

Electron Transfer. 70. Reductions of Oxyhalogens by Vitamin B_{12r} (Cob(II)alamin)¹

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Vitamin B_{12r} (cob(II)alamin), the Co(II) derivative of vitamin B₁₂, reduces ClO₃⁻, BrO₃⁻, IO₃⁻, and ClO₂⁻ to the corresponding halide ions in acid solution and *o*-iodosobenzoic acid to the *o*-iodo acid. Specific rates for these reductions have been measured and their acid dependencies examined. In each case, the overall rate is determined by the first step in the reaction sequence, the initial 1e reduction of the oxyhalogen. Each of the B_{12r}-halate reactions is first order in [H⁺]; the B_{12r}-ClO₂⁻ reaction exhibits both an [acid]-independent and first-order-[H⁺] term, whereas reduction of iodosobenzoic acid features an inverse-[H⁺] term. The B_{12r}-IO₃⁻ reaction, but none of the others, is strongly autocatalytic, probably reflecting the reaction of the product I⁻ with IO₃⁻ to form the very reactive oxidant, I₂. Vitamin B_{12s}, the Co(I) derivative of B₁₂, reduces ClO₃⁻ about 10⁴ times as rapidly as B_{12r}, a rate ratio too small to be compatible with the 0.78-V difference in the formal potentials of the two reductants on the basis of the Marcus model for outer-sphere electron-transfer processes. It is proposed that the B_{12r}-ClO₃⁻ reaction (and, by implication, the reactions with BrO₃⁻, IO₃⁻, and ClO₂⁻) proceeds mainly by an inner-sphere route that utilizes an oxygen bridge between Co(II) and halogen. The path for the B_{12s}-ClO₃⁻ reaction is uncertain, nor can we say whether this reduction involves transfer of a single electron or whether it is initiated by a 2e transaction, forming of a Co(III) intermediate that undergoes comproportionation with B_{12s} to form 2 units of Co(II).

The two reduced forms of vitamin B₁₂ are cob(II)alamin (B_{12r}) and cob(I)alamin (B_{12s}). The potential for the latter is about 0.8 V more negative than that for the former,² and as expected, B_{12s} is by far the more rapid reductant. Interest in the electron-transfer reactions of B_{12s} has recently intensified,³ and it has been noted that many oxidants that react smoothly with this Co(I) species, at rates measurable by conventional mixing techniques or by stop-flow techniques, react inconveniently slowly with its Co(II) counterpart. Rather less attention has been paid to the oxidations of B_{12r},⁴ although it is recognized that a number of its reactions with stronger oxidants (e.g., peroxide derivatives and elemental halogens) may be monitored without difficulty.

The present study deals mainly with the reactions of cob(II)alamin with oxyhalogen species. In one instance (ClO₃⁻) we have been able directly to compare specific rates for reduction by B_{12r} and B_{12s}.

Experimental Section

Materials. Sodium chlorate and sodium iodate (Baker and Adamson), sodium bromate (Sargent Chemicals), hydroxocobalamin hydrochloride (Sigma Chemicals), glycine (Aldrich Chemicals), *o*-iodosobenzoic acid (Pfaltz and Bauer), and sodium chlorite^{5,6} (Alfa

Chemicals) were used as received. Lithium perchlorate, for use in kinetic experiments, was prepared as described.⁷ All reactions were carried out under N₂ in distilled water that had been previously boiled and purged with N₂ for at least 4 h. Cob(II)alamin was generated by reaction of the Co(III) complex hydroxocobalamin hydrochloride with zinc amalgam,^{4b} a reduction that was generally complete in less than 1 min. If this reaction was allowed to proceed for 5 min or more, B_{12r} was further reduced to B_{12s}, as shown by the change of color from yellow to gray, the fading of the Co^{II} spectral peaks at 470 and 312 nm, and the growth of Co^I peaks at 387, 560, and 680 nm.^{3b} Because of the extreme sensitivity of B_{12s} solutions to traces of oxygen, the latter reductant was generated in the vessel to be used for reaction^{3b,8} and transfers between vessels were avoided. Solutions of B_{12r} could be transferred without difficulty by using syringe techniques.

Stoichiometric Studies. The stoichiometries of seven of the more rapid reactions, taking the Co^{II} or Co^I complex in excess, were determined by adding a measured deficiency of oxidant to the reduced vitamin B₁₂ solution, waiting 30–80 min for completion of the reaction,⁹ and then measuring the increase in absorbance at 350 nm (for Co^{II} to Co^{III} conversions) or the decrease in absorbance at 387 nm (for Co^I to Co^{II} conversions). These changes, after small corrections for the slow loss of reductant in the absence of coreagent, were compared to those observed when the cobalt reductant was treated with excess oxidant. Representative results appear in Table I.

