Contribution from the Department of Chemistry,
Kent State University, Kent, Ohio 44242

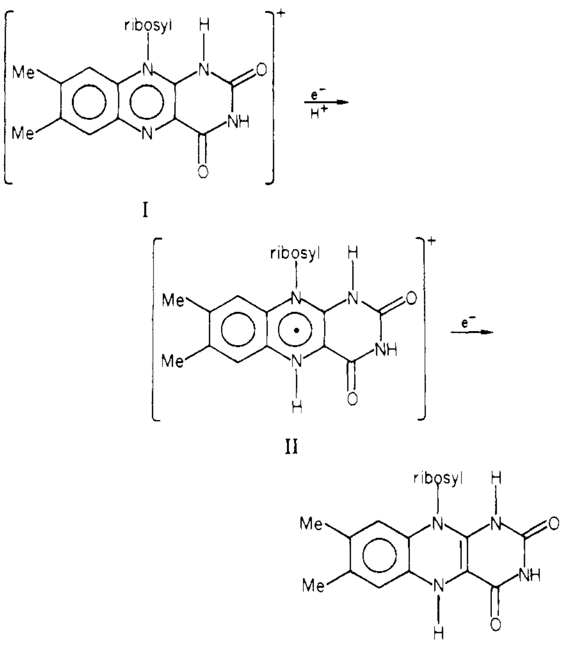
Electron Transfer. 52. Reactions of Dihydroriboflavin with Metal-Center Oxidants[1]

A. N. SINGH, VANGALUR S. SRINIVASAN,[2] and E. S. GOULD*

Received July 7, 1981

Riboflavin is reduced by excess V^{2+} or Eu^{2+} in aqueous $HClO_4$ to the dihydro derivative ("RbH_2", III), which may be oxidized to the corresponding semiquinone, II, by a variety of metal-center oxidants. Reactions of RbH_2 with a series of substitution-inert cobalt(III) complexes conform to a rate law (eq 2) pointing to the partition of the dihydro reductant into an inactive protonated form and a reactive deprotonated form, with pK_{HA} for this partition estimated as 0.89. The reactivity pattern for these Co(III) complexes is similar to that for oxidations of the semiquinone, Rb·, but distinctly different from patterns for reactions of Cr(II), Eu(II), U(III), and Ti(III), each of which may utilize inner-sphere paths if available. In particular, there is no indication of bridging by bound carboxyl, nor is there evidence of rate enhancement by chelating or reducible functions. Reductions of these complexes by RbH_2 thus appear to be outer sphere. The oxidation of RbH_2 with VO_2^{2+} is inverse first order in H^+ in the range 0.20–1.40 M H^+, suggesting a reaction sequence (eq 4) proceeding through a VO^{2+}–RbH_2 intermediate complex, from which two protons have been removed. RbH_2 (an even-electron molecule) is considerably more reactive than its semiquinone, Rb· (an odd-electron species), with the ratio of specific rates, $k_{RbH_2}/k_{Rb\cdot}$ (25 °C, 1.3 M H^+), approximately 10^2 throughout the study. The kinetic advantage that RbH_2 enjoys probably results from a combination of its more negative formal potential, its zero charge, and, presumably, a more rapid self-exchange.

Flavins, the most important and versatile of the oxidation coenzymes,[3] may undergo both one- and two-electron reductions, yielding, respectively, radical (semiquinone) and dihydro species, as exemplified by the reductions of riboflavin (I) in strongly acid solutions (eq 1). In an earlier work[4] we examined the reaction of the semiquinone (II) with a number of oxidizing metal centers, including a variety of substitution-inert cobalt(III) complexes and presented evidence that this radical reacts in its deprotonated form via outer-sphere paths, even in systems featuring very effective bridging groups. The present extension deals with one-electron oxidations of the dihydro derivative III, a reductant considerably more reactive than radical II, its "odd-electron comember" in the indicated electron-transfer series.



