Inorg. Chem. **2001,** *40,* 5701−5703 **5701**

Mononuclear Hydroxamate Five-Coordinate Nickel(II) Complexes: Structural and Spectroscopic Characterization

M. Dolores Santana,[†] Gabriel García,*[,†] José Pérez,[‡] Elíes Molins,[§] and Gregorio López[†]

Departamento de Química Inorgánica, Universidad de Murcia, 30071 Murcia, Spain, Departamento de Ingeniería Minera, Geológica y Cartográfica, Universidad Politécnica de Cartagena, 30203 Cartagena, Spain, and Institut de Ciència de Materials, CSIC, Campus Universitari de Bellaterra, 08193 Cerdanyola, Spain

Received March 19, 2001

Introduction

Hydroxamic acids constitute a very important class of chelating agents, and their complexes are ubiquitous in biological systems.[1] The coordination chemistry of hydroxamic acids and their derivatives has received considerable attention in modeling of the biological function, in particular, inhibition of urease activity.[2] Urease is a nickel-containing metalloenzyme[3−5] that catalyzes the hydrolysis of urea to form ammonia and carbamate, and it can be inhibited by a variety of agents including thiols[6] and hydroxamic acids.[7] The structure of *Bacillus pasteurii* urease inhibited with acetohydroxamic acid has been solved at 1.55 Å.[8] The structure clearly shows the binding mode of the inhibitor anion symmetrically bridging the two Ni ions in the active site through the hydroxamate oxygen and chelating one Ni ion through the carbonyl oxygen. The two Ni ions in the active site are separated by a distance of 3.53 Å.

The {O,μ-O} bridging function of the hydroxamic moiety has been observed in a few dinuclear complexes used as structural models of the inhibited urease, obtained by substitution of carboxylate ligands by hydroxamates in octahedral compounds with preorganized dimeric structure.[9,10] On the other hand, the {O,O} chelating mode has been observed in the reported nickel complexes in an octahedral structure supported by magnetic moments and IR and electronic spectra that have not been structurally evidenced in the solid state.[11] Recently, Pecoraro et al.[12] have reported nickel complexes containing deprotonated salicylhydroxamic acid as a binucleating ligand with the carbonyl and hydroximate oxygens bound to one nickel and the phenolate oxygen and imine nitrogen chelating an adjacent nickel atom. Herein, we report the crystal structure and the spectroscopic studies of a mononuclear nickel pentacoordinate hydroxamate complex that reveals a {O,O} chelating mode of the hydroxamate, and it is the only crystallographically characterized example of a hydroxamate derivative in a distorted square pyramidal geometry.

Experimental Section

Materials. The complexes [Ni([12]aneN$_3$-mc)(μ-OH)]$_2$(PF$_6$)$_2$ ([12]aneN$_3$-mc = 2,4,4-trimethyl-1,5,9-triazacyclododec-1-ene, [12]aneN$_3$-mc1, or 2,4,4,9-tetramethyl-1,5,9-triazacyclododec-1-ene, [12]aneN$_3$-mc2) were synthesized by procedures previously described.[13,14] All commercial reagents were obtained from Aldrich Co. and used without further purification. Solvents were dried and distilled by general methods before use.

Physical Measurements. C, H, and N analyses were carried out with a microanalyzer Carlo Erba model EA 1108. IR spectra were recorded on a Perkin-Elmer 16F PC FT-IR spectrophotometer using Nujol mulls between polyethylene sheets. The NMR spectra of (CD$_3$)$_2$CO solutions were recorded on a Bruker model AC 200E (standard SiMe$_4$) or a Varian Unity 300 spectrometer. The UV/vis spectra (in acetone) were recorded on a Hitachi 2000V spectrophotometer for the 300−800 nm range. Fast atom bombardment (FAB) mass spectra were run on a Fisons VG Autospec spectrometer operating in the FAB$^+$ mode. Magnetic susceptibility measurements were measured on polycrystalline samples in the temperature range 100−300 K with a Quantum Desing SQUID susceptometer. It was calibrated with Hg[Co(NCS)$_4$]. Diamagnetic corrections were estimated from Pascal's constants. The magnetic data were also corrected for the temperature-independent paramagnetism (100×10^{-6} cm^3 mol^{-1} per Ni atom).