Kinetic Studies. Rates were estimated from measurements of changes in absorbance using a Cary 14 recording spectrophotometer. For reactions of B_{12r}, the increase in absorbance at 350 nm (a cob(III)alamin peak) was monitored; for reactions of B_{12s}, decreases in absorbance at 387 nm were followed. Special precautions in handling B_{12s} have been described.^{3b,10} Acidities were regulated by additions of known concentrations of HClO₄ and glycine. Total ionic strength was maintained near 0.50 M by adding LiClO₄. Except as noted below, reactions were first order each in oxidant and cobalt but were carried out under pseudo-first-order conditions such that less than 20% of the reagent in excess was consumed during the course of the reaction. Conversions were followed for at least 5 half-lives. Rate constants from successive half-life values within a run generally agreed

- (1) Support of this work by the National Science Foundation is gratefully acknowledged.
- (2) Formal potentials of -0.48 V for B_{12s} and +0.30 V for B_{12r} at pH 1 (vs. NHE) have been reported: Lexa, D.; Saveant, J.-M. *Acc. Chem. Res.* **1983**, *16*, 235. Both of these values are strongly pH dependent. Redox reactions of B₁₂ are further complicated by the equilibrium between the internally benzimidazole-coordinated ("base-on") and protonated-benzimidazole ("base-off") forms, but only the latter is important in the acidity range considered here.
- (3) See, for example: (a) Lexa, D.; Saveant, J.-M. *J. Am. Chem. Soc.* **1976**, *98*, 2652. (b) Itabashi, E.; Parekh, H. V.; Mark, H. B., Jr. *Anal. Lett.* **1978**, *B11*, 515. (c) Kaufmann, E. J.; Espenson, J. H. *J. Am. Chem. Soc.* **1977**, *99*, 7051. (d) Ryan, D. A.; Espenson, J. H.; Meyerstein, D.; Mulac, W. A. *Inorg. Chem.* **1978**, *17*, 3725. (e) Espenson, J. H.; Gjerde, H. B. *Ibid.* **1980**, *19*, 3549. (f) Banks, R. G. S.; Henderson, R. J.; Pratt, J. M. *J. Chem. Soc. A* **1968**, 2886. (g) Balasubramanian, P. N.; Gould, E. S. *Inorg. Chem.* **1983**, *22*, 2365.
- (4) See, for example: (a) Espenson, J. H.; Martin, A. H. *J. Am. Chem. Soc.* **1977**, *99*, 5953. (b) Heckman, R. A.; Espenson, J. H. *Inorg. Chem.* **1979**, *19*, 38.
- (5) The purity of this sample of NaClO₂, as estimated by the method of Kolthoff and co-workers,⁶ was 78.0%, in agreement with the value 80% given on the label. Attempted recrystallization did not improve its quality. Since the impurities were taken to be NaCl (which does not react with B_{12r}) and NaClO₃ (which reacts much more slowly than NaClO₂), this oxidant was used as received and a correction made for the estimated purity.
- (6) Kolthoff, I. M.; Sandell, E. B.; Meehan, E. J.; Bruckenstein, S. "Quantitative Chemical Analysis", 4th ed.; Collier-Macmillan: Toronto, 1969; p 852.

- (7) Dockal, E. R.; Everhart, E. T.; Gould, E. S. *J. Am. Chem. Soc.* **1971**, *93*, 5661.
- (8) Loar, M. K.; Sens, M. A.; Loar, G. W.; Gould, E. S. *J. Am. Chem. Soc.* **1978**, *100*, 330 (footnote 6).
- (9) Stoichiometric studies of the slow reaction of B_{12r} with ClO₃⁻ could not be carried out since consumption of reductant by traces of air slowly leaking into the vessel became competitive with the primary reaction.
- (10) Balasubramanian, P. N.; Gould, E. S. *Inorg. Chem.* **1984**, *23*, 824 (footnote 9). Because of the extreme sensitivity of B_{12s} to traces of oxygen, solutions of that reductant more dilute than 6 × 10⁻⁵ M could not be handled satisfactorily. In contrast, reproducible results could be obtained from experiments using 10⁻⁶ M B_{12r}. Reflecting this difference, lower limits for bimolecular reductions with B_{12r}, obtained by our mixing techniques, lie near 10⁴ M⁻¹ s⁻¹, while those for B_{12s} fall near 10³ M⁻¹ s⁻¹ (see, for example, Table III).

Table I. Stoichiometries of the Reactions of B_{12r} and B_{12s} with Oxyhalogen Species^a

oxidant	reductant	[H ⁺], M	10 ⁵ [Co], M	10 ⁵ [Ox], M	10 ⁵ Δ[Co], M	Δ[Co]/Δ[Ox]
BrO ₃ ⁻	B _{12r}	0.080	4.40	0.42	2.64	6.3
			8.80	0.84	5.50	6.5
			8.80	0.71	4.49	6.4
IO ₃ ⁻	B _{12r}	0.080	6.10	0.65	3.95	6.1
			6.10	0.56	3.23	5.8
			7.20	0.86	5.52	6.5
			8.80	0.86	5.35	6.3
ClO ₃ ⁻	B _{12s}	0.044	4.00	0.37	2.40	6.5
			6.40	0.65	3.94	6.0
			8.40	0.75	4.57	6.1
			8.70	0.44	2.86	6.5
BrO ₃ ⁻	B _{12s}	0.044	4.20	0.166	1.02	6.2
			4.24	0.50	3.18	6.4
			5.94	0.33	1.98	6.0
			5.94	0.42	2.57	6.4
IO ₃ ⁻	B _{12s}	0.044	4.20	0.20	1.35	6.7
			4.60	0.20	1.25	6.2
			6.00	0.47	2.98	6.3
			6.20	0.34	2.07	6.2
ClO ₂ ⁻	B _{12r}	0.044	4.45	0.58	1.69	3.6
			4.45	1.16	3.16	3.4
ClO ⁻	B _{12r}	0.001 ^b	4.05	2.98	2.60	0.87
			4.05	1.49	1.18	0.79
<i>o</i> -IOC ₆ H ₄ COOH	B _{12r}	0.11	4.00	1.30	2.76	2.12
			5.75	2.07	3.98	1.91
			7.10	2.60	5.49	2.10

