Synthesis and Characterization of 18-Membered Unsymmetrical Dinucleating [N_{10}] Macrocycle i.e. [L^1.2HClO_4] and 26-Membered Unsymmetrical Dinucleating [N_{12}] Macrocycle i.e. [L^2.2HClO_4]
INTRODUCTION

The survey of literature regarding the synthetic methods reported for a wide variety of macrocyclic ligands, their reactivity towards metal ions as well as their utility to serve as models for biological systems has been reviewed in chapter-1.

There has been considerable interest in the chemistry of binucleating macrocycles capable of incorporating two metal centers and the topic has been the subject of several recent reviews\(^1\).

This interest has arisen due to the occurrence of binuclear metal centers in enzymes such as red kidney bean purple acid phosphatase\(^2\) and urease\(^3\). Metal complexes of some binucleating hexaaza macrocycles form host-guest complexes with a range of anions such as maleate, pyrophosphate and triphosphate\(^4\). In addition they can display catalytic activity in the hydrolysis of phosphate derivatives\(^5\) and peptidase\(^6\).

Binuclear centers containing transition elements such as iron and copper are common among metallo-proteins\(^7\). These centers often function by binding and activating substrates. The individual metal ions found at the binuclear center, however, may have quite distinct role in the overall function. As for example, the active sites in erythrocyte super oxide dismutase (SOD), bind one metal ion to the substrate while the presence of other metal ion is responsible for maintaining the
structural integrity of the active sites. In such cases, it is often found that the binuclear site of the metalloenzyme situates its metal ions in chemically distinct environments. Four distinct environments can be readily identified in respect of metal ions binding which are:

1. Symmetric, i.e. identical donor atoms bound to each metal in similar geometries.
2. Donor asymmetry i.e. different types of donor atoms bound to each metal.
3. Geometrical asymmetry i.e. inequivalent geometrical spatial arrangement of the donor atoms about each metal.
4. Coordination number asymmetry i.e. an unequal number of donor atoms coordinated to each metal.

All these possibilities can be illustrated diagrammatically as shown in (fig. 2.1).

![Diagram showing classification of metal coordination environments](image)

**Fig. 2.1**: Classification of metal coordination environments found in metalloproteins containing multinuclear metal centers. M is general transition metal and W, X, Y and Z represents hetrotom donors (e.g. N, O, S, etc.).
The individual metals of binuclear centers have been found to possess donor asymmetry in, for example, cobalt-based methionine aminopeptidase\textsuperscript{9}, bovine SOD\textsuperscript{10}, and the trizinc enzyme phospholipase C\textsuperscript{11}. Geometric asymmetry of metalloprotein binuclear sites has been reported\textsuperscript{12} for the B2 protein active iron site of ribonucleotide reductase and certain adducts of the dicopper site of hemocyanin\textsuperscript{13-15}. There are several examples of binuclear metalloproteins where coordination number asymmetry is known or proposed. These include some copper-containing tyrosinases\textsuperscript{16}, hemerythrin\textsuperscript{17}, uteroferrin\textsuperscript{18} and the hydroxylase component of soluble methane mono-oxygenase\textsuperscript{19-20}. The asymmetric nature of a number of homodinuclear or heterodinuclear transition metal-derived metallobiosites where the individual metal ions are capable to have quite distinct roles in the functioning of the metalloenzyme concerned have led to search for carefully designed unsymmetric dinucleating ligands. Such ligands can result in dinuclear complexes capable of acting as models for the metallobiosites\textsuperscript{1, 21}. It is also possible that any combination of these types of asymmetry may occur in a single binuclear enzyme. Coordination asymmetry in metalloenzymes presents the possibility of “open” coordination sites for direct interaction of one metal center with substrate. It is becoming apparent that coordination number asymmetry exists in a number of metalloproteins and may be responsible for imparting unique reactivity\textsuperscript{22-24}. However, the effects that geometric or coordination
number asymmetry have on the physical properties and function of binuclear sites are much less studied. The reason for this appears to stem from a lack of suitable model systems. Complexes having geometric\textsuperscript{25(a,b)} or coordination number asymmetry\textsuperscript{25(c,d)} are reported to be formed but are rare. The rational design of ligands that can induce coordination number asymmetry in binuclear complexes is a desirable target for developing a more complete description of spectroscopic and chemical reactivity properties related to metalloenzyme systems.

Dinucleating macrocyclic ligands with dissimilar coordination sites are of particular importance because hetero-dinuclear complexes derived from such macrocycles are thermodynamically stable and kinetically retarded with regard to metal dissociation and metal substitution\textsuperscript{26,27} relative to metal complexes of acyclic ligands. Macrocyclic ligands can provide a well-defined environment for the bound metal ions and influence their physico-chemical properties\textsuperscript{28}.

