Structure and Gas-Phase Stability of Zn(II)—Molecule Complexes

M. SMIEŠKO and M. REMKO*

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Comenius University, SK-832 32 Bratislava
e-mail: remko@fpharm.uniba.sk

Density Functional Theory method at the B3LYP level with large "triple zeta" 6-311+G(d,p) basis set was used to study structural and thermodynamic parameters of complexes of bivalent zinc cation with selected ligands acting as Lewis bases: H_2CS, HNO_2, H_2NCHS, CH_3XH, CH_3X, HCXXH, HCXX$^-$, imidazole, 1,3-oxazole, 1,3-thiazole, Y—PH(=O)O$^-$, Y—SHO$_2$ where X = O, S and Y = H, OH, NH$_2$. Ligands binding to zinc bivalent cation *via* sulfur atom, due to its "soft" (polarizable) character, generally showed higher interaction enthalpies in comparison with corresponding oxygen analogues with "hard" (less polarizable) character. This rule applies for both monodentate and bidentate ligands. Derivatives of phosphonic acid exhibit higher interaction enthalpies and lower entropies than structurally related derivatives of sulfonic acid. In the series of 5-membered heterocyclic ligands the interaction enthalpies and Gibbs energies decrease in the order imidazole, 1,3-thiazole, 1,3-oxazole.

Zinc bivalent cation plays an important role in the function of numerous metalloenzymes (*e.g.* angiotensin-converting enzyme, thermolysin). Due to its unique character – redox stability and variable coordination number allowing multiple geometry arrangements, which result from the special electron configuration (filled 3*d* orbital, vacant 4*s* orbital) – in the majority of these enzymes zinc cation Zn^{2+} is directly involved in the catalytic mechanism [1]. It has been shown that presence of a potent Zn^{2+}-binding functional group in the molecule of inhibitor may significantly influence the overall binding affinity to the enzyme active site (*e.g.* up to 60 % in human carboxylic anhydrase II inhibitors) [2]. However, well-balanced profile of other physicochemical properties, *e.g.* lipophilicity, dissociation constant and structural parameters, of inhibitor is required in order to achieve a good inhibition. The optimization of the zinc—ligand interaction from steric and electronic point of view is desirable, because it may lead to improving binding affinity of respective inhibitor. As direct experimental determination of thermodynamic parameters for these interactions is impossible, high-level *ab initio* theoretical methods can in principle provide a wealth of information inaccessible by current experimental techniques. Recently, there has been a growing interest in the theoretical modeling of the metal ions − Lewis base complexes [3]. In this area density functional theory methods have proved their usefulness and accuracy [4—15].

Most frequently occurring zinc-binding functional groups in the molecules of metalloenzyme inhibitors have been objects of several previous theoretical studies. Functional groups containing oxygen, nitrogen, and sulfur atoms binding directly to bivalent zinc cation were studied at the B3LYP/LANL2DZ level [16]. *Ab initio* and SIBFA (Sum of Interaction Between Fragments *ab initio* computed) methods were applied in study of bidentate zinc ligands based on α-sulfanylacylamides [17] and glycine [18]. Binding of hydroxamic acid derivatives to bivalent zinc cation was studied at B3LYP/6-311+G(2*d*,2*p*) level [19]. Recently, two-layer ONIOM method was used to characterize 46 gas-phase complexes of neutral and anionic ligands with Zn^{2+} [20]. Imidazole and imidazolate as natural ligands of bivalent zinc cation present in the active sites of metalloenzymes have been thoroughly studied at various levels of theory [21—23].

The main objective of this study was to investigate binding of monodentate and bidentate ligands isosteric to zinc-binding functional groups of presently used metalloproteinase inhibitors. Special attention was paid to structural and thermodynamic parameters of zinc—ligand complexes through theoretical modeling of such bonding.

COMPUTATIONAL DETAILS

The starting geometries of ligands and their respective complexes with bivalent zinc cation were built in the most stable conformation as shown in Formulae. All complexes were geometry-optimized with the

---

*The author to whom the correspondence should be addressed.