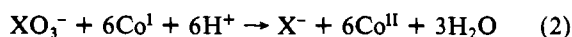
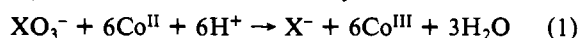
^a Reactions of B_{12r} were followed at 350 nm; those of B_{12s} were followed at 387 nm (see text). ^b HClO₄-glycine buffer.

to within 5% (correcting, where necessary, for the slight consumption of the reagent in excess), and average values did not differ significantly from those obtained from slopes of logarithmic plots of absorbance differences against reaction times. Specific rates from replicate runs with the oxidant in excess checked to better than 8%, whereas reproducibility with the reductant in excess was perceptibly poorer. Specific rates obtained from curves with the oxidant in excess were in agreement with those with reductant in excess, provided account was taken of the stoichiometry of the conversion (6:1 for BrO₃⁻ and ClO₃⁻; 4:1 for ClO₂⁻). Except for the IO₃⁻ reaction, examination of kinetic profiles gave no indication of intermediates formed or destroyed on a time scale comparable to that for the measured disappearance of reductant. Moreover, no sharp drop in absorbance occurred immediately after addition of oxidant, thus ruling out the rapid formation of a partially reduced halogen species. In the reaction of B_{12s} with excess chlorate, the subsequent oxidation of the initial product, B_{12r}, to Co(III) was slow enough so that no difficulty was encountered in monitoring the primary reaction. Temperatures were kept at 25.0 ± 0.2 °C during the entire series of experiments.

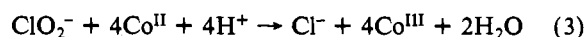
The reaction of iodate with cob(II)alamin did not yield the usual exponential kinetic traces. Instead, a curve having steadily increasing slope (during the first 90% of the reaction) was obtained. This behavior is diagnostic of autocatalysis (see following section); for this reaction, rates were estimated from initial slopes.

Results and Discussion

Reactions of each of the halate anions, both with excess cob(II)alamin and with its Co(I) analogue are seen (Table I) to consume very nearly 6 mol of reductant, indicating that each halogen(V) oxidant is reduced cleanly to the 1- state:



A similar conclusion applies to the reduction of chlorite (which consumes nearly 4 eq of B_{12r}), whereas *o*-iodosobenzoic acid is converted to the iodo-substituted aromatic:



Marked departures from the expected 2:1 stoichiometry are observed for the reaction of B_{12r} with hypochlorite, suggesting

that this very active oxidant is attacking the corrin ring system or a side chain, as well as the cobalt(II) center.

Kinetic data pertaining to two representative systems, bromate + B_{12r} and chlorate + B_{12s}, appear in Table II. Both reactions are seen to be strongly acid dependent. The B_{12r}-BrO₃⁻ reaction is very nearly first order in [H⁺], whereas the rate law for the B_{12s}-ClO₃⁻ reactions exhibits a kinetic acidity dependence of the type $a + b[\text{H}^+]$. There is no evidence of kinetic saturation within the acidity ranges examined. The observed 6:1 relationship between the loss of reductant (with halate in excess) and loss of halate (with reductant in excess) (Table II) indicates that under both sets of conditions we are observing the reduction of halate to halide. The straightforward exponential decay curves generated with the oxidant in excess, in conjunction with the absence of an initial sharp drop in absorbance, tell us that the overall rate is being determined by the first step in the sequence, the initial attack on halate. It may then be inferred that halates are reduced more slowly than any of the halogen oxidation states intervening between 5+ and 1-, a conclusion in accord with the rapidity of the B_{12r}-ClO₂⁻ reaction noted here. Specific rates for the reactions in this series are summarized in Table III.

Except for the reduction of *o*-iodosobenzoic acid, rate laws for all reactions in this series feature a prominent term first order in [H⁺], and for each of the B_{12r}-halate reactions no other kinetic term is observed.¹¹ Since the pK_a for B_{12r} has been recorded to be near 3.0,² i.e., well above the pH range examined for these systems, this [H⁺] dependence must be taken to arise from protonation of the oxidants. Bimolecular specific rates for reduction of the reactive acidic halogen(V) species, XO₃H, may then be obtained by multiplying the tabulated specific rates by the recorded¹² acidity constants for the halic acids. The resulting values (M⁻¹ s⁻¹ at 25 °C) are

(11) An earlier observation (Boos, R. N.; Carr, J. E.; Conn, J. B. *Science* **1953**, *117*, 603) that BrO₃⁻ does not oxidize cob(II)alamin at a measurable rate at pH 9.3 is in accord with the absence of an acid-independent term in the rate law for this reaction.