The polyaza macrocycles of the type (3k)-ane[N\textsubscript{k}] have been shown to produce bimetallic complexes\textsuperscript{29} when K\geq 6. However, for (4k)-ane[N\textsubscript{6}] type where K\geq 6 giving a (24)-ane[N\textsubscript{6}] as for example, [1,5,9,13,17,21]hexaazacyclotetracosane macrocyclic tends to encapsulate\textsuperscript{30} only one metal ion in its cavity. Template reaction utilizing the “2:2” condensation of a diamine with 2,6 diformly-4-methyl phenol was the first one pot reaction giving a dinuclear complex\textsuperscript{31}. Later on, attempts to obtain macrocycles with different lateral chains
through stepwise cyclization using two dissimilar alkyldiamines by template procedure were also successful\textsuperscript{32}. Most of the earlier efforts concentrated for isolating symmetrical macrocycles primarily because of their ease of synthesis\textsuperscript{33}. There are reports\textsuperscript{34} of large macrocycles with two or more cavities but possessing only identical biting sites (symmetrical macrocycles) to encapsulate the metal ions. However, there are relatively less reports\textsuperscript{35}, regarding metal ion encapsulation in large unsymmetrical macrocycles containing more than one type of metal binding sites. The unsymmetrical macrocycles so far reported\textsuperscript{32,36}, usually involved heteroatomic centers like $N_2O_2$, $N_2O_4$, $N_4O_2$. Polyazamacrocycles $[N_k]$ (where $k \leq 8$) with different environments for the aza groups are known\textsuperscript{36}. However, to our knowledge, big macrocycles with $K > 8$ having unsymmetrical aza groups capable to encapsulate more than one metal ion are scarce\textsuperscript{35,37}. A route to obtain unsymmetrical $[N_6]$ macrocycle has recently been developed\textsuperscript{37} which utilizes multi-step procedure incorporating a suitable precursor generated in-situ by an N-acetylated amine, N-acetylpropane 1,3-diamine in presence of suitable metal ions. A few metal ion free polyaza macrocycles containing endocylic substitution in the rings have been reported\textsuperscript{38} from this laboratory.

A one pot synthetic procedure utilizing N-acetylaniline to generate an intermediate capping agent for cyclizing the appropriate diamines in the absence of any metal ion (non-template procedure) to
obtain metal ions free unsymmetrical polyaza macrocycles has recently been exploited in this laboratory\textsuperscript{39,40}.

In this chapter the synthesis and characterization of 18-membered unsymmetrical $[N_{10}]$ dinucleating macrocycle, $[2,8,11,17]$tetramethyl $[3,5,7,12,14,16]$hexaphenyl $[1,3,5,7,9,10,12,14,16,18]$decaazaoctadeca $[2,8,11,17]$tetraene dihydroperchlorate i.e. $[L^1\cdot 2\text{HClO}_4]$ and 26-membered unsymmetrical $[N_{12}]$ dinucleating macrocycle, $[2,12,15,25]$tetramethyl $[3,11,16,24]$tetraphenyl $[1,3,5,9,11,13,14,16,18,22,24,26]$dodecaazahexacosa $[2,12,15,25]$ tetraene dihydroperchlorate i.e. $[L^2\cdot 2\text{HClO}_4]$ have been described. The schemes for the formation of the these macrocycles have also been proposed on the basis of their physico-chemical and spectroschopic data like FAB–mass, IR, UV-visible, NMR etc.
EXPERIMENTAL

Reagents used:

Ethyl acetate (S.D. Fine, India), Aniline (Qualigens, India), 1,3-diaminopropane (E.Merck, Germany), Hydrazine hydrate (BDH, India), Perchloric acid (70%) (Merck, India), and Formaldehyde (37-41%) (Merck, India) were used as received. Solvents were purified and dried before their use by reported method.

Physical Measurements:

IR spectra were recorded as KBr discs on a Perkin Elmer model spectrum GX and H\textsuperscript{1} NMR spectra of samples in d\textsubscript{6}-DMSO on a Bruker DRX 300 spectrometer using TMS as internal reference. Electronic spectra and conductivities of 10\textsuperscript{-3}M solution in DMSO were recorded on a Cintra-5GBS UV-visible spectrophotometer and Systronics-305 Conductivity Bridge respectively. FAB mass spectra of the ligands were recorded in m-nitrobenzyl alcohol (NBA) matrix using Jeol/SX-102 spectrometer. Results of microanalysis were obtained from analytical laboratory of RSIC, Central Drug Research Institute, Lucknow, India.
Synthesis of $[2,8,11,17]\text{tetramethyl } [3,5,7,12,14,16]\text{hexaphenyl } [1,3,5,7,9,10,12,14,16,18]\text{decaaza} \text{deca} [2,8,11,17] \text{tetraene dihydroperchlorate i.e. } [L^1.2\text{HClO}_4]$: 

