Volume 26
Number 19
September 23, 1987

Inorganic Chemistry

Communications

Four- and Five-Coordinate Cobalt(II) Thiolate Complexes: Models for the Catalytic Site of Alcohol Dehydrogenase

Sir:

The catalytic zinc in liver alcohol dehydrogenase (LADH) is coordinated by two cysteines, a histidine, and a water molecule.[1,2] There is a controversy whether the substrate displaces the water molecule with the zinc remaining four-coordinate or whether the substrate binds without displacement of H_2O to give a five-coordinate intermediate state.[3,5,6] Many spectroscopic studies relating to this mechanistic question have been made on the cobalt-substituted LADH, whose structure and activity are quite similar to the native zinc enzyme.[3,4] Spectroscopic evidence supporting five-coordinate intermediate states comes from the proposed relationship of the zero-field splitting of Co(II) complexes with coordination number and from ^{17}O relaxation studies.[5] Electronic spectroscopy provides a major argument against the five-coordinate states: there are no significant differences in the extinction coefficients of the ligand field bands in the spectrum of the cobalt enzyme upon transition from the initial tetrahedral state to the proposed five-coordinate intermediate states.[6] We report the synthesis and structure determination of a series of bis(thiolate)cobalt complexes, which are spectroscopic models for the catalytic center in LADH.

The reaction of $Co(SR)_2$ (SR = S-2,4,6-*i*-$Pr_3C_6H_2$ or S-2,6-*i*-$Pr_2C_6H_3$)[7] with 2 equiv of pyridine or 1-methylimidazole in CH_3CN gives $Co(SR)_2L_2$ complexes in high yield.[8,9] [Co(S-2,4,6-*i*-$Pr_3C_6H_2)_2(py)_2$] (**1**) was previously shown to have a distorted tetrahedral structure by X-ray diffraction.[9] The structure of **1** closely reproduces the [(cys-S)$_2$Zn(imid)(his)] coordination unit of the structurally characterized imidazole inhibited enzyme; in both structures the rings of the nitrogen donor ligands are nearly orthogonal.[10]

When bidentate ligands such as bipyridine or phenanthroline are substituted for the monodentate nitrogen bases, five-coordinate complexes of formulation [$Co(SR)_2(L)(CH_3CN)$] (L = bpy, phen) are obtained.[11] The X-ray crystal structure of [Co(S-2,6-*i*-$Pr_2C_6H_3)_2(bpy)(CH_3CN)$] (**2**) reveals it to be monomeric with a distorted trigonal-bipyramidal geometry (Figure 1).[12] The two thiolates occupy equatorial positions, the bpy ligand spans an axial–equatorial edge and the CH_3CN, which comes from the solvent, occupies an axial position. Well-characterized examples of five-coordinate Co(II) complexes are limited in number.

When the same reaction was performed with a less sterically hindered thiolate ligand, the resultant complex is a dimer, [Co-(S-2,3,5,6-$Me_4C_6H)_2(bpy)]_2$ (**3**) (Figure 1).[13] The cobalt ions are five-coordinate with an asymmetric dithiolate bridge.[14] The difference in the nuclearity of compounds **2** and **3** reflects the reduced tendency of the more steric thiolates to bridge metal centers.[15] The structures of **2** and **3** also indicate the tendency of cobalt to become five coordinate.

Complexes **1** and **2** and their respective derivatives are monomeric four- and five-coordinate complexes with very similar ligand sets. They should make a good test case for spectroscopic methods that claim to be able to distinguish differences in the coordination number in Co(II) complexes and proteins.[5,6,16] The electronic spectra of [Co(S-2,4,6-*i*-$Pr_3C_6H_2)_2$(1-Me-imid)$_2$] in toluene and in CH_3CN (Figure 2) are similar; the position and extinction of the ligand field bands are consistent with tetrahedral

---

(1) Eklund, H.; Brändén, C.-I. In *Zinc Enzymes*; Spiro, T. G., Ed.; Wiley: New York, 1983.

(2) Klinman, J. P. *CRC Crit. Rev. Biochem.* **1981**, *10*, 39.

(3) (a) Zeppezauer, M.; Andersson, I.; Dietrich, H.; Gerber, M.; Maret, W.; Schneider, G.; Schneider-Bernlöhr, H. *J. Mol. Catal.* **1984**, *23*, 377. (b) Zeppezauer, M. In *Coordination Chemistry of Metalloenzymes*; Bertini, I., Drago, R., Luchinat, C., Eds.; Reidel: Dordrecht, The Netherlands, 1983.

(4) Schneider, G.; Eklund, H.; Cedergren-Zeppezauer, E.; Zeppezauer, M. *Proc. Natl. Acad. Sci. U.S.A.* **1983**, *80*, 5289.

