°C for 2 h to give a yellow-orange solution. The solvent was carefully distilled off and reserved for a second reaction, the residue taken up in CH_2Cl_2 and separated by TLC, eluting with CH_2Cl_2 (30%)/hexane (70%). Extraction of a pale yellow band gave ^{13}C-labeled [$HOs_3(CO)_9(\mu_3:\eta^2:\eta^1:\eta^2\text{-}C_5C^*H_7)$] in ca. 40% yield. The dienyl complex was converted to [$Os_3(CO)_9(\mu_3:\eta^2:\eta^2:\eta^2\text{-}C_5C^*H_6)$] following the procedure described previously.[6a]

Solution NMR Experiments. Solution NMR spectra were obtained using a Bruker AM400 spectrometer operating at 400.1 MHz for ^1H and 100.6 MHz for ^{13}C. Samples were dissolved in CD_2Cl_2, and spectra were recorded in 5-mm tubes. For low temperature two-dimensional experiments samples were prepared at room temperature, cooled to ca. 200 K, and filtered to give saturated solutions (approximate concentrations of 55 and 32 mg mL^{-1} for the ethylene and styrene complexes, respectively). Temperature calibration was achieved with a methanol NMR thermometer using the method of van Geet.[56]

With the exception of the ^1H-^{13}C chemical shift correlation spectra, all two-dimensional spectra were recorded phase sensitively using the Marion-Wuthrich TPPI method,[27] and Lorentzian-to-Gaussian apodization was used in each dimension.

Acquisition Conditions. Double-Quantum-Filtered COSY.[57] t_1 was incremented in 256 steps to a maximum of 256/(2×SW1) s, and the data were zero filled to 512 words prior to Fourier transformation. Thirty-two scans per increment were recorded. Acquisition time in t_2 was 0.45 s giving 2048 real data points. Relaxation delay between experiments was 0.45 s.

Two-Dimensional CAMELSPIN.[15a] The mixing time consisted of a CW spin locking field of duration 0.2 s and field strength, $\gamma B_1/2\pi$, of 3.0 kHz. The same field strength was used for the remainder of the radio frequency pulses. t_1 was incremented in 256 steps to a maximum of 256/(2×SW1) s, and the data were zero filled to 512 words prior to Fourier transformation. Sixteen scans per increment were recorded. Acquisition time in t_2 was 0.2 s giving 2048 real data points. Relaxation delay between experiments was 0.6 s.

Two-Dimensional Exchange Spectra.[23] Carbon spectra were recorded using broadband proton decoupling (WALTZ-16).[58] t_1 was incremented in 256 steps to a maximum of 256/(2×SW1) s, and the data were zero filled to 512 words prior to Fourier transformation. Two hundred fifty-six scans were recorded for each increment. Acquisition time in t_2 was 0.51 s giving 4096 real data points. Relaxation delay between experiments was 0.25 s.

^1H-^{13}C Chemical Shift Correlation.[59] t_1 was incremented in 64 steps to a maximum of 64/SW1 s, and the data were zero filled to 128 words prior to Fourier transformation. Five hundred twelve scans were recorded per increment. Acquisiton time in t_2 was 0.21 s giving 2048 real data points. Relaxation delay was 1.0 s. An absolute value display was taken.

^1H and ^{13}C longitudinal relaxation times were recorded using an inversion-recovery sequence. Steady state NOE difference spectra were recorded in the usual way.[60]

Solid State NMR Experiments. ^{13}C CP/MAS NMR spectra were recorded at 50.32 MHz using a Bruker CXP200 spectrometer equipped with a multinuclear, proton-enhanced, double-bearing magic angle sample spinning probe, a high power proton decoupler, and an Aspect 2000 data system. A single contact spin-lock CP sequence with flip back of ^1H magnetization and with a proton rf field of 17 G was used.[61] Dry nitrogen was used for both spinning and bearing gases. Temperature regulation was of the bearing gas and temperature measurement was of the bearing exhaust close to the sample. Temperature calibration below room temperature was achieved with the samarium ethanoate tetrahydrate Curie law chemical shift thermometer previously calibrated against the phase transition of *d*-camphor[62] and above room temperature with the phase transitions of cobaltocenium hexafluorophosphate[63] and 1,4-diazabicyclo-[2,2,2]-octane.[62] The system was allowed to equilibrate at each new temperature for 1 h before spectral accumulation was commenced. The intensity of the ferrocene NMR resonance was measured at each temperature under otherwise identical conditions to provide a degree of temperature-dependent intensity calibration for the probe. Approximately 250 mg of a sample enriched to about 15% with ^{13}CO, together with a small amount of potassium bromide (the ^{79}Br resonance of which was used to set the magic angle[64] at each temperature), was packed into a 7-mm zirconia rotor with a Kel-F top. Typically 1000-2000 transients, with a relaxation delay of 3-15 s, were accumulated for each spectrum in the organic ligand region, and up to 600 transients, with a relaxation delay of 30-60 s, for the carbonyl region.

