Synthesis and Spectral, Thermal and Structural Characterization of a Vitamin B13 Complex of Nickel(II) with 2-Aminothiazole, *mer*-[Ni(HOr)(H_2O)$_2$(ata)$_2$]

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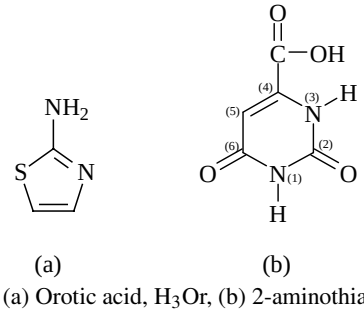
The *mer*-bis(2-aminothiazole)diaqua-orotato-nickel(II) complex, *mer*-[Ni(HOr)(H_2O)$_2$(ata)$_2$] (**1**), was synthesized and characterized by spectral (IR and UV/vis) and thermal studies. In addition, the crystal structure of the complex was determined by single crystal X-ray diffraction. The complex crystallizes in the triclinic system, space group $P\bar{1}$. The orotate ligand is coordinated to the nickel(II) atom through a nitrogen atom of the pyrimidine ring and an oxygen atom of the carboxylate group as a bidentate dianion. The coordination of the Ni(II) ion is extended to six by the two 2-aminothiazoles (ata) and two water molecules. The thermal decomposition has been studied in a static air atmosphere.

Key words: Orotato Complex, Vitamin B13 Complex, 2-Aminothiazole

Introduction

Aminothiazoles are a group of biologically important compounds having a wide range of activities such as anti-tumor, anti-anoxic and anti-oxidant properties [1, 2]. Previous reports have shown that aminothiazoles possess anti-oxidant activity and inhibit lipid peroxidation [2, 3]. 2-Aminothiazoles [Scheme 1. (a)] are known mainly as biologically active compounds with a broad range of activities and as intermediates in the synthesis of antibiotics, well known sulfa drugs, and some dyes [4]. Metal complexes of vitamin B13 [orotic acid, uracil-4-carboxylic acid, 1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidine carboxylic acid, H_3Or, Scheme 1. (b)] and its derivatives continue to attract attention because of their multidentate functionality and their pivotal role in bioinorganic chemistry [5]. Orotic acid is a precursor in the biosynthesis of pyrimidine bases and nucleic acids in living organisms [6] and has been widely exploited in medicine. Besides its biological importance, vitamin B13 is also an interesting potentially multidentate ligand. It can be coordinated to metal ions through the nitrogen atoms, the two carbonyl oxygen and the carboxylate oxygen atoms as a monodentate, bidentate and polydentate donor. The most common coordination mode of



Scheme 1. (a) Orotic acid, H_3Or, (b) 2-aminothiazole, ata.

HOr^{2-} is ligation through the deprotonated nitrogen atom of the pyrimidine and one carboxylate oxygen atom so forming a five-membered chelate ring. Crystal structures were described for mononuclear Ni(II)-orotate complexes with triethanolamine [7], 4-methylimidazole [8], imidazole [9], nicotine amide [10], water [11, 12], 2,2′-bipyridylamine, 1,10-phenanthroline, and 2,9-dimethyl-1-1,10-phenanthroline [13], with the orotate ligands acting as bidentate donors. In polymeric [Ni(HOr)(H_2O)$_3$]$_n$ [13, 14] and [Ni(HOr)(NH_3)-(H_2O)$_2$]$_n$ [15] complexes, orotate acts as a bridging ligand [orotato-N(3), O_{acid}, O(6) or O(2)]. In some of the complexes, orotate acts as a counter ion [15 – 18]. Orotic acid exhibits a double or triple hydrogen-bonding functionality, depending on the metal coor-

dination mode. The potential for molecular recognition of organic molecules may have interesting implications in both pharmaceutical and materials chemistry, where the orotate or hydrogenorotate anions can be used as versatile synthons for the assembly of metal-organic supramolecular architectures [19]. In this study, we describe the synthesis, spectroscopic (IR and UV/vis), thermal and structural characterization of *mer*-[Ni(HOr)(H_2O)$_2$(ata)$_2$] (**1**).

