

Ligand-Exchange Processes on Solvated Zinc Cations: Water Exchange on $[\text{Zn}(\text{H}_2\text{O})_4(\text{L})]^{2+} \cdot 2\text{H}_2\text{O}$ (L = Heterocyclic Ligand)

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Dedicated to Professor Paul von Ragué Schleyer on the occasion of his 80th birthday

Abstract: The water-exchange mechanisms of $[\text{Zn}(\text{H}_2\text{O})_4(\text{L})]^{2+} \cdot 2\text{H}_2\text{O}$ (L = imidazole, pyrazole, 1,2,4-triazole, pyridine, 4-cyanopyridine, 4-aminopyridine, 2-azaphosphole, 2-azafuran, 2-azathiophene, and 2-azaselenophene) have been investigated by DFT calculations (RB3LYP/6-311+G**). The results support limiting associative reaction pathways that involve the formation of six-coordinate intermediates $[\text{Zn}(\text{H}_2\text{O})_5(\text{L})]^{2+} \cdot \text{H}_2\text{O}$. The basicity of the coordinated heterocyclic ligands shows a good correlation with the activation barriers, structural parameters, and stability of the transition and intermediate states.

Keywords: density functional calculations • exchange interactions • reaction mechanisms • water chemistry • zinc

Introduction

Understanding the mechanisms of solvent-exchange reactions of metal ions in solution is essential for the understanding of the reactivity of metals ions in chemical and biological systems. Zinc is the second most abundant transition metal in living organisms and plays an important role in structural, catalytic, and enzymatic processes.^[1,2] Zinc enzymes are related to hormonal actions and brain pathologies, and are involved in synthetic, hydrolytic, hydration, and degradation processes.^[3,4,5]

The effect of the coordination of heteroaromatic ligands including nitrogen donors on water-exchange reactions of hydrated Zn^{II} is important for a better understanding of the

structure–reactivity correlation of the active site of a large number of zinc enzymes.^[6] Heterocyclic ligands occur in natural products, such as nucleic acids, plant alkaloids, vitamins, proteins, anthocyanins, flavones, heme pigments, and chlorophyll.^[7] Heterocyclic azoles are also known as building blocks of many antibiotics, anticancer agents, fungicides, and several other drugs.^[8,9]

A characteristic property of molecules with N donors is their gas-phase proton affinity, which is defined as the negative value of the enthalpy change for the reaction between a proton and the chemical species in the gas phase. Usually an electrically neutral species is investigated to form its conjugate acid.^[10] Ion-cyclotron resonance (ICR) spectroscopy and chemical ionization (CI) measurements are primary experimental methods used to measure the gas-phase proton affinity. These measurements are experimentally difficult to perform and to interpret.^[11] Modern computational methods can give very accurate values for the proton affinity of molecules.^[12]

The number of coordinated ligands around the Zn^{II} ion is variable. In both zinc-finger proteins and enzymes, zinc is usually tetrahedrally coordinated, but in some catalytic binding sites it is found to be pentacoordinate and rarely hexacoordinate.^[13,14] Hartmann et al.^[15] studied the water-exchange mechanism of $[\text{Zn}(\text{H}_2\text{O})_n]^{2+} \cdot m\text{H}_2\text{O}$ with $n = 3-6$ and $m = 0-2$, in which n and m represent the number of water molecules in the first and second coordination spheres, respectively. X-ray crystal analysis has revealed that Zn^{II} complexes with a chiral Schiff base can exist as five-coordinate

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Lewis acid–Lewis base complexes in the solid state.^[16] The presence of a vacant coordination site in Zn^{II} complexes is essential for catalytic processes with Lewis bases.^[17]

In terms of experimental mechanistic information on water-exchange reactions, the sign of the activation volume (ΔV^\ddagger) is considered as important evidence for the assignment of the underlying mechanism.^[18,19] A positive sign suggests that the exchange mechanism has a dissociative character, whereas associative reactions are characterized by negative activation volumes. Rotzinger^[20] suggested as a quantum-chemical descriptor for the activation volume that the sign of the change in the sum of all M–O bond lengths ($\Delta\Sigma$) during the activation process should agree with the sign of ΔV^\ddagger .

On the basis of structural and energetic data, the water-exchange mechanism for $[Zn(H_2O)_6]^{2+}$ was found to be a limiting dissociative (D) mechanism that involves the formation of a five-coordinate intermediate by using hybrid density functional theory (DFT, here B3LYP).^[21] The results are in good agreement with ab initio calculations and self-consistent reaction field methods.^[22] Recently we studied the exchange of HCN on $[Zn(HCN)_6]^{2+} \cdot HCN$ using density functional theory. The computed structural parameters and activation energies showed that the activation barrier of the dissociative mechanism (7 kcal mol⁻¹) is clearly more favorable than for the interchange mechanism (15.9 kcal mol⁻¹).^[23] HCN exchange also exhibits a D type mechanism as for water exchange in $[Zn(H_2O)_6]^{2+}$. The water-exchange mechanisms of $[Zn(H_2O)_4(L)]^{2+} \cdot 2H_2O$ (L = NH₃, CH₃NH₂, (CH₃)₂NH, and (CH₃)₃N) are characterized by a limiting associative (A) pathway that involves the formation of a six-coordinate intermediate, $[Zn(H_2O)_5(L)]^{2+} \cdot H_2O$.^[24]

The primary goal of the present work was to elucidate the water-exchange mechanisms of complexes of the type $[Zn(H_2O)_4(L)]^{2+} \cdot 2H_2O$ (L = imidazole, pyrazole, 1,2,4-triazole, pyridine, 4-cyanopyridine, 4-aminopyridine, 2-azaphosphole, 2-azafuran, 2-azathiophene, and 2-azaselenophene), and to gain more insight into the influence of the basicity of the heterocyclic ligands on the stability of the transition and intermediate states in terms of an associative exchange mechanism. In this respect, Morokuma, Marzilli, et al.^[25] were able to show by DFT calculations that addition of a Zn^{2+} ion to an imidazole molecule had a similar effect as protonation of the ligand's nitrogen donor, whereas at the same time the heterocycle lowered the charge on the Zn^{2+} ion more than water. We, therefore, wondered whether such effects can be correlated with well-defined physical properties, such as pK_{H^+} values or gas-phase proton affinities.

