Contribution from the Department of Chemistry,
University of Cincinnati, Cincinnati, Ohio 45221

Transmethylation of Methylmetal Compounds by Methylcobalamin

John S. Thayer

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The reaction between methylcobalamin and metal compounds plays a major role in biological transmethylation and in the natural cycling of metals through the environment.[1] Kinetic studies have appeared for inorganic mercuric,[2,3] lead,[4] platinum,[4] and palladium[5] compounds. Little work, however, has been reported on the corresponding reaction of organometals. Bertilsson and Neujahr[6] reported that organomercurials reacted with methylcobalamin but gave no specific rate data. Wood and co-workers indicated a second-order rate constant of 6.2×10^{-2} s^{-1} M^{-1} for the reaction between methylmercuric acetate and methylcobalamin.[2,7] Chu and Gruenwedel reported a value of 0.254 s^{-1} M^{-1} for the corresponding reaction of CH_3HgOH.[8] This paper describes some kinetic studies on the reaction of methylcobalamin with various methyl derivatives of heavier metals.

Experimental Section

Materials. Methylmetal compounds were purchased from various commercial sources and recrystallized before reaction. Tetramethylarsonium and -stibonium iodides were prepared from $(CH_3)_3As$ or $(CH_3)_3Sb$ and methyl iodide. Methylcobalamin was purchased from Sigma Chemical Co.

Reactions were run in sealed flasks, using a buffered acetic acid medium (HOAc 0.10 M; NaOAc 0.10 M; pH 4.55). Due to the photosensitivity of methylcobalamin, the reaction vessels were wrapped in aluminum foil and kept in darkened cupboards at room temperature. A typical run would use 25 mL total solution with the methylmetal concentration between 10^{-2} and 10^{-3} M and the methylcobalamin concentration at 10^{-4} M or less. Most reactions were done with the methylmetal in at least 20-fold excess.

Spectroscopic Determinations. All samples were run on a Cary 14 recording visible/ultraviolet spectrophotometer. Since the extinction coefficients for methylcobalamin and aquocobalamin at 520 and 350 nm have been reported (7.68×10^3 and 1.07×10^4 cm^{-1} M^{-1} for the methyl species; 7.61×10^3 and 2.19×10^4 cm^{-1} M^{-1} for the aquo species),[6] the extent of reaction could be determined from the ratios of absorbances at these wavelengths. The ratio varied from 1.39 in pure methylcobalamin to 2.88 in pure aquocobalamin and was calibrated against mixtures of known concentrations. Since some methylmetals reacted extremely slowly, solutions of methylcobalamin were run as controls. These controls showed no change in the peak ratios over a period of 2 weeks.

Results and Discussion

Under pseudo-first-order conditions, the rate equation takes the form

$$\text{rate} = K[CH_3HgOAc]^n[CH_3B_{12}] = k_{obsd}[CH_3B_{12}] \qquad (1a)$$

where

$$k_{obsd} = K[CH_3HgOAc]^n \qquad (1b)$$

Equation 1b in logarithmic form becomes

$$\log k_{obsd} = \log K + n \log [CH_3B_{12}] \qquad (1c)$$

A log–log plot of k_{obsd} vs. $[CH_3B_{12}]$ should give a straight line whose slope will be n and whose intercept will be log K. Figure 1 shows such a plot for methylmercuric acetate. The slope of the line is 0.978, indicating that the reaction is first order with respect to $[CH_3HgOAc]$. A similar first-order dependence has been reported for mercuric ion[2,9] and for tetrachloropalladate(II) ion.[5] Since reactions were performed under pseudo-first-order conditions, a plot of k_{obsd} vs. $[CH_3HgOAc]$ should give a straight line, from whose slope K can be determined. Figure 2 shows such a plot. The slope gives a value of $K = 6.88 \times 10^{-2}$ s^{-1} M^{-1}, in reasonable agreement with the literature values and with the value obtained from the log–log plot. In the same way, the reaction orders and rate constants were determined for various other methylmetal compounds. These are listed in Table I.

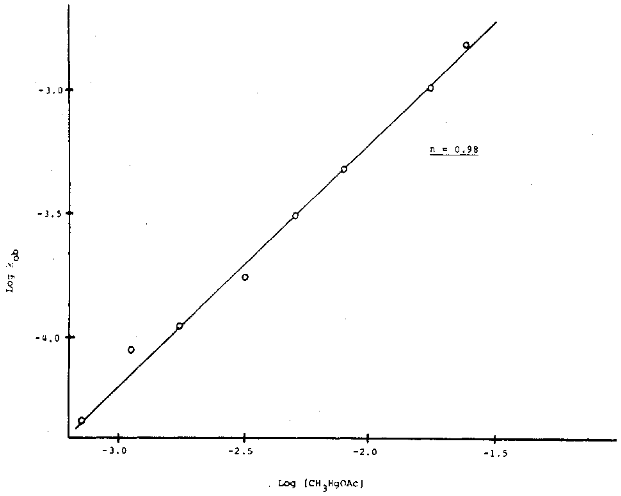

Figure 1. Plot of log k_{obsd} vs. log $[CH_3HgOAc]$. The slope ($n = 0.98$) indicates first-order dependence on $[CH_3HgOAc]$.