(5) (a) Makinen, M. W.; Kuo, L. C.; Yim, M. B.; Wells, G. B.; Fukuyama, J. M.; Kim, J. E. *J. Am. Chem. Soc.* **1985**, *107*, 5245. (b) Makinen, M. W.; Kuo, L. C.; Yim, M. B.; Maret, W.; Wells, G. B. *J. Mol. Catal.* **1984**, *23*, 179. (c) Makinen, M. W.; Maret, W.; Yim, M. B. *Proc. Natl. Acad. Sci. U.S.A.* **1983**, *80*, 2584. (d) Makinen, M. W.; Wells, G. B. *Met. Ions Biol. Syst.* **1987**, *22*, 129.

(6) (a) Bertini, I.; Gerber, M.; Lanini, G; Luchinat, C.; Maret, W.; Rawer, S.; Zeppezauer, M. *J. Am. Chem. Soc.* **1984**, *106*, 1826. (b) Bertini, I.; Luchinat, C. *Adv. Inorg. Biochem.* **1984**, *6*, 71. (c) Bertini, I.; Luchinat, C. *Met. Ions Biol. Syst.* **1983**, *15*, 101.

(7) [S-2,4,6-*i*-$Pr_3C_6H_2$] = 2,4,6-triisopropylbenzenethiolate; [S-2,6-*i*-$Pr_2C_6H_3$] = 2,6-diisopropylbenzenethiolate; [S-2,3,5,6-Me_4C_6H] = 2,3,5,6-tetramethylbenzenethiolate.

(8) In a typical reaction, the nitrogen base was added to a green CH_3CN solution of $Co(SR)_2$, which was generated in situ by the reaction of $CoCl_2 \cdot 6H_2O$ with 2 equiv of LiSR.

(9) Corwin, D. T., Jr.; Gruff, E. S.; Koch, S. A. *J. Chem. Soc., Chem. Commun.* **1987**, 966.

(10) Eklund, H.; Samama, J.-P.; Wallen L. *Biochemistry* **1982**, *21*, 4858.

(11) [Co(S-2,6-*i*-$Pr_2C_6H_3)_2(bpy)(CH_3CN)$] (**2**). Electronic spectrum (CH_3CN): 686 nm (193), 586 (sh) (486), 541 (sh) (706), 461 (sh) (2640), 399 (5960), 291 (18 900) nm. Crystal data: $a = 11.389$ (4) Å, $b = 15.847$ (7) Å, $c = 10.972$ (5) Å, $\alpha = 92.42$ (3)°, $\beta = 96.92$ (3)°, $\gamma = 71.21$ (3)°, $V = 1861$ (2) Å^3, triclinic, $P\bar{1}$, R (R_w) = 0.076 (0.088) for 2192 unique data.

(12) Bond distances (Å) and angles (deg) for **2**: Co–S1, 2.265 (3); Co–S2, 2.300 (3); Co–N1, 2.086 (7); Co–N2, 2.118 (7); Co–N3, 2.146 (8); S1–Co–S2, 124.6 (1); S1–Co–N1, 111.5 (2); S1–Co–N2, 97.2 (2); S1–Co–N3, 91.4 (2); S2–Co–N1, 123.1 (2); S2–Co–N2, 87.3 (2); S2–Co–N3, 94.6 (2); N1–Co–N2, 76.8 (3); N1–Co–N3, 92.5 (3); N2–Co–N3, 168.2 (3).

(13) [Co(S-2,3,5,6-$Me_4C_6H)_2(bpy)]_2$ (**3**). Crystal data: $a = 15.088$ (6) Å, $b = 18.163$ (7) Å, $c = 10.344$ (5) Å, $\alpha = 93.12$ (3)°, $\beta = 93.39$ (3)°, $\gamma = 84.93$ (3)°, $V = 2815(4)$ Å^3, $Z = 2$, triclinic, $P\bar{1}$. R (R_w) = 0.050 (0.063) for 4058 unique data.

(14) Bond distance (Å) and angles (deg) for **3**: Co1–S1, 2.585 (2); Co1–S1′, 2.326 (2); Co1–S3, 2.266 (2); Co1–N1, 2.094 (5); Co1–N2, 2.142 (5); S1–Co1–S3, 101.19 (7); S1–Co1–S1′ 77.4 (2); S1–Co1–N1, 93.1 (2); S1–Co1–N2, 157.2 (2); S3–Co1–N1, 107.2 (2); S3–Co1–N2, 101.3 (2); N1–Co1–N2, 76.8 (2).

(15) Koch, S. A.; Fikar, R.; Millar, M.; O'Sullivan, T. *Inorg. Chem.* **1984**, *23*, 121.

