

## A STUDY ON THE HETEROCYCLIC LIGANDS WITH A REFERENCE OF THEIR METALLIC COMPLEXES

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### ABSTRACT

The formation of stable complexes by heterocyclic ligands with a variety of metal ions is an essential part of the field of coordination chemistry. This exhaustive research investigates the synthesis, characterisation, and reactivity of heterocyclic ligands, with a special emphasis on the complexes of these ligands with metallic atoms. In order to make progress in domains such as catalysis, material science, and medicinal chemistry, it is vital to have a solid understanding of the characteristics and behaviors of these ligands. The investigation starts with an investigation into the synthesis of a wide variety of heterocyclic ligands. These ligands include derivatives of pyridine, imidazole, and pyrrole. Several different methods of synthetic synthesis are discussed, with an emphasis placed on the significance of ligand design and functionalization. In order to validate ligand structures, certain spectroscopic and structural characterisation methods, such as nuclear magnetic resonance (NMR) spectroscopy and X-ray crystallography, are utilized. As the research moves forward, it looks at the coordination chemistry of these heterocyclic ligands with a variety of metal ions.

**Keywords:** *Heterocyclic Ligands, Metallic Complexes*

### INTRODUCTION

In this study, we investigate the process of metallic complex formation, with the goal of clarifying the elements that influence the stability, shape, and reactivity of complexes. The importance of these complexes in catalytic processes, both in terms of their function in industrial applications and their impact on the environment, is emphasized by the fact that the emphasis is focused on the role that these complexes play. In this study, we investigate the electrical and optical characteristics of these metallic complexes in order to demonstrate their potential application in fields such as photovoltaics and luminous materials. By establishing a correlation between the structure of ligands and the complicated characteristics of complex systems, we provide insights into the rational design of novel materials with functions that are specifically suited. In addition, the biological significance of heterocyclic ligands and their metal complexes is investigated as part of this study. In this article, we examine the process of developing medications that are based on metals and compare and contrast the reactions of various metallic centers in biological contexts. This work presents an in-depth analysis of heterocyclic ligands as well as the metallic complexes containing those ligands. By investigating their synthesis, coordination chemistry, and a variety of applications, we want to make a contribution to the expanding body of knowledge that exists within the subject of inorganic chemistry and its significance to a variety of other scientific fields.

a new 1Hbenzo[d]imidazol-1-yl)quinolin-8-ol ligand was synthesized, along with its complexes with Co(II), Ni(II), Cu(II), and Zn(II). the results of this synthesis are reported. In order to characterize the new ligand and the metal(II) complexes it forms, a number of different analytical and spectroscopic methods were utilized.

Investigations into the ability of the produced ligand and its metal complexes to inhibit the growth of bacteria and fungi were carried out. In addition, the cytotoxicity of these complexes was examined using a variety of human cancer cell lines.

The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were obtained by utilizing TMS as an internal solvent and DMSO ( $d_6$ ) as a solvent throughout the recording process on a Bruker Avance-400 and Bruker Avance-100 MHz NMR equipment, respectively. The Perkin-Elmer LCMS PE Sciex API/65 Spectrophotometer was utilized in order to get the mass spectra. FT-IR spectra were obtained by using KBr discs and an Avatar 360 spectrophotometer from Nicolet, Madison, United States. The wavenumber range for this measurement was  $4000\text{--}400\text{ cm}^{-1}$ . The melting points were obtained using a Buchi 530 melting point equipment with open capillary tubes at one end, and the results have not been modified. The pre-coated TLC plates manufactured by Merck were utilized. Utilizing a Perkin-Elmer model 240C analyzer, we were able to do elemental analysis on carbon, hydrogen, and nitrogen. For the purpose of recording the UV-Vis spectra, a UV-Vis double beam spectrophotometer was utilized. The measurements of molar conductance were performed with the assistance of a digital electronic conductivity meter. The Gouy technique was utilized to carry out magnetic measurements while the apparatus was kept at room temperature.

