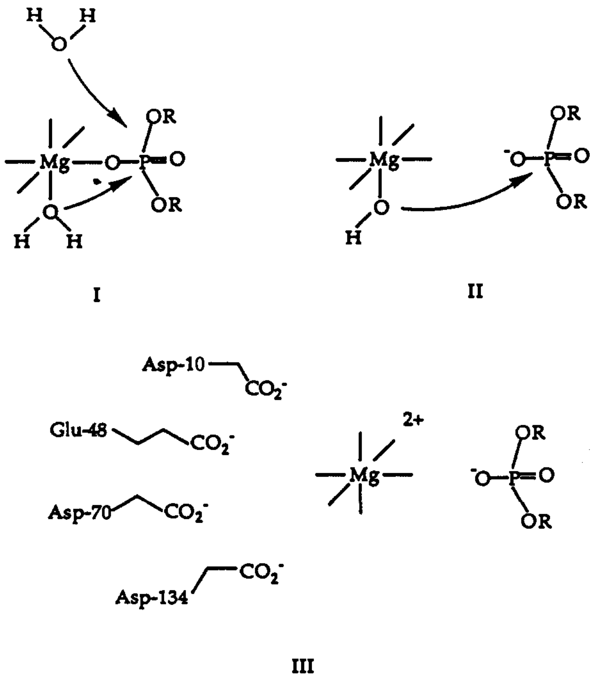

Figure 1. Schematic representation of three possible mechanistic roles for $Mg^{2+}(aq)$ as a RNase H cofactor: (1) Lewis acid/template activation of the phosphodiester backbone toward nucleophilic attack; (II) activation of nucleophilic water $[Mg(OH)^+]$; (III) outer-sphere-complex formation [Asp10 (2.0 Å), Glu48 (4.2 Å), Asp70 (4.5 Å), Asp134 (4.9 Å); distances from active-site carboxylates to Mg^{2+} are noted in parentheses[17]]. Possible roles for the bound cation are described in the text.

Table I. Kinetic Parameters for RNase H Digestion of $([^3H]\text{-A}\cdot\text{dT})_{20}$ with a Variety of Metallocofactors[a,b]

M^{n+}	V_{max}, μM s^{-1}	K_m, μM
$Co(NH_3)_6^{3+}$	0.31 ± 0.02	1.0 ± 0.2
$Co(en)_3^{3+}$	0.19 ± 0.01	0.57 ± 0.08
$Mg(aq)^{2+}$	0.33 ± 0.01	1.0 ± 0.1
$Mn(aq)^{2+}$	0.13 ± 0.01	0.36 ± 0.08
$Ca(aq)^{2+}$	0.047 ± 0.009	0.2 ± 0.1

[a] Each result is the average of at least three experiments. [b] The reaction mixture (20 μL) contained the following: 10 mM M^{n+}, 40 mM Tris (pH 7.5), 100 mM KCl, 5% (w/v) sucrose, 0.1 mM DTT, $([^3H]\text{-A}\cdot\text{dT}_{20}$ (2 × 10^4 cpm), RNase H (1 unit). After incubation (37 °C, 30 min), the reaction mixture was stored on ice and quenched with 7% $HClO_4$ (20 μL, 0 °C, 30 min). The mixture was then centrifuged (14000 rpm, 30 min) and the supernatant (10 μL) added to scintillation fluid (10 mL). Substrate concentration varied from 94 nM to 4.4 μM.

H, $Co(NH_3)_6^{3+}$ inhibits the reaction of DNase I. Presumably $Co(NH_3)_6^{3+}$ binds at the active site but cannot coordinate directly to the phosphate backbone to activate the diester to attack by a Glu-His-OH relay, as previously proposed for this enzyme.[10]

In this paper we have described a simple test to identify the active coordination state of the metal cofactor for metallonuclease enzymes. This will be of value in the design of inhibitor complexes for HIV RNase H activity. Comparisons of enzyme activity when using metal cofactors with well-defined coordination states offers considerable insight on the mechanistic role of the metal cation.[19]

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Supplementary Material Available: A figure displaying the Michaelis-Menten data used to generate Table I (1 page). Ordering information is given on any current masthead page.

