Sterically Induced, Spontaneous Co–C Bond Homolysis and β-Elimination Reactions of Primary and Secondary Organocobalamins[1]

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Abstract: Sterically hindered secondary alkylcobalamins carrying hydrogen in the β-position decompose in neutral aqueous solutions spontaneously by way of β-elimination. The cleavage of the Co–C bond in these compounds is caused by "upward" distortions of the corrin ligand in response to the attachment of the axial base, 5,6-dimethylbenzimidazole, as well as by thermal motions of the corrin ligand system. Organocobalamins carrying organic groups which lack hydrogen in the β-position cannot decompose by way of the β-elimination mechanism. It is demonstrated on the basis of experiments with the prototype compounds neopentyl- and benzylcobalamin that such cobalamins decompose spontaneously with Co–C bond *homolysis*. Under strictly anaerobic conditions, the resulting vitamin B_{12r} and organic radicals recombine with high efficiency to regenerate the Co–C bond. Aerobically, vitamin B_{12r} and the organic radicals are rapidly oxidized, rendering these cobalamins highly oxygen sensitive in neutral aqueous solution. This is in significant contrast to the behavior of secondary alkylcobalamins undergoing spontaneous, concerted β-elimination. Further insight into the mechanism of Co–C bond cleavage reactions is provided by the results of measurements of the activation parameters [$\Delta H^{\circ\ddagger}$, $\Delta S^{\circ\ddagger}$, and $\Delta G^{\circ\ddagger}$] of Co–C bond thermolysis in neopentyl-, benzyl-, isopropyl-, and isobutylcorrins. From the $\Delta H^{\circ\ddagger}$ values the Co–C bond dissociation energies of these organocorrins were estimated to range between 20 and 32 kcal·mol^{-1}.

Until recently, secondary alkylcobalamins (Figure 1) were considered too unstable to be isolated due to steric restrictions imposed by the corrin ligand. We have found,[2] however, that such organocorrins are capable of existence because the corrin ligand can adopt "downward" distorted configurations in response to the steric demands of the cobalt-bound secondary alkyl group. These distortions can become sufficient to rupture the coordinative bond between the axial base (5,6-dimethylbenzimidazole, DMBZ) and the corrin cobalt atom, causing all acyclic secondary alkylcobalamins to exist predominantly in the "base-off" form. In neutral solutions, the unprotonated, appended DMBZ seeks to reattach itself to the corrin cobalt atom because of its affinity for the δ+ charged Co(III) ion. Reattachment of the DMBZ to cobalt causes "upward" configurational adjustments of the corrin ligand which promote the spontaneous cleavage of the Co–C bond. If the DMBZ is protonated, upward distortions of the corrin ligand can still occur through thermal motions, but these cause Co–C bond cleavage with much lower probability. It is therefore possible to isolate many secondary alkylcobalamins in the protonated base-off form.

In alkylcobalamins which carry hydrogen in the β-position, spontaneous dealkylation produces olefins and vitamin B_{12s}. In the prototype compound, isopropylcobalamin, this decomposition was judged to be essentially concerted,[2] since the yields of propylene were unaffected by the presence of oxygen. Since β-elimination in secondary alkylcobalamins is so greatly favored over other possible dealkylation pathways, we decided to study the spontaneous decomposition of a number of sterically hindered organocorrins which lack hydrogen in the β-position. In these corrins, the Co–C bond must cleave homolytically, generating vitamin B_{12r} and organic radicals. In anaerobic aqueous solution, recombination of these homolysis products to the original organocorrins will be the main reaction; it has been shown that methyl radicals react with vitamin B_{12r} at near diffusion-controlled rates.[3]

Aerobically, these cobalamins should suffer irreversible decomposition, however, due to oxidation reactions of the free organic radicals and of vitamin B_{12r}. Since isopropylcobalamin undergoes spontaneous decomposition in neutral solution at essentially the same rate aerobically and anaerobically,[2] cobalamins decomposing by homolytic Co–C bond cleavage would exhibit distinctly different behavior compared to spontaneously decomposing secondary alkylcobalamins.

In this paper, we describe studies with neopentylcobalamin, I,

I II

as the prototype, and with benzylcobalamin, II, as an example subject to both steric and electronic labilization toward Co–C homolysis. In addition, results of studies with the corresponding cobinamides and with isopropyl- and isobutylcobalamin are included for comparative purposes.

Results

Preparation and Properties of Neopentyl- and Benzylcorrins. Neopentylcobalamin is formed by the reaction of neopentyl halides with vitamin B_{12s}[4] but cannot be readily isolated by conventional methods as it is oxygen sensitive in solution. The same is true for benzylcobalamin, whose synthesis in solution has been described by several authors,[5-7] none of whom accomplished its isolation as a solid.

We have found that both neopentyl- and benzylcobalamin are significantly less oxygen sensitive in the protonated base-off form. A convenient method of synthesis consists of the reaction of vitamin B_{12s} with neopentyl iodide or benzyl bromide, respectively, in acidic (NH_4Br-buffered) methanol. This produces the organocobalamins in the protonated base-off form, whose isolation is described in the Experimental Section. The protonated base-off salts are stable on storage at 4 °C for extended periods. The corresponding cobinamides are sufficiently stable to be prepared and isolated by conventional methods of organocobalamin synthesis.

(1) Paper No. 52 of a series entitled "Studies on Vitamin B_{12} and Related Compounds". Presented, in part, at the Third European Symposium on Vitamin B_{12} and Intrinsic Factor, March 5-8, 1979, Zurich, Switzerland. Also see the published Proceedings (B. Zagalak and W. Friedrich, Eds.), pp 511-528 (1979).

