2014

Studies on the Transition Metal Complexes of Schiff Bases with Heterocyclic Amines

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University of Rajshahi

EXAMINER'S COPY

Studies on the Transition Metal Complexes of Schiff Bases with Heterocyclic Amines

A Thesis Submitted to the University of Rajshahi, Bangladesh in Partial Fulfilment of the Requirements for the Award of the Degree of Doctor of Philosophy in Chemistry

Submitted by

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RAJSHAHI-6205

June, 2014

Dedicated To

My Parents
and
Beloved Daughters

Declaration

I thereby declare that the whole of the work submitted as a thesis entitled " Studies on the Transition Metal Complexes of Schiff Bases with Heterocyclic Amines" for the degree of Doctor of Philosophy in Chemistry from University of Rajshahi is the result of my own investigation except where due acknowledgements has been given. The thesis has not been concurrently submitted in substance for any other Degree, Award, Diploma, Associate ship or Fellowship. The work has been carried out under the supervision of Professor Dr. M. Saidul Islam, Department of Chemistry, University of Rajshahi, and Professor Dr. M. Abdul Jalil Miah, Department of Chemistry, University of Rajshahi, Rajshahi-6205, Bangladesh was my Co-supervisor.

Laijuma 16.06.2014

Date: 16/06/2014 *University of Rajshahi* *Rajshahi, Bangladesh.*	*(Laila Arjuman Banu)* *Author*

Declaration Certificate

This is to certify that the thesis entitled " Studies on the Transition Metal Complexes of Schiff Bases with Heterocyclic Amines" is a bonafide record of research work done by Laila Arjuman Banu under our joint supervision and guidance. We further certify that no part of the thesis has been submitted to any other University or institute for any degree, Diploma, Associate ship, Fellowship or similar title to the candidate. The candidate has fulfilled all terms and conditions of the Ph.D course including presentation of the results of her study in seminars held in the Department of Chemistry, University of Rajshahi, Bangladesh.

We have gone through the final draft of the thesis and recommended its submission for the degree of Doctor of Philosophy in Chemistry since it is in conformity with the regulation of this University and accepted standard with respect to originality and quality.

16-6-2014

Prof. Dr. M. Saidul Islam	*Prof. Dr. M. Abdul Jalil Miah*
Supervisor	*Co-supervisor*
Department of Chemistry	*Department of Chemistry*
University of Rajshahi	*University of Rajshahi*

Acknowledgement

All praises to Almighty Allah who gave me strength, patience and ability to perform my research work successfully.

I would like to express my best regards, heartfelt gratefulness, deep appreciation to my honorable, amicable, dynamic and beloved supervisor, **Dr. M. Saidul Islam**, Professor, Department of Chemistry, University of Rajshahi, for his dedicated supervision, proficient guidance, priceless suggestions, generous help, encouragement and co-operation throughout the entire period of my research work as well as to prepare this dissertation. I am really indebted a lot to him and I feel proud for giving me such an opportunity to work in close association with him.

I would like to offer my extraordinary indebtedness and gratitude to Dr. M. Entazul Haque, Professor and Chairman, Department of Chemistry, University of Rajshahi, for his valuable suggestions, inspiration and support during the course of my research work.

Special indebtedness and gratitude to Dr. M. T. H. Tarafder , Professor, Department of Chemistry, University of Rajshahi, for his valuable suggestions and inspiration during the period of my research work.

I am highly grateful to all of my teachers and colleagues, Department of Chemistry, University of Rajshahi, for their cordial help during my research work.

I express heartiest thanks to my student Md. Shafiqul Islam, Lecturer, Department of Pharmacy, Varendra University, for his endless co-operation during my research work.

I owe warm thanks to all of my research students especially Md. Sher Ali, Md. Abul Basar and Md. Khaled Bin Walid for their cordial behavior and their support throughout my research.

I never forget the unquestioned support and sacrifices by my husband Md. Shafeul Alam. Without his support and encouragement it could not be possible for to do this research work. I also acknowledge the affection and sacrifice by my beloved daughters Quantum and Crystal during my whole research period.

My sincere gratitude and honour to my parents. I am also thankful to my other family members.

Last of all I want to express my deepest regard and gratitude to all of my teachers from my Primary level to Post-graduation level of my study life. Without their blessings I could not step up this position.

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ABSTRACT

With an aim to prepare some model complexes, six ligands were prepared. They are arranged in three series depending on nature of the ligands and their donating capability. A variety of aldehydes and a verity of primary amines were used to prepare different Schiff base lignads. The thesis also extended to synthesis and characterization of some transition metal complexes containing Schiff base as primary ligands and heterocyclic amines as secondary lignads.

The complexes were isolated in solid form and characterized on the basis of elemental analysis, conductivity, magnetic measurements, UV, IR and NMR spectral analysis and crystallographic analysis also.

The Schiff base complexes were screened for biological activities such as antibacterial, antifungal, cytotoxicity and antioxidant properties.

For description, we have divided the whole thesis into three sections viz. section A, B, & C.

SECTION-A

This section contains two chapters (chapter I-II)

CHAPTER-1

This is an introductory chapter. This chapter is designed to provide sufficient background and usefulness of the present study.

CHAPTER-II

This chapter describes the experimental techniques, which include the chemicals, physical measurements, and analytical techniques.

SECTION-B

This chapter contains four chapters (chapter III-VI)

Dharmarajan *et. al.* [109] have reported the synthesis and evaluation of various diclofenac acid hydrazones and amides for *invitro* and *invivo* antimicrobial activities against *Mycobacterium tuberculosis.*

Schiff base tetrazamacrocyclic ligand and its complexes of the types, $[MLX_2]$ and $[CuL]X_2$ [M= Co(II), Ni(II), Zn(II); X= Cl^-, NO_3^-] synthesized and characterized by elemental analyses, mass, ^{1}H-NMR, IR, UV-Viss, magnetic susceptibility and molar conductance data.

The complexes shown antimicrobial activity against various pathogens. [110-111]

Lei *et. al.* [112-113] have reported the synthesis of a series of Schiff bases (Fig. 4) by reacting 5-Chlorosalicyldehyde and primary amines. The compounds were assayed for antibacterial and antifungal activities. It is also reported that salicylaldehyde derivatives, with one or more halo-atoms in the aromatic ring, showed variety of biological activities.

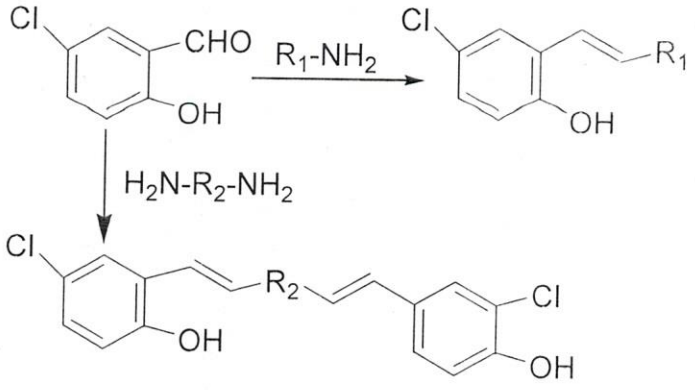
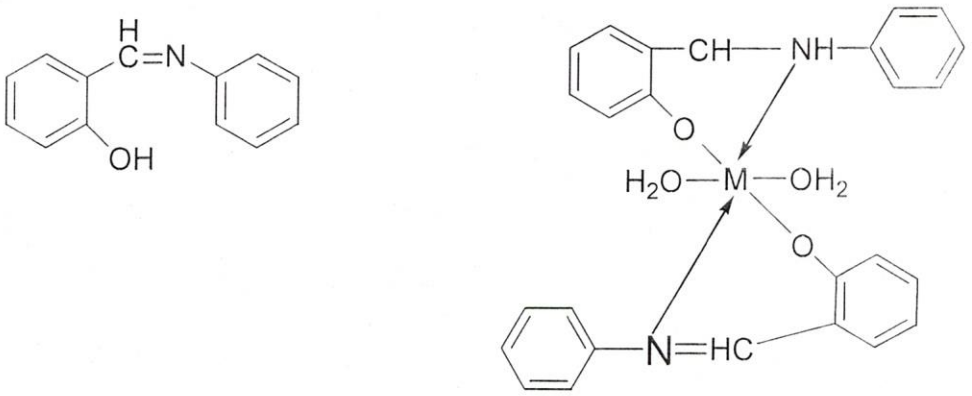


Fig. 4- Synthesis of the Schiff bases

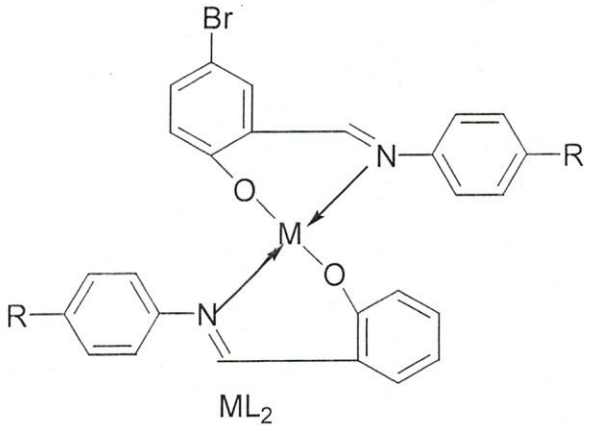
Rehman *et. al.*[114] have reported the synthesis and characterization of a Schiff base (Fig. 5) derived from aniline and salicylaldehyde and its transition metal complexes. Elemental analysis, IR and NMR techniques were used to investigate the chemical structure of the complexes. Biological screening of the complexes reveals that the Schiff base complexes show significant activity against all microorganisms.



Where, M=Mn, Co, Zn

Fig.5- Complexes of the Schiff base

A novel Schiff base ligand (Fig. 6) derived from 5-bromo salicylaldehyde and 4-substituted amines and its transition complexes with Co(II), Ni(II) and Cu(II) have been synthesized.[115] The antimicrobial activity properties of the ligands and their metal complexes have been studied.



M=Co(II), Ni(II), Cu(II), and R=F,I

Fig. 6- General structure of metal complexes

A series of biologically active pyrazine- derived Schiff base ligands (Fig. 7) have been synthesized by the condensation reaction of 2-aminopyrazine with salicylaldehyde and acetamido benzyaldehyde. Then their Co(II), Ni(II) and Zn(II) complexes have been prepared. The biological evaluation of the simple uncomplexed studied the DNA clevage and antibacterial activity of the Schiff base transition metal complexes.[116]

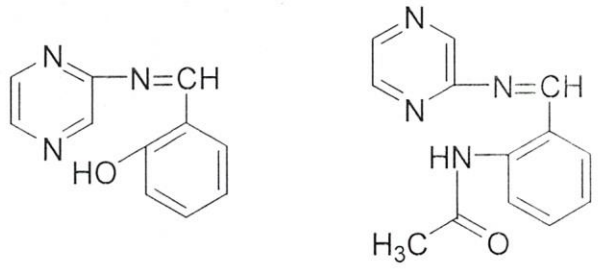
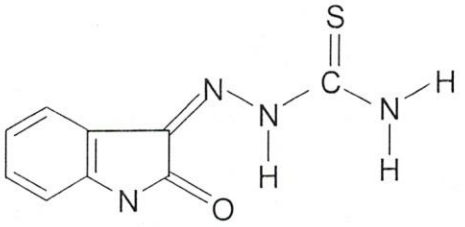
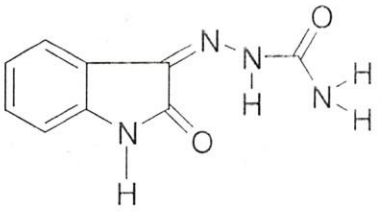


Fig.7- Pyrazine-derived Schiff base

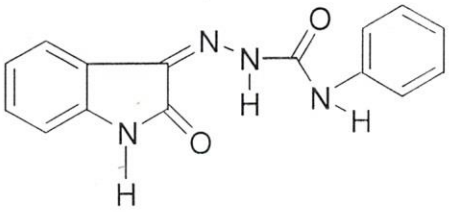
A media consisting of isatin-Schiff bases (Fig. 8) was developed to maximize the production of antibiotics Hexaene H-85 Azalomycine β by *Streptomyces hygroscopicus*.[117]



isatin-3-thiosemicarbazone



isatin-3-semicarbazone



isatin-3-phenylhydrazone

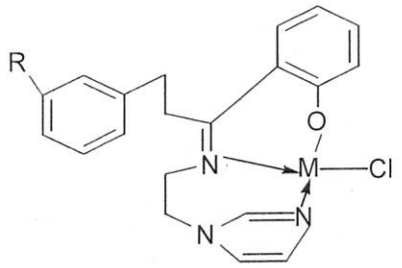
Fig.8- Structure of Schiff bases

Singh *et. al.*[118] have reported the synthesis of new Zn(II) complexes by the reactions of Zn(II) acetate with Schiff bases. All these Schiff bases and their complexes have also been screened for their antibacterial activities.

Schiff base, N,N□-bis (2-hydroxy-1-naphthaldimine) 1,3-diamino-propanol (napdapOH) reacts with metal chlorides to form dinuclear complexes of the type $(M_2L_2)nCl_2$. Where, M= Ni, Cu, Fe.

The characterization of the newly formed compounds was done by ^{1}H-NMR, UV-Viss and IR spectroscopy and elemental analysis. The invitro antibacterial activity of the metal complexes was studied and compared with that of free ligands.[119]

Kalanithi *et. al.*[120] have reported the synthesis of tridentate chelate complexes (Fi g. 9) of Co(II), Ni(II), Cu(II) and Zn(II) from the chalcone based ligands.



M= Co(II), Ni(II), Cu(II), and Zn(II)

HL_1, R=H
HL_2, R=CH_3
HL_3, R=NO_2

Fig. 9 Proposed structure of the metal(II) complexes

A series of 4-substituted-emonimethyltetrazole quinoline with appropriate amine were obtained by refluxing in dioxane (Fig. 10). They were evaluated for their anti-inflammatory and antimicrobial activities.[121]

CHAPTER-III

SYNTHESIS & CHACTERIZATION OF Co (II), Ni (II) & Cu (II) COMPLEXES OF TRIDENTATE SCHIFF BASE WITH HETEROCYCLIC AMINES.

Some Schiff base complexes of Co (II), Ni (II) & Cu (II) containing heterocyclic amines have been prepared. The complexes were isolated from the reaction in solid forms and characterized on the basis of elemental analysis, conductivity, magnetic measurements, UV and IR spectroscopic studies.

The complexes have the general composition, [M(SB)L]; where

M= Co (II), Ni (II) & Cu (II)

SB= Prepared Schiff bases

L=Heterocyclic amines.

The observed values of magnetic moments and electronic spectral data confirm that all the complexes have tetrahedral/square planar geometry.

The strong band at (1633-1604) cm^{-1} is due to the (C=N) group, these values are somewhat lower than the free ligand indicating the coordination with the metal atoms through nitrogen atom.

CHAPTER-IV

SYNTHESIS & CHARACTERIZATION OF LIGHTER & HEAVIER TRANSITION METAL COMPLEXES WITH SCHIFF BASES & HETEROCYCLIC AMINES.

This chapter reports the synthesis and characterization of lighter and heavier transition metal complexes with Schiff base and heterocyclic amines. The complexes were characterized on the basis of elemental analysis, physical properties, UV, IR and NMR spectral studies.

The observed values of magnetic moments of the Co (II) and Cu (II) complexes are paramagnetic and Ni (II) and heavier transition metal complexes are diamagnetic in nature.

CHAPTER-V

SYNTHESIS & CHARACTERIZATION OF HEAVIER TRANSITION METAL COMPLEXES WITH SCHIFF BASES & HETEROCYCLIC AMINES.

Two Schiff base ligands have been prepared by the condensation with a variety of aldehydes and SBDTC/SMDTC.

A number of heavier transition metal complexes have been synthesized and characterized. A close observation on the structure of the ligands reveals that all the Schiff bases contain a thiocarbonyl group and a proton adjacent to it. The IR spectra of the ligands show that Schiff bases do not show any peak at around 2570 cm^{-1} attributed to S-H stretching mode indicating that in the solid state it remains in the thioketo form. The spectra of Schiff bases exhibit bands at 3300 cm^{-1} which may be assigned to the ν (N-H) bands. The band at ca. 1600 cm^{-1} may be assigned to the ν (C=N) of the azomethine group. In case of complexes it is shifted by lower frequencies, which indicate the coordination of azomethine nitrogen to metal ion.

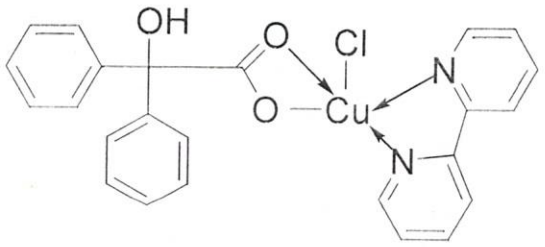
The ^{1}H-NMR spectra of the complexes can account all the protons of the ligand in complexes except phenolic proton and thiolo sulphur proton which are lost during complexes formation i, e, deprotonation of the ligand. This is the evidence of coordination via phenolic oxygen and thiolo sulphur atom of the ligand.

CHAPTER-VI

PREPARATION & CRYSTALLOGRAPHIC STRUCTURE DETERMINATION OF Cu (II) COMPLEX.

For recent structural studies on metal complexes of anions derived from benzilic acid. The Cu (II) atom in the title complex, $[Cu(C_{14}H_{11}O_3)Cl(C_{10}H_8N_2)]$, exists within a ClN_2O_2 donor set defined by a chloride ion, an asymmetrically chelating carboxylate ligand, and a symmetrically chelating 2, 2′-bipyridine molecule.

The coordination geometry is square pyramidal with the axial site occupied by the O atom forming the weaker Cu-O interaction. The hydroxy group forms an intermolecular hydrogen bond with the axial O atom, as well as an intermolecular O-H.... Cl hydrogen bond. The latter leads to the formation of [100] supramolecular chains in the crystal, with the Cu (II) atoms lying in a line. Here in, the crystal and molecular structure of a mononuclear Cu (II) complex is given below.



Molecular structure of a mononuclear Cu(II) complex

SECTION-C

This section contains five chapters (Chapter VII-XI)

CHAPTER-VII

This is an introductory chapter of biological activity. This chapter is designed to provide sufficient background and usefulness of the present study.

CHAPTER-(VIII-XI)

Biological activity such as antibacterial, antifungal, cytotoxicity and antioxidant activities of the complexes.

All the complexes of metals under investigations showed more or less activities against the pathogenic bacteria tested. The results also revealed that among all the tested samples, the [Th(SB-B_2)Q], Schiff base of SBDTC and Schiff base of SMDTC showed strong activity against the gram positive and gram negative bacteria.

The test complexes were found to show significant activity against the brine shrimp nauplii. In this bioassay, the mortality rate of brine shrimp was found to increase with the increase of concentration of the samples. There is a positive correlation between brine shrimp toxicity and cytotoxicity.

From the zone of inhibition, it is observed that some complexes showed highest antifungal activity towards all the fungi used. But some complexes showed lowest activity and some complexes were found to be fully inactive against the three pathogenic fungi.

Antioxidant activity of a synthetic compound can be measured using the scavenging potential of that compound for the trapping of free redicals. Among the three samples, the Schiff base of SMDTC showed strong antioxidant activity, [Ni (SB-A_2)IQ] showed less antioxidant activity.

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CHAPTER-ONE

INTRODUCTION

1.1. GENERAL INTRODUCTION

Coordination compounds, the term is usually used in inorganic chemistry include compounds composed of a metal atom or ion and one or more ligands (atoms, ions or molecules), that can formally think of as donating electrons to the metal. The name coordination compound comes from the coordinate covalent bond, which historically was considered to be formed by the donation of a pair of electrons from one atom to another. Since these compounds are usually formed by the donation of electron pair from ligands to metals so, the name is appropriate. Coordinate covalent bonds are identical to covalent bonds that are formally formed by the combination of one electron from each atom. Only the formal electron counting distinguishes them from each other. Coordination compounds are also called acid-base adducts and popularly recognized complexes or charged, complex ions.

Complex/coordination compounds are also addition compounds, which have the following properties:

i) These compounds retain their identities in the solid as well as when dissolved in water or any other ionic solvent.

ii) Their properties are completely different from those of their individual constituents.

Inorganic chemists tried to use the advances in the theory of organic bonding and the simple ideas of ionic charges to explain bonding in coordination compounds, but found the theories were inadequate.

In this regard, one theory, proposed first by Blomstrand[1] and further developed by Jorgensen[2]. Although the history of bonding and the interpretation of reactions of coordination compounds were really begun by Alfred Werner[3] which is popularly known as "Werner's coordination theory". The independent approaches of Sidgwick[4] and Lowery[5] were invaluable in systematizing of rapidly accumulating information on coordination compounds that suggested the principal valences of Werner are involved when electron transference occurs and the auxiliary or secondary valencies are satisfied by the electron pairs donated by the coordinating species takes place. Although the electron pair donor-acceptor approach made by Lewis[6] is still useful for many Lewis acid-base interactions in forming complexes. It is apparent that the bonding in complex species involving metal ions require more detailed considerations. Pauling[7] used his valence bond approach to explain differences in magnetic behavior among coordination compounds using either 3d or 4d orbital of the metal ions. Griffith and Orgel[8] developed and popularized the use of ligand field theory, derived from the crystal field theory of Bethe[9] and Van Vleck[10] on the behavior of metal ions in crystals and from the molecular orbital treatment of Van Vleck[11]. From the earlier works, the wide-spread influence of the works of Bjerrum[12] on metal-amine formation has led to a more general acceptance of the concept of complex formation and stimulated further studies. He made substantial advances in the areas of kinetics, thermodynamic stability, mechanism of reaction, stereochemistry, oxidation-reduction, synthesis and magneto chemistry, etc.

An already different metal atom ligated with different ligands has been established and their bonding pattern with the crystal geometry has also been developed. But the designing of ligands with the free or protein-bound metal ions has created a recent focus in medicinal inorganic research. [13-15]

The science of coordination chemistry, an extremely attractive field in modern researches, though of comparatively recent origin, is now in a state of rapid advance and has received much attention with its successful results. Extensive researches in the field of coordination chemistry are being done and the number of published of research papers and reviews in the inorganic literature are growing exponentially. This is now a central part due to an extensive and important involvement of such complexes in bioinorganic chemistry. For example, iron and copper play extensive roles in the form of coordination complexes in a wide number of key physiological and numerous essential proteins and enzymes.

Interactions between metals and medicines are becoming important subjects for study since the activities of some drugs are influenced by their interactions with metals. A number of studies have been carried out on the relationship between the effectiveness of some medicines and their coordination properties of metal ions. [16-19]

Every year thousands of compounds are synthesized and many of them are subjected to pharmacological screening to determine if they have useful biological activity. But all are not equally popular due to their different efficacy, safety and toxicity to the host also.

Biological and medicinal properties of transition metal complexes and their mechanisms of action is now a modern drug discovery program. This topic has been dominated in recent years by the use of iron complexes in the clinical trial of cancer but covers a broad field ranging from effects on bacteria, viruses etc. Use of gold complexes in arthritis and nitroprusside as a vasodilator platinum based complexes. Cisplatin is one of the most effective drugs for treating testicular, ovarian, bladder and neck cancers[20]. Now various tumor cell lines are growing resistance to cisplatin e, g, and acquired cisplatin resistance in some preclinical tumor models. These problems have led the scientists to explore new and potent bioactive complexes, which may come in the modern clinical trial. Synthetic chemical compounds constitute important source of various bioactive compounds such as antimicrobial[21] and anticancer[22] compounds.

Toxic compound can usually be tolerated in low doses and can exhibit therapeutic effects within narrow concentration ranges and biochemical essential elements can become toxic at high doses. [23]

The pharmaceutical use of metal complexes therefore has excellent potential. Broad arrays of medicinal applications of metal complexes have been investigated and several recent reviews summarize in these fields. [24]

The chemistry of Schiff base complexes has attracted a great deal of attention ever since Pfeiffer[25-27] carried out his pioneering research in the 1930's. Metal chelates of Schiff basses have been reviewed by Holm *et at.*[28] The properties of the metal ion complexes are often strongly depended on the ligand structure. Because of a considerable synthetic flexibility of the formation of Schiff base ligands of diverse structural type, it is possible to affect certain stereo chemical and electronic changes and some related

properties of the metal complexes by using suitably designed Schiff basses as ligands. Beside that, Schiff bases produce stable metal complexes. So it is easy to carry out clinical trial in animals to determine the role of the complexes in normal or diseased biological system.

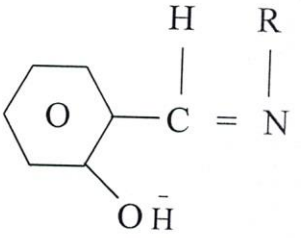
Schiff base is by definition of any derivative formed by the condensation between aldehydes/ketones with primary amines. Schiff base generally formed by condensation of primary amine with a carbonyl compound according to the following equation:

Where, R'=H or CH_3 and R=Aliphatic/aromatic group.

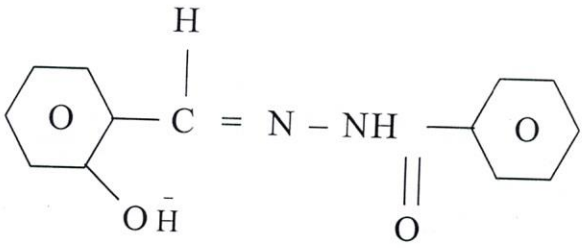
Schiff base contains a functional group (>C=N-) and the nitrogen atom connected to aryl/alkyl group but not with hydrogen atom.

The Schiff base ligands also formed by the condensation of diamine and diketone lose the acidic proton and behave as a chelating agent with the loss of acidic protons.

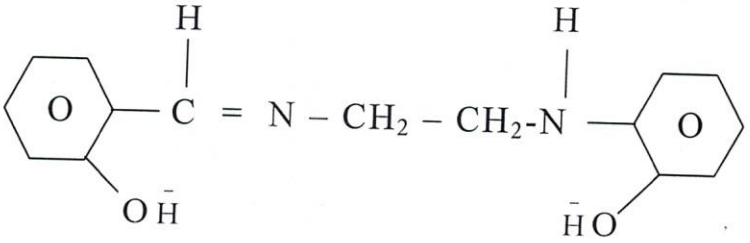
It is well known that the basses are effective chelating agents if either the carbonyl compound or the amine or both contain electron rich functional groups near the condensation site. Depending on the number of coordinating atoms present in the molecule, Schiff basses may act as mono, bi, tri or tetra dentate ligands and can form usually five or six membered chelate rings after reaction with a metal ion.



Bidentate Schiff



Tridentate Schiff base

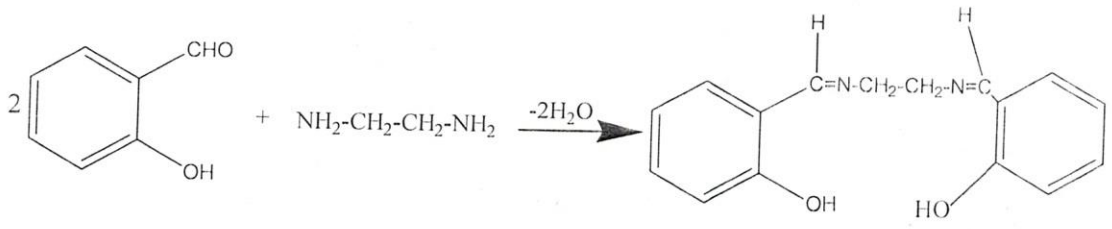


Tetradentate Schiff base

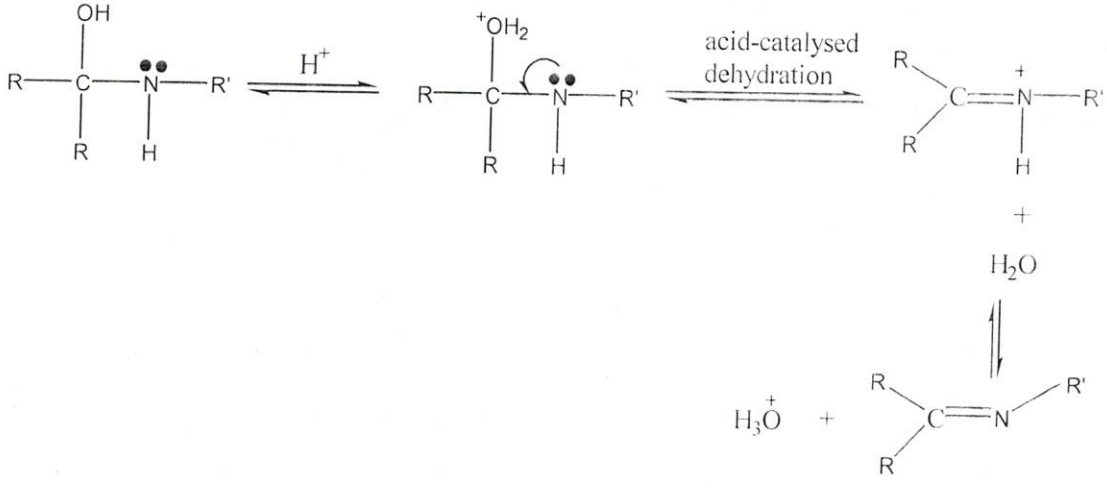
Schiff base as a ligand with the metal ion now created a deep connection between the biological activity and the catalytic eligibility for the different reactions generally planned.

It is crystalline and weakly basic in nature, readily hydrolyzed by water and form carbonyl compounds and amine reversibly. It could be used for different chemical intermediates, perfume, in different dye staffs, rubber accelerator and in liquid crystal for the modern electronic devices.

One of the best nitrogen, oxygen donor Schiff base ligands is bis-salicylaldehyde elhylenediimine.



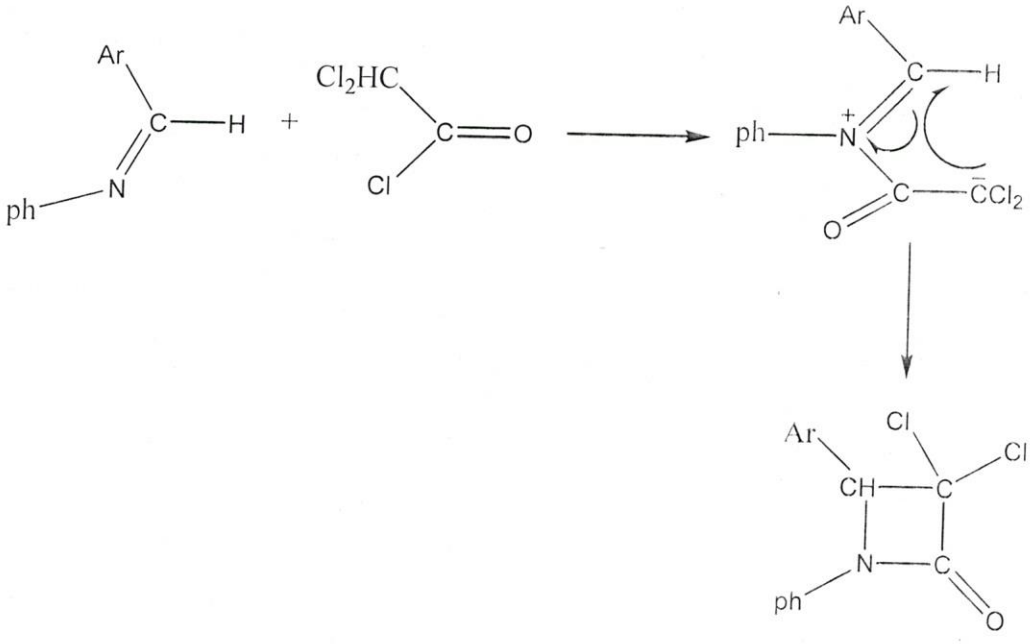
The mechanism of Schiff base formation is another variation on the theme of neucleophilic addition to the carbonyl group. In this reaction amine acts as neucleophile. At first, the amine reacts with the carbon positive center of aldehydes/ketones to give an unstable adduct, which is called carbinolamine. The carbinolamine loses one molecule of water either by acid or by base-catalyzed pathway.



The dehydration of carbinolamines is also catalyzed by base. This reaction is somewhat analogous to the E_2 elimination of alkyl halides however it is not concerned but it precedes two steps through an anionic intermediate. Thus the Schiff base formation is really a sequence of two types of reaction i.e., addition followed by elimination.[29]

Schiff bases of aliphatic aldehydes are relatively unstable and readily polymerizable[30-32] while those of aromatic aldehydes having effective conjugation are more stable. [33-36]

Schiff base have a large number of synthetic uses in organic chemistry, some of which are given as acylation of Schiff bases[37-38] by acid anhydrides, acid chlorides and acyl cyanides is initiated by attack at the nitrogen atom and leads to net addition of the acylating agent to the carbon nitrogen double bond. Reactions of this type have been put to good use in natural product syntheses.



The facility of minimum salt hydrolysis has been put to use in a synthesis of secondary amines from primary amines which involves conversion into the aldimine ($R^1CH=NR^2$) and then by alkylation into the iminium salt [$R^1CH=N^+R^2(R^3)X^-$] followed by hydrolysis to give the secondary amines (R^2NHR^3). Because of the involvement of Schiff base hydrolysis in a number of enzyme-mediated processes, the detailed

mechanism of the hydrolytic cleavage of carbon-nitrogen double bonds become the subject of close scrutiny both under invivo and under invitro conditions.[39-40] Imine hydrolysis is also a key step in the Sommelet, Stephen and Sonn-Muller[41-43] and Ceatterman and Gatterman[44] aldehyde syntheses.

Alkoxides add in the expected fashion to Schiff bases[45], giving the corresponding α-alkoxy amino compounds. This type of addition provides the key step in an elegant "one pot" stereospecific synthesis of penicillin intermediates, which can be further elaborated, to new cephalosporin derivatives.

Schiff bases are important class of compound due to their flexibility, structural similarities with natural biological substances and also due to the presence of imine (-N=H), which imports in elucidating the mechanism of transformation and racemization reaction in biological system. These novel compounds could also act as valuable ligands whose biological activity has been shown to increase on complexation.

Schiff bases are the important compound owing to their wide range of biological activities[46-47] and industrial application.[48] They have also been found to possess the pharmacological activities such as antimalarial[49], anticancer [50], antibacterial[51], antifungal[52], antitubercular[53], antimicrobial[54] and antiviral.[55]

Complexes of transition metal ions with ONS Schiff base ligands were synthesized and their biological activity were studied also by Gunthkal *et al.*[56] Patil and co-warkers[57] synthesized the Schiff base ligand complexes and also studied their antibacterial activity.

The azomethine linkage and hetero aromatic moiety in the synthesized complexes exhibit extensive biological activities.[58-59]

Amino Schiff bases[60] derived from aromatic and heterocyclic amine possess high activity against human tumor cell lines. Aryl-azo Schiff bases[61] exhibit anticancer activity. Diorgano-tin (iv) complexes and Schiff base[62] show antitumor activities in vitro and inhibit interaction of KBHCT-8 and BEL- 7402 tumor cell lines.

Several Schiff bases possess radical scavenging[63] analgestic[64] and anti-oxidative action.[65] Schiff base of chitoson and carboxy methyl-chitoson shows an antioxidant activity such as superoxide and hydroxyl scavenging.[66]

Heterocyclic compounds may be inorganic, most contain at least one carbon atom, and one or more atoms of elements other than carbon within the ring structure, such as sulfur, oxygen or nitrogen.[67]

Heterocyclic amines also sometime referred to as HCAs, are chemical compounds containing at least one heterocyclic ring which by definition has atoms at least two different elements, plus the compound has at least one amine group. The heterocyclic amines, although they contain tertiary nitrogen, coordinate readily with metal ions.

Heterocyclic moieties can be found in a large number of compounds, which display biological activity. The biological activity of the compounds is mainly dependent on their molecular structure.

The heterocyclic amine complexes with platinum and copper have been used as antitumor[68] and antibacterial agents.[69] Derivatives of copper and tin of 9-hydroxyquinoline are antifouling agents[70] and 8-

hydroxyquinoline itself protects the industrial oil from the growth of bacteria and fungi in them. The chlorinated species of 8- hydroxyquinoline has been proved as antibacterial and antifungal agents and the imido derivatives are administered to overcome zinc deficiency in animals. Most of the heterocyclic amines are used as corrosion inhibitor.

There are many organic, inorganic, aromatic and heterocyclic compounds, which are employed as biologically active agents. Among these, the compounds containing sulphur are highly effective.

The addition compounds are formed by the union of two substances, whose molecules apparently already have the normal valence requirements of their constituent atoms satisfied, has long been established. The classical example is ammonia-boron trifluoride, H_3 N: BF_3 discovered in 1809 by Gay Lussac and Thenard. They suggested that the bond formed between the two component molecules probably of the covalent shared electron-pair type seems reasonable. Such a shared electron-pair bond might be considered to establish by the donor-acceptor action. An atom in the donor molecule having a lone pair of electrons in the valence shell which can donate for sharing with an atom in the acceptor molecule and has suitable unoccupied orbital.[71]

In spite of the prevalence of such bonding in systems such as the Grignard reagent and the Fridel Crafts intermediates. The fact is that numerous other important cases of catalytic action may reasonably be accounted for by assuming addition compound formation. Very little attention has been given to the quantitative aspects of donor acceptor action.

The chemistry of metal complexes or addition compounds is now the most active research field of inorganic Chemistry. A survey of articles in recent issues of the Journal of Inorganic Chemistry indicates that perhaps 70% could be considered to deal with metal complexes or addition compounds. Progress in this area of chemistry has received an added impetus because of its many applications to chemical industry and biology. The rapidly developing field of bioinorganic chemistry is centered on the presence of metal complexes or addition compounds in living systems.

1.2. LITERATURE SURVEY

Schiff base compounds and their metal complexes have been extensively investigated due to their wide range of applications including catalysts, [72-73] medicine, [74-75] crystal engineering, [76] anti-corrosion agent. [77-78]

Aromatic Schiff bases or their metal complexes catalyse reactions on oxygenation,[79-80] hydrolysis,[81] electro-reduction,[82] and decomposition.[83] Four coordinated Co(II) Schiff base chelate complexes[79] show catalytic activity in oxygenation of alkene. Metaloporphyrins[80] oxidize phenols (naphthol). Some copper complexes, derived with amino acids, enhance (10-50 times) hydrolysis rate[81] more than simple copper (II) ion. Synthetic iron (II) Schiff base complex exhibits catalytic activity towards electro-reduction of oxygen.[82] Some metal complexes of a polymer bound Schiff base show catalytic activity on decomposition of hydrogen peroxide and oxidation of ascorbic acid.[83] Cyanohydrins cobaltate complexes exhibit catalytic activity.[84]

Several Schiff bases possess anti-inflammatory, allergic inhibitors reducing activity,[85] radical scavenging activity,[85] analgesic,[86] and antioxidative action.[87]

Thiazole derived Schiff bases[88] show analgestic and anti-inflammatory activity. Schiff base of Chitosan and carboxymethyl-chitosan shows an antioxidant activity such as superoxide and hydroxyl scavenging.[89] Furan semicarbazone metal complexes exhibit significant anthelmintic and analgestic activity.[90]

Salicylidiene anthanilic acid[91] possess anti-ulcer activity and complexation behaviour with copper complexes, which show an increase in antiulcer activity.

Some Schiff bases and their metal complexes[92] containing Cu, Ni, Zn and Co were synthesized from salicylaldehyde, 2,4-dihydroxy-benzaldehyde, glycine and L-alanine and possess antitumor activity. Amino Schiff bases[93] derived with aromatic and heterocyclic amine possess high acitivity against human tumor cell lines. Aryl-azo Schiff bases[94] exhibit anticancer activity.

Schiff bases having chelation with nitrogen, oxygen etc donors and their complexes have been used as drugs and reported to possess a wide variety of biological activities against bacteria, fungi and certain type of tumors and they have also many pharmaceutical properties. [95-99]

Imine or azomethine groups are present in various natural, naturally derived and non-natural compounds. The imine group present in such compounds has been shown to be critical to their biological activities.[100-102]

This thesis concentrates on the synthesis and biological activities of Schiff bases and their complexes.

Complexes of Co (II) and Ni(II) with new Schiff bases (Fig. 1). Some of the complexes were screened for their anti-bacterial and anti-fungal activity, and one representative Co (II) complex was evaluated for oxytocic.[103]

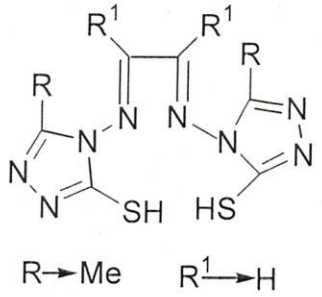
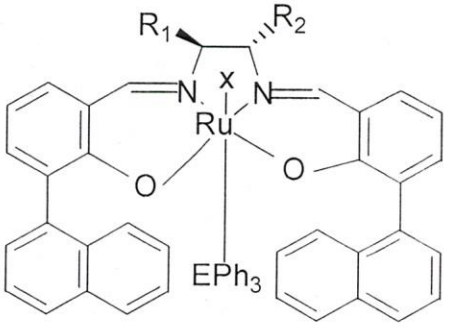


Fig 1:Complexes of Co(II) and Ni(II) with schiff bases.

Daniel *et. al.*[104-108] have reported the synthesis of chiral Schiff base of ruthenium (III) of the type [RuX(LL□) (EPh_3)]; (Where X= Cl^-/ Br^-; LL□= Chiral Schiff base; E= P or As) (Fig. 2)



L_1 $R_1=R_2=(CH_2)_2$
L_2 $R_1=H$; $R_2=CH_3$
L_3 $R_1=R_2=C_6H_5$

Fig.2. Ruthenium(III) Complexes

The catalytic and antibacterial activities have also been carried out for these new complexes.

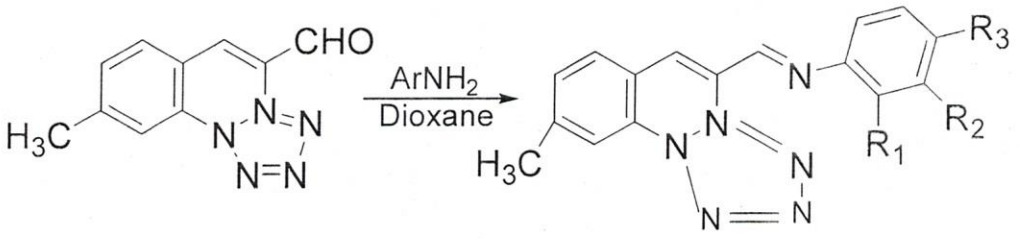


Fig. 10- Synthesis scheme of Schiff bases

Isoniazid is the first line antitubercular medication used in the treatment and prevention of tuberculosis. In this modern world drug discovery involves medicinal chemistry along with other important fields like CADD (Computer Aided Drug Discovery), 3D QSAR, X-Ray crystallography and pharmacokinetic studies etc. Present work includes structure based design, synthesis and biological evaluation of some novel Isoniazid,[122-123] derivatives with sulphanamides [124-126] and aldehydes followed by benzoylation of Schiff bases.[127]

Nalini *et. al.*[128] have synthesized some novel biologically active Isoniazid derivatives substituted with sulphonamides and aldehydes (Fig. 11). Synthesized compounds were screened for antimicrobial and antitubercular activities and compared with known standards.

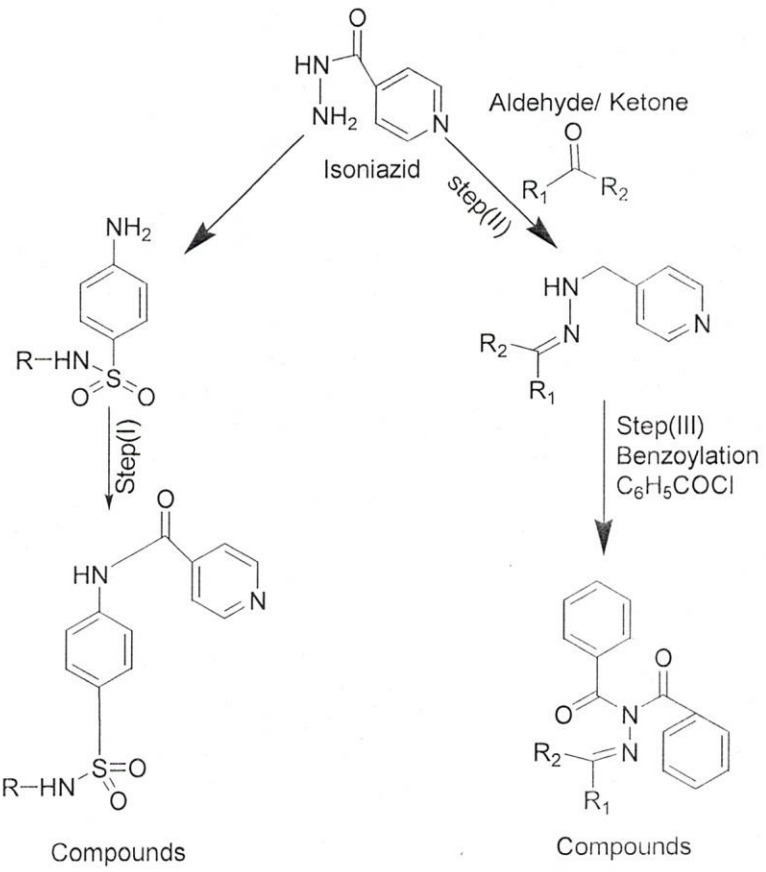


Fig.11- Novel Isonized Derivatives

Heterocycles form by far the largest of classical divisions of organic chemistry and are of immense importance biologically and industrially. The majority of pharmaceuticals and biologically active agro-chemicals are heterocyclic while countless additives and modifiers used in industrial applications ranging from cosmetics, reprography, information storage and plastics are heterocyclic in nature. They have contributed to the development of society from a biological and industrial point of view as well as to the understanding of life processes and to the efforts to improve the quality of life. Among the approximately 20 million chemical compounds identified by the end of second millennium, more than two-

thirds are fully or partially aromatic and approximately half are heterocyclic.[129] Many natural drugs[130-133] such papavarine, theobromine, quinine, emetine, theophylline, atropine, procaine, codeine, reserpine and morphine are heterocycles. Almost all the compounds we know as synthetic drugs such as diazepam, chloropromazine, isoniazid, metronidazole, anidothymidine are also heterocycle.

Synthetic heterocycles have widespread therapeutic uses such as antibacterial, anti-HIV activity, antitubercular, antimalarial, hdrbicidal, analgestic, anti-inflammatory, anticonvulsant, anticancer and lijjpid peroxidation inhibitor, hypontics, antitumoral, anthelmintic and insecticidal agents.[134-140]

There are larger number of synthetic compounds with other important applications such as anticorrosive agents, agrochemicals,photostabilizers, dyestaff, booster agent, antioxidant in rubber and flavouring agent.[141-146]

The pyrrolidines derivatives such as levetiracetam and brivaraccetum are used in epilepsy.[147] Levetiracetam has potential benefits for other psychiatric and neurologic conditions such as tourette syndrome, autism and anxiety disorder. Zonisamide is a sulfonamide anticonvulsant approved for use as an adjunctive therapy in adults with partial onset seizures.[148]

Prazosin and terazosin belong to the class of alpha-adrenergic blockers which lower blood pressure by reluxing blood vessels.[149]

Candesartan, telmisartan, valsartan and irvesartan are angiotensin II receptor antagonist used for the treatment of high blood pressure.[150]

Theophylline is the most widely used though generally as a derivative for example aminophylline and theobryl are soluble derivatives of theobromine and are more powerful diuretic than theophylline.[151]

1.3.AIMS OF THE PRESENT WORK

The importance and application of metal complexes in analytical chemistry is well known. [152] The ligands play an important role in some biological system and its function is related at least, in part, to its chelating ability with metals. [153] The investigations of metal complexes have been subjected to various physico-chemical investigations including IR, UV-Viss, magnetic susceptibility, NMR, X-ray crystallography studies. The reports are undoubtedly important but there are many points, which needs further investigation particularly for understanding of their role in biological and industrial field.

The main objectives of our research is-

i. To prepare a variety of Schiff base ligands i.e. bidentate, tridentate ligands with mainly O, N and S donor atoms and to characterize them by different techniques.

ii. To synthesize the lighter and heavier transition metal complexes of those ligands with heterocyclic amines under suitable conditions.

iii. To characterize the transition metal complexes by different physical, analytical, spectroscopic and X-ray crystallography data.

iv. To test all the ligands and the complexes for antimicrobial study such as antibacterial, cytotoxicity, antifungal and antioxidant properties. The results will be compared among themselves as well as with standard fungicide and antibiotics.

Moreover, these studies raised a number of questions, which make further study of the characteristics of the metal complexes, their functions as antitumor, anticancer, medicinal properties etc.

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CHAPTER - TWO

EXPERIMENTAL TECHNIQUES

2.1 THE CHEMICALS

2.1.1 Metals

Uranyl nitrate was received from BDH Chemicals Ltd., England, and Zirconyl nitrate and Thorium nitrate were obtained from Loba Chemic Pvt. Ltd. India. Cobalt chloride, Cupric chloride and Nickel chloride were obtained from BDH Chemicals Ltd., England.

2.1.2 Ligands

Ligands such as pyridine, 2-picoline, 4-picoline and glycine were from E. Marck, Germany. Quinoline, iso-quinoline were obtained from BDH, England.

2.1.3 Other reagents

Dimethyl sulfoxide and N-**dimethyl** formamide were used as supplied by E. Marck, Germany. Acetone was obtained from BDH, England and salicaylaldehyde was obtained from Hopkin and Williams Ltd. England.

2.1.4 Ethanol

Absolute ethanol was obtained by refluxing 99% ethanol (Carew & Co., Bangladesh) with resublimed iodine and magnesium turnings and then distilling. The solvent was then stored in contact with Linde molecular sieves type 4A, which had been heated to 350-400°C and cooled in a desiccator.

2.2 PHYSICAL MEASUREMENTS

2.2.1 Weighing

The weighing operation was performed on a METTLER PM 200 electronic balance.

2.2.2 Melting point measurement

The melting or decomposition temperature of all the prepared metal complexes were observed in an electrothermal melting point apparatus model No. AZ6512. It was however, not possible to measure the melting points beyond 300°C.

2.2.3 Conductivity

Conductivity measurements of the complexes were carried out in dimethyl sulfoxide (DMSO). The conductivity viz.. the molar conductivites were obtained using the following formula: $\lambda = \frac{1000}{c}$ x cell constant x observed conductivity.

10^{-3} M solutions of the complexes were employed for this purpose. The electrical conductance measurements were made at room temperature using a WPACM 35 conductivity meter and a dip-cell with a platinized electrode. The cell was calibrated with 0.01 N, 0.001 N potassium chloride solution and it had a cell constant of 1.065. The conductance of the pure solvent was determined. Some of the conductivities were also measured in PTI-18 digital conductivity meter.

2.2.4 Magnetic measurement

The SHERWOD SCIENTIFIC Magnetic Susceptibility Balance was used for the present investigation.

(i) Working principle of the balance

The magnetic Susceptibility Balance works on the basis of a stationary sample and moving magnets. The pairs of magnets are placed at opposite ends of a beam so placing the system in balance. Introduction of the sample between the poles of one pair of magnets produces a deflection of the beam, which is registered by means of phototransistor. A current is made to pass through a coil mounted between the poles of the other pair of magnets, producing a force restoring the system to balance. All the position of equilibrium, the current through the coil proportional to the force exerted but he sample can be measured as a voltage grope.

The following general expression for mass susceptibility χ_g in C.G. S unit may be derived in the same manner as for the traditional Gouy method.

$\chi_g=(1/m)[c(r-r_0)+ \chi_{vair}A]$ ... ...(1)

Where,

C= Proportionality Constant.

M= Mass of the sample (in gm).

L= Length of the sample (in cm)

R= Susceptibility of the tube with sample.

R_0= Susceptibility of the empty tube (Normally-`ve').

A= Cross section area of the tube (in cm^2)

χ_{vair} =Volume susceptibility of the displaced air, for powdered sample the air correction term χ_{vair} may normally be ignored.

C, the constant of proportionality is related to the calibration constant of a given balance by the following formula:

$C=C_{Bal}/10^9$ ... ... (II)

From (I) and (II), we get

$\chi_g=C_{Bal}\times1\times(R-R_0)/10^9\times m$ ... ... (III)

(ii) Calibration of the balance

The magnetic susceptibility Balance (M.S.B) must be calibrated at its intended work place. The balance is to be used mainly for solid sample, then a solid calibrate [preferably Hg $(SCN)_4$] is recommended since some of the systematic errors in packing may cancel[1]

(iii) Experimental procedure

1. The zero knob of the magnetic susceptibility was turned until numerical display shows zero (000) and calibration sample, $HgCo(SCN)_4$ was inserted into sample holder. It then allowed to settle reading the numerical display.

2. Reading was recorded and calibration constant was calculated from the formula:

C_{Bal} $=C_{Tube}/(R-R_0)$

$=(1766.842)/[2830-(-17)]$

$=2.086$ ... ... (IV)

From (III) and (IV), we get

$\chi_g=2.086\times1\times(R-R_0)10^9\times m$ ... ... (V)

(iv) Operation of the balance

1. The range knob was turned to the XI scale was allowed to 10 minutes warm up period before use.

2. The zero knob adjusted until the display reads 000. The zero was adjusted on each side.

3. An empty sample tube of known weight was placed into the tube guide and was taken the reading, R_0.

4. The sample was packed and noted the sample mass, m in gram and the sample length, 1 in cm.

5. The packed sample tube was placed into the tube guide and was taken the reading, R.

The mass susceptibility, χ_g is calculated by using the following formula:

$\chi_g=2.086\square 1\square(R-R_o)/10^9\square m$

The temperature was recorded from thermometer situated in the balance room.