Hydrazine hydrate (6.05 ml, 0.099 mol) was mixed with 30ml of methanol in a two necked round bottomed flask placed on a constant temperature bath. Perchloric acid (10 ml, 0.099 mol) was added drop wise with continuous stirring maintaining the temperature of the reaction mixture at room temperature. N-acetylaniline (94 ml, 0.199 mol) was dropped slowly through a dropping funnel with continuous stirring and the reaction mixture was further stirred for 18 hours. Reaction was monitored by recording UV-visible spectrum of the reaction mixture at intervals which indicated formation of a species having C=N bonds. The disappearance of a band at 320nm, characteristic of the $n \rightarrow \pi^*$ transition of $(-\text{CO-NH-})$ group of N-acetylaniline with a concomitant appearance of a new band at 385 nm is indicative of the formation of new species in the solution. The band at 385 nm is characteristic of the $\pi \rightarrow \pi^*$ transition reported for the C=N bond in the molecule. This reasonably indicates that the condensation process generated an intermediate species containing C=N bond in the molecular unit. Formaldehyde (20.3 ml, 0.299 mol) was added drop wise with continuous stirring over a period of one hour, which produced slight milkiness in the solution. It was again stirred overnight at room temperature.
Aniline (9.1 ml, 0.099 mol) and formaldehyde (20.3 ml, 0.299 mol) taken in separate dropping funnels were dropped in the reaction mixture at a slow dropping rate which gave an exothermic reaction. The temperature of the reaction mixture was maintained at room temperature which was again stirred continuously over-night. This has afforded a yellow coloured solid product. The product was filtered off, washed with methanol and dried under vacuum, (yield = 27.82 g or 29%, mp = 128-130°C). The solid was soluble in 1,4-dioxane and dimethyl sulfoxide. The recrystallization of the compound has produced only amorphous solids.

Table-2.1: Analytical and Molar conductance ($\Lambda_m$) data of [L$^1$.2HClO$_4$]:

<table>
<thead>
<tr>
<th></th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
<th>$\Lambda_m$ (cm$^2$ ohm$^{-1}$ mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observed</td>
<td>59.61</td>
<td>5.16</td>
<td>14.48</td>
<td>17.0</td>
</tr>
<tr>
<td>Calcd. For</td>
<td>[C$<em>{48}$H$</em>{52}$ N$_{10}$Cl$_2$O$_8$]</td>
<td>59.62</td>
<td>5.17</td>
<td>14.49</td>
</tr>
</tbody>
</table>

UV-visible spectrum: $\Lambda_{max} = 385$ nm ($\varepsilon = 1507$ lit. mol$^{-1}$ cm$^{-1}$)
Physico-chemical and spectroscopic data of [2,8,11,17]tetramethyl [3,5,7,12,14,16]hexaphenyl [1,3,5,7,9,10,12,14,16,18]decaazaoctadeca [2,8,11,17]tetraene dihydroperchlorate i.e. [L^2.2HClO_4]:

Table-2.2: Important frequencies (cm⁻¹) observed in IR spectra of the ligand and their assignments:

<table>
<thead>
<tr>
<th>Assignments</th>
<th>v(N-N)</th>
<th>v(C=N)</th>
<th>v(C-N)</th>
<th>v(C-N)</th>
<th>v_1</th>
<th>v_2</th>
<th>v_3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Band position</td>
<td>933_s</td>
<td>987_s</td>
<td>1613_vs</td>
<td>1245_s</td>
<td>1348_s</td>
<td>1172_m</td>
<td>1075_s</td>
</tr>
</tbody>
</table>

s = strong, vs = very strong, m = medium, w = weak

Table-2.3: Ion abundance for ligand and its fragmentation* peaks observed in FAB-mass spectrum of [L^2.2HClO_4]:

<table>
<thead>
<tr>
<th>m/z</th>
<th>Assignments</th>
<th>%Abundance</th>
<th>m/z</th>
<th>Assignments</th>
<th>%Abundance</th>
</tr>
</thead>
<tbody>
<tr>
<td>766</td>
<td>[L^1]^+</td>
<td>62</td>
<td>212</td>
<td>[(C_6H_5NHCH_2)_2]^+</td>
<td>60</td>
</tr>
<tr>
<td>1100</td>
<td>[L^1.2HClO_4+Bq-2H]^+</td>
<td>58</td>
<td>154</td>
<td>[(C_6H_5)^+</td>
<td>70</td>
</tr>
<tr>
<td>1055</td>
<td>[L^1+Rn]^+</td>
<td>52</td>
<td>120</td>
<td>[(C_6H_5NHCH_2N)]^+</td>
<td>80</td>
</tr>
<tr>
<td>383</td>
<td>½[L^1]^+</td>
<td>30</td>
<td>106</td>
<td>[(C_6H_5NHCH_2]^+</td>
<td>100</td>
</tr>
<tr>
<td>308</td>
<td>[(C_6H_3)_2]^+</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*NBA (m-Nitrobenzyl alcohol) was used as the matrix for FAB recording which give its peaks at [m/z = 136, 137, 154, 289, 307].
*Bq = NBA (136), Rn = NBA (289)

