$(PCy_3)(pyridine)_x][Fe_2(CO)_8(\mu\text{-}CuPCy_3)]$ (**4c**). Pyridine can be removed by prolonged pumping under high vacuum, and **1** is recovered.

Addition of 1 equiv of $[Cu(CH_3CN)_4]PF_6$ and PCy_3 to **4b** also yields **1**. On the other hand, the reaction between **1** and $Na_2[Fe_2(CO)_8]$ in THF results in **4a**. Sodium amalgam reacts with **1** to reduce Cu(I) in the cluster to Cu(0). The overall reaction proceeds in two steps as shown in Scheme II. Similarly, the reaction of **1** with KH reduces Cu(I) and proceeds in two steps. In both reactions above, the intermediate products are sodium and potassium salts of **4** (**4a,d**).

Both **1** and **4** are protonated by $HBF_4{\cdot}OEt_2$. Protonation of **1** causes the reduction of Cu(I) to Cu(0) and the oxidation of $[Fe_2(CO)_8]^{2-}$ to $Fe_3(CO)_{12}$. Protonation of **4a** with 1 equiv of $HBF_4{\cdot}OEt_2$ produces $^1/_2$ equiv of **1** and a mixture of intractable materials. Protonation of **4a** with HCl was also performed in THF-d_8 at −80 °C. The reaction was monitored by variable-temperature ^1H and ^{31}P NMR spectroscopy. The attempt to observe possible intermediate products $[(\mu\text{-}H)Fe_2(CO)_8(\mu\text{-}CuPCy_3)]$ and $H_2Fe_2(CO)_8$ failed; instead, **1** was observed even at −80 °C. The other products or decomposed material could not be definitely identified.

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Supplementary Material Available: Listings of calculated hydrogen atom positional parameters, anisotropic thermal parameters, bond distances, and bond angles for **1**, **3**, **4b**·0.5THF, and **7** (28 pages); listings of structure factor amplitudes (168 pages). Ordering information is given on any current masthead page.

Palladium(II)-Catalyzed Exchange and Isomerization Reactions. 14.[1] Kinetics and Stereochemistry of the Isomerization and Water Exchange of 2-(Methyl-d_3)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol in Aqueous Solution Catalyzed by $PdCl_4^{2-}$: Two New Mechanistic Probes for Catalytic Chemistry

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The isomerization of 2-(methyl-d_3)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol (**2a**) into an equilibrium mixture of **2a** and 2-methyl-4-(methyl-d_3)-1,1,1,5,5,5-hexafluoro-3-penten-2-ol (**2b**) in aqueous solution was studied by ^1H and ^2H NMR, under the Wacker conditions of low chloride (<1.0 M) and acid (<0.5 M) concentrations. The rate expression under these conditions is rate = $k_i[PdCl_4^{2-}][\mathbf{2a}]/[H^+][Cl^-]^2$, with $k_i = 1.05 \times 10^{-6}$ s^{-1}. The exchange of **2a** with ^{18}O-enriched water was studied by ^{13}C NMR using isotope-induced shift methods and the rate of exchange was found to be the same as the rate of isomerization within experimental error. This result requires that isomerization and exchange occur by a hydroxypalladation route, rather than through palladium(IV)-π-allyl intermediates. The rate expression for isomerization at low chloride concentrations is identical with the rate expression for the Wacker oxidation of ethene to acetaldehyde. This result is inconsistent with a proton inhibition arising from equilibrium hydroxypalladation but is consistent with proton loss from the Pd(II) coordination sphere in a preequilibrium step followed by a cis hydroxypalladation occurring from within the coordination sphere of the palladium(II). Stereochemical studies were conducted with chiral (*E*)-**2a**. The observed result was the formation of chiral **2b** with the opposite configuration of the initial **2a**. This result is also consistent only with cis hydroxypalladation; so both kinetic and stereochemical mechanistic probes give the same result.

Introduction

The fact that most catalytic reactions involve several steps makes the interpretation of kinetic data in terms of mechanisms ambiguous in such complicated systems. For instance, in the Wacker process for the oxidation of olefins to aldehydes and ketones in aqueous solution by $PdCl_4^{2-}$, the kinetic rate expression, given by eq 1, can be interpreted in several ways. Although most workers agree the $[Cl^-]^2$ inhibition results from displacement of two chlorides by olefin and water in the Pd(II) coordination sphere in rapid preequilibria, there is considerable disagreement as to the source of the proton inhibition. The kinetics are consistent with (a) cis addition by coordinated hydroxyl in the slow step, eq 2, or (b) trans attack by external water in an equilibrium step, eq 3.[2] In the second mechanism, decomposition of the adduct is rate determining.

$$\text{rate} = k[PdCl_4^{2-}][\text{olefin}]/[H^+][Cl^-]^2 \qquad (1)$$

The arguments in favor of one or the other of the proposed mechanisms are based on (1) stereochemical results,[3-5] (2) comparisons of kinetic and competitive isotope

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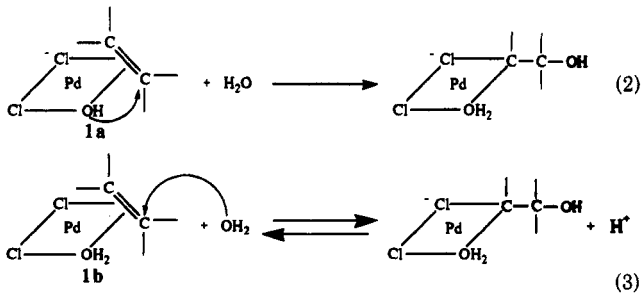


