Five-Coordination and Adduct Formation in $Co^{III}-$Corrinoids Dissecting Ligand Substitution into Its Component Steps

Mohamed S. A. Hamza,[a,c] Rudi van Eldik,*[a] Pascal L. S. Harper,[b] John M. Pratt,*[b] and Eric A. Betterton[d]

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The equilibria between the five- and six-coordinate species of alkylcobinamide and cobalamin (base-off) have been studied using high-pressure spectroscopic techniques. The addition of a water molecule to the five-coordinate complex is accompanied by a volume decrease of 12 $cm^3 \cdot mol^{-1}$.

Introduction

The mechanisms of ligand substitution reactions can be divided into the two extremes of limiting dissociative (D) and associative (A) mechanisms, linked by a broad range of interchange (I) mechanisms involving the formation of some weak, non-bonded "outer-sphere" (OS) adduct or intermediate between the entering and/or leaving ligand and the complex,[1] but few such adducts have been reported.[2] Good evidence for several such OS intermediates has recently been obtained from kinetic studies of both ligand substitution[3] in the six-coordinate $Co^{III}-$corrinoids (derivatives of vitamin B_{12})[4] and of the methylation of five-coordinate $Co^{II}-$corrinoids by MeI in the presence of thiols.[5] As will be shown here, the $Co^{III}-$corrinoids also offer an unusual opportunity to observe analogues of the five-coordinate intermediate of the limiting D mechanism, and of adducts with both five- and six-coordinate forms under equilibrium (i.e. non-reacting) conditions. In addition they offer the opportunity to establish a link between kinetically deduced transient intermediates and directly observable stable species.

Co−corrinoids with only amide side-chains are termed *cobinamides* (Cbi), those with the attached nucleotide (as in B_{12} itself) *cobalamins* (Cbl), and those where the amides have been esterified (usually as the Me ester) *cobesters* (Cbs); protonation and displacement of the coordinated nucleotide base in a Cbl gives a coordination sphere identical to that of a Cbi. UV/Vis spectrophotometry provides the main tool for kinetic and other studies.[4b] Both axial sites are surrounded by a hydrophobic cylinder of the exocyclic substituents, projecting roughly normal to the corrin ring, and an outer ring of hydrophilic amide groups. Comparing a Cbi with the analogous Cbs provides a test for possible involvement of the side-chains in, e.g. adduct formation. $Co^{III}-$corrinoids with the more typical axial ligands used in kinetic studies are red and six-coordinate. There is, however, good evidence that Cbi's (and protonated Cbl's) with stronger donor ligands (e.g. vinyl, methyl, sulfite, or dialkyl phosphite) exist as temperature-dependent mixtures of yellow five-coordinate and red six-coordinate aqua (solvato) forms based on UV/Vis, EXAFS, and NMR measurements.[4a,6] No other explanation for the available data has been put forward. Increasing temperature favours the yellow five-coordinate form, and with diethyl phosphite[7] as ligand it has also been shown qualitatively that increasing pressure favours the red six-coordinate form. No structural data on the yellow forms have yet been reported and more evidence for the reversible coordination of H_2O is clearly desirable.

We have now quantitatively studied the pressure dependence (up to 150 MPa) of the spectra of both vinyl-Cbi (VCbi, $4 \cdot 10^{-5}$ M, pH = 7, unbuffered solution) and protonated methyl-Cbl ($3 \cdot 10^{-5}$ M MeCbl/0.5 M $HClO_4$) in aqueous solution, which contain 70 and 90%, respectively, of the yellow form at ambient pressure and 20 °C,[6a] in order to determine the reaction volumes for conversion of the yellow to red forms according to Equation (1).

