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Palladium(II)-catalyzed exchange and isomerization reactions. XVI [1] The kinetics and stereochemistry of the oxidation and isomerization of hexafluoro allylic alcohols in aqueous solution catalyzed by $PdCl_3$(pyridine)$^-$

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Abstract

Further mechanistic studies on the $PdCl_3$(pyridine)$^-$ catalytic system in aqueous solution are described using the tetrasubstituted allylic alcohol, (*E*)-2-methyl-d_3-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol, **3a**, and the trisubstituted allylic alcohol, (*E*)-4-Methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol, **6**, as substrates. At low [Cl^-] the $PdCl_4^{2-}$ catalyzed isomerization of **3a**, which can only undergo isomerization into its allylic isomer, was previously found to obey the Wacker rate expression: $k_i[PdCl_4^{2-}][\mathbf{3a}]/[H^+][Cl^-]^2$. In contrast, the rate expression for isomerization of **3a** by [$PdCl_3(Py)^-$] at low [Cl^-] was found to be: $rate_i = k_i[PdCl_3(Py)^-][\mathbf{3a}]/[Cl^-]$. This rate expression is of the same form as that previously found for the isomerization of **3a** by $PdCl_4^{2-}$ at high [Cl^-]. This result strongly suggests that the hydroxypalladation by $PdCl_3(Py)^-$ at low [Cl^-] is a *trans* process as opposed to a *cis* process with $PdCl_4^{2-}$. This expectation was confirmed by stereochemical studies with chiral **3a**. The stereochemistry of addition for $PdCl_3(Py)^-$ was identical to that for $PdCl_4^{2-}$ at high [Cl^-]. Independent stereochemical studies have shown this addition to be *trans*. With $PdCl_3(Py)^-$ there are two possible routes for olefin oxidation. A *cis* process similar to that found for $PdCl_4^{2-}$ or a *trans* process analogous to that previously proposed to explain the *trans* stereochemistry found at high [Cl^-]. Stereochemical studies with **6**, which can undergo oxidation, showed that both processes are operative with $PdCl_3(Py)^-$ at [Cl^-] = 0.05 M. Thus addition of a pyridine to the coordination sphere of Pd(II) causes a profound change in reactivity.

Keywords: Wacker; Isomerization; Oxidation; Palladium(II); Stereochemistry; Modified catalyst

1. Introduction

The mechanism of the aqueous $PdCl_4^{2-}$ catalyzed oxidation of ethene to ethanal (Wacker reaction) has generated considerable controversy. The rate expression under low [Cl^-] conditions was found to be given by Eq. (1) (for general discussion and references, see [1]):

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

The kinetics and deuterium isotope effects were best explained by the mechanism, shown

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[1] For Part XV see Ref. [9].

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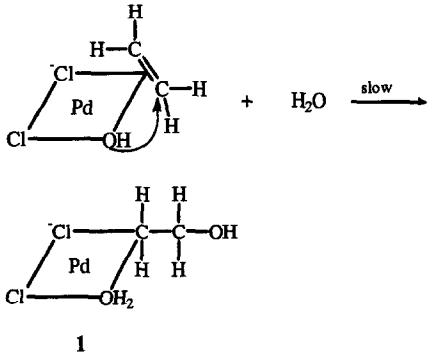
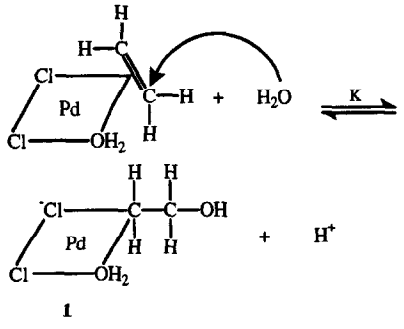
in Eq. (2), involving *cis* attack of coordinated hydroxide in the slow step [2].



(2)

However, more recent stereochemical studies have suggested that, in fact, the addition of Pd(II) and hydroxyl is a *trans* process. Thus, at high [Cl^-] (> 3 M), 2-chloroethanol becomes a major product [3]. Making use of this fact, in a very elegant stereochemical study, (*E*)- and (*Z*)-ethene-d_2 were oxidized at high [Cl^-] (3.3 M) in the $CuCl_2$ promoted reaction to give 2-chloroethanol-d_2 [4]. The configurations of the chloroethanols obtained from the two deuteriated ethenes were consistent only with *trans* hydroxypalladation. As shown in Eq. (3), based on these studies, the generally accepted mechanism for the Wacker reaction involves *trans* attack on a Pd(II)-ethene π-complex.

