Inorg. Chem. **2002**, *41*, 2981–2986

Novel Reactivity Mode of Hydroxamic Acids: A Metalla-Pinner Reaction

Konstantin V. Luzyanin,[†] Vadim Yu. Kukushkin,*[,†] Maxim L. Kuznetsov,[‡] Dmitrii A. Garnovskii,[‡] Matti Haukka,[§] and Armando J. L. Pombeiro*[,‡]

St. Petersburg State University, 198504 Stary Petergof, Russian Federation, Centro de Química Estrutural, Complexo I, Instituto Superior Técnico, Av. Rovisco Pais, 1049-001 Lisbon, Portugal, and Department of Chemistry, University of Joensuu, P.O. Box 111, FIN-8010 Joensuu, Finland

Received February 21, 2002

The reaction between the nitrile complex *trans*-$[PtCl_4(EtCN)_2]$ and benzohydroxamic acids $RC_6H_4C(=O)NHOH$ (R = *p*-MeO, *p*-Me, H, *p*-Cl, *o*-HO) proceeds smoothly in CH_2Cl_2 at ∼45 °C for 2–3 h (sealed tube) or under focused 300 W microwave irradiation for ∼15 min at 50 °C giving, after workup, good yields of the imino complexes $[PtCl_4\{NH{=}C(Et)ON{=}C(OH)(C_6H_4R)\}_2]$ which derived from a novel metalla-Pinner reaction. The complexes $[PtCl_4\{NH{=}C(Et)ON{=}C(OH)(C_6H_4R)\}_2]$ were characterized by elemental analyses (C, H, N), FAB mass spectrometry, and IR and ^1H and $^{13}C\{^1H\}$ spectroscopies, and $[PtCl_4\{NH{=}C(Et)ON{=}C(OH)(Ph)\}_2]$ (as the bis-dimethyl sulfoxide solvate), by X-ray single-crystal diffraction. The latter disclosed its overall *trans*-configuration with the iminoacyl species in the hydroximic tautomeric form in *E*-configuration which is held by N—H···N hydrogen bond between the imine =N*H* atom and the hydroximic N atom.

Introduction

Hydroxamic acids and metal hydroxamates are among the most studied compounds owing to their high applicability in diverse areas and significance in life processes. In bioinorganic chemistry, they are the subject of rapt attention as inhibitors of enzymes, for example, peroxidases,[1] ureases,[2] and matrix metalloproteinase,[3] and siderophores for iron(III).[4] In medicine, these acids have recently been widely used as key functional groups of potential therapeutics targeting cardiovascular diseases, HIV, and Alzheimer's disease.[5] Hydroxamic acid based chelation therapy is useful for the treatment of cancer,[6] metal poisoning,[7] iron-overload,[8] malaria,[9] allergic diseases,[10] and tuberculosis.[11] In agriculture, they play an important role in the chemical defense of cereals against pests such as insects and pathogenic fungi and bacteria[12] and as plant growth regulators.[13] Some other

* To whom correspondence should be addressed. E-mail: kukushkin@vk2100.spb.edu (V.Yu.K.); pombeiro@ist.utl.pt (A.J.L.P.).
[†] St. Petersburg State University.
[‡] Instituto Superior Técnico.
[§] University of Joensuu.

(1) O'Brien, E. C.; Farkas, E.; Gil, M. J.; Fitzgerald, D.; Castineras, A.; Nolan, K. B. *J. Inorg. Biochem.* **2000**, *79*, 47. (b) Tsukamoto, K.; Itakura, H.; Sato, K.; Fukuyama, K.; Miura, S.; Takahashi, S.; Ikezawa, H.; Hosoya, T. *Biochemistry* **1999**, *38*, 12558.
(2) Benini, S.; Rypniewski, W. R.; Wilson, K. S.; Miletti, S.; Ciurli, S.; Mangani, S. *J. Biol. Inorg. Chem.* **2000**, *5*, 110. (b) Zhang, Y.; Li, D.; Houtman, J. C.; Witiak, D. T.; Seltzer, J.; Bertics, P. J.; Lauhon, C. T. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 2823. (c) Brown, D. A.; Cuffe, L. P.; Fitzpatrick, N. J.; Glass, W. K.; Herlihy, K.; Nimir, H.; Deeg, O.; Errington, W.; Kemp, T. J. *Chem. Commun.* **1998**, 2433. (d) 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.
(3) Porter, J. R.; Millican, T. A.; Morphy, J. R. *Expert Opin. Ther. Pat.* **1995**, *5*, 1287; *Chem. Abstr.* **1996**, *124*, 80174. (b) Hidalgo, M.; Eckhardt, S. G. *J. Natl. Cancer Inst.* **2001**, *93*, 178. (c) Yamamoto, M.; Hirayama, R.; Naruse, K.; Yoshino, K.; Shimada, A.; Inoue, S.; Kayagaki, N.; Yagita, H.; Okumura, K.; Ikeda, S. *Drug Des. Discovery* **1999**, *16*, 119. (d) Steinman, D. H.; Curtin, M. L.; Garland, R. B.; Davidsen, S. K.; Heyman, H. R.; Holms, J. H.; Albert, D. H.; Magoc, T. J.; Nagy, I. B.; Marcotte, P. A.; Li, J.; Morgan, D. W.; Hutchins, C.; Summers, J. B. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 2087. (e) Hooper, N. M.; Turner, A. J. *Biochem. Soc. Trans.* **2000**, *28*, 441−6.
(4) Albrecht-Gary, A. M.; Libman, J.; Shanzer, A. *Pure Appl. Chem.* **1996**, *68*, 1243. (b) Crumbliss, A. L. *Coord. Chem. Rev.* **1990**, *105*, 155. (c) Hara, Y.; Shen, L.; Tsubouchi, A.; Akiyama, M.; Umemoto, K. *Inorg. Chem.* **2000**, *39*, 5074.
(5) El Yazal, J.; Pang, Y.-P. *J. Phys. Chem. B* **2000**, *104*, 6499. (b) El Yazal, J.; Pang, Y.-P. *J. Phys. Chem. A* **1999**, *103*, 8346.
(6) Steward, W. P.; Thomas, A. L. *Expert Opin. Invest. Drugs* **2000**, *9*, 2913. (b) Steward, W. P. *Cancer Chemother. Pharmacol.* **1999**, *43*, Suppl. S56−60. (c) Brammer, R.; Buckels, J.; Bramhall, S. *Int. J. Clin. Pract.* **2000**, *54*, 373−381.
(7) Domingo, J. L. *Reprod. Toxicol.* **1998**, *12*, 499−510; *Chem. Abstr.* **1998**, *129*, 311786.
(8) Turcot, I.; Stintzi, A.; Xu, J.; Raymond, K. N. *J. Biol. Inorg. Chem.* **2000**, *5*, 634. (b) Richardson, D. R.; Ponka, P. *J. Lab. Clin. Med.* **1998**, *131*, 306.
(9) Cabantchik, Z. I. *Parasitol. Today* **1995**, *11*, 74; *Chem. Abstr.* **1995**, *122*, 229826. (b) Tsafack, A.; Golenser, J.; Libman, J.; Shanzer, A.; Cabantchik, Z. I. *Mol. Pharmacol.* **1995**, *47*, 403; *Chem. Abstr.* **1995**, *122*, 230213.
(10) Igeta, K.; Tobetto, K.; Saiki, I.; Odake, S.; Fujisawa, T.; Matsuo, T.; Oku, T. PCT Int. Appl. WO 00 03,703, 2000; *Chem. Abstr.* **2000**, *132*, 117536.
(11) Miller, M. J. *Chem. Rev.* **1989**, *89*, 1563 and references therein.