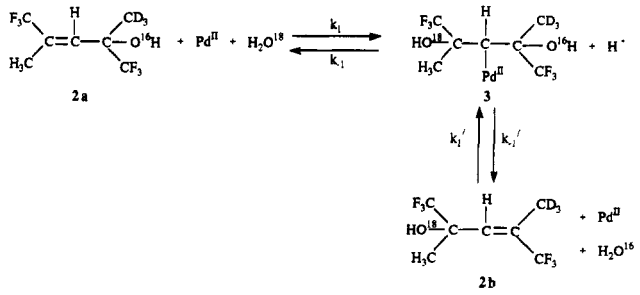
effects,[6] (3) secondary isotope effects,[6c,7] and (4) demonstration of the rate-determining step by the oxidation of deuterated allylic alcohols that will undergo measurable isomerization if hydroxypalladation is reversible.[8] All of these methods have their shortcomings. Thus in the case of (1), since the usual carbonyl products do not give stereochemical information, the reaction conditions must be changed drastically to obtain the type of products that give stereochemical information. There is a strong possibility that such changes in conditions may alter the mode of hydroxypalladation. In one case[4] such a mechanistic alteration has been demonstrated.[9] With (2) and (3) the arguments are based on subtle effects, and in the case of (4), the demonstration is definitive but it is an argument against a mechanism and the evidence provides no positive data in favor of a certain reaction path. Thus there is a need for mechanistic probes that will allow the determination of the kinetics and stereochemistry of oxypalladation independent of the complication of oxidation.

The strategy for designing a kinetic probe involves studying the kinetics of a mechanistically very simple reaction for which the rate-determining step is known to be hydroxypalladation. This reaction is the isomerization and water exchange of an allylic alcohol made unsymmetrical by substituting a methyl-d_3 for a regular methyl at one end of the allylic alcohol. Now, in addition, this alcohol cannot have any hydrogens at the end carbons or else it would undergo oxidation by Wacker chemistry to give carbonyl products. Thus a tetrasubstituted allylic alcohol is required. It was found that a 1,1,3,3-tetramethyl allylic alcohol was unstable to water addition under the acid conditions of the Wacker reaction but 2-(methyl-d_3)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol (**2a**) gave the required hydrolytic stability. The reason the rate-determining step for the water exchange and isomerization of this olefin is hydroxypalladation can be seen from examination of Scheme I. In a completely symmetrical exchange such as this one, the value of $k_1 = k_1'$ and $k_{-1} = k_{-1}'$, so half the time that **2a** is converted to **3**, **3** reverts to **2a**, and half the time it goes to **2b**. Thus the rate depends only on the rate of formation of **3**, not on its equilibrium concentration. The important result is that if hydroxypalladation occurs by an equilibrium process such as shown in eq 3, the proton inhibition term will not appear in the rate expression and the rate expression for exchange will be given by eq 4.[4]

$$\text{rate} = k[PdCl_4^{2-}][\text{olefin}]/[Cl^-]^2 \qquad (4)$$

The stereochemical probe involves the determination of the optical and geometric configuration of the isomerization product formed from one geometric isomer of a chiral allylic alcohol, which has a high barrier to free rotation. The allyl alcohol chosen for the present studies was actually the *E* isomer of chiral **2a**. The trifluoromethyl groups that were required for hydrolytic stability also provided steric hindrance, which resulted in restricted rotation. Computer calculation of energies show that the OH group is restricted to a position facing one plane of the molecule, since the OH and CF_3 groups are forced into a configuration in which they are furthest from the CH_3 group.[10] The face to which the Pd(II) is directed will depend on the absolute configuration of the starting alcohol. The directing influence of the hydroxyl group is predicted from Cram's rule[11] and has been confirmed for several epoxidation[12] as well as other reactions.[13] Partial 1,2 chirality transfer has been demonstrated for the palladium(II)-catalyzed addition of a phenyl group (Heck reaction) to chiral 3-methylbut-3-en-2-ol.[14]

Scheme I



The possible reaction sequences for the (−)-(*R*)-(*E*)-**2** isomer are outlined in Scheme II. Trans hydroxypalladation gives the adduct **3a**, which, by the principle of microscopic reversibility, would undergo dehydroxypalladation to give **2b**, which has the same *R* configuration corresponding to the starting alcohol but is the *Z* geometric isomer. On the other hand, cis addition gives the intermediate **3b**, which decomposes to the product **2b** with the *S*-(+) configuration and the *E* geometric configuration.

