SYNTHESIS, CHARACTERISATION AND PHYSICOCHEMICAL STUDIES OF SOME POLYPHENOLIC COMPOUNDS

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By

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Certificate

It is certified that the work contained in the thesis entitled "**SYNTHESIS, CHARACTERISATION AND PHYSICOCHEMICAL STUDIES OF SOME POLYPHENOLIC COMPOUNDS**" by Ms. Jyotirekha G. Handique, a student of the Department of Chemistry, Indian Institute of Technology, Guwahati for the award of the degree of Doctor of Philosophy has been carried out under my supervision and that this work has not been submitted elsewhere for a degree.

September, 2001

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CONTENTS

CHAPTER 1

POLYPHENOLIC COMPOUNDS: AN OVERVIEW

1.1 Brief introduction

Polyphenolic compounds are usually referred to a diverse group of naturally occurring compounds containing multiple phenolic functionalities[1]. These compounds are commonly found in higher plants. They have synthetic, medicinal and industrial value. Naturally occurring polyphenols are known to have numerous biological activities. They are found to be potential candidate for use as drugs, for example[1], in disease like AIDS, heart ailments, ulcer formation, bacterial infection, mutagenesis and neural disorders. Plant polyphenols are also responsible for flower colouration[2-5]. The prime factor for colouration of flower is supramolecular interaction. Stacking of aromatic nuclei, keto-enol tautomerism and pH also effect the change of colour in polyphenols.

From chemical point of view, polyphenols can react with one-electron oxidants, which prevents free radical formation in biological systems. Such single electron oxidation processes are considered to be the key steps of polyphenols while acting as drugs[6]. The ability of these compounds to interact with metal ions such as Fe^{2+}, which is capable of generating free radical has significance in their bioactivity. However, some polyphenols under special circumstances may behave as pro-oxidant[1]. The other important aspects of these polyphenols are the interactions of available multiple polar functional groups for selective and unselective binding with biologically important molecules such as proteins. Because of the presence of

multiple phenol functionalities, they interact with proteins so strongly, that precipitation of protein-polyphenol complexes occurs frequently, which is the basis of their use in the tanning process of leather[7].

The foregoing discussion gives us a description of polyphenolic compounds referring to few naturally occurring systems, as classified by phytochemists. While making a general classification of polyphenolic compounds it would be inappropriate if we do not account for the synthetic compounds possessing multiple units of phenolic group. For this purpose, the simplest building blocks of polyphenols and their possible arrangements to construct them in a repeated manner is important. Again, those polymers indirectly derived from phenols, but having functionalised phenolic units also need to be taken care, in such classification. The tailor-made polyphenolic compounds having multiple number of phenolic units have their own importance. Novolacs and resols are well known industrial polymers because of their excellent toughness and temperature-resistance. Nowadays, phenolic resins have numerous applications in modern technological fields, such as in synthetic fibres, in computer technology (photoresists, microchips) and in aerospace technology[8]. About 6-8% of worldwide production of phenolic resins, mainly resols, novolaks, alkylphenol resins and esterified resins are consumed as coating and printing inks. Some calixarene analogues, having a bowl shape and with long flexible alkyl substituents have been found to show mesogenic properties[9]. Chromatographic separation materials also have been designed from polyphenolic compounds. Some calixarenes have been used as gas chromatography stationary phase[10-12]. Recently, two resorcarene derivatives have been used for separation of

substituted benzenes[13]. Poly (phenylene oxide) polymers have been used to support metal complex catalyst. Functionalised poly (2,6-dimethylphenylene oxide) and poly (2,6-diphenylphenylene oxide) have been used to support titanium hydrogenation catalyst and rhodium hydroformylation catalyst[14]. These polymers are also thermally stable and mechanically stronger than other organic polymeric supports like polystyrene[15].

The classification of natural polyphenols is mainly based on the types of building blocks that appear as repeated units. The prominent textbooks and synthetic chemist have classified the different naturally occurring polyphenols on the basis of the three repeated building blocks[16] namely (i) leucoanthocyanidins [**1.1**] (ii) flavone glycosides [**1.II**] and (iii) esters and amides of hydroxycinnamic acids [**1.III**].

A general classification of polyphenol would not be complete if simple systems (scheme 1.1) irrespective of cyclic and open nature are not included.

Compounds having repeated phenolic building blocks with direct C-C bonds or with some intervening atoms, represented by [**1.IV**] are also referred to as polyphenols. The building blocks in such systems may generally be comprised of two repeated entities, one is the phenolic aromatic part and other is the linker. Schematically one can represent such system with the scheme **1.1**

Besides the polyphenolic compounds that are included in the above classifications, phenolic compounds arranged in organized arrays in space through weak interactions with or without intervening molecules also needs attention. Such systems can have replication of reactivity of aggregated multiple phenolic groups in organized manner. In addition to these, more complicated systems may also be created by star or dendrimeric type of polyphenolic compounds, which are compiled as a miscellaneous category and discussed in the subsection **1.2.4** of this chapter.

1.2 Classification of polyphenolic compounds

A general classification of polyphenols can be represented by scheme 1.2

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In the next subsections, the descriptions of polyphenols and their synthetic and structural aspects are presented.

1.2.1 Naturally occurring polyphenolic compounds

1.2.1a Proanthocyanidin derivatives

These oligomers contain two to six units of or high molecular weight polymer of flavan-3-ol[16]. The flavan-3-ol units are joined to each other at 4- to 8-positions and in some cases at 4- to 6- positions by direct C-C bonds, as shown in **scheme 1.3**. The synthesis of oligomer of proathocyanidin starts from the phenolic

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flavan-3-ols which undergoes stereospecific nucleophilic condensation with a quinone methide unit. This dimer further condenses with a quinone methide and the process proceeds to form oligomers and polymers with C-4 to C-8 and to a lesser extent with C-4 to C-6 interflavan bonds.

1.2.1b Galloyl and hexahydroxydiphenyl ester derivatives

In this class, different gallic and hexahydrodiphenic acid derivatives are present as esters of a polyol (usually D-glucose) at the core of the polyphenolic ester[16]. The pentagalloyl-D-glucose [**1.V**] is the principal precursor, from which some other member of this class have been chemically synthesized[17].

Higher oligomers and polymers of this type of esters comprise two very well known sub-classes of polyphenols, namely, gallotannins and ellagitannins. It is assumed that the hexahydroxydiphenoyl esters and their derivatives are formed by oxidative coupling reactions of adjacent galloyl ester groups (**scheme 1.4**).

Lactonisation of hexahydroxydiphenic ester by acid yields ellagic acid (bis-lactone of hexahydroxydiphenic acid); ellagitannins are derived from these lactones. There are different structures of ellagitannins which mainly originate from (a) the different extent of galloylation, (b) the intramolecular oxidative C-C coupling of galloyl

groups, (c) the dehydrogenative and hydrolytic cleavage of galloyl group/s of aromatic rings and (d) oligmerisation via oxidative C-O coupling reaction[18].

Alternatively, intramolecular C-C coupling of galloyl ester groups results in the formation of hexahydroxydiphenoyl esters with decreased conformational flexibility (**scheme 1.5**).

1.2.1c Hydroxy cinnamic acid derivatives

These are the condensation oligomers of mono lignols, namely, p-coumaryl alcohol, coniferyl alcohol and sinapyl alcohol[1,19,20]. Lignin is one such example formed from the oxidative polymerization of coniferyl alcohol. Lignin is a reticulated polyphenol, having three main functions in plants. They provide mechanical support, play role in conduction of water and also provide protection against biodegradation in plants. The formation of lignin involves various radicals of coniferyl alcohol as shown in **scheme 1.6**.

1.2.1d Phloroglucinol derivatives

These oligomers are derived from phloroglucinol subunits. They are formed by oxidative C-C and C-O coupling reactions of phloroglucinol. One example[16] of

this class is furofureckol [**1.VI**]. It has four units of phloroglucinol that are condensed by both C-C and C-O coupling. They are found in marine brown algae.

1.2.2 Synthetic polyphenolic compounds

In the case of a naturally occurring polyphenolic compound one has to make a retrospection of the natural product to get the monomeric building blocks. This may and may not lead to identify a less complicated phenolic counterpart. This happens primarily due to the fact that biological processes are complicated and original simple phenolic components may get first transformed to another one through multiple or single step transformations and this particular part may appear as the repeated building blocks.

But for synthetic polyphenolic compounds having relatively simple building blocks such complicacies can be avoided as the synthetic protocol for monomeric unit is known. While visualizing a polyphenolic compound the representative pictures having repeated phenolic units with the linker are illustrated by **scheme 1.1**. Hence, it can be stated that while in biological field making correlation between a polyphenol with its simple building blocks is retrospective, in synthetic field, one

usually starts from the primary units. The other important point in synthetic chemistry is to look for a reagent that would provide a basis for polymerization reaction in the desired direction. Thus, the construction of polyphenolic compounds from certain simple building blocks with synthetic methodology is important. These are highlighted in the following subsections with the possible application and their physicochemical properties.

1.2.2a Polyphenolics without intervening atoms

These are the simplest polyphenols that can be formed by multiple phenolic units via direct C-C bond between aromatic part of phenols. They can either be open chain or cyclic.

Open chain

It is very easy to visualize the phenolic oligomers having direct C-C bond. But in reality there is limited number of such systems due to their instability toward oxidations and also limited chemical methodology to construct uniform chain. Oxidative radical coupling reaction is used for synthesis of such oligomers. For example, phenols with one or two of its reactive positions blocked by alkyl groups, on oxidation by a Cu(II) salt yield dimer or trimer, [**1.VII, 1.VIII**]. However, drastic reaction conditions are required which may also degrade the oligomers[21].

The oxidative reactions of naphthols give C-C bonded low molecular weight compounds and majority of the products obtained from such reactions are binaphthols[22]. One of the promising reaction that provides a route to synthesise a C-C bonded polyphenolic is the palladium catalysed coupling reaction of aromatic boric esters with a halobenzene (**Scheme 1.7**)[23].

In a recent report, poly naphthalenic compounds of methyl ether of 2,3-naphthalenediol[24] is studied. Helical structure as well as interesting optical properties are obtained in such compounds.

The enzyme catalysed reaction of phenolic compounds also leads to C-C bonded polyphenols. The first example of enzymatic polymerisation of various phenol derivatives was done by an enzyme called Horse Radish Peroxidase(HRP)[25]. Enzymatic polymerisation of phenols and alkyl phenols by HRP showed that the position and chain length of the alkyl group highly affect the chain length of the oligomer. The medium of polymerisation also has role in molecular weight of the

resultant polyphenol. It has been observed that polymerisation of phenols in reverse micellar system resulted in the formation of higher molecular weight polyphenols in comparison to those formed in aqueous organic solvent.

Cyclic

Spherands are cyclic oligomers of aromatic compounds and the first report of this type was that of a cyclohexametaphenylene system. This compound was synthesized[26] from *p*-cresol, which was first oxidatively coupled by using $FeCl_3$ to get a trimer. Bromination of the trimer, followed by methylation and further treatment with butyl lithium leads to the corresponding spherand (**scheme 1.8**).

1.2.2b Polyphenols with intervening carbon atom

Phenol-aldehyde oligomers

The controlled condensation reaction between phenol and an aldehyde, such as formaldehyde[27] gives either a cyclic or open chain polyphenolic compounds. Depending on the reaction conditions, the condensation leads to a range of products.

Baeyer in 1872[27,28] first reported the condensation reaction of phenols and aldehydes. The reaction of aldehyde and phenol in both basic and acidic media lead to the formation of methylol groups (CH_2OH) at 2 and 6 (*ortho*) and/or at 4 (*para*) positions with respect to the phenolic –OH. Subsequent chain growth may result from two types of condensations: a) condensation between two methylol phenols resulting in CH_2OCH_2 bridges and/or b) further condensation of methylol group with *ortho* and *para* position of phenols resulting in CH_2 bridges between phenolic rings (**scheme 1.9**).

Such oligomers can be classified into the following groups:

Open chain

Novolacs are open chain condensation oligomer of phenol with aldehyde. The term novolac has come from Latin word *novo*: new and Sanskrit *lac*: hundred

thousand. These oligomers were used as a substitute for shellac, the purified secretions (lac) of the larvae of the insect *Kerria lacca*[20]. A hundred thousand insects are needed to produce one ounce (28.4 g) of shellac. These oligomers/polymers are prepared by reacting phenol with formaldehyde under acidic conditions. The molar ratio of phenol-aldehyde below 1:1 gives limited crosslinks, however, use of excess formaldehyde leads to crosslinked products [**1.IX**].

To construct the uniform polyphenol units as shown in [**1.VIII**] one needs to address the *ortho* and *para* selectivity on the aromatic part during the condensation reaction. It is generally observed that at a low pH, condensation at the *para* position and at a pH of about 3-5, condensation at the *ortho* position is favoured.

An unsubstituted phenol having *o*- and *p*- positions free yields condensation products without selectivity, thereby giving highly irregular crosslinked products. Hunter et al[29] prepared phenol-aldehyde linear oligomers upto five phenolic rings

starting with appropriately functionalised diphenylmethane derivatives (**scheme 1.10**).

Cyclic

Calixarenes

Phenols with *para*-substituted alkyl group, upon condensation with aldehydes under specific reaction conditions give cyclic oligomers, which are called[27, 28] calixarenes. The term calixarene was introduced by Gutsche, as these molecules have cuplike coformation when the all aryl groups orient in the same direction (Latin: calix- cuplike)[28]. These cyclic oligomers are designated as 'calixarenes' and a bracketed number between the prefix calix- and the suffix –arene is used to show the size of the ring. The prefix of the substituted phenol is written

ahead of these. For example, the cyclic tetramer, obtained from *p*-t-butyl phenol with formaldehyde is designated as *p*-*t*-butylcalix[4]arene.

The ring size also varies[28] depending upon reaction conditions. A base catalysed condensation reaction of *para* alkyl-substituted phenols with formaldehyde affords tetra-, hexa- and octameric macrocyclic products [**1.X, 1.X1**, **1.XII**], whereas acid catalysed condensation of resorcinol with aliphatic and aromatic aldehyde give cyclic tetrameric products [**1.XIII**][28]. Increase in number of hydroxy group in the aromatic part drastically effects the conformation and physical as well as chemical properties of these systems. On alkylation and silylation of the phenolic hydroxyls[30] or on functionalisation of the ring the cavity size changes. For example, the resorcinol derived cyclic tetramer, termed as resorc[4]arene [**1.XIII**] provide deeper cavities than a usual calix[n]arene. The cyclic trimer, cycloveratrylene prepared from catechol[31], after transformation into chiral derivatives was used as a preorganising matrix for the design of receptors for transition metals[32].

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Cyclic tetrameric condensation products from 1- and 2-naphthol and formaldehyde analogous to calixarenes also have been prepared[33-36]. These are termed as calix[n]naphthalenes. For example, reaction of 1-naphthol can occur at the C-2 and C-4 positions which are *ortho*- and *para*- to the hydroxyl group and three isomeric bis(1-hydroxynaphthyl)methanes can be obtained in the first condensation step. These are *o*-*o*-, *p*-*p*- and *o*-*p*- products and on further condensation should yield four isomers (**scheme 1.12**). Three isomers, [**1.XIV, 1.XV, 1.XVI],** have only been isolated. These cyclic compounds are reported to have deeper cavities than calixarenes for inclusion.

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However, condensation of *p*-*t*-butylphenol with formaldehyde in basic medium leads to a mixture of cyclic compounds containing not only methylene, but also dimethylene ether bridge[27]. They are shown in **scheme 1.13.**

Under drastic reaction conditions, cleavage of methylene bridges and restructuring of phenolic units were observed. This kind of rearrangement allows the formation of calix[4]arenes from calix[8]arenes. Calixarenes can be synthesized either by stepwise conversion so as to prepare a synthetic precursor ready for cyclisation (stepwise synthesis, **scheme 1.12**)[28] or by taking a synthetic

precursor that would combine to give the desired cyclic calix[n]arenes (straightforward synthesis, **scheme 1.14**).

Spherand type calixarene

These are calixarene analogues, synthesised by the condensation of bisphenol[**1.17**] with formaldehyde in the presence of a base (**scheme 1.15**)[37]. These can be considered as hybrids of calixarenes and spherands and in turn, their stereochemistry is also more complex than calixarenes with two arrangements (R- and S-) being inherently present in bisphenol. Mild oxidation of calixarenes affords spirodienone derivatives of calixarenes (**Scheme 1.15**). Spherand type calixarenes[**1.XVIII**] have also been modified to yield spirodienone derivatives[**1.XIX**][38].

1.2.2c Polyphenols with intervening heteroatoms

Open chain

Poly-phenylene-ether

These compounds are derived from phenolic compounds, having intervening oxygen bridges. One of such examples is shown in **scheme 1.16**[39].

This class of oligomer has interesting optical properties[40], and they also have application as engineering plastics [41, 42, 43]. The oxidative coupling reactions are used to prepare this kind of oligomers[44]. Enzyme catalysed oxidative polymerisation reactions are also useful in synthesizing such polyphenols[27].

Polyphenolic compounds with intervening sulphur atom/s

A series of acyclic *p*-methyl- and *p*-t-butyl phenol and formaldehyde tetramer [**1.XX**], in which some, or all, of methylene bridge(s) are replaced by sulphur bridge(s) have been synthesized[45].

Cyclic

Calixarenes with other hetero atoms

Oxacalixarenes and thiacalixarene are calixarenes in which methylene bridges are replaced by oxygen or sulphur atom respectively. Each of these classes can be divided to homobridged and heterobridged depending on uniformity of distribution of the heteroatoms[46].

Oxacalixarenes

These are calixarene analogues, in which, CH_2OCH_2 bridges replace CH_2 bridges completely (homooxacalixarenes) or partially (heterooxacalixarenes) between the aromatic units[47]. Gutsche and co-worker[48] reported a general and direct method for preparation of oxacalixarenes by thermal dehydration of bishydroxymethylated phenols, which is shown in **scheme 1.17**.

Hexahomotrioxacalix[3]arenes have been prepared by stepwise synthesis based on cyclisation of the linear trimer [**1.XXI**] (**scheme 1.18**). But in the process an irregular cyclic compound, that is, heptahomotetraoxacalix[3]arene[**1.XXII**] was also formed.

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Recently, oxacalixnaphthalenes [e.g.**1.XXIII** and **1.XXIV**] also have been synthesized to combine both the features of oxacalixarene, that is additional CH_2OCH_2 groups for more binding sites and of calixnaphthalenes, having deeper cavities[49].

Thiacalixarene

Thiacalixarenes have –S- bridges instead of $–CH_2-$ bridges in a typical calixarene. First report of this type are 2,8,14,20- tetrathiacalix[4]arene [**1.XXV**] and 5,11,17,23-tetra-*tert*-butyl-2,8,14,20-tetrathiacalix[4]arene [**1.XXVI**][50]. These compounds after alkylation have been found to possess interesting properties both in the solid state and in solution[51].

Different conformers of thiacalixarenes can be prepared by alkylation. It has been observed that while in case of smaller alkyl groups like ethyl, all four conformers, namely, cone, partial cone, 1,2-alternate, 1,3-alternate are present at room temperature. But in case of bigger groups, like propyl, the interconversion takes place only at high temperature[52].

These thiacalixarenes are also found to have larger cavity than that of analogous calixarenes[53]. Oxidation of the sulphur bridges to sulphones or sulphoxide moieties can create new ligands out of these groups with potentially interesting complexation abilities[54-56].

1.2.2d Miscellaneous

Repeated phenolic units in polymeric chain

This class of compounds is not strictly polyphenols but the oligomers with phenolic units in regular intervals. Two examples of such oligomer or polymer are

the polystyrene containing phenolic functionality [**1.XXVII**] and epoxy resins containing phenolic functionality [**1.XXVIII**][57].

Chiral binaphthyl compound [**1.XXIX**] catalyses asymmetric addition of dialkyl and diaryl zinc to aldehydes. However, the recoverability of the catalyst could be improved when its polymeric counterpart [**1.XXX**][58] is used.

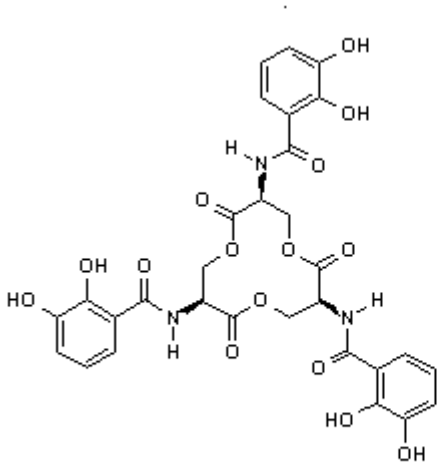
Branched chain type

This is a class of polyphenolic compound where branches polypheolic units are anchored to central core molecule. The first of its kind [**1.XXXI**] was synthesised by acid catalysed cross linking of novolac by using an N-methoxy methylated melamine cross-linker[59].

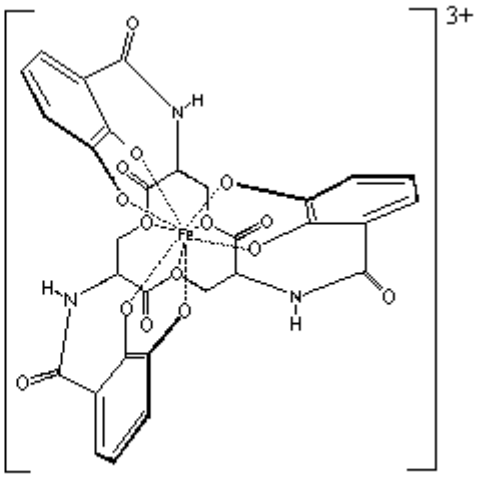
Star type polyphenol

In this type of polyphenol multiple numbers of phenolic units are grown on sequential manner from a central core molecule in different direction in organized manner and several repeated branching can occur. One such type of polyphenol[60,61] is naturally occurring enterobactin. This is involved in iron transport by

complexation of Fe^{3+}. Such polyphenolic compound serve as hexadentate chelate ligands called siderophores. Figure [**1.XXXIII**] is the iron complex of a siderophore [**1.XXXII**]. For understanding the ion transport in biological systems, this type of synthetic polyphenolic compounds can be of immense help.



1.XXXII



1.XXXIII

Polyphenols held by weak forces

As already stated, polyphenolic compounds have the provision for extensive H-bonding, in many cases they are found to exist as H-bonded clusters or aggregates[62]. In these aggregates charge transfer interactions, keto-enol tautomerism

are factors that contribute to make the aggregates/clusters well defined[63]. For example, hydroquinone is the simplest example of dihydroxyphenol, which exists in the form of aggregate. Depending on the arrangement of the aggregated units it can exist in α, β and γ form. Of late, Aoyama and his co-worker have reported some polyphenolic systems that are held together by intervening atoms to give interesting structures[64] as well as catalytic activities[65]. They have developed a solid Bronsted base catalyst[65] for some base-promoted organic reaction by immobilising La^{3+} in a H-bonded tetraphenol network [**1.XXXIV**]. This is an amorphous 1:2 co-ordination polymer composed of tetraanionic polyphenoxide and hydroxylanthanum dications with O^{-}----$[LaOH]^{2+}$ -- O^{-} bridges.

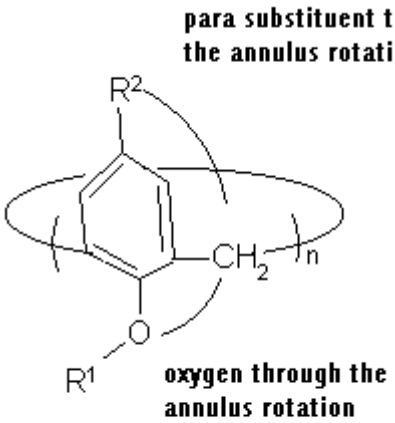
In another report, they have designed a diamondoid organic lattice by using a tetraphenol as a node and benzoquinone as a spacer[64] [**1.XXXV**].

1.3 Special features of polyphenolic compounds

Assisted by both intra- and intermolecular H-bonding, polyphenolic compounds show interesting conformational, inclusion and complexation behaviour.

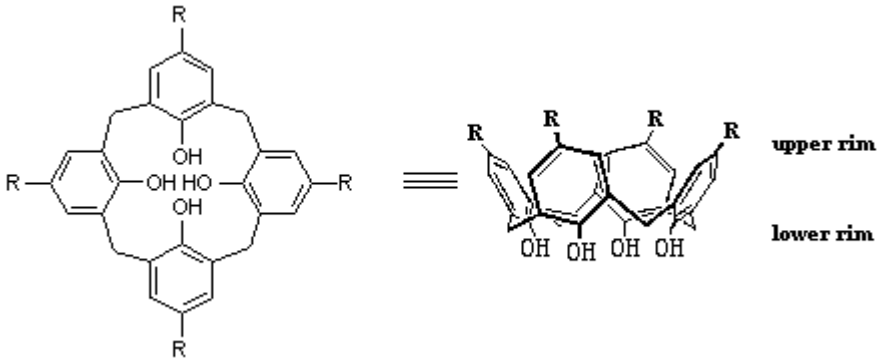
1.3.1 Conformational flexibility

Conformational flexibility of polyphenolic compounds is best understood in calixarenes. This can also be manipulated according to desired direction by introducing appropriate functional groups either in the upper rim or in the lower rim or in the both. In calixarenes, phenolic units are held by methylene bridges and are flexible for conformational changes. They show spectacular conformational behaviour on changing solvent, temperature and on further funtionalisation. This flexibility is due to the possible orientations of phenol units. Such conformational flexibility may occur through two mechanisms: the oxygen-through-the annulus rotation and the para-substituent-through-the annulus rotation [**1.XXXVI**][66].

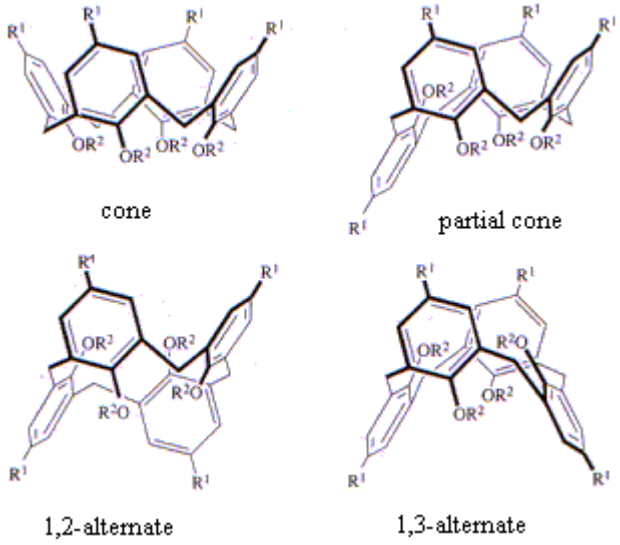


[1.XXXVI]

These are the two mechanisms of rotation by which the calixarenes adopt cup or cone coformation. These conformers are stabilized by the intramolecular hydrogen-bonding interaction between –OH groups. For a typical calixarene, there are two different zones in its cone like conformation. The lower zone contains the phenolic hydroxy groups and the upper zone contains the alkyl-substituted *para*-positions of the constituent phenols, which are called the 'lower rim' and 'upper rim' respectively.



In the case of O-alkylated calixarenes, the intramolecular H-bonding is not present and the through the annulus rotation of the aryl ring changes from the hydroxy counterpart. Thus, they give different type of conformations, which is illustrated by taking the example of tetra-O-alkylated calix[4]arene.

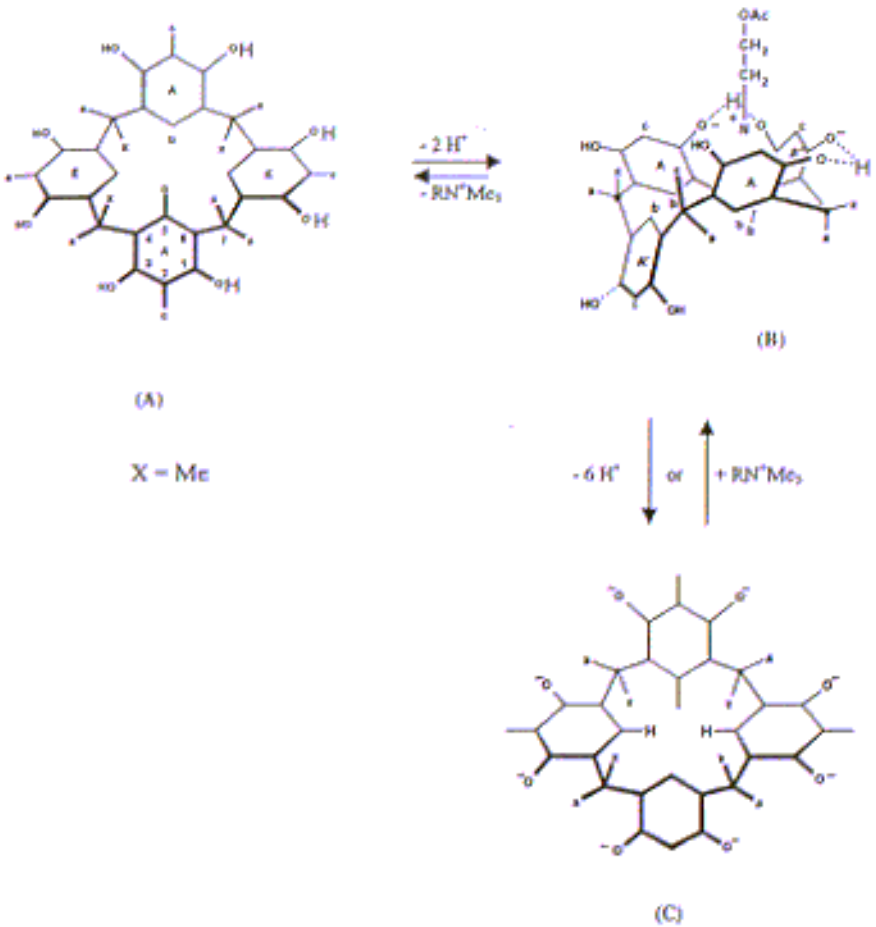


For higher calixarenes, the number of possible conformations is much higher than calix[4]arene. Because of their unique molecular structure with the possibility of 'shaping' and 'tuning', they have been widely investigated as molecular scaffolds and as building blocks in designing suitable molecular structure for supramolecular studies[28, 66].

One very striking complexation behaviour of resorcarene with ammonium ion is studied[67,68] in the light of their different conformational changes (**scheme 1.20**). As a function of pH, the resorc[4]arene shows three different conformations

[A, B and C]. Only one conformer [B] is capable of complexing with ammonium ion. Out of the other two conformers, one can complex with ammonium ion when it changes its conformation. In this process it has to absorb two protons from the solution, thus showing the behaviour of a proton pump.

These features were discussed in the section dealing with calixarenes and are not discussed further. However, to show the utility of such conformational outcome, the behaviour of a resorcarene to work as a proton pump is highlighted here.



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1.3.2 Non covalent interactions

1.3.2a H-bonding

Phenols and in turn, polyphenolic compounds show amphiphatic behaviour since the phenolic hydroxy groups are hydrophilic while the aromatic rings are hydrophobic. Because of the presence of multiple hydroxyl groups, phenolic compounds can form extensive hydrogen bonding. The binding with a substrate with H-bonding becomes very strong as a result of multiple site binding and this explains the complexation of polyphenols with various substrates capable of making H-bonds. Conformational mobility also contributes to a great extent, which facilitates multiple site binding. As an example, complexation of polyphenols with proteins may be cited, where strong association results from the conformational mobility in both substrates. Again, the binding of polyphenols with a protein with a loose, random coil conformation results in strong binding in comparison to complexation of polyphenols with globular protein[16].

In case of natural polyphenolics, there are numerous examples of molecular recognition. Complexation between caffeine and polyphenols due to weak

intermolecular forces has long been studied. The black tea polyphenol theaflavin [**1.XXXVIII**] has been found to complex with caffeine[**1.XXXVII**][69], which is the cause of formation of turbidity in tea infusion at temperature < 60°C.

Effect of H-bonding on acidity

Calix arenes are the best examples for demonstrating the effect of H-bonding in their coformational and binding behaviour. Large number of hydroxyl groups in polyphenolic compounds may undergo intramolecular H-bonding, which can persist even in aqueous solution. This is reflected in anomalously low first pK_a value of the following calixarenes, in comparison to their respective phenols[68,70]. This lowering of pK_a is attributed to

H-bond stabilization of the respective phenolate anions. In another example of resorcarene, pK_a for the first four protons is two units lower than that of resorcinol, whereas the pK_a of the remaining four protons involved in the especially strong H-bonds is above even methanol.

1.3.2b Consequence of non-covalent interaction and preferential structure

Recognition of neutral species

Resorcarene derivative [**1.XXXIX**] binds selectively with cytidine[71]. It was attributed to possible complementary hydrogen bonding. The host resorc[4]arene has a bowl shaped aromatic cavity equipped with four distinct H-bonding sites.

Recognition of amino acids by calixarenes involves simultaneous recognition of ammonium group, carboxylate group and the side chain. This is however, sometimes difficult, because strong solvation shields zwitterionic heads from attractive interactions of ionic binding sites. Again, proximity of counter charges in an amino acid also reduces the complexing ability. Hence the side chain should be the decisive factor for selectivity, which is exploited to some extent, by taking the weak hydrophobic interaction and mere repulsion of the recognizing molecule.

Kobayashi *et al*[72] used calixarene tetrasulphonate[**1.XL**] for this purpose, where the side chain length and the size of aromatic ring in the side chain contributed to the recognition of different amino acids.

Cation recognition

Selective recognition of cations is very much necessary in both analytical and clinical chemistry. For example, the selective recognition of NH_4^+ from monovalent metal ions, particularly, K^+, has attracted considerable interest in clinical chemistry[73]. In measuring urea content in blood after converting it into NH_4^+, K^+ always cause problem because of similar size. Functional calixarenes, exhibiting chemoselective properties in recognition of these cations have been reported by Swager and his co-workers[74, 75].

Chiral recognition

Chiral recognition has been of immense importance in biological as well as analytical chemistry. Polyphenolic compounds have the potentiality for designing molecular host for chiral recognition. Araki *et al*[76] had shown ability of homooxacalixarenes for chiral recognition of α-amino acid derivatives.

The origin of many flower colour has been attributed to anthocyanins. The pattern of assembling of various components also has a major role in the variation of colour. Precise molecular recognition like chiral recognition also occurs in these assemblies[77]. For the blue colour of *Salvia patens,* it has been demonstrated that, the gross structure of the pigment is the result of chiral molecular recognition of six molecules of an anthocyanin, six molecules of a flavone and two metal atoms, where multiple phenolic functionalities of the anthocyanin and flavone units play a major role[78].

1.3.3 Inclusion

Polyphenolic compounds and their parent phenols are widely used for their ability to include organic and inorganic compounds and hence they modify the properties of a large variety of guest molecules. Whether it is cyclic or open chain compounds, they can form inclusion complexes. Many of them can trap common solvent molecules such as CH_2Cl_2, toluene etc. However, in the case of cyclic counterparts, two types of inclusion complex have been observed. In the first type one molecule of guest is held inside the cavity of one host molecule whereas in the second type two molecules of host face each other by upper rim to encapsulate one guest molecule. The first report of the type having ingested molecule is a 1:1 complex between *p-tert*-butyl-calix[4]arene and toluene[79,80] and an example of the other type is the 1:2 complex between anisole and *p-t-butyl*-calix[4]arene[81].

Although calixarenes have been studied for their inclusion of charged organic species or α-amino acids, of late, inclusion of radical by calixarenes also has been reported[82]. In this report, inclusion of benzyl *tert*-butyl nitroxide[**1.XLI**] was used to probe its inclusion in two water-soluble calixarene viz. Pentasodium 25,26,27,28-tetrahydroxycalix[4]arene-5,11,17,23-tetrasulphonate[**1.XLII**] and tetrasodium-25,26,27,28-tetrakis(carboxymethoxy)calix[4]arene[**1.XLIII**].

Homooxacalixarenes also have been tuned to generate dimeric capsules which have served as a versatile host for [60]fullerene[83,84,85]. Certain calix-arenes have shown their ability for selective inclusion[86-89]. *p-tert*-butyl-calix[8]arene can be used to selectively separate [60]-fullerene from a mixture containing C_{60} and C_{70} fullerenes. There is a formation of 1:1 clathrate in which a C_{60} guest molecule

is bound within the cavity of the host molecule. The inclusion behaviour of calixnaphthalenes in different solvents also has been studied with fullerene as guest[90]. There are also examples in which aggregating units of calixarenes can trap an amine[91].

