J. Am. Chem. Soc. **1989**, *111*, 4497–4498

Active Site Model of Urease: Synthesis, Structure, and Magnetic Properties of a Binuclear Ni(II) Complex Containing a Polyimidazole Ligand

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Received August 1, 1988

There is growing interest in the active site structures and catalytic functions of Ni^{II}-containing metalloproteins.[1] Probably the best known but still poorly understood nickel-containing enzyme is jack bean urease (urea amido hydrolase).[2,3] Isolated from Japanese jack beans by Sumner in 1926,[3] urease is known to catalyze the hydrolysis of urea[4] at a rate 10^{14} times faster than the spontaneous degradation of the amide in water. Only recently has urease been shown to contain two Ni^{II} ions per molecule of protein,[2a] both of which are thought to be intimately involved in the hydrolysis process.[5] Recent EXAFS studies[6,7] suggest that both Ni^{II} ions are octahedral in geometry and coordinated to histidine ligands; however, the Ni–Ni separation is still not known. Blakeley et al.[2b,5] have suggested that a dihydroxodiaminomethane-bridged intermediate forms following hydroxide ion attack on an O-coordinated urea carbonyl carbon atom, which decomposes forming a bound carbamate ion. More recent evidence supporting a binuclear active site in urease comes from magnetization studies on the protein by Wilcox.[8] A weak antiferromagnetic exchange interaction was detected between Ni^{II} ions indicative of close Ni–Ni separation (<4 Å) in the protein. β-Mercaptoethanol is known to bind reversibly to urease, resulting in the formation of a diamagnetic complex, presumably due to the presence of a strong antiferromagnetic exchange interaction through a sulfur-bridged complex.

We wish to report herein the synthesis and properties of a binuclear Ni^{II} complex of the phenol-containing polyimidazole ligand, Hbimp = 2,6-bis[(bis((1-methylimidazol-2-yl)methyl)-amino)methyl]-4-methylphenol. Biologically relevant ligands such as imidazoles and phenolate and acetate ions have been employed in this study to model the active site of urease because they approximate the amino acid residues presumed to be bound to the Ni^{II} ions.[6]

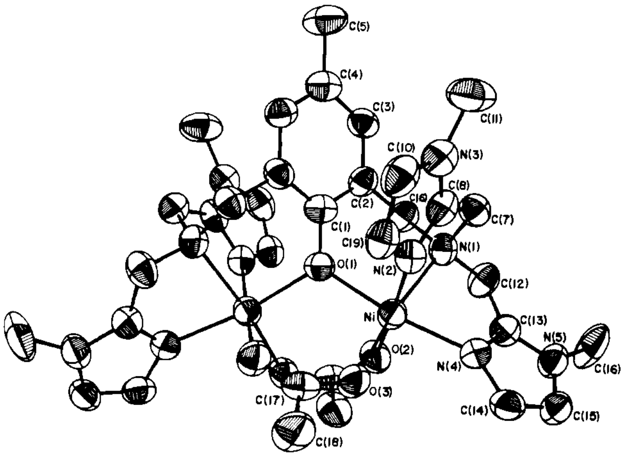

Figure 1. A view of the $[Ni_2(bimp)(\mu\text{-}OAc)_2]^+$ cation which lies on a crystallographic 2-fold axis. Selected bond distances (Å) and angles (deg) are as follows: Ni–O(1) = 2.010 (3); Ni–O(2) = 2.100 (5); Ni–O(3) = 2.019 (5); Ni–N(1) = 2.178 (5); Ni–N(2) = 2.073 (5); Ni–N(4) = 2.101 (5); Ni–Ni′ = 3.422 (4); Ni–O(1)–Ni′ = 116.7 (5).

$[Ni_2(bimp)(\mu\text{-}OAc)_2]\cdot ClO_4\cdot CH_3OH$ (**1**) is prepared by reaction of 2 equiv of nickel(II) acetate·dihydrate with 1 equiv of bimp and sodium perchlorate in methanol. The resulting turquoise-colored precipitate is recrystallized from methanol affording light green crystals. The structure[10] of **1** is shown in Figure 1. The complex contains a μ-phenoxo di-μ-acetato bridged structure and imidazole-containing pendants that complete the octahedral geometry around each Ni^{II} ion. Similar structures have been observed for Fe[11a–d,12] and Mn[9,11e–f] complexes of bimp and related ligands; however, this is the first example of a triply bridged μ-phenoxo di-μ-acetato Ni_2^{II} complex. Recently, Wieghardt and co-workers[13] reported the synthesis and characterization of a μ-hydroxo di-μ-acetato bridged Ni_2^{II} complex, containing the tridentate cyclic amine ligand, *N,N′,N″*-trimethyl-1,4,7-triazacyclononane (TACN). A μ-aqua di-μ-acetato bridged dinickel complex also has been reported.[14] The Ni–Ni separation in **1** is 3.422 (4) Å, while the average Ni–N distance of 2.171 (7) Å and Ni–O distance of 2.044 (5) Å are typical of octahedral Ni(II) complexes[15] and compare favorably with lengths reported for