Table-2.4: Positions of resonance peaks δ (ppm) observed in _1^H NMR of [L^1.2HClO_4] and their assignments:

<table>
<thead>
<tr>
<th>Assignments</th>
<th>H_3C–N&lt;</th>
<th>H_3C–N–^N</th>
<th>H_2C–C=N</th>
<th>H_2C–^N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak Positions</td>
<td>6.64 (10H)</td>
<td>7.14 (20H)</td>
<td>4.17 (12H)</td>
<td>2.50 (8H)</td>
</tr>
</tbody>
</table>

It was synthesized in the same manner as described above for L¹.2HClO₄. In a two necked round bottomed flask hydrazine hydrate (6.05 ml, 0.099 mol) taken in methanol (30 cm³), was stirred at room temperature. Perchloric acid (10 ml, 0.099 mol) was added drop wise with continuous stirring and then N-acetylaniline (94 ml, 0.199 mol) was added slowly through a dropping funnel with continuous stirring. Like [L¹.2HClO₄], the reaction was monitored periodically by recording the UV-visible spectrum of the reaction mixture which indicated formation of a species having C=N bonds. The disappearance of a band at 320 nm, characteristic of n → π* transition of (−CO−NH−) group of N-acetylaniline with a concomitant appearance of a new band at 398 nm indicates the formation of the intermediate species containing C=N bond in the molecular unit. Formaldehyde (20.3 ml, 0.299 mol) was added drop-wise to the reaction mixture which was again stirred over night at room temperature. 1,3-diaminopropane (8.4 ml, 0.099 mol) and formaldehyde (20.3 ml, 0.299 mol) taken in two separate dropping funnels fitted with the reaction flask, were dropped simultaneously to the reaction mixture at a slow dropping rate which gave an exothermic reaction. The temperature of the reaction mixture was maintained at room temperature and again stirred continuously for
two days. This produced an oily yellow coloured mass. Methanol (200 ml) was added in this and the reaction mixture was again stirred for 8 hours which afforded a light yellow coloured solid product. The product was filtered off, washed with methanol and dried under vacuum (Yield = 12.85 g or 14%, m.p. = 280°C (dec.). The solid was soluble in 1,4-dioxane and dimethyl sulphoxide. Here too, recrystalization of the solid provided only amorphous compound.

Table-2.5: Analytical and Molar Conductance ($A_m$) data of [L$^2$.2HClO$_4$]:

<table>
<thead>
<tr>
<th></th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
<th>$A_m$ (cm$^2$ ohm$^{-1}$ mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observed</td>
<td>54.30</td>
<td>6.02</td>
<td>18.10</td>
<td>11.0</td>
</tr>
<tr>
<td>Calcd. For [C$<em>{42}$H$</em>{58}$N$_{12}$Cl$_2$O$_8$]</td>
<td>54.31</td>
<td>6.03</td>
<td>18.10</td>
<td></td>
</tr>
</tbody>
</table>

UV-visible spectrum: $\lambda_{\text{max}} = 398$ nm ($\varepsilon = 1490$ lit mol$^{-1}$ cm$^{-1}$).

### Table-2.6: Important frequencies (cm\(^{-1}\)) observed in IR spectra of the ligand and their assignments:

<table>
<thead>
<tr>
<th>Assignments</th>
<th>v(N-N)</th>
<th>v(C=N)</th>
<th>v(N-H)</th>
<th>v(C-N)</th>
<th>v1</th>
<th>v2</th>
<th>v3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Band Positions</td>
<td>933(\text{m})</td>
<td>1613(\text{s})</td>
<td>3397(\text{s})</td>
<td>1243(\text{s})</td>
<td>1346(\text{s})</td>
<td>1171(\text{m})</td>
<td>1078(\text{w})</td>
</tr>
</tbody>
</table>