(2) J. H. Grate and G. N. Schrauzer, *J. Am. Chem. Soc.*, **101**, 4601 (1979).

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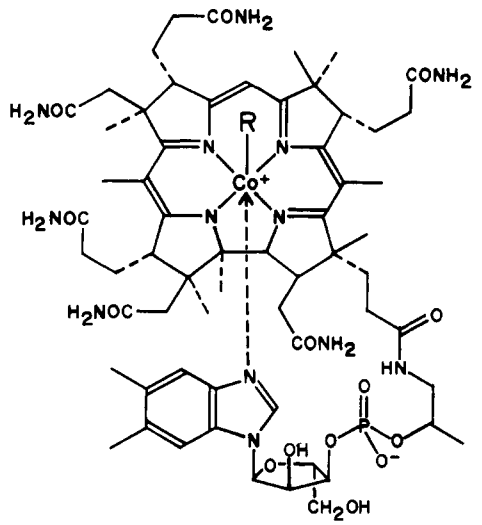


Figure 1. The structure of alkylcobalamins in the base-on form. Cobinamides lack the axial base and phosphoribosyl moieties.

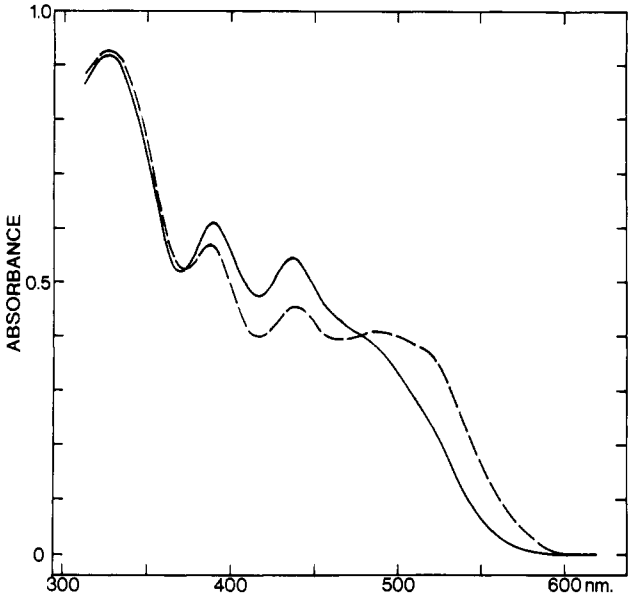
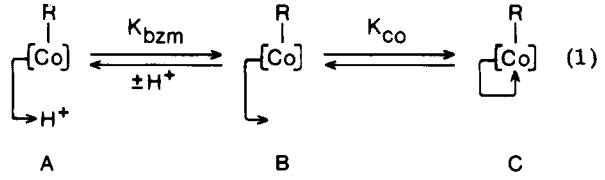


Figure 2. Absorption spectra of neopentylcobalamin in acidic (—) and neutral (---) solutions (60 μM).

Optical absorption spectra of the cobalamins in neutral and acidic solutions are shown in Figures 2 and 3. The base-off forms of the cobalamins are isospectral with the corresponding cobinamides. It may be seen that neopentyl- and benzylcobalamin each exist in neutral solution partly in the base-off form. The relative concentrations of the base-off protonated, base-off unprotonated, and base-on forms are determined by the pH and the magnitude of K_{co} as shown in eq 1; pK_{bzm} is taken as 4.70.[8]



(1)

Values of K_a, defined as in eq 2, were measured by spectro-

$$K_a = ([B] + [C])[H^+]/[A] = K_{bzm}(K_{co} + 1) \quad (2)$$

photometric titrations in anaerobic aqueous solution for both

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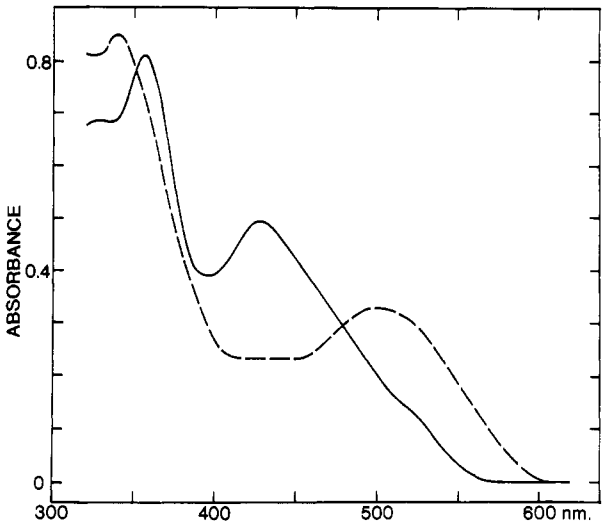

Figure 3. Absorption spectra of benzylcobalamin in acidic (—) and neutral (---) solutions (40 μM).

Table I. Values for pK_a and K_{co} for Neopentyl, Benzyl, and Other Alkylcobalamins

organic group	pK_a	K_{co}
neopentyl	4.55[a]	0.4
benzyl	4.25[a]	2
isobutyl	4.20[b]	2
n-propyl	3.84[c]	6
methyl	2.72[c]	95

[a] This work, ±0.05. [b] Reference 2, loc. cit. (±0.05). [c] Reference 13, loc. cit.

neopentyl- and benzylcobalamin and are given in Table I together with those of selected other alkylcobalamins.

