Inorganica Chimica Acta, 50 (1981) 95–99

Activation Parameters for the Axial Water Substitution Reaction in some Vit. B_{12} Model Compounds

R. DREOS-GARLATTI, G. TAUZHER, G. COSTA

Istituto di Chimica, Università di Trieste, P. le Europa 1, 34127 Trieste, Italy

and M. GREEN

Department of Chemistry, University of York, Heslington, York YO1 5DD, U.K.

Received December 19, 1980

The activation parameters for the axial water substitution reactions of the organometallic complexes $RCo(DH)_2H_2O$ ($R = CH_3$) and $RCo\{(DO)(DOH)pn\}H_2O^+$ ($R = CH_3$, C_2H_5) are reported. Comparison with the activation parameters of the corresponding reactions of the aquocobalamin suggests that the lability of the biological complex is mainly due to entropy effects.

Furthermore the effects of the variation of the equatorial chelating ring and the effects of the variation of the R group for a given type of complexes on the activation parameters are considered. The corresponding changes in ΔH^* and ΔS^* values are discussed in terms of electronic and steric effects.

Introduction

The substitution reactions of the water ligand in Co(III) complexes containing a planar or nearly planar chelating ring, are currently of great interest, owing to the analogy between the chemical properties of these complexes and the Vit B_{12} coenzymes [1]. The most widely used approach to the study of the reaction mechanism is a comparative analysis of the rate changes resulting from the variation of the incoming ligand [2–7]. In spite of the relatively large amount of the rate constants data, there are few cases for which the activation parameters have been determined, although they could afford some information on the transition state.

The substitution reactions of aquocobalamin were investigated some time ago by Randall and Alberty [2, 3] and more recently reexamined by Thusius [4]. The reactions were found to be quite rapid and the rate constants nearly independent of the nature of the incoming ligand. This result is consistent with a transition state where both entering and leaving group are loosely bound to the cobalt atom. On the other hand the 'model' cobalamin complexes, nitro and iodo-aquo (bis-dimethylglyoximato) Co(III), are substitution inert and the rates are in some measure sensitive to the nature of the entering group [5].

The difference between the two classes of complexes arises from the large differences in the activation entropies, which are positive for cobalamin and somewhat negative for cobaloxime. Thusius suggests that the cobalamines and the cobaloximes may react by a different mechanism [4]. The large negative activation entropies and the rather small activation enthalpies for the latter complexes could be indicative of significant bond formation in the activated complex.

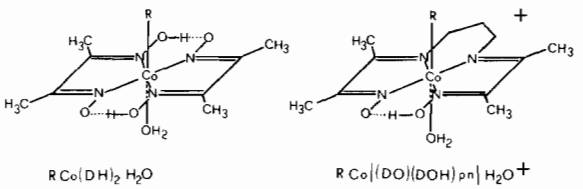

Fig. 1.

When an alkyl group is present in axial position in the cobaloximes [7], and in the related Co{(DO)(DOH)pn} complexes [6] (Fig. 1), the substitution of the water ligand in *trans* position is very rapid and involves a dissociative type of activation. In view of the similarity in the substitution lability between these complexes and the aquocobalamin, it would be interesting to extend the comparison to the activation parameters. Another aspect which we have examined is the effect of the variation of the axial group on the activation parameters. This could lead to a deeper understanding of the origin of the dramatic differences observed in the rate constants, when the ligand *trans* to the water molecule is varied.

Experimental

Materials

Samples of the complexes $[RCo\{(DO)(DOH)pn\}H_2O]^+ClO_4^-$, where R = CH_3 or C_2H_5, and CH_3-$Co(DH)_2H_2O$ were prepared according to previously reported methods [8, 9].

All other chemical were analytical grade and were used without further purification.

Ammonia solutions were standardized by potentiometric titration against 0.1 *M* HCl. Sodium thiocyanate solutions were standardized by titration with $AgNO_3$. The thiourea solutions were prepared from a known weight of reagent.

Apparatus and Experimental Procedure

For pH measurement a Radiometer pH-meter type pH M4 equipped with a glass/calomel couple of electrodes was used.

The kinetics were followed by a Durrum-Gibson Model D-130 stopped-flow spectrophotometer equipped with a Kel-F valve block. Since it has been noticed that kinetic data obtained by this type of instruments at other than ambient temperature may be affected by significant errors [10], we wish to report in details the experimental procedure followed by us in order to minimize these errors. This may be an argument of special interest when, as in the present case, the kinetic data are used for the calculation of activation parameters.

The trouble arises from a non uniform distribution of temperature across the sample. This leads to the same thermal artifact originally described by Gibson [11].

