

Scientific paper

Two Zinc(II) Complexes with Similar Hydrazone Ligands: Syntheses, Crystal Structures and Antibacterial Activities

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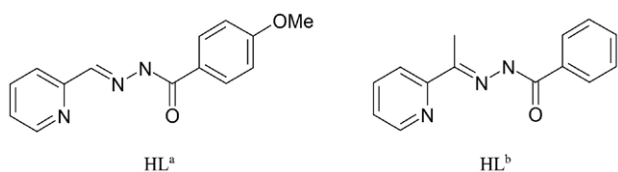
Abstract

A pair of new mononuclear zinc(II) complexes with hydrazone ligands 4-methoxybenzoic acid (1-pyridin-2-yl-methylidene)hydrazide (HL^a) and benzoic acid (1-pyridin-2-ylethylidene)hydrazide (HL^b) were prepared. They are [Zn(L^a)₂] (1) and [Zn(L^b)₂] (2). The complexes were characterized by physico-chemical methods and single crystal X-ray determination. The tridentate hydrazone ligands coordinate to the Zn atoms through the pyridine nitrogen, imino nitrogen and enolate oxygen atoms. The Zn atom in each complex is six coordinated by two hydrazone ligands, to form octahedral coordination. The complexes have effective activities against the bacteria *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas fluorescens*.

Keywords: Schiff base; Zinc complex; Crystal structure; Antibacterial activity

1. Introduction

Schiff bases are readily synthesized by the condensation reaction of aldehydes with primary amines, which have been widely investigated for their antibacterial and antitumor activities.¹ The metal complexes of Schiff bases have also received much attention due to their contribution to the development of coordination chemistry related to catalysis and enzymatic reactions, magnetism and molecular architectures,² as well as biological activities.³ The Schiff bases 4-methoxybenzoic acid (1-pyridin-2-yl-methylidene)hydrazide (HL^a; Scheme 1) and benzoic acid (1-pyridin-2-ylethylidene)hydrazide (HL^b; Scheme 1) are interesting tridentate hydrazone-type ligands, which possess potential antibacterial activities.⁴ In this paper, two new mononuclear zinc(II) complexes, [Zn(L^a)₂] (1) and [Zn(L^b)₂] (2), have been synthesized and structurally characterized. The antibacterial activities against *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas fluorescens*, were evaluated for the complexes.



Scheme 1. The Schiff bases, HL^a and HL^b.

2. Experimental

2. 1. Materials and Measurements

Pyridine-2-carbaldehyde, pyridine-2-ethanone, 4-methoxybenzohydrazide, and benzohydrazide with AR grade were obtained from Aldrich and used as received. Elemental analyses (C, H, N) were performed using a Perkin-Elmer 240C analytical instrument. Infrared spectra were recorded on a Nicolet 5DX FT-IR spectrophotometer with KBr pellets. UV-vis spectra were recorded on a Lambda 900 spectrophotometer.

2. 2. Synthesis of Complex 1

Pyridine-2-ethanone (1.21 g, 0.01 mol) and 4-methoxybenzohydrazide (1.66 g, 0.01 mol) were stirred in 30 mL methanol at room temperature for 20 min. Then, zinc nitrate hexahydrate (2.97 g, 0.01 mol) dissolved in 30 mL methanol was added dropwise to the solution. The mixture was further stirred for 30 min and filtered. The filtrate was evaporated slowly in air to give colorless block-like single crystals, which were washed three times with methanol and dried in open air. Yield: 55%. Found: C, 59.72; H, 4.71; N, 14.13. Anal. Calcd. for C₃₀H₂₈N₆O₄Zn: C, 59.86; H, 4.69; N, 13.96%. IR data (cm⁻¹, KBr pellet): 1602, 1585, 1562, 1511, 1495, 1455, 1407, 1361, 1317, 1300, 1289, 1247, 1171, 1097, 1063, 1042, 1027, 905, 840, 765, 680, 635, 618.

UV-Vis data (λ_{\max} (nm), ϵ (L mol⁻¹ cm⁻¹): 276 (1.23 × 10³), 325 (1.38 × 10³), 370 (1.45 × 10³).

