Recent Advances in Synthesis, Characterization and Biological Activity of Nano Sized Schiff Base Amino Acid Cu(II) Complexes

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ABSTRACT

The Alpha-amino acids Azomethine amino ligands were created by combining L-phenylalanine (P) and DL-tryptophan (T) with 3-methoxysalicylaldehyde (MS) or 4-diethylamino salicylaldehyde (DS). We checked the infrared, 1H, and 13C nuclear magnetic resonance, as well as the melting temperature, for every ligand. Fe (II) and Cu (II) complexes with novel nanoscale structures were generated when the azomethine amino ligands were combined with metal salts. In a dynamic air environment, the separated complexes were studied using thermal analysis (TGA), infrared spectra, ultraviolet-visible spectra, and elemental analysis. From the thermal data, the kinetic and Redfern parameters were calculated. A lack of electrolysis is supported by the low molar conductance values of the complexes. According to the results of the magnetic susceptibility experiments, the complexes under study are paramagnetic. Additionally, spectrophotometric determinations of the produced complexes' stability constants were made. The analytical findings show that amino acid Schiff bases coordinate with Fe (II) and Cu (II) ions in octahedral geometry, according to the general formula [M(HL)2]. and act as dibasic tridentate ONO ligands. liquid water. Using transmission electron microscopy, the size of the produced complexes' particles was measured and found to be nanoscale. Additionally, against some bacteria (+ve), The ligands and their complexes were evaluated for their antibacterial activity against Escherichia coli (-ve) and Micrococcus luteus (+ve), as well as fungi (+ve) such Aspergillus Niger, Candida glabrata, and Saccharomyces cerevisiae. Metal complexes, according to these investigations, are more effective against bacteria and fungi than their equivalent ligands. Through the use of spectrum investigations, viscosity tests, and gel electrophoreses, seeing the complexes' interaction with CT-DNA. The fact that the produced complexes may potentially intercalate with DNA was also uncovered.

KEYWORDS

Azomethine, Amino acid, TGA, TEM, Antimicrobial, DNA interaction.

I. INTRODUCTION

Transition metal Recent years have seen a surge in the study of Schiff base complexes as more and more people become interested in their possible uses in fields as diverse as medicine, ecology, industry, and biology. Types of macrocyclic complexes that comprise tetradentate ligands and first-row transition metal ions have been the subject of much study. Among the several essential biological functions performed by iron, zinc, and copper ions—the three most prevalent metal ions in the human body—are the production of RNA and DNA, regulating enzyme and gene expression, enhancing protein structure and function. Various viewpoints have focused on the synthesis and activity investigations of Cu (II) complexes because of their significance in biological processes. There have been reports of fungicidal, bactericidal, antiviral, and antitubercular activities shown by Complexes involving Schiff bases and amino acids with first-row transition metals, especially copper (II). Cu (II) complexes containing amino acid Schiff bases have potent biological actionhas garnered a lot of interest. There is some evidence that Schiff bases and metal complexes may have anticancer medicinal uses. Antimicrobial and antifungal properties are only two of the several significant biological actions shown by these substances. When enzymes interact with carbonyl or amino groups on substrates, Schiff bases seem to play a significant role as reaction intermediates in a variety of these processes. Schiff base complexes are intriguing in bioinorganic chemistry because of the synthetic models they can give for metal-containing sites in metalloproteins and the advances they can make in medicinal chemistry. So, there are many analytical, therapeutic, and biological uses for Schiff bases and complexes. In addition, salicylaldehyde and diamine derivative complexes with transition metals have been the subject of much research. Their ability to serve serving as oxygen-introducing catalysts for organic biological substrates is the reason for this.

Because of their structural diversity and ease of preparation, Schiff base complexes have long been regarded as a key stereochemical model in the fields of main group and transition metal coordination chemistry. Antitumor, antibacterial, and antioxidant properties are just a few of the many biological uses for metal complexes of Schiff bases. The economic and biological significance of transition metal Schiff base complexes makes them an attractive research target.

