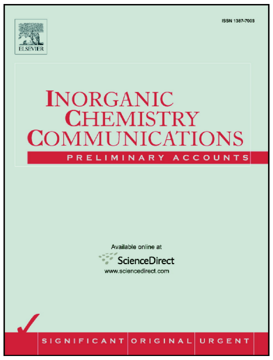

Zinc(II) coordination polymer on the base of 3′-(1H-tetrazol-5-yl)-[1,1′-biphenyl]-4-carboxylic acid: Synthesis, crystal structure and antimicrobial properties

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Zinc(II) coordination polymer on the base of 3'-(1*H*-tetrazol-5-*yl*)-[1,1'-biphenyl]-4-carboxylic acid: Synthesis, crystal structure and antimicrobial properties

Lucian G. Bahrin [a], *Irina Rosca* [a], *Lilia Clima* [a], *Sergiu Shova* [a], *Dana Bejan* [a], *Alina Nicolescu* [a], *Narcisa-Laura Marangoci* [a], *Monica C. Sardaru* [a], *Vasile Lozan* [a,b] *and Alexandru Rotaru* [a,*]

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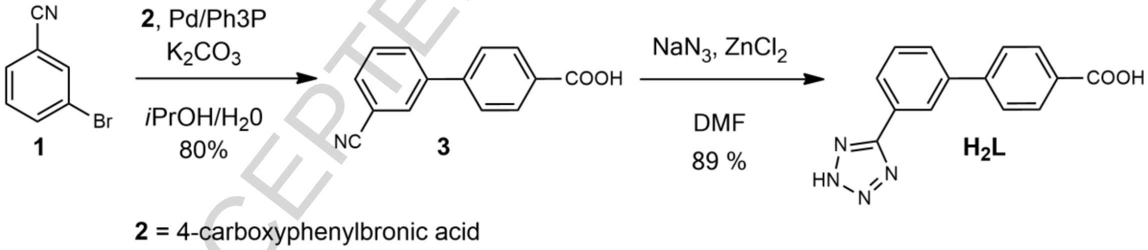
In recent years there has been an emergent interest in the development of coordination polymers owing to their interesting variety of architectures and their intriguing potential applications in areas including hydrogen storage [1-3], adsorption [4], luminescence [5-7], catalysis [8-10] and biological activity [11, 12]. These applications consequently lead to an increasing demand in the design of new ligands which by means of coordination bonding, hydrogen bonding, aromatic–stacking interactions or van der Waals forces would contribute to the formation of polymeric structures which might extend in one, two or three dimensions [13]. Owing to its unique structure and properties, tetrazole and its derivatives have been the subject of intense research and applications in a vast variety of fields including greener explosive materials and pyrotechnics [14, 15], fragments in pharmaceutical drugs (anti-bacterial, anti-allergic, anti-inflammatory, and anti-fungal) [16], or construction of metal–organic frameworks [17, 18]. This comes as a consequence of tetrazole aromaticity, excellent coordination capability and the possibility of more or less straightforward introduction of chemical moieties in its structure. Especially, substituted tetrazolate derivatives containing carboxylate group have attracted great attention due to the fact that they can act as a class of excellent polydentate ligands, which might or already have been utilized in the construction of coordination polymers with structural varieties and novel performances [19, 20]. This interest is dictated by the their bifunctional feature and versatile bonding modes, which coordinate to metal ions via O atoms of carboxyl groups and N atoms of the tetrazole ring, acting as monodentate [21], bidentate [22], tridentate [23] and tetradentate [24] bridge. Besides the interesting structural properties of tetrazole containing complexes, not less interesting are their peculiar properties like increased biological activity which might be considerably accelerated due to the presence of a metal ion in their structure. In this regard, synthesis of new tetrazole containing ligands and preparation of metal complexes with metals, especially with transition metal including Cu(II), Ni(II), Co(II) and Zn(II) with subsequent investigation of biological activity of both the new ligand and its metal complex is of a particular importance. Transitions row metal ions are both essential and toxic to microorganisms and zinc, occurring as the divalent cation Zn^{2+}, is the second most abundant transition metal in humans and has its important role related to the immune system, interacting with up to 10% of all human proteins [25-27]. Zn(II) concentrations are elevated in response to inflammations and bacterial infections as a consequence of Zn(II) release from damage or apoptotic cells. Interestingly, even though many tetrazole containing derivatives as ligands and their metal complexes with Cu(II), Ni(II) and Co(II) possessing biological activity are known and available in the literature, there are only few reports regarding Zn(II) coordination compounds activity when compared to the initial ligand [28-29]. Thus, antibacterial activity of Zn(II) tetrazole derivatives complexes was reported only by Krishna and co-workers [29], were they have investigated and compared the inhibitory action of the new ligands and their Zn(II) complexes against *Bacillus subtilis*, *Staphylococcus aureus*, *Proteus vulgaris*, *Aspergillus niger* and *Candida albicans.*

