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Modeling Nickel Hydrogenases: Synthesis and Structure of a Distorted Octahedral Complex with an Unprecedented [NiS_4H_2] Core

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Hydrogenases comprise a fundamental group of bacterial enzymes that catalyze the reversible oxidation of dihydrogen to protons and, thus, play a key role in molecular bioenergetics.[1] Interest in hydrogenases has intensified in recent years since unequivocal structural information was obtained using X-ray crystallography for the NiFe−hydrogenase extracted from *Desulfovibrio gigas*.[2] Numerous elegant synthetic,[3] spectroscopic,[4] and theoretical[5] studies have provided further insight into the structure and function of NiFe hydrogenases. It is now clear that the active site consists of a dinuclear nickel−iron complex in a sulfur-rich environment, with the nickel atom surrounded by four cysteine groups in a geometry that has been described as either square pyramidal with a missing basal ligand or octahedral with two cis coordination vacancies (Figure 1).[6] Despite these efforts, the exact nature of the catalytic cycle and the redox properties of nickel (i.e., the factors affecting the stabilization of Ni(I) and Ni(III) species) remain uncertain. Seeking to investigate new structural and functional model compounds for nickel hydrogenases, we set out to apply the poly(mercaptoimidazolyl)borate ligand system[7] to this endeavor. In this regard, bis(mercaptoimidazolyl)borates (Bm^R) are attractive soft donor ligands because of their coordinative flexibility and ease of preparation, and they have recently been used in zinc bioinorganic chemistry[8] and in the design of potential radiopharmaceutical agents.[9] We present here the synthesis, characterization, and preliminary electrochemical studies of a complex having structural features that closely resemble those of the nickel center in the active states (the so-called "Ni−B" or "Ni−SI" forms)[10] of NiFe hydrogenases.

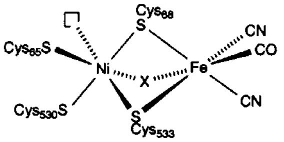
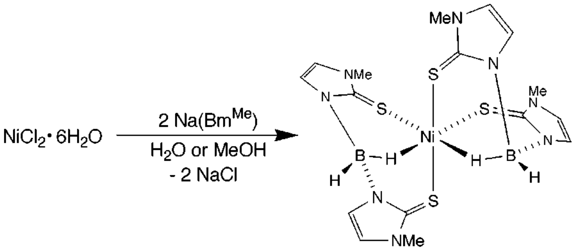


Figure 1. Representation of the active site in the NiFe hydrogenase extracted from *D. gigas* showing a vacant coordination site (open square) and the additional bridging oxo or hydroxo ligand (X) present only in the oxidized (inactive) form of the enzyme.

The yellow nickel(II) complex $Ni(Bm^{Me})_2$ was readily prepared (76% yield) by mixing aqueous or methanolic solutions of $NiCl_2 \cdot 6H_2O$ and the sodium salt of the bis(2-mercapto-1-methylimidazolyl)borate anion in a 1:2 ratio (eq 1).[11]



(1)

It is an air stable, thermally robust solid, slightly soluble in benzene, tetrahydrofuran, methanol, or acetonitrile, but more so in chloroform and dimethyl sulfoxide, and it has been characterized by a combination of analytical and spectroscopic techniques.[12] The presence of Ni···H−B interactions, precedented in poly(mercaptoimidazolyl)borate chemistry,[13] was verified in the solid state by the observation of two ν_{B-H} stretching bands (2403 & 2250 cm^{-1}) in its IR spectrum and subsequently confirmed by an X-ray diffraction study (vide infra). The paramagnetism of $Ni(Bm^{Me})_2$ ($\mu_{eff} = 3.1\ \mu_B$)[14] is typical of an $S = 1$ ground state

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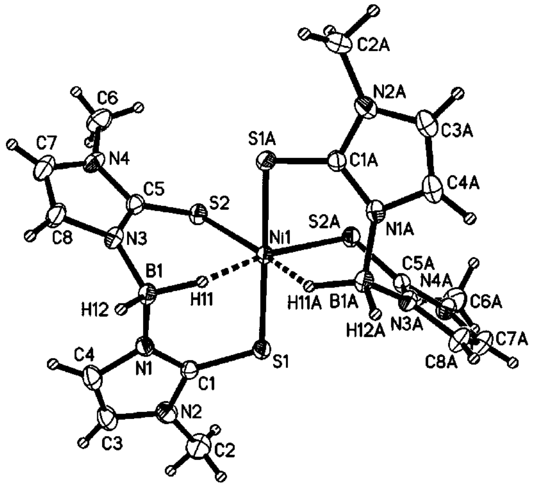

Figure 2. Molecular structure of Ni(Bm^{Me})$_2$. Selected bond lengths (Å) and angles (deg): Ni−S1 2.3616(13), Ni−S2 2.3896(13), Ni−H11 1.863(9); S1−Ni−S1A 172.92(1), S1−Ni−S2 95.69(1), S1−Ni−S2A 88.99(1), S2−Ni−S2A 97.31(1), H11−Ni1−H11A 77.4(4).

and is also manifested in solution by broad, contact-shifted resonances in its ^{1}H NMR spectrum.

