

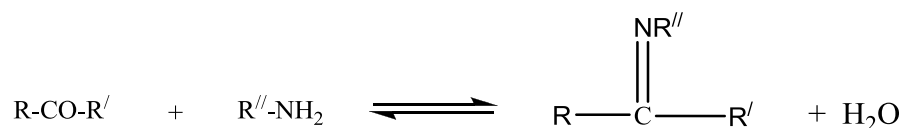
CHAPTER 2

LITERATURE REVIEW

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2.1 Schiff bases and their metal complexes

Schiff bases were firstly discovered by Schiff in 1864 as a product of the condensation reaction between carbonyl compounds and primary amines.



Schiff bases that contain aryl substituents were substantially more stable and more readily synthesized, while those which contain alkyl substituents are relatively unstable and tend to polymerize[5,6].

Schiff bases are widely employed as ligands in coordination chemistry [7, 8]. This is because they are readily available, versatile and have tunable properties which depend on the starting materials (primary amine and carbonyl precursors). They exhibit various reactivities and functionalities. Moreover, the number, the nature and the relative position of the donor atoms of a Schiff base ligand allow a good control over stereochemistry of the metallic centres, as well as the number of the metal ions within homo- and heteropolynuclear complexes. All these advantages make Schiff bases very good ligands to form metal complexes that are of interest in bioinorganic chemistry, catalysis, encapsulation, transport and separation processes [9, 10].

Salicylaldehyde and its derivatives are useful carbonyl precursors for the synthesis of a large variety of Schiff bases. Examples are their reaction with monoamines, diamines with two primary amino groups, or diamines with one primary

and one tertiary amino group. In the last case, the condensation reaction leads to tridentate (NNO) Schiff bases [11-13]. Additional coordinating groups attached to salicylaldehyde increase not only the denticity of the resulting Schiff bases, but also their versatility and ability to generate polynuclear complexes. An example of such salicylaldehyde derivative is 3-methoxysalicylaldehyde (*o*-vanilin), which was largely employed for the synthesis of compartmental ligands [14, 15].

Another very important Schiff bases are those of tetradentate ligands having N_2O_2 or N_4 donor sets, such as bis(salicylaldehyde)ethylenediimine, salenH₂ and bis(salicylaldehyde)phenylenediimine, salphenH₂ (Figure 2.1). Their metal complexes were found to have catalytic activity for epoxidation reactions [16-18].

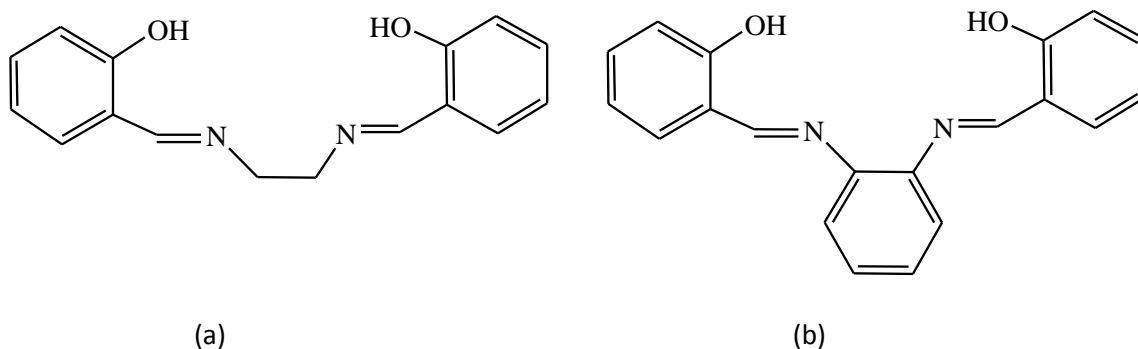


Figure 2.1 The structural formula of (a) salenH₂; (b) salphenH₂

During the past two decades, metal complexes with Schiff bases as ligands have been amongst the most widely studied coordination compounds. Schiff base complexes have been studied extensively due to various reasons like manifestation of novel structural features, up-normal magnetic properties and relevance to biological processes. Considerable attention had been paid to the chemistry of the metal complexes of Schiff bases containing nitrogen and other donors. This may be attributed to their stability, biological activity and potential applications in many fields such as oxidation catalysis, electrochemistry etc. [19, 20]. Schiff base complexes have also applications in clinical [21] and analytical fields [22]. Some Schiff bases are used as model molecules for biological oxygen carrier systems [23]. Tetradentate Schiff bases complexes are well known to form stable complexes, where the coordination takes place through the N_2O_2 donor set [24-26]. Complexes of transition metal ions with polydentate Schiff bases containing nitrogen and oxygen donor atoms play an important role in biological systems and represent interesting models for metalloenzymes that catalyze the reduction of dinitrogen and dioxygen [27, 28]