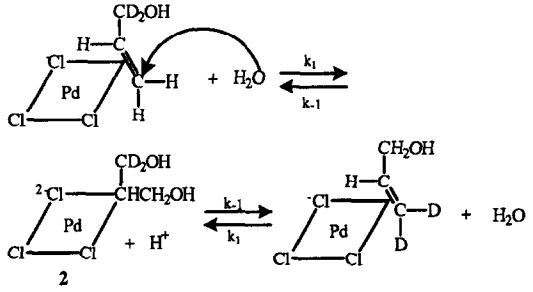


(3)

However, there is now a growing body of evidence that there are two modes of addition: one that predominates at low [Cl^-] and another that predominates at high [Cl^-]. Furthermore the two modes of addition apparently have opposite stereochemistries. Thus, allyl alcohol-1,1- and 3,3-d_2, are oxidized to Wacker products [5] by the rate expression given by Eq. (1) at low [Cl^-] [6]. However, at [Cl^-] > 2.0 M, these allyl alcohols undergo a non-oxidative isomerization and solvent exchange which obeys the rate expression given by Eq. (4) [7]. This rate expression,

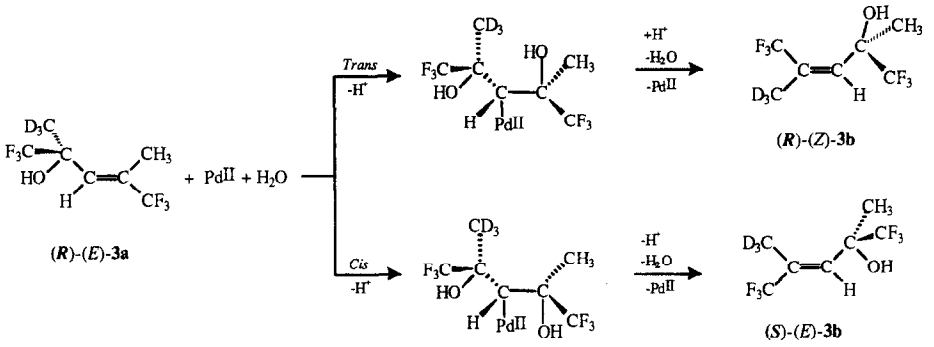
$$\text{rate} = k[PdCl_4^{2-}][\text{olefin}]/[Cl^-], \qquad (4)$$

is consistent with *trans* attack on a trichloropalladium(II)-olefin π-complex. The reaction scheme is shown in Eq. (5),



(5)

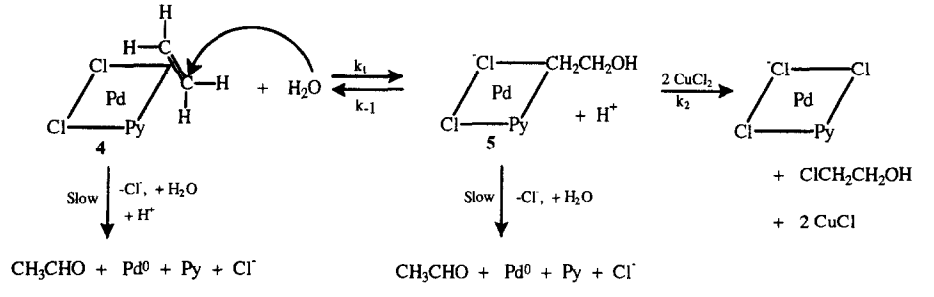
where the intermediate **2** cannot oxidatively decompose but can only reverse the hydroxypalladation to give isomerized allyl alcohol-d_2. Apparently, the reason **2** is stable to oxidative decomposition is the fact it does not have a labile coordination site for hydride transfer which would initiate oxidative decomposition. Note that the intermediate **1** in Eq. (3) *does* have a labile aquo containing coordination site. Furthermore, in two previous papers by the authors the kinetics and stereochemistry of the allylic isomerization of the tetrasubstituted allylic alcohol (*E*)-2-methyl-d_3-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol, (*E*)-**3a**, into an equilibrium mixture of **3a** and 2-methyl-4-methyl-d_3-1,1,1,5,5,5-hexafluoro-3-penten-2-ol, **3b**, in aqueous solution, was studied by ^1H and ^2H NMR, under conditions of both low (< 1.0



