Kinetics of Substitution of Co-ordinated Carbanions in Cobalt(III) Corrinoids

By H. A. O. HILL, J. M. PRATT,[†] S. RIDSDALE, F. R. WILLIAMS, and R. J. P. WILLIAMS*
(*Inorganic Chemistry Laboratory, South Parks Road, Oxford* OX1 3QR)

Summary Kinetic studies on the Ag^{I}- and Hg^{II}-assisted substitution of co-ordinated carbanions in Co^{III} corrinoids show that (i) Ag^{I} assists the removal of CN^- while Hg^{II} assists the removal of organo-ligands, (ii) steric hindrance stabilises Et, Pr^n, and Pr^i, relative to Me, (iii) steric compression and/or electronic changes destabilise Pr^i relative to Pr^n, and (iv) 5,6-dimethylbenzimidazole (bzm) shows a *trans*-labilising effect relative to H_2O.

COBALT(III) corrinoids, which contain the tetradentate corrin ring present in vitamin B_{12}, can be prepared with a wide range of carbanions as one of the axial ligands (X). In previous papers we have studied the effect of the co-ordinated carbanion on the properties of the other ligands in the complex (*cis*- and *trans*-effects).[1] We are now interested in establishing whether reactions which involve the carbanions themselves show any regular pattern. Since the Co–C bond is usually inert (in the dark) we have studied ligand substitution reactions assisted by Ag^{I} and Hg^{II}; and in order to examine the effect of the *trans*-ligand (Y) upon the substitutions we have used both cobalamins, where Y is 5,6-dimethylbenzimidazole (bzm) attached to the corrin ring by a nucleoside side-chain, and the cobinamides, where Y is H_2O or absent.[2]

The reactions and equilibria observed are shown in the Table; additional equilibria, involving the displacement of (bzm) from co-ordination to the cobalt by complexing with Ag^{I} or Hg^{II}, are omitted from the Table, but have been allowed for in calculating the rate constants. These appear to be the first kinetic data reported for ligand substitution reactions involving a variety of organo-ligands. All the reactions lead to the formation of the corresponding aquo-complex. The reaction of methylcobalamin with Hg^{II} was shown by mass spectrometry to give $MeHg^+$ and it is assumed that the other reactions also involve electrophilic attack of Hg^{II} on the carbanion. Ag^{I} and Hg^{II} provide an interesting contrast. Ag^{I} removes CN^- (presumably *via* the formation of Co–CN–Ag), removes organo-ligands slowly if at all, but exhibits equilibria which can be ascribed to the formation of, for example, CoC≡C–Ag and Co–CHAg-CH_2. The following points can be made about the reactions of Hg^{II}: (i) Hg^{II} is a better electrophile towards co-ordinated Me than I_2 (methylcobalamin reacts slowly with I_2 in aqueous methanol)[3] or H^+ (methylcobalamin is stable even in concentrated H_2SO_4).[4] (ii) Substitution of one H in Me to give Et, Pr^n, *etc.*, stabilises the ligand, presumably by sterically hindering the approach of Hg^{II} to the co-ordinated carbon atom. (iii) Substitution of a second H in Me, however, to give Pr^i labilises the ligand. The change from primary to secondary alkyl will alter the electron density and the electronic structure of the Co–C unit, but the most important factor is probably the weakening of the Co–C bond by steric compression within the secondary alkyl ligand and between it and the corrin ring. (iv) (Bzm) exerts a *trans*-labilising effect compared to H_2O in the three cases where data are available (X = vinyl, Me, and Et). A similar *trans*-labilising effect of (bzm) compared to H_2O has been observed in unpublished work on other reactions, *e.g.* the reactions of the methyl complex with BH_4^- to give methane (reduction) and of the s-butyl complex with BH_4^- to give butenes (elimination) are faster for the cobalamin than for the cobinamide; and isopropylcobinamide can be prepared by the reaction of the cobalt(I) complex with MeI in the presence of an excess of BH_4^- while the cobalamin cannot, presumably because the latter is decomposed too rapidly.

Reactions[a] *and equilibria between* Co^{III} *corrinoids and* Ag^{I} *or* Hg^{II}

X	$Y = H_2O$ (or absent) $+Hg(OAc)_2$	Y = (bzm) $+Hg(OAc)_2$	Y = (bzm) $+AgNO_3$
–CN	$<10^{-5}$	$<10^{-5}$	$8{\cdot}6 \times 10^{-2}$
–C≡CH	[b]		Eqm.[c]
$–CH{=}CH_2$	$1{\cdot}75 \times 10^{-1}$	$7{\cdot}05 \times 10^{-1}$	Eqm.[c]
Me	$1{\cdot}2 \times 10^{-1}$	$3{\cdot}7 \times 10^{2}$	[d]
Et	$<10^{-5}$	2×10^{-1}	[d]
Pr^n	$<10^{-5}$		
Pr^i	$3{\cdot}8 \times 10^{-3}$		
C_5-Deoxyadenosyl (B_{12} Coenzyme)	$<10^{-5}$	$<10^{-5}$	

[a] The values are second-order rate constants in units of $mole^{-1}sec^{-1}$ at 30°. X and Y are the two axial ligands.

[b] Reaction observed, but rate constant not determined.

[c] An instantaneously established equilibrium is observed, involving the carbanion.

[d] No reaction or equilibrium observed [except displacement of (bzm) from co-ordination to the cobalt].

The mechanism by which the Co–C bond in the enzyme-bound coenzymes (C_5-deoxyadenosylcorrinoids) is broken is not yet known. Our results show that the maximum rate of, for example, cleavage of the Co–Me bond is observed when the organo-ligand is simultaneously attacked directly by a strong reagent and activated by the ligand (or second reagent) in the *trans*-position. The enzyme-bound co-enzyme may be activated by a similar "push-and-pull" mechanism.[‡]

We thank Dr. L. Mervyn and Glaxo Laboratories for the gift of certain corrinoids and the Medical Research Council for financial assistance.

(*Received, January* 27*th*, 1970; *Com.* 124.)

[†] Present address: Imperial Chemical Industries Limited, Petrochemical and Polymer Laboratory, P.O. Box 11, The Heath, Runcorn, Cheshire.

[‡] *Note added in proof.* J. M. Wood, F. Scott Kennedy, and C. G. Rosen, *Nature*, 1968, **220**, 123, have observed methyl transfer to mercury from vitamin B_{12} in methane-producing bacteria.

[1] R. A. Firth, H. A. O. Hill, J. M. Pratt, R. G. Thorp, and R. J. P. Williams, *J. Chem. Soc.* (*A*), 1968, 2428 and 1969, 381.
[2] R. A. Firth, H. A. O. Hill, B. E. Mann, J. M. Pratt, R. G. Thorp, and R. J. P. Williams, *J. Chem. Soc.* (*A*), 1968, 2419.
[3] K. Bernhauer and E. Irion, *Biochem. Z.*, 1964, **339**, 521.
[4] J. M. Pratt, *J. Chem. Soc.*, 1964, 5154.