(12) (a) Choppin, G. R.; Ensor, D. D. *J. Inorg. Nucl. Chem.* **1977**, *39*, 1226. (b) Naidich, S.; Ricci, J. F. *J. Am. Chem. Soc.* **1939**, *61*, 3268.

Table II. Kinetic Data for the Oxidation of Vitamin B_{12s} (Cob(I)alamin) with Chlorate and Oxidation of B_{12r} (Cob(II)alamin) with Bromate^a

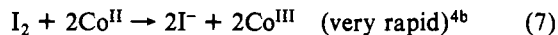
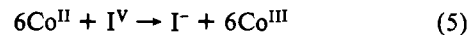
10 ⁵ [Ox], M	10 ⁵ [Red], M	10 ² [H ⁺], M	k _{obsd} ^b	k ₂ ^c
B _{12s} + ClO ₃ ⁻ System				
11.1	6.16	0.132	1.70	1.53
22.2	6.16	0.132	3.5	1.55
44.4	6.16	0.132	6.7	1.52
9.76	6.16	1.05	7.9	8.1
9.76	6.16	0.71	6.6	6.8
9.00	6.16	0.60	4.6	5.1
9.00	6.16	0.43	3.0	3.3
9.00	6.16	0.24	2.4	2.7
9.00	6.16	0.18	2.0	2.3
9.00	6.16	0.132	1.39	1.54
9.00	6.16	0.059	0.90	1.00
0.22	7.15	0.132	2.4	2.1
0.22	7.22	0.245	3.0	2.5
0.22	7.21	0.60	5.0	4.2
0.22	7.10	0.70	6.6	5.8
0.22	7.10	1.05	9.2	7.8
B _{12r} + BrO ₃ ⁻ System				
9.64	4.28	3.6	1.28	1.33
24.1	4.28	3.6	3.6	1.49
48.2	4.28	3.6	7.2	1.51
9.36	4.28	1.4	0.78	0.83
9.64	4.28	2.5	1.13	1.17
9.64	4.28	5.8	2.3	2.4
9.36	4.28	10.0	5.1	5.4
8.50	4.28	15.6	6.7	7.9
9.36	4.28	19.2	9.1	9.8
9.36	4.28	3.6 ^d	2.3	2.4
9.36	4.28	3.6 ^e	1.76	1.88
0.20	7.06	51	3.2	26
0.20	7.10	38	2.4	20
0.20	7.10	24.3	1.54	13.4
0.20	7.10	13.9	0.91	7.8
0.20	7.10	7.2	0.51	4.3

^a Reactions were carried out at 25.0 °C; the supporting electrolyte was LiClO₄ (μ = 0.50). B_{12s}-ClO₃⁻ reactions were buffered with glycine and its hydroperchlorate. ^b Pseudo-first-order rate constants (in s⁻¹ × 10²) = -d[Red]/dt[Red]⁻¹. ^c Second-order rate constants (in M⁻¹ s⁻¹ × 10⁻²), obtained by dividing k_{obsd} by [Ox] when the oxidant was in excess or by [Red]/6 when the reductant was in excess. ^d μ = 0.11 M. ^e μ = 0.28 M.

3.7 × 10³ for HClO₃, 1.0 × 10⁶ for HBrO₃, but only 7 for HIO₃. The kinetic advantage that bromate enjoys over chlorate in redox reactions has been noted by other workers¹³ but has not been satisfactorily explained. Since we are, in effect, monitoring the initial slow step, the reduction of pentapositive to tetrapositive halogen, any rationalization of trends must take into account the properties of the latter state, and in the case of Br(IV) and I(IV), such intermediates, although almost certainly intervening in other 1e reductions of halates,^{13c,14} have thus far been chemically elusive.

The B_{12r} reaction with IO₃⁻, but not with ClO₃⁻ or BrO₃⁻, is strongly autocatalytic. Data in Table IV, pertaining to a typical B_{12r}-IO₃⁻ run (at 0.080 M H⁺), demonstrate that rates

increase by a factor of 4 within a single run. The catalytic species here is doubtless I⁻, which, when added as such to the primary reaction mixture, has been found to accelerate the primary reaction markedly. We suggest that the catalytic sequence (eq 5-7) involves formation of I₂, which has been



shown^{4b} to react with B_{12r} rapidly ($k = 6 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$) under conditions similar to ours. The rate law for the reaction of IO₃⁻ with I⁻ (reaction 6), which may be taken to be the kinetic bottleneck in the catalytic sequence, has been shown¹⁵ to be of the form $k_6[\text{I}^-]^2[\text{IO}_3^-][\text{H}^+]^2$, where k_6 pertains to the consumption of IO₃⁻. For a combination of the uncatalyzed and catalyzed paths, we may then write

