

SYNTHESIS AND STRUCTURE OF IRON(III) COMPLEX WITH 2-ACETILPYRIDINE-AMINOGUANIDINE

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Abstract: Schiff bases represent an interesting class of compounds due to a wide range of possible applications, especially their biological activity. Having in mind that the biological activity of the ligand could be closely related to its coordinating properties, we examined the synthesis and structure of a novel Fe(III) complex with the Schiff base of aminoguanidine and 2-acetylpyridine.

Bis(ligand) complex of iron(III), of the formula $[\text{Fe}(\text{L}-\text{H})_2]_2(\text{NCS})\text{Cl}$, was obtained by the reaction of FeCl_3 and the thiocyanate ligand salt in a mole ratio 1:1 in the presence of lithium-acetate as a deprotonating agent. The complex is obtained in the form of brown single crystals and is characterized by elemental analysis data, conductometric measurements, IR spectra, and X-ray analysis. The latter revealed that the chelating ligand is coordinated in its monoanionic form *via* pyridine, azomethine, and nitrogen atoms of the aminoguanidine fragment, forming octahedral environment.

Keywords: Schiff bases, guanylhydrazones, transition metal complexes, X-ray crystallography.

1. INTRODUCTION

Schiff bases are a promising class of compounds because of easy synthetic routes and a wide range of applications. Some of these compounds show significant antioxidant [1], anticonvulsant [2], and diuretic activities [3], while the others are used for the preparation of drugs, as catalysts, sensors, for gas storage and purification, etc. These structures are often stabilized by hydrogen and halogen bonds, as well as $\pi \dots \pi$ stacking interactions, thus could be used as thermo-resistant materials, pharmaceutical products, optoelectronic devices [3]. The presence of metal ions in these structures could enhance the properties of the ligands themselves, especially the biological activity [4]. Doğan et al. [5] call this ligand class „exclusive ligands” because they can coordinate to different metals and have rich coordination chemistry.

Among this large group of compounds, derivatives of aminoguanidine occupy a special place with a wide range of pharmacological applications [6]. Having in mind all the above, in the last decade, we have thoroughly investigated the coordination chemistry of Schiff bases of aminoguanidine.

Since 2-acetylpyridine derivatives and their

complexes have shown the antitumor and cytotoxic activity [7], it became of interest to synthesize and characterize the Schiff base of these two compounds and its complexation abilities. Recently, copper(II) complexes with 2-acetylpyridine-aminoguanidine have been synthesized and structurally characterized and their interactions with the chemotherapeutic drug, cisplatin, were investigated [8,9].

Schiff base complexes with iron are important in medicinal chemistry [10], as biomimetic functional models [11] for iron-containing enzymes, but also as catalysts [12].

As the continuation of our previous research, bearing in mind the mentioned importance of iron complexes, in this paper, the synthesis and characterization of iron(III) complex with the Schiff base of aminoguanidine and 2-acetylpyridine are described.

2. EXPERIMENTAL

2.1. Reagents

All chemicals used were commercially available products of analytical reagent grade, except for the ligand 2-acetylpyridine-aminoguanidinium

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dithiocyanate (L·2HNCS) which was prepared as described earlier [13].

2.2. Synthesis of the complex $[\text{Fe}(\text{L}-\text{H})_2]_2(\text{NCS})\text{Cl}$

The mixture of 0.075 g (0.25 mmol) of thiocyanate ligand salt (L·2HNCS) and 0.050 g (0.5 mmol) LiOAc is dissolved in 5 cm³ of water. Upon mild heating of the mixture, 0.040 g (0.25 mmol) FeCl₃ is added and heated until complete dissolution. A week later from the dark-red solution dark single crystals were filtered and washed with water and EtOH. Yield: 0.039 g (68 %).

2.3. Analytical methods

Elemental analyses (C, H, N, and S) of air-dried compounds were carried out by standard micro-methods. Molar conductivity measurements of freshly prepared 1 mM solutions were performed on a Jenway 4010 conductivity meter. IR spectra were recorded on a Nicolet Nexus 670 FTIR (Thermo Scientific) spectrophotometer, in the range of 400–4000 cm⁻¹ by the KBr pellet technique. Melting points were measured on a *Nagema* hot stage microscope *Rapido*.

