

Hexaaquanickel diorotate(1-)  
dihydrate at 150 KLarry R. Falvello, Daniel Ferrer, Tatiana Soler\* and  
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Received 12 February 2003

Accepted 28 February 2003

Online 21 March 2003

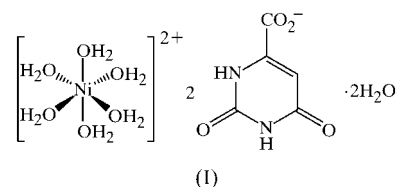
In hexaaquanickel bis(2,6-dioxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate) dihydrate,  $[\text{Ni}(\text{H}_2\text{O})_6](\text{C}_5\text{H}_3\text{N}_2\text{O}_4)_2 \cdot 2\text{H}_2\text{O}$ , the nickel cation is coordinated by six aqua ligands and only associated with the two orotate ions through hydrogen bonds. The structure is isotypic with the magnesium and zinc analogues. The metal cation sits on a crystallographic center of inversion that relates the water molecules and the organic anions. The orotate moieties form an unbonded one-dimensional chain mediated by a hydrogen-bonded self-recognition interaction. The hexaaquanickel complex molecules bridge these chains laterally, acting as molecular clamps that bring neighboring layers nearer than expected. As a result of this three-dimensional arrangement, a short contact of 3.166 (5) Å is observed between two C atoms of two adjacent ribbons.

## Comment

Orotic acid (6-uracilic acid,  $\text{OrH}_2$ ) and some of its derivatives are of great importance in biological systems, due to their role as precursors of pyrimidine nucleosides (Rawn, 1989), and they are found in the cells and body fluids of many living organisms. Metal orotates are widely applied in medicine, e.g. platinum, palladium and nickel orotates with a wide variety of substituents have been screened as therapeutic agents for cancer (Sabat *et al.*, 1980; Karipides & Thomas, 1986; Castan *et al.*, 1990). However, recent interest has focused on the proposed biological function of orotic acid as a carrier, which underlies the successful application of metal orotates in therapies for a variety of metal deficiencies, such as calcium, magnesium, zinc or iron.

$\text{OrH}_2$  can act as a dibasic acid, depending on the pH range. The acid functions are the exocyclic carboxylate group ( $\text{p}K_a = 2.09$ ) and the 1-imino position ( $\text{p}K_a = 9.28$ ), so in the pH range of approximately 5–9, deprotonation of orotic acid yields orotate(1-) salts containing  $\text{OrH}^-$  (Kaneti & Golovinski, 1971). Only in very alkaline solutions or in the presence of strong coordination centers are orotate(2-) ions present in significant quantities.

A great number of orotate(2-) complexes have been characterized structurally (Mutikainen & Lumme, 1980; Mentzafos *et al.*, 1987; Mutikainen, 1989; Hodgson & Asplund, 1990), but less has been written about the equally important complexes of orotate(1-). Some examples are the coordination compounds of lithium and magnesium orotate(1-) (Bach *et al.*, 1990; Lutz, 2001) and the coordination complex of zinc orotate(1-) (Kumberger *et al.*, 1993).

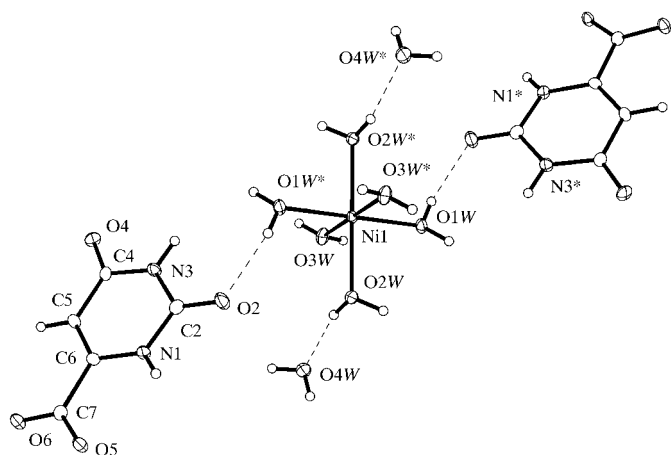


In this paper, we report the preparation and crystal structure of a water-rich nickel orotate(1-) complex, (I). The importance of this compound, as happens with the zinc and magnesium analogues, lies in its similarity to the metal-orotate species found in aqueous solution. Such structural similarity could enhance its possible pharmacological interest.