s = strong, m = medium, w = weak

### Table-2.7: Ion abundance for ligand and its fragmentation* peaks observed in FAB-mass spectrum of [L^2 .2HClO_4]:

<table>
<thead>
<tr>
<th>m/z</th>
<th>Assignments</th>
<th>%Abundance</th>
</tr>
</thead>
<tbody>
<tr>
<td>728</td>
<td>[L^2]^+</td>
<td>70</td>
</tr>
<tr>
<td>1232</td>
<td>[L^2-2HClO_4+Pz-3H]^+</td>
<td>66</td>
</tr>
<tr>
<td>1035</td>
<td>[L^2+Pz]^+</td>
<td>64</td>
</tr>
<tr>
<td>713</td>
<td>[L^2-CH_3]^+</td>
<td>40</td>
</tr>
<tr>
<td>651</td>
<td>[L^2- C_6H_5]^+</td>
<td>20</td>
</tr>
<tr>
<td>448</td>
<td>[\frac{1}{2} L^2+ C_6H_5N_3]^+</td>
<td>22</td>
</tr>
<tr>
<td>441</td>
<td>[\frac{1}{2} L^2+ C_6H_5]^+</td>
<td>20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>m/z</th>
<th>Assignments</th>
<th>%Abundance</th>
</tr>
</thead>
<tbody>
<tr>
<td>419</td>
<td>[\frac{1}{2} L^2 . NCNCH_3]^+</td>
<td>25</td>
</tr>
<tr>
<td>364</td>
<td>\frac{1}{2} [L^2]^+</td>
<td>35</td>
</tr>
<tr>
<td>212</td>
<td>[(C_6H_5NHCH_2)_2]^+</td>
<td>68</td>
</tr>
<tr>
<td>154</td>
<td>[(C_6H_5)_2]^+</td>
<td>50</td>
</tr>
<tr>
<td>120</td>
<td>[C_6H_5NHCH_2 . N]^+</td>
<td>95</td>
</tr>
<tr>
<td>118</td>
<td>[C_6H_5NC.CH_3]^+</td>
<td>80</td>
</tr>
<tr>
<td>106</td>
<td>[C_6H_5NHCH_2]^+</td>
<td>100</td>
</tr>
</tbody>
</table>

*NBA (m-nitrobenzyl alcohol) was used as the matrix for FAB recording which give its peaks at [m/z = 136,137,154,289,307].

*Pz = NBA (307)

### Table-2.8: Position of Resonance peaks δ (in ppm) observed in \(^1\text{H}-\text{NMR}\) of [L^2 .2HClO_4] and their assignments:

<table>
<thead>
<tr>
<th>Assignments</th>
<th>CH(_2)</th>
<th>H(_2)C-NC&lt;</th>
<th>H(_2)C=C-N</th>
<th>H(_2)C=CN</th>
<th>NH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak Position</td>
<td>2.8</td>
<td>7.0</td>
<td>4.01</td>
<td>2.49</td>
<td>5.8</td>
</tr>
<tr>
<td>(12H)</td>
<td>(20H)</td>
<td>(12H)</td>
<td>(8H)</td>
<td>(4H)</td>
<td></td>
</tr>
</tbody>
</table>

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RESULTS AND DISCUSSION

Formation of L\(^1\).2HClO\(_4\):