(16) (a) Lever, A. B. P. *Inorganic Electronic Spectroscopy*; Elsevier: Amsterdam, 1984; pp 480–505. (b) Banci, L.; Bencini, A.; Benellki, C.; Gatteschi, D.; Zanchini, C. *Struct. Bonding* (*Berlin*) **1982**, *52*, 37.

0020-1669/87/1326-3079$01.50/0

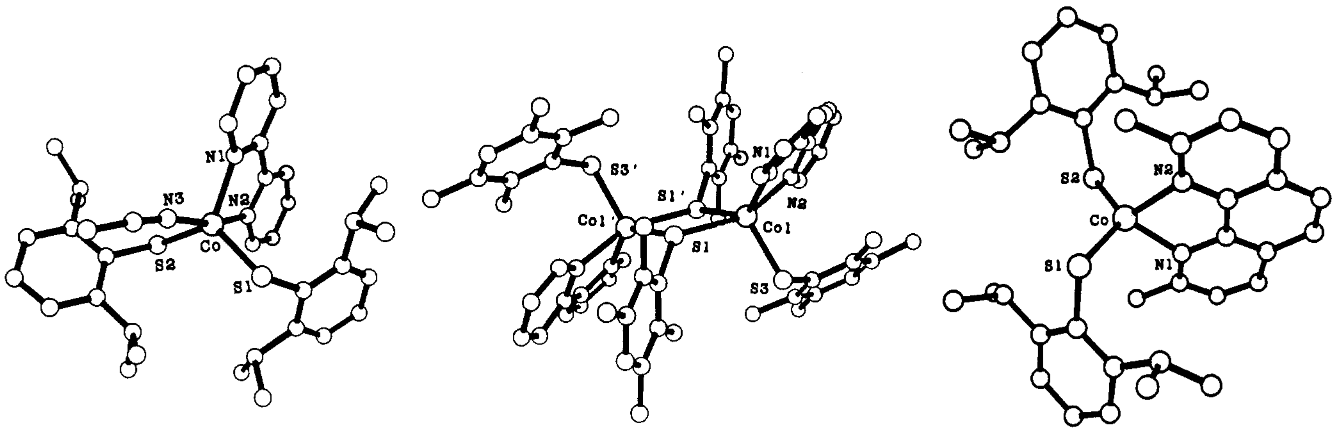

Figure 1. Structural diagrams (left to right) of $[Co(S\text{-}2,6\text{-}i\text{-}Pr_2C_6H_3)_2(bpy)(CH_3CN)]$, $[Co(S\text{-}2,3,5,6\text{-}Me_4C_6H)_2(bpy)]_2$, and $[Co(S\text{-}2,6\text{-}i\text{-}Pr_2C_6H_3)_2(2,9\text{-}Me_2phen)]$.

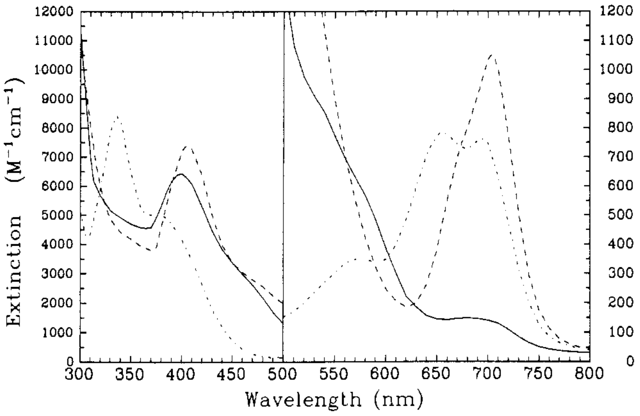

Figure 2. Electronic spectra (CH_3CN solutions) of $[Co(S\text{-}2,4,6\text{-}i\text{-}Pr_3C_6H_2)_2(1\text{-}Me\text{-}imid)_2]$ (·-·), $[Co(S\text{-}2,6\text{-}i\text{-}Pr_2C_6H_3)_2(phen)(CH_3CN)]$ (—), and $[Co(S\text{-}2,6\text{-}i\text{-}Pr_2C_6H_3)_2(2,9\text{-}Me_2phen)]$ (---).

coordination.[16] Moreover, the spectra are very similar to the spectrum of the $[(cys\text{-}S)_2Co(pyrazole)(his)]$ unit of the pyrazole-inhibited cobalt(II)-substituted catalytic center of LADH.[3b] The electronic spectra of **2** and its phen analogue in CH_3CN show markedly reduced extinctions for ligand field bands in the visible and in the near-infrared regions (Figure 2).[11] Reduced extinction for the ligand field bands in five- vs. four-coordinate Co(II) complexes is well established for complexes with nitrogen and oxygen donor ligands.[6,16] This result indicates that five-coordinate $[Co^{II}(S\text{-}cys)_2]$ centers should also be expected to have reduced extinction coefficients. The electronic spectrum of **2** in CH_3CN is very similar to that of the Co enzymes to which bpy has been added.[17] On the basis of the analogy of the structure of the phen-bound Zn enzyme,[18] the bpy-bound Co(LADH) is also five-coordinate.

