



## Synthesis and spectral characterisation of hydrazone based 14-membered octaaza macrocyclic Ni(II) complexes

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### ABSTRACT

Schiff base condensation of benzil bis(hydrazone) with formaldehyde, acetone and benzaldehyde and its nickel(II) complexes were synthesised. Preparation of the free ligands was accomplished by refluxing benzil with hydrazine derivatives in 1:10 mole ratios in ethylene glycol. The spectral characterisation of hydrazone based 14-membered octaaza macrocyclic complexes of nickel(II) was undertaken. The ligand, benzil bis(hydrazone) and complexes were characterized by FTIR, UV-visible, <sup>1</sup>H NMR, Mass spectroscopy. The results of the investigations support the formulation of each of the complexes as a metal ion surrounded by a planar, quadridentate ligand. Thus, the data provide strong support for the conclusion that the macrocyclic complexes were actually prepared.

**Key words:** Schiff base, benzil bis(hydrazone), macrocycle, nickel(II) complex.

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### INTRODUCTION

There is a growing interest in the design and synthesis of the macrocyclic complexes of hydrazones because of their applications as anticancer, antiviral, antibacterial and antifungal agents [1-3] and they are considered as useful models for biological systems. The hydrazones are the building block for the present work as hydrazones and their derivatives constitute a versatile class of compounds in organic chemistry. These compounds have interesting biological properties, such as anti – inflammatory, analgesic, anticonvulsant, antituberculous, antitumor, anti – HIV and antimicrobial activity [4-6]. Hydrazones are important compounds for drug design, as possible ligands for metal complexes, organocatalysis and also for the syntheses of heterocyclic compounds [7-9]. The ease of preparation, increased hydrolytic stability relative to imines because of the delocalization of the imine double bond due to the presence of electronegative group and the tendency toward crystallinity are all desirable characteristics of hydrazones. Due to these traits, hydrazones have been under study for a long time. Hydrazones contain two connected nitrogen atoms of different nature and a C-N double bond that is conjugated with a lone pair of the terminal nitrogen atom. These structural fragments are mainly responsible for the physical and chemical properties of hydrazones. Both nitrogen atoms of the hydrazine group are nucleophilic, although the amino type nitrogen is more reactive. The carbon atom of hydrazine group has both nucleophilic and electrophilic character [10,11].

The introduction of functional groups in the hydrazone molecules expands the scope of use of the latter in organic synthesis. Moreover, the combination of the hydrazono group with other functional groups leads to compounds with unique physical and chemical properties. Hydrazones containing a halo atom in  $\alpha$  or  $\beta$  – positions generate nitrile imines [12] and 1,2-diaza-1,3-butadiene [13] are active intermediates in cycloaddition chemistry. The amidrazones and thiosemicarbazones are well documented because of their biological activity and use in the synthesis of heterocyclic compounds [14].

The benzil bis(hydrazone) macrocyclic complexes are chemically more reactive because the six membered chelate rings contain hydrazone linkages which are very reactive due to the presence of nucleophilic nitrogen. The reactivity of benzil bis(hydrazones) greatly widens the scope of this compound as a precursor for the synthesis of variety bulkier, aromatic rich molecules. Schiff base condensation of bis(hydrazone) with suitable aldehydes and ketones would form a macrocyclic and macro acyclic molecules which will have more number of nitrogen atoms, and this will behave as better coordinating ligands for variety of metal atoms/ions. Hence, the synthesis and spectral characterisation of hydrazone based 14-membered octaaza macrocyclic complexes of nickel(II) was undertaken.

## EXPERIMENTAL SECTION

### Preparation of benzil bis(hydrazone)

Benzil (10.5 g, 50 mmol) was dissolved in 100 ml of ethylene glycol and hydrazine hydrate (24.3 ml, 500 mmol) was added to it. The resulting yellow solution was refluxed for 3 h and then it was left in the air. After 20 h the precipitated white microcrystalline compound was filtered off and washed successively with 100 ml of water and 25 ml of diethylether. The compound was dried in air. The compound was recrystallized from warm methanol. Yield 8.32 g. The compound was soluble in diethylether, acetonitrile, chloroform, and acetone.

