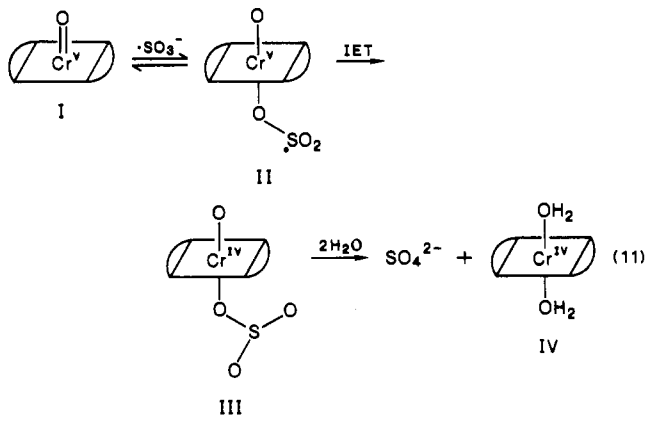
anion $SO_3^{\bullet-}$ (k_2/k_4 = 20–35) points to an inner-sphere path for the Cr^V–S^5 reaction, (3). The latter is represented schematically as (11), in which formation of the precursor complex, II, from



the $SO_3^{\bullet-}$ radical anion and the Cr(V) chelate I precedes internal electron transfer (IET) to form the Cr(IV)–S(VI) intermediate, III, which features an electron-deficient sulfur atom. Complex III then undergoes rapid hydration (at sulfur) and aquation (at Cr^{IV}) to yield the $Cr^{IV}(H_2O)_2$ complex, IV.[33] We cannot say why such a mechanism (or one related to it) is favored for the Cr^V–S^5 reaction but not for the remaining steps in the proposed series, (2), (4), and (5). We note, however, that Cr^V–S^5 may be the only one of the four steps that involves interaction between a radical and oxo-bound chromium center.[34]

Finally, it may be asked whether additional systems will exhibit the type of kinetic behavior observed here. If we retain the same oxidant, three constraints are imposed on the reductant. First, it must be able to entertain both 1e and 2e changes, with the 1e product stable enough to undergo partition between subsequent reaction paths; reagents in this class include nitrite, dithionite, chlorite, vanadium(III), substituted hydroquinones, and aromatic amines. Second, the lower oxidation state must react more rapidly with Cr(IV) than with Cr(V) (in accord with the relative formal potentials of the two oxidants);[28] this is probably the case for each of the indicated reductants. Most important, there must be a reversal of relative oxidation rates (pertaining to Cr^{IV} and Cr^V) in going from the reductant to the 1e intermediate; i.e., this intermediate must react more rapidly with Cr^V than with Cr^{IV}. Experience with earlier systems[6,8,13] suggests that metal-center reductants are unlikely to fulfill the latter requirement. However the behavior of oxygenated reductants and more complicated organic molecules remains to be examined.

Acknowledgment. The authors are indebted to Dr. Kenneth Long, Dr. V. S. Srinivasan, and Dr. Y.-T. Fanchiang for early experiments that initiated interest in this system. We are also grateful to Dr. J. W. Reed, Dr. R. D. Cornelius, Dr. K. Chandra, and H. A. Thompson for assistance with computer procedures and to Professors M. Manes, J. H. Espenson, I. R. Epstein, and K. Kustin for unusually helpful discussions.

Registry No. I, 84622-43-5; HSO_3^-, 15181-46-1; Cr^{4+}, 15723-28-1.

(33) It is assumed that loss of the monodentate sulfate ligand from the Cr(IV) center is much more rapid than loss of the chelating carboxylato group. Our experiments yield no evidence for formation of significant quantities of a (sulfato)chromium(III) product.

(34) The ligand configuration about Cr(IV) in solution is, at present, uncertain. Although a 5-coordinate oxo ion (analogous to that in Cr^V and V^{IV}) is not unreasonable, an octahedral configuration (analogous that in Cr^{III}) has also been suggested. See, for example: Espenson, J. H. *Acc. Chem. Res.* **1970**, *3*, 347.