When cold water placed in both the drive syringes is injected into the warm cuvette, a rise in absorption is observed which comes down again, as the water temperature rises and approaches the temperature of the cuvette. An opposite sequence of absorbance changes is observed when warm water is injected into the cold cuvette. Such alterations can be avoided by maintaining the same temperature level in the drive syringes and in the cuvette.

In our procedure the temperature control was performed separately for the cuvette and for the syringes well by two distinct thermostating systems. This allows the independent regulation of the temperature. When the liquid in the thermostat bath containing the drive syringes reaches a given constant temperature, the temperature of the thermostat of the cuvette is adjusted until no sign of curvature is observed in the oscilloscopic trace, when water is injected into the cuvette. Efficient control of temperature is assured by the fact that a modest temperature gradient induces large change in absorbance. The experiment temperature is read on a thermometer immersed in the liquid of the thermostat bath. Further cautions have been also followed according to Chattopadhayay and Coetzee [10].

The redetermination of the ΔH^* value for the reaction of Ni(II) with 2,2'bipyridine gives a value of 12.4 kcal M^{-1}, which is in satisfactory agreement with that reported by the above authors (11.7 kcal M^{-1}). On the contrary, the activation parameters data for the reaction of CH_3–$Co(DH)_2H_2O$ with SCN^- (ΔH^* = 4.43 ± 0.23 kcal M^{-1}; ΔS^* 0.26 ± 0.76 u.e.) are considerably dissimilar from those reported by other authors (ΔH^* = 17.5 ± 0.4 kcal M^{-1}; ΔS^* 10 ± 1.5 u.e.) [12].

We are unable to give any explanation for the observed discrepancy.

Results

The substitution reactions of the coordinated water in some organometallic complexes of Co(III) (eqn. 1) were studied at various temperatures in the range 14–43 °C. The temperature was maintained constant within ±0.2 °C.

$$RCo(chel)H_2O + L \rightleftarrows RCo(chel)L + H_2O \quad (1)$$

with R = CH_3, C_2H_5

chel = $(DH)_2$, $\{(DO)(DOH)pn\}$

L = NH_3, SCN^-, thiourea

The kinetic measurements were performed in aqueous solution, at I = 1 *M* ($NaNO_3$) under pseudo first order conditions, maintained with a large excess of the incoming ligand. The initial concentration of the complexes was $2–4 \times 10^{-4}$ *M*; the ligand concentrations range from 4×10^{-3} to 0.2 *M*.

These complexes behave as weak acids; the pK_a for the deprotonation of the coordinated water is 12.31 for $CH_3Co\{(DO)(DOH)pn\}H_2O^+$, 12.55 for $C_2H_5Co\{(DO)(DOH)pn\}H_2O^+$ [13] and 12.68 for $CH_3Co(DH)_2H_2O$ [14]. Consequently when NH_3 was the incoming ligand it was necessary to buffer the reagent solutions. These solutions were prepared by addition of equivalent amounts of NH_3 and NH_4NO_3. Under these conditions and at the ligand concentration used, the correction to the ammonia concentration needed to account for the dissociation is negligible. The resulting pH of the solutions was about 9.3. At this pH value the complexes are almost completely in the form of aquocomplexes. The observed pseudo first order rate constants (k_{obs}) were obtained from the slopes of the linear plots of $\log(A_t - A_\infty)$ *vs.* t, where A_t is the optical absorbance at time t and A_∞ is the final absorbance.

The k_{obs} values show a linear dependence on the concentration of the entering ligand, L, according to the expression

$$k_{obs} = k_1[L] + k_{-1} \quad (2)$$

TABLE I. Rate Constants for the Water Ligand Substitution Reactions at I = 1 *M* ($NaNO_3$), at Various Temperatures.

$CH_3CO\{(DO)(DOH)pn\}H_2O^+ + L^{0,-} \rightleftharpoons CH_3Co\{(DO)(DOH)pn\}L^{+,0} + H_2O$

L = SCN^-			L = thiourea		
t °C	$k_1(M^{-1}\,sec^{-1})$	$k_{-1}(sec^{-1})$	t °C	$k_1(M^{-1}\,sec^{-1})$	$k_{-1}(sec^{-1})$
16.6	218.3 ± 3.9	1.7 ± 0.3	17.5	103.1 ± 1.0	2.1 ± 0.1
23.4	391.3 ± 13.9	4.1 ± 0.9	22.6	165.9 ± 2.1	3.9 ± 0.3
30.4	613.5 ± 24.8	10.5 ± 1.6	29.1	252.5 ± 3.2	9.2 ± 0.4
36.2	924.1 ± 42.9	21.9 ± 2.9	34.5	373.1 ± 3.8	16.0 ± 0.5
42.8	1475.1 ± 78.8	38.9 ± 5.4	41.4	591.9 ± 19.4	33.5 ± 2.5