[Ni([12]aneN$_3$-mc1)(Ah)]PF$_6$ 1. The compound acetohydroxamic acid (HAh, 26 mg, 0.340 mmol) was added to a solution of [Ni([12]aneN$_3$-mc1)(μ-OH)]$_2$(PF$_6$)$_2$ (150 mg, 0.170 mmol) in acetone (20 mL). The reaction was stirred for 1 h, during which time the mixture became a bright blue solution. Acetone was then removed under reduced pressure until ∼10 mL. After addition of ether (25 mL), the resulting blue solid was filtered off, washed with ether, and air dried. Yield: 0.138 g (83%). Anal. Calcd for C$_{14}$H$_{29}$N$_4$O$_2$PF$_6$Ni: C, 34.4; H, 6.0; N, 11.5. Found: C, 34.4; H, 6.2; N, 11.4. FAB (+ve) *m*/*z*: 343 [M]$^+$. ^{1}H NMR (CD$_3$)$_2$CO) δ: 334.8 (α-CH), 317.5 (α-CH), 219.8 (α-CH), 179.8 (α-CH), 104.8 (α-CH), 98.7 (α-CH), 30.5 (4-Me), 24.9 (2H, α-CH), 19.1 (4-Me), 3.4 (Me, Ah), −9.7 (β-CH), −11.2 (β-CH), −12.1 (β-CH), −17.5 (2-Me), −26.9 (β-CH), −32.0 (β-CH), −36.4 (β-CH). ϵ_{584} 38 M^{-1} cm^{-1}, ϵ_{360} 570 M^{-1} cm^{-1}. Principal IR bands cm^{-1}: 3294, 3266, 3176, 1660, 1612, 1546, 1460, 1302, 1080.

[Ni([12]aneN$_3$-mc2)(Ah)]PF$_6$ 2. To a suspension of [Ni([12]aneN$_3$-mc2)(μ-OH)]$_2$(PF$_6$)$_2$ (150 mg, 0.170 mmol) in acetone (20 mL) was added HAh (26 mg, 0.340 mmol). The mixture was heated under reflux with stirring for 2 h. The solvent was removed under reduced pressure until ∼10 mL. After addition of ether (25 mL), a solid product was obtained as a green solid that was filtered off, washed with diethyl ether, and air dried. Yield: 0.137 g (80%). Anal. Calcd for C$_{15}$H$_{31}$N$_4$O$_2$-

---

* To whom correspondence should be addressed. E-mail: ggarcia@um.es.
[†] Universidad de Murcia.
[‡] Universidad Politécnica de Cartagena.
[§] Institut de Ciència de Materials, Bellaterra.

(1) Kurzak, B.; Kozlowski H.; Farkas, E. *Coord. Chem. Rev.* **1992**, *114*, 169.

(2) Pearson, M. A.; Michel, L. O.; Hausinger, R. P.; Karplus, P. A. *Biochemistry* **1997**, *36*, 8164.

(3) Jabri, E.; Carr, M. B.; Hausinger, R. P.; Karplus, P. A. *Science* **1995**, *268*, 998.

(4) Hausinger,R. P. Urease. In *Biochemistry of Nickel*; Plenum Press: New York, 1993; pp 23−57.

(5) Mobley, H. L. T.; Hausinger, R. P. *Microbiol Rev.* **1989**, *53*, 85.

(6) (a) Todd, M. J.; Hausinger, R. P. *J. Biol. Chem.* **1989**, *264*, 15835. (b) Takishima, K.; Suga, T.; Mamiya, G. *Eur. J. Biochem.* **1988**, *175*, 151.

(7) (a) Hase, J.; Kobashi, K. *J. Biochem.* (*Tokyo*) **1967**, *62*, 293. (b) Kehl, H. *Chemistry and Biology of Hydroxamic Acids*; Karger: New York, 1982.

(8) Benini, S.; Rypniewski, W. R.; Wilson, K. S.; Miletti, S.; Ciurli, S.; Mangani, S. *JBIC*, *J. Biol. Inorg. Chem.* **2000**, *5*, 110.

(9) Stemmler, A. J., Kampf, J. W.; Kirk, M. L.; Pecoraro, V. L. *J. Am. Chem. Soc.* **1995**, *117*, 6368.

