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Palladium(II)-Catalyzed Isomerization of (*Z*)-1,4-Diacetoxy-2-Butene: Solvent Effects

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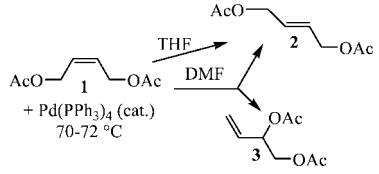
The isomerization of (Z)-1,4-diacetoxy-2-butene (**1**) catalyzed by $PdCl_2(MeCN)_2$ was studied in THF and DMF. The reaction occurs more rapidly in THF than in DMF, but in both solvents it did not proceed to complete consumption of the substrate and led to a mixture of **1**, (*E*)-1,4-diacetoxy-2-butene (**2**), and 1,2-diacetoxy-3-butene (**3**). The formation of **2** is more favored in DMF than in THF. The reactivity of **1** and the solvent effect differ strongly from those previously obtained with $Pd(PPh_3)_4$ as the catalyst. Interpretations are provided for the crucial role of the nature of both solvent and intermediates on the course of the isomerizations.

Introduction

The 1,3-transposition of allylic acetates in the presence of catalytic amounts of palladium complexes is a well known reaction[1,2] that has been extensively used in synthetic organic chemistry. The mechanism of this reaction depends on the oxidation state of palladium.

An η^3-allylpalladium intermediate is usually admitted from Pd^0 catalysis,[3] but we have demonstrated the influence of the polarity of the solvent on the mechanism of the Pd^0-catalyzed isomerization of (*Z*)-1,4-diacetoxy-2-butene (**1**).[4] In the presence of $Pd(PPh_3)_4$, **1** was selectively isomerized to (*E*)-1,4-diacetoxy-2-butene (**2**) in THF while both **2** and 1,2-diacetoxy-3-butene (**3**) were simultaneously obtained in DMF (Scheme 1). A set of experiments led to the conclusion that the involvements of an η^1-allylpalladium in the former solvent and of a cationic η^3-allylpalladium in the latter are the key intermediates that are derived from **1**.



Scheme 1.

The [3,3] sigmatropic rearrangement of allylic acetates through an 1,3-acetoxonium ion type intermediate is usually admitted with Pd^{II} catalysts,[3,5–7] especially when $PdCl_2(RCN)_2$ is used with solvents such as THF, PhMe, and CH_2Cl_2.[8–11] Another mechanism was proposed for when $PdCl_2$ in AcOH or $Pd(OAc)_2$ alone was used; this mechanism involves the addition of Pd^{II} and acetate across the double bond followed by the regeneration of the catalyst from β-elimination of the acetate, specifically, an acetoxypalladation–deacetoxypalladation sequence.[9,12] It was also envisaged that the isomerization of linalyl acetate could imply the cleavage of the C–OAc bond to afford an intermediate having an allylic cation moiety and the 6,7-C=C bond coordinated to $(AcOPdCl_2)^-$.[13] To the best of our knowledge, the Pd^{II}-catalyzed isomerization of 1,2-diacetoxy-3-ene and 1,4-diacetoxy-2-ene type compounds has only been reported from 6,7-diacetoxy-8-tetradecene[11] and 1-substituted-1,4-diacetoxy-4-phenyl-2-butenes.[14] With these last substrates, the acetate transfer occurs only from the benzylic position and leads to the complete rearrangement of the substrate into the corresponding 1-substituted-1,2-diacetoxy-4-phenyl-3-butenes.[14]

The unexpected results obtained from **1** at 70–72 °C under Pd^0 catalysis led us to examine the isomerization of **1**, **2**, and **3** under Pd^{II} catalysis; this study is here reported.

Results

The reaction of **1** at 70–72 °C in THF in the presence of 0.05 equiv. of $PdCl_2(MeCN)_2$ (**4**) led to the formation of **2** and **3**. No products other than **1**, **2**, and **3** were detected from monitoring the course of the reaction by GC and ^1H NMR spectroscopy. After heating for 6 h, the diacetate proportions evolved very moderately (Figure 1, Table S1). The

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addition of a new batch of **4** after 24 h heating led only to a slight increase in the conversion of **1**. Switching from THF as solvent to DMF slowed down the reaction, but increased the conversion of **1** (Figure 1, Table S2). In both solvents, it was impossible to reach the complete transformation of **1**.