In coordination chemistry, the heterocyclic coordinating compounds that are concerned with azo ligands, particularly thiazole azo ligands, and with their metallic ions in their coordinated chelate pattern are the ligands that play a fundamental and essential function. They are necessary to life because they play a very key part in the metabolic processes of many living cells, which makes them highly important in industrial technology, biological systems, and routine. They are of considerable relevance because to the special features that they possess, which make them very important. Physicochemical features can be attributed to the metal chelates of ligands that contain hetero-atom donor sets. Thiazole azo ligands have the capacity to coordinate with a diverse selection of metallic ions as a result of their stable and vividly colored metal complexes, which are due to the hard nitrogen, oxygen, and soft sulfur donor atoms in their structure.

When compared with organic molecules, the ligand complexes of metallic ions have distinct structures; as a result, the forms that it may take cover a wide variety of coordination geometries. It is intriguing to examine molecules that contain both S and N atoms because of the strong antifungal, antibacterial, and anticancer properties that these compounds exhibit. Thiazolylazo complexing agents have been used effectively in the determination of a wide variety of metal ions, and they have garnered a lot of attention due to the fact that they are sensitive chromogenic reagents that can be used in spectrophotometry, liquid chromatography, and extraction photometry in a variety of ways, including solid phase, liquid – liquid, and cloud point extraction. Compounds containing thiazolyl azo are essential for the production of certain applications such as biological activity and are used in intermediates. Due to the great sensitivity and selectivity of thiazolylazo reagents as analytical reagents, these azo reagents have garnered a lot of attention in the field of analysis. Due to the fact that this group of azo dyes is a (-acidic) azo imine, quite a few of these dyes have been synthesized, and their capacities as chelating reagents have been investigated. Synthesis of a new thiazolyl azo ligand with a number of complexes of the azo dye ligand and characterization using a variety of analytical and spectroscopic methods was the goal of this study. In addition, the bioactive relevance of the ligand and the metal complexes it forms was researched.

PAHs, or polycyclic aromatic hydrocarbons, have made a significant contribution to the field of materials science thanks to the desired electrical and self-assembly capabilities that they possess. Heterocyclic PAHs,

which are part of a select group of PAHs, are extremely valuable for use in organic light-emitting diodes, electroluminescent materials, and solar cells. Indeed, the inclusion of heteroatoms into these systems results in a number of functional and electrical benefits. This involves the development of nitrogen-functional handles for use in synthetic manipulations, the ability to N-coordinate to metal centers, the possibility for donor–acceptor systems, and the utilization of nitrogen-based materials in stimuli-responsive applications.<sup>5</sup> As a result, it is extremely desired to have access to heterocyclic PAHs through the use of synthetic techniques that are both succinct and flexible.<sup>6</sup> The assembly of fused rings around a core heterocyclic building block using a technique known as annulative p-extension (APEX) is one method that has proven to be effective in the study of heterocyclic PAHs.

The utilization of arynes synthesized in situ presents a tempting method for accomplishing this goal, despite the fact that such intermediates have traditionally been avoided due to the high level of reactivity they exhibit. However, the strain-driven reactivity of arynes, in conjunction with the capability to form numerous bonds in a single step under moderate circumstances, has recently led to the utilization of arynes as modular building blocks in a broad variety of applications. One of these applications is the synthesis of PAHs. On the other hand, heterocyclic arynes, also known as hetarynes, have only been employed in PAH production in very small amounts. This is partially attributable to the fact that the moderate, fluoride-mediated production of heterocyclic arynes (hetarynes) has just recently become prevalent in the past ten years.<sup>12</sup> Additionally, the capacity to access and modify indole-derived arynes (indolynes) and their derivatives is significantly different from that of benzyne chemistry. This is because indole-derived arynes are produced from indoles.

Compounds with an azomethine group have a broad spectrum of biological value. Schiff bases, which are created from amino and carbonyl compounds that function as significant ligands, co-ordinate with metal through the group, which is having a wide range of research (Bader et al., Schiff bases are prepared from amino and carbonyl compounds that act as key ligands. According to Giri et al. (2015), the study of metal complexes formed from Schiff base is motivated by the complexes' fascinating features, which include biological characteristics, enzymatic reactions, catalysis, and electrochemical investigations. Due to the presence of an imines group, compounds that include Schiff bases exhibit flexibility with natural biological substances. This is because imines are required for the transformation and racemization reaction that takes place in biological systems.