The amount of isomerization, as determined by NMR, will be compared with the amount of *S*-(+) isomer formed. Since reisomerization would give back the starting configuration by both types of addition, with cis addition the amount of isomerization should equal the amount of *S*-(+) isomer formed. For trans addition, the *R*-(−) configuration should be formed but geometric isomerization should be observed. Note that the determination of absolute configuration is not crucial to this study since the two chiral centers are chemically the same except for the small effect of the substitution of a methyl-d_3 for a nondeuterated

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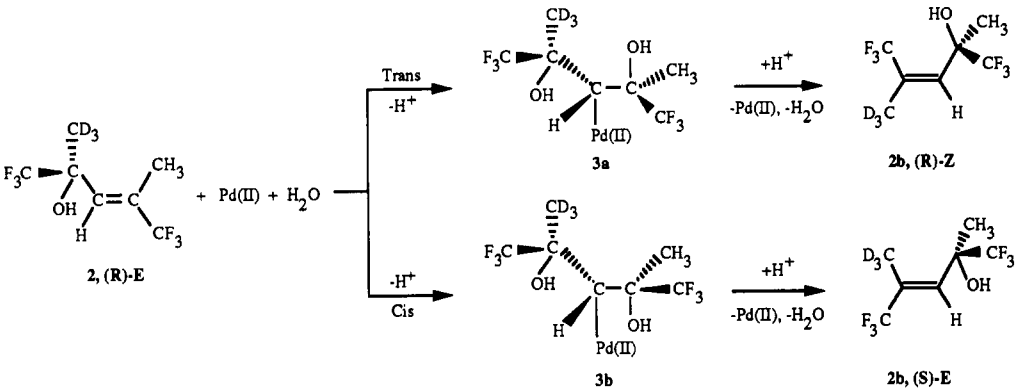
Scheme II



methyl. This difference would not have an appreciable effect on rotation or GLC retention times of their esters. Thus all that is needed is a knowledge of whether retention or inversion of the chiral center has occurred and if geometric isomerization takes place. It is important to emphasize that the experiment requires that the rate of optical and/or geometric change be the same as the rate of isomerization, since this result ensures only one type of hydroxypallation is occurring. Thus, assume that rotation is not restricted to any extent. In that case either trans or cis hydroxypalladation, which could occur at both faces of the olefin, would also give eventual racemization because both will give the (*R*)- and (*S*)-**2b** isomers. *However, both types of addition would give a rate of formation of* (*S*)-***2b***, *which is one-half that of isomerization, because each time* (*S*)-***2b*** *is formed an equal amount of* (*R*)-***2b*** *is formed.*

Results

All kinetic runs were carried out at 25 °C. Preliminary control experiments revealed that there was no oxidation evident over 24 h under all reaction conditions. There was no acid- or chloride-catalyzed isomerization observed in the absence of $PdCl_4^{2-}$. Under all reaction conditions dehydration of the alcohol species was not observed.

The isomerization data are given in Table I. The data clearly indicate an acid inhibition term. In runs 5–7, for which $[PdCl_4^{2-}]$ and $[Cl^-]$ remain constant, the rate decreases steadily as $[H^+]$ increases. The fact that the values of k_i, which were calculated from eq 5, remain constant

$$\text{rate} = k_i[PdCl_4^{2-}][C_7H_5D_3F_6O]/[H^+][Cl^-]^2 \quad (5)$$

indicate the rate expression is of the form of eq 1 rather than eq 4. The value of k_i is 1.05×10^{-6} M^2 s^{-1}.

The ^{18}O exchange rates were measured using the ^{18}O isotope effect on the ^{13}C NMR.[15] Rate constants for exchange under two sets of reaction conditions are also given in Table I. The value of k_{ex}, also calculated on the basis of eq 5, is the same as the value of k_i. The fact that $k_i = k_{ex}$ is important because this result is predicted by Scheme I but is *not* predicted by an exchange mechanism involving Pd(IV) π-allyl intermediates, a mechanism that has previously been observed for a Pd(II)-catalyzed isomerization.[16] As shown in eq 6, this last mechanism predicts that the rate of isomerization is *half* the rate of exchange; so the two mechanisms can be distinguished if both exchange and isomerization are measured.[17] The results in the present work clearly indicate the reaction mechanism is the hydroxypalladation–dehydroxypalladation route given by Scheme I.[18]

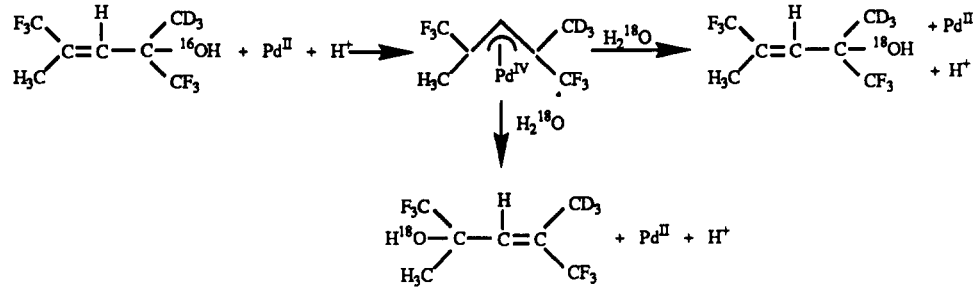
Table I. Rates of Isomerization and ^{18}O Exchange of 2-(Methyl-d_3)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol under Wacker Conditions[a]

run	$[PdCl_4^{2-}]$	$[H^+]$[b]	$[Cl^-]$[c]	10^5k_{obsd}, s^{-1}	$10^6(k_i$ or $k_{ex})$,[d] s^{-1}
			Isomerization		
1	0.007	0.05	0.5	7.7	1.4
2	0.015	0.05	0.5	13	1.1
3	0.008	0.10	0.25	15	1.2
4	0.016	0.10	1.0	1.3	0.81
5	0.008	0.05	0.5	6.0	0.94
6	0.008	0.15	0.5	2.1	0.98
7	0.008	0.20	0.5	1.5	0.91
8	0.008	0.10	0.20	23	1.2
9	0.008	0.10	0.75	1.7	1.2
10	0.004	0.10	0.50	1.5	1.0
11	0.032	0.40	0.50	3.5	1.1
					av 1.1
			^{18}O Exchange		
12	0.008	0.10	0.5	3.62	1.1
13	0.008	0.05	1.0	1.47	0.92