(10) Arnold, M.; Brown, D. A.; Deeg, O.; Errington, W.; Haase, W.; Herlihy, K.; Kemp, T. J.; Nimir, H.; Werner, R. *Inorg. Chem.* **1998**, *37*, 2920.

(11) (a) Brown, D. A.; Roche, A. L. *Inorg. Chem.* **1983**, *22*, 2199. (b) Brown, D. A.; McKeith, D.; Glass, W. K. *Inorg. Chim. Acta* **1979**, *35*, 57.

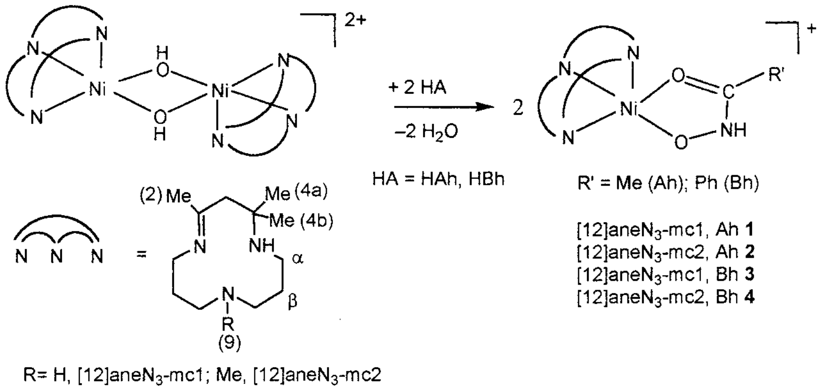
(12) Psomas, G.; Stemmler, A. J.; Dendrinou-Samara, C.; Bodwin, J. J.; Schneider, M.; Alexiou, M.; Kampf, J. W.; Kessissoglou, D. P.; Pecoraro, V. L. *Inorg. Chem.* **2001**, *40*, 1562.

(13) Martin, J. W. L.; Johnston, J. H.; Curtis, N. F. *J. Chem. Soc., Dalton Trans.* **1978**, 68.

(14) Escuer, A.; Vicente, R.; Ribas, J. *Polyhedron* **1992**, *11*, 453.

10.1021/ic010298+ CCC: $20.00

Scheme 1. Synthesis of Complexes **1−4** and Proton Labeling



PF$_6$Ni: C, 35.8; H, 6.2; N, 11.1. Found: C, 35.6 H, 6.3; N, 11.1. FAB (+ve) *m*/*z*: 357 [M]$^+$. ^{1}H NMR (CD$_3$)$_2$CO) δ: 262.0 (α-CH), 255.5 (α-CH), 237.4 (α-CH), 168.8 (α-CH), 100.7 (N-Me), 112.4 (α-CH), 91.1 (α-CH), 33.3 (α-CH), 29.6 (4-Me), 26.1 (α-CH), 19.2 (4-Me), 8.9 (Me, Ah), −6.6 (*β*-CH), −10.9 (*β*-CH), −12.0 (*β*-CH), −18.3 (2-Me), −26.3 (*β*-CH), −33.8 (*β*-CH), −35.9 (*β*-CH). ϵ_{587} 34 M^{-1} cm^{-1}, ϵ_{365} 541 M^{-1} cm^{-1}. Principal IR bands cm^{-1}: 3380, 3196, 1660, 1600, 1532, 1462, 1306, 1078.

[Ni([12]aneN$_3$-mc1)(Bh)]PF$_6$ 3. The compound was prepared in a way similar to that for **1** using benzohydroxamic acid (HBh, 47 mg, 0.340 mmol) and [Ni([12]aneN$_3$-mc1)(μ-OH)]$_2$(PF$_6$)$_2$ (150 mg, 0.170 mmol). A blue solid was obtained. Yield: 0.161 g (86%). Anal. Calcd for C$_{19}$H$_{31}$N$_4$O$_2$PF$_6$Ni: C, 41.4; H, 5.7; N, 10.2. Found: C, 41.4; H, 5.9; N, 10.0. FAB (+ve) *m*/*z*: 405 [M]$^+$. ^{1}H NMR (CD$_3$)$_2$CO) δ: 337.0 (α-CH), 320.9 (α-CH), 221.7 (α-CH), 183.3 (α-CH), 102.7 (α-CH), 99.0 (α-CH), 31.3 (4-Me), 25.4(2H, α-CH), 19.0 (4-Me), 9.3 (Ph, Bh), −9.4 (*β*-CH), −11.2 (*β*-CH), −12.1 (*β*-CH), −17.4 (2-Me), −26.9 (*β*-CH), −31.7 (*β*-CH), −36.3 (*β*-CH). ϵ_{583} 44 M^{-1} cm^{-1}, ϵ_{369} 894 M^{-1} cm^{-1}. Principal IR bands cm^{-1}: 3298, 3284, 3174, 1666, 1598, 1518, 1459, 1316, 1052.

