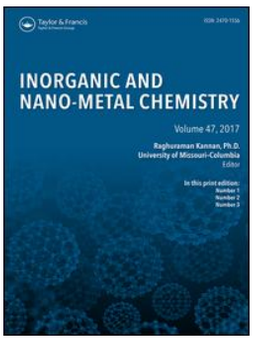


Inorganic and Nano-Metal Chemistry

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/lsrt21

Synthesis and characterization of a manganese(II) complex containing N(sp^2)$_4$-donor Schiff base ligand and interaction toward biomacromolecules

Mohammad Hakimi , Behjat Tarani , Zahra Mardani , Hassan Hassani , Monika Kučeráková & Eliska Skorepova

To cite this article: Mohammad Hakimi , Behjat Tarani , Zahra Mardani , Hassan Hassani , Monika Kučeráková & Eliska Skorepova (2020): Synthesis and characterization of a manganese(II) complex containing N(sp^2)$_4$-donor Schiff base ligand and interaction toward biomacromolecules, Inorganic and Nano-Metal Chemistry, DOI: 10.1080/24701556.2020.1852250

To link to this article: https://doi.org/10.1080/24701556.2020.1852250

INORGANIC AND NANO-METAL CHEMISTRY
https://doi.org/10.1080/24701556.2020.1852250

Synthesis and characterization of a manganese(II) complex containing $N(sp^2)_4$-donor Schiff base ligand and interaction toward biomacromolecules

Mohammad Hakimi[a], Behjat Tarani[a], Zahra Mardani[b], Hassan Hassani[a], Monika Kučeráková[c], and Eliska Skorepova[c]

[a]Department of Chemistry, Payame Noor University, Tehran, Iran; [b]Inorganic Chemistry Department, Faculty of Chemistry, Urmia University, Urmia, Iran; [c]Institute of Physic, Czech Academy of Sciences, Prague, Czech Republic

ABSTRACT

In this work, an N_4-donor Schiff base ligand, *N,N'*-(propane-1,2-diyl)bis(1-phenyl-1-(pyridin-2-yl)methanimine) (PPPM) and its Mn(II) complex, $[Mn(PPPM)(OAc)_2]\cdot 3H_2O$ (**1**), were prepared and identified by elemental analysis, FT-IR, ^{1}H NMR spectroscopy as well single-crystal X-ray diffraction. X-ray structure analysis of **1** revealed a distorted square-face bicapped trigonal prism geometry around manganese atom with MnN_4O_4 environment containing an N_4-donor PPPM and two O_2-donor acetato ligands. The ligand has a chiral center on carbon atom which leads to the formation of a racemic mixture of complex **1**. In the crystal structure of complex, intermolecular hydrogen bonds form $R_4^4(8)$ hydrogen bond motifs. The ability of two optical isomers of PPPM ligand and manganese complex to interact with 10 selected biomacromolecules (BRAF kinase, CatB, DNA gyrase, HDAC7, rHA, RNR, TrxR, TS, Top II, B-DNA) was investigated by docking studies. These studies revealed that $PPPM^{R,S}$ and $\mathbf{1}^{R,S}$ isomers can bind to these molecules better than doxorubicin (except B-DNA).

ARTICLE HISTORY
Received 12 May 2020
Accepted 18 October 2020

KEYWORDS
Manganese(II) complex; docking study; biomacromolecule; Schiff base; crystal structure

Introduction

Schiff base compounds attract considerable interest due to their wide range of applications such as chemosensors,[1,2] OLED,[3] photochromic materials,[4] catalysts,[5–7] and anti-corrosion agents.[8] Schiff base ligands and their complexes show interesting pharmacological activities such as antimicrobial,[9] anticancer,[10,11] antibacterial,[12] antifungal,[12] and antioxidative.[13] The cleavage of plasmid DNA by Schiff base complexes has been well reported.[14,15] Also, interaction of these compounds with biomacromolecules have been studied by docking studies.[10,11,16–18]

The coordination complexes as well as their applications have been largely previously reported in literatures.[19–21] Transition metals such as copper, iron, and manganese are involved in multiple biological processes, from electron transfer to catalysis to structural roles, and are frequently associated with active sites of proteins and enzymes.[22] However, dysregulation of some of these essential metals during normal biochemical processing has been implicated in the development of various pathological disorders, such as cancer.[23] The research shows that the metal ion is the most significant factor in the design of medicine Schiff base complexes.[24] An important property of metals is that they form positively charged ions in aqueous solution that can bind to negatively charged biological molecules.[22,25]

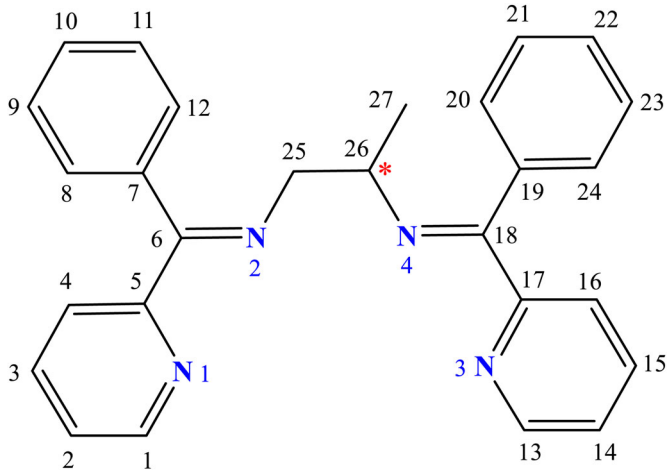
Manganese, with rich coordination geometry and versatile oxidation state, is well known biogenic metal and entrenched in the medicine and biology areas.[26] Manganese is a necessary element occurring in the biological systems and tis trace amounts are essential to life.[27] Thus, many manganese complexes derived from Schiff base have been synthesized and evaluated for their applications as biomedical field.[28,29] Some manganese complexes have shown considerable promise in superoxide dismutase (SOD) and catalase-like activity which could be a perspective for the creation of new medicines with wide applications.[30,31] A variety of activities such as inhibit endogenous NMT,[32] HAS[33] and BSA[27,34] binding, antioxidant,[35] anticancer,[36,37] antimicrobial[37] has been observed for complexes of manganese. Also interaction of these complexes with DNA has been established by experimental[38,39] and theoretical (docking) methods[17] and researchers have established that these compounds can overcome drug resistant cancers.[40]

In order to extend the chemistry of this class of compounds, in this work, preparation, characterization (elemental analysis, FT-IR, ^{1}H NMR spectroscopy) and crystal structure of a manganese(II) complex, $[Mn(PPPM)(OAc)_2]\cdot 3H_2O$ (**1**), with *N,N'*-(propane-1,2-diyl)bis(1-phenyl-1-(pyridin-2-yl)methanimine) (PPPM) ligand (Scheme 1) are presented.

CONTACT Mohammad Hakimi mohakimi@yahoo.com Department of Chemistry, Payame Noor University, 19395-4697 Tehran, Iran.

Supplemental data for this article can be accessed at the publisher's website.

CCDC Number 1941242 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Center, 12, Union Road, Cambridge CB2 1EZ, UK. deposit@ccdc.cam.ac.uk.



Scheme 1. Structure of the *N,N′*-(propane-1,2-diyl)bis(1-phenyl-1-(pyridin-2-yl)methanimine) (PPPM) ligand with atom numbering.

