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mer-Diaquabis(1*H*-imidazole-κN^3)-(orotato-κ$^2N^3$,O^4)nickel(II)

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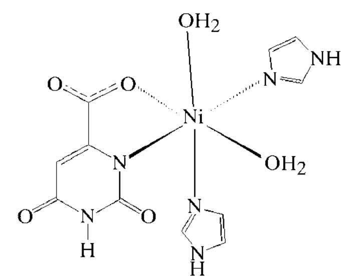
The title mononuclear complex, $[Ni(C_5H_2N_2O_4)(C_3H_4N_2)_2(H_2O)_2]$ or $[Ni(HOr)(im)_2(H_2O)_2]$ (im is imidazole and H_3Or is orotic acid, or 2,6-dioxo-1,2,3,6-tetrahydropyrimidine-4-carboxylic acid), has been synthesized and the crystal structure determination is reported. The Ni^{II} ion in the complex has a distorted octahedral coordination geometry comprised of one deprotonated pyrimidine N atom and the adjacent carboxylate O atom of the orotate ligand, two tertiary imidazole N atoms and two aqua ligands. An extensive three-dimensional network of O*W*—H···O and N—H···O hydrogen bonds, and π–π and π–ring interactions are responsible for crystal stabilization.

Comment

Orotic acid (H_3Or, vitamin B_{13}) and its metal complexes continue to attract attention because of its multidentate functionality and its great significance in living organisms as a precursor of pyrimidine nucleosides (Genchev, 1970; Rawn, 1989; Lalioti *et al.*, 1998). For these reasons, metal orotates have recently attracted growing attention in medicine. Furthermore, nickel, magnesium, palladium and platinum orotate complexes have been screened as therapeutic agents for cancer treatment (Sabat *et al.*, 1980; Karipides & Thomas, 1986; Castan *et al.*, 1990; Kumberger *et al.*, 1993). Orotic acid and its anions, *viz*. H_2Or^-, HOr^{2-} and Or^{3-}, besides being biologically important, are also potentially interesting multidentate ligands, especially above the deprotonation pH values, coordinating to metal ions through the N atoms, the two carbonyl O atoms and the carboxylate O atoms. H_3Or can act as a dibasic acid, depending on the pH range. In the pH range 3–9, orotic acid exists mainly as the readily coordinating monodeprotonated HOr^{2-} anion (the carboxylic acid group has a pK_a value of 2.07; Bach *et al.*, 1990; Lutz, 2001). In basic solutions (pH 9), both the carboxyl group and a heterocylic N atom are deprotonated, so the anion acts as a bidentate ligand. Existing studies of its coordination complexes demonstrate that it occurs as a dianion, often coordinating *via* the N atom and carboxylic acid group, so forming a five-membered chelate ring (Mutikainen, 1987; Mutikainen *et al.*, 1996; Maistralis *et al.*, 2000; Wysokinski *et al.*, 2002; Icbudak *et al.*, 2003; Ölmez *et al.*, 2004). In polymeric orotic acid complexes, the orotate anion bridges the metal ions through the carboxylate group and N and O atoms, forming one-dimensional polymeric chains (Castan *et al.*, 1998; Ha *et al.*, 1999; Sun *et al.*, 2002). Imidazole is of considerable interest as a ligand because its presence in many biological systems (Valle & Wacker, 1970; Tamura *et al.*, 1987), for example, in the histidyl residue of proteins, provides a potential binding site for metal ions. Imidazole is a monodentate ligand and forms complexes with metal ions through its tertiary N atom (Brooks & Davidson, 1960; Davis & Smith, 1971; Wang *et al.*, 2000; Hao *et al.*, 2000). In this paper, we report the preparation and crystal structure of the title complex, (I), incorporating both oratate and imidazole ligands. This compound might be of interest in pharmacological studies.