Results and Discussion

Magnetic susceptibility and UV/vis spectrum

The Ni(II) complex exhibits a magnetic moment of 2.92 BM, which corresponds to two unpaired electrons. The UV/vis spectrum of a solution in H_2O exhibits absorption bands at 394 (ε = 18 L mol^{-1} cm^{-1}), 638 (ε = 5) and 895 nm (ε = 4), assigned to the $^3A_{2g} \rightarrow {}^3T_{1g}$ (P), $^3A_{2g} \rightarrow {}^3T_{1g}$ and $^3A_{2g} \rightarrow {}^3T_{2g}$ *d-d* transitions, respectively. The Δ_o value for Ni(II) has been calculated as 11170 cm^{-1} [21].

IR Spectrum

The most significant frequencies in the IR spectrum of **1** are given in Table 1. The spectrum shows a strong band at 3453 cm^{-1} due to aqua ligands. The bands at 3350 and 3292 cm^{-1} are attributed to the NH_2 stretching vibration of the ata ligands. The weak band at 2937 cm^{-1} is due to ν_{CH} vibrations. The carbonyl stretching bands of the free orotic acid observed at 1729 and 1719 cm^{-1} ($\nu_{C=O(acid)} + \nu_{C(2)=O}$) and 1700 cm^{-1} [$\nu_{C(6)=O} + \nu_{ring}$] [22] are shifted to 1650 and 1625 cm^{-1} in the spectrum of **1**. This shift indicates that the orotate ligand is coordinated as a dianion through the nitrogen atom of the pyrimidine ring and an oxygen atom of the carboxylate group. The intense band at 1592 cm^{-1} corresponds to ν_{CC} vibrations of the pyrimidine ring, while the $\nu_{(C=N)}$ and $\nu_{(C-N)}$ vibrations are observed at 1534 and 1280 cm^{-1}, respectively.

Thermal analysis

The thermal decomposition of **1** was followed by DTG up to 1000 °C in a static air atmosphere. The first stage at 147 – 200 °C is related to the release of two water ligands with an endothermic effect (DTG_{max} = 197 °C, mass loss found 9.12 %, calcd. 8.03 %). The following stages at 201 – 448 °C are related to the decomposition of the ata ligand and decarboxylation of the orotate ligand. The strong exothermic stage is associated with the burning of the organic residue. The final decomposition product is NiO. The total mass loss is 82.80 % (calcd. 83.37 %) for the 30 – 525 °C temperature range.

Table 1. IR spectral data of **1** (cm^{-1}) and of orotic acid.

Assignment	Orotic acid [22]	**1**[a]
ν(OH)	3241 sh	3453 s
ν(NH_2)	–	3350, 3292 s
ν($N_{(3)}$H)	3154 m	3139 s
ν($N_{(1)}$H)	3137 m	–
ν(CH)	3099 s	2937 w
ν($C=O_{acid} + C_{(2)}=O$)	1729, 1719 vs	1650 vs
ν($C_{(6)}=O$) + ν_{ring}	1700 vs	1625 vs
ν(C=C) + ν_{ring}	1653 vs	1592 vs
ν(C=N)	1435 s	1492, 1535 m
ν(C=S)	–	1209 m

[a] Abbreviations: w – weak; m – medium; s – strong; vs – very strong; b – broad.

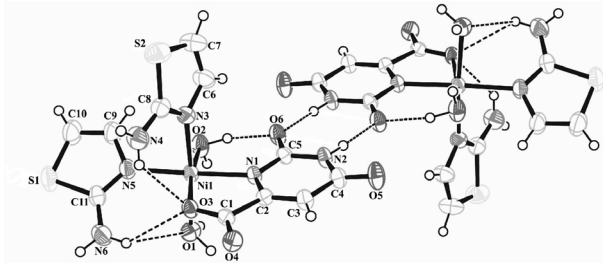


Fig. 1. The AD:DA pairs present in the crystal structure of **1**, showing the intra- and some of the intermolecular hydrogen bonding.

