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NMR Studies of Mononuclear Octahedral Ni(II) Complexes Supported by Tris((2-pyridyl)methyl)amine-Type Ligands

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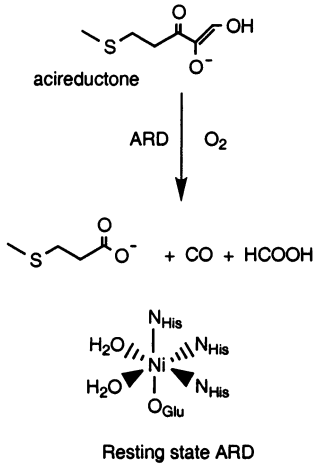
The recent discovery of acireductone dioxygenase (ARD), a metalloenzyme containing a mononuclear octahedral Ni(II) center, necessitates the development of model systems for evaluating the role of the metal center in substrate oxidation chemistry. In this work, three Ni(II) complexes of an aryl-appended tris((2-pyridyl)methyl)amine ligand (6-Ph_2TPA, *N*,*N*-bis((6-phenyl-2-pyridyl)methyl)-*N*-((2-pyridyl)methyl)amine), [(6-Ph_2TPA)Ni(CH_3CN)(CH_3OH)]$(ClO_4)_2$ (**1**), [(6-Ph_2TPA)Ni(ONHC(O)CH_3)]ClO_4 (**3**), and [(6-Ph_2TPA)Ni–Cl(CH_3CN)]ClO_4 (**4**), and one Ni(II) complex of tris((2-pyridyl)methyl)amine, [(TPA)Ni(CH_3CN)(H_2O)]$(ClO_4)_2$ (**2**), have been characterized in acetonitrile solution using conductance methods and NMR spectroscopy. In acetonitrile solution, **1**–**4** have monomeric cations that exhibit isotropically shifted ^{1}H NMR resonances. Full assignment of these resonances was achieved using one- and two-dimensional ^{1}H NMR techniques and ^{2}H NMR of analogues having deuteration of the supporting chelate ligand. COSY cross peaks were observed for pyridyl protons of the 6-Ph_2TPA ligand in **1** and **3**. This study lays the groundwork for using NMR methods to examine chemical reactions of **1** and **2** with model substrates of relevance to ARD.

Introduction

A new nickel enzyme, acireductone dioxygenase (ARD), was recently identified which catalyzes the oxidative breakdown of acireductone (1,2-dihydroxy-3-keto-5-methylthiopentene) to 2-methylthiopropionate, carbon monoxide, and formate in *Klebsiella pneumoniae* (Scheme 1).[1] This reaction is a shunt out of the methionine salvage pathway, and its biological relevance remains under investigation.[2] X-ray absorption spectroscopic studies of ARD suggest a resting state structure having an octahedral Ni(II) center ligated by six O/N-donors, including 3−4 histidine ligands.[3] Subsequent conserved domain homology modeling of the active site in ARD via comparison with jack bean canavalin suggests the presence of three histidine ligands and one glutamate donor

Scheme 1



to the Ni(II) center.[4] In the presence of the acireductone substrate, the nickel center retains an octahedral coordination environment, albeit the oxygen content of the primary coordination environment appears to be higher. Best fits of the EXAFS data for the enzyme/substrate complex suggest

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bidentate coordination of acireductone to the mononuclear nickel center, with displacement of one of the histidine residues.

ARD represents the first example of a nickel-containing dioxygenase.[5,6] The chemistry of this enzyme is intriguing for several reasons, including the fact that removal of the Ni(II) ion, followed by replacement with Fe(II), yields an enzyme (ARD′) that catalyzes the breakdown of acireductone into different products, specifically the α-ketoacid precursor of methionine and formate.[1] This is the only reported example in the literature of a metal-dependent change in reaction products starting from the same substrate in a biological system. The key difference between the reaction pathways of ARD and ARD′ appears to involve the internal site of attack (C(2) or C(3)) on the substrate by an initially formed hydroperoxide radical or anion at C(1) of the metal-bound acireductone. A current hypothesis is that the metal ion present in ARD/ARD′ must influence the structure of the substrate adduct, and thereby determine the site of attack of the reactive hydroperoxide radical or anion.[4]

In this work, we have investigated whether NMR methods can be used for the solution characterization of mononuclear octahedral Ni(II) complexes having tris((2-pyridyl)methyl)-amine (TPA)-type supporting ligands. At the outset of this work, literature precedent suggested that monomeric octahedral Ni(II) complexes typically exhibit resonances that are considerably broader (typically at least 1 order of magnitude) than those observed for pseudotetrahedral and high-spin pentacoordinate Ni(II) species or dimeric nickel complexes.[7−9] We demonstrate here that use of one-dimensional ^{1}H and ^{2}H NMR methods, as well as two-dimensional ^{1}H COSY spectra, enables the full assignment of the ^{1}H NMR resonances of octahedral mononuclear Ni(II) complexes supported by tris((2-pyridyl)methyl)amine-type ligands. In addition, we demonstrate that one-dimensional ^{1}H NMR spectra of mononuclear octahedral Ni(II) complexes, supported by an aryl-appended tris((2-pyridyl)methyl)amine ligand (6-Ph$_2$TPA, *N*,*N*-bis((6-phenyl-2-pyridyl)methyl)-*N*-((2-pyridyl)methyl)amine), exhibit significant changes as a function of the anion bound to the octahedral Ni(II) center. The results of this study provide evidence that NMR methods, including one-dimensional ^{1}H NMR, will be valuable tools for monitoring model reactions of relevance to the chemistry of Ni(II)-containing acireductone dioxygenase.

Experimental Section

General Methods. All reagents and solvents were obtained from commercial sources and were used as received unless otherwise noted. Solvents were dried according to published procedures and were distilled under N_2 prior to use.[10] Air and water sensitive manipulations were performed in an MBraun Unilab glovebox under an atmosphere of purified N_2. The ligands TPA (tris((2-pyridyl)-methyl)amine),[11] d_6-TPA,[12] and 6-Ph$_2$TPA[13] and the Ni(II) complexes [(6-Ph$_2$TPA)Ni(CH$_3$CN)(CH$_3$OH)](ClO$_4$)$_2$ (**1**)[13] and [(6-Ph$_2$TPA)Ni(ONHC(O)CH$_3$)]ClO$_4$ (**3**)[13] were prepared according to literature procedures.

Physical Methods. General. Conductance measurements for **1**−**4** were made at 22(1) °C using a YSI model 31A conductivity bridge with a cell having a cell constant of 1.0 cm^{-1} and using [(TPA)Cu−Cl]ClO$_4$[14] as a 1:1 electrolyte standard. Preparation of the solvent (acetonitrile) and standard solutions for conductance measurements and subsequent data analysis were performed as previously described.[15] UV−visible spectra of **2** and **4** were collected on a Hewlett-Packard 8453 diode array spectrophotometer. IR spectra of **2** and **4** were recorded on a Shimadzu FTIR-8400 spectrometer as KBr pellets. Low-resolution electron impact mass spectroscopic data for (6-Ph)$_2$-d_6-TPA and (6-Ph)$_2$-d_2-TPA and fast atom bombardment mass spectroscopic data for **2** and **4** were obtained at the Mass Spectrometry Facility, Department of Chemistry, University of California, Riverside. Elemental analyses were performed by Atlantic Microlabs of Norcross, GA.

NMR Methods. All NMR spectra were recorded on a Bruker ARX-400 NMR spectrometer. Temperature calibration curves were recorded for the temperature range 198−298 K using methanol and 298−358 K using ethylene glycol.[16] Chemical shifts (in ppm) are referenced to the residual solvent peak(s) in C*H*D$_2$CN (^{1}H, 1.94 (quintet) ppm). A typical one-dimensional ^{1}H NMR spectrum of **1**−**4** consists of 16K data points, 300 scans, and a 250 ms relaxation delay. An exponential weighting function (lb = 30 Hz) was used during processing. The 90° pulse (8.9 μs) was calibrated at 302 K. Longitudinal relaxation times (T_1) were measured using the inversion−recovery pulse sequence (180°−τ−90°) method. ^{2}H NMR spectra were obtained at 302 K on a Bruker ARX-400 operating at 61.43 MHz using an unlocked system. Magnitude ^{1}H COSY spectra for **1** and **3** were obtained in CD$_3$CN at 302 K. These spectra were typically obtained with 512 data points in the F1 dimension and 1024 data points in the F2 dimension with a delay time of 150 ms. An unshifted sine-bell squared function and zero filling to 2048 data points were applied prior to Fourier transformation in both dimensions. Temperature dependence data for **1**−**4** was processed using standard least-squares fit procedures.

