

*Dedicated to the memory of  
Professor Petru Spacu (1906–1995)*

## Ni(II) TERNARY COMPLEXES CONTAINING DIIMINE AND CYSTEINE

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This paper deals with the synthesis and characterization of new ternary [Ni(diimine)(thiolate)<sub>2</sub>] complexes where diimine is 2,2'-bipyridine (bpy) or its 4,4'-derivates: 4,4'-dimethyl-2,2'-bipyridine (dmbpy) and 4,4'-dinitro-2,2'-bipyridine (dnbpy) and thiolate is thioaminoacid cysteine (Cys) or its methylic ester (CysMe) in which Ni lies in a square planar N<sub>2</sub>S<sub>2</sub> environment. The investigation on the presence of ligand-ligand electron transfer processes in these complex compounds and of the factors these processes depends on are also studied. The complex compounds are suitable for being metalloenzyme simple *in vitro* models.

### INTRODUCTION

Biomolecules play a key role in basic life processes. The complexity of their structure, properties and functions has determined, in the last years, many researchers to create simple laboratory models for the active site of metalloenzymes.<sup>1</sup>

The total of five types of nickel enzymes known so far contrasts with greater number of enzymes containing iron or zinc, which raises the question as to what is the special function of nickel in these enzymes. The use of nickel by organisms implies that it confers an enhanced catalytic efficiency which compensates for the extra metabolic costs incurred by the cell. These costs include the effort expended in maintaining specific systems for nickel uptake, storage, and probably insertion into enzymes. For nickel sites in proteins, the formal oxidation state may also be difficult to determine, owing to charge delocalization. However, simple model complexes are useful to establish the effect of different ligand types.<sup>2</sup>

Ni(II) ions are characterized by higher affinity toward nitrogenous-based ligands than Zn(II) ions<sup>3</sup> and this explains the requirement for Ni(II) ions, in place of the more common Zn(II) in hydrolytic enzymes.

The aminoacid cysteine is the most frequently occurring ligand of nickel in the active centre of nickel containing enzymes. Sulfur coordination is an important feature in metalloenzymes and the covalency and soft environment are possible prerequisites for efficient charge transfer.

Aromatic diimines, such as 2,2'-bipyridine provide a ligand-ligand charge-transfer (LLCT) absorption with particularly large solvatochromic shifts of complexes.<sup>4</sup> A wide variety of thiolates and dithiolates are known to coordinate to transition metals and several have been utilized for square-planar mixed-ligand systems.

The synthesis of a large number of substituted derivatives of 2,2'-bipyridine has led to the discovery that substitution in the 4, 4'-positions has a profound effect upon the stabilities, oxidation reduction potentials and color intensities of the metal complexes.

The photochemical and redox properties of these complexes can be varied through appropriate substitution on the pyridine rings. The derivatization of a 2,2'-bipyridyl ligand with electron donating/withdrawing groups in the 4,4'-positions has been a popular means of controlling the redox

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potential of transition metal bipyridil complexes. The 4,4' disubstitution pattern is desirable, not only because it is the synthetically simplest to prepare but also because substitution at these positions offers no steric complications on complexation.<sup>5</sup>

Recently, the crystalline structure of a novel active site of an unusual bifunctional enzyme carbon monoxide dehydrogenase/acetyl CoA synthase (CODH/ACS)<sup>6</sup> was reported. This structure contains a square-planar Ni ion coordinated to a Cys – Gly – Cys motif in which two deprotonated amide nitrogen atoms comprise one half of the square plane and the two cysteine thiolates comprise the other half.

This paper deals with the synthesis and characterization of two new types of complexes  $[M(\text{bpyR})(\text{Cys})_2]$  and  $[M(\text{bpyR})(\text{MeCys})_2]$ , (where  $R = 2\text{H}, 2\text{CH}_3, 2\text{NO}_2$ ) that may be considered as simple models for an active site of a nickel enzyme.

## RESULTS AND DISCUSSION

Complexes of  $[M(\text{diimine})(\text{thiolate})_2]$  type where  $M = \text{Ni(II)}, \text{Zn(II)}$ , diimine is 2,2'-bipyridine (bpy) or its 4,4'-derivates: 4,4'-dimethyl-2,2'-bipyridine (dmbpy) and 4,4'-dinitro-2,2'-bipyridine (dnbpy) and thiolate is thioaminoacid cysteine (Cys) or its methylic ester (CysMe) have been separated from the ternary systems  $M(\text{II})$  salt – bpy or bpy derivate – cysteine or cysteine methylic ester varying the following experimental conditions:

- the nature of metal salt;
- the nature of acceptor molecule;
- the nature of donor molecule.