$CH_3Co(DH)_2H_2O + L^{0,-} \rightleftharpoons CH_3Co(DH)_2L^{0,-} + H_2O$

L = SCN^-			L = thiourea		
t °C	$k_1(M^{-1}\,sec^{-1})$	$k_{-1}(sec^{-1})$	t °C	$k_1(M^{-1}\,sec^{-1})$	$k^{-1}(sec^{-1})$
16	81.7 ± 0.9	1.35 ± 0.06	17.2	65.0 ± 0.6	1.13 ± 0.06
21	133.7 ± 1.0	2.0 ± 0.06	22.8	118.3 ± 1.9	1.4 ± 0.3
26	198.1 ± 3.7	3.6 ± 0.2	29.1	188.4 ± 2.9	3.5 ± 0.4
31.6	314.0 ± 5.7	6.5 ± 0.3	35.4	297.0 ± 7.1	8.1 ± 0.8
36	449.9 ± 9.9	10.8 ± 0.6	41.6	505.5 ± 13.7	14.4 ± 1.7
42.6	762.8 ± 12.2	20.1 ± 0.7			

$RCo\{(DO)(DOH)pn\}H_2O^+ + NH_3 \longrightarrow RCo\{(DO)(DOH)pn\}NH_3^+ + H_2O$

R = CH_3		R = C_2H_5	
t °C	$k_1(M^{-1}\,sec^{-1})$	t °C	$k_1(M^{-1}\,sec^{-1})$
14.5	2.53 ± 0.08	16.1	46.8 ± 0.6
20	4.61 ± 0.05	23.8	93.4 ± 1.3
25	7.1 ± 0.2	29.6	156.2 ± 1.6
29.6	11.7 ± 0.2	35.4	254.3 ± 3.3
33.6	16.5 ± 0.2	41.6	451.7 ± 6.9
42.4	37.4 ± 0.4		

Values of k_1 and k_{-1}, calculated by a linear least squares analysis, are summarized in Table I as a function of the temperature.

No intercept has been observed for L = NH_3, owing to the high formation constants of the ammino complexes [13].

The activation parameters ΔH^* and ΔS^* were calculated by fitting the k_1–T data to the Eyring equation in the exponential form

$$k_1 = \frac{kT}{h} e^{-\Delta H^*/RT} e^{+\Delta S^*/R} \quad (3)$$

by a non linear least squares analysis, each value of k_1 being weighted as $1/\sigma^2_{k_1}$. Initial parameters estimates for this analysis were determined from the slope and the intercept of the linear form of the Eyring equation:

$$\ln k_1/T = \ln \frac{k}{h} - \frac{\Delta H^*}{RT} + \frac{\Delta S^*}{R} \quad (4)$$

The ΔH^* and ΔS^* values are collected in Table II. All errors reported in this work are simple standard deviations. The computer program used was SPSS (Statistical Package for Social Sciences) version 8.0, June 79, running on the CDC CYBER 170/720 of the University of Trieste.

Discussion

It has to be expected that for the reactions involving a dissociative activation process the ΔH^* values should be relatively independent on the nature of the incoming ligand, as it is at best loosely bound

TABLE II. Activation Parameters for the Water Ligand Substitution Reactions.

Reaction	k_1 (M^{-1} sec^{-1}) at 25 °C	ΔH^* (kcal M^{-1})	ΔS^* (e.u.)
$CH_3Co\{(DO)(DOH)pn\}H_2O^+ + SCN^-$	422.4[a]	12.60 ± 0.26	−4.26 ± 0.88
$CH_3Co\{(DO)(DOH)pn\}H_2O^+$ + thiourea	192.1[a]	12.39 ± 0.28	−6.53 ± 0.93
$CH_3Co\{(DO)(DOH)pn\}H_2O^+ + NH_3$	7.55[a]	16.60 ± 0.18	1.16 ± 0.58
$C_2H_5Co\{(DO)(DOH)pn\}H_2O^+ + NH_3$	105.2[a]	15.46 ± 0.23	2.57 ± 0.75
$CH_3Co(DH)_2H_2O + SCN^-$	187.1[a]	14.43 ± 0.23	0.26 ± 0.76
$CH_3Co(DH)_2H_2O$ + thiourea	132.4[a]	14.62 ± 0.50	0.21 ± 0.19
$NO_2Co(DH)_2H_2O + SCN^-$	5.8×10^{-4} [b]	19.10 ± 1.2	−9 ± 4
Aquocobalamin + SCN^-	2300[c]	17.10 ± 0.4	14 ± 1

