



iJRASET

International Journal For Research in
Applied Science and Engineering Technology



INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

Volume: 13 Issue: IV Month of publication: April 2025

DOI: <https://doi.org/10.22214/ijraset.2025.64981>

www.ijraset.com

Call:  08813907089

E-mail ID: ijraset@gmail.com

Synthesis, Characterization, and Antioxidant Activities of N-(Diphenylmethene) hydrazine carbothiohydrazide a new Schiff Bases Derived from Substituted benzophenones and their Complexes

Dr. Sanjay Kumar

Department of Chemistry, Patna University, Patna

I. INTRODUCTION

The use of metals for medicinal purposes has been exploited since very ancient times; for instance, silver has been used as a disinfectant agent for water and milk for thousands of years¹. Similarly, the application of gold in medicine can be dated back to 2500 BC and throughout the entire history of humanity it is possible to find traces of several applications of this noble metal to treat various diseases². Indeed, in the 19th century the complex dicyanoaurate(I) ($K[Au(CN)_2]$) was proposed by Koch for its bacteriostatic properties to fight tubercle bacillus, while in the 20th century, gold complexes were introduced to treat rheumatoid arthritis, leading to the approval of Auranofin by FDA in 1985. This latter compound is today the reference compound for gold complexes and, on the ground of the so-called repurposing strategy, has been proposed as promising anticancer agent and entered several clinical trials in US, some of which are still ongoing^{3,4}.

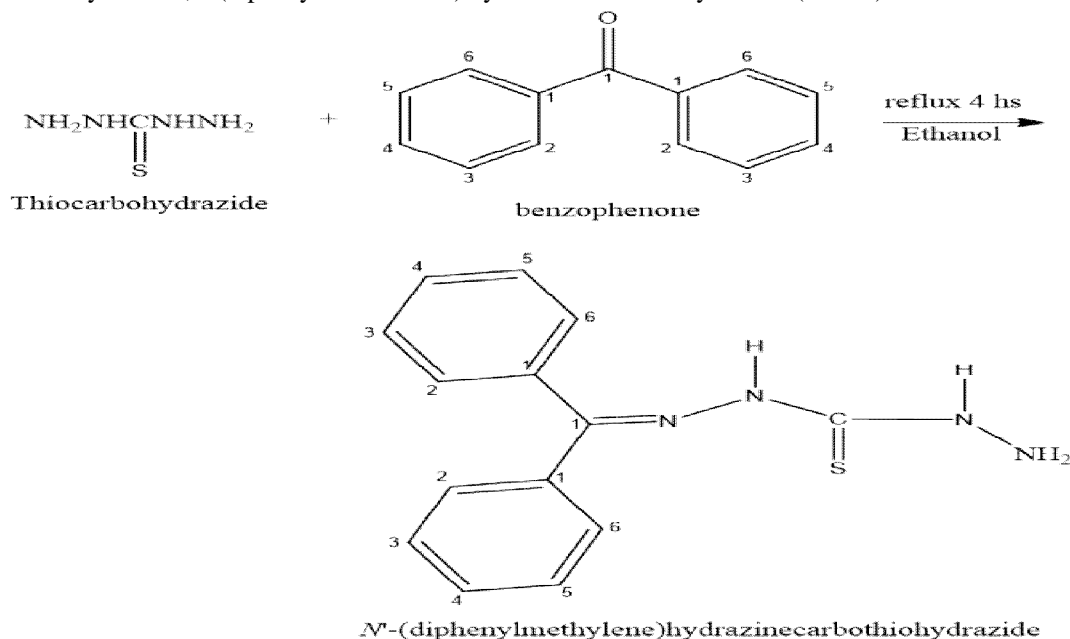
Beyond silver and gold, several bismuth, antimony and mercury compounds have been employed to combat bacterial and parasitic diseases. In this view, bismuth salts and antimony complexes have been proposed and used for eradication of *Helicobacter pylori* infection, and against leishmaniasis respectively⁵. Also, arsenic, in the form of trioxide (As_2O_3), is nowadays one of the reference drugs for the treatment of acute promyelocytic leukemia⁶. Several inorganic complexes are also used for diagnostic medicine as in the case of gadolinium-based contrast agents, ^{99m}Tc compounds for myocardial perfusion imaging⁷ and ⁶⁴Cu for PET imaging⁸. However, the most important impulse to the research of metal-based drugs with medicinal properties came from the serendipitous discovery of the antitumor features of cisplatin by Rosenberg and Loretta Van Camp in 1965⁹. Cisplatin was approved in 1978 by the FDA, and this event triggered enormous efforts by scientists in search of innovative and ameliorated inorganic anticancer drugs, leading to the approval worldwide of carboplatin and oxaliplatin analogs. This makes platinum-based drugs an essential arsenal for first- and second-line anticancer chemotherapy used in about 50% of clinical protocols¹⁰.

Metals complexes offer an extremely versatile and reliable tool for the development of improved medicinal compounds. Indeed, it is possible to finely tune the chemical properties of these complexes by controlling the metal center oxidation state and selecting the most appropriate ligands for each application. Thus, it is not surprising that the challenge in the development of innovative and improved metal-based drugs largely overlaps with the development of innovative and ameliorated ligands for the functional metal element.

