spin-only ($\mu_{\text{s.o.}}$) value of 12.96 μ_{B} for the twelve unpaired electrons.

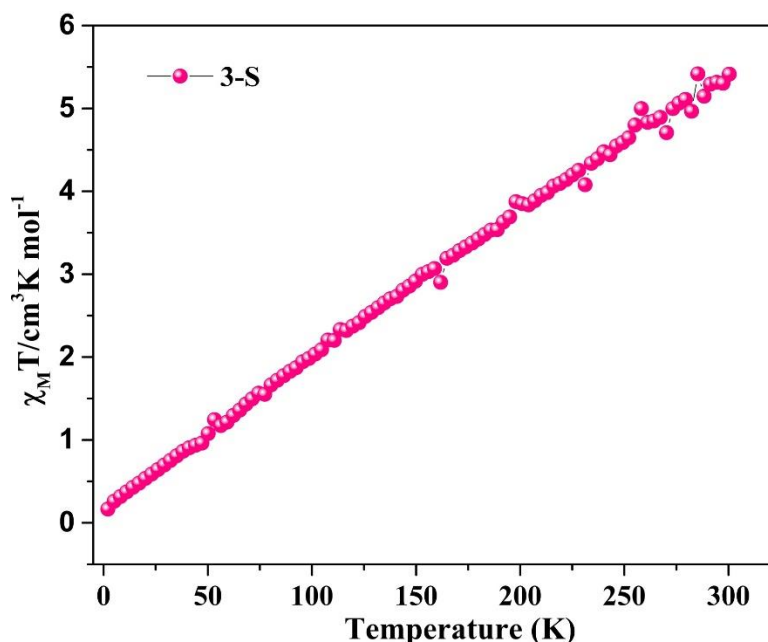


Figure 5.5: $\chi_{\text{M}}T$ Vs T plot for cage **3-S**.

The EPR spectra of the bromanilate derived cages **5-R** and **5-S** again displayed a singlet at room temperature with $g = 2.0026$ (Figure 5.6a). Unlike **3-R** and **3-S**, intensity of the EPR signal decreases with decreasing temperature from 270 to 100 K (Figure 5b). This suggests that the radicals located at the adjacent bromanilate fragments interact with opposite spins. In fact, at 77 K there is no EPR signal observed for both **5-R** and **5-S** signifying the singlet nature of these radicals (Figure 5.6c). Furthermore, the initial squid magnetometric measurements show a diamagnetic behaviour for the cages **5-R** and **5-S** confirming the singlet nature of the radical spins in them.

It is interesting to note that the spin cages have been formed for the unsubstituted anilate and bromanilate ligands while neutral cages have been obtained for the fluoranilate linkers. This could be due to the higher electron withdrawing nature of the F-atoms on the fluoranilate moieties increase the HOMO-LUMO gap in the system and thereby destabilizing the radical state.

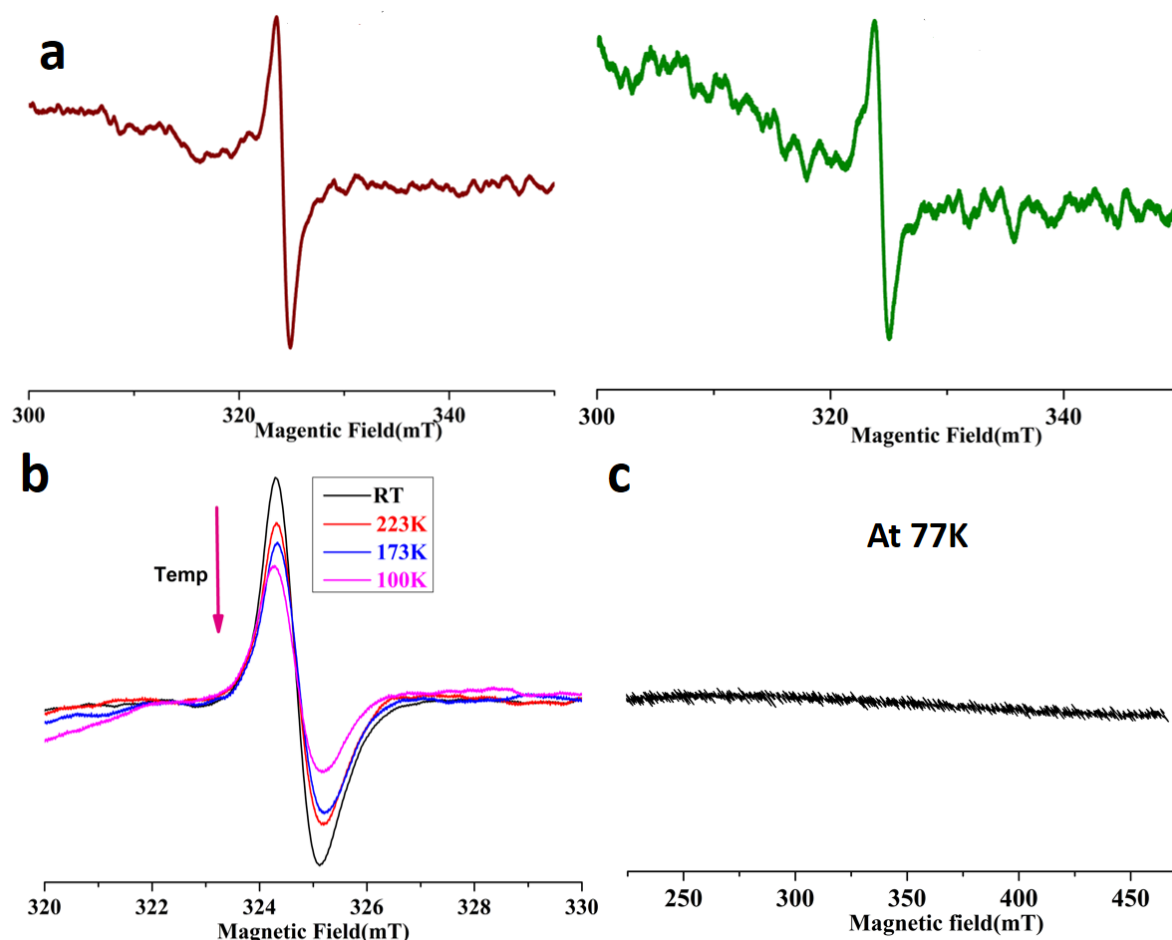


Figure 5.6: a) EPR spectra of singlet diradical cages 5-R and 5-S. b) variable Temperature of EPR spectra of cage 5-S d) at 77K.

5.3.4 Computational results:

Further insights on the radical properties of these cages have been obtained by computational studies on the 3-S cage. Since the molecule is a very large cluster, we have modeled the structure by fragmenting it to its idealized repeat unit. Because the molecule is completely symmetric, we expect an uniform exchange between the radicals. For the calculations, two unique models were assumed. In one case, the unique Pd₃ core has been kept intact at one side and the ligating environment of the Pd atoms across the three bridging radical ligands were retained identical to the original Pd₃ core. In the second model the coordination around the Pd atoms across the dmbq ligand were terminated with H atoms. From the spin density plot it is clear in that both the cases the spin distribution is nearly same regardless the environment (H or the original P-derived N and O chelation) at the terminal Pd atoms. The spin density plots show that there is delocalisation of the unpaired electron on the O atom with the C of the aromatic ring (Figure 5.7). Moreover, the absence of prominent spin densities on the Pd atoms

suggest no or very weak interactions between the radicals of the neighbouring dhbq motifs. Furthermore, exchange interactions were calculated by using the phi simulation software and by DFT methods. Since the radicals are much distant apart from one another via sp³ bridging bond, the exchange is found to be weak as compared to the radical-radical exchange for the organic magnetic systems. Since only half of the structure is taken for the computation by considering only 3 DHBQ motifs, the exchange calculated from the DFT calculation is deviating slightly from the phi simulated exchange values (Figure 5.6). Among the two models, the second model where H is attached to the terminal Pd gives an exchange values of -85 cm⁻¹ where as the exchange value from phi simulation is found to be -80 cm⁻¹. In both the cases the exchange interactions are found to be anti-ferromagnetic in nature.

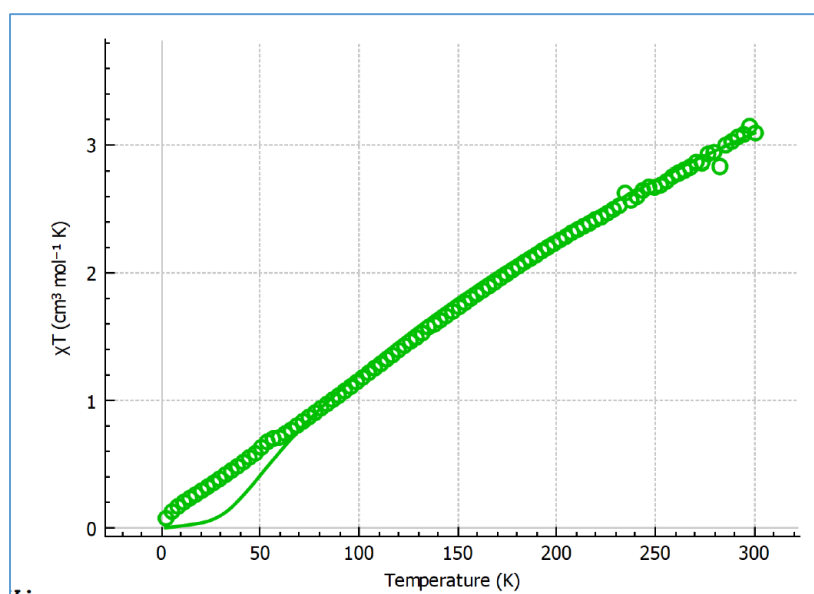


Figure 5.6: Phi simulated χT vs T plots for DHBQ-Pd cage complex.

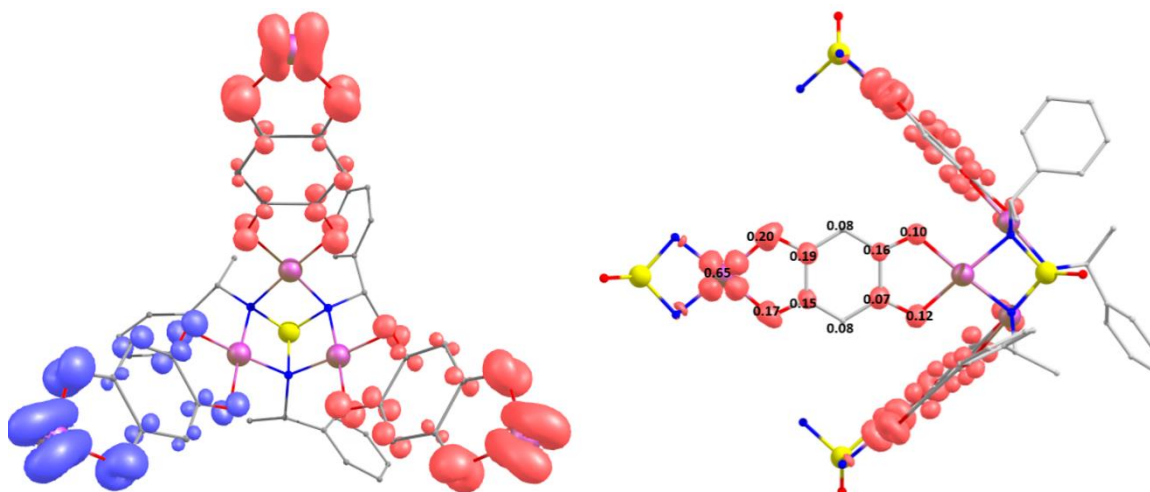


Figure 5.7: Spin density plots for the 3-S cage fragment with terminal broken symmetry states with Pd atoms across the three bridging radical ligands substituted with (a) terminal H-atoms and (b) with N_{imido} and O_{anilate} coordination.

5.4 Conclusion

In conclusion, utilizing a family of anilate based linkers, chiral Pd(II) cage assemblies with polyradical frameworks have been built. While the anilate and bromanilate linkers form the stable radical pairs on the cage framework, the fluoranilate linkers stabilize the neutral cages. The formation of the tetrahedral cage assemblies have been confirmed MALDI-TOF, ³¹P-NMR and single-crystal X-ray diffraction analysis in case of **4-R** and **4-S**. The EPR, magnetic measurements and theoretical calculations show that the diradicals in each of the [d_hbq²⁻]^{••} linkers in the cages **3-R** and **3-S** exist in the triplet state, whereas the [C₆Br₂O₄²⁻]^{••} diradical dianions in **5-R** and **5-S** exist in the singlet ground state. Currently, we are investigating the magnetic properties of the other cages along with computational studies to support the nature of diradicals in these spin-cages. The present work provides insights for design and synthesis of stable metal organic and organic cage frameworks containing polyradicaloid structures with enormous potential in the area of spin-electronic devices.

5.5 References

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End of Chapter 5



Chapter 6



**Thesis Conclusion and Future
Perspectives**

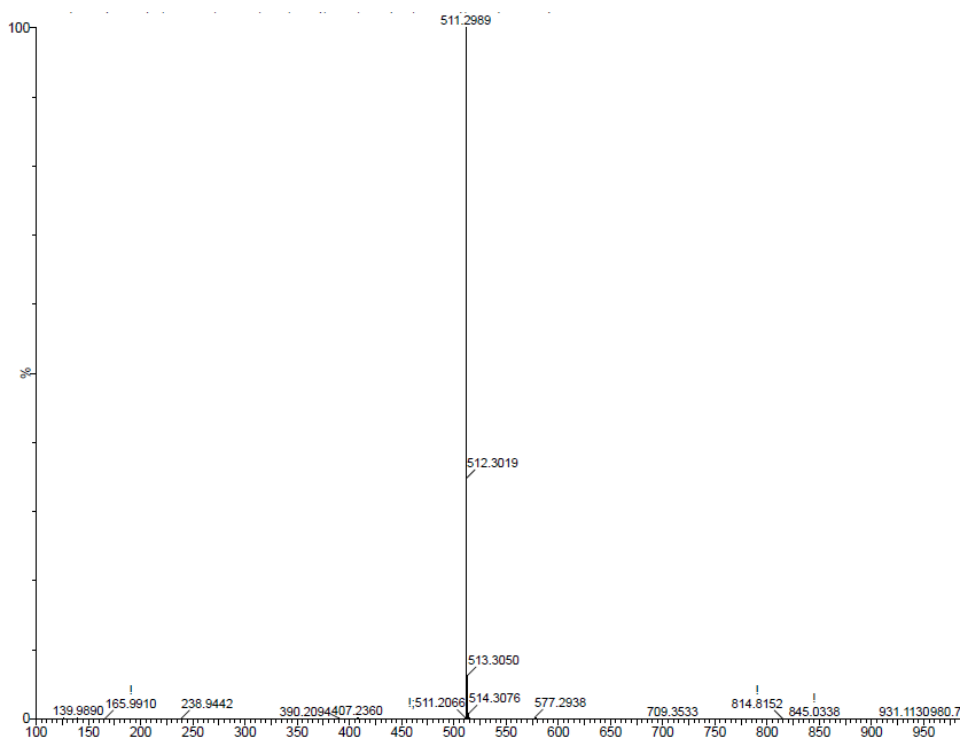
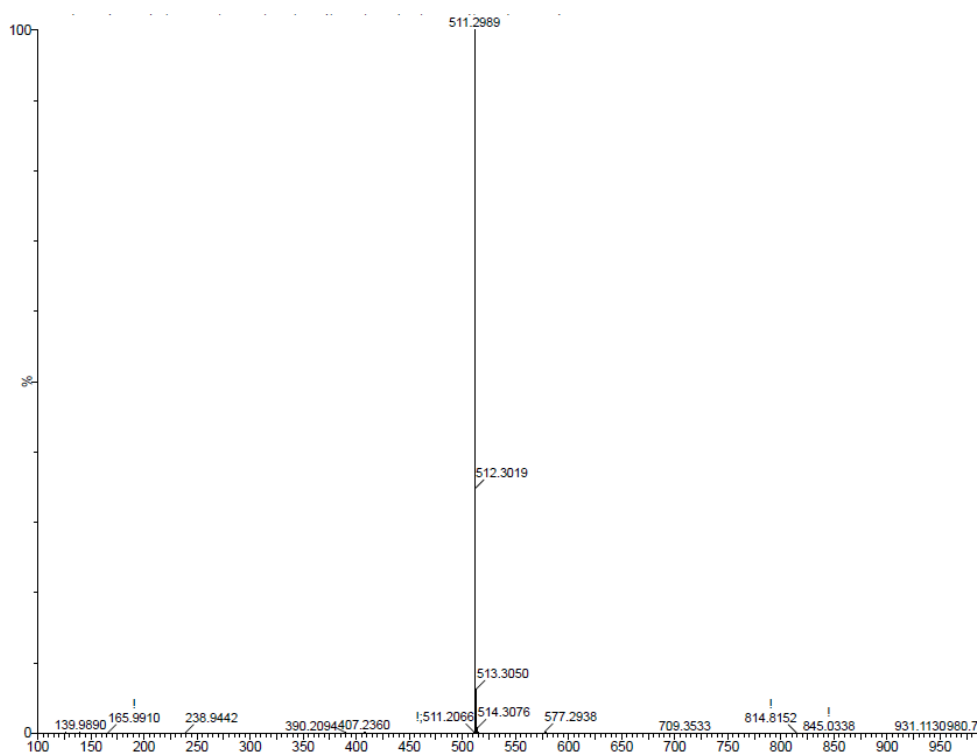
In summary, this thesis demonstrates the synthesis of chiral metal-organic cages and simple chiral organic assemblies derived from chiral amino P(V) motifs and their functional studies in the domains of host-guest chemistry, chiral recognition and separation. In chapter 2 We have described the synthesis of novel chiral aminophosphonium salts and studied their chiral recognition behavior by using enantiomers of mandelic acid and phenylglycinol with high binding selectivity. Also, synthesis and structures of enantiopure salts of phosphonium anilates have described in this chapter. These phosphonium anilates exhibit interesting hydrogen bonded 2-D frameworks. Chiral neutral tetrahedral Pd(II) cages derived from chiral imido(phosphate) trianions (obtained via the deprotonation of the corresponding phosphoramidate ligands), Pd(II) ions and oxalate dianions have been described in the Chapter 3. These cages were shown to resolve small racemic molecules with various functional groups such as epoxide, lactone and ketones. Neutral chiral tetrahedral cages consisting of chiral tris(imido) phosphate trianions, Pd(II) ions and chloranilate linkers were described in Chapter 4. Moreover, it is interesting to note that subtle variation in the linker backbone leads to an increase in the enantioselectivity towards a series of 4-halostyrene oxides In chapter 5, Pd(II) cages with anilate, bromanilate, fluoranilate linkers were prepared and studied for their radical forming behaviour. Interestingly, we found that anilate and bromanilate tethered chiral cages were diradical in nature, as evidenced from EPR, magnetic measurements and computational calculations. In the future, it will be interesting to develop of water-soluble chiral metal-organic cages and study chiral recognition and separation capabilities in aqueous media. Also, the synthesis of chiral spin cages would be fascinating in the area of spintronics and electronic devices.

End of Chapter 6



Appendix



**Figure A.2.1:** MALDI-TOF spectra of P-R4.**Figure A.2.2:** MALDI-TOF spectra of P-S4.

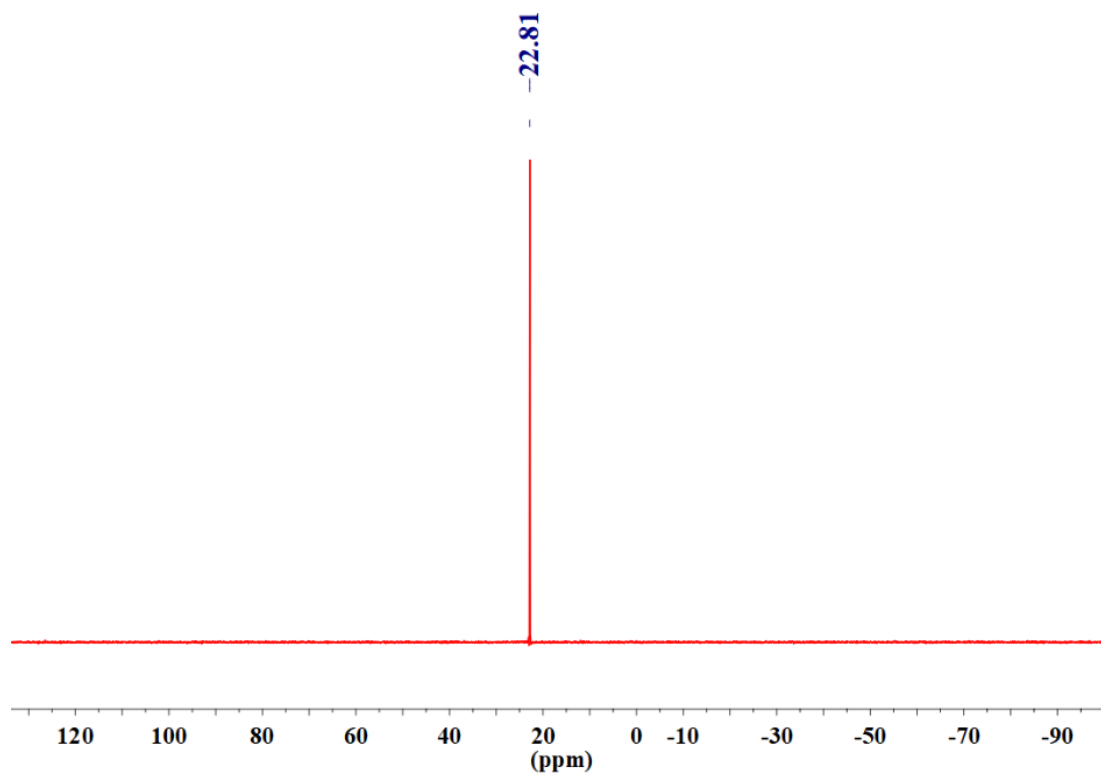


Figure A.2.3: ^{31}P NMR spectra of P-R4.

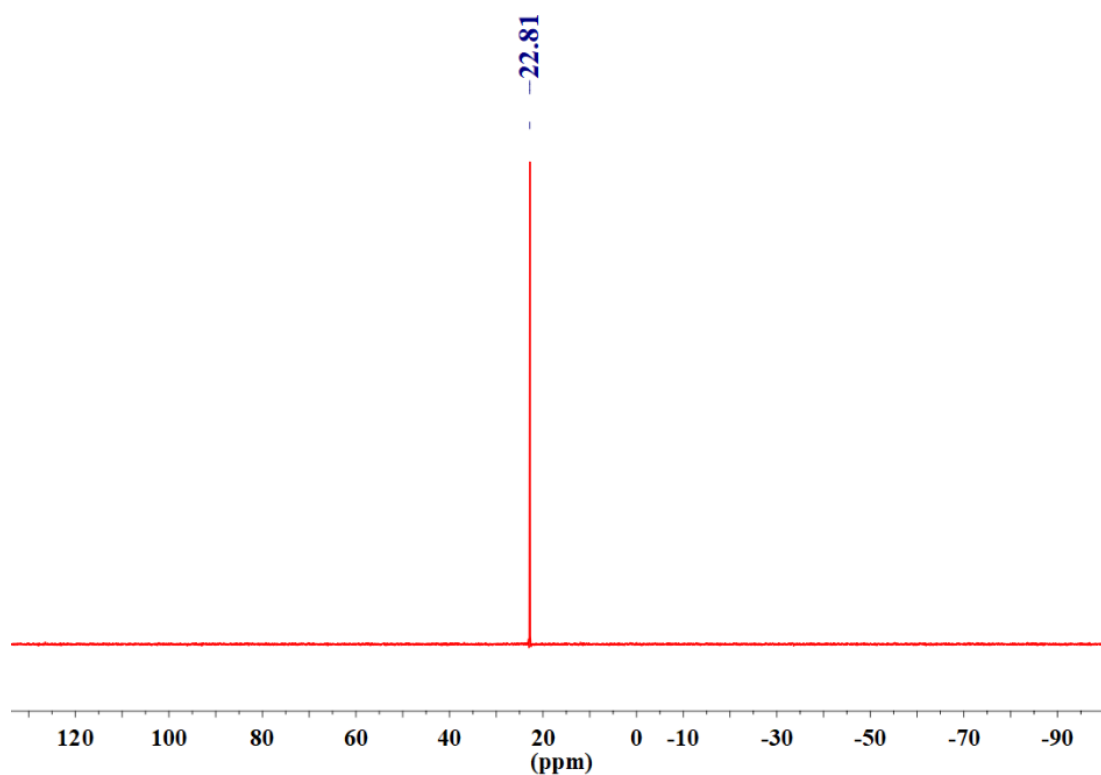
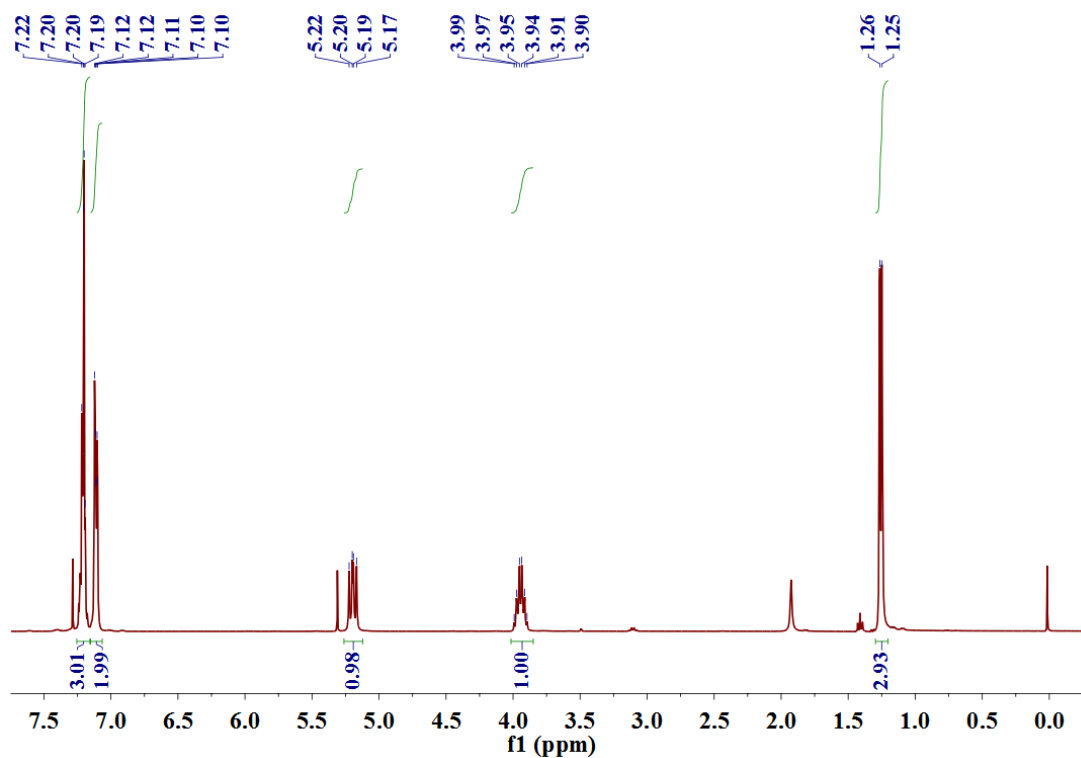
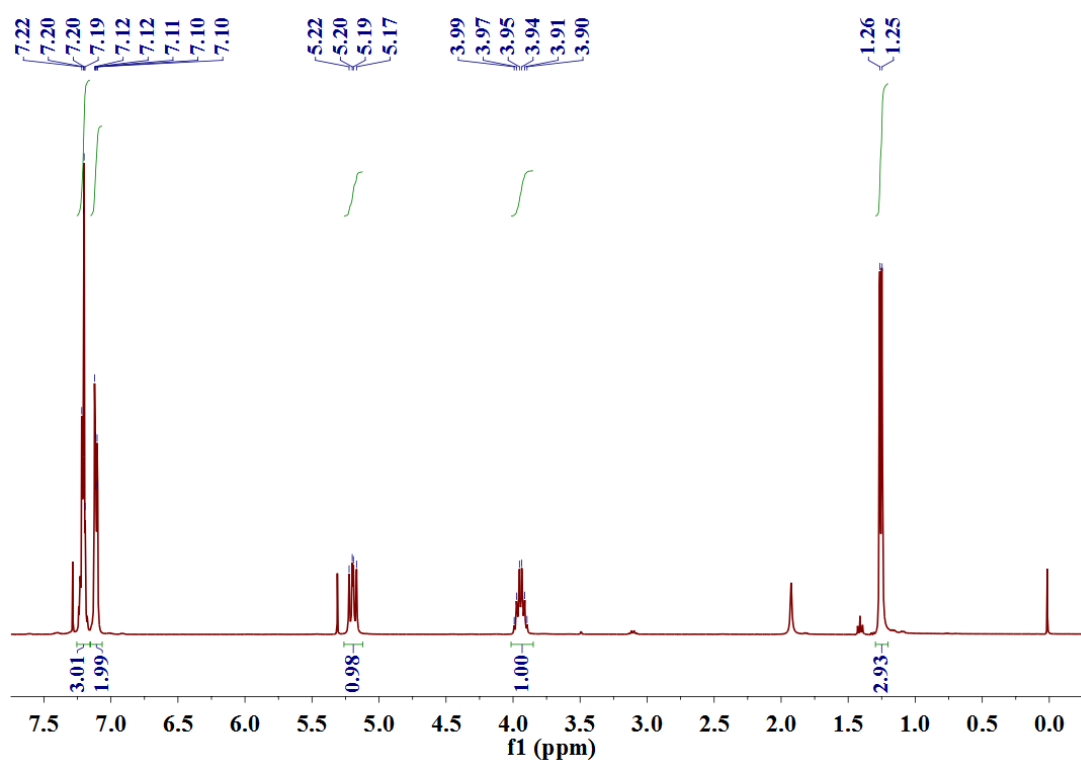
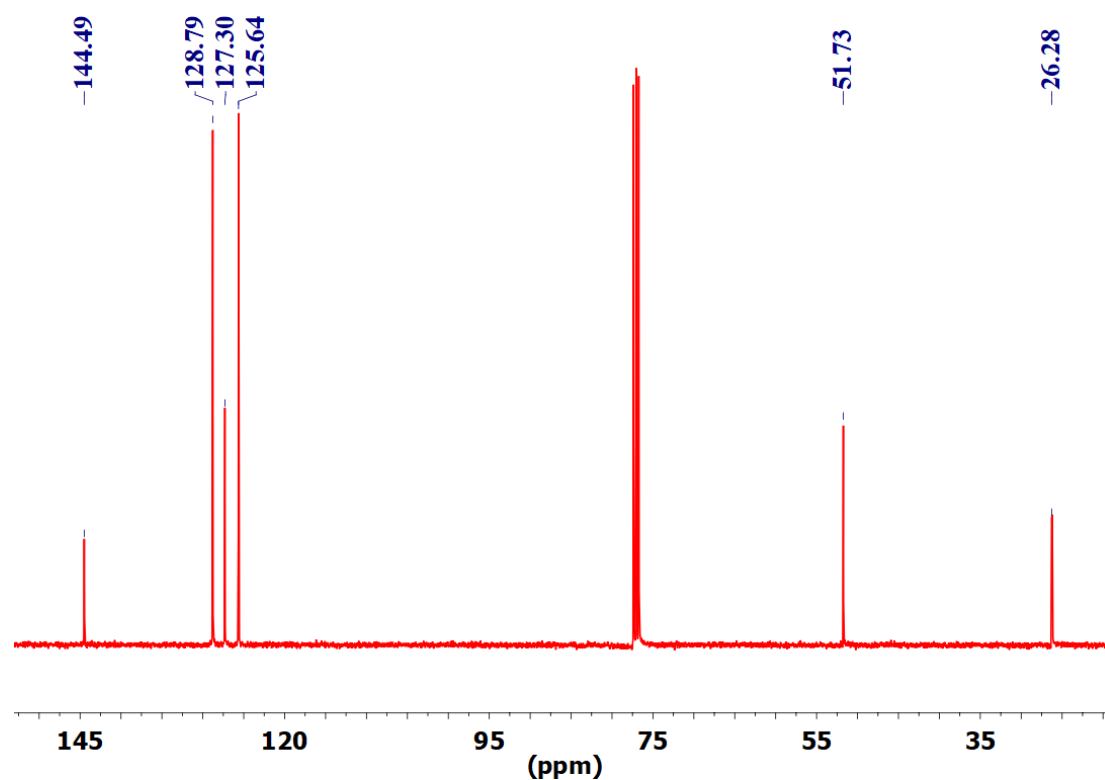
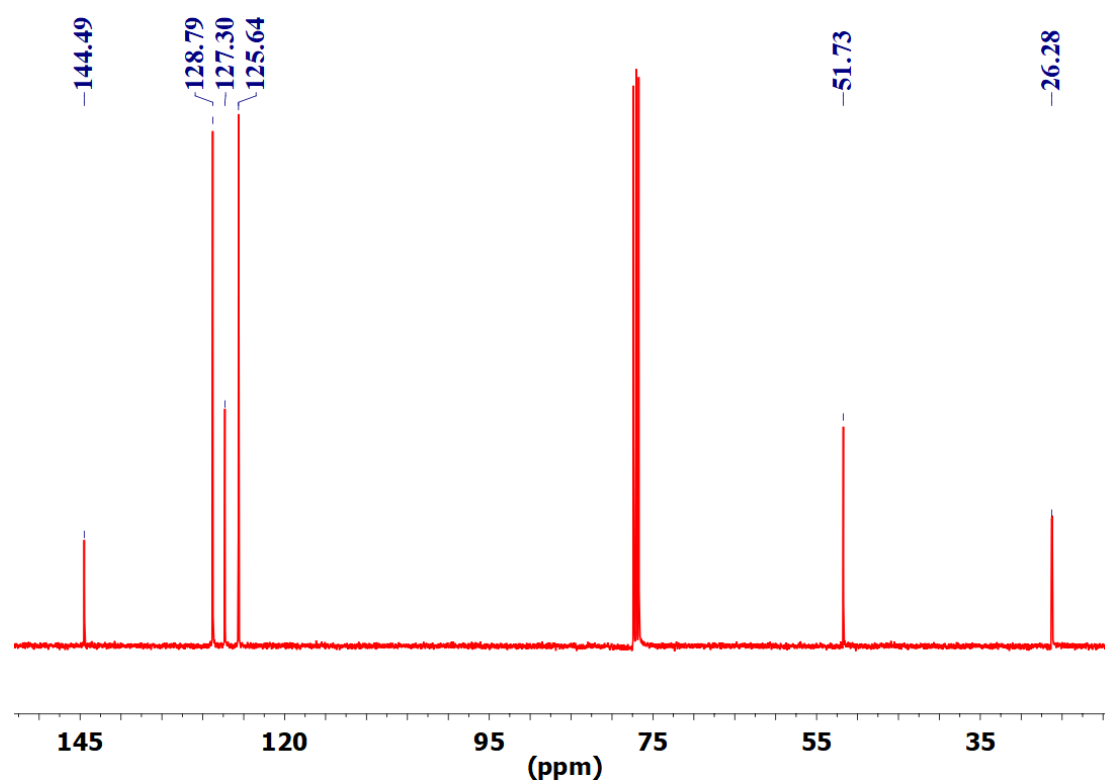


Figure A.2.4: ^{31}P NMR spectra of P-S4.

Figure A.2.5: ¹H NMR spectra of P-R₄.Figure A.2.6: ¹H NMR spectra of P-S₄.

Figure A.2.7: ^{31}C NMR spectra of P-R₄.Figure A.2.8: ^{31}C NMR spectra of P-S₄.

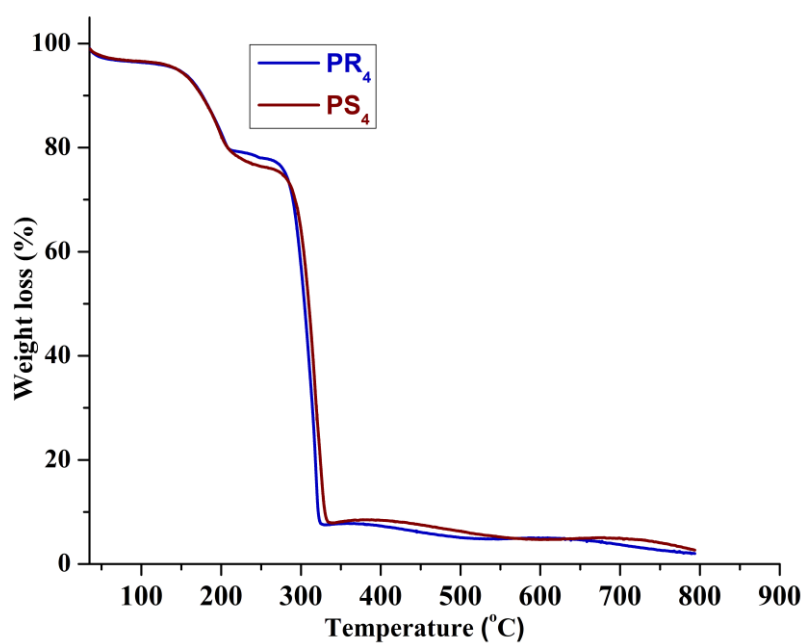


Figure A.2.9: TGA graph of P-R₄ and P-S₄.

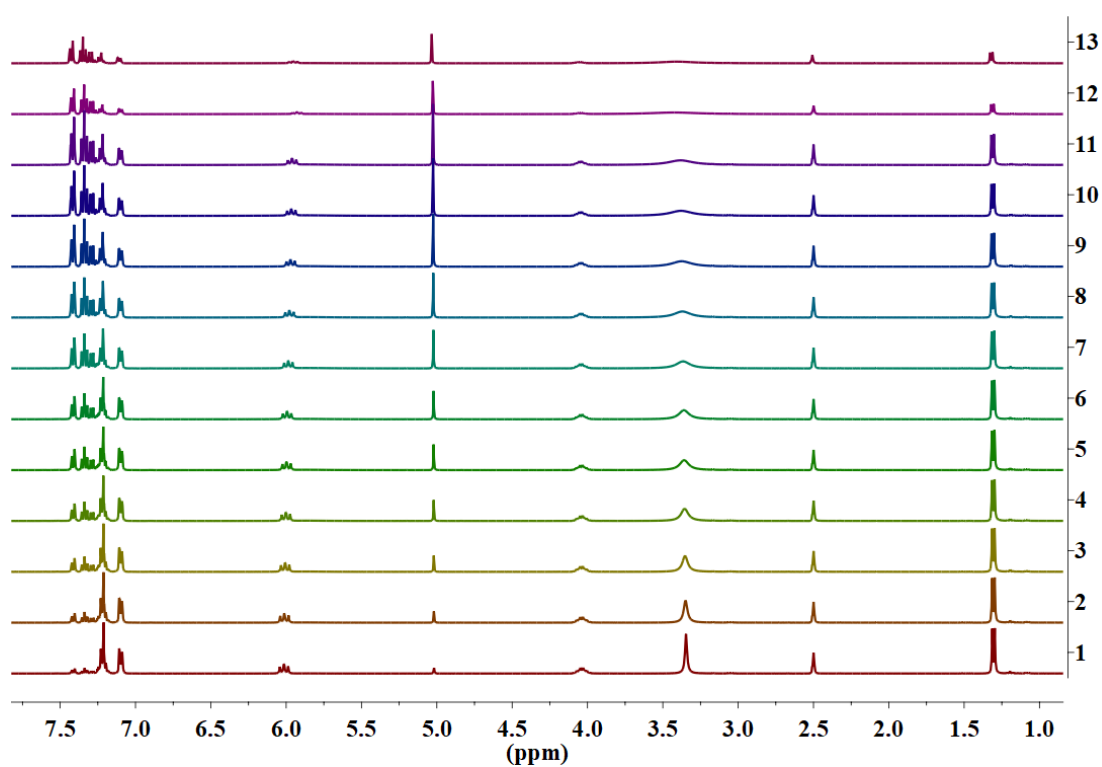


Figure A.2.10: Stacked ¹H NMR titration plot for P-R₄ with R-MA.

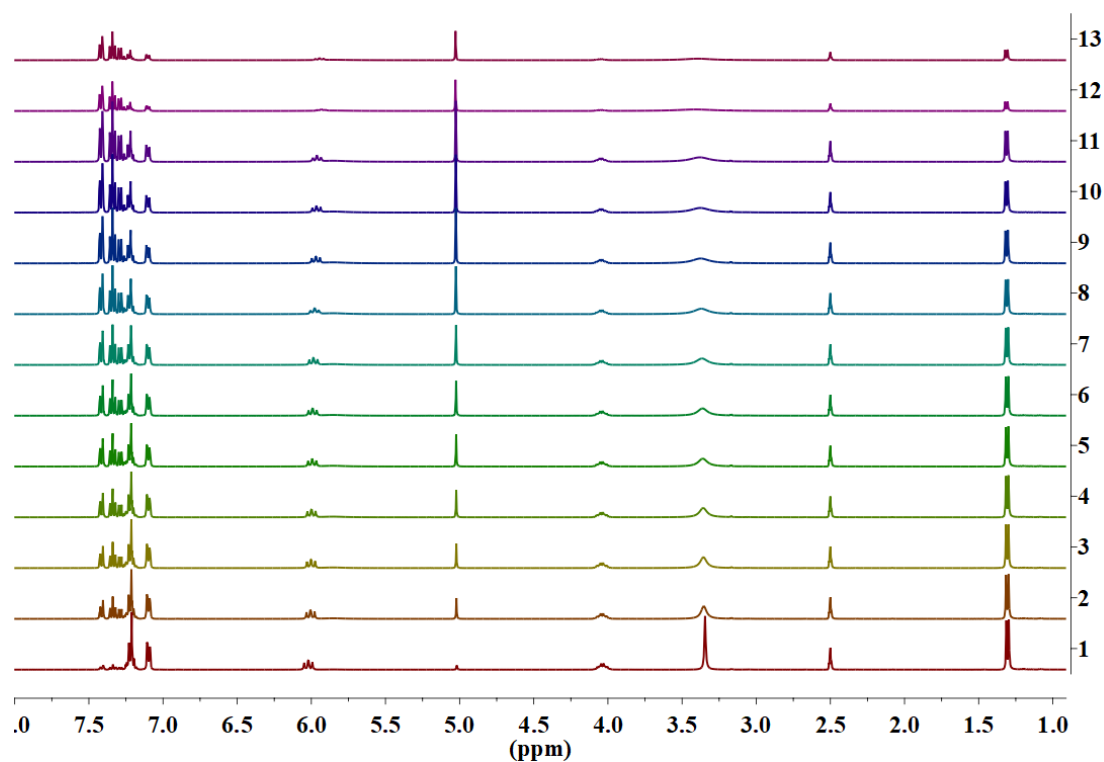


Figure A.2.11: Stacked ^1H NMR titration plot for P-S₄ with S-MA.

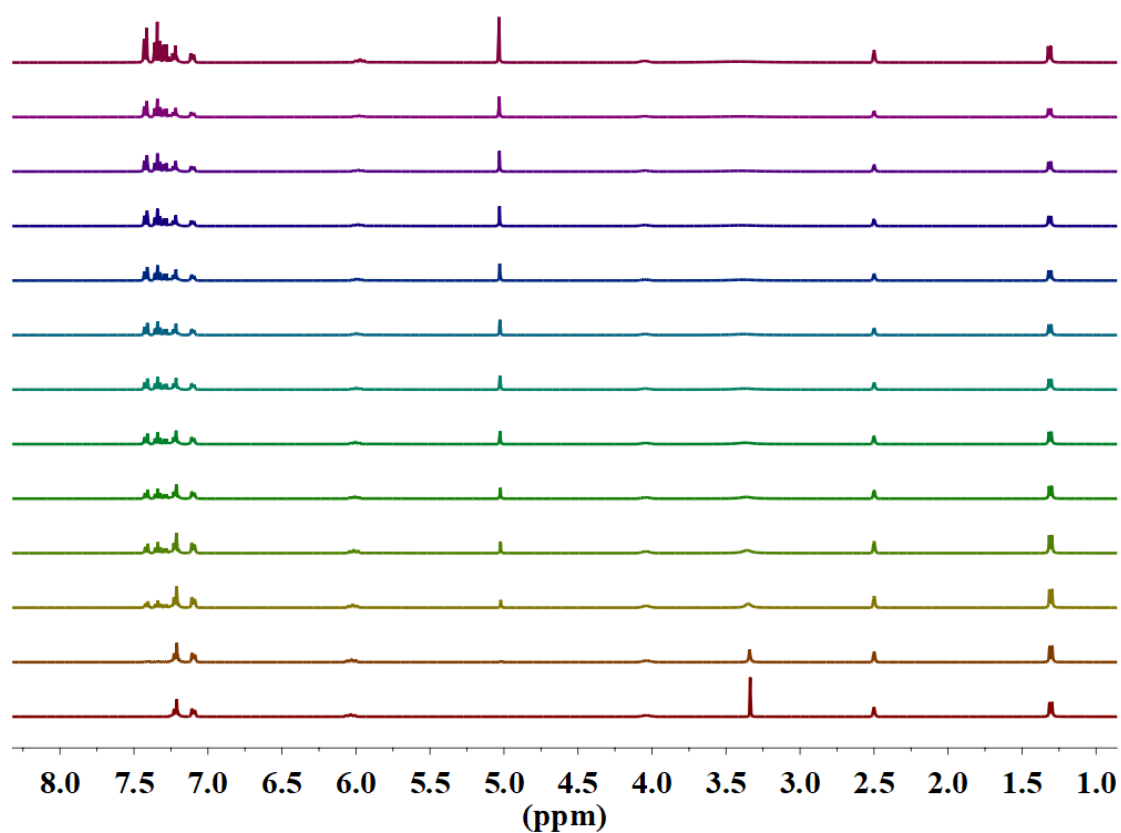


Figure A.2.12: Stacked ^1H NMR titration plot for P-S₄ with R-MA.

