Synthesis of Transition-Metal Complexes by Cycloaddition and Their Application in Catalysis

M.Sc. Thesis

By **JYOTI KUMARI**



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Synthesis of Transition-Metal Complexes by Cycloaddition and Their Application in catalysis

A THESIS Submitted in partial fulfillment of the requirements for the award of the degree of Master of Science

> *by* **Jyoti Kumari**



DISCIPLINE OF CHEMISTRY INDIAN INSTITUTE OF TECHNOLOGY INDORE JUNE 2017



INDIAN INSTITUTE OF TECHNOLOGY INDORE

CANDIDATE'S DECLARATION

I hereby certify that the work which is being presented in the thesis entitled "Synthesis of transition-metal complexes by cycloaddition and their application in catalysis" in the partial fulfillment of the requirements for the award of the degree of MASTER OF SCIENCE and submitted in the DISCIPLINE OF CHEMISTRY at INDIAN INSTITUTE OF TECHNOLOGY INDORE, is an authentic record of my own work carried out during the time period from July 2016 to June 2017 under the supervision of Dr. Suman Mukhopadhyay, Associate Professor, Indian Institute of Technology Indore.

The matter presented in this thesis has not been submitted by me for the award of any other degree of this or any other institute.

JYOTI KUMARI

This is to certify that the above statement made by the candidate is correct to the best of our knowledge.

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DEDICATED TO MY PARENTS

Abstract

The present thesis focuses on design and syntheses of mono- and dinuclear copper and cobalt tetrazolato complexes by metal mediated [2+3] cycloaddition reaction between copper and cobalt bound azide $[Cu(bipy)(N_3)_2]_n$, $[Cu(phen)(N_3)_2]_n$ and $[Co(Me_2en)_2(N_3)_2]$ {bipy=2,2 bipyridyl, phen=1,10 phenanthroline and $(Me_2en)_2=N,N'$ dimethylethylenediamine } and different organonitriles e.g. benzonitrile, 4cyanobenzonitrile and 4-pyridinebenzonitrile. Catalytic properties of the synthesized copper tetrazolato complexes have been examined which act as a homogeneous catalysis for the oxidation of benzene into phenol, benzoquinone and catechol and interactions of cobalt complexes with bovine serum albumin (BSA) are also explored.

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ACRONYMS

Acronym	Meaning	
BSA	Bovine serum albumin	
Calcd.	Calculated	
DMF	Dimethylforamide	
En	Ethylene diamine	
ESI-MS	Electrospray Ionisation –Mass Spectroscopy	
GOF	Goodness of Fitting	
GC	Gas Chromatography	
IR	Infrared	
MW	Microwave	
MOFs	Metal-organic Framework	
MeOH	Methanol	
μ	Represents bridging	
Pytz	5-(4-pyridyl)tetrazolate	
4-Clptz	5-(4-chloropyridyl)tetrazolate	
Me ₂ en	N,N' dimethylethylene diamine	

NOMENCLATURE

Å	Wavelength
α	Alfa
β	Beta
Å	Angstrom
nm	Nanometer
cm	Centimeter
0	Degree
Mmol	Millimol
mL	Milliliter
a.u	Arbitary Unit

Chapter 1

Introduction

1.1 General Introduction:

In early 19th century, Alfred Werner also known as "Father of Coordination Chemistry" put forward his theory of modern coordination chemistry which elaborates the structure and bonding in coordination complexes. Coordination chemistry offers the possibility to examine the metal ligand interaction in various natural processes which have immense importance in biology and materials. The fine interplay of interaction between the interaction of ligands and metal ion can impart specialized properties in metal complexes so that they can be utilized in material and medicinal science and biology research. Among various organic ligands nitrogen containing hetrocycles have shown some interesting advantage as with intermediate binding capacity with metal ion it can be effectivly utilized for many areas including catalysis, material sciences and biological applications. A careful tuning of the azole based ligands can produce compounds with improved activity. Utilization of heterocyclic ligands in coordination chemistry has shown remarkable applications in medicinal chemistry, material chemistry [1,2], organic synthesis ,gas generating composition [3], biochemical, pharmaceutical, catalytic [4], medicinal chemistry [5] and anti-corrosion species [6]. Among the heterocyclic ligands tetrazole have generated a great interest owing to their ability to coordinate in different modes to contribute in synthesizing mono- and polymeric metal complexes (Figure 1.1).



Figure 1.1 Structure of monomeric complex

However, though interactions of various tetrazoles ligands with group 10 transition metals have been widely investigated by researchers [4, 7–9], the chemistry of other transition metal complexes with tetrazolato ion are less developed. Tetrazole ligands have the unique ability to form bridging coordination bond which leads to formation of multidimensional coordination polymers exhibiting great structural diversity associated with interesting catalytic, optical, magnetic, membrane and absorption properties. Both tetrazole and its derivatives, normally the 5-substituted derivatives, can act as polydentate ligands exhibiting several coordination modes. 1- and 2-substituted tetrazoles are often used for the construction of coordination networks [10–12]. Different transition metals have shown their ability to form wide range of tetrazole compounds in which octahedral, tetrahedral, square planar and square pyramidal geometry are predominant.

Synthesis of tetrazolato complexes mainly take place in two different approaches. Tetrazoles can be utilized itself as a ligand with a metal precursor or it can be generated in situ by cycloaddition of organonitrile and inorganic azide. In recent years many metal tetrazolato complexes have been generated using the [2+3] cycloaddition method. However, most of tetrazoles complexes are associated with group 10 transition metals, particularly platinum and palladium. Apart from those some limited examples of some other transition metal elements of tetrazolato complexes are reported [13, 14]. Our interest in tetrazoles concerns their use as precursors for the formation of new functionalized polytetrazole macromolecules, which have potential applications as catalyst for benzene oxidation. The direct oxidation of benzene to phenol [15, 16] has recently attracted much attention and has been investigated extensively as a promising route for phenol production. This is because of the inertness of C-H bonds especially, in saturated hydrocarbons, where the bond energy amount to 400 kJmol⁻¹[17]. Secondly a one-step process for the production of any molecule is more advantageous. Generally phenol is produced industrially mainly by a three-step reaction process with low phenol yields, low atomic efficiency and the formation of explosive intermediates [18].

1.2 History and preparation of the tetrazoles

Tetrazoles were discovered more than one hundred years ago by swedish chemist Bladin in 1885. First report was in 1901 wherein 5aminotetrazole was made by the reaction of hydrazoic acid (HN₃) with cyanamide. Treatment of hydrazoic acid with cyanide results in the formation of 5-substituted tetrazole derivatives which was first reported by Hantzsch and Vagt [19]. The [3+2] cycloaddition between hydrazoic acid and cyanide derivatives is a well known and one of the most efficient routes [20]. Unfortunately, hydrazoic acid is highly explosive, toxic, and volatile. Practically, the use of sodium azide as substrate in place of the hydrazoic acid would be efficient and convenient; however, the [2+3] cycloaddition energy barrier is significantly lower with hydrazoic acid than with azide ion. To overcome this energy limitation, reactions have been designed either to control the hydrazoic acid formation [21] or to use a large excess of azide ions in the presence of metal catalysts or strong Lewis Acids. In 2001, Demko and Sharpless [22] established that, using zinc salt as a catalyst, the cycloaddition reaction facilitated. The corresponding tetrazole obtained at high temp. 100° C with reaction time 6 to 48 h (Scheme 1.1). That is the safer and exceptionally efficient process for transforming nitriles into tetrazoles in water; the only other reagents are sodium azide and a zinc salt.

