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Ni (II) COMPLEX OF DINITROPHENYLHYDRAZONE: SYNTHESIS, CHARACTERIZATION, AND ADMET PREDICTION

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ABSTRACT

This study reports the synthesis, characterization, and ADMET prediction of a new dinitrophenyl hydrazone ligand obtained through the condensation of 2,4-dinitrophenylhydrazine (2,4-DNP) and 2-hydroxy-1,2-diphenylethan-1-one (benzoin), together with its corresponding Ni (II) complex. The synthesized compounds were characterized using melting point determination, molar conductivity measurements, UV-Visible spectroscopy, FT-IR spectroscopy, and ^{1}H and ^{13}C NMR analyses. The compounds were obtained in good yields, while molar conductivity values of 111 and 72 S cm² mol⁻¹ for the ligand and Ni (II) complex, respectively, indicated their electrolytic nature. Spectroscopic investigations confirmed successful complex formation through coordination of the azomethine nitrogen (C=N) and nitro oxygen (-NO_2) donor sites to the Ni (II) ion. The present study further investigates the ADMET profiles of the synthesized compounds using SwissADME and ProTox-II tools. ADMET prediction results suggested that metal complexation improved gastrointestinal absorption, aqueous solubility, and oral bioavailability. Toxicity predictions further indicated differences in the toxicity profiles of the ligand and metal complex, with both compounds falling within acceptable toxicity classes for preliminary drug discovery considerations. Overall, the study demonstrates the potential of the synthesized compounds as promising candidates for pharmacological exploration, therefore, further studies are recommended to experimentally validate the predicted pharmacokinetic and toxicological properties.

Keywords: Benzoin, Ni (II), Pharmacokinetic, Dinitrophenylhydrazone, ADMET.

1. Introduction

Diabetes Hydrazone functional groups are increasingly recognized as key structural motifs in bioactive compounds (Wahbeh & Milkowski, 2019) with numerous clinically relevant pharmaceutical agents incorporating this moiety (Çakmak *et al*., 2024). Owing to their broad pharmacological relevance, hydrazone-based compounds have garnered considerable attention from the medicinal chemistry community (Ibraheem *et al*., 2024). Researchers have been actively synthesizing these derivatives and

evaluating their biological potential through *in vitro* studies (Sıcak *et al*., 2025). Collectively, these investigations have demonstrated that hydrazone compounds exhibit a wide spectrum of pharmacological activities including analgesic, anti-inflammatory, antitubercular, anticancer and antibacterial (Czyżewska *et al*., 2025; Tumosienė *et al*., 2025) effects with the specific activity largely dependent on the nature of their substituents.

Transition metal complexes constitute a versatile and rapidly expanding area of research in chemistry, biochemistry, and medicine. Their distinctive electronic properties, rich reactivity patterns, and diverse coordination geometries make them valuable tools for probing fundamental chemical principles and for understanding how metal-based species interact with biological molecules and cellular systems, thereby informing novel therapeutic strategies for a broad spectrum of diseases (Abdolmaleki *et al*., 2025; Berhanu, 2023)

Ni (II) hydrazone complexes exhibit enhanced pharmacological potential because of their favorable redox behavior, the nature of the hydrazone ligand, the identity of the metal center, and the resulting coordination geometry, all of which modulate reactivity toward biological substrates and cellular targets (Kumar *et al*., 2024; Vrdoljak *et al*., 2023). Therefore, complexation of organic hydrazone ligands with transition metals often improves medicinal properties by enhancing stability, solubility, and bioavailability, while also facilitating targeted delivery to specific tissues or organelles, which can result in higher efficacy and reduced off-target toxicity compared with the free ligands (Anitha *et al*., 2025; Ugochukwu *et al*., 2021; Otuokere *et al*., 2020). In addition, coordination can alter the pharmacokinetic and pharmacodynamic profiles of the drug, including distribution, plasma-protein binding, and metabolic stability, potentially leading to improved therapeutic outcomes (Naeini *et al*., 2024). Transition metal complexes have demonstrated significant therapeutic potential in diverse disease areas, including cancer, microbial infections, and neurological disorders (Otuokere *et al*., 2022), with modern metallodrugs and metal-based formulations offering mechanisms beyond conventional organic agents, such as DNA distortion, redox-mediated cytotoxicity, enzyme inhibition, and modulation of metal-homeostasis pathways (Robert *et al*., 2025; Tan *et al*., 2025; Kostova, 2024; Otuokere *et al*., 2022; Edozie *et al*., 2020; Otuokere *et al*., 2019).

To better understand and predict these biological effects, theoretical and computational chemistry approaches have become indispensable tools in modern research. In modern drug design, theoretical and computational approaches have gained great importance as computational approaches are adapted to circumvent the high costs of unnecessary use of resources and time. In particular, ADMET contains the pharmacokinetic profile of a compound (drug molecule) and plays a significant role in determining its pharmacodynamics activities (Eberendu *et al*., 2025; Otuokere *et al*., 2019). A good drug candidate can be consumed in the desired time as well as distributed through the entire body for its efficient action and metabolism. Moreover, they are to be easily metabolised and eliminated from blood stream without causing any toxic effects. These properties are summed up by the term ADME (absorption, distribution, metabolism and elimination) or better ADMET when toxicity studies are included. In addition, the lead compounds ought to possess the physicochemical properties set by different drug filters such as Lipinski`s rule of five (RO5) to be regarded as drug-like compounds. Some studies have shown that drug failed at clinical trials due to its adverse side effect and their toxicity which has been proven to be very detrimental and expensive in the drug development (Venkataraman *et al*., 2025; Fu *et al*., 2024; Niu *et al*., 2024). It is time consuming, tedious and costly to evaluate drug-likeness and ADMET parameters of lead compounds using conventional

methods. Although computational methods are not confirmatory, they do provide information of the most likely drug-like compounds out of an array of compounds.