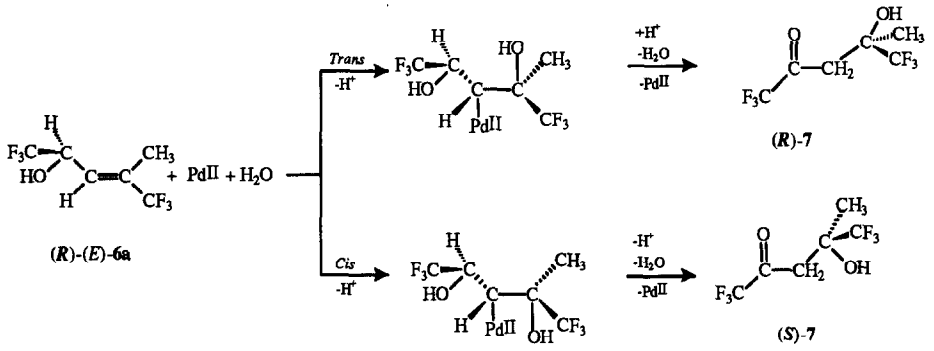
Scheme 1.

M) [8] and high (> 2.0 M) [9] chloride concentrations. The complete reaction sequence with stereochemical implications for chiral **3a** is outlined in Scheme 1. The assignments of absolute configuration are made by the Mosher acid procedure which is not been proved to be completely reliable for tertiary alcohols [10]. However, as discussed previously, the experiment does not depend on absolute configurations but the relative configurations of the starting material and product [8]. The rate expression under low [Cl^-] conditions was found to be given by Eq. (1) while the rate expression at high [Cl^-] is given by Eq. (4). The results at low [Cl^-] provided kinetic evidence for the route shown in Eq. (1). However the most significant result is that *the stereochemistry of addition was different at low and high [Cl^-]*! Since both the kinetics and stereochemical studies with (*E*)- and (*Z*)-ethene-d_2 are consistent with *trans* addition at high [Cl^-], the stereochemistry must be *cis* at low [Cl^-] and *trans* at high [Cl^-].

In a previous paper the oxidation of ethene by $PdCl_3(Py)^-$ was studied to test the *cis* and *trans* addition mechanisms [11]. The *cis* mechanism predicted a strong retardation of rate from that found for $PdCl_4^{2-}$ and a stabilization of the intermediate hydroxypalladation adduct so that it is more readily intercepted by $CuCl_2$ to give 2-chloroethanol. The *trans* mechanism predicts little change in rate or the trapping of the hydroxypalladation adduct by $CuCl_2$. It was found that replacement of a chloride in the coordination sphere of Pd(II) by a neutral pyridine ligand (1) reduced the value of the rate constant for the oxidation by a factor of about 750, and (2) made the intermediate hydroxypalladation adduct stable enough to be intercepted by $CuCl_2$ to give 2-chloroethanol at chloride concentrations as low as 0.2 M. With $PdCl_4^{2-}$ a chloride concentration of at least 3 M is required before any appreciable amount of 2-chloroethanol is formed [3]. This demonstration of the ability to change the reactivity of a catalyst by addition of neutral ligands was certainly the most important result of the previous paper.



Scheme 2.



Scheme 3.

The overall picture that emerges is shown in Scheme 2. The predominant reaction appears to be *trans* hydroxypalladation to give an intermediate which is stable enough to be intercepted by $CuCl_2$. Of course this addition would not be detected with ethene as substrate because the ethene would not undergo any detectable change in the addition–elimination cycle. The present study will employ the chiral allylic alcohol, **3a**, mentioned above, to determine the kinetics and relative stereochemistries of $PdCl_3(Py)^-$ as compared with $PdCl_4^{2-}$.

Another question which arises concerning Scheme 2 is the route for acetaldehyde formation. As shown **4** could decompose by the usual Wacker route or **5**, the intermediate formed by *trans* hydroxypalladation, could be the source of acetaldehyde. One possible way for distinguishing between two routes is stereochemistry. Previous studies indicate the route involving **4** proceeds by *cis* addition while the route involving **5** would occur by *trans* addition. Of course acetaldehyde does not give stereochemical information but the trisubstituted allyl alcohol, (*E*)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol, **6**, does permit determination of modes of addition. The reaction sequence is outlined in Scheme 3. Again the absolute configuration of the product is not known for certain so the results will indicate the relative stereochemistries of addition of $PdCl_3(Py)^-$ and $PdCl_4^{2-}$.

