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First-Transition-Metal Complexes Containing the Ligands 6-Amino-6-methylperhydro-1,4-diazepine (AAZ) and a New Functionalized Derivative: Can AAZ Act as a Mimetic Ligand for 1,4,7-Triazacyclononane?

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The structure and physicochemistry of the $[Ni^{II}(AAZ)_2](ClO_4)_2$ (**1**) complex (AAZ = 6-amino-6-methylperhydro-1,4-diazepine), as a system that is able to mimic some important chelate properties of 1,4,7-triazacyclononane, are reported. The syntheses of a new unsymmetric AAZ-functionalized ligand and the structure of its first heterodinuclear $Fe^{III}Zn^{II}$ complex are also presented.

Since the original synthesis of the cyclic amine 1,4,7-triazacyclononane ([9]aneN3) in 1972,[1] more than 900 papers involving [9]aneN3 itself and a diversity of multidentate-functionalized derivatives and their metal complexes have been reported in the literature.[2] In fact, it has been recognized that [9]aneN3 is a strong facial tridentate chelating ligand that plays a significant role in the stabilization of several inorganic structural motifs, including transition-metal complexes,[3] bioinorganic model complexes,[4] and several other materials.[5] However, it should be noted that, despite the advantageous properties of [9]aneN3 mentioned above, its synthesis is extremely laborious and expensive in terms of both time and cost. Thus, it is evident that the search for facial tridentate amine ligands that are able to mimic the structural and physicochemical properties of [9]aneN3 is a matter of great interest.

Very recently, Aime et al.[6] reported the synthesis of the tridentate 6-amino-6-methylperhydro-1,4-diazepine (AAZ) ligand as an intermediate in the preparation of the heptadentate 6-amino-6-methylperhydro-1,4-diazepinetetraacetic acid (AAZTA) ligand. In the same paper, it was demonstrated that the chelate properties of the $[Gd(AAZTA)]^-$ complex make this system an excellent candidate for the development of a new class of magnetic resonance imaging agents. However, no good crystals for X-ray analysis have been obtained, and thus the coordination mode of AAZ remains unknown.

The fact that the synthesis of AAZ is simple[6] and employs readily available and cheap chemicals, along with the lack of any structural data on this system, led us to investigate its tridentate chelating ability in relation to transition-metal ions. In this Communication, we present the crystal structure of $[Ni^{II}(AAZ)_2](ClO_4)_2$ (**1**) as being the first structure involving the AAZ ligand, together with results from physicochemical studies in solution. A comparison between $[Ni^{II}(AAZ)_2]^{2+}$ and $[Ni^{II}([9]aneN3)_2]^{2+}$ (**2**) reveals significant similarities in their structural parameters as well as in their solution properties.[7] In addition, the synthesis of the new unsymmetrical dinucleating $H_2AAZBPMP$ ligand and the X-ray structure of the dinuclear $[Fe^{III}Zn^{II}(AAZBPMP)(\mu\text{-}OMe)(\mu\text{-}OAc)](ClO_4)$ (**3**) complex are presented. It should be emphasized that the use of unsymmetrical ligands is a convenient strategy in mimicking structural and catalytic properties of mixed-valence metalloenzymes.[8]

The tridentate AAZ ligand was synthesized as described in the literature,[6] while $H_2AAZBPMP$ was prepared in situ through a condensation reaction of AAZ with 2-{[(2-hydroxybenzyl)(2-pyridylmethyl)amino]methyl}-4-methyl-6-formylphenol[9] in MeOH under reflux for 24 h.

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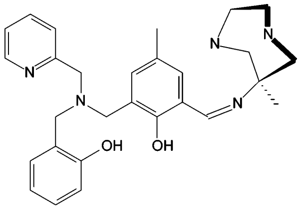