Metal complexes of tetradentate ligands having N_2O_2 or N_4 donor sets were studied [16]. Electrochemical and spectrochemical studies of Co(salen) and Co(salphen) showed that both compounds formed adducts with oxygen and exhibited catalytic activities for oxygen reduction. Furthermore, complexes of chromium, manganese, nickel and ruthenium with Schiff bases having N_2O_2 and N_4 donor atoms were found to be catalytic for epoxidation reactions [29]. These complexes bound reversibly to molecular oxygen with a change in the oxidation state of the metal [30, 31].

Reactions of those Schiff bases with group 6 and 8 metal carbonyls have been studied recently [32-34]. Reactions of $M(\text{CO})_6$ ($M = \text{Cr}, \text{Mo}$) with the Schiff base bis(2-hydroxyacetophenone)ethylenediimine (hapenH₂) in air gave the oxo derivative $M(\text{O})(\text{hapen})$ with the metal in the +4 formal oxidation state. The dihydride complex $\text{MoH}_2(\text{CO})(\text{hapen})$ was also isolated under reduced pressure [32]. On the other hand, reaction of hapenH₂ with $\text{Ru}_3(\text{CO})_{12}$ resulted in the formation of the dicarbonyl derivative $\text{Ru}(\text{CO})_2(\text{hapenH}_2)$ [34]. Reaction of bis(salicylaldehyde)ethylenediimine (salenH₂) with $\text{Cr}(\text{CO})_6$ under reduced pressure yielded the dicarbonyl derivative $\text{Cr}(\text{CO})_2(\text{salenH}_2)$ with the chromium atom in the zero oxidation state, while its reaction with $\text{Mo}(\text{CO})_6$ in air gave the paramagnetic oxo metal complexes $\text{Mo}(\text{CO})(\text{O})(\text{salen})$ with a +IV metal oxidation state and a high-spin d^2 configuration [32] ((Figure 2.2).

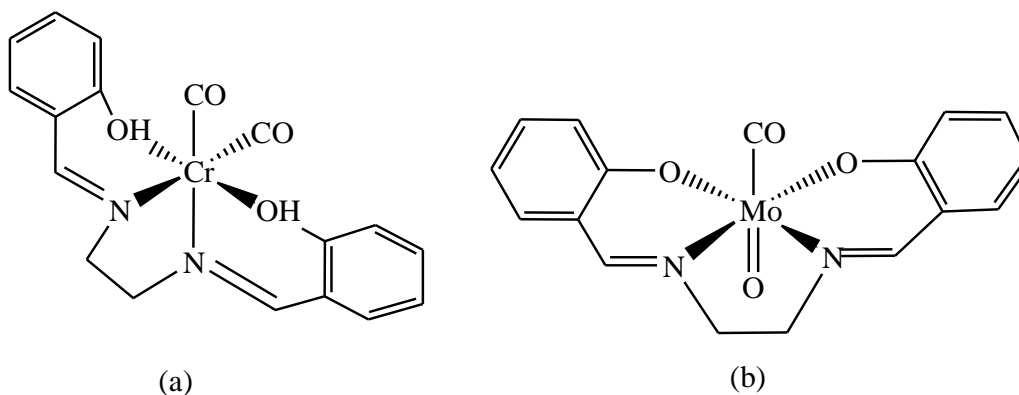


Figure 2.2 SalenH₂ complexes of (a) Cr(0) and (b) Mo(IV+)

Recently, reactions of $M(CO)_6$ ($M = Cr, Mo$ and W) with *N*-salicylidene-2-hydroxyaniline ($shaH_2$) (Figure 2.3) were reported.