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Electron Transfer. 79. Reductions of Organic Disulfides by Vitamin B_{12s} (Cob(I)alamin)[1]

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Vitamin B_{12s} (cob(I)alamin) reacts rapidly and completely with organic disulfides in aqueous media, yielding the corresponding thiols and cob(II)alamin, whereas reactions of the cobalt(II) complex with disulfides are slow and incomplete. Reactions are first order in both B_{12s} and disulfide and are generally accelerated three- to sevenfold by monoprotonation of a basic site on the oxidant. Rate enhancements resulting from diprotonation (when it occurs) are slight. Reduction of the monoanion of dithiodiacetic acid (I) is unexpectedly rapid, suggesting destabilization of the S–S bond by internal hydrogen bonding. Two different reaction sequences for the series, one involving a thiyl (RS•) intermediate and the other proceeding through a Co(III) transient, are consistent with the data at hand.

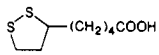
Earlier reports[2] by Espenson and co-workers described reductions of peroxides with cobalt(II) macrocycles, including vitamin B_{12r} (cob(II)alamin). These reactions were generally rapid, and analysis of the results suggested some diversity of mechanistic detail. It therefore appeared reasonable to examine analogous reductions of organic disulfides (RSSR). The principal reduction products, in aqueous media, were expected to be the corresponding thiols, with the overall transformations thus being closely related to those of importance in a variety of biosystems.[3] In our hands, however, reductions of disulfides with B_{12r} proved to be slow and incomplete, even at very low pHs, possibly reflecting the small difference in formal potentials of the reacting species.[4–6]

We therefore turned to reactions of disulfides with the much stronger reductant, vitamin B_{12s} (cob(I)alamin). As anticipated,[7,8]

(1) Sponsorship of this work by the National Science Foundation (Grant No. 8313253) is gratefully acknowledged.
(2) (a) Espenson, J. H.; Martin, A. H. *J. Am. Chem. Soc.* **1977**, *99*, 5953. (b) Heckman, R. A.; Espenson, J. H. *Inorg. Chem.* **1979**, *18*, 38.
(3) See, for example: Ziegler, D. M. *Annu. Rev. Biochem.* **1985**, *54*, 305.
(4) Formal potentials (vs. NHE at pH 1) for B_{12r} and B_{12s} have been reported as +0.30 and –0.48 V, respectively;[5] both of these values are strongly pH dependent. Formal potentials for thiol–disulfide systems that are devoid of strongly electron-attracting or electron-repelling groups lie between +0.02 and +0.30 V at pH 0, and between –0.20 and –0.40 V at pH 7.[6]
(5) Lexa, D.; Saveant, J.-M. *Acc. Chem. Res.* **1983**, *16*, 235.
(6) See, for example: Clark, W. M. *Oxidation-Reduction Potentials of Organic Systems*; Williams and Wilkins: Baltimore, MD, 1960; p 486.
(7) The difference in formal potentials of B_{12r} and B_{12s} corresponds, by the Marcus model for outer-sphere reactions,[8] to a $10^{6.5}$-fold difference in specific rates. Substantial changes in this ratio are expected if one or both of these reductants utilizes an inner-sphere path.

0020-1669/86/1325-3353$01.50/0

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

disulfide (SS)	pH	$10^5[SS]_0$	$10^5[B_{12s}]_0$	$10^5\Delta[B_{12s}]$	$\Delta[B_{12s}]/\Delta[SS]$
$(HOOCCH_2S)_2$ (I)	3.0	1.08	3.18	2.22	2.05
		1.57	5.67	3.29	2.09
		2.05	7.10	4.47	2.19
	6.9	0.70	4.43	1.65	2.37
		1.37	5.13	2.91	2.12
		2.73	6.60	5.56	2.03
$(HOCH_2CH_2S)_2$ (II)	3.8	0.74	5.80	1.59	2.14
	4.0	2.51	6.70	5.45	2.17
	5.2	1.82	5.57	3.82	2.10
$[^-OOCCH(NH_3^+)CH_2S]_2$ (III)	3.7	1.37	4.40	2.83	2.06
	3.8	2.58	6.77	5.53	2.15
 IV	4.6	0.88	3.27	2.02	2.30
	5.0	1.06	5.80	2.04	1.92
4,4′-$(py)_2S_2$[b] (V)	3.7	1.64	5.20	3.30	2.01

[a] Reactions were monitored at 387 nm; all concentrations in M. [b] "Aldrithiol-4".

these were rapid, but some fell within the range measurable by stopped-flow spectrophotometry.

