EurJIC
European Journal of Inorganic Chemistry

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Zinc(II) Complexes of N,N-Di(2-picolyl)hydrazones

Authors: David Barsoum; Lawrence Kyeremeh-Mensah; Quinton Meisner; Ronald Clark; Eric Masson; Lei Zhu

To be cited as: Eur. J. Inorg. Chem. 10.1002/ejic.201601066

Link to VoR: http://dx.doi.org/10.1002/ejic.201601066

WILEY-VCH

Zinc(II) Complexes of *N*,*N*-Di(2-picolyl)hydrazones

David N. Barsoum,[a] Lawrence Kyeremeh-Mensah,[b] Quinton J. Meisner,[a] Ronald J. Clark,[a] Eric Masson,[b,*] Lei Zhu[a,*]

a. Department of Chemistry and Biochemistry, Florida State University, 95 Chieftan Way, Tallahassee, FL 32306-4390. Email: lzhu@chem.fsu.edu; URL: http://chem.fsu.edu/zhu

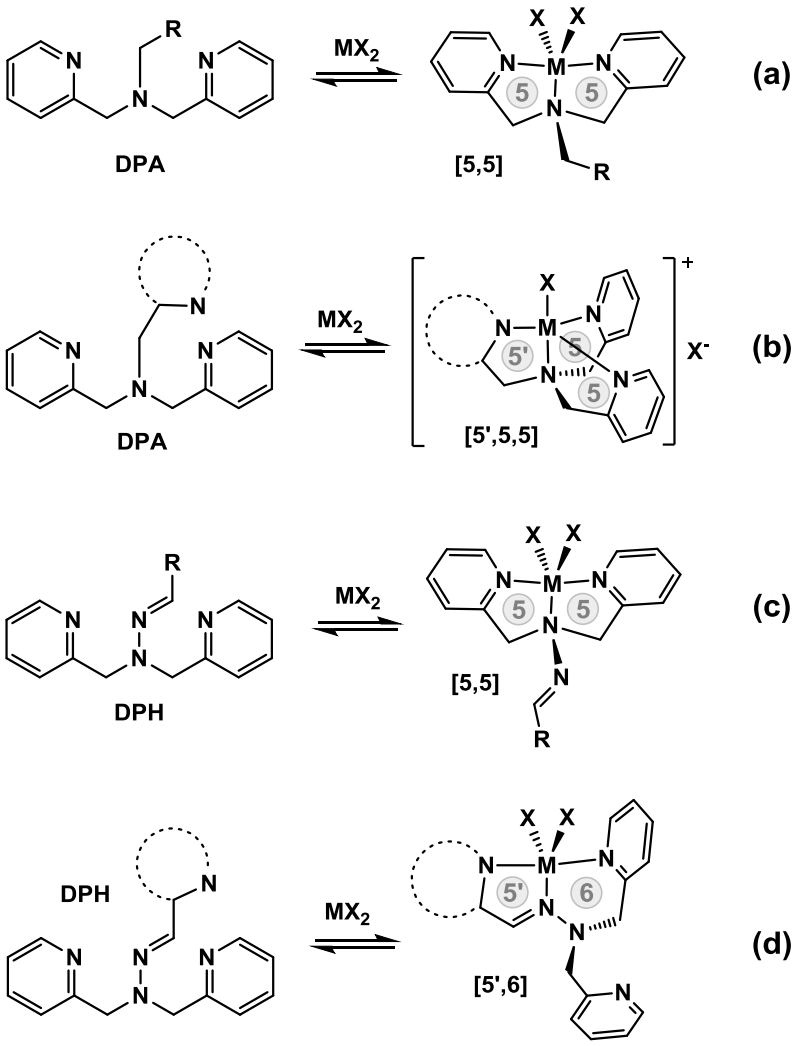
b. Department of Chemistry and Biochemistry, Ohio University, Athens, Ohio 45701. Email: masson@ohio.edu; URL: http://www.phy.ohiou.edu/~eric/Masson_group/

Abstract. We report *N*,*N*-di(2-picolyl)hydrazone (DPH) ligands that are capable of binding metal ions in two isomeric forms depending on the nature of the hydrazone substituent. When the hydrazone substituent is not coordinating, the metal ion prefers the *N*,*N*-di(2-picolyl)amino (DPA) site, which is a known tridentate ligand that anchors on the sp^3-hybridized amino nitrogen. When the hydrazone substituent is coordinating, the metal ion instead anchors on the sp^2-hybridized imino nitrogen to afford a different structural isomer. Zinc(II) is used as a representative transition metal ion for characterizing the coordination chemistry of DPH in both solution and solid states.

Key words. Zinc, hydrazone, di(2-picolyl)hydrazone, DPH

Introduction

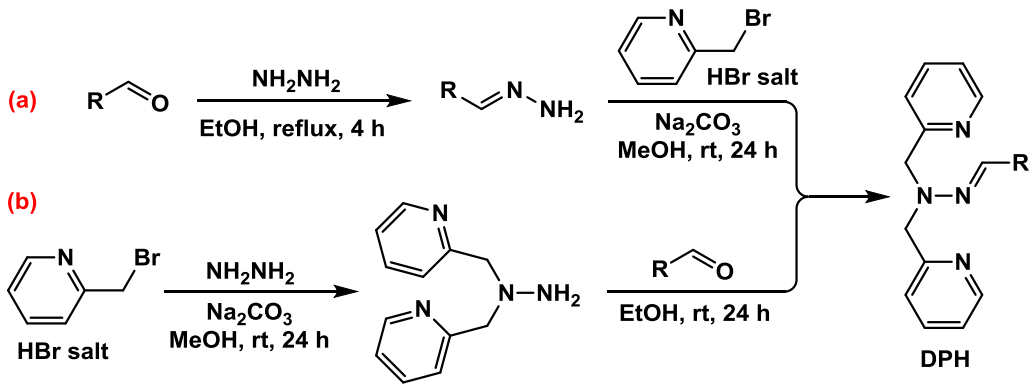
N,*N*-Di(2-picolyl)amines (DPAs, Scheme 1a) are frequently used tridentate ligands in coordination chemistry.[1] DPA forms metal complexes that contain two 5-membered chelate rings (designated as the [5,5] isomer in Scheme 1a). When the amino nitrogen is alkylated with an ancillary ligand, the overall ligand may become tetradentate to afford a complex of [n',5,5] coordination mode (n = 5 in Scheme 1b; The "prime" refers to the chelate ring involving the ancillary ligand, the numbers without prime are the sizes of chelate rings involving the pyridyl groups on the DPA portion).[2] In this work, we introduce *N*,*N*-di(2-picolyl)hydrazone (DPH, Scheme 1c), a ligand that, in addition to possessing the [5,5] binding mode of DPA (Scheme 1c), is capable of forming 6-membered chelate rings that anchor on the imino (sp^2) nitrogen (Scheme 1d). Therefore, the DPH ligands could retain the high thermodynamic stabilities of the DPA metal complexes, while gaining the possibility of switching between coordination modes (e.g., [5,5] and [5',6] in Schemes 1c and 1d), and consequently allowing the access to the rich dynamic properties of hydrazones. The coordination chemistry of hydrazones and acyl hydrazones has been explored in developing molecular machines,[3] sensors,[4] and other stimulus-responsive materials.[5] The photoisomerizable hydrazone C=N bond has been employed in controlling the structures of metal coordination complexes.[5a, 5d, 6] These interesting properties of hydrazones inherent in DPH ligands will be explored in the future. In this paper we establish the coordination chemistry of DPH ligands via the characterization of their zinc(II) complexes in both solid and solution states.



Scheme 1. *N*,*N*-Di(2-picolyl)amine (DPA, a/b) and *N*,*N*-di(2-picolyl)hydrazone (DPH, c/d). X is a monodentate ligand. 'R' in (a) and (c) is a non-coordinating substituent; a nitrogen-anchored ancillary ligand is defined by the dotted curve in b and d, and engages in 5-membered chelate rings (5' in d).