(V) The magnetic moment

Form the measurement of magnetic moment, one can fond the number of unpaired electrons present in the system and the possible configuration and also the structure.

If a substance is placed in a field of intensity H gauss, the magnetic induction of the field within the substance is given by:

$B=H+4\pi I$

Where, I= Intensity of magnetization induced by the field.

H is called the volume susceptibility of the substance, and is given by the symbol χ_v in most cases; a more useful quantity is the magnetic Susceptibility per unit mass susceptibnility, χ_g equal to χ_v/d where d is the density of the substanbce in gm/cm^3. It is convenient to regard χ_v as dimensionless and χ_g as having the dimensions of reciprocal density.

The molar susceptibility, χ_m is the product of χ_g and the molecular or formula weight of the substance.

For compounds containing a paramagnetic ion, χ_m will be less than the susceptibility per gram of the paramagnetic ion, χ_m^{corr} because of the diamagnetic contribution of the other groups or ligands present. Since magnetic moments are additive, χ_m^{corr} can be obtained from χ_m by the addition of the appropriate corrections[2].

For paramagnetic metal ions, it is customary to obtain the effective magnetic moments, μ_{eff} Bohr Magnetones (B.M.). μ_{eff} and χ_m^{corr} are related by the following expression:

$(\mu_{eff})^2=3kT.\ \chi_m^{corr}/NB^2$

Where,

N=Avogadro's number, B= Bohr Magneton

K= Boltzman constant, T=Absolute temperature

Hence,

$\mu_{eff}=2.828\sqrt{\chi_m^{corr}\times T}$

The magnetic moment was calculated by using the above equation.

Table2.1: Unpaired spins and magnetic moments

No. of unpaired electrons (n)	Total spin angular moment (s)	Spin only magnetic moments
1	½	1.73
2	1	2.83
3	1.5	3.87
4	2	4.90
5	2.5	5.92

The stereochemistry of metal complexes may well be understood from the value of magnetic moment measurements.

2.2.5 Electronic Spectra

Electronic absorption spectra were obtained on a LKB Ultrospec K 4053 spectrophotometer. The spectra of the complexes were recorded in DMSO using quartz cell of 1 cm path length.

The visible and ultraviolet spectroscopy is a simple but powerful tool which gives information on the geometries of the complex molecules, in a typical transition of metal complexes, the observed spectrum, in general, consists of a series of crystal field bands, which are in the visible region and depend largely on the donor atom of the ligand and on the metal ion. The crystal field transitions are of two types: one is the intense spin allowed transitions and other is the lower intensity spin-forbidden transition, which appear as shoulders on the spin allowed transitions. The ultraviolet spectrum is complicated and consists of electronic transitions between the ligand and the metal (charge transfer), and also transitions within the ligand itself which are usually $\pi \rightarrow \pi^*$ or $\delta \rightarrow \pi^*$ transitions. The bands in the electronic spectra represent different vibration transitions according to the electronic charge; each band is made up of a number of fine lines due to the changes in rotational energy superposed on the electronic and vibrational energy changes.

2.2.6 Infrared spectra

Infrared spectra (as KBr disc) were recorded on a SIMADUZU FTIR-8400 (Japan) infrared spectrometer as KBr pellets in the region 4000-200 cm^{-1} in the Central Science Lab., Rajshahi University, Rajshahi.

The samples were kept in an agate mortar, thoroughly powdered with potassuium bromide and then transferred in a mini-disc holder and a disc was made by hand press. The KBr disc was mounted in the sample cavity of the machine. The spectra were calibrated against 1601.8 ch^{-1}peak of the polystyrene film.

2.2.7 Nuclear Magnetic Resonance (NMR) Spectra

Proton NMR in DMSO-d_6 were obtained with a NMR spectrometer from England.

2.2.8 Mass Spectra

Mass spectra of some complexes were obtained from the chemistry Department, University of Stirling, U. K.

2.2.9. Thin Layer Chromatography (TLC)

Thin layer chromatography provides a means of separation, purification and identification of a mixture of compounds. This technique involves an absorbent (usually silica gel) as a stationary phase and a solvent or solvent mixture as the mobile phase. Due to the differences in mobility of the components. They are separated from each other by the solvent.

TLC Plates

The cleaned grease free glass plates (20 cm × 5 cm) were washed with water followed by acetone and dried in an electrical oven. The plates were then placed on a frame (Quick-fit, England) and the spreader was placed in position. A suspension of silica gel (25cm in 55 cm^3 distilled water) was transferred to the open spreader, set with appropriate thickness and the spreader was drawn across the plates. A uniform layer of absorbent was obtained. The glass plates thus coated with silica gel (e. Merck, TLC grade)

were allowed to stay in position at room temperature until the surface became completely dried. These plates were then left for 2 hours in an oven at 60° c for activation and then these were ready for use.

Procedure

The solutions of the components under investigation were spotted with glass capillaries to the TLC plates about 2 cm from the bottom. The plates were then placed downwards in a chromatographic tank so that the spotted marks remained above the solvent surface. The tank contained the developing solvent or solvent mixture. The plates were removed when the solvent front reached 1.5 cm below the upper edge. The plates were then dried and the chromatograms were developed by putting them in an iodine chamber.

2.3 ANALYTICAL TECHNIQUES

2.3.1 Antibacterial activity

Antibacterial activity was determined by agar discs diffusion method[3-4] this method was developed by Bondi and standardized by Bauer et al. in 1966 for susceptibility test.

2.3.2 Antifungal activity

For determining the antifungal activity of test complexes had been selected by using disc diffusion technique, because it is essentially a quantitative or semi quantitative test indicating the sensitivity or resistance

of microorganism to the test material and then confirm by determining the MIC of test complexes against fungus.

2.3.3 Cytotoxic effect

Brine shrimp lethality bioassay is a recent development in the bioassay for the bioactive compounds. Here, in vivo lethality in a simple zoological organism (brine shrimp nauplii) is used as a convenient monitor for screening and fractionation in the discovery of new bioactive products.

In this bioassay, the mortality rate of brine shrimp was found to be increased with the increase in concentration of the samples and a plot of percent mortality versus log concentration on the graph paper produced and approximate linear correlation between them.[5-6]

2.3.4 Antitumor activity

An essential part of drug development is the testing of potential new compounds against animal tumours both in vitro and in vivo. In vitro tests determine whether the compound has any effect against neoplasm or not and in vivo tests[7] determine dose response curves on animals bearing transplanted tumour giving an indication of the effects of the new drugs not only on the tumour but also on the host, indicating its toxicity and therapeutic index.

2.3.5 Determination of antioxidant property

Total antioxidant capacity of different compounds were determined by the method of Prieto *et. al.*,[8] with some modifications.

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CHAPTER–3

STUDIES ON THE Co (II), Ni(II) AND Cu(II) COMPLEXES OF TRIDENTATE SCHIFF BASES WITH HETEROCYCLIC AMINES

3.1. INTRODUCTION

The Schiff base ligands are derived by the condensation of an active carbonyl group and a primary amine and contain the azomethine group (=C=N-). These bases can be effective chelating agents either the carbonyl compound as the amine or both contain potentially coordinating functional groups near the site of condensation.

The Schiff base ligands have been used as mono, di or chelating ligands. Westland and Tarafder[1] synthesized a dinegetively charged tridentate ONO chelating agent from the condensation of **salicyldehyde** and **O-aminophenol**. They have also synthesized another Schiff base containing ONO donor sequence from the condensation of **salicyldehyde** and **O-aminobenzoic** acid.

A number of complexes containing NNS, ONS and ONN donor sequence have been studied in our laboratory [2-4]. However, nothing seems to have been done so far on complexation of ligands having ONN and ONO donor sequence. These kinds of ligands provide intriguing chemistry with both lighter and heavier transition metals.

Schiff base constitute a very important group of N,O donor chelating ligands.[5-9].Another group of ligands containing azomethine (=C=N-) found in Schiff base is constituted by hydrazones which have also been used as ligands though they are not as widely studied [10-12] as Schiff base. Schiff bases and their metal complexes are well known to have pronounced biological activities [13-17] and form an important class of

compounds in medicinal and pharmaceutical field and azomethine linkage might be responsible for the biological activities of the Schiff bases.[18-21]

Keeping these facts in view we here in report the preparation and characterization of the Schiff base metal complexes with heterocyclic amines. Then we have tried to evaluate their biological activity such as antimicrobial, antifungal and antitumor properties.

3.2. EXPERIMENTAL PROCEDURE

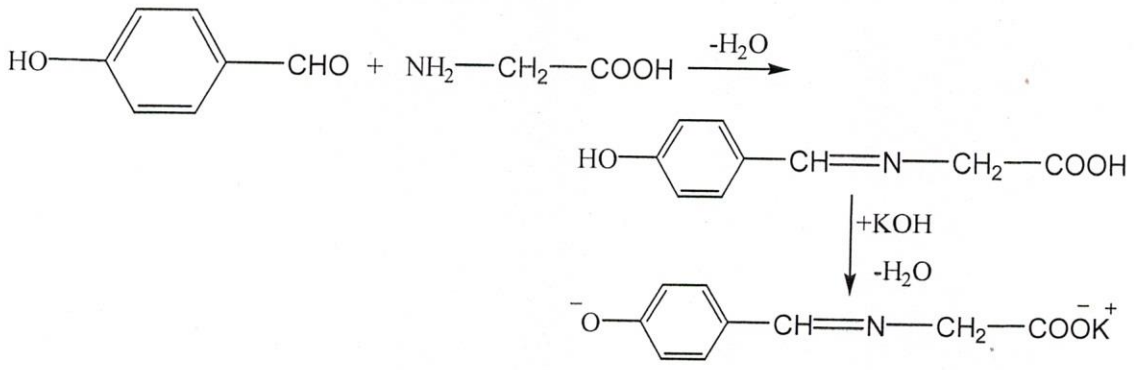
3.2.1. Reagents: As stated in chapter 2 Page No 40.

3.2.2. Physical measurements: As stated in chapter 2 Page No. 41.

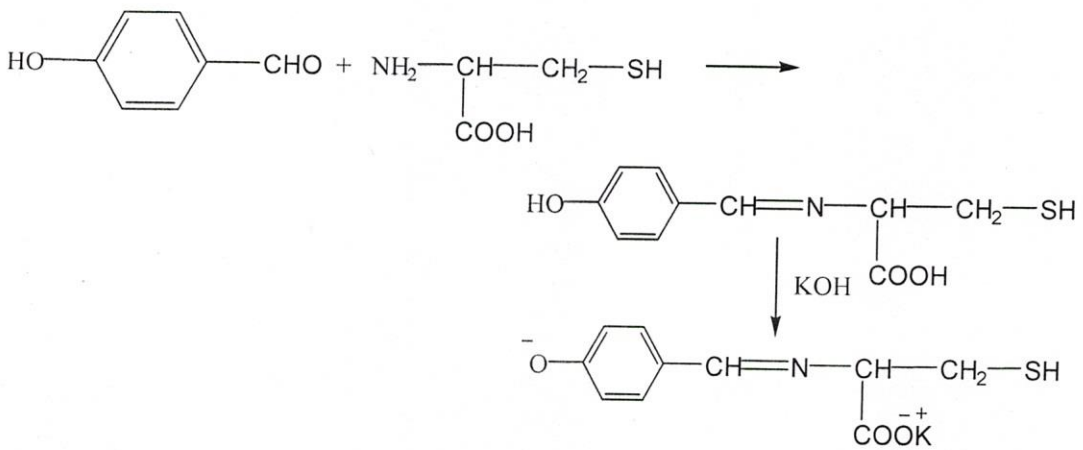
3.3. General method of preparation of tridentate Schiff bases

P-hydroxybenzaldehyde (4.8848g, 0.04mole) dissolved in 20ml absolute ethanol was added slowly with constant stirring to a solution of glycine/L(+) cystine(0.04mole) in water in the presence of potassium

hydroxide . The solution was refluxed for 4-5 hrs.The liquid Schiff base was prepared by the distillation process.



Schiff base for glycine($SB\text{-}A_1$)



Schiff base for L(+) cystine ($SB\text{-}A_2$)

3.3.2: Preparation Procedures of($SB\text{-}A_1$)/ ($SB\text{-}A_2$) complexes:

The complexes have the general formula [M(SB)L]; where , M=Ni(II),Co(II), Cu(II)

L=Heterocyclic amine [Quinoline , Pyridine, Iso-quinoline ,2-Picoline and 4- Picoline].

SB=Schiff base ligands such as (**$SB\text{-}A_1$**)/(**$SB\text{-}A_2$**)

In a typical preparation 0.002mole of metal salts and 0.002mole of **(SB-A_1)/(SB-A_2)** were separately dissolved in minimum amount of absolute alcohol and then the solution were mixed together and heated on water both for an hour. Then an ethanolic solution of L, 0.002 mole was added to the above solution .The resultant mixture was heated under reflux on a water bath for 2 hrs and then cooled .The colored precipitate so formed, was filtered, washed with hot ethanol and dried in a vacuum desiccator over anhydrous $CaCl_2$.

3.4. RESULTS AND DISCUSSION

3.4.1. Physical properties:

Some physical properties viz., color, melting point , magnetic moments and conductance values are given in (Table-3.4.1).The complexes were soluble in water , N,N'–dimethyl formamide and dimethyl sulfoxide . The conductance values of the complexes in DMSO indicated that the complexes were non-electrolyte in nature.[22] The values of magnetic moment in Bohr Magneton of the complexes are in good agreement with their respective structures[23-28].

Table -3.4.1: Physical properties for SB Complexes:

No.	Complexes	Colour	Melting point or decomposition temperature (±5°C)	Molar conductance (ohm^{-1} cm^2 mol^{-1})	μ_{eff}(B.M.)
1	[Ni(SB-A_1)2-pic]	Yellow	250	9.00	2.90
2	[Ni(SB-A_1)Py]	Red	180	1.28	3.00
3	[Ni(SB-A_1)Q]	Reddish Brown	210	1.00	3.25
4	[Co(SB-A_1)IQ]	Greenish Yellow	230	1.50	4.05
5	[Co(SB-A_2)Q]	Deep Blue	240	2.20	4.00
6	[Ni(SB-A_2)IQ]	Brown	220	6.50	3.15
7	[Cu(SB-A_2)Q]	Black	210	5.40	1.90
8	[Cu(SB-A_2)4-Pic]	Black	240	5.50	1.95

3.4.2 Electronic Spectra:

The electronic spectra of Co (II) complexes in DMSO gave bands corresponding to the transitions $^4T_{2g} \rightarrow {}^4T_{1g}$, $^4T_{2g} \rightarrow {}^4A_{2g}$ and charge transfer respectively, which are in good agreement with the tetrahedral structure.

The electronic spectra of Ni(II) complexes gave three bands corresponding to the transitions $^1A_{1g} \rightarrow {}^1B_{1u}$, $^1A_{2g} \rightarrow {}^1A_{2u}$ and $^1A_{1g} \rightarrow {}^1E_u$ respectively.

Cu(II) complexes in DMSO gave three bands due to the transitions $^2B_{1g} \rightarrow {}^2A_{1g}$, $^2B_{1g} \rightarrow {}^2E_g$ and charge transfer.

These bands of Ni (II) and Cu(II) complexes are consistent with square planar geometry.[29-33]

Table-3.4.2: UV-visible spectral bands of the SB complexes:

No.	Complexes	Band I (in nm)	Band II (in nm)	Band III (in nm)
1	[Ni(SB-A_1)2-Pic]	355	412	472
2	[Ni(SB-A_1)Py]	355	412	472
3	[Ni(SB-A_1)Q]	355	412	472
4	[Co(SB-A_1)IQ]	300	400	500
5	[Co(SB-A_2)Q]	350	420	550
6	[Ni(SB-A_2)IQ]	340	400	510
7	[Cu(SB-A_2)Q]	340	420	500
8	[Cu(SB-A_2)4-Pic]	350	420	520

3.4.3. IR Studies

The strong band at (1633-1604) cm-^{1} is due to the (C=N) group and other two bands at (1400-1500) cm^{-1} and (1200-1300) cm-^{1} for the asymmetric and symmetric stretching vibration of (-COO) group respectively. These values are somewhat lower than the free ligand indicating the coordination with the metal atoms. Two distinct bands at (510-530) and (390-490) cm^{-1} for the stretching vibrations of (M-O) and (M-N) bands indicated the complexation of (C-O) and (C=N) group respectively.[30-33] From the above observation it may be concluded that Schiff base ligand behaves as tridentate dinegative ligand.

Table-3.4.3: IR bands for SB Ligands and complexes

No.	Complexes	ν(C=N) cm^{-1}	ν_{asym} (COO) cm^{-1}	ν_{sym} (COO) cm^{-1}	ν_{asym} (N-C) cm^{-1}	ν_{sym}(N-C) cm^{-1}	ν(M-O) cm^{-1}	ν(M-N) cm^{-1}	ν(O-H) cm^{-1}
A_1	Ligand(SB- A_1)	1640	1580	1372	-	-	-	-	-
1	[Ni(SB- A_1)2-pic]	1620	1467	1293	827	745	524	485	3400
2	[Ni(SB - A_1)Py]	1619	1467	1294	822	745	523	483	3435
3	[Ni(SB- A_1)Q]	1608	1467	1292	810	744	523	483	3054
4	[Co(SB - A_1)IQ]	1604	1476	1277	827	746	512	390	3429
A_2	Ligand(SB-A_2)	1650	1590	1382					
5	[Co(SB-A_2)Q]	1620	1509	1377	810	740	529	488	3434
6	[Ni(SB-A_2)IQ]	1633	1500	1278	826	750	535	484	3324
7	[Cu(SB-A_2)Q]	1607	1508	1313	810	759	523	399	3446
8	[Cu(SB- A_2)4Pic]	1619	1506	1231	814	758	578	493	3449

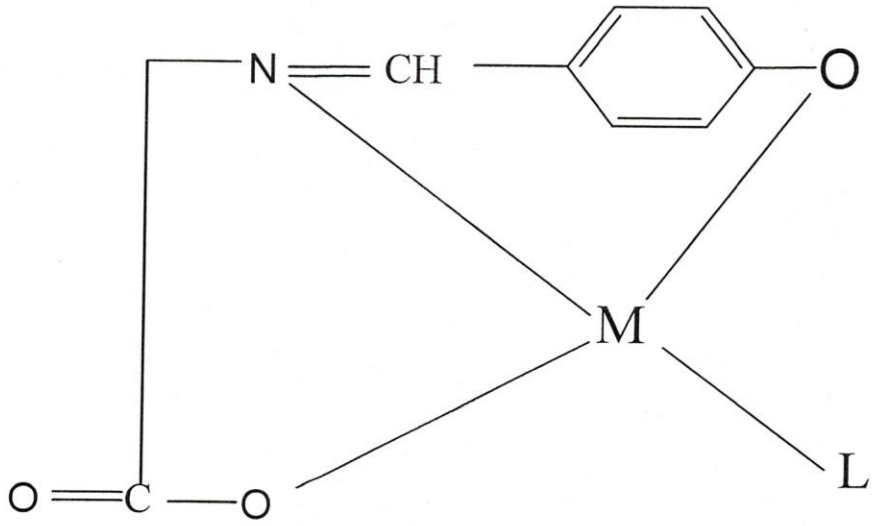
3.4.4. ^{1}H NMR Studies.

From the ^{1}H NMR spectra of the complex [Ni(SB- A_2)IQ], that the Schiff base ligand and hetero-ligand have taken part in the complexation. From the peak heights of the protons it is clear that isoquinoline and salicylaldehyde (phenyl protons) and Schiff base (azomethine protons) have taken part in the complexation reaction with Ni(II) metal ion. The complex shows separate peak at 3.3 ppm for $-CH_2$ protons.

Complexes	Phenyl proton(ppm)	Azomethine Proton(ppm)	$-CH_2$ proton(ppm)
[Ni(SB- A_2)IQ]	6.7	8	3.32

3.5 CONCLUSION

From the above informations and data the probable structure of the complex is given below



where, M = Co(II), Ni(II) and Cu(II)
L = Heterocyclic amines

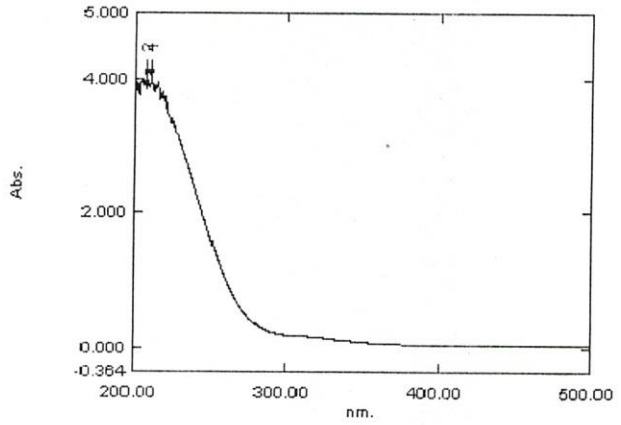


Fig. 3.1: UV-visible spectrum of the complex [[Ni(SB- A_1)2-pic].

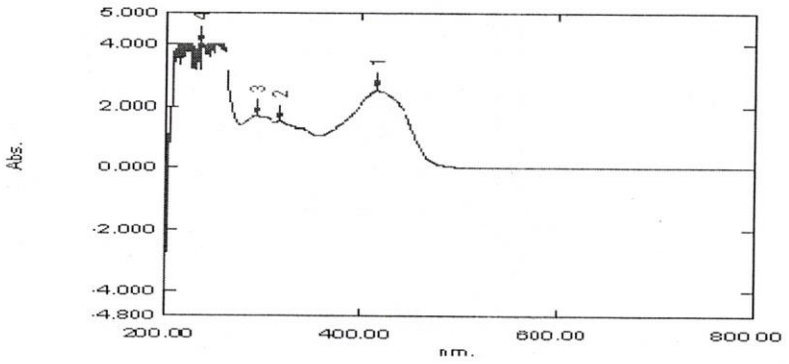


Fig. 3.2: UV-visible spectrum of the complex [[Ni(SB - A_1)Py]]

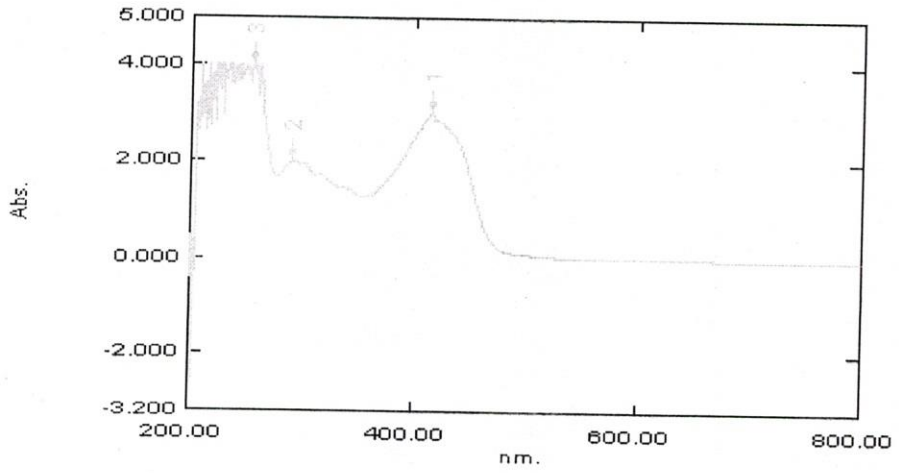


Fig. 3.3: UV-visible spectrum of the complex [Co(SB-A_1)IQ].

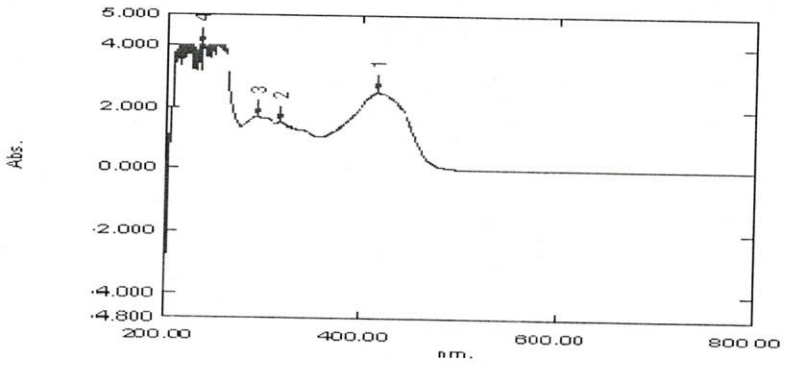


Fig. 3.4: UV-visible spectrum of the complex [Co(SB- A_2)Q].

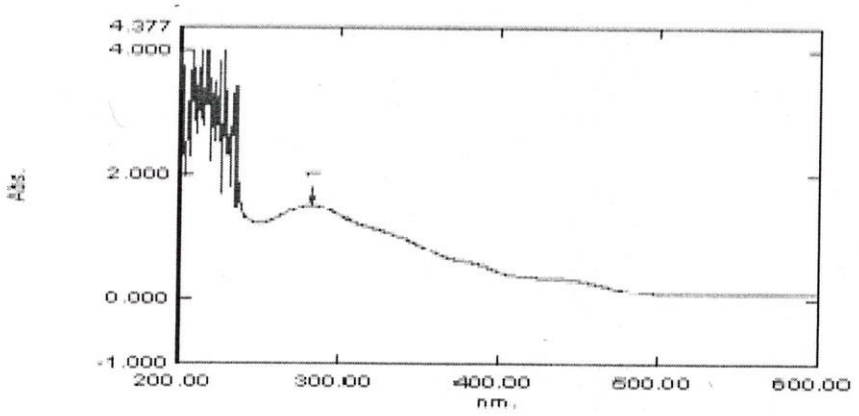


Fig. 3.5: UV-visible spectrum of the complex [Cu(SB-A_2)4-Pic].

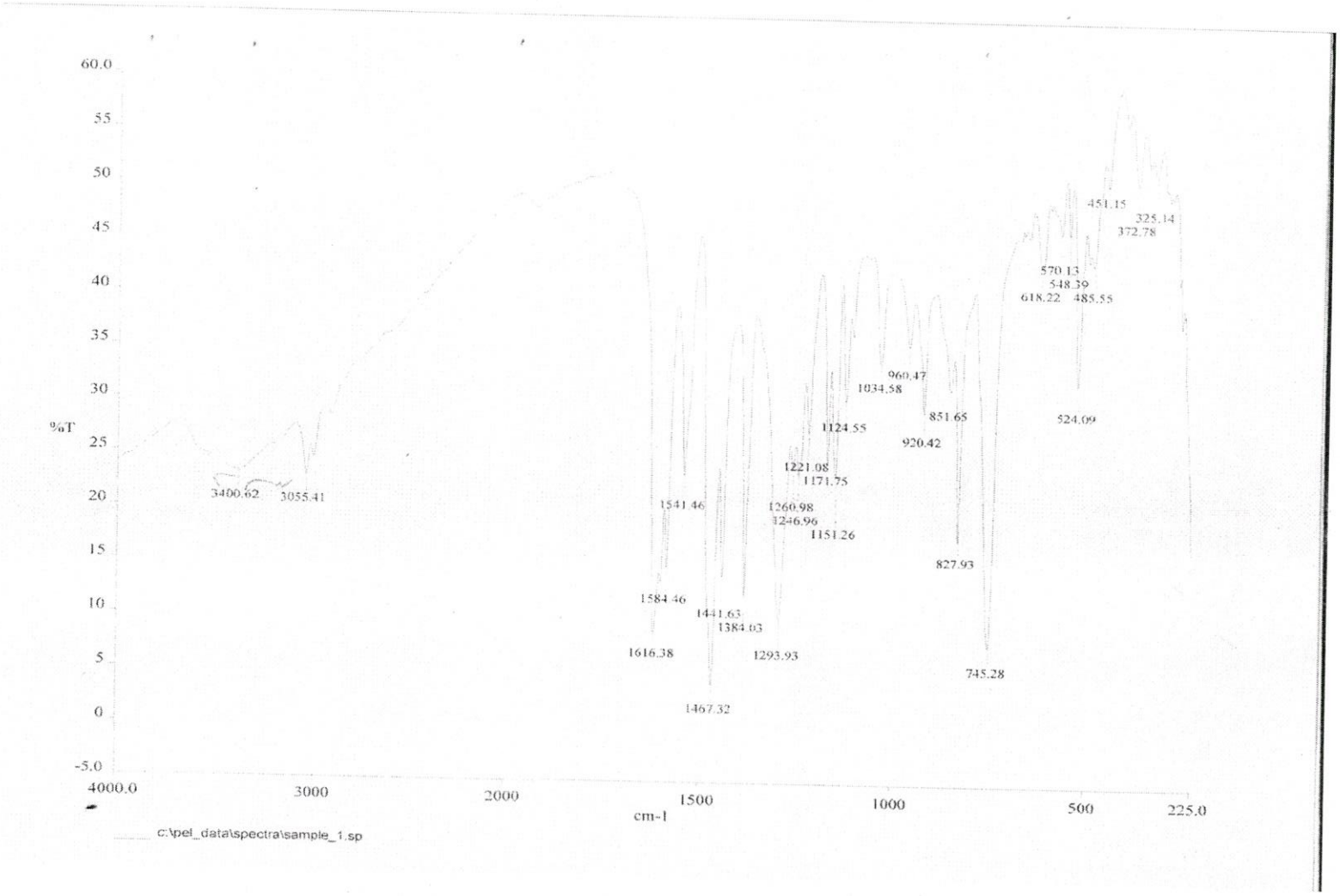


Fig. 3.6: FTIR spectrum of the complex [Ni(II)(SB-A_1)2-Pic]

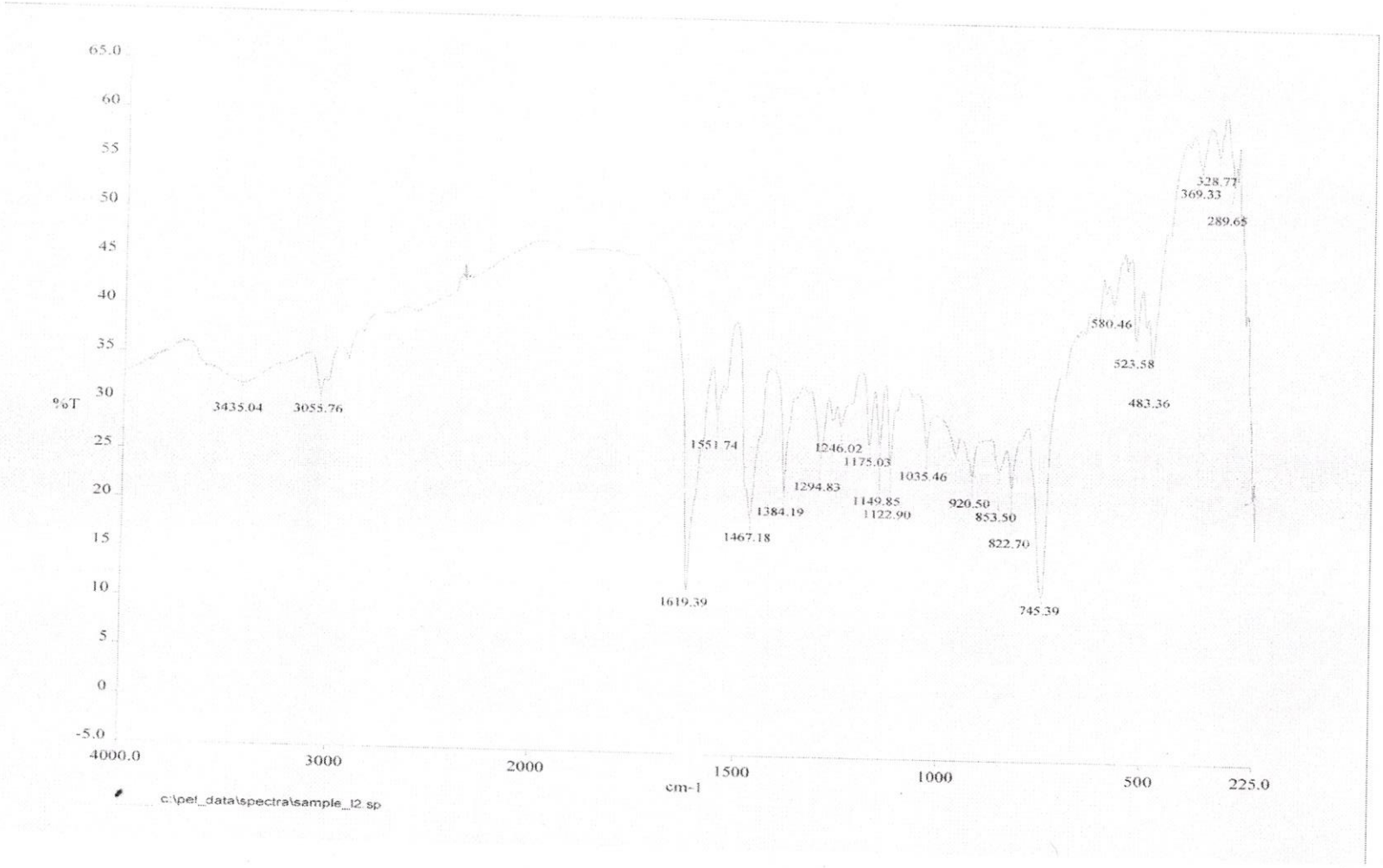


Fig. 3.7: FTIR spectrum of the complex [Ni(II)(SB-A_1)Py]

Fig. 3.8: FTIR spectrum of the complex [Ni(II)(SB-A_1)Q]

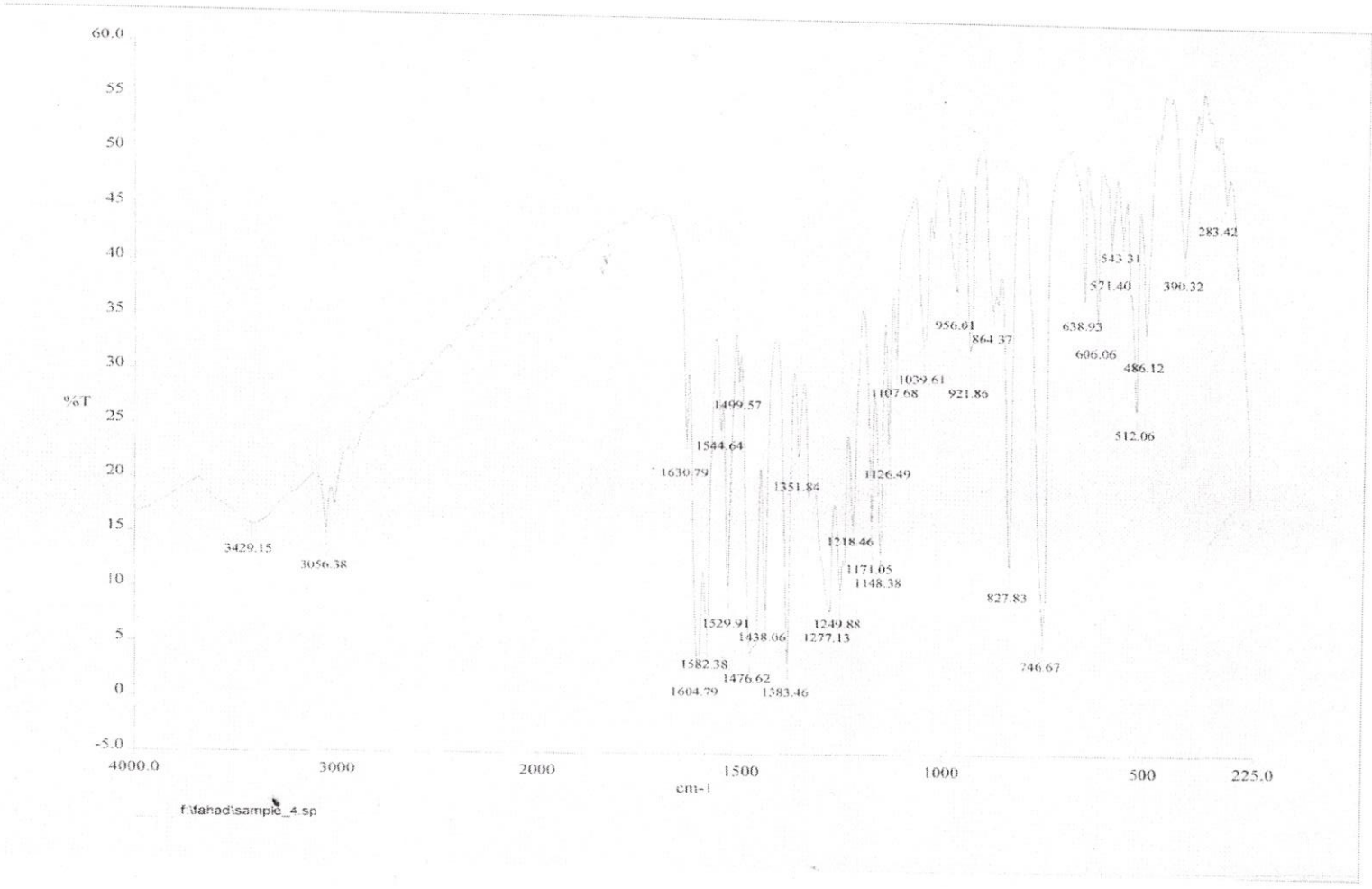


Fig. 3.9: FTIR spectrum of the complex [Co(II)(SB-A_1)IQ]

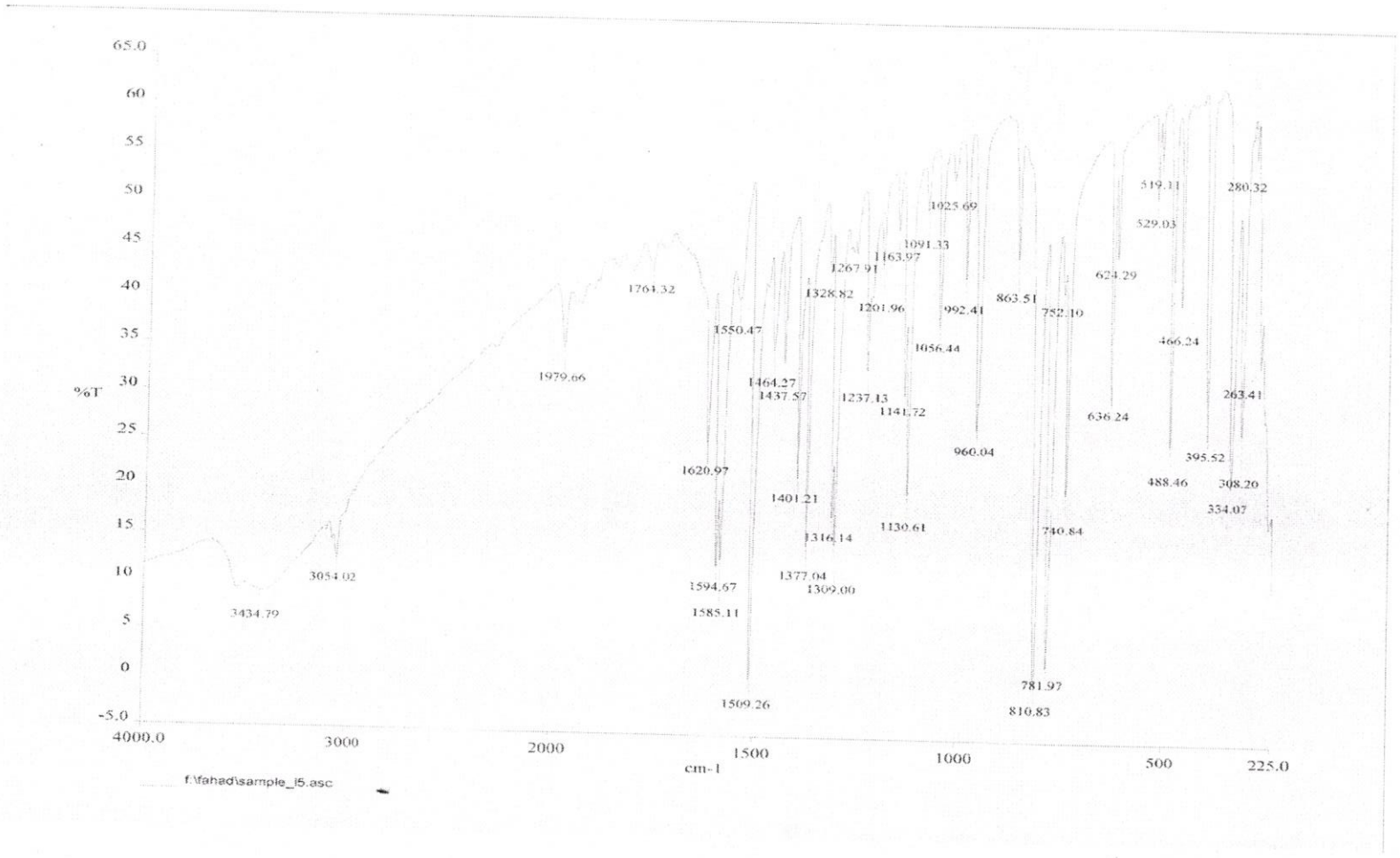


Fig. 3.10: FTIR spectrum of the complex [Co(II)(SB-A_2)Q]

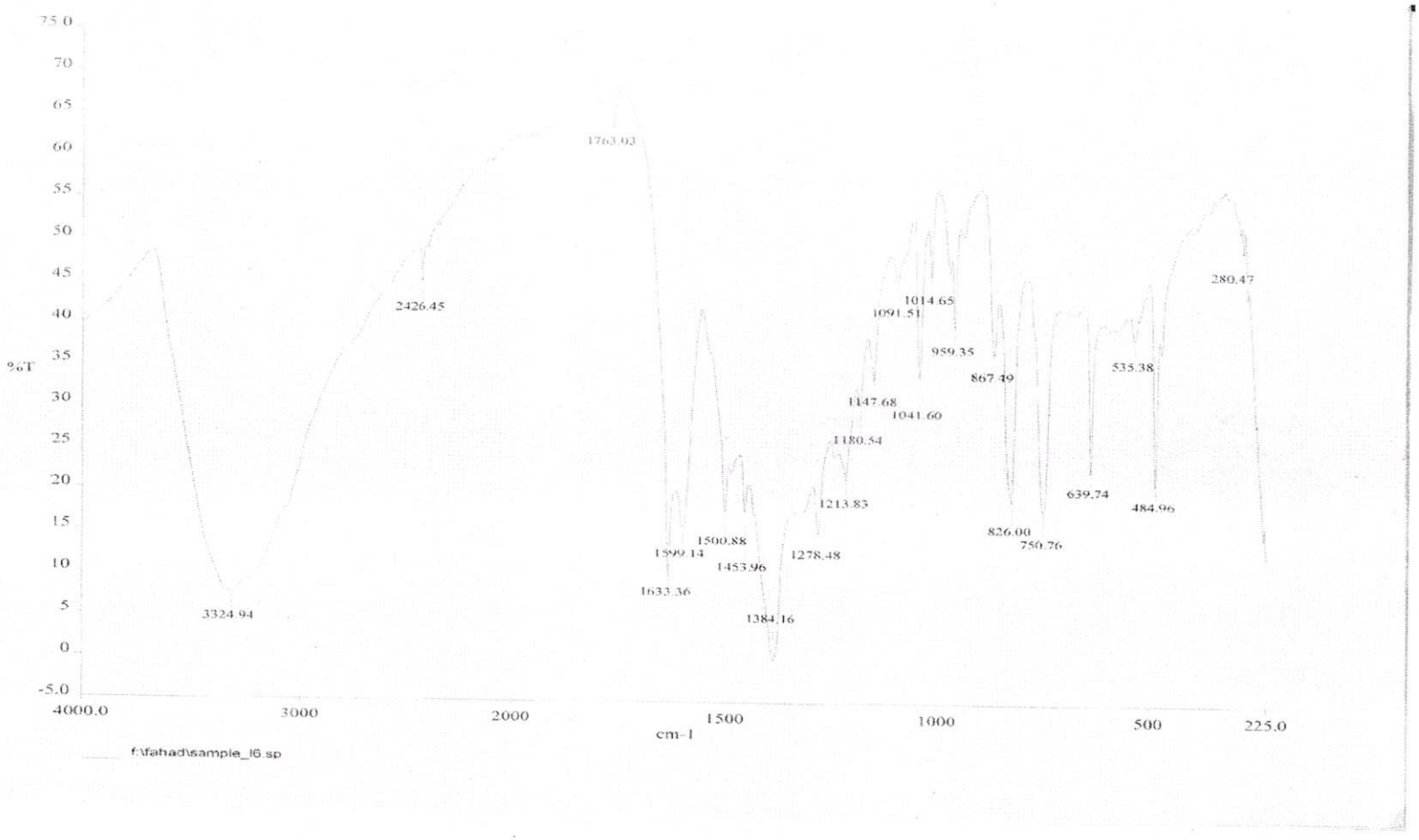


Fig. 3.11: FTIR spectrum of the complex [Ni(II)(SB-A_2)IQ]

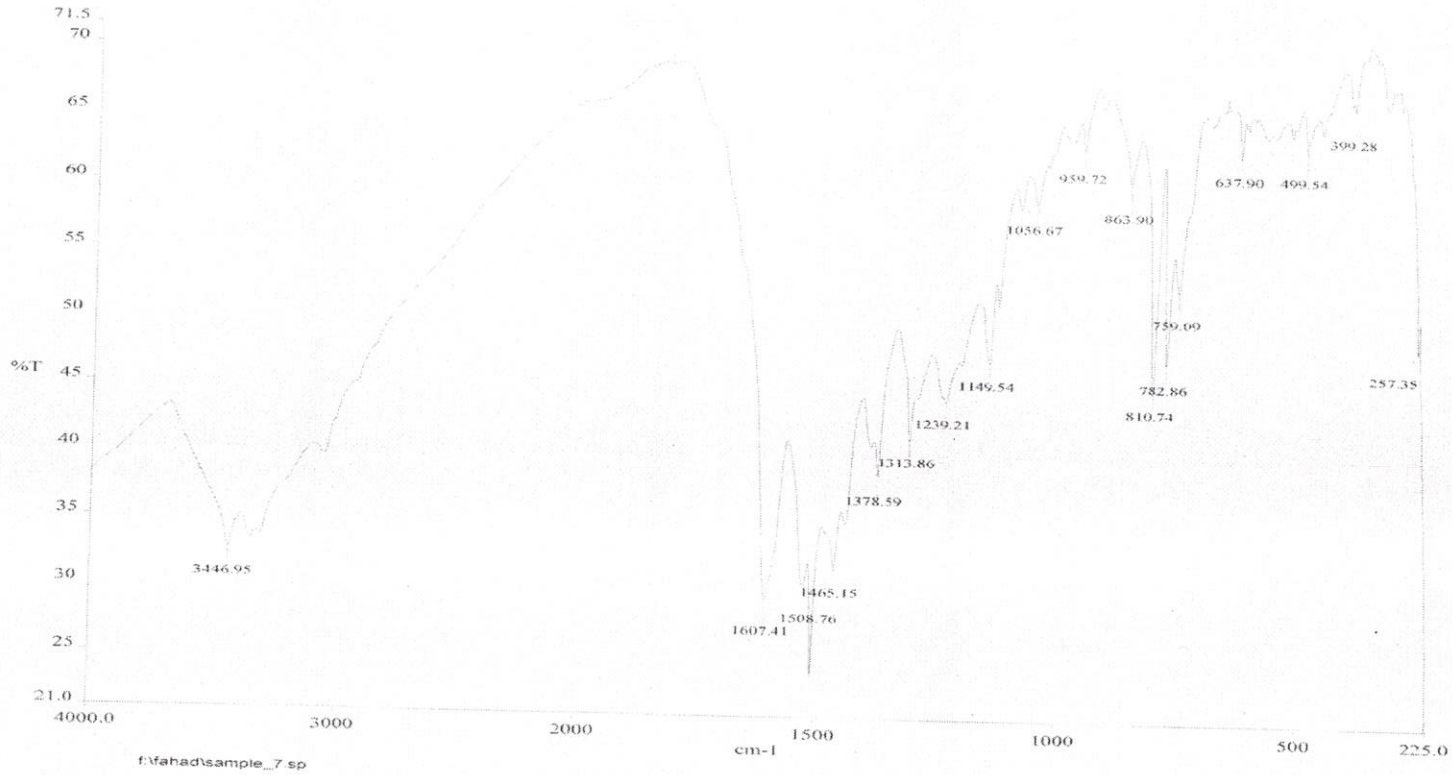


Fig. 3.12: FTIR spectrum of the complex [Cu(II)(SB-A_2)Q]

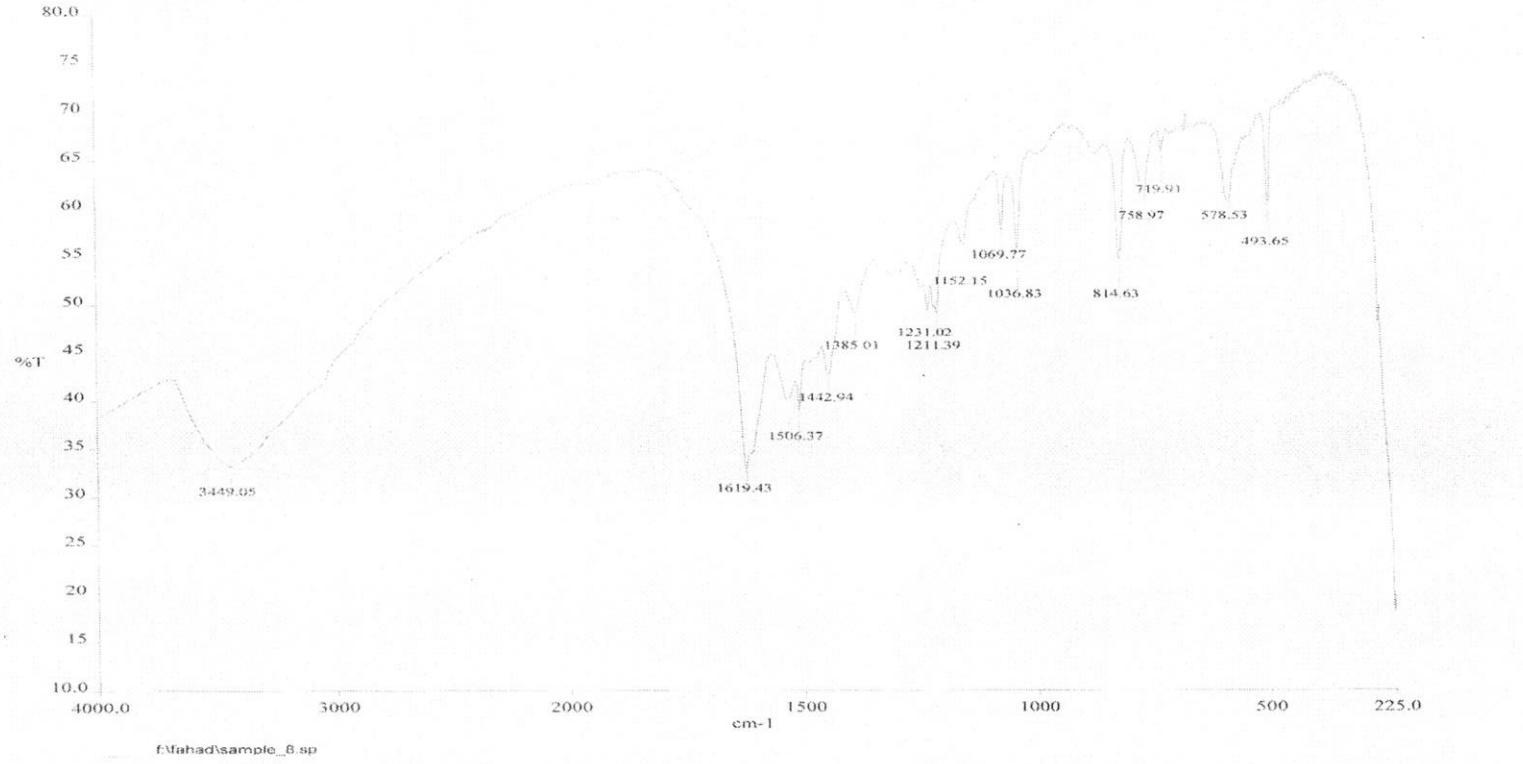


Fig. 3.13: FTIR spectrum of the complex [Cu(II)(SB-A_2)4-Pic]

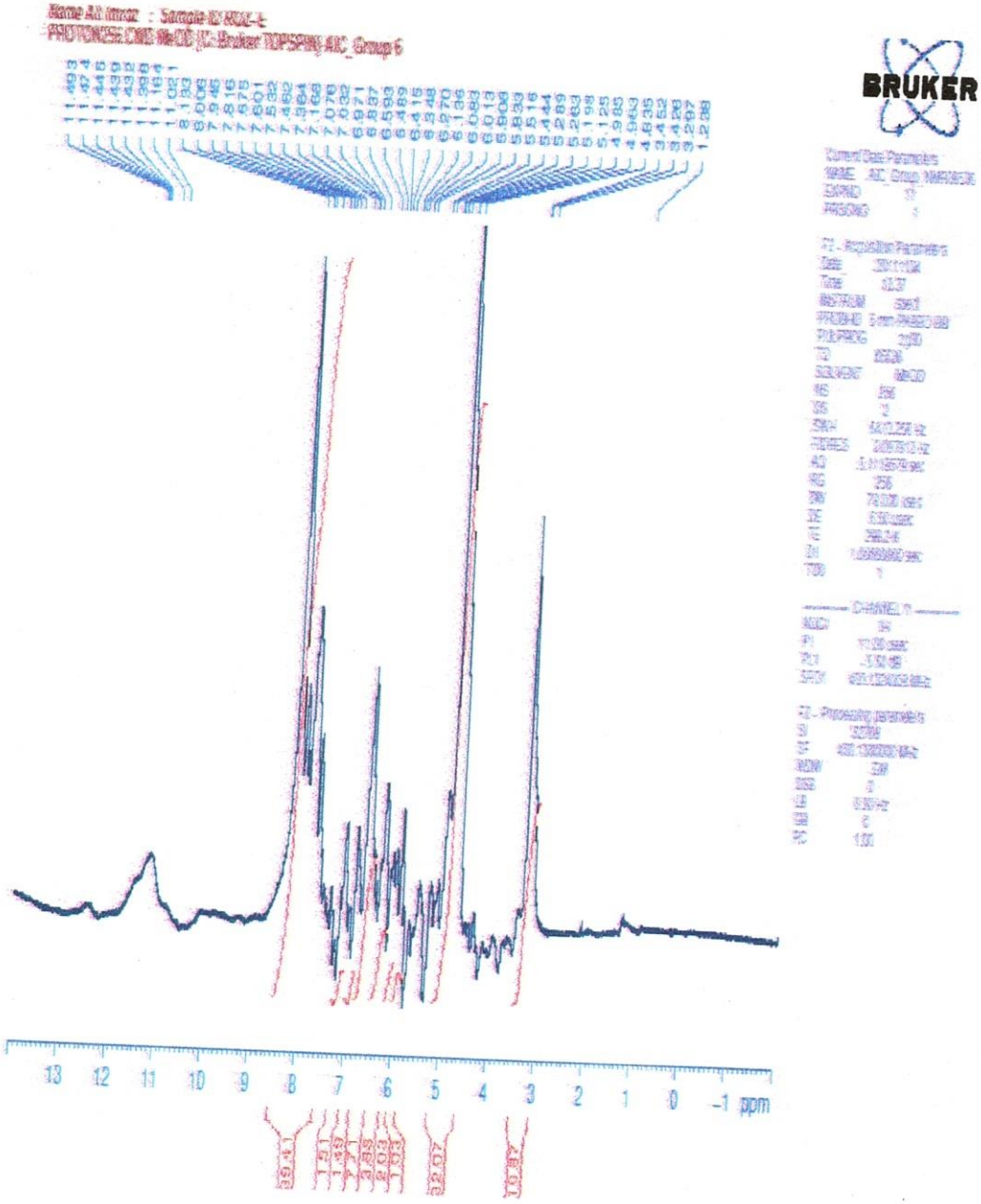


Fig. 3.14 ^{1}H-NMR spectrum of Complex [Ni(II)(SB-A_2)IQ]

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CHAPTER -FOUR

STUDIES ON THE LIGHTER AND HEAVIER METAL COMPLEXES WITH SCHIFF BASES AND HETEROCYCLIC AMINES.