$$\text{rate} = -d[\text{B}_{12r}]/dt = k_5[\text{B}_{12r}][\text{IO}_3^-][\text{H}^+] + 6k_6[\text{I}^-]^2[\text{IO}_3^-][\text{H}^+]^2 \quad (8)$$

in which the factor 6 in the second term accommodates the B_{12r}/IO₃⁻ stoichiometry in the catalytic sequence. If IO₃⁻ is taken in large excess, [B_{12r}]₀ is represented as a , and the extent of reaction is represented as x , (8) may be rewritten as

$$\text{rate} = [\text{H}^+][\text{IO}_3^-][k_5(a-x) + 6k_6(x/6)^2[\text{H}^+]] \quad (9)$$

and a plot of the function $\text{rate}/[\text{H}^+][\text{IO}_3^-] - k_5(a-x)$ vs. $x^2[\text{H}^+]/6$ should have k_6 as slope. Such a plot, from the data in Table IV, yields a value $4.8 \times 10^8 \text{ M}^{-4} \text{ s}^{-1}$ at $\mu = 0.50$.¹⁶ As expected,¹⁷ this falls significantly below that the recorded for the extrapolated (to $\mu = 0$) figure¹⁵ ($1.3 \times 10^9 \text{ M}^{-4} \text{ s}^{-1}$).

Autocatalysis is not observed during the reductions of BrO₃⁻ and ClO₃⁻, for with these oxidants the uncatalyzed reaction is much more rapid than that with IO₃⁻, whereas the halate-halide reactions analogous to (6) are much slower. In a run with [B_{12r}] = 4 × 10⁻⁵ M, [BrO₃⁻] = 4 × 10⁻⁴ M, and [H⁺] = 0.10 M, for example, the loss of B_{12r} by the primary reaction occurs at a rate 7 × 10⁻⁶ M s⁻¹. When this reaction is half-complete ([Br⁻] = 3.3 × 10⁻⁶ M), the rate of loss of BrO₃⁻ from reaction with Br⁻ may be calculated¹⁸ as 3.8 × 10⁻¹¹ M s⁻¹. A similar comparison for ClO₃⁻ (at the 0.01 M level) yields 3 × 10⁻⁷ M s⁻¹ as the initial rate of the primary reaction, but a value less than 10⁻²² M s⁻¹ for the rate of the halide-halate reaction¹⁹ when the primary reaction is half-complete.

Although protonation of the oxidant appears to be necessary for the halate-B_{12r} reactions, the more facile oxidant, ClO₂⁻,

- (15) Abel, E.; Stadler, F. Z. *Phys. Chem. Stoichiom. Verwandtschaftsl.* **1926**, *122*, 49. The indicated expression appears to apply to systems in which [I⁻] > 10⁻⁶ M. A different rate law, first order in [I⁻], has been proposed for much lower concentrations of I⁻ (Dushman, S. J. *Phys. Chem.* **1904**, *8*, 483). See also: Myers, O. E.; Kennedy, J. W. *J. Am. Chem. Soc.* **1950**, *72*, 897.
- (16) This plot and analogous plots at other acidities are found to curve downward at low values of [B_{12r}], possibly reflecting a partial shift in the rate-determining step from (6) to (7).
- (17) A reaction in which an activated complex of net charge 1- is formed from a combination of three 1- ions and two 1+ ions should feature a substantial negative kinetic salt effect.
- (18) Birk and Kozub^{14c} have recorded the rate law for the BrO₃⁻-Br⁻ reaction as

$$-d[\text{BrO}_3^-]/dt = 2.86[\text{Br}^-][\text{BrO}_3^-][\text{H}^+]^2 \quad (10)$$

at 25 °C and μ = 0.5.

- (19) The rate law for the reaction of Cl⁻ with ClO₃⁻ in aqueous acidic solutions has been reported to be

$$-d[\text{ClO}_3^-]/dt = 0.001[\text{H}^+]^4[\text{ClO}_3^-]^2[\text{Cl}^-]^2 \quad (11)$$

at 50 °C. Luther, R.; MacDougall, F. H. Z. *pHys. Chem., Stoichiom. Verwandtschaftsl.* **1908**, *62*, 199.

- (13) See, for example: (a) Downs, A. J.; Adams, C. J. "Comprehensive Inorganic Chemistry"; Bailar, J. C., Jr.; Ed.; Pergamon Press: Oxford, 1973; Collect. Vol. II, p 1432. (b) Latimer, W. L. "Oxidation Potentials", 2nd ed.; Prentice-Hall: Englewood Cliffs, NJ, 1952; Chapter 5. (c) Anbar, M.; Neta, P. *J. Inorg. Nucl. Chem.* **1966**, *28*, 1645.
- (14) See, for example: (a) Thompson, R. C.; Gordon, G. *Inorg. Chem.* **1966**, *5*, 557. (b) Birk, J. P. *Ibid.* **1973**, *12*, 2468. (c) Birk, J. P.; Kozub, S. G. *Ibid.* **1973**, *12*, 2460. (d) Thompson, R. C. *Ibid.* **1975**, *14*, 1280. (e) Bakac, A.; Thornton, A. T.; Sykes, A. G. *Ibid.* **1976**, *15*, 274. (f) Cornelius, R. D.; Gordon, G. *Ibid.* **1976**, *15*, 1002. (g) Birk, J. P. *Ibid.* **1978**, *17*, 504.