### Synthesis of macrocyclic complexes

#### Synthesis of $[\text{Ni}(\text{C}_{30}\text{H}_{28}\text{N}_8)](\text{ClO}_4)_2$

Formaldehyde (789 mg, 10 mmol) of 38% aqueous solution was added to a solution of  $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$  (1.82 g, 5 mmol) in 15 mL of acetonitrile. To this stirred blue solution, benzil bis(hydrazone) (2.38 g, 10 mmol) was added. One drop of the concentrated perchloric acid was added to catalyse the condensation reaction and the solution was stirred for 1 h and 30 minutes at room temperature. Diethyl ether (25 mL) was slowly added to the red – brown solution to induce precipitation of the product. The greyish green precipitates were filtered and washed with diethylether and dried in vacuum. Yield 2.27 g; mp = 150 °C – 160 °C (dec.)

#### Synthesis of $[\text{Ni}(\text{C}_{34}\text{H}_{36}\text{N}_8)](\text{ClO}_4)_2$

To a vigorously stirred blue solution of  $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$  (365.69 mg, 1 mmol) in 3 mL of acetonitrile, acetone (116 mg, 2 mmol) was added. To this blue coloured solution, benzil bis(hydrazone) (476 mg, 2 mmol) was added. One drop of concentrated perchloric acid was added to catalyse the condensation reaction. The reaction was refluxed for 4 h and left for precipitation. The formed brown colour precipitate was filtered and washed with diethylether and dried in vacuum. Yield 0.41 g; mp = 160 °C -170 °C (dec.)

#### Synthesis of $[\text{Ni}(\text{C}_{42}\text{H}_{36}\text{N}_8)](\text{ClO}_4)_2$

Benzaldehyde (318.39 mg, 3 mmol) was added to a vigorously stirred blue solution of  $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$  (548.53 mg, 1.5 mmol) in 4.5 mL acetonitrile. To this solution, benzil bis(hydrazone) (714 mg, 3 mmol) and a drop of concentrated perchloric acid was added to catalyse the condensation reaction. The reaction mixture was stirred overnight for precipitation at room temperature. The white precipitates were filtered and washed with diethyl ether and dried in vacuum. Yield 0.77 g; mp = 160 °C – 170 °C (dec.)

### Spectral Characterisation

Infrared spectra were recorded using potassium bromide plates on a Perkin–Elmer Spectrum RX-I FT–IR Spectrophotometer in the range of 4000 – 350  $\text{cm}^{-1}$ . Ultraviolet and visible spectra were recorded on a Perkin–Elmer Lambda 25 UV–Visible Spectrophotometer controlled by the Win Lab software through computer. The spectra were recorded in the region 200 – 800 nm in acetonitrile using a matched pair of Teflon stoppered quartz cell of path length 1 cm. The  $^1\text{H}$  NMR spectra were recorded on a Bruker – Avance 300 MHz spectrometer at room temperature using  $\text{CDCl}_3$  or  $\text{DMSO}-d_6$  as solvent. TMS was used as the internal reference. The electrospray ionization mass spectra were recorded on a Micromass Quattro II Triple Quadrupole Mass Spectrometer. The sample was dissolved in chloroform methanol/acetonitrile/water and introduced into the ESI source through a syringe pump at the rate of 5  $\mu\text{L}/\text{min}$ . the ESI capillary was set at 3.5 V and the cone voltage was 40 V. the spectra was collected in 6 s scans and the hard copies are averaged spectra of 6-8 scans.

## RESULTS AND DISCUSSION

### Characterization: Infrared spectra

The important IR frequencies of free benzil bis(hydrazone) and Ni(II) complexes formed due to the condensation of benzil bis(hydrazone) and formaldehyde, acetone and benzaldehyde are present in the table 1. The IR spectra of free benzil bis(hydrazone) was compared with the spectra of the Ni(II) complexes in order to study the binding mode of the ligand to the metal ion in the complexes. A strong band is observed for free benzil bis(hydrazone) at around 1620.89  $\text{cm}^{-1}$  characteristic of the azomethine (C=N) stretching vibration. In the metal chelates the band

characteristic of the azomethine group is shifted to 1600 – 1570  $\text{cm}^{-1}$ . The lower value may be due to the drift of the lone pair density of the azomethine nitrogen towards the metal atom, indicating the coordination occurred through the nitrogen of the C=N group.