Because of their structural diversity, ease of production, and crucial roles in the coordination chemistry of transition metals and major groups, Schiff bases and their metal complexes have been the subject of substantial research. Condensation of active carbonyl with primary amines in an appropriate solvent is the key step in their synthesis. These metal complexes are synthesized by combining a metal precursor with the Schiff-base ligand in the right proportions under controlled laboratory circumstances. Schiff bases and metal complexes have a plethora of documented uses (7, 8). Chelating ligands in coordination chemistry, catalysts, a dye, initiators in polymerization, and luminous compounds are some of the ways these compounds have been used by researchers. In terms of biology, they have been evaluated as agents that combat bacteria, fungi, tumors, viruses, and insecticides. From 32 to 34Since the discovery of cisplatin 35 in the 1970s and auranofin 36,37 in the 1990s, researchers within the realm of pharmaceutical research and development have been interested in metal complexes as potential new drugs.38 This study summarizes 39 investigations that demonstrated the anticancer potential of copper(Cu) complexes as a chemical that might block proteosomes, produce reactive oxygen species (ROS), and cause DNA damage, all of which would lead to the death of cancer cells.

II. LITERATURE REVIEW

Nida Asif et.al (2023) The Zinc oxide nanoparticles (ZnONPs) have attracted the interest of researchers worldwide due to their biocompatibility, low toxicity, sustainability, and cost-effectiveness, making them the most employed metal oxide nanoparticles. The optical, electronics, and food packaging industries are where they really shine as potential competitors. biomedicine because to their distinctive chemical and optical characteristics. In comparison to chemical and physical approaches, biological methods that use green or natural pathways are less harmful to the environment, easier to implement, and need fewer potentially dangerous procedures. Also, ZnONPs may significantly increase pharmacophore bioactivity, and they're less toxic and biodegradable. Due to their ability to increase ROS formation and release Zn^{2+} ions, which induce cell death, they are key players in cell apoptosis. In addition, these ZnONPs complement wound healing components and biosensing components that detect trace levels of biomarkers associated with certain diseases. In summary, this review delves into the synthesis and latest advancements in ZnONPs derived from various green sources, including but not limited to: components like as stems, leaves, bark, roots, fruits, flowers, microbes, algae, and proteins. Additionally, it clarifies their medicinal applications, such as antibacterial, antioxidant, antidiabetic, anticancer, anti-inflammatory, antiviral, wound healing, medication administration, and related mechanisms of action. The paper concludes by outlining the potential future uses and research directions for biosynthesized ZnONPs.

Meng Liu et.al (2024) An essential heterogeneous catalyst is a metal or metal oxide species encased in zeolites. They have been a focus of study due to their performances, which consistently surpass those of typical supported catalysts in several critical processes. Significant progress has been made in synthesizing, characterizing, and performing with metal species (often clusters of metals and metal oxides) found in zeolites. Two novel approaches to metal species encapsulation, post-treatment and in-situ synthesis, are presented and discussed here. Metal species in zeolite-encapsulated catalysts are studied using a number of important methods, such as chemisorption, electron microscopy, X-ray absorption (XAS), and Fourier transform infrared spectroscopy of CO (FTIR-CO). Research like this verifies that metal species may be effectively contained in zeolites while retaining their unique physiochemical characteristics. It is also possible to determine the encapsulation fraction using a probe molecular titration test. The emphasis is on the activity, selectivity, and stability of zeolite-encapsulated metal catalysts when it comes to their catalytic performance. We conclude with a brief overview of the uses of metal catalysts encased in zeolites for reactions involving hydrogen.

