SYNTHESIS & CHARACTERIZATION OF SOME NON-HEME N-DONOR BASED TRANSITION METAL COMPOUNDS

DISSERTATION

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CHAPTER 1

INTRODUCTION

1.1 PART-A

The chemistry of first row transition metal complexes containing non-heme *N*-donor ligands is an area of research with growing attention in todays world. In metalloenzymes a metal active site plays a vital role in biochemical reactions. The chemistry of synthetic polydentate ligands with main group elements as well as transition elements have been extensively studied for many many years because of their extensive stability and flexibility. Thus, polydentate ligands are readily used in catalysis, biological chemistry and many other biomimetic applications where in the model system approach can provide valuable guidance to eventually study the real systems. In biomimetic chemistry, metal complexes are designed in such a special way such that they resemble the active site of metalloenzymes and correlate their structure-function relationship. In recent years, a large amount of work has been carried out on understanding the roles of high valent and nickle-oxygen intermediates in a variety of biomimetic oxidations.

In hydrogen gas generation and oxygen gas evolution the role of nickle(II) compounds is documented. For several metalloenzymes, nickel(II) compounds have been used as the models and they display special DNA- binding cleavage activities and antimicrobial properties in biological system. They are also used in various reactions like cross-coupling reaction, alkaline oxidation and electrolytic water oxidation as catalysts. The present multiple donor atoms that is the polydentate ligands provide greater complex stability for metal binding compared with monodentate analogues due to the chelate where in they form the ring structure which makes the ligand more stable. Many Nickle complexes have shown efficient activity as an antioxidant and antimicrobial agent against several microorganisms. The most common coordination number for d-block metal complexes with polydentate ligand systems are four, five and six.

The elements of the first row transition metal series are abundant and available for specific functions as they exhibit a variety of coordination numbers and the flexible geometries over sp, sp^2 *and* sp^3 hybridisation of carbon. The late transition metals viz. cobalt and nickle have been less investigated in biomimetic studies due to their limited scope in biology. These ligands become coordinatively unsaturated when metal is bonded to them and when it has one or two binding site bonded to labile solvent molecule which can further be used for catalysis. These labile solvent molecules can be replaced by bidentate N-donor ligands like 1,10-Phenathroline thus saturating the metal site and their properties can be studied. The nickel complexes of 1,10-Phenanthroline and 2,2' bipyridine derivatives have exhibited the property of binding and cleavage of DNA residues. Several non-heme iron catalysts on combining with H_2O_2 have shown slightly higher selective oxidation activity including steriospecific and oxygen independent hydroxylation of inactivated alkanes. Many tetradentate bis (quinolyl)-diamine and bis (quinolylmethyl)dipamine ligands were prepared by Nielson and co-workers.

Some of the non-heme ligands that are extensively studied are given in the scheme below:

tris(pyridine-2-ylmethyl)amine

N^1,N^1-dimethyl-N^2,N^2-bis(quinolin-2-ylmethyl)ethane-1,2-dimine

N^1,N^2-di(quinolin-8-yl)ethane-1,2-diamine

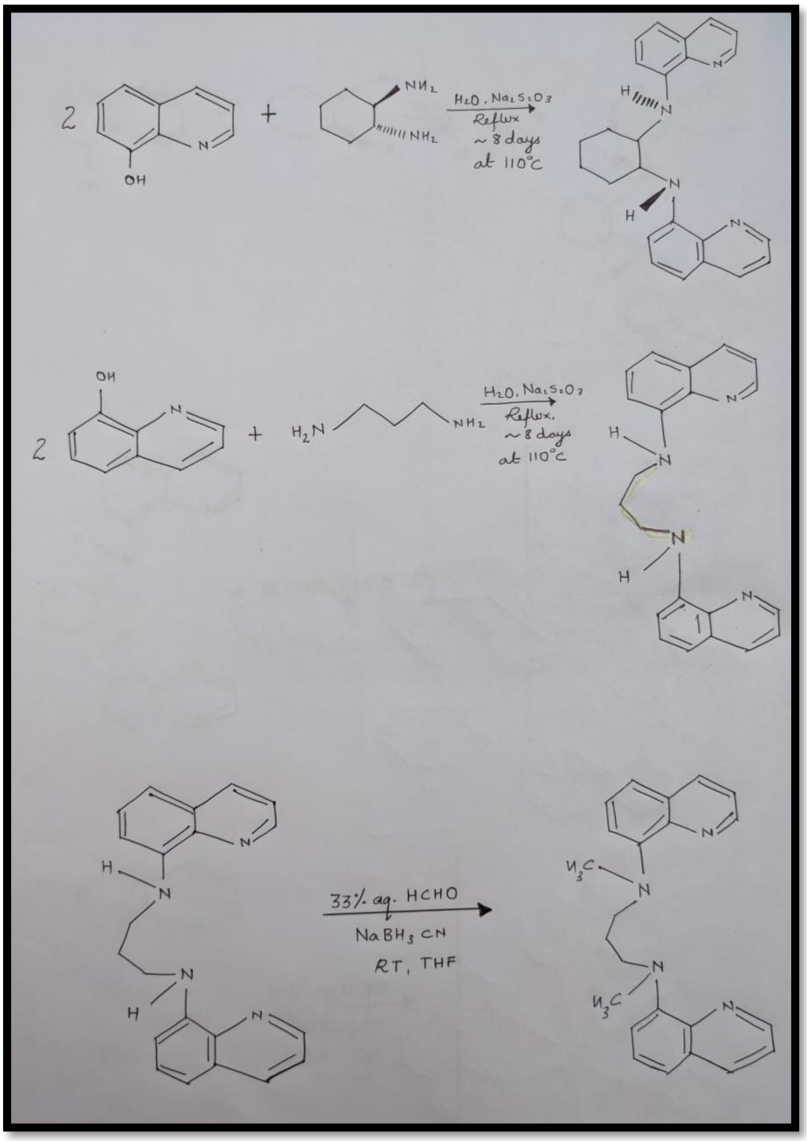
N^1,N^2-dimethyl-N^1,N^2-di(quinolin-8-yl)ethane-1,2-diamine