A crucial determinant in developing potent therapeutic agents is the appropriate selection of precursors for ligand synthesis. 2,4-Dinitrophenylhydrazine (2,4-DNP), an analog of hydrazine (H_2N-NH_2), plays a vital role in biological and pharmaceutical applications through its reactive hydrazone derivatives and, moreover, an essential class of drugs (Çetin & Dede, 2025; Wang *et al*., 2024). The 2,4-dinitrophenyl moiety acts as a strong electron-withdrawing group, modulating electronic properties via resonance and inductive effects, which stabilizes the hydrazone linkage. This enhances reactivity and enables non-covalent interactions like π-π stacking and charge-transfer, supporting molecular recognition and supramolecular assembly. Nitrogen and oxygen donor atoms in the structure facilitate coordination, ideal for bioinorganic applications (Robert *et al*., 2025). Integration of the dinitrophenylhydrazone into ligands like DPHD boosts drug-likeness, complying with Lipinski's Rule of Five and showing favorable ADME profiles which amplifies the bioactive properties in metal complexes after complexation.

Similarly, Benzoin, a hydroxy ketone bearing two phenyl rings, serves as a key precursor for synthesizing hydrazone-metal complexes with promising drug-like and biological activities. Recently, studies have indicated that benzoin and its derivatives have potential in the development of biological compounds thus, attracting attention (Robert *et al*., 2025; Çetin & Dede, 2025). This background supports the rationale for selecting benzoin as a starting material in the design of new bioactive compound. To the best of our knowledge, there is lack of report on the synthesis of benzoin-dinitrophenylhydrazine derivative and its Ni (II) complex, followed by a comprehensive investigation combining experimental characterization and ADMET profiling. This integrated approach not only provides detailed structural, spectral, and pharmacokinetic insights but also highlights the potential of these compounds as promising bioactive agents, thereby offering a significant contribution to the development of metal-based therapeutics.

Considering all these factors, the primary objective of this work was to synthesize new dinitrophenylhydrazone ligand from benzoin and 2,4-DNP, together with its Ni (II) complex. Additionally, a comprehensive characterization of the compounds was conducted using various spectroscopic methods in conjunction with ADMET predictions were conducted to assess the pharmacokinetic behavior and drug-like properties of the synthesized compounds. All the findings confirm these active compounds as possible metal-based medicines with potential therapeutic agent.

2. Materials and methods

2.1 Materials and physical measurements

The reagents used were of analytical grade. They are methanol, ethanol, hexane, dimethylsulfoxide, 2,4-dinitrophenylhydrazine, 2-Hydroxy-1,2-diphenylethan-1-one, Nickel (II) chloride. Melting points were determined using a Gallenkamp melting point apparatus. The molar conductivities of the compounds in dimethylformamide at room temperature were determined using an OMEGA digital conductometer (CD5126 by OMEGA industry, UK). Solubility was carried out in test tubes using various solvents such as distilled water, methanol, ethanol, hexane and dimethylsulfoxide. The electronic absorption spectra were obtained with a Thermo Scientific Orion Aquamate 8100 Uv-Vis Spectrophotometer in the range 800-200

nm.. The infrared spectra of the complexes, as pressed KBr disc, were recorded on an Agilent Cary 630 FT-IR in the region 4000-400 cm^{-1}. The Nuclear magnetic resonance of the compounds in chloroform were recorded on a Nanalysis-X685 (60MHz)**.** Swiss ADME online platform (http://www.swissadme.ch) was used to predict the ADME properties, the drug-like characteristics, and possible drug-drug interactions. The toxicological predictions were produced based on the ProTox-II web tool (tox.charite.de/).

2.2 Synthesis of DPHD

The DPHD ligand was synthesized by following a modified version of the procedure as described in literature by Eberendu *et al*. (2025). 0.01 mole (1.98 g) of 2,4-dinitrophenylhydrazine (2,4-DNP) was dissolved in an acidified methanolic medium prepared from concentrated sulfuric acid (10 mL), distilled water (15 mL), and methanol (25 mL). The mixture was gently warmed and filtered to obtain a clear reaction solution. 0.01 mole (2.12 g) of 2-hydroxy-1,2-diphenylethan-1-one (benzoin) was gradually added to the filtrate with continuous stirring and heated to near boiling (Figure 2.2a). The resulting precipitate was allowed to cool to room temperature, after which it was recrystallized from methanol and dried in a desiccator.

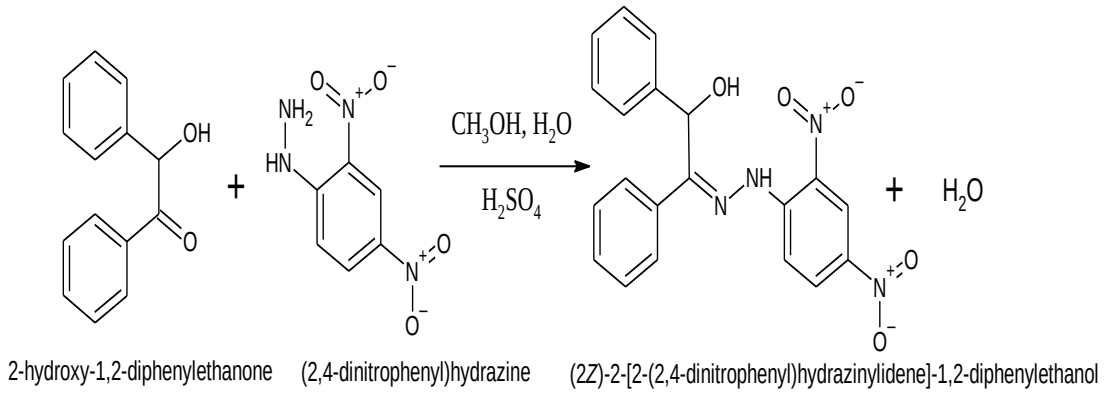


Figure 2.2a: Synthesis of DPHD Ligand

2.3 Synthesis of [Ni(DPHD)]

The [Ni(DPHD)] complex was synthesized by following a modified version of the procedure as described in literature by Eberendu *et al*. (2025). 0.01 mole (3.92 g) of the DPHD ligand was dissolved in 10 mL of hot methanol and added dropwise to a hot methanolic solution (10 mL) containing 0.01 mole (2.37 g) of $NiCl_2 \cdot 6H_2O$ under continuous stirring for 5 min. A colored precipitate gradually formed indicating complex formation and the precipitate was separated by filtration process. The solid precipitate was washed several times with distilled water and methanol to purify the precipitates. The reaction equation is shown in Equation (2.3a).

