Studies on Cobaloxime Compounds. IV. The Polarography of Cobaloximes

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Various types of cobaloximes, *e.g.*, *Co*-alkyl derivatives with different bases as an axial ligand and polymeric cobaloximes with the general formula of $Co(OH)(DH)_2$(Copoly—AM-VPy) (DH: dimethylglyoximato monoanion) in which Copoly—AM-VPy is a low-molecular-weight copolymer of acrylamide and 4-vinylpyridine, were prepared, and their half-wave potentials in cathodic reduction were compared to each other and to those of a few vitamin B_{12} compounds. All of them showed a single irreversible cathodic wave. Methyl- and cyanocobaloximes were reduced at more negative potentials than the corresponding methylcobalamin and cyanocobalamin(vitamin B_{12}). The half-wave potential of methylcobaloxime shifted in the direction of the more negative potentials as the donating strength of the axial base increased. This was correlated with the charge-transfer transition energies of those cobaloximes as determined from their electronic spectra. The polymeric cobaloximes were reduced at less negative potentials than the others.

The cobaloxime compounds have properties quite similar to those of vitamin B_{12} compounds in their chemical reactivity, as have been established especially by Schrauzer *et al.*[1] The oxidation and reduction of cobalt in those complexes are the most important steps in many of the reactions. The polarographic reduction is a useful means inasmuch as the half-wave potentials can be considered as resulting solely from the ease of the reduction of each complex itself, since mercury cathode has a common reducing power which can be controlled in any way; this is different from the reduction with other chemical reducing reagents, that is, the result of two reactants, *i.e.*, the complex and a reagent.

The polarographic behavior of cobaloximes has been studied extensively by Maki[2] and by Schrauzer *et al.*[3] Maki reported that $K[Co(CN)_2(DH)_2]\cdot 3/2H_2O$[4] showed a single irreversible wave at -1.105 V *vs.* SCE in 0.5 M Na_2SO_4; they attributed this wave to a two-electron reduction from Co(III) to Co(I). Schrauzer *et al.* reported the half-wave potentials of several cobaloximes. For example, $CoCl(DH)_2(py)$ yields three cathodic waves, at -0.10, -1.0, and -1.27 V, *vs.* the Ag/AgCl electrode at 25°C in a 50% aqueous ethanolic solution, while there were four waves, at -0.67, -1.44, -2.42, and -3.06 V *vs.* Ag/0.10 M $AgNO_3$ at 25°C in acetonitrile. The first wave corresponds to the reduction of Co(III) to Co(II); the second, to Co(II)—Co(I), and the third, to Co(I)—Co(0), whereas the fourth is due to the reduction of pyridine. They have also reported the polarographic reduction of some alkylcobaloximes, which show two irreversible waves in acetonitrile. For instance, $CH_3Co(DH)_2(H_2O)$ yields two cathodic waves, at -1.7 and -2.42 V *vs.* Ag/0.10 M $AgNO_3$. From a comparison between these alkylcobaloximes and $CoCl(DH)_2(py)$, they have deduced that the organocobaloximes are complexes of Co(II).

In this work, various types of cobaloximes, *e.g.*, *Co*-methyl derivatives with different axial bases and *Co*-alkylcobaloximes with pyridine as a common axial base were synthesized. The half-wave potentials of these cobaloximes were determined under the same conditions and were compared to each other and also to those of other several cobaloximes and vitamin B_{12} derivatives. The dependence of the ease of reduction upon the kind of the axial ligand was discussed. The results will be described below.

Experimental

Materials. All the alkylcobaloximes were synthesized mostly by the methods of Schrauzer and have been reported in previous publications.[5-7] The cyanocobalamin and methylcobalamin were kindly supplied by the Eisai Co. All the other reagents used in the measurements were of a G. R. grade and were obtained from commercial sources.

Measurements. The polarographic measurements were made with a Yanagimoto potential-controlled Polarograph (model PA102) at 25°C. All the complexes were dissolved in a 0.1 N K_2SO_4 aqueous solution. Before each determination, nitrogen gas was bubbled through the solution for 10 min. Two ppm of a copolymer of acrylamide and 4-vinylpyridine (Copoly—AM-VPy, AM : VPy molar ratio = 14.5, $M_n = 1500$) were added to each solution in order to diminish the maximum wave. The characteristics of the capillary used were as follows: $m = 0.684$ mg/sec and $t = 4.55$ sec, the values of which were measured in a 0.1 N K_2SO_4 aqueous solution.