Table III. Specific Rates for the Oxidation of Vitamin B_{12r} (Cob(II)alamin) and B_{12s} (Cob(I)alamin) with Oxyhalogen Species

oxidant (Ox)	reductant	[H ⁺], M	pK _a (HOx)	k ^a
ClO ₃ ⁻	B _{12r}	0.02-0.41	-2.7 ^b	7.4[H ⁺]
ClO ₃ ⁻	B _{12s}	0.0005-0.010		90 + (6.9 × 10 ⁴)[H ⁺]
ClO ₂ ⁻	B _{12r}	0.0002-0.004	1.66 ^d	2.1 × 10 ⁴ + (5.6 × 10 ⁷)[H ⁺]
BrO ₃ ⁻	B _{12r}	0.010-0.50	-2.3 ^b	(5.2 × 10 ³)[H ⁺]
BrO ₃ ⁻	B _{12s}	10 ⁻⁵ -10 ⁻²		>10 ³
IO ₃ ⁻	B _{12r}	0.010-0.10	0.5 ^c	22[H ⁺] ^e
IO ₃ ⁻	B _{12s}	10 ⁻⁵ -10 ⁻²		>10 ³
o-C ₆ H ₄ (COOH)(IO)	B _{12r}	0.0040-0.13	7.4 ^f	72 + 3.5[H ⁺] ⁻¹

^a Second-order specific rates in M⁻¹ s⁻¹, calculated as indicated in Table II. Reactions were carried out at 25 °C; μ = 0.52 M (LiClO₄ - HClO₄). ^b Choppin, G. R.; Ensor, D. D. *J. Inorg. Nucl. Chem.* 1977, 39, 1226. ^c Naidich, S.; Ricci, J. F. *J. Am. Chem. Soc.* 1939, 61, 3268. The value recorded by these authors (0.79, μ = 0) has been adjusted to μ = 0.5 M. ^d Smith, R. M.; Martell, A. E. "Critical Stability Constants"; Plenum Press: New York, 1976; Vol. 4, p 134. ^e Autocatalytic reaction; specific rate was determined from initial rate. ^f Value for the uncharged iodoso acid (Caraway, W. T.; Hellerman, L. *J. Am. Chem. Soc.* 1953, 75, 5334.)

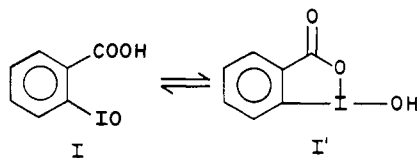
Table IV. Autocatalysis in the Reaction of Vitamin B_{12r} with Iodate^a

time, s	10 ⁵ [B _{12r}], M	rate ^b	time, s	10 ⁵ [B _{12r}], M	rate ^b
0	4.05	2.8	198	2.52	7.2
112	3.38	4.3	244	1.96	8.8
162	2.95	5.6	264	1.53	10.6

^a Data refer to a single kinetic run, in which [B_{12r}]₀ = 4.05 × 10⁻⁴ M, [IO₃⁻] = 4.2 × 10⁻⁴ M, [H⁺] = 0.08 M, μ = 0.50 (LiClO₄ - HClO₄), and T = 25 °C. ^b Instantaneous rates, -d[B_{12r}]/dt, M s⁻¹ × 10⁸.

is seen to react in both its protonated and nonprotonated forms. As with ClO₃⁻ and BrO₃⁻, undistorted kinetic curves, with both oxidant and reductant in excess, indicate that here again, the initial 1e reduction, giving a Cl(II) species, is rate determining.²⁰

Of the oxidants considered here, only *o*-iodosobenzoic acid (I) features the inverse-[H⁺] path in its reduction by B_{12r}.



This path, the major one at [H⁺] values below 0.05 M, may reflect deprotonation of the oxidant or of the reductant (kinetics alone is noncommittal on this point). We favor the latter alternative. Aside from the circumstance that deprotonation of a reductant generally makes it more reactive (whereas the reverse is usually true for an oxidant), we point out that if attack by B_{12r} on the iodoso anion were predominant, it would occur at a bimolecular specific rate (obtained by dividing the inverse-[H⁺] coefficient by the known²¹ K_a for the iodoso acid, 4 × 10⁻⁶) near 10⁸ M⁻¹ s⁻¹. This very high value appears much less reasonable than a specific rate near 3500 M⁻¹ s⁻¹, which

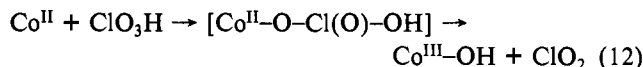
(20) (a) The known disproportionation of HClO₂ to ClO₂, ClO₃⁻, and Cl⁻ is much too slow to compete significantly with reduction by B_{12r} under our conditions. Perceptible departures from the expected 4:1 stoichiometry for the B_{12r}-ClO₂⁻ reaction (Table I) may be attributed, at least in part, to oxidation of ClO₂⁻ by traces of O₂, forming the sluggishly reacting ClO₃⁻. (b) A reviewer suggests the possibility that one or more of these reductions by B_{12r} is initiated by a two-electron transaction, giving a Co(IV) chelate, which would then be expected to undergo rapid disproportionation with unreacted B_{12r}. Although our data do not preclude such a sequence, we find no substantial experimental precedent for such a d⁵ cobalt species and therefore consider such a mechanism to be relatively unlikely.