$$NiCl_2.6H_2O + C_{20}H_{16}N_4O_5 \rightarrow [Ni(C_{20}H_{16}N_4O_5)] + 6H_2O + Cl_2 \qquad (2.3a)$$

3 Results and Discussion

Table 3.1 shows that the DPHD ligand was orange in colour while its [Ni(DPHD)] complex exhibited a greenish-yellow colour which was different from that of the ligand. The observed color change is attributed to electronic delocalization within the compound which confirms a successful coordination, consistent with findings reported in recent studies on hydrazone complexes (Chaltsev *et al*., 2024). The ligand and its [Ni(DPHD)] complex have high melting points of 110 ^{o}C and 137 ^{o}C, respectively. Çetin & Dede, (2025), in their studies reported that hydrazone complexes exhibit higher melting points than their free ligands due to stronger intermolecular interactions and increased lattice energy from metal coordination. The ligand recorded a high percentage yield of 89 % and [Ni(DPHD)] complex yielded 78 %, reflecting highly efficient hydrazone condensation contrasted by typical chelation and purification losses in Ni (II) coordination chemistry (Robert *et al*., 2025). The DPHD ligand and its [Ni(DPHD)] complex showed a molar conductivity of 111 $S.cm^2.mol^{-1}$ and 72 $S.cm^2.mol^{-1}$ respectively, indicating their electrolytic nature. The decrease in conductivity upon complexation indicates reduced ionic mobility and a lower degree of dissociation in solution. This may be attributed to coordination of the ligand donor atoms to the Ni (II) center, leading to the formation of a more stable chelated structure with reduced charge mobility (Umasare *et al*., 2024). Table 3.2 shows that both DPHD and [Ni(DPHD)] complex were readily soluble in dimethylsulfoxide (DMSO), slightly soluble in distilled water, methanol and ethanol, and insoluble in hexane. This solubility behaviour reflects their moderate polarity due to the presence of hydrazone and nitro groups together with aromatic rings. The high solubility in DMSO is attributed to its strong solvating ability toward hydrazone compounds and their metal complexes, consistent with related studies on hydrazone based complexes (Kumar *et al*., 2023).

Table 3.1: Physical properties of the compounds

Compounds	Colour	Yield(%)	Molar Conductance ($S.cm^2.mol^{-1}$)	M.P(^{o}C)
DPHD	Orange	89	111	110
[Ni(DPHD)]	Greenish yellow	78	72	137

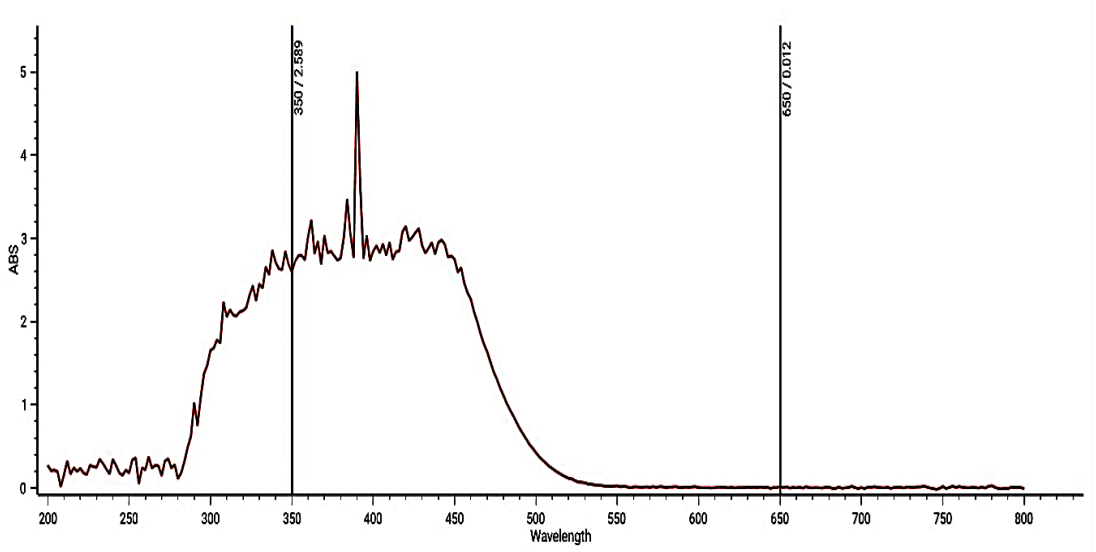
Table 3.2: The Solubility profile of the compounds

Compounds	Hexane	Distilled water	Methanol	Ethanol	DMSO
DPHD	INS	SLS	SLS	SLS	SLB
[Ni(DPHD)]	INS	SLS	SLS	SLS	SLB

****SLS - Slightly soluble, INS - Insoluble, SLB - Soluble**

UV-visible spectroscopy

A comparison of the Uv-vis spectrum of the ligand and its metal complex was made in Figure 3.1. The spectra exhibited distinct electronic transitions which confirmed successful coordination of the ligand to the metal centre and these shifts also specified changes in the electronic environment. The DPHD ligand exhibited prominent absorption bands at λ = 305-330 nm and 380-390 nm which was assigned π-π* and n-π* transitions of the aromatic rings and azomethine chromophores, respectively. Upon coordination to Ni (II) centre, these bands shifted slightly to λ = 305-340 nm and 370-400 nm with a new band detected at 430 nm. The bathochromic shifts indicate coordination of the ligand donor atoms to the Ni (II) centre resulting in increased electron delocalization within the chelate ring (Saleh *et al*., 2026). According to ligand field theory, coordination of the DPHD ligand creates a crystal field around the Ni (II) center generates a crystal field that splits the metal d-orbitals, giving rise to additional electronic transitions characteristics of Ni (II) hydrazone (Basaran *et al*., 2024; Umasare *et al*., 2024). The new absorption band at 430 nm is attributed to a d-d transition, confirming complex formation and strong metal-ligand interactions as commonly observed in Ni (II) complexes (Islam *et al*., 2026).