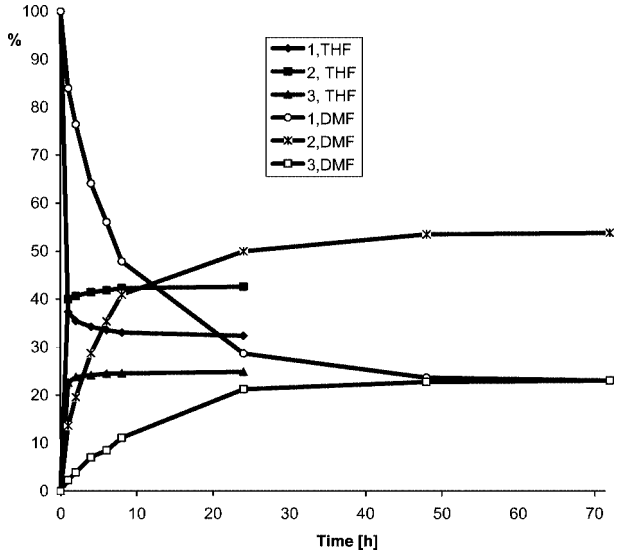


Figure 1. Evolution over time of the diacetate proportions obtained from the $PdCl_2(MeCN)_2$-catalyzed reaction of (*Z*)-1,4-diacetoxy-2-butene (**1**) at 70–72 °C in either THF or DMF.

Diacetates **2** and **3** were also subjected to $PdCl_2(MeCN)_2$ catalysis under the same conditions (Figure 2, Table S3). Isomerizations of **2** into **3** and **3** into **2** without production of **1** were obtained; they occurred more rapidly in THF than in DMF. A deposit of palladium was observed in DMF especially with **3** as the substrate. This catalyst degradation did not allow more than 20% conversion of **3** in DMF to be obtained.

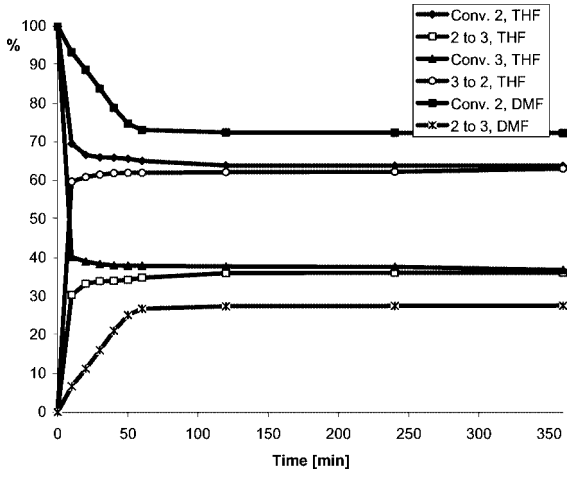


Figure 2. $PdCl_2(MeCN)_2$-catalyzed isomerization of (*E*)-1,4-diacetoxy-2-butene (**2**) and 1,2-diacetoxy-3-butene (**3**) at 70–72 °C.

To slow down the isomerization of **1** in THF, this reaction was repeated at room temperature (Figure 3, Table S4).