H_2AAZBPMP

The molecular structure of the mononuclear cation in complex **1**[10,11] (Figure 1) reveals a centrosymmetric structure with two AAZ ligand molecules facially coordinated to the Ni^{II} ion, forming a highly distorted octahedron, in which the 1,4-diazepine seven-membered ring adopts a pseudochair configuration. In the structure, the trigonal distortion (regarded as a pseudo-3-fold axis) is such that the N−Ni−N angles average is 80.33(10)° when all nitrogens come from one AAZ ligand (intraligand bond angles) and, similarly, the N−Ni−N average is 99.60(10)° for the interligand bond angles, which should be 90° in a regular octahedron. It is worth noting that these values are comparable to those of 81.6(3) and 98.4(1)° observed in the centrosymmetric $[Ni^{II}([9]aneN3)_2]^{2+}$ cation[7a] because AAZ is a 1,4-diaza ligand, with the third donor nitrogen being a primary amine. Similarly, the average Ni−N bond length of 2.113(2) Å for $[Ni^{II}(AAZ)_2]^{2+}$ is in full agreement with the value of 2.116(9) Å determined for $[Ni^{II}([9]aneN3)_2]^{2+}$. Therefore, structurally these complexes are very similar.

We have also carried out a series of physicochemical studies, including electrochemistry, potentiometric titration, and UV−vis spectroscopy for $[Ni^{II}(AAZ)_2]^{2+}$ under experimental conditions identical with those utilized for $[Ni^{II}([9]aneN3)_2]^{2+}$. For comparison purposes, the data are summarized in Table 1 for both complexes.

The electronic absorption spectrum of **1** in water at 20 °C is shown in Figure S1 in the Supporting Information and reveals three maxima, typical of an octahedral NiN6 chromophore.[7d] The absorption maxima at 12 500, 19 400, and 28 800 cm^{-1} can be attributed to the $^3A_{2g} \rightarrow {}^3T_{2g}$, $^3A_{2g} \rightarrow {}^3T_{2g}(F)$, and $^3A_{2g} \rightarrow {}^3T_{2g}(P)$ transitions, respectively, and these are comparable to those observed in the spectrum of $[Ni^{II}([9]aneN3)_2]^{2+}$, mainly the value of D_q, which is 1250 cm^{-1} for both complexes. In addition, the shoulder at 11 000 cm^{-1}, which appears on the low-energy side of the 12 500 cm^{-1} band, is also consistent with $D_q > 1200$ cm^{-1} observed for $[Ni^{II}([9]aneN3)_2]^{2+}$.[7d]

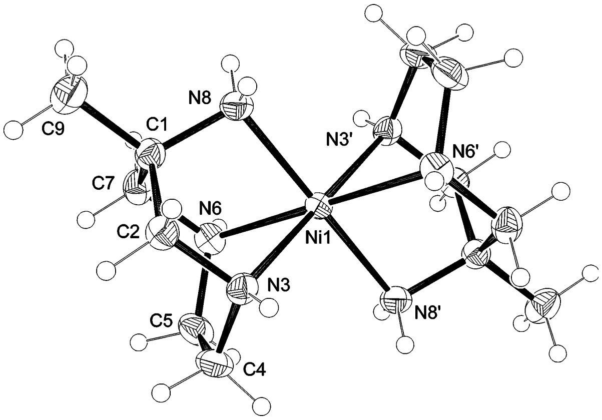

Figure 1. ORTEP of the cation $[Ni^{II}(AAZ)_2]^{2+}$. Ellipsoid at the 40% probability level and H atoms with arbitrary size. Selected bond lengths and angles (Å and deg): Ni1−N3, 2.132(2); Ni1−N6, 2.119(2); Ni1−N8, 2.090(2); N8−Ni1−N6, 83.36(9); N8−Ni1−N6^i, 96.64(9); N8−Ni1−N3^i, 97.36(9); N6−Ni1−N3^i, 105.00(9); N8−Ni1−N3, 82.64(9); N8^i −Ni1−N3, 97.36(9); N6−Ni1−N3, 75.00(9). (i) −*x*, −*y*, −*z*.

