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Hydrophobic Vitamin B_{12}

8. Carbon-Skeleton Rearrangement Reactions Catalyzed by Hydrophobic Vitamin B_{12} in Octopus Azaparacyclophane

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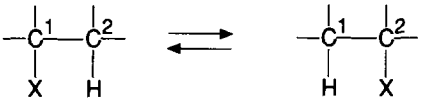
Heptapropyl cobyrinate perchlorate catalyzed the carbon-skeleton rearrangements, which convert 2-acetyl-2-ethoxycarbonylpropane, 2-cyano-2-ethoxycarbonylpropane, 1-acetyl-1-ethoxycarbonylethane, and diethyl β-methyl-DL-aspartate into 1-acetyl-2-ethoxycarbonylpropane, 2-cyano-1-ethoxycarbonylpropane and 1-cyano-2-ethoxycarbonylpropane, 1-acetyl-2-ethoxycarbonylethane, and diethyl glutamate, respectively, in an octopus cyclophane placed in aqueous carbonate buffer (pH 7.0) at 20.0°C by utilizing vanadium trichloride as a cocatalyst under aerobic photolysis conditions. The migratory aptitude of the electron-withdrawing groups was found to follow the sequence: CN ≈ $CO_2C_2H_5$ < $COCH_3$. Yields of the rearrangement products were very low in the absence of heptapropyl cobyrinate perchlorate.

INTRODUCTION

Among vitamin B_{12}-dependent enzymatic reactions, isomerization reactions, which lead to intramolecular 1,2-migration of various functional groups, have been attracting much attention because of the novel nature of these reactions from the viewpoint of organic chemistry (Eq. [1]). In particular, carbon-skeleton rearrangement reactions, mediated by methylmalonyl-CoA mutase, glutamate mutase, and α-methyleneglutarate mutase, do not require additional cofactors, different from other isomerization reactions, and radical intermediates have not been detected by ESR in these reactions (*1*). This raised questions whether the reactions proceed via radical or anionic mechanisms, and whether the cobalt of vitamin B_{12} coenzyme participates in the rearrangement process. Thus, clarification of the reaction mechanisms involved has become a challenging area of biomimetic research, and relevant model reaction systems have been developed and investigated in view of their physicochemical behavior and reactivity (*2*). Cobaloxime,



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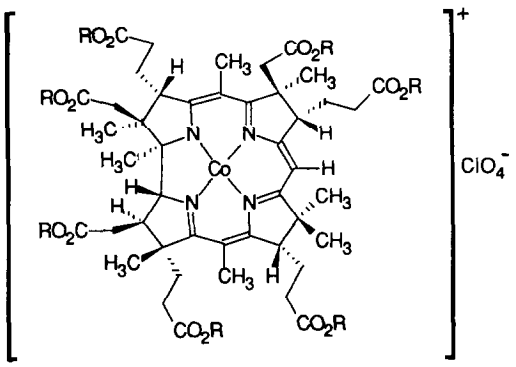
bis(dimethylglyoximato)cobalt, developed by Schrauzer *et al.*, is capable of forming the cobalt–carbon bond with various ligands in a manner as confirmed with vitamin B_{12} (*3*). However, this cobalt complex is not considered to be a good model complex since its redox behavior is much different from that of vitamin B_{12} (*4*). On the other hand, various model reactions have been carried out by utilizing vitamin B_{12} itself in aqueous media due to the solubility problem of this coenzyme (*5*). As a consequence, the reactivity was found to be much lower relative to that of the enzymatic systems.

The naturally occurring apoproteins, which provide relevant reaction sites for vitamin B_{12}, are considered to play crucial roles that lead to desolvation and close association of reacting species (*1*). In this regard, we have been interested in the catalytic activity of vitamin B_{12} in hydrophobic microenvironments, to simulate the catalytic functions of the holoenzymes concerned. Various macrocyclic compounds have been studied extensively in view of their potential for functional simulation of enzymes (*6*). It is required for our study to develop macrocycles which provide a three-dimensionally extended cavity so that a bulky vitamin B_{12} model complex can be incorporated into it. From this viewpoint, we have prepared an octopus cyclophane having eight hydrocarbon chains, $APC[C_2Lys\text{-}(C_5N^+)2C_{14}]_4$, that behaves as an effective cationic host over a wide pH range in aqueous media (*7*). To achieve complete incorporation of a vitamin B_{12} model into a hydrophobic microenvironment provided by the octopus cyclophane, the naturally occurring vitamin B_{12}, cobalamin, needs to be chemically modified. We have prepared hydrophobic vitamin B_{12} derivatives which have carboxylic ester groups in place of the peripheral amide moieties of cobalamin (*8, 9*) and found that the hydrophobic vitamin B_{12} is incorporated into the octopus cyclophane in a 1 : 1 molar ratio (*10, 11*).