(I)

The crystal structure of (I) is presented in Fig. 1. The Ni^{II} ion has a distorted octahedral coordination geometry comprised of atom N1 and a carboxylate O atom from a doubly deprotonated bidentate orotate ligand, two aqua O atoms and two tertiary N atoms from imidazole molecules. Atoms N1 and O3 are bonded to Ni1 to form a five-membered chelate ring [N1—Ni1 = 2.0719 (15) Å and O3—Ni1 =

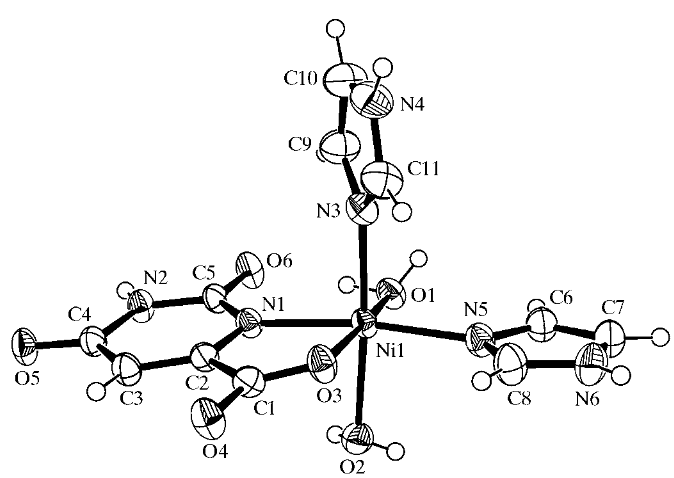


Figure 1
The molecular structure of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

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2.0635 (12) Å], water atom O1 [Ni—O1 = 2.0716 (13) Å] and imidazole atom N5 [Ni—N5 = 2.0721 (16) Å] form the equatorial plane, and water atom O2 [Ni—O2 = 2.162 (14) Å] and imidazole atom N3 [Ni—N3 = 2.0745 (16) Å] are in the apical positions of the Ni^{II} coordination octahedron. The equatorial plane is approximately planar, with an r.m.s. deviation of 0.0432 Å, and the largest deviation from the mean plane is 0.0805 (6) Å for atom Ni1. For the two symmetry-unrelated $Ni-O_{aqua}$ bond lengths, we might expect to observe two similar values; in fact, they are quite different (see above). This is apparently due to the strong intramolecular hydrogen-bonding interaction between atom H1*A* of the aqua ligand and exocyclic atom O6 [Fig. 2; O1···O6 = 2.712 (19) Å]. This interaction is also the reason that the molecule forms the *mer* instead of the *fac* isomer. All the 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 angle subtended at the Ni atom by the orotate ligand is 80.12 (5)°, which is in agreement with values previously reported for other orotate-containing Ni^{II} complexes (Sabat *et al.*, 1980; Wysokinski *et al.*, 2002). This 'bite' angle is far from the ideal value of 90° because of the constrained geometry of the orotate ligand.

The orotate ligand in (I) is essentially planar (r.m.s. deviation = 0.0444 Å), with a slight deviation from planarity arising from the non-zero torsion angle between the carboxylate group and the ring [N1—C2—C1—O3 = 2.5 (2)°]. This torsion angle indicates that distortion of the orotate ligand caused by coordination to the Ni^{II} ion is even less than in uncoordinated orotic acid [5.9 (4) (Falvello *et al.*, 2003) and 5.0 (2)° (Bulut *et al.*, 2003)]. Of all the N—C bonds in the uracyclic ring of the orotate ligand, N1—C5 and N1—C2 are the shortest, with values of 1.346 (2) and 1.355 (2) Å, respectively. This indicates a considerable π-electron delocalization within the C3—C2—N1—C5 skeleton. The C═O bond lengths for exocyclic atoms O5 and O6 are 1.257 (2) and 1.252 (2) Å, respectively. These values are slightly longer than those in typical orotate complexes and this can be attributed to the intermolecular hydrogen bonding (Table 2).

