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Mononuclear nitrogen/sulfur-ligated cobalt(ii) methoxide complexes: Structural, EPR, paramagnetic ^{1}H NMR, and electrochemical investigations

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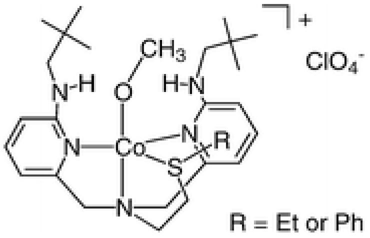
Abstract

The first examples of mononuclear nitrogen/sulfur-ligated Co(II) alkoxide complexes, species of relevance to a reactive intermediate observed for Co(II)-substituted liver alcohol dehydrogenase, have been isolated and characterized by multiple methods including X-ray crystallography, EPR, paramagnetic ^{1}H NMR, and cyclic voltammetry.

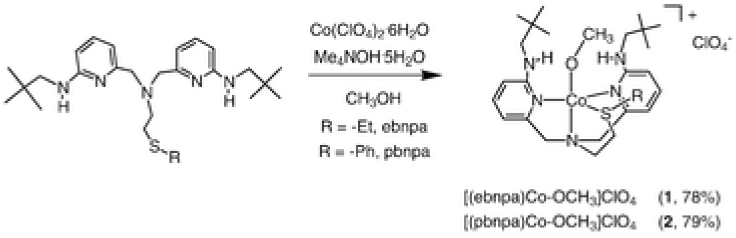


Mononuclear alkoxide complexes of the late transition metals are rare, due in part to the propensity of alkoxide ligands to bridge metal centers.[1] To date, four mononuclear Co(ii) complexes having terminal alkoxide ligation have been structurally characterized.[2,3] One of these is a tetrahedral cationic N_3-ligated Co(ii) ethoxide complex isolated using a chelate ligand that encapsulates the alkoxide moiety within a hydrophobic pocket.[2] The others are tetrahedral or trigonal planar species having bulky –O–C(*t*-Bu)$_3$ or –O–C(Ph)$_3$ ligation.[3]

In the zinc enzyme liver alcohol dehydrogenase (LADH), a nitrogen/sulfur-ligated zinc alkoxide species is proposed to be the reactive moiety for hydride transfer to NAD$^+$ during alcohol oxidation.[4] This alkoxide moiety is stabilized *via* hydrogen-bonding to a nearby amino acid residue (Ser48).[4,5] As zinc is spectroscopically silent (d^{10}), evidence for the proposed alkoxide intermediate in the alcohol dehydrogenase catalytic cycle has been obtained *via*UV-vis studies of a Co(ii)-substituted form of enzyme that retains catalytic activity, albeit 50–70% less than that of the native enzyme.[6]

We have previously shown that a mononuclear nitrogen/sulfur-ligated zinc methoxide complex can be isolated using a mixed nitrogen/sulfur chelate ligand which provides two internal hydrogen bond donors to the zinc-bound alkoxide oxygen atom.[7] To date, there are no examples in the chemical literature of structurally-related mononuclear zinc and cobalt alkoxide complexes of relevance to LADH. Thus, there is no chemical precedent for understanding how Co(ii) substitution in LADH may influence the chemical reactivity of the metal alkoxide moiety. Outlined herein are studies toward evaluating the chemical properties of mononuclear cobalt methoxide complexes supported by a specific nitrogen/sulfur chelate ligand.

Treatment of ebnpa[7] or pbnpa[8] with an equimolar amount of Co(ii)$(ClO_4)_2\cdot 6H_2O$ and $Me_4NOH\cdot 5H_2O$ in dry methanol (Scheme 1), followed by work-up and recrystallization from CH_3OH/Et_2O yielded green crystalline samples of [(ebnpa)Co–OCH_3]ClO_4 (**1**) and [(pbnpa)Co–OCH_3]ClO_4 (**2**) in yields of 78–79%. Single crystals of these complexes suitable for X-ray crystallographic studies were obtained *via*crystallization of each from $MeOH/Et_2O$ in the presence of Me_4NClO_4.‡ Complexes **1** and **2** have been characterized by elemental analysis, X-ray crystallography, EPR, paramagnetic ^{1}H NMR, cyclic voltammetry, UV-vis and FTIR. Analogues of **1** having deuteration at the alkoxide methyl group and selected positions of the ebnpa chelate ligand have been generated to enable assignment of paramagnetic ^{1}H NMR resonances (see ESI†).



