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INTERACTION OF DISULFIDES WITH METHYLCOBALOXIME

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Summary

Base-catalyzed hydrolysis of disulfides has been found to be accelerated by the presence of methyl(aquo)cobaloxime and to lead to the formation of methyl-(thiolato)cobaloximes. This acceleration is prevented in the presence of a large excess of pyridine suggesting that disulfides associate to methylcobaloxime at the labile, axial ligand position. If such association occurs, it must be quite weak since no direct spectroscopic evidence for interaction of disulfides with methyl-cobaloxime in the absence of base could be obtained.

Introduction

Methylcobaloxime, like other alkyl cobaloximes, is well known to form complexes with organic amines, thiols and alkyl sulfides [1—4], alkyl sulfoxides, phosphines, and phosphites [5,6], various inorganic Lewis bases [7], and carbon monoxide [8]. During recent experiments on the interaction of disulfides with methyl(aquo)cobaloxime in aqueous base, we discovered an apparent enhancement of the rate of base-catalyzed disulfide hydrolysis (eq. 1) leading to the for-

$$\begin{array}{l} R—S—S—R + OH^- \rightarrow RS^- + RSOH \\ \qquad\qquad\qquad\qquad\qquad\quad \downarrow \\ \qquad\qquad\qquad\qquad\qquad\quad \text{stable products} \end{array} \qquad (1)$$

mation of methyl(thiolato)cobaloximes. The current report describes experiments which suggest, although they do not prove, that this reaction occurs via pre-equilibrium formation of an extremely weak axially liganded complex of disulfide with methylcobaloxime.

Results and discussion

2-Hydroxyethyl disulfide has essentially no effect on the electronic spectrum of methyl(aquo)cobaloxime at pH 6.5 in phosphate buffer even when employed

TABLE 1

NMR CHEMICAL SHIFTS FOR METHYLCOBALOXIME AND METHYL DISULFIDE IN METHANOL-d_4/D_2O (50% v/v) [a]

Sample	Chemical shift (ppm) (Assignment)			
	Initial	+ NaOD [b] (Immed.)	+ NaOD (+ 2 hr)	+ KCN (+ 20 min) [c]
$CH_3Co(D_2H_2)HOH$ + CH_3SSCH_3	0.75 ($\underline{CH_3}Co(D_2H_2)HOH$) 2.24 ($CH_3Co(\underline{D_2H_2})HOH$) 2.43 ($\underline{CH_3}SS\underline{CH_3}$)	0.40 ($\underline{CH_3}Co(D_2H_2)OH^-$) 2.19 [d] ($CH_3Co(\underline{D_2H_2})OH^-$) 2.43 ($\underline{CH_3}SS\underline{CH_3}$)	0.69 ($\underline{CH_3}Co(D_2H_2)S\underline{CH_3}^-$) 1.28 ($CH_3Co(D_2H_2)\underline{SCH_3}^-$) 2.18 [d] ($CH_3Co(\underline{D_2H_2})SCH_3$)	0.79 ($\underline{CH_3}Co(D_2H_2)CN^-$) 1.94 ($\underline{CH_3}S^-$) 2.14 [d] ($CH_3Co(\underline{D_2H_2})CN^-$)
$CH_3Co(D_2H_2)HOH$	0.72 ($\underline{CH_3}Co(D_2H_2)HOH$) 2.23 ($CH_3Co(\underline{D_2H_2})HOH$)	0.39 ($\underline{CH_3}Co(D_2H_2)OH^-$) 2.19 [d] ($CH_3Co(\underline{D_2H_2})OH^-$)	0.39 ($\underline{CH_3}Co(D_2H_2)OH^-$) 2.19 [d] ($CH_3Co(\underline{D_2H_2})OH^-$)	0.79 ($\underline{CH_3}Co(D_2H_2)CN^-$) 2.13 [d] ($CH_3Co(\underline{D_2H_2})CN^-$)
CH_3SSCH_3	2.43 ($\underline{CH_3}SS\underline{CH_3}$)	2.43 ($\underline{CH_3}SS\underline{CH_3}$)	2.45 ($\underline{CH_3}SS\underline{CH_3}$)	2.45 ($\underline{CH_3}SS\underline{CH_3}$) 1.94 ($\underline{CH_3}S^-$)
CH_3SH	2.05 ($\underline{CH_3}SH$)	1.95 ($\underline{CH_3}S^-$)	1.95 ($\underline{CH_3}S^-$)	1.96 ($\underline{CH_3}S^-$)
$CH_3Co(D_2H_2)HOH$ + CH_3SH	0.75 ($\underline{CH_3}Co(D_2H_2)HOH$) 2.05 ($\underline{CH_3}SH$) 2.23 ($CH_3Co(\underline{D_2H_2})HOH$)	0.70 ($\underline{CH_3}Co(D_2H_2)SCH_3^-$) 1.30 ($CH_3Co(D_2H_2)\underline{SCH_3}^-$) 2.17 [d] ($CH_3Co(\underline{D_2H_2})SCH_3^-$)	0.70 ($\underline{CH_3}Co(D_2H_2)SCH_3^-$) 1.29 ($CH_3Co(D_2H_2)\underline{SCH_3}^-$) 2.18 [d] ($CH_3Co(\underline{D_2H_2})SCH_3^-$)	0.79 ($\underline{CH_3}Co(D_2H_2)CN^-$) 1.95 ($\underline{CH_3}S^-$) 2.14 [d] ($CH_3Co(\underline{D_2H_2})CN^-$)

