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Hydrophobic Vitamin B$_{12}$. Part 20:[#] Supernucleophilicity of Co(I) Heptamethyl Cobyrinate toward Various Organic Halides

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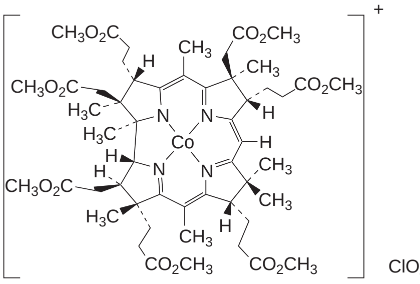
Heptamethyl cobyrinate, hydrophobic vitamin B$_{12}$, was reduced to its Co(I) species by a reaction with sodium tetrahydroborate, which reacted with various organic halides, such as CH_2Cl_2, $CHCl_3$, CCl_4, $CHBrCl_2$, $CHBr_3$, CCl_3CH_3, $CFCl_3$, and $BrCH_2CH_2CH_3$, to form the corresponding alkylated complexes with dehalogenation. The alkylated complexes were characterized by elemental analyses and ESI-MS, and the photo-lability of the alkylated complexes was confirmed by the UV–vis absorption spectral change. The fashion for cleavage of the cobalt–carbon bond under irradiation with visible light was investigated by an ESR spin-trapping technique. The redox behavior of a series of alkylated complexes was investigated by cyclic voltammetry. The alkylated complexes showed an irreversible reduction peak at −1.21 to −1.29 V vs Ag–AgCl, which showed cleavage of the cobalt–carbon bond by electrolysis.

Cobalamin-dependent enzymes catalyze various molecular transformations that are of particular interest from the viewpoint of organometallic and catalytic chemistry.[1–5] One of the most significant properties of the cobalamin is a high nucleophilicity toward several alkyl halides to form an alkylated complex with dehalogenation.[6–8] Such reductive dehalogenation reactions are presently of great interest, primarily because of their potential use in the treatment of halogenated solvent wastes as well as in remedial approaches to remove such chemicals from contaminated soil and water.[9,10] Recently, it has been demonstrated that certain bacteria can use tetrachloroethene as an electron acceptor by reducing it to *cis*-dichoroethene.[2,11] *Reductive dehalogenase* contains cobalamin as a cofactor.[2,11] Thus, the substantial ability of cobalamin for reductive dehalogenation prompted us to investigate the reactivity of a cobalamin derivative for the degradation of various organic halides. We have been dealing with a hydrophobic vitamin B$_{12}$, heptamethyl cobyrinate perchlorate [Cob(II)7C$_1$ester]ClO$_4$, which has ester groups in place of the peripheral amide moieties of the naturally occurring cobalamin, as shown in Chart 1;[12] also, (II) in [Cob(II)7C$_1$ester]ClO$_4$ shows the oxidation state of cobalt. We performed the dechlorination of 1,1-bis(4-chlorophenyl)-2,2,2-trichloroethane (DDT) catalyzed by a hydrophobic vitamin B$_{12}$ under electrochemical and photochemical conditions.[13,14] During the course of these studies, hydrophobic vitamin B$_{12}$ was found to act as an excellent catalyst for the dehalogenation of chlorinated organic compounds. Thus, in the present work we carried out a systematic study concerning the reactivity of the Co(I) species of hydrophobic vitamin B$_{12}$ toward various organic halides, such as chloroform, dichloromethane, and tetrachloromethane, etc., as shown in Scheme 1. Such compounds are widely known as environmental pollutants.