The presence of the cobalt-bound alkyl groups was also confirmed by their susceptibility to photolysis by visible light. In aerobic aqueous solution, neopentylcobalamin undergoes rapid photolysis, yielding vitamin B_{12a}, neopentane (≲0.1%), isobutene, and oxygen-containing products, including pivalaldehyde, formaldehyde, and acetone. In strictly anaerobic solution, however, photolysis proceeds very slowly, with only slight decomposition observed even after 1 h of continuous irradiation. Such behavior is also observed with methylcobalamin[3,9-11] and is indicative of efficient recombination of neopentyl radicals with vitamin B_{12r}. In anaerobic solutions containing 2-propanol as a source of abstractable hydrogen,[12] photolysis produces vitamin B_{12r} more rapidly and neopentane is formed in near quantitative yields. Benzylcobalamin on aerobic photolysis likewise yields vitamin B_{12a}, with benzaldehyde as a major product. Under anaerobic conditions, it is photolyzed to vitamin B_{12r} at a slower rate than aerobically but faster than neopentylcobalamin; bibenzyl and traces of toluene were detected as photolysis products.

Spontaneous Co–C Bond Cleavage of Neopentyl- and Benzylcorrins in Solution. Under anaerobic conditions in the dark, neutral aqueous solutions of neopentylcobalamin decompose only very slowly. Dealkylation was observed to proceed at a slow rate initially but appears to become extremely slow on further dark storage. After 8 months of storage, vitamin B_{12r} was observed spectrophotometrically, but still 15% of the original neopentylcobalamin was detectable.

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Table II. Observed Rates and Calculated Activation Parameters for the Aerobic Thermal Decomposition of Several Organocorrins in Aqueous Solution

organocorrin	soln	temp, °C	k_{obsd}, s^{-1}	$t_{1/2}$	$\Delta H^{\circ\ddagger}$, kcal·mol^{-1}	$\Delta S^{\circ\ddagger}$, eu	$\Delta G^{\circ\ddagger}$, kcal·mol^{-1}
neopentylcobalamin	1.0 M H_3PO_4	25	2.9×10^{-7}	28 days			
	pH 7.0[a]	25	1.5×10^{-4}	75 min	23.4 ± 0.2[b]	2.6 ± 0.1[b]	22.6 ± 0.2[c]
	pH 7.0	32	3.9×10^{-4}	30 min			
	pH 7.0	42	1.4×10^{-3}	8 min			
	pH 7.0	53	4.8×10^{-3}	2.4 min			
	pH 7.0	60	1.1×10^{-2}	63 s			
neopentylcobinamide	1.0 M H_3PO_4	25	2.4×10^{-7}	33 days			
	pH 7.0	25	1.1×10^{-7}	73 days			
	pH 7.0	60	3.9×10^{-5}	293 min	32.1 ± 0.1	17.3 ± 0.4	26.9 ± 0.3
	pH 7.0	74	2.8×10^{-4}	41 min			
	pH 7.0	87.5	1.7×10^{-3}	6.8 min			
benzylcobalamin	1.0 M H_3PO_4	30	2.8×10^{-5}	410 min			
	pH 7.0	8	1.9×10^{-4}	61 min	24.6 ± 0.6	12.3 ± 2.0	20.9 ± 1.2
	pH 7.0	10	2.8×10^{-4}	41 min			
	pH 7.0	16	7.7×10^{-4}	15 min			
	pH 7.0	24	2.3×10^{-3}	5.0 min			
	pH 7.0	25.5	2.7×10^{-3}	4.3 min			
benzylcobinamide	1.0 M H_3PO_4	30	2.9×10^{-5}	400 min			
	pH 7.0	33	3.6×10^{-5}	320 min	26.9 ± 0.5	9.2 ± 1.5	24.3 ± 0.9
	pH 7.0	45	2.4×10^{-4}	48 min			
	pH 7.0	60	1.5×10^{-3}	7.8 min			
	pH 7.0	74	7.9×10^{-3}	88 s			
isopropylcobalamin	pH 7.0	6	3.3×10^{-4}	35 min	20.7 ± 0.5	−0.3 ± 1.8	20.8 ± 1.0
	pH 7.0	15	1.0×10^{-3}	11.5 min			
	pH 7.0	25	3.8×10^{-3}	3.0 min			
isopropylcobinamide	0.1 M H_3PO_4	45.5	5.8×10^{-5}	200 min	28.3 ± 0.2	10.8 ± 0.7	25.1 ± 0.4
	0.1 M H_3PO_4	59	3.9×10^{-4}	30 min			
	0.1 M H_3PO_4	75	2.8×10^{-3}	4.1 min			
isobutylcobalamin	pH 7.0	59	1.1×10^{-4}	108 min	26.8 ± 0.4	3.8 ± 1.2	25.7 ± 0.8
	pH 7.0	73	5.5×10^{-4}	21 min			
	pH 7.0	88.5	3.3×10^{-3}	3.5 min			

[a] 0.10 M phosphate (Na^+) buffer. [b] Uncertainties correspond to standard deviations of the slopes and intercepts of ln (k_{obsd}/T) vs. ($1/T$). [c] Uncertainties are the sums of those from the standard deviations of the enthalpies and entropies.