1.3.4 Cation-π-interaction

Among the non-covalent interactions, cation-π interaction[92] plays a significant role in designing utility material as well as in molecular biology. Understanding of this interaction in model systems provides evidence that a hydrophobic binding site comprised of aromatic rings can compete with full aqueous solvation in the binding of highly solvated cations. Polyphenolic compounds, bind quaternary ammonium and some iminium ions[67]. Schneider *et al*[67,68] have reported resorcarene hosts to show cation-π interaction. However, in these cases it was difficult to quantify the relative importance of cation-π vs. conventional ion pair interactions, since the anionic groups, used to solubilise the hosts also made their way to close proximity to the cationic centers on the hosts.

1.3.5 Metal binding

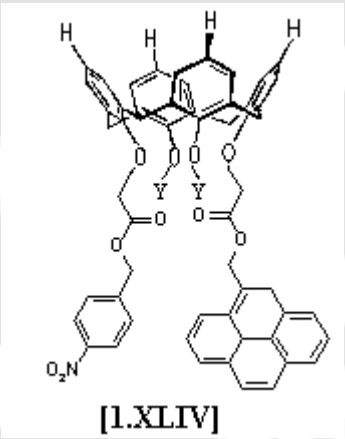
1.3.5a Ionophoric character

The ligands, which are capable of forming stable complexes with charged hydrophilic species are ionophores. The resultant complexes are most often lipophilic and thus they are easily transported into lipophilic phases. Many natural and synthetic ionophores, hence, can be used as transmembrane carriers for ions and as phase transfer catalyst. Ionophoric complexation is fairly specific, and ionophores can discriminate between metal cations of different size and different charge.

Certain polyphenolic compounds also have the potentiality of being ionophore. Particularly, calixcrownethers have high discrimination ability for K^+/Na^+ [93].

1.3.5b Chemical sensor

The presence of a cation guest in the cavity of an appropriately functionalised calixarene can be sensed by fluorescence study. The calixarene [**1.XLIV**], containing a fluorescent pyrene group and a *p*-nitrobenzyl quencer[94] is not fluorescent. But the presence of a cation in the cavity makes the lower rim more open, thereby compelling the fluorophore and the quencher spatially apart. As a result of this new conformation, the complex becomes fluorescent. These types of receptor are thus, potential candidates for ion sensors based on fluorescence.

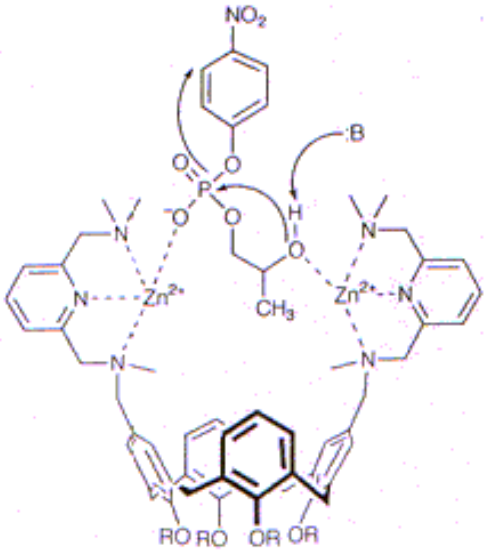


[1.XLIV]

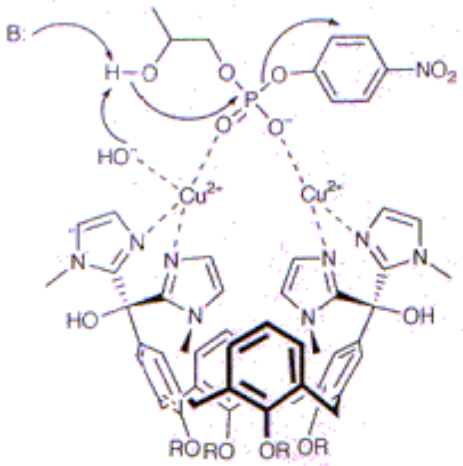
1.4 Biomimicking

Polyphenolic compounds can provide wide scopes for mimicking biological systems. For example, after proper funtionalisation, calixarenes provide dynamic preorganisation of molecular structures to mimick catalytic activity of many biological enzymes. Although, the lower rim, namely the phenolic –OH groups can easily be functionalised, it can be well speculated that functionalisation at the upper rim will provide more flexibility to the molecule, thereby providing more scope for designing enzyme models with different steric requirements[95].

Phosphodiesters are the functional groups linking nucleosides in RNA and DNA, the development of synthetic catalysts capable of cutting these linkages have medical applications. Appropriately functionalised calixarenes can act as dinuclear metalophosphodiesterase. Models [**1.XLV**] and [**1.XLVI**] of this kind of bimimicking has been demonstrated[96,97].



[1.XLVI]



[1.XLVI]

Understanding and manipulating protein-protein interactions is of prime interest in medicinal chemistry as these provide insights into many biological processes. Enzyme active sites are most often present in the interior of protein structures.

In one of the examples of antibody mimick, calixarene skeleton has been found to bind to basic residues on surface of α-chymotrypsin[98].

1.5 Scope of the work

In the foregoing discussions illustrations are made so as to provide a general classifications of polyphenolic compounds with a critical view to evaluate their emerging applications. Scope for designing different types of molecular architecture from structural variations in polyphenolic compounds has been a key factor for obtaining insight to biologically important processes. Polyphenols with intervening carbon as linker have proved to be potential entities in analytical, biological and material chemistry. Cyclic counterparts of this type of polyphenols such as calixarenes, resorcarenes, cycloveratrylenes etc. have been extensively studied for their ability to recognise guest molecules. Open chain counterparts of such polyphenolic compounds are expected to provide wider scope for conformational variation than the cyclic oligomers. But in comparison to the cyclic oligomers, the synthesis and applications of linear counterparts have not been explored with equal endeavour. The cyclic systems have some preorganised conformations, but the linear polyphenolic compounds ought to have flexibility that may bring forth increased number of preferred conformations as well as complexity to the system. Another aspect, which can be explored in the case of linear oligomers is the projections of the hydroxyl groups in different dielectric medium. Variations on hydrophobic and hydrophilic units on the chain of polyphenolic oligomers may lead to solvent induced or guest induced conformational changes that in turn might provide new optical or electronic properties.

The proton transfer processes are being studied with great interest to understand the photochemical as well as electrochemical processes. In this regard special attentions are put on quinonic types of compounds. In biological systems the

quinone units are in supramolecular environment, thus, their electrochemical properties in confined environment have great importance. The calixarenes have provided scope for such studies with the quinonic units either being anchored to the ring or encapsulated in the cavity. However, open chain polyphenolic compounds having folded structures to recognize quinones are not being studied. This leaves wide scope for pursuing such chemistry.

It is mentioned earlier that the polyphenolic compounds are of prime concern in supported catalysis for their close relevance to biological transformations. For such supported reactions the polyphenolic support can be either in the form of an isolated polyphenolic compound that binds to substrates or in the form of a supported catalyst formed *in situ* for further reaction. The metal catalysed oxidative as well as reductive reactions can be the best choice for study of such reactions.

CHAPTER 2

SYNTHESIS, CHARACTERISATION AND PHYSICOCHEMICAL STUDIES OF PYROGALLOL-ALDEHYDE OLIGOMERS

2.1 Background

In chapter 1, we have elaborated various aspects of polyphenolic compounds to delineate the structural, physicochemical and utility of different types of polyphenols. We have been able to illustrate the need of studying linear polyphenolic systems.

Conformational flexibility may arise in linear polyphenols having intervening carbon atoms as well as in the polyphenols having intervening hetero-atoms. In the later case the systems having C-O bond as bridge are interesting due to their relevance to biologically occurring systems. Again, if both hydrophilic and hydrophobic units are introduced on a conformationally flexible polymer backbone, the resulting oligomer/polymers may attain interesting molecular architecture. Such architecture may be used for molecular recognition, and is expected to possess solvent dependent property (such as solvatochromicity) due to flexibility of the chain. To impart both hydrophilic and hydrophobic functional groups on the polymer backbone, condensation reaction between phenol and aldehyde is a suitable method. This reaction has scope for structural modification in either of the two components. Polymers having such variation of hydrophilic and hydrophobic groups could be represented as shown in figure **2.1.** Phenolic units being the hydrophilic part, aldehyde units can be chosen with different extent of hydrophobicity.

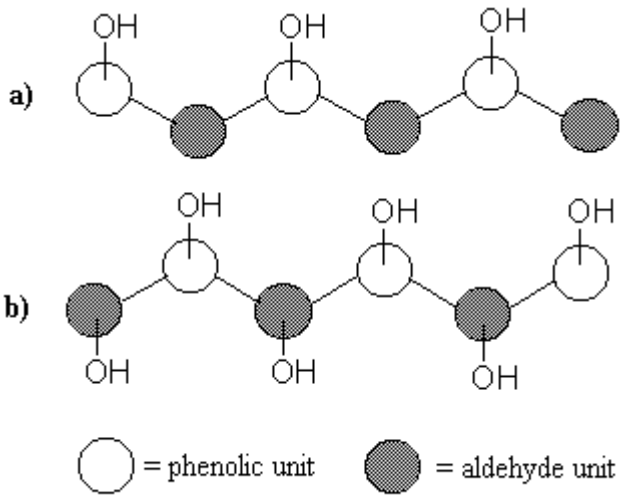


Figure 2.1: Representative skeleton of conformationally flexible phenol-aldehyde oligomer having hydrophilic groups on a) phenolic units only and on b) aldehyde units also.

To obtain a linear oligomer from condensation reaction of a phenol with aldehyde, some important factors have to be taken into account. In a phenolic system, both the *o*-, and *p*- positions, i. e. 2-, 4- and 6- carbons of the phenolic ring [**2.I**] with respect to the carbon having the hydroxyl group are activated. Hence, condensation may occur at all these three positions.

Phenols with both *o*- and *p*- positions free yield crosslinked products also alongwith the linear oligomer. Usually, a 1:1 mixture of a phenol having substituent at one of the *o*- and *p*- position and the aldehyde is expected to yield a linear or cyclic oligomer without crosslinking. Oligomers without crosslinking have been obtained in such cases, but cyclic compounds are predominant to give well-known calixarene family.

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Indian Institute of Technology Guwahati

We are interested in synthesis as well as properties of linear polyphenolic oligomers having hydrophilic units in the polymer backbone. We have chosen 1,2,3-trihydroxybenzene (pyrogallol) as the phenolic component for the condensation reaction. The reasons that have prompted us to choose pyrogallol are as follows. From synthetic point of view pyrogallol has the potentiality to yield linear product. In pyrogallol, there are three phenolic -OH groups, which would allow condensation reaction at only two positions, namely at 4- and 6- positions (2.**II**). Position 4- is *ortho*- to 3-OH group and *para*- to 1-OH. Hence the *meta*-deactivating effect due to 2-OH is minimized. Similarly, position 6- is *ortho*- to 1-OH and *para*- to 3-OH, hence the *meta*- deactivating effect due to 2-OH is minimized. The remaining position 5- is *meta*- to both 1- and 3-OH. The combined *meta*- deactivating effects rule out any condensation at this position, since the *para*-activation due to 2-OH has been minimized.

Other reasons are the available examples of analogous compounds that have interesting physicochemical properties. Several naturally occurring compounds, such as gallotannins[1], ellagitannins[18], lignin[19] and plant pigment anthocyanins[55] etc. contain pyrogallol unit as the building block. Out of them, the tannin group of compounds binds to selective molecules[7] and the lignin[19] has the capacity to retain water alongwith its primary function of imparting mechanical strength to plant systems. These types of function of the systems are related to multiple phenolic functionalities and even hydrophobic stacking where the pyrogallol groups are constrained to a rigid, inflexible, sterically hindered conformation[5].

There are also examples of cyclic polyphenolic systems derived from pyrogallol units, which showed recognition of α-amino acids[72] and mesophasic property leading to liquid crystal behaviour[76].

2.2 Condensation reaction of pyrogallol with aldehydes

The oligomers, **2.III-VI,** were prepared by condensation of pyrogallol with corresponding aldehydes by conventional method similar to the reported one in the literature[20] for analogous compounds. The oligomers of pyrogallol and different aldehydes (**2.III-2.VI**) were prepared by acid catalysed condensation reaction (given in section **5.3.1**).

Equation 2.1: Building blocks of oligomers **2.III-2.VI** from condensation of pyrogallol and aldehydes

The literature on condensation reactions of an aldehyde with phenolic compounds suggests that formation of the cyclic oligomers, namely calixarenes and their analogues is thermodynamically favorable process[20]. The reaction procedure reported earlier for formation of cyclic calix arenes from pyrogallol with aldehydes involves long reaction time and drastic reaction conditions[72]. Our reactions were performed with mild conditions than the reported procedure for cyclic counterparts. We also get cyclic component in our reaction but while synthesizing the linear oligomers we had disregarded the cyclic counterpart.

2.3 Characterisation of the oligomers

The product of condensation of pyrogallol and benzaldehyde (**2.III**) is found to be soluble in methanol, ethanol, 1-propanol, 2-propanol, acetonitrile, DMSO, DMF, THF etc. The absence of strong band due to carbonyl group of the parent

aldehyde at ~1700 cm^{-1} in the IR spectra of each of the oligomer suggests formation of the oligomers. A representative IR spectra of such oligomer is shown in figure **2.2**. The IR spectra of each of these oligomers show strong and broad peak for the OH group in the region 2800-3600cm^{-1}. The absorbances in the region of 2800-2900 cm^{-1} in each case, suggests presence of hydrogen bonding in the system.

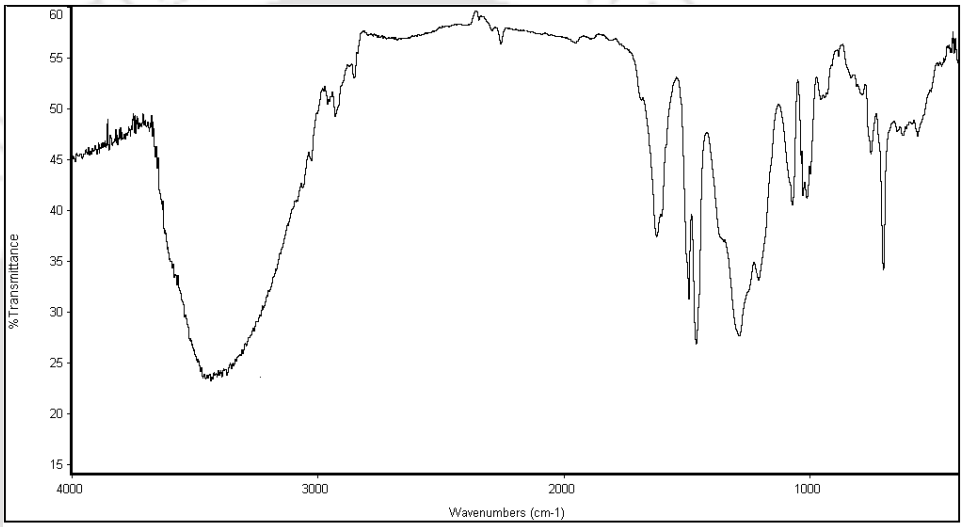


Figure 2.2: Infrared spectra of **2.III** as thin film prepared in acetonitrile

2.3.1 GPC analysis of the oligomers

Gel Permeation Chromatography has been proved to be an effective technique to ascertain the distribution of molecular weight of polymeric/oligomeric compounds. In case of the oligomers, **2.III-2.VI,** GPC data (Table **2.1**) have shown that the polydispersity of each of the the oligomers is close to unity. This implies that the molecular weight distributions of the oligomers are very narrow. Molecular weight distributions are in the range 2000 - 4000.

Table 2.1

GPC data of the oligomers

Oligomers	**Mn, Mw** (THF)	Polydispersity
2.III	1209, 1252	1.036
2.IV	2199, 2248	1.022
2.V	1399, 1540	1.101
2.VI	2469, 2484	1.006

2.3.2 Mass spectral analysis

Since the oligomers show narrow molecular weight distribution, mass spectral studies can be of great help in ascertaining the exact molecular weight of the oligomers. The mass fragments of the oligomers can be of help to describe the uniformity and the fragmentation pattern. For illustration, the MALDI mass spectra of **2.III** and **2.IV** (figure **2.3a** and **2.3b**) are discussed here.

Figure 2.3a: MALDI mass spectra of **2.III**

The MALDI mass spectra of **2.III** shows peak distributions at m/e 2036.7, 1821.3, 1604.2, 1391.5, 1178.7, 1085.3, 981.8, 961.2, 872.7(base peak), 767.5 and 646.3, which reflect loss of -CH(C_6H_5)-, -$C_6H_4O_3$CH(C_6H_5)- and –CH(C_6H_5) $C_6H_4O_3$CH(C_6H_5)- fragments from the polymer chain. The base peak appears at 872.7 (m/e) and it corresponds to [-(C_6H_5)CH-$C_6H_4O_3$]$_3$$C_6H_4O_3C_6H_5$CH(OH) showing that it might have got released from a linear chain of the polymer.

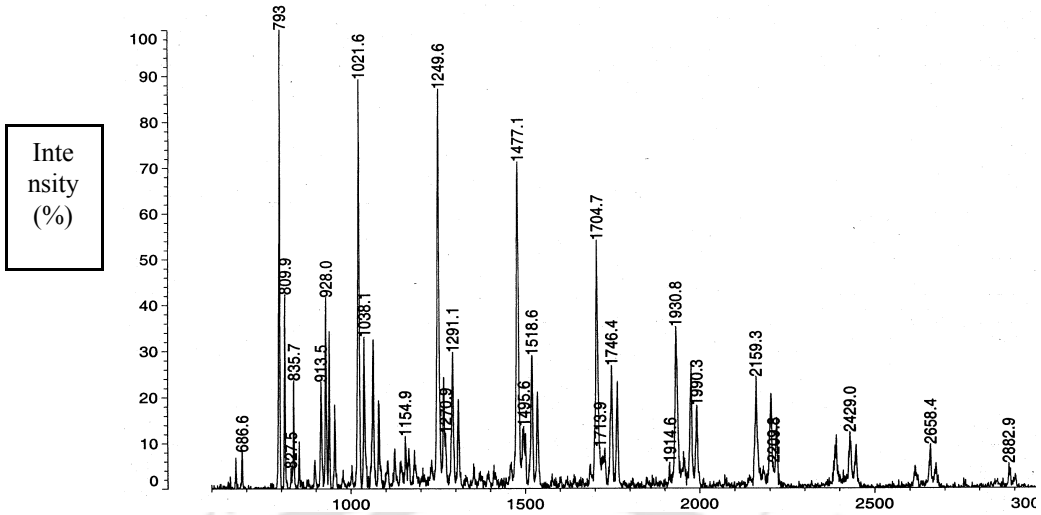


Figure 2.3b: MALDI mass spectra of **2.IV**

The base peak in the case of **2.IV** at 793.6 (m/e) is the Ag salt having three units of basic building block of **2.IV,** i.e. $-CH[C_6H_4(CH_3)]C_6H_4O_3-$ (**figure 2.3b)**. The m/e values in the spectrum at 2658.4, 2429.0, 2159.3, 1930.8, 1704.7, 1477.1, 1249.6, 1021.6, and 793.6 correspond to loss of fragments such as $-CH[C_6H_4(CH_3)C_6H_4O_3-$ from a linear oligomer having uniform repeated units of

-CH[$C_6H_4(CH_3)C_6H_4O_3$- in the chain. The peak at m/e 928 corresponds to a fragment –CH.[$C_6H_4O_3CH(C_6H_5)]_3C_6H_4O_3CHOH(C_6H_5)$ and the peak at m/e 1704.7 is assigned to $(C_6H_5)C(OH)[C_6H_4O_3CH(C_6H_5)]_6COH(C_6H_5)$.

In the MALDI mass spectrum of **2.V** (given in section **5.3.1**) the m/e values appear at 2466.0, 2222.1, 1978.0, 1733.3, 1490.3, 1246.1 1006.2 and 1002.0, which explains uniform sequential loss of the building block -CH[$C_6H_4(OCH_3)]C_6H_4O_3$- from the linear chain of the polymer. The base peak at 1002.0 is assigned to –[CH{$C_6H_4(OCH_3)$}$C_6H_4O_3]_4CHC_6H_4O$• and the peak at 1006.0 m/e is assigned to Ag salt having four unit of the building block –CH[$C_6H_4(OCH_3)]C_6H_4O_3$-.

2.3.3 NMR study of the oligomers

Nuclear Magnetic Resonance spectroscopy is an efficient tool for ascertaining the structure, conformation and end group analysis of oligomers. The presence of an end group in an oligomer can be seen in its ^1H NMR spectra as signals with low integration, if the signals are not buried in the signals due to the protons of the entire chain.

The ^1H NMR spectra of the product of condensation oligomer of pyrogallol and acetaldehyde (**2.VI**) shows no signal for an end group, suggesting the formation of a cyclic oligomer rather than a linear one (figure **2.4)** and is confirmed from its integration ratio.

We have recorded the ^{1}H NMR spectra of **2.III** in two different solvents namely methanol-d_4 and DMSO-d_6. This was done with a view that the methanol-d_4 having labile deuterium would exchange protons of the OH groups of the oligomer and make the spectra less complicated. To look for the possibility of solvent effect on the structure, spectra was taken in a second solvent.

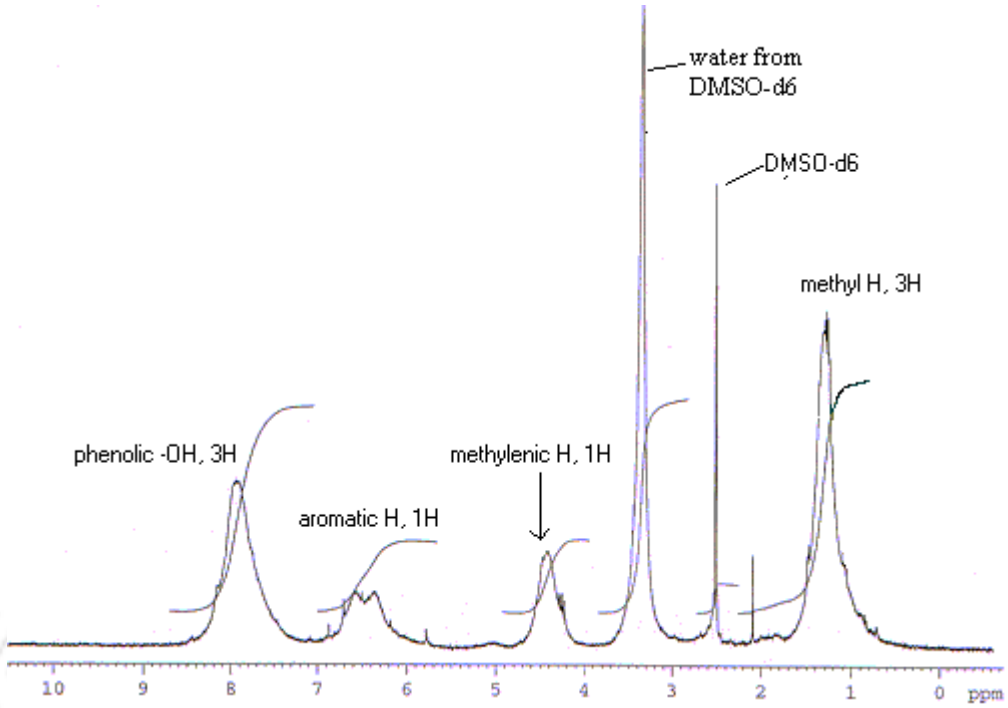


Figure 2.4: 400 MHz ^{1}H NMR spectra of **2.VI** in **DMSO-d$_6$**

The ^{1}H NMR spectra of **2.III** in methanol-d_4 (figure **2.5a**) has two triplets (δ 7.5 ppm, J = 4 Hz and δ 7.6 ppm, J = 4 Hz) and a doublet (δ 7.9 ppm, J = 4 Hz) at a lower field and they are believed to arise from the aromatic ring of the aldehydic part. The integration value supports them to arise from the end group which would be a phenyl group attached to a methylene carbon bearing a hydroxyl group. It is likely that the majority of the products in the condensation reaction of aldehyde with pyrogallol arise as open chain compound because the end group can have H-bonded effect so that elimination of water molecule is reduced (structure is shown in figure **2.11** on page ---.

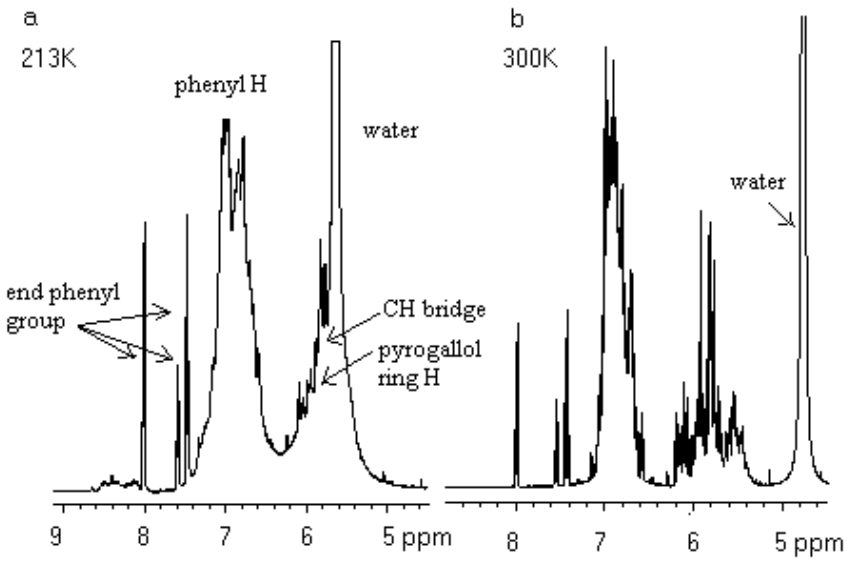


Figure 2.5: ^{1}H NMR spectra in CD_3OD of **2.III** (a) at $-60^{0}C$, at (b) $30^{0}C$

The two solvents do not distinguish the above signals as the J values are not changing. However, in case of the spectra in methanol-d_4 there is only one set of the above three peaks. But in the spectra in DMSO-d_6 a minor triplet at δ 7.15 and another unresolved peak at δ 7.3 ppm partially buried in the signal due to protons of –OH groups of the phenolic units. This difference is possible if the oligomer is present in different conformations in different solvents and also may be due to the exchanging nature of CD_3OD with phenolic groups. However, the possibility of more set of such signals with low intensity due to end group, being present as buried in the multiplet at 6.4-7.4 could not be ruled out. This possibility, in fact, was found to be true from study of UV-visible absorption of the oligomers, which is discussed in section **2.4.1.**

TH-87_984501

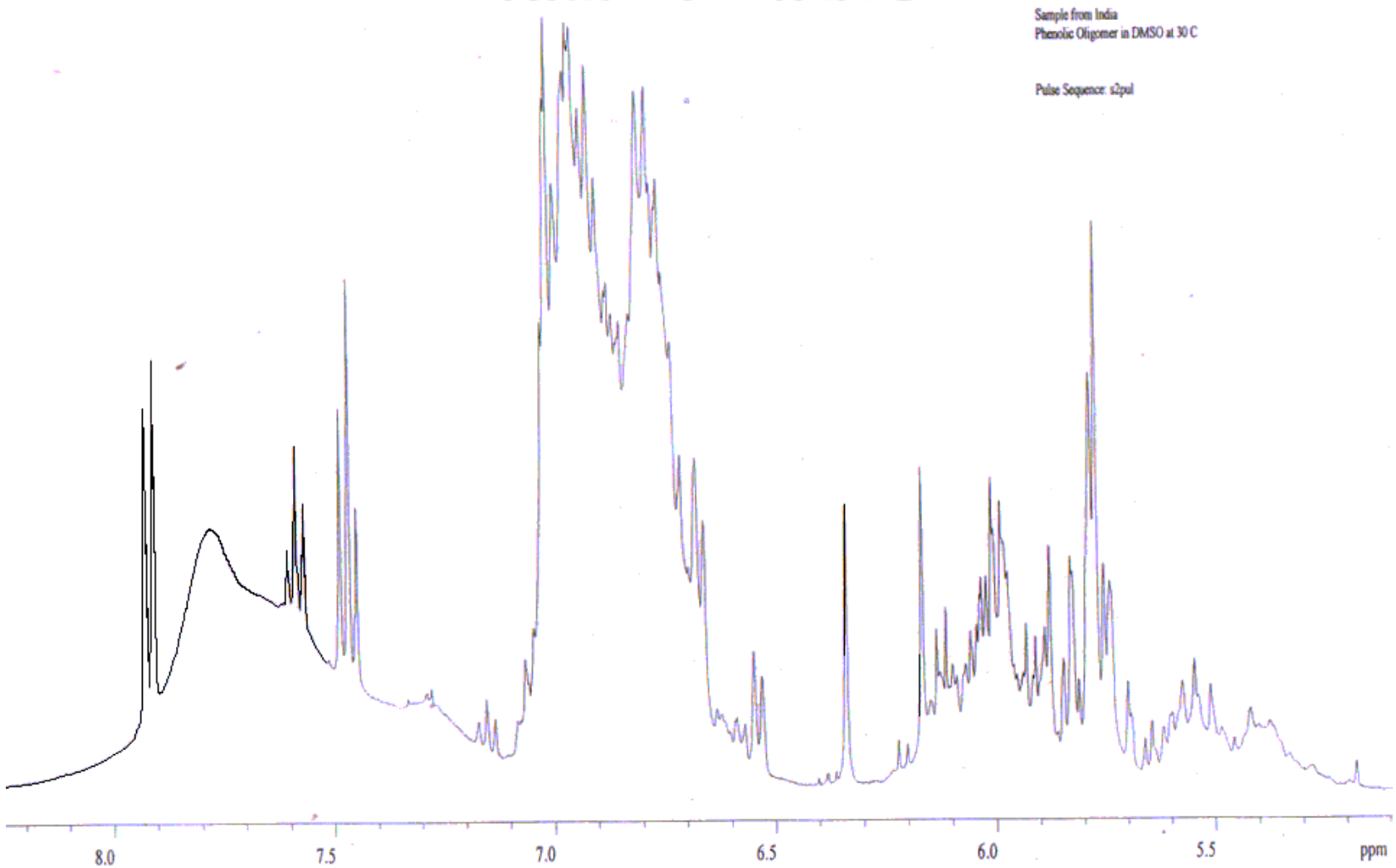
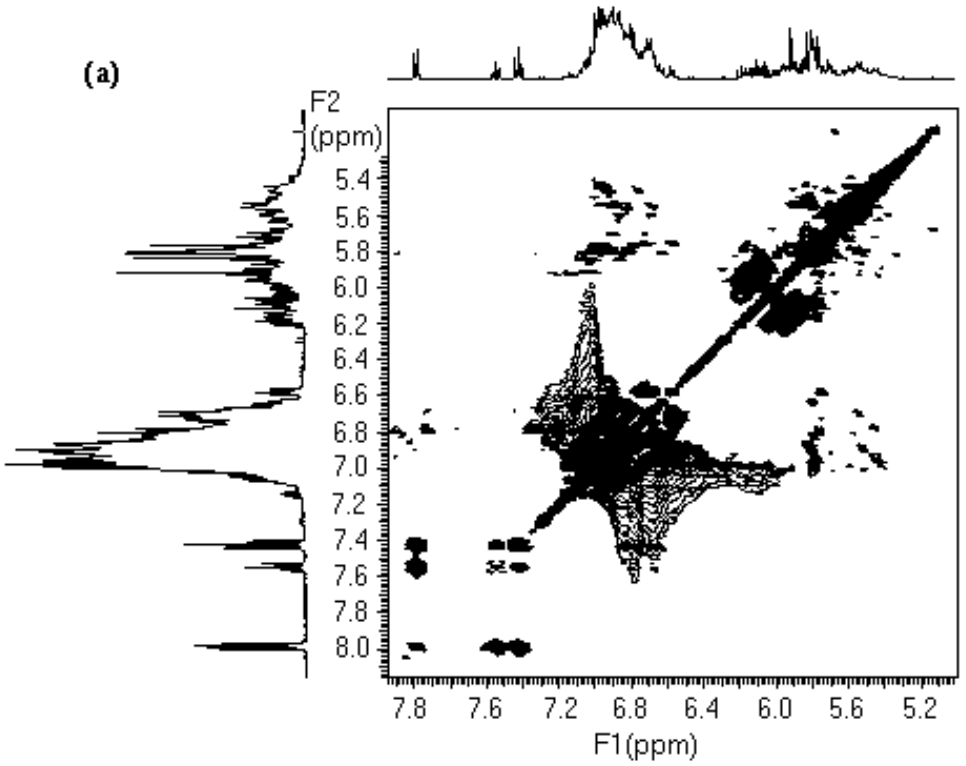

Sample from India
Phenolic Oligomer in DMSO at 30 C
Pulse Sequence: s2pul
8.0
7.5
7.0
6.5
6.0
5.5
ppm

Figure **2.6:** ^{1}H NMR spectra of **2.III** in DMSO-d_6

The ^{1}H NMR spectra of the sample **2.III** in methanol-d_4, recorded at two different temperatures, viz. $30^{0}C$ and at $-60^{0}C$, are shown in figure **2.6a** and **2.6b**. The signals from the phenyl group attached to the main chain that appeared as multiplet in the region of 6.6-7.2 ppm are narrowed on cooling and the signals in the region of 5.4-6.4 are largely effected in which the majority of the multiplets are convulsed to a set of mutiplets spreading from 5.7 to 6.2 ppm. Since these signals originate from hydrogens in aromatic counterpart and also from the hydrogen attached to the bridging carbon between two pyrogallol building blocks, cooling hinders the conformational changes and this forces the oligomer to have a rigid geometry. The proton signal of water of methanol-d_4 originally present at 4.75 ppm shifts to 5.6 ppm, and appears with the multiplets of the C-H proton and the proton from pyrogallol unit. This effect clearly indicates the hydrophilic interaction of the compound with water molecules in solvent and water of crystallisation. This results are also supported by elemental analysis and thermogravimetry presented in section.

The NMR signals of the oligomers in the aromatic region are not clearly differentiated in a normal ^{1}H NMR. But the 2D-HOMO-COSY of **2.III** in two different solvents has clear differentiation in the correlation (figure **2.7a, 2.7b**) showing that the systems are in different conformations in two different solvents. Although the peak separations of individual H are difficult because of the possibility of interacting and non-interacting conformational states, nevertheless the observation of highly symmetric spectra suggests the orderliness and the regular conformational patterns present in the system. Again in case of the spectra in CD_3OD, one doublet

and two triplets (a, b and c in figure **2.7a**) at δ 8, 7.6 and 7.4 ppm respectively show that they are co-related. It clearly indicates that they are from the same C_6H_5- group, which we assigned as the end C_6H_5- group.


(a)
F2
(ppm)
5.4
5.6
5.8
6.0
6.2
6.4
6.6
6.8
7.0
7.2
7.4
7.6
7.8
8.0
7.8
7.6
7.2
6.8
6.4
6.0
5.6
5.2
F1(ppm)

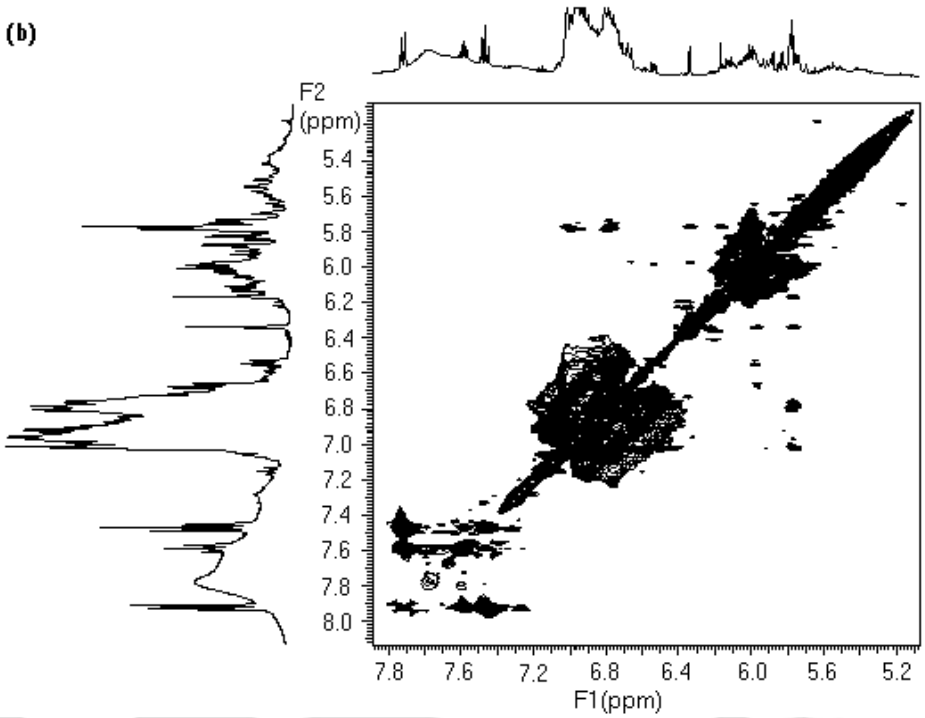


Figure 2.7: 2D-^{1}H HOMOCOSY NMR spectra of **2.III** in (a) CD_3OD (b) DMSO-d_6

The ^{1}H NMR spectra of **2.V** in DMSO-d_6 and CD_3OD (figure **2.9a** and **2.9b**) are different which shows the presence of different conformers in the solution. This could be ascertained by taking the help of integration, as well as from the shift of the A_2B_2 type of protons present in the aromatic ring of the *para* substituted end group.

