Palladium(II)-Catalyzed Exchange and Isomerization Reactions. 13.[1] Palladium(II) Chloride Catalyzed Exchange and Isomerization of 2-(Methyl-d_3)-4-methyl-3-penten-2-ol and Its Ethyl Ether in Methanol

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The kinetics of the palladium(II)-catalyzed exchange of 2-(methyl-d_3)-4-methyl-3-penten-2-ol (**1a**) with solvent methanol as well as its isomerization to the methyl ether of its allylic isomer, 2-methyl-4-(methyl-d_3)-2-methoxy-3-pentene, were studied. Under all conditions, the rates of exchange and isomerization were the same, indicating that both processes were proceeding by an oxypalladation–deoxypalladation mechanism. As expected, no oxidation was observed with this tetrasubstituted allyl alcohol since there were no β-hydrogens to shift to form carbonyl products. There were two regimes of kinetic behavior. At low chloride concentration ($[Cl^-] \leq 1.2$ M) the rate expression is rate = $k[PdCl_4^{2-}][\text{allyl alcohol}]/[H^+][Cl^-]^2$. This rate expression is of the same form as that found for the oxidation of olefins in water and methanol. At high chloride concentration ($[Cl^-] \geq 1.5$ M) the rate expression is rate = $k[PdCl_4^{2-}][\text{allyl alcohol}]/[Cl^-]$, a rate expression previously found for nonoxidative exchange and isomerization in water. Next the reactions of allyl alcohols containing β-hydrogens were tested. Both allyl alcohol and 4-methyl-3-penten-2-ol gave their respective oxidations products, 3-methoxypropanol and 4-methyl-4-methoxy-2-pentanone, at low $[Cl^-]$. However, at high $[Cl^-]$, both gave exchange but no oxidation products. These products were 3-methoxy-1-propene from allyl alcohol and 4-methyl-4-methoxy-2-pentene and 2-methyl-4-methoxy-2-pentene from 4-methyl-3-penten-2-ol. The ethyl ether of nondeuterated **1a** was prepared and its exchange with methanol at low $[Cl^-]$ was studied. Its rate expression for exchange is rate = $k[PdCl_4^{2-}][\text{allyl ether}]/[H^+][Cl^-]^2$. The fact that exchange of the ethyl ether at low $[Cl^-]$ obeys the same rate expression as oxidation has mechanistic implications which are discussed.

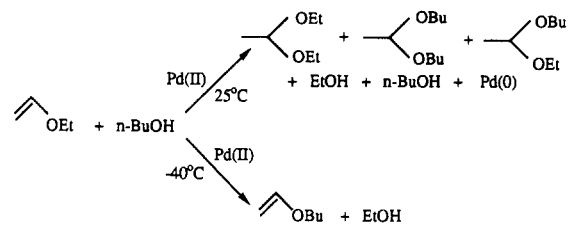
Introduction

The exchange of vinylic and allylic esters, chlorides and ethers with alcohol solvents has been the subject of several patents.[2] The most fundamental mechanistic study was by McKeon and co-workers[3] who found that the ether exchange was not as readily carried out as the ester exchange in carboxylic acid solvents.[4] If the reaction with vinyl ethers is carried out at room temperature, the only products were acetals and alcohols with the precipitation of Pd metal. At −40 °C an equilibrium mixture of vinyl ethers is obtained with no precipitation of Pd metal. An example is the reaction of ethyl vinyl ether with 1-butanol shown in Scheme I, the Pd(II) being in the form of $(PhCN)_2PdCl_2$.

Further studies indicated that the oxidation reaction forming acetals, which occurred above −25 °C, was catalyzed by HCl formed when $(CH_3CN)_2PdCl_2$ was reduced. If the reaction mixture is buffered with NaH_2PO_4, the exchange to give vinyl ethers occurred at 25 °C, although some Pd metal still precipitated. Finally 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.[3]

Thus, the mechanism of exchange to give vinyl and allylic ethers is poorly understood and needs clarification if conditions for achieving useful exchange reactions are to be defined. The strategy which will be employed involves kinetic studies of the exchange and isomerization of tetrasubstituted allylic alcohols which *cannot* be oxidized by hydride shift to give acetals and ketals. Consider the exchange and isomerization reactions shown in Scheme II where the allyl alcohol **1a** is easily prepared by adding methyl-d_3-magnesium iodide to mesityl oxide. Because of the bulk of the methyl groups the Pd(II) will add to the center carbon to give **2** and the carbons in **2** bonded to the hydroxyl or methoxyl groups contain no hydrogens to shift to give oxidation oxidative decomposition so only exchange and isomerization can occur. In the present study, the exchange can be followed by the appearance of the OCH_3 peak by ^1H NMR. This mechanistic probe will first be used to determine the types of oxypalladations which occur under various reaction conditions. Then allyl alcohols containing β-hydrogens will be reacted to see which of these oxypalladation routes are oxidative and which give only the desired exchange. In this study the only ligands on Pd(II) will be chloride.