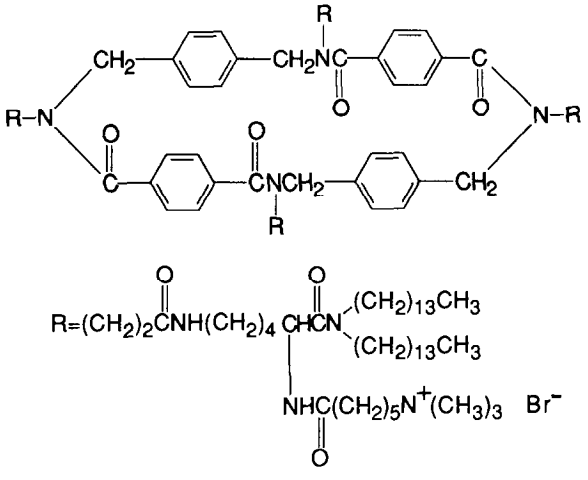
Even though real reaction mechanisms involved in the carbon-skeleton rearrangements mediated by the vitamin B_{12}-dependent enzymes are not clarified at the present stage, radical mechanisms are considered to be the most plausible mechanisms for other 1,2-migration reactions on the basis of various evidences (*12*). In this regard, rearrangement reactions, promoting 1,2-migration of a thioester or an acyl group via formation of substrate radical intermediates generated by reaction of the corresponding bromides with *n*-Bu_3SnH and 2,2′-azobisisobutyronitrile, were investigated in methanol or benzene without a vitamin B_{12} model at relatively high temperatures (60–114°C) in connection with biological reactions (*13, 14*). In those reactions, an acyl group readily migrated (yield, ca. 80%), but a thioester group was not a good migrating group (yield, 1–9%). However, any relevant apoprotein models, which are capable of generating substrate radicals in the dark, have not been developed up to now. To compromise on these circumstances, we have been adopting photolysis conditions to generate substrate radicals. We have found previously that carbon-skeleton rearrangement reactions of alkyl ligands bound to a hydrophobic vitamin B_{12}, as simulation of the methylmalonyl-CoA mutase reaction, were markedly favored in the hydrophobic cavity provided by the octopus cyclophane under anaerobic photolysis conditions at ordinary temperatures (*11*).

In this work, we examined carbon-skeleton rearrangements catalyzed by a



R = n-C_3H_7

[Cob(II)7C_3ester]ClO_4



APC[C_2Lys(C_5N^+)2C_{14}]$_4$

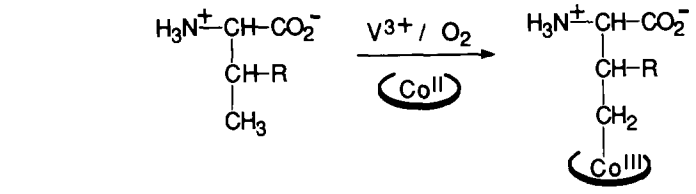
hydrophobic vitamin B_{12}, [Cob(II)7C_3ester]ClO_4, in the octopus cyclophane, in combination with a substrate-activation process provided by vanadium trichloride and atmospheric oxygen under irradiation with visible light to set up a true artificial holoenzyme system that achieves turnover of the catalyst species.

RESULTS AND DISCUSSION

We have previously investigated the carbon-skeleton rearrangement reactions of alkyl ligands bound to the hydrophobic vitamin B_{12}, as shown by Eqs. [3] and [4], and the rearrangements were found to be markedly favored in the hydropho-

bic cavity of APC[C_2Lys(C_5N^+)2C_{14}]$_4$ provided in aqueous media, relative to those carried out in methanol and benzene, under anaerobic photolysis conditions at ordinary temperatures (*11*). There are various methods for preparation of hydrophobic vitamin B_{12} derivatives bearing various alkyl ligands (*15–18*). In our previous study, hydrophobic vitamin B_{12} derivatives, **1** and **2**, were prepared by the reaction of Cob(I)7C_3ester with the corresponding alkyl bromides (*11*). Meanwhile, a combination of molecular oxygen and vanadium(III) ions as oxidizing and reducing reagents, respectively, readily converts a methyl substituent into the corresponding radical species which then undergoes coupling with a Co^{II} species as reported by Schrauzer *et al.* (Eq. [2]) (*19–22*). We adopted their method in this work and prepared alkylated complexes, **1–4** (refer to Eqs. [3]–[6], respectively), from 2-acetyl-2-ethoxycarbonylpropane, 2-cyano-2-ethoxycarbonylpropane, 1-acetyl-1-ethoxycarbonylethane, and diethyl β-methyl-DL-aspartate, respectively (refer to Experimental).

We have previously observed that the conversion of diethyl β-methyl-DL-aspartate into diethyl glutamate, as catalyzed by [Cob(II)7C_3ester]ClO_4, takes place



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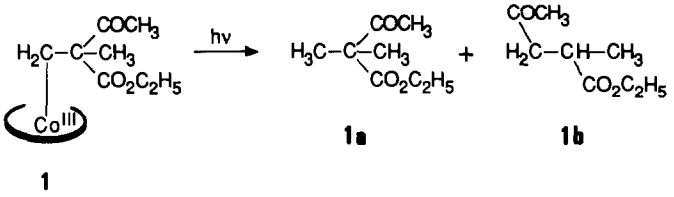
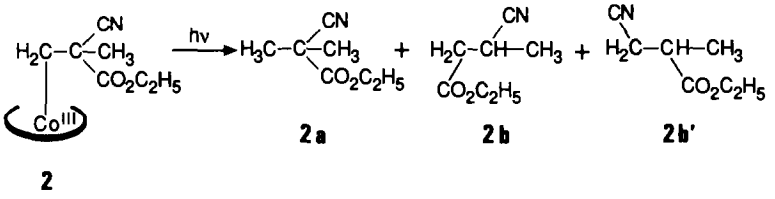


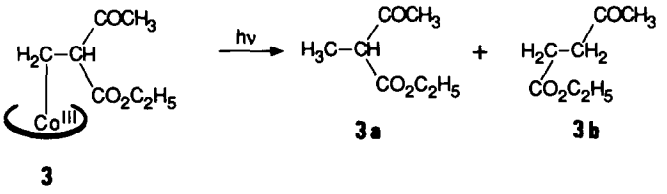
1 1a 1b

[3]