2. Results

2.1. Isomerization kinetics

The data for the kinetics of isomerization are listed in Table 1. Examination of the data indicates that the rate expression given in Eq. (4) is obeyed. Thus, in runs 1–3, where $[H^+] = 0.4$ M and $[PdCl_3(Py)^-]$ remains constant at 0.01 M, the value of k_{obs} decreases by about a factor of

Table 1
Rates of isomerization of 2-methyl-d_3-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol (**3a**) with $PdPyCl_3^-$ as catalyst [a]

Run	$[PdPyCl_3^-]$	$[H^+]$ [b]	$[Cl^-]$ [c]	$10^6 \times k_{obsd}$ [d] (s^{-1})	$10^4 \times k_i$ [e] (s^{-1})
1	0.01	0.40	0.20	9.8	2.0
2	0.01	0.40	0.40	5.6	2.2
3	0.01	0.40	0.60	3.2	1.9
4	0.02	0.40	0.80	5.3	2.1
5	0.04	0.20	1.0	5.7	1.4
6	0.08	0.80	0.60	25	1.9
7	0.08	0.60	0.60	25	1.9
8	0.005	0.20	0.20	3.9	1.6
				average	1.6

[a] All runs were carried out in aqueous solution at 25°C; quinone (0.10 M) was added to prevent the formation of palladium(0); in all runs, initial $[C_7H_5D_3F_6O] = 0.044$ M. Ionic strength was kept constant at 2.0 M using $LiClO_4$.
[b] Added as $HClO_4$.
[c] Added as LiCl.
[d] 1st order rate constant for **3a** disappearance. Data were treated as a reaction approaching equilibrium.
[e] k_i were calculated assuming that the rate expression given in Eq. (4) was operative, and $[PdCl_3(Py)^-]$ and $[Cl^-]$ were constant for each run.

Table 2
Stereochemistry of the isomerization products from chiral (E)-2-methyl-d_3-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol (**3a**) in aqueous acid solution [a], catalyzed by palladium(II)

Substrate		$[Cl^-]$	Catalyst	Product		
config	% ee [b]			% isomerization [c]	% S [d]	% R [d]
R [e]	100	0.05	$PdCl_4^{2-}$	48	50 [f]	50
S [e]	100	0.05	$PdCl_4^{2-}$	50	50	50 [f]
R [g]	100	3.5	$PdCl_4^{2-}$	27(25) [h]	0	100
S [g]	100	2.0	$PdCl_4^{2-}$	35(32) [h]	100	0
R	100	0.05	$PdCl_3(Py)^-$	40	15 [f]	85
S	100	0.05	$PdCl_3(Py)^-$	25	93	7 [f]
R	100	0.20	$PdCl_3(Py)^-$	28(28) [h]	0	100
S	100	0.20	$PdCl_3(Py)^-$	32(30) [h]	100	0

[a] Acid and Pd(II) concentrations were kept constant at 0.20 M 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] Maximum % isomerization obtainable is 50%. This is determined by ^2H NMR of the CD_3 resonance.
[d] Determined by GC retention times and ^1H NMR of the MTPA diastereomers.
[e] Data from [8].
[f] GLC retention time as well as collection by preparative GLC followed by ^1H NMR analysis indicated this fraction was entirely the (*E*)-geometric isomer. In addition ^1H NMR of the complete reaction mixture indicated only the (*E*) isomer was present.
[g] Data from [9].
[h] The values in parentheses are the % of (*Z*)-geometric isomer found in the reaction mixture.

2 when the $[Cl^-]$ is doubled and decreases by a factor of 3 when $[Cl^-]$ is increased by a factor of 3, indicating a $[Cl^-]$ inhibition term. In regard to the dependence on $[H^+]$, the rate does not change in runs 6 and 7 where $[H^+]$ is varied, indicating a zero order dependence on acid. In runs 3 and 6, $[PdCl_3(Py)^-]$ is increased by a factor of 8 at constant $[Cl^-]$, and the rate increases by the same factor, indicating a 1st order dependence on $[PdCl_3(Py)^-]$. For the overall data, k_i remains constant within experimental error when calculated by Eq. (4) indicating this is the correct expression. When k_i is calculated according to Eq. (1), the values of k_i vary over a wide range.