I

II

III

(1)

Experimental Section

Materials. Riboflavin, an Aldrich product, was used as received; master solutions 0.001 M in coenzyme were prepared in deaerated 1.0 M $HClO_4$ immediately before each series of experiments. Solutions of $Eu(ClO_4)_2$,[5a] $VO(ClO_4)_2$,[5b,c] and $Ru(NH_3)_6Cl_3$[6] were prepared as described. Master solutions of $UO_2(ClO_4)_2$ and $Fe(ClO_4)_3$ were prepared from the hydrated perchlorates (Alfa products) and were standardized spectrophotometrically.[7] Cobalt complexes not available from previous studies[8] were prepared by literature procedures.[8a,9,10]

Rate Measurements. The dihydro derivative of riboflavin (III) was generated at the 10^{-4} M level by treatment of solutions of riboflavin in 0.1-1.3 M $HClO_4$ with excess $Eu(ClO_4)_2$. All preparations were carried out under nitrogen in 1.00-cm spectrophotometer cells sealed by rubber serum caps. It was necessary to add, in addition to the quantity of Eu^{2+} needed to accomplish the two-electron reduction of the flavin, enough of this reductant to consume variable traces of oxygen in solution and adsorbed on the inner surface of the vessel. Incomplete reduction to the dihydro compound yielded solutions exhibiting the red color characteristic of riboflavin semiquinone (II) in strongly acid solution (λ_{max} = 495 nm).[4] In practice, satisfactory results were achieved by adding sufficient Eu^{2+} to obtain a solution remaining colorless for 10–15 min, waiting until the first trace of pink (presumably reflecting slow leakage of oxygen) appeared, and then adding the oxidant.[11]

Rates of oxidation of the dihydro species to the radical cation (II) were then estimated from measurements of absorbance increases at 495 nm on a Cary 14 spectrophotometer.[8c] Reactions were first order in dihydro compound and oxidant but were carried out under pseudo-first-order conditions, with the oxidant in greater than 10-fold

---

(1) Joint sponsorship of this work by the donors of the Petroleum Research Fund, administered by the American Chemical Society, by the National Science Foundation (Grant 8022881), and by the Biomedical Research Support Grant Program, Division of Research Resources, National Institutes of Health (Grant BRSG S07 RR-07182), is gratefully acknowledged.

(2) On leave from Vivekananda College, Mylapore, Madras, India.

(3) For recent reviews, see: (a) Hemmerich, P. *Adv. Chem. Ser.* **1977**, *No. 162*, 312. (b) Walsh, C., *Annu. Rev. Biochem.* **1978**, *47*, 881. (c) Bruice, T. C. *Acc. Chem. Res.* **1980**, *13*, 256.

(4) Singh, A. N.; Gelerinter, E.; Gould, E. S. *Inorg. Chem.*, preceding paper in this issue.

(5) (a) Dockal, E. R.; Gould, E. S. *J. Am. Chem. Soc.* **1972**, *94*, 6673. (b) Guenther, P. R.; Linck, R. G. *Ibid.* **1969**, *91*, 3769. (c) Linck, R. G. *Inorg. Chem.* **1970**, *9*, 2529.

(6) Fan, F.-R. F.; Gould, E. S. *Inorg. Chem.* **1974**, *13*, 2547.

(7) IUPAC Spectrophotometric Data"; Butterworths: London, 1963; pp 223 (Fe^{3+}), 550 (UO_2^{2+}).

(8) (a) Fan, F.-R. F.; Gould, E. S. *Inorg. Chem.* **1974**, *13*, 2639. (b) Fanchiang, Y.-T.; Carlson, R. R.; Thamburaj, P. K.; Gould, E. S. *J. Am. Chem. Soc.* **1977**, *99*, 1073. (c) Wu, M.-Y.; Paton, S. J.; Fanchiang, Y.-T.; Gelerinter, E.; Gould, E. S. *Inorg. Chem.* **1978**, *17*, 326.

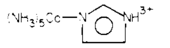
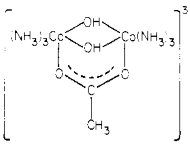
(9) (a) Gould, E. S.; Taube, H. *J. Am. Chem. Soc.* **1964**, *86*, 1318. (b) Linhard, M.; Siebert, H. *Z. Anorg. Allg. Chem.* **1969**, *364*, 24. (c) Siebert, H.; Tremmel, G. *Ibid.* **1972**, *390*, 292. (d) Wieghardt, K. *Ibid.* **1972**, *391*, 142. (e) Wieghardt, K. *J. Chem. Soc., Dalton Trans.* **1973**, 2548.

