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Characterization of a Simple Vitamin B_{12} Model Complex and Its Catalysis in Electrochemical Carbon-Skeleton Rearrangement

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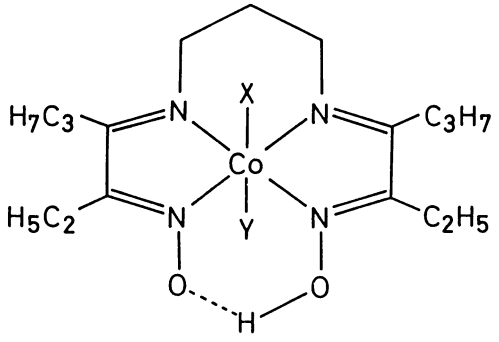
The electrochemical carbon-skeleton rearrangement reaction of 2,2-bis(ethoxycarbonyl)-1-bromopropane was catalyzed by the cobalt complex of 2,10-diethyl-3,9-dipropyl-1,4,8,11-tetraazaundeca-1,3,-8,10-tetraene-1,10-diol, which was characterized by ESR spectroscopy and cyclic voltammetry.

Various isomerization reactions, which are known to be catalyzed by vitamin B_{12}-dependent enzymes, have not been investigated under electrochemical conditions in the presence of vitamin B_{12} and its model complexes. Recently, we have found that the controlled-potential electrolysis of 2,2-bis(ethoxycarbonyl)-1-bromopropane, a model substrate for methylmalonyl-CoA mutase, was catalyzed by a hydrophobic vitamin B_{12} in N,N-dimethylformamide (DMF) to give 1,2-bis(ethoxycarbonyl)-propane as a major product in the dark.[1] This is the first example for the carbon-skeleton rearrangement reaction catalyzed by a vitamin B_{12} model under electrochemical conditions. This finding prompted us to develop a simple model complex, which shows redox behavior analogous to that of vitamin B_{12} with respect to the nuclear cobalt and catalyzes the isomerization reaction in a similar manner. We report here on the electrochemical carbon-skeleton rearrangement catalyzed by a model complex which was derived from the Costa's complex[2] by its modification.

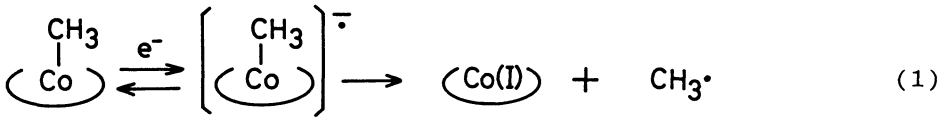
Various simple cobalt complexes have been synthesized as vitamin B_{12} models,[3] but most of those complexes cannot be qualified as favorable models in view of their redox potentials with respect to the central cobalt, which are primarily controlled by basicity of equatorial ligands. Since the corrinoid skeleton of vitamin B_{12} behaves as a monoanionic ligand, it is most appropriate to employ such an equatorial ligand to prepare a model complex. In this regard, we became interested in



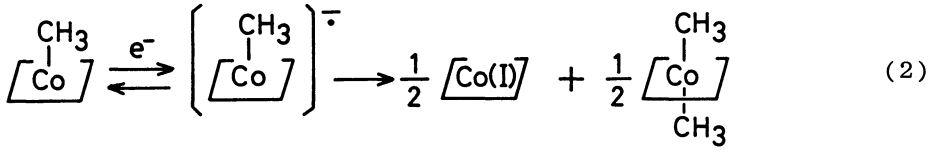
$[Co^{III}\{(C_2C_3)(DO)(DOH)pn\}Cl_2]$ (**1**): X = Y = Cl
$[Co^{III}\{(C_2C_3)(DO)(DOH)pn\}Br_2]$ (**2**): X = Y = Br
$[Co^{III}\{(C_2C_3)(DO)(DOH)pn\}I_2]$ (**3**): X = Y = I
$[Co^{II}\{(C_2C_3)(DO)(DOH)pn\}(H_2O)_2]B(C_6H_5)_4$ (**4**): X = Y = H_2O
$[Co^{III}\{(C_2C_3)(DO)(DOH)pn\}(CH_3)(H_2O)]ClO_4$ (**5**): X = CH_3, Y = H_2O
$[Co^{III}\{(C_2C_3)(DO)(DOH)pn\}(CH_3)_2]$ (**6**): X = Y = CH_3

