An oxido-bridged dinickel(II) complex with L-alanine derived spiro ligand from an unusual mannich aminomethylation

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The crystal structure of a centrosymmetric dinuclear nickel(II) complex, formed from the reaction of bis(L-alaninato)nickel(II) with formaldehyde and methylamine, shows two bridging 2,4,8,10-tetramethyl-5-oxido-5′-carboxylato-$2\lambda^5$,4,8,10-tetraazaspiro[5.5]undec-2-en(234-del)-ylium ligands, L, and two formato ligands; each nickel atom exists in a *trans*-N_2O_4 octahedral geometry with an average (μ-O)–Ni distance of 2.033(1) Å and Ni$\cdots$Ni*i* distance of 2.894(1) Å. Formation of L implies an unprecedented deamination step involving activation of both the α-carbon and the α-methyl hydrogen atoms of the L-alaninato moiety.

Keywords: Dinickel(II) complex; L-Alanine; Mannich aminomethylation; Deamination; Crystal structure

1. Introduction

The biological importance of nickel is seen from its presence in six types of metalloenzymes, namely, ureases, hydrogenases, methyl coenzyme M reductase, carbon monoxide dehydrogenase, acetylcoenzyme A synthase, and nickel superoxide dismutase [1]. Urease, the only nickel-containing metallohydrolase, catalyses the hydrolysis of urea to ammonia and carbon dioxide [2]. The microbial urease from Klebsiella aerogenes has been found to contain two nickel(II) ions, which are 3.5 Å apart within

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the dinuclear active site [2]. In order to understand the mechanism of the hydrolysis of urea, various researchers have synthesized dinickel(II) complexes to provide models for urease [2–6].

In contrast, mononuclear nickel(II) complexes with chelated amino acids show anomalous behavior as these complexes retard amino acid racemization, while other metal complexes of the same amino acids enhance it [7]. A similar behavior has been observed while investigating the Mannich aminomethylation of bis(α-aminoacidato)metal(II) complexes [8–13]. Methylamine (methanamine) catalyzes the reaction of bis(L-alaninato)copper(II), **1a**, with formaldehyde in the pH range 6.0–9.0 to yield a bis(4-methyloxazolidine-4′-carboxylato)copper(II) complex, which has been previously synthesized in basic solution [14]. Other bis(L-alaninato)metal(II) complexes (metal = nickel, zinc), however, do not react similarly with formaldehyde even in the presence of bases [14]. Both **1a** and bis(L-alaninato)zinc(II), **1b**, undergo Mannich aminomethylation with formaldehyde and ammonia to yield metal(II) complexes of $3N,7N$-(1,3,5,7-tetraazabicyclo-[3.3.1]nonyl)dipropionate; bis(L-alaninato)nickel(II), **1c**, is unreactive and yields hexamine in all cases [11]. In the Mannich aminomethylation reaction of **1**, reaction occurs at the amino nitrogen while the α-carbon and the α-methyl groups of the chelated L-alanine are unreactive [11–14]. Unexpectedly, **1c** reacts with neutralized formaldehyde and methylamine to yield a dinickel(II) complex. Both the activation of the methyl protons of the alanine moiety and the deamination of alanine to yield the pyruvate in the present Mannich reaction of **1c** are unprecedented.

2. Experimental

2.1. *Synthesis*

The dimer was obtained by allowing the bluish solution mixture of **1c** (1.2 g, 0.005 mol), formaldehyde (10 mL, 40% aqueous solution) previously neutralized with aqueous sodium hydroxide, and methylamine (amount added to raise pH to ~8.2) to stand at room temperature until it changed to a green solution. No attempt was made to exclude air. Slow evaporation of the green solution afforded green cuboidal crystals suitable for X-ray structure analysis. The whole process of color change and formation of crystals took about a month (yield, 1.0 g; 45% based on theoretical maximum yield of 0.0025 mol). Elemental analysis: found (%): C, 34.98; H, 7.20; N, 15.54. Calculated for $C_{26}H_{60}N_8O_{18}Ni_2$ (%): C, 35.15; H, 7.04; N, 15.77. IR (KBr, cm^{-1}): 3354s, 3020w, 2973w, 2820w, 2740w, 1702s, 1598s, 1475m, 1438w, 1412w, 1398w, 1381m, 1360s, 1304w, 1243w, 1223m, 1212m, 1179m, 1166m, 1130m, 1104m, 1080m, 1062m, 1042m, 1020w, 983w, 962w, 944m, 824m, 794m, 657m, 536m, 487m, 444m, 420m, 403m, 380w.