Experimental

Materials. All solvents and chemicals used in the synthesis were of reagent grade, and were used without further purification. For electrochemical studies, *N*,*N*-dimethylformamide (DMF) was stirred for one day in the presence of BaO under a nitrogen atmosphere, and distilled under reduced pressure. The distillation was performed with the exclusion of light, and DMF thus purified was stored in a refrigerator under nitrogen in the presence of activated molecular sieves, 4A. Tetrabutylammonium perchlorate (n-Bu$_4$NClO$_4$) was purchased from Nakalai Chemicals (special grade) and dried at room temperature under a vacuum before use. Heptamethyl cobyrinate perchlorate, [Cob(II)7C$_1$ester]ClO$_4$, was synthesized by a previously reported method.[12,15] α-Phenyl *N*-(*t*-butyl)nitrone (PBN) was purchased from Aldrich and was used without further purification.

Synthesis of [(CH$_2$Cl)Cob(III)7C$_1$ester]ClO$_4$ (1). A methanol solution (100 mL) of [Cob(II)7C$_1$ester]ClO$_4$ (30 mg, 2.6×10^{-5} mol) was deoxygenated by bubbling nitrogen gas through



Hydrophobic vitamin B$_{12}$
[Cob(II)7C$_1$ester]ClO$_4$

Chart 1.

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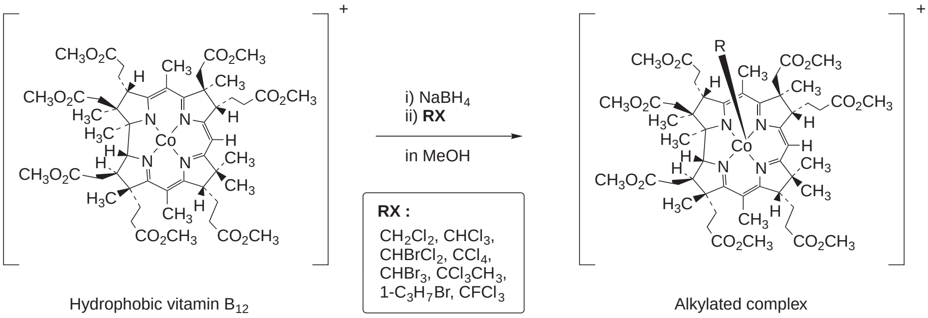


R = CH$_2$Cl (**1**), CHCl$_2$ (**2**), CCl$_3$ (**3**), CHBr$_2$ (**4**)
CCl$_2$CH$_3$ (**5**), 1-C$_3$H$_7$ (**6**), CFCl$_2$ (**7**)

Scheme 1.

it for 15 min at 303 K, and sodium tetrahydroborate (300 mg, 7.9×10^{-3} mol) was added to the deoxygenated solution with vigorous stirring under a nitrogen atmosphere. The following operations were carried out in the dark. When the solution turned dark green, dichloromethane (CH_2Cl_2) (1 g, 1.2×10^{-2} mol) was added to it. The resulting solution was stirred for 5 min at room temperature, and 30% (w/w) aqueous perchloric acid (3 mL) was carefully added to it in order to decompose any excess of sodium tetrahydroborate. With adding dichloromethane (extracting solvent) and water, the organic layer was separated using a separation funnel. After drying over anhydrous Na_2SO_4, the dichloromethane extract was evaporated to dryness, and the resulting powder was collected by suction filtration. After being dried in vacuo, the product was reprecipitated from benzene upon the addition of *n*-hexane to afford a brown powder. Yield: 19 mg (63%). Found: C, 53.71; H, 6.50; N, 4.75%. Calcd for $C_{53}H_{75}N_4Cl_2Co_1O_{18}$: C, 53.67; H, 6.37; N, 4.72%. UV–vis (in CH_2Cl_2): [λ_{max}/nm], 263, 305, 380$_{sh}$, 462. ESI MS: $(M - ClO_4)^+$, 1085.6 (calcd for $M - ClO_4$, 1085.4); $(M - Cl - ClO_4)^+$, 1051.5.