(10) We are grateful to Professor K. Wieghardt for samples of some of the cobalt(III) complexes used.

(11) When the described procedure was used, oxidation of the dihydro compound by adventitious oxygen was, in general, negligibly slow in comparison to reaction with the added metal-center oxidant. However, in our hands, satisfactory data for these systems could not be obtained when reactions were carried out in 10-cm cells (reaction volume 30 cm^3).

0020-1669/82/1321-1236$01.25/0

Table I. Kinetic Data for Reactions of the Dihydro Derivative of Riboflavin with Cobalt(III) Oxidants[a]

oxidant	$[H^+]$[b]	k_{obsd}[c]	k_{calcd}[d]
$(NH_3)_5Co(py)^{3+}$	0.10	84	83.5
	0.30	42	43.4
	0.50	28	29.1
	0.70	21	22.1
	0.90	18.7	17.7
	1.10	17.7	14.7
	1.30	15.2	12.7
$(NH_3)_5Co(DMF)^{3+}$	0.10	138	137
	0.30	69	71.5
	0.50	45	48.2
	0.70	37	36.5
	0.90	32	29.6
	1.10	28	24.6
	1.30	24	21.0
 IV	0.10	24	23.7
	0.30	12.9	12.7
	0.50	8.7	8.70
	0.70	6.8	6.64
	0.90	5.6	5.33
	1.10	4.1	4.50
	1.30	3.2	3.70
 V	0.10	66	66.5
	0.30	37	36.9
	0.50	27	25.6
	0.70	21	19.7
	0.90	14.8	15.9
	1.10	11.9	13.0
	1.30	10.0	11.2

[a] Reactions were carried out at 25.0° with $\mu = 1.30$, $[RbH_2] = 1.0 \times 10^{-4}$ M, and [oxidant] = 0.0007-0.003 M. [b] $[H^+]$ values in M. [c] k values in $M^{-1}\ s^{-1}$. [d] Values calculated as $k_{lim}K_{HA} \cdot (K_{HA} + [H^+])^{-1}$; parameters k_{lim} and K_{HA} for each oxidation are listed in Table II.

excess. When the effect of acidity variation was being examined, the concentration of added $HClO_4$ was allowed to vary while the total ionic strength was maintained near 1.3 M by addition of thrice-recrystallized $LiClO_4$. Reactions were generally followed for at least 4 half-lives. Rate constants obtained from successive half-life values within a run agreed to within 6%, whereas specific rates from replicate runs checked to better than 8%. Some backward drift in the "infinity reading", reflecting further oxidation of the semiquinone reaction product to riboflavin, was sometimes observed, but since such oxidations were much slower than the primary reactions, this drift did not seriously interfere with evaluation of specific rates. Temperatures were kept at 25.0 ± 0.2 °C during the entire series of kinetic runs.

Electronic spectra of solutions obtained from the oxidation of the dihydro derivative with cobalt(III) complexes were indistinguishable from the spectrum of the radical cation (II).

Results and Discussion

The redox reactions of interest are initiated in solutions where all but a small portion of the riboflavin taken is in the dihydro form, the remainder (1-5%) being the semiquinone. Comparison of the estimated formal reduction potential of the semiquinone (0.150 V[4]) with that of Eu^{3+} (−0.379 V[12]) assures us that in such solutions virtually all added Eu^{2+} has been oxidized to the tripositive state and that reaction of the added oxidant with Eu^{2+} plays no role in these systems.

Kinetic acidity dependencies have been examined for oxidations by three $(NH_3)_5Co^{III}$ derivatives and for the bridged μ-acetato cobalt(III) dimer. Note (Table I) that these four oxidants follow similar patterns—rates increase with decreasing acidity, but the trend is less sharp than that corresponding to a simple proportionality to $[H^+]^{-1}$, particularly at lower acidities. These dependencies conform to eq 2, applicable to a system in which the oxidant or reductant is distributed between a basic form, which reacts at a limiting specific rate, k_{lim}, and an unreactive acidic form having an acidity constant K_{HA}. Values of the parameters k_{lim} and K_{HA} giving the closest agreement between observed specific rates and those rates calculated by (2) are summarized in Table II. The K_{HA} values pertaining to oxidations by the three complexes are seen to be nearly the same. Because none of these cobalt(III) derivatives features protons that are removable near the acidity range studied, we infer that it is the dihydroflavin that is undergoing partial deprotonation, that pK_{HA} for the protonated form is 0.89 (at $\mu = 1.3$), and that the protonated form has negligible reactivity under the conditions chosen.