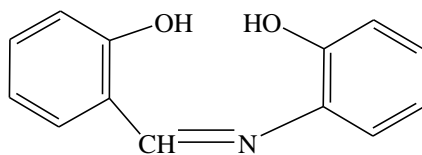


Figure 2.3 The structural formula of $shaH_2$

Under reduced pressure, the reaction yielded $CrO_2(CO)_2(shaH_2)$ and $W(CO)_2(shaH)_2$ (Figure 2.4), while in air the reaction yielded $MoO(sha)$ and $Mo_2O_4(sha)_2$ (Figure 2.5) [2]. Structural studies of the complexes revealed that $shaH_2$ binds to the metal through the oxygen atoms of the hydroxyl groups and the nitrogen atom of the imine group. Thus, the type of ligand and the reaction conditions play a vital role in determining the type of products isolated.

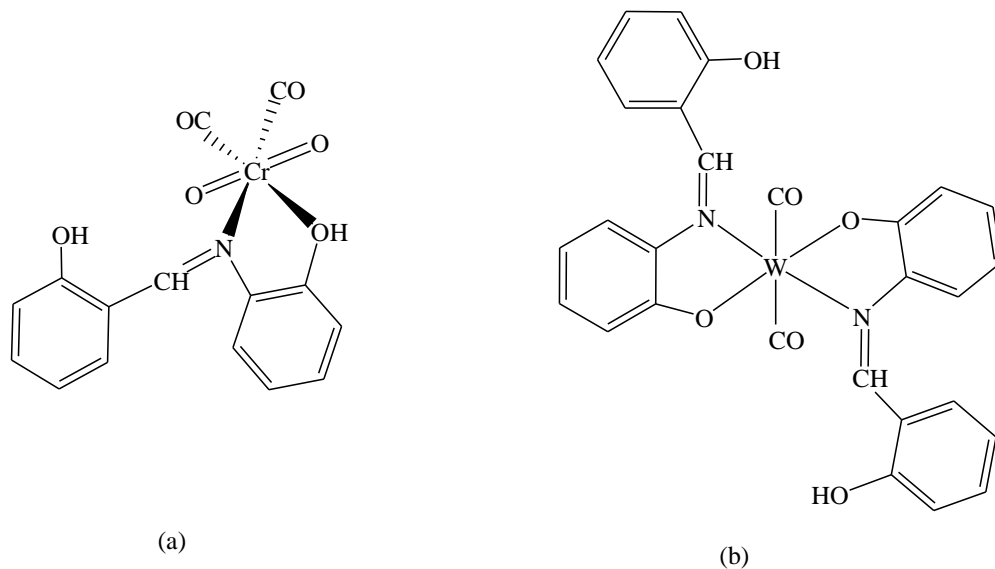


Figure 2.4 $shaH_2$ complexes of (a) Cr ; and (b) W , formed under reduced pressure