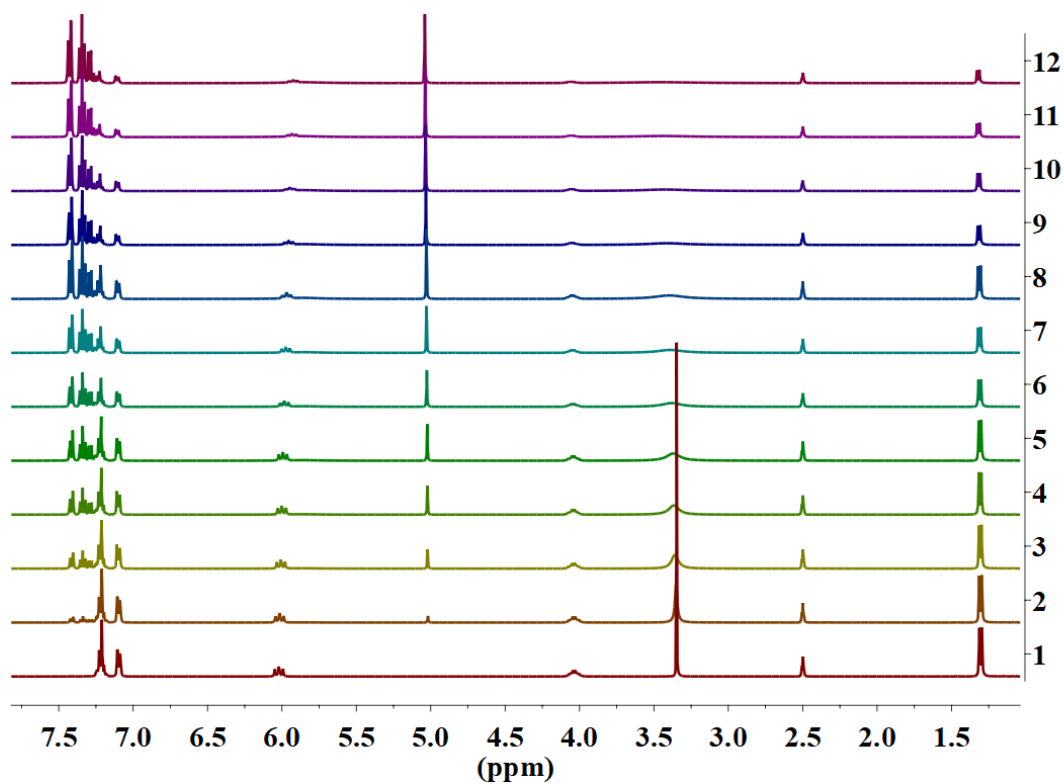


Figure A.2.13: Stacked ^1H NMR titration plot for P-S₄ with S-MA.

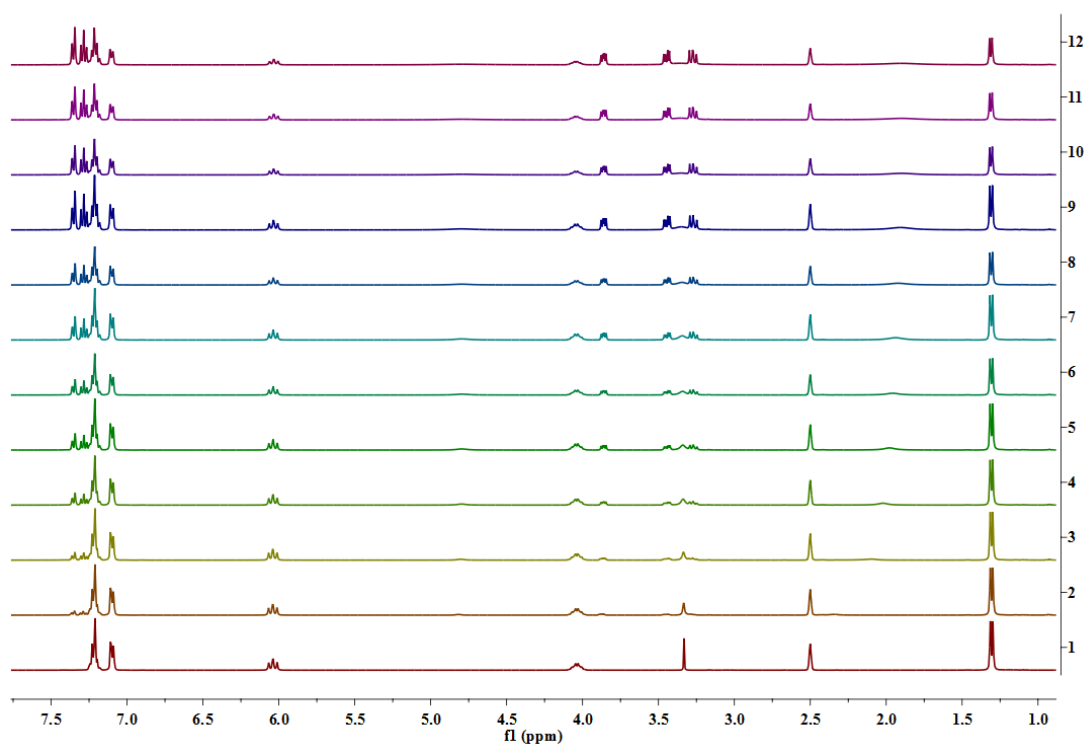


Figure A.2.14: Stacked ^1H NMR titration plot for P-R₄ with R-PG.

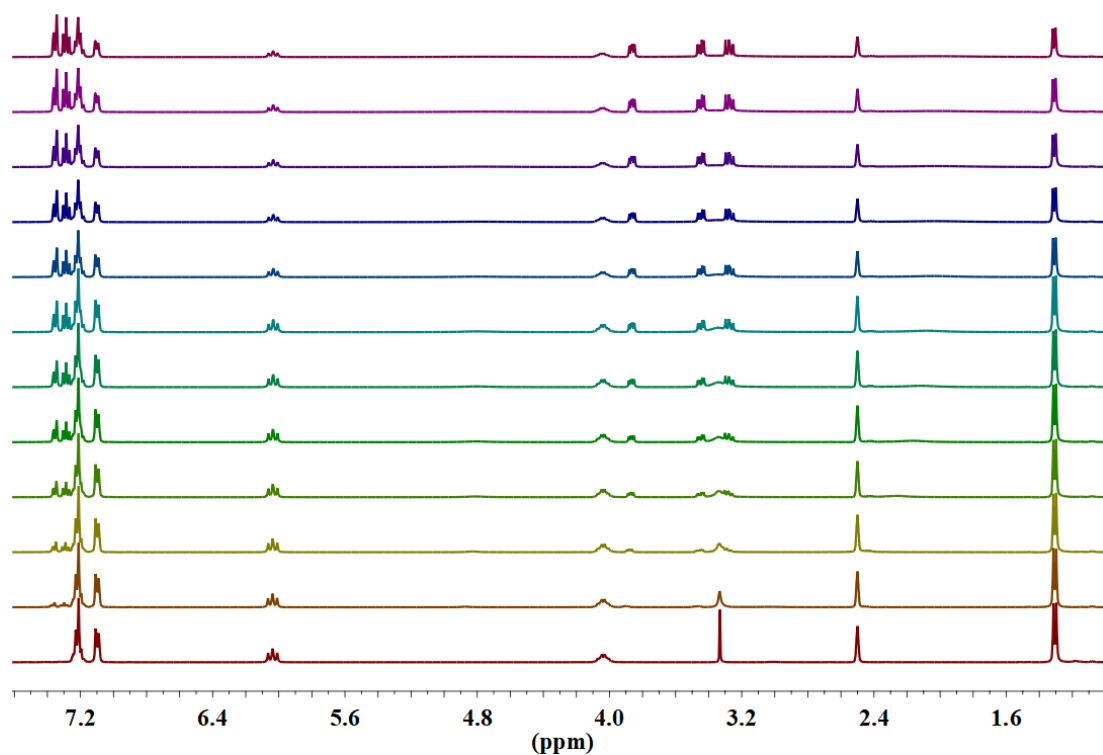


Figure A.2.15: Stacked ^1H NMR titration plot for P-S₄ with R-PG.

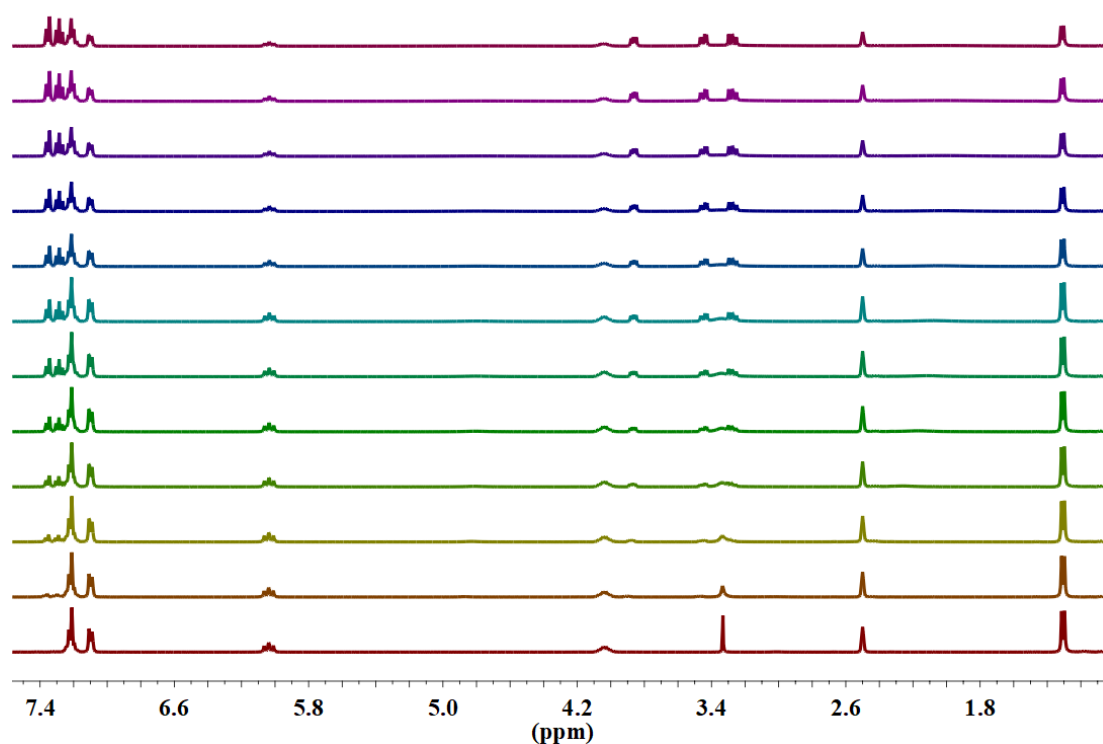


Figure A.2.16: Stacked ^1H NMR titration plot for P-S₄ with R-PG.

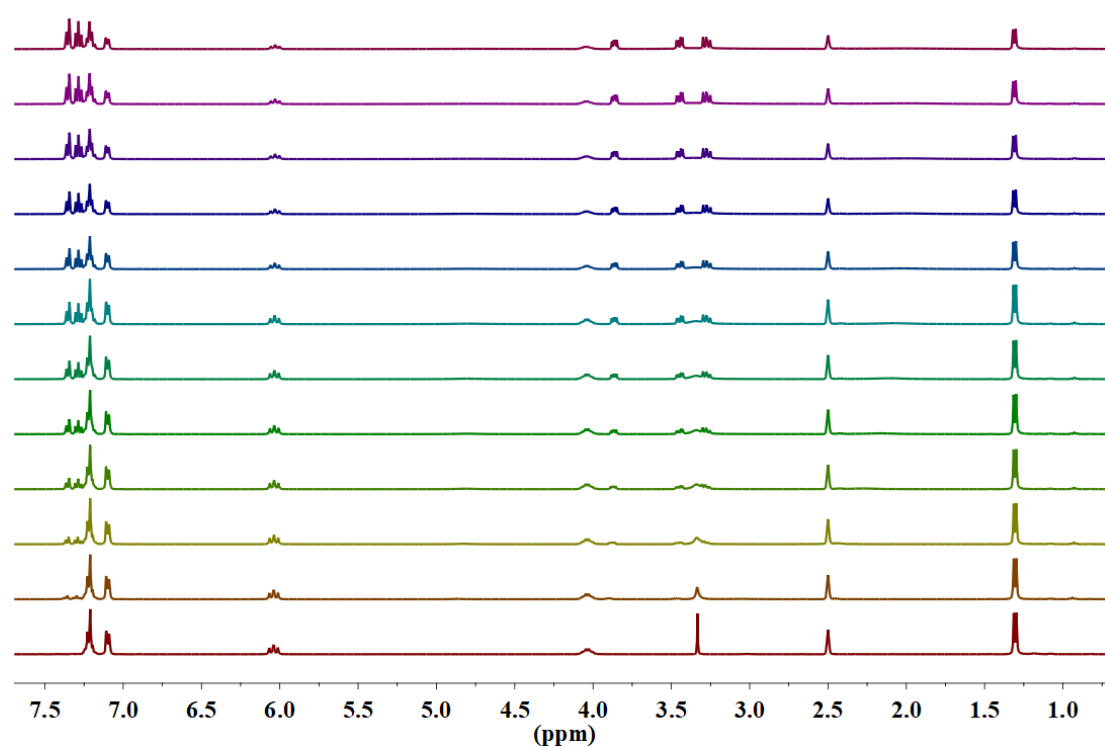


Figure A.2.17: Stacked ^1H NMR titration plot for P-S_4 with S-PG .

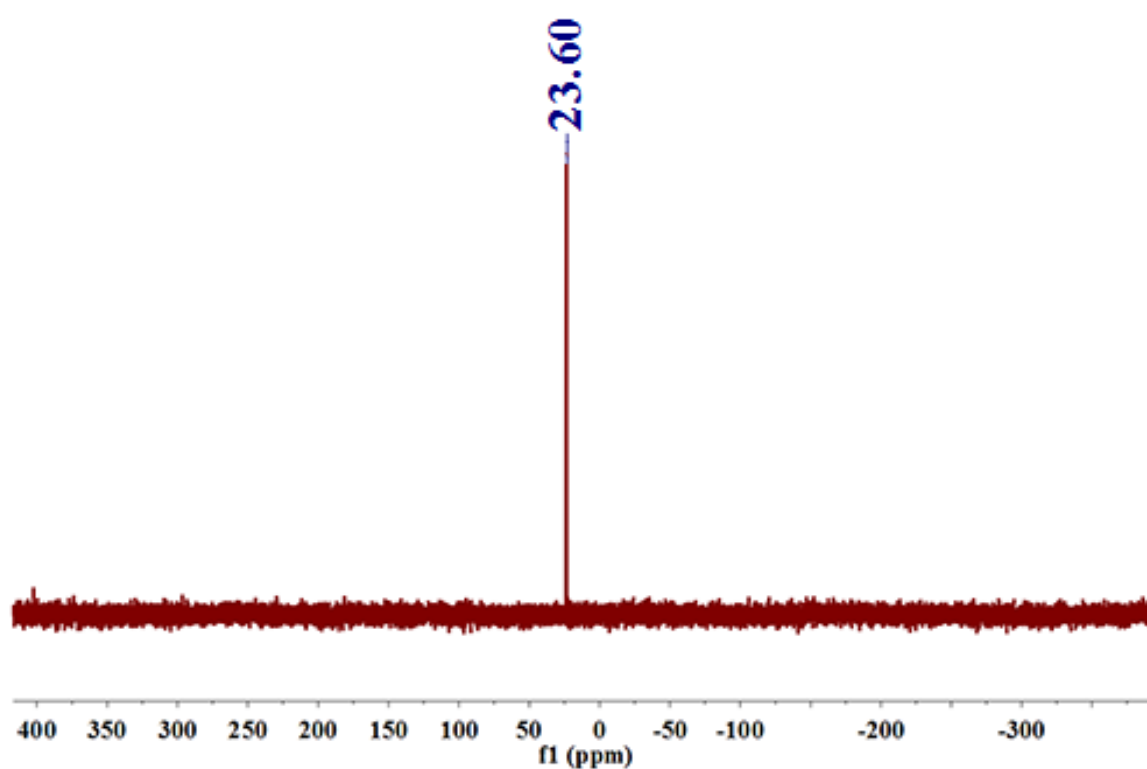


Figure A.2.18: ^{31}P NMR of phosphonium anilate PD-R .

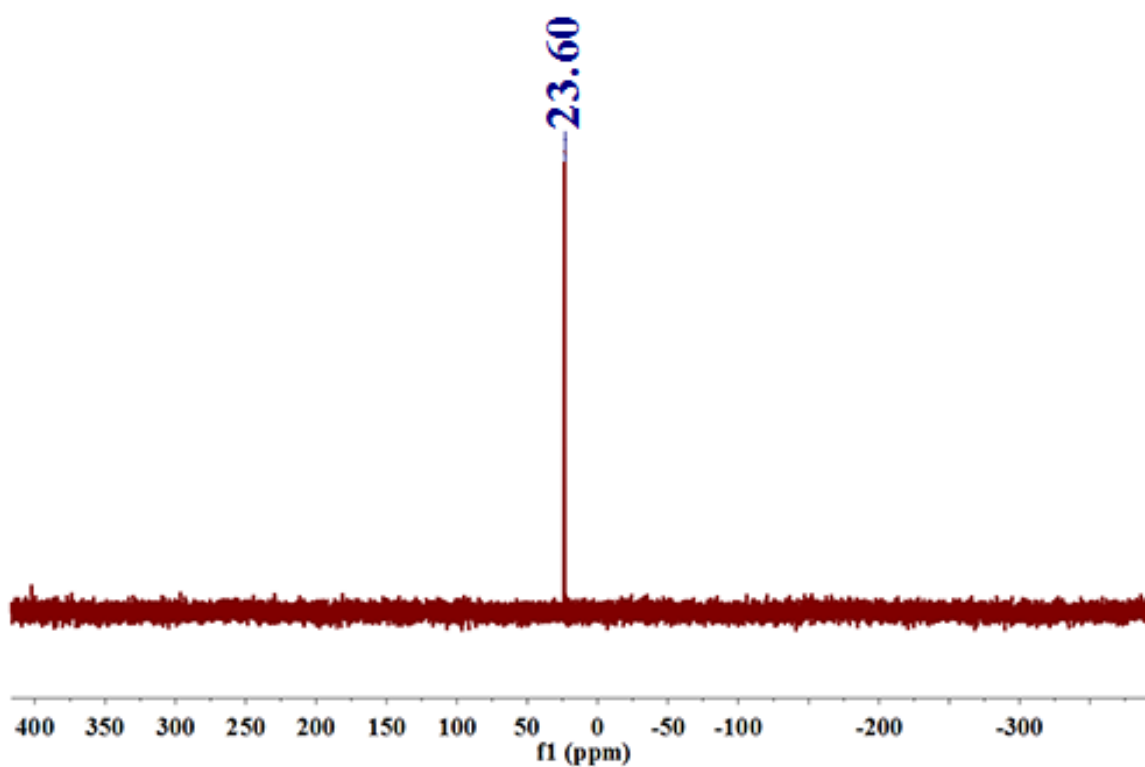


Figure A.2.19: ^{31}P NMR of phosphonium anilate PD-S.

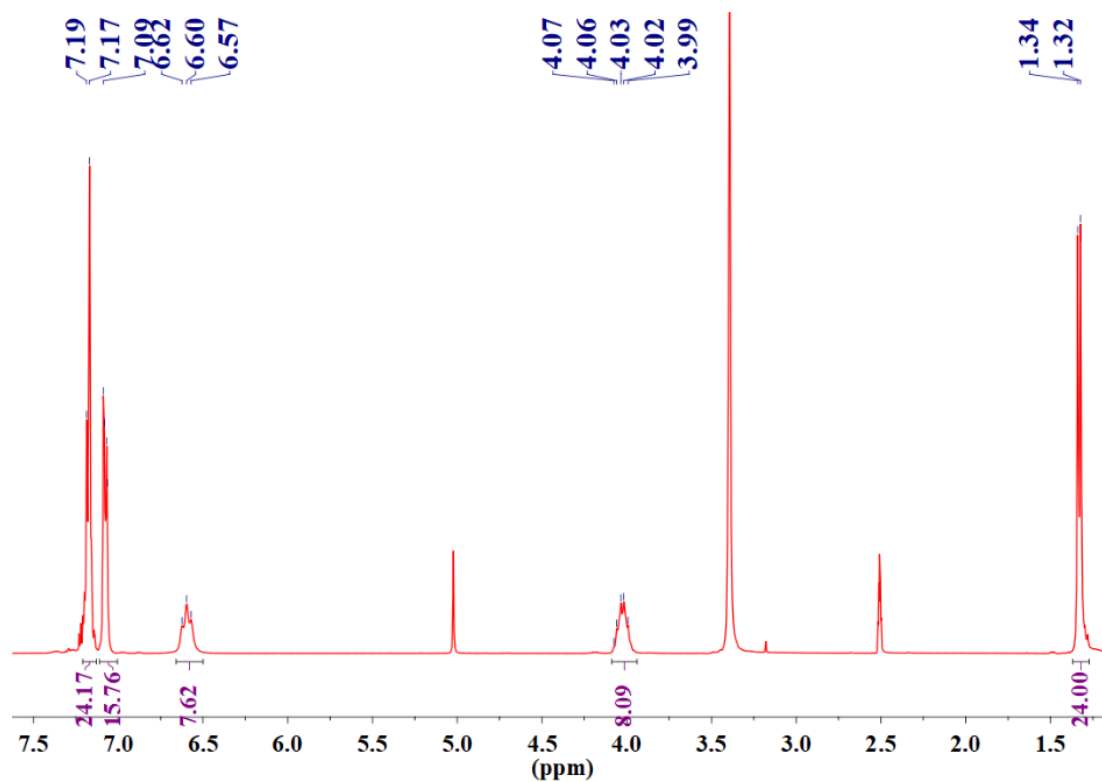


Figure A.2.20: ^1H NMR of phosphonium anilate PD-R.

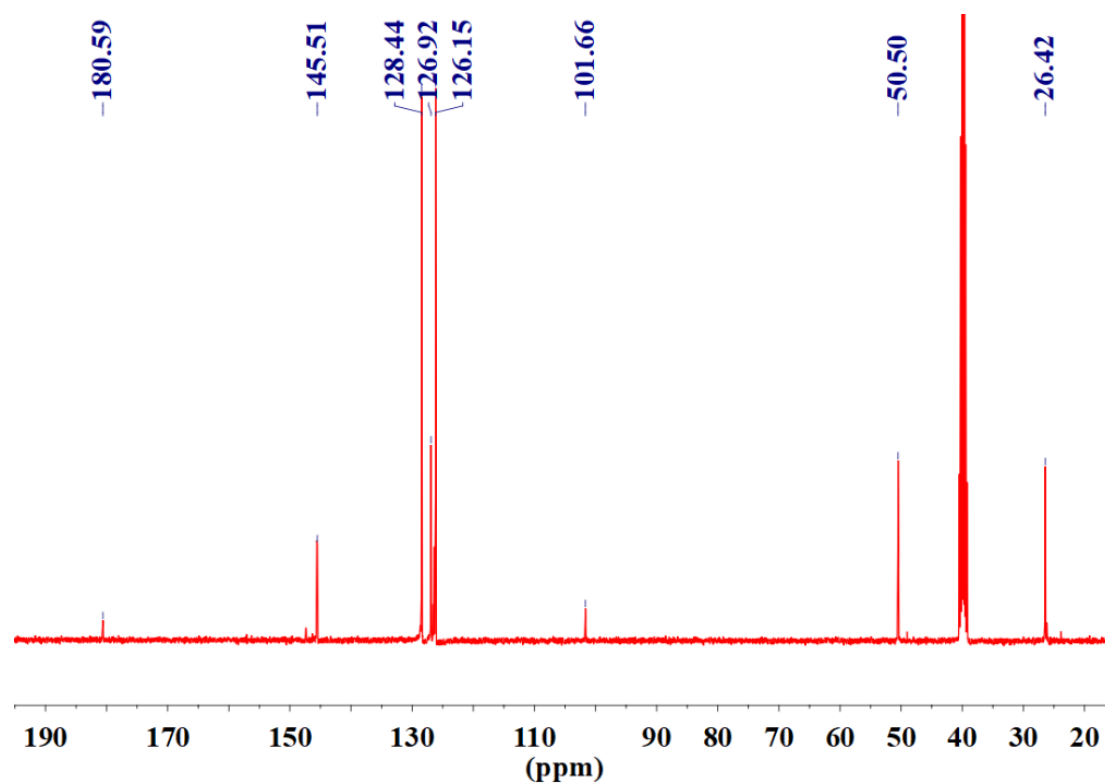


Figure A.2.21: ^{13}C NMR of phosphonium anilate PD-R.

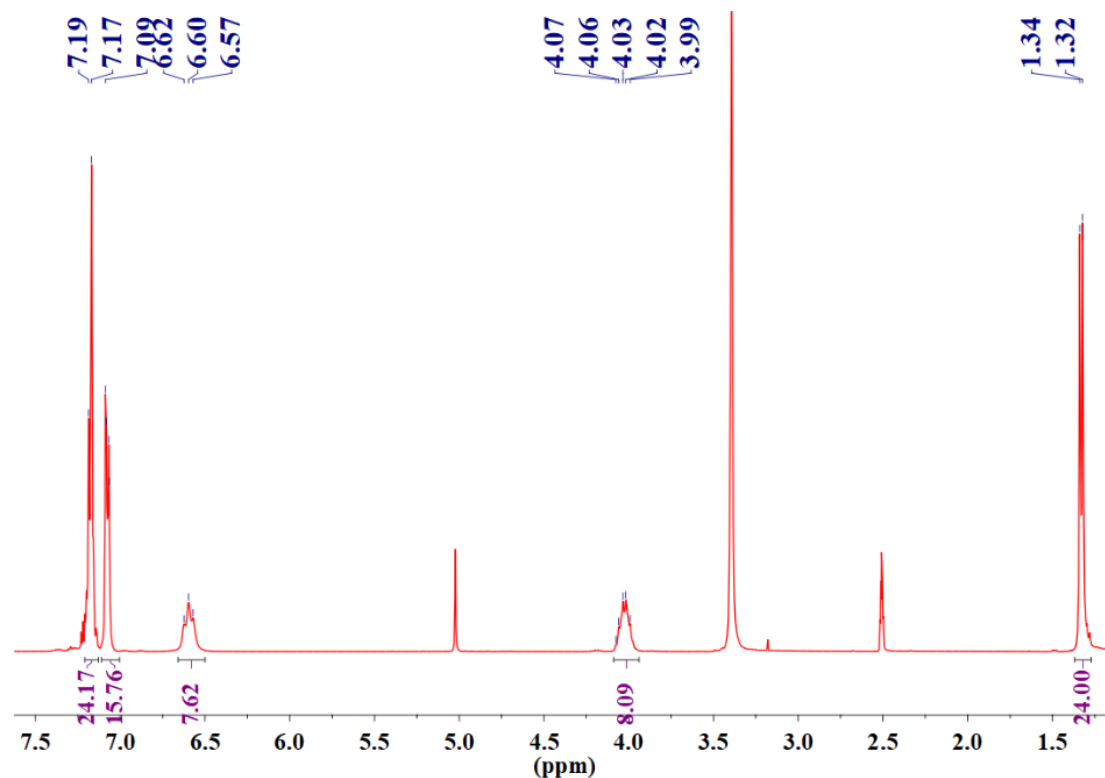


Figure A.2.22: ^1H NMR of phosphonium anilate PD-S.

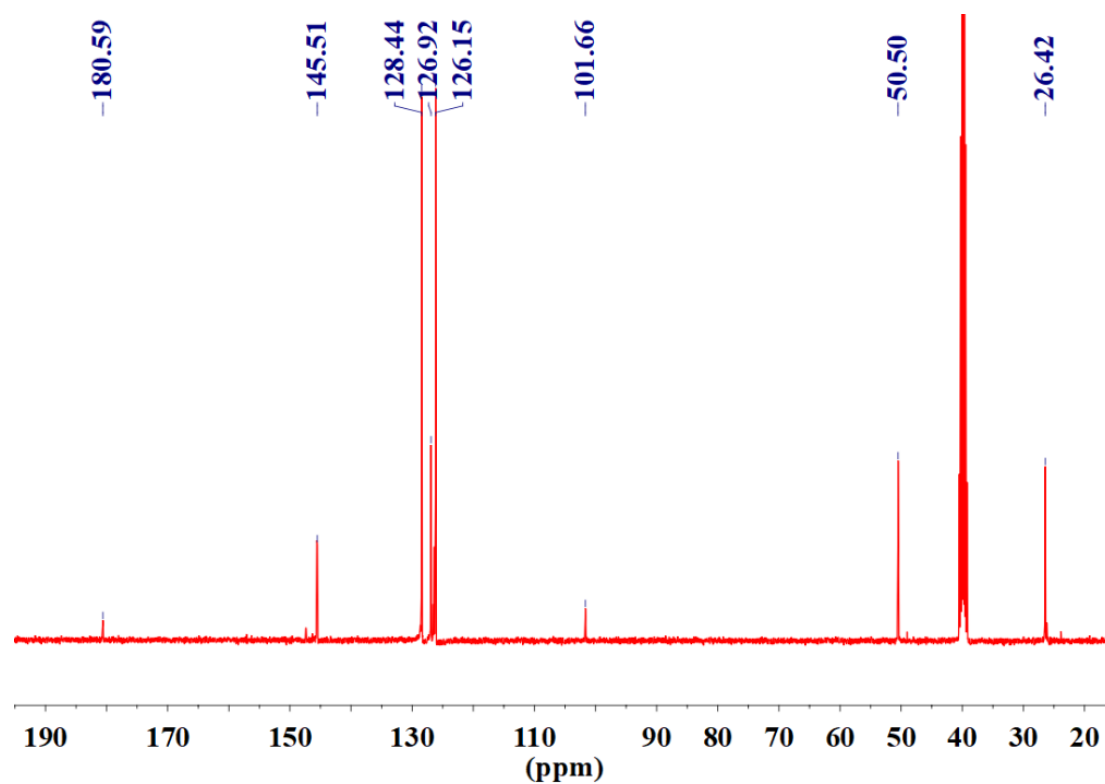


Figure A.2.23: ¹H NMR of phosphonium anilate PD-S.

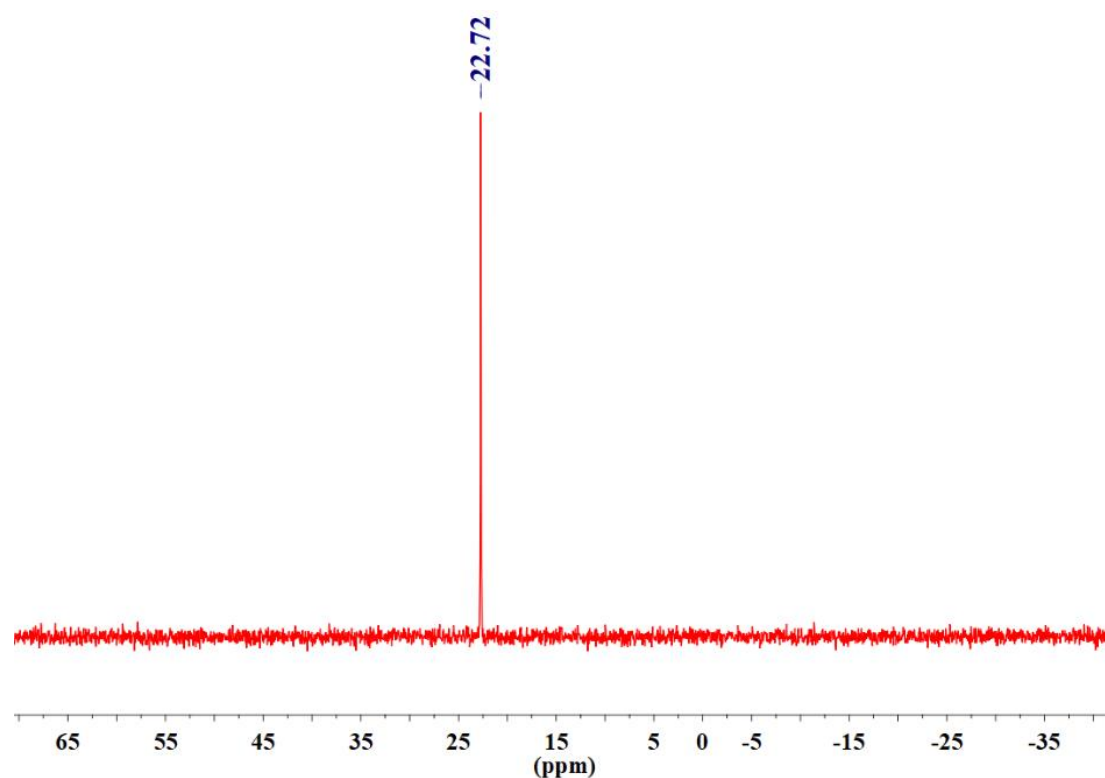


Figure A.2.24: ¹⁹F NMR of phosphonium fluoranilate PF-R.

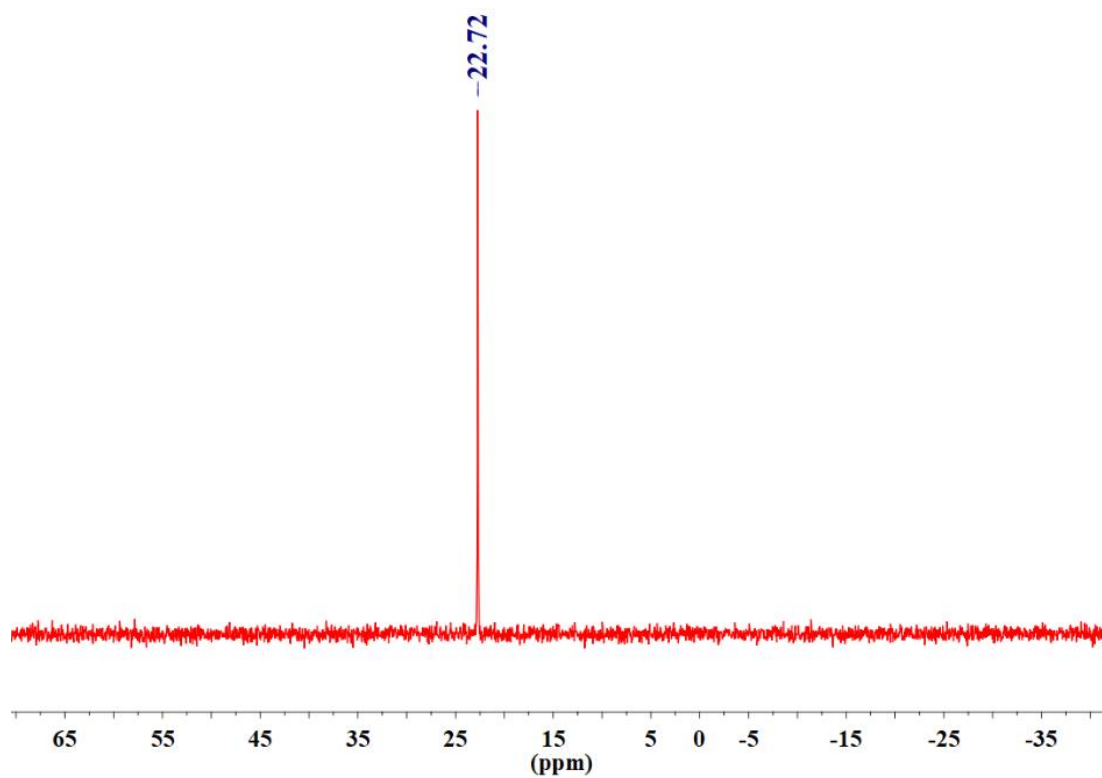


Figure A.2.25: ^{19}F NMR of phosphonium fluoranilate PF-S.

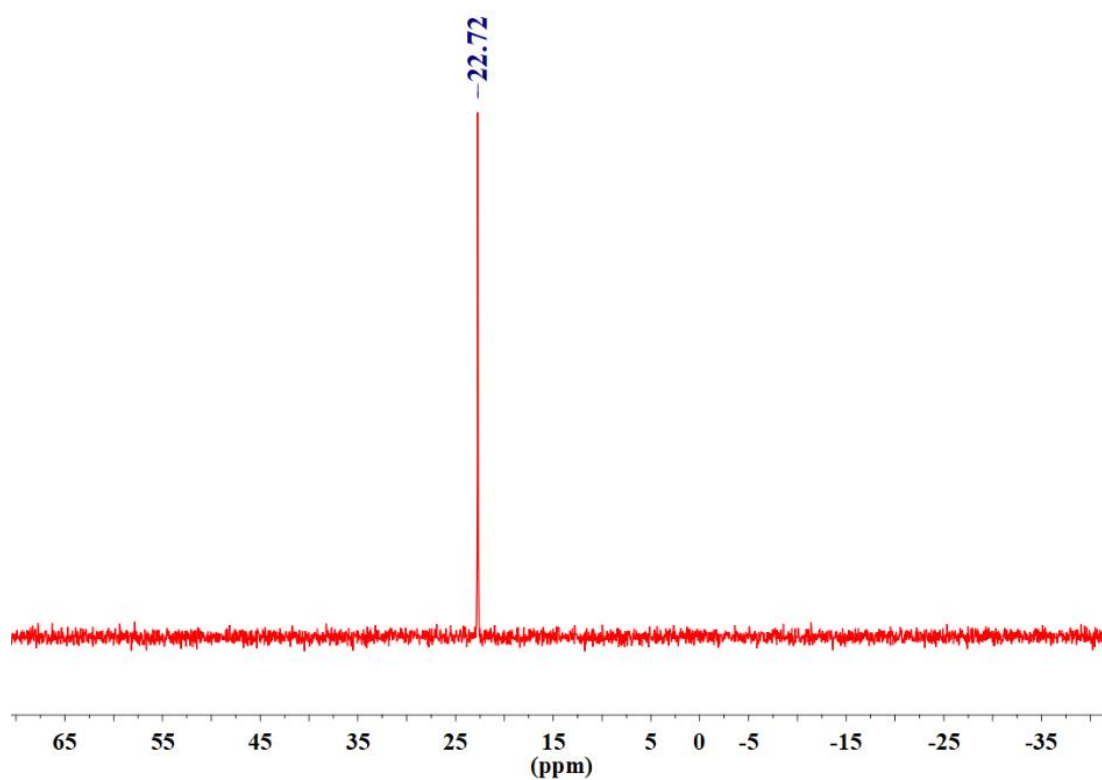


Figure A.2.26: ^{31}P NMR of phosphonium fluoranilate PF-R.

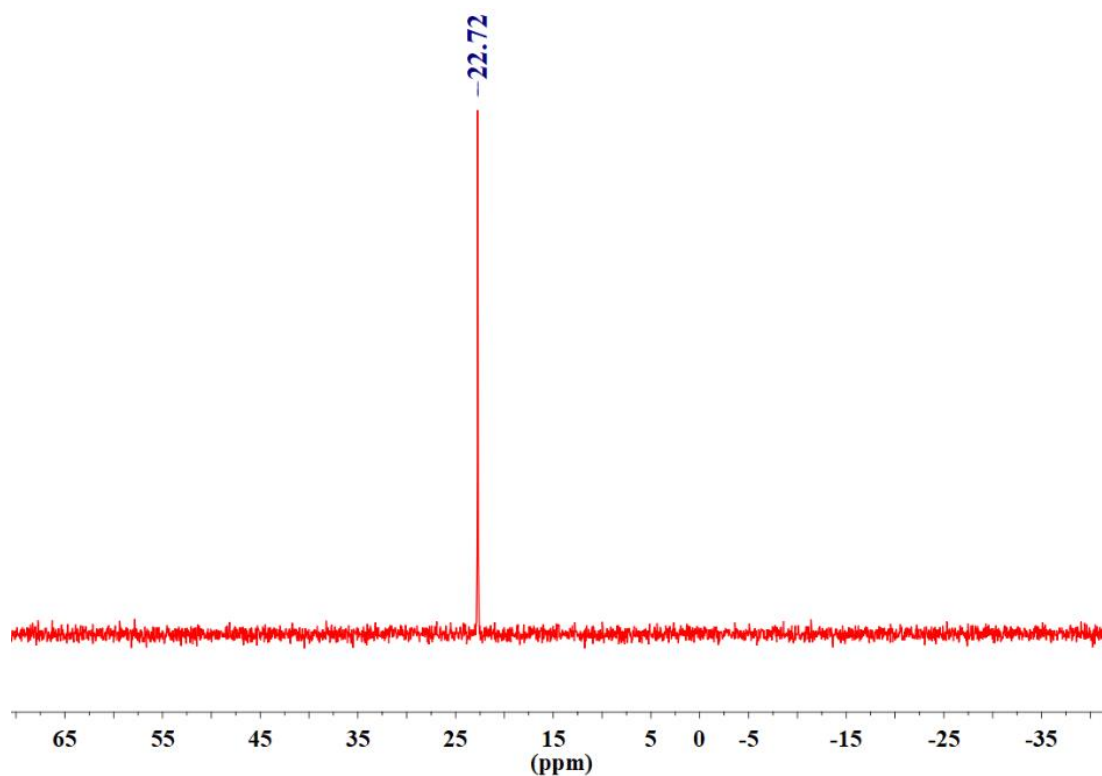


Figure A.2.27: ^{31}P NMR of phosphonium fluoranilate PF-S.

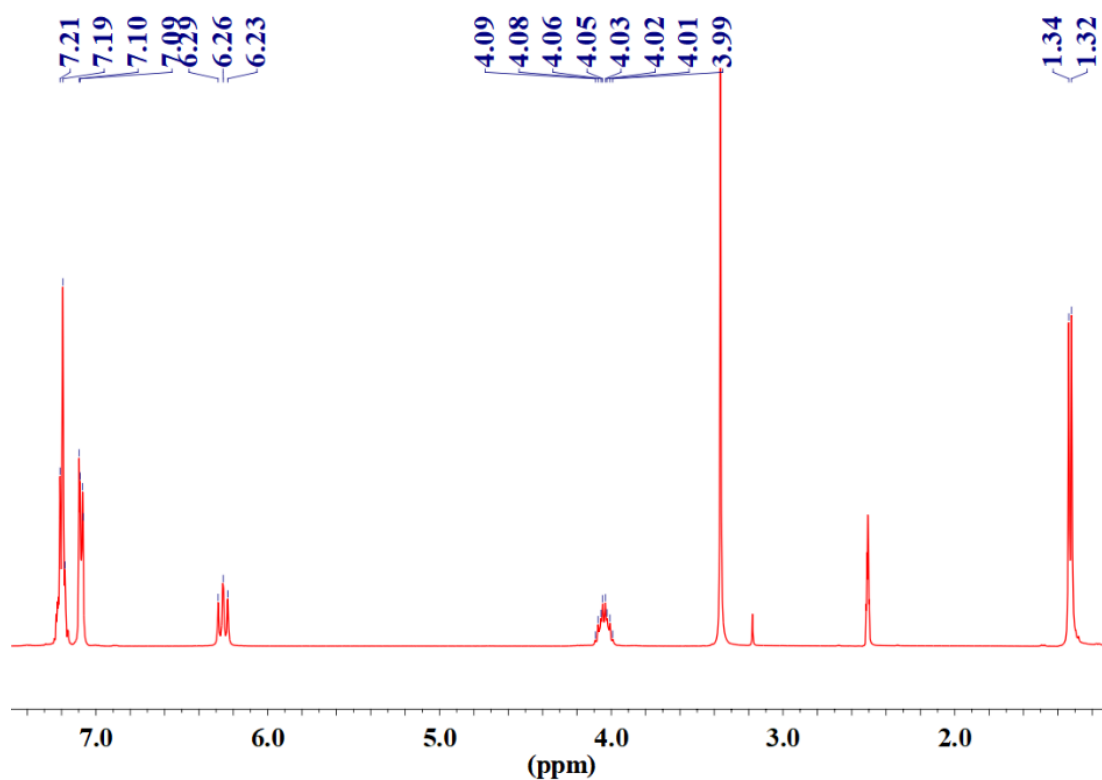


Figure A.2.28: ^1H NMR of phosphonium fluoranilate PF-R.