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Selective γ C-H Bond Cleavage in Alkoxides: 2-Propanol on Mo(110)

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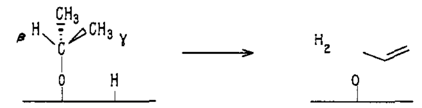
The kinetic stability of alkoxides adsorbed on Cu(110) and Ag(110) has been correlated with the strength of the C-H bond adjacent to the oxygen atom. The presence of the electronegative oxygen atom renders the C-H bond for the carbon bound to oxygen 4-7 kcal/mol weaker than the other C-H bonds in the complex. The radical formed from homolytic C-H bond cleavage is stabilized by the electronegative oxygen; hence, the bond dissociation energy is lowered.[1] The weaker C-H bond for the position β to the metal center in alkoxides bound to metals results in a propensity for β-hydrogen elimination. Indeed, when the C-O bond is retained and a product of selective dehydrogenation is isolated, β C-H bonds are preferentially cleaved in alkoxides bound either to metal surfaces[1-8] or to metal clusters.[9-12] The reactions of alkoxides on metal surfaces have been studied more extensively on the later transition-metal surfaces with relatively fewer reports on earlier transition metals, i.e., Mo. In addition, the absence of β-hydrogens in the alkoxide increases its kinetic stability with respect to dehydrogenation, as seen with *tert*-butoxide on Cu(110) and Ag(110).[1,2] In fact, the alkoxide C-O bond is retained on most transition-metal surfaces. For example, CO and H_2 are the primary products from methoxide decomposition on Mo(100).[13,14] Some exceptions are seen, however, in the reactions of methanol on W(100)[15] and Ti(0001),[16] methanol and ethanol on Fe(100),[17] and methanol on Pt(110)-(1×1).[18] C-O bond retention is also seen during the reaction of 2-propanol on MoO_3;[19] acetone is a primary product.

Alkoxide reactivity on Mo(110) is distinctly different from that on most other transition-metal surfaces. Importantly, the C-O bonds of alkoxides are cleaved on Mo. In addition, we report here that the C-H bond in 2-propoxide γ to Mo is cleaved, while the β C-H bonds remain *intact* (eq 1). Reactions of selectively



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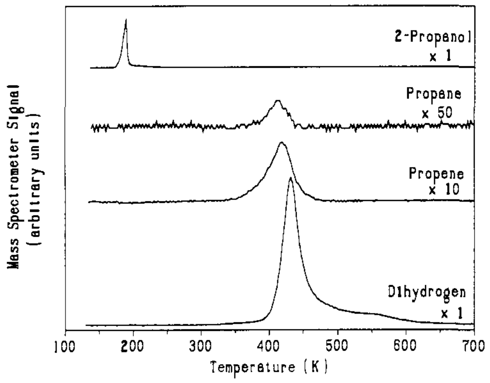

Figure 1. Temperature-programmed reaction of a saturation coverage of 2-propanol on Mo(110) adsorbed at 120 K. The most intense masses were monitored in each case: dihydrogen (*m/e* 2), propene (*m/e* 41), propane (*m/e* 43), and 2-propanol (*m/e* 45). All spectra were corrected for 2-propanol fragmentation, but the propene spectrum was not corrected for propane fragmentation. The heating rate used was 10 K/s.

labeled 2-propanol on Mo(110) unequivocally demonstrate that γ elimination exclusively occurs on Mo(110). Indeed, we propose that the preference for γ over β elimination is evidence for substantial C–O bond breaking prior to C–H bond cleavage.

All experiments were performed in an ultrahigh-vacuum chamber described previously[20] with a base pressure of $\leq 2 \times 10^{-10}$ Torr. The chamber was equipped with X-ray photoelectron, Auger electron, and mass spectroscopies and low-energy electron diffraction.

Temperature-programmed reaction of 2-propanol on Mo(110) yields two hydrocarbon products via C–O bond scission: propene and propane. Nonselective decomposition affording atomic carbon and oxygen and gaseous H_2 is a competing process (Figure 1). 2-Propanol multilayers sublime from the surface below 250 K in a peak centered at 180 K. All masses between *m/e* 2 and 80 were monitored during the reaction of 2-propanol. No oxygen-containing or other hydrocarbon products were detected.