In addition to the expected biological properties of the Schiff base ligand PPPM, binding to Mn^{2+} ion makes this complex a good choice for biologically active compounds. For study of the biological activities of two possible isomers (R and S) of PPPM and also **1**, docking calculations were run to investigate the possibility of an interaction between these compounds with 10 protein targets,[10,16,18,41–43] including: BRAF kinase, Cathepsin B (CatB), DNA gyrase, Histone deacetylase (HDAC7), recombinant Human albumin (rHA), Ribonucleotide reductases (RNR), Thioredoxin reductase (TrxR), Thymidylate synthase (TS), Topoisomerase II (Top II) along with B-DNA. These proteins were selected either due to their reported roles in cancer growth or as transport agents that affect drug pharmacokinetic properties (e.g. rHA). The DNA gyrase was included to study the possibility of anticancer properties and their activity as antimalarial agents.[44] The knowledge gained from docking on the B-DNA should be useful for the development of potential probes for DNA structure and new therapeutic agents for cancer and other diseases.[45]

Experimental

Materials and measurements

All starting chemicals and solvents were reagent or analytical grade and used as received. The infrared spectra of KBr pellets in the range of 400–4000 cm^{-1} were recorded with a FT-IR 8400-Shimadzu spectrometer. The carbon, hydrogen, and nitrogen contents were determined in a Thermo Finnigan Flash Elemental Analyzer 1112 EA. The melting points were determined with a Barnsted Electrothermal 9200 electrically heated apparatus. ^{1}H NMR spectrum was recorded on a Bruker Aspect 3000 instrument operating at 250 MHz; chemical shifts are given in parts per million, with values in reference to an internal standard of TMS.

Preparation of N,N′-(propane-1,2-diyl)bis(1-phenyl-1-(pyridin-2-yl)methanimine), PPPM

The PPPM ligand was prepared as described in literature[46] with some modifications. 0.07 g (1 mmol) of 1,2-diaminopropane, dissolved in methanol (5 mL), was added dropwise with stirring to 0.37 g (2 mmol) of 2-benzoylpyridine in methanol (20 mL) and the resulting solution was stirred for 1 h at room temperature and then was refluxed for 6 h. A thick brown oil was obtained and the redundant precursors removed by rotary evaporation. Yield: 0.32 g, 79%. Anal. Calcd for $C_{27}H_{24}N_4$ (404.52): C, 80.17; H, 5.98; N, 13.85. Found C, 79.19; H, 6.12; N, 14.07. IR (KBr disk): 3053 (ν C–H)^{ar}, 2963 (ν_{as} C–H), 1663 (ν C=N)^{imine}, 1628 (ν C=N)^{py}, 1566 (ν C=C)^{ar}, 1449 (δ_{as} CH_2), 1395 (δ_s CH_2), 1045 (ν C–N), 750 and 700 (γ py) cm^{-1}. ^{1}H NMR (250 MHz, DMSO-d_6): δ = 8.70 (d, 2H, C^1H, $C^{13}H$), 8.44 (d, 2H, C^4H, $C^{16}H$), 7.15–8.03 (m, 14H, CH^{ar}), 2.99–3.23 (m, 2H, $C^{25}H_2$), 2.30–2.40 (m, 1H, $C^{26}H$), 1.03 (d, 3H, $C^{27}H_3$) ppm.

Preparation of [Mn(PPPM)(OAc)$_2$]·3H$_2$O

$Mn(OAc)_2$ (1 mmol, 0.17 g) was dissolved in methanol (5 ml) and added with stirring to the methanol solution (10 ml) of the PPPM (1 mmol, 0.40 g). The reaction mixture was stirred at 60 °C for 4 h. The solution was left for slow evaporation at room temperature. Then the resultant precipitate was filtered off, washed with methanol, and recrystallization from acetonitrile. After six days, brown crystals of complex were formed and collected by filtration. Yield 0.52 g, 82%. M.p. 156 °C. Anal. Calcd for $C_{31}H_{36}MnN_4O_7$ (631.6): C, 58.95; H, 5.75; N, 8.87. Found C, 59.05; H, 5.78; N, 9.08. IR (KBr): 3391 (ν_{as} O–H), 3301 (ν_s O–H), 3057 (ν C–H)^{ar}, 2958 (ν_{as} CH_2 and/or CH_3), 2930 (ν_s CH_2 and/or CH_3), 1656 (δ H_2O), 1636 (ν C=N)^{imine}, 1578 (ν C=N)^{py}, 1567 (ν C=C)^{ar}, 1565 (ν_{as} COO)^{Oac}, 1437 (ν_s COO)^{Oac}, 1430 (δ_{as} CH_2), 1395 (δ_s CH_2), 1049 (ν C–N), 750 and 708 (γ py), 667 (δ OCO)^{Oac}, 629 (ρ_r H_2O), 550 (ρ_w H_2O) cm^{-1}.

Computational details

The structure of ligand was optimized with the Gaussian 09 software[47] and calculated for an isolated molecule using Density Functional Theory (DFT)[48] at the B3LYP/6-31 + G level of theory (Figure 1).

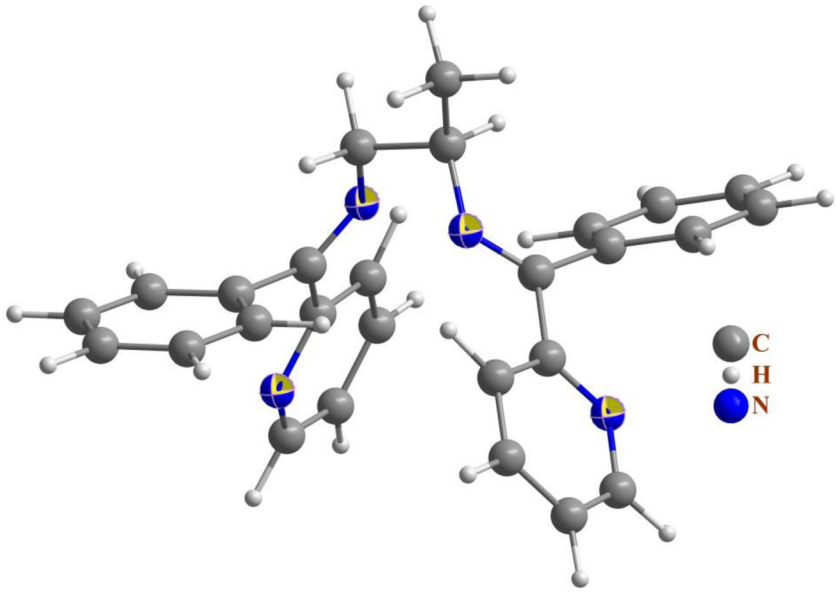


Figure 1. Optimized structure of the PPPM.

Table 1. Crystal structure data and structure refinement of complex **1**.

Empirical formula	$C_{31}H_{36}MnN_4O_7$
Formula weight, g mol^{-1}	631.6
Crystal size, mm^3	0.12 × 0.08 × 0.05
Temperature, K	95
Crystal system	Monoclinic
Space group	*C* 2/*c*
Unit cell dimensions	
a, Å	24.7851(3)
b, Å	8.2661(1)
c, Å	29.9111(4)
β, °	99.1923(12)
Volume, Å^3	6049.37(13)
Z	8
Calculated density, g cm^{-3}	1.387
Absorption coefficient, mm^{-1}	4.00
F(0 0 0), *e*	2648
θ range data collection, °	3.6–74.3
h, *k*, *l* ranges	$-30 \leq h \leq 30$, $-10 \leq k \leq 10$, $-36 \leq l \leq 37$
Reflections collected/independent/R_{int}	43,147/6149 / 0.037
Data/ref. parameters	6149/413
*R*1/*wR*2 ($I > 3\sigma(I)$)	0.0334/0.0817
*R*1/*wR*2 (all data)	0.0357/0.0825
Goodness-of-fit on F^2	2.12
Largest diff. peak/hole, *e* Å^{-3}	0.40/−0.46

Docking details

The pdb files 4r5y, 3ai8, 5cdn, 3c0z, 2bx8, 1peo, 3qfa, 1njb, 4gfh, 1bna for the 10 receptors, BRAF kinase, Cathepsin B (CatB), DNA gyrase, Histone deacetylase (HDAC7), recombinant Human albumin (rHA), Ribonucleotide reductases (RNR), Thioredoxin reductase (TrxR), Thymidylate synthase (TS), Topoisomerase II (Top II), B-DNA, respectively, used in this research were obtained from the Protein Data Bank (pdb).[49] The full version of Genetic Optimization for Ligand Docking (GOLD) 5.5[50] was used for the docking studies. The Hermes visualizer in the GOLD Suite was used to further prepare the ligand, complex, and the receptors for docking. The cif file of the complex and optimized structure of ligand (Figure 1) were used for the docking studies. The region of interest used for GOLD docking was defined as all the protein residues within 6 Å of the reference ligand "A" that accompanied the downloaded protein. For B-DNA, the region of interest was defined on DNA backbone within 10 Å of the O2, DT19 atom for minor groove. All free water molecules in the structure of the proteins were deleted before docking. Default values of all other parameters were used and the compounds were submitted to 10 genetic algorithm runs using the GOLDScore fitness function.

