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Demethylation of Methylcobalamin by Platinum(IV)/Platinum(II) Couples. Methyl Transfer within a Trinuclear Intermediate

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The kinetics of the demethylation of methylcobalamin (CH_3-B_{12}) by mixtures of Pt(IV) ($PtCl_6^{2-}$, $Pt(CN)_4Cl_2^{2-}$, $Pt(CN)_5Cl^{2-}$, $Pt(CN)_5I^{2-}$, $Pt(CN)_6^{2-}$) and Pt(II) ($PtCl_4^{2-}$, $Pt(CN)_4^{2-}$) in aqueous solution are consistent with reversible complexation of CH_3-B_{12} with Pt(II) to form a binuclear intermediate, followed by reversible reaction of this complex with Pt(IV) to form a trinuclear intermediate prior to the rate-limiting step. Spectroscopic evidence (UV-visible region) is presented for both $CH_3\text{-}B_{12}\cdots Pt^{II}$ and the trinuclear intermediate, and the equilibrium constants obtained thereby agree well with those determined from the kinetics. Evidence is presented in support of a Pt(II) bond in the binuclear intermediate at a site close to the Co-C bond. Reaction of this intermediate with Pt(IV) leads to a halide-bridged $(CH_3\text{-}B_{12})\cdots Pt\cdots X\cdots Pt$ species. The rate constant for the rate-limiting step is found to be nearly identical for the "base-on", "base-off", and "base-absent" forms of CH_3-B_{12} (base = 5,6-dimethylbenzimidazole ribofuranoside phosphate group). This lack of dependence on the axial ligand is taken as evidence against direct attack by the bound platinum group on the Co-C bond and instead favors electron transfer from an orbital on the corrin ring to the bound platinum group in the rate-limiting step, followed by rapid methyl transfer.

Introduction

In the preceding paper,[2] we established the stoichiometry for the demethylation of methylcobalamin (CH_3-B_{12}) by platinum(IV)/platinum(II) combinations (eq 1). Our

$$CH_3\text{-}B_{12} + PtL_4^{2-} + PtL'_4XY^{2-} \xrightarrow{H_2O} H_2O\text{-}B_{12}^+ + CH_3PtL_4X^{2-} + PtL'_4{}^{2-} + Y^- \quad (1)$$

earlier kinetic study with $PtCl_6^{2-}/PtCl_4^{2-}$ [3] suggested a reaction in which the initial step in methyl transfer is a reversible complexation of the reactant (Pt(II)) with the organometal (CH_3-B_{12}) rather than direct attack on the carbon-metal bond.

We describe here a more detailed kinetic study to include combinations of $PtCl_6^{2-}$, $Pt(CN)_4Cl_2^{2-}$, $Pt(CN)_5Cl^{2-}$, $Pt(CN)_5I^{2-}$, and $Pt(CN)_6^{2-}$ as Pt(IV) complexes, with $PtCl_4^{2-}$ and $Pt(CN)_4^{2-}$ as Pt(II) complexes. This expanded study has given us more insight into the reaction mechanism. The kinetic analysis has provided us with evidence for two intermediates along the reaction path, and spectral evidence for these two intermediates has been obtained as well. The reactivity pattern for the above series allows some conclusions to be drawn about the structures of these intermediates. And finally, this expanded study has given clues to the nature of methyl-transfer step itself.

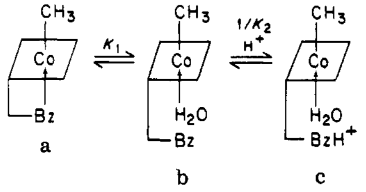
Experimental Section

Materials. The source and purification of $Na_2PtCl_6{\cdot}6H_2O$, K_2PtCl_4, $Na_2Pt(CN)_4$, $Na_2Pt(CN)_4Cl_2$, $Na_2Pt(CN)_5Cl$, and CH_3-B_{12} have been described.[2] Chlorine gas was bubbled through the Na_2PtCl_6 solution during recrystallization to eliminate any Pt(II) impurities. The compounds $Na_2Pt(CN)_5I$[4] and $Na_2Pt(CN)_6$[5] were synthesized and purified according to literature methods. Methylcobinamide (CH_3-B_{12} devoid of the ribonucleotide side chain) was a gift from H. Hogenkamp.[6] Concentrations of CH_3-B_{12} and H_2O-B_{12}^+ in solution were determined from their absorption spectra by using published molar absorptivities.[7]

Rate and Equilibrium Measurements. Reaction rates and equilibrium constants for the $CH_3\text{-}B_{12}\cdots$platinum intermediates were determined spectrophotometrically (GCA/McPherson spectrophotometer). Rates were measured by the absorbance increase at 351 nm (γ band of H_2O-B_{12}^+). All reactions were performed at 23 ± 0.3 °C under dim light. Ionic strength was maintained at 1.0 M with NaCl. To avoid hydrolysis,[8] stock solutions of $PtCl_4^{2-}$ (in 1.0 M NaCl) were never stored for more than 1 h. The pH was controlled in the range 1-7 with HCl or phosphate, as appropriate. A large excess of Pt(II) and Pt(IV) with respect to CH_3-B_{12} was used in all rate measurements, so that both $[Pt^{II}]$ and $[Pt^{IV}]$ would remain essentially constant. The range of CH_3-B_{12} concentration was $(3\text{-}50) \times 10^{-6}$ M. Plots of $\log (A_\infty - A_t)$ vs. time gave straight lines for more than 85% of the reaction, demonstrating first-order dependence on $[CH_3\text{-}B_{12}]$.[3]

Results

The base-on to base-off equilibrium for CH_3-B_{12} (eq 2, Bz = 5,6-dimethylbenzimidazole ribofuranoside phosphate side chain base) was found to be important for the demethylation by the $PtCl_6^{2-}/PtCl_4^{2-}$ couple.[3] The value of



(2)

pK_2 is taken to be 5.0, which is the pK_a of dicyanocobalamin ($NCB_{12}CN$-BzH^+) in 1.0 M KCl at 25 °C.[9a] This is close to the pK_a of free 5,6-dimethylbenzimidazole (4.7).[9b] The value of pK_1 was determined by a spectrophotometric technique[3] to be 2.0 in 1.0 M NaCl at 23 °C, which are the actual conditions of the experiments described in this report.