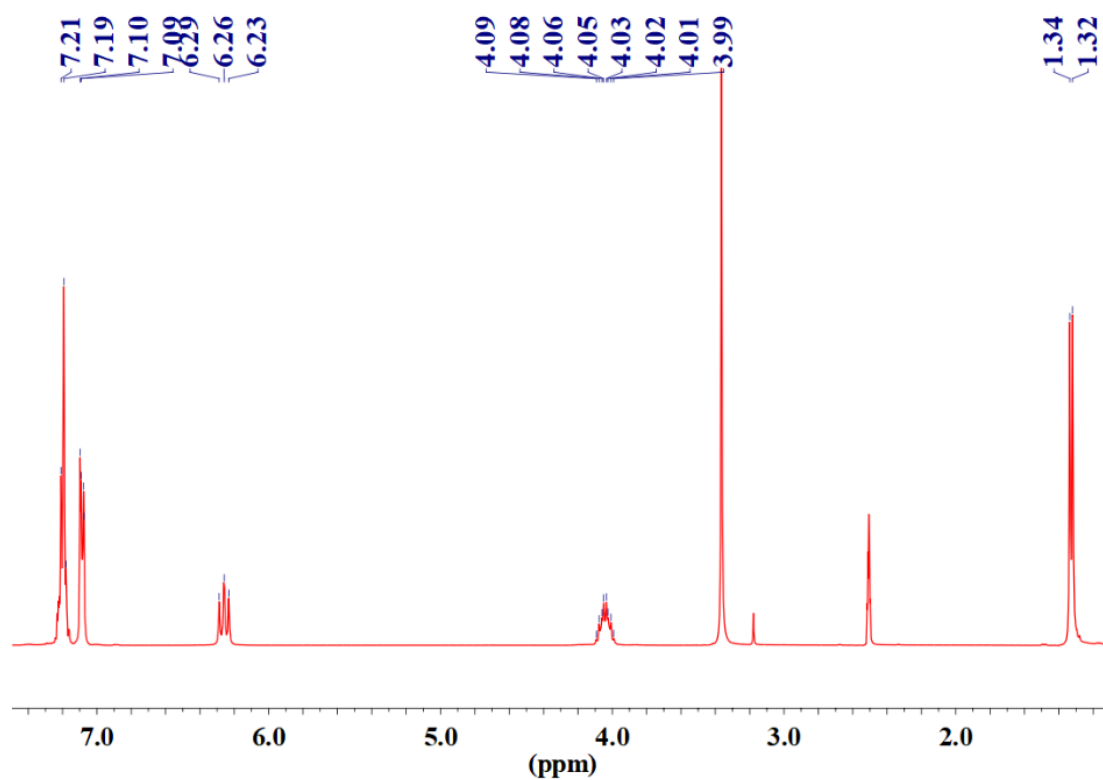


Figure A.2.29: ¹H NMR of phosphonium fluoranilate PF-S.

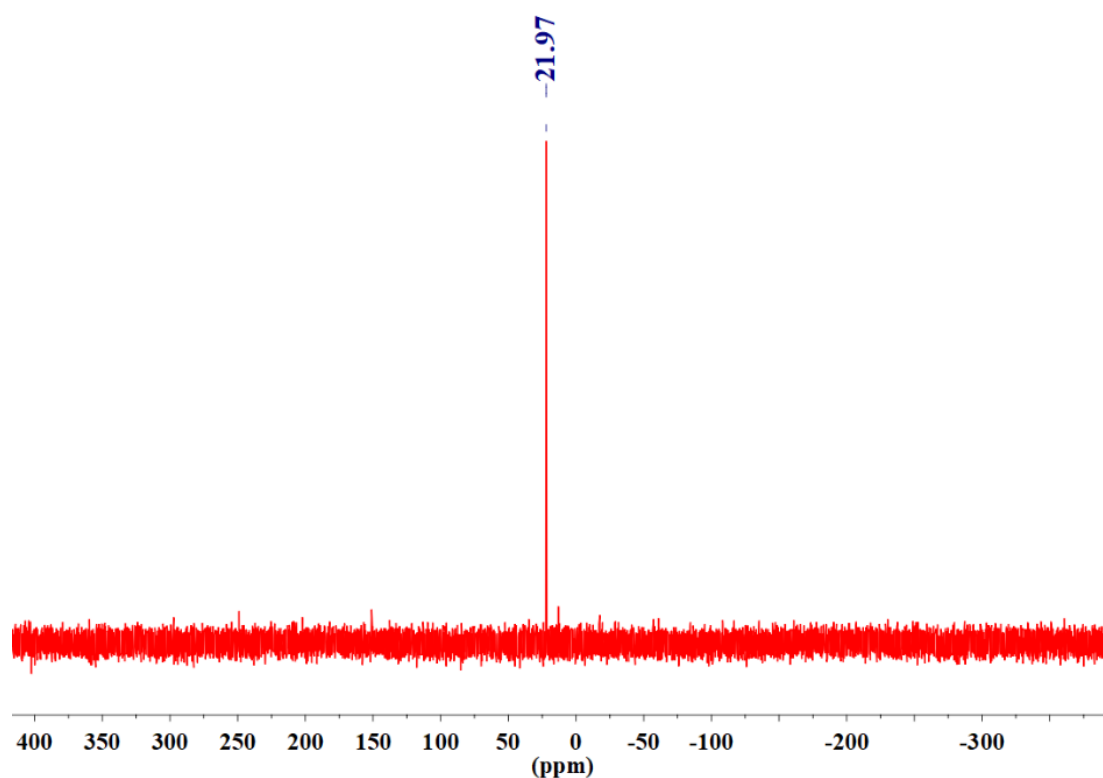


Figure A.2.30: ³¹P NMR of phosphonium chloranilate PC-R.

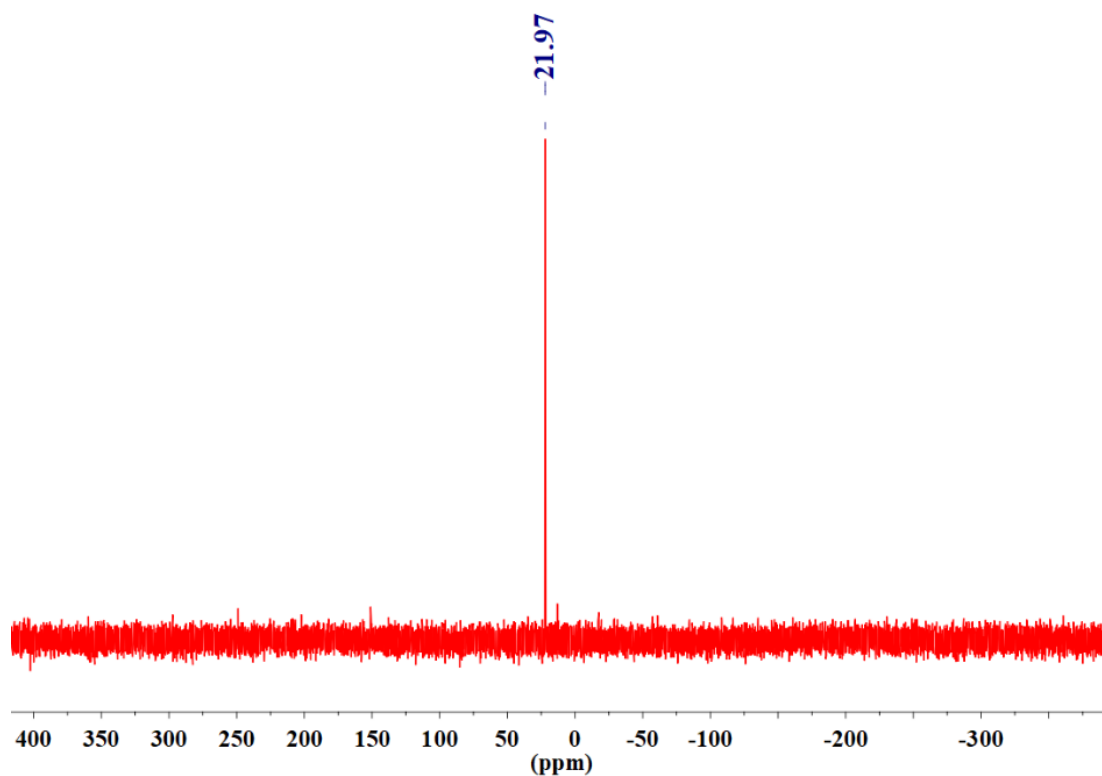


Figure A.2.31: ^{31}P NMR of phosphonium chloranilate PC-S.

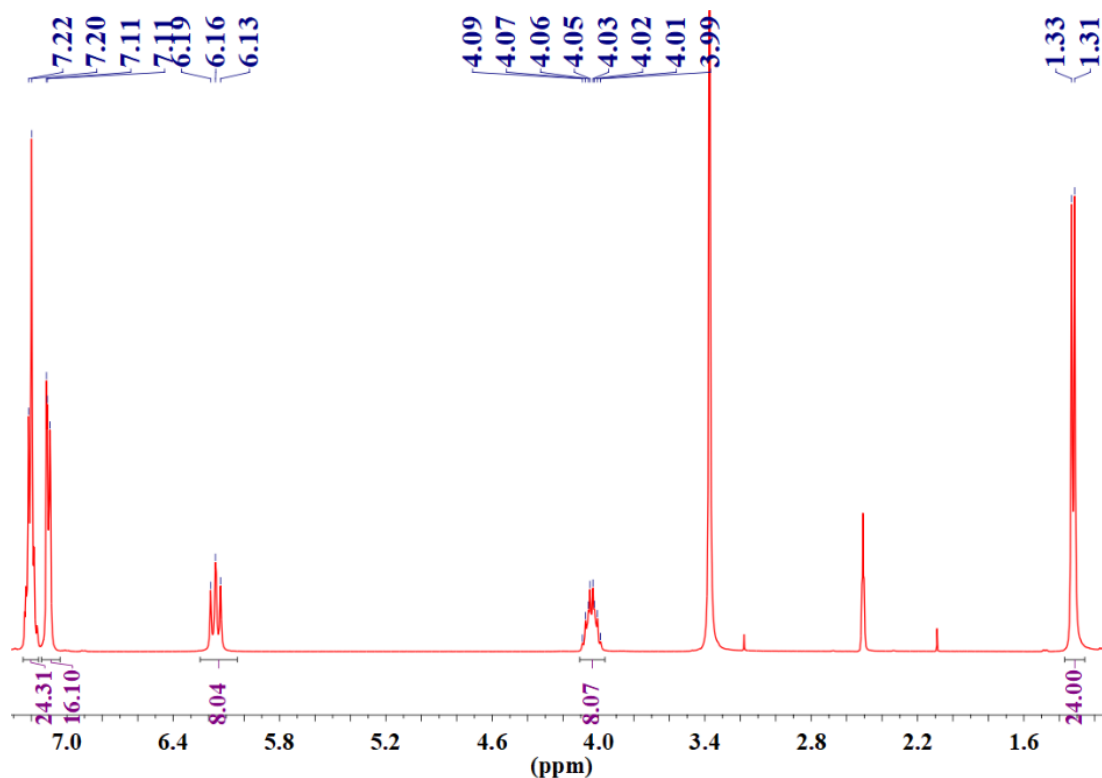


Figure A.2.32: ^1H NMR of phosphonium chloranilate PC-R.

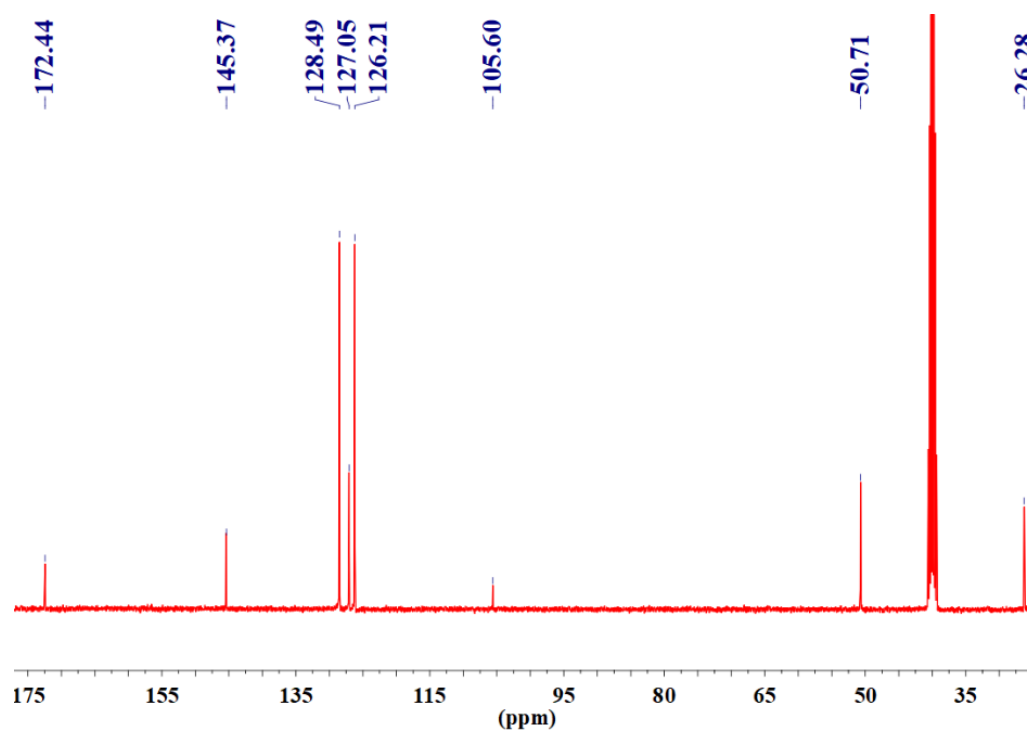


Figure A.2.33: ^{31}C NMR of phosphonium chloranilate PC-R.

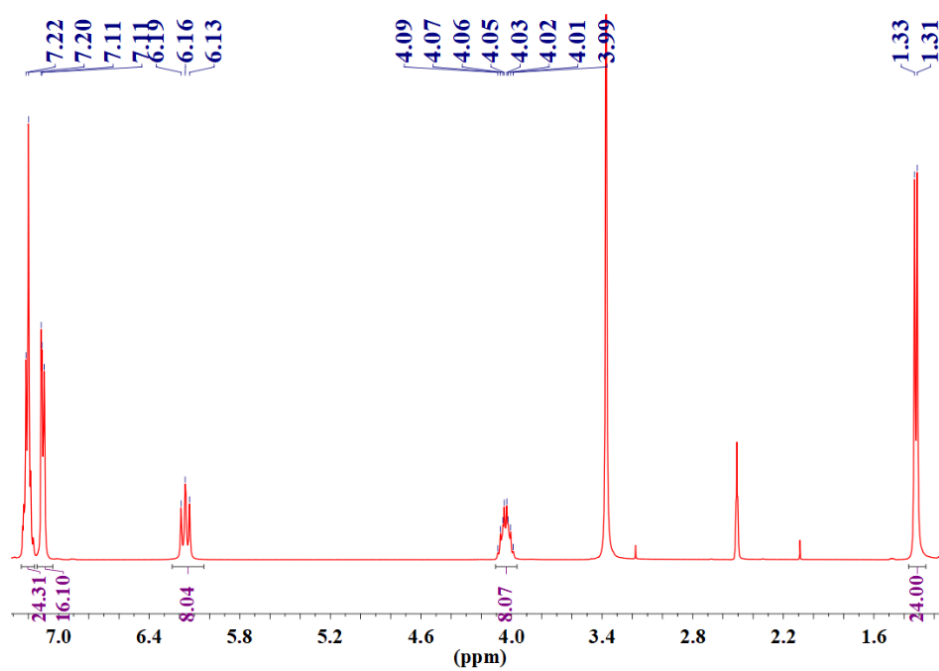


Figure A.2.34: ^1H NMR of phosphonium chloranilate PC-S.

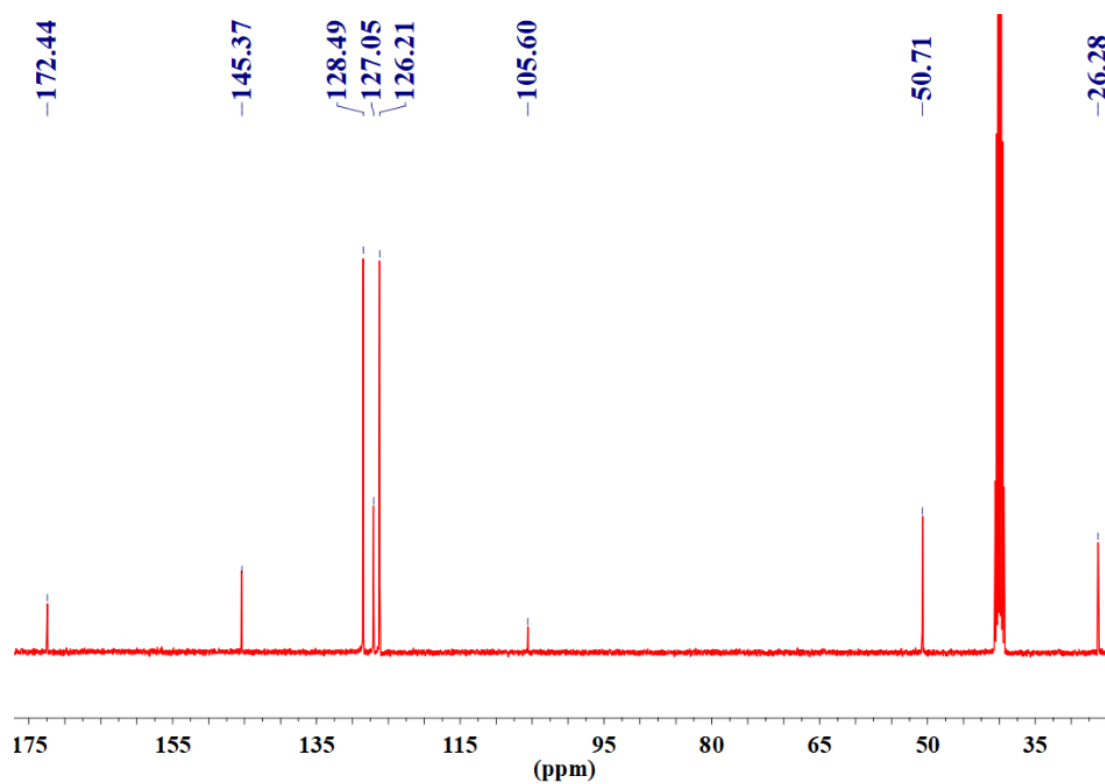


Figure A.2.35: ^{31}C NMR of phosphonium chloranilate PC-S.

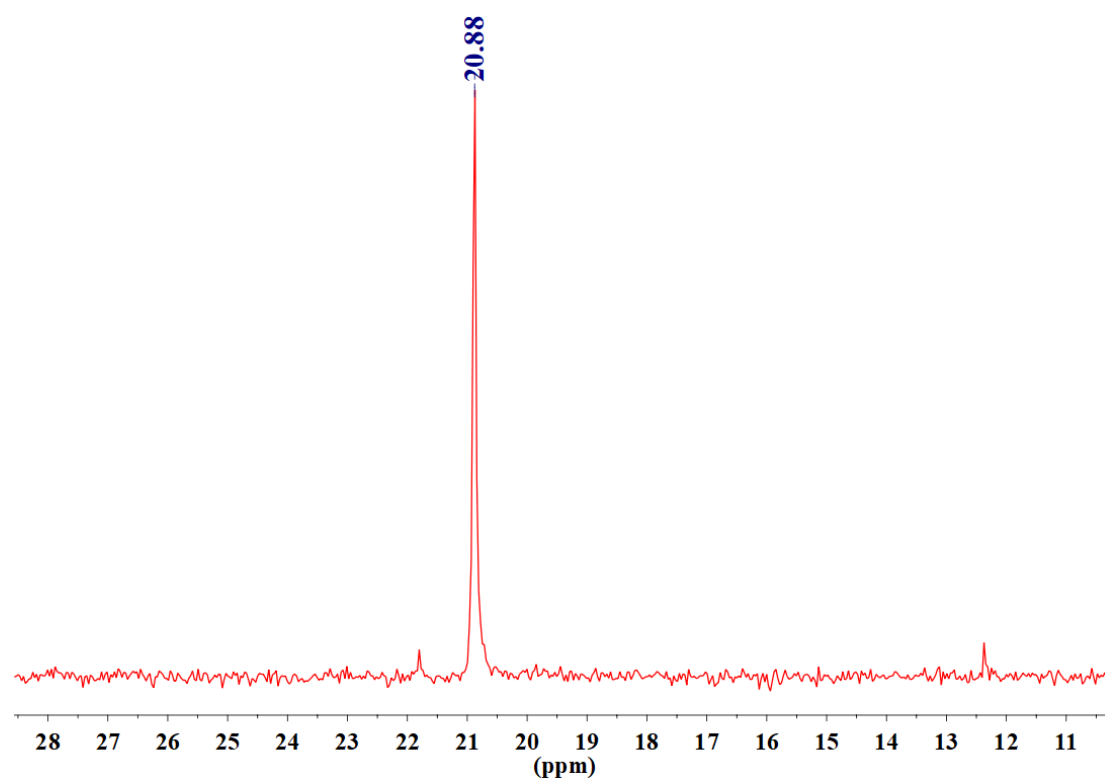


Figure A.2.36: ^{31}P NMR of phosphonium bromanilate PB-R.

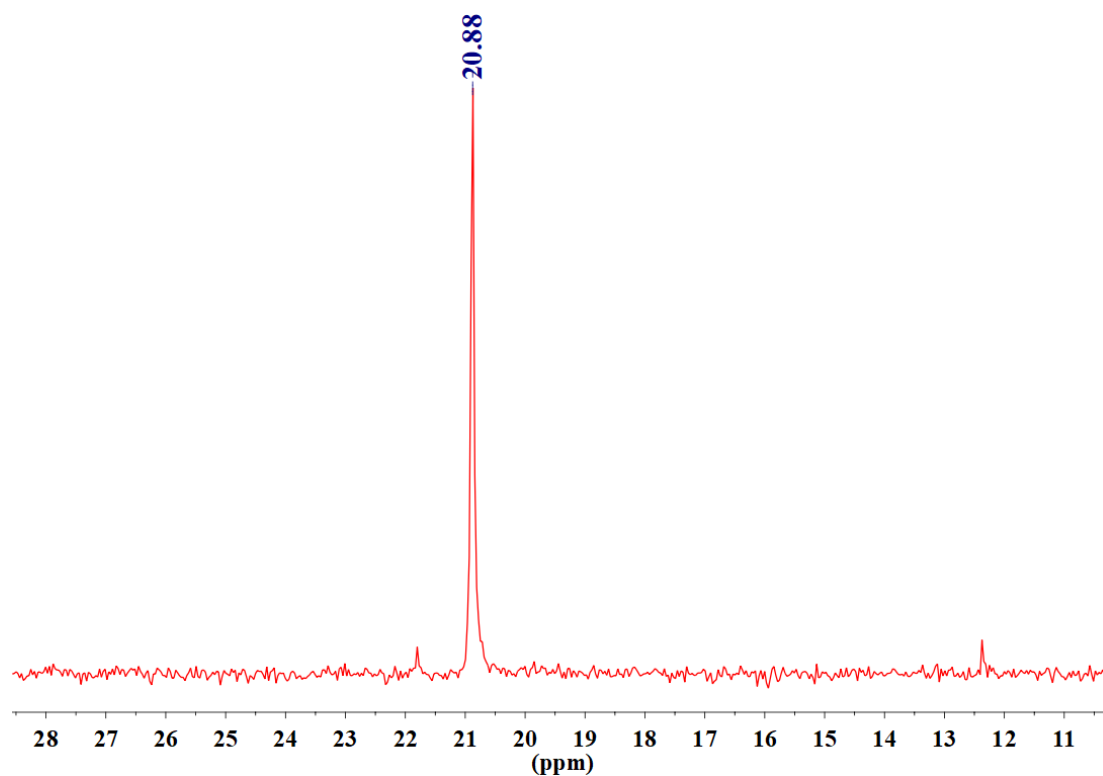


Figure A.2.37: ^{31}P NMR of phosphonium bromanilate PB-S.

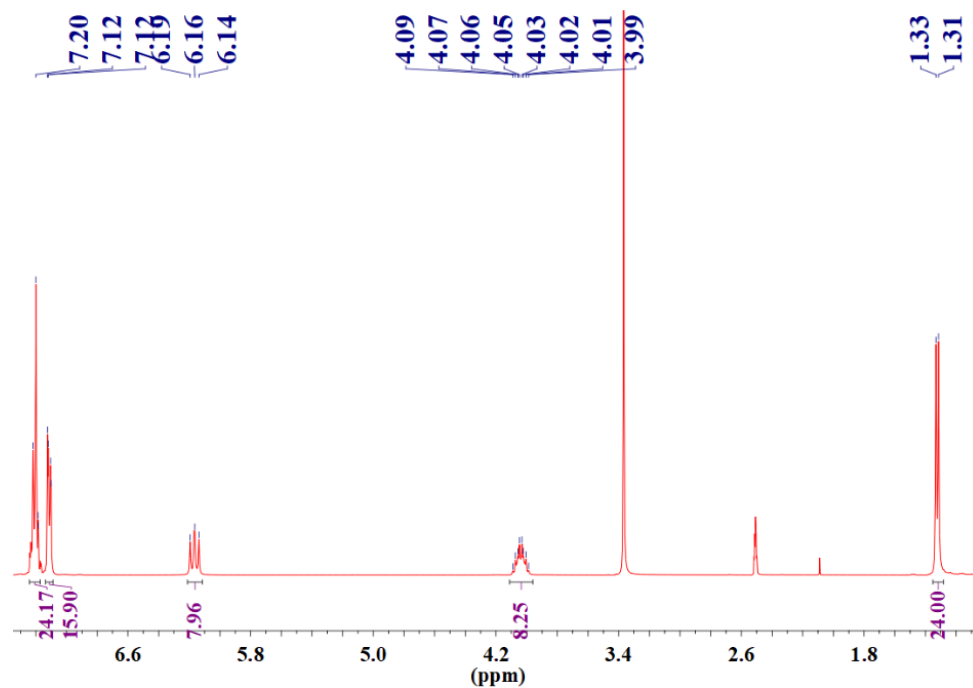


Figure A.2.38: ^1H NMR of phosphonium bromanilate PB-R.

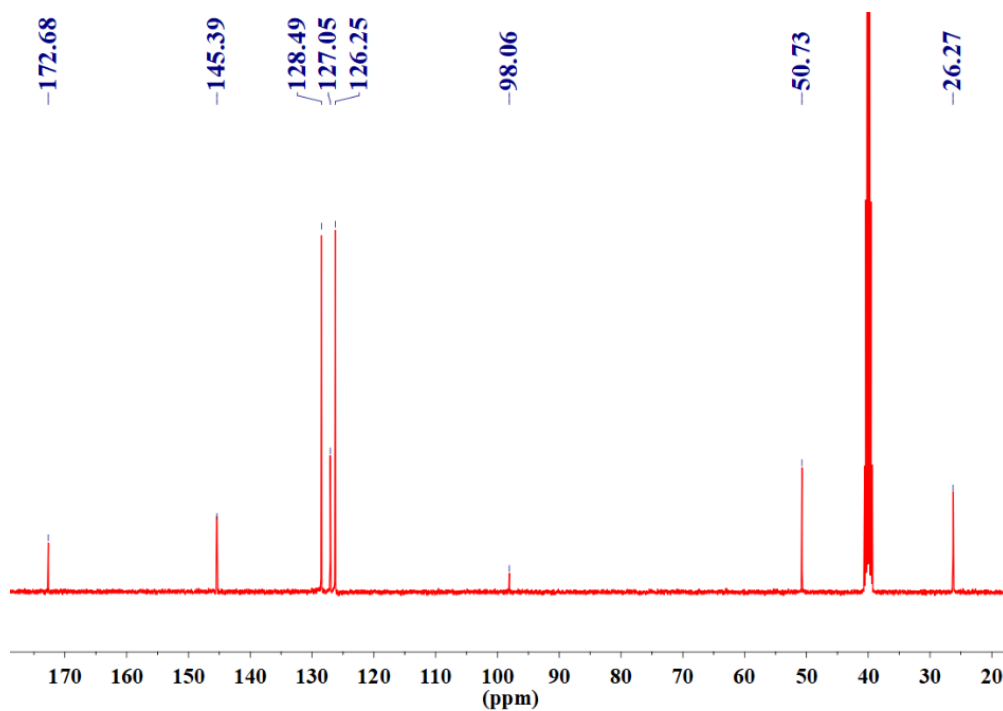


Figure A.2.39: ^{13}C NMR of phosphonium bromanilate PB-R.

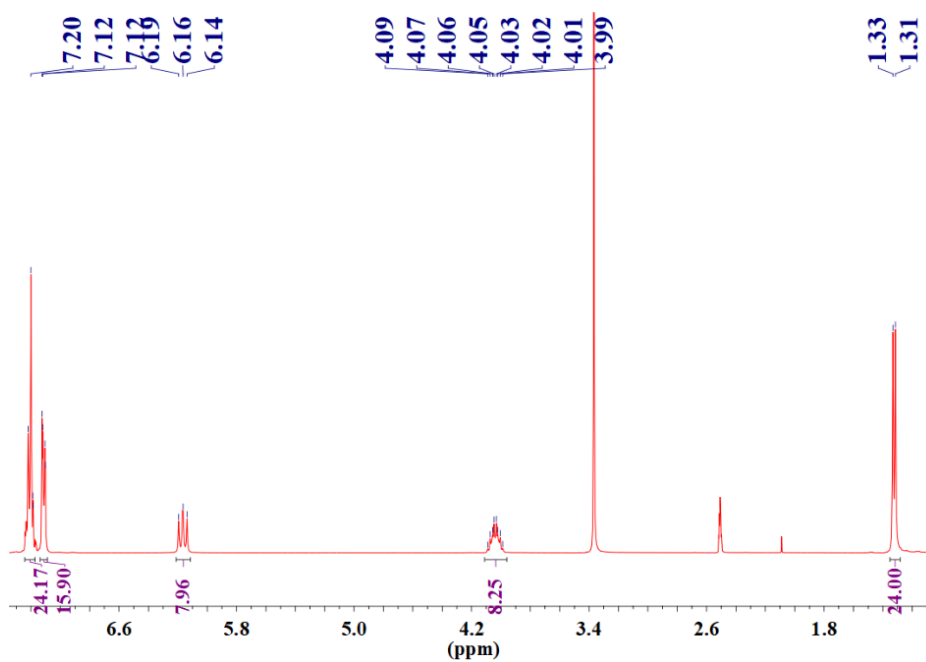


Figure A.2.40: ^1H NMR of phosphonium bromanilate PB-S.

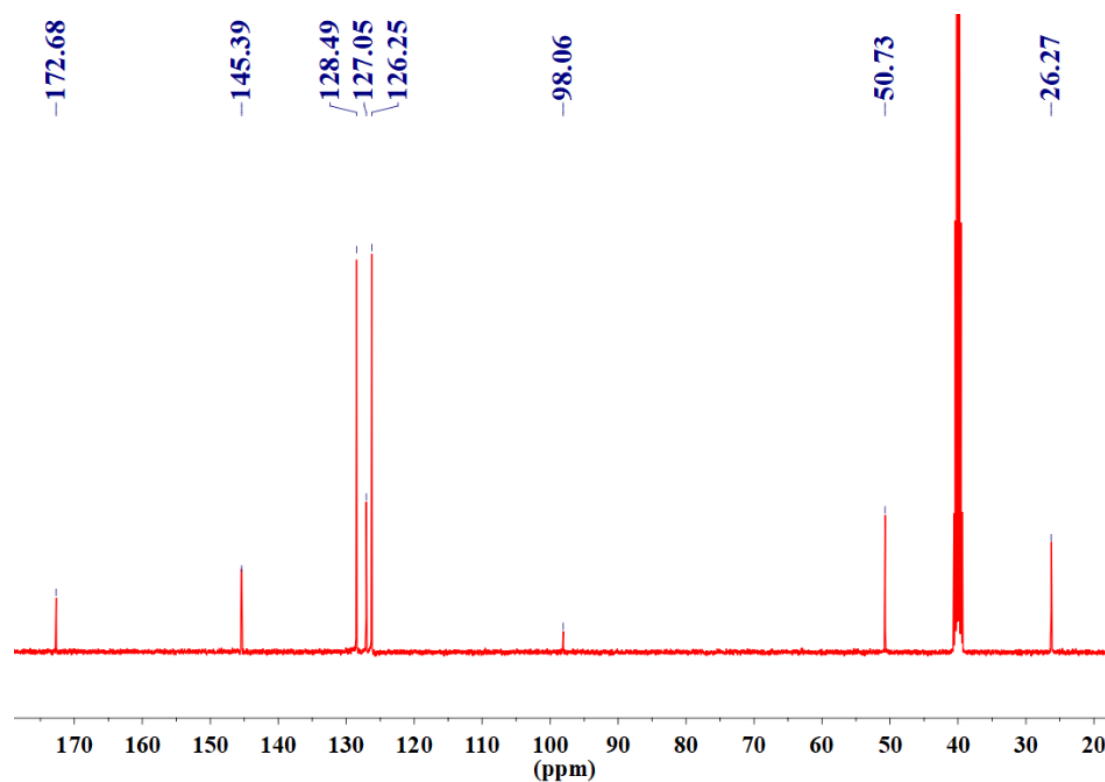


Figure A.2.41: ^{31}C NMR of phosphonium bromanilate PB-S.

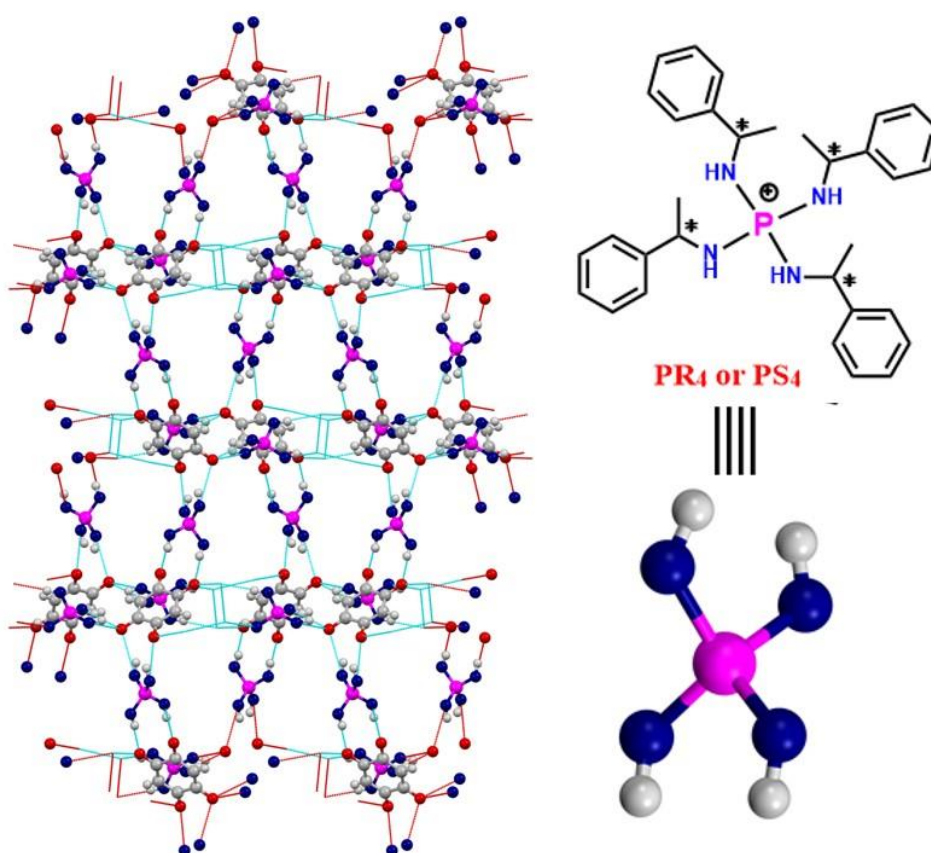


Figure A.2.42: 2*2*2 packing structure of hydrogen bonded networks of phosphonium anilate PD-**R** or PD-**S** (chiral α -methyl benzyl groups are omitted for clarity).

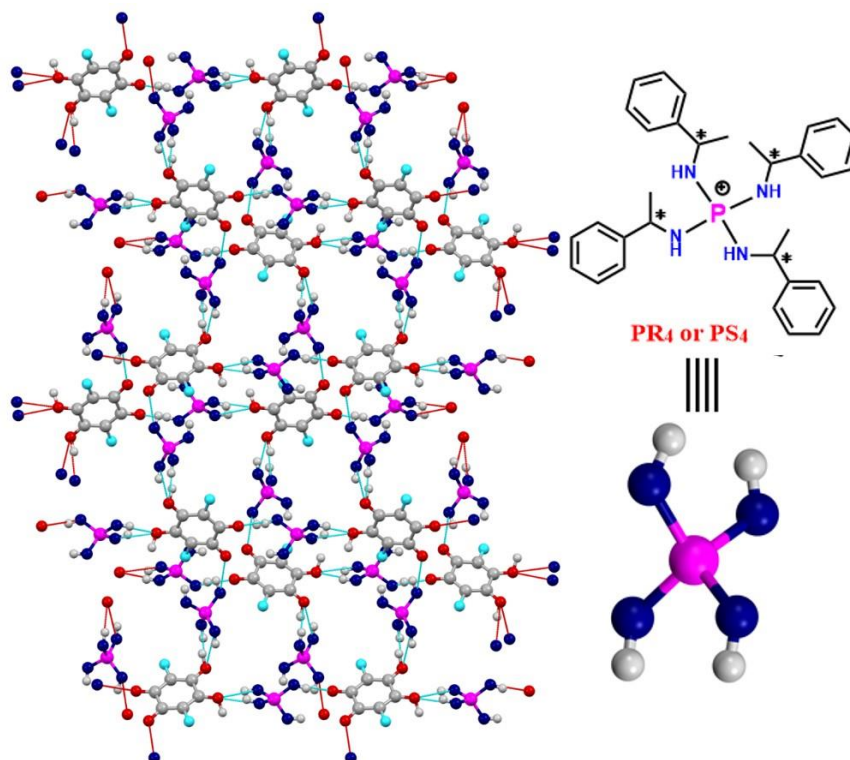


Figure A.2.43: 2*2*2 packing structure of phosphonium Fluoranilate PF-**R** or PF-**S** chiral α -methyl benzyl groups are omitted for clarity.

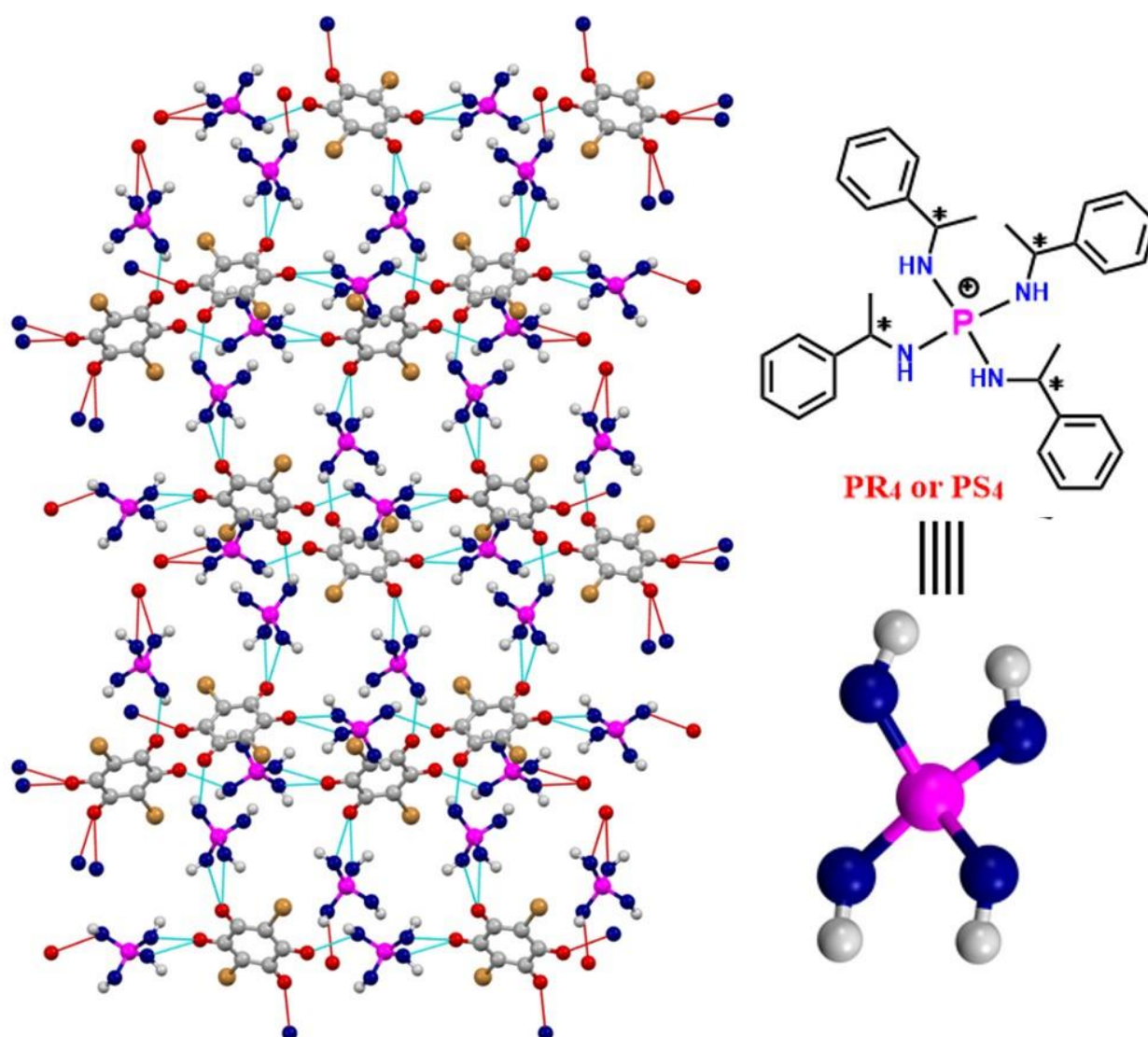
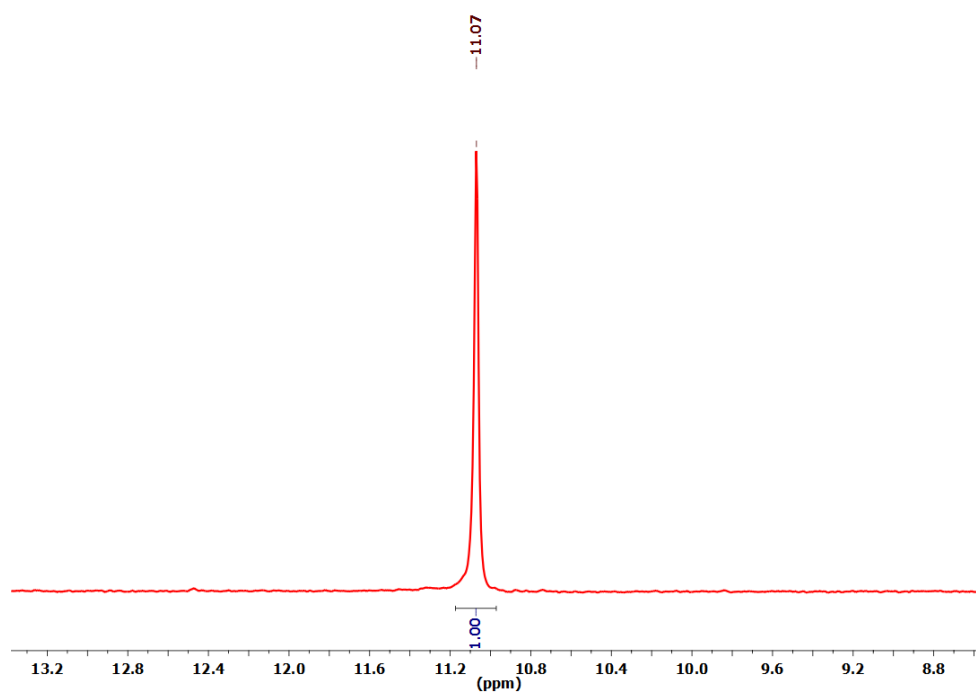
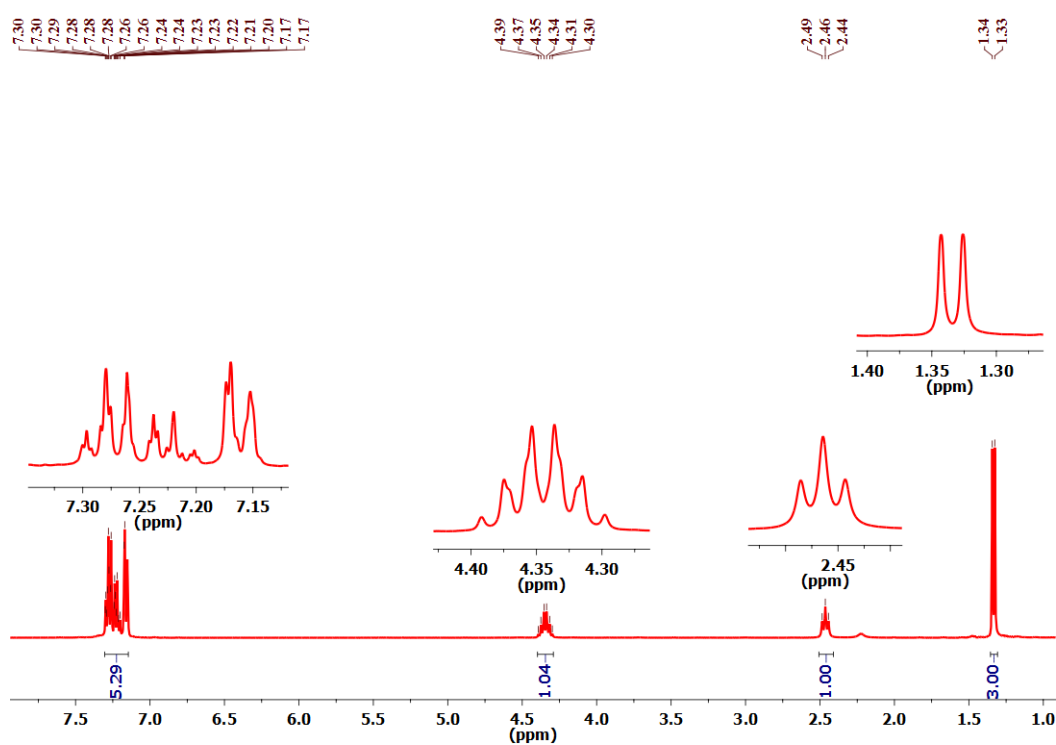


Figure A.2.44: 2*2*2 packing structure of phosphonium bromanilate PB-R or PB-S chiral α -methyl benzyl groups are omitted for clarity.