**Molecular electrical conductivity** measurements established that all synthesized complexes are nonelectrolytes.

The **FT-IR spectra** have been recorded to confirm our suppositions regarding the coordination mode of the ligands, the experimental data being assigned according to the literature.

In Fig. 1 are presented FT-IR spectra of Ni(II) complex compounds containing 4,4'-dimethyl 2,2'-bipyridine.

The infrared spectra of cysteine exhibit significant features in  $\nu(\text{H}_3\text{N}^+)$  and  $\nu(\text{COO}^-)$  regions. In cysteine the peaks at  $3000\text{ cm}^{-1}$  and  $2946\text{ cm}^{-1}$  were assigned to  $\nu(\text{N-H})$  asymmetric and symmetric stretching vibrations. The peak at  $2731\text{ cm}^{-1}$  was assigned to  $\nu(\text{C-H})$  stretching frequency. The asymmetric and symmetric stretching vibrations of carboxylate group of cysteine were observed at  $1582\text{ cm}^{-1}$  and  $1404\text{ cm}^{-1}$ . The peak due to  $\nu(\text{S-H})$  was observed at  $2600\text{ cm}^{-1}$ . The peaks due to  $\text{NH}_3^+$  twisting and rocking and  $\text{COO}^-$  wagging frequencies were observed in the range  $1200\text{--}600\text{ cm}^{-1}$ .

The infrared spectra of all synthesized complexes showed characteristic bands positions, shifts and intensities which can be correlated to monodentate S Cysteine coordination. The absence of  $\nu(\text{S-H})$  frequency in the spectra of complexes is a proof of the deprotonation of the S-H group on binding with the metal. The spectra did not show any broad band around  $3400\text{ cm}^{-1}$  indicating the non coordination of water molecules.

In the region  $1570\text{--}1620\text{ cm}^{-1}$  in the spectra of complexes all bands assigned to  $\nu(\text{C-C}), \nu(\text{C-N})$  ( $1570, 1595, 1620\text{ cm}^{-1}$ ) are shifted towards higher frequencies in comparison to unbounded bpy or bpy derivatives what indicates that these N-donors are coordinated to metal.

To better understand the most probable electronic structure of the studied complex compounds, we have examined their absorption properties. At first glance the reflectance UV VIS spectra appear very similar to those of other  $[\text{Ni(II)}(\text{diimine})(\text{dithiol})]$  complexes. An intense, structured band maximizing near  $250\text{--}300\text{ nm}$  is attributed to the lowest diimine-centered spin-allowed  $\pi\text{--}\pi^*$  transition and also to the cysteine ligand. The spectra present another two bands, one relatively intense around  $500\text{ nm}$  assigned to  $b_{1g} \rightarrow b_{2g}$  ( ${}^1A_{1g} \rightarrow {}^1A_{2g}$ ) transition and the other one, more intense, around  $400\text{ nm}$  assigned to  $b_{1g} \rightarrow a_{1g}$  ( ${}^1A_{1g} \rightarrow {}^1B_{1g}$ ) transition (Fig. 2).

The absence of a band in the range of  $900\text{--}1200\text{ nm}$  is a real proof for a square-planar geometry of complexes.

The oxidative decomposition of the complex compound  $[\text{Ni}(\text{dmbpy})(\text{Cys})_2]$  (Fig. 3) begins around  $65^\circ\text{C}$  and ends at  $710^\circ\text{C}$  with eight peaks in the DTA curve: the first and the second endothermic and the rest exothermic. Among all these peaks the sixth and the seventh are strongly exothermic and the last one ( $627\text{--}710^\circ\text{C}$ ) represents the oxidation of metallic nickel to nickel oxide associated to a weight growth<sup>7</sup>. This oxidation of metallic nickel to nickel oxide also occurs to another malic acid Fe-Ni complex compound<sup>8</sup>, and in this case nickel identification was made by X-ray diffractometry.