Preliminary Considerations for the Demethylation Reaction. Ligand-exchange reactions between the starting Pt(IV) and Pt(II) complexes used in this study do not

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Table I. Kinetic Parameters for the Demethylation of Base-on CH_3-B_{12} by Mixtures of Pt(IV) and Pt(II) Complexes[a, b]

	Pt(II)					
	$PtCl_4^{2-}$		$Pt(CN)_4^{2-}$			
Pt(IV)	k', M^{-1} s^{-1}	$10^{-3}K_3$, M^{-1}	k', M^{-1} s^{-1}	10^3k, s^{-1}	$10^{-3}K_3$, M^{-1}	$10^{-3}K_4$, M^{-1}
$PtCl_6^{2-}$	1.1×10^2 [c]	3.4 [c]	3.5		3.5	
$Pt(CN)_4Cl_2^{2-}$	1.5×10	5.1		3.0	2.0	8.1
$Pt(CN)_5Cl^{2-}$	very slow			3.6	6.5	1.0
$Pt(CN)_5I^{2-}$	no reaction			no reaction		
$Pt(CN)_6^{2-}$	no reaction			no reaction		

[a] pH 7.2 (0.1 M phosphate). [b] Variance in these parameters is ±10%. [c] From ref 3; all others from this work.

occur.[10] Hydrolysis of $PtCl_4^{2-}$ in 1.0 M NaCl is slow enough to be unimportant,[8] and all other Pt(II) and Pt(IV) complexes are inert to hydrolysis[11] under the reaction conditions employed here.

Pt(II) complexes do not demethylate CH_3-B_{12} even after a few days. It has been reported that prolonged incubation of CH_3-B_{12} with $PtCl_4^{2-}$ results in demethylation.[12] We have found that a very high concentration of unpurified Na_2PtCl_4 will demethylate CH_3-B_{12}. This is most likely due to contamination with Pt(IV) compounds because recrystallization eliminates this activity. On the other hand, there does appear to be a pathway for demethylaton by Pt(IV) complexes alone. These reactions, which also produce H_2O-B_{12}^+, are much slower than the Pt(IV)/Pt(II) demethylation. At low initial Pt(IV) concentrations, a lag period followed by an exponential phase is usually observed, which suggests that the Pt(IV)/Pt(II) route becomes competitive due to Pt(II) generation. The Pt(IV)/Pt(II) route generates CH_3Pt^{IV} products in the absence of chloride.[2] By contrast, the Pt(IV) alone route generates CH_3Cl and no CH_3Pt^{IV} compounds in the absence of added chloride.

Kinetics. "Base-on" CH_3-B_{12}. "Base-on" CH_3-B_{12} (**a**) is the predominant B_{12} species in solution at pH 7.2; demethylation is largely confined to this form at this pH. The Pt(IV)/Pt(II) couples can be grouped into two categories according to the rate laws in Pt(IV) and Pt(II). Group I is exemplified by the $PtCl_6^{2-}/PtCl_4^{2-}$ system described previously.[3] The rate law is first order in Pt(IV). However, dependence on Pt(II) is first order at low concentrations and progressively changes to zero order at high concentrations. These results imply a preequilibrium such as the one presented in eq 3 and the rate law in eq 5.

$$CH_3\text{-}B_{12} + \text{Pt(II)} \overset{K_3}{\rightleftharpoons} \underset{\textbf{A}}{CH_3\text{-}B_{12}\cdots Pt^{II}} \qquad (3)$$

$$\textbf{A} + \text{Pt(IV)} \xrightarrow{k'} \text{products} \qquad (4)$$

$$\frac{d[H_2O\text{-}B_{12}^+]}{dt} = k_{obsd}[CH_3\text{-}B_{12}] \qquad (5)$$

$$k_{obsd} = \frac{k'K_3[Pt^{II}][Pt^{IV}]}{1 + K_3[Pt^{II}]}$$

This pattern is also followed by the couples $Pt(CN)_4Cl_2^{2-}/PtCl_4^{2-}$ and $PtCl_6^{2-}/Pt(CN)_4^{2-}$. Figure 1A shows plots of k_{obsd} vs. $[Pt^{IV}]$ and Figure 1B shows plots of $[Pt^{IV}]/k_{obsd}$ vs. $1/[Pt^{II}]$. From these plots the values of k' and K_3 are derived via eq 5 and are listed in Table I.

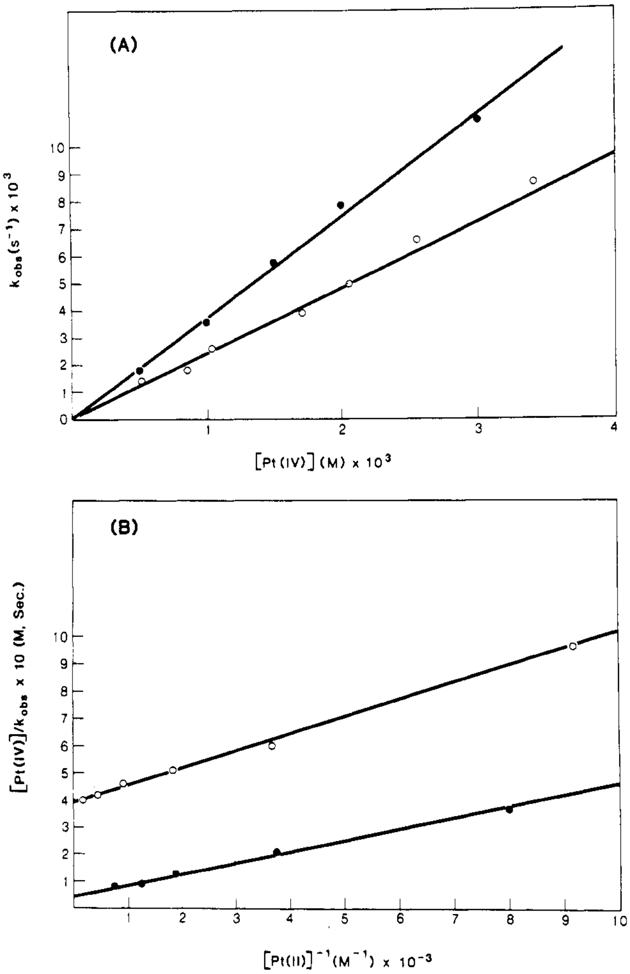

Figure 1. Kinetic data for the demethylation of CH_3-B_{12} by $PtCl_6^{2-}/Pt(CN)_4^{2-}$ (○) and $Pt(CN)_4Cl_2^{2-}/PtCl_4^{2-}$ (●) couples at pH 7.2: (A) plots of k_{obsd} vs. $[Pt^{IV}]$ at a constant $[Pt^{II}]$; (B) plots of $[Pt(IV)]/k_{obsd}$ vs. $[Pt(II)]^{-1}$.