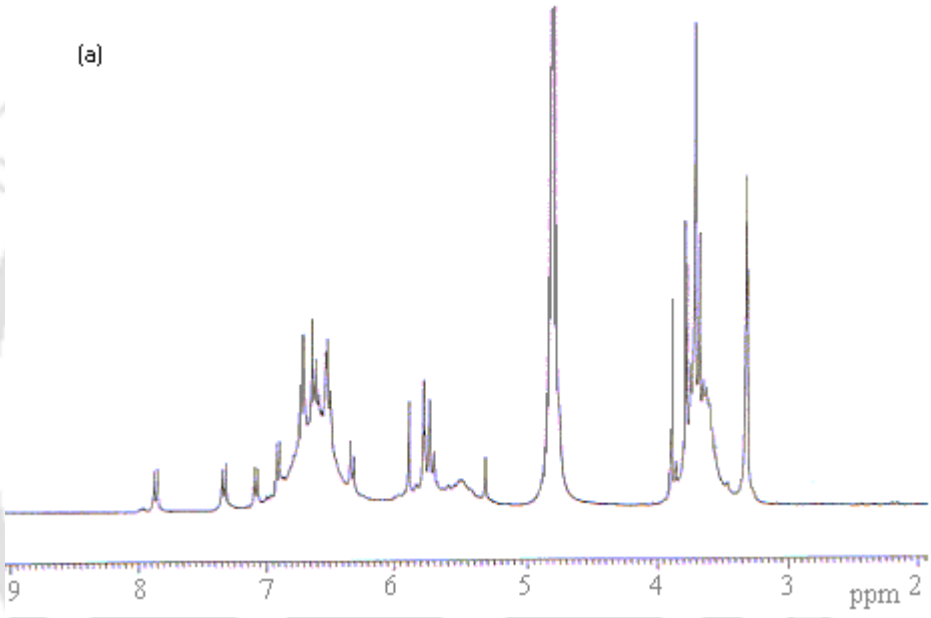


Figure **2.8:** 400 MHz ^{1}H NMR spectrum of **2.V (a)** in CD_3OD and (b) in DMSO-d_6

The spectra of **2.V** shows three pairs of doublets, a, b and c as shown in figure **2.8a** with J-values of 11.5 Hz. The J-values (*o*-coupling) suggest them to be aromatic protons from $CH_3C_6H_4$- group (A_2B_2) pattern. These must be the end groups which are in different environments. In DMSO-d_6, all the three pairs are not clearly distinguishable, but they appeared as unresolved peaks. The presence of all these sets of signals in two different solvents indicates that the oligomer is in different conformations in both the solvents. In fact, it was substantiated by UV-visible spectra of the compound too. In contrast to the case of **2.V**, one absorption peak was observed for **2.III** in methanol. One important point to be noted is that although three sets of A_2B_2 signals for the end groups of the conformers are observed the integrations vary from solvent to solvent.

The ^{1}H NMR spectra of **2.IV** in DMSO-d_6 (given in section **5.3.1**) also shows presence of end *p*-$CH_3C_6H_4$- groups (three different pairs of doublets in the aromatic region) in different environments, suggesting the presence of linear system with different conformations.

2.3.3a Thermogravimetry of the oligomer 3.III

It has been already mentioned that temperature dependent NMR spectra show interaction of the oligomer with water present in the solvent. The results can be correlated to thermogravimetry also.

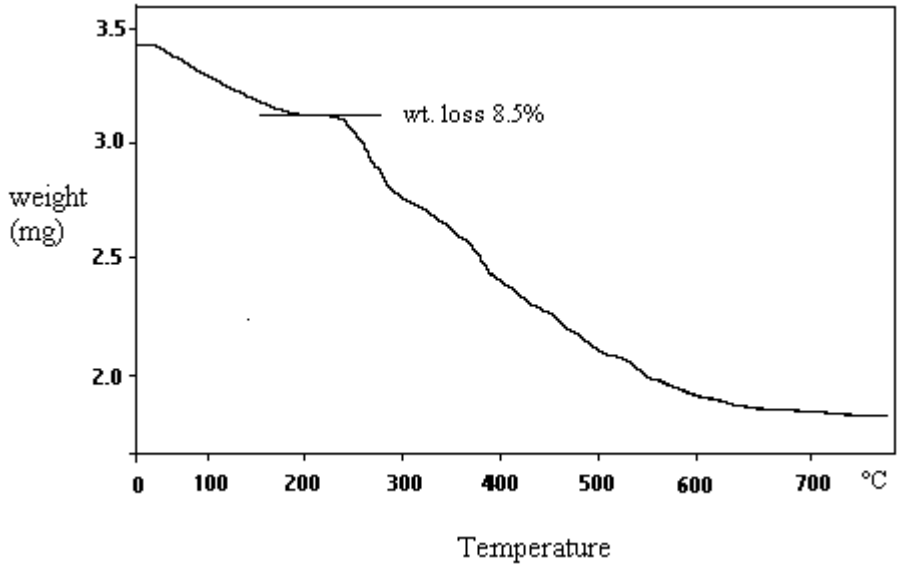


Figure **2.9**: Thermogram of **2.III**

The thermogravimetric analysis suggests that the compounds are hygroscopic. As an illustrative case, on heating there is loss of 8.5% weight in the region of 80-200^{0}C from **2.III** (Figure **2.9**). This weight loss is attributed to water molecules, held by the oligomers through H-bonding. The thermogravimetric results

are in good agreement with the elemental analyses also. For example, the calculated percentage values of C and H are 72.9 and 4.7 respectively for each building block of **2.III**. But the experimental results do not agree with this composition. However, on taking account of hydrated water molecule the composition was considered as $C_{13}H_{10}O_3.1.25\ H_2O$. For this composition, C and H are calculated to be 66.0 and 5.3 respectively. This result is in good agreement with the experimental values 66.4 and 5.41 for C and H respectively. This observation also suggests the oligomers to have tendency for strong hydrophilic interaction.

2.4 Physicochemical studies of the oligomers

2.4.1 Solvatochromicity of the oligomers

The oligomers having both hydrophilic and hydrophobic units on their polymeric backbone, are expected to attain different conformations in different solvents, which will be reflected in their electronic spectra as shift of the absorption bands. The solvent dependent shift of the absorption bands in the UV-visible spectra of a compound is termed as solvatochromicity[100]. The oligomers **2.III-2.V** have shown solvatochromic behaviour, which is illustrated here by taking **2.III** as a typical example. The oligomer **2.III** has a single absorption maximum at 478 nm in methanol. It shows two overlapping absorptions at 427nm and 500nm in aprotic solvent such as acetonitrile and dimethylsulphoxide that favours hydrophobic interactions (Figure **2.10a** and **2.10b**).

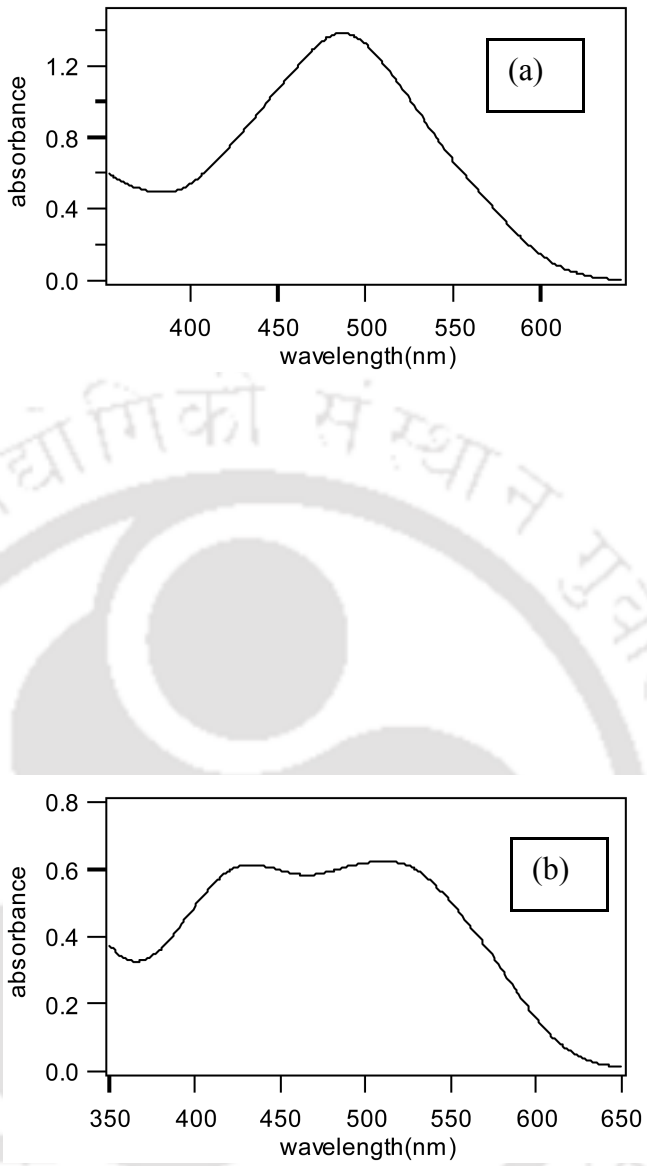


Figure **2.10:** UV-visible spectra of **2.III** in (a) methanol and in (b) acetonitrile

The absorbance at 427nm and 500nm are attributed to two forms of the oligomers, in one form all the hydroxyl groups are projecting in one direction (**X**) and in the other, every alternate ring containing hydroxyl groups projects in one direction of the oligomer (**Y**) (figure **2.11**). In methanol the oligomer has absorption at 478 nm due to a state **Z** (say) which is equivalent to **X** but the hydrophilic part would project out in this state. The state is bound state with highly protic solvents, such as methanol.

Figure 2.11: Two possible structures of oligomer **2.III**

The compound has a single absorption in methanol but as the chain length of such protic solvent is increased the shape of the absorption changes due to increase in hydrophobic interaction. The effect of different protic solvents on the electronic spectra of the oligomers can be seen from the variation of the visible spactra on

changing the solvent. Such changes in **2.III,** observed from use of different alcohols with varied chain length are shown in figure **2.12.**

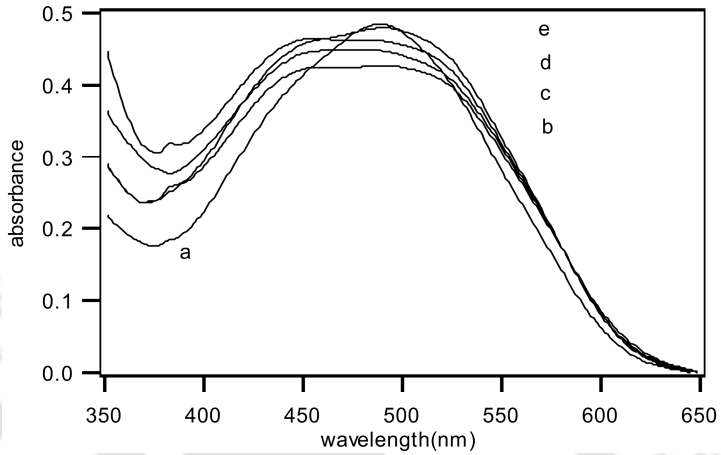
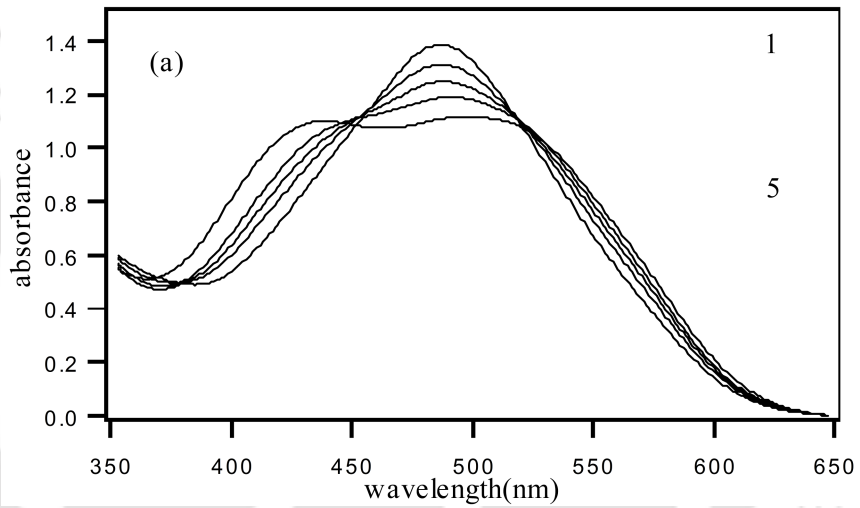


Figure **2.12**: **2.III** in alcohols a) methanol, b) ethanol c) 2-propanol, d) n-butanol and e) 1-propanol.

Thus, the effect of solvent on the conformational changes could be ascertained by using mixed solvent systems. UV-visible spectroscopic analysis has been proved to be effective for determination of solution composition[101]. Overlapping UV-Visible spectra can be rationally resolved for quantitative analysis of composition of different species present in a solution[101]. It has been made even more effective by analysis of matrix from the superimposed absorption spectra of two (or more) different species[68].

We have used matrix analysis of the UV-visible spectra of the oligomers to find out the composition of different conformers in a solution. For this purpose we had studied the electronic spectra of the oligomers with two mixed solvents systems namely acetonitrile-methanol and dimethylsulphoxide-methanol. The changes that occur on addition of dimethylsulphoxide to a methanol solution of **2.III,** as well as to acetonitrile a methanol solution of **2.III** are shown in figure **2.13a** and **2.13b**.



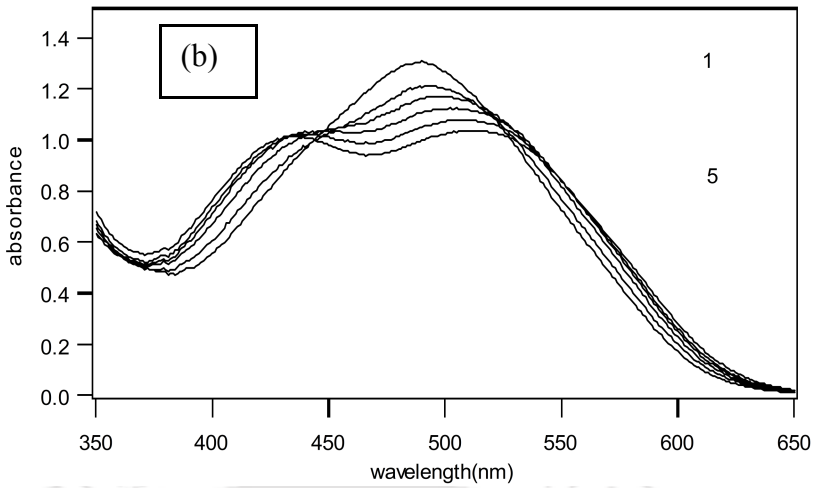


Figure **2.13:** The solvatochromicity of **2.III** with composition of **(a)** acetonitrile and methanol (1)-(5) 1: 0; 1:5; 1:2; 1:1; 0: 1 **(b)** dimethylsuphoxide and methanol (1)-(5) 0: 1; 1:5; 1:2; 2:1; 1:0.

As only one absorbance is resulted from the methanolic solution with a normal Gaussian shape (figure **2.10a**), it is assumed that it is due to one conformation and it is present in methanolic solution in 100%. This spectra has been denoted by a function f_1, which is a function of absorption and wavelength. The acetonitrile solution of the oligomer has two distinct absorptions and so it may be assumed to comprise of two normal Gaussian functions f_2 and f_3. The two distinct absorption maxima from acetonitrile solution could be sorted out by extrapolating the mirror image of each part as shown in figure **2.14**, which are represented by functions, f_2 and f_3.

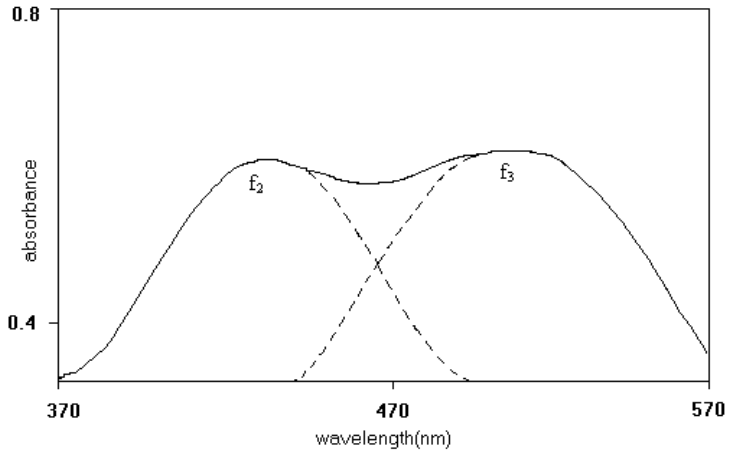


Figure **2.14**: Functions, f_2 and f_3, for **X** and **Y**(figure **2.11**) obtained by extrapolation of spectra of **2.III** in acetonitrile (figure **2.10b**),

The functions f_2 and f_3 are also functions of two variables viz. wavelength and absorbance. So if one has to represent such a function a series of absorbance data from different wavelength has to be collected and it would be simple, if the wavelength range is same for all the functions. We have recorded the data on absorbance against wavelength at each 1nm interval on IGOR software package on an IBM Pentium PC.

Under this circumstance, we can define absorbance for the methanol profile as '$x_{1(n)}$', where, 'x' is the absorbance at wavelength 'n' in methanol solution and

'n' varies from 370 nm to 570 nm. Similarly, for f_2 and f_3 also, we get two series of data '$x_{2(n)}$' and '$x_{3(n)}$' respectively.

Notations used for the analysis, where, x = absorbance of a given solution, which is defined by the subscripts as follows	
$x_{(n)}$	n = particular wavelength 1 = for the solution in methanol (f_1) 2 and 3 = for the two components of the solution in acetonitrile, having λ_{max} at ~ 435 nm and ~ 500 nm respectively
$x_{1(n)}$	
$x_{2(n)}$	
$x_{3(n)}$	

Now, for a solution in a mixture of solvent, we get another function, F (say), which can now be represented as

$$C_1f_1 + C_2f_2 + C_3f_3 = F$$

where, the co-efficients C_1, C_2 and C_3 represent the contribution of each conformer species, represented by f_1, f_2 and f_3 in the solution under consideration. The representative matrices can now be constructed from the data collected in IGOR, as follows:

Now let the above equation be represented as $\Rightarrow A \times B = C$

$$\Rightarrow B = A^{-1} \times C$$

Now, with the help of the matrices C and A, by using MATLAB package on an IBM Pentium computer, it could be possible to find out the composition of the three states i.e. C_1, C_2 and C_3 in different solvent compositions and these are tabulated in **table 2.2**. While doing the calculations we have made use of the following assumptions: (a) the methanolic solution contains exclusively one conformer and (b) the acetonitrile solution has two conformers and these are present in equal proportions.

Table 2.2

The ratio of $\mathbf{C_1}$, $\mathbf{C_2}$ and $\mathbf{C_3}$ in different solvent compositions

Solvent composition	Ratio of solvent	Ratios of $C_1 : C_2 : C_3$
CH_3OH : CH_3CN	5 : 1	0.76 : 0.10 : 0.14
	2 : 1	0.64 : 0.16 : 0.20
	1 : 1	0.54 : 0.20 : 0.26
	0 : 1	0.41 : 0.24 : 0.34
CH_3OH : DMSO	5 : 1	0.58 : 0.22 : 0.20
	2 : 1	0.52 : 0.20 : 0.27
	1 : 2	0.33 : 0.32 : 0.35
	0 : 1	0.29 : 0.33 : 0.38

The results support that the more amount of hydrophilic solvent methanol generates state $\mathbf{C_1}$ through hydrophilic interaction of the solvent with state $\mathbf{C_2}$ and $\mathbf{C_3}$. The results are further confirmed by simulating the graphs with the help of normal Gaussian function using Microcal Origin software as described below.

The functions, can be represented by a general function, $f_{(x)}$, where,

A = Area

x_c = Centre

W = Width

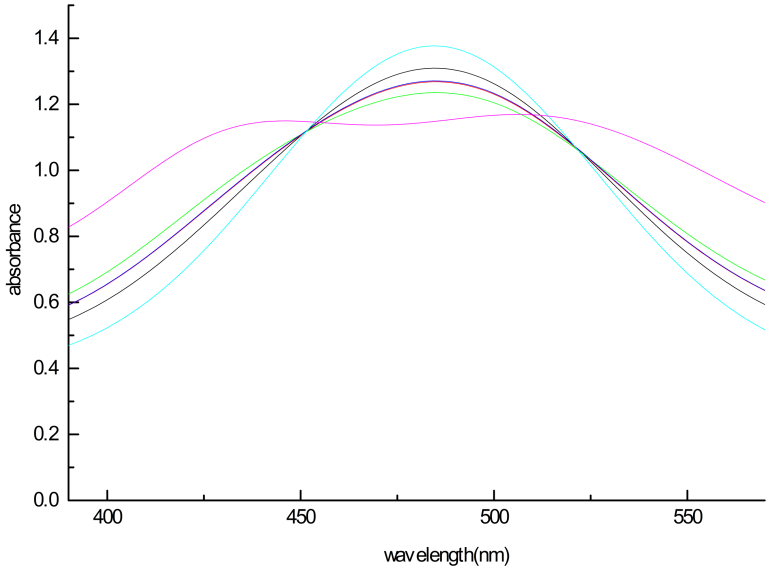
Offset = Yo

The A, x_c, W and Y_0 can be ascertained by fitting the equation (1) type function with the help of Microcal Origin software to the function or the function generated by drawing mirror image of the exponential(?) part of it as represented earlier (figure **2.14**). The individual equations for f_1, f_2 and f_3 were obtained by putting the values of absorption against wavelength. They are

Now, putting the values of C_1, C_2 and C_3 in equation

$$C_1f_1 + C_2f_2 + C_3f_3 = F$$

for each function, F, we have got the simulated graphs. The corresponding graph for spectra showing solvatochromic behaviour of **2.III** in figure **2.12a** is shown in figure **2.15**. It reflects the original nature of the spectra. So, it can be concluded that the assumptions made to find out the composition C_1, C_2 and C_3 were rational.


absorbance
wavelength(nm)
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
400
450
500
550

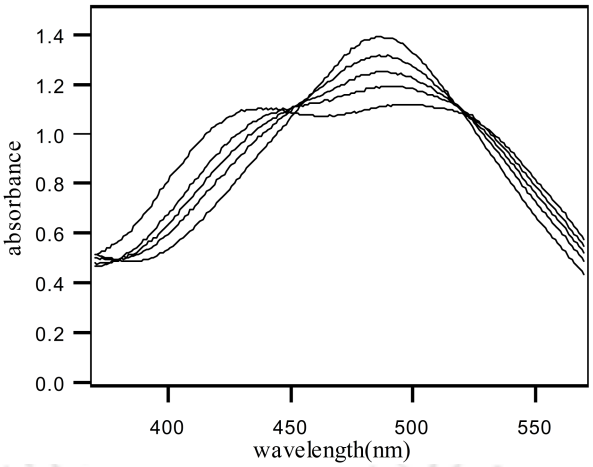


Figure **2.15**: (a) Simulated graph and (b) the spectra in the range 370-570 nm from spectra given in figure **2.13a**

2.4.2 The effect of different amines on the electronic spectra of the oligomer

In chapter 1, recognition of amino acid by polyphenolic system has been cited[72]. Chapman et al[102] reported encapsulation of pyrazine in polyphenolic system. Schneider et al[67] used recognition of tetraalkyl ammonium salt by resorcarene derivatives to construct allosteric proton pump. In another recent report[103], the size and shape selectivity for diamines by a tetrahydroxy cavitand have been reported. With similar philosophy in mind we studied the visible spectra of the oligomers in presence of different amines.

Pyrogallol itself can interact with organic amine such as *t*-butylamine. Before studying the behaviour of the oligomer on interaction with the amines, it would appropriate to see the interaction of pyrogallol with amines. As a typical example, we have chosen to use *t*-butylamine. Addition of *t*-butylamine in aliquots to a solution of pyrogallol shows growth at 267nm and after the ratio of pyrogallol to *t*-butylamine becomes 1:1 another absorption maximum at 333nm grows on subsequent addition (**Fig 2.16**).

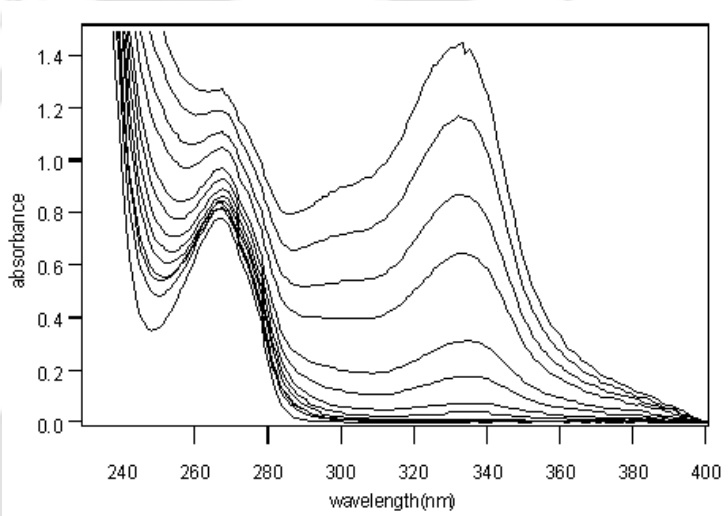


Figure 2.16: UV-visible spectra of pyrogallol (1.3 mg) in acetonitrile (3 cm^3), with subsequent addition of t-butylamine with (1) 0 mM, for (2) to (5) with 0.5, 1, 1.5 and 2 µl of *t*-butylamine; for (6) to (13) 1µl of t-butylamine in each aliquot to solution 5).

Quantitative measurement of amine addition gives the amount to reach the maximum absorption correspond to 1:1 molar ratio, suggesting that at first stage an ion-pair of *t*-butylamine with one equivalent protons takes place followed by the next ion pairs. The growth in absorption at 267nm and 333nm as increase in concentration of the *t*-butylamine is shown in figure **2.17**. These results clearly indicate that the proton attached to the central hydroxyl group (that means the 4-OH proton) is first lost followed by the other two to form ion pairs.

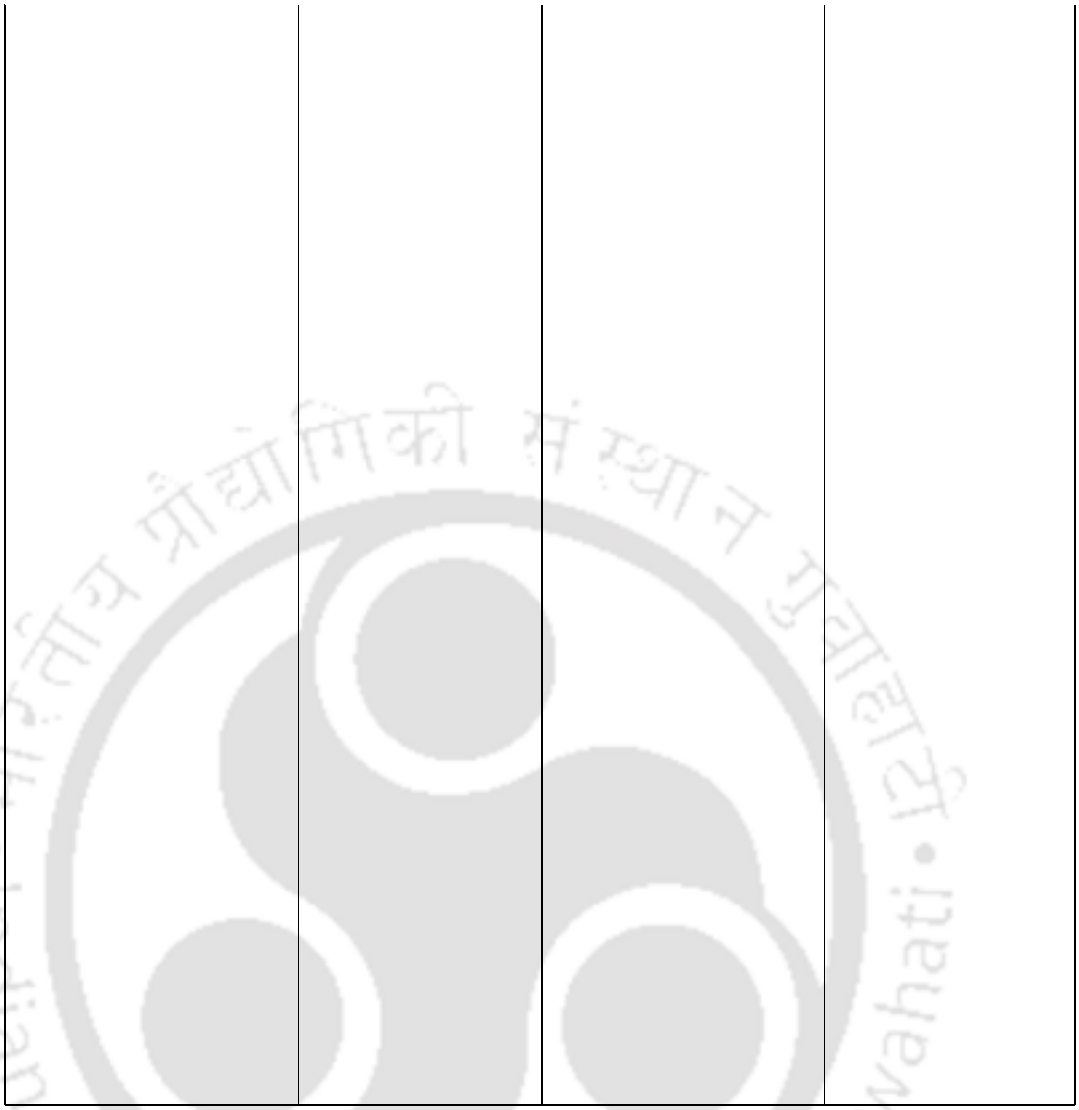
Figure **2.17**: Growth of absorption of pyrogallol at 267 nm and 333 nm on increasing concentration of *t*-butylamine.

The effect of amine on the absorption spectra of the oligomers is illustrated by taking **2.III** as a typical example. The absorption maxima of the oligomer **2.III** in acetonitrile occur at 427nm and 500nm. The two absorption maxima of the oligomer **2.III** are changed significantly when treated with organic amines. The change in absorbance at 427 nm or 500 nm not necessarily leads to the same type of absorption profile. The change of absorption occurs at lower or higher side of these absorption maxima depending on the amine used. Based on the effect on the absorption spectra of the oligomer **2.III,** the amines are categorized into four types, namely, **A**, **B**, **C** and **D**. Type **A** causes absorption change at 427 and 500nm with growth of new absorption maximum at 566nm, type **B** increases the absorbance at 427nm, type **C** enhances the absorbance at 427 nm and 500nm and type **D** does not significantly effect the absorptions at 427nm and 500nm of the oligomer **2.III.** Different types of the amines that fall under four different categories are listed in **Table 2.3**.