Aerobically, neopentylcobalamin in neutral solution decomposes rapidly to vitamin B_{12a} and organic products derived from the neopentyl residue, i.e., neopentane (≲0.1%), isobutene, pivalaldehyde, formaldehyde, etc., as from the photolysis of neopentylcobalamin under aerobic conditions. The rate of decomposition is first order in the cobalamin; a typical example of repetitive spectral scans during aerobic decomposition is shown in Figure 4. At 25 °C, the half-life of neopentylcobalamin in neutral aqueous solutions is 75 min; at acidic pH the half-life is close to 1 month. Neopentylcobinamide is similarly long-lived in both acidic and neutral solutions. Under an atmosphere of pure oxygen, neopentylcobalamin decomposes in neutral solution at the same rate as under air.

Benzylcobalamin in aerobic neutral aqueous solution decomposes to vitamin B_{12a} and oxidation products of the benzyl radical (mainly benzaldehyde), with a half-life of only 5 min at 24 °C. Under *strictly* anaerobic conditions, however, the rate of spontaneous decomposition at room temperature is too slow to be measured accurately; after 1 h at room temperature, only slight decomposition (ca. 1%) was detectable spectrophotometrically. The aerobic half-life of benzylcobalamin in the protonated base-off form is ca. 7 h at 30 °C, comparable to that of benzylcobinamide in both neutral and acidic solutions (see Table II).

Activation Parameters of Thermal Co–C Bond Cleavage Reactions. Rates of dealkylation of neopentyl-, benzyl-, isopropyl-, and isobutylcorrins in aerobic aqueous solutions were determined spectrophotometrically in temperature ranges between 5 and 90 °C (Table II). The first-order appearance of the cobalt(III) corrin spectrum occurred with sharp isosbestic points in all cases. Plots of ln ($k_{obsd.}/T$) vs. $1/T$ were linear over the temperature ranges studied; the observed $\Delta H^{\circ\ddagger}$, $\Delta S^{\circ\ddagger}$, and $\Delta G^{\circ\ddagger}$ values are given in Table II.

Effects of Oxygen on the Spontaneous Decompositions of Isopropyl- and Isobutylcobalamin. The observed effects of oxygen on the spontaneous decompositions of neopentyl- and benzylcobalamin prompted a further examination of the influence of oxygen on the spontaneous decomposition of alkylcobalamins which carry hydrogen in the β-position. The aim of these experiments was to use O_2 as a scavenger of any free organic radicals generated during the process of spontaneous Co–C bond cleavage. In accord with our previous observations,[2] the yields of propylene from isopropylcobalamin under aerobic and anaerobic conditions are virtually identical. Isobutylcobalamin, on aerobic thermolysis in neutral solution at 90 °C, however, yields only half the amount of isobutene as is formed under argon (Table III). Its rate of decomposition at 73 °C is approximately twice as fast in aerobic

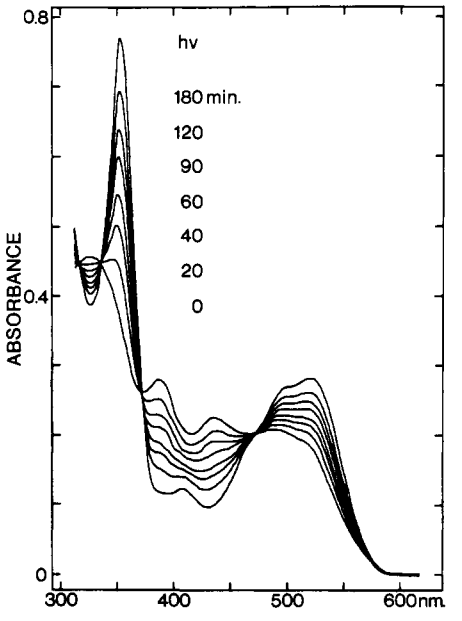

Figure 4. Repetitive spectral scans during the aerobic decomposition of neopentylcobalamin (30 μM) in 0.10 M phosphate (Na^+) buffer (pH 7.0). The final spectrum was recorded after photolysis of the remaining neopentylcobalamin.

Table III. Relative Yields of Isobutene from Thermal and Photochemical Decomposition of Isobutylcobalamin under Aerobic and Anaerobic Conditions

dec condtns	rel yield, %
dark, pH 7, 90 °C, Ar	100
dark, pH 7, 90 °C, air	49
$h\nu$, pH 7, 25 °C, Ar	100
$h\nu$, pH 7, 25 °C, air	28

Table IV. K_{Co} Values and Room-Temperature Half-Lives of Four Alkylcobalamins

alkyl group	ethyl[a]	*n*-propyl[a]	isobutyl[a]	neopentyl
no. of β-CH_3 groups	0	1	2	3
K_{Co}	6	6	2	0.4
$t_{1/2}$	6 months	4–5 months	14 days	75 min

[a] Data from ref 2, loc. cit.

neutral solution ($t_{1/2}$ = 21 min) as under anaerobic conditions ($t_{1/2}$ = 45 min). The presence of oxygen also decreases the yield of isobutene on photolysis at room temperature. In contrast, the photolysis yields of propylene from isopropylcobalamin in acidic solution are unaffected by the presence of air in the gas phase.