Scheme 1: Non-heme Ligands

In recent years, the structural and spectroscopic elucidation of nickel(II)- superoxide and nickel(III)-peroxide of tetramethylated cyclams has attracted the attention of bioinorganic chemists in the modelling chemistr. Although a large amount of research on non-heme nickel(II) compounds has been carried out, our understanding in this area suggests that there is scope in designing the new topological ligands which stabilise nickel(II) ion.

Synthesis of $BQCNMe_2$ was done initially by addition of n-butyl lithium in hexane to $BQCNH_2$ in THF and stirring at -78˚C followed by addition of methyl iodide. This conditions were difficult to attain and maintain. This particular procedure was then modified by reacting $BQNHC_2$ in THF with $NaBH_3CN$ and formaldehyde and overnight stirring at room temperature. Complexation was done using Nickel as the central metal ion. This was further reacted with auxillary ligands such as bipyridine with replacement of labile CH_3CN molecules. And all the compounds were tested for their catalytic activity in hydroxylation of alkanes using m-CPBA as oxidant under catalytic conditions. And it was proposed that the intermediate [Ni(II)-O-(BQCN)(CH_3CN)] is responsible for hydroxylation of alkanes giving alcohols as the major product.

In the present work, we have synthsized and studied some of the non-heme ligands like N,N′-Bis(quinoline-8-yl)cyclohexane-1,2-diamine (BQCN-H$_2$), and N,N′-dimethyl-N,N′-di(quinoline-8-yl)cyclohexane-1,2-diamine (BQCN-Me$_2$). We have reported synthesis, characterisation, and reactivity of two dual site aqua mononuclear nickel(II) compounds stabilised by N,N′-Bis(quinoline-8-yl)cyclohexane-1,2-diamine (BQCN-H$_2$), and N,N′-dimethyl-N,N′-di(quinoline-8-yl)cyclohexane-1,2-diamine (BQCN-Me$_2$). The two water molecules in BQCN-H$_2$ and BQCN-Me$_2$ are replaced by auxillary bidentate ethylenediamine (en), imidazole (imi) and monodentate 1,10-phenanthroline (phen), bipyridine (bpy) and bipyrimidine (bpm) affording seven nickel(II) compounds along with the two ligands.



Scheme 2: Synthesis of Non-heme Ligands

The experimental details, instrumentation and characterisation techniques are discussed in the following chapters.

PART B

Porphyrins are a group of heterocyclic macrocycle organic compounds, composed of four modified pyrrole subunits interconnected at their α carbon atoms via methine bridges (=CH-). The porphyrin ring structure is aromatic, with a total of 26 electrons in the conjugated system. Porphyrin macrocycles have been the subject of intense study in the last century because they are widely distributed in nature, usually as metal complexes of either iron or magnesium. As such, they serve as the prosthetic group in a wide variety of primary metabolites, such as haemoglobin, myoglobins, cytochromes, catalases, peroxidases, chlorophylls, and bacteriochlorophylls; Porphyrin macrocycles are not only important for understanding various biological processes as they are biological processes but also have applications in divergent fields including catalysis of organic reaction and the photodynamic therapy of cancer. One result of the large conjugated system is that porphyrin molecules typically have very intense absorption bands in the visible region and may be deeply coloured.