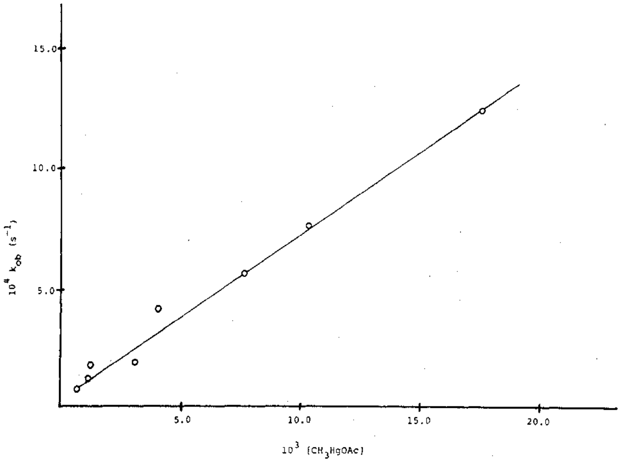

Figure 2. Plot of k_{obsd} vs. $[CH_3HgOAc]$. The slope yields $K = 0.0688$ s^{-1} M^{-1}.

Table I. Rate Constants and Reaction Order for Methylcobalamin–Methylmetal Reaction

compd	runs	order[a]	K,[b] s^{-1} M^{-1}
CH_3HgOAc	8	0.978	6.21×10^{-2}, 6.88×10^{-2}
$(CH_3)_2TlOAc$	5	0.887	2.99×10^{-4}, 3.94×10^{-4}
$(CH_3)_3PbOAc$	6	0.922	2.70×10^{-4}, 3.46×10^{-4}
$(CH_3)_3SnOAc$	6	0.87	3.0×10^{-5}, 4.5×10^{-5}
$(CH_3)_3TeI$	5	0.947	1.34×10^{-4}, 1.62×10^{-4}
$(CH_3)_4PI$	4	1.01	6.38×10^{-4}, 5.85×10^{-4}
$(CH_3)_4AsI$	5	0.997	1.66×10^{-3}, 1.53×10^{-3}
$(CH_3)_4SbI$	4	1.04	1.63×10^{-4}, 1.38×10^{-4}
$CH_3AsO_3Na_2$	2	no reacn obsd	
$(CH_3)_2AsO_2Na$	2	no reacn obsd	

[a] Slope of line in log–log plot. [b] First column is value obtained from log–log plot; second column is value obtained from k_{obsd}–[methylmetal] plot.

DeSimone et al.[2] reported that mercuric ion and methylcobalamin react to form a "base-off" complex; a similar complex was reported for tetrachloropalladate ion by Scovell.[5] We found no evidence for any such complex formation in our systems. Chu and Gruenwedel[9] reported that no "base-off" complex was formed when $[CH_3Hg^+] = 4.8 \times 10^{-5}$ M and

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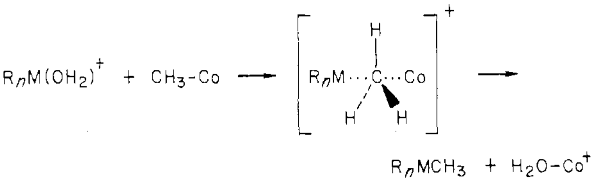
$[CH_3B_{12}] = 7.6 \times 10^{-5}$ M. The highest $[CH_3HgOAc]$ we used was 0.0178 M which, using the dissociation constant of 2.8 $\times 10^{-4}$ reported by Maguire et al.,[10] should give $[CH_3Hg^+] = 5.0 \times 10^5$ M. Under these conditions, no "base-off" complex would be expected.

Methylmercuric and methylplatinum compounds were reported in the reaction with mercuric salts[2] and hexachloroplatinate(IV) ion.[4] An unstable $CH_3PdCl_3^{2-}$ intermediate was postulated in the tetrachloropalladate reaction,[5] decomposing to give the detected products CH_3Cl and palladium metal. Wood et al. reported that treatment of CH_3HgOAc with $^{14}CH_3B_{12}$, followed by extraction with toluene, caused much of the label to pass into the toluene layer, presumably through formation of $^{14}CH_3HgCH_3$.[7] When we reacted CH_3HgOAc and CH_3B_{12} in a sealed vessel and subsequently evacuated the gaseous layer into a NaCl gas cell, we found infrared peaks at 2900, 1440, 1195, 781, and 700 cm^{-1}, very close to values assigned for the vibrational spectrum of dimethylmercury.[11] The Hg–C stretching vibration at 540 cm^{-1} could not be detected with any certainty, due to cell end absorption. Reaction between $(CH_3)_4AsI$ and CH_3B_{12} gave the characteristic, unpleasant odor of $(CH_3)_3As$. The corresponding reaction of $(CH_3)_3TeI$ gave $(CH_3)_2Te$, also detectable by its odor, and some elemental Te, presumably by decomposition of the initially formed $(CH_3)_4Te$.[12] Neither $(CH_3)_4AsI$ nor $(CH_3)_3TeI$ gave an odor in the absence of methylcobalamin.