$$k = k_{lim}K_{HA}/(K_{HA} + [H^+]) \qquad (2)$$

Table II. Kinetic Parameters for Acid-Dependent Reactions of Cobalt(III) Complexes with the Dihydro Derivative of Riboflavin

oxidant	k_{lim}[a]	K_{HA}[a]
$(NH_3)_5Co(py)^{3+}$	156 ± 11	0.12 ± 0.01
$(NH_3)_5Co(DMF)^{3+}$	252 ± 16	0.12 ± 0.01
IV	41.4 ± 1.7	0.13 ± 0.01
V	111 ± 6	0.15 ± 0.01

[a] The parameters k_{lim} and K_{HA} appear in eq 2. Values in the table were obtained by nonlinear least-squares refinement of unweighted kinetic data by minimizing $(k_{obsd} - k_{calcd})^2$.

Since partition of the dihydro compound between protonation levels is not affected by alteration of the cobalt(III) oxidant, we may estimate limiting specific rates, applicable to reactions of additional complexes with the deprotonated dihydro derivative, from measurements at a single acidity. Table III lists measured specific rates and calculated limiting values for a variety of $(NH_3)_5Co^{III}$ complexes, and Table IV gives the corresponding values for several μ-carboxylato dinuclear cobalt(III) complexes similar to the μ-acetato derivative (V). Note, however, that this treatment may not be extended to oxidations by the mononuclear acetato and 2,6-pyridinedicarboxylato complexes, both of which undergo partial protonation in the $[H^+]$ range studied.[13-15]

Oxidations of the dihydroflavin, "RbH_2", with substitution-inert cobalt(III) complexes generate a reactivity pattern similar to that for oxidations of the related cation radical, Rb·,[4] but distinctly different from the patterns for Cr(II),[16] Eu(II),[8a] U(III),[17] and Ti(III),[18] each of which may utilize inner-sphere paths if suitable bridging functions are accessible (specific rates for Rb· and Cr(II) are included in Table III for comparison). With RbH_2, the various carboxylato comlexes are reduced at specific rates near those for the pyridine and imidazole (IV) derivatives of $Co(NH_3)_5^{III}$, which are now recognized to utilize only outer-sphere paths in electron transfer.[4,6] Hence, there is no significant rate enhancement reflecting bridging action by bound carboxyl. Further marked accelerations attributable, in the Cr(II) series, to the presence of chelating or reducible groups (such as α-keto or pyridinecarboxylato functions) likewise do not appear in the reactions of the dihydro reductant. Among the bridged dimeric oxidants (Table IV), the μ-acetato complex (V) is reduced by RbH_2 at a rate quite comparable to those for the pyruvato, glyoxalato, and benzoylformato analogues, again contrasting with Cr(II) and Eu(II) reductions, which have been found to be strikingly accelerated (10^2-10^4) by incorporation of the α-C=O func-

---

(12) Biedermann, G.; Silber, H. R. *Acta Chem. Scand.* **1973**, *27*, 3761.

(13) (a) Barrett, M. B.; Swinehart, J. H.; Taube, H. *Inorg. Chem.* **1971**, *10*, 1983. (b) Gould, E. S. *J. Am. Chem. Soc.* **1974**, *96*, 2373.

(14) Deprotonation of the aquo complex $(NH_3)_5Co(H_2O)^{3+}$ ($pK_A = 6.2$[15]) is without appreciable effect in the acidity range studied.

(15) Splinter, R. C.; Harris, S. J.; Tobias, R. S. *Inorg. Chem.* **1968**, *7*, 901.

(16) Taube, H.; Gould, E. S. *Acc. Chem. Res.* **1969**, *2*, 321.