Table 2.3

Classification of the amines based on the effect on absorption spectrum of the oligomer **2.III**. (pk_a values of the amines are shown against each)

Type **A**	Type **B**	Type **C**	Type **D**
Growth of λ_{max} (new) at 560-570nm	Growth of λ_{max} at ~ 430nm	Growth of λ_{max} at 427 as well as 500nm	Insignificant change on λ_{max}



The behaviors of four types of amines are illustrated in figure **2.18a-h**. Figure **2.18a** illustrates the growth of absorption at 566nm on addition of *t*-butyl amine representing one example of amine of type **A**. Two other examples showing similar behavior are shown in figure **2.18b-c**. In figure 6d an example of amine of type **B** is shown in which benzidine is used as an amine. The behavior of type **C** amine is demonstrated in figure **2.18e-g**, whereas figure 6h shows the example of type **D** amine. The interaction of 1,2-phenylenediamine results in growth of absorption at

500nm but slightly effect the absorption at 427nm (**Fig 2.18g**). This amine is included in the type **C.**

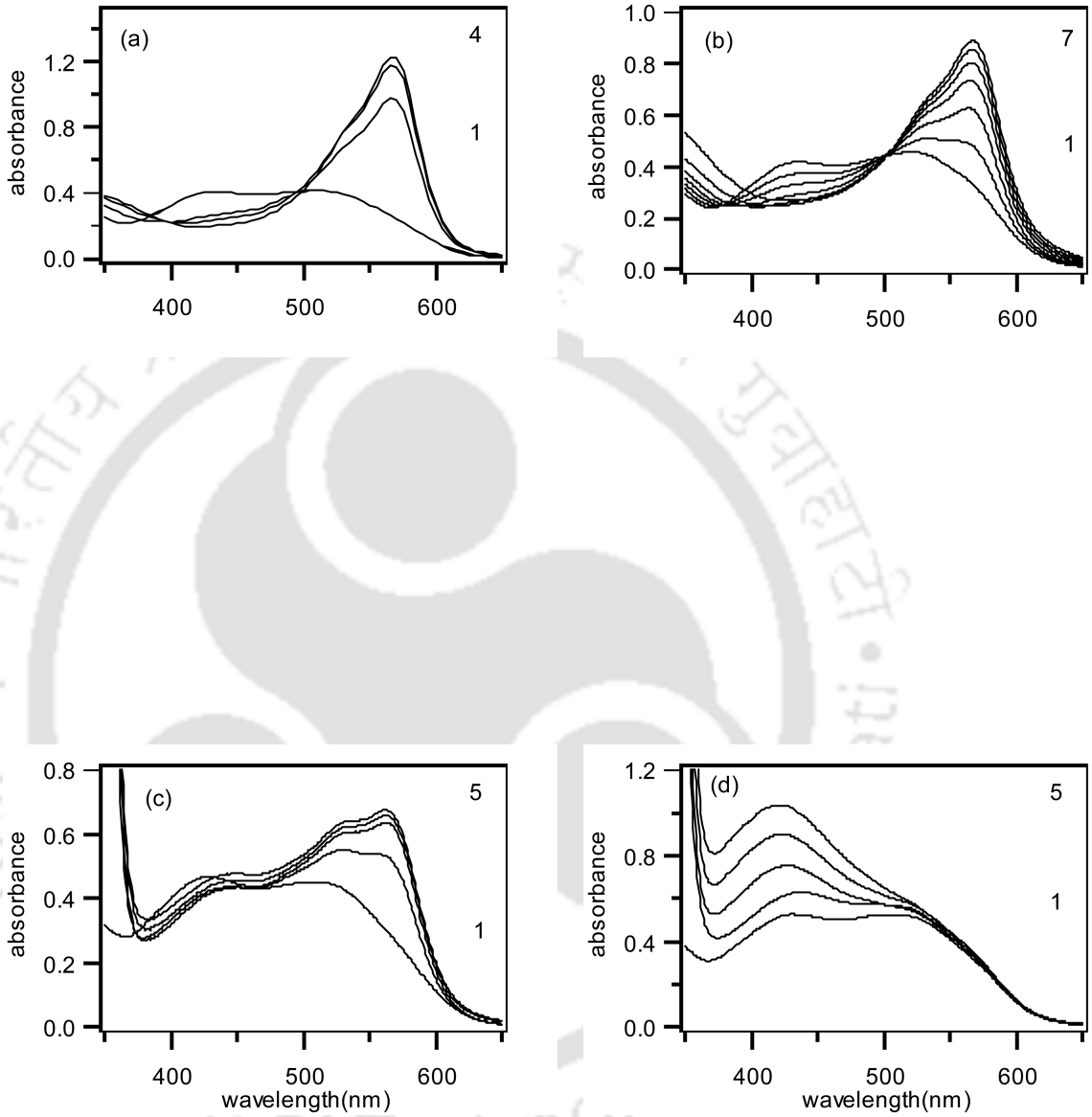


Figure 2.18: UV-visible spectra of a solution of **III** (9 mg) in acetonitrile (3 cm^3) on addition of different amines with:

(a) 1) 0 mM 2) 4.7×10^{-3} mM 3) 9.4×10^{-3} mM and 4) 14×10^{-3}mM of *t*-butylamine
(b) 1) 0 mM 2) to7) addition of 1.5×10^{-7} mM of ethylenediamine in each aliquot
(c) 1) 0 mM 2) 7.9×10^{-2} mM 3) 15.8×10^{-2} mM 4) 23.9×10^{-2} mM and 5) 31.7×10^{-2} mM of imidazole
(d) 1) 0 mM 2) 2.7×10^{-2} mM 3) 5.5×10-2 mM 4) 8.3×10^{-2} mM and 5) 11.1×10^{-2} mM of benzidine

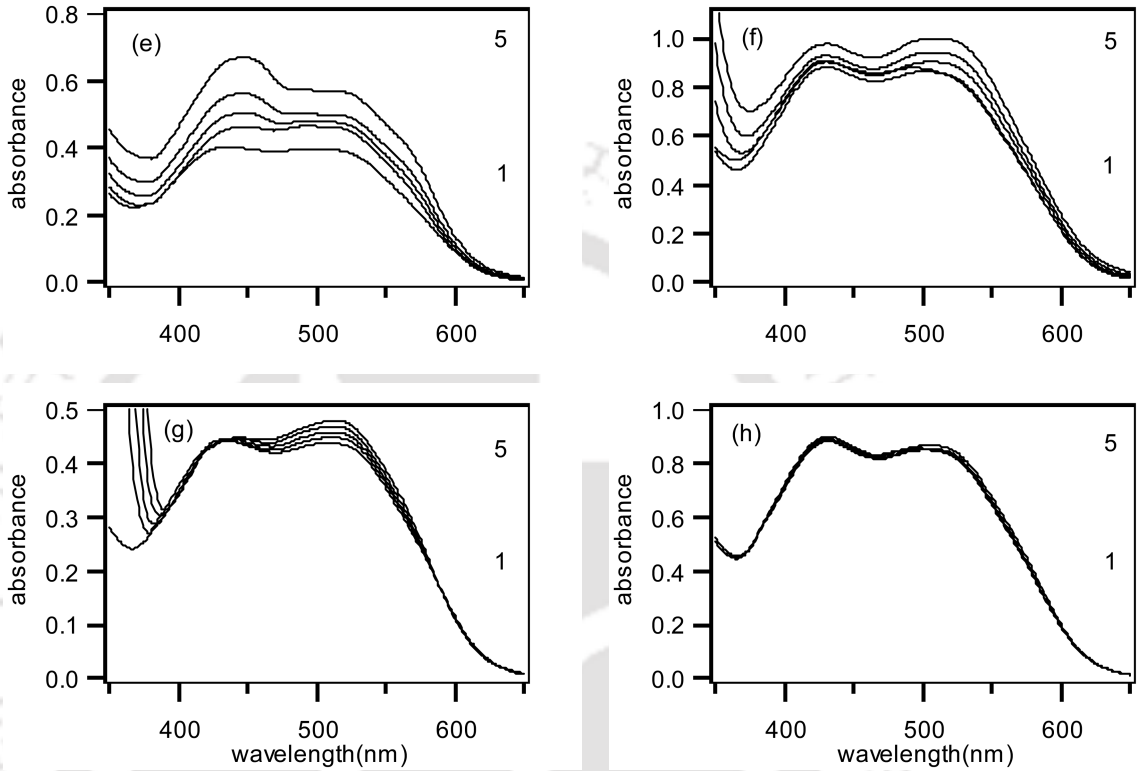


Figure 2.18: (Contd.)
(e) 1) 0 mM 2) 9.2×10^{-2} mM 3) 18.4×10^{-2} mM 4) 27.7×10^{-2} mM and 5) 37×10^{-2} mM of 1,2-phenylenediamine
(f) 1) 0 mM 2) 23×10^{-3} mM 3) 45×10^{-3} mM and 4) 68.8×10^{-3} mM of 4-iodoaniline
(g) 1) 0 mM 2) 2×10^{-3} mM 3) 4.2×10^{-3} mM 4) 6.2×10^{-3} mM and 5) 8.3×10^{-3} mM 1-naphthylamine
(h) 1) 0 mM 2) 1×10^{-2} mM 3) 2×10^{-2} mM and 4) 7.5×10^{-2} mM of aniline.

As already stated, the absorbances at 427nm and 500nm in aprotic solvent are attributed to two forms of the oligomers, **(X)** and (**Y**) (**Fig 2.11**) and in highly protic neutral substrates as well as solvent another state **Z** results giving an absorption at 470 nm. Hence, change of absorbance at these wavelengths can be explained in terms of conformational changes.

Increase in absorptions at both the places on addition of type **C** amine is due to stabilisation of the stacks of aromatic rings through interaction with -OH group of both the conformers. Such interaction leads to ion pairs having quinonic structure that can be formed through resonance structure. The type **D** amine causes no disruption of the intramolecular hydrogen bonding in the system.

The type **B** amine, such as the bifunctional rigid amine benzidine cannot be accommodated in the structure (**X**) containing intramolecular hydrogen bonding. Benzidine has two aromatic rings intervening the amine groups and the two end of the amines are at greater distance then analogous rigid diamine namely 1,4-phenylenediamine. However, the molecule benzidine has proper size to confine itself into the space between the alternate pyrogallol rings in form (**Y**) (figure **2.19**).

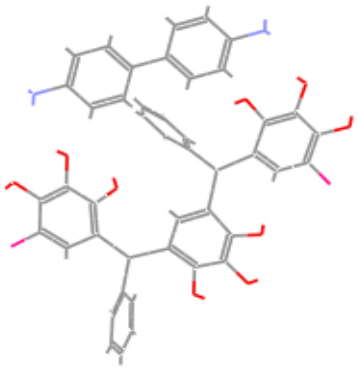


Figure **2.19**: Model showing proximity of benzidine to a part of oligomer **2.III**.

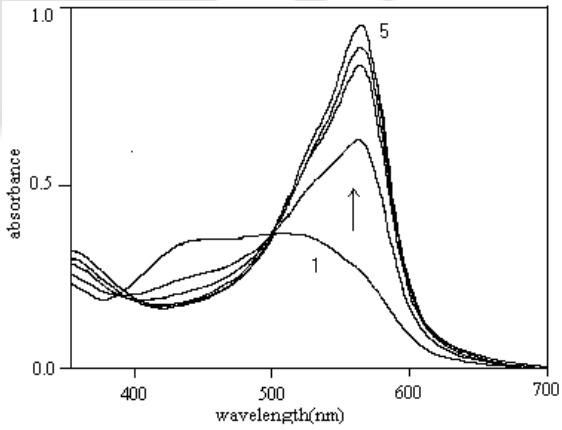


Figure **2.20**: Effect of *t*-butylamine on the spectra of **2.IV.**

The effect of amines on spectra is same for the other oligomers also and an example is shown in **figure 2.20**.

The observation would be incomplete if the effect of concentration of various amines on the respective new absorptions is not evaluated. Following are some graphs representing this effect in case of a few representative amines. These are

recorded in case of **2.III**. The M_W value, which is 1209, has been considered to be its molecular weight, as it showed polydispersity to be around unity. In case of *t*-butylamine it shows that a maximum absorption at 566 nm has been attained at the oligomer-amine ratio of 1:10. Similarly, for imidazole the ratio is 1:42.6. But in case of ethylenediamine, a dramatic change is noticed in the ratio, which is 1:0.00012 (figure **2.21a-c**).

(a)

(b)

(c)

Figure **2.21:** Effect of concentration of amine on the new absorption of oligomer **2.III** at 566 nm (a) *t*-butylamine, (b) imidazole and (c) ethylenediamine.

Similar study was carried on type B amine also. For benzidine, oligomer to amine ratio is 1: 15, while it is 1: 37 (figure **2.22a-b**) in case of 1,2-phenylenediamine. These results indicate that it is not purely a binding of amine to form ion-pairs, that in turn may give rise to change in colour, but more of a recognition of different amines that gives rise to such colour change.

Figure **2.22**: The effect of concentration of amine on the absorption of **2.III** at 427 nm (a) benzidine and (b) 1,2-phenylenediamine

2.4.3 Design of chemically driven reversible optical switches

Switching is referred to a process, by which two (or more) different states of a system can be changed by application of a stimulus.[104] The stimulus may be optical, electrical or chemical. Different characteristics of the two different states provide scope for reading out the signal for change of the state. In case of a chemical system, change of electronic absorption is one of the important read-out mechanisms, by which the change of optical wavelength due to the change of the state of the system can be observed and recorded. In other words, this switching leads to switching of optical wavelength. Again a switch, which switches optical wavelength is called optical switch.

The type **A** amines form ion pairs with the oligomer and generates new state and thus can be used to device chemically driven optical switch. Absorption changes in such a switch is shown in figure **2.23**.

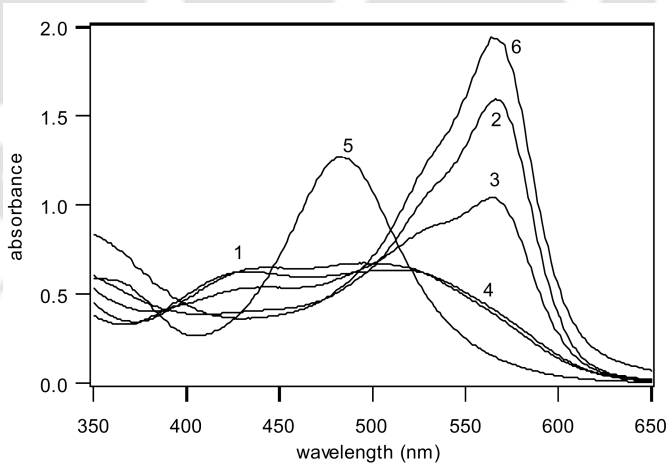


Figure **2.23:** UV-visible spectra of a solution of **2.III** (3 mg) in acetonitrile (3 cm^3) with 1) none 2) 0.5 µl of *t*-butylamine 3)-5) 1µl of HCl (1N) in each aliquot to solution 2) and 6) 2 µl of *t*-butyl amine to 5).

The oligomer **2.III** on interaction with *t*-butylamine leads to strong absorption at 563nm and this absorption diminishes on addition of hydrochloric acid

a new absorption maximum at 475nm is observed. On addition of excess *t*-butylamine, this absorption is lost and the absorption at 563nm develops (**figure 2.22**). This cycle can be reversibly done and we have successfully tested reversibility of such cycle to six times without degradation of the oligomers.

Such phenomenon can be explained by the reversible binding of acid and base as shown in **scheme 2.1**.

The hydroxyl groups of the oligomer initially form ion pair through reversible binding showing growth in the absorbance at 563 nm. A new state is generated on treatment with acid returns to the state generated from interaction with amine. This state has absorbance at 475 nm. An identical state as of the one

generated from treatment with amine followed by mineral acid can also be generated through interaction of the oligomer with a quaternary ammonium salts directly. Thus, the new state that grows at 473nm is identified to occur from recognition of quaternary ammonium salt from independent study (figure **2.24**).

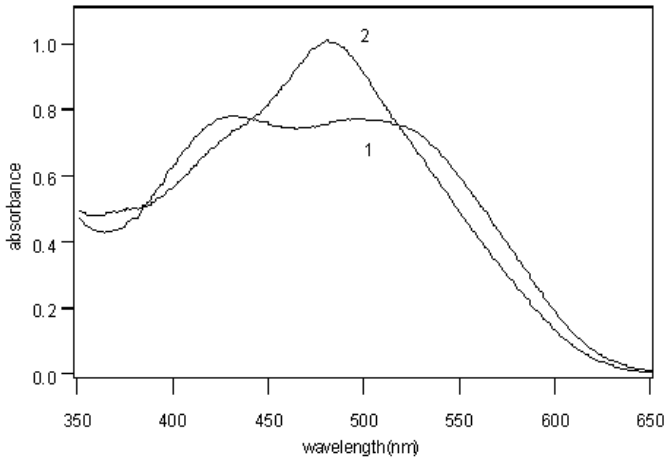


Figure 2.24: UV-visible spectra of a solution of **2.III** (3 mg) in acetonitrile (3 cm^3) with 1) none and 2) 6.4 mg tertrabutylammonium bromide

The chemically driven optical switch can be designed from the type **B** amine also. For example benzidine allows growth of absorption at 423nm of **2.III** which can be switched to 474nm by addition of perchloric acid (figure **2.25**).

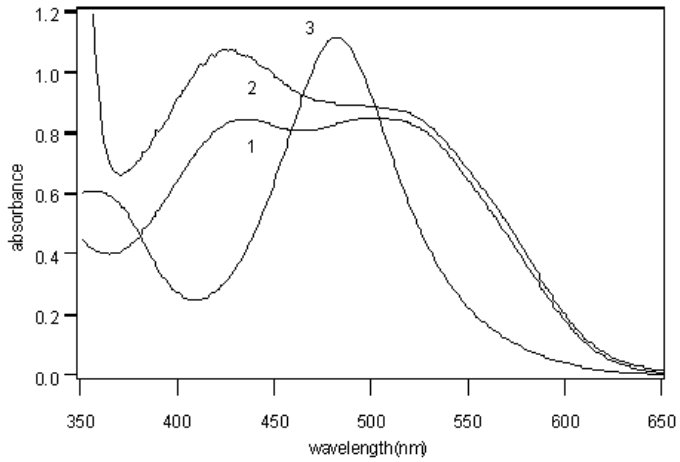


Figure 2.25: UV-visible spectra of a solution of **2.III** (3 mg) in acetonitrile (3 cm^3) with 1) none 2) 5 mg of benzidine, 3) 5 µl of $HClO_4$ (70%) was added to 2).

One may put forward at this stage that the device of the switch is purely an acid-base chemistry involving quinonic intermediates. But it would be inappropriate to explain in this manner as the amines having comparable pk_a values may have the totally different effect on the absorbance. For example first pk_a of aniline is 4.60 and that of benzidine is 4.66, but they have different effects on the electronic spectra (refer **table 2.3**) of the oligomer **2.III**. Similarly, pyridine has pk_a 5.23 whereas p-methyl aniline has pk_a 5.10 but they have very different effect on electronic spectra. No doubt the basicity is one key factor but the conformational change due to the hydrophobicity and hydrophilicity of the oligomer is the prime factor in design of such switch. We have recorded GPC of the sample by adding amine to solutions of **2.III** in different solvent. This did not give any evidence on aggregation of two or multiple units of oligomers.

Literature suggests that suitably designed calixarenes can recognize anion also[19]. Effects of the anions of the quaternary ammonium salts on the bound state

with quaternary salts are tested with a set of anions. The visible spectra of the quaternary ammonium salt of *t*-butylamine with perchlorate, chloride, bromide, sulphate anions do not show significant shift in the absorption spectrum. The variation of anions on the quarternary salts shows a slight difference in the new λ_{max} to the extent of + or -10nm precluding the interaction of an anion. However, there is significant effect of anion when optical switching is done with benzidine. Different acids such as perchloric acid, hydrochloric acid shows shift in the λ_{max}. Treatment of **2.III** with benzidine and perchloric acid respectively gives rise to absorption at 474 nm whereas the similar state generated from benzidine and hydrochloric acid with **2.III** has absorption at 481 nm. This shows that the different states created by different anions of the quaternary ammonium salts of diamine with a rigid frame, has significant effect on binding. The effect is probably due to the bound state with the quaternary ammonium salt that would have to accommodate two anions within it. Foregoing discussions makes it clear that optical switch can be derived from the oligomers that are prepared from condensation of aromatic aldehydes with pyrogallol.

2.4.4 Electrochemical study

Cyclic polyphenolic compounds such as calixarenes on appropriate functionalisation are expected to pave way for designing redox-switch having analogy to enzymes[106]. To study the electrochemistry of the calixarenes an electroactive site in the calixarenes is to be present in the ring. An elegant demonstration on such system was given by Gomez-Kaifer *et.al.*[107]. The calixarenes may provide a means to study electrochemical properties of external electroactive guest molecule in a confined environment. With this methodology the electrochemistry of quinone systems with different hosts is well established[108-110]. Another aspect of studying electrochemical properties in confined medium is to assess a supramolecular environment having close analogy to biological systems. Since we are dealing with linear chains and these recognize amines we have studied the electrochemical behaviour of an electroactive aromatic diamine namely 1,4-phenylenediamine. This electrochemical study has another facet as aromatic amines provide a way to synthesis of polyanilinic compounds and also would provide information to design redox switch[110]. The 1,4-phenylenediamine can transform into benzenoid units and thus can throw light on proton transfer and redox properties of the amine units[111].

As mentioned earlier that 1,4-phenylenediamine is recognised by the oligomers (**2.III-2.V**). A schematic representation of such recognition is shown in figure **2.26**.

Figure **2.26**: Schematic representation of recognition of 1,4-phenylenediamine

The 1,4-phenylenediamine has two reversible redox cycles $E_{1/2}$ at 334 mV and $E_{1/2}$ at 863 mV due to the formation of cationic radicals (Fig **2.27**).

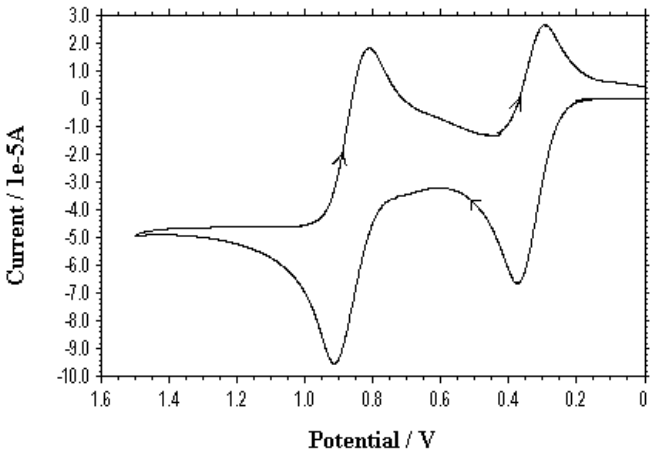
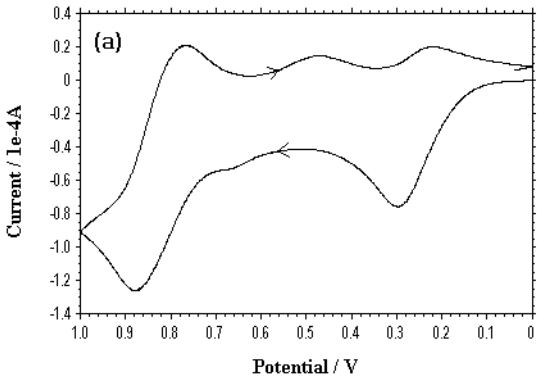
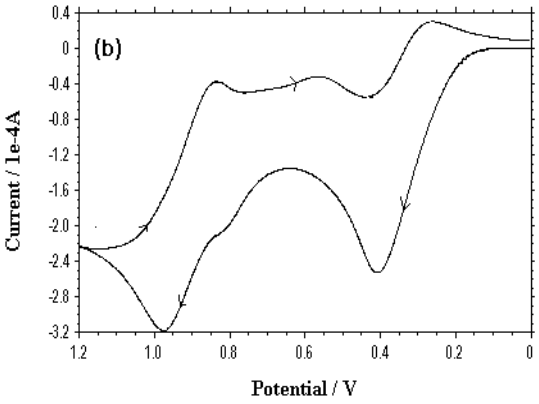


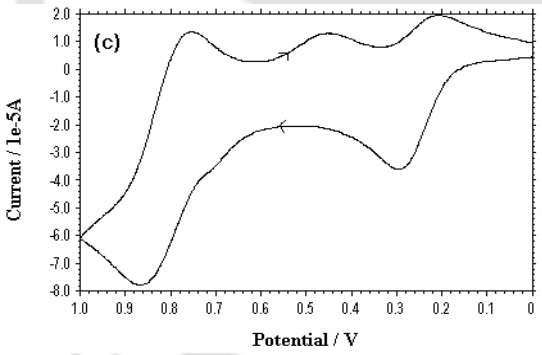
Figure **2.27**: Cyclic voltammogram of 1,4-phenylenediamine in acetonitrile (3ml) with tetrabutylammoniumperchlorate(0.1M) as supporting electrolyte. Scan rate = 100mV /sec

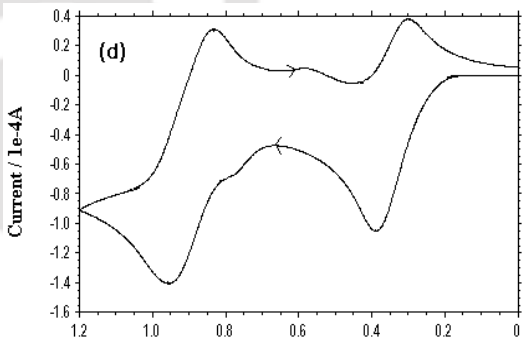
Overall electrochemical process taking place is represented in **scheme 2.2**, where 1,4-phenylenediamine can have benzene-benzenoid structures on electrochemical oxidation and reduction reactions. The first reversible cycle with $E_{1/2}$ at 334 mV is due to a cationic radical, this radical in the second reversible cycle at $E_{1/2}$ 863 mV transforms to a diimine.

The overall redox reactions of 1,4-phenylenediamine in the presence of the oligomers are not effected but positions of $E_{1/2}$ of the original reversible cycles are shifted from the original positions and also become quasireversible. Figure **2.28a-d** are the cyclic voltamograms of the 1,4-phenylenediamine with different oligomers, viz. **2.III-2.VI** which show that the usual redox reactions of 1,4-phenylenediamine (**scheme 2.2**) are taking place, but their shapes suggest that these electrochemical reactions tend to be quasireversible on recognition.


(a)
Current / 1e-4A
Potential / V


(b)
Current / 1e-4A
Potential / V


(c)
Current / 1e-5A
Potential / V


(d)
Current / 1e-4A

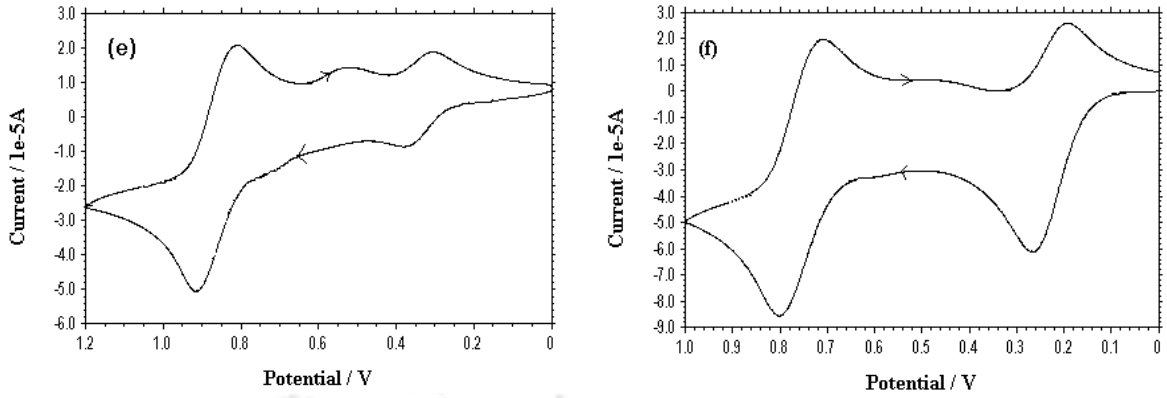


Figure **2.28**: Cyclic vltammogram of 1,4-phenylene diamine (in acetonitrile) in presence of various substrates, (a) **2.III,** (b) **2.IV**, (c) **2.V,** (d) **2.VI** (e) **2.VII** and (f) **2.VIII.** Supporting electrolyte: tetrabutylammoniumperchlorate(0.1M), Scan rate = 100mV /sec

It is also worth comparing the results with open chain ethers that may have suitable geometry for recognition of 1,4-phenylenediamine. The two such ethers (**2.VII** and **2.VIII**) having similar geometry are chosen.

The ether **2.VII** shows slight shift in the $E_{1/2}$ values of 1,4-phenylenediamine from that of its free state, whereas in the case of **2.VIII** the $E_{1/2}$ values are less by 114 and 107 mV respectively (figure **2.28**e-f). This suggests that the 1,4-phenylenediamine is embedded in the ethers and the binding ability of **2.VIII** is higher than that of **2.VII**.

It is worth noting that the cyclic calixarene having six phenolic units in the ring (**2.IX**) shows insignificant change in the redox potentials of 1,4-phenylenediamine (entry 8 of table **2.4**) but the shape of the cyclic voltamogram is indicative of being bound to the calixarene. For a comparative study a cyclic siloxane (**2.X**) is also studied, in this case there is a slight shift in the electrochemical properties of 1,4-phenylenediamine without affecting the overall redox processes.

The oligomer **2.III** and **2.V**shift the potentials towards lower value but in the case of **2.IV** there is only slight shifts on the redox potentials. The $E_{1/2}$ values of 1,4-phenylenediamine with different substrates are listed in table **2.4**.

Table **2.4**
The $E_{1/2}$ values of 1,4-phenylenediamine

in the presence of different substrates

Entry No.	Substrate	$E_{1/2}$'s in mV
1	None	334, 863
2	**2.III**	259, 822
3	**2.IV**	336, 897
4	**2.V**	251, 809
5	**2.VI**.	345, 890
6	**2.VII**	345, 861
7	**2.VIII**	230, 756
8	**2.IX**	346, 859
9	**2.X**	252, 790

As benzidine also showed definite effect on the electronic properties of the oligomers, the electrochemistry of benzidine was also studied in presence of the oligomers. Benzidine has one redox cycle at $E_{1/2}$ 529.5 mV and an oxidation wave at 953 mV. In presence of the oligomers, the redox cycle becomes irreversible. However, the positions of the oxidation peaks are not shifted (figure **2.29**). It implies that, benzidine after oxidation gets bound to the oligomer.

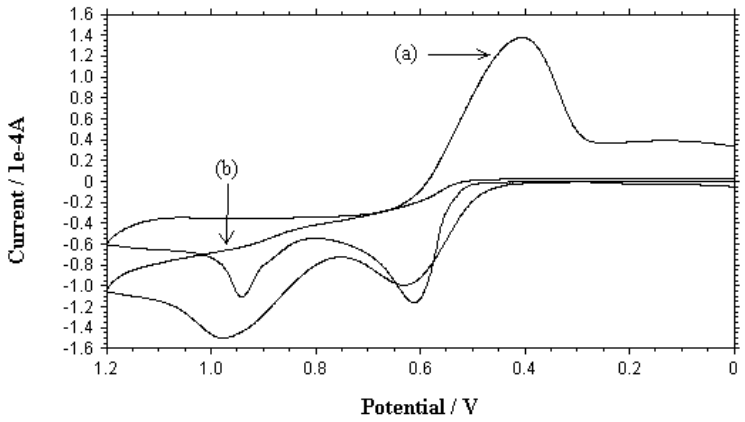


Figure **2.29**: Cyclic voltammogram of (a) benzidine and (b) benzidine and **2.III**

The electrochemistry of quinonic compounds is of great value in understanding the role of quinone in photosynthetic energy conversion[112]. The electrochemical property of the quinonic compounds in a confined environment

throws light on the mechanistic aspects of biological redox reactions[105]. The redox properties of free quinones and the quinones bound to a host vary and a large reduction in reduction potential is observed[113]. Thus redox properties of the donor and acceptor counterparts in a charge transfer complex are to vary from the original counterpart[107].

Study of the cyclic voltamogram of 1,4-naphthoquinone alone and with the oligomers under study showed that there is no considerable change on the cyclic voltamogram of 1,4-naphthoquinone in presence of the oligomers (figure **2.30**).

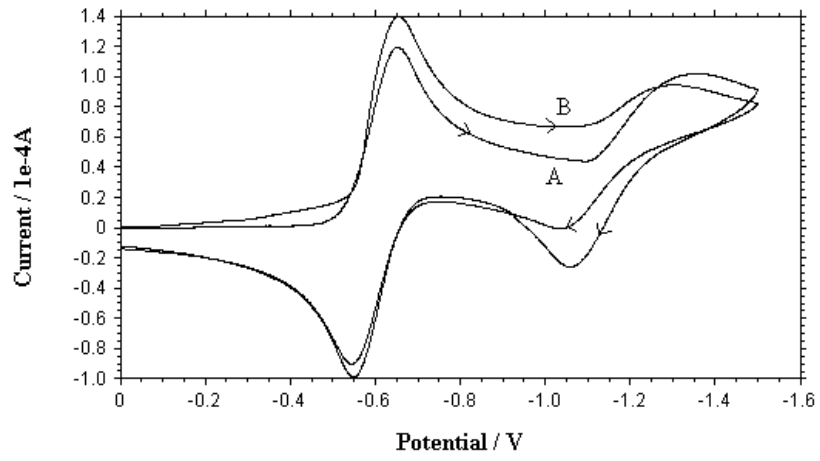


Figure **2.30**: Cyclic voltamogram (A) of 1,4-naphthoquinone and (B) of 1,4-naphthoquinone with **2.III**.

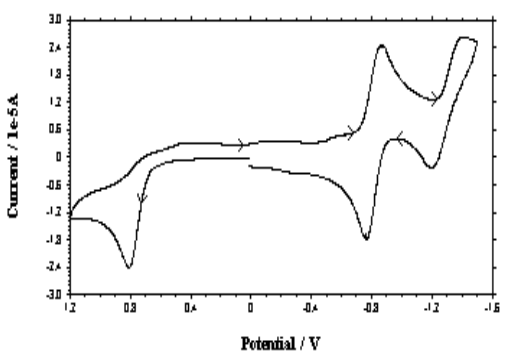
It implies that the quinonic unit was not bound to the oligomers. In order to bring a quinonic unit to the proximity of the oligomers and to have a bound state we studied the electrochemistry of the charge transfer complexes, prepared from quinonic compounds. In this study, the first system we have studied is the charge transfer complex of 1,4-phenylenediamine with 1,4-naphthoquinone (**2.XI**).

This system is chosen with the reasons that, the capability of the oligomers (**2.III-2.V**) to recognize the 1,4-phenylenediamine is expected to bring the quinone either within the hydrophilic cage of the oligomer or to the vicinity of the oligomer for further interaction (figure **2.31**).

The cyclic voltamograms of charge transfer complex of 1,4-naphthoquinone with 1,4-phenylenediamine (**2.XI**) and that of the charge transfer complex with oligomer **2.III** are shown figure **2.32a-b**. 1,4-naphthoquinone has two reversible one-electron redox cycles with $E_{1/2}$ at –584mV and –993mV and 1,4-phenylenediamine has two reversible redox cycles with $E_{1/2}$ at 334 mV and 836 mV respectively[114].

The charge transfer adduct does not have these two redox cycles and instead has only one oxidation wave at 809 mV and two reversible cycles with $E_{1/2}$ at -815mV and –1272mV.

The reversible redox cycles at the –ve side are attributed to the two redox processes that may occur to equilibrate between 1,4-naphthalene-diol and 1,4-naphthaquinone. The charge transfer complex on interaction with the oligomer (**2.III**) results in loss of the two original cycles in the –ve side but has one quasireversible cycle with $E_{1/2}$ at –884 mV. The system was found to be electroactive and it is observed that the reduction potential in the second cycle increases towards the negative side, however the oxidation peak at –700 mV remained unchanged. The new reduction peak with $E_{1/2}$ –884 mV in the first cycle shifts to the –ve side in the second cycle to a peak with $E_{1/2}$ –1011 mV. This suggests that the quinonic part of the charge transfer complex (**2.XI**) on generation of anionic radical is further stabilized (figure **2.32b**). This occurs as the radical so formed is embedded within the oligomer.



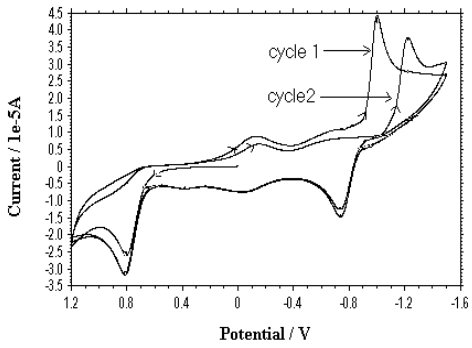


Figure **2.32**: Cyclic voltamogram of (a) **2.XI** and (b) **2.XI** in presence of **2.III**

It is also a pertinent issue to explore the ability of the oligomers to recognize quinonic units from equivalent structures. The understanding of the space isomers of charge transfer complexes would add more dimensions to the space interaction in supramolecular isomerisation. If the donor and acceptor have provision of hydrogen bonding and also have possibility of interchange of conjugation between the donor and acceptor (scheme **2.3**) they may have equivalent structures. These molecules could also probably help in designing equivalent structures formed via proton transfer through space and also from exchange of conjugation between two organic motifs shown in scheme **2.3**.

One simple system we have taken up for such study is the pairs derived from 1,4-naphthoquinone (NQ) with 1,4-benzenediol (BD) and 1,4-naphthalenediol (ND) with 1,4-benzoquinone (BQ). They should have structure **2.XII** and **2.XIII** respectively.

It has been possible to prepare only **2.XII** while attempt to prepare **2.XIII** from ND and BQ yielded NQ and BD (scheme **2.4**).

The reaction of equimolar amount of NQ with BD leading to the formation of charge transfer complex **2.XII** can be seen in the UV-visible spectrum. The intensity

of absorption of original BD is enhanced with a minor increase in the intensity of absorption of the peak at 334 nm of NQ. This was observed for the solution of the equimolar mixture of NQ and BD and also from isolated adduct.

In the ^{1}H NMR spectrum of **2.XII** (figure **2.32a**)**,** there are two multiplets at 7.8 and 8.0 ppm from the two sets of non-equivalent protons at 5, 8 and 6, 7 positions. It has a singlet at 7.1 ppm from the protons located at 2 and 3 positions of the naphthalenic ring. These peaks are slightly different from that of free NQ. The protons from the BD counterpart appear at 6.6 and at 8.6 ppm. The free BD has NMR signals very close to these signals at 6.5 and 8.5 ppm. Apparently, no new signal other than the original counterpart appeared in the spectrum. The signals of NQ appear at 7.0, 7.8 and 8.1 ppm, whereas these are obtained at 7.1, 7.8 and 8.0 ppm in the crude product of NQ with BD

The ^{1}H NMR spectrum of crude reaction mixture of the reaction of equimolar amount of NQ and BD as well as that of ND with BQ (figure **2.32b**) are identical except the later pair has an additional singlet at 6.9 ppm. The proton signal of free BQ at 6.8 ppm, appeared at 6.9 ppm in the product. The 1,4-napthalenediol has proton signals at 6.4, 6.7, 8.2, 9.3 ppm which were not observed in the case of the reaction product of ND with BQ. Since the products from the reaction of ND with BQ and NQ with BD were same, there must be an equilibrium between the two pairs. The small shift in the chemical shift and non-observation of strong charge transfer absorption at a higher wave length than the original counterparts makes us to believe that in solution the charge transfer interaction is less prominent than a

hydrogen bonding interaction as shown as **2.XIV** rather than truly π- interacting stacked structure. It is to be noted that the powder diffraction pattern of the two

Figure **2.33:** ^{13}H NMR (400MHz) spectra of (a) the adduct of NQ and BD and (b) the crude product mixture of equimolar ND with BQ.

adducts are much different from each other confirming the structures in solid state to be different from the structures in solution.

The results are also supported by the ^{13}C NMR of the products of crude mixture in each cases. In the case of the reaction of NQ with BD the reaction mixture has seven signals in the aromatic region and out of which one is due to carbonyl. Whereas in the case of the reaction mixture of ND with BQ the reaction mixture has nine signal of which seven are common to the earlier case and two are from 1,4-benzoquinone (figure **2.34**).