[Ni([12]aneN$_3$-mc2)(Bh)]PF$_6$ 4. Complex **4** was prepared in a fashion analogous to that for **2**, starting from [Ni([12]aneN$_3$-mc2)(μ-OH)]$_2$(PF$_6$)$_2$ (150 mg, 0.170 mmol) and HBh (47 mg, 0.340 mmol). A green solid was obtained. Yield: 0.115 g (60%). Anal. Calcd for C$_{20}$H$_{33}$N$_4$O$_2$PF$_6$Ni: C, 42.5; H, 5.9; N, 9.9. Found; C, 42.3; H, 5.9; N, 9.9. FAB (+ve) *m*/*z*: 419 [M]$^+$. ^{1}H NMR (CD$_3$)$_2$CO) δ: 265.7 (α-CH), 260.0 (α-CH), 239.7 (α-CH), 173.2 (α-CH), 110.3 (α-CH), 102.4 (N-Me), 92.3 (α-CH), 33.8 (α-CH), 30.9 (4-Me), 26.7 (α-CH), 19.4 (4-Me), 9.4 (Ph, Bh), −6.5 (*β*-CH), −10.9 (*β*-CH), −12.1 (*β*-CH), −18.4 (2-Me), −26.4 (*β*-CH), −33.9 (*β*-CH), −36.2 (*β*-CH). ϵ_{587} 84 M^{-1} cm^{-1}, ϵ_{362} 802 M^{-1} cm^{-1}. Principal IR bands cm^{-1}: 3264, 3188, 1660, 1600, 1532, 1457,1308, 1068.

X-ray Crystallography. Crystals of [Ni([12]aneN$_3$-mc2)(Ah)]PF$_6$ **2** were obtained by slow diethyl ether diffusion onto an acetone solution. A single crystal (approximate dimensions 0.20 × 0.20 × 0.30 mm) was mounted on an Enraf-Nonius CAD4 diffractometer equipped with a graphite monochromator for Mo Kα radiation. The crystallographic data are shown in Table 1. Accurate cell parameters were determined by least-squares fitting of 25 high-angle reflections. The scan method was $\omega - 2\Theta$ with the range of *hkl* ($-9 \le h \le 9$, $-24 \le k \le 0$, $-15 \le l \le 15$) corresponding to $2\Theta_{\max} = 50°$. Empirical ψ-scan mode absorption was made. The structure was solved by direct methods SHELXS-97[15] and refined by full-matrix least-squares techniques using anisotropic thermal parameters for non-H atoms. The final *R* factor was 0.0429 [$R_w = 0.1136$ where $w = 1/\sigma^2(F_0^2) + (0.0776\,P)^2 + 1.71P$ and $P = F_0^2 + 2F_c^2)/3$] over 2693 observed reflections [$I > 2\sigma(I)$].

Table 1. Crystallographic Data for Complex **2**

formula	C$_{15}$H$_{31}$F$_6$N$_4$NiO$_2$P
M	503.12
T (K)	273(2)
crystal system	monoclinic
space group	$P21/n$
λ (Mo Kα) (Å)	0.71073
a (Å)	7.750(9)
b (Å)	20.931(9)
c (Å)	13.286(6)
β (deg)	104.02
V (Å^3)	2091(3)^3
Z	4
ρ_{calc} (g cm^{-3})	1.598
R1 [$I > 2\sigma(I)$]	0.0429
wR2 (all data)	0.1287
GOF	0.984
measured reflections	7347
independent reflns	3683