Scheme I



In both water[5] and methanol[6] the rate expression for acyclic olefin oxidation under Wacker conditions is given by eq 1, while, under conditions where oxidation is very

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

(1) Part 12: Gregor, N.; Zaw, K.; Henry, P. M. *Organometallics* **1984**, *3*, 1251.
(2) For general discussion and references, see: Henry, P. M. *Palladium Catalyzed Oxidation of Hydrocarbons*; D. Reidel: Dordrecht, Holland, 1980; pp 138–140.
(3) (a) McKeon, J. E.; Fitton, P.; Griswold, A. A. *Tetrahedron* **1972**, *28*, 227. (b) McKeon, J. E.; Fitton, P. *Tetrahedron* **1972**, *28*, 233.
(4) Henry, P. M. *Acc. Chem. Res.* **1973**, *6*, 16.
(5) (a) Henry, P. M. *J. Am. Chem. Soc.* **1964**, *86*, 3246. (b) Henry, P. M. *J. Am. Chem. Soc.* **1966**, *88*, 1595. (c) Wan, W. K.; Zaw, K.; Henry, P. M. *Organometallics* **1988**, *7*, 1677. (d) Zaw, K.; Henry, P. M. *J. Org. Chem.* **1990**, *55*, 1842.
(6) Henry, P. M.; Lee, H. B. *Can. J. Chem.* **1976**, *54*, 1726.

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Scheme II

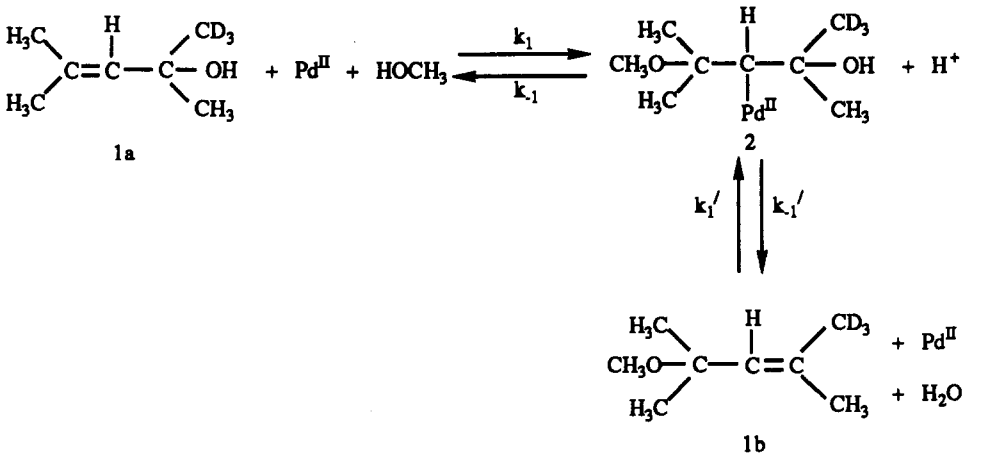


Table I. Rates of Exchange and Isomerization of 2-(Methyl-d_3)-4-methyl-3-penten-2-ol in Methanol at Low Chloride Concentrations[a,b]

run	10^3[$CHCl_2CO_2H$], M	10^5[H^+],[c] M	[Cl^-], M	10^3[$PdCl_4^{2-}$], M	$10^3 k_{obsd}$, s^{-1} [d]	$10^6 k_{ex}$, $M^2\ s^{-1}$ [e]
1	5.1	1.4	0.63	2.0	2.1 (1.7)	5.9
2	5.1	1.4	0.60	4.0	4.0 (3.8)	5.1
3	5.1	1.4	0.63	8.0	8.1 (8.5)	5.7
4	5.1	1.4	0.61	16.0	16.0 (16.2)	5.2
5	5.1	1.4	1.2	4.0	1.0 (1.0)	4.9
6	5.1	1.4	0.32	4.0	18.0 (16.5)	6.5
7	10.2	2.8	0.60	4.0	2.0 (2.1)	5.1
8	20.4	5.6	0.63	4.0	0.97 (0.90)	4.9
9	40.9	11.3	0.60	4.0	0.53 (0.50)	5.4
					average	5.5

[a] [Cl1−] ≤ 1.2 M. [b] [allyl alcohol] = 0.171 M. [c] Calculated by using a K_a of 4.0×10^{-7} for dichloroacetic acid.[28] [d] Values outside parentheses are those for exchange while values inside parentheses are those for isomerization. [e] Calculated assuming the rate expression is that given by eq 1.

slow ([Cl^-] > 3.0 M), a nonoxidative exchange reaction was found in aqueous solution. The rate expression for the exchange is given by eq 2.

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

Results

Control Experiments. Studies of the stability of **1a** in the presence of dichloroacetic acid in methanol indicated that in the presence of 0.10 M dichloroacetic acid the allyl alcohol was stable for up to 15 min without any observable change. However, after 30 min under these conditions the formation of 2-(methyl-d_3)-4-methyl-1,3-pentadiene, a dehydration product, was observed. Under the acid conditions of the study, which are similar to those previously used to study ethylene oxidation, [$Cl_2HCCOOH$] = 0.0005–0.01 M,[6] the starting allyl alcohol was stable in methanol for the time required to make the longest kinetic run. It was also stable indefinitely in the presence of 3.0 M LiCl.