The platinum couples $Pt(CN)_4Cl_2^{2-}/Pt(CN)_4^{2-}$ and $Pt(CN)_5Cl^{2-}/Pt(CN)_4^{2-}$ comprise a second group of reactions that show a progression from first-order to zero-order behavior with increasing concentrations for *both* Pt(IV) and Pt(II). This implies that Pt(IV) as well as Pt(II) is involved in a complexation prior to the rate-determining step. One interpretation of this is the formation of a trinuclear intermediate **B** in eq 6, where the k_{obsd} of eq 5 is then expressed by eq 7.

$$\textbf{A} + \text{Pt(IV)} \overset{K_4}{\rightleftharpoons} \underset{\textbf{B}}{CH_3\text{-}B_{12}\cdots Pt^{II}\cdots Pt^{IV}} \xrightarrow{k} \text{products} \qquad (6)$$

$$k_{obsd} = \frac{kK_3K_4[Pt^{II}][Pt^{IV}]}{1 + K_3[Pt^{II}] + K_3K_4[Pt^{II}][Pt^{IV}]} \qquad (7)$$

Accordingly, plots of k_{obsd}^{-1} vs. $[Pt^{IV}]^{-1}$ at each (constant) $[Pt^{II}]$ give an intercept = k^{-1} and slope = (1 + K_3-

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[10] For a review of the Pt(II)-catalyzed ligand substitution reactions of Pt(IV) complexes, see: (a) Mason, W. R. *Coord. Chem. Rev.* **1972**, *7*, 241. Also see: (b) Elding, L. I.; Gustafson, L. *Inorg. Chim. Acta* **1977**, *24*, 239.

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Table II. Comparison of Experimental vs. Calculated k_{obsd} for Demethylation by Mixtures of $Pt(CN)_4Cl_2{}^{2-}$ and $Pt(CN)_4{}^{2-}$ [a]

$10^3[Pt(CN)_4Cl_2{}^{2-}]$, M	$10^3[Pt(CN)_4{}^{2-}]$, M	10^3k_{obsd}, s^{-1}	
		exptl	calcd [b]
0.195	0.287	1.1	1.1
0.389	0.287	1.6	1.6
0.584	0.287	1.7	1.9
0.973	0.287	2.1	2.2
1.95	0.287	2.8	2.6
2.92	0.287	3.2	2.7
0.214	0.542	1.7	1.6
0.268	0.542	1.7	1.6
0.535	0.542	2.2	2.1
0.803	0.542	2.5	2.3
1.07	0.542	2.7	2.5
2.14	0.542	3.3	2.7
0.95	1.15	1.5	1.6
0.389	1.15	1.9	2.0
0.584	1.15	2.2	2.3
0.973	1.15	2.4	2.5
2.92	1.15	3.0	2.8
0.195	2.87	1.6	1.7
0.389	2.87	1.8	2.2
0.973	2.87	2.4	2.6

[a] $[CH_3\text{-}B_{12}] \approx 10^{-5}$ M; pH 7.2 (0.1 M phosphate).
[b] Calculated on the basis of eq 7 and appropriate constants therein. Average deviation from experimental value, 7.6%.

$[Pt^{II}])/kK_3K_4[Pt^{II}]$. Plots of slope vs. $[Pt^{II}]^{-1}$ then yield K_3 and K_4. The values of k, K_3, and K_4 derived from these data are listed in Table I.

The validity of the reaction sequence proposed in eq 6 is supported by good agreement between experimental k_{obsd} and k_{obsd} calculated according to eq 7 for $Pt(CN)_4Cl_2{}^{2-}/Pt(CN)_4{}^{2-}$ (Table II). Agreement is equally good for the $Pt(CN)_5Cl^{2-}/Pt(CN)_4{}^{2-}$ couple.

The demethylation mechanisms for both groups of platinum couples can be unified if it is assumed that K_4 for group I couples is small enough that the intermediate B does not form in appreciable amounts; that is, the K_3K_4 term in the denominator of eq 7 remains small. If this assumption is true, then $k' = kK_4$.

Kinetics. "Base-on" vs. "Base-off" Forms. The reaction sequence of eq 3 and 4 (or eq 3 and 6) may also be applied to the unprotonated and protonated base-off forms of $CH_3\text{-}B_{12}$ (**b** and **c** of eq 2). As the pH of the solution is lowered **c** increases in concentration, whereas **b** is always present in very low concentration. The reaction with the $PtCl_6{}^{2-}/Pt(CN)_4{}^{2-}$ couple at pH 1–3 follows the kinetic pattern of group I (i.e., first order in $[Pt^{IV}]$, Figure 2A) and is therefore described by the reaction sequence in eq 3 and 4 and fits the rate law presented in eq 5. In this case "$CH_3\text{-}B_{12}$" is taken to represent all three forms of methylcobalamin in solution. In order to separate out the contributions of the individual forms, it is necessary to consider the analogous eq 8.

$$k_{obsd} = ((k^aK_2K_3{}^a + k^bK_1K_2K_3{}^b + k^cK_1K_3{}^c[H^+])[Pt^{II}] \times [Pt^{IV}])/(K_2 + K_1K_2 + K_1[H^+] + K_2K_3{}^a[Pt^{II}] + K_1K_2K_3{}^b[Pt^{II}] + K_1K_3{}^c[H^+][Pt^{II}]) \quad (8)$$

By taking into account the fact that $K_1 \gg K_2$ and assuming that both the unprotonated and protonated base-off species have similar reactivity (i.e., $K_3{}^b \simeq K_3{}^c$ and $k^b \simeq k^c$), eq 8 can be simplified to

$$k_{obsd} = \frac{(k^aK_2K_3{}^a + k^cK_1K_3{}^c[H^+])[Pt^{II}][Pt^{IV}]}{K_2 + K_1[H^+] + K_2K_3{}^a[Pt^{II}] + K_1K_3{}^c[H^+][Pt^{II}]} \quad (9)$$