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(10) Data were collected on an irregular green plate of dimensions 0.15 × 0.30 × 0.50 mm coated with epoxy at 295 K using Mo Kα radiation (λ = 0.71073 Å; 2θ = 50° on an Enraf-Nonius CAD-4 diffractometer) and corrected for linear decay of intensities (8.4% decay); reflection averaging gave agreement on I = 2.6%. The structure was solved and refined (SDP package) using 1607 unique reflections having $I > 3\sigma(I)$. Crystallographic data: monoclinic space group $C2/c$; a = 13.466 (3) Å, b = 20.849 (3) Å, c = 15.049 (4) Å, β = 94.66(1)°, V = 4211.2 Å^3, and Z = 4; R = 5.2%, R_w = 6.9%; d_{obsd} = 1.53 (1) g/cm^3; d_{calcd} = 1.54 g/cm^3. *Caution*! Although the compound described herein was not found to be shock sensitive, care should be taken in handling all perchlorate salts.

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0002-7863/89/1511-4497$01.50/0

$Ni_2(\mu\text{-}OH)(\mu\text{-}OAc)_2(TACN)^+$.[13]

In acetonitrile **1** displays three broad absorption bands at 373 (ϵ = 60.0 M^{-1} cm^{-1}), 622 (ϵ = 20.4 M^{-1} cm^{-1}), and 1037 nm (ϵ = 25.4 M^{-1} cm^{-1}). These peaks are assigned to the $^3A_{2g} \rightarrow {}^3T_{1g}(P)$, $^3T_{1g}(F)$, and $^3T_{2g}(F)$ transitions expected for octahedral d^8 ions.[16] A weak absorption also is observed at 767 nm due to the spin forbidden $^3A_{2g} \rightarrow {}^1E_{1g}$ transition. Evaluation of the data with a d^8 energy level diagram[17] gives D_q = 970 cm^{-1} and $B \simeq 940$ cm^{-1}. Urease also displays three prominent bands in the visible and near-IR region at 407, 745, and 1060 nm.[5] Addition of excess ammonium carbamate to an aqueous solution of **1** results in the formation of a bridged carbamate complex[18] which displays clean isobestic behavior and absorption peaks at 370 (ϵ = 220.0 M^{-1} cm^{-1}), 615 (ϵ = 26.0 M^{-1} cm^{-1}), 768 (ϵ = 6.0 M^{-1} cm^{-1}) and 1015 (ϵ = 25.0 M^{-1} cm^{-1}). The reactivity of the carbamate complex toward strong base as well as **1** with urea and other known substrates of urease are under investigation.

The electrochemical properties of **1** have been studied by cyclic voltammetry. A single quasireversible one-electron[20] redox wave is observed in acetonitrile at +0.94 V vs Ag/AgCl corresponding to the $Ni^{II}Ni^{II}/Ni^{II}Ni^{III}$ couple. Similar electrochemical behavior has been reported for the $[Ni_2(\mu\text{-}OH)(\mu\text{-}OAc)_2(TACN)]$[13] ion and related Ni^{II} complexes.[21] Efforts to isolate the mixed-valence $[Ni^{II}Ni^{III}$ (bimp) $(\mu\text{-}OAc)_2]^{2+}$ complex are in progress.

The solid-state variable-temperature magnetic susceptibility of **1** has been measured between 300.9 and 5.5 K. The effective magnetic moment of the cation changes gradually from 4.69 μ_B/complex at 300.9 K to 2.88 μ_B/complex at 5.5 K[22] suggesting the presence of a weak antiferromagnetic exchange interaction. The data were least-squares (25 × 25) fit by a full-matrix diagonalization approach which includes both an isotropic exchange interaction ($H = -2J\hat{S}_1\cdot\hat{S}_2$) as well as single-ion zero-field splitting (DS_z^2 where D is the axial zero-field-splitting parameter) for each Ni(II) ion to give g = 2.2, D = −0.02 cm^{-1}, and J = −1.9 cm^{-1}. The weak exchange interaction is consistent with the magnetic data discussed earlier for urease.[8]

Acknowledgment. We are thankful for support from the National Science Foundation (Grant RII-8610671) and the Commonwealth of Kentucky through the Kentucky EPSCoR Program (R.M.B.) and National Institutes of Health Grant HL13652 (D.N.H.). Dr. C. Trapp's contribution in determining ligand field parameters for **1** are acknowledged.