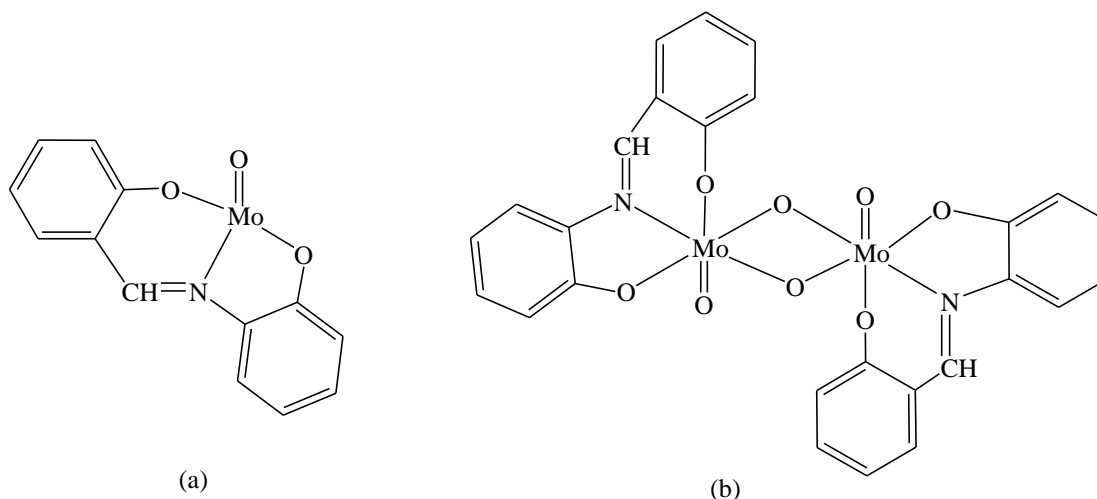


Figure 2.5 ShaH₂ complexes of Mo formed in air

Interaction of metal carbonyls $M(\text{CO})_6$ ($M = \text{Cr}, \text{Mo}$ and W) with the tetradentate Schiff base, bis(salicylaldehyde)phenylenediimine (salphenH₂) was studied in THF [3]. Under reduced pressure, the reaction with $\text{Cr}(\text{CO})_6$ and $\text{Mo}(\text{CO})_6$ yielded $\text{Cr}(\text{CO})_2(\text{salphen})$ and $\text{MoO}(\text{CO})(\text{salphen})$ respectively, while in air the reaction yielded $\text{MoO}_2(\text{salphenH})_2$ and $\text{W}_2\text{O}_6(\text{salphenH}_2)$. All complexes were characterized by elemental analysis, mass spectrometry and IR and ¹H-NMR spectroscopies. Spectroscopic studies supported the proposed structures. The UV-vis spectra of the complexes in different solvents showed bands due to either metal-to-ligand or ligand-to-metal charge transfer transition.

Several Schiff base complexes contain two or more metal ions [35, 36]. There is increasing evidence that binuclear transition metal complexes have played important roles in the development of coordination chemistry. Examples are models for more complex systems of polymetallic or cluster catalyzed reactions, and applications of mixed metal systems in organic synthesis [20]. In addition, they act as models in bioinorganic

chemistry [37]. The development of a large number and varieties of binucleating ligands has led to the successful synthesis of a variety of homo and hetero-binuclear metal complexes [38]. An evolution started few decades ago toward hetero-bimetallic complexes, but still limited number of these complexes are known and fully structurally characterized. The literature survey reported that Schiff base and their complexes possess good luminescence and pigmentation properties. A number of Schiff base metal complexes were also reported to be a great utility in pharmacological and biological aspects. These properties depend on the structure of ligand and the nature of metal ion [35-38].

2.2 Biological and antioxidant activities

Schiff bases and their metal complexes play an important role in the field of biology due to their interesting biological activities. Many of them have been synthesized, characterized and tested for various biological applications. Among those triazines which are known to possess interesting biological activities: they act as anti-bacterial, anti-viral, antimalarial and anti-inflammatory agents among others.[39,40] Their anticancer, antileukemia and anti-HIV activities have also been evaluated and found to show promising properties in some instances.[41-43] The therapeutic properties of certain salicylaldehyde and indoles are also reported and show bactericidal activity.[44] It is known that the existence of metal ions bonded to biologically active compounds may enhance their activities.[45-49]. Scientific research proved that non-biologically active compounds become biologically active and less biologically active compounds become more active upon coordination/chelation with metal ions.[50]

Free radicals containing one or more unpaired electrons are produced in normal or pathological cell metabolism. They are formed in living organisms in different ways, including normal aerobic respiration, stimulated polymorphonuclear leukocytes and macrophages, and peroxisomes. They are natural by-products of our body's metabolism. High levels of free radicals and reactive oxygen species (ROS), including hydrogen peroxide (H_2O_2), extremely reactive hydroxyl radicals, and several other free radicals produced by cells, would cause damage to lipids, proteins and DNA, and thus may lead to various diseases such as carcinogenesis, drug-associated toxicity, inflammation, atherogenesis and aging in aerobic organisms.[51-53] So the significance of free radicals and ROS in the pathogenesis of multifarious diseases has attracted considerable attention. Antioxidants are currently fabricated as the drug candidates to

counter these diseases. Minor dietary compositions have been seriously considered to combat the ill effects of free radicals and ROS.