Condensation reaction of N-acetylaniline with hydrazine hydrate takes place in 2:1 mol ratio in presence of HClO\(_4\) in methanol, producing an intermediate species which contains C\(=\)N bonds. The reaction was monitored by periodically recording the UV-visible spectrum of the reaction mixture which indicated formation of a species having C\(=\)N bonds. The disappearance of a band at 320 nm, characteristic\(^{35}\) of the \(n \rightarrow \pi^*\) transition of (-CO-NH-) group of N-acetylaniline with a concomitant appearance of a new band at 385 nm, is indicative of the formation of new species in the solution. The band at 385 nm is characteristic of the \(\pi \rightarrow \pi^*\) transition reported\(^{42}\) for the C\(=\)N bond in the molecule. This reasonably indicates that the condensation process generated an intermediate species containing C\(=\)N bonds in the molecular unit. Further reaction of the intermediate (in-situ) with a capping agent i.e. mixture of HCHO and aniline (2:1 mol ratio) induces the cyclization process giving a fairly air stable yellow coloured amorphous solid product reasonably, via a 2:2 cyclization process. Analytical data (Table-2.1) of the solid product \(L^1.2\text{HClO}_4\) are consistent with the molecular formula \(C_{48}H_{50}N_{10}.2\text{HClO}_4\ [C_{48}H_{52}N_{10}Cl_2O_8]\). The FAB mass spectrum of solid exhibited the
molecular ion peak \([L^1]^+ \text{ (m/z = 766)}\), along with various relevant peaks generated from the thermal fragmentation process (Table-2.3). The appearance of fragments like \([L^1 \cdot 2\text{HClO}_4 + \text{Bq-2H}]^+ \text{ (m/z = 1100)}\), \([L^1 + \text{Rn}]^+ \text{ (m/z = 1055)}\), (NBA = metanitro benzyl alcohol having its own fragmentations at m/z = 136 (Bq), 137, 154, 289 (Rn), 307) along with other fragments like \(\frac{1}{2}[L^1]^+ \text{ (m/z = 383)}\), \([\text{C}_6\text{H}_5\text{S}]^+ \text{ (m/z = 308)}\), \([\text{C}_6\text{H}_5\text{NHCH}]^2_2\) \text{ (m/z = 212)}\), \([\text{C}_6\text{H}_5\text{S}]_2^+ \text{ (m/z = 154)}\), \([\text{C}_6\text{H}_5\text{NHCH}_2\text{N}]^+ \text{ (m/z = 120)}\) and \([\text{C}_6\text{H}_5\text{NHCH}_2]^+ \text{ (m/z = 106)}\) in good percent abundance is consistent with the presence of these substituents / groups in the framework of the macrocyclic moiety. The important bands observed in the IR spectrum of the compound are summarized in (Table-2.2). The observed important bands are characteristic of \(\nu(\text{N-N})\), \(\nu(\text{C=N})\), \(\nu(\text{C=N})\) aliphatic, \(\nu(\text{C=N})\) aromatic, \(\nu(\text{C=C})\) and \(\nu(\text{C-H})\) fundamental stretching vibrations. The spectrum does not show the strong broad band in the region 1700-1750 cm\(^{-1}\) reported\(^{37}\) for \(\nu(\text{C=O})\) stretching vibration of the N-acetylaniline. However, there is appearance of new strong absorption band at around 1600 cm\(^{-1}\) characteristic\(^{37}\) of \(\nu(\text{C=N})\) stretching vibration. The spectrum also contains a band of strong intensity at \(\sim 1000 \text{ cm}^{-1}\) indicating the presence of N–N bond in the molecular unit. The disappearance of fundamental vibrations due to \(\text{C=O}\) bond stretching frequency with the concomitant appearance of sharp bands for \(\text{C=N}\) and \(\text{N–N}\) bond frequencies indicates the cyclization process giving the final product which contains the \(\text{C=N}\) as
well as N—N bonds. Additional frequencies, characteristic of \( \nu(C—N) \) stretching vibration along with the vibrations of \( \text{CeH}_5, \text{CH}_3, \) and \( C—C \) bands also appeared at their appropriate positions. The spectrum also contained frequencies characteristic of the fundamental vibrations \( (\nu_1, \nu_2, \nu_3) \) of the counter \( \text{ClO}_4^- \) ion, at the reported positions. The observed splitting of the band in the region \( (1050-1130) \text{ cm}^{-1} \) for characteristic \( \nu_2 \) stretching vibration of perchlorate group is indicative of a lowering of the \( \text{ClO}_4^- \) symmetry from perfect \( T_d \) symmetry observed for the free anion to a reduced \( (C_{3v} \) or \( C_{2v} \)) symmetry. The reduction in symmetry is observed when \( \text{ClO}_4^- \) group is involved in bonding either through one oxygen or two oxygen atoms effecting \( C_{3v} \) or \( C_{2v} \) symmetry, respectively of the perchlorate group. The ligand behaved as a non-electrolyte \( (\text{Table } 2.1) \) in dimethyl sulfoxide, an ionising high dielectric constant \( (\varepsilon = 46) \) solvent, supporting the presence of a strong cation-anion interaction between the \([L.2H]^2+\) and the counter \( \text{ClO}_4^- \) ion in the solution. It is reasonable to suggest that the \( \text{ClO}_4^- \) ion is encapsulated in the cavity of the present macrocyclic ligand. There are few reports in the literature \( ^{30} \) indicating that protonated form of polyaza macrocycles having large cavities as in \([1,4,7,10,13,16]\text{hexaazacyclooctadecane} \) \([1,5,9,13,17,21]\text{hexaazacyclooctatetracosane}\) and\([1,5,9,13,17,21,25,29] \text{octazacyclodotriacontan}\) form stable complexes with various organic as
well as inorganic anions such as succinate, Cl \(^{-}\), NO\(_3\) \(^{-}\) and complex anions. This has also been confirmed from the IR data of L\(^{1}\).2HClO\(_4\) where too, encapsulation of the counter ClO\(_4\) \(^{-}\) ion has been evidenced from observed splitting of \(\nu_2\) vibration mode (Table-2.2) into a doublet at 1075 cm\(^{-1}\) and 1118 cm\(^{-1}\). The encapsulation of ClO\(_4\) \(^{-}\) ions in the macrocyclic cavities can be illustrated as in Fig. 2.2. The \(^1\)H-NMR spectrum of L\(^{1}\).2HClO\(_4\) (Table-2.4) recorded in \(d_6\)-DMSO showed signals characteristic of the protons from H\(_{5}\)C=N\(_{\text{<}}\) (6.68, 10H); H\(_{5}\)C=N\(_{\text{\rangle}}\) (7.18, 20H), H\(_3\)C=C=N (4.18, 12H); \(\text{H}_2\text{C} \equiv \text{N}\) (2.58, 8H). The UV-visible spectrum of the ligand showed band at 385 nm assignable to the excitation from the filled \(\pi\) bonded electron of C=N (HOMO) to an empty antibonding \(\pi^*\) orbital (LUMO) i.e. \(\pi \rightarrow \pi^*\) transition of the polyaza moiety. In view of the strong support from physico-chemical and spectroscopic data, the whole process of the formation of the macrocyclic ligand salt [2,8,11,17]tetramethyl [3,5,7,12,14,16]hexaphenyl [1,3,5,7,9,10,12,14,16,18]decaazaoctadeca [2,8,11,17]tetraene dihydroperchlorate i.e. L\(^{1}\).2HClO\(_4\) can be considered as involving 2:2 cyclization in accordance with the scheme-1 shown in (Fig. 2.2). First step (step 1) of the scheme shows the formation of the intermediate species while step 2 indicates the capping mechanism involving cyclization process resulting in the macrocyclic moiety.
Scheme -1