Results and Discussion

All the cobalt complexes examined in this work showed a single irreversible cathodic wave under these conditions. These results were in good agreement with those on $K[Co(CN)_2(DH)_2]\cdot 3/2H_2O$ obtained by Maki, and not with those on the cobaloxime derivatives obtained by Schrauzer. According to Maki's results, which were obtained under conditions more similar to ours, this wave can be attributed to Co(III)—

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[1] *E. g.*, G. N. Schrauzer and J. Kohnle, *Chem. Ber.*, **97**, 3056 (1964); G. N. Schrauzer, *Accounts Chem. Res.*, **1**, 97 (1968).

[2] N. Maki, *Kagaku*, **16**, 202 (1961); *Nature*, **188**, 227 (1960).

[3] G. N. Schrauzer, R. J. Windgassen, and J. Kohnle, *Chem. Ber.*, **98**, 3324 (1965); G. N. Schrauzer and R. J. Windgassen, *J. Amer. Chem. Soc.*, **88**, 3738 (1966).

[4] DH means the dimethylglyoximato monoanion.

[5] N. Yamazaki and Y. Hohokabe, *Chem. Commun.*, **1968**, 829.

[6] N. Yamazaki and Y. Hohokabe, This Bulletin, **44**, 63 (1971).

[7] N. Yamazaki and Y. Hohokabe, submitted to this Bulletin.

Co(I) reduction. Most of the cobaloximes were reduced at more negative potentials than $Co(H_2O)_6^{2+}$, probably as a result of a strong interaction of dimethylglyoxime ligands with cobalt.

Many alkyl derivatives, especially hydroxypropyl and methyl derivatives, have been synthesized as model vitamin B_{12} compounds,[6] and their electronic and infrared absorption spectra, and also the effect on a B_{12}-dependent enzymatic reaction, have been reported.[6-8]

The reduction waves of these analogs and vitamin B_{12} compounds under the same conditions are compared in Table 1. Methylcobalamin or cyanocobalamin was reduced at a less negative potential than the corresponding methyl- or cyanocobaloximes. For example, methyl(pyridine)cobaloxime was reduced at a potential more negative by −0.11 V than that of methylcobalamin. Planary-coordinating-dimethylglyoxime ligands in cobaloximes seem to charge more electrons to cobalt atoms than does corrin in cobalamin.

TABLE 1. HALF-WAVE POTENTIALS OF METHYL- AND CYANO-COBALOXIMES, AND -COBALAMINS

Each material was dissolved in 0.1 N K_2SO_4 at the concentration of 3.0×10^{-4} M, unless indicated. Measurement was done at 25°C. Estimated errors were ±0.01 unless indicated.

Material[a]	$E_{1/2}$ (V *vs.* SCE)	$n\alpha$[d]
$Co(CN)(DH)_2(py)$[b]	−1.19[d]	0.33
Cyanocobalamin[c]	−1.09	0.41
$CH_3Co(DH)_2(H_2O)$	−1.26	0.31
$CH_3Co(DH)_2$(nico)	−1.28	0.29
$CH_3Co(DH)_2$(tolu)	−1.28	0.30
$CH_3Co(DH)_2$(py)	−1.31	0.33
$CH_3Co(DH)_2$(pico)	−1.33	0.35
$CH_3Co(DH)_2$(imd)	−1.40	0.27
Methylcobalamin[c]	−1.20	0.25
$[Co(H_2O)_6]Cl_2$	−1.21	0.37

a) py; pyridine. nico; nicotinamide. tolu; *p*-toluidine. pico; γ-picoline. imd; imidazole.
b) 0.6×10^{-4} M. c) 1.0×10^{-4} M. d) ±0.02.

The half-wave potentials of *Co*-methylcobaloximes are affected by another axial ligand. As the electron-donating power of the axial base increases, the potential shifts to more negative potentials. The relationship between the pK_a of the axial base and the half-wave potential of the cobaloxime is shown in Fig. 1. The order of the ease of reduction coincided with that of the spectrochemical shift of methylcobaloximes;[7] *i.e.*, the charge-transfer transition energies of methylcobaloximes decreased in this order: (imidazole)-, (γ-picoline)-, (pyridine)-, (*p*-toluidine)-, (nicotinamide)-, and aquocobaloxime. Therefore, the half-wave potentials measured in this experiment are considered to be a measure of the reducibility of the Co atom in these complexes.

