Model compounds for co-enzyme B_{12}: kinetic data for cobalt–alkyl bond dissociation reactions

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Abstract

The effects of pressure and temperature on the rates of the thermal homolytic fission of the cobalt–carbon bond in some organocobalt model compounds for co-enzyme B_{12} has been determined. The investigated model systems comprise six-coordinated benzyl complexes of dimethylglyoxime with nitrogen and phosphorus coordinated axial ligands and five- and six-coordinated butyl complexes of the Schiff base bis(salicylidene)ethylenediamine. The observed activation volumes, reported for the first time for this type of compound, are discussed in terms of the cage model and solvent dependence. The observed activation enthalpies, a measure for the cobalt–carbon bond dissociation energies, are discussed in terms of steric and electronic factors of the *trans*-ligand. Finally, an isokinetic relationship and the influence of the coordination number are mentioned.

Introduction

Vitamin B_{12}, which is isolated from the cell as cyanocobalamin, exists naturally as hydroxocobalamin, methylcobalamin and adenosylcobalamin, the latter two of which are functional co-enzymes [1, 2]. Adenosylcobalamin is involved in several enzyme-catalyzed rearrangement reactions. The first step in these reactions seems to involve facile homolytic fission of the cobalt–carbon bond to generate a 5′-deoxyadenosyl radical and a Co(II) corrinoid [1–3].

To identify the factors that might cause the weakening of the cobalt–carbon bond, various groups have examined the influence of electronic and steric parameters on the cobalt–carbon bond dissociation energy of co-enzyme B_{12} model compounds. These include alkyl derivatives of cobaloximes and cobalt complexes of Schiff bases [3–8]. Generally speaking, alkylcobaloximes can only be investigated as six-coordinated complexes with an axial ligand such as pyridine or a tertiary phosphine, whereas alkylcobalt complexes of Schiff bases can in principle be investigated with or without an axial ligand (six- or five-coordinated) [3–12]. The influence of the axial ligand on the cobalt–carbon bond dissociation energy has been discussed both in terms of electronic factors (nitrogen donors) and steric factors (phosphorus donors), a rather confusing situation [4]. Further, solvent effects will influence the results to some extent [13].

The most popular method to investigate the cobalt–carbon bond dissociation has been the kinetic method using radical trapping procedures. So far, only temperature dependent studies have been performed. However, it is well-known that pressure dependent studies increase the reliability of suggested reaction mechanisms and interpretations of reaction kinetics [14].

The present paper describes kinetic results for thermally induced cobalt–carbon bond cleavage in two groups of model compounds. The first group consists of six-coordinated benzyl complexes of H_2dmg (dimethylglyoxime or 2,3-butanedione dioxime) with nitrogen and phosphorus coordinated axial ligands. The second group consists of five- and six-coordinated butyl complexes of the Schiff base H_2salen (bis(salicylidene)ethylenediamine or 2,2′-[1,2-ethanediylbis(nitrilomethylidyne)]diphenol).
Both temperature and pressure dependence have been studied, so enthalpies, entropies and volumes of activation will be presented. Further, the temperature dependence of the volumes of activation and the influence of the solvent have been investigated.

This is the first report of activation volumes for cobalt–carbon bond cleavage in organometallic B_{12} models.

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Experimental

Material

Solvents were purchased as analytical grade, saturated with nitrogen gas before use and, if necessary, dried by routine methods. The radical trap 2,2,6,6-tetramethylpiperidine 1-oxide (tempo) was used without further purification. $[C_6H_5CH_2Co(Hdmg)_2\text{-}[S(CH_3)_2]]$ was prepared according to Schrauzer [15]. $[C_6H_5CH_2Co(Hdmg)_2L]$, L = PMe_3, PEt_3, PBu_3, PPh_3, PCy_3 (tricyclohexylphosphine), pyridine and 4-cyanopyridine, were prepared in solution from the dimethyl sulfide complex using an excess of ligand, as checked by UV–Vis and ^1H NMR spectra. H_2salen and $[C_4H_9Co(salen)]$ were prepared according to published methods [16, 17] and identified using UV–Vis and ^1H NMR spectra. $[C_4H_9Co(salen)L]$, L = PCy_3 and pyridine, were again prepared in solution.

