via carboxylate bridging, to another cationic center, i.e., that it is present principally as a Cr^{IV}–Fe^{III} complex. Analogous dinuclear species may intervene with other cationic reductants.[46] Comparable variability in $\epsilon_{Cr(IV)}$ is encountered with anionic reductants such as thiolactate[15] and 2,3-dihydroxybenzoate.[45] In these instances Cr(IV)–carboxylate association occurs, and this is reflected in the incorporation of carboxyl groups in the resulting Cr(III) products.

(46) In addition, association between Cr(IV) and Cr(V) centers in solution may come into play when the latter oxidation state is a major component. When Cr(IV) is generated from Cr(V) chelate II by using a deficiency of $(Mo^V)_2$ in 0.1 M ligand acid, the rate at which Cr(IV) decays (by oxidation of ligand acid) is found to be inversely proportional to [Cr(V)] remaining. The implication here is that the active oxidant is a Cr(IV) species, formed in a preequilibrium involving dissociation of a (predominant) Cr^{IV}–Cr^V complex.

Acknowledgment. We are grateful to Dr. S. K. Ghosh for help in computational procedures, to Dr. R. N. Bose for valuable discussions, and to Ms. Arla McPherson for technical assistance.

Registry No. I, 40804-49-7; [II]Na, 97042-89-2; 2-ethyl-2-hydroxybutanoic acid, 3639-21-2.

Supplementary Material Available: Table IV, giving stoichiometric data for the $(Mo^V)_2$–Cr^V reaction, and Table V, listing reaction conditions (2 pages). Ordering information is given on any current masthead page.

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Electron Transfer. 104. Reductions of Pyridinecarboxamides with Vitamin B_{12s} (Cob(I)alamin)[1]

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Vitamin B_{12s} (cob(I)alamin) is oxidized to its Co^{II} analogue by pyridinecarboxamides in aqueous buffers. The amides are reduced in multiples of two units. With B_{12s} in excess, the 3- and 4-$CONH_2$ substituted pyridines consume six units of Co^I, whereas the 2-isomer consumes nearly four. With the amide in excess, conversions are principally to a dihydro species which, in the case of nicotinamide, is predominantly a 1,6-dihydro derivative. Further partial conversion to tetrahydro compounds results in nonexponential kinetic profiles which have been treated by numerical integration methods to yield specific rates for both reaction steps. In all cases, that for reduction of the dihydro compound is greater than that for its aromatic precursor. All reactions are accelerated by H^+. The various observed $[H^+]$ dependencies reflect partition of one or both redox partners into acidic and basic forms and, in some instances, additional contributions from paths involving extraprotonated species which are stoichiometrically minor but exceptionally reactive. The 4-$CONH_2$ amide is reduced about 10^2 times as rapidly as the 3-$CONH_2$ under comparable conditions, a selectivity similar to that recognized for 1e reductions of these amides but different from that expected for 2e transfers, suggesting that these reactions, although net 2e changes, proceed in 1e steps with the overall rate determined by the initial transfer.

Vitamin B_{12s} (cob(I)alamin, the cobalt(I) analogue of B_{12a}), the formal potential of which has been recorded as −0.62 V at pH 5 and −0.50 V at pH 3,[2] is one of the strongest reductants that can be readily handled in aqueous solution.[3] Moreover, it is remarkably diverse in its reactions. In reducing a variety of unsaturated organic species,[4] it functions as a 2e donor, whereas its reactions with the metal centers Co^{III},[5] Eu^{III},[6] Ti^{IV},[6] and V^{III}[7] are necessarily 1e transactions. Reductions of organics have been utilized in synthetic procedures,[4a,8] and mechanistic questions have also been considered.[4b,c]

This contribution pertains to the reductions, using B_{12s}, of five pyridinecarboxamides, including both the physiologically important 3-$CONH_2$ derivative (niacinamide)[9] and its 4-substituted isomer, which has achieved prominence as a ligand used in fundamental redox studies elsewhere.[10] We present evidence that although these reductions involve net changes of two electrons, both electrons are not transferred in a single act.