Results and Discussion

Two routes were used for the synthesis of DPH ligands (Scheme 2). Route (a) began with the condensation of an aldehyde and hydrazine to afford a hydrazone, followed by alkylation with 2-picolyl bromide. In order to accommodate functionalized hydrazones that might undergo undesirable alkylation, route (b) was used that switched the order of condensation and alkylation. Hydrazine was alkylated to afford *N*,*N*-di(2-picolyl)hydrazine,[7] followed by condensation with an aldehyde to result in the DPH ligand.



Scheme 2. Synthesis of DPH ligands.

DPH ligands **1**-**3** are shown in Figure 1. Compound **1** has a non-binding hydrazone substituent, while **2** and **3** offer an extra ligand (phenol(ate) or pyridine, respectively) in addition to the two hydrazone nitrogens and the two picolyl groups. The structures of the zinc(II) complexes of **1**-**3** reveal the influence of the hydrazone ancillary component on the preferred binding mode of DPH, [5,5] or [5',6] (Schemes 1c and 1d). Neither [6,6] nor [5',6,6] (not drawn) was observed in this study.

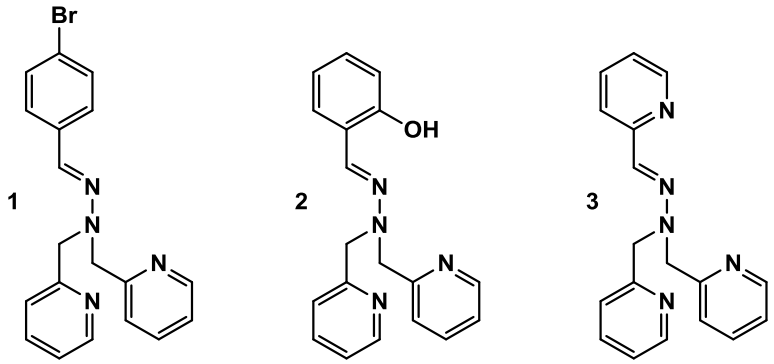


Figure 1. Structures of DPH ligands **1**-**3**.

The zinc(II) complexes of ligands **1**-**3** were prepared by mixing a ligand and $ZnCl_2$ (or $Zn(ClO_4)_2 \cdot 6H_2O$ in one case) in 2/1 or 1/1 ligand/zinc(II) molar ratio in acetonitrile. Upon solvent removal, the precipitated zinc(II) complex was isolated and washed with diethyl ether. Afterwards, the solid was redissolved in acetonitrile, and diethyl ether was allowed to diffuse into the acetonitrile solution of the complex until single crystals formed. Both [Zn(**1**)Cl_2] and [Zn(**2**)Cl_2] adopt the [5,5] binding mode as shown in single crystal structures (Figure 2). The distorted trigonal bipyramidal geometry of zinc(II) in both complexes is similar to that of zinc(II)/DPA complexes.[8] The hydroxy group in [Zn(**2**)Cl_2] forms a hydrogen bond with the imino nitrogen[9] instead of coordinating with zinc(II). These observations suggest that compound **2**

prefers the [5,5] coordination mode over [6',6] when the neutral 2-hydroxyphenyl moiety engages in an intramolecular hydrogen bond.[10]

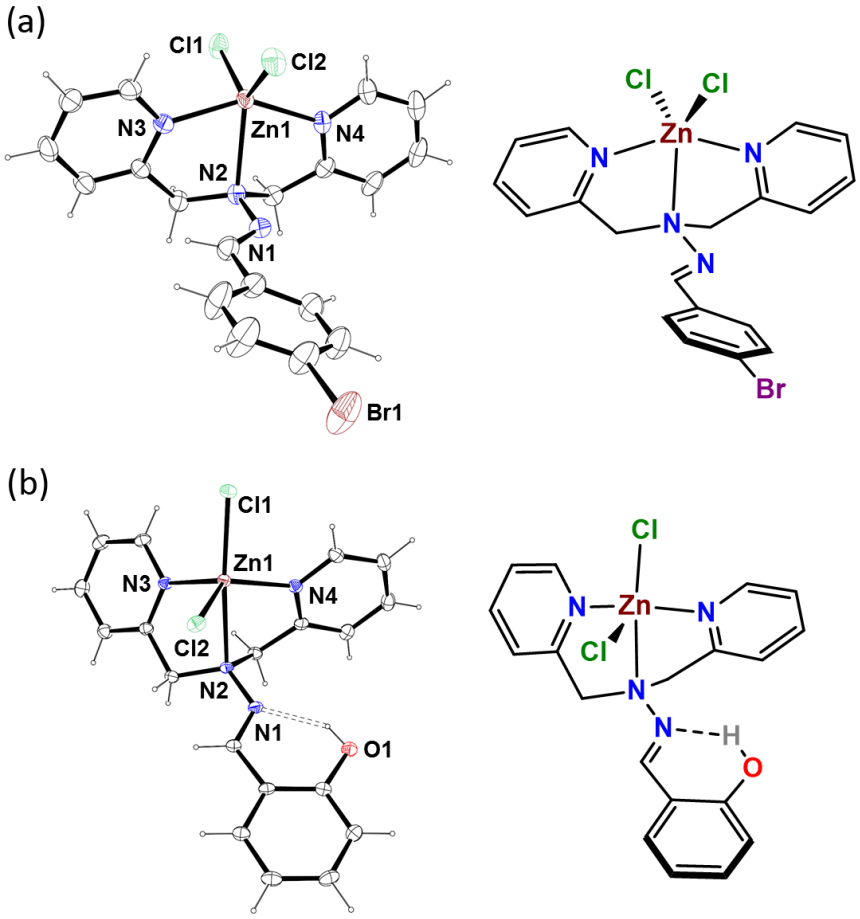


Figure 2. ORTEP (left, 50% ellipsoid) and ChemDraw structures (right) of (a) [Zn(**1**)Cl_2] (CCDC 1446279) and (b) [Zn(**2**)Cl_2] (CCDC 1446280). Selected distances (Å): (a) N1-N2 = 1.406(4); N2-Zn1 = 2.374(4); N3-Zn1 = 2.107(3); N4-Zn1 = 2.083(3); Zn1-Cl1 = 2.2872(9); Zn1-Cl2 = 2.267(1). (b) N1-N2 = 1.401(2); N2-Zn1 = 2.486(1); N3-Zn1 = 2.070(1); N4-Zn1 = 2.091(1); Zn1-Cl1 = 2.2996(5); Zn1-Cl2 = 2.2580(4).

The single crystal structure of [Zn(**3**)Cl_2] is shown in Figure 3a. The hydrazone pyridyl group and one of the picolyl groups bind zinc(II) to afford a 5- and a 6-membered chelate rings, respectively, to result in a [5',6] isomer (Figure 3a). The two remaining positions of the penta-coordinated zinc(II) are occupied by chloride counter ions, thus leaving one picolyl group of **3** unbound. The structure of [Zn(**3**)$_2$]$(ClO_4)_2$ (Figure 3b), a complex of ZnL_2 stoichiometry, replicates the [5',6] binding mode in the ZnL complex. The ligand is tridentate, and is *meridional* in the complex. The stereochemistry of [Zn(**3**)$_2$]$(ClO_4)_2$ differs from the that of the [Zn(DPA)$_2$]X_2 complexes, of which only *cis-facial* isomers have been observed.[11]