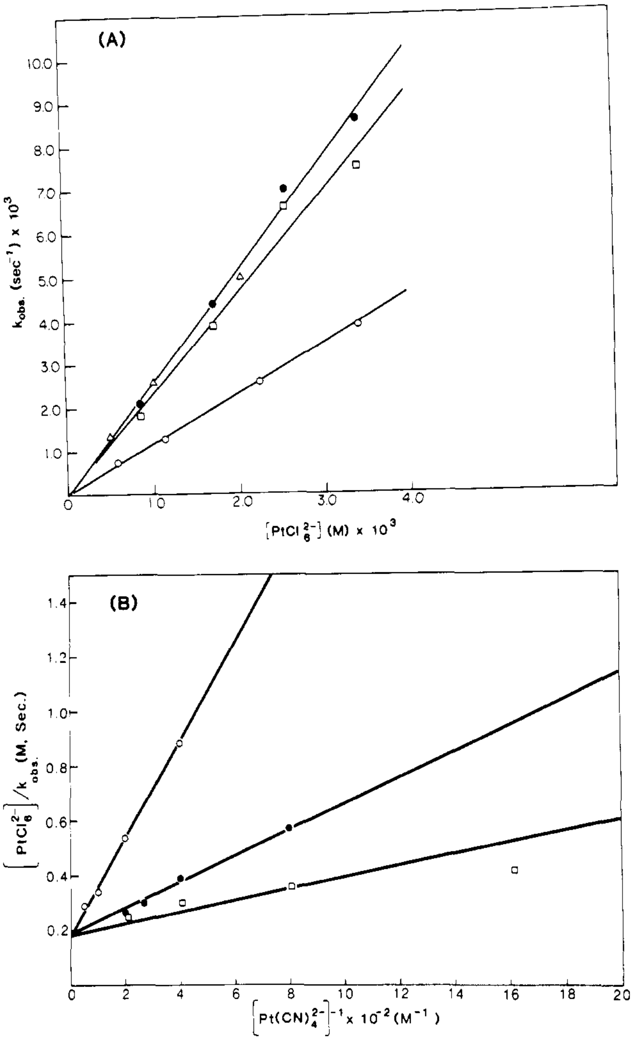

Figure 2. Kinetic data for the demethylation of $CH_3\text{-}B_{12}$ by $PtCl_6{}^{2-}/Pt(CN)_4{}^{2-}$ in acid solution. (A) Plots of k_{obsd} vs. $[PtCl_6{}^{2-}]$ at constant $[Pt(CN)_4{}^{2-}]$: ●, pH 7.2, $[Pt(CN)_4{}^{2-}] = 1.09 \times 10^{-3}$ M; ○, pH 1.00, $[Pt(CN)_4{}^{2-}] = 2.50 \times 10^{-3}$ M; □, pH 2.00, $[Pt(CN)_4{}^{2-}] = 2.50 \times 10^{-3}$ M; △, pH 3.00, $[Pt(CN)_4{}^{2-}] = 1.71 \times 10^{-3}$ M; (B) Plots of $[PtCl_6{}^{2-}]/k_{obsd}$ vs. $[Pt(CN)_4{}^{2-}]^{-1}$: ○, pH 1.0; ●, pH 2.0 □, pH 3.0.

Plots of $[Pt^{IV}]/k_{obsd}$ vs. $[Pt^{II}]^{-1}$ should, according to this rate law, give straight lines with intercepts and slopes given in eq 10 and 11.

$$\text{intercept} = \frac{K_2K_3{}^a + K_1K_3{}^c[H^+]}{k^aK_2K_3{}^a + k^cK_1K_3{}^c[H^+]} \quad (10)$$

$$\text{slope} = \frac{K_2 + K_1[H^+]}{k^aK_2K_3{}^a + k^cK_1K_3{}^c[H^+]} \quad (11)$$

The plots (Figure 2B) show that the intercepts are almost independent of pH. This result has two possible explanations: (1) That $K_2K_3{}^a \gg K_1K_3{}^c[H^+]$ and $k^aK_2K_3{}^a \gg k^cK_1K_3{}^c[H^+]$. (This would mean that the decrease in the rate with increasing $[H^+]$ is due only to the progressive removal of the base-on form from the reaction.) The value of k^a calculated under this assumption, when substituted into (11) gives $K_3{}^a = 1.2 \times 10^4$ M^{-1} (at pH 1), which does not agree with K_3 obtained at pH 7.2 (Table I). (2) That $k^a \simeq k^c$. Under this assumption, $K_3{}^c$ is calculated (from eq 11 at the pHs 1 and 2[13]) to be 6 (±2) × 10^2 M^{-1}.

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[13] Data obtained at pH 3.0 cannot be used to evaluate $K_3{}^c$ because the contribution to k_{obsd} from the base-off path is very small at this pH, introducing a large uncertainty to the value of $K_3{}^c$.

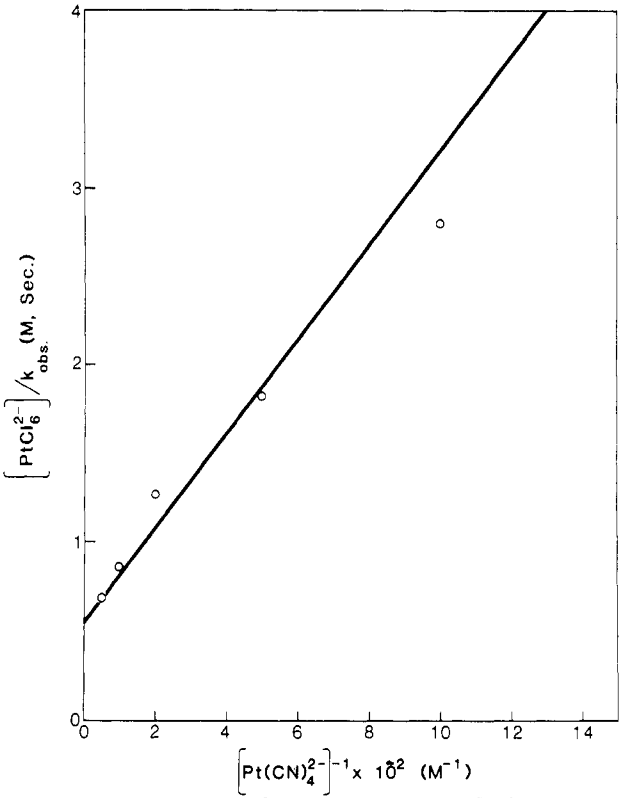

Figure 3. Plots of $[PtCl_6^{2-}]/k_{obsd}$ vs. $[Pt(CN)_4^{2-}]^{-1}$ for the demethylation of methylcobinamide by $PtCl_6^{2-}/Pt(CN)_4^{2-}$ at pH 7.2.

This contention that $k^a \simeq k^c$ is supported by our kinetic studies with methylcobinamide, a CH_3-B_{12} analogue that does not contain the side chain base and is therefore present in solution only in the base-off form. Methylcobinamide gives kinetic results similar to those of CH_3-B_{12}. The reaction with the $PtCl_6^{2-}/Pt(CN)_4^{2-}$ couple is first order in Pt(IV) and first to zero order in Pt(II) and is suitably described by eq 5. Plots of $[PtCl_6^{2-}]/k_{obsd}$ vs. $[Pt(CN)_4^{2-}]^{-1}$ (Figure 3) are linear and give rise to $k^c = 1.9$ (±0.3) M^{-1} s^{-1} and $K_3^c = 2.3$ (±0.5) × 10^2 M^{-1}. Note that k^c and K_3^c for methylcobinamide are almost identical with the corresponding values for protonated base-off CH_3-B_{12}.