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Supplementary Material Available: Figures showing variable temperature ^1H and $^{13}C\{^1H\}$ NMR spectra for complexes **3** and **4**, ^1H two-dimensional CAMELSPIN spectrum of **3**, and $^{13}C\{^1H\}$ two-dimensional EXSY spectrum of **1** and a table of two-dimensional EXSY peak intensity data for **3** (8 pages). Ordering information is given on any current masthead page.

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Development and Mechanistic Study of a New Aldehyde Decarbonylation Catalyst

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Abstract: $Rh_2(PMe_3)_2(CO)_2Cl_2$ (**2**) has been found to catalyze the decarbonylation of aldehydes to give the corresponding alkanes. Reaction rates are comparable to those of the most active nonradical systems previously reported. A mechanistic study indicates that the turnover-limiting reaction step includes addition of the aldehydic C-H bond to an intact molecule of **2**; ligand dissociation or cleavage of the chloride bridge does not occur prior to the C-H addition step. This conclusion is based on kinetic studies ($d[R'H]/dt = k_{obs}[2][R'CHO]$; $R' = n\text{-}C_{11}H_{23}$; $k_{obs} = 2.2 \times 10^{-4}$ M^{-1} s^{-1}; $\Delta S^* = -26$ eu) and the observation of a significant kinetic isotope effect ($k_{RCHO/RCDO} > 1.8$).

Our interest in the catalytic carbonylation of hydrocarbons has led us to consider the development of catalysts for the reverse reaction. In addition to its obvious relevance to alkane carbonylation, the decarbonylation of aldehydes is a useful and im-

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portant reaction in organic synthesis.[1,2] The most commonly used reagent for this purpose in Wilkinson's catalyst, $Rh(PPh_3)_3Cl$, which stoichiometrically effects decarbonylation at or near room temperature to give $Rh(PPh_3)_2(CO)Cl$. Only at elevated temperatures (>200 °C), however, is that system catalytic.[1,2] While more efficient catalytic systems have been reported, such as $[Rh\{Ph_2P(CH_2)_nPPh_3\}_2]^+$ and Ru(tetraphenylporphyrin)$(PPh_3)_2$,[2,3] as of yet none have been found to be of practical utility. The development of such systems is clearly of interest, especially in view of the very high cost of rhodium.[4] Herein we report the development of a new decarbonylation catalyst and a mechanistic study which elucidates the nature of the transition state of the turnover-limiting reaction step.

Our study of the alkane carbonylation catalyst $Rh(PMe_3)_2(CO)Cl$[5] led us to examine the properties of $Rh_2(PMe_3)_4Cl_2$.[6] We found that it efficiently decarbonylates aldehydes. Reaction 1

$$Rh_2(PMe_3)_4Cl_2 + 2RCHO \rightarrow 2Rh(PMe_3)_2(CO)Cl + 2RH \quad (R = Me, Et, Ph) \quad (1)$$

takes place rapidly (<1 h) at 26 °C even in the presence of only 1 equiv of aldehyde (10 mM). To our knowledge, $Rh_2(PMe_3)_4Cl_2$ is therefore the most active decarbonylation reagent known.

The thermal loss of CO from $Rh(PMe_3)_2(CO)Cl$, if it occurred, could lead to the completion of a catalytic decarbonylation cycle containing eq 1 as the actual decarbonylation step. In fact, no significant catalysis is observed even with solutions of $Rh(PMe_3)_2(CO)Cl$ in neat benzaldehyde at high temperatures (e.g., a 7 mM $Rh(PMe_3)_2(CO)Cl$ solution at 115 °C for 48 h afforded 0.7 mM benzene). However, a report by Poilblanc[7] indicates that the dicarbonyl analogue, $Rh(PMe_3)(CO)_2Cl$ (**1**), loses CO under mild conditions. We therefore examined the reactivity of the corresponding dimer, $Rh_2(PMe_3)_2(CO)_2Cl_2$ (**2**), and found that like $Rh_2(PMe_3)_4Cl_2$ it effects decarbonylation, albeit less rapidly, yielding **1**. The same product, **1**, results from the addition of

$$\underset{\mathbf{2}}{Rh_2(PMe_3)_2(CO)_2Cl_2} + 2RCHO \xrightarrow{\text{ca. 100 °C}} \underset{\mathbf{1}}{2Rh(PMe_3)(CO)_2Cl} + 2RH \quad (R = Me, Et, Ph) \quad (2)$$