Schiff bases and their metal complexes have a considerable contribution among the efforts put to rectify this problem. Ye Zhang and co-workers[54] introduced a series of different Schiff base links at position 4 to 7-benzyloxycoumarine structure in order to enhance the donor-acceptor electronic effect and to increase the electronic fluidity to a well known coumarine derivatives that display promising antioxidant activity. Their efforts reached a conclusion that some of the compounds showed better radical scavenging activities than butylated hydroxy toluene (BHT), a commercially available antioxidant, in DPPH assay; other compounds demonstrated better ABTS⁺ radical scavenging activities than BHT; and exhibited stronger superoxide anion radical scavenging activities than butylated hydroxy anisol (BHA); and ascorbic acid.[54]

Further more, Schiff base ligands derived from 4,4'-(2-hydroxy-5-isopropylbenzene-1,3-diyl) bis [methylidenenitrilo] - bis(2,6-di-tert-butylphenol); 4,4'-(2-hydroxy-5-tertbutylbenzene-1,3-diyl) bis [methylidenenitrilo]} bis (2,6-di -tert -butylphenol) and their transition metal complexes [Cu(II), Co(II), Ni(II), Pd(II) and Ru(III) were synthesized, characterized and evaluated for their antioxidant properties using the stable DPPH• method.[55] Solutions of the sterically hindered Schiff base ligands showed DPPH• scavenging activity. Free radical scavenging activity of the sterically hindered Schiff base ligands also increased with increasing concentration. The scavenging effect of the Schiff base ligands and standards at 200 µg/ml on the DPPH• radical are in the order of BHT > tocopherol > ethanol extract of ligand1 > water extract of ligand 2 and were 94%, 91%, 83%, and 69%, respectively, at the same concentration (200 µg/ml). These

results indicate that the Schiff base ligands have a noticeable effect on the scavenging of free radicals. These compounds may limit free radical damage occurring in the human body. The antioxidant activity of ligands were attributed to various mechanisms, among which are prevention of chain initiation, binding of transition metal ion catalysts, decomposition of peroxides, prevention of continued hydrogen abstraction, reductive capacity, and radical scavenging[55]

Schiff base metal complexes were also reported to possess potential antioxidant activity towards superoxide anions and hydroxyl free radicals. Yang Wang and co-workers reported the synthesis of cobalt (II), nickel (II) and iron (II) Schiff base complexes derived from 2-carboxy-benzaldehydebenzoylhydrazone; and 2 carboxybenzaldehyde-(4'-methoxy) benzoylhydrazone. The study demonstrated that the complexes have activity in the suppression of O_2^{-2} anions and $OH\bullet$ radicals. In general, the antioxidative activities increased as the concentration of these complexes increased up to a selected extent. The complexes exhibit more effective antioxidant power than the ligands and the series of the latter ligand are better than the series of the former [56].

2.3 Elemental analysis

To determine the precise amounts of elements (carbon, hydrogen, nitrogen, sulphur) present in an unknown substance, a quantitative analysis is required. Commercially available elemental analyzers are capable of determining simultaneously the percentages of carbon, hydrogen and nitrogen in a compound. In these instruments the sample is burned in a stream of oxygen. The gaseous products are converted to carbon dioxide, water, and nitrogen, which can be detected via gas chromatography, using thermal conductivity detectors. The precise amount of each gas produced in the combustion is determined by integration of the corresponding gas chromatography peaks [57].

2.4 FTIR spectroscopy

The infrared portion of the electromagnetic spectrum is divided into three regions: near-, mid- and far- infrared, named for their relation to the visible spectrum. The far-infrared, approximately $400\text{--}10\text{ cm}^{-1}$ ($1000\text{--}30\text{ }\mu\text{m}$), lying adjacent to the microwave region, has low energy and may be used for rotational spectroscopy. The mid-infrared, approximately $4000\text{--}400\text{ cm}^{-1}$ ($30\text{--}2.5\text{ }\mu\text{m}$) may be used to study the fundamental vibrations and associated rotational-vibrational structure. The higher energy near-IR, approximately $14000\text{--}4000\text{ cm}^{-1}$ ($2.5\text{--}0.8\text{ }\mu\text{m}$) can excite overtone or harmonic vibrations. The names and classifications of these subregions are merely conventions. They are neither strict division nor based on exact molecular or electromagnetic properties.