Crystal structure determination

A suitable crystal of **1** was chosen and its X-ray analysis was performed at 95 K using a SuperNova diffractometer with a micro-focus sealed tube, mirrors-collimated Cu Kα radiation ($\lambda = 1.54184$ Å), and CCD detector Atlas S2. The data were

Table 2. Selected bond lengths (Å) and angles (°) for complex **1** with estimated standard deviations in parentheses.

Bond lengths		Angles	
Mn1–N1	2.392(1)	N1–Mn1–N2a	67.27(8)
Mn1–N2a	2.372(3)	N1–Mn1–N3	155.61(4)
Mn1–N3	2.359(1)	N1–Mn1–O2	94.61(4)
Mn1–N4a	2.341(7)	O1–Mn1–O2	55.25(4)
Mn1–O1	2.360(1)	O2–Mn1–O4	165.53(5)
Mn1–O2	2.348(1)	O3–Mn1–O1	83.30(4)
Mn1–O3	2.397(1)	O3–Mn1–O2	138.18(4)
Mn1–O4	2.288(1)	O3–Mn1–O4	55.37(5)

Table 3. Hydrogen bond dimensions (Å and °) in complex **1**.[a]

D–H···A	*d*(D–H)	*d*(H···A)	*d*(D···A)	<(DHA)
O5–H1o5···O4^{i}	0.87	1.94	2.813(2)	176
O5–H2o5···O2	0.83	2.14	2.9665(19)	176
O6–H1o6···O7^{ii}	0.95	1.88	2.818(2)	172
O6–H2o6···O1^{iii}	0.95	1.77	2.713(2)	174
O7–H1o7···O3^{iv}	0.95	1.87	2.795(2)	163
O7–H2o7···O6	0.952	1.852	2.774(2)	162

aSymmetry operators: i $-x+1/2, y-1/2, -z+1/2$; ii $-x+3/2, -y+1/2, -z$; iii $x+1/2, y-1/2, z$; iv $-x+1, y, -z+1/2$.

processed with CrysAlis.[51] The structure was solved with the charge flipping algorithm by Superflip[52] and refined by full-matrix least-squares on F^2 using program Jana2006.[53] Anisotropic displacement parameters were used for all non-hydrogen atoms. Hydrogen atoms on carbon were kept at geometrically expected positions and refined as riding atoms with $U_{iso} = 1.2\,U_{eq}$ of the corresponding parent atom. Positions of hydrogen atoms on water were found in the residual electron density map using the software MCE[54] and refined using a restraint that all O–H bond lengths should be close to 0.95 Å. For hydrogen atoms of water, U_{iso} was kept as $1.2\,U_{eq}$ of the corresponding parent oxygen. The middle bridging part of the ligand was disordered (N4–C30–C29–(C31)–C30–N2). The disorder was modeled using the rigid body refinement feature in Jana2006 and the occupancy of the major component was 0.590(2).

Selected crystallographic data are presented in Table 1. Diagrams of the molecular structure were created using Ortep-III[55,56] and Diamond.[57] Selected bond lengths are displayed in Table 2 and hydrogen bond geometries in Table 3.

Results and discussion

The PPPM ligand was prepared by the condensation of propane-1,2-diamine and 2-benzoyl pyridine. Reaction between manganese(II) acetate with PPPM provided complex **1**. The complex is air-stable and soluble in DMSO.

Spectroscopic studies

In the IR spectrum of the PPPM and **1**, bands at above and below 3000 cm^{-1} are due to the C–H modes of the aromatic rings (phenyl and pyridine) and aliphatic moieties (propane moiety and acetato ligand), respectively. The imine and pyridine units of the ligand are effected the IR spectrum at about 1650 cm^{-1} owing to the ν (C=N).[58] These bands are shifted by 27 and 50 cm^{-1} to lower frequencies after coordination to the manganese, confirming the N_4-donation of the ligand. Similar result has been observed for PPPM derivatives.[17]

The presence of the water molecule in **1** affects the IR spectrum in three regions, including broad peaks above 3300–3400 cm^{-1} for asymmetric and symmetric O–H stretches, 1656 cm^{-1} for H_2O bending and 200–600 cm^{-1} for "librational modes". These modes are due to rotational oscillations of the water molecules restricted by interactions with neighboring atoms and they are classified into three types (wagging (ρ_w), twisting (ρ_t), and rocking (ρ_r)) depending upon the direction of the principal axis of rotation.[12,13]

In the FT-IR spectrum of **1**, three bands at 1565, 1437, and 667 cm^{-1} were assigned to the ν_{as} (COO), ν_s (COO), and δ (OCO) respectively,[59] confirming the presence of the acetate unit in this complex. The differences between asymmetric (ν_{as}) and symmetric (ν_s) stretching of the acetate group (Δ) can reveal its coordination type. Compared with Δ value for the acetate salt, monodentate complexes exhibit much larger Δ values (164 cm^{-1}) while in bidentate complexes these values are significantly lower.[60,61] The Δ value for **1** is calculated as 128 cm^{-1} which corresponds to the bidentate acetate ligand.

The ^{1}H NMR spectrum of the PPPM revealed that this structure is containing the aromatic (7.5–9.0 ppm) and aliphatic (5.19 ppm) portions. Among the aromatic protons, the nearest one to the nitrogen atom of the pyridine ring is observed at the lowest magnetic field.

Crystal and molecular structure of $[Mn(PPPM)(OAc)_2]\cdot 3H_2O$

In the crystal structure of **1** (Figure 2), the manganese atom is coordinated by four nitrogen atoms of one PPPM and four oxygen atoms of two bidentate acetato ligands to form a distorted square-face bicapped trigonal prism, MnN_4O_4 (Figure 3), geometry. Study of the CSD database[62] revealed that this environment is rare and there are only nine examples[17,63–69] for such geometry around the manganese atom, in which all nitrogen atoms belong to one tetradentate ligand. In this structure, bond lengths average of four Mn–N (2.366 Å) is comparable with that of the Mn–O (2.348 Å) bond lengths.

In **1**, the PPPM ligand acts as a tetradentate $N_2^{imine}N_2^{py}$-donor, forming three five-membered chelate rings. Among them, the central chelate ring is non-planar (r.m.s deviation: 0.262 Å for C30a) while two side rings are almost planar (r.m.s deviations: 0.078 Å for C6, 0.089 Å for N4a). The dihedral angle between planes through the four coordinated nitrogen atoms and four coordinated oxygen atoms is 86.29°, confirming that the PPPM ligand has perpendicular direction to the acetato ligands. Also, two pyridine rings lie on a plane formed by four coordinated nitrogen atoms (dihedral angles average of 4.10°), while phenyl rings are rotated by 76.65° (angles average) from this plane. The PPPM ligand has a chiral center on C29 atom and the crystals of **1** are a racemic mixture of *R* and *S* isomers in alternate layers. In fact, there is a crystallographic disorder in the

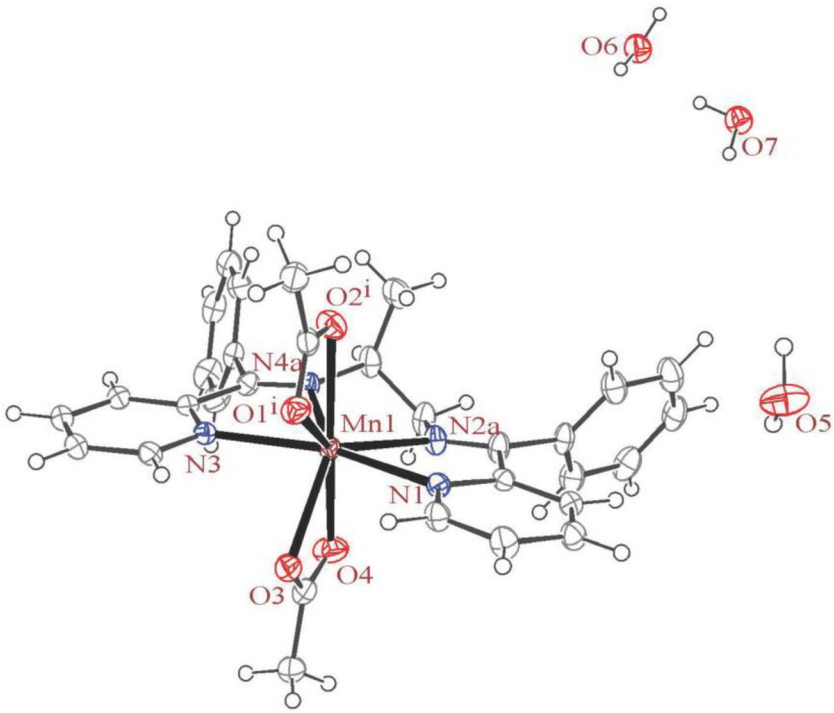


Figure 2. Ortep-III diagram of the molecular structure of complex **1**. The ellipsoids are drawn at the 50% probability level.