*Crystal structure of **1***

The details of the crystal structure are given in Table 2. The molecular structure is shown in Fig. 1. Selected bond distances and angles are given in Table 3. The crystal structure consists of discrete [Ni(HOr)(H_2O)$_2$(ata)$_2$] molecules. The Ni(II) ion has a distorted octahedral configuration with a bidentate HOr^{2-} ligand, two water and two ata ligands (Fig. 1). The N and O atoms of the orotate anion are bonded to the metal cation to form a five-membered chelate ring [Ni(1)–N(1) = 2.055 (2) and Ni(1)–O(1) = 2.049(2) Å]. All N–Ni–N, N–Ni–O and O–Ni–O bond angles deviate significantly from 90 or 180°, which is presumably a result of the steric constraints arising from the shape of the ligands. The C–O distances are almost equal in the uncoordinated HOr^{2-} anion and its Ni(II) and Li(I) complexes [23]. In **1**, the C–O bond lengths are in the range 1.254(3) – 1.244(3) Å, which is comparable with those in similar Ni(II) complexes [8, 17].

Table 2. Crystal data and structure refinement parameters for **1**.

Empirical formula	$C_{11}H_{14}N_6O_6S_2Ni$
Formula weight [g mol^{-1}]	449.11
Crystal size [mm^3]	$0.220 \times 0.157 \times 0.070$
Temperature [K]	293(2)
Wavelength (MoK_α) [Å]	0.71073
Crystal system	triclinic
Space group	$P\bar{1}$
Unit cell dimensions:	
a, b, c [Å]	8.294(1), 8.710(1),12.060(1)
α, β, γ [°]	97.42(7), 99.00(1), 95.78(7)
V [Å^3]	846.8(1)
Z	2
Absorption coefficient [mm^{-1}]	1.436
$D_{calc.}$ [Mg m^{-3}]	1.761
θ range for data collection [deg]	2.51–28.01
Measured reflections	13465
Independent reflections	3990
Absorption correction	integration
Final R indices [$F^2 \geq 2\sigma(F^2)$]	R_1 = 0.0469; wR_2 = 0.1826
	R_1 (all data) = 0.9600
Goodness-of-fit on F^2	0.974
Largest difference peak and hole [e Å^{-3}]	0.725 / −0.962

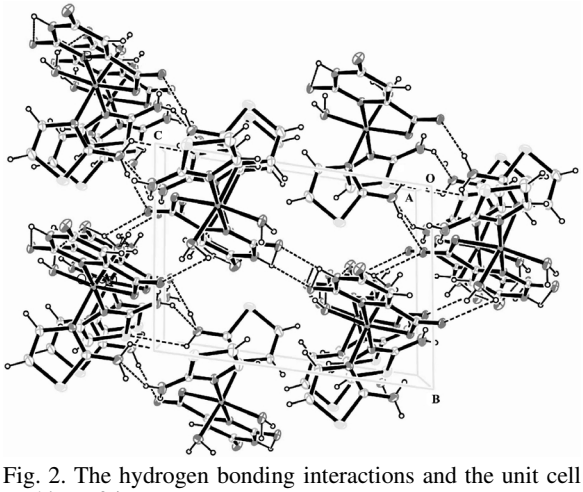


Fig. 2. The hydrogen bonding interactions and the unit cell packing of **1**.

The orotato ligand is almost planar (the r.m.s deviations are 0.0593 Å). A comparison of the Ni–O1, Ni–N3, M–N_{ata} distances, and the O1–Ni–N3 and N_{ata}–M–N_{ata} angles for the orotate and ata metal complexes is given in Table 4.