Discussion

Under strictly anaerobic conditions in neutral aqueous solutions, neopentyl- and benzylcobalamin appear to be as stable as normal, sterically unrestricted organocobalamins. Aerobically, however, they decompose within minutes to hours and thus exhibit a clearly anomalous behavior which is not observed with simple organocorrins. The corresponding cobinamides are much more long-lived under aerobic conditions, just as neopentyl- and benzylcobalamin are in the protonated base-off forms in acidic solutions (see Table II). This shows that in neutral solutions the Co–C bonds of neopentyl- and benzylcobalamin are cleaved by coordination of the appended DMBZ, just as was observed in our study of secondary alkylcobalamins.[2] Neopentylcobalamin and benzylcobalamin, however, undergo spontaneous homolytic Co–C bond cleavage rather than syn-β-elimination. The Co–C bond cleavage is initiated by upward motions of portions of the corrin ligand in the base-on form to yield a close pair of vitamin B_{12r} and the neopentyl or benzyl radical, as is exemplified in Figure 5 for neopentylcobalamin. In strictly anaerobic aqueous solution, recombination of the two species to the original organocorrin occurs with high efficiency. Aerobically, oxidation reactions cause irreversible decomposition. The observed slow rates of aerobic decomposition of neopentyl- and benzylcobinamide show that the homolyses of the Co–C bonds can also be induced through thermal motions of the axial base-free corrin ligand, albeit with much lower efficiency.

The neopentyl and benzyl residues are not as sterically demanding as typical secondary alkyl groups. Accordingly, neopentyl- and benzylcobalamin can exist partially in the base-on form, just as is observed with other primary organocobalamins. The opposing steric demands of the organic groups and the axial base are reflected in the magnitudes of the K_{Co} values as given in Table I. In the series ethyl-, *n*-propyl-, isobutyl-, neopentylcobalamin, axial base coordination decreases with increasing size of the alkyl residue, while rates of spontaneous (aerobic) Co–C bond cleavage increase by orders of magnitude, as may be seen from Table IV. It is of interest to note that the base-off spectrum of neopentylcobalamin resembles that of isopropylcobalamin,[2] suggesting a similarly distorted corrin ligand, although isopropylcobalamin does not exist measurably in the base-on form. The benzyl group is more electron withdrawing than simple alkyl groups, but its steric demands still result in a relatively low K_{Co} value for benzylcobalamin, which is close to that of isobutylcobalamin (see Table I). The rate of aerobic decomposition of benzylcobalamin in neutral solution at room temperature ($t_{1/2}$ = 5 min), however, is far greater than that of isobutylcobalamin ($t_{1/2}$ = 14 days[2]). Since benzylcobinamide and the protonated base-off form of benzylcobalamin are also relatively short-lived under aerobic conditions (see Table II), it follows clearly that the Co–C bond in benzylcorrins is also substantially labilized by electronic effects.

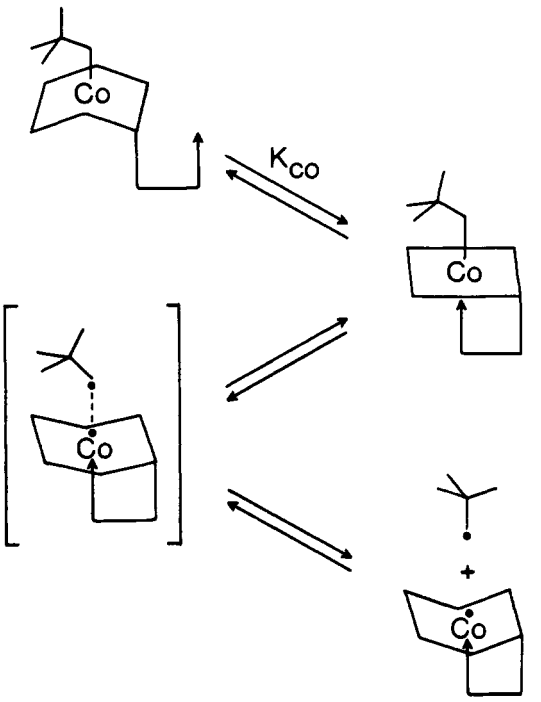

Figure 5. Schematic representation of the corrin conformational changes in the axial base induced homolytic Co–C bond cleavage of neopentylcobalamin.

The oxygen sensitivity of neopentyl- and benzylcorrins in aqueous solutions in the dark is taken as evidence for the occurrence of spontaneous Co–C bond homolysis. The organic radical and cobalt(II) corrin generated react with O_2 to presumably yield organoperoxycorrins as is shown in eq 3; the same is

$$\begin{array}{l} \overset{R}{\underset{|}{[Co]}} \rightleftharpoons [Co^{II}] + R\cdot \xrightarrow{O_2} [Co^{II}] + ROO\cdot \longrightarrow \\ \qquad\qquad \overset{OOR}{\underset{|}{[Co]}} \longrightarrow [Co^{III}] + \text{oxidized products} \end{array} \quad (3)$$

also postulated for the aerobic photolysis reactions of these compounds. In analogy to eq 3, benzylperoxocobaloxime has been isolated from the aerobic photolysis and thermolysis of benzylcobaloxime.[14] Our reason for suggesting such intermediates in eq 3 arises from the fact that cobalt(III) corrins are formed during the aerobic photolyses and dark decompositions of neopentyl- and benzylcorrins often at rates faster than the cobalt(II) corrins are oxidized by oxygen under otherwise identical conditions.

Our previous work[2] indicated that the elimination of propylene from isopropylcobalamin occurs in an essentially concerted manner, without the intermediate formation of free isopropyl radicals, since the yield of propylene is virtually unaffected by the presence of oxygen. The effect of oxygen on the rate of thermal decomposition of isobutylcobalamin in neutral solution and on the resulting yield of isobutene (see Table III), however, show that for this derivative a substantial fraction of the alkyl groups can be scavenged by oxygen. Thus, β-elimination and Co–C bond homolysis can be competitive processes which both are initiated by a lengthening of the Co–C bond.

