

chloroformate, pyridine, CH_2Cl_2 .

- (25) Anal. Calcd for $\text{C}_{16}\text{H}_{25}\text{NO}_3$: C, 72.96; H, 9.57; N, 5.32. Found: C, 73.02; H, 9.65; N, 5.31.
 (26) We thank Professor K. Yamada for providing a generous sample of natural dendrobine used for comparative purposes.
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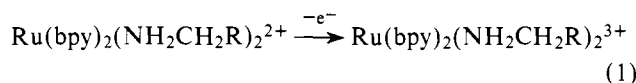
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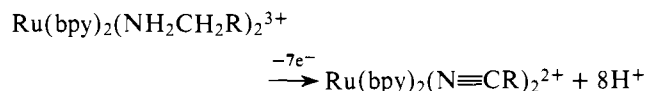
Oxobis(2,2'-bipyridine)pyridineruthenium(IV) Ion, $[(\text{bpy})_2(\text{py})\text{Ru}=\text{O}]^{2+}$

Sir:

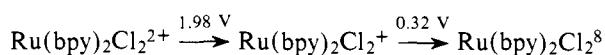
The earlier work of Dwyer and coworkers¹ and our more recent results have shown that for polypyridine complexes of ruthenium there is an extensive and reversible Ru(III)/Ru(II) redox chemistry.² This is especially true for *cis*-bis(2,2'-bipyridine) complexes where systematic changes in the remaining two inner coordination sphere ligands lead to predictable changes in redox potentials and charge-transfer spectra.² Polypyridine Ru(III)-Ru(II) couples have been of great value in studying electron-transfer processes in outer-sphere reactions,³ in mixed-valence complexes,⁴ and in reactions involving metal complex excited states.^{4,5} In some cases, Ru(III) complexes are unstable toward subsequent oxidation of a bound ligand (e.g., eq 1).⁶



In others Ru(IV) is an accessible oxidation state,

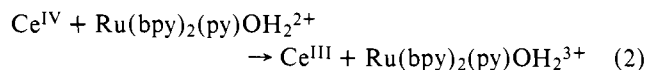


although with two bipyridine ligands only at high redox potentials as shown by the potentials below (vs. SCE) for the *cis*-dichloro Ru(IV)-Ru(III) and Ru(III)-Ru(II) couples.⁷



Complexes of Ru in high oxidation states are known. The preparations usually involve the addition of ligands to solutions containing RuO_4 and products form which contain both the added ligand and oxo groups. Examples include RuO_4py_2 , $[\text{Ru}(\text{O})_2(\text{NH}_3)_4]\text{Cl}_2$, and $\text{Cs}_3[\text{Ru}(\text{O})(\text{CN})_4(\text{CNO})_2]$.⁹ It is possible to show a direct connection between the lower and higher oxidation state chemistries of ruthenium using complexes which contain bound water or other ligands which have dissociable protons.

As shown by a spectrophotometric titration in 1.0 M HClO_4 , the Ru(II) complex *cis*- $\text{Ru}(\text{bpy})_2(\text{py})\text{OH}_2^{2+}$ (py is pyridine)¹⁰ is oxidized by Ce(IV) to Ru(III) (eq 2).

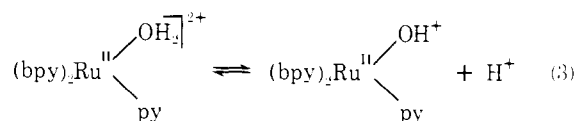


Upon oxidation, spectral changes occur which are typical for oxidation of Ru(II) to Ru(III):^{3b} (1) the $\pi^*(\text{bpy}) \leftarrow \text{Ru}(\text{II})$ absorption band at λ_{max} 470 (ϵ 8400) disappears; (2) The pattern of $\pi^*(\text{bpy}) \leftarrow \pi(\text{bpy})$ absorption bands in the ultraviolet changes predictably (λ_{max} 290 nm (ϵ 57 200) \rightarrow λ_{max} 303 nm (ϵ 26 600) and 312 (26 200)). Surprisingly, however, we find that the Ru(III) complex undergoes a second one-electron oxidation by Ce(IV) to give a new species which has

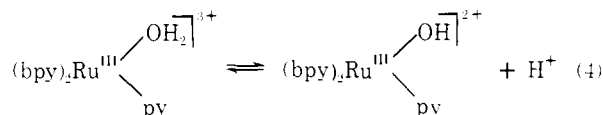
significant absorption bands only in the ultraviolet (λ_{max} 300 nm (ϵ 23 100), 248 (28 500)).¹¹

