However, chromatography delivers a single product **12** which arises by equilibration to the thermodynamically most stable one and desilylation of the silyl ester. NMR spectroscopy establishes the axial nature of the carboxylic acid group. MM-2 calculations support the notion that J_{ab} for **12** should be around 0–2 Hz, whereas the same coupling for the compound epimeric at the carboxyl-bearing carbon should be 4–7 Hz. These predictions correspond well to the observed couplings of the parent adduct (<1 and 6.0 Hz, respectively). The appearance of H_a at δ 3.69 as a broad singlet (J < 1 Hz) supports the assignment as the exo carboxylic acid; consideration of A-strain effects also predicts the axial carboxylic acid to be more stable. MM-2 calculations support the higher stability for the axial isomer too.

To determine the initial bonding site in the tropone partner, a double-labeling experiment is necessary. In this case, the 2-methyltropone was reacted with **7**, which undergoes in situ carboxylation prior to cycloaddition (entry 8). As for the case of entry 5, a stereoisomeric mixture initially forms which equilibrates to the exo carboxylic acid product depicted. The presence of an isolated AB pattern for the allylic methylene group (δ 2.65 and 2.42, J = 13.5 Hz) and a broad singlet for the allylic methine proton (δ 3.69) establishes both the regio- and stereochemistry.

In contrast to the reaction of dienes with tropone where several modes of reaction have been observed,[3] the reaction of the bifunctional conjunctive reagent **4** and its analogues with tropone proceeds only via the [6 + 3] mode. Furthermore, the reaction is highly chemo- and regioselective and, in the case of electron-withdrawing groups, highly diastereoselective. The versatility of the bridging ketone and the ease with which such a one-carbon bridge may be cleaved make these adducts flexible nine-membered ring intermediates. The ability of the cyclic TMM precursor of entry 7 to participate demonstrates the rapidity with which polycyclic systems may be constructed. it appears that these TMM synthons can permit an approach to a number of odd-membered rings via [2n + 3] cycloadditions. So far, syntheses of five- (n = 1) and nine-membered (n = 3) rings have been proven to be feasible. In both cases, the question of concerted vs. stepwise reactions must be considered open. The developing parallel between the reactions of these bifunctional conjunctive reagents and those of dienes, especially electron-rich dienes such as Danishefsky's diene,[12] begins to suggest that similar mechanisms may be involved.

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Kinetics of ^{13}CO Exchange with ^{12}CO in $[HM_3(^{12}CO)_{11}]^-$ and $[DM_3(^{12}CO)_{11}]^-$ (M = Ru or Os): Relationship between Exchange Pathway and Catalytic Activity in the Catalysis of the Water Gas Shift Reaction

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The anion $[HRu_3(CO)_{11}]^-$ has been implicated as an active participant in the catalysis of the water gas shift reaction.[1,2] On the other hand, $[HOs_3(CO)_{11}]^-$ is less active under similar conditions.[3] The kinetics of ^{13}CO exchange with ^{12}CO in $[HM_3(^{12}CO)_{11}]^-$ and $[DM_3(^{12}CO)_{11}]^-$ (M = Ru, Os) in THF[4] provide further insight into the nature of the catalysis of the water gas shift reaction by $[HRu_3(CO)_{11}]^-$ and reveal a basis for the apparent difference in activity between $[HRu_3(CO)_{11}]^-$ and $[HOs_3(CO)_{11}]^-$.

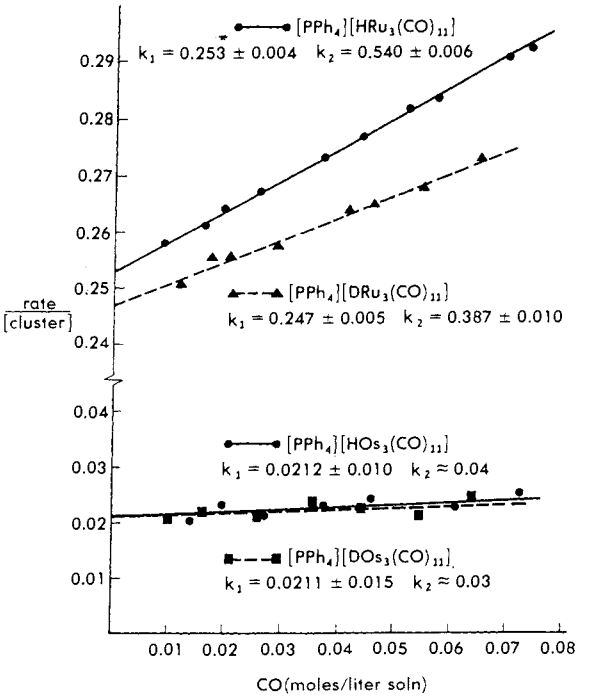

Figure 1. Plot of rate/[cluster] vs. CO concentration in solution.