Methods and measurements

Samples were handled if necessary under nitrogen in a Vacuum Atmosphere Corporation glovebox. The water and oxygen levels were maintained under 5 ppm using a specially designed high capacity gas purification system. Kinetic measurements under pressure (0.1 to 150 MPa) were performed in a high pressure cell [18], which was placed in a Zeiss M4 QII spectrophotometer supplied with an Oriel Xenon arc-lamp with a photofeedback control unit to get a sufficiently high and stable signal. A computer controlled shutter was placed in the lightbeam to exclude photolysis during slow reactions. The reaction temperature was measured with a thermocouple placed in direct contact with the solution and was kept constant within 0.2 °C using thermostatic baths. Conventional temperature dependent kinetic measurements were conducted on a Beckman Acta CIII, a Beckman UV 5230 and a Beckman DU 70 spectrophotometer, equipped with kinetic sets. ^1H NMR spectra were obtained on a Bruker WH-90 spectrometer and UV–Vis spectra were made with a Beckman Acta MIV spectrophotometer.

Kinetic studies were carried out photometrically at 370 (for the cobaloximes), 660 (for $[C_4H_9Co(salen)]$), 530 (for $[C_4H_9Co(salen)(pyridine)]$) and 360 (for $[C_4H_9Co(salen)(PCy_3)]$) nm. The complex concentration was varied between 10^{-5} and 10^{-4} M. Excess tempo (10^{-2} M) was used as radical scavenger. The concentration of the axial ligand was varied between 10^{-2} and 10^{-1} M. Reactions were followed for at least three half-lives and 2–3 independent runs were made. From the temperature dependence of the rate constants (6–9 measurements) the enthalpy and entropy of activation were obtained by a weighted least-squares Eyring analysis. From the pressure dependence of the rate constants (5–9 measurements) the volume of activation was calculated with a weighted linear least-squares regression routine on the basis of the formula: $\ln k_{obs} = \ln k_0 -)\Delta V^{\neq}_{obs}/RT)P$. Nearly all plots of $\ln k_{obs}$ versus pressure showed linear dependence within the measured pressure range. Only the reaction of $[C_6H_5CH_2Co(Hdmg)_2(pyridine)]$ gave a significant increase in the accuracy of the fit, when a second order term was added [14].

Results and discussion

It is well established that in the presence of a radical trap, the reaction scheme for the cobalt–carbon bond dissociation in organocobalt B_{12} models [RCo(chel)L] can be described by the following equations [5–8].

$$[RCo(chel)L] \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [Co(chel)L]^{\cdot} + R^{\cdot}$$

$$R^{\cdot} + trap \xrightarrow{k_2} R\text{-trap}$$

Overall: $[RCo(chel)L] + trap \longrightarrow [Co(chel)L]^{\cdot} + R\text{-trap}$

Usually, only the limiting rates with excess trap, in the region where $k_{obs} = k_1$ (independent of the trap concentration), are determined [5–8]. This method worked well in the present case, as checked by the dependence of the cobalt–carbon bond cleavage rate on the trap concentration. The trap tempo is capable of fast and irreversible scavenging of the benzyl and butyl radicals [5].

In the case of the system $[C_4H_9Co(salen)]$/pyridine complications occur because of the equilibrium between five- and six-coordinated species in solution, even in the presence of a large excess of pyridine.

$$[C_4H_9Co(salen)] + pyridine \overset{K}{\rightleftharpoons} [C_4H_9Co(salen)(pyridine)]$$

Under these conditions the observed rate-law becomes

$$k_{obs} = \frac{k_5 + k_6 K[\text{pyridine}]}{1 + K[\text{pyridine}]}$$

where k_5 and k_6 are the rate constants for the thermal cobalt–carbon bond cleavage reaction of the five- and six-coordinated complex, respectively. In this case it was therefore necessary to perform the measurements (at every temperature and pressure) in dependence of the pyridine concentration. This gives the additional advantage that k_5 can be determined

separately. We obtained excellent agreement between k_5 and its activation parameters in pure solvent and the solvent/pyridine mixtures. With tricyclohexylphosphine as ligand, the six-coordinated complex is readily formed when an excess of ligand is used; so the usual scheme can be used in this case. In Table 1 kinetic data for cobalt–alkyl bond dissociation reactions of the organocobalt B_{12} models [RCo(chel)L] are listed.