2.4. Single-crystal X-ray diffraction

Single-crystal X-ray diffraction data for compound $[\text{Fe}(\text{L}-\text{H})_2]_2(\text{NCS})\text{Cl}$ were collected on an Oxford Diffraction Gemini S diffractometer equipped with a CCD detector, using monochromatized Mo *K* α radiation ($\lambda = 0.71073 \text{ \AA}$). Data reduction and empirical absorption correction were performed with CrysAlisPRO [14]. The structures were solved by direct methods using SHELXS and refined on F^2 by full-matrix least-squares using SHELXL [15]. All non-hydrogen atoms were refined anisotropically. H atoms attached to C atoms were placed at the geometrically calculated positions with the C–H distances fixed to 0.93 and 0.96 Å from the aromatic and methyl C atoms, respectively. H atoms attached to N atoms were located in difference Fourier maps and refined using distance restraints. The U_{iso} values of the H atoms were approximated by U_{eq} values of their carrier atoms. Crystallographic details for structure analysis are summarized in Table 1. The figures were produced using MERCURY [16].

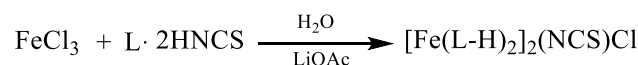
Table 1. Crystallographic and refinement details

Crystal data	$[\text{Fe}(\text{L}-\text{H})_2]_2(\text{NCS})\text{Cl}$
Chemical formula	$\text{Fe}_2\text{C}_{33}\text{H}_{40}\text{N}_{21}\text{SCl}$
M_r	910.06
Crystal system	Triclinic
Space group	$P\bar{1}$
Temperature (K)	293(2)
a (Å)	11.5383(3)
b (Å)	12.7155(4)
c (Å)	15.9651(5)
α (°)	97.300(3)
β (°)	97.667(2)
γ (°)	94.172(2)
V (Å ³)	2253.08(12)
Z	4
Radiation type	Mo <i>K</i> α
<i>Data collection</i>	
Diffractometer	Gemini S (Oxford Diffraction)
Absorption correction	Gaussian
μ (mm ⁻¹)	0.786
Measured reflections	24966
Independent reflections	10617
Observed reflections	8204
$[I > 2\sigma(I)]$	
R_{int}	0.0240
<i>Refinement</i>	
$R[F^2 > 2\sigma(F^2)]$	0.080
$wR(F^2)$	0.265
S	1.090
No. of reflections	10617
No. of parameters	537
No. of restraints	12
H-atom treatment	Mixed

3. RESULTS AND DISCUSSION

3.1. Synthesis and physicochemical properties of the complex $[\text{Fe}(\text{L}-\text{H})_2]_2(\text{NCS})\text{Cl}$

Bis (ligand) complex of iron(III) was obtained in the reaction of FeCl₃ and the thiocyanate ligand salt in molar ratio 1:1, in the presence of LiOAc as deprotonating agent (Scheme 1). The obtained complex shows good solubility in DMF, while it is poorly soluble in MeOH and EtOH.



Scheme 1. Synthesis of the complex

The molar conductivity of the complex corresponds to a 3:1 type of electrolyte [17], which is in concordance with the coordination formula (Table 2).

It is interesting to mention that a similar reaction with chloride ligand salt and with ammonia used for deprotonation of the ligand yielded in the formation of

the complex of the formula $[\text{Fe}(\text{L}-\text{H})_2]\text{Cl}\cdot 6\text{H}_2\text{O}$ [18]. However, the latter complex crystallizes in the tetragonal crystal system, *i.e.* has higher symmetry, probably due to the presence of only one sort of counter-ion.

Table 2. Elemental analysis and molar conductivity data

Formula (sum formula)	Found (calculated), %			λ_M [$\text{Scm}^2\text{mol}^{-1}$] (DMF)
	C	H	N	
$[\text{Fe}(\text{L}-\text{H})_2]_2(\text{NCS})\text{Cl}$ ($\text{Fe}_2\text{C}_{33}\text{H}_{40}\text{N}_{21}\text{SCl}$)	43.28 (43.57)	4.20 (4.40)	32.18 (32.33)	291