**Figure A3.1:** ³¹P NMR of ligand X^{SS}H₃.**Figure A3.2:** ¹H NMR of ligand X^{SS}H₃.

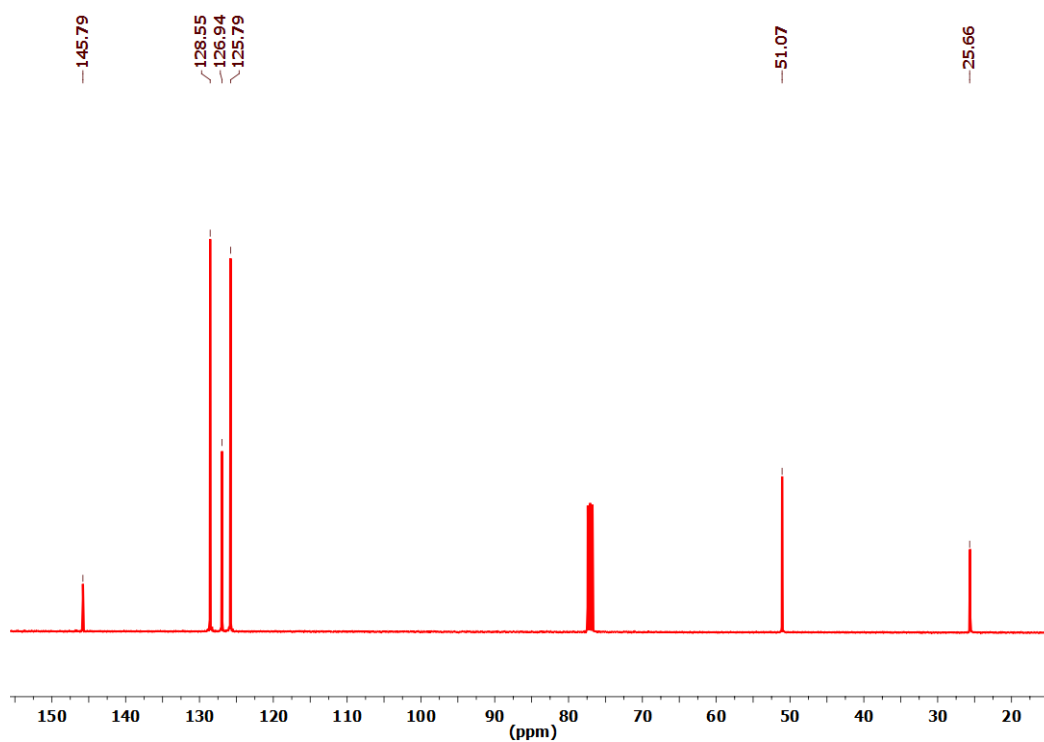


Figure A3.3: ^{13}C NMR of ligand $\text{X}^{\text{SSS}}\text{H}_3$

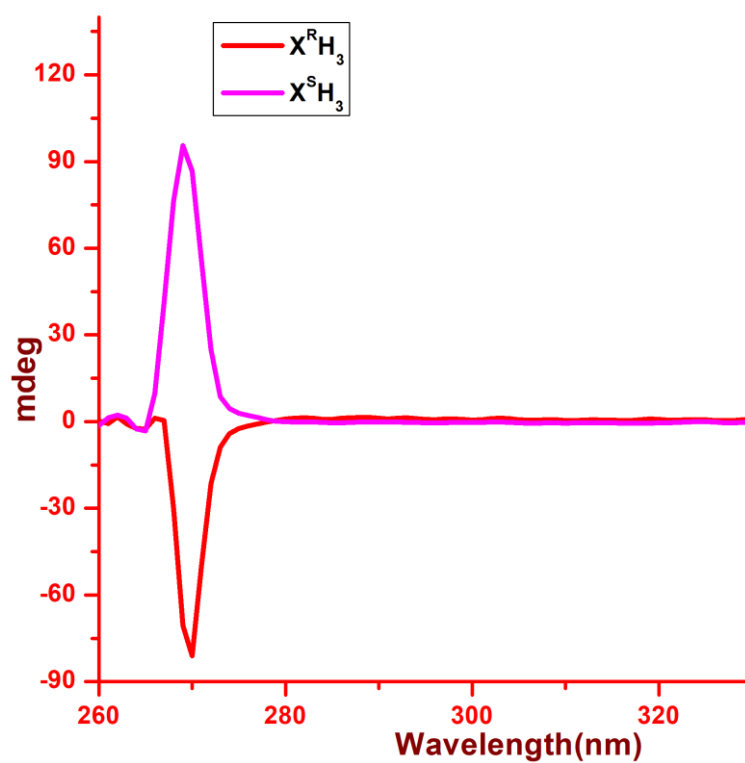


Figure A3.4: CD spectra of ligands $\text{X}^{\text{RRR}}\text{H}_3$ and $\text{X}^{\text{SSS}}\text{H}_3$ in DCM.

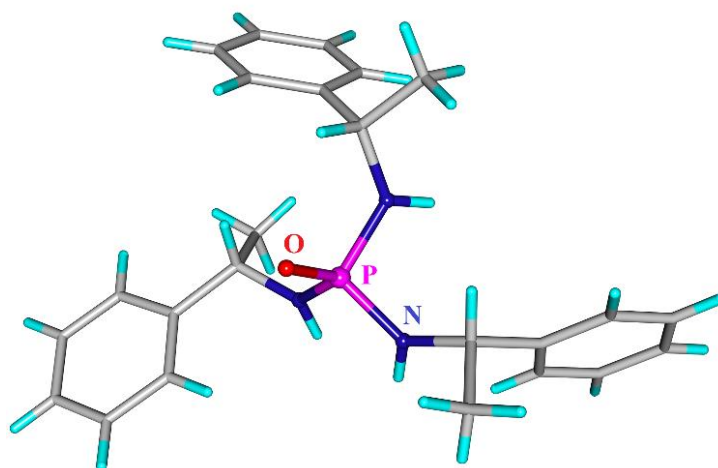


Figure A3.5: Crystal structures of Ligand X^{SS}H₃.

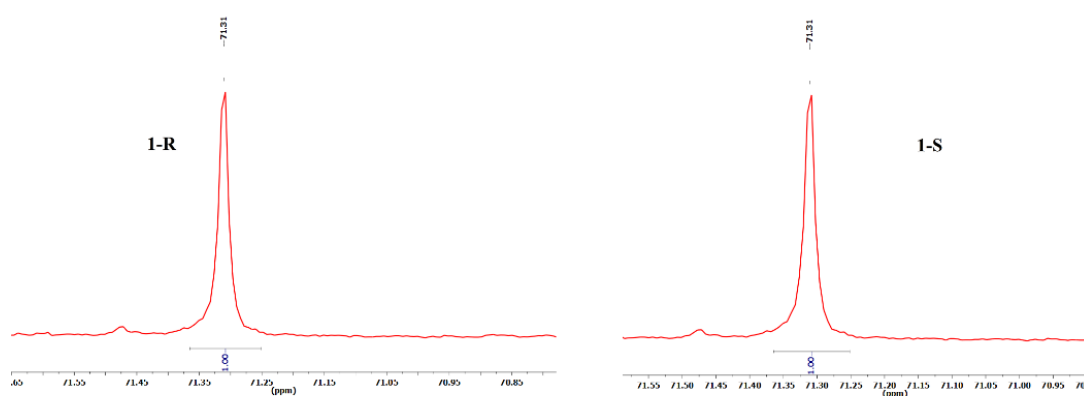


Figure A3.6: ³¹P NMR spectra of **1-R** and **1-S**.

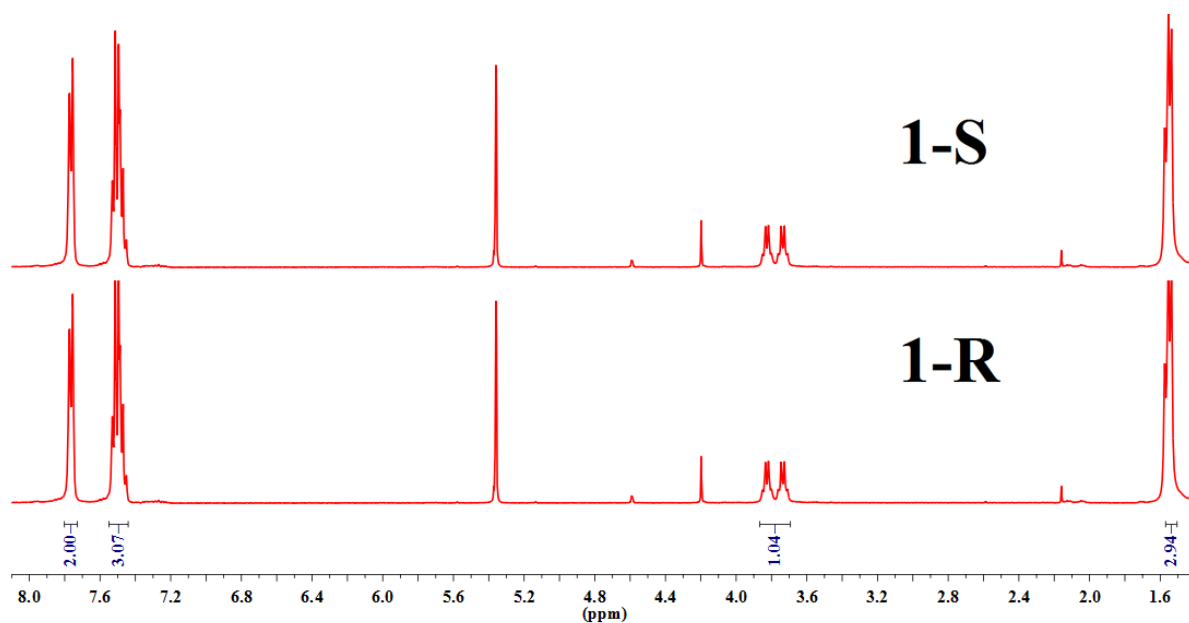


Figure A3.7: ^1H NMR spectra of **1-R** and **1-S**.

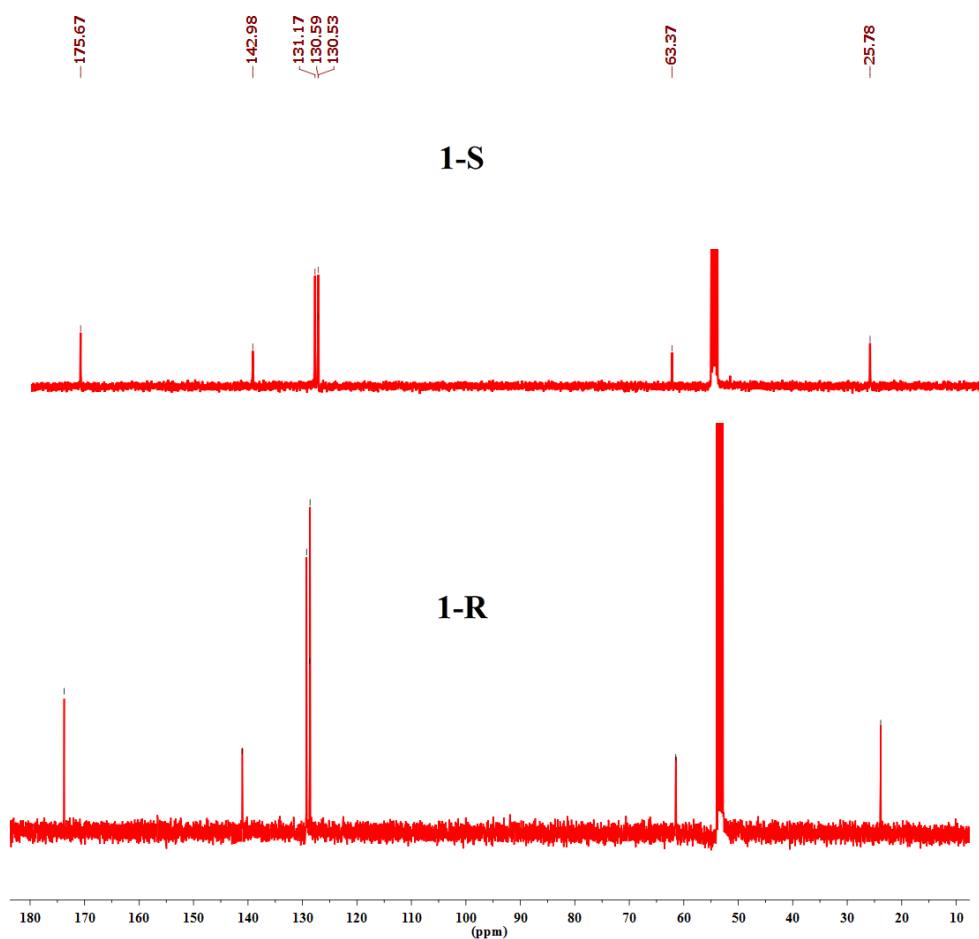


Figure A3.8: ^{13}C NMR spectra of **1-R** and **1-S**.

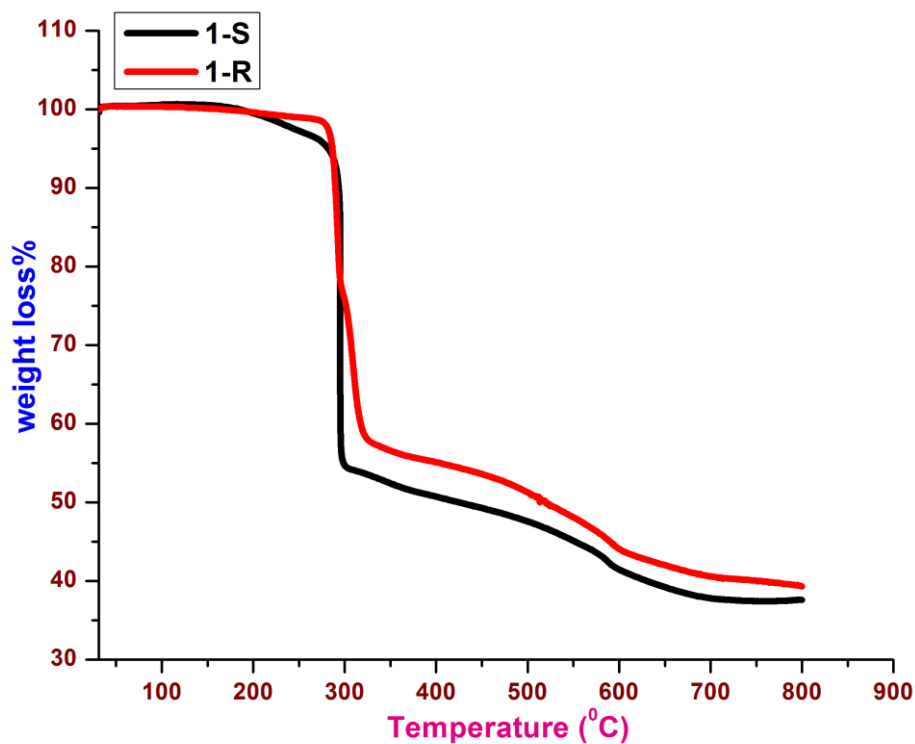


Figure A3.9: TGA curves of cages 1-R and 1-S.

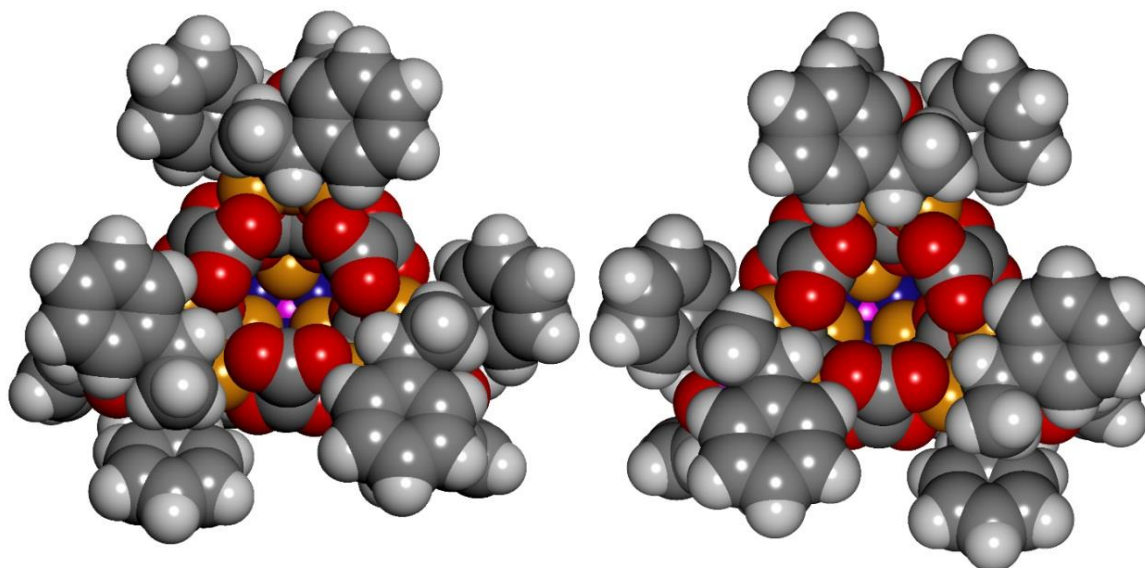


Figure A3.10: Space-filling view of cage 1-R and 1-S showing the definite intrinsic pockets

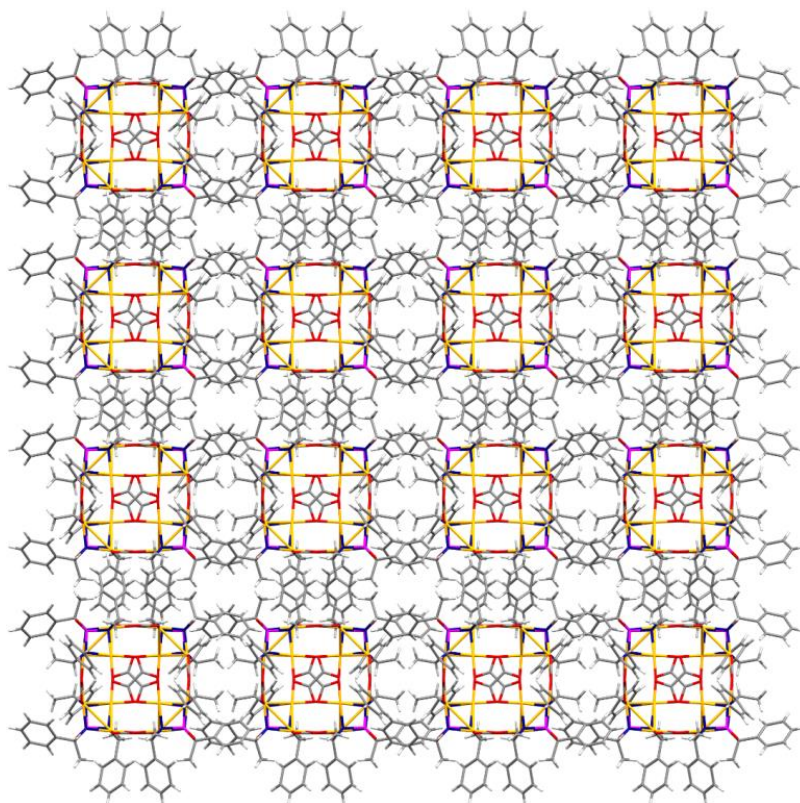


Figure A3.11: View of packing of the cage 1-R along the a-axis.

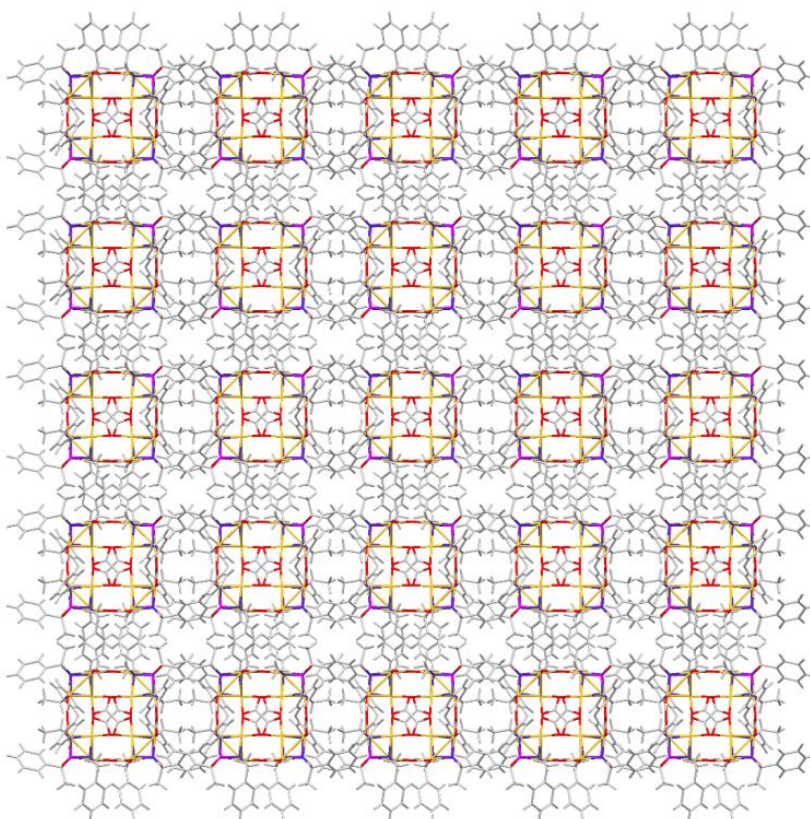


Figure A3.12: View of packing of the cage 1-S along the a-axis.

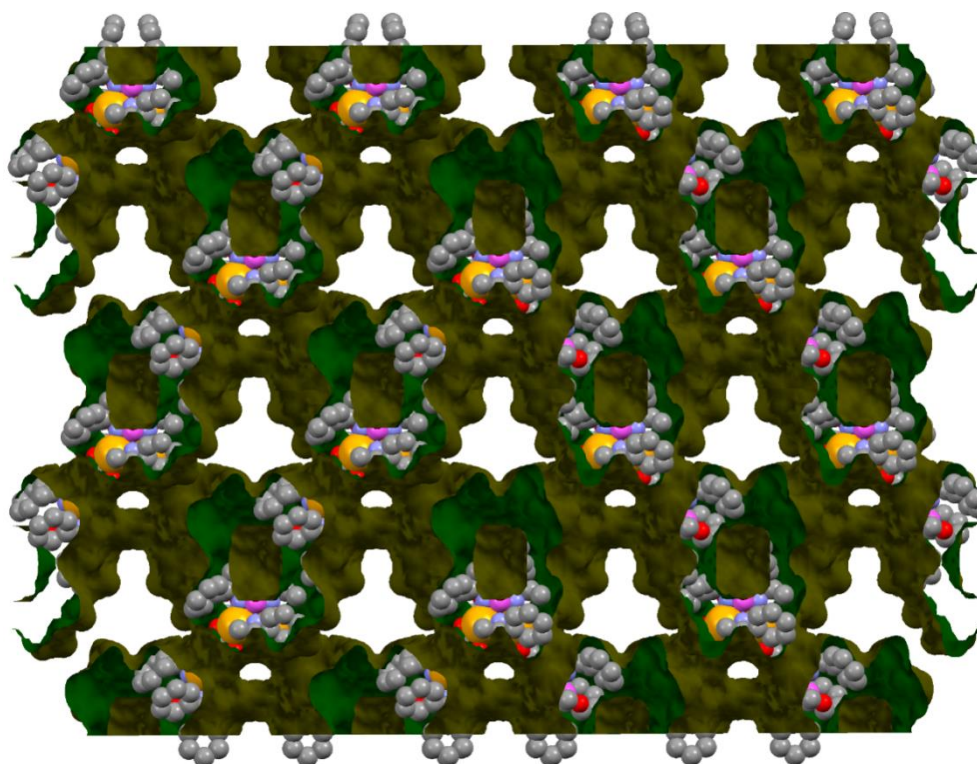


Figure A3.13: Connolly surface view of the packing structure of **1-S** computed by Mercury software³ showing the location and shape of both the intrinsic (small) and extrinsic (large) cavities.

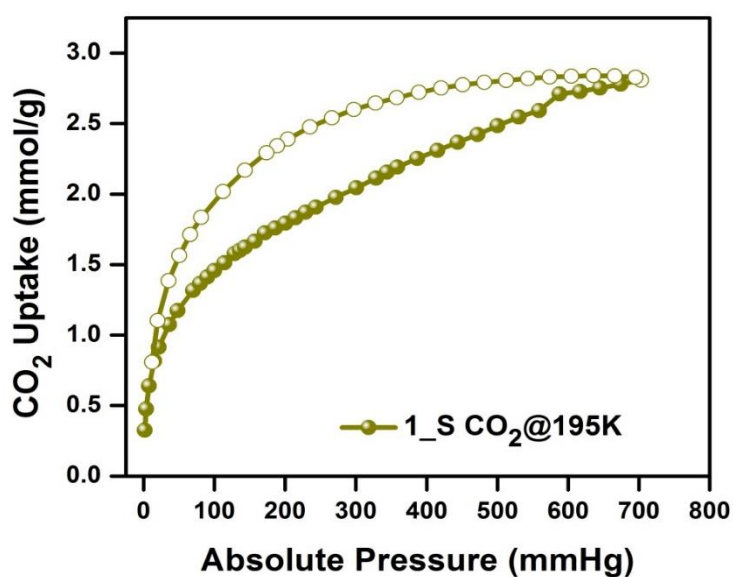


Figure A3.14: CO₂ absorption measurement data of **1-S** at 195K.

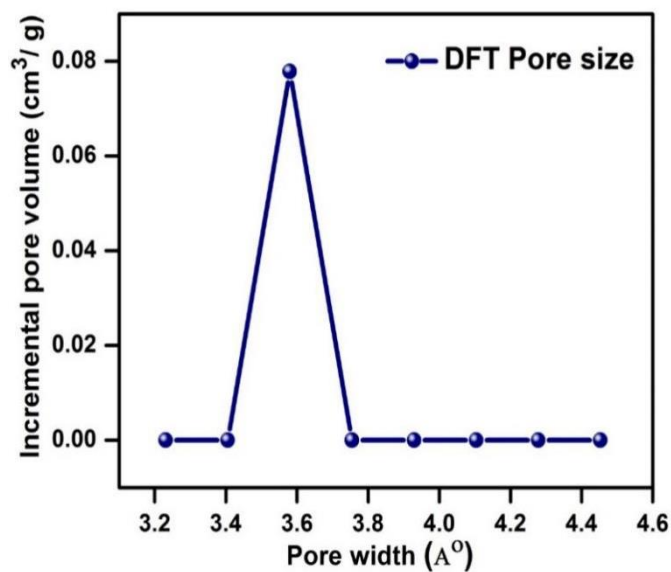


Figure A3.15: DFT derived pore size for cage 1-S.

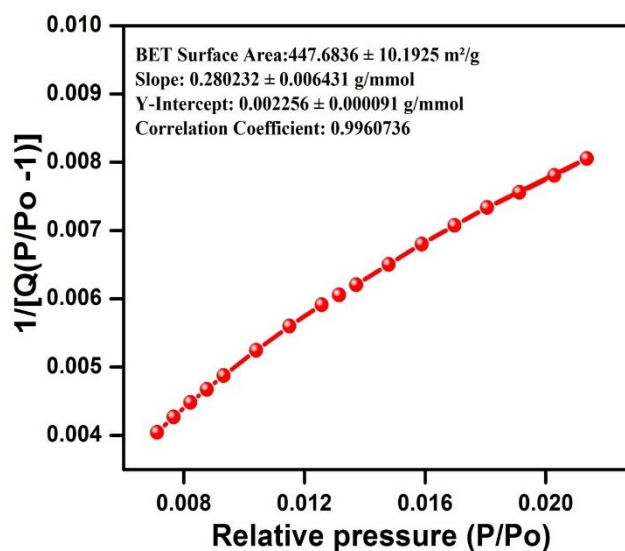


Figure A3.16: Calculated BET surface area for the cage 1-S.

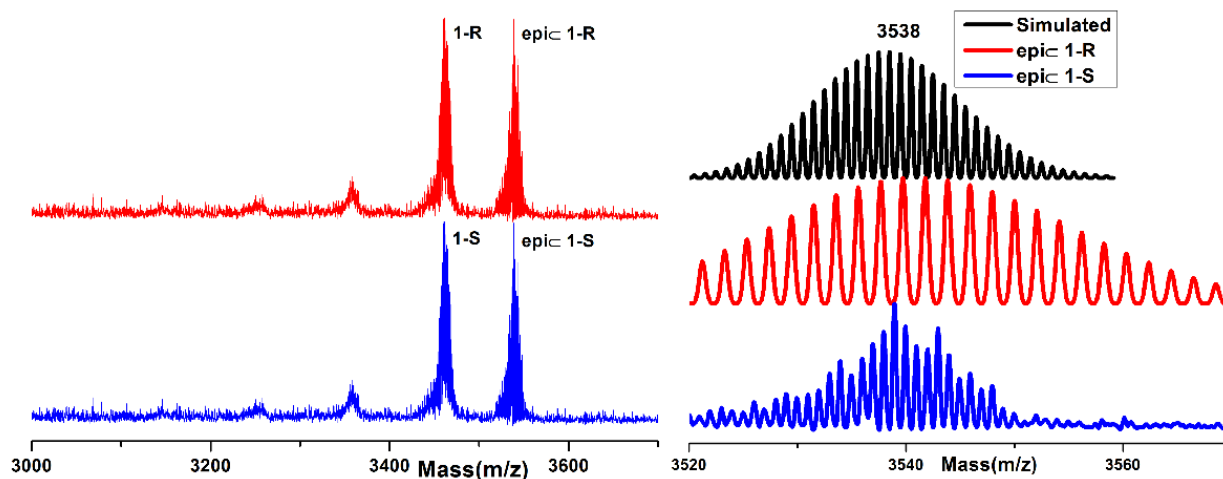


Figure A3.17: MALDI-TOF spectra of $\pm\text{epi}\epsilon 1\text{-R}$ and $\pm\text{epi}\epsilon 1\text{-S}$ and their isotopic distribution of peaks.

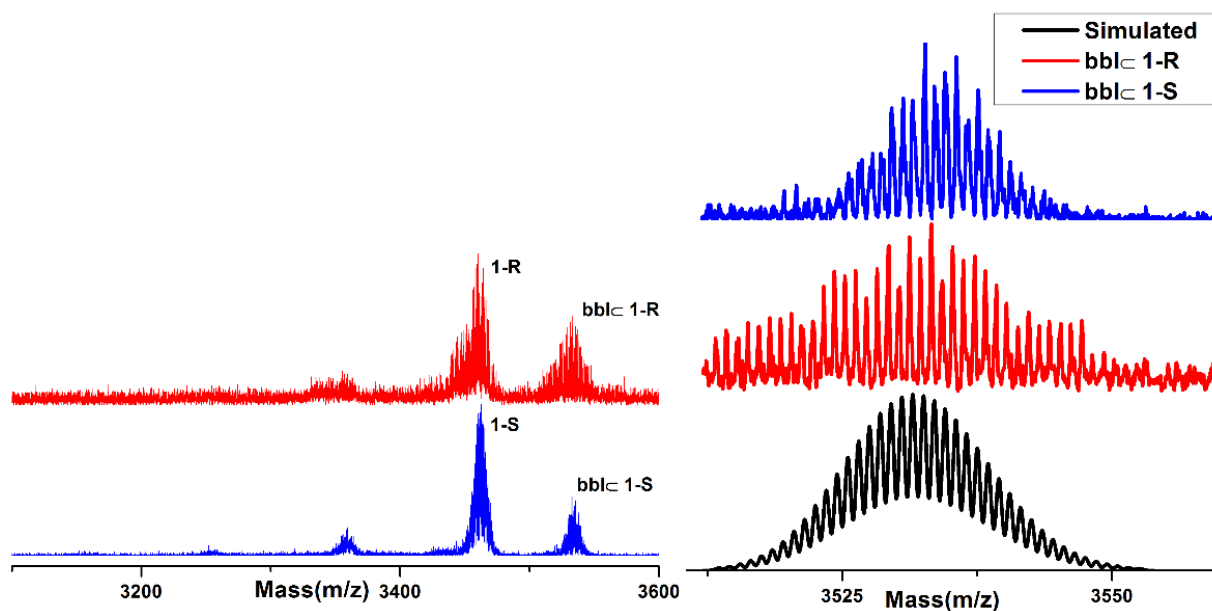


Figure A3.18: MALDI-TOF spectra of $\pm\text{bbl}\epsilon 1\text{-R}$ and $\pm\text{bbl}\epsilon 1\text{-S}$ and their isotopic distribution of peaks.

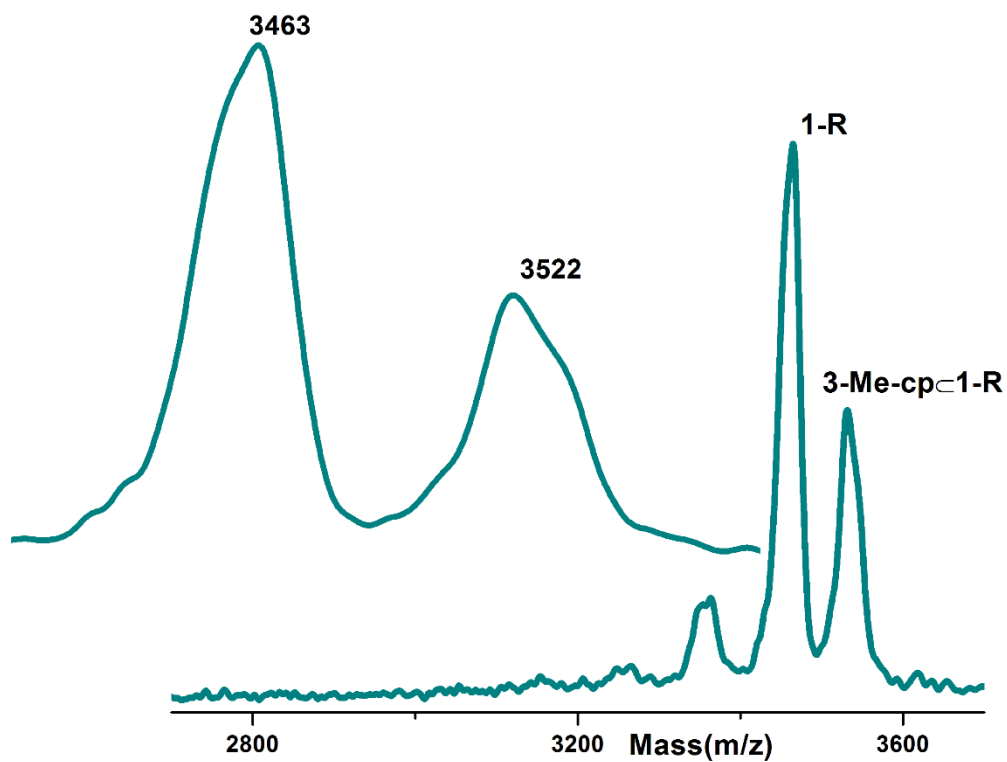


Figure A3.19: MALDI-TOF spectra of $\pm 3\text{-Me-cp}<1\text{-R}$ in the linear mode.

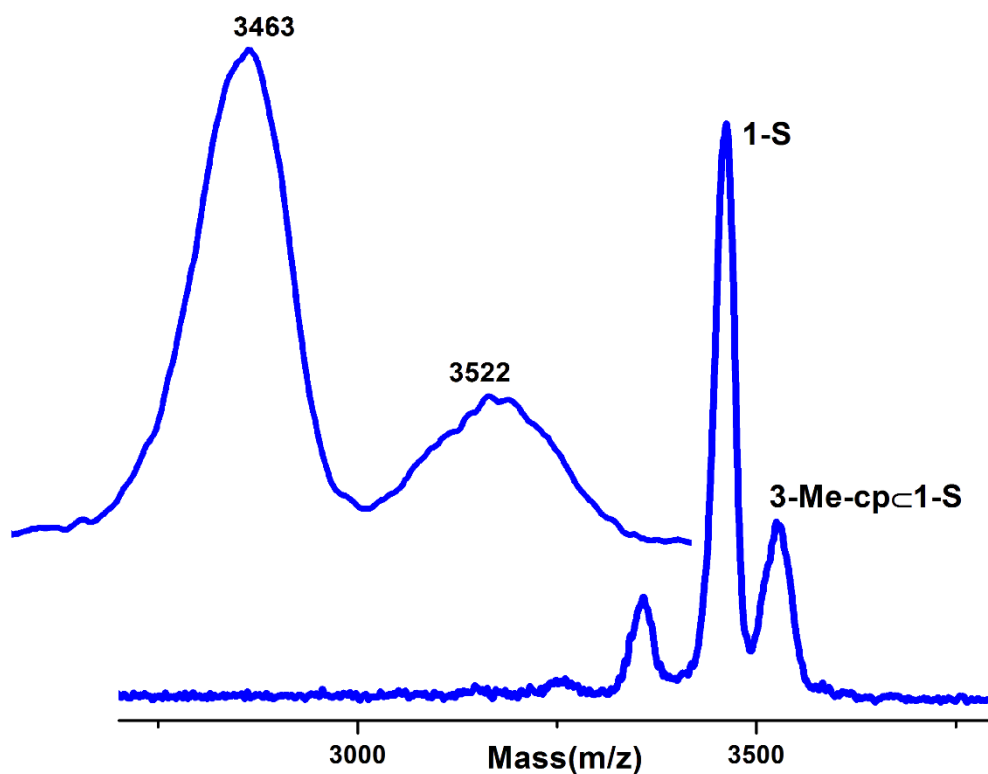


Figure A3.20: MALDI-TOF spectra of $\pm 3\text{-Me-cp}<1\text{-S}$ in linear mode.

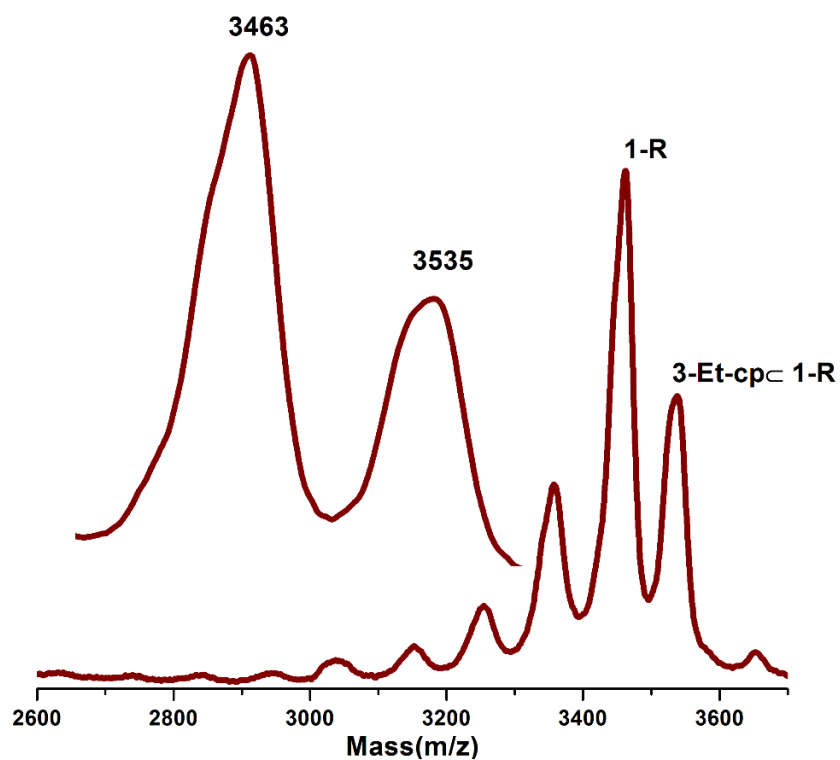


Figure A3.21: MALDI-TOF spectra of $\pm 3\text{-Et-cp}<1\text{-R}$ in linear mode.

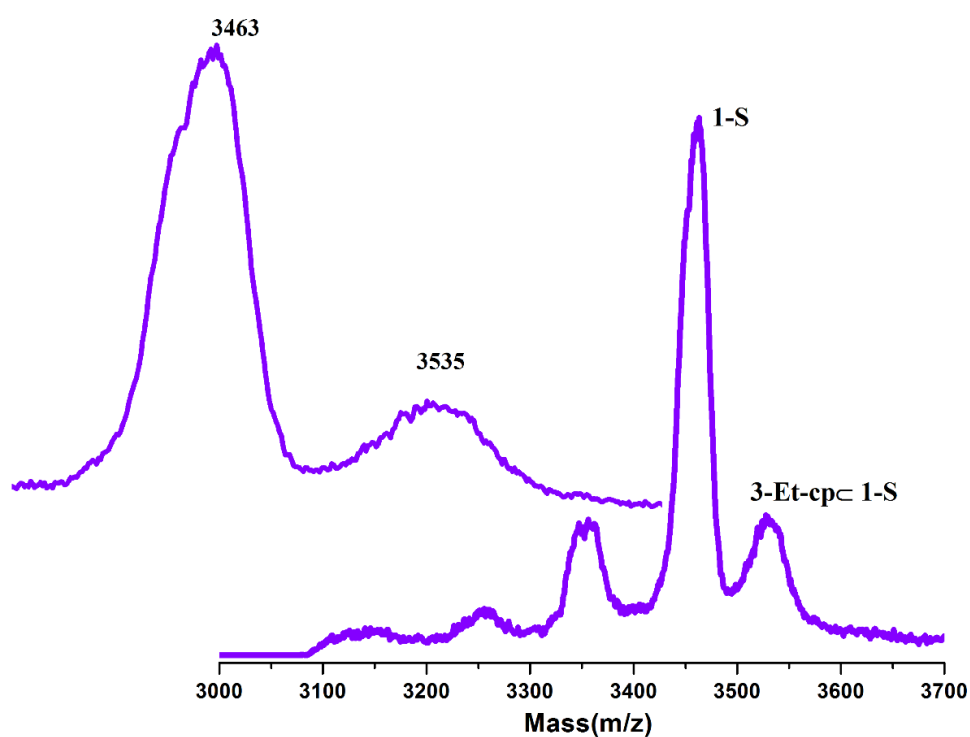


Figure A3.22: MALDI-TOF spectra of $\pm 3\text{-Et-cp}<1\text{-S}$ in linear mode.