2. 3. Synthesis of Complex 2

Pyridine-2-ethanone (1.21 g, 0.01 mol) and benzohydrazide (1.36 g, 0.01 mol) were stirred in 30 mL methanol at room temperature for 20 min. Then, zinc nitrate hexahydrate (2.97 g, 0.01 mol) dissolved in 30 mL methanol was added dropwise to the solution. The mixture was further stirred for 30 min and filtered. The filtrate was evaporated slowly in air to give colorless block-like single crystals, which were washed three times with methanol and dried in open air. Yield: 61%. Found: C, 26.21; H, 4.53; N, 15.40. Anal. Calcd. for C₂₈H₂₄N₆O₂Zn: C, 62.06; H, 4.46; N, 15.51%. IR data (cm⁻¹, KBr pellet): 1595, 1587, 1562, 1498, 1460, 1431, 1357, 1316, 1293, 1169, 1160, 1095, 1060, 1041, 903, 776, 746, 708, 683, 637. UV-Vis data (λ_{\max} (nm), ϵ (L mol⁻¹ cm⁻¹): 270 (1.12 × 10³), 310 (1.29 × 10³), 365 (1.30 × 10²).

2. 4. X-ray Crystallography

Single crystal structural diffraction was performed on a Bruker Smart 1000 CCD area-detector diffractometer with graphite monochromatized Mo-K α radiation ($\lambda = 0.71073$ Å). Diffraction data for the complexes were collected by ω scan mode at 298(2) K. Data reduction and cell refinement were performed by the SMART and SAINT programs.⁵ Empirical absorption correction was applied by using SADABS.⁶ Structures of the complexes were solved by direct method and refined with the full-matrix least-squares technique using SHELXL97.⁷ The non-H atoms in the structures were subjected to refined anisotropic refinement. All hydrogen atoms were located in geometrically and treated with the riding mode. Crystallographic data and experimental details for the complexes are summarized in Table 1. Selected bond lengths and angles for the complexes are listed in Table 2.

2. 5. Antibacterial Test

Antibacterial activities of the Schiff bases and the complexes were tested *in vitro* against *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas fluorescens* using MH medium (Mueller–Hinton medium: casein hydrolysate 17.5 g, soluble starch 1.5 g, beef extract 1000 mL) in triplicate. The minimum inhibitory concentrations (MIC) of the test compounds were determined by a colorimetric method using the dye MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide). A solution of the compound (50 μ g mL⁻¹) in DMSO was prepared and graded quantities of the test compounds were incorporated in specified quantity of sterilized liquid MH medium. A specified quantity of the medium containing the compound was poured into microtitration plates. Sus-

Table 1. Crystallographic and experimental data for the complexes.

	1	2
Chemical formula	C ₃₀ H ₂₈ N ₆ O ₄ Zn	
C ₂₈ H ₂₄ N ₆ O ₂ Zn		
Formula weight	601.95	541.90
T (K)	298(2)	298(2)
crystal system	orthorhombic	monoclinic
space group	<i>Pbca</i>	<i>Cc</i>
<i>a</i> (Å)	11.9317(7)	10.3526(13)
<i>b</i> (Å)	10.1046(6)	19.287(2)
<i>c</i> (Å)	47.2193(18)	12.3879(19)
β (°)	90	90.536(2)
<i>V</i> (Å ³)	5693.0(5)	2473.3(6)
<i>Z</i>	8	4
ρ (g/cm ³)	1.405	1.455
μ (Mo-K α) (mm ⁻¹)	0.909	1.032
<i>F</i> (000)	2496	1120
No. of measured reflections	32450	7154
No. of unique reflections	5299	3379
No. of observed reflections	3633	3003
Parameters	374	337
<i>R</i> _{int}	0.0500	0.0372
Goodness of fit on <i>F</i> ²	1.136	1.045
<i>R</i> ₁ , <i>wR</i> ₂ [<i>I</i> ≥ 2 σ (<i>I</i>)] ^a	0.0490, 0.0962	0.0771, 0.2050
<i>R</i> ₁ , <i>wR</i> ₂ (all data) ^a	0.0801, 0.1078	0.0847, 0.2118
Highest peak and deepest hole (e Å ⁻³)	0.250, -0.321	0.745, -0.490

$$^a R_1 = \sum |F_o| - |F_c| / \sum |F_o|, wR_2 = [\sum w(F_o^2 - F_c^2)^2 / \sum w(F_o^2)]^{1/2}.$$