Kinetics. The exchange and isomerization of 2-(methyl-d_3)-4-methyl-3-penten-2-ol in methanol catalyzed by Li_2PdCl_4 was first studied under reaction conditions which gave rapid ethene oxidation.[6] Data are given in Table I. Each run was plotted as a first-order reaction in the allyl alcohol concentration and correlation coefficients of greater than 0.96 were obtained, indicating the reaction was indeed first order in [allyl alcohol]. The kinetics are consistent with the expression given by eq 1. The value of k_{ex}, calculated assuming eq 1, remains quite constant considering the complexity of the rate expression, confirming that eq 1 is the correct rate expression for the reaction. The values of the isomerization rate constant were also determined by the scrambling of the deuterium label. It was necessary to demonstrate that $k_{ex} = k_{ism}$ to prove that the reaction is not proceeding by a mechanism involving Pd(IV) π-allyl species.[1,7]

The exchange and isomerization was next studied at [Cl^-] ≥ 1.5 M. The kinetic data is given in Table II. The fact that the value of k_{ex}, assuming a rate expression of the form of eq 2, is constant indicates that eq 2 is the correct rate expression. Since the rates of isomerization are the same as the rates of exchange within experimental error, Scheme II must be operative.

The data for the exchange of the ethyl ether of nondeuterated 1 given in Table III clearly indicates a rate expression of the form of eq 1. The first-order dependence on [$PdCl_4^{2-}$] is shown by runs 19–21 while runs 19, 22, and 23 indicate a 1/[Cl^-]^2 dependence. The first-order acid inhibition is demonstrated by runs 19, 24, and 25.

Product Studies. The product, **1b**, in Scheme I was identified by its ^1H and ^2H NMR spectrum. At equilibrium, integration of the resonances indicated a 50–50 mixture of **1a** and **1b**. The oxidation, exchange, and isomerization products for allyl alcohol, **3**, and 4-methyl-3-penten-2-ol, **4**, were studied under similar conditions; at low chloride concentrations, [Cl^-] ≤ 1.2 M, and at high chloride concentrations, [Cl^-] ≥ 1.5 M. Oxidation was the only process obtained for both unsaturated alcohols at low [Cl^-]. The oxidation product of allyl alcohol, 3-methoxypropanal, $CH_3OCH_2CH_2CHO$,[8] and of **4** (4-methyl-4-

(7) Ng, F. T. T.; Henry, P. M. *J. Org. Chem.* **1973**, *38*, 3338.
(8) Cardellach, J.; Estopa, C.; Font, J.; Morenzo-Mañas, M.; Ortuño, R. M.; Sanchez-ferrando, F.; Valle, S.; Vilamajop, L. *Tetrahedron* **1982**, *28*, 2377.

Table II. Rates of Exchange and Isomerization of 2-(Methyl-d_3)-4-methyl-3-penten-2-ol in Methanol at High Chloride Concentration[a,b]

run	$10^4[Cl_2HCCO_2H]$, M	$10^5[H^+]$,[c] M	$[Cl^-]$, M	$10^3[PdCl_4^{2-}]$, M	$10^4 k_{obsd}$, s^{-1}[d]	$10^5 k_{ex}$, $M^2\ s^{-1}$[e]
10	5.1	1.4	2.0	4.0	2.9 (3.1)	1.5
11	5.1	1.4	1.5	4.0	3.6 (4.0)	1.4
12	5.1	1.4	2.5	4.0	2.2 (2.2)	1.4
13	10.2	2.8	2.0	4.0	3.0 (2.9)	1.5
14	20.4	5.6	2.0	4.0	2.9 (3.0)	1.5
15	5.1	1.4	2.0	8.0	5.7 (5.0)	1.4
16	5.1	1.4	2.0	16.0	12.8 (13.3)	1.6
17	5.1	1.4	2.0	2.0	1.4 (1.7)	1.4
18	5.1	1.4	3.0	4.0	1.8 (2.1)	1.4
					average	1.4

[a] $[Cl^-] \geq 1.5$ M. [b] [allyl alcohol] = 0.171 M. [c] Calculated by using a K_a of 4.0×10^{-7} for dichloroacetic acid.[28] [d] Values outside parentheses are those for exchange while values inside parentheses are those for isomerization. [e] Calculated assuming the rate expression is that given by eq 2.

Table III. Rates of Exchange and Isomerization of 2,4-Dimethyl-2-ethoxy-3-pentene in Methanol at Low Chloride Concentrations[a,b]

run	$10^3[CHCl_2CO_2H]$, M	$10^5[H^+]$,[c] M	$[Cl^-]$, M	$10^3[PdCl_4^{2-}]$, M	$10^4 k_{obsd}$, s^{-1}[d]	$10^6 k_{ex}$, $M^2\ s^{-1}$[e]
19	5.1	1.4	0.60	4.0	10.1	1.3
20	5.1	1.4	0.60	12.0	28.5	1.2
21	5.1	1.4	0.60	16.0	35.7	1.1
22	5.1	1.4	1.2	4.0	2.5	1.2
23	5.1	1.4	0.3	4.0	42.8	1.4
24	10.2	2.8	0.60	4.0	5.5	1.4
25	20.4	5.6	0.63	4.0	2.9	1.5
					average	1.3

[a] $[Cl^-] \leq 1.2$ M. [b] [allyl ether] = 0.171 M. [c] Calculated by using a K_a of 4.0×10^{-7} for dichloroacetic acid.[28] [d] Values outside parentheses are those for exchange while values inside parentheses are those for isomerization. [e] Calculated assuming the rate expression is that given by eq 1.

methoxy-2-pentanone, $CH_3O(CH_3)_2CCH_2C(=O)CH_3$)[9] were identified by comparing their ^1H NMR spectra with those reported. At higher $[Cl^-]$ no oxidation was obtained, but exchange was observed for allyl alcohol, and both exchange and isomerization were obtained for 4-methyl-3-penten-2-ol in methanol. The exchange product from allyl alcohol, 3-methoxy-1-propene, $CH_3OCH_2CH{=}CH_2$,[10a] the exchange product from 4, 4-methyl-4-methoxy-2-pentene ($CH_3O(CH_3)_2CCH{=}CHCH_3$),[10b] as well as the isomerization product, 2-methyl-4-methoxy-2-pentene ($(CH_3)_2C{=}CHCH(CH_3)OCH_3$),[10b] were also identified by comparing their ^1H NMR spectra with those reported.