Here in, we present synthesis and characterization of 3’-(2*H*-tetrazol-5-*yl*)-[1,1’-biphenyl]-4-carboxylic acid as novel ligand and preparation of its coordination polymers with Zn(II), followed by the antimicrobial investigations of both the ligand and metal complex against three different reference strains: *Escherichia coli*, *Staphylococcus aureus* and *Candida albicans*.

Synthesis of 3'-(*2H*-tetrazol-5-*yl*)-[1,1'-biphenyl]-4-carboxylic acid (**H_2L**), referred as ligand in following descriptions, was achieved via two steps straightforward synthesis as shown in scheme 1.



Scheme 1. Synthetic pathway of 3'-(*2H*-tetrazol-5-*yl*)-[1,1'-biphenyl]-4-carboxylic acid (**H_2L**).

The proposed synthetic pathways involved a Suzuki – Myaura coupling of 3-bromobenzonitrile **1** with 4-carboxyphenylbronic acid **2**, using palladium acetate as catalyst [30]. Subsequently, the nitrile moiety of **3** was converted to a tetrazole ring using sodium azide in the presence of zinc chloride as catalyst, yielding the desired product in 72% yield, over two steps. The final compound **H_2L** was characterized using NMR, ESI-MS and IR spectroscopy. Thus, in the ^{1}H-NMR spectrum of **H_2L**, the signal present at 16.90 ppm as a very broad singlet belongs to the tetrazole H atom, while the signal present at 13.11 ppm displays the presence of the carboxylic H atom. The ^{13}C-NMR spectrum of **H_2L** reveals the presence of the carboxyl and tetrazole C atoms at 167.5 and 155.6 ppm respectively, with the signals present between 143.6 ppm and 125.4 ppm belonging to the aromatic C atoms. The IR spectrum of **H_2L** displays two absorption bands, at 3124 and 3040 cm^{-1}, assigned to the N-H and O-H stretching vibrations, while the signal present at 1686 cm^{-1} was assigned to the C=O stretching vibration.

To investigate the possibility for the formation of a coordination compound between the new ligand and Zn(II), we performed the reaction between **H_2L** and $Zn(NO_3)_2{*}6H_2O$. We have found that at 4:1 ratio, a crystalline compound was obtained in good yield, using a mixture of dimethylformamide, methanol and water as solvent. The isolated crystals were characterized by IR and X-ray diffraction. The first piece of evidence that supports the formation of a complex is provided by the IR spectrum of the isolated compound. Thus, the bands at 3124 and 3040 cm^{-1} present in the IR spectrum of **H_2L**, which were assigned to the tetrazole N-H and carboxyl O-H stretching vibrations, are no longer present in the IR spectrum of the complex. Instead a new band is observed at 3485 cm^{-1}, assigned to the water molecules present in the complex. Also, the band belonging to the carboxyl C=O stretching vibration, found at 1686 cm^{-1} in the IR spectrum of **H_2L**, is replaced by a new band, present at around 1591 cm^{-1}, which suggests the presence of a carboxylate group.