Infrared spectroscopy exploits the fact that molecules have specific frequencies at which they rotate or vibrate corresponding to discrete energy levels (vibrational modes). These resonant frequencies are determined by the shape of the molecular potential energy surfaces, the masses of the atoms and, by the associated vibronic coupling. In order for a vibrational mode in a molecule to be IR active, it must be associated with changes in the permanent dipole. In particular, in the Born-Oppenheimer and harmonic approximations, i.e. when the molecular Hamiltonian corresponding to the electronic ground state can be approximated by a harmonic oscillator in the neighborhood of the equilibrium molecular geometry, the resonant frequencies are determined by the normal modes corresponding to the molecular electronic ground state potential energy surface. Nevertheless, the resonant frequencies can be in a first approach related to the strength of the bond, and the mass of the atoms at either end of it. Thus, the frequency of the vibrations can be associated with a particular bond type.

Simple diatomic molecules have only one bond, which may stretch. More complex molecules have many bonds, and vibrations can be conjugated, leading to infrared absorptions at characteristic frequencies that may be related to chemical groups. For example, the atoms in a CH₂ group, commonly found in organic compounds can vibrate in six different ways: symmetrical and antisymmetrical stretching, and 4 different bending modes: scissoring, wagging, rocking and twisting [58-62].

2.5 NMR spectroscopy

Nuclear magnetic resonance spectroscopy (NMR) is a technique which exploits the magnetic properties of certain nuclei. The most important applications for the organic chemist are proton NMR and carbon-13 NMR spectroscopy. In principle, NMR is applicable to any nucleus possessing spin.

Many information can be obtained from an NMR spectrum. Much like using infrared spectroscopy to identify functional groups, analysis of a 1D NMR spectrum provides information on the number and type of chemical entities in a molecule. However, NMR provides much more information than IR.

The impact of NMR spectroscopy on the natural sciences has been substantial. It can, among other things, be used to study mixtures of analytes, to understand dynamic effects such as change in temperature and reaction mechanisms, and is an invaluable tool in understanding protein and nucleic acid structure and function. It can be applied to a wide variety of samples, both in the solution and the solid state.

When placed in a magnetic field, NMR active nuclei (such as ^1H or ^{13}C) absorb at a frequency characteristic of the isotope. The resonant frequency, energy of the absorption and the intensity of the signal are proportional to the strength of the magnetic field. For example, in a 21 tesla magnetic field, protons resonate at 900 MHz. It is

common to refer to a 21 T magnet as a 900 MHz magnet, although different nuclei resonate at a different frequency at this field strength.

Depending on the local chemical environment, different protons in a molecule resonate at slightly different frequencies. Since both this frequency shift and the fundamental resonant frequency are directly proportional to the strength of the magnetic field, the shift is converted into a field-independent dimensionless value known as the chemical shift. The chemical shift is reported as a relative measure from some reference resonance frequency. For the nuclei ^1H , ^{13}C , and ^{29}Si , TMS (tetramethylsilane) is commonly used as a reference. This difference between the frequency of the signal and the frequency of the reference is divided by frequency of the reference signal to give the chemical shift. The frequency shifts are extremely small in comparison to the fundamental NMR frequency. A typical frequency shift might be 100 Hz, compared to a fundamental NMR frequency of 100 MHz, so the chemical shift is generally expressed in parts per million (ppm) [63].

By understanding different chemical environments, the chemical shift can be used to obtain some structural information about the molecule in a sample. The conversion of the raw data to this information is called assigning the spectrum. For example, for the ^1H -NMR spectrum for ethanol ($\text{CH}_3\text{CH}_2\text{OH}$), one would expect three specific signals at three specific chemical shifts: one for the CH_3 group, one for the CH_2 group and one for the OH group. A typical CH_3 group has a shift around 1 ppm, a CH_2 attached to an OH has a shift of around 4 ppm and an OH has a shift around 2–3 ppm depending on the solvent used.

Because of molecular motion at room temperature, the three methyl protons *average* out during the course of the NMR experiment (which typically requires a few ms). These protons become degenerate and form a peak at the same chemical shift which is difficult to interpret in more complicated NMR experiments. The shape and size of peaks are indicators of chemical structure too. In the example above—the proton spectrum of ethanol—the CH₃ peak would be three times as large as the OH. Similarly the CH₂ peak would be twice the size of the OH peak but only 2/3 the size of the CH₃ peak.