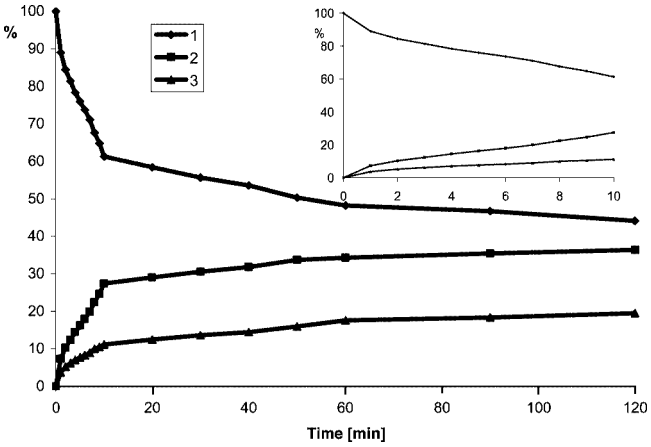
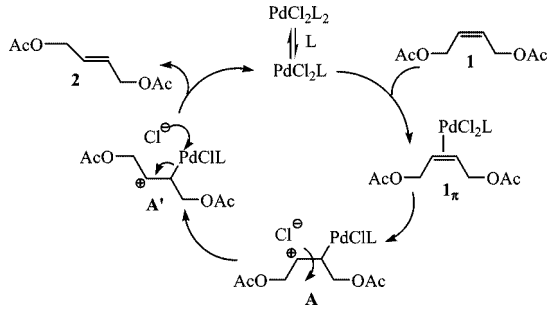


Figure 3. Evolution over time of the diacetate proportions obtained from the $PdCl_2(MeCN)_2$-catalyzed reaction of (*Z*)-1,4-diacetoxy-2-butene (**1**) at room temperature in THF.

Discussion

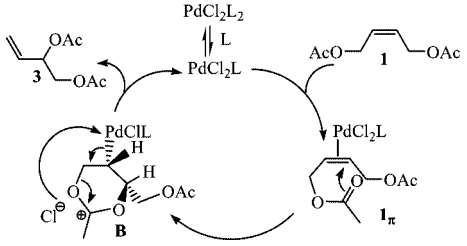
From comparison of the results depicted in Figures 1 and 3 with those previously obtained in the presence of $Pd(PPh_3)_4$,[4] it appears that the efficiency of the Pd-catalyzed isomerization of **1** depends dramatically on the oxidation state of the catalyst. Indeed, the complete conversion of **1** was obtained with $Pd(PPh_3)_4$ but not with $PdCl_2(MeCN)_2$. Moreover, the solvent effect on the reactivity and selectivity are quite different.

The (*Z*/*E*) isomerization of double bonds under Pd^{II} catalysis is well-documented.[15–19] For the mechanism, the intermediate formation of an η^3-allyl(hydrido)palladium(IV) complex was envisaged[18] but subsequent studies ruled out such a possibility.[19,20] Spencer et al. suggested either the formation of a carbocation from the interaction of the C=C bond with $PdCl_2(MeCN)_2$, followed by rotation around the $ClPdC–C^+$ bond and regeneration of the catalyst, or the *trans* addition of $PdCl_2$ to the C=C bond followed by rotation and *syn* β-elimination of $PdCl_2$.[19] It is known that $PdCl_2(RCN)_2$ forms olefin complexes,[21] and theoretical studies have shown that (1) the coordination of $CH_2=CH_2$ to Pd^{II} results in the lowering of the C=C torsional barrier[17] and (2) ethylene coordinated to a Pd atom is positively charged.[22] It is not possible to distinguish between the two mechanistic possibilities proposed by Spencer. Nevertheless, our reaction was carried out in the absence of added chloride,[23] and Sen and Lai have shown that the Pd^{II}-catalyzed migration of C=C bonds occurs via the $Pd^{II}–C–C^+$ intermediate.[24] Consequently, the first proposal of Spencer seems to be the most adequate to explain the **1** → **2** isomerization (Scheme 2).



Scheme 2.

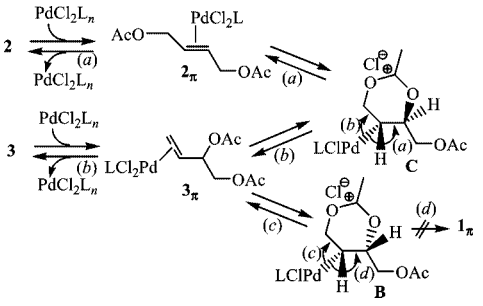
The other reaction pathway from **1** and **4** is the formation of 1,3-acetoxonium ion **B** (Scheme 3). According to the literature,[1,2] particularly the allylic transposition of acetates with 100% chirality transfer,[10,11,25] **B** is produced via the intramolecular *trans* addition of the carbonyl of one ester moiety to the Pd-coordinated double bond.