Quantum-chemical methods: Following the approach used by Hartmann et al.,^[21] and for comparability with recent studies on solvent exchange on Li^+ ,^[26] Be^{2+} ,^[27] and Al^{3+} ions,^[23,28] we fully optimized the structures at the RB3LYP/6-311+G** level of theory^[29] and evaluated the energy by RMP2(full)/6-311+G**//RB3LYP/6-311+G**.^[30] The influence of bulk solvent was probed by using the CPCM-formalism^[31] and water as solvent, that is, RB3LYP(CPCM)/6-

311+G**//RB3LYP/6-311+G**. The complexes were characterized as local minima or transition states by computation of vibrational frequencies (RB3LYP/6-311+G**). To obtain insight into the aromaticity of the ligands, nucleus-independent chemical shift (NICS) calculations^[32] were performed at the same level of theory (RB3LYP/6-311+G**//RB3LYP/6-311+G**). The Gaussian 03 suite of programs was used throughout.^[33]

Results and Discussion

Formation of $[Zn(H_2O)_4L]^{2+} \cdot 2H_2O$: As demonstrated earlier,^[24] Zn^{2+} prefers fivefold coordination in $[Zn(H_2O)_4(L)]^{2+}$, owing to the influence of the coordinated N-donor ligand, whereby the electronic and steric effects of the ligand have a significant influence on the stability of Zn^{2+} complexes.^[24] The reaction of NH₃ with $[Zn(H_2O)_6]^{2+}$ clearly favors the formation of $[Zn(H_2O)_4(NH_3)]^{2+} \cdot 2H_2O$ according to our earlier DFT calculations (RB3LYP/6-311+G**).^[24] To answer the question which is the most stable species in solution, we investigated by way of a typical example the reaction of 2-azafuran with $[Zn(H_2O)_6]^{2+}$. The rate constant for water exchange on $[Zn(H_2O)_6]^{2+}$ is about 10^7 s⁻¹,^[34] with the result that $[Zn(H_2O)_6]^{2+}$ exists in equilibrium with the almost isoenergetic $[Zn(H_2O)_5]^{2+} \cdot H_2O$ species on the basis of different DFT calculations.^[15,24] Figure 1 shows the relative stabilities of the different species that can be formed in the reaction of 2-azafuran with $[Zn(H_2O)_6]^{2+}$. Addition of one 2-azafuran molecule to $[Zn(H_2O)_6]^{2+}$ results in the for-

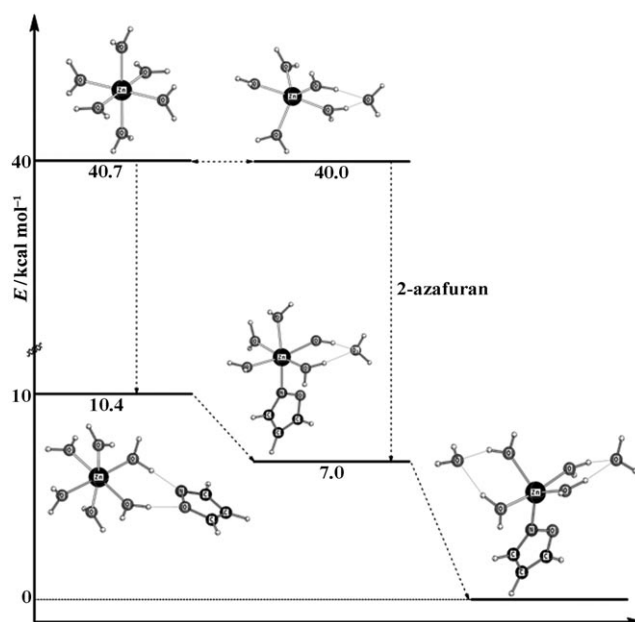


Figure 1. Schematic presentation of the calculated (RB3LYP/6-311+G**) energies of the different species formed in the reaction of 2-azafuran with $[Zn(H_2O)_6]^{2+}$ to form $[Zn(H_2O)_4(2\text{-azafuran})]^{2+} \cdot 2H_2O$ as the most stable species.

mation of the $\{[\text{Zn}(\text{H}_2\text{O})_6]^{2+} \cdot (2\text{-azafuran})\}$ adduct, which is $30.3 \text{ kcal mol}^{-1}$ more stable in energy. This energy difference is in good agreement with the addition of molecules (such as water) to form the second coordination sphere, and is surely somewhat exaggerated as compared to the case with included solvent in earlier work.^[24,27] The 2-azafuran ligand binds through two hydrogen bonds to two water molecules in the $\{[\text{Zn}(\text{H}_2\text{O})_6]^{2+} \cdot (2\text{-azafuran})\}$ complex. Rearrangement of $\{[\text{Zn}(\text{H}_2\text{O})_6]^{2+} \cdot (2\text{-azafuran})\}$ leads to $\{[\text{Zn}(\text{H}_2\text{O})_5(2\text{-azafuran})]^{2+} \cdot \text{H}_2\text{O}\}$ ($3.4 \text{ kcal mol}^{-1}$ more stable) and to the most stable complex $\{[\text{Zn}(\text{H}_2\text{O})_4(2\text{-azafuran})]^{2+} \cdot 2\text{H}_2\text{O}\}$ ($7.0 \text{ kcal mol}^{-1}$ more stable than $\{[\text{Zn}(\text{H}_2\text{O})_5(2\text{-azafuran})]^{2+} \cdot \text{H}_2\text{O}\}$) as shown in Figure 1.