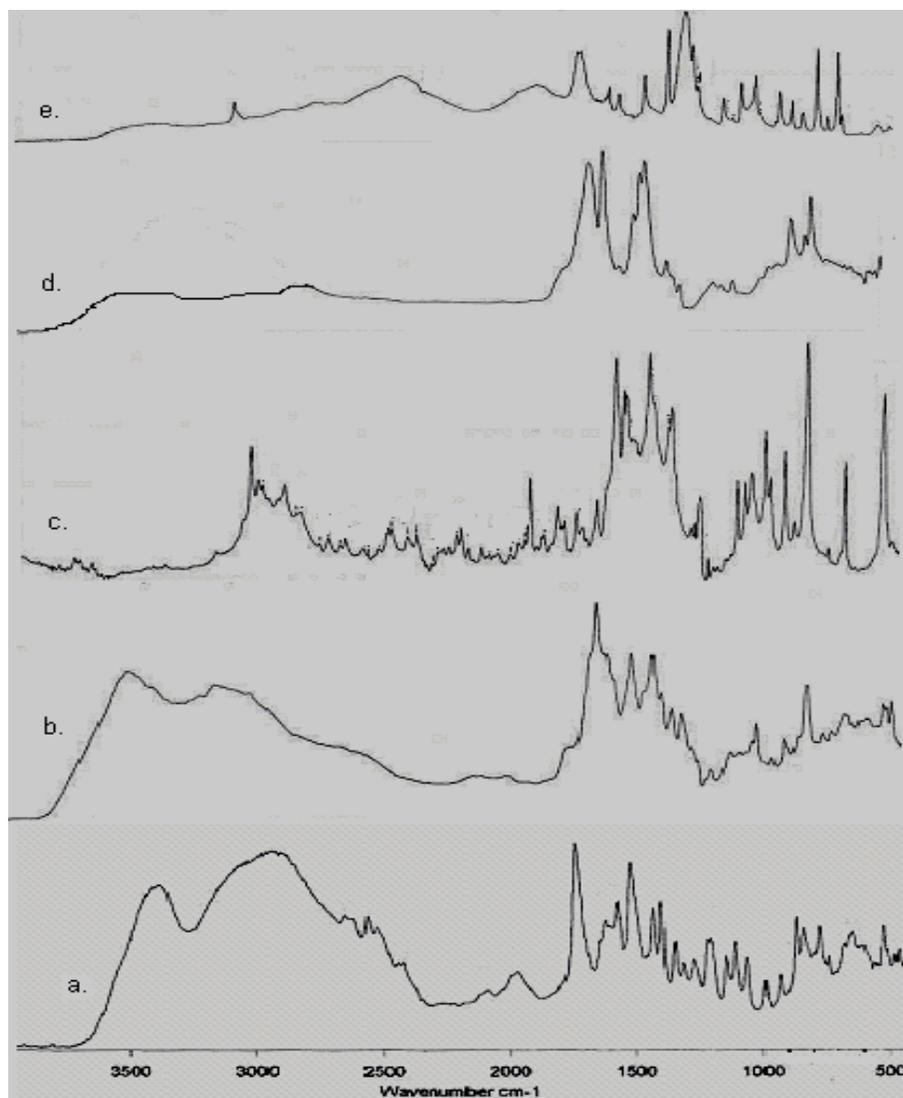


Fig. 1 – Infrared spectra of: a. Cys; b.  $[\text{Ni}(\text{dmdpy})(\text{Cys})_2]$ ; c. dmdpy; d.  $[\text{Ni}(\text{dmdpy})(\text{CysMe})_2]$ ; e. CysMe in the  $4000\text{-}400\text{ cm}^{-1}$  range.

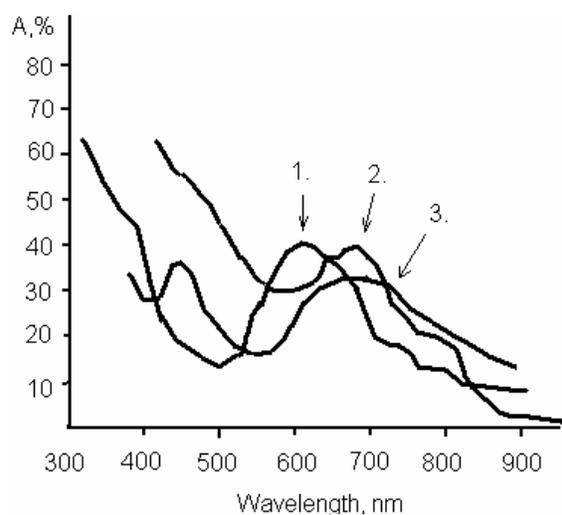


Fig. 2 – Reflectance spectra of: 1.  $[\text{Ni}(\text{dmbpy})(\text{Cys})_2]$ ; 2.  $[\text{Ni}(\text{bpy})(\text{Cys})_2]$ ; 3.  $[\text{Ni}(\text{dnbpy})(\text{Cys})_2]$ .