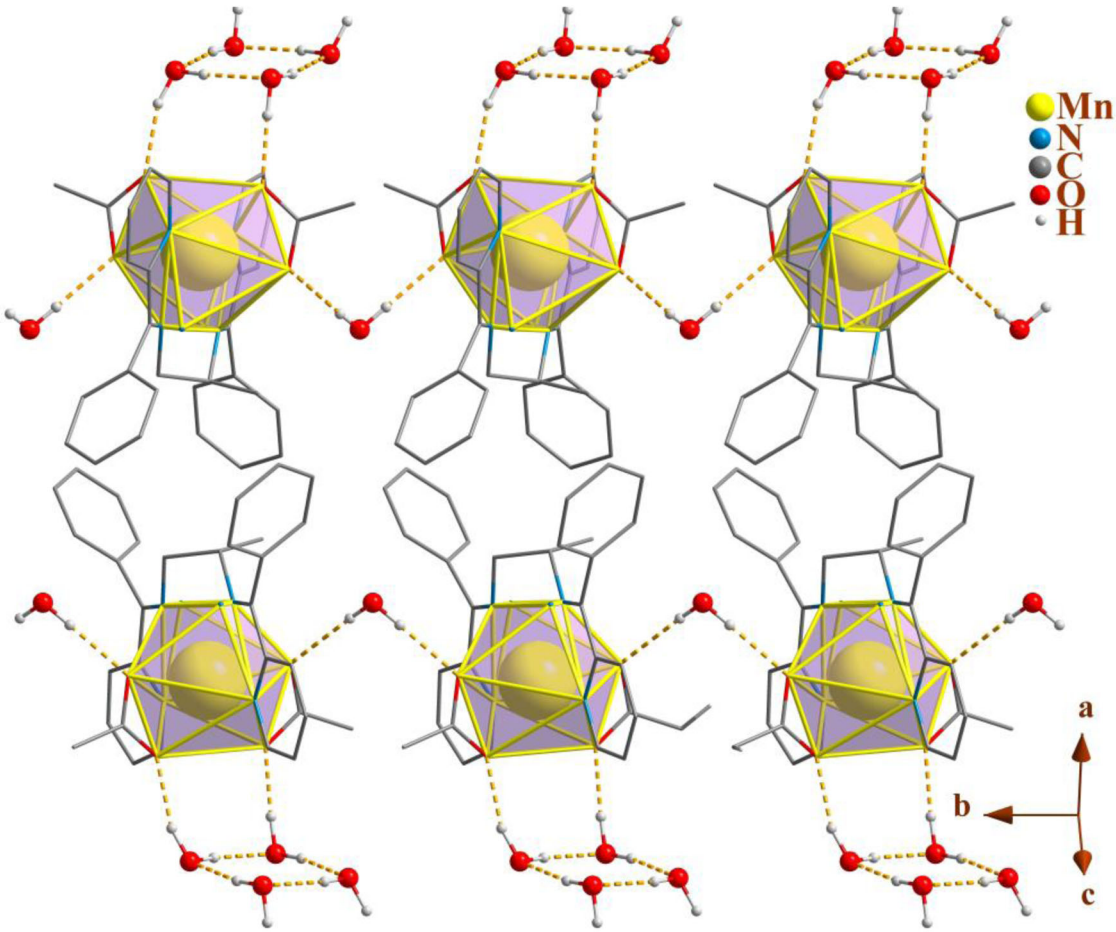


Figure 3. Packing of molecules **1** in the crystal showing the hydrogen bonds and $R_4^4(8)$ hydrogen bond motifs. Each MnN_4O_4 unit is shown as a polyhedron.

Table 4. The calculated fitness values for the optical isomers of PPPM ligand and complex **1** along with the doxorubicin.

	B-DNA MIN	BRAF-KINASE	CATB	DNA-GYRASE	HDAC7	RHA	RNR	TRXR	TS	TOP II
$PPPM^R$	65.20	60.84	46.54	69.29	69.01	57.99	55.84	71.63	58.58	62.27
$PPPM^S$	68.91	57.52	56.47	52.18	69.17	58.47	55.45	43.39	55.61	65.73
COMPLEX $\mathbf{1}^S$	49.89	47.28	35.32	71.90	58.94	60.13	47.17	−1.39	60.55	66.71
COMPLEX $\mathbf{1}^R$	51.95	49.49	54.84	44.10	42.65	50.43	36.91	34.05	60.01	65.68
DOXORUBICIN	83.10	54.21	25.95	52.97	50.73	50.10	49.18	66.70	53.34	59.05

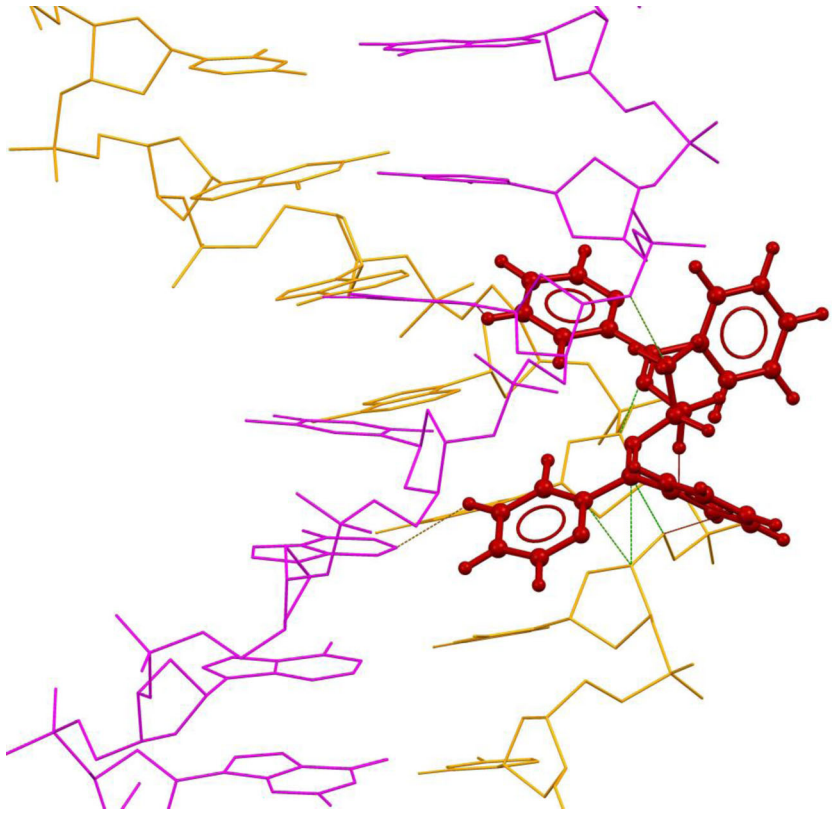


Figure 4. Docking study results showing the interaction between the $PPPM^R$ and B-DNA (minor groove).