1st Step

\[ 2C_6H_5NH-CO-CH_3 + H_2N-NH_2 \xrightarrow{\text{HClO}_4} [C_6H_5-N-C=N-N-C-N=C-C_6H_5] \cdot \text{HClO}_4 - 2H_2O \]

2nd Step

\[ [C_6H_5-N-C=N-N=C-N=C_6H_5] \cdot \text{HClO}_4 + C_6H_5NH_2 + 2\text{HCHO} \]

Fig. 2.2: Scheme showing the mechanism for the formation of \( L^1 \cdot 2\text{HClO}_4 \)
Formation of \( L^2.2\text{HClO}_4 \):

The in-situ capping reaction of the intermediate species formed in the solution by condensation of N-acetylaniline and hydrazine hydrate with 1,3-diaminopropane and formaldehyde (1:2 mol ratio) follows the same reaction path resulting in \( L^2.2\text{HClO}_4 \) as a stable light yellow coloured solid compound similar to that discussed for the formation of macrocyclic ligand \( L^1.2\text{HClO}_4 \). Here too, the course of the reaction has been monitored by recording the UV-visible spectra of the reaction mixture at regular intervals which indicates formation of a species having \( \text{C}=\text{N} \) bonds. The disappearance of a band at 320 nm characteristic\(^{35} \) of the \( \text{n} \rightarrow \pi^* \) transition of \((-\text{CO-NH-})\) group of N-acetylaniline with a concomitant appearance of a new band at 398 nm is indicative of the formation of new species in the solution. The band at 398 nm is characteristic of the \( \pi \rightarrow \pi^* \) transition reported\(^{42} \) for the \( \text{C}=\text{N} \) bond in the molecule. This reasonably indicates that the condensation process generates an intermediate species containing \( \text{C}=\text{N} \) bonds in the molecular unit. Further reaction of the intermediate (in-situ) with a capping agent i.e. mixture of HCHO and 1,3-diaminopropane (2:1 mol ratio) induces the cyclization process giving a fairly air stable light yellow coloured amorphous solid product, reasonably, via a 2:2 cyclization process. Analytical data (Table 2.5) of the solid product \( L^2.2\text{HClO}_4 \) are consistent with the molecular formula \( \text{C}_{42}\text{H}_{56}\text{N}_{12}.2\text{HClO}_4 \ [\text{C}_{42}\text{H}_{58}\text{N}_{12}\text{Cl}_2\text{O}_8] \). The FAB-mass spectrum of solid
exhibited the molecular ion peak $[L^2]^+ (m/z=728)$, along with various relevant peaks generated from the thermal fragmentation process (Table 2.7). The appearance of fragments like $[L^2.2HClO_4+Pz-3H]^+ (m/z=1232)$, $[L^2+ Pz]^+ (m/z=1035)$, (NBA= metanitro benzyl alcohol having its own fragmentations at m/z = 136, 137, 154, 289, 307 (Pz)), $[L^2-CH_3]^+ (m/z=713)$, $[L^2-C_6H_5]^+ (m/z=651)$, $[\frac{1}{2}L^2+C_3H_6N_3]^+ (m/z=448)$, $[\frac{1}{2}L^2+C_6H_5]^+ (m/z=441)$, $[\frac{1}{2}L^2.NCNCH_3]^+ (m/z=419)$, $\frac{1}{2}[L^2]^+ (m/z=364)$, $[(C_6H_5NHCH_2)_2]^+ (m/z=212)$, $[(C_6H_5)_2]^+ (m/z=154)$, $[C_6H_5NHCH_2N]^+ (m/z=120)$, $[C_6H_5NC.CH_3]^+ (m/z=118)$, $[C_6H_5NHCH_2]^+ (m/z=106)$, in good percent abundance are consistent with the presence of these substituents/groups in the frame work of the macrocyclic moiety. The important bands observed in the IR spectrum of the compound are summarized in (Table-2.6). The observed important bands are characteristic of $\nu(N-N)$, $\nu(NH)$, $\nu(C-N)$, $\nu(C-C)$ and $\nu(C-H)$ fundamental stretching vibrations. The spectrum does not show the strong broad band in the region 1700-1750 cm$^{-1}$ reported$^{37}$ for $\nu(C=O)$ stretching vibration of the N-acetylaniline. However, there is appearance of new strong absorption band at around 1600 cm$^{-1}$ characteristic$^{37}$ of $\nu(C=N)$ stretching vibration. The spectrum also contains a band of strong intensity at $\sim$1000 cm$^{-1}$ indicating the presence of N–N bond in the molecular unit. The disappearance of fundamental vibrations due to C=O bond stretching frequency with the concomitant appearance of sharp bands for C=N and N–N bond
frequencies indicate the cyclization process giving the final product which contains the C=\text{N} as well as N–N bonds. Additional frequencies characteristic of v(C–N) stretching vibration along with the vibration of C₆H₅, CH₃ and C–C bonds also appeared at their appropriate positions. The spectrum also contained frequencies characteristic of the fundamental vibrations (ν₁, ν₂, ν₃) of the counter ClO₄⁻ ion, at the reported⁴³ positions. The observed splitting of the band in the region (1050–1130) cm⁻¹ characteristic of ν₂ stretching vibration of perchlorate group is indicative of a lowering of the ClO₄⁻ symmetry from perfect T₄d symmetry observed for the free anion to a reduced (C₃v or C₂v) symmetry. The reduction in symmetry is observed when ClO₄ group is bonded either through one oxygen or two oxygen atoms effecting C₃v or C₂v symmetry of the perchlorate group. The ligand behaved as a non-electrolyte⁴⁴ (Table-2.5) in dimethyl sulfoxide (DMSO), an ionizing high dielectric constant (ε=46) solvent, supporting the presence of a strong cation-anion interaction between the [L.2H]²⁺ and the counter ClO₄⁻ ion in the solution. It is reasonable to suggest that the ClO₄⁻ ion is encapsulated in the cavity of the macrocyclic ligand. This has also been confirmed with the IR data of [L².2HClO₄]. The encapsulation of ClO₄⁻ ions in the macrocyclic cavities can be illustrated as in Fig. 2.3.