Activation volumes

The observed activation volume varies from 12.4–34.3 $cm^3\ mol^{-1}$. Because of the nature of the reactions, it was necessary to determine the activation volumes at different temperatures. It is known that the volume of activation is generally not very sensitive to variation in temperature [14]. This was checked for the systems $[C_6H_5CH_2Co(Hdmg)_2(PBu_3)]$, $[C_6H_5CH_2Co(Hdmg)_2(PPh_3)]$ and $[C_4H_9Co(salen)(PCy_3)]$. The results (Table 1) confirm this behaviour, so activation volumes determined at different temperatures can be compared. The large positive values found for the volumes of activation can be explained in two, fundamentally different, ways. This first way is simply that homolysis is characterized by strongly positive volumes of activation as reported by Swaddle and co-workers [19, 20] for some simple organometallic cobalt(III) and chromium(III) complexes in aqueous solution. The second explanation is more sophisticated and deals also with the observed solvent dependence of the activation volume:

It has recently been advocated that this type of organometallic homolytic fission reaction can best be interpreted by the cage model [21–23]

$$[M\text{-}R] \rightleftharpoons [M^{\cdot}\ {}^{\cdot}R] \rightleftharpoons M^{\cdot} + {}^{\cdot}R \xrightarrow{trap} \text{trapped products}$$

cage pair free radicals

Arguments have been presented that organometallic systems show high cage efficiencies [21–23], in agreement with the absence of a temperature dependence of the observed activation volume.

If we assume that besides the diffusion barrier no extra barrier to escape from the cage exists, the observed activation volume will contain a solvent contribution: the pseudo volume of activation, $\Delta V^{\neq}_{\eta}$ (also called the transport contribution) [24]. The 'real' homolytic volume of activation can then be approximated by $\Delta V^{\neq}_{h} = \Delta V^{\neq}_{obs} - \Delta V^{\neq}_{\eta}$. For the solvents used in this investigation, the following values have been reported [25] for $\Delta V^{\neq}_{\eta}$ (in $cm^3\ mol^{-1}$): toluene, 22.0; methanol, 8.3; acetone, 15.9; iodoethane, 11.0. Applying this correction to the values for $\Delta V^{\neq}_{obs}$ in Table 1 results in $\Delta V^{\neq}_{h}$ values that vary from -2.0 to 12.3 $cm^3\ mol^{-1}$. These values are (much) smaller than those reported by Swaddle and co-workers [19, 20] for aqueous solutions (15–35 $cm^3\ mol^{-1}$) for which $\Delta V^{\neq}_{\eta} = 0.16$ $cm^3\ mol^{-1}$. Small values for $\Delta V^{\neq}_{h}$ imply that the transition state for cage formation must be comparatively early. This behaviour mimicks C–C homolysis, for which the work of Neuman [26] indicates that the transition states for homolytic scission are in the order of 2 to 3% larger in volume than the ground state radical initiators. Nevertheless, desolvation of the caged pair on separation seems to play a role in some of the systems studied by us. It is obvious that more data are needed to decide which explanation is the more realistic one. Particularly data for water as solvent would be valuable but in this case solubility problems can be expected. We are now investigating this matter further.