From our X-ray crystallographic analysis at 150 K we found that the nickel-containing compound is isotypic with the previously reported magnesium and zinc orotate(1-) compounds. The structure is formed by a cationic hexaaquanickel complex hydrogen bonded to two  $\text{OrH}^-$  counter-ions.

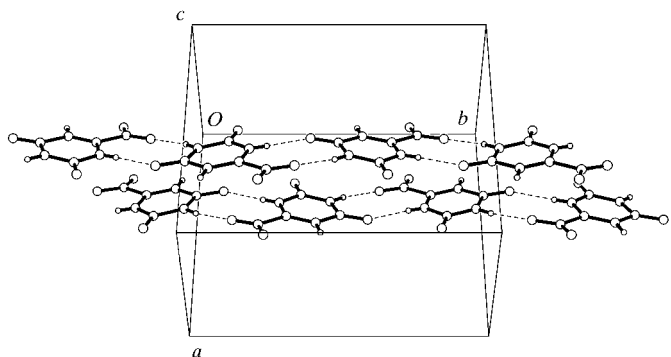
In (I), the nickel cation sits on a crystallographic center of inversion that relates the water molecules of the coordination shell, the orotate anions and the uncoordinated water molecules. The orotate anion is essentially planar, with a slight deviation from planarity arising from the small non-zero torsion angle between the carboxylate group and the ring [ $\text{N1}-\text{C6}-\text{C7}-\text{O5} = 5.9 (4)^\circ$ ]. The angles formed at the amide  $\text{C}=\text{O}$  group of the urea fragment,  $\text{N3}-\text{C2}-\text{O2}$  and  $\text{N1}-\text{C2}-\text{O2}$ , are essentially equal, but as the chemical environment of the  $\text{C4}=\text{O4}$  carbonyl group is not symmetrical, the angles around it are quite different [ $\text{N3}-\text{C4}-\text{O4} = 119.8 (3)^\circ$  and  $\text{C5}-\text{C4}-\text{O4} = 125.1 (3)^\circ$ ]. The same deviation from symmetry is observed in the structure of the ammonium salt of the orotate anion (Solbakk, 1971). The orotate moiety seems to have a degree of plasticity involving coordination to metal centers. In the Cu (Mutikainen & Lumme, 1980) and Ni (Sabat *et al.*, 1980) complexes of  $\text{Or}^{2-}$ , the  $\text{C2}-\text{N1}-\text{C6}$  angle is smaller [ $117.9 (2)$  and  $118.3 (3)^\circ$ , respectively] than that found in either orotic acid [ $122.7 (2)^\circ$ ; Takusagawa & Shimada, 1973] or (I) [ $122.8 (3)^\circ$ ]. The carboxylate  $\text{C}-\text{O}$  distances also display some variability, depending upon their environment. When unligated or when bound to Ni or Li (Lutz, 2001), the two  $\text{C}-\text{O}$  distances are practically equal. When  $\text{OrH}^-$  is bound to uranium through a carboxylate O atom, however, the  $\text{C}-\text{O}$  bond involving the ligated O atom is longer [ $1.275 (5)$  versus  $1.221 (6)$  Å], probably as a result of greater covalency in the  $\text{U}-\text{O}$  bond (Mentzafos *et al.*, 1987).