4.1. INTRODUCTION

Many complexes of different Schiff bases have been reported by a number of authors.[1-7] These complexes have attracted special attention due to their wide range of application in analytical chemistry,[8-12] biological and industrial field.[13-17] Most probably Above and Cerbelcv[18-19] were the first workers to synthesize the Schiff base of salicyldehyde and thiosemicarbazide.

Sharma *et. al.* [20] worked on some Iridium (III) complexes derived from Schiff base and aminocarboxylic acids and characterized them by some modern techniques. Ahmed *et al.*[21] prepared complexes of Ni (II) with Schiff base derived from the condensation of 7-hydroxy-5-methoxy-2-methyl amino acids. Complexes of Zr(IV) and Ti(III) with tridentate Schiff base derived from glycine and Salicyldehyde and amine bases were studied by Islam *et al.*[22] Tarafder *et. al.*[23] studied the thiocyanato complexes of Ni(II), Co(II) and Zn(II) . Bovy kin and Barba[24] investigated the complex formed by divalent Ni(II) and Cu(II) with derivatives of salicyldehyde thiosemicarbazone. These kinds of Schiff base ligands provide intriguing chemistry with both the lighter and heavier transition metals.

In this thesis we report the synthesis and characterization of lighter and heavier transition metal complexes with Schiff base and heterocyclic amines.

4.2. EXPERIMENTAL PROCEDURE

4.2.1. Reagents:

As stated in chapter 2 Page No 40.

4.2.2. Physical Measurements: As stated in chapter 2 Page No 41.

4.3.1. General Method of Preparation of Schiff Bases ($SB\text{-}B_1$)/ ($SB\text{-}B_2$):

The Schiff bases were prepared by the condensation of salicyldehyde with O-aminophenol/ ethylenediamine. Solution of salicylaldehyde (1.7g, 0.014 mol) in absolute ethanol (20ml) was added to an ethanolic solution of O-aminophenol / ethylenediamine (0.014mol). The mixture was heated to reduce the volume to 25ml, and then it was cooled in an ice bath. The colored product was isolated and washed with hot ethanol and dried in a vacuum desiccator over anhydrous $CaCl_2$.

4.3.2. General method for the preparation of (SB-B_1)/ (SB-B_2) complexes:

General formula: [M(SB-B_1)/ (SB-B_2)L];Where, M=Co(II), Ni (II), Cu(II), U(VI), Th(IV) and Zr(II).

L=Heterocyclic amines/ Quinoline, Iso-quinoline, 2-picoline and 4-picoline.

4.3 PROCEDURE

0.002mole of metal salt, 0.002mole of SB- B_1/ SB-B_2 and 0.004 mole of KOH were separately dissolved in ethanol and then the solution were mixed and heated on a water bath for half an hour. Then an ethanolic solution of 0.002mole was added to the mixed solution. The resultant mixture was heated under reflux on a water bath for 2hours and then cooled. The coloured precipitate so formed was filtered, washed with hot ethanol and dried in a vacuum desiccator over anhydrous $CaCl_2$.

The formation of the complexes can be shown by the following reactions:

$H_2L' + 2KOH \longrightarrow K_2L' + 2H_2O$

$MCl + K_2L' + L \longrightarrow ML'L + 2KCl$

Where, M= Co (II), Ni (II), Cu (II), U (VI), Th (IV) and Zr (II).

H_2L' ⟶ Schiff bases (SB- B_1)/ (SB-B_2)

L' ⟶ Deprotonated Schiff bases

L ⟶ Heterocyclic amines e,g, Quinoline, Isoquinoline, 2-Picoline and 4-Picoline.

4.4.RESULTS AND DISCUSSION

4.4.1. Physical properties of the complexes:

The physical properties of the complexes are given in Table 4.4.1(a) and 4.4.1(b). The molar conductance in DMSO indicate that the lighter metal complexes are non electrolyte in nature and the heavier metal complexes are electrolyte in nature.[25] The magnetic susceptibility measurement showed that the complexes of Co(II) and Cu(II) were paramagnetic in nature and the Ni(II) was diamagnetic and heavier metal complexes are diamagnetic in nature also.

Table 4.4.1 (a): Physical properties of the complexes:

No.	Complex	Colour	Meltig point	Molar Conductace Ohm^{-1}Cm^{2}mol^{-1}	Magnetic moment μ_{eff} (B.M.)
1	[Co(SB-B_1)Q]	Black	210	2.0	1.86
2	[Co(SB- B_1)IQ]	Brown	245	2.1	1.73
3	[Co(SB- B_1) (2-Pic)]	Ash	230	3.0	1.89
4	[Co(SB- B_1)(4-Pic)]	Brown	229	2.4	1.98
5	[Ni(SB- B_1)Q]	Greenish yellow	280	2.2	1.68
6	[Ni(SB- B_1)IQ]	Red	235	2.4	Dia
7	[Ni(SB- B_1) (2-Pic)]	Green	260	2.6	Dia
8	[Ni(SB- B_1)(4-Pic)]	Greenish	240	2.9	Dia
9	[Cu(SB- B_1)Q]	Green	225	2.1	1.87
10	[Cu(SB- B_1)IQ]	Black	210	6.1	1.98
11	[Cu(SB- B_1) (2-Pic)]	Deep green	240	3.9	1.90
12	[Cu(SB- B_1)(4-Pic)]	Blue	220	4.5	2.10

Table 4.4.1 (b): Physical properties of the complexes:

No.	Complex	Colour	Melting point	Molar Conductace $Ohm^{-1}Cm^2mol^{-1}$	Magnetic moment μ_{eff} (B.M.)
1	[U(SB- B_2) Q]	Yellow	210	82.50	-0.434
2	[U(SB- B_2)IQ]	Greenish Yellow	198	73.90	0.414
3	[U(SB- B_2) (Py)]	Yellow	165	78.30	0.644
4	[U(SB- B_2)(2-Pic)]	Orange Red	185	75.40	-0.525
5	[Th(SB- B_2)Q]	White	138	73.70	-0.216
6	[Th(SB- B_2)IQ]	Cream	152	88.40	-0.465
7	[Th(SB- B_2) (Py)]	Light Yellow	145	75.70	0.326
8	[Th(SB- B_2)(2-Pic)]	Light Yellow	130	73.72	0.495
9	[Zr(SB- B_2)Q]	Cream	140	74.40	-0.29
10	[Zr(SB- B_2)IQ]	White	122	77.20	-0.432
11	[Zr(SB- B_2) (Py)]	Brown	135	79.80	Dia
12	[Zr(SB- B_2)(2-Pic)]	Cream	132	84.30	Dia

Where, SB- B_1: $C_{13}H_9NO_2H_2$, Q : Quinoline, IQ : Iso-quinoline, 2-Pic : 2-Picoline and 4-Pic : 4-Picoline

4.4.2. Electronic spectra of the complexes:

The UV-vis spectra of the complexes [Co(SB-B_1)L] in Table -4.4.2 (a) showed three absorption bands at 480, 540, 580 nm respectively.

The compound [Ni(SB- B_1))L] showed absorption at 420, 362, and 320 nm which correspond to $^1A_{2g} \rightarrow {}^1A_{2g}$, $^1A_{1g} \rightarrow {}^1B_{1g}$, and $^1A_{1g} \rightarrow {}^1E_{1g}$ transitions in D_{4h} symmetry, respectively.

The UV-vis spectrum of the complexes [Cu(SB-B_1)L] showed three absorption bands at 410, 640, nm for $^2B_{1g} \rightarrow {}^2A_{1g}$ and charge transfer transition respectively.

The electronic spectral data (Table-4.4.2 (b)) of the complexes showed bands between 230-360 nm region due to the charge transfer band only.[28]

Table -4.4.2 (a) Electronic spectral data

Complexes	Band-I in nm	Band-II in nm	Band-III in nm
[Co(SB- B_1)L]	480	540	580
[Ni(SB- B_1)L]	320	362	420
[Cu(SB- B_1)L]	410	480	640

Table -4.4.2 (b) Electronic spectral data

Complexes	λ_{max}(nm)	
Ligand	300	340
[U(SB- B_2)Q]	298	345
[U(SB- B_2)IQ]	255	345
[U(SB- B_2) (Py)]	260	290
[U(SB- B_2)(2-Pic)]	280	325
[Th(SB- B_2)Q]	250	300
[Th(SB- B_2)IQ]	240	350
[Th(SB- B_2) (Py)]	264	314
[Th(SB- B_2)(2-Pic)]	230	315
[Zr(SB- B_2)Q]	260	295
[Zr(SB- B_2)IQ]	315	350
[Zr(SB- B_2) (Py)]	310	360
[Zr(SB- B_2)(2-Pic)]	320	370

4.4.3. IR Studies of the complexes:

The infrared spectral data were shown in Table-4.4.3(a). The Schiff base ($C_{13}H_9NO_2H_2$) behaves as tridentate di-negative ligand coordinating at the imino nitrogen and two oxygen atoms. In the complexes, the shift of ν(C=N) mode to lower frequencies i.e., (1550-1610) cm^{-1} Table-4.4.3 (a) indicates that bond formation takes place through the imino nitrogen atom[26]. The ν(O-H) band observed in the free Schiff base disappears upon coordination, which indicates deprotonation, and coordination at the oxygen site. Furthermore, the presence of ν(M-O) and ν(M-N) linkages of bands at

(535-505) and (415-400) cm^{-1}, respectively were observed for all the complexes. [27]

Infrared spectral data have been presented in Table-4.4.3 (b). The complexes display ν(C=N) bands at (1638-1550) cm^{-1} which was significantly lower than the values of the Schiff base ν(C=N) at 1650 cm^{-1}. These indicate the coordination of Schiff base through their C=N group. The U(VI) complexes display ν(M=O) modes in the region (936-825) cm^{-1} . Further, the modes of ν(M-O) and ν(M-N) were observed at the region (836-725) and (501-459)cm^{-1} respectively. The complexes display ν(N-H) modes in the region of (3468-3435) cm^{-1}.

Table-4.4.3 (a): IR spectral data

No.	Complexes	ν(C=N) cm^{-1}	ν_{asym} (C-H) of aromatic cm^{-1}	ν(M-O) cm^{-1}	ν(M-N) cm^{-1}	ν(O-H) cm^{-1}
1	Ligand/(SB- B_1)	1632	-	-	-	3415
2	[Co(SB-B_1)L]	1610	3040	535	415	-
3	[Ni(SB-B_1)L]	1580	3000	520	410	-
4	[Cu(SB-B_1)L]	1550	3100	505	400	-

Table-4.4.3 (b): IR spectral data

No.	Complexes	ν(N-H) cm^{-1}	ν (C=N) cm^{-1}	ν (M=O) cm^{-1}	ν(M-O) cm^{-1}	ν(M-N) cm^{-1}
1	Ligand/(SB- B_2)	3450	1650	-	-	-
2	[U(SB- B_2)Q]	3468	1579	882	725	501
3	[U(SB- B_2) (Py)]	3459	1629	918	760	463
4	[U(SB- B_2)(2-Pic)]	3435	1550	825	724	459
5	[Th(SB- B_2)Q]	3466	1620	-	750	501
6	[Th(SB- B_2) (Py)]	3460	1629	-	754	456
7	[Zr(SB- B_2)Q]	3468		-	836	463
8	[Zr(SB- B_2) (Py)]	3436	1638	-	825	457

4.4.4. ^{1}H NMR Studies of the complexes:

The NMR spectra of complexes can account all the protons of the ligand in complexes except phenolic proton which are lost during complex formation i,e. deprotonation of the ligand .This is the evidence of coordination via, phenolic oxygen of the ligand. A singlet in the range of 7-8 ppm was found due to azomethine proton of the ligand. Multiplet peaks in the range of 6-7 ppm are due to phenyl protons of salicyldehyde.

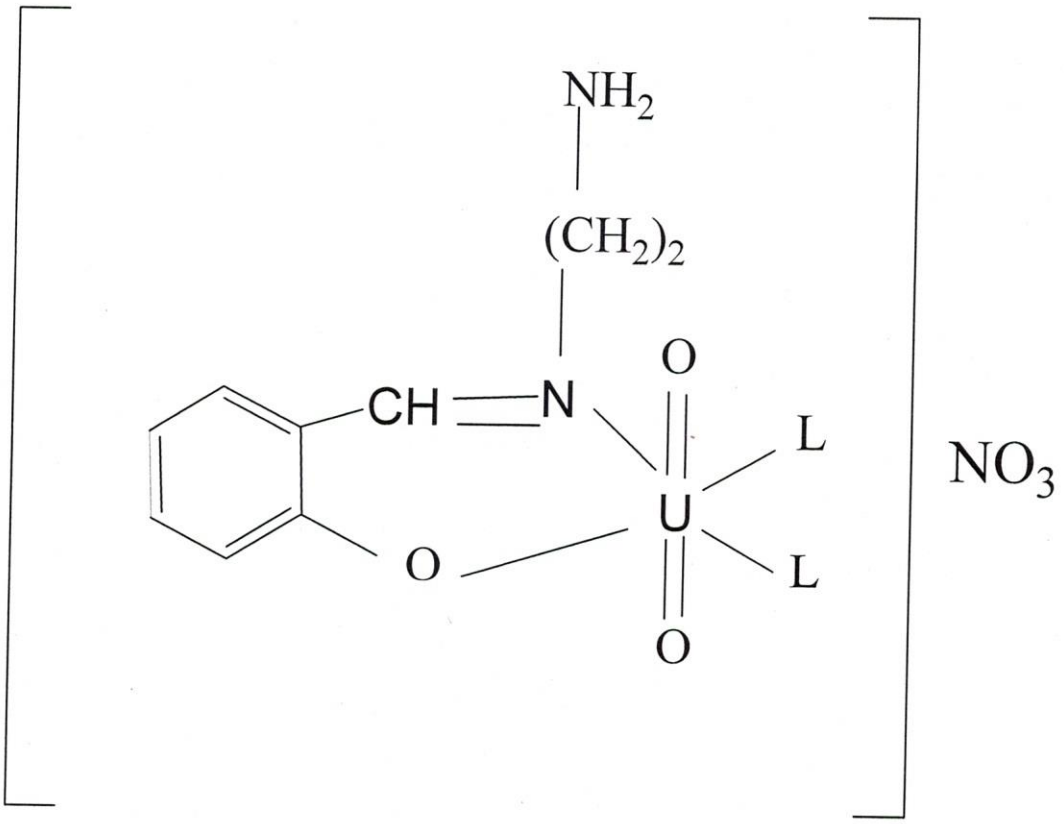
The complexes show two separate peaks at 3.3ppm (for $-CH_2$ proton) and 9.5ppm (for $-NH_2$ proton).

Table-4.4: ^{1}H NMR spectral data

Complexes	Phenyl proton(ppm)	Azomethine Proton(ppm)	$-CH_2$ proton(ppm)	$-NH_2$ proton(ppm)
[U(SB- B_2)Q]	6.96	7.61	3.33	9.465
[Th(SB- B_2) (Py)]	6.95	7.40	3.90	8.58
[Zr(SB- B_2)Q]	6.78	7.84	3.59	9.75

4.5 CONCLUSION

From the above informations and data the probable structure of the complex [U(SB-B_2)L] is given below



Where, L= Heterocyclic amines

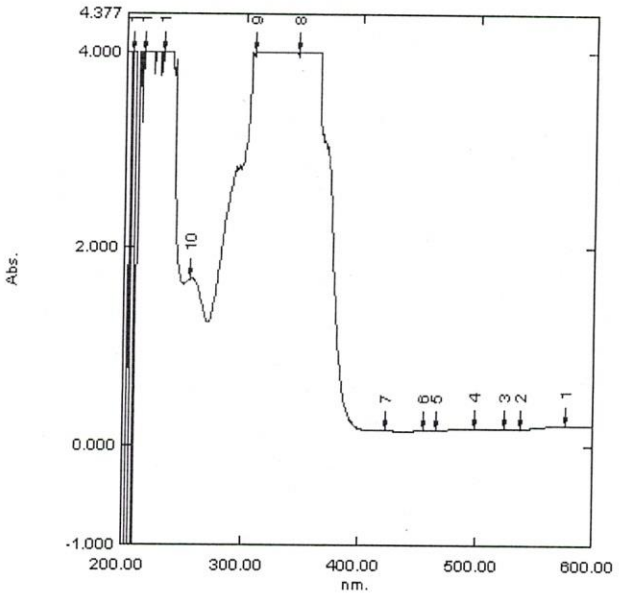


Fig.4.1: UV Spectrum of [Co(SB-B_1)L]

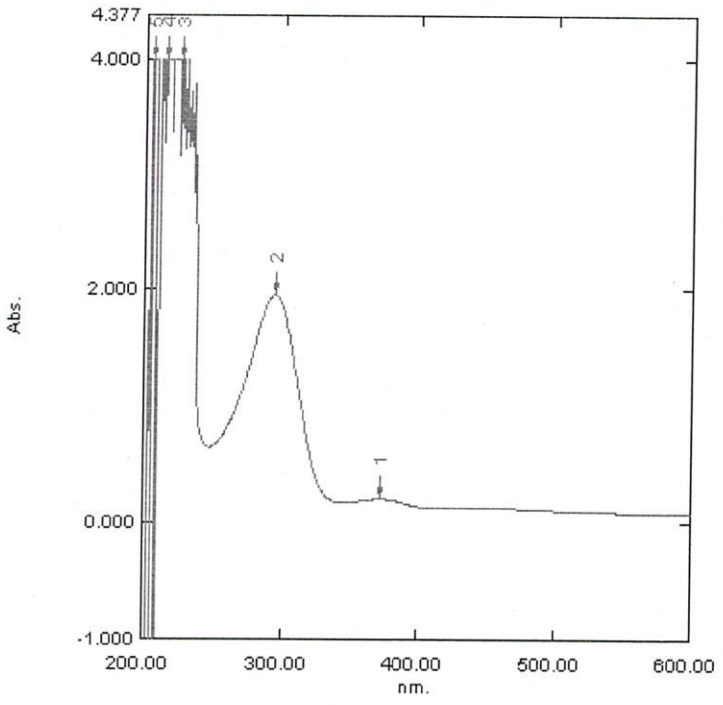


Fig.4.2: UV Spectrum of [Ni(SB-B_1)L]

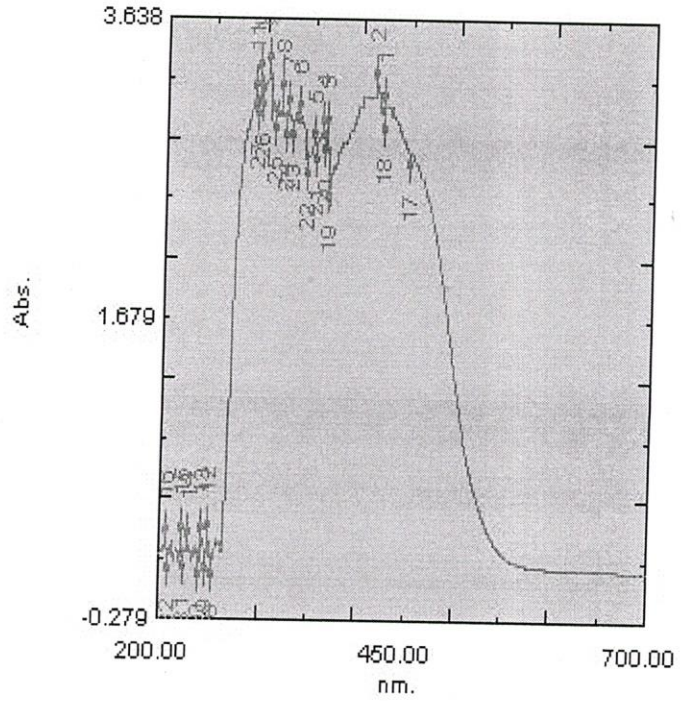


Fig.4.3: UV Spectrum of [U(SB-B_2)Q]

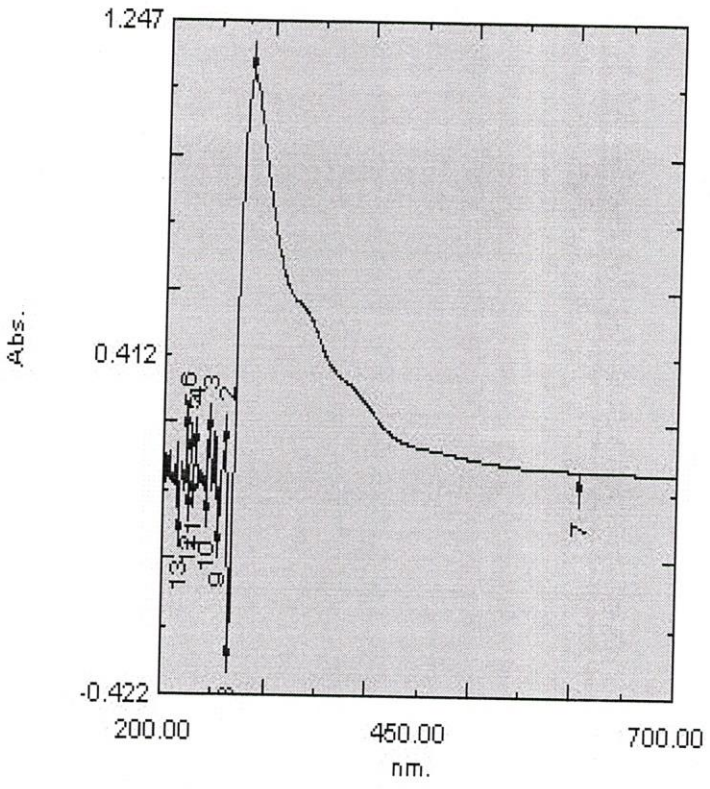


Fig.4.4: UV Spectrum of [U(SB-B_2)IQ]

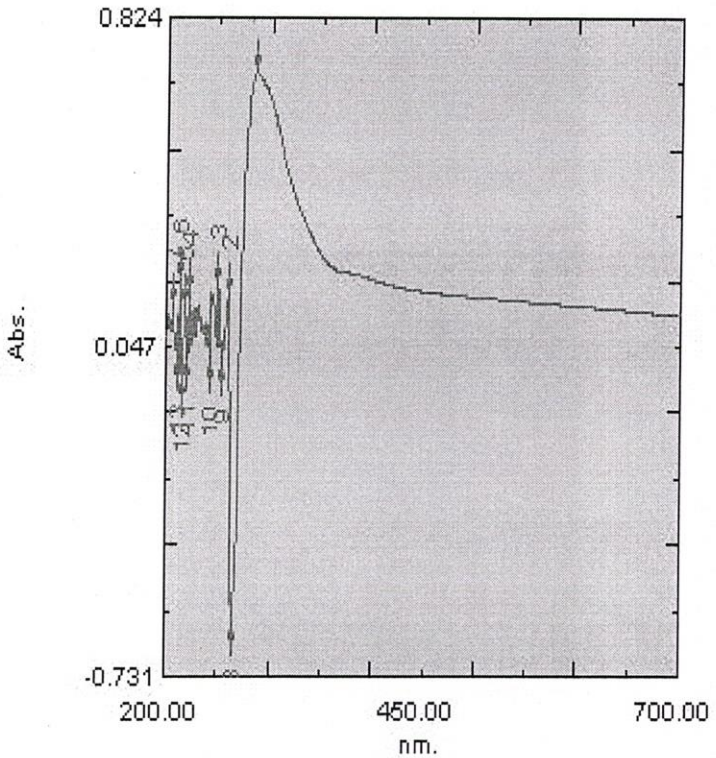


Fig.4.5: UV Spectrum of [Th(SB-B_2)Q]

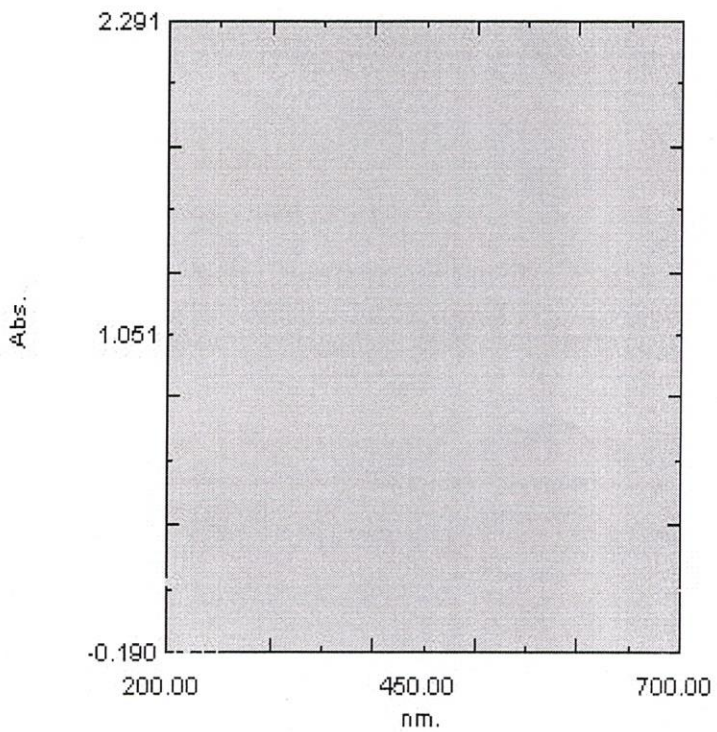


Fig.4.6: UV Spectrum of [Th(SB-B_2)IQ]

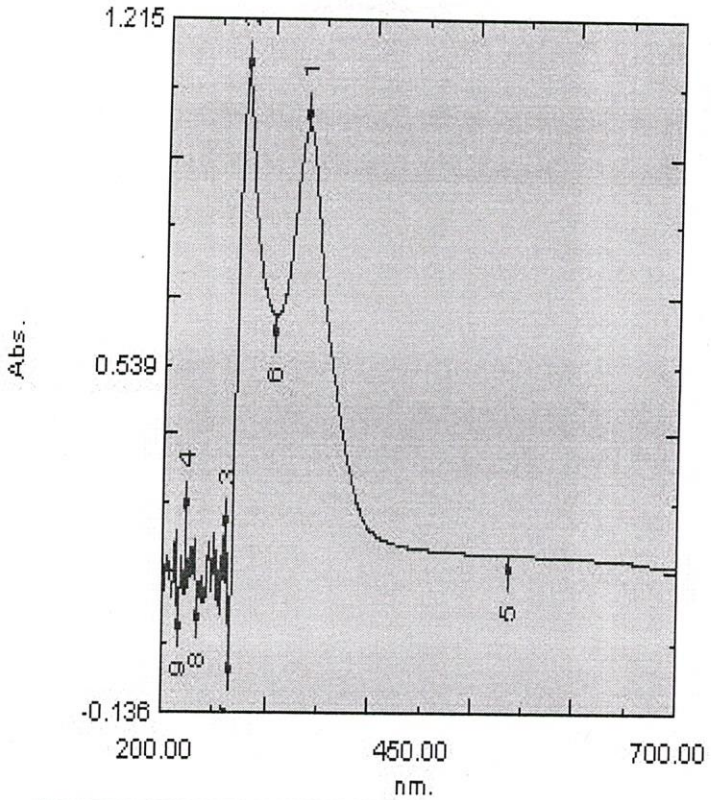


Fig.4.7: UV Spectrum of [Zr(SB-B_2)Q]

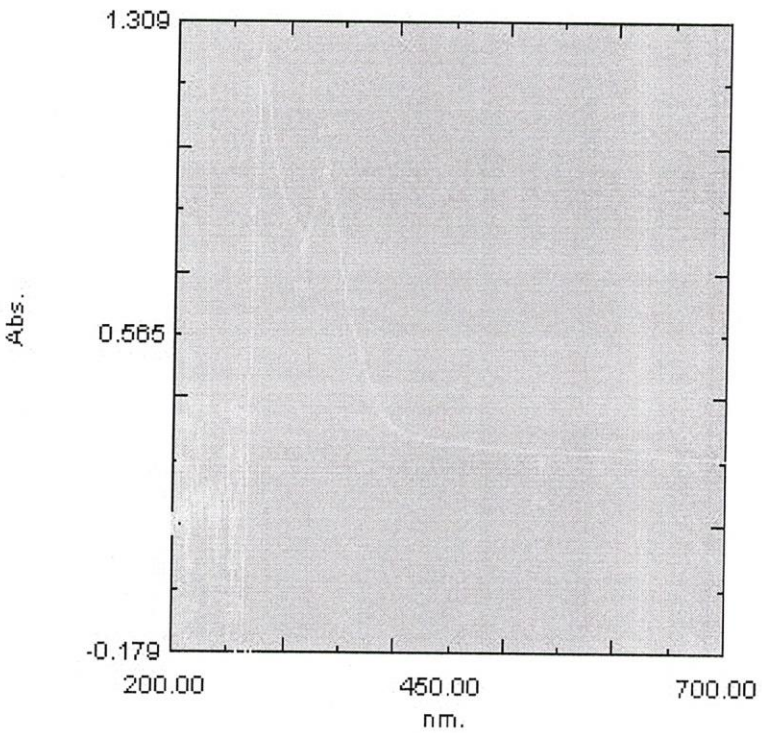


Fig.4.8: UV Spectrum of [Zr(SB-B_2)IQ]

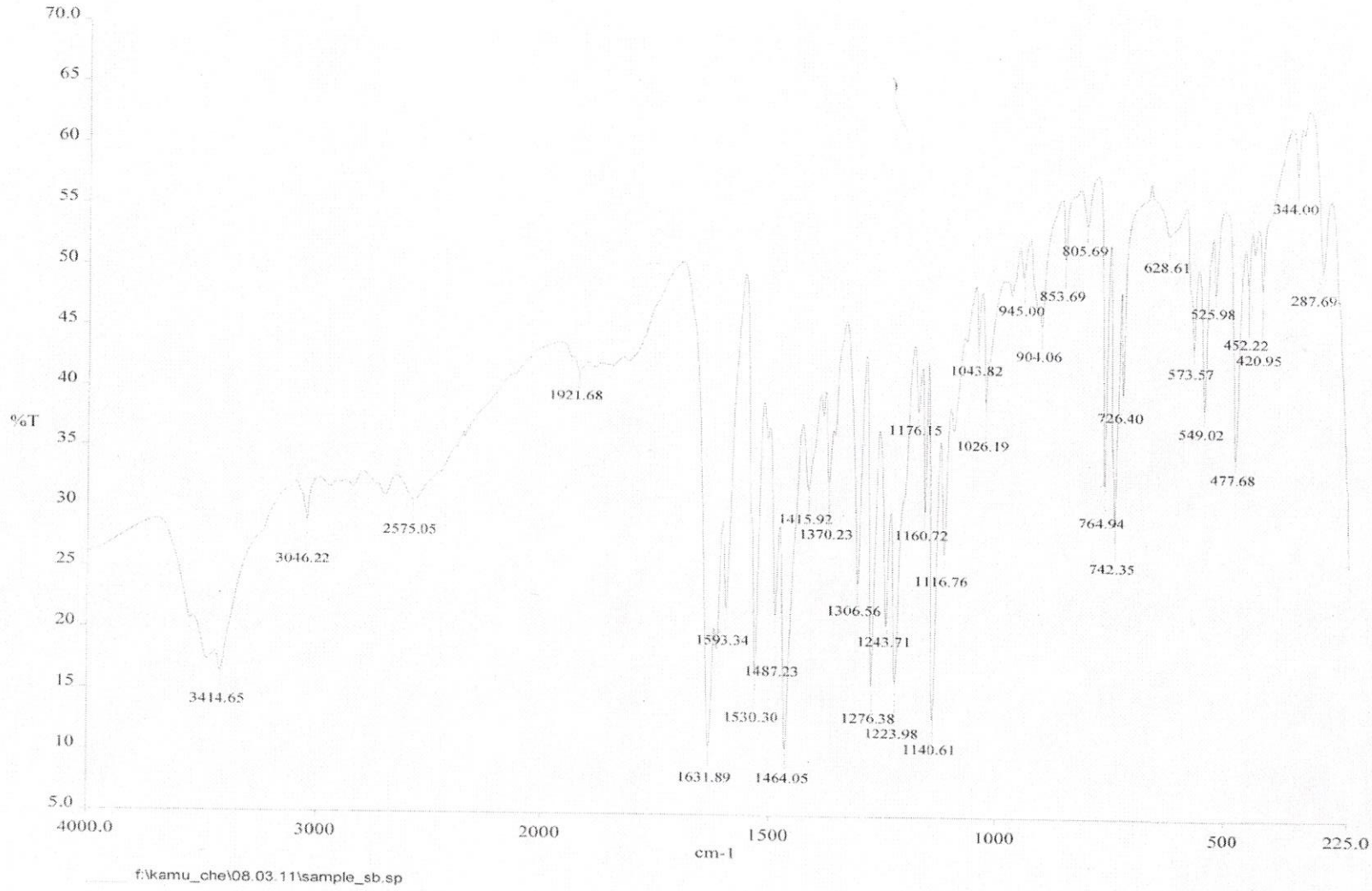


Fig. 4.9: FTIR spectrum of the complex [SB-B_1]

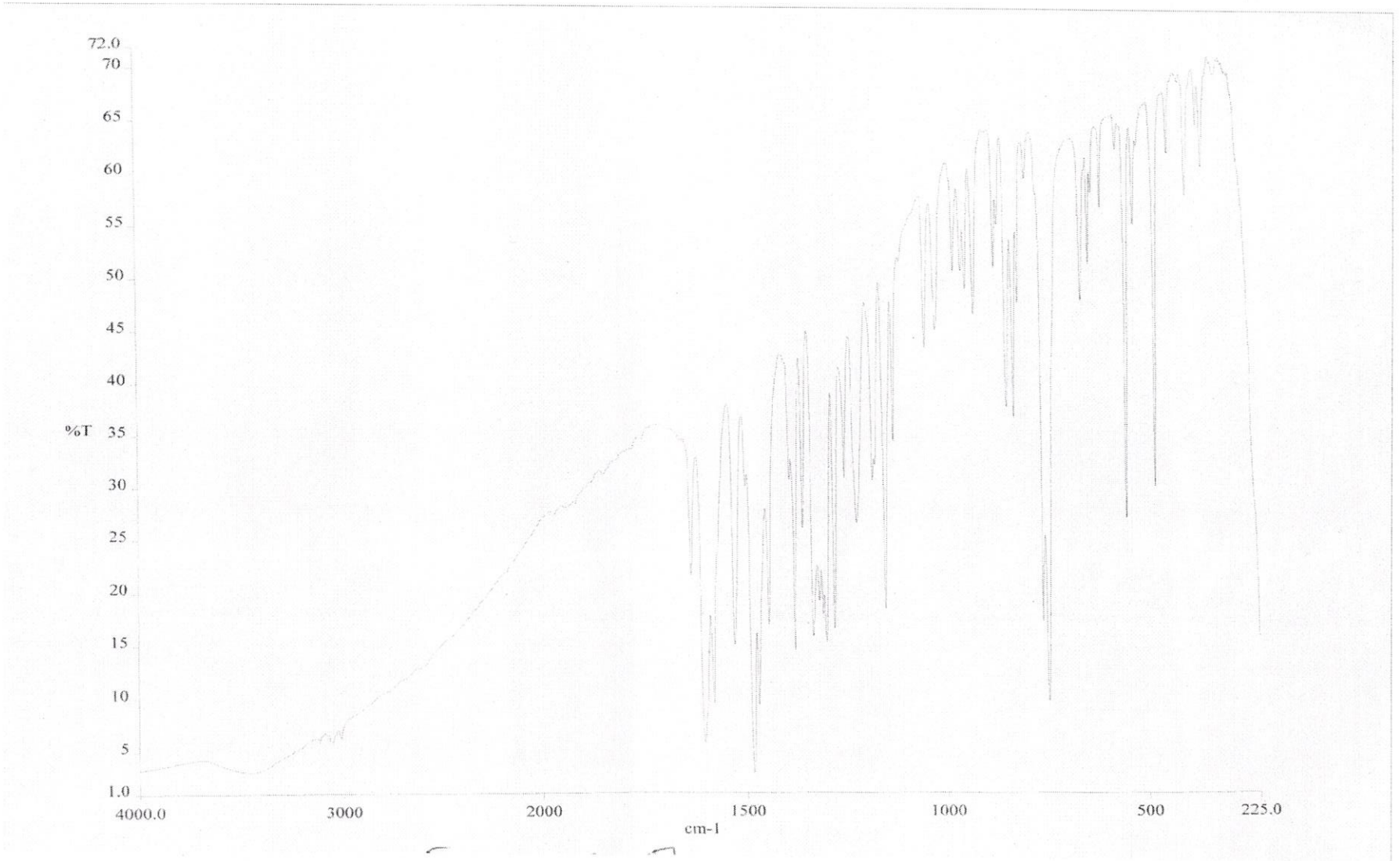


Fig. 4.10: FTIR spectrum of the complex [Co(II)(SB-B_1)IQ]

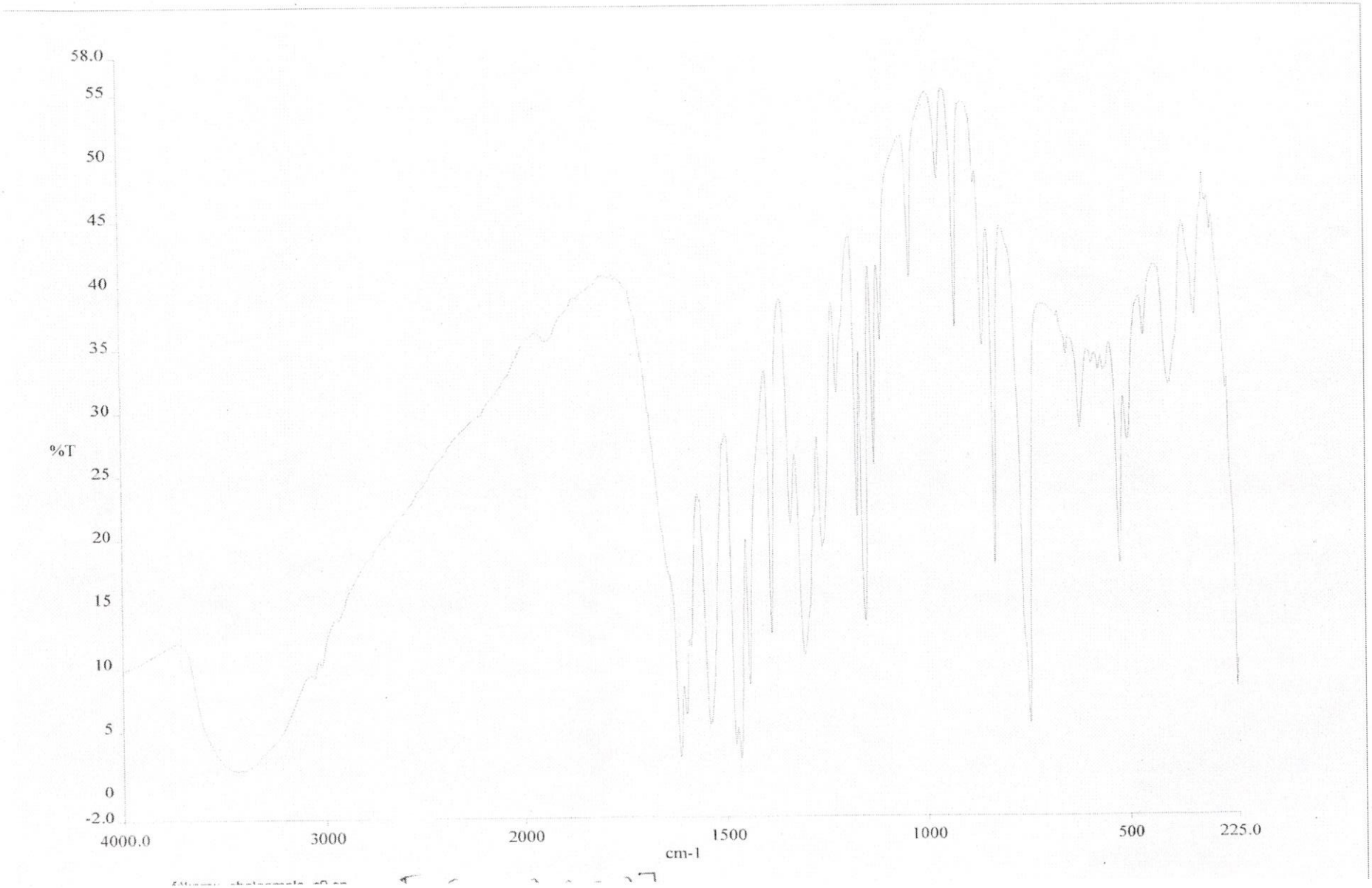


Fig. 4.11: FTIR spectrum of the complex [Ni(II)(SB-B_1)2-Pic]

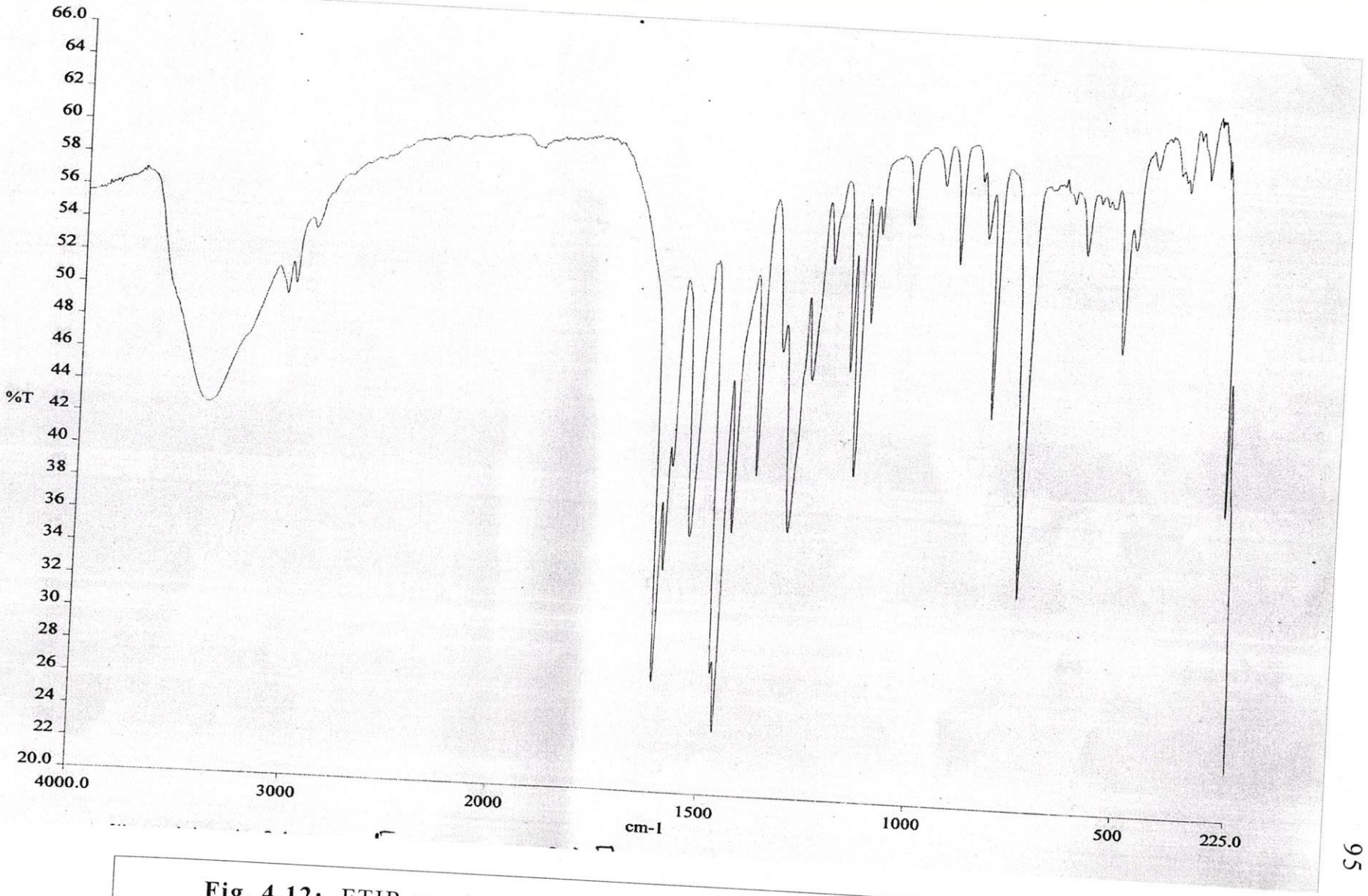


Fig. 4.12: FTIR spectrum of the complex [Ni(II)(SB-B_1)Py]

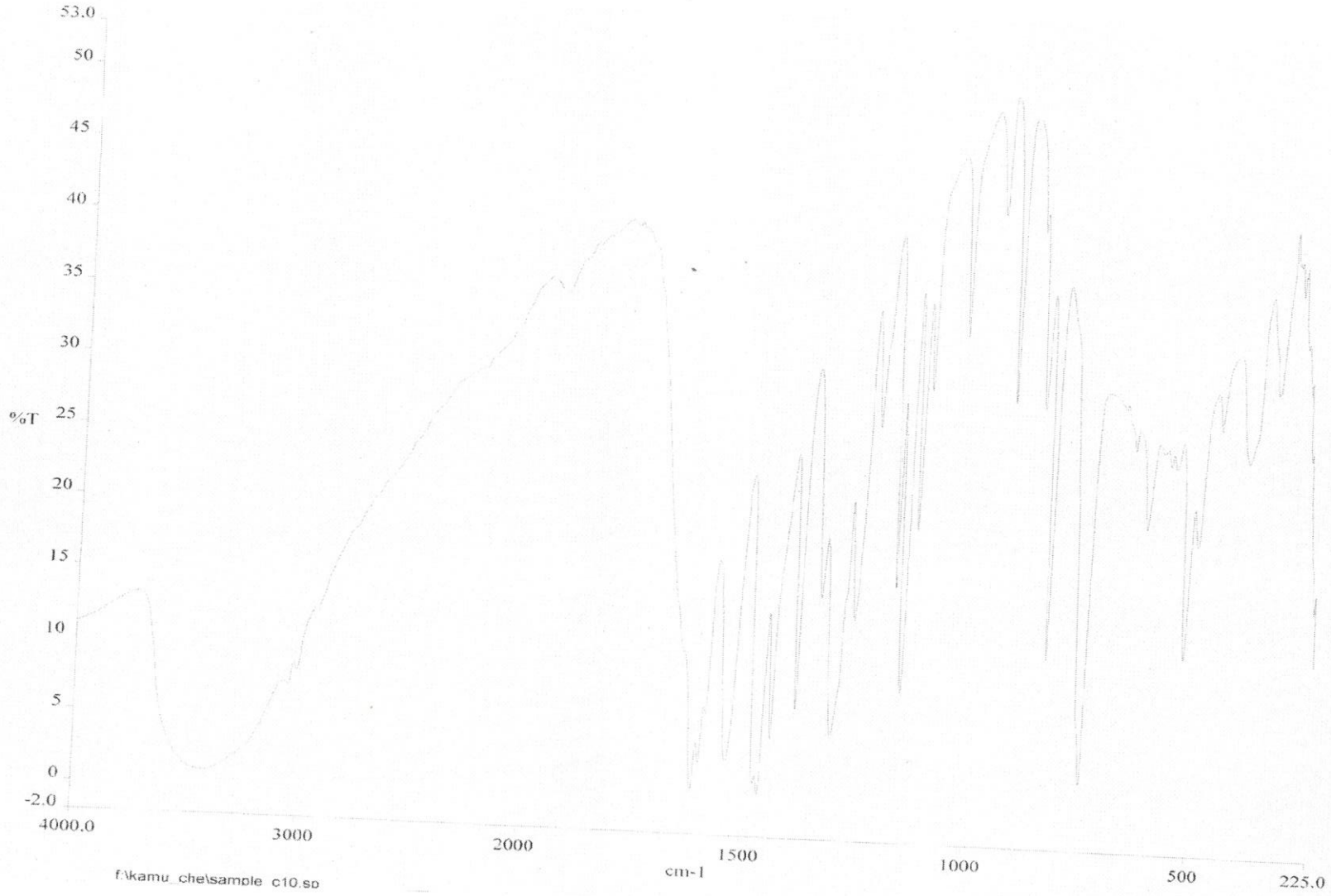


Fig. 4.13: FTIR spectrum of the complex [Ni(II)(SB-B_1)4-Pic]

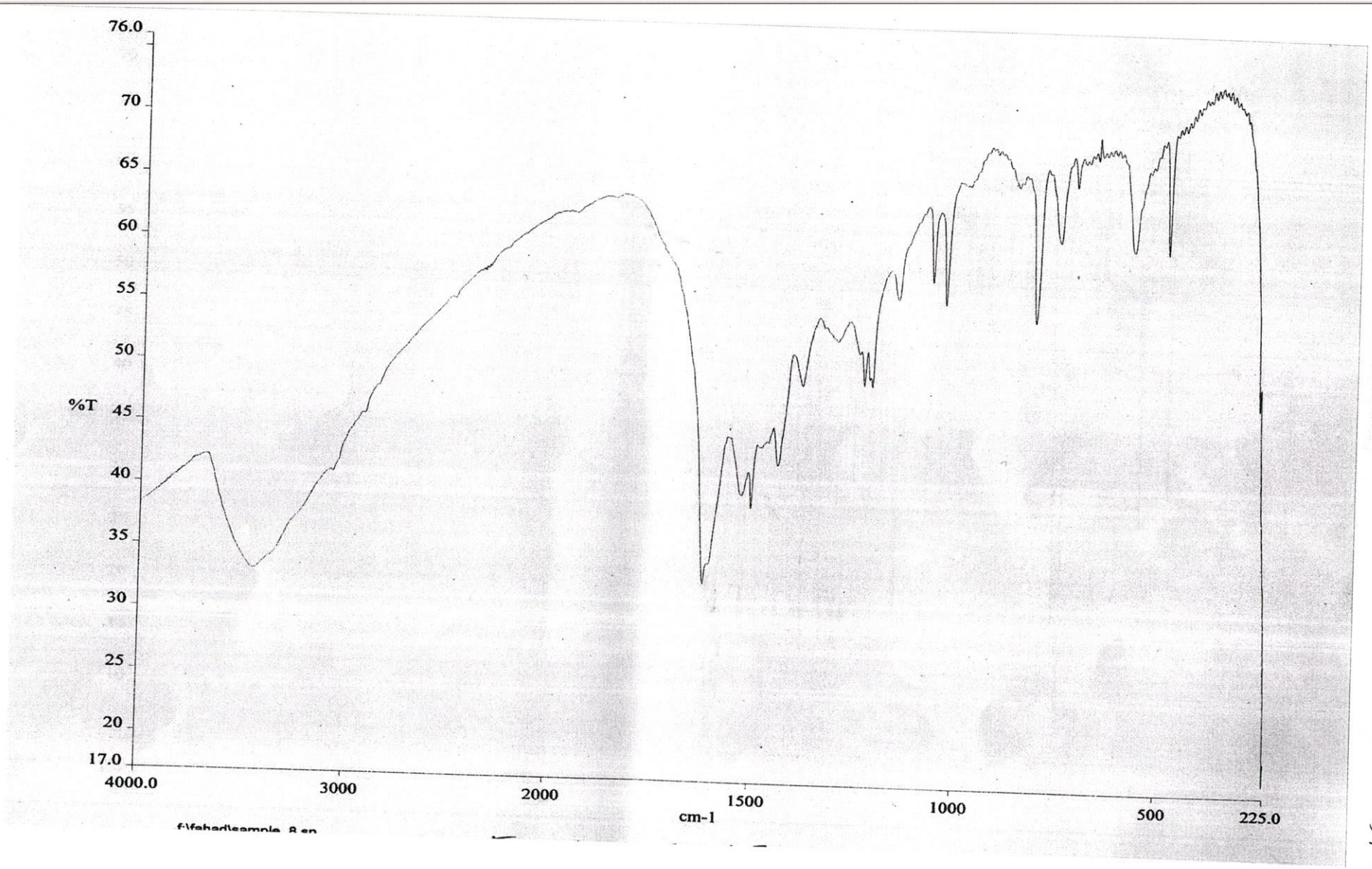


Fig. 4.14: FTIR spectrum of the complex [Cu(II)(SB-B_1)IQ]

