Synthesis, Spectroscopy and X-ray Crystallography Structure of Pyridine 4-Carbaldehyde Semicarbazone Schiff Base Ligand

Farzaneh Mahmoudi a,*, Saeed Farhadi b,*, Michal Dusek b, Morgane Poupon b

a Department of Chemistry, Lorestan University, Khoramabad 68151-44316, Iran
b Institute of Physics of the Czech Academy of Sciences, Na Slovance 2, 18221 Prague 8, Czech Republic

ARTICLE INFO
Received: 09 November 2019
Revised: 16 December 2019
Accepted: 05 January 2020
Available online: 22 January 2020

KEYWORDS
Semicarbazone
Schiff base ligand
Crystal structure
Spectroscopy

ABSTRACT
In this work, pyridine 4-carbaldehyde semicarbazone Schiff base ligand (HL) was synthesized with condensation of pyridine 4-carbaldehyde and semicarbazide hydrochloride in reflux method. The HL was characterized using the CHN elemental analysis, FT-IR, UV-Vis, and 1H NMR spectroscopy. The single crystals of HL prepared and used for the X-ray crystallography. Single-crystal X-ray diffraction revealed that, HL crystallized in a triclinic system with the space group P-1. The FT-IR spectra and X-ray crystallography results suggested that the HL ligand is in keto form.

GRAPHICAL ABSTRACT

Pyridine 4-carbaldehyde semicarbazone Schiff base ligand (HL)

* Corresponding author's E-mail address: farzanehmahmoudi@yahoo.com (F. Mahmoudi), sfarhadi1348@yahoo.com (S. Farhadi)
**Introduction**

Schiff bases are known as imines or azomethines and are used as ligands for synthesis of complexes using different metal ions. They are obtained from condensation reaction of primary amines and aldehydes or ketones. Often, aldehydes react faster and better than ketones because of the steric and electronic effects [1-3]. For many years, they have been introduced as chelating ligands in transition metal coordination chemistry, because of easy synthesis routes, extensive availability and versatility of structure related to their potential applications in catalysis, analytical, pharmacological, and magnetism [4-5]. Schiff bases are also used as significant intermediates for synthesis of various bioactive materials [6-9]. Countless Schiff bases and their coordination complexes with outstanding antimicrobial activity, antifungal, and anticancer abilities have been reported [8-13]. The Schiff bases with pyridine ring have received more attention in literature [14-15]. The semicarbazones and thiosemicarbazones usually behave as chelating ligands, which are versatile in both neutral and anionic forms [16-18]. Metal complexes of semicarbazones and thiosemicarbazones have gained special attention due to their importance in medicine and biological system [19-20]. Furthermore, the metal complexes of semicarbazones have demonstrated antimicrobial [21,22], anticancer [23], and antiviral activities [24,25]. The first report for synthesis of pyridine 2-carbaldehyde semicarbazone ligand dates in 1955 [26,27], discovering its antifungal activity. Keeping on that, we reported several transition metal compounds based on this ligand [25, 28-30]. Herein we synthesized a new semicarbazone ligand by the reaction of semicarbazide hydrochloride and pyridine 4-carbaldehyde under reflux conditions and characterized it with several analyses. Furthermore the structure of the HL was determined using the X-ray crystallography and discussed completely.

**Experimental**

**General**

The chemicals and solvents contains pyridine 4-carbaldehyde, semicarbazide hydrochloride and ethanol were purchased from Merck. Fourier-transform infrared spectra were recorded on Shimadzu FT-IR 8400 S (Japan) using KBr pellet. Microanalyses were carried out using a Heraeus CHN–O– Rapid analyzer. The uncorrected melting point was measured on an Electrothermal 9100 apparatus. \(^1\)H NMR spectra were recorded on a Bruker AVANCE 300-MHz instruments at room temperature with the signal of the free deuterated methanol, CD\(_2\)OD solvent using TMS as internal reference. UV-Vis spectrum was recorded on a Carry 100 Conc Varian spectrophotometer.