I   *II*   *III*   *IV*   *V*

VI   *VII*   *VIII*   *IX*   *X*

XI   *XII*   *XIII*   *XIV*   *XV*
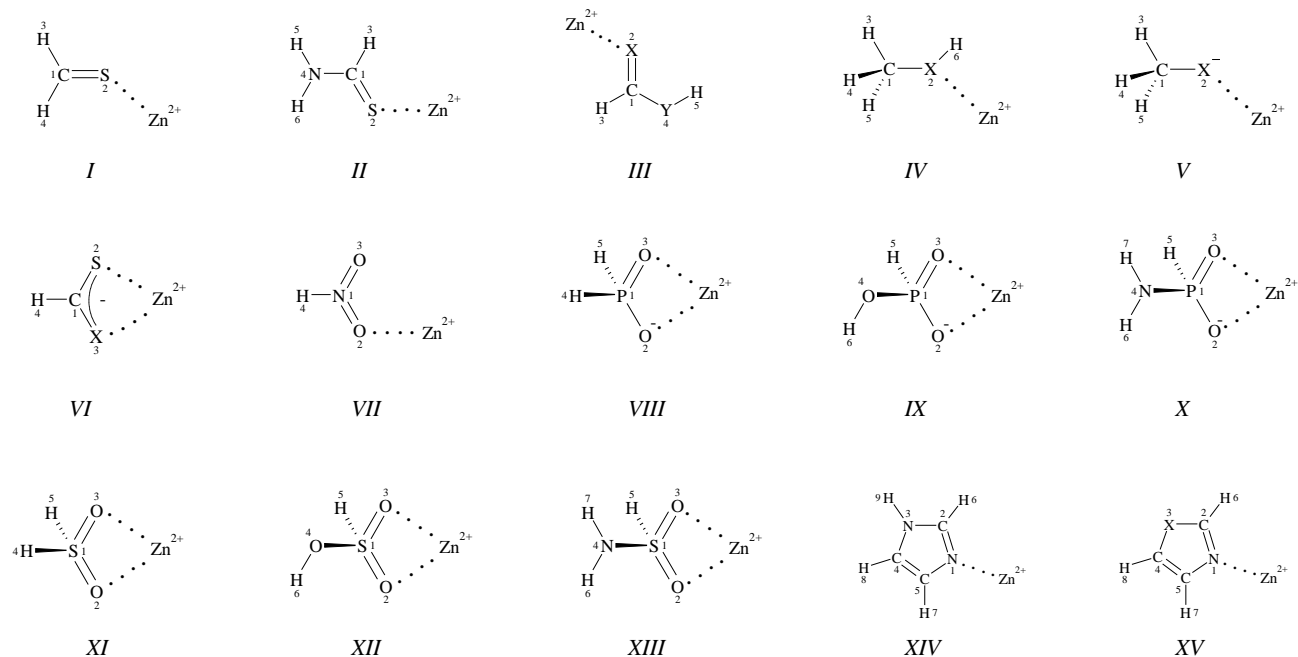
Formulae. Structural formulae of complexes studied with atom numbering (X, Y = S, O).

Gaussian 98 program [24] employing the Becke3LYP hybrid functional of the density functional theory [25—29] with the basis set as implemented in the Gaussian 98 package of computer codes [24]. For Zn we used the 6-311+G(d,p) Wachters—Hay [30, 31] all-electron basis set.

Formation of studied complexes can be described by the reaction

$$\mathrm{Zn}^{2+}(g) + \mathrm{L}(g) \longrightarrow \mathrm{Zn}^{2+}\cdots \mathrm{L}(g) \qquad (A)$$
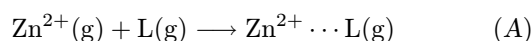
where L represents ligand part of the complex and $\mathrm{Zn}^{2+}\cdots\mathrm{L}$ represents final complex. The gas-phase interaction enthalpy ΔH for reaction (A) is defined by eqns (1—3). The calculations of enthalpies and Gibbs energies were performed at 298.15 K.

