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SYNTHESIS, SPECTROSCOPIC, THERMAL AND BIOLOGICAL ASPECTS OF NICKEL(II) COMPLEXES WITH HYDANTOIN

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ABSTRACT

A series of organic hydantoin-compounds containing Nickel as an inorganic element for enhancing the pharmacological activity was synthesized. They have been characterized by elemental analysis, (FT-IR, 1H &13 C NMR, and electronic) spectra, magnetic measurements and thermal studies. A magnetic moment and reflectance spectral study reveals that an octahedral geometry has been assigned to all the prepared complexes. Ligands (Ln) and their metal complexes were screened for their in-vitro antimicrobial activity against some microorganisms. The results showed some lower to moderate activities.

Keywords – Synthesis, spectroscopic, hydantoin.

1. INTRODUCTION

In more general sense, hydantoins can refer to chemical compounds, which have substituent groups bonded to a hydantoin ring skeleton structure. For example, phenytoin has two phenyl groups substituted onto the number 5 carbon in a hydantoin molecule[1]. Hydantoin was first isolated in 1861 by adolf von baeyer in the course of his study of uric acid. He obtained it by hydrogenation of allantoin, hence the name. urech in 1873[2] synthesized the derivative 5-methyl hydantoin from alanine sulfate and potassium cyanate in what is now known as the urech hydantoin. Dian kammeyer and co-workers[3] reported direct synthesis of hydantoins and ita chemical derivatives. These compounds have been utilized for purposes as diverse as disinfectants, biocide agents. G. B. Rown, T. M. Delorey and co-workers[4] reported sodium channel binding and anticonvulsant activities of hydantoins containing conformationally constrained 5-phenyl substituents.

Nosrat O. Mahmoodi and co-workers[5] reported one-pot synthesis of hydantoins, an efficient method was utilized for the synthesis of hydantoins starting with ketones, benzoin, benzil, phenanthrene-dione and aldehydes. Two main and convenient procedures using either KCN and $(NH_4)_2CO_3$ or Urea and NaOH, Ethanol were examined[5,6].

Salicylic acid is involved in endogenous signaling, mediating in plant defense against pathogens. It plays a role in the resistance to pathogens by inducing the production of pathogenesis-related proteins[8,9]. Salicylic acid is known for its ability to ease aches and pains and reduce fevers. These medicinal properties, particularly fever relief, have been known since ancient times, and it is used as an anti-inflammatory drug[10]. Mesalazine is formed from the prodrug balsalazide along with the inert carrier molecule 4-aminobenzoyl-beta-alanine[11]. L. A. Christensen and B. A. Jacobsen reported 5-amino salicylic acid : its clinical and pharmaceutical applications[12].

2. MATERIALS AND METHODS

2.2 Materials

In this study we used analytical grade chemicals for our laboratory work. 4 - Amino salicylic acid, concentrated hydrochloric acid, ethanol, formaldehyde, dimethyl formamide and $Ni(NO_3)_2 \cdot 3H_2O$ were purchased form the E. Merck (India) Limited, Mumbai.

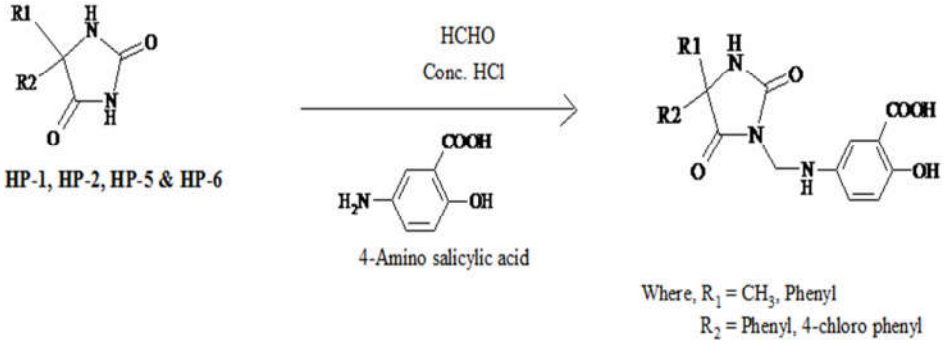

Fig. 1: Scheme of reaction

2.3 Methods

A mixture of various hydantoin derivatives (0.01 mole) and formaldehyde (40%, 1.5 ml) and concentrated hydrochloric acid (1 to 2 drops) in iso propyl alcohol (20 ml) was stirred at 50-55^{0}C with a solution of 4-amino salicylic acid (0.01 mole) in iso propyl alcohol (10 ml) for 15 hrs. The solid product that separated out on standing for a 1 hrs was collected by filtration, washed with iso propyl alcohol & dried. It was recrystallized from iso propyl alcohol to yield the compounds, where we obtained in 65-80% of yield.