CO gas to a solution of **2**.[8] Although reaction 2 is not catalytic

$$\mathbf{2} + 2CO \xrightarrow{\text{room temp}} 2\,\mathbf{1} \quad (3)$$

in a closed vessel, purging the resulting solution with argon (even at 25 °C) regenerates the starting material (eq 4), thus completing a catalytic cycle (eq 5). Continuous purging during the reaction

$$\mathbf{1} \xrightarrow{\text{Ar purge, } -CO} \mathbf{2} \quad (4)$$

$$RCHO \xrightarrow[\text{Ar purge}]{\text{2 (ca. 100 °C)}} RH + CO\uparrow \quad (5)$$

allows a catalytic reaction to proceed at rates approximately equal to those of the fastest previously reported nonradical system, $[Rh(Ph_2P(CH_2)_3PPh_2)_2]^+$,[2] for example, 3.6 turnovers/h at 100 °C (R = n-$C_{11}H_{23}$).[9] A 50% conversion (ca. 225 turnovers) was effected with a 10 mM solution of **2** after 72 h; no significant catalyst decomposition was observed afterwards as monitored by IR spectroscopy. Whereas some[1,3] (though not all[2]) decarbonylation systems afford significant quantities of the corresponding alkene from aliphatic aldehydes, undecane was the only significant product observed from dodecanal; less than 2% undecene was formed (GC). We suggest that as this system is completely unoptimized, there is considerable potential for the development of related systems with greater, more practical, levels of reactivity. In part for this reason, we have probed the kinetics of eq 2 and attempted to elucidate the nature of the rate-determining step (rds).

A priori, several mechanisms for eq 2 could be envisaged. In particular, the importance of three-coordinate rhodium intermediates in oxidative addition reactions[10,11] combined with the

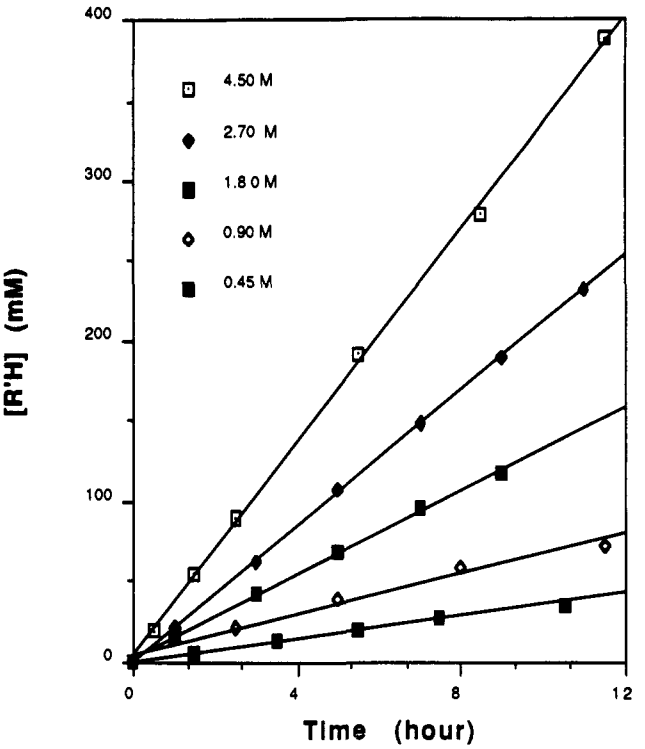

Figure 1. Formation of R'H at different R'CHO concentration in 2-undecanone; 10 mM **2**, 100 °C.

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(3) (a) Domazetia, G.; Tarpey, B.; Dolphin, D.; James, B. R. *J. Chem. Soc., Chem. Commun.* **1980**, 939–940. (b) Domazetis, G.; James, B. R.; Tarpey, B.; Dolphin, D. In *Catalytic Activation of Carbon Monoxide*; ACS Symposium Series 152; American Chemical Society: Washington, DC, 1981; pp 243–252.

(4) The price (Johnson-Matthey) of $RhCl_3$ hydrate is presently $2377/25 g.

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(8) With the addition of less than a stoichiometric quantity of CO gas, or before reaction 2 reaches completion (in the absence of an argon purge), the following equilibrium is observed: $\mathbf{2} + \mathbf{1} \rightleftharpoons Rh_2(PMe_3)(CO)_3Cl_2 + Rh(PMe_3)_2(CO)Cl$ ($K_{eq} = 0.4$). Because this equilibrium is rapidly established, we have been unable to experimentally determine if **1** is the kinetic product of reactions 2 and 3. It is possible for example that $Rh_2(PMe_3)(CO)_3Cl_2$ plus free PMe_3 is the kinetic product although, in view of the relative strengths of the rhodium–phosphine bond versus the halide bridge,[12] this does not seem likely.

(9) $[Rh(Ph_2P(CH_2)_3PPh_2)_2][BF_4]$, probably the most active nonradical decarbonylation catalyst reported to date,[2] decarbonylates heptanal with 31 turnovers/h at 115 °C. Complex **2** decarbonylates dodecanal with 3.6 turnovers/h at 100 °C. Because we analyze the reaction solution, and therefore use high molecular weight species and moderate temperatures, while Pignolet et al. analyzed the volatile products, it is difficult to directly compare the two systems with precision.