Since allylic alcohols react with Pd(II) salts to form π-allyl species which could serve as catalysts,[11] the π-allyl palladium(II) chloride from $PdCl_4^{2-}$ and nondeuterated **1** was prepared and its spectroscopic properties determined. It was then dissolved in methanol containing all the ingredients of a reaction mixture except Li_2PdCl_4. The reaction mixture was worked up in the usual fashion and it was found that the palladium(II)–π-allyl could be detected by ^1H and ^2H NMR. It could then be shown the π-allyl species was not present in any of the regular kinetic runs since no resonances due to this species were observed.

Discussion

The results of this study clearly indicate conditions for conducting exchange reactions in methanol solvent while avoiding the complication of oxidation. At low $[Cl^-]$ the kinetics follow the Wacker rate expression, eq 1, and only oxidation of both allyl alcohol and **4** occurs as shown in eqs 3 and 4.[12]

$$\underset{\mathbf{3}}{CH_2{=}CHCH_2OH} \xrightarrow[CH_3OH]{PdCl_4^{2-}} CH_3OCH_2CH_2CH{=}O \qquad (3)$$

$$\underset{\mathbf{4}}{(CH_3)_2C{=}CHCH(CH_3)OH} \xrightarrow[CH_3OH]{PdCl_4^{2-}} CH_3O(CH_3)_2CCH_2C(CH_3)(=O) \qquad (4)$$

At high $[Cl^-]$ the kinetics obey eq 2 and only exchange is observed without any oxidation. As shown in eqs 5 and 6 the products are allylic ethers. In the case of **4** the

$$\underset{\mathbf{3}}{CH_2{=}CHCH_2OH} \xrightarrow[CH_3OH]{PdCl_4^{2-}} CH_3OCH_2CH{=}CH_2 \qquad (5)$$

$$\underset{\mathbf{4}}{(CH_3)_2C{=}CHCH(CH_3)OH} \xrightarrow[CH_3OH]{PdCl_4^{2-}} \underset{\mathbf{5}}{CH_3O(CH_3)_2C{=}CH(CH_3)} \xrightarrow[CH_3OH]{PdCl_4^{2-}} \underset{\mathbf{6}}{(CH_3)_2C{=}CHCH(CH_3)OCH_3} \qquad (6)$$

secondary isomerization occurs to give mainly **6** with smaller amounts of **5**.[12]

It is almost certain that both oxidation and exchange proceed through oxypalladation intermediates analogous to **2** in Scheme II. The question is how does high $[Cl^-]$

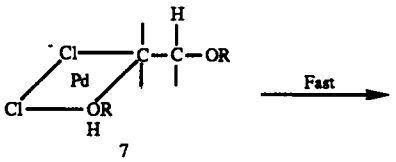
(9) Sadtler Research Laboratories, *Nuclear Magnetic Resonance Spectra, Chemical Shift Index*; ref 9279M.

(10) (a) Kirmse, W.; Rode, J.; Rode, K. *Chem. Ber.* **1986**, *119*, 3672. (b) Grandi, R.; Messerotti, W.; Pagnoni, U. M.; Trave, R. *J. Org. Chem.* **1977**, *42*, 1352.

(11) Keim, W. *Transition Metals in Homogeneous Catalysis*; G. M. Schrauzer, Ed.; Marcel Dekker, Inc.: New York, 1971; pp 59–91.

(12) Although the change from oxidation to exchange products with increasing $[Cl^-]$ was fairly sharp, there were chloride concentrations at which both were present. Thus for allyl Alcohol at $[Cl^-] = 1.5$ M the ratio of oxidation to exchange products was 3/1 while at $[Cl^-] = 2.5$ M only 1% was oxidation product. With **4**, at $[Cl^-] = 1.5$ M, oxidation product was 25% of the total and no oxidation was observed at $[Cl^-] = 2.5$ M. The amount of initial exchange product, **5**, was, at most, 7% of the total exchange product.

stabilize **2** from oxidative decay when one or more of the methyls are replaced by hydrogens? The only reasonable conclusion is that external chloride is inhibiting equilibra that open up labile sites on Pd(II) leading to hydride shift which occurs at low [Cl^-] as shown in eq 7. Possible