[a] All runs are in aqueous solution at 25 °C; quinone (0.10 M) added to all runs to prevent the formation of Pd(0). In all runs initial $[C_7H_5D_3F_6O]$ = 0.044 M. $LiClO_4$ was added to bring the ionic strength (μ) to 2.0 M. [b] Added as $HClO_4$. [c] Added as LiCl. [d] k_i and k_{ex} were calculated for runs 1–13, assuming the rate expression given in eq 1 is operative and $[PdCl_4^{2-}]$, $[H^+]$, and $[Cl^-]$ are constant for each run.

The enantiomers of **2** were resolved by preparative GLC of their (*S*)-(+)-α-(trifluoromethyl)phenylacetate ((+)-MTPA) esters. Their absolute configuration was assigned by the induced chemical shift of the signals of the methoxy

(15) Risley, J. M.; Etten, R. L. *J. Am. Chem. Soc.* **1979**, *101*, 252.
(16) Ng, F. T. T.; Henry, P. M. *J. Org. Chem.* **1973**, *38*, 3338.
(17) The fact that $k_i = k_{ex}$ also eliminates a mechanism proposed by a referee: palladium(II) acts as a Lewis acid to remove the hydroxyl group and give an allylic carbonium ion, which reacts with water to give exchange and isomerization. Such a mechanism would also predict that k_i is $^1/_2k_{ex}$.
(18) A referee has suggested an S_N2' mechanism in which the hydroxide attacks olefin in the π-complex **1b**, shifting the double bond without the intermediate hydroxypalladation adduct, to give the observed isomerization. The only role of the palladium would be as a Lewis acid catalyst to remove the alcohol hydroxyl. It is not clear why such a mechanism should be so stereospecific. Also the preferred stereochemistry would seem to be addition of hydroxide on the face of the olefin opposite to that of the Pd(II), which is not the observed result. In addition it is not clear why the kinetics should follow the Wacker rate expression. These kinetics require that the $PdCl_4^{2-}$ first form a π-complex with the olefin, releasing a chloride (K_1), followed by replacement of a second chloride by H_2O (K_2) to give **1b**, which is attacked by hydroxide. In any case this mechanism can be shown to be untenable because the rate of the hydroxide attack on **1b** would have to be of the order of a diffusion-controlled process in aqueous solution. For space reasons a detailed calculation will not be given here but has been given elsewhere.[19] If maximum values of 0.5 for K_1 and 0.025 for K_2 are used, it can be shown that the rate of hydroxide attack must be 8×10^{15} times faster than k_i in Table I. Since $k_i = 10^6$ s^{-1}, this rate must be $\sim 10^9$ s^{-1} or about 10 times faster than a diffusion-controlled process in aqueous solution and thus impossible.
(19) Wan, W. K.; Zaw, K.; Henry, P. M. *Organometallics* **1988**, *7*, 1677.



(6)

Table II. Stereochemistry of the Isomerization of (*E*)-2-(Methyl-d_3)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol under Wacker Conditions[a]

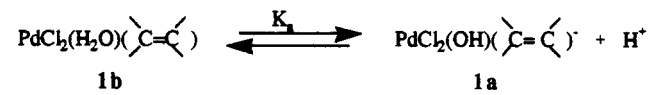
substrate				product		
config	% ee[b]	[Cl⁻]	[catalyst]	% isomerization[c]	% *S*[d]	% *R*[d]
R	100	0.10	$PdCl_4^{2-}$	30	32.5[e]	67.5
R	100	0.05	$PdCl_4^{2-}$	48	50.0[e]	50.0
S	100	0.10	$PdCl_4^{2-}$	25	72.5	27.5[e]
S	100	0.05	$PdCl_4^{2-}$	50	50.0	50.0[e]

[a] Acid and $PdCl_4^{2-}$ concentrations were kept constant at 0.20 and 0.05 M, respectively. [b] Determined by ^1H NMR of the OCH_3 singlet of the MTPA ester and GC peaks of the *RR* and *RS* diastereomers respectively. [c] This is determined by ^2H NMR of the CD_3 resonance. [d] Determined by GC retention times of the MTPA diastereomers. [e] Obtained as the *E* geometric isomer.

protons by $Eu(fod)_3$ shift reagent.[20] The *E* configuration of **2** was assigned on the basis of ^1H NOE experiments on the ketone from which **2** was prepared as well as differences in the NMR and IR of the two geometric isomers due to the more hindered rotation in the *Z* isomer. The product, **2a**, was resolved as above and the absolute configuration of the enantiomers assigned in the same fashion. The two optical isomers of **2** were regenerated by reaction with $LiAlH_4$ and isomerized under the conditions of the Wacker reaction. The product, **2b**, was isolated, the (*S*)-(+)-MTPA esters were again prepared, and the optical purity was determined by analytical GLC and ^1H NMR. The results are summarized in Table II. These results clearly indicate that isomerization occurs with inversion of configuration. According to Scheme II, this result is consistent only with cis hydroxypalladation under the conditions of the isomerization. These are the same as the Wacker oxidation conditions.

