First Evidence That the Mechanism of Catalytic Hydrogenation with Homogeneous Palladium and Rhodium Catalysts Is Strongly Influenced by Substrate Polarity

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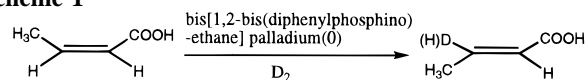*University of Cambridge, Lensfield Road*
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Received December 4, 1996

Homogeneous palladium and rhodium catalysts have assumed an important position in synthetic chemistry because of their utility in the semireduction of alkynes[1−2] and the asymmetric reduction of prochiral alkenes.[3−6] Although there have been many studies conducted, the electronic mode in which the transition metal hydrogen species adds to the double bond of the alkene has never been determined. It has been reported that the geminal hydrogens of terminal alkenes can be exchanged by deuterium with homogeneous catalysts.[7−9] We have recently found that during the reduction of *cis*-alkenes, such as *cis*-crotonic acid, with deuterium some *trans*-alkenes are formed that contain one deuterium atom (Scheme 1). This identifies that deuterium is directly involved in the isomerization of the *cis*-alkenes and has allowed us to investigate for the first time the electronic properties of the hydrogen bonded to the metal, by determining how electron-donating or -withdrawing groups conjugated to the double bond influence the location of the hydrogen addition. If the metal hydrogen bond is polarized in the catalyst, the hydrogen should selectively add to the most electronically favored end of the double bond.
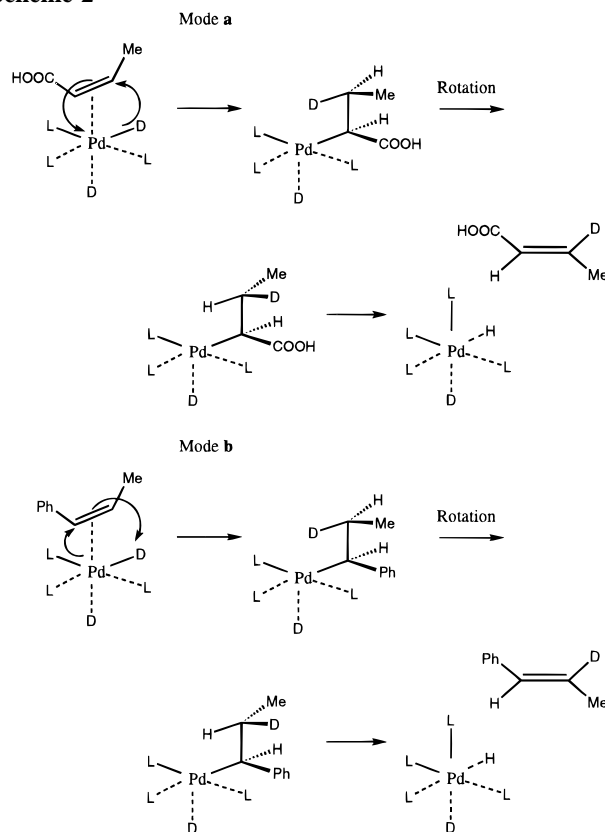
We report in this paper that by using this methodology we have been able to demonstrate that the palladium hydrogen bond can be polarized in either mode (**a**) $Pd^{\delta+}-H^{\delta-}$ or (**b**) $Pd^{\delta-}-H^{\delta+}$), whereas the rhodium catalyst studied is dominated by mode **a** ($Rh^{\delta+}-H^{\delta-}$). This provides strong evidence that the mechanism of catalytic hydrogenation with homogeneous catalysts is a two electron process that can be dramatically affected by the Coulombic nature of the substrate.