In nondonor solvents, the spectra of **2** and its phen analogue show extinctions that indicate tetrahedral coordination. This result is consistent with the dissociation of the coordinated CH_3CN to give a four-coordinate complex. A further control experiment was done in which the phen ligand was replaced by 2,9-dimethyl-1,10-phenanthroline. It was anticipated that the steric effect of the two methyl groups ortho to the nitrogens would discourage five-coordination. X-ray crystallography established that $[Co(S\text{-}2,6\text{-}i\text{-}Pr_2C_6H_3)_2(2,9\text{-}Me_2phen)]$ (**4**) is indeed four-coordinate in the solid state even though it was crystallized from CH_3CN (Figure 1).[19,20] The electronic spectra of **4** in both CH_3CN (Figure 1) and in $CHCl_3$ are similar to the spectra of **2** in nondonor solvents with extinction coefficients that are in agreement with tetrahedral coordination.[19]

We have demonstrated that suitable modifications of the ligands can control the coordination geometry of bis(thiolate)cobalt(II) complexes. Our model studies support the view that the catalytic metal center in LADH remains four-coordinate during the enzymatic mechanism.

Acknowledgment is made to the National Institutes of Health for financial support (Grant GM-31849) and to Professor J. Lauher for use of the ROTOCHEM molecular graphics programs.

Supplementary Material Available: Tables of crystallographic data, fractional atomic coordinates, and isotropic and anisotropic thermal parameters and a plot of the electronic spectra in the near-infrared region (15 pages). Ordering information is given on any masthead page.

---

(17) Syvertsen, C.; McKinley-McKee, J. S. *J. Inorg. Biochem.* **1984**, *22*, 43.

(18) Boiwe, T.; Brändén, C.-I. *Eur. J. Biochem.* **1977**, *77*, 173.

(19) $[Co(S\text{-}2,6\text{-}i\text{-}Pr_2C_6H_3)_2(2,9\text{-}Me_2phen)]$ (**4**). Crystal data: $a = 12.548$ (5) Å, $b = 17.30$ (1) Å, $c = 16.82$ (1) Å, $\beta = 101.99$ (6)°, $V = 3573$ (8) Å^3, $Z = 4$, monoclinic, $P2_1/n$, R (R_w) = 0.042 (0.047) for 1929 unique data. Electronic spectrum (CH_3CN):1710 (52), 1170 (63), 852 (35), 704 (1050), 674 (sh) (745), 475 (sh) (2680), 406 (7400), 315 (sh) (7330), 263 (27 800) nm.

(20) Bond distances (Å) and angles (deg) for **4**: Co–S1, 2.242 (2); Co–S2, 2.246 (2); Co–N1, 2.065 (5); Co–N2, 2.045 (5); S1–Co–S2, 124.80 (7); S1–Co–N1, 115.7 (2); S1–Co–N2, 104.0 (2); S2–Co–N1, 105.6 (2); S2–Co–N2, 117.3 (2); N1–Co–N2, 81.7 (2).

Department of Chemistry
State University of New York at Stony Brook
Stony Brook, New York 11794

Douglas T. Corwin, Jr.
Ronald Fikar
Stephen A. Koch*

Received March 27, 1987

$(CH_3C_5H_4)_2TiS_2SiMe_2$: A Reactive Complex Containing an Si–S Ligand

Sir:

While the coordination chemistry of carbon–sulfur ligands is vast, very little is known about silicon–sulfur ligands.[1] Such species are of interest because they should prove as structurally variable as their carbon-based analogues but more reactive. Silanethiolates represent a bridge between organic thiolates and the thiometalates.[2] This paper summarizes our preliminary

---

(1) Ungurenasu, C.; Haiduc, I. *Rev. Roum. Chim.* **1968**, *13*, 657. Nametkin, N. S.; Tyurin, V. D.; Aleksandrov, G. G.; Kuźmin, O. V.; Nekhaev, A. I.; Andrianov, V. G.; Mavlonov, M.; Struchkov, Tu. T. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1979**, 1353. Seyferth, D.; Henderson, R. S.; Song, L.-C. *Organometallics* **1982**, *1*, 125.

(2) Krebs, B. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 113. Müller, A.; Diemann, E.; Jostes, R.; Bögge, H. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 934.

0020-1669/87/1326-3080$01.50/0