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[a] Institute for Inorganic Chemistry, University of Erlangen-Nürnberg,
Egerlandstraße 1, Erlangen 91058, Germany
[b] Department of Chemistry, Imperial College of Science, Technology and Medicine,
London SW1 2AY, UK
[c] Department of Chemistry, Faculty of Science, Ain Shams University,
Abbassia, Cairo, Egypt
[d] Department of Atmospheric Science, University of Arizona,
Tucson, AZ 85721-0081, USA

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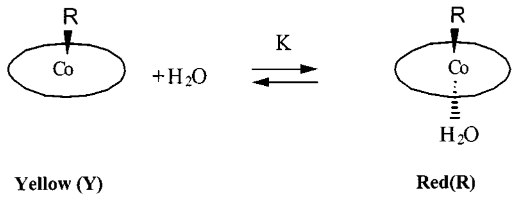

(1)

Calculations[8] suggest a volume of activation ($\Delta V^{\#}$) of $+13.1\ cm^3 \cdot mol^{-1}$ for a limiting D mechanism of ligand substitution involving the loss of coordinated H_2O in an octahedral complex and such a value may be taken as diagnostic of the loss of coordinated H_2O in the conversion of the red to yellow forms. In addition, possible adduct formation has been studied with the five-coordinate VCbi and vinyl-Cbs (VCbs), and the six-coordinate dicyano-Cbi (DCCbi) and dicyano-Cbs (DCCbs).

Results and Discussion

Increasing pressure *p* displaces the observed equilibrium from the yellow (Y) towards the red (R) form both for VCbi and MeCbl/H$^+$, as shown in Figures 1 and 2. Figure 1 shows distinct isosbestic points at 372, 447, and 536 nm, and a significant absorbance increase at the shoulder at 482 nm in the case of Vcbi. In addition, distinct isosbestic points at 385, 473, and 584 nm, and a significant increase in the absorbance at 490 nm were observed in the case of MeCbl/H$^+$ (Figure 2). The effect of pressure on the UV/Vis spectra suggests the formation of a six-coordinate species, since it is known that these (assumed) five-coordinate corrinoids exhibit maxima at 451 and 458 nm, respectively, and their six-coordinate corrinoid forms at ca. 495 and 503 nm, respectively.[6a] Values of the equilibrium constant ($K = [R]/[Y]$) as a function of *p* were calculated from the increase in absorbance at 490 nm using the optical density ratio of the two bands for the fully formed R and Y derived from the temperature-dependence studies as described in the literature.[6a] The slopes of the plots of ln *K* versus *p* (see Figures 3 and 4) gave values (in duplicate experiments) for the reaction volume $\Delta V = -12.4 \pm 1.0$ and $-12.5 \pm 1.2\ cm^3 \cdot mol^{-1}$ for the conversion of Y to R in VCbi and MeCbl/H$^+$, respectively. Their identical values underline the close parallel between Cbi's and protonated Cbl's, and their agreement with the theoretical value of $-13.1\ cm^3 \cdot mol^{-1}$ (see above) confirms that conversion of the Y to R form involves the coordination of one molecule of H_2O by the five-coordinate Y form. Formation of the R form is therefore favoured both by increasing pressure ($\Delta V \approx -12.5\ cm^3 \cdot mol^{-1}$) and by decreasing temperature ($\Delta S = -22 \pm 2$ e.u. reported for (diethyl phosphito)Cbl in aqueous acidic solution).[7]

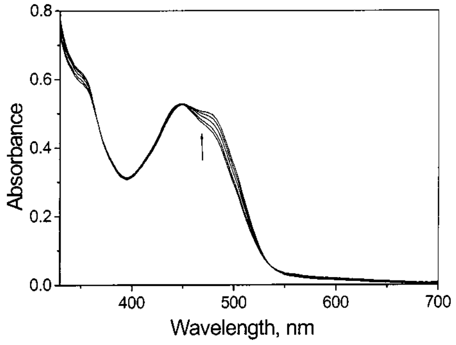

Figure 1. UV/Vis spectra of vinylcobinamide, recorded as a function of pressure (0.1, 30, 70, 110, and 150 MPa, accompanied by an increase in absorbance around 490 nm)

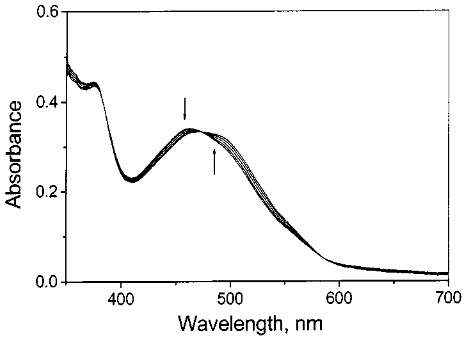

Figure 2. UV/Vis spectra of methylcobalamin (base-off form), recorded as a function of pressure (0.1, 30, 70, 110, and 150 MPa, accompanied by an increase in absorbance around 500 nm)