10.1021/ic025554c CCC: $22.00
Published on Web 05/04/2002

practical areas involving hydroxamic acids and their complexes include removal of toxic elements by solvent extraction,[14] usage as efficient and environmentally friendly corrosion inhibitors,[15] applications as collectors for flotation of minerals,[16] antioxidant acivity,[17] and their potential as redox switches for electronic devices.[18]

Amazingly, such a broad spectrum of activity of hydroxamic acids is almost exclusively associated with *only one type of chemical reactions*; that is, their ability to bind a large variety of metal ions forms, in the vast majority of cases, *O,O* five-membered chelate rings[19−21] (bridging[22,23] and monodentate[24] coordination modes are also known, although scarce), and these complexes are often characterized by very high stability constants.[21] Although hydroxamic acids have been known for over a century,[25] their reactivity modes involving metal centers, besides the complex forming properties, are practically unexplored; among the rare exceptions are the recently described deoxygenation of the N−OH group occurring at Os(III) and Rh(I) centers,[26] Ni(II)-assisted hydroxylamine elimination,[23] and reductive cleavage of the N−O bond with SmI_2.[27]

In recent years, our group has been involved in investigations of the reactivity of metal-activated nitriles, a topic that has recently been reviewed by two of us.[28] In particular, the reaction between platinum(IV) complexes $[PtCl_4(RCN)_2]$ (R = alkyl, benzyl, phenyl),[29−31] and also nitrile complexes of Pt(II),[32] Rh(III),[33] and Re(IV),[34] with such N*OH* nucleophiles as oximes, RR′C═NOH, and dialkyl hydroxylamines, R_2-NOH, giving a C−O bond upon addition of the OH group across the nitrile group of metal-activated RCN, have been observed. As a continuation of this project, we focused our attention on hydroxamic acids as potential N*OH* nucleophiles (where the N *amide* atom in the sp^2 hybridization[35] is different of the sp^3 *amine* nitrogen in hydroxylamines) and found, instead of the conventional chelation, a novel reactivity pattern for those species, that is, their involvement in a new metalla-Pinner type reaction leading to their *O*-addition to the nitrile carbon. In organic chemistry, the Pinner reaction,[28] interaction between an organonitrile and an alcohol which is typically performed in the presence of substantial amounts of hydrogen chloride, is widely applicable for the preparation of imino esters which are, in turn, useful as synthons for further versatile conversions. We have now extended this type of reaction to hydroxamic acids in a novel metal-mediated process.

Experimental Section

Materials and Instrumentation. Hydroxamic acids were synthesized in accord with the published method.[20] Solvents were obtained from commercial sources and used as received while dichloromethane was conventionally dried. The complex $[PtCl_4(EtCN)_2]$ was prepared as previously described.[36] C, H, and N elemental analyses were carried out by the Microanalytical Service of the Instituto Superior Técnico. For TLC, Merck UV 254 SiO_2 plates have been used. Positive-ion FAB mass spectra were obtained on a Trio 2000 instrument by bombarding 3-nitrobenzyl alcohol (NBA) matrixes of the samples with 8 keV ($\sim 1.28 \times 10^{15}$ J) Xe atoms. Mass calibration for data system acquisition was achieved using CsI. Infrared spectra (4000−400 cm^{-1}) were recorded on a BIO-RAD FTS 3000MX instrument in KBr pellets. ^1H and $^{13}C\{^1H\}$ NMR spectra were measured on a Varian UNITY 300 spectrometer at ambient temperature. The microwave experiments