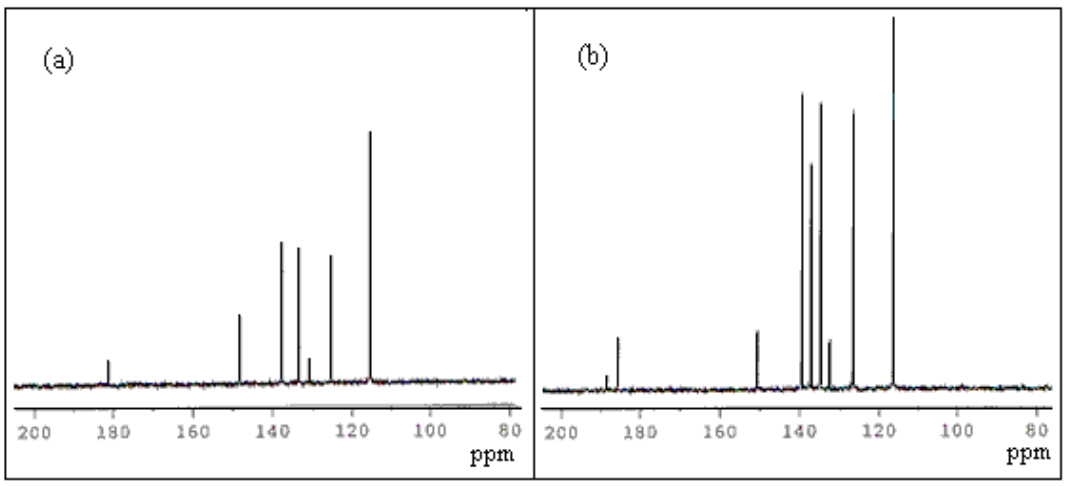


Figure **2.34:** ^{13}C NMR (400MHz) spectra of (a) the adduct of NQ and BD and (b) the crude product mixture of equimolar ND with BQ.

The proton NMR integration of the products of the reaction shows that only 50% of the 1,4-benzoquinone is transformed from 1,4-benzenediol and the 1,4-naphthalenediol completely got converted to 1,4-naphthoquinone. These results support that the reaction must be passing through an incomplete equilibrium and an additional process in operation that oxidizes the 1,4-naphthalenediol. Another possibility is that the reaction may proceed without a charge transfer interaction. To ascertain these the visible spectra of the reactions were monitored with time at one minute's intervals and observed that the reaction of ND with BQ leads to initial

increase in absorption at 334nm. This absorption reaches a maximum value and then decays (figure **2.35**).

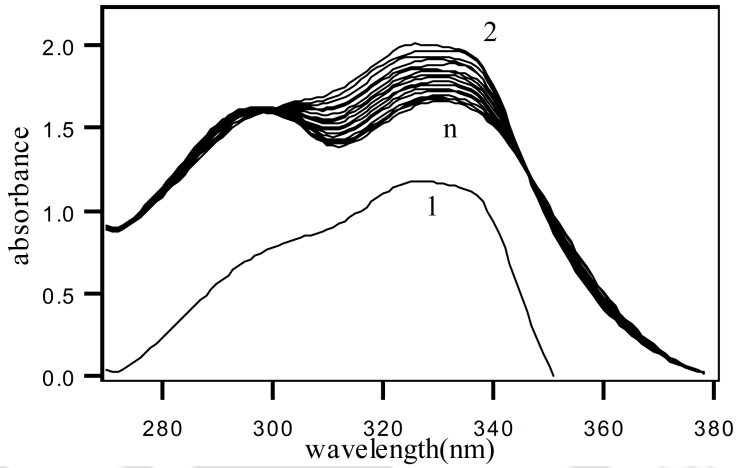


Figure **2.35** : UV-visible spectra of an equimolar mixture of 1,4-naphthalenediol (0.002mmol) and 1,4-benzoquinone (0.002mmol) in acetonitrile (3ml) 1) after 1minute of mixing, 2-n) after every minute from the initial plot 1).

During this decay there is increase in the absorbance at 294 nm that is due to the formation of 1,4-benzenediol. As mentioned earlier that there is an incomplete equilibrium between BQ and BD in the presence of ND. In this reaction all the ND got oxidized, but BD is partially reduced. The transformation of ND by an external agent or alternative way cannot be ruled out. To check such possibilities, to a solution of 1,4-naphthalenediol in acetonitrile hydrogen peroxide was added in an independent experiment. This did not change the visible spectra of the solution. But

on addition of a trace amount of 1,4-benzoquinone to this the peak intensity at 324 nm was enhanced. After laps of few seconds the absorption at 324nm started decreasing and growth at 294nm (figure **2.36**) took place.

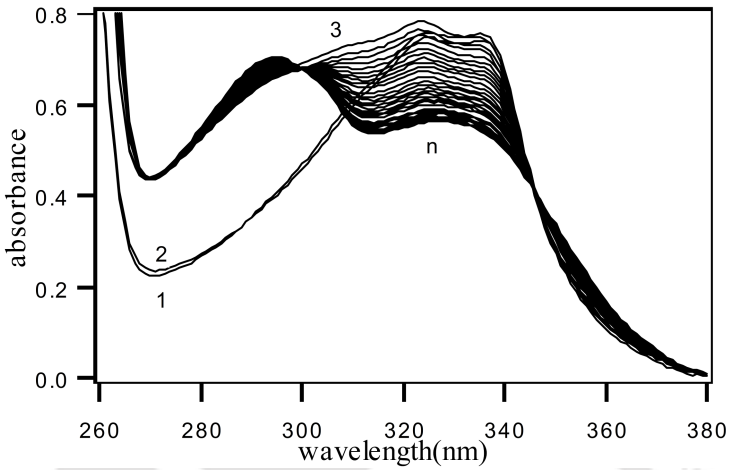


Figure **2.36**: UV-visible spectra of 1)1,4-naphthalenediol (0.00055mmol in 3ml acetonitrile) 2) 1,4-naphthalendiol with hydrogen peroxide (5µl, 6%) 3-n) scans with intervals of one minute after addition of 1,4-benzoquinone (trace amount) to 2).

This supported that the BQ was causing a catalytic effect on oxidation of ND in the presence of oxidant. Similar observation was also observed when tertiary-butylhydroperoxide was used as oxidant. These results also supported the fact the ND oxidation by BQ accompanies a parallel process. The yield of BQ in the above reaction slightly increases when anhydrous solvent was used. Thus the results

can be explained by considering the proton transfer process in a highly hydrogen bonded network of the charge transfer adduct (scheme **2.4**).

The conversion of the 1,4-naphthalenediol by hydrogen peroxide was not possible at ambient condition without addition of trace amount of 1,4-benzoquinone. This suggests that the hydroperoxide can participate in the proton transfer process through hydrogen bonded structure as shown in scheme 2. The water molecule shown in the scheme to terminate such process comes from the solvent. Control

experiments were carried to confirm the interconversion of 1,4-naphthalenediol to 1,4-napthoquinone the out by recording UV-visible spectra of the mixtures of ND and BQ with different concentration ratios. It was observed that the conversion of 1,4-naphthalenediol to 1,4-naphthoquinone was independent of the concentration of BQ. This observation also favoured the mechanism shown in scheme **2.4** rather than a possible alternative path involving radical.

The IR spectra of the two isomeric counterparts in solid state clearly indicate this formation. The system **2.XII** has only one carbonyl signal at 1650^{-1}, whereas in the case of crude product of ND and BQ, there are two carbonyl frequencies at 1650 cm^{-1} and 1630 cm^{-1} (figure **2.37**), one is due to naphthoquinone and the other is due to benzoquinone.

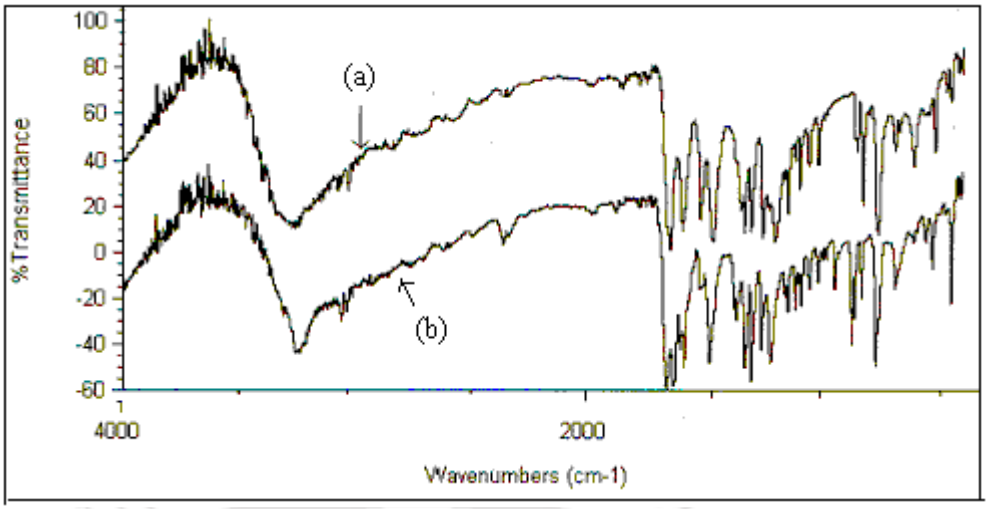


Figure **2.37**: **IR** spectra of (a) the adduct of NQ and BD and (b) the crude product mixture of equimolar ND with BQ (as KBr pellet)

Data on heat of formation (-77.89126 kcal/mol for side-on alignment and –84.07083 kcal/mol for stacking alignment for **2.XII** and –64.98432 kcal/mol for **2.XIII**) also support this formation, since the energy difference of at least 13 kcal suggests that **2.XII** is more stable.

The above observations support that **2.XII** and **2.XIII** can co-exist in solution with considerable charge delocalisation (**scheme 2.3**), however, low energy difference makes **2.XIII** to get converted to **2.XII** in solution. The ^{1}H NMR integration of **2.XII** and **2.XIII** shows that only 50% of the 1,4-benzoquinone is

transformed from 1,4-benzenediol and 1,4-naphthalenediol completely got converted to 1,4-naphthoquinone. These results support that the reaction must be passing through an incomplete equilibrium and an additional process in operation that oxidizes the 1,4-naphthalenediol. Another possibility is that the reaction may proceed without a charge transfer interaction.

To ascertain these the visible spectra of the reactions were monitored with time at one minutes intervals and observed that the reaction of ND with BQ leads to initial increase in absorption at 334nm. This absorption reaches a maximum value and then decays (figure **2.36**). During this decay there is increase in the absorbance at 294 nm that is due to the formation of 1,4-benzenediol. As mentioned earlier that there is an incomplete equilibrium between BQ and BD in the presence of ND. In this reaction all the ND got oxidized, but BD is partially reduced. The transformation of ND by an external agent or alternative way cannot be ruled out.

To check such possibilities, to a solution of 1,4-naphthalenediol in acetonitrile hydrogen peroxide was added in an independent experiment. This did not change the visible spectra of the solution. But on addition of a trace amount of 1,4-benzoquinone to this the peak intensity at 324 nm was enhanced. After few seconds the absorption at 324 nm started decreasing and growth at 294 nm (figure **2.37**) took place.

This supported that the BQ was causing a catalytic effect on oxidation of ND in the presence of oxidant. Similar observation was also observed when tertiary-butylhydroperoxide was used as oxidant. These results also supported the fact the ND oxidation by BQ accompanies a parallel process. The yield of BQ in the above reaction slightly increases when anhydrous solvent was used. Thus the results

can be explained by considering the proton transfer process in a highly hydrogen bonded network of the charge transfer adduct (scheme **2.4**).

The conversion of the 1,4-naphthalenediol by hydrogen peroxide was not possible at ambient condition without addition of trace amount of 1,4-benzoquinone. This suggests that the hydrogen peroxide can participate in the proton transfer process through hydrogen bonded structure as shown in scheme **2.4**. The water molecule shown in the scheme to terminate such process comes from the solvent. Control experiments were carried to confirm the interconversion of 1,4-naphthalenediol to 1,4-napthoquinone by recording UV-visible spectra of the mixtures of ND and BQ with different concentration ratios. It was observed that the conversion of 1,4-naphthalenediol to 1,4-naphthoquinone was independent of the concentration of BQ. This observation also favoured the mechanism shown in scheme **2.4** rather than a possible alternative path involving radical.

Since **2.XII** could be obtained as stable in solution, we have checked its cyclic voltamogarm in the negative side and observed two couples arising from the reduction of 1,4-naphthoquinone to 1,4-naphthoquinone radical monoanion and dianion. It has one oxidation wave at 1030 mV and a reduction wave at 337 mV in the above range (figure **2.38**). On a slow scan rate, only the oxidation wave remains.

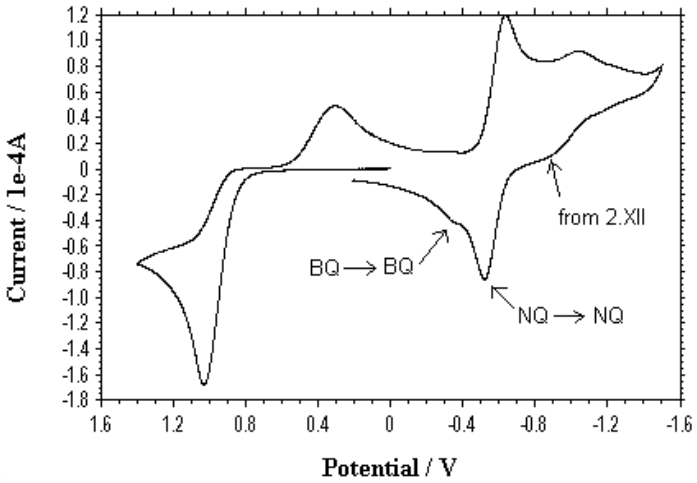


Figure **2.38**: Cyclic voltammogram of **2.XII**

However, **2.XIV** showed two pairs of redox potentials arising from the two quinonic units. Although the identical number of peaks for reduction and oxidation of the 1,4-naphthoquinone and 1,4-benzoquinone are observed the redox pairs are shifted in each case from a free state showing them to be bound state. For example free state of the 1,4-naphthoquinone has oxidations at –539 and –937mV and reduction peaks at –621 and -1100 mV respectively. The benzoquinone has oxidation at –307mV and reduction at -472 mV. The cyclic voltamograms of **2.XII** and the crude product of naphthalenediol and benzoquinone in the region of 0 to -1.5V region are shown in figure **2.38** and **2.39**.

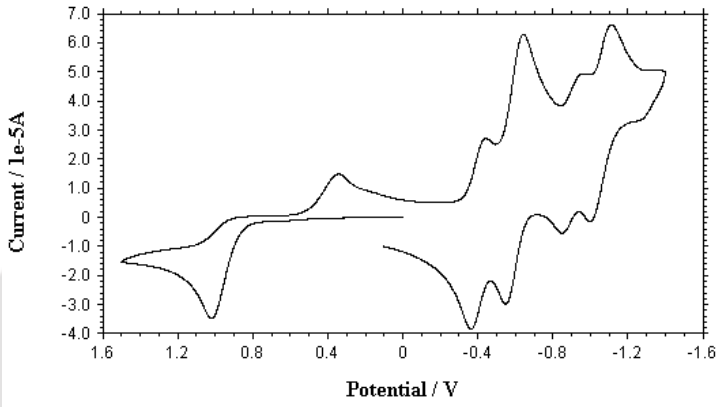


Figure **2.39** : Cyclic voltammogram of crude product of ND and BQ

The electrochemical processes of **2.XII** and that of the crude reaction mixture of reaction of ND with BQ that arise from dissociation of the charge transfer adducts can be represented by the scheme **2.5**.

At slow scan rate (1mV/sec) the reduction peak that were present in the positive side (310mV) disappeared. In the case of the crude reaction mixture of ND and BQ a negative scan led to an additional redox couple having oxidation at -928mV and reduction at –1040mV. This couple is assigned to a redox couple of 1,4-naphthoquinone and 1,4-naphthoquinone anionic radical formed through electrochemical reduction[114]. In the cyclic voltamogram of **2.XII** in the first cycle do not lead to the reduction peak at -430mV and oxidation peak at –316mV but after multiple cycles and sufficient lapse of time degradation of the charge transfer complex to give detectable amount of 1,4–benzoquinone This led to the growth of this redox couple for 1,4-benzoquinone and its anionic radical.

Thus, all the results described above supports that **2.XII** and **2.XII** can co-exist, however, low energy difference makes **2.XIII** to get converted to **2.XII** in solution. To understand the interconversion several scans of freshly prepared equimolar solutions of NQ and BD (figure **2.40**) and that of ND and BQ (figure **2.41**) were recorded.

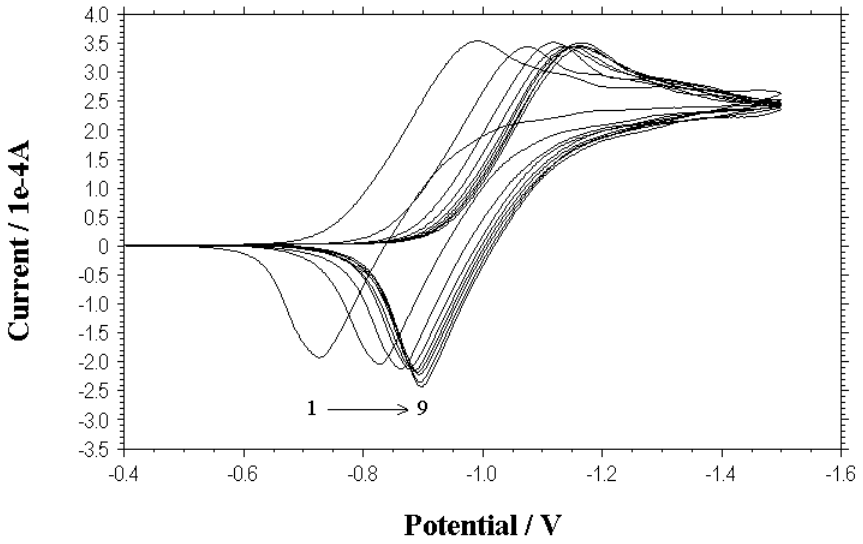


Figure **2.40**: Formation of charge transfer adduct monitored by cyclic voltamograms of equimolar amount of 1,4-naphthoquinone (0.001mmol) with 1,4-benzenediol (0.001mmol) in acetonitrile (3ml) with tetrabutylammonium-perchlorate(0.1M) as supporting electrolyte (from scan 1 to 9). Scan rate = 100mV /sec

In the later case we have observed as soon as the NQ and BD are mixed the two redox couple in the negative side appears as only one. This couple further shifts towards negative side and attains a stable state after about 20minutes, showing the stability of the **2.XII**. However, the similar study with an equimolar mixture of ND and BQ has led to the decrease in the oxidation potential of 1,4-benzoquinone and increase in the oxidation potential of 1,4-naphthoquinone. It had shown growth of

the redox potential of **2.XII** (as observed in the earlier with other pair) as well as additional redox couple is assigned to the isomer **2.XIII** (figure **2.41**). All these studies support that the isomers **2.XII** and **2.XIII** are formed in solution however, the **2.XIII** gets converted to **2.XII**.

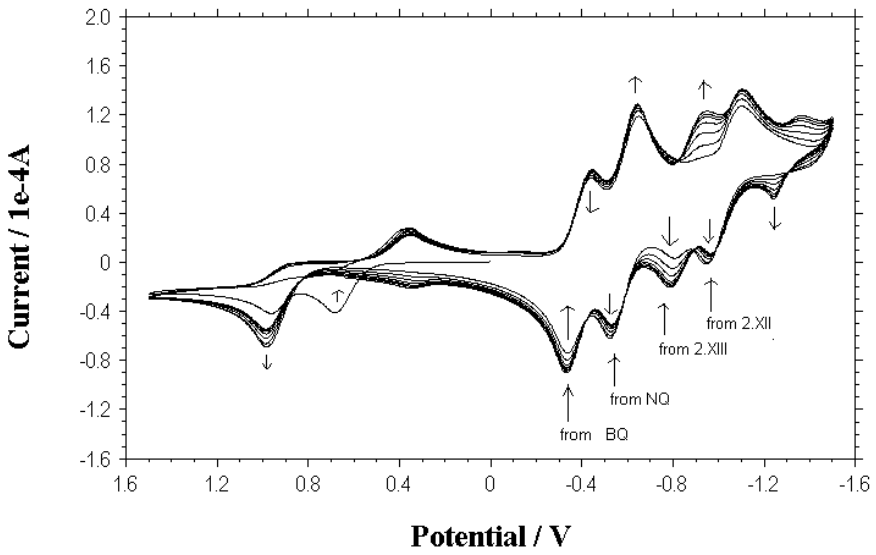


Figure **2.41**: Formation of charge transfer adduct monitored by cyclic voltamograms of equimolar amount of 1,4-naphthalenediol(0.001mmol) with 1,4-benzoquinone (0.001mmol) in acetonitrile (3ml) with tetrabutylammoniumperchlorate(0.1M) as supporting electrolyte. Scan rate = 100mV /sec

The electrochemical behaviour of **2.XII** and the crude product of ND and BQ has been studied in presence of oligomers **2.III-2.V**. It has been observed that the oligomers are able to recognize quinonic species from this type of equivalent structures also.

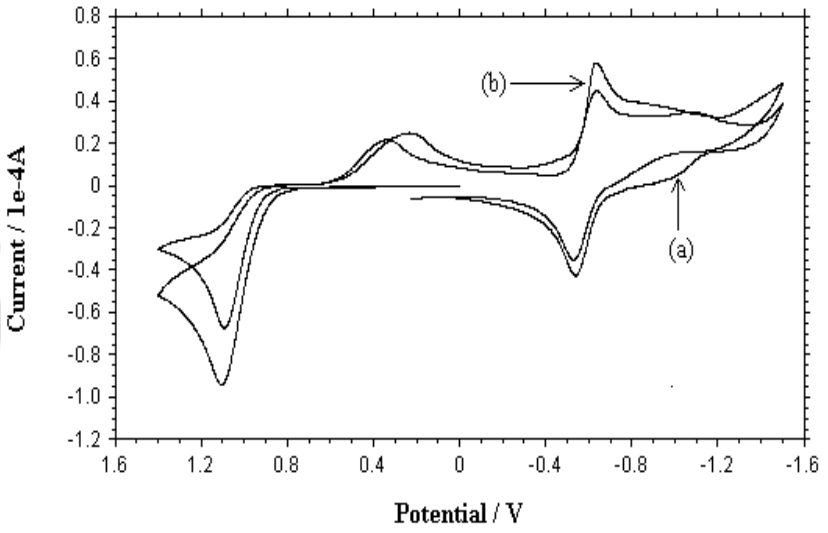


Figure **2.41** : Cyclic voltammogram of (a) **2.XII** and (b) **2.XII** and **2.III**.

The cyclic voltamograms of **2.XII** and the crude product of ND and BQ in presence of the oligomer **2.III** (figure **2.42b** and **2.43b**) are identical. So, these

suggest that the biradical species formed in both the systems upon electrochemical reduction (scheme **2.3**) are stabilized upon binding with the oligomer.

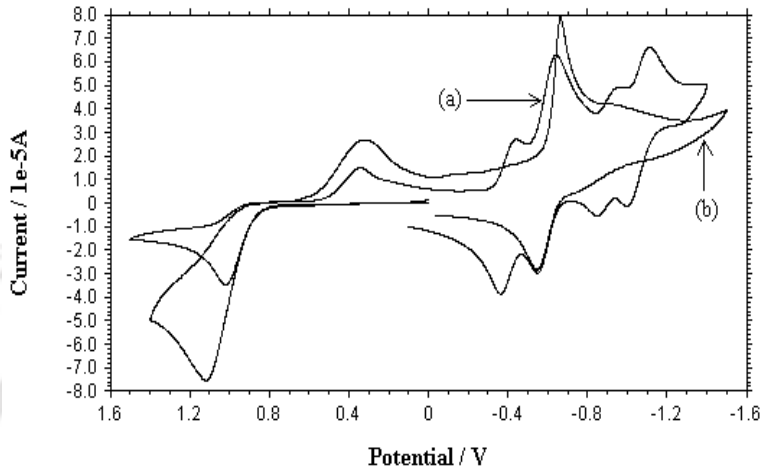


Figure **2.43**: Cyclic voltammogram of (a) crude product of ND and BQ and (b) that with **2.III**

2.4.5 The oligomers as supports in hydrolysis

Supramolecular chemistry has made significant breakways to establish simple hydrolytic reactions that occur in biology by various enzymes[110-111]. The hydrophobic confinement is one effect that provides extra performance and selectivity in such reactions[115-118]. The capability to recognize amine substrates,

especially quaternary ammonium salts have prompted us to look for reactions which would pass through extrusion of an ammonium species. The hydrolysis of oxime and imine functionalities to a carbonyl group is selected for such purpose. The oxime/imine itself are recognized by the oligomers and the hydrolysis of oxime/imine gives ammonium salt that is further recognized by the oligomers. Possible path for such hydrolysis of oximes and imines in presence of the oligomer is shown in scheme **2.6**.

To check the above possibility shown in scheme **2.6**, a set of experiments was performed on selected oximes and imines in presence of H_2SO_4. The reactions were performed after optimization of the amount of the polyphenol **2.III** to get an optimum yield at ambient temperature.

The results of such experiments when compared from the GC traces, obtained at a particular time interval from control experiments with or without the polyphenol. We have observed that neither H_2SO_4 nor the oligomer with H_2SO_4 led to 100% of the oximes and imines at room temperature. But we could get best yield of 80% when oligomers are used as support.

The comparative results on the rate of hydrolysis of oximes and imines are summarized in table **2.4**. The results indicate that the rate of hydrolysis of the oximes and imines are enhanced by the oligomers in acidic medium.

Experimental details are given in section **5.3.1**

Table **2.4**
Comparative result on acid hydrolysis of imine and oxime in the presence of oligomer **2.III**

Substrate (**S**)	Relative ratio of time taken for hydrolysis of **S** in the presence and absence of **2.III**
	1.67
	1.67
	1.53
	1.64

However, this leaves a question whether such reactions could be facilitated at high temperature. But we did not checked the reactions at high temperature for the following reasons; a) we are interested in a system which could be resembling a biological system performing at room temperature and b) we have already observed in the case of NMR of **2.III** that the molecules change their conformation on heating. To avid such complicacies, we have not tested the reactions at high temperature.

2.4.6 Conclusions_

Linear oligomers, prepared from the condensation reaction of pyrogallol and aldehyde show solvatochromic behaviour. They show change in chemical shifts upon interaction with amines.

It has been possible to make broad based classification of interaction of amines with the oligomers**.** Based upon the interaction of amines and further addition of acid, it is possible to design chemically driven optical switch from these oligomers.

The electrochemical study distinguishes a bound state of 1,4-phenylenediamine with the oligomer. Electrochemical study reveals that the oligomers can distinguish a quinonic unit, which is present as a charge transfer complex or as

The capability of them to recognize quaternary ammonium salts is utilized to show the role of the oligomers as support in hydrolysis of oximes and imines.

CHAPTER 3

SYNTHESIS, CHARACTERISATION AND UTILISATION OF MONO- AND DI-HYDROXYNAPHTHALENE OLIGOMERS

3.1 Background

The importance of polyphenolic compounds in the field of analytical, industrial and biological chemistry has already been elaborated in the previous chapters. Polyphenolic compounds having intervening carbon have been considered in chapter 2 and some of their physicochemical studies were carried out. In chapter 1, the importance of polynaphthalenic compounds with intervening carbons has also been emphasised. Naphthalenic units have multiple sites for the C-C bond formation. This makes it more difficult to analyse and interpret the products from a reaction of naphthalenic compounds. Similar difficulties can be anticipated for constructing multiple of naphthalenic units bridged by intervening oxygen atoms. However, there is a clear advantage of C-O bond formation on a naphthalenic compound by metal catalysed reaction over acid catalysed C-C bond formation. A metal catalysed oxidative reaction can impart selectivity during coupling of naphthalenic units.

The compounds having phenol units with intervening oxygen atoms are generally termed as polyphenylene ethers. Polyphenylene ethers, have found wide application in material chemistry, as engineering plastic[8], photosensitive polymers[119] and as coating materials[120]. Polyphenylene ethers find applications in

synthetic chemistry[121] and are constituent of biologically important molecules such as lignin[19]. Cyclic polyphenylethers, namely, oxacalixarenes and oxacalixnaphthalenes show the ability to trap guest molecule and hence, have been used for molecular recognition[122].

In addition to these, phenolic and related aggregates, prepared by copper promoted oxidative polymerisation and having copper(II) ions[123] possess the property of thermoelectric switch. The organised aggregates having π-stacks of aromatic rings are able to trap radical[124], ion[92] and decide fate of a catalytic reaction[125]. Oxidation of dihydroxy aromatic compounds can give charge-transfer complexes or quinonic compounds[126]. A charge transfer complex having organised packing with metal ion/s has interesting electronic properties[127]. Thus, there has been increasing interest on the catalytic reactions of phenolic compounds by copper complexes having core of Cu_2O_2[43, 128-131]. However, the understanding of oxidative reactions of phenolic compounds in terms of selectivity is yet to be achieved.

Acetal or enzyme catalysed oxidative polymerization is a suitable method[132] for synthesis of polyphenols. This reaction is of fundamental importance in view of its relevance in the biosynthesis and biomimetic synthesis of diverse natural products[133].

3.2 Oxidative polymerisation of phenols: Brief review

Oxidative coupling of phenols is usually achieved by the use of organic peroxides and/or by transition metal catalyst[134]. Various oxidants, such as $FeCl_3$[135-136], $Mn(acac)_3$[137-138], alkaline $K_3Fe(CN)_6$[139], Cu(II)-amine complexes[140-142], VOF_3[143] and thallium trifluoroacetate[144] have so far been proved particularly useful. Out of these, Cu(II)-derived agents have been found to be very effective. To describe oxidative coupling of phenols, the main variables to be considered are a) **substrate**-which may be a unionized phenol or phenolate anion, b) **reagent**-which may be homogeneous or heterogeneous and c) **pathway**.

Oxidation of phenols with all its *o*- and *p*- positions free, yields an aryloxy radical with loss of one proton and one electron (**scheme 3.1**).

Radical mechanism may proceed through two possible paths: a) **radical coupling** and b) **radical substitution**. The first path will lead to: **three modes of**

C-C coupling giving three different products namely, *ortho-ortho*, *para-para* and *ortho-para* C-C coupled dimers. The second path will lead to: **two modes of C-O bonding** to give two different products, namely, C_{orto}-O and C_{para}-O products. In case of 3,5-dimethyl phenol, where steric effect would not be a major factor to preclude coupling at either of these positions, a total of five products should be obtained (**scheme 3.2**).

Foregoing discussion clearly shows the diversity of products in an oxidative coupling of phenols. However spin density calculation at the carbon centers could help one to predict the selectivity in the product formation. It has been shown from ESR studies on alkyl-substituted phenoxyl radical that the spin density at the para-position is almost twice of that at the ortho-position[145]. Again frontier

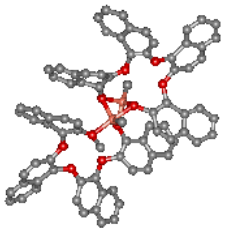
molecular orbital theory supports preferential coupling of delocalised radical at the site of highest spin density[146]. Hence, aryloxy coupling should yield *para-para* coupled dimer as the major product.

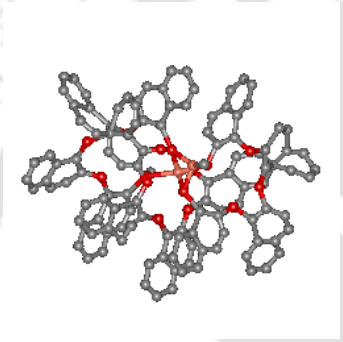
3.3 Oxidative oligomerisation of 2-naphthol

The use of environmentally benign nature of reagents used for oxidative polymerisation reaction is an important issue. Since, most of these transition metal oxidants are associated with high degree of toxicity, the development of simpler and safer reagent is a need of the day. In a recent study, our group of researchers have demonstrated that the activated aromatic compounds can be hydroxylated or oligomerised by environmentally safe copper complexes[123]. Encouraged by these results, we envisaged the ability of the reagents for oxidative oligomerisation for naphthols. It has already been discussed in chapter I that polyphenols having intervening C and/or O, derived from both 1- and 2-naphthols, namely calixnaphthalenes and oxacalixnaphthalenes provide deeper cavities for inclusion of guest molecules. But the ability of the linear counterpart has not yet been explored. The cyclic oligomers, mentioned above, have been synthesised from condensation reaction of naphthols and aldehydes. On the other hand, oxidative oligomerisation of naphthols could be a useful route for synthesis of polynaphthalene systems having intervening O atoms. But the existing reports on oxidative coupling of naphthols show only dimerisation of naphthol through C-C coupling to yield symmetrical binaphthol molecule (**3.1**)[112]. So there is ample scope for exploration of

oxidative reaction of naphthols, which could lead to C-O bonded long chain polynaphthylenic ethers.

The reaction of 2-naphthol (described in section **5.3.2**) with catalytic amount of *cis*-bisglycinatocopper(II) monohydrate in the presence of hydrogen peroxide gives compounds **3.II** and **3.III** through hydroxylation cum oxidative coupling reaction (equation **3.1**).





From the analytical data given below, it was found that the compound **3.II** contains a Cu_2O_2 core held by two tetramers of 2-naphthols and the axial ligands are 2-naphthol and water, while **3.III** contains three units of tetramers which hold two copper centers. In the case of **3.III,** out of the three tetramer units, one is neutral and others are in oxo-form. The compounds are characterised by their elemental analysis, IR, FAB mass, ESR spectra and magnetic moment.

The O-H stretching vibration of the compound appears at 3182 cm^{-1} whereas in 2-naphthol it appears at 2951 cm^{-1}. The characteristic C-O stretch of the complex appears at 1201cm^{-1}. The complex has a characteristic visible absorption at 472 nm due to dimeric oxo-bridged core of copper(II). The Cu_2O_2 core in biologically related systems[128,129,147-148] has a characteristic absorption in a similar region. The complex has also another absorption at 333 nm from the ligand. It has fluorescence emission at 547nm on excitation at 401nm. The ^1H NMR was not much informative and shows only broad aromatic signals.

The FAB mass spectra (spectra shown in section **5.3.2**) of the compound **3.II** shows highest ion peak at 663 and at 665. These peaks are assigned to mass ions of L-Cu-$O^{+\cdot}$ (where L=ligand) due to two isotopes of copper. Such fragment is formed through heterolytic cleavage of the complex. The mass at 647 and 649(m/z) are due to L-$Cu^{+\cdot}$. Similarly the signals at 584, 568, 444, 424(m/z) are due to the subsequent losses of Cu, O, $C_{10}H_6$ from this part. The oligomer having four naphthalene units is

formed through hydroxylation cum C-O bond formation of hydroxylated 2-naphthol with unreacted 2-naphthol. Similar hydroxylation cum oligomerisation of *p*-phenylphenol is catalysed by Cu_2O_2 dimeric core[43]. Hence it is assumed that a Cu_2O_2 core has been formed during the reaction which catalysed the formation of an oligomer with four naphthalene units and then the Cu_2O_2 core is held by two oligomer units. Elemental analysis suggests a composition of $C_{90}H_{57}O_{12}Cu_2$, which indicates the presence of one 2-naphthol unit and water as axial ligand.

The magnetic moment (in emu) of the complex at 25°C is field dependant and with an increasing trend on increase of field from 2KGauss to 10 KGauss (figure **3.1a**). This indicates the presence of an exchange coupling in the system.

Figure **3.1**: Change of magnetic moment of (a) **3.II** (10.6 mg) and (b) **3.III** (2.4 mg) with field strength

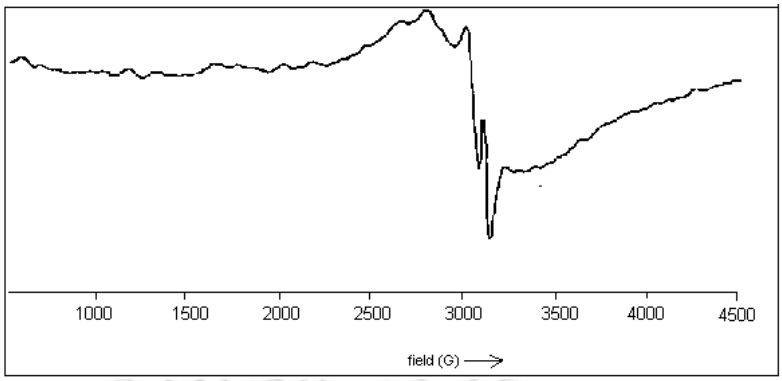


Figure 3.2: The ESR spectra of **3.II** (solid) at 25^0C; Field setting 2500 G central field, 9.04 GHz microwave frequency and 1500G sweep width.