Pinki Punia et.al (2021) In response to the widespread problem of insufficient potable water, scientists from all around the world are working to develop more effective and economical ways of purifying polluted water. Researchers are now doing experiments with several kinds of nanoparticles to determine their potential for treating wastewater that has been contaminated or otherwise compromised. Extensive testing has been conducted on a wide variety of nanoparticles to establish their suitability for the treatment of polluted and untreated wastewater. These nanoparticles include carbon-based, semiconductor, ceramic, polymeric, metal, magnetic, and many more types. Depending on their structural, electrical, magnetic, physical, and chemical properties, various nanoparticles have distinct benefits. It has been shown that nanoparticles, like nano ferrites, may be separated, regenerated, and reused several times without compromising their characteristics. This can lead to a substantial decrease in operational expenses. In order to produce the nanoparticles, this paper gives a comprehensive overview of the several synthesis and characterization methods. Additionally, this research summarizes the most recent advancements, particularly throughout the last two decades, in the use of nanoparticles to effectively filter out harmful pathogens, organic contaminants, and metals from water. To that end, this study will focus on nanoparticles and their derivatives and their boundless potential for use in treating polluted water and other pollutants.

Ze Liao et.al (2022) The widespread and persistent degradation of our natural environment by endocrine-disrupting chemicals (EDCs) is a direct result of their mass manufacture and widespread use. In both humans and aquatic species, even modest amounts of EDC exposure may lead to metabolic problems, issues with sexual development, and problems with reproduction. One viable and long-term option for EDC removal from wastewater is adsorption treatment, especially when combined with nanocomposites. Graphene, carbon nanotubes, carbon fibers, carbon dots, carbon sponges, magnetic carbon nanomaterials, and other carbon-based nanomaterials might be used to efficiently remove EDCs from wastewater. We cover the theory of adsorption, the important uses of carbon nanocomposites in removing various EDCs, and the latest developments in the production and characterization of carbon nanocomposite materials. We also compare carbon nanocomposites to other adsorbents and examine the aspects that influence their usage in EDC elimination. An important reason why this review is important is that it encourages the creation of nanocomposites for wastewater purification.

Isaac K. Tetteh et.al (2024) Carbon derivatives (OCDs) and activated carbons (ACs) have a long and storied history that goes all the way back to antiquity. Using both biomass and non-biomass sources, this article discusses the latest developments in the synthesis, characterization, and environmental applications of these adsorbents driven by demand. Before breaking down and analyzing the topic to shed light on modern carbon-based adsorbents, it identifies pertinent literature sources and knowledge gaps. Both traditional and cutting-edge syntheses are emphasized. Also included are the most recent developments in the field of adsorbent characterization and remediation. Chemical or physical activation, either in a single step or a combination of the two, is a standard component in AC synthesis. Problems related to combinatorics are investigated. Various advanced approaches are detailed, including one- or two-step processes including hydrothermal carbonization/activation and microwave-assisted irradiation. The majority of organic carbon derivatives (OCDs), such as carbon nanotubes, nanofibers, and dots, need sophisticated syntheses, such as nanotechnology. Nowadays, cutting-edge methods such as Characterization of ACs and OCDs is accomplished by the use of X-ray diffraction (XRD), thermogravimetric analysis (TGA), scanning electron microscopy (SEM), nitrogen (N2) adsorption, and Fourier transform infrared spectroscopy (FTIR). We can learn more about their structures, characteristics, and potential efficacies with the use of these methods. We evaluate their reliability efficacy in cleaning air, water, and dirt. Depending on the kind of activation, the precursor's origin, synthesis process, product characteristics, and quality were all factors in the best percent elimination efficiency. As an example, activating neem leaves chemically with H3PO4 and Cr6+ with Fe nanoparticles from tea extracts both yielded 100% success, however activating rice husk physically only resulted in 91.8% success for Cr3+. The activation of H3PO4 was the lowest, although their differential absorptivity's for other metals were considerable as well. This analysis takes into account the ongoing quest for appropriate replacements by researchers as a result of the high cost, arduous procedures involved in generating and recovering ACs, and their lack of selectivity. Additionally, the topic of developing new ACs and OCDs for environmental cleanup using artificial intelligence (AI) approaches is covered. Lastly, recommendations for further study are provided.