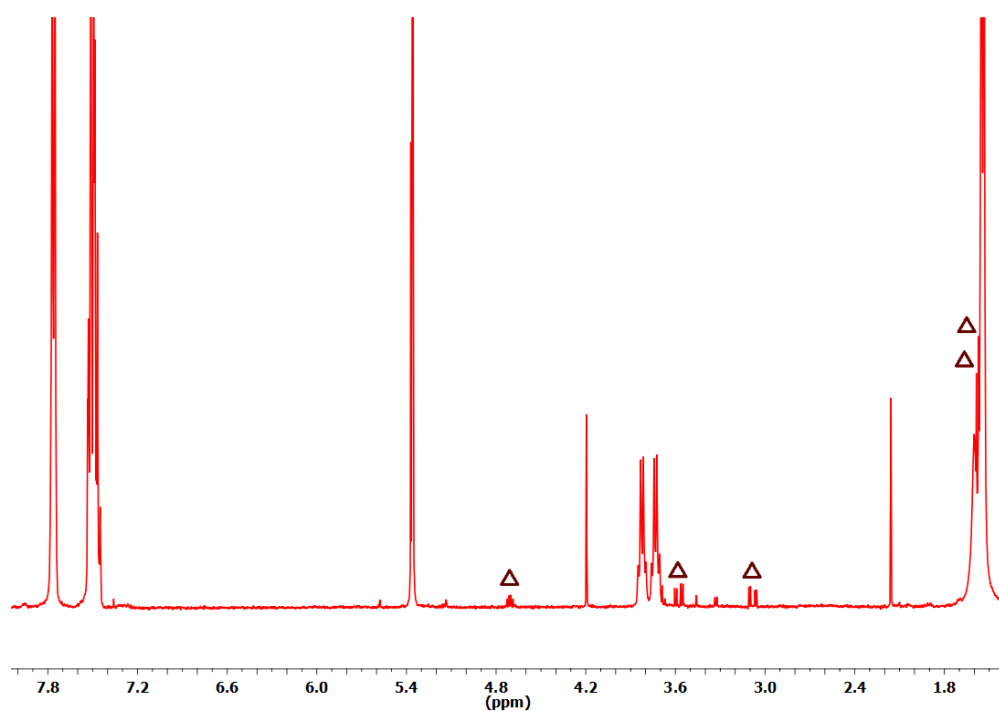


Figure A3.23: ^1H NMR of $\text{bbl}\subset\text{1-R}$ and the signals of β -butyrolactone are cartooned by the symbol Δ .

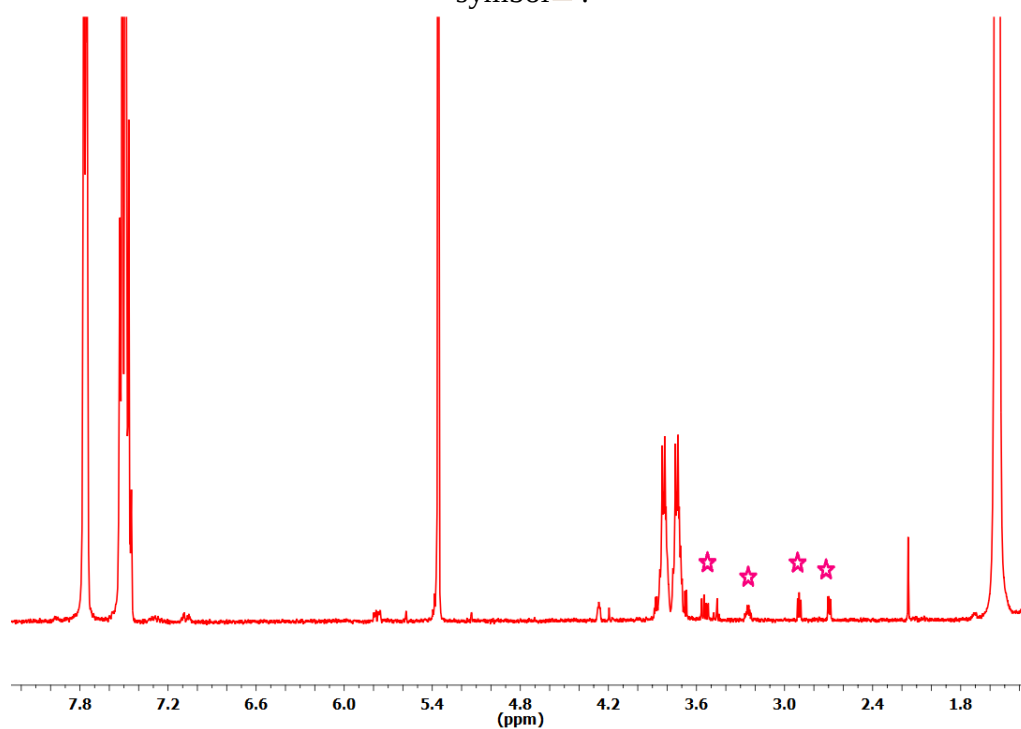


Figure A3.24: ^1H NMR of $\text{epi}\subset\text{1-R}$ and the signals of epichlorohydrin are cartooned by $\star$.

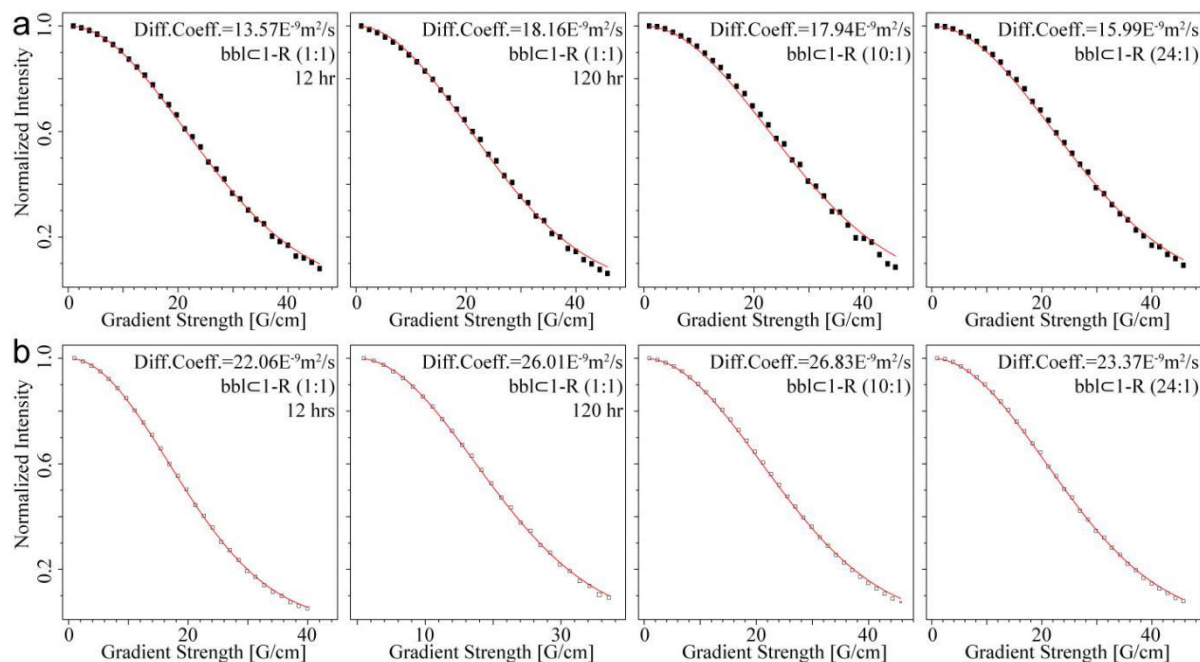


Figure A3.25: Integral decay profile of (a) host protons (filled box) and (b) guest protons (open box) for $(\pm)\text{bbl-C1-R}$ systems.

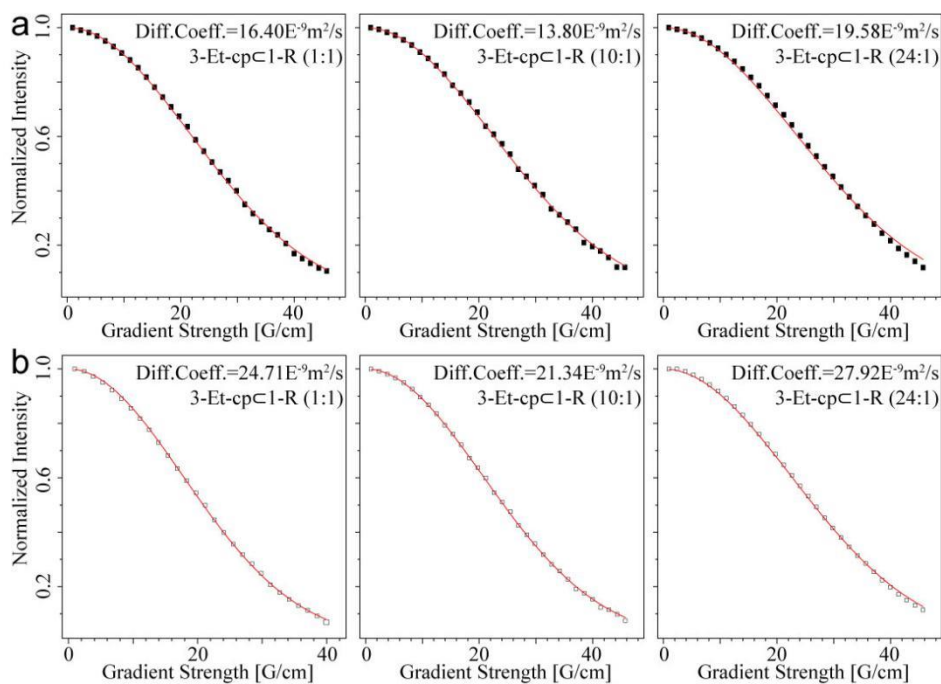


Figure A3.26: Integral decay profile of (a) host protons (filled box) and (b) guest protons (open box) for $(\pm)3\text{-Et-cp-C1-R}$ systems

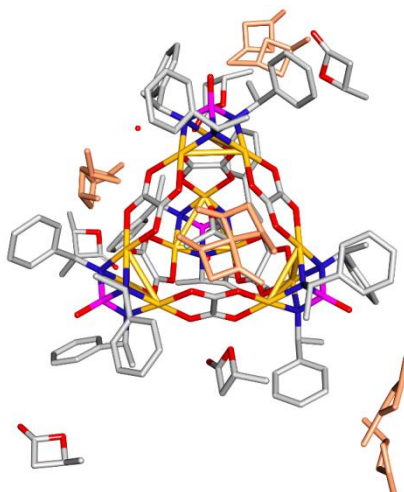


Figure A3.27: Molecular structure of $\pm\text{bbl}\subset\pm\mathbf{1}$ with disordered bbl guest molecules shown in light orange colour.

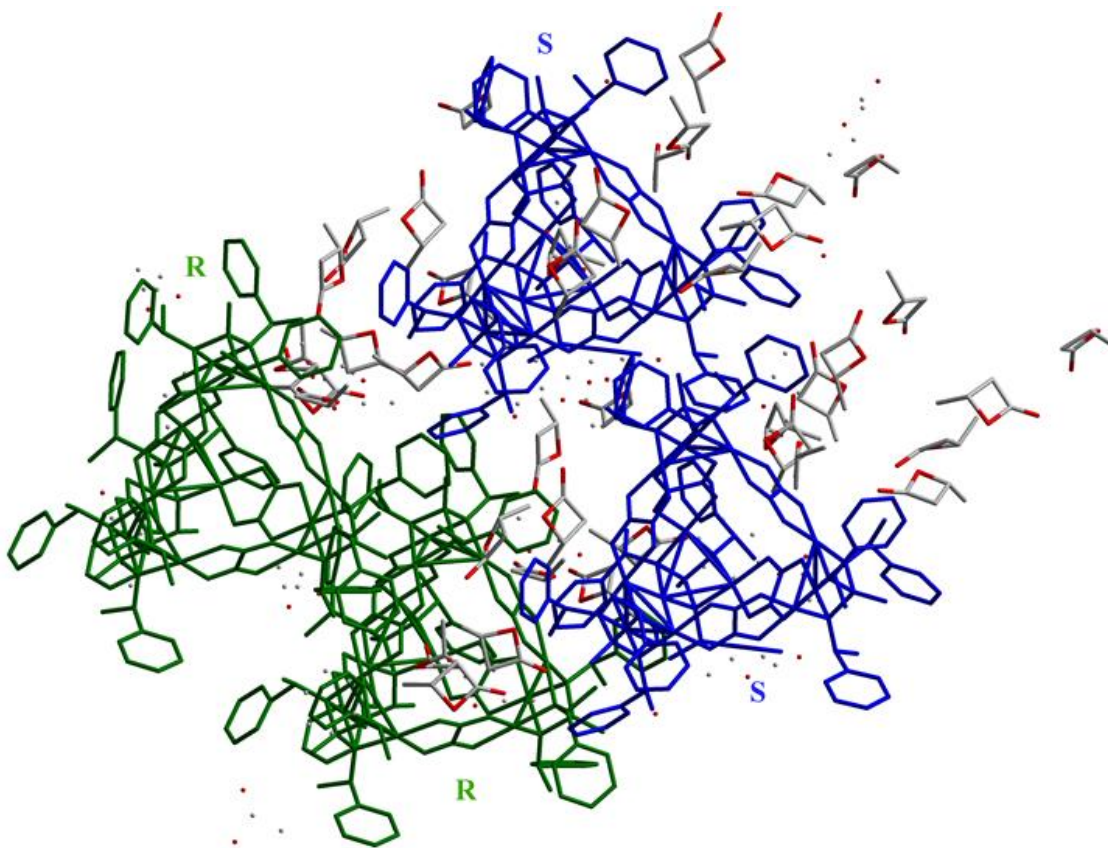


Figure A3.28: 2x2x2 packing structure of $\pm\text{bbl}\subset\pm\mathbf{1}$ showing both location of bbl guests at the intrinsic (green colour) and extrinsic cavities orders (blue) and disordered (orange).

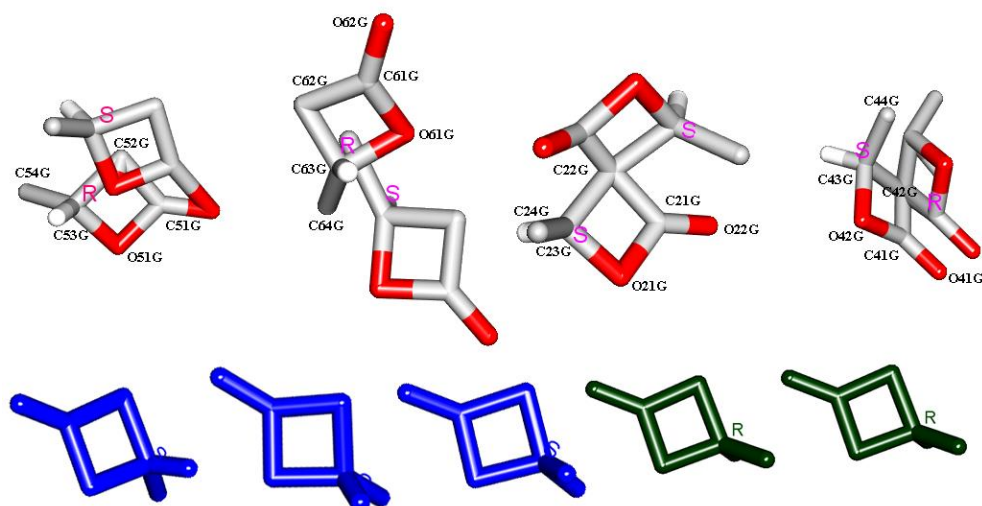


Figure A3.29: $\pm\text{bbl}\subset\pm\mathbf{1}$ showing both disordered (top) and ordered bbl (bottom) guests present in the extrinsic cavities: S-bbl shown in blue and R-bbl shown in green.

GC Methods for the Enantiomeric Separation of the Chiral Guest Molecules

1. Enantiomeric separation of epichlorohydrin

Column used: Supelco γ -dex (30 m* 0.25 mm * 0.25 μm),

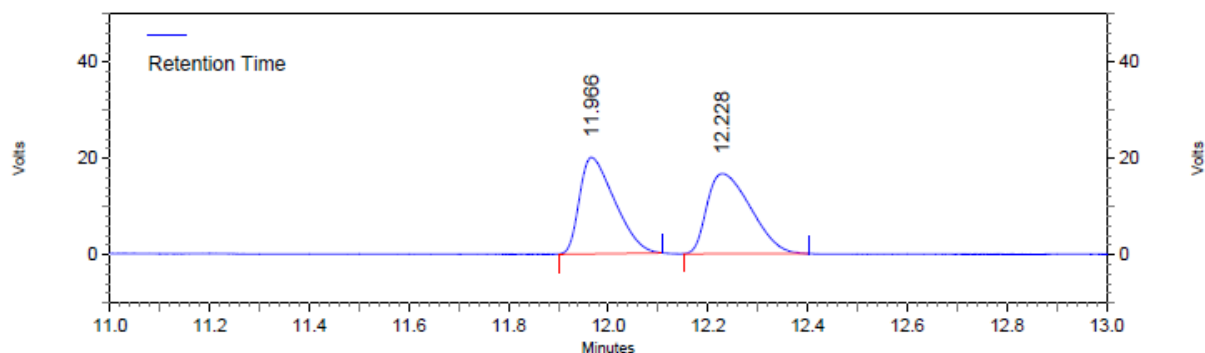
Split ratio 30:1,

Inlet temperature 210 $^{\circ}\text{C}$,

Column pressure 7 psi,

Temperature programme: started at 50 $^{\circ}\text{C}$, hold for 2 mins then heated at rate of 10 $^{\circ}\text{C}$ to 100 $^{\circ}\text{C}$ followed by heating at rate of 2 $^{\circ}\text{C}$ to 160 $^{\circ}\text{C}$. Finally it was heated at the rate of 10 $^{\circ}\text{C}$ to Maximum temperature (210 $^{\circ}\text{C}$).

(a) Neat $\pm\text{epi}$:



Front Signal Results				
Retention Time	Area	Area %	Height	Height %
11.966	755741	49.20	154033	54.60
12.228	780432	50.80	128089	45.40
Totals				
	1536173	100.00	282122	100.00

Figure A3.30: GC chromatogram and analysis plot showing the resolved peaks for rac-epichlorohydrin.

(a) $\pm$ epi With 1-R:

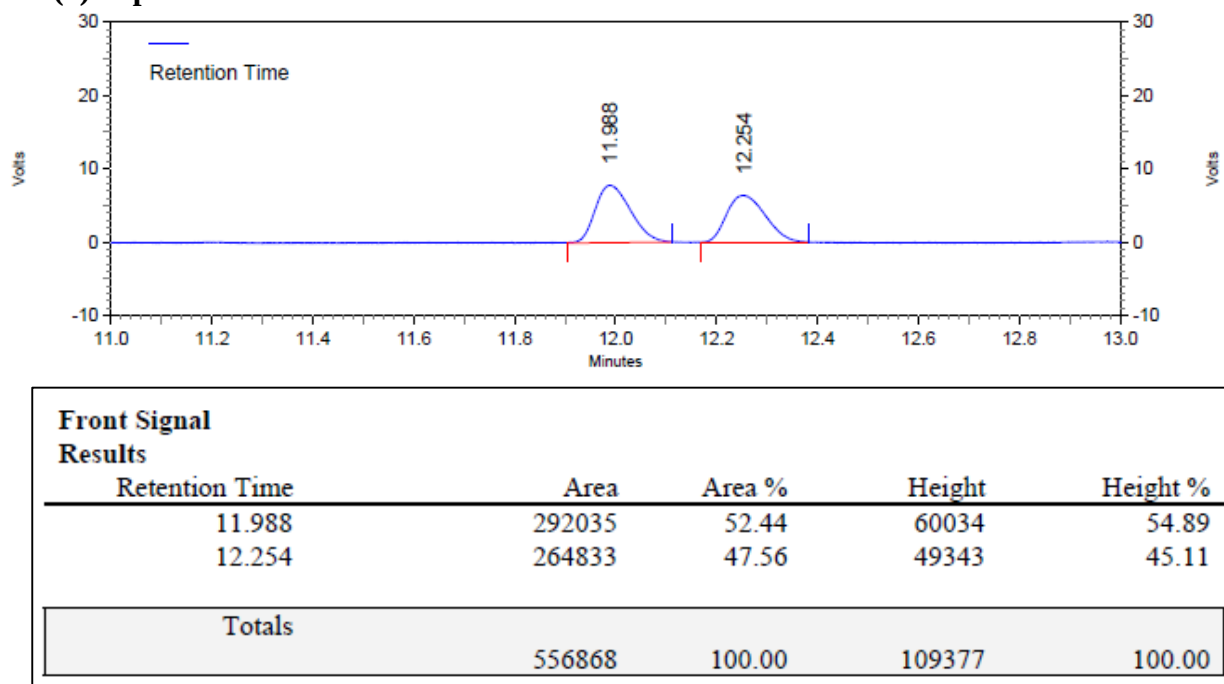
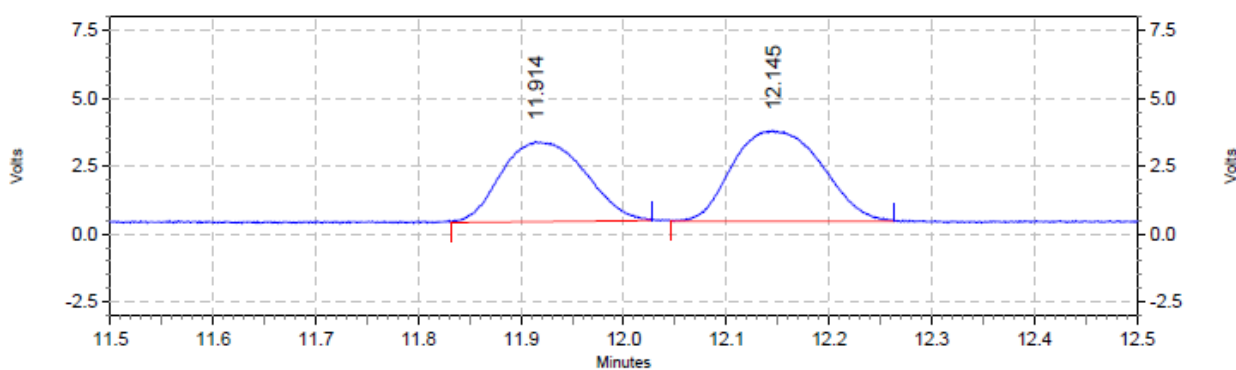


Figure A3.31: GC chromatogram and analysis plot for the resolved peaks of epichlorohydrin extracted from 1-R cage showing 6% *ee*.

(a) $\pm$ epi With 1-S:



Front Signal Results				
Retention Time	Area	Area %	Height	Height %
11.914	128946	45.22	22729	46.84
12.145	156231	54.78	25799	53.16
Totals	285177	100.00	48528	100.00

Figure A3.32: GC chromatogram and analysis plot for the resolved peaks of epichlorohydrin extracted from 1-S cage showing 10% *ee*.

2. Enantiomeric separation of β -butyrolactone:

Column used: Supelco β -dex (30 m* 0.25 mm * 0.25 μ m),

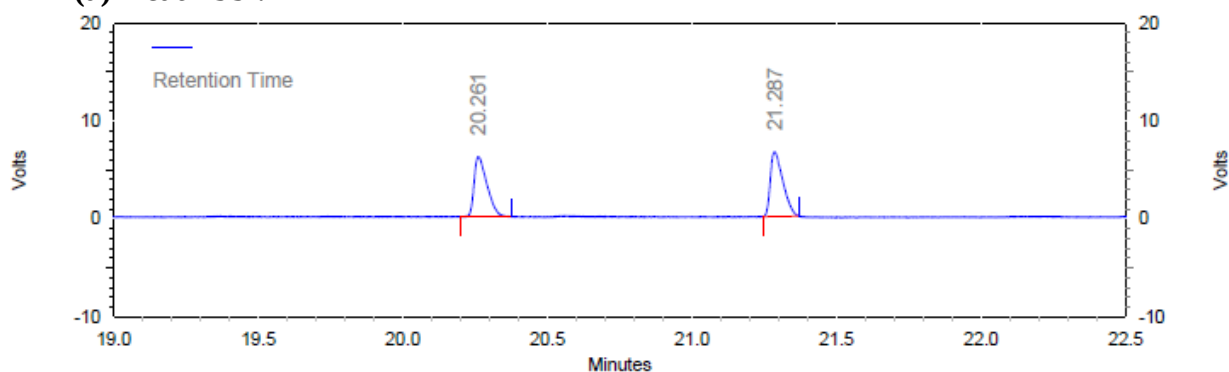
Split ratio 30:1,

Inlet temperature 210 $^{\circ}$ C,

Column pressure 15.1 psi

Temperature programme: started at 80 $^{\circ}$ C, hold for 1 mins then heated at the rate of 4 $^{\circ}$ C to 160 $^{\circ}$ C. Finally heated at the rate of 10 $^{\circ}$ C to 210 $^{\circ}$ C and hold for 2 mins

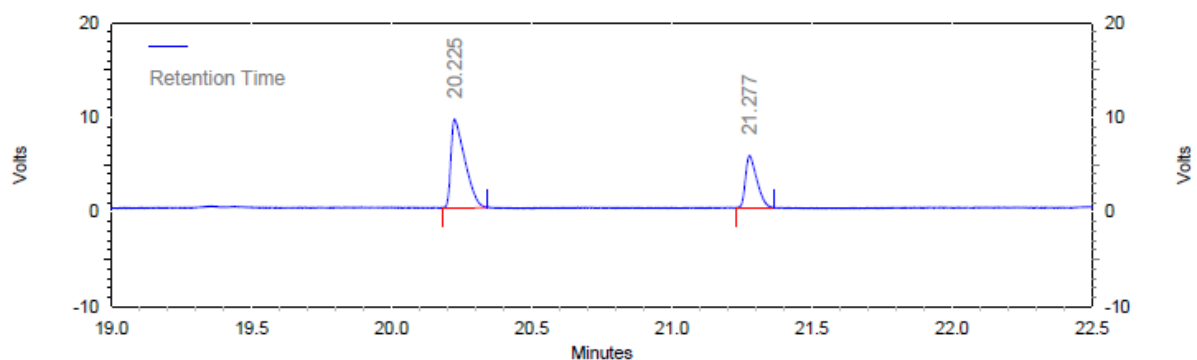
(a) Neat $\pm$ bbl:



Front Signal Results				
Retention Time	Area	Area %	Height	Height %
20.261	147976	49.13	47414	48.30
21.287	153187	50.87	50753	51.70
Totals	301163	100.00	98167	100.00

Figure A3.33: GC chromatogram and analysis plot showing the resolved peaks for rac- β -butyrolactone.

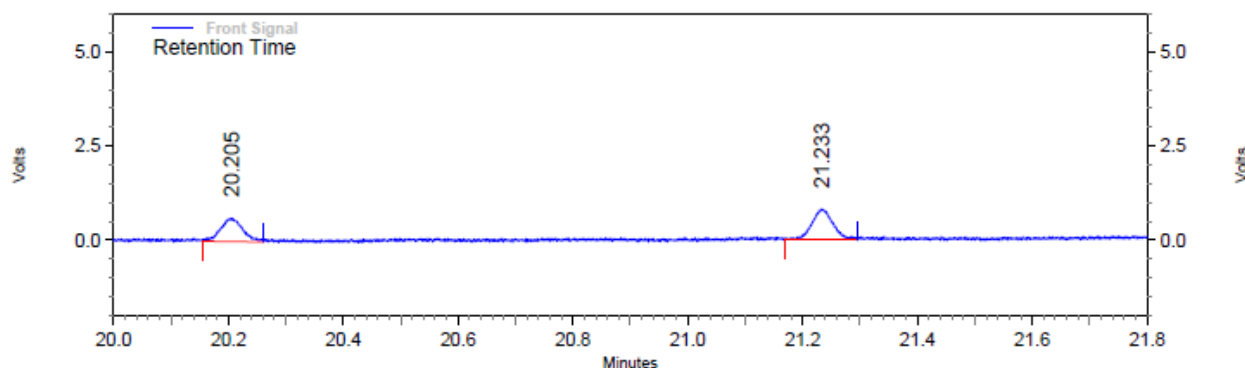
(b) $\pm$ bbl with 1-R:



Front Signal Results				
Retention Time	Area	Area %	Height	Height %
20.225	249952	67.23	72382	62.89
21.277	121844	32.77	42709	37.11
Totals	371796	100.00	115091	100.00

Figure A3.34: GC chromatogram and analysis plot for the resolved peaks of bbl extracted from 1-R cage showing 34% ee.

(a) $\pm$ bbl with 1-S:



Front Signal Results				
Retention Time	Area	Area %	Height	Height %
20.205	12749	43.38	4830	43.21
21.233	16643	56.62	6349	56.79
Totals	29392	100.00	11179	100.00

Figure A3.35: GC chromatogram and analysis plot for the resolved peaks of bbl extracted from 1-S cage showing 14% ee.

Enantiomeric separation of 3-methylcyclopentanone:

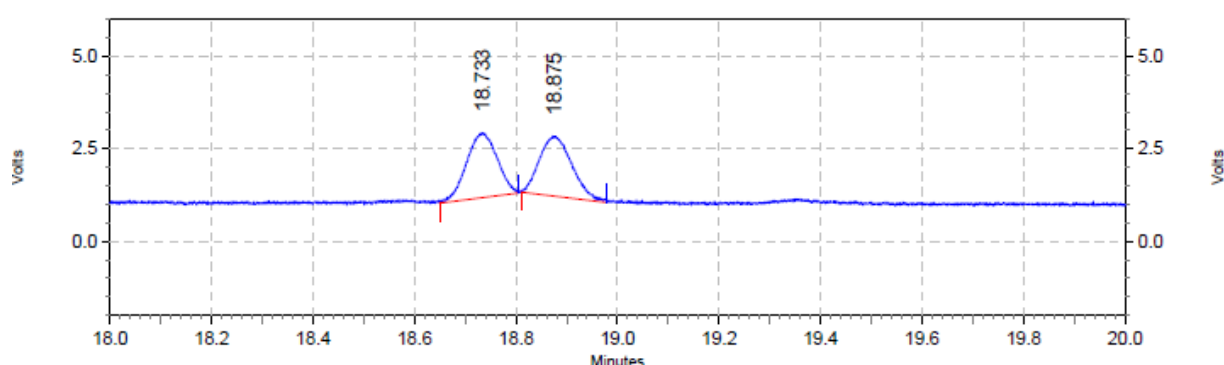
Column used: Supelco β -dex (30 m* 0.25 mm * 0.25 μ m),

Split ratio 30:1,

Inlet temperature 210 $^{\circ}$ C,

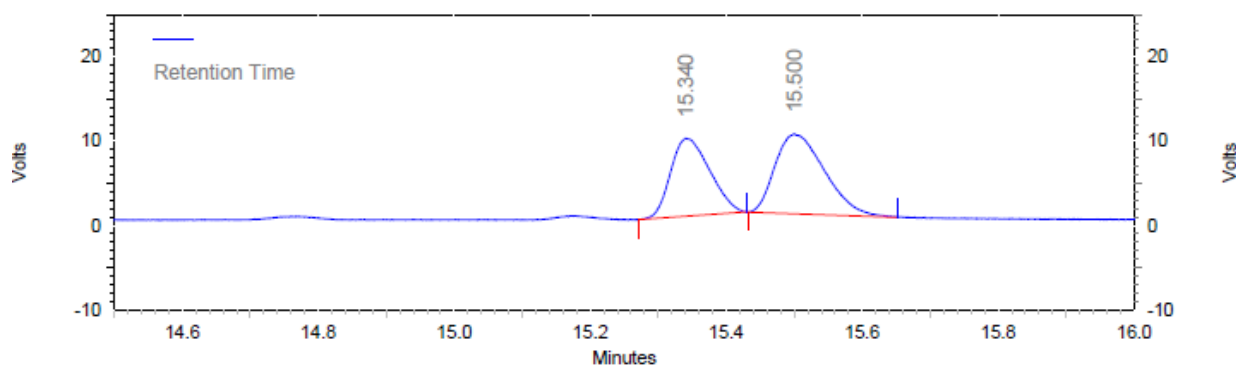
Column pressure 7 psi

Temperature programme: started at 50 $^{\circ}$ C, then ramped at the rate of 10 $^{\circ}$ C to 90 $^{\circ}$ C then heated at the rate of 3 $^{\circ}$ C to 130 $^{\circ}$ C hold for 3 mins It was further heated at the rate of 2 $^{\circ}$ C to 150 $^{\circ}$ C.Finally heated at the rate of 10 $^{\circ}$ C to 210 $^{\circ}$ C

(a) Neat $\pm$ 3-Me-cp:

Front Signal Results				
Retention Time	Area	Area %	Height	Height %
18.733	56507	50.43	13506	51.94
18.875	55535	49.57	12495	48.06
Totals	112042	100.00	26001	100.00

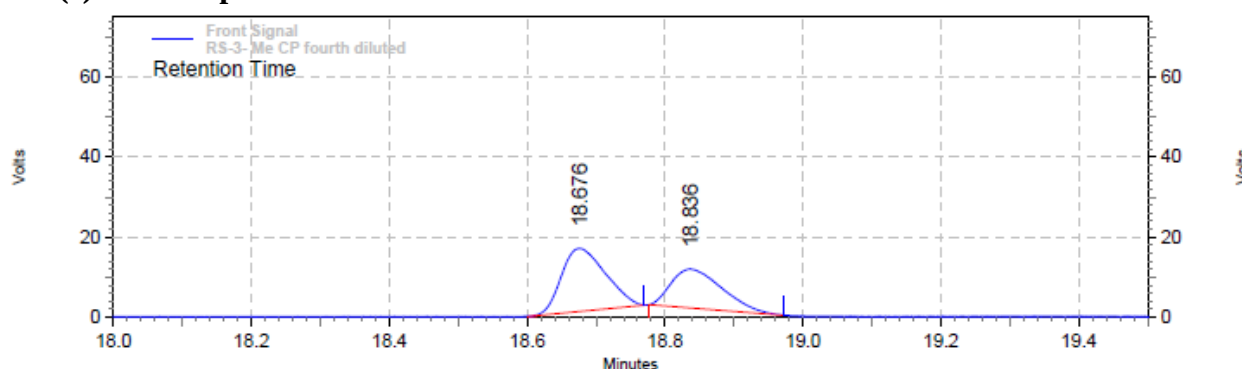
Figure A3.36: GC chromatogram and analysis plot showing the resolved peaks for rac-3-methylcyclopentanone.

(b) $\pm$ 3-Me-cp with 1-R:

Front Signal Results				
Retention Time	Area	Area %	Height	Height %
15.340	283033	43.51	71050	49.41
15.500	367454	56.49	72752	50.59
Totals	650487	100.00	143802	100.00

Figure A3.37: GC chromatogram and analysis plot for the resolved peaks of 3-Me-cp extracted from **1-R** cage showing 14% *ee*.

(c) $\pm$ 3-Me-cp with 1-S



Front Signal Results				
Retention Time	Area	Area %	Height	Height %
18.676	534751	58.09	121036	61.77
18.836	385745	41.91	74900	38.23
Totals	920496	100.00	195936	100.00

Figure A3.38: GC chromatogram and analysis plot for the resolved peaks of 3-Me-cp extracted from **1-S** cage showing 16% *ee*.

Enantiomeric separation of 3-ethylcyclopentanone:

Column used: Supelco β -dex (30 m* 0.25 mm * 0.25 μ m),

Split ratio 30:1,

Inlet temperature 210 $^{\circ}$ C,

Column pressure 7 psi

Temperature programme: started at 50 $^{\circ}$ C, and heated at the rate of 10 $^{\circ}$ C to 90 $^{\circ}$ C. It was further heated at the rate of 3 $^{\circ}$ C to 130 $^{\circ}$ C and hold for hold for 3 mins. Again it was heated at the rate of 2 $^{\circ}$ C to 150 $^{\circ}$ C. Finally it was heated at the rate of 10 $^{\circ}$ C to 210 $^{\circ}$ C.

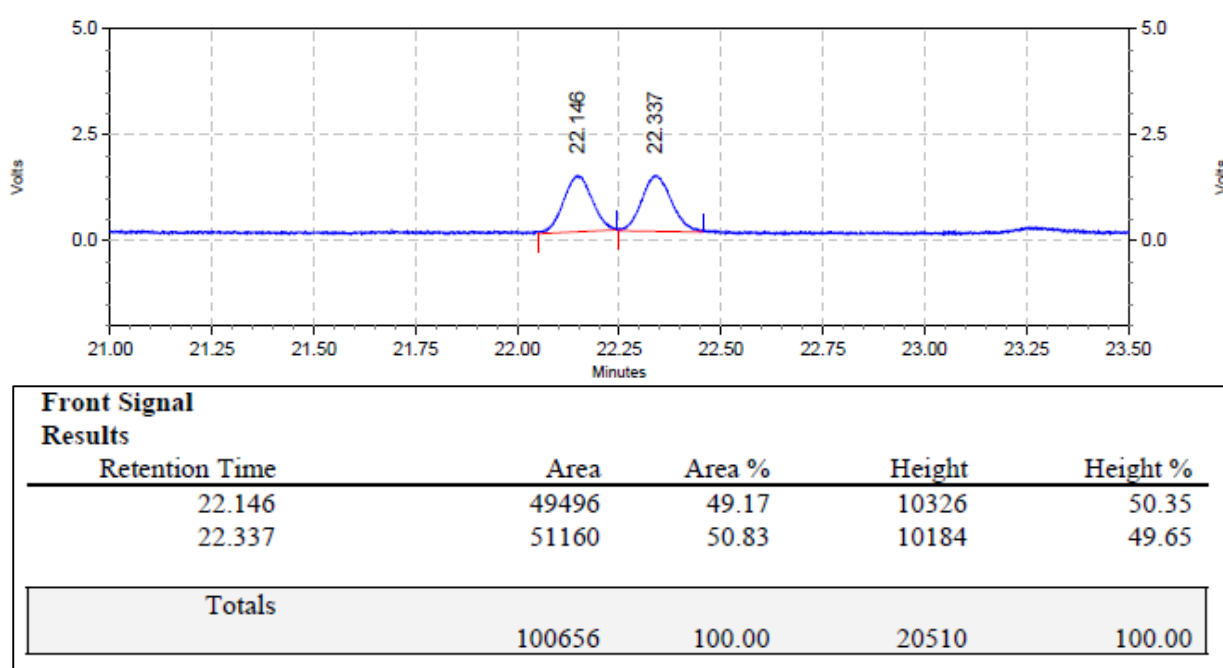
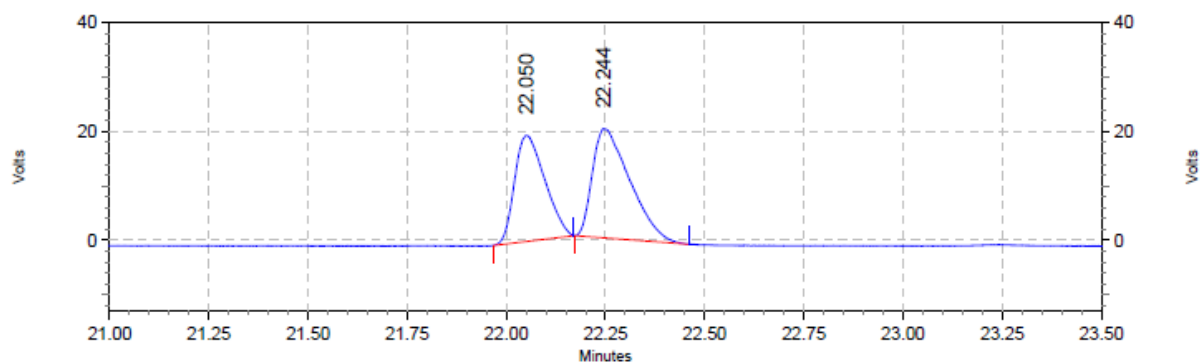
(a) Neat ± 3 -Et-cp:

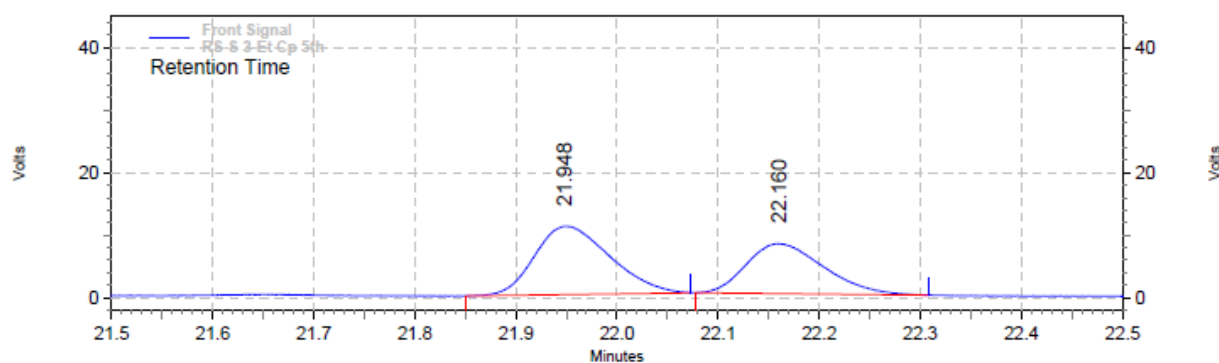
Figure A3.39: GC chromatogram and analysis plot showing the resolved peaks for rac-
-3-ethylcyclopentanone.

(b) ± 3 -Et-cp with 1-R:

Front Signal Results				
Retention Time	Area	Area %	Height	Height %
22.050	794248	43.93	149918	49.26
22.244	1013781	56.07	154401	50.74
Totals				
	1808029	100.00	304319	100.00

Figure A3.40: GC chromatogram and analysis plot for the resolved peaks of 3-Et-cp extracted from 1-R cage showing 12% ee.

(c) 3-Et-cp with 1-S:



Front Signal Results				
Retention Time	Area	Area %	Height	Height %
21.948	434606	57.09	84147	57.77
22.160	326657	42.91	61504	42.23
Totals				
	761263	100.00	145651	100.00

Figure A3.41: GC chromatogram and analysis plot for the resolved peaks of 3-Et-cp extracted from 1-S cage showing 14% ee.

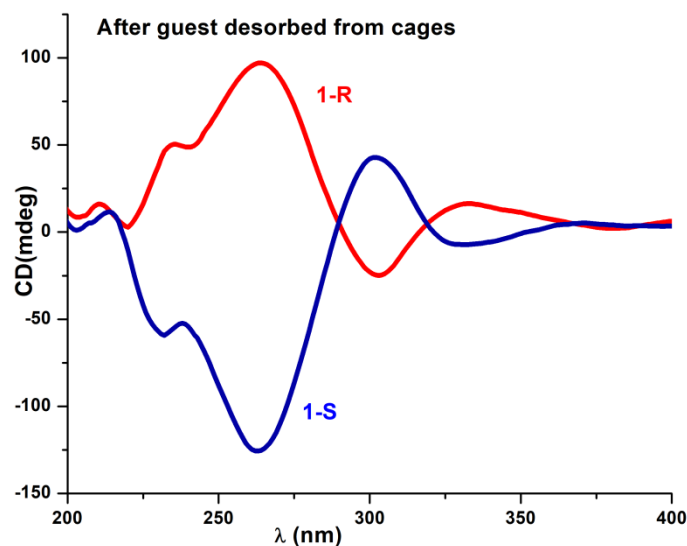


Figure A3.42: CD spectra of **1-R** and **1-S** cages obtained after desorbing bbl guest molecules.