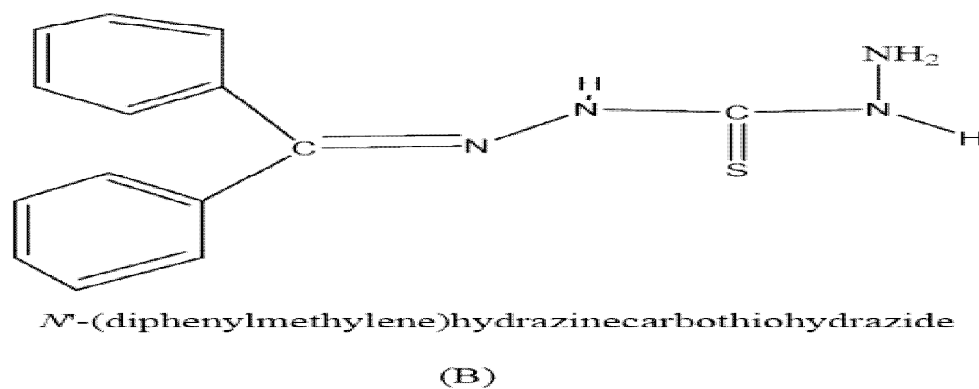
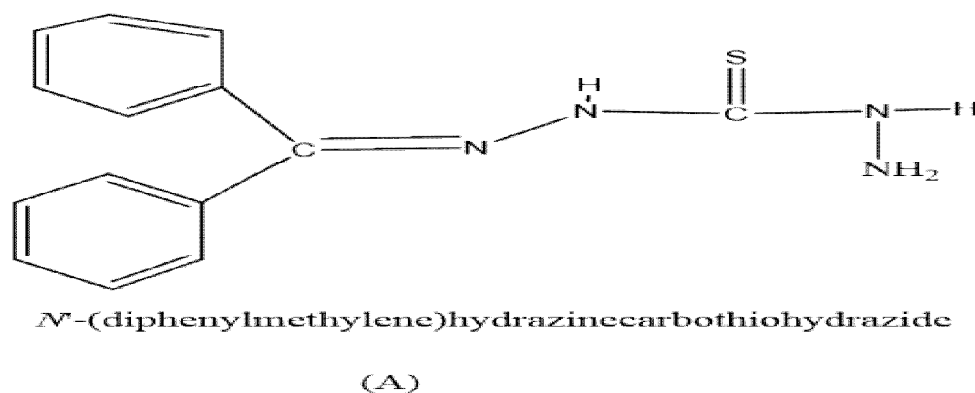
Among several ligands, thiosemicarbazones (TSCs), are a very attractive class of metal-chelating ligands, able to coordinate many transition metals through the sulfur as well as the azomethinic nitrogen atoms¹¹. They can act as N, S-multidentate ligands, and moreover, it is possible to modulate the binding properties/stoichiometries through the insertion of other heteroatoms into the backbone structure (i.e., phenolic or pyridyl moieties). They have a great variety of biological properties, both as free ligands and as metal complexes, and several studies have been published reporting on thiosemicarbazone-based complexes with medicinal applications¹²⁻²¹.

Beyond TSCs, in recent years, there has been growing interest in the coordination chemistry of thiocarbohydrazones (TCHs) compounds that share the general formula depicted in [Scheme 1a-c](#) and that can be considered the higher homologues of TSCs ([Scheme 1d](#)).

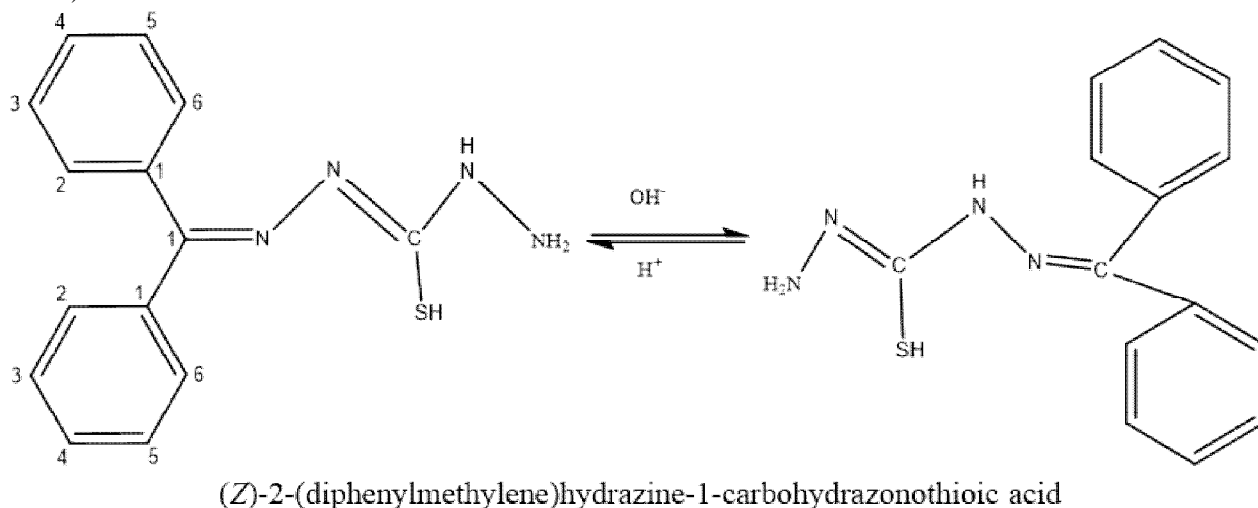
The first synthesis of these systems is dated 1925 and described the condensation of ketones and aldehydes with thiocarbohydrazide²². The earliest employ of this derivatives relied the hetero-ring closure of the aldehyde derived thiocarbohydrazones²²⁻²⁴. The condensation of benzophenone with thiocarbohydrazide in ethanol acidified with a few drop of glacial acetic acid results in the formation of thiocarbohydrazone, N (diphenylmethene) hydrazine thiocarbohydrazone (DTCH).