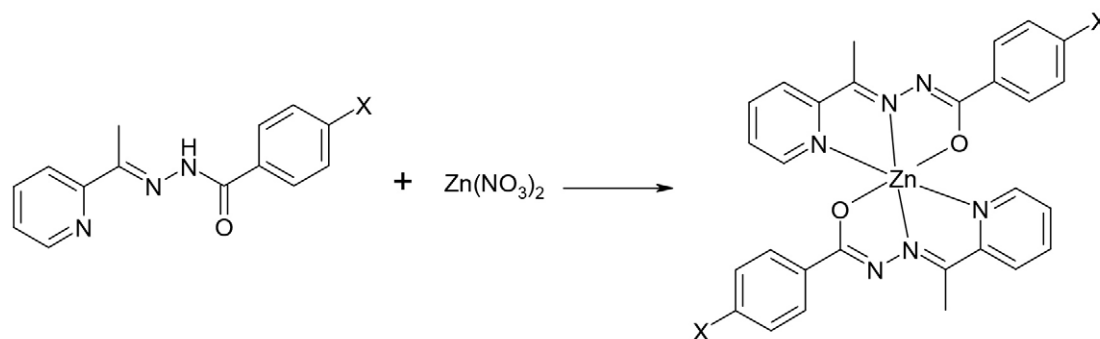
Table 2. Selected bond lengths (Å) and angles (°) for the complexes.

		1	
Bond lengths			
Zn1–N2	2.055(2)	Zn1–N5	2.058(2)
Zn1–O1	2.099(2)	Zn1–O3	2.136(2)
Zn1–N4	2.197(3)	Zn1–N1	2.212(3)
Bond angles			
N2–Zn1–N5	174.18(10)	N2–Zn1–O1	75.79(9)
N5–Zn1–O1	109.85(9)	N2–Zn1–O3	103.22(9)
N5–Zn1–O3	74.85(9)	O1–Zn1–O3	99.04(10)
N2–Zn1–N4	106.59(10)	N5–Zn1–N4	75.12(10)
O1–Zn1–N4	91.76(10)	O3–Zn1–N4	149.97(9)
N2–Zn1–N1	74.44(10)	N5–Zn1–N1	100.09(10)
O1–Zn1–N1	149.59(9)	O3–Zn1–N1	93.62(10)
N4–Zn1–N1	90.86(11)		
		2	
Bond lengths			
Zn1–N2	2.030(9)	Zn1–N5	2.062(8)
Zn1–O2	2.106(7)	Zn1–O1	2.137(7)
Zn1–N1	2.184(9)	Zn1–N4	2.199(8)
Bond angles			
N2–Zn1–N5	173.0(3)	N2–Zn1–O2	102.9(3)
N5–Zn1–O2	73.4(3)	N2–Zn1–O1	74.9(3)
N5–Zn1–O1	99.6(3)	O2–Zn1–O1	99.7(3)
N2–Zn1–N1	74.9(4)	N5–Zn1–N1	110.9(4)
O2–Zn1–N1	92.7(4)	O1–Zn1–N1	149.2(3)
N2–Zn1–N4	108.5(3)	N5–Zn1–N4	75.9(4)
O2–Zn1–N4	147.9(3)	O1–Zn1–N4	94.6(3)
N1–Zn1–N4	89.3(4)		

pension of the microorganism was prepared to contain about 10^5 colony forming units cfu mL^{-1} and applied to microtitration plates with serially diluted compounds in DMSO to be tested and incubated at 37°C for 24 h. After the MICs were visually determined on each of the microtitration plates, $50\ \mu\text{L}$ of PBS (Phosphate Buffered Saline $0.01\ \text{mol L}^{-1}$, pH 7.4: $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ 2.9 g, KH_2PO_4 0.2 g, NaCl 8.0 g, KCl 0.2 g, distilled water 1000 mL) containing 2 mg of MTT was added to each well. Incubation was continued at room temperature for 4–5 h. The content of each well was removed, and $100\ \mu\text{L}$ of isopropyl alcohol containing 5% $1.0\ \text{mol L}^{-1}$ HCl was added to extract the dye. After 12 h of incubation at room temperature, the optical density (OD) was measured with a microplate reader at 550 nm.

3. Results and Discussion

The complexes were readily prepared by the reaction of the Schiff bases and zinc nitrate in methanol (Scheme 2).



Scheme 2. Synthetic procedure of the complexes. X = OCH_3 for 1, and H for 2.