PPPM ligand atoms N4–C30–C29–(C31)–C30–N2 (the bringing section of PPPM). The molecule of PPPM is almost symmetrical with only the methyl C31 violating this. This then enables the ligand to bind to the metal in the lattice in a disordered fashion, where both enantiomers are overlaid and the refined occupancy of the major component is 0.590(2).

In this structure, there are strong O–H···O hydrogen bonds (strong hydrogen bonds are in range of 1.5–2.2 Å[70]), between water molecules as well as between water and the acetato ligand. The O–H···O hydrogen bonds participate in the formation of a $R_4^4(8)$ hydrogen bond motif (four acceptors, four donors with degree of 8)[71,72] between four water molecules (Figure 3).

Docking studies

For the prediction and comparison of the biological activity of the ligand and complex **1** along with their two possible optical isomers, interactions of these four compounds with 10 macromolecule receptors using Gold[50] docking software were studied. The Gold docking results are reported in terms of the values of fitness, where "fitness" expresses ability of the investigated compound to take part in the docking interaction.[10,16,17,41–43,73] In Table 4, we present the best binding results out of the favorable ten ones predicted by Gold, and compare the obtained scores with those of the famous anticancer drug, doxorubicin (a cancer medication that interferes with the growth and spread of cancer cells in the body[74]).

Analysis of Table 4 shows that all studied structures can be consider as biologically active compounds.[10,16,17,41–43,73] The best predicted targets for $\mathbf{1}^S$, $\mathbf{1}^R$, $PPPM^S$, and $PPPM^R$ are DNA gyrase, Top II, HDAC7, and TrxR, respectively. This observation revealed that the presence of a chiral atom on PPPM ligand highly affected binding ability of the corresponding optical isomers. Based on the calculated fitness values, ligand and its complex show different tendency to the protein molecules, for example one or two isomers of PPPM can interact with the BRAF Kinase, CatB, HDAC7, RNR, and TrxR proteins better than the **1** while the complex isomers bind to the other proteins stronger than the ligand isomers. Docking studies revealed that the optical isomers of ligand and complex have different binding abilities and can

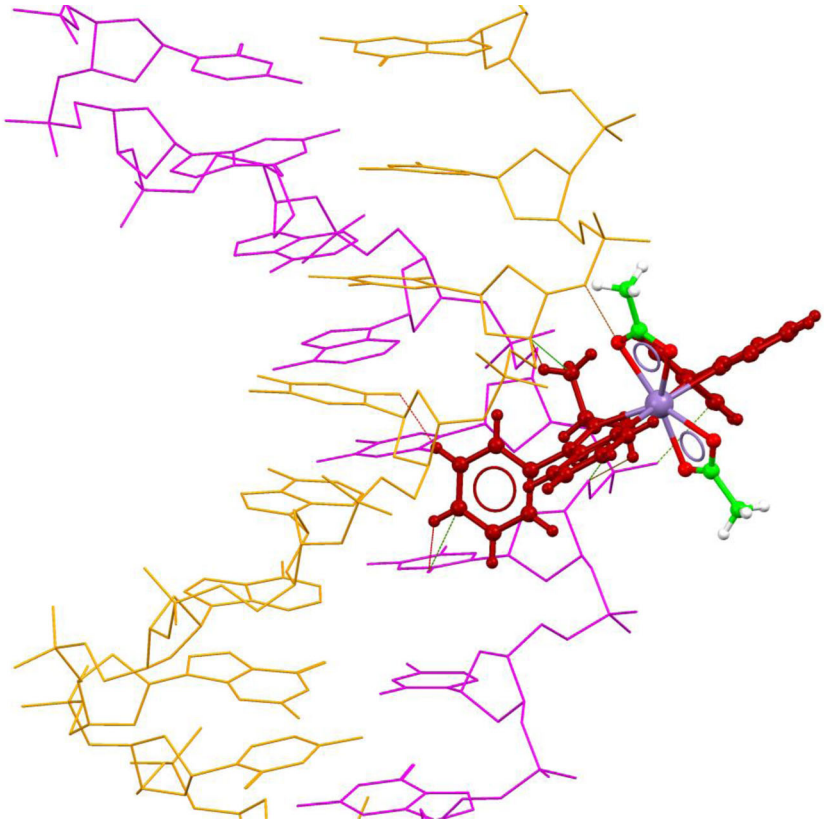


Figure 5. Docking study results showing the interaction between the Complex $\mathbf{1}^{S}$ and B-DNA (minor groove).

attach selectively to the biomacromolecules. Also these compounds can place in the minor groove of the DNA molecule which make these compounds a good choice for DNA binding studies. Data of the Table 4 revealed that the isomers of ligand or complex **1** or both of them have higher fitness values than doxorubicin in interaction toward all studied targets (except B-DNA), therefore we suggest that anticancer activities of these compounds should be studied. The docking results of the interaction between the $PPPM^{R}$ and complex $\mathbf{1}^{S}$ with B-DNA (minor groove) are shown in Figures 4 and 5, respectively.

Conclusion

In this work, a new complex of manganese(II), $[Mn(PPPM)(OAc)_2]\cdot 3H_2O$ (**1**), with *N*,*N*'-(propane-1,2-diyl)-bis(1-phenyl-1-(pyridin-2-yl)methanimine) (PPPM) was synthesized and spectral properties of the complex as well as the ligand were investigated. In the structure of **1**, the manganese atom has a MnN_4O_4 environment with a distorted square-face bicapped trigonal prism geometry formed by one N_4-donor PPPM ligand and two O_2-donor acetato ligands. In the crystal packing of **1**, the strong O–H···O interactions form a $R_4^4(8)$ hydrogen bond motif between four water molecules. The docking studies on the complex and its ligand revealed that these compounds might be biologically active by interacting with 10 biomacromolecules (BRAF kinase, CatB, DNA gyrase, HDAC7, rHA, RNR, TrxR, TS, Top II, and B-DNA). The best predicted targets for $\mathbf{1}^{S}$, $\mathbf{1}^{R}$, $PPPM^{S}$, and $PPPM^{R}$ are DNA gyrase, Top II, HDAC7, and TrxR, respectively. This study showed that two optical isomers of ligand and complex have different tendency to bimacromolecules. Docking calculations revealed that the fitness values of the ligand and complex are higher than that of doxorubicin (except B-DNA), thus we suggest that studying anticancer activities of these compounds could bring interesting results.

Acknowledgements

MD and MK thank Tereza Václavů from the Institute of Physics for measurement of the data set of complex **1**. The crystallographic part was supported by the project 18-10504S of the Czech Science Foundation and used instruments of the CzechNanoLab Research Infrastructure supported by MEYS CR (LM2018110). We would like to acknowledge Dr. Keyvan Moeini for CSD studies and the FAIRE (Frank H. Allen International Research and Education Programme) award of the Cambridge Structural Database, for supplying the access to the CSD softwares package.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

The crystallographic part was supported by the project 18-10504S of the Czech Science Foundation using instruments of the ASTRA laboratory established within the Operation Program Prague Competitiveness – project CZ.2.16/3.1.00/24510.