**Synthesis of pyridine 4-carbaldehyde semicarbazone (HL)**

At first, semicarbazide hydrochloride (10 mmol, 1.1 g) was added to 40 mL ethanol in a round bottom flask and heated at 75 °C. It refluxed for 2 h at this temperature till dissolved completely in ethanol. Then pyridine 4-carbaldehyde (10 mmol, 1 mL) was dissolved in 10 mL ethanol and was added dropwise to the above solution under reflux condition. The mixture was refluxed on water bath for 6 h at 75 °C and the precipitate of HL was formed. After cooling the solution to room temperature, the precipitate was collected, washed with ethanol, dried in air and used without further purification. Yield: 1.8 g (83%), [m.p. 153 °C]. For synthesis of single crystals of HL with slow evaporation method, after collecting the precipitate, the solution of reaction was kept at room temperature. After 5 days, the white crystals of HL were formed at vessel of reaction. The crystals were collected and dried at room temperature. Anal. Calcd for C\(_7\)H\(_{13}\)ClN\(_4\)O\(_3\): C, 35.5; H, 5.65; N, 23.67. Found: C, 35.7; H, 5.52; N, 23.80. Characteristic FT-IR data (KBr, cm\(^{-1}\)):...
3386 m, \( \nu (\text{NH}_2) \); 3220 m, \( \nu (\text{N-H}) \); 1704 s, \( \nu (\text{C=O}) \); 1604 s, \( \nu (\text{C=N}) \); 1087 s, \( \nu (\text{N-N}) \).

**Scheme 1.** Synthesis of pyridine 4-carbaldehyde semicarbazone Schiff base ligand (HL)

![Scheme 1](image)

**Table 1.** Crystal and structure refinement data for HL

| Chemical Formula | C7H13CIN4O3 |
|------------------|-------------|
| Formula weight   | 236.66      |
| Crystal description | Plate, transparent |
| Crystal size (mm) | 0.13 x 0.13 x 0.04 |
| Temperature (K)  | 95          |
| Crystal system   | triclinic   |
| Space group      | P-1         |
| \( a (\text{Å}) \) | 4.6415 (1)  |
| \( b (\text{Å}) \) | 8.8704 (3)  |
| \( c (\text{Å}) \) | 14.1176 (5) |
| \( \alpha (^\circ) \) | 104.918 (3) |
| \( \beta (^\circ) \) | 95.654 (3)  |
| \( \gamma (^\circ) \) | 100.799 (3) |
| Volume (\( \text{Å}^3 \)) | 545.08 (3) |
| \( Z \) | 2 |
| \( \rho \) calculated (g/cm\(^3\)) | 1.442 |
| \( \mu (\text{mm}^{-1}) \) | 3.112 |
| Largest diff. peak and hole (e\( \text{Å}^{-3} \)) | 0.28-0.31 |
| Final R indices [I>3\( \sigma(I) \)] | 0.0352 (2033) |
| Final R indices (all data) | 0.0953 (2194) |

**Crystallographic analysis**

The single crystal X-ray diffraction experiments were performed using a Super Nova four circles diffractometer equipped with an Atlas S2 detector and an micro focus source (Cu-K\(_{\alpha}\)average = 1.5418 Å). The data were collected at 95 K on a single crystal of suitable size (0.13 x 0.13 x 0.04 mm\(^3\)), using \( \omega \) scans and detector-sample distance 53 mm. The diffracted intensities were collected up to 75.420° (-5 ≤ \( h \) ≤ 5; -11 ≤ \( k \) ≤ 10 and -17 ≤ \( l \) ≤ 16). The experimental details are summarized in Table 1.

The structure has a triclinic unit cell with \( a = 4.6415 \text{ Å} \), \( b = 8.8704 \text{ Å} \), \( c = 14.1176 \text{ Å} \), \( \alpha = 104.918^\circ \), \( \beta = 95.654^\circ \) and \( \gamma = 100.799^\circ \). The data reduction and absorption correction were done by the software Crys Alis Pro [31], merging of symmetry equivalent reflections yielded \( R_{int} = 0.056 \). The structure was solved by charge flipping (Super flip [32]) for space group P-1. The refinement was performed with the software Jana 2006. The anisotropic displacement parameters (ADP) were used for N, C, O and Cl. The hydrogens atoms were inserted are insert by symmetry and positions were refined for nitrogen and oxygen atoms. The hydrogen ADP are restrained for 1.2 times \( U_{eq} \). The final merit factor are \( R_{obs} = 3.52\% \) and \( wR_{all} = 9.53\% \).