The twice-oxidized product precipitates from concentrated solutions as the perchlorate salt. Using the method of Feltham and Hayter,¹² conductivity studies in aqueous solution show that the cation has a +2 charge. In addition to the usual bpy and ClO_4^- bands in the infrared, a sharp intense band appears at 792 cm^{-1} (Nujol mull) which is within the range expected ($785\text{--}850\text{ cm}^{-1}$) for a $\text{Ru}=\text{O}$ stretching vibration.^{9a,13} The assignment of the band as $\nu(\text{Ru}=\text{O})$ is supported by the shift of the band to 752 cm^{-1} in the ^{18}O -labeled complex (752 cm^{-1} calculated). Magnetic susceptibility measurements on the salt at room temperature using the Faraday technique¹⁴ gave $\mu_{\text{eff}} = 2.95\ \mu_{\text{B}}$ which is slightly higher than the spin-only value for two unpaired spins ($2.83\ \mu_{\text{B}}$) and is consistent with the presence of a d^4 , paramagnetic Ru(IV) ion. Elemental analyses are consistent with the product being the perchlorate salt of the Ru(IV) complex $(\text{bpy})_2(\text{py})\text{Ru}=\text{O}^{2+}$. Anal. Calcd for $[\text{Ru}(\text{bpy})_2(\text{py})\text{O}](\text{ClO}_4)_2$: C, 42.44; N, 9.90; H, 2.99. Found: C, 42.17; N, 9.85; H, 2.74.

We have investigated the acid-base and redox properties of the Ru(II)-Ru(III)-Ru(IV) system using spectral and electrochemical techniques (cyclic voltammetry, coulometry, and potentiometric titrations). A spectrophotometric titration shows that $\text{Ru}(\text{bpy})_2(\text{py})\text{OH}_2^{2+}$ is a weak acid having $\text{p}K_{\text{a}}$ (25 °C) ~ 10.8 in 0.333 M NaSO_4 (eq 3). In 1.0 M HClO_4 , ox-



idation of $\text{Ru}(\text{bpy})_2(\text{py})\text{OH}_2^{2+}$ at +0.90 V vs. the SCE (saturated calomel electrode) occurs with $n = 1$ (n is the electrochemical stoichiometry determined by coulometry) to give Ru(III) primarily as the aquo ion $\text{Ru}(\text{bpy})_2(\text{py})\text{OH}_2^{3+}$. Reduction of the Ru(III) complex to Ru(II) also occurs with $n = 1$. The Ru(III) complex is a strong acid, $\text{p}K_{\text{a}}$ (25 °C) = 0.85 ± 0.03 in 1 M $\text{HClO}_4/\text{LiClO}_4$ (eq 4). Apparently, the



remarkably enhanced acidity following oxidation of Ru(II) to Ru(III) comes from stabilization of the electron-deficient Ru(III) site by $\text{p}(\text{OH}^-) \rightarrow d\pi(\text{Ru}(\text{III}))$ electron donation. A new, intense absorption band appears for the hydroxo complex (λ_{max} 372 nm (ϵ 5560)) whose origin probably lies in a ligand to metal charge-transfer transition ($d\pi(\text{Ru}(\text{III})) \leftarrow \text{p}(\text{OH}^-)$).¹⁵

Across the pH interval 0-7 in $\text{HClO}_4/\text{LiClO}_4$ solutions containing $\text{Ru}(\text{bpy})_2(\text{py})\text{OH}_2^{2+}$, cyclic voltammograms (see Figure 1) show the expected Ru(III)/Ru(II) wave which is reversible and a Ru(IV)/Ru(III) wave which appears only at low scan rates. The difficulty with the Ru(IV)/Ru(III) wave is not understood. The peak to peak separation appears to be independent of sweep rate, but, at high sweep rates, both oxidation and reduction peaks disappear. The same effect is observed at Au wire and glassy carbon electrodes. In any case, coulometric oxidation of $\text{Ru}(\text{bpy})_2(\text{py})\text{H}_2\text{O}^{2+}$ past the second wave occurs with $n = 2$ to give $\text{Ru}(\text{bpy})_2(\text{py})\text{O}^{2+}$ which is reduced to the Ru(II) complex with $n = 2$. Reduction potentials (uncorrected for activity coefficients) vs. the SCE were obtained for the two couples by a potentiometric titration using Ce(IV) in 1.0 M HClO_4 . The values shown in eq 5 and 6 have been corrected for the partial deprotonation of $\text{Ru}(\text{bpy})_2(\text{py})\text{OH}_2^{3+}$. Above pH 2, where $\text{Ru}(\text{bpy})_2(\text{py})\text{OH}_2^{2+}$ is the dominant form of Ru(III), the Ru(IV)/Ru(III) and