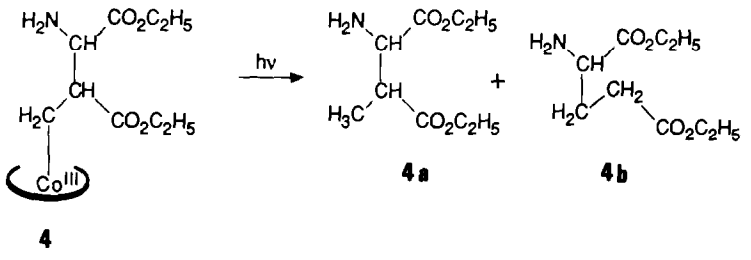
2 2a 2b 2b'

[4]



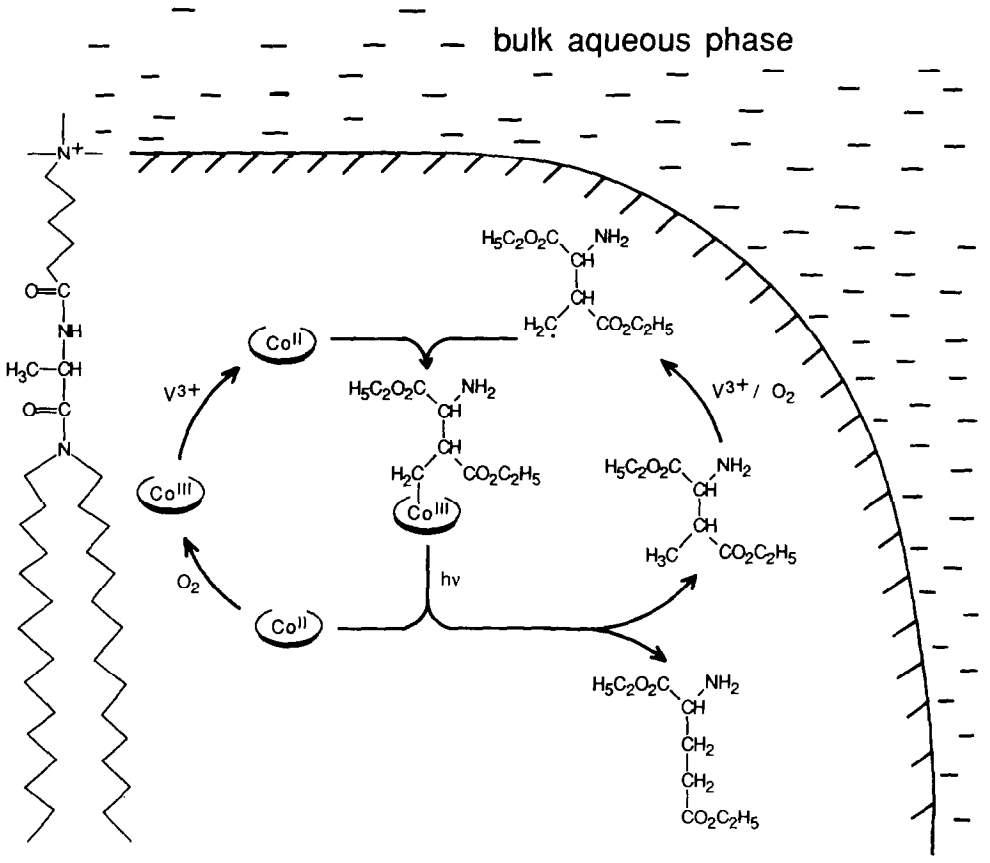
3 3a 3b

[5]



[6]

readily in single-compartment vesicles of *N,N*-dihexadecyl-*N*$^{\alpha}$-[6-(trimethylammonio)hexanoyl]-L-alaninamide bromide under aerobic photolysis conditions, by utilizing vanadium trichloride as a cocatalyst for activation of the substrate species (*23*). We have proposed a catalytic cycle shown in Scheme 1 as the most plausible cycle on the basis of the following experimental facts. (i) The corresponding alkylated complex was formed by the reaction of [Cob(II)7C$_3$ester]ClO$_4$



SCHEME 1

and diethyl β-methyl-DL-aspartate in the presence of vanadium trichloride under aerobic conditions. Without vanadium trichloride under otherwise identical conditions, the alkylated complex was not detected and the rearrangement product was not obtained at all. (ii) Such an alkylated complex was inactive in the dark, but gave the corresponding rearrangement product in single-compartment vesicles under irradiation with visible light. (iii) The cobalt(II) complex generated by the photolysis was autoxidized to the cobalt(III) species under aerobic conditions, which was then reduced by vanadium(III) ions to afford the original cobalt(II) species. (iv) In the absence of the substrate under otherwise identical conditions, the cobalt(II) species remained unchanged.