Table A3.1: Specific rotation (α_D) values for cages **1-R** and **1-S** after desorbing bbl guests and its comparison with as-made samples

Cages	α_D
1-R (as made)	+666°
1-R (after bbl desorp.)	+668°
1-S (as made)	-684°
1-S (after bbl dessorp.)	-679°

Table A3.2: Unit-cell parameters for the crystals obtained by re-crystallization after desorbing bbl guest molecules.

1-R Crystal 1	1-R Crystal 2	1-R Crystal 3
$a = 28.01 \text{ \AA}; \alpha = 90^\circ$ $b = 28.01 \text{ \AA}; \beta = 90^\circ$	$a = 27.93 \text{ \AA}; \alpha = 90^\circ$ $b = 27.93 \text{ \AA}; \beta = 90^\circ$	$a = 27.37 \text{ \AA}; \alpha = 90^\circ$ $b = 27.37 \text{ \AA}; \beta = 90^\circ$

$c = 28.01 \text{ \AA}; \gamma = 90^\circ$ Volume = $21969 \text{ \AA}^3$	$c = 27.93 \text{ \AA}; \gamma = 90^\circ$ Volume = $21795 \text{ \AA}^3$	$c = 27.37 \text{ \AA}; \gamma = 90^\circ$ Volume = $20503 \text{ \AA}^3$
1-S Crystal 1	1-S Crystal 2	1-S Crystal 3
$a = 27.78(4) \text{ \AA}; \alpha = 90^\circ$ $b = 27.78(4) \text{ \AA}; \beta = 90^\circ$ $c = 27.78(4) \text{ \AA}; \gamma = 90^\circ$ Volume = $21852 \text{ \AA}^3$	$a = 27.83(4) \text{ \AA}; \alpha = 90^\circ$ $b = 27.83(4) \text{ \AA}; \beta = 90^\circ$ $c = 27.83(4) \text{ \AA}; \gamma = 90^\circ$ Volume = $21549 \text{ \AA}^3$	$a = 28.07(6) \text{ \AA}; \alpha = 90^\circ$ $b = 28.07(6) \text{ \AA}; \beta = 90^\circ$ $c = 28.07(6) \text{ \AA}; \gamma = 90^\circ$ Volume = $22124 \text{ \AA}^3$

Table A4.1 Selected bond lengths (Å) and bond angles (°) for 2-R and 2-S in I23 phase.

CAGE	Bond Lengths		Bond Angles
2-R	Pd01-N1	1.999(9)	N1-Pd01-O3 100.3(3)
	Pd01-O3	2.031(8)	N1-Pd01-N1 77.0(6)
	Pd01-N1	2.037(9)	O3-Pd01-N1 176.9(4)
	Pd01-O2	2.050(7)	N1-Pd01-O2 178.8(4)
	Pd01-P1	2.738(4)	O3-Pd01-O2 80.8(3)
	Pd01-Pd01	3.1151(16)	N1-Pd01-O2 101.9(3)
	Pd01-Pd01	3.1151(16)	N1-Pd01-P1 38.5(3)
	Cl1-C11	1.704(12)	O3-Pd01-P1 138.8(2)
	P1-O1	1.450(13)	N1-Pd01-P1 38.6(3)
	P1-N1	1.711(10)	O2-Pd01-P1 140.4(2)
	P1-N1	1.711(10)	N1-Pd01-Pd01 39.9(3)
	P1-N1	1.711(10)	O3-Pd01-Pd01 95.8(2)
	P1-Pd01	2.738(4)	N1-Pd01-Pd01 81.2(3)
	P1-Pd01	2.738(4)	O2-Pd01-Pd01 139.56(19)
	O2-C9	1.282(12)	P1-Pd01-Pd01 55.32(5)
	O3-C10	1.233(12)	N1-Pd01-Pd01 81.7(3)
	N1-C2	1.528(17)	O3-Pd01-Pd01 139.4(2)
	N1-Pd01	2.037(9)	N1-Pd01-Pd01 39.0(2)
	C1-C2	1.55(2)	O2-Pd01-Pd01 97.1(2)
	C1-H1A	0.9600	P1-Pd01-Pd01 55.32(5)
	C1-H1B	0.9600	Pd01-Pd01-Pd01 60.0
	C1-H1C	0.9600	O1-P1-N1 122.0(3)
	C2-C3	1.43(2)	O1-P1-N1 122.0(3)
	C2-H2	0.9800	N1-P1-N1 94.6(4)
	C3-C4	1.3900	O1-P1-N1 122.0(3)

C3-C8	1.3900	N1-P1-N1 94.6(4)
C4-C5	1.3900	N1-P1-N1 94.6(4)
C4-H4	0.9300	O1-P1-Pd01 138.93(6)
C5-C6	1.3900	N1-P1-Pd01 48.0(3)
C5-H5	0.9300	N1-P1-Pd01 46.7(3)
C6-C7	1.3900	N1-P1-Pd01 99.1(3)
C6-H6	0.9300	O1-P1-Pd01 138.93(6)
C7-C8	1.3900	N1-P1-Pd01 46.7(3)
C7-H7	0.9300	N1-P1-Pd01 99.1(3)
C8-H8	0.9300	N1-P1-Pd01 48.0(3)
C9-C11	1.380(14)	Pd01-P1-Pd01 69.35(10)
C9-C10	1.566(16)	O1-P1-Pd01 138.93(6)
C10-C11	1.400(15)	N1-P1-Pd01 99.1(3)
C11-C9	1.380(14)	N1-P1-Pd01 48.0(3)
		N1-P1-Pd01 46.7(3)
		Pd01-P1-Pd01 69.35(10)
		Pd01-P1-Pd01 69.35(10)
		C9-O2-Pd01 112.5(7)
		C10-O3-Pd01 115.7(8)
		C2-N1-P1 125.7(7)
		C2-N1-Pd01 117.6(8)
		P1-N1-Pd01 94.8(5)
		C2-N1-Pd01 118.7(9)
		P1-N1-Pd01 93.4(4)
		Pd01-N1-Pd01 101.0(4)
		C2-C1-H1A 109.5
		C2-C1-H1B 109.5

	H1A-C1-H1B 109.5
	C2-C1-H1C 109.5
	H1A-C1-H1C 109.5
	H1B-C1-H1C 109.5
	C3-C2-N1 113.9(13)
	C3-C2-C1 116.1(13)
	N1-C2-C1 109.6(14)
	C3-C2-H2 105.4
	N1-C2-H2 105.4
	C1-C2-H2 105.4
	C4-C3-C8 120.0
	C4-C3-C2 123.4(11)
	C8-C3-C2 116.5(11)
	C5-C4-C3 120.0
	C5-C4-H4 120.0
	C3-C4-H4 120.0
	C6-C5-C4 120.0
	C6-C5-H5 120.0
	C4-C5-H5 120.0
	C5-C6-C7 120.0
	C5-C6-H6 120.0
	C7-C6-H6 120.0
	C6-C7-C8 120.0
	C6-C7-H7 120.0
	C8-C7-H7 120.0
	C7-C8-C3 120.0
	C7-C8-H8 120.0

			C3-C8-H8 120.0 O2-C9-C11 123.3(10) O2-C9-C10 115.9(9) C11-C9-C10 120.7(10) O3-C10-C11 126.4(11) O3-C10-C9 114.8(10) C11-C10-C9 118.7(9) C9-C11-C10 120.5(10) C9-C11-Cl1 119.6(9) C10-C11-Cl1 119.9(9)
2-S	Pd1-N1	2.013(7)	N1-Pd1-N1 76.9(4)
	Pd1-N1	2.028(8)	N1-Pd1-O1L 100.0(3)
	Pd1-O1L	2.029(7)	N1-Pd1-O1L 176.4(3)
	Pd1-O2L	2.046(6)	N1-Pd1-O2L 178.0(3)
	Pd1-P1	2.739(3)	N1-Pd1-O2L 102.2(3)
	Pd1-Pd1	3.0837(14)	O1L-Pd1-O2L 80.9(2)
	Pd1-Pd1	3.0837(14)	N1-Pd1-P1 38.4(2)
	P1-O1	1.449(10)	N1-Pd1-P1 38.5(2)
	P1-N1	1.708(8)	O1L-Pd1-P1 138.42(17)
	P1-N1	1.708(8)	O2L-Pd1-P1 140.63(17)
	P1-N1	1.708(8)	N1-Pd1-Pd1 82.0(2)
	P1-Pd1	2.739(3)	N1-Pd1-Pd1 40.10(19)
	P1-Pd1	2.739(3)	O1L-Pd1-Pd1 138.23(18)
	N1-C1	1.504(15)	O2L-Pd1-Pd1 96.15(18)
	N1-Pd1	2.013(7)	P1-Pd1-Pd1 55.75(4)
	C1-C3	1.408(17)	N1-Pd1-Pd1 40.5(2)
	C1-C2	1.58(2)	N1-Pd1-Pd1 81.8(2)

C1-H1	0.9800	O1L-Pd1-Pd1 94.71(19)
C2-H2A	0.9600	O2L-Pd1-Pd1 137.84(16)
C2-H2B	0.9600	P1-Pd1-Pd1 55.75(4)
C2-H2C	0.9600	Pd1-Pd1-Pd1 60.0
C3-C4	1.3900	O1-P1-N1 121.9(2)
C3-C8	1.3900	O1-P1-N1 121.9(2)
C4-C5	1.3900	N1-P1-N1 94.7(3)
C4-H4	0.9300	O1-P1-N1 121.9(2)
C5-C6	1.3900	N1-P1-N1 94.7(3)
C5-H5	0.9300	N1-P1-N1 94.7(3)
C6-C7	1.3900	O1-P1-Pd1 139.46(5)
C6-H6	0.9300	N1-P1-Pd1 98.7(3)
C7-C8	1.3900	N1-P1-Pd1 47.6(3)
C7-H7	0.9300	N1-P1-Pd1 47.1(3)
C8-H8	0.9300	O1-P1-Pd1 139.46(5)
C1L-O1L	1.228(10)	N1-P1-Pd1 47.6(3)
C1L-C2L	1.407(12)	N1-P1-Pd1 47.1(3)
C1L-C3L	1.558(12)	N1-P1-Pd1 98.7(3)
C2L-C3L	1.385(12)	Pd1-P1-Pd1 68.51(8)
C2L-C11	1.725(9)	O1-P1-Pd1 139.46(5)
C3L-O2L	1.280(10)	N1-P1-Pd1 47.1(3)
C3L-C1L	1.558(12)	N1-P1-Pd1 98.7(3)
O2L-Pd1	2.046(6)	N1-P1-Pd1 47.6(3)
		Pd1-P1-Pd1 68.51(8)
		Pd1-P1-Pd1 68.51(8)
		C1-N1-P1 126.2(6)
		C1-N1-Pd1 117.4(7)

	P1-N1-Pd1 94.4(4)
	C1-N1-Pd1 119.4(7)
	P1-N1-Pd1 93.9(4)
	Pd1-N1-Pd1 99.4(3)
	C3-C1-N1 114.5(11)
	C3-C1-C2 112.0(10)
	N1-C1-C2 112.1(12)
	C3-C1-H1 105.8
	N1-C1-H1 105.8
	C2-C1-H1 105.8
	C1-C2-H2A 109.5
	C1-C2-H2B 109.5
	H2A-C2-H2B 109.5
	C1-C2-H2C 109.5
	H2A-C2-H2C 109.5
	H2B-C2-H2C 109.5
	C4-C3-C8 120.0
	C4-C3-C1 125.5(9)
	C8-C3-C1 114.3(9)
	C3-C4-C5 120.0
	C3-C4-H4 120.0
	C5-C4-H4 120.0
	C6-C5-C4 120.0
	C6-C5-H5 120.0
	C4-C5-H5 120.0
	C7-C6-C5 120.0
	C7-C6-H6 120.0

	C5-C6-H6 120.0
	C6-C7-C8 120.0
	C6-C7-H7 120.0
	C8-C7-H7 120.0
	C7-C8-C3 120.0
	C7-C8-H8 120.0
	C3-C8-H8 120.0
	O1L-C1L-C2L 126.8(9)
	O1L-C1L-C3L 116.0(8)
	C2L-C1L-C3L 117.2(8)
	C3L-C2L-C1L 121.9(8)
	C3L-C2L-Cl1 119.0(7)
	C1L-C2L-Cl1 119.1(7)
	O2L-C3L-C2L 123.7(8)
	O2L-C3L-C1L 115.4(7)
	C2L-C3L-C1L 120.9(7)
	C1L-O1L-Pd1 114.9(6)
	C3L-O2L-Pd1 112.7(5)

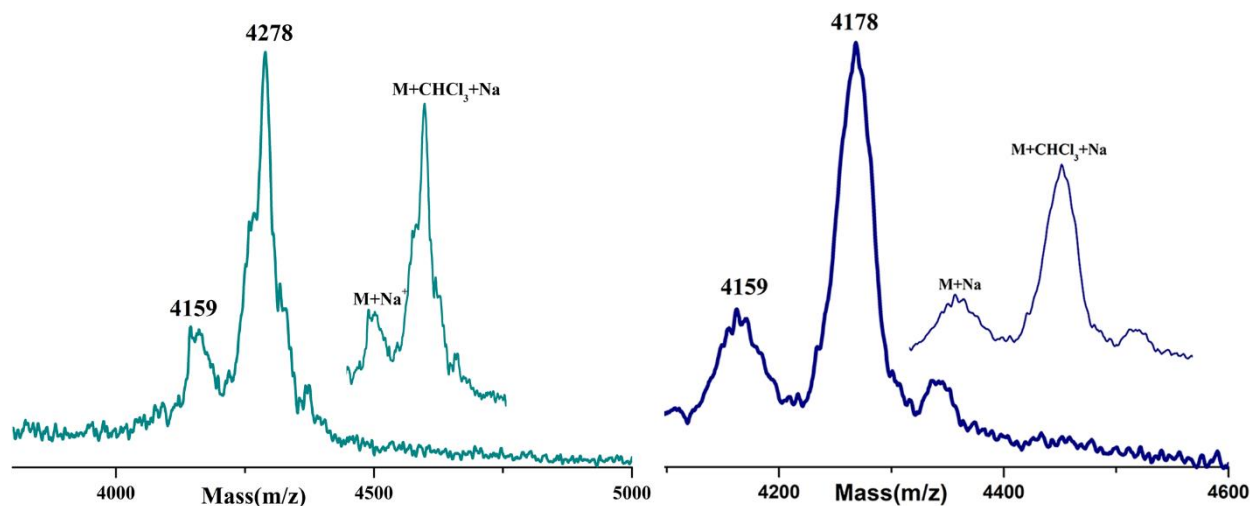


Figure A4.1: MALDI-TOF (Linear mode) spectrum of 2-R (left) and 2-S (right).

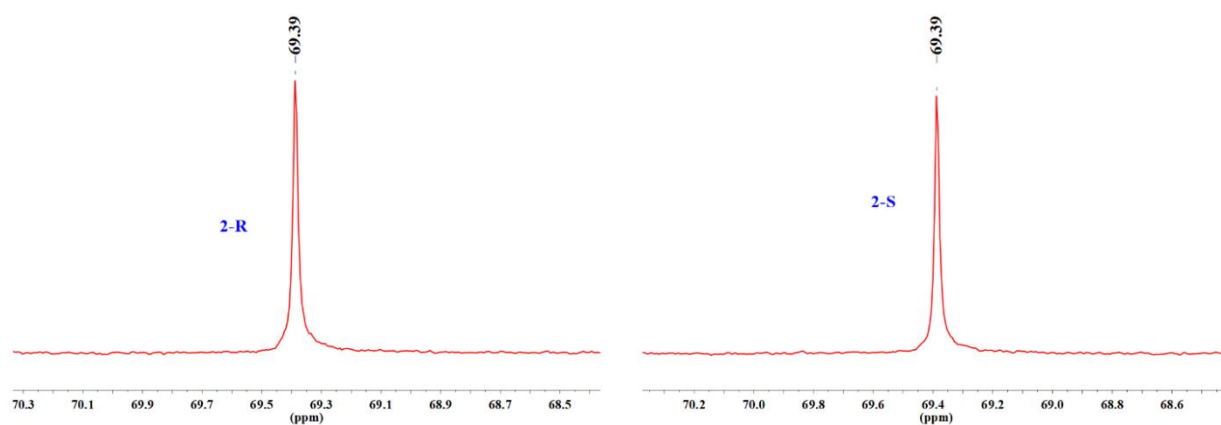
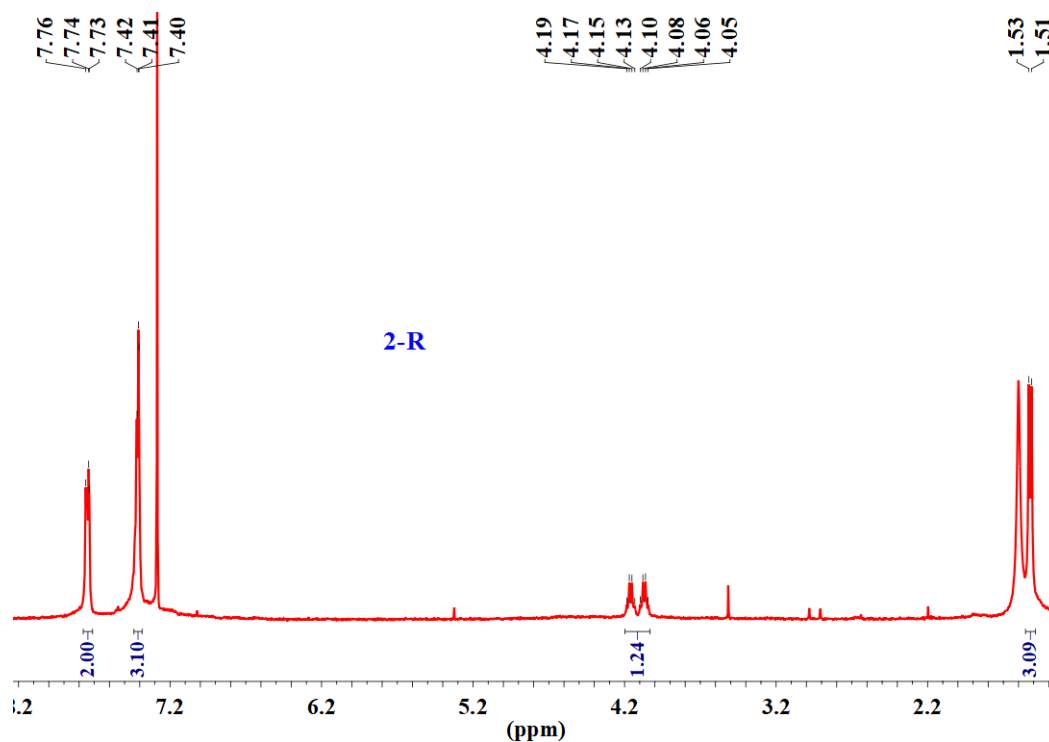
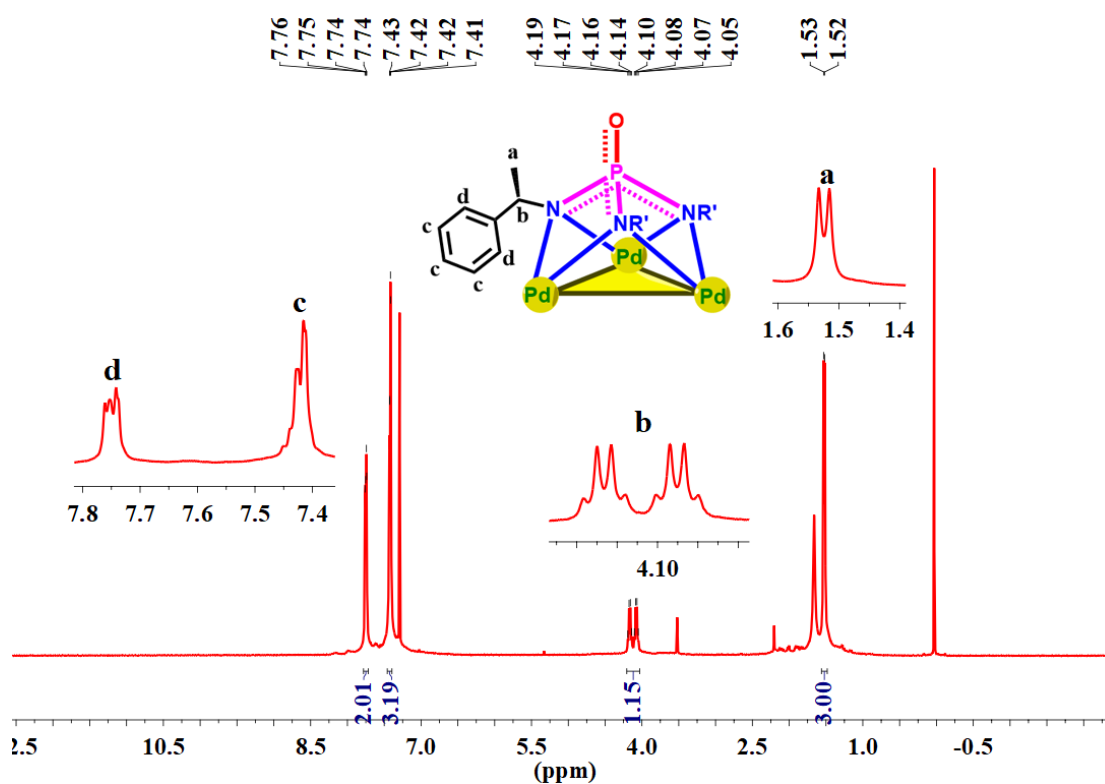
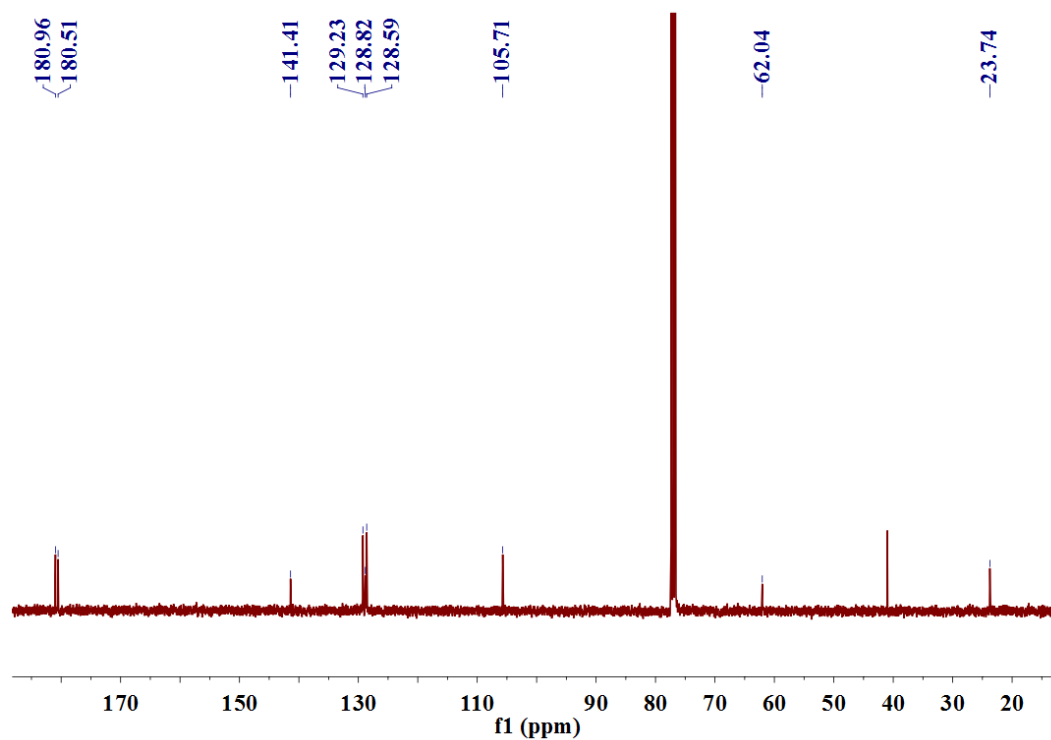
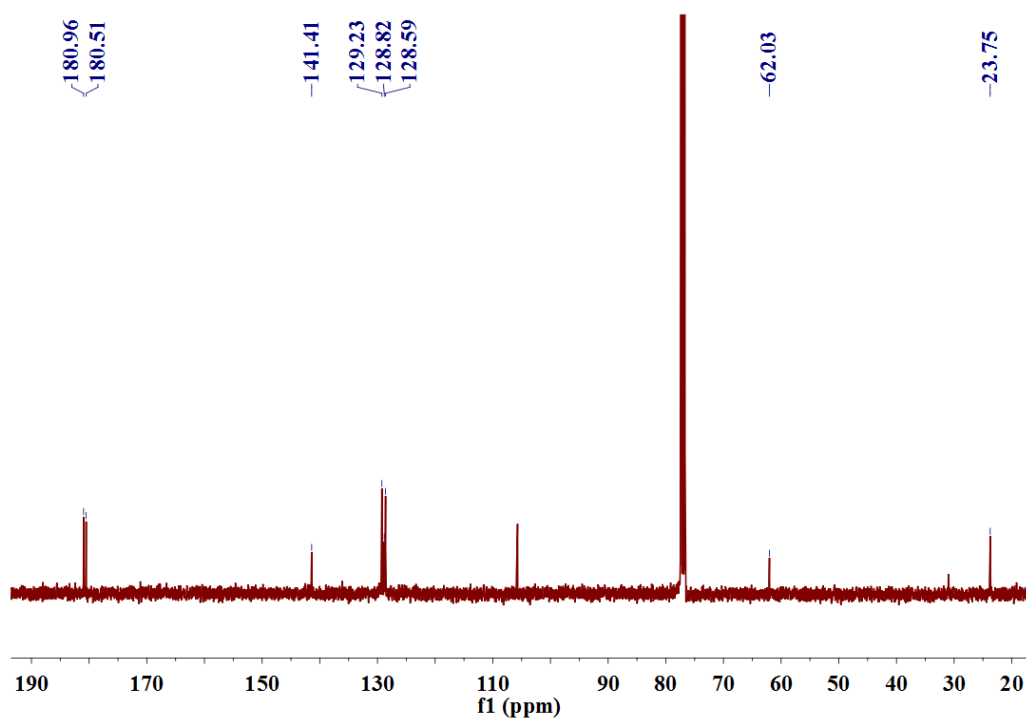


Figure A4.2: ^{31}P NMR spectra of 2-R and 2-S.

Figure A4.3: ^1H NMR spectrum of 2-R.Figure A4.4: ^1H NMR spectrum of 2-S.

**Figure A4.5:** ¹³C NMR spectra of 2-R.**Figure A4.6:** ¹³C NMR spectra of 2-S.

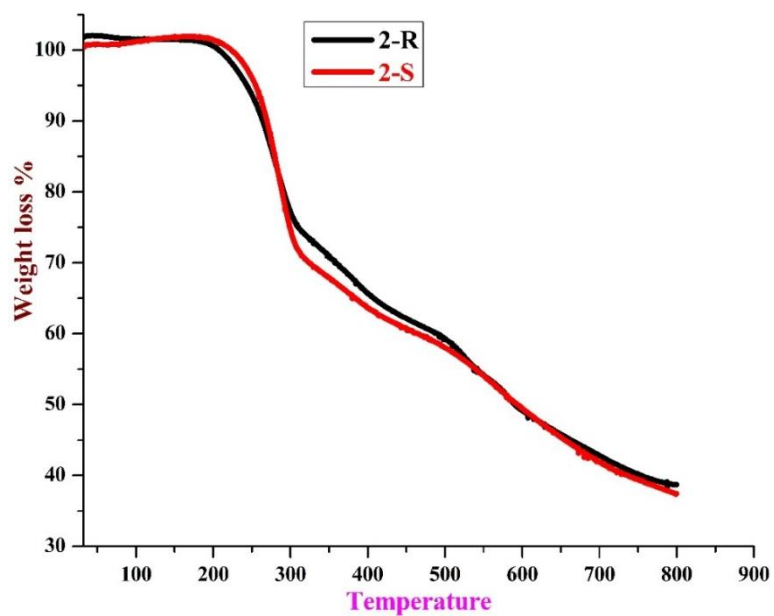


Figure A4.7: TGA graph of 2-R and 2-S.

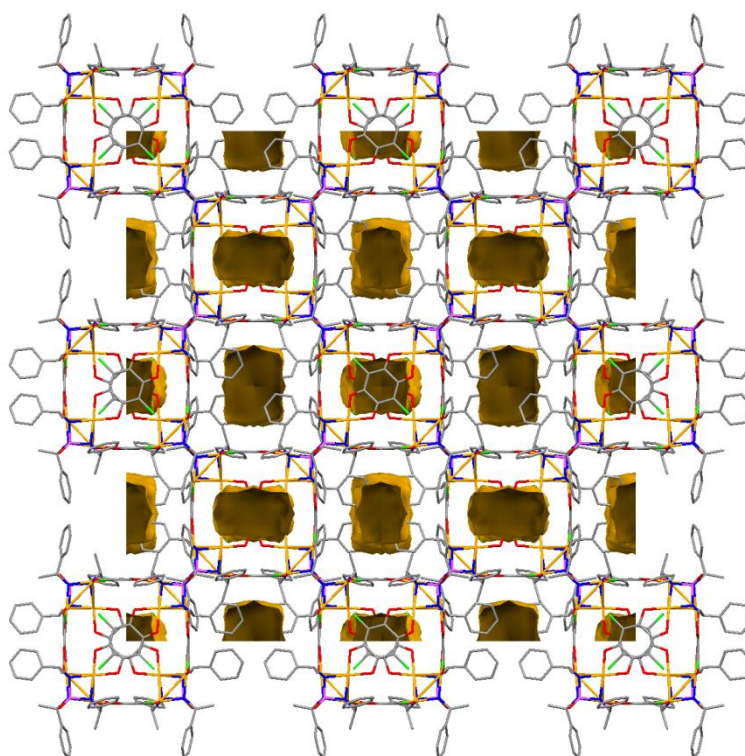


Figure A4.8: 2*2*2 Packing structure of 2-R along with its solvent accessible surface in cubic I_{23} phase.

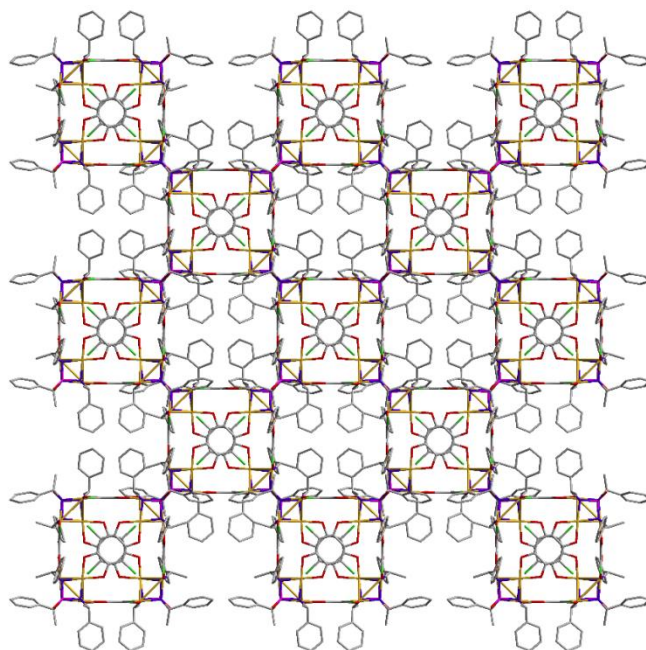
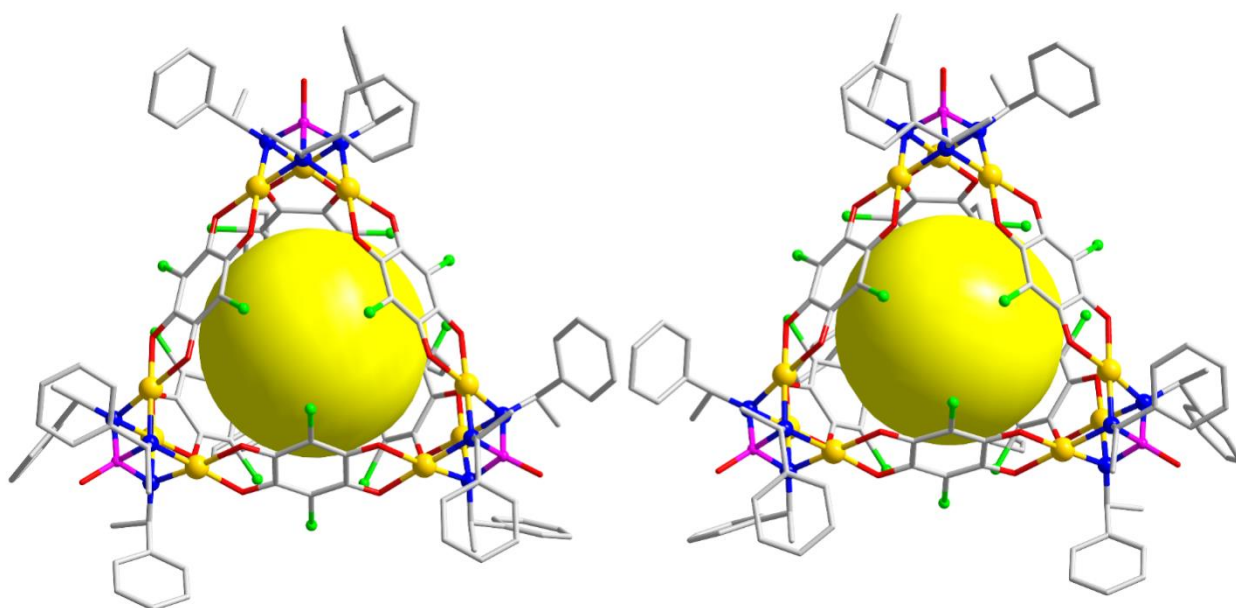


Figure A4.9: 2*2*2 Packing structure of 2-S in cubic $I23$ phase.



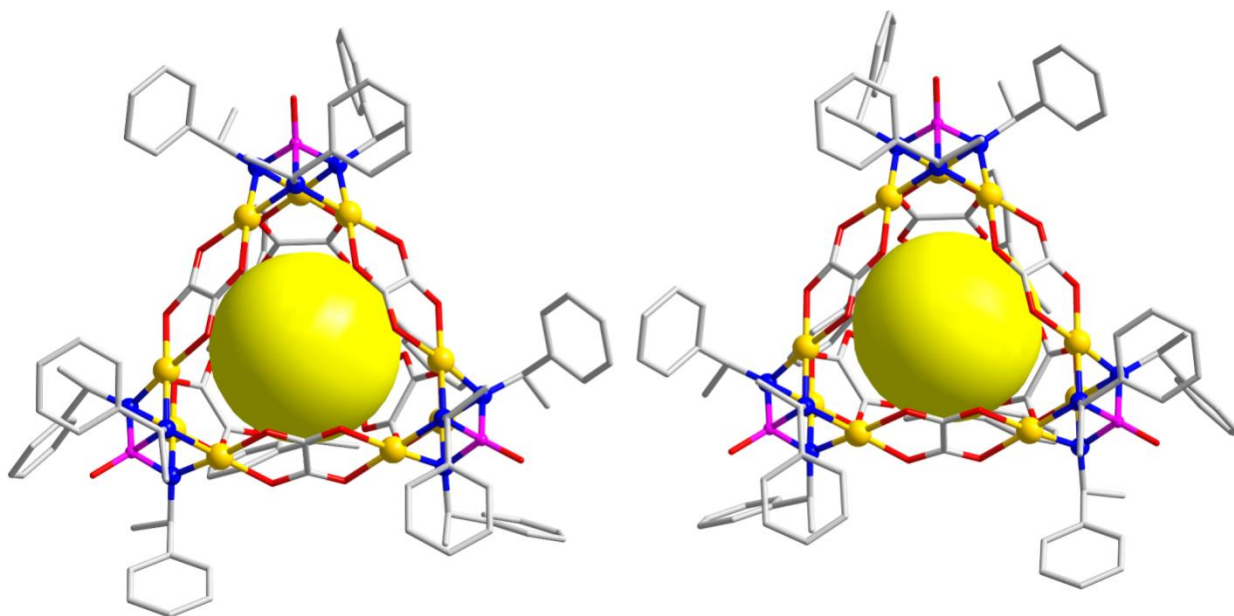


Figure A4.10: Structural similarities of **2-R** and **2-S** with that of **1-R** and **1-S**. Yellow spheres represent the intrinsic voids of these cages: $224 \text{ \AA}^3$ for **2-R** and **2-S** and $86 \text{ \AA}^3$ for **1-R** and **1-S**.

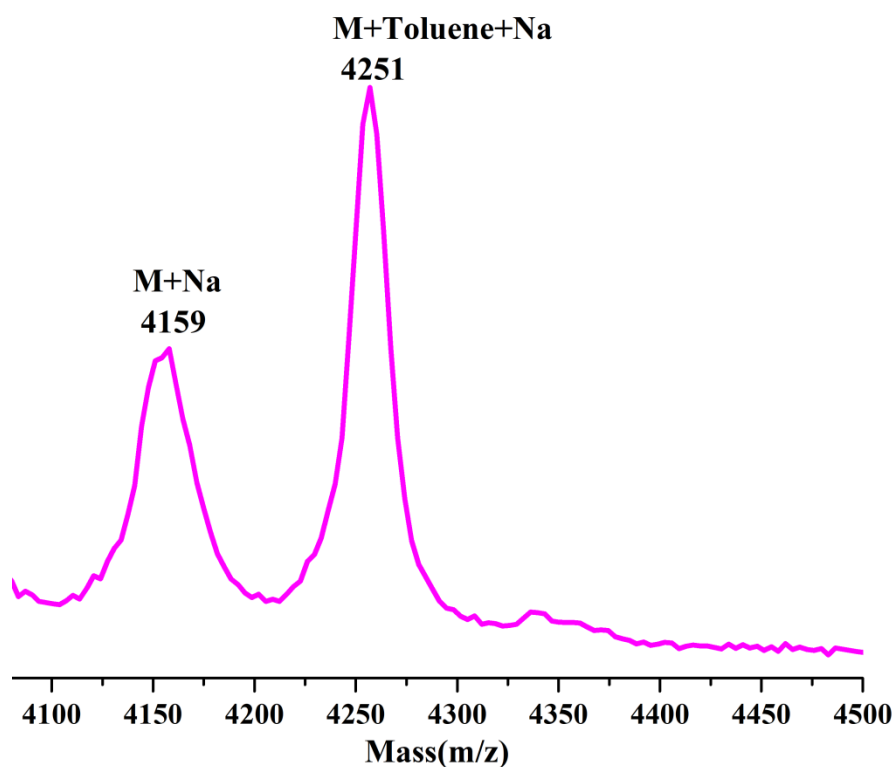


Figure A4.11: MALDI-TOF (Linear mode) spectrum of Toluene $\subset$ **2-S**.

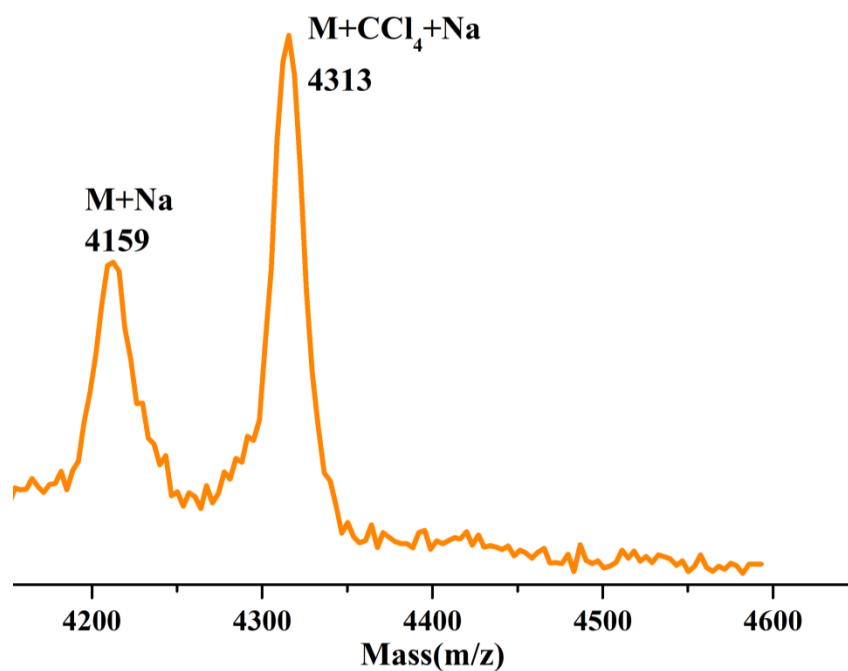


Figure A4.12: MALDI-TOF (Linear mode) spectrum of $CCl_4 + 2-S$.

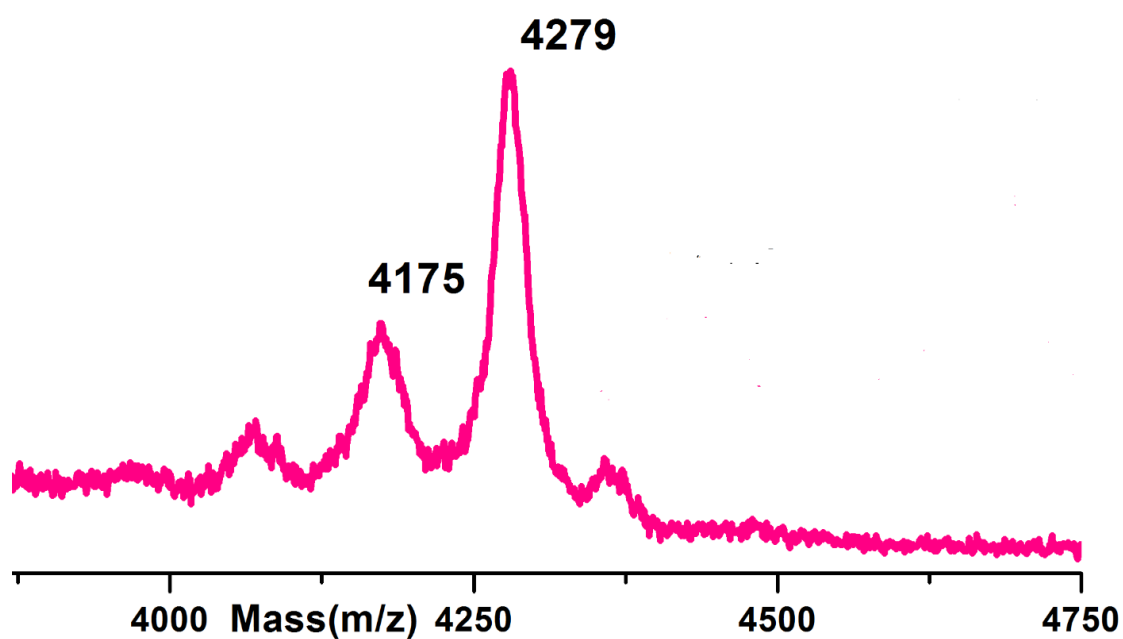


Figure A4.13: MALDI-TOF Mass spectra of $\pm SO$ treated with 2-R.