(10) For a closely related and well-characterized example of addition (of H_2) to a square-planar Rh(I) complex (proceeding via ligand loss), see: (a) Halpern, J. *Inorg. Chim. Acta* **1981**, *50*, 11–19. (b) Halpern, J.; Wong, C. S. *J. Chem. Soc., Chem. Commun.* **1973**, 629.

(11) Milstein has demonstrated that R–H bond reductive elimination from $Rh(PMe_3)_3Cl(R)(H)$ proceeds via prior ligand loss and thus by the principle of microscopic reversibility the oxidative addition must proceed via three-coordinate complexes. Particularly noteworthy is the case where RH = PhCHO: (a) Milstein, D. *Acc. Chem. Res.* **1984**, *17*, 221–226. (b) Milstein, D. *Organometallics* **1982**, *1*, 1549–1551.

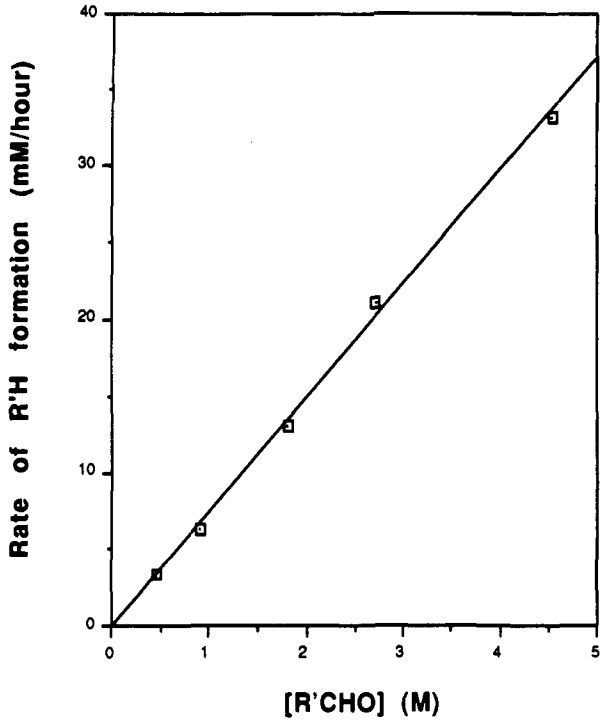


Figure 2. Rate of R'H formation at different R'CHO concentration; values obtained from data plotted in Figure 1.

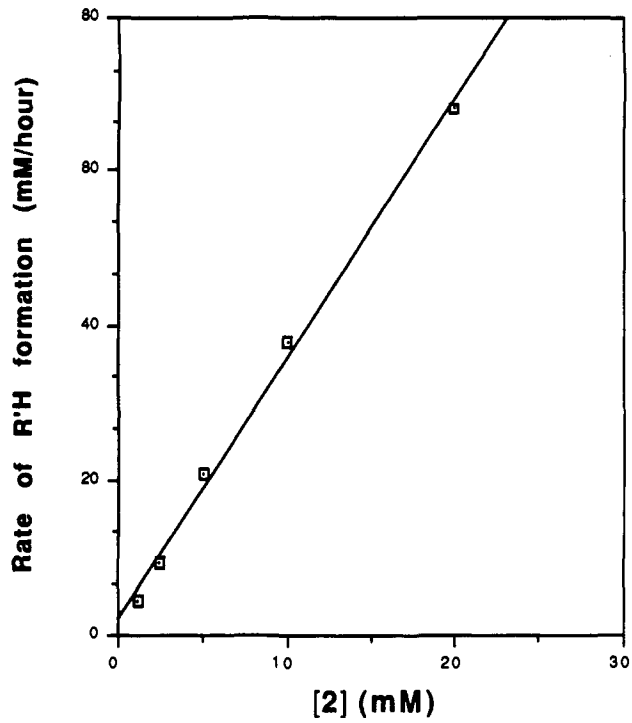


Figure 3. Rate of R'H formation as a function of [2] in neat R'CHO at 100 °C.

relative weakness of the chloride bridge[12] might suggest that cleavage of the bridge prior to reaction with aldehyde is a likely pathway (eqs 6 and 7). Further support of such a pathway comes

$$2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} 2Rh(PMe_3)(CO)Cl \qquad (6)$$

$$Rh(PMe_3)(CO)Cl + RCHO \xrightarrow{k_2} 1 + RH \qquad (7)$$

from mechanistic studies by Wong and Halpern on the $Rh(PPh_3)_3Cl$ stoichiometric decarbonylation[13] and by Pignolet on the $[Rh(Ph_2PC_3H_6PPh_2)_2]^+$ catalytic reaction.[2] In both cases, phosphine loss is indicated to be the first step, and in the limit of high [RCHO], it is rate-determining.