$$\Delta H^{\mathrm{o}} = \Delta E^{\mathrm{o}} + \Delta pV \qquad (1)$$
$$\Delta H^{\mathrm{o}} = \left[E^{\mathrm{o}}_{\mathrm{Zn}^{2+}\cdots\mathrm{L}} - \left(E^{\mathrm{o}}_{\mathrm{Zn}^{2+}} + E^{\mathrm{o}}_{\mathrm{L}} \right) \right] + \Delta pV \qquad (2)$$
$$\Delta H^{\mathrm{o}} = E^{\mathrm{o}}_{\mathrm{Zn}^{2+}\cdots\mathrm{L}} - E^{\mathrm{o}}_{\mathrm{Zn}^{2+}} - E^{\mathrm{o}}_{\mathrm{L}} - RT \qquad (3)$$

where $E^{\mathrm{o}}_{\mathrm{Zn}^{2+}\cdots\mathrm{L}}$ is energy of the complex, $E^{\mathrm{o}}_{\mathrm{Zn}^{2+}}$ is energy of bivalent zinc cation, and $E^{\mathrm{o}}_{\mathrm{L}}$ is energy of ligand at $T = 298.15$ K. In eqn (3) the term ΔpV is substituted with $-RT$, as one mole of gas is lost with the reaction (A).

RESULTS AND DISCUSSION

All molecular structures were first fully optimized at the B3LYP level of theory. At the optimized geometries, vibrational frequency calculations were performed to obtain the zero-point energy and to estimate the thermal corrections to the enthalpy, H

and entropy, S. An analysis of the harmonic vibrational frequencies of the optimized species revealed that all complexes are minima (no imaginary frequencies). The selected structural parameters of optimized ligands and complexes are summarized in Tables 1 and 2. The relative enthalpies and Gibbs energies of various isomeric complexes of the systems studied with respect to the most stable species are reported in Table 3. Both the neutral and deprotonated species were considered in several sets of complexes (Formulae).

Optimization of complexes *I* and *II* (for the denotation of complexes see Table 3) resulted in planar arrangement. In the complex *II*, which is more stable in *E*-arrangement, *i.e.* the dihedral angle $\phi[\mathrm{N}(4)$—C(1)—S(2)—$\mathrm{Zn}^{2+}] = 180°$, the electron-donating effect of NH_2 group causes increased negative charge on sulfur atom and the distance between Zn^{2+} and sulfur atom is by 0.011 nm shorter than in complex *I*. In both complexes *I* and *II* the bonding angle $\alpha(\mathrm{C}(1)$—S(2)—$\mathrm{Zn}^{2+})$ is far from linear (108.9° and 106.7°, respectively) and zinc atom is positioned in the direction of one of the sulfur lone pairs. In oxygen atom-containing complex *Va* with ligand $\mathrm{CH_3O^-}$ the distance between Zn^{2+} and oxygen atom is by 0.006 nm shorter than in complex *IVa* with ligand $\mathrm{CH_3OH}$. In the sulfur-containing complexes *Vb* with ligand $\mathrm{CH_3S^-}$ the distance between Zn^{2+} and oxygen atom is by 0.015 nm shorter than in complex *IVb* with ligand $\mathrm{CH_3SH}$. Planar arrangement was observed after optimization of sulfur analogue of formate anion $\mathrm{HC(=O)S^-}$ and in the complex *VIb* ($\mathrm{HC(=S)S^-}\cdots\mathrm{Zn}^{2+}$). Interestingly, planar complex *VII* with ligand $\mathrm{HNO_2}$, which is isosteric to formate anion, forms a monodentate complex with Zn^{2+} that is by 9.4 kJ mol^{-1} more stable

Table 1. Structural Parameters of Complexes with Bivalent Zinc Ion I—XIII ($d_i/10^{-10}$ m); $\alpha_i/°$; $\phi_i/°$)