Single crystal X-ray diffraction study has confirmed the complexation of **H_2L** and Zn(II) ion and the results are shown in Fig. 1, Table S1 and Table S2. The asymmetric part of the structure comprises two Zn(II) ions, one double deprotonated ligand **L^{2-}**, one formate anion ($HCOO^-$) and one coordinated and one co-crystalized water molecules, so that the charge balance is in agreement with the formation of species $[Zn_3L_2(HCOO)_2(H_2O)_2]\cdot 2H_2O$ (**4**).

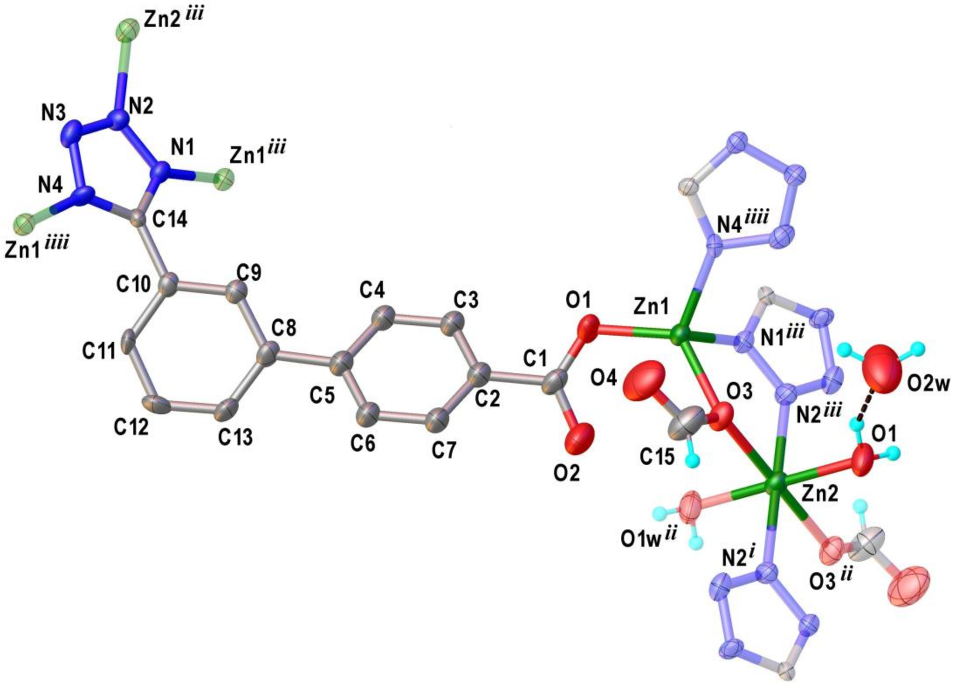


Fig. 1. Extended asymmetric unit in the crystal of **4** with atom labelling scheme and thermal ellipsoids at 50% probability level. Only the major component of disordered part is shown. Atoms generated by symmetry operation are shown semi-transparent. (Symmetry code: ^{1}1 - *x*,1 - *y*, 1 - *z*; ^{2}2 - *x*, 1 - *y*, 2 - z; ^{3}1 - *x*, -0.5 + *y*, 0.5 – *z*.)