Table I. Stoichiometries of the Reactions of Vitamin B_{12s} (Cob(I)alamin) with Pyridinecarboxamides[a]

amide (Py–R)	mmol of PyR × 10^4	mmol of B_{12s} × 10^4	Δmmol of B_{12s} × 10^4	$\Delta[B_{12s}]/\Delta[PyR]$
2-$CONH_2$	2.6	16.0	10.4	4.0
	4.0	24	15.3	3.8
	2.0	24	7.8	3.9
3-$CONH_2$	0.33	4.0	2.04	6.1
	0.66	4.0	4.0	6.1
	0.45	4.0	2.66	5.9
3-$CONHCH_3$	1.00	8.0	4.0	4.0
	1.50	8.0	6.0	4.0
	0.50	8.0	2.1	4.2
4-$CONH_2$[b]	0.40	4.0	2.5	6.3
	0.50	4.0	3.1	6.2
	0.67	4.0	3.9	5.6
1-CH_3-4-$CONH_2$,[b,c]	1.33	8.0	7.4	5.6
	0.80	8.0	4.6	5.8
	0.67	8.0	3.9	5.8

[a] Reactions were carried out in solutions buffered with 0.05 M each of glycine and its hydrochloride, unless otherwise indicated, and were monitored at 470–500 nm. [b] Faster reactions carried out in HOAc–OAc^- buffer. [c] 1-Methyl-4-carbamoylpyridinium perchlorate.

(1) Sponsorship of this work by the National Science Foundation (Grants 8313253 and 8619472) is gratefully acknowledged.
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(3) By way of comparison, the strongest reductant among readily preparable hydrated metal cations is U^{3+} ($E^\circ = -0.63$ V) (Ahrland, S.; Liljenzin, J. O.; Rydberg, J. *Comprehensive Inorganic Chemistry*; Pergamon: Oxford, U.K., 1973; Vol. 5, p 519).
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Experimental Section

Materials. Pyridinecarboxamides (Tokyo Chemical Industry or Aldrich Products) and hydroxocobalamin hydrochloride (Sigma) were used as received or after recrystallization from water (which process did not significantly affect the results). Sodium perchlorate, used as a supporting electrolyte in kinetic experiments, was prepared in solution by treatment of $NaHCO_3$ with $HClO_4$; solutions were adjusted to pH 5.5–6.0 and were sparged with purified N_2 for at least 3 h.

N-Methylisonicotinamide perchlorate (1-methyl-4-carbamoyl-pyridinium perchlorate) was prepared by methylation of the ring nitrogen of isonicotinamide in aqueous solution using methyl iodide as described.[11] The resulting substituted pyridinium iodide, which crystallized from the reaction mixture, was treated with a slight excess of aqueous $AgClO_4$ at 40–50 °C, the precipitated AgI was removed by filtration, the excess Ag^+ was precipitated by dropwise addition of HCl, and the filtered solution was carefully concentrated by rotary evaporation. The white perchlorate, which separated on cooling to 0 °C, was crystallized from aqueous $HClO_4$. Although no problems were encountered in handling this salt, it is recommended that no more than 500 mg be prepared in a single lot.

Cob(I)alamin was generated from the cobalt(III) complex, hydroxocobalamin hydrochloride, in stoppered spectrophotometric cells by reduction with zinc amalgam in acid solution.[12]

Stoichiometric Studies. Stoichiometries of all reactions, each with B_{12s} in excess, were determined in buffered media by generating Co^I in acid solution, buffering the solution, adding a deficiency of the amide in water, waiting about 20 min, and then measuring the increase in absorbance at 470–500 nm.[13] The resulting changes were compared to those occurring when B_{12s} reacted with excess oxidant. Corrections were made for the slow change in absorbance (less than 5%) when B_{12s} was kept in the medium used in the absence of pyridine derivatives. Results are summarized in Table I.

Kinetic Measurements and Estimation of Specific Rates. Rates were estimated from measurements of decreases of absorbance at 387 nm by using either a Cary 14 or a Beckman Model 5260 recording spectrophotometer. The reductant, B_{12s}, was generated directly from B_{12a} in the optical cell as described.[12] Acidities were regulated by the addition of known quantities of glycine or acetate buffers before reduction to Co^I, and pH values were checked at the conclusion of each redox experiment. Acidity ranges chosen were those that yielded measurable rates. Total ionic strength was maintained at 0.5 M by addition of $NaClO_4$. Kinetic runs were carried out with the oxidant (the pyridine amide) in 10- to 50-fold excess.

Reactions did not generate straightforward exponential decay curves. Observed half-life periods increased progressively during the course of each reaction, but the increase was much less marked than that corresponding to a second-order profile. This effect could not be attributed to autoinhibition, for if a fresh sample of B_{12s} was added to a spent reaction mixture, the initial rate was that observed for the previous sample.[14] The electronic spectrum of the cobalt product corresponded, in all cases, to that of B_{12r} (cob(II)alamin).[12,15] Isosbestic points at 343, 416, and 543 nm were observed.

Nearly all kinetic curves could be fitted to a sequence featuring partial conversion of the pyridine amide to a dihydro product and thence, to a lesser extent, to a tetrahydro product (see Discussion). Such fits were accomplished initially with the program INTEGRAL to produce curves that were compared to those observed.[16,17] Selected specific rates giving approximate agreement between observed and calculated absorbances were refined further by using an iterative nonlinear least-squares procedure.[18,19] Parameters resulting from these refinements reproduced the observed curves closely.