[a] Varian T-60 NMR spectrometer, 35°C, all shifts in ppm downfield from DSS. All resonances are singlets. [b] Final [NaOD] 1.4 *M*. [c] Final [KCN] 0.24 *M*. [d] Intensity decreases with time due to H—D exchange [9].

in 200-fold excess. However, in 0.2 *N* KOH spectral changes ensue immediately, characterized by a large increase in absorption at 322 nm. The final spectrum (after correction for excess disulfide) is essentially identical to that of the 2-mercaptoethanolate complex of methylcobaloxime [1] ($\epsilon_{322} = 9.55 \times 10^3\ M^{-1}\ cm^{-1}$, $\epsilon_{302} = 8.85 \times 10^3\ M^{-1}\ cm^{-1}$).

This reaction has been further investigated by ^1H NMR spectroscopy. A typical experiment is shown in Table 1 in which methyl(aquo)cobaloxime (0.11 *M*) was incubated with methyl disulfide (0.11 *M*) in methanol-d_4/D_2O (50% v/v). In the absence of base the resonances were essentially unperturbed from their values as individual components in the same solvent (Table 1). Upon addition of NaOD (final concentration 1.4 *N*) an immediate spectral change occurs characterized by a shift of the cobalt-bound methyl resonance from 0.75 to 0.40 ppm and a shift of the equatorial methyl resonance from 2.24 to 2.19 ppm. These spectral changes reflect conversion of methyl(aquo)cobaloxime to the hydroxo complex, as shown in Table 1. Slower spectral changes (half-time about 15 min) begin immediately, characterized by a shift of the cobalt-bound methyl resonance to 0.69 ppm, appearance of a new resonance at 1.28 ppm, and disappearance of the methyl disulfide resonance at 2.43 ppm.

The final spectrum of the product may be assigned to the methyl thiolato complex of methylcobaloxime based on the following two observations: (1) Independent generation of $CH_3Co(D_2H_2)SCH_3^-$ (from $CH_3Co(D_2H_2)HOH$, CH_3SH, and NaOD, Table 1) confirms the assignments of the resonances at ca. 0.70 ppm and ca. 1.30 ppm as the cobalt-bound methyl group and the coordinated methyl thiolate anion, respectively; and (2) Displacement of CH_3S^- from $CH_3Co(D_2H_2)SCH_3^-$ formed by either route by cyanide ion (0.24 *M*) leads to the generation of methyl(cyano)cobaloxime (characterized by resonances at 0.79 ppm for the cobalt-bound methyl and 2.14 ppm for the equatorial methyls) and a new resonance at 1.95 ppm assigned to free methyl thiolate anion. Strictly analogous results have been obtained with benzyl disulfide and 2-hydroxyethyl disulfide. The NMR assignments for the products of these reactions are shown in Table 2.