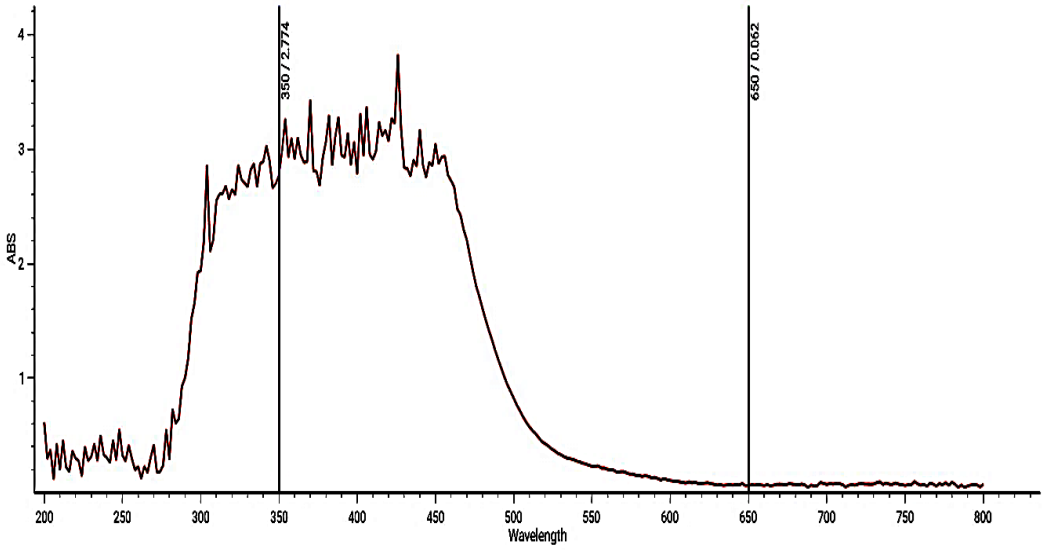


Figure 3.1: UV/VIS spectrum for DPHD and [Ni(DPHD)]

Infrared spectra

To verify the formation of the complex, the infrared spectrum of the ligand is compared with that of the complex which is showed in Figure 3.2. The IR spectra of the DPHD ligand show an intensive band around 1658 cm^{-1} assigned to the azomethine group (-C=N) which shifted to 1610 cm^{-1} in the metal complex. This signifies electron donation from the azomethine nitrogen to the Ni (II) center, which decreases the C = N bond order (Venkatesh *et al*., 2026; El-Boraey & El-Gammal, 2025). The weak broad band at 3380 cm^{-1} and 3227 cm^{-1} were assigned to hydroxyl (-OH) and amine (-NH) stretching vibrations (Mbe-Majoumo *et al*., 2024), respectively while [Ni(DPHD)] complex exhibited bands at 3376 cm^{-1} and 3231 cm^{-1}, indicating that the phenolic oxygen and the -NH group did not actively participate in coordination. This was further confirmed by the absence of C-O band and a slight shift observed at the -NH band for the complex (Venkatesh *et al*., 2026). The characteristic band at 1386 cm^{-1} in the ligand spectra was assigned to the frequency vibration of aromatic -NO_2. A noticeable shift in the IR band of the [Ni(DPHD)] complex was observed at 1338 cm^{-1} indicating that this functional group participates in bonding. Similar shifts suggesting coordination were also observed by Robert *et al.* (2025) and Eberendu *et al*. (2025).