As it was confirmed by single-crystal XRD (*vide infra*) the chelating ligand is coordinated in the usual tridentate NNN manner, *via* pyridine, azomethine, and the nitrogen atom of the imino group of aminoguanidine moiety. This mode of coordination was primarily suggested by the comparison of the IR spectra of the complex (Figure 1) and the ligand salt (Figure 2). The negative shift of $\nu(\text{C}=\text{N})$ band in the spectrum of the complex (1628 cm^{-1}) compared with its position in the spectrum of the ligand (1680 cm^{-1} [13]) points to the coordination

of the azomethine nitrogen atom. The $\nu(\text{CN})$ band is shifted towards lower wavenumbers and suggests the coordination of aminoguanidine fragment. Due to the coordination of the pyridine nitrogen, weak bands ascribed to deformations of the pyridine ring in (604 cm^{-1}) and out of a plane (405 cm^{-1}) suffer a positive shift [19] and could be found at 655 cm^{-1} and 437 cm^{-1} in the spectrum of the complex. Finally, the band originating from the free NCS^- ion is found at ca. 2050 cm^{-1} in both the spectra [19].

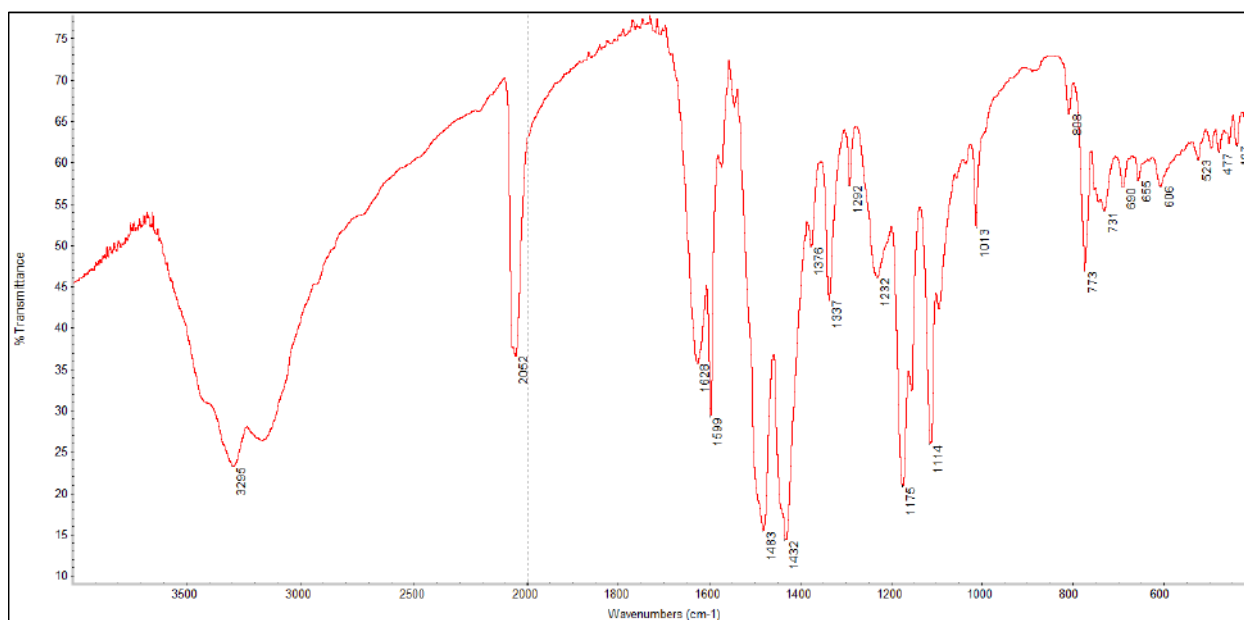


Figure 1. IR spectrum of the complex

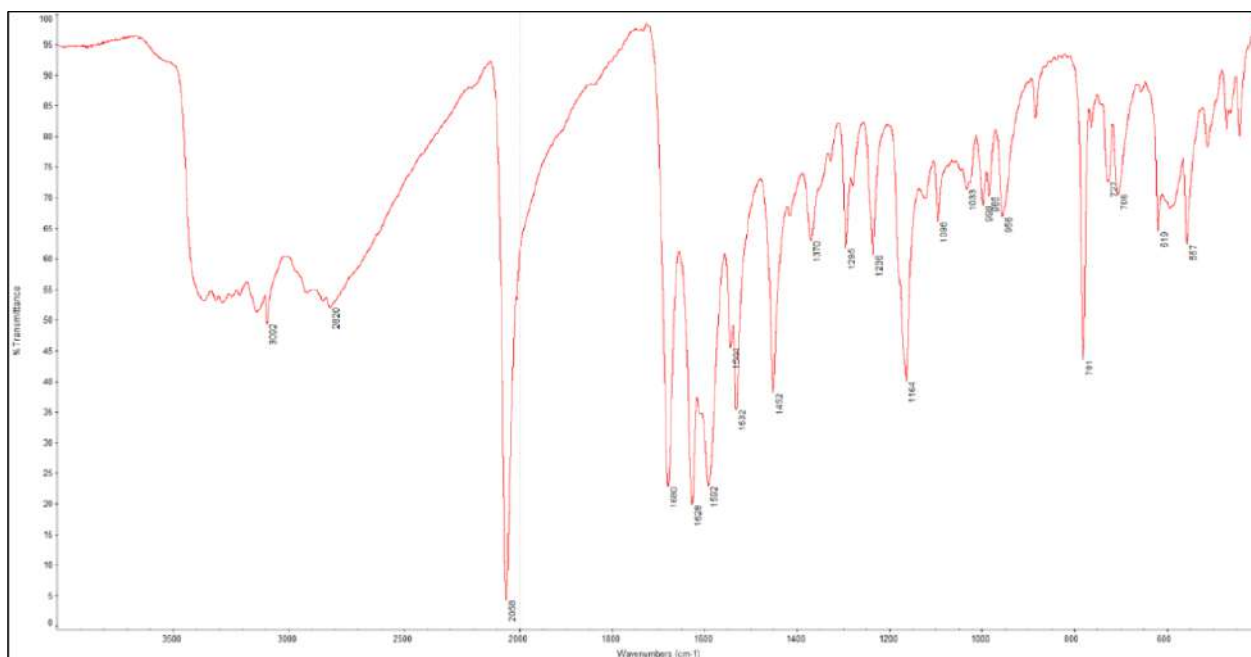


Figure 2. IR spectrum of the ligand L-2HNCS [13]

3.2. Crystal structure

As was mentioned above, this complex cation is also found in the earlier described complex of the formula $[\text{Fe}(\text{L}-\text{H})_2]\text{Cl}\cdot 6\text{H}_2\text{O}$ [18], thus it would be interesting to make a comparative analysis of the two structures and the structure of the ligand (Figure 3.). Figure 4. represents complex cations in the asymmetric unit, while counter-ions are omitted due to clarity. Having that in mind, in Table 3. selected bond lengths and angle values for the complexes $[\text{Fe}(\text{L}-\text{H})_2](\text{NCS})\text{Cl}$ and $[\text{Fe}(\text{L}-\text{H})_2]\text{Cl}\cdot 6\text{H}_2\text{O}$, and the thiocyanate ligand salt are given.