The methylthiolato complex of methylcobaloxime was obtained as its tetraphenylarsonium salt (an orange, hygroscopic solid) from reaction mixtures containing methyl disulfide and methyl(aquo)cobaloxime in aqueous-methanolic (50% v/v) base, following addition of tetraphenylarsonium chloride. This material had identical NMR spectral characteristics to the $CH_3Co(D_2H_2)SCH_3^-$ complex prepared in situ (i.e. column 3 of Table 1) with the addition of a multiplet resonance (7.58—8.05 ppm, 20.2 protons relative to 12.0 protons at 2.15 ppm) assigned to the tetraphenylarsonium cation. Unfortunately, when this hygroscopic compound was dried at room temperature under reduced pressure it lost methane thiol (as detected by NMR spectroscopy) preventing elemental analysis to confirm its empirical formula.

Base-catalyzed disulfide hydrolysis (eq. 1) was studied by UV spectroscopy and found to be much too slow to account for methyl(thiolato)cobaloxime formation in the experiments described above. Methyl disulfide was found to be cleaved by hydroxide ion with a rate constant of $5.0 \times 10^{-4}\ M^{-1}\ min^{-1}$ at 25°C, while the apparent rate constant for the formation of $CH_3Co(D_2H_2)SCH_3^-$ in the experiment described in Table 1 (35°C, 1.4 *N* NaOD) was about $4.6 \times 10^{-2}\ min^{-1}$.

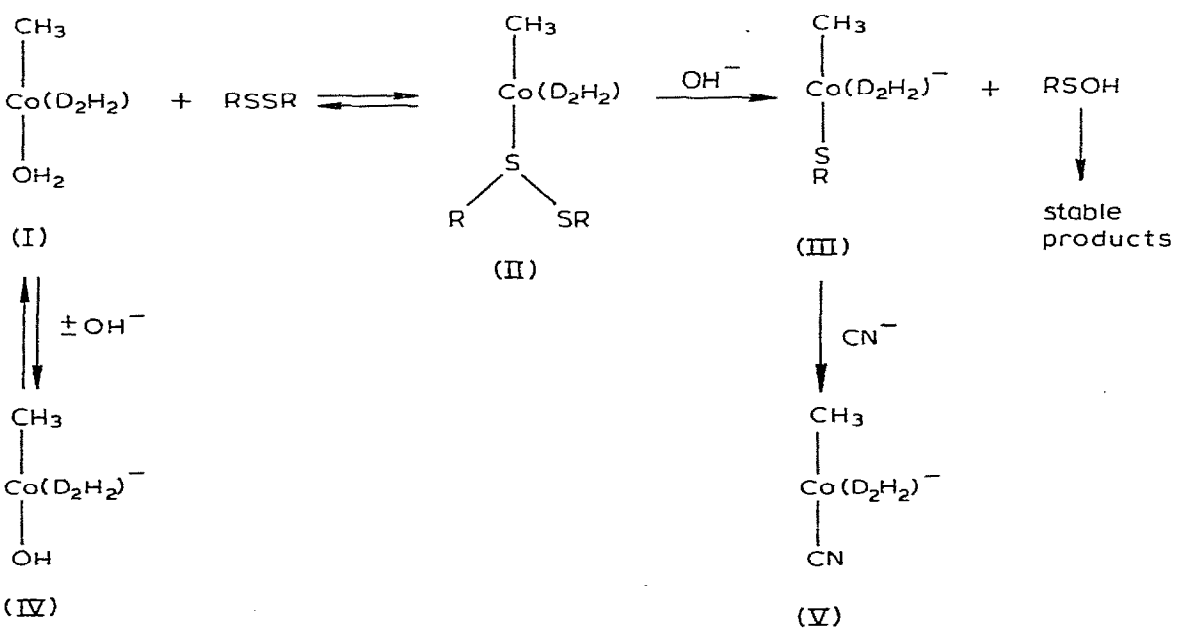
TABLE 2

NMR SPECTRA OF THE PRODUCTS OF THE REACTION OF DISULFIDES WITH METHYL(AQUO)-COBALOXIME IN AQUEOUS-METHANOLIC BASE [a]