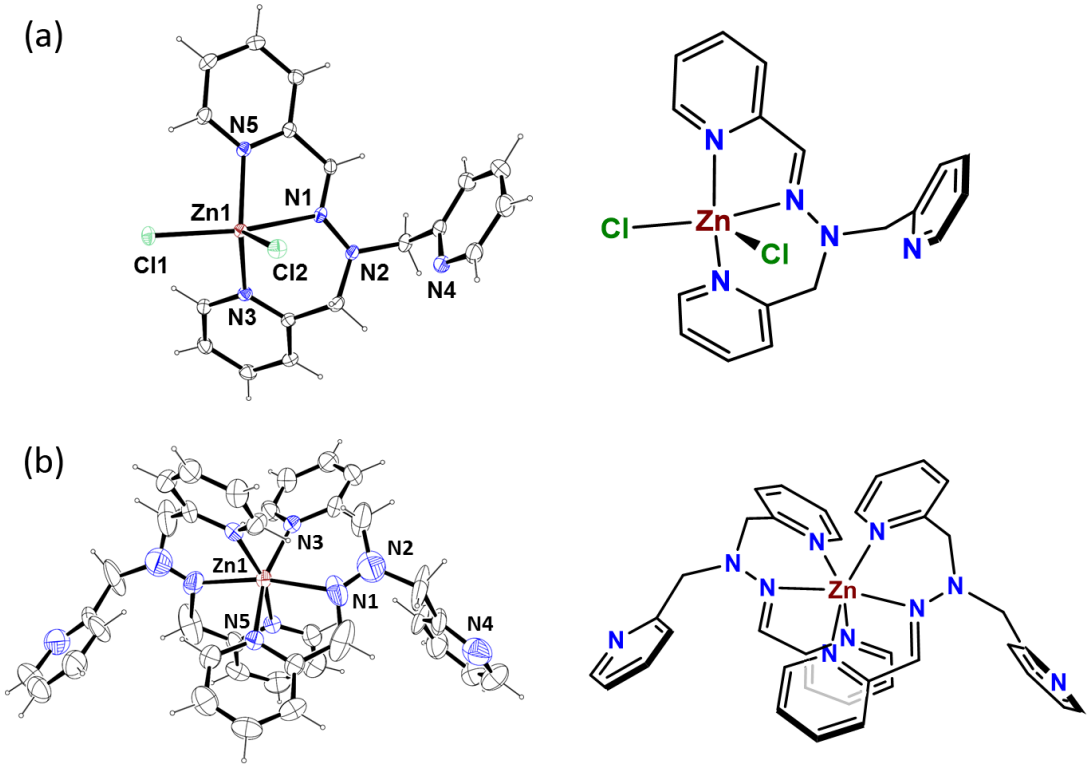


Figure 3. ORTEP (left, 50% ellipsoid) and ChemDraw structures of (a) [Zn(**3**)Cl_2] (CCDC 1446281) and (b) $[Zn(\mathbf{3})_2]^{2+}$ (CCDC 1446282). Selected distances (Å): (a) N1-N2 = 1.337(2); N1-Zn1 = 2.302(2); N3-Zn1 = 2.113(2); N5-Zn1 = 2.110(2); Zn1-Cl1 = 2.345(1); Zn1-Cl2 = 2.270(1). (b) N1-N2 = 1.22(1); N1-Zn1 = 2.203(9); N3-Zn1 = 2.142(6); N5-Zn1 = 2.149(5).

The ^{1}H NMR spectrum of ligand **1** in CD_3CN shows two chemically equivalent 2-picolyl groups (Figure 4, bottom). Upon addition of $Zn(ClO_4)_2$ to form the ZnL complex, the pyridyl proton signals (a-d) are all shifted downfield due to the deshielding effect from the zinc(II) center (top). Additionally, the protons in the methylene group appear as a pair of doublets typical of an AX or an AB spin system. These chemical shift patterns are similar to those of the ZnL complexes of DPAs.[8b, 11] Based on this information, we conclude that the solution structure of [Zn(**1**)]$(ClO_4)_2$ is of the [5,5] coordination mode (Scheme 1a), in which zinc(II) binds the DPA moiety to form two 5-membered chelate rings, as observed in the solid state (Figure 2a).

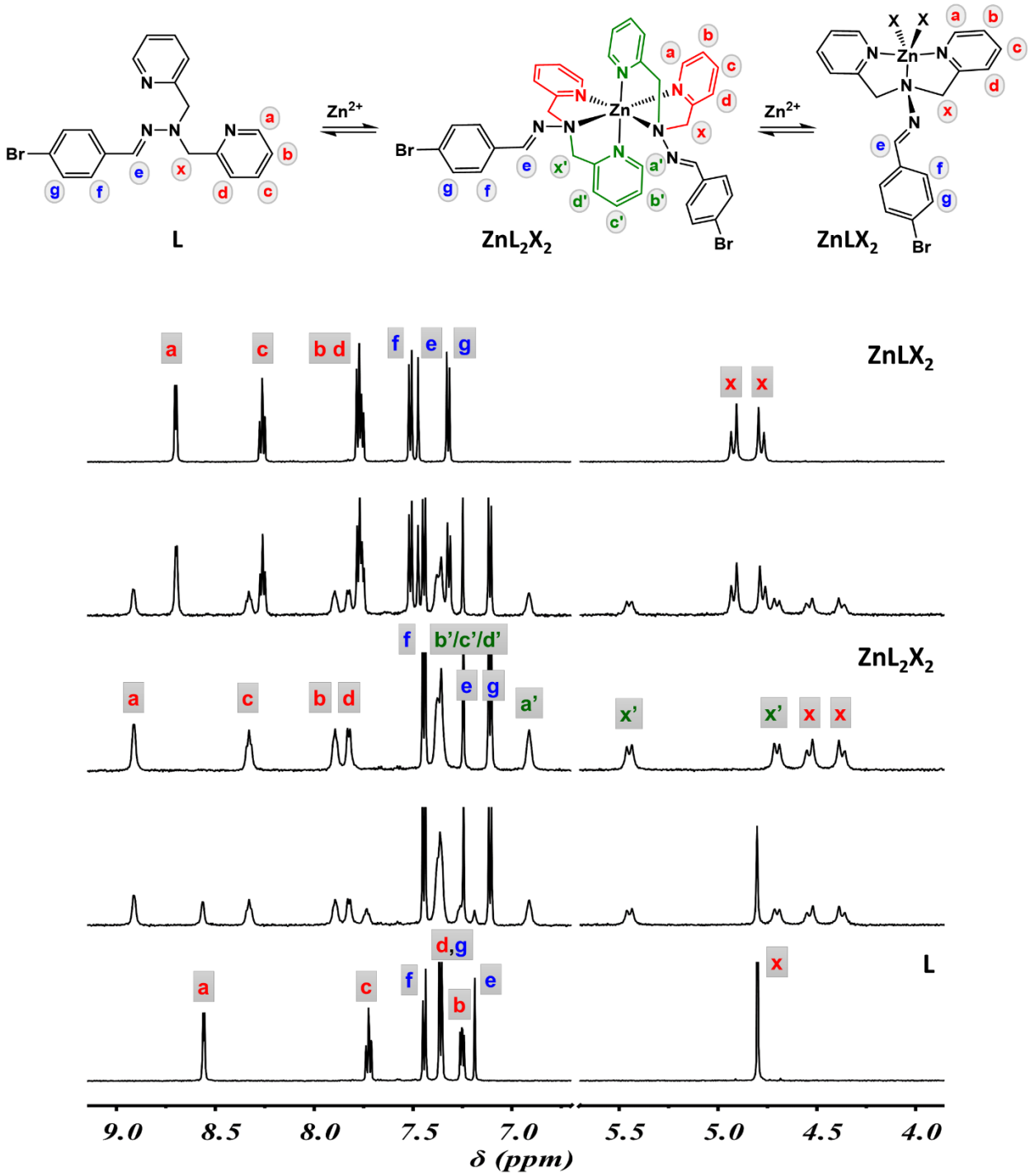


Figure 4. The ^{1}H NMR (500 MHz, CD_3CN) spectra of DPH ligand **1** in the presence of increasing [$Zn(ClO_4)_2$], from bottom up. The scheme of zinc(II) complex formation is shown on the very top. X = counter ion or solvent. The proton assignments of L, ZnL_2X_2, and $ZnLX_2$ species are shown.

At zinc(II)/ligand = ½ ratio, $[Zn(\mathbf{1})_2](ClO_4)_2$ was observed in solution (ZnL_2X_2 in Figure 4). The spectrum contains two sets of pyridyl protons (a-d and a'-d') and four methylene doublets (x and x'). Previously we showed that $[Zn(DPA)_2]X_2$ complexes exhibit *cis-facial* stereochemistry in both solution and solid states.[11] The chemical shift pattern of $[Zn(\mathbf{1})_2](ClO_4)_2$ (Figure 4, middle) closely resembles that of $[Zn(DPA)_2]X_2$. Therefore, we conclude that $[Zn(\mathbf{1})_2](ClO_4)_2$ also forms the *cis-facial* isomer of the [5,5] coordination mode in solution, as drawn in the scheme on the top of Figure 4.