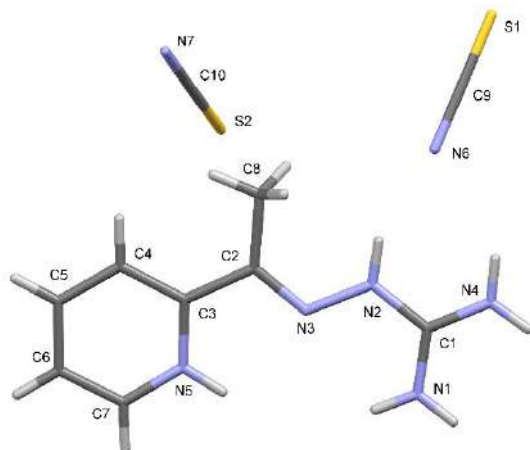


Figure 3. Structure of the ligand, L-2HNCS

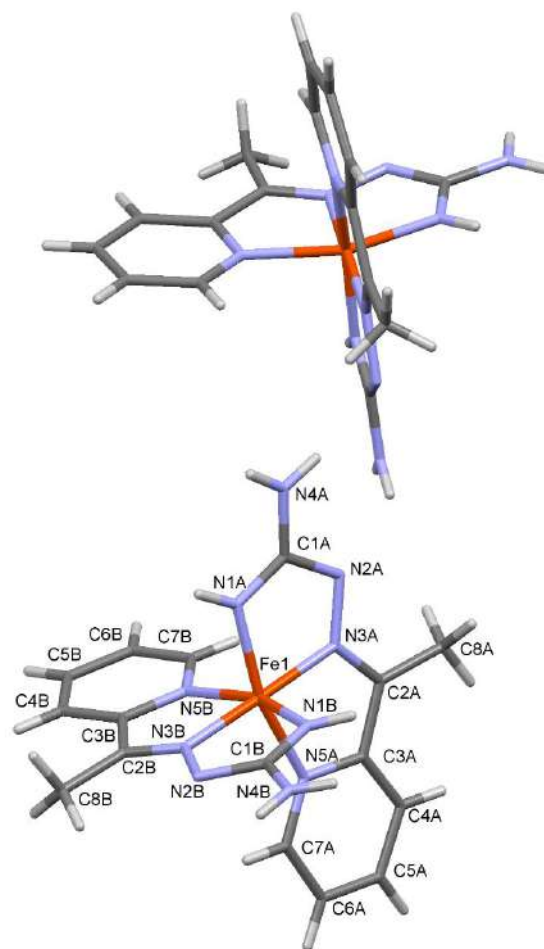


Figure 4. Structure of the complex

Table 3. Selected bond lengths and angle values

Bond	Lengths, Å		
	[Fe(L-H) ₂]Cl·6H ₂ O	[Fe(L-H) ₂] ₂ (NCS)Cl	L·2HNCS
Fe–N1	1.884(5)-1.932(5)	1.879(4)-1.893(5)	–
Fe–N3	1.889(5)-1.911(6)	1.892(3)-1.900(3)	–
Fe–N5	1.529(7)-1.578(4)	1.964(4)-1.976(4)	–
C1–N1	1.305(9)-1.324(7)	1.316(6)-1.356(6)	1.302(5)
C1–N2	1.346(7)-1.360(7)	1.347(6)-1.356(6)	1.343(4)
C1–N4	1.327(7)-1.340(7)	1.346(5)-1.364(7)	1.317(4)
N2–N3	1.335(9)-1.369(6)	1.347(4)-1.364(7)	1.364(3)
C2–N3	1.287(9)-1.322(7)	1.288(6)-1.314(6)	1.283(3)
Bond	Angles, °		
	[Fe(L-H) ₂]Cl·6H ₂ O	[Fe(L-H) ₂] ₂ (NCS)Cl	L·2HNCS
C3–N5–C7	119.4(5)-120(5)	119.2(4)-120.3(4)	123.7(2)
C1–N2–N3	107.1(3)-108.3(5)	106.6(4)-108.3(4)	118.0(2)
N3B–Fe–N3A	178.5(2)	177.7(2)	–
N5B–Fe–N1B	160.8(2)	160.9(2)	–
N1A–Fe–N5A	161.1(2)	161.4(2)	–

The asymmetric unit of the complex [Fe(L-H)₂]₂(NCS)Cl consists of two complex cations [Fe(L-H)₂]⁺, and one chloride and one thiocyanate as counterions. In this complex chelating ligand is coordinated in the usual tridentate NNN mode, through pyridine (N5), azomethine (N3) and, the imino nitrogen atom of aminoguanidine moiety (N1), forming two five-membered metallocycles.

Due to the presence of LiOAc, as a deprotonating agent, the Schiff base is deprotonated, thus coordinated in its monoanionic form. The deprotonation of the pyridine N-atom, which takes place before coordination, causes the shrinkage of the C3–N5–C7, which has a value of 123.7(2) ° in the structure of the ligand [13] for ca. 4°. Similarly, the deprotonation of the N2 atom, as well as the coordination of the aminoguanidine residue, leads to shrinkage of the C1–N2–N3 angle for 10–11°. It should be mentioned that this change in angle value is less pronounced in the complexes containing the neutral form of the ligand with the protonated N2 atom [13].

The Fe(III) ion is situated in the slightly distorted octahedral environment of two monoanions of the chelating ligand. Even though the bis(ligand) complex is obtained, the ligand preserved a high degree of planarity. The values of trans angle N3B–Fe–N3A are near the theoretical value, while the others deviate from this value for ca. 10°. The dihedral angles between the chelate rings have values in the range of 2.41–4.18°.

In the complex [Fe(L-H)₂]₂(NCS)Cl all Fe–N bond lengths are in the range of 1.879(4)–1.976(4) Å, with the longest distance between the metal ion and pyridine nitrogen atom (N5), as it was found in

the structure of [Fe(L-H)₂]Cl·6H₂O as well. All intraligand C–N bonds are longer than double and shorter than single, except for the C2–N3 bond, which has a length that corresponds to a localized double bond. This trend is found in all the other complexes with this ligand [13] and is a consequence of electron delocalization in the aminoguanidine residue.