Supplementary Material Available: Tables containing atomic positional parameters, isotropic and anisotropic thermal parameters, selected bond lengths and angles, and magnetic data and figures of electrochemical and electronic spectral properties for $[Ni_2(bimp)(\mu\text{-}OAc)_2]ClO_4\cdot CH_3OH$ (**1**) are available (12 pages); table of observed and calculated structure factors (6 pages). Ordering information is given on any current masthead page.

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(18) The same di-μ-carbamate complex can be prepared by reaction of 2 equiv of nickel(II) perchlorate and ammonium carbamate with bimp in a methanol solution. The compound analyzes correctly for the formula $[Ni_2(bimp)(\mu\text{-}O_2CNH_2)_2]\cdot ClO_4\cdot CH_3OH$.

(19) Inhibitors such as phosphoramidates and dihydrogen phosphate monoanion also are thought to bridge the nickel ions in urease, requiring the Ni–Ni separation to be less than 6 Å, further supporting the proposal of a binuclear active site.

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(22) Compound **1** also displays an X-band EPR spectrum at 4.2 K (with features at g = 6.67, 4.17, 2.24 and 2.17) for both a microcrystalline-powdered sample and frozen acetonitrile solution of the complex.

Thermal and Photochemical Rearrangements of Methyliridium Phosphido Complexes: Formation of a Cyclometalated Hydride by α-Abstraction of a Coordinated Alkyl Ligand

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Received November 21, 1988

One of the fundamental reactions of mononuclear hydrocarbyl metal complexes is the α-elimination or α-abstraction process.[1] Although this process is quite well-documented[2] for the earlier transition metals, recent studies[3] have suggested that complexes of the later metals are also amenable to this process. In particular, we have previously reported the photochemical generation of an iridium methylidene[4] and the unusual mode of dihydrogen activation by a terminal phosphide complex,[5] both processes apparently involving elimination or transfer of an α-hydrogen from a coordinated hydrocarbyl group. In this paper we provide yet another example of this type of reaction in the *thermal* rearrangement of iridium(III) methyl complexes containing terminal phosphide ligands. Also presented is the contrasting apparent coupling of an alkyl and a terminal phosphide ligand under *photochemical* conditions to give a coordinated phosphine.

The iridium(III) diphenylphosphido complex[5] $Ir(CH_3)PPh_2[N(SiMe_2CH_2PPh_2)_2]$, **1a**, is thermally unstable; at 50 °C in the dark, deep purple solutions of **1a** slowly (5 h) fade to light yellow to generate the octahedral hydride complex[6] *fac*-$Ir(\eta^2\text{-}CH_2PPh_2)H[N(SiMe_2CH_2PPh_2)_2]$, **2a**, in high yield. The X-ray crystal structure[7] of **2a** is shown in Figure 1 along with some pertinent bond parameters. The ancillary tridentate ligand has isomerized to the facial coordination mode with the hydride trans to the amide donor; the η^2-CH_2PPh_2 moiety occupies the remaining cis sites of the distorted octahedron. Although **2a** is stable in the solid state under an inert atmosphere, further heating in solution results in the *irreversible* formation of the iridium(I) complex $Ir(PMePh_2)[N(SiMe_2CH_2PPh_2)_2]$, **3a**. Photolysis[8] of the Ir(III) phosphide complex **1a** at room temperature results in the direct formation of the Ir(I) complex **3a** with no evidence for the intermediacy of the cyclometalated hydride complex **2a**. These

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(6) Analytical and NMR data are contained in the Supplementary Material.

(7) Crystals of *fac*-$Ir(\eta^2\text{-}CH_2PPh_2)H[N(SiMe_2CH_2PPh_2)_2]$ (**2a**) are monclinic having the cell constants 9.253 (2) Å, 21.950 (5) Å, 20.081 (4) Å, and 90.74 (2)°; other crystal data are Z = 4 and space group $P2_1/c$. The structure was solved by conventional heavy-atom techniques and was refined in blocks (with the Ir atom in every cycle) using least-squares procedures to R = 0.0356 and R_w = 0.0370 for 4448 reflections having $I > 3\sigma(I)$ collected at 20 ± 1° with Mo Kα radiation on a Nicolet R3 diffractometer. All the atoms were refined anisotropically except for the hydrogen atom on iridium which was refined isotropically; all other hydrogens were fixed in idealized positions. Full details will be reported elsewhere.

(8) The photolysis of **1a** was carried out using a 275 W sunlamp for 24 h at room temperature; however, photolysis of the more thermally labile complex **1b** required use of a N_2 laser with the sample maintained at −30 °C.

0002-7863/89/1511-4498\$01.50/0