Discussion

For the first time in mechanistic studies of catalytic palladium(II) both kinetics and stereochemistry have been determined under the same reaction conditions and, as might be expected, they reinforce each other. First consider the kinetic studies on the exchange and isomerizations reactions. As discussed in the Introduction, an equilibrium hydroxypalladation mechanism for the exchange, such as that shown show in eq 3, would have predicted a rate expression without a proton inhibition term, eq 4. The fact that the actual rate expression is eq 5, which is of the same form as the Wacker rate expression, eq 1, requires that the proton loss in the exchange studies must occur prior to the hydroxypalladation step. A mechanism that will fulfill this requirement would involve two initial fast equilibria to replace two chlorides by olefin and water forming the aquo π-complex **1b**, which would then release a proton in a acid–base equilibrium shown in eq 7 to give the hydroxo π-complex, **1a**. The hydroxypalladation step would then involve the cis hydroxy insertion shown in eq 2.



(7)

On the other hand the stereochemical results also provide definite independent evidence for a cis hydroxypalladation. The most likely cis insertion mechanism in light of the rate expression is that given by eq 2.

Although the present results cannot be taken as absolute evidence for cis hydroxypalladation in the Wacker reaction becuase the two reactions are different, they certainly provide very strong evidence for this type of addition. The reaction conditions are the same for both reactions as are the rate expressions. It is difficult to imagine that Pd(II) would add one way for exchange and another for oxidation. Also other evidence suggests cis addition. A very interesting study by Bryndza involves the reaction of a methylplatinum(II) compound containing both a coordinated methoxide and methyl with tetrafluoroethylene to give a methoxyplatination adduct.[21] By use of CD_3OD in the solvent, Bryndza was able to demonstrate that the methoxide originated in the coordination sphere of the Pt(II) and that the methoxide insertion was at least 3 orders of magnitude faster than the methyl insertion. This is a very significant result since Pt(II) and Pd(II) chemistries are analogous and the more stable Pt(II) organometallics are often used as models for Pd(II) catalytic chemistry. This result is important in the present context because it demonstrates the ease of methoxide insertion in a d^8 complex and, in fact, it goes much more readily than carbon insertion. This facility could explain the reason Pd(II) might prefer the mechanism given by eq 2. Secondary isotope effects with $CH_2{=}CD_2$ have also been used to imply the mechanism of hydroxypalladation.[6c,7] The product ratio of $CH_2DCDO/CHD_2CHO = 0.89$ has been interpreted in terms of rate-determining hydroxypalladation but not equilibrium hydroxypalladation, an interpretation compatible with the present results.

In another study Bäckvall and co-workers have published calculations suggesting hydroxide ligands will always migrate more slowly to coordinated olefins than an alkyl ligand on four-coordinate Pd(II) complexes.[22] The authors are not in a position to judge the validity of these calculations but the results of the present study certainly appear inconsistent with them.

How can the present results be reconciled with the elegant stereochemical studies of Bäckvall, Åkermark, and

(20) (a) Yamaguchi, S.; Yasuhara, F.; Kabuto, K. *Tetrahedron* **1976**, *32*, 1363. (b) Yamaguchi, S.; Yasuhara, F. *Tetrahedron Lett.* **1977**, 89. (c) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1963**, *34*, 2543. (d) Dale, D. L.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.

(21) Bryndza, H. E. *Organometallics* **1985**, *4*, 406.

(22) Bäckvall, J. E.; Bjorkman, E. E.; Pettersson, L.; Siegbahn, P. *J. Am. Chem. Soc.* **1984**, *106*, 4369.

Ljunggren, who, using $CuCl_2$ to trap the intermediate hydroxypalladation adduct to give 2-chloroethanol, showed that the addition was trans by the configuration of the product from ethene-*1,2-d*$_2$?[4] Their reaction conditions involved high chloride concentrations, which greatly retarded the rate of oxidation. It was later shown that under these conditions the main process was a nonoxidative exchange and isomerization reaction, whose rate expression is given by eq 8.[9] This rate expression is consistent only

$$\text{rate} = k[PdCl_4^{2-}][\text{olefin}]/[Cl^-] \quad (8)$$

with a trans attack of water in a matter similar to that shown in eq 3 but with a chloride replacing the aquo ligand in **1b**. The extra chloride must stabilize the hydroxypalladation adduct against oxidative decomposition to carbonyl product in the absence of $CuCl_2$, but apparently $CuCl_2$ can intercept the intermediate causing it to decompose to 2-chlorethanol. Thus there is no conflict between the present studies and those at high chloride concentrations. The kinetics simply indicate different modes of hydroxypalladation are taking place under the two sets of conditions. If two different types of addition can occur in water it would be expected that changing the solvent might also have a profound effect on the mode of oxypalladation. Thus both cis[23] and trans[24,25] addition have been observed in nonaqueous and mixed aqueous solvents. Even the identity of the olefin can be important under the Wacker oxidation conditions. For the cyclic olefins, cyclohexene and 2-cyclohexenol, the rate expression for oxidation is not eq 1 but rather eq 8, indicating the mode of hydroxypalladation is different from that for acyclic olefins.[26-28] The kinetics, as well as deuterium-labeling studies,[28] are consistent with trans addition.