The central part of the structure is built up from a centrosymmetric tri-nuclear core, as shown in Fig. 2. The tri-nuclear cluster is consolidated due to the bridging structural function of two tetrazole fragment and two formate anions. The formate anions act as bidentate-bridging ligands being coordinated in μ_2-η^2:η^0 mode. The Zn2 atom occupies a special position on the inversion center, while Zn2 and symmetrically related Zn2(2 – *x*, 1 – *y*, 2 – *z*) are located in general positions with Zn1⋯Zn1′ separation at 7.116(2) Å. The Zn1···Zn2 distance is of 3.5580(9) Å. The Zn2 atom is hexa-coordinated by a set N_2O_4 donors in slightly distorted octahedral geometry. The apical Zn1-N2 bond distances of 2.260(6) Å are significant longer compared with Zn2-O1*w* of 2.018(5) and Zn2-O3 of 2.103(4) Å in equatorial plane. The N_2O_2 coordination environment of Zn1 atom is completed by one nitrogen atom from tetrazole fragment and one oxygen atom from carboxylate group of L^{2-} ligand resulting in a distorted tetrahedral coordination.

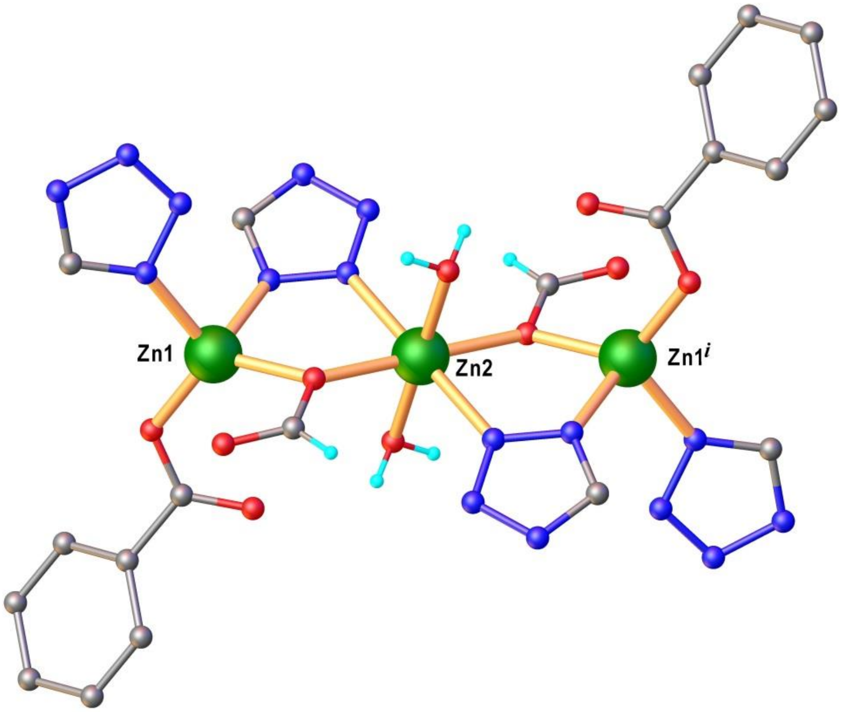


Fig. 2. View of the central trinuclear core $\{Zn_3(\mu\text{-tetrazole})_2(\mu_2\text{-formate})_2\}^{2-}$ in the crystal structure of **4**. Non-relevant H-atoms are omitted.

As shown in Fig. 1, 3'-(*2H*-tetrazol-5-yl)-[1,1'-biphenyl]-4-carboxylic acid behaves as tetra-dentate double-deprotonated ligand. Three nitrogen atoms from tetrazole fragment and one oxygen atom from carboxylate group are coordinated to four different zinc atoms. The carboxylate group of L^{2-} fulfills a function of monodentate ligand being coordinated in $\eta^1:\eta^0$ mode. In the crystal the tri-nuclear clusters and tetradentate ligand L^{2-} as tri-nodal linkers are interconnected via inversion center to form a strongly compacted three-dimensional coordination polymer. A partial view of the $\mathbf{\{[Zn_3L_2(HCOO)_2(H_2O)_2]\}_n}$. coordination network is presented in Fig. 3a,b. It is to note, that due to tri-nodal character of the organic linker, each tri-nuclear unit is directly interconnected with ten symmetry related metal-clusters. A topological view of the 3D coordination polymer is shown in Fig. 3b.