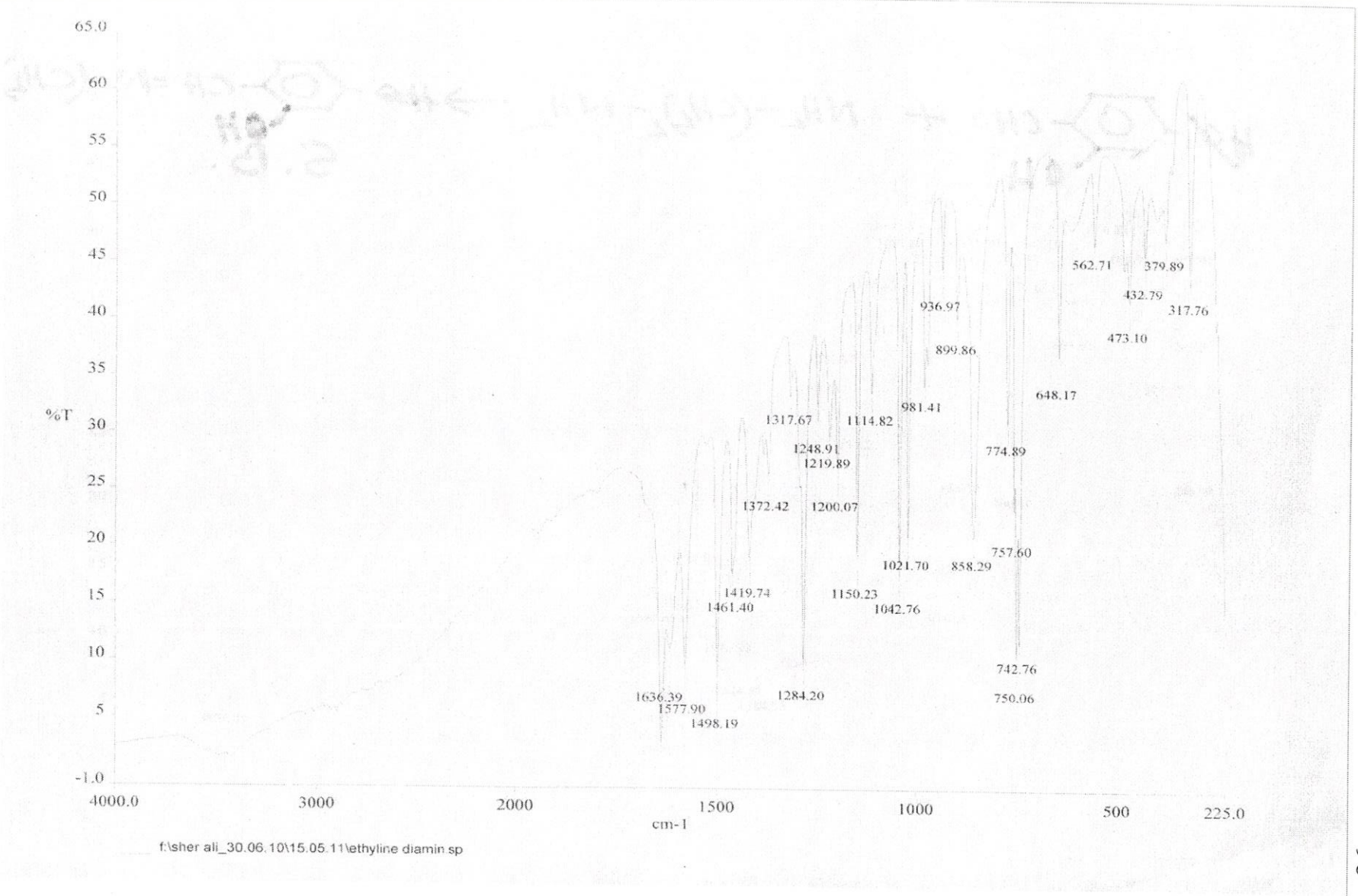


Fig. 4.15: FTIR spectrum of the Schiff Base [SB-B_2]

Fig. 4.16: FTIR spectrum of the complex [U(VI)(SB-B_2)Q]

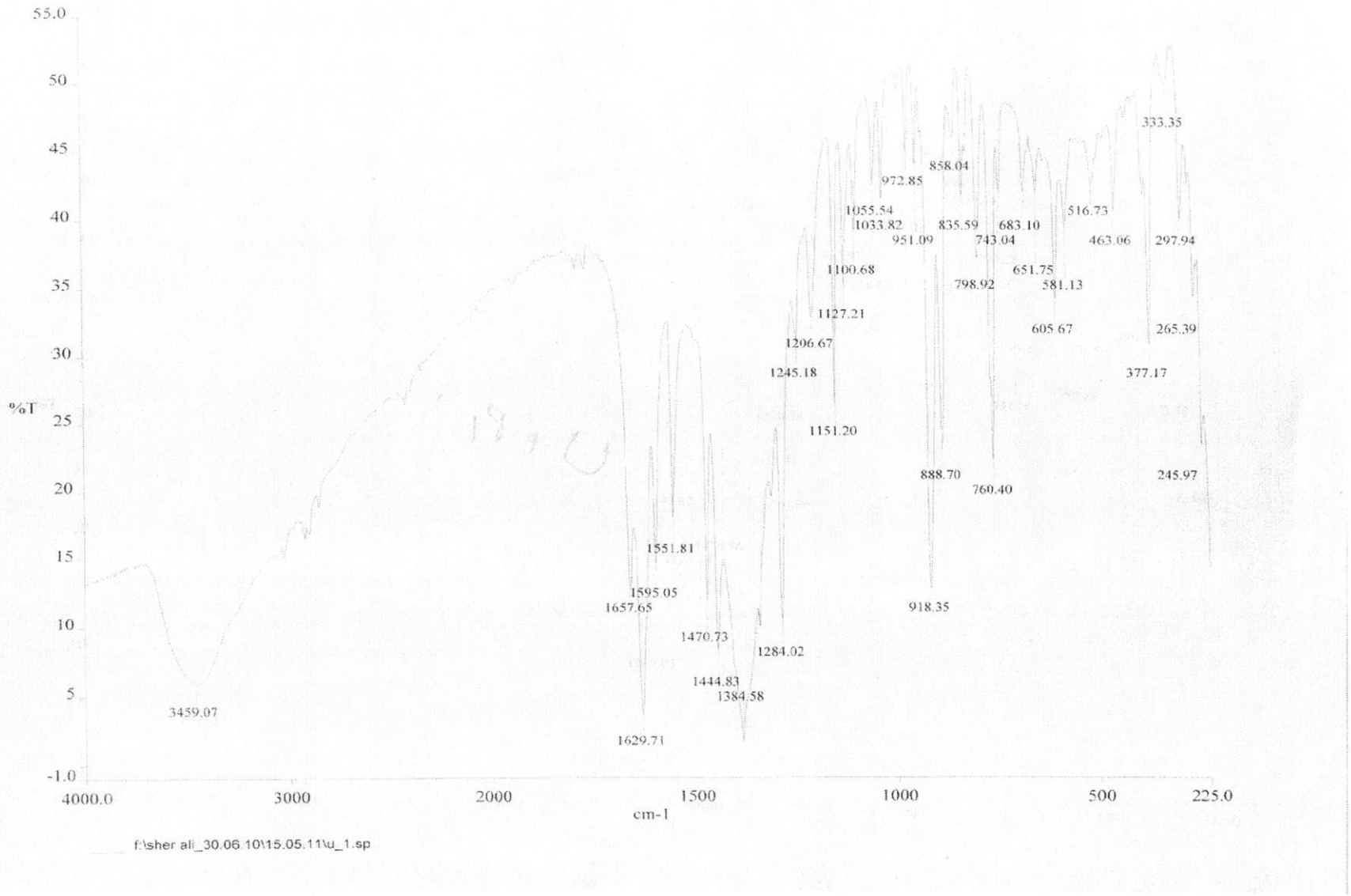


Fig. 4.17: FTIR spectrum of the complex [U(VI)(SB-B_2)Py]

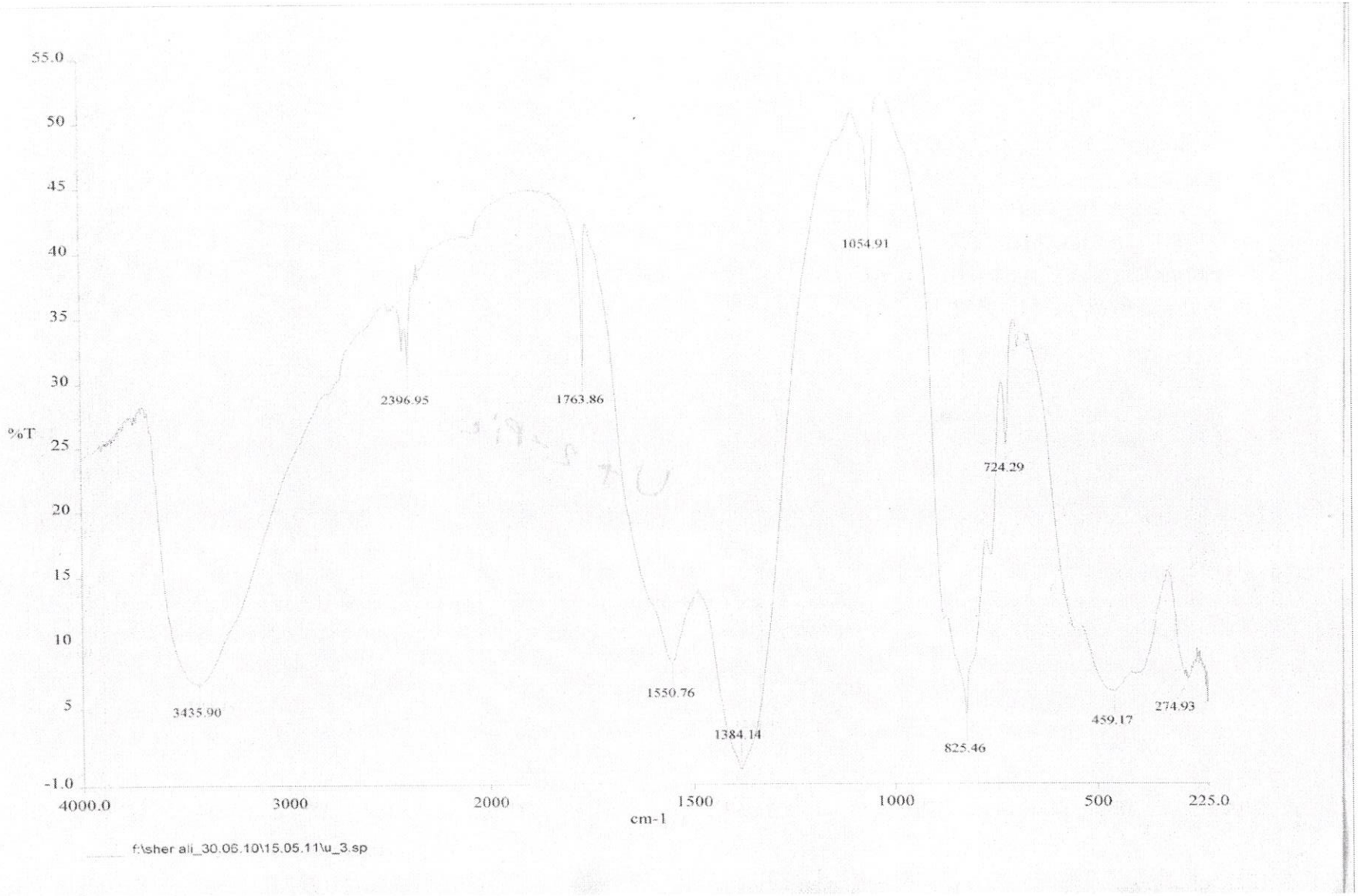


Fig. 4.18: FTIR spectrum of the complex [U(VI)(SB-B_2)2-Pic]

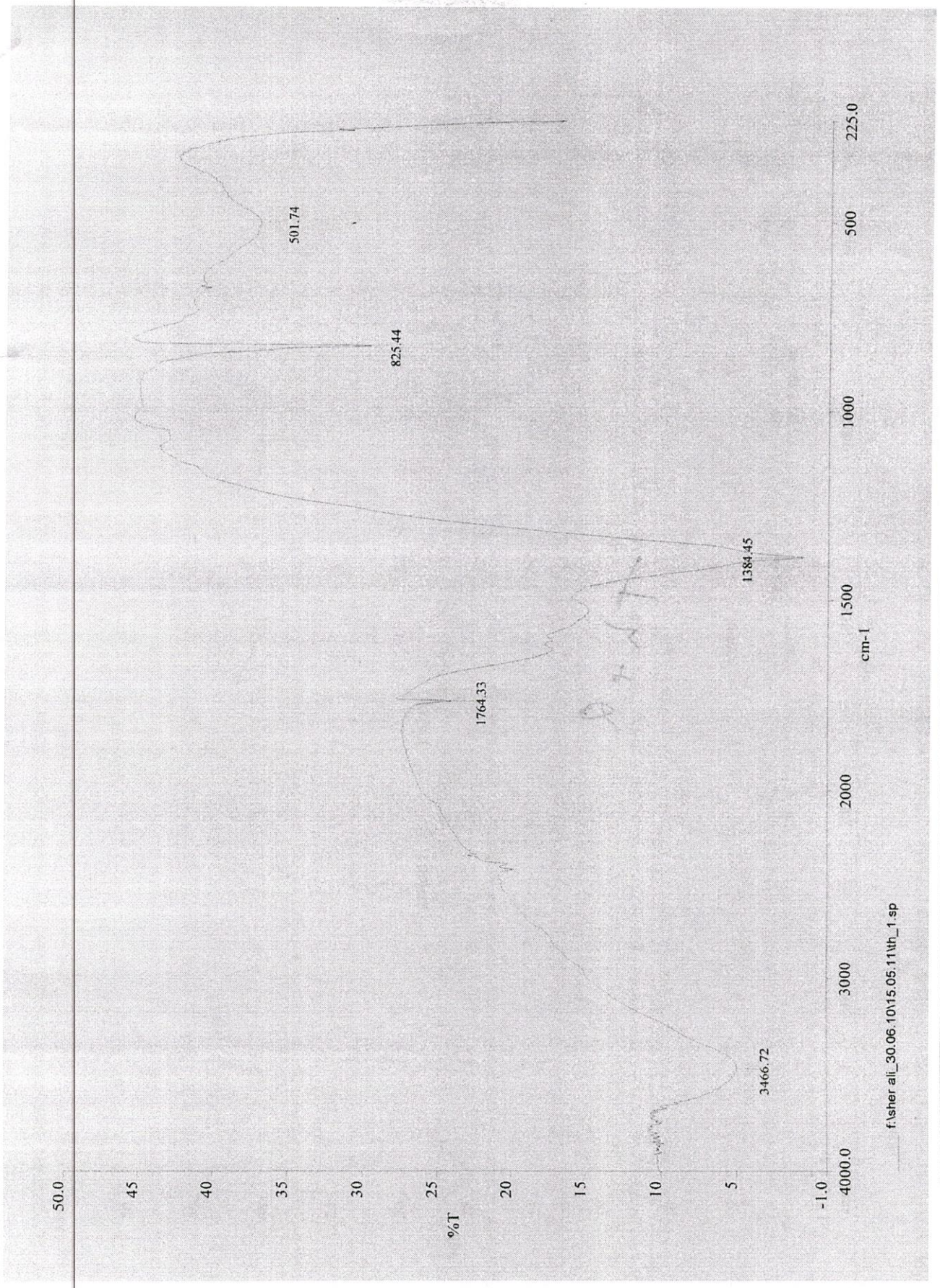


Fig. 4.19: FTIR spectrum of the complex [Th(IV)(SB-B_2)Q]

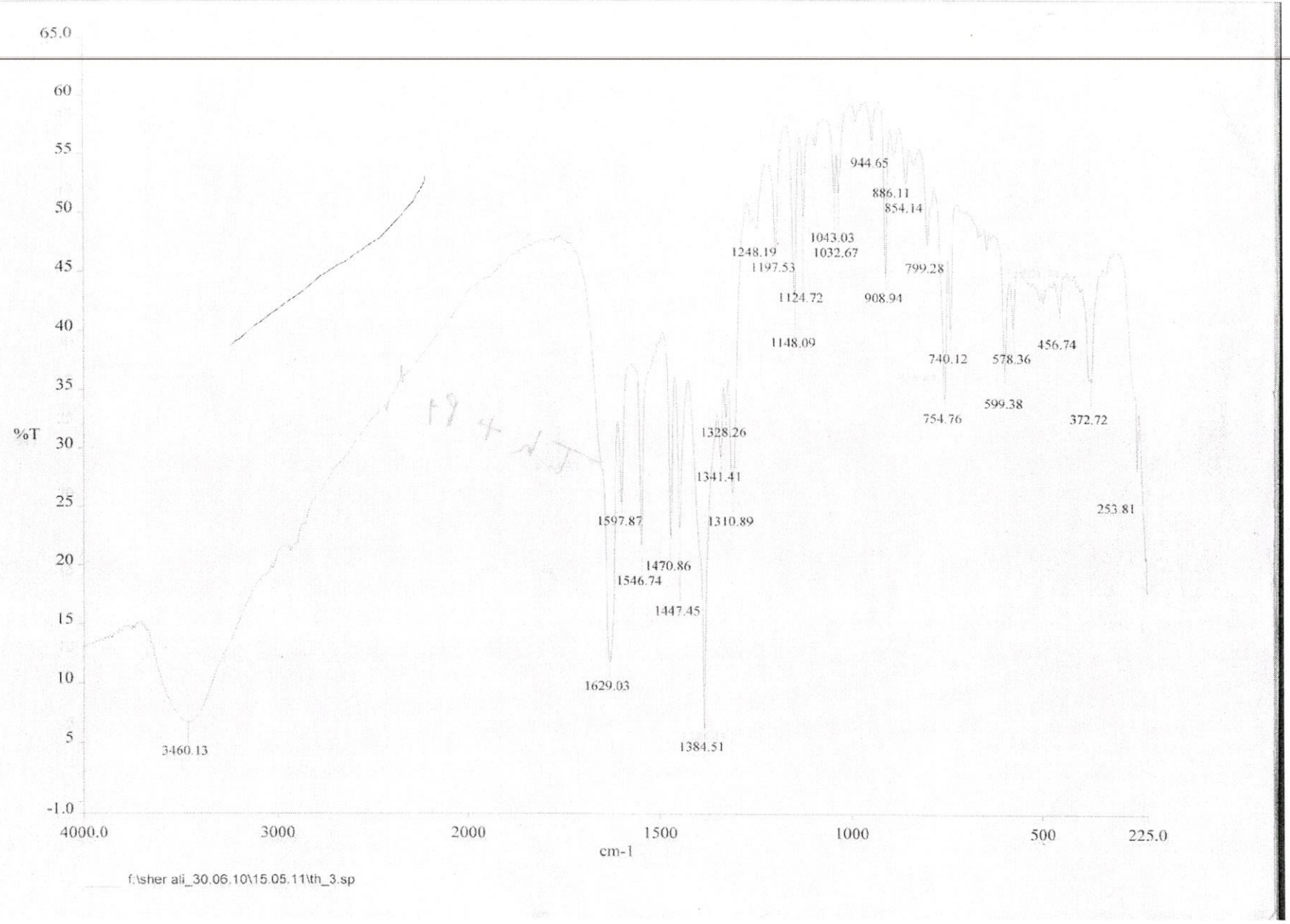


Fig. 4.20: FTIR spectrum of the complex [Th(IV)(SB-B_2)Py]

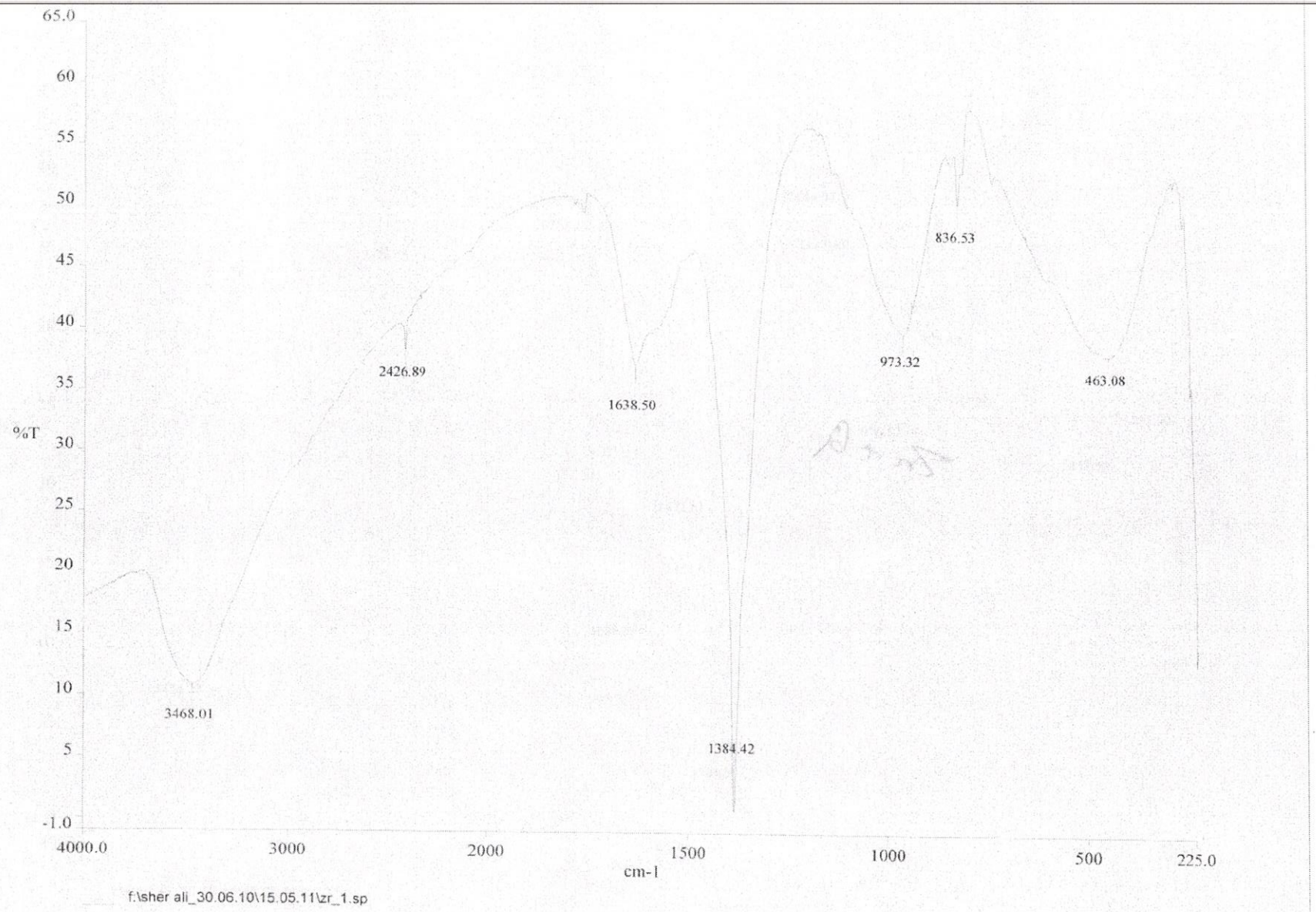


Fig. 4.21: FTIR spectrum of the complex [Zr(VI)(SB-B_2)Q]

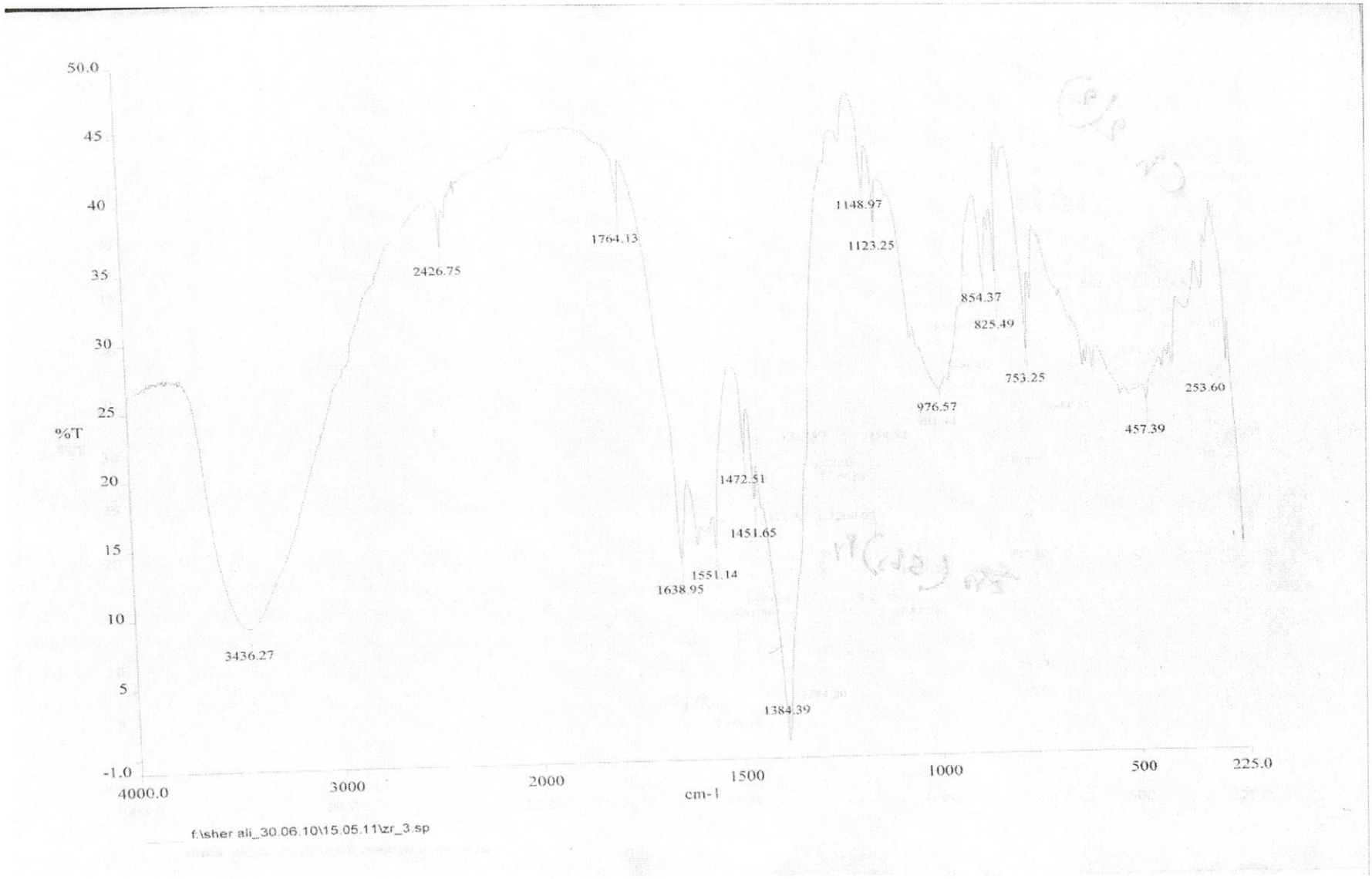


Fig. 4.22: FTIR spectrum of the complex [Zr(IV)(SB-B_2)Py]

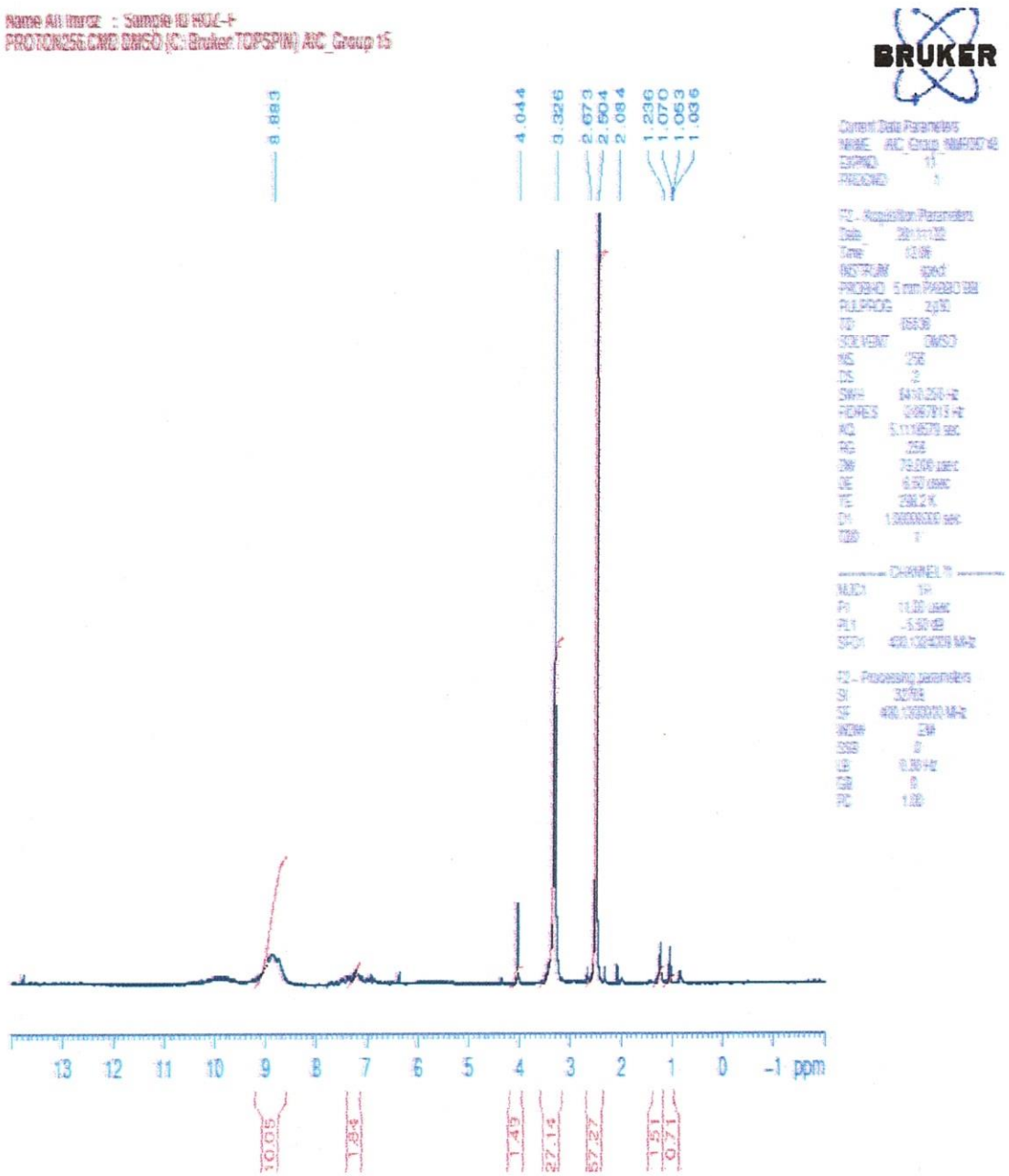


Fig. 4.23: ^{1}H-NMR spectrum of Complex[Cu(II)SB-B_1)4-Pic]

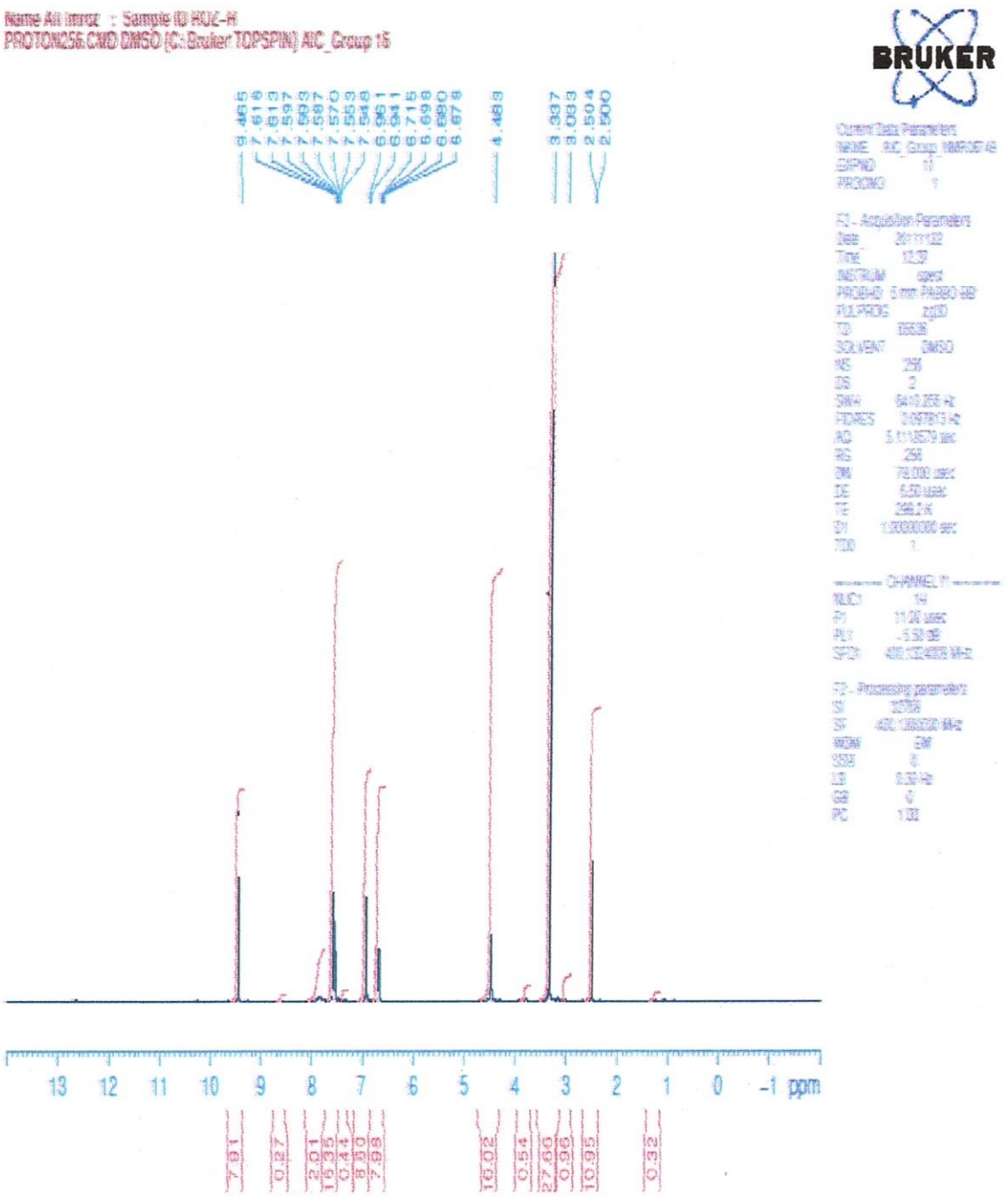


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Fig. 4.24: ^{1}H-NMR spectrum of Complex[U(VI)(SB-B_2)Q]

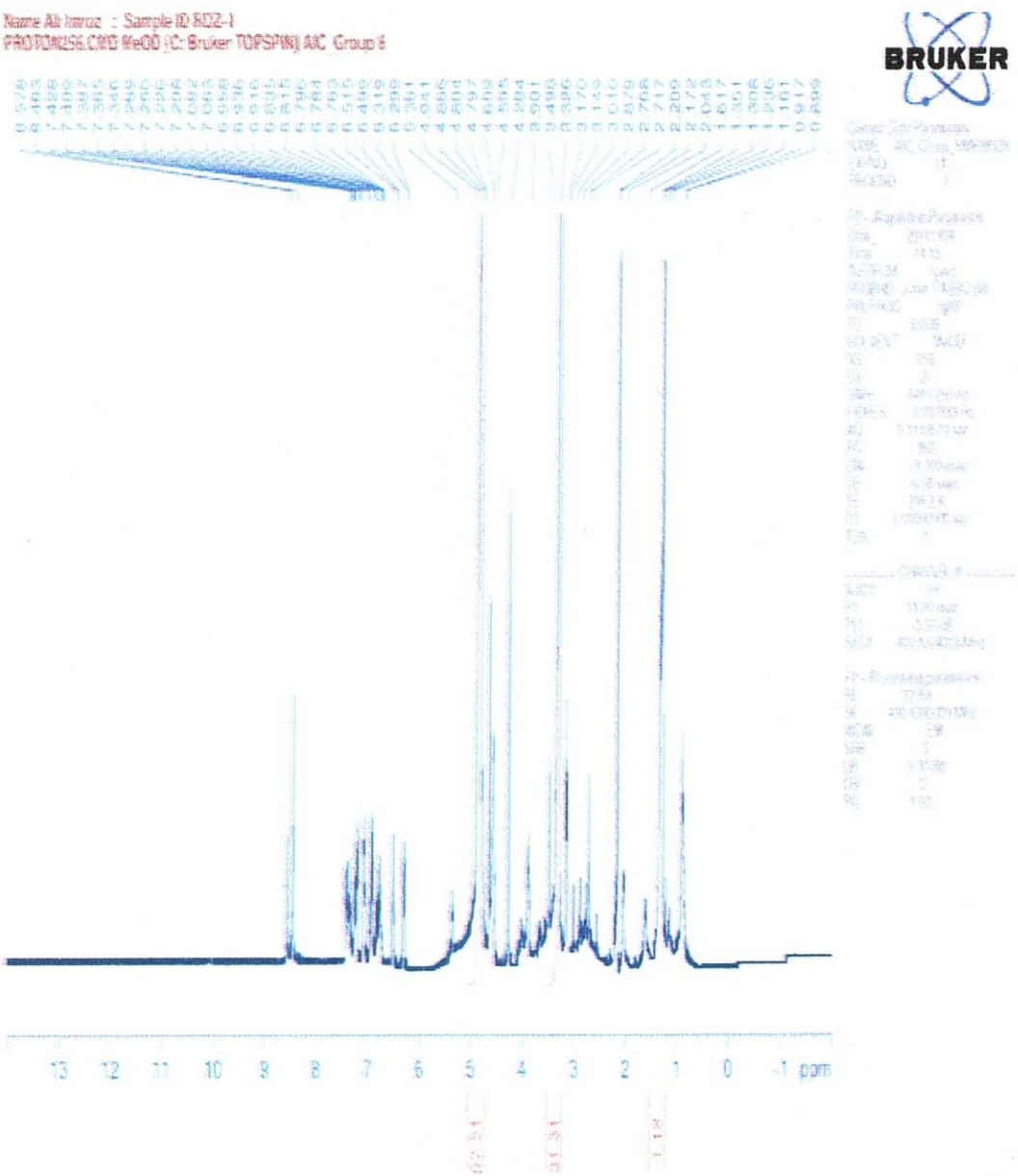

Fig. 4.25: ^{1}H-NMR spectrum of Complex[Zr(IV)(SM-C_1)Q]

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CHAPTER -FIVE

STUDIES ON THE HEAVIER METAL COMPLEXES WITH SCHIFF BASES AND HETEROCYCLIC AMINES

5.1. INTRODUCTION

The dithiocarbazate (NH_2NHCS_2) and its substituted derivatives have been investigated as ligand for a long time.[1-4]

These compounds have received much attention for further studies because i) they provide an interesting series of ligands whose properties can be greatly modified by introducing different organic constituents, thereby causing a variation of ultimate donor properties (ii) the interaction of these donor to metal ions gives complexes of different geometries and properties and (iii) these complexes are potentially biologically active.

There are two series of ligands which were prepared by condensation of i) salicylaldehyde with s-benzyldithiocarbazate and ii) p-anisylaldehyde with s-methyldithiocarbazate are reported in this chapter.

The Schiff base behaves as uninegative bidentate ligand and coordinate through thioenolic sulfur and azomethine nitrogen atoms.

Some new heavier metal complexes formed with Schiff base and heterocyclic amines have been reported in this chapter.

5.2. EXPERIMENTAL PROCEDURE

5.2.1. Reagents: As stated in chapter 2 Page No 40.

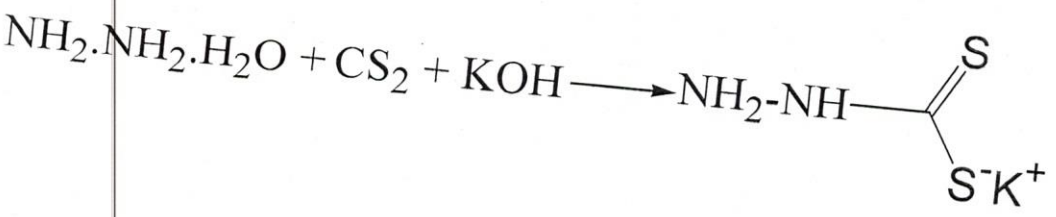
5.2.2. Physical Measurements: As stated in chapter 2 Page No 41.

5.3. Preparation Procedure of Schiff bases

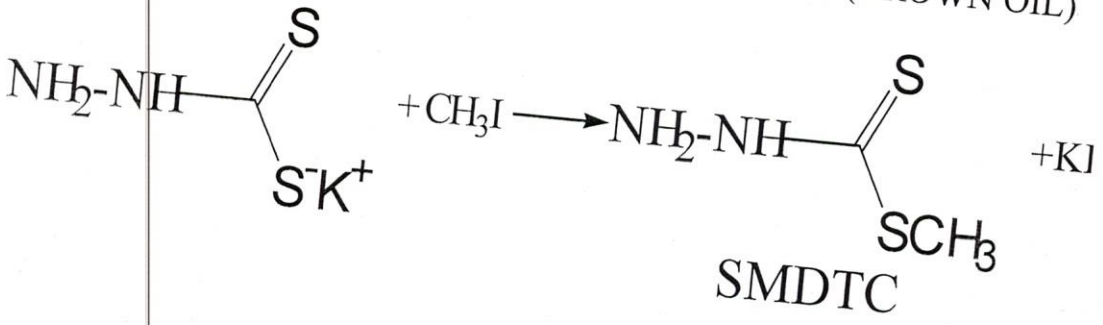
5.3.1. Preparation of S-methyldithiocarbzate (SMDTC)

PROCEDURE

SMDTC was prepared as literature method. Potassium hydroxide (0.4mol) was completely dissolved in 140mL of 90% ethanol and the mixture was cooled. Then the solution of hydrazine hydrate (0.4mol) was added slowly with stirring. A solution of CS_2 (0.4mol) was then added dropwise from a burette with constant stirring over a period of an hour. The resulting yellow oil was separated by separating funnel and dissolved in 40% ice ethanol (40mL). Methyl iodide (0.4mol) was added from a burette drop wise with vigorous mechanical stirring. After the complete addition of methyl iodide the mixture stirred for further ten minutes. Then 200mL of ice cooled water was added in it and stirring was continued for further 20minutes.The product was separated by filtration, washed with water and dried in air. The purred product recrystallized from ethanol, dried in a vacuum desiccators over anhydrous $CaCl_2$.Meting point 80^0C.



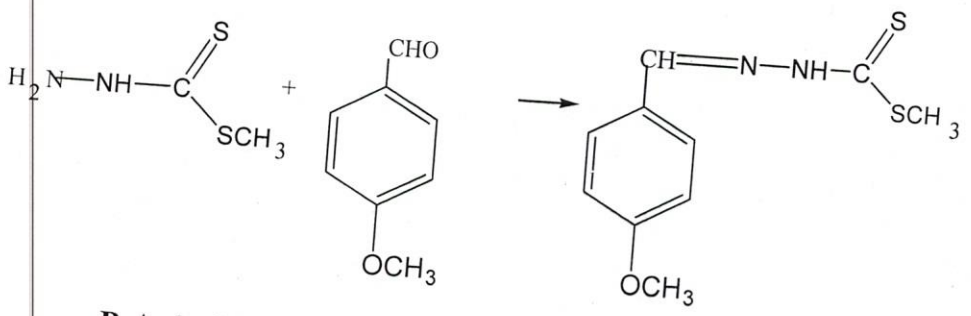
KDTCA (BROWN OIL)



SMDTC

5.3.2. Preparation of the Schiff base (SMDTC with P-anisyladehyde):

SMDTC (0.4 mol) was dissolved in hot absolute ethanol (70-80 ml). P-anisaldehyde (0.4mol) in hot absolute ethanol (40 ml) was added and the mixture was heated for 40 min and then cooled. The white precipitate which has formed was separated and dried in *vacuo* over anhydrous $CaCl_2$. The white precipitate, which has formed was separated and dried in *vacuo* over anhydrous $CaCl_2$.



P-Anisaldehyde Schiff base of SMDTC

5.3.3. General method for the preparation of the complexes with Schiff base, SMDTC:

PROCEDURE

Metal salt with hydrate {[U $(NO_3)_2.6H_2O$](1mmol),[$Th(NO_3)_4.5H_2O$] (1mmol) and [$Zr(NO_3)_2.5H_2O$](1mmol)} was dissolved in absolute ethanol (30 ml). The Schiff base SMDTC (1 mmol) in hot absolute ethanol (30 ml) and heterocyclic amines (2mmol) in absolute ethanol (30ml) were added to the metal solution. The mixture were then refluxed for 45 mins and then cooled. The precipitate was filtered off and washed with hot ethanol and dried in vacuo over anhydrous $CaCl_2$.

5.4. RESULTS AND DISCUSSION

5.4.1. Physical properties:

The physical properties of the complexes are shown in Table- (5.1). The molar conductance of 10^{-3} M solution of the complexes in DMSO were measured at 30^0C. The molar conductance values (Table-5.1) indicates that the U(VI)and Th(IV) complexes are highly electrolyte and Zr(IV) complexes are non-electrolyte.

The observed values of effective magnetic moment (μ_{eff}) at room temperature are given in Table-5.1. The magnetic moment values indicated that these complexes are diamagnetic in nature and this revealed that there was no change in the oxidation states of the metal ions upon complex formation.

Table 5.1: Some physical properties of the SMDTC Schiff base complexes:

No.	Complexes	Color	Melting/ Decomposition Point(^{0}C)	Molar Conductance $Ohm^{-1}Cm^2mol^{-1}$	Magnetic moment μ_{eff} (B.M.)
1	SMDTC	White	81	-	-
2	Ligand(SB—C_1)	White	165	-	-
3	U(SB—C_1)Q	Gray	245	82.40	Dia
4	U(SB—C_1)IQ	Brown	240	75.20	Dia
5	Th(SB—C_1)Q	Light Cream	230	80.10	Dia
6	Th(SB—C_1)IQ	White	232	73.52	Dia
7	Zr (SB—C_1)Q	Deep yellow	225	4.70	Dia
8	Zr(SB—C_1)IQ	Light yellow	230	5.10	Dia

Where, SMDTC: s-methyldithiocarbazate ,SB—C_1: SMDTC of Schiff Base, Q: Quinoline, IQ= Iso-quinoline.

5.4.2. Electronic Spectra:

The electronic spectral data (Table-5.2) of the complexes showed bands between 230-370 nm regions due to the charge transfers band only.[5]

Table 5.2: The electronic spectral data of the SMDTC Schiff base complexes:

No.	Complexes	λ_{max}
1	U(SB—C_1)Q	380
2	U(SB—C_1)IQ	375
3	Th(SB—C_1)Q	370
4	Th(SB—C_1)IQ	365
5	Zr(SB—C_1)Q	380
6	Zr(SB—C_1)IQ	375

5.4.3. IR studies of complexes:

The IR spectrum (Table-5.3) of the Schiff base showed strong bands at 3121 cm^{-1}. This was attributed to the secondary amine ν(N-H) mode of the free ligands. The disappearance of ν(N-H) bands in their spectra of the metal complexes suggests deprotonation and consequent co-ordination through the thiolate anions. The Schiff base also showed strong bands at 1650cm^{-1}. These are assigned to the ν(C=N) modes for free ligand. In the metal complexes, this stretching band shifted to lower frequencies, due to the lowering of the C=N bond order as a result of the metal-nitrogen bond formation. The ν(C=S) mode observed in the free ligand disappeared in the complexes. Thus the Schiff base coordinate to the metal through the thiolate sulphur and the β-nitrogen as evident from IR spectrum showing bands at 290cm^{-1} and 540cm^{-1}, corresponding to ν(M-S) and ν(M-N) stretching modes, respectively.[6]

Table 5.3: Selected IR absorption bands of SMDTC Schiff base complexes:

No	Complexes	ν(NH_2) cm^{-1}	ν(NH) cm^{-1}	ν(C=S) cm^{-1}	ν(C=N) cm^{-1}	ν(C-S) cm^{-1}	ν(O=M=O) cm^{-1}	ν(M-N) cm^{-1}	ν(M-S) cm^{-1}
1	SMDTC	3365	3200	1064	-	-	-	-	-
2	Ligand(SB—C_1)	-	3121	1026	1650	-	-	-	-
3	U(SB—C_1)Q	-	-	-	1634	856	945	487	271
4	U(SB—C_1)IQ	-	-	-	1634	850	919	435	280
5	Th(SB—C_1)Q	-	-	-	1631	840	-	518	253
6	Th(SB—C_1)IQ	-	-	-	1570	833	-	518	290
7	Zr(SB—C_1)Q	-	-	-	1598	825	-	540	279
8	Zr(SB—C_1)IQ	-	-	-	1590	835	-	472	253

5.4.4. ^{1}H NMR studies of complexes:

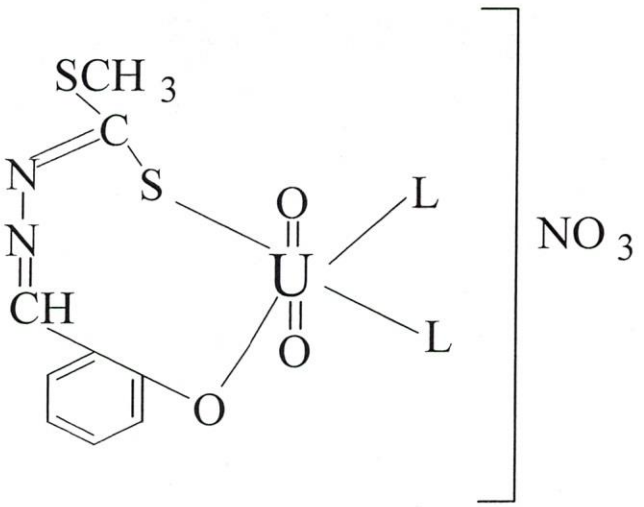
The ^{1}H NMR spectral data are given in Table-5.4.The NMR spectra of the complexes can account all the protons of the ligand in complex except thiolo sulphur proton, which are lost during complex formation i.e., deprotonation of the ligand. This is the evidence of coordination via. thiolo sulphur atom of the ligand. Multiplet peaks in the range of 7-9 ppm are due to phenyl protons. A singlet in the range of 8-9 ppm is due to azomethine proton of the ligand. The peak of $-SCH_3$ proton appears in the range of 2.6 ppm. These peaks are common for all complexes.[7]

Table 5.4: Selected ^{1}H NMR spectra of SMDTC Schiff base complexes:

Complexes	Phenyl proton(ppm)	Azomethine proton(ppm)	$-SCH_3$ proton(ppm)	$-OCH_3$ proton(ppm)
Zr(SB—C_1)Q	6.986	8.39	2.59	3.86

CONCLUSION

From the above informations and data the probable structure of the [U(SB-C_1)L] complex is given below

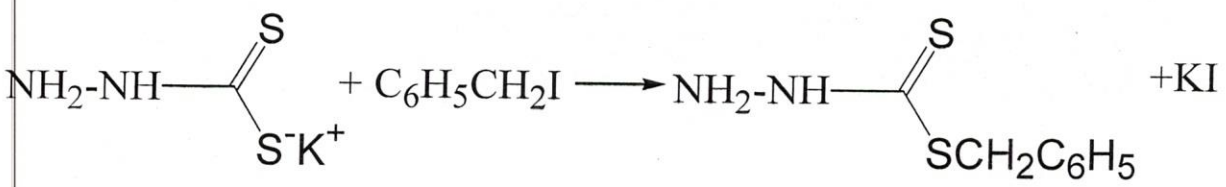


Where, L = Heterocyclic Amines

5.5. PREPARATION PROCEDURE

5.5.1. Preparation of S-benzyldithiocarbzate (SBDTC):

This compound was prepared by the method developed by Ali and Tarafder[4].