(12) Gierl, A.; Frey, M. *Novartis Found. Symp*. **1999**, *223*, 150; *Chem. Abstr*. **2000**, *133*, 263823.
(13) Rentzea, C.; Rademacher, W.; Harreus, A.; Jung, J. Eur. Pat. Appl. EP 350,693, 1990; *Chem. Abstr*. **1990**, *113*, 40433. (b) Moser, H.; Schurter, R. Ger. Offen. 2,709,854, 1977; *Chem. Abstr*. **1977**, *87*, 201125.
(14) Szymanowski, J. *Miner. Process. Extr. Metall. Rev*. **1998**, *18*, 389; *Chem. Abstr*. **2000**, *133*, 284426. (b) Szymanowski, J. *Pol. J. Appl. Chem*. **1996**, *40*, 3; *Chem. Abstr*. **1997**, *126*, 146462.
(15) Kalman, E.; Felhosi, I.; Karman, F. H.; Lukovits, I.; Telegdi, J.; Palinkas, G. *Mater. Sci. Technol*. **2000**, *19* (Pt. 1), 471; *Chem. Abstr*. **2000**, *134*, 20007.
(16) Willis, M. J.; Mathur, S.; Young, R. H. *Adv. Flotation Technol.*, Proceedings of Symposium of Society for Mining, Metallurgy, and Exploration, Littleton, CO, 1999; Parekh, B. K., Miller, J. D., Eds.; p 219; *Chem. Abstr*. **1999**, *132*, 95954. (b) Lee, J. S.; Nagaraj, D. R.; Coe, J. E. *Miner. Eng*. **1998**, *11*, 929; *Chem. Abstr*. **1998**, *129*, 292133.
(17) Collis, C. S.; Rice-Evans, C. A. *Antioxid. Health Dis*. **1997**, *4*, 409; *Chem. Abstr*. **1997**, *127*, 185242.
(18) Inouye, M. *Kagaku (Kyoto)* **1995**, *50*, 512; *Chem. Abstr*. **1995**, *123*, 157215.
(19) Larin, G. M. *Russ. J. Coord. Chem*. **1999**, *25*, 750. (b) Kurzak, B.; Kozlowski, H.; Farkas, E. *Coord. Chem. Rev*. **1992**, *114*, 169. (c) Agraval, I. K. *Usp. Khim*. **1979**, *48*, 1773−1803. (d) Mizukami, S.; Nagata, K. *Coord. Chem. Rev*. **1968**, *3*, 267.
(20) Chatterjee, B. *Coord. Chem. Rev*. **1978**, *26*, 281.
(21) For general compilation of stability constants see: Menon, S. K.; Agrawal, Y. K. *Rev. Inorg. Chem*. **1996**, *16*, 1. (b) For metal complex formation properties of the naturally occurring hydroxamate-type siderophore desferrioxamine B see: Kiss, T.; Farkas, E. *J. Inclusion Phenom. Mol. Recognit. Chem*. **1998**, *32*, 385. (c) For stability constants of Al complexes see: Yokel, R. A. *J. Toxicol. Environ. Health* **1994**, *41*, 131.
(22) Benini, S.; Rypniewski, K. S.; Wilson, K. S.; Miletti, S.; Ciurli, S.; Mangani, S. *J. Biol. Inorg. Chem*. **2000**, *5*, 110.
(23) Brown, D. A.; Cuffe, L. P.; Fitzpatrick, N. J.; Glass, W. K.; Herlihy, K.; Nimir, H.; Deeg, O.; Errington, W.; Kemp, T. J. *Chem. Commun*. **1998**, 2433.
(24) Scolnick, L. R.; Clements, A. M.; Liao, J.; Crenshaw, L.; Helberg, M.; May, J.; Dean, T. R.; Christianson, D. W. *J. Am. Chem. Soc*. **1997**, *119*, 850.
(25) Kikugawa, Y. *Rev. Heteroat. Chem*. **1996**, *15*, 263; *Chem. Abstr*. **1997**, *126*, 59462. (b) Kikugawa Y. *Yakugaku Zasshi* **1995**, *115*, 909.
(26) Das, A.; Basuli, F.; Falvello, L. R.; Bhattacharya, S. *Inorg. Chem*. **2001**, *40*, 4085. (b) Das, A.; Basuli, F.; Peng, S.-M.; Bhattacharya, S. *Inorg. Chem*. **2002**, *41*, 440.
(27) Keck, G. E.; Wager, T. T.; McHardy, S. F. *Tetrahedron* **1999**, *55*, 11755.
(28) Kukushkin, V. Yu.; Pombeiro, A. J. L. *Chem. Rev*., in press.
(29) Kukushkin, V. Yu.; Pakhomova, T. B.; Bokach, N. A.; Wagner, G.; Kuznetsov, M. L.; Galanski, M.; Pombeiro, A. J. L. *Inorg. Chem*. **2000**, *39*, 216. (b) Kukushkin, V. Yu.; Pakhomova, T. B.; Kukushkin, Yu. N.; Herrmann, R.; Wagner, G.; Pombeiro, A. J. L. *Inorg. Chem*. **1998**, *37*, 6511.
(30) Kuznetsov, M. L.; Bokach, N. A.; Kukushkin, V. Yu.; Pakkanen, T.; Wagner, G.; Pombeiro, A. J. L. *J. Chem. Soc., Dalton Trans*. **2000**, 4683.
(31) Wagner, G.; Pombeiro, A. J. L.; Kukushkin, Yu. N.; Pakhomova, T. B.; Ryabov, A. D.; Kukushkin, V. Yu. *Inorg. Chim. Acta* **1999**, *292*, 272.
(32) Ferreira, C. M. P.; Guedes da Silva, M. F. C.; Fraústo da Silva, J. J. R.; Pombeiro, A. J. L.; Kukushkin, V. Yu.; Michelin, R. A. *Inorg. Chem*. **2001**, *40*, 1134.
(33) Kukushkin, V. Yu.; Ilichev, I. V.; Zhdanova, M. A.; Wagner, G.; Pombeiro, A. J. L. *J. Chem. Soc., Dalton Trans*. **2000**, 1567. (b) Kukushkin, V. Yu.; Ilichev, I. V.; Wagner, G.; Fraústo da Silva, J. J. R.; Pombeiro, A. J. L. *J. Chem. Soc., Dalton Trans.* **1999**, 3047.
(34) Wagner, G.; Pombeiro, A. J. L.; Bokach, N. A.; Kukushkin, V. Yu. *J. Chem. Soc., Dalton Trans.* **1999**, 4083.
(35) Podlaha, J.; Cisarova, I.; Soukupova, L.; Schraml, J. *Collect. Czech. Chem. Commun*. **2000**, *65*, 1273.
(36) Luzyanin, K. V.; Haukka, M.; Bokach, N. A.; Kuznetsov, M. L.; Kukushkin, V. Yu.; Pombeiro, A. J. L. *J. Chem. Soc., Dalton Trans*. **2002**, 1882.

Table 1. Crystal Data for *trans*-[$PtCl_4${*E*-NH=C(Et)ON=C(OH)Ph}$_2$]·2(Me_2SO)

empirical formula	$C_{24}H_{36}Cl_4N_4O_6PtS_2$
fw	877.58
temp, K	150(2)
λ, Å	0.71073
cryst syst	triclinic
space group	$P\bar{1}$ (No. 2)
a, Å	7.9885(2)
b, Å	8.6198(2)
c, Å	12.4855(3)
α, deg	87.562(1)
β, deg	75.856(1)
γ, deg	86.901(1)
V, Å^3	832.08(3)
Z	1
θ-range, deg	3.75−27.46
ρ_{calcd}, g/cm^3	1.751
μ(Mo Kα), mm^{-1}	4.705
reflns collected/unique	7928/3756
R_{int}	0.0464
R1[a] ($I \geq 2\sigma$)	0.0270
wR2[b] ($I \geq 2\sigma$)	0.0648

[a] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$. [b] $wR2 = [\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]]^{1/2}$.

were performed in a CEM focused microwave synthesis system (model Discover).