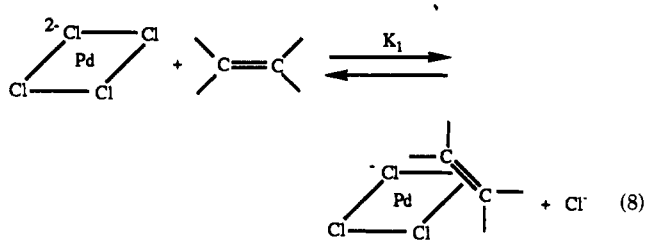


7

$$Pd(0) + 2Cl^- + H^+ + \text{HC(H)=O} \quad (7)$$

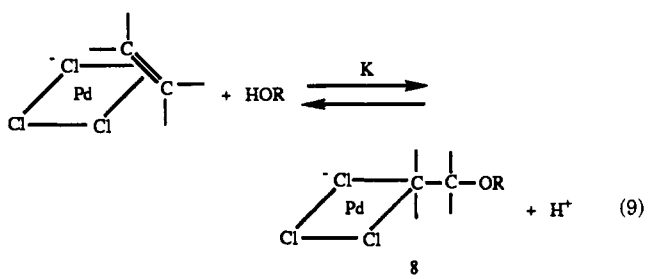
detailed mechanisms are discussed elsewhere[13] but the important point for present discussion is that, at low [Cl^-], a labile coordination site containing CH_3OH is present which is necessary for hydride shift.

The mode of oxypalladation at low [Cl^-] is changed from one that requires two chlorides to dissociate from the coordination sphere of Pd(II) to one at high [Cl^-] that requires only one chloride to dissociate. Thus high chloride is changing the mechanism of the palladium(II) catalysis. The kinetics are consistent with trans methoxypalladation. Since olefin activation by π-complex formation is always a necessary step in palladium(II) catalysis, the first power chloride inhibition must result from the equilibrium shown in eq 8. Since the kinetics only allow for one species to



(8)

be coordinated to Pd(II), the methanol must attack from outside the coordination sphere of the Pd(II) as shown in eq 9. As opposed to **7**, **8** must be stabilized against oxi-



(9)

8

dative decomposition by the hydride shift shown in eq 7. Thus **8** can only reverse the oxypalladation step to give exchange. The stabilization of the intermediate methoxypalladation adduct by high [Cl^-] has the secondary effect of changing somewhat the mode of addition. Of course it is possible that the stereochemistry of addition of methanol at low chloride is also trans but the removal of the second chloride to give a neutral Pd(II) species may make the addition more facile under low [Cl^-] conditions.

Certainly the stability of Pd(II) oxypalladation adducts containing strongly coordinating neutral groups is well documented. Thus olefins containing heteroatoms such as nitrogen and sulfur have long been know to form stable oxypalladation adducts[14] as have chelating diolefins.[15]

(13) Reference 2, pp 74–78.

Some interesting mechanistic studies have been carried out with use of methoxypalladation adducts of chelating olefins containing nitrogen donor atoms.[16] In another study it was demonstrated that a Pd(II)–π-complex containing η^5-C_5H_5 and phosphine ligands was converted to a stable methoxypalladation adduct by trans attack of methanol.[17] No doubt the reason for the stability of these adducts results from the fact that the strongly complexing ligands prevent formation of labile coordination sites on Pd(II) and thus inhibit the oxidative decomposition by β-hydrogen transfer shown in eq 7. There is kinetic evidence that vacant coordination sites are required for the decomposition of oxypalladation intermediates[18] and there is also evidence that such sites are required for decomposition of Pt(II) alkyls.[19] In the present study the Pd(II) species has been stabilized to the extent that it does not oxidatively decompose but still undergoes demethoxypalladation at such a rate that the intermediate adduct does not build up and the reaction becomes catalytic in Pd(II).

The success of the diamine complexes of palladium(II) acetate is, no doubt, also due to the stabilization of the oxypalladation intermediate by the strongly complexing diamine groups.[3]

The oxidation products from allyl alcohol at low chloride deserve brief comment. The only product was 3-methoxypropanal (eq 3) which arose from addition of Pd(II) to the center carbon as shown in eq 10 followed by a hydride shift from the alcohol carbon. A hydride shift from the

$$\underset{\mathbf{3}}{CH_2{=}CHCH_2OH} \xrightarrow[CH_3OH]{Pd(II)} H^+ + CH_3OCH_2C(Pd^{II})HCH_2OH \xrightarrow[CH_3OH]{-Pd(0)} CH_3OCH_2CH_2CH{=}O \quad (10)$$

carbon containing the CH_3O group would have given $(CH_3O)_2CHCH_2CH_2OH$ which was not observed. Apparently hydride shift from an alcoholic carbon is much preferred over a shift from an ether carbon, a result which is not too surprising. Secondly, the oxidation of allyl alcohol in water gave a 12–15% yield of α-hydroxyacetone (acetol) which would correspond to the dimethyl ketal in methanol. As shown in eq 11 the ketal would be formed by addition of Pd(II) to the end carbon to give **10** followed by oxidative decomposition to give **11**. The hydroxyl

$$\mathbf{3} + Pd(II) + CH_3OH \xrightarrow{-H^+} \underset{\mathbf{10}}{Pd^{II}CH_2CH(OCH_3)CH_2OH} \xrightarrow{-Pd(0)} \underset{\mathbf{11}}{CH_3C(OCH_3)_2CH_2OH} \quad (11)$$