Water-exchange mechanism of $[\text{Zn}(\text{H}_2\text{O})_4\text{L}]^{2+} \cdot 2\text{H}_2\text{O}$: The calculated (RB3LYP/6-311+G**) structures of $[\text{Zn}(\text{H}_2\text{O})_4(\text{L})]^{2+} \cdot 2\text{H}_2\text{O}$ (reactant/product A), $\{[\text{Zn}(\text{H}_2\text{O})_5(\text{L})]^{2+} \cdot \text{H}_2\text{O}\}^\ddagger$ (transition state B), and $[\text{Zn}(\text{H}_2\text{O})_5(\text{L})]^{2+} \cdot \text{H}_2\text{O}$ (intermediate C) are shown in Figure 2 for L=pyrazole (for L=imidazole, 1,2,4-triazole, pyridine, 4-cyanopyridine, 4-aminopyridine, 2-azaphosphole, 2-azafuran, 2-azathiophene, and 2-azaselenophene see Figures S1–S9 in the Supporting Information). The presented mechanisms all follow the same general reaction path. The reactant contains one heteroaromatic ligand (L) and four coordinated water molecules in the first coordination sphere and two water molecules in the second sphere bound through hydrogen bonding. One of the water molecules in the second coordination sphere moves toward the metal ion by breaking a hydrogen bond with one of the water molecules in the first coordination sphere to form a transition state typical for an associative reaction pathway $\{[\text{Zn}(\text{H}_2\text{O})_5(\text{L})]^{2+} \cdot \text{H}_2\text{O}\}^\ddagger$ (see Figure 2B). The intermediate is then formed by means of cleavage of the second already weakened hydrogen bond to form a stable six-coordinate complex, $[\text{Zn}(\text{H}_2\text{O})_5(\text{L})]^{2+} \cdot \text{H}_2\text{O}$ (see Figure 2C). Note that the six-coordinate intermediate is only a metastable species and will lose one coordinated water molecule via a transition state similar to the first to form the more stable five-coordinate complex, $[\text{Zn}(\text{H}_2\text{O})_4(\text{pyrazole})]^{2+} \cdot 2\text{H}_2\text{O}$ (see Figure 2A). The corresponding energy profiles are summarized in Figure 3.

The calculated energy values (B3LYP, MP2, and CPCM) of the transition and intermediate states for the water-exchange reaction of $[\text{Zn}(\text{H}_2\text{O})_4(\text{L})]^{2+} \cdot 2\text{H}_2\text{O}$ (L=imidazole, pyrazole, 1,2,4-triazole, pyridine, 4-cyanopyridine, 4-aminopyridine, 2-azaphosphole, 2-azafuran, 2-azathiophene, and 2-azaselenophene) are summarized in Table 1. The activation barriers to reach the transition state between the reactant and intermediate states are in all cases higher than the connected local minima. The calculated reaction energies (RB3LYP/6-311+G** + ZPE(RB3LYP/6-311+G**)) can be corroborated by MP2(full) energy calculations (MP2-(full)/6-311+G**//RB3LYP/6-311+G** + ZPE(RB3LYP/6-311+G**)), by which the well-documented energetic underestimation of transition states is shown.^[27,30,35]

Probing the solvent effects by CPCM single-point calculation (RB3LYP(CPCM:H₂O)/6-311+G**//RB3LYP/6-311+

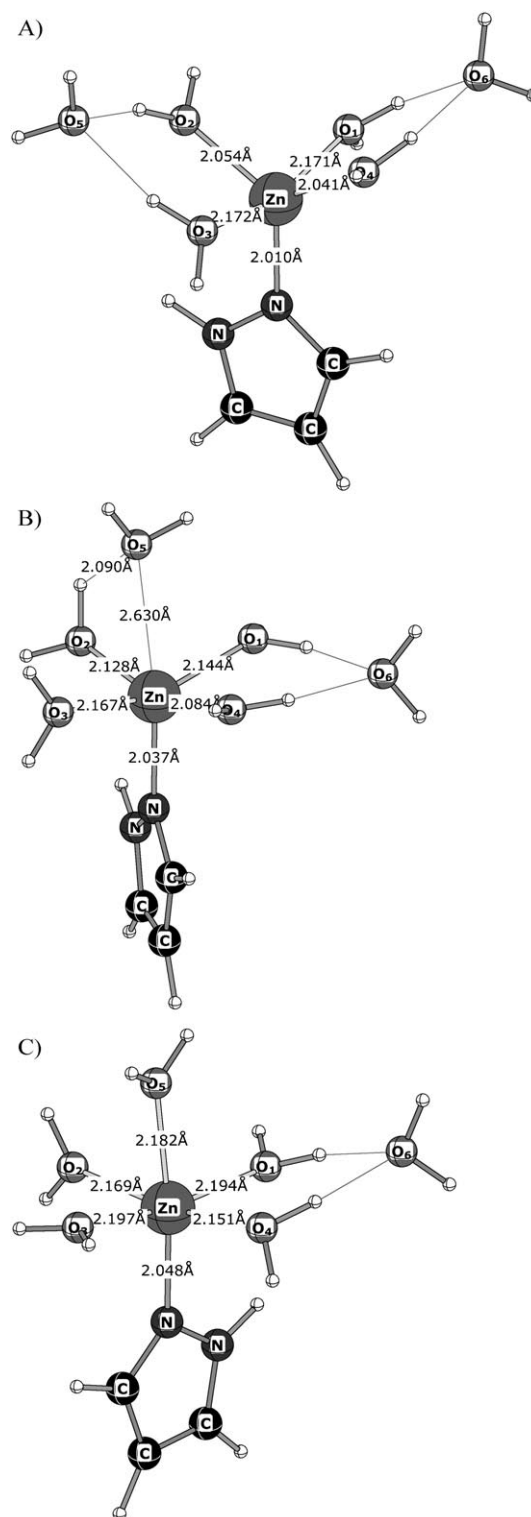


Figure 2. Calculated structures (RB3LYP/6-311+G**) of A) $[\text{Zn}(\text{H}_2\text{O})_4(\text{pyrazole})]^{2+} \cdot 2\text{H}_2\text{O}$, B) $\{[\text{Zn}(\text{H}_2\text{O})_5(\text{pyrazole})]^{2+} \cdot \text{H}_2\text{O}\}^\ddagger$, and C) $[\text{Zn}(\text{H}_2\text{O})_5(\text{pyrazole})]^{2+} \cdot \text{H}_2\text{O}$. Relative energies are presented in Figure 3 and Table 1.