N-(Diphenylmethene) hydrazine carbothiohydrazide (DTCH) has different donor sites and it can exist in the following orientations of donor sites (A and B) also.



Due to the bulky size of diphenylketone, the hydrozone formed DTCH is expected to get stabilised with only one ketone molecule. As expected bis(diphenylmethylene) thiohydrazide could be obtained by rigorous refluxing in ethanol in slightly acidic medium. The ligand DTC contains thiocarbohydrazide in two or three orientation of $-NH-NH_2$ and thiocarbonyl group ($>C=S$). The molecule in neutral or acidic medium expected exist in thione tautomer. The thiol tautomer will be expected to be formed in basic medium (as shown below).



In neutral or slightly acidic medium it is expected that the ligand will coordinate as bidental neutral molecule. The orientation of third donor sites to coordinate with the same metal as tridentate donor molecule is improbable due to steric reason. The ligand has been used to prepare complexes of Cu(II), Ni(II), Zn(II), Cd(II), Co(II) and Mn(II). It has been found that the ligand fails to form pure Mn(II) complexes both in neutral and basic medium.

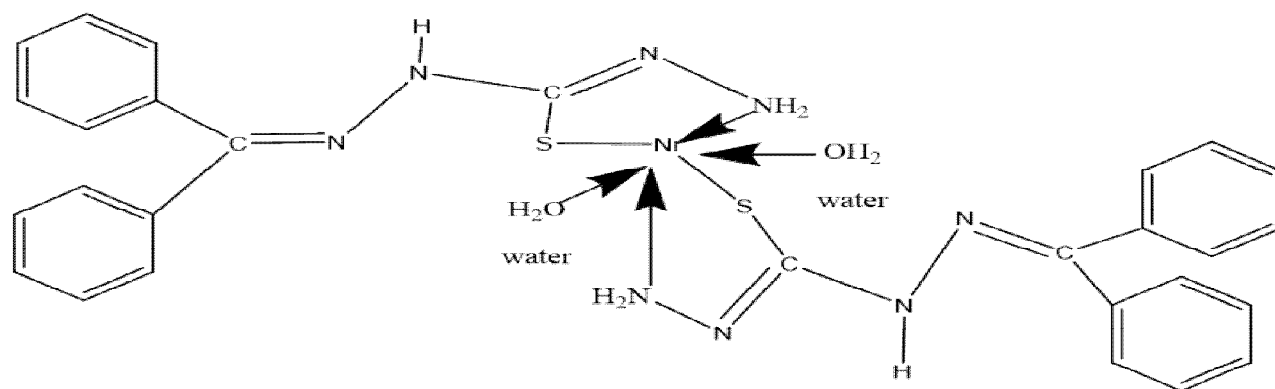
EXPERIMENTAL

Preparation of complexes with Co(II) and Ni(II) with DTCH.

Diaquo bis [diphenyl ketone thio carbo hydrazone Co(II)] and Diaquo bis [diphenyl ketone thio carbo hydra zone Ni(II)]

$[M(DTCH)_2(H_2O)_2]$

Procedure:- About 0.1 milli mole metal chloride was dissolved in 20 ml aqueous ethanol and treated with 0.21 milli mole of ligand (DTCH) in hot ethanol. The mixed solution were heated on steam bath for fifteen minutes and p^H of the solution was raised by adding dilute ammonia drop wise when the complex was digested on steam bath for ten to fifteen minutes and allow to cool at room temperature. The complex were filtered on a Buckner funnel and washed with cold aqueous ethanol (20%) and dried in a desiccator for two to three days. The dried sample were analysed and their magnetic moment value were recorded on Gouy balance at room temperature. The analytical results magnetic moment value of complexes are recorded in Table-A.