Scheme 1.1 Synthesis of tetrazole by eco- friendly way.

The most convenient route to 5-substituted 1H-tetrazoles is the addition of azide ion to nitriles [23]. There are three more methods by which this transformation can be carried out; those that make use of tin or silicon azides[24], those that use strong Lewis acids and those that are run in acidic media [25,26]. However, these traditional cycloaddition reactions have some drawbacks like expensive and toxic metals and severe water sensitivity. The few other methods that seek to avoid hydrazoic acid liberation during the reaction, by avoiding acidic conditions, require a very large excess of sodium azide. In addition, all of the known methods use organic solvents, in particular, dipolar aprotic solvents such as DMF. So, the most convenient way of preparation of tetrazoles by [2+3] cycloaddition reaction between metal ligated azide and cyanide group using DMF as a solvent

1.3 Applications of tetrazoles :

As tetrazole possess so much versatility in coordination, they serve a wide range of applications which are mentioned below:-

1.3.1 Medicinal chemistry:

Tetrazole is used as a drug in medicinal chemistry; it is most frequently used as a nonclassical bioisostere of carboxylic acid moieties in biologically active molecules [27]. Bioisosterism is a smart method used in drug design to rationally modify the structure of the lead compound using bioisosteres [28, 29] which could enhance the desired biological or physiological properties without significant changes in chemical structure. Tetrazole exhibiting a planar structure, can stabilize a negative charge by delocalizing electron. This distribution of charge increases the interaction of receptor- ligand. In addition, tetrazolate anions are more lipophilic which benefits the passing of drug molecules through cell membranes. More over the nitrogen rich tetrazoles provide more opportunities to form hydrogen bonds with the recognition sites of receptor. However, the main motto for development of tetrazole-containing drugs is to improve the ADME (Absorption, Distribution, Metabolism, and Elimination).





Antiflammatory



treatment of diabetes



Aganist ulcer caused by acetic acid derivatives

Figure 1.2: Selected drugs in the tetrazole series.

1.3.2. Tetrazole frameworks in gas storage

In tetrazole there are four donor nitrogen atom. Due to the incorporation of accessible nitrogen-donor groups into the pore walls of porous materials this research has received considerable attention as materials for strategic gas absorbent such as CO₂ and H₂. They dramatically affect the gas uptake capacity and selectivity of the materials, especially for CO₂ capture on account of the dipolequadrupole interactions between the polarizable CO₂ molecule and the accessible nitrogen site. Literature reports also indicated that the incorporation of accessible nitrogen-donor groups into the pore walls of the porous materials could enhance the CO₂ uptake capacity and selectivity [2, 30-33]. A 3-D -NH functionalized zeolitic tetrazolate framework (Cd-4TP) has been reported (Figure 1.5). Cd-4TP shows high $CO_2(273K)$ and $H_2(77K)$ uptake due to the presence of tetrazole nitrogen [34].



Figure 1.3 Gas adsorption isotherms of Cd-4TP-1. (a) N_2 adsorption isotherms for Cd-4TP-1 (b) Hydrogen adsorption isotherms for Cd-4TP-1 at 77 K and 1 atm pressure. (c) CO₂ adsorption isotherms for Cd-4TP-1 at 273 K and 1 atm pressure. The filled and open circles represent adsorption and desorption, respectively. (d) Crystal structure of Cd-4TP-1 MOF.

1.4 [2+3] cycloaddition reaction

[2+3] cycloaddition reaction also known as click reaction was introduced by K. B. Sharpless in 2001 to describe reactions that are high yielding, wide in scope, create only byproducts [35]. The general application of 1,3-dipoles in chemistry was first established by Huisgen in the 1960s [36]. 1, 3-dipolar cycloaddition has been used in the construction of 5-membered ring systems. This concept was developed in parallel with the interest within the pharmaceutical, materials, and other industries in capabilities for generating large libraries of monomeric, polymeric and bridging compounds for screening in discovery research.

The 1,3-dipolar cycloaddition is a chemical reaction between a 1,3dipole and a dipolarophile to form a five-membered ring. Currently, 1,3-dipolar cycloaddition is an important route to the regioand stereoselective synthesis of five-membered heterocycles and their ring-opened acyclic derivatives.



Scheme 1.2: Schematic representation of [2+3] cycloaddition.

1.5 Generation of tetrazole ligand

In recent years many metal tetrazolate complexes have been synthesized using the [2+3] cycloadditions of metal ligated azides and nitriles. There are few examples of tetrazolate complexes, however in most of these cases the tetrazole itself has been used as the ligand [37]. It has been generated by in situ [2 + 3] cycloaddition of an azide and a nitrile in a hydrothermal process [38]. The advantage of the in situ method is that all the reactions take place in one step from the reactants. Secondly it is highly efficient, and environmentally friendly. There are many other methods for synthesis of tetrazole complexes (1) by classical controlled method (2) uncontrolled synthesis of tetrazole complexes by solvothermal, microwave and refluxing methods. Out of these methods microwave and refluxing ways are mainly used.

1.5.1 Generation of tetrazole as ligand by microwave irradiation method

The cycloaddition reaction has been carried out in mild condition by irradiating the solution of metal complex in the presence of organonitriles by microwave reactor. DMF has been used as reaction medium and it takes about 3h at 130° C. This method greatly accelerates the reactions, leading to the products only in 3 h to give the comparable yield which can be obtained after 12 h under conventional heating (Scheme 1.3) [39].



Scheme1.3 Schematic presentation for the formation of cobalt(III)-tetrazolato complex by microwave method.

1.6.2 Generation of tetrazole ligand by refluxing method

Treatment of the diazido platinum(II) complex with different organonitriles in refluxing DMF yielded tetrazolato complex bis(pyridyltetrazolato)platinum complex isolated as white crystalline solids in moderate yields (ca. 60-55%) [40–46]. The tetrazolato complexes were obtained via [2+3] cycloaddition of the organonitriles with the ligated azides (scheme 1.4).



Scheme 1.4 Synthesis of [Pt (N₄CR)₂(PPh₃)] by refluxing method.

<u>1.6 Organization of thesis:</u>

In continuation of investigation on metal ligated cycloaddition reactions between different organonitriles and coordinated azide and aiming to contribute to the development of the synthesis of novel 5-substituted tetrazole complexes, preferably using refluxing conditions, synthesis of novel Cu(II) and Co(II) complexes have been taken up with the 4-cyanobenzonitrile (pytz) and 4-chlorobenzonitrile (4-Clptz) keeping in the mind to explore potentially versatile coordination nature of these ligands.