Application of the steady-state approximation to [Rh(PMe$_3$)(CO)Cl] (eqs 6 and 7) yields the rate law eq 8. In the limit k_2[RCHO] $\gg 16k_{-1}k_1$[**2**], the predicted rate expression is d[RH]/dt = $2k_1$[**2**], while the limit k_2[RCHO] $\ll 16k_{-1}k_1$[**2**] yields d[RH]/dt = k_2[RCHO]$\{k_1/k_{-1}$[**2**]$\}^{1/2}$.

$$d[RH]/dt = \frac{k_2[RCHO]\{-k_2[RCHO] + (k_2^2[RCHO]^2 + 16k_{-1}k_1[\mathbf{2}])^{1/2}\}}{4k_{-1}} \qquad (8)$$

Under an argon purge, at 100 °C, decarbonylation obeys the rate law d[R'H]/dt = k_{obs}[**2**][R'CHO] (R' = n-$C_{11}H_{23}$; k_{obs} = 2.2×10^{-4} M^{-1} s^{-1}) over the range [R'CHO] = 0.45–4.5 M (Figures 1 and 2) and [**2**] = 1.25–20 mM (Figure 3). Aldehyde concentration was varied by dilution in 2-undecanone as solvent, thereby largely preserving the bulk properties of the solution (an experiment with 1.8 M R'CHO in hexadecane gave a rate only slightly greater than that in ketone[14]). The observed kinetics argue strongly against bridge cleavage prior to the rds (eqs 6 and 7) or as a rds prior to reaction with aldehyde: k_2[RCHO] $\gg k_{-1}$[Rh(PMe$_3$)(CO)Cl]. Similarly, the observed rate expression argues against phosphine loss either as a rds or as a preequilibrium.[15] A rate-determining loss of CO may be ruled out and a

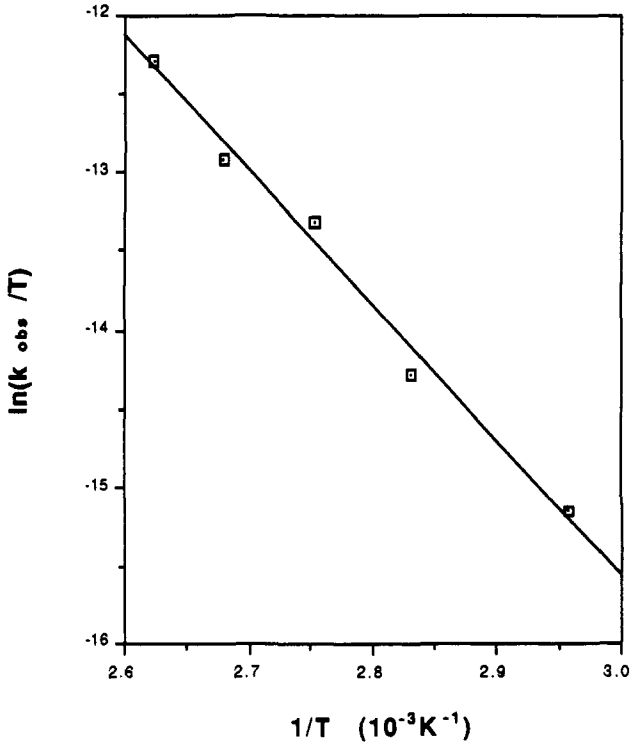


Figure 4. Eyring plot for the catalytic decarbonylation of R'CHO (eq 5) in the temperature range 65–108 °C; 10 mM **2** in neat R'CHO.

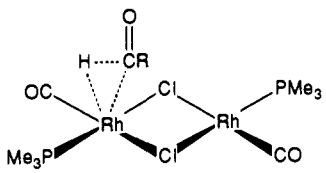
(12) Drago, R. S.; Miller, J. G.; Hoselton, M. A.; Farris, R. D.; Desmond, M. J. *J. Am. Chem. Soc.* **1983**, *105*, 444–449.

(13) Wong, C. S. Ph.D. Thesis, University of Chicago, 1973.

(14) A solution of R'CHO (1.8 M) and **2** (5 mM) in hexadecane solvent yielded 8.8 mM undecane h^{-1} as compared with 6.6 mM h^{-1} from a similar 2-undecanone solution. Presumably this difference results from a slight (and nearly equal) degree of complexation of **2** with the aldehyde and ketone but not with hexadecane.

(15) Direct determination of the effect of PMe$_3$ concentration on the reaction rate was impossible due to the following reaction (which goes to apparent completion): **2** + PMe$_3$ → Rh(PMe$_3$)$_2$(CO)Cl. However, any equilibrium concentration of PMe$_3$ in a solution of **2** would be dependent on [**2**]. Thus, the first-order dependence on [**2**] of the rate of reaction 5 is inconsistent with a preequilibrium loss of PMe$_3$.