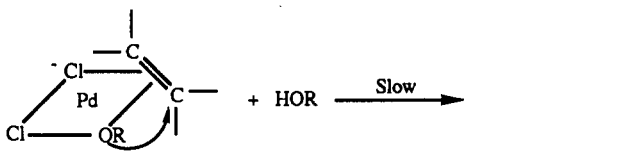
group is known to direct Pd(II) to the carbon next to the carbon containing the hydroxyl in hydroxypalladations in aqueous solution.[5d,20] For allyl alcohol the preference for center carbon (eq 10) to end carbon (eq 11) is 2.5 to one. Since **11** is not detected in methanol, the preference must

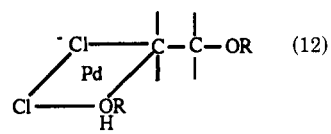
(14) Reference 2, pp 38–40.
(15) (a) Stille, J. K.; James, D. E. *J. Organomet. Chem.* **1976**, *108*, 401. (b) Chatt, J.; Vallarano, L. M.; Venanzi, L. M. *J. Chem. Soc.* **1957**, 2496; 3413. (c) White, D. A. *J. Chem. Soc. (A)* **1971**, 145. (d) Reference 3, pp 224–234.
(16) Alyea, E. C.; Dias, S. A.; Ferguson, G.; McAlees, A. J.; McCrindle, R.; Roberts, P. J. *J. Am. Chem. Soc.* **1977**, *99*, 4985.
(17) Majima, T.; Kurosawa, H. *J. Chem. Soc., Chem. Commun.* **1977**, 610.
(18) Winstein, S. W.; Mc Caskie, J.; Lee, H.-B.; Henry, P. M. *J. Am. Chem. Soc.* **1976**, *98*, 6913.
(19) Whitesides, G. M.; Gaasch, J. F.; Stedronsky, E. R. *J. Am. Chem. Soc.* **1972**, *94*, 5258.
(20) Zaw, K.; Lautens, M.; Henry, P. M. *Organometallics* **1985**, *4*, 1286.

be must higher. This is also not surprising since methanol has a lower dieletric constant than water and is a poorer solvating solvent so the directing effect of the O–H···Cl–Pd hydrogen bonding interaction might be expected to be stronger in methanol than in water. On the other hand the differences in rate at low [Cl^-] between the alcohol, **1a** (Table I), and its ethyl ether (Table III) is a little more than four with the alcohol being the faster. This result suggests that the hydrogen bonding effect does not greatly increase the value of K_1 in eq 8 or, if it does, this effect is counterbalanced by a slowing of a later process in the reaction scheme. It could be that stabilization of the π-complex slows the rate of oxypalladation.

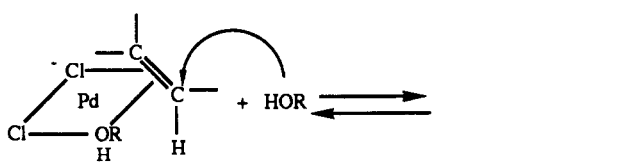
It is surprising that the absolute rate of exchange of **1a** at low chloride concentrations is so fast. In fact it is almost exactly the same as the corresponding rate of oxidation of ethene in methanol.[6,21] The increased substitution on the double bond would have been expected to decrease the rates of oxypalladation. Thus, in aqueous solution 2-buten-1-ol, which is much less substituted than **1a**, is oxidized at a rate 0.025 times that of ethene.[5d] The reason for the high reactivity of **1a** toward methoxypalladation is unknown but it does indicate that these highly substituted olefins are suitable models for their less hindered counterparts.

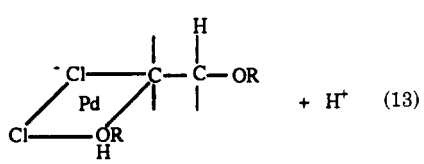
The kinetic results for the exchange of the ethyl ether at low chloride give a clue as to possible modes of methoxypalladation under these conditions. Of particular interest is the fact that the rate expression for exchange is identical with that found for oxidation of ethene in methanol (eq 1) and ethene and other acyclic olefins in water.[5] The rate expression is consistent with the following routes. (1) Cis addition of Pd(II) and coordinated hydroxide or methoxide (oxypalladation) in the slow step as shown in eq 12 or (2) trans attack by external solvent in an equilibrium step as shown in eq 13. This equilibrium would not be detected unless some change in the olefin such as isomerization occurred every time the addition–elimination sequence took place.





(12)





(13)

The first mechanism was originally selected on the basis of isotope effects,[5a,22] but more recent stereochemical studies indicate hydroxypalladation under certain conditions occurs by trans attack of water from outside the coordination sphere of palladium(II).[15a,23-25] The validity of extrapolating the results of these studies to the conditions of the aqueous olefin oxidation has been discussed.[1] Also, more recent oxidation and isomerization studies with deuterated allyl alcohols indicated hydroxypalladation was the slow step of the oxidation, a result consistent with the route given in eq 12.