Many porphyrins are naturally occurring; one of the best known porphyrins is heme, the pigment in red blood cells, a cofactor of the protein haemoglobin. Porphyrin systems are important in different biological processes as they are biologically accessible compounds whose functions can be varied by changing the metal, its oxidation state, or the nature of the oraganic substituents on the porphyrin structure. It is a general principle that evolution tends to proceed by modifying structures and functions that are already present in an organism rather than producing new ones. Many new synthetic methods of metalloporphyrins have been developed, including the tautemerization of pyrrole and the self-condensation of dipyrromethene. The synthesis of substituted tetraphenylporphyrin copmpunds via the tautemerization of benzaldehyde and pyrrole has also been improved by using different organic oxidants, carboxylic acids and solvents.

The easiest porphyrin to be synthesized is Tetraphenylporphyrin (TPP) which was prepared by reacting pyrrole along with benzaldehyde under acidic conditions. The synthesis was first reported by Rothemund who chose to carry out the reaction in sealed glass tubes at high temperature which was later studied and modified by Adler and peferred to use the technique of refluxing propionic acid instead of sealed tube chemistry and obtained 20-25% good yield of TPP. This inconsequential procedure involved addition of equimolar amounts of pyrrole and banzaldehyde to refluxing propionic acid. Almost heating about for one half hour, the misture was allowed to cool and the product(TPP) was filtered off.

The synthesis was finally successful and optimised by Limdsey's group which showed that excellent yields of a wide variety of tetraarylporphyrins can be obtained using a high dilution two step reaction between arylaldehydes and pyrrole, in presence of Lewis acid catalyst (usually BF_3-etherate). In the second step of the reaction, the initial product (a colourless porphyrinogen) was oxidised to porphyrin using a quinine for example 2,3-dicholoro-5,6-dicyanobenzoquinone (DDQ). Material isolated from the Rothemund and Adler/Longo approaches was highly crystalline but was nonethelesscontaminated with about 5% or less of 5,10,15,20-tetraphenylchlorin. Brief treatment of the product with DDQ (which was the final step in the most recent Lindsey procedure) obtained transformation of 5,10,15,20-tetraphenylchlorin into porphyrin.

The porphyrin macrocycles contain 22 conjugated π-electrons, but only 18of these are important for making its conjugated aromatic network. The *meso*-position are the most electronically reactive positions at the porphyrin periphery and also generally the most preferential sites for electrophilic aromatic substitutions, additions and radical reactions. While , the β-pyrrolic positions are the most sterically accessible and can also undergo the same type of reactions. All naturally occurring porphyrins are metal complexes and therefore porphyrins can be readily metalated with a wide variety of metal ions. The innerpyrrolenine nitrogen atoms of porphyrins can be protonated to give the corresponding mono-, or di-cations, and the NH groups can be deprotonated to produce di-anions. The metal ions play an important role in terms of imductive effect on the π-electrons system and also strongly influence the chemical reactivity, photophysical properties and biological functions of porphyrin macrocycles. Metalloporphyrins are porphyrin molecules in which most of the metal occupies the vacant space and the inner nitrogen atoms are deprotonated. Spectral properties of porphyrins also changes, with the addition of different kinds of metals. The method used to confirm the product formation is UV-visible spectroscopy as it gives information about the absorption peak and wavelength of absorption.

PROPERTIES

The characterisation techniques used to characterise the compound formed are usually UV-visible spectroscopy, NMR spectroscopy, IR spectroscopy, fluorescence, etc. The properties of transition metal complexes such as variable coordination environments, structural diversity are responsible for their wide use in several disciplines of science. In biomimetic chemistry, the high valent metal complexes (such as Fe(IV), Ru(IV), Ru(VI), Mn(V), Fe(III), etc) have been extensively exploited in organic oxidations such as C-H activation, oxygen transfer reactions, alcohol oxidation, deformylation reactions. Apart from this work, in bioinorganic chemistry nickel(II) complexes have been explored as model complexes of several metalloenzymes. The Ni(II) complexes are gaining importance since they exhibit antimicrobial and DNA binding and cleaving activities. In addition, the nickel(II) complexes are also known to catalyse a wide range of organic reactions. Therefore, the understanding of the structural features of the nickel(II) complexes has become of a prime importance, especially to coordination chemists.

1.3:Instrumentation

IR SPECTROSCOPY

The infrared portion of the electromagnetic spectrum is usually divided into three regions, that is the near-, mid-, and far-infrared, named for their relation to the visible spectrum. Infrared Spectroscopy or Vibrational Spectroscopy involves the interaction of infrared radiation with matter. The higher energy near-IR, approximately 14000-4000 cm^{-1} (0.8-2.5µm wavelength) can excite overtone or harmonic vibrations. The mid-infrared, approximately 4000-400 cm^{-1} (2.5-25 µm) may be used to study the fundamental vibrations and associated rotational-vibrational structure. The far-infrared, approximately 400-10 cm^{-1} (25-100 µm), lying adjacent to the microwave region. In order for a vibrational mode in a sample to be “IR active”, it must be associated with changes in the dipole moment. It can be used to determine the different functional groups present in the compound. Infrared spectroscopy exploits the fact that molecules absord frequencies that are characteristic of their structure. Theses absorptions occur at resonant frequencies, i.e: the frequency of the absorbed radiation matches the vibrational frequency.