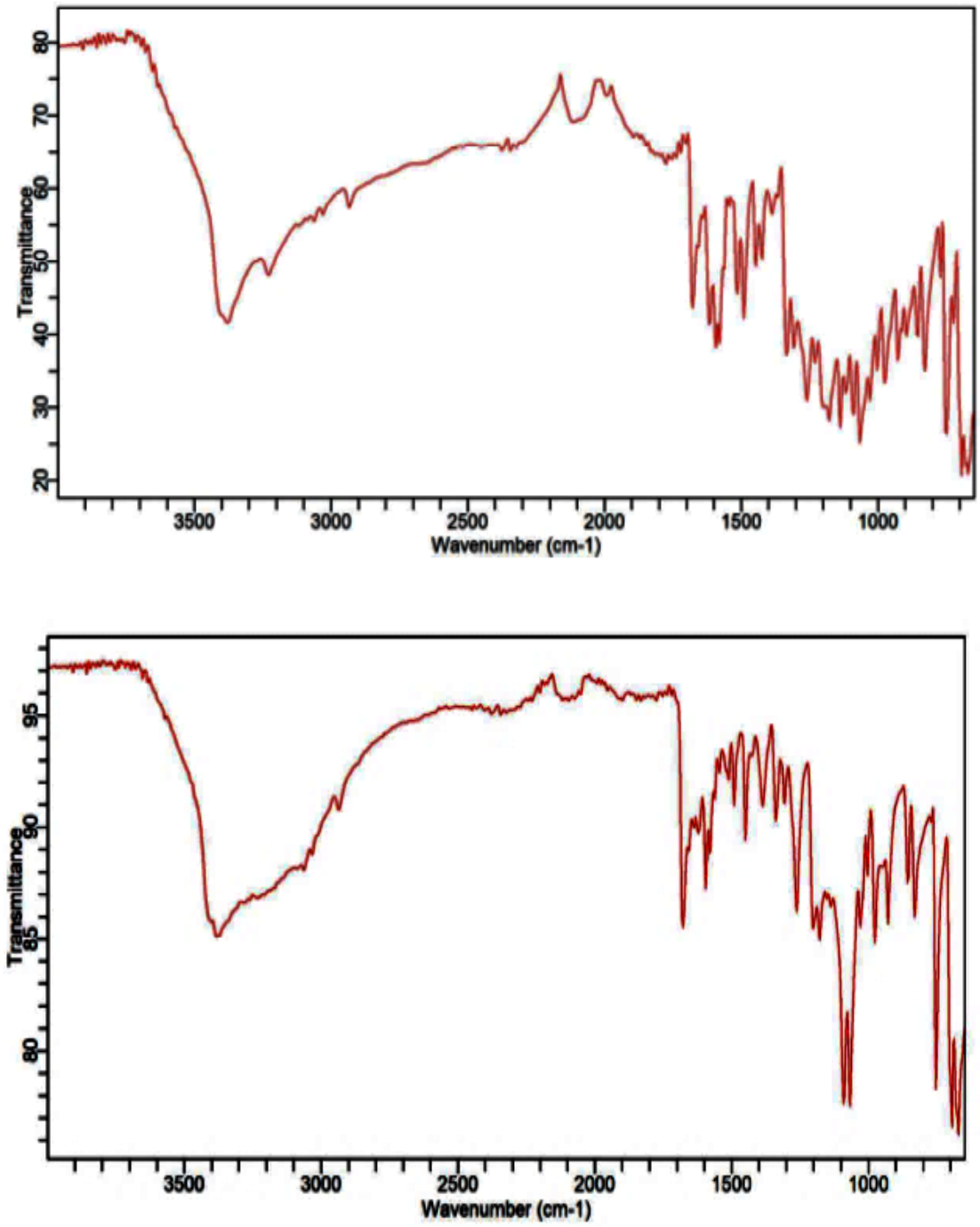


Figure 3.2:FTIR spectra for DPHD and [Ni(DPHD)]

Nuclear magnetic resonance (NMR)

The ^{1}H NMR spectrum (Figure 3.3) of DPHD revealed the presence of aromatic protons from phenyl groups and 2,4-DNP in the region δ 7.3 – 7.9 ppm. Upon complexation, the [Ni(DPHD)] complex showed a slight downfield shift to δ 7.4–7.9 ppm, attributable to changes in electron density around the ligand framework caused by coordination to the Ni (II) ion (Qurban *et al*., 2022). The azomethine proton (HC=N) appeared as a distinct signal at δ 8.5 ppm in the free ligand but became broadened and overlapped with the aromatic

proton signals in the metal complex. This behavior suggests the involvement of the azomethine nitrogen in coordination and may result from coordination-induced line broadening and chemical shift changes (El-Boraey & El-Gammal, 2025). These spectral features are consistent with the proposed structure of the hydrazone ligand and provide evidence for successful complex formation.

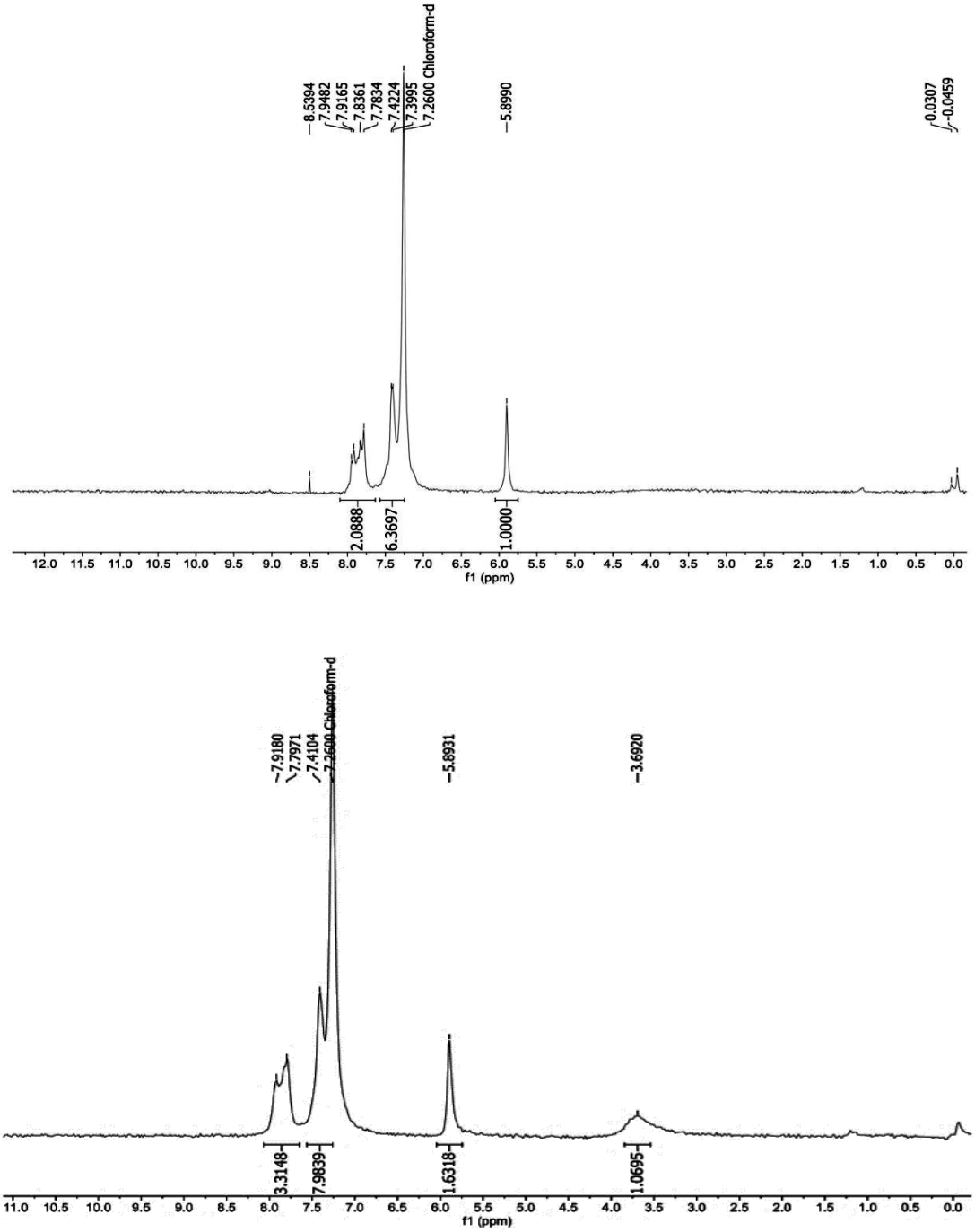
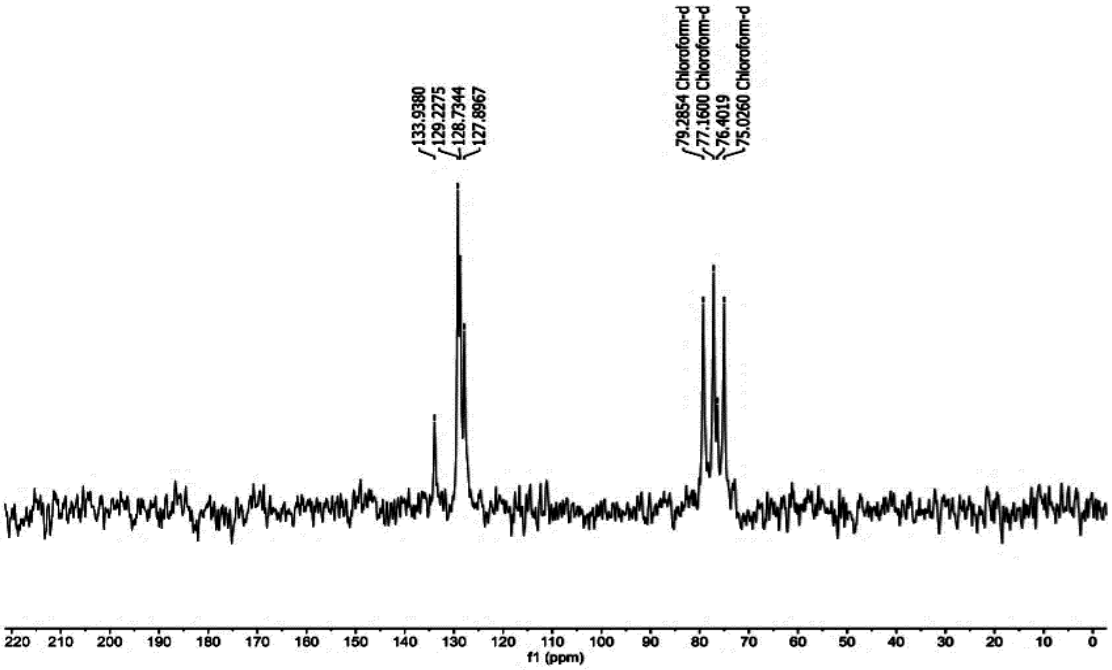