**Results and discussions**

Most of the semicarbazone ligands display keto-enol tautomerism in coordination to metal ion centers as neutral or deprotonated ligands [16-20]. Preparation of the pyridine 4-carbaldehyde semicarbazone ligand (HL) was revealed by infrared spectroscopy (Figure 1). The FT-IR spectrum of HL revealed a strong
band at 1704 cm\(^{-1}\) and two medium bands at 3386 and 3220 cm\(^{-1}\) for C=O, –NH\(_2\) and N–H stretching, and a sharp band at 1087 related to N–N bond. Observation of sharp band corresponding to C=O bond, suggests the keto form for HL and interestingly presence of a strong band at 1604 cm\(^{-1}\) reveals the imine functionality in HL. The bands at 2754 and 2986 cm\(^{-1}\) correspond to C–H bond of aldehyde. The strong bands at 1419 cm\(^{-1}\) and 1450-1580 cm\(^{-1}\) are related to aliphatic C–N bonds and aromatic C=C bonds, respectively. The low energy in-plane and out of plane vibrations of pyridine ring are observed at 655 and 451 cm\(^{-1}\) respectively. Interestingly observation of bands at 3429 and 1640 cm\(^{-1}\) corresponding to stretching and bending vibrations of water, confirms presence of lattice water molecules in structure of HL.

The \(^1\)H NMR spectrum of HL is demonstrated in Figure 2. The singlet resonances are observed at \(\delta=10.413, 10.391\) and 9.963 ppm, which are assigned to semicarbazide NH (\(^{3}\)NH), hydrogenated pyridine nitrogen (\(^{1}\)NH) and aldehyde CH groups (\(^{6}\)CH), respectively.

**Figure 1.** FT-IR spectrum of HL

![FT-IR spectrum of HL](image)

**Figure 2.** \(^1\)H NMR spectrum of HL in CD\(_3\)OD

![\(^1\)H NMR spectrum of HL in CD\(_3\)OD](image)
The broad small peaks at the range of 9.2-9.4 ppm are related to NH$_2$ group of semicarbazone (\(\text{^4NH}_2\)). The observed peaks at \(\delta=9.985\) and 9.631 ppm belong to the pyridine protons. The peaks at 6.524 ppm can assigned to water molecules in structure of HL and the peaks at 4.929 and 4.933 ppm are related to use CD$_3$OD solvent for analysis.

Electronical spectra of the HL measured in methanol solvent (Figure 3). Observation of absorption bands at 224 and 328 nm corresponding to intra-ligand \(\pi \rightarrow \pi^*\) transitions of the pyridin ring and imine group confirms successful synthesis of HL \([28-30]\).

Structure of the HL is depicted in Figure 4. It crystallizes in a triclinic system, with the space group of \(P-1\). X-ray crystal analysis revealed that, the structure of the HL contained a Schiff base molecule, two water molecules, and one anionic chlorine atom. The structural formula of the HL can be summarized as \(\text{[H}_2\text{L}^+\text{Cl}^-\text{(H}_2\text{O})_2\text{]}\). According to the FI-IR data, the HL is not deprotonated and it is in inert form of ligand. In fact, the HL by keeping its hydrogen atom located on N3 atom exists in keto form. Moreover, the nitrogen of the pyridine ring is protonated, giving the ligand a positive charge, and a chlorine atom is located in the structure as a counter-ion. The observed chlorine atom in the structure of HL is from the semicarbazide hydrochloride, which used for synthesis of HL.

The shortest bond distances of the pyridine ring are 1.347 and 1.339 Å for N3–C4 and N3–C6 respectively. The C–C or C= C distances of pyridine ring are between 1.375 Å and 1.400 Å. The selected bond distances and angles of HL are summarized at Table 2. The C=N bond length of HL is 1.285 Å which is in good consistent with the C=N bond distances in similar ligands \([20-29]\). Although the HL contains an aromatic cycle, there is no \(\pi \rightarrow \pi\) stacking interaction in its structure. Presence of two water molecules and chlorine ion in structure of HL plays an important role in hydrogen bond interactions, expanding the structure in three dimensions. Table 3 provides more details on the hydrogen bonding interactions in HL. Figure 5a illustrates the available individual hydrogen bonds in the structure of HL. The N4–H1N4···O1 and O3–H3O3···O1 hydrogen bonds connect molecules into layers (Figure 5b), and the layers are interconnected by hydrogen bonds of the water molecules and chloride ions.