adopting the Costa's model complex[2] and modified it by placing alkyl groups in its peripheral sites so that the resulting complex becomes soluble in various organic solvents. 2,10-Diethyl-3,9-dipropyl-1,4,8,11-tetraazaundeca-1,3,8,10-tetraene-1,10-diol, $(C_2C_3)(DOH)_2pn$, and its cobalt complexes with various axial ligands were prepared (refer to the structural formulae in the preceding page)[4] by referring to the reported procedures[5] along with some modifications. Complex **4** is a typical low-spin Co^{II} complex in the light of its ESR spectrum; $g_{\parallel} = 2.00$, $g_{\perp} = 2.38$, and $A_{\parallel}^{Co} = 104 \times 10^{-4}$ cm^{-1} (in chloroform at 77 K). When pyridine was added in two- to ten-fold molar excess over a quantity of the cobalt complex, only one pyridine molecule was coordinated to the central cobalt at its axial site: the superhyperfine structure due to the interaction between the nitrogen nucleus (I = 1) and the cobalt nucleus (I = 7/2) was observed in the $g_{\parallel}$ region; $g_{\parallel} = 2.00$, $g_{\perp} = 2.28$, $A_{\parallel}^{Co} = 83 \times 10^{-4}$ cm^{-1}, and $A_{\parallel}^{N} = 14 \times 10^{-4}$ cm^{-1}. In the presence of a large excess of pyridine (ca. 500-fold), however, both axial sites of the central cobalt were occupied by pyridine molecules as confirmed by ESR spectroscopy. These ESR behavior and the corresponding spin Hamiltonian parameters are comparable to those observed for a hydrophobic vitamin B_{12r} having a corrinoid ligand.[6]

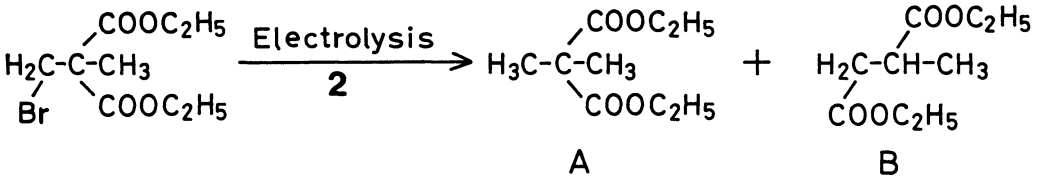
The redox behavior of the present complexes was investigated in DMF by means of cyclic voltammetry. The reversible Co(II)/Co(I) redox couple for **4** was observed at -0.69 V vs. Ag/AgCl. As for the complexes with halogen ligands such as **1**, **2**, and **3**, their Co(II)/Co(I) redox couples were observed in the range of -0.69 to -0.70 V vs. Ag/AgCl. These values are very close to those observed for the hydrophobic vitamin B_{12}[7] and aquacobalamin;[8] -0.61 V vs. SCE in DMF and -0.74 V vs. SCE in water, respectively. The Co(II)/Co(I) redox potential for cobaloxime, a vitamin B_{12} model frequently used, was observed by far in a more cathodic range relative to these values; -1.11 V vs. SCE in acetonitrile.[2] In the course of the initial sweep of cyclic voltammetry applied on **5**, a single irreversible reduction peak, which is assigned to the one-electron reduction intermediate, was observed at -1.50 V vs. Ag/AgCl, while somewhat weaker peaks (-1.36 and -0.65 V vs. Ag/AgCl) were observed in the anodic sweep; the latter being attributed to the Co(I)/Co(II) oxidation. A Co(II)/Co(I) reduction peak was then detected at -0.90 V vs. Ag/AgCl in the cathodic sweep. Such behavior is similar to that observed for the methylated hydrophobic vitamin B_{12}.[1] The one-electron reduction intermediate of the present complex is less labile than that of the methylated hydrophobic vitamin B_{12} in the cobalt—carbon bond cleavage, since the ratio between anodic and cathodic peak currents (i_{pa}/i_{pc}) was 0.54 for the present methylated complex while 0.23 for the methylated hydrophobic vitamin B_{12} at the identical sweep rate (100 mV s^{-1}). The one-electron reduction potential for **5** is close to those for the methylated hydrophobic vitamin B_{12} and methylcobinamide; -1.32 V vs. SCE in DMF[1] and -1.46 V vs. SCE in DMF—1-propanol (1:1 v/v),[8] respectively. However, the corresponding potential for methylcobaloxime is -2.2 V vs. SCE in acetonitrile at -26 °C,[2] which is by far in a more cathodic range relative to the value for vitamin B_{12} and must arise from the difference in ligand nature; the present and corrinoid ligands are monoanionic, while the cobaloxime ligand is dianionic. As to the cobalt—carbon bond cleavage of the one-electron reduction intermediate, the methylated hydrophobic vitamin B_{12} undergoes the cleavage by the irreversible homolysis shown in



(1)



(2)



(3)

Table 1. Product analyses for controlled-potential electrolysis of 2,2-bis(ethoxycarbonyl)-1-bromopropane as catalyzed by **2**[a)]