The [5,5] isomers of $[Zn(\mathbf{2})](ClO_4)_2$ and $[Zn(\mathbf{2})_2](ClO_4)_2$ were also observed in CD_3CN (Figure S1, Supporting Information). The large chemical shift values of the hydroxyl proton (δ = 10.2 and 9.6 ppm, respectively) in both complexes suggest that the OH group forms a hydrogen bond with the imino nitrogen. Thus, the imino nitrogen is not engaged in binding, leaving the zinc(II) ion to be taken up by the DPA moiety.

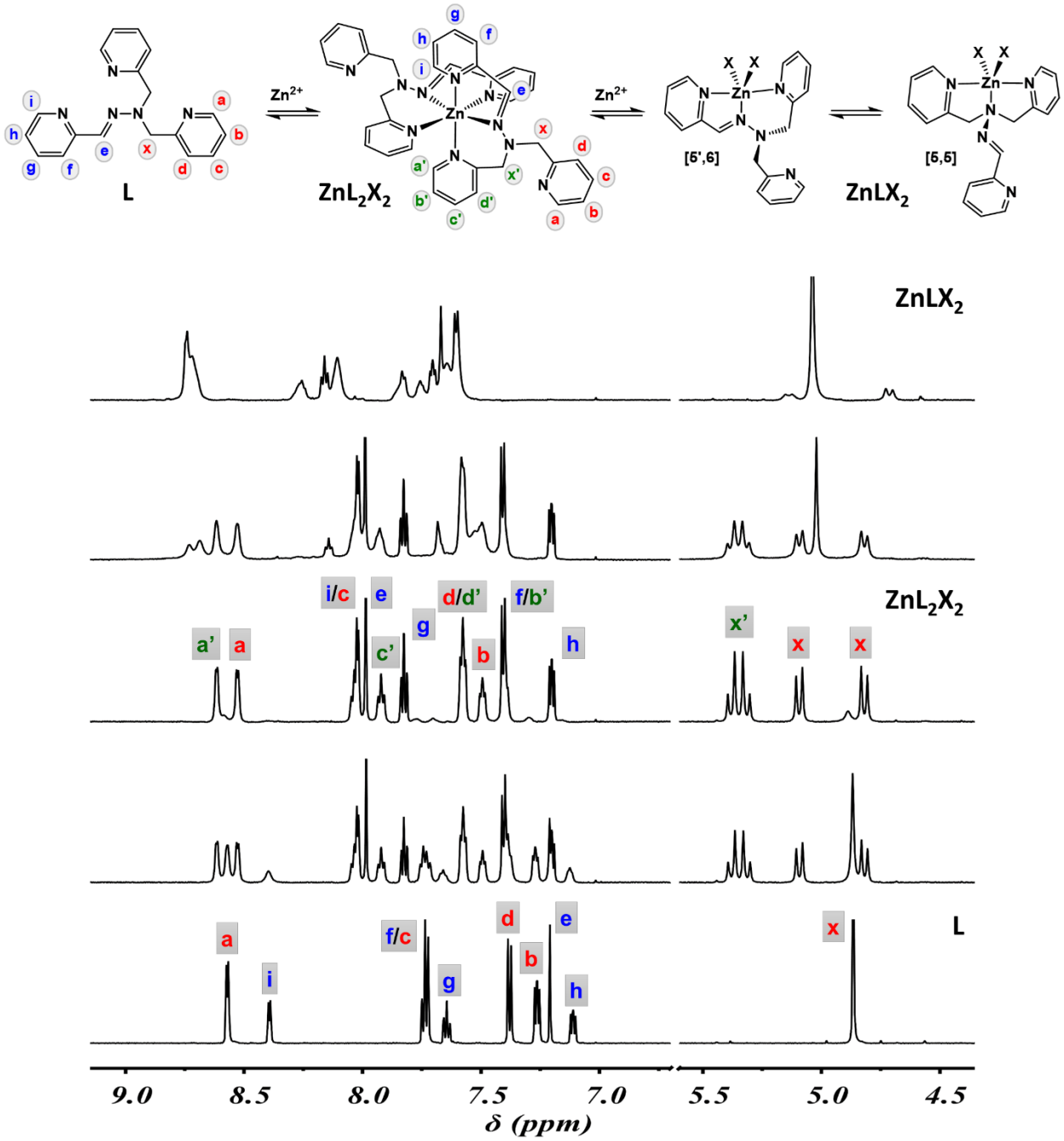


Figure 5. The ^{1}H NMR (500 MHz, CD_3CN) spectra of DPH ligand **3** in the presence of increasing [$Zn(ClO_4)_2$], from bottom up. The scheme of zinc(II) complex formation is shown on top. X = counter ion or solvent. The proton assignments of L and ZnL_2X_2 are shown. The spectra a repeat experiment with more data points are shown in Figure S2, Supporting Information.

Titrating $Zn(ClO_4)_2$ into a CD_3CN solution of ligand **3** led to the formation of a ZnL_2 complex [Zn(**3**)$_2$]$(ClO_4)_2$, followed by that of a ZnL complex [Zn(**3**)]$(ClO_4)_2$ (Figure 5). In [Zn(**3**)$_2$]$(ClO_4)_2$, three

chemically non-equivalent pyridyl groups were observed; one from the hydrazone pyridyl and two from the two picolyl groups. The protons of $[Zn(\mathbf{3})_2](ClO_4)_2$ were assigned using a combination of 2D NMR techniques (Figures S24-S28). The hydrazone proton 'e' of ligand **3** underwent a large downfield shift from 7.20 to 7.97 ppm upon forming $[Zn(\mathbf{3})_2](ClO_4)_2$, which suggests that in addition to one of the picolyl groups, the hydrazone pyridyl coordinates with zinc(II) in the complex. This conclusion is in contrast with that of ligand **1**. The hydrazone proton 'e' of ligand **1** remained relatively unchanged upon forming the ZnL_2 complex (from 7.20 to 7.25 ppm, see Figure 4), an indication that the hydrazone moiety is not bound with zinc(II) in that complex.

Most proton peaks of the presumed ZnL complex $[Zn(\mathbf{3})](ClO_4)_2$ broadened in the last spectrum of the titration experiment (top, Figure 5), suggesting that an equilibrium between the [5'6] and [5,5] isomers occurs on the time scale of ^{1}H NMR. Instead of a pair of doublets for the methylene groups expected in zinc(II)/DPA complexes, including the zinc(II) complexes of DPH ligands **1** and **2**, a singlet that is assigned to the [5',6] isomer accounting for most methylene protons was observed.

The distribution between [5,5] and [5',6] isomers of of $[Zn(\mathbf{3})](ClO_4)_2$ was studied using variable temperature (VT) ^{1}H NMR experiments, by recording the ^{1}H NMR spectra from -30 to +75 °C (Figure 6). The spectrum recorded at -30 °C (Figure 6, spectrum a) presents the expected two doublets at δ = 5.07 and 4.68 ppm, which are assigned to the picolylic hydrogens of the complex in a [5,5] isomer. The two singlets at δ = 5.16 and 4.92 ppm are assigned to the picolylic hydrogen nuclei of the [5',6]-coordinated complex (defined in Scheme 1d). They indicate that (1) Zn switches coordination from one picolyl ligand to the other slowly on the ^{1}H NMR time scale upon rotation along the N-N bond of the hydrazone, and (2) the 6-membered chelate ring is flexible on the NMR time scale.