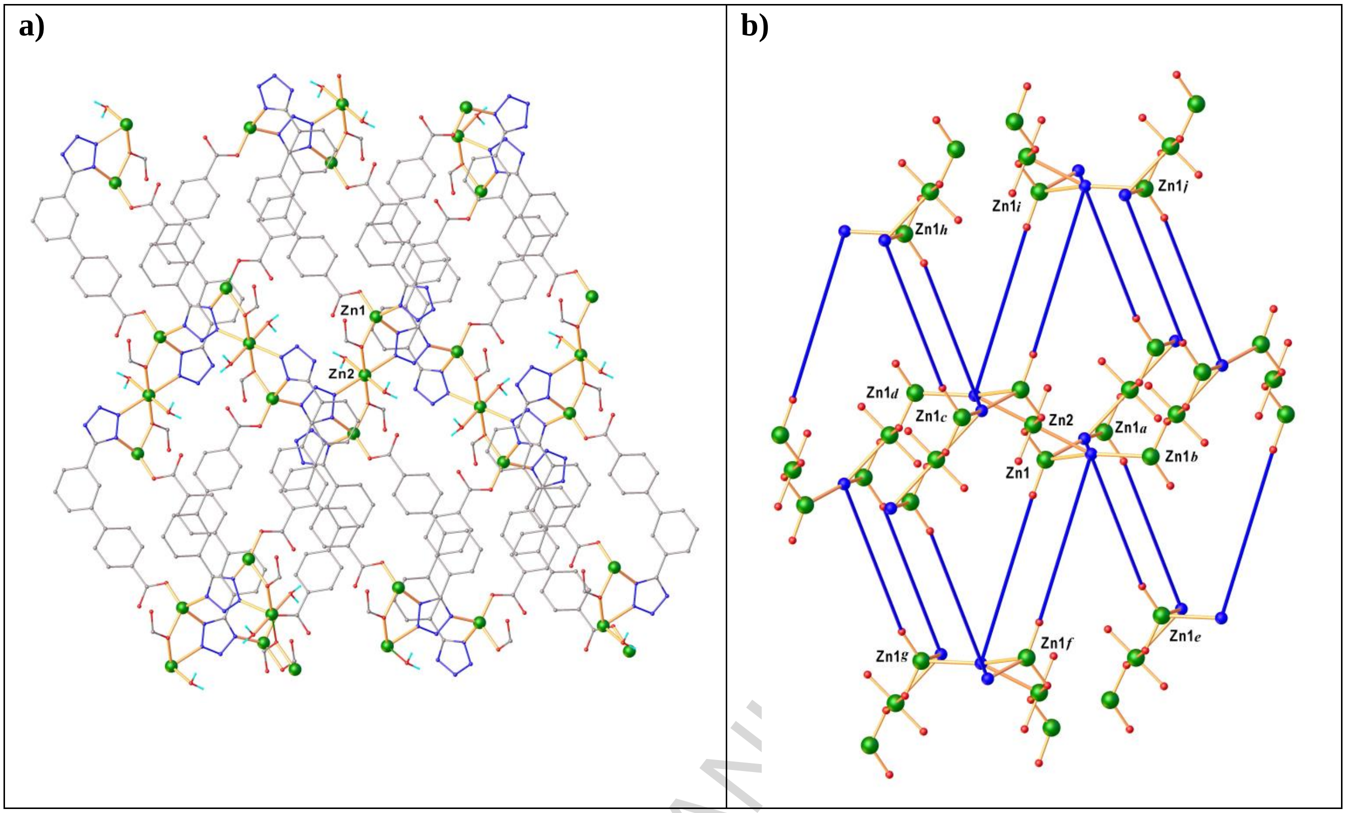


Fig. 3. a) A section of packing diagram in the crystal structure of **$\{[Zn_3L_2(HCOO)_2(H_2O)_2]\}_n$**. Co-crystalized water molecules are not shown for clarity; b) topological view of coordination network. Metal-ligands bonds are shown in orange, while the tri-nodal linkers are replaced by blue lines with tetrazole rings as blue spheres. (Symmetry codes for equivalent atoms Zn1: $^{a)}x$, 0.5 – y, -0.5 + z; $^{b)}$ -x, 0.5 – y, 0.5 + z; $^{c)}$ 2 - x, 0.5 – y, 2.5 - z; $^{d)}$ 1.5 - x, 0.5 – y, 2.5 – z; $^{e)}$1 - x, -0.5 – y, 0.5 – z; $^{f)}$ 1 - x, 1 – y, 1 – z; $^{g)}$ 1 - x, 0.5 – y, 0.5 – z; $^{h)}$ 1 + x, 1.5 – y, 1.5 + z; $^{i)}$ 1 + x, y, 1 + z; $^{j)}$ 1 - x, 1.5 – y, 1.5 + z;)

Powder Xray diffraction (PXRD) patterns were recorded for bulky sample **4** in order to check the phase purity. All the peaks presented in the experimental patterns matched well with the simulated patterns generated from single-crystal diffraction data (Fig. S1), indicating a pure phase of the bulky sample.

Thermal gravimetric analysis (TGA) was performed to evaluate the thermal stability of compound **4** (Fig. S2). The decomposition process took place in multiple stages. The first step occurred from 30 to 230 °C with a slight mass loss~ 7%, assigned to the release of coordinated and guest water molecules (calcd. 8.1%). The following decomposition stages in the range of 230–700 °C were assigned to the loss of the ligands.

To evaluate the antimicrobial activity of both **H_2L** and coordination polymer **4**, the agar disk diffusion method [31] which consists in adding the compounds to the culture medium, pre-inoculated with the microbial suspension, and measuring the inhibition zone around the film disks after 24 h of incubation was utilized (Fig. S3). Thus, compounds **H_2L** and **4** showed no antimicrobial activity against the reference strains *S. aureus* and *C. albicans* (data not presented), but proved to have selective antibacterial activity against *E. coli*. Data on the average inhibition diameters of the inhibition zones are presented in Table 1.