2.2. *Physical measurement and X-ray crystallography*

C, H and N microanalysis of the dinickel(II) complex, **2**, was carried out with a Perkin–Elmer 2400 C, H, N, S and O elemental analyser. A Perkin–Elmer 1000 FT-IR spectrophotometer was used to obtain the infrared spectrum of the compound. A solid diffuse reflectance spectrum of the complex as an MgO disc was recorded on

a Hitachi 330 spectrophotometer. UV-vis spectroscopic measurement on an aqueous solution of **2** was carried out on a Shimadzu UV-160 spectrophotometer. Electrospray ionisation mass spectra (ESI-MS) of **2** were obtained by using a Finnigan MAT LCQ with a spray voltage of 4.5 kV. The solvent was a 1 : 1 v/v water/methanol mixture and the mass spectrum was collected for different heating capillary temperatures (at 100 and 150°C). The diffraction data for **2** were collected on a Siemens CCD area-detector diffractometer at 168 K for a crystal of size $0.50 \times 0.50 \times 0.50$ mm using the ω-scan technique. Lorentz-polarization correction and multi-scan absorption correction were applied [15]. The structure was solved and refined by using SHELXS-97 and SHELXL-97, respectively [16, 17]. The structure was refined from 3240 reflections to $R = 0.0324$ and $wR = 0.0899$. The carbon-bound hydrogen atoms were generated geometrically, and were included in the refinement in the riding model approximation. The water hydrogen atoms were located from difference Fourier maps, and were refined with a distance restraint of O–H 0.85 ± 0.01 Å. Crystal data, selected bond lengths and angles and hydrogen bonding parameters are listed in tables 1 and 2. Complete bond lengths and bond angles, and other crystal data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre (CCDC No. 215135).

Table 1.   Crystal data and structure refinement.

Formula	$C_{26}H_{60}N_8O_{18}Ni_2$	a (Å)	23.747(2)
Formula weight	890.24	b (Å)	9.8239(7)
Crystal system	Monoclinic	c (Å)	18.843(1)
Space group	$C2/c$	α (°)	116.401(1)
V (Å^3)	3862.1(5)	T (K)	168
D_c (g cm^{-3})	1.531	Z	4
$F(000)$	1888	λ (Å)	0.71073
μ (mm^{-1})	1.058		
Index ranges	$-28 \leq h \leq 29$;	θ range (°)	1.91–26.38
	$-11 \leq k \leq 12$;		
	$-22 \leq l \leq 23$		
Data [$I > 2\sigma(I)$]	3240	Reflections	3929
R [$I > 2\sigma(I)$]	0.032	Goodness-of-fit on F^2	1.054
wR	0.090	R (all data)	0.042
		wR	0.093

Table 2.   Selected bond lengths (Å) and angles (°).

Ni1–O1	2.079(1)	O1–Ni1–O3	78.8(1)
Ni1–O3	2.045(1)	O1–Ni1–O3i	167.3(1)
Ni1–O3i	2.021(1)	O1–Ni1–O4	97.0(1)
Ni1–O4	2.027(2)	O1–Ni1–N3i	99.2(1)
Ni1–N3i	2.190(2)	O1–Ni1–N4	91.3(1)
Ni1–N4	2.300(2)	O3–Ni1–O3i	89.2(1)
Ni1$\cdots$Ni1i	2.894(1)	O3–Ni1–O4	175.2(1)
		O3–Ni1–N3i	88.9(1)
		O3–Ni1–N4	86.8(1)
		O3i–Ni1–O4	95.1(1)
		O3i–Ni1–N3i	84.6(1)
		O3i–Ni1–N4	83.8(1)
		O4–Ni1–N3i	89.4(1)
		O4–Ni1–N4	95.7(1)
		N3i–Ni1–N4	167.6(1)

Symmetry transformation: $i = 1/2 - x, 1/2 - y, 1 - z$.

3. Results and discussion

3.1. *Crystal structure*

The crystal structure of **2** (figure 1), shows two nickel(II) atoms, two zwitterionic oxido-bridging ligands, 2,4,8,10-tetramethyl-5-oxido-5′-carboxylato-$2\lambda^5$,4,8,10-tetraaza-spiro[5.5]undec-2-en(234-del)-ylium, two formate ions and eight uncoordinated water molecules (not shown). This complex is formulated as $[Ni(C_{12}H_{21}N_4O_3)(HCOO)]_2 \cdot 8H_2O$. Each nickel(II) atom has a distorted octahedral geometry. The ligating atoms (2N, 4O) consist of a formate oxygen atom, an amine nitrogen atom (derived from methylamine), carboxylate oxygen and μ-oxido atoms found on the same spiro ligand; and an amine nitrogen and μ-oxido atoms of the second spiro ligand. The four equatorial ligating atoms are oxygen atoms bearing a formal uninegative charge and their Ni–O distances ranges from 2.021(1) to 2.047(1) Å; the two elongated axial Ni–N distances average 2.245 Å. The $[Ni(C_{12}H_{21}N_4O_3)(HCOO)]_2$ complex interacts with uncoordinated water molecules to form a three-dimensional network.