3. 1. Crystal Structure Description

Molecular structures of complexes 1 and 2 are shown in Figures 1 and 2, respectively. The Zn atom in each complex is coordinated by two hydrazone ligands, to form octahedral coordination geometry. The hydrazone ligand

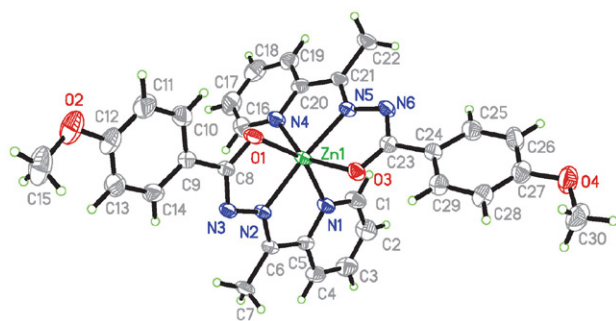


Figure 1. Molecular structures of complex 1 with ellipsoids at 30% probability.

coordinates to the Zn atom through the pyridine nitrogen, imino nitrogen and enolate oxygen atoms. The coordinate bond lengths in the two complexes are comparable to each other, and also similar to those observed in zinc complexes with similar ligands.⁸ The hydrazone ligands adopt *trans* configuration with respect to the methyldene unit. The shorter distances of the C–N bonds and the longer distances of the C–O bonds for the $-\text{C}(\text{O})-\text{NH}-$ units than usual, suggest conjugation effect in the hydrazone molecules. The dihedral angles among the benzene rings and the pyridine rings of the hydrazone ligands are $3.4(5)^\circ$ and $20.9(5)^\circ$ for 1, and $7.4(3)^\circ$ and $19.5(3)^\circ$ for 2.

3. 2. IR and Electronic Spectra

In the spectra of the complexes, the characteristic absorption of the $\nu(\text{C}=\text{N})$ vibrations are located at $1602\ \text{cm}^{-1}$ for 1 and $1595\ \text{cm}^{-1}$ for 2.⁹ In the UV–Vis spectra of the complexes, the absorptions centered about 270 nm and 320 nm are attributed to the $\pi-\pi^*$ and $n-\pi^*$ transitions of the azomethine chromophores.¹⁰ The absorptions cen-

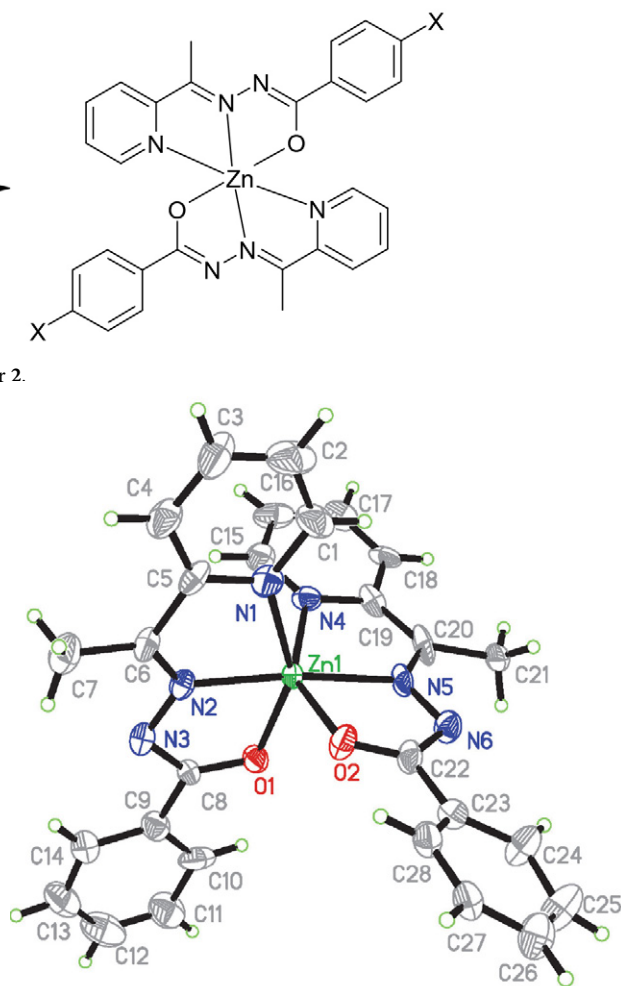


Figure 2. Molecular structures of complex 2 with ellipsoids at 30% probability.

tered about 370 nm may attribute to the ligand to metal charge transfer.