The important point is that general statements to the effect that oxygen nucleophiles attack olefins in a trans fashion are meaningless because the mode of addition could depend on the olefin and reaction conditions. The final proof of the mechanism of the Wacker reaction must be stereochemical studies under the conditions of rapid olefin oxidation to aldehydes and ketones. This will not be a simple task because the products are carbonyl, but, in order to be valid, the stereochemical studies must be carried out with an olefin that has been shown to obey the Wacker kinetics given in eq 1.

Experimental Section

Starting Materials. The palladous chloride was purchased from AESAR. 1,1,1-Trifluoroacetone, sodium (pellets in xylene), phosphorus pentoxide, and methyl-d_3-magnesium iodide (Aldrich, Sure seal) were purchased from Aldrich Chemicals and used without further purification. [^{18}O]water (1.5 atom % and 97 atom %) was obtained from MSD Isotopes Inc. All other chemicals were of reagent grade.

Isomerization Kinetics. The isomerization of 2-(methyl-d_3)-4-methyl-1,1,1,4,4,4-hexafluoro-3-penten-2-ol was monitored by using ^{2}H NMR. The reaction was run on a 10-mL scale. Four experimental points were taken for each run. The first three 2-mL aliquots of the mixture were extracted with 3–5-mL portions of methylene chloride. For the final sample the remainder of the reaction mixture was used. After the mixture was dried with $MgSO_4$ and filtered and the methylene chloride evaporated at room temperature, the crude concentrate was dissolved in $CHCl_3$ and the solution analyzed by ^{2}H NMR, using a Varian VXR 300 NMR instrument. The percent isomerization was determined by comparing the area of the singlet peak at 1.6 ppm corresponding to CD_3 in 2-(methyl-d_3)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol with the area of the singlet peak at 2.2 ppm corresponding to CD_3 in 2-methyl-4-(methyl-d_3)-1,1,1,5,5,5-hexafluoro-3-penten-2-ol. $CDCl_3$ (7.24 ppm) was used as internal standard. The data were plotted as a reaction approaching equilibrium.[29a] A plot of ln (50% − % isomerization) versus time was made on semilog paper and the half-life read off at the 25% point. Since the value of the equilibrium constant for the isomerization is equal to 1, the rates of the forward and the reverse reactions are identical and the value of the slope of ln (50% − % isomerization) = $-2k_{obsd}$. The value of k_i was calculated by assuming the following rate expression is the correct one: $k_{obsd} = k_i[PdCl_4^{2-}]/[H^+][Cl^-]^2$.

^{18}O Exchange Kinetics. The experimental procedures were similar to those for the isomerization studies. The ^{18}O isotopic effect on the ^{13}C NMR was a useful tool in studying the exchange kinetics of this system.[15] An upfield ^{18}O isotopic shift of the alcohol carbon was obtained, which was dependent on the amount of ^{18}O in the molecule. After suitable amounts of the $HClO_4$, Li_2PdCl_4, and LiCl stock solutions were mixed, the solution was diluted with a mixture of 1.5 atom % and 97 atom % water-^{18}O. ^{13}C NMR were run on the Varian VXR 300 NMR. Approximately 3000 transients gave the required sensitivity. The percent ^{18}O in the alcohol mixture [2-(methyl-d_3)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol and 2-methyl-4-(methyl-d_3)-2-(hydroxy-^{18}O)-1,1,1,5,5,5-hexafluoro-3-pentene] was determined by a comparison of the intensities of the ^{13}C parent peak at 74 ppm ($^2J_{FC}$ = 3 Hz) with the intensities of the product peak at the same resonance, but shifted upfield by 0.08 ppm. Control experiments in the absence of Pd(II) indicated that there was no observable acid-catalyzed exchange. The data were treated by the equation for isotopic exchange.[29b] From the known amount of $H_2{}^{18}O$, $H_2{}^{16}O$, and allyl alcohol, the percent ^{18}O at equilibrium could be calculated and thus the fraction of exchange, F, at each sampling time. Plots of log $(1 - F)$ versus time on semilog paper were linear. From the slope the value of k_{obsd} (=R in ref 29b) was then calculated from eq 9. The value of k_{ex} was then calculated from k_{obsd}, assuming that eq 1 is the correct rate expression.

$$k_{obsd} = \text{slope}\,\frac{([H_2{}^{18}O] + [H_2{}^{16}O])[\text{allyl alcohol}]}{([H_2{}^{18}O] + [H_2{}^{16}O]) + [\text{allyl alcohol}]} \quad (9)$$