UV-VISIBLE SPECTROSCOPY

UV-Visible Spectroscopy involves the promotion of the electrons from the ground state to higher energy or excited state. It is an electronic spectroscopy and involves ultraviolet and visible radiations. UV-Visible Spectroscopy is also known as Absorption Spectroscopy. It obeys Beer-Lambertz Law which states that: “When a beam of monochromatic radiation is passed through a solution of an absorbing substance, the amount of light absorbed is directly proportional to the concentration of absorbing substance and the path length of the medium. This is the basic principle of UV-Visible Spectroscopy. The main uses of UV-Visible Spectroscopy is in determination of different analytes specially transition metal ions, conjugated organic compounds and biological macromolecules. The other uses are to study the rate of the reaction.

C, H, N ELEMENTAL ANALYSIS

This analysis gives the elemental composition of the sample. It is a combustion analysis wherein the sample is burnt in excess of oxygen and the composition of the combustion product is determined by calculating the mass of the combustion products.

^{1}H NMR STUDIES

This technique can be used to find the number of different protons or carbon present in the compound. The reference compound used here is tetramethysilane(TMS). ^{1}H NMR is Nuclear Magnetic Resonance is a property of the nucleus of an atom, concerned with what is known as *Nuclear Spin* (I). Although isotopes can have a variety of values for I, the most useful for spectroscopy are those nuclei which have I=1/2. The most commonly studied nuclei are ^{1}H and ^{13}C. When a nuclei with I=1/2 is placed in a magnetic field, it can either align itself with the field (lower energy) or against (higher energy). If radiowaves are applied, nuclei in the lower energy state can absorb the energy and jump to the higher energy state which depends on the strength of magnetic field and the magnetic properties of isotopes of atoms.

CHAPTER 2

EXPERIMENTAL DETAILS

2.1 Materials and Methods

8-hydroxyquinoline, 1,2-diaminecyclohexane, sodium thiosulphate, ethanol, acetonitrile, Nickle percholorate hexahydrate, galcial acetic acid, formaldehyde, diethyl ether, ethylenediamine, 1,10-phenanthroline, imidazole, bipyridine, bipyrimindin, choloroform.

All the chemicals were purchased from the commercial sources and used without further purification. The starting Ni(II) and $Ni(ClO_4).6H_2O$ was prepared by the slow addition of conc. $HClO_4$ to the aqeousof $NiCO_3$ followed by recrystallisation in water. The ligands N,N′-Bis(quinoline-8-yl)cyclohexane-1,2-diamine ($BQCN-H_2$), and N,N′-dimethyl-N,N′-di(quinoline-8-yl)cyclohexane-1,2-diamine ($BQCN-Me_2$) were prepared according to the literature procedure. The UV-Vis spectra were recorded in Acetonitrile (CH_3CN) and methanol in the range 200-1000nm using Agilent diode array 8453 UV-Vis Spectrophotometer. The ^1H NMR spectra were recorded on Bruker Advance III 400 MHz NMR Spectrometer. The compounds were diluted in KBr powder and the infrared were recorded in the region 4000-400 cm^{-1} using Shimadzu (IR Prestige-21) FT-IR Spectrometer. Elemental Analysis was recorded on Elemental Variomicro Cube CHN Analyser. Cyclic Volatammetry was carried out to know the redox potentials obtained from cyclic voltammograms (CV) and differential pulse voltammograms (DPV) on Electrochemical Workstation-CH Instrument. In CV / DPV measurements, a glass vessel containing sample solution was equipped with a Pt disc (working electrode), Pt wire (counter electrode), reference electrode, $Ag/AgNo_3$ (0.01M) and tetrabutylammonium hexafluorophosphate ($TBAPF_6$) as supporting electrolyte. The sample solutions were purged with N_2 gas for around 15 minutes before each measurement. The powder X-Ray Diffractometer patterns were obtained using a Panalytical Xpert3 Powder X-ray Diffractometer using Cu Kα radiation.

2.2:Synthesis of N,Ń-Bis(quinolin-8-yl)cyclohexane-1,2-diamine (BQCN-H_2)

A mixture of 8-hydroxyquinolin (35g, 241mmol) was taken in a 1000mL round bottom flask. To this 1,2-diaminecyclohexane (15mL, 120.9mmol) and sodium thiosulphate (46.8g, 241mmol) was added along with 800mL of water and was refluxed at 110˚C in oil bath for about 8 days. Then the solution was allowed to cool to room temperature and sodium hydroxide was added dropwise to maintain the pH till alkaline (pH>12). The resuktant mixture was extracted twice with DCM (60mL) and the organic layer was collected in another 500mL round bottom flask and ethanol was added and the mixture was reduced to dryness by using Rota Vapour. The solid obtained was refrigerated overnight, filtered using Buchner Funnel and dried which gave pale yellow coloured crystalline solid.