In the light of the above accomplishments, a novel substrate-activation process, composed of molecular oxygen and vanadium trichloride, was coupled with the mediator system, constituted with [Cob(II)7C_3ester]ClO_4 and APC[C_2Lys-(C_5N^+)2C_{14}]$_4$, to carry out the catalytic carbon-skeleton rearrangements. Equimolar amounts of [Cob(II)7C_3ester]ClO_4 and APC[C_2Lys(C_5N^+)2C_{14}]$_4$ and a large excess of vanadium trichloride were dissolved in aqueous carbonate buffer (pH 7.0) containing a sufficiently excess amount of a substrate, 2-acetyl-2-ethoxycarbonylpropane (**1a**), 2-cyano-2-ethoxycarbonylpropane (**2a**), 1-acetyl-1-ethoxycarbonylethane (**3a**), or diethyl β-methyl-DL-aspartate (**4a**, a mixture of *erythro*- and *threo*-diastereoisomers), and the reaction mixture was irradiated with visible light at 20.0°C under aerobic conditions. In the absence of substrate species under otherwise identical conditions, [Cob(II)7C_3ester]$^+$ remained unchanged for a sufficiently prolonged period of time. The results, given in Figs. 1–4, apparently indicate that the reactions proceed catalytically and the substrates are expected to be completely converted into the corresponding rearrangement products after a sufficient period of time. The rearrangement products were obtained in the following yields based on the amount of the hydrophobic vitamin B_{12} for 70 h of the reaction period: **1b**, 710%; **2b** + **2b′**, 480%; **3b**, 670%; **4b**, 200%. The yields based on amounts of respective substrates for the same reaction period were as follows: **1b**, 12%; **2b** + **2b′**, 7.5%; **3b**, 11%; **4b**, 3.5%. On the other hand, much smaller amounts of the rearrangement products were detected without the hydrophobic vitamin B_{12} under otherwise identical conditions.

The alkylated complexes were formed in the course of the catalytic reaction since such complexes were detected by electronic spectroscopy in the dark (Fig. 5; the reaction mixture was extracted with dichloromethane since a large excess of vanadium trichloride obscured the overall spectrum). Without vanadium trichloride under otherwise identical conditions, the alkylated complexes were not detected in the dark and the rearrangement products were not obtained at all under photolysis conditions. The substrate must be activated by vanadium(III) ions and molecular oxygen, and the resulting radical species undergoes coupling with [Cob(II)7C_3ester]$^+$ to give the corresponding alkylated complex, as confirmed by separate experiments described above. The alkylated complex is subjected to homolytic cleavage to afford the original substrate (**1a**, **2a**, **3a**, or **4a**) and the rearrangement product(s) (**1b**, **2b** and **2b′**, **3b**, or **4b**) under irradiation with visible light; the original substrate thus obtained participates in the catalytic cycle. The cobalt(II) species generated by the homolytic cleavage was autoxidized to afford

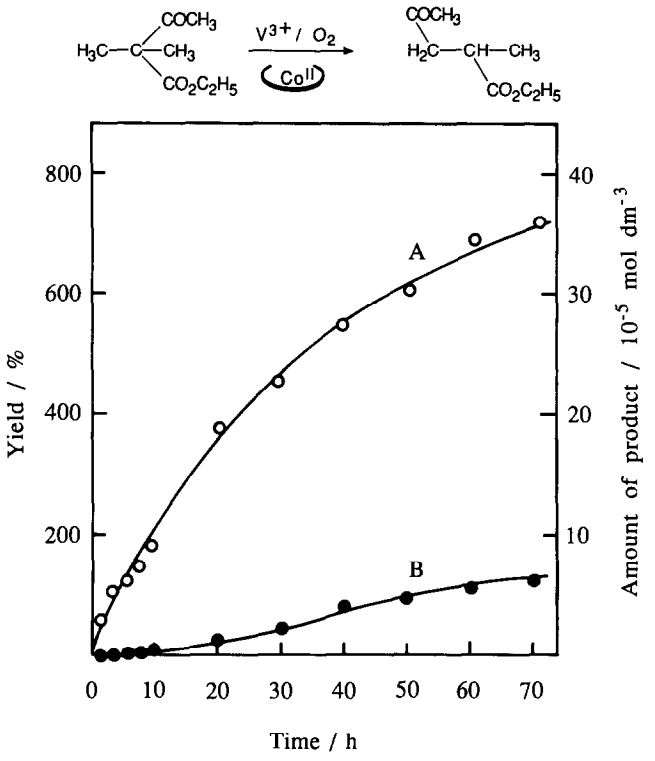


FIG. 1. Conversion of 2-acetyl-2-ethoxycarbonylpropane into 1-acetyl-2-ethoxycarbonylpropane in the octopus cyclophane under aerobic irradiation conditions at pH 7.0 and 20.0°C: APC[C_2Lys-(C_5N^+)2C_{14}]$_4$, 5.0×10^{-5} mol dm^{-3}; 2-acetyl-2-ethoxycarbonylpropane (substrate), 3.0×10^{-3} mol dm^{-3}; vanadium trichloride, 0.1 mol dm^{-3}. (A) [Cob(II)7C_3ester]ClO_4 added (5.0×10^{-5} mol dm^{-3}); (B) without [Cob(II)7C_3ester]ClO_4. The yield is based on the amount of [Cob(II)7C_3ester]ClO_4.

the cobalt(III) complex under aerobic conditions (*10*) (refer to Fig. 5B), which was then reduced by vanadium(III) ions to give the original cobalt(II) species. Therefore, vanadium trichloride acts not only as an activator for molecular oxygen to afford the substrate radical, but also as a reductant for the hydrophobic vitamin B_{12}, retaining the complex in the reactive Co^{II} state. The overall reaction cycle is shown in Fig. 6.