Scheme 1

Representations of the cations of **1** and **2** are shown in Fig. 1. Similar to the zinc ion in [(ebnpa)Zn–OCH$_3$]ClO$_4$ (τ = 0.84, 0.88),[7,9,10] the Co(ii) centers of **1** and **2** each exhibit a slightly distorted trigonal bipyramidal geometry (**1**: τ = 0.90; **2**: τ = 0.93)[9] with the pyridylnitrogen donors and the thioether sulfur in the pseudo trigonal plane. For **1**, **2**, and [(ebnpa)Zn–OCH$_3$]ClO$_4$, a prominent equatorial angular deviation from the expected 120° involves an acute N(py)–M–N(py) bond angle (**1**: 111.84(5)°, **2**: 110.61(6)°, [(ebnpa)Zn–OCH$_3$]ClO$_4$:[10] 113.2(4)°/111.9(4)°). The axial Co–O and Co–N(am) distances in **1** (Table 1) are slightly longer (~0.02 Å) than similar linkages in **2**. The equatorial Co–N(py) and Co–S distances in **1** are shorter than those found in **2**, which is, in part, an indication of enhanced donor ability of the –SEt substituent of **1***versus* the –SPh donor of **2**. The Co(ii) derivative **1** exhibits similar bond distances to its zinc analogue [(ebnpa)Zn–OCH$_3$]ClO$_4$, with the largest deviation being in the metal–sulfur unit (~0.05 Å), where the Co(ii) complex has a shorter M–S interaction (Table 1). The general similarity of the bond distances in **1** and [(ebnpa)Zn–OCH$_3$]ClO$_4$ is consistent with the nearly identical ionic radii of five-coordinate Co(ii) and Zn(ii) (81 and 82 pm, respectively).[11] Finally, the Co–O(1)–C angles in **1** and **2** (126.12(11)° and 122.18(12)°, respectively) are the most acute reported to date for mononuclear cobalt alkoxide linkages,[2,3] and are generally similar to the angles observed for the two independent cations of [(ebnpa)Zn–OCH$_3$]ClO$_4$ (123.1(8)° and 124.5(8)°).[10]

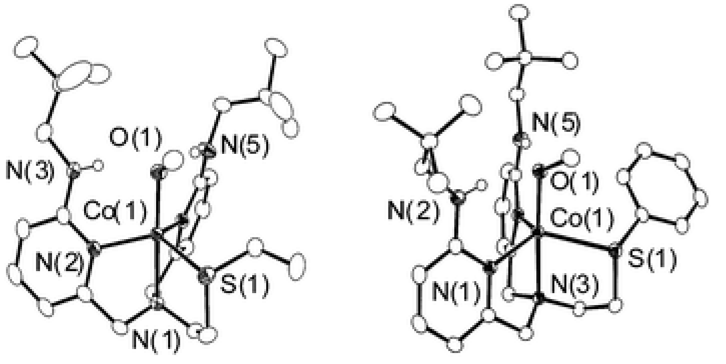


Fig. 1 Representations of the cationic portions of **1** and **2**. See Table 1 for selected bond distances.

Table 1 Selected bond distances (Å) in **1**, **2**, and [(ebnpa)Zn–OCH$_3$]ClO$_4$[7]

Compound	τ^a	**M–O**	**M–N(py)**	**M–N(am)**	**M–S**
1	0.90	1.9302(11)	2.0852(12), 2.0885(12)	2.1919(13)	2.4387(4)
2	0.93	1.9125(12)	2.1023(14), 2.1060(15)	2.1741(14)	2.5023(5)
[(ebnpa)Zn–OCH$_3$]ClO$_4$[10]	0.84	1.953(8)	2.095(9), 2.076(9)	2.212(10)	2.490(3)
	0.88	1.948(8)	2.086(10), 2.105(9)	2.192(10)	2.496(3)

a A. W. Addison, T. N. Rao, J. Reedijk, J. van Rijn and G. C. Verschoor, J. Chem. Soc., Dalton Trans., 1984, 1349.

Preliminary EPR analysis of **1** and **2** (0.46 and 0.49 mM, respectively) indicates that both complexes are high spin. As shown in Fig. S1, each complex exhibits a well-defined $S = 3/2$ $M_s = |\pm 1/2\rangle$ signal indicating a system having modest spin–orbit coupling and a high degree of rhombic distortion of the axial zero-field splitting. Simulation of the line shape for **1** yielded $g(x,y)$ = 2.395, g_z = 2.060, $A_y(^{59}\text{Co})$ = 0.0068 cm^{-1}, and E/D = 0.233.

These parameters suggest an electronically distorted 5- or 6-coordinate site with little electron delocalization away from the Co(ii) ion. Uneven intensities of the resolved hyperfine lines in the spectrum of **2**, centered at $g_{\mathrm{eff}} \sim 6$, indicate the presence of two species. Nevertheless, computer simulations show these species to be extremely similar in terms of electronic structure.