Reductions of the ring-methylated derivative of isonicotinamide, which were much more rapid than those of the other amides, gave still more complex decay curves, each involving at least three kinetic components. Although such profiles were not analyzed in detail, an initial half-life period of ca. 4.5 s was noted when the oxidant was taken at the 1.2×10^{-4} M level, corresponding to a bimolecular rate constant near 10^3 M^{-1} s^{-1} (pH 4.6) for the rapid component. Solutions of benzamide and dimethylformamide (amides devoid of the pyridine function) did not react with B_{12s} under our conditions.

Examination of the Nicotinamide Reduction Products. Reaction mixtures (1 mL) contained 6.5×10^{-3} mmol of B_{12s} and 9.8×10^{-3} mmol of nicotinamide (pH 3.8). These were allowed to react for 30 min, after which the products were absorbed on a column of Bio-gel P-2 (200–400 mesh; exclusion limit 1800 Da). Products were slowly eluted with water. An initial fraction (10 mL) was colored and exhibited spectra characteristic of a mixture of the Co^{II} and Co^{III} forms of B_{12}; an ensuing colorless fraction (also about 10 mL) displayed no absorbance in the visible or UV region. A colorless fraction (ca. 30 mL) following the latter showed maxima at 270 and 350 nm, $Abs_{270}/Abs_{350} = 1.33$. Spectra of subsequent fractions were featureless.

Results

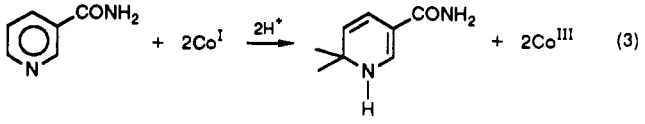
Stoichiometric determinations, made with B_{12s} in excess (Table I), indicate that this reductant reacts with pyridine amides in multiples of two oxidation units. Nicotinamide and isonicotinamide (the 3- and 4-$CONH_2$ substituted oxidants) consume very nearly six units of Co^I, being thus converted to hexahydro derivatives

$$Py(CONH_2) + 6Co^I + 6H^+ \rightarrow PyH_6(CONH_2) + 6Co^{II} \quad (1)$$

whereas the more slowly reacting 2-$CONH_2$ and 3-$CONHCH_3$ amides are reduced only to tetrahydro species

$$Py(CONHR) + 4Co^I + 4H^+ \rightarrow PyH_4(CONHR) + 4Co^{II} \quad (2)$$

In our kinetic experiments, carried out with the amide in excess, reduction should proceed mainly to the dihydro level. Although a mixture of isomers would be expected, the spectrum of the production from nicotinamide (λ_{max} = 270 and 350 nm) corresponds to that reported for the 1,6-dihydro compound, I,[20] in-



(3)

I

dicating that B_{12s}, like $NaBH_4$, attacks principally at the α-carbon on the less hindered side of the pyridine ring. In the absence of reported spectra of dihydro derivatives of the 2- and 4-amides,[21] reductions of these isomers may be taken to proceed in a similar manner.

The nonexponential kinetic traces obtained with the amides in large excess tell us that more than one reaction is occurring on

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(12) Balasubramanian, P. N.; Gould, E. S. *Inorg. Chem.* **1983**, *22*, 2635.
(13) Monitoring these stoichiometric experiments near the very strong B_{12s} peak at 387 nm, using very dilute solutions of Co^I, was less successful since loss of reductant (probably reflecting slow leakage of air) became more troublesome during the course of these relatively slow conversions. Reductions of *N*-methylnicotinamide were so sluggish that reliable stoichiometric data could not be obtained with this amide.
(14) The possibility that we were observing parallel reactions of two similarly colored Co^I species was eliminated by showing that B_{12s} prepared from hydroxocobalamin hydrochloride behaved identically with that prepared from the corresponding purified acetate. We thank Professor L. Marzilli for a sample of the latter.
(15) Bonnet, R. *Chem. Rev.* **1963**, *63*, 573.
(16) Kinetic fits, which utilized a fourth-order Runge-Kutta integration technique,[17] were accomplished by a FORTRAN-77 program on an IBM 3081D computer system. The FORTRAN-IV version of the program, for which we thank Professor Gilbert Gordon (Miami University, Oxford, OH), was modified to incorporate the appropriate differential equations and stoichiometric relationships.
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Table II. Kinetic Data for the Reaction of Vitamin B_{12s} (Cob(I)alanin) with 4-Pyridinecarboxamide (Isonicotinamide)[a]