The analytical and spectral data of compounds are described.

IR, NMR and C^{13} spectra of Lingand -1

5-Methyl-3-(salicylic acid-1-yl-amino methyl)-5-phenyl-imidazolidine-2,4-dione :

Infrared Spectral Features (cm^{-1})

3362 -NH of amine, 2855, 1446 -CH_3 and N-CH_2-N linkage, 2890 -Aromatic C-H stretchin 1626-C=O, 1240 -C-NH, 3453 –OH, 1667 -CO of COOH, 3503 -OH of COOH.

NMR spectral Features (δ, ppm)

7.11-8.07 (multiplet, aromatic C-H protons), 4.74 (2H singlet,CH_2) of N-CH_2, 1.4 (3H singlet,CH_3), 4.50 (H of -OH), 10.50 (H of -COOH).

^{13}CMR spectral Features (δ, ppm)

113-145 (Benzene), 170 (C of –C=O), 32 (C-CH_3), 46 (N-CH_2-N), 173 (C of –COOH), 157 (C of C-OH).

IR, NMR and C^{13} spectra of Lingand-4

5-Phenyl-3-(Salicylic acid-1-yl-amino methyl)-5-(4-chloro phenyl)-imidazolidine-2,4-dione:

Infrared Spectral Features (cm^{-1})

3363 -NH of amine, 2855,1446 -CH_3 and N-CH_2-N linkage,1626,1500 Aromatic C-H stretching 1667 -C=O, 1240 -C-NH, 3452 –OH, 1667 -CO of COOH, 3500 -OH of COOH.

NMR spectral Features (δ, ppm)

7.11-8.07 (multiplet, aromatic C-H protons), 4.74 (2H singlet,CH_2) of N-CH_2, 4.50 (H of -OH), 10.50 (H of -COOH).

^{13}CMR spectral Features (δ, ppm)

113-145 (Benzene), 170 (C of –C=O), 46 (N-CH_2-N), 173 (C of –COOH), 157 (C of C-OH).

Then this ligand was used for making the derivatives of Nickle complexes as follows. General procedure for the complexation:

2.3.1 Preparation of metal complexes

The ligand was dissolved in aqueous alkali and filtered through G-1 funnel. It was stirred well and 1:1 HCl-H_2O mixture was added drop wise to precipitate the ligand. The solid was filtered, washed with boiling water then with petroleum ether and air-dried. The dried ligand sample was used for the preparation of metal complexes.

The synthesis of metal complex comprises the two steps:

[A] Preparation of sodium salt of solution of ligand sample (i.e. Reagent)

All the ligands used for the preparation of their sodium salt solution. The general procedure is as follows:

A dried ligand sample (0.1 M) was stirred in 100 ml of 1:1 mixture of acetone-ethanol. Calculated amount of aqueous solution of 1 M NaOH was added drop wise to the ligand solution. During neutralization some pasty precipitates appeared. Minimum amount of water was added to dissolve the precipitates. The resulting solution with little turbidity was diluted to 250ml by water and then designated as reagent solution. This turbid solution was used as such for preparing all metal complexes. Hence details will not be given henceforth about the preparation of this reagent solution.

[B] Preparation metal complexes of ligands

The sodium salt solution (25ml containing 0.01M ligand) of each ligand was added drop wise to a solution of cupric nitrate hexahydrate (0.01 mole) in 100 ml of water with rapid stirring. The so called pH of the resultant solution was 4.5. A greenish blue solid precipitated out. It was allowed to settle. Then it was digested on water bath at 70ºC for about 2 hours. The solid mass was filtered, washed with 1:1 mixture of water–ethanol and finally with acetone, and air-dried, yield was 65-68%. The resulting complex was powdered well and further dried at 70ºC over a period of 24 hrs.

Here are the structures of newly prepared metal complexes.