Spectral Evidence for Reaction Intermediates. CH_3-B_{12}···Pt^{II}. The UV–visible spectra of CH_3-B_{12} (4.5 × 10^{-5} M) alone and with $Pt(CN)_4^{2-}$ (0.010 M) are presented in Figure 4. The α and γ bands (515 and 340 nm, respectively) of CH_3-B_{12} in the presence of the platinum compound are blue-shifted ~3 nm, and a shoulder appears at 355 nm. These spectral changes are reversible and time independent and cease when $[Pt(CN)_4^{2-}]$ reaches a level of about 10^{-2} M. (At this concentration, the ratio $[CH_3\text{-}B_{12}\cdots Pt^{II}]/[CH_3\text{-}B_{12}]$ is calculated to be 20 according to the K_3 value determined from kinetics (Table I).) The equilibrium constant is calculated to be 4 (±2) × 10^3 M^{-1} from absorbance changes at 355 nm. This value is in excellent agreement with K_3 determined from the kinetics. Similar changes in the CH_3-B_{12} spectrum occur with $PtCl_4^{2-}$ except the shoulder at 355 nm is not as prominent. An equilibrium constant of 3 (±2) × 10^3 M^{-1} is obtained, which is also in good agreement with the kinetic study.

By contrast, the ^1H NMR spectrum of CH_3-B_{12} is largely unaffected by $PtCl_4^{2-}$ or $Pt(CN)_4^{2-}$ (0.008 ppm maximum shift) under conditions that predict almost complete complex formation (i.e., $[CH_3\text{-}B_{12}] = 1$ mM; $[Pt^{II}] = 5$ mM).

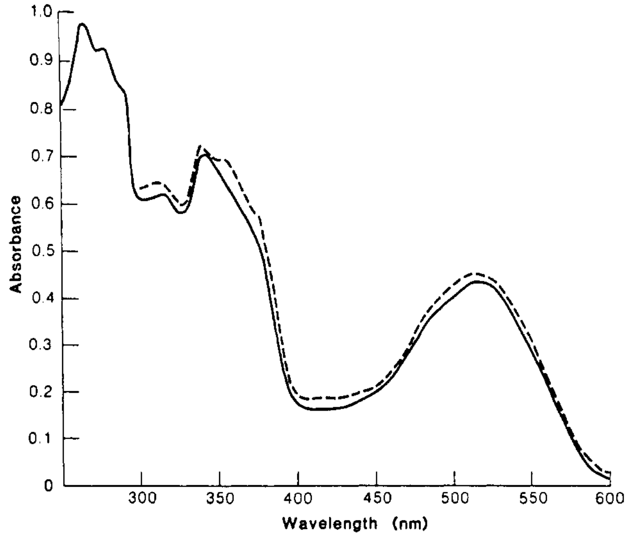

Figure 4. Effect of $Pt(CN)_4^{2-}$ on the visible spectrum of CH_3-B_{12} at pH 7.2; (—), CH_3-B_{12} alone (4.5 × 10^{-5} M); (···) CH_3-B_{12} (4.5 × 10^{-5} M) and $Pt(CN)_4^{2-}$ (1.0 × 10^{-2} M).

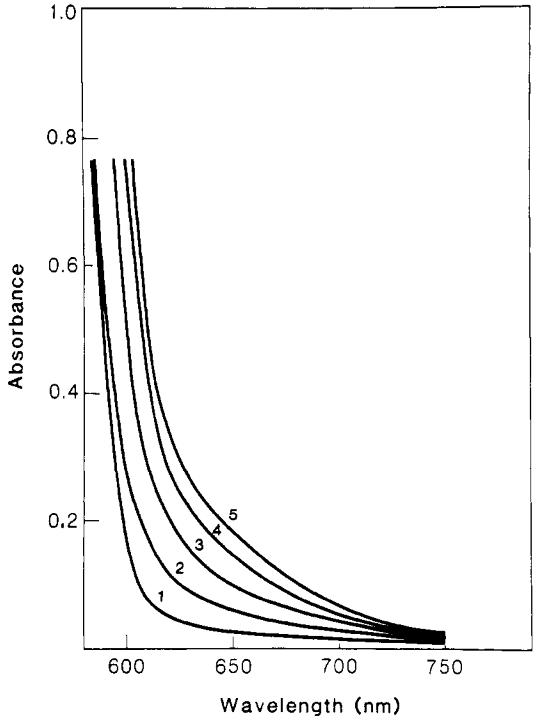

Figure 5. Spectral evidence for the trinuclear intermediate B using $Pt(CN)_5Cl^{2-}$ and $Pt(CN)_4^{2-}$ as reactants with CH_3-B_{12}: $[CH_3\text{-}B_{12}] = 0.52$ (spectrum 1), 0.52 (spectrum 2), 1.04 (spectrum 3), 1.56 (spectrum 4), and 2.08 mM (spectrum 5); $[Na_2Pt(CN)_4] = [Na_2Pt(CN)_5Cl] = 5.0$ mM except for spectrum 1, which is CH_3-B_{12} alone.

Spectral Evidence for the Trinuclear Intermediate. The reaction of CH_3-B_{12} with the $Pt(CN)_5Cl^{2-}/Pt(CN)_4^{2-}$ couple is slow, yet K_4 for this system is indicated to be large (Table I). Thus, the electronic spectrum can be examined for evidence of a trinuclear intermediate as governed by K_4 (eq 6). CH_3-B_{12} does not absorb significantly from 630 to 750 nm even at a concentration as high as 1.5 × 10^{-3} M. However, when both $Pt(CN)_5Cl^{2-}$ and $Pt(CN)_4^{2-}$ are present with CH_3-B_{12} in solution a significant absorbance in this region occurs before any observable H_2O-B_{12}^+ is formed (Figure 5).[14] The experiments were carried out

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[14] Note that similar spectral study in the wavelength range 250–600 nm is not feasible because of the very large difference in the total absorbance and absorbance change due to the addition of $Pt(CN)_4^{2-}$ and $Pt(CN)_5Cl^{2-}$.

at constant platinum concentrations that were high enough to quantitatively convert CH_3-B_{12} to the new intermediate, as demonstrated in spectra 1–5. This new species has a molar absorptivity of 1.87×10^2 M^{-1} cm^{-1} at 630 nm (ϵ_{630} for CH_3-B_{12} = 63 M^{-1} cm^{-1}). A combination of any two of the compounds CH_3-B_{12}, $Pt(CN)_5Cl^{2-}$, and $Pt(CN)_4^{2-}$ fails to increase the absorbance in this region of the spectrum. A combination of $Pt(CN)_6^{2-}$ or $Pt(CN)_5I^{2-}$ with $Pt(CN)_4^{2-}$ and CH_3-B_{12}, at the same concentrations, also fails to produce absorbance in this region, and these two Pt(IV) complexes show no reactivity in the demethylation reaction with Pt(II).