**Figure 3.** UV-Vis spectra of HL

**Figure 4.** Crystal structure of HL
Figure 5. (a) View of hydrogen bonding interactions in HL, (b) Expansion of HL with intermolecular interactions in three dimensions (green)

Table 2. Selected Bond Distances (Å) and Angles (°) of HL

| Atom 1 | Atom 2 | distance (Å) | Atom 1 | Atom 2 | distance (Å) |
|--------|--------|--------------|--------|--------|--------------|
| C5     | O1     | 1.2450 (18)  | N4     | C5     | 1.3833 (19)  |
|        | N1     | 1.3259 (18)  |        | H1N4   | 0.87 (2)     |
| O2     | H1O2   | 0.85 (2)     | C1     | C3     | 1.4002 (19)  |
| O3     | H1O3   | 0.87 (2)     |        | C4     | 1.375 (2)    |
| H2O2   |        |              |        |        |              |
| O3     | H2O3   | 0.83 (3)     |        | H1C1   | 0.96         |
| N1     | H1N1   | 0.75 (2)     | C2     | C3     | 1.463 (2)    |
|        | H2N1   | 0.84 (2)     |        | C7     | 1.397 (2)    |
| N2     | N4     | 1.3527 (18)  | C4     | H1C4   | 0.96         |
|        | C2     | 1.2846 (19)  |        | C6     | 1.380 (2)    |
| N3     | C4     | 1.347 (2)    |        | H1C6   | 0.96         |
|        | C6     | 1.3391 (19)  |        | C7     | 0.96         |
|        | H1N3   | 0.82 (2)     |        | Cl1    | 3.0579 (14)  |

| Atom 1 | Atom 2 | Atom 3 | Angle (°) | Atom 1 | Atom 2 | Atom 3 | Angle (°) |
|--------|--------|--------|-----------|--------|--------|--------|-----------|
| H1O2   | O2     | H2O2   | 100 (2)   | N2     | C2     | C3     | 118.40 (12) |
| H1O3   | O3     | H2O3   | 110 (2)   | N2     | C2     | H1C2   | 120.8     |
| C5     | N1     | H1N1   | 119.4 (14)| C3     | C2     | H1C2   | 120.8     |
| C5     | N1     | H2N1   | 119.3 (15)| C1     | C3     | C2     | 121.85 (13) |
| H1N1   | N1     | H2N1   | 120.3 (19)| C1     | C3     | C7     | 118.95 (13) |
| N4     | N2     | C2     | 116.77 (11)| C2     | C3     | C7     | 119.20 (12) |
| Cl1    | N3     | C4     | 113.31 (9)| N3     | C4     | C1     | 120.04 (13) |
| Cl1    | N3     | C6     | 124.17 (10)| N3     | C4     | H1C4   | 119.98 |
| Cl1    | N3     | H1N3   | 4.4 (14)| C1     | C4     | H1C4   | 119.98 |
| C4     | N3     | C6     | 122.50 (14)| O1     | C5     | N1     | 124.89 (14) |
| C4     | N3     | H1N3   | 117.7 (14)| O1     | C5     | N4     | 117.78 (12) |
| C6     | N3     | H1N3   | 119.7 (14)| N1     | C5     | N4     | 117.33 (13) |
| N2     | N4     | C5     | 119.41 (11)| N3     | C6     | C7     | 119.76 (14) |
| N2     | N4     | H1N4   | 121.5 (14)| N3     | C6     | H1C6   | 120.12 |
| C5     | N4     | H1N4   | 117.7 (14)| C7     | C6     | H1C6   | 120.12 |
| C3     | C1     | C4     | 119.23 (14)| C3     | C7     | C6     | 119.52 (13) |
| C3     | C1     | H1C1   | 120.38 | C3     | C7     | H1C7   | 120.24 |