Parameter	I	II	IIIa	IIIb	IIIc	IVa	IVb	Va	Vb	VIa	VIb	VII	VIII	IX	X	XI	XII	XIII
			X = O Y = S	X = S Y = O	X = S Y = S	X = O	X = S	X = O	X = S	X = O	X = S	X = S						
d[C(1)—X(2)]	1.631	1.743	1.295	1.723	1.713	1.570	1.860	1.428	1.838	1.731	1.692	1.306	1.581	1.579	1.583	1.518	1.515	1.524
d[C(1)—H(3)]	1.099	1.087	1.093	1.091	1.088	1.086	1.090	1.102	1.096	1.250	1.692	1.166	1.581	1.579	1.594	1.518	1.516	1.538
d[C(1)—H(4)]	1.090	1.290	1.671	1.262	1.665	1.087	1.088	1.091	1.087	1.098	1.094	1.058	1.405	1.570	1.624	1.380	1.531	1.575
d[C(1)—H(5)]						1.090	1.099	1.091	1.087				1.405	1.394	1.399	1.380	1.368	1.368
d[X(2)—H(6)]						0.978	1.366											
d[N(4)—H(5)]		1.022	1.363	0.984	1.364													
d[N(4)—H(6)]		1.022												0.968	1.012		0.987	1.025
d[N(4)—H(7)]															1.013			1.023
d[X(2)···Zn^{2+}]	2.372	2.262	1.856	2.290	2.286	1.864	2.346	1.801	2.196	2.295	2.337	1.899	1.944	1.939	1.939	2.058	2.039	2.041
d[X(3)···Zn^{2+}]										2.053	2.337	3.181	1.944	1.939	1.921	2.058	2.042	1.998
α[X(2)—C(1)—H(3)]	114.6	122.0	121.9	123.7	121.5	105.7	107.1	102.1	101.8	122.3	127.4	126.5	102.2	101.4	100.7	104.5	103.0	101.6
α[X(2)—C(1)—H(4)]	127.8	120.8		123.0	125.7	106.2	112.1	112.7	112.1	118.1	116.3	110.7	111.6	115.2	111.1	111.7	116.4	111.3
α[X(2)—C(1)—H(5)]						102.8	101.9	112.7	112.1				111.6	112.5	114.0	111.7	112.3	113.8
α[C(1)—N(4)—H(5)]	120.3		97.3	120.1	99.4													
α[C(1)—N(4)—H(6)]	124.0																	
α[Z(1)—N(4)—H(5)]														122.2	122.0		122.7	119.5
α[C(1)—N(4)—H(6)]															120.8			120.5
α[C(1)—X(2)—Zn^{2+}]	108.9	106.7	135.5	106.5	107.9	110.3	100.1	126.7	105.9	72.6	75.8	126.3	89.6	90.2	90.2	92.0	92.9	92.6
ϕ[H(3)—X(2)—C(1)—H(4)]	180.0	180.0	180.0	180.0	180.0	130.7	109.9	115.9	116.0	180.0	180.0	180.0						
ϕ[H(3)—X(2)—C(1)—H(5)]						121.9	125.6	-128.1	-128.1									
ϕ[H(3)—X(2)—C(1)—H(6)]						-117.6	-115.6	-128.1										
ϕ[H(5)—Y(4)—C(1)—H(3)]			180.0	180.0	180.0	161.8	-170.8											
ϕ[H(4)—C(1)—X(2)—H(6)]						-76.3	-45.3											
ϕ[H(5)—C(1)—X(2)—H(6)]						44.2	73.5											
ϕ[X(1)—N(4)—H(5)—H(6)]	180.0	180.0																
ϕ[O(2)—S(1)—N(4)—H(6)]														-58.6	38.5		-59.5	155.9
ϕ[O(2)—S(1)—N(4)—H(7)]															-158.9			-42.5
ϕ[H(3)—C(1)—X(2)—Zn^{2+}]	180.0	0.0	0.0	0.0	0.0	-33.2	-71.7	180.0	180.0	0.0	0.0	0.0	0.0	0.9	0.8	0.0	0.5	0.8