Experimental Section

Materials. Organic disulfides (Aldrich Chemical and Pfaltz and Bauer), hydroxocobalamine hydrochloride (Sigma), sodium borohydride,[9] (Fisher) and phthalic acid (Aldrich) were used as received, as were phosphate, carbonate, borate, and glycine buffer components (Fisher). Lithium perchlorate, for use in kinetic experiments, was prepared as described.[10a] All reactions were carried out under oxygen-free N_2 in distilled water that had been previously boiled and sparged with N_2 for at least 4 h.

Cob(I)alamin was generated in solution from the cobalt(III) complex, hydroxocobalamin hydrochloride. Reduction in acidic solutions was carried out with zinc amalgam,[10b] whereas reduction in basic solution[11] utilized sodium borohydride in the presence of catalytic amounts of $PdCl_4^{2-}$. For stoichiometric experiments, B_{12s} solutions were prepared in spectrophotometric cells,[10b] for kinetic runs, solutions of B_{12s} were generated externally and then transferred under N_2 to the reservoir syringe of the stop-flow instrument.

Stoichiometric Studies. Stoichiometries of the reactions, with B_{12s} in excess, were determined in buffered media by adding a deficiency of disulfide to the B_{12s} solution, waiting only 30–60 s, and then measuring the decreases in absorbance at 387 nm. These changes were compared with those observed when B_{12s} was treated with excess disulfide. When B_{12s} was generated in acid solution, the solution was buffered before reaction; when B_{12s} was generated with $NaBH_4$, the buffering species were instead added to the disulfide. Corrections were made for the slight but measurable (less than 5%) loss in absorbance when the corresponding volume of water or aqueous buffer, devoid of disulfide, was added to the B_{12s} solution. Representative results appear in Table I.

Estimation of Acidity Constants. Acidity constants (23 °C, 0.2 M $LiClO_4$) for cystine and for the dihydrochlorides of cystamine and cystine dimethyl ester were estimated by partial titration with NaOH. Since each of these disulfides has two pK_A values separated by a relatively small interval,[12] data (pH readings) were treated by Speakman's procedure.[13] Thioctic acid (IV) is only slightly soluble (0.004 M, 23 °C) in the medium used; its single pK value was estimated by a partition method in which the solid acid was allowed to equilibrate with 0.056 M aqueous sodium acetate, after which the total acidity in the supernatant solution was determined.[14]

Kinetic Studies. Rates were estimated from measurements of decreases in absorbance at 387 nm by using a Durrum-Gibson stopped-flow spectrophotometer. Acidities were regulated by addition of known concentrations of phosphate, carbonate, phthalate, or borate buffers to the disulfide solutions before mixing;[15a] pH values of the resulting solutions were checked experimentally. Total ionic strength was generally maintained near 0.20 M by addition of $LiClO_4$. Reactions were first order each in disulfide and B_{12s} but were carried out under pseudo-first-order conditions with the disulfide usually in greater than tenfold excess. Changing the concentration of borohydride (from 4×10^{-4} to 1×10^{-3} M) did not significantly affect the rate of the primary reaction.[15b]

Conversions were generally followed to at least 5 half-lives. Replicate reactions, with the same pair of master solutions, were carried out until decay curves for two successive runs superimposed. Agreement between rate constants, obtained from logarithmic plots of absorbance differences against reaction times, was better than 6% (for runs with different master solutions) at the highest pHs used. However, results became progressively less precise as the acidity was raised, reflecting the increased rate of hydrogen bubble formation from the added borohydride. Agreement between runs in phthalate buffers (pH near 5) was not better than 9%, whereas acceptable kinetic measurements in glycine buffers (pH near 3) could generally not be carried out by our methods. Relatively large uncertainties in the initial concentrations of B_{12s} that had been transferred appeared to preclude reliable kinetic runs under second-order conditions.