G** + ZPE(RB3LYP/6-311+G**)), shows that the inclusion of solvent effects stabilizes the transition and intermediate states, and also lowers the activation barriers. The

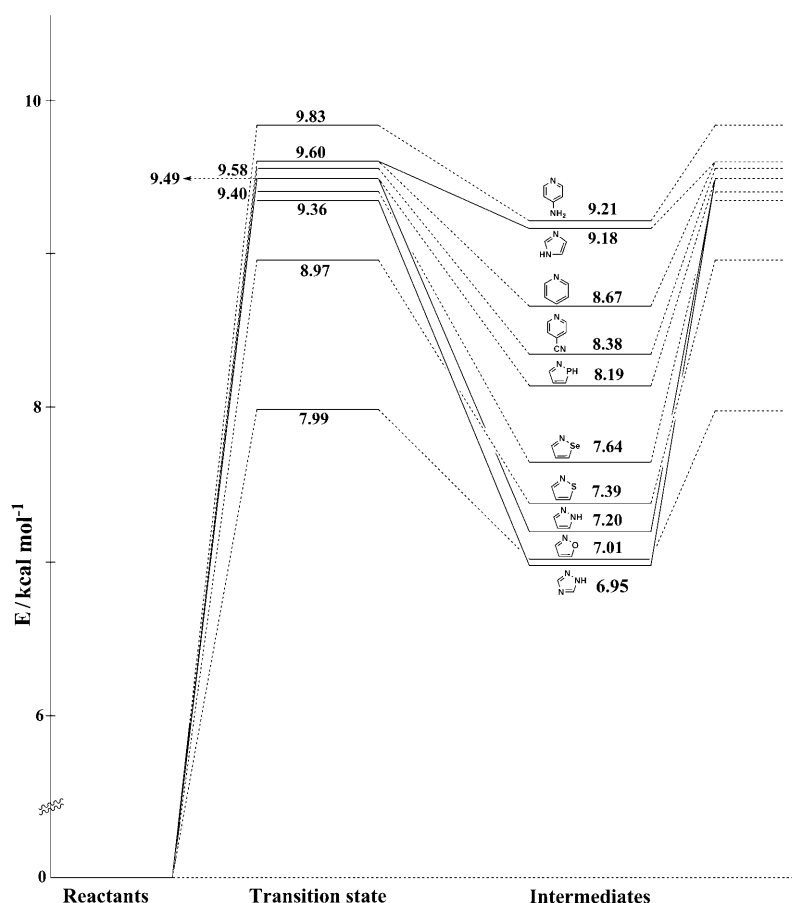


Figure 3. Calculated (RB3LYP/6-311 + G**) energy profile for water exchange on $[\text{Zn}(\text{H}_2\text{O})_4(\text{L})]^{2+} \cdot 2\text{H}_2\text{O}$ (L = imidazole, pyrazole, 1,2,4-triazole, pyridine, 4-cyanopyridine, 4-aminopyridine, 2-azaphosphole, 2-azafuran, 2-azathiophene, and 2-azaselenophene). Note that only the reaction up to the intermediate is presented and the symmetric loss of water from the first coordination sphere to complete the exchange process of the degenerated reaction is omitted for clarity.

Table 1. Calculated relative energies for water exchange on $[\text{Zn}(\text{H}_2\text{O})_4(\text{L})]^{2+} \cdot 2\text{H}_2\text{O}$.^[a]

Ligand	$\text{p}K_{\text{H}^+}$	Proton affinity [kcal mol ⁻¹]	ΔE (transition state) [kcal mol ⁻¹]			ΔE (intermediate) [kcal mol ⁻¹]		
			B3LYP	MP2	CPCM	B3LYP	MP2	CPCM
imidazole	6.95 ^[37]	224.6	9.60	6.57	2.46	9.18	5.13	0.44
pyrazole	2.48 ^[38]	213.1	9.49	6.62	2.95	7.20	3.19	-0.89
1,2,4-triazole	1.17 ^[39]	200.4	9.36	6.56	2.52	6.95	2.91	-1.47
4-aminopyridine	9.87 ^[40]	235.1	9.83	6.47	2.90	9.21	4.82	0.61
pyridine	5.25 ^[41]	221.9	9.60	6.48	2.28	8.67	4.34	-0.65
4-cyanopyridine	1.90 ^[42]	210.1	9.58	6.54	2.22	8.38	4.06	-1.33
2-azaphosphole	–	220.1	9.49	6.65	2.96	8.19	4.23	-0.7
2-azafuran	–	201.5	7.99	5.37	2.72	7.01	2.86	-1.83
2-azathiophene	–	210.6	8.97	6.13	2.38	7.39	3.58	-1.66
2-azaselenophene	–	214.6	9.40	6.33	2.49	7.64	3.76	-1.42

^[a] B3LYP: RB3LYP/6-311 + G**//RB3LYP/6-311 + G** + ZPE (RB3LYP/6-311 + G**); MP2: MP2(full)/6-311 + G**//RB3LYP/6-311 + G** + ZPE (RB3LYP/6-311 + G**); CPCM: RB3LYP(CPCM: H₂O)/6-311 + G**//RB3LYP/6-311 + G** + ZPE (RB3LYP/6-311 + G**).

extra stabilization of the solvent influence makes the intermediate, within the accuracy of the solvent method, energetically equal with the reactant. Along with the relatively low activation energies, we expect a fast water-exchange process following an associative mechanism, similar to that found

for sp^3 -hybridized ligands (L = NH_3 , NH_2CH_3 , $\text{NH}(\text{CH}_3)_2$, and $\text{N}(\text{CH}_3)_3$).^[24] In contrast, solvent exchange on $[\text{Zn}(\text{H}_2\text{O})_6]^{2+}$ ^[21] and $[\text{Zn}(\text{HCN})_6]^{2+} \cdot \text{HCN}$ ^[36] was found to follow a dissociative mechanism. These observations are in good agreement since dissociative and associative ligand-exchange processes are closely related and mainly controlled by the coordination number of the reactant state at the local energy minimum.

The water-exchange mechanism for the $[\text{Zn}(\text{H}_2\text{O})_4(\text{L})]^{2+} \cdot 2\text{H}_2\text{O}$ complexes shows an associative pathway, owing to the existing vacant coordination site on the metal ion. The Zn–O, Zn...OH₂^{second sphere}, and Zn–N bond lengths for the studied complexes and their sum are reported in Table 2. The elongation or compression of a given bond during the activation processes also affects the bond lengths of the other “spectator” ligands.^[20] Therefore, the changes in all the bond lengths, or their sum abbreviated by $\Delta\Sigma$ (Table 2), is a reasonable descriptor for the experimentally measurable volume of activation. The calculated negative values of $\Delta\Sigma$ for all investigated complexes clearly show compression during the reaction process and therefore verify the associative character of the water-exchange process.