Uniquely, each spiro ligand chelates to a nickel(II) via the pyruvate moiety and bridges the two nickel(II) atoms by using (i) the oxido oxygen atom (O3) of the pyruvate moiety and (ii) two separate nitrogen atoms (N3 and N4) of one six-membered diaza ring (N3–C8–C7–C12–N4). The four-membered bridging ring (Ni1–O3–Ni*i*–O3*i*) has a bite angle of 89.2(1)° and this does not cause severe distortion of nickel(II) octahedral geometry, unlike a similar oxido-bridged diiron(III) dimer with a bite angle
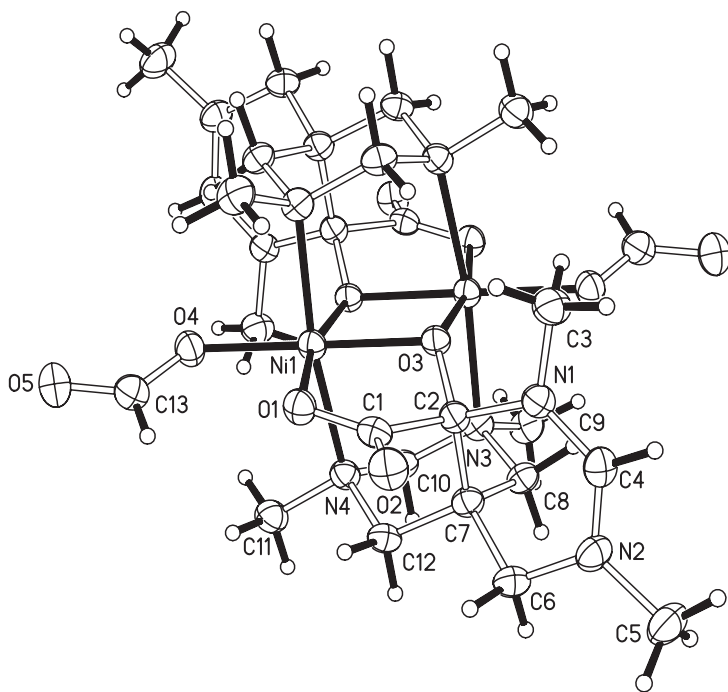

Figure 1. ORTEP drawing with thermal ellipsoids for non-hydrogen atoms at 50% probability. Unlabelled atoms are generated by the symmetry transformation $1/2 - x, 1/2 - y, 1 - z$.

of 76.2° [18]. The Ni1–O3–Ni*i* bridging angle of 90.8(1)° in **2** is significantly smaller than those formed by bridging phenolate oxygen (97.4°, 118.0°) in other dinickel(II) complexes [4, 5] but is comparable to that formed by a single-atom O-bridged urea (91.4(1)°) in a dinickel(II) complex with three different bridging groups [4]. The Ni1···Ni1*i* distance of 2.894(1) Å in **2** is shorter than 2.966(1) Å found in the above O-bridged urea complex [4], other dinickel(II) complexes (3.085, 3.431, 3.376, 3.4–3.5 Å) [3, 5, 19, 20] and some ureases (3.5, 3.7 Å) [21, 22]. Thus far, **2** has the shortest Ni···Ni distance among the reported models of urease. Besides the possibility of mimicking the hydrolytic property of ureases, complex **2** may show antiferromagnetic exchange coupling because of its significantly shorter Ni···Ni bond distance [4].

Coordination of the diaza ring (at N3 and N4) apparently results in a chair-conformation and a common shift in amine nitrogen orbital hybridization towards sp^3. In contrast, the other uncoordinated six-membered diaza ring has a two-open-flap-envelope conformation and its amine nitrogen atoms (N1 and N2) exhibit more sp^2 hybridization for bonding, as evidenced by shorter N1–C4 and N2–C4 bond lengths (average, 1.312(2) Å) compared to the corresponding N3–C10 and N4–C10 bond lengths (average, 1.483(2) Å) in the former diaza ring, and the co-planarity of N1–C4–N2–C6 atoms. The planar C4 atom seems to be part of a delocalized imminium where the positive charge resonates between the N1 and N2 atoms. This delocalized system is supported by the fact that both N1–C4 and N2–C4 bonds are intermediate between an imine C=N double bond (1.267(3)–1.287(5) Å) and a C–N single bond (amine 1.458–1.53 Å, pyridines 1.342–1.367 Å) [23].