Percentage yield obtained was: 33.5%

Molecular Formula: $C_{24}H_{24}N_4$

2.3: Synthesis of [Ni(BQCN-H_2)(H_2O)$_2$](ClO_4)$_2$

The solution containing ligand (BQCN-H_2) (0.5g, 1,36mmol) was dissolved in minimum amount of DCM and this was slowly added in a dropwise manner to the round bottom flask containing Nickel Perchlorate [Ni(ClO_4)$_2$.6H_2O] (0.497g, 1.36mmol) along with acetonitrile at Room Temperature and the reaction mixture was stirred on a magnetic stirrer for about 12 hours. To this mixture distilled diethyl ether was added dropwise with continuous stirring and purple coloured solid was obtained. The resultant solid was washed and dried using diethyl ether.

Percentage yield obtained: 88%

Molecular Formula: $C_{28}H_{30}Cl_2NiN_6O_8$

2.4: Synthesis of [Ni(BQCN-Me$_2$)(H_2O)$_2$](ClO_4)$_2$

The solution containing ligand (BQCN-Me$_2$) (0.5g, 1,36mmol) was dissolved in minimum amount of DCM and this was slowly added in a dropwise manner to the round bottom flask containing Nickel Perchlorate [Ni(ClO_4)$_2$.6H_2O] (0.497g, 1.36mmol) along with acetonitrile at Room Temperature and the reaction mixture was stirred on a magnetic stirrer for about 12 hours. To this mixture distilled diethyl ether was added dropwise with continuous stirring and purple coloured solid was obtained. The resultant solid was washed and dried using diethyl ether.

Percentage yield obtained: 71%

Molecular Formula: $C_{28}H_{28}\,Me_2Cl_2NiN_6O_8$

2.5: Preparation of [Ni(BQCN-H_2)(en)](ClO_4)$_2$

The compound [Ni(BQCN-H_2)(H_2O)$_2$](ClO_4)$_2$ (0.5g, 1.36mmol) was taken in a 25mL round bottom flask and to this solution of Ethylenediamine (20.1µL, 3.02mmol) was added dropwise dissolved in minimum amount of acetonitrile. This mixture was stirred overnight (12hrs) on a magnetic stirrer at 25 ° C. Colour change observed was from pale yellow to dark brown. After 12 hours brown coloured was extracted using diethyl ether and dried. The obtained compound was than isolated for crystal formation using Slow Diffusion Technique. Shinny brown crystals were obtained and characterised further using various methods.

2.6: Preparation of [Ni(BQCN-H_2)(phen)](ClO_4)$_2$

The compound [Ni(BQCN-H_2)(H_2O)$_2$](ClO_4)$_2$ (0.5g, 1.36mmol) was taken in a 25mL round bottom flask and to this solution of 1,10-phenanthrolin (20.1µL, 3.02mmol) was added dropwise dissolved in minimum amount of acetonitrile. This mixture was stirred overnight (12hrs) on a magnetic stirrer at 25 ° C. Colour change observed was from pale yellow to creamish yellow. After 12 hours compound was extracted using diethyl ether and dried. The obtained compound was than isolated for crystal formation using Slow Diffusion Technique. Pale yellow crystals were obtained and characterised further using various methods.

2.7: Preparation of [Ni(BQCN-H_2)(imi)](ClO_4)$_2$

The compound [Ni(BQCN-H_2)(H_2O)$_2$](ClO_4)$_2$ (0.5g, 1.36mmol) was taken in a 25mL round bottom flask and to this powder of imidazol (0.0411g, 6.04mmol) was added dropwise dissolved in minimum amount of acetonitrile. This mixture was stirred overnight (12hrs) on a magnetic stirrer at 25 ° C. Colour change observed was from pale yellow to light green. After 12 hours compound was extracted using diethyl ether and dried. The obtained compound was than isolated for crystal formation using Slow Diffusion Technique. Green crystals were obtained and characterised further using various methods.

2.8: Preparation of [Ni(BQCN-Me_2)(phen)](ClO_4)$_2$

The compound [Ni(BQCN-Me_2)(H_2O)$_2$](ClO_4)$_2$ (0.5g, 1.36mmol) was taken in a 25mL round bottom flask and to this 1,10-phenanthrolin (20.8µL, 3.04mmol, 2eqv) was added dropwise dissolved in minimum amount of acetonitrile. This mixture was stirred overnight (12hrs) on a magnetic stirrer at 25 ° C. After 12 hours compound was extracted using diethyl ether and dried. The obtained compound was than isolated for crystal formation using Slow Diffusion Technique. Light yellow crystals were obtained and characterised further using various methods.