CAUTION! *Perchlorate salts of metal complexes with organic ligands are potentially explosive. Only small amounts of material should be prepared, and these should be handled with great care.*[17]

[(TPA)Ni(CH$_3$CN)(H$_2$O)](ClO$_4$)$_2$ (2).[18] To a solution of TPA (48 mg, 0.16 mmol) in CH$_3$CN (∼2 mL) was added a CH$_3$CN (∼2 mL) solution of Ni(ClO$_4$)$_2$·6H$_2$O (60 mg, 0.16 mmol). This

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produced a purple reaction mixture that was stirred at room temperature for 1 h. An excess of Et_2O (~60 mL) was added, and the solution was cooled at (~−18 °C) overnight. A purple solid that had deposited was carefully dried under vacuum in four separate portions. The solid was then recrystallized from CH_3CN/Et_2O at room temperature, resulting in the deposition of red-purple batches of needle-type crystals (77 mg, 77%): UV−vis, nm (ϵ, M^{-1} cm^{-1}) 385 (30), 531 (17), 853 (19); FTIR (KBr, cm^{-1}) 3399 (ν_{OH}), 1100 (ν_{ClO4}), 625 (ν_{ClO4}); FAB-MS (CH_3CN/NBA), *m*/*z* (relative intensity), 447 ([M − ClO_4 − H_2O − CH_3CN]$^+$, 100%); μ_{eff} (302 K) = 2.92 μ_B. Anal. Calcd for $C_{20}H_{25}N_5Cl_2O_9Ni$: C, 39.67; H, 3.83; N, 11.57. Found: C, 39.32; H, 3.85; N, 11.56.

[(6-Ph_2TPA)Ni−Cl(CH_3CN)]ClO_4 (4). To a solution of Ni(ClO_4)$_2$·6H_2O (40 mg, 0.11 mmol) in CH_3CN was added a slurry of 6-Ph_2TPA (48 mg, 0.11 mmol) in CH_3CN. The resulting mixture was stirred for ~1 h. To this solution was added a slurry of Me_4NCl (12 mg, 0.11 mmol) in CH_3CN, and the resulting solution was stirred for 1 h. During this time, the color of the reaction mixture changed from brown to bright green. The solvent was then removed under reduced pressure, and the green residue was redissolved in CH_2Cl_2, filtered through a glass wool/Celite plug, and evaporated to dryness. Recrystallization from CH_3CN/Et_2O at ambient temperature yielded green crystals suitable for X-ray crystallography (82 mg, 73%): UV−vis, nm (ϵ, M^{-1} cm^{-1}) 370 (36), 598 (8), 1007 (8); FTIR (KBr, cm^{-1}) 2319 (ν_{CH3CN}), 1094 (ν_{ClO4}), 623 (ν_{ClO4}); FAB-MS (CH_3CN/NBA), *m*/*z* (relative intensity), 535 ([M − ClO_4 − CH_3CN]$^+$, 100%). Anal. Calcd for $C_{32}H_{29}N_5Cl_2O_5Ni$: C, 56.76; H, 4.32; N, 10.34. Found: C, 56.53; H, 4.16; N, 9.85.

6-(d_5-Ph)$_2$TPA. The preparation of 6-(d_5-Ph)$_2$TPA followed a synthetic route similar to that reported for 6-Ph_2TPA except using appropriately deuterated precursors.[13] d_5-6-phenyl-2-pyridinecarboxyaldehyde was prepared from 6-bromopicolylaldehyde and d_5-$PhB(OH)_2$ (Aldrich, 98%-*d*) following a method reported by Canary and co-workers for the protio analogue (yield: 37%):[19] ^{1}H NMR (CD_3CN, 400 MHz) δ 10.09 (d, J = 0.7 Hz, 1H), 8.12 (dd, J_1 = 7.9 Hz, J_2 = 1.3 Hz, 1H), 8.03 (td, J_1 = 7.7 Hz, J_2 = 0.8 Hz, 1H), 7.88 (dd, J_1 = 7.5 Hz, J_2 = 0.8 Hz, 1H). d_5-6-Phenyl-2-pyridinemethanol was prepared via the reduction of d_5-6-phenyl-2-pyridinecarboxyaldehyde with $NaBH_4$ in methanol/water (yield: 72%):[13] ^{1}H NMR (CD_3CN, 400 MHz) δ 7.85−7.80 (m, 1H), 7.73 (d, J = 7.9 Hz, 1H), 7.34 (d, J = 7.6 Hz, 1H), 4.70 (d, J = 5.3 Hz, 2H), 3.75 (t, J = 5.6 Hz, 1H). The halide derivative d_5-2-(chloromethyl)-6-phenylpyridine hydrochloride was prepared from treatment of d_5-phenyl-2-pyridinemethanol with freshly distilled $SOCl_2$ (yield: 98%): ^{1}H NMR (CD_3CN, 400 MHz) δ 8.26−8.22 (m, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 7.8 Hz, 1H), 5.23 (s, 2H). Preparation of *N*,*N*-bis((6-(d_5-phenyl)-2-pyridyl)methyl)-*N*-((2-pyridyl)methyl)amine (6-(d_5-Ph)$_2$TPA) was achieved via treatment of 2 equiv of d_5-2-(chloromethyl)-6-phenylpyridine hydrochloride with 1 equiv of 2-pyridylmethylamine in CH_3CN in the presence of sodium carbonate and tetrabutylammonium bromide. The product obtained from this reaction was isolated and purified as previously described (yield: 62%):[13] ^{1}H NMR (CD_3CN, 400 MHz) δ 8.49 (m, 1H), 7.80−7.76 (m, 2H), 7.72−7.68 (m, 4H), 7.55 (d, J = 7.5 Hz, 2H), 7.20−7.17 (m, 1H), 3.96 (s, 6H); ^{2}H NMR (CD_3CN, 61.43 MHz) δ 8.2, 8.1, 7.5 ppm; LREI-MS *m*/*z* (relative intensity), 453 ([M + H]$^+$, 40%).

[((6-(d_5-Ph))$_2$TPA)Ni(CH_3CN)(CH_3OH)](ClO_4)$_2$ (1-d_{10}), [((6-(d_5-Ph))$_2$TPA)Ni(ONHC(O)CH_3)]ClO_4 (3-d_{10}), and [((6-(d_5-Ph))$_2$TPA)Ni−Cl(CH_3CN)]ClO_4 (4-d_{10}) were prepared using 6-(d_5-Ph)$_2$TPA following synthetic methods identical to those described for protio analogues.[13]

(6-Ph)$_2$-d_6-TPA. This was prepared in a manner similar to that reported by Karlin and co-workers for d_6-tris((2-pyridyl)methyl)-amine.[12] To solid (6-Ph)$_2$TPA (250 mg, 0.576 mmol) in a round-bottom flask was added $CH_3C(O)OD$ (25 mL, Aldrich, 98%). The resulting solution was refluxed under nitrogen for 48 h. After cooling to ambient temperature, 5 M NaOH (~30 mL) and CH_2Cl_2 (~45 mL) were added. The reaction mixture was then stirred for an additional 3 h, at which point the organic layer was separated, dried over sodium sulfate, and filtered, and the solvent was removed under reduced pressure. This yielded a white powder in quantitative yield that was used without further purification: ^{1}H NMR (CD_3CN, 400 MHz) δ 8.49 (d, J = 4.8 Hz, 1H), 8.06−8.02 (m, 4H), 7.80−7.76 (m, 2H), 7.72−7.67 (m, 4H), 7.56 (d, J = 7.6 Hz, 2H), 7.49−7.40 (m, 6H), 7.20−7.18 (m, 1H); ^{2}H NMR (CD_3CN, 61.43 MHz) δ 4.0 ppm; LREI-MS *m*/*z* (relative intensity), 449 ([M + H]$^+$, 100%).