Exchange between ^{13}CO and ^{12}CO in $[HRu_3(^{12}CO)_{11}]^-$ in THF[4] (20–30 °C, 0.001–0.01 M $[HRu_3(CO)_{11}]^-$, 0.0007–0.033 M CO) appears to occur through parallel first- and second-order reactions. The overall rate expression for the forward exchange reaction is given by eq A, where concentrations are given in moles per liter

$$\text{rate} = k_1[\text{cluster}] + k_2[\text{cluster}][\text{CO}] \qquad \text{(A)}$$

of solution. A plot of rate/[cluster] vs. [CO] is linear (Figure 1). For $[PPh_4][HRu_3(CO)_{11}]$ at 298 K, $k_1 = 0.253 \pm 0.004$ s^{-1} and $k_2 = 0.540 \pm 0.006$ M^{-1} s^{-1}. For k_1, $\Delta H_1^{\ddagger} = 19.8 \pm 0.6$ kcal/mol and $\Delta S_1^{\ddagger} = 5.3 \pm 1.5$ cal/mol K; for k_2, $\Delta H_2^{\ddagger} = 14.1 \pm 0.5$ kcal/mol and $\Delta S_2^{\ddagger} = -8.0 \pm 1.7$ cal/mol K. Entropies of activation, $\Delta S_1^{\ddagger}$ and $\Delta S_2^{\ddagger}$, are consistent with dissociative and associative processes, respectively. Thus, at low ^{13}CO concentration an apparent dissociative step forming $[HRu_3(CO)_{10}]^-$ plus CO appears to dominate the exchange process. The dissociative pathway confirms a suggestion by Darensbourg,[8a] and k_1 is

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(4) (a) Kinetic measurements were made by using a thermostated gas infrared cell with a cold finger to hold the continuously stirred reaction solution. Reaction conditions: 0.1–2.5 atm of ^{13}CO; 20.0 ± 0.2 to 35.0 ± 0.2 °C; anion concentration = 0.001–0.01 M. With the $[PPh_4]^+$ counterion and under these conditions, $Ru_3(CO)_{12}$ does not appear to form.[1] The forward reaction was followed by monitoring the 2171-cm^{-1} band of free ^{12}CO as it appeared in the gas phase over the stirred solution. A Mattson Instruments Cygnus 25 FTIR spectrometer was programmed to collect spectra at desired intervals and acquisition times. Time vs. absorbance data were analyzed by using a standard rate-fitting computer program and the McKay equation for isotopic exchange.[5] The solubility of CO in THF was determined over the temperature and pressure range employed in this study by using a modification of a known procedure.[6] At 1 atm of CO pressure, its solubility in THF is 0.0109 ± 0.0005 M (25 °C) and 0.0117 ± 0.0003 M (30 °C). Its solubility in THF increases with increasing temperature, consistent with results from other ether solvents.[7]
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consistent with results of Ford[8b] for the kinetics of PPh_3 exchange with $[PPN][HRu_3(CO)_{11}]$.[8] On the basis of Ford's work,[8b] intramolecular CO exchange is probably stereoselective. Since intermolecular CO exchange is slower than intramolecular scrambling of CO's in the cluster, we employ a statistical correction factor of $^1/_{11}$ in the rate calculation.

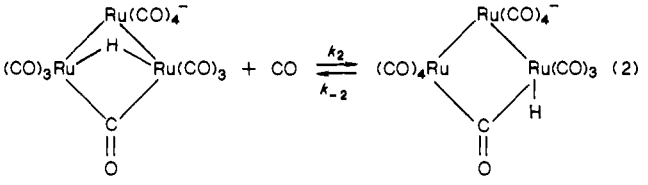
The associative exchange pathway becomes increasingly significant (reaction 1) with increasing ^{13}CO concentration (increasing ^{13}CO pressure).

$$[HRu_3(^{12}CO)_{11}]^- + {}^{13}CO \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} [HRu_3(^{13}CO)(^{12}CO)_{11}]^- \quad (1a)$$

$$[HRu_3(^{13}CO)(^{12}CO)_{11}]^- \underset{k'_2}{\overset{k'_{-2}}{\rightleftharpoons}} [HRu_3(^{13}CO)(^{12}CO)_{10}]^- + {}^{12}CO \quad (1b)$$

$$[HRu_3(^{12}CO)_{11}]^- + {}^{13}CO \rightleftarrows [HRu_3(^{13}CO)(^{12}CO)_{10}]^- + {}^{12}CO \quad (1)$$

The following steps have been proposed in the reaction of $[HRu_3(CO)_{11}]^-$ with CO and H_2O in the water gas shift reaction:[1,2]



$$[HRu_3(CO)_{12}]^- + H_2O \xrightarrow{k_3} Ru_3(CO)_{12} + H_2 + OH^- \quad (3)$$

$$[HRu_3(CO)_{11}]^- + H_2O + CO \xrightarrow{k_4} Ru_3(CO)_{12} + H_2 + OH^- \quad (4)$$

The catalytic cycle is completed by reaction of the $Ru_3(CO)_{12}$ with OH^- to regenerate $[HRu_3(CO)_{11}]^-$.