Chapter 2: This chapter includes review of past work and project motivation:

Chapter 3: This chapter includes materials, instruments and the experimental procedure used to synthesize the metal tetrazole complexes. It also includes experimental techniques employed to study their BSA binding properties and catalytic properties.

Chapter 4: In this chapter results have been discussed which were obtained after the synthesis and application study of the metal complexes.

Chapter 5: This chapter concludes the described work and also looks for possible future scope and applications.

Chapter 2

Review of past work and project motivation

Interactions of tetrazole ligands with different metal atoms have been widely investigated by different researchers in the past few years [47]. Tetrazoles are very interesting ligand in coordination chemistry because of its versatile binding sites (scheme 2.1), comparable pKa values with carboxylic acids and possibility of formation of polynuclear metal complexes.



Scheme 2.1 Different binding sites of tetrazoles

Metal tetrazole complexes have a broad area of application in catalysis, gas adsorption material and luminescent materials. These complexes have shown applications in the area of biology by targeting different biomolecules as well as some complexes have shown magnetic susceptibility properties too.

2.1 Catalytic activity:

Metal-tetrazolato complexes have been extensively used for catalysis in last few years. Mukhopadhyay et al has reported synthesis of Cutetrazole complexes by the cycloaddition reaction between sodium azide and 4-cyanopyridine in the presence of a copper (II) salt and their catalytic properties towards the oxidation of secondary alcohols under mild and green conditions [figure 2.1].



Figure 2.1 Synthesis of Cu (II)-tetrazole complexes.

Investigations on their catalytic properties disclosed that reported complexes act as active catalyst precursors towards the microwaveassisted homogeneous oxidation of secondary alcohols (1phenylethanol, cyclohexanol, 2-hexanol, 3-hexanol, 2-octanol and 3octanol) with tert-butylhydroperoxide, leading to the yields of the corresponding ketones up to 86% (TOF = 430 h⁻¹) and 58% (TOF290 h⁻¹) in the oxidation of 1-phenylethanol and cyclohexanol, respectively, after 1 h under low power (10 W) microwave irradiation, and in the absence of any added solvent or additive. Again metal tetrazole complexes have shown catalytic activity towards different coupling reactions. Yang et al has reported synthesis of tetrazole ligand stabilized NHC-Pd complexes from the dimeric precursor $[Pd(\mu-Cl)(Cl)(NHC)]_2$ with different tetrazole ligands and their promising catalytic activity in the coupling reactions [48].

2.2 Gas Storage:

Metal tetrazolato complexes have shown great gas adsorption properties as well. Banerjee et al has reported syntheses of Cu(II) complexes with predesigned ligands 4-(1H-tetrazole-5-yl)benzoic acid (4-TBA) and 2-fluoro-4-(1H-tetrazole-5-yl)benzacid(2F-4-TBA),which have shown N₂ and CO₂ adsorption property at 298K (figure 2.2) [34].



Figure 2.2 N_2 adsorption isotherms below 1.0 bar for Cu-TBA-1 (blue) and Cu-TBA-2 (red) at 77 K. Filled and open circles represent adsorption and desorption data, respectively. Pores available for N_2 gas adsorption in the Cu-TBA-1 and -2 are shown with a yellow ball in the inset.

<u>2.3 Magnetic properties:</u>

There are several reports where metal tetrazolato complexes have shown interesting magnetic properties. Mukhopadhyay et al investigated the reaction of a mono-azido nickel compound $[Ni(L)(N_3)]$ [HL=chloro-2-{(2-(dimethylamino)ethylimino)methyl}phenol] with various organonitriles and their magnetic properties [figure 2.3] [49].



Figure 2.3 Antiferromagnetic interactions between the nickel centres

Song et al reported preparation of Co-tetrazole complexes using 4substituted tetrazole–benzoate ligands, 4-aminophenyl-1H-tetrazole (HL¹) and 4-carboxyphenyl-1H-tetrazole (HL²). The prepared complexes have shown spin-canted antiferromagnetism at low temperature [50].

2.4 Luminescence properties:

Metal tetrazolato complexes have shown significant luminescence properties as reported in literature. Bunzli et al. described that Anionic tridentate benzimidazole-pyridine-tetrazolates evolves as a new class of "soft" nitrogen chromophore ligands that can be coordinated to lanthanide to give luminescent and redox-active complexes. The ligands form neutral complexes with lanthanum and europium and efficiently sensitize the red luminescence of europium. Excitation spectra of the europium complexes in the solid and DCM solution upon monitoring the ${}^{5}D_{0}\rightarrow{}^{7}F_{2}$ emission band. The samples were optically thick (saturated signal) at <375 nm. The sharp lines at 395 nm and 463 nm are the ${}^{5}L_{6}\leftarrow{}^{7}F_{0,1}$ and ${}^{5}D_{2}\leftarrow{}^{7}F_{0,1}$ transitions of Eu(III) [51].



Figure 2.4 Luminescence property of Eu(III)-tetrazole complexes

Again Stagni et al has illustrated protonation deprotonation protocol for Re-tetrazolato complexes for their luminescent properties [52].



Figure 2.5 Protonation- deprotonation scheme

2.5 Biological applications:

The binding mode of different biomolecules with tetrazolato metal complexes has attracted much attention recently because of their site specific binding properties and wide range of applications [53]. Mukhopadhyay et al. has reported synthesis of two new mononuclear water soluble copper(II) complexes, $[Cu{(5-pyrazinyl)tetrazolate}_2]$ (1,10-phenanthroline)] and [Cu{(5-pyrazinyl)tetrazolate}(1,10phenanthroline)₂](NO₃) (N₃), using the metal mediated [2 + 3]reaction between copper bound cycloaddition azide and pyrazinecarbonitrile [54] (figure 2.6).



Figure 2.6 Molecular structure of $[Cu(phen)(pzta)_2](H_2O)$ and $[Cu(phen)_2(pzta)](NO_3)$

Both the complexes have shown promising interactions with Bovine Serum albumin (BSA) as well as ct DNA by quenching the fluorescence intensity with increased concentration of the sample [figure2.7].



Figure2.7FluorescencequenchingofBSAbycomplex[Cu(phen)(pzta)_2](H_2O)

Again Komeda et. Al. reported synthesis of antitumor-active tetrazolato-bridged dinuclear platinum(II) complexes and their interaction with DNA by circular dichroism (CD) and fluorescence microscopy (FM) [54] figure 2.8.



Figure 2.8: Tetrazolato bridged dinuclear platinum complex against pancreatic cancer.

Studying all these previous reports on metal tetrazole complexes, synthesis of new tetrazolato complexes of copper and cobalt metal have been taken up. In case of Cu(II), two known copper complexes $[Cu(bipy)_2(N_3)_2]_n$, $[Cu(phen)(N_3)_2]_n$ have been prepared as the starting metrial according to the reported procedure [55,56] and in case of Co(II), new complex, $[Co(dm_2en)_2(N_3)_2]$ [dm₂en =N.N'а dimethylethylenediamine] have been utilized. These complexes are then allowed to react with different organonitriles e.g. benzonitrile, 4cyanopyridine and 4-chlorobenzonitrile to furnish tetrazolato complexes. BSA binding activity and benzene oxidation property have also been carried out for the prepared complexes.