[((6-Ph)$_2$-d_6-TPA)Ni(CH_3CN)(CH_3OH)](ClO_4)$_2$ (1-d_6), [((6-Ph)$_2$-d_6-TPA)Ni(ONHC(O)CH_3)]ClO_4 (3-d_6), and [((6-Ph)$_2$-d_6-TPA)Ni−Cl(CH_3CN)]ClO_4 (4-d_6) were prepared using (6-Ph)$_2$-d_6-TPA following synthetic methods identical to those described for protio analogues.[13]

(6-Ph)$_2$-d_2-TPA. The preparation of (6-Ph)$_2$-d_2-TPA followed a synthetic route similar to that reported for 6-Ph_2TPA except for an initial step involving reduction of 6-phenyl-2-pyridinecarboxyaldehyde.[13] Specifically, d_1-6-phenyl-2-pyridinemethanol was prepared via the reduction of 6-phenyl-2-pyridinecarboxyaldehyde (780 mg, 4.26 mmol) with $LiAlD_4$ (250 mg, 5.96 mmol) in dry THF (55 mL). The $LiAlD_4$ was placed in a 500 mL round-bottom flask in 40 mL of THF. To this solution was carefully added a THF (15 mL) solution of 6-phenyl-2-pyridinecarboxyaldehyde. Following stirring of the resulting mixture for ~15 min at ambient temperature, D_2O (~10 mL) was added. The solution was then extracted with CH_2Cl_2. The organic fractions were dried over Na_2SO_4 and filtered, and the solvent was removed under reduced pressure, yielding a yellow oil (640 mg, 88%): ^{1}H NMR (CD_3CN, 400 MHz) δ 8.09−8.07 (m, 2H), 7.85−7.82 (m, 1H), 7.74 (d, J = 7.7 Hz, 1H), 7.52−7.40 (m, 3H), 7.35 (d, J = 7.5 Hz, 1H), 4.69 (s, 1H). d_1-2-(Chloromethyl)-6-phenylpyridine hydrochloride was prepared from treatment of d_1-phenyl-2-pyridinemethanol with freshly distilled $SOCl_2$ (yield: 99%): ^{1}H NMR (CD_3CN, 400 MHz) δ 8.42−8.38 (m, 1H), 8.09−8.05 (m, 3H), 7.90 (d, J = 7.8 Hz, 1H), 7.67−7.58 (m, 3H), 5.36 (s, 1H). *N*,*N*-Bis((6-(phenyl)-2-pyridyl)-d_1-methyl)-*N*-((2-pyridyl)methyl)amine ((6-Ph)$_2$-d_2-TPA) was generated via treatment of 2 equiv of d_1-2-(chloromethyl)-6-phenylpyridine hydrochloride with 1 equiv of 2-pyridylmethylamine in CH_3CN in the presence of sodium carbonate and tetrabutylammonium bromide. The product obtained from this reaction was isolated and purified as previously described (yield: 35%):[13] ^{1}H NMR (CD_3CN, 400 MHz) δ 8.49 (dt, J_1 = 4.8 Hz, J_2 = 1.4 Hz, 1H), 8.07−8.04 (m, 4H), 7.80−7.77 (m, 2H), 7.72−7.68 (m, 4H), 7.55 (d, J = 7.6 Hz, 2H), 7.49−7.40 (m, 6H), 3.99−3.93 (br, 4H); ^{2}H NMR (CD_3CN, 61.43 MHz) δ 4.0 ppm; LREI-MS *m*/*z* (relative intensity), 445 ([M + H]$^+$, 100%).

[((6-Ph)$_2$-d_2-TPA)Ni(CH_3CN)(CH_3OH)](ClO_4)$_2$ (1-d_2), [((6-Ph)$_2$-d_2-TPA)Ni(ONHC(O)CH_3)]ClO_4 (3-d_2), and [((6-Ph)$_2$-d_2-TPA)Ni−Cl(CH_3CN)]ClO_4 (4-d_2) were prepared using (6-Ph)$_2$TPA following synthetic methods identical to those described for protio analogues.[13]

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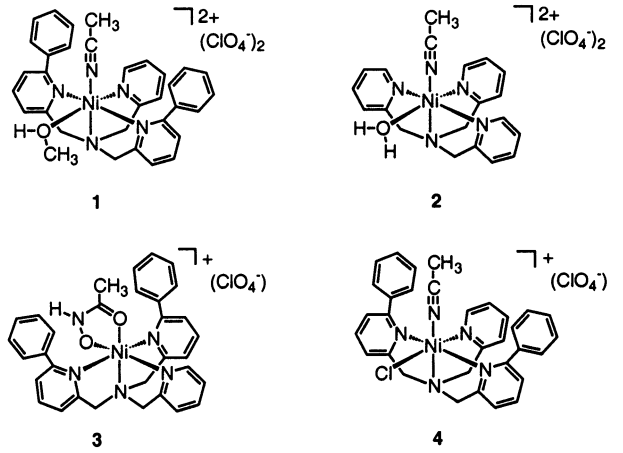

Figure 1. Mononuclear nickel(II) complexes examined using one- and two-dimensional ^{1}H NMR.

[(d_6-TPA)Ni(CH$_3$CN)(H$_2$O)](ClO$_4$)$_2$ (2-d_6). This was prepared using d_6-TPA in a manner identical to the synthetic procedure described for [(TPA)Ni(CH$_3$CN)(H$_2$O)](ClO$_4$)$_2$ (**2**).

X-ray Crystallography. A crystal of **4** was mounted on a glass fiber with traces of viscous oil and then transferred to a Nonius KappaCCD diffractometer with Mo Kα radiation ($\lambda = 0.71073$ Å) for data collection at 150(1) K. An initial set of cell constants was obtained from 10 frames of data that were collected with an oscillation range of 1 deg/frame and an exposure time of 20 s/frame. Final cell constants were determined from a set of strong reflections from the actual data collection. For the data set collected for **4**, each reflection was indexed, integrated, and corrected for Lorentz, polarization, and absorption effects using DENZO-SMN and SCALEPAC.[20] All of the non-hydrogen atoms were refined with anisotropic displacement coefficients.

Structure Solution and Refinement. Complex **4** crystallizes in the space group $P2_1/n$. Two noncoordinated acetonitrile molecules were found in the asymmetric unit. All hydrogen atoms except those on C(34) and C(36) of the noncoordinated CH$_3$CN solvent molecules were located and refined independently using SHELXL97.

Results and Discussion

Preparation and Characterization of Mononuclear Octahedral Ni(II) Complexes. We are pursuing a project directed at the development of synthetic model systems relevant to the nickel-containing enzyme acireductone dioxygenase (ARD). As a portion of our work in this area, we have reported the synthesis and structural characterization of [(6-Ph$_2$TPA)Ni(CH$_3$CN)(CH$_3$OH)](ClO$_4$)$_2$ (**1**) and [(6-Ph$_2$TPA)Ni(ONHC(O)CH$_3$)]ClO$_4$ (**3**) (Figure 1).[13] Notably, the isolation of **3** provides evidence that the 6-Ph$_2$TPA ligand can support octahedral Ni(II) complexes having a chelating bidentate anion akin to a proposed substrate-bound form of ARD.