10^3[amide]	[HOAc]	[OAc^-]	pH	k_1[b]	k_2[b]
1.25	0.050	0.050	4.79	19.3 (17.8)	127 (119)
2.5	0.050	0.050	4.76	18.9 (18.4)	116 (121)
2.5[c]	0.050	0.050	4.73	18.3 (18.9)	163 (123)
1.25	0.10	0.10	4.76	19.1 (18.4)	122 (121)
1.25	0.10	0.050	4.55	26 (22)	108 (132)
1.25	0.20	0.050	4.05	33 (36)	138 (148)
1.25	0.30	0.050	3.87	39 (42)	138 (148)
1.25	0.40	0.050	3.78	50 (45)	177 (152)
2.5	0.050	0.10	5.04	14.3 (13.8)	96 (101)
2.5	0.050	0.20	5.23	9.7 (11.1)	81 (85)

[a] Reactions were carried out at 25 °C in HOAc–OAc^- buffers; μ = 0.50 M ($NaClO_4$). $[B_{12s}] = 8.0 \times 10^{-5}$ M unless otherwise indicated. [b] Specific rates (M^{-1} s^{-1}) for reactions 4 and 5 in text, obtained from nonlinear least-squares refinements in which absorbances were compared with those resulting from the differential equations (7) and (8). Parenthetical values are calculated from eqs 10 and 11 by using parameters listed in text. [c] $[B_{12s}] = 4.0 \times 10^{-5}$ M.

Table III. Kinetic Data for the Reaction of Vitamin B_{12s} (Cob(I)alamin) with 3-Pyridinecarboxamide (Nicotinamide)[a]

10^3[amide]	[$GlyH^+$]	[Gly]	pH	k_1[b]	k_2[b]
5.0	0.050	0.20	3.42	0.47 (0.47)	4.4 (4.7)
5.0	0.050	0.10	3.11	0.63 (0.48)	8.0 (6.6)
5.0	0.050	0.050	2.72	0.80 (0.84)	13.4 (14.4)
5.0	0.10	0.050	2.45	2.4 (2.0)	33 (33)
5.0	0.20	0.050	2.24	4.3 (4.5)	76 (70)
5.0	0.30	0.050	2.06	10.6 (9.7)	156 (142)
5.0	0.40	0.050	1.99	13.8 (13.1)	171 (189)
5.0	0.050	0.050	2.72	0.99 (0.84)	14.2 (14.4)
10.0	0.050	0.050	2.69	0.81 (0.89)	14.4 (15.3)
20.0	0.050	0.050	2.73	0.68 (0.82)	14.6 (14.0)
5.0[c]	0.050	0.050	2.72	0.83 (0.84)	14.1 (14.5)
5.0[d]	0.050	0.050	2.71	0.86 (0.86)	14.9 (14.8)
5.0	0.30	0.30	2.69	0.91 (0.89)	15.0 (15.3)

[a] Reactions were run at 25 °C in glycine buffers; μ = 0.50 M ($NaClO_4$). $[B_{12s}] = 8.0 \times 10^{-5}$ M unless otherwise indicated. [b] Bimolecular rate constants (M^{-1} s^{-1}) for 2e and 4e reductions of nicotinamide (reactions 4 and 5 in text), obtained from refinement of kinetics data (refs 16 and 18). Parenthetical values are calculated from eqs 12 and 13 by using parameters in text. [c] $[B_{12s}] = 4.0 \times 10^{-5}$ M. [d] $[B_{12s}] = 1.6 \times 10^{-4}$ M.

the time scale examined. Such curves are analyzed in terms of sequence 4–6, in which rates for (4) and (5) would be expected

$$Py + Co^{I} \xrightarrow[k_1]{H^+} PyH_2 + Co^{III} \quad (4)$$

$$PyH_2 + Co^{I} \xrightarrow[k_2]{H^+} PyH_4 + Co^{III} \quad (5)$$

$$Co^{I} + Co^{III} \rightarrow 2Co^{II} \quad \text{(rapid)} \quad (6)$$

to be [H^+]-dependent.[22] Step 6, the $Co^{I/III}$ comproportionation, is known to be rapid enough ($k > 10^7$ M^{-1} s^{-1})[23] to allow its combination with (4) and (5). This sequence then generates the differential equations (7)–(9). To treat our systems, eqs 7 and 8 were chosen, a 5-s interval between kinetic points was taken, and values of k_1 and k_2 were allowed to vary. Numerical integration[17] then yielded the concentrations of Py, PyH_2, PyH_4, Co^I, and Co^{II} at each point. Incorporation of the molar absorbances of the two B_{12} species (Co^I and Co^{II}) gave calculated values for the optical density of the solution. Values of k_1 and k_2 giving an approximate fit to the observed decay were used as trial values for the final least-squares refinement.[18]

$$\frac{-d[Py]}{dt} = k_1[Py][Co^I] \quad (7)$$

$$\frac{-d[Co^I]}{dt} = 2k_1[Py][Co^I] + 2k_2[PyH_2][Co^I] \quad (8)$$

$$\frac{d[PyH_2]}{dt} = k_1[Py][Co^I] - k_2[PyH_2][Co^I] \quad (9)$$

(22) With the oxidant in excess, this sequence may be shown to result in nearly exponential decay curves if $k_1 \geq k_2$ or if $k_2/k_1 > 10^2$. Profiles of the type observed then imply that k_2 is greater than k_1, but not too much greater.