Chapter 3

Experimental Section

3.1 Reagent and Chemicals:

All the chemicals and solvents used in the experiments are commercially available; reagents are of analytical grade and used without further purification. All experiments were carried out in an open atmosphere. Cu (II) nitrate trihydrate, Co(II) nitrate hexahydrate, 1,10-phenanthroline mono hydrate, 2,2–bipyridyl, sodium azide, 4cyanopyridine, 4-chlorobenzonitrile and benzonitrile were purchased from Merck-India Chemical Company. Benzene was purchased from Sigma and used without further purification.

Caution! Azide and tetrazolate compounds are potentially explosive. Only a small amount of material should be prepared and handled with care.

3.2 Methods and Instrumentation

Elemental analysis for Carbon, Hydrogen and Nitrogen were performed on a ThermoFlash 2000 elemental analyzer. Infrared spectra were recorded in the 4000–400 cm⁻¹ with a BRUKER TENSOR 27 instrument using KBr pellets. Mass spectrometric analyses were done on Bruker-Daltonics, microTOF-Q II mass spectrometer. Electrospray mass spectra (ESI-MS) were run with an ion-trap instrument (Bruker-Daltonics, microTOF-Q II Mass Spectrometer) equipped with an electrospray ion source. NMR spectra were recorded on a BrukerAvance 400 spectrometer. Chemical shifts are referenced to internal solvent resonances and reported relative to tetramethylsilane (TMS).

The catalytic oxidations of benzene were carried out in an open atmosphere in a 50 mL round-bottom flask fitted to a water condenser.
Gas Chromatographic(GC) analyses were performed in a FISONS Instruments GC 8000 series gas chromatograph with a FID detector and a capillary column (DB-WAX, column length: 30 m; internal diameter: 0.32 mm) and the Jasco-Borwin v.1.50 software. The temperature of injection was 240 °C. The initial temperature was maintained at 100 °C for 1 min, then raised 10 °C/min to 180 °C and held at this temperature for 1 min. Helium was used as the carrier gas. GC-MS analyses were carried out using a Perkin Elmer Clarus 600 C instrument (He as the carrier gas). The ionization voltage was 70 eV. Gas chromatography was conducted in the temperature-programming mode, using a SGE BPX5 column (30 m×0.25 mm×0.25 μ m). The internal standard method was used for product quantification.

3.3 X-ray crystallography

Single crystal X-ray structural analyses of Complexes **1** and **3** were performed on a CCD Agilent Technologies SUPER NOVA diffractometer. Data for the complex **1** and **3** were collected at 293(2) K using graphite-monochromatic MoK α radiation ($\lambda \alpha$ = 1.54184 A). The CrysAlisPro CCD software was used for the data collection. The strategy for the data collection was evaluated by using the CrysAlisPro CCD software. The structures were solved by direct methods using the SHELXS-97 and refined using full matrix least-squares with the SHELXL-97 refining on F².

The positions of all the atoms were obtained by direct methods. All non-hydrogen atoms were refined anisotropically. The remaining hydrogen atoms were placed in geometrically constrained positions and refined with isotropic temperature factors, generally 1.2Ueq of their parent atoms. The contribution of solvent electron density was removed by the SQUEEZE routine in PLATON [57]. The crystal and refinement data were summarized in Table 4.1, and selected bond distances and bond angles for **1** and **3** are depicted in Tables 4.2 and 4.3 respectively.

3.4 Synthesis of metal azide and tetrazolato complexes:

3.4.1 Synthesis of Copper (II) azide complexes

The copper azide complexes $[Cu(bipy)(N_3)_2]_n$ and $[Cu(phen)(N_3)_2]_n$ were prepared according to the previously reported procedure [55,56]by reacting 0.24g (1mmol) of Cu(NO₃)₂.3H₂0 with 0.20g (1mmol) of HL{HL= 1,10 phenothroline / 2,2-bipyridyl} by addition of 0.13g (2 mmol) of NaN₃ in 30 mL of methanol for 2h. The green precipitate formed upon complexation was removed *via* filtration. The resulting precipitate was filtered and washed several times with ether and analyzed.

3.4.2 Synthesis of $[Cu_2(bipy)_2(4-Clptz)_4](1)$

The dinuclear complex **1** was prepared by reacting 0.11 g (0.37 mmol) of $[Cu(bipy)(N_3)_2]_n$ with 0.40g (3 mmol) of 4-chlorobenzonitrile in 20 mL of DMF. The reaction mixture was stirred under reflux condition for 12 hrs at 130° C. The solvent was removed *in vacuo* and the resulting oily residue was treated with diethyl ether to obtain a greenish blue powder. The resulting residue was allowed to stand for crystallization at 298K. Upon very slow evaporation of the solvent, blue coloured needle like crystal was obtained after 20-21 days (reaction scheme 3.1).

Anal.Calcd.for Complex 1: $C_{24}H_{16}Cl_2CuN_{10}$: C 49.79; H 2.79; N 24.20%. Found: C 50.02; H 2.98; N 24.78%. ESI-MS (positive ion, CH₃OH) m/z: 577.1 [M]⁺ (calcd 577.02). IR (cm⁻¹, KBr, selected peak): 3438(s), 3070(w), 1661(s), 1605(s), 1503(m), 1437 (s) , 1317(m), 1251(w), 1170(w), 1090(m), 1008(m).

3.4.3 Synthesis of [Cu₂(bipy)₂(pytz)₄](2)

The dinuclear complex **2** was prepared by reacting 0.11g (0.37 mmol) of $[Cu(bipy)(N_3)_2]_n$ with 0.40g (3 mmol) of 4-cyanopyridine in 20 mL

of DMF. The reaction mixture was stirred under reflux condition for 12 hrs at 130° C. The solvent was then removed in vacuo and the resulting oily residue was washed several times with diethyl ether to obtain a violet blue powder (reaction scheme 3.1).

Anal.Calcd.for Complex **2**: C₄₄H₃₂Cu₂N₂₄: C 51.61; H 3.15; N 32.83%. Found: C 52.52; H 3.22; N 32.63%. ESI-MS (positive ion, CH₃OH) m/z: 876.02 [M]⁺ (calcd 876.14). IR (cm⁻¹, KBr, selected peak): 3429(s), 2924(s) ,1677(s), 1517(m), 1420(s), 1260(w), 1296(w), 1219(w), 1072)(w), 1039(m).



Scheme 3.1: Schematic representation for the synthesis of complexes $[Cu_2(bipy)_2 (4-Clptz)_4]$ (1) and $[Cu_2(bipy)_2(pytz)_4](2)$ using different organonitriles.