bis(((Z)-2-(diphenylmethylene)hydrazineyl)(hydrazineylidene)methyl)thio)nickel

TABLE - A
ANALYTICAL RESULTS AND COLOUR OF THE COMPLEXES

S. No.	Complex	% Element: Found/ (Calc .)						μ_{eff} 30-31°C in B.M
		COLOUR	M	C	N	S	H	
1	[DTCH] LIGAND	Yellow		62.17	21.05	11.25	5.16	Diamagnetic
2	[Ni(DTCH) ₂ (H ₂ O) ₂]	Yellowish brown	19.37	51.23	17.65	9.78	1.79	3.42

TABLE — B
SOLUBILITY AND ELECTRICAL CONDUCTANCE DATA (31° C)

Complex	Qualitative value in solvents				Molar conductance value Ohm ⁻¹ mol ⁻¹ cm ² {DMF}
	Water	Methanol	Benzene	DMF	
[DTCH]	INS	SL S	SI S	FS	12
[Ni(DTCH) ₂ (H ₂ O) ₂]	INS	SL S	SIS	FS	6

TABLE-IR		
I.R. SPECTRAL BANDS OF LIGAND		
S.No	Band Positions in cm ⁻¹	Assignments
1	3228.69	$\sqrt{(\text{NH}_2)}$
2	3149.69	$\sqrt{(\text{NH})}$
3	3103.53	$\sqrt{(\text{NH}_2)}$
4	2924.77	$\sqrt{(\text{C-H})}$ phenyl ring
5	1603.79	$\sqrt{(\text{C=N})}$
6	1498.49	$\delta(\text{NH})$ Thioamide I
7	1443.34	$\delta(\text{C-H})$ phenyl group skeletal
8	1319.59	$\delta(\text{C-H})$
9	1297.25	$\sqrt{(\text{C-C})}$
10	1235.63	$\sqrt{(\text{N-N})}$
11	1216.48	$\sqrt{(\text{C-N})}$
12	1198.06	$\sqrt{(\text{C-N})}$
13	1069.40	$\sqrt{(\text{C=S})}$
14	953.65	$\delta(\text{C-C})$ Phenyl rings + Phenyl rings(Ph-C)
15	917.96	$\delta(\text{C-C})$ Phenyl rings + Phenyl rings(Ph-C)
16	826.67	$\delta(\text{C-C})$ Phenyl rings + Phenyl rings(Ph-C)
17	768.36	Ortho substituted $\delta(\text{C-H})$ vibration
18	692.28	Ortho substituted $\delta(\text{C-H})$ vibration
19	668.36	$\delta(\text{C-C}) + \delta(\text{N-N}) + \text{ring deformation vibration}$
20	650.02	$\delta(\text{C-C}) + \delta(\text{N-N}) + \text{ring deformation vibration}$
21	626.07	$\delta(\text{C-C}) + \delta(\text{N-N}) + \text{ring deformation vibration}$
22	454.83	$\delta(\text{C-C}) + \delta(\text{N-N}) + \text{ring deformation vibration}$
23	419.48	$\delta(\text{C-C}) + \delta(\text{N-N}) + \text{ring deformation vibration}$

TABLE-IR ₃		
I.R. SPECTRAL BANDS OF COMPLEX		
S.No	Band Positions in cm ⁻¹	Assignments
1	3421.09	$\sqrt{(\text{H}_2\text{O})}$
2	3246.34	$\sqrt{(\text{NH}_2)}$
3	3171.12	$\sqrt{(\text{NH})}$
4	3029.90	$\sqrt{(\text{C-H})}$ phenyl ring
5	2930.86	$\sqrt{(\text{C-H})}$ phenyl ring
6	1635.68	$\sqrt{(\text{C=N})}$ ketoimine
7	1484.29	$\delta(\text{NH})$ thioamide I
8	1441.05	phenyl ring skeletal vibration
9	1313.88	$\delta(\text{C-H})$ phenyl ring
10	1297.42	Phenyl ring skeletal vibration.
11	1270.07	Thioamide II
12	1231.66	Phenyl ring skeletal vibration
13	1191.92	Phenyl ring skeletal vibration
14	1124.50	$\sqrt{(\text{N-N})}$ Phenyl ring skeletal vibration
15	1015.81	$\sqrt{(\text{C-N})}$ Phenyl ring skeletal vibration
16	952.06	$\sqrt{(\text{C=S})}$
17	907.78	Phenyl ring skeletal vibration
18	824.61	Ortho substituted phenyl ring
19	773.37	Ortho substituted phenyl ring
20	758.55	$\delta(\text{C-H})$ vibration
21	724.94	$\sqrt{(\text{C-S})}$ deprotonated thiol
22	682.58	Ring deformation vibration
23	655.73	Ring deformation vibration
24	625.21	Ring deformation vibration
25	482.63	Ring deformation vibration
26	454.63	Ring deformation vibration
27	419.62	$\sqrt{(\text{M-N})} + \sqrt{(\text{M-O})}$