Activation enthalpies

The activation enthalpies are a measure for the cobalt–carbon bond dissociation energies [3–8]. They have to be corrected by a factor depending on the viscosity of the solvent; in the case of toluene this correction amounts to 8.3 $kJ\ mol^{-1}$ [13]. It has been argued that both steric factors and electronic factors of the *trans*-ligand influence the value of the activation enthalpy for cobalt–carbon bond cleavage. In the case of phosphorus donors steric factors would dominate and in the case of nitrogen donors electronic factors [4]. For a number of PR_3 complexes, the activation enthalpy exhibited a marked (inverse) dependence on the size of the ligand, expressed in the cone angle, while no systematic dependence on pK_a was found [6]. However, the use of pK_a measurements in such an analysis suffers from the fact that it may be solvent dependent. It has been suggested that relative lone pair ionization potentials and proton-affinities in the gas phase offer a better way of comparison [27]. Nevertheless, our measurements give values in the same range as obtained earlier [6] although a combination of activation enthalpy and entropy (i.e. the rate constant) gives a better fit than the activation enthalpy alone. Now it seems somewhat artificial to specify an exclusive steric effect for phosphorus donors and an exclusive electronic effect for nitrogen donors. The size of the cone angle, for instance, will also influence the donor and acceptor properties of the PR_3 ligand.

It has been said that increasing the size of the *trans*-ligand induces cobalt–carbon bond lengthening and weakening due to conformational distortion of the equatorial ligand away from the *trans*-ligand and towards the alkyl group [4]. This mechanism has been postulated to account for the enzyme-accelerated cobalt–carbon homolysis in co-enzyme B_{12} itself: the rate enhancement is believed to result

TABLE 1. Kinetic data for cobalt–alkyl bond dissociation reactions of organocobalt compounds [RCo(chel)L]

R	Chelate[a]	L	Solvent	$\Delta V^{\ddagger}_{obs}$ ($cm^3\ mol^{-1}$) (Temperature (°C))	$\Delta H^{\ddagger}_{obs}$ ($kJ\ mol^{-1}$)	$\Delta S^{\ddagger}_{obs}$ ($J\ K^{-1}\ mol^{-1}$)	Temperature range (°C)	$10^4 \times k_{calc}$[b] (75 °C) (s^{-1})
$C_6H_5CH_2$	$(Hdmg)_2$	PMe_3	toluene	32.6 ± 0.6(108.3)	133.2 ± 2.8	51.6 ± 7.3	80–112	0.373
$C_6H_5CH_2$	$(Hdmg)_2$	PEt_3	toluene	23.1 ± 0.3(93.2)	108.9 ± 0.8	2.3 ± 2.2	72–101	4.39
$C_6H_5CH_2$	$(Hdmg)_2$	PBu_3	toluene	22.5 ± 0.2(56.0)	126.4 ± 6.5	48.7 ± 17.6	78–99	2.76
$C_6H_5CH_2$	$(Hdmg)_2$	PBu_3	toluene	21.8 ± 1.2(82.6)				
$C_6H_5CH_2$	$(Hdmg)_2$	PBu_3	methanol	12.4 ± 0.6(79.6)				
$C_6H_5CH_2$	$(Hdmg)_2$	PPh_3	toluene	21.4 ± 0.5(49.0)	95.5 ± 0.6	−23.0 ± 1.8	44–81	21.4
$C_6H_5CH_2$	$(Hdmg)_2$	PPh_3	toluene	20.2 ± 0.4(68.4)				
$C_6H_5CH_2$	$(Hdmg)_2$	PCy_3	toluene	24.7 ± 0.8(49.0)	113.4 ± 1.3	47.9 ± 3.8	32–59	223
$C_6H_5CH_2$	$(Hdmg)_2$	pyridine	toluene	32.2 ± 1.1[c](92.2)	108.7 ± 2.7	−2.6 ± 7.3	78–99	2.61
$C_6H_5CH_2$	$(Hdmg)_2$	4-CN-pyridine	toluene	29.6 ± 0.3(78.9)	142.0 ± 4.1	94.9 ± 11.5	61–85	3.26
C_4H_9	salen		acetone	23.1 ± 0.4(48.5)	116.2 ± 2.4	45.0 ± 7.5	32–54	59.9
C_4H_9	salen		iodoethane	17.0 ± 0.7(48.5)				
C_4H_9	salen		toluene	20.8 ± 1.3(48.5)	102.3 ± 1.3	2.9 ± 4.0	43–77	46.1
C_4H_9	salen		toluene	20.0 ± 3.3(69.4)	102.1 ± 2.2	2.3 ± 6.4	50–77	46.0
C_4H_9	salen	pyridine	toluene	34.3 ± 3.2(69.4)	144.9 ± 2.7	116.4 ± 6.4	50–77	15.9
C_4H_9	salen	PCy_3	toluene	25.5 ± 1.8(48.5)	120.0 ± 1.6	59.3 ± 5.0	33–63	90.0
C_4H_9	salen	PCy_3	toluene	25.1 ± 1.5(55.7)				