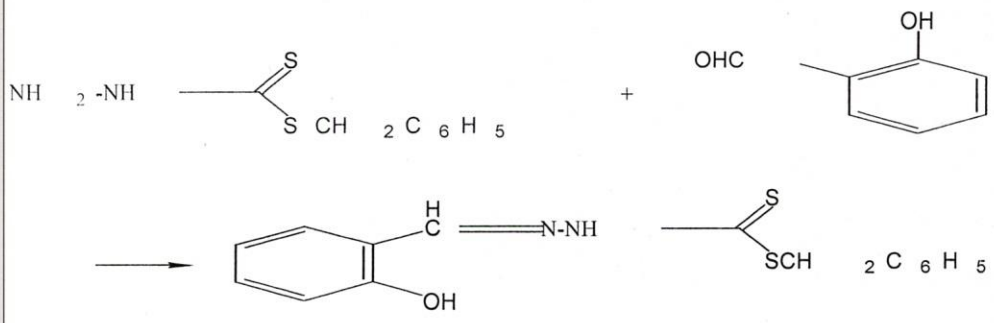


SBDTC

5.5.2. Preparation of the Schiff base (SBDTC with Salicyldehyde):

PROCEDURE:

A hot solution of salicyldehyde (0.4mol) in absolute ethanol was mixed with a hot solution of SBDTC (0.4mol) in the same solvent. The mixture was then heated on a hot plate for 20 minutes. After reducing volume a white colored product appeared which was filtered off. This product was washed with dry ethanol for several times and dried in a vacuum desiccator over anhydrous $CaCl_2$.



Schiff base of SBDTC

5.5.3. General method for the preparation of the complexes with Schiff base of SBDTC:

Metal salt with hydrate {$[U(NO_3)_2.6H_2O]$(1mmol),$[Th(NO_3)_4.5H_2O]$ (1mmol) and $[Zr(NO_3)_2.5H_2O]$(1mmol)} was dissolved in absolute ethanol (30 ml). The Schiff base SBDTC (1 mmol) in hot absolute ethanol (30 ml) and heterocyclic amines (2mmol) in absolute ethanol (30ml) were added to the metal solution. The mixture were then refluxed for 45 mins and then cooled. The precipitate was filtered off and washed with hot ethanol and dried in vacuo over anhydrous $CaCl_2$.

5.6. Results and Discussion

5.6.1. Physical properties:

The physical properties of the complexes are shown in Table- 5.5. The molar conductances of 10^{-3} M solution of the complexes in DMSO were measured at 30^0C. The molar conductance values (Table-5.5) indicated that the U(VI) Th(IV) complexes are highly electrolyte whereas Zr(IV) complexes are non-electrolyte.

The observed values of effective magnetic moment (μ_{eff}) at room temperature are given in Table-5.5. The magnetic moment values indicated that these complexes are diamagnetic in nature and this revealed that there was no change in the oxidation states of the metal ions upon complex formation.

Table 5.5: Some physical and analytical data of the SBDTC Schiff base complexes:

No.	Complexes	Color	Melting/ Decomposition Point (^{o}C)	Conductance In $ohm^{-1}m^2mol^{-1}$	Magnetic moment in nm
1	SBDTC	Gray	-	9.80	Dia
2	Ligand (SB-C_2)	White	-	4.40	Dia
3	U(SB-C_2)Q	Brown	245	85.45	Dia
4	U(SB-C_2)IQ	Brown	240	80.50	Dia
5	Th(SB-C_2)Q	Cream	250	75.45	Dia
6	Th(SB-C_2)IQ	Cream	230	76.50	Dia
7	Zr(SB-C_2)Q	Brown	220	4.70	Dia
8	Zr(SB-C_2)IQ	Brown	210	4.90	Dia

Where, SBDTC: s-benzyldithiocarbazate, SB-C_2: SBDTC Schiff Base, Q: Quinoline, IQ= Iso-quinoline.

5.6.2. Electronic Spectra:

The electronic spectral data (Table-5.6) of the complexes showed bands between 360-390 nm regions due to the charge transfers band only.[5]

Table 5.6: The electronic spectral data of the SBDTC Schiff base complexes:

No.	complexes	λ_{max} in nm
1	U(SB-C_2)Q	380
2	U(SB-C_2)IQ	360
3	Th(SB-C_2)Q	370
4	Th(SB-C_2)IQ	380
5	Zr(SB-C_2)Q	390
6	Zr(SB-C_2)IQ	380

5.6.3. IR studies:

The Schiff bases have two protons (the phenolic and the NH proton) which may be lost during the course of its reaction with a metal ion. It can therefore, act as a doubly deprotonated or a singly deprotonated species depending upon the nature of the metal salts being used. Although the ligands have a number of donor atoms, because of steric factor it can only donate maximum through azomethine nitrogen, thioketo sulfur and phenolic oxygen. So the ligands can act as bidentate or tridentate mononegative or dinegative ligand depending on the nature of metal used.

Characteristic IR frequencies of the ligand and their complexes are listed in Table-5.7.The IR data of the complexes show the presence of a broad band at about (3430-3460) cm^{-1} due to ν(OH) stretch indicate the presence of uncoordinate phenolic -OH group.

The Schiff base complexes exhibit a sharp strong band at (1630-1620) cm^{-1} due to ν(C=N) stretching frequency which indicate the coordination of azomethine nitrogen to metal ion[6].

A medium strong band at about (520-570) cm^{-1} for the complexes are assigned to ν(M-N) stretching frequency[7]. This band is absent in the free ligand. A week band in the range of (450-470) cm^{-1} is due to the metal-sulfur stretching frequency[8] was observed.

So from the above discussion, it is clear that the ligand is attached with the metal ion via, azomethine nitrogen and thiol sulfur atom and the ligand is acting as bidentate uninegetive.

Table 5.7 : Selected IR absorption bands of SBDTC Schiff base complexes:

No	Complexes	ν(NH_2) cm^{-1}	V(C=S) cm^{-1}	ν(C=N) cm^{-1}	ν(C-S) cm^{-1}	ν(O=M=O) cm^{-1}	ν(M-N) cm^{-1}	ν(M-S) cm^{-1}	V(OH) cm^{-1}
1	SBDTC	3458	1051	-	951	-	-	-	-
2	Ligand(SB-C_2)	-	1026	1650	948	-	-	-	3467
3	U(SB-C_2)Q	-	-	1621	890	970	566	467	3467
4	U(SB-C_2)IQ	-	-	1622	894	969	565	466	3467
5	Th(SB-C_2)Q	-	-	1622	870	-	519	450	3435
6	Th(SB-C_2)IQ	-	-	1631	880	-	521	430	3436
7	Zr(SB-C_2)Q	-	-	1623	894	-	565	459	3467
8	Zr(SB-C_2)IQ	-	-	1625	895	-	565	459	3466

5.6.4. ^{1}H NMR studies of the complexes:

The ^{1}H NMR spectral data of the complexes are given in Table-5.8. Multiplet peaks in the range of 7-9 ppm are due to phenyl proton of salicyladehyde and benzyl moiety. The range is large because different groups are attached to the phenyl group. A singlet in the range of 8-9 ppm is due to azomethine proton of the ligand.[9] The peak of $-SCH_2$ proton appears in the range of 3-4 ppm. These peaks are common for all of the complexes.

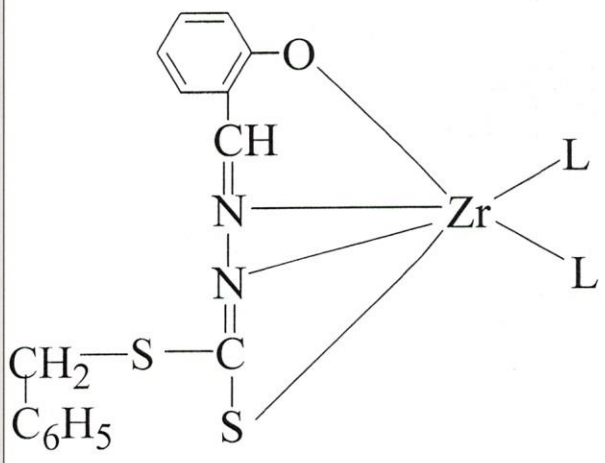
A singlet in the range of 11-12 ppm is due to the hydrogen bond proton of the SBDTC ligand.

Table 5.8: ^{1}H NMR studies of the complexes:

Complexes	Phenyl proton(ppm)	Azomethine proton(ppm)	$-SCH_2-$ proton(ppm)	-NH proton(ppm)
Zr(SB-C_2)Q	6.95-7.70	9.01	3.30	11.21
U(SB-C_2)Q	7.50-7.75	9.01	3.32	11.21

CONCLUSION

From the above information and data the probable structure of the complex [Z(SB-C_2)L] is given below



Where, L = Heterocyclic Amines

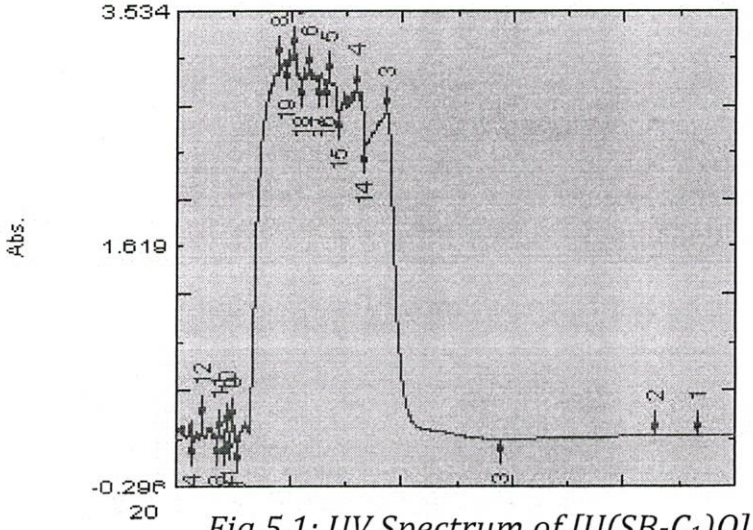


Fig.5.1: UV Spectrum of [U(SB-C_1)Q]

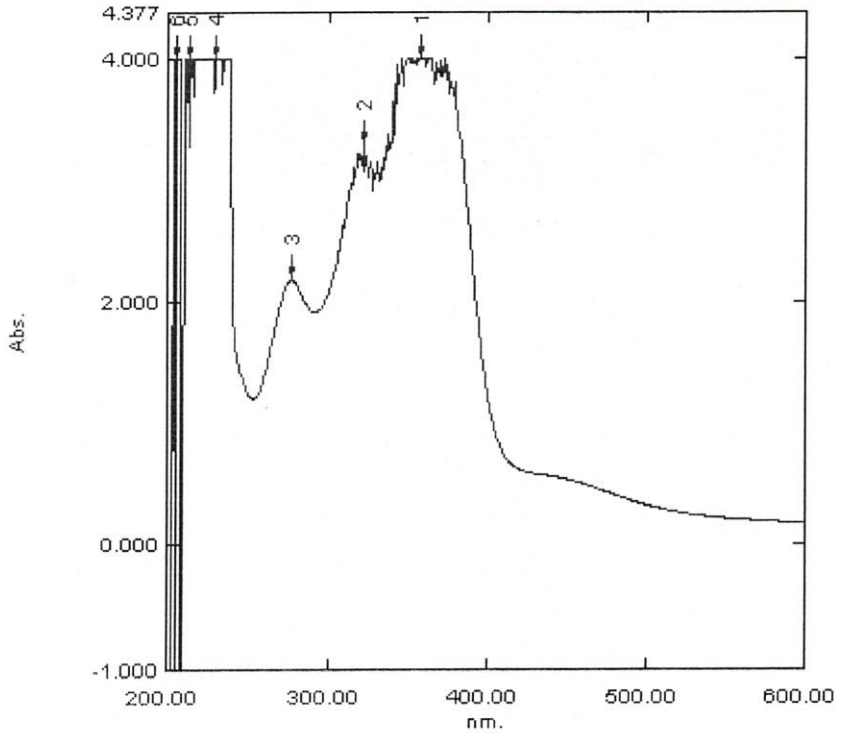


Fig: 5.2: *UV Spectrum of* [Th(SB- C_1)IQ]

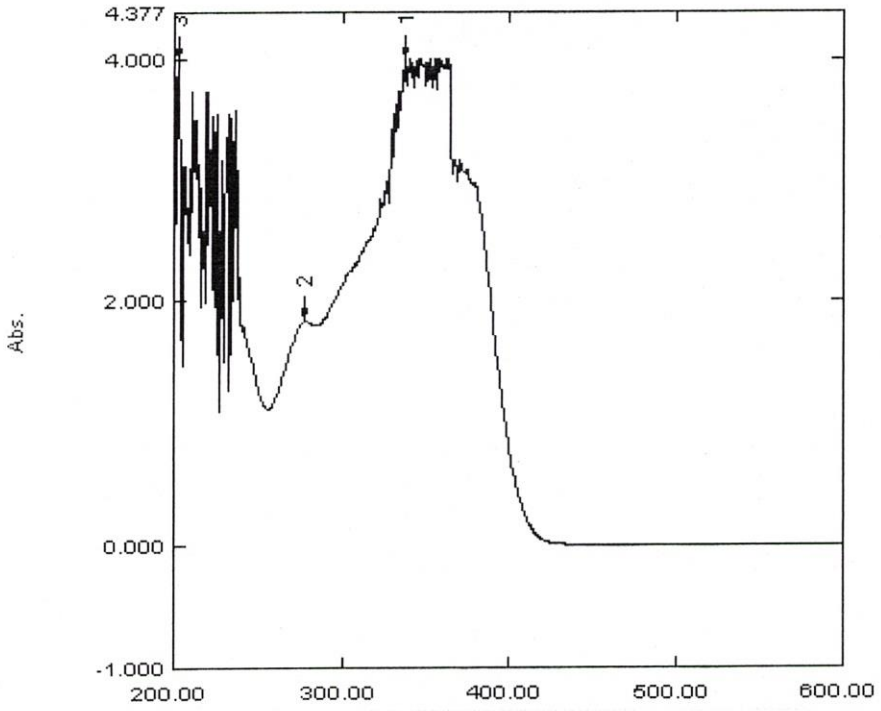


Fig. 5.3: *UV Spectrum of* [Zr(SB- C_1)Q]

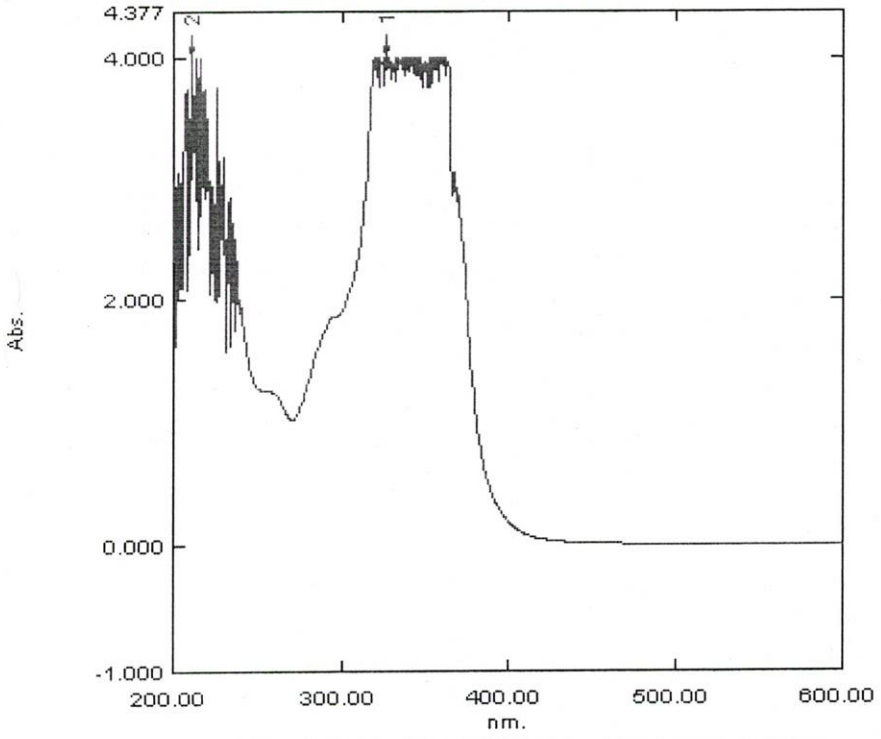


Fig:5.4: *UV Spectrum of* [U(SB- C_2)Q]

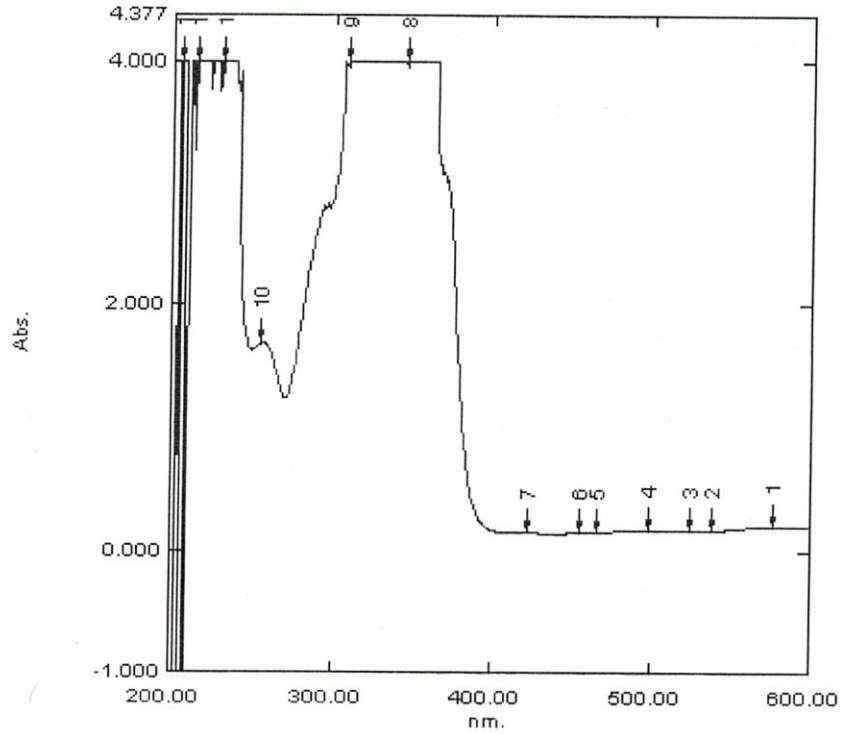


Fig: 5.5: *UV Spectrum of* [Th(SB- C_2)IQ]

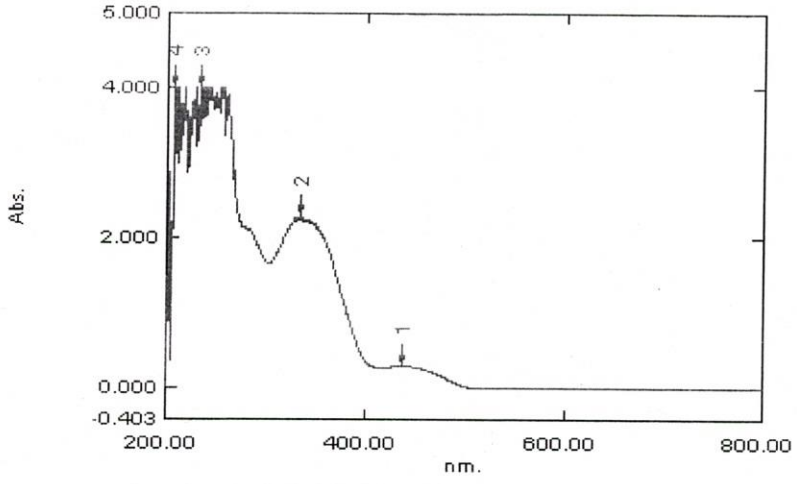


Fig: 5.6: *UV Spectrum of* [Zr(SB- C_2)Q]

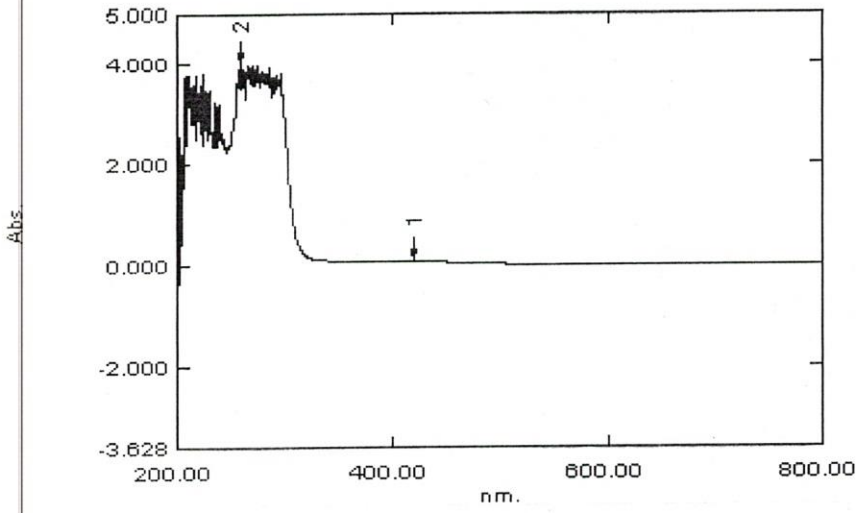


Fig: 5.7: *UV Spectrum of* Schiff Base of SMDTC

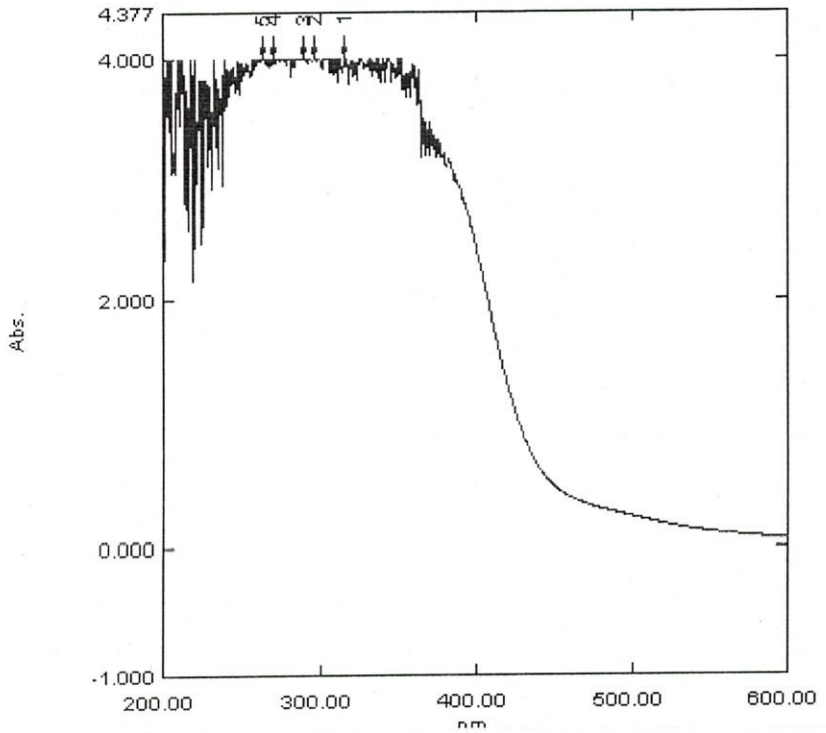


Fig: 5.8: *UV Spectrum of* Schiff Base of SBDTC

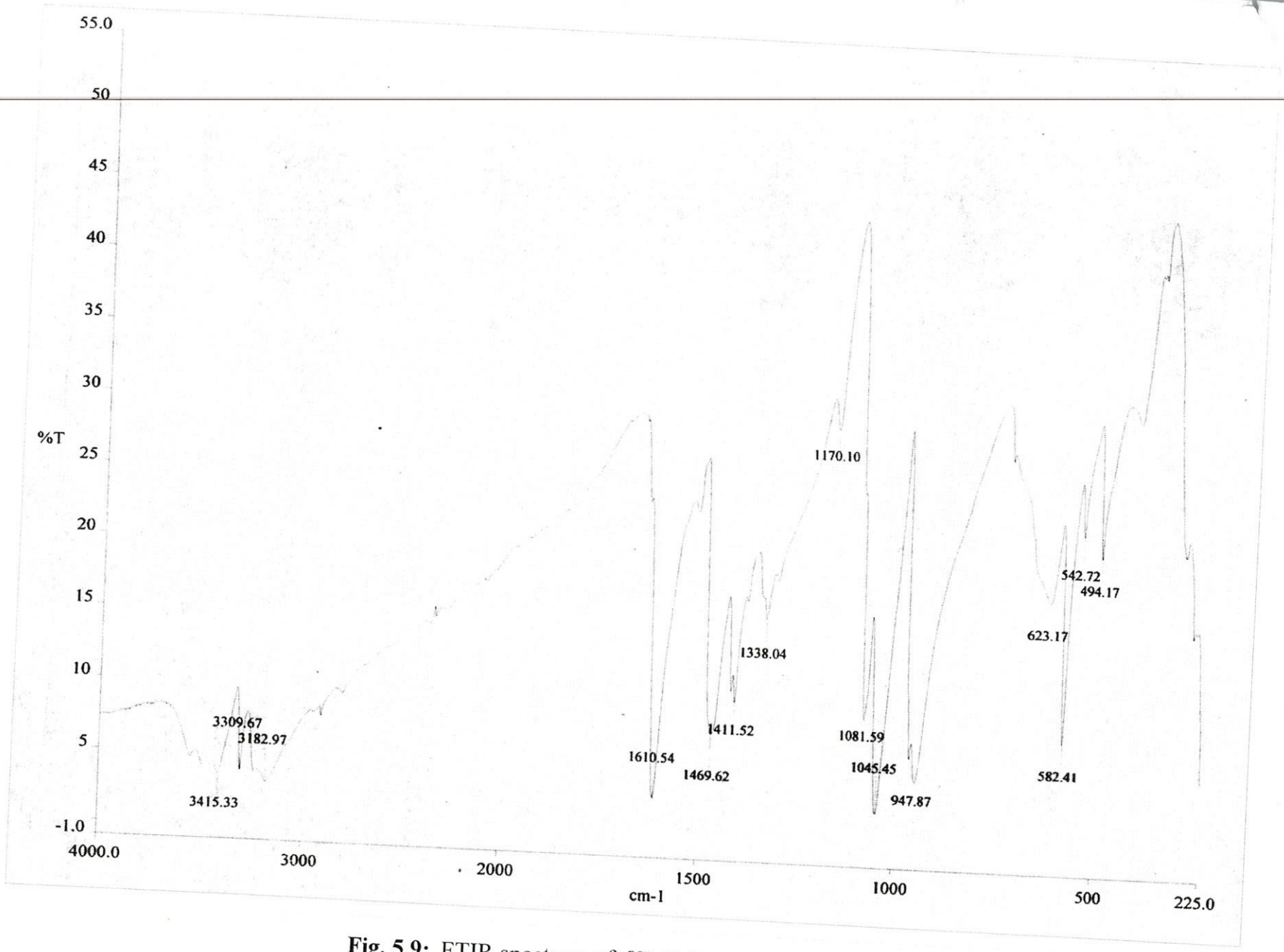


Fig. 5.9: FTIR spectrum of [SMDTC]

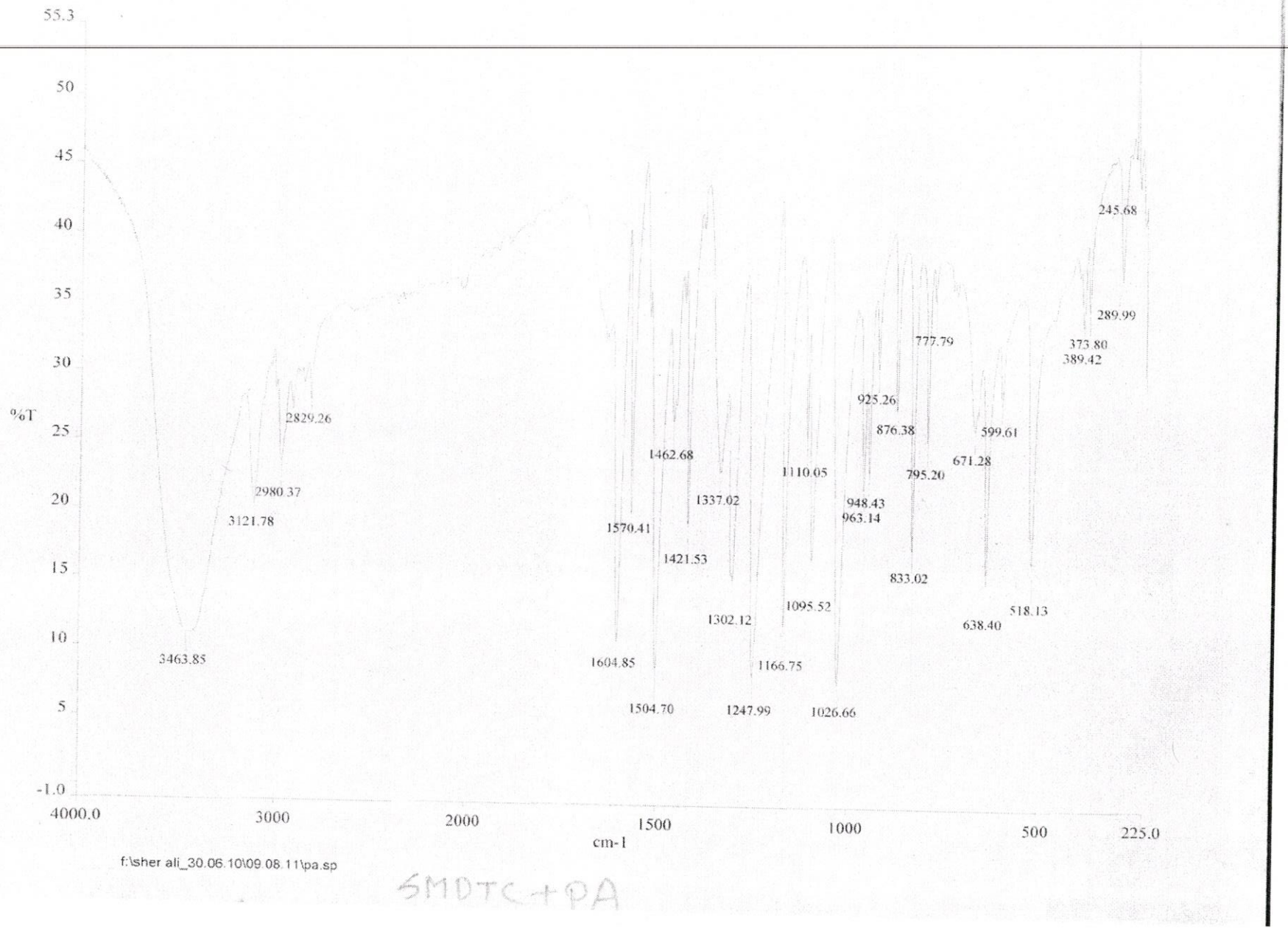


Fig. 5.10: FTIR spectrum of the [SB-C_1]

Fig. 5.11: FTIR spectrum of the complex [Zr(SB-C_1)IQ]

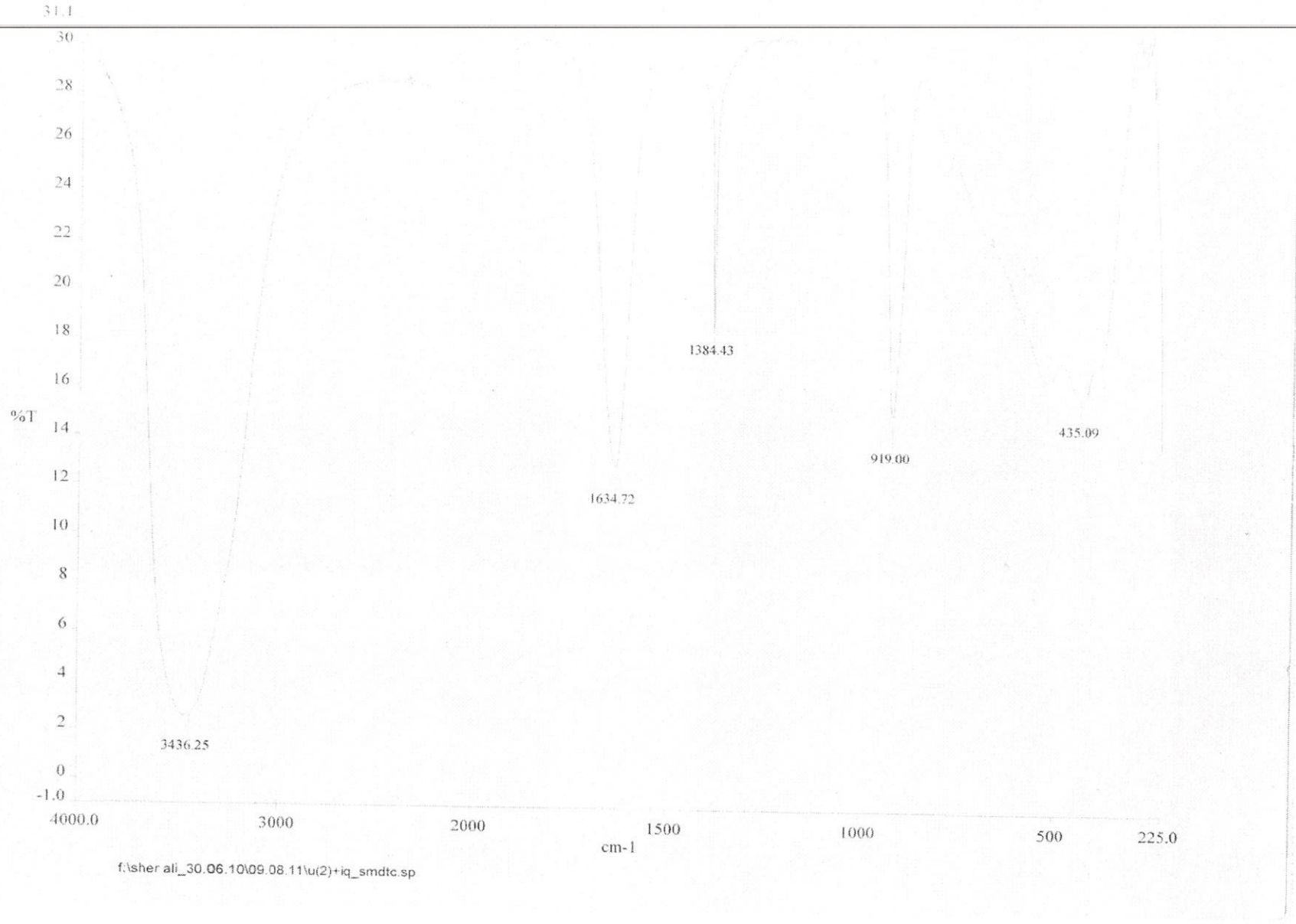


Fig. 5.12: FTIR spectrum of the complex [U(SB-C_1)IQ]

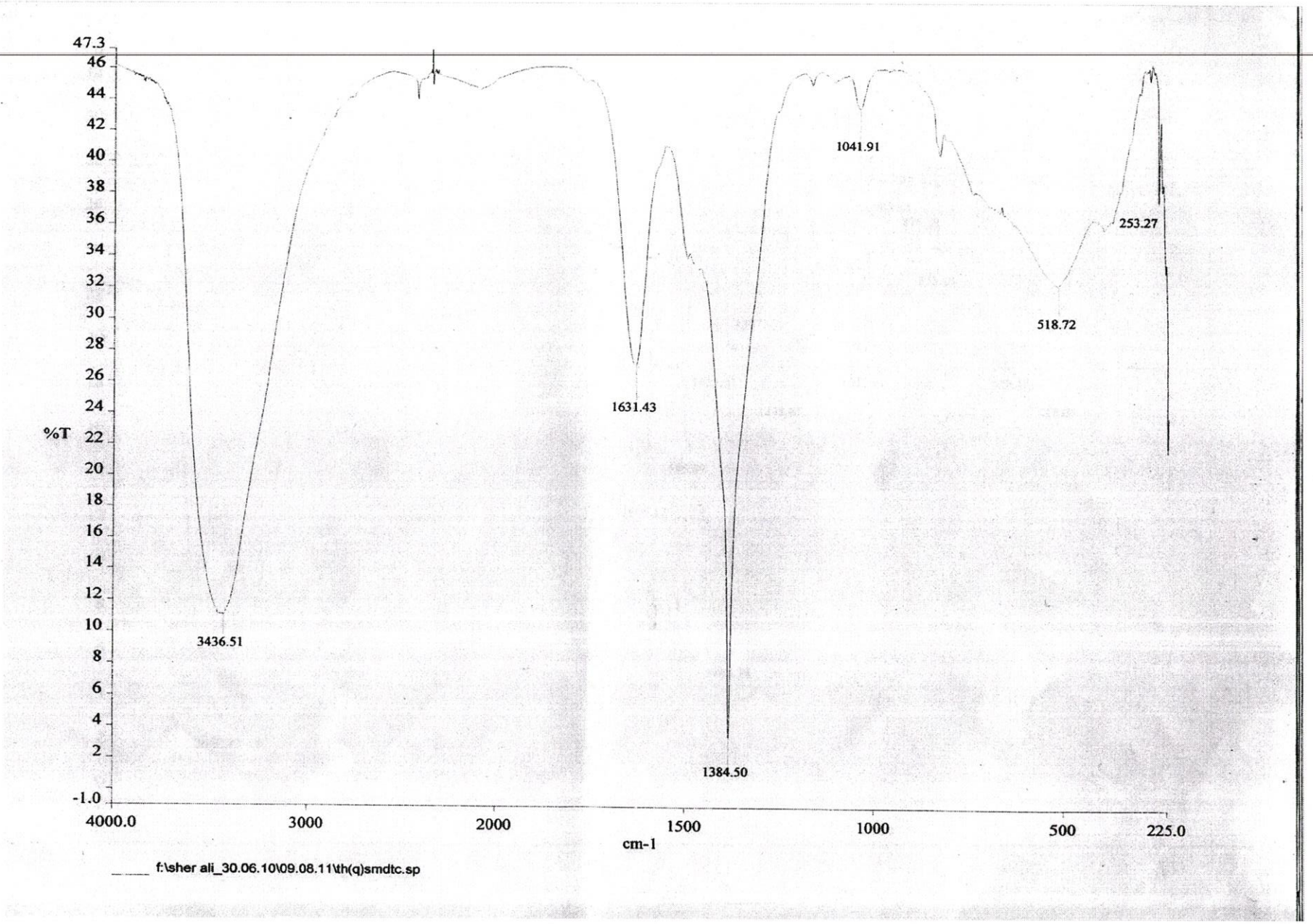


Fig. 5.13: FTIR spectrum of the complex [Th(SB-C_1)Q]

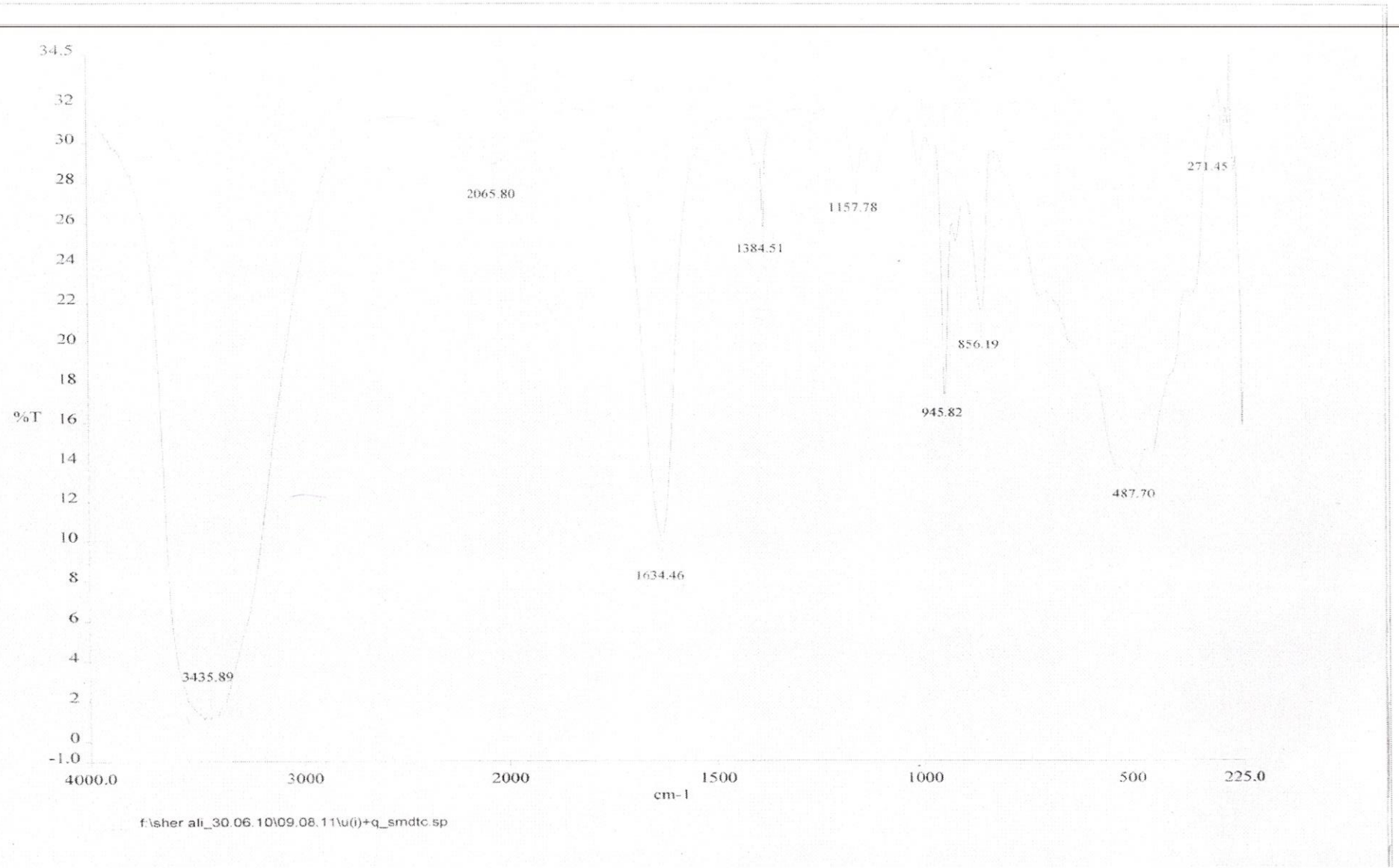


Fig. 5.14: FTIR spectrum of the complex [U(SB-C_1)Q]

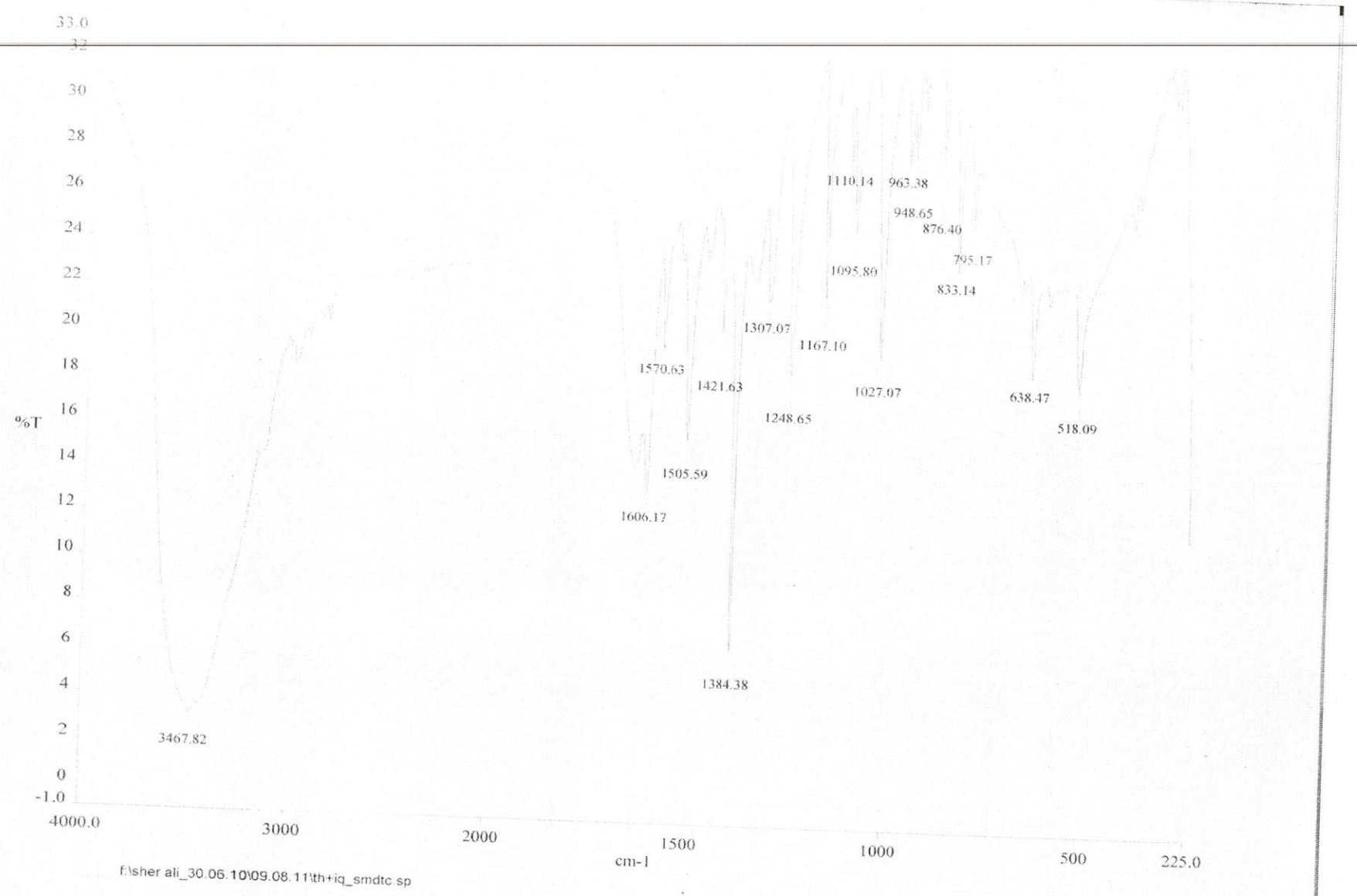


Fig. 5.15: FTIR spectrum of the complex [Th(SB-C_1)IQ]

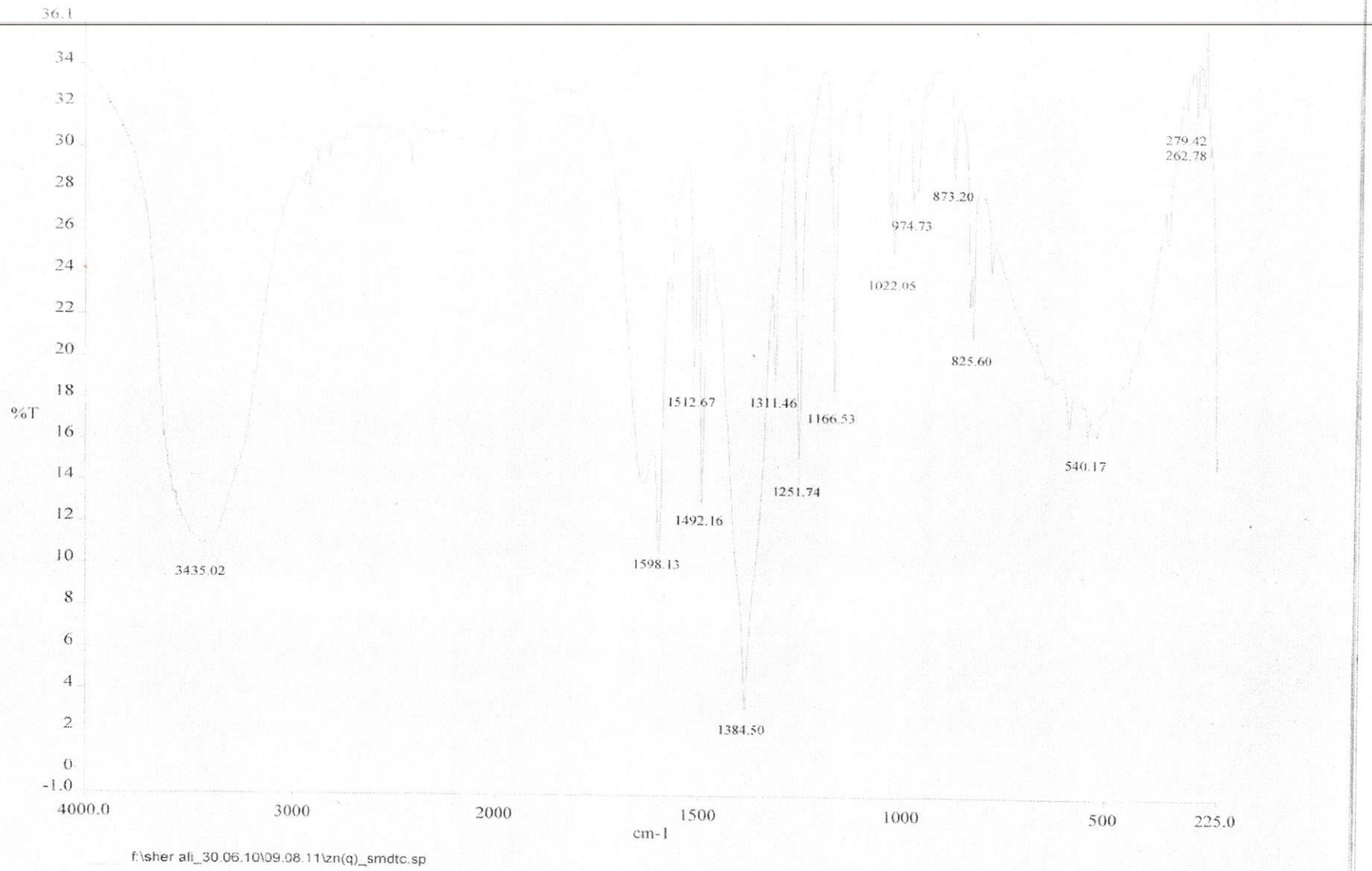


Fig. 5.16: FTIR spectrum of the complex [Zr(SB-C_1)Q]

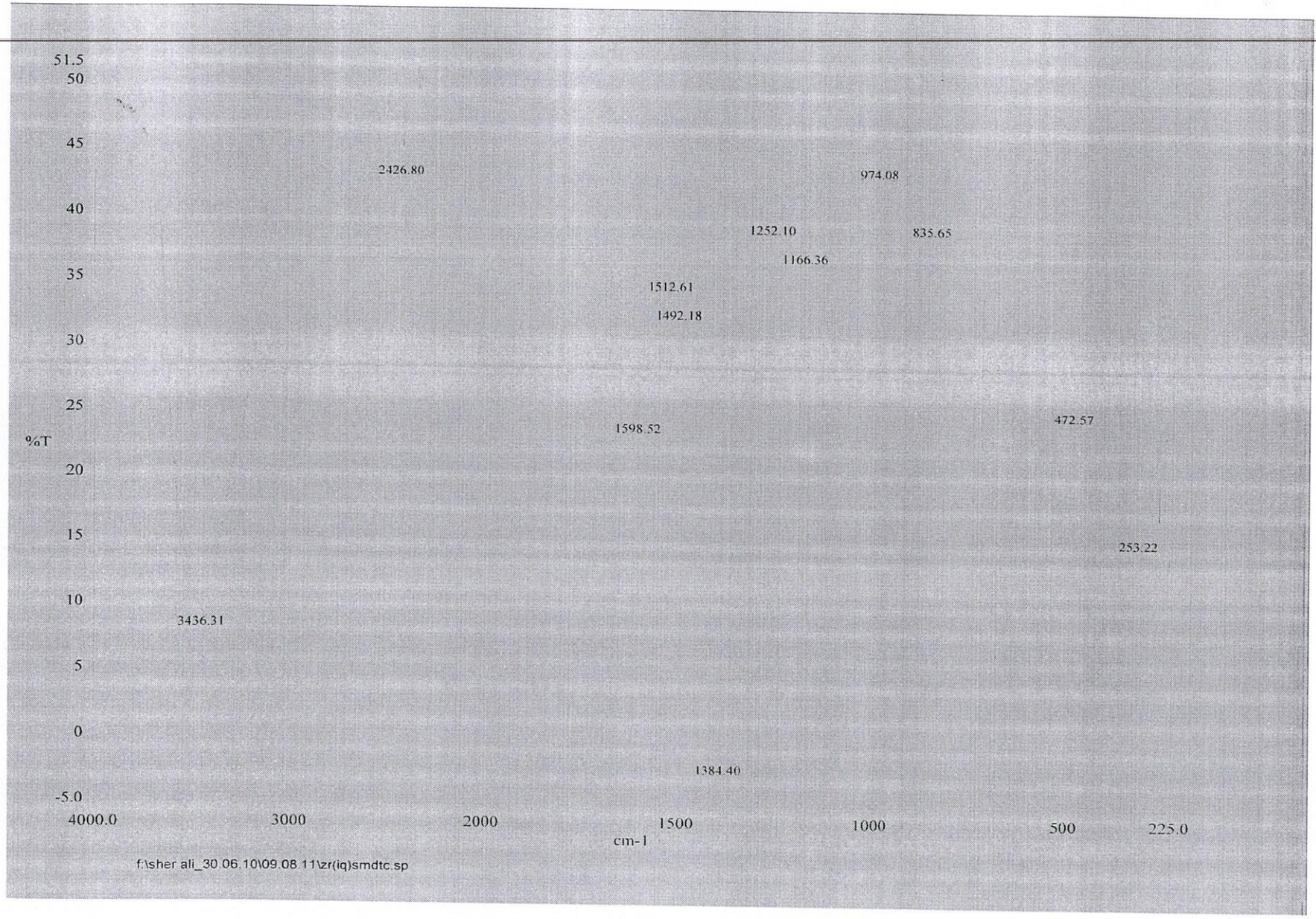


Fig. 5.17: FTIR spectrum of the complex [Zr(SB-C_1)Q]