Disulfide	Chemical shift (ppm) (Assignment)	
	+ NaOD	+ KCN [b]
$(C_6H_5CH_2S)_2$	0.63 (s) $(\underline{CH_3}Co(D_2H_2)SCH_2C_6H_5^-)$ 2.12 (s) [c] $(CH_3Co(\underline{D_2H_2})SCH_2C_6H_5^-)$ 3.15 (s) $(CH_3Co(D_2H_2)S\underline{CH_2}C_6H_5^-)$ 7.00—7.43 (m) $(CH_3Co(D_2H_2)SCH_2\underline{C_6H_5}^-)$	0.80 (s) $(\underline{CH_3}Co(D_2H_2)CN^-)$ 2.12 (s) [c] $(CH_3Co(\underline{D_2H_2})CN^-)$ 3.66 (s) $(\underline{C_6H_5CH_2}S^-)$ 7.00—7.50 (m) $(\underline{C_6H_5}CH_2S^-)$
$(HOCH_2CH_2S)_2$	0.70 (s) $(\underline{CH_3}Co(D_2H_2)SCH_2CH_2OH^-)$ 1.93 (t) $(CH_3Co(D_2H_2)S\underline{CH_2}CH_2OH^-)$ 2.22 (s, [c] $(CH_3Co(\underline{D_2H_2})SCH_2CH_2OH^-)$ 3.57 (t) $(CH_3Co(D_2H_2)SCH_2\underline{CH_2}OH^-)$	0.79 (s) $(\underline{CH_3}Co(D_2H_2)CN^-)$ 2.14 (s) [c] $(CH_3Co(\underline{D_2H_2})CN^-)$ 2.28 (t) $(HOCH_2\underline{CH_2}S^-)$ 3.26 (t) $(HO\underline{CH_2}CH_2S^-)$

[a] Varian T-60 Spectrometer, 35°C. All shifts in ppm downfield from DSS. Conditions $(C_6H_5CH_2S)_2$-0.28 *M* NaOD, 98% methanol-d_4-D_2O (v/v). $(HOCH_2CH_2S)_2$-0.55 *M* NaOD, 50% methanol-d_4-D_2O (v/v). [b] Final [KCN] = 0.24 M. [c] Intensity decreases with time due to H—D exchange [9].

SCHEME 1



The appropriate rate constants for 2-hydroxyethyl disulfide were 1.7×10^{-3} M^{-1} min^{-1} at 25°C and about 8.7×10^{-2} min^{-1} (35°C, 0.56 *N* NaOD) respectively.

These results are consistent with Scheme 1 in which the apparent enhancement of base-catalyzed disulfide hydrolysis by methyl(aquo)cobaloxime is attributed to equilibrium formation of an axially liganded disulfide complex of methylcobaloxime (species II). The expected displacement of electron density from disulfide sulfur to cobalt in II would be expected to enhance the rate of hydroxide ion attack on the disulfide function. It must, however, be noted that no direct evidence for the formation of II with any disulfide could be obtained. The failure of disulfides to perturb either the ^1H NMR or electronic spectrum of methyl(aquo)cobaloxime in neutral aqueous solution, even when employed in large excess, implies that if species II does exist, the equilibrium constant for its formation must be quite low.

Indirect evidence for the intermediacy of species II in the base-catalyzed formation of methyl(thiolato)cobaloximes from methyl(aquo)cobaloxime and disulfides was obtained from experiments in which the formation of thiolato products (III) was inhibited by the presence of excess pyridine. Pyridine is known to be a good axial ligand for methylcobaloxime and would be expected to compete successfully with disulfides for the axial ligand position in this complex as shown in Scheme 2.