The following alkylated complexes (**2**–**7**) were synthesized by the same method as for **1**:

Synthesis of [(CHCl$_2$)Cob(III)7C$_1$ester]ClO$_4$ (2). Chloroform ($CHCl_3$) was used as substrate in place of CH_2Cl_2. Yield: 61%. Found: C, 52.31; H, 6.40; N, 4.75%. Calcd for $C_{53}H_{74}N_4Cl_3Co_1O_{18}$: C, 52.16; H, 6.11; N, 4.59%. UV–vis (in CH_2Cl_2): [λ_{max}/nm], 262, 305, 378$_{sh}$, 458. ESI MS: $(M - ClO_4)^+$, 1119.4 (calcd for $M - ClO_4$, 1119.4); $(M - Cl - ClO_4)^+$, 1085.4; $(M - Cl_2 - ClO_4)^+$, 1051.5. Bromodichloromethane ($CHBrCl_2$), used as a substrate, afforded the same product. Yield: 69%.

Synthesis of [(CCl$_3$)Cob(III)7C$_1$ester]ClO$_4$ (3). Tetrachloromethane (CCl_4) was used as substrate in place of CH_2Cl_2. Yield: 55%. Found: C, 50.69; H, 5.81; N, 4.74%. Calcd for $C_{53}H_{73}N_4Cl_4Co_1O_{18}$: C, 50.73; H, 5.86; N, 4.46%. UV–vis (in CH_2Cl_2): [λ_{max}/nm], 262, 305, 382$_{sh}$, 447. ESI MS: $(M - Cl - ClO_4)^+$, 1119.5 (calcd for $M - Cl - ClO_4$, 1119.4); $(M - Cl_2 - ClO_4)^+$, 1085.6; $(M - Cl_3 - ClO_4)^+$, 1051.6.

Synthesis of [(CHBr$_2$)Cob(III)7C$_1$ester]ClO$_4$ (4). Bromoform ($CHBr_3$) was used as substrate in place of CH_2Cl_2. Yield: 52%. Found: C, 48.33; H, 5.65; N, 4.45%. Calcd for $C_{53}H_{74}N_4Br_2Cl_1Co_1O_{18}$: C, 48.62; H, 5.70; N, 4.28%. UV–vis (in CH_2Cl_2): [λ_{max}/nm], 305, 320, 459. ESI MS: $(M - ClO_4)^+$, 1207.4 (calcd for $M - ClO_4$, 1207.3); $(M - Br - ClO_4 + H)^+$, 1129.5; $(M - Br_2 - ClO_4 + 2H)^+$, 1051.6.

Synthesis of [(CCl$_2$CH$_3$)Cob(III)7C$_1$ester]ClO$_4$ (5). 1,1,1-Trichloroethane (CCl_3CH_3) was used as substrate in place of CH_2Cl_2. Yield: 22%. UV–vis (in CH_2Cl_2): [λ_{max}/nm], 315, 466. ESI MS: $(M - ClO_4 + 2H)^+$, 1135.5 (calcd for $M - ClO_4$, 1133.4); $(M - Cl - ClO_4)^+$, 1097.5; $(M - Cl_2 - ClO_4)^+$, 1063.6.

Synthesis of [(C$_3$H$_7$)Cob(III)7C$_1$ester]ClO$_4$ (6). 1-Bromopropane was used as substrate in place of CH_2Cl_2. Yield: 47%. UV–vis (in CH_2Cl_2): [λ_{max}/nm], 263, 303, 380, 443. ESI MS: $(M - ClO_4)^+$, 1079.5 (calcd for $M - ClO_4$, 1079.5).

Synthesis of [(CFCl$_2$)Cob(III)7C$_1$ester]ClO$_4$ (7). Fluorotrichloromethane (CCl_3F) was used as substrate in place of CH_2Cl_2. Yield: 41%. Found: C, 51.33; H, 5.65; N, 4.45%. Calcd for $C_{53}H_{73}N_4Cl_3Co_1F_1O_{18}$: C, 51.40; H, 5.94; N, 4.52%. UV–vis (in CH_2Cl_2): [λ_{max}/nm], 261, 303, 383$_{sh}$, 454. ESI MS: $(M - ClO_4)^+$, 1137.4 (calcd for $M - ClO_4$, 1137.4); $(M - Cl - F - ClO_4)^+$, 1083.3.