The ESR spectrum of the compound at 25^0C has two signals; one at 3025G (g =1.89) having resemblance to copper(II) centre with distorted tetrahedral geometry[149]. The other signal at 3125G (g =1.95) is due to a radical stabilised by the copper center[124] (figure **3.2**). The radical is presumably a Cu-O· radical formed by homolytic cleavage of the complex .

In the mass spectra, the highest mass of compound **3.III** is identical to **3.II** showing it to be due to a fragmented ion (spectra shown in section **5.3.2**). The elemental analysis suggests a composition of $C_{120}H_{76}O_{15}Cu_2$. This composition is in agreement with a structure that consists of three units of a tetramer of 2-naphthol,

which hold two copper centers. In this case also, the ^{1}H NMR spectra gives aromatic signals as unresolved multiplets. Unlike the compound **3.II**, the ESR spectra of this compound shows only a broad signal at 3025G (g = 1.89) due to copper(II) centers. The magnetic moment (in emu) at 25°C is dependant on the applied field (figure **3.1b**). This result supports exchange coupling between the two copper(II) centers.

Our group of researchers have recently found that copper(II) containing dihydroxy aromatics and aminohydroxy aromatic compounds possess property as thermoelectric switch[123,150-153] i.e. the temperature dependence of the resistance of films prepared from these compounds has a normal Gaussian shape (experimental detail in **section 5.1.11**). This means it increases initially and then decreases exponentially after a limiting temperature. In the present study it is observed that the electrical resistance of a film prepared from a chloroform solution of **3.II** decreases in the region of temperature 90-150^{0}C (figure **3.3**) having resemblance to behaviour of a semiconductor.

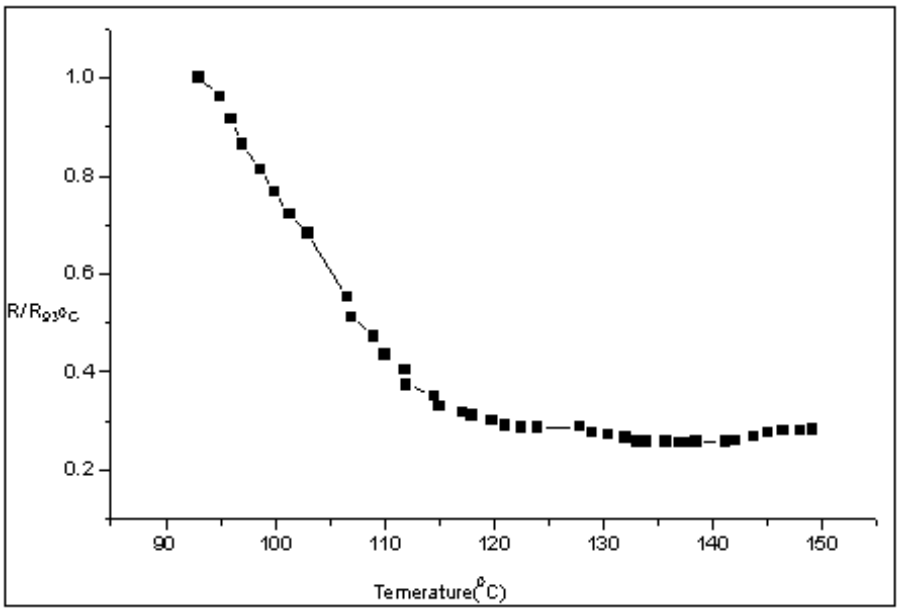


Figure 3.3: Plot of resistance (R) normalised to resistance at 93^0C (R_{93^0C}) vs temperature of **3.II**

Compound **3.II** has identical ESR spectra at 100^0C with that at 30°C. Differential scanning calorimetry shows an exothermic process in the region of 90-160^{o}C (figure **3.4**).

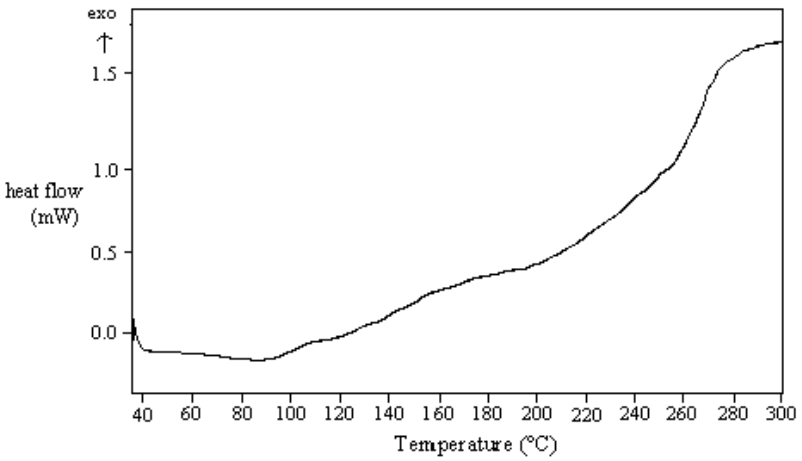


Figure **3.4:** DSC curve of **3.II**

Thermogravimetry shows that there is about 3.8% weight loss of **3.II** in the region 90-160°C (figure **3.5**).

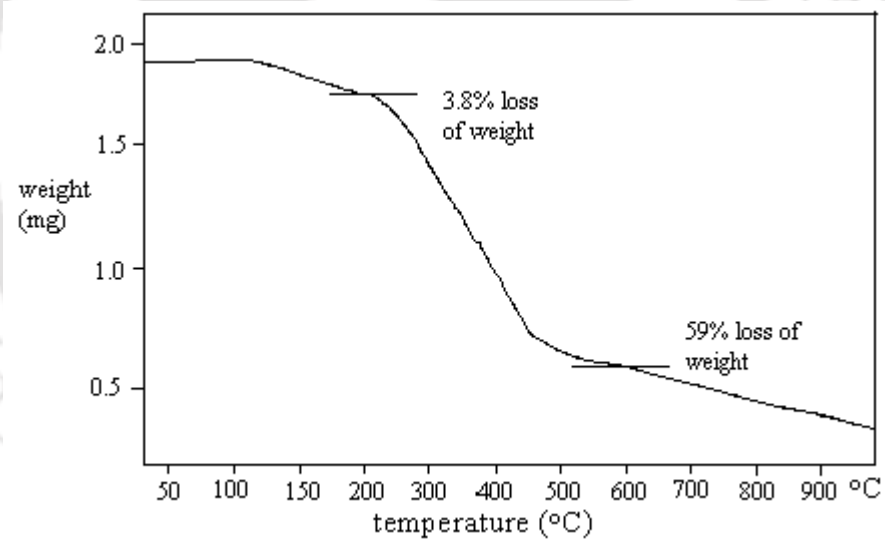


Figure **3.5:**Thermogram of **3.II**

This weight loss can be correlated to the loss of the solvent molecules from the co-ordination sphere. The compound is thermally unstable above 220^0C and decomposes to lose 59% of its weight on heating to 550^0C. Based on all these observations we suggest that the decrease in the resistance in the region of 90-160^0C

occurs due to the loss of the solvent molecules from the co-ordination sphere as well as from the interstices. In copper(II) containing hydroquinone aggregate[153] and also in the copper(II) containing dihydroxyphenolic aggregates, the change in co-ordination around copper(II) centre on heating gives a resistance profile that passes through a normal Gaussian shape[123].

The oxo-bridged cores of manganese are catalytic centers for peroxo bond formation and the Cu_2O_2 cores are believed to be responsible for cleavage of O-O bond in biological system[128]. It is believed that Cu(III) intermediates are involved in such cleavage in biological systems[129,131]. The compound **3.II** reacts with O-O bonded compounds, hydrogenperoxide and tertiarybutylhydroperoxide in dichloromethane, acetonitrile etc. The relative rate of such reactions could be ascertained from the decay of the absorption at 472 nm (figure **3.6**).

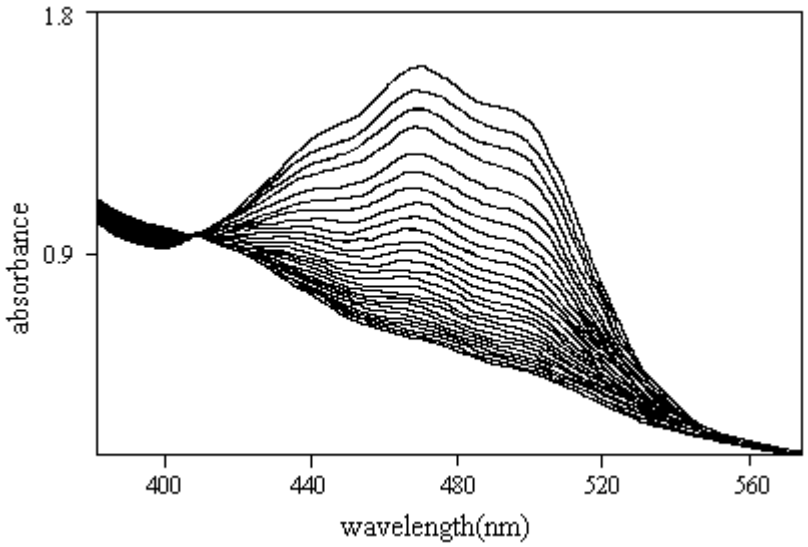


Figure 3.6: Decay of absorption at 472nm at a time interval of one minute of **3.II** on reaction with hydrogenperoxide (**3.II**= 0.0013mmol, [H_2O_2]=0.01mmol)

This suggests decomposition of the dimeric copper(II)-copper(II) center on reaction with peroxides. In the reaction of hydrogen peroxide oxygen was not evolved showing a probable involvement of homolytic cleavage. The decrease in the absorbance at 472nm accompanies an isosebestic point at 420nm and is indicative of its conversion to another single product in solution. In all the cases 2-naphthol was

obtained after reaction with peroxides. Probably this was formed during the reaction of peroxide with copper core and it loses the axial 2-naphthol ligand. The relative rates of oxidation are found to be solvent dependant and are in the order of dichloromethane > methanol > acetonitrile (figure **3.7**).

The change of absorbance at 472 nm in methanol and dichloromethane has a decay profile without an induction time showing a spontaneous process. But in the case of acetonitrile there is an induction time after which only decay takes place. This has two implications. Firstly it implicates the utility of the intermediate for use as catalyst. Secondly, its instability after an induction period implies the involvement of preformed species, which is presumably a radical species.

Figure **3.7:** Decay of absorbance of **3.II** at 472 nm versus time on addition of *t*-butyl hydroperoxide (A) in dichloromethane, (B) in methanol and (C) in acetonitrile

Figure **3.8**: Decay of absorbance of **3.II** at 472 nm in methanol
on treatment with (A) H_2O_2 and (B) *t*-butylhydroperoxide

Again, decomposition of the dimeric copper(II)-copper(II) center by *t*-butyl hydroperoxide is faster than hydrogen peroxide (figure **3.8**). Solvent effect on the rate indicates involvement of hydrogen bonding in the transition state. The decomposition of hydrogen peroxide through cyclic H-bonded intermediate is established[154].

Here, the slow rate of decay of absorption at 472 nm in acetonitrile suggested that the copper(II) center is stabilized in acetoinitrile for a considerable time (figure **3.9**), which is indicative of the potentiality of acetonitrile as appropriate solvent for reaction, where this species is involved. The compound **3.II** also reacts with reducing agent such as hydrazine hydrate, loses the absorption peak at 472nm. The absorption at 472nm of **3.II** is also bleached on irradiation by a tungsten lamp.

Figure **3.9**: Decay of absorbance of **3.II** on treatment with *t*-butyl hydroperoxide (A) in dichloromethane and (B) in acetonitrile

A metal catalysed oxidation of 2-naphthol usually gives binaphthol[121,149]. Binaphthol was not formed in the reaction of the 2-naphthol with *cis*-bisglycinato copper(II) monohydrate in hydrogen peroxide and this precludes a C-C coupling product.

The reaction of 2-naphthol with tertiarybutylhydroperoxide (procedure is given in section **5.3.2**) is catalysed by *cis*-bisglycinatocopper(II) monohydrate leading to tetrameric product **3.IV** (equation **3.2**).

The compound **3.IV** is characterized by its NMR, IR, mass spectra and its elemental analysis. ^{1}H NMR spectra in $CDCl_3$ shows peak at 1.5-1.8(m, 9H), which is due to *t*-butyl group. The presence of the tertiary butyloxy group on the oligomer suggests it to pass through an initial transfer of butyloxy group from tert-butylhydroperoxide. The IR spectra show one peak at 1266 cm^{-1}, which is characteristic of an aryl peroxy group. The elemental analysis confirms the composition for a tetramer of 2-naphthol (analytical data in section **5.3.2**).

3.3 Synthesis, characterisation and physicochemical studies of naphthalenediol oligomers

Naphthalenediols having hydroxyl groups at 1,3-, 1,6-, 2,3- and 2,7- have been taken for this study. Oligomerisation reaction was carried out at room temperature by using hydrogen peroxide with catalytic amount of

cis-bisglycinato-Cu(II) monohydrate (experimental details in section **5.3.2**). Naphthalenediols, namely, 1,3-, 1,6-, 2,3- and 2,7- naphthalenediols were oligomerised to give C-O bonded oligomers (**3.V-3.VIII**) respectively.

1,5- naphthalenediol was found to be unaffected by the reaction. The reaction of 1,4-naphthalenediol yielded a mixture (**3.IX**) of 1,4-naphthalenediol and 1,4-naphthoquinone, rather than an oligomer.

3.3.1 Characterisation of the oligomers:

The oligomers are obtained as mixtures of isomers from unpreferential attack of the naphthaloxy radical produced during oligomerization. Gel Permeation Chromatography has shown that **3.V-VIII** are low molecular weight oligomers. The (Mn, Mw) values of the oligomers are shown in Table **3.1**.

Table **3.1**

The GPC data of the oligomers of naphthalenediols prepared by catalytic reactions of *cis-bisglycinato* copper (II) monohydrate and hydrogenperoxide.

Oligomers derived from	M_n, M_W

1,3- Naphthalenediol	3418, 3629
1,6- Naphthalenediol	1079, 1080; 2193, 3306
2,7- Naphthalenediol	2551, 2979
2,3- Naphthalenediol	m/z 637 (LSIMS)-tetramer

The selectivity in isomer being a major issue for pursuing further studies we have done a theoretical calculation on the electron density of the naphthalenediol. The charge density at each carbon centre of each naphthalenediol under consideration was calculated. The charge densities in Mulliken scale calculated by AM1 calculation of the naphthalenediols are listed in Table **3.2**.

Table **3.2**

Charge densities at different carbon centres of naphthalenediols

(in Mulliken's scale)

Carbon no.	Naphthalenediols					
	1,3-	1,4-	1,5-	1,6-	2,3-	2,7-
1	0.14009	0.06656	0.08634	0.10976	-0.22624	-0.21607
2	-0.35844	-0.24404	-0.27321	-0.29645	0.01571	0.08202
3	0.11500	-0.24403	-0.16096	-0.13611	0.07856	-0.26480
4	-0.24048	0.06655	-0.18181	-0.21676	-0.18710	-0.12176
5	-0.19430	-0.15993	0.08637	-0.21999	-0.17136	-0.12174
6	-0.16641	-0.19048	-0.27326	0.08499	-0.18846	-0.26484
7	-0.21294	-0.19052	-0.16100	-0.27063	-0.18845	0.08203
8	-0.13718	-0.15990	-0.18177	-0.10706	-0.17316	-0.21607
9	-0.09171	-0.03350	-0.03334	-0.09391	-0.04073	0.02118
10	0.01352	-0.03346	-0.03336	0.01503	-0.03853	-0.11142

Preferential C-O bond formation would occur at a place higher electron density. To illustrate the oligomerisation reaction, here we have chosen 1,6-naphthalenediol as a typical example. The data (Table **3.2**) indicate that the potential sites for such bond formation in the 1,6-naphthalenediol are at C2, C7 positions of the rings. Out of these two, C2 has more electron densities and this is the most probable site for a C-O bond formation through a radical mechanism. The next options for coupling reactions are at C4 and C5. However, the steric factors and the electronic factors are less favourable than the attack at C2 and C7 positions. Thus, the most favourable structures of the oligomer (**VI**) are A and B which are shown in equation **3.3**. Oligomerization reaction of 1,6-naphthalenediol with *cis*-bisglycinato copper (II) monohydrate in the presence of hydrogenperoxide to give C-O bonded oligomer is shown in equation **3.3.** It has an absorption maximum at 334 nm (ε= 16,666g^{-1} cm^{-1}).

The mass spectrum of the oligomer of 1,6-naphthalenediol in the range of is shown in figure **3.10**. The oligomer has the mass fragments corresponding to sequential loss of di and tri-hydroxynaphthalene units. For example it has mass fragments (*m/e*) at 476 (trimer), 666 (tetramer), 808 (pentamer), 969 (hexamer), 1108 (heptamer), 1140 (hydroxylated heptamer), 1298 (hydroxylated octamer) and also at 1472, 1646, 1836, etc. for corresponding combination of 9, 10, 11 units, respectively.

Figure **3.10 :** MALDI mass spectrum of **3.VI**, [inset: that in the range of 800-2000 (m/e)]

The synthetic methodology used in the above reactions allows the reaction to pass through a radical mechanism[131]. The electron spin resonance study of the oligomer shows that a radical is trapped in it. This radical is stable under ambient

conditions. It is trapped in the network of the oligomer of 1, 6-naphthalendiol and has a sharp ESR signal at 1.93 g (Fig. **3.11**)

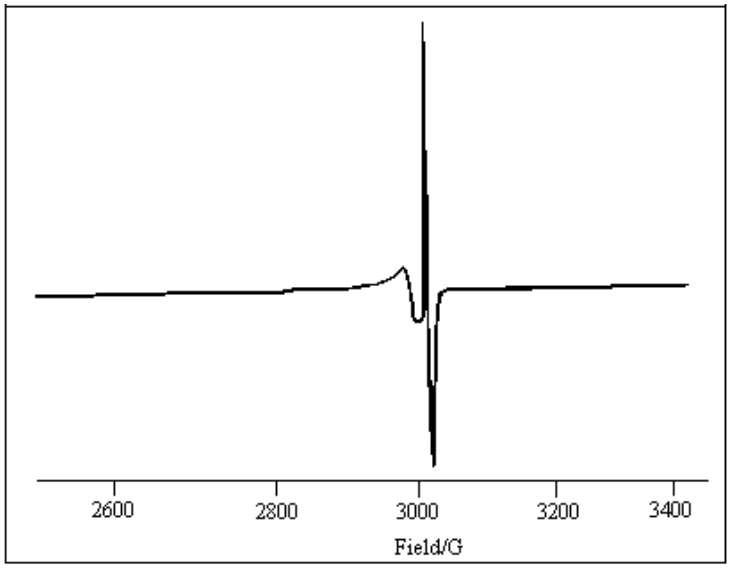


Figure **3.11:** ESR spectra of **3.VI.** Field setting 2500G central field, 9.04 microwave frequency and 1500 sweep width

There is a minor ESR signal adjacent to the above signal and it is assigned to the copper center. Probably a Cu(II)-O· radical is trapped inside the polymeric

matrix. Such a radical may be due to degradation of Cu_2O_2 core during the oxidative oligomerization reaction.

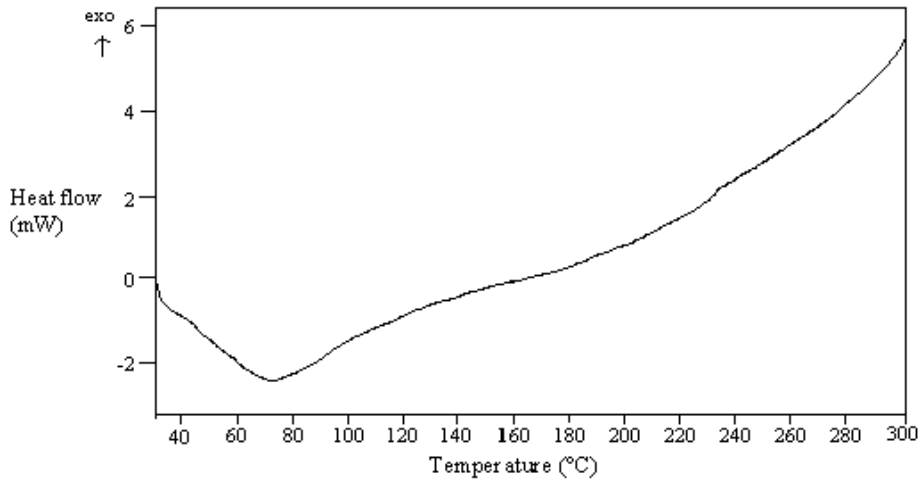


Figure **3.12:** DSC of **3.VI**

The oligomer has an endothermic process at 30°C-160°C, as shown by the DSC graph (figure **3.12**). This process is due to loss of water molecule from the interstices in **3.VI.**

The hygroscopicity is reflected in the thermal analysis of the samples as well as in the elemental analysis. The corresponding loss of weight is reflected in the thermogram (figure **3.13**). The thermogravimetry shows continuous weight loss beyond this region also and this is due to oxidative degradation of the oligomer. The thermogravimetric data alongwith the elemental analysis are in good agreement with a composition of $(C_{10}H_6O_3.\ 0.75H_2O)_n$ [Elemental analysis: calculated C, 63.6, H, 3.98; found C, 63.18, H, 3.84].

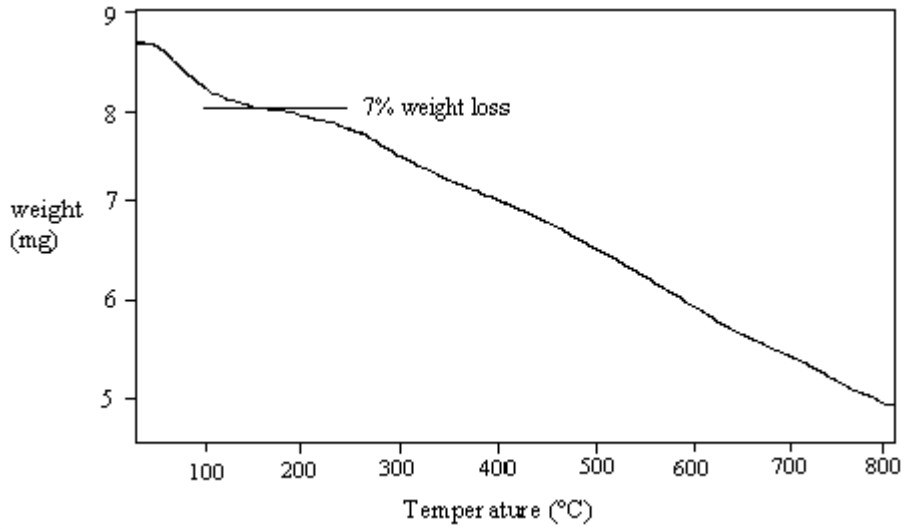


Figure **3.13 :** Thermogram of 1,6-naphthalenediol oligomer (**3.VI**)

Due to the capability to hold water molecules by the oligomer and as they are hygroscopic and aggregated through the hydrogen bonding among the hydroxyl groups present in it or through the water molecules in the interstices. it shows interesting electrical properties. The film of the oligomer has resistance profile that increases on heating and has a trend similar to metallic property. Presumably, presence of the radical along with H-bonding in the system imbibes additional

conductivity to the film of the oligomer. Thermal energy can cause disruption of H-bonds, which makes the film to loss the proton conductivity present in the system contributing to increase of resistance with temperature.

The reaction of 1,4-napthalenediol yielded a black solid (**3.IX**) and the elemental analysis, NMR, IR suggest that it is a mixture of 1,4-napthoquinone and 1,4-napthalenediol. The ESR spectra has a sharp signal at 3250G (g=2.02) due to a radical and two broad signals at 2975G (g=1.86) and 1375G (g=1.14) from the copper(II) centre stabilised through a radical (fig **3.14**).

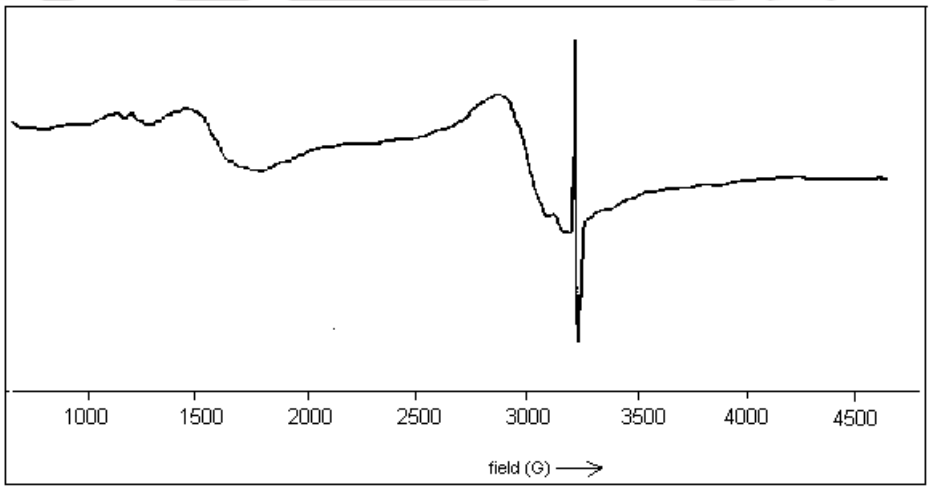


Figure **3.14**: ESR spectra of **3.IX** at 25°C; Field setting 2500 G central field,

9.04 GHz microwave frequency and 1500 G sweep width.

The signal 1375G suggests the radical to be stabilised by the metal centre[134]. The copper concentration in the complex is of the order of ~1%. The unit is believed to have a metal stabilised napthalenediol radical whose effect is relayed through a possible π-stacks through a charge-transfer interaction.

The extensive π-stacks of charge transfer complex having copper ions are well established[127]. Further support to aggregation is reflected in the DSC (figure **3.15**) where the melting point of the starting 1,4-napthalenediol (m.p. is not observed.

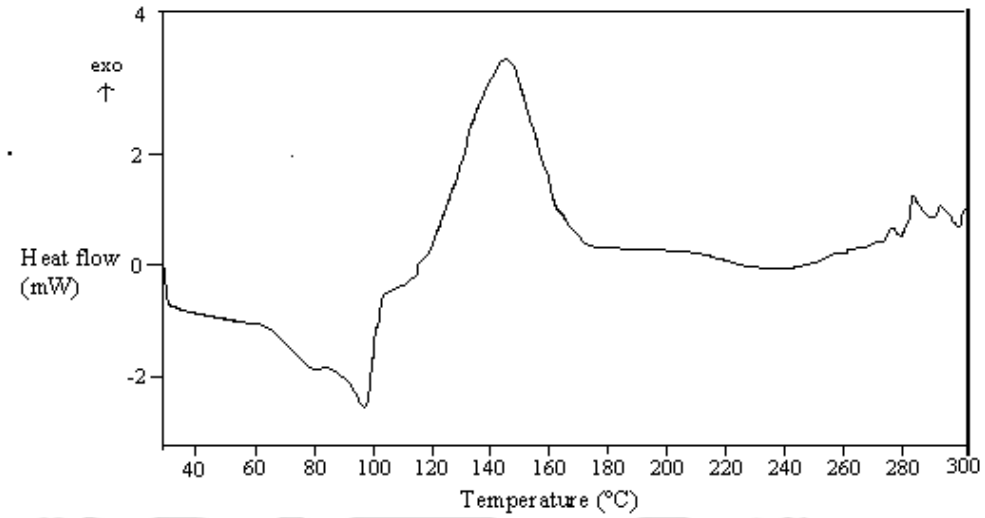


Figure **3.15** : DSC curve of **IX**

Due to paucity of getting suitable crystal for diffraction study, it is difficult to draw a structure fitting the metal ion within this aggregate. The resistance of a film prepared from **3.IX** continuously increases in the region of 30-160^{0}C (15 fold) suggesting the disruption of π-stacks in the system on heating.

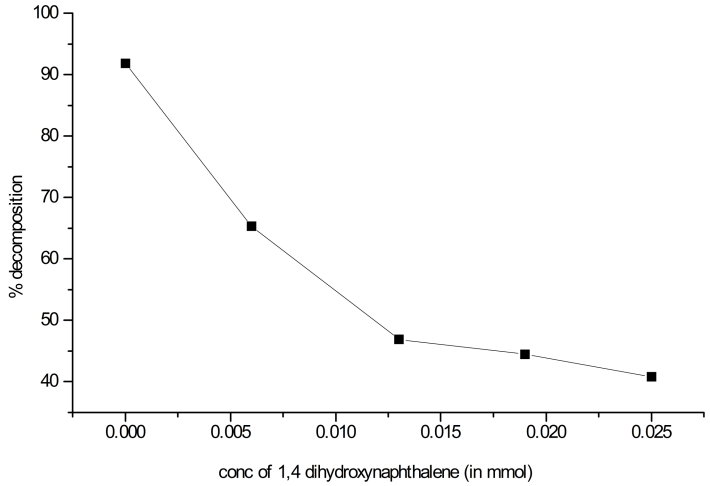


Figure **3.16**: Decomposition of H_2O_2 by **3.IX** with increase of concentration

The decomposition of hydrogen peroxide by **3.IX** is less as compared to an identical reaction of *cis*-bisglycinato copper(II) monohydrate as evident from the observation from the *in situ* reactivity study of complex **3.IX** (experimental details in section **5.3.2**). Thus, with a fixed amount of *cis*-bisglycinatocopper(II) monohydrate

the decomposition of hydrogen peroxide is reduced as the concentration of 1,4-naphthalenediol is increased (figure **3.16**).

1.1.2 Naphthalenediol oligomers as support in oxidation reactions:

Another aspect of polyphenolic compounds is their potentiality as support for reagents in oxidation reactions. This aspect has been less exploited. A suitable ligand environment around copper ion enhances catalytic activity of many oxidative reactions. Keeping this in mind, we have studied few oxidative reactions of copper complexes in the presence of the polymers prepared from the oxidative reaction of 1,6-naphthalenediol. This demonstrates the effect of hydrophobic confinement on copper intermediates during oxidative reaction of copper[II] with hydrogen peroxide.

Copper (II) complexes in basic medium get precipitated as copper (II) hydroxide. For example, the reaction of copper(II) acetate with H_2O_2 gives yellow precipitate. This can inhibit the catalytic effect of a copper (II) complex. Such drawback is anticipated to minimize if a supported reagent can provide some extra stability to a reactive species[155,156] on a hydrophobic confinement[131,157-159] on copper can be imparted. In addition to that when two competitive oxidative reactions are performed by the same oxidant it is possible that the formation of one product favors other reaction. As an illustrative example if one considers the one pot competitive oxidation reaction between benzaldehyde to benzoic acid and polymerization on 1,6-naphthalenediol it is observed that both the reactions proceed simultaneously (Eq. **3.4**).

The presence of 1,6-naphthalenediol, slightly improves the yield of benzoic acid. Thus, it is necessary to know the effect on enhancement of oxidation of benzaldehyde is by the naphthalenediol or by a supported catalyst formed during polymerization of the naphthalenediol. During metal catalyzed oxidative reactions naphthols are added to act as promoter[159]. However, these studies do not discuss the possible role of the promoters as supported reagent.

The redox stability of the oligomer is one of the criteria to act as support in an oxidative catalytic reaction. The cyclic voltamogram of the oligomer of 1,6-naphthalenediol has shown two minor oxidation waves at 1019 mV and at 819 mV with a minor reduction peak at 203 mV. There is no significant change of these peaks on multiple cycles suggesting it to be stable potential range of 0-1500 mV. As the oligomer of 1,6-naphthalenediol contains a stable radical and also electrochemically stable it should be useful in initiating further radical reactions. We

have utilized the reactivity of this radical in the presence as well as absence of a metal ion/s. The catalytic reactions were carried out as one pot reaction with the oligomer and the reactions with specified amount as shown in Table **3.3**. The reactions were monitored by gas chromatography with the aid of FID detector and SE-30 capillary column. The results are summarized in Table **3.3**.

Table **3.3**

The catalytic study of oligomer of 1, 6-naphthalenediol

Entry no.	Cis-bisglycinato Cu(II) (mM)	Amount of oligomer (mg.)	Yield (%)*
Benzyl alcohol (2 mM) + H_2O_2(8.83 mM) → Benzaldehyde+Benzoic acid			
1	-	-	14, 0.4
2	0.1	-	9, 0.25
3	-	16	15, nil
4	0.05	16	26, 6
5	0.1	16	16, 8
6	0.05	32	22, 1
Benzaldehyde (2 mM)+H_2O_2(4.4 mM) →Benzoic acid			
7	-	-	42
8	0.02	-	49
9	0.05	-	50
10	-	16	45
11	-	32	45
12	0.05	16	80
13	0.05	32	88
Benzamide (2mM) + H_2O_2 (8.83 mM) → Benzoic acid			
14	-	-	Nil
15	0.2	-	17
16	0.25	-	18
17	-	40	53
18	-	48	54
19	0.02	40	63

Benzanilide (2 mM) + H_2O_2 → Benzoic acid			
20	0.2	-	32
21	0.2	40	65

*The yields are based on GC data and comparison with authentic sample.

It is observed that this oligomer containing a radical can catalyze variety of oxidation reaction such as hydrolysis of benzamide, oxidation of aldehydes, etc. The results suggest that the reactivity of copper(II) complexes is enhanced by the oligomer 1,6-naphthalenediol. The effect may be attributed to a possible stabilization of transient peroxo species by a hydrophobic confinement. In the first part of this chapter it has been demonstrated that the phenolic oligomer can stabilize Cu_2O_2 core.

This study demonstrates the effect of hydrophobic confinement that can contribute to the reactivity of oxidative reactions of copper complexes where copper-oxo/peroxo species participates. This also demonstrates the possibility of multiple cycle reactions that can occur during competitive oxidation versus oligomerization reactions.

The catalytic ability to oxidize benzaldehyde to benzoic acid by cis-bisglycinatocopper(II) monohydrate in hydrogen peroxide is also enhanced when the oxidation is performed with catalytic amount of **3.IX** containing analogous copper(II) catalyst concentration. Similarly the complex **3.IX** has superior catalytic activity than the parent of *cis*-bisglycinatocopper(II) monohydrate in hydrogen peroxide to oxidize amide bond in benzamide to give benzoic acid.