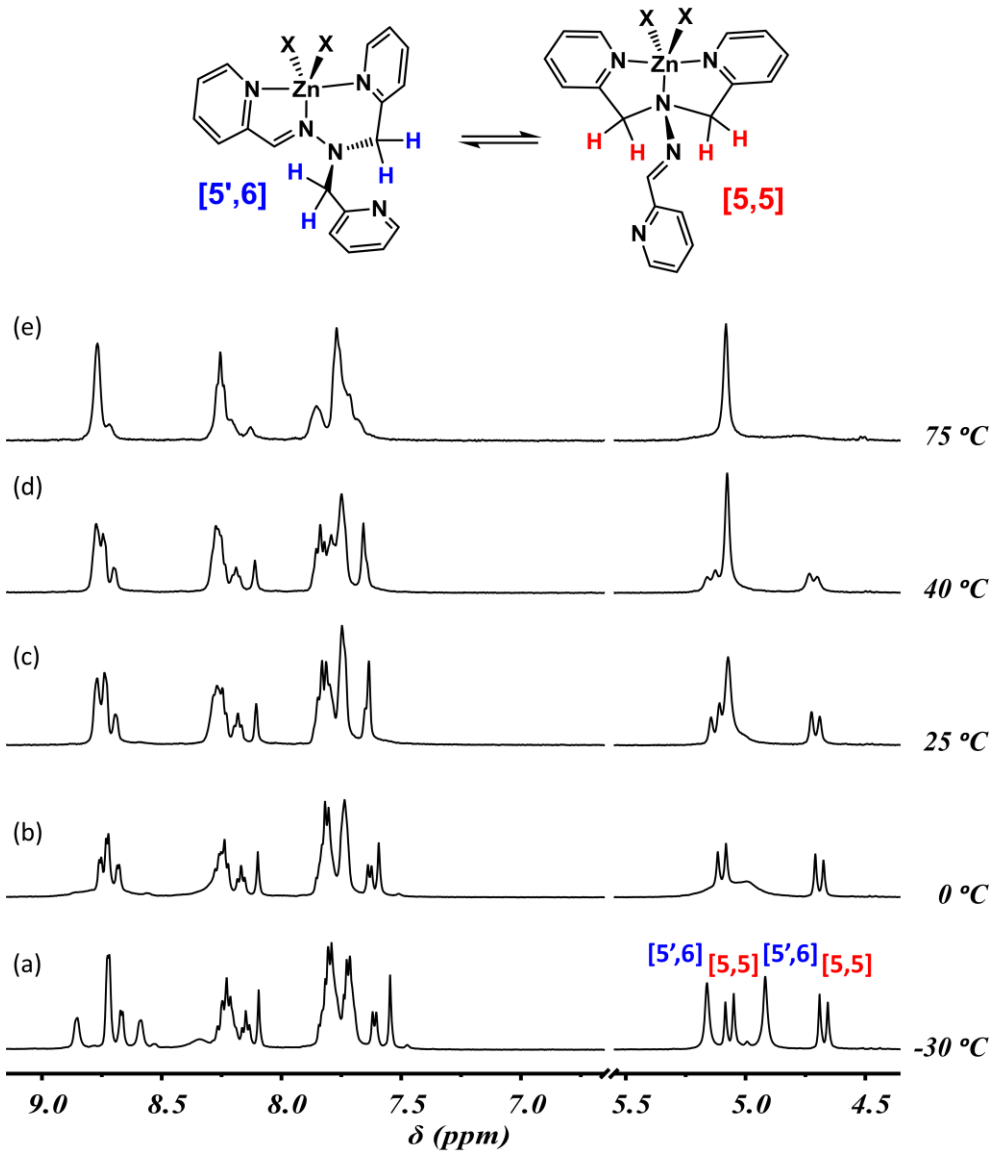


Figure 6. Variable temperature ^{1}H NMR (500 MHz, CD_3CN) of [Zn(**3**)X_2] (X = counter ion or solvent) from -30 to 75 °C (spectra a-e). The counter ion in this experiment is perchlorate. The CH_2 protons in [5',6] and [5,5] coordination isomers are marked in blue and red, respectively, in both structures on top and the spectrum at the bottom.

Coalescence between the two picolylic singlets of the [5',6] isomer of [Zn(**3**)]$(ClO_4)_2$ was observed at approximately 0 °C (Figure 6, spectrum b); this corresponds to a free energy of activation of 13 kcal/mol for the zinc(II)-pyridyl exchange. The same mechanism in the [5,5] isomer is more energy costly, and the coalescence of the two picolylic AX doublets is initiated at temperatures at or above 75 °C; this corresponds to a 16.5 kcal/mol barrier for the exchange process (Figure 6, spectrum e). The same barrier was measured for complex [Zn(**1**)]$(ClO_4)_2$, which exclusively adopts the [5,5] coordination mode (Figure S3). Fast interconversion between the [5,5] and [5',6] coordination modes of [Zn(**3**)]$(ClO_4)_2$, leading to a

unique singlet for all picolylic hydrogens was never observed, as the spectra recorded at higher temperatures lacked proper resolution.

To support the structural assignment of $[Zn(\mathbf{3})]^{2+}$ complexes and their relative stabilities in acetonitrile, we compared the stabilities of [5,5] and [5',6] isomers of $[Zn(\mathbf{3})(CH_3CN)]^{2+}$ using density functional theory (DFT) calculations. We used the dispersion-corrected PBE0-D3(BJ) functional, as this hybrid functional has been shown to accurately optimize transition metal-ligand complexes.[12] The functional was validated by screening the conformations of complex $[Zn(\mathbf{3})]Cl_2$ ([5',6] isomer; see Figure 3a) using def2-TZVP basis sets, and comparing the structure of the most stable conformer with the one obtained by X-ray diffraction. A high degree of overlapping was observed for both structures.

The geometries of complex $[Zn(\mathbf{3})(CH_3CN)]^{2+}$ in both [5,5] (Figure S6) and [5',6] (Figure S7) coordination modes were optimized at the PBE0-D3(BJ)/def2-TZVP level (coordinates available in the Supporting Information), and the energies were refined with the PW6B95-D3(BJ) functional[13] in single-point calculations. Replacing chlorides with acetonitrile ligands did not significantly affect the overall geometry of the complexes. Enthalpic and entropic contributions to the total energies were obtained by vibrational analysis, and solvation energies were calculated with the IEFPCM continuum solvation model[14] (details in Supporting Information). The electronic contribution to the equilibrium favors the [5',6] coordination mode by 2.1 kcal/mol over its [5,5] isomer, and entropic as well as enthalpic contributions increase the preference for the [5',6] isomer to 2.4 kcal/mol at -30 °C. While the stability of the [5',6] isomer is overestimated (a 64:36 [5',6]/[5,5] ratio in solution corresponds to a 0.3 kcal/mol advantage for the [5',6] isomer), calculations do predict the preferred coordination mode correctly. An increasing preference for the [5',6] isomer at a higher temperature is also obtained *in silico* (a 0.2 kcal/mol gain between -30 and 75 °C).

The ratio between [5',6]- and [5,5] isomers of $[Zn(\mathbf{3})](ClO_4)_2$ is not only sensitive to temperature (64:36 at -30 °C and 78:22 at 40 °C, see Figure 6), but also to the polarity or ionic strength of the medium. The coordination mode of [5,5] becomes increasingly favorable upon addition of excess amounts of $Zn(ClO_4)_2$ or $LiClO_4$, with [5',6]/[5,5] ratios shifting from 64:36 to 56:44 in the presence of 15 equiv. $Zn(ClO_4)_2$ or 3.0 equiv. $Zn(ClO_4)_2$ and 24 equiv. $LiClO_4$ (relative to ligand **3**) at -30 °C (Figure S4).

To the contrary, trace amounts of water (up to 0.3%) significantly tilted the balance towards the [5',6] isomer (from 64% to 82% and 96% in the presence of 12 and 36 equiv. water, Figure S5). We propose that water replaces acetonitrile ligands, and interacts not only with the zinc(II) center, but also with the nitrogen atom of one of the picolyl units via hydrogen bonding (see Figure 7). In that arrangement, DFT calculations showed a 4.5 kcal/mol preference for the [5',6] isomer over the [5,5] analog, a 2.1 kcal/mol increase in computed stability compared to anhydrous conditions.