X-ray Structure Determination of *trans*-[$PtCl_4${NH=C(Et)-ON=C(OH)Ph}$_2$]·2(Me_2SO). The X-ray diffraction data were collected on a Nonius Kappa CCD diffractometer using Mo Kα radiation ($\lambda = 0.71073$ Å) and the Collect[37] data collection program. The Denzo-Scalepack[38] program package was used for cell refinements and data reduction. The structure was solved by direct methods using the SIR97 program.[39] An empirical absorption correction based on equivalent reflections[40] was applied to data ($T_{max}/T_{min} = 0.38569$ and 0.21172). The structure was refined with the SHELXL97[41] program and the WinGX graphical user interface.[42] Pt was placed on a center of symmetry, and the asymmetric unit contained half of the *trans*-[$PtCl_4${NH=C(Et)ON=C(OH)Ph}$_2$] molecule. The sulfur atom in the Me_2SO solvent molecule was disordered in two positions with occupation parameters of ~0.9 and 0.1. Hydrogens H(1) and H(2), bonded to nitrogen and oxygen, respectively, were located from the difference Fourier map and refined isotropically. All other hydrogens were placed in idealized positions and were fixed or constrained to ride on their parent atom. Crystallographic data are summarized in Table 1, and selected bond lengths and angles, in the Figure 1 legend.

Computational Details. The full geometry optimization of all structures has been carried out at the restricted Hartree−Fock level of theory with help of the GAMESS[43] program package. Symmetry operations were not applied. The single-point calculations at the MP2[44] level on the basis of the equilibrium Hartree−Fock geometries also have been performed in order to take into account the electron correlation effects. A quasirelativistic Stuttgart pseudopotential described 60 core electrons, and the appropriate contracted basis set (8s7p6d)/[6s5p3d] for the platinum atom[45] was used. The standard basis set of Gauss functions 6-31G[46,47] was selected for all other atoms, and d-type polarization functions with exponent 0.75[47,48] were added for the Cl atoms. The Hessian matrix was calculated numerically for all structures in order to prove the location of correct minima (all structures have no imaginary frequencies), and the zero-point vibrational energies have been estimated. The starting conformation of *trans*-[$PtCl_4$(N≡CMe)-{N(H)=C(Me)ONC(OH)Me}] (**HI**) corresponded to the experimental structure from this work. For *trans*-[$PtCl_4$(N≡CMe){N(H)=C(Me)ON(H)C(=O)Me}] (**HA**), the experimental structural data are unavailable, and in order to check all possible conformations of this form, the calculations have been carried out on the basis of the structures with the different conformation of the N(H)=C(Me)-ON(H)C(=O)Me fragment.

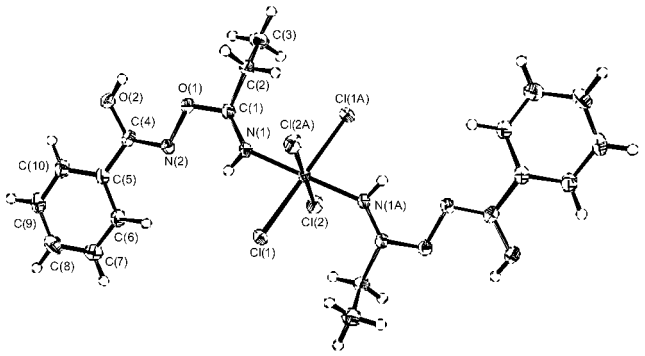


Figure 1. ORTEP drawing of *trans*-[$PtCl_4${NH=C(Et)ON=C(OH)Ph}$_2$]·2(Me_2SO) with the atomic numbering scheme (two Me_2SO molecules are omitted for clarity). The thermal ellipsoids are drawn at the 50% probability level. Selected bond lengths (Å) and angles (deg): Pt(1)−Cl(1) 2.3147(8), Pt(1)−Cl(2) 2.3193(8), Pt(1)−N(1) 2.028(3), N(1)−C(1) 1.277(4), C(1)−C(2) 1.494(4), C(1)−O(1) 1.345(4), O(1)−N(2) 1.443(4), N(2)−C(4) 1.291-(4), C(4)−O(2) 1.316(4), C(4)−C(5) 1.481(5), Cl(1)−Pt(1)−Cl(2) 91.11(3), Cl(1)−Pt(1)−N(1) 84.62(8), Cl(2)−Pt(1)−N(1) 88.38(9), Pt(1)−N(1)−C(1) 134.8(2), N(1)−C(1)−O(1) 120.7(3), O(1)−N(2)−C(4) 108.1(3), N(2)−C(4)−O(2) 127.3(3).

Addition of $RC_6H_4C(=O)NHOH$ (R = *p*-MeO, *p*-Me, H, *p*-Cl, *o*-HO) to *trans*-[$PtCl_4(EtCN)_2$]. In a typical experiment, *trans*-[$PtCl_4(EtCN)_2$] (0.050 g, 0.11 mmol) is dissolved in dichloromethane (5 mL) at 20−25 °C, the hydroxamic acid (0.22 mmol) is added, and the reaction mixture is heated in a sealed tube at 45−47 °C for 2−3 h until the hydroxamic acid is dissolved. The orange solution is evaporated to ~$^1/_2$ of its initial volume, and diethyl ether (2 mL) is added. An excess of the hydroxamic acid precipitates and is removed by filtration. In the case of *p*-methoxybenzohydroxamic acid, the filtrate is evaporated to dryness, and diethyl ether (5 mL) is added to the residue formed giving a yellow solution, which is left to stand overnight in a closed flask. The bright yellow crystals formed are filtered off and dried in air at room temperature. In the case of other acids, the filtrate is