Entry	Electrolysis conditions					Yield/%[e)]	
	Potential V vs. Ag/AgCl	Irradiation[b)]	Additive[c)]	Charge[d)] F mol^{-1}	Period h	A	B
1	-1.0	Irradiation	Imidazole	0.6	26	ca. 2	Trace
2	-1.5	In the dark	None	0.5	24	Trace	Trace
3	-1.5	In the dark	Imidazole	2.0	14	16—20	18—26
4	-1.8	In the dark	None	0.5	24	1—2	Trace
5	-1.8	In the dark	Imidazole	2.0	10	35—40	40—47
6	-2.0	In the dark	None	2.0	7	7—11	1—2
7	-2.0	In the dark	Imidazole	2.0	6	20—25	55—61

a) Electrolysis was carried out in a two-compartment cell equipped with Pt electrodes at 20 ± 2 °C under argon atmosphere. Starting solutions composed of: **2**, 30 mg (5.5 x 10^{-5} mol); 2,2-bis(ethoxycarbonyl)-1-bromopropane, 1.0 g (3.8 x 10^{-3} mol); 30 mL of DMF containing 0.05 mol dm^{-3} tetrabutylammonium tetrafluoroborate. b) Irradiation with a 300-W tungsten lamp from a distance of 50 cm. c) Imidazole, 100 mg (1.47 x 10^{-3} mol). d) Electrical charge passed per mol of the substrate. e) Based on an initial amount of the substrate; the rest was the unreacted substrate; analyzed by GLC; refer to structures in Eq. 3 for A and B.

Eq. 1.[1)] On the other hand, the disproportionation reaction (Eq. 2) takes place with the present complex as clarified for similar complexes by Elliott et al.[2)] The dimethylated complex (**6**) did not show any reduction peak over the potential range from 0 to -2.0 V vs. SCE in DMF. When a large excess of imidazole was added, the disproportionation reaction did not occur.

On the basis of the above study on redox behavior, the catalytic function of **2** was investigated by using 2,2-bis(ethoxycarbonyl)-1-bromopropane as a substrate under electrochemical conditions (refer to Eq. 3). The reaction cycle proceeds in the following manner: the Co^{III} complex is converted into the Co^{I} species by elec-

trochemical reduction, and the corresponding alkylated complex is generated by the reaction of the super-nucleophilic Co^{I} with the substrate; the alkylated complex is decomposed by photolysis or electrolysis to afford the products, and the cobalt complex acts as a mediator repeatedly. The following findings are based on the product analyses under various conditions (Table 1). (i) Products A and B were scarcely detected without imidazole at every potential in the range of -1.0 to -2.0 V vs. Ag/AgCl. (ii) The rearrangement product (B) was largely obtained at -1.5, -1.8, and -2.0 V vs. Ag/AgCl in the presence of imidazole. (iii) The rearrangement reaction proceeds more favorably under stronger reduction conditions.

On careful comparison between the electrochemical carbon-skeleton rearrangement reactions catalyzed by the present simple vitamin B_{12} model and the hydrophobic vitamin B_{12},[1] some comments need to be made. (i) The hydrophobic vitamin B_{12} does not require an organic base for the catalytic reaction, while a base such as imidazole is essential to the reaction catalyzed by the present complex. Imidazole must be bound to the nuclear cobalt of the alkylated vitamin B_{12} model, so that the cobalt—carbon bond is effectively activated by the trans effect arising from the coordinated axial base. When imidazole is not present, the corresponding dialkylated complex (refer to Eq. 2), that is inactive for both electrolysis and photolysis, is formed in the course of reaction, and consequently the catalytic reaction does not take place efficiently. (ii) The hydrophobic vitamin B_{12} requires a proton source for the formation of product B during the electrolysis at -1.5 V vs. Ag/AgCl, while the present model complex affords the product in a significant yield without such an additive under the comparable conditions.

References

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2) C. M. Elliott, E. Hershenhart, R. G. Finke, and B. L. Smith, J. Am. Chem. Soc., 103, 5558 (1981).
3) See for example: J. Halpern, "Chemistry and Significance of Vitamin B_{12} Model System," in "B_{12}," ed by D. Dolphin, John Wiley, New York (1982), Vol. 1, pp. 501—542.
4) All new compounds were characterized fully by analytical and spectroscopic methods; elemental analyses for selected complexes are as follows. Found (**2**): C, 37.72; H, 5.72; N, 10.33%. Calcd for $C_{17}H_{31}N_4Br_2CoO_2$ (**2**): C, 37.66; H, 5.76; N, 10.33%. Found (**4**): C, 66.63; H, 7.51; N, 7.79%. Calcd for $C_{41}H_{55}N_4BCoO_4$ (**4**): C, 66.76; H, 7.51; N, 7.60%. Found (**5**): C, 41.96; H, 6.98; N, 10.84%. Calcd for $C_{18}H_{36}N_4ClCoO_7$ (**5**): C, 41.99; H, 7.05; N, 10.88%.
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