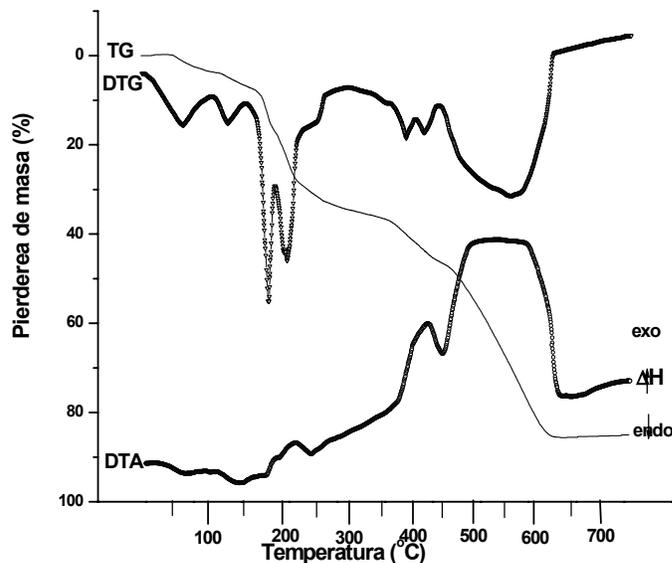


Fig. 3 – Thermal behaviour of complex compound [Ni(dmbpy)(Cys)<sub>2</sub>].

In Table 1 are presented the temperature range and the weight loss for all processes associated to oxidative decomposition of the complex compound [Ni(dmbpy)(Cys)<sub>2</sub>].

Table 1

Processes associated to oxidative decomposition of the complex compound [Ni(dmbpy)(Cys)<sub>2</sub>]

Process	T <sub>i</sub> – T <sub>f</sub> (°C)	T <sub>m</sub> (°C)	Weight loss, (%)
1	65 – 124	88	4.44
2	124 – 152	143	3.03
3	152 – 191	179	10.15
4	191 – 328	210	18.13
5	328 – 408	392	6.84
6	408 – 443	422	4.04
7	443 – 627	553	38.70
8	627 -710*	660	0.31
Total			85.02

\* weight growth

In the complex compound [Ni(dmbpy)(Cys)<sub>2</sub>] 4,4'-dimethyl 2,2'-bipyridine decomposes before cysteine, and the seventh process starts from Ni(Cys)<sub>2</sub> according to the thermal behaviour of another nickel(II) complex compounds containing acids or aminoacids and neutral molecules with nitrogen as donor atom<sup>9</sup> in which neutral molecule decomposes first.

The temperatures at the onset of decomposition suggest that the complexes are thermally more stable comparing to the ligands due to coordination.

The complex compound containing 4,4'-dimethyl 2,2'-bipyridine is more thermally stable comparing to the complex compound containing 2,2'-bipyridine or 4,4'-dinitro 2,2'-bipyridine respectively.

Formation of nickel oxide, respectively zinc oxide, occurs at comparable temperature for the same type of complex compound.

The low values of magnetic susceptibilities, presented in Table 2, under that for the paramagnetic, octahedral species of Ni(II) (under 3.2 BM) sustain a possible equilibrium square-planar (diamagnetic) ↔ octahedral (paramagnetic) that is probably present in crystalline lattice of the studied complexes.

Considering that the obtained complexes are of the type [Ni(diimine)(thiolate)<sub>2</sub>] which contain two different ligands in which one is more easily reduced and the other more easily oxidized, it is very probable that the relative band from the reflectance spectra of the complexes in visible range is not only a d-d band but also a CT band (probably the CT band is overlapped over a d-d one).