Figure 3.3: ^{1}H-NMR spectra for DPHD and [Ni(DPHD)]

Figure 3.4 shows the ^{13}C-NMR spectra for the ligands and [Ni(DPHD)] complex. The peaks at δ 75.02 - 79.28 ppm are from deuterated chloroform solvent ($CDCl_3$) and are consistent with common literature

values (Marchetti *et al*., 2022). The peaks at δ 127.89 ppm, 128.73 ppm, and 129.22 ppm were assigned to aromatic carbons and this multiplet signals suggest substituted aromatic rings, appeared at δ 127.96 - 133.96 ppm for [Ni(DPHD)] complex. These are consistent with reported values in the literature for similar phenyl groups for hydrazone compounds (Saheeb & Damdoom, 2020). The imine carbon (-C=N) signal appeared at δ 133.93 ppm in the free ligand and shifted downfield to δ 134.04–139.26 ppm upon complexation, indicating deshielding due to coordination of the azomethine nitrogen atom to the Ni (II) ion. This observation supports the involvement of the azomethine group in metal coordination, as previously reported by Salah *et al*. (2019). The peak at δ 76.40 ppm for DPHD and δ 76.38 ppm for [Ni(DPHD)] complex was assigned carbon to which the -OH group is attached.



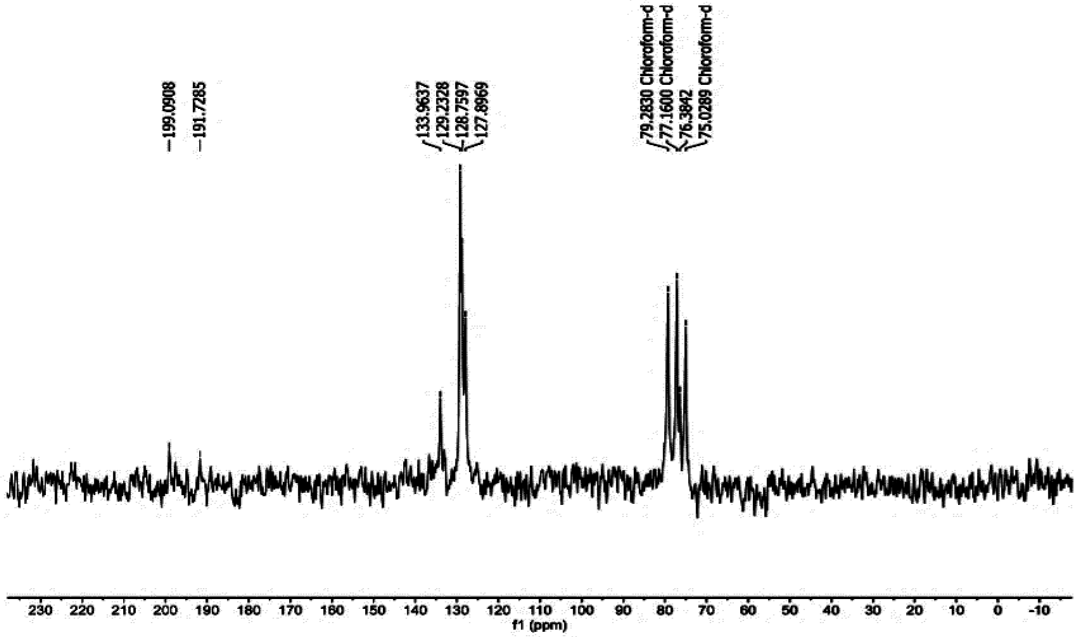


Figure 3.4: ^{13}C-NMR spectra for DPHD and [Ni(DPHD)]

Based on the spectroscopic studies, the structures in Figure 3.5 have been proposed for the ligand and its [Ni(DPHD)] complex