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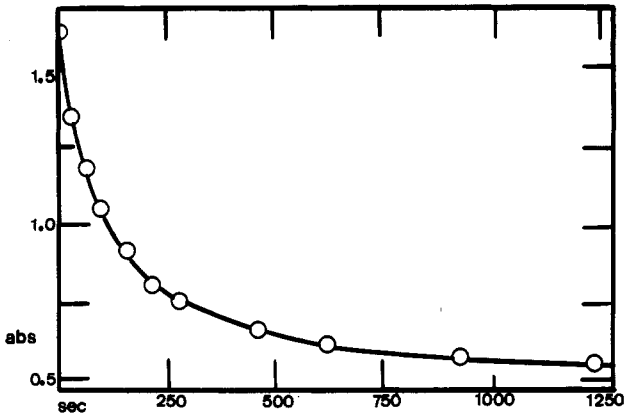

Figure 1. Kinetic profile at 387 nm for the reaction of vitamin B_{12s} (Cob(I)alamin) (8.0×10^{-5} M) with nicotinamide (5.0×10^{-3} M) at 25 °C. The supporting medium was 0.05 M each in glycine and its hydroperchlorate and 0.45 M in $NaClO_4$; the pH was 2.75. The solid line is the experimental curve, whereas the circles represent absorbances calculated from integration of the differential equations (7) and (8) in the text. The parameters k_1 and k_2 were taken as 0.99 and 14.2 M^{-1} s^{-1}. Extinction coefficients used (M^{-1} cm^{-1}): B_{12s} (Co^I), 21×10^3; B_{12r} (Co^{II}), 6.5×10^3. Optical path length: 1.00 cm.

Table IV. Rate Laws for the Reactions of Vitamin B_{12s} (Cob(I)alamin) with Pyridinecarboxamides[a]

amide	pH	rate law[b]
4-$CONH_2$	3.87–5.23	$k_1 = \left(\frac{[H^+]}{K_R + [H^+]}\right) + \left(\frac{k_{Py}K_{PyH} + k_{PyH}[H^+]}{K_{PyH} + [H^+]}\right)$ $k_2 = \frac{K_{PyH}[H^+]}{K_R + [H^+]}$
3-$CONH_2$	1.99–3.42	$k_1 = k_{PyH} + k'[H^+]^2$ $k_2 = k_{PyH} + k'[H^+] + k'[H^+]^2$
2-$CONH_2$	2.13–3.30	$k_1 = \left(\frac{[H^+]}{K_{PyH} + [H^+]}\right) + (k_{PyH} + k'[H^+])$ $k_2 = k'[H^+] + k'[H^+]^2$
3-$CONHCH_3$	2.18–3.19	$k_{1,2} = k'[H^+]$
1-CH_3-3-$CONH_2$	2.10–2.89	$k_{1,2} = k_{Py} + k'[H^+]$

[a] Reactions were carried out at 25 °C; μ = 0.5 M ($NaClO_4$). Experiments were monitored at 387 nm. [b] Values of k_1 and k_2 (specific rates for the first and second stages of reduction) were obtained from least-squares refinements in which observed absorbances were compared to those obtained by integration of differential equations based on sequence 4–6 (see text and refs 16–18). The value of K_R, referring to protonation of B_{12s}, was taken as 5.0×10^{-6} M^{-1}.[4c]

Tables II and III list refined values of k_1 and k_2 for the reactions of B_{12s} with nicotinamide and its 4-$CONH_2$ isomer. Calculated absorbances for a typical nicotinamide run are compared with the corresponding experimental curve in Figure 1. The more reactive of these oxidants, isonicotinamide, was examined at pH 3.7–5.2. Within this range, both the amide (pK_{PyH} of its conjugate acid = 3.67)[24] and B_{12s} (pK_R = 5.3)[4c] are partially protonated. If, on