(17) (a) Wang, R. T.; Espenson, J. H. *J. Am. Chem. Soc.* **1971**, *93*, 380. (b) Loar, M. K.; Sens, M. A.; Loar, G. W.; Gould, E. S. *Inorg. Chem.* **1978**, *17*, 330.

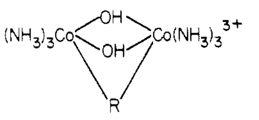
(18) Martin, A. H.; Gould, E. S. *Inorg. Chem.* **1976**, *15*, 1934.

Table III. Specific Rates for Oxidations of the Dihydro Derivative of Riboflavin with Pentaamminecobalt(III) Complexes, $R(NH_3)_5Co^{III}$

ligand, R	k_{obsd}[a]	k_{lim}[b]	$k_{Rb\cdot}$[a,c]	k_{Cr}[d]
ethylenediamine[e]	0.21	2.3		2×10^{-5}
imidazole (IV)	3.2	41[f]		4×10^{-4}
pyrazole	14.5	160		0.0023
pyridine	15.2	156[f]	0.29	0.0040
N,N-dimethylformamide	24	2.5×10^2[f]	0.22	0.0070
N,N-dimethylnicotinamide	54	6.0×10^2	0.99	0.030
glycinato (O bound)	2.3	25		0.064
N-acetylglycinato	9.0	99		0.30
acetato	18.0	*g*	0.26	0.35[h]
formato	17.0	187	0.15	7.2
aquo	50	5.5×10^2	0.50	$3.1/[H^+]$
maleato	8.0	88		2.0×10^2
pyruvato	7.5	83		10×10^3
benzoylformato	11.0	121	0.14	$>10^4$
2,6-pyridinedicarboxylato	12.0	*g*		$1.5 \times 10^4/[H^+]$
azido	23.0	2.5×10^2		$\sim 3 \times 10^5$
fluoro	3.3	36	0.11	4×10^5
chloro	15.4	170	0.20	3×10^6

[a] Specific rates ($M^{-1}\ s^{-1}$) for reactions at 25 °C in 1.3 M $HClO_4$. [b] Limiting specific rates calculated, unless otherwise indicated, as $k_{lim} = k_{obsd}(1 + [H^+]/K_{HA})$, where $[H^+]$ is 1.3 M and K_{HA} is taken as 0.13 M. [c] Reference 4. [d] Specific rates for reduction by Cr^{2+} at 25 °C ($\mu = 1.0$). Values are taken largely from ref 6 and 8a. [e] $Co(en)_3^{3+}$. [f] Values obtained by nonlinear least-squares refinement of kinetic data (see Table II). [g] Limiting rate not calculated because of complications arising from partial protonation of oxidant (see ref 13). [h] Limiting (inner-sphere) rate at low acidities.[13a]

Table IV. Specific Rates for Oxidations of the Dihydro Derivative of Riboflavin with Bridged Dimeric Cobalt(III) Complexes



bridging ligand, R	k_{obsd}[a]	k_{lim}[b]
acetato	10.0	111[c]
glyoxalato	22	2.5×10^2
o-aldehydobenzoato	36	4.0×10^2
pyruvato	34	3.8×10^2
benzoylformato	72	7.9×10^2
p-aldehydobenzoato	86	9.5×10^2

[a] Specific rates ($M^{-1}\ s^{-1}$) for reactions at 25 °C in 1.3 M $HClO_4$. [b] Limiting specific rates calculated, unless otherwise indicated, as $k_{lim} = k_{obsd}(1 + [H^+]/K_{HA})$, where $[H^+] = 1.3$ M and K_{HA} is taken as 0.13 M. [c] Value obtained by nonlinear least-squares refinement of kinetic data pertaining to acid dependency (see Tables I and II).

tion,[19] the latter presumably providing an inner-sphere path for use of the metal-center reductants.