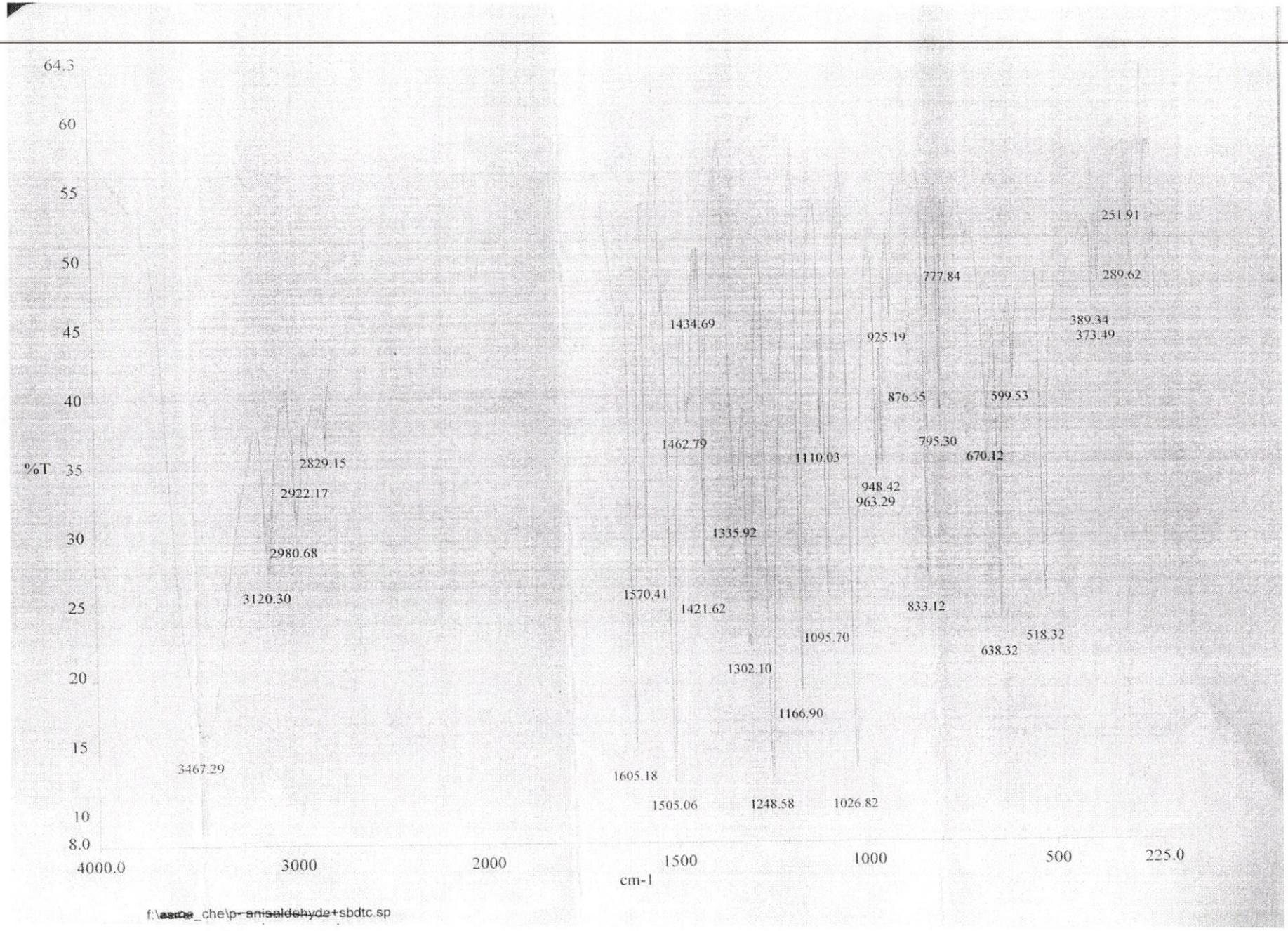


Fig. 5.18: FTIR spectrum of the Schiff Base [SB-C_2]

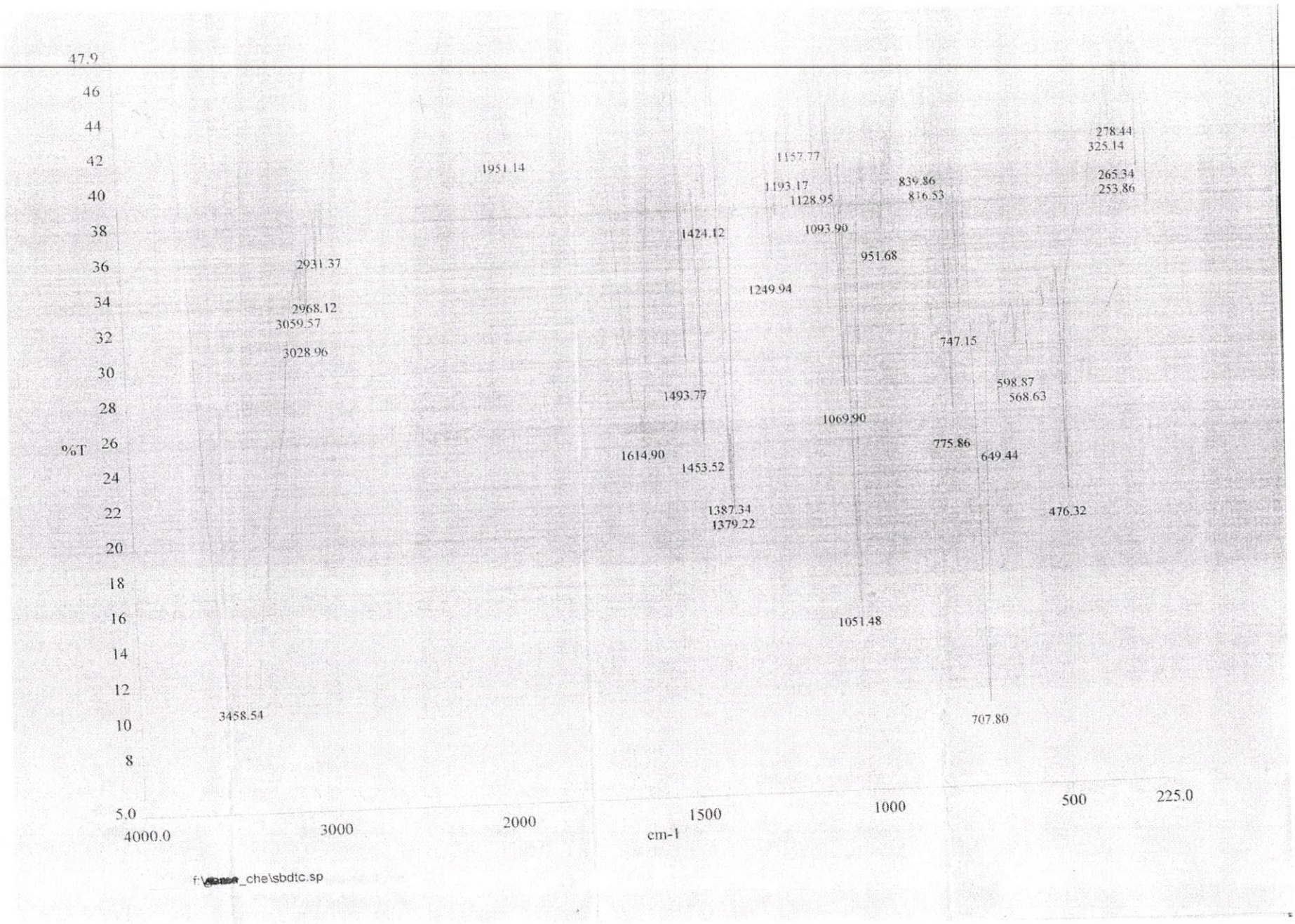


Fig. 5.19: FTIR spectrum of SBDTC

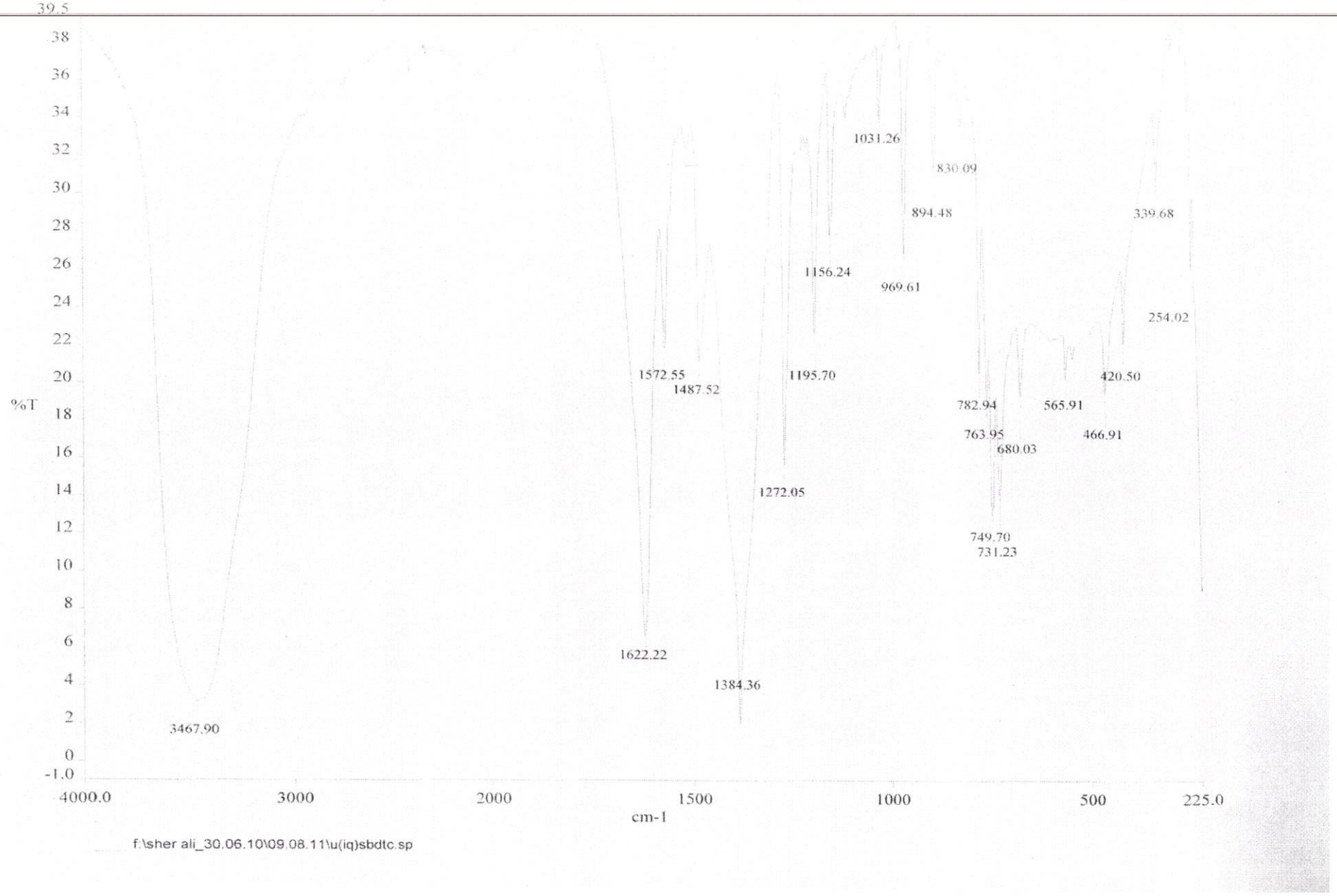


Fig. 5.20: FTIR spectrum of the complex [U(SB-C_2)IQ]

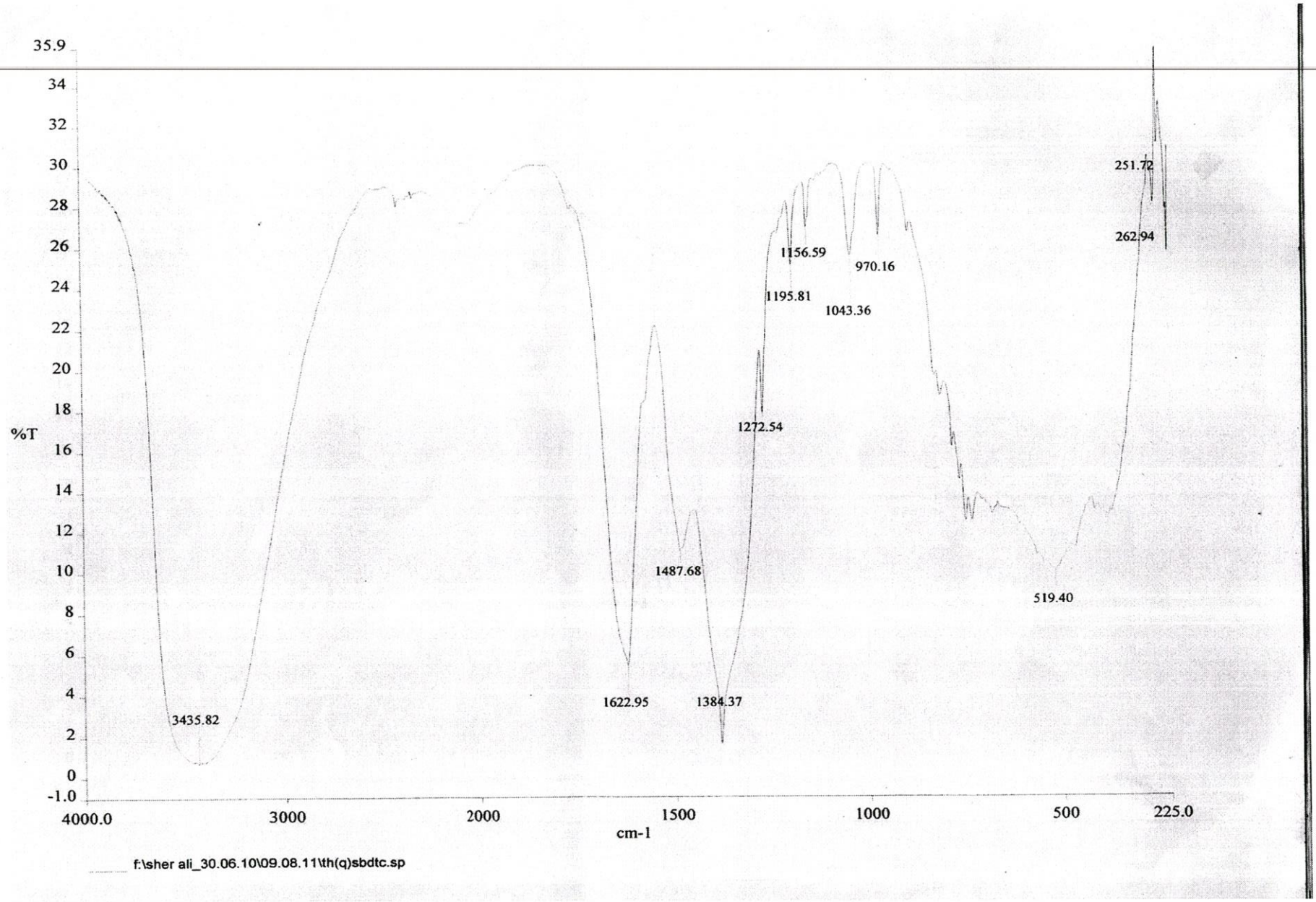


Fig. 5.21: FTIR spectrum of the complex [Th(SB-C_2)Q]

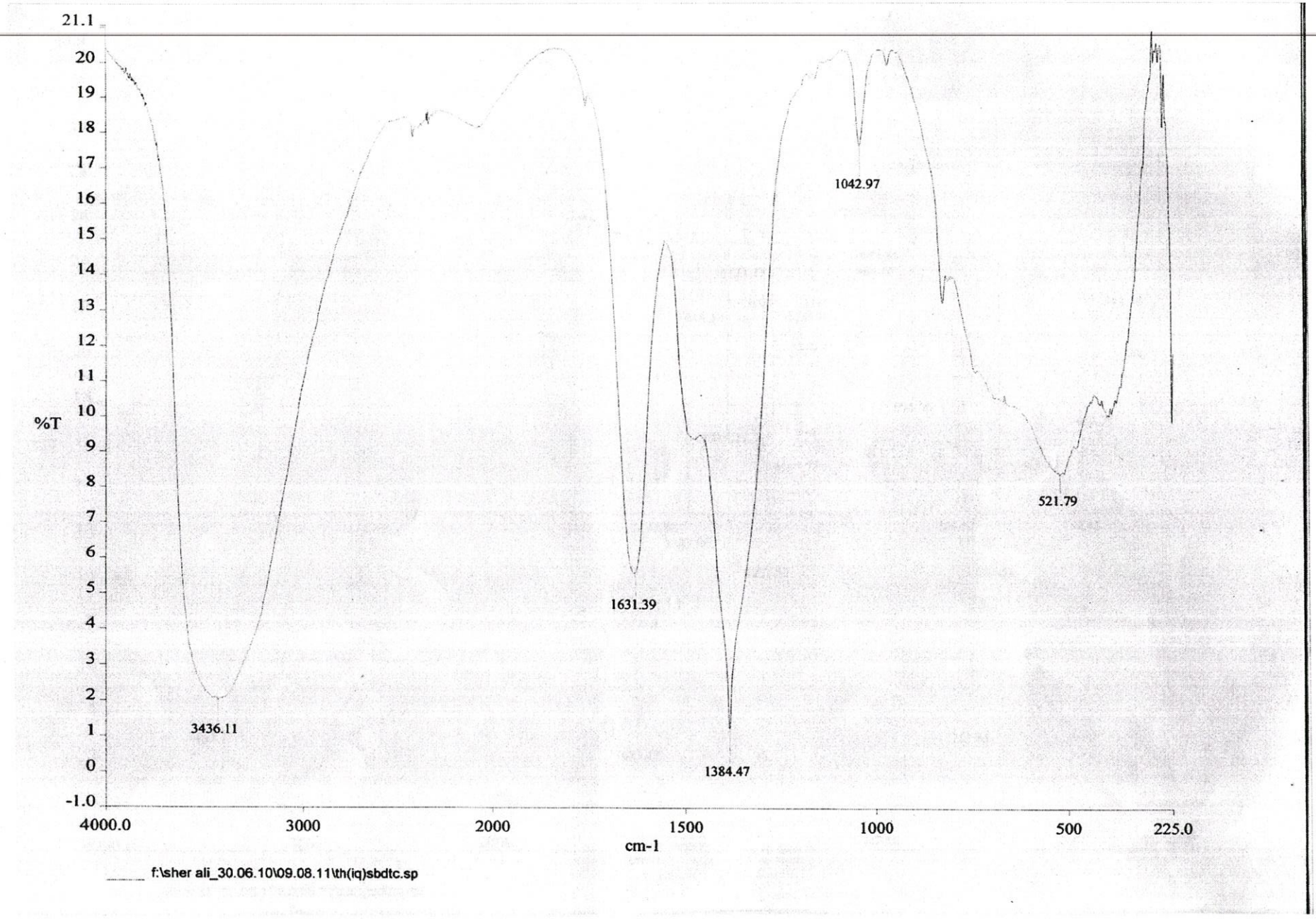


Fig. 5.22: FTIR spectrum of the complex [Th(SB-C_2)IQ]

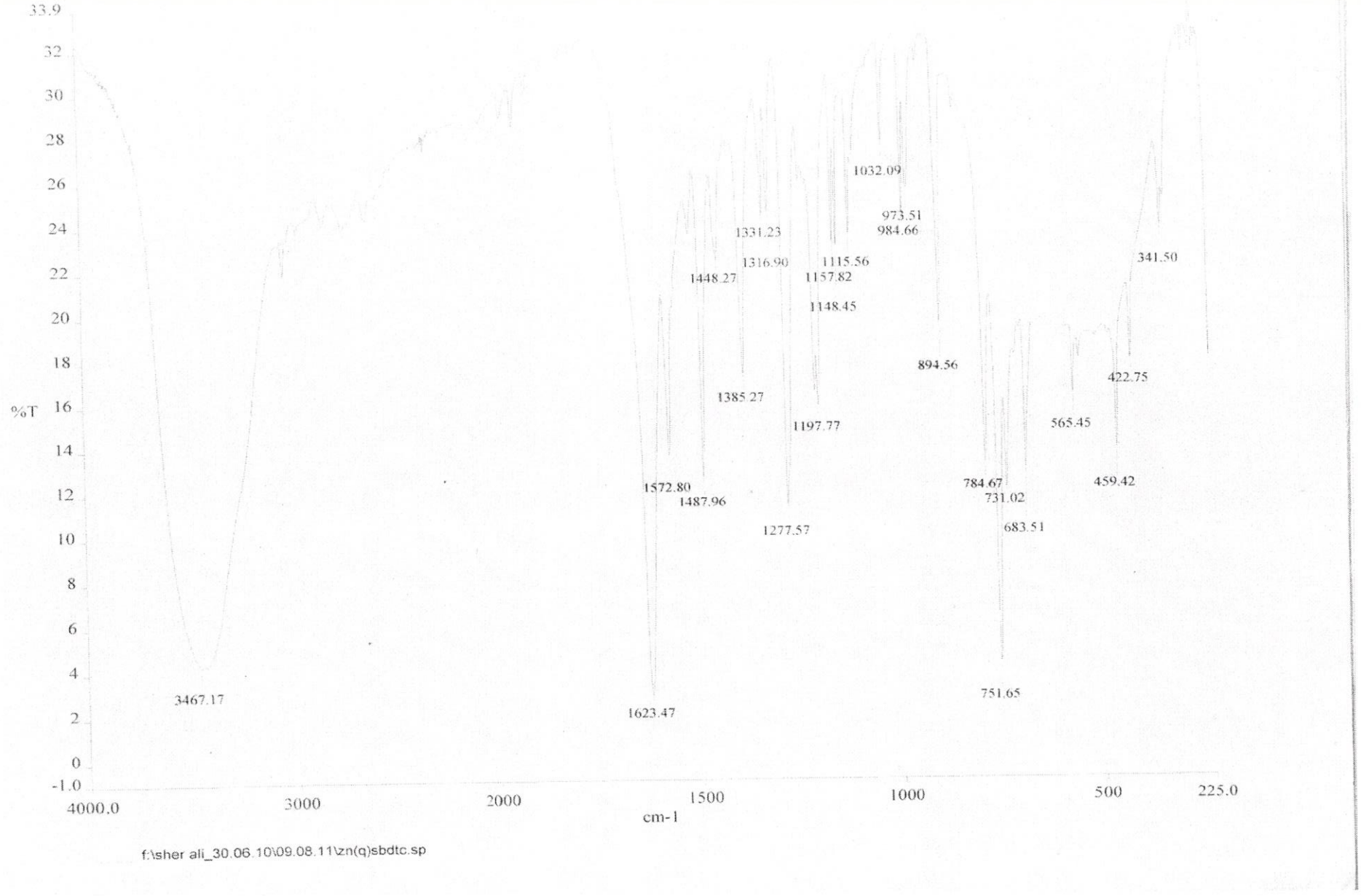


Fig. 5.23: FTIR spectrum of the complex [Zr(SB-C_2)Q]

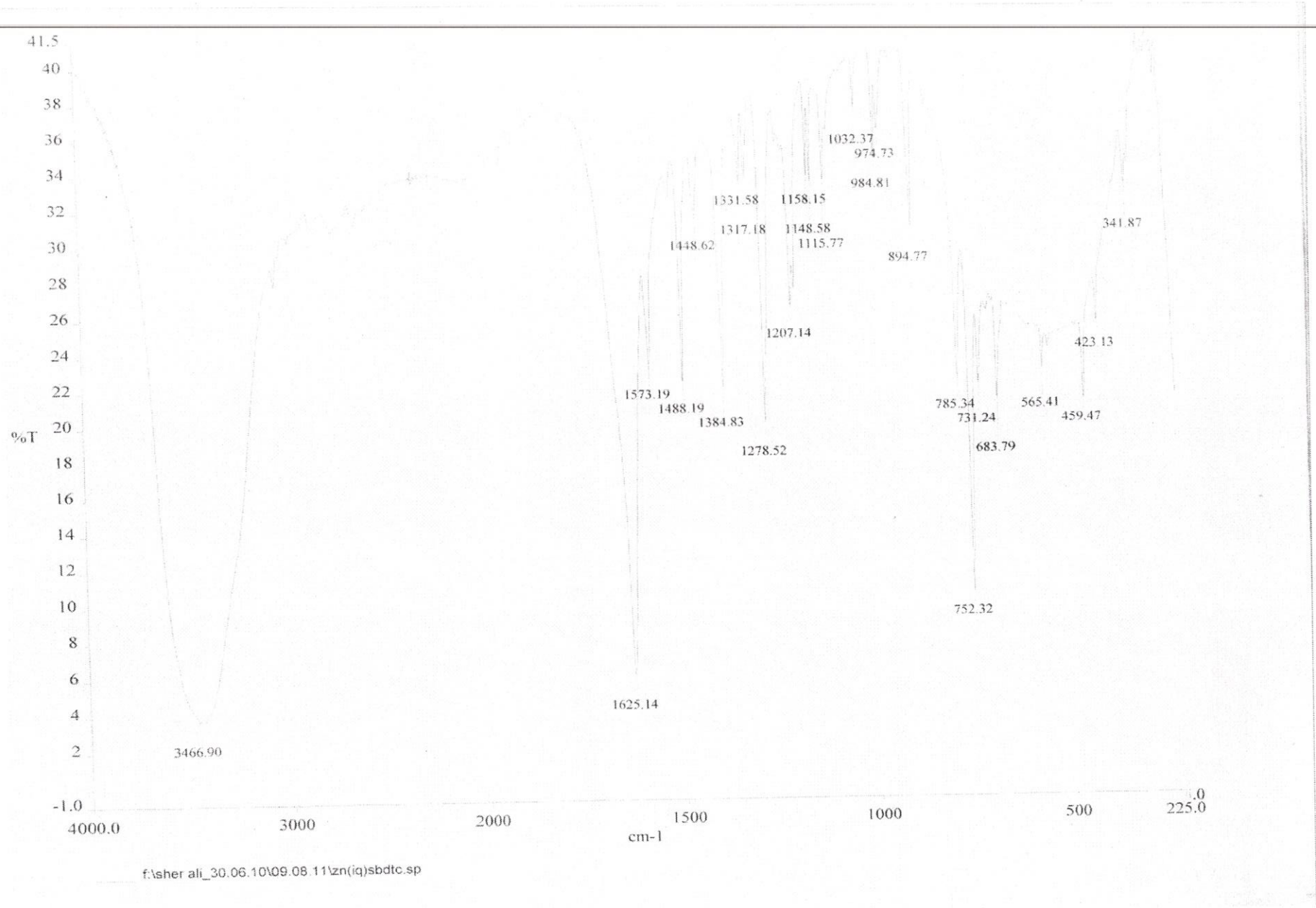


Fig.5.24: FTIR spectrum of the complex [Zr(SB-C_2)IQ]

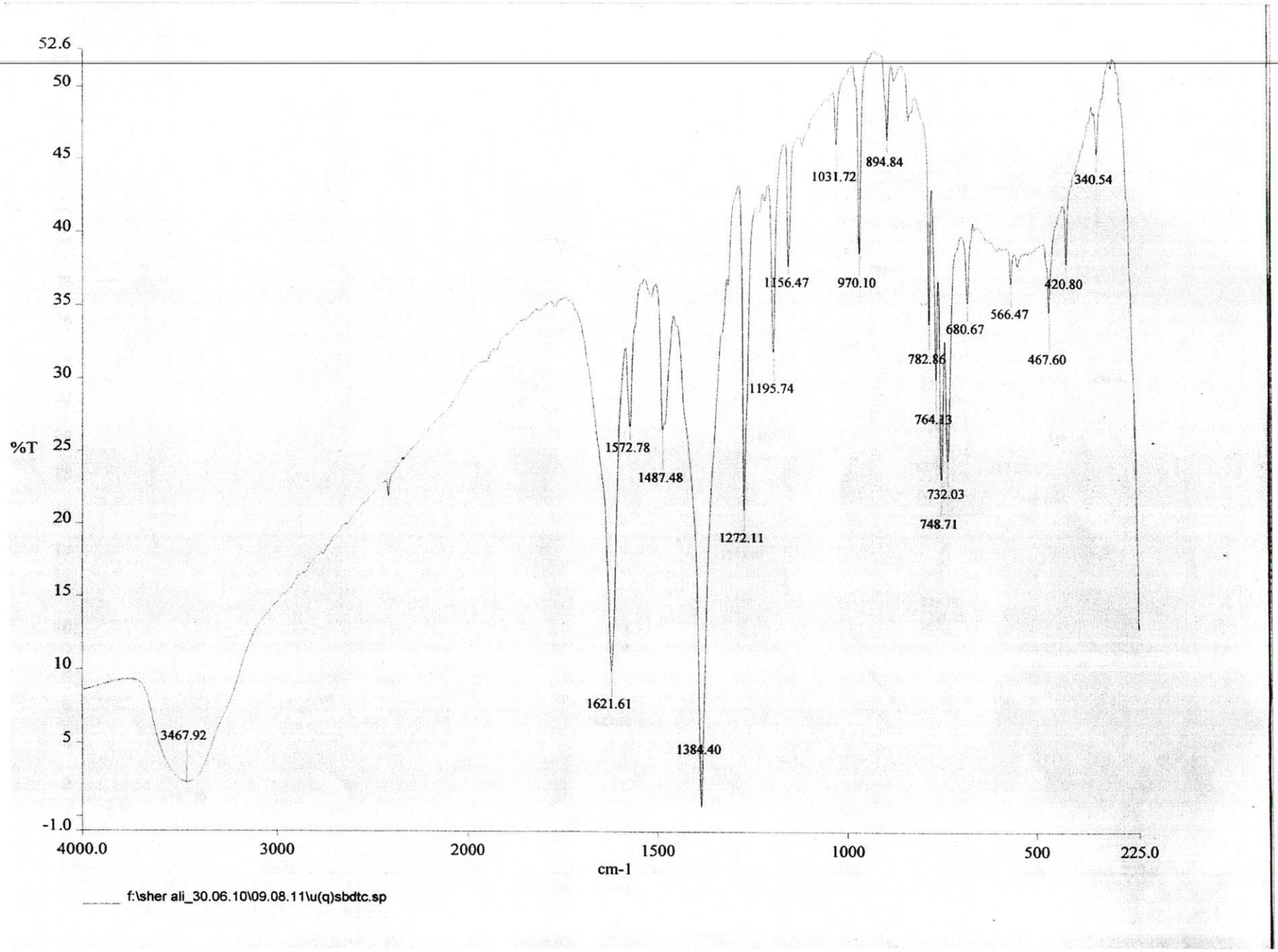


Fig. 5.25: FTIR spectrum of the complex [U(SB-C_2)Q]

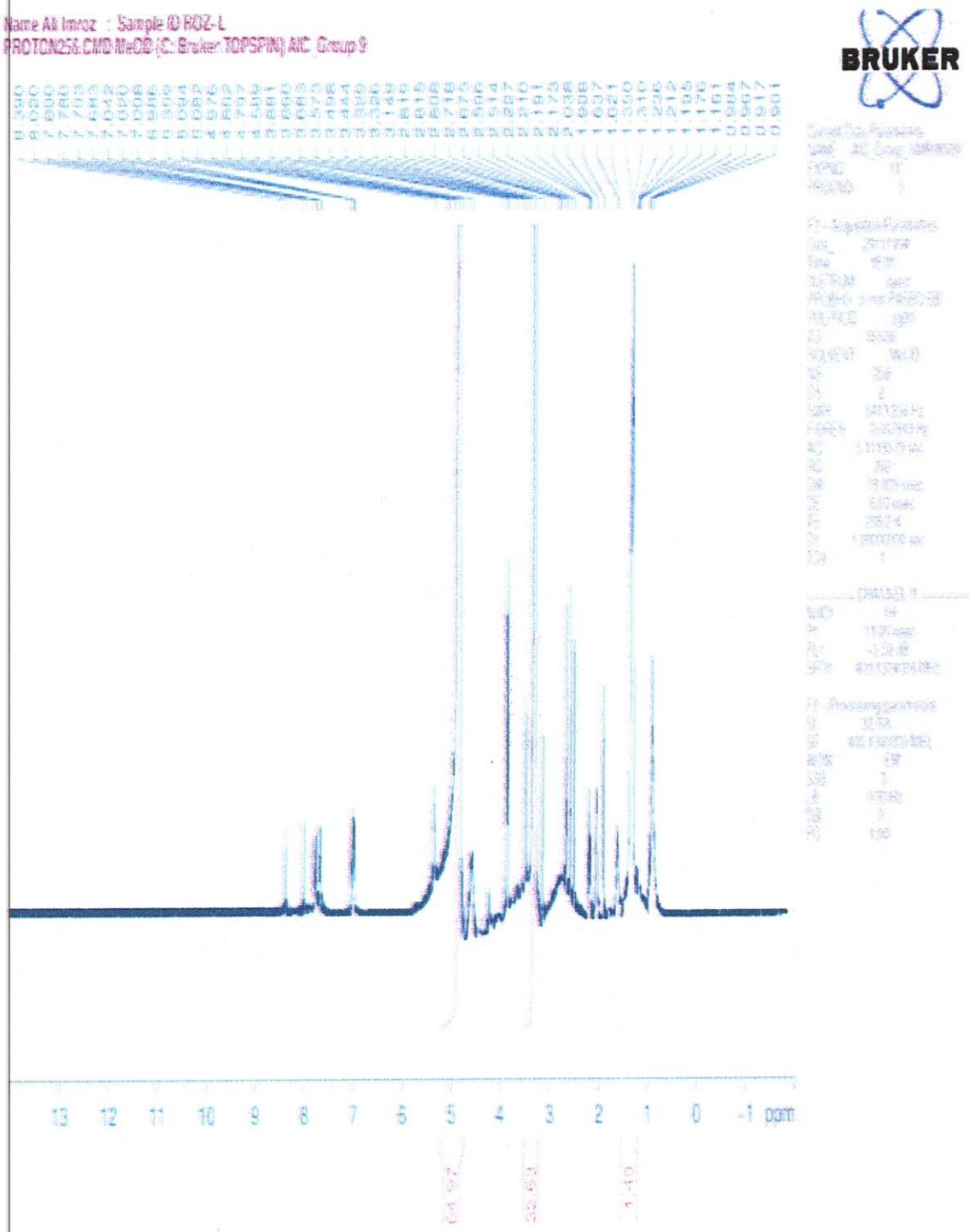


Fig. 5.26: ^{1}H-NMR spectrum of [Zr(SB-C_1)Q]

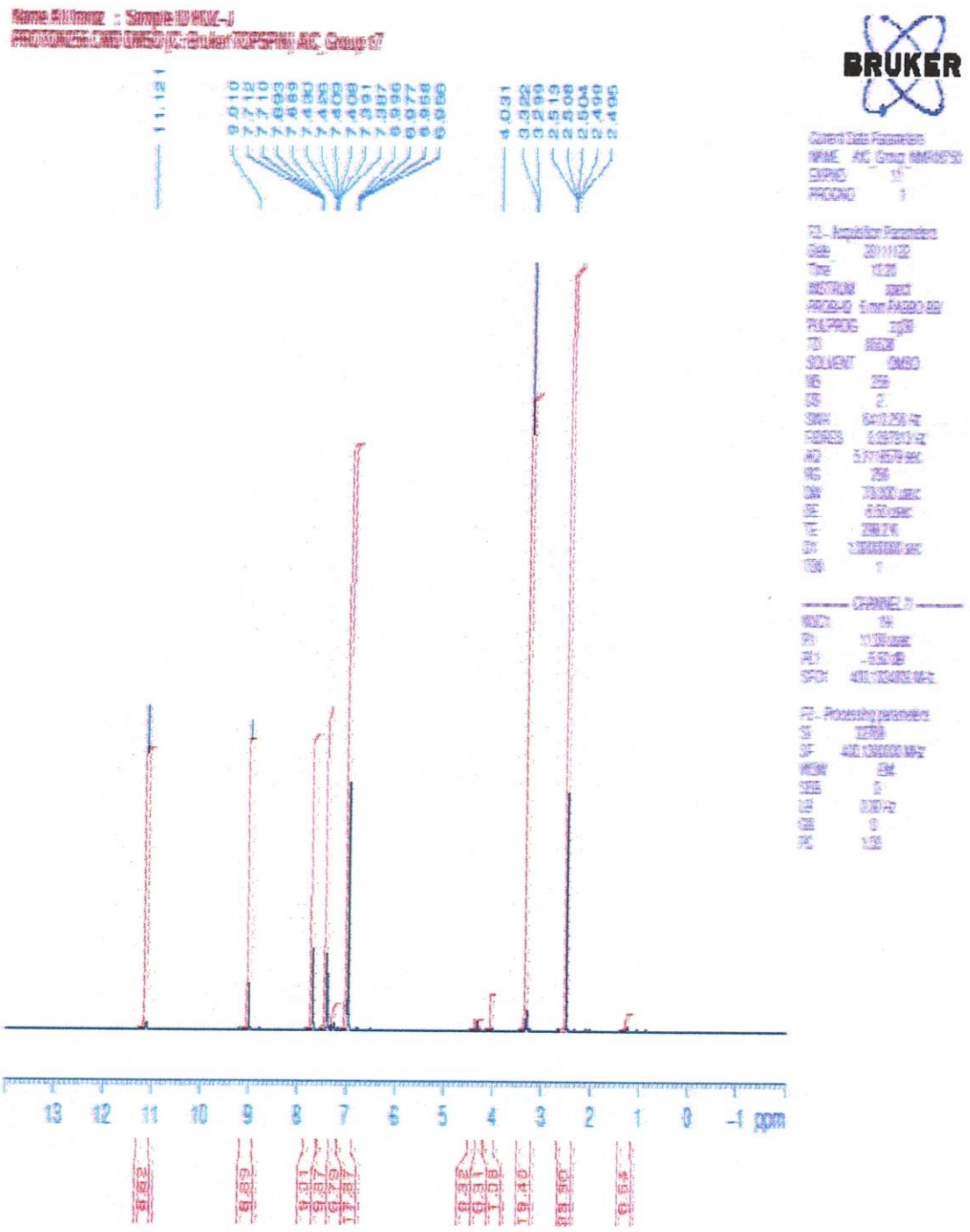


Fig. 5.27: ^{1}H-NMR spectrum of [Zr(SB-C_2)Q]

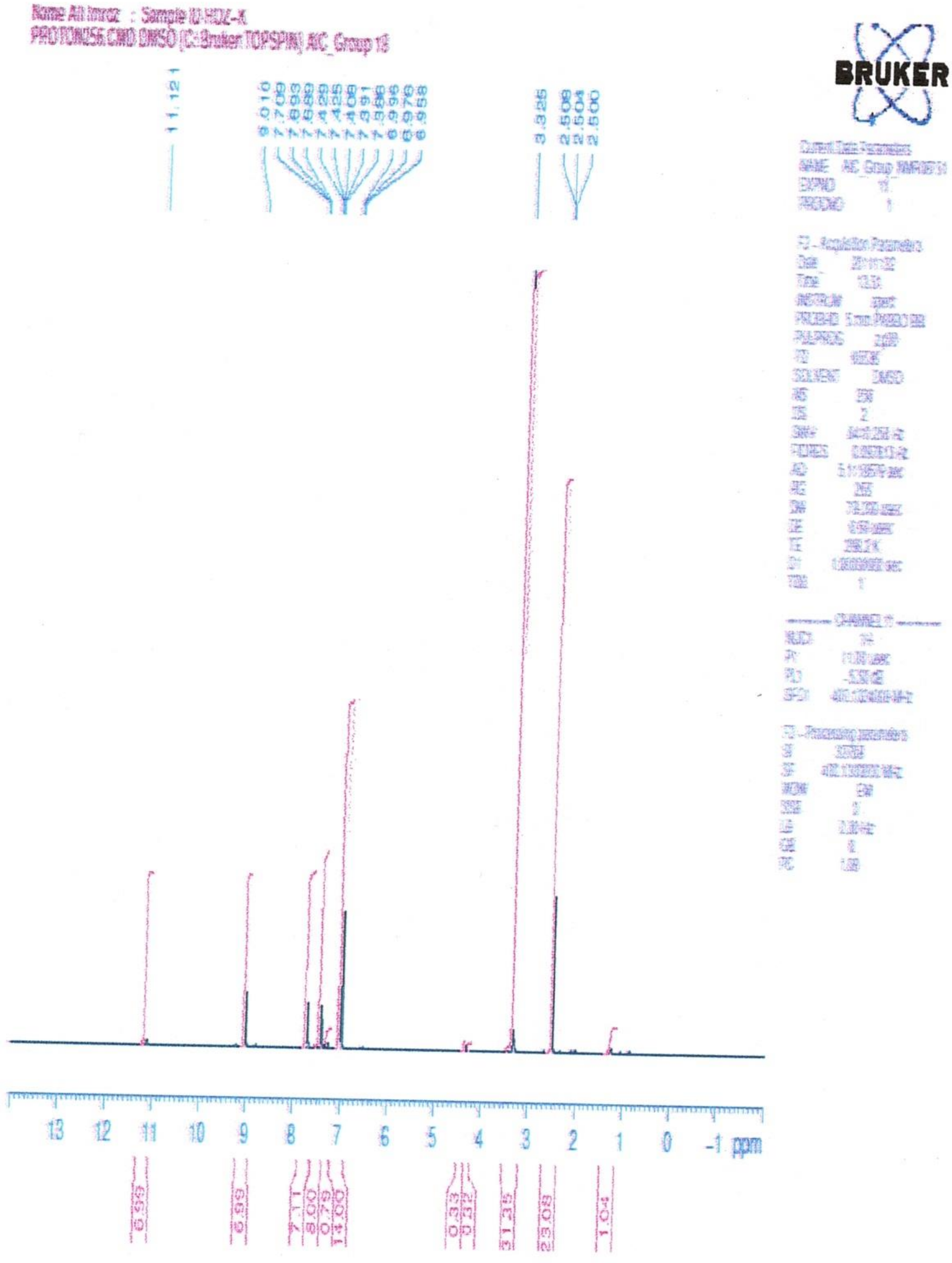


Fig. 5.28: ^{1}H-NMR spectrum of Complex[U(SB-C$_2$)Q]

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CHAPTER-VI

PREPARATION & CRYSTALLOGRAPHIC STRUCTURE DETERMINATION OF Cu (II) COMPLEX

6.1. INTRODUCTION

X-ray crystallography is a tool used for determining the atomic and molecular structure of a crystal.

Since many materials can form crystals-such as salts, metals, minerals, semiconductors, as well as various inorganic, organic and biological molecules X-ray crystallography is the fundamental tool in the development of determining the structure of the complex. In its first decades of use, this method determined the size of atoms, the lengths and types of chemical bonds, and the atomic-scale differences among various materials, especially minerals and alloys. The method also reveled the structure and function of many biological molecules, including vitamins, drugs, proteins and nucleic acids such as DNA. X-ray crystallography is still the chief method for characterizing the atomic structure of new materials and in discerning materials that appear similar by other experiments. X-ray crystal structure can also serve as the basis for designing pharmaceuticals against diseases.

The first application of X-ray crystallography was found in metallurgy[1-6]. Since that success, X-ray crystal structures of proteins, nucleic acids and other biological molecules have been determined.

Scientists now use X-ray crystallography routinely to determine how a pharmaceutical drug interacts with its protein target and what changes might improve it[7].

The Cu (II) atom in the title complex, [Cu ($C_{14}H_{11}O_3$) Cl ($C_{10}H_8N_2$)], exists within a ClN_2O_2 donor set defined by a chloride ion, an asymmetrically chelating carboxylate ligand, and a symmetrically chelating 2,2-bipyrdine molecule.

6.2. EXPERIMENTAL PROCEDURE

6.2.1. Reagents: As stated in chapter 2 Page No 40.

6.2.2. Physical Measurements: As stated in chapter 2 Page No 41.

6.2.3. X-ray crystal structure determination

The X-ray crystallography of these crystals was carried out at the University of Malaya, Malaysia.

6.3. Preparation procedure

A mixture of copper chloride (O.134g, 1m mol), benzilic acid (0.228 g.1 mmol), 2,2-bipyridine (0.196g 1m mol) and Et_3N (0.1 g, 1m mol) was placed into methanol (40 ml) and the resultant solution was heated to 223K for 0.5h. Initial precipitates were filtered off and the filtrate was allowed to stand for several days. Blue blocks of the title compound were collected, washed with methanol and air-dried at room temperature. *M.P.* 457K.

6.4. RESULTS & DISCUSSION

Recent structural investigations of benzilate complexes have confirmed that anions derived from benzilic acid can function as multidentate ligands with versatile coordination modes[12, 13]. Herein, the crystal and molecular structure of a mononuclear Cu^{11} complex, (fig.6.1), is described.

The Cu atom in (fig.6.2) is coordinated by a C1, an asymmetrically chelating carboxylate anion, and a symmetrically chelating 2,2 bipyridine ligand, Table 1. The asymmetric mode of coordination of the carboxylate is reflected in the disparate C --- O bond distances with the longer Cl --- O1 distance [1.285(8) Å] being associated with the shorter Cu --- O1 interaction, and the short Cl ---- O2 distance [1.204(7) Å] associated with the weaker Cu --- O2 contact. The resultant ClN_2O_2 donor set defines a square pyramid. This assignment is based on the value calculated for τ of 0.07 for the Cu atom, which compares to the τ values of 0.0 and 1.0 for ideal square pyramidal and trigonal bi-pyramidal geometries, respectively[14]. In this description, the weakly coordinating 02 atom defines the axial site. White not participating in direct coordination to the Cu atom, the hydroxyl group forms an intramolecular hydrogen bond with the 02 atom as well as an intermolecular O --- H...C1 hydrogen bond, Table 2. The latter leads to the generation of supramolecular chains along the axis, (fig. 6.3), were by the Cu atom lie on a line.

Crystal data[8] and refinement[9] details are given in table 1., Fig.1., showing the atom labeling scheme, was drawn with 70% displacement ellipsoid using ORTEP-3[10] and the remaining figures were drawn with DIAMOND[11].

The molecular structure and atom numbering scheme for the complex (2, 2́- Bipyridine – κ^2 N, Ń) chloride (2 –hy-droxy-2, 2 – diphenylacetato 2- κ^2 O^1, $O^{1'}$) copper (II) is shown in Fig.1 and selected atomic distances and angles are shown in table -2, and table -3. The Cu (II) atom, which is bonded with Cl1, O1, O2, N1 and N2 atoms complete the square pyramidal coordination geometry.

Table 6.1: Crystal data and refinement details for the complex (2, 2́- Bipyridine – κ^2 N, Ń) chloride (2 –hy-droxy-2, 2 – diphenylacetato 2- κ^2 O^1, $O^{1'}$) copper (II)

Empirical formula	$[Cu(C_{14}H_{11}O_3)\ Cl\ (C_{10}H_8N_2)]$
Formula weight	482.40
Crystal habit, color	Block, Blue
Crystal system	Monoclinic
Space group	P2/c
a (Å)	7.1537(9)
b (Å)	15.7277(19)
c (Å)	18.601(4)
Volume ($Å^3$)	2073.5(5)
Z	4
Density, Dx (Mgm^{-3})	1.545
Absorption coefficient (mm^{-1})	1.21
F(000)	988
Crystal size (mm)	0.20×0.15×0.10
Reflections collected	8454
Independent reflections	3651
R_{int}	0.053
Reflections with $I \geq 2\sigma(I)$	2719
Number of parameters	281
R indices [all data]	R1=0.060, wR2=0.238

Table 2: Selected bond lengths (A°) and angles (°) for the complex (2, 2́- Bipyridine – κ^2 N, Ń) chloride (2 –hydroxy-2, 2 – diphenylacetato 2- κ^2 O^1, $O^{1'}$) copper (II)

Cu-Cl1	2.2301(18)
Cu-O1	1.971(4)
Cu-O2	2.476(4)
Cu-N1	2.006(5)
Cu-N2	1.976(5)
N1-C15	1.329(8)
N1-C19	1.333(9)
N2-C24	1.345(8)
N2-C20	1.353(8)
O1-C1	1.285(8)
O2-C1	1.204(7)
O3-C2	1.421(7)
$O3-H3_0$	0.8200
C1-C2	1.567(8)
C2-C3	1.527(8)
C2-C9	1.537(8)
C3-C4	1.379(9)
C3- C8	1.395(9)
O1- Cu-N2	160.0(2)
O1- Cu-N1	92.9(2)
N2- Cu-N1	81.4(2)
O1- Cu-Cl	95.35(14)
N2-Cu-1	96.91(15)
C10-C9-C2	120.8(5)
C14-C9-C2	120.6(5)

Table 6.3: Hydrogen bonding parameters (D-H...A; A°) for the complex (2, 2- Bipyridine – κ^2 N, N) chloride (2 – hydroxy-2, 2 – diphenylacetato 2- κ^2 O^1, O^1) copper (II)

D-H...A	D-H	H...A	D...A	D-H...A
O3-H3o...O2	0.82	2.19	2.622(6)	113
O3- H3o...Cl1	0.82	2.62	3.328(5)	146

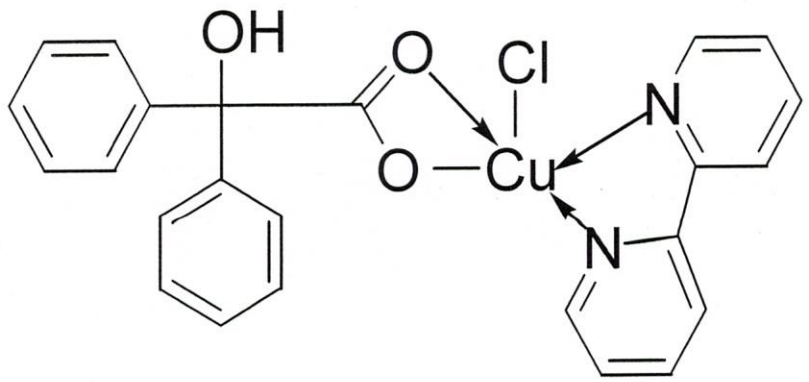

Fig.6.1:Molecular structure of a mononuclear Cu(II) complex

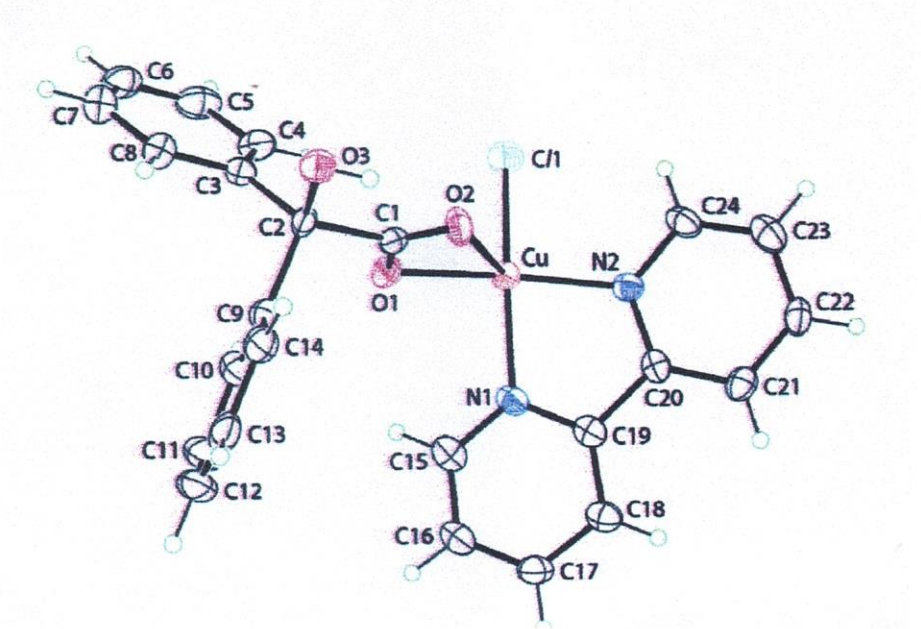

Fig.6.2: Molecular structure of Cu(II) complex showing displacement ellipsoids at the 50% probability level

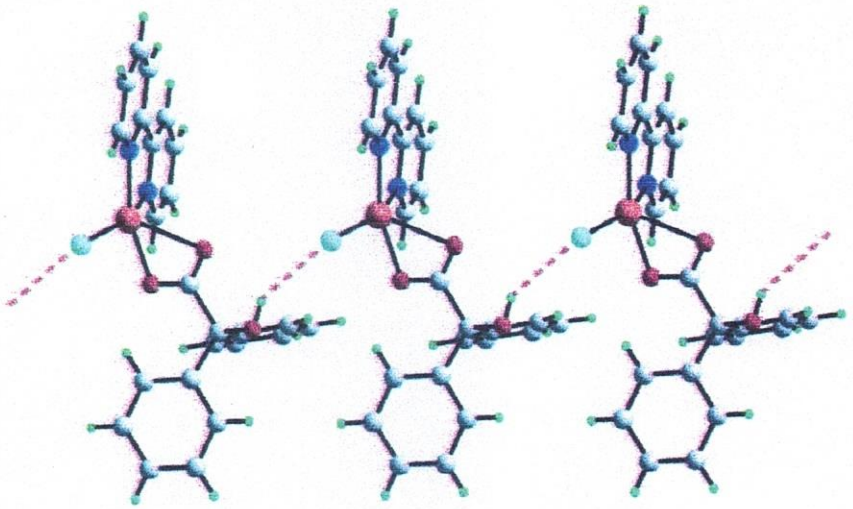

Fig.6.3: Supramolecular chain along the α axis in Cu(II) mediated by O-H....Cl hydrogen bonds (shown as orange dashed lines)

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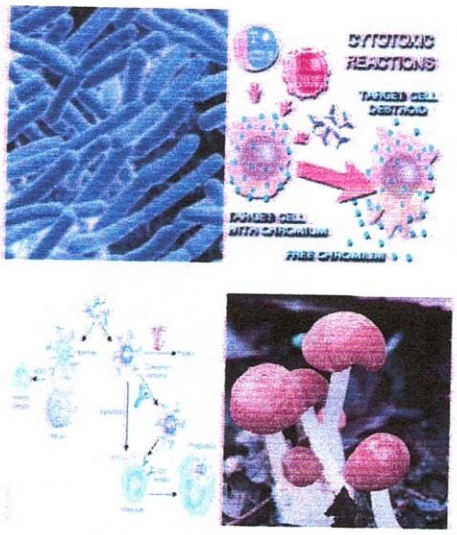
CHAPTER - SEVEN



INTRODUCTORY DISCUSSION OF BIOLOGICAL ACTIVITY OF SCHIFF BASE TRANSITION METAL COMPLEXES

The treatment of diseases due to bacterial, viral, fungal invasion by chemical compounds was studied successfully without affecting the tissues of the host and any other side effects. These antibiotics are developing resistance to the pathogenic organism day by day. In the 3rd world countries like Bangladesh, irrational use of antibiotics is a major cause of such resistance. So, it is no doubt important to discover newer, safer and more effective antibiotics. Biological and medicinal properties of transition metal complexes and their mechanisms of action is now a very important tool for the modern drug discovery program. Synthetic chemical compounds constitute important sources of various bioactive compounds such as antimicrobial[1] and anticancer[2] compounds.