The overall formation constant for this new species is calculated from the spectral changes to be 4.8 (±1.8) × 10^6 M^{-2}. The details are available in the supplementary material. This value is in good agreement with the kinetically derived K_3K_4 (Table I).

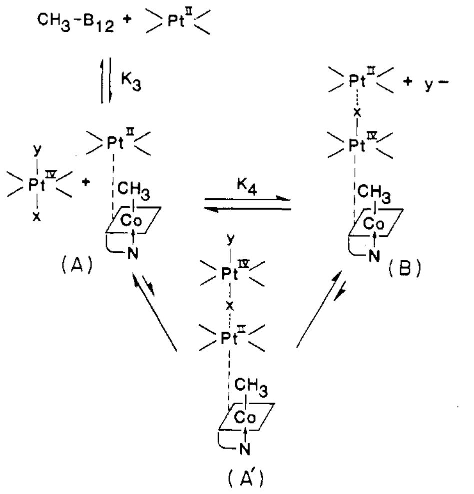
Discussion

The stoichiometry for the methyl-transfer reaction is given in eq 1. Assuming the mechanism is the same for all Pt(IV)/Pt(II) couples, our kinetic data are best described by reactions 3 and 6.

Before any further discussion of this mechanism, it is worthwhile at this point to eliminate some other schemes. First, a mechanism involving the reaction of Pt(II) with Pt(IV) to generate a reactive Pt(III) intermediate can be eliminated because it requires the kinetic orders in Pt(II) and Pt(IV) to be identical under all reaction conditions—first order if [Pt^{III}] is very low or first to zero order if [Pt^{III}] is significant. We have clearly demonstrated that Pt(II) and Pt(IV) show very different kinetic behavior. Second, and for the same reason, a mechanism involving the reaction of Pt(IV) with Pt(II) to form a binuclear Pt(IV)–Pt(II) intermediate prior to the complexation or reaction with CH_3-B_{12} can also be ruled out. Third, a mechanism similar to that in eq 3 and 6, except that the roles of Pt(IV) and Pt(II) are switched (i.e., Pt(IV) complexes with CH_3-B_{12} first), can be eliminated on the grounds that it would require the kinetic order in a given Pt(IV) complex to be independent of the Pt(II) complex used. Our kinetic study shows that this is not the case. The reaction with $Pt(CN)_4Cl_2^{2-}$ is first order in Pt(IV) at all concentrations when $PtCl_4^{2-}$ is used, but changes from first to zero order with increasing concentration of $Pt(CN)_4^{2-}$. Finally, a mechanism in which Pt(II) is the first platinum species to complex with CH_3-B_{12}, as depicted in eq 3, is entirely consistent with these kinetic data. Table I shows that K_3 for a given Pt(II) complex is independent of the Pt(IV) complex used.

The mechanism of eq 3 and 6 is presented in Scheme I in greater detail. It is possible to infer structural information about the two intermediates from our results. The Pt(II) atom in A is likely to be bonded to a site in the vicinity of the Co–C bond. This conclusion is supported by the following observations: (1) The methylplatinum product arises from methyltransfer to the Pt(II) reactant.[2] (2) Methyl radicals are not produced at significant concentrations because HCHO and HCOOH are not found in those reactions performed in the presence of oxygen. This was checked by ^1H and ^{13}C NMR. The limits of detection of these species are such that we were able to see clearly the HCHO ^{13}C resonance upon photolysis of 90% ^{13}C $^{13}CH_3$-B_{12} (which is known to produce HCHO[15]) at a concentration which was 5% of that used in these product studies. The absence of these products is important because it implies that methyl transfer occurs during a CH_3-B_{12}-to-Pt(II) encounter.

Scheme I



What is the nature of the bond in A? A bond between Pt(II) and the benzimidazole 3-nitrogen can be ruled out because changes in the UV–visible spectrum, or the ^1H NMR spectrum,[16] that are characteristic of base-off CH_3-B_{12} do not occur, even at high Pt(II) concentrations. Coordination of Pt(II) to an acetamide or propionamide group on the periphery of the corrin ring is unlikely because demethylation rates are unaffected by the addition of 1 M $HCONH_2$ or CH_3CONH_2 in our experiments, and such binding should be competitively inhibited by exogenous amide. Also, amides are known to be very weak ligands towards Pt(II).[17] It is possible that the binding energy is due in part to electrostatic attraction from ion pairing between the dinegatively charged Pt(II) complex and the positively charged cobalt macrocycle. The similarity in K_3 for $PtCl_4^{2-}$ and $Pt(CN)_4^{2-}$ is consistent with ion pairing. However, this is not likely to be the only force of attraction between Pt(II) and CH_3-B_{12} in this medium (i.e., 1 M NaCl), because competition with sodium ions, which are present at greater than 10^5[CH_3-B_{12}], would be expected to interfere with such a reaction.

Another possible type of bonding in A is Pt(II) interaction with the orbitals of the corrin ring to form a π complex similar to the well-known syngergic donor/acceptor bond between transition-metal complexes, including Pt(II), and olefins or polyenes. The spectral changes of CH_3-B_{12} on formation of A are not inconsistent with Pt interaction with the corrin ring π system. The α and γ bands in the electronic spectrum of CH_3-B_{12} have been attributed to $\pi \rightarrow \pi^*$ transitions involving orbitals centered largely on the corrin π conjugated system.[18] Upon bonding with a Pt(II) complex, the gap between π and the π^* orbitals is expected to increase after overlap with the appropriate σ and π orbitals centered on the platinum, and this is what is observed; the α and γ bands of CH_3-B_{12} are blue-shifted ~3 nm (Figure 4). The absence of changes in the ^1H NMR spectrum of CH_3-B_{12} on formation of A is not unexpected for this type of bonding. Olefinic protons, especially in highly substituted olefins, do not shift

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dramatically on coordination to Pt(II) compounds, and the magnitude and direction of the shifts are dependent on the net change in electron density of the olefin, which is close to zero in most cases.[19] CH_3-B_{12} has one olefinic proton on a trisubstituted double bond. Allylic protons, of which CH_3-B_{12} has several, are normally shifted very little, or not at all, on coordination to Pt(II) complexes.[19]