(21) Caraway, W. T.; Hellerman, L. *J. Am. Chem. Soc.* 1953, 75, 5334. This value, which we have confirmed potentiometrically, is obviously uncharacteristically high for an ortho-substituted benzoic acid, (for which a pK less than 5 would be expected). In conjunction with other data, it has led a number of workers to propose that *o*-iodosobenzoic acid exists predominantly in the cyclic form I'. For a summary of these arguments, see: Baker, G. P.; Mann, F. G.; Sheppard, N.; Tetlow, A. *J. Chem. Soc.* 1965, 3721.

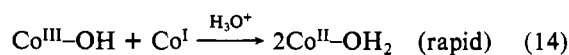
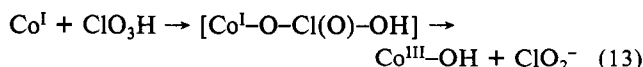
would be calculated in an analogous manner for reaction of the uncharged oxidant with the deprotonated form of cob(II)alamin, (pK_a = 3.0).² Note also that inverse-[acid] rate dependencies have recently been observed for B_{12r} reductions of metal-center oxidants that are devoid of appreciably acidic hydrogens.²²

Of the reductions by the cobalt(I) derivative, B_{12s}, only that of ClO₃⁻ proceeds slowly enough to allow rate estimates by our techniques. Comparison with the B_{12r}-ClO₃⁻ reaction is complicated by the appearance of two terms in the rate law for B_{12s}, but the ratio of [H⁺]-dependent terms is seen to be 10⁴. Although one must be cautious in drawing mechanistic conclusions from a single ratio, this value makes it unlikely that both cobalamin reductants react with ClO₃⁻ by simple outer-sphere single-electron transfers. The difference in formal potentials of the two reductants, 0.78 V,² corresponds, by the Marcus model,²³ to a 10^{6.5}-fold difference in specific rates. Moreover, Lexa² has presented data indicating that self-exchange in the Co^I-Co^{II} corrin system is significantly more rapid than that in the Co^{II}-Co^{III} system, a difference that should further favor reduction by B_{12s}. The departure from the outer-sphere model is thus in the direction pointing to a substantial inner-sphere component²⁴ for reduction by B_{12r} and leaves upon the question in the case of B_{12s}.

Since both B_{12r} (5-covalent Co^{II}) and B_{12s} (4-covalent Co^I) are coordinatively unsaturated under the conditions used, we can envisage inner-sphere paths utilizing oxygen bridges for both reductants. That involving B_{12r} is necessarily a one-electron transaction, (12), but as in earlier studies of reductions



by B_{12s},^{3a,10} there is a major ambiguity associated with the Co(I) reductant. We cannot say as yet whether we are dealing with the transfer of a single electron (in a manner analogous to (12)) or whether this reaction is initiated by a two-electron change, forming Co(III), which then very rapidly^{3c,d} undergoes comproportionation:



On one hand, evidence pointing to 2e initiation has been

(22) It has been found, example, (Balasubramanian, P. N., unpublished experiments, 1983) that (NH₃)₂CoCl²⁺ and its bromo analogue react with B_{12r} at rates inversely proportional to [H⁺].

(23) Marcus, R. A. *J. Chem. Phys.* 1956, 24, 866, 979. It is assumed that an increase in ΔG[‡] resulting from an increase in the standard potential of the reductant is half the increase in ΔG[°]. (See, for example: Hush, N. S. *Trans. Faraday Soc.* 1961, 57, 557.)

(24) See, for example: Gould, E. S. *Inorg. Chem.* 1979, 18, 900.

presented for B_{12s} reductions of nitrate³⁸ and substituted hydroxylamines¹⁰ in acid solution, and an analogous route has been proposed for reduction of N_2O at higher pH.²⁵ At the same time, however, Bakac and co-workers^{14e} have demonstrated that reductions of BrO_3^- and IO_3^- by V^{2+} (which, like B_{12s} , can undergo either 1e or 2e changes) proceed by sin-

gle-electron transfers, and experiments of Gordon and Tewari²⁶ point to the same conclusion for the $V^{2+}-ClO_3^-$ reaction. Reservation of judgment on this point appears to be advisable.

Registry No. B_{12s} , 18534-66-2; B_{12r} , 14463-33-3; ClO_3^- , 14866-68-3; BrO_3^- , 15541-45-4; IO_3^- , 15454-31-6; ClO_2^- , 14998-27-7; *o*-iodosobenzoic acid, 304-91-6.