than the bidentate one. In complexes *VIII—XIII* with ligands derived from phosphonic and sulfonic acids Zn^{2+} is bound to the ligand bidentately and the dihedral angle $\phi[O(3)—Y(1)—O(2)—Zn^{2+}]$, Y = P, S, is close to $0°$. In the complexes *VIII, IX, XI,* and *XII* the interatomic distances between zinc and oxygen atom are almost equal, but in complexes *X* and *XIII* one distance is by 0.002 nm and 0.004 nm shorter than the other (Table 1). Sulfur-containing ligands HC(=X)Y, analogues of formic acid and their complexes with Zn^{2+}, have the planar arrangement. The ligand HC(=O)SH is by 18.0 kJ mol^{-1} more stable than tautomer HC(=S)OH. This can be explained by the fact that the "soft" polarizable sulfur atom of thiol group is a better donor of electrons than "hard" (less polarizable) oxygen atom of hydroxyl group. However, complex HC(SH)O$\cdots$$Zn^{2+}$ is by 44.4 kJ mol^{-1} less stable than complex HC(OH)S$\cdots$$Zn^{2+}$ showing that sulfur is a better zinc ligand than oxygen. In the series of 5-membered heterocyclic ligands, the shortest distance between dication of zinc atom and coordinating nitrogen atom $d[N(1)—Zn^{2+}] = 0.188$ nm was found for imidazole, which is due to its nonstrained ring geometry and highly delocalized system of π-electrons pushing the lone pair of coordinating nitrogen atom out of the molecule (Table 2). Respective oxygen- and sulfur-containing analogues of imidazole are less aromatic. 1,3-Oxazole contains a highly electronegative oxygen atom, which decreases beneficial π-electron delocalization and the sharp bonding angle of the sulfur atom in 1,3-thiazole$\cdots$$Zn^{2+}$, $\alpha[C(2)—S(3)—C(4)] = 91.3°$ in *XVb* and causes an excessive ring strain and hinders the delocalization.

The calculated interaction enthalpies $\Delta H°$, entropies $\Delta S°$, and Gibbs energies $\Delta G°$ are summarized in Table 3. For comparison thermodynamic data from similar study [10] are also included. The interaction enthalpies $\Delta H°$ of studied ligands with Zn^{2+} decrease in the order:

CH_3S^-, CH_3O^-, $HCSS^-$, $HCSO^-$, $H_2N—PH(=O)O^-$, $H_2P(=O)O^-$, HO—PH(=O)O$^-$, $H_2N—CHS$ (markedly), imidazole, HCSSH, 1,3-thiazole, 1,3-oxazole, HCSOH, $H_2N—SHO_2$, CH_3SH, H_2CS, HCOSH, H_2SO_2, HO—SHO_2, CH_3OH, HNO_2.

Generally, negatively charged ligands have much larger interaction enthalpies and Gibbs energies than respective neutral ligands due to the strong electrostatic interaction. However, the interaction enthalpy and Gibbs energy depend on the type of atom directly bound to Zn^{2+}, *e.g.* sulfur-containing ligands exhibit larger interaction enthalpies and Gibbs energies than their oxygen analogues. Tighter binding of sulfur-containing ligands in comparison to oxygen-containing ones is supported by more favourable entropic contribution. One exception are complexation entropies of ligands CH_3OH ($\Delta S° = -91.0$ J mol^{-1}

Table 2. Structural Parameters of Complexes with Bivalent Zinc Ion *XIV* and *XV* (Interatomic Distances $d_i/10^{-10}$ m); $\alpha_i/°$)