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Table V. Kinetic Parameters Pertaining to the Reactions of Vitamin B_{12s} (Cob(I)alamin) with Pyridinecarboxamides[a]

amide		pK_{PyH}	k_{Py}, M^{-1} s^{-1}	k_{PyH}, M^{-1} s^{-1}	k', M^{-2} s^{-1}	k'', M^{-3} s^{-1}
4-$CONH_2$	k_1	3.67	18.8 ± 1.1	82 ± 7		
	k_2			156 ± 7		
3-$CONH_2$	k_1	3.47		0.40 ± 0.07		(1.30 ± 0.02) × 10^5
	k_2			3.3 ± 0.5	(3.0 ± 0.7) × 10^3	
2-$CONH_2$	k_1	1.8		3.7 ± 0.3	(1.3 ± 0.2) × 10^3	
	k_2				(2.5 ± 0.4) × 10^3	(1.07 ± 0.22) × 10^6
3-$CONHCH_3$	k_1	3.5			163 ± 8	
	k_2				(5.7 ± 0.3) × 10^3	
1-CH_3-3-$CONH_2$[b]	k_1	0.024 ± 0.004[c]			10.7 ± 1.4	
	k_2	1.92 ± 41[c]			(5.5 ± 1.2) × 10^2	

[a] Reactions were carried out at 25 °C; μ = 0.5 M ($NaClO_4$). Values of k_1 and k_2 (specific rates for the first and second stages of reduction) were obtained as described in Table IV. Specific rates k_{Py} and k_{PyH} refer to the deprotonated and ring-protonated forms of the oxidants; k' and k'' refer to "extraprotonated" paths. Values of pK_{PyH} were taken from ref 24. [b] 1-Methyl-3-carbamoylpyridinium perchlorate. [c] Contribution from the ring-methylated amide.

the basis of earlier studies,[4b,c] the nonprotonated form of B_{12s} is assumed to be unreactive, operation of the two protonation equilibria leads to eq 10, where k_{Py} and k_{PyH} are specific rates

$$(k_1)_{obsd} = \left(\frac{[H^+]}{K_R + [H^+]}\right)\left(\frac{k_{Py}K_{PyH} + k_{PyH}[H^+]}{K_{PyH} + [H^+]}\right) \quad (10)$$

for the two forms of the oxidant. Refinement of data in terms of (10) yields k_{Py} = 18.8 ± 1.1 and k_{PyH} = 82 ± 7 M^{-1} s^{-1}.[25]

A simpler relationship, (11), applies to k_2, which pertains to the reduction of the dihydro compound, since conversion of the latter increases the basicity of the ring nitrogen[26] so that pro-

$$(k_2)_{obsd} = \frac{k_{PyH}[H^+]}{K_R + [H^+]} \quad (11)$$

tonation of the oxidant is virtually complete. Hence, variation of k_2 with $[H^+]$ simply reflects the partial protonation of B_{12s}. From (11) we calculate a limiting specific rate, k_{PyH} = 156 ± 7 M^{-1} s^{-1}.

The slower reduction of the 3-amide, nicotinamide, examined at pH 2.0–3.5, is unusually sensitive to acidity. Values for k_1 conform to the binomial expression (12), where k_{PyH} = 0.40 ±

$$(k_1)_{obsd} = k_{PyH} + k''[H^+]^2 \quad (12)$$

0.07 M^{-1} s^{-1} and k'' = (1.30 ± 0.02) × 10^5 M^{-3} s^{-1}. The prominence of the k'' term within the $[H^+]$ range studied indicates that this step proceeds mainly through an activated complex featuring the two redox partners plus two extra protons.[27] If one of these is associated with the Co^I center of B_{12s}[28] and the other with the $-CONH_2$ group of the oxidant, the bimolecular rate constant for this path, obtained by multiplying k' by the two appropriate deprotonation constants,[29] exceeds 10^7 M^{-1} s^{-1}. The second (k_2) stage of reduction of this amide is similarly sensitive to pH, with the expression for the $[H^+]$ dependence (13) exhibiting both $[H^+]$-

$$(k_2)_{obsd} = k_{PyH} + k'[H^+] + k''[H^+]^2 \quad (13)$$

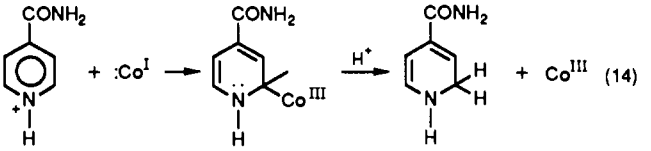
and $[H^+]^2$-proportional terms, where k_{PyH} = 3.3 ± 0.5 M^{-1} s^{-1}, k' = (3.0 ± 0.7) × 10^3 M^{-2} s^{-1}, and k'' = (1.47 ± 0.15) × 10^6 M^{-3} s^{-1}. The "extramonoprotonated" term (k') terms in (13) may reflect additional protonation of either the oxidant or the reductant.