Chart I. Proposed Structure of the Transition State of the Rate-Limiting Reaction Step of Equation 5



preequilibrium loss of CO also seems unlikely as we observe that the reaction rate is independent of the rate of argon purge (20–60 mL/min). In addition, an Eyring plot reveals that the entropy of activation of reaction 5 is $\Delta S^{\ddagger} = -26$ eu (Figure 4; $\Delta H^{\ddagger} = 17.3$ kcal mol^{-1}), consistent with a transition state in which an aldehyde molecule is associated with an intact molecule of the dimer, i.e., [**2**·R′CHO]. The direct participation of a four-coordinate rhodium center in a decarbonylation reaction has precedent; $Rh(PPh_3)_2LCl$ (L = DMF, MeCN) is reported to react (stoichiometrically) without prior loss of ligand.[13]

Intermolecular pathways can be ruled out by labeling experiments involving mixtures, e.g., R′CDO and *n*-$C_7H_{15}CHO$, which demonstrate that the alkyl group and the H atom of the resulting alkane are derived from the same molecule of aldehyde. The alkanes produced from such mixtures were of essentially the same isotopic composition (GC/MS) as those resulting from the decarbonylation of separate solutions of the two aldehydes.[16]

The rate of the stoichiometric reaction, eq 2 (i.e., in the absence of an argon purge), is found not to vary significantly for the first 60 min during which time the reaction proceeds to ca. 15% completion (65 °C).[8] This initial rate is found to be approximately equal to that of the catalytic decarbonylation.[18] These observations, and the fact that the catalytic rate is independent of the rate of argon bubbling, argue against the possibility of the reactive catalyst being a minor carbonylated species in equilibrium under the catalytic conditions, for example, $Rh_2(PMe_3)(CO)_3Cl_2$.[8]

The question of the reactive site of the aldehyde molecule can be addressed as follows. Rate-limiting associative cleavage of the bridge by the aldehyde carbonyl group (the C=O double bond or an oxygen lone pair) is consistent with the observed rate law. However, two arguments rule out such a possibility: (1) Because aldehyde concentration is varied in a ketone solvent, the first-order dependence on [aldehyde] would not be expected if carbonyl attack is rate-determining unless the reactivity of the carbonyl group of the ketone is completely negligible versus that of the aldehyde; this seems highly unlikely. (2) A significant and reproducible isotope effect was observed; $k_{RCHO/RCDO} > 1.8$, in independent experiments.[19] The isotope effect can only be reconciled with carbonyl attack prior to C–H bond attack if the carbonyl attack is reversible.[20] However, a preequilibrium involving aldehyde coordinated to a fragment such as $Rh(PMe_3)(CO)Cl$ is inconsistent with the observed first-order dependence on [**2**]. We may thus conclude that in the transition state, which is of the stoichiometry [**2**·R′CHO], partial or complete cleavage of the aldehydic C–H bond has taken place (Chart I). In view of the aforementioned examples of mononuclear four-coordinate decarbonylation reagents, $Rh(PPh_3)_2ClL$,[13] there seems no reason in our case to invoke participation of both metal centers. Instead, we suggest that a simple oxidative addition occurs at one of the two four-coordinate rhodium centers of **2**, similar to the reaction of the related dimer, $Rh_2(PPh_3)_4Cl_2$, with H_2, to give the asymmetric Rh(III)/Rh(I) adduct.[21] The aldehydic C-H bond addition may be followed by or may proceed concertedly with halide bridge cleavage to give the unsaturated species $Rh(PMe_3)(CO)Cl(RCO)H$ which could undergo alkyl migration and then reductive elimination of RH. The fate of the other rhodium center, $Rh(PMe_3)(CO)Cl$, is unknown; the observed kinetics are consistent either with a completely efficient reaction of this fragment with aldehyde (to give a second alkane molecule) or with complete dimerization to give back **2**.

Conclusion

A mechanistic study of a new aldehyde decarbonylation catalyst, **2**, has revealed the nature of the transition state of the turnover limiting step: C–H bond addition to an undissociated molecule of **2**. Although this system affords no obvious practical advantages over the Pignolet system[2] (similar rates are found at similar temperatures), it offers a significant opportunity for optimization or "fine-tuning" based on the mechanistic conclusions. Thus, we are currently attempting to develop both more reactive analogues of **2** and also related monomeric complexes, i.e., $Rh(PR_3)(CO)(halogen)L$. The use of systems like **2** for the reverse reaction, carbonylation, is clearly prohibited by the fact that CO reacts with **2** to give **1** (eq 3). However, related (i.e., four-coordinate Rh(I)) systems which are stable under CO atmosphere should in principle also be able to effect decarbonylation under CO atmosphere. (Such systems, however, may be less reactive than **2** since the reaction of **2** with the abstracted CO molecule may provide a significant driving force for its reactivity.) We have found this to be the case for at least one such system: $Rh(pyridine)(CO)_2Cl$ does catalyze aldehyde decarbonylation under CO atmosphere, and preliminary mechanistic studies indicate that like **2** it reacts via an associative pathway.[22]

Experimental Section

2 was prepared according to the method of Poilblanc.[7] Dodecanal, heptanal, and 2-undecanone were purchased from Aldrich and used after drying over magnesium sulfate and distilling. The catalytic reaction (eq 5) was followed by GC, using a 5% OV-101 80/100 Chromosorb column.