2.9: Preparation of [Ni(BQCN-H_2)(bpm)](ClO_4)$_2$

The compound [Ni(BQCN-H_2)(H_2O)$_2$](ClO_4)$_2$ (0.5g, 1.36mmol) was taken in a 25mL round bottom flask and to this powder of bipyrimidine (0.0477g, 3.02mmol) was added dropwise dissolved in minimum amount of acetonitrile. This mixture was stirred overnight (12hrs) on a magnetic stirrer at 25 ° C. Colour change observed was from pale yellow to off white. After 12 hours compound was extracted using diethyl ether and dried. The obtained compound was than isolated for crystal formation using Slow Diffusion Technique. Colourless crystals were obtained and characterised further using various methods.

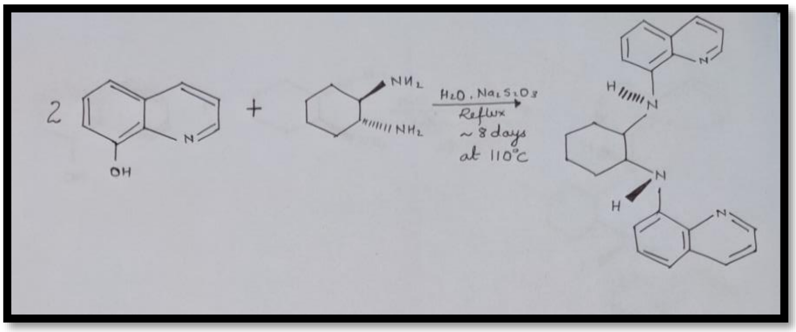
2.10: Preparation of Nickel Perchlorate [Ni(ClO_4)$_2$.6H_2O]

Nickel perchlorate was prepared by adding perchloric acid dropwise to the slurry made by dissolving appropriate amount of Nickel carbonate in 10mL of water with continuous stirring on magnetic stirrer till clear solution is obtained. This was followed by recrystallisation of the product to get green crystals.

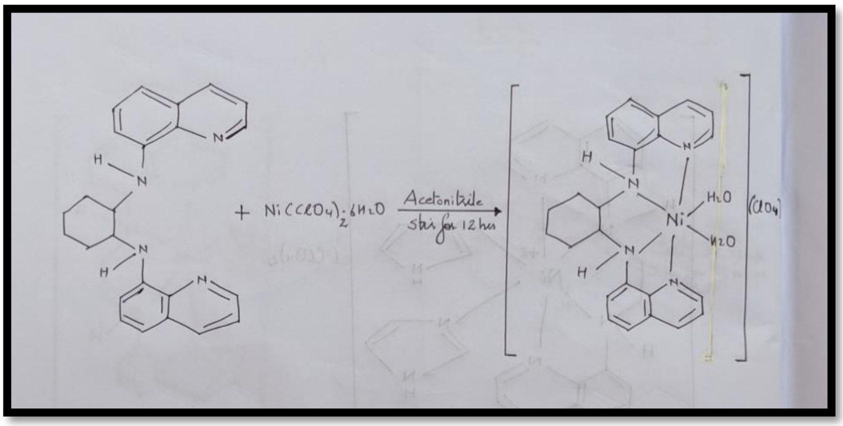
CHAPTER 3

RESULTS AND DISCUSSION

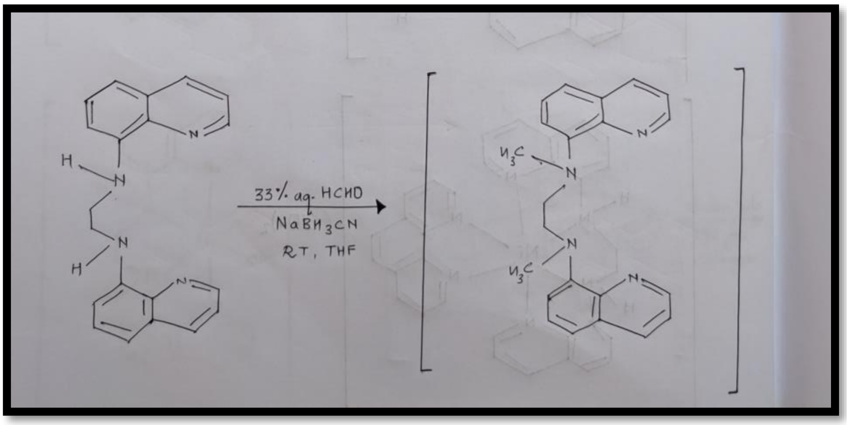
3.1: Scheme for the synthesis of N,Ń-Bis(quinolin-8-yl)cyclohexane-1,2-diamine (BQCNH^{2})