Discussion

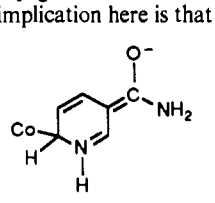
Rate laws for reductions of each of the amides studied are listed in Table IV, whereas estimated kinetic parameters are collected in Table V. Each of the amides undergoes a two-stage reduction analogous to that observed for the 3- and 4-$CONH_2$ oxidants. Although operation of the second stage is reflected in the observed nonexponential kinetic profiles, numerical integrations, using the appropriate rate constants,[16,17] indicate that the resulting tetrahydro compound(s) constitute only a minor fraction (2–15%) of the reduced pyridine product.

All reactions are accelerated by H^+, but the acid dependencies, as indicated, are not the same throughout. The protonation of B_{12s} (pK = 5.3) need be considered only for reduction of isonicotinamide, for the slower reactions are carried out at higher acidities where the reductant exists nearly exclusively in its protonated form. Partial conversion to ring-protonated forms may be kinetically significant for the aromatic amides taken (k_1 component; pK_{Py} = 2–4) but not for their more basic dihydro derivatives (k_2 components). The appearance of $[H^+]$- and $[H^+]^2$-proportional terms underlines the importance of contributions involving "extraprotonated" species which are stoichiometrically negligible but kinetically effective. Why such terms are observed only in some cases, and whether additional protonated routes might be detected if the range of acidities were expanded remain unanswered questions.

The most noteworthy aspect of this work is the marked acceleration resulting from substitution of a 4-$CONH_2$ group on the pyridine ring. Previous studies[4b,c] of the reactions of B_{12s} with unsaturated species suggest that the first reduction is initiated by sequence 14. However, the ease with which the 4-amide is



reduced brings to mind the reactivity pattern reported for the 1e reductions of such aromatics,[30] whereas a 2e transfer indicated in (14) would be expected to be favored by a 3-$CONH_2$ substituent, reflecting conjugative stabilization of the C–Co^{III} intermediate (II). The implication here is that the reactions at hand,



II

(25) The error limits cited here and elsewhere are estimated standard deviations (σ values), derived from least-squares refinements of kinetic data in terms of the indicated $[H^+]$ dependencies. See, for example: Harris, D. C. *Quantitative Chemical Analysis*, 2nd ed.; Freeman: New York, 1987; p 55.

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(27) In our examination of the reduction of nicotinamide (pK_A = 3.47)[24] in glycine buffers, appreciable conversion of the amide to its nonprotonated form occurs at the upper end of the pH range where reaction is slowest. Our data in this region are too few and of insufficient precision to allow evaluation of k_a and k_{HA} in the presence of a strong $[H^+]^2$-proportional term.

(28) Lexa, D.; Saveant, J.-M. *J. Am. Chem. Soc.* **1976**, *98*, 2652. These workers have presented evidence for a second protonation of B_{12s} near pH 1, whereas Pillai[4c] has assigned a pK_A = 0.0 for this protonation.

(29) The pK_A value for protonation of the amide group is taken to be −2.0, i.e., very nearly equal to that recorded for benzamide. See, for example: Arnett, E. M. *Prog. Phys. Org. Chem.* **1963**, *1*, 223 (Table XVI).

(30) See, for example: Loar, M. K.; Fanchiang, Y.-T.; Gould, E. S. *Inorg. Chem.* **1978**, *17*, 3689.

although net 2e changes, proceed in 1e steps, with the overall rate determined by the initial transfer. The resulting radical may then react quickly with a second Co^{I} center or may undergo bimolecular disproportionation, yielding equivalent quantities of the dihydro compound and the original aromatic. Substantial chain termination by radical dimerization is not consistent with the observed stoichiometry.

Although additional systems should be examined, it thus appears that B_{12s} reductions of pyridine amides differ from those of α,β-unsaturated dicarboxylic acids and their esters where the superior reactivity of alkyne-derived oxidants and the overall stereospecificity of their conversion to alkenes support the intermediacy of a carbanion-like adduct, formed in a 2e process without intervention of an odd-electron species.[4b,c]

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Supplementary Material Available: Tables VI-VIII, giving kinetic data for the reactions of 2-pyridinecarboxamide, *N*-methylnicotinamide, and 1-methyl-3-carbamoylpyridinium perchlorate with B_{12s} (3 pages). Ordering information is given on any current masthead page.