We have previously investigated the identical carbon-skeleton rearrangement reactions by utilizing alkyl bromides as substrates under anaerobic electrochemical conditions in the dark, and the reactions were found to proceed via formation of anionic intermediates (*24–26*). The migratory aptitude among the acetyl, cyano, and ethoxycarbonyl groups increases as follows: CN < $CO_2C_2H_5$ < $COCH_3$. Under the present conditions, the turnover numbers with respect to the catalyst species, [Cob(II)7C_3ester]$^+$, are as follows after 70 h of reaction period: acetyl, 7.1 (**1a**) and 6.7 (**3a**); ethoxycarbonyl, 5.2 (calibrated due to a competing reaction); cyano, 4.3 (calibrated due to a competing reaction); ethoxycarbonyl or amino

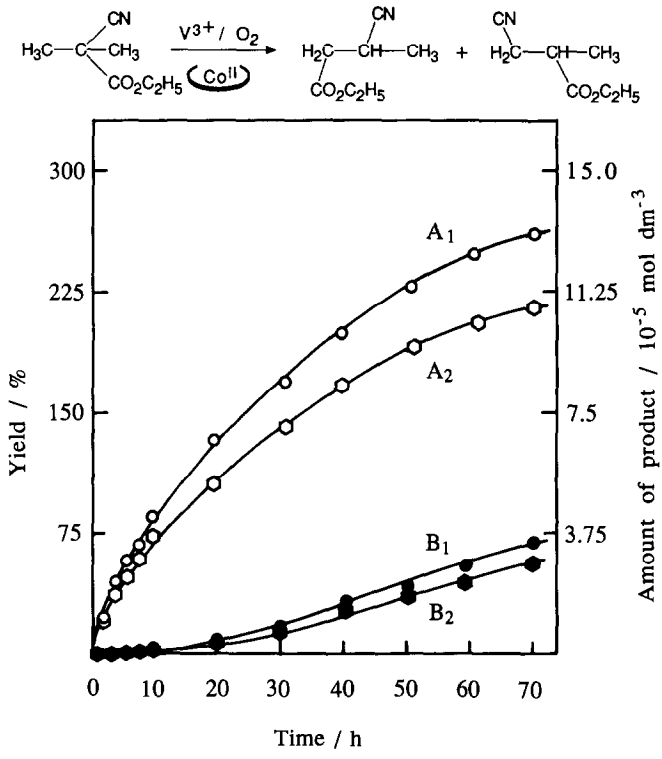


FIG. 2. Conversion of 2-cyano-2-ethoxycarbonylpropane into 2-cyano-1-ethoxycarbonylpropane (A_1 and B_1) and 1-cyano-2-ethoxycarbonylpropane (A_2 and B_2) in the octopus cyclophane under aerobic irradiation conditions; reaction conditions are identical to those given in Fig. 1. (A_1 and A_2) [Cob(II)7C_3ester]ClO_4 added (total, 5.0×10^{-5} mol dm^{-3}); (B_1 and B_2) without [Cob(II)7C_3ester]ClO_4.

(ethoxycarbonyl)methyl, 2.0. Thus, the acetyl group also migrates most readily, but both cyano and ethoxycarbonyl groups undergo migration at a comparable aptitude. The reaction mechanism, radical or anionic, seems to control the migratory aptitude of electron-withdrawing groups. The conversion of diethyl β-methyl-DL-asparate into diethyl glutamate is somewhat enhanced in single-compartment vesicles relative to the same reaction in the octopus cyclophane (*23*). However, these results cannot be directly compared with each other since the medium conditions are not identical; pH 1.0 for the vesicular system and pH 7.0 for the present system.

CONCLUSION

The octopus cyclophane was found to be effective as an apoenzyme model for functional simulation of vitamin B_{12}-dependent enzymes. The real catalytic cycle for carbon-skeleton rearrangements is now established by utilizing a combination

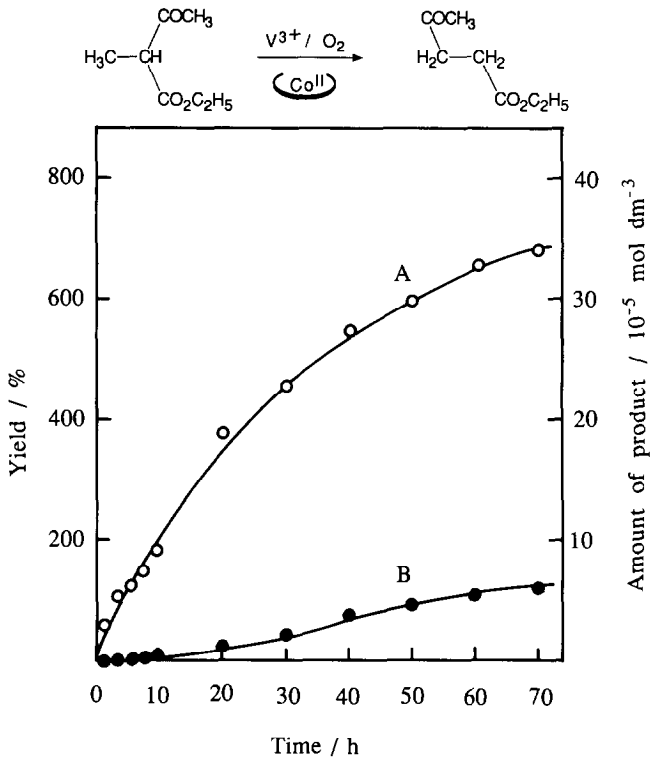


FIG. 3. Conversion of 1-acetyl-1-ethoxycarbonylethane into 1-acetyl-2-ethoxycarbonylethane in the octopus cyclophane under aerobic irradiation conditions; reaction conditions are identical to those given in Fig. 1.

of vanadium(III) ions and molecular oxygen for activation of substrate species without using activated substrates such as halogenated ones. In the light of the present study, the following became evident.