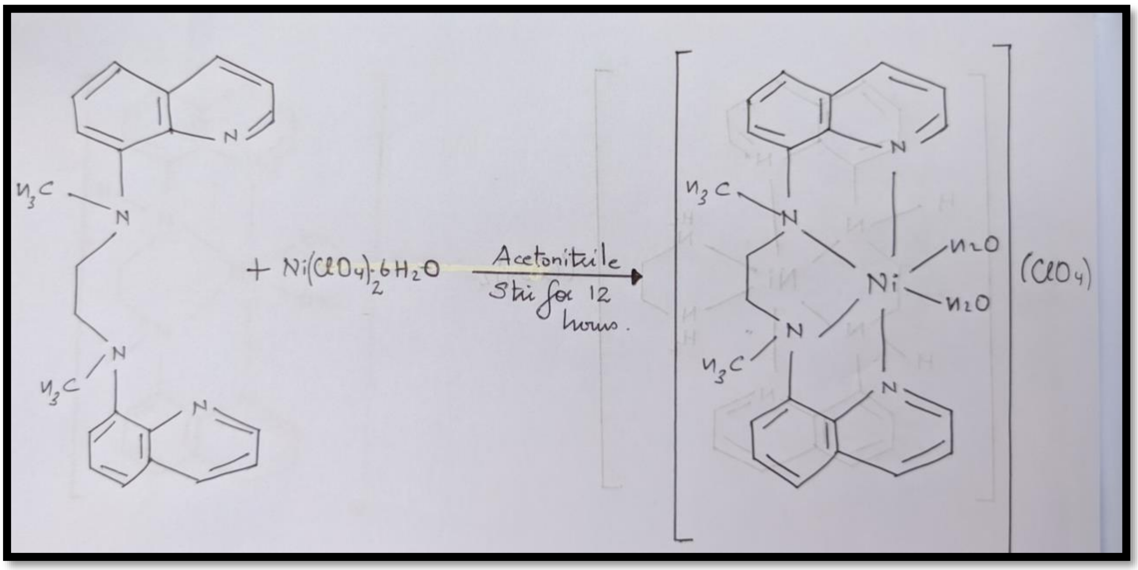
3.2: Scheme for the synthesis of [Ni(BQCN-H^{2})(H_2O)$_2$](ClO_4)$_2$



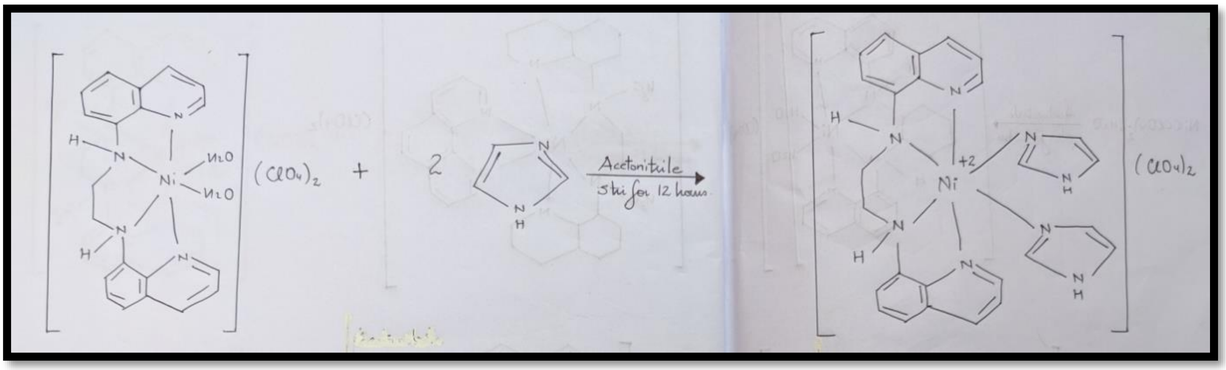
3.3: Scheme for the synthesis of N,Ń-Dimethyl-N,Ń-bis(quinolin-8-yl)cyclohexane-1,2-diamine (BQCH-Me$_2$)



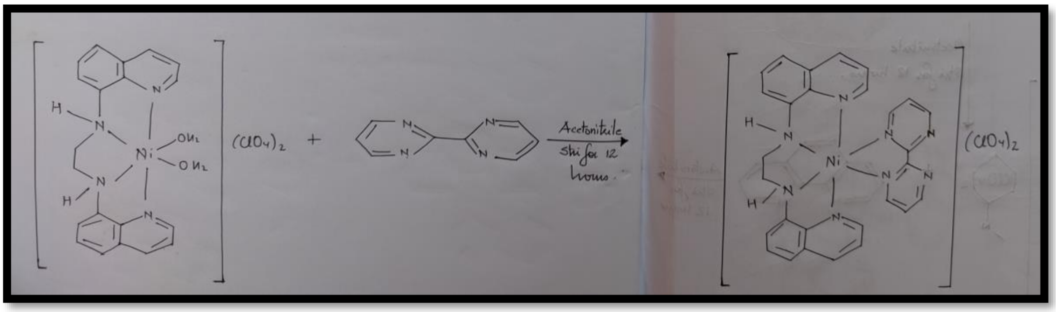
3.4: Scheme for the synthesis of [Ni(BQCN-Me$_2$)(H$_2$O)](ClO$_4$)$_2$