Parameter	*XIV* X = N	*XVa* X = O	*XVb* X = S
$d[N(1)—C(2)]$	1.357	1.338	1.344
$d[C(2)—N(3)]$	1.326	1.296	1.687
$d[N(3)—C(4)]$	1.383	1.379	1.734
$d[C(4)—C(5)]$	1.357	1.345	1.351
$d[C(5)—N(1)]$	1.407	1.420	1.405
$d[C(2)—H(6)]$	1.080	1.082	1.082
$d[N(3)—H(9)]$	1.019		
$d[C(5)—H(7)]$	1.078	1.079	1.081
$d[C(4)—H(8)]$	1.080	1.080	1.083
$d[N(1)\cdots Zn^{2+}]$	1.881	1.895	1.904
$\alpha[N(1)—C(2)—N(3)]$	107.5	110.1	112.0
$\alpha[C(2)—X(3)—C(4)]$	110.5	108.9	91.3
$\alpha[N(3)—C(4)—C(5)]$	106.9	108.2	111.3
$\alpha[C(4)—C(5)—N(1)]$	106.7	105.6	111.7
$\alpha[N(1)—C(2)—H(6)]$	127.2	129.6	125.1
$\alpha[N(1)—C(5)—H(7)]$	123.6	123.9	121.2
$\alpha[C(5)—C(4)—H(8)]$	130.4	134.7	127.9
$\alpha[C(2)—N(3)—H(9)]$	124.3		
$\alpha[C(2)—N(1)—Zn^{2+}]$	126.5	126.9	124.9
$\alpha[C(5)—N(1)—Zn^{2+}]$	125.1	125.9	121.4

K^{-1}) and CH_3SH ($\Delta S° = -98.4$ J mol^{-1} K^{-1}). The binding affinity of sulfur analogues of formic acid increases with the number of sulfur atoms in the molecule. Interaction enthalpy and Gibbs energy of ligand HCOSH binding to Zn^{2+} *via* oxygen atom is by 62.4 kJ mol^{-1} lower than of its tautomer HCSOH binding to Zn^{2+} *via* sulfur atom. Due to lower electronegativity of phosphorus, the derivatives of phosphonic acid show larger interaction enthalpies and Gibbs energies than respective derivatives of sulfonic acid, which allows better polarization of P—O bonds than of S—O ones. In both phosphonic and sulfonic acid derivatives amino substituent on central atom (phosphorus and sulfur) increases interaction enthalpy and Gibbs energy by positive mesomeric effect, while hydroxyl group withdraws electrons from central atom, which results in the decrease of interaction enthalpy and Gibbs energy. In the series of 5-membered heterocyclic ligands imidazole is the best Zn^{2+} ligand and the interaction enthalpy and Gibbs energy correlates with aromatic character of the ring system. Interaction enthalpy and Gibbs energy of ligand HNO_2, which is isosteric to formate anion, is rather weak ($\Delta H° = -457.2$ kJ mol^{-1} and $\Delta G° = -428.0$ kJ mol^{-1}), due to its neutral charge and higher electronegativity of nitrogen atom in comparison to carbon atom of formate.

Unfortunately, accurate experimental energetic values for zinc complexes of this ligand family are not available. However, when compared to experimental values, B3LYP level of theory provides excellent gas-phase basicities and metal affinities for organic

Table 3. Calculated Gas-Phase Enthalpies ΔH°, Entropies ΔS°, and Gibbs Energies ΔG° of the Zinc—Ligand Complexes Studied ($T = 298.15$ K)