The trinuclear complex between CH_3-B_{12}, Pt(II), and Pt(IV) is detected kinetically as an intermediate in systems where K_4 is large—$Pt(CN)_4Cl_2{}^{2-}/Pt(CN)_4{}^{2-}$ and $Pt(CN)_5Cl^{2-}/Pt(CN)_4{}^{2-}$. The steps leading to this intermediate are outlined in Scheme I. Initially, the reaction of Pt(IV) with A could lead to the complex A′, which is unfavorable because Pt(II) does not readily become six-coordinate. However, a switch in the oxidation states of the platinum atoms via a formal two-electron transfer through the chloride bridging ligand could lead to B, concomitant with elimination of the ligand Y^-. The central Pt(IV) atom in B would then be stable as a six-coordinate metal. Transformations of a similar kind are well-known in Pt(II)-catalyzed ligand exchange reactions of Pt(IV) complexes, which also proceed through a bridged binuclear intermediate or transition state and result in a switch in oxidation states between the two platinum atoms:[10]

$$\begin{aligned} X\text{-}Pt^{IV}L_4\text{-}Z + Pt^{II}L'_4 + Y^- &\rightarrow X\text{-}Pt^{IV}L_4\text{-}Z\cdots Pt^{II}L'_4\text{-}Y \\ &\rightleftharpoons X\text{-}Pt^{II}L_4\cdots Z\text{-}Pt^{IV}L'_4\text{-}Y \rightarrow \\ &\qquad X^- + Pt^{II}L_4 + Z\text{-}Pt^{IV}L'_4\text{-}Y \end{aligned}$$

The structure that we propose for B also follows from several other observations. (1) The intermediate CH_3-$B_{12}\cdots Pt(CN)_4{}^{2-}\cdots Pt(CN)_5Cl^{2-}$ absorbs in the region 630–750 nm (Figure 5). Solid mixed valence platinum complexes with halide bridging ligands (i.e., $Y\text{-}PtL_4\text{-}X\cdots PtL_4$) are reported to absorb strongly in this region.[20] (2) The structure of B is supported by the relative reactivity for the Pt(IV) complexes:

$$Pt(CN)_4Cl_2{}^{2-} > Pt(CN)_5Cl^{2-} > Pt(CN)_6{}^{2-}$$

The rationale for this is that $Pt(CN)_5Cl^{2-}$ is less reactive than $Pt(CN)_4Cl_2{}^{2-}$ because cyanide is a poorer leaving group than chloride in the reaction A′ $\rightleftharpoons$ B; this is reflected in the value of K_4, which is eight fold smaller for $Pt(CN)_5Cl^{2-}$ (Table I). This order is also found for the Pt(II)-catalyzed ligand exchange reactions.[10a] The negligible reactivity of $Pt(CN)_6{}^{2-}$ must also be due in part to the reduced leaving ability of CN^-. An additional factor that makes $Pt(CN)_6{}^{2-}$ less reactive than $Pt(CN)_5Cl^{2-}$ could be reduced ability of CN^- over Cl^- to mediate the electron-transfer process in the bridge position. (Cyanide has not been evaluated as a bridging ligand in the Pt(II)-catalyzed ligand exchange reactions. However, Br^- is preferred over CN^- for the bridge position in $Pt(CN)_5Br^{2-}$.) Or it may be simply that the extreme stability of $Pt(CN)_6{}^{2-}$ precludes net reaction. Consistent with the former is the fact that $Pt(CN)_6{}^{2-}$ does not form observable concentrations of the trinuclear intermediate by UV–visible spectroscopy. (3) The rate constant k for the rate-determining step is almost identical for $Pt(CN)_4Cl_2{}^{2-}$ and $Pt(CN)_5Cl^{2-}$ in the demethylation reaction with $Pt(CN)_4{}^{2-}$ (Table I). This indicates a common intermediate for these reactions. (4) The alternative structure to B for the trinuclear intermediate is one in which both platinum complexes have separate binding sites on CH_3-B_{12}. This is less credible, in view of the requirement that follows from the kinetic study that binding of Pt(IV) must be triggered by binding of Pt(II).

Finally, from these results we can comment on the mechanism of methyl transfer to platinum. Direct attack by bound platinum in the intermediate B on the Co–C bond (i.e., formally electrophilic attack) is unlikely on the basis of the kinetic results which show that the rate constant for the rate-determining step is insensitive to the presence or absence of the axial benzimidazole ligand. It is known that the axial ligand trans to the organo group has a large effect on the rate of heterolytic reactions of the Co–C bond of organocobalamins or their model compounds.[21,22] Therefore, the comparable rate constants for the base-on and base-off forms of CH_3-B_{12} can be taken as strong evidence that direct attack on the Co–C bond does not occur by the bound platinum in the rate-limiting step.

A mechanism for the rate-limiting step that is in better agreement with the lack of influence by axial ligand is an electron transfer to the bound platinum from the corrin ring π system (eq 12). These electrons are less susceptible to effects of the axial ligand than the Co–C bond electrons.

$$\underset{B}{CH_3\text{-}B_{12}\cdots Pt^{IV}\text{-}X\cdots Pt^{II}} \rightarrow (CH_3\text{-}B_{12})^+(Pt^{III}\text{-}X\cdots Pt^{II})^- \qquad (12)$$

Electron transfer may be succeeded by either rapid methyl transfer to platinum within the solvent-caged radical pair (eq 12) or by dissociation of the radical pair followed by reencounter with methyltransfer. Each of these post rate-limiting steps may be considered homolytic attack of the reduced platinum on the methyl carbon of CH_3-$B_{12}{}^+$ (i.e., $CH_3\cdot$ transfer).[23]

The evidence disfavors a mechanism in which CH_3-$B_{12}{}^{+}\cdot$ cleaves to form methyl radicals free in solution because of the absence of oxygenated products typically found when $CH_3\cdot$ is generated in the presence of oxygen (e.g., when CH_3-B_{12} is photolyzed[15]). Oxygen can be expected to compete successfully with reactive platinum intermediates, because the rate of reaction of $CH_3\cdot$ with O_2 is near the diffusion-controlled limit and the concentration of O_2 in water under air is about 10^{-4}–10^{-3} M, which is considerably higher than one would expect the concentration of any free reactive platinum reactants. Homolytic cleavage of the carbon–cobalt bond of one-electron-oxidized dimethylcobalt macrocycles to give methyl radicals has been reported,[24] however.