The crystal is stabilized by strong intermolecular H bonds N–H···O, O–H···O *etc*. The details of this hydrogen bonding are given in Table 5. The orotate ligand is involved in hydrogen bonds with neighboring orotate ligands and aqua ligands through its N and O atoms. As shown in Figs. 1 and 2, each of the HOr^{2-} ligands is doubly H-bonded to a corresponding HOr^{2-} ligand of another Ni(II) complex. These DA:AD type hydrogen bonds involve the pyrimidine carbonyl and the amide N–H groups [N(2)···O(6)^{i} 2.826(3) Å, H···O(6)^{i} 1.98 Å, N(2)–H···O(6)^{i} 170.1°; i: $2-x$, $1-y$, $1-z$]. Double hydrogen bonds are found in nature in guanine tetrads (or G quartets) [24] which are stabilized by a central sodium ion. Some of these interactions are illustrated in Fig. 2. There are also hydrogen bonds between ata and aqua ligands.

Table 3. Selected bond lengths (Å) and angles (°) in **1**.

Ni1–O2	2.107(2)	Ni1–N1	2.055(2)
Ni1–O3	2.049(2)	Ni1–N5	2.080(3)
N5–C11	1.307(4)	S1–C10	1.719(4)
N3–C8	1.313(4)	S2–C7	1.714(5)
N6–C11	1.339(4)	C9–C10	1.332(5)
N4–C8	1.346(4)	C7–C6	1.343(5)
S1–C11	1.735(3)	N5–C9	1.385(4)
S2–C8	1.728(3)	N3–C6	1.374(4)
O3–Ni1–N3	92.03(9)	O3–Ni1–O1	83.89(9)
N1–Ni1–N3	90.10(10)	N1–Ni1–O1	93.65(9)
N5–Ni1–N3	87.57(10)	N5–Ni1–O1	88.67(10)
O2–Ni1–N3	95.00(10)	O1–Ni1–O2	89.61(10)
C11–N5–C9	110.4(3)	C9–C10–S1	110.0(3)
C8–N3–C6	110.9(3)	C6–C7–S2	110.2(3)
N3–C8–N4	125.1(3)	N3–C8–S2	113.7(2)
N5–C11–N6	124.4(3)	N5–C11–S1	113.9(2)
N4–C8–S2	121.2(2)	C10–C9–N5	116.3(3)
N6–C11–S1	121.7(3)	C7–C6–N3	115.7(3)
C10–S1–C11	89.45(17)	C7–S2–C8	89.54(17)

Table 5. Hydrogen bonding interactions in **1**.

D–H···A	d(D–H) (Å)	d(H···A) (Å)	d(D···A) (Å)	<(DHA) (°)
N2–H2···O6^{i}	0.86	1.98	2.826(3)	170.1
N4–H4A···S1^{ii}	0.86	2.80	3.292(3)	118.1
N4–H4B···O4^{iii}	0.86	2.03	2.861(3)	162.8
N6–H6B···N4^{ii}	0.86	2.54	3.320(4)	151.0
O1–H1A···O5^{iv}	0.92(2)	1.90(5)	2.682(3)	141(6)
O1–H1B···O4^{v}	0.93(2)	1.79(2)	2.714(3)	173(6)
O2–H2B···O5^{iv}	0.93(2)	2.20(6)	2.953(4)	137(7)
N4–H4A···O3	0.86	2.18	2.867(3)	136.1
N6–H6A···O1	0.86	2.55	3.090(4)	121.3
N6–H6A···O3	0.86	2.58	3.246(4)	135.6
O2–H2A···O6	0.93(2)	1.77(3)	2.633(3)	153(5)

Symmetry operations: ^{i} $2-x$, $1-y$, $1-z$; ^{ii} $1-x$, $-y$, $2-z$; ^{iii} $2-x$, $-y$, $2-z$; ^{iv} $x-1$, y, z; ^{v} $2-x$, $1-y$, $2-z$.