(16) The mass spectrum (GC–MS) of the resulting heptane from these reactions was identical to that from authentic C_7H_{16}; i.e., less than 2% $C_7H_{15}D$ was formed. The mass spectrum of the undecane was nearly identical (<5% deviation) to that resulting from the decarbonylation of R′CDO in the absence of octanal. In both the experiment and the control the resulting undecane did contain significant amounts of R′H (ca. 38%). However, in view of the isotopic composition of the heptane, and the fact that R′H forms in the absence of octanal, it is clear that the protium is not derived from a crossover decarbonylation pathway. Rather, it results from a significant isotopic impurity in the dodecanal[17] (ca. 20% R′CHO; IR, MS, ^{1}H NMR) multiplied by an isotope effect (vide infra) with a possible contribution from H/D exchange with PMe_3 or the alkyl groups. Very similar results were obtained from an experiment with R′CHO and *n*-$C_8H_{17}CDO$.[17]

(17) R′CDO and *n*-$C_8H_{17}CDO$ were synthesized by a published modification of the Rosenmund reaction, R′C(O)Cl or *n*-$C_8H_{17}C(O)Cl$ and D_2 over 5% Pd/C: Burghstahler, A. W.; Weigel, L. O.; Shaefer, C. G. *Synthesis* **1976**, *11*, 767–768.

(18) We have only been able to accurately determine the initial stoichiometric rate based on the formation of rhodium-containing products, $Rh_2(PMe_3)(CO)_3Cl_2$ and $Rh(PMe_3)_2(CO)Cl$,[8] and the disappearance of **2** (IR spectroscopy) rather than on the basis of alkane produced which is less than 1.0 mM. The calculated pseudo-first-order rate constant (65 °C) is 6×10^{-5} s^{-1}, versus 9×10^{-5} s^{-1} for the catalytic reaction. While this discrepancy may be due to a second pathway operative only under the catalytic conditions, we feel that it is more likely due to either (a) experimental error in our IR determination of the concentrations of products in the complicated equilibrium mixture[8] or (b) a significant equilibrium concentration of free CO under these conditions. We are presently trying to determine if such an equilibrium is in effect.

(19) The actual ratio of observed rates in the two independent experiments (R′CHO/R′CDO) was 1.9:1. The deuterated dodecanal contained 20% R′CHO.[17] With *n*-$C_8H_{17}CHO$/*n*-$C_8H_{17}CDO$ (10% *n*-$C_8H_{17}CHO$ impurity) the ratio was 1.8:1. Presumably, with isotopically pure deuterioaldehydes the observed rates would be slightly slower and the ratios thus slightly higher.

(20) Fairly similar isotope effects have been found in the aldehyde decarbonylation studies of refs 2 ($k_H/k_D = 1.6$) and 13 (1.55). Isotope effects for simple, direct, C–H oxidative addition reactions have subsequently been determined and found to generally be rather small ($k_H/k_D < 2$). Thus, the value found in this work (>1.8) and even that of refs 2 and 13 is certainly consistent with a primary isotope effect and not indicative of a secondary effect. In fact, the values for aldehyde decarbonylation are higher than those for simple C–H addition. This is probably due to a late transition state since the addition reactions leading to decarbonylation are endoergic whereas the reactions leading to stable insertion products (and directly measurable C–H-(D) addition isotope effects) are exoergic and the transition states probably contains a relatively intact C–H bond. (a) For the oxidative addition of cyclohexane C–H(D) bonds to $(C_5Me_5)Ir(PMe_3)$ a kinetic isotope effect $k_H/k_D = 1.38$ has been found: Janowicz, A. H.; Bergman, R. G. *J. Am. Chem. Soc.* **1983**, *105*, 3929–3939. (b) For the insertion of $(C_5Me_5)Rh(PMe_3)$ into the C–H(D) bonds of benzene $k_H/k_D = 1.4$ has been found: Jones, W. D.; Feher, F. J. *J. Am. Chem. Soc.* **1986**, *108*, 4814–4819. (c) For insertion of $(C_5Me_5)Rh(PMe_3)$ into hexane C–H(D) bonds, $k_H/k_D = 1.1$: Periana, R. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 7332–7346.

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The identity of the decarbonylation product, undecane, was verified by comparison with an authentic sample (Aldrich) using the OV-101 column and was additionally confirmed by comparison on a 50-m HP-1 (cross-linked methylsilicone gum phase) capillary column where it could be distinguished clearly from undecene. The absence of undecene was checked by taking the GC of the final reaction mixtures on the capillary column. Dodecanal-d_1 and heptanal-d_1 were prepared using the modified Rosenmund reduction method of dodecanoyl chloride developed by Burgstahler.[17] The preparation was done with 16 mL of dodecanoyl chloride, purchased from Aldrich and distilled before use. Prolonged reaction times were necessary (48 h) for completion of the reaction. The product was identified by GC, FTIR, NMR, and GC-MS. All rhodium reactions were conducted under inert atmosphere. High-purity argon was passed through purification towers containing MnO and 4A molecular sieves before being bubbled through catalytic reaction solutions.