2.2. Stereochemistry of isomerization

The stereochemical results are listed in Table 2. Also included for comparison are stereochemical results previously reported for $PdCl_4^{2-}$ at low [8] and high [9] chloride concentrations. First consider the results with $PdCl_4^{2-}$ as catalyst. In run 1, using (*R*)-(*E*)-**3a** as substrate at $[Cl^-] = 0.05$ M, when ^2H NMR indicated the starting material was 48% isomerized, 50% of the (*R*)-isomer was converted to (*S*)-**3b** with the (*E*) geometric configuration. As shown in Scheme 1, this result is consistent only with *cis* addition to the most stable π-complex. In run 2, using (*S*)-(*E*)-**3b**, the result is also consistent with *cis* addition to the most stable π-complex. At high $[Cl^-]$, $PdCl_4^{2-}$ gave results consistent only with *trans* addition to the most stable π-complex. Both the (*R*)- and (*S*)-isomers (runs 3 and 4) gave no inversion of configuration and the % isomerization was equal to the amount of (*Z*) geometric isomer formed. As shown in

Table 3
Summary of stereochemistry results for the oxidation of (*E*)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol (**6**) [a]

Starting alcohol		$[Cl^-]$	Catalyst	Products		
config	% ee [b]	(M)		config	% ee oxidation	% isomerized
(*R*)-(−)	99.2	0.1	$PdCl_4^{2-}$	(*S*)-(+)	100	0 [c]
(*S*)-(+)	100	0.3	$PdCl_4^{2-}$	(*R*)-(−)	97.0	0 [c]
(*R*)-(−)	99.2	0.05	$PdCl_3(Py)^-$	(*S*)-(+)	22	17 [d]
(*S*)-(+)	100	0.05	$PdCl_3(Py)^-$	(*R*)-(−)	12	12 [d]

[a] All runs are in water at 25°C. $[H^+] = 0.1$ M, $[PdCl_4^{2-}] = 0.05$ M for each run. Ionic strength, μ, is adjusted to 2.0 M with $LiClO_4$. All runs were carried out over a 50 h period.
[b] ee = Enantiomeric excess.
[c] No isomerization product was observed.
[d] Isomerization product is 2-hydroxy-2-methyl-1,1,1,5,5,5-hexafluoro-3-pentene.

Scheme 1 this result is consistent with *trans* addition.

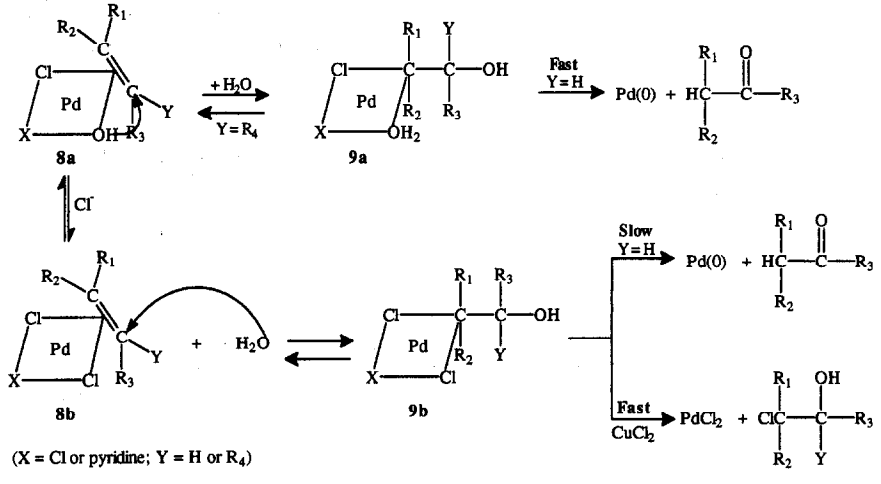
The results with $PdCl_3(Py)^-$ depended on the chloride concentration. At $[Cl^-] = 0.05$ M, the inversion of configuration is observed but the % inversion is consistently lower than the % isomerization. For the (*R*)-enantiomer, while the % isomerization is 40%, the % inversion is only 15%. For the (*S*)-enantiomer, the corresponding values were 25% and 7%. At $[Cl^-] = 0.2$ M the results with $PdCl_3(Py)^-$ are more definitive. Retention of configuration with formation of the (*Z*) geometric isomer is the observed result. According to Scheme 1 this result is consistent with *trans* addition to the most stable π-complex. Whatever the absolute stereochemistry of addition, these results clearly show that the hydroxypalladation mode for $PdCl_3(Py)^-$ at low $[Cl^-]$ is opposite that for $PdCl_4^{2-}$.

