Evidence for a (π-Allyl)palladium Intermediate in the Quinone-based Palladium-catalysed Allylic Acetoxylation

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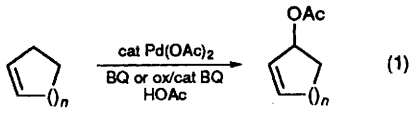
The mechanism of the quinone-based palladium-catalysed allylic acetoxylation of cyclohexene is studied using 1,2-dideuteriocyclohexene (55–70% D) as substrate; the distribution of the deuterium label in the product, determined by ^{1}H NMR spectroscopy, is that expected for a (π-allyl)palladium intermediate.

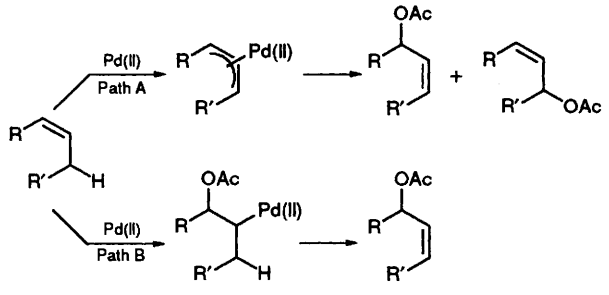
Palladium-catalysed allylic oxidation has developed into a synthetically useful method. In particular, cyclic olefins are oxidised to their corresponding allylic acetates in excellent yields and high selectivity employing *p*-benzoquinone (BQ) as stoichiometric oxidant or electron-transfer mediator [eqn. (1)].[1] The mechanism of this Pd^{II}-catalysed transformation has



(1)

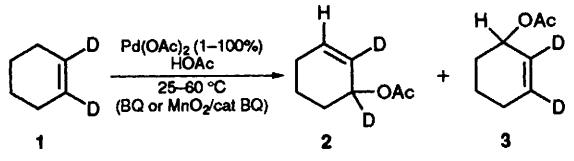
been subject to debate, and two alternative principal pathways have been put forward (Scheme 1).[2–6] One mechanism involves formation of a (π-allyl)palladium intermediate *via* allylic C–H bond activation[7] followed by a nucleophilic attack by acetate[8] (path A). The other proceeds *via* an acetoxypalladation-β-elimination sequence (path B).[2,4]

The mechanism seems to depend upon both the substrate and the oxidation system.[2] Thus, Winstein[3] and Henry[4] obtained results that indicated an acetoxypalladation pathway (Scheme 1, path B) when employing $Pd(OAc)_2$ (stoichiometric) or $PdCl_2$–$CuCl_2$ as oxidants, respectively. On the other hand, Wolfe[5] and Frankel[6] proved that a π-allyl route (Scheme 1, path A) predominates with other reoxidation systems. Although the quinone-based allylic acetoxylation [eqn. (1)] has been assumed to proceed *via* a (π-allyl)palladium(II) intermediate,[1] conclusive evidence for such a mechanism is lacking. In this communication, we provide evidence for the (π-allyl) route in the allylic acetoxylation of cyclohexene.



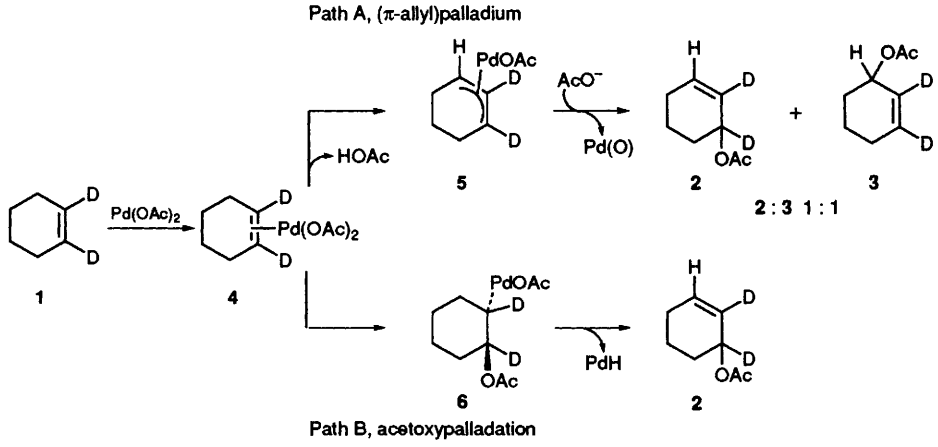
Scheme 1 (π-Allyl) route (A) *vs.* oxypalladation route (B) in allylic acetoxylation