Table 1. Antibacterial activity of **H_2L** (left) and **4** (right) against the references strains (mm).

Strain	**Inhibition zone H_2L (mm)**	**Inhibition zone 4 (mm)**
S. aureus	-	-
E. coli	20 ± 0.05 mm	16 ± 0.31 mm
C. albicans	-	-

Zn(II) is an essential micronutrient for bacteria, although it has significant toxicity at high concentrations [32-34]. Zinc is able to protect the human organism against *E. coli* maybe due to its combined effect on host tissues (helping the immunity) [35] and in the same inhibiting the pathogen [36].

As proven by the present study, resistance to zinc was noticed to be associated with *S. aureus* [37]. On the other hand the resistance of the fungal strain to zinc may be due to the fact that *C. albicans* secrets a scavenger protein (a ‘zincophore”) Pra 1, which sequesters zinc from the host cells and re-associates with the fungus via co-expressed zinc transporter Zrt1 [38], thus zinc is improving *C. albicans* growth.

In this work, we successfully synthesized and characterized 3’-(1*H*-tetrazol-5-*yl*)-[1,1’-biphenyl]-4-carboxylic acid as a novel ligand, as well as a coordination polymer with Zn(II). The crystal structure analysis of the resulted coordination polymer revealed that the central part of the structure is built up from a centrosymmetric tri-nuclear core, while the tri-nuclear cluster is consolidated due to the bridging structural function of two tetrazole fragments and two formate anions. Both the ligand and the coordination polymer have been tested for antimicrobial activity against three different reference strains, showing a selective activity of the investigated compounds against *Escherichia coli*.