(i) A combination of vanadium trichloride and atmospheric oxygen abstracts a hydrogen atom from the terminal methyl substituent of a substrate species to form the corresponding radical species, which then undergoes reaction with $[Cob(II)7C_3ester]^+$ to form the alkylated complex.

(ii) The nuclear bivalent cobalt of the hydrophobic vitamin B_{12} promotes the rearrangement reaction via formation of a tight pair with the radical intermediate which is generated via homolytic cleavage of the cobalt–carbon bond upon photolysis of the alkylated complex with visible light (*11*). Even though the substrate radical is formed by the substrate-activation process performed by the combination of vanadium(III) ions and molecular oxygen, a yield of the rearrangement product is very low in the absence of the hydrophobic vitamin B_{12} under otherwise identical conditions.

(iii) The rearrangement reactions of the present alkyl ligands bound to the hydrophobic vitamin B_{12} do not proceed in homogeneous solutions such as in

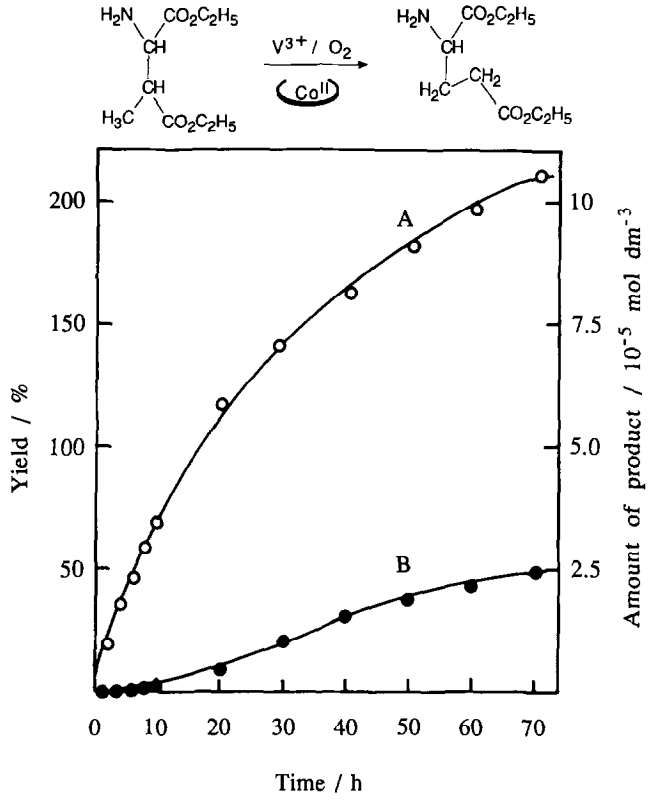


FIG. 4. Conversion of diethyl β-methyl-DL-aspartate into diethyl glutamate in the octopus cyclophane under aerobic irradiation conditions; reaction conditions are identical to those given in Fig. 1.

methanol and benzene, as clarified previously (*11*). We have investigated the photolysis reactions of alkylated complexes **1** and **2** in benzene at various temperatures without participation of the octopus cyclophane; the yields of **1b** and **2b** + **2b'** were markedly increased in a temperature range below the melting point of benzene compared with those observed above it (*11*). In addition, the molecular motion of the guest molecule incorporated into the octopus cyclophane is very restricted and the guest molecule is desolvated to a significant extent (*11*). The 1,2-migration of the electron-withdrawing groups must arise from both repression of molecular motion and desolvation effects operating on the alkylated cobalt complexes situated in the octopus cyclophane.

(iv) The migratory aptitude of the present electron-withdrawing groups follows the sequence: $CN \approx CO_2C_2H_5 < COCH_3$. Since the real migrating group in diethyl β-methyl-DL-aspartate is not known at present, we refrain from defining a migratory tendency of the functional groups involved in it.

The present artificial holoenzyme system is capable of simulating catalytic functions exerted by methylmalonyl-CoA mutase and glutamate mutase and expected to be utilized with other nonenzymatic rearrangement reactions which go through similar reaction mechanisms.

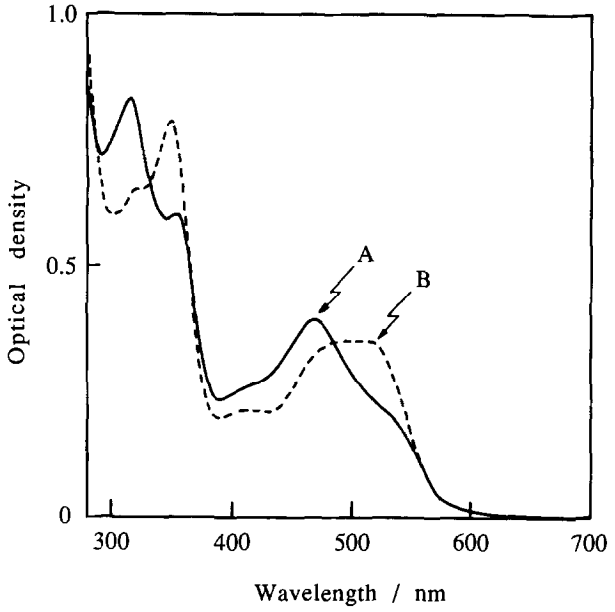


FIG. 5. (A) Electronic spectrum of a dichloromethane extract after 1 h of the reaction of [Cob(II)7C_3ester]ClO_4 (5.0×10^{-5} mol dm^{-3}) with 2-acetyl-2-ethoxycarbonylpropane (3.0×10^{-3} mol dm^{-3}) in the presence of APC[C_2Lys(C_5N^+)2C_{14}]$_4$ (5.0×10^{-5} mol dm^{-3}) and vanadium trichloride (0.1 mol dm^{-3}) in the dark under aerobic conditions at pH 7.0 and 20.0°C; formation of alkylated complex **1**. (B) Electronic spectrum of a sample obtained by irradiation of sample A with a 500-W tungsten lamp at a distance of 30 cm for 5 min under aerobic conditions; formation of the cobalt(III) species.