In summary, this study shows that a binding site is available on CH_3-B_{12} for platinum and perhaps other metals. Binding can be followed by an intracomplex redox

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[23] An alternative mechanism has been proposed by a reviewer:

$$\begin{aligned} &B \rightarrow CH_3Co^{III}\cdots Pt^{III}\text{-}X\text{-}Pt^{III}\ (C) \rightarrow \\ &\{Co^{II} + CH_3Pt^{IV} + XPt^{III}\}\ \text{(solvent cage)} \rightarrow Co^{III} + CH_3Pt^{IV} + XPt^{II} \end{aligned}$$

This was suggested from the observations that (a) S_H2 reactions on R–Co^{III} are facile (McHatton, R. C.; Espensen, J. H.; Bakac, A. *J. Am. Chem. Soc.* **1982**, *104*, 3531) and (b) that two-electron transfers like Pt(II)/Pt(IV) may proceed kinetically via two one-electron steps (Finke, R. G.; Voegeli, R. H.; Laganis, E. D.; Bockelheide V. *Organometallics* **1983**, *2*, 347 and references therein). C can also be considered an intermediate in the transformation A′ $\rightleftharpoons$ B. The above reaction is consistent with the kinetic results that demand a buildup of a trinuclear intermediate (i.e., zero order in Pt^{IV} at high $[Pt^{IV}]$), provided that the rate of C → B is faster than C → products. Since axial ligand effects on the rates of S_H2 reactions on R–Co^{III} are virtually unknown, the alternative mechanism cannot be eliminated.

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reaction, culminating in the cleavage of the Co-C bond and transfer of the organo group to the reduced attacking metal. This reaction mechanism is reminiscent of the reactions by I_2 and other electrophiles on organometallic compounds of Pb and Sn, which were shown to occur by charge-transfer complexation, electron transfer to form a radical pair, and finally transfer of the organo group to the electrophile within the radical pair.[25] The sequence of steps for the platinum-CH_3-B_{12} reaction is similar, but the nature of the interactions is qualitatively different. The CH_3-B_{12}···Pt^{II} intermediate, for example, is probably not a charge-transfer complex of the traditional definition. And, whereas electron transfer from R_4Pb or R_4Sn occurs from a carbon-metal orbital, the electron transferred from CH_3-B_{12} to platinum probably does not. Thus, the breaking of the Co-C bond arises from interactions elsewhere in the molecule and not directly on the Co-C bond. This may have implications for the mechanisms of methylcobalamin-dependent enzymatic reactions.

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Registry No. CH_3-B_{12}, 13422-55-4; H_2O-B_{12}^+, 13422-52-1; $PtCl_6^{2-}$, 16871-54-8; $Pt(CN)_4Cl_2^{2-}$, 38725-65-4; $Pt(CN)_5Cl^{2-}$, 38725-82-5; $Pt(CN)_5I^{2-}$, 45000-44-0; $Pt(CN)_6^{2-}$, 41517-45-7; $PtCl_4^{2-}$, 13965-91-8; $Pt(CN)_4^{2-}$, 15004-88-3.

Supplementary Material Available: Plot to determine the formation constant of the trinuclear intermediate from absorbance changes at 630 nm for the demethylation by $Pt(CN)_5Cl^{2-}$/$Pt(CN)_4^{2-}$ (2 pages). Ordering information is given on any current masthead page.

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[25] For a recent review on the charge-transfer and electron-transfer reactions of organometallic compounds, see: Kochi, J. K. *Pure Appl. Chem.* **1980**, *52*, 571.

Linking Molybdenum or Tungsten with Platinum. The Synthesis and Molecular Structure of PtMo(μ-Ph_2Ppy)(μ-CO)$(CO)_2Cl_2$ (Ph_2Ppy = 2-(Diphenylphosphino)pyridine)

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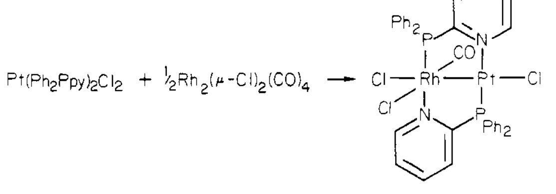
Reaction of $Pt(Ph_2Ppy)_2Cl_2$ (Ph_2Ppy is 2-(diphenylphosphino)pyridine) with (bicycloheptadiene)$Mo(CO)_4$ or $(CH_3CN)_3W(CO)_3$ produces $PtMo(\mu\text{-}Ph_2Ppy)_2(\mu\text{-}CO)(CO)_2Cl_2$ (98% yield) or $PtW(\mu\text{-}Ph_2Ppy)_2(\mu\text{-}CO)(CO)_2Cl_2$ (67% yield), respectively. Infrared and $^{31}P\{^1H\}$ NMR spectra indicate that the Mo and W complexes have similar structures. $PtMo(\mu\text{-}Ph_2Ppy)_2(\mu\text{-}CO)(CO)_2Cl_2$ is also formed in the reaction between $Mo(Ph_2Ppy)_2(CO)_4$ (phosphorus-bound Ph_2Ppy) and (1,5-cyclooctadiene)$PtCl_2$. Red $PtMo(\mu\text{-}Ph_2Ppy)_2(\mu\text{-}CO)(CO)_2Cl_2$ crystallizes in the orthorhombic space group $I2cb$ ($\bar{c}ba$ of $Iba2$, No. 45) with a = 13.784 (6) Å, b = 17.677 (5) Å, c = 31.915 (13) Å, Z = 8, and V = 7776.6 (5) Å^3. The structure was refined to a conventional R value of 0.060 by using 3777 significant reflections and 232 parameters. The structure of the binuclear complex indicates that it possesses a Pt-Mo bond (2.845 (1) Å long) and a semibridging carbonyl group. Additional ligating atoms about Pt are 2P and Cl and about Mo are 2N, 2C (from CO), and Cl. The two bridging Ph_2Ppy ligands assume a head-to-head arrangement with a trans-P-Pt-P unit and a cis-N-Mo-N unit.

Introduction

In a recent series of articles,[1-7] we have shown that a variety of both homo- and heterobinuclear complexes that involve group 8 metal atoms can be synthesized by using 2-(diphenylphosphino)pyridine (Ph_2Ppy) as a bridging ligand. The strategy used in the synthesis of these compounds involves the initial binding of Ph_2Ppy to one metal through a phosphorus atom. In a subsequent reaction with a second metal complex, the binuclear compound is formed. Examples of this latter step are shown in eq 1[1,6] and 2.[7] A common feature to all known reactions of this type is the addition of one metal-halide bond to the second metal center. We believe that this behavior is a consequence of the rigid nature of the bridging ligand. This rigidity, in the case of a trans pair of bridging Ph_2Ppy ligands, appears to limit the M-M separation to distances less than 2.7 Å.[2]



(1)

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