Kinetic profiles gave no indication of intermediates formed or destroyed on a time scale comparable to that for the measured disappearance of B_{12s}. No sharp drops in absorbance immediately after mixing were noted, thus ruling out the rapid formation of a partially reduced sulfur intermediate. In all cases, the electronic spectrum of the oxidation product corresponded to that of B_{12r} (cob(II)alamin).[10b,16]

Results and Discussion

Reductions of each of the disulfides with excess B_{12s} are seen to consume very nearly 2 mol of Co(I) (Table I). The net reactions may thus be represented

$$R_2S_2 + 2Co(I) + 2H^+ \rightarrow 2RSH + 2Co(II) \qquad (1)$$

The persistence of 2:1 stoichiometry with the pyridyl-substituted disulfide (V) indicates that, under the conditions used, reduction of the pyridine ring is much slower than that of the S–S linkage.

Representative kinetic data are assembled in Table II. Specific rates for most reactions in the series are seen to increase with acidity, a trend that may be attributed to partial protonation of

(8) Marcus, R. A. *J. Chem. Phys.* **1956**, *24*, 866, 979.
(9) Reproducibility in kinetic runs was best when freshly opened $NaBH_4$ was used to reduce the Co(III) complex. After a given container had been opened several times and allowed to stand, kinetic results became erratic.
(10) (a) Dockal, E. R.; Everhart, E. T.; Gould, E. S. *J. Am. Chem. Soc.* **1971**, *93*, 5661. (b) Balasubramanian, P. N.; Gould, E. S. *Inorg. Chem.* **1983**, *22*, 2635.
(11) (a) Kaufmann, E. J.; Espenson, J. H. *J. Am. Chem. Soc.* **1977**, *99*, 7051. (b) Balasubramanian, P. N.; Reed, J. W.; Gould, E. S. *Inorg. Chem.* **1985**, *24*, 1794.
(12) Cystine, with two carboxyl and two amino groups, has four pK_A's. The two lowest, involving the carboxyls, have been estimated as 1.7 and <1.0 and therefore play no part in the present study. See, for example: White, A.; Handler, P.; Smith, E. L. *Principles of Biochemistry*, 5th ed.; McGraw-Hill: New York, 1973; p 104.
(13) (a) Speakman, J. C. *J. Chem. Soc.* **1940**, 855. (b) See also: Sarjeant, E. P. *Potentiometry and Potentiometric Titrations*; Wiley: New York, 1984; p 342.
(14) See, for example: Sherrill, M. S. *A Course of Laboratory Experiments in Physicochemical Principles*; Macmillan: New York, 1924; p 64.
(15) (a) Experiments with cystine dimethyl ester as oxidant were carried out immediately after preparation of the solution to minimize complications due to hydrolysis of the ester. (b) As in previous work,[11b] experimental ambiguity resulted from reaction of traces of O_2 on mixing B_{12s} and coreagent solutions. In the absence of disulfides, decay curves were observed, having half-life periods near 2 s at pH 10 and near 40 ms at pH 5.4. Disulfide concentrations were therefore adjusted so that the primary reactions were much more rapid than these, and the order in disulfide was checked.
(16) Bonnet, R. *Chem. Rev.* **1963**, *63*, 573.

Table II. Representative Kinetic Data for the Oxidation of Vitamin B_{12s} (Cob(I)alamin) with Organic Disulfides at 23 °C[a]