Measurements. Elemental analyses were obtained from the Service Center of Elementary Analysis of Organic Compounds at Kyushu University. The UV–vis absorption spectra were measured on a Hitachi U-3300 spectrophotometer at room temperature. Electrospray ionization (ESI) mass spectra were obtained on a PE SCIEX API III, and PerSeptive Biosystem Mariner™. All measurements of photo-labile alkylated complexes were performed in a dark room under dim light.

Cyclic Voltammetry. Cyclic voltammograms (CV) were obtained using a BAS CV 50W electrochemical analyzer. A three-electrode cell equipped with a 1.6-mm diameter platinum wire as the working and counter electrodes was used. An Ag–AgCl (3.0 mol dm^{-3} NaCl) electrode served as a reference. Nonaqueous DMF solutions containing an alkylated cobalt complex (1.0×10^{-3} mol dm^{-3}) and *n*-Bu$_4$NClO$_4$ (1.0×10^{-1} mol dm^{-3}) were deaerated prior to each measurement, and an argon atmosphere was maintained inside the cell throughout each measurement. All measurements were carried out at room temperature. The $E_{1/2}$ value of ferrocene/ferrocenium (Fc/Fc$^+$) was 0.56 V vs Ag–AgCl with this setup.

Measurements of ESR Spectra. The ESR spectra were obtained on a JEOL JES-FE1G X-band spectrometer equipped with an Advantest TR-5213 microwave counter and an Echo Electronics EFM-200 NMR field meter. The ESR spectra observed after photolysis of alkylated complexes (5.0×10^{-4} mol dm^{-3}) in the presence of PBN (2.0×10^{-1} mol dm^{-3}) were measured in methanol at room temperature under a completely degassed condition by freeze–pump–thaw cycles. Irradiation of visible light was done with a 500-W tungsten lamp.

Results and Discussion

Syntheses and Characterization of Alkylated Cobalt Complexes. The hydrophobic vitamin B_{12}, [Cob(II)7C_1-ester]ClO_4 reproduces the $E_{1/2}$ value for Co^{II}/Co^{I} in base-off aquacobalamin, and can easily be reduced to a Co(I) species by the reaction of some chemical reducing reagent, or by an electrochemical reduction.[16,17] A reaction of [Cob(II)-7C_1ester]ClO_4 with sodium tetrahydroborate in methanol afforded a greenish-blue solution, which showed a strong π–π^* transition band at 390 nm. This is a typical spectrum for the Co(I) species for hydrophobic vitamin B_{12}.[16,17] A subsequent reaction with CH_2Cl_2 immediately changed the color of the solution to dark brown. The resulting dark-brown product was photo-sensitive. Figure 1 shows the UV–vis absorption spectra of this product before (Line A) and after (Line B) irradiation with visible light under aerobic conditions. This spectral change is characteristic of a compound with a cobalt–carbon bond.[18] Insight into the nature of this photo-sensitive species was also obtained from ESI-MS. ESI-MS has been found to be applicable to the characterization of unstable compounds, including organometallic compounds due to the mildness of the ionization method.[19,20] The introduction of a methanol solution of the complex into the ESI mass spectrometer in the dark afforded a positive ion mass spectrum with the most prominent peak cluster at m/z 1085.6, which has a mass value consistent with the ions $[M - ClO_4]^+$, as shown in Fig. 2. A satisfactory elemental analysis for the product was also obtained. Thus, a compound with a cobalt–carbon bond for hydrophobic vitamin B_{12} was formed in the reaction of CH_2Cl_2.