EXPERIMENTAL

General Analyses and Measurements

Elemental analyses were performed at the Microanalysis Center of Kyushu University. A Beckman Φ71 pH meter equipped with a Beckman 39505 combined electrode was used for pH measurements after calibration with a combination of appropriate standard aqueous buffers. Electronic absorption spectra were recorded with a Hitachi 340 or a Hitachi 220A spectrophotometer, while infrared spectra were taken on a JASCO IR-810 spectrophotometer. GLC analyses were carried out with a Shimadzu GC-9A apparatus equipped with a Shimadzu C-R3A-FFC Chromatopac for data processing. ^1H NMR spectra were taken on a Hitachi R-24B or a JEOL JNM-FX100 spectrometer, while mass spectroscopic analyses were performed on a JEOL JMS-01SG-2 spectrometer.

Materials

Heptapropyl cobyrinate perchlorate, [Cob(II)7C_3ester]ClO_4, and an octopus cyclophane, APC[C_2Lys(C_5N^+)2C_{14}]$_4$, were prepared with reference to methods reported previously (*7,9*). Vanadium trichloride of guaranteed reagent was ob-

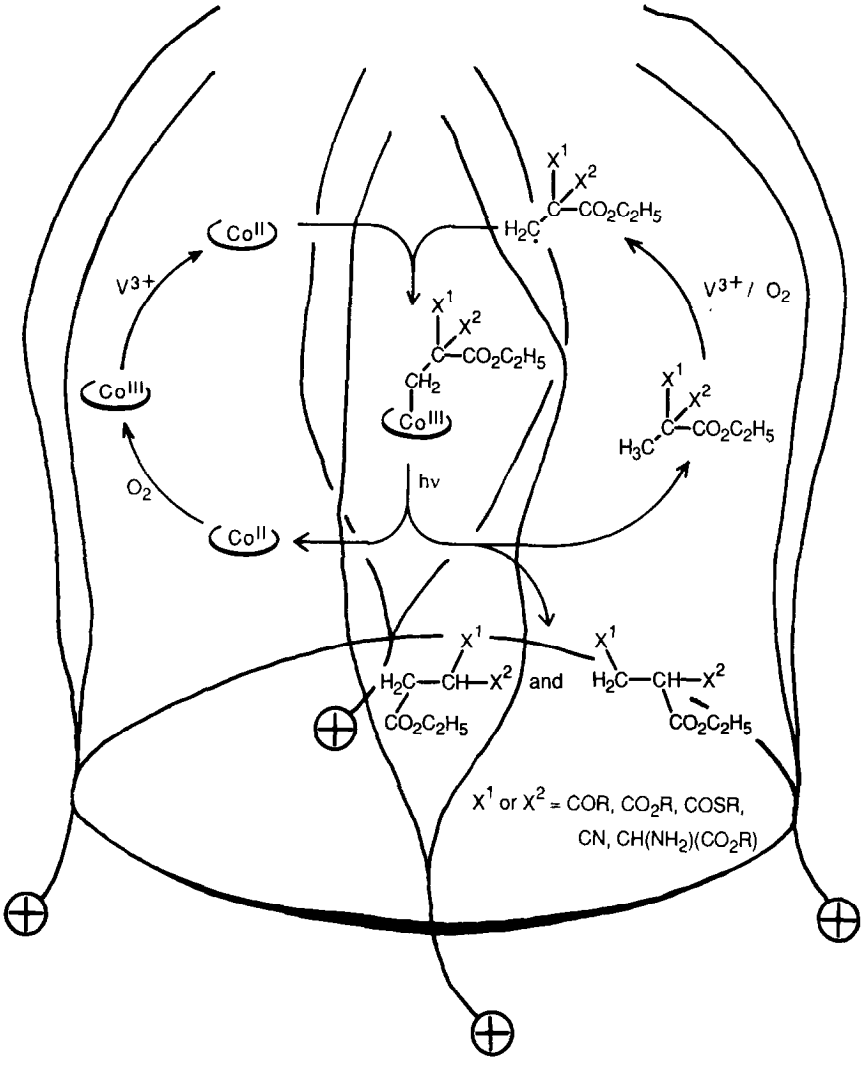


FIG. 6. Schematic representation of catalytic carbon-skeleton rearrangement in the octopus cyclophane.