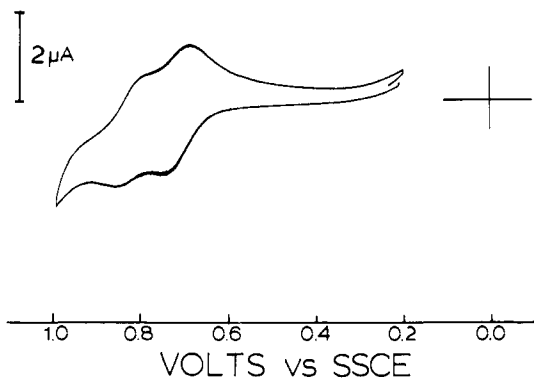
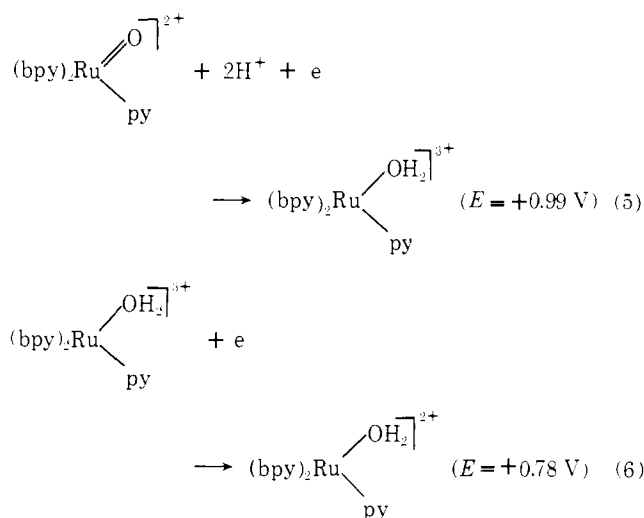


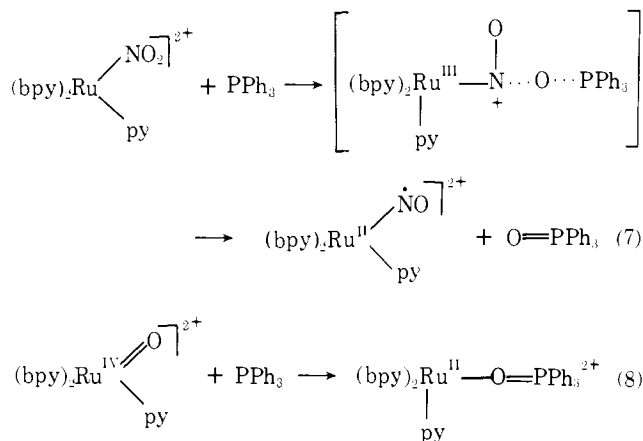
Figure 1. Cyclic voltammogram of $\text{Ru}(\text{bpy})_2(\text{py})\text{OH}_2^{2+}$ at a gold wire electrode in 0.01 M HClO_4 /0.10 M LiClO_4 vs. the saturated sodium chloride calomel electrode using a scan rate of 20 mV/s.



$\text{Ru}(\text{III})/\text{Ru}(\text{II})$ potentials both shift ca. -59 mV per pH unit increase as expected. At pH 7, the two potentials are $+0.53$ and $+0.42$ V vs. the SCE, respectively. Thus, in the pH interval 0–7, $\text{Ru}(\text{III})$ is stable with respect to disproportionation and can be generated rapidly by mixing solutions containing $\text{Ru}(\text{II})$ and $\text{Ru}(\text{IV})$.¹⁶ The reduction potential data are remarkable at least in comparison with the $\text{Ru}(\text{bpy})_2\text{Cl}_2^{2+/+}$ couple. The much lower $\text{Ru}(\text{IV})/\text{Ru}(\text{III})$ potential suggests that the presence of the oxo ligand leads to extensive stabilization of the $\text{Ru}(\text{IV})$ state, presumably by $p(\text{O}^{2-}) \rightarrow d\pi(\text{Ru}(\text{IV}))$ electron donation.¹⁷ The electrophilic nature of the oxo group is indicated by the fact that it does not appear to be protonated in the pH range 0–7 as shown by the absence of spectral changes throughout this pH region.