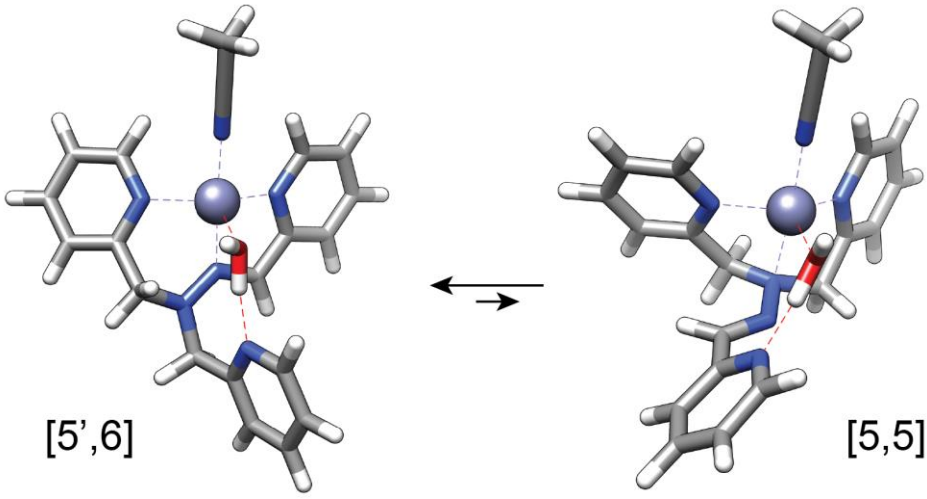


Figure 7. Stabilization of the [5',6] isomer of [Zn(**3**)]$(ClO_4)_2$ to the expense of its [5,5] analog in wet acetonitrile. Structures optimized at the TPSS-D3(BJ)/def2-TZVP level.

Conclusion

In summary, *N*,*N*-Di(2-picolyl)hydrazone (DPH) ligands can use either nitrogen atoms in the N(sp^3)-N(sp^2) bond to anchor metal ion coordination. In zinc(II) complexes, the hydrazone substituent influences which nitrogen is involved in multidentate coordination. When the hydrazone substituent is not coordinating, DPH forms complexes that are anchored on the sp^3 amino nitrogen as with *N*,*N*-Di(2-picolyl)amines. When the hydrazone component is 2-pyridyl, zinc(II) shifts to bind at the sp^2 imino nitrogen with the assistance from the 2-pyridyl. DPH complexes of other metal ions will be studied in the future, in addition to developing methods to switch binding between amino and imino nitrogens, likely by means of hydrazone photochemistry.

Experimental Section

1) Materials and general methods. Reagents and solvents were purchased from various commercial sources and were used without further purification unless otherwise noted. All reactions were carried out in oven- or flame-dried glassware. Analytical thin-layer chromatography (TLC) was performed using pre-coated TLC plates with silica gel 60 F254 or with aluminum oxide 60 F254 neutral. Flash column chromatography was performed using 40-63 μm (230-400 mesh) silica gel or alumina (80-200 mesh, pH 9-10) as the stationary phases. ^{1}H NMR spectra were recorded at 300, 500, or 600 MHz, while ^{13}C NMR spectra were recorded at 125 or 150 MHz. All chemical shifts were reported in δ units relative to tetramethylsilane. High resolution mass spectra (HRMS) were obtained at the Mass Spectrometry Laboratory at FSU using a time-of-flight analyzer. Elemental analysis was conducted at Atlantic Microlab, Inc.

2) Synthesis and characterization of new compounds

4-bromobenzaldehyde hydrazone.[15] 4-Bromobenzaldehyde (3.8 g, 20 mmol) was added to a flame-dried round-bottom flask purged with argon, and diluted with absolute ethanol (15 mL). Hydrazine (2.6 g, 80 mmol) was then carefully added dropwise over 5 min at rt. The reaction mixture was stirred at the refluxing temperature (78 °C). After 4 h, the reaction mixture was allowed to cool to rt, diluted with ethyl acetate (80 mL), and washed with saturated brine (3 x 75 mL) to afford the desired product to use in the next step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm 7.68 (s, 1H), 7.47 (d, *J* = 5.1 Hz, 2H), 7.41 (d, *J* = 5.1 Hz, 2H), 5.57 (s, 2H).

Compound 1. 2-Picolylbromide hydrobromide (253 mg, 1.0 mmol) and Na_2CO_3 (212 mg, 2.0 mmol) were added to a round-bottom flask purged with argon, followed by the addition of methanol (3 mL). The reaction mixture was stirred for 5 min before the addition of 4-bromobenzaldehyde hydrazone obtained from the previous step (100 mg, 0.5 mmol). After stirring for 24 h at rt, the reaction mixture was passed through a K_2CO_3 pad and diluted with dichloromethane. Solvent was removed under reduced pressure and the crude product was purified via silica gel column chromatography eluted with dichloromethane (100 mL), then ethyl acetate (100 mL), to afford the pure product as a yellow oil (23% yield in two steps). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 8.56 (d, *J* = 4.6 Hz, 2H), 7.64 (t, *J* = 7.7 Hz, 2H), 7.38 (d, *J* = 8.6 Hz, 2H), 7.33 (d, *J* = 8.8 Hz, 4H), 7.18 (t, *J* = 5.6 Hz, 2H), 7.07 (s, 1H), 4.77 (s, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 157.9, 159.6, 137.0, 135.9, 131.7, 131.2, 127.3, 122.5, 121.2, 60.8; HRMS (ESI+) (m/z): $[M+H]^+$ calcd for $C_{19}H_{18}BrN_4$ 381.0715, found 381.0706.

***N*,*N*-Di(2-picolyl)hydrazine.** 2-picolylbromide hydrobromide (101 mg, 0.399 mmol) and Na_2CO_3 (90 mg, 0.85 mmol) were added to a flame-dried round-bottom flask purged with argon, followed by the addition of methanol (1.5 mL). Hydrazine (6 μL, 0.2 mmol) was added dropwise to the reaction mixture and stirred at rt for 24 h before passing through a pad of K_2CO_3. The crude product was loaded onto an alumina gel column and eluted with dichloromethane, then dichloromethane/ethyl acetate 50:50, then 1 up to 4% methanol in dichloromethane. The product was unable to be purified any further and was used directly in the next reaction.

Compound 2. The crude *N*,*N*-di(2-picolyl)hydrazine from the previous step (150 mg, ~0.7 mmol) was diluted with absolute ethanol (3 mL) and added to a round-bottom flask purged with argon. 2-Hydroxybenzaldehyde (85 mg, 0.70 mmol) was then added to the reaction mixture and stirred at rt for 24 h. The reaction mixture was then diluted with dichloromethane and placed under reduced pressure to remove the solvent. The residue was loaded on a short silica gel column and eluted with ethyl acetate in dichloromethane in three segments (0, 50, and 100% ethyl acetate) to afford the pure product as a white solid (34 mg, 15% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm 11.22 (s, 1H), 8.59 (d, *J* = 5.6 Hz, 2H), 7.67 (t, *J* = 7.7 Hz, 2H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.36 (s, 1H), 7.21 (t, *J* = 5.0 Hz, 2H), 7.11 (t, *J* = 8.6 Hz, 1H), 6.92 (d, *J* = 1.6 Hz, 1H), 6.87 (d, *J* = 1.6 Hz, 1H) 6.76 (t, *J* = 6.4 Hz, 1H), 4.74 (s, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm 157.1, 157.0, 149.8, 138.1, 137.1, 129.4, 129.1, 122.8, 122.4, 119.6, 119.2, 116.5, 60.8; HRMS (ESI+) (m/z): $[M+H]^+$ calcd for $C_{19}H_{18}N_4ONa$: 341.1378; found 341.1373.

Compound 3. To a flame-dried round-bottom flask, 2-picolylbromide hydrobromide (2.5 g, 10 mmol) and potassium carbonate (1.45 g, 10.5 mmol) were dissolved in 38 mL of MeOH. After stirring for 10 min, hydrazine (160 μL, 5.10 mmol) was added dropwise to the mixture and stirred overnight. After stirring for 24 h, the reaction mixture was heated to 70 °C and picolinaldehyde (476 μL, 5.00 mmol) was added. The new reaction mixture was then stirred for an additional 24 h before cooling to rt. The mixture was diluted with EtOAc (150 mL) and washed with deionized water (75 mL x 3) and saturated brine (75 mL). The crude product was then purified on an alumina column using dichloromethane and slowly increasing the amount of EtOAc (1% increments). A yellow oil was obtained (607 mg, 40% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm 8.53 (ddd,[16] *J* = 5.0, 2.0, 1.0 Hz, 2H), 8.41 (ddd, *J* = 5.0, 2.0, 1.0 Hz, 1H), 7.76 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.60 (td, *J* = 8.0, 2.0 Hz, 2H), 7.56 (td, *J* = 8.0, 2.0 Hz, 1H), 7.29 (dt, *J* = 8.0, 1.0 Hz, 2H), 7.25 (s, 1H), 7.14 (ddd, *J* = 8.0, 5.0, 1.0 Hz, 2H), 7.03 (ddd, *J* = 8.0, 5.0, 1.0 Hz, 1H), 4.83(s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm 157.3, 155.8, 149.7, 149.1, 136.9, 136.2, 132.0, 122.5, 122.0, 121.8, 119.2, 60.4; HRMS (ESI+) (m/z): $[M+H]^+$ calcd for $C_{18}H_{18}N_5$: 304.1562; found: 304.1558.