Stability correlations: A very characteristic value for a basic molecule is the $\text{p}K_{\text{H}^+}$ value that characterizes the binding of a H^+ ion and is therefore related to the complexation of a metal ion. Experimental $\text{p}K_{\text{H}^+}$ data for some of the ligands are given in Table 1. A graphical correlation of the calculated activation energy and the stability of the intermediates with the $\text{p}K_{\text{H}^+}$ values leads to linear relationships on considering the ring size of the N-donor ligand (see Figure 4). The stabilization of the intermediate and transition states for five- and six-membered aromatic rings correlate with the basicity

Table 2. Selected structural parameters (RB3LYP/6-311+G**) for the $[\text{Zn}(\text{H}_2\text{O})_4(\text{L})]^{2+} \cdot 2\text{H}_2\text{O}$ and $[\text{Zn}(\text{H}_2\text{O})_5(\text{L})]^{2+} \cdot \text{H}_2\text{O}$ complexes. Values of r are given in [Å].

Ligand	$[\text{Zn}(\text{H}_2\text{O})_4(\text{L})]^{2+} \cdot 2\text{H}_2\text{O}$				$[\text{Zn}(\text{H}_2\text{O})_5(\text{L})]^{2+} \cdot \text{H}_2\text{O}$				$\Delta\Sigma = \Sigma r_2 - \Sigma r_1$ [Å]
	$r_1(\text{Zn}-\text{O})$	$r_1(\text{Zn}-\text{N})$	$r_1(\text{Zn}\cdots\text{O})$	Σr_1	$r_2(\text{Zn}-\text{O})$	$r_2(\text{Zn}-\text{N})$	$r_2(\text{Zn}\cdots\text{O})$	Σr_2	
imidazole	2.05, 2.05, 2.18, 2.18	2.00	3.96, 3.96	18.38	2.12, 2.11, 2.17, 2.14	2.03	3.94, 2.60	17.11	-1.27
pyrazole	2.04, 2.05, 2.17, 2.17	2.00	3.94, 3.95	18.32	2.08, 2.14, 2.13, 2.16	2.04	3.92, 2.63	17.08	-1.24
1,2,4-triazole	2.05, 2.04, 2.15, 2.20	2.02	3.96, 3.93	18.35	2.08, 2.11, 2.13, 2.16	2.06	3.92, 2.65	17.09	-1.26
4-aminopyridine	2.05, 2.05, 2.19, 2.19	1.99	3.97, 3.97	18.41	2.16, 2.11, 2.14, 2.18	2.03	3.94, 2.53	17.13	-1.28
pyridine	2.05, 2.05, 2.18, 2.18	2.02	3.95, 3.95	18.38	2.14, 2.12, 2.12, 2.17	2.06	3.93, 2.58	17.12	-1.26
4-cyanopyridine	2.05, 2.17, 2.05, 2.17	2.03	3.94, 3.94	18.35	2.14, 2.10, 2.12, 2.17	2.07	3.93, 2.60	17.13	-1.22
2-azaphosphole	2.18, 2.05, 2.18, 2.05	2.01	3.96, 3.96	18.39	2.11, 2.13, 2.12, 2.16	2.04	3.99, 2.67	17.22	-1.17
2-azafuran	2.13, 2.04, 2.15, 2.05	2.04	3.91, 3.93	18.25	2.14, 2.09, 2.10, 2.08	2.07	3.95, 2.75	17.18	-1.07
2-azathiophene	2.05, 2.04, 2.17, 2.05	2.02	3.94, 3.94	18.21	2.09, 2.13, 2.11, 2.16	2.05	3.94, 2.66	17.14	-1.07
2-azaselenophene	2.17, 2.05, 2.17, 2.05	2.01	3.95, 3.95	18.35	2.17, 2.10, 2.14, 2.12	2.05	3.94, 2.61	17.13	-1.22

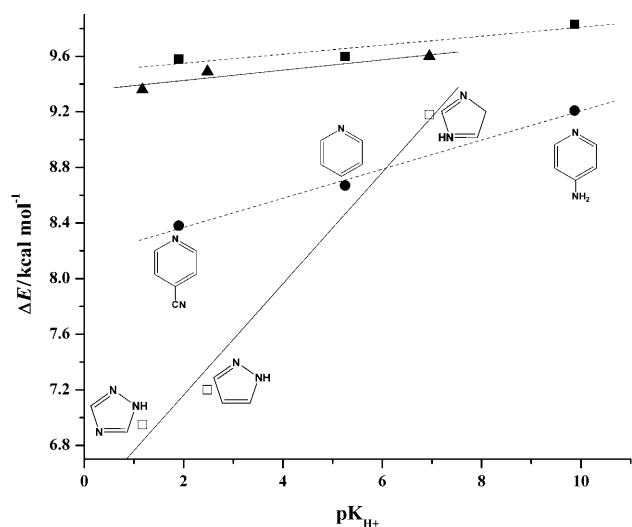


Figure 4. Correlation between the experimental $\text{p}K_{\text{H}^+}$ value and the calculated (RB3LYP/6-311+G**) activation energy, and energy gap between the reactant and intermediate states. ■: Transition state (six-membered ring), ●: intermediate (six-membered ring) ▲: transition state (five-membered ring), □: intermediate (five-membered ring).

of the N-donor atom. Strong bases end up in higher activation barriers and a smaller energy gap between the transition and intermediate states. This can easily be rationalized, as the higher basicity goes along with a better donor ability of the N atom and a decrease in the stability of the complex.

In computational chemistry the gas-phase proton affinity is a widely applied descriptor for the basicity of a molecule.^[43,44] Therefore, the proton affinity of imidazole, pyrazole, 1,2,4-triazole, pyridine, 4-cyanopyridine, 4-aminopyridine, 2-azaphosphole, 2-azafuran, 2-azathiophene, and 2-azaselenophene were calculated by (B3LYP/6-311+G**) to gain more information on the basicity of these ligands (see Table 1). As in the case of the experimental $\text{p}K_{\text{H}^+}$ values, a good correlation was obtained between the activation energy and the proton affinity, as well as between the energy gap between reactant and intermediate states and the calculated gas-phase proton affinity (see Figure 5). The calculated activation energy and the reactant-intermediate