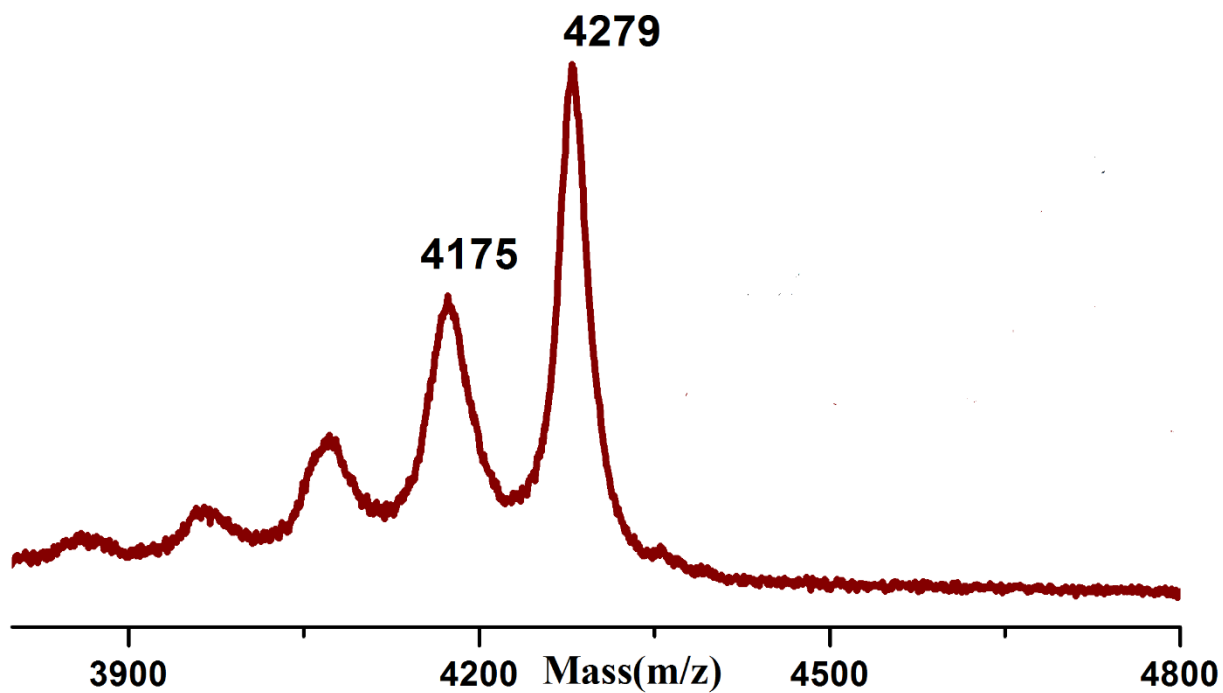


Figure A4.14: MALDI-TOF Mass spectra of $\pm$ SO treated with 2-S.

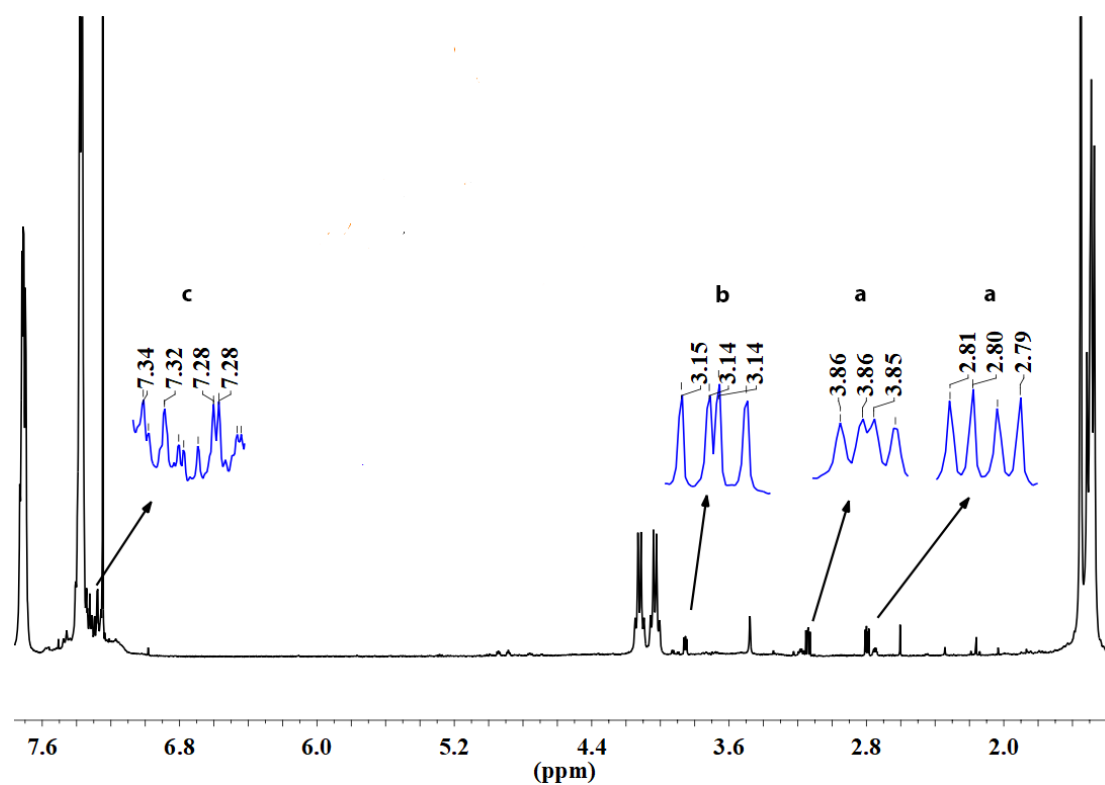


Figure A4.15: ^1H NMR spectra of $\pm$ SO treated with 2-R.

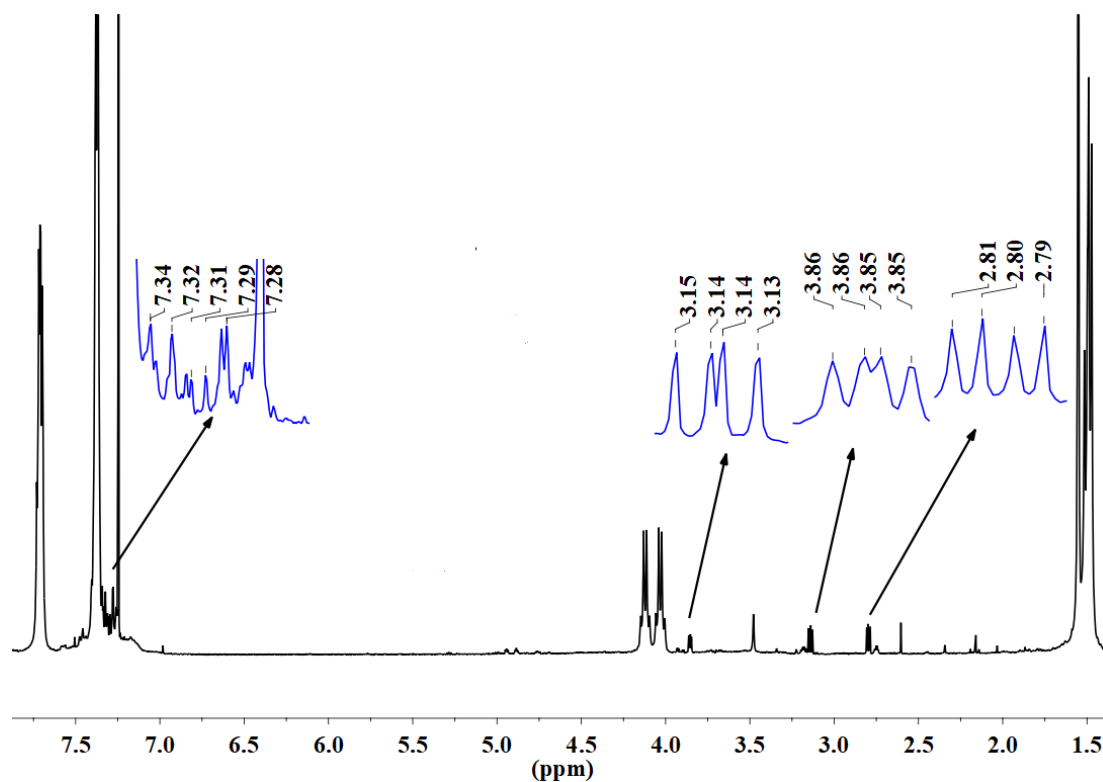


Figure A4.16: ¹H NMR spectra of $\pm$ SO treated with 2-S.

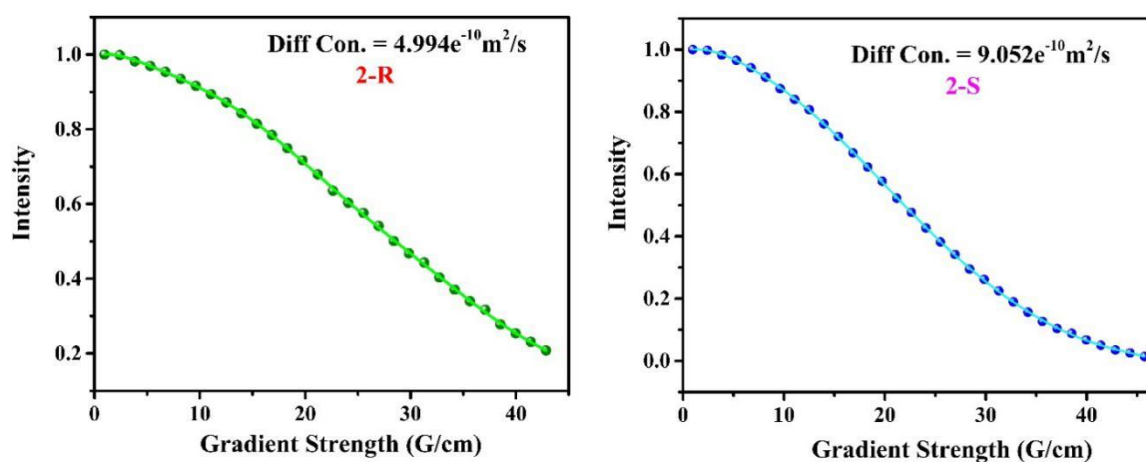


Figure A4.17: ¹H- DOSY NMR spectra of cages 2-R and 2-S.

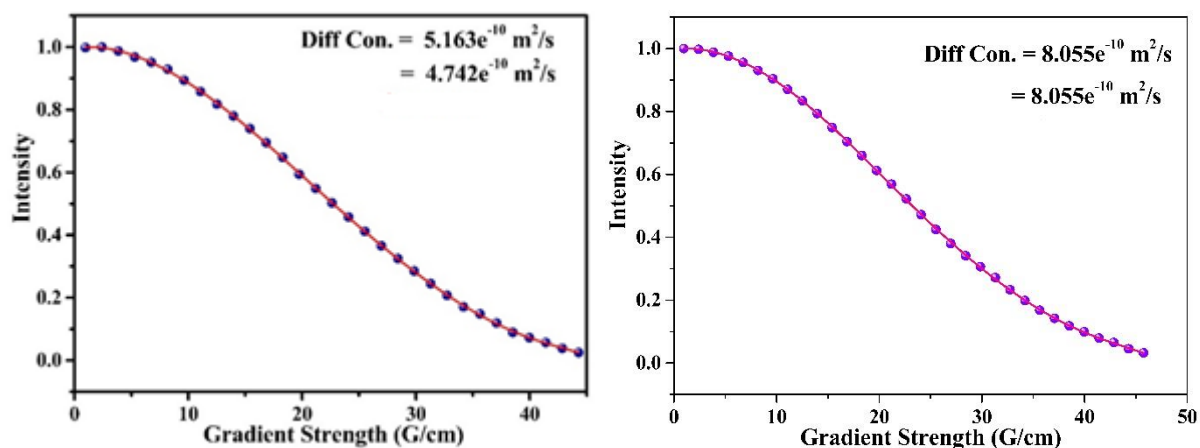


Figure A4.18: ^1H -DOSY NMR spectra of cages 2-R and 2-S treated with $\pm\text{SO}$.

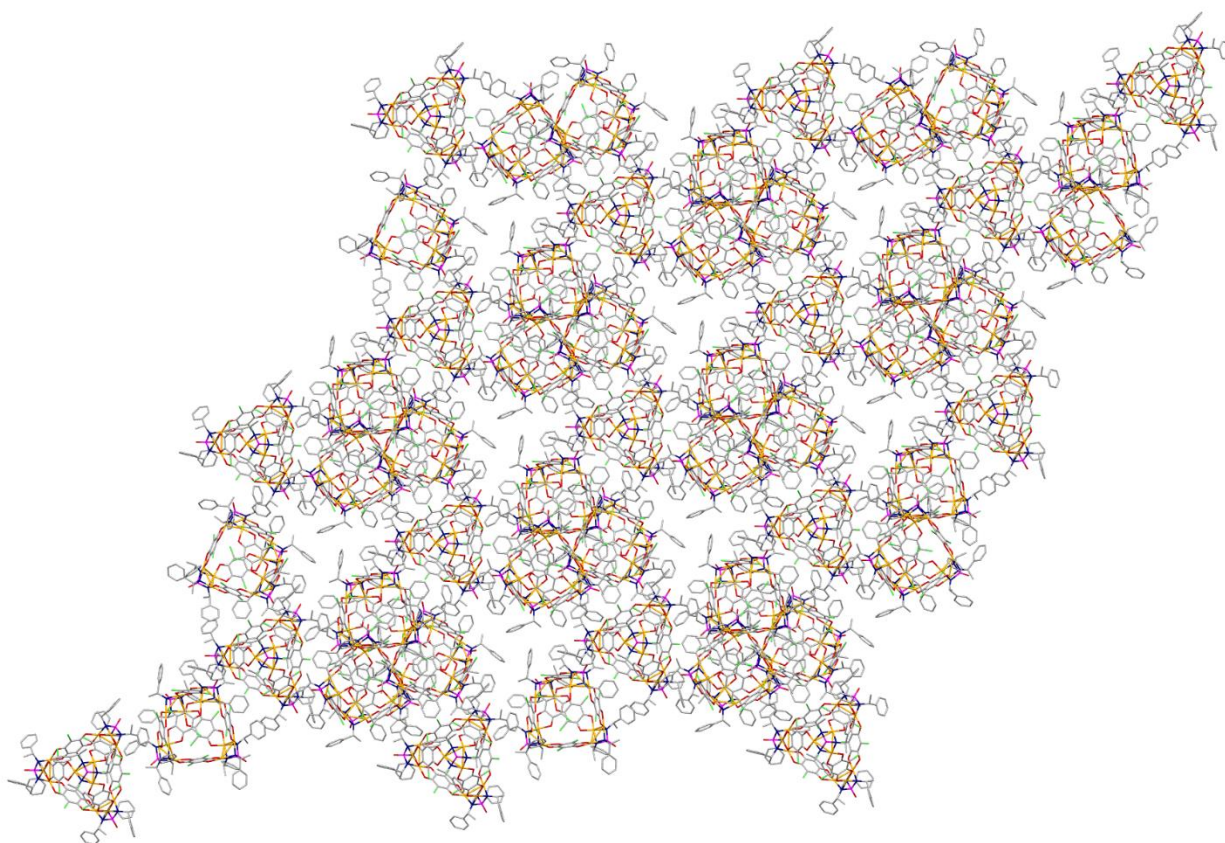


Figure A4.19: SCXRD generated packing structure of $\pm\text{SO}$ treated 2-R crystallized in the $R3$ space group and its $2 \times 2 \times 2$ packing structure.

Chiral HPLC chromatogram for $\pm$ SO

Chiral HPLC chromatogram for $\pm$ SO were performed by using the ChiralCel OD-H column with a flow rate of 0.5 mL/min using 99:1 hexane: isopropanol solvents eluents.

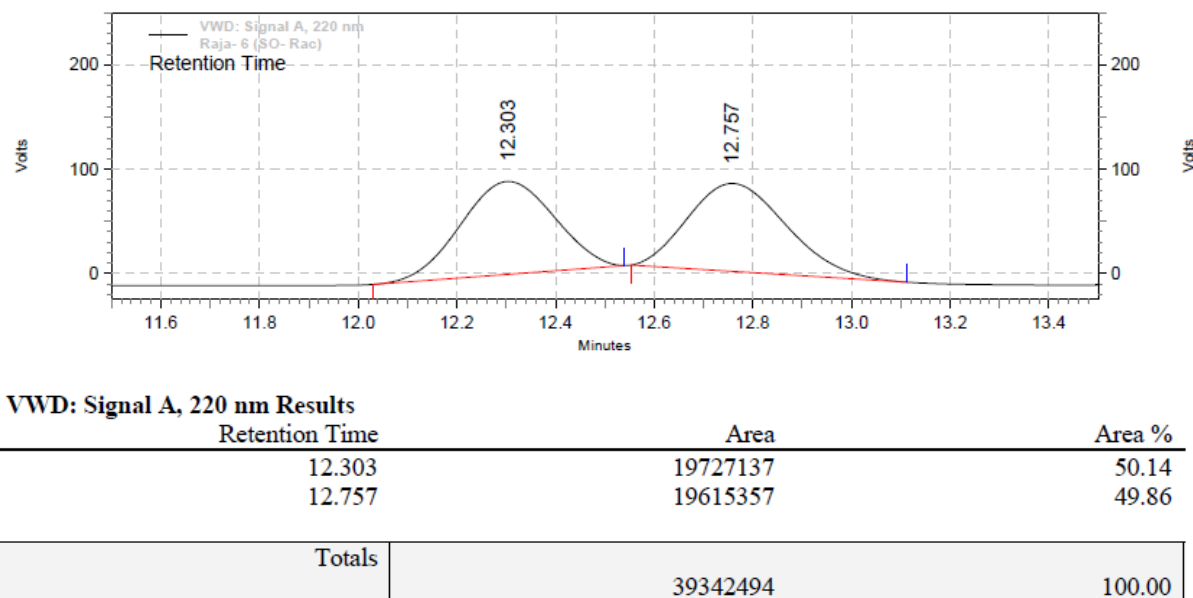


Figure A4.20: Chiral HPLC chromatogram for untreated $\pm$ SO.

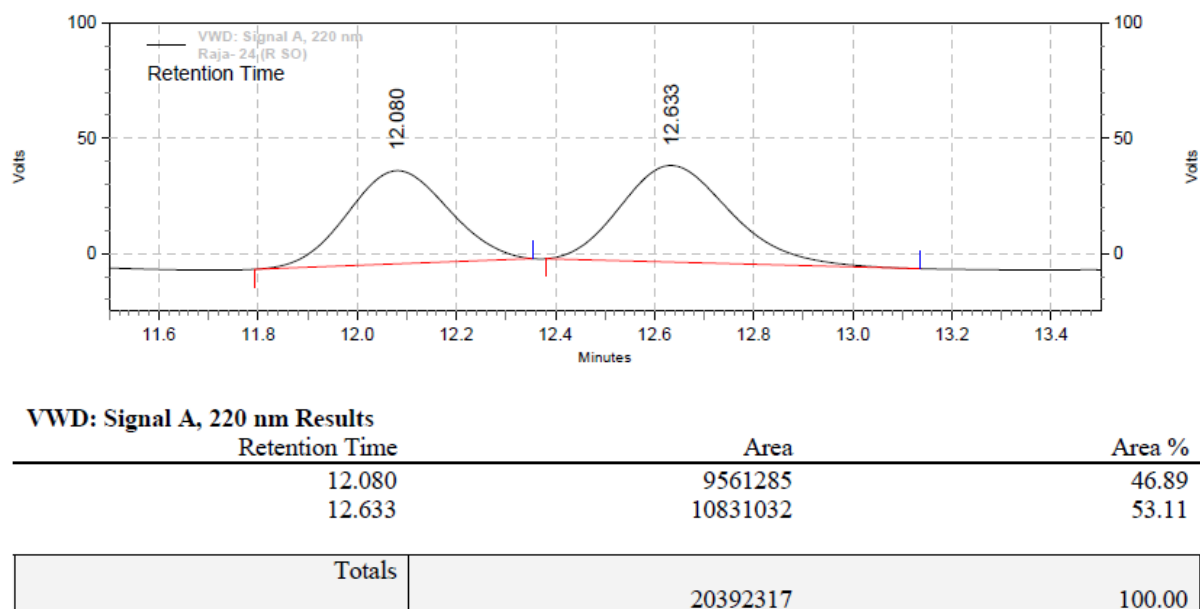


Figure A4.21: Chiral HPLC chromatogram for separation of $\pm$ SO by 2-R, ee = 7%.

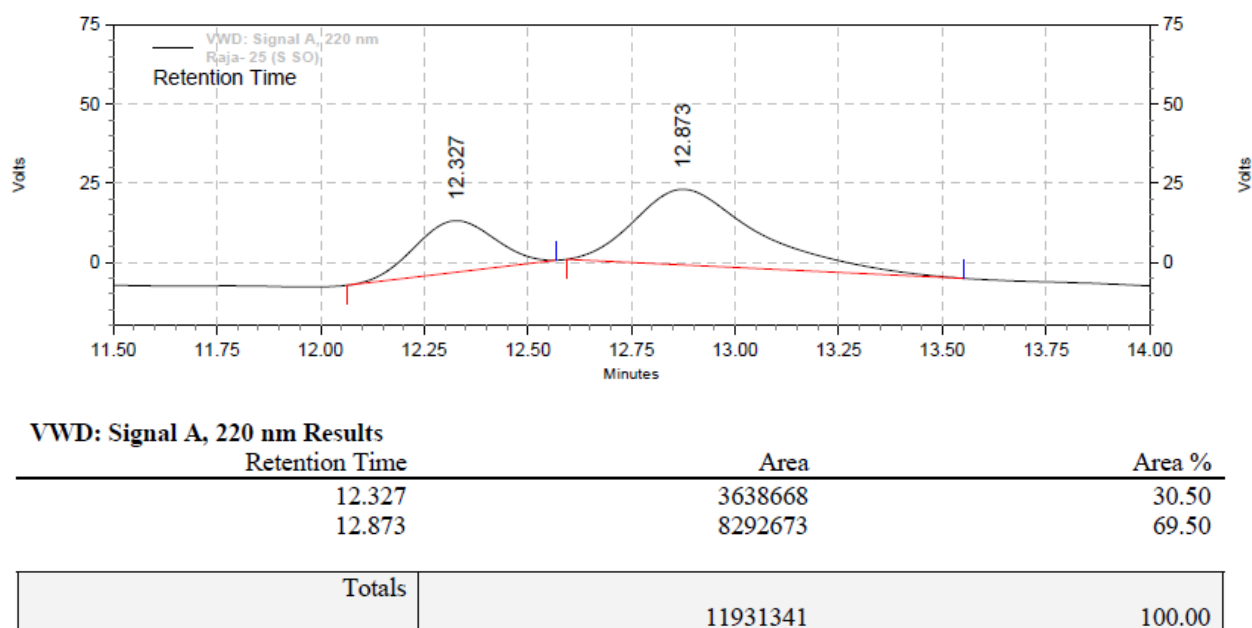


Figure A4.22: Chiral HPLC chromatogram for separation of $\pm$ SO by 2-S, $ee = 39\%$.

Chiral HPLC chromatogram for $\pm$ F-SO

Chiral HPLC chromatogram for $\pm$ F-SO were performed by using the ChiralCel OD-H column with a flow rate of 0.5 mL/min using 98:2 hexane: isopropanol solvents eluents.

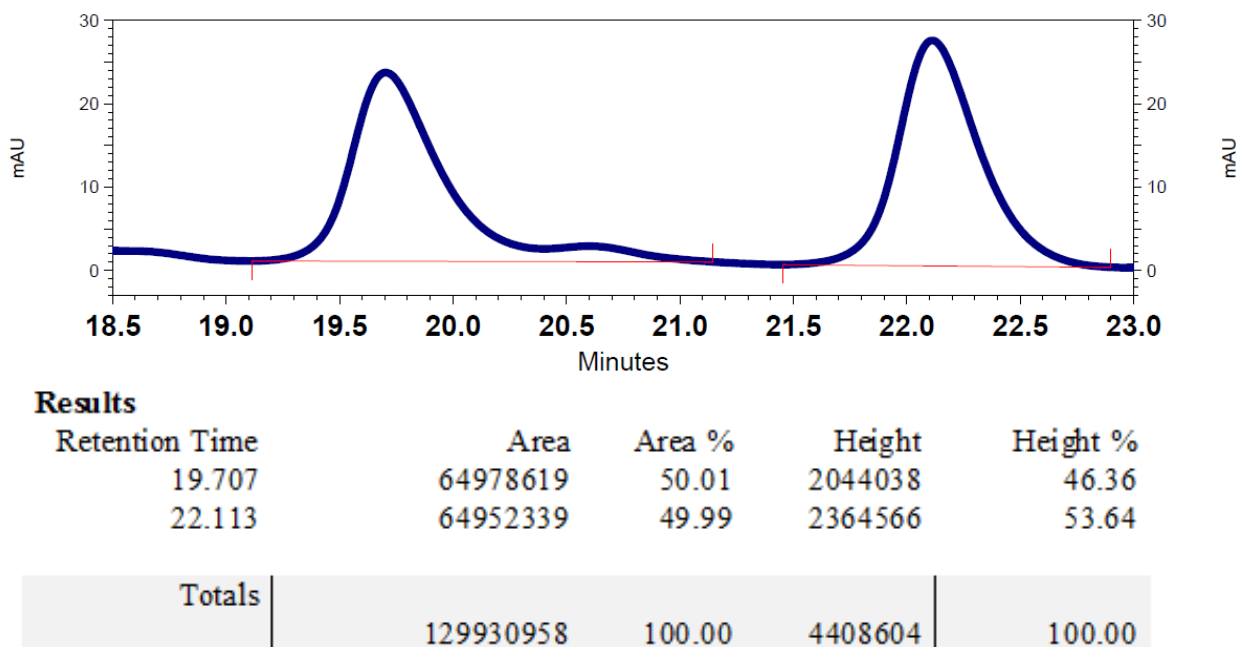
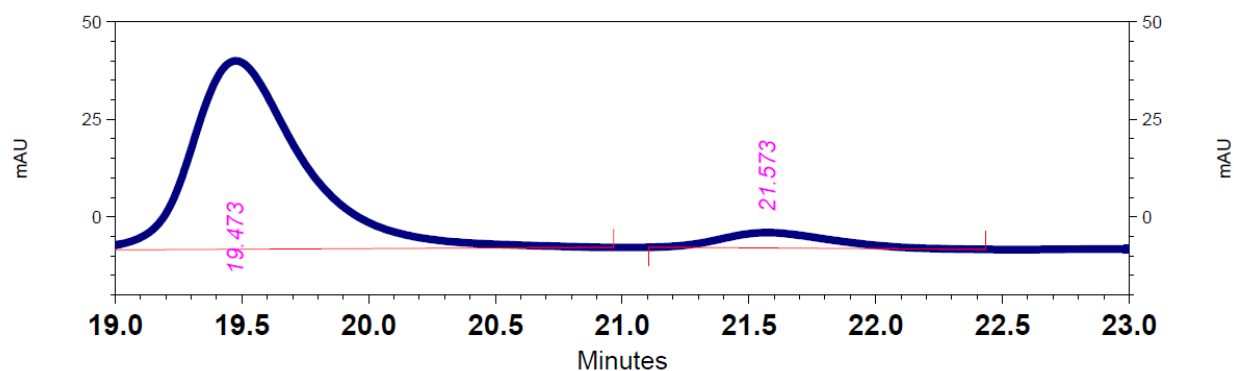


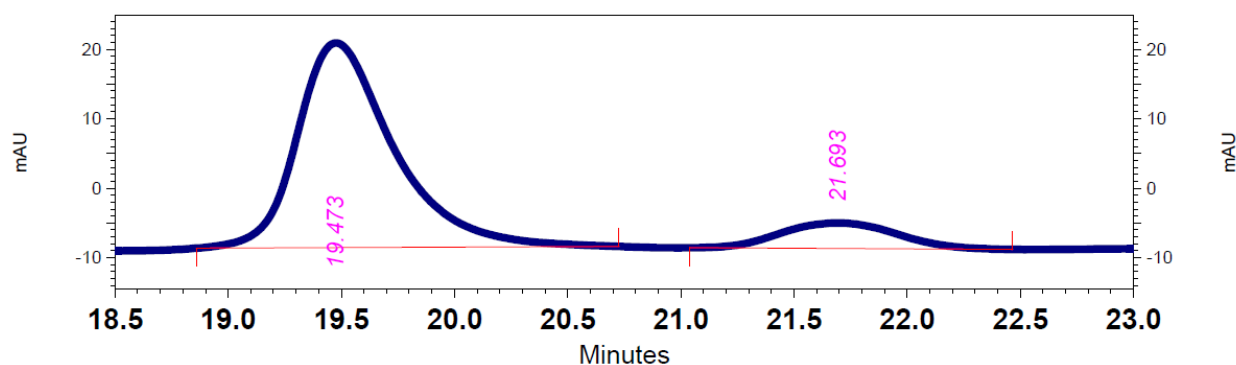
Figure A4.23: Chiral GC chromatogram for untreated $\pm$ F-SO.

**Results**

Retention Time	Area	Area %	Height	Height %
19.473	119690020	90.45	3421087	89.69
21.587	12631178	9.55	393405	10.31

Totals	132321198	100.00	3814492	100.00
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Figure A4.24: Chiral HPLC chromatogram for separation of $\pm$ F-SO by 2-R, $ee = 80\%$.

**Results**

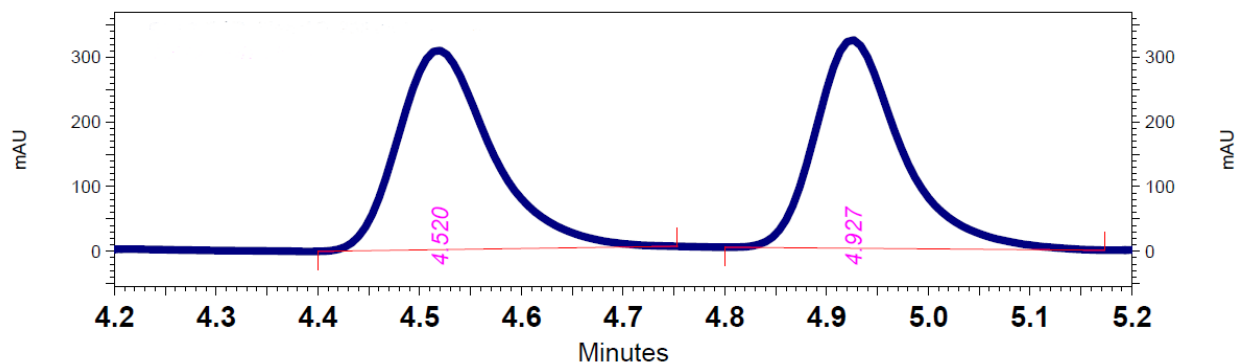
Retention Time	Area	Area %	Height	Height %
19.473	3081121	89.43	101243	89.44
21.573	252425	10.57	8280	10.56

Totals	3333546	100.00	109523	100.00
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Figure A4.25: Chiral HPLC chromatogram for separation of $\pm$ F-SO by 2-S, $ee = 78\%$.

Chiral HPLC chromatogram for $\pm$ Cl-SO

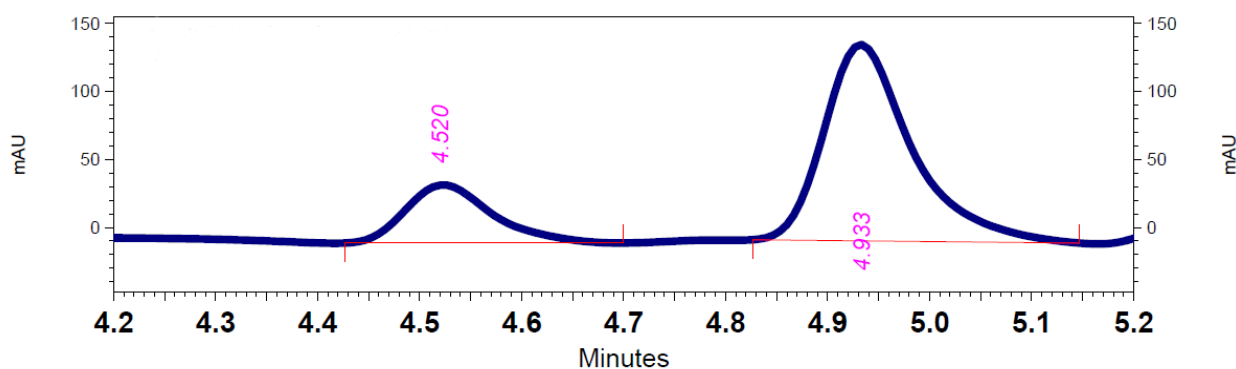
Chiral HPLC chromatogram for $\pm$ Cl-SO were performed by using the ChiralCel OD-H column with a flow rate of 1 mL/min using 90:10 hexane: isopropanol solvents eluents.



Results

Retention Time	Area	Area %	Height	Height %
4.520	4143924	50.92	646721	48.90
4.927	3993921	49.08	675938	51.10
Totals	8137845	100.00	1322659	100.00

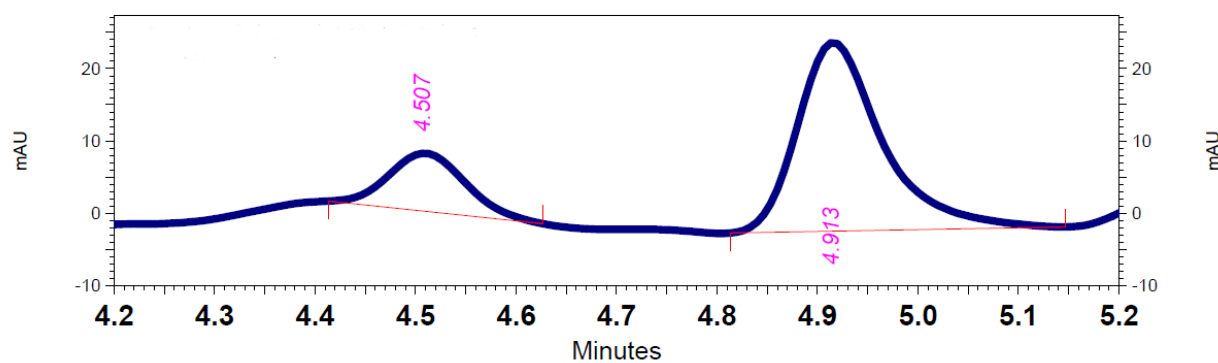
Figure A4.26: Chiral GC chromatogram for untreated $\pm$ Cl-SO.



Results

Retention Time	Area	Area %	Height	Height %
4.507	89313	21.69	16633	23.34
4.913	322373	78.31	54624	76.66
Totals	411686	100.00	71257	100.00

Figure A4.27: Chiral HPLC chromatogram for separation of $\pm$ Cl-SO by 2-R, *ee* = 57%.

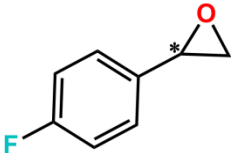
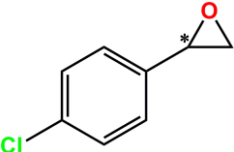


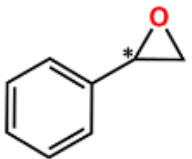
230 nm/Bw:4 nm

Results

Retention Time	Area	Area %	Height	Height %
4.507	89584	21.75	16706	23.42
4.913	322373	78.25	54624	76.58
Totals	411957	100.00	71330	100.00

Figure A4.28: Chiral HPLC chromatogram for separation of $\pm$ Cl-SO by 2-S, $ee = 56\%$.**Table A4.2:** Summary of HPLC-separation results for the racemic guest molecules by 2-R and 2-S.

Guest	1 st Run	2 nd Run	3 rd Run
			
% ee resolved by 2-R	80 (R)	80 (R)	78 (R)
% ee resolved by 2-S	78 (R)	78 (R)	78 (R)
Guest	1 st Run	2 nd Run	3 rd Run
			
% ee resolved by 2-R	57 (R)	57 (R)	56 (R)

% ee resolved by 2-S	56 (R)	56 (R)	56 (R)
Guest 	1 st Run	2 nd Run	3 rd Run
% ee resolved by 2-R	7 (R)	7 (R)	7 (R)
% ee resolved by 2-S	39 (R)	39 (R)	39 (R)

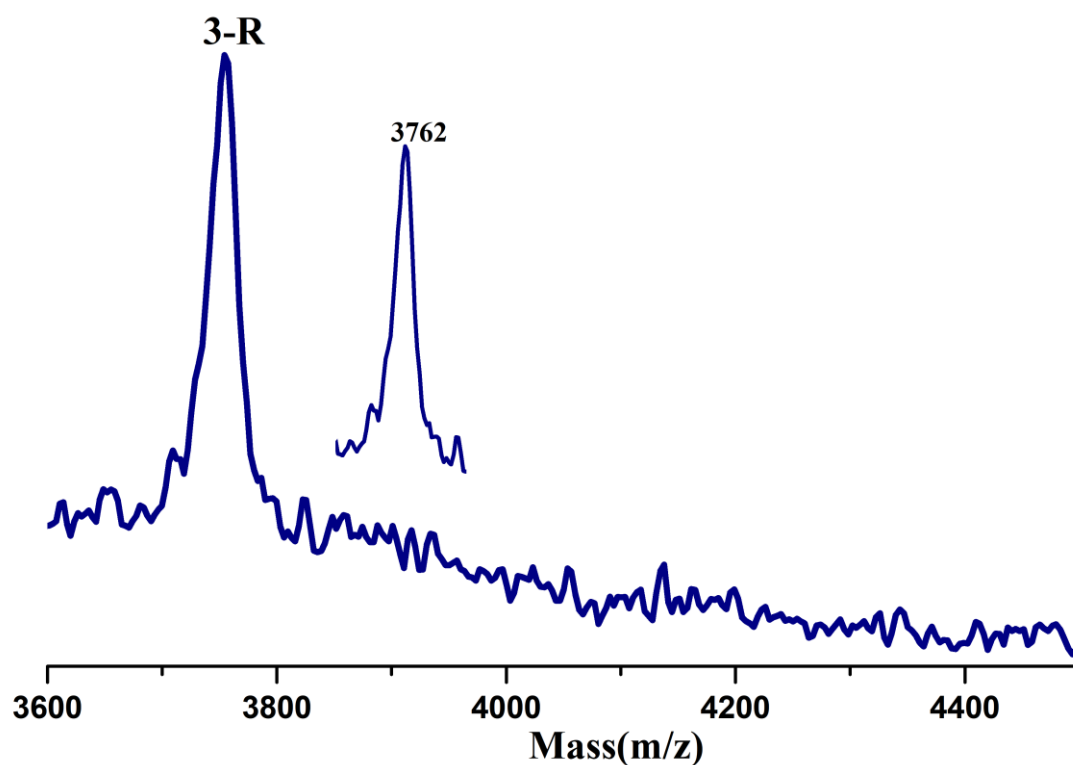


Figure A5.1: MALDI-TOF (Linear mode) spectra of spin cage 3-R.

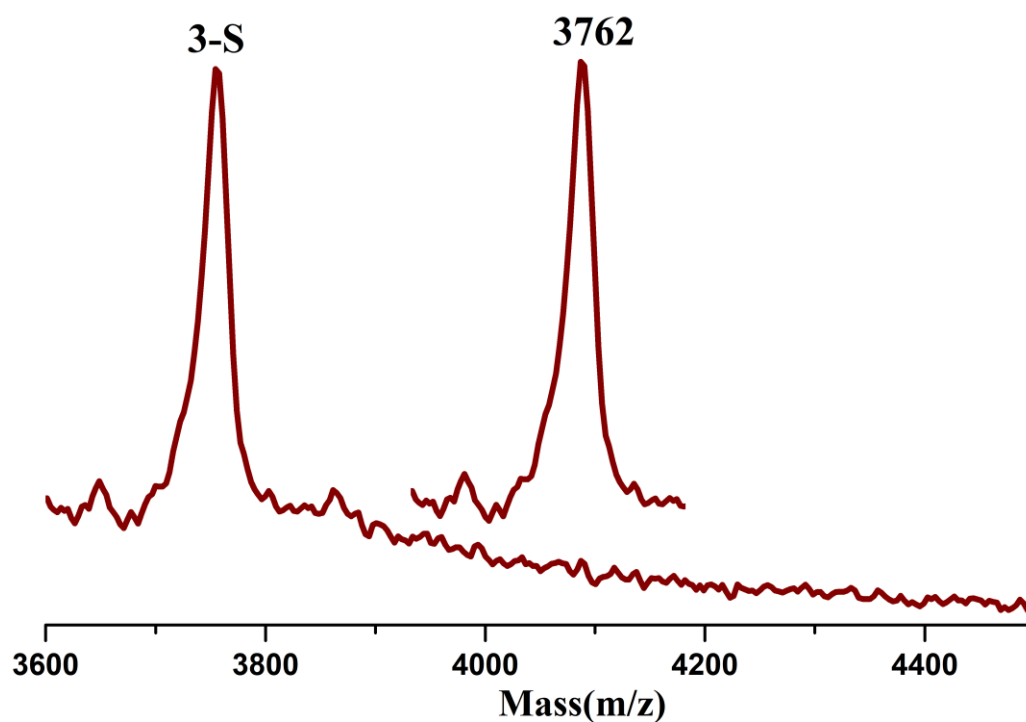


Figure A5.2: MALDI-TOF (Linear mode) spectra of racemic spin cage 3-S.

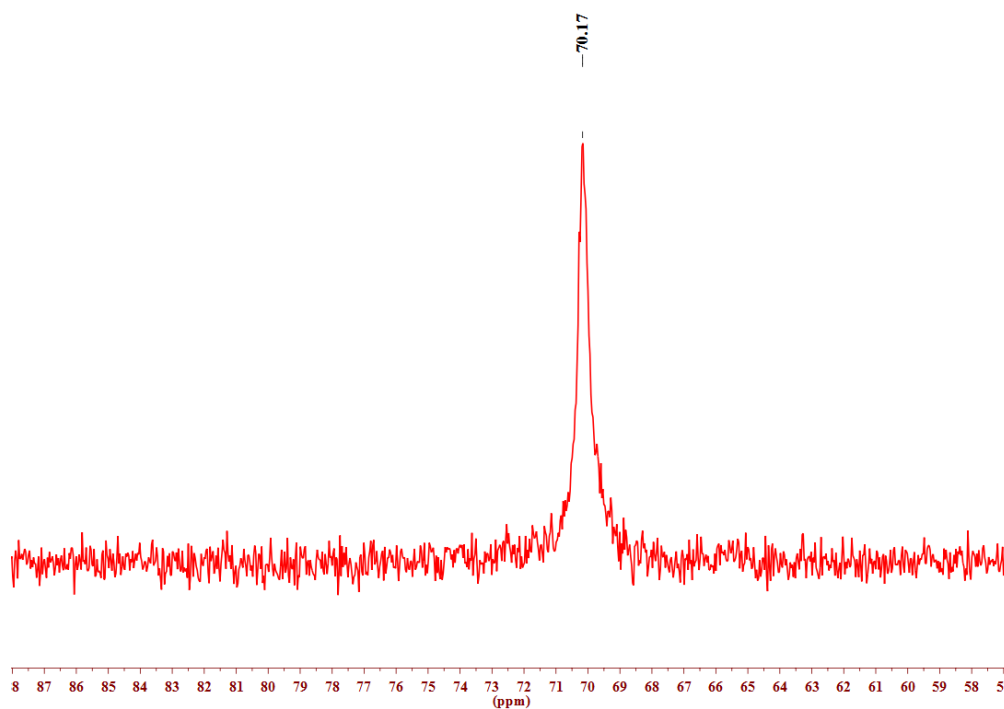


Figure A5.3: ^{31}P NMR of cage 3-S.

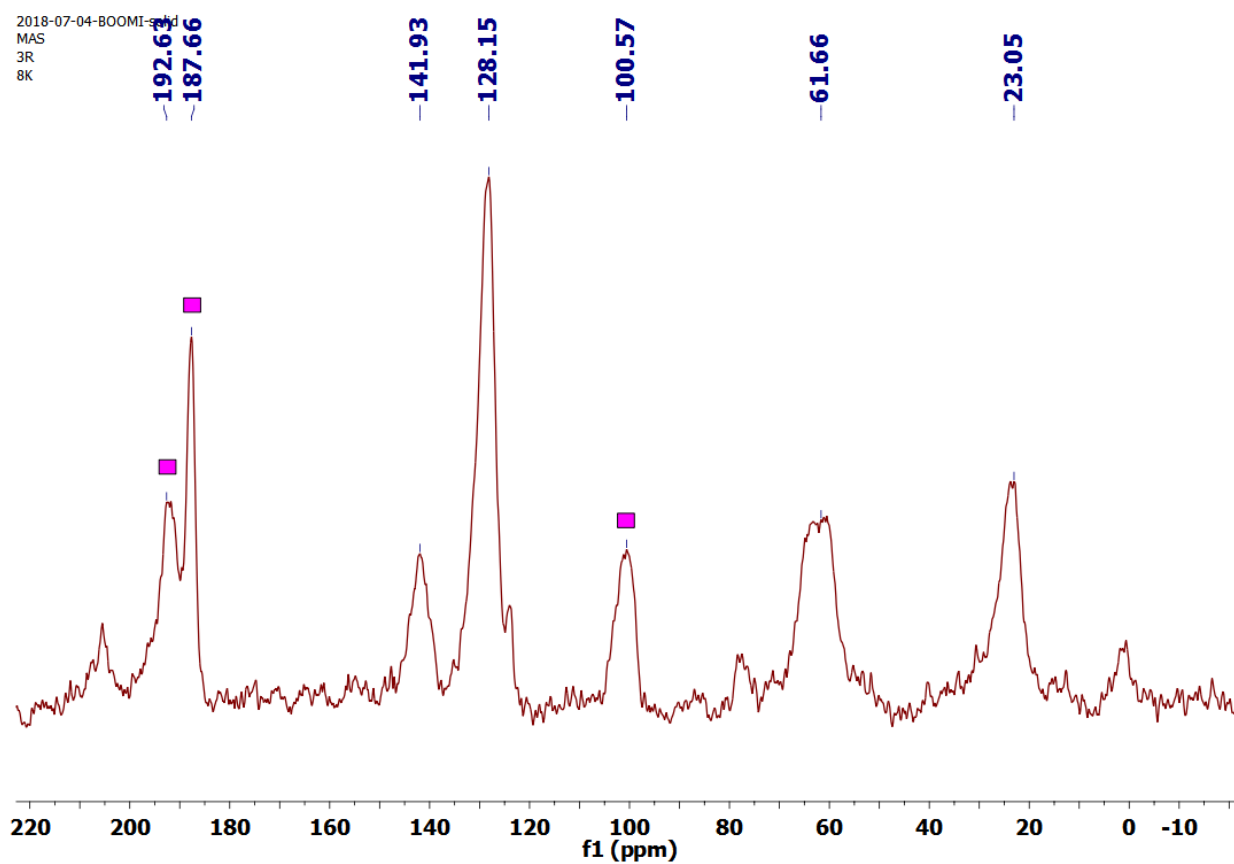


Figure A5.4: Solid state ^{13}C NMR spectra of cage 3-R (dhbq linker signals are denoted in pink colour square).