Complex [Zn(1)Cl$_2$]. Compound **1** (25.0 mg, 0.0656 mmol) was dissolved in CH_3CN (391 μL, 0.168 mM) in a vial. $ZnCl_2$ (13.6 mg, 0.10 mmol) was dissolved in CH_3CN (597 μL, 0.168 mM) and added to the solution of **1**. The reaction mixture was stirred for 15 min before concentrated under reduced pressure. The resulting complex was then washed with diethyl ether three times and vacuum dried. The complex was dissolved in CH_3CN (0.5 mL) and filtered through a layer of glass microfiber into a small vial. The small vial containing the complex was then placed into a larger vial containing diethyl ether. After 5 days, single crystals were obtained (CCDC 1446279). Anal. calcd for $C_{19}H_{17}BrCl_2N_4Zn$: C, 44.09; H, 3.31; N, 10.83, found: C, 43.92; H, 3.29; N, 10.79.

Complex [Zn(1)$_2$](ClO$_4$)$_2$. ^{1}H NMR (500 MHz, CD_3CN) was acquired during the ^{1}H NMR Zn(II) titration experiment: ^{1}H NMR (500 MHz, CD_3CN): δ/ppm 8.91 (m, 2H), 8.33 (t, *J* = 5.8 Hz, 2H), 7.89 (m, 2H), 7.83 (d, *J* = 5.8 Hz, 2H), 7.44 (m, 4H), 7.38-7.36 (m, 6H), 7.25 (s, 2H), 7.11 (m, 4H), 6.91 (m, 2H), 5.45 (d, *J* = 13.2 Hz, 2H), 4.70 (d, *J* = 11.8 Hz, 2H), 4.54 (d, *J* = 15.2 Hz, 2H), 4.38 (d, *J* = 13.3 Hz, 2H).

Complex [Zn(1)](ClO$_4$)$_2$. ^{1}H NMR (500 MHz, CD_3CN) was acquired during the ^{1}H NMR Zn(II) titration experiment: δ/ppm 8.70 (d, *J* = 4.1 Hz, 2H), 8.26 (td, *J* = 6.5, 1.3 Hz, 2H), 7.79-7.75 (m, 4H), 7.51 (m, 2H), 7.47 (s, 1H), 7.32 (m, 2H), 4.92 (d, *J* = 14.0 Hz, 2H), 4.78 (d, *J* = 13.4 Hz, 2H).

Complex [Zn(2)Cl$_2$]. Compound **2** (32 mg, 0.10 mmol) was dissolved in CH_3CN (298 μL) in a vial. $ZnCl_2$ (14 mg, 0.10 mmol) was dissolved in CH_3CN (597 μL, 0.168 mM) and added to the solution of **2**. The reaction mixture was stirred for 15 min then concentrated under reduced pressure. The complex was then washed with diethyl ether twice and concentrated. The complex was dissolved in CH_3CN (0.5 mL) and filtered through a layer of glass microfiber into a small vial. The small vial containing the complex was then placed into a larger vial containing diethyl ether. After 1-2 days, single crystals were obtained (CCDC 1446280). Anal. calcd for $C_{19}H_{18}Cl_2N_4OZn$: C, 50.19; H, 3.99; N, 12.32, found: C, 50.79; H, 4.24; N, 12.13.

Complex [Zn(2)$_2$](ClO$_4$)$_2$. ^{1}H NMR (500 MHz, CD_3CN) was acquired during the ^{1}H NMR Zn(II) titration experiment: δ/ppm 9.53 (s, 2H), 8.81 (m, 2H), 8.36 (m, 2H), 7.89 (m, 4H), 7.55 (s, 2H), 7.48 (m, 2H), 7.44

(m, 2H), 7.37 (m, 2H), 7.29 (t, *J* = 6.3 Hz, 2H), 6.95 (d, *J* = 6.3 Hz, 2H), 6.84 (m, 4H), 6.77 (d, *J* = 7.1 Hz, 2H), 5.38 (m, 2H), 4.70 (m, 2H), 4.53 (m, 2H), 4.43 (m, 2H).

Complex [Zn(2)]$(ClO_4)_2$. ^{1}H NMR (500 MHz, CD_3CN) was acquired during the ^{1}H NMR Zn(II) titration experiment: δ/ppm 10.02 (s, 1H), 8.72 (d, *J* = 3.6 Hz, 4H), 8.29 (td, *J* = 6.6, 1.2 Hz, 4H), 7.82 (d, *J* = 6.7 Hz, 4H), 7.78 (t, *J* = 5.1 Hz, 4H), 7.70 (m, 2H), 7.30 (m, 2H), 7.17 (dd, *J* = 6.4, 1.2 Hz, 2H), 6.88 (m, 2H), 6.82 (d, *J* = 6.8 Hz, 2H), 4.98 (d, *J* = 13.4 Hz, 4H), 4.83 (d, *J* = 13.7 Hz, 4H).

Complex [Zn(3)$_2$]$(ClO_4)_2$·$(CH_3CN)_2$. Compound **3** (10.3 mg, 34.0 μmol) was dissolved in CH_3CN (2 mL) and added to $Zn(ClO_4)_2$·$6H_2O$ (5.70 mg, 15.3 μmol) to give a clear light yellow solution. The solvent was removed under reduced pressure to give a light yellow powder, which was washed with diethyl ether (3 x 1.5 mL). The solid was then dissolved in CH_3CN (1.5 mL), passed through glass wool and left in a sealed vessel containing diethyl ether, which was allowed to diffuse by vapor for 1.5 wk. The supernatant was removed by decanting and the solid washed twice with diethyl ether (1 mL) to give clear light yellow crystals (CCDC 1446282). ^{1}H NMR (500 MHz, CD_3CN) was acquired during the Zn(II) titration experiment: δ/ppm 8.59 (d, *J* = 4.2 Hz, 2H), 8.50 (d, *J* = 4.8 Hz, 2H), 8.02-7.99 (m, 4H), 7.97 (s, 2H), 7.89 (t, *J* = 7.3 Hz, 2H), 7.80 (td, *J* = 7.8, 1.5 Hz, 2H), 7.55 (m, 4H), 7.47 (t, *J* = 6.4 Hz, 2H), 7.40-7.35 (m, 4H), 7.17 (ddd, *J* = 7.7, 5.2, 1.2 Hz, 2H), 5.36 (d, *J* = 17.4 Hz, 2H), 5.29 (d, *J* = 17.3 Hz, 2H), 5.07 (d, *J* = 15.7 Hz, 2H), 4.79 (d, *J* = 15.6 Hz, 2H). Anal. calcd for $C_{40}H_{40}Cl_2N_{12}O_8Zn$: C, 50.41; H, 4.23; N, 17.64, found: C, 50.00; H, 4.16; N, 17.34.

Complex [Zn(3)Cl_2]. Compound **3** (7.10 mg, 23.4 μmol) was dissolved in CH_3CN (2 mL) and added to $ZnCl_2$ (3.10 mg, 22.8 μmol) to give a clear light yellow solution. The solvent was removed under reduced pressure to give an off-white powder, which was washed with diethyl ether (3 x 1.5 mL). The solid was then dissolved in CH_3CN (1.5 mL), passed through glass wool and then left in a sealed vessel containing diethyl ether which was allowed to diffuse by vapor for 1.5 wk. The supernatant was then removed by decanting and washing twice with diethyl ether (1 mL) to give a light tan crystalline solid (CCDC 1446281). Anal. calcd for $C_{18}H_{17}Cl_2N_5Zn$: C, 49.18; H, 3.90; N, 15.93, found: C, 48.91; H, 3.98; N, 15.91.