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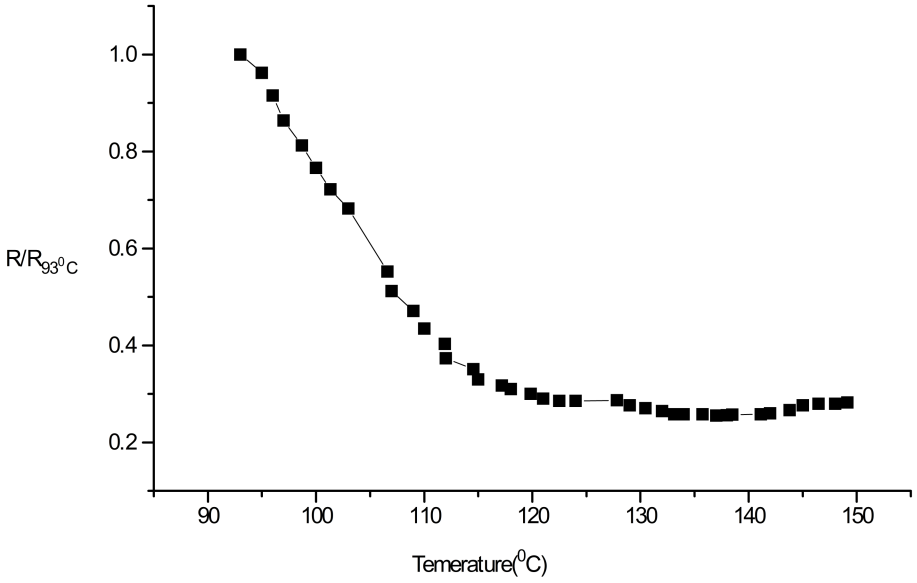
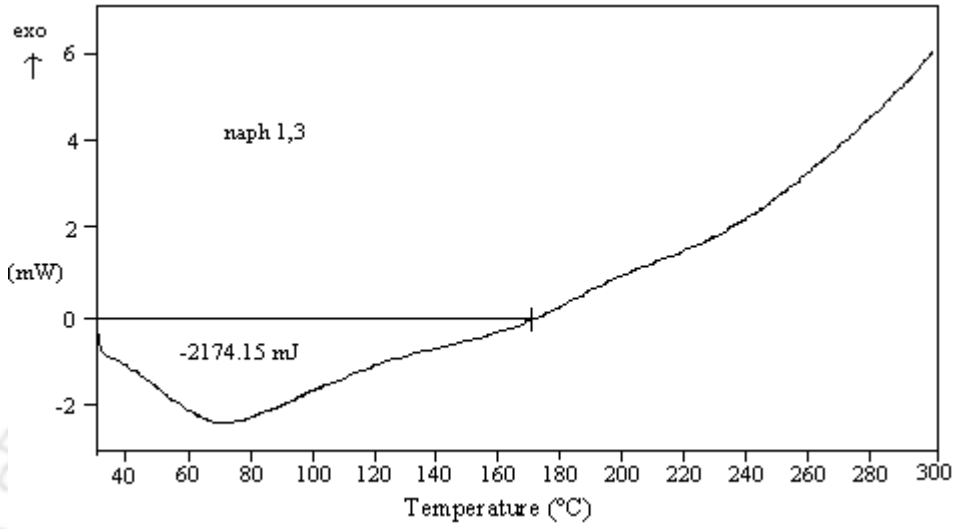
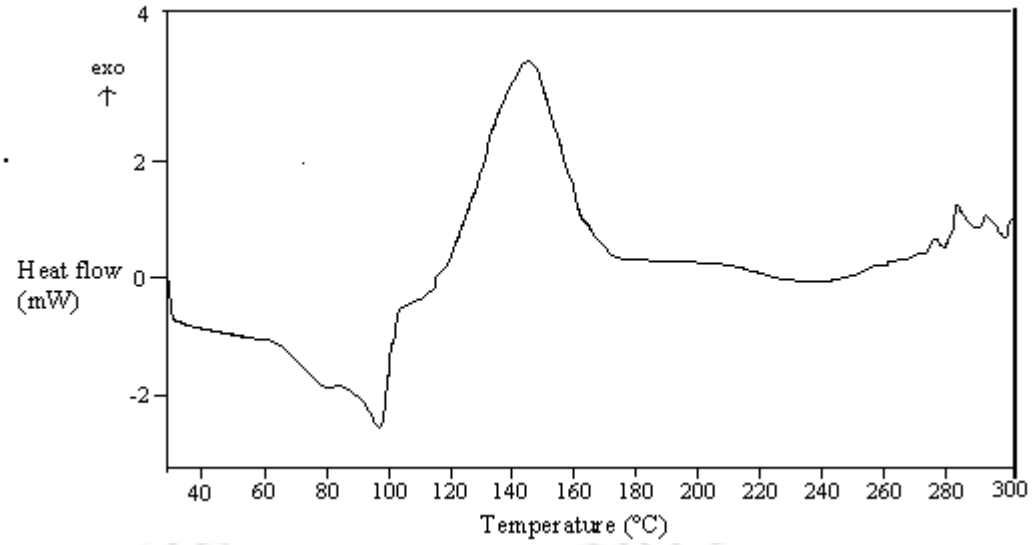
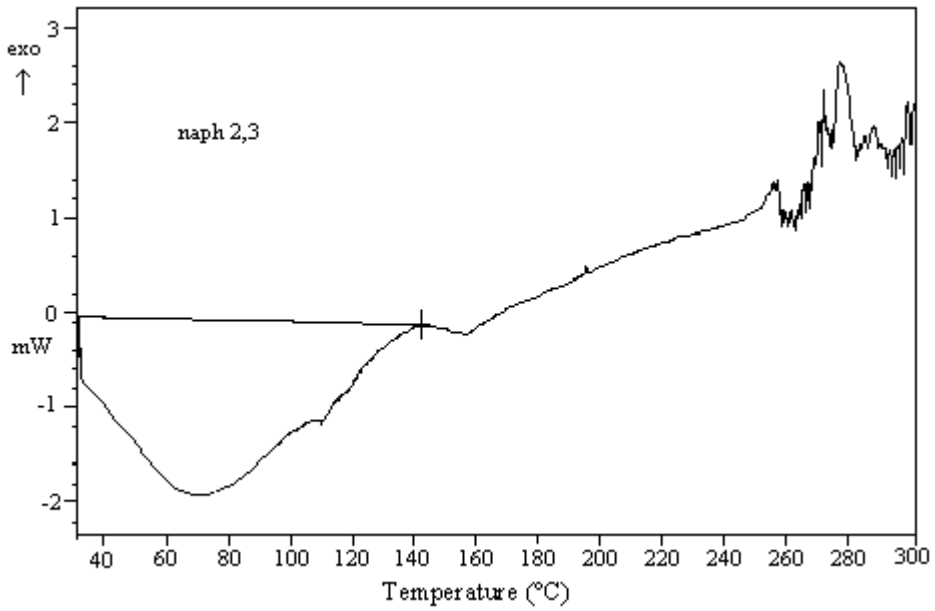
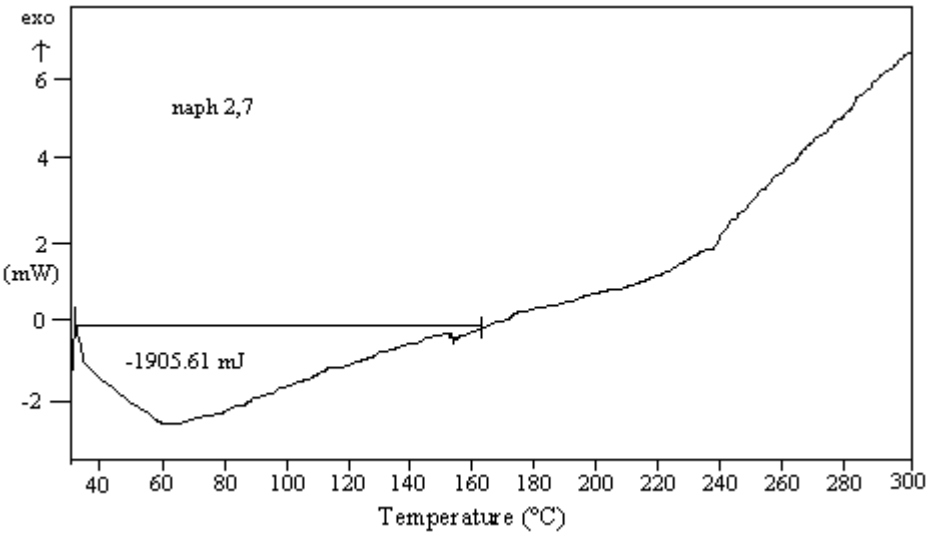


The dimeric copper compound **3.III** catalyses oxidation of benzaldehyde to benzoic acid in hydrogen peroxide.


exo
naph 1,3
(mW)
-2174.15 mJ
Temperature (°C)


exo
Heat flow
(mW)
Temperature (°C)





1,4- Naphthalenediol	2065, 2751
1,5- Naphthalenediol	2551, 2790

CHAPTER 4

POLYPHENOLS IN SUPPORTED BOROHYDRIDE REDUCTIONS AND ITS COMPARISON WITH METAL MEDIATED BOROHYDRIDE REDUCTIONS

4.1 Background

Reduction of organic compounds is a common reaction extensively used in synthetic chemistry and in industry[160-162]. Borohydrides continue to contribute an important share in this field of synthetic chemistry[163]. The role of support in borohydride reductions, is an important point to explore. Borohydride exchange resin (BER) has been reported to be effective in solvent purification, generation of volatile metal hydrides and reduction of metal ions and some aldehydes[164]. Borohydride supported on amberlite is exclusively used as a mild reducing reagent. This supported borohydride reagent also exhibited selectivity in the reduction of ∝,β-unsaturated carbonyl compounds to corresponding unsaturated alcohols[165].

For selectivity in reduction of aldehydes and ketones in presence of other functional groups, sodium borohydride has been a better reagent of choice[166]. The reducing property of sodium borohydride is substantially modified by presence of metal salts[167]. In studying the selectivity of reduction by sodium borohydride, the reduction reaction of ∝,β-unsaturated carbonyl compounds has been thoroughly exploited and continues to attract attention[168-173].

Reduction of an ∝,β-unsaturated carbonyl compounds can lead to three compounds (**scheme 4.1)**. They are (i) allylic alcohol (**4.1**) resulting from attack on the carbonyl functional groups, (ii) saturated carbonyl compound (**4.2**) resulting from attack on the double bond and (iii) saturated alcohol (**4.3**) resulting from the subsequent reduction of saturated carbonyl compounds, generally observed in the presence of proton donors (most frequently the solvent)[163].

Selective hydrogenation of ∝,β-unsaturated carbonyl compound is a frequent synthetic problem in synthesis of large number of fine chemicals, particularly in flavour and fragrance chemistry and in pharmaceuticals. Although various reagents are developed for selective reductions of ∝,β-unsaturated carbonyl compounds, many are associated with complex reaction work up, low yield etc.

Regioselectivity of the reduction depends on several factors[163]. These are (a) structure of the starting compound (b) nature of the solvent and (c) nature of the reagent. For example, presence of sterically hindered double, electrophilic assistance by a protic solvent and assistance by a cation associated with the reagent and an added Lewis acid promote reduction of the carbonyl functional group. In contrast, reduction of the double bond is preferred under the following circumstances, viz., (i) if a bulkier reagent is used, (ii) if the reagent is associated with a cation such as ammonium cation, capable of inducing electrophilic assistance, or with a transition metal such copper or (iii) the reaction is carried in an aprotic media, which strongly solvate alkaline cations.

We have discussed in the second chapter how ammonium cation can be recognized by polyphenols. Thus a BH_4^- unit attached to an ammonium cation would be able to form ion pair with polyphenolic compound and affect the course of reduction.

It is established that reduction of unsaturated compounds can efficiently be carried out by the reaction of hydrated nickelchloride in the presence of radical anions[174]. However, such reactions require generation of anion radicals by reactive alkali metals, which need extensive care in handling. The incorporation of deuterium from preformed deuterohydrated nickelchloride to unsaturated organic compounds makes these reactions attractive and exploration of new reagents have increasing demand[175]. Reports are available on partial incorporation of deuterium on carbonyl

compounds by borohydride anions without a catalyst as well as in the presence of late transition metal complexes[176,177].

In the light of the foregoing reports, we explored (i) the possibility of using polyphenols as support in borohydride reduction and (ii) the use of nickel catalysts to modify the course of the reduction of ∝,β-unsaturated carbonyl compounds under neutral condition and also on the incorporation of deuterium from solvent containing active deuterium into the products in such reactions.

The polyphenolic compounds, **2.III-2.IV** have been found to recognize ammonium ions as reported in chapter 2. Again the role of ammonium ion in ammonium borohydride reduction is already highlighted. We have chosen tetramethyl ammonium borohydride for reduction of carbonyl compounds and used the reagent alone and with the polyphenols as support.

4.2 Reduction of carbonyl compound with tetramethylammonium borohydride in presence of the oligomer 2.III

The polyphenolic compound, **2.III** have been found to recognize ammonium ions as reported in chapter 2. So we have studied the reduction of benzaldehyde and cinnamaldehyde by tetramethylammonium borohydride with and without the presence of oligomer **2.III**. The results with oligomer **3.III** have shown that the reaction rate of reduction of benzaldehyde to benzyl alcohol is enhanced. For example, 98% conversion of benzaldehyde to benzyl alcohol took place in 20

minutes, when it is treated with NMe_4BH_4 at 0°C, in methanol, whereas in identical condition this conversion was achieved in 10 minutes in presence of **2.III**.

For reduction of ∝,β-unsaturated carbonyl compound we have chosen cinnamaldehyde. The reaction yielded cinnamyl alcohol without affecting the double bond. This reaction was compared with the reduction of cinnamaldehyde in presence of a cyclic polyphenol, 4-*t*-butylcalix[6]arene (**2.IX**). It is noticed that the amount of conversion of cinnamaldehyde to cinnamyl alcohol is lowered by the use of this cyclic polyphenol, whereas in presence of linear polyphenol **2.III** the conversion is enhanced. The results are shown in table **4.1**. It may be inferred from the results above that the rate of the reduction is greatly facilitated by open chain polyphenol which recognizes the cation. But cyclic calix arenes are not very susceptible for such process due their poor solubility in the solvent.

Table **4.1**
Results of reduction of cinnamaldehyde

Entry No.	Substrate	Reaction condition	Time	%conversion to cinnamyl alcohol
1.		NMe_4BH_4, O°C, MeOH	1 hour	84.7%
2.	-do-	-do-, **2.IX**	-do-	75.6%

3.	-do-	-do-, **2.III**	20 min	90.53%

4.3 Reduction of α,β-unsaturated carbonyl compounds with sodium borohydride in presence of nickel catalyst

The reaction of *trans*-3-phenyl-2-propenal with sodium borohydride and catalytic amount of $Ni(bpy)Cl_2$ (bpy = 2,2′ bipyridine) leads to *trans*-3-phenyl-2-propen-1-ol along with 3-phenyl propan-1-ol within 30 minutes. The reaction is applicable to other α,β-unsaturated carbonyl compounds (scheme **4.2**) and is substrate dependent and the results on the product ratios of unsaturated (**U**) and saturated (**S**) alcohols are shown in table **4.2**.

It would be reasonable to compare the catalytic activity of different nickel salts with that of nickel bipyridyl chloride. We have chosen bis-triphenylphosphinenickel(II)chloride $[Ni(PPH_3)_2Cl_2]$ (preparation procedure

given in section **5.4.1**), nickel(II)acetate and nickel(II)chloride hexahydrate for this purpose. The catalytic reactivity was tested by comparing the percentage conversion of *trans*-3-phenyl-2-propenal at 15 minutes time interval in each independent experiment and reactivity was found to be in the order of $Ni(bpy)Cl_2$ > bis-triphenylphosphinenickel(II)chloride > nickel(II)acetate > nickel(II)chloride hexahydrate. The product ratios of saturated and unsaturated (U : S as in scheme **4.2**) are effected by the nickel catalyst and in each case the saturated (S) and unsaturated products were formed in approximately equal ratios except in the case of $Ni(bpy)Cl_2$. In this case the maximum selectivity on the formation of unsaturated alcohol was observed (>90%).

The significant feature of these reactions is the transfer of active deuterium from the solvent containing active deuterium during reduction to form C-D bond. It was observed that the reaction of *trans*-3-phenyl-2-propenal in deuterium oxide with $Ni(bpy)Cl_2$ as catalyst gave *trans*-3-phenyl-2-propen-1-ol with incorporation of deuterium at α and γ positions in 43:57 ratio. Deuterium incorporation from D_2O does not occur without the use of nickel catalyst (scheme **4.3**).

Table 4.2
Results on $Ni(bpy)Cl_2$ catalysed reduction

Entry	Substrate	Ratio of U: S (as in scheme **4.2**)	% conversion to alcohol
1.		36: 64	98
2.		84:16	96
3.		81:19	90
4.		100:0	98

5.		100:0	100
6.		94: 6	100
7.		83: 17	96

Similar results were also observed from the reaction of sodiumborohydride in methanol-d_4.

Table 4.3
Results on deuterium incorporation

Sl No.	Substrate	Ratio of **U** : **S** (as in scheme **4.2**)
1[a]		94 : 6
2[b]		100 : 0 (no deuteriumon **U**)
3[c]		91 : 9 (ratio of α and γ deuterated on **U** is 43 : 57)
4[d]		93 : 7 (ratio of α and γ deuterated on **U** is 46 :54)

a = in the absence of $Ni(bpy)Cl_2$; b = Without $Ni(bpy)Cl_2$ catalyst in CD_3OD,

c = with $Ni(bpy)Cl_2$ catalyst in D_2O, d = with $Ni(bpy)Cl_2$ catalyst in CD_3OD.

The reaction of *trans*-3-phenyl-2-propenal with sodiumborohydride in the presence of $Ni(bpy)Cl_2$ catalyst has yielded the deuterated saturated and unsaturated alcohols. The **figure 4.1(a)** and **(b)** are the ^1H NMR spectra of the reaction mixture in which the reduction of *trans*-3-phenyl-2-propenal with sodium borohydride carried out in methanol-d_4 without and with $Ni(bpy)Cl_2$.

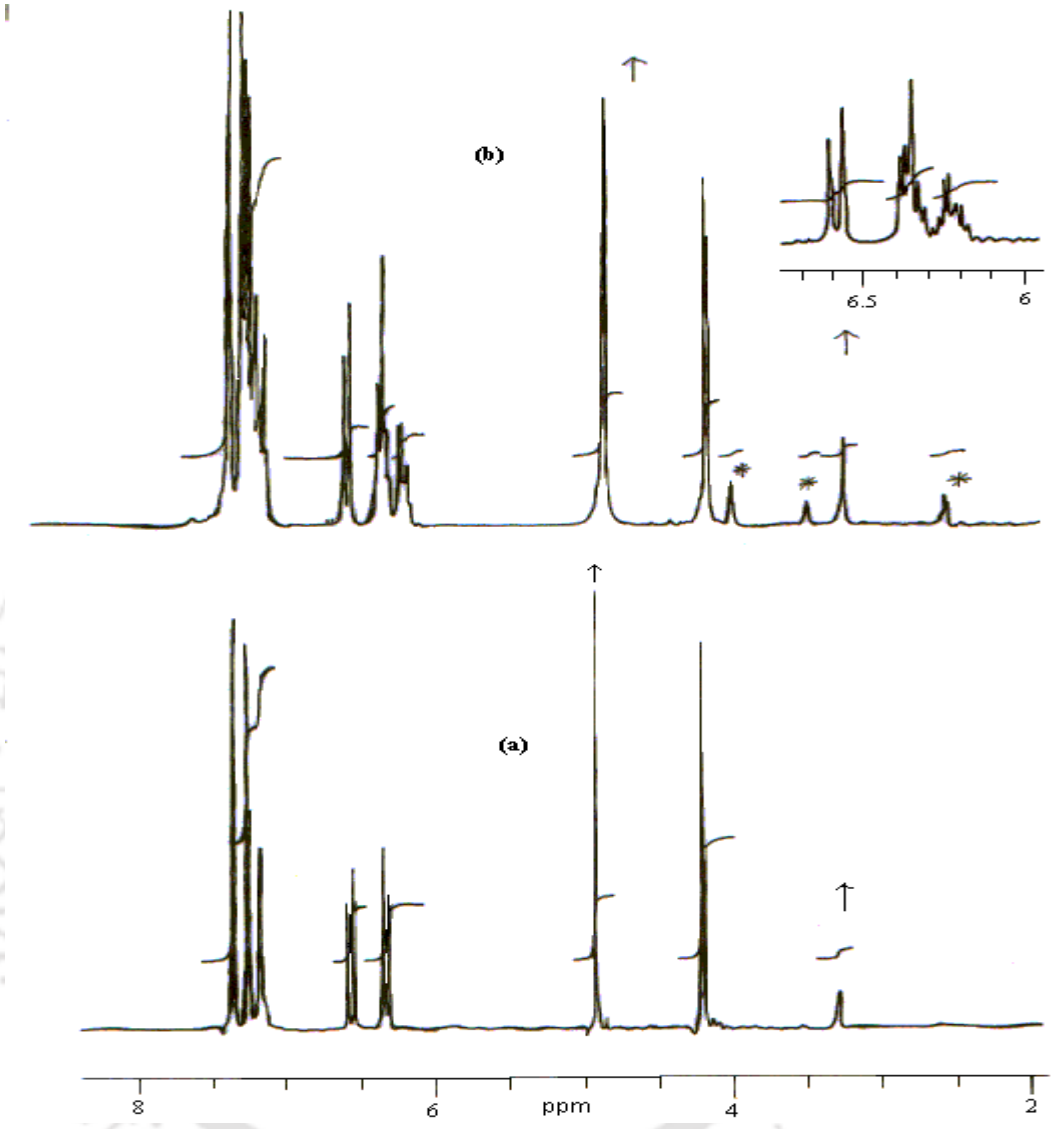


Figure **4.1**: ^{1}H NMR spectra (400 MHz) of the reaction mixture of *trans*-3-phenyl-2-propenal with sodium borohydride in methanol-d_4 (a) without and (b) with Ni(bpy)Cl_2.(* are signals from the saturated alcohol and ↑ are from the solvent). Inset is the expansion of α and β-proton signals of (b)

The multiplicity of α and γ protons in ^{1}H NMR clearly discerns the incorporation of deuterium at these positions when the Ni(bpy)Cl_2 was used as a catalyst. In the undeuterated *trans*-3-phenyl-2-propen-1-ol, the α and γ protons appear at 6.56δ as doublet (J= 18Hz, trans coupling) and at 6.34δ as doublet of triplet (18, 9Hz respectively). However, in the product obtained from reaction in CD_3OD by Ni^{2+}/BH_4^- system, the coupling pattern of the signal at 6.56δ is not affected but becomes slightly broadened due to the presence of deuterium with I=1 and the signal at 6.34δ appears as multiplet due to the presence of deuterium at α and γ position. The integrations confirm the ratio of deuterium at α and γ position as 46:54. The proton signal at 4.21δ appearing as a doublet of multiplet (J = 9Hz) from saturated carbon (γ-position) also indicates the deuterium being incorporated at γ-position. Only the *trans* unsaturated alcohol was obtained in these reactions. About 7% 3-phenyl propan-1-ol was also obtained on reduction by Ni^{2+}/BH_4^- system.

A plausible path leading to the incorporation of deuterium during the reduction of the α-β-unsaturated carbonyl compound is shown in **scheme 4.4**. The generation of reduced nickel(0) complexes similar to [**A**] (scheme **4.4**) by reducing

agents is established[178-180]. A methanolic solution of $Ni(bpy)Cl_2$ has its absorption maximum at 296nm and 306nm due to metal to ligand charge transfer[181] (spectra 1 in figure **4.2**. These absorptions disappear after addition of sodium borohydride (spectra 2 in figure **4.2**) and a new absorption at 282nm develops (spectra 3 in figure **4.2**). The absorption at 282 nm starts decaying after this and after some time the absorptions for $Ni(bpy)Cl_2$ at 296 and 306 nm start recovering (spectra 3 to n in figure **4.2**).

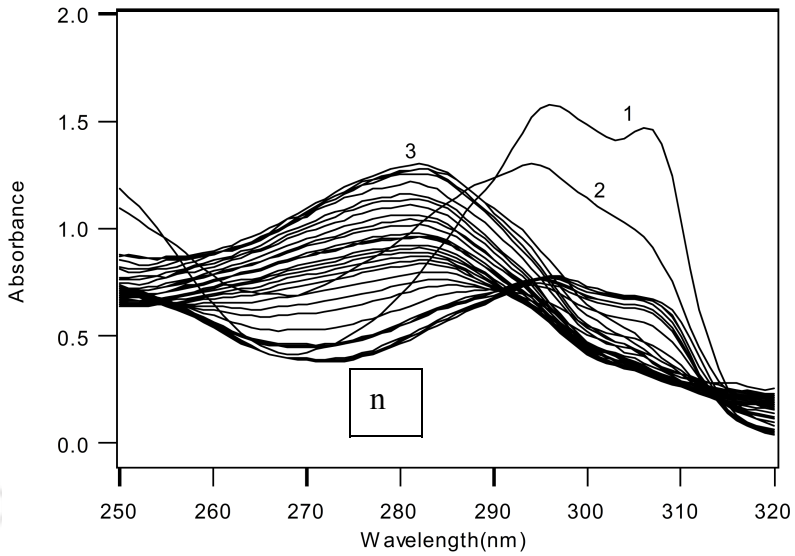


Figure **4.2**: Change of absorbance of a methanolic solution containing Ni(bpy)Cl_2 (0.023 mM) with sodium borohydride (0.05 mM) as recorded with 2 minute's time interval

Vigorous hydrogen gas evolution occurs initially and once the borohydride is consumed, the two absorption maxima at 296 and 306nm reappear and the absorption at 282nm disappears. This suggests that an intermediate[180] of Ni(0) of the type [**A**] having absorption at 282nm gets converted to Ni(II) species during dehydrogenative coupling reaction[178-180]. A similar pattern on the change of

absorbance was also observed during the reduction reaction of *trans*-3-phenyl-2-propenal by sodiumborohydride in the presence of $Ni(bpy)Cl_2$ in methanol. An oxidative addition and reductive elimination process may be favourable to explain the equidistribution of deuterium at α and γ-position. Since the exchange of deuterium at α and γ-positions were approximately equal, it suggests intermediacy of π-allylic type of complex in the

reaction. There are several structural possibilities of such intermediates and in view of the inability to isolate such intermediate/s the discussion is minimised. The

existing literature suggests that the carbonyl compounds can be partially deuterated by sodium borohydride[176]. Heavy metal salts such as that of platinum[177] enhance the partial deuteration of carbonyl compound by sodiumborohydride in deuterated solvents. However, our reactions are performed under neutral condition and the selective carbonyl reduction of α-β unsaturated carbonyl compounds are observed. The dehydrogenative coupling reactions by other hydride such as deuterosilanes in the presence of transition metal catalyst also allow hydrogenation of olefins through deuterium scrambling on the products[182-183].

This study showed the catalytic effect of $Ni(bpy)Cl_2$ during the sodiumborohydride reduction and also has shown that the deuterium can be partially incorporated from a deuterated solvent containing active deuterium to an α-β-unsaturated carbonyl compound. In case of the polyphenol supported borohydride reduction, it has been noticed that no reduction of double bonds occur with exclusive formation of the unsaturated alcohol only. Again in comparison to reduction of carbonyl compounds with tetramethyl ammonium borohydride alone, reduction with the same reagent in presence of the oligomer was found to be faster.

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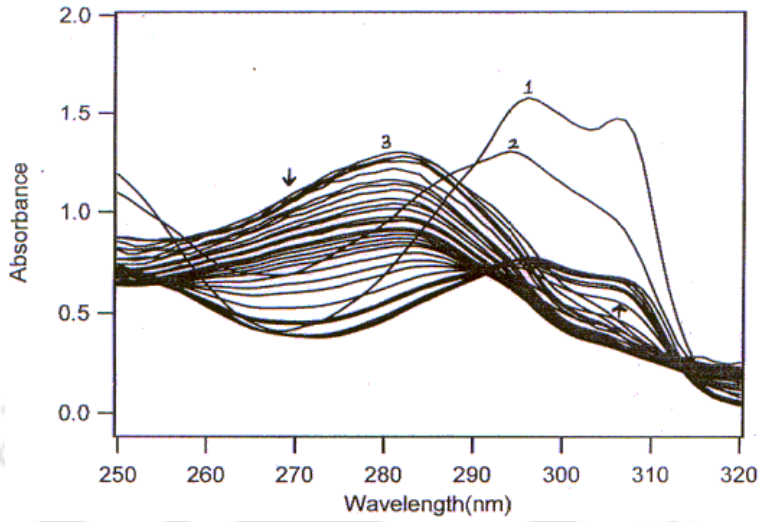
Indian Institute of Technology Guwahati


2.0
1.5
1.0
0.5
0.0
Absorbance
250
260
270
280
290
300
310
320
Wavelength(nm)
1
2
3

CHAPTER 5

EXPERIMENTAL

5.1 General Instruments/Equipment used for analytical purpose

5.1.1 Infrared spectra

Infrared spectra of the compounds were recorded either on a Nicolet Impact-410 Fourier Transform Infra Red spectrophotometer or a Perkin-Elmer Infrared spectrophotometer. Spectra were recorded either as KBr pellet or as nujol mull or as thin film.

5.1.2 UV-visible spectra

UV-visible spectra were recorded by dissolving the stipulated amount of the substrate/s in appropriate solvent and on a Hitachi UV-visible U-2001 spectrophotometer.

The interactions of amines (chapter 2) were studied by recording visible spectra of oligomers in acetonitrile solution. In each case definite amount of amine was dissolved in acetonitrile and added in aliquot with the help of a microsyringe. For solvatochromicity study, the electronic spectral data on absorbance at each 1nm interval were collected and used for simulation purpose with the aid of IGOR software package on an IBM PC. For simulation purpose the matrices were constructed directly from the data of a normal Gaussian shape spectra or from the data of extrapolated peak constructed by addition of mirror image of one half of the spectra in the case of overlapping peaks. The matrices were constructed to find out the component of each species with the aid of the

data available from the experiment by literature procedure[68]. In these cases MATLAB software package was used in an IBM Pentium PC to obtain the relative contribution of each states.

5.1.3 Nuclear Magnetic Resonance spectra

Majority of the ^{1}H NMR and ^{13}C NMR spectra were recorded either on a Bruker 400 MHz or on a JEOL Ex-400 NMR spectrometer using TMS as internal standard. These were recorded at Sophisticated Instrumentation Facility, Indian Institute of Science, Bangalore, Indian Institute of Chemical Biology, Kolkata, Indian Association of Cultivation of Science, Kolkata and Tokyo Institute of Technology, Japan,

5.1.4 Mass spectra

The Matrix Assisted Laser Desorption Ionisation (MALDI) mass spectra were recorded as matrix in AgTFA on a Kratos PC-Kompact mass spectrometer in positive ion mode. It was done in Molecular Biophysics Division, Indian Institute of Science, Bangalore The LSI mass spectra were recorded on a VG Auto Spec M mass spectrometer using either glycerol or m-nitrobenzyl alcohol as matrix at Indian Institute of Chemical Technology, Hyderabad.

5.1.5 Electron Spin Resonance Spectra

The ESR measurements were done on X-band of an EPR-E-112 ESR spectrometer at Regional Sophisticated Instrumentation Centre, Indian Institute of Technology, Madras, Chennai. A quartz cell was used for X-band measurements.

In all these measurements diphenyl picryl hydrazyl radical (DPPH) was used as the standard.

5.1.6 Elemental analysis

The elemental analyses were done on a Perkin-Elmer PE 2400 series II CHN analyzer 2400. For a few samples, the elemental analyses were done at Central Drug Research Institute, Lucknow and at Indian Association of Cultivation of Science, Kolkata.

5.1.7 Gel Permeation Chromatography

The GPC were done on a Water 600 GPC system with Refractive Index detector (Waters 2421 RI detector) with ultrastyragel® column and THF as eluent. The flow rate was 5 mL/min. The calibration curves for GPC analyses were obtained using polystyrene standards.

5.1.8 Thermal analysis

The thermal analyses were carried on a Mettler-Toledo TGA/SDTA 851^e and DSC 821^e thermal analyser. Thermogravimetric measurements were conducted under pure nitrogen gas either in an alumina or in a platinum crucible. Differential Scanning Calorimetric experiments were done under air in an aluminium or in a platinum crucible. In both DSC and TG, the heating rate was maintained as either 5°C/min or 10°C/min.

5.1.9 Electrochemical Analysis

Cyclic Voltametry

The cyclic voltamograms were recorded with an electrochemical analyzer CH Instrument with three electrode systems comprising of Ag/AgCl reference electrode, two platinum electrodes as working and auxiliary electrodes. The

measurements were done in dry acetonitrile (HPLC grade, distilled over CaH_2) with tetrabutylammonium perchlorate as supporting electrolyte. The EMF values are with reference to ferrocene as standard.

The electrochemical studies were performed by dissolving 2 mg each of the oligomer in acetonitrile (5 cm^3) with 200 mg of the tetrabutylammonium perchlorate as supporting electrolyte with scan speed 0.1 mV/s. Pure nitrogen gas was passed through the solution before recording of the voltammogram.

5.1.10 Gas Chromatographic Analysis

Catalytic reactions were monitored by gas chromatography on a Hewlett Packard HP 6890 GC system with the aid of FID detector by using SE-30 capillary column. In most of the cases, oven, injector and detector temperature were set at 150°C, 220°C and 220°C. In all cases N_2 was used as a carrier gas with 4.8 bar inlet pressure. The results were recorded on an HP 3395 integrator.

5.1.11 Conductivity Measurement

Conductivity of the material was measured over a range of temperature on a Hewlett Packard 34401 multimeter, Keithley 6512 programmable electrometer and agronics 93-C DC power supply unit. The measurements were based on the principle of measuring the resistivity changes as well as resistance with change of temperature.

Material under investigation was taken as a thin film, made by spreading a paste of the sample in a solvent, on a small, thin mica sheet. After removing the solvent by slow evaporation, the mica sheet was placed in a set up, specially

designed for the measurement (figure **5.1**). The mica sheet was placed between the two probes and the copper block, such that the two probes just touch the film. The resistance versus resistivity was recorded. The temperature was obtained from the corresponding resistivity by using the conversion table.

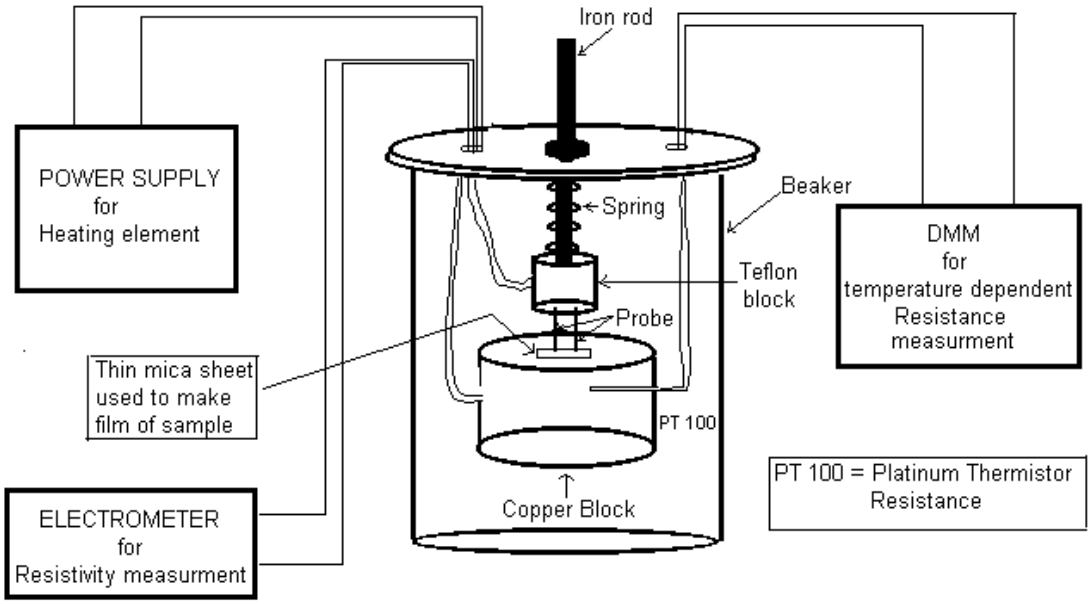


Figure 5.1: Two probe method for conductivity measurement

5.1.12 Magnetic measurement

Magnetic measurements were done on a Vibrating Sample Magnetometer at Regional Sophisticated Instrumentation Centre, Indian Institute of Technology, Chennai.

5.1.13 Calculation of heat of formation and charge density

Heat of formation of **2.XII** and **2.XIII** and charge densities of different naphthalenediols were calculated by using AM1 calculation.

5.2 Reagents and solvents

General reagents and solvents, used in this study are of reagent grade and purchased from E. Merck, Germany, Sigma Aldrich, USA, Glaxo Laboratories (India) limited, and S.D. Fine Chemicals Limited. Solvents were purified by standard procedure[184]. Pyrogallol, benzaldehyde, substituted benzaldehydes, different amines, 1- and 2-naphthols and tertiary butylhydroperoxide (70% in water) used in this study are purchased from Aldrich, USA and different naphthalenediols are purchased from Kanto Chemicals, Japan and used without further purification. The α-β unsaturated carbonyl compounds used in this study were either prepared by standard procedure[184] or procured from Aldrich, USA and used as obtained.

5.3 Synthetic Methods and Analytical Data

5.3.1 Experimental Details of Chapter 2

Synthesis of 2.III-2.VI

Typical procedure (2.III): A solution containing benzaldehyde (1060mg, 10mmol), pyrogallol (1260mg, 10mmol) and oxalic acid (100mg, 0.8mmol) in dry ethanol (10ml) were refluxed for 3hrs. A viscous brick red solution was obtained. The solvent was removed under reduced pressure and then washed with

water (2X 25ml). The dark red viscous gel thus obtained after decantation of water was further dried under vacuum. Prior to decantation of the gel a white solid was obtained which was discarded. Yield: 930mg.

Analytical data

2.III: IR (KBr, cm^{-1}) 3369 (bs), 3000(m) 1688(m) 1623(s), 1495 (s), 1464(s), 1286(s), 1207(s), 1068 (s), 1012 (s), 953 (w), 750 (m), 702 (s). **^{1}H NMR** (400 MHz, DMSO-d_6) δ(ppm) 5.2-8.2 (m); **Mn, Mw** (THF) 1209, 1252**;** **MALDI mass**: (m/e) 2036.7, 2244.3, 1821.3, 1604.2, 1625.3, 1391.5, 1373.4, 1177.7, 1085.3, 981.8, 872.7 (100% intensity); **Elemental anal:** Calc for $C_{13}H_{10}O_3$. 1.25 H_2O, C 65.95 H 5.34; Found C 66.54, H 5.66.