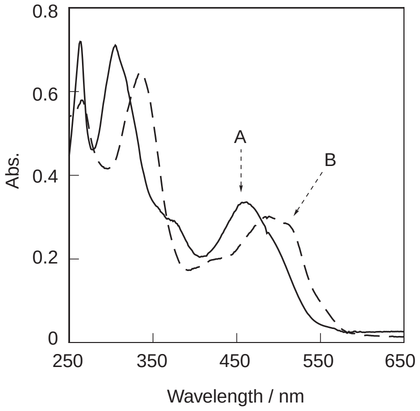


Fig. 1. UV–vis absorption spectra of [(CH_2Cl)Cob(III)-7C_1ester]ClO_4 (**1**) in CH_2Cl_2 (solid line) and after irradiation with visible light (broken line).

Similarly, other organic halides (alkylated reagents: $CHCl_3$, $CHBrCl_2$, CCl_4, $CHBr_3$, CCl_3CH_3) also react with the Co(I) species of hydrophobic vitamin B_{12} to afford the corresponding alkylated complexes with dehalogenation. These chlorinated and brominated organic compounds have been widely used in industrial processes, and are the major environmental pollutants commonly found in soil, groundwater, and the atmosphere.[9,21] Fluorotrichloromethane ($CFCl_3$), so-called CFC-11, also reacted with hydrophobic vitamin B_{12}. 1-Bromopropane substitute for ozone layer-depleting chlorofluorocarbons, is thought to cause hemotopoietic and reproductive hazards,[22] which also reacted with hydrophobic vitamin B_{12} with dehalogenation. In this way, the Co(I) species of hydrophobic vitamin B_{12} reacted with various organic halides to form alkylated compounds with dehalogenation.

Electronic Spectra of Alkylated Complexes. One of the most convenient methods for identifying particular cobalamin derivatives is electronic absorption spectroscopy. As mentioned above, an alkylated complex gave the characteristic photo-sensitive UV–vis absorption spectrum, as shown in Fig. 1. It is known that the electronic spectra of the cobalamin derivatives are quite sensitive to axial ligands.[23] In the alkylated complex, subtle changes did not affect the spectrum (γ-band), but the visible region (α-band) was sensitive to the number of chlorines attached to the carbon, which was bonded onto the cobalt atom, as shown in Fig. 3. Indeed, the electronegativity of the substituent at the carbon atom attached to the cobalt ion exhibited a good linear relationship with the α-band, as shown in Fig. 4.

Cleavage of Cobalt–Carbon Bonds. The cobalt–carbon bond of alkylated cobalt complexes undergoes a variety of cleavage reactions via homolytic or heterolytic pathways, as shown in Scheme 2.[24,25] The manner of photolysis for **1**, **2**, and **3** was investigated by UV–vis and ESR spectroscopies.

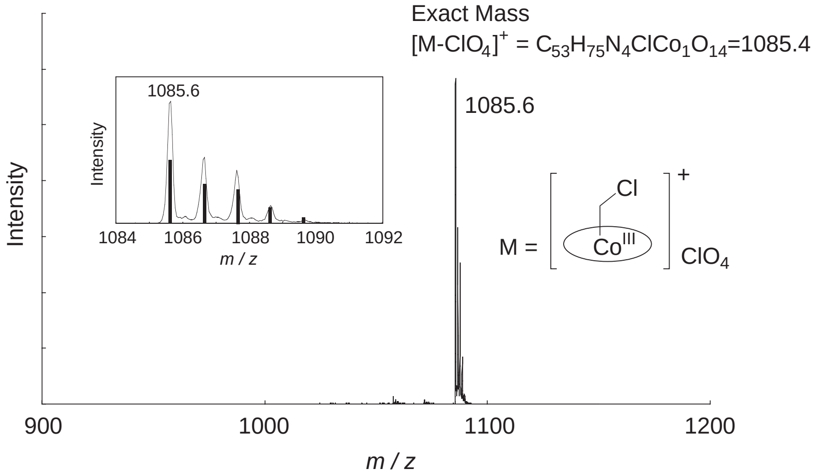


Fig. 2. ESI-mass spectrum of [(CH_2Cl)Cob(III)7C_1ester]ClO_4 (**1**).