Additionally, it has been shown that metal complexes generated from schiff base ligands can act as oxygen transporters. Schiff base is utilized to produce metal complexes, which are then put to use in modern research due to the DNA-binding and cleavage capabilities it possesses under physiological conditions. Schiff base metal complexes have been the subject of substantial research because of their flexibility in the realm of industry. These complexes have biological activities such as anticancer, antifungal, antiviral, anticonvulsant, anti-inflammatory, and antibacterial properties, and they are beneficial in the treatment of inflammatory illnesses such as rheumatoid arthritis. Due to the stereochemical, electrochemical, and electrical characteristics of transition metal complexes with ligands comprising N, S, and N, O donors, there has been a lot of research done on these complexes. The reactivity of metal ions in the transmethylation process is the primary focus of the research of transition metal ions generated from Schiff bases. Complexes of silver that have the I oxidation state provide an excellent inhibitor against mosaic virus. In this study, we presented the synthesis and characterization of newly created metal complexes with oxidation numbers of (II), (IV) with Schiff bases including heterocyclic moieties. These metal complexes were freshly prepared.

## OBJECTIVES

1. The study Heterocyclic ligands play a pivotal role in coordination chemistry, forming stable complexes with various metal ions.
2. The study investigates the coordination chemistry of these heterocyclic ligands with diverse metal ions.

## RESEARCH METHODOLOGY

Sigma was the source for both the aminoantipyrine and the indole-3-carboxaldehyde. Merck was the supplier for the metal chlorides that were acquired. The AnalaR grade was utilized for all other compounds that were used. Before being put to use, the solvents were cleaned up with a distillation process. EDTA titration was used to assess the amount of metal contained in the complexes. A Perkin-Elmer elemental analyzer was utilized in order to carry out the elemental analysis. At room temperature and using a calibrated digital conductivity meter, conductivity readings were taken from newly produced 10<sup>-3</sup> M solutions in DMSO. The infrared spectra were obtained by using a JASCO FT/IR-410 spectrometer to collect data in KBr pellet across the frequency range of 4000–400 cm<sup>-1</sup>. A Perkin Elmer Lambda-25 UV/VIS spectrometer was utilized in order to record electronic spectra. The diamagnetic adjustments were done using Pascal's constant, and the cyclic voltammetric measurements were carried out in a Bio-Analytical system (BAS) model CV-50W electrochemical analyzer. The magnetic measurements at room temperature were carried out using a Guoy balance. A reference Ag/AgCl electrode, an auxiliary platinum electrode, and a working glassy electrode were the three components that made up the three-electrode cell. The electrolyte that was employed to assist the reaction was tetrabutylammonium perchlorate.

## Synthesis of metal Schiff base complexes

### In vitro antimicrobial activity

Antibacterial and antifungal activities of the ligand and its complexes were tested in vitro against the bacterial species *Escherichia coli*, *Bacillus subtilis*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*; fungal species, *Aspergillus niger*, *Aspergillus flavus*, and *Candida albicans* by the disk diffusion method. Results showed that the ligand and its complexes were Amikacin was considered the gold standard for treating bacterial infections, whereas nystatin was considered the gold standard for treating fungal infections. Petri plates with nutrient agar medium were used to cultivate the organisms to be tested. After being synthesized in DMF, the compounds were soaked in a filter paper disk of 5 millimeters in diameter and 1 millimeter in thickness. The disks were then placed on the plates that had been seeded previously and incubated at 37 degrees Celsius. After 24 hours for bacterial species and 72 hours for fungal species, the width of the inhibition zone that surrounded each disk was measured.

### DNA cleavage analysis

The chemicals were each included in the pUC18 DNA sample in their own unique fashion. After two hours of incubation at 37 degrees Celsius, the sample mixes were analyzed. The electrophoresis of the samples was performed by weighing 300 mg of agarose and then dissolving it by boiling it in 25 ml of TAE buffer (4.84 g Tris base, pH 8.0, 0.5 M EDTA/1 L). This was done in order to separate the samples according to their molecular weights. After the gel had cooled to a temperature of 55 degrees Celsius, it was put into a gel cassette that was

equipped with a comb, and then it was left to harden. After carefully removing the comb, the gel was then transferred into the electrophoresis chamber, which had been filled with TAE buffer. A DNA sample was carefully placed into the wells, along with a standard DNA marker, and then a steady 100 V of electricity was pushed through the gel until the dye front reached the end of the gel. This process was repeated until the dye front reached the end of the gel. After removing the gel, it was stained with ETBR solution at a concentration of 10 micrograms per milliliter for 10–15 minutes, and then the bands were examined using a UV transilluminator.