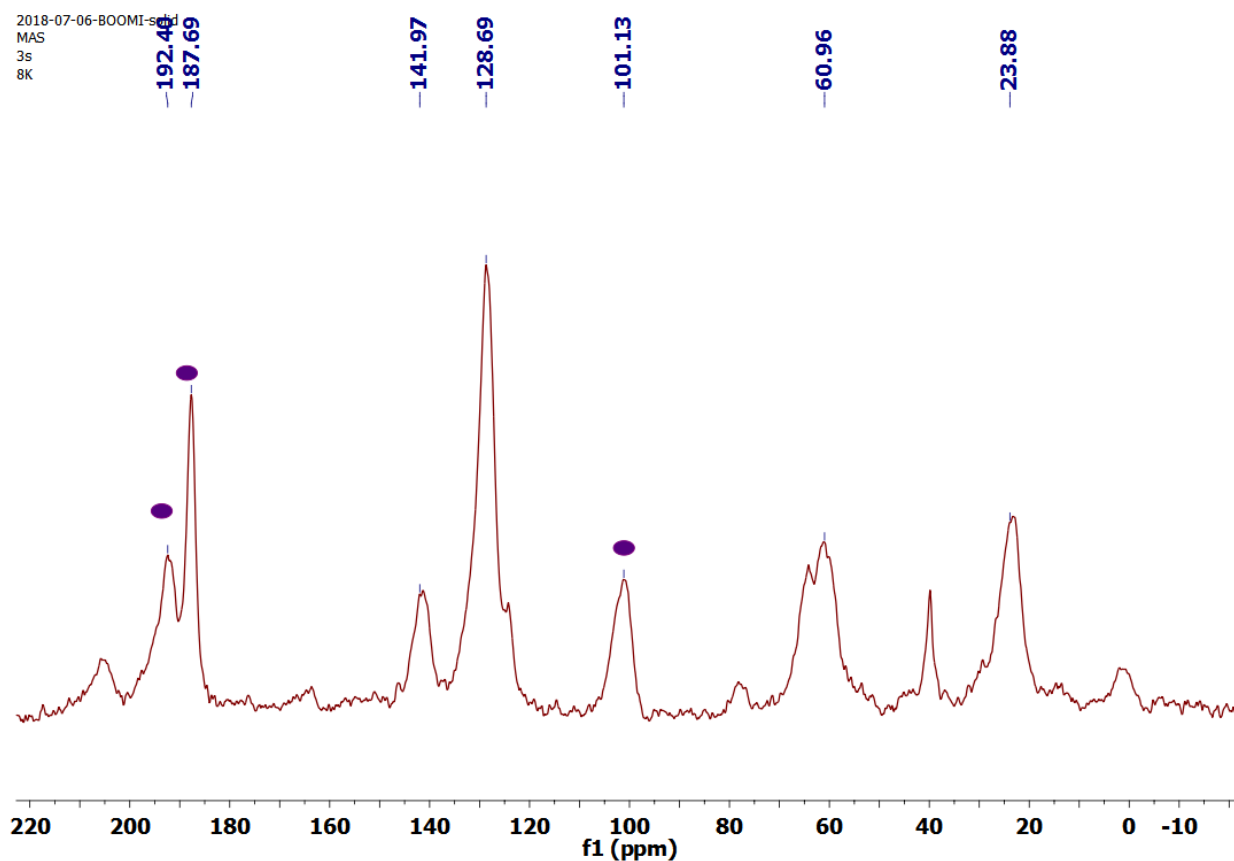


Figure A5.5: Solid state ^{13}C NMR spectra of cage 3-S (dhbq linker signals are denoted in purple colour circle).

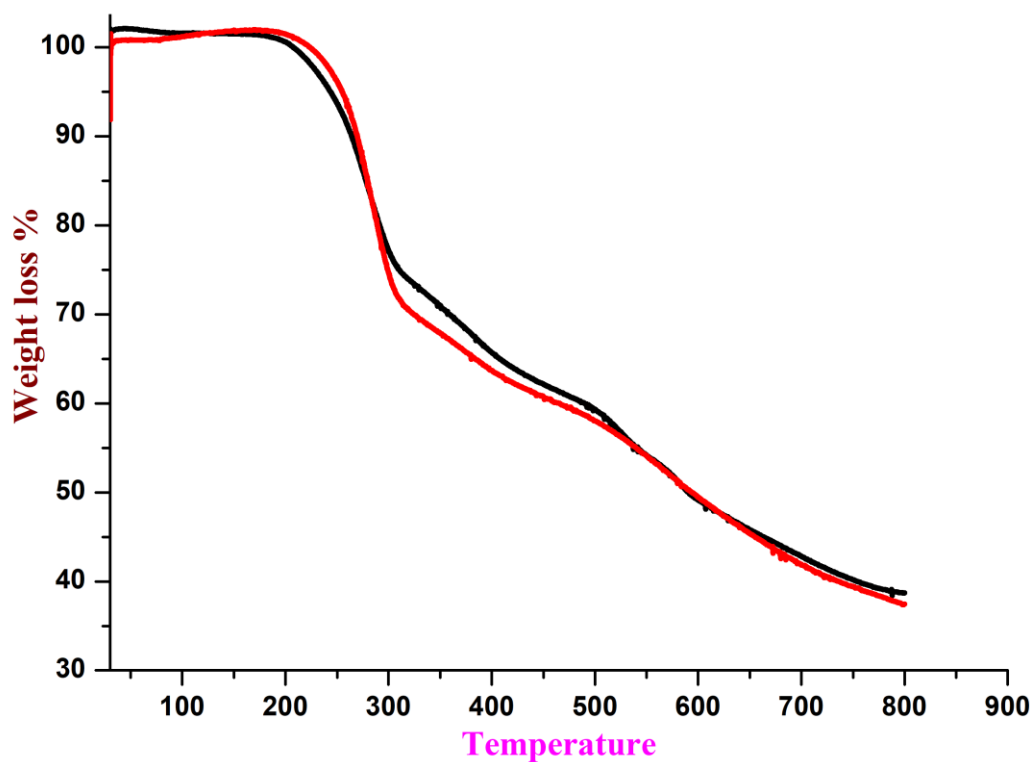


Figure A5.6: TGA graph of 3-R (red) and 3-S (black).

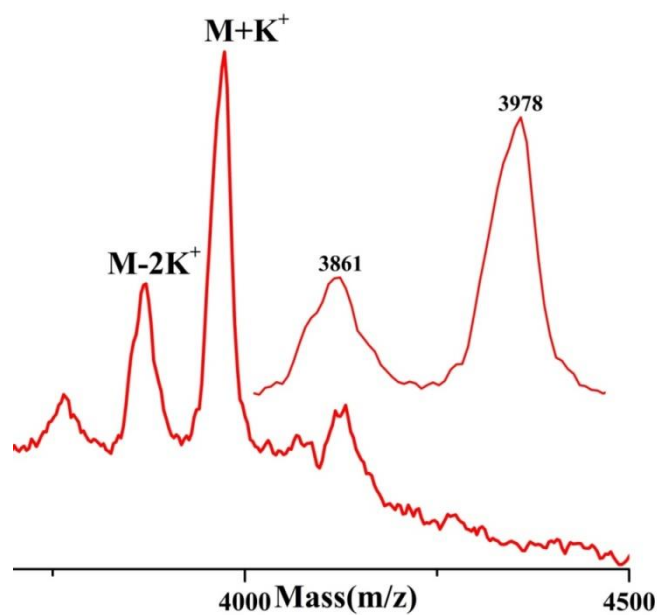


Figure A5.7: MALDI-TOF spectra of cage 4-R.

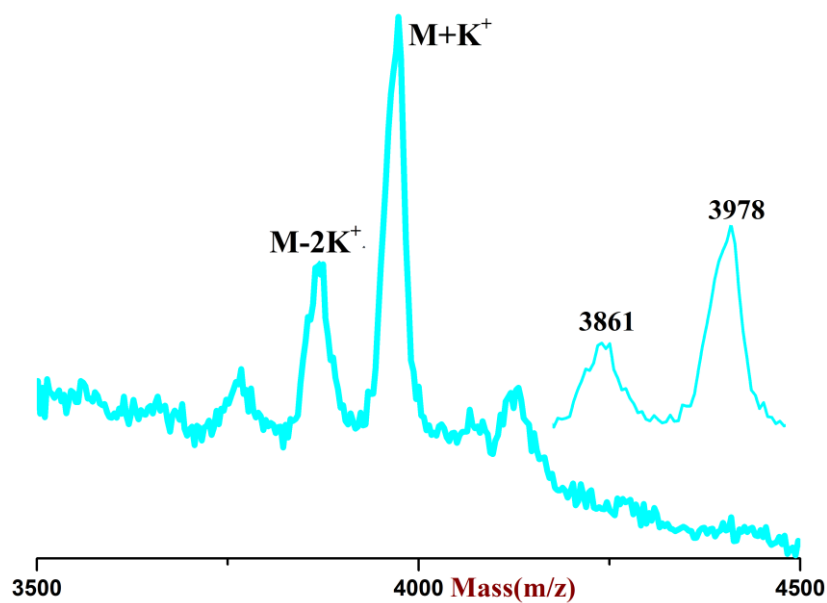


Figure A5.8: MALDI-TOF spectra of cage 4-S.

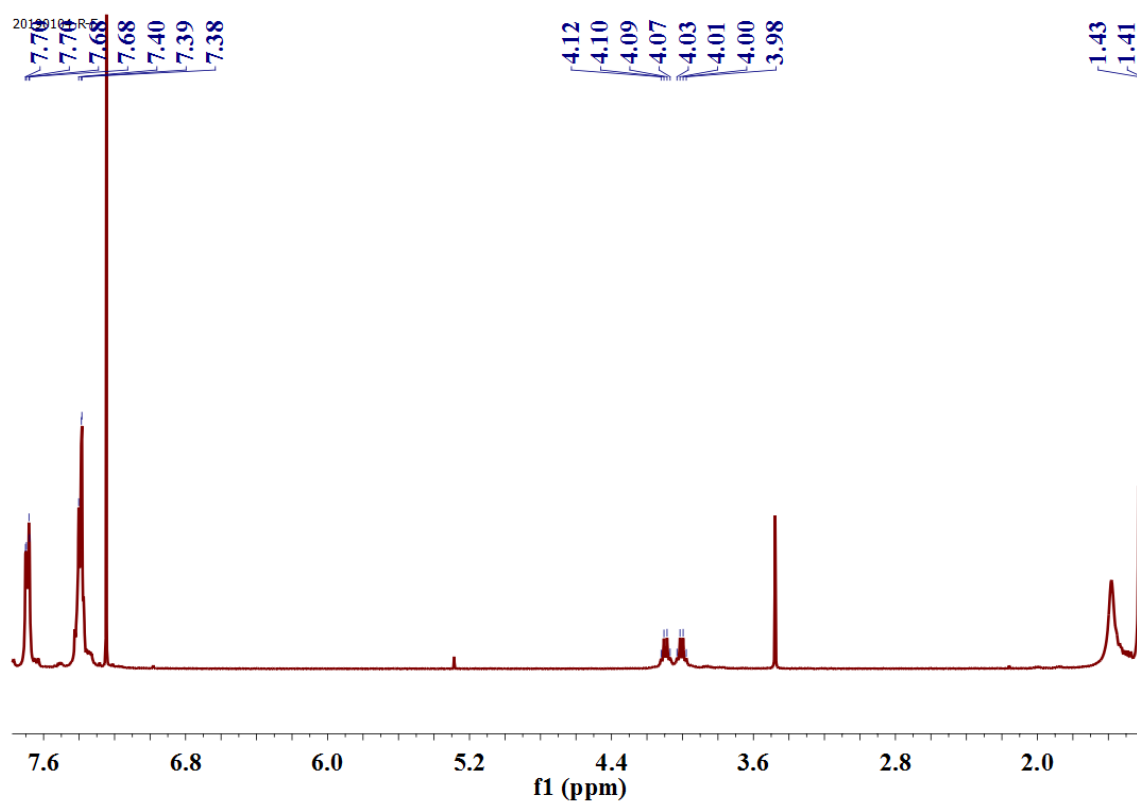


Figure A5.9: 1H NMR of fluoranilate tethered chiral cage 4-R.

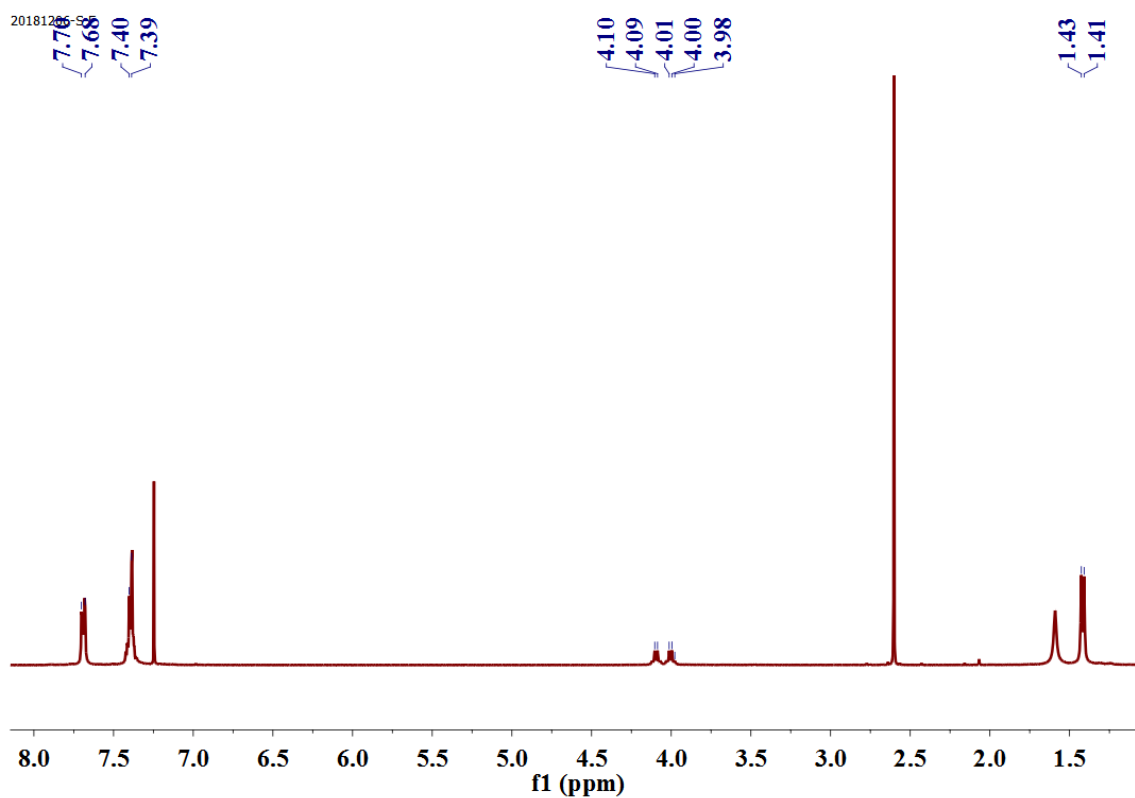


Figure A5.10: ^1H NMR of fluoranilate tethered chiral cage 4-S.

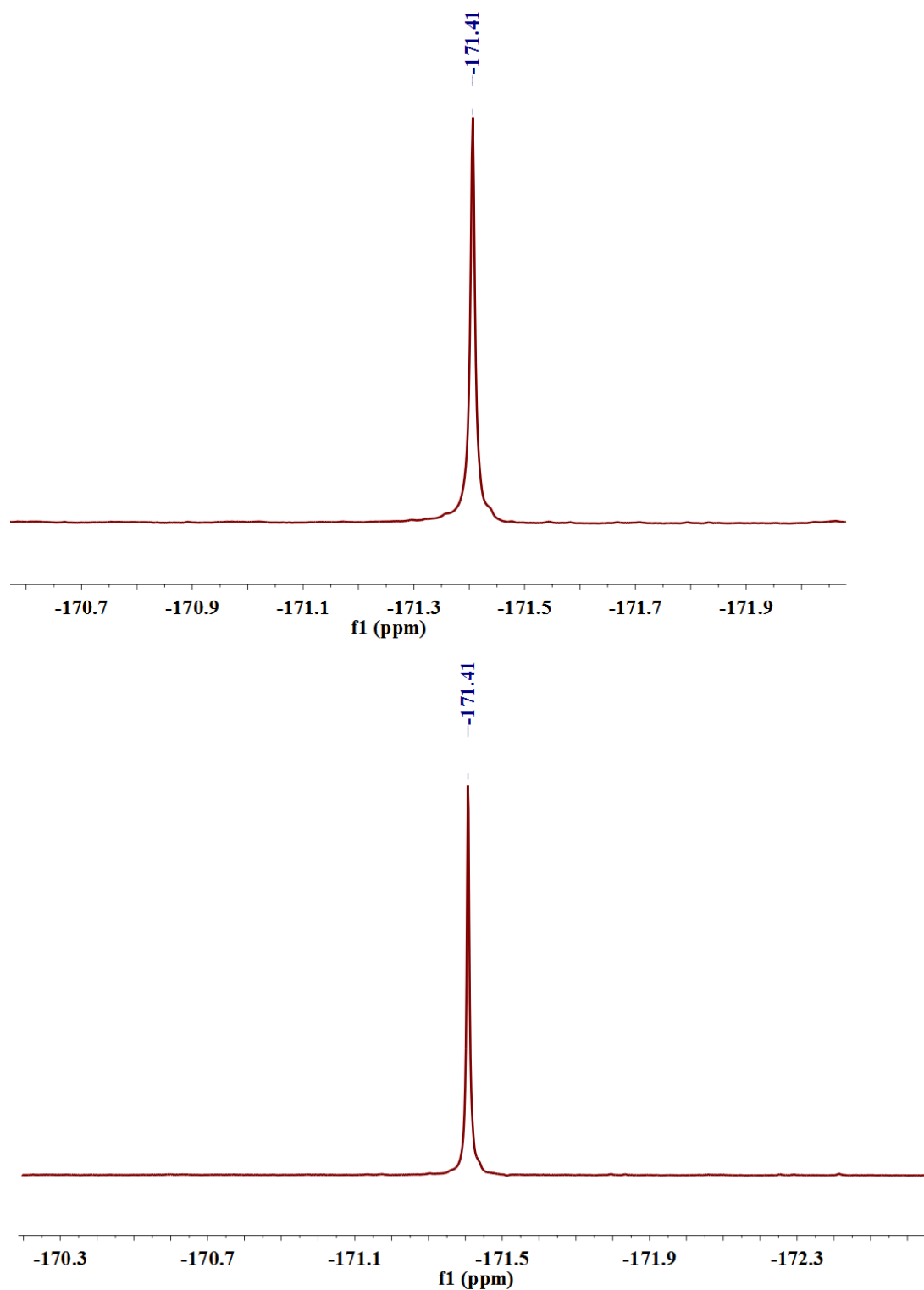


Figure A5.11: ^{19}F NMR of 4-R(Top) and 4-S(Bottom) cages.

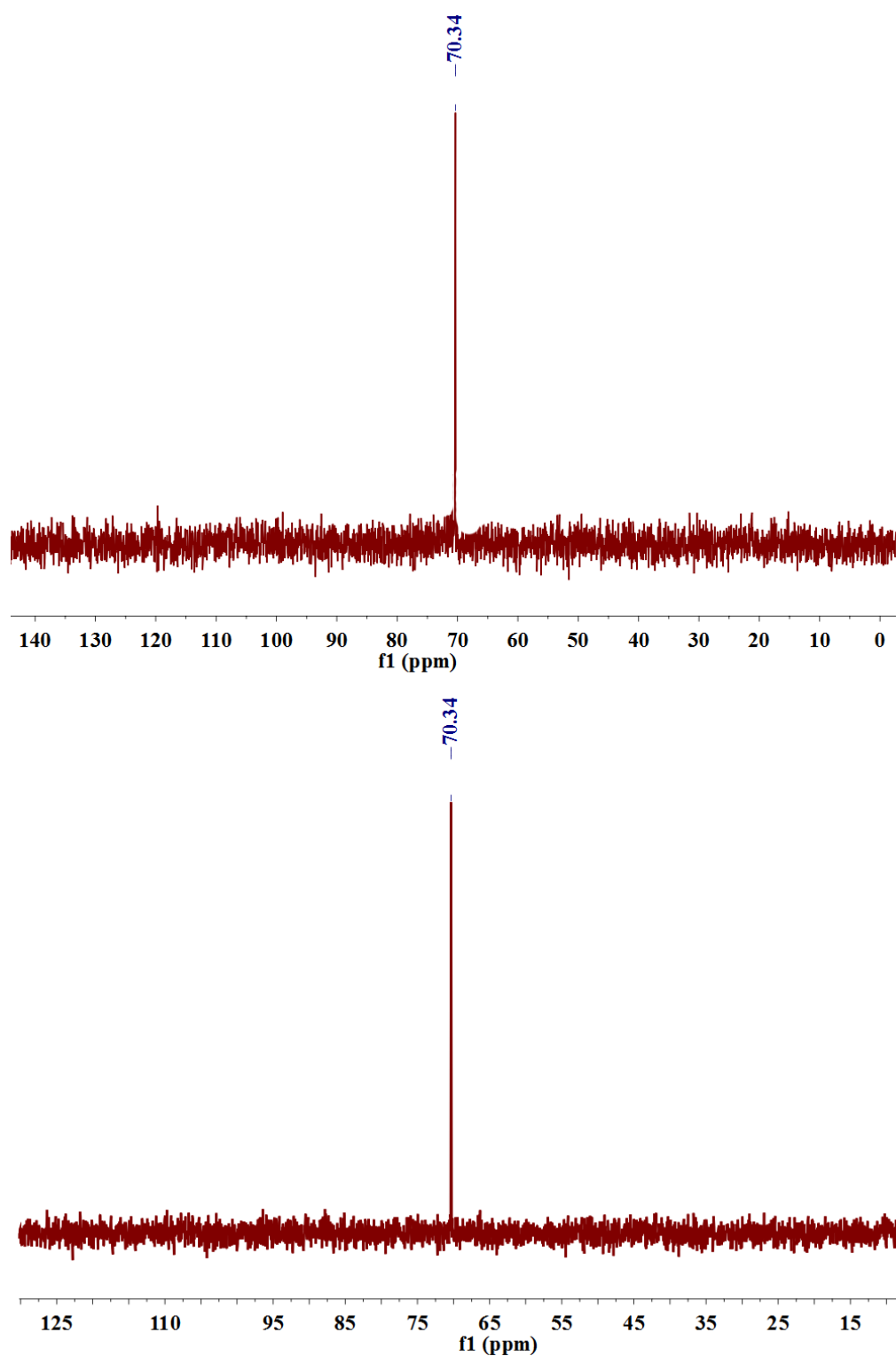


Figure A5.12: ^{31}P NMR of 4-R (Top) and 4-S (Bottom) cages.

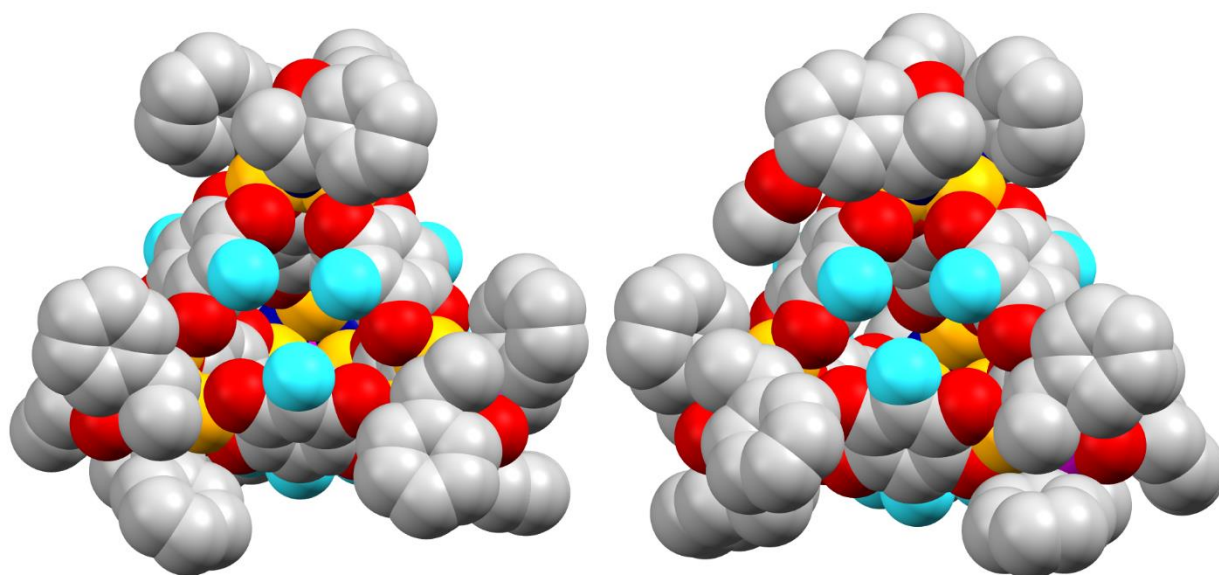


Figure A5.13: Space filling representations of 4-R (left) and 4-S (right).

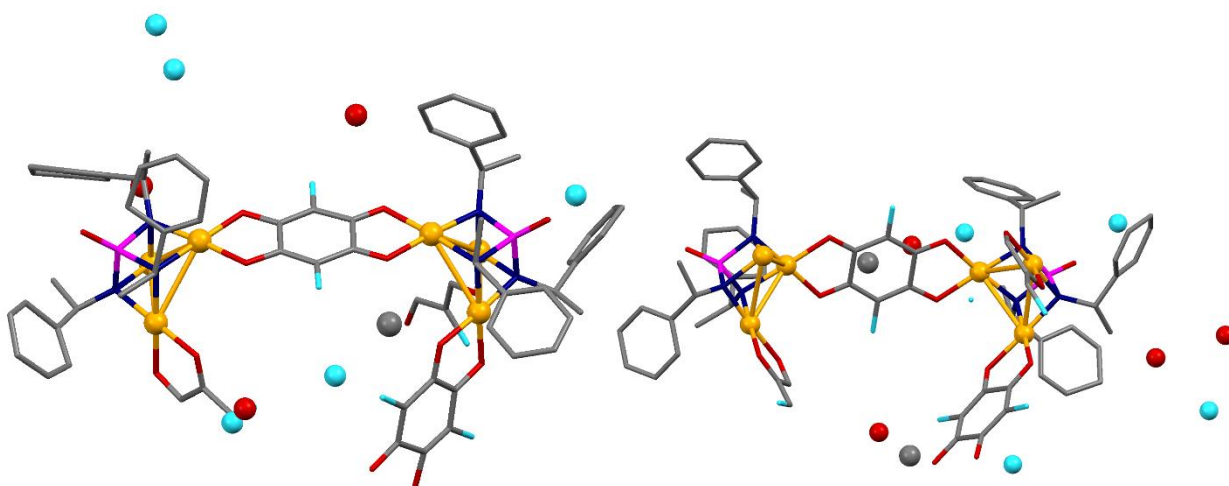


Figure A5.14: Asymmetric unit for cage 4-R and 4-S.

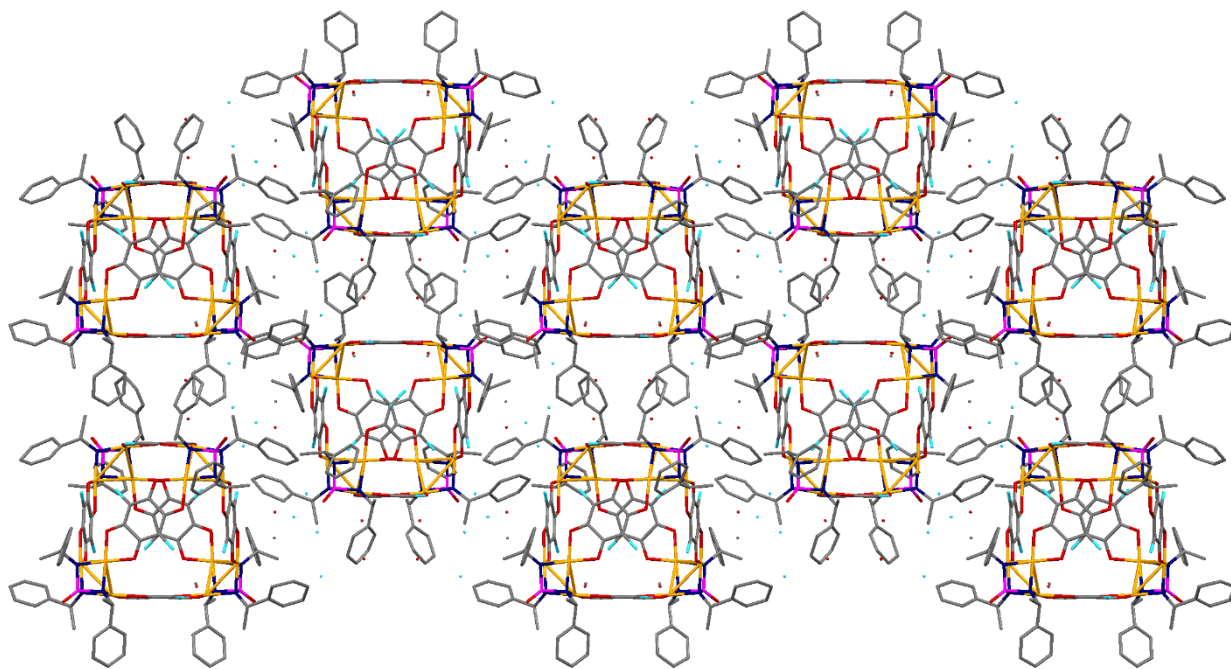


Figure A5.15: 2*2*2 Packing structure of 4-R with solvent molecules and anions.

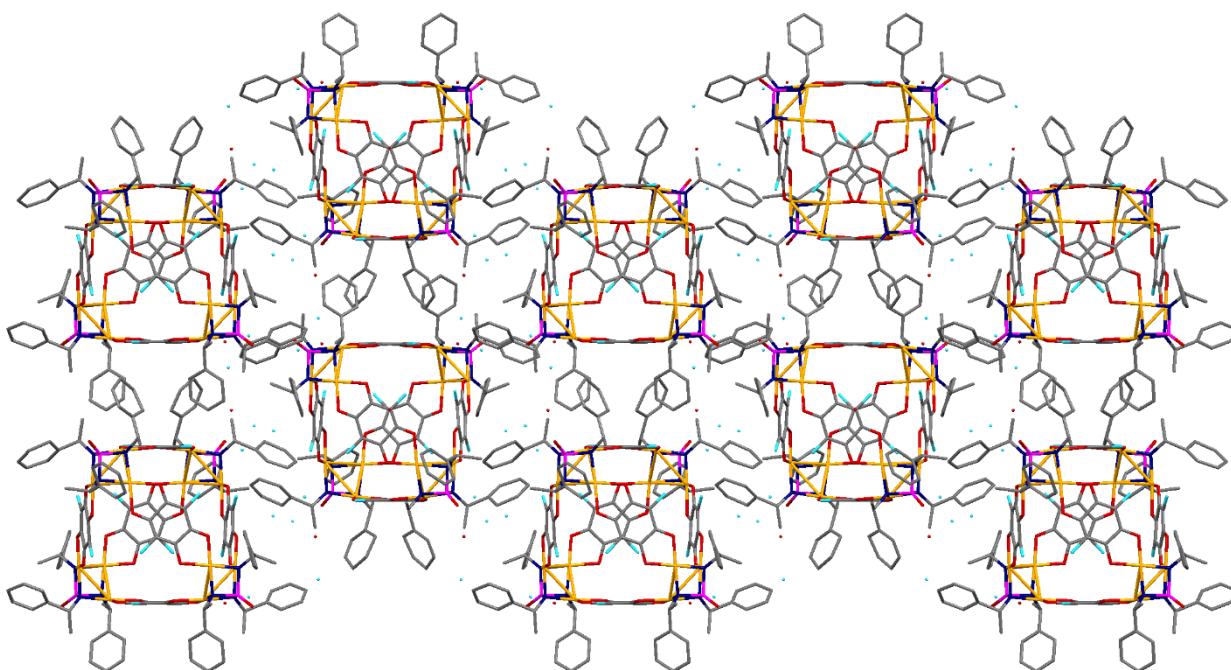


Figure A5.16: 2*2*2 Packing structure of 4-S with solvent molecules and anions.

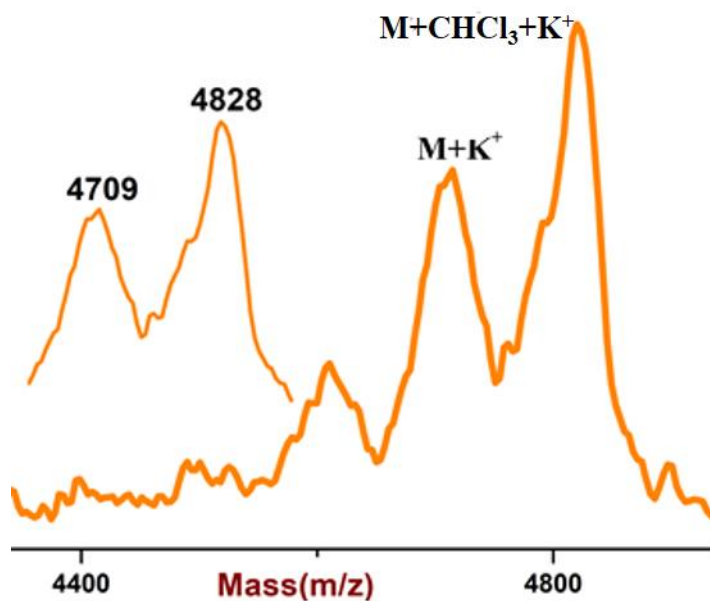


Figure A5.17: MADLI-TOF spectra of singlet diradical cages 5-R

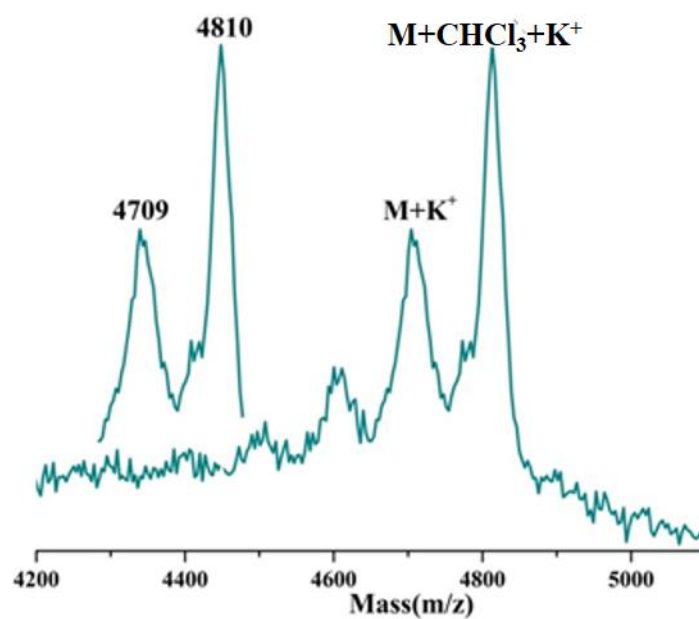


Figure A5.18: MADLI-TOF spectra of singlet diradical cages 5-S.

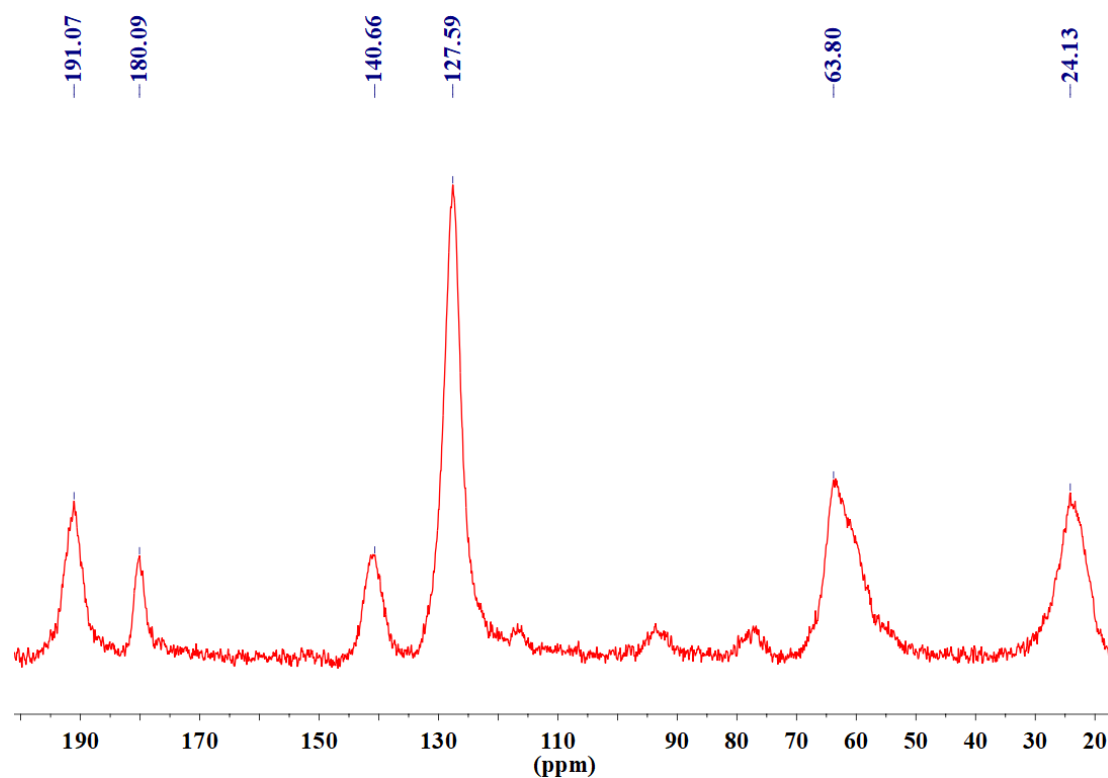


Figure A5.19: Solid state ^{13}C NMR of singlet diradical cages 5-R.

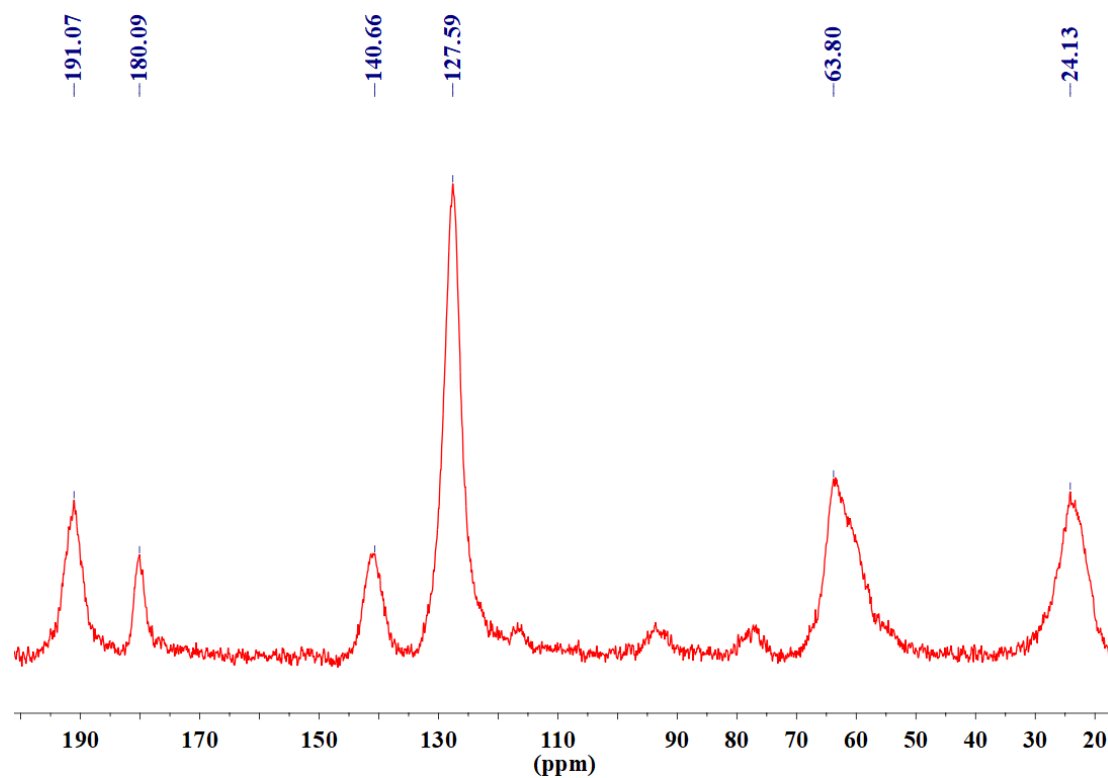


Figure A5.20: Solid state ^{13}C NMR of singlet diradical cages 5-S.

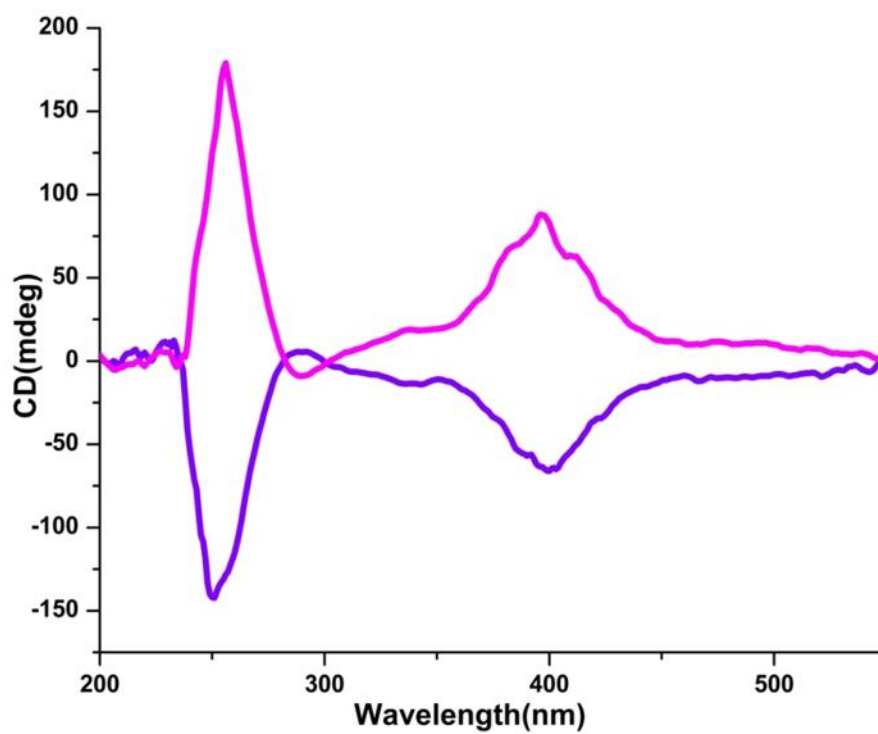


Figure A5.21: CD spectra of singlet diradical cages 5-R and 5-S.