Thus, the rate pattern for reductions by RbH_2 (with specific substituent effects virtually absent) indicates that this species reacts with cobalt(III) complexes via an outer-sphere path, a conclusion in keeping with our observation that the oxidation product from these reactions is the radical cation, Rb•, which has suffered no modification of its ring system. It is instructive to compare the RbH_2 pattern to that for reductions by $Ru(NH_3)_6^{2+}$,[20,21] which is often considered (although not without reservation[22]) to be a compulsory outer-sphere oxidant. Although the log-log plot (Figure 1), which utilizes the k_{lim} values for RbH_2, appears to approach linearity, serious divergences are perceptible. Among points at the slow end of the scale, scatter is more severe than that observed in the analogous cross relation between specific rates involving only metal-center reductants,[6,8a,17b] yet this scatter is not sufficiently systematic to sustain a convincing explanation. More distressingly, the point for reduction of $(NH_3)_5CoCl^{2+}$ (not shown) lies far off the regression line drawn, reflecting a specific rate for reduction of this complex by $Ru(NH_3)_6^{2+}$ ($2.6 \times 10^2\ M^{-1}\ s^{-1}$, 25 °C, $\mu = 0.50$)[21] that is 10^3 times that consistent with the indicated linear relationship. Similarly striking positive departures by this chloro oxidant have been observed when the $Ru(NH_3)_6^{2+}$ pattern has been plotted against those for reductions by the riboflavin radical cation,[4] by the radical and dihydro derivative of phenazine,[23] and by the dihydro derivative of 1-deazariboflavin.[23] Indeed, it appears that this divergence generally arises when $Ru(NH_3)_6^{2+}$ rates are compared to those for electron transfer from aromatic donors, whether the latter be even- or odd-electron species. We hesitate to attribute the enhancement to a substantial inner-

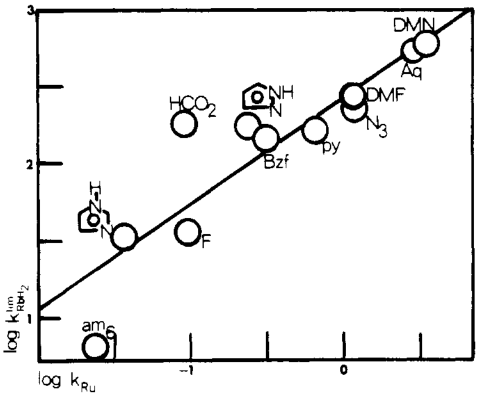


Figure 1. log–log plot comparing the specific rates of reduction of pentaamminecobalt(III) complexes, $R(NH_3)_5Co^{III}$, by $Ru(NH_3)_6^{2+}$ ($\mu = 0.50$, supporting electrolyte LiCl) and by the dihydro derivative of riboflavin, RbH_2. The latter set are limiting values, obtained from eq 2, with use of measured specific rates in conjunction with the p*K* of the dihydro compound (0.89 at $\mu = 1.30$). Bzf = benzoylformato; DMN = *N,N*-dimethylnicotinamide. The regression line shown corresponds to the equation $\log k_{RbH_2} = 0.68 \log k_{Ru} + 2.42$.

---

(19) Srinivasan, V. S., unpublished experiments, Kent State University, 1980–1981.

(20) Specific rates for reduction by $Ru(NH_3)_6^{2+}$ (k_{Ru} values) are taken principally from reports by Endicott[21] and by Fan.[6] These generally refer to reactions carried out in 0.1 M HCl, $\mu = 0.50$.

(21) Endicott, J. F.; Taube, H. *J. Am. Chem. Soc.* **1964**, *86*, 1686.

(22) See, for example: Earley, J. E. *Prog. Inorg. Chem.* **1970**, *13*, 243.

(23) Singh, A. N., unpublished experiments, Kent State University, 1981. Stated in different terms, these aromatic donors have been found to reduce $(NH_3)_5CoCl^{2+}$ 2–5 times as rapidly as the corresponding fluoro-substituted oxidant, whereas with $Ru(NH_3)_6^{2+}$ as reductant, this ratio of rates exceeds 2×10^3.