III. EXPERIMENTAL

Chemicals

Chemicals including 3-methoxy salicylaldehyde ($C_8H_8O_3$), 4-the amino acids phenylalanine (P) and DL-tryptophane (T), calf thymus DNA (CT-DNA), and the metal ions Cu (CH_3COO) were used for detailed manufacture.2. The purest forms of water and $(NH_4)_2$ Fe $(SO_4)_2.6H_2O$ were procured from Sigma-Aldrich.

Instruments

The melting points and locations of breakdown of the complexes of the separated ligands were recorded using a melting point instrument, the Cimarec 3 Thermolque. The amounts of carbon, hydrogen, and nitrogen were determined using a Perkin Elmer (2400) CHNS analyzer. The KBr pellets were subjected to infrared spectra (4000-400 cm-1) using the Shimadzu FT-IR model 8101 spectrometer. Bruker spectral measurements of 1HNMR and 13CNMR were obtained using DMSO as an internal reference. At a pace of 10 degrees min-1, the TG/DT analyses were recorded using a Shimadzu company 60 H. While capturing the UV-Vis spectra, a PG spectrophotometer type T+80 was used at 298k. At room temperature, we measured the magnetic susceptibility of the metal complexes using a Gouy balance and Hg [Co $(SCN)_4$] as a calibrant. The molar conductance was measured using an Elico CM-180 conductometer with solutions in DMSO containing 1 mmol L-1. We utilized a HANNA 211 pH meter with a CL-51B combination electrode and an operating voltage of 298 kHz to test the pH. As a prerequisite to taking any readings, the meter was pH-calibrated using standard buffers at 4.02 and 9.18, respectively. To screen for microbes, agar well diffusion was used. In order to measure the viscosity, the viscometer was heated to 25 o C in a thermos-stated water bath. Using a UV transilluminator, the gel electrophoresis was seen and recorded using a Panasonic DMC-LZ5 Lumix Digital Camera.

Synthesis of Schiff base ligands

3-Methoxysalicylaldehyde OR 4-L-Phenylalanine OR DL-Tryptophandiethylamino salicylaldehyde were used to produce three Schiff bases. The following procedure was used to generate the imine derivatives of DL-Tryptophan (T) or LPhenylalanine (P). L-Phenylalanine or DLTryptophan, five millimoles of either 3-methoxysalicylaldehyde (0.76 g) or 4-diethylaminosalicylaldehyde (0.995 g) were dissolved in thirty millimoles of heated ethanol. The mixture was allowed to cool to room temperature after being refluxed while stirring for 2 hours. After incubating for 24 hours, the precipitate was strained and rinsed with heated ethanol. Using proton NMR measurements, we checked that the chemicals we got were real and pure. Table 1 shows amino acid Schiff bases and their structures that were produced for this investigation.