The orotate molecule seems to have a degree of elasticity with regard to its coordination to metal centres. In complexes of HOr^{2-} with Ni (this work; Sabat *et al.*, 1980; Wysonkinski *et al.*, 2002), Cu (Mutikainen & Lumme, 1980) and Zn (Mutikainen, 1987), the C5—N1—C2 angle is smaller [118.25 (15), 118.3 (3), 118.9 (11), 117.9 (2) and 118.1 (4)°, respectively] than that found in orotic acid [122.8 (3) (Takusagawa & Shimada, 1973), 123.07 (14) (Bulut *et al.*, 2003) and 122.8 (3)° (Falvello *et al.*, 2003)]. This shrinkage of the C5—N1—C2 angle is due to the metal coordination at N1, which causes widening of the adjacent N1—C2—C3 and N1—C5—N2 angles to 124.79 (16) and 118.01 (15)°, respectively [120.82 (16) and 115.15 (14)°, respectively, in Bulut *et al.* (2003)].

The carboxylate C—O distances in the orotate anion also display some variability, depending on their environment. The C—O distances are practically equal in the uncoordinated HOr^{2-} anion and its Ni^{II} and Li complexes (Lutz, 2001). In (I), the C—O bond lengths are in the range 1.248 (2)–1.253 (2) Å, which is comparable with those in similar Ni^{II} complexes (Sabat *et al.*, 1980; Wysokinski *et al.*, 2002). However, in the Co^{II}, Cu^{II} (Icbudak *et al.*, 2003) and Mg^{II} (Mutikainen *et al.*, 1996) complexes of HOr^{2-}, the carboxylate group is asymmetric [C—O = 1.278 (2)–1.223 (3), 1.270 (4)–1.240 (4) and 1.262 (2)–1.243 (2) Å, respectively].

The two imidazole rings in (I) are individually planar, with r.m.s. deviations of 0.0028 and 0.0007 Å, and the maximum deviations from these planes are 0.0039 (15) Å for atom N4 and 0.0010 (13) Å for atom C7. These planes are approximately perpendicular, with a dihedral angle of 88.17 (8)°. The dihedral angles between the orotate ligand and the imidazole groups are 81.43 (6) and 10.98 (11)°. The internal geometries are as expected, with the bond lengths N3—C11 [1.306 (3) Å], N5—C8 [1.321 (2) Å], C9—C10 [1.346 (3) Å] and C6—C7 [1.348 (3) Å] corresponding exactly to typical double-bond lengths. These values are comparable with those in mixed-ligand imidazole–Ni^{II} complexes (Wang *et al.*, 2000; Hao *et al.*, 2000; Gao *et al.*, 2004).

The crystal packing of (I) is formed *via* intermolecular hydrogen bonding, and π–π and π–ring interactions. It can be seen from Fig. 2 that the two orotate molecules are joined by two N2—H4···O5 hydrogen bonds (Table 2), which leads to the formation of a centrosymmetric dimer of (I) in the crystal unit cell. A similar behaviour was also reported in the work of Wysokinski *et al.* (2002). Two aqua ligands and imidazole atoms N4 and N6 also form intermolecular hydrogen-bonding interactions, through carboxylate atom O4 and exocylic carbonyl atoms O5 and O6 (see Table 2 for details).

In the extended structure of (I), shown in Fig. 2, there are also weak π–π and π–ring interactions. An intermolecular π–π contact occurs between the two symmetry-related imidazole rings (N3-coordinated, hereinafter ring *A*) of neighbouring molecules. Ring *A* is oriented in such a way that the perpendicular distance from *A* to A^{vii} is 3.351 Å, the closest interatomic distance being C10···C11^{vii} [3.438 (4) Å; symmetry code: (vii) $1 - x$, $-y$, $1 - z$]. The distance between the ring centroids is 3.6610 (14) Å. The other imidazole ring (N5-