## Materials and instrumentation

All of the solvents, organic compounds, and inorganic salts that were utilized in this work were extremely pure before being put to use and did not require any additional purification steps. These chemicals were purchased from companies such as Sigma-Aldrich, Merck, BDH, Fluka, and Scharlau. The HMRS measurements were carried out using DMSO-d<sub>6</sub> serving as the measurement solvent and TMS acting as the internal standard reference on a Bruker model 500-UltraShield 300 MHz spectrometer. The Shimadzu Agilent Technologies model 5973C was utilized for the collection of mass spectra. KBr pellets were used in the recording of Fourier Transform Infrared (FT-IR) spectra, which was done using a Shimadzu model 8400s FT-IR spectrometer scanning at a range between 4000 and 400 cm<sup>-1</sup>. The Shimadzu model UV-1650 UV-Visible spectrophotometer was used to take the readings for the UV-Visible spectra. Absolute ethanol was used as the measuring solvent while performing double-beam scanning throughout a wavelength range of 200-1100 nm. Shimadzu model XRD-6000 spectroscopy was used to carry out the process of X-ray diffraction. In addition, we employed a digital pH meter made by JENWAY of England, model 3505, for the pH adjustment. A TESCAN model MIRA3 (FESEM) was utilized in both the field emission scanning electron microscope and the energy dispersive X-ray imaging processes. The OMEGA Digital Melting Point Apparatus model MPS10-120 was utilized in order to get the melting points, which were recorded in an open capillary tube.

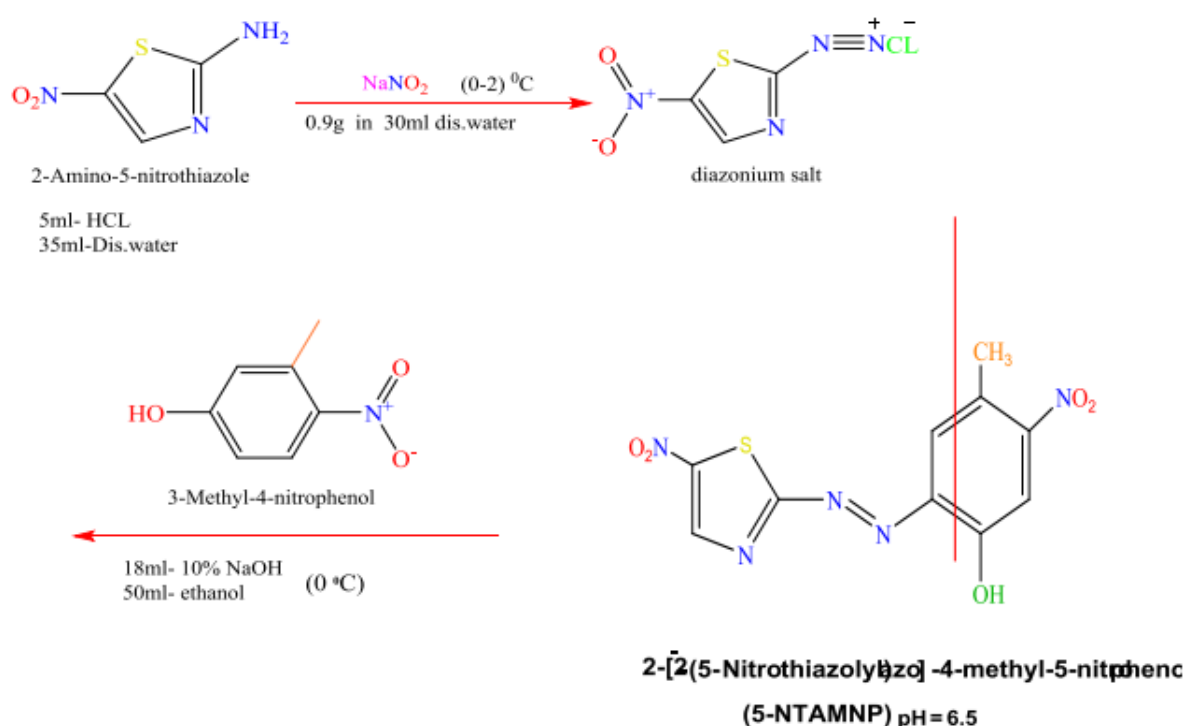


Figure 1. Synthesis of thiazolyl azo dye ligand (5-NTAMNP).