Results and Discussion

The hydroxide ligand in complexes [Ni([12]aneN$_3$-mc)(μ-OH)]$_2$(PF$_6$)$_2$ is a weak base and a very good leaving group. For this reason, [Ni([12]aneN$_3$-mc)(μ-OH)]$_2$(PF$_6$)$_2$ reacts with acids producing H$_2$O and the complex containing the acid anion as a nickel-bound ligand.[16] Both aceto- and benzohydroxamic acids react with [Ni([12]aneN$_3$-mc)(μ-OH)]$_2$(PF$_6$)$_2$ giving the desired hydroxamate derivatives **1−4** presented in Scheme 1. The identity of these complexes could be unambiguously inferred from their spectra (see the Experimental Section). The IR spectra contain the expected absorptions attributed to the hydroxamate ligand: v(NH) at 3196−3174 cm^{-1}, v(CO) at 1600 cm^{-1}, v(CN) at 1546−1518 cm^{-1}. The general pattern of the infrared spectra supports coordination via ketonic oxygen atom and the oxygen atom of the deprotonated NHO$^-$ group, as reported previously for monomeric nickel complexes containing alkylhydroxamic acids.[10,11] The IR spectra show the bands assigned to v(N−H) (~3300 cm^{-1}) and v(C=N) (~1660 cm^{-1}) of the coordinated macrocycle and strong bands at 840 and 560 cm^{-1} due to the hexafluorophosphate anion.

The electronic spectra of complexes **1−4** (see Experimental Section), measured in acetone, are very similar and understood in C_{4v} symmetry with bands in the 600 and 360 nm regions, which could be assigned to $^3B_1(F) \rightarrow {}^3E(F)$ and $^3B_1(F) \rightarrow {}^3A_2, {}^3E(P)$ transitions, respectively. Both $\lambda_{\max}$ values and molar absorptivities are consistent with a distorted pentacoordinate environment around nickel(II).[16,17]

---

(15) Sheldrick, G. M. *SHELXS-97*; University of Göttingen, Germany, 1997.

(16) (a) Santana, M. D.; Rufete, A.; Sánchez, G.; García, G.; López, G.; Casabó, J.; Molins, E.; Miravitlles, C. *Inorg. Chim. Acta* **1997**, *255*, 21. (b) Santana, M. D.; Rufete, A.; García, G.; López, G.; Casabó, J.; Cabrero, A.; Molins, E.; Miravitlles, C. *Polyhedron* **1997**, *16*, 3713. (c) Santana, M. D.; García, G.; Rufete, A.; Sánchez, G.; Ramírez de Arellano, M. C.; López, G. *Inorg. Chem. Commun.* **1998**, *1*, 267. (d) Santana, M. D.; García, G.; Rufete, A.; Ramírez de Arellano, M. C.; López, G. *J. Chem. Soc., Dalton Trans.* **2000**, 619.

(17) Lever, A. B. P. *Inorganic electronic spectroscopy*; Elsevier: Amsterdam, 1984; pp 513−520.

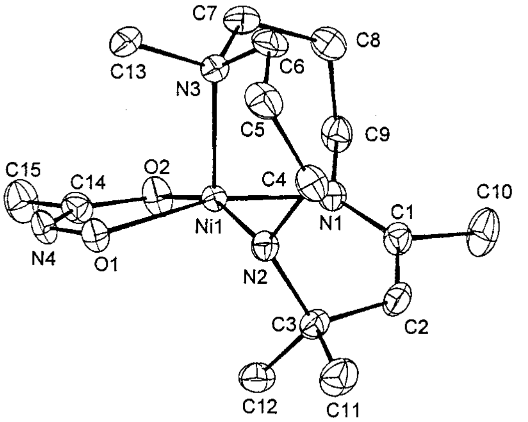


Figure 1. ORTEP plot of the cation of [Ni([12]aneN_3-mc2)(Ah)]PF_6 **2** with the labeling scheme.