disulfide	pH	$10^{-5}k^b$	disulfide	pH	$10^{-5}k^b$
dithiodiacetic acid (I)	6.52	0.67 (0.65)[c]	cystine dimethyl ester	10.39	11.0 (11.4)[d]
	6.18	0.76 (0.81)		8.87	12.5 (11.6)
	5.78	1.32 (1.27)		8.51	13.5 (11.9)
	5.40	2.4 (2.3)		8.25	13.5 (12.3)
	4.96	6.4 (5.5)		7.19	17.8 (18.3)
	4.72	7.9 (9.2)		5.92	26 (25)
	4.46	17 (16)	cystamine (VI)	10.48	5.6 (4.8)[d]
dithiodiethanol (II)	7.15	11		10.28	5.8 (5.4)
	4.17	10		9.98	6.4 (7.0)
cystine (III)	10.52	0.52 (0.48)[d]		9.70	9.0 (9.2)
	10.05	0.49 (0.59)		9.05	14.3 (15.4)
	9.78	0.81 (0.74)		8.95	17.2 (16.6)
	9.00	1.70 (1.74)		8.47	19.7 (19.8)
	8.94	1.90 (1.86)		8.35	22 (20)
	8.54	2.8 (2.7)		8.22	22 (21)
	8.23	2.8 (3.2)		5.92	22 (23)
	6.82	4.1 (4.2)	dithiosalicyclic acid (VII)	10.51	12.9
	4.26	4.3 (4.2)		9.89	13.5
thioctic acid (IV)	7.17	3.4 (3.3)[e]		6.53	18.4
	6.51	3.5 (3.3)	*trans*-1,2-dithiane-4,5-diol (VIII)	8.13	0.29
	5.93	4.2 (3.9)		4.81	0.31
	5.28	4.5 (5.4)	aldrithiol-4 (V)	7.37	>25
	5.04	6.5 (6.3)	3,3-dithiodipropionic acid	6.70	>25
	4.75	7.7 (7.7)	6,6′-dithiodinicotinic acid (IX)	10.39	>44
	4.51	9.1 (8.8)			

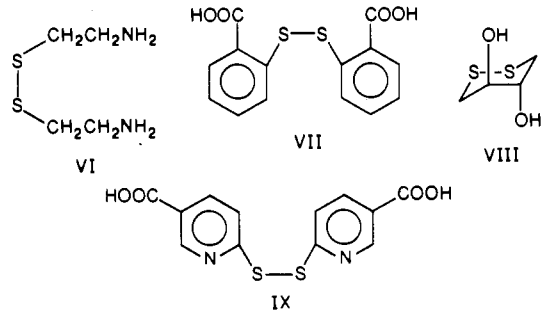
[a] The supporting electrolyte was $LiClO_4$ (μ = 0.20 M). Carbonate, borate, phosphate, and phthalate buffers (see Experimental Section) were used. $[B_{12s}] = 2 \times 10^{-5}$ to 6×10^{-5} M; [disulfide] = 2×10^{-3} to 6×10^{-4} M; $[PdCl_4^{2-}] = 6 \times 10^{-6}$ M; $[BH_4^-] = 4 \times 10^{-4}$ M. [b] Second-order rate constants, M^{-1} s^{-1}. [c] Calculated values (in parentheses) obtained from eq 4 in text, taking k_A as 5.1×10^4 M^{-1} $^{-1}$ and k_{HA}/K_{HA} as 4.5×10^{10} M^{-2} s^{-1}. [d] Calculated values (in parentheses) obtained from eq 2 in text by using parameters listed in Table III. [e] Calculated values (in parentheses) obtained from eq 3 in text.

Table III. Kinetic Parameters for the Oxidation of Vitamin B_{12s} (Cob(I)alamin) with Organic Disulfides at 23 °C, μ = 0.20 M

disulfide	k_0[a]	k_1[a]	k_2[a]	pK_1	pK_2
cystine (III)[b]	0.40 ± 0.05	2.9 ± 0.2	4.2 ± 0.2	8.08	8.96
cystine dimethyl ester[b]	11.4 ± 0.5	30 ± 4	23 ± 5	5.99	6.96
cystamine (VI)[b]	3.0 ± 0.4	13.7 ± 0.9	21 ± 1	8.77	9.61
thioctic acid (IV)[c]	3.3 ± 0.2	11.6 ± 0.4		4.80	
dithiodiacetic acid (I)[d]	0.51 ± 0.09	95 ± 4		2.88[e]	3.67[e]
dithiosalicyclic acid (VII)	12 ± 2	>20			
dithiodiethanol (II)	11 ± 1				
trans-1,2-dithiane-4,5-diol (VIII)	0.27 ± 0.02				

[a] Specific rates (M^{-1} s^{-1} $\times$ 10^{-5}) pertaining to the unprotonated (k_0), monoprotonated (k_1), and diprotonated (k_2) forms of the disulfide oxidants, obtained by nonlinear least-squares treatment of kinetic data using eq 2, 3, or 4 (see text). [b] Refinement used eq 2. [c] Refinement used eq 3. [d] Refinement used eq 4. [e] Reference 17.

the oxidants rather than B_{12s} since rates for diithiodiethanol (II) and the diol of 1,2-dithiane (VIII), which are devoid of carboxylate or amine functions, are pH-independent within the range studied.