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Electron Transfer. 106. Stabilized Aqueous Chromium(IV), As Prepared from the Chromium(VI)-Arsenic(III) Reaction[1]

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Reduction of $HCrO_4^-$ with H_3AsO_3 in solutions buffered by 2-ethyl-2-hydroxybutanoic acid (LigH) and its salt (Lig^-) yields stabilized pink solutions of Cr(IV). This atypical state is oxidized to a bis chelate of Cr(V) with excess Cr(VI), is reduced very slowly to chelated Cr(III) with excess Lig^-, but does not react with As(III). Variation of absorbance with [Lig^-] points to partition of Cr(IV) (eq 4) into two forms, II (ϵ_{510} = 53 ± 22) and II-Lig (ϵ_{510} = 2460 ± 70 M^{-1} cm^{-1}), related by a ligation constant of 90 ± 8 M^{-1} (25 °C; μ = 0.50 M). The Cr(VI)-As(III) system features a $Cr^{VI}As^{III}$ complex (K = 340 ± 60 M^{-1}). Reduction to Cr(IV) (rate law 6) proceeds through two paths, the first involving extra units of H^+ and Lig^- and the second requiring 2 H^+ and 2 Lig^-. The reaction $Cr^{IV} + Cr^{VI} \rightarrow 2Cr^{V}$ in this buffer appears to entail a $Cr^{IV}Cr^{VI}$ complex (K = 50 ± 9 M^{-1}) and proceeds through a combination of an acid-independent route and a [H^+]-proportional route. This comproportionation corresponds to that observed when Cr(VI) is reduced with $Mo_2O_4^{2+}$ in the same medium. Chromium(IV) solutions prepared by reduction with excess As(III) are more stable than those prepared by using $Mo_2O_4^{2+}$, U(IV), or Sn(II), for the latter three reagents can undergo less favored 1e$^-$ changes in the presence of the strongly oxidizing Cr(IV) center. Analogous 1e$^-$ oxidation of As(III) cannot compete with the reduction of Cr(IV) by the ligand anion used.

Although chromium(IV) is generally considered to be an atypical oxidation state, awareness is increasing as to its role in the redox chemistry of that element. Kinetic studies have implicated this state as an intermediate in the reactions of chromium(VI) with both organic[2] and inorganic[3] reductants, and preparative oxidations using Cr(IV), generated in situ, have been described.[4] Of the Cr(IV) compounds that have been isolated and characterized,[5] nearly all undergo decomposition in aqueous media. A small number of diperoxo ammine complexes,[6] such as $Cr^{IV}(NH_3)_3(O_2)_2$, decompose only slowly in water, but the behavior of the metal center in such complexes is significantly modified by the presence of two peroxo ligands and by the expanded coordination sphere about seven-covalent chromium.

Chromium(IV) derivatives of 2-hydroxy carboxylates have been detected as transients when Cr(V) chelates derived from carboxylato ligands of this type are reduced with the 1e$^-$ reagents U(IV), Fe(III), and VO^{2+}[7] or with species that can undergo both one- or two-electron reductions (such as bisulfite, nitrite, and ascorbate).[8] However, examination of such systems is complicated by the further rapid reductions of Cr(IV) by 1e$^-$ transactions.

We recently[9] reported the preparation of more stable Cr(IV) complexes in solution by treatment of Cr(VI) with the cationic reductant $[Mo^{V}_2O_4(H_2O)_6]^{2+}$ in aqueous media buffered by 2-ethyl-2-hydroxybutanoic acid $[(C_2H_5)_2C(OH)COOH]$ (I) and its anion. The persistance of Cr(IV) in such systems results, in part, from the difficulty associated with the reactions of $(Mo^{V})_2$ derivatives with 1e$^-$ oxidants,[10] reactions that often appear to entail

Table I. Stoichiometry of the Cr(VI)-As(III) Reactions[a]

10^4-[Cr^{VI}], M	10^4-[As^{III}], M	10^4-Δ[Cr^{VI}], M	10^4-Δ[As^{III}], M	Δ[Cr^{VI}]/Δ[As^{III}]
1.50	5.0		1.63	1.08
3.0	5.0		2.95	0.98
4.0	5.0		3.9	0.96
1.9[b]	7.5		2.05	0.93
3.8[b]	7.5		3.7	1.03
100	15.0	31		2.08
100	30	58		1.94
100	45	86		1.91
9.0[c]	4.0	2.7		0.67
9.0[c]	8.0	5.2		0.65
9.0[c]	12.0	7.7		0.64

[a] Cr^{VI} was added as $Na_2Cr_2O_7$; As^{III}, as H_3AsO_3. Solutions (pH 3.3) were buffered with equal concentrations (0.05 M) of the ligand hydroxy acid (I) and its sodium salt unless otherwise indicated. Reactions were monitored at 510 nm. [b] [HLig] = [Lig^-] = 5 × 10^{-3} M. [c] Reactions in 0.10 M $HClO_4$, carried out in the absence of ligating acid; these were monitored at 350 nm. Reaction time = 30 min.

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