Generally, in the polarographic reduction, the electron from the mercury cathode is transferred to the lowest vacant orbital of the reductant. According to molecular orbital theory, non-bonding orbitals (d_{xy}, d_{yz}, d_{zx}) are filled with 6 electrons in the case of an octahedral Co(III) complex, and the antibonding orbital (σ^*) is the lowest vacant one which is formed with the formation of the corresponding bonding orbital (σ) by the interaction of the d_{z^2} orbital of the central metal with suitable orbitals of axial ligands. Therefore, the potential at which the reduction of the complex occurs probably depends directly upon the absolute energy level of the lowest vacant orbital, and not necessarily upon the energy difference between σ and σ^*. Since the stronger interaction of the axial-base component causes increasing negative potentials of the reduction, as has been mentioned above, it is considered that a strong interaction of the base results in raising the absolute energy level of σ^*. If the absolute energy level of σ is assumed to be less affected by the formation of molecular orbitals between cobalt and ligands than that of σ^*, the energy difference between σ and σ^*, *i.e.*, ν_I, which can be determined by studying the electronic spectrum, should increase with the interaction of the ligands in the complex.

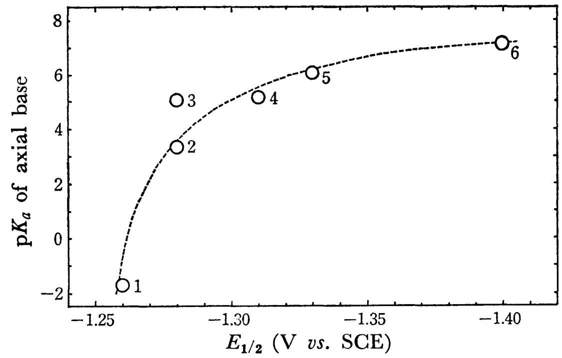

Fig. 1. The relationship between pK_a of the axial base and the half-wave potential of the methylcobaloxime, $CH_3Co(DH)_2B$.
B: 1, H_2O; 2, nicotinamide; 3, *p*-toluidine; 4, pyridine; 5, γ-picoline; 6, imidazole.

In short, $\Delta E_{1/2}$ which is the difference between a half-wave potential of methylcobaloxime and that of a given cobaloxime as a criterion, and $\Delta\nu_I$, which is the difference in charge-transfer transition energy between them, are expected to be correlated. Using as a criterion methylaquocobaloxime, in which coordinating water is considered to be the weakest ligand among the ligands examined in this work, we could obtain the correlation between $\Delta\nu_I$ and $\Delta E_{1/2}$; it is illustrated in Fig. 2. Methyl(imidazole)cobaloxime is not included here because its ν_I is obscurely shown as a shoulder band on its electronic spectrum. As is shown in Fig. 2, there is clearly a relationship between $\Delta\nu_I$ and $\Delta E_{1/2}$, supporting the argument just presented. In other words, as has been discussed above, a strongly-interacting ligand raises the σ^* orbital, while the level of σ is less affected, resulting in making the reduction potential more negative and in raising

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8) Y. Hohokabe and N. Yamazaki, This Bulletin, **44**, 798 (1971).

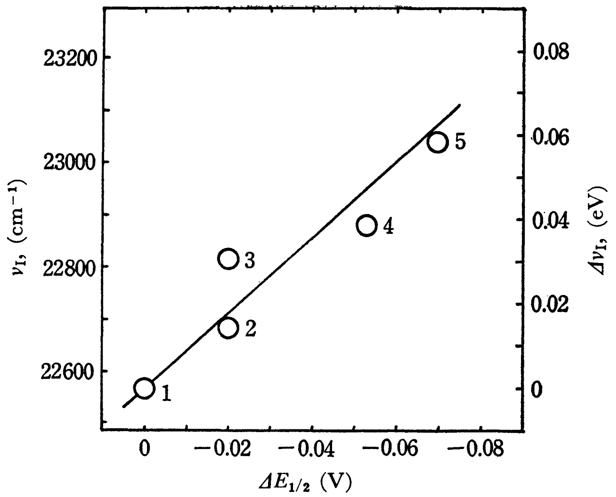

Fig. 2. The correlation between $\Delta\nu_I$ and $\Delta E_{1/2}$ of methylcobaloximes.
The data of methylaquocobaloxime were adopted as a standard for the calculation of $\Delta\nu_I$ and $\Delta E_{1/2}$. ν_I is the lowest charge-transfer transition energy which had been obtained directly from electronic spectral data.[7]
1, H_2O; 2, nicotinamide; 3, *p*-toluidine; 4, pyridine; 5, *γ*-picoline.