## DATA ANALYSIS

We began our synthetic experiments by pursuing a Pd-catalyzed annulation reaction of bromobiaryls **13**–**23** with N-Me-4,5-indolyne precursor, the latter of which is accessible in a single step from its commercially available N-H derivative. In this reaction, the bromobiaryls are converted into the indolyne precursor. During the beginning stages of our research, we explored the conditions for the annulation of carbocyclic arynes using 2-bromobiphenyl as the aryl halide coupling partner. These conditions were described by Larock. This resulted in the creation of **16** with a yield of just 43%, underscoring the difficulties that were previously stated in connection with the use of N-containing heterarynes in metal catalyzed processes in comparison to more straightforward arynes. In previous research<sup>24–26</sup>, we found that metal-catalyzed trappings of heterocyclic strained intermediates require careful optimization. This is due to the fact that such reactions require that a transient strained intermediate be generated at a rate that allows for efficient reaction with an in situ generated organometallic species while simultaneously minimizing decomposition pathways that are commonly seen in strained intermediate chemistry. The combination of co-solvents, in particular, is regarded to be significant for modifying the rate of hetaryne synthesis. In the end, we observed that the required reaction took place more effectively by utilizing a ratio of co-solvents consisting of acetonitrile and toluene.<sup>27</sup> With the most optimum.

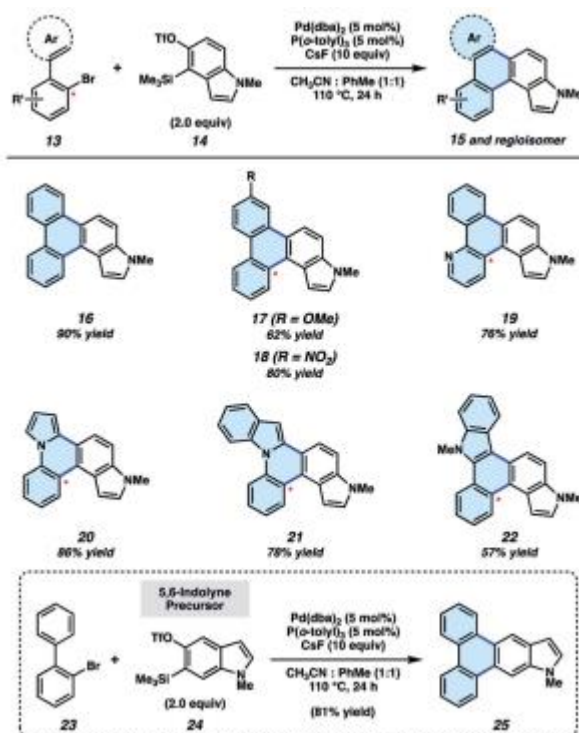


Figure 2 p-extension of indolynes. Yields for 17–22 reflect isolated yields of a mixture of regioisomers (1–1.5: 1; for details).

Conditions, with a yield of 90 percent may be reached. There is also the potential for the approach to make use of substituted biaryls. For instance, methoxy- and nitro-substituted biaryls proceeded through the annulation process without any problems, resulting in the delivery of adducts **17** and **18** with yields of 62% and 80%, respectively. In these situations, mixes of regioisomers are generated, and the amounts of each kind are

approximately equal.<sup>28</sup> Utilizing heterocyclic derivatives of 2-bromobiphenyls allowed us to achieve another one of our goals, which was to introduce more heteroatoms into the products. Utilization of a pyridyl substrate led to the production of 19 with a yield of 76%. molecule 19 is an intriguing aza-analog of the parent molecule 16. In addition to this, we were successful in exchanging one of the phenyl rings for either pyrrole or indole units, as evidenced by the creation of 20–22. Last but not least, we carried out the annulation of 2-bromobiphenyl with 5,6-indolyne precursor 24, which resulted in adduct 25 being produced with an 81% rate of success. The findings that are displayed in Figure 3 not only verify our technique for achieving the p-extension of heterocyclic building blocks, but they also enable access to heteroatom-containing PAHs that have a varied range of electrical and structural characteristics.