The reaction sequence shown in Scheme III provides, in principle, another means of choosing between the two routes. As opposed to Scheme II, the two oxygen containing groups in **2'** have about the same tendency to eliminate, so $k_{-1} = k_{-1}'$ and the oxypalladation step becomes the rate-determining step for both exchange and isomerization because exchange occurs half the time that oxypalladation occurs. This is the reason no proton inhibition appears in eq 2 for the exchange and isomerization in aqueous solution at high chloride concentration. If this condition is met the proton inhibition cannot result from the equilibrium shown in eq 13. In other words, if eq 13 were the reason for the proton inhibition in the oxidation, the rate expression for the exchange would be given by eq 14. The only reasonable conclusion is that a rate expression such as eq 1 for a symmetrical exchange indicates the proton release occurs before the oxypalladation step takes place.[26]

$$\text{rate} = k_{ex}[PdCl_4^{2-}][\text{olefin}]/[Cl^-]^2 \qquad (14)$$

Of course, the final answer to the Wacker mechanism will be stereochemical evidence in aqueous solution. However this study as well as at least one other[1] has demonstrated that the mode of oxypalladation can change with chloride concentration even in the same solvent so interpretation of stereochemical studies must be done very carefully. The authors believe that stereochemical data for Wacker chemistry are valid only under conditions of the rapid olefin oxidation (low [Cl^-] in aqueous solution) and with olefins whose oxidation kinetics obey eq 1.

Experimental Section

Starting Materials. The palladium(II) chloride was purchased from Aesar. The methanol, HPLC grade from Aldrich Chemicals (Sureseal), was dried further with trimethyl orthoformate. All other chemicals were of reagent grade. Stock solutions of the following compositions were prepared: 0.2 M in Li_2PdCl_4, 2.0 M in LiCl, 2.0 M in dichloracetic acid, 3.0 M in $LiClO_4$. Reaction mixtures were prepared by diluting these stock solutions.

Kinetics. The rate of exchange and isomerization were studied simultaneously on a 25-mL scale by working up 5-mL portions of the reaction mixture at various times. The 5-mL aliquots were pipetted into 25 mL of CH_2Cl_2 which was then washed with two 25-mL portions of water followed by 25 mL of saturated sodium bicarbonate and again with 25 mL of water. The organic layer was then dried over anhydrous $MgSO_4$ and evaporated slowly at room temperature. ^1H and ^2H NMR spectra were obtained for each workup. NMR spectra were recorded on a Varian 300 MHz VXR 300 instrument at 20 °C. The rate of exchange was studied by using ^1H NMR, by measuring the increase in the areas of the OCH_3 singlet at 3.25 ppm and the CH singlet at 5.10 ppm corresponding to 2-methoxy-2-methyl-4-(methyl-d_3)-3-pentene, against the decrease in the area of the CH singlet at 5.34 ppm corresponding to 2-(methyl-d_3)-4-methyl-3-pentene-2-ol. The isomerization was followed by using ^2H NMR, by measuring the

(21) The value of k_{ex} in Table I is equivalent to kK_1 in ref 6.
(22) (a) Henry, P. M. *J. Org. Chem.* **1973**, *38*, 2415. (b) Kosaki, M.; Isemura, M.; Kitaura, K.; Shinoda, S.; Saito, Y. *J. Mol. Catal.* **1977**, *2*, 351. (c) Saito, Y.; Shinoda, S. *J. Mol. Catal.* **1980**, *9*, 461.
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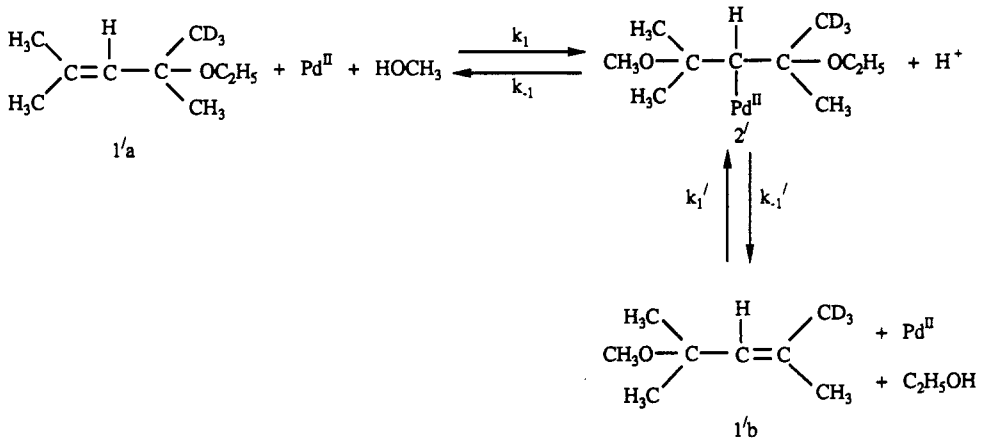
(26) See Ref 2, pp 41–84, for a complete discussion of possible mechanisms.

Scheme III



increase in the area of the peak at 1.2 ppm corresponding to 2-methoxy-2-(methyl-d_3)-4-methyl-3-pentene against the decrease in the area of the peaks at 1.6–2.0 ppm corresponding to the starting alcohol. The data for isomerization were treated as a first-order reaction in **1a** approaching equilibrium.[27] A plot of log (50% – percent isomerized) vs time was made on semilog paper and the half-life read off at the 25% point. Since the value for the equilibrium constant for the isomerization is equal to 1, the rates for the forward and reverse reactions are identical, and the value of the slope of the plot of ln (50% – percent isomerized) vs time = $-2k_{obsd}$. Since isomerization of **1b** would give the methyl ether of **1a**, the final reaction mixture consists of a 50–50 mixture of the methyl ether of **1a** and **1b**.