3.4.4. Synthesis of [Cu₂(phen)₂(4-Clpytz)₄] (3)

The dinuclear complex **3** was prepared by reacting 0.11g (0.37 mmol) of $[Cu(phen)(N_3)_2]_n$ with 0.41g (3 mmol) of 4-chlorobenzonitrile in 20 mL of DMF. The reaction mixture was stirred under reflux condition for 12 hrs at 130° C. The solvent was removed in vacuo and the resulting oily residue was treated with diethyl ether to obtain a

greenish blue powder. The resulting residue was allowed to stand for crystallization at 298K. Upon very slow evaporation of the solvent, blue coloured needle like crystal was obtained after 20-21 days (reaction scheme 3.2).

Anal.Calcd. for Complex-**3**: $C_{29}H_{23}$ Cl₂CuN₁₁O: C 51.61; H 3.15; N 32.83%. Found: C 52.52; H 3.22; N 32.63%. ESI-MS (positive ion, CH₃OH) m/z: 699.3[M+Na]⁺ (calcd 699.08). IR (cm⁻¹, KBr, selected peak): 3430 (s), 2923 (m), 1610 (s), 1422 (m), 1026 (w).

3.4.5 Synthesis of $[Cu_2(phen)_2)(pytz)_4]$ (4)

The dinuclear complex **4** was prepared by reacting 0.12g (0.37 mmol) of $[Cu(phen)(N_3)_2]_n$ with 0.30 g (3 mmol) of 4-cyanopyridine in 20 mL of DMF. The reaction mixture was stirred under reflux condition for 12 hrs at 130° C. The solvent was then removed in vacuo and the resulting oily residue was washed several times with diethyl ether (reaction scheme 3.2).

Anal.Calcd.for Complex-4 : $C_{44}H_{32}Cu_2N_{24}$: C 53.78.61; H 3.01; N 31.36%. Found: C 53.02.; H 2.93.; N 32.2%. ESI-MS (positive ion, CH₃OH) m/z: 536.1 [M]⁺ (calcd 536.01). IR (cm⁻¹, KBr, selected peak): 3445(s), 2924(w), 1631(s), 1515(m), 1428(m), 1375(s), 1219(w), 1144(w),1000(w).





Scheme 3.2: Schematic representation for the synthesis of complexes $[Cu_2(phen)_2(4-Clptz)_4](3)$ and $[Cu_2(phen)_2(pytz)_4](4)$ using different organonitriles.

Synthesis of Co(II) complexes:

3.4.6. Synthesis of $[Co(Me_2en)_2(N_3)_2]$ (5)

The mononuclear complex **5** was prepared by reacting of 0.14 g of $Cu(NO_3)_2 \cdot 6H_2O$ (0.5mmol) with 1 mmol of N ,N' dimethylethylenediamine in 20 mL of DMF. The reaction mixture was stirred at room temperature for 10 min. After 10 min. 0.06 g of NaN₃ (1 mmol) (in 10ml methanol) was added dropwise with constant stirring until dark brown precipitate was obtained. It was stirred for 2 h and then filtered. The resulting precipitate was washed several times with diethyl ether (reaction scheme 3.3).

Anal.Calcd.for Complex **5**: $C_8H_{24}CoN_{11}O_3$ (382.14): C 25.20; H 6.34; N 40.41 O 12.59%. Found: C 25.02.; H 6.93.; N 39.26%. ESI-MS (positive ion, CH₃OH) m/z: 319.2 [M]⁺ (calcd 319.28). IR (cm⁻¹, KBr, selected peak): 3448(s), 2925(w), 2052(s), 1635(m), 1383(s).



Scheme 3.3 Schematic representation for the synthesis of complexes5

3.4.7. Synthesis of [Co(Me₂en)₂(4-Clptz)₂] (6)

The mononuclear complex **6** was prepared by reacting 0.12g (0.37 mmol) of complex 5 with 0.14 g (1.00 mmol) of 4-chlorobenzonitrile in 20 mL of DMF. The reaction mixture was stirred under reflux condition for 12 hrs at 130° C. The solvent was then removed in vacuo and resulting oily residue was treated with diethyl ether (reaction scheme 3.4).

Complex6: $C_{22}H_{32}C_{21}CoN_{13}O_3$: m/z: 412.9 [M]⁺ (calcd 413.01). IR (cm⁻¹, KBr, selected peak): 3439(s), 2928(w), 1663(s), 1442(s), 1382(s), 1092(m), 837(m).

3.4.8. Synthesis of [Co(Me₂en)₂(4-pytz)₂] (7)

The mononuclear complex **7** was prepared by reacting 0.11g (0.37 mmol) of complex 5 with 0.10 g (1.00 mmol) of 4-cyanobenzonitrile in 20 mL of DMF. The reaction mixture was stirred under reflux condition for 12 hrs at 130° C. The solvent was then removed in vacuo and resulting oily residue was treated with diethyl ether (reaction scheme 3.4).

Complex-7: $C_{20}H_{32}CoN_{15}O_3$: ESI-MS (positive ion, CH₃OH) m/z: 529.1 [M]⁺ (calcd 528.01). IR (cm⁻¹, KBr, selected peak): 3439(s), 2928(w), 1663(s), 1442(s), 1382(s), 1092(m), 837(m).

3.4.9 Synthesis of [Co(Me2en)₂)(4-pytz)₂] (8)

The mononuclear complex **8** was prepared by reacting 0.11g (0.37 mmol) of complex 5 with 0.10 g (1.00 mmol) of benzonitrile in 20 mL of DMF. The reaction mixture was stirred under reflux condition for 12 hrs at 130° C. The solvent was then removed in vacuo and resulting oily residue was treated with diethyl ether (reaction scheme 3.4).

Complex-8: C₂₂H₃₄CoN₁₃O₃: ESI-MS (positive ion, CH₃OH) m/z: 442.1. IR (cm⁻¹, KBr, selected peak): 3425(s), 1662(s), 1379(s), 1102 (m), 835(m).



Scheme 3.4 Schematic representation for the synthesis of complex 6, 7 and 8.

3.5 Oxidation of benzene using Copper tetrazolato complex:

The catalytic oxidations of benzene were carried out in 25mL reaction flask under refluxing conditions. To the reaction vessel, 0.01 g of catalyst was suspended in acetonitrile (3mL). To it, benzene (1.2 mmol), and hydrogen-peroxide (0.083 mol) were added. The reaction mixture was heated to 70 $^{\circ}$ C and stirred vigorously for 3 h. Solution aliquots

were taken and analysed by GC. The catalytic oxidation of benzene leads to multiple reaction products phenol, catechol, benzoquinone (reaction scheme 3.5). The major products of the reaction was phenol. Blank experiments in the absence of catalysts, were performed under the studied reaction conditions.



Scheme 3.5: Oxidation of benzene to phenol ,benzoquinone and catechol with hydrogen peroxide catalysed by the copper complexes 1-4

3.6 BSA interaction study

The protein binding studies of these complexes were investigated using bovine serum albumin (BSA) by means of fluorescence spectroscopy recording excitation at 295 nm and the corresponding emission at 340 nm. The excitation and emission slit widths and scan rates were kept constant throughout the experiment. A 10 μ M stock solution of BSA was prepared using Tris-HCl buffer (pH ~7.4) solution and stored at 4°C for further use. Stock solutions of complexes 1-4 (1 mM in strength) were also prepared in Tris-HCl buffer and 5% DMSO. Fluorescence intensity of 2 mL stock solution of BSA was measured and recorded as blank. Thereafter it was titrated by successive additions of 10 μ L of the respective stock solution of complexes (upto $\mu L).$ The fluorescence data was further analyzed by the Stern–Volmer equation.