[a]H_2dmg = 2,3-butanedione dioxime; H_2salen = bis(salicylidene)ethylenediamine. [b]Calculated from the activation parameters. [c]Quadratic fit ($\Delta\beta^{\ddagger}_{obs} = 1.2 \pm 0.2 \times 10^{-2}\ cm^3\ mol^{-1}\ MPa^{-1}$).

from steric distortion of the protein-bound co-enzyme (e.g., an upward conformational distortion of the corrin ring, movement of the benzimidazole base toward the corrin ring) while electronic effects of the *trans*-ligand are considered less important [28]. However, this view is not supported by structural studies of cob(II)alamin, the structure of the cobalt(II) corrin being strikingly similar to that of the corrin moiety of co-enzyme B_{12} [28]. Further, NMR studies indicate that the solution structures of the base-on and base-off forms of co-enzyme B_{12} are remarkably similar and no evidence was found to indicate a change in corrin pucker on dissociation of the *trans*-ligand [29]. All this suggests that the effect of the *trans*-ligand on properties of B_{12} and its model compounds can best be expressed in terms of electronic factors; in this aspect the concept of 'negative catalysis' has recently been invoked [30].

Activation entropies

Halpern [7, 8] has discussed the linear correlation observed for $\Delta H^{\neq}$ and $\Delta S^{\neq}$ in the case of organocobalt B_{12} models. Usually, such isokinetic plots reflect nothing more than the interdependence between $\Delta H^{\neq}$ and $\Delta S^{\neq}$, but Halpern's considerations lead him to the conclusion that the trends of dependence are genuine and not of such artificial origin. One of the considerations is that the slopes of plots of $\Delta H^{\neq}$ versus $\Delta S^{\neq}$ are consistently significant higher than the mean temperature of the measurements. If we use all data from Table 1 that have been collected in the same solvent (toluene), we obtain an isokinetic plot with a slope of 352 K. Because this is rather close to the mean temperature of the measurements, it seems more likely to explain the linear correlation between $\Delta H^{\neq}$ and $\Delta S^{\neq}$ in the usual way [8].

Much emphasis has been placed on the possible correlation between $\Delta V^{\neq}$ and $\Delta S^{\neq}$ [14]. However, usually data do not correlate well [14] and the present case is no exception.

General

Organocobaloximes that have been suggested as B_{12} models are usually six-coordinated. The more electron-rich Schiff base models have been found as five- and six-coordinated species. In the solid state potentially five-coordinated species [RCo(salen)] are known to dimerize, but for dilute solutions in poorly coordinating solvents five-coordination presents no problem [4]. Homolysis of the cobalt–carbon bonds results in, formally, cobalt(II) complexes. For the cobaloximes, all transformations are thus from six-coordinated Co(III) to five-coordinated Co(II), whereas for the salen models both six-coordinated Co(III) to five-coordinated Co(II) and five-coordinated Co(III) to four-coordinated Co(II) do occur. Interest for the different behaviour of these species comes from the suggestion that in the co-enzyme B_{12} system, the bond from cobalt to the *trans*-ligand is broken during catalysis [29, 31]. For Table 1 it can be seen that for the salen complexes the activation enthalpy is higher for the six-coordinated species. However, the rate constant (i.e. a combination of $\Delta H^{\neq}$ and $\Delta S^{\neq}$) shows no definite direction. We did try to extend this series with other phosphine ligands, but unfortunately $P(OMe)_3$, PMe_3, PBu_3 and PPh_3 react directly with the salen ligand and/or the radical trap used.

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