The reaction mixture was prepared in a 25-mL volumetric flask. The temperature was kept constant at 25 ± 0.1 °C in a constant temperature water bath. Quinone was added to each run to prevent the formation of palladium–π-allyl species and as the reoxidant for atomic palladium(0). For kinetic runs at $[Cl^-] \leq 1.2$ M, the ionic strength, μ, was maintained at 2.0 M with the addition of the appropriate number of moles of $LiClO_4$. The allyl alcohol was kept at 0.171 M for each run. H^+ was added in the form of dichloroacetic acid, which is reported to have a K_a of 4×10^{-7} in methanol.[28]

Product Identification. The isomerization product **1b** was identified by comparison of its spectra with that of the nondeuterated analogue reported in the literature.[29] The products from **4** and allyl alcohol at low and high chloride concentrations were identified by working up the reaction mixtures and comparing their ^1H NMR spectra with those reported in the literature. In the case of exchange and isomerization of **4** at high $[Cl^-]$, the two products, **5** and **6**, were separated by column chromatography with use of a 2-cm × 6-cm silica gel column with 20:80 methylene chloride–petroleum ether as eluant. The 20-mL samples that were collected were evaporated at room temperature. The fractions were identified by NMR. Their relative amounts were determined from a reaction mixture before separation.

Preparation of 2-(Methyl-d_3)-4-methyl-3-penten-2-ol.[30] To 100 mL of 1.0 M CD_3MgI in anhydrous ether was added 9.0 g (0.09 mol) of mesityl oxide, previously dried over anhydrous $MgSO_4$, under a flow of nitrogen. This was stirred for 1 h and then neutralized with 100 mL of 5% HCl. It was stirred until all the precipitate was dissolved. The ether layer was separated and the aqueous layer neutralized with saturated $NaHCO_3$. It was then extracted with 4 × 50 mL portions of ether which were combined, washed with saturated Na_2SO_4, and dried over anhydrous $MgSO_4$. The solvent was air evaporated. Weight = 6.4 g. Yield = 61%. The product was identified by comparing its ^1H NMR spectra with that of its nondeuterated analogue reported in the literature.[31] 300-MHz ^1H NMR ($CDCl_3$): δ = 1.31 (s, 3 H), 1.71 (s, 3 H), 1.87 (s, 3 H), 5.34 (s, 1 H). ^2H NMR ($CHCl_3$) 1.30 (s, 3 D). ^{13}C NMR ($CDCl_3$): δ = 132, 134, 71, 31, 27, 19.

Preparation of 4-Methyl-3-penten-2-ol.[32] Mesityl oxide (5.7 g, 0.06 mol) was dissolved in 150 mL of 0.4 M $CeCl_3$ in methanol. After the mixture was stirred for 10 mins at room temperature 2.3 g (0.06 mol) of $NaBH_4$ was added rapidly. This was allowed to stir for an additional 5 min and then hydrolyzed with 150 mL of cold saturated ammonium chloride. This was extracted with methylene chloride and dried over anhydrous $MgSO_4$ and the solvent air evaporated. Yield = 4.2 g (70%). 300-MHz ^1H NMR ($CDCl_3$): δ = 1.13 (d, 3 H), 1.61 (s, 3 H), 1.65 (s, 3 H), 2.79 (s, OH), 4.45 (q, 1 H), 5.13 (d, 1 H).[6] ^{13}C NMR ($CDCl_3$): δ = 134, 130, 65, 26, 24, 18.

Preparation of 2,4-Dimethyl-2-ethoxy-3-pentene. A 0.44-g sample of palladium(II) chloride (0.0025 mol), and 0.32 g of lithium chloride (0.0075 mol) were dissolved in anhydrous ethanol. After all the $PdCl_2$ dissolved excess anhydrous $MgSO_4$ was added followed by 3.0 g of 2,4-dimethyl-3-penten-2-ol (0.0026 mol). This was allowed to stir for 48 h at room temperature in a capped Erlenmeyer flask. After 25 mL of $CHCl_3$ was added to the mixture and it was washed with four 25-mL portions of distilled water, the organic phase was dried ($MgSO_4$), and evaporated to give 2.5 g of 2,4-dimethyl-2-ethoxy-3-pentene (0.0018 mol), 69% yield. 300-MHz ^1H NMR ($CDCl_3$): δ = 1.12 (t, 3 H), 1.25 (s, 6 H), 1.66 (s, 3 H), 1.76 (s, 3 H), 3.30 (qr, 2 H), 5.04 (s, 1 H). ^{13}C NMR ($CDCl_3$) δ = 18.0, 19.5, 23.5, 24.5, 58, 75, 130, 133.

Preparation of Dichloro(1,1,3,3-tetramethylallyl)palladium(II). 2,4-Dimethyl-3-penten-2-ol (1 g) was dissolved in 25 mL of 0.20 M Li_2PdCl_4 in dry methanol. This was stirred for 10 h. Methylene chloride (50 mL) was added and the resulting solution washed with 4 × 50-mL portions of saturated sodium carbonate. The organic phase was dried over anhydrous $MgSO_4$ and evaporated under vacuum. Golden yellow crystals were obtained. Weight = 0.56 g. Yield = 40%. MP dec = 123 °C. 300-MHz ^1H NMR ($CDCl_3$): δ = 1.5 (m, 12 H), 4.75 (s, 1 H). ^{13}C NMR ($CDCl_3$): δ = 28, 31, 132, 133, 134.

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