Cystine (III), its dimethyl ester, and cystamine (VI) are partitioned between nonprotonated, monoprotonated, and diprotonated species. The dependence of rate on acidity then should be described by (2), where k_{obsd} is the second-order rate constant ob-

$$k_{obsd} = \frac{k_0K_1K_2 + k_1K_1[H^+] + k_2[H^+]^2}{K_1K_2 + K_1[H^+] + [H^+]^2} \quad (2)$$

served at a given acidity, k_0, k_1, and k_2 represent the rate constants associated with the three protonation levels, and K_1 and K_2 are the acidity constants for the di- and monoprotonated forms. Nonlinear least-squares treatment of the kinetic data for these disulfides, in conjunction with the experimental acidity constants in the medium used, yields specific rates listed in Table III for the individual protonation levels. Values of rate constants, calculated from (2), are compared with observed rates in Table II.

For thioctic acid (IV), with a single acidic site, the simpler expression (eq 3) applies; (k_{HA} and k_A refer to the protonated and

$$k_{obsd} = \frac{k_AK_{HA} + k_{HA}[H^+]}{K_{HA} + [H^+]} \quad (3)$$

nonprotonated forms of the oxidants). Acidity constants for dithiodiacetic acid (I) (pK_1 = 2.88; pK_2 = 3.67)[17] lie well above the acidity range examined, and here relationship 3 undergoes further simplification to the binomial expression (4). For the

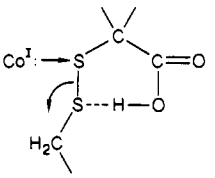
$$k_{obsd} = k_A + k_{HA}[H^+]/K_{HA} \quad (4)$$

dibasic acid, plots of k_{obsd} vs. $[H^+]$ are very nearly linear. There is no trace of upward concavity, indicating that additional acceleration reflecting a contribution from the diprotonated form

(17) Martell, A. E.; Smith, R. M. *Critical Stability Constants*; Plenum: New York, 1982; Vol. 5, First Supplement, p 324. These values are recorded for 25 °C, μ = 1.0.

is negligible in our acidity range.

The increases in rates accompanying protonations of the oxidant, a feature observed for a wide variety of oxidations in solution, reflects, at least in part, electron withdrawal from the electron-acceptor site. For the amino-substituted disulfides, this effect is a modest one (a three- to sevenfold acceleration) and is even less pronounced for the second protonation (k_2 values) than for the first.[18] An extension of this reasoning accounts, at least in part, for the differences in the k_0 values, as the negatively charged oxidants, derived from deprotonation of carboxylic acids, are seen to react substantially more slowly than the uncharged disulfides. The 200-fold rate enhancement on protonation of the anion of dithiodiacetic acid (I) hints that intramolecular hydrogen bonding to sulfur (X) further weakens the S–S bond or stabilizes the



X

departing thiyl group (or both). This additional acceleration is not observed for thioctic acid (IV), in which the protonation site lies much farther from the redox center. The relatively sluggish reduction of the *trans*-diol of 1,2-dithiane (VIII) suggests either that this disulfide enjoys some stabilization by incorporation into a six-membered ring or that the axial hydroxy groups serve to hinder approach of the bulky reductant.