Experimental Section

All chemicals were purchased as analytical grade. The IR spectrum was obtained with a Bruker Tensor 27 FT-IR spectrometer using KBr pellets in the 4000 – 400 cm^{-1} range. Elemental analyses for C, H and N were performed using a Carlo Erba 1106 microanalyzer. The magnetic susceptibility measurement was performed at r. t. using a Sher-

Table 4. Comparison of the bond lengths and angles of selected Ni-HOr complexes and [$ZnCl_2$(ata)$_2$].

Complexes	Ni–O1 (Å)	Ni–N3 (Å)	O1–Ni–N3 (°)	M–N_{ata} (Å)/N_{ata}–M–N_{ata} (°)
[Ni(HOr)(H_2O)$_4$]·H_2O [20]	2.023(3)	2.049(3)	80.0(1)	–
[Ni(HOr)(H_2O)$_3$]$_n$ [14]	2.064(2)	2.056(2)	79.41(7)	–
[Ni(HOr)(H_2O)$_3$(na)]·2H_2O [10]	2.073(1)	2.048(2)	80.21(6)	–
[Ni(HOr)(H_2O)(4-mim)$_3$]$_2$ · 5H_2O [8]	2.078(2)/2.061(2)	2.084(2)/2.118(2)	79.66(6)/79.92(6)	–
[Ni(HOr)(H_2O)$_2$(im)$_2$] [9]	2.064(1)	2.072(2)	80.12(5)	–
[Ni(HOr)(bipy)(H_2O)$_2$]·2H_2O [11]	2.053(3)	2.067(3)	79.47(11)	–
[Ni(HOr)(NH_3)(H_2O)$_2$]$_n$ [19]	2.08(1)	2.08(1)	78.7(5)	–
[Ni(HOr)(H_2O)(tea)]·H_2O [7]	2.029(1)	2.085(2)	80.08(6)	–
[$ZnCl_2$(ata)$_2$] [29]	–	–	–	2.024(2), 2.011(2)/109.59(2)
[NiHOr(H_2O)$_2$(ata)$_2$] (this work)	2.100(2)	2.108(2)	83.89(9)	2.080 (3), 2.108(3)/87.6(1)

wood Scientific MXI model Gouy magnetic balance. The UV/vis spectrum was obtained for an aqueous solution of the complex (10^{-3} M) with a Unicam UV2 spectrometer in the range 900 – 190 nm. A Perkin Elmer Diamond TG/DTA thermal analyzer was used to record simultaneous TG, DTG and DTA curves in static air atmosphere at a heating rate of 10 °C min^{-1} in the temperature range 20 – 1000 °C using platinum crucibles.

*mer-[Ni(HOr)(H_2O)$_2$(ata)$_2$] (**1**)*

A solution of 2-aminothiazole (0.51 g, 5 mmol) in ethanol (10 mL) was added dropwise and with stirring to a solution of [Ni(HOr)(H_2O)$_4$]·H_2O [20] (0.76 g, 2.5 mmol) in distilled water (30 mL). The solution was heated to 60 °C in a temperature-controlled bath and stirred for 5 h. The reaction mixture was then cooled to r. t. The blue crystals formed were filtered, washed with ethanol and dried in air. $C_{11}H_{14}N_6O_6S_2Ni$ (449.11): calcd. C 29.42, H 3.16, N 18.71; found C 29.34, H 3.16, N 18.73.

Crystallographic analysis

Diffraction experiments were carried out at 296 K on a Stoe IPDS diffractometer. The structure was solved by Direct Methods using the program SHELXS-97 [25]. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares methods with SHELXL-97 [25]. All hydrogen atoms except H1A, H1B, H2A and H2B were located. Data collection: X-Area; cell refinement: X-Area; data reduction: X-RED [26]; molecular graphics: ORTEP-3 for Windows [27]; software used to prepare material for publication: WinGX [28].

CCDC 632158 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

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