After proving that the p-extension of indoles could be accomplished with the help of indolynes, we set out to establish a similar chemical reaction utilizing the carbazole heterocycle. In comparison to their indole counterparts, carbazoles have an extra aromatic ring. Carbazoles are useful in applications including medicinal chemistry, complete synthesis of natural products, and materials-based applications. In contrast, arylene-derived carbazoles, also known as carbazolyne, have only had limited application in the field of chemical synthesis. Examples from more recent times include the production of carbazolyne via the hexadehydro-Diels–Alder reaction, the utilization of a silyl precursor, and the utilization of traditional dehydrohalogenation chemistry.

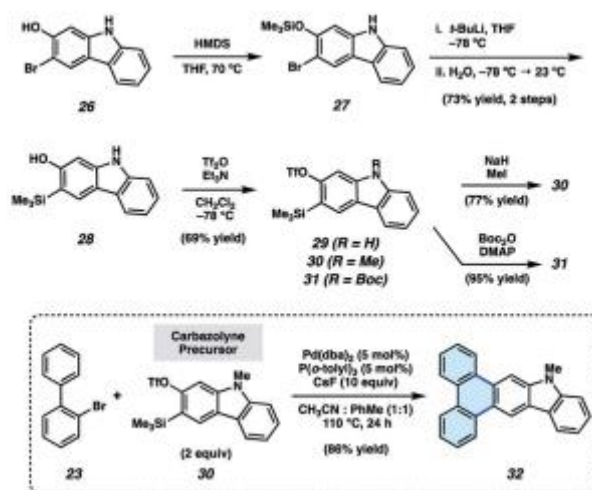
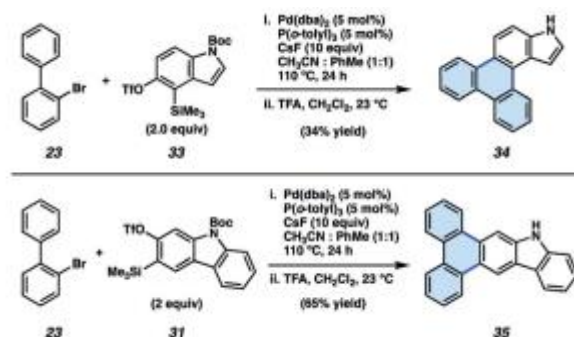


Figure 3 Synthesis of Carbazolyne Precursors.

We developed the concise approach to carbazolyne precursors shown in hydroxycarbazole because silyl precursors to carbazolynes were not known in the literature. Hydroxycarbazole (26) was treated with HMDS to afford silyl ether which, in turn, was carried forward in a retroBrook rearrangement sequence to afford silyl alcohol. The production of silyl with a yield of 69% went off without a hitch thanks to tri. Through the processes of methylation and Boc-protection, respectively, the N–H molecule was converted into the protected derivatives and NMe-carbazolyne precursor was utilized in our p-extension approach, and the circumstances used were those that had been previously improved. It came as a pleasant surprise to find that the reaction between 2-bromobiphenyl and N-me-carbazolyne precursor catalyzed by Pd produced p-extended carbazole with an 86% yield. This is an illustration of the trapping of a carbazolyne intermediate that was catalyzed by a transition metal. Particularly noteworthy is the fact that this makes it possible to incorporate a carbazole moiety into a p-extended system in a single step. Using the approach that we developed, we also attempted to find out if it was

possible to obtain N–H derivatives of the indole and carbazole annulation products that we developed. In the end, it was discovered that N–H products could be obtained by using N-Boc protected hetaryne precursors in our methods. After subjecting 23 and the indolyne precursor to the conditions that are typical for our reactions, a treatment with acid (TFA) is performed in order to eliminate.



**Figure 4 Synthesis Of N–H Products 34 And 35.**

## CONCLUSION

We investigate the process of metallic complex formation, with the goal of clarifying the elements that influence the stability, shape, and reactivity of complexes. The importance of these complexes in catalytic processes, both in terms of their function in industrial applications and their impact on the environment, is emphasized by the fact that the emphasis is focused on the role that these complexes play. In this study, we investigate the electrical and optical characteristics of these metallic complexes in order to demonstrate their potential application in fields such as photovoltaics and luminous materials. By establishing a correlation between the structure of ligands and the complicated characteristics of complex systems, we provide insights into the rational design of novel materials with functions that are specifically suited.