[a] Interpolated from the rate constants determined at temperatures other than 25 °C. [b] From ref. 5. [c] From ref. 4.

in the transition state. The ΔS^* values should be slightly positive because the transition state would be more loose than the initial state owing to the relief of the steric strain [15]. From the data of Table II it appears that the activation enthalpies for all these complexes vary over a rather narrow range with charges of incoming ligand, according to the well established dissociative nature of the activation process. The activation entropies are positive for aquocobalamin, about zero for $CH_3Co(DH)_2H_2O$ and slightly negative for $CH_3Co\{(DO)(DOH)pn\}H_2O^+$. However they never reach the very negative values typical of the substitution reactions involving an associative mechanism [15]. This result suggests that the amount of the dissociative character of the reaction mechanism decreases in the sequence: aquocobalamin > $CH_3Co(DH)_2H_2O$ > $CH_3Co\{(DO)(DOH)pn\}H_2O^+$.

Aquocobalamin is about 10 times more labile than the organometallic model complexes, although they exhibit relatively low values of activation enthalpy (Table II). Probably these small ΔH^* values arise mainly from a weak cobalt–water bond in the ground state. A comparison of the cobalt–water bond lengths is not possible as structural data concerning the aquocobalamin are not available. However, it has been suggested that the acid strength of an aquocomplex could afford an indirect estimate of the metal–oxygen bond strength: the stronger the acid, the stronger the metal oxygen bond [15]. The high pK_a values of the organometallic model complexes (see Results) in comparison with the low pK_a value for aquocobalamin, 7.55 ± 0.2 [2], supports the hypothesis of a stronger cobalt–water bond in the ground state for the latter complexes. Hence the lability of the biological complex is mainly due to entropy effects. Thusius came to the same conclusion on the basis of the comparison of the activation parameters of the aquocobalamin with those of the inert iodo aquo and nitroaquo complexes [4].

It may be observed that the presence of an alkyl group in the trans position in the cobaloximes highly enhances the rate of the substitution of the water ligand [6, 7] which becomes very similar to that of the aquocobalamin. However the causes of the lability of the organometallic synthetic complexes and those of the aquocobalamin remain still different.

Comparison between $CH_3Co\{(DO)(DOH)pn\}H_2O^+$ and $CH_3Co(DH)_2H_2O$ is more difficult because differences are small. However it can be observed that the ΔH^* values for $CH_3Co(DH)_2H_2O$ are higher than that for $CH_3Co\{(DO)(DOH)pn\}H_2O^+$ when SCN^- and thiourea are the incoming ligands (Table II). The higher ΔH^* values may reflect both a stronger cobalt water bond in the ground state and a weaker cobalt water bond in the transition state. Probably in this case both effects are present.

A stronger cobalt water bond in the ground state is suggested by the X-ray structural data, the Co–O bond lengths being 2.05 Å for $CH_3Co(DH)_2H_2O$ [16] and 2.14 Å for $CH_3Co\{(DO)(DOH)pn\}H_2O^+$ [17]. An opposite trend would be observed if the bond lengths were dependent only on the relative degree of electrodonation from the equatorial chelate to the metal center. In fact these complexes differ in the replacement of the -OHO- group by the $-(CH_2)_3-$ group (Fig. 1). Since the -OHO- group carries a net negative charge it should be relatively more electron releasing than the $-(CH_2)_3-$ group and the electronic charge should increase from {(DO)(DOH)pn} to $(DH)_2$ complexes. Many properties vary according to this sequence [18–21]. Thus the trend observed for bond lengths must be caused by steric effects, which contribute to a lengthening of the Co–OH_2 bond in the $CH_3Co\{(DO)(DOH)pn\}H_2O^+$ relative to $CH_3Co(DH)_2H_2O$ and concomitantly to a decrease in the ΔH^* values for this complex.

The hypothesis of a weaker cobalt–water bond for $CH_3Co(DH)_2H_2O$ in the transition state is in accord with the initial suggestion, based on the consideration of the ΔS^* values, of a higher degree of dissociative

character in the reaction mechanism of this complex.