Modern analysis software allows analysis of the size of peaks to understand how many protons give rise to the peak. This is known as integration—a mathematical process which calculates the area under a graph (essentially what a spectrum is). The analyst must integrate the peak and not measure its height because the peaks also have *width*—and thus its size is dependent on its area not its height. However, it should be mentioned that the number of protons, or any other observed nucleus, is only proportional to the intensity, or the integral, of the NMR signal, in the very simplest one-dimensional NMR experiments. In more elaborate experiments, for instance, experiments typically used to obtain carbon-13 NMR spectra, the integral of the signals depends on the relaxation rate of the nucleus, and its scalar and dipolar coupling constants. Very often these factors are poorly understood - therefore, the integral of the NMR signal is very difficult to interpret in more complicated NMR experiments [64].

2.6 Ultraviolet-visible spectroscopy

Ultraviolet-visible spectroscopy or ultraviolet-visible spectrophotometry (UV-Vis or UV/Vis) involves the spectroscopy of photons in the UV-visible region. This means it uses light in the visible and adjacent (near ultraviolet (UV) and near infrared (NIR)) ranges. The absorption in the visible ranges directly affects the color of the chemicals involved. In this region of the electromagnetic spectrum, molecules undergo electronic transitions. This technique is complementary to fluorescence spectroscopy, in that fluorescence deals with transitions from the excited state to the ground state, while absorption measures transitions from the ground state to the excited state.

UV/Vis spectroscopy is routinely used in the quantitative determination of solutions of transition metal ions and highly conjugated organic compounds.

- Solutions of transition metal ions can be coloured (i.e., absorb visible light) because d electrons within the metal atoms can be excited from one electronic state to another. The colour of metal ion solutions is strongly affected by the presence of other species, such as certain anions or ligands. For instance, the colour of a dilute solution of copper sulfate is a very light blue; adding ammonia intensifies the colour and changes the wavelength of maximum absorption (λ_{max}).
- Organic compounds, especially those with a high degree of conjugation, also absorb light in the UV or visible regions of the electromagnetic spectrum. The solvents for these determinations are often water for water soluble compounds, or

ethanol for organic-soluble compounds. (Organic solvents may have significant UV absorption; not all solvents are suitable for use in UV spectroscopy. Ethanol absorbs very weakly at most wavelengths.) Solvent polarity and pH can affect the absorption spectrum of an organic compound. Tyrosine, for example, increases in absorption maxima and molar extinction coefficient when pH increases from 6 to 13 or when solvent polarity decreases.

- While charge transfer complexes also give rise to colours, the colours are often too intense to be used for quantitative measurement.

The Beer-Lambert law states that the absorbance of a solution is directly proportional to the concentration of the absorbing species in the solution and the path length. Thus, for a fixed path length, UV/VIS spectroscopy can be used to determine the concentration of the absorber in a solution. It is necessary to know how quickly the absorbance changes with concentration. This can be taken from references (tables of molar extinction coefficients), or more accurately, determined from a calibration curve [65].

2.7 Thermogravimetric analysis (TGA)

Thermogravimetry is one of the oldest thermal analytical procedures used in chemistry.

It is a simple analytical technique that measures the weight loss (or weight gain) of a material as a function of temperature.

As materials are heated, they can lose weight from a simple process such as drying, or from chemical reactions that liberate gases. Some materials can gain weight by reacting with the atmosphere in the testing environment.

Since weight loss and gain are disruptive processes to the sample material or batch, knowledge of the magnitude and temperature range of those reactions are necessary in order to design adequate thermal ramps and holds during those critical reaction periods.

A sample of the test material is placed into a high alumina cup that is supported on, or suspended from an analytical balance located outside the furnace chamber. The balance is zeroed, and the sample cup is heated according to a predetermined thermal cycle or heating rate. The balance sends the weight signal to the computer for storage, along with the sample temperature and the elapsed time.

The TGA curve plots the TGA signal, converted to percent weight change on the Y-axis against the reference material temperature on the X-axis.

TGA is commonly employed in research and testing to determine characteristics of materials such as polymers, resins, and rubbers, to determine degradation temperatures, absorbed moisture content of materials, the level of inorganic and organic components in materials, decomposition points of explosives, and solvent residues. It is also often used to estimate the corrosion kinetics in high temperature oxidation, heat resistance and measurement of the ash content in samples [66].