Microorganism like fungi cause plant disease and are also responsible for poor yield of crops, which can cause significant loss to the farming community. The chemicals, which have the ability to kill fungi, are called fungicides; suitable fungicide should be toxic to the parasite or inhibit the growth of its spore without causing phytotoxicity. A good fungicide should be capable of even distribution from the spraying or dusting on the surface to be covered. It should be remaining on the surface without running off and should stick to the surface after drying. Again a good fungicide should be as least toxic as possible to human beings and cattle. The treatment of diseases due to fungal invasion by chemical compounds were studied and used successfully without affecting the tissues of the host and other side effects.

There are many organic, inorganic, aromatic and heterocyclic compounds. Which are effective as antibacterial and antifungal agents. Salt of toxic metals and organic acids and organic compounds of mercury and sulfur, quinine and heterocyclic nitrogenous compounds are familiar and these are major fungicides. Among these sulfur-

containing compounds is highly effective and popular fungicide. Our interest was to see weather our synthesized ligands and their metal complexes are effective or not against some selected bacteria and fungi.

Transition metal complexes were also found to have physiological properties[3]. In all cases where transition metal complexes are used as drugs, the systems are designed so that upon ligand dissociation, cleavage or elimination, the metal is delivered as the cationic species[4].

The cytotoxicity of the metal raises the possibility of using transition metal complexes as potential prodrugs in conjunction with known anticancer compounds. More, specially, by binding a known anti tumor agent as the dissociating ligand, we may have the capability of using a transition metal as a delivery system for antitumor agents.

Brine shrimp lethality bioassay is an assay procedure for the bioactive compounds, which indicate cytotoxicity as well as anticancer, antiviral, pesticidal etc activity.[5] Bioactive compounds is almost cytotoxic in high doses[6]. Pharmacology is simply toxic at a lower dose or at higher dose. Thus in vivo lethality is a simple zoological organism (brine shrimp napulii) can be used as a convenient monitor for the screening and fractionation in the discovery of new bioactive synthetic products[7,8].

Sulpher-nitrogen ligands and their complexes have been reported to be biologically versatile compounds possessing antiviral[9], antibacterial[10] antipyretic fungicide[11] and have analgesic activities. Franch and Co-workers[12-14] studied the carcinostatics activity of thiosemi-carbazones containing heterocyclic nitrogen and they sugested that these compounds, by loss of a proton from their tautomatic thiol form, act as tridentate chelating agents, sequestering metal ions, which are involved in carcinogenesis.

Many cancers are known to have viruses associated with them and a few cancers believed to be actually caused by viruses consequently, and anticancer drug may actually be an antiviral agent[15]. Kirschmmer[16] have observed that the proteins and nucleic acid proteins of viruses are effective chelating agents and the aim of the metallotherapeutic designer is to alter the virus by metal chelating so that the viral activity is diminished. These workers have pointed out that moderately stable metal chelates are necessary, since the metal ion must not be so weakly bound as to be free enough to be complexes by amino acids and enzymes present in the body be able to be selective in regard to benign and malignant viruses.

It is apparent that thermodynamic stability of the metal chelates is less important than kinetic consideration. Cancer growth is dependent on the reproduction of the malignant cells having a kinetic advantage over the body defense mechanism. Therefore the metal complex is effective and sufficiently labile to out space the cancer growth.[17] From the recent study of the anti- tumor activities of some neutral complexes of the type PtA_2X_2 (A = amine; X = halogen), it has been suggested that kinetic factors are important in determining the effective dose of metal complexes. It is clear that a study on the synthesis and characterization of new sulphur-nitrogen chelating agent and their metal complexes would be useful in the discovery of anticancer and antiviral drugs.

Table–7.1: Complex abbreviation for biological activity

No.	Complexes	Symbol
1	[Ni(SB-A_1)2-Pic]	L_1
2	[Ni(SB-A_2)IQ]	L_6
3	[Cu(SB-A_2)4-pic]	L_8
4	[Zr(SB-C_1)Q]	S_1
5	[Th(SB-C_1)Q]	S_2
6	[U(SB-C_1)Q]	S_3
7	[Zr(SB-C_2)IQ]	S_4
8	[Th(SB-C_2)Q]	S_5
9	[U(SB-C_2)IQ]	S_6
10	[Zr(SB-B_2)Q]	S_1^1
11	[Zr(SB-B_2)Py]	S_1^3
12	[U(SB-B_2)Q]	S_2^1
13	[U(SB-B_2)Py]	S_2^3
14	[Th(SB-B_2)Q]	S_3^1
15	[Th(SB-B_2)Py]	S_3^3
16	[Ni(SB-B_1)2-Pic]	C_7
17	[Cu(SB-B_1)4-pic]	C_{12}
18	Schiff base of SBDTC/C_2	SBDTC
19	Schiff base of SMDTC/C_1	SMDTC
20	Et-Di/B_2	Et-Di

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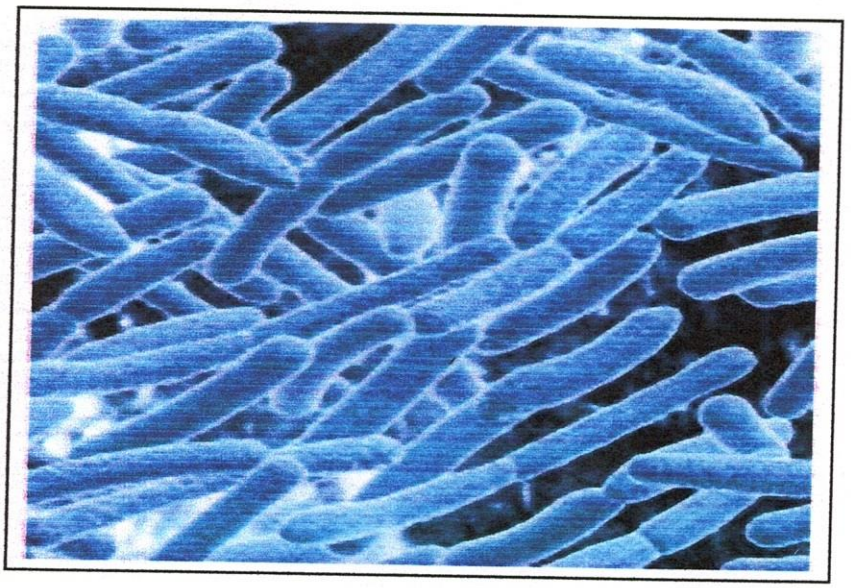
CHAPTER - EIGHT



ANTIBACTERIAL ACTIVITIES OF LIGHTER AND HEAVIER TRANSITION METAL COMPEXES

8.1. INTRODUCTION AND PRINCIPLE

Any chemical or biological agent that either kills or inhibits the growth of microorganism is called antimicrobial agent. The susceptibility of microorganism to antimicrobial agent can be determined in *vitro* by a number of methods. The disc diffusion technique [1,2] is widely acceptable for preliminary investigation of materials, which were suspected to posses' antimicrobial properties. Diffusion procedure was normally used for qualitative test, which allocates organism of the susceptible intermediate (moderately susceptible) or resistant categories.

The dried filter paper discs containing the test material was usually applied to the test plate containing the culture of microorganisms. These were kept at low temperature (4°C) for 24 hours. Initially the dried discs absorbed water from the surrounding test medium and the drug was dissolved. The drug migrates through the adjacent test medium by concentration gradient of the drug according to physical law that governs diffusion of molecules through an agar gel[3]. As a result, there was a gradual change of drug concentration in the agar surrounding each disc. Then the plates were incubated in an incubator at 37°C for 6 hours. Activities of test samples were expressed by measuring the zone of inhibition observed around the area of the disc.

As the antibiotic diffusion progresses microbial multiplication also proceeds. After an initial lag phase, a logarithmic growth phase is initiated and at that moment bacterial multiplication proceeds more rapidly than the drug can diffuse. Therefore, the bacterial cells, which were not inhibited by the antimicrobial agents, will continue to multiply

until a lawn of grown can be visualised. No growth will appear in the area where drug was present in inhibitory concentration.

Generally more susceptible the test organism the larger was the circular zone of inhibition. Antimicrobial activities of the test sample were expressed by measuring the zone of inhibition observed around the area of the disc. The diameter of the inhibition was usually measured to understand the extent of inhibition in different concentration. The compounds, which showed inhibition diameters of 20 mm and above, were considered strongly antimicrobial[4].

The size of the inhibitory zones depends on the following principle factors.

i. Intrinsic antimicrobial sensitivity of the test sample.
ii. Growth rate of the test microorganism.
iii. Diffusion rate of the drug that was related to its water solubility.
iv. Number of concentration of the freshly seeded test organism.
v. Amount of the test sample on disc.
vi. Thickness of the test medium in the Petri dishes.
vii. Thickness of the filter paper disc.

8.2. APPARATUS AND REAGENTS

i. Micropipette.
ii. Autoclave.
iii. Incubator
iv. Refrigerator.
v. Filter paper disc.
vi. Petri dishes.
vii. Inoculation loop.
viii. Sterile cotton.
ix. Sterile forceps.
x. Spirit lamp.
xi. Laminar air flow unit.
xii. Nutrient agar.

8.3. METHOD

The test organisms were pathogenic for human beings. For this reason, all steps of the work were done with high precaution and aseptic condition that were mentioned below. All steps of the work were carried out at microbiology laboratory at Pharmacy Department at Rajshahi University.

8.4.TEST OF ORGANISMS USED FOR THE STUDY

Three pathogenic bacteria were selected for the test, two of which were gram negative and other was gram positive.

List of The Test Pathogenic Bacteria

Gram Negative

Escherichia coli

Shegilla dysenteriae

Gram Positive

Bacillus subtilis

Agro bactrium

8.4.1.CULTURE MEDIA

Nutrient agar medium was used as culture media. The instant nutrient agar (DIFCO) medium was weighed and then reconstituted with distilled water in a conical flask according to specification (2.3% w/v). The formulation of nutrient agar media (DIFCO) was as follows:

Nutrient agar (mast diagnostics)

Formulation	Grams /litre
Peptone A	6.0
Yeast extract	2.0
Beef extract	1.0
Sodium chloride	5.0
Agar	14.0
Distilled water sq. to 1000 mL	

Total 28 grams of powder was weighed and dispersed in one litre of distilled water allowed to shake for 10 minutes, rotated to mixed and then sterilised by autoclaving for 15 minutes at 121°C. Then medium was cooled to 40-45°C and mixed well, then poured in to plates.

8.4.2.PREPARATION OF FRESH CULTURE

The liquid culture was called broth culture. The culture media without agar powder per litre.

Formulation	Grams /litre
Bacto tryptone	10.0 g
Bacto yeast extract	5.0 g
NaCl	10.0 g

The pH was adjusted to 7.5 with sodium hydroxide.

Trpytone, NaCl and yeast extract of calculated amount were taken in a conical flask and distilled water was added (volume should be less then 1 litre) the contents were heated in water bath to make a clear solution. The pH of the solution was then adjusted to 7.5 using NaOH or HCl as necessary. Distilled water was added sufficiently to make the final volume (1-liter). Again the total volume was heated on a water bath to obtain a clear solution. The conical flask was plugged with cotton and then autoclaved for 15 minutes at 120°C.

50 ml of broth medium was transferred in a conical flask. The test microorganisms of pure culture were streaked on the nutrient broth media with the help of sterile loop in an aseptic condition and incubated at 37°C for 24 hours. The broth culture thus obtained was considered as fresh culture. Fresh culture of this type was always used throughout the sensitivity testing.

8.4.3.PREPARATION OF THE CULTURE PLATE

A small bottle containing 10 ml sterile nutrient broth was taken and the test organism from the pure culture transferred to this bottle with the help of an inoculation loop in an aseptic condition. After inoculation the bottle was subjected to incubation at 37°C for 24 hours to provide sufficient time and temperature for the growth of the test organism.

To 100 ml of the nutrient agar, 1 ml of the prepared culture was added and was mixed thoroughly with shaking. A 25 ml portion of this culture was poured in to a petridish and the petridish was rotated several times first in clockwise direction and then in anticlockwise direction in order to facilitate homogeneous distribution of the test organism. The media were poured into petridish on a level horizontal surface so as to give a uniform depth of approximately 4 mm. The petridish was kept undisturbed for about 15 minutes during which it was solidified. After complete solidification of the media, 4-5 holes were made inside it with the help of a brother.

Just before using plates with lids agar were placed in an incubator (25°C) for about 10-15 minutes until the execs of surface moisture was lost by evaporation. There should be no droplets of water on observing their antibacterial activities. The species *Bacillus megatrium* was taken as test organism.

8.4.4.PREPARATION OF DISCS

A. Sample discs.

i. Solutions of the compounds were prepared in respective solvents so that 10 μL contained 100 μg of the compounds.

ii. Filter paper disc were taken in petridish and sterilised by oven at 110°C for 1 hour.

iii. 10 μL of the solutions were placed on the discs with the help of a micropipette thus discs containing 100 μg compounds were prepared.

iv. These discs were than air-dried.

B. Standard Disc

Ready made *kanamycin* K–30 μg/disc containing 30 μg/disc of antibiotic *kanamycin* were used as standard disc.

8.4.5.PLACEMENT OF THE DISC AND INCUBATION

The solidified agar plates were seeded with the 100μL of fresh culture with the help of a micropipette and spread the microorganisms with the help of a sterile spreader in an aseptic condition.

The prepared discs of samples were placed gently on the freshly seeded solidified agar plates with a sterile forceps. Standard disc were also placed on the test plate to compare the effect of the test sample and to nullify the effect of solvent respectively.

The plates were then kept in a refrigerator at 4°C for 24 hours in order that the materials had sufficient time to diffuse to a considerable area of the plates. After this the plates were incubated at 37°C for 6 hours.

8.4.6.CALCULATION OF THE ZONE OF INHIBITION

After incubation the diameter of the zone of inhibitions were observed and measured in mm by a transparent scale, result, obtained from these is listed in the Table. 8.1.

Table-8.1: Antibacterial activity of the complexes (1-21) and *Kanamycin.*

No	Complexes	Zone of inhibition, diameter in nm			
		Gram Negative		Gram Positive	
		E. coli	*Shigella dysenteriae*	*Agro bactrium*	*Bacillus subtilis*
1	[Ni(SB-A_1)2-Pic]	07	07	10	07
2	[Ni(SB-A_2)IQ]	07	07	08	08
3	[Cu(SB-A_2)4-pic]	09	06	08	12
4	[Zr(SB-C_1)Q]	07	08	08	06
5	[Th(SB-C_1)Q]	07	10	06	06
6	[U(SB-C_1)Q]	08	07	07	07
7	[Zr(SB-C_2)IQ]	08	06	06	07
8	[Th(SB-C_2)Q]	10	11	08	10
9	[U(SB-C_2)IQ]	08	08	09	06
10	[Zr(SB-B_2)Q]	07	06	06	06
11	[Zr(SB-B_2)Py]	08	08	08	06
12	[U(SB-B_2)Q]	07	09	08	07
13	[U(SB-B_2)Py]	07	08	06	08
14	[Th(SB-B_2)Q]	09	12	21	09
15	[Th(SB-B_2)Py]	08	07	06	06
16	[Ni(SB-B_1)2-Pic]	10	06	06	07
17	[Cu(SB-B_1)4-pic]	07	07	07	06
18	Schiff SBDTC/C2	16	13	20	17
19	Schiff SMDTC/C1	25	21	22	24
20	Et-Di/B_2	08	17	09	06
21	*Kanamycin -30*	28	20	21	25

8.4. RESULTS AND DISCUSSION

It has been observed that some drugs increase the activity when administered as metal complexes or their metal chelates[5]. The antibacterial activities of the metal complexes of Schiff bases were recorded against four pathogenic bacteria.

We have studied the antibacterial activity of the Schiff base ligands and their transition metal complexes with some selected bacteria. Among them two are Gram positive and two are Gram negative . Gram was a scientist who had classified bacteria as positive and negative on the basis of their cell wall chemical structure.

Gram negative:

Escherichia coli.

Shigella dysenteriae

Gram positive:

Bacillus subtilis

Agro bactrium.

The results of inhibition zone of some selected bacteria due to the effect of the test compounds are presented in Table 8.2. From the result it is clear that all the complexes of metals under investigations showed more or less activities against the four pathogenic bacteria. From the zone of inhibition it is observed that among the heavier metal complexes the Th(IV) complexes (complex 8 & 14) showed strong activity against both the Gram positive and Gram negative bacteria. The U(VI) and Zr(IV) complexes showed moderate activities against both Gram positive and Gram negative bacteria. Results also illustrate that the lighter transition

metal complexes, only the complex 3 showed moderate activity against Gram-positive bacteria. But rest of the complexes were less effective against Gram positive and Gram negative bacteria. Of them, the ligands (derived from SBDTC & SMDTC) were the most effective against Gram positive and Gram-negative bacteria. They showed almost equal zone of inhibition as kanamycin does, which was a standard antibiotic. In our cases ligands are more effective towards the bacteria than the complexes. If we compare the effectiveness of the ligands and their complexes against Gram positive and Gram-negative bacteria, we should see that the test complexes showed more or less effectiveness in both the cases. But it seems that the test complexes showed better performance in case of Gram-positive bacteria.

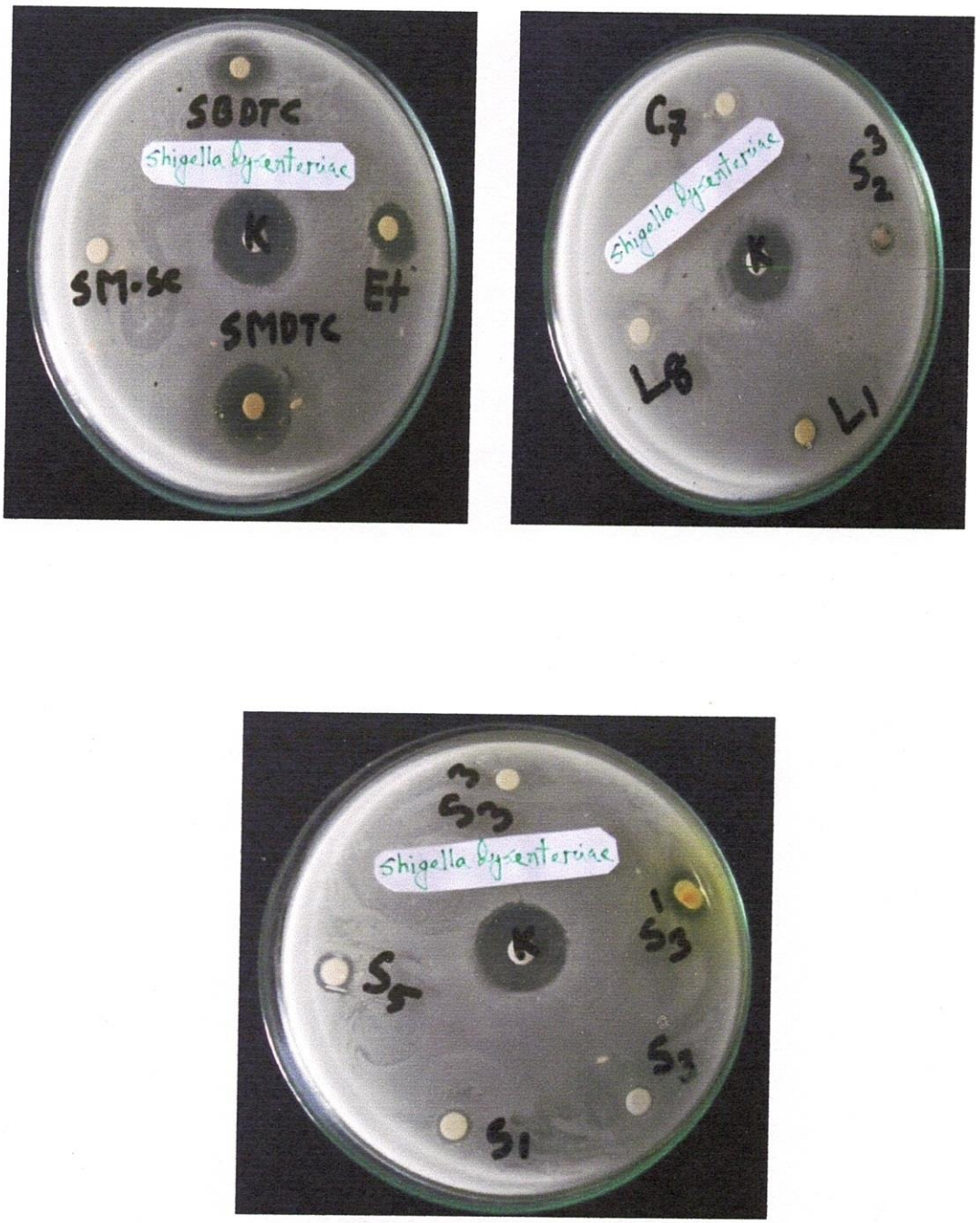


Fig. 8.1: Photographic representation of Zone of inhibition of the complexes against *Shigella dysenteriae*.

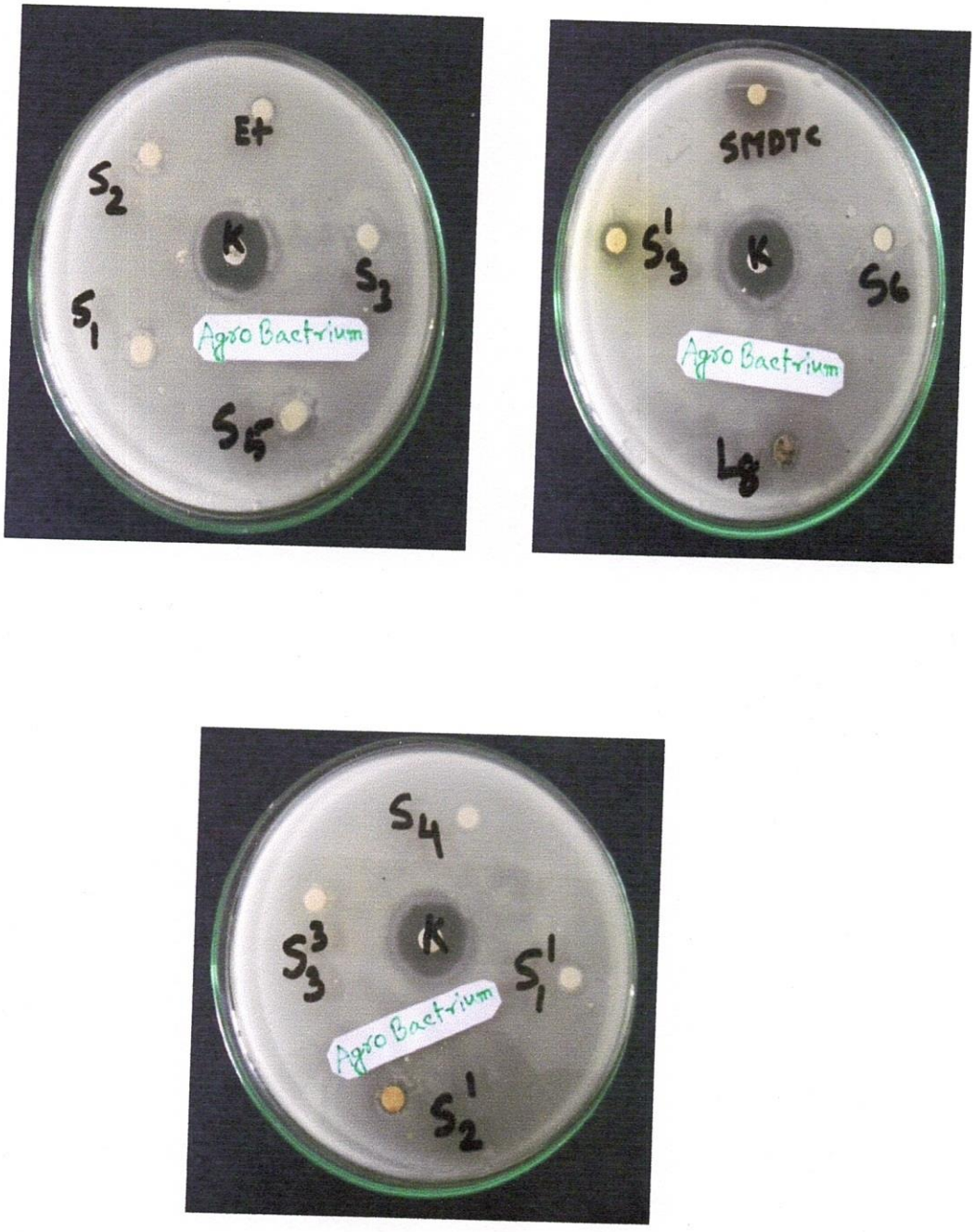


Fig. 8.2: Photographic representation of Zone of inhibition of the complexes against *Agro. Bactrium.*

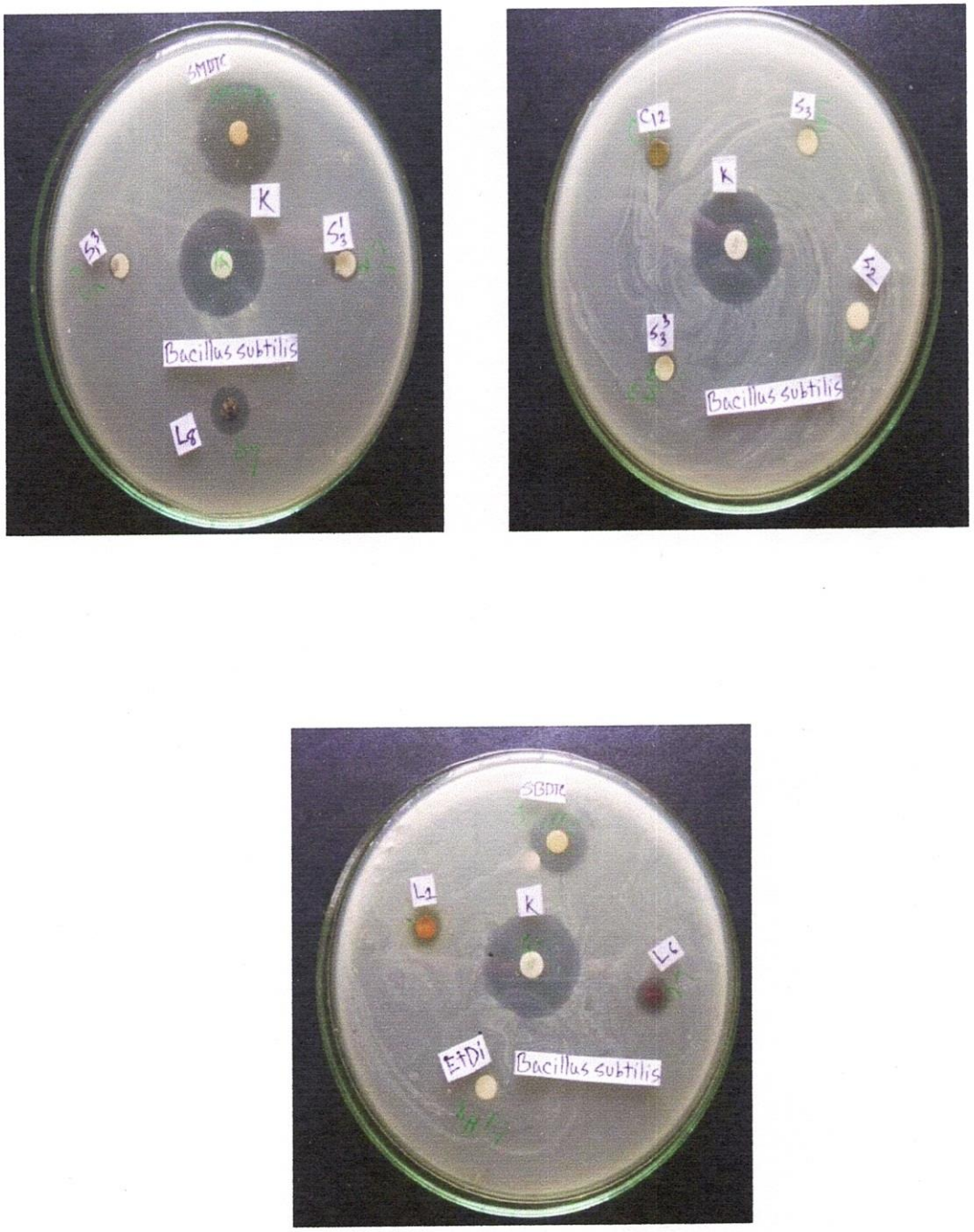


Fig. 8.3: Photographic representation of Zone of inhibition of the complexes against *Bacillus subtilis*.

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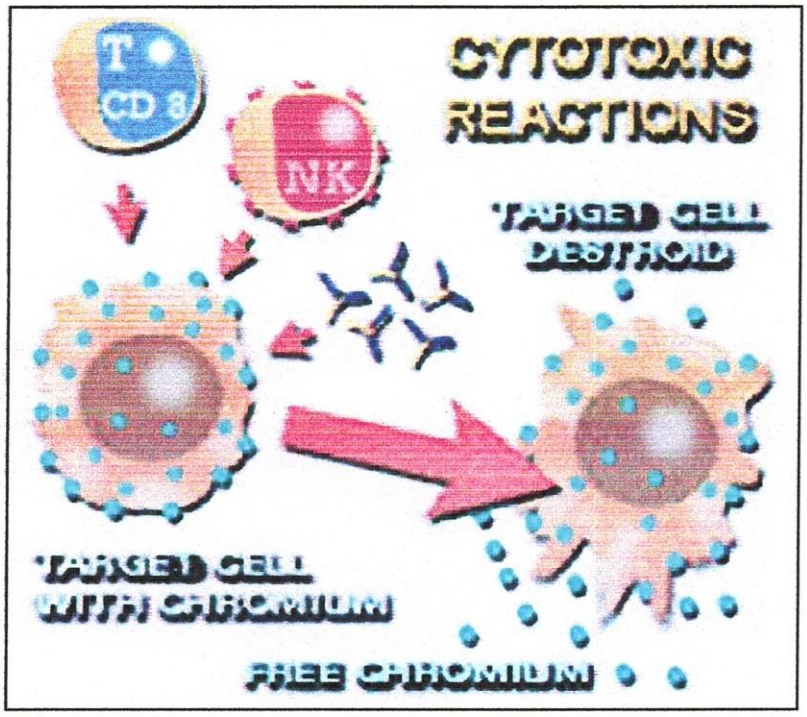
CHAPTER-NINE



STUDY OF BRINE SHRIMP LETHALITY OF LIGHTER AND HEAVIER TRANSITION METAL COMPLEXES

9.1. INTRODUCTION

Bio-assay usually involves comparison of unknown preparation with a standard.

Brine Shrimp lethality bioassay is a development in the bioassay for the bioactive compounds. Transition metal complexes can be tested for their bioactivity by this method. Here, *in vivo* lethality in a simple zoological organism (brine shrimp nauplii) is used as a convenient monitor for screening and fractionation in the discovery of new bioactive products. This bioassay indicates cytotoxicity as well as a wide range of pharmacological activities of the compounds.[1]

This test is known as the "Brine Shrimp Lethality Bioassay"

In all cases where transition metal complexes are used as drugs, the systems are designed so that complexes are dissociated, cleavage or eliminated. As a result the metal is delivered as the cytotoxic species. [2] Gunthkal .*et all.* [3] have synthesized ONS donor Schiff base complexes and studied their cytotoxic effect.

The brine shrimp bioassay has advantage of being rapid (24hrs) inexpensive and simple. [4] It easily utilizes a large number of organisms for statistical validation and requires no special equipment and a relatively small amount of sample. Furthermore, it does not require animal serum, as it is needed for cytotoxicities. This bioassay is indicative of cytotoxicity and a wide range of pharmacological activities of natural products.[5] Bioactive compounds is almost always toxic in high doses. [6-7]

9.2. MATERIALS

i. *Artemia Salina Leach* (brine shrimp eggs),

ii. Sea salt (From fish store)

iii. Small tank with perforated diving dam to grow shrimp, cover and lamp to attract shrimp.

iv. Pipettes (5 mL and 1mL)

v. Micropipettes (10 -200 μL)

vi. Vials (2mL)

vii. Magnifying glass

9.3. PROCEDURE

i. **Preparation of seawater:** 38 gm of pure NaCl was dissolved in distilled water to make 1 litre solution and this filtered off.

ii. **Hatching of Shrimps:** Sea water was kept in the small tank and shrimp eggs were added to the one side of the perforated tank where constant oxygen supply was carried out and constant temperature was maintained and then this side was covered. Two days were allowed for the shrimp to hatch as nauplii (larvae). The hatched shrimps were attracted to the lamp. On the other side of the divided tank through the perforation in the dam, these nauplii were taken for bioassay.

iii. **Preparation of Samples:** Test complexes were dissolved in 200mL DMSO to get a concentration of 5 μg/mL.

iv. **Application of test solution and nauplii to the vials:** 10, 20, 40, 80 and 160 μL of the test solution were taken in vials and 5mL of the sea water was added to each vial containing 10 brine

shrimp nauplii so that the concentration of the sample in the vials were 10, 20, 40, 80 and 160 respectively. Three vials were used for each concentration and a control was used containing 10 µl of the solvent and 10 nauplii in 5 ml of seawater. A magnifying glass was used for convenience counting of the nauplii.

v. **Counting of the nauplii:** After 24 hours the vials were observed and number of survivors in each vial were counted and noted. From this data, the percentage of mortality of nauplii was calculated at each concentration.

vi. The probity analysis was used to determine the lethality of 50 and 50% mortality levels,

vii. LC_{50} was obtained from the graph (Fig.1, Fig.2, Fig.3, and Fig.4).

9.4. RESULTS AND DISCUSSION

There is a positive correlation between brine shrimp toxicity and cytotoxicity. In this bioassay, the mortality rate of brine shrimp was found to increase with the increase of concentration of the samples and a plot of percent mortality versus log of concentration on the graph paper was produced and approximate linear correlation between them was found.

The rate of mortality of brine shrimp nauplii was found to be increased with the increase of concentration for all the complexes (Fig. 9.1-9.4). The lethality values for 50 (LC_{50}) are shown in Tables 9.1-9.4. From the Tables 9.1 and 9.2 it is shown that the complexes of L-1, L-4, L-7, L-8, C-7 and C- 12 exhibit more toxic to brine shrimp compared to other complexes of lighter metal complexes.

However, in case of heavier transition metal complexes of S1/1, S-2, S-3 and S-6 showed more toxic to the lower concentration of LC_{50} values. On the other hand, the complexes of S1/3, S-4 and S-5 showed less toxic effect to the brine shrimp compared to other heavier transition metal complexes.

The present investigations clearly showed that the lighter transition metal complexes were found to be more toxic to brine shrimp than the heavier transition metal complexes.

The test complexes were found to show significant activity against the brine shrimp nauplii (Table-9.1-9.4 and Fig.9.1-9.4). Using the bioassay a number of novel antitumor and pesticidal natural products have been previously isolated.[8] The positive response obtained in this assay suggests that the test complexes may contain antitumor, antimicrobial property. The test complexes showed positive results in brine shrimp lethality bioassay. So these complexes are bioactive.

Table-9.1: Brine shrimp lethality bioassay for test complexes.

Sample Abbreviation	Complexes	24 h Exposure
		LC_{50} (µg/mL)
L-1	[Ni(SB- A_1)2-pic]	14.45
L-4	[Co(SB- A_1)IQ]	16.98
L-6	[Ni(SB- A_2)IQ]	20.41
L-7	[Cu(SB- A_2)Q]	14.45
L-8	[Cu(SB- A_2)4-Pic]	13.18

Table-9.2: Brine shrimp lethality bioassay for test complexes.

Sample Abbreviation	Complexes	24h Exposure
		LC_{50} (µg/mL)
C-7	[Ni(SB- B_1)2-pic]	12.58
C-12	[Cu(SB- B_1)4-Pic]	15.13

Table-9.3: Brine shrimp lethality bioassay for test complexes.

Sample Abbreviation	Complexes	24h Exposure
		LC_{50} (µg/ mL)
S 1/1	[Zr(SB- B_2)Q]	17.78
S1/3	[Zr(SB- B_2)Py]	39.80
S2/1	[U(SB- B_2)Q]	28.84
S2/3	[U(SB- B_2)Py]	28.84
S3/1	Th(SB- B_2)Q]	22.38
S3/3	Th(SB- B_2)Py]	28.84

Table-9.4: Brine shrimp lethality bioassay for test complexes.

Sample Abbreviation	Complexes	24 h Exposure
		LC_{50} (µg/mL)
S-1	[Zr(SB- C_1)Q]	20.84
S-2	[Th(SB- C_1)Q]	14.45
S-3	[U(SB- C_1)Q]	17.37
S-4	[Zr(SB- C_2)Q]	40.73
S-5	Th(SB- C_2)Q]	40.73
S-6	[U(SB- C_2)Q]	14.45

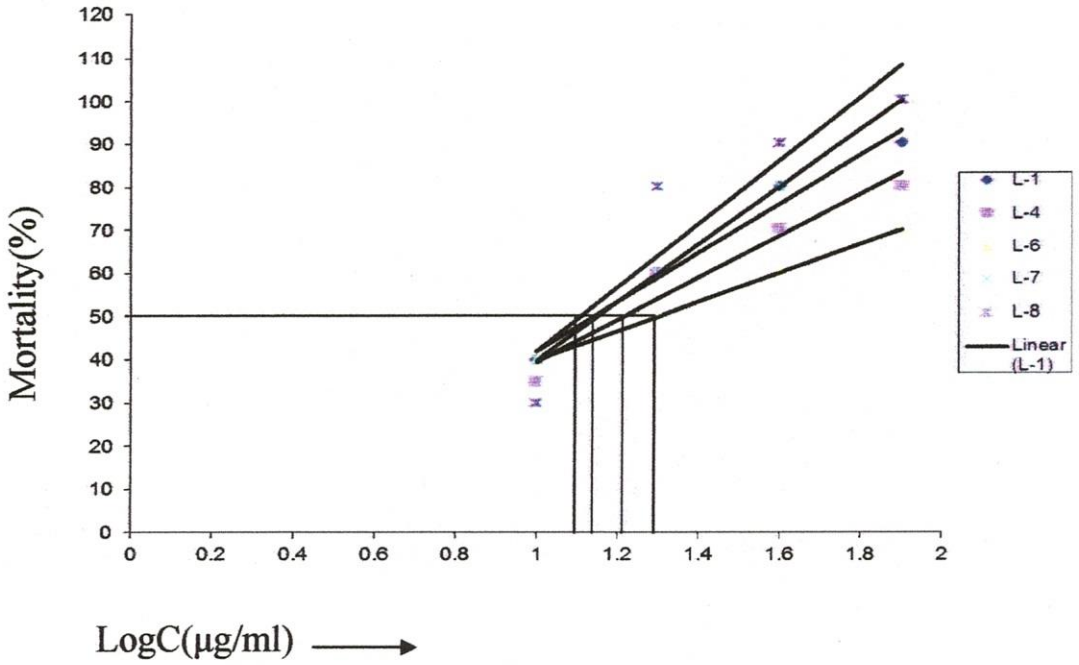


Fig- 9.1: Toxicity effect of complexes on the mortality of Brine shrimp at 24 h exposure

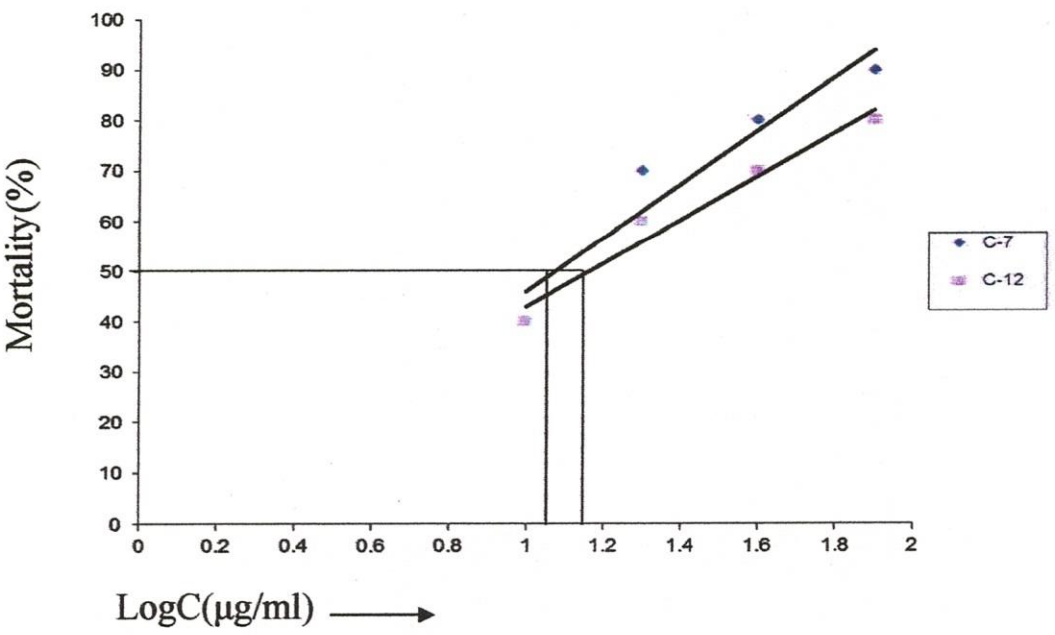


Fig- 9.2: Toxicity effect of complexes on the mortality of Brine shrimp at 24 h exposure

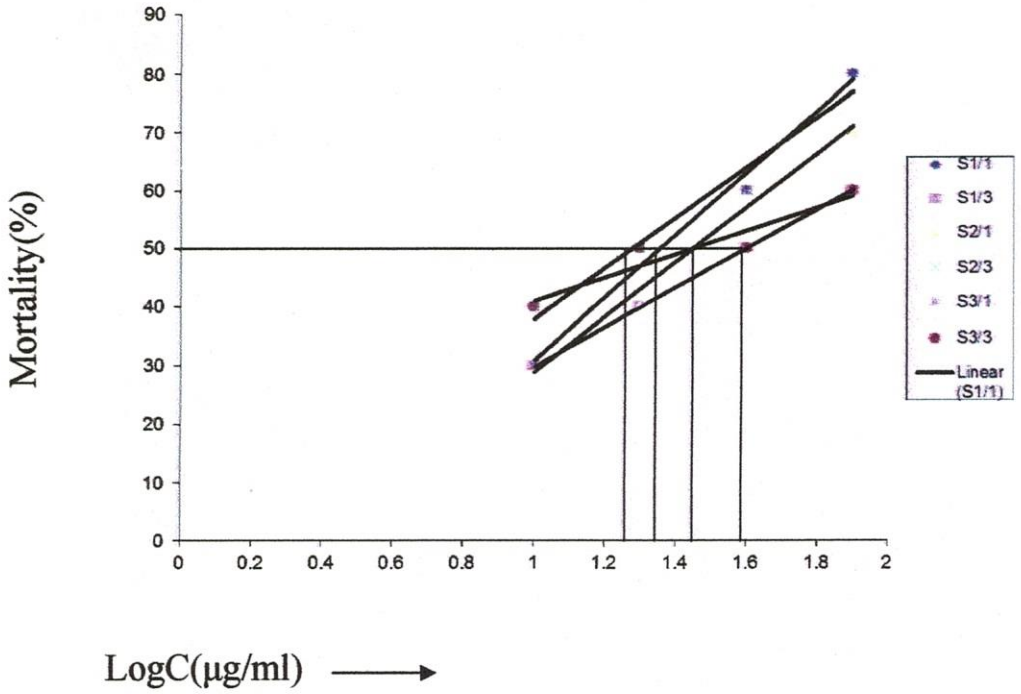


Fig.9.3: Toxicity effect of complexes on the mortality of brine shrimp at 24h exposure

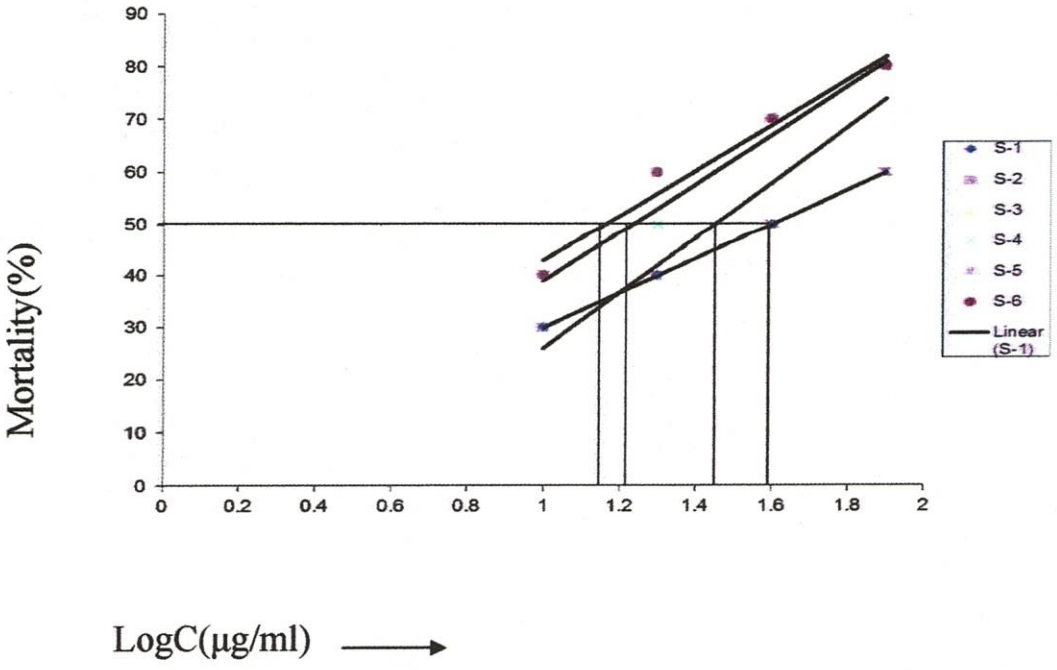


Fig.9.4: Toxicity effect of complexes on the mortality of brine shrimp at 24h exposure

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CHAPTER - TEN

ANTIFUNGAL ACTIVITY OF LIGHTER AND HEAVIER TRANSITION METAL COMPLEXES

10.1. INTRODUCTION

Fungi are eukaryotic organism. So fungal cell contain nucleus, mitochondria, ER and ribosome but fungal cell membrane contains ergosterol and symosterol and cell wall consists primary chitin. Some fungi are restricted to plants and do not causes human diseases but others natural habitat is environment and human beings.

The chemicals, which have the ability to kill fungi, are called fungicides. Some chemicals simply inhibit the fungal growth temporarily without killing. If the fungus were free from such substances, it would revive. Such chemical is called fungistant and the phenomenon of temporarily inhibiting the growth is called fungistasis. Suitable fungicide should be toxic to the parasite or inhibit the growth of its spore without causing phytotoxicity. Again a good fungicide should be capable of even distribution from the spraying or dusting machines on to the surface to be covered should remain on the surface without running off and should stick to the surface after drying. A good fungicide should be as least toxic as possible to human beings and cattle. This will eliminate dangers of accidental poisoning and make it safer for an operator to work.

For determination the antifungal activity of test complexes had been selected by using disc diffusion technique, because it is essentially a quantitative or semi quantitative test indicating the sensitivity or resistance of the confirm by determining the MIC of test compound against these fungus.

Heterocyclic bases have a great importance in biological and industrial fields. Most of the heterocyclic bases are used as corrosion inhibitors [1] and as antibacterial, anticonvulsive, antifungal and antifouling agent. The chlorinated species of 8-hydroxyqinoline has been proved as antibacterial and antifungal agents. [2] The di-iodo derivative is administered to overcome Zn deficiency in animals. [3] Patil *et. al* [4] have prepared Schiff base ligand complexes and their antifungal activity were studied.
Rashid and co-workers studied complexes of chromium synthesized and their cytotoxicity and antimicrobial activity. [5]

Salt of toxic metals and organic acids and organic compounds of mercury and sulphur quinine and heterocyclic nitrogenous compounds are familiar and major fungicides. Among these the compounds containing sulphur are highly effective and popular fungicide. Most of them are derivatives of dithiocarbamic acids.
Organotin(IV) compounds have been extensively studied as wood preservatives, agrochemical matricides and fungicides.[6,7]

10.2.ANTIFUNGUL ACTIVITY TESTING

The antifungal activity of the complexes was carried out against *Saccharromyces, Aspergillus* and *Candida albicans* using disc diffusion technique.

10.3. CULTURE MEDIA

i. PDA (Potato, Dextrose, Agar) media:

PDA medium was used as culture media composition of the PDA medium for 1000 mL is as follows:

1. Potato (cutting piece)	200g
2. D-glucose	20g
3. Agar for solidify	20g
4. Distilled water	1000mL

To prepare PDA medium potatoes were cut into pieces and weighed. About 200g were boiled in 1000 mL of distilled water for an hour, filtered and volume was made up to 1000 mL by adding distilled water. Glucose and agar were added then stirred. The pH of the medium was then adjusted 5- 6 which is acidic in nature. The medium was then sterilized at 121°C under pressure for 15 minutes.

ii. Sobouraud medium

The composition of the sobouraud medium for 1000 mL is as follows:

1. Glucose	20 g
2. Agar powder	20 g

3. Peptone 10 g

4. Distilled water 1000 mL

To prepare sobouraud medium, the amount of each constituent was calculated from the above chart. Peptone and glucose of above-mentioned amount were taken in a conical flask and distilled water was added. The contents were heated in a water bath to make a clear solution. The pH of the solution was then adjusted at 6.5. Required amount of powder was added to the solution and distilled water was added sufficiently to make the final volume (1L). The total volume was again heated in a water bath to obtain a clear solution. The medium was then sterilized at 121°C at 151 b pressures for 15 minutes.

10.4. RESULTS AND DISCUSSION

The results of percent inhibition of mycelia growth on incubation with the test complexes in medium are shown in Table 10.1-10.4. The overall result indicates that, all the fungi taken in the experiment are very much sensitive to most of the test complexes.

From the zone of inhibition it is observed that the lighter transition metal complexes 1 & 2 (in Table 10.1) and complexes 6 & 7 (in Table 10.2) showed significant activity towards all the fungi used. In other cases the complexes showed good percent of inhibition on the growth of fungus with few exceptions. The results also showed that the heavier transition metal complexes 1& 3 (in Table 10.3) moderately active against the fungi used. But in case of other complexes all fungi showed comparatively weak

sensitivity. It is interesting to note that some lighter transition metal complexes and some heavier transition metal complexes are fully inactive against all the fungi used.