The molecular structure of Ni(Bm^{Me})$_2$ was determined by single-crystal X-ray diffraction (Figure 2).[15] The six-coordinate complex contains a [NiS$_4$H$_2$] core that has never before been observed in nickel chemistry.[16] The distorted octahedral metal center is surrounded by two tridentate [Bm^{Me}]$^-$ groups (i.e., a κ^3-*S,S,BH* coordination mode for each ligand), with the two Ni···H−B interactions in mutually cis positions. The Ni−H bond lengths in Ni(Bm^{Me})$_2$ [1.863(9) Å] are within the range of corresponding values observed in the only three other nickel complexes containing such bonds that have been structurally characterized,[17] but they are clearly longer than the typical Ni−H bond distances found in authentic nickel hydride complexes (ca. 1.46 Å).[18] Most significantly, the constrained geometry of the four sulfur donor atoms ($S{-}Ni{-}S_{trans} \approx 173°$, $S{-}Ni{-}S_{cis} \approx 89{-}97°$) is quite similar to that postulated for the nickel center in the active form of NiFe hydrogenase (e.g., $SCys_{65}{-}Ni{-}SCys_{530} = 89°$).[2b] Furthermore, the Ni−S bond lengths, 2.3616(13) and 2.3896(10) Å, are within the range of Ni−SCys bond distances observed in the structure of NiFe hydrogenase (2.2−2.6 Å).[2b]

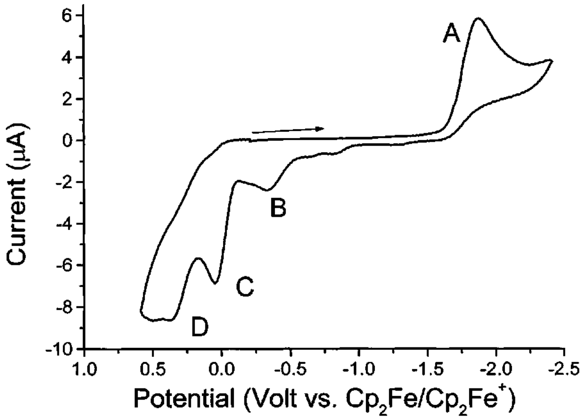

Figure 3. Cyclic voltammogram of a 0.5 mM solution of Ni(Bm^{Me})$_2$ in acetonitrile containing TBAPF$_6$ as the supporting electrolyte (0.1 M). The scan was initiated in the negative potential direction, and a glassy carbon disk working electrode was used; scan rate = 200 mV/s.

Cyclic voltammetry experiments established that Ni(Bm^{Me})$_2$ is susceptible to both electrochemical reduction and oxidation (Figure 3).[19] In particular, a chemically irreversible reduction of Ni(Bm^{Me})$_2$ (wave A, $Ep_c = -1.87$ V) is followed by a homogeneous reaction after electron transfer, the ultimate product of which undergoes a chemically irreversible oxidation (wave B, $Ep_a = -0.34$ V). Ni(Bm^{Me})$_2$ also undergoes a chemically irreversible oxidation (wave C, $Ep_a = 0.04$ V), the product(s) of which can also be further oxidized (wave D, $Ep_a = 0.37$ V). A detailed study of the processes giving rise to the observed electrochemical activity of this and related nickel complexes is in progress.

In summary, we have prepared and characterized Ni(Bm^{Me})$_2$, the first bis(mercaptoimidazolyl)borate complex of nickel. X-ray crystallography confirmed the formation of a novel [NiS$_4$H$_2$] species having two cis Ni···H−B interactions and an overall distorted octahedral geometry, thereby providing a structural model compound for the nickel center in the active form of NiFe hydrogenases. The reactivity of Ni(Bm^R)$_2$ and the syntheses of related tris(mercaptoimidazolyl)borate derivatives (Tm^R)NiX are currently under investigation.

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Supporting Information Available: Experimental details, characterization data, and X-ray crystallographic tables for Ni(Bm^{Me})$_2$ (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) Crystal data for Ni(Bm^{Me})$_2$·2MeCN (at 150 K): orthorhombic, *Pccn* (No. 56), $a = 13.731(7)$, $b = 14.177(7)$, $c = 15.234(8)$ Å, $V = 2965(2)$ Å^3, $Z = 4$. The structure was refined by full-matrix least-squares on F to give final indices $R_1 = 0.035$ and $wR_2 = 0.038$ for 3385 independent reflections [$I > 3\sigma(I)$].

(16) Distorted tetrahedral [MS$_4$H$_2$] cores having also two vicinal but considerably longer M···H−B contacts (2.1−2.6 Å) are present in the tris(mercaptoimidazolyl)borate complexes M(Tm^{Ph})$_2$ (M = Fe, Co) and in the bis(mercaptoimidazolyl)(pyrazolyl)borate complex Cd(pzBm^{Me})$_2$. See ref 13c and: Kimblin, C.; Bridgewater, B. M.; Churchill, D. G.; Hascall, T.; Parkin. G. *Inorg. Chem.* **2000**, *39*, 4240−4243.

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