2.IV: IR (KBr, cm^{-1}) 3396(bs), 2830(w), 1674(s), 1605(s), 1508(s), 1463(s), 1287(s), 1208(s), 1070(w), 1019(s), 956(w), 809(s); **^{1}H NMR** (400MHz, DMSO-d_6) δ(ppm) 7.3-8.2(m, 8H), 2.1-2.3(m, 3H); **M_n, M_w** (THF) 2199, 2248. **MALDI mass** (m/e) 793.6 (100%), 809.9, 928.0, 1021.6, 1038.1, 1249.6, 1270.9, 1291.1, 1477.1, 1518.6, 1704.7, 1746.4, 1930.8, 1990.3, 2159.3, 2209.8, 2429.0, 2658.4, 2882.9. **Elemental analysis** Calculated for $C_{14}H_{12}O_3.0.5H_2O$, C 70.88, H 5.48; Found, C 70.07, H 5.59. **Thermogravimetry** shows 3.8% loss of weight at the temperature range of 150-200°C.

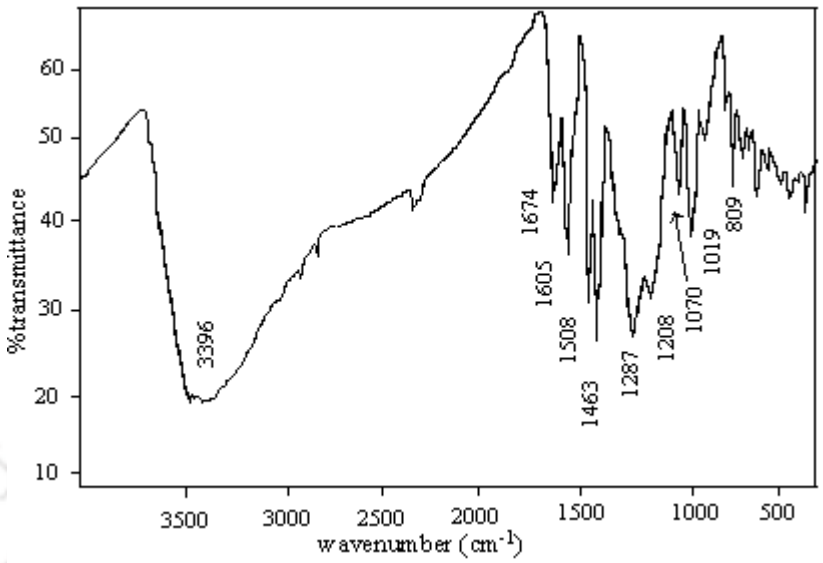


Figure **5.2**: IR spectra of **2.IV** (as KBr pellet)

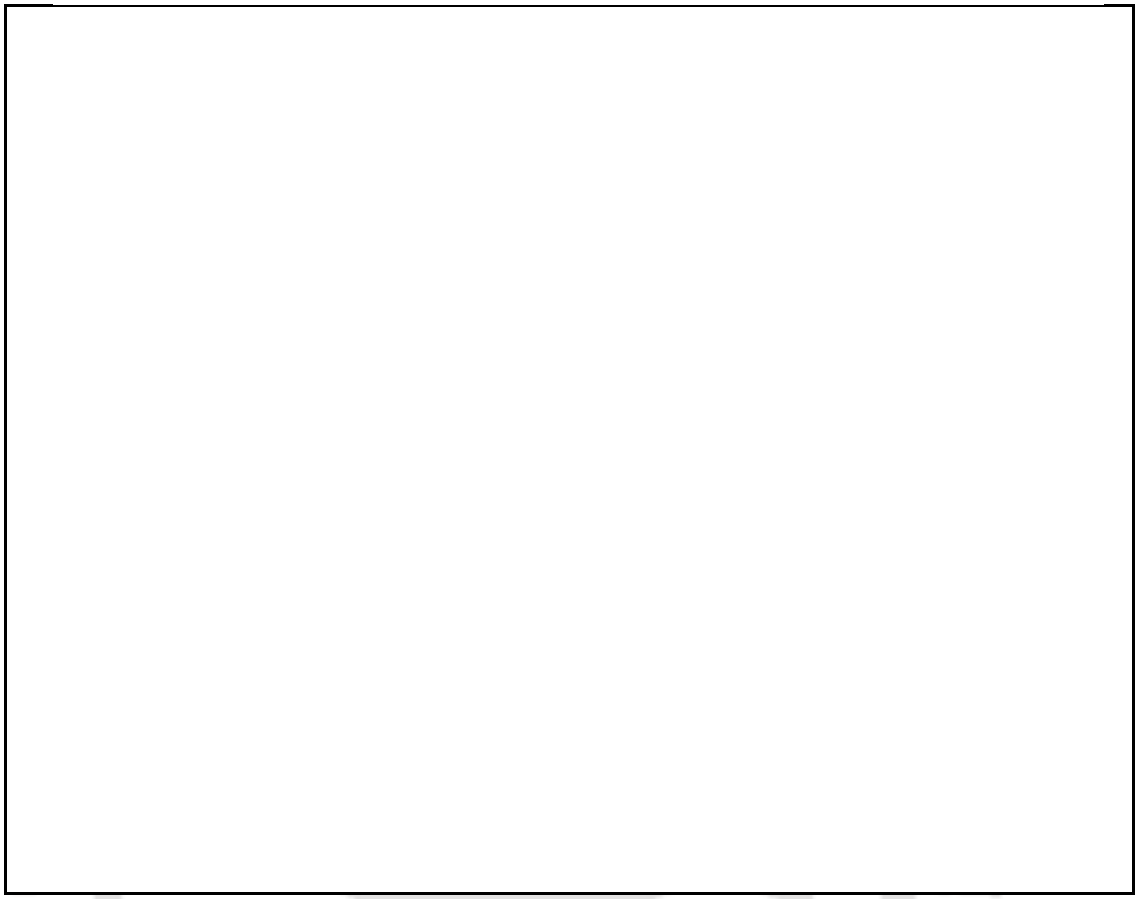


Figure **5.3**: 400 MHz ^{1}H NMR spectra of **3.IV** in DMSO-d_6.

2.V: **IR** (KBr, cm^{-1}) 3465 (bs), 2837(ws), 1609(s), 1463(s), 1245 (s), 1072(m), 1025(s), 826(m). **^{1}H NMR** (400 MHz, DMSO-d_6); δ(ppm) 6.3-7.9 (m, 8H), 3.5-3.9 (m, 3H). **MALDI mass** (m/e) 1002.0(100%), 1250.1, 1490.3, 1733.3, 1978.0, 2222.1, 2466.0. **Elemental analysis**: Calculated for $C_{14}H_{12}O_4.0.8\ H_2O$, C 65.01 H 5.26; Found C 65.46, H 5.19.

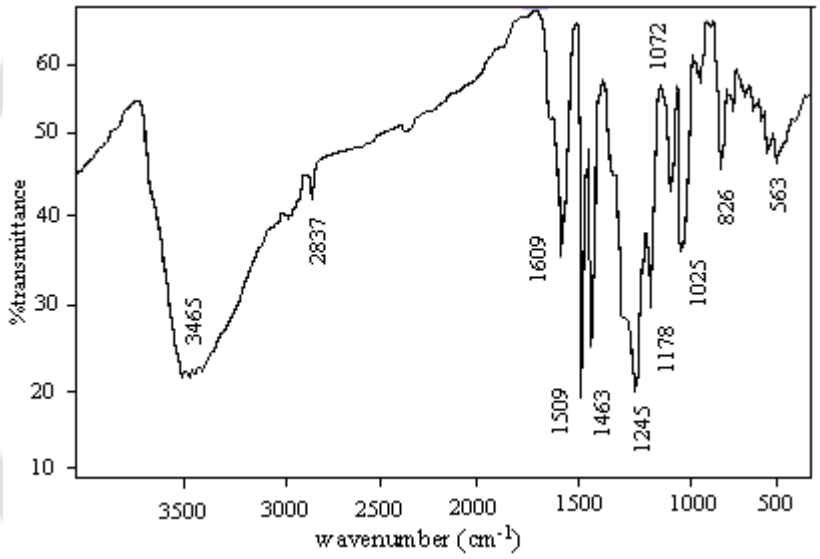


Figure **5.4**: IR spectra of **3.V**(as KBr pellet)

Figure **5.5:** MALDI mass spectra of **3.V**

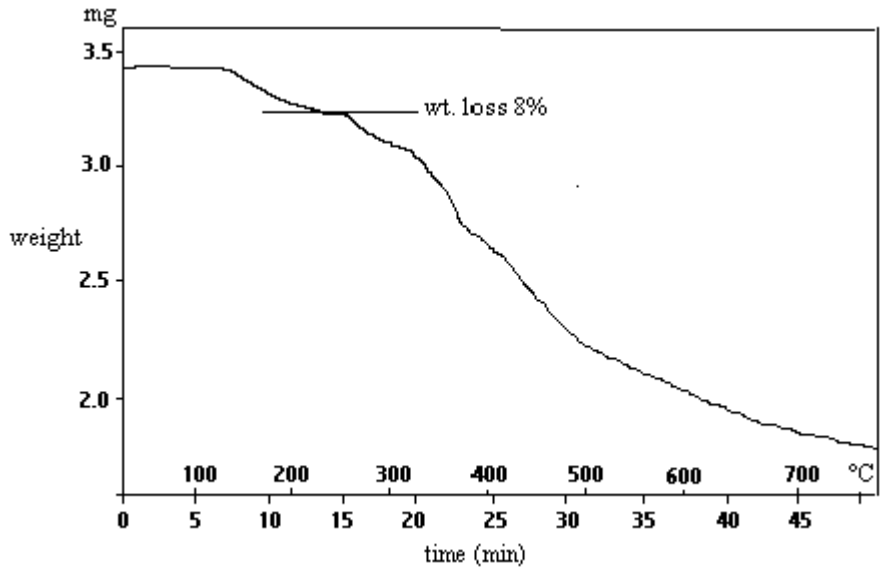


Figure **5.6:** Thermogram of **3.V**

2.VI: IR (KBr, cm^{-1}), 3434(bs), 2963(m), 1624(s), 1499(s), 1464(s), 1284(s), 1096(s), 1035(w), 949(w), 873(w). **^{1}H NMR** (400MHz, DMSO-d_6), δ(ppm) 6.2-7.4(m, 4H), 4.2-4.7(m, 1H), 1-1.5 (m, 3H); **M_n, M_w** (THF) 2469, 2484. **Elemental analysis** Calculated for $(C_8H_8O_3)_4.3H_2O$, C 58.00, H 5.74; Found C 57.4, H 5.66. Thermogravimetric study shows 8% weight loss in

150°-220°C corresponding to loss of water molecule from the interstices. This substantiates the corrected molecular formula.

General method for synthesis of 1,1-di-(2′-methoxyphenoxy)-methane(VII) and 1,2-di-(2′-methoxyphenoxy)-ethane (VIII)[184]

Two equivalents of 2-methoxyphenol (620mg, 50 mM) was taken in acetone (0.05 dm^3) with one equivalent of the halide [for **VII**, diiodomethane (668mg, 25mM) and for **VIII**, 1,2-dibromoethane (470mg, 25 mM)] and anhydrous K_2CO_3 (7g, 50 mM) in a round bottom flask and refluxed with vigorous stirring at 80°C for 18 hours. The resulting solution was filtered. Acetone was removed by distillation under reduced pressure and the residue after addition of water, extracted with dichloromethane. The dichloromethane extract after washing with dilute NaOH solution and water was dried over Na_2SO_4. The product was then obtained after removal of the solvent under reduced pressure. Yield: for **2.VII,** 507 mg (78 %), for **2.VIII,** 465mg (68 %).

Analytical data

2.VII: M.P. 84°C. **IR** (nujol, cm^{-1}) 1600(s), 1518(bs), 1475(bs), 1425(m), 1382(m), 1330(s), 1310(w), 1250(bs), 1230(s), 1180(s), 1150(s), 1120(s), 1010(bs), 755(s), 680(m). **^{1}H NMR** (400MHz, $CDCl_3$): δ (ppm), 7.3-7.7, (m, 8H), 6.2(s, 2H), 4.3 (s, 6H); **^{13}C NMR** (400 MHz, $CDCl_3$): δ(ppm) 150.50,

146.66., 123.73, 121.39, 118.43, 112.53, 93.73, 56.28; **Elemental analysis**: Calculated for $C_{15}H_{16}O_4$ C 69.23, H, 6.15; Found C, 68.99, H 6.53.

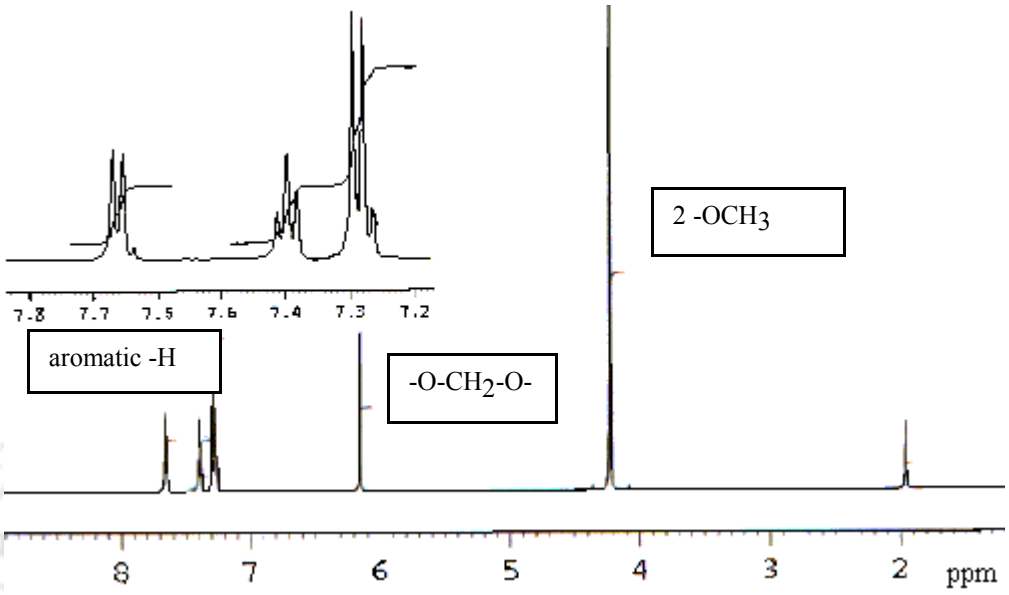


Figure **5.7:** ^{1}H NMR spectra of **2.VII** (in $CDCl_3$)

2.VIII: M.P. 140°C. **IR** (nujol) 1580(s), 1500(s), 1478(s), 1458(s), 1370(m), 1340(m), 1320(w), 1250(s), 1220(s), 1181(s), 1120(s), 1055(m), 1037(m), 1018(s), 900(w), 775(m), 750(s), 737(s). **^{1}H NMR** (400 MHz, $CDCl_3$): δ(ppm) 7.5-7.2(m, 8H), 4.8(s, 4H), 4.2(s, 6H); **^{13}C NMR** (400MHz, $CDCl_3$): δ(ppm) 150.17, 14865, 122.14, 121.35, 114.76, 112.58, 68.04, 56.38; **Elemental analysis**: Calculated for $C_{16}H_{18}O_4$; C 70.07; H 6.57; Found C 70.21; H, 6.53

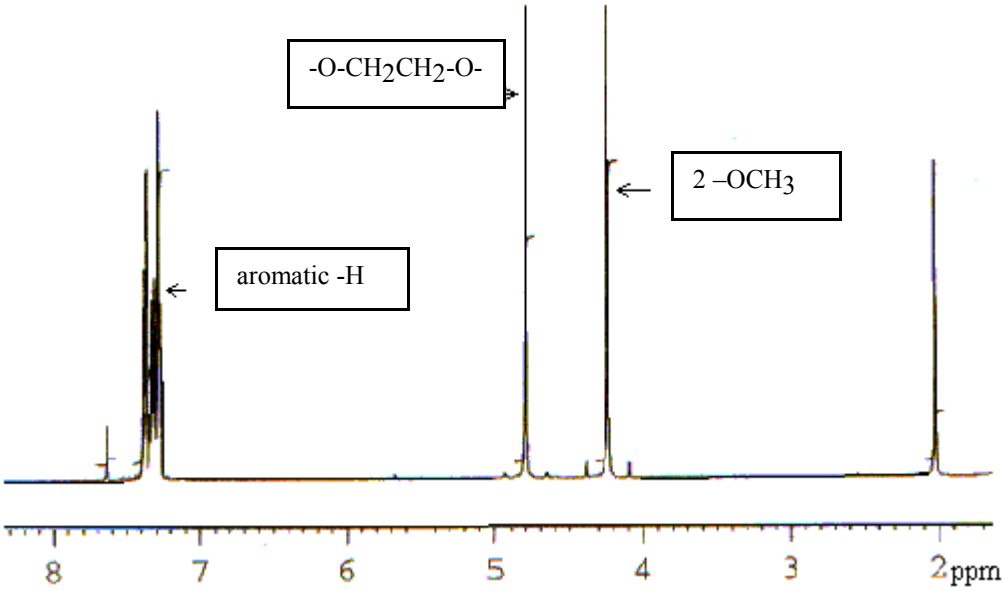


Figure **5.8:** ^{1}H NMR spectra of **2.VIII**(in $CDCl_3$)

Preparation of charge transfer complexes

1,4-phenylenediamine with 1,4-naphthoquinone (IX)

A solution of 1,4-naphthoquinone (316mg, 2mM) and 1,4-phenylenediamine in ethanol (0.025dm^3) was mixed with stirring and

refluxed on a water bath for 15 min. The solvent was removed under reduced pressure to get a black solid, which was recrystallised from cold ethanol. Yield: 527 mg. **IR** (KBr, cm^{-1}) 3316(s), 1672(s), 1629(s), 1600(s), 1563(s), 1512(s), 1432(m), 1352(s), 1309(s), 1265(s), 1250(s), 1120(m), 996(s), 843(m), 821(s). **^{1}H NMR** (400 MHz, $CDCl_3$, δ) 6.72-8.10 (m, 8H), 6.20 (s, 2H), 3.82(bs, 4H); **^{13}C NMR** (400 MHz, $CDCl_3$, δ): 135.24, 132.49, 126.79, 126.53, 125.31, 116.19, 102.65. **Elemental analysis** Calculated for $C_{10}H_6O_2.C_6H_8N_2$ %C 72.18, %H 5.26, %N 10.52; Found C, 72.67, H, 4.96, N, 10.38. λ_{max} (CH_2Cl_2) 496 nm (ε = 4563 M^{-1} cm^{-1}).

Adduct of 1,4-naphthoquinone with 1,4-benzenediol (2.XII)

Saturated solutions of 1,4-naphthoquinone (158 mg, 1mM) and 1,4-benzenediol (110 mg, 1 mM), in dehydrated ethanol (0.01 dm^3 for each) were mixed together with constant stirring and the solution was refluxed at 80^0C for 30 minutes. The solvent was then removed under reduced pressure. The reddish brown solid so obtained was recrystallised from cold ethanol (yield 265 mg). **IR**(KBr, cm^{-1}) 3250(bs), 1653(s), 1593(s), 1520(s), 1460(s), 1348(s), 1224(s), 1208(s), 1102(s), 830(s), 771(s); **^{1}HNMR** (400 MHz, $CDCl_3$, δ, ppm) 8.6(s), 8(m), 7.8(m), 7.1(s), 6.6(s); **^{13}CNMR** (400 MHz, DMSO-d_6, δ, ppm) 185.7,

150.6, 139.6, 135.0, 132.4, 126.7, 116.5 **Elemental analysis** calculated for $C_{16}H_{12}O_4$, C 71.64, H 4.47; found C 71.14, H 4.69.

Adduct of 1,4-benzoquinone with 1,4-naphthalenediol

Saturated solutions of 1,4-naphthalenediol (160 mg, 1mM) and 1,4-benzoquinone (108 mg, 1 mM) in acetone (0.01 dm^3 for each) were mixed together and allowed to stand at room temperature. The solvent was removed under reduced pressure and the black solid so obtained was recrystallised from acetone (yield : 268 mg). **IR** (KBr, cm^{-1}) 3257(bs), 1659(s), 1633 (s), 1586(s), 1480(s), 1367(s), 1334(s), 1301(s), 1268(s), 1222(s), 877(s), 784(s); **^{1}HNMR** (400 MHz, $CDCl_3$, δ, ppm) 8.6(s), 8.0(s), 7.8(m), 7.1(s), 6.9(s), 6.6(s); **^{13}CNMR** (400 MHz, DMSO-d_6, δ, ppm) 188.5, 185.6, 150.6, 139.6, 137.4, 135.1, 132.4, 126.7, 116.5; **Elemental analysis** Calculated for $C_{16}H_{12}O_4$, C 71.64, H 4.47; found C 71.52, H, 4.08.

Preparation of oximes[184]

A typical preparation (*p*-methylbenzaldoxime): 1 gm (15 mM) of hydroxylamine hydrochloride was taken with 2 gm crystallized Na-acetate in 8 mL ethanol. About 1.5 mL (12.5 mM) of *p*-methylbenzaldehyde was mixed with it and shaked well until a clear solution was obtained. The solution was warmed on a water bath for 10 minutes. Crystallization of the oxime took place on cooling. The oxime was filtered and washed with water and then recrystallised from ethanol. Yield: 1.6 gm. M.P. 79°C.

Preparation of imines[184]

A typical preparation (N-benzylideneaniline): 1mL (10 mM) of benzaldehyde was taken in 8 mL of ethanol and 0.9mL (10 mM) of aniline was added to the above solution with stirring. The mixture was warmed on a water bath for 15 minutes. The precipitate so obtained was filtered, washed with cold ethanol and recrystsllised from ethanol. Yield 1.5 gm. M.P. 52°C.

Hydrolysis of oximes and imines

In separate experiments, solutions of oxime or imine (0.5 mmol) in 5 ml aqueous acetonitrile (H_2O: CH_3CN; 2:1) were treated with H_2SO_4 (1M, 0.3 ml) in the presence and absence of **2.III** (30 mg) were stirred at room temperature. Aliquots of the reaction mixtures were taken in 1hr time interval and extracted with CH_2Cl_2. The CH_2Cl_2 extract was washed with water and dried over Na_2SO_4. The products were analysed by recording their gas chromatogram and comparing with authentic samples at different time intervals.

5.3.2 Experimental Details of Chapter 3

Preparation of cis-bisglycinatocopper(II) monohydrate[185]

Copper(II) sulphate pentahydrate (3.0 g, 12.0 mM) was dissolved in 17 mL of hydrochloric acid (1M). Glycine (1.5 g, 20.0 mM) was added to this solution with stirring and the resulting solution was warmed over a water bath for 1 hour. To this solution, solid sodium hydrogen carbonate was added until the precipitation was complete. The precipitate was filtered and then recrystallised

from hot water. The resulting product was dried in an oven. **IR** (KBr, cm^{-1}): 3280(bs), 2992(m), 1600(s), 1388(s), 1328(s), 1156(s), 1063(s), 917(s). **UV-vis** λ_{max} 630 nm.

The reaction of 2-naphthol with hydrogenperoxide and cis-bisglycinatocopper(II)

2-naphthol (290mg, 2mmol), cis-bisglycinatocopper(II)monohydrate (48mg, 0.2mmol) and hydrogenperoxide ($1cm^3$, 30% v/v) were taken together in a mixed solvent of acetonitrile and water (2:1 ratio) and stirred at 70^0C for four hours. The reaction mixture was allowed to cool and the acetonitrile was removed under reduced pressure and the remaining paste was purified by column chromatography to obtain **3.II** and **3.III**. The isolated yield of **3.II** and **3.III** in pure form are 25mg and 48mg respectively.

Analytical data of 3.II: **IR** (film) 3469(s), 2925(m), 2825(m), 1629 (s), 521(s), 1461(s), 1266(s), 12199s), 1145(s), 809(s), 755(s). **FAB mass** (m/e): 663, 647, 584, 516, 444,413, 391, 363, 355, 351, 281, 255, 221, 207, 167. **Elemental analysis** Calculated for $C_{90}H_{59}O_{12}Cu_2$, C 74.22, H 3.91 found C 74.96, H 4.01.

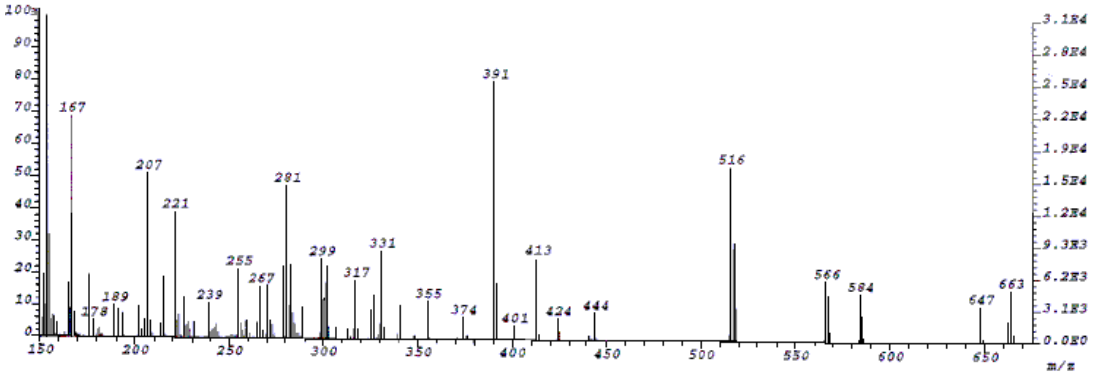


Figure **5.11**: FAB mass spectrum **3.II**

Analytical data of <u>3.III</u>: **IR** (film) 3182(s), 1626(s), 1606(s), 1475(s), 1371(s), 1273 (s), 1201(s), 815(s), 756(s) **FAB mass** (m/e) 663, 584, 565, 444, 391, 355, 323, 302, 281, 255, 226, 207, 176, 154, 136, 107, 95, 83,69, 55. **Elemental analysis** Calculated for $C_{120}H_{76}O_{15}Cu_2$ C, 76.47 H, 4.04; found C, 76.93, H, 4.72

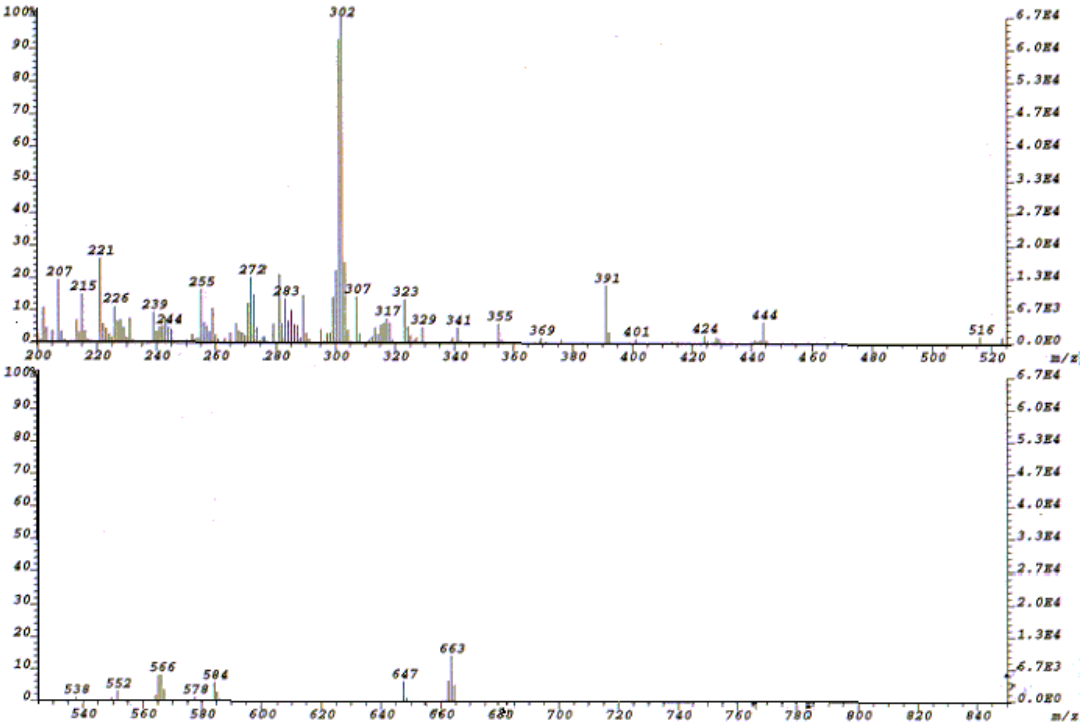


Figure **5.12:** FAB mass spectrum of **3.III**

The reaction of 2-naphthol with tertiarybutylhydroperoxide and cis-bisglycinatocopper(II)

2-naphthol (290mg, 2mM) *cis*-bisglycinatocopper(II)monohydrate (48mg, 0.2mM) and tertiarybutylhydroperoxide (0.3cm^3, 70%) were taken together in a mixed solvent of acetonitrile and water (2:1 ratio) and stirred at 70^0C for one hour. The reaction mixture was allowed to cool and the acetonitrile was removed under reduced pressure and the remaining paste was extracted with dichloromethane (0.025 dm^3). The extracted mixture after evaporation of dichloromethane was put over a silica gel column and purified to obtain **3.IV** (isolated yield in pure form 60 mg). **IR** (film, cm^{-1}) 3496(s), 2925(s), 1629(s), 1521(w), 1461(w), 1266(w), 1145(w), 810(m), 756(m). **^{1}H NMR** ($CDCl_3$) 11.9 (s, 1H) 6.2-10(m, 24H), 1.5-1.8(m, 9H). **Elemental analysis** Calculated for $C_{44}H_{32}O_6$ C, 80.48 H, 4.87 found C, 80.42 H, 4.85.

Preparation of naphthalenediol oligomers (3.V-3.VIII)

Typical preparation procedure (3.V)

The 1,6-naphthalenediol (320 mg, 2mM), *cis*-bisglycinato copper (II) monohydrate (4,6 mg, 0.02 mM) and hydrogen peroxide (30% v/v, 0.5 cm^3) were reacted together in acetonitrile (0.002 dm^3) at room temperature for 2 h. After removal of the solvent under reduced pressure the residue obtained was washed with water (0.002 dm^3x5) which on drying under reduced pressure yielded the oligomer as a black solid (yield: 370 mg). **IR** (KBr) 3400(bs), 1600(vs), 1400 (s),

1360 (s), 1280 (bs). **^{1}H NMR** (400 MHz, DMSO-d_6 8.5-6 (m); **Elemental analysis** Calculated for $(C_{10}H_6O_3.\ 0.75H_2O)_n$ C, 63.6, H, 3.98; Found C, 63.18, H, 3.84. Copper (II) content estimated was found to be 0.5-1%.

Estimation of copper

Estimation of copper was done by standard iodometric procedure[186] by adding potassium iodide to the test solution and titrating the liberated iodine with sodium thiosulphate solution. Sodium thiosulphate solution was standardized by iodometric titration by using potassium dichromate solution as primary standard.

Analytical data of 3.V-3.VIII

Oligomers, derived from	**IR (KBr, cm^{-1})**	**Elemental analysis**	**Calculated composition**
1,3-	3500(s), 1600(s), 1420(m), 1380(m), 790(w)	C 65.08 H 3.61	
2,3-	3420(s), 1395(m), 1360(m), 740(w)	C 65.44 H 4.25	
2,7-	3420(s), 1640(s), 1600(s), 1390(m), 1355 (m), 840(w)	C 62.14 H 4.19	

Preparation of 3.IX

A mixture of 1,4-napthalenediol (400mg, 2.53mmol) and *cis*-bisglycinatocopper(II) (6.2mg, 0.027mmol) with hydrogen-peroxide (1cm^3,

30%) was stirred at room temperature for 15 minutes. On removal of the solvent from this reaction mixture under reduced pressure gave a black mass (413.6 mg). **Elemental analysis**: Calculated for found %C 68.64, %H 3.68. **IR** (film) 3300(bs), 1700(s), 1600(s), 1325(s), 1300(s), 1150(s), 1125(s), 900(s), 800(s). **^{1}H NMR** (DMSO-d_6) 9.3(s), 7.9(dm), 7.4(m), 7.1(s), 6.65(s). **ESR** 2975G (g=1.86), 1375G (g=1.14). The reactivity of this compound was studied *in situ* for oxidation of aldehydes. A typical oxidation reaction studied is as follows: To a well stirred mixture of benzaldehyde (318mg 3mmol) and hydrogen peroxide (0.5 cm^3, 30%), the catalyst (20mg) was added and stirred at 80^0C for two hours and product was analysed by GC extracting the reaction mixture with dichloromethane (2 cm^3).

Decomposition of hydrogen peroxide in presence of 3.IX

12 mg (0.05 mM) of cis-bis glycinato Cu(II) monohydrate was taken in acetonitrile(5 mL) and **3.IX** was added to this solution. To the solution added 1 mL of 30% H_2O_2 solution in water and the residual H_2O_2 was estimated[186] after 20 minutes. The experiment was done with different amounts (0 mM, 0.0052 mM, 0.013 mM, 0.019 mM, 0.025 mM) of **3.IX.**

Oxidation of benzaldehyde

Hydrolysis of benzamide

5.3.3 Experimental Details of Chapter 4

Preparation of Dichloro(bipyridyl)nickel(II) chloride [Ni(bpy)Cl_2][187]

1.19 gm (0.5 mM) of $NiCl_2.6H_2O$ was taken in 50 cm^3 of glacial acetic acid and refluxed for 30 minutes until a colour change from green to yellow is achieved. The acid was decanted and the residue was washed with butanol (2×40 cm^3). A solution of 2,2′-bipyridyl (0.78 gm, 0.5 mM) in butanol (75 cm^3) was added to the solid and the mixture was refluxed until a light green precipitate appeared. The reaction mixture was allowed to cool to room temperature and the light green Ni(bipy)Cl_2 was collected by filtration and dried well under vacuum. Yield: 0.8 gm.

Preparation of Dichlorobis(triphenylphosphine)nickel(II) chloride $[Ni(PPH_3)_2Cl_2]$[188]

1.19 gm (0.5 mM) of $NiCl_2.6H_2O$ was taken in 50 cm^3 of glacial acetic acid and refluxed for 30 minutes until a colour change from green to yellow is achieved. The acid was decanted and the residue was washed with butanol (2×40 cm^3). A solution of triphenylphosphine (2.62 gm, 1 mM) in butanol (75 cm^3) was added to the solid and the mixture was refluxed until a pink precipitate appeared. The reaction mixture was allowed to cool to room temperature and the pink $Ni(PPh_3)_2Cl_2$ was collected by filtration and dried well under vacuum. Yield: 2.3 gm.

Synthesis of α-β unsaturated carbonyl compounds[184]

Typical procedure for benzylidene acetophenone or 1,3-diphenylprop-2-en-1-one: 2 g of sodium hydroxide was taken in 20 mL of water and 10 mL of ethanol in a 100 mL round bottomed flask. The temperature was maintained at 25°C by immersing the flask in an ice-water bath. To this solution added freshly distilled acetophenone (5 g, 40 mM) and benzaldehyde (4 mL, 40 mM) and stirred vigourously at about 25°C for 3 hours. The resultant thick solution was left overnight in a refrigerator and then filtered the product under suction, washed with cold water until the washing is no longer alkaline and then with ice cold ethanol. Yield: 8 g, m.p. 52°C. The product was recrystallised from water.

The reduction of α-β unsaturated carbonyl compounds[184]

To a well stirred solution containing α-β unsaturated carbonyl compound (1mM), $Ni(bpy)Cl_2$ (0.01mM) in methanol ($2cm^3$), the $NaBH_4$ (2mM) was added in portions. A rapid reaction took place with vigorous gas evolution and the reaction mixture was stirred for half an hour at room temperature (25^0C). The solution turned black. To the reaction mixture dichloromethane ($20cm^3$) was added followed by addition of hydrochloric acid (1% in $5cm^3$ water). The dichloromethane layer was separated and dried over anhydrous sodium sulphate and filtered. Removal of the solvent under reduced pressure gave the corresponding alcohols in near quantitative yield (refer table **4.3**). The products were purified by column chromatography except in the case of reduced product of crotonaldehyde where purification was done by distillation. The saturated and unsaturated alcohols were obtained as mixture.