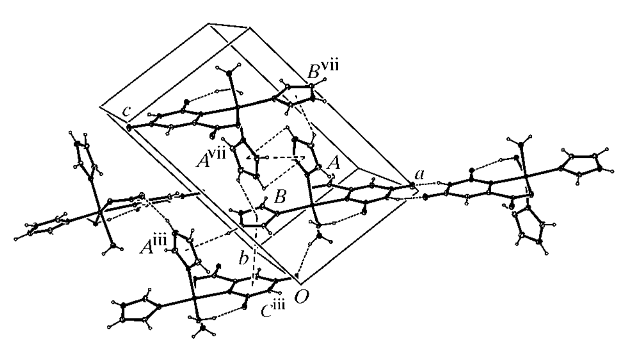

Figure 2
The three-dimensional structure of (I). Dashed lines indicate the hydrogen bonds, as well as the π–π and π–ring interactions. [Symmetry codes: (iii) $x - 1$, y, z; (vii) $1 - x$, $-y$, $1 - z$.]

coordinated, ring *B*) also forms an intermolecular π–π contact, with the uracilate ring (*C*) of the orotate ligand. Rings *B* and *C* are oriented in such a way that the perpendicular distance from *B* to *C* is 3.578 Å, the closest interatomic distance is C6···C4^{iii} [3.443 (3) Å; symmetry code: (iii) $x - 1, y, z$] and the dihedral angle between the planes of the rings is 10.8°. The distance between the ring centroids is 3.9717 (12) Å. Rings *A* and *B* are also involved in intermolecular N—H···π and C—H···π interactions with the imidazole N and C atoms. With regard to the N—H···π contact, for two neighbouring *A* rings, the distance between atom H11 and the centre of ring *A* (*CgA*) is 3.35 (3) Å, the distance between atom H11 and the plane of ring *A* is 3.31 (3) Å, and the N4—H11···*CgA* angle is 84 (2)°. In addition, there are also two C—H···π interactions between rings *A* and *B*. For the C10—H10···π contact, the distance between atom H10 and the centre of ring *B* (*CgB*) is 2.91 Å, the distance between atom H10 and the plane of ring *B* is 2.81 Å, and the C10—H10···*CgB* angle is 137°. For the C7—H7···π contact, the distance between atom H7 and the centre of ring *A* is 3.01 Å, the distance between atom H7 and the plane of ring *A* is 3.00 Å, and the C7—H7···*CgA* angle is 173°.

Experimental

For the preparation of [Ni(HOr)$(H_2O)_4$]·H_2O, a mixture of a solution of $NiCl_2·6H_2O$ (1.19 g, 5 mmol) in distilled water (25 ml) and a solution of $NaHCO_3$ (0.42 g, 5 mmol) in distilled water (25 ml) was added dropwise with stirring at 353 K to a suspension of orotic acid (0.87 g, 5 mmol) in distilled water (25 ml). The resulting mixture was refluxed with stirring for 24 h at 353 K in a temperature-controlled bath and, after evolution of CO_2, the clear solution was cooled to room temperature. The green crystals which formed were filtered off and washed successively with 10 ml portions of cold distilled water and acetone and dried *in vacuo*. For the preparation of [Ni(HOr)(im)$_2$$(H_2O)_2$], (I), a solution of imidazole (0.55 g, 4 mmol) in ethanol (10 ml) was added dropwise with stirring to a solution of [Ni(HOr)$(H_2O)_4$]·H_2O (0.62 g, 2 mmol) in distilled water (50 ml). The mixture was heated to 333 K in a temperature-controlled bath and refluxed with stirring for 12 h at 333 K. The reaction mixture was then cooled to room temperature. The blue crystals of (I) which formed were filtered off and washed successively with 10 ml portions of cold distilled water and ethanol and dried *in vacuo*.