Scheme 3.

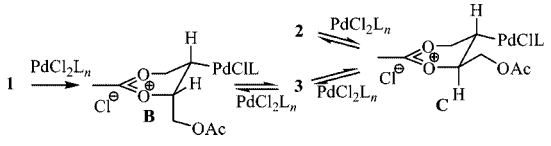
In THF, the isomerization reactions catalyzed by **4** lead to the thermodynamic equilibrium between **2** and **3** (**2/3** ≈ 1.7, Figures 1 and 2, Tables S1 and S3) already observed under Pd^0 catalysis.[4] In contrast, the **2/3** ratio becomes apparently stable for a value of ca. 2.3 (Figure 1) or 2.6 (Figure 2) in DMF. This strong difference between the final **2/3** ratios obtained in THF and DMF could be due to the solvent effect on the equilibria[26,27] or, more probably, to the destruction in DMF of the catalyst with time. Indeed, the addition of a new batch of **4** to the 2.3 mixture of **2** and **3** in DMF decreased the **2/3** ratio (Table S2). The Pd^{II}-catalyzed **2** → **3** and **3** → **2** isomerizations are due to [3,3] sigmatropic rearrangements involving acetoxonium ion **C** (Scheme 4). Acetoxonium ion **B** is also produced from **3**, but given the absence of the formation of **1** from **3** (Figure 2, Table S3), its only reactive pathway is the back reaction leading to $\mathbf{3}_\pi$ (Scheme 4).

The palladium oxidation state depending reactivity of **1**, namely complete transformation with $Pd(PPh_3)_4$[4] but not with $PdCl_2(MeCN)_2$, is difficult to rationalize because both catalysts involve the formation of an η^2-palladium complex as the first step. The only partial conversion of **1** under Pd^{II} catalysis is not justified by the mechanisms depicted in Schemes 2 and 3. The slower $PdCl_2$-induced rearrangement of (*Z*)-allylic acetates relative to the corresponding (*E*) isomers[2,9,10b,28] could be invoked, but is not a sufficient reason. A possible explanation is issued from reports of Golding et al.[3,7,28] According to these authors, the isomerization of (*E*,*Z*)-4-acetoxy-hepta-2,5-diene occurs preferentially at the (*E*) double bond with $PdCl_2(MeCN)_2$ to afford (3*E*,5*Z*)-2-acetoxy-hepta-3,5-diene, whereas the reaction with $Pd(PPh_3)_4$ involves the (*Z*) double bond and leads to (3*E*,5*E*)-2-acetoxy-hepta-3,5-diene.[3] The observations of Golding led us to suspect that the interaction of Pd^{II} species with the C=C bond of **2** and **3** is easier than with the (*Z*) double bond of **1**; this preference would lead to a reaction occurring almost exclusively with **2** and/or **3** when the relative concentration of **1** decreases to a given level. From the results depicted in Figure 1, this level depends on the solvent. This could be due to the influence of the nature of the solvent on the conformation of the substrates.[26]



Scheme 4.

The preference for reactions from **2** and/or **3** rather than from **1** can be, in part, also explained by comparing the steric interactions developed in acetoxonium ions **B** and **C**, as well as their formation and their reactive pathways (Scheme 5). All substituents of **C** are quasiequatorial while **B** possesses a quasiaxial substituent. Consequently, the formation of **C** that is produced from **2** and **3** and leads to both **2** and **3**, is likely easier than that of **B** that is produced from **1** and **3** but evolves to only **3**.



Scheme 5.