Paramagnetic ^{1}H NMR has been used extensively to characterize active site structural features and reactions of Co(ii)-substituted zinc enzymes including LADH.[12] We have found NMR useful for analyzing the solution properties of **1** and **2**. Shown in Fig. S2 is the ^{1}H NMR spectrum of a 2.3 mM solution of **1** in CD_3CN at 302 K. On the basis of integration, T_1 values, deuteration and complementary ^{2}H NMR studies, and comparison of the observed spectral features of **1** with those of **2** (Fig. S3) at a similar concentration, we have assigned several of the proton resonances of **1** (Table S1). For example, a single neopentyl methyl resonance is easily identifiable at 10.6 ppm. The β-protons of the pyridyl rings of **1** appear as two sharp singlets at 66.3 and 50.7 ppm, respectively, with the γ-H (*para* to the pyridylnitrogen) being observed at 7.3 ppm. The observation of only one set of pyridylproton resonances indicates that an effective plane of symmetry is present for **1** in CD_3CN solution. Selective deuteration of the neopentyl methylene position of the ebnpa ligand (using **1-*d*$_4$-n**) enabled the identification of two resonances at 6.1 and 3.7 ppm, each of which integrates to 2H, consistent with the "inner" and "outer" chemical environment of these protons in the solid state structure of **1**. Although a resonance for the alkoxide methyl protons could not be identified in the ^{1}H NMR spectrum of **1**, using [(ebnpa)Co–OCD_3]ClO_4 (**1-*d*$_3$**) and ^{2}H NMR, the alkoxide methyl proton resonance was identified at ∼79 ppm. Notably, acquisition of ^{1}H NMR spectra of **1** and **2** at higher concentrations (*e.g.* ∼24–26 mM, Fig. S4 and S5) indicates the presence of two species for each complex. We currently speculate that the second species for each is a dimeric complex, as the single set of resonances for the low concentration species for **1** and **2** can be regenerated *via* dilution of the higher concentration solutions.

Compounds **1** and **2** each exhibit a single, quasi-reversible ($i_{\mathrm{pa}} \gg i_{\mathrm{pc}}$) redox couple (Fig. S6) at ∼1460 and ∼1483 mV, respectively, *versus*SCE. The reversibility of these couples is not influenced by changes in potential scan range or rate. The anodic peak current (i_{pa}) for each oxidative wave is of similar magnitude to the anodic current of an internal standard ferrocene/ferrocenium couple. Since both the analyte and ferrocene were present in approximately equal concentrations in these experiments, the parity of the two anodic currents suggests that the observed oxidative processes correspond to the removal of one electron from the original cobalt(ii) alkoxide complexes.

In conclusion, the isolation of **1** under the same conditions used for the zinc analogue [(ebnpa)Zn–OCH_3]ClO_4 suggests similar hydrolytic stability for the Co(ii) and Zn(ii) methoxide derivatives. This observation leads us to hypothesize that the Co(ii)–OR species that is spectroscopically observable for Co(ii)-containing LADH is of similar hydrolytic stability to the proposed Zn(ii)–OR intermediate in the catalytic cycle of the native enzyme. However, from these studies we also note that unlike [(ebnpa)Zn–OCH_3]ClO_4, **1** and **2** exhibit concentration dependent ^{1}H NMR features, suggestive of the presence of a monomer/dimer equilibrium in acetonitrile solution.

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Footnotes

1. † Electronic supplementary information (ESI) available: Experimental details, and Figs. S1 (EPR spectra of **1** and **2** in MeOH soln.), S2 and S4 (^{1}H NMR spectra of **1** in CD_3CN), S3 and S5 (^{1}H NMR spectra of **2** in CD_3CN), S6 (cyclic voltammetry of **1** and **2**) and Table S1 (^{1}H NMR features of **1** and **2** in CD_3CN at 302 K). See http://www.rsc.org/suppdata/dt/b4/b408177c/
2. ‡ *Crystal data*: for **1**: $C_{27}H_{46}ClCoN_5O_5S$, M = 647.13, triclinic, space group $P\bar{1}$, a = 8.5503(2), b = 13.7775(2), c = 14.6350(4) Å, α = 77.3731(14), β = 89.8851(12), γ = 74.0184(14)°, V = 1614.20(6) Å^3, Z = 2, μ = 0.721 mm^{-1}. Using Mo Kα radiation (0.71073 Å), a total of 11777 reflections were collected ($6.32 < 2\vartheta < 55.02°$), of which 7305 were independent. Refinement converged to R_1 = 0.0323, wR_2 = 0.0768 ($I > 2\sigma I$) and R_1 = 0.0410, wR_2 = 0.0819 (all data). The perchlorate anion was disordered over two positions. For **2**: $C_{31}H_{46}ClCoN_5O_5S$, M = 695.17, triclinic, space group $P\bar{1}$, a = 10.8800(2), b = 12.0599(3), c = 13.9550(4) Å, α = 72.8711(10), β = 77.7458(15), γ = 75.1747(14)°, V = 1672.92(7) Å^3, Z = 2, μ = 0.701 mm^{-1}. Using Mo Kα radiation (0.71073 Å), a total of 12007 reflections were collected ($6.32 < 2\vartheta < 55.00°$), of which 7611 were independent. Refinement converged to R_1 = 0.0350, wR_2 = 0.0739 ($I > 2\sigma I$) and R_1 = 0.0502, wR_2 = 0.0808 (all data). CCDC reference numbers: **1**, 240280; **2**, 240281. See http://www.rsc.org/suppdata/dt/b4/b408177c/ for crystallographic data in CIF or other electronic format.