In a typical experiment (Table 3), methyl(pyridine)cobaloxime (0.1 *M*) was incubated with methyl disulfide (0.1 *M*) in methanol-d_4/pyridine-d_5/D_2O (33/33/34, v/v/v). Addition of NaOD (final concentration 1.4 *N*) causes immediate shifts of the cobalt-bound methyl resonance from 1.05 to 1.31 ppm and the equatorial methyl resonance from 2.21 to 2.10 ppm. These shifts reflect the partial formation of species V (Scheme 2) by ionization of an equatorial oxime proton for which there is ample evidence from previous work [2,3]. No subsequent spectral changes occur except the time dependent decrease in signal inten-

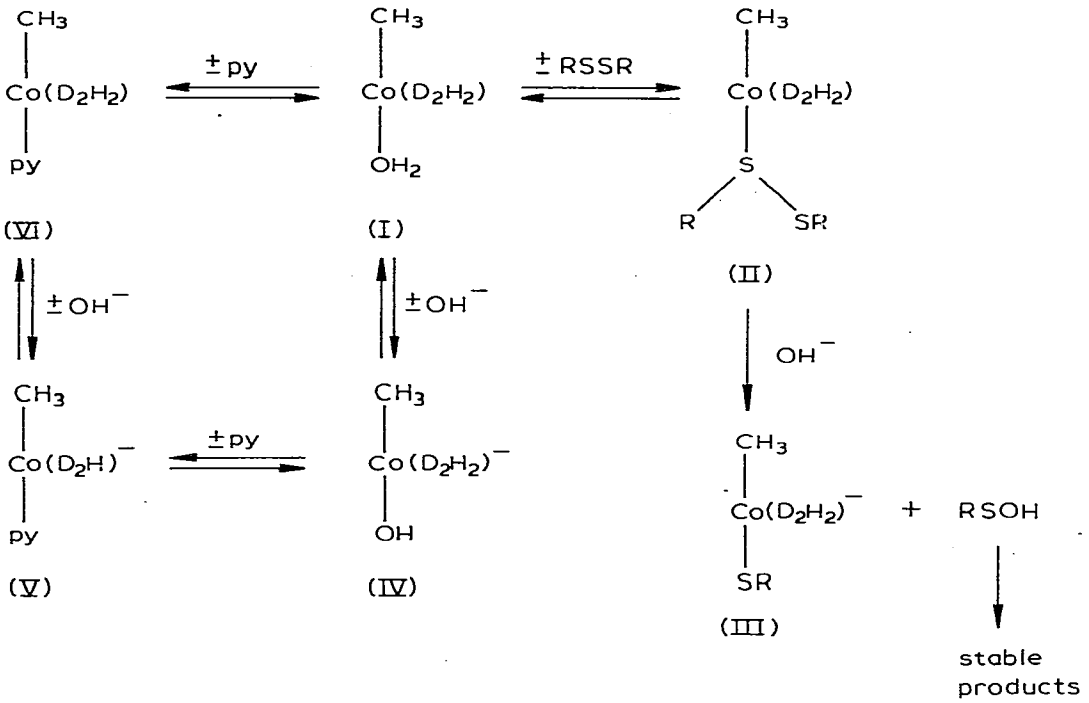
TABLE 3

NMR CHEMICAL SHIFTS FOR METHYL(PYRIDINE)COBALOXIME AND METHYL DISULFIDE IN METHANOL-d_4/PYRIDINE-d_5/D_2O [a]

Sample	Chemical shift (ppm) (Assignment)		
	Initial	+ NaOD [b] (Immed.)	+ NaOD [b] (+10 h)
$CH_3Co(D_2H_2)py$ + CH_3SSCH_3	1.05 ($\underline{CH_3}Co(D_2H_2)py$)	1.31 ($\underline{CH_3}Co(D_2H)py^-$)	1.31 ($\underline{CH_3}Co(D_2H)py^-$)
	2.21 ($CH_3Co(\underline{D_2H_2})py$)	2.10 [c] ($CH_3Co(\underline{D_2H})py^-$)	2.10 [c] ($CH_3Co(\underline{D_2H})py^-$)
	2.40 ($\underline{CH_3}SS\underline{CH_3}$)	2.40 ($\underline{CH_3}SS\underline{CH_3}$)	2.40 ($\underline{CH_3}SS\underline{CH_3}$)
$CH_3Co(D_2H_2)py$	1.04 ($\underline{CH_3}Co(D_2H_2)py$)	1.33 ($\underline{CH_3}Co(D_2H)py^-$)	1.32 ($\underline{CH_3}Co(D_2H)py^-$)
	2.19 ($CH_3Co(\underline{D_2H_2})py$)	2.12 [c] ($CH_3Co(\underline{D_2H})py^-$)	2.11 [c] ($CH_3Co(\underline{D_2H})py^-$)