ORCID

Zahra Mardani http://orcid.org/0000-0002-3749-5399

References

1. Dong, W.-K.; Li, X.-L.; Wang, L.; Zhang, Y.; Ding, Y.-J. A New Application of Salamo-Type Bisoximes: As a Relay–Sensor for Zn2+/Cu2+ and Its Novel Complexes for Successive Sensing of H+/OH−. *Sensor. Actuat.* **2016**, *B229*, 370–378.
2. Wang, B.-J.; Dong, W.-K.; Zhang, Y.; Akogun, S. F. A. Novel Relay-Sensor for Highly Sensitive and Selective Detection of Zn2+/Pic − and Fluorescence on/off Switch Response of H+/OH−. *Sensor. Actuat.* **2017**, *B247*, 254–264.
3. Che, C.-M.; Chan, S.-C.; Xiang, H.-F.; Chan, M. C. W.; Liu, Y.; Wang, Y. Tetradentate Schiff Base Platinum(II) Complexes as New Class of Phosphorescent Materials for High-Efficiency and White-Light Electroluminescent Devices. *Chem. Commun.* **2004**, 1484–1485. DOI: 10.1039/b402318h.
4. Margerum, J. D.; Miller, L. J. *Photochromism*; Interscience, Wiley: New York, **1971**; p 569.
5. Gupta, K. C.; Sutar, A. K. Catalytic Activities of Schiff Base Transition Metal Complexes. *Coord. Chem. Rev.* **2008**, *252*, 1420–1450. DOI: 10.1016/j.ccr.2007.09.005.
6. Kannappan, R.; Matsumoto, M.; Hallren, J.; Nicholas, K. M. New Chiral Schiff Base–Zinc Complexes and Their Esterolytic Catalytic Activity. *J. Mol. Catal.* **2011**, *A339*, 72–78.
7. Li, L.-H.; Dong, W.-K.; Zhang, Y.; Akogun, S. F.; Xu, L. Syntheses, Structures and Catecholase Activities of Homo- and Hetero-Trinuclear Cobalt(II) Complexes Constructed from an Acyclic Naphthalenediol-Based Bis(Salamo)-Type Ligand. Appl. Organometal. Chem. **2017**, *31*, e3818. DOI: 10.1002/aoc.3818.
8. Ahamad, I.; Prasad, R.; Quraishi, M. A. Thermodynamic, Electrochemical and Quantum Chemical Investigation of Some Schiff Bases as Corrosion Inhibitors for Mild Steel in Hydrochloric Acid Solutions. *Corros. Sci.* **2010**, *52*, 933–942. DOI: 10.1016/j.corsci.2009.11.016.
9. Zhang, M.; Xian, D.-M.; Li, H.-H.; Zhang, J.-C.; You, Z.-L. Synthesis and Structures of Halo-Substituted Aroylhydrazones with Antimicrobial Activity. *Aust. J. Chem.* **2012**, *65*, 343–350. DOI: 10.1071/CH11424.
10. Saghatforoush, L.; Moeini, K.; Hosseini-Yazdi, S. A.; Mardani, Z.; Hajabbas-Farshchi, A.; Jameson, H. T.; Telfer, S. G.; Woollins, J. D. Theoretical and Experimental Investigation of Anticancer Activities of an Acyclic and Symmetrical Compartmental Schiff Base Ligand and Its Co(II). *RSC Adv.* **2018**, *8*, 35625–35639. DOI: 10.1039/C8RA07463A.
11. Saghatforoush, L.; Moeini, K.; Hosseini-Yazdi, S. A.; Mardani, Z.; Bakhtiari, A.; Hajabbas-Farshchi, A.; Honarvar, S.; Abdelbaky, M. S. M. Effective Anticancer Activities of an Acyclic Symmetrical Compartmental Schiff Base Ligand and Its Co(II), Cu(II) and Zn(II) Complexes against the Human Leukemia Cell Line K562. *Polyhedron* **2019**, *170*, 312–324. DOI: 10.1016/j.poly.2019.05.057.
12. Shanker, K.; Rohini, R.; Ravinder, V.; Reddy, P. M.; Ho, Y.-P. Ru(II) Complexes of N4 and N2O2 Macrocyclic Schiff Base Ligands: Their Antibacterial and Antifungal Studies. *Spectrochim. Acta A Mol. Biomol. Spectrosc.* **2009**, *73*, 205–211. DOI: 10.1016/j.saa.2009.01.021.
13. Li, Y.; Yang, Z.-Y. DNA Binding Affinity and Antioxidative Activity of Copper(II) and Zinc(II) Complexes with a Novel Hesperetin Schiff Base Ligand. *Inorg. Chim. Acta* **2009**, *362*, 4823–4831. DOI: 10.1016/j.ica.2009.07.008.
14. Morrow, J. R.; Kolasa, K. A. Cleavage of DNA by Nickel Complexes. *Inorg. Chim. Acta* **1992**, *195*, 245–248. DOI: 10.1016/S0020-1693(00)85319-0.
15. Tiwari, A. D.; Mishra, A. K.; Mishra, S. B.; Mamba, B. B.; Maji, B.; Bhattacharya, S. Synthesis and DNA Binding Studies of Ni(II), Co(II), Cu(II) and Zn(II) Metal Complexes of N1,N5-Bis[Pyridine-2-Methylene]-Thiocarbohydrazone Schiff-Base Ligand. *Spectrochim. Acta A Mol. Biomol. Spectrosc.* **2011**, *79*, 1050–1056. DOI: 10.1016/j.saa.2011.04.018.
16. Mardani, Z.; Hakimi, M.; Moeini, K.; Mohr, F. Reaction of 2-[(2-Aminoethyl)Amino]Ethanol with Pyridine-2-Carbaldehyde and Complexation of the Products with Cu(II) and Cd(II) along with Docking Studies. *Acta Crystallogr.* **2019**, *C75*, 951–959.
17. Hakimi, M.; Tarani, B.; Mardani, Z.; Moeini, K.; Kučeráková, M.; Dušek, M. Spectral, Structural, Theoretical and Docking Studies of a Mn(II) Complex with an N4-Donor Ligand. *J. Chem. Res.* **2018**, *42*, 623–627. DOI: 10.3184/174751918X15422215897056.
18. Hakimi, M.; Ahmadi, S.; Mardani, Z.; Mohr, F. Docking Studies on an N4-Donor Schiff Base Ligand and Its Cu(II) Complex Supported by Structural, Spectral and Theoretical Studies. *J. Chem. Res.* **2019**, *43*, 170–178. DOI: 10.1177/1747519819857505.
19. Fan, L.; Liu, Z.; Zhang, Y.; Wang, F.; Zhao, D.; Yang, J.; Zhang, X. Electrochemical, and Magenetic Properties of 2D Coordination Polymers Based on the Mixed Ligands p-Terphenyl-2,2′′,5′′,5′′′-Tetracarboxylate Acid and 1,10-Phenanthroline. *New J. Chem.* **2019**, *43*, 13349–13356. DOI: 10.1039/C9NJ03530C.
20. Fan, L.; Zhang, Y.; Liang, J.; Wang, X.; Lv, H.; Wang, J.; Zhao, L.; Zhang, X. Structural Diversity, Magnetic Properties, and Luminescence Sensing of Five 3D Coordination Polymers Derived from Designed 3,5-Di(2′,4′-Dicarboxylphenyl)Benozoic Acid. *CrystEngComm* **2018**, *20*, 4752–4762. DOI: 10.1039/C8CE00877A.
21. Fan, L.; Wang, F.; Zhao, D.; Sun, X.; Chen, H.; Wang, H.; Zhang, X. Two Cadmium(II) Coordination Polymers as Multi-Functional Luminescent Sensors for the Detection of Cr(VI) Anions, Dichloronitroaniline Pesticide, and Nitrofuran Antibiotic in Aqueous Media. *Spectrochim. Acta A Mol. Biomol. Spectrosc.* **2020**, A*239*, 118467 DOI: 10.1016/j.saa.2020.118467.
22. Orvig, C.; Abrams, M. J. Medicinal Inorganic Chemistry: Introduction. Chem. Rev. **1999**, *99*, 2201–2204. DOI: 10.1021/cr980419w.
23. Yaman, M.; Kaya, G.; Yekeler, H. Distribution of Trace Metal Concentrations in Paired Cancerous and Non-Cancerous Human Stomach Tissues. *World J. Gastroenterol.* **2007**, *13*, 612–618. DOI: 10.3748/wjg.v13.i4.612.
24. Arjmand, F.; Muddassir, M.; Khan, R. H. Chiral Preference of l-Tryptophan Derived Metal-Based Antitumor Agent of Late 3d-Metal Ions (Co(II), Cu(II) and Zn(II)) in Comparison to d- and dl-Tryptophan Analogues: Their in Vitro Reactivity Towards CT DNA, 5′-GMP and 5′-TMP. *Eur. J. Inorg. Chem.* **2010**, *45*, 3549–3557.
25. Haas, K. L.; Franz, K. J. Application of Metal Coordination Chemistry to Explore and Manipulate Cell Biology. Chem. Rev. **2009**, *109*, 4921–4960. DOI: 10.1021/cr900134a.
26. Rebouças, J. S.; Spasojević, I.; Batinić-Haberle, I. Pure Manganese(III) 5,10,15,20-Tetrakis(4-Benzoic Acid)Porphyrin (MnTBAP) is Not a Superoxide Dismutase Mimic in Aqueous Systems: A Case of Structure–Activity Relationship as a Watchdog Mechanism in Experimental Therapeutics and Biology. J. Biol. Inorg. Chem. **2008**, *13*, 289–302. DOI: 10.1007/s00775-007-0324-9.
27. Li, Z.; Yan, H.; Liu, K.; Huang, X.; Niu, M. Syntheses, Structures, DNA/BSA Binding and Cytotoxic Activity Studies of Chiral Alcohol-Amine Schiff Base Manganese (II/III) Complexes. *J. Mol. Struct.* **2019**, *1195*, 470–478. DOI: 10.1016/j.molstruc.2019.05.110.
28. Dehkordi, M. N.; Bordbar, A. K.; Lincoln, P.; Mirkhani, V. Spectroscopic Study on the Interaction of ct-DNA with Manganese Salen Complex Containing Triphenyl Phosphonium Groups. *Spectrochim. Acta A Mol. Biomol. Spectrosc.* **2012**, *90*, 50–54. DOI: 10.1016/j.saa.2012.01.015.
29. Zhu, L.-N.; Gao, H.-R.; Wang, H.-X.; Xu, M.-Y.; Li, X.-Z. Synthesis, Crystal Structures, and DNA Cleavage Activities of Manganese(II) Complexes: A Good Example of the Synergy