DeSimone et al.[2] have proposed that transmethylation of mercuric salts occurs through electrophilic attack on the carbanionic methyl group, followed by cleavage of the Co–C bond. Our observations are consistent with this mechanism, which is represented in eq 2. Since the methyl group bonds to the metal as an electron-donating carbanion, methylmetal compounds should be less electrophilic than inorganic analogues and thereby react more slowly with methylcobalamin. This indeed is observed for Hg(II),[2] Tl(III),[13] and Pb(IV).[13]



(2)

Methylmercuric ion[2] and trimethyllead ion[14,15] are known to undergo methylation through biological processes. The volatile products play an important role in the movement of these metals through the environment. Our work indicates that this might also happen for other methylmetal compounds, including the previously unsuspected "onium" salts of group 5 and 6 elements. Preliminary observations further suggest that similar reactions occur with other organometals, particularly ones of mercury, lead, and tin that have numerous biocidal applications, with the implication that unexpected and undesired reactions of these compounds may occur under environmental conditions. We are currently investigating these possibilities.

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Registry No. Methylcobalamin, 13422-55-4; CH_3HgOAc, 108-07-6; $(CH_3)_2TlOAc$, 18000-46-9; $(CH_3)_3PbOAc$, 5711-19-3; $(CH_3)_3SnOAc$, 1118-14-5; $(CH_3)_3TeI$, 18987-26-3; $(CH_3)_4PI$, 993-11-3; $(CH_3)_4AsI$, 5814-20-0; $(CH_3)_4SbI$, 2185-78-6.

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Contribution from the Department of Chemistry,
Purdue University, West Lafayette, Indiana 47907,
and the School of Chemistry, University of Bath,
Bath BA2 7AY, United Kingdom

Conversion of the Molybdenum(III) Halides to Metal–Metal Bonded Dimers of the Type $Mo_2X_4L_4$ by Dimethylamine and Tertiary Phosphines[1]

J. E. Armstrong,[2a] D. A. Edwards,*[2b] J. J. Maguire,[2b]
and R. A. Walton*[2a]

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Access to the chemistry of those molybdenum(II) halides and their derivatives, which contain the metal–metal bonded Mo_2^{4+} core, invariably utilizes molybdenum(II) acetate, $Mo_2(O_2CCH_3)_4$, as the initial synthetic starting material.[3–15] An important class of such complexes are those of the type $Mo_2X_4L_4$ (X = Cl, Br, I; L = neutral donor) which are prepared via the molybdenum(II) complexes $K_4Mo_2Cl_8$,[3] $(NH_4)_5Mo_2Cl_9{\cdot}H_2O$,[6,7,12] β-MoX_2 (X = Cl, Br, I),[3,4] and $(picH)_2[Mo_2X_6(H_2O)_2]$ (pic = 4-methylpyridine; X = Br, I),[14,15] or the molybdenum(III) derivatives $Cs_3Mo_2X_8H$ (X = Cl, Br).[7] The use of $Cs_3Mo_2X_8H$ in the synthesis of the pyridine complexes $Mo_2X_4(py)_4$ is of particular interest,[7] since upon reaction of pyridine with the corresponding enneahalodimolybdenum(III) derivatives $Cs_3Mo_2X_9$ or by use of much more forcing conditions in its reaction with $Cs_3Mo_2X_8H$, only the monomeric molybdenum(III) species *mer*-$MoX_3(py)_3$ can be isolated.[8] While the transformation of $Mo_2X_8H^{3-}$ to *mer*-$MoX_3(py)_3$ is believed to proceed, *at least in part*, through the intermediacy of the molybdenum(II) derivatives $Mo_2X_4(py)_4$, there is no evidence to support such a mechanism in the case of the conversion of $Mo_2X_9^{3-}$ to *mer*-$MoX_3(py)_3$. Likewise, the reactions of $Cr_2Cl_9^{3-}$ and $W_2Cl_9^{3-}$ to produce *mer*-$CrCl_3(py)_3$[16,17] and $W_2Cl_6(py)_4$,[18] respectively, do not appear to involve the formation of chromium(II) or tungsten(II) intermediates. The surprising differences which exist between the reactions of $Mo_2X_8H^{3-}$ and $Mo_2X_9^{3-}$ have led us to investigate certain aspects of the reactivity of the parent trihalides MoX_3 (X = Cl, Br). We now report details of the

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