Pure *cis*-alkenes with a variety of different functional groups attached (to the double bond) were individually isomerized using deuterium gas and either the palladium or rhodium catalyst to give a mixture of the labeled *trans*-alkene (10−45%) and alkane. NMR analysis of the *trans*-alkenes clearly showed that the deuterium is not evenly distributed across the double bond (Table 1). Deuterium is found only to be present in crotonic acid (**1**) and ethyl crotonate (**2**) at the carbon remote to the carbonyl group when the isomerization is carried out with bis-[1,2-bis(diphenylphosphino)ethane]palladium(0). α,β-Unsatur-

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Scheme 1

Scheme 2

ated compounds, such as crotonic acid, are polarized so that the carbon remote to carbonyl group is electron deficient (compared to the carbon next to the functional group) and readily react at this position with nucleophilic species. The deuterium distribution in **1** and **2** would therefore be consistent with the palladium−hydrogen bond being polarized so that the hydrogen was electronegative and the palladium electropositive (mode **a** $Pd^{\delta+}-H^{\delta-}$) just prior to their addition to the double bond. The intermediate formed after addition can then receive another hydrogen from the palladium to form the saturated alkane or rotate with the subsequent elimination of the hydrogen attached to the remote carbon to give the deuterated *trans*-alkene (Scheme 2).

To investigate how a functional group with the opposite characteristics to a carbonyl group might influence the mode of addition of the palladium hydrogen species to the double bond, compounds containing a phenyl group conjugated to the double bond were studied using unlabeled **3** and the *cis*-isomer of **4** (Table 1). The aromatic group, particularly with a *p*-methoxy substituent, will polarize the double bond so that the remote carbon is electron rich compared to the one next to the functional group. The deuterium distribution in compounds **3** and **4** (formed using the palladium catalyst) shows that the label is located solely in the position remote to the aromatic group. This result is completely opposite to what would be predicted if the palladium hydrogen bond is polarized in mode **a** ($Pd^{\delta+}-H^{\delta-}$) as was proposed for crotonic acid (**1**) and ethyl crotonate (**2**). More consistent with this regioselectivity of the deuteration would be for the palladium−hydrogen bond to be polarized in the opposite way (mode **b** $Pd^{\delta-}-H^{\delta+}$) so that the palladium was electronegative and the hydrogen electropositive (Scheme 2).

Table 1

isomerization product	catalyst[a]	deuterium distribution (%)		relative ratio of deuterium (%)	
		I	II	I	II
1 H₃C–C=C COOH	Pd	64	0	100	0
2 H₃C–C=C COOEt	Pd	59	0	100	0
3 MeO–⬡–C=C	Pd	0	*Cis* 32[b] *Trans* 32	0	100
	Rh	0	0	0	0
4 ⬡–C=C–C₂H₅	Pd	0	65	0	100
5 ⬡–C=C–COOH	Pd	37	6	86	14
	Rh	22	0	100	0
6 ⬡(OMe)–C=C–COOH	Pd	41	15	73	27
7 MeO–⬡–C=C–COOH	Pd	22	24	48	52
8 ⬡–C=C–OMe	Pd	37	4	90	10
	Rh	0	55	0	100

a Pd: bis[1,2-bis(diphenylphosphino)ethane]palladium(0). Rh: chlorotris(triphenylphosphine)rhodium(I) (Wilkinson's catalyst). *b Cis/trans* refers to the deuterium being *cis/trans* to the aromatic group. Some compound was identified with 2 deuteriums in the terminal position of the double bond. The proportion of this compound increased with a longer reaction time as did that of the monodeuterated species.

To further investigate which mode of addition is preferred, *cis*-alkenes with functional groups conjugated to both ends of the double bond were isomerized with deuterium and the palladium catalyst. The results show for *cis*-isomer of cinnamic acid (**5**) that either position can be deuterated; 86% of the deuterium is remote to the carbonyl group with only 14% remote to the phenyl group. The double bond of **5** is strongly polarized and can therefore promote both modes of addition, however, the deuterium distribution shows that mode **a** is favored. Compounds **6** and **7** differ from **5** by having an *o*- or *p*-methoxy group in the aromatic ring and result in a significant increase in the proportion of deuterium remote to this aromatic group compared to the same position in **5**. The aromatic ring substituted with an *o*- or *p*-methoxy group will be more electron releasing than the phenyl ring of cinnamic acid and hence may aid attack of an electrophilic hydrogen on the carbon remote to this group.