II. RESULTS AND DISCUSSION

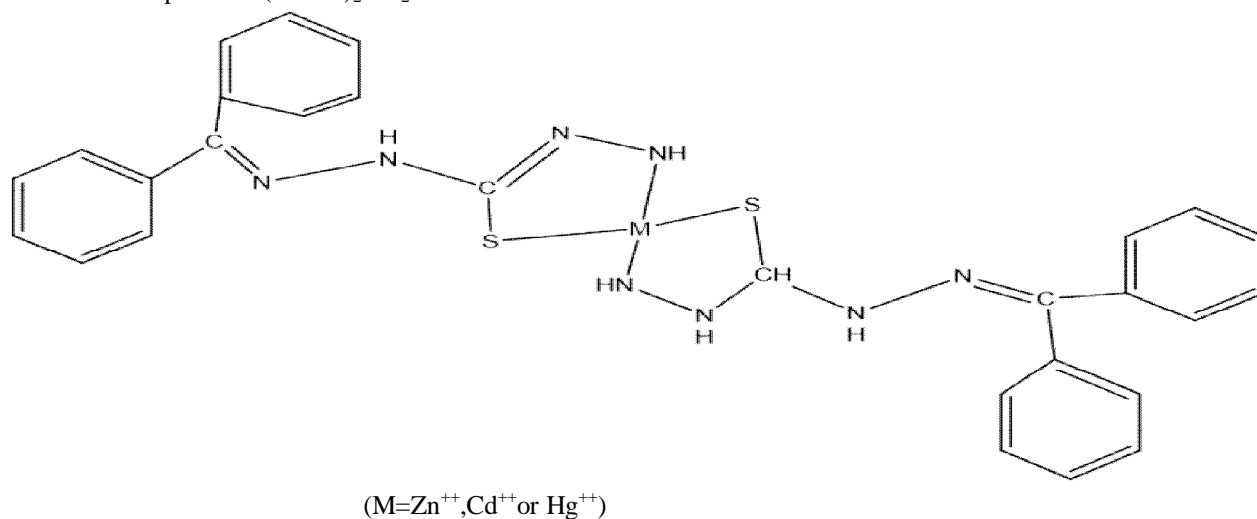
Diphenylketone thiocarbohydrazone (DTCH).

N-(diphenylmethylene) hydrazine carbothiohydrazide contain two bulky phenyl group adjacent to hydrazinoyl methylene ($>\text{C=N-}$) nitrogen and it is expected that ($>\text{C=N-}$) should be reluctant to form coordinate bond with metal atom. The thiol sulphur and terminal hydrazine nitrogen (NH_2) is suitable site to form chelate ring with metal atom. The elemental analysis of complexes of bivalent metal atom Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) corresponds to composition $\text{M}(\text{DTC})_2 \cdot n\text{H}_2\text{O}$ ($n=2$ or zero). The complexes are almost insoluble in cold and hot water but slightly dissolve in hot ethanol and methanol. These complexes however dissolve in appreciably in Dimethyl formamide and dimethyl sulphoxide. The electrical conductance value of these complexes were determined qualitatively to as certain it's non ionic character. The electrical conductance value at $31-32^\circ\text{C}$ in dimethyl formide were found almost negligible ($6-8 \text{ ohm}^{-1}\text{cm}^{-2}$) supporting their non-ion character. The magnetic susceptibility of these complexes were determined by Gouy process at room temperature ($31.5-32^\circ\text{C}$) as expected Zn(II), Cd(II) and Hg(II) (d^{10} electronic system) complexes are diamagnetic and Co(II), Ni(II) and Cu(II) complexes are paramagnetic system. The magnetic susceptibility value of Co(II) complex $[\text{Co}(\text{DTC})_2(\text{H}_2\text{O})]$ was found 4.86 B.M and that of Ni(II) complexes $[\text{Ni}(\text{DTC})_2(\text{H}_2\text{O})]$ value was 3.42 BM. The Magnetic moment of Co(II) and Ni(II) within the range expected for octahedral complexes of respective metal ion.