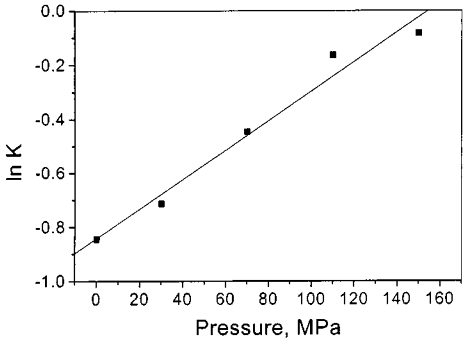

Figure 3. ln *K* versus pressure for the equilibrium between the five- and six-coordinate species of vinylcobinamide according to Equation (1); the best fit of the data (solid line) gives $\Delta V = -12.4 \pm 1.0\ cm^3 \cdot mol^{-1}$

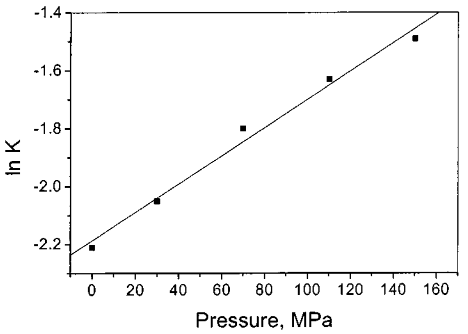

Figure 4. ln *K* versus pressure for the equilibrium between the five- and six-coordinate species of methylcobalamin (base-off) according to Equation (1); the best fit of the data (solid line) gives $\Delta V = -12.5 \pm 1.2\ cm^3 \cdot mol^{-1}$

Initial experiments on adduct formation by VCbi showed that the addition of the structure-breakers[9] KI and $NaClO_4$ (but not the structure-makers[9] NaCl and NaF), of sodium iodoacetate (but not sodium acetate), and of MeI all caused an immediate and significant change in the spectrum, indicating a shift from the R to the Y form, with distinct isosbestic points observed at least in the case of $NaClO_4$. A similar positive result was obtained for VCbs with KI and $NaClO_4$ (a negative result was obtained with NaCl). All these observations suggest that the solute (as adduct or ion-pair) binds in the hydrophobic cavity close enough to the Co metal centre to destabilise the coordinated H_2O and favour the five-coordinate form. By contrast, hydroxide (as well as imidazole, etc.) forms a red six-coordinate complex.[10] Binding constants of $K = 3.0 \pm 0.4\ \mathrm{M}^{-1}$ and $1.5 \pm 0.5\ \mathrm{M}^{-1}$ were obtained for VCbi with iodide (phosphate buffer pH = 7.25, up to 0.4 M KI) and perchlorate (unbuffered solution, up to 2 M $NaClO_4$), respectively.

Comparison of the spectrum of DCCbi (with a slight excess of cyanide to suppress ligand substitution) in 1 M solutions of a range of solutes showed no detectable difference (from that in water alone) with urea, NH_2OH, ethylene glycol (i.e. very hydrophilic compounds), NaOH, NaF, and sodium acetate (structure-making anions), KF or Me_4NF. Differences, however, were observed in the presence of imidazole, pyridine, 2,6-dimethylpyridine, NaBr and NaI (structure-breaking anions), sodium iodoacetate, and MeI. These changes were not reversed by adding more cyanide (i.e. do not involve displacement of coordinated cyanide) and, at least with iodide, did not vary with the Co concentration (i.e. not due to aggregation). All the observed changes were characterised by a similar broadening of both the α, β and γ bands (at 580, 540, and 367 nm, respectively) with a decrease in absorbance but no significant shift in λ_{max}, an increase in the 400−450 nm region and a cross-over (or even an isosbestic point) at ca. 460 and 600 nm; cf. the so-called Ham effect.[11] Similar experiments with DCCbs showed changes with both pyridine and KI in aqueous solution but no change with urea or ethylene glycol, while no changes were observed even with pyridine or KI in methanol or with pyridine in chloroform. The tests for solute, solvent and side-chains all suggest that the solute interacts with some hydrophobic part of the corrin structure, which is probably (as with VCbi) the cavity around one or both of the axial coordination sites, but interaction with its external walls cannot be excluded. Binding constants could not reliably be determined from the small changes in spectra. On re-examining the reported failure of cyano-Cbl (vitamin B_{12} itself) and dicyano-Cbl (nucleotide base displaced from coordination by cyanide) to fluoresce,[12] however, it was found that DCCbi in methanol fluoresces in the visible region with a maximum at 603 nm (when excited at 500 nm) but that this is quenched by adding imidazole or benziminazole (modelling the 3,5-dimethylbenzimidazole present in the Cbl's) and not restored by adding more cyanide (i.e. quenching does not involve displacement of coordinated cyanide). A binding constant K of ca. 14 M^{-1} for DCCbi with imidazole was calculated from the decreasing emission at 603 nm with increasing imidazole concentration in unbuffered methanol (containing ca 10^{-3} M KCN). This is comparable to the value of $K = 12$ to 16 M^{-1} for aquapentaammineruthenium(II) with the incoming methylpyrazinium ion.[2]