Table 2  
Magnetic susceptibilities

Complex compound	Magnetic susceptibility, BM
[Ni(bpy)(Cys) <sub>2</sub> ]	1.790268
[Ni(bpy)(CysMe) <sub>2</sub> ]	1.733533
[Ni(dmbpy)(Cys) <sub>2</sub> ]	1.933318
[Ni(dmbpy)(CysMe) <sub>2</sub> ]	1.875462
[Ni(dnbpy)(Cys) <sub>2</sub> ]	1.791869
[Ni(dnbpy)(CysMe) <sub>2</sub> ]	1.763453
[Zn(bpy)(Cys) <sub>2</sub> ]	0.028179
[Zn(bpy)(CysMe) <sub>2</sub> ]	0.046574
[Zn(dmbpy)(Cys) <sub>2</sub> ]	0.068786
[Zn(dmbpy)(CysMe) <sub>2</sub> ]	0.053248
[Zn(dnbpy)(Cys) <sub>2</sub> ]	0.201539
[Zn(dnbpy)(CysMe) <sub>2</sub> ]	0.235689

To support this idea and to assign the nature of the CT band ( $L \rightarrow M$ ;  $M \rightarrow L$ ;  $L \rightarrow L'$ ) we have studied the reflectance spectra of  $[\text{Zn(II)(diimine)(thiolate)}_2]$  complexes.

Replacing Ni(II) ion in  $[\text{Ni(bpyR)(Cys)}_2]$  or  $[\text{Ni(bpyR)(MeCys)}_2]$  chromophore with Zn(II) give complexes which absorb in visible range (500-550 nm). Such bands are very probable  $\pi-\pi^*$  bands (ligand-ligand bands) because Zn(II) ( $d^{10}$ ) does not absorb in visible range and MLCT or LMCT bands are also very little possible for Zn(II) (due to the Zn high redox potential).

An increasing of both the wavelength and the intensity of the charge transfer to diimine absorption band from Zn(II) complexes to Ni(II) complexes is observed (Fig. 4). This trend in wavelength follows the trend in the second ionization potentials of metals.

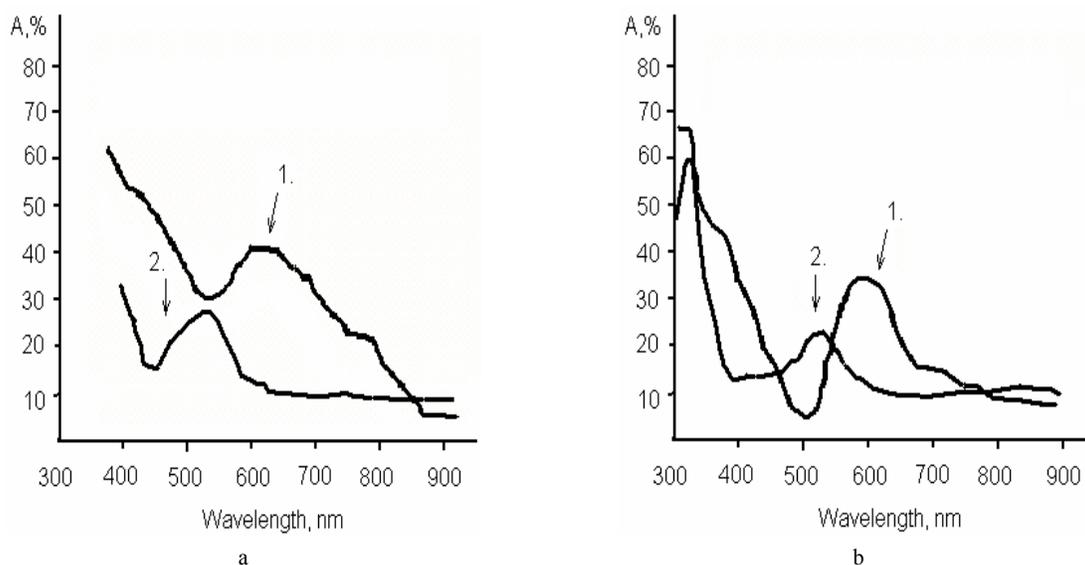


Fig. 4 – Reflectance spectra of Ni(II) and Zn(II) complexes respectively: 1b.  $[\text{Ni(dmdpy)(Cys)}_2]$ ; 2b.  $[\text{Zn(dmdpy)(Cys)}_2]$ ; 1a.  $[\text{Ni(dpy)(Cys)}_2]$ ; 2a.  $[\text{Zn(dpy)(Cys)}_2]$ .