the charge-transfer transition energy ($\sigma \rightarrow \sigma^*$). This is well supported by the fact that the slope of the $\Delta\nu_I$ *vs.* $\Delta E_{1/2}$ plots is around 0.9; this shows that the differentiations are of the same degree in both series.

Many (pyridine)cobaloximes with various kinds of another axial ligand were also examined; the results are shown in Table 2. Simple alkyl derivatives were reduced at nearly the same potential, while benzyl and hydroxypropyl derivatives were at less negative potentials. The argument which has just described in the case of methylcobaloximes, *i.e.*, that a strongly coordinating ligand raises the level of the antibonding orbital, could not be ascertained in (pyridine)-cobaloximes with a different axial ligand, such as Cl, CN, and alkyl, because the low solubility of chloro- and cyano-cobaloximes in water prevented us from determining their spectrochemical sequences in those (pyridine)cobaloxime series. However, speaking only of alkyl derivatives, the relationship between ν_I and $E_{1/2}$ was not observed. Benzyl and hydroxyalkyl ligands have substituents of different natures, such as the aromatic ring and the hydroxy group respectively, so that the affinity of the complex to the electrode might differ from those of simple alkyl derivatives.

Table 2. Half-wave potentials of various (pyridine)cobaloximes: $CoX(DH)_2$(pyridine), or $RCo(DH)_2$(pyridine)

Each material was dissolved in 0.1 N K_2SO_4 at the concentration of 3.0×10^{-4} M, unless indicated. Measurement was done at 25°C. Estimated errors were ±0.01 unless indicated.

Material X or R	$E_{1/2}$ (V *vs.* SCE)	$n\alpha$[d)]
CN[a)]	−1.19[d)]	0.33
$C_6H_5CH_2$[b)]	−1.20[d)]	0.74[e)]
$CH_3CH(OH)CH_2$	−1.24[d)]	0.35
$HOCH_2CH(OH)CH_2$	−1.26	0.27
$HOCH_2CH(CH_3)$	−1.27[d)]	0.28
Cl[c)]	−1.28	0.31
$CH_3CH_2CH_2$	−1.30	0.33
$CH_3CH(CH_3)$	−1.30	0.31
CH_3	−1.31	0.33
CH_3CH_2	−1.31	0.32

a) 0.6×10^{-4} M. b) 1.0×10^{-4} M. c) 1.5×10^{-4} M. d) ±0.02. e) ±0.05.

The ease of the reduction depends, of course, on the electron affinity of the cobalt atom in the complex. In addition, it is known that the half-wave potential is governed by the rate of the reduction reaction at the cathode in the irreversible reduction; *i.e.*, the higher the rate of reduction reaction, the less negative the potential. The higher rate of the reduction reaction will be attained by the larger value of the rate constant of the electrode reaction. This is probably the consequence of the closer distance between the cathode and the reactant (Co atom), and of the electron affinity of the cobalt atom in the complex.

It is expected that a strongly electron-attractive ligand facilitates the reduction of the complex. Since the Hammett σ constants are considered to be a measure of the electronic properties of the ligand, the half-wave potentials of (pyridine)cobaloximes are correlated with the constants of their axial ligands in Figs. 3 and

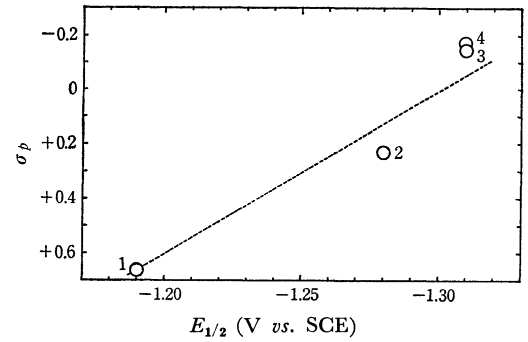

Fig. 3. The relationship between the Hammett constant σ_p and the half-wave potential of (pyridine)cobaloximes: $CoX(DH)_2$(pyridine).
X: 1, CN; 2, Cl; 3, CH_3CH_2; 4, CH_3.