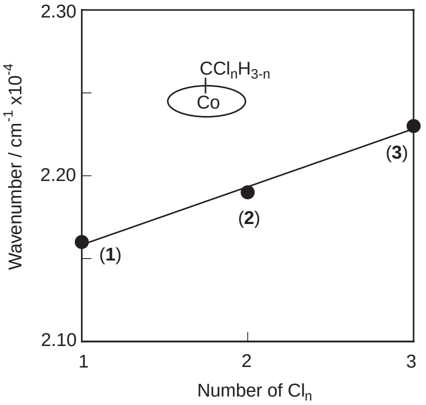


Fig. 3. Plots of wavenumber for various alkylated complexes, $[(CCl_nH_{3-n})Cob(III)7C_1ester]ClO_4$ (**1**, **2**, and **3**).

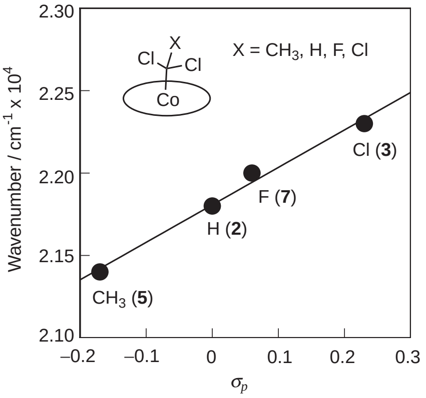
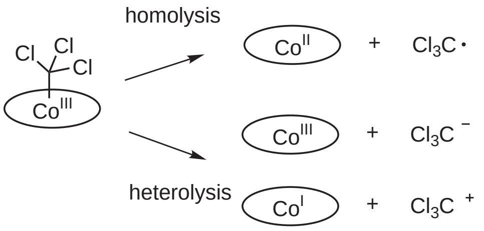


Fig. 4. Hammett plots of wavenumber for various alkylated complexes, $[(XCCl_2)Cob(III)7C_1ester]ClO_4$ (**2**, **3**, **5**, and **7**).



Scheme 2.

The UV–vis spectrum of **3** in MeOH was changed to absorption maxima at 266, 315, 405_{sh}, and 468 nm after the irradiation of visible light under anaerobic condition, and the resulting spectrum was identical to that of the Co(II) state. The reaction was also followed by the ESR spin-trapping technique with PBN. An ESR signal attributable to the PBN spin adduct was observed after the photolysis of **3** under anaerobic condition at $g = 2.006$ ($A_N = 14.5$ G, $A_H = 5.9$ G; 10^4 G $= 1$ Tesla), as shown in Fig. 5. It is obvious from these results that the photolysis causes a homolytic cleavage of the cobalt–carbon bond for **3**. A similar spectral behavior was also observed in the cases of **1** and **2**.

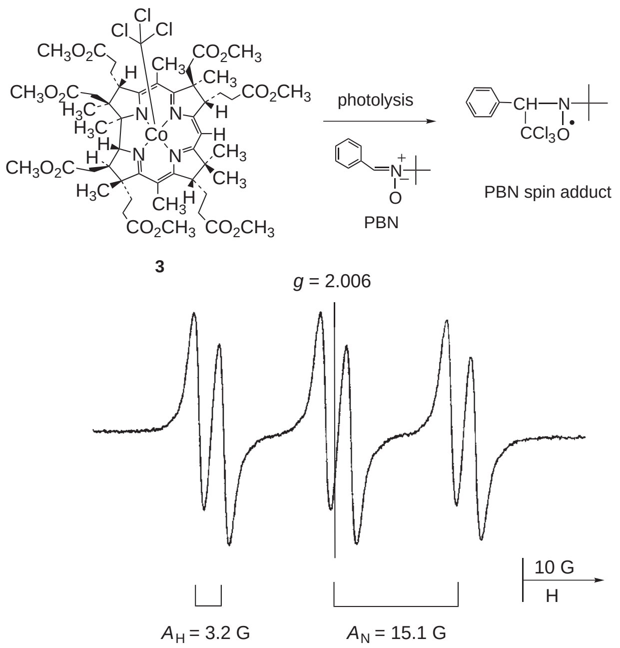


Fig. 5. ESR spectrum observed during photolysis of a MeOH solution containing $[(CCl_3)Cob(III)7C_1ester]ClO_4$ (**3**) (5.0×10^{-4} mol dm^{-3}) and PBN (2.0×10^{-1} mol dm^{-3}) under anaerobic condition.

