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Evidence for Intermediates in the Substitution Reactions of a Vitamin B_{12} Model Compound

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Summary Kinetic studies on the substitution of alkylaquo-1,3-bis(biacetyl monoximeimino)propanatocobalt ions reveal evidence for intermediate complexes when the incoming ligand contains an aromatic group.

THE kinetics of substitution by various ligands of the aquo-group in complexes of the type, $[RCo\{(DOH)(DO)(pn)\}H_2O]^+$, (I),[1] hereafter MH_2O, where R is alkyl, have been studied. Reactions were investigated spectrophotometrically using the stopped-flow technique at 25·0 ± 0·2° in water maintained at 1M ionic strength using $NaNO_3$.

The results fall into two categories:

(i) When the incoming ligand, L, is SCN^-, N_3^-, NH_3, piperidine, or morpholine, a linear relationship is observed:

$$\text{Rate} = a[MH_2O][L]$$

up to the highest practicable concentrations of L (2·0M for NH_3, otherwise 0·2M). Data are given in Table 1. Such variations as there are in a appear to be governed largely by the charge on L (see Table 1). Thus, like the corresponding reactions[2] of aquomethylbis(dimethylglyoximato)cobalt, these processes are S_N1.

(ii) If L is imidazole, benzylamine, pyridine, or 4-methylpyridine, curves of the following form are obtained:

$$\text{Rate} = b[MH_2O][L]/(c + [L])$$

Moreover, the calculated limiting rates as $[L] \rightarrow \infty$, that is $b[MH_2O]$, are dependent on the ligand L (see Table 2). Thus, for these four ligands the process cannot be *lim* S_N1 as in (1) and (2), as then the limiting rate is completely independent of L, being equal to $k_2[MH_2O]$, $b \equiv k_1$ and $c \equiv k_{-1}/k_2$).

$$MH_2O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} M + H_2O \qquad (1)$$

$$M + L \xrightarrow{k_2} ML \qquad (2)$$

Therefore, a scheme is suggested as in (3) and (4), in which an intermediate, $MH_2O{\cdot}L$, is produced in pre-equilibrium.

$$MH_2O + L \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} MH_2O{\cdot}L \qquad (3)$$

$$MH_2O{\cdot}L \xrightarrow{k_4} ML + H_2O \qquad (4)$$

Then if $k_4 << k_{-3}$ and $K_3 = k_3/k_{-3}$, $b \equiv k_4$ and $c \equiv 1/K_3$, while the limiting rate as $[L] \rightarrow \infty$ is $k_4[MH_2O]$ and hence is dependent on the nature of L observed. When [L] is small, the rate becomes $K_3k_4[MH_2O][L]$ (in which range $b/c \equiv a \equiv K_3k_4$), conforming to the observed first-order kinetics in L. The scheme suggested for the ligands in category (ii) is thus completely compatible with our observations.

Table 1

Values of $a/\text{M}^{-1}\,\text{s}^{-1}$

L/R	Me	Et
SCN^-	397·0 ± 5·0	
N_3^-	339·0 ± 4·0	3360 ± 90
NH_3	7·05 ± 0·08	
Piperidine	1·09 ± 0·02	
Morpholine	0·47 ± 0·01	

Data obtained by least-squares regression of rate/[MH_2O] against [L]; errors are standard deviations; correlation coefficients ⩾ 0·996.

It could be argued that in the case of the five ligands in category (i), use of higher concentrations of L would reveal the presence of an intermediate. In principle this is true, since an interchange process, such as in (i), involves the exchange of ligands between spheres in an outer sphere complex.[3] However the stabilities, *vis-à-vis* reaction (3), of the intermediates produced by imidazole, benzylamine, pyridine, and 4-methylpyridine are much greater than those of any intermediates formed by the other five ligands. The upper limits which the data allow to be placed on K_3 type terms of 0·02 M^{-1} for NH_3 and 0·08 M^{-1} for SCN^-, N_3^-, piperidine, and morpholine in general are much lower than the values given in Table 2 for $1/c$, that is K_3.

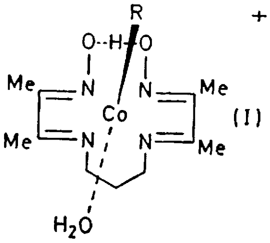
Table 2

Values of b and c

L	R	b/s^{-1}	$(1/c)/\text{M}^{-1}$	$(b/c)/\text{M}^{-1}\,\text{s}^{-1}$
Imidazole	Me	430 ± 90	0·26 ± 0·06	110·0 ± 1·0
	Et	2570 ± 180	0·63 ± 0·05	1613·0 ± 9·0
Benzylamine	Me	67·0 ± 27·0	0·12 ± 0·05	8·55 ± 0·05
Pyridine	Me	104·0 ± 5·0	1·00 ± 0·09	104·0 ± 4·0
	Et	1030 ± 50	1·53 ± 0·09	1580 ± 20
4-Methylpyridine	Me	83·0 ± 180·0	1·81 ± 0·16	150·0 ± 6·0

Data obtained by least-squares linear regression of [MH_2O]/rate against 1/[L]; errors are standard deviations; correlation coefficients: L = py, R = Me, 0·990; L = 4-Mepy, R = Me, 0·991; otherwise, > 0·999.

What then causes some of the ligands to form unusually stable intermediates with (I)? None of them carry a charge to form the ion pair normally observed in a pre-equilibrium process.[4] There is no correlation with their basicities; pK_a at 25°: NH_3, 9·2;[5] piperidine, 11·1; morpholine, 8·3; imidazole, 7·1; benzylamine, 9·3; pyridine, 5·2; 4-methylpyridine, 6·0.[6] Nor do they all possess aromatic amino-groups. However, they do all contain aromatic groups. We suggest that these are used in forming the intermediates, perhaps through a π–π interaction with the conjugated system of the {(DOH)(DO)(pn)} ligand.



(I)

In view of the evidence here, it now seems possible that (I) could form the same sort of intermediate in acetone containing 1% water.[7] For R = Me, K_3 would be approximately 5·6 M^{-1} for imidazole and benzimidazole. There is no evidence for intermediates in the substitution reactions in water of aquocobalamin[8] and the aquoalkylbis(dimethylglyoximato)cobalt[2] complexes. In contrast, the kinetics in aqueous solution of exchange of water for cyanide and thiocyanate (neither aromatic) in cobalt haematoporphyrin[9] are compatible with the formation of intermediates with K_3 between 6 and 100 M^{-1}.

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