Crystal data

[Ni$(C_5H_2N_2O_4)(C_3H_4N_2)_2(H_2O)_2$]
M_r = 384.97
Monoclinic, $P2_1/c$
a = 8.6201 (6) Å
b = 13.5104 (7) Å
c = 13.5612 (10) Å
β = 99.627 (6)°
V = 1557.11 (18) Å^3
Z = 4
D_x = 1.642 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 20 639 reflections
θ = 1.5–28.5°
μ = 1.29 mm^{-1}
T = 293 (2) K
Prism, blue
0.30 × 0.27 × 0.24 mm

Data collection

Stoe IPDS-2 CCD diffractometer
ω scans
Absorption correction: by integration (*X-RED*32; Stoe & Cie, 2002)
T_{min} = 0.701, T_{max} = 0.755
21 831 measured reflections
3068 independent reflections
2658 reflections with $I > 2\sigma(I)$
R_{int} = 0.044
θ_{max} = 26.0°
$h = -10 \rightarrow 10$
$k = -16 \rightarrow 16$
$l = -16 \rightarrow 16$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.027
$wR(F^2)$ = 0.072
S = 1.06
3068 reflections
245 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0482P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.52 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

Ni1—O3	2.0635 (12)	O5—C4	1.257 (2)
Ni1—O1	2.0716 (13)	O6—C5	1.252 (2)
Ni1—N1	2.0719 (15)	N1—C5	1.346 (2)
Ni1—N5	2.0721 (16)	N1—C2	1.355 (2)
Ni1—N3	2.0745 (16)	N3—C11	1.306 (3)
Ni1—O2	2.1620 (14)	N5—C8	1.321 (2)
O3—C1	1.248 (2)	C6—C7	1.348 (3)
O4—C1	1.253 (2)	C9—C10	1.346 (3)
O3—Ni1—O1	172.26 (5)	N1—Ni1—N3	92.33 (6)
O3—Ni1—N1	80.12 (5)	N5—Ni1—N3	94.09 (6)
O1—Ni1—N1	93.41 (6)	O3—Ni1—O2	86.83 (5)
O3—Ni1—N5	93.99 (6)	O1—Ni1—O2	88.23 (5)
O1—Ni1—N5	91.95 (6)	N1—Ni1—O2	83.59 (6)
N1—Ni1—N5	171.37 (6)	N5—Ni1—O2	89.83 (6)
O3—Ni1—N3	91.01 (6)	N3—Ni1—O2	175.66 (6)
O1—Ni1—N3	93.51 (6)	C5—N1—C2	118.25 (15)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1*A*···O6	0.86 (3)	1.88 (3)	2.712 (2)	162 (3)
O1—H1*B*···O4^{i}	0.85 (2)	1.84 (2)	2.686 (2)	176 (3)
O2—H2*A*···O6^{ii}	0.84 (2)	2.00 (2)	2.820 (2)	168 (3)
O2—H2*B*···O5^{iii}	0.81 (2)	2.05 (2)	2.796 (2)	153 (3)
N2—H4···O5^{iv}	0.84 (2)	2.05 (2)	2.869 (2)	165 (2)
N6—H6···O5^{v}	0.84 (2)	2.06 (2)	2.880 (2)	166 (3)
N4—H11···O4^{vi}	0.85 (2)	2.08 (2)	2.885 (2)	160 (3)

Symmetry codes: (i) $1 - x, y - \frac{1}{2}, \frac{1}{2} - z$; (ii) $1 - x, -y, -z$; (iii) $x - 1, y, z$; (iv) $2 - x, -y, -z$; (v) $x - 1, \frac{1}{2} - y, \frac{1}{2} + z$; (vi) $x, \frac{1}{2} - y, \frac{1}{2} + z$.

H atoms bound to C atoms were placed in calculated positions, with C—H = 0.93 Å, and were allowed to ride on their parent atoms, with $U_{iso}(H) = 1.2U_{eq}(C)$. The remaining H atoms were located in a difference map and refined, with O—H distances restrained to 0.85 (2) Å and N—H distances restrained to 0.87 (2) Å.

Data collection: *X-AREA* (Stoe & Cie, 2002); cell refinement: *X-AREA*; data reduction: *X-RED*32 (Stoe & Cie, 2002); program(s) used to solve structure: *SIR*97 (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*III (Burnett & Johnson, 1996); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1765). Services for accessing these data are described at the back of the journal.

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