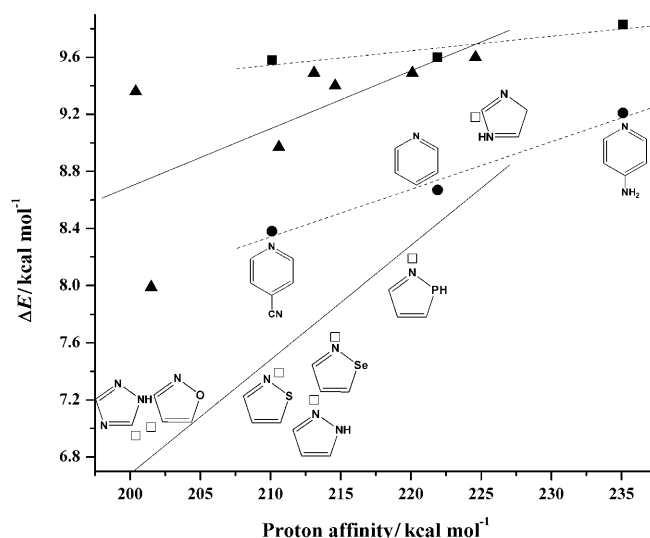


Figure 5. Correlation between the calculated (RB3LYP/6-311+G**) proton affinity and the calculated (RB3LYP/6-311+G**) activation energy, and energy gap between the reactant and intermediate states. ■: Transition state (six-membered ring), ●: intermediate (six-membered ring) ▲: transition state (five-membered ring), □: intermediate (five-membered ring)

energy gap are higher in the case of six-membered rings (Figures 4 and 5). This is attributed mainly to steric effects.

Increasing the basicity is associated with increasing the ability for σ donation and decreasing the ability for the aromatic ligands to function as π acceptors.^[45] Therefore, the intermediate of $[\text{Zn}(\text{H}_2\text{O})_5(\text{L})]^{2+} \cdot \text{H}_2\text{O}$ in the case of 1,2,4-triazole is more stable than in the case of 4-aminopyridine, as 4-aminopyridine is more basic ($\text{p}K_{\text{H}^+} = 9.87$) and a worse π acceptor than 1,2,4-triazole ($\text{p}K_{\text{H}^+} = 1.17$). The NH_2 group on the pyridine ring has an electronic donor ability in the case of 4-aminopyridine, whereas in contrast the cyano group is electron withdrawing in the case of 4-cyanopyridine. The substituent on the pyridine ligand plays a very important role in terms of the basicity of the ligand. Interestingly, in the case of the nitrogen heterocyclic ligands of five-membered rings, we found that the basicity of the ligand decreases with increasing electronegativity of the atom directly bound to the nitrogen donor. 1,2,4-triazole and 2-azafuran

have a lower basicity, owing to the presence of nitrogen and oxygen in the direct neighborhood.

The electron density on the central metal plays a significant role in the energy difference between the transition and intermediate states in the water-exchange mechanism. In this respect, it is instructive to compare the data of the present study on heterocyclic ligands with our earlier work on alkyl amine ligands.^[24] Whereas in the case of the alkyl amine ligands (formal sp^3 -hybridized N donors) the transition state-intermediate energy difference is between 0.1 and 1.4 kcal mol⁻¹,^[24] it is between 0.4 and 2.4 kcal mol⁻¹ in the case of formally sp^2 -hybridized N-donor heterocyclic aromatic ligands. We attribute this difference to the improved stabilization of the intermediates by π -acceptor ligands (hetero aromatic ligands) than by purely σ -donor ligands such as the alkyl amines.

The calculated (B3LYP/6-311+G**) structural parameters of the reactants $[Zn(H_2O)_5(L)]^{2+}$ and $[Zn(H_2O)_4(L)]^{2+} \cdot 2H_2O$, the transition states $\{[Zn(H_2O)_5(L)]^{2+} \cdot H_2O\}^\ddagger$ and the intermediates $[Zn(H_2O)_5(L)]^{2+} \cdot H_2O$ are depicted in Figures 2, 6, and S1–S11 (see the Supporting Information) and summarized in Table 3. The calculated structural data of

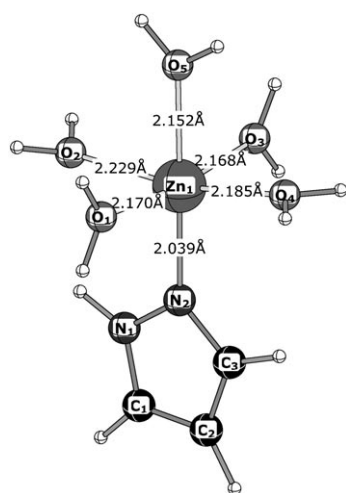


Figure 6. Calculated structure (RB3LYP/6-311+G**) of $[Zn(H_2O)_5-(pyrazole)]^{2+}$.

Table 3. Bond lengths and angles in the calculated structures (RB3LYP/6-311+G**) of $[Zn(H_2O)_5(L)]^{2+}$, $[Zn(H_2O)_4(L)]^{2+} \cdot 2H_2O$, $\{[Zn(H_2O)_5(L)]^{2+} \cdot H_2O\}^\ddagger$, and $[Zn(H_2O)_5(L)]^{2+} \cdot H_2O$.

Ligand	$[Zn(H_2O)_5(L)]^{2+}$ PG = C_7		$[Zn(H_2O)_4(L)]^{2+} \cdot 2H_2O$ PG = C_7		$Zn \cdots O_{axial}$ [Å]	$\{[Zn(H_2O)_5(L)]^{2+} \cdot H_2O\}^\ddagger$ PG = C_7			$[Zn(H_2O)_5(L) \cdot H_2O]^{2+}$ PG = C_7	
	$Zn-O_{axial}$ [Å]	O1-Zn-O3 [°]	$Zn \cdots OH_2$ second sphere [Å]	O2-Zn-O4 [°]		$Zn-O_{equatorial}$ [Å]	$d(O2 \cdots O5)$ [Å]	O2-Zn-O4 [°]	$Zn-O_{axial}$ [Å]	O2-Zn-O4 [°]
imidazole	2.16	164.6	3.96	119.5	2.60	2.12	3.15	159.3	2.19	161.3
pyrazole	2.15	169.1	3.94	121.9	2.63	2.13	3.14	159.9	2.18	167.8
1,2,4-triazole	2.15	171.1	3.93	115.2	2.65	2.11	3.13	159.7	2.18	169.8
4-aminopyridine	2.16	159.9	3.97	118.7	2.53	2.14	3.17	158.4	2.18	163.3
pyridine	2.17	162.1	3.95	120.9	2.58	2.12	3.15	156.3	2.18	162.6
4-cyanopyridine	2.16	163.5	3.94	122.1	2.60	2.12	3.15	158.6	2.18	164.1
2-azaphosphole	2.16	164.4	3.96	118.8	2.67	2.12	3.15	157.7	2.18	164.3
2-azafuran	2.15	168.9	3.91	116.1	2.75	2.08	3.17	163.5	2.18	168.3
2-azathiophene	2.16	166.1	3.94	120.7	2.66	2.11	3.15	155.5	2.18	165.4
2-azaselenophene	2.16	165.9	3.95	120.6	2.61	2.12	3.16	158.4	2.18	165.4

$[Zn(H_2O)_4(L)]^{2+} \cdot 2H_2O$ clearly show that there is an influence of the ligand basicity on the structures, for example, the distance between the central Zn^{2+} ion and the water molecule in the second coordination sphere depends on the basicity of the coordinated ligand L.