Table 1. Physicochemical Properties of **1** and **2** at 25 °C[a]

compound	ν_{max}, cm^{-1} (ϵ, M^{-1} cm^{-1})	$E_{1/2}$, mV vs NHE	pK_{a1}; pK_{a2}; pK_{a3}	log β_1; log β_2
$[Ni^{II}(AAZ)_2]^{2+}$ [b]	28 800 (20.0); 19 400 (8); 12 500 (7.6); 11 000 (sh)	1046	2.10; 6.37; 9.26	11.39; 6.54
$[Ni^{II}([9]aneN3)_2]^{2+}$	30 300 (12.0); 20 000 (9.0); 12 500 (9.0); 11 500 (sh)[c]	950[d]	nd; 6.82; 10.42[c]	16.24; nd[c]

[a] In aqueous solution. [b]This work. [c]Reference 7d. [d]Reference 7c. nd: not determined.

A comparison of the stability constant for the AAZ ligand protonation/deprotonation (Figure S2 in the Supporting Information) with that for the [9]aneN3 system reveals further similarities between the two systems, with the monoprotonated $HAAZ^+$ species being present in more than 90% at pH ∼ 8.0. As with the [9]aneN3 ligand,[7d] the first dissociation for the AAZ ligand is that of a strong acid ($pK_{a1} = 2.1$). Figure S3 in the Supporting Information shows the species distribution curves for the Ni^{II}(AAZ) system in a 1:2.2 metal ion/ligand ratio (the ligand is present in a concentration of 10% above a ratio of 1:2 metal/ligand). As can be visualized from Figure S3 in the Supporting Information, the metal ion is complexed at pH values above 2.0, forming the $[Ni(AAZ)]^{2+}$ species, which reaches a maximum formation of 99.2% at pH = 4.6 as the only complex species. The $[Ni(AAZ)_2]^{2+}$ species is formed at pH values above 5.0. It reaches a maximum formation at pH = 10, where it is 99.8% formed. As this species is forming, the H_2AAZ^{2+} species decreases and the curve for $[Ni(AAZ)_2]^{2+}$ rises. The free monoprotonated and completely deprotonated species of the ligands, $HAAZ^+$ and AAZ, are formed because the ligand

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(10) The AAZ ligand reacts with $Ni(ClO_4)_2 \cdot 6H_2O$ in a CH_3CN solution (stoichiometry 2:1) to form the stable $[Ni^{II}(AAZ)_2](ClO_4)_2$ (**1**) complex. Lilac crystals of **1** suitable for X-ray analysis were obtained after allowing the solution to stand at room temperature for 2 days. Complex **3** was prepared by simultaneously adding methanolic solutions of $Zn(OAc)_2 \cdot 6H_2O$ (0.5 mmol) and $Fe(ClO_4)_3 \cdot 9H_2O$ (0.5 mmol) to a methanolic solution containing the ligand H_2AAZBPMP (∼0.5 mmol, generated in situ) and NaOAc (1.0 mmol) with stirring to yield a dark purple solution. After allowing the solution to stand for a few days at room temperature, suitable crystals for X-ray analysis were formed. Complexes **1** and **3** gave satisfactory elemental CHN analysis.

(11) X-ray analysis. Complex **1**: $C_{12}H_{30}Cl_2N_6NiO_8$, fw 516.03, monoclinic, $P2_1/n$, $a = 9.3031(7)$ Å, $b = 13.749(1)$ Å, $c = 9.383(1)$ Å, $\beta = 119.673(5)°$, $V = 1042.79(19)$ Å^3, $Z = 2$, $\mu = 1.239$ mm^{-1}, unique 1851 [R(int) = 0.0147], parameters 149, GOF(F^2) = 1.067, R1 = 0.0311, wR2 = 0.0817. Complex **3**: $C_{31}H_{39}ClFeN_5O_9Zn$, fw 782.34, triclinic, $P\bar{1}$, $a = 11.561(3)$ Å, $b = 12.747(2)$ Å, $c = 13.333(2)$ Å, $\alpha = 98.03(2)°$, $\beta = 99.01(1)°$, $\gamma = 115.28(1)°$, $V = 1707.2(6)$ Å^3, $Z = 2$, $\mu = 1.265$ mm^{-1}, unique 6068 [R(int) = 0.0404], parameters 433, GOF(F^2) = 1.022, R1 = 0.0501, wR2 = 0.1447.

is in excess, and they reach a maximum of 20% and 10%, respectively. At this point, it is important to note that even though the stability constant (log $\beta_1 = 11.39$) for the formation of the $[Ni(AAZ)]^{2+}$ species is ~5 orders of magnitude lower than that observed for $[Ni^{II}([9]aneN3)]^{2+}$, it is significantly higher (~10^4) than that observed for the formation of the $[Ni^{II}(AAZ)_2]^{2+}$ complex. Such an unexpected behavior and the magnitude of D_q is most probably related to severe steric constraints imposed by the AAZ ligand, in full agreement with the interpretation given for the nickel(II) 1,4,7-triazacyclononane system.