Reaction 1a of the exchange pathway from the kinetic results is consistent with suggested reaction 2. Exchange of ^{13}CO with ^{12}CO in the study of ^{13}CO exchange in the deuteriated cluster $[PPh_4][DRu_3(CO)_{11}]$ shows that the deuterium label has little effect on k_1 (Figure 1) but that k_2 decreases significantly: $k_2(H)/k_2(D) = 1.40$; $k_1 = 0.247 \pm 0.005$ s^{-1}; $k_2 = 0.387 \pm 0.010$ M^{-1} s^{-1}. The dominant isotope effect[9] is consistent with our suggestion[1a] that in the associative step bridge-hydrogen displacement to a terminal position occurs. Since the intermediate does not reach detectable concentrations in the reaction medium, we invoke the steady-state approximation and set the rate constant for H_2 liberation, k_4, equal to $k_2k_3/(k_{-2} + k_3)$.

The value of k_4 is estimated to be about 1.3×10^{-3} M^{-1} s^{-1} for the liberation of H_2 from an aqueous solution 0.01 M in $K[HRu_3(CO)_{11}]$, 25 °C under 1 atm of CO[1a] (eq 3), with [CO] equal to its solubility in water.[10] Unless k_2 is subject to major solvent effects, the low value of k_4 compared to k_2 implies that $k_{-2} >> k_3$, i.e., $k_4 \sim k_2k_3/k_{-2}$. Therefore, reaction 3 approximates a preequilibrium step prior to rate-limiting release of H_2 in the second step. The rate of HD evolution from the reaction of $[DRu_3(CO)_{11}]^-$ with H_2O under 1 atm of CO is significantly smaller[1a] than the rate of H_2 evolution from the reaction of $[HRu_3(CO)_{11}]^-$ with H_2O. Thus the kinetic isotope effect on the overall reaction is larger than the kinetic isotope effect found for reaction 2, and an additional contribution from k_3 is thereby implied as expected for the making of an H–H (H–D) bond accompanied by the breaking of a Ru–H (Ru–D) bond.

The rate of ^{13}CO exchange with ^{12}CO in $[HOs_3(CO)_{11}]^-$ also obeys the overall forward rate given by eq A (Figure 1). For $[PPh_4][HOs_3(CO)_{11}]$ at 298 K, $k_1 = 0.0212 \pm 0.0010$ s^{-1} and $k_2 \sim 0.04$ M^{-1} s^{-1}. For k_1, $\Delta H_1^{\ddagger} = 23.9 \pm 0.7$ kcal/mol and $\Delta S_1^{\ddagger} = 13.9 \pm 2.3$ cal/mol K.

For $[HOs_3(CO)_{11}]^-$, the rate of exchange is relatively insensitive to ^{13}CO concentration. This poorer ability to participate in an associative reaction, we believe, accounts for the lower activity of $[HOs_3(CO)_{11}]^-$ than that of $[HRu_3(CO)_{11}]^-$ in the catalysis of the water gas shift reaction.

For the exchange of ^{13}CO with ^{12}CO in $[PPh_4][DOs_3(CO)_{11}]$, the value of k_1 is essentially unaffected. For $[PPh_4][DOs_3(CO)_{11}]$ at 298 K, $k_1 = 0.0211 \pm 0.0015$ s^{-1} and $k_2 \sim 0.03$ M^{-1} s^{-1}.

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Chirality of Intermediates in Thiamin Catalysis: Structure of (+)-2-(1-Hydroxyethyl)-3,4-dimethyl-5-(2-hydroxyethyl)thiazolium Iodide, the Absolute Stereochemistry of the Enantiomers of 2-(1-Hydroxyethyl)thiamin, and Enzymic Reaction of the Diphosphates

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The decarboxylation of pyruvate is catalyzed by enzymes which utilize thiamin diphosphate (TDP) as a cofactor.[2] The enzyme-bound covalent adduct of TDP and pyruvate loses CO_2 and is protonated to form the adduct of acetaldehyde, 2-(1-hydroxyethyl)thiamin diphosphate (HETDP).[2,3] Although TDP, the substrates, and products are achiral, the intermediates are chiral with the stereocenter at the carbon atom derived from C2 of pyruvate.[4] Optically active HETDP has been isolated from pyruvate dehydrogenase[5] and 2-(1-hydroxyethyl)thiamin (HET) has been resolved.[6,7] The absolute stereochemistry of the materials is unknown. We now report the unambiguous determination of the absolute stereochemistries through X-ray crystallographic analysis of a derivative and the reaction of each enantiomer of HETDP with pyruvate decarboxylase.

2-(1-Hydroxyethyl)thiamin (HET) was prepared and resolved as the 1:1 salt of (−)-2,3-dibenzoyltartaric acid.[7] The HET released by HCl treatment of the salt is optically active: (+)-HET ($[\alpha]^{25}_D$ +12.5° ± 0.1°). The salt of HET and (+)-2,3-dibenzoyltartaric acid was also prepared and treatment with HCl released (−)-HET ($[\alpha]^{25}_D$ −12.5 ± 0.1°). (+)-HET was converted to (−)-2-(1-hydroxyethyl)-3,4-dimethyl-5-(2-hydroxyethyl)thiazolium iodide ((−)-HETI) by reaction with sodium sulfite[8,9]

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