Table V. Kinetic Data for Reaction[a] of the Dihydro Derivative of Riboflavin with VO^{2+}

$[H^+]$	k	$[H^+]$	k
0.20	35	1.00	7.1
0.40	17.0	1.20	5.9
0.60	11.6	1.40	5.0
0.80	9.3		

[a] Reactions were carried out at 25.0 °C with $\mu = 1.40$ ($HClO_4$ + $LiClO_4$), $[RbH_2]_0 = 1.0 \times 10^{-4}$ M, and $[VO_2^{2+}] = 0.0013$–0.012 M. k values in $M^{-1}\ s^{-1}$.

sphere contribution to the Ru(II) reduction (although the direction of the effect is in accord with this) for such a path would presumably require expansion of the coordination octahedron about this metal center, a process that has, in the past, been suggested[24] but not yet demonstrated. We suspect instead that a favorable path for the $Co(NH_3)_5Cl^{2+}$–$Ru(NH_3)_6^{2+}$ reaction, in which the reducing metal center approaches the oxidant through the chloride ligand, is inaccessible to the aromatic reductants (because of repulsion between the chloro substituent and the electron-rich π regions sandwiching the rings) and that the aromatics therefore approach the oxidant in the vicinity of an octahedral face determined by three of the ammonia nitrogens. We are astonished, however, that this difference in path is associated with such a marked difference in rate.

Data pertaining to the reaction of RbH_2 with VO^{2+} in the acidity range 0.2–1.40 M H^+ are summarized in Table V. This oxidant, in contrast to the cobalt(III) complexes examined, adheres closely to an inverse-$[H^+]$ dependency (eq 3).

$$\text{rate} = (7.0\ s^{-1})[VO^{2+}][RbH_2][H^+]^{-1} \qquad (25\ °C,\ \mu = 1.4) \qquad (3)$$

There is, in this instance, no indication of kinetic saturation in the $[H^+]$ range examined, indicating the involvement of a protonation equilibrium for which pK_{HA} exceeds 2. Since coordination of VO_2^{2+} to the dihydro reductant would be expected to shift its primary pK_{HA} to below 0.89, rather than to raise it, it appears here that we are dealing with a second deprotonation, i.e.

$$VO^{2+} + RbH_2 \rightleftarrows VORbH_2^{2+} \xrightarrow[pK << 1]{-H^+} [CB]' \underset{pK > 2}{\overset{-H^+}{\rightleftarrows}} [CB]'' \rightarrow \text{products} \qquad (4)$$

Note that in the proposed sequence, the second conjugate base, $[CB]''$, is taken to be the reactive intermediate.[25] Whether the second proton is lost from the flavin ring system or from water in the primary coordination sphere of vanadium is, at this point, an open question.[26]

We find it of interest that the dihydro derivative of riboflavin, an even-electron molecule, is a considerably more reactive reductant than the semiquinone, Rb·, an odd-electron species. Comparing reactions of the two in 1.3 M $HClO_4$ (Table III), we note $k_{RbH_2}/k_{Rb\cdot}$ to be near 10^2 for each of the various cobalt(III) oxidants; a similar ratio applies to oxidations by VO^{2+} and UO_2^{2+}.[4] Two features of the dihydro compound that may be presumed to contribute to this rate difference are its more negative reduction potential and its zero net charge. The difference in formal potentials of the two reductants (0.070 V)[4] corresponds, with assumption of adherence to Marcus' model,[27] to a rate ratio of $10^{0.6}$ or 4, whereas it may be estimated that the unit positive charge of the protonated semiquinone, II, contributes an additional factor of about 2 to this difference.[28-30] The small residual kinetic advantage (very roughly a factor of 10) enjoyed by the dihydro reductant may be reasonably attributed to a difference in self-exchange rates in the two aromatic systems, but experimental confirmation of this point is obviously desirable.

Acknowledgment. We thank Professors Albert Haim and Robert G. Linck for valuable discussions.