Preparation of 4-Methyl-1,1,1,5,5,5-hexafluoro-4-hydroxypentan-2-one.[30] One gram atom of sodium pellets was prepared in xylene and the xylene removed by means of a sintered-glass filterstick. The sodium pellets were washed twice with ethyl ether and covered with 200 mL of anhydrous ethyl ether. With vigorous stirring 60 g (1.3 mol) of absolute ethanol was added to the sodium over 30 min. To this well-stirred ether solution of sodium ethoxide, whose temperature was kept below 0 °C, was added 100 g (0.89 mol) of 1,1,1-trifluoroacetone. After the solution had been stirred for 1–2 h, it was poured into a mixture of 100 mL of concentrated sulfuric acid and 1000 g of ice. The solid hydrate was filtered and the aqueous layer neutralized with sodium hydroxide solution and extracted with ethyl ether solvent. Both the residue and the ether extract were combined and distilled, giving 69% yield of crude condensation product, bp 78–98 °C. This crude product was distilled over P_2O_5 giving an overall yield of 65%, bp 82 °C. 300 MHz ^{1}H NMR ($CDCl_3$): δ 1.52 (s, 3 H), 2.88, 3.25 (AB quartet, J_{AB} = 18 Hz, 2 H). ^{13}C ($CDCl_3$): δ 20, 40, 73 ($^2J_{FC}$ = 3 Hz), 78 ($^2J_{FC}$ = 3 Hz), 115 ($^1J_{FC}$ = 14 Hz), 125 ($^1J_{FC}$ = 14 Hz), 189. IR (neat): 3500, 1770, 1200 cm^{-1}.

Preparation and Characterization of (*E*)- and (*Z*)-4-Methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-one. To 20 g of 4-hydroxy-4-methyl-1,1,1,5,5,5-hexafluoro-2-pentanone was added

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dropwise 10 mL of 20% oleum over 15 min. The mixture was refluxed for 6 h and distilled, giving 18 g (91%) of product with an E/Z ratio of 95.5:4.5. These conformers were separated by GC on a 20 ft × 0.85 in. DCQF-1 column, at 120 °C, with a helium flow rate of 20 mL/min., after fractional distillation.

The E isomer had a boiling point of 76 °C and a retention time of 12 min. ^{1}H NMR ($CDCl_3$): δ 2.41 (s, 3 H), 6.92 (s, 1 H) ^{1}H NMR NOE experiment: irradiation at δ 6.92 (vinyl H) produces at 2.41 (1.6%, methyl). ^{13}C ($CDCl_3$): δ 16, 117, 119, 121, 150, 180. IR (neat): 3100, 2960, 1735, 1650, 1200, 1100, 735 cm^{-1}. Anal. Calcd for $C_6H_4F_6O$: C, 34.97; H, 1.96. Found: C, 34.91, H, 1.90.

The Z isomer had a boiling point of 95 °C and a retention time of 33 min. Spectroscopic data for the Z isomer are as follows. ^{1}H NMR ($CDCl_3$): δ 1.74 (s, 3 H), 6.00 (s, 1 H) ^{1}H NMR NOE experiment: irradiation at δ 6.92 (vinyl H) produces enhancement at 1.74 (36%, methyl). ^{13}C ($CHCl_3$): δ 20, 80, 96, 119.5, 120, 122, 124, 128, 144. IR (neat): 3110, 3000, 2960, 1750, 1690, 1635, 1180, 735 cm^{-1}. Anal. Calcd for $C_6H_4F_6O$: C, 34.97; H, 1.96. Found: C, 35.05; H, 1.63.

The structures of the two isomers were assigned on the basis of the NOESY experiment and the fact that the complicated IR and NMR spectras of the Z isomer could be explained by the larger barrier to rotation in this isomer. Calculations show that the barrier to rotation is twice as high for the Z isomer as for the E isomer. This would explain the two carbonyl bands (1680 and 1750 cm^{-1}) and the complicated ^{13}C and ^{1}H NMR's for the Z isomer.

Preparation of (*E*)-2-(Methyl-d_3)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol. To 15 mL of 1.0 M (0.015 mol) methyl-d_3-magnesium iodide in anhydrous ethyl ether was added 1.82 g (0.0081 mol) of (*E*)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-one under a flow of nitrogen. The solution was stirred for 30 min and hydrolyzed with 100 mL of 5% hydrochloric acid. The aqueous layer was separated and neutralized with a saturated solution of sodium carbonate and extracted with two 50-mL portions of ethyl ether. The ether layers were combined, washed with a saturated solution of sodium sulfite, dried (anhydrous magnesium sulfate), and distilled, giving 69% yield of 2-(methyl-d_3)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol, bp 76 °C. 300-MHz ^{1}H NMR ($CDCl_3$): δ 2.12 (s, 3 H), 3.40 (s, OH), 6.18 (s, 1 H). ^{2}H ($CHCl_3$): δ 1.49 (s, 3 D). ^{13}C ($CDCl_3$): δ 12, 22 (CD_3), 74 ($^2J_{FC}$ = 3 Hz), 124 ($^1J_{F2C}$ = 14 Hz), 126 ($^1J_{FC}$ = 14 Hz), 129, 133 ($^2J_{FC}$ = 3 Hz). IR (neat): 3450, 3020, 2900, 2250, 1150 cm^{-1}. Anal. Calcd for $C_7H_5D_3F_6O$: C, 36.37; H, 3.55. Found: C, 36.87; H, 3.56.

Preparation of (*S*)-(+)-α-Methoxy-α-(trifluoromethyl)-phenylacetyl Chloride ([(+)-MTPA-Cl]).[20] (*R*)-(+)-α-Methoxy-α-(trifluoromethyl)phenylacetic acid ((*R*)-(+)-MTPA), 41 g, thionyl chloride, 75 mL (distilled practical grade), and sodium chloride, 0.5 g, were refluxed together for 50 h. After excess thionyl chloride was removed by vacuum evaporation, the residue was distilled to give 43.8 g of (*S*)-(+)-MTPA-Cl, 90% yield. bp = 54–56 °C (1mm), $[\alpha^{22}_D]$ = 128.7 ± 0.2°.