The most important structural feature of (I) is the extensive network of hydrogen bonds, which not only connect the orotate(1-) anions to the nickel complex, but also relate



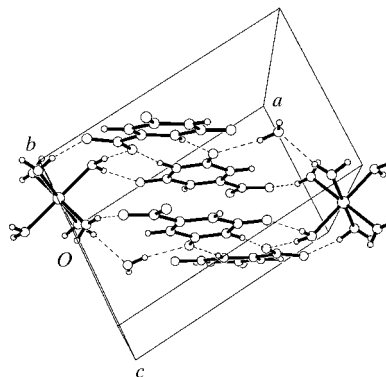
**Figure 1**  
Displacement-ellipsoid plot of hexaaquanickel diorotate(1<sup>-</sup>) dihydrate. Non-H atoms are represented by 50% probability ellipsoids and H atoms are shown as small spheres of arbitrary size [symmetry code: (i)  $-x, 1 - y, -z$ ].

adjacent anions through the O atoms of carbonyl and carboxylate groups and the two N atoms of the ring. This self-recognition of the orotate ions leads to the formation of stacked ribbons which propagate parallel to the *b* axis of the cell (Fig. 2). This pattern is also found in the structure of the ammonium salt of the orotate anion (Solbakk, 1971), where the orotate ribbons are interconnected through hydrogen bonds with the ammonium ions and water molecules. The hydrogen bonds linking the orotate ribbons in (I) follow a pattern of the type  $R_2^2(9)$  (Bernstein *et al.*, 1995). Adjacent ribbons are bridged laterally by  $[\text{Ni}(\text{H}_2\text{O})_6]^{2+}$  cations, the aqua ligands of which act as hydrogen-bond donors to the carbonyl and carboxylate O atoms of the orotate anions, forming an  $R_3^3(8)$  motif on one side of the ribbon and an  $R_3^3(13)$  motif on the other (Fig. 3). The hexaaquanickel complex cations act as molecular clamps, which force the neighboring ribbons to approach each other more closely than expected, producing a short contact between two C atoms of neighboring layers [ $\text{C}6 \cdots \text{C}7^i = 3.166(5) \text{ \AA}$ ; symmetry code: (i)  $x, \frac{1}{2} - y, -\frac{1}{2} + z$ ].



**Figure 2**  
The orientation inside the cell of the ribbons formed by orotate self-recognition.

The differences in bond lengths and angles between (I) and the isotopic Mg- and Zn-containing structures can be attributed to the difference in size of the metal cations, and follow the pattern found for hexaaqua compounds of the first *d*-block series in the case of the complexes of nickel and zinc (Cotton *et al.*, 1993). The structures found in these examples of divalent metal complexes differ notably from that of lithium orotate monohydrate. In that compound, the orotate moiety binds



**Figure 3**  
Partial view of the packing, showing the stacking of the orotate ribbons and the connection through the hexaaquanickel complex cations.

directly to the metal cation. The  $\text{Li}^+$  cation is surrounded by a tetrahedral environment consisting of a water molecule and three orotate moieties displaying three coordination modes. Conversely, each orotate anion is ligated to three  $\text{Li}^+$  ions. The three-dimensional arrangement in lithium orotate monohydrate consists of two-dimensional layers instead of ribbons, which are connected to each other by  $\text{O}-\text{H} \cdots \text{O}$  and  $\text{N}-\text{H} \cdots \text{O}$  hydrogen bonds, some of them bifurcated.

## Experimental

Crystals of (I) were grown by slow evaporation at room temperature from an aqueous mixture of  $\text{NiCl}_2$ , orotic acid (purchased from Aldrich) and ammonium hydroxide in a 1:2:2 molar ratio.

### Crystal data

$[\text{Ni}(\text{H}_2\text{O})_6](\text{C}_5\text{H}_3\text{N}_2\text{O}_4)_2 \cdot 2\text{H}_2\text{O}$   
 $M_r = 513.03$   
 Monoclinic,  $P2_1/c$   
 $a = 10.7908(10) \text{ \AA}$   
 $b = 12.8626(10) \text{ \AA}$   
 $c = 6.8482(10) \text{ \AA}$   
 $\beta = 97.932(12)^\circ$   
 $V = 941.42(18) \text{ \AA}^3$   
 $Z = 2$

$D_x = 1.810 \text{ Mg m}^{-3}$   
 Mo  $K\alpha$  radiation  
 Cell parameters from 25 reflections  
 $\theta = 10.5\text{--}17.3^\circ$   
 $\mu = 1.13 \text{ mm}^{-1}$   
 $T = 150(2) \text{ K}$   
 Plate, pale blue  
 $0.20 \times 0.11 \times 0.02 \text{ mm}$