To obtain further insight into spontaneous Co–C bond cleavage reactions of sterically crowded organocorrins, we determined activation parameters for a number of compounds. Halpern has recently suggested[15] that the $\Delta H^{\circ *}$ values for the cleavage of Co–C

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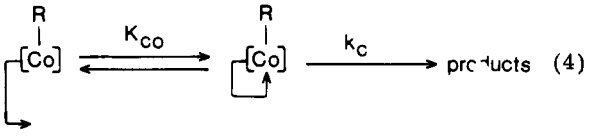
bonds in organocobaloximes should be very close to the Co–C bond dissociation enthalpies. This should also be true for alkylcobinamides. For alkylcobalamins in neutral solution, the observed rates of decomposition involve both the axial base coordination constant and the rate of Co–C bond cleavage (see eq 4).[2] Since k_{obsd}, the



(4)

rate of thermal (spontaneous) decomposition, is defined by eq 5,

$$k_{obsd} = K_{co}k_c/(K_{co} + 1) \quad (5)$$

the activation parameters for thermolysis of organocobalamins in neutral solution include contributions from the coordination equilibria. Axial base coordination was observed to decrease with increasing temperature, but over the temperature ranges of our experiments these effects are small, judging from the changes of the optical absorption spectra of partially base-on organocobalamins with temperature. The differences in the observed $\Delta H^{\circ\ddagger}$ values between organocobalamins and the respective organocobinamides are attributed to largely reflect Co–C bond labilization as a result of axial base coordination. The activation enthalpies of the organocorrins measured herein lie between 20 and 32 kcal·mol^{-1}. A range of 20–33 kcal·mol^{-1} was recently reported for a number of secondary alkylcobaloximes.[15] The same authors also predicted the Co–C bond homolysis activation enthalpy of benzylcobalamin to be 15–20 kcal·mol^{-1} (assuming $\Delta S^{\circ\ddagger} \simeq 0$), and Co–C bond dissociation energies of primary alkylcobalamins of 20–30 kcal·mol^{-1}. Our work produced a slightly larger $\Delta H^{\circ\ddagger}$ for benzylcobalamin (24.6 ± 0.6 kcal·mol^{-1}), with a $\Delta S^{\circ\ddagger}$ of 12.3 ± 2.0 eu, which is clearly a larger $\Delta S^{\circ\ddagger}$ than was observed for the alkylcobalamins of our study. This suggests that the Co–C bond in benzylcobalamin is cleaved with less assistance by the DMBZ-induced upward movements of the corrin ligand because of its lower thermodynamic strength. The $\Delta S^{\circ\ddagger}$ values for thermolysis of all the organocobinamides studied are also positive and in the range of 9–18 eu. We interpret these values to suggest that the Co–C bond cleavage of the organocobinamides occurs without involving the comparatively ordered corrin configuration which is created by DMBZ coordination in the cobalamins. The order imposed on the corrin ligand by the organic residue is lost in the product cobinamide. In the alkylcobalamins, however, order imposed by axial base coordination is preserved in the transition state. This results in smaller $\Delta S^{\circ\ddagger}$ values (−0.3 to +3.8 eu), regardless of whether the Co–C bond is cleaved by homolysis or by β-elimination.

Our work shows that spontaneous Co–C bond cleavage reactions of organocobalamins can occur by both overall heterolytic and homolytic mechanisms at ambient temperatures with the assistance of the axial DMBZ and the corrin ligand. We have previously[2] described such reactions as "mechanochemical" since they are induced by conformational motions of the corrin ligand and have pointed out that the energy requirements for Co–C bond cleavage of corrinoid coenzymes or organocobalt intermediates in enzymatic reactions could thereby be further lowered through interactions of the corrins with enzyme proteins.

Experimental Section

Materials. Vitamin B_{12a} (hydroxocobalamin) and vitamin B_{12} (cyanocobalamin, USP) were obtained from Merck, Sharp and Dohme Research Laboratories, Rahway, N.J. Diaquocobinamide was obtained from vitamin B_{12} via dicyanocobinamide as described in ref 16. Neopentyl iodide was prepared from neopentyl alcohol by reacting the tosylate with excess sodium iodide in peroxide-free diglyme at 120 °C and purified by vacuum distillation. Argon was freed of oxygen by two Cr^{2+} scrubbers in series. All other reagents and chemicals were commercial products and were used as received.

Methods and Instrumentation. Organocorrinoids were handled in a darkened laboratory with the dimmest light possible. When being handled in light, cobalamins were stored in aluminum foil wrapped glassware. Optical absorption spectra of cobalamin solutions were recorded on a Beckman DK-2A recording spectrophotometer equipped with a temperature-regulated cell block. Hydrocarbons were determined with a Hewlett-Packard Model 700 gas chromatograph equipped with an 8 ft × $^1/_8$ in. column of octane/Porasil C (GC Durapak, Waters Associates), with He as the carrier gas and flame ionization detection. Photolyses of organocorrins were performed at 15-cm distance from a 150-W tungsten floodlamp with air-stream cooling.

Preparation of Organocorrinoids. Isopropylcobalamin and isobutylcobalamin were prepared from hydridocobalamin and the corresponding alkyl bromides as outlined in ref 2.