3) X-ray crystallography

Crystals were mounted on a nylon loop with the use of heavy oil. The samples were generally cooled to -170 °C for data collection. No phase change on cooling was ever evident. Full data were taken on a Bruker SMART APEX II diffractometer using a detector distance of 6 cm. The number of frames taken was 2,400 using 0.3 degree omega scans with 20 seconds of frame collection time. Integration was performed using the program SAINT which is part of the Bruker suite of programs. Absorption corrections were made using SADABS. XPREP was used to obtain an indication of the space group and the structure was typically solved by direct methods and refined by SHELXTL. The non-hydrogen atoms were refined anisotropically. Typically the hydrogen atoms could be found during the least squares refinement, but in practice they are constrained as a riding model. The .cif files have been deposited in the Cambridge Crystallographic Data Centre (CCDC), referenced by the following CCDC numbers: [Zn(**1**)Cl_2]: 1446279; [Zn(**2**)Cl_2]: 1446280; [Zn(**3**)Cl_2]: 1446281; and [Zn(**3**)$_2$]$(ClO_4)_2$: 1446282.

Acknowledgments. This work was supported by the National Science Foundation (CHE1213574 to L.Z. and CHE1507321 to E.M.). D.N.B was supported by the Delos F. and Frances L. Detar Undergraduate Research Award.

References

[1] a) G. Anderegg, F. Wenk, *Helv. Chim. Acta* **1967**, *50*, 2330-2332; b) J. K. Romary, J. D. Barger, J. E. Bunds, *Inorg. Chem.* **1968**, *7*, 1142-1145.

[2] a) C. S. Allen, C.-L. Chuang, M. Cornebise, J. W. Canary, *Inorg. Chim. Acta* **1995**, *239*, 29-37; b) A. Blackman, *Polyhedron* **2005**, *24*, 1-39; c) E. A. Lewis, W. B. Tolman, *Chem. Rev.* **2004**, *104*, 1047-1076; d) L. M. Mirica, X. Ottenwaelder, T. D. P. Stack, *Chem. Rev.* **2004**, *104*, 1013-1045; e) Z. Dai, J. W. Canary, *New J. Chem.* **2007**, *31*, 1708-1718.

[3] a) X. Su, T. F. Robbins, I. Aprahamian, *Angew. Chem. Int. Ed.* **2011**, *50*, 1841-1844; b) D. Ray, J. T. Foy, R. P. Hughes, I. Aprahamian, *Nat. Chem.* **2012**, *4*, 757-762.

[4] a) N. Li, Y. Xiang, X. Chen, A. Tong, *Talanta* **2009**, *79*, 327-332; b) L. Wang, W. Qin, W. Liu, *Inorg. Chem. Commun.* **2010**, *13*, 1122-1125; c) Y. Zhou, H. N. Kim, J. Yoon, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 125-128; d) L. Y. Zhao, Q. L. Mi, G. K. Wang, J. H. Chen, J. F. Zhang, Q. H. Zhao, Y. Zhou, *Tetrahedron Lett.* **2013**, *54*, 3353-3358; e) B. K. Datta, D. Thiyagarajan, S. Samanta, A. Ramesh, G. Das, *Org. Biomol. Chem.* **2014**, *12*, 4975–4982; f) J. Wang, Y. Li, N. G. Patel, G. Zhang, D. Zhou, Y. Pang, *Chem. Commun.* **2014**, *50*, 12258-12261.

[5] a) M. N. Chaur, D. Collado, J.-M. Lehn, *Chem. Eur. J.* **2011**, *17*, 248-258; b) G. Vantomme, J.-M. Lehn, *Chem. Eur. J.* **2014**, *20*, 16188-16193; c) G. Vantomme, N. Hafezi, J.-M. Lehn, *Chem. Sci.* **2014**, *5*, 1475-1483; d) A. T. Franks, D. Peng, W. Yang, K. J. Franz, *Inorg. Chem.* **2014**, *53*, 1397-1405; e) X. Su, I. Aprahamian, *Chem. Soc. Rev.* **2014**, *43*, 1963-1981.

[6] F. Kitamura, K. Sawaguchi, A. Mori, S. Takagi, T. Suzuki, A. Kobayashi, M. Kato, K. Nakajima, *Inorg. Chem.* **2015**, *54*, 8436–8448.

[7] U. Ragnarsson, *Chem. Soc. Rev.* **2001**, *30*, 205-213.

[8] a) L. Zhang, R. J. Clark, L. Zhu, *Chem. Eur. J.* **2008**, *14*, 2894-2903; b) J. T. Simmons, J. R. Allen, D. R. Morris, R. J. Clark, C. W. Levenson, M. W. Davidson, L. Zhu, *Inorg. Chem.* **2013**, *52*, 5838-5850; c) S. I. Kirin, P. Dübon, T. Weyhermüller, E. Bill, N. Metzler-Nolte, *Inorg. Chem.* **2005**, *44*, 5405–5415.

[9] X. Wang, J. W. Canary, *Bioconjugate Chem.* **2012**, *23*, 2329−2334.

[10] Attempts were made to prepare the zinc(II) complex of deprotonated ligand **2**, only to afford complexed mixtures unresolvable from the ^{1}H NMR data.

[11] J. T. Simmons, Z. Yuan, K. L. Daykin, B. T. Nguyen, R. J. Clark, M. Shatruk, L. Zhu, *Supramol. Chem.* **2014**, *26*, 214-222.

[12] a) M. Bühl, C. Reimann, D. A. Pantazis, T. Bredow, F. Neese, *J. Chem. Theory Comput.* **2008**, *4*, 1449-1459; b) J. Vícha, M. Patzschke, R. Marek, *Phys. Chem. Chem. Phys.* **2013**, *15*, 7740-7754.

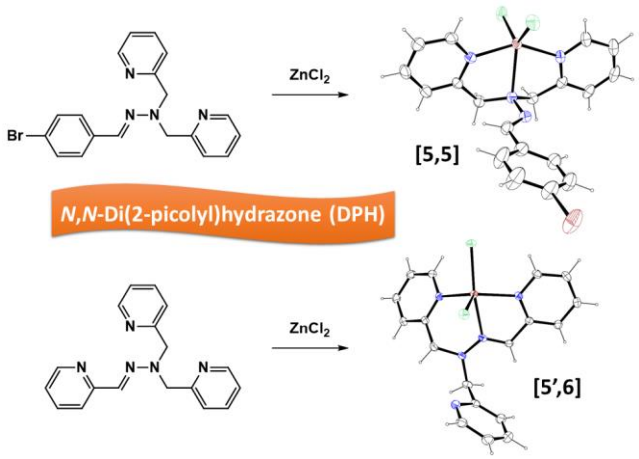
[13] a) S. Grimme, S. Ehrlich, L. Goerigk, *J. Comput. Chem.* **2011**, *32*, 1456-1465; b) S. Grimme, J. Antony, S. Ehrlich, H. Krieg, *J. Chem. Phys.* **2010**, *132*, 154104; c) Y. Zhao, D. G. Truhlar, *J. Phys. Chem. A* **2005**, *109*, 5656-5667.

[14] a) R. Improta, G. Scalmani, M. J. Frisch, V. Barone, *J. Chem. Phys.* **2007**, *127*, 074504; b) R. Improta, V. Barone, G. Scalmani, M. J. Frisch, *J. Chem. Phys.* **2006**, *125*, 054103; c) J. Tomasi, B. Mennucci, R. Cammi, *Chem. Rev.* **2005**, *105*, 2999-3093.

[15] A. V. Shastin, V. N. Korotchenko, V. G. Nenajdenko, E. S. Balenkova, *Tetrahedron* **2000**, *56*, 6557–6563.

[16] $^{5}J_{HH}$ coupling (between protons para to each other on an aryl ring) are not usually resolved; however we did see it in this case.

For the Table of Contents:



N,N-di(2-picolyl)hydrazone (DPH) ligands are capable of binding metal ions in two coordination modes that anchor on either the sp^3 amino or the sp^2 imino nitrogen atom, depending on the nature of the hydrazone moiety.