### Data collection

Enraf-Nonius CAD-4 diffractometer  
 $\omega$ - $\theta$  scans  
 Absorption correction:  $\psi$  scan (Kopfmann & Huber, 1968)  
 $T_{\min} = 0.906, T_{\max} = 0.993$   
 2326 measured reflections  
 2148 independent reflections  
 1562 reflections with  $I > 2\sigma(I)$

$R_{\text{int}} = 0.038$   
 $\theta_{\text{max}} = 27.5^\circ$   
 $h = -14 \rightarrow 13$   
 $k = -16 \rightarrow 0$   
 $l = 0 \rightarrow 8$   
 3 standard reflections  
 frequency: 30 min  
 intensity decay: 8.0%

## Refinement

Refinement on  $F^2$   
 $R[F^2 > 2\sigma(F^2)] = 0.047$   
 $wR(F^2) = 0.119$   
 $S = 1.00$   
 2148 reflections  
 172 parameters

H atoms treated by a mixture of independent and constrained refinement  
 $w = 1/[\sigma^2(F_o^2) + (0.045P)^2]$   
 where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{\max} = 0.005$   
 $\Delta\rho_{\max} = 0.41 \text{ e } \text{\AA}^{-3}$   
 $\Delta\rho_{\min} = -0.49 \text{ e } \text{\AA}^{-3}$

Table 1

Selected geometric parameters ( $\text{\AA}$ ,  $^\circ$ ).

Ni1—O1W	2.016 (2)	Ni1—O2W	2.074 (2)
Ni1—O3W	2.068 (3)		
O1W—Ni1—O3W	84.92 (11)	O3W—Ni1—O2W	89.06 (10)
O1W—Ni1—O2W	90.34 (10)		

Table 2

Hydrogen-bonding geometry ( $\text{\AA}$ ,  $^\circ$ ).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O1W—H1A $\cdots$ O2 <sup>vi</sup>	0.73 (4)	2.01 (4)	2.728 (4)	169 (5)
O1W—H1B $\cdots$ O5 <sup>iii</sup>	0.95 (4)	1.72 (4)	2.663 (3)	172 (4)
O2W—H2A $\cdots$ O4W	0.82 (4)	1.98 (4)	2.782 (4)	165 (4)
O2W—H2B $\cdots$ O6 <sup>iii</sup>	0.86 (4)	1.87 (4)	2.714 (3)	168 (4)
O3W—H3A $\cdots$ O4W <sup>iv</sup>	0.80 (5)	2.03 (5)	2.812 (4)	168 (4)
O3W—H3B $\cdots$ O6 <sup>i</sup>	0.83 (5)	1.96 (5)	2.769 (4)	164 (4)
O4W—H4A $\cdots$ O2W <sup>v</sup>	0.74 (4)	2.26 (4)	2.952 (4)	154 (4)
O4W—H4B $\cdots$ O4 <sup>i</sup>	0.82 (5)	2.06 (5)	2.878 (4)	170 (4)
N1—H1N $\cdots$ O4 <sup>vii</sup>	0.78 (4)	2.22 (4)	2.978 (4)	165 (4)
N3—H3N $\cdots$ O5 <sup>ii</sup>	0.90 (4)	1.99 (4)	2.860 (4)	164 (4)

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

All of the H atoms were found in a difference Fourier map and, except for the orotate H5 atom, their positions were refined freely with  $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{parent atom})$ . Atom H5 was placed geometrically and refined as riding, with  $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ .

Data collection: *CAD-4/PC* (Enraf–Nonius, 1996); cell refinement: *CAD-4/PC*; data reduction: *XCAD4* (Harms & Wocadlo, 1995);

program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Siemens, 1996); software used to prepare material for publication: *SHELXL97*.

TS thanks the Ministry of Education, Culture and Sports (Spain) for a Postdoctoral Fellowship. Funding from the Ministry of Science and Technology (Spain), under grant BQU2002-00554, is gratefully acknowledged.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: LN1162). Services for accessing these data are described at the back of the journal.

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