Finally we wish to consider the effect of the axial group trans to the water molecule on the activation parameters. The organocobaloximes are about 10^5 times more labile than the corresponding nitro and iodoaquocomplexes (Table II). This very high rate enhancement is due both to decrease in the activation enthalpy and to increase in the activation entropy. However the enthalpy effect, which essentially reflects the change in the strength of the cobalt–water bond is determinant. In this connection we recall that a change of ΔS^* of 4.6 u.e. causes a 10 fold change in the reaction rate if ΔH^* remains constant; if ΔS^* remains constant the rate changes by a factor of 10 for a change of ΔH^* of 1.36 kcal M^{-1} at 25 °C [22].

The data for the ammonia ligation to CH_3 and $C_2H_5Co\{(DO)(DOH)pn\}H_2O^+$ can be used to evaluate the effect of the variation of the R group. The increase in the rate constants on going from CH_3 to C_2H_5 derivative is consistent with a dissociative mechanism. Also in this case both enthalpic and entropic effects contribute to the rate enhancement, but the enthalpic effects are predominant.

Thus for a given chelating equatorial ligand the change of the axial ligand *trans* to the water molecule affects the strength of the cobalt water bond, and therefore the ΔH^* values, rather than the ΔS^* values. This result is in accord with the finding of Marzilli *et al.* [23] that when the bulkiness of the R group in the organocobaloxime increases the bonds between the cobalt atom and the axial ligands become longer and the equatorial ligand is relatively unaffected by the steric strain.

It may be concluded that the rate of the water substitution reaction by the dissociative mechanism appears to the efficiently tuned by electronic and by steric effects. The latter are active both directly on the activation entropy and indirectly on the activation enthalpies through the variation of the axial water–cobalt bond length.

References

1 G. N. Schrauzer, *Angew. Chem. Int. Ed. Engl., 15,* 417 (1976).
2 W. C. Randall and R. A. Alberty, *Biochemistry, 5,* 3189 (1966).
3 W. C. Randall and R. A. Alberty, *Biochemistry, 6,* 1520 (1967).
4 D. Thusius, *J. Am. Chem. Soc., 93,* 2629 (1971).
5 D. N. Hague and J. Halpern, *Inorg. Chem., 6,* 2059 (1967).
6 G. Tauzher, R. Dreos, G. Costa and M. Green, *Chem. Comm.,* 414 (1973).
7 A. L. Crumbliss and W. K. Wilmarth, *J. Am. Chem. Soc., 92,* 2593 (1970).
8 G. N. Schrauzer and R. J. Windgassen, *J. Am. Chem. Soc., 88,* 3738 (1966).
9 G. Costa, G. Mestroni and E. de Savorgnani, *Inorg. Chim. Acta, 3,* 323 (1969).
10 F. K. Chattopadhyay and J. F. Coetzee, *Anal. Chem., 44,* 2117 (1972).
11 Q. H. Gibson, 'Rapid Mixing and Sampling Techniques in Biochemistry', edited by B. Chance, R. H. Eisenhardt, Q. H. Gibson and K. K. Lonberg-Halm, Academic Press, New York, p. 116 (1964).
12 T. Sakurai, J. P. Fox and L. L. Ingraham, *Inorg. Chem., 10,* 1105 (1971).
13 G. Tauzher, R. Dreos, G. Costa and M. Green, *Inorg. Chem., 19,* 3790 (1980).
14 K. L. Brown and R. G. Kallen, *J. Am. Chem. Soc., 94,* 1814 (1972).
15 F. Basolo and R. Pearson, 'Mechanisms of Inorganic Reactions', J. Wiley and Sons Inc., N.Y. (1967).
16 D. L. McFadden and A. T. McPhail, *J. Chem. Soc. Dalton,* 363 (1974).
17 S. Brückner, M. Calligaris, G. Nardin and L. Randaccio, *Inorg. Chim. Acta, 3,* 278 (1969).
18 A. Bigotto, G. Costa, G. Mestroni, G. Pellizer, A. Puxeddu, E. Reisenhofer, L. Stefani and G. Tauzher, *Inorg. Chim. Acta Rev., 4,* 41 (1970).
19 J. H. Espenson, W. R. Bushey and M. E. Chmielewski, *Inorg. Chem., 14,* 1302 (1975).
20 G. Mestroni, C. Cocevar and G. Costa, *Gazz. Chim. It., 103,* 273 (1973).
21 R. J. Guschl and T. L. Brown, *Inorg. Chem., 13,* 959 (1974).
22 J. F. Bunnett in A. Weissberger Ed., 'Techniques of Chemistry', Vol. VI, Part I, p. 405, Interscience, N.Y. (1974).
23 L. G. Marzilli, P. J. Toscano, L. Randaccio, N. Bresciani Pahor and M. Calligaris, *J. Am. Chem. Soc., 101,* 6754 (1979).