2.3. Stereochemistry of oxidation

The results are listed in Table 3. The results with $PdCl_4^{2-}$ are inversion of configuration with almost quantitative chirality transfer. In the case of $PdCl_3(Py)^-$ a chloride concentration of 0.05 M had to be employed since higher $[Cl^-]$ gave isomerization almost exclusively. Even at $[Cl^-] = 0.05$ isomerization was a serious side reaction. The stereochemical result was mainly inversion but the % ee was much lower than the starting material. This result, of course, indicates two modes of hydroxypalladation are occurring simultaneously.

3. Discussion

The results of all the previous studies discussed in the Introduction can be best accommodated by the overall reaction sequence shown in Scheme 4. The Wacker oxidation route is shown in the top portion where **8a** (X = Cl; $[Cl^-] < 1.0$ M) is produced by the reaction of $PdCl_4^{2-}$ with olefin and water followed by dissociation of a proton. The intermediate **9a**, when formed from olefins with β-hydrogens, is very reactive and rapidly decomposes to give Wacker oxidation products. In fact, deuterium labeling studies with ethene and allyl alcohol show that the intermediate, **9a**, decomposes to products every time it is formed. Only with tetrasubstituted alcohols such as **3** is the reverse reaction observed. The *cis* addition is postulated because exchange studies with **3a** (Scheme 1) are only consistent with opposite stereochemistries of addition at high and low $[Cl^-]$ [8,9]. The stereochemical studies of Bäckvall, Åkermark and



Scheme 4.

Ljunggren clearly prove *trans* addition at high $[Cl^-]$ so hydroxypalladation must be *cis* at low $[Cl^-]$. Kinetic results are consistent with these modes of addition.

For the $PdCl_4^{2-}$ system the lower pathway involving **8b** ($X = Cl^-$) becomes important at $[Cl^-] > 2.0$ M. The intermediate **9b**, formed by *trans* hydroxypalladation of **8b**, is much more stable than **9a** and does not tend to decompose to carbonyl products. The evidence for this stability is the fact that allyl alcohol, which rapidly undergoes Wacker oxidation at low $[Cl^-]$, only undergoes the exchange shown in Eq. (5) at $[Cl^-] > 2$ M. The increased stability of **9b** allows it to be intercepted by $CuCl_2$ to give chlorohydrins.

A recent paper investigated the effect on the reaction pathways shown in Scheme 4 of placing the neutral ligand, pyridine, in the coordination sphere of Pd(II) [11]. This substitution of pyridine for chloride resulted in a large decrease in the rate of acetaldehyde production, a result attributed to inhibition of formation of **8a** (X = pyridine) due to electronic factors. In addition the formation of β-chloroethanol occurred at much lower $[Cl^-]$ (0.2 M) than with $PdCl_4^{2-}$ (> 2 M). This results is best explained by increased stability of **9b** when X = pyridine.

The present paper provides further insight into the detailed reaction sequence shown in Scheme 4. First the data permit an estimation of the rate constants for *cis* and *trans* addition. These rate constants demonstrate that *trans* addition predominates at chloride and proton concentrations above 0.2 M. Second, the data reveal that oxidation can occur by further reaction of *both* **4** and **5**. At $[Cl^-] = 0.05$ M, the overall rates of oxidation by these two species is about equal.

Since the copper promoted reaction with $PdCl_3(Py)^-$ occurred at chloride concentrations as low as 0.2 M, the reaction must follow the lower route in Scheme 4 above this chloride concentration. Using **3a** as a kinetic and stereochemical probe, it was found that the kinetics of exchange did, in fact, obey Eq. (4) at low $[Cl^-]$, a finding consistent with *trans* addition. The stereochemical results confirmed the profound change in mechanism produced by the catalyst modification. The stereochemistry result was exactly opposite that found for $PdCl_4^{2-}$ at low $[Cl^-]$. In fact the stereochemistry of hydroxypalladation was identical to that found for $PdCl_4^{2-}$ under conditions of high $[Cl^-]$; conditions under which independent stereochemical studies give strong evidence for *trans* addition [4].