The close agreement between our experimentally determined volumes of reaction and the calculated value provides strong evidence that the equilibrium of interest involves the simple coordination of H_2O by the yellow five-coordinate corrinoid to produce the red six-coordinate form. Conversely, it provides the first experimental value for (and support for the calculated value of) the limiting volume of activation required in discussing D and I_d mechanisms of ligand substitution. Our results also demonstrate that both the five-coordinate VCbi and the six-coordinate DCCbi can form directly observable stable adducts and ion-pairs; the solutes are probably located within the hydrophobic cylinder surrounding the Co ion which, in effect, acts like a calixarene. The qualitatively similar behaviour of iodide, iodoacetate, and MeI demonstrates that the corrin ring can promote the formation of adducts as potential intermediates in reactions ranging from nucleophiles with Co^{III} to electrophiles (such as MeI) with Co^{II} and Co^{I}. The Co^{III}−corrinoids offer a unique opportunity to see how, as the donor power of one axial ligand is increased in the established order of the *trans* effect [e.g. $H_2O <$ DMB (nucleotide base) $< OH^- < CN^- <$ acetylide < vinyl < methyl < ethyl],[4a] the unstable five-coordinate intermediate for ligand substitution in the other axial position will become the stable yellow five-coordinate form, a transient OS intermediate will become a stable adduct, and the observed low volumes of activation ($\Delta V^{\#} = +4$ to $+8$ $cm^3\ mol^{-1}$),[3c−3d,13] typical of an I_d mechanism, will increase to the reaction volume ($\Delta V = +12.5\ cm^3{\cdot}mol^{-1}$), denoting a limiting D mechanism.

Experimental Section

The pH of the solutions was measured using a Mettler Delta 350 pH meter. It was calibrated with standard buffer solutions at pH = 4 and 7. UV/Vis spectra were recorded with Shimadzu UV-2101 or Cary 5 spectrophotometers. UV/Vis spectra under high pressure were recorded with the Shimadzu spectrophotometer utilizing a home-made high-pressure unit.[14] Emission spectra of degassed methanolic solutions were recorded with a Spex Fluorimax 2. All the instruments used in this work were thermostated to 25 °C. Values of ΔV were calculated from the slope ($= -\Delta V/RT$) of plots of ln K versus pressure. Methylcobalamin was purchased from Sigma. Dicyanocobinamide was prepared as described in the literature[15] by treating cyanocobalamin with trifluoromethanesulfonic acid and then adding cyanide. Dicyanocobester was prepared by heating cyanocobalamin under reflux in a solution of methanol containing 1 M H_2SO_4 under N_2 for 4 d, and then adding cyanide.[16] Vinylcobinamide was prepared by treating Co^I−cobinamide with acetylene and vinylcobester by an analogous reaction.[17] The purity of the prepared complexes was checked by UV/Vis spectroscopy and thin layer chromatography, and the results were found to be in excellent agreement with data reported in the literature. The preparation of solutions and measurements were carried out in diffuse light since all the alkylcobalamins are known to be very light-sensitive.

Acknowledgments

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