The cyclic voltammogram (CV) of **1** (Figure S4 in the Supporting Information) in an aqueous 0.1 M $LiClO_4$ solution reveals one reversible wave (scan rate: 10−200 mV s^{-1}) in the 0.00−1.10 V potential range vs Ag/AgCl, which is assigned to the $[Ni(AAZ)_2]^{3+/2+}$ couple. The redox potential of $E_{1/2} = 1046$ mV vs NHE indicates that the Ni^{III} is a strong oxidant and it is only slightly anodically shifted when compared to the corresponding $E_{1/2}$ value of 950 mV observed in $[Ni^{II}([9]aneN3)_2]^{2+}$.[7c]

Finally, aiming to functionalize the AAZ ligand, a common feature observed for [9]aneN3,[2,3] we have synthesized, in situ, the unsymmetrical dinucleating $H_2AAZBPMP$ ligand. In fact, in this sense, AAZ has an inherent advantage over [9]aneN3 because it has two distinct amine functions in its structure, and this, of course, can be used to simplify several organic synthetic procedures. Here we used the primary amine of AAZ to further conjugate it with a carbonyl group. Because the $H_2AAZBPMP$ ligand is completely unsymmetric, with its harder site (NNO donor) being adequately projected for coordination to M^{III} centers, as observed for other dinucleating ligands containing this tridentade core,[8] the synthesis of the heterodinuclear complex **3** is straightforward.[10] An ORTEP drawing of the cation in **3** is shown in Figure 2, while the main bond lengths and angles are given in the figure caption.