From the earlier considerations, the spiro ligand, L, is depicted as shown in figure 2. Its chemical formula is $[C_{12}H_{21}N_4O_3]^-$. At a heating capillary temperature of 100°C, the electrospray ionization mass spectrum of the dinickel(II) complex **2** shows a m/z peak of 701.2 (100%) which can be ascribed to $[Ni_2(C_{12}H_{21}N_4O_3)_2 (HCOO)]^+$, **3**, with a calculated mass of 701.10 while an m/z 328.04 ($\sim$10%) corresponds to $[Ni(C_{12}H_{21}N_4O_3)]^+$, **4**, with a calculated mass of 328.04. On increasing the capillary temperature to 150°C, the m/z 701.2 peak disappears and the m/z peak 328.2 increases in intensity to 100%. Presumably, **4** arises from the dissociation of **3**.

Formation of L may be initiated by conversion of the L-alaninate to pyruvate. This conversion must involve C–N bond cleavage, and this may be akin to cleavage
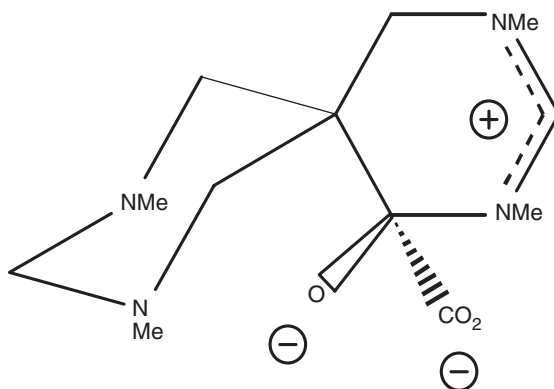
Figure 2. Structure of the spiro ligand, L.

of the C–N bond in the conversion of urea to ammonia in dinickel(II) complexes and ureases, where the very electronegative nickel ions are postulated to act together to activate the normally inert urea and to polarize the C–NH$_2$ bond [3, 24]. This involvement of the dinickel is suggested because it has been found that the mononuclear Ni(L-ala)$_2$ is not reactive in Aldol-type and Mannich aminomethylation reactions [11–14]. Support for this also comes from an earlier investigation where the hydroxide-bridged dinuclear nickel complex, [Ni$_2$(μ-OH)(μ-OH$_2$)(bdptz)(H$_2$O)$_2$] (OTs)$_3$, catalyzes the decomposition of urea to ammonia and cyanate while the mononuclear nickel species, [Ni(terpy)(OH$_2$)$_3$](OTs)$_2$, is inactive under identical conditions [3]. Although such deaminations of α-amino acids are commonly enzyme catalyzed, the present deamination of L-alaninate is unusual and as of yet it is uncertain how this occurs. However, similar non-enzymatic deamination of amino acids by pyridoxal in the presence of transition metal cations or complexes has been reported [25–27]. Chelation of pyruvate to the nickel can activate the keto-carbon atom to attack by a nucleophile and increase the acidity of the methyl protons; this activation is similar to cobalt(III) coordinated 2-iminopropanoate (e.g. [(NH$_3$)$_4$Co(NH=C(CH$_3$) COO]$^{2+}$) in which the metal ion activates the imine carbon to attack by a nucleophile and makes the imine NH and CH$_3$ groups more acidic [28, 29]. The postulated pyruvate complex may react, as an acidic substrate, with formaldehyde and methylamine to yield the final coordinated tetraazaspiro ligand, L. Although the use of aliphatic amine (including methylamine) and formaldehyde in template synthesis of polyaza macrocycles is widely reported [30, 31], the present reaction is the first to yield a polyaza spiro ligand. Lastly, the formate can arise from a Canizzarro reaction of formaldehyde with itself in the presence of the strong base NaOH.

3.2. *Electronic spectrum*

In the solid state, the green dinickel(II) complex, **2**, exhibits three transitions at 260, 395 and 660 nm due to LMCT, $^3A_{2g} \rightarrow ^3T_{1g}(P)$ and $^3A_{2g} \rightarrow ^3T_{1g}(F)$, respectively. These transitions are typical of nickel in an octahedral environment [32, 33]. That six-coordination of the nickel has been retained in aqueous solution is shown by the corresponding transitions at 222 ($\varepsilon = 26{,}600 \, \mathrm{M^{-1} \, cm^{-1}}$), 397 ($\varepsilon = 47 \, \mathrm{M^{-1} \, cm^{-1}}$) and 695 nm ($\varepsilon = 21 \, \mathrm{M^{-1} \, cm^{-1}}$). The visible absorption of the aqueous solution of this compound is comparable to that of the green [Ni(H$_2$O)$_6$]$^{2+}$ which has λ_{max} values at 400 nm (25,000 cm^{-1}) and 714 nm (14,000 cm^{-1}) [34].

Acknowledgements

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