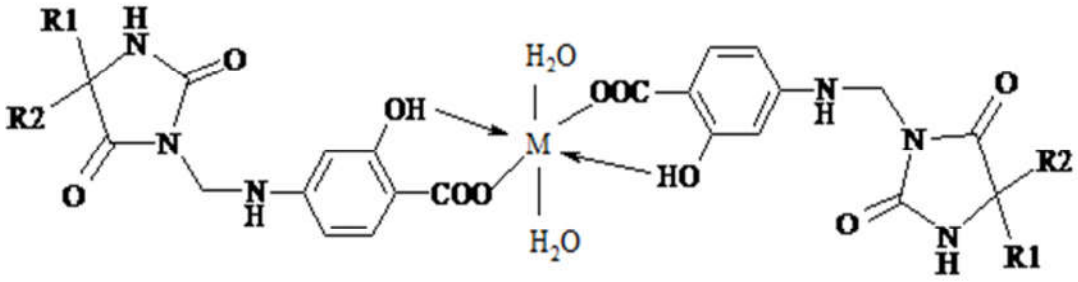

Fig. 2: Metal complex where M = Ni(II)

For Complex-1 $R_1 = CH_3$, $R_2 =$ Ph

For Complex-2 $R_1 = CH_3$, $R_2 =$ Ph-Cl

For Complex-3 $R_1 =$ Ph, $R_2 =$ Ph

For Complex-4 $R_1 =$ Ph, $R_2 =$ Ph-Cl

3. RESULTS AND DISCUSSION

3.1 Elemental analysis

Elemental analysis of all four complexes are shown in Table - 1.

Table 1: Elemental analysis of all four complexes

Metal Comp.	M.Wt gm /mole	Yield %	Elemental analysis									
			%Metal		%C		%H		%N		%Cl	
			Cald.	Found	Cald.	Found	Cald.	Cald.	Cald.	Found	Cald.	Found
1	803	65	7.34	7.30	53.79	53.80	4.48	4.40	10.46	10.40	-	-
2	872	64	6.76	6.70	49.54	49.50	3.90	3.90	9.63	9.60	8.14	8.10
3	927	65	6.36	6.30	59.54	59.50	4.31	4.30	9.06	9.00	-	-
4	996	65	5.92	6.00	55.42	55.50	3.81	3.80	8.43	8.40	7.12	7.10

3.2 IR Spectroscopy

The examination of IR spectra of metal complexes reveals that IR spectra of metal complexes of each series are identical in almost all aspects.

a) All the IR spectra have identical bands at their respective positions.

b) Most of the bands appeared in the spectra of corresponding ligand are observed at the similar position in the IR spectra of their metal complexes.

c) The band due to CO of COOH group appeared in the spectra of ligand is almost vanished in the spectra of complexes. The new strong band around 1600 cm^{-1} is appeared and this might be responsible for COO^- anion. This is expected as the COOH group of ligand is participating in metal complex formation.

d) Only a new band at 1095 cm^{-1} had appeared in the spectra of metal complexes. This may be assigned to V_{c-o} of C-O-Metal bond formation.

3.3 Magnetic susceptibility

The results of magnetic properties of all newly prepared complexes are summarized in Table-2.

Table 2: Magnetic properties

Metal complexes	χ_g X10 ^{6} (cgs)	χ_m X10 ^{6} (cgs)	Magnetic moment μ_{eff} (B.M.)	$\mu_{eff}=\sqrt{n(n+2)}$ (B.M.)	Expected μ_{eff} (B.M.)	Cond. λ_M (Ω^{-1} cm^2 mol^{-1})
1	5.32	4272	3.22	2.84	2.9-3.4	8.22
2	4.89	4272	3.22	2.84	2.9-3.4	7.88
3	4.55	4219	3.20	2.84	2.9-3.4	8.10
4	4.28	4272	3.22	2.84	2.9-3.4	8.22

χ_M = Molar Conductivity (Ω^{-1} cm^2 mol^{-1}) χ_g = Gram Susceptibility (cgs)

3.4 Reflectance spectral data of Ni^{2+} complexes

The results of magnetic properties of all newly prepared complexes are depicted in Table-3.

Table-3 : Magnetic properties

Metal Complexes	Observed transition energies (cm^{-1})	
	$^3A_{2g} \rightarrow {}^3T_{1g}$ (P)	$^3A_{2g} \rightarrow {}^3T_{1g}$ (F)
1	24113	15192
2	22242	15792
3	22183	14120
4	22491	13118

A magnetic moment and reflectance spectral study reveals that an octahedral geometry has been assigned to all the prepared complexes. Ligands

3.5 Antimicrobial Activity Study

Ligands (Ln) and their metal complexes were screened for their *in-vitro* antimicrobial activity against some microorganisms. The study has been conducted according to the method adopted by Cruickshank et al[13]. The results of the antimicrobial studies are represented in Table-4.

Table 4:

Compound	Zone of Inhibition (in mm)			
	Gram positive		Gram negative	
	B.Subtillis	S.Aureus	E.Coli	Ps.Aeruginosa
1	14	12	17	17
2	10	13	11	09
3	12	12	11	11
4	12	11	09	13

The results showed some lower to moderate activities.

4. ACKNOWLEDGEMENT

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