An absorption band was observed around 2945 – 2900  $\text{cm}^{-1}$  the characteristic of the aliphatic (C-H) stretching vibration which indicates the condensation of the carbonyl functional group with the amino groups. The bands for C-N stretching and N-N stretching have become very prominent in the macrocyclic complexes.

**Table 1: Characteristic IR bands ( $\text{cm}^{-1}$ ) of the compounds studied**

S. No	Compounds	$\nu(\text{N-H})$	$\nu(\text{C-H})$	$\nu(\text{C=N})$	$\nu(\text{C-N})$	$\nu(\text{N-N})$	$\nu(\text{M-N})$
1	Benzil bis(hydrazone)	3351.57, 3191.37	-	1620.89	-	1158.98	-
2	$[\text{Ni}(\text{C}_{34}\text{H}_{36}\text{N}_8)](\text{ClO}_4)_2$	3377.67	2912.08	1600.48	1235.6	1113.29	580.48
3	$[\text{Ni}(\text{C}_{30}\text{H}_{28}\text{N}_8)](\text{ClO}_4)_2$	3287.64	2941.53	1580.29	1266.84	1112.23	589.89
4	$[\text{Ni}(\text{C}_{42}\text{H}_{36}\text{N}_8)](\text{ClO}_4)_2$	3212.06	-	1604.24	1250.31	1145.07	509.42

### Electronic Spectra

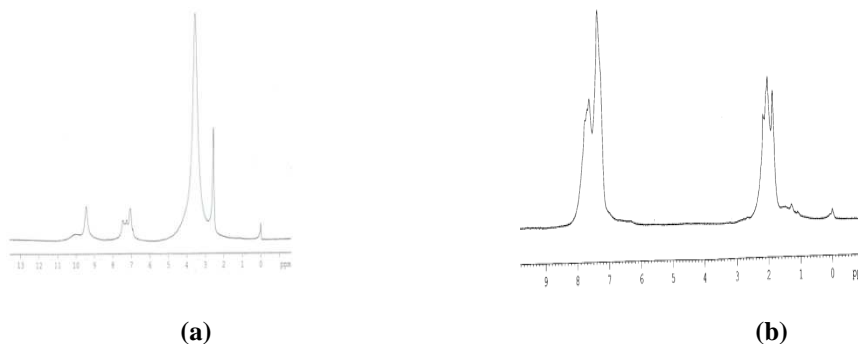
On comparing the electronic spectra of free benzil bis(hydrazone) and the macrocyclic complexes, free benzil bis(hydrazone) transition band due to  $\pi\text{-}\pi^*$  transition is shifted to higher energy in the complexes (table 2). The shoulders in the complexes are assigned to  $\pi\text{-}\pi^*$  of aromatic ring, ligand to metal charge transfer,  $n\text{-}\pi^*$  transitions.

**Table 2: Absorption Spectral data (nm) of Benzil bis(hydrazone) and its Complexes**

S. No	Compounds	Absorption( $\lambda_{\text{max}}$ )	
		$\pi\text{-}\pi^*$ (Benzene/imino)	$n\text{-}\pi^*$ (Azomethine)
1	Benzil bis(hydrazone)	273.32	-
2	$[\text{Ni}(\text{C}_{34}\text{H}_{36}\text{N}_8)](\text{ClO}_4)_2$	270.01	314.32
3	$[\text{Ni}(\text{C}_{30}\text{H}_{28}\text{N}_8)](\text{ClO}_4)_2$	289.02	435.74
4	$[\text{Ni}(\text{C}_{42}\text{H}_{36}\text{N}_8)](\text{ClO}_4)_2$	250.54	314.49

### $^1\text{H}$ NMR Spectrum

The  $^1\text{H}$  NMR spectrum (fig 1a) of  $[\text{Ni}(\text{C}_{30}\text{H}_{28}\text{N}_8)](\text{ClO}_4)_2$  in  $\text{DMSO-d}_6$  shows the multiplet at 7.48 – 7.05  $\delta$  which is assigned to protons (20 protons) of the four aromatic rings. The poor solubility of the compound in most of the deuterated solvents did not allow us to characterise the presence of aliphatic protons.