The results clearly show that steric effects have only a minor role on the regioselectivity of the metal hydrogen addition to the double bond of these substrates since compound **7** containing a *p*-methoxy group is sterically no more demanding than cinnamic acid (**5**).

When the same approach was used to investigate the electronic properties of a rhodium catalyst [chlorotris(triphenylphosphine)rhodium(I)], the results with compounds **3**, **5**, and **8** (Table 1) reveal that compared with the palladium catalyst rhodium−hydrogen addition occurs predominantly by mode **a** ($Rh^{\delta+}$−$H^{\delta-}$). This difference in electronic properties as highlighted for enol ether **8** (Figure 1) cannot be explained by the metal's influence on a one-electron process.[10] This strongly suggests that catalytic hydrogenation with homogeneous cata-
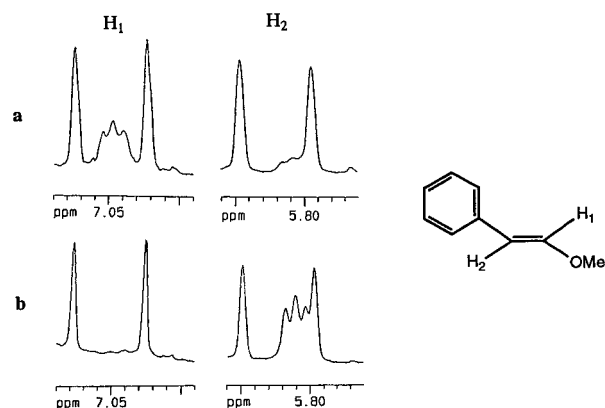

Figure 1. Part of the ¹H NMR spectrum (250 MHz, CDCl₃) (double bond region) for the *trans*-enol ether **8** formed by the isomerization of the *cis*-isomer using D₂ and (a) bis[1,2-bis(diphenylphosphino)ethane]-palladium(0) or (b) chlorotris(triphenylphosphine)rhodium(I). The triplets observed inside the doublets show deuterium hydrogen coupling that occurs in the labeled compound.

lysts is most likely a two-electron process that, for palladium, is strongly influenced by the Coulombic properties of the substrate.

Previous work has established that the formation of *trans*-alkenes by β-elimination occurs with *cis*-geometry[11] (Scheme 2) and would predict 100% incorporation of deuterium into alkenes **1−8**. Intriguingly, the level of deuterium incorporated is substantially less (Table 1), suggesting either a different mechanism is taking place or there are competing mechanisms.

It is possible that the addition of metal and hydrogen to the double bond is not concerted. If the metal adds first to the double bond of the *cis*-alkene, to give a charged intermediate whose lifetime was sufficient for rotation to take place to the *trans*-conformation, then isomerization could occur without incorporation of deuterium. Alternatively, hydrogen could add first to the double bond to give a charged intermediate that again would allow rotation to take place, with the double bond being reformed by elimination of a hydrogen or a deuterium. This last step might be subject to a kinetic isotope effect and should give at least a 50% incorporation of deuterium into the *trans*-alkene. Having functional groups conjugated to the double bond that are capable of stabilizing such charged intermediates might favor these stepwise pathways and explain why such molecules isomerize readily during hydrogenation compared to simple *cis*-alkenes.

The identification that the mode of addition is strongly governed by the polarity of the substrate should greatly aid the understanding of asymmetric reduction of alkenes as it affords an insight into the likely structure of the intermediate formed during their hydrogenation.[12] The approach reported here should also prove useful for the rational design of new catalysts, as their electronic properties can be readily determined using this methodology.

Supporting Information Available: Experimental details and spectroscopic and analytical data for compounds **1−8** (6 pages). See any current masthead page for ordering and Internet access instructions.

JA964179I

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