Neopentyl- and Benzylcobalamin. Hydroxocobalamin, 250 mg, was dissolved in 10 mL of 5% NH_4Br in absolute methanol in a 15-mL capacity centrifuge tube. After deaeration with argon, 1 g of zinc dust was added, the tube was capped with a rubber septum, and argon flushing was continued by passing the inert gas through injection needles for gas inlet and outlet. The formation of vitamin B_{12s} was quantitative within a few minutes. Thereafter, 0.05 mL of neopentyl iodide was injected, producing the yellow-orange base-off protonated organocobalamin virtually instantly. Argon flushing was continued several minutes to ensure complete reaction. (Prolonged exposure of the product to the zinc results in net yield losses due to reductive dealkylation.) The zinc was removed by centrifugation and the supernatant poured into 100 mL of 1 N HCl. The cobalamin was extracted into a minimal volume of 1:1 phenol/chloroform (v/v). After evaporation of the chloroform, the cobalamin was precipitated by pouring the phenolic extract into 50 mL of diethyl ether and collected by centrifugation. The product cobalamin[17] was washed repeatedly with ether, dried in vacuo, and stored in the dark at 4 °C. The purity of samples was monitored spectrally and by thin-layer chromatography on cellulose with 10:3:7 *n*-butanol/acetic acid/water as the eluant, which separates organocobalamins in the protonated base-off form from unalkylated vitamin B_{12a}. Neopentylcobalamin optical absorption spectra: at pH 7 in H_2O, 326 nm ($\epsilon = 1.55 \times 10^4$ M^{-1} cm^{-1}), 388 (9.46×10^3), 439 (7.52×10^3), 487 (6.78×10^3); at pH 2 in H_2O, 326 nm ($\epsilon = 1.53 \times 10^4$ M^{-1} cm^{-1}), 389 (1.02×10^4), 437 (9.05×10^3).

Benzylcobalamin was prepared analogously, on 1/5 the scale of neopentylcobalamin (see above), by using benzyl bromide as the alkylating agent. Spectra: at pH 7 in H_2O, 339 nm ($\epsilon = 2.12 \times 10^4$ M^{-1} cm^{-1}), 500 (8.17×10^3); at pH 2 in H_2O, 356 (2.02×10^4), 428 (1.23×10^4).

Organocobinamides. A solution of diaquocobinamide, 10 mg, in 1 mL of H_2O was deaerated with argon. Sodium borohydride, 25 mg, was added to generate the Co(I) nucleophile. A 25-μL sample of the alkylating agent (neopentyl iodide, benzyl bromide, or isopropyl bromide) was added and the reaction was allowed to proceed for several minutes during which the mixture was shaken. The solution was subsequently poured into 20 mL of 1 M HCl and the cobinamide extracted into a minimal volume of phenol/chloroform (1:1). After evaporation of the chloroform, ether was added to precipitate the cobinamide. It was collected by centrifugation, redissolved in a minimal volume of methanol, reprecipitated with ether, collected, and dried. The product was purified on a 1.5 × 20-cm column of CM-cellulose with 10 mM sodium phosphate (pH 7) as the eluant and recovered from the major band by phenol extraction and precipitation as above.

Spectrophotometric Titrations. A solution of the organocobalamin in 50 mL of 10 mM citric acid was placed in a silicone septumed vial and deaerated exhaustively with argon. From this solution, 2.5-mL samples were transferred with an Ar-flushed syringe into a silicone septumed, deaerated cuvette. Small volumes of deaerated sodium hydroxide solutions of appropriate concentrations were injected to adjust the pH and the spectra recorded. The solutions were displaced from the curvette with argon for later pH measurement. The titration was completed in less than 1 h. Absorbance vs. pH data was evaluated at 439 and 520 nm for neopentylcobalamin and at 428 and 520 nm for benzylcobalamin. In each case, the resulting pK_a's agreed within 0.05 pH unit.

Kinetic Measurements. The rates of aerobic decomposition were determined by recording repetitive spectral scans. The decomposition of the cobalamins in neutral solution were initiated by adding a drop of a 0.1 M H_3PO_4 solution of the cobalamin into a cuvette containing 0.1 M sodium phosphate at pH 7.0. Toward the end of each reaction, the remaining organocorrinoid was photolyzed to obtain the t_∞ spectrum. Sharp isosbestic points were observed, and the first-order rate constants were evaluated from the absorbance changes at the wavelength of the γ-band of the cobalt(III) corrin. For benzylcobinamide in neutral so-

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(17) Isolated in the protonated base-off form, the cobalamins are orange-yellow rather than cherry red; the counterion is chloride and was detected by flame spectroscopy of solutions of the cobalamins in H_2O.

lution, the rate constants were evaluated at 428 nm.

For the slow decompositions of neopentylcobinamide and protonated base-off neopentylcobalamin at room temperature, solutions were stored in the dark, and at appropriate times, spectra of aliquots were recorded before and after photolysis. First-order rate constants were determined from the slopes of ln $[1 - (A_t/A_{h\nu})]$ vs. time, where A_t is the absorbance at time t and $A_{h\nu}$ is the corresponding absorbance after photolysis, measured at the wavelength of the cobalt(III) corrin γ-band.

The anaerobic decomposition of isobutylcobalamin was followed under an atmosphere of argon and produced vitamin B_{12s}, which more slowly was oxidized by protons to vitamin B_{12r}. The first-order rate constant was determined at 540 nm, a vitamin B_{12s}-vitamin B_{12r} isosbestic point.

Hydrocarbon Product Analysis. In typical experiments, 0.1 mL of a solution of the organocobalamin in 0.1 M H_3PO_4 was injected into a serum capped vial of 38-mL capacity which contained 5 mL of the buffered reaction solvent. For anaerobic conditions, both of the solutions were first rigorously deaerated with argon. After completion of the reactions, hydrocarbons in the gas phase were analyzed by GLPC. The identities and yields of products were determined by comparison with standards.

Carbonylic Product Identification. In the terminal solutions from aerobic decompositions of 25-mg samples of the cobalamins, carbonylic reaction products were converted into the 2,4-dinitrophenylhydrazones by adding 5 mL of a saturated (ca. 4 mg/mL) solution of 2,4-dinitrophenylhydrazine in 2 N HCl. The derivatized products were extracted into hexane and identified against standards by thin-layer chromatography on silica gel, using 1:1 hexanes/diethyl ether as the eluant for the products from neopentylcobalamin and benzene for benzaldehyde/DNPH from benzylcobalamin.

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Aspects of the Hydrogenation of Carbon Disulfide by Transition-Metal Cluster Compounds. The Reactions of Carbon Disulfide with Hydridotriosmium-Carbonyl Clusters

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Abstract: The reactions of CS_2 with $H_2Os_3(CO)_{10}$ (Ia) and $H_2Os_3(CO)_9[P(CH_3)_2C_6H_5]$ (Ib) are reported. Both clusters react with CS_2 to produce dicluster complexes of formula $(\mu\text{-}S_2CH_2)[HOs_3(CO)_9L]_2$ (L = CO, IIa; L = $P(CH_3)_2C_6H_5$, IIb). IIa was analyzed crystallographically: space group $P\bar{1}$, a = 10.093 (3) Å, b = 13.289 (2) Å, c = 13.865 (3) Å, α = 84.53 (2)°, β = 75.44 (2)°, γ = 88.24 (2)°, Z = 2, ρ_{calcd} = 3.30 g/cm³. For 3795 reflections ($F^2 \geq 3\sigma(F)^2$) R = 0.048 and R_w = 0.055. IIa contains a methanedithiolato ligand linking two triosmium clusters. The C–S distances at 1.85 Å are typical of carbon–sulfur single bonds. The S–C–S angle at 104.4 (7)° is approximately tetrahedral. In the formation of IIa two cluster complexes have reacted with a single molecule of CS_2 and each has transferred one hydride ligand to the carbon atom. A dithioformato complex $(\mu\text{-}S_2CH)HOs_3(CO)_9[P(CH_3)_2C_6H_5]$ (IIIb) and a thioformaldehyde complex $(\mu\text{-}SCH_2)(\mu_3\text{-}S)Os_3(CO)_9[P(CH_3)_2C_6H_5]$ (IVb) were also isolated from the reaction of Ib with CS_2. IVb has been analyzed crystallographically: space group $P2_1/c$, a = 10.001 (2) Å, b = 13.523 (3) Å, c = 18.660 (5) Å, β = 91.26 (2)°, Z = 4, ρ_{calcd} = 2.74 g/cm³. For 3404 reflections ($F^2 \geq 3.0\sigma(F)^2$) R = 0.058 and R_w = 0.067. IVb contains a thioformaldehyde ligand which is π bonded to one osmium atom C–S = 1.79 (1) Å while the sulfur atom simultaneously serves as a bridge across two osmium atoms. It also contains a triply-bridging inorganic sulfide ligand in a cluster of three osmium atoms which has only one osmium–osmium bond. When heated, both IIIb and IVb decarbonylate to form the complex $(\mu_3\text{-}\eta^2\text{-}SCH_2)(\mu_3\text{-}S)Os_3(CO)_8[P(CH_3)_2C_6H_5]$ (Vb). Vb was also analyzed crystallographically: space group $P\bar{1}$, at −35 °C, a = 9.103 (4) Å, b = 11.722 (4) Å, c = 11.819 (2) Å, α = 71.87 (2)°, β = 79.66 (2), γ = 82.20 (3)°, Z = 2, ρ_{calcd} = 2.86 g/cm³. For 3668 reflections ($F^2 \geq 3.0\sigma(F)^2$) R = 0.037 and R_w = 0.041. Vb contains a triply-bridging thioformaldehyde ligand with the sulfur atom directly bridging two osmium atoms and the carbon atom bonded solely to the third. The C–S distance is 1.869 (6) Å. Vb also contains a triply-bridging inorganic sulfide ligand, but unlike IVb the cluster has two osmium–osmium bonds. Mechanisms for the formation of all products are proposed and discussed. It was shown that dithioformato cluster complexes are not intermediates in the formation of IIa and IIb as demonstrated by the inability of the complexes $(\mu\text{-}S_2CH)HOs_3(CO)_{10}$ (IIIa), prepared by an independent method, and IIIb to be converted into the dicluster complexes.

Introduction

There has been much interest in transition-metal cluster compounds as a possible source for a new class of homogeneous catalysts.[1] Polynuclear coordination[2] and metal–metal bond cleavage[3] and formation[4] processes may serve as new means for the activation of small molecules. We are attempting to define the roles of these processes in the cluster-assisted hydrogenations of small unsaturated molecules.

Our earlier study of the $H_2Os_3(CO)_{10}$–isocyanide system provided insight into the roles of multiple coordination and isocyanide insertion in the cluster-catalyzed hydrogenation of isocyanide molecules.[5] We have now undertaken a study of the interaction of osmium hydride clusters with heterocumulenes[6] X = C = Y (X,Y = O, S, or NR) with the hope that they might provide some

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