X-ray photoelectron spectra are consistent with 2-propoxide as the sole intermediate on the surface after annealing to 200 K, the temperature past that of multilayer sublimation (Figure 2). The two peaks present in the C(1*s*) spectra at 286.5 and 285.1 eV are assigned as the carbon bound to the oxygen (286.5 eV) and the two methyl carbons (285.1 eV). Carbon(1*s*) binding energies for ethoxide on Fe(100)[17] are 285.5 and 284.5 eV and that for methoxide on Mo(110) is 286.4 eV.[21]

The high C(1*s*) binding energies clearly demonstrate that the majority of C–O bonds remain intact,[22] and the observed 1:2 ratio between the peaks is consistent with a 2-propoxide skeleton. This conclusion is supported by the observation of a single O(1*s*) peak at 531.9 eV, characteristic of covalently bonded oxygen. Atomic oxygen has an O(1*s*) binding energy of 529.9 eV,[21] while binding energies of 530.7–531.2 eV have been observed for alkoxides on other metal surfaces.[3,17] Preliminary high-resolution electron energy loss studies give firm support for the identification of the 2-propoxide intermediate: the loss associated with the O–H stretch disappears after 2-propanol multilayers are heated to 250 K while all other losses remain essentially the same.

No spectroscopic changes are observed until hydrocarbon formation commences, consistent with a 2-propoxide reaction intermediate. The maximum coverage of 2-propoxide was estimated to be $\Theta_O = 0.28$ on the basis of X-ray photoelectron spectra. At the maximum coverage, ~70% of the adsorbed 2-propoxide forms hydrocarbons, while 30% nonselectively decomposes, on the basis of X-ray photoelectron and Auger electron data.[23]

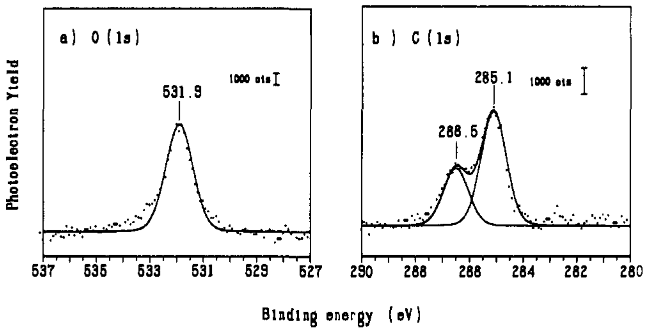

Figure 2. (a) O(1*s*) and (b) C(1*s*) X-ray photoelectron spectra of a saturation coverage of 2-propanol annealed to 200 K. The tail to higher binding energy observed in the O(1*s*) spectra is found to be present in all studies of oxygen-containing molecules on Mo(110) and is attributed to core–hole lifetimes, electron–hole pairs, or phonon creation, which asymmetrically broaden core peaks on the high binding energy side.

Selective dehydrogenation at the γ position is observed during temperature-programmed reaction of $(CD_3)_2CHOH$ or $(CH_3)_2CDOH$ on Mo(110). Only propene-d_5 is formed from $(CD_3)_2CHOH$ and only propene-d_1 is formed from $(CH_3)_2CDOH$ reaction.[24] Clearly, the C–H bond γ to the surface is selectively cleaved. Furthermore, the lack of other isotopes of propene in the reaction of $(CD_3)_2CHOH$ demonstrates that there is no reversible C–H bond breaking. Notably, there is only a small difference in the kinetics for propene formation from the two different isotopically labeled molecules even though a C–H bond is broken in $(CH_3)_2CDOH$ and a C–D bond in $(CD_3)_2CHOH$. The peak temperatures differ by less than 5 K, indicating that C–H(D) bond breaking is not rate limiting.

The observed selective γ C–H and accompanying C–O bond scission in 2-propanol induced by Mo(110) is in sharp contrast to 2-propanol reactivity on Cu(110),[3] Fe(100),[17] Rh(111)-(2×1)-O,[25] or Pd(111)-O.[8] In these cases, β dehydrogenation affords acetone.

We propose that the observed selective γ dehydrogenation is the result of a substantial amount of C–O bond breaking prior to C–H bond activation. Removal of the oxygen eliminates the stabilization of the radical produced from β elimination. Furthermore, only a small kinetic isotope effect for C–H vs C–D bond breaking is strong evidence that C–O bond breaking is the rate-limiting step in the formation of propene from 2-propanol. The isopropyl radical formed from C–O bond scission should facilely eliminate a methyl hydrogen to afford propene.

The reactivity of Mo(110) is proposed to be, in part, due to the strong Mo–O bond, estimated to be ~132 kcal/mol.[26] Given the rapid kinetics for deoxygenation, there may also be a substantial amount of C–O bond weakening upon adsorption. There is clearly a strong driving force for C–O bond scission due to the large Mo–O bond enthalpy, which would lower the barrier for oxygen elimination. Theoretical and more detailed spectroscopic studies of the Mo–alkoxide bonding are planned to evaluate the extent of C–O bond weakening to test our hypothesis.

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