Complex	Interaction	$\Delta H^\circ/(\text{kJ mol}^{-1})$	$\Delta S^\circ/(\text{J mol}^{-1}\,\text{K}^1)$	$\Delta G^\circ/(\text{kJ mol}^{-1})$
I	$H_2CS\cdots Zn^{2+}$	−611.8	−97.2	−582.8
II	$H_2NC(H){=}S\cdots Zn^{2+}$	−758.7	−96.5	−729.9
IIIa	$HC(SH){=}O\cdots Zn^{2+}$	−581.3	−102.1	−550.8
IIIb	$HC(OH){=}S\cdots Zn^{2+}$	−643.7	−96.3	−615.0
IIIc	$HC(SH){=}S\cdots Zn^{2+}$	−710.0	−96.0	−681.4
IVa	$CH_3OH\cdots Zn^{2+}$	−513.5	−91.0	−486.3
IVb	$CH_3SH\cdots Zn^{2+}$	−621.0	−98.4	−591.7
Va	$CH_3O^{(-)}\cdots Zn^{2+}$	−1812.7	−98.4	−1783.3
Vb	$CH_3S^{(-)}\cdots Zn^{2+}$	−1821.5	−94.0	−1793.5
VIa	$HCSO^{(-)}\cdots Zn^{2+}$	−1745.5	−110.7	−1712.5
VIb	$HCSS^{(-)}\cdots Zn^{2+}$	−1792.1	−111.7	−1758.8
VII	$HNO_2\cdots Zn^{2+}$	−457.2	−98.0	−428.0
VIII	$H_2PO_2\cdots Zn^{2+}$	−1716.6	−113.9	−1682.7
IX	$H_2PO_3\cdots Zn^{2+}$	−1697.7	−115.4	−1663.3
X	$H_2NHPO_2\cdots Zn^{2+}$	−1744.1	−111.5	−1710.9
XI	$H_2SO_2\cdots Zn^{2+}$	−561.5	−107.7	−529.4
XII	$H_2SO_3\cdots Zn^{2+}$	−560.0	−112.6	−526.5
XIII	$H_2NHSO_2\cdots Zn^{2+}$	−632.0	−110.9	−598.9
XIV	$Imidazole\cdots Zn^{2+}$	−753.9	−108.5	−721.6
XVa	$1,3\text{-Oxazole}\cdots Zn^{2+}$	−659.3	−98.4	−629.9
XVb	$1,3\text{-Thiazole}\cdots Zn^{2+}$	−707.6	−102.8	−676.9
XVI[a]	$H_2CO\cdots Zn^{2+}$	−485.3	−108.8	−452.7
XVII[a]	$H_2NCHO\cdots Zn^{2+}$	−646.0	−113.8	−612.1
XVIII[a]	$HCOOH\cdots Zn^{2+}$	−530.9	−110.0	−498.3
XIX[a]	$HCOO^{(-)}\cdots Zn^{2+}$	−1707.1	−114.2	−1673.2
XX[a]	$H_2O\cdots Zn^{2+}$	−433.5	−94.6	−405.4
XXI[a]	$H_2S\cdots Zn^{2+}$	−525.1	−96.7	−496.2
XXII[a]	$HO^{(-)}\cdots Zn^{2+}$	−1824.2	−97.1	−1795.4
XXIII[a]	$HS^{(-)}\cdots Zn^{2+}$	−1770.3	−86.2	−1744.7

a)Taken from Ref. [10].

compounds containing different groups [32, 33]. The Becke 3LYP DFT binding energies are comparable with those obtained at the correlated MP2 level [33] and are in good agreement with available experimental data [10, 33].

CONCLUSION

Ab initio DFT study of 21 biologically relevant ligands and their complexes with Zn^{2+} helped to assess relative trends of their gas-phase interaction enthalpies and Gibbs energies. The results show that the ligands binding to zinc atom *via* sulfur atom are able to form tighter interaction with Zn^{2+} due to "soft" (polarizable) character of sulfur atom in comparison to "hard" (less polarizable) character of oxygen analogues. The derivatives of phosphonic acid are better zinc ligands than respective sulfonic acid derivatives. The binding affinity of 5-membered heterocyclic ligands revealed a positive correlation between aromaticity and interaction enthalpy and Gibbs energy.

REFERENCES

1. McCall, K. A., Huang, C., and Fierke, C. A., *J. Nutr. 130*, 1437S (2000).
2. Kimura, E., *Acc. Chem. Res. 34*, 171 (2001).
3. Noodleman, L., Lovell, T., Han, W.-G., Li, J., and Himo, F., *Chem. Rev. 104*, 459 (2004).
4. Ryde, U., *Biophys. J. 77*, 2777 (1999).
5. Remko, M. and Rode, B. M., *Chem. Phys. Lett. 316*, 489 (2000).
6. Deerfield II, D. W., Carter, C. W., Jr., and Pedersen, L. G., *Int. J. Quantum Chem. 83*, 150 (2001).
7. Cheng, F., Zhang, R., Luo, X., Shen, J., Li, X., Gu, J., Zhu, W., Shen, J., Sagi, I., Ji, R., Chen, K., and Jiang, H., *J. Phys. Chem. B 106*, 4552 (2002).
8. Peschke, M., Blades, A. T., and Kebarle, P., *J. Am. Chem. Soc. 122*, 10440 (2000).
9. Diaz, N., Suarez, D., and Merz, K. M., Jr., *Chem. Phys. Lett. 326*, 288 (2000).
10. Remko, M. and Rode, B. M., *J. Mol. Struct. (Theochem) 505*, 269 (2000).
11. Dudev, T. and Lim, C., *J. Phys. Chem. B 105*, 4446 (2001).
12. Smith, G. D., Bell, R., Borodin, O., and Jaffe, R. L., *J. Phys. Chem. A 105*, 6506 (2001).
13. Remko, M. and Rode, B. M., *Phys. Chem. Chem. Phys. 3,* 4667 (2001).