Two additional complexes have been prepared and characterized for NMR studies. First, an analogue of **1**, supported by the tris((2-pyridyl)methyl)amine ligand, [(TPA)Ni(CH$_3$CN)(H$_2$O)](ClO$_4$)$_2$ (**2**), was prepared in 73% yield via treatment of TPA with an equimolar amount of Ni(ClO$_4$)$_2$·6H$_2$O, followed by recrystallization from CH$_3$CN/Et$_2$O. A new mononuclear nickel chloride complex [(6-Ph$_2$TPA)NiCl(CH$_3$CN)]ClO$_4$ (**4**) was prepared via the synthetic pathway shown in Scheme 2. Both **2** and **4** were characterized by UV−vis, FTIR, FAB-MS, conductance and elemental analysis. The chloride derivative **4** was also characterized by single-crystal X-ray crystallography (Table 1). The cationic portion of **4** is shown in Figure 2. Overall, the mononuclear Ni(II) cation exhibits a slightly distorted octahedral geometry with the chloride ion positioned in the plane of the pyridyl nitrogen donors of the 6-Ph$_2$TPA ligand. A coordinated acetonitrile solvent molecule is positioned between the two phenyl substituents of the 6-Ph$_2$TPA chelate ligand as has been previously observed for **1**. The average Ni−N$_{py}$ bond length (Table 2) for the phenyl-substituted pyridyl donors in **4** (Ni−N$_{PhPy}$: 2.24 Å) is slightly longer than the analogous average distance for **1** (2.21 Å). This elongation could be due to reduced Lewis acidity for the Ni(II) center in **4** (relative to **1**) due to coordination of the chloride anion. The

Scheme 2

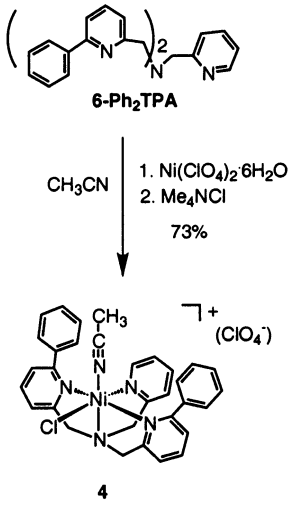

Table 1. Summary of X-ray Data Collection and Refinement for **4·2CH$_3$CN**[a]

empirical formula	$C_{36}H_{35}N_7Cl_2O_4Ni$
formula weight	759.32
crystal system	monoclinic
space group	$P2_1/n$
a (Å)	15.4913(4)
b (Å)	10.0769(3)
c (Å)	23.3121(5)
α (deg)	
β (deg)	99.4683(15)
γ (deg)	
V (Å^3)	3589.54(16)
Z	4
density (calcd), Mg m^{-3}	1.405
temp (K)	150(1)
crystal size (mm^3)	0.33 × 0.25 × 0.09
diffractometer	Nonius KappaCCD
abs coeff (mm^{-1})	0.739
2θ max (deg)	54.96
reflections collected	13801
indep reflections	8095
variable parameters	570
$R1$/w$R2$[b]	0.0543/0.1302
GOF (F^2)	1.038
largest diff (e Å^{-3})	0.811/−0.612

[a] Radiation used: Mo Kα ($\lambda = 0.71073$ Å). [b] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$; w$R2 = [\sum[w(F_o^2 - F_c^2)^2]/[\sum(F_o^2)^2]]^{1/2}$ where $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$.

(20) Otwinowski, Z.; Minor, W. *Methods Enzymol.* **1997**, *276*, 307−326.

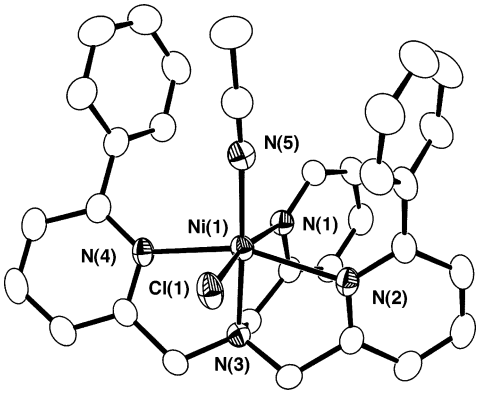

Figure 2. ORTEP representation of the cationic portion of **4·2CH$_3$CN**. Ellipsoids are plotted at the 50% probability level. All hydrogen atoms omitted for clarity.

Table 2. Selected Bond Distances (Å) and Angles (deg) for **4·2CH$_3$CN**[a]

Ni−N(1)	2.088(2)	N(3)−Ni(1)−N(5)	174.63(10)
Ni−N(2)	2.272(2)	N(4)−Ni(1)−N(2)	157.67(10)
Ni−N(3)	2.081(3)	N(1)−Ni(1)−Cl(1)	169.73(7)
Ni−N(4)	2.213(2)	N(5)−Ni(1)−N(1)	93.79(10)
Ni−N(5)	2.034(3)	N(5)−Ni(1)−N(2)	103.94(10)
Ni−Cl(1)	2.364(1)	N(5)−Ni(1)−Cl(1)	90.21(8)
		N(5)−Ni(1)−N(4)	98.35(10)
		N(1)−Ni(1)−N(2)	79.62(9)
		N(3)−Ni(1)−N(1)	83.04(10)
		N(1)−Ni(1)−N(4)	97.64(9)

[a] Estimated standard deviations in the last significant figure are given in parentheses.

remaining Ni−N distances in **4** (Ni−N$_{Py}$ 2.088(2), Ni−N$_{amine}$ 2.081(3), Ni−N$_{CH3CN}$ 2.034(3) Å) are within experimental error of those found in **1** (Ni−N$_{Py}$ 2.065(4), Ni−N$_{amine}$ 2.082(4), Ni−N$_{CH3CN}$ 2.044(4) Å). It is worth noting that a nickel chloride complex of the TPA ligand ([(TPANi)$_2$(μ-Cl)$_2$](ClO$_4$)$_2$) has been previously reported in the literature. The solid-state structure of this complex contains a dinuclear cation with two bridging chloride anions.[21]

Conductance Measurements. To confirm that the mononuclear structures of **1**−**4** are retained in CH$_3$CN solution, a series of conductance measurements were performed. Onsager plots for data collected for **1**−**4** are shown in Figure 3 along with the 1:1 standard [(TPA)Cu−Cl]ClO$_4$.[14] Two distinct groups of slopes are observed, consistent with 1:1 electrolyte behavior of **3**, **4**, and [(TPA)Cu−Cl]ClO$_4$, and 1:2 behavior of **1** and **2** in CH$_3$CN solution.

NMR Studies. General. Examples of the use of NMR methods for the solution characterization of paramagnetic Ni(II) complexes have previously appeared in the literature.[22−31] However, these studies focused on synthetic complexes that are not structurally relevant to the nickel center in ARD or for which mononuclear solid-state structures have not been reported.[8,9,22−31] In this study, using 1D and 2D ^{1}H NMR and ^{2}H NMR, we have fully assigned the proton NMR resonance of four mononuclear octahedral Ni(II) complexes of relevance to the active site nickel center in acireductone dioxygenase (ARD). These complexes have

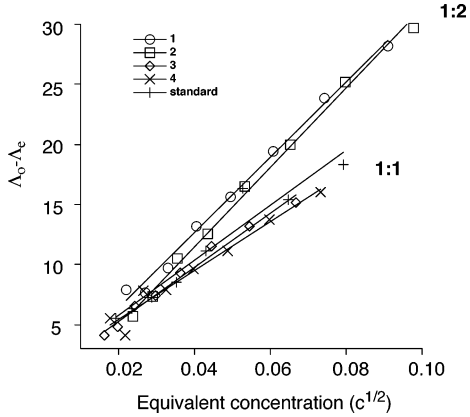

Figure 3. Onsager plots for **1**−**4** and the 1:1 standard [(TPA)Cu−Cl]ClO$_4$.

four nitrogen donors from the chelate ligand as an initial motif for modeling the protein contribution to the ligand environment in the enzyme active site. In **1** and **2**, two cis coordination positions are occupied by solvent molecules, akin to the proposed metal-coordinated waters in resting state ARD.[4] In **3**, a bidentate ligand (hydroxamate) is coordinated to the Ni(II) center, a structure that has some relevance to a proposed substrate adduct in the enzyme.[4] Notably, three of these complexes (**1**, **3**, and **4**) have been characterized by X-ray crystallography,[13] and the X-ray structure of a close analogue of **2** has been reported in the literature.[18] Conductance measurements, performed over a range of concentrations for **1**−**4**, yielded data that could be fit to the Onsager law, revealing 1:2 electrolyte behavior for **1** and **2**, and 1:1