The magnetic moment value of Cu(II) complexes $[\text{Cu}(\text{DTC})_2(\text{H}_2\text{O})](1.85\text{B.M})$ was also similar to octahedral copper(II) complexes. The complexes are stable at room temperature and up to temperature $(110-120^\circ\text{C})$. On heated aqua complexes $[\text{M}(\text{DTC})_2(\text{H}_2\text{O})][\text{M}=\text{Co}(\text{II}), \text{Ni}(\text{II}) \text{ and } \text{Cu}(\text{II})]$ starts losing water and become almost anhydrous at $(160-180^\circ\text{C})$. The retention of water molecule by complexes below 120°C suggested the co-ordination nature of water molecule. The presence of water molecule in complexes is also supported by a broad band near $3320-3430\text{ cm}^{-1}$ in IR spectra of complexes. The complexes on heating above $230-250^\circ\text{C}$ started decomposition suggested that hydrazine part get detached from phenyl part. The infrared spectra of complexes and free ligands were determined in KBr optics. The IR spectrum of ligands shows NH_2 and NH stretching bands at $3228, 3149$ and 2924 cm^{-1} . The phenyl ring C-H stretch assigned to a band at 3103 cm^{-1} . The methylene part $\sqrt{(\text{C}=\text{N})}$ stretch of the ligand is observed at $1443, 1319, 1249$ and 1235 cm^{-1} . are attributed to skeletal vibrations of phenyl ring. The I.R bands located at $1216, 1198, 1069, 1067$ and 919 cm^{-1} are attributed $\sqrt{(\text{C}-\text{N})}$, $\sqrt{(\text{N}-\text{N})}$ and $\sqrt{(\text{K}-\text{C})}$ vibration of free ligand molecule. The I.R band at 952 cm^{-1} of free ligand is assigned to thiol group $\sqrt{(\text{C}=\text{S})}$ vibration which disappear in its complexes and shifted to lower frequency. The IR bands of ligand located at $826, 768, 692, 668\text{ cm}^{-1}$ are assigned to phenyl ring out of plane (C-H) stretches and IR bands at 1635 cm^{-1} (Fig-IR-2) which is due to $\sqrt{(\text{C}=\text{N})}$ band to higher wave number supported it is free and not the bonding site of ligand molecule. The $\delta(\text{NH}_2)$ of ligand located at 1498 cm^{-1} is shifted to lower frequency and observed near 1484 cm^{-1} suggested to coordinated nature of terminal hydrazine NH_2 nitrogen. The IR bands of free ligands has been found shifted to some extent in complexes (prominent bands are shown in IR Table¹⁻⁵). The electronic spectrum of ligand in ethanol shows three electronic transitions located at $213, 254$ and 312 cm^{-1} assigned to $\sigma-\sigma^*, \pi-\pi^*$ and $n-\pi^*$ transition. The $n-\pi^*$ transition located at 312 cm^{-1} is fairly weak as it is spin forbidden transition. The electronic absorption spectrum of complexes shows strong absorption below 420 cm^{-1} attributable from charge transfer transition and no d-d transition could be located definitely in solution.

III. CONCLUSIONS

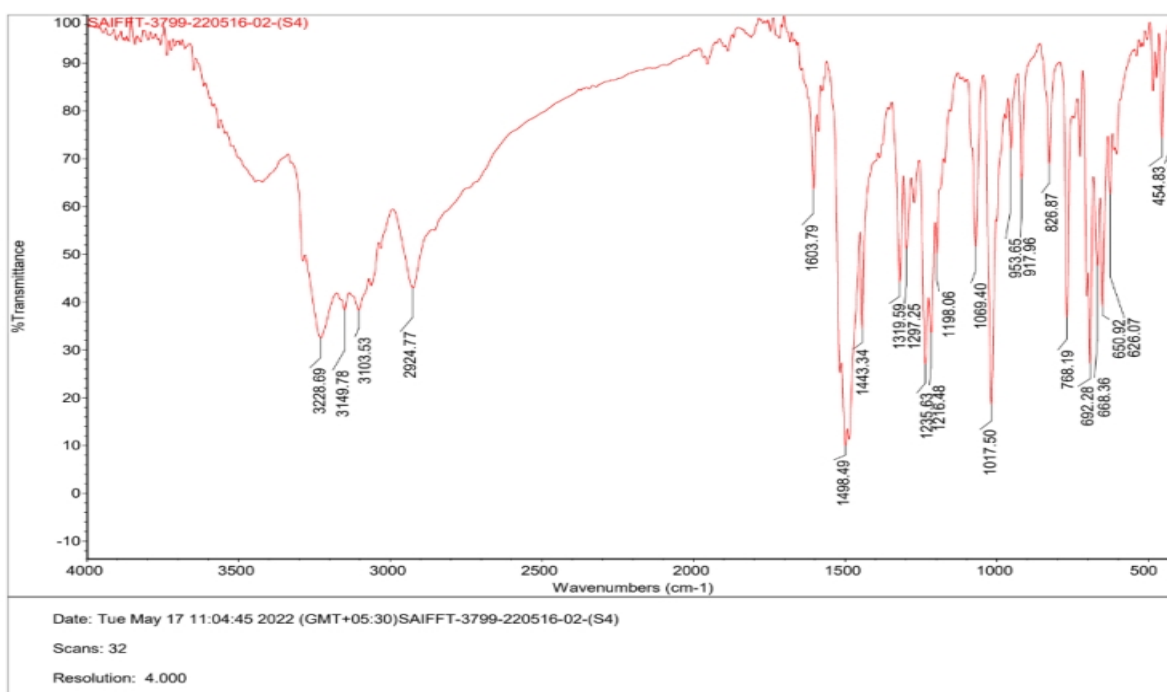
Thus on basis of electric conductance, magnetic susceptibility and I.R. spectral studies the following structures are tentatively suggested for the complexes $\text{M}(\text{DTCH})_2.n\text{H}_2\text{O}$