Such complex compounds which present ligand  $\rightarrow$  ligand charge transfer are suitable for being simple models of metalloenzyme active situs regarding the electron transfer processes associated with biocatalytic reactions.

## EXPERIMENTAL

Ligand 4,4'-dinitro 2,2'-bipyridine was synthesized in three steps by original method based on literature data.<sup>4,10,11</sup>

a. 2,2'-bipyridine  $N,N'$ -dioxid. WARNING: This reaction is potentially explosive. 2,2'-bipyridine (10g, 64 mmol), hydrogen peroxide (13 cm<sup>3</sup>, 100 vol.), and glacial ethanoic acid (75 cm<sup>3</sup>) were heated at 80°C for 3 hours. Hydrogen peroxide (9 cm<sup>3</sup>, 100 vol.)

was added and heating was continued for 4 hours. The colourless solution was cooled to room temperature and added slowly to propanone (11), precipitating a white solid of 2,2'-bipyridine N,N'-dioxide which is collected by filtration and air dried (11 g, 90%). This product is commonly used as obtained from the above preparation, but recrystallisation from a large volume of ethanol gave transparent white plates, m.p. 312-315<sup>0</sup>C (decomp.)

b. 4,4'-dinitro 2,2'-bipyridine N,N'-dioxide. To a mixture of 2,2'-bipyridine N,N'-dioxid (5 g, 27 mmol) and oleum sulphuric acid (1:2 v/v, 25 cm<sup>3</sup>) in an ice bath, nitric acid (fuming, 20 cm<sup>3</sup>) was added slowly. The mixture was heated to 100<sup>0</sup>C for 6 hours, with the reflux condenser fitted with a calcium chloride drying tube. After this time it was cooled to room temperature and cautiously poured onto crushed ice (50 g) and water (50 cm<sup>3</sup>) to give a yellow solid. This was collected by filtration, washed with water and air dried to give 4,4'-dinitro 2,2'-bipyridine N,N'-dioxid (3.75 g, 49%) m. p. 272-275<sup>0</sup>C.

c. 4,4'-dinitro 2,2'-bipyridine. A suspension of 1.5 g (5.4 mmol) of 4,4'-dinitro 2,2'-bipyridine N,N'-dioxid in 23 ml of anhydrous chloroform was cooled to 0<sup>0</sup>C and 3 ml (34 mmol) of phosphorus trichloride was added. The mixture was heated at reflux over a water-bath for one hour, cooled to room temperature and poured into a mixture of ice and water. The resulting suspension was made alkaline with aqueous sodium hydroxide and 1.3 g of unchanged starting material recovered by filtration. The aqueous layer of the filtrate was extracted with several portions of fresh chloroform and discarded. The combined chloroform portions were evaporated to a crystalline residue (0.2 g, m.p.182-185<sup>0</sup>C) which was recrystallized from 95% ethanol to yield 0.12 g of orange needles, m.p. 191.5-194.5<sup>0</sup>C. Repeated recrystallizations from the same solvent raised the melting point to 195-197<sup>0</sup>C.

Anal. Found: C 49.17; N 22.33. Calc. C 48.78; N 22.76.

### Complex compounds synthesis

Complexes were synthesized by mixing a DMF solution containing 1:2 ratios of bpy or bpy derivatives (1mmol) and cysteine or cysteine methyl ester (2mmol) which were added simultaneously and independently to a nickel chloride DMF solution (1mmol). The resulting solution was concentrated on a water bath until the green precipitates have been obtained. The precipitates were filtered and washed with ethanol, ethylic ether and dried in air.

**Molar electrical conductivities** have been recorded in DMSO solutions at 25<sup>0</sup>C, with a OK 102/1 Radelkis Conductometer with a 0.1 S – 0.5 S measuring range.

**FT-IR spectra** have been recorded with a Perkin-Elmer spectrophotometer using KBr pellets as reference in the 4000-400 cm<sup>-1</sup> range.

**<sup>1</sup>H NMR** have been recorded in DMSO using a Bruker Avance DRX 400 Spectrometer at room temperature.

**Electronic reflectance spectra** were recorded using a Specord M 40 Carl Zeiss Jena with MgO as standard.

**Magnetic measurements** were carried out using a Faraday balance at room temperature using Mohr salt as standard.

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