Figure 7 and Figure S12 in the Supporting Information report correlations between the distance between the Zn^{2+} ion and the equatorial water molecule in the second coordination sphere and the proton affinities for different N-donor ligands and the experimental pK_{H^+} values, respectively (see Tables 1 and 3). The good correlation between the ligand basicity and the distance between the central Zn^{2+} ion and the water molecule in the second coordination sphere suggests that the transfer rate of the water molecule from the second to the first coordination sphere increases on increasing the basicity of the coordinated heterocyclic ligand. On passing through the typical transition state for a limiting associative mechanism, the distance between the zinc ion and the water molecule in the second coordination sphere ($Zn \cdots OH_2$) is shortened by (1.16, 1.44 Å) from (3.91, 3.97 Å)

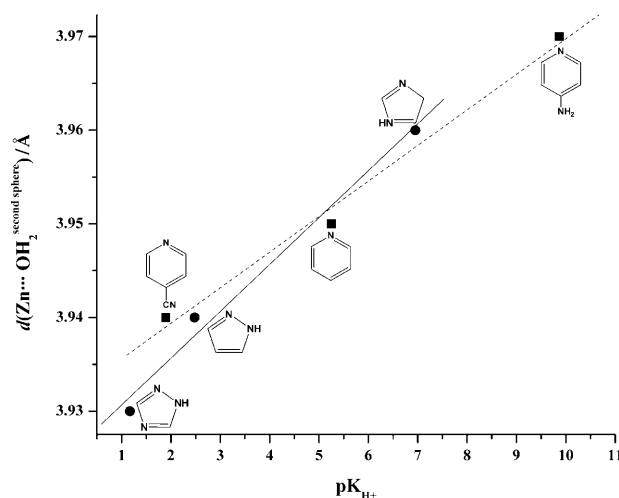


Figure 7. Correlation between the experimental pK_{H^+} value and the distance between the Zn^{2+} ion and the water molecule in the second coordination sphere $[Zn(H_2O)_4(L)]^{2+} \cdot 2H_2O$. ●: five-membered ring, ■: six-membered ring.

in $[\text{Zn}(\text{H}_2\text{O})_4(\text{L})]^{2+} \cdot 2\text{H}_2\text{O}$ to (2.75, 2.53 Å) in $\{[\text{Zn}(\text{H}_2\text{O})_5(\text{L})]^{2+} \cdot \text{H}_2\text{O}\}^\ddagger$ for $\text{L} = 2\text{-azafuran}$ and 4-aminopyridine , respectively.

Interestingly, the bond lengths $\text{Zn}\cdots\text{O}^{\text{axial}}$ and $\text{Zn}-\text{N}^{\text{axial}}$ (Å) in the transition state go along with the basicity, that is, a clear sign for the dependence on the electronic density on the central Zn^{2+} ion. In Figure 8 and Figure S13 in the Supporting Information, the calculated bond lengths $\text{Zn}\cdots\text{O}^{\text{axial}}$

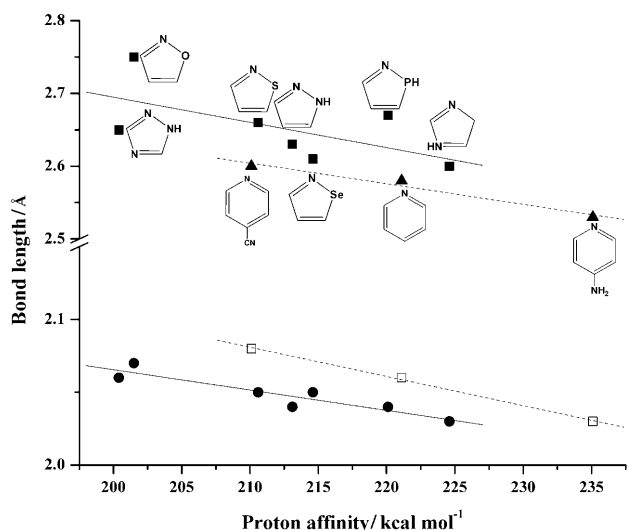


Figure 8. Correlation between the calculated (RB3LYP/6-311+G**) $\text{Zn}-\text{L}$ bond length in $\{[\text{Zn}(\text{H}_2\text{O})_5(\text{L})\cdot\text{H}_2\text{O}]^{2+}\}^\ddagger$ and the calculated (RB3LYP/6-311+G**) proton affinity. ■: $\text{Zn}\cdots\text{O}^{\text{axial}}$ (five-membered ring), ●: $\text{Zn}-\text{N}$ (five-membered ring), ▲: $\text{Zn}\cdots\text{O}^{\text{axial}}$ (six-membered ring), □: $\text{Zn}-\text{N}$ (six-membered ring).

and $\text{Zn}-\text{N}^{\text{axial}}$ are plotted as a function of the basicity of the coordinated ligands (L). A shortening of the $\text{Zn}\cdots\text{O}^{\text{axial}}$ and $\text{Zn}-\text{N}^{\text{axial}}$ bond lengths on increasing the basicity is clearly observed. This, however, can be attributed to the electronic repulsion effect for the shortening of the $\text{Zn}\cdots\text{O}^{\text{axial}}$ bond length, that is, the more basic ligand is a better σ donor and increases the electron density on the central Zn^{2+} ion. Owing to the electronic repulsion effect, the $\text{Zn}-\text{O}$ bond length and the distance between the equatorial water molecules are elongated (Table 3) in the first coordination sphere; therefore the entering water molecule faces weaker repulsion by the water molecules in the first sphere in the case of a higher-ligand basicity. The attraction of the coordinated ligands to the divalent central ion increases by increasing their basicity and this causes shortening of $\text{Zn}-\text{N}^{\text{axial}}$ bond. The $\text{O}1-\text{Zn}-\text{O}3$ angle in $[\text{Zn}(\text{H}_2\text{O})_5(\text{L})]^{2+}$ decreases on increasing the basicity of the coordinated ligand (see Figures 6, 9, and S10, S11, and S14 in the Supporting Information, as well as Table 3) according to the electronic repulsion.