Chapter 4

Results and Discussion

4.1 Synthesis and characterization:

The metal polymer complex $[Cu(bipy)(N_3)_2]_n$ and $[Cu(phen)(N_3)_2]_n$ were prepared according to reported methods [55,56] by stirring $Cu(NO_3)_2.3H_2O(0.24g,1mmol)$ and $L^1(1mmol)\{L^1=1,10\ phenothroline\}$ / 2,2-bipyridyl} with NaN₃ in 30 mL of methanol for 2 h. Upon reaction of $[Cu(bipy)(N_3)_2]_n$ with 4-chlorobenzonitrile (1:2 molar ratio) in DMF, a violet coloured solution was obtained, which upon concentration and slow evaporation furnished blue needle shaped crystals of $[Cu_2(bipy)_2 \{5-(4-chlorophenyl)tetrazolato\}_2]$ (complex 1) (Scheme 3.1). However, using of $[Cu(phen)(N_3)_2]_n$ with 4chlorobenzonitrile and following a similar procedure like the synthesis of complex 1 resulted in the formation of blue colour crystal of $[Cu_2(phen)_2{5-(4-chlorophenyl)tetrazolato}_2]$ (complex 3) (Scheme 3.2). For preparation of complexes 2 and 4, 2:1 molar ratio of organonitrile to metal ligated azide was used in the same reaction conditions as those employed for complex 1 (Scheme 3.1 and 3.2). The chelating bidentate tetrazolato completes the octahedral geometry surrounding the copper centre and helps to break down the polymeric complex to dimeric entity. In case of cobalt tetrazole, new cobalt (III) diazido complex (5) was synthesized first and it was utilized for tetrazolato ligand synthesis. The ratio between metal (cobalt) to azide is 1:2 for complex 5 which has been further used for preparation of different tetrazolato complexes. Upon reaction of complex 5 with different organonitriles 4-chlorobenzonitrile, 4-cyanopyridine and benzonitrile (1:2 molar ratio) in DMF, a reddish-brown coloured solution was obtained.

All the complexes have been characterized by various spectroscopic technique. Both complex 1 and 3 have been characterized by IR and ESI-MS spectroscopy, elemental analyses and single crystal X-ray

crystallography. Complexes 2 and 4 have been characterized by IR, elemental analysis and ESI-MS spectroscopy. Crystals could not be obtained for complexes 5, 6, 7 and 8. However compositions of these complexes have been ascertained from IR and ESI-MS spectroscopy and elemental analyses.

4.1.1. FT -IR spectra:

Synthesis of tetrazolato complexes have been monitored by IR spectroscopy. Disappearance of azide stretching band at about 2047 cm⁻¹ have been closely followed with progress of reaction in refluxing condition. A new band was obtained for complexes 1-4 in the range of 1610-1678 cm⁻¹ in IR spectra (Figure 4.1- 4.4) indicating the formation of tetrazolato moiety [58,59] and there is no azide in these complexes. The IR spectrum of complex 5 displays a strong band at 2050 cm⁻¹ due to the asymmetric stretching vibration of the coordinated azido group. The band at $\bar{\nu} = 1383$ cm⁻¹ for complex 5 indicates presence of free nitrate ligand [53] in complex , whereas for complexes 6-8, the same band occurs at $\bar{\nu} = 1383$ cm⁻¹, 1382 cm⁻¹, 1378 cm⁻¹, and 1379 cm⁻¹ respectively. Complexes 6-8 show a strong band at around 1650 cm⁻¹, which can be attributed to the coordinated tetrazole group.



Figure 4.1 IR spectrum of complex



Figure 4.2 IR spectrum of complex 2



Figure 4.3: IR spectrum of complex 3.



Figure 4.4 : IR spectrum of complex 4.



Figure 4.5 IR spectrum of complex 5.



Figure 4.6.IR spectrum of complex 6.



Figure 4.7: IR spectrum of complex 7.



Figure 4.8: IR spectrum of complex 8

4.1.3. Mass spectra:

In the ESI-MS of all the bis(tetrazolato) complexes the molecular ion peaks have been observed, confirming the presence of the bistetrazolate ligands in the metal complexes. The ESI-MS spectrum for the complex 1-4 show peaks at 577.1, 876.02, 699.3, and at 536.1 which corresponds to the cationic complex of [Cu(bipy){5-(4chlorophenyl)-tetrazolato $_{2}+H^{+}$, $[Cu_2(bipy)_2){5-(4-pyridyl)$ tetrazolato $]_3]^+$, [Cu(phen) $\{5-(4-chlorophenyl)-tetrazolato\}_2+Na]^+$, and $[Cu_2(phen){5-(4-pyridyl)-tetrazolato}_2+H]^+$, respectively (Figure 4.9-4.12). However the ESI-MS spectra for the complex 5-8 show the peaks at 319.2, 601.1, 529.1 and 529 which corresponds to the molecular ion peak of $[CoL_2(N_3)_2]^+$, $[CoL_2\{5-(4-chlorophenyl)$ tetrazolato $_{2}^{+}$, $[CoL_{2}{5-(4-pyridyl)-tetrazolato}_{2}^{+}$ and $[CoL_{2}{5-(4-pyridyl)-tetrazolato}_{2}^{+}$ {L= pyridyl)-tetrazolato $\{2\}^+$ N,N'-dimethylethylenediamine} respectively (Figure 4.13-4.16).



Figure 4.9: ESI-MS spectrum of complex 1



Figure 4.10: ESI-MS spectrum of complex 2



Figure 4.11: ESI-MS spectrum of complex 3



Figure 4.12: ESI-MS spectrum of complex 4



Figure 4.13: ESI-MS spectrum of complex 5



Figure 4.14: ESI-MS spectrum of complex 6



Figure 4.15: ESI-MS spectrum of complex 7.



Figure 4.16: ESI-MS spectrum of complex 8

4.1.4. X-ray crystallography:

The nature of the complexes 1 and 3 have been unambiguously determined by single–crystal X-ray crystallography. Two copper ions are found to be forming dimeric compound with penta-coordinated geometry around the metal centre through N donor sites. The details of data collection conditions and parameters of refinement process are given in Table 4.3. Complexes 1 and 3 crystallizes in the triclinic system and space group P-1. However, the selected bond lengths and angles are given in Table 4.2 and 4.3.