[a] Varian T-60 NMR Spectrometer, 35°C. All shifts in ppm downfield from DSS. Solvent composition 33/33/34 (v/v/v). All resonances are singlets. [b] Final [NaOD] = 1.4 *M*. [c] Intensity decreases with time due to H—D exchange [9].

SCHEME 2



sity of the equatorial methyl resonance due to base-catalyzed H—D exchange previously described by Cartãno and Ingraham [9]. Throughout the experiment (for 20 h after the addition of NaOD) the methyl disulfide resonance at 2.40 ppm was unperturbed.

These experiments show that the axial ligand position of methylcobaloxime is involved in the apparent enhancement of base-catalyzed disulfide hydrolysis and suggest that formation of the disulfide adduct of methylcobaloxime (II in Schemes 1 and 2) is a likely mechanism for this effect.

Experimental

Methyl(aquo)cobaloxime was synthesized as described by Schrauzer [10].

Electronic spectra were obtained with a Cary 14 Recording Spectrophotometer, whose sample compartment was thermostatted at 25.0 ± 0.1°C for kinetic determinations. The interaction of disulfides with methyl(aquo)cobaloxime was studied using divided compartment spectrophotometer cells. All solutions were made 2×10^{-4} *M* in EDTA to retard the air oxidation of thiolate anions [1]. Ionic strength was maintained at 1.0 *M* with added KCl and glass distilled, deionized water was used throughout.

Apparent first order rate constants (in 0.2 *N* KOH) for the base-catalyzed hydrolysis of disulfides in the absence of methyl(aquo)cobaloxime were obtained from the time dependence of the increase in UV absorbance of basic solutions of disulfides due to formation of the strongly absorbing thiolate anions

using the method of initial slopes [11]. The molar extinction coefficients for the thiolate anions were independently determined to be 5.66×10^3 M^{-1} cm^{-1} (235 nm) for 2-mercaptoethanol, and 5.50×10^3 M^{-1} cm^{-1} (237 nm) for methanethiol.

^1H NMR spectra were recorded on a Varian T-60 NMR spectrometer with sample probe maintained at 35°C. Some samples contained DSS * as an internal reference. In other samples, methanol-d_4 was used as an internal reference and shifts relative to DSS were calculated from the measured shift of methanol-d_4 from DSS in the same solvent.

Preparation of $[CH_3Co(D_2H_2)SCH_3^-][As(Ph)_4^+]$

0.75 g (2.3 mmole) methyl(aquo)cobaloxime was placed in a 100 ml three-necked round-bottomed flask. 0.275 g (2.9 mmole) methyl disulfide was added in 25 ml of methanol and the flask was purged with argon for 30 min. 25 ml of aqueous 1.0 *N* KOH was then added via a pressure equalizing addition funnel and the reaction mixture was stirred overnight under continuous argon purge. 0.97 g (2.3 mmole) tetraphenylaronium chloride was then dissolved in a few ml of methanol and added. The solvent volume was reduced to approximately half-volume on a rotary flash evaporator and 1.08 g of orange powder was obtained by suction filtration. The product was air dried on a Büchner funnel. Yield 63%; NMR (methanol-d_4/D_2O, 50% v/v, δ(DSS) 0.66 (S, 3.03 H), 1.30 (S, 2.86 H), 2.15 (S, 12.00 H), 7.58—8.05 (m, 20.2 H).

Acknowledgments

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* DSS = 2,2-dimethyl-2-sila-5-pentanesodiumsulfolene.