The ¹H-NMR spectrum of L².2HClO₄ (Table-2.8) recorded in d₆-
DMSO showed signals that are characteristic of the protons from NH (5.8δ, 4H), H₃C=N (2.49δ, 8H); H₅C=N (4.01δ, 12H); H₅C₆=N (7.0δ, 20H) and CH₂ (2.8δ, 12H).

The UV-visible spectrum of the ligand showed band at 398 nm assignable to the excitation from the filled π bonded electron of C=N (HOMO) to an empty antibonding π* orbital (LUMO) i.e. π → π* transition of the polyaza moiety. The formation of the macrocyclic ligand salt [2,12,15,25]tetramethyl [3,11,16,24]tetraphenyl[1,3,5,9,11,13,14,16,18,22,24,26] dodecaazahexacosa [2,12,15,25]tetraane dihydro-perchlorate i.e. [L²·2HClO₄] can be considered as involving 2:2 cyclization in accordance with the scheme-2 shown in (Fig. 2.3). First step (step-1) of the scheme-2 shows the formation of intermediate species while step-2 indicates the capping mechanism involving cyclization process resulting in the macrocyclic moiety.
Scheme – 2

1st Step

\[ 2\text{C}_6\text{H}_5\text{NH}–\text{CO}–\text{CH}_3 + \text{H}_2\text{N}–\text{NH}_2 \xrightarrow{\text{HClO}_4} [\text{C}_6\text{H}_5–\text{N}–\text{C}–\text{N}–\text{N}–\text{C}–\text{N}–\text{C}_6\text{H}_5] \cdot \text{HClO}_4 - 2\text{H}_2\text{O} \]

2nd Step

\[ \text{H}_3\text{N}(\text{CH}_2)_3\text{NH}_2 + 2\text{HCHO} \rightarrow [\text{H}_2\text{C}–\text{N}–(\text{CH}_2)_3–\text{N}=\text{CH}_2] + 2\text{H}_2\text{O} \]

\[ [\text{C}_6\text{H}_5–\text{N}–\text{C}=\text{N}–\text{N}=\text{C}–\text{N}–\text{C}_6\text{H}_5] \cdot \text{HClO}_4 + [\text{H}_2\text{C}–\text{N}–(\text{CH}_2)_3–\text{N}=\text{CH}_2] \]

Fig. 2.3: Scheme showing the mechanism for the formation of \( \text{L}^2 \cdot \text{2HClO}_4 \)
REFERENCES:


7. For reviews on binuclear enzymes and models see:


    


    