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(26) Gordon, G.; Tewari, P. H. *J. Phys. Chem.* **1976**, *70*, 200.

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Oxidation-Reduction Reactions of Complexes with Macrocyclic Ligands. Role of Kinetic Factors in Distinguishing Mechanistic Pathways in Reactions of Copper(I) Complexes with Coordinated Dioxygen¹

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The rates of reaction between several simple copper(I) complexes and the coordinated dioxygen moiety of $Co([14]aneN_4)(OH_2)O_2^{2+}$ ($[14]aneN_4 = 1,4,8,11$ -tetraazacyclotetradecane) have been examined. The very rapid reactions are inferred to span a mechanistic range from simple electron transfer for simple Cu^I (polypyridyl) complexes to transient μ -peroxo ($Co-O-O-Cu$) adduct formation for $CuCl_3^{2-}$ and $Cu(C_2H_4)^+$. The discrimination between mechanistic pathways is attributed to intrinsic kinetic factors rather than to the thermodynamics of $Cu^{II}-(O_2^{2-})$ bond formation.

Introduction

Copper-containing enzymes mediate the reduction of dioxygen in several biological systems. The role of the copper is variously ascribed to O_2 binding or to electron transport to the reaction center.² Despite the interest in these enzymatic systems, and despite the commonly recognized catalytic role of copper compounds in redox processes, there are many perplexing features of the oxidation-reduction chemistry of copper complexes. For example, the large differences in copper(I) and copper(II) stereochemistry ought to lead to very large reorganizational barriers to oxidation-reduction processes involving complexes in these oxidation states. Thus, electron-transfer reactions of the aquocopper(II)-aquocopper(I) couple are quite sluggish,³ in apparent contradiction to the often observed catalytic role of copper couples.

Owing to the obvious problems of detecting very small amounts of short-lived, reactive intermediates, there have been few direct studies of the reactions of 1:1 dioxygen adducts of transition-metal complexes. However, we have recently found that the 1:1 adduct of O_2 and $Co([14]aneN_4)(OH_2)_2^{2+}$ ⁴ is relatively strongly absorbing and that $Co([14]aneN_4)-$

$(OH_2)O_2^{2+}$ persists long enough in dilute aqueous solution that many of its simple reactions may be investigated.⁵ Our work with the $Co([14]aneN_4)(OH_2)O_2^{2+}$ intermediate has shown that the coordinated dioxygen moiety has a relatively small intrinsic barrier to electron transfer, that it is only a mild reducing agent ($E^f \approx 0.3$ V vs. NHE), and that any selectivity of simple inner-sphere over outer-sphere electron-transfer processes has appeared to originate in the very large stability of the $M-O$ bonds of the μ -peroxo products.^{5c,d}

We have undertaken the present study to determine whether the reactivity patterns in copper-oxygen systems are dictated largely by product stabilities, as seems the case for many reactions of coordinated superoxide, or whether the differences in copper(I) and copper(II) stereochemistries are important in dictating the reaction pathway.

Experimental Section

Materials. Copper(I) chloride (99.999%) and Cu_2O (99.95%) were obtained from Alfa Chemicals. Tetrakis(acetonitrile)copper(I) perchlorate was synthesized from Cu_2O by the method of Hemmerich and Sigwart.⁶

The macrocyclic ligands $[14]aneN_4$ ⁷ and $Me_6[14]-4,11$ -diene N_4 ^{4,8} and the complexes $[Co(Me_6[14]-4,11\text{-diene}N_4)(OH_2)_2](ClO_4)_3$,⁹ $[Co(Me_4[14]tetraeneN_4)(OH_2)](ClO_4)_3$,¹⁰ and $Co(Me_4[14]tetrae-$

(1) Partial support of this research by the National Institutes of Health (Grant AM14341) is gratefully acknowledged.

(2) For reviews see: (a) Solomon, E. I. In "Copper Coordination Chemistry: Biochemical and Inorganic Perspectives"; Karlin, K. D.; Zubieta, J., Eds.; Adenine Press, Guildford, NY, 1983, p 1. (b) Zuberbühler, A. D. *Ibid.*, p 237. (c) Rogic, M. M.; Swerdloff, M. D.; Demmin, T. R. *Ibid.*, p 259. (d) Gray, H. B.; Solomon, E. I. In "Copper Proteins"; Spiro, T. G., Ed.; Wiley: New York, 1982; Vol. I, p 1. (e) Solomon, E. I. *Ibid.*, p 41. (f) Malmström, B. G. In "Metal Ion Activation of Dioxygen"; Spiro, T. G., Ed.; Wiley: New York, 1980; p 181.

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(4) Ligand abbreviations: $[14]aneN_4$ (cyclam) = 1,4,8,11-tetraazacyclotetradecane; $Me_6[14]-4,11$ -diene N_4 = 5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradeca-4,11-diene; tpy = 2,2',2''-terpyridine; 4,4'- Me_2 bpy = 4,4'-dimethyl-2,2'-bipyridine; bpy = 2,2'-bipyridine; im = imidazole.

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