between Metal Ions Prompting DNA Cleavage. *Eur. J. Inorg. Chem.* **2014**, *2014*, 2396–2405. DOI: 10.1002/ejic.201400044.
30. Weiss, H.; Riley, D. P. Therapeutic Aspects of Manganese (II)-Based Superoxide Dismutase Mimics. In Uses of Inorganic Chemistry in Medicine; The Royal Society of Chemistry: Cambridge, **1999**, pp 77–92.
31. Ghosh, K.; Tyagi, N.; Kumar, P. Role of Carboxamido Nitrogen in Mononuclear Manganese Complex: Superoxide Scavenging Activity and Nuclease Activity. *Inorg. Chem. Commun.* **2010**, *13*, 380–383. DOI: 10.1016/j.inoche.2009.12.028.
32. Shrivastav, A.; Singh, N. K.; Tripathi, P.; George, T.; Dimmock, J. R.; Sharma, R. K. Copper(II) and Manganese(III) Complexes of N'-[(2-Hydroxy Phenyl) Carbonothioyl] Pyridine-2-Carbohydrazide: Novel Therapeutic Agents for Cancer. *Biochim* **2006**, *88*, 1209–1216. DOI: 10.1016/j.biochi.2006.03.004.
33. Geromichalos, G. D.; Tarushi, A.; Lafazanis, K.; Pantazaki, A. A.; Kessissoglou, D. P.; Psomas, G. In Vitro and in Silico Study of the Biological Activity of Manganese(III) Inverse-[9-MC-3]-Metallacrowns and Manganese(II) Complexes with the Anti-Inflammatory Drugs Diclofenac or Indomethacin. J. Inorg. Biochem. **2018**, *187*, 41–55. DOI: 10.1016/j.jinorgbio.2018.07.007.
34. Tarushi, A.; Zampakou, M.; Perontsis, S.; Lafazanis, K.; Pantazaki, A. A.; Hatzidimitriou, A. G.; Geromichalos, G. D.; Psomas, G. Manganese(II) Complexes of Tolfenamic Acid or Naproxen in Polymeric Structures or Encapsulated in [15-MC-5] Manganese(III) Metallacrowns: Structure and Biological Activity. *Inorg. Chim. Acta* **2018**, *483*, 579–592. DOI: 10.1016/j.ica.2018.09.001.
35. Kaya, B.; Kaya, K.; Koca, A.; Ülküseven, B. Thiosemicarbazide-Based Iron(III) and Manganese(III) Complexes. Structural, Electrochemical Characterization and Antioxidant Activity. *Polyhedron* **2019**, *173*, 114130. DOI: 10.1016/j.poly.2019.114130.
36. Icsel, C.; Yilmaz, V. T.; Aydinlik, Ş.; Aygun, M. New Manganese(II), Iron(II), Cobalt(II), Nickel(II) and Copper(II) Saccharinate Complexes of 2,6-Bis(2-Benzimidazolyl)Pyridine as Potential Anticancer Agents. *Eur. J. Inorg. Chem.* **2020**, *202*, 112535.
37. El-Shwiniy, W. H.; Shehab, W. S.; Zordok, W. A. Spectral, Thermal, DFT Calculations, Anticancer and Antimicrobial Studies for Bivalent Manganese Complexes of Pyrano[2,3-d]Pyrimidine Derivatives. *J. Mol. Struct.* **2020**, *1199*, 126993. DOI: 10.1016/j.molstruc.2019.126993.
38. Ghosh, K.; Tyagi, N.; Kumar, P.; Singh, U. P.; Goel, N. Stabilization of Mn(II) and Mn(III) in Mononuclear Complexes Derived from Tridentate Ligands with N2O Donors: Synthesis, Crystal Structure, Superoxide Dismutase Activity and DNA Interaction Studies. J. Inorg. Biochem. **2010**, *104*, 9–18. DOI: 10.1016/j.jinorgbio.2009.09.014.
39. Sharma, D.; Revanasiddappa, H. D.; Jayalakshmi, B. DNA/BSA Interaction and In Vitro Antimicrobial Studies of Mn(III) Complexes Bearing Bidentate N, O Donor Schiff Bases. *J. Iran. Chem. Soc.* **2020**, *17*, 43–58. DOI: 10.1007/s13738-019-01745-9.
40. Ghosh, R. D.; Banerjee, K.; Das, S.; Ganguly, A.; Chakraborty, P.; Sarkar, A.; Chatterjee, M.; Choudhuri, S. K. A Novel Manganese Complex, Mn-(II) N-(2-Hydroxy Acetophenone) Glycinate Overcomes Multidrug-Resistance in Cancer. Eur. J. Pharm. Sci. **2013**, *49*, 737–747. DOI: 10.1016/j.ejps.2013.05.002.
41. Marandi, F.; Moeini, K.; Alizadeh, F.; Mardani, Z.; Quah, C. K.; Loh, W.-S.; Woollins, J. D. Treatment of Cadmium(II) and Zinc(II) with N 2 -Donor Linkages in Presence of β-Diketone Ligand; Supported by Structural, Spectral, Theoretical and Docking Studies. *Inorg. Chim. Acta* **2018**, *482*, 717–725. DOI: 10.1016/j.ica.2018.07.014.
42. Mardani, Z.; Kazemshoar-Duzduzani, R.; Moeini, K.; Hajabbas-Farshchi, A.; Carpenter-Warren, C.; Slawin, A. M. Z.; Woollins, J. D. Anticancer Activities of a β-Amino Alcohol Ligand and Nanoparticles of Its Copper(ii) and Zinc(ii) Complexes Evaluated by Experimental and Theoretical Methods. *RSC Adv.* **2018**, *8*, 28810–28824. DOI: 10.1039/C8RA04578J.
43. Hakimi, M.; Sadeghi, F.; Feizi, N.; Moeini, K.; Kucerakova, M.; Dusek, M. Investigation of the Effect of the N-Oxidation Process on the Interaction of Selected Pyridine Compounds with Biomacromolecules: Structural, Spectral, Theoretical and Docking Studies. *Acta Crystallogr.* **2019**, *C75*, 750–757.
44. Adeniyi, A. A.; Ajibade, P. A. Comparing the Suitability of Autodock, Gold and Glide for the Docking and Predicting the Possible Targets of Ru(II)-Based Complexes as Anticancer Agents. *Molecules* **2013**, *18*, 3760–3778. DOI: 10.3390/molecules18043760.
45. Moghadam, N. H.; Salehzadeh, S.; Shahabadi, N. Spectroscopic and Molecular Docking Studies on the Interaction of Antiviral Drug Nevirapine with Calf Thymus DNA. *Nucleos. Nusleot. Nucl.* **2017**, *36*, 553–570.
46. Abedi, M.; Khandar, A. A.; Gargari, M. S.; Gurbanov, A. V.; Hosseini, S. A.; Mahmoudi, G. Syntheses, Characterization, and Crystal Structures of a Dinuclear Complex and Coordination Polymer of Mercury(II) with Schiff Base Ligands Containing N3 and N4Donors. Z. *Anorg. Allg.* Chem. **2014**, *640*, 2193–2197. DOI: 10.1002/zaac.201400273.
47. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; et al. Gaussian 09; Gaussian, Inc.: Wallingford, CT, **2009**.
48. Perdew, J. P. Density-Functional Approximation for the Correlation Energy of the Inhomogeneous Electron Gas. *Phys. Rev.* **1986**, *B33*, 8822–8824.
49. Gavezzotti, A. Are Crystal Structures Predictable? *Acc. Chem. Res.* **1994**, *27*, 309–314. DOI: 10.1021/ar00046a004.
50. Jones, G.; Willett, P.; Glen, R. C.; Leach, A. R.; Taylor, R. Development and Validation of a Genetic Algorithm for Flexible Docking. J. Mol. Biol. **1997**, *267*, 727–748. DOI: 10.1006/jmbi.1996.0897.
51. Rigaku Oxford Diffraction, *CrysAlisPro Software System, Version 1.171.xx.xx*; Rigaku Corporation: Oxford, **2018**.
52. Palatinus, L.; Chapuis, G. SUPERFLIP – A Computer Program for the Solution of Crystal Structures by Charge Flipping in Arbitrary Dimensions. J. Appl. Crystallogr. **2007**, *40*, 786–790. DOI: 10.1107/S0021889807029238.
53. Petříček, V.; Dušek, M.; Palatinus, L. Crystallographic Computing System JANA2006: General Features. *ZKRI* **2014**, *229*, 345–352.
54. Rohlicek, J.; Husak, M. MCE2005 – A New Version of a Program for Fast Interactive Visualization of Electron and Similar Density Maps Optimized for Small Molecules. *J. Appl. Crystallogr.* **2007**, *40*, 600–601.
55. Farrugia, L. J. ORTEP-3 for Windows – A Version of ORTEP-III with a Graphical User Interface (GUI). J. Appl. Crystallogr. **1997**, *30*, 565–565. DOI: 10.1107/S0021889897003117.
56. Burnett, M. N.; Johnson, C. K. *Ortep-III, Report ORNL-6895*; Oak Ridge National Laboratory: Oak Ridge, TN, **1996**.
57. Bergerhof, G.; Berndt, M.; Brandenburg, K. Evaluation of Crystallographic Data with the Program DIAMOND. *J. Res. Natl. Stand. Technol.* **1996**, *101*, 221–225.
58. Hakimi, M.; Mardani, Z.; Moeini, K.; Schuh, E.; Mohr, F. Complexation to Cadmium(II) of a Tetradentate Ligand Resulting from the Condensation of 2-Pyridinecarbaldehyde with N-(2-Aminoethyl)Propane-1,3-Diamine. *ZNB* **2013**, *68*, 267–271. DOI: 10.5560/znb.2013-2294.
59. Marandi, F.; Moeini, K.; Rudbari Hadi, A. Sonochemical Synthesis and Characterization of Three Nano Zinc(II) Coordination Polymers; Precursors for Preparation of Zinc(II) Oxide Nanoparticles. *ZNB* **2016**, *71b*, 959–965.
60. Nakamoto, K. *Infrared and Raman Spectra of Inorganic and Coordination Compounds*, 6th ed.; John Wiley: Hoboken, **2009**; p 232.
61. Hakimi, M.; Moeini, K.; Mardani, Z.; Khorrami, F. Crystal Structure and Characterization of a New Eight Coordinated Cadmium Complex. *J. Korean Chem. Soc.* **2013**, *57*, 352–356. DOI: 10.5012/jkcs.2013.57.3.352.