3. 3. Antibacterial Activity

The Schiff bases and the two complexes were screened *in vitro* for antibacterial activities against *Bacillus*

Table 3. Antibacterial results (MIC ($\mu\text{g mL}^{-1}$)).

Compound	<i>Bacillus subtilis</i>	<i>Staphylococcus aureus</i>	<i>Escherichia coli</i>	<i>Pseudomonas fluorescens</i>
HL ¹	43.1	18.5	32.6	> 100
HL ²	63.7	32.8	51.2	> 100
1	10.2	7.8	15.4	28.5
2	17.8	19.2	27.5	45.3
Penicillin	1.3	2.1	> 100	> 100

subtilis, *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas fluorescens* by the MTT method. The MICs of the compounds against the bacteria are presented in Table 3. Penicillin was used as reference drug.

The Schiff base HL¹ shows medium antibacterial activities against *Staphylococcus aureus*, weak activities against *Bacillus subtilis* and *Escherichia coli*, and no activity against *Pseudomonas fluorescens*. The Schiff base HL² shows weak activities against *Bacillus subtilis*, *Staphylococcus aureus* and *Escherichia coli*, and no activity against *Pseudomonas fluorescens*. In general, the zinc complexes have stronger activities against all bacteria than the free Schiff bases. The antibacterial activities of complex **1** are better than those of complex **2**. Complex **1** shows strong activities against *Bacillus subtilis* and *Staphylococcus aureus*, medium activity against *Escherichia coli*, and weak activities against *Pseudomonas fluorescens*. Complex **2** shows medium activities against *Bacillus subtilis*, *Staphylococcus aureus* and *Escherichia coli*, and weak activity against *Pseudomonas fluorescens*. As for *Escherichia coli* and *Pseudomonas fluorescens*, both complexes have more activities than Penicillin, which deserves further investigation.

4. Conclusion

We report the syntheses and crystal structures of two new mononuclear zinc(II) complexes with tridentate hydrazone ligands. The Zn atoms are in octahedral coordination. Both complexes have effective activities against the bacteria *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas fluorescens*.

Supplementary material

CCDC reference numbers 1578771 (**1**) and 1578772 (**2**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at

www.ccdc.cam.ac.uk, or from Cambridge Crystallographic Data Center, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk.

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5. References

- (a) Z. H. Chohan, M. ul-Hassan, K. M. Khan, C. T. Supuran. *J. Enzyme Inhib. Med. Chem.* **2005**, *20*, 183–188; DOI:10.1080/14756360500043257
- (b) J. Zhang, F. Pan, H. Cheng, W. Du. *Russ. J. Coord. Chem.* **2010**, *36*, 514–519; DOI:10.1134/S1070328410070067
- (c) A. Iqbal, H. L. Siddiqui, C. M. Ashraf, M. H. Bukhari, C. M. Akram. *Chem. Pharm. Bull.* **2007**, *55*, 1070–1072. DOI:10.1248/cpb.55.1070
- (a) A. Lalehzari, J. Desper, C. J. Levy. *Inorg. Chem.* **2008**, *47*, 1120–1126; DOI:10.1021/ic702015u
- (b) L. Xu, Y. Li, M. Duan, Y. Li, M. Han, J. Wu, Y. Wang, K. Dong, Z. You. *Polyhedron* **2019**, *165*, 138–142; DOI:10.1016/j.poly.2019.03.016
- (c) Y. Li, L. Xu, M. Duan, B. Zhang, Y. Wang, Y. Guan, J. Wu, C. Jing, Z. You. *Polyhedron* **2019**, *166*, 146–152; DOI:10.1016/j.poly.2019.03.051
- (d) M. Duan, Y. Li, L. Xu, H. Yang, F. Luo, Y. Guan, B. Zhang, C. Jing, Z. You. *Inorg. Chem. Commun.* **2019**, *100*, 27–31. DOI:10.1016/j.inoche.2018.12.009
- (a) G. B. Baghalli, P. G. Avaji, S. A. Patil, P. S. Badami. *Eur. J. Med. Chem.* **2008**, *43*, 2639–2649; DOI:10.1016/j.ejmech.2008.02.013
- (b) Z. H. Chohan, M. Arif, A. Rashid. *J. Enzyme Inhib. Med. Chem.* **2008**, *23*, 785–796; DOI:10.1080/14756360701450145
- (c) Z. H. Chohan, M. Arif, Z. Shafiq, M. Yaqub, C. T. Supuran. *J. Enzyme Inhib. Med. Chem.* **2006**, *21*, 95–103; DOI:10.1080/14756360500456806
- (d) Y. Li, L. Xu, M. Duan, J. Wu, Y. Wang, K. Dong, M. Han, Z. You. *Inorg. Chem. Commun.* **2019**, *105*, 212–216; DOI:10.1016/j.inoche.2019.05.011