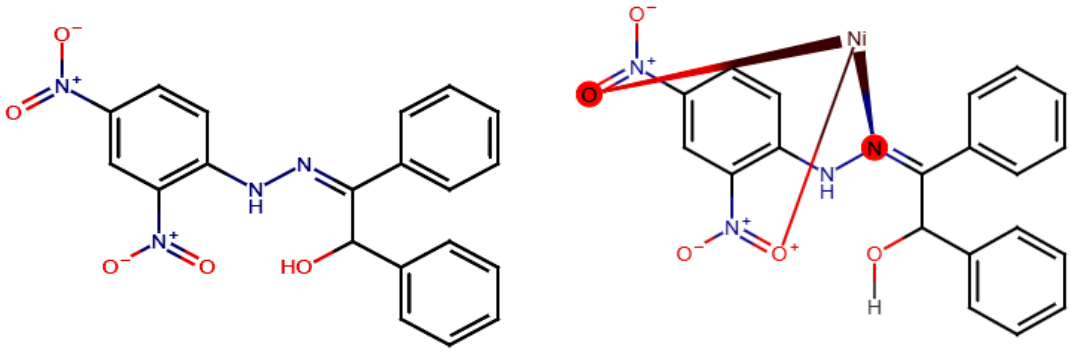


Figure 3.5: Proposed structure for DPHD and [Ni(DPHD)]

***In silico* studies**

The DPHD ligand and its [Ni(DPHD)] complex have been studied for drug-likeness properties using *in silico* tools like SwissADME.

Drug-likeness prediction

Lipinski rule of five (RO5) is a predictive model postulated by Lipinski *et al*. (2004) used for assessing the suitability of small molecules particularly concerning their absorption and permeation. The RO5 states that for a compound to be considered orally active, it should not violate more than one of the set criteria. The predictions as shown in Table 3.3, the compounds exhibited zero violations of RO5, indicating strong compliance with this key criterion for oral drug-likeness. Therefore, the compounds hold potential as effective oral drugs.

ADME predictions

The ADME studies (Table 3.3) predicted both compounds to exhibit a Topological Polar Surface Area (TPSA) below the threshold value of 140 Å^2 which is in compliance with Lipinski *et al*. (2004) rule for the requirement of potential oral drug candidate. The predicted Log *S* values using the ESOL model demonstrate that the [Ni(DPHD)] complex (Log *S* = −4.29) is more water-soluble compared to the DPHD ligand (Log *S* = −5.89), indicating enhanced bioavailability which aligns with Landolsi *et al*. (2026), who reported enhanced solubility and bioavailability characteristics for a novel Ni (II) complex. Aqueous solubility is a critical factor determining how well a drug will be absorbed into the bloodstream and reach its target. Both the DPHD ligand and [Ni(DPHD)] complex exhibited an identical predicted bioavailability score of 0.55, indicating that these compounds would be available in good proportion after digestion. Similar results from Carvalho Souza *et al*. (2022) support the suitability of Ni (II) complexes for oral drug development. Pan-assay interference compounds (PAINS) are substructures known to cause off-target effects and false positives in drug discovery. They are sometimes referred to as frequent hits or promiscuous chemicals (Otuokere *et al.*, 2025; Magalhães *et al.*, 2021). In our predictive model, none of the compounds exhibited PAINS which is a positive indicator of their specificity and potential safety in further testing. The

synthetic accessibility prediction scores for the compounds shows easy route of synthesis (Robert *et al*., 2025).

Enzyme Interaction Prediction

The ADMET analysis (Table 3.3) further revealed the interactions predicted between the cytochromes and the test compounds. Cytochrome P450 (CYP) enzyme family are crucial for drug metabolism as they regulate the biotransformation of over 90% of medications (Testa & Krämer, 2008). The DPHD ligand is predicted to inhibit CYP2C19 and CYP2C9, while the [Ni(DPHD)] complex shows no inhibition of any CYP isoforms, indicating that coordination with Ni (II) eliminates potential drug-drug interaction risks associated with CYP enzyme inhibition. This absence of CYP inhibition in [Ni(DPHD)] suggests improved safety and reduced risk of drug interactions compared to the ligand, which aligns with recent Ni (II) ADMET studies exhibiting favorable pharmacokinetic properties without CYP inhibition (Saha *et al*., 2026). The skin permeation predictions gave coefficients (Log Kp < -7 cm/s), indicating poor transdermal absorption. This suggests that the test compounds are less suitable for transdermal delivery but advantageous for oral or parenteral administration, minimizing dermal exposure risks (Etim *et al*., 2025).

Bioavailability radar

The bioavailability radar provides a rapid assessment of drug-likeness based on six physicochemical properties: lipophilicity, size, polarity, solubility, flexibility, and saturation (Ritchie *et al*., 2011; Lovering *et al*., 2009). As shown in Table 3.3, the DPHD ligand was predicted to have poor oral bioavailability due to deviations in molecular size and flexibility whereas the [Ni(DPHD)] complex fell closer to the optimal range, suggesting improved oral bioavailability. These results indicate that metal complexation enhanced the ligand's drug-likeness and oral absorption potential.

BOILED-Egg

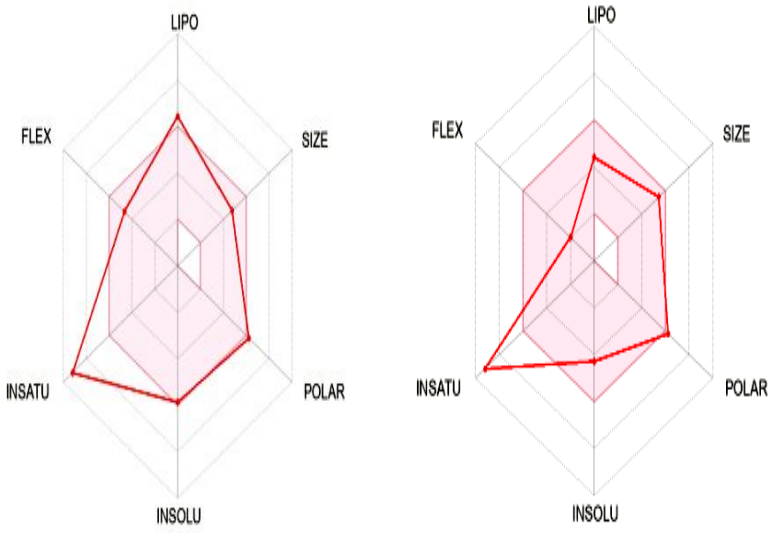
The BOILED-Egg model predicts passive gastrointestinal absorption (HIA) and blood-brain barrier (BBB) permeation based on molecular lipophilicity (WLOGP) and polarity (TPSA) (Daina & Zoete, 2016). As shown in Table 3.3, the DPHD ligand appeared as a blue coloured dot outside both the white (HIA) and yolk (BBB) regions, meaning it will not be well absorbed by the intestines and has limited BBB permeation. In contrast, the [Ni(DPHD)] complex exhited blue coloured dot within the white region, meaning it has better intestinal absorption and oral bioavailability. The blue dot labeled as PGP^+ indicates that the test compounds are P-gp substrate that may be easily effluxed by P-glycoprotein transporters (Rathi *et al*., 2026).