Acknowledgements

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References

[1] N.L. Rosi, J. Eckert, M. Eddaoudi, D.T. Vodak, J. Kim, M. Keeffe, O.M. Yaghi, Science 300 (2003) 1127.

[2] J.L. Rowsell, O.M. Yaghi, Angew. Chem. Int. Ed. 44 (2005) 4670–4679.

[3] D. Sun, S. Ma, Y. Ke, D.J. Collins, H.-C. Zhou, J. Am. Chem. Soc. 128 (2006) 3896–3897.

[4] J.-M. Lin, C.-T. He, P.-Q. Liao, D.-D. Zhou, J.-P. Zhang, X.-M. Chen, SCIENCE CHINA Chem. 59 (2016) 970–974.

[5] L.-Y. Zhang, G.-F. Liu, S.-L. Zheng, B.-H. Ye, X.-M. Zhang, X.-M. Chen, Eur. J. Inorg. Chem. 2003 (2003) 2965–2971.

[6] S. Zhao, T.-R. Zheng, Y.-Q. Zhang, X.-X. Lv, B.-L. Li, Y. Zhang, Polyhedron 121 (2017) 61–69.

[7] R.W. Huang, Y.S. Wei, X.Y. Dong, X.H. Wu, C.X. Du, S.Q. Zang, T.C.W. Mak, Nat. Chem. 9 (2017) 689–697.

[8] X.M. Gao, D.-S. Li, J.-J. Wang, F. Fu, Y.-P. Wu, H.-M. Hu, J.-W. Wang, CrystEngComm 10 (2008) 479-482.

[9] X.C. Huang, Y.Y. Lin, J.P. Zhang, X.M. Chen, Angew. Chem. Int. Ed. 45 (2006) 1557–1559.

[10] L. Chen, Q. Chen, M. Wu, F. Jiang, M. Hong, Acc. Chem. Res. 48 (2015) 201–210.

[11] H.S. Wang, Coord. Chem. Rev. 349 (2017) 139-155.

[12] M. Paul, K. Sarkar, J. Deb, P. Dastidar, Chem.-A Eur. J. 23 (2017) 5736-5747.

[13] S.R. Batten, N.R. Champness, Philos, Trans. R. Soc. A Math. Phys. Eng. Sci. 375 (2016) 20160032.

[14] J.J. Sabatini, J. D. Moretti, Chem. Eur. J. 19 (2013) 12839-12845.

[15] J.J. Sabatini, A.V. Nagori, G. Chen, P. Chu, R. Damavarapu, T.M. Klapötke, Chem.-A Eur. J. 18 (2012) 628-631.

[16] V.A. Ostrovskii, R.E. Trifonov, E.A. Popova, Russ. Chem. Bull. 61 (2012) 768-780.

[17] A.J. Mota, A. Rodriquez-Dieguez, M.A. Palacios, J.M. Herrera, D. Luneau, E. Colacio, Inorg. Chem. 49 (2010) 8986-8996.

[18] M.H. Zeng, B. Wang, X.Y. Wang, W.X. Zhang, X.M. Chen, S. Gao, Inorg. Chem. 45 (2006) 7069-7076.

[19] F. He, M.L. Tong, X.L. Yu, X.M. Chen, Inorg. Chem. 44 (2005) 559-565.

[20] H.Y. Yang, L.K. Li, J. Wu, H.W. Hou, B. Xiao, Y.T. Fan, Chem.-A Eur. J. 15 (2009) 4049-4056.

[21] J. Zhao, Z.Z. Hu, X.G. Zheng, S.W. Ng, Acta Crystallogr. Sect. E. 65 (2009) m1601(Structure Rep.Online).

[22] D.G. Ding, M.L. Zhang, L.C. Li, Y.T. Fan, H.W. Hou, J. Coord. Chem. 62 (2009) 2675-2681.

[23] Y.L. Bai, J. Tao, R.B. Huang, L.S. Zheng, S.L. Zheng, K. Oshida, Y. Einaga, Chem. Commun. 15 (2008) 1753-1755.