- (e) Z. You, H. Yu, B. Zheng, C. Zhang, C. Lv, K. Li, L. Pan. *Inorg. Chim. Acta* **2018**, 469, 44–50; DOI:10.1016/j.ica.2017.09.011
- (f) H.-L. Zhu, X.-Z. Zhang, Y. Gu, A. Liu, F. Liu, Z. You, Y. Li. *Acta Chim. Slov.* **2016**, 63, 721–725.
4. (a) M. Zhang, D.-M. Xian, H.-H. Li, J.-C. Zhang, Z.-L. You. *Aust. J. Chem.* **2012**, 65, 343–350; DOI:10.1071/CH11424
- (b) P. G. Avaji, C. H. V. Kumar, S. A. Patil, K. N. Shivananda, C. Nagaraju. *Eur. J. Med. Chem.* **2009**, 44, 3552–3559; DOI:10.1016/j.ejmech.2009.03.032
- (c) M. J. Hearn, M. H. Cynamon, M. F. Chen, R. Coppins, J. Davis, H. J.-O. Kang, A. Noble, B. Tu-Sekine, M. S. Terrot, D. Trombino, M. Thai, E. R. Webster, R. Wilson. *Eur. J. Med. Chem.* **2009**, 44, 4169–4178. DOI:10.1016/j.ejmech.2009.05.009
5. Bruker. *SMART and SAINT*. Bruker AXS, Madison, WI, 2002.
6. G. M. Sheldrick. *SADABS. Program for Empirical Absorption Correction of Area Detector*; University of Göttingen, Germany, 1996.
7. G. M. Sheldrick. *SHELXTL V5.1 Software Reference Manual*; Bruker AXS, Inc., Madison, WI, 1997.
8. (a) H.-H. Li, Z.-L. You, C.-L. Zhang, M. Yang, L.-N. Gao, L. Wang. *Inorg. Chem. Commun.* **2013**, 29, 118–122; DOI:10.1016/j.inoche.2012.12.023
- (b) Z.-L. You, M. Zhang, D.-M. Xian. *Dalton Trans.* **2012**, 41, 2515–2524; DOI:10.1039/c1dt11566a
- (c) S. Basak, S. Sen, S. Banerjee, S. Mitra, G. Rosair, M. T. G. Rodriguez. *Polyhedron* **2007**, 26, 5104–5112. DOI:10.1016/j.poly.2007.07.025
9. X.-M. Hu, L.-W. Xue, G.-Q. Zhao, Y.-J. Han. *Synth. React. Inorg. Met.-Org. Nano-Met. Chem.* **2012**, 42, 557–562. DOI:10.1080/15533174.2011.613884
10. L.-W. Xue, X. Wang, G.-Q. Zhao. *Synth. React. Inorg. Met.-Org. Nano-Met. Chem.* **2012**, 42, 1334–1338. DOI:10.1080/15533174.2012.680139

Povzetek

Sintetizirali smo dva nova enojedrna cinkova(II) kompleksa s hidrazonskima ligandoma 4-metoksibenzojsko kislino (1-piridin-2-iletidiliden)hidrazidom (HL^a) in benzojsko kislino (1-piridin-2-iletidiliden)hidrazidom (HL^b), [Zn(L^a)₂] (1) in [Zn(L^b)₂] (2). Kompleksa sta bila okarakterizirana s fiziko-kemijskimi metodami in monokristalno rentgensko difrakcijo. Tridentatna hidrazonska liganda se koordinirata na Zn atom preko piridinskega dušikovega atoma, iminskega dušikovega atoma in enolatnega kisikovega atoma. Zn atom v obeh kompleksih ima koordinacijsko število šest in je koordiniran z dvema hidrazonskima ligandoma v oktaedrični geometriji. Kompleksa sta učinkovita proti bakterijam *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* in *Pseudomonas fluorescens*.



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