The stereochemistry results in Table 2 for $PdCl_3(Py)^-$ catalyzed isomerization of **3a** at $[Cl^-] = 0.05$ M are consistent only with both *cis* and *trans* addition taking place simultaneously. For the run starting with the (*R*)-isomer the fraction proceeding by *cis* addition can be calculated by dividing the % *S* by the % isomerized or $15/40 = 0.38$. In the same fashion the same quantity can be obtained for the run starting with the (*S*) isomer by dividing the % *R* by the % isomerized or $7/25 = 0.28$. Thus the fraction proceeding by *cis* addition is ~ 0.35. Using the average value of $k_i(trans)$ of 1.6×10^{-4} s^{-1}, the value of k(observed) for *trans* addition, k_{obtr}, can be calculated for the reaction conditions ($[Cl^-] = 0.05$ M, $[Pd(II)] = 0.05$ M, $[H^+] = 0.2$ M) of the stereochemical experiments using Eq. (4). This value of k_{obtr} is 1.6×10^{-4} s^{-1} which accounts for 0.65 of the total rate of isomerization. The corresponding value for *cis* addition, k_{obcs}, can now be readily calculated to be 9×10^{-5} s^{-1}. Inserting this value as well as the concentrations of the reactants, listed above, in Eq. (1) produces a value of $k_i(cis) = 9 \times 10^{-7}$ M^2 s^{-1} for *cis* addition. Now these k_i values permit a rough calculation of the fraction reacting by the *cis* addition route for any set of reaction conditions. [2] Thus, for run 8 (Table 1), which has the lowest values of

[2] The ratio of rates is given by the expression: $k_{obcs}(cis)/k_{obtr}(trans) = (9 \times 10^{-7}\ M^2\ s^{-1})[Pd(II)]/[H^+][Cl^-]^2/(1.6 \times 10^{-4}\ s^{-1})[Pd(II)]/[Cl^-] = 5.6 \times 10^{-3}\ M^2/[H^+][Cl^-]$. The fraction of the total proceeding by the *cis* route is then $k_{obcs}(cis)/(k_{obtr}(trans) + k_{obsd}(cis))$.

$[Cl^-]$ and $[H^+]$, the fraction proceeding by the *cis* route is calculated to be 0.12. This amount is just beyond experimental error. For run 1 this same fraction is about 0.06. For the rest of the runs the *cis* route is insignificant.

These findings have some significance for Pd(II) catalysis in general. For instance they explain some of the previously observed *trans* hydroxypalladations which were used as evidence for *trans* addition under Wacker conditions. *Trans* addition has been observed in several reactions where the Pd(II) contains a neutral ligand in its coordination sphere. These include hydroxypalladation of chelating diolefins [12] and methoxy- and hydroxy-palladation under a carbon monoxide atmosphere [13,14]. The CO bonds very strongly to Pd(II) to give Pd(II) carbonyls analogous to $PdCl_3(Py)^-$ [15]. Also studies on the exchange of vinyl ethers found that precipitation of Pd metal was a serious side reaction at temperatures above −25°C [16]. However two chelating diamine complexes of palladium(II) acetate, (L-L)$Pd(OAc)_2$ (L-L = 2,2′-bipyridine or 1,10-phenanthroline), were found to be effective catalysts for exchange at temperatures up to 80°C. This result is, no doubt, another example of stabilization of a Pd(II) catalyst against oxidative decomposition by neutral amine ligands.

Another question which arises is the identity of the intermediate, **4** or **5** (Scheme 2), which gives the ethanal product. If the pathway proceeds via **4**, the mechanism would be analogous to that proposed for the reaction at low $[Cl^-]$. This path would involve first replacing a chloride in the coordination sphere with water followed by dissociation of a proton in an equilibrium reaction. Then *cis* attack of hydroxide (Eq. (2)) would give the intermediate that would decompose to **7** (Scheme 3). If **5** is the intermediate, the route would be analogous to that proposed to explain *trans* addition of water (Eq. (3)) [4]. *trans* equilibrium hydroxypalladation would be followed by loss of another chloride to put water in the coordination sphere. This would provide the labile coordination site necessary for hydride transfer to give **7**. Both routes would give Eq. (1) as the rate expression. Of course there is always the possibility both mechanisms are operative simultaneously. The stereochemical studies using the trisubstituted allylic alcohol, **6**, outlined in Scheme 3, confirm that both routes are operative. Thus at $[Cl^-] = 0.05$, about 60% of the reaction proceeds through **4** and the remainder via **5**. *Thus the trans addition mechanism, shown in Eq. (3), invoked to explain the stereochemical results at high $[Cl^-]$, is actually operative to some extent with $PdCl_3(Py)^-$.*

Some insight into the competition between isomerization and oxidation is provided by comparing the present results with those in Table 2. As shown in Table 3, at $[Cl^-] = 0.05$ M isomerization is competitive with oxidation and at higher $[Cl^-]$ the yield of **7** was too low for analysis because of the different chloride dependencies for oxidation (Eq. (1)) and isomerization (Eq. (4)). The interesting point is that *the chloride concentration at which cis addition in Table 2 for isomerization of **3a*** becomes important is approximately the same as that of which the oxidation of **6** becomes appreciable. This result indicates that, while *trans* addition *can* result in oxidation, *cis* addition leads only to oxidation, a conclusion in agreement with earlier deuterium isotope effect studies [2].