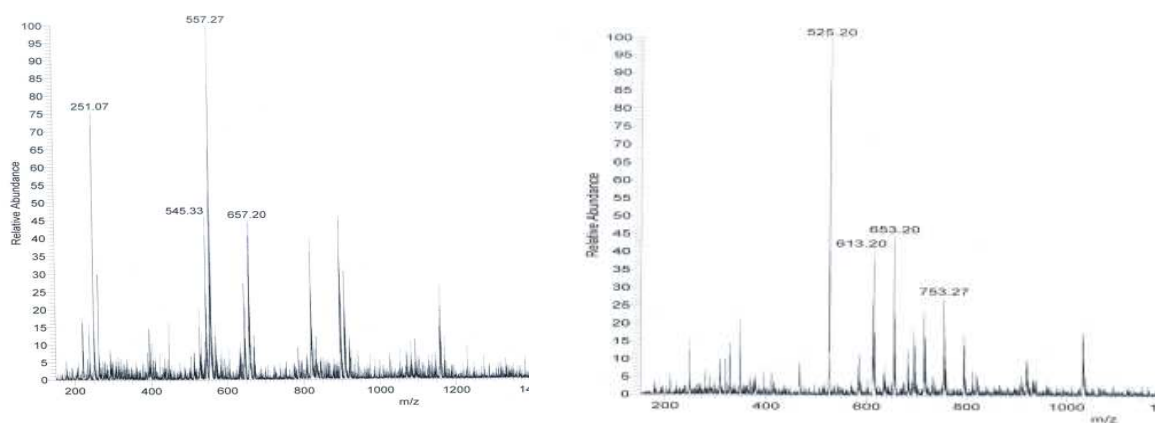


**Fig 1:  $^1\text{H}$  NMR Spectrum of (a)  $[\text{Ni}(\text{C}_{30}\text{H}_{28}\text{N}_8)](\text{ClO}_4)_2$  (b)  $[\text{Ni}(\text{C}_{34}\text{H}_{36}\text{N}_8)](\text{ClO}_4)_2$**

The  $^1\text{H}$  NMR spectrum (fig 1b) of  $[\text{Ni}(\text{C}_{34}\text{H}_{36}\text{N}_8)](\text{ClO}_4)_2$  in  $\text{CDCl}_3$  shows the multiplet at 7.75 – 7.35  $\delta$  which is assigned to protons (20 protons) of the four aromatic rings. The multiplet in aliphatic region at 2.16 – 1.86  $\delta$  corresponds to methyl protons (12 protons).

### ESI Mass Spectra

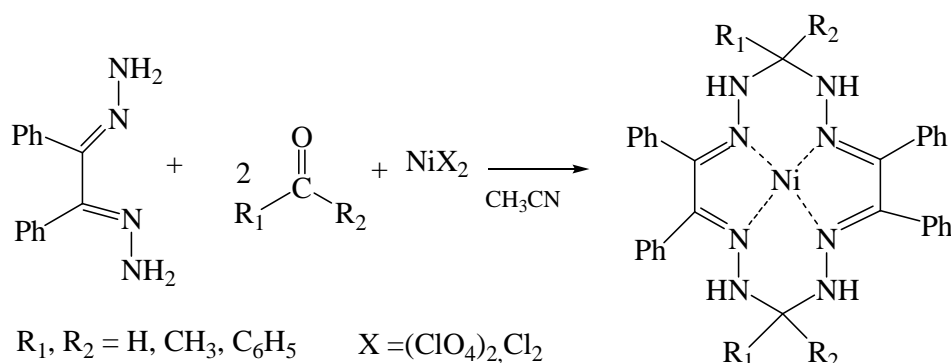
The ESI spectrum of the complex (Fig 2)  $[\text{Ni}(\text{C}_{30}\text{H}_{28}\text{N}_8)](\text{ClO}_4)_2$  showed a molecular ion peak at  $m/z$  557 which is equivalent to  $[\text{Ni}(\text{C}_{30}\text{H}_{28}\text{N}_8)-1]$ . The peak at  $m/z$  657.20, assigned to  $[\{\text{Ni}(\text{C}_{30}\text{H}_{28}\text{N}_8)\}(\text{ClO}_4)]$ . The peak at  $m/z$  545 is due to the loss of  $-\text{CH}$  group  $[\text{Ni}(\text{C}_{30}\text{H}_{28}\text{N}_8)]$ .