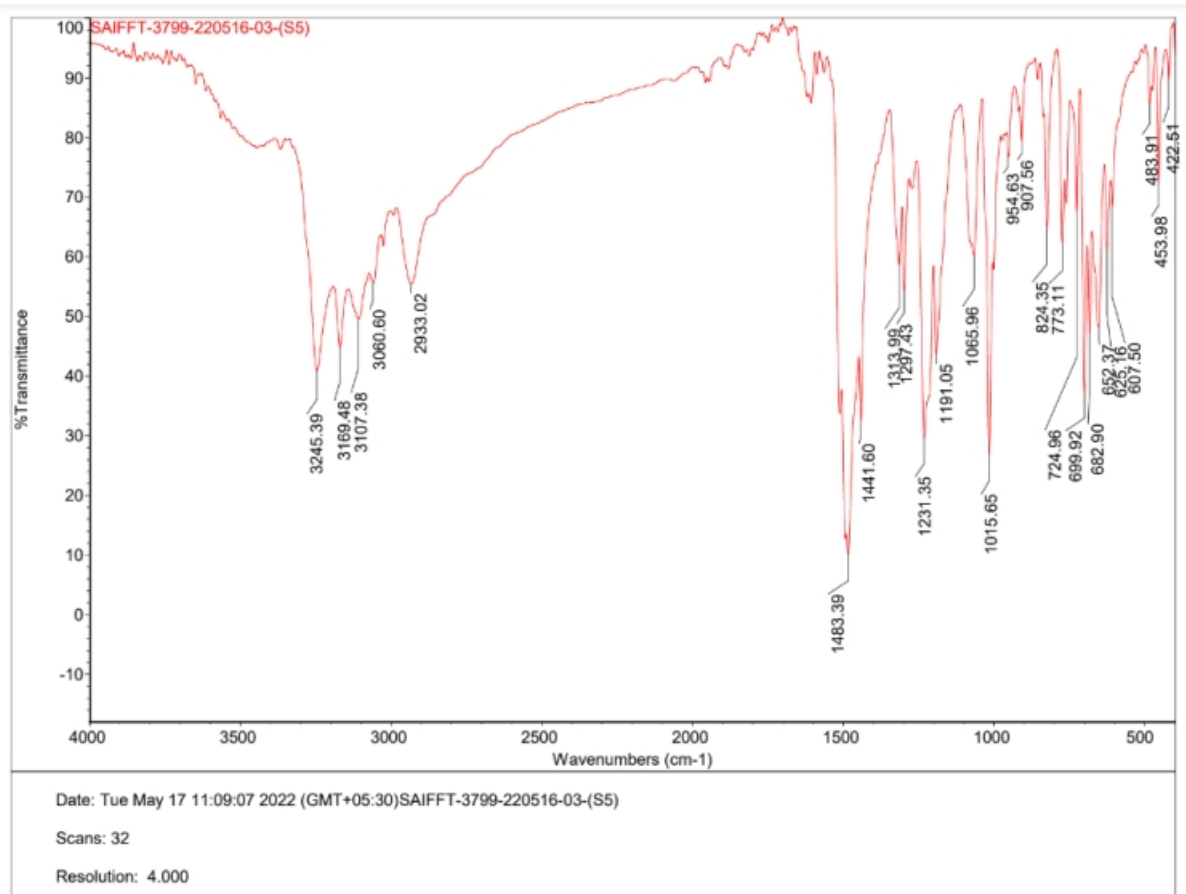
REFERENCES

- [1] Silvestry-Rodriguez, N.; Sicairos-Ruelas, E.E.; Gerba, C.P.; Bright, K.R. Silver as A Disinfectant; Springer: New York, NY, USA, 2007; pp. 23–45.
- [2] Pricker, S.P. Medical uses of gold compounds: Past, present and future. Gold Bull. 1996, 29, 53–60.
- [3] Database of Privately and Publicly Funded Clinical Studies Conducted around the World. Available online: <https://clinicaltrials.gov/> (accessed on 10 November 2019).
- [4] Marzo, T.; Massai, L.; Pratesi, A.; Stefanini, M.; Cirri, D.; Magherini, F.; Becatti, M.; Landini, I.; Nobili, S.; Mini, E.; et al. Replacement of the Thiosugar of Auranofin with Iodide Enhances the Anticancer Potency in a Mouse Model of Ovarian Cancer. ACS Med. Chem. Lett. 2019, 10, 656–660.
- [5] Marzo, T.; Cirri, D.; Pollini, S.; Prato, M.; Fallani, S.; Cassetta, M.I.; Novelli, A.; Rossolini, G.M.; Messori, L. Auranofin and its Analogues Show Potent Antimicrobial Activity against Multidrug-Resistant Pathogens: Structure-Activity Relationships. CHEMMEDCHEM 2018, 13, 2448–2454.
- [6] List, A.; Beran, M.; DiPersio, J.; Slack, J.; Vey, N.; Rosenfeld, C.S.; Greenberg, P. Opportunities for Trisenox® (arsenic trioxide) in the treatment of myelodysplastic syndromes. Leukemia 2003, 17, 1499–1507.
- [7] Lippard, S.J. Metals in Medicine; University Science Books: Mill Valley, CA, USA, 1994.
- [8] Niccoli Asabella, A.; Cascini, G.L.; Altini, C.; Paparella, D.; Notaristefano, A.; Rubini, G. The copper radioisotopes: A systematic review with special interest to ^{64}Cu . BioMed Res. Int. 2014, 2014.