Schleyer's nucleus independent chemical shifts (NICS) have become the most widely used aromaticity probe, owing to their simplicity and efficiency.^[32] NICS is typically computed at ring centers (non-weighted mean of the heavy

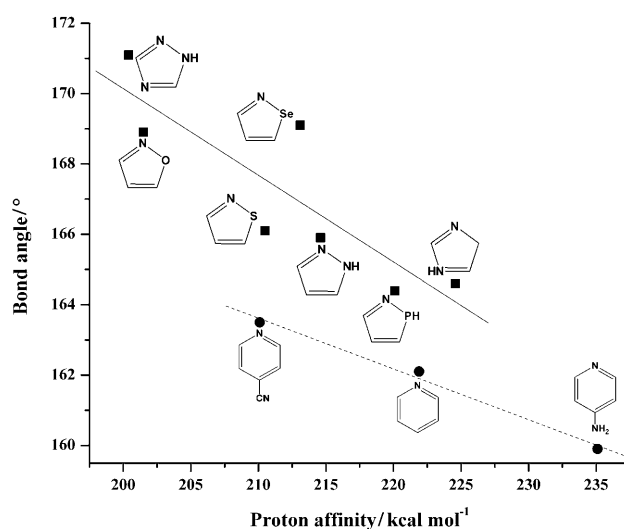


Figure 9. Correlation between the calculated (RB3LYP/6-311+G**) bond angles of $[\text{Zn}(\text{H}_2\text{O})_5(\text{L})]^{2+}$ and the proton affinity. ■: $\text{O}1-\text{Zn}-\text{O}3$ (five-membered ring), ●: $\text{O}1-\text{Zn}-\text{O}3$ (six-membered ring).

atoms) and 1 Å perpendicular to the ring's plain.^[46] Exemplarily testing of the pyrazole and pyridine ligands' aromaticity by NICS calculations showed nearly no change throughout the reaction (reactant, transition, and intermediate states), indicating that the aromaticity of the ligand is not affected by the ligand exchange reaction on the coordinated zinc ion (Table 4). Comparison with literature values shows that NICS(1) values, considered not to be influenced by σ -donor effects,^[32b] show nearly the same values as for the protonated ligands. The observation that complexation with closed shell metal ions does not influence the NICS values is in accordance with earlier observations.^[27d,47]

Table 4. NICS_(total) (RB3LYP/6-311+G**) values for L, LH^+ , $[\text{Zn}(\text{H}_2\text{O})_4(\text{L})]^{2+} \cdot 2\text{H}_2\text{O}$, $\{[\text{Zn}(\text{H}_2\text{O})_5(\text{L})]^{2+} \cdot \text{H}_2\text{O}\}^\ddagger$, and $[\text{Zn}(\text{H}_2\text{O})_5(\text{L})\cdot\text{H}_2\text{O}]^{2+}$ (L = pyridine and pyrazole).

Compound	NICS(0) _(total)	NICS(1) _(total)
pyridine ($\text{C}_5\text{H}_5\text{N}$) ^[46]	-6.82	-10.17
protonated pyridine ($\text{C}_5\text{H}_6\text{NH}$) ^[46]	-7.75	-9.89
$[\text{Zn}(\text{H}_2\text{O})_4(\text{pyridine})]^{2+} \cdot 2\text{H}_2\text{O}$	-7.09	-9.86
$\{[\text{Zn}(\text{H}_2\text{O})_5(\text{pyridine})\cdot\text{H}_2\text{O}]^{2+}\}^\ddagger$	-6.97	-9.89
$[\text{Zn}(\text{H}_2\text{O})_5(\text{pyridine})]^{2+} \cdot \text{H}_2\text{O}$	-7.13	-9.94
pyrazole ($\text{C}_3\text{H}_4\text{N}_2$) ^[46]	-13.61	-10.09
protonated pyrazole ($\text{C}_3\text{H}_4\text{N}_2\text{H}$) ⁺	-14.57	-10.75
$[\text{Zn}(\text{H}_2\text{O})_4(\text{pyrazole})]^{2+} \cdot 2\text{H}_2\text{O}$	-13.93	-10.99
$\{[\text{Zn}(\text{H}_2\text{O})_5(\text{pyrazole})\cdot\text{H}_2\text{O}]^{2+}\}^\ddagger$	-13.71	-10.95
$[\text{Zn}(\text{H}_2\text{O})_5(\text{pyrazole})]^{2+} \cdot \text{H}_2\text{O}$	-13.62	-10.93

Conclusion

On the basis of quantum-chemical calculations we showed that the water-exchange reaction on $[\text{Zn}(\text{H}_2\text{O})_4(\text{L})]^{2+} \cdot 2\text{H}_2\text{O}$ (L = imidazole, pyrazole, 1,2,4-triazole, 4-aminopyridine, pyridine, 4-cyanopyridine 2-azaphosphole, 2-azafuran, 2-azathiophene, and 2-azaselenophene) follows an associative

mechanism, as a result of the vacant coordination site on the five-coordinate Zn^{2+} ion. The negative values of $\Delta\Sigma$ (Table 2) show a compression during the reaction process, verifying an associative mechanism. The activation barriers and structural parameters depend on the basicity and steric effects of the coordinated heterocyclic ligands. The stabilization of the intermediate and transition states decreases on increasing the basicity and the size of the heterocyclic ligands as a result of steric effect. The good correlation found between the ligand basicity and the distance between the central metal atom and the water molecule in the second coordination sphere, suggests that the transfer rate of the water molecule from the second to the first coordination sphere increases by increasing the basicity of the coordinated heterocyclic ligand. The shortening of the $Zn\cdots O^{axial}$ and $Zn-N^{axial}$ bond lengths on increasing the basicity can be attributed to the electronic repulsion effect in the case of $Zn\cdots O^{axial}$ and increasing the attraction of the ligand to the central ion in the case of $Zn-N^{axial}$. A test on the aromaticity of the pyrazole and pyridine ligands by NICS calculations showed nearly no change throughout the reaction (reactant, transition, and intermediate states), indicating that the aromaticity of the ligand is not affected by coordination to divalent zinc ion.

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