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ALKYL GROUP TRANSFER FROM COBALT TO MERCURY: THE REACTION OF ALKYLCOBALAMINS, ALKYLCOBALOXIMES AND OF RELATED COMPOUNDS WITH MERCURIC ACETATE

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Mercuric salts have been shown to inhibit the corrin dependent biosynthesis of methane by Methanobacillus omelianskii (1), presumably by reacting with the methylated corrin cofactor prior to its reductive demethylation. Nonenzymatically the reaction of alkylcobalamins with mercuric salts was reported to yield mercury dialkyls if conducted in the presence of metallic zinc as the reducing agent (1). However, Hill et al. (2), subsequently observed that the cleavage of the Co-C bond in alkylcobalamins by mercuric salts occurs by electrophilic attack and does not require reducing conditions. The reaction is believed to yield organomercurials as principal products since the ion CH_3-Hg^+ was detected by mass spectroscopy among the products of the reaction of methylcobalamin with mercuric acetate. Since Co-Hg transalkylation reactions of cobalamins and cobaloximes have not been studied in detail, we have investigated the reactions of cobaloximes (3) and of vitamin B_{12} derivatives with mercuric salts. The reaction of the cobaloxime(I) nucleophile with methylmercuric chloride has previously been shown to yield methylcobaloxime (4). The reverse transfer of organic groups from cobalt to mercury occurs in high yields by reacting acetate buffered aqueous solutions of mercuric acetate with alkyl, aralkyl and arylcobaloximes (eq. 1)(5):

$$\overset{R}{|}(Co) + Hg(OAc)_2 \xrightarrow[pH\ 2\text{-}5,\ 20^\circ,\ 70\text{-}90\%]{} (Co^{III}) + R\text{-}Hg\text{-}OAc + OAc^- \qquad (1)$$

(R + e.g. $-CH_3$, $-C_2H_5$, $-CH_2C_6H_5$, $-C_6H_5$).

Following the intensity decrease of the characteristic Co-C bond charge transfer transition (6) of alkylcobaloximes spectrophotometrically it was established that the reaction is first order in mercuric acetate and alkylcobaloxime, the dealkylation presumably occurs by a

SE_2 mechanism, with $HgOAc^+$ or an equivalent species as the attacking electrophile (7). The rates of dealkylation are pH dependent and vary with the degree of dissociation of the mercuric salt employed. Mercuric phosphate, for example, dealkylates methylcobaloxime at considerably higher rates than mercuric acetate.

Observed second-order rate constants for a number of reactions are summarized in Table I.

TABLE I

Second-order Rate Constants ($mole^{-1}sec^{-1}$ at 26°) of the Reactions of Organocobalt Complexes with Mercuric Acetate. Measurements Performed in Aqueous 0.1 M NaOAc/HOAc Buffer, Initial Concentration of $Hg(OAc)_2$ Usually 1.0 M.

R	Axial Base[(a)]:	In-Plane Ligand[(b)]	k_2[(c)]
$-CH_3$	pyridine	Dmg	$(6.6 \pm 0.1)\cdot 10^{-2}$
$-C_2H_5$	pyridine	Dmg	$(7.7 \pm 0.3)\cdot 10^{-4}$
$n\text{-}C_3H_7$	pyridine	Dmg	$(7.0 \pm 0.2)\cdot 10^{-4}$
$-CH_2\text{-}CH(CH_3)_2$	pyridine	Dmg	$(2.02 \pm 0.02)\cdot 10^{-4}$
$-CH_2\text{-}C(CH_3)_3$	pyridine	Dmg	$(9.2 \pm 0.3)\cdot 10^{-5}$
$-CH_2CH_2CH(CH_3)_2$	pyridine	Dmg	$(5.9 \pm 0.7)\cdot 10^{-4}$
Secondary alkyls	pyridine	Dmg	$<10^{-6}$
$-CH_3$	5,6-Dmbz	corrin	(300±27)
$-C_2H_5$	5,6-Dmbz	corrin	$(1.3 \pm 0.1)\cdot 10^{-4}$
$n\text{-}C_3H_7$	5,6-Dmbz	corrin	$(2.9 \pm 0.3)\cdot 10^{-5}$
$i\text{-}C_3H_7$	5,6-Dmbz	corrin	$(3.5 \pm 0.2)\cdot 10^{-5}$
$-CH_3$	H_2O	corrin	$(6.4 \pm 0.1)\cdot 10^{-2}$
$-C_2H_5$	H_2O	corrin	$(5.7 \pm 0.2)\cdot 10^{-5}$
$n\text{-}C_3H_7$	H_2O	corrin	$(1.7 \pm 0.3)\cdot 10^{-5}$
$i\text{-}C_3H_7$	H_2O	corrin	$(1.1 \pm 0.4)\cdot 10^{-5}$

(a) The axial base is in most cases displaced by water during the experiments. Dmbz = Dimethylbenzimidazole.
(b) Dmg = Dimethyglyoxime.
(c) Error limits denote maximal deviation from average value of k_2. $k_2 = \frac{k_1}{[Hg(OAc)_2]}$

The rate of dealkylation depends significantly on steric factors, i.e. the accessibility of the carbon atom attached to cobalt and to some extent on the in-plane ligand. Secondary alkylcobaloximes are essentially unreactive at room temperature for steric reasons, while β-substituted alkylcobaloxime derivatives still react more slowly than γ-substituted alkyl derivatives. The influence of the axial base component is indicated by the fact that methylcobalamin is dealkylated 10^4 times faster than methylcobinamide and methylcobaloxime. The rates of reaction of higher alkylcobalamins do not differ significantly from those of the corresponding cobinamide and cobaloxime derivatives (Table I). The absence of the kinetic trans-effect in these reactions is due to the fact that the first step of the reaction of the higher alkylcobalamins consists in the rapid formation of a complex between mercuric acetate and the 5,6-dimethylbenzimidazole attached to the corrin ring (8). The actual dealkylation step takes place at a slow rate with k_2 values as shown in Table I. Contrary to some of the data reported in Ref. 2, no evidence for a special labilization of the Co-C bond in isopropyl cobalamin and isopropylcobinamide was found. However, the trans-effect in methylcobalamin is real and possible because of the tighter binding of the 5,6-dimethylbenzimidazole to cobalt. This increases the electron density on the metal and renders the methyl group more susceptible to electrophilic attack.

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(5) The organomercury acetates formed according to eq 1 were isolated on a preparative scale and identified by comparison with authentic samples, as well as by conversion into the organomercuric chlorides on reaction with aqueous HCl.

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(7) The reaction should take place with inversion of configuration at the α-carbon atom. The low reactivity of secondary alkylcobaloximes in the reaction with mercuric acetate has thus far precluded demonstration of this inversion of configuration.

(8) This complex formation is accompanied by the characteristic red-yellow shift associated with the removal of the benzimidazole from the corrin cobalt atom. **The alkylcobalamin** be regenerated by the addition of excess pyridine.