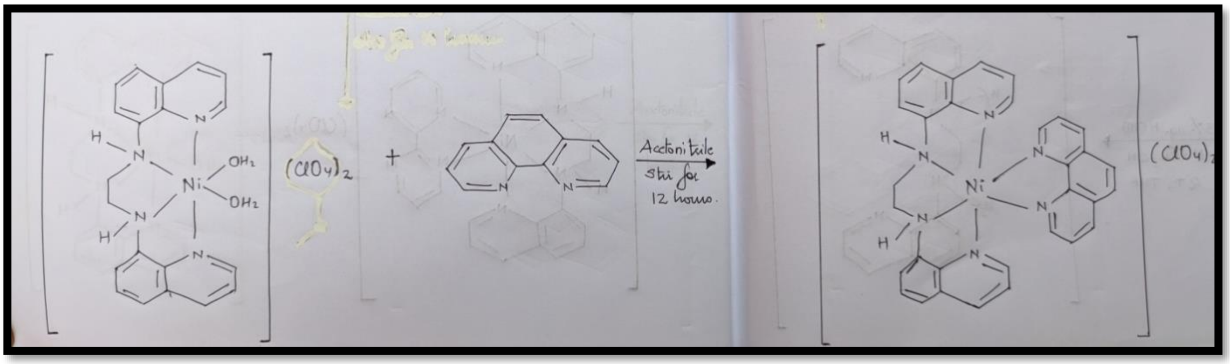
3.5: Scheme for the synthesis of [Ni(BQCN-H$_2$)(imi)](ClO$_4$)$_2$



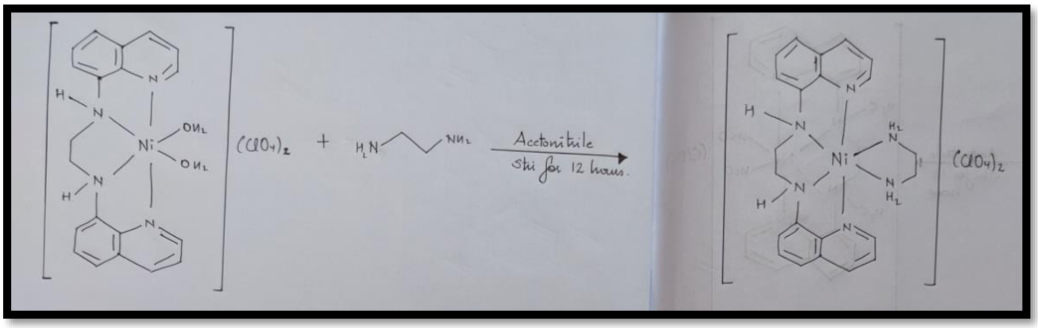
3.6: Scheme for the synthesis of [Ni(BQCN-H$_2$)(bpm)](ClO$_4$)$_2$



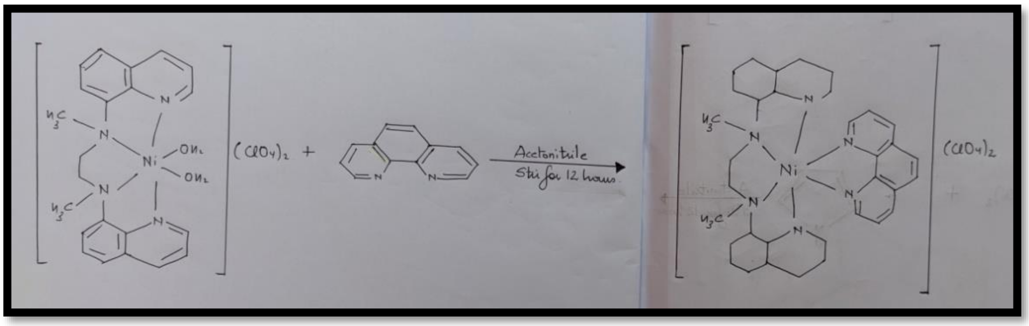
3.7: Scheme for the synthesis of [Ni(BQCN-H$_2$)(phen)](ClO$_4$)



3.8: Scheme for the synthesis of [Ni(BQCN-H$_2$)(en)](ClO$_4$)$_2$



3.9: Scheme for the synthesius of [Ni(BQCN-Me$_2$)(phen)](ClO$_4$)$_2$



CHAPTER 5

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