**Fig 2:** Mass spectrum of (a)  $[\text{Ni}(\text{C}_{30}\text{H}_{28}\text{N}_8)](\text{ClO}_4)_2$  (b)  $[\text{Ni}(\text{C}_{34}\text{H}_{36}\text{N}_8)](\text{ClO}_4)_2$

The ESI spectrum of the complex  $[\text{Ni}(\text{C}_{34}\text{H}_{36}\text{N}_8)](\text{ClO}_4)_2$  showed a molecular ion peak at  $m/z$  613.20 which is equivalent to  $[\text{Ni}(\text{C}_{34}\text{H}_{36}\text{N}_8) - 1]$ . The peaks at  $m/z$  753, 653, 525 assigned to  $[\{\text{Ni}(\text{C}_{34}\text{H}_{36}\text{N}_8)\}(\text{ClO}_4) + \text{K}]$ ,  $[\text{Ni}(\text{C}_{34}\text{H}_{36}\text{N}_8) + \text{K}]$ ,  $[\text{Ni}(\text{C}_{28}\text{H}_{20}\text{N}_8)]$  respectively.

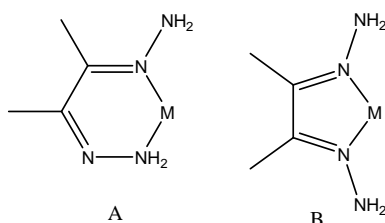
### General Reaction Scheme



### Scheme: Synthesis of benzil bis(hydrazone) complexes

Octaazabis ( $\alpha$ -diimine) macrocyclic complexes were prepared by reacting 2 equiv of Benzil dihydrazone with 2 equiv of the appropriate aldehyde or ketone in the presence of 1 equiv of divalent transition metal ( $\text{M} = \text{Ni}^{+2}$ ). The free amino groups of coordinated benzil bis(hydrazone) are ideally oriented for ring closure by reaction with carbonyl functional group to give six-membered chelate ring and ultimately octaaza-14-membered ring macrocyclic complexes. Condensation reactions with formaldehyde, acetone, and benzaldehyde led to the successful macrocyclic synthesis with Ni(II). The condensation reaction occur at slower rate with acetones.

The possibility of syn-anti and anti-anti isomerization among the free dihydrazone ligands and their octaaza complexes was considered. Both isomers of benzil dihydrazone are capable of forming metal chelates with the syn-anti configuration forming six-membered chelate rings, **A**, while the anti-anti configuration yields five-membered  $\alpha$ -diimine chelate rings, **B**.



The syn-anti configuration of a number of cyclic 1,2-dihydrazones was observed by Baldwin and co-workers. However, the NMR spectrum of benzil dihydrazone indicates the anti-anti configuration. The  $\pi$ -acceptor property of

the  $\alpha$ -diimine moieties enhances their chelating tendency with metals of significant  $\pi$ -donor tendency. Therefore the cyclization products of (B) obtained from condensation of benzil dihydrazone with aldehydes is expected to yield products having the symmetrical anti-anti structure.

### CONCLUSION

Present study demonstrates the feasibility of synthesizing 14-membered octaaza macrocyclic complexes. The synthesized benzil-bihydrazone acted as bidentate ligand. The template condensation of benzil bis(hydrazone) with aldehyde and ketone lead to the synthesis of 14-membered octaazabis ( $\alpha$ -diimine) macrocyclic complexes of Ni(II). The metal ion is coordinated through the azomethine nitrogen atom in the hydrazones. The bonding of the ligand to metal ion was confirmed by FT-IR, NMR, Mass and electronic data. These macrocyclic complexes can act as a building block for new supramolecular assemblies which could have potential photophysical or biological properties.

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