Preparation and Resolution of (*E*)-2-(Methyl-d_3)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-yl α-Methoxy-α-(trifluoromethyl)phenylacetate. (*E*)-2-(Methyl-d_3)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol, 0.3078 g (0.148 mmol), and distilled (*S*)-(+)-MTPA-Cl, 0.0379 g (0.15 mmols), were mixed in CCl_4, 5 drops, and dry pyridine, 5 mL, and allowed to reflux for 12 h. Water, 1 mL, was added and the reaction mixture transferred to a separatory funnel containing 20 mL of ether. The ether solution was washed successively with dilute HCl, saturated $NaHCO_3$, and water. It was then dried ($MgSO_4$), filtered, and vacuum evaporated. The residue was dissolved in $CDCl_3$ for NMR studies. 300-MHz ^{1}H NMR ($CDCl_3$): δ 2.13 (s, 3 H), 3.45 (m, 3 H), 7.3–7.7 (m, 5 H). ^{13}C ($CDCl_3$): δ 16, 33, 53, 56, 74, 85, 96, 123, 126, 127, 128, 130, 131, 133, 161.

The diastereomers were separated by GC using a 20 ft × 0.21 in. DCQF-1 column at 185 °C and flow rate of 60 mL/min. Retention times were 114 min for the RS diastereomer and 138 min for the RR diastereomer. Eu(fod)$_3$ shift studies were done in the usual manner and subsequent hydrolysis with $LiAlH_4$ revealed that (−)-*R*-*E* had $[\alpha^{22}_D]_{max}$ = −9.3 ± 0.3° (*c* 2.0, $CHCl_3$) and (+)-*S*-*E* had $[\alpha^{22}_D]_{max}$ = +9.5 ± 0.1° (*c* 2.0, $CHCl_3$).

Preparation and Resolution of (*Z*)-2,4-Dimethyl-1,1,1,5,5,5-hexafluoro-3-penten-2-yl α-Methoxy-α-(trifluoromethyl)phenylacetate. The alcohol, 2,4-dimethyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol was prepared in the usual manner by Grignard reaction of CH_3MgI with (*Z*)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-one. 300-MHz ^{1}H NMR ($CDCl_3$): δ 1.55 (3 H), 2.1 (s, 3 H), 2.7 (OH), 6.15 (s, 1 H). ^{13}C ($CDCl_3$): δ 11, 15, 20, 74, 118, 121, 128.5, 132.

The MTPA diastereomers were synthesized by the previously described procedure. 300-MHz ^{1}H NMR ($CDCl_3$): δ 1.5–1.7 (3 H), 2.1 (s, 3 H), 3.7 (s, 3 H), 5.9–6.3 (1 H), 7.4–7.8 (m, 5 H). ^{13}C ($CDCl_3$): δ 16.5, 20, 22, 50, 56, 70, 116, 122, 125, 128, 129, 130, 132, 140. LIS studies were done with Eu(fod)$_3$ and results indicated that the *RR* diastereomer had a retention time of 38 min and the *RS*, 43.5 min. The two isomers were collected from a 20 ft × 0.21 in. DCQF-1 column at 190 °C, helium flow rate 60 mL/min.

Analysis of Stereochemical Reaction Mixtures. The reactions were run on a 10-mL scale as for the kinetic runs. However, for the stereochemical studies the entire reaction mixture was worked up. The MTPA esters were prepared and analyzed by GLC to determine the distribution of optical and geometric isomers. In addition the ^{1}H NMR of the esters was taken to confirm the distributions.

Registry No. **2**, (*R*)-*E*, 135818-48-3; **2**, (*S*)-*E*, 135818-49-4; (*R*)-(+)-MTPA, 20445-31-2; (*S*)-(+)-MTPA-Cl, 20445-33-4; CH_3MgI, 917-64-6; O_2, 7782-44-7; 1,1,1-trifluoroacetate, 421-50-1; 4-methyl-1,1,1,5,5,5-hexafluoro-4-hydroxypentan-2-one, 649-65-0; (*E*)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-one, 135708-32-6; (*Z*)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-one, 135708-33-7; methyl-d_3-magnesium, 41251-37-0; (*E*)-2-(methyl-d_3)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol, 135708-34-8; (*R*,*R*)-(*E*)-2-(methyl-d_3)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-yl [α-methoxy-α-(trifluoromethyl)phenyl]acetate, 135708-35-9; (*R*,*S*)-(*E*)-2-(methyl-d_3)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-yl [α-methoxy-α-(trifluoromethyl)phenyl]acetate, 135708-36-0; (*Z*)-2,4-dimethyl-1,1,1,5,5,5-hexafluoro-3-penten-3-ol, 135734-19-9; (*R*,*R*)-(*Z*)-2,4-dimethyl-1,1,1,5,5,5-hexafluoro-3-penten-2-yl [α-methoxy-α-(trifluoromethyl)phenyl]acetate, 135708-37-1; (*R*,*S*)-(*Z*)-2,4-dimethyl-1,1,1,5,5,5-hexafluoro-3-penten-2-yl [α-methoxy-α-(trifluoromethyl)phenyl]acetate, 135708-38-2; 2-(methyl-d_3)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol, 135708-39-3; palladous chloride, 7647-10-1.