All NMR spectra were obtained with a Varian XL-200 spectrometer. IR spectra were obtained with a Mattson Cygnus 100 spectrophotometer. A Varian 3400 GC interfaced with a Finnigan-Mat 8230 high-resolution magnetic sector mass spectrometer, using electron ionization (70 eV), was used for all GC-MS analyses.

Catalytic reactions (eq 5) were carried out in a bubbler constructed of a cell (9-cm length, 2.5-cm diameter) fused to a Vigreux condenser (15 cm) on top of which was attached an inlet/outlet adapter. The inlet was fitted with a Kontes high-vacuum stopcock and extended through a glass capillary tube through the condenser to the bottom of the cell. The outlet was also fitted with a similar stopcock, used to adjust the flow rate, and joined to a flow meter. A GC sampling port (an Ace-Thred adjustable electrode adapter) was placed near the outlet. In a typical experiment, 4 mL of solution is placed in the cell, the flow rate of purified argon is adjusted, and the condenser is cooled with water at 0 °C. To monitor the reaction, the cell is taken out of the oil bath and is immediately placed in an ice bath to quench the reaction. The reaction solution is shaken so as to dissolve any material which might be on the inner walls of the condenser and a sample is taken for GC analysis.

The stoichiometric reaction (eq 2) was monitored by FTIR. Two procedures were followed. The reaction was carried out either (a) in a thermostated IR cell or (b) in an Ace-Thred-fitted cell immersed in a thermostated oil bath. Samples were then transferred by syringe into an IR cell. The reason for the use of the latter procedure was to ensure that temperatures in both the stoichiometric and the catalytic cases were identical. The results from both procedures were in good agreement. The concentration of the alkane (using both procedures) was derived from the concentration of $Rh(PMe_3)_2(CO)Cl$ product and calculated using eq 9,

$$[R'H] = \tfrac{1}{2}\{20\ \text{mM} - y \pm [(-20\ \text{mM} + y)^2 - 8y(10\ \text{mM} + y - y/K_{eq})]^{1/2}\} \quad (9)$$

where y is the concentration of $Rh(PMe_3)_2(CO)Cl$ (mM) as determined spectroscopically. This expression was derived from eq 2 and the equilibrium in ref 8 for a 10 mM initial concentration of **2** (the solution obtained by subtracting the radical expression is used for the early stages of the reaction). The equilibrium constant, $K_{eq} = 0.4$, was determined by adding substoichiometric amounts of carbon monoxide to solutions of **2** and then monitoring the concentrations of $Rh(PMe_3)_2(CO)Cl$ and **2**. This value was in agreement with that obtained by monitoring reaction 2 before completion. We were also able to use an alternative expression to determine the stoichiometric reaction rate, eq 10, where x is the

$$[R'H] = 20\ \text{mM} - 2(x + y) \quad (10)$$

spectroscopically determined concentration of **2**. Equation 10 gave results in agreement with eq 9, but the determination of small changes in [**2**] introduced additional scatter into the data and we therefore relied on eq 9.

C-O stretching frequencies (cm^{-1}) in the infrared spectrum are as follows (dodecanal solvent; extinction coefficient in parentheses in units of M^{-1} cm^{-1}): **1**, 2001 (2200), 2086 (1500); **2**, 1975 (3900); $Rh(PMe_3)_2(CO)Cl$, 1960.5 (2100); $Rh_2(PMe_3)(CO)_3Cl_2$, 2089 (ca. 2400), 2019 (ca. 2500), 1990 (ca. 1800).

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Registry No. 1, 31340-72-4; **2**, 49634-24-4; dodecanol, 112-53-8; undecane, 1120-21-4; deuterium, 7782-39-0.

Total Synthesis of (-)-Hikizimycin Employing the Strategy of Two-Directional Chain Synthesis

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Abstract: Hikizimycin (anthelmycin) is a nucleoside antibiotic and anthelmintic agent that represents the most structurally complex member of the long-chain carbohydrate class of natural products. The undecose moiety of hikizimycin was constructed efficiently by employing the strategy of two-directional chain synthesis. A description of this approach, including the advantages and challenges, is provided. In addition, the methods that were utilized to solve the remaining problems associated with the synthesis of hikizimycin are reported. The synthesis confirms the assigned structure of the natural product.

Introduction

Hikizimycin (also named anthelmycin) is a nucleoside disaccharide that was isolated from the fermentation broth of *Streptomyces* A-5[1] and *Streptomyces longissimus*[2] and shown to possess significant anthelmintic activity against a variety of common parasites.[3] Hikizimycin belongs to an important class of natural products that incorporate, within their structure, long-chain carbohydrate moieties.[4] These molecules, which include tunicamycins,[5] herbicidins,[6] and neuraminic acids,[7] have stimulated much interest due to their complex structures and to their ability to exert a profound influence on a variety of biological processes. Hikizimycin is comprised of a cytosine base, a 3-

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