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Table 3. ^{1}H NMR Chemical Shifts for **1**−**4** in CD_3CN at 302 K

assignment	chem shift (ppm)[a]	$\Delta\nu_{1/2}$ (Hz)[b]	T_{1exp} (ms)[c]	rel area
	[(6-Ph_2TPA)Ni(CH_3CN)(CH_3OH)](ClO_4)$_2$ (**1**)			
α	∼176	4000	*d*	*d*
β	58.0, 50.4	280, 270	3, 3	1, 1
β′	53.0, 39.9	370, 290	3, 2	2, 2
γ	15.5	71	9	1
γ′	8.5	*d*	7	2
CH_2 (PhPy)[e]	∼158, ∼36[e]	3000	*d*, *d*	*d*, *d*
CH_2 (Py)	∼77	2900	<1	*d*
Ph	8.4, 6.6	*d*, 700	8, <1	6, 4
	[(TPA)Ni(CH_3CN)(H_2O)](ClO_4)$_2$ (**2**)			
α	∼142	4900	*d*	*d*
β	52, 50	720, 710	2, 3	3, 3
γ	14.3	100	7	3
CH_2	∼79	7200	*d*	*d*
	[(6-Ph_2TPA)Ni(ONHC(O)CH_3)]ClO_4 (**3**)			
α	160	900	*d*	∼1
β	47.5, 41.8	80, 80	10, 11	1, 1
β′	38.8, 29.3	100, 100	13, 7	2, 2
γ	14.8	46	29	1
γ′	6.4	49	25	1
CH_2 (PhPy)[e]	143, 45	600, 500	*d*, <1	2, 2
CH_2 (Py)	51	370	1	2
Ph	8.2, 8.0, 4.7	60, 55, 220	25, 19, 2	2, 4, 4
N−H	128[f]	500	*d*	1
CH_3	9.0	83	7	3
	[(6-Ph_2TPA)Ni−Cl(CH_3CN)]ClO_4 (**4**)			
α	∼170	∼10000	*d*	*d*
β	54.6, 37	220, 390	6, 3	*d*
β′	∼52, ∼42	780, 720	*a*, 3	*d*
γ	14.8	72	13	1
γ′	10[g]	360	12	2
CH_2 (PhPy)	∼192,[e] ∼21	*d*, 1750	<1	*d*
CH_2 (Py)	∼76	1900	<1	*d*
Ph	*d*, 8.6, 6.9	*d*, 50, 250	*d*, 17, 7	*d*

[a] Chemical shifts in ppm relative to the residual solvent peak of C*H*D_2CN (^{1}H, 1.94 (quintet) ppm). [b] Line widths are full width at half-maximum. [c] T_1 values were obtained at 400 MHz. [d] Could not be observed/determined. [e] Located using complex supported by (6-Ph_2)-d_2-TPA ligand. [f] Peak disappears upon addition of D_2O to a CD_3CN solution of **3**. [g] Located using complex supported by 6-(d_5-Ph)$_2$TPA ligand.

behavior for **3** and **4**.[32] Thus, all of the complexes reported in this study are mononuclear in CH_3CN solution.

^{1}H NMR spectra of **1**−**4** were collected at 29 °C in d_3-acetonitrile solution. Chemical shifts, relative areas, line widths, and T_1 values for **1**−**4** are given in Table 3. All of the complexes exhibit several isotropically shifted ^{1}H NMR resonances spread over a chemical shift range of ∼150−180 ppm.

Assignment of Resonances: [(6-Ph_2TPA)Ni(CH_3CN)(CH_3OH)](ClO_4)$_2$ (1). Initial assignment of the resonances for **1** (Figure 4) was made on the basis of integrated intensity and T_1 values. Four resonances found in the region of 39−58 ppm are assigned as the *β*-H's of the pyridyl and phenyl-substituted pyridyl rings (Figure 5). Two of these resonances (53.0 and 39.9 ppm) integrate to two protons each, and thus are associated with the phenyl-appended pyridyl moieties. The remaining two signals (58.0 and 50.4 ppm) in this region each integrate to one proton and are assigned to the unsubstituted pyridyl group. The T_1 values for the *β*-H's of **1** are all similar, falling in the range of 2−3 ms. The observation of only four pyridyl *β*-resonances indicates that

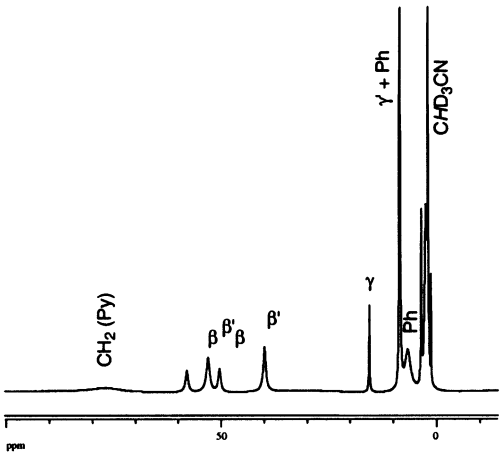

Figure 4. ^{1}H NMR spectrum of **1** in CD_3CN at 302 K. Spectrum was referenced to the residual proton solvent signal of C*H*D_2CN at 1.94 ppm.

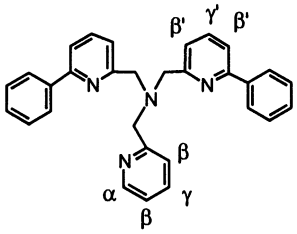

Figure 5. Labeling scheme for (6-Ph_2)TPA ligand.

in CH_3CN solution **1** has an effective plane of symmetry that yields equivalent phenyl-appended pyridyl substituents. A sharp resonance at 15.5 ppm (T_1 = 9 ms), integrating to 1H, is assigned as the *γ*-H of the unsubstituted pyridyl ring. A resonance at 8.5 ppm, having a similar T_1 value (7 ms), that could be integrated in the ^{1}H NMR spectrum of the d_{10}-analogue [((6-(d_5−Ph))$_2$TPA)Ni(CH_3CN)(CH_3OH)](ClO_4)$_2$ (**1**-d_{10}, Figure 6), is assigned as the *γ*′ resonance. Confirmation of these assignments was achieved using two-dimensional ^{1}H NMR techniques. A magnetic COSY spectrum of **1** (Figures S5 and S6, Supporting Information), recorded at 29 °C, shows clear cross peaks between the resonances at 53.0/39.9 ppm (*β*′) and 8.5 ppm (*γ*′), and 58.0/50.4 ppm (*β*) and 15.5 ppm (*γ*).

Resonances found at 8.4 (T_1 = 8 ms) and 6.6 (T_1 = <1 ms) ppm in the one-dimensional ^{1}H NMR spectrum of **1** were conclusively identified as belonging to the phenyl appendages via deuterium substitution using [((6-(d_5−Ph))$_2$-TPA)Ni(CH_3CN)(CH_3OH)](ClO_4)$_2$ (**1**-d_{10}). The ^{2}H NMR spectrum of **1**-d_{10} displays two overlapping resonances (8.5 and 8.4 ppm) and a third broad resonance at 6.6 ppm. On the basis of peak intensity and T_1 values, we assign the resonance at ∼6.6 ppm to the ortho hydrogens of the phenyl groups.