- [9] Rosenberg, B.; Van Camp, L.; Krigas, T. Inhibition of Cell Division in Escherichia coli by Electrolysis Products from a Platinum Electrode. *Nature* 1965, 205, 698–699. [
- [10] Barry, N.P.E.; Sadler, P.J. Exploration of the medical periodic table: Towards new targets. *Chem. Commun.* 2013, 49, 5106.
- [11] Giorgio, P. Thiosemicarbazone Metal Complexes: From Structure to Activity. *Open Crystallogr. J.* 2008, 3, 16–28.
- [12] Donnelly, P.S.; Caragounis, A.; Du, T.; Laughton, K.M.; Volitakis, I.; Cherny, R.A.; Sharples, R.A.; Hill, A.F.; Li, Q.-X.; Masters, C.L.; et al. Selective Intracellular Release of Copper and Zinc Ions from Bis(thiosemicarbazone) Complexes Reduces Levels of Alzheimer Disease Amyloid- β Peptide. *J. Biol. Chem.* 2008, 283, 4568–4577.
- [13] Paterson, B.M.; Donnelly, P.S. Copper complexes of bis(thiosemicarbazones): From chemotherapeutics to diagnostic and therapeutic radiopharmaceuticals. *Chem. Soc. Rev.* 2011, 40, 3005–3018.
- [14] Jyothi, N.R.; Farook, N.A.M.; Cho, M.; Shim, J. Cytotoxic activities of thiosemicarbazones and their metal complexes. *Asian J. Chem.* 2013, 25, 5841–5843.
- [15] Shim, J.; Jyothi, N.R.; Farook, N.A.M. Biological applications of thiosemicarbazones and their metal complexes. *Asian J. Chem.* 2013, 25, 5838–5840. *Pharmaceuticals* 2020, 13, 4 16 of 19
- [16] Moorthy, N.S.H.N.; Cerqueira, N.M.F.S.A.; Ramos, M.J.; Fernandes, P.A. Aryl- and heteroarylthiosemicarbazone derivatives and their metal complexes: A pharmacological template. *Recent Pat. Anti-Cancer Drug Discov.* 2013, 8, 168–182. [
- [17] Jansson, P.J.; Kalinowski, D.S.; Lane, D.J.R.; Kovacevic, Z.; Seebacher, N.A.; Fouani, L.; Sahni, S.; Merlot, A.M.; Richardson, D.R. The renaissance of polypharmacology in the development of anti-cancer therapeutics: Inhibition of the “Triad of Death” in cancer by Di-2-pyridylketone thiosemicarbazones. *Pharmacol. Res.* 2015, 100, 255–260.
- [18] Silva, B.V.; Silva, B.N.M. Thio- and Semicarbazones: Hope in the Search for Treatment of Leishmaniasis and Chagas Disease. *Med. Chem.* 2017, 13, 110–126.
- [19] Prajapati, N.P.; Patel, H.D. Novel thiosemicarbazone derivatives and their metal complexes: Recent development. *Synth. Commun.* 2019, 49, 2767–2804.
- [20] Namiecinska, E.; Sobiesiak, M.; Malecka, M.; Guga, P.; Rozalska, B.; Budzisz, E. Antimicrobial and structural properties of metal ions complexes with thiosemicarbazide motif and related heterocyclic compounds. *Curr. Med. Chem.* 2019, 26, 664–693. [CrossRef]
- [21] Haldys, K.; Latajka, R. Thiosemicarbazones with tyrosinase inhibitory activity. *MedChemComm* 2019, 10, 378–389. [CrossRef]
- [22] Guha, P.C.; Dey, S.C. Hetero-ring formations with thiocarbohydrazide. II. Condensations with diketones and aldehydes. *Q. J. Indian Chem. Soc.* 1925, 2, 225–239.
- [23] Guha, P.K.; Roychoudhury, S.K. Hetero-ring formations with thiocarbohydrazide. IV. Reactions of 1-phenylthiocarbohydrazide. *J. Indian Chem. Soc.* 1928, 5, 163–174.
- [24] Guha, P.C.; Roychoudhury, S.K. Hetero-ring formations with thiocarbohydrazide. III. Reactions of substituted thiocarbohydrazides. *J. Indian Chem. Soc.* 1928, 5, 149–161.
- [25] French, F.A.; Blanz, E.J. The Carcinostatic Activity of Thiosemicarbazones of Formyl Heteroaromatic Compounds. 1 III. Primary Correlation. *J. Med. Chem.* 1966, 9, 585–589. [CrossRef] [PubMed]
- [26] Wiles, D.M.; Suprunchuk, T. Preparation and fungistatic properties of thiocarbohydrazones. *J. Med. Chem.* 1970, 13, 323–324. [CrossRef] [PubMed]
- [27] Cano Pavon, J.M.; Garcia de Torres, A.; Cristofol Alcaraz, E.; Siles Cordero, M.T.; Vereda Alonso, E. Analytical applications of thiocarbohydrazones. A review. *Quim. Anal.* 1994, 13, 5–10.



I.R. OF THE LIGAND



I.R OF THE COMPLEX



10.22214/IJRASET



45.98



IMPACT FACTOR:
7.129



IMPACT FACTOR:
7.429



INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

Call : 08813907089  (24*7 Support on Whatsapp)