Table 4.1 Crystal data and structure refinement parameters for complex 1 and 3

Complex	1	3	
Empiricalformula	$C_{24}H_{16}Cl_2CuN_{10}$	$C_{29}H_{23}Cl_2CuN_{11}O$	
Formula weight	578.92	676.02	
Crystal system	Triclinic	Triclinic	
Space group	P -1	P -1	
a (Å)	10.3605(6)	9.2379(3)	
b (Å)	11.9690(6)	11.0834(4)	
c (Å)	13.2453(4)	14.8844(7)	
α (°)	115.420(4)	92.250(4)	
β (°)	101.677(4)	94.780(3)	
γ	94.725(4)	100.985(3)	
V [Å ³]	1425.92(13)	1488.48(10)	
λ (Å)	1.54184	1.54184	
ρcalcd (mg m ⁻³)	1.348	1.508	
Z	2	2	
T (K)	293(2)	293(2)	
μ (mm ⁻¹)	3.064	3.061	
F(000)	586	690	
Crystal size (mm ³)	0.260 x 0.190	0.330 x 0.270	
GOF	x 0.130	x 0.210	
θ ranges (°)	1.076	1.055	
Reflections	3.831 - 71.349	4.8740 -70.627	
collected/unique	5398 / 5398	5592/ 4721	
[I>2sigma(I)]	R1 = 0.0539,	R1 = 0.0644,	
R indices (all	wR2 = 0.1681	wR2 =0.1904	

data)	R1 = 0.0584,	R1 = 0.0719,
	wR2 = 0.1731	wR2 =0.206

Table 4.2: Selected bond lengths (Å) and bond angles (°) for complex 1 % (A) = (A) + (A)

Cu(1)-N(2)	1.980(2)	N(2)-Cu(1)-N(6)	90.65(10)
Cu(1)-N(6)	1.996(2)	N(2)-Cu(1)-N(9)	162.53(10)
Cu(1)-N(9)	2.023(2)	N(6)-Cu(1)-N(9)	93.18(10)
Cu(1)-N(10)	2.030(2)	N(2)-Cu(1)-N(10)	91.94(10)
Cu(1)N(7)#1	2.187(2)	N(6)-Cu(1)-N(10)	163.71(10)
Cl(1)-C(12)	1.746(4)	N(9)-Cu(1)-N(10)	79.80(10)
Cl(2)-C(5)	1.754(4)	N(2)-Cu(1)-N(7)#1	98.51(10)
N(1)-C(1)	1.331(4)	N(6)-Cu(1)-N(7)#1	99.11(9)
N(1)-N(2)	1.336(3)	N(9)-Cu(1)-N(7)#1	97.70(9)
N(2)-N(3)	1.318(4)	N(10)-Cu(1)N(7)#1	96.40(9)
N(3)-N(4)	1.316(4)	N(3)-N(2)-Cu(1)	123.9(2)
N(4)-C(1)	1.328(4)	N(1)-N(2)-Cu(1)	124.8(2)
N(5)-C(8)	1.319(4)	N(7)-N(6)-Cu(1)	128.90(19)
N(5)-N(6)	1.340(3)	N(5)-N(6)-Cu(1)	121.32(18)
N(7)Cu(1)#1	2.187(2)	N(6)-N(7)-Cu(1)#1	131.70(19)
N(8)-C(8)	1.330(4)	N(8)-N(7)-Cu(1)#1	119.37(17)

Cu1 N6	1.999(3)	N6 Cu1 N2	88.82(11)
Cu1 N2	2.001(3)	N6 Cu1 N10	171.76(12)
Cu1 N10	2.045(3)	N2 Cu1 N10	88.89(11)
Cu1 N9	2.063(2)	N6 Cu1 N9	98.97(11)
Cu1 N3	2.251(3)	N2 Cu1 N9	161.05(12)
Cl1 C5	1.746(5)	N10 Cu1 N9	93.38(11)
N1 N2	1.332(4)	N6 Cu1 N3	94.83(11)
N2 N3	1.315(4)	N2 Cu1 N3	101.18(11)
N3 N4	1.338(4)	N10 Cu1 N3	93.38(11)
N3 Cu1	2.251(3)	N9 Cu1 N3	95.38(10)
N4 C1	1.334(4)	N3 N2 Cu1	126.9(2)
N5 C8	1.326(4)	N1 N2 Cu1	122.3(2)
N5 N6	1.336(4)	N2 N3 Cu1	131.9(2)
N6 N7	1.317(4)	N4 N3 Cu1	119.7(2)
N7 N8	1.313(5)	N7 N6 Cu1	123.1(2)
N8 C8	1.338(5)	N5 N6 Cu1	126.5(2)
N9 C15	1.321(5)	C26 N9 Cu1	112.0(2)
N9 C26	1.359(4)	C24 N10 Cu1	128.9(2)
N10 C25	1.361(4)	C25 N10 Cu1	112.8(2)]

Table 4.3: Selected bond lengths (Å) and bond angles (°) for complex3

$\underline{4.1.4.1 \text{ Crystal structure of } [Cu_2(bipy)_2 (4-Clptz)_4] (1)}$

The accurate structure of complex **1** was determined by single crystal X-ray crystallographic study. The crystal structure of complex 1 is

shown in figure 4.15. The title compound $[Cu_2(bipy)_2\{5-(4$ chlorophenyl)-tetrazolato $_{4}$ (1) has bridging tetrazolato ligand to generate a dimer and crystallizes in the triclinic system and space group P-1 (Table 4.1). The copper ion are found to be forming dimeric compounds with pentacoordinated geometry surrounding the metal centre. There are two types of tetrazolato ligand: one acting as a terminal ligand and the other exhibiting a bridging ligand in other words, adopting simultaneously asymmetric end-on and end-to-end bridging modes. The bipyridyl molecule acts as a chelating ligand. The bidentate bipyridyl moiety coordinates the copper centres in equatorial plane whereas two tetrazolato ligand make bridged between the copper centre through N²N³ mode. One of the tetrazolato nitrogen coordinate to the basal plane whereas nitrogen from other tetrazole ligand coordinates axially to fulfill the square pyramidal geometry. The fifth position is again occupied by the terazolato nitrogen in monodentate fashion for the both copper centres. The distance between metal and coordination atoms and the angles observed are similar to earlier [54]. The space configuration of five-coordinated complexes could be well defined by the τ value [$\tau = (\beta - \alpha)/60$ where α and β being the two largest coordination angles], $\tau = 0$ for an ideal square pyramid as well as $\tau = 1$ for an ideal triangular bipyramid. For complex **1** the value of τ has been found to be 0.01, thus it forms square pyramidal geometry. Complex 1 has been found to be forming a H-bonded 1D linear and cage chain through C24-H24..... N10 and C15-H15.....N9. Hydrogen bonded interaction among the different molecules induce a cage kind of structure as indicated in figure 4.18 and 4.19.



Figure 4.17: Molecular structure of $[Cu_2 (bipy)_2 (4-Clptz)_4] (1)$ with the atomic numbering scheme.



Figure 4.18: 1-D linear polymeric chain structure of complex 1 closely packed via H-bonding through C24-H24..... N10 and C15-H15.....N9.



Figure 4.19: 1-D cage polymeric chain structure of complex 1 closely packed via H-bonding through through C24-H24..... N10 and C15-H15.....N9.