Although the results of this study speak to structure–reactivity relationships in the reduction of disulfides, they appear to be silent in regard to an important facet of these systems. Two fundamentally different reaction sequences are consistent with the reaction products, the stoichiometry, and the observed kinetic behavior. In both sequences, the rate-determining step is the initial attack of Co(I) on the disulfide function, with subsequent steps being rapid. The first possibility is a homolytic route related to the reductions of Fe(III) and $Co(en)_3^{3+}$ by B_{12s};[19,20] this involves intervention of a thiyl ($RS^\bullet$) radical

$$R_2S_2 + Co^I \rightarrow RS\text{–}Co^{II} + RS^\bullet \quad (5)$$

$$RS^\bullet + Co^I \rightarrow RS\text{–}Co^{II} \quad \text{(rapid)} \quad (6)$$

$$2RS\text{–}Co^{II} \rightarrow 2RS^- + 2Co^{II} \quad \text{(rapid)} \quad (7)$$

An alternative path (implied by structure X) is similar to that suggested for reductions of nitrate and substituted hydroxylamines.[10b,21] This route features heterolytic attack by strongly nucleophilic[22] Co(I), yielding a Co(III) intermediate, which, on the basis of reported behavior,[11a,23] may be assumed to react very rapidly with a second Co(I)

$$R_2S_2 + Co^I \rightarrow RS^- + RS\text{–}Co^{III} \quad (8)$$

$$RS\text{–}Co^{III} + Co^I \rightarrow RS\text{–}Co^{II} + Co^{II} \quad \text{(rapid)} \quad (9)$$

$$RS\text{–}Co^{II} \rightarrow RS^- + Co(II) \quad \text{(rapid)} \quad (10)$$

Aquation of the $RS\text{–}Co^{II}$ intermediate to give aquo-substituted cob(II)alamin, a step common to both sequences, would be expected likewise to be rapid.[24]

This ambiguity of reaction path is analogous to that encountered in the oxidation of B_{12s} by oxyhalogen anions.[11b] In both instances, simplicity of kinetic pattern is obtained at the cost of mechanistic insight.[25]

Acknowledgment. The authors are grateful to Professor R. N. Bose for help in computing procedures and to Professor Paul Sampson for valuable discussions.

Registry No. I, 505-73-7; I (monoanion), 103422-90-8; II, 1892-29-1; III, 56-89-3; III (dianion), 58823-23-7; III (monoanion), 103422-91-9; III (monoprotonated), 103422-92-0; III (diprotonated), 58823-22-6; III (dimethyl ester), 1069-29-0; III (dimethyl ester)·2HCl, 30925-07-6; III (dimethyl ester) (monoprotonated), 103422-93-1; IV, 62-46-4; V, 2645-22-9; VI, 51-85-4; VI (monoprotonated), 103422-94-2; VII, 119-80-2; VIII, 14193-38-5; IX, 15658-35-2; cystamine dihydrochloride, 56-17-7; 3,3-dithiodipropionic acid, 1119-62-6.

(18) Calculated k_1 and k_2 values for cystine dimethyl ester (Table III) imply that protonation of the unipositive cation decreases reactivity. However, the difference between specific rates lies barely outside the uncertainties for both values and is most probably not real.
(19) Carlson, R. R., unpublished experiments, Kent State University, 1984.
(20) Balasubramanian, P. N.; Gould, E. S. *Inorg. Chem.* **1985**, *24*, 1791.
(21) Balasubramanian, P. N.; Gould, E. S. *Inorg. Chem.* **1984**, *23*, 824.
(22) Schrauzer, G. N.; Deutsch, E.; Windgassen, R. J. *J. Am. Chem. Soc.* **1968**, *90*, 2441.
(23) Ryan, D. A.; Espenson, J. H.; Meyerstein, D.; Mulac, W. A. *Inorg. Chem.* **1978**, *17*, 3725.
(24) The substitution lability of axial substituents in cob(III)alamin derivatives has been demonstrated: Thusius, D. *J. Am. Chem. Soc.* **1971**, *93*, 2629. Ligand exchange in the corresponding Co(II) complexes, for which ligand field stabilization is less marked, should be even more rapid.
(25) A reviewer has asked us to suggest a future experimental approach that might resolve the indicated mechanistic ambiguity. Differentiation is complicated by the ease with which the usual "radical-trapping reagents" are undoubtedly reduced with B_{12s}. If dimerization of $RS^\bullet$ radicals, formed in the initial step of the homolytic mechanism, competes favorably with their further reaction with B_{12s} (reaction 6), it may be that "scrambling" experiments with a mixture of doubly isotopically labeled and unlabeled disulfides and a deficiency of B_{12s} will prove informative.