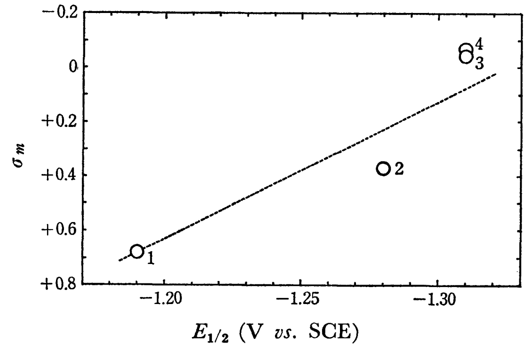

Fig. 4. The relationship between the Hammett constant σ_m and the half-wave potential of (pyridine)cobaloximes: $CoX(DH)_2$ (pyridine).
X: 1, CN; 2, Cl; 3, CH_3CH_2; 4, CH_3.

TABLE 3. HALF-WAVE POTENTIALS OF POLYMERIC COBALOXIMES AND OTHERS

Measurement was done in 0.1 N K_2SO_4 at 25°C. Copoly—AM-VPy means a copolymer of acrylamide (AM) and 4-vinylpyridine (VPy). The molecular weight and AM : VPy molar ratio are: a, 1400 and 13.7; b, 3000 and 11.9, respectively.[4] The concentration was: a, b, 2.0×10^{-4} M (Co); c, 3.0×10^{-4} M. Estimated errors were: d, ±0.01; e, ±0.02; f, ±0.04.

Material	$E_{1/2}$ (V *vs.* SCE)	$n\alpha^{\mathrm{e}}$
Co(OH)(DH)$_2$(Copoly—AM-VPy)$^{\mathrm{a}}$	-1.15^{e}	0.70
Co(OH)(DH)$_2$(Copoly—AM-VPy)$^{\mathrm{b}}$	-1.16^{d}	0.60
CoCl(DH)$_2$(H$_2$O)$^{\mathrm{c}}$)	-1.22^{f}	0.36
Co(OH)(DH)$_2$(H$_2$O)$^{\mathrm{c}}$	-1.26^{d}	0.25

4. The complex with an electron-attractive ligand is reduced at a less negative potential, as has been expected. However, it was found, from an investigation of the infrared spectra of cobaloximes,[6] that the electron-attractive ligand in the sixth position causes stronger interaction between Co and the fifth ligand, *i.e.*, the axial base, in turn resulting in an increase in the electron density of the equatorial moiety in the cobaloxime. The observation of the polarographic behavior seems to be inconsistent with that of the infrared spectra. It is also expected, however, that the electron from the mercury cathode is transferred to Co through an electron-attractive ligand, such as CN or Cl; this facilitates the reduction of the central cobalt atom, irrespective of the electron density of the Co in the complex.

The polymeric cobaloximes have also been prepared and described previously.[5,9] They are reduced at less negative potentials than other, analogous monomeric cobaloximes, as is shown in Table 2. The half-wave potentials of polymeric cobaloximes were expected to be more negative than that of hydroxoaquocobaloxime. Nevertheless, the reduction of the former was observed to take place at a less negative potential than that of the latter. This might be due to a polymer effect, by which the existence of amide groups in the neighborhood of the Co moiety facilitated the electron-transfer from the cathode to the complex. The addition of the same copolymer to the other monomeric cobaloximes did not change their half-wave potentials, but only diminished the maximum wave which was generally observed in the absence of a surface-active agent. Since polyacrylamide is known as a surface-active agent, the facilitating effect of the polymeric ligand on the reduction of the polymeric cobaloxime may be attributed to the strong adhesion of polymeric cobaloxime to the dropping mercury cathode, thus facilitating reduction reaction by the electron of mercury cathode. The half-wave potential was not affected by a change in the molecular weight of the polymeric ligand.

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[9] The half-wave potentials of polymeric cobaloximes reported previously had more negative values, but they may have been incorrectly standardized.