In conclusion, this study demonstrates the need for a detailed and accurate knowledge of the mechanism of a catalytic process. Only with such knowledge can the catalyst be modified to give new catalytic chemistry.

4. Experimental section

4.1. Materials

The palladium(II) chloride was purchased from AESAR and the LiCl, 1,1,1-trifluoroacetone and $Eu(fod)_3$ were purchased from Aldrich Chemical. $KPdCl_3(Py)$ was prepared

and its stock solutions analyzed as described previously [9]. All other chemicals were of reagent grade. Stock solutions of the following compositions were prepared: 0.2 M in $KPdCl_3(Py)$, 2.0 M in LiCl, 2.0 M in perchloric acid and 3.0 M in $LiClO_4$. Reaction mixtures were prepared by diluting these stock solutions.

4.2. Physical measurements

All ^1H NMRs were recorded on a Varian VXR 300 NMR spectrometer. GLC analyses were carried out using a Perkin Elmer Sigma 3B gas chromatograph.

4.3. Preparation of racemic-(E)-4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol, (Luché reduction) [17]

One mmol each of methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-one, prepared as described previously [8], and $CeCl_3 \cdot 7H_2O$, were dissolved in 2.5 ml of methanol. $NaBH_4$ (38 mg, 1 mmol) was added in one portion with stirring. H_2 gas evolution was accompanied by a temperature rise (approx. 35–40°C). Stirring was continued for 3–5 min before the pH was adjusted to neutrality with dilute aqueous HCl. The mixture was extracted with ether, dried over $MgSO_4$, and the solvent evaporated. The crude residue was distilled over P_2O_5 yielding 91% of product, bp 118–122°C.

4.4. Preparation of MPTA Ester of 6 [10]

4-Methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-ol, 0.3078 g (0.148 mmol) and distilled (*S*)-(+)-α-methoxy-α-(trifluoromethyl)-phenylacetyl chloride ((*S*)-(+)-MTPA-Cl), 0.0379 g (0.15 mmol) were mixed in 5 ml dry pyridine containing 5 drops of CCl_4, and allowed to stand in a stoppered flask for 12 h. Water, 1 ml, was added and the reaction mixture was transferred to a separatory funnel containing 20 ml 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 ^1H NMR ($CDCl_3$): $\delta = 2.05$ (m, 3H), 3.50 (m, 3H), 5.80–6.30 (m, 2H), 7.30–7.70 (m, 5H). ^{13}C ($CHCl_3$): 11.7, 55.7, 67.6, 120, 124, 127, 127.2, 128.6, 130.1, 138.9, 165. IR (neat): 3090, 2990, 2970, 2850, 1765, 1590, 1500, 1450, 1190, 1130, 770, 700. Anal. Calcd for $C_{16}H_{13}F_9O_3$: C, 45.30; H, 3.09. Found: C, 45.38; H, 3.08.

4.5. Resolution of the diastereo isomers of 4-methyl-1,1,1,5,5,5-hexafluoro-3-penten-2-yl-α-methoxy-α-trifluoromethyl-phenylacetate

Each of the diastereomers were collected from a 20 ft × 0.21 in. DCQF-1 column at 195°C, helium flow rate 60 ml/min. Retention times were 174 and 180 min for the respective diastereomers. Each diastereomer was reduced by lithium aluminum hydride (1:4, $LiAlH_4$:ester), in anhydrous ether. The ether phase was dried over $MgSO_4$ and distilled giving the pure enantiomer.

4.6. Kinetic studies

The isomerization of 2-methyl-d_3-4-methyl-1,1,1,4,4,4-hexafluoro-3-penten-2-ol was monitored by ^2H NMR using a Varian 300 VXR NMR. The experimental procedure has been described [8].

4.7. 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 ^1H NMR of the esters was taken to confirm the distributions.

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