## REFERENCES

1. Peters, A. T., & Freeman, H. S. (1991). *Colour chemistry: the design and synthesis of organic dyes and pigments*. Elsevier Applied Science. Sole distributor in the USA and Canada, Elsevier Science Pub. Co..
2. Roblin Jr, R. O., Williams, J. H., Winnek, P. S., & English, J. P. (1940). Chemotherapy. II. Some Sulfanilamido Heterocycles. *Journal of the American Chemical Society*, 62(8), 2002-2005.
3. J.D. Edward, M.N. Hughes and K.J. Rutt, *J. Chem. Soc. (A)*, 2101-2105 (1969).
4. Sharma, S. (2017). 2-(5-Chlorobenzo [d] thiazol-2-ylimino) thiazolidin-4-one derivatives as an antimicrobial agent. *Arabian Journal of Chemistry*, 10, S531-S538
5. Ali, M. A., Mirza, A. H., Ting, W. Y., Hamid, M. H. S., Bernhardt, P. V., & Butcher, R. J. (2012). Mixed-ligand nickel (II) and copper (II) complexes of tridentate ONS and NNS ligands derived from S-alkyldithiocarbazates with the saccharinate ion as a coligand. *Polyhedron*, 48(1), 167-173.



6. Biswas, S., Pramanik, A. K., & Mondal, T. K. (2015). Palladium (II) complex with thiazole containing tridentate ONN donor ligand: Synthesis, X-ray structure and DFT computation. *Journal of Molecular Structure*, 1088, 28-33.
7. Haas, K. L., & Franz, K. J. (2009). Application of metal coordination chemistry to explore and manipulate cell biology. *Chemical reviews*, 109(10), 4921-4960.
8. Jana, S., Jana, M. S., Sarkar, D., Paira, M. K., & Mondal, T. K. (2013). Ruthenium carbonyl complexes of 3-(2-(methylthio) phenylazo)-4-hydroxy-3-penten-2-one: Synthesis, spectral characterization, electronic structure and catalytic activity. *Journal of Molecular Structure*, 1054, 83-88.
9. Bazel, Y., Tupys, A., Ostapiuk, Y., Tymoshuk, O., Imrich, J., & Šandrejová, J. (2018). A simple non-extractive green method for the spectrophotometric sequential injection determination of copper (ii) with novel thiazolylazo dyes. *RSC Advances*, 8(29), 15940-15950.
10. Yadav, P. S., & Senthilkumar, G. P. (2011). Benzothiazole: different methods of synthesis and diverse biological activities. *International journal of pharmaceutical sciences and drug research*, 01-07.
11. Fan, X., Zhu, C., & Zhang, G. (1998). Synthesis of 2-[2-(5-methylbenzothiazolyl) azo]-5-dimethylaminobenzoic acid and its application to the spectrophotometric determination of nickel. *Analyst*, 123(1), 109-112.
12. Karipcin, F., Dede, B., Percin-Ozkorucuklu, S., & Kabalcilar, E. (2010). Mn (II), Co (II) and Ni (II) complexes of 4-(2-thiazolylazo) resorcinol: Syntheses, characterization, catalase-like activity, thermal and electrochemical behaviour. *Dyes and Pigments*, 84(1), 14- 18.
13. Wang, M., Lin, J. M., Qu, F., Shan, X., & Chen, Z. (2004). On-capillary complexation of metal ions with 4-(2-thiazolylazo) resorcinol in capillary electrophoresis. *Journal of Chromatography A*, 1029(1-2), 249-254.
14. Al-Adilee, K. J., Abedalrazaq, K. A., & Al-Hamdiny, Z. M. (2013). Synthesis and Spectroscopic Properties of Some Transition Metal Complexes with New Azo-Dyes Derived From Thiazole and Imidazole. *Asian Journal of Chemistry*, 25(18).
15. Al-Adilee, K., & Kyhoiesh, H. A. (2017). Preparation and identification of some metal complexes with new heterocyclic azo dye ligand 2-[2-(1-Hydroxy-4-Chloro phenyl) azo]-imidazole and their spectral and thermal studies. *Journal of Molecular Structure*, 1137, 160-178.