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55424-74-3; 20, 112818-18-5; 21, 32811-25-9; 22, 35293-39-1; 23, 90646-75-6; 24, 113507-56-5; coenzyme B₁₂, 13870-90-1.

Supplementary Material Available: Table VIII containing representative material balances for the reaction of various bromides with (*n*-Bu)₃SnH (1 page). Ordering information is given on any current masthead page.

Thermal Decomposition and Cobalt–Carbon Bond Dissociation Energies of Organocobalamins: Neopentyl-, (Cyclopentylmethyl)-, (Cyclohexylmethyl)-, (Tetrahydrofurfuryl)- and ((Tetrahydro-2*H*-pyryl)methyl)cobalamin

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Abstract: The title compounds were prepared and characterized and their thermal decomposition reactions were studied in aqueous solutions of varying pH and containing varying concentrations of cob(II)alamin (B₁₂) and of bis(dimethylglyoximate)cobalt(II), [Co(DH)₂]. Homolytic cobalt–carbon bond dissociation pathways were identified through competitive trapping of the resulting free radicals according to the following scheme: R-B₁₂ ⇌ R• + B₁₂; R• + Co(DH)₂ → R-Co(DH)₂. Determination of the kinetics of these reactions yielded (after correction for the base on–base off equilibria) the following values of the activation parameters: R = neopentyl, Δ*H*[‡] = 26.7 ± 1.2 kcal/mol, Δ*S*[‡] = 15 ± 5 cal/(mol K); R = cyclopentylmethyl, Δ*H*[‡] = 26.8 ± 2 kcal/mol; Δ*S*[‡] = 3 ± 6 cal/(mol K). From these measurements the Co–C bond dissociation energies of the base-on forms of neopentyl-B₁₂ and cyclopentylmethyl-B₁₂ were deduced to be ca. 24 kcal/mol. In ethylene glycol Δ*H*[‡] for homolytic dissociation of the Co–C bond of neopentyl-B₁₂ was found to be about 4 kcal/mol higher than in aqueous solution.

It is now widely accepted that coenzyme B₁₂ dependent rearrangements are initiated by enzyme-induced homolytic dissociation of the coenzyme cobalt–carbon bond to generate a 5'-deoxyadenosyl radical.¹⁻⁵

Accordingly, a knowledge of the Co–C bond dissociation energy of this and related organocobalt compounds, and of the factors that influence such bond dissociation energies and that may contribute to enzyme-induced bond weakening and dissociation, is important to an understanding of the coenzyme's role. In this context we have previously determined the Co–C bond dissociation energies of a variety of organocobalt complexes (coenzyme B₁₂ models) in which the nature of the equatorial ligand (porphyrin, Schiff base, etc.), the cobalt-bonded alkyl group, and the trans-axial ligand (amine, phosphine, etc.) were varied.⁶⁻⁹ Such prior

studies have included determination of the Co–C bond dissociation energy of coenzyme B₁₂ itself ((5'-deoxyadenosyl)cobalamin), for which values ranging from 26 to 30 kcal/mol have been reported.^{10,11} Attention also is directed to several other earlier studies on the thermal decomposition of cobalamins.¹²

In this paper we report studies on the thermal decomposition of several other cobalamins (R-B₁₂) and, in some cases, determination of their Co–C bond dissociation energies. A particular objective was to attempt to identify distinctive features that might be associated with the 5'-deoxyadenosyl moiety as compared with other organic substituents. These studies also bear on the validity of one of the procedures that has previously been employed to determine the Co–C bond dissociation energy of coenzyme B₁₂.¹⁰

Results and Discussion

General. The general approach used in these studies parallels that employed in several earlier investigations.^{7,8,10,11,12a,13} Co–R bond dissociation energies were deduced from measurements of the kinetics of the homolytic bond dissociation reactions in the presence of a radical trap (in the present study bis(dimethyl-

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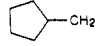
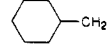
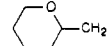
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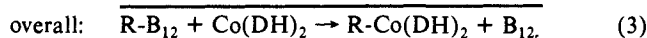
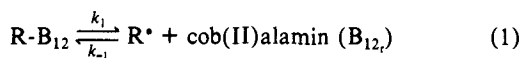
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Table I. Base On-Base Off Equilibria of Organocobalamins (R-B₁₂)

R	pK _a (25 °C)	temp range of measts, °C	ΔH' (pH), kcal/mol	ΔS' (pH), cal/(mol K)
(CH ₃) ₃ CCH ₂	5.07 ± 0.03	10.2–30.6	5.9 ± 0.3 (6.9)	20 ± 1 (6.9)
	3.99 ± 0.05	26.8–54.6	7.2 ± 0.3 (7.6) 3.9 ± 0.2 (5.0)	20 ± 1 (7.6) 12 ± 1 (5.0)
	4.08 ± 0.02			
	3.44 ± 0.01			

glyoximato)cobalt(II), abbreviated Co(DH)₂, which forms significantly stronger cobalt-carbon bonds than cobalamin)^{8a} according to the scheme of eq 1–3.



Under pseudo-first-order conditions (Co(DH)₂ and B₁₂, constant) this scheme yields

$$-\frac{1}{[\text{R-B}_{12}]} \frac{d[\text{R-B}_{12}]}{dt} = k_{\text{obsd}} = \frac{k_1 k_2 [\text{Co(DH)}_2]}{k_{-1} [\text{B}_{12}] + k_2 [\text{Co(DH)}_2]} \quad (4)$$

which rearranges to

$$\frac{1}{k_{\text{obsd}}} = \frac{1}{k_1} + \frac{k_{-1} [\text{B}_{12}]}{k_1 k_2 [\text{Co(DH)}_2]} \quad (5)$$

The Co-R bond dissociation energy (*D*_{Co-R}) may be derived from the kinetic measurements through the relation

$$D_{\text{Co-R}} = \Delta H_1^* - \Delta H_{-1}^* \quad (6)$$

In cases where information is available it has been concluded that the recombination reaction (*k*₋₁) is diffusion controlled.¹⁴ Thus, Δ*H*₋₁^{*} corresponds to the activation enthalpy for a diffusion-controlled reaction, which, in turn, can be approximated by Δ*H*^{*} for viscous flow.¹⁵ For water, this ranges from about 3 kcal/mol at 20 °C to 2 kcal/mol at 100 °C.¹⁶

Correction for Base On-Base Off Equilibria. Cobalamins are known to undergo reversible dissociation of the pendant axial 5,6-dimethylbenzimidazole and thus to exist in solution as an equilibrium mixture of the "base-on" [RCo-N], "base-off" [R-Co N], and "protonated-base-off" [RCo NH⁺] forms. The concentrations of these species are related through the equations

$$[\text{R-B}_{12}] = [\text{RCo-N}] + [\text{R-Co N}] + [\text{RCo NH}^+] \quad (7)$$

$$K_{\text{on-off}} = [\text{R-Co N}]/[\text{RCo-N}] \quad (8)$$

$$K_a = ([\text{R-Co N}] + [\text{RCo NH}^+])/[\text{RCo-N}] [\text{H}^+] \quad (9)$$

$$K'_{\text{on-off}} = ([\text{R-Co N}] + [\text{RCo NH}^+])/[\text{RCo-N}] \quad (10)$$

Values of p*K*_a, *K*_{on-off}, and *K*'_{on-off}, determined as described in the Experimental Section, are listed in Table I. The p*K*_a of free 5,6-dimethylbenzimidazole (and, hence, presumably of [RCo N]) has been estimated to be ca. 5.5 (25 °C, *I* = 0.1 M).¹⁷ Thus,

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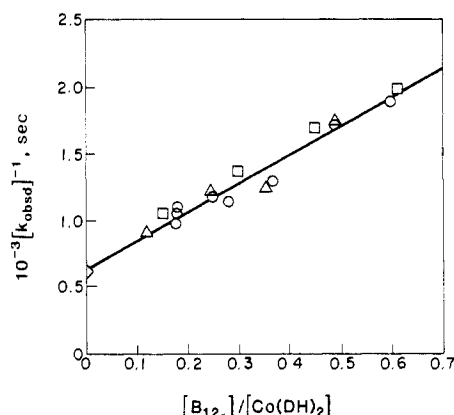


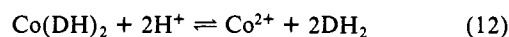
Figure 1. Plots of $[k_{\text{obsd}}]^{-1}$ vs $[\text{B}_{12}]/[\text{Co(DH)}_2]$ for the reaction of (CH₃)₃CCH₂-B₁₂ with [Co(DH)₂] at 40.5 °C, pH 6.8. (O) 1.2 × 10⁻³ M B₁₂; (□) 2.6 × 10⁻³ M Co(DH)₂; (Δ) 1.5 × 10⁻³ M Co(DH)₂; (◇) limiting rate with excess Co(DH)₂ (*k*_{obsd} ~ *k*₁).

the degree of protonation of [RCo N] is small at pH ≥ 7 and, under these conditions, *K*_{on-off} ~ *K*'_{on-off}.

In view of the much higher thermal stability of the base-off and protonated-base-off forms,¹⁸ their contributions to the Co-C bond dissociation reaction (eq 1) may be neglected and the measured values of *k*₁ must be corrected to reflect only the contributions of the base-on form; i.e.

$$(k_1)_{\text{corr}} = k_1 [\text{R-B}_{12}]/[\text{RCo-N}] = k_1 (1 + K'_{\text{on-off}}) \quad (11)$$

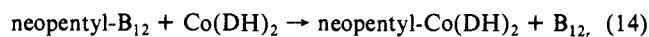
Dissociation of Co(DH)₂. Because Co(DH)₂ undergoes OH⁻-induced irreversible decomposition at the higher temperatures required for the study of some of these reactions,¹⁹ it was necessary, in some cases, to lower the pH of the reaction solutions to the range 4–5. Under these conditions Co(DH)₂ undergoes reversible dissociation, according to eq 12 and 13, so that the solution contains a mixture of Co(DH)₂ and Co²⁺.²⁰



$$\frac{[\text{Co}^{2+}][\text{DH}_2]^2}{[\text{Co(DH)}_2][\text{H}^+]^2} = K_{\text{DH}_2} \quad (13)$$

This equilibrium could be monitored spectrophotometrically by measuring the intensity of the absorbance of Co(DH)₂ at 462 nm (*ε*_{max} = 1.9 × 10³ M⁻¹ cm⁻¹). From such measurements, encompassing the initial pH range 4.3–5.0 and initial concentration ranges 1.0 × 10⁻³ to 6.3 × 10⁻³ M Co(DH)₂ and 0 to 8.4 × 10⁻³ M excess DH₂, *K*_{DH₂} was determined to be (3.0 ± 0.7) × 10⁵ at 25 °C in 0.3 M acetate buffer. This value was insensitive to temperature variations over the range 30–100 °C.

Neopentylcobalamin. (a) In Aqueous Solution at pH 6.8. The reaction of neopentyl-B₁₂ with Co(DH)₂ in aqueous solution at pH 6.8 (where dissociation of Co(DH)₂ according to eq 12 is negligible) was found to exhibit the stoichiometry of eq 14.



This is confirmed by the following observations: (i) The UV-visible spectrum of a solution containing initially 1.4 × 10⁻⁴ M each of neopentyl-B₁₂ and Co(DH)₂ (0.1 M phosphate buffer, pH 6.8), after reacting at 80 °C for 5 h, matched that of a synthetic solution containing 1.4 × 10⁻⁴ M each of neopentyl-Co(DH)₂ and B₁₂. (ii) In several experiments it was found by ¹H NMR that,

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Table II. Stoichiometries of the Reactions of Neopentylcobalamin with "Co(DH)₂"

pH	temp, °C	time, h	10 ³ × init concn, M		10 ³ × final concn, M			ΣB ₁₂	Σ(CH ₃) ₃ CCH ₂
			(CH ₃) ₃ CCH ₂ -B ₁₂	"Co(DH) ₂ "	B _{12a}	(CH ₃) ₃ CCH ₂ -B ₁₂	(CH ₃) ₃ CCH ₂ -Co(DH) ₂		
6.8	45	1.5	1.1	7.8	1.58 ^a	0	1.29 ^b	1.58	1.29
6.8	80	5	3.5	5.0	3.6	0	3.6	3.6	3.6
6.8	45	1.5	1.1	7.8	1.58 ^a	0	1.29 ^b	1.58	1.29
4.3	60	29	1.0	1.5	0.9	0.1	0.89	1.0	0.99
4.3	60	9	1.0	5.0	1.03	0	1.06	1.03	1.06
4.3	70	18	1.0	1.6	0.91	0.1	0.86	1.01	0.96

^a0.44 × 10⁻³ M B_{12a} present initially; Δ[B_{12a}] = 1.14 M. ^b0.30 × 10⁻³ M (CH₃)₃CCH₂-B₁₂ present initially; Δ[(CH₃)₃CCH₂-B₁₂] = 0.99 M.

following reaction of neopentyl-B₁₂ with Co(DH)₂ (and after passing O₂ through the solution to oxidize the paramagnetic B₁₂ product to B_{12a}), the concentrations of neopentyl-Co(DH)₂ and B_{12a} correspond to the concentration of reacted neopentyl-B₁₂ (Table II).

The kinetics of reaction 14 were examined at 40.5 °C. The results of experiments encompassing the initial concentration ranges, 3.0 × 10⁻⁴ to 1.2 × 10⁻³ M B₁₂, and 2.0 × 10⁻³ to 6.8 × 10⁻³ M Co(DH)₂, conformed to eq 5 as depicted in Figure 1. These measurements yield $k_1 = (1.65 \pm 0.15) \times 10^{-3} \text{ s}^{-1}$ and $k_{-1}/k_2 = 3.5 \pm 0.3$.

k_1 was determined at other temperatures (25–45 °C) from measurements under limiting conditions (large excess Co(DH)₂, no added B₁₂) such that $k_2[\text{Co}(\text{DH})_2] \gg k_{-1}[\text{B}_{12}]$; hence $k_{\text{obsd}} \approx k_1$. The results, listed in Table II, yield $\Delta H_1^\ddagger = 23.1 \pm 0.7 \text{ kcal/mol}$ and $\Delta S_1^\ddagger = 2 \pm 2 \text{ cal/(mol K)}$. These values are in good agreement with those reported in an earlier study using O₂ as radical scavenger, $\Delta H_1^\ddagger = 23.4 \pm 0.2 \text{ kcal/mol}$, $\Delta S_1^\ddagger = 1.6 \pm 0.1 \text{ cal/(mol K)}$.^{12b} After correction of the rate constants in Table II according to eq 11, $(\Delta H_1^\ddagger)_{\text{corr}} = 26.7 \pm 1.2 \text{ kcal/mol}$ and $(\Delta S_1^\ddagger)_{\text{corr}} = 15 \pm 5 \text{ cal/(mol K)}$. Subtracting $\Delta H_{-1}^\ddagger \sim 3 \text{ kcal/mol}$ leads to a value of 24 ± 2 kcal/mol for the neopentyl-B₁₂ bond dissociation energy, $D_{\text{neopentyl-B}_{12}}$.

(b) In Aqueous Solution at pH 4.3. To establish whether Co(DH)₂ also was effective as a radical trap at lower pHs where it was partially or largely dissociated into Co²⁺ and DH₂ (eq 12),^{10,11,20} the reaction between neopentyl-B₁₂ and Co(DH)₂ also was examined at pH 4.3.

The data in Table II demonstrate that, under these conditions, the stoichiometry of eq 14 still is obeyed, transfer of the neopentyl radical from B₁₂ to Co(DH)₂ being essentially quantitative. The kinetics of the reaction at 35.2 °C were examined with initial solution compositions ranging from 3.0 × 10⁻³ to 6.9 × 10⁻³ M "Co(DH)₂" and 3.1 × 10⁻⁴ to 1.2 × 10⁻³ M B₁₂. Under these conditions, the reaction was found to obey the rate law of eq 15,

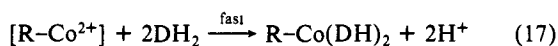
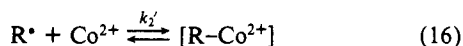
$$k_{\text{obsd}} = \frac{k_1'k_2'[\text{"Co}(\text{DH})_2\text{"}]}{k_{-1}'[\text{B}_{12}] + k_2'[\text{"Co}(\text{DH})_2\text{"}]} \quad (15)$$

which is essentially the same as eq 4 but with ["Co(DH)₂"] = [Co(DH)₂] + [Co²⁺]. These measurements yield the values $k_1' = (1.7 \pm 0.3) \times 10^{-4} \text{ s}^{-1}$ and $k_{-1}'/k_2' = 13 \pm 3$ (compared with $k_{-1}/k_2 = 3.5$ at 40.5 °C). Thus, we estimate the efficiency of "Co(DH)₂" as a radical trap at pH 4.3 to be about one-quarter that at pH 6.8 where dissociation of Co(DH)₂ is negligible.

Two interpretations may be accorded to the trapping of the neopentyl radicals at pH 4.3:

(i) Trapping is effected wholly by undissociated Co(DH)₂ which is present under these conditions, in accord with eq 2.

(ii) Trapping also is effected by the Co²⁺ ion to yield a transient neopentyl-Co²⁺ adduct which reacts rapidly with DH₂ to form the observed neopentyl-Co(DH)₂ product (eq 16 and 17). (Because of the reversibility of reaction 16, Co²⁺ is not expected to be an effective radical trap in the absence of DH₂.)



Because more than 90% of the Co(DH)₂ is dissociated into Co²⁺ and DH₂ at pH 4.3, it seems unlikely that the relatively efficient

radical trapping under these conditions is due entirely to undissociated Co(DH)₂. Accordingly, we favor the interpretation of eq 16 and 17, which invokes radical trapping also by Co²⁺. Indeed, Kochi²¹ has reported evidence for such trapping of alkyl radicals by Co²⁺ and formation of transient [R-Co²⁺] adducts. In any event, it is clear that "Co(DH)₂" does function as an efficient radical trap at pH 4.3 and can be used to determine the kinetics of alkyl-B₁₂ bond dissociation under these conditions. This point is noteworthy, since the appropriateness of such a procedure has been questioned.^{11b}

(c) In Ethylene Glycol Solution. Because of discrepancies in earlier measurements on the thermal decomposition of (5'-deoxyadenosyl)cobalamin in aqueous and in ethylene glycol solutions,^{10,11} it was of interest to extend these studies on neopentyl-B₁₂, where both the stoichiometry and mechanisms are unequivocal, to ethylene glycol.

Decomposition of neopentyl-B₁₂ in ethylene glycol over the temperature range 20–50 °C, under limiting conditions (initially ca. 2 × 10⁻⁴ neopentyl-B₁₂, 5 × 10⁻³ M Co(DH)₂), exhibited excellent pseudo-first-order kinetics and yielded the values of k_1 listed in Table III and the activation parameters $\Delta H_1^\ddagger = 26.8 \pm 0.3 \text{ kcal/mol}$ and $\Delta S_1^\ddagger = 13 \pm 1 \text{ cal/(mol K)}$ (vs 23.1 ± 0.7 kcal/mol and 2 ± 2 cal/(mol K) in aqueous solution at pH 6.8). Preliminary measurements yield estimates of 10 ± 1 kcal/mol and 34 ± 5 cal/(mol K) for $\Delta H'$ and $\Delta S'$, respectively, for neopentyl-B₁₂ in ethylene glycol. Using these values to correct for the base on-base off equilibrium yields $(\Delta H_1^\ddagger)_{\text{corr}} = 33 \pm 2 \text{ kcal/mol}$ and $(\Delta S_1^\ddagger)_{\text{corr}} = 35 \pm 10 \text{ cal/(mol K)}$ (vs 26.7 ± 1.2 kcal/mol and 15 ± 5 cal/(mol K) in aqueous solution at pH 6.8). The differences, $\Delta\Delta H_1^\ddagger = 3.7 \pm 1 \text{ kcal/mol}$ and $(\Delta\Delta S_1^\ddagger)_{\text{corr}} = 6 \pm 3 \text{ cal/mol}$, parallel those found earlier for the homolytic Co-C bond dissociation reactions of several other organocobalt compounds (benzyl-Co(DH)₂ and benzyl-Co(porphyrin) in toluene and ethylene glycol ($\Delta\Delta H^\ddagger = 4\text{--}6 \text{ kcal/mol}$),^{8a} presumably reflecting the higher viscosity of ethylene glycol compared with that of water and toluene. Accordingly, a difference of several kcal/mol between ΔH^\ddagger for the homolytic dissociation of the Co-C bond in 5'-deoxyadenosyl-B₁₂ in ethylene glycol and in water is not unexpected.^{10,11}

(Cyclopentylmethyl)cobalamin (c-C₅H₉CH₂-B₁₂). **(a) In the Absence of Co(DH)₂.** Since higher temperatures (60–80 °C) were required for the decomposition of c-C₅H₉CH₂-B₁₂ to proceed at conveniently measurable rates, this reaction was studied at pH 5.0. Under these conditions the extent of protonation of c-C₅H₉CH₂-B₁₂ is less than 10%. At the same time "Co(DH)₂" was found to be stable.

At 74 °C, c-C₅H₉CH₂-B₁₂ decomposed in the absence of "Co(DH)₂", with a half-life of ca. 50 min, to form B₁₂, in quantitative yield (spectrophotometric).²² The kinetic behavior, described below, and the pattern of organic products are accommodated by Scheme I.

In the absence of "Co(DH)₂", the principal organic product, after thermolysis of c-C₅H₉CH₂-B₁₂ for 6 h at 75 °C (identified by ¹H NMR following extraction with C₆D₆), was found to be

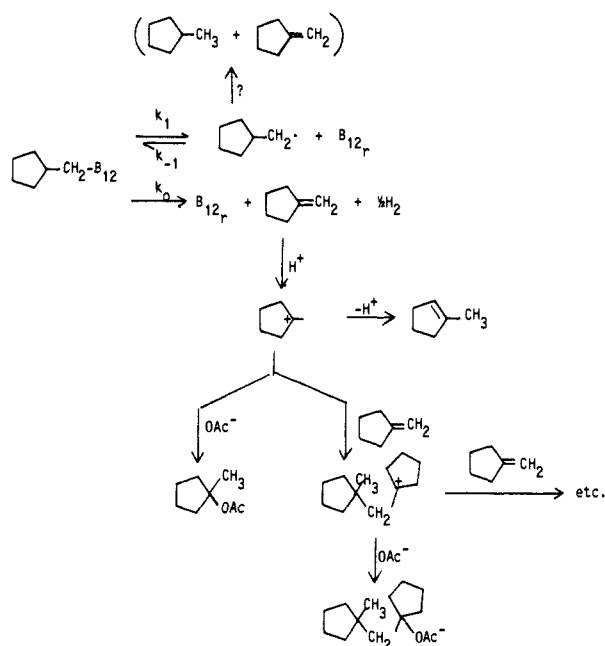
(21) Kochi, J. K.; Rust, F. F. *J. Am. Chem. Soc.* 1961, 83, 2017.

(22) B₁₂ decomposes spontaneously in acidic solutions at high temperatures to form B_{12a}.^{11b} However, the rate is much lower than the time scale of this reaction: $t_{1/2} \sim 360 \text{ min}$ at 100 °C, pH 4.3. Hence it would appear that B₁₂ is the primary product of the reaction.

Table III. Kinetic Data for Homolytic R-B₁₂ Bond Dissociation^a

R	pH	temp. °C	uncorrected			corrected ^b		
			10 ⁴ k ₁ , s ⁻¹	ΔH ₁ [*] , kcal/mol	ΔS ₁ [*] , cal/(mol K)	10 ⁴ k ₁ , s ⁻¹	ΔH ₁ [*] , kcal/mol	ΔS ₁ [*] , cal/(mol K)
(CH ₃) ₃ CCH ₂	6.8	25.4	2.12			4.70		
(CH ₃) ₃ CCH ₂	6.8	30.0	3.69			8.97		
(CH ₃) ₃ CCH ₂	6.8	30.7	4.26			10.5		
(CH ₃) ₃ CCH ₂	6.8	35.5	7.45			20.3		
(CH ₃) ₃ CCH ₂	6.8	35.2	8.46			23.0		
(CH ₃) ₃ CCH ₂	6.8	40.0	14.7			44.0		
(CH ₃) ₃ CCH ₂	6.8	40.6	16.5			49.4		
(CH ₃) ₃ CCH ₂	6.8	45.4	24.8			81.8		
(CH ₃) ₃ CCH ₂	6.8	45.6	24.9			82.1		
(CH ₃) ₃ CCH ₂	6.8			23.1 ± 0.7	2 ± 2		26.7 ± 1.2	15 ± 5
(CH ₃) ₃ CCH ₂	c	20.4	0.40			0.92		
(CH ₃) ₃ CCH ₂	c	20.8	0.42			0.90		
(CH ₃) ₃ CCH ₂	c	30.0	1.65			5.43		
(CH ₃) ₃ CCH ₂	c	30.8	1.80			5.44		
(CH ₃) ₃ CCH ₂	c	40.0	6.82			29.1		
(CH ₃) ₃ CCH ₂	c	40.6	7.71			33.6		
(CH ₃) ₃ CCH ₂	c	50.0	27.3			172		
(CH ₃) ₃ CCH ₂	c			26.8 ± 0.3 ^c	13 ± 1 ^c		33 ± 2 ^c	35 ± 10 ^c
c-C ₅ H ₉ -CH ₂	5.0	58	0.26			0.47		
c-C ₅ H ₉ -CH ₂	5.0	63	0.45			0.86		
c-C ₅ H ₉ -CH ₂	5.0	68	0.98			1.95		
c-C ₅ H ₉ -CH ₂	5.0	73	1.30			2.70		
c-C ₅ H ₉ -CH ₂	5.0	78	2.49			5.35		
c-C ₅ H ₉ -CH ₂	5.0			25.2 ± 1.7	-3 ± 5		26.8 ± 2	3 ± 6

^aIn aqueous solution unless designated otherwise. ^bCorrected for base on-base off equilibrium; data for base-on form. ^cIn ethylene glycol.

Scheme I Possible Pathways for the Decomposition of c-C₅H₉CH₂-B₁₂ in Acetate Buffer

1-methylcyclopentane (together with unidentified products associated with resonances at 1.71, 1.40, 1.02, and 1.01 ppm). The absence of methylcyclopentane under these conditions is not unexpected. Since the formation of the cyclopentylmethyl radical is reversible, and of methylenecyclopentane irreversible, most of the product would be expected to be derived from the latter. Failure to observe methylenecyclopentane also is expected. In a control experiment methylenecyclopentane (5 × 10⁻³ M) in 0.1 M pH 5 acetate buffer was heated at 75 °C for 1 h and found to be unstable. In addition to unreacted methylenecyclopentane the ¹H NMR spectrum of the C₆D₆ extracts exhibited resonances at 2.51, 2.33, and 2.02 ppm attributable to methylcyclopentane and resonances at 1.71, 1.40, 1.03, and 1.02 ppm, corresponding to those of the unidentified products of the thermal decomposition of c-C₅H₉CH₂-B₁₂. Thus, it would appear that the latter arise from further reactions of methylenecyclopentane formed according

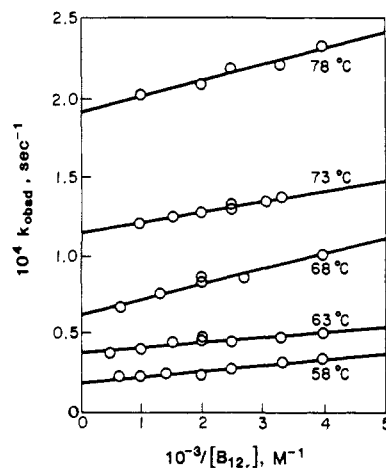


Figure 2. Dependence of k_{obsd} on $[\text{B}_{12r}]^{-1}$ for the decomposition of c-C₅H₉CH₂-B₁₂ (pH 5.0).

Table IV. Kinetic Data for (Cyclopentylmethyl)cobalamin (pH 5.0)

temp, °C	10 ⁴ k ₀ , s ⁻¹	10 ⁴ (k _{obsd}) _{lim} , s ⁻¹	10 ⁴ k ₁ , s ⁻¹
58	0.20	0.46	0.26
63	0.37	0.82	0.45
68	0.63	1.61	0.98
73	1.15	2.46	1.30
78	1.92	4.41	2.49

to Scheme I. Such possible products include the hydroxide or acetate of the 1-methylcyclopentyl carbonium ion or of the addition product of the latter to methylenecyclopentane.

According to Scheme I it should be possible to suppress the homolytic dissociation pathway by addition of B_{12r}, and, in this way, to determine, in the limit, the rate constant of the olefin elimination pathway, k_0 . The plots of k_{obsd} vs $[\text{B}_{12r}]^{-1}$ in Figure 2 are consistent with this and yield the values of k_0 listed in Table IV and the activation parameters $\Delta H_0^* = 25.4 \pm 0.3$ and $\Delta S_0^* = -4 \pm 2$ cal/(mol K).

(b) In the Presence of Co(DH)₂. Scheme I anticipates that, in the presence of "Co(DH)₂", the cyclopentylmethyl radical produced in the homolytic dissociation step should be trapped to form c-C₅H₉CH₂-Co(DH)₂. To test this, c-C₅H₉CH₂-B₁₂ (1.0

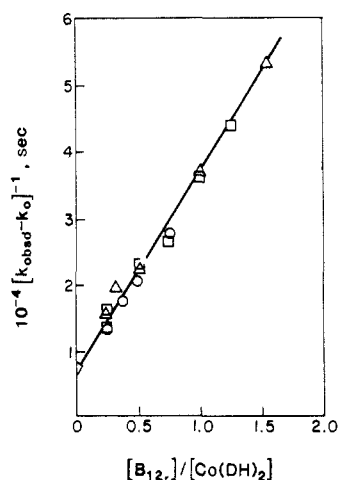
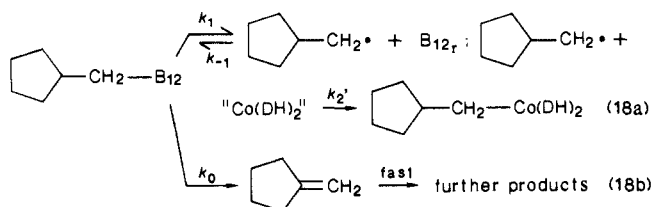


Figure 3. Plots of $(k_{\text{obsd}} - k_0)^{-1}$ vs $[B_{12}]/[Co(DH)_2]$ for the decomposition of $c\text{-C}_5\text{H}_9\text{CH}_2\text{-B}_{12}$ at 73.0 °C, pH 5.0. (○) 4.0×10^{-3} M $Co(DH)_2$; (□) 2.0×10^{-3} M $Co(DH)_2$; (△) 1.0×10^{-3} M B_{12} ; (◇) limiting value with excess $Co(DH)_2$ ($k_{\text{obsd}} - k_0 \approx k_1$).

$\times 10^{-3}$ M in D_2O containing 0.1 M pD 5.0 CD_3COO^- buffer) was heated at 75 °C for 20 min in the presence of a large excess (5×10^{-3} M) of $Co(DH)_2$ followed by passing O_2 through for 30 min to oxidize B_{12} , and unreacted $Co(DH)_2$. The 1H NMR spectrum of the resulting solution contained signals corresponding to a quantitative yield (1.0×10^{-3} M) of B_{12a} and 4.7×10^{-4} M $c\text{-C}_5\text{H}_9\text{CH}_2\text{-Co(DH)}_2$. Thus it is concluded that 47% of the $c\text{-C}_5\text{H}_9\text{CH}_2\text{-B}_{12}$ decomposes by the homolytic pathway under these conditions.

The kinetic scheme for the reaction of $c\text{-C}_5\text{H}_9\text{CH}_2\text{-B}_{12}$ in the presence of $Co(DH)_2$ and B_{12} , corresponds to



The resulting rate law

$$\frac{1}{[c\text{-C}_5\text{H}_9\text{CH}_2\text{-B}_{12}]} \frac{d[c\text{-C}_5\text{H}_9\text{CH}_2\text{-B}_{12}]}{dt} = k_{\text{obsd}} = \frac{k_0 + \frac{k_1 k_2' [Co(DH)_2]}{k_{-1} [B_{12}] + k_2' [Co(DH)_2]}}{\quad} \quad (19)$$

rearranges to

$$(k_{\text{obsd}} - k_0)^{-1} = \frac{1}{k_1} + \frac{k_{-1} [B_{12}]}{k_1 k_2' [Co(DH)_2]} \quad (20)$$

The rates of the reaction of $c\text{-C}_5\text{H}_9\text{CH}_2\text{-B}_{12}$ were monitored spectrophotometrically at 73 °C and pH 5.0 in a series of experiments encompassing the initial concentration ranges 1.0×10^{-4} to 2.0×10^{-4} M B_{12} , and 6.5×10^{-4} to 4.0×10^{-3} M $Co(DH)_2$. The kinetics conformed to pseudo-first-order behavior, yielding values of k_{obsd} . Combining these with the values of k_0 in Table III leads to the linear plot of $(k_{\text{obsd}} - k_0)^{-1}$ vs $[B_{12}]/[Co(DH)_2]$ depicted in Figure 3 in accord with eq 20. These measurements yield $k_1 = (1.30 \pm 0.11) \times 10^{-4} \text{ s}^{-1}$ and $k_{-1}/k_2' = 3.8 \pm 0.3$.

In the limit when $k_2' [Co(DH)_2] \gg k_{-1} [B_{12}]$, eq 19 reduces to $k_{\text{obsd}} = k_0 + k_1$. Values of k_{obsd} determined under these limiting conditions at temperatures ranging from 58 to 78 °C are listed in Table IV together with the values of k_0 determined earlier and the resulting values of k_1 obtained by difference. These yield $\Delta H_1^\ddagger = 25.2 \pm 1.7 \text{ kcal/mol}$ and $\Delta S_1^\ddagger = -3 \pm 5 \text{ cal/(mol K)}$. Correcting for the base on-base off equilibrium yields $(\Delta H_1^\ddagger)_{\text{corr}} = 26.8 \pm 2 \text{ kcal/mol}$ and $(\Delta S_1^\ddagger)_{\text{corr}} = 3 \pm 6 \text{ cal/(mol K)}$. Thus,

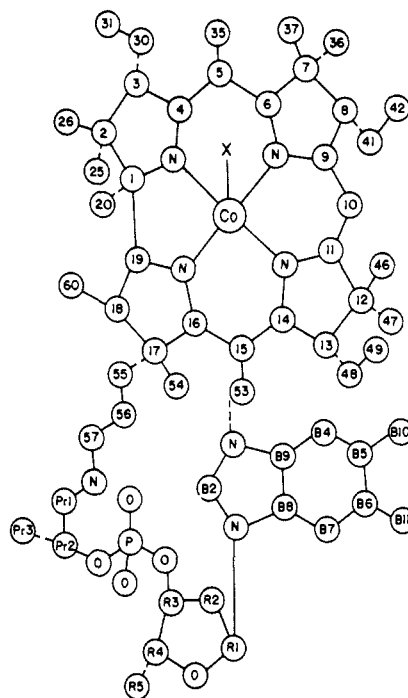


Figure 4. IUPAC numbering scheme for carbon atoms of alkylcobalamins (X = alkyl group).

we deduce the Co-C bond dissociation energy to be $24 \pm 2 \text{ kcal/mol}$.

A knowledge of the values of k_0 and of k_1 and k_{-1}/k_2' permits prediction of the product distribution. Under the limiting conditions just described, the yield of $c\text{-C}_5\text{H}_9\text{CH}_2\text{-Co(DH)}_2$ should correspond to k_1/k_{obsd} , i.e., $1.30 \times 10^{-4} \text{ s}^{-1}/2.46 \times 10^{-4} \text{ s}^{-1} = 0.53$ at 73 °C. This is close to the yield of 47% at 75 °C reported above.

It is striking that the activation parameters for k_0 and k_1 are virtually identical. Thus, $\Delta H_0^\ddagger = 25.3 \text{ kcal/mol}$, $\Delta H_1^\ddagger = 25.2 \text{ kcal/mol}$; $\Delta S_0^\ddagger = -4 \text{ cal/(mol K)}$, $\Delta S_1^\ddagger = -3 \text{ cal/(mol K)}$. This suggests that the two processes share a common rate-determining step, namely homolytic Co-C bond dissociation to yield a geminate $c\text{-C}_5\text{H}_9\text{CH}_2\cdot, B_{12r}$ radical pair. The two products, i.e., radical and olefin, could then arise from competing geminate pair separation and cage H-atom transfer, i.e., $c\text{-C}_5\text{H}_9\text{CH}_2\cdot, B_{12r} \rightarrow c\text{-C}_5\text{H}_9\text{CH}=\text{CH}_2 + \text{H-B}_{12r}$; $\text{H-B}_{12r} \rightarrow B_{12r} + 1/2 \text{H}_2$. We have previously proposed a similar mechanism for the olefin-forming reaction $\text{PhCH(CH}_3\text{)-Co(DH)}_2 \rightarrow \text{Co(DH)}_2 + \text{PhCH}=\text{CH}_2 + 1/2 \text{H}_2$.^{6b} Other olefin-elimination reactions have been similarly interpreted.²³

(Cyclohexylmethyl)cobalamin ($c\text{-C}_6\text{H}_{11}\text{CH}_2\text{-B}_{12}$). The behavior of $c\text{-C}_6\text{H}_{11}\text{CH}_2\text{-B}_{12}$ closely paralleled that of $c\text{-C}_5\text{H}_9\text{CH}_2\text{-B}_{12}$. The two compounds exhibited similar pK_a 's (4.06 and 3.99, respectively). A pH 6.8 solution of $c\text{-C}_6\text{H}_{11}\text{CH}_2\text{-B}_{12}$ was stable at room temperature for at least 24 h, and higher temperatures were required to observe decomposition. At pH 5.0 (in the absence of $Co(DH)_2$), $c\text{-C}_6\text{H}_{11}\text{CH}_2\text{-B}_{12}$ decomposed at 75 °C with a half-life of ca. 70 min to form B_{12} , in quantitative yield (spectrophotometric). Following decomposition at 75 °C for 6 h the 1H NMR spectrum of a C_6D_6 extract contained signals due to methylenecyclohexane and 1-methylcyclohexene, in the ratio 5:7, together with minor unidentified resonances at 1.68, 1.415, 1.04, and 1.02 ppm. The last three signals also could be observed in the spectrum of a sample of authentic methylenecyclohexane decomposed under the same conditions. No methylcyclohexane could be detected.

As in the case of $c\text{-C}_5\text{H}_9\text{CH}_2\text{-B}_{12}$, the decomposition of $c\text{-C}_6\text{H}_{11}\text{CH}_2\text{-B}_{12}$ (in the absence of $Co(DH)_2$) was inhibited by added B_{12} ; thus, at 75 °C, pH 5, $k_{\text{obsd}} = 1.39 \times 10^{-4}$, 1.29×10^{-4} , and $1.14 \times 10^{-4} \text{ s}^{-1}$ at 5.0×10^{-4} , 1.0×10^{-3} , and 2.0×10^{-3} M

(23) Baldwin, D. A.; Betterton, E. A.; Chemaly, S. M.; Pratt, J. M. *J. Chem. Soc., Dalton Trans.* **1985**, 1613.

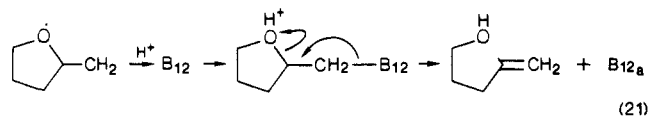
Table V. ¹H NMR Spectra of Alkylcobalamins^a

assign ^b	ethyl ^c	neopentyl pD 4.3 ^d	cyclopentylmethyl			cyclohexyl- methyl pD 5.0 ^d	tetrahydro- furfuryl pD 6.8 ^e	(tetrahydro-2H- pyrilyl)methyl (pD 6.8) ^f
			pD 6.8 ^e	pD 5.0 ^d	pD 4.3 ^d			
B(2)H	6.991	9.190	7.110	7.428	8.236	7.744	6.960, 6.984	6.983, 6.965
B(4)H	6.245	7.413	6.376	6.537	6.976	6.696	6.260, 6.360	6.235, 6.222
B(7)H	7.166	7.510	7.162	7.215	7.354	7.264	7.176, 7.164	7.164, 7.157
B(10)H ₃	2.212		2.220	2.191	2.200/2.180		2.216	2.219
B(11)H ₃	2.212	2.194/2.160	2.220	2.191		2.188/2.180	2.216	2.219
R(1)H	6.245	6.500	6.250	6.283	6.390	6.330	6.260	6.265
Pr(3)H ₃	1.209	1.172	1.220	1.205	1.185	1.196	1.218	1.224
C(10)H	6.041	6.978	6.128	6.240	6.552	6.380	5.988, 6.048	6.035, 5.995
C(20)H ₃	0.520	0.614	0.438	0.483	0.604	0.528	0.504, 0.418	0.508, 0.454
C(25)H ₃	1.386	(1.624) ^g	1.400	(1.428) ^g	(1.624) ^g	(1.456) ^g	(1.420) ^g	(1.467) ^g
C(35)H ₃	2.495	2.384	2.504	2.483	2.440	2.440	2.500	2.507
C(36)H ₃	1.778	1.838	1.820	1.815	1.820	1.820	1.786, 1.858	1.833, 1.783
C(46)H ₃	1.043	1.210	1.244	1.226	1.180	1.234	1.178, 1.280	1.289, 1.213
C(47)H ₃	1.441	1.418	1.344	1.356	1.384	1.366	(1.350) ^g	(1.367, 1.357) ^g
C(53)H ₃	2.476	2.384	2.480	2.463	2.430	2.450	2.500	2.493
C(54)H ₃	1.386	(1.392) ^g	1.400	(1.397) ^g	(1.392) ^g	(1.400) ^g	(1.396) ^g	(1.399, 1.393) ^g
X(1) ^h	0.846/0.566	i/0.920						
X(2) ^h	-0.594		-0.360	-0.430	-0.540	-1.007		
X(3) ^h		0.086	{ 0.380, 0.560/	{ 0.376, 0.536/	{ 0.312, 0.412/	l	{ 1.070, 0.991	} 0.9960, 0.820
X(4) ^h			{ 0.908, 0.991/	{ 0.896, 0.946/	{ 0.804, 0.816/	l	{ 0.980, 0.560, 0.380	
X(5) ^h			{ 1.070 ^{i,k}	{ 1.056, 1.137/	{ 0.980, 1.090/	1.642/1.558	3.58, 3.40	
X(6) ^h						l		
X(7) ^h						l		3.69, 3.46, 3.34, 2.93

^aChemical shifts (δ) downfield from (trimethylsilyl)propionic acid (TSP). ^bBased on numbering scheme in Figure 4 (cf. ref 27 and 28). ^cFrom ref 27. ^d0.1 M acetate buffer in D₂O at 36 °C. ^e0.1 M phosphate buffer in D₂O at 36 °C. ^f0.1 M phosphate buffer in D₂O at 23 °C. ^gTentative assignments. ^hAlkyl group carbon atoms numbered in sequence starting from Co-bonded carbon atom. ⁱNot observed due to overlap with other resonances. ^jThese single-proton resonances belonging to the cyclopentylmethyl group could not be assigned. ^kOverlap with adjacent large peak. ^lSignals for these 10 protons appear between 0.9 and 0.3 ppm.

B₁₂, respectively. Extrapolation to [B₁₂]⁻¹ = 0 yielded $k_0 = 1.1 \times 10^{-4} \text{ s}^{-1}$, close to the value $1.15 \times 10^{-4} \text{ s}^{-1}$ at 73 °C previously determined for c-C₆H₁₁CH₂-B₁₂. Because of the similarity of behavior to the latter, the study of c-C₆H₁₁CH₂-B₁₂ was not pursued further.

(Tetrahydrofurfuryl)cobalamin (THF-B₁₂). The study of this compound was of interest because it incorporates an analogue of one of the structural elements (the deoxyribose moiety) of (5'-deoxyadenosyl)cobalamin. THF-B₁₂ was only moderately stable in aqueous solution at pH 6.8, decomposition being detectable after 10 h at 15 °C under an inert atmosphere. Decomposition was accelerated by acid, so that the half-life for decomposition at 25 °C was ca. 60 min at pH 5.0 and less than 5 min at pH 2.2. The product of decomposition was aquocob(III)alamin (B_{12a}). Thus, it appears that decomposition is induced by protonation of the oxygen atoms in accord with eq 21



Because of this instability it proved impossible to study the homolytic Co-C bond dissociation reaction or to measure the pK_a of THF-B₁₂. It is remarkable that the stability of the structurally related (5'-deoxyadenosyl)cobalamin is so much greater than that of THF-B₁₂ notwithstanding probably more severe steric crowding.

((Tetrahydro-2H-pyryl)methyl)cobalamin (THP-B₁₂). The behavior of this compound paralleled that of THF-B₁₂, although it exhibited somewhat greater stability. In aqueous solution at pH 6.8 it was stable for ca. 2 days at 25 °C. The half-life for its decomposition (to B_{12a}) at 36 °C was 36 h at pH 4.3 and 12.5 h at pH 2.5. Decomposition was sufficiently slow to permit measurement of the pK_a (3.44 ± 0.01) but not to study the homolytic Co-C bond dissociation.

Experimental Section

General. All manipulations were performed in the dark under N₂ with rigorous exclusion of air.

Instrumentation. ¹H NMR spectra were recorded in D₂O or C₆D₆ solution using The University of Chicago 500-MHz spectrometer. Chemical shifts are referenced with respect to internal sodium 3-(trimethylsilyl)propionate-*d*₄ (TSP-*d*₄) or TMS, respectively. The solvent peak was suppressed by irradiating the water signal. UV-visible spectra were recorded on a Perkin-Elmer Lambda 7 or Lambda 5 spectrophotometer, equipped with a thermostated cell connected to a circulating constant-temperature bath (± 0.2 °C). The pH of the buffer solutions

was measured relative to a standardized Orion Ag/AgCl electrode using a Radiometer PHM 64 pH meter.

Starting Materials. Vitamin B₁₂ (cyanocobalamin), dimethylglyoxime, cyclopentylmethanol, tetrahydrofurfuryl alcohol, methylcyclopentane, methylenecyclopentane, and methylcyclohexane were used without purification. Neopentyl bromide, cyclohexylmethyl iodide, and 2-(bromomethyl)tetrahydro-2H-pyran were purified by vacuum distillation. Cyclopentylmethyl iodide and tetrahydrofurfuryl iodide were prepared by the procedure of Rydon.²⁴

Cobalamins. Cob(II)alamin (B₁₂),²⁵ hydroxocob(III)alamin (B_{12a}),²⁶ and neopentylcobalamin^{12b} were prepared by literature procedures.

(Cyclopentylmethyl)cobalamin. B_{12a} (0.25 g, 0.186 mmol) was dissolved in 10 mL of N₂-saturated 5% NH₄Br methanol solution. Zn dust (1 g) was added to the cherry red solution and the color changed immediately to dark green, indicating the formation of B₁₂. Cyclopentylmethyl iodide (0.03 mL, 0.285 mmol) was injected into the B₁₂ solution, resulting in orange (cyclopentylmethyl)cobalamin within a few minutes. After the Zn dust was removed by centrifugation, the orange supernatant was mixed with 100 mL of 1 M aqueous HCl solution in a separatory funnel. The organocobalamin was extracted into 15 mL of a 1:1 chloroform-phenol mixture and precipitated by addition of 50 mL of ether. The orange precipitate was collected by centrifugation and washed repeatedly with ether until the phenol was completely removed. The recovered solid was dried in vacuo overnight. Yield, 0.18 g (0.127 mmol, 68% based on B_{12a}). UV-visible, λ_{max} ($10^{-3}\epsilon_{\text{max}}$): pH 7.6, 522.5 (8.58), 450.0 (3.95); pH 5.0, 518.0 (7.65), 449.0 (4.115), 380.0 (7.50).

(Cyclohexylmethyl)cobalamin. B_{12a} (0.1 g, 0.074 mmol) was dissolved in 5 mL of N₂-saturated 5% NH₄Br methanol solution. Zn dust (0.4 g) was added to the cherry red solution, resulting in an immediate color change to greenish black, indicating formation of B₁₂. Addition of 0.03 mL of cyclohexylmethyl bromide resulted in a color change to red-orange within a few minutes. After centrifugation of the orange suspension, the supernatant was mixed with 50 mL of 1 M aqueous HCl. The organocobalamin was extracted into 10 mL of a 1:1 mixture of chloroform and phenol and precipitated by addition of 100 mL of ether. The orange solid was recovered by centrifugation and washed with ether until phenol was completely removed. The product was dried in vacuo overnight. Yield, 0.06 g (0.042 mmol, 57% based on B_{12a}). UV-visible, λ_{max} ($10^{-3}\epsilon_{\text{max}}$): pH 6.8, 518 (6.70), 440 (4.14); pH 5.0, 518 (6.50), 442 (4.25), 380 (6.99).

(Tetrahydrofurfuryl)cobalamin. B_{12a} (0.25 g, 0.19 mmol) was dissolved in 10 mL of N₂-saturated methanol. Addition of 0.05 g of NaBH₄ (0.13 mmol) to the cherry red solution resulted in an immediate color change to dark green, indicating the formation of B₁₂. Tetrahydrofurfuryl iodide (0.03 mL, 0.29 mmol) was injected into the brown solution, resulting in a color change to pink. After 1 h of stirring to complete the reaction, 80 mL of water was added, and the organocobalamin was

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(25) Blaser, H. U.; Halpern, J. *J. Am. Chem. Soc.* 1980, 102, 1684.

(26) Bernhart, K.; Wagner, O. *Biochem. Z.* 1963, 357, 366.

extracted into 15 mL of 1:1 phenol-chloroform. Ether (150 mL) was added to precipitate the organocobalamin. The pink solid was recovered by centrifugation, washed repeatedly with ether, and dried under vacuum. Yield, 0.15 g (0.11 mmol, 56% based on B_{12}). UV-visible, λ_{\max} ($10^{-3}\epsilon_{\max}$): pH 6.8, 520 (8.41), 368 (10.80), 355 (13.67).

((Tetrahydro-2H-pyryl)methyl)cobalamin. B_{12a} (0.25 g, 0.19 mmol) was dissolved in 10 mL of methanol. The resulting cherry red solution was saturated with N_2 , and 0.05 g of $NaBH_4$ (0.13 mmol) was added to produce a dark green solution of B_{12} . Addition of 0.03 mL of 2-(bromomethyl)tetrahydro-2H-pyran resulted in an immediate color change to pinkish red. After 1 h of stirring under N_2 to complete the reaction, the solution was mixed with 100 mL of water, and the organocobalamin was extracted into 15 mL of 1:1 phenol-chloroform. Ether (150 mL) was added to the phenol-chloroform layer to precipitate the organocobalamin. The pink-red solid was recovered by centrifugation and washed with ether. The product was dried in vacuo overnight. UV-visible, λ_{\max} ($10^{-3}\epsilon_{\max}$): pH 6.8, 521 (6.76), 372 (9.02), 340 (11.72).

The 1H NMR spectra of the cobalamins are detailed in Table V. Chemical shift assignments are based on comparisons with the published spectra of ethylcobalamin²⁷ and (5'-deoxyadenosyl)cobalamin²⁸ and on the pH dependencies of the resonances.

Organobis(dimethylglyoximate)cobalt(III) Complexes ($[R-Co(DH)_2]$). Dimethyl sulfide adducts of neopentyl-Co(DH)₂ and *c*-C₆H₅CH₂-Co(DH)₂ were prepared by literature procedures.²⁹ The dimethyl sulfide ligands were removed by dissolving the adducts in N_2 -saturated water and evaporating to dryness under vacuum.

Solvents and Buffers. Buffer solutions (0.1 M) for UV-visible spectral studies were prepared by using CH₃COOH-CH₃COONa for pH 3-5 and K₂HPO₄-KH₂PO₄ for pH 6-8 in deionized distilled water that was previously boiled and stored under N_2 . Buffer solutions (0.1 M) for 1H NMR spectral studies were prepared with CD₃COOD-CD₃COONa for pD 3-5 and K₂HPO₄-KH₂PO₄ for pD 6-8 in 99.8% D₂O. Ethylene glycol was purified by a literature procedure.³⁰

Identification and Quantification of Thermolysis Products by 1H NMR. Samples for 1H NMR analysis were prepared in a flask equipped with a high-vacuum valve and a side arm. After the desired quantity of the solid compound was weighed and dissolved in N_2 -saturated D₂O buffer solution, the valve was closed and the flask placed in a thermostated oil bath (± 0.5 °C). The reaction mixture was cooled and sampled periodically under a N_2 atmosphere. Subsequently, the sample was oxidized by air, and a known concentration of internal reference (TSP-*d*₄) was

added. The thermolysis products were identified by comparison with the 1H NMR spectra of authentic compounds and quantified by integration and comparison with the internal reference.

Kinetics Measurements. Samples for kinetic studies were prepared in a 1-cm Pyrex glass cell equipped with a high-vacuum valve and a side arm. The desired quantity of the solid compound was dissolved in the N_2 -saturated aqueous buffer solution or ethylene glycol in the cell. The cell was closed and placed in the thermostated cell compartment of the UV-visible spectrophotometer or (with concordant results) in a thermostated oil bath. In the former case, the disappearance of the alkylcobalamins and appearance of B_{12} were continuously monitored by measuring the absorbance at 650 nm. (No decomposition was observed when organocobalamin solutions were irradiated at this wavelength for 24 h at 25 °C.) In the latter case, the cell was removed from the oil bath periodically, cooled immediately, and placed in the thermostated cell compartment (25 °C), and the absorbance at 650 nm was recorded. These operations were performed in the dark.

The kinetic measurements were performed under pseudo-first-order conditions and the reactions followed for at least 3 half-lives. First-order rate constants were computed by linear least-squares regression.

Base On-Base Off Equilibrium Constants. Alkylcobalamin solutions (1×10^{-4} to 2×10^{-4} M) were prepared as for the kinetic measurements. Spectra were recorded over the pH range 2-7 and pK_a values, defined by eq 9, were determined by fitting spectral titration curves at ca. 522 nm. Values of ΔH° and ΔS° listed in Table I were determined by linear least-squares regression fitting of the temperature dependence of the absorbance (A_{obsd}) at 522.5 nm (520 nm in the case of ethylene glycol) to the equation

$$\ln [(A_\alpha - A_{\text{obsd}})/(A_{\text{obsd}} - A_0)] = -\Delta H^\circ/RT + \Delta S^\circ/R \quad (22)$$

The absorbance of the base-off form (A_0) was assumed to be that of the limiting protonated form, i.e., $[Co NH^+]$, at low pH. The absorbance of the base-on form (A_α) was determined from the fitting procedure. The measured absorbances were corrected for thermal expansion of the solutions. Values of $(k_1)_{\text{corr}}$ were computed according to eq 11.

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Registry No. B_{12} , 13422-51-0; Co(DH)₂, 36451-49-7; neopentylcobalamin, 71721-47-6; (cyclopentylmethyl)cobalamin, 113779-31-0; (cyclohexylmethyl)cobalamin, 113779-32-1; (tetrahydrofurfuryl)cobalamin, 75642-83-0; ((tetrahydro-2H-pyryl)methyl)cobalamin, 113792-90-8; cyclopentylmethyl iodide, 27935-87-1; cyclohexylmethyl bromide, 2550-36-9; tetrahydrofurfuryl iodide, 5831-70-9; 2-(bromomethyl)tetrahydro-2H-pyran, 34723-82-5.

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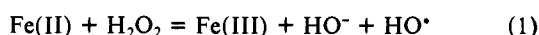
Reduction of Hydrogen Peroxide by the Ferrous Iron Chelate of Diethylenetriamine-*N,N,N',N'',N''*-pentaacetate

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Abstract: Ferrous iron complexed with diethylenetriamine-*N,N,N',N'',N''*-pentaacetate (DTPA) reacts with hydrogen peroxide in neutral aqueous solution at room temperature to yield an oxidizing species that is not scavenged by *tert*-butyl alcohol, under conditions where >90% of hydroxyl radical would be scavenged. Further, the oxidizing species reacts with Fe^{II}DTPA³⁻ and H₂O₂ at virtually the same rate, in contrast to the known behavior of the hydroxyl radical. These observations, the effects of methanol on the reaction, and the kinetic and stoichiometric results of the experiments clearly establish that the oxidizing species produced is not the hydroxyl radical, but an iron-oxo species such as the ferryl ion. The oxidizing species is formed in an apparent first-order reaction, when either hydrogen peroxide or Fe^{II}DTPA³⁻ is in kinetic excess. The bimolecular reaction rate constant is $(1.37 \pm 0.07) \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$.

The reduction of hydrogen peroxide by iron chelates is a well-known reaction.¹ In acid solution, it appears that the reduction produces the hydroxyl radical (HO[•]) (eq 1). This is the



key reaction in the production of hydroxylated products by Fenton's reagent in strongly acid solutions. The rate in acid solution has been measured.²⁻⁸ Acid solution values have been

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