Table 1: The amino acid ligands produced using the Schiff base

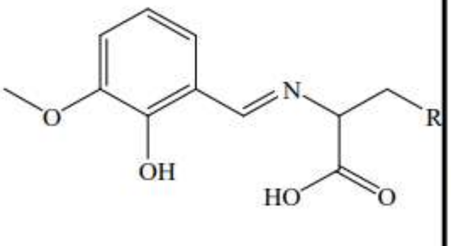
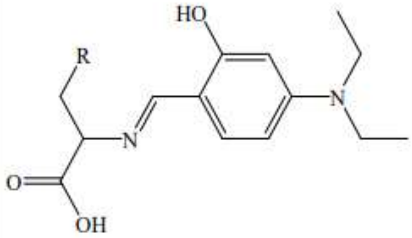
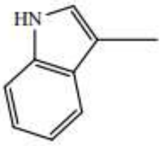
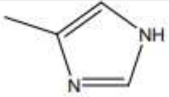
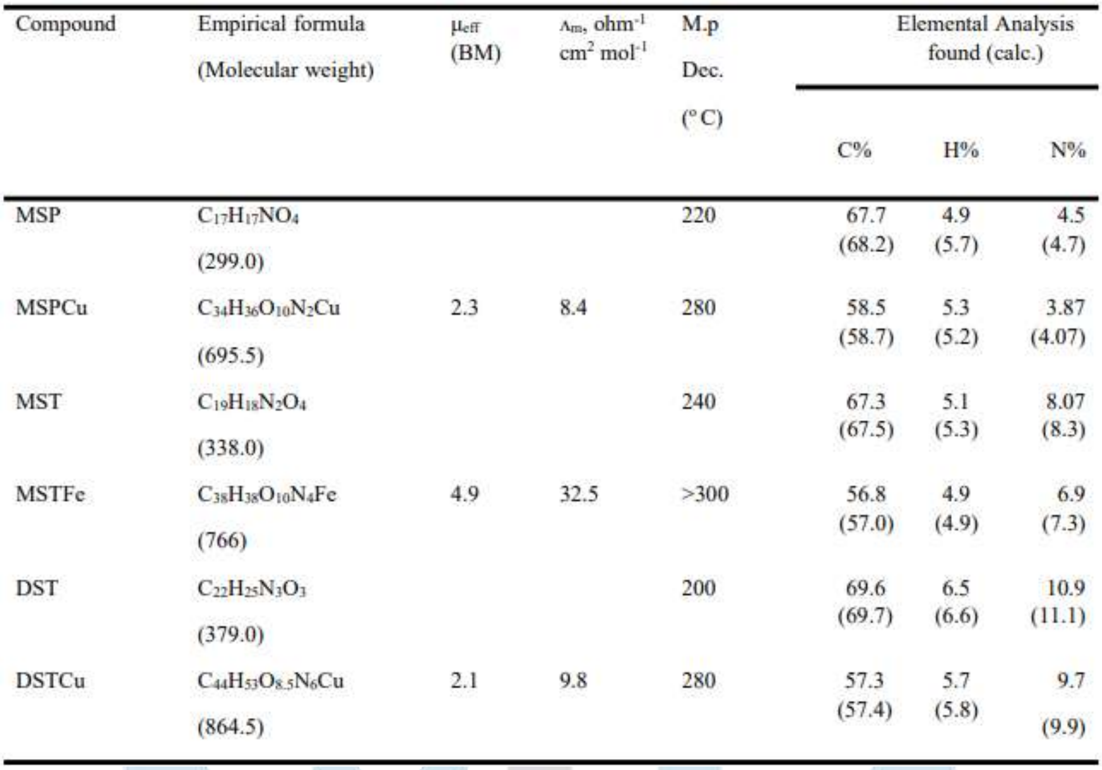
				**Side Chain**
Aldehyde	Ligand Abbreviation	Aldehyde	Ligand Abbreviation	**R**
3-methoxysalicyladehyde	MSP	4-diethylaminosalicylaldehyde	DSP	
	MST		DST	
			DSH	

Table 2:nuclear magnetic resonance (HNMR) spectra of the ligands for Schiff bases that were studied

Comp.	^{1}H NMR (δ, ppm), in DMSO
MSP	13.6 (s, 1H, COOH), 8.4(s, 1H, CH=N), 7.4 – 6.6(m, 8H - Ar), 4.3(s, 1H, OH), 3.9(m, 1H, CH), 3. 8(S, 3H, OCH_3), 3.2 (d, 2H, CH_2).
MST	13.8-13.6 (s,1H,COOH),10.9 (s,1H,NH), 8.2 (s, 1H, CH=N), 7.5 – 6.5(m, 8H - Ar), 4.2(s, 1H, OH), 3.0(d, 2H, CH_2), 3.8 (S, 3H, OCH_3), 3.7(m, 1H, CH),
DST	11.5 (s, 1H, COOH), 9.5(s, 1H,NH), 8.3(s, 1H, CH=N), 6.0 - 7.5(m, 8H – Ar), 4.3(s, 1H, OH), 3.3 (q, 4H, $2CH_2$-CH_3), 2.7 (d, 2H, CH_2 - Ar), 0.9 - 1.2 (t, 6H, $2CH_3$-CH_2), 3.5 (s, 1H, CH).