The presence of an effective plane of symmetry for **1** in CD_3CN solution, as suggested by observation of equivalent PhPy donors (vida supra), indicates that a total of three methylene proton resonances should be observed. At 29 °C, three broad resonances are identifiable at ∼176, 158, and 77 ppm, each of which has a peak width of ≥2900 Hz. These resonances were conclusively identified as methylene protons of the chelate ligand via examination of the ^{1}H and ^{2}H NMR

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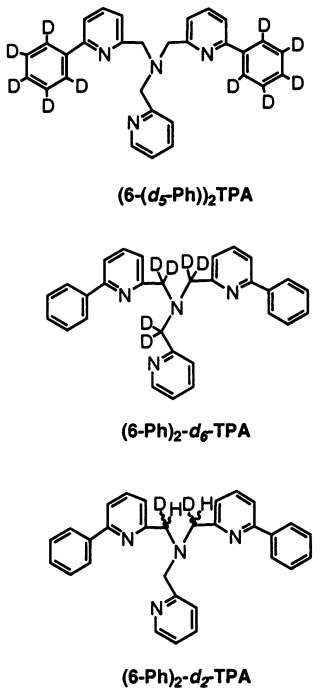

Figure 6. Deuterated ligands.

spectra of the deuterated analogue [((6-Ph)$_2$-d_6-TPA)Ni(CH$_3$CN)(CH$_3$OH)](ClO$_4$)$_2$ (**1**-d_6, Figure 6) in which all of the methylene protons were replaced by deuterons. Specifically, resonances at ~163, 75, and ~39 ppm are observed in the ^{2}H NMR spectrum of **1**-d_6. We attribute the subtle differences in chemical shift between the ^{2}H NMR resonances and those in the ^{1}H NMR spectrum to the broad nature of the peaks, particularly in the ^{1}H NMR spectrum. On the basis of literature precedent,[33,34] we assign the most downfield shifted (~158 ppm in the ^{1}H NMR spectrum) of the methylene proton resonances to H_{eq}, the methylene proton on each PhPy arm that has a dihedral angle (Ni−N−C−H) closer to 180°. A dramatic difference in chemical shift for H_{eq} and H_{ax} is expected for the PhPy geminal methylene protons due to chelate ring formation, which results in different hyperfine contact shift and relaxation times for each proton. Use of a d_2-functionalized ligand having a racemic 50:50 H:D content for the PhPy methylene units (Figure 6) confirmed the assignment of the resonances at ~163 and 39 ppm in the ^{2}H NMR spectrum of **1**-d_6 as being the two independent signals expected for the geminal PhPy methylene deuterons. The signal at ~39 ppm corresponds to a peak observed in ^{1}H NMR spectrum of **1** at ~36 ppm when the sample is heated to ≥65 °C. The final signal in the ^{2}H NMR spectrum of **1**-d_6 at 75 ppm is assigned as the expected methylene resonance for the Py linker deuterons. Finally, the signal at ~176 ppm ($\Delta\nu_{1/2}$ ~4000 Hz) in the ^{1}H NMR spectrum of **1** is assigned as the α-H of the unsubstituted pyridyl ring. The large isotropic shift and broad nature of this resonance is consistent with the close proximity of this proton to the paramagnetic Ni(II) center (Ni(I)···H 3.17 Å).

A broad resonance in the ^{1}H NMR spectrum of **1** in CD$_3$CN, found at ~3.5 ppm, is assigned to the methyl protons of methanol. The observed chemical shift of this resonance, which is slightly downfield of the expected chemical shift of free methanol (3.28 ppm) in CD$_3$CN solution under diamagnetic conditions, indicates that the Ni(II)-coordinated methanol undergoes exchange with the deuterated solvent. A second broad peak found at ~2.4 ppm indicates the presence of trace water in the sample (2.13 ppm in CD$_3$CN under diamagnetic conditions). A clear resonance for CH$_3$CN, which is a ligand to the Ni(II) center in the solid-state structure of **1**, could not be identified and may be overlapping with the above-mentioned 2.4 ppm resonance.

[(TPA)Ni(CH$_3$CN)(H$_2$O)](ClO$_4$)$_2$ (2). Five broad hyperfine-shifted resonances are observed in the ^{1}H NMR spectrum of **2** in CD$_3$CN. Two resonances at 52 (T_1 = 2 ms) and 50 (T_1 = 3 ms) ppm, respectively, each of which integrates to three protons, are assigned as the pyridyl β-protons. The sharpest signal in the spectrum ($\Delta\nu_{1/2}$ = 100 Hz, T_1 = 7 ms) is found at 14.3 ppm and integrates to three protons. This resonance is assigned as the pyridyl γ-protons. The observation of only one set of pyridyl β- and γ-protons suggests a rearrangement of the unsymmetrical ligand environment that is rapid on the NMR time scale and results in similar chemical shifts for all the pyridyl protons of **2**. Consistent with this hypothesis is the observation of a single broad methylene proton resonance centered at ~79 ppm ($\Delta\nu_{1/2}$ ~7200 Hz). The ^{2}H NMR spectrum of the d_6 analogue complex [(d_6-TPA)Ni(CH$_3$CN)(H$_2$O)](ClO$_4$)$_2$ (**2**-d_6) contains two broad resonances centered at ~79 and 68 ppm, suggesting similar chemical environments for the methylene deuterons. A broad resonance in the ^{1}H NMR spectrum of **2** at ~142 ppm is assigned as the signal for the pyridyl α-proton. Finally, a broad peak at ~2.46 ppm is tentatively assigned as being for H$_2$O and CH$_3$CN, which are displaced from the Ni(II) center via exchange with CD$_3$CN.

[(6-Ph$_2$TPA)Ni(ONHC(O)CH$_3$)]ClO$_4$ (3). Of all the complexes in this study, the sharpest ^{1}H NMR resonances at 29 °C are observed for **3** (Figure 7 (top)), a complex which has some structural relevance to a proposed substrate adduct for ARD.[4] Whereas the Py and PhPy β-proton resonances in **1** have peak widths at half-height of ~280−370 Hz, analogous resonances in **3**, found at 47.5, 41.8, 38.8, and 29.3 ppm, have $\Delta\nu_{1/2}$ = 80−100 Hz. The γ- and γ′-proton resonances are easily identifiable for **3** at 14.8 and 6.4 ppm, respectively. This complex was amenable to study by two-dimensional ^{1}H COSY NMR (Figure 8), which confirmed the assignment of all of the β- and γ-hydrogens. Unlike **1**, all three resonances of the phenyl substituents are easily observed at 29 °C (8.2 (T_1 = 25 ms), 8.0 (T_1 = 19 ms), and 4.7 (T_1 = 2 ms) ppm). ^{2}H NMR studies of **3**-d_{10} confirmed the assignment of these resonances. The 4.7 ppm resonance in **3** exhibits the shortest T_1 value, suggesting that this signal is for the ortho protons of the phenyl rings.[35] Three broad resonances (143 ppm ($\Delta\nu_{1/2}$ = 600 Hz), 51 ppm ($\Delta\nu_{1/2}$ = 370 Hz), and 45.4 ppm ($\Delta\nu_{1/2}$ = 500 Hz) ppm) in the ^{1}H

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(34) Holm, R. H.; Hawkins, C. J. In *NMR of Paramagnetic Molecules: Principles and Applications*; La Mar, G. N., Horrocks, W. D., Jr., Holm, R. H., Eds.; Academic Press: New York, 1973; pp 243−332.

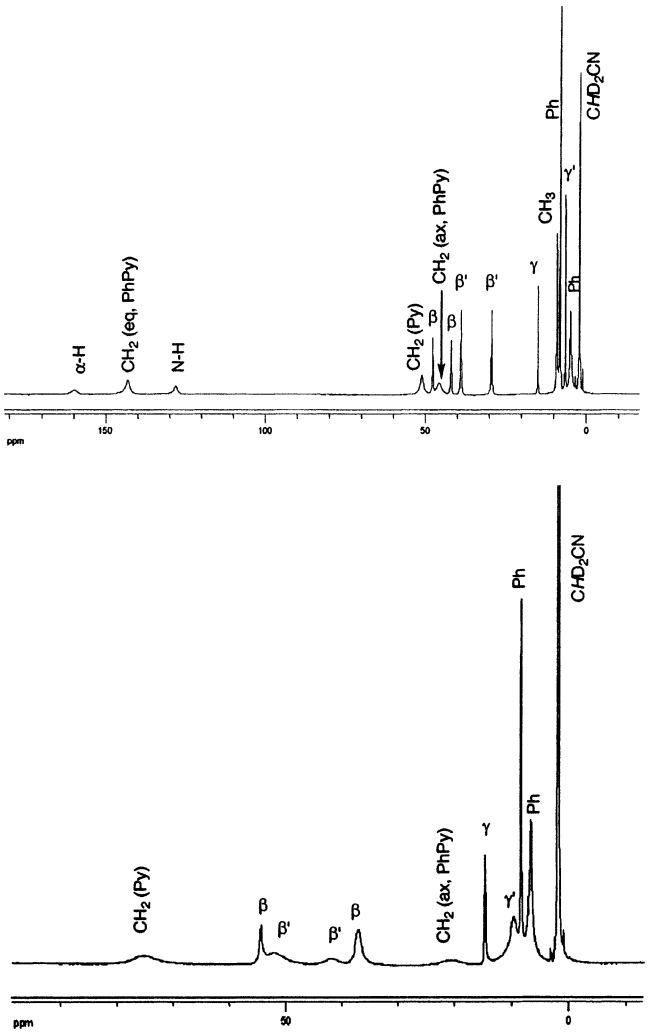

Figure 7. Top: ^{1}H NMR spectrum of **3.** Bottom: A portion of the ^{1}H NMR spectrum of **4**. Spectra were obtained in CD_3CN at 302 K and were referenced to the residual proton solvent signal of C*H*D$_2$CN at 1.94 ppm.