tained from Wako Pure Chemical Industries, Ltd. (Osaka, Japan), and used without further purification. Substrate species, 2-acetyl-2-ethoxycarbonylpropane (**1a**) and 2-cyano-2-ethoxycarbonylpropane (**2a**) were prepared according to reported procedures (*26*), and the products were purified by distillation under reduced pressure. 1-Acetyl-1-ethoxycarbonylethane (**3a**) was purchased from Aldrich Chemical Co., Inc. (Milwaukee, WI). Diethyl β-methyl-DL-asparate (**4a**) was prepared by esterification of β-methyl-DL-aspartic acid in a manner similar to that adopted for esterification of various α-amino acids (*27*). Authentic samples, 1-acetyl-2-ethoxycarbonylpropane (**1b**), 2-cyano-1-ethoxycarbonylpropane (**2b**), and 1-cyano-2-ethoxycabonylpropane (**2b′**), were prepared after reported procedures (*26*). 1-Acetyl-2-ethoxycarbonylethane (**3b**) and diethyl glutamate (**4b**) were

purchased from Aldrich Chemical Co., Inc., and Fluka Chemie AG (Switzerland), respectively. All the substrate and authentic samples were used after confirmation of their purity by GLC and elemental analyses. Alkylated derivatives of heptapropyl cobyrinate perchlorate were prepared as described below.

Heptapropyl 3-amino-2,3-bis(ethoxycarbonyl)propylcobyrinate perchlorate (**4**) was prepared as follows. A methanol solution (100 ml) of heptapropyl cobyrinate perchlorate (300 mg, 2.2×10^{-4} mol) and diethyl β-methyl-DL-asparate (100 mg, 4.2×10^{-4} mol) was mixed with 60 ml of aqueous sodium carbonate buffer (0.02 mol dm^{-3}, pH 11.2), and 25 ml of 15% (w/w) aqueous perchloric acid containing vanadium trichloride (50 mg, 3.2×10^{-4} mol) was added to the resulting mixture. The solution was stirred vigorously for 5 min at room temperature, and for a further 1 h after air was introduced into it for 2 min. The product was extracted with dichloromethane and purified on a column of Sephadex LH-20 with methanol as an eluant to give a brown solid: yield 151 mg (46%); ir (KBr) 2945 (CH str.), 1725 (ester C=O str.), and 1100 and 620 cm^{-1} (ClO_4^- str.); λ_{max} (CH_2Cl_2) 271 (ε 2.40×10^4), 311 (2.20×10^4), 350sh (0.88×10^4), 405sh (0.74×10^4), and 458 nm (1.03×10^4). *Anal.* Calcd for $C_{75}H_{117}ClCoN_5O_{22} \cdot 1.5H_2O$: C, 57.66; H, 7.74; N, 4.48%. Found: C, 57.53; H, 7.45; N, 4.38%.

Heptapropyl 2-acetyl-2-ethoxycarbonylpropylcobyrinate perchlorate (**1**), heptapropyl 2-cyano-2-ethoxycarbonylpropylcobyrinate perchlorate (**2**), and heptapropyl 2-acetyl-2-ethoxycarbonylethylcobyrinate perchlorate (**3**) were prepared according to analogous procedures. Since these compounds are quite photosensitive, these were identified by infrared and electronic spectroscopy.

1: ir (KBr) 2950 (CH str.), 1730 (ester C=O str.), and 1100 and 620 cm^{-1} (ClO_4^- str.); λ_{max} (CH_2Cl_2) 273 (ε 2.19×10^4), 309 (2.41×10^4), 376sh (0.87×10^4), and 456 nm (1.03×10^4).

2: ir (KBr) 2940 (CH str.), 1730 (ester C=O str.), and 1100 and 620 cm^{-1} (ClO_4^- str.); λ_{max} 269 (ε 2.20×10^4), 310 (2.37×10^4), 378sh (0.84×10^4), and 458 nm (1.03×10^4).

3: ir (KBr) 2947 (CH str.), 1730 (ester C=O str.), and 1100 and 620 cm^{-1} (ClO_4^- str.); λ_{max} 274 (ε 2.20×10^4), 308 (2.41×10^4), 379sh (0.88×10^4), and 457 nm (1.13×10^4).

Catalytic Reaction

A dichloromethane solution (5 ml) containing equimolar quantities of APC-$[C_2Lys(C_5N^+)2C_{14}]_4$ and [Cob(II)7C_3ester]ClO_4 (1.0×10^{-6} mol each) and a substrate (6.0×10^{-5} mol) was evaporated *in vacuo* to remove the solvent completely, and the residue was dissolved in aqueous sodium carbonate buffer (0.02 mol dm^{-3}, pH 11.2; 20 ml). Aqueous 15% (w/w) perchloric acid (5 ml) containing vanadium trichloride (0.1 mol dm^{-3}) was added to the solution and pH of the resulting mixture was adjusted to 7.0 with aqueous 15% (w/w) sodium hydroxide. The reaction mixture was irradiated with a 500-W tungsten lamp at a distance of 30 cm along with air bubbling at 20.0°C. Samples were taken out at appropriate time intervals, extracted with dichloromethane (20 ml ×3). The dichloromethane extract was evaporated to dryness, and an appropriate amount of diethyl ether (500

μl) was added to it. The products were identified by means of GLC, with coinjection of authentic samples into columns of Silicone DC-550 (Shimadzu Co., Japan) and Silicone SE-30 (Gasukuro Kogyo, Inc., Japan). A capillary column of Polyethylene Glycol-20M (Gasukuro Kogyo, Inc.) was used for identification of isomers having similar structures. Quantitative analyses of the products were carried out by GLC on the basis of correlation lines established independently by using authentic samples. The rearrangement products separated by preparative GLC were also identified by means of ^{1}H NMR and mass spectroscopic measurements. The identical procedure was adopted for reactions without [Cob(II)7C_3ester]ClO_4. No oxygenation products were detected by GLC under the present experimental conditions.

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