Table 3: Physical and analytical information on ligands and complexes of Schiff bases with amino acids



Compound	Empirical formula (Molecular weight)	μ_{eff} (BM)	Λ_m, ohm^{-1} cm^2 mol^{-1}	M.p Dec. (° C)	Elemental Analysis found (calc.)		
					C%	H%	N%
MSP	$C_{17}H_{17}NO_4$ (299.0)			220	67.7 (68.2)	4.9 (5.7)	4.5 (4.7)
MSPCu	$C_{34}H_{36}O_{10}N_2Cu$ (695.5)	2.3	8.4	280	58.5 (58.7)	5.3 (5.2)	3.87 (4.07)
MST	$C_{19}H_{18}N_2O_4$ (338.0)			240	67.3 (67.5)	5.1 (5.3)	8.07 (8.3)
MSTFe	$C_{38}H_{38}O_{10}N_4Fe$ (766)	4.9	32.5	>300	56.8 (57.0)	4.9 (4.9)	6.9 (7.3)
DST	$C_{22}H_{25}N_3O_3$ (379.0)			200	69.6 (69.7)	6.5 (6.6)	10.9 (11.1)
DSTCu	$C_{44}H_{53}O_{8.5}N_6Cu$ (864.5)	2.1	9.8	280	57.3 (57.4)	5.7 (5.8)	9.7 (9.9)

Synthesis of the investigated complexes

To create three new complexes, 40 ml of amino acid solutions were mixed together with 50 ml of heated ethanolic solutions of either 4-diethylamino salicylaldehyde (5 mmole, 0.995 g) or 3-methoxy salicylaldehyde (5 mmole, 0.76 g). Five millimoles of phenyl alanine (0.825 g) or tryptophan (1.045 g) were dissolved to make the amino acid solutions. After that, it was agitated for an hour at 70 degrees Celsius. Next, combine 0.98 g of (NH4)2Fe (SO4)2.6H2O) with 2.5 mmole of Cu (CH3COO)2. H2O in 30 ml of aqueous-ethanol with 40 ml of Cu (CH3COO)2. H2O in 0.5 g. Glacial acetic acid was used in small amounts to prevent the oxidation of iron (II). For three hours, the ingredients were mixed while left at room temperature. Colors altered for MSPCu (yellow to green), DSTCu (blue), and MSTFe (dark brown). Overnight, the resulting product evaporated. Following filtration and a water wash, the resulting solid product was vacuum dried over anhydrous CaCl2.

IV. RESULTS AND DISCUSSION

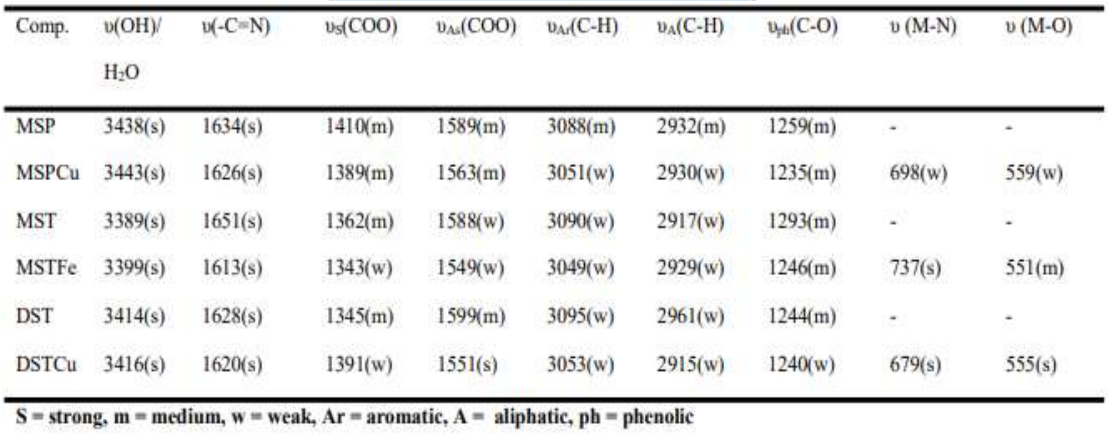
IR spectra

You can see the results of the infrared spectra in Table 4. Infrared spectra provide important details about the The metal atom is bonded to a functional group. With respect to purpose of researching how metal complexes bind to Schiff bases. A comparison is made between the complex spectra and the infrared spectra the unbound ligand. These complexes' linked water molecules have a wide band at the range of 3443–3389 cm-1, which is blamed on their □ (OH) vibration.