Registry No. III, 13345-95-4; IV, 38716-02-8; V, 46240-70-4; $(NH_3)_5Co(py)^{3+}$, 31011-67-3; $(NH_3)_5Co(DMF)^{3+}$, 31125-61-8; $Co(en)_3^{3+}$, 14878-41-2; $(NH_3)_5Co(pyrazine)^{3+}$, 38671-07-7; $(NH_3)_5Co(DMN)^{3+}$, 31011-70-8; $(NH_3)_5Co(gly)^{2+}$, 44982-38-9; $(NH_3)_5Co(N\text{-}Acgly)^{2+}$, 80327-72-6; $(NH_3)_5Co(CH_3CO_2)^{2+}$, 16632-78-3; $(NH_3)_5Co(HCO_2)^{2+}$, 19173-64-9; $(NH_3)_5Co(H_2O)^{3+}$, 14403-82-8; $(NH_3)_5Co(O_2CCH{=}CHCO_2H)^{2+}$, 17712-86-6; $(NH_3)_5Co(CH_3COCO_2)^{2+}$, 19306-91-3; $(NH_3)_5Co(Bzf)^{2+}$, 49861-82-7; $(NH_3)_5Co(2\text{-}CO_2H\text{-}6\text{-}CO_2C_5H_3N)^{2+}$, 67662-34-4; $(NH_3)_5Co(N_3)^{2+}$, 14403-83-9; $(NH_3)_5CoF^{2+}$, 15392-06-0; $(NH_3)_5CoCl^{2+}$, 14970-14-0; $(NH_3)_3Co(\mu\text{-}OH)_2(\mu\text{-}HCOCO_2)Co(NH_3)_3^{3+}$, 80327-73-7; $(NH_3)_3Co(\mu\text{-}OH)_2(\mu\text{-}o\text{-}C_6H_4CO_2(CHO))Co(NH_3)_3^{3+}$, 52362-79-5; $(NH_3)_3Co(\mu\text{-}OH)_2(\mu\text{-}CH_3COCO_2)Co(NH_3)_3^{3+}$, 80327-74-8; $(NH_3)_3Co(\mu\text{-}OH)_2(\mu\text{-}Bzf)Co(NH_3)_3^{3+}$, 80327-75-9; $(NH_3)_3Co(\mu\text{-}OH)_2(\mu\text{-}p\text{-}C_6H_4CO_2(CHO))Co(NH_3)_3^{3+}$, 52375-30-1; VO^{2+}, 20644-97-7.

---

(24) See, for example: (a) Endicott, J. F.; Taube, H. *Inorg. Chem.* **1965**, *4*, 473. (b) Ford, P. C.; Kuempel, J. R.; Taube, H. *Ibid.* **1968**, *7*, 1976.

(25) For additional instances in which activation for a redox process requires loss of two protons, see: (a) Kirwin, J. B.; Peat, F. D.; Proll, J. D.; Sutcliffe, L. H. *J. Phys. Chem.* **1963**, *67*, 1717. (b) Martin, A. H.; Gould, E. S. *Inorg. Chem.* **1975**, *14*, 873.

(26) Preliminary experiments indicate that the reaction of the dihydro derivative of riboflavin with $Ru(NH_3)_6^{3+}$ ($k = 10\ M^{-1}\ s^{-1}$ at 25 °C in 1.3 M $HClO_4$) and with UO_2^{2+} ($k = 65\ M^{-1}\ s^{-1}$) can be monitored with conventional mixing techniques, whereas the reaction with $Fe(ClO_4)_3$ ($k = 3 \times 10^4\ M^{-1}\ s^{-1}$) falls into the stopped-flow region. Acid dependencies for these reactions have not been determined, nor has the effect of salts having donor anions been investigated.

(27) It is assumed here than an increase in ΔG^* resulting from an increase in the standard potential of the reductant is half the increase in $\Delta G°$. See, for example: (a) Hush, N. S. *Trans. Faraday Soc.* **1961**, *57*, 557. (b) Chou, M.; Creutz, C.; Sutin, N. V. *J. Am. Chem. Soc.* **1977**, *99*, 5615.

(28) The electrostatic work, w, associated with reduction of a tripositive $(NH_3)_5Co^{III}$ derivative with the riboflavin radical ion, Rb·, may be estimated as follows:[29]

$$w = (4.3 \times 10^{-8})(+1)(+3)/a(1 + (3.3 \times 10^7)\mu^{1/2}a)$$

where a is the distance of closest aproach (in cm). The latter parameter is, in turn, estimated by adding the distance between the Co(III) center and the periphery of the coordinated ammonia (3.4×10^{-8} cm)[30] to the half-thickness of the π-electron cloud (1.9×10^{-8} cm). The contribution of this work term to ΔG^* is again taken to be $w/2$.

(29) Phillips, J.; Haim, A. *Inorg. Chem.* **1980**, *19*, 76.

(30) See, for example: Beattie, J. K.; Binstead, R. A.; Broccardo, B. *Inorg. Chem.* **1978**, *17*, 1822.