[24] S.J. Li, H. Wang, W.D. Song, S.W. Hu, P.W. Qin, Acta Crystallogr. Sect. E. 66 (2010) m160(Structure Rep.Online).

[25] L. Rink, P. Gabriel, Biometals 14 (2001) 367-383.

[26] W.C. Fischer, R.E. Black, Annu. Rev. Nutr. 24 (2004) 255-275.

[27] K.J. Waldronm, J.C. Rutherford, D. Ford, N.J. Robinson, Nature 460 (2009) 823-830.

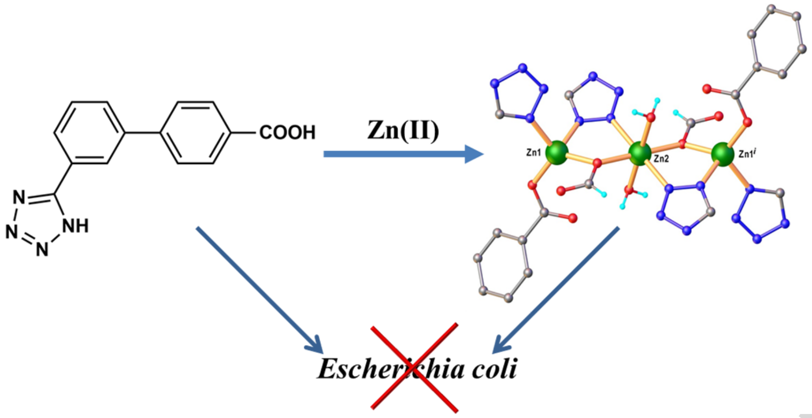
[28] A. Haleel, P. Arthi, N. Dastagiri Reddy, V. Veena, N. Sakthivel, Y. Arun, P.T. Perumal, A. Kalilur Rahiman, RSC Adv. 4 (2014) 60816-60830.

[29] B. Umamaheswara Rao, V. Krishna, G. Nageswara Rao, Asian J. Chem. 27(2) (2015) 4405-4410.

[30] B.E. Huff, T.M. Koenig, D. Mitchell, M.A. Staszak, Org. Synth. 10 (2004) 102.

[31] D.F. Brown, D. Kothari, J. Clin. Pathol. 28 (1975) 779–83.
[32] S. Silver, Gene 179 (1996) 9-19.
[33] M.R. Bruins, S. Kapil, F.W. Oehme, Ecotoxicol. Environ. Saf. 45 (2000) 198-207.
[34] B.D. Corbin, E.H. Seeley, A. Raab, J. Feldmann, M.R. Miller, V.J. Torres, K.L. Anderson, B.M. Dattilo, P.M. Dunman, R. Gerads, R.M.Caprioli, W. Nacken, W.J. Chazin, E.P. Skaar, Science 319 (2008) 962-965.
[35] J.K. Crane, T.M. Naeher, I. Sheulgina, C. Zhu, E.C. Beodeker, Infect. Immun. 75 (2007) 5974-5984.
[36] J.K. Crane, J.E. Broome, R.M. Reddinger, B.B. Werth, BMC Microbiol. 14 (2014) 145-161.
[37] R. Nair, D. Thapaliya, Y. Su, T.C. Smith, Infect. Control. Hosp. Epidemiol. 35 (2014) 32-39.
[38] F. Citiulo, I.D. Jacobsen, P. Miramon, L. Schild, S. Brunke, P. Zipfel, M. Brock, B. Hube, D. Wilson, PLos Pathogens, 8(6) (2012) e1002777.

Graphical abstract



Highlights

- New rigid ligand containing tetrazol and carboxylic moieties has been synthesized and characterized.
- The ligand is able to form crystalline coordination polymer with Zn(II).
- The antimicrobial activity of both ligand and Zn(II) coordination polymer was evaluated and compared.