Table 2. Selected Bond Lengths (Å) and Angles (Deg) for **2**

Ni(1)−O(1)	2.002(5)	O(1)−Ni(1)−O(2)	81.4(2)
Ni(1)−O(2)	2.009(6)	O(1)−Ni(1)−N(2)	90.9(2)
Ni(1)−N(2)	2.036(7)	O(2)−Ni(1)−N(2)	159.2(3)
Ni(1)−N(1)	2.036(6)	O(1)−Ni(1)−N(1)	162.2(3)
Ni(1)−N(3)	2.064(7)	O(2)−Ni(1)−N(1)	90.7(3)
		N(2)−Ni(1)−N(1)	90.9(3)
		O(1)−Ni(1)−N(3)	103.8(3)
		O(2)−Ni(1)−N(3)	98.3(3)
		N(2)−Ni(1)−N(3)	102.3(3)
		N(3)−Ni(1)−N(1)	93.1(3)

The ^1H NMR spectra for complexes **1−4** show the resonance line pattern observed for the [12]aneN_3-macrocycle ligands that has been assigned on the basis of previous studies of nickel macrocyclic complexes.[16] The α-methylene protons shift downfield (∼330−25 ppm), whereas the β-methylene protons shift upfield (∼−7 to −36 ppm) with regard to the diamagnetic position. Equatorial protons are expected to experience larger contact shifts than axial protons and therefore the most downfield resonances are due to α-CH_{eq} and the most upfield ones to β-CH_{eq}.[18] The isotropically shifted ^1H NMR signals observed for methyl groups (2-Me, ∼−18 ppm, 4-Me(a, b), ∼30 and ∼19 ppm, and 9-Me−N, ∼95 ppm) can be initially assigned by inspection of their peak areas as well as methyl and phenyl groups of hydroxamates.

The crystal of complex **2** consists of [Ni([12]aneN_3-mc2)(Ah)]$^+$ cations and PF_6^- anions held together by electrostatic interactions. The structure of the cation is shown in Figure 1 with selected bond lengths and angles given in Table 2. The nickel atom is pentacoordinate, with a square pyramid arrangement of the chelating atoms. The three nitrogen atoms of the N_3 macrocycle occupy the apical position and two adjacent basal ones, whereas the other two basal positions correspond to the hydroxamate group. The nickel atom is 0.328(3) Å out of the basal plane (N1,N2,O1,O2, rmsd = 0.028) toward atom N3. This plane is nearly coplanar to the O1−N4−C14−O2 mean plane, the angle between both planes being 3.9(4)°. The two Ni−O bond lengths are similar (2.002(5) and 2.009(6) Å), and the hydroxamate ligand provides a close-to-ideally planar chelate ring (maximum deviation 0.06 Å for O2). The distances Ni−O are shorter than those found in acetohydroxamate dinuclear octahedral complexes of Ni(II).[9,10] However, these distances are very similar to that reported for the structure of *B. pasteurii* urease inhibited with acetohydroxamic acid.[8] The macrocycle is coordinated facially, with the imine chelate ring in the basal plane of the square pyramid. A feature of the structure is the presence of the methyl group (C12) close to the vacant octahedral coordination site, 2.91 Å from the nickel(II) ion. The closest contact between two cationic complexes is 2.282 Å for H2 and O1; this distance is longer than that of the majority of hydrogen bonds.

The effective magnetic moments for these compounds at roon temperature are in the 3.10−2.97 μ_B range, and they remain constant in the temperature range 100−300 K. The magnetic moments, at room temperature, estimated by NMR measurements in solution are in the 2.99−2.95 μ_B range. These values are those expected for magnetically isolated Ni(II) ions with a spin triplet ($S = 1$) ground state.

It has been suggested that the inhibition of urease by hydroxamic acids involves the coordinative saturation of two nickel centers with a 5/5 coordination number set.[8] All the reported inhibited-urease models[9,10] showed nickel atoms in an octahedral environment, and those were prepared by acetate displacement. The synthesis of complex **2** is based on the reaction between a bridging hydroxo ligand and the hydroxamic acid, and it represents the first example of a hydroxamate derivative bound to a nickel atom in a five-coordinate environment. Finally, to our knowledge, the mechanism of urease inhibition is not well established and the presence of a pentacoordinate nickel(II) moiety containing hydroxamate acting as chelate should not be ruled out.

Acknowledgment. This work has been supported by the Dirección General de Enseñanza Superior e Investigación Científica (PB97/1036). Dr F. Lloret of the University of Valencia, Spain, is thanked for measuring magnetic susceptibilities.

Supporting Information Available: X-ray crystallographic data and CIF files for obtained compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

IC010298+

---

[18] La Mar, G. N., Horrocks, W., Jr., Holm, R. H., Eds. *NMR of Paramagnetic Molecules*; Academic Press: New York, 1973; p 243.