The solvent also impacts the rate of the conversion of **1**, and the selectivity of this process as exemplified in Figures 1 (Table S1 and S2) and 4 (Table S5), respectively. For a conversion of 16%, the **2/3** ratios were ca. 2 and 6 in THF and DMF, respectively (Figure 4). As expected, the concurrent **2** → **3** isomerization led to the decrease in these differences with the reaction time. These results show that in a polar solvent such as DMF,[29] in which separated ions should be produced,[30] the $PdCl_2(MeCN)_2$-catalyzed reaction of **1** involves mainly the (*Z*) → (*E*) isomerization of the C=C bond, specifically, a reaction via carbocation **A** as depicted in Scheme 2 rather than via acetoxonium ion **B** (Scheme 3). The equilibrium between carbocations **A** and **A′** is independent of a reaction with Cl^- (Scheme 2) whereas the **B** → **3** pathway requires Cl^- (Scheme 3). In DMF, the chloride anion is more solvated than in THF; consequently, it is less prone to react with the PdClL moiety, hence the increase in the (*Z*) → (*E*) isomerization compared to the 1,3-transposi-

tion. This solvent effect on the selectivity differs strongly from the one previously observed under Pd^0 catalysis[4] since (1) in THF, $Pd(PPh_3)_4$ leads to the exclusive or almost exclusive isomerization of **1** into **2**, while $PdCl_2(MeCN)_2$ affords a ca. 2:1 mixture of **2** and **3** and (2) in DMF, both $PdCl_2(MeCN)_2$ and $Pd(PPh_3)_4$ lead to **2** and **3** from **1**, but the formation of **2** is more privileged by the Pd^{II} catalyst. The differences in the conversion rates with the nature of the solvent (Figure 1) can also be explained by the differences in the solvation of the ionic intermediates that are more stabilized in DMF than in THF, and, consequently, they should evolve more slowly towards the products.

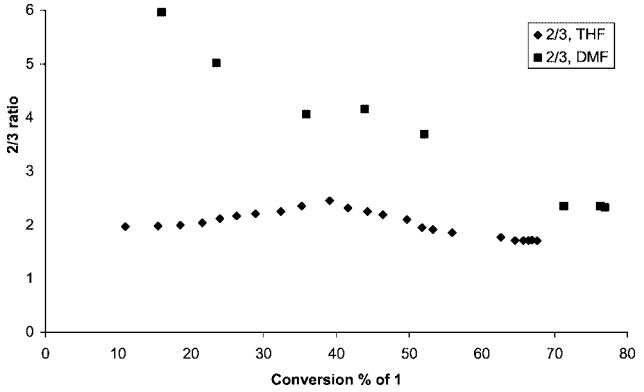


Figure 4. Influence of the solvent and the conversion on the ratio of diacetates **2** and **3** obtained from **1**.

Experimental Section

General: THF was distilled from sodium/benzophenone under an argon atmosphere. Diacetates **1**, **2**, and **3** and $PdCl_2(MeCN)_2$ were prepared as previously reported.[4,31] NMR spectra were obtained with a Bruker AC 250 spectrometer. GC analysis were performed with an HP6890 apparatus equipped with DB1 capillary column (length: 25 m, diameter: 0.32 mm) and an HP 3395 integrator.

General Isomerization Procedure and Determination of the Acetate Ratios: To a solution of **1**, **2**, or **3** (700 mg, 4.07 mmol) in dry THF or DMF (15 mL) under an atmosphere of argon was added $PdCl_2(MeCN)_2$ (52.8 mg, 0.05 equiv.), and the mixture was warmed in a bath heated at 70–72 °C. Samples were removed from the reaction mixture at the times mentioned in the tables, filtered through Celite, and then analyzed by GC. ^{1}H NMR spectroscopic analyses were carried out after evaporation of the solvent followed by dissolution of the residues in $CDCl_3$.

GC analysis: Gas: nitrogen (4 bar); injector and detector temperatures: 250 °C; oven temperature: 70 °C for 5 min, then 2 °C/min till 200 °C; internal standard: nonane; retention times, nonane: 4.67 min, **3**: 10.08 min, **1**: 16.12 min, **2**: 17.08 min.

^{1}H NMR spectroscopic analysis: The ratios between the different acetates were established from the respective integrations of the CH_2 of **1** (δ = 4.62 ppm) and **2** (δ = 4.58 ppm), and the C*H* proton of **3** (δ = 5.74 ppm); the precision of the integrations was estimated to be ± 3%.

Supporting Information (see footnote on the first page of this article): Tables S1, S2, S3, S4, and S5.

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