Table 3.3: ADMET properties of DPHD and [Ni(DPHD)] complex

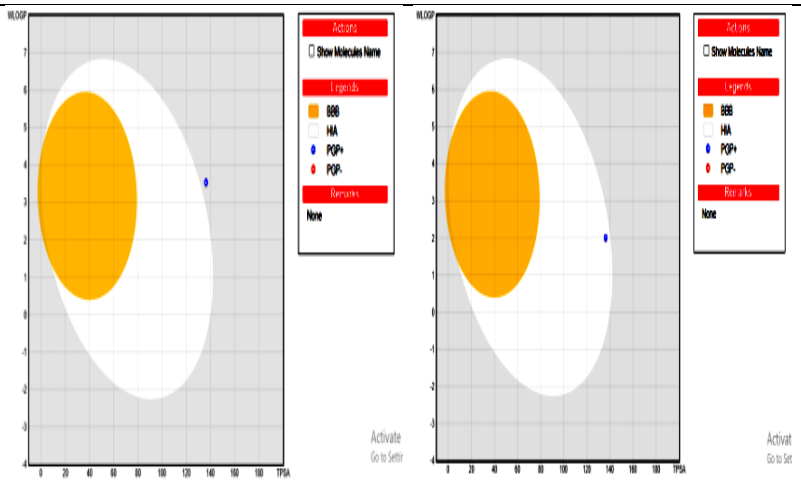
Physicochemical Properties		
Formular	DPHD	[Ni(DPHD)]
Molecular weight (g/mol)	392.36	451.06
Num. H-bond acceptors	6	5
Num. H-bond donors	2	2
Molar Refractivity	112.02	124.93
TPSA ($Å^2$)	136.26	136.26
	Lipophilicity	
Log *P*	-0.37	-4.73

	Water Solubility	
Log *S* (ESOL)	-5.89	-4.29
Class	Moderately soluble	Moderately soluble
	Pharmacokinetics	
GI absorption	Low	High
BBB permeant	No	No
P-gp substrate	Yes	Yes
CYP1A2 inhibitor	No	No
CYP2C19 inhibitor	Yes	No
CYP2C9 inhibitor	Yes	No
CYP2D6 inhibitor	No	No
CY3A4 inhibitor	No	No
Log K_p (skin permeation) (cm/s)	-4.61	-7.47
	Druglikeness	
Lipinski	Yes, 0 violation	Yes, 0 violation
Bioavailability Score	0.55	0.55
	Medicinal Chemistry	
PAINS	0 alert	0 alert
Synthetic accessibility	4.01	5.42

Bioavailability radar



Boiled Egg diadram



	Toxicity Assessment	
Predicted LD_{50} (mg/Kg)	2690	900
Predicted toxicity class	5	4

Toxicity studies

Toxicity assessment is a crucial component of therapeutic drug development because it provides an early indication of the safety profile of potential drug candidates (Amorim *et al*., 2024). The Globally Harmonized System classifies the toxicity of compounds into six classes based on their LD_{50} values; the higher the class number, the lower the toxicity (Morris-Schaffer & McCoy, 2021). The DPHD ligand exhibited a predicted oral LD_{50} of 2690 mg kg^{-1} and was classified as GHS Class V, indicating low acute toxicity. Upon coordination with Ni (II), the LD_{50} decreased to 900 mg kg^{-1}, placing the [Ni(DPHD)] complex in GHS Class IV and suggesting a moderate increase in toxicity. Similar observations have been reported for Ni (II) Schiff base complexes with favorable pharmacological properties and acceptable toxicity profiles (Saha *et al*., 2026). Despite the observed increase in toxicity, the [Ni(DPHD)] complex remains within the moderately toxic category and does not fall into the highly toxic Classes I-III, indicating an acceptable predicted safety profile.

4. Conclusion

This study successfully synthesized a new hydrazone ligand through the condensation of 2,4-dinitrophenylhydrazine (2,4-DNP) and 2-hydroxy-1,2-diphenyl-ethan-1-one (benzoin), together with its corresponding Ni (II) complex, in high yields of 89% and 78%, respectively. The isolated compounds were air stable and exhibited distinct physicochemical properties, including a colour change from orange for the free ligand to greenish-yellow for the Ni (II) complex and an increase in melting point upon complexation, indicating enhanced thermal stability. Spectroscopic characterization by UV-Vis, FTIR, and NMR analyses confirmed the successful formation of the hydrazone ligand and its coordination to the Ni (II) ion through the azomethine nitrogen (C=N) and nitro (NO_2) oxygen donor atoms. The appearance of d-d transition bands in the electronic spectrum of the complex and the observed shifts in characteristic FTIR absorption bands further supported the proposed coordination mode. To complement the experimental study, ADMET prediction was performed. ADMET prediction revealed favorable pharmacokinetic properties, acceptable

oral bioavailability, and moderate toxicity profiles for both compounds, highlighting their potential as promising bioactive candidates.

Overall, the combined experimental and ADMET predictions demonstrate that Ni (II) complexation enhances certain physicochemical and pharmacokinetic characteristics of the ligand while maintaining desirable drug-likeness properties. Nevertheless, further *in vitro* and *in vivo* studies are required to validate the predicted biological activities, pharmacokinetic behavior, safety profiles, and also to establish their suitability for potential therapeutic applications.

Authors' Contribution

UFR carried out the experimental work, interpreted the results, and drafted the initial manuscript. IEO conceptualized and supervised the study, led in result interpretation and manuscript revision. JCN supervised the research and critically reviewed the manuscript. JCA drafted the initial manuscript, reviewed and edited the manuscript, resources. All authors reviewed and endorsed the final manuscript.

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