To distinguish between the two mechanistic pathways (Scheme 1), a symmetrically deuteriated cyclohexene, 1,2-dideuteriocyclohexene **1** was used as substrate.[9]† Palladium-catalysed allylic oxidation of **1** employing $Pd(OAc)_2$ as catalyst and *p*-benzoquinone (2 equiv.) as oxidant in acetic acid[1] afforded a 1 : 1 mixture of the deuteriated products **2** and **3**, as determined by ^{1}H NMR spectroscopy. The same result was obtained when employing catalytic amounts of *p*-benzoquinone with MnO_2 as the oxidant. The results are summarised in Table 1.



1 2 3 (2)

In Scheme 2, the expected outcome of an allylic acetoxylation of 1,2-dideuteriocyclohexene is shown. For both mechanisms the initial step would be a coordination of palladium(II) to the double bond to give **4**. Then, either cleavage of the activated allylic C–H bond[7] to yield a (π-allyl)palladium complex **5**, or a *trans* attack[4] by acetate to yield **6** occurs. Both pathways would yield a dideuterated 1-acetoxy-2-cyclohexene with the deuterium label intact at C-2. If neglecting the secondary isotope effect,[10] the (π-allyl) pathway would give equal amounts of the products **2** and **3**. The acetoxypalladation pathway should, on the other hand, yield only the 1,2-dideuterated allylic acetate **2**. For an olefin containing less deuterium, the reasoning is analogous, since the amount of deuterium at position 2 in the product always reflects the degree of deuteration of the olefin.‡ In Table 1, the theoretical distribution of the deuterium label for the two pathways have been calculated.§ The observed distribution is in excellent agreement with that expected from a mechanism involving a (π-allyl)palladium intermediate.¶



Scheme 2

Table 1 Some reaction conditions for the allylic acetoxylation of 1,2-dideuteriocyclohexene (55–70% D)[a,‡]

				^{1}H NMR (3-H : 2-H : 1-H)[b]		
% $Pd(OAc)_2$	Oxidant	T/°C	% D‡	π-Allyl[c]	Acetoxypalladation[d]	Observed[e]
100	Pd^{II}[e]	60	55	1.61 : 1 : 1.61	2.22 : 1 : 1	1.64 : 1 : 1.64
5	BQ (200%)	60	65	1.93 : 1 : 1.93	2.70 : 1 : 1	1.94 : 1 : 1.97
5	BQ (200%)	25				1.88 : 1 : 1.84
1	MnO_2 (110%)[f]	60	70	2.17 : 1 : 2.17	3.33 : 1 : 1	2.33 : 1 : 2.22
2	MnO_2 (110%)[f]	60				2.29 : 1 : 2.22

[a] The reactions were carried out on a 0.25 mmol scale in reagent grade acetic acid. [b] The integral of 2-H of 1-acetoxy-2-cyclohexene was used to normalise the integrals of protons 1- and 3-H.§ [c] Calculated values. [d] Estimated error ±0.02. [e] No reoxidant for Pd^0. [f] See ref. 1*a*,*b*.

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Footnotes

† An investigation of a palladium-mediated allylic acetoxylation with HNO_2–HNO_3–$Hg(OAc)_2$ as reoxidation system using 3,3,6,6-tetradeuteriocyclohexene was carried out by Wolfe *et al.*[5b]

‡ The amount of deuterium (x_D) in the two vinylic positions was determined by ^{1}H NMR spectroscopy from the ratio of the relative integral of the vinylic signal (I_{rel}) to that of the non-deuteriated compound (which is 2). Thus x_D can be defined by $x_D = 1 - (I_{rel}/2)$, and vary between 0 and 1, with the latter figure representing complete deuteriation in both vinylic positions, *i.e.* 1,2-dideuteriocyclohexene.

§ The mechanism involving acetoxypalladation would give an ^{1}H NMR integration ratio for protons 3-H, 2-H and 1-H of 1-acetