The Chemistry of Vitamin B_{12}. Part 25.[1] Mechanism of the β-Elimination of Olefins from Alkylcorrinoids; Evidence for an Initial Homolytic Fission of the Co–C bond †

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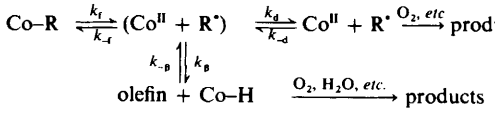
Equilibrium constants ($\log_{10} K$/dm^3 mol^{-1}) have been determined for the co-ordination of imidazole by the five-co-ordinate alkylcobinamides with R (= alkyl) = Me (0.9), Et (−0.5), neopentyl (np) (−1.4), Pr^i (< −1.9), and cyclohexyl (C_6) (< −1.9) in aqueous solution at 25 °C; this confirms that contact between dbzm (the heterocyclic base, 5,6-dimethylbenzimidazole, in the cobalamin side-chain) and the corrin ring can play only a minor part in the similar effect of varying R on the co-ordination of dbzm. The maximum (pH- and p_{O_2}-independent) rates of decomposition of np- and C_6-cobalamin (at 36 °C) and of the corresponding cobinamides (at 80 °C) have been determined. Comparison of present and published kinetic data show that changing R (from Et to np and C_6) and changing from six- to five-co-ordination (for both R = np and C_6) produce very similar and large changes in rate, irrespective of whether the overall reaction corresponds to homolytic fission (R = np) or β-elimination (R = C_6); this provides indirect evidence that both reactions involve a common first step, *viz.* homolytic fission of the Co–C bond to produce a caged (Co^{II} + radical) pair. The decomposition of C_6-cobinamide in air at pH 1 and 25 °C is catalysed by vanadyl ions in solution and by cobalt boride in suspension. Me- and C_6-cobinamide are both diamagnetic.

β-Elimination and the reverse addition of olefins to a metal–hydrogen bond are well known reactions in organometallic chemistry; see for example, ref. 2. A good example is provided by the reversible interconversion of the square-planar Pt^{II} complexes *trans*-[$Pt(PPh_3)_2ClX$] [X = H (+ ethylene) or Et]. It is generally accepted that the mechanism involves a single concerted four-centre transition state and requires a vacant co-ordination site;[2] the fact that Pt^{II} complexes undergo ligand substitution by an associative (S_N2) mechanism[3] shows that the additional co-ordination site is readily accessible. In this paper we present evidence that β-elimination in the alkylcorrinoids probably proceeds by a different two-step mechanism, which involves an initial homolytic fission (h.f.)‡ of the Co–C bond [equation (1)].

$$\text{Co–R} \rightleftharpoons \text{Co–H} (+ \text{ olefin}) \longrightarrow Co^{I} + H^{+} \longrightarrow Co^{II} + \tfrac{1}{2} H_2 \quad (1)$$

Alkylcorrinoids can undergo β-elimination either thermally or photochemically and from either the six- or five-co-ordinate forms; good examples are the thermal decomposition of Pr^i- and C_6-cobalamin at room temperature and the photolysis of Et-cobalamin.[4] The evidence that the yellow 'base-off' alkylcorrinoids (cobinamides and acidified cobalamins) are five-co-ordinate has been reviewed[4] and is supported by the high rate of reaction ($k_2 \geqslant 10^8$ dm^3 mol^{-1} s^{-1}) of Me-cobinamide with cyanide.[5] β-Elimination has been studied only in aqueous solution where complications arise [see equation (1)] because the hydride[1] loses a proton (*cf.* other Co-H complexes[6]), with pK *ca.* +1,[7] to give the Co^{I} complex, which decomposes under N_2 by an extraordinary oscillating reaction to give Co^{II},[8] while



Scheme.

decomposition at pH < 1 is very fast.[1,6] Evidence for the intermediate formation of the hydride is, however, provided by the formation of some HD from β-elimination in D_2O.[9] The rate is very sensitive to both the steric effect of the alkyl ligand R (see below) and to the presence or absence of the second axial ligand, which may change the rate of Co–C bond fission by factors of up to 10^{10} and 10^4 respectively;[4,9] the effect of a change in the nature of the second axial ligand has not yet been studied quantitatively.

Three facts suggest that β-elimination from alkylcorrinoids does not involve the additional co-ordination site required by the concerted mechanism. (*a*) Six-cordinate Co^{III} corrinoids, like other Co^{III} complexes, undergo ligand substitution by a dissociative (S_N1) mechanism.[5,10] (*b*) Equilibrium constants for the co-ordination of substituted amines by aquocobalamin are more sensitive to steric hindrance than with any other metal ion yet studied.[11] (*c*) The six-co-ordinate alkylcobalamins are more labile than their five-co-ordinate analogues.[4,9,12] The alternative to a concerted mechanism is a two-step mechanism (first discussed in the corrinoid field for the photolysis of alkylcobalamins[13]), in which h.f. of the Co–C bond occurs in the first step and the H atom is transferred from the radical to the Co in the second step, *i.e.* β-elimination shares the same first step as overall h.f. Overall h.f. is exemplified by the thermal decomposition of np-cobalamin[4,9,12] at room temperature and by the photolysis of Me-cobalamin and the cobalamin coenzyme.[4] It has recently been shown by picosecond flash photolysis that the immediate product from the photolysis of both Me-cobalamin and the coenzyme is a caged (Co^{II} + radical) pair with kinetic properties distinct from those of the separated Co^{II} and free radical.[14] It is reasonable to assume that thermal h.f.

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† *Non-S.I. units employed:* B.M. = 0.927 × 10^{-23} A m^2, c.g.s.u. = S.I. × $10^6/4\pi$.

‡ Abbreviations: h.f. = homolytic fission, dac = diaquocobinamide, im = imidazole, dbzm = the base (5,6-dimethylbenzimidazole) present in the cobalamin side-chain, R = alkyl ligands and radicals, C_n = *n*-membered cycloalkyl ligands and radicals, np = neopentyl (CH_2CMe_3).

Table 1. Effect of increasing steric compression around co-ordinated C_α on the properties of alkylcorrinoids

R	$A_{440}:A_{460}$ [a]	R-cobinamide + im $\log_{10} K$ [b]	R-cobalamin pK [c]	Rate of Co–C fission in R-cobalamin [d] $t_{\frac{1}{2}}$ (temp./°C)
Me	0.90	[0.9]	2.6	≥1 yr (r.t.) [e]
Et	[1.03]	[−0.5]	3.9	6 months (r.t.) [e]
Pr^i	1.23	[< −1.9]	≥4.5	3 min (25) [e]
np	1.22	[−1.4]	4.7 ± 0.2	60 min (25) [f]
C_6	1.27	[< −1.9]	4.7 ± 0.2	21 min (25) [f,g]

New results and values are enclosed in square brackets.

[a] Of the protonated, five-co-ordinate (E) forms of the alkylcobalamins. Values from ref. 17 except that for R = Et, which has been recalculated (*cf.* previous value 1.08). [b] K is defined by equation (2). The concentration of the six-co-ordinate aquo-form of the alkylcobinamide is negligible except for R = Me (~10% at 20 °C).[15b] [c] pK for protonation of dbzm, *i.e.* for conversion of the (A) + (C) forms to the (E) forms of the alkylcobalamins. Values from ref. 4. [d] Experimentally observed values of $t_{\frac{1}{2}}$ in air, uncorrected for the presence of the relatively inert five-co-ordinate (C) form. [e] Ref. 9. [f] Ref. 12. [g] See also Results and Discussion sections.

also proceeds *via* a caged intermediate, as shown in the Scheme where the caged intermediate is enclosed in brackets. The presumed[15a] five-co-ordinate structure of the Co^{II} product is supported by the very fast rate of reaction of B_{12r} with methyl radicals ($k_2 \sim 2 \times 10^9$ dm^3 mol^{-1} s^{-1}) to reform the Co–Me bond.[16]

To establish the mechanism of β-elimination, evidence for or against the occurrence of the caged pair as a reaction intermediate is needed. The very fast rates of reaction of the caged pair[14] preclude direct detection in the case of thermal β-elimination, but the occurrence of two different overall routes of Co–C bond fission (h.f. and β-elimination) and the existence of two major rate-determining factors (R and co-ordination number) provide the opportunity for using indirect methods. If β-elimination and h.f. share a common intermediate, then the maximum rate of decomposition by either route will be determined by the same rate constants (k_f and k_{-f} of Scheme) and hence show a similar dependence on the two main variables (R and co-ordination number), irrespective of whether the overall reaction involves h.f. or β-elimination. It has been shown that the alkyl ligands R can be placed in virtually a single order (*viz.* R = Me ~ C_3 < Et ~ Pr^n < Bu^i ~ C_4 < Pr^i, np, C_5, C_6) from their effect on the u.v.–visible spectra (which can be considered as a ground-state effect) and on equilibrium constants for the co-ordination of ligands in the *trans* position (thermodynamic effect), and that this represents the order of increasing steric compression around the co-ordinated C_α;[4,12,17-19] selected data are given in Table 1. We have therefore made a detailed study of the decomposition of the six-co-ordinate cobalamins and the five-co-ordinate cobinamides with R = np and C_6, which occupy similar positions in the steric order and yet decompose by overall h.f. (np) and mainly or entirely by overall β-elimination (C_6).[4]

Two possible complicating factors must be eliminated before the steric order can be used to test for correlations between h.f. and β-elimination. First, it has been argued[9,20] that the labilising effect of dbzm on the Co–C bond of bulky alkyl groups is transmitted mainly through contact between dbzm and the C(5)–C(6) part of the corrin ring, rather than through the Co atom, the equatorial N atoms, and the co-ordinated C_α. This suggestion can be tested by comparing the dependence of the equilibrium constants for the co-ordination of imidazole (which cannot interact with the corrin ring) and dbzm and the converse labilisation of the Co–C bond by imidazole and by dbzm. We have therefore studied the co-ordination of imidazole by the cobinamides with R = Me, Et, Pr^i, np, and C_6 and include the result for R = vinyl, which was determined at the same time. Secondly, the spectra of the five-co-ordinate alkylcorrinoids show that the first band may occur at either *ca.* 460 nm (*e.g.* R = Me) or at *ca.* 440 nm (*e.g.* R = C_6) and that the ratio $A_{440}:A_{460}$ is a sensitive indicator of the position of R in the steric order (see Table 1).[4,17] Superposition of the spectra for different R groups gives a semblance of isosbestic points at *ca.* 450 and *ca.* 480 nm, with intensity moving from the band at 460 nm into lower energy transitions as well as into the band at 440 nm, when R is changed from Me to C_6 (see Figure 6 of ref. 2); in view of the possible existence of paramagnetic alkyl–Co^{III} complexes,[21] this could represent a spin-dependent (*i.e.* singlet–triplet) equilibrium. The cobalamin coenzyme is diamagnetic in both its red six-co-ordinate and yellow ($\lambda_{max.}$ = 458 nm) five-co-ordinate forms,[15c] but no alkylcorrinoid with a band at *ca.* 440 nm has yet been studied. We have therefore determined the magnetic susceptibility of Me- and C_6-cobinamide as representatives of compounds with maxima at *ca.* 460 and 440 nm respectively.

The aims of this paper are, therefore, (*i*) to determine and compare the maximum rates of Co–C bond fission in the np/C_6-cobalamins/cobinamides as evidence for the mechanism of β-elimination, (*ii*) to determine equilibrium constants for the co-ordination of imidazole by various alkylcobinamides, and (*iii*) to determine the magnetic susceptibility of C_6-cobinamide and other cobinamides. Our main arguments and conclusions concerning (*i*) have been reported in brief elsewhere.[19]

Experimental

Materials.—Samples of vitamins B_{12} and B_{12a} were kindly given by Mr. A. P. Domleo of Glaxo-Allenbury (Pty) Limited. D_2O (Merck, uvasol), Bu^{t}OH (Merck, zur Analyse), MeI (Merck), and neopentyl bromide (Fluka) were all used as received. EtBr and Pr^{i}I (both Hopkin and Williams) and cyclohexyl bromide (Emmanuel) were redistilled before use. Imidazole (Aldrich) was recrystallised three times from benzene before use. Nitrogen (Afrox, Germiston, Transvaal) was used without further purification.

Preparation of Cobalamins and Cobinamides.—Cyanoaquocobinamide[22] and dac[23] were prepared as previously described, as were vinyl- and the alkyl-cobinamides,[22] *except* that the starting material was dac instead of cyanoaquocobinamide. Precautions against photolysis were taken when handling and studying all organocorrinoids. Attempts were made to develop a method for the quantitative reduction of dac to the Co^{II} cobinamide, in the absence of excess reducing agent and potential ligands, for use in magnetic studies. In agreement with the relative redox potentials,[24] qualitative tests showed that dac is reduced much more readily than aquocobalamin and Co^{II} cobinamide oxidised (*e.g.* by O_2) much less readily than the Co^{II}

cobalamin (B_{12r}). Diaquocobanamide is readily reduced (within 15 min) by a suspension of zinc dust in neutral water and by AR-grade methanol (over several hours) unless freshly distilled from $KMnO_4$; reduction may be brought about simply by freeze-drying[23] or by removing the solvent on a rotary evaporator.[25] We also find that dac undergoes self-reduction in neutral, homogeneous solution on heating (*e.g.* to 80 °C) but, rather surprisingly, complete reduction could not be achieved even on prolonged heating under N_2. Conversely, reducing dac with a trace of tetrahydroborate (to give mainly Co^{II} with some Co^{I}), followed by acidification to decompose excess tetrahydroborate, always produces a mixture of Co^{II} and Co^{III}. The Co^{II}–Co^{III} cobinamide system behaves as though it tends towards some equilibrium or steady-state balance between the valencies, regardless of the direction of approach. The cause of this peculiar behaviour has not been investigated, but may be connected with the interconversion of conformational isomers (of unknown structure), which is observed for both cobalamins and cobinamides on heating and which may affect the redox potentials.[26–28] Diaquocobinamide can also be reduced by CO,[29] but we found that the reduction of dac by CO or by formate was always accompanied by considerable formation of 'stable yellow corrinoids'.[15d,30] We were finally obliged to use solutions prepared by the freeze-drying of dac, whose spectra indicated the presence of *ca.* $\frac{2}{3}$ Co^{II} and $\frac{1}{3}$ Co^{III}.

U.v.–Visible Spectra.—These were recorded with a JASCO Uvidec-1 spectrophotometer in thermostatted 1-cm cells.

Magnetic Susceptibility Measurements.—Magnetic susceptibilities were determined by Evans's n.m.r. method[31] using a Bruker WP80 Fourier-transform 80-MHz n.m.r. spectrometer at 27 °C with an estimated resolution of 0.1 Hz. The outer tube (i.d. = 4 mm) contained 2% v/v Bu^tOH and *ca.* 10^{-2} mol dm^{-3} of the corrinoid in D_2O and, in order to give signals of approximately equal height, the inner tube (o.d. = 2.5 mm, i.d. = 1.3 mm) contained 6% v/v Bu^tOH in D_2O. Values of $\mu_{eff.}$ were calculated from the observed splittings (Δf) by using the values of -0.6413×10^{-6} c.g.s. for the gram susceptibility of 2% Bu^tOH in D_2O at 25 °C,[32] and -0.69×10^{-6} c.g.s. for the diamagnetic correction (as reported for B_{12} itself).[33]

Buffers.—The following buffers were used (all with I = 0.2 mol dm^{-3}): pH 4.0, acetic acid–NaO_2CMe; pH 7.1—8.1, Na_2HPO_4–NaH_2PO_4; pH 8.8—10.4, Na_2CO_3–$NaHCO_3$. 0.05 and 0.005 mol dm^{-3} H_2SO_4 were used for pH 1.1 and 2.0 respectively.

Results

Co-ordination of Imidazole by Vinyl- and Alkyl-cobinamides.—Equilibrium constants K (where only the axial ligands are given)

$$K = \frac{[\text{R–Co–im}]}{([\text{R–Co–OH}_2] + [\text{R–Co}])\,[\text{im}]} \qquad (2)$$

for the co-ordination of imidazole by cobinamides with R = vinyl, Me, or Et were determined in buffers of pH 8.8 at 25 °C. For each cobinamide separate solutions were prepared containing a fixed cobalt concentration (*ca.* 2×10^{-5} mol dm^{-3}) and varying concentrations of imidazole (up to 1 mol dm^{-3} for the vinyl and Me complexes and up to 4 mol dm^{-3} for the Et complex, which increased the pH to 9.6). The spectra were scanned over the range 300—650 nm; all equilibria were established instantaneously and reasonable isosbestic points were observed. The products were all red with absorption bands at 329, 365, and 519 nm (R = vinyl); 344, 363, 376 (sh), and 525 nm (R = Me); and approximately 342, 360, 380 (sh), and 500 nm (R = Et). Plots of A_{525} against imidazole concentration showed that complete formation of the product was not attained, and the data were therefore evaluated by the method of Newton and Arcand[34] to obtain values of A_∞. Plots of log ($|A - A_0|/|A_\infty - A|$) *versus* log [im] were then used to confirm the stoicheiometry (one im per Co) and to derive values of $K_{obs.}$ which were corrected for the small amount of protonated imidazole (pK taken as 7.2) to give K = 18.6 ± 1.7, 8.55 ± 0.6, and 0.35 ± 0.03 dm^3 mol^{-1} for R = vinyl, Me, and Et respectively or $\log_{10} K$ = 1.3, 0.9, and −0.5. Compare the value of K = 11 dm^3 mol^{-1} for R = Me previously reported by Pailes and Hogenkamp.[35]

The spectrum of np-cobinamide showed the appearance of a shoulder at ~520 nm at very high concentrations of imidazole only. Assuming that the spectrum of the imidazole complex of np-cobinamide is the same as that of the imidazole complex of Me-cobinamide, the spectrum around 520 nm indicates the formation of *ca.* 15% of the imidazole adduct in 4.5 mol dm^{-3} imidazole (buffer present, pH measured as 9.7); hence K = $15/(85 \times 4.5) = 4 \times 10^{-2}$ dm^3 mol^{-1} or $\log_{10} K = -1.4$. No analogous change in the spectrum was observed with either C_6- or Pr^i-cobinamide in 4.5 mol dm^{-3} imidazole; assuming that 5% formation of the red imidazole adduct would be observed gives $\log_{10} K < -1.9$. C_6-cobinamide decomposes in unbuffered 4.5 mol dm^{-3} imidazole in air at 50 °C to give the bis(imidazole)–Co^{III} complex (λ_γ = 359 nm) with isosbestic points and first-order kinetics ($t_{\frac{1}{2}}$ = 210 min), but shows no detectable (< 3%) decomposition over 2 h in a buffer of comparable pH (10.43) in the absence of imidazole. The values of log K are included in Table 1.

Magnetic Susceptibilities of Cobinamides.—No splitting (Δf = 0.0 ± 0.1 Hz) was observed for *ca.* 10^{-2} mol dm^{-3} solutions of cyanoaquocobinamide (Factor B), Me- or C_6-cobinamide (all in deionised water), or for dicyanocobinamide (Factor B in unbuffered 0.01 mol dm^{-3} NaCN solution), *i.e.* they are all, as expected, diamagnetic. As an additional and more sensitive test for possible differences between Me- and C_6-cobinamide, identical concentrations of the former and latter were placed in the inner tube (as reference) and outer tube (as sample) respectively; again no splitting was detected. Since it proved impossible (see Experimental section) to obtain a quantitative reduction of dac to the Co^{II} complex in the absence of excess reducing agent (*e.g.* BH_4^-, which would cause partial reduction to Co^{I} and cause the evolution of bubbles of H_2) or potential ligands (*e.g.* thiols), we were unable to make a quantitative determination of the magnetic moment of the Co^{II} complex and have used the sample containing *ca.* $\frac{2}{3}$ Co^{II} and $\frac{1}{3}$ Co^{III} (as determined from the spectrum) simply to check the applicability of the method. No magnetic moment has yet been determined for any mononuclear Co^{II} corrinoid; a single unpaired electron would give a spin-only value of $\mu_{eff.}$ = 1.73 B.M., but higher values are always found for low-spin d^7 Co^{II} ions due to orbital contribution (*e.g.*, $\mu_{eff.}$ = 2.72 B.M. for Co^{II}–phthalocyanine).[36] A solution of 4.9×10^{-3} mol dm^{-3} Co^{II} cobinamide (containing 2.4×10^{-3} mol dm^{-3} dac) gave Δf = 1.65 and 1.82 (±0.1) Hz in two separate experiments (average 1.7 Hz), which corresponds to $\mu_{eff.}$ = 1.9 B.M.

Rates of Decomposition of Alkylcorrinoids.—The rates of decomposition of the four alkylcorrinoids (*viz.* C_6/np-cobalamin/cobinamide) were studied by u.v.–visible spectrophotometry using (1.5—3.0) $\times 10^{-5}$ mol dm^{-3} aqueous solutions in a thermostatted cell. The aim was to obtain maximum rates of decomposition and to establish that these were independent of both pH and p_{O_2}. The experimental conditions and results are given in Table 2. In order to obtain convenient rates the more inert cobinamides were studied at 80 °C. Our original intention

Table 2. Rates of thermal decomposition of C_6- and np-corrinoids

Compound	Temp. (°C)	pH	% O_2[a]	Product[b]	$10^2 k_1$/min^{-1}	$t_{\frac{1}{2}}$/min
C_6-cobalamin	25	7.1	100	Co^{III}	0.79	88
C_6-cobinamide	r.t.	7.1	100	Co^{III}	*c*	
np-cobalamin	25	7.1	100	Co^{III}	1.02	68
np-cobinamide	25	7.1	100	Co^{III}	*c*	
C_6-cobalamin	36	7.1	0	Co^{I}		20—30[d]
		7.1	20	Co^{III}	3.5	20
		7.1	100	Co^{III}	3.7	19
		8.1	100	Co^{III}	3.4	21
		9.2	100	Co^{III}	3.2	22
		10.2	100	Co^{III}	3.4	21
np-cobalamin	36	7.1	0	Co^{II}	*e*	
		7.1	4	Co^{III}	4.3	16
		7.1	20	Co^{III}	5.3	13
		7.1	100	Co^{III}	4.6	15
		9.2	100	Co^{III}	4.3	16
C_6-cobinamide	80	1.1	0	Co^{III}	2.0[f]	35[f]
		1.1	1	Co^{III}	6.0	12
		1.1	2	Co^{III}	5.1	14
		1.1	4	Co^{III}	4.6	15
		1.1	20	Co^{III}	5.3	13
		1.1	100	Co^{III}	5.8	12
		2.0	100	Co^{III}	4.6	15
		4.0	100	Co^{III} + Sy		⩽20
		8.0	100	Co^{II} + Sy		10—25
		8.0	0	Co^{II}		31—37
np-cobinamide	80	1.0	0	Co^{II}	*g*	
		1.0	20	Co^{III}	5.6	12
		1.0	100	Co^{III}	6.2	11
		7.9	0	Co^{II}	*h*	
		7.9	20	Co^{III}	4.2	16
		7.9	100	Co^{III}	4.6	15

[a] In O_2–N_2 mixtures. [b] Identified from the spectra (see text); Sy is a stable yellow corrinoid.[15d,30] [c] ⩽3% in 1 d. [d] The initially formed Co^{I} decomposed to Co^{II} by an oscillating reaction[8] with a periodicity of *ca.* 5 min; the overlap of the reactions, together with the oscillations, prevented an accurate determination of $t_{\frac{1}{2}}$. Several separate experiments all indicated $t_{\frac{1}{2}}$ = 20—30 min. [e] Very slow; *cf.* refs. 12 and 20. [f] Average of three separate values (35, 35, and 36 min). [g] ~33% decomposition in 1 h. [h] ~23% decomposition in 1 h.

of studying the cobinamides (at 80 °C) and cobalamins (at 35 °C) at the same pH (*ca.* 7) was frustrated by the fact (see Table 2) that decomposition of the cobinamides at pH ⩾ 4 gives a mixture of products which prevents the determination of reasonable kinetic plots, while the protonation of dbzm at pK ~ 4.7 (see Table 1) prevents the study of the cobalamins at pH ⩽ 5. In all these experiments the cell was closed with a rubber septum pierced by two syringe needles, which were used for passing the appropriate N_2–O_2 mixture through the solution for 10 min at room temperature before the reaction was initiated by placing the cell in the heated cell-holder.

For each set of conditions the reaction was first studied by following the change with time of the whole spectrum from 300 to 600 nm in order to establish the presence or absence of isosbestic points and to identify the products from the position of their absorption bands,[15] *viz.* 350 and 357 nm (aquo- and hydroxo-cobalamin), 473 and 470 nm ('base-on' and 'base-off' forms of the Co^{II} B_{12r}), 387 nm (Co^{I} B_{12s}), and *ca.* 460 nm (stable yellow corrinoid, in which the conjugation has been broken).[30] In those cases where a value of k_1 is listed (Table 2), the reaction showed reasonable isosbestic points and gave a single major product and the kinetics were then studied in further experiments under identical conditions by following the increase in optical density at the wavelength of the product. The reaction was followed for at least five half-lives; in all cases the observed end-point agreed within experimental error with that calculated from the known absorption coefficients of the initial and final corrinoids. Changes in optical density over the first 5 min were ignored in order to allow time for the solution to reach the stated temperature. The derived first-order kinetic plots were all linear over at least four half-lives.

We have shown previously that both cobalamins (R = np or C_6) exist at 25 °C as a mixture of the red, six-co-ordinate, 'base-on' (A) form and the yellow, five-co-ordinate, 'base-off' but unprotonated (C) form.[18] Comparing the spectra at 25 and 36 °C showed no significant differences over the whole range 300—600 nm; for both cobalamins, therefore, the fraction present in each form remains essentially the same at the two temperatures, *viz.* 60% (A) for R = np and 20% for R = C_5.[18]

Discussion

Present results on the co-ordination of imidazole by cobinamides provide further evidence on the nature of the *trans*-effect both for the ligands from H_2O to Et (usually denoted by X), where electronic effects predominate, and for the simple alkyl ligands (R) where steric effects predominate. Inclusion of our value for vinylcobinamide shows that $\log_{10} K$ (dm^3 mol^{-1}) for the substitution of co-ordinated H_2O by imidazole (and/or the simple co-ordination of imidazole by the five-co-ordinate form) falls with X in the order H_2O (7.5) > dbzm (4.6) > CN^- (4.1)[15e] > HC≡C– (3.4)[37] > CH_2=CH– (1.3) > Me (0.9) > Et (−0.5), as already found for the co-ordination of cyanide.[5] The data for R = Me, Et, Pr^i, np, and C_6 show (see Table 1) that there are comparable falls in the equilibrium constants for the co-ordination of imidazole and dbzm (*i.e.* rise in the pK) with R = Me > Et > np > Pr^i, C_6. In addition, it has been established that the Co–C bond in the C_6- (this paper), np-,[12]

Table 3. Comparison of the maximum rates of thermal decomposition of C_6/np-cobalamins/cobinamides

Compound	Temp. (°C)	$t_{\frac{1}{2}}$ R = C_6	$t_{\frac{1}{2}}$ R = np	ratio (C_6/np)
Six-co-ordinate cobalamins,[a] pH 7	25	18 min	41 min	0.44
	36	4.2 min	9 min	0.47
Five-co-ordinate cobalamins, in 1 mol dm^{-3} H_3PO_4	25	67 d[b]	28 d[c]	2.4
Five-co-ordinate cobinamides, pH 1	80	12 min	11 min	1.1

[a] Values correspond to 100% of the six-co-ordinate (A) form and have been calculated by multiplying the experimentally observed values of 80 and 68 min at 25 °C and 21 and 15 min at 36 °C (see Table 2) by the fraction present in the mixture as the (A) form, *viz.* 0.2 and 0.6 for R = C_6 and np respectively. [b] Ref. 9. [c] Ref. 20.

and Pr^i-cobinamides[9] can be labilised by high concentrations of imidazole (presumably *via* the intermediate formation of the six-co-ordinate imidazole adduct), as well as by the presence of co-ordinated dbzm. These results show that little, if any, of the effect of R on the binding constant for dbzm or the reverse effect of dbzm on the lability of the Co–C bond can be ascribed[9] to contact *via* the C(5)–C(6) region of the corrin ring.

The magnetic susceptibilities show that the yellow, five-co-ordinate Me- and C_6-cobinamides, like the protonated form of the coenzyme,[15c] are diamagnetic; all the alkylcorrinoids to be discussed here, whether five- or six-co-ordinate, can therefore be assumed to be diamagnetic. There appears to be only one remaining complication regarding the starting materials which must be borne in mind when analysing the kinetic data of Table 2, *viz.* that np- and C_6-cobalamins exist in neutral solution as a mixture of *ca.* 60 and 20% respectively (at 25 °C) of the red, six-co-ordinate 'base-on' (A) form, together with the yellow, five-co-ordinate but unprotonated 'base-off' (C) form;[18] the spectra suggest (see Results section) that we can adopt the same values at 36 °C.

The main points shown by Table 2 can be summarised as follows. (*a*) The decomposition of C_6-cobalamin at pH 7 under N_2 gives B_{12s}, as characterised both by its spectrum and by its decomposition to B_{12r}, by an oscillating reaction (*cf.* ref. 8); this appears to be the first spectroscopic identification of Co^I as the product of thermal β-elimination. (*b*) C_6-cobalamin and -cobinamide both decompose relatively rapidly even in the absence of O_2, as expected[4,9] for β-elimination. (*c*) np-cobalamin and -cobinamide decompose far more slowly in the absence of O_2, as expected[4,9] for h.f. (*d*) The presence of O_2 increases the rate of decomposition of all four compounds, except possibly C_6-cobalamin. The maximum stimulating effect of O_2 is reached at low levels of O_2 ($\leqslant 1\%$ O_2 for C_6-cobinamide). It *appears* that O_2 also increases the rate of decomposition of C_6-cobalamin, but this could not be established quantitatively because of complications due to the unusual kinetics of the decomposition of Co^I (see Results section); this does, however, seem likely in view of the report that the yield of alkane to alkene is increased by the presence of dithioerythritol.[38] (*e*) The rates of all four reactions studied in detail are virtually pH-independent. In addition, we have found (*f*) that vanadyl ions in solution and particles of cobalt boride in suspension are good catalysts for the decomposition of C_6-cobinamide (but not np-cobinamide) in air at 25 °C; this appears to be the first report of a catalysed decomposition of an alkylcorrinoid. Several other observations may be explained by similar catalytic effects. We previously observed $t_{\frac{1}{2}}$ of *ca.* 21 and 60 min for the decomposition of C_6- and np-cobalamin respectively (in air at 25 °C) when the cobalamins were prepared by a method in which $Co(NO_3)_2$ was added in order to catalyse the reduction of B_{12a} to B_{12s} by tetrahydroborate;[12] Grate and Schrauzer[9] also reported that C_6-cobalamin decomposed faster than np-cobalamin ($t_{\frac{1}{2}}$ = 44 and 75 min respectively in air at 25 °C). In the present work, however, B_{12a} is reduced without the addition of a catalyst and we find $t_{\frac{1}{2}}$ of *ca.* 90 and 70 min respectively (see Table 2), *i.e.* the rate of C_6-cobalamin is reduced while that of np-cobalamin remains unchanged. Omitting the catalyst is a prerequisite for detecting Co^I as the product both of the photolysis[8] and of the thermolysis (this paper) of C_6-cobalamin; the addition of catalyst produces Co^{II}.[8] There appear to be a number of redox-catalysed reactions of corrinoids waiting to be explored.

The above results have removed two anomalies regarding C_6-cobalamin (*viz.* failure to detect Co^I and the possible role of catalysts), established that all the rates are pH-independent (as required by the proposed mechanisms), and provided values for the maximum (p_{O_2} independent) rates of decomposition; these are given in Table 3 as values of $t_{\frac{1}{2}}$. For the cobalamins in neutral solution the observed values of $t_{\frac{1}{2}}$ have been corrected to correspond to 100% of the six-co-ordinate (A) form by assuming that the (C) form is inert. To provide a value for the five-co-ordinate forms at 25 °C we have used Schrauzer's values[9,20] for the acidified cobalamins; our own experiments (see Table 2) suggest that the cobinamides decompose more than 10^2 times more slowly than the cobalamins, *i.e.* they are in qualitative agreement. Comparison of the results for the cobinamides at 80 °C and the acidified cobalamins at 25 °C shows that the ratio of the lability of the Co–C_6 and Co–np bonds is not very sensitive to temperature.

We can now test for the mechanism of β-elimination as follows. If β-elimination involves a two-step mechanism which shares a common intermediate with h.f. (Scheme), then we would expect, first, that a change in R (to a position higher in the steric order) would cause a similar increase in the lability of the Co–C bond towards both β-elimination and h.f. and, secondly, that a change from six- to five-co-ordination would cause a similar decrease in lability. If, on the other hand, β-elimination involves a totally different one-step mechanism then, first, there is no reason to expect that a change in R would have a similar effect on β-elimination and h.f. (any similarity would be purely fortuitous) and, secondly, one would expect that a change from six- to five-co-ordination would have a markedly different effect and probably even increase the rate of β-elimination. With R = Et, a ligand low in the steric order (see Table 1), Et-cobalamin decomposes very slowly with $t_{\frac{1}{2}} \sim 6$ months[9] [uncorrected for the presence of 20% of the (C) form][18] by β-elimination. Then if Et is replaced by np or C_6, both of which occupy similar and much higher positions in the steric order (see Table 1), $t_{\frac{1}{2}}$ falls to 41 and 18 min respectively (Table 3), which corresponds to labilisation by factors of

0.6×10^4 and 1.5×10^4. If we then convert the six-co-ordinate cobalamins to the five-co-ordinate forms $t_{\frac{1}{2}}$ increases from 41 min to 28 d (*i.e.* by 1.0×10^3) for R = np and from 18 min to 67 d (5.4×10^3) for R = C_6, yet the ratio of the lability of the Co–C_6 to the Co–np bonds remains the same within a factor of five (see Table 3), *i.e.* a change in co-ordination number has the same effect on Co–C lability, regardless of whether Co–C bond fission involves h.f. or β-elimination.

These results show that a change in R and a change in co-ordination number both have a very similar effect on the rate, irrespective of whether the Co–C bond fission leads to overall h.f. or β-elimination, and confirm *both* the predictions based on a common first step for h.f. and β-elimination. We therefore conclude that β-elimination in the alkylcorrinoids (both five- and six-co-ordinate, and probably photochemical as well as thermal) occurs *via* the Scheme involving an initial h.f. to give a caged (Co^{II} + radical) pair and, conversely, that the reverse addition of olefins to the hydride to give alkylcorrinoids, which can be observed in glacial acetic acid,[1,39] also proceeds *via* the caged pair.

It has been argued that the β-elimination of Pr^i-cobalamin must be concerted since the yields of propylene are unaffected by the presence of O_2;[20] the validity of this argument can be tested as follows. Since the rates of diffusion of free radicals are virtually independent of size, k_d will be *ca.* 10^9 s^{-1} for R = Pr^i as well as Me[16] and, since the reaction yields an olefin, $k_\beta > k_d$. If we then assume that $k_\beta > 10^9$ s^{-1} and that O_2 reacts with the caged radical at a rate similar to that with the free methyl radical (*viz.* 5×10^9 dm^3 mol^{-1} s^{-1}),[16] then the relatively low solubility of O_2 in water (*ca.* 10^{-3})[32] will give a maximum rate of $\sim 5 \times 10^6$ s^{-1} for reaction with the caged radical; this will not readily be detected in competition with k_β and, conversely, will not significantly affect the rate of β-elimination. The good correlation between the effect of varying the cycloalkyl ring size (C_5—C_8) on the rates of decomposition of the acidified cobalamins (*i.e.* five-co-ordinate forms) and of the Cope elimination of cycloalkylamine oxides has been adduced as evidence for the concerted *syn*-elimination of olefins in the former reaction;[9] the correlation with the rates of homolytic fission of cycloalkyl-substituted azoalkanes[40] is, however, at least as good.

The structure of the caged pair has not previously been discussed. We assume that conversion of the six-co-ordinate alkylcobalamin into a caged pair involves movement of the cobalt atom out of the plane of the corrin ring towards the co-ordinated N atom of dbzm (*cf.* the displacement of *ca.* 0.11 Å observed in a five-co-ordinate iodide-bridged binuclear Co^{II} corrinoid),[15f] possibly coupled with a change from a singlet to a triplet ground state. Since simple alkyl radicals (*e.g.* Et, Pr^i, C_6) have a planar structure,[40] their formation would be accompanied by a corresponding movement of C_α away from the plane of the corrin ring.

Our present results and arguments appear to provide the first experimental evidence for β-elimination *via* h.f. in any metal–alkyl complexes.

Acknowledgements

We thank Mr. A. P. Domleo of Glaxo-Allenbury (Pty) Ltd. for the gift of samples of vitamins B_{12} and B_{12a}, the Council for Scientific and Industrial Research for financial support, and Miss Janine Aron for help with some of the experiments.

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Received 8*th May* 1984; *Paper* 4/731