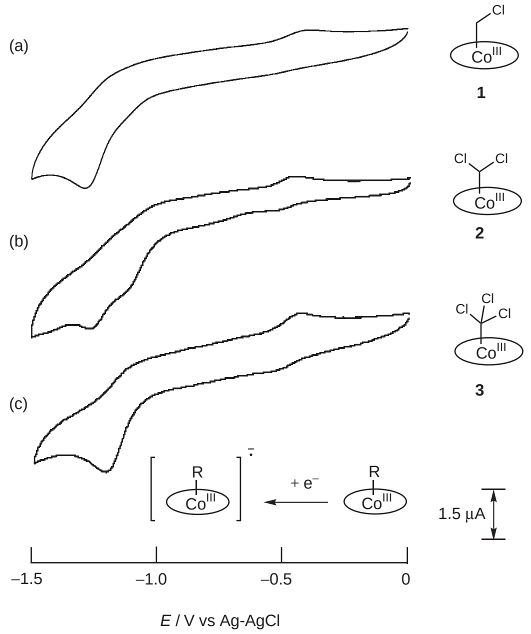


Fig. 6. Cyclic voltammograms of various alkylated complexes in DMF containing 0.1 mol dm^{-3} n-Bu_4NClO_4 at room temperature in the dark; sweep rate: 100 mV s^{-1}. (a) **1**, (b) **2**, and (c) **3**.

Redox Behavior of the Alkylated Complexes. The redox behavior of alkylated complexes was investigated by cyclic voltammetry in DMF. The cyclic voltammograms of alkylated complexes, **1**, **2**, and **3** are shown in Fig. 6. A single irreversible reduction peak, assigned to a one-electron reduction of the alkylated complex, was observed at -1.29 V vs Ag–AgCl for **1**. In the cases of **2** and **3**, the corresponding irreversible

Table 1. Redox Potentials for the Various Alkylated Complexes[a)]

$[(CH_{3-n}Cl_n)Cob(III)7C_1ester]^+$	Reduction /vs Ag–AgCl	n/Number of Cl
$[(CH_3)Cob(III)7C_1ester]^+$	−1.32	0
1 ($n = 1$)	−1.29	1
2 ($n = 2$)	−1.27	2
3 ($n = 3$)	−1.21	3

a) Working and counter electrode: Pt, [complex] $= 1.0 \times 10^{-3}$ M, $[n\text{-}Bu_4NClO_4] = 0.1$ M, under Ar atomosphere at room temperature. Scan rate, 100 mV/s. Solvent, DMF.

reduction peaks were observed at −1.27 V and −1.21 V vs Ag–AgCl, respectively (Table 1). A slight anodic shift of the reduction potential is due to the number of chlorine substituents on the carbon atom attached to the cobalt ion. In any event, these voltammograms indicate that the alkylated complexes are decomposed by electrolysis in a potential range more cathodic than −1.3 V vs Ag–AgCl. These results show the possibility for catalytic dehalogenation of chlorinated organic compounds by hydrophobic vitamin B_{12}.

In conclusion, the Co(I) form of hydrophobic vitamin B_{12} reacted with various organic halides to form an alkylated complex with dehalogenation. It is very interesting that even bulky halide compounds, such as CCl_4 and CCl_3CH_3, can react with the Co(I) species of hydrophobic vitamin B_{12} to form cobalt-haloalkyl complexes. Such organic halides are widely known as environment pollutants. Catalytic dehalogenation of various organic halides, achieved by hydrophobic vitamin B_{12}, is currently under investigation in our laboratory.

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