(37) *Collect*, data collection software; Nonius B.V.: Delft, The Netherlands, 1997−2000.
(38) Otwinowski, Z.; Minor, W. Processing of X-ray Diffraction Data Collected in Oscillation Mode. In *Macromolecular Crystallography, Part A*; Carter, C. W., Jr., Sweet, R. M., Eds.; Methods in Enzymology Volume 276; Academic Press: New York, 1997; pp 307−326.
(39) Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G. L.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A. G. G.; Polidori, G.; Spagna, R. *J. Appl. Crystallogr*. **1999**, *32*, 115.
(40) Sheldrick, G. M. *SHELXTL*, Version 5.1; Bruker Analytical X-ray Systems, Bruker AXS, Inc.: Madison, WI, 1998.
(41) Sheldrick, G. M. *SHELXL97*, Program for Crystal Structure Refinement; University of Göttingen: Göttingen, Germany, 1997.
(42) Farrugia, L. J. *J. Appl. Crystallogr*. **1999**, *32*, 837.
(43) Schmidt, M. W.; Baldridge, K. K.; Boatz, J. A.; Elbert, S. T.; Gordon, M. S.; Jensen, J. H.; Koseki, S.; Matsunaga, N.; Nguyen, K. A.; Su, S. J.; Windus, T. L.; Dupuis, M.; Montgomery, J. A. *J. Comput. Chem*. **1993**, *14*, 1347.
(44) Møller, C.; Plesset, M. S. *Phys. Rev*. **1934**, *46*, 618. (b) Binkley, J. S.; Pople, J. A. *Int. J. Quantum. Chem*. **1975**, *9*, 229.
(45) Andrae, D.; Haeussermann, U.; Dolg, M.; Stoll, H.; Preuss, H. *Theor. Chim. Acta* **1990**, *77*, 123.
(46) Ditchfield, R.; Hehre, W. J.; Pople, J. A. *J. Chem. Phys*. **1971**, *54*, 724. (b) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys*. **1972**, *56*, 2257.
(47) Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S.; DeFrees, D. J.; Pople, J. A. *J. Chem. Phys*. **1982**, *77*, 3654.
(48) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213.

evaporated to dryness and the solid washed with pentane. Yields are 70−80%, based on Pt. The reaction is accelerated by focused 300 W microwave irradiation and completed for ∼15 min at 50 °C giving the same isolated yields.

[PtCl$_4${NH=C(Et)ON=C(OH)(C$_6$H$_4$OMe-*p*)}$_2$]. Anal. Calcd for $C_{22}H_{28}N_4Cl_4O_6Pt$: C, 33.81; H, 3.61; N, 7.17%. Found: C, 33.49; H, 3.71; N, 7.00%. FAB$^+$-MS, *m*/*z*: 783 [M + H], 710 [M − 2Cl], 674 [M − 3Cl + H]. TLC on SiO_2: R_f = 0.38 (eluent $Me_2CO/CHCl_3$ = 3:1). IR spectrum (selected bands), cm^{-1}: 3265 mw ν(N−H), 1709 (variable intensity, see text) ν(C=O), 1669 m and 1608 s ν(C=N), 1256 s ν(C−OMe), 1024 s ν(O−Me), 839 s δ(C−H) (aryl). ^{1}H NMR spectrum in DMSO-d_6, δ: 1.29 (t, *J* 7.5 Hz, 3*H*, CH_2*Me*), 3.12 (quart, *J* 7.5 Hz, 2*H*, C*H*$_2$Me), 3.82 (s, 3*H*, O*Me*), 7.10 (d, *J* 8.8 Hz, 2*H*, meta) and 7.79 (d, *J* 8.8 Hz, 2*H*, ortho) (aryl), 8.56 (s, br, 1*H*, C=N*H*). ^{13}C{^{1}H} NMR in DMSO-d_6, δ: 10.8 (CH_3) and 26.0 (CH_2) (Et), 55.2 (O*C*H$_3$), 114.0, 114.3, 114.9 and 119.8 (*C*$_6$H$_4$OMe), 164.8 and 176.6 (C=O and HN=*C*).

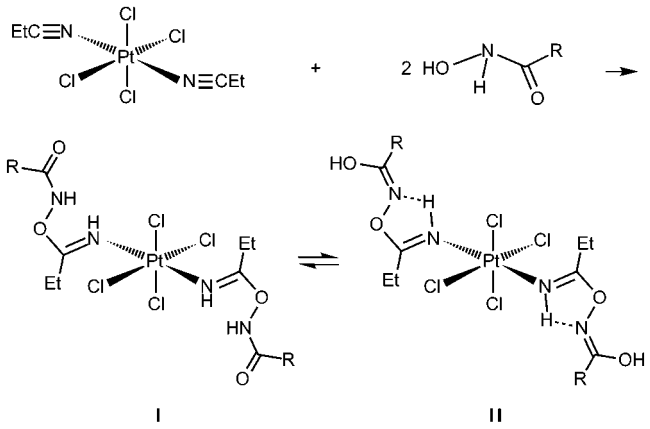
[PtCl$_4${NH=C(Et)ON=C(OH)(C$_6$H$_4$Me-*p*)}$_2$]·$^1/_2$Et$_2$O. Anal. Calcd for $C_{22}H_{28}N_4Cl_4O_4Pt\cdot{}^1/_2Et_2O$: C, 36.65; H, 4.23; N, 7.12%. Found: C, 36.52; H, 4.25; N, 7.22%. FAB$^+$-MS, *m*/*z*: 749 [M + H], 713 [M − Cl], 642 [M − 3Cl − H], 606 [M − 4Cl − H]. TLC on SiO_2: R_f = 0.61 (eluent $Me_2CO/CHCl_3$ = 3:1). IR spectrum (selected bands), cm^{-1}: 3273 mw ν(N−H), 1705 (variable intensity, see text) ν(C=O), 1648 and 1611 s ν(C=N), 827 m δ(C−H) (aryl). ^{1}H NMR spectrum in DMSO-d_6, δ: 1.31 (t, *J* 7.2 Hz, 3*H*, CH_2*Me*), 3.14 (quart, *J* 7.2 Hz, 2*H*, C*H*$_2$Me), 2.39 (s, 3*H*, C*Me*), 7.38 (d, *J* 7.8 Hz, 2*H*, meta) and 7.74 (d, *J* 7.8 Hz, 2*H*, ortho) (aryl), 8.58 (s, br, 1*H*, C=N*H*), 11.12 (s, br, 1*H*, O*H*). ^{13}C{^{1}H} NMR in DMSO-d_6, δ: 10.9 (CH_3) and 21.0 (CH_2) (Et), 20.4 (C$_6$H$_4$*C*H$_3$), 118.0, 118.3, 126.9, 128.7, 129.1 and 129.9 (*C*$_6$H$_4$Me), 164.3 and 179.7 (C=O and HN=*C*). The solvated Et_2O has been detected in the NMR spectra.