Our primary interest in $(\text{bpy})_2(\text{py})\text{Ru}=\text{O}^{2+}$ and related complexes is in their possible applications as oxidation catalysts. In appropriate complexes, it may be possible to mimic the reactivity of RuO_4 or OsO_4 and, because of the high chemical stability imparted by the Ru –bipyridine linkages, it may be possible to recycle them through a series of redox cycles. We recently reported that nitro complexes of $\text{Ru}(\text{III})$ can act as oxygen atom transfer reagents where the essential features in terms of the observed reactivity are probably the existence of both a transferrable oxygen and two one-electron acceptor sites, one at the metal ($\text{Ru}(\text{III}) \rightarrow \text{Ru}(\text{II})$) and one at a bound ligand ($\text{RuNO}^+ \rightarrow \text{RuNO}\cdot$) (eq 7).^{18,19} The $\text{Ru}^{\text{IV}}=\text{O}$ complex has the same properties except that a single two-electron acceptor site exists at the metal.

In acetonitrile solution, $(\text{bpy})_2(\text{py})\text{Ru}=\text{O}^{2+}$ undergoes a rapid reaction with PPh_3 to give an intermediate ($\lambda_{\text{max}} 479$ nm ($\epsilon 8820$)) which appears to be the triphenylphosphine oxide complex (eq 8). The initial reaction is stoichiometric as written



and is followed by a slower ($t_{1/2} = 100$ min at 25.0 °C) solvolysis of the bound $\text{O}=\text{PPh}_3$ group (eq 9). The latter reaction

$$(\text{bpy})_2\text{Ru}(\text{py})\text{OPPh}_3^{2+} + \text{CH}_3\text{CN} \longrightarrow (\text{bpy})_2\text{Ru}(\text{py})\text{CH}_3\text{CN}^{2+} + \text{OPPh}_3 \quad (9)$$

occurs quantitatively as shown by visible spectral analysis for $\text{Ru}(\text{bpy})_2(\text{py})\text{CH}_3\text{CN}^{2+}$ ($\lambda_{\text{max}} 437$ ($\epsilon 7730$)) and infrared analysis for the phosphine oxide ($\nu(\text{P}=\text{O})$ at 1194 cm^{-1}). In fact, intermediates containing oxo groups may be the catalytic agents in the ruthenium-catalyzed oxidation of alcohols to aldehydes and ketones by amine N -oxides,²⁰ and we are currently investigating the reactivity of $\text{Ru}(\text{bpy})_2(\text{py})\text{O}^{2+}$ toward a variety of organic substrates.

Acknowledgments are made to the National Science Foundation under Grants MPS75-11867 and CHE77-04961 for support of this research and to Professor Richard Palmer of Duke University for his assistance with the magnetic measurements.

References and Notes

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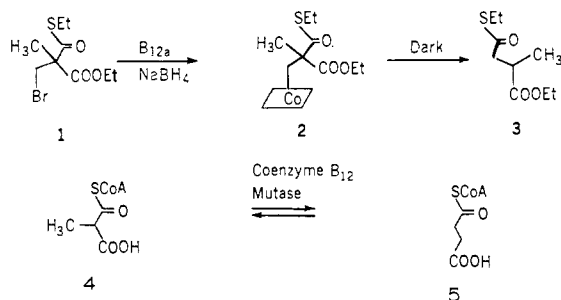
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Mechanism of Action of Coenzyme B₁₂. An Overall Anionic Mechanism for Carbon-Skeleton Rearrangement in a Model Reaction

Sir:

It was recently shown that the dimethyl malonate-cobalamin complex **2** undergoes exclusive rearrangement of the

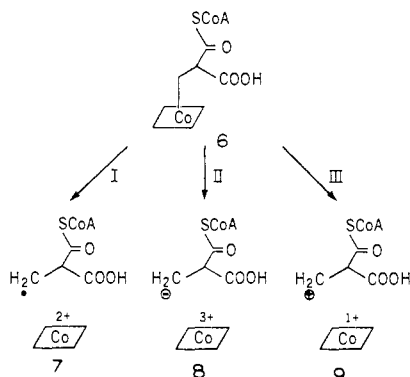


thioester group during the dark reaction **1** → **3** as an analogy for the methylmalonyl CoA → succinyl CoA (**4** → **5**) interconversion mediated by methylmalonyl CoA mutase which contains coenzyme B₁₂ as a cofactor.^{2,3}