All hydrogen-donors of the chelating ligand are involved in the formation of weak H-bonds with chloride ion, sulfur atom of thiocyanate ion, and the hydrazine nitrogen atom of the neighboring ligand molecule.

The packing of the structural units of the complex is presented in Figure 5.

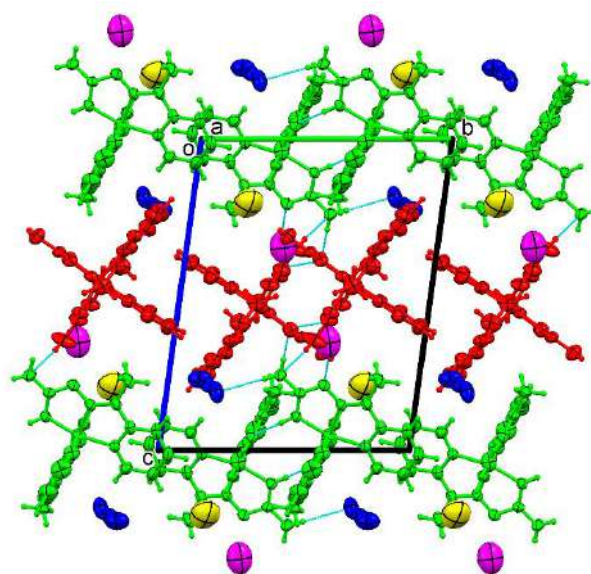


Figure 5. Packing of the structural units of the complex [Fe(L-H)₂]₂(NCS)Cl

4. CONCLUSION

The synthesis, some physicochemical and structural properties of the novel iron(III) complex with 2-acetylpyridine-aminoguanidine, of the formula $[\text{Fe}(\text{L}-\text{H})_2]_2(\text{NCS})\text{Cl}$, are presented. The reaction of an aqueous solution of FeCl_3 and the thiocyanate ligand salt in molar ratio 1:1, in the presence of LiOAc , yielded in the formation of single crystals of the titled bis(ligand) complex. The complex is characterized by elemental analysis, conductometric measurements, IR spectroscopy, and single-crystal X-ray analysis. The structural parameters of the obtained complex were compared to those of a similar structure containing the same complex cation, as well as the structure of the thiocyanate salt of the ligand. The tridentate NNN coordination of the Schiff base in its monoanionic form is found, and the effects of the deprotonation and coordination on the structure of the ligand are pointed out. Considering the mentioned biological importance of both ligand precursors, the ligand itself, as well as the iron complexes in general, some further research is going to be done to examine the antioxidant activity of the complex.

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СИНТЕЗА И СТРУКТУРА КОМПЛЕКСА ГВОЖЂА(III) СА 2-АЦЕТИЛПИРИДИН-АМИНОГВАНИДИНОМ

Сажетак: Већ неколико деценија Шифове базе аминогванидина привлаче пажњу истраживача захваљујући широком спектру потенцијалне примене, а пре свега биолошке активности. Због чињенице да је врло често биолошка активност лиганда уско повезана са њиховим комплексирајућим способностима, у овом раду биће описана синтеза и структура комплекса гвожђа(III) са Шифовом базом аминогванидина и 2-ацетилпиридина.

У реакцији гвожђе(III)-хлорида и тиоцијанатне соли лиганда у молском односу 1 : 1, у присуству литијум-ацетата као агенса за депротонацију, добијен је бис(лиганд) комплекс формуле $[\text{Fe}(\text{L}-\text{H})_2]_2(\text{NCS})\text{Cl}$. Добијени комплекс је чврста, кристална супстанца мрке боје, добро растворна у диметилформамиду, а нешто слабије у метанолу и етанолу. Састав и структура комплекса претпостављени су на основу података елементарне анализе, кондуктометријских мерења и IR спектра, а једнозначно потврђени рендгенском структурном анализом. Асиметрична јединица комплекса састоји се из два $[\text{Fe}(\text{L}-\text{H})_2]^+$ јона, једног хлоридног и једног тиоцијанатног јона. Хелатни лиганд је координован у моноанјонској форми на NNN тридентатни начин и то преко пиридинског, азометинског и имино атома азота аминогванидинског фрагмента, дајући октаедарско окружење око гвожђа(III).

Кључне речи: Шифове базе, гванилхидразони, комплекси прелазних метала, рендгенска структурна анализа.



Paper received: 20 August 2020
Paper accepted: 18 February 2021