62. Allen, F. H. The Cambridge Structural Database: A Quarter of a Million Crystal Structures and Rising. *Acta Crystallogr.* **2002**, *B58*, 380–388.
63. Ratilainen, J.; Airola, K.; Fröhlich, R.; Nieger, M.; Rissanen, K. Synthesis of a Tetradentate Piperazine Ligand and a Structural Study of Its Coordination Compounds. *Polyhedron* **1999**, *18*, 2265–2273. DOI: 10.1016/S0277-5387(99)00117-5.
64. Qiang, Z.; Zhi, S.; Hao, Y.; Hui-Zhen, S. Coordination Modes of Polypyridyl Quinoxaline with Hg(II), Pb(II), Co(II) and Mn(II). *Chinese J. Struct. Chem.* **2016**, *35*, 69–76.
65. Wang, S.; Westmoreland, T. D. Correlation of Relaxivity with Coordination Number in Six-, Seven-, and Eight-Coordinate Mn(II) Complexes of Pendant-Arm Cyclen Derivatives. Inorg. Chem. **2009**, *48*, 719–727. DOI: 10.1021/ic8003068.
66. Louloudi, M.; Nastopoulos, V.; Gourbatsis, S.; Perlepes, S. P.; Hadjiliadis, N. Eight-Coordination in Nitrato Manganese(II) Complexes with Tetradentate di-Schiff Bases Derived from 2-Pyridyl Ketones: Preparation, Characterization and Catalytic Activity for Alkene Epoxidation. *Inorg. Chem. Commun.* **1999**, *2*, 479–483. DOI: 10.1016/S1387-7003(99)00127-6.
67. Hwang, I. C.; Ha, K. Diacetato[N,N'-Bis-(2-Pyridylmethyl-Idene)Cyclo-Hexane-1,2-Diamine]Manganese(II) Hexa-Hydrate. *Acta Crystallogr.* **2008**, *E64*, m453.
68. Mikuriya, M.; Hatano, Y.; Asato, E. Variable Coordination Geometries in Manganese(II): Eight-, Seven-, and Six-Coordinate Mn(II) Complexes with Pyridyl-Containing Schiff-Base Ligands. *Chem. Lett.* **1996**, *25*, 849–850. DOI: 10.1246/cl.1996.849.
69. Baldeau, S. M.; Slinn, C. H.; Krebs, B.; Rompel, A. Rompel, A. Five Manganese(II) Complexes with Seven- or Eight-Coordinated Mn(II), Revealing Different Coordination Modes for the Nitrato Ligands. *Inorg. Chim. Acta* **2004**, *357*, 3295–3303. DOI: 10.1016/j.ica.2004.03.021.
70. Desiraju, G. R.; Steiner, T. *The Weak Hydrogen Bond: In Structural Chemistry and Biology*; Oxford University Press: Oxford, **2001**.
71. Hakimi, M.; Mardani, Z.; Moeini, K.; Mohr, F.; Fernandes, M. A. Palladium, Cadmium and Mercury Complexes of 2-((2-((2-Hydroxyethyl)Amino)Ethyl)Amino)Cyclohexanol: Synthesis, Structural, Spectral and Solution Studies. *Polyhedron* **2014**, *67*, 27–35. DOI: 10.1016/j.poly.2013.08.065.
72. Hakimi, M.; Moeini, K.; Mardani, Z.; Mohr, F. Microwave-Assisted Template Synthesis of Diazacyclam-Based Macrocyclic Copper Complex and Forming Octahedral, Square Planar and Square Pyramidal Geometries by Ion Exchanging and Introducing a Novel 2D Square-Grid Copper–Mercury Coordination Polymer. *Polyhedron* **2014**, *70*, 92–100. DOI: 10.1016/j.poly.2013.12.033.
73. Marandi, F.; Moeini, K.; Arkak, A.; Mardani, Z.; Krautscheid, H. Docking Studies to Evaluate the Biological Activities of the Co(II) and Ni(II) Complexes Containing the Triazine Unit: Supported by Structural, Spectral, and Theoretical Studies. *J. Coord. Chem.* **2018**, *71*, 3893–3911. DOI: 10.1080/00958972.2018.1543871.
74. Webpage, https://www.drugs.com/mtm/doxorubicin.html (accessed July 19, 2018).