NMR spectrum of **3** disappear upon deuteration of the methylene linkers (using **3**-d_6). Correspondingly, a ^{2}H NMR spectrum of **3**-d_6 has three resonances at ∼141, 50, and 45 ppm, consistent with three methylene signals as is observed for **1**. A ^{2}H NMR spectrum of **3**-d_2 indicates that the signals at ∼141 and 45 ppm are the expected geminal methylene deuteron resonances of the PhPy appendages.

Two broad downfield-shifted resonances (∼160 and 128 ppm) are present in the ^{1}H NMR spectrum of **3**-d_6. The signal at 128 ppm disappears when **3** is treated with D_2O in dry CD_3CN, consistent with assignment of this peak as the hydroxamate N−*H* proton resonance. A resonance at 9.0 ppm is assigned, on the basis of integration, as the methyl resonance for the hydroxamate ligand. Finally, the signal at ∼160 ppm in the ^{1}H NMR spectrum of **3** is assigned as the pyridyl α-proton resonance.

[(6-Ph$_2$TPA)Ni−Cl(CH$_3$CN)]ClO$_4$ (4). Resonances in the ^{1}H NMR spectrum of **4** at 29 °C are considerably broader than those observed for **1** and **3** under identical conditions (Figure 7 (bottom)). Comparison of the chemical shifts and peak widths of the ^{1}H NMR resonances of **4** over a 10-fold concentration range (∼1.5−15 mM) yields no change in the spectral features, suggesting that the observed peak broadening is not due to formation of multinuclear species. This conclusion is supported by conductance measurements of **3** in CH_3CN solution, which indicate that the complex behaves as a 1:1 electrolyte.

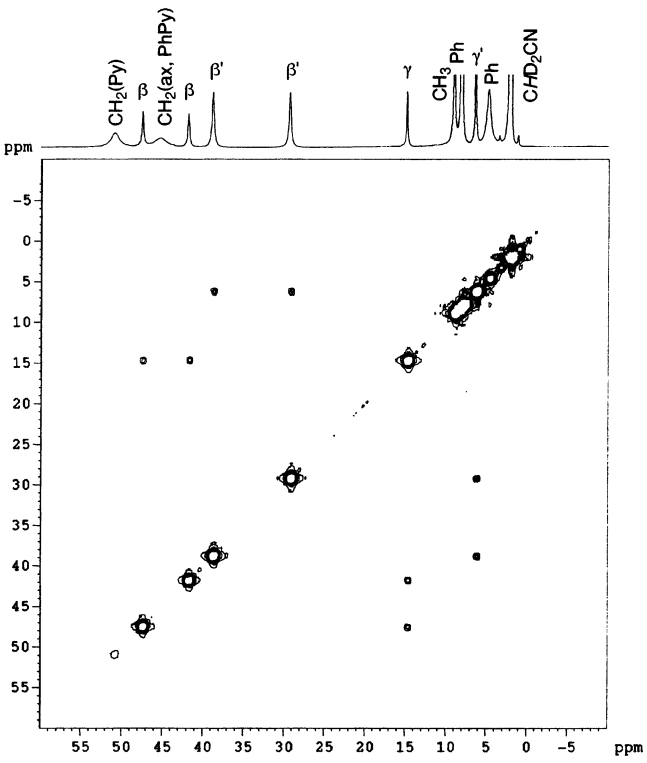

Figure 8. ^{1}H COSY spectrum of **3** obtained at 400 MHz at 302 K in CD_3CN solution.

The resonances for the β-H's in **4** appear as two relatively sharp (54.6 and 37 ppm) and two broad resonances (∼52 and ∼42 ppm) at 29 °C. The γ-H's for the pyridyl and phenyl-appended pyridyl rings can be assigned on the basis of integration to peaks at 14.8 and ∼10 ppm, respectively. Two resonances associated with the phenyl appendages are present in the ^{1}H NMR spectrum of **4** at 8.6 and 6.6 ppm. A ^{2}H NMR spectrum of **4**-d_{10} revealed peaks at 11.2, 8.6, and 6.8 ppm. The most downfield of these resonances is very broad in the ^{2}H NMR spectrum of **4**-d_{10}. Thus, it is likely that the corresponding signal in the ^{1}H NMR spectrum of **4** is broadened into the baseline and/or is unobservable due to overlap with the γ'-proton resonance. Two methylene resonances have been assigned in the ^{1}H NMR spectrum of **4** at ∼76 and ∼21 ppm. These assignments were confirmed via examination of the **4**-d_6 analogue using ^{2}H NMR, where signals are present at 74 ppm and ∼25 ppm. In the ^{2}H NMR spectrum of **4**-d_6 a third very broad resonance is present at ∼192 ppm. The assignment of the resonance as H_{eq} was confirmed via examination of the deuterated analogue [((6-Ph)$_2$-d_2-TPA)Ni−Cl(CH$_3$CN)]ClO$_4$ by ^{2}H NMR, which revealed a very broad feature at ∼190−200 ppm, and a second signal at ∼26 ppm (H_{ax}). Similar to the assignments made for **1** and **3**, these resonances correspond to the geminal

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deuterons of the PhPy methylene linkages. The pyridyl α-H in **4** is assigned to a very broad feature ($\Delta\nu_{1/2} \geq 10000$ Hz) at ~170 ppm. A broad peak at ~2.14 ppm is assigned as protio acetonitrile, which has been displaced from the metal center by CD_3CN.

Temperature Dependence of Chemical Shifts. Examination of the ^{1}H NMR spectra of **1**−**4** over a temperature range of 259−346 K revealed that the majority of resonances sharpened and moved toward the diamagnetic region with increasing temperature, thus showing typical Curie law behavior (Figures S1−S4, Supporting Information). Fits for $1/T$ vs δ (ppm) plots for the resonances of **1**−**4** gave correlation coefficients in the range of 0.95−0.99. Selected resonances for **1**−**4** exhibit a small degree of anti-Curie behavior.[36] These include two aromatic resonances for **1** (γ' and a Ph resonance), one phenyl resonance of **3**, and the γ' resonances of **3** and **4**. Intercepts for selected resonances on the $1/T$ vs δ (ppm) plots differ significantly from the expected diamagnetic shift at 0 K (Table 4; e.g. α, β, and CH_2(Ph) resonances in **1**, β/β', Ph, CH_2(PhPy), and N−H resonances in **3**, and α, β/β, γ', CH_2(PhPy), CH_2Py, and Ph resonances in **4**) suggesting small deviations from the Curie law. For pseudo-octahedral Ni(II) centers, zero-field splitting (D),[9,37] wherein $D \ll$ thermal energy k_BT, may influence both $1/T$ (contact) and $1/T^2$ (dipolar) contributions to the temperature dependence of the hyperfine chemical shift.[38] In an attempt to probe the role of D in the deviations from the Curie Law observed for **1**−**4**, the temperature dependence of the chemical shifts was also fit using a second-order polynomial equation (Table 4). However, similar to the results reported by Belle and co-workers for dimeric Ni(II) complexes having pseudo-octahedral metal centers,[9] no significant improvement in fit quality, as evidenced by comparison of correlation coefficients (~0.95−0.99), was observed in the polynomial plots, thus precluding further interpretation of the influence of zero-field splitting on the observed chemical shifts.