[PtCl$_4${NH=C(Et)ON=C(OH)Ph}$_2$]·$^1/_2$CH$_2$Cl$_2$. Anal. Calcd for $C_{20}H_{24}N_4Cl_4O_4Pt\cdot{}^1/_2CH_2Cl_2$: C, 32.24; H, 3.30; N, 7.34%. Found: C, 32.26; H, 3.53; N, 7.00%. FAB$^+$-MS, *m*/*z*: 650 [M − 2Cl], 614 [M − 3Cl − H], 579 [M − 4Cl]. TLC on SiO_2: R_f = 0.50 (eluent $Me_2CO/CHCl_3$ = 3:1). IR spectrum (selected bands), cm^{-1}: 3216 mw ν(N−H), 1710 (variable intensity, see text) ν(C=O), 1663 and 1609 s ν(C=N), 832 s δ(C−H) (aryl). ^{1}H NMR spectrum in $CDCl_3$, δ: 1.35 (t, J_{HH} 7.5 Hz, 3*H*, CH_2*Me*), 3.18 (quart, J_{HH} 7.5 Hz, 2*H*, C*H*$_2$Me), 7.40−7.51 (m, 3*H*, meta + para) and 7.74 (m, 2*H*, ortho) (*Ph*), 8.70 (br, 1*H*, C=N*H*), 11.31 (s, br, 1*H*, O*H*). ^{13}C{^{1}H} NMR in DMSO-d_6, δ: 11.0 (CH_3) and 24.3 (CH_2) (Et), 127.2, 128.9, 129.7 and 132.6 (*Ph*), 162.8 and 178.5 (C=O and HN=*C*). The solvated CH_2Cl_2 has been detected in the NMR spectra.

[PtCl$_4${NH=C(Et)ON=C(OH)(C$_6$H$_4$Cl-*p*)}$_2$]. Anal. Calcd for $C_{20}H_{22}N_4Cl_6O_4Pt$: C, 30.40; H, 2.81; N, 7.09%. Found: C, 30.18; H, 2.95; N, 7.00%. FAB$^+$-MS, *m*/*z*: 755 [M − Cl], 717 [M − 2Cl + H], 683 [M − 3Cl], 647 [M − 4Cl]. TLC on SiO_2: R_f = 0.38 (eluent $Me_2CO/CHCl_3$ = 3:1). IR spectrum (selected bands), cm^{-1}: 3270 mw ν(N−H), 1711 (variable intensity, see text) ν(C=O), 1665 and 1619 s ν(C=N), 1092 s ν(Aryl−Cl), 839 s δ(C−H) (aryl). ^{1}H NMR spectrum in DMSO-d_6, δ: 1.29 (t, *J* 7.5 Hz, 3*H*, CH_2*Me*), 3.12 (quart, *J* 7.5 Hz, 2*H*, C*H*$_2$Me), 3.82 (s, 3*H*, O*Me*), 7.51 (d, *J* 8.6 Hz, 2*H*, meta) and 7.83 (d, *J* 8.6 Hz, 2*H*, ortho) (aryl), 8.57 (s, br, 1*H*, C=N*H*), 11.25 (s, br, 1*H*, O*H*). ^{13}C{^{1}H} NMR in DMSO-d_6, δ: 11.0 (CH_3) and 21.5 (CH_2) (Et), 128.5, 128.7, 129.1 and 129.4 (*C*$_6$H$_4$OCl-*p*), 176.5 and 166.7 (C=O and HN=*C*).

[PtCl$_4${NH=C(Et)ON=C(OH)(C$_6$H$_4$OH-*o*)}$_2$]. In the case of salycylhydroxamic acid, the addition is not selective, and the reaction gives a mixture of products. The target addition product was detected in the mixture and characterized as indicated later.

Scheme 1



However, our attempts to isolate [PtCl$_4${NH=C(Et)ON=C(OH)-(C$_6$H$_4$OH-*o*)}$_2$] in the pure form by recrystallization or by column chromatography failed because of either thermal instability of the compound or decomposition on SiO_2, respectively. FAB$^+$-MS, *m*/*z*: 717 [M − Cl], 681 [M − 2Cl], 645 [M − 3Cl]. IR spectrum (selected bands), cm^{-1}: 3559 m ν(O−H), 3260 mw ν(N−H), 1728 (variable intensity, see text) ν(C=O), 1697 s and 1611 m ν(C=N), 1082 m ν(Aryl−Cl), 829 s δ(C−H) (aryl). ^{1}H NMR spectrum in DMSO-d_6, δ: 0.97 (t, *J* 7.5 Hz, 3*H*, CH_2*Me*), 2.04 (quart, *J* 7.5 Hz, 2*H*, C*H*$_2$Me), 6.91−7.26 (m, 4*H*) (aryl), 8.30 (s, br, 1*H*, C=N*H*), 11.62 (s, 1*H*, OH). ^{13}C{^{1}H} NMR in DMSO-d_6, δ: 11.0 (CH_3) and 23.5 (CH_2) (Et), 126.5, 127.5, 128.1, 128.7, 129.1 and 129.4 (*C*$_6$H$_4$OH-*o*), 166.5 and 176.8 (C=O and HN=*C*).

Results and Discussion

The reaction between the nitrile complex *trans*-[PtCl$_4$-(EtCN)$_2$] (addressed for this study because of its rather good solubility in CH_2Cl_2) and benzohydroxamic acids RC$_6$H$_4$C-(=O)NHOH (R = *p*-MeO, *p*-Me, H, *p*-Cl, *o*-HO) proceeds smoothly in CH_2Cl_2 at ∼45 °C for 2−3 h (sealed tube), and subsequent workup allowed the isolation of new complexes in good yields. The reaction is accelerated by focused 300 W microwave irradiation and completed for ∼15 min at 50 °C giving the compounds in 70%−80%. The satisfactory elemental analyses and coherent FAB-MS and NMR data favor the addition of the hydroxamic acids to the nitrile carbon atom giving the iminoacylated products, which, in principle, can be obtained in two tautomeric forms, I and II (Scheme 1).