14. Ai, H., Bu, Y., and Han, K., *J. Chem. Phys. 118,* 10973 (2003).
15. Remko, M. and Rode, B. M., *Struct. Chem. 15*, 223 (2004).
16. Cini, R., *J. Biomol. Struct. Dyn. 16*, 1225 (1999).
17. Tiraboschi, G., Fournié-Zaluski, M. C., Roques, B. P., and Gresh, N., *J. Comput. Chem. 22*, 1038 (2001).
18. Rogalewicz, F., Ohanessian, G., and Gresh, N., *J. Comput. Chem. 21*, 963 (2000).
19. Yazal, J. E. and Pang, Y. P., *J. Phys. Chem. B 104*, 6499 (2000).
20. Remko, M. and Garaj, V., *Mol. Phys. 101*, 2357 (2003).
21. Yazal, J. E. and Pang, Y. P., *J. Phys. Chem. B 103*, 8773 (1999).
22. Yazal, J. E., Roe, R. R., and Pang, Y. P., *J. Phys. Chem. B 104*, 6662 (2000).
23. Smieško, M. and Remko, M., *J. Biomol. Struct. Dyn. 20*, 759 (2003).
24. *Gaussian 98*, Revision A.11.4. Frisch, M. J., Trucks, G. W., Schlegel, H. B., Scuseria, G. E., Robb, M. A., Cheeseman, J. R., Zakrzewski, V. G., Montgomery, J. A., Jr., Stratmann, R. E., Burant, J. C., Dapprich, S., Millam, J. M., Daniels, A. D., Kudin, K. N., Strain, M. C., Farkas, O., Tomasi, J., Barone, V., Cossi, M., Cammi, R., Mennucci, B., Pomelli, C., Adamo, C., Clifford, S., Ochterski, J., Petersson, G. A., Ayala, P. Y., Cui, Q., Morokuma, K., Rega, N., Salvador, P., Dannenberg, J. J., Malick, D. K., Rabuck, A. D., Raghavachari, K., Foresman, J. B., Cioslowski, J., Ortiz, J. V., Baboul, A. G., Stefanov, B. B., Liu, G., Liashenko, A., Piskorz, P., Komaromi, I., Gomperts, R., Martin, R. L., Fox, D. J., Keith, T., Al-Laham, M. A., Peng, C. Y., Nanayakkara, A., Challacombe, M., Gill, P. M. W., Johnson, B., Chen, W., Wong, M. W., Andres, J. L., Gonzalez, C., Head-Gordon, M., Replogle, E. S., and Pople, J. A., Gaussian, Pittsburgh, PA, 2002.
25. Becke, A. D., *Phys. Rev. A 38*, 3098 (1988).
26. Becke, A. D., *J. Chem. Phys. 98*, 5648 (1993).
27. Lee, C., Yang, W., and Parr, R. G., *Phys. Rev. B 37*, 785 (1988).
28. Parr, R. G. and Yang, W., *Density-Functional Theory of Atoms and Molecules.* Oxford University Press, Oxford, 1989.
29. Neumann, R., Nobes, R. H., and Handy, N. C., *Mol. Phys. 87*, 1 (1996).
30. Wachters, A. J. H., *J. Chem. Phys. 52*, 1033 (1970).
31. Hay, P. J., *J. Chem. Phys. 66*, 4377 (1977).
32. Remko, M., *Chem. Pap. 52*, 637 (1998).
33. Remko, M., *Mol. Phys. 91*, 929 (1997).