When we compare the sensitivity of all the fungi with a fungicide Nystain, we observed that the all fungi were more sensitive towards lighter transition metal complexes but less sensitive towards heavier transition metal complexes. As our complexes very much effectively inhibit the growth of these fungi, they may turn to be a good fungicide after extensive research.

Table –10.1: Antifungal activity of the complexes against Saccharromycess(SC), Aspergillus niger (AN), Candida albicaus(CA).

No.	Complexes	Diameter of zone inhibition (mm) 200μg/disc		
		SC	AN	CA
1	[Ni(SB- A_1)2-pic]	20	23	25
2	[Ni(SB- A_2)IQ]	22	18	20
3	[Cu(SB- A_2)4-Pic]	8	9	7
4	Nystain	20	20	18

Table-10.2: Antifungal activity of the complexes against Saccharromycess(SC), Aspergillus niger (AN), Candida albicaus(CA).

No.	Complexes	Diameter of zone inhibition (mm) 200μg/disc		
		SC	AN	CA
1	[Co(SB- B_1)(4-Pic)]	9	8	10
2	[Ni(SB- B_1)IQ]	vp	vp	vp
3	[Ni(SB- B_1) (2-Pic)]	vp	vp	vp
4	[Ni(SB- B_1)(4-Pic)]	10	18	22
5	[Cu(SB- B_1)(4-Pic)]	20	Vp	Vp
6	[Zn(SB- B_1)Q]	18	22	23
7	[Co(SB- B_1)IQ]	22	20	16
8	Nystain	20	20	18

Where : vp= very poor

Table-10.3: Antifungal activity of the complexes against Saccharromycess(SC), Aspergillus niger (AN), Candida albicaus(CA).

No.	Complexes	Diameter of zone inhibition (mm) 200µg/disc		
		SC	AN	CA
1	[Zr(SB- B_2)Py]	16	18	20
2	[U(SB- B_2)Q]	18	10	14
3	[U(SB- B_2)2-Pic]	20	16	15
4	[Th(SB- B_2)Py]	13	11	10
5	[Th(SB- B_2)Q]	vp	vp	vp
6	Nystain	20	20	18

Table-10.4: Antifungal activity of the complexes against Saccharromycess(SC), Aspergillus niger (AN), Candida albicaus(CA).

No.	Complexes	Diameter of zone inhibition (mm) 200µg/disc		
		SC	AN	CA
1	[U(SB- C_1)IQ]	vp	vp	vp
2	[Zr(SB- C_1)Q]	vp	vp	vp
3	[U(SB- C_2)IQ]	vp	vp	vp
4	[Th(SB- C_2)IQ]	10	8	9
5	[Zr(SB- C_2)IQ]	vp	vp	vp
6	Nystain	20	20	18

Where : vp= very poor

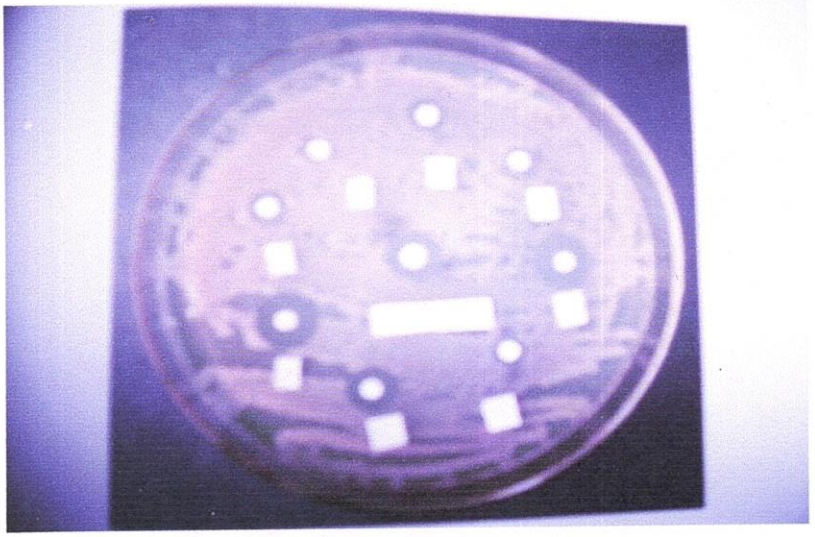

Fig.10.1: Photographic representation of zone of inhibition of the complexes against *Candida Albicause*

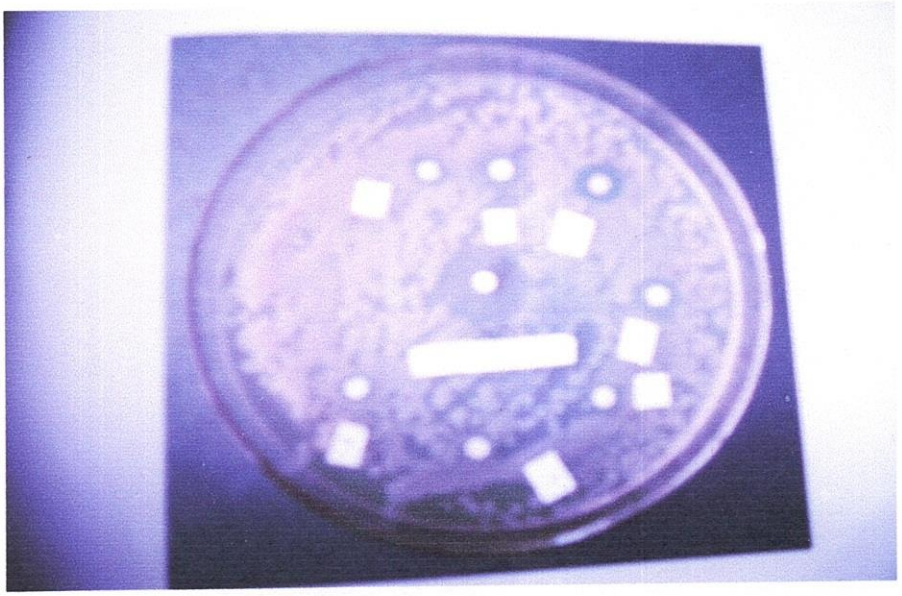

Fig.10.2: Photographic representation of zone of inhibition of the complexes against *Candida Albicause*

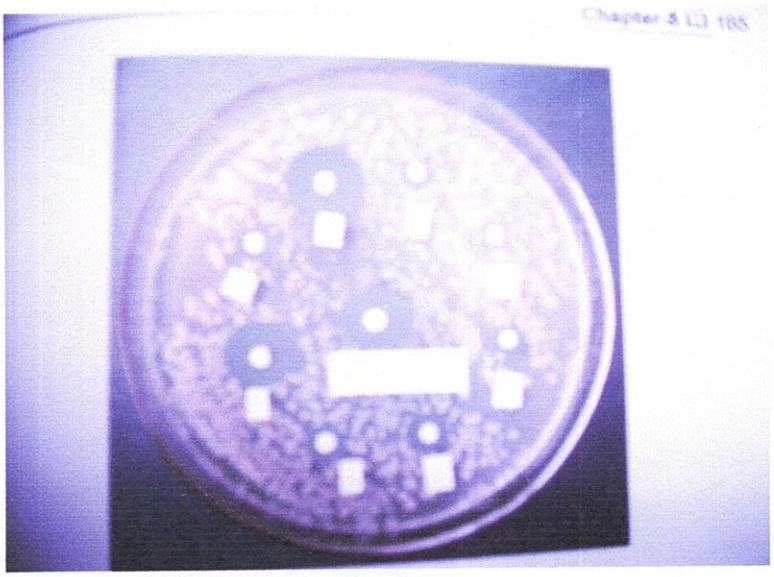

Fig.10.3: Photographic representation of zone of inhibition of the complexes against *Aspergillus Niger*

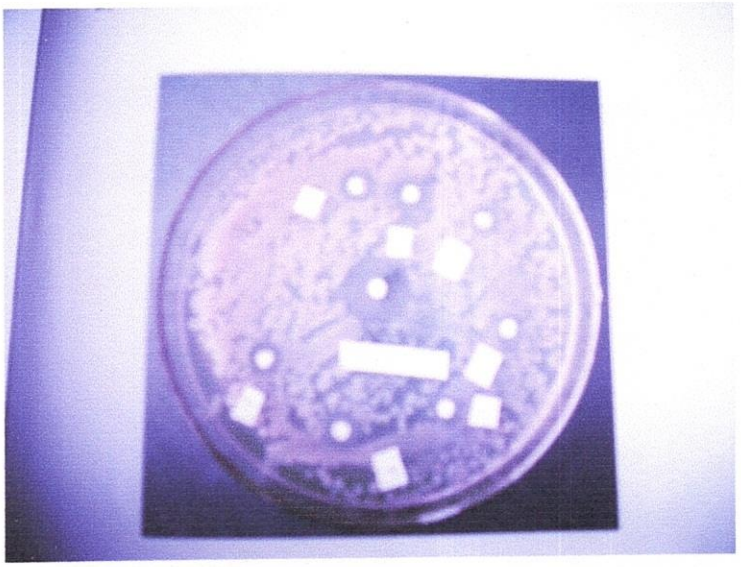

Fig.10.4: Photographic representation of zone of inhibition of the complexes against *Aspergillus Niger*

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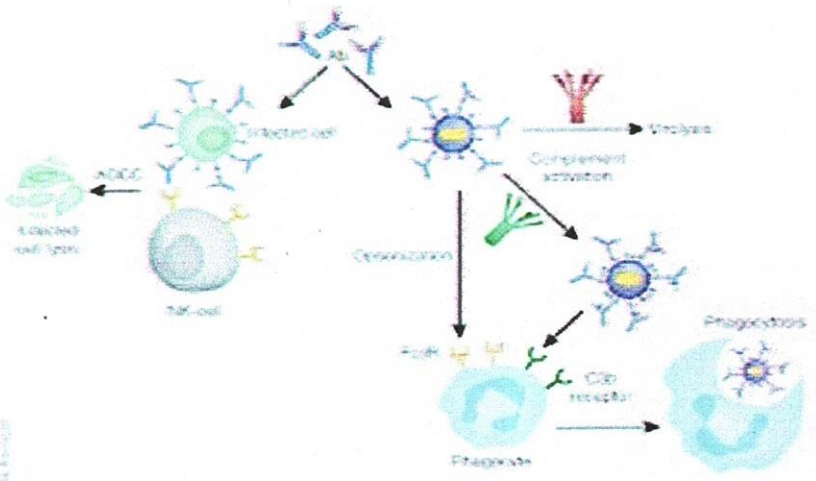
CHAPTER - ELEVEN



ANTIOXIDANT PROPERTIES OF SCHIFF BASE COMPLEXES

11.1. INTRODUCTION

The preparation and study of inorganic compounds containing biologically important ligands become easier because metal ions used are active in many biological processes.[1-3] the fact that transition metals are essential metallic elements and exhibit great biological activity when associated with certain metal electronic transfer reaction or the storage of iron[4-6] has critical attention in the study of system.

Antioxidants are the compounds, which terminate the attack of reactive species like free radicals and prevent it from ageing and different disease associated with oxidative damages inside the body system.[7]Antioxidant activity of a synthetic compound can be measured using the scavenging potential of that compound for the trapping of free radicals.

These free radicals can oxidize bio-molecules viz. nucleic acids, proteins, lipids, DNA, tissue damage and can initiate degenerative diseases. Oxidative damage plays a significantly pathological role in human disease such as cancer, cirrhosis and arthritis etc.[8-9]

Almost all organisms are protected to some extent by free radical damage by enzymes. Such as super-oxide dismutase and catalase or compounds such as ascorbic acid, tocopherols, phenolic acids, polyphenols, fiavonoids and glutathione.[10] However, antioxidant supplements or dietary antioxidants may be sources of protection that the body needs to protect against the damaging effects of free radicals.[11] presently, synthetic antioxidants are widely used because they are effective and cheaper than natural antioxidants.

Drugs with antioxidant mechanisms are being widely proposed as starting point for the development of new therapeutic interventions in several pathological disorders associated with oxidant damage, caused

by reactive oxygen species (ROS) under conditions of "Oxidative stress".[24-26] This term refers to an imbalance between ROS production and elimination, and it is characterized by reduction in the responsible for their metabolism antioxidant defences. [27, 28] Oxidative stress apears to be an important part of many human diseases including cancer.[29-31] All organism contain a complex net work of antioxidant metabolites and enzymes that work together to prevent oxidative damage to cellular components, such as DNA, Proteins and Lipids caused by ROS produced during cellular metabolism.[32-34] The Schiff base ligands are highly significant in bioinorganic chemistry, catalysis, extraction of metal ions from solution and many more. Also, they are highly significant from the biological point of view.[35-36]

Keeping the above facts in mind and in continuation of our research work, in the present thesis we report the synthesis and characterization and antioxidant property of transition metal complexes of Schiff bases with heterocyclic amines.

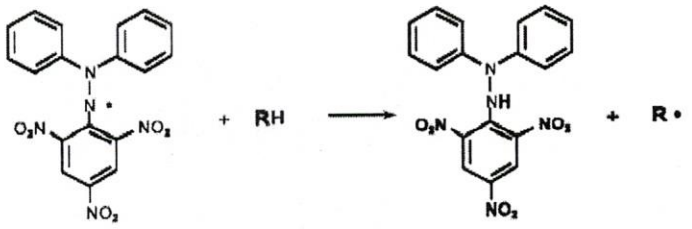
11.2.METHOD AND MATERIALS

11.2.1 DPPH (1, 1-diphenyl-2-picrylhydrazyl) RADICAL SCANVENZING ASSAY

DPPH was used to evaluate the free radical scavenging capacity of different samples.[37-38]

11.2.2. PRINCIPLE

The 1, 1-diphenyl-2-picrylhydrazyl radical (DPPH) has been widely used to evaluate the free radical scavenging capacity of antioxidants. DPPH free radical is reduced to the corresponding hydrazine when it reacts with hydrogen donors. DPPH can make stable free radicals in aqueous or methanol solution. With this method, it was possible to determine the antiradical power of an antioxidant activity by measurement of the decrease in the absorbance of DPPH at 517 nm. Resulting from a color change from purple to yellow the absorbance decreased when the DPPH was scavenged by an antioxidant, through donation of hydrogen to form a stable DPPH molecule. In the radical form, this molecule had an absorbance at 517 nm, which disappeared after acceptance of an electron or hydrogen radical from an antioxidant compound to become a stable diamagnetic molecule.



DPPH
517 nm

11.2.3. MATERIALS AND APPARATUS

a. DPPH (Sigma chemical company, USA)
b. Methanol (Sigma chemical company, USA)
c. Butylated hydroxy toluene (BHT) (Merck, Germany)

d. Pipette (1-10 ml)

e. UV-spectrophotometer (Shimadzu, USA)

11.2.4. EXPERIMENTAL PROCEDURE

1 ml methanol solutions of the different samples at different concentrations were taken into the test tubes.

1. 2.4 ml of methanol solution of DPPH was added into each of the test tubes.
2. The test tubes were then incubated at RT for 30 mines in dark place to complete the reaction.
3. Then the absorbances of the solutions were measured at 517 nm using a spectrophotometer against blank.
4. The percentage (%) of inhibition activity was calculated from the following equation:

$$\% I = \{(A_o - A_1)/A_o\} \times 100$$

Where,

A_0 is the absorbance of the control and

A_1 is the absorbance of the samples.

Then % of inhibition was plotted against concentration and IC_{50} was calculated from the graph.

11.3. RESULT AND DISCUSSION

The antioxidant activity of the samples was evaluated by the widely used and most reliable DPPH radical scavenging assay method. This antioxidant assay is based on the ability of the samples to scavenge the stable DPPH radical that contains an odd electron. This radical gives absorbance at 517 nm and decolorizes after neutralization by the antioxidants. Increasing of the concentration of the samples increases the activity. In this test the ascorbic acid was used as standard. Among the three samples the Schiff base of SMDTC had very antioxidant activity even higher than the standard ascorbic acid and the Schiff base of SBDTC had moderate antioxidant activity but the L_6 beyond the range of antioxidant activity. To calculate IC_{50} values of ascorbic acid, Schiff base of SBDTC and Schiff base of SMDTC were 5.75, 22, and 2.20 μg/ml respectively.

Radical scavenging activities are very important to prevent the deleterious role of free radical in the development of many types of diseases including cancer. DPPH (1, 1-diphenyl-2-picryl-hydrazyl) free radical scavenging is an accepted mechanism that has been used extensively to predict antioxidant activities by which antioxidants act to inhibit the free radical generation. Our investigation revealed that the Schiff base of SMDTC had free radical scavenging activity with IC_{50} 2.20 μg/ml which was closely resemble to that of ascorbic acid (standard) with IC_{50} of 5.75μg/ml. Our samples showed moderate to significant free radical scavenging activity and the lowest activity found in L_6 with IC_{50} value beyond the range (shown in Tab. 11.1 and Fig.

11.1). The results indicate that the samples with their proton-donating ability could serve as free radical inhibitors or scavengers and might act as primary antioxidants.

Table 11.1: DPPH radical scavenging activity of the different samples and Ascorbic acid (Std.) at different concentrations:

Name of sample	Concentration (µg/ml)	% of scavenging			Mean of % of scavenging	% of scavenging Mean ± STD
		a	b	c		
Ascorbic acid	5	45.9	46.43	46.12	46.14	46.14±0.23
	10	65.86	67.21	65.55	66.21	66.21±0.88
	20	95.33	95.60	95.78	95.57	95.57±0.23
	40	95.97	96.08	95.77	95.94	95.94±0.16
	80	96.29	96.27	96.23	96.26	96.26±0.03
	160	96.29	96.31	96.28	96.29	96.29±0.015
	320	96.31	96.30	96.29	96.30	96.30±0.01
Schiff base of SBDTC	5	10.22	10.51	10.36	10.36	10.36±0.14
	10	22.29	22.59	21.97	22.28	22.28±0.31
	20	45.01	45.22	45.17	45.13	45.13±0.11
	40	90.62	90.44	90.49	90.52	90.52±0.09
	80	95.89	95.77	95.82	95.83	95.83±0.06

	160	96.04	95.96	95.98	95.99	95.99±0.04
	320	96.04	96.14	96.08	96.09	96.09±0.05
L_6	5	3.89	3.66	3.69	3.72	3.72±0.12
	10	6.26	6.46	6.43	6.38	6.38±0.11
	20	10.91	10.63	11.04	10.86	10.86±0.21
	40	21.83	22.07	22.11	22.00	22.00±0.15
	80	31.94	32.17	31.74	31.95	31.95±0.22
	160	37.72	37.31	37.50	37.51	37.51±0.20
	320	41.73	41.33	41.67	41.58	41.58±0.22
Schiff base of SMDTC	5	87.03	86.91	86.82	86.92	86.92±0.10
	10	94.03	94.30	93.94	94.09	94.09±0.19
	20	94.84	94.69	94.80	94.78	94.78±0.08
	40	95	94.93	95.06	95.00	95.00±0.06
	80	95.16	95.13	95.10	95.13	95.13±0.03
	160	95.16	95.14	95.17	95.16	95.16±0.02
	320	95.16	95.15	95.17	95.16	95.16±0.01

Table 11.2: IC_{50} values of the different samples

Name of Samples	**IC_{50} Values**
Ascorbic acid	5.75
Schiff base of SMDTC/C1	2.20
Schiff base of SBDTC/C2	22

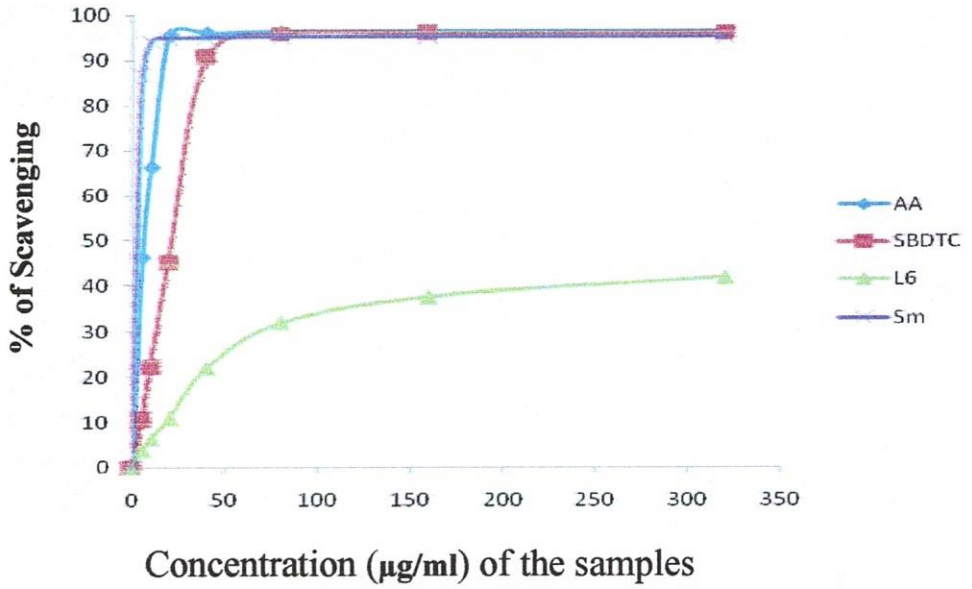


Fig. 11.1: Determination of DPPH radical scavenging activity.

Where, AA ⟶ Ascorbic acid, SBDTC ⟶ Schiff Base of SBDTC,

Sm ⟶ Schiff Base of SMDTC .

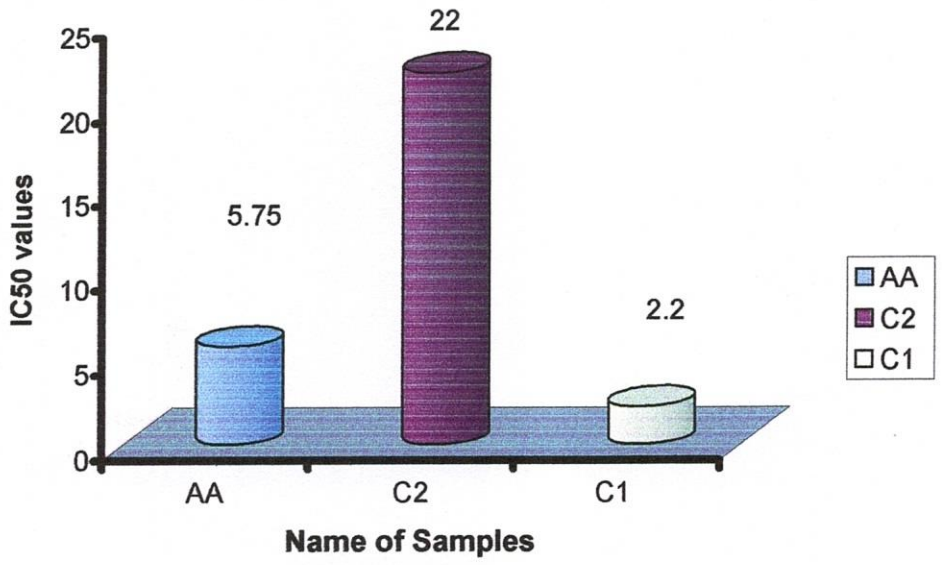


Fig. 11.2: IC_{50} values of different samples.

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APPENDIX

Acta Crystallographica Section E
Structure Reports

ISSN 1600-5368

(2,2′-Bipyridine-κ^2N,N')chlorido(2-hydroxy-2,2-diphenylacetato-$\kappa^2O^1,O^{1'}$)-copper(II)

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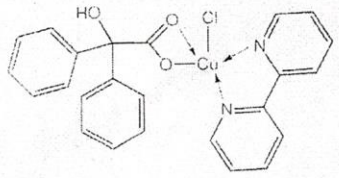
Received 25 February 2011; accepted 25 February 2011

Key indicators: single-crystal X-ray study; T = 293 K; mean σ(C–C) = 0.010 Å; R factor = 0.060; wR factor = 0.238; data-to-parameter ratio = 13.0.

The Cu(II) atom in the title complex, $[Cu(C_{14}H_{11}O_3)Cl(C_{10}H_8N_2)]$, exists within a ClN_2O_2 donor set defined by a chloride ion, an asymmetrically chelating carboxylate ligand, and a symmetrically chelating 2,2′-bipyridine molecule. The coordination geometry is square pyramidal with the axial site occupied by the O atom forming the weaker Cu—O interaction. The hydroxy group forms an intramolecular hydrogen bond with the axial O atom, as well as an intermolecular O—H···Cl hydrogen bond. The latter leads to the formation of [100] supramolecular chains in the crystal, with the Cu(II) atoms lying in a line.

Related literature

For recent structural studies on metal complexes of anions derived from benzilic acid, see: Yang *et al.* (2010); Reza *et al.* (2010). For additional structural analysis, see: Addison *et al.* (1984); Spek (2009).



Experimental

Crystal data

$[Cu(C_{14}H_{11}O_3)Cl(C_{10}H_8N_2)]$
M_r = 482.40
Monoclinic, $P2_1/c$
a = 7.1537 (9) Å
b = 15.7277 (19) Å
c = 18.601 (4) Å
β = 97.806 (14)°
V = 2073.5 (5) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 1.21 mm^{-1}
T = 293 K
0.20 × 0.15 × 0.10 mm

Data collection

Agilent SuperNova Dual diffractometer with an Atlas detector
Absorption correction: multi-scan (*CrysAlis PRO*; Agilent, 2010)
T_{min} = 0.571, T_{max} = 1.000
8454 measured reflections
3651 independent reflections
2719 reflections with $I > 2\sigma(I)$
R_{int} = 0.053

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.060
$wR(F^2)$ = 0.238
S = 1.03
3651 reflections
281 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.91 e Å^{-3}
$\Delta\rho_{min}$ = −1.42 e Å^{-3}

Table 1
Selected bond lengths (Å).

Cu—Cl1	2.2301 (18)	Cu—N1	2.006 (5)
Cu—O1	1.971 (4)	Cu—N2	1.976 (5)
Cu—O2	2.476 (4)		

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O3—H3*o*···O2	0.82	2.19	2.622 (6)	113
O3—H3*o*···Cl1^i	0.82	2.62	3.328 (5)	146

Symmetry code: (i) $x+1, y, z$.

Data collection: *CrysAlis PRO* (Agilent, 2010); cell refinement: *CrysAlis PRO*; data reduction: *CrysAlis PRO*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3* (Farrugia, 1997) and *DIAMOND* (Brandenburg, 2006); software used to prepare material for publication: *publCIF* (Westrip, 2010).

MYR, LAB and MSI thank Dr T. G. Roy for special assistance. The authors also thank Rajshahi University for the provision of their central laboratory facilities and the University of Malaya for support of the crystallographic facility.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: HB5805).

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Acta Cryst. (2011). E67, m399 [doi:10.1107/S160053681100729X]

(2,2'-Bipyridine-κ^2N,N')chlorido(2-hydroxy-2,2-diphenylacetato-$\kappa^2O^1,O^{1'}$)copper(II)

M. Y. Reza, L. A. Banu, M. S. Islam, S. W. Ng and E. R. T. Tiekink

Comment

Recent structural investigations of benzilate complexes have confirmed that anions derived from benzilic acid can function as multidentate ligands with versatile coordination modes (Reza *et al.*, 2010; Yang *et al.*, 2010). Herein, the crystal and molecular structure of a mononuclear Cu^{II} complex, (I), is described.

The Cu atom in (I) is coordinated by a Cl, an asymmetrically chelating carboxylate anion, and a symmetrically chelating 2,2'-bipyridine ligand, Table 1. The asymmetric mode of coordination of the carboxylate is reflected in the disparate C—O bond distances with the longer C1—O1 distance [1.285 (8) Å] being associated with the shorter Cu—O1 interaction, and the short C1—O2 distance [1.204 (7) Å] associated with the weaker Cu—O2 contact. The resultant ClN_2O_2 donor set defines a square pyramid. This assignment is based on the value calculated for τ of 0.07 for the Cu atom, which compares to the τ values of 0.0 and 1.0 for ideal square pyramidal and trigonal bi-pyramidal geometries, respectively (Spek, 2009; Addison *et al.*, 1984). In this description, the weakly coordinating O2 atom defines the axial site. While not participating in direct coordination to the Cu atom, the hydroxyl group forms an intramolecular hydrogen bond with the O2 atom as well as an intermolecular O—H···Cl hydrogen bond, Table 2. The latter leads to the generation of supramolecular chains along the *a* axis, Fig. 2, whereby the Cu atoms lie on a line.

Experimental

A mixture of copper chloride (0.134 g,1 mmol), benzilic acid (0.228 g, 1 mmol), 2,2'-bipyridine (0.196 g, 1 mmol) and Et_3N (0.1 g, 1 mmol) was placed into methanol (40 ml) and the resultant solution was heated to 323 K for 0.5 h. Initial precipitates were filtered off and the filtrate was allowed to stand for several days. Blue blocks of the title compound were collected, washed with methanol and air-dried at room temperature. *M*. pt. 457 K.

Refinement

The O– and C-bound H atoms were geometrically placed (O—H = 0.82 Å and C–H = 0.93 Å) and refined as riding with $U_{iso}(H) = zU_{eq}$(carrier atom); z = 1.5 for O and z = 1.2 for C. The maximum and minimum residual electron density peaks of 0.91 and 1.42 e $Å^{-3}$, respectively, were located 0.93 Å and 0.78 Å from the N1 and Cu atoms, respectively.

supplementary materials

Figures

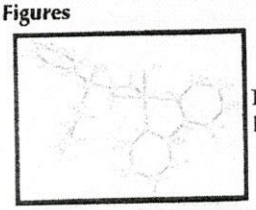

Fig. 1. Molecular structure of (I), showing displacement ellipsoids at the 50% probability level.

Fig. 2. Supramolecular chain along the *a* axis in (I) mediated by O—H···Cl hydrogen bonds (shown as orange dashed lines).

(2,2'-Bipyridine-κ^2N,N')chlorido(2-hydroxy-2,2- diphenylacetato-$\kappa^2O^1,O^{1'}$)copper(II)

Crystal data

$[Cu(C_{14}H_{11}O_3)Cl(C_{10}H_8N_2)]$
$M_r = 482.40$
Monoclinic, $P2_1/c$
Hall symbol: -P 2ybc
$a = 7.1537\ (9)$ Å
$b = 15.7277\ (19)$ Å
$c = 18.601\ (4)$ Å
$\beta = 97.806\ (14)°$
$V = 2073.5\ (5)$ Å^3
$Z = 4$
$F(000) = 988$
$D_x = 1.545$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 3252 reflections
$\theta = 2.6–29.4°$
$\mu = 1.21$ mm^{-1}
$T = 293$ K
Block, blue
0.20 × 0.15 × 0.10 mm

Data collection

Agilent SuperNova Dual diffractometer with an Atlas detector
Radiation source: SuperNova (Mo) X-ray Source
Mirror
Detector resolution: 10.4041 pixels mm^{-1}
ω scans
Absorption correction: multi-scan (*CrysAlis PRO*; Agilent, 2010)
$T_{min} = 0.571$, $T_{max} = 1.000$
8454 measured reflections
3651 independent reflections
2719 reflections with $I > 2\sigma(I)$
$R_{int} = 0.053$
$\theta_{max} = 25.0°$, $\theta_{min} = 2.6°$
$h = -8\rightarrow8$
$k = -18\rightarrow17$
$l = -21\rightarrow22$

Refinement

Refinement on F^2
Least-squares matrix: full
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map

$R[F^2 > 2\sigma(F^2)] = 0.060$	Hydrogen site location: inferred from neighbouring sites
$wR(F^2) = 0.238$	H-atom parameters constrained
$S = 1.03$	$w = 1/[\sigma^2(F_o^2) + (0.1324P)^2 + 7.2136P]$ where $P = (F_o^2 + 2F_c^2)/3$
3651 reflections	$(\Delta/\sigma)_{max} < 0.001$
281 parameters	$\Delta\rho_{max} = 0.91$ e Å^{-3}
0 restraints	$\Delta\rho_{min} = -1.42$ e Å^{-3}

Special details

Geometry. All s.u.'s (except the s.u. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell s.u.'s are taken into account individually in the estimation of s.u.'s in distances, angles and torsion angles; correlations between s.u.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell s.u.'s is used for estimating s.u.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit *S* are based on F^2, conventional *R*-factors *R* are based on *F*, with *F* set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on *F*, and *R*- factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
Cu	0.63293 (10)	0.44986 (4)	0.36367 (4)	0.0351 (3)
Cl1	0.4262 (2)	0.34756 (11)	0.32669 (10)	0.0475 (5)
N1	0.7215 (8)	0.5629 (3)	0.4053 (3)	0.0390 (13)
N2	0.6723 (7)	0.4182 (3)	0.4674 (3)	0.0337 (11)
O1	0.6859 (6)	0.4804 (3)	0.2657 (2)	0.0401 (10)
O2	0.9191 (6)	0.3986 (3)	0.3158 (2)	0.0415 (11)
O3	1.0661 (7)	0.3757 (3)	0.1956 (2)	0.0438 (11)
H3o	1.1135	0.3685	0.2378	0.066*
C1	0.8391 (9)	0.4378 (4)	0.2651 (3)	0.0330 (14)
C2	0.9273 (9)	0.4407 (4)	0.1925 (3)	0.0307 (13)
C3	0.7914 (9)	0.4235 (4)	0.1234 (3)	0.0350 (13)
C4	0.6016 (10)	0.4065 (4)	0.1209 (4)	0.0457 (16)
H4	0.5468	0.4054	0.1634	0.055*
C5	0.4940 (11)	0.3911 (5)	0.0554 (5)	0.058 (2)
H5	0.3653	0.3811	0.0536	0.070*
C6	0.5752 (13)	0.3905 (5)	−0.0080 (4)	0.062 (2)
H6	0.5008	0.3794	−0.0520	0.074*
C7	0.7616 (13)	0.4058 (5)	−0.0067 (4)	0.061 (2)
H7	0.8161	0.4044	−0.0493	0.073*
C8	0.8696 (11)	0.4236 (5)	0.0586 (4)	0.0490 (17)
H8	0.9971	0.4358	0.0596	0.059*
C9	1.0175 (8)	0.5291 (4)	0.1890 (3)	0.0342 (13)
C10	0.9071 (10)	0.6006 (4)	0.1767 (4)	0.0414 (15)
H10	0.7765	0.5952	0.1684	0.050*

C11	0.9891 (12)	0.6816 (4)	0.1764 (4)	0.0550 (19)
H11	0.9129	0.7295	0.1691	0.066*
C12	1.1818 (12)	0.6901 (5)	0.1871 (4)	0.057 (2)
H12	1.2369	0.7435	0.1861	0.068*
C13	1.2907 (10)	0.6200 (5)	0.1991 (3)	0.0491 (18)
H13	1.4213	0.6259	0.2060	0.059*
C14	1.2124 (9)	0.5387 (4)	0.2013 (4)	0.0413 (15)
H14	1.2900	0.4915	0.2108	0.050*
C15	0.7393 (9)	0.6339 (4)	0.3682 (4)	0.0448 (16)
H15	0.7052	0.6331	0.3182	0.054*
C16	0.8060 (10)	0.7086 (4)	0.4006 (4)	0.0466 (16)
H16	0.8175	0.7571	0.3730	0.056*
C17	0.8541 (10)	0.7101 (4)	0.4732 (4)	0.0464 (16)
H17	0.8988	0.7599	0.4964	0.056*
C18	0.8367 (9)	0.6366 (4)	0.5133 (4)	0.0410 (15)
H18	0.8700	0.6364	0.5634	0.049*
C19	0.7685 (8)	0.5635 (4)	0.4772 (4)	0.0339 (14)
C20	0.7432 (8)	0.4810 (4)	0.5129 (3)	0.0319 (13)
C21	0.7927 (9)	0.4669 (4)	0.5869 (3)	0.0393 (15)
H21	0.8404	0.5107	0.6177	0.047*
C22	0.7690 (10)	0.3860 (4)	0.6135 (3)	0.0431 (16)
H22	0.8011	0.3748	0.6627	0.052*
C23	0.6981 (10)	0.3219 (4)	0.5670 (4)	0.0484 (17)
H23	0.6828	0.2672	0.5844	0.058*
C24	0.6505 (10)	0.3403 (4)	0.4949 (4)	0.0432 (16)
H24	0.6012	0.2972	0.4637	0.052*

Atomic displacement parameters ($Å^2$)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cu	0.0404 (5)	0.0315 (5)	0.0357 (5)	0.0002 (3)	0.0137 (4)	−0.0010 (3)
Cl1	0.0425 (9)	0.0453 (9)	0.0547 (11)	−0.0055 (7)	0.0066 (8)	−0.0046 (8)
N1	0.050 (3)	0.027 (2)	0.045 (3)	0.001 (2)	0.025 (3)	−0.001 (2)
N2	0.034 (3)	0.032 (3)	0.037 (3)	−0.003 (2)	0.009 (2)	−0.003 (2)
O1	0.053 (3)	0.042 (2)	0.029 (2)	0.005 (2)	0.018 (2)	−0.0053 (19)
O2	0.050 (3)	0.043 (2)	0.032 (2)	0.003 (2)	0.009 (2)	0.012 (2)
O3	0.058 (3)	0.033 (2)	0.042 (3)	0.017 (2)	0.012 (2)	−0.002 (2)
C1	0.045 (3)	0.026 (3)	0.029 (3)	−0.007 (3)	0.011 (3)	−0.006 (2)
C2	0.040 (3)	0.032 (3)	0.019 (3)	0.005 (2)	0.002 (2)	−0.001 (2)
C3	0.045 (3)	0.025 (3)	0.035 (3)	0.003 (3)	0.005 (3)	−0.001 (3)
C4	0.046 (4)	0.041 (4)	0.052 (4)	−0.005 (3)	0.010 (3)	−0.010 (3)
C5	0.050 (4)	0.045 (4)	0.075 (6)	−0.004 (3)	−0.009 (4)	−0.010 (4)
C6	0.086 (6)	0.043 (4)	0.046 (5)	−0.002 (4)	−0.025 (4)	−0.004 (3)
C7	0.090 (6)	0.053 (4)	0.041 (4)	−0.008 (4)	0.014 (4)	0.001 (3)
C8	0.063 (4)	0.048 (4)	0.037 (4)	−0.005 (4)	0.012 (3)	−0.003 (3)
C9	0.038 (3)	0.033 (3)	0.034 (3)	−0.001 (3)	0.014 (3)	−0.006 (3)
C10	0.043 (3)	0.038 (3)	0.045 (4)	0.003 (3)	0.011 (3)	0.004 (3)
C11	0.070 (5)	0.030 (3)	0.067 (5)	0.002 (3)	0.019 (4)	0.001 (3)

C12	0.075 (5)	0.038 (4)	0.063 (5)	−0.020 (4)	0.030 (4)	−0.007 (3)
C13	0.052 (4)	0.069 (5)	0.028 (3)	−0.021 (4)	0.012 (3)	−0.007 (3)
C14	0.044 (4)	0.044 (4)	0.038 (4)	0.002 (3)	0.013 (3)	−0.002 (3)
C15	0.040 (4)	0.041 (4)	0.053 (4)	0.000 (3)	0.005 (3)	0.009 (3)
C16	0.050 (4)	0.034 (3)	0.058 (5)	−0.001 (3)	0.016 (3)	0.007 (3)
C17	0.058 (4)	0.033 (3)	0.049 (4)	−0.006 (3)	0.011 (3)	−0.008 (3)
C18	0.040 (3)	0.034 (3)	0.051 (4)	0.000 (3)	0.012 (3)	−0.002 (3)
C19	0.028 (3)	0.033 (3)	0.044 (4)	0.002 (2)	0.016 (3)	0.001 (3)
C20	0.028 (3)	0.035 (3)	0.034 (3)	0.005 (2)	0.010 (2)	0.005 (3)
C21	0.043 (4)	0.044 (3)	0.033 (3)	0.004 (3)	0.011 (3)	−0.006 (3)
C22	0.052 (4)	0.052 (4)	0.026 (3)	0.006 (3)	0.008 (3)	0.007 (3)
C23	0.051 (4)	0.040 (4)	0.058 (5)	0.003 (3)	0.021 (3)	0.011 (3)
C24	0.050 (4)	0.030 (3)	0.053 (4)	−0.004 (3)	0.022 (3)	0.004 (3)

Geometric parameters (Å, °)

Cu—Cl1	2.2301 (18)	C9—C14	1.390 (9)
Cu—O1	1.971 (4)	C10—C11	1.403 (9)
Cu—O2	2.476 (4)	C10—H10	0.9300
Cu—N1	2.006 (5)	C11—C12	1.372 (11)
Cu—N2	1.976 (5)	C11—H11	0.9300
N1—C15	1.329 (8)	C12—C13	1.351 (11)
N1—C19	1.333 (9)	C12—H12	0.9300
N2—C24	1.345 (8)	C13—C14	1.399 (10)
N2—C20	1.353 (8)	C13—H13	0.9300
O1—C1	1.285 (8)	C14—H14	0.9300
O2—C1	1.204 (7)	C15—C16	1.376 (10)
O3—C2	1.421 (7)	C15—H15	0.9300
O3—H3o	0.8200	C16—C17	1.348 (10)
C1—C2	1.567 (8)	C16—H16	0.9300
C2—C3	1.527 (8)	C17—C18	1.390 (9)
C2—C9	1.537 (8)	C17—H17	0.9300
C3—C4	1.379 (9)	C18—C19	1.387 (9)
C3—C8	1.395 (9)	C18—H18	0.9300
C4—C5	1.371 (10)	C19—C20	1.481 (8)
C4—H4	0.9300	C20—C21	1.391 (9)
C5—C6	1.385 (12)	C21—C22	1.384 (9)
C5—H5	0.9300	C21—H21	0.9300
C6—C7	1.352 (12)	C22—C23	1.379 (10)
C6—H6	0.9300	C22—H22	0.9300
C7—C8	1.377 (11)	C23—C24	1.370 (10)
C7—H7	0.9300	C23—H23	0.9300
C8—H8	0.9300	C24—H24	0.9300
C9—C10	1.375 (9)		
O1—Cu—N2	160.9 (2)	C10—C9—C2	120.8 (5)
O1—Cu—N1	92.9 (2)	C14—C9—C2	120.6 (5)
N2—Cu—N1	81.4 (2)	C9—C10—C11	120.8 (6)
O1—Cu—Cl1	95.35 (14)	C9—C10—H10	119.6
N2—Cu—Cl1	96.91 (15)	C11—C10—H10	119.6

N1—Cu—Cl1	156.84 (16)	C12—C11—C10	120.0 (7)
O1—Cu—O2	58.31 (16)	C12—C11—H11	120.0
N2—Cu—O2	104.72 (18)	C10—C11—H11	120.0
N1—Cu—O2	101.21 (18)	C13—C12—C11	119.3 (6)
Cl1—Cu—O2	101.55 (12)	C13—C12—H12	120.3
C15—N1—C19	119.0 (6)	C11—C12—H12	120.3
C15—N1—Cu	126.3 (5)	C12—C13—C14	121.7 (7)
C19—N1—Cu	114.6 (4)	C12—C13—H13	119.1
C24—N2—C20	118.7 (6)	C14—C13—H13	119.1
C24—N2—Cu	126.3 (4)	C9—C14—C13	119.5 (6)
C20—N2—Cu	114.8 (4)	C9—C14—H14	120.3
C1—O1—Cu	98.7 (4)	C13—C14—H14	120.3
C1—O2—Cu	77.7 (4)	N1—C15—C16	122.9 (7)
C2—O3—H3o	109.5	N1—C15—H15	118.6
O2—C1—O1	125.2 (6)	C16—C15—H15	118.6
O2—C1—C2	119.0 (5)	C17—C16—C15	118.7 (6)
O1—C1—C2	115.8 (5)	C17—C16—H16	120.7
O3—C2—C3	105.5 (4)	C15—C16—H16	120.7
O3—C2—C9	111.0 (5)	C16—C17—C18	119.6 (6)
C3—C2—C9	110.4 (5)	C16—C17—H17	120.2
O3—C2—C1	107.8 (5)	C18—C17—H17	120.2
C3—C2—C1	115.8 (5)	C19—C18—C17	118.7 (6)
C9—C2—C1	106.4 (4)	C19—C18—H18	120.7
C4—C3—C8	118.6 (6)	C17—C18—H18	120.7
C4—C3—C2	125.1 (6)	N1—C19—C18	121.1 (6)
C8—C3—C2	116.3 (6)	N1—C19—C20	114.5 (5)
C3—C4—C5	119.8 (7)	C18—C19—C20	124.4 (6)
C3—C4—H4	120.1	N2—C20—C21	121.8 (6)
C5—C4—H4	120.1	N2—C20—C19	114.6 (5)
C4—C5—C6	120.5 (7)	C21—C20—C19	123.6 (6)
C4—C5—H5	119.7	C22—C21—C20	118.2 (6)
C6—C5—H5	119.7	C22—C21—H21	120.9
C7—C6—C5	120.7 (7)	C20—C21—H21	120.9
C7—C6—H6	119.7	C23—C22—C21	120.1 (6)
C5—C6—H6	119.7	C23—C22—H22	119.9
C6—C7—C8	119.1 (8)	C21—C22—H22	119.9
C6—C7—H7	120.5	C24—C23—C22	118.7 (6)
C8—C7—H7	120.5	C24—C23—H23	120.6
C7—C8—C3	121.3 (7)	C22—C23—H23	120.6
C7—C8—H8	119.4	N2—C24—C23	122.6 (6)
C3—C8—H8	119.4	N2—C24—H24	118.7
C10—C9—C14	118.6 (6)	C23—C24—H24	118.7
O1—Cu—N1—C15	19.3 (6)	C5—C6—C7—C8	−1.1 (12)
N2—Cu—N1—C15	−179.0 (6)	C6—C7—C8—C3	1.9 (12)
Cl1—Cu—N1—C15	−91.6 (6)	C4—C3—C8—C7	−1.0 (10)
O2—Cu—N1—C15	77.6 (5)	C2—C3—C8—C7	177.7 (6)
O1—Cu—N1—C19	−159.5 (4)	O3—C2—C9—C10	171.8 (5)
N2—Cu—N1—C19	2.2 (4)	C3—C2—C9—C10	55.3 (7)
Cl1—Cu—N1—C19	89.6 (6)	C1—C2—C9—C10	−71.2 (7)

O2—Cu—N1—C19	−101.2 (4)	O3—C2—C9—C14	−10.8 (8)
O1—Cu—N2—C24	−103.3 (7)	C3—C2—C9—C14	−127.3 (6)
N1—Cu—N2—C24	−177.1 (5)	C1—C2—C9—C14	106.2 (6)
Cl1—Cu—N2—C24	26.2 (5)	C14—C9—C10—C11	−0.1 (10)
O2—Cu—N2—C24	−77.7 (5)	C2—C9—C10—C11	177.4 (6)
O1—Cu—N2—C20	70.8 (7)	C9—C10—C11—C12	1.4 (11)
N1—Cu—N2—C20	−3.0 (4)	C10—C11—C12—C13	−1.2 (12)
Cl1—Cu—N2—C20	−159.7 (4)	C11—C12—C13—C14	−0.3 (11)
O2—Cu—N2—C20	96.4 (4)	C10—C9—C14—C13	−1.4 (9)
N2—Cu—O1—C1	31.7 (7)	C2—C9—C14—C13	−178.9 (6)
N1—Cu—O1—C1	103.6 (4)	C12—C13—C14—C9	1.6 (10)
Cl1—Cu—O1—C1	−98.1 (3)	C19—N1—C15—C16	0.6 (10)
O2—Cu—O1—C1	2.2 (3)	Cu—N1—C15—C16	−178.2 (5)
O1—Cu—O2—C1	−2.4 (3)	N1—C15—C16—C17	−0.5 (10)
N2—Cu—O2—C1	−172.8 (4)	C15—C16—C17—C18	0.4 (10)
N1—Cu—O2—C1	−88.9 (4)	C16—C17—C18—C19	−0.4 (10)
Cl1—Cu—O2—C1	86.8 (3)	C15—N1—C19—C18	−0.6 (9)
Cu—O2—C1—O1	3.8 (5)	Cu—N1—C19—C18	178.4 (4)
Cu—O2—C1—C2	−177.9 (5)	C15—N1—C19—C20	−179.9 (5)
Cu—O1—C1—O2	−4.7 (7)	Cu—N1—C19—C20	−1.0 (6)
Cu—O1—C1—C2	177.0 (4)	C17—C18—C19—N1	0.5 (9)
O2—C1—C2—O3	15.2 (7)	C17—C18—C19—C20	179.8 (6)
O1—C1—C2—O3	−166.4 (5)	C24—N2—C20—C21	−0.3 (8)
O2—C1—C2—C3	133.0 (6)	Cu—N2—C20—C21	−174.9 (4)
O1—C1—C2—C3	−48.6 (7)	C24—N2—C20—C19	177.8 (5)
O2—C1—C2—C9	−103.9 (6)	Cu—N2—C20—C19	3.3 (6)
O1—C1—C2—C9	74.5 (6)	N1—C19—C20—N2	−1.4 (7)
O3—C2—C3—C4	119.4 (6)	C18—C19—C20—N2	179.2 (5)
C9—C2—C3—C4	−120.7 (6)	N1—C19—C20—C21	176.7 (6)
C1—C2—C3—C4	0.3 (8)	C18—C19—C20—C21	−2.7 (9)
O3—C2—C3—C8	−59.2 (7)	N2—C20—C21—C22	0.5 (9)
C9—C2—C3—C8	60.8 (7)	C19—C20—C21—C22	−177.5 (6)
C1—C2—C3—C8	−178.3 (5)	C20—C21—C22—C23	0.0 (10)
C8—C3—C4—C5	−0.8 (10)	C21—C22—C23—C24	−0.6 (10)
C2—C3—C4—C5	−179.3 (6)	C20—N2—C24—C23	−0.3 (9)
C3—C4—C5—C6	1.6 (11)	Cu—N2—C24—C23	173.6 (5)
C4—C5—C6—C7	−0.7 (12)	C22—C23—C24—N2	0.8 (10)

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O3—H3o···O2	0.82	2.19	2.622 (6)	113
O3—H3o···Cl1^{i}	0.82	2.62	3.328 (5)	146

Symmetry codes: (i) *x*+1, *y*, *z*.

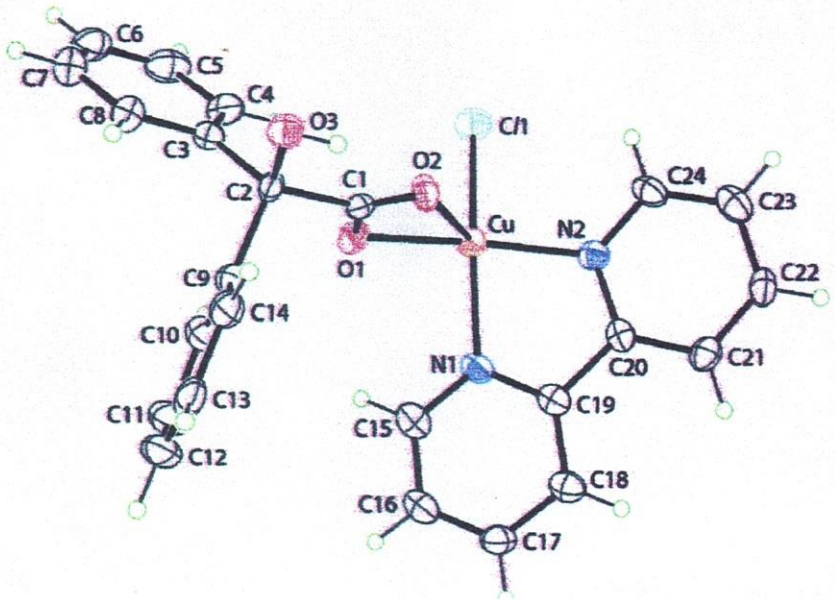

Fig.1: Molecular structure of Cu(II) complex showing displacement ellipsoids at the 50% probability level

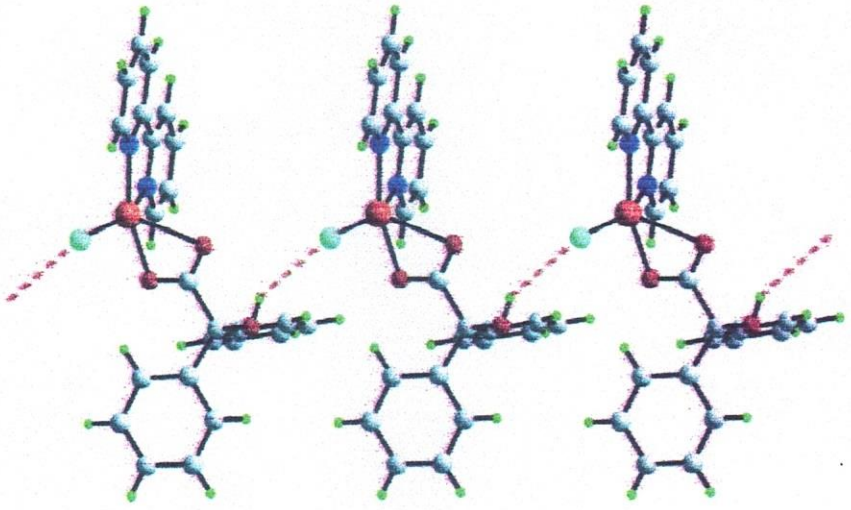

Fig.2: Supramolecular chain along the α axis in Cu(II) mediated by

O-H....Cl hydrogen bonds (shown as orange dashed lines)