4.1.4.2 Crystal structure of $[Cu_2(bipy)_2\{5-(4-chlorophenyl)-tetrazolato\}_4(3)$

Complexes 3 crystallizes in the triclinic system and space group P-1. It consists of two Cu(II) ions consisting of two bridging tetrazole , two terinal tetrazole and two phenothroline acting as chelating ligand in two different metal center showing five coordination site (Figure 4.20). The chelating bidentate phenothroline moiety coordinates the copper centre in equatorial plane whereas two tetrazolato ligand make bridge between the copper centre through N², N³ mode. One of the tetrazolato nitrogen coordinates to this basal plane whereas nitrogen from other tetrazole ligand coordinates axially . All are coordinated to the metal centre through N-atom resulting in the expected distorted square pyramidal geometry (τ_5 =0.17). All the bond distances and bond angles are similar to earlier report in literature. The bond angles reveal that complex 2 occurs in distorted square pyramidal geometry .



Figure 4.20: Molecular structure of $[Cu_2(phen)_2{5-(4-chlorophenyl)-tetrazolato}_4(3)$

4.2 Catalytic activity for the oxidation of benzene :

Catalytic oxidation of hydrocarbons is an important class of reaction from the view point of the environments as well as for the production of the specialty chemicals. Among hydrocarbon oxidation of benzene has been widely studied with different transition metal complexes under relatively mild condition. Benzene tends to produce phenol upon oxidation which tends to get over oxidized to form catechol and quinones. In this particular study oxidation of benzene has been studied in presence of complex 1-4 as a probable oxidation catalyst. Different reaction conditions have been explored for an optimum set of reaction condition for most efficient activity of the metal complex under relatively mild condition.



Scheme 4.1. Oxidation of benzene to phenol ,benzoquinone and catechol with hydrogen peroxide catalysed by the copper complexes 1-4.

Under optimized (70 °C, 3 h of refluxing and 1 mole % of Cu catalyst relatively to benzene) conditions, acetonitrile solvent with hydrogen peroxide as a oxidant lead to excellent yields of the oxygenated products with almost 100% of conversion for compound 1. The reaction mixture has shown unprecedented selectivity towards formation of phenol as production of up to 81% of phenol has been detected in GC. The selectivity for the phenol is relatively lower for compound 2-4 as 76, 75 and 78% of phenol has been detected, respectively. Catechol and benzoquinoneare the two other products detected by GC-MS analysis under the above conditions, however formation of these products are found to be much lower in terms of yield. All the results of oxidation study is combined in table 1. A blank reaction, in the absence of any catalyst, were carried out under the studied reaction conditions and no significant conversion and selectivity for product was observed . If compared with reported oxidation of benzene to phenol [60] the present system show encouraging conversion and selectivity under mild reaction conditions.

Catalyst	Phenol	Benzoquinone	Catechol	%Conversion	TON
1	91.60	-	8.40	100	37
2	76.69	0.56	21.41	98.66	31
3	75.97	-	21.67	97.64	24
4	78.42	7.05	5.31	90.78	32

 Table 4.4 Product selectivity (%) and % conversion

4.3 Interaction with bovine serum albumin (BSA) :

Interaction of bovine serum albumin (BSA) with synthesized cobalt complexes were studied through spectroscopic method. It is well known that the interaction between metal complex and protein leads to the quenching of the fluorescence of the BSA protein and it may happen because of dynamic or static interaction [61]. The absorption peak for BSA is visible at 278 nm arising from the presence of aromatic amino acids (Try, tyr and phe) [62]. A fix amount of BSA solution was titrated with an increasing concentration of complex leading to a continuous decrease in initial fluorescence intensity for the fluorophore with a red shift (figure 4.21). This is an indication of the interaction between BSA and the complex.



Figure 4.21: Fluorescence quenching of BSA by complex 5

To get further insight in the quenching process, the fluorescence quenching data were analyzed with Stern-Volmer equation, [63] (graph shown in Figure 4.22) according to which :

$$\frac{F_0}{F} = 1 + k_q \tau_0 [Q] = 1 + K_{SV} [Q]$$

where F_0 and F are the fluorescence intensities in the absence and the presence of a quencher, k_q is the bimolecular quenching rate constant, τ_0 is the average lifetime of fluorophore in the absence of a quencher and [Q] is the concentration of a quencher (metal complexes). K_{SV} is the Stern–Volmer quenching constant in M^{-1} .The K_b value obtained for complexes **5** were found to be in order of 10^3 showing affinity for protein binding with $K_b = 8.04 \times 10^3$ (M^{-1}).



Figure 4.22 Stern volmer plot for complex 5

The binding constant (K_b) and number of binding sites (n) have been determined by Scatchard plot (Figure 4.23), equation of which is given

$$\log \left[\frac{F_0 - F}{F} \right] = \log K_b + n \log [Q]$$



Figure 4.23 Scatchard plot for complex 5

The calculated values of Ksv, n and kq for the interaction of the complexes with the BSA are given in Table 4.4 indicating a good BSA binding tendency of the complex.

Table 4.5: Ksv, n and kq value for complex 5

Catalyst	K _{SV} (M ⁻¹)	$k_q (M^{-1} s^{-1})$	K _b (M ⁻¹)	n
	1.04 x 10 ⁴	1.7 x 10 ¹²	8.04 x 10 ³	0.97

Chapter 5

Conclusion

In conclusion four new dinuclear Cu(II)-tetrazolato complexes 1-4 have been synthesized by means of 1,3-dipolar cycloaddition between copper ligated azide and different organonitriles. The structural characterization of the complexes were established by various physicochemical experiments including single crystal X-ray diffraction studies ,infrared spectroscopy, elemental analyses and mass spectroscopy. Single crystal X-ray diffraction results revealed that complex 1 has square pyramidal and complex 3 has distorted square pyramidal geometry around the metal ion. These complexes exhibited a good promising catalytic activity concomitant with a high selectivity for the oxidation of benzene to phenol, benzoquinone and catechol mixture using hydrogen peroxide as a oxidant. The selectivity for phenol is relatively higher for complex 1 as 91%. These catalytic compounds present several advantages in terms of sustainability: they are fast, use an alternative green energy source (MW), facile work-up process and use of a non-toxic and cheap metal ion as catalyst.

Using cobalt metal new diazido complex and three monomeric tetrazolato complexes have been synthesised successfully. The cobalt complexes are also studied for BSA activity. Only cobalt(III) diazido complexes showed appreciable protein binding activity when examined using BSA protein.

Scope of future work

As dimeric copper complexes have shown interesting oxdiation property towards benzene oxidation therefore, synthesis of higher nuclear complexes with tetrazole ligands could be taken up as future plan which could show more prominent oxidation properties in relatively milder conditions.

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APPENDIX –A



Figure A.1 1 – D chain polymeric structure for complex 1



Figure A.2 3 – D chain polymeric structure for complex 1



Figure A.3 1 – D chain polymeric structure for complex 3



Figure A.4 Hydrogen bonded 1 –D chain polymeric structure for complex 3