The aromatic bond's stretching vibrations and □ (C - H) aliphatic bonds may be attributed to the bands seen in the 3095-3049 cm-1 and 2961-2915 cm-1 sections, respectively. The recognizable ϕ(C=N) band situated between 1651 and 1628 cm-1 range is shown by the ligands.

compounds with (In the range of 1626-1613 cm-1, C=N) were identified, although Reduced (C=N) bond order as a result of coordination bonding between the metal and the nitrogen lone pair in imine compounds is indicated by a usually decreased (C=N) stretching frequency. The ligands' □ υ (C - O). (phenolic) vibrations are seen at 1293-1244 cm-1, however in complexes, they shift to a lower frequency range, indicating coordinated phenolic oxygen. The ligands also exhibit intense bands at (1410 - 1345 cm-1) and (1599 - 1588) cm-1, which represent the symmetric and asymmetric stretching frequencies of the organic ligand's (COOH) group, respectively. The frequencies of the symmetric and asymmetric bands were reduced throughout the complex's formation. The difference between the COO-group's symmetry and asymmetry stretching vibrations demonstrated the coordination of amino acid Schiff bases. Two more bands were found at 737–679 cm-1 and 559–551 cm-1, respectively. These bands could be connected to the stretching of □υ(M-N) and □υ(M-O).

Table 4: The examined Schiff base amino acid ligands and their complexes' infrared spectrum



Comp.	υ(OH)/ H_2O	υ(-C=N)	υ_{S}(COO)	υ_{As}(COO)	υ_{Ar}(C-H)	υ_{A}(C-H)	υ_{ph}(C-O)	υ (M-N)	υ (M-O)
MSP	3438(s)	1634(s)	1410(m)	1589(m)	3088(m)	2932(m)	1259(m)	-	-
MSPCu	3443(s)	1626(s)	1389(m)	1563(m)	3051(w)	2930(w)	1235(m)	698(w)	559(w)
MST	3389(s)	1651(s)	1362(m)	1588(w)	3090(w)	2917(w)	1293(m)	-	-
MSTFe	3399(s)	1613(s)	1343(w)	1549(w)	3049(w)	2929(w)	1246(m)	737(s)	551(m)
DST	3414(s)	1628(s)	1345(m)	1599(m)	3095(w)	2961(w)	1244(m)	-	-
DSTCu	3416(s)	1620(s)	1391(w)	1551(s)	3053(w)	2915(w)	1240(w)	679(s)	555(s)

S = strong, m = medium, w = weak, Ar = aromatic, A = aliphatic, ph = phenolic

V. CONCLUSION

This paper presents the synthesis of novel Schiff base ligands of the dibasic tridentate ONO amino acid and its iron (II) and copper (II) complexes. Analytical data, infrared, electrical, 1H nuclear magnetic resonance, molar conductance, and thermal tests have all verified the complexes' structures. Analytical and spectral investigations led to the proposal of an octahedral geometry for the general formula [M(HL)2] for the Fe (II) and Cu (II) complexes. water in liquid form. The complexes that are made do not undergo electrolysis. Here is the sequence in which the Kf values that were acquired increased:

DSTCu>MSTFe after MSPCu. Research on their thermal stability has shown that the complexes do in fact exhibit stability. In contrast to ligands, the antimicrobial and antifungal properties of the produced Schiff base metal complexes are superior. The intercalative method is used for the DNA binding investigation. Results from this study may pave the way for better knowledge of how metal (II) complexes interact with nucleic acids, which in turn could aid in the creation of probes to study DNA structure and conformation or novel therapeutic agents to treat certain diseases.

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