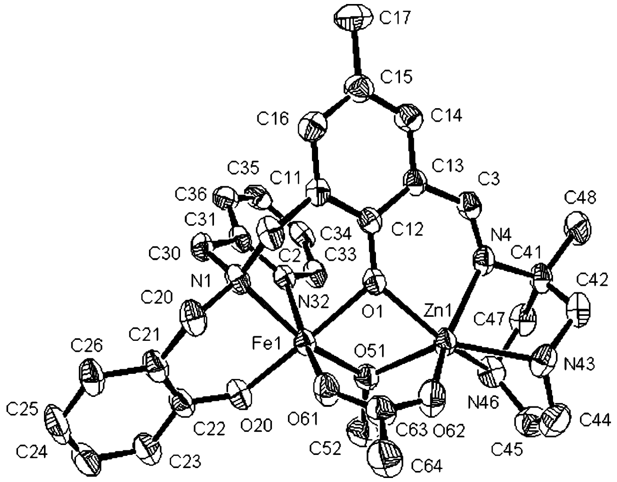

Figure 2. ORTEP of the cation of complex **3**. Ellipsoid at the 40% probability level. Selected bond lengths and angles (Å and deg): Fe1−O20, 1.883(3); Fe1−O51, 1.924(3); Fe1−O61, 2.029(3); Fe1−O1, 2.053(3); Fe1−N32, 2.157(4); Fe1−N1, 2.195(4); Zn1−O51, 2.063(3); Zn1−N4, 2.082(4); Zn1−O62, 2.101(4); Zn1−O1, 2.161(3); Zn1−N43, 2.216(4); Zn1−N46, 2.257(4); Fe1−Zn1, 3.079(1); O20−Fe1−O51, 100.39(14); O20−Fe1−O61, 93.21(15); O51−Fe1−O61, 96.34(15); O20−Fe1−O1, 176.85(14); O51−Fe1−O1, 82.75(13); O61−Fe1−O1, 86.12(14); O20−Fe1−N32, 95.68(15); O51−Fe1−N32, 92.06(14); O61−Fe1−N32, 166.48(15); O1−Fe1−N32, 84.45(13); O20−Fe1−N1, 88.33(15); O51−Fe1−N1, 166.40(15); O61−Fe1−N1, 93.55(15); O1−Fe1−N1, 88.65(13); N32−Fe1−N1, 76.58(14); O51−Zn1−N4, 126.16(15); O51−Zn1−O62, 89.02(15); N4−Zn1−O62, 138.53(17); O51−Zn1−O1, 77.00(12); N4−Zn1−O1, 82.16(14); O62−Zn1−O1, 86.18(14); O51−Zn1−N43, 145.69(15); N4−Zn1−N43, 79.37(16); O62−Zn1−N43, 80.77(15); O1−Zn1−N43, 134.11(14); O51−Zn1−N46, 88.80(15); N4−Zn1−N46, 81.33(16); O62−Zn1−N46, 125.30(17); O1−Zn1−N46, 145.55(15); N43−Zn1−N46, 71.40(16); C12−O1−Fe1, 126.3(3); C12−O1−Zn1, 132.5(3); Fe1−O1−Zn1, 93.86(13); C22−O20−Fe1, 134.1(3); Fe1−O51−Zn1, 101.09(14); Fe1−O51−Zn1, 101.09(14).

The molecular structure[11] of **3** shows that in the dinuclear $[Fe^{III}Zn^{II}(AAZBPMP)(\mu\text{-}OMe)(\mu\text{-}OAc)]^+$ unit the Fe^{III} and Zn^{II} ions are bridged by the phenolate oxygen O1 of $AAZBPMP^{2-}$ and by exogenous carboxylate and methoxy groups. While the two nitrogens N1 and N32, from the tertiary amine and the pyridine group and the oxygen O20 of the terminal phenolate complete the N_2O_4 coordination of Fe^{III}, the N_3O_3 coordination sphere of Zn^{II} is complemented by the three nitrogens N4, N43, and N46 of the AAZ pendent arm. The bond lengths around the Fe^{III} average to 2.040(3) Å, a value that is in agreement with those observed in other dinuclear $Fe^{III}M^{II}$ complexes containing the [*N*-(2-hydroxybenzyl)(2-pyridylmethyl)amine], HBPA) structural unit.[8] Zn^{II} lies in a highly distorted octahedral coordination environment because of severe steric constraints imposed by the imine−AAZ pendent arm, and as expected, the bonds around Zn^{II} are significantly longer and average to 2.146(3) Å. The $Zn-N_{imine}$ bond length is ~0.15 Å longer than the $Zn-N_{amine}$ bond lengths, and this can be attributed to the higher basicity of the imine nitrogen. In the dinuclear $\{Fe^{III}(\mu\text{-}OMe)(\mu\text{-}OAc)Zn^{II}\}$ core, the Fe^{III} and Zn^{II} centers are 3.08 Å apart, a distance that is comparable to the $Fe^{III}\cdots Zn^{II}$ distance observed in the active site of red kidney bean purple acid phosphatase.[8a] It is important to note that, although in the synthesis of **3** an excess of acetate was used, only one OAc^- bridging group was incorporated into the heterodinuclear unit, a result that indicates that the imine−AAZ pendent arm in the $H_2AAZBPMP$ ligand most probably plays the main role in the easy obtention of **3**. It should be noted that the synthesis of unsymmetrical $M^{II}(\mu\text{-}OAc)_2M^{III}$ complexes containing the 2,6-diaminomethyl-4-methylphenol moiety is a common feature already described in the literature.[8]

In summary, the easy and cheap synthesis of AZZ[6] and the similarities of the structural and physicochemical properties of AAZ and its nickel complex with [9]aneN3, together with the structure of the $Fe^{III}Zn^{II}$ complex obtained from a AAZ-functionalized ligand, highlight this system as being a prominent candidate to mimic important properties of 1,4,7-triazacyclononane.

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Supporting Information Available: X-ray crystallographic details for complexes **1** and **3** in CIF format. Figures S1−S4 showing a UV−vis spectrum, protonation constants, stability constants, and CVs, respectively (PDF). This material is available free of charge via the Internet at http://pubs.acs.org or www.ccdc.cam.ac.uk (CCDC 271565 and 271566).

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