Symmetry codes: (i) x−1, y, z+1; (ii) x+1, y, z−1
Table 3. Selected hydrogen bonding parameters in HL (D = donor, H = hydrogen and A = acceptor)

| D-H.A   | D (D-H) (Å) | D (H.A) (Å) | D (D.A) (Å) | (D-H.A) (°) |
|---------|-------------|-------------|-------------|-------------|
| C2–H1C2···O3\textsuperscript{iii} | 0.96       | 2.49        | 3.4013 (18) | 158.72      |
| N1–H1N1···O2\textsuperscript{v}  | 0.84 (2)  | 2.26 (2)     | 3.0087 (18) | 149.6 (17)  |
| N1–H2N1···O3\textsuperscript{iv} | 0.84 (2)  | 2.04 (2)     | 2.8602 (16) | 163.7 (19)  |
| N4–H1N4···O1\textsuperscript{v} | 0.87 (2)  | 1.97 (2)     | 2.8370 (16) | 174.2 (18)  |
| O3–H1O3···O1\textsuperscript{vi} | 0.83 (3)  | 1.98 (2)     | 2.7833 (17) | 160.7 (18)  |
| O3–H2O3···O2\textsuperscript{vi} | 0.75 (2)  | 2.11 (3)     | 2.8555 (18) | 173 (2)     |
| O2–H1O2···Cl1\textsuperscript{vii} | 0.85 (2)  | 2.28 (2)     | 3.1281 (12) | 177 (2)     |
| O2–H2O2···Cl1\textsuperscript{vi} | 0.87 (2)  | 2.28 (2)     | 3.1418 (11) | 173 (2)     |

Symmetry codes: (ii) x+1, y, z−1; (iii) −x+2, −y+1, −z; (iv) −x+1, −y, −z; (v) −x+1, −y+1, −z; (vi) x+1, y, z; (vii) x−1, y, z.

Conclusion

In this research study, a Schiff base ligand named pyridine 4-carbaldehyde semicarbazone (HL) was synthesized and fully characterized. The results of the CHN elemental analysis, FT-IR, UV-Vis and $^1$H NMR spectroscopies confirmed the successful synthesis of the HL. The X-ray crystallography of single crystals of HL revealed its structural formula as [$\text{H}_2\text{L}$]$^+$Cl$^-$($\text{H}_2\text{O}$)$_2$. Presence of several hydrogen bonding interaction in structure of HL expanded its structure in three dimensions. Also it was found that, the HL can be utilized as an interesting tridendate NNO donor ligand for synthesis of novel complexes with different metal ions.

Appendix A. supplementary data

CCDC 1494841 contains the supplementary crystallographic data for the structure reported in this paper. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

Acknowledgment

The authors would like to acknowledge Lorestan University for supporting this work. The crystallographic part was supported by the project 18-10504S of the Czech Science Foundation using instruments of the ASTRA lab established within the Operation program Prague Competitiveness-project CZ.2.16/3.1.00/24510.

Disclosure statement

No potential conflict of interest was reported by the authors.

References

[1] A.L. Berhanu, I. Mohiuddin, A.K. Malik, J.S. Aulakh, V. Kumar, K.H. Kim, *Trend. Analyst. Chem.*, 2019, 116, 74–91.
[2] B. Bansod, T. Kumar, R. Thakur, S. Rana, I. Singh, *Biosens. Bioelectron.*, 2017, 94, 443–455.
[3] X. Liu, J.R. Hamon, *Coord. Chem. Rev.*, 2019, 389, 94–118.
[4] B. Shaabani, A.A. Khandar, F. Mahmoudi, S.S. Balula, L. Cunha-Silva, *J. Mol. Struct.*, 2013, 1045, 55–61.
[5] B. Shaabani, A.A. Khandar, M. Dusek, M. Pojarova, F. Mahmoudi, *Inorg. Chim. Acta*, 2013, 394, 563–568.
[6] Y. Echegoyen, I. Suelves, M.J. Lazaro, M.L. Sanjuan, R. Moliner, *Appl. Cat. A*, 2007, 333, 229–237.
[7] S. Nayak, P. Gamez, B. Kozlevcar, A. Pevec, O. Roubeau, S. Dehnen, J. Reedijk, *Polyhedron*, 2010, 29, 2291–2296.
[8] S. Uddin, S. Hossain, A. Latif, R. Karim, R.K. Mohapatra, K.E. Zahan, *Am. J. Heterocycl. Chem.*, 2019, 5, 27–36.
How to cite this manuscript: Farzaneh Mahmoudi, Saeed Farhadi, Michal Dusek, Morgane Poupon, Synthesis, Spectroscopy and X-ray Crystallography Structure of Pyridine 4-Carbaldehyde Semicarbazone Schiff Base Ligand, Adv. J. Chem. A, 2020, 3(4), 534–541.

Copyright © 2020 by SPC (Sami Publishing Company)+ is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.