In spite of the accumulation of evidence pointing towards a homolytic cobalt-carbon bond cleavage⁴ of coenzyme B₁₂ and of the subsequently formed hypothetical intermediate such as **7** as part of the catalytic cycle (Scheme I, route I), there is abundant in vitro analogy for ionic mechanisms in the chemistry of alkyl cobalamins portrayed by routes II (carbanion **8**)⁵ and III (carbocation **9**).⁶ Most of the enzyme-catalyzed reactions involving coenzyme B₁₂ are without precedent in terms of known organic reactions,⁷ whilst mechanisms involving a reactive free radical⁴ in a vicinal migration have little parallel with chemical experience. Thus, although the first (and last) committed steps in the enzymatic reaction of coenzyme B₁₂ probably involve homolysis of the cobalt-carbon bond at C-5' of the adenosyl moiety, the rearrangement of the substrate might stem from an ionic or radical mechanism operating on a covalently attached intermediate such as **6** (Scheme I).

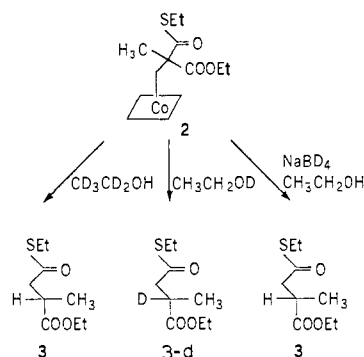
We now wish to report some of our observations which suggest an overall anionic mechanistic feature for carbon-

Scheme I



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Scheme II



skeleton rearrangement in the model reaction. We have examined the mechanism of the facile thioester migration,¹ **1** → **3**, which requires abstraction of hydrogen from the reaction milieu, using deuterium label as a probe for possible differentiation among the various mechanisms depicted in Scheme I as a first step toward understanding the methylmalonyl CoA mutase conversion, at least in terms of a viable chemical model. Experiments designed to trap analogs of the various possible intermediates, namely radical, carbanion, and carbonium ion, were performed as follows (Scheme II). (1) The use of CD₃CD₂OH as a solvent constitutes a probe for the involvement of possible radical intermediates and should lead to incorporation of deuterium from ethanol-*d*₅⁸ into the rearranged product. No deuterium incorporation was observed in the conversion of **1** to **3**. (2) Generation of an anionic species could be readily demonstrated by employing CH₃CH₂OD as solvent. Thus, the reaction of bromo ester **1** with hydroxycobalamin (B_{12a}), CH₃CH₂OD, and NaBH₄ in the dark under N₂ over 1–5 h gave 33–44%⁹ of the completely deuterium-incorporated rearranged product **3-d**, whose NMR and mass spectra¹⁰ locates the deuterium label exclusively at C-3. In comparing the ¹H NMR of **3-d** with that of **3**, the methyl singlet at δ 1.21 becomes a sharp doublet (*J* = 6.6 Hz) and the well-resolved AB pattern of the –CH₂– protons has additional multiplicity due to spin-spin coupling with the methine proton. Integration of the ¹H NMR of **3** shows one additional proton than in **3-d** at δ 2.98 with complex coupling superimposed on the other resonances. (3) The presence of a cationic species would result in incorporation of the deuterium label from NaBD₄ in the rearranged product **3-d**. When a competition experiment was run in CH₃CH₂OH in the presence of NaBD₄, the rearranged ester was not deuterated, thus making the intervention of a cationic species unlikely.

It should be pointed out that the overall carbanionic deuteration does not necessarily support the notion that the skeletal rearrangement is taking place at the stage of the carbanionic intermediate. In fact, the bromo ester **1** was found to rearrange, although in much poorer yields and under different conditions, to the product **3** upon reductive treatment with NaBH₄ or zinc in aprotic solvent at elevated temperature. From these results we conclude that the overall mechanism for the present model reaction is anionic, and that possibly the skeletal rearrangement may take place at the radical (or radical anion) stage, followed by a rapid second electron reduction to give the carbanionic intermediate which is then protonated by the reaction medium. It is also to be noted that, in the enzymatic rearrangement, no hydrogen exchange between the substrate and the medium takes place, perhaps because of an intimate association between 5'-deoxyadenosine and the reaction site of the enzyme.

Further model studies on the development of the catalytic action by coenzyme B₁₂ and on the nature of the rearrangement reactions involving cobalamin, both as reagent and catalyst, are in progress.