Comparison of the NMR Features of 1−4. The most striking difference between the ^{1}H NMR spectral features of the 6-Ph_2TPA- and TPA-ligated complexes is the observation of distinct β and γ resonances for the pyridyl rings of the Py and PhPy appendages in 6-Ph_2TPA derivatives. In **1**, **3**, and **4**, the β' and γ' resonances of the PhPy donors appear upfield of the analogous Py ring protons, with the hydroxamate complex **3** exhibiting the smallest PhPy β' and γ' hyperfine shifts. The larger shifts observed for the Py versus PhPy ring protons indicates differences in ligand field and spin distribution for these two types of donors in the chelate ligands. In this regard, it is important to note that the length of the Ni−N_{py} bond in **1**, **3**, and **4** is ~0.15−0.19 Å shorter than the average Ni−N_{PhPy} distance in these complexes, with the greatest difference in N_{Py} and $N_{PhPy(av)}$ bond lengths (~0.19 Å) being identified for **3**. Thus, the smaller hyperfine shifts for the PhPy pyridyl ring protons, which involve a significant contact contribution, is consistent with the longer distance of these hydrogen atoms from the paramagnetic Ni(II) center.

Table 4. Temperature Dependence of Chemical Shifts

		Curie plot[b]		polynomial plot[c]		
assignment	δ (ppm)[a]	δ_{int} (ppm)	$a \times 10^{-3}$ (ppm·K)	δ_{dia} (ppm)	$a' \times 10^{-3}$ (ppm·K)	$b' \times 10^{-5}$ (ppm·K^2)
		[(6-Ph_2TPA)Ni(CH_3CN)(CH_3OH)](ClO_4)$_2$ (**1**)				
α	~176	−58.67	68.9	8.49	25.2	70.8
β	58.0	6.99	14.8	7.70	14.4	0.6
	50.4	14.54	10.3	7.18	14.8	−6.9
β'	53.0	9.67	12.4	7.70	13.7	−2.0
	39.9	5.43	10.0	7.56	8.8	1.9
γ	15.5	7.24	2.4	7.70	2.1	0.4
γ'	8.5	9.19	−0.3	7.77	0.5	−1.2
CH_2 (PhPy)	~158	5.68	44.6	3.96	45.6	−1.4
	~36[d]					
CH_2 (Py)	~77	21.16	15.7	3.96	26.7	−17.6
Ph	8.4	7.88, 7.28	0.2, 0.3	7.45	0.4, 0.2	0.4, 0.1
	6.6	7.70	−0.3	8.04	−0.6	0.3
		[(TPA)Ni(CH_3CN)(H_2O)](ClO_4)$_2$ (**2**)				
α	~142	7.25	41.2	8.48	40.7	0.6
β	52	4.55	14.3	7.58	12.5	2.7
	50	4.53	13.7	7.20	12.1	2.5
γ	14.3	6.60	2.3	7.71	1.7	1.0
CH_2	~79	7.70	22.0	3.84	24.6	−4.1
		[(6-Ph_2TPA)Ni($ONHC(O)CH_3$)]ClO_4 (**3**)				
α	160	8.92	45.6	8.49	45.8	−0.3
β	47.5	5.79	12.6	7.70	11.5	1.7
	41.8	−2.29	12.4	7.18	6.8	8.4
β'	38.8	12.47	8.9	7.70	11.7	−4.2
	29.3	−3.85	10.0	7.56	3.2	10.0
γ	14.8	6.85	2.4	7.70	1.9	0.8
γ'	6.4	11.27	−1.5	7.77	0.6	−3.1
CH_2 (PhPy)	143	−27.01	51.6	3.96	33.0	27.7
	45	43.07	0.7	3.96	24.3	−35.5
CH_2 (Py)	51	1.27	15.1	3.96	13.4	2.4
Ph	8.2	7.44	0.2	7.45	0.2	0.009
	8.0	6.76	0.4	7.45	−0.04	0.6
	4.7	11.47	−2.0	8.04	0.007	−3.0
N−H	128	−19.81	44.5	8.98	27.5	25.0
CH_3	9.0	−1.99	3.3	1.76	1.1	3.3
		[(6-Ph_2TPA)Ni−Cl(CH_3CN)]ClO_4 (**4**)				
α	~170	14.46	45.9	8.49	49.1	−4.2
β	54.6	1.82	15.6	7.70	12.1	5.2
	37	−19.07	18.1	7.18	2.4	23.3
β'	~52	33.75	5.3	7.70	20.9	−23.1
	~42	13.52	7.0	7.56	10.6	−5.3
γ	14.8	8.63	1.8	7.70	2.4	−0.8
γ'	10	30.03	−6.2	7.77	7.2	−20.0
CH_2 (PhPy)	~192	17.79	38.2	3.96	45.8	−10.3
	~21	7.57	4.0	3.96	6.1	−2.8
CH_2 (Py)	~76	14.51	18.1	3.96	24.4	−9.3
Ph	8.6	7.98	0.2	7.45	0.5	−0.5
	6.9	−2.15	2.7	8.04	−3.4	9.1

[a] Observed chemical shift (ppm) at 302 K. [b] Fit of change in chemical shift (ppm) with temperature (K) according to the Curie law ($\delta_{obs} = \delta_{int} + a/T$), where δ_{int} is the intercept at $T = 0$ K and a is the Curie slope. [c] Fit of change in chemical shift (ppm) with temperature (K) according to a polynomial function ($\delta_{obs} = \delta_{int} + a'/T + b'/T^2$), where δ_{int} is the chemical shift of the diamagnetic resonance of the free ligand. [d] Variable temperature chemical shift data not obtained.

Comparison of ^{1}H NMR Properties of 1−4 with Iron Complexes Ligated by Tris((2-pyridyl)methyl)amine-Type Ligands. Extensive paramagnetic ^{1}H NMR studies on tris((2-pyridyl)methyl)amine-ligated iron complexes have been reported by Que and co-workers.[35,39] Similar to the octahedral Ni(II) complexes described here, six-coordinate Fe(II) complexes of TPA exhibit a pattern of isotropically shifted pyridine resonances in the order α-H > β-H > γ-H

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consistent with a σ delocalization mechanism. NMR characterization of iron complexes of monoaryl-appended tris((2-pyridyl)methyl)amine ligands (6-PhTPA and (6-(4-OCH_3-Ph)-TPA)) have also been reported.[35,40] Similar to the ^{1}H NMR spectroscopic properties of **1**, **3**, and **4**, the six-coordinate Fe(II) cation $[(6\text{-PhTPA})Fe(CD_3CN)_2]^+$ in CD_3CN solution exhibits a 2:1 pattern of β-H resonances, indicating an effective mirror plane within the cation in solution. Mandon and co-workers have characterized the Fe(II) complex $[(6\text{-}Ph_2TPA)FeCl_2]$ in which one PhPy arm is dissociated from the metal both in the solid state and in CH_3CN solution. In this case, two resonances at 2.1 and 1.8 ppm, respectively, were assigned to protons of the uncoordinated pyridyl ring. A distinct set of resonances for the phenyl substituent of the uncoordinated PhPy donor was not identified. No evidence for PhPy dissociation in **1**−**4** was found in the NMR studies outlined herein.

Summary and Perspective

Examples of mononuclear octahedral Ni(II) complexes for which both the solid-state structure is known and the paramagnetic ^{1}H NMR resonances have been fully assigned are rare. In this work, we have completely assigned the proton resonances of synthetic mononuclear octahedral nickel(II) complexes of relevance to ARD using 1D and 2D ^{1}H NMR methods, as well as ^{2}H NMR. Our success in this endeavor suggests that NMR methods will be viable for monitoring reactions of **1** and **2** with model acireductone substrates. As the active site nickel center in ARD is ligated by four protein-derived residues, including three histidine donors, initial model studies involving Ni(II) complexes of tris((2-pyridyl)methyl)amine-type ligands are appropriate.

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Supporting Information Available: Isotropic shift vs 1/*T* plots for **1**−**4** (Figures S1−S4); magnitude ^{1}H COSY spectra for **1** and **3** (Figures S5 and S6); X-ray crystallographic CIF file for **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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