The products of the reaction show no bands of ν(C≡N) stretching vibrations but display two intense bands in the range 1697−1611 cm^{-1} due to ν(C=N),[29] and one more band at ∼1710 cm^{-1}, whose intensity varies randomly from sample to sample within the same compound and also depends on the R radical of the reagent. If the later band can be attributed to ν(C=O), and this assumption is supported by the conducted quantum chemical calculations, in the hydroxamic form I (Scheme 1), the results obtained give collateral evidence in favor of concurrent formation of the two tautomers in a ratio which depends on both experimental conditions and type of hydroxamic acid employed.

All the complexes exhibit rather poor solubility in the most common solvents, and NMR spectra were obtained only in dmso-d_6 where the compounds gradually decompose (∼50%

degradation is observed for ~3−4 h) to give some yet unidentified reddish-brown Pt-containing species and EtC(=O)NH_2. However, measuring the spectra soon after dissolution allowed the observation of only one set of signals from one tautomeric form, and these peaks were attributed to the HN=C(Et) part of the hydroxamic/hydroximic functionality.

In one case, a crystalline material, that is, [$PtCl_4${NH=C(Et)-ON=C(OH)Ph}$_2$], appeared soon after dissolution of the complex in dmso-d_6, and these crystals were subject to X-ray study. The coordination polyhedron of the bis-solvated complex is a slightly distorted octahedron, Figure 1.

The Pt−Cl and Pt−N bond lengths and also all bond angles around the Pt center are normal, and they are of typical values for other platinum(IV) complexes.[29,49] The imine ligands are mutually trans. The two C=N bonds are equal within 3σ [1.277(4) and 1.291(4) Å], and they agree well with typical values for the C=N double bonds;[50] concurrently, the C−O bond [1.316(4) Å] is a typical single bond. Inspection of these values clearly indicates that the iminoacylated ligand is stabilized in the hydroximic tautomeric form (II) in the *E*-configuration with N−H···H hydrogen bond between the imine C=N*H* atom and the hydroximic nitrogen with the following observed distances and angles: N(1)−H(1) 0.85(5), N(1)···N(2) 2.559(3), N(1)−H(1)···N(2) 2.11(5), and the angle N(1)−H(1)···N(2) is 113(4)°. Unfortunately, comparison of the IR spectra of [$PtCl_4${NH=C(Et)-ON=C(OH)Ph}$_2$] *before* the dissolution in dmso-d_6 and *after* the isolation of the bis-solvate was not constructive because in the latter case the two dimethyl sulfoxide molecules in the lattice strongly affect the fingerprint area.

The isolation of the complex in the pure hydroximic form is unusual insofar as it is well-documented by both theoretical[5,51] and experimental studies that the hydroxamic form is the dominant one in free hydroxamic acids,[52] metal hydroxamates,[53] and *O*-acylated or *O*-silylated hydroxamic acids.[54] We assumed, albeit based on so far scarce experimental data, that the coordination led to a higher stabilization of the II form, and to get additional arguments favoring this assumption, a theoretical study on the relative stabilities of the two tautomeric forms has been conducted.

Table 2. Calculated Total Energies E_{tot} (Hartree), Zero-Point Energies, ZPE (kcal/mol) and Relative Energies, E_{rel} (kcal/mol) with the Most Stable Isomer as a Reference

	HF//HF			MP2//HF	
	E_{tot}	ZPE	E_{rel}[a]	E_{tot}	E_{rel}
HI	−2502.800085	124.83	0.72 (0.48)	2504.640755	2.02
HA1	−2502.801239	125.07	0.0 (0.0)	2504.643972	0.0
HA2	−2502.799745	124.82	0.93 (0.71)	2504.641026	1.85
HA3	−2502.795449	124.94	3.63 (3.50)	2504.636135	4.92
HA4	−2502.794768	125.04	4.06 (4.06)	2504.634886	5.70

[a] Values in parentheses include zero-point corrections.

The full geometry optimization of the two model compounds bearing the iminoacyl ligands in the hydroximic and the hydroxamic forms, that is, *trans*-[$PtCl_4$(N≡CMe){N(H)=C(Me)ONC(OH)Me}] (HI) and *trans*-[$PtCl_4$(N≡CMe){N(H)=C(Me)ON(H)C(=O)Me}] (HA), has been performed. The conformation of the equilibrium structure of HI and the H-bonding pattern correspond to the experimental ones, and the main calculated bond lengths are in very good agreement with the experimental X-ray data (the maximum deviation of 0.043 Å for the Pt−Cl bonds and not higher than 0.021 Å for the other bonds). For HA, four minima, associated with four structures (HA1−4, Table 2) having different conformations of the hydroxamic moiety, were located on the potential energy surface; the bond lengths for all the HA structures are very close to each other. The calculations at the Hartree−Fock level show that the difference of the total energies of HI and the most energetically favorable HA structures (HA1 and HA2; the schematic representation of HA1 is given in Scheme 1 as I) is small and does not exceed 1 kcal/mol; the zero-point correction additionally decreases this difference. The electron correlation correction at MP2//HF level increases the relative stability of HA1 and HA2 although the energy difference between HI and HA1 is still rather small, that is, 2.02 kcal/mol. Hence, the theoretical study gives further support to our assumptions stating that in the coordinated ligands both forms have comparable stability. We also anticipate that the addition of the hydroxamic acids gives a mixture of HA and HI tautomers which then (R = Ph) crystallizes from dimethyl sulfoxide preferably in the HI form.

In conclusion, it is worthwhile to mention that: (i) The addition of hydroxamic acids across the C≡N bond is platinum(IV)-mediated because ^{1}H NMR experiments show that noncoordinated EtCN does not react with the hydroxamic acids under the reaction or even harsher (45 °C, 5 d) conditions. Moreover, it has been reported that namely nitriles are formed upon pyrolysis of hydroxamic acids[55] or their deoxygenation, for example, by PBr_3.[56] The imino-

(49) Orpen, A. G.; Brammer, L.; Allen, F. H.; Kennard, O.; Watson, D. G.; Taylor, R. *J. Chem. Soc., Dalton Trans*. **1989**, S1. (b) Bokach, N. A.; Haukka, M.; Pombeiro, A. J. L.; Morozkina, S. N.; Kukushkin, V. Yu. *Inorg. Chim. Acta*, accepted for publication. (c) Ryabov, A. D.; Kazankov, G. M.; Panyashkina, I. M.; Grozovsky, O. V.; Dyachenko, O. G.; Polyakov, V. A.; Kuzmina, L. G. *J. Chem. Soc., Dalton Trans*. **1997**, 4385.

(50) Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1987**, S1.

(51) Remko, M.; Sefcikova, J. *THEOCHEM* **2000**, *528*, 287. (b) El Yazal, J.; Pang, Y.-P. *J. Phys. Chem. A* **1999**, *103*, 8346. (c) Remko, M.; Mach, P.; Schleyer, P.; Exner, O. *THEOCHEM* **1993**, *98*, 139. (d) Turi, L.; Dannenberg, J. J.; Rama, J.; Ventura, O. N. *J. Phys. Chem*. **1992**, *96*, 3709. (e) Fitzpatrick, N. J.; Mageswaran, R. *Polyhedron* **1989**, *8*, 2255.

(52) Salmon, L.; Prost, E.; Merienne, C.; Hardre, R.; Morgant, G. *Carbohydr. Res*. **2001**, *335*, 195. (b) Hoshino, Y.; Murase, N.; Oishi, M.; Yamamoto, H. *Bull. Chem. Soc. Jpn*. **2000**, *73*, 1653. (c) Henriksen, A.; Schuller, D. J.; Meno, K.; Welinder, K. G.; Smith, A. T.; Gajhede, M. *Biochemistry* **1998**, *37*, 8054.

(53) Santana, M. D.; Garcia, G.; Perez, J.; Molins, E.; Lopez, G. *Inorg. Chem*. **2001**, *40*, 570. (b) Swiatek-Kozlowska, J.; Fritsky, I. O.; Dobosz, A.; Karaczyn, A.; Dudarenko, N. M.; Sliva, T. Yu; Gumienna-Kontecka, E.; Jerzykiewicz, L. *J. Chem. Soc., Dalton Trans*. **2000**, 4064. (c) Chen, W.; Gao, S.; Liu, S.-X. *Acta Crystallogr., Sect. C* **1999**, *C55*, 531. (d) Gaynor, D.; Starikova, Z. A.; Haase, W.; Nolan, K. B. *J. Chem. Soc., Dalton Trans*. **2001**, 1578.

(54) Artemenko, A. I.; Anufriev, E. K.; Tikunova, I. V.; Exner, O. *Zh. Prikl. Spektrosk*. **1980**, *33*, 131; *Chem. Abstr*. **1981**, *94*, 46316. (b) Schraml, J.; Kvicalova, M.; Blechta, V.; Soukupova, L.; Exner, O.; Boldhaus, H.-M.; Erdt, F.; Bliefert, C. *Magn. Reson. Chem*. **2000**, *38*, 795.

(55) Shahnaz, F. *Gov. Rep. Announce. Index (U. S.)* **1993**, *93* (4), Abstract No. 308,980; *Chem. Abstr*. **1994**, *120*, 216694.

acylated products of our study are presumably formed by nucleophilic attack of the OH group of the hydroxamic acids on the activated carbon atom of the platinum(IV)-bound organonitrile, a process similar to that for the addition of oximes.[28−34] (ii) Although the metal-mediated hydroxamic acid−nitrile coupling is entirely unusual, it is still reasonable to expect the *addition* with platinum nitrile complexes because the soft metal center has less pronounced ability to *bind* such hard bases as hydroxamates. Indeed, to the best of our knowledge, platinum hydroxamates are unknown, and moreover, there are only scarce reports of hydroxamates of some other platinum group metal ions.[57] (iii) The study establishes a novel type of metalla-Pinner reaction with potential application in organic synthesis of imine compounds with the hydroxamic/hydroximic function. Moreover, it is anticipated the extension of this investigation to bifunctional hydroxamic acids to obtain compounds with remote unligated −C(═O)(H)NOH groups which may be useful for further complexation, for example, with hard metal centers, and construction of heterometallic systems[58,59] with potential application in the material science and this project is underway in our group.

Acknowledgment. K.V.L. and V.Yu.K. express gratitude to the International Science Foundation (Soros Foundation) for the fellowships, while K.V.L. additionally thanks the Centro de Química Estrutural, Complexo I, Instituto Superior Técnico, Portugal, for a grant. M.L.K., D.A.G., and V.Yu.K. are very much obliged to the PRAXIS XXI and POCTI programs (Portugal) for the grants BPD16369/98//BPD/5558/2001, BPD16368/98, and BCC16428/98, correspondingly. A.J.L.P. and V.Yu.K. are grateful to the FCT (Foundation for Science and Technology) and the PRAXIS XXI and POCTI programs for financial support of these studies.

Supporting Information Available: Tables S1−S6 listing crystallographic data, atomic coordinates, bond lengths and bond angles, anisotropic displacement parameters, hydrogen coordinates and isotropic displacement parameters, and torsion angles. X-ray crystallographic files in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

IC025554C

(56) Liguori, A.; Sindona, G.; Romeo, G.; Uccella, N. *Synthesis* **1987**, 168.
(57) Mishra, R. S. *J. Indian Chem. Soc.* **1969**, *46*, 1074.
(58) For review see: Garnovskii, A. D.; Sadimenko, A. P.; Uraev, A. I.; Vasilchenko, I. S.; Garnovskii, D. A. *Russ. J. Coord. Chem.* **2000**, *26*, 311.
(59) For recent works see: Darensbourg, D. J.; Adams, M. J.; Yarbrough, J. C. *Inorg. Chem.* **2001**, *40*, 6543. Scoles, L.; Yamamota, J. H.; Brissieux, L.; Sterenberg, B. T.; Udachin, K. A.; Carty, A. J. *Inorg. Chem.* **2001**, *40*, 6731. Darensbourg, D. J.; Lee, W. Z.; Yarbrough, J. C. *Inorg. Chem.* **2001**, *40*, 6533. Tanase, T.; Inukai, H.; Onaka, T.; Kato, M.; Yano, Sh.; Lippard, S. J. *Inorg. Chem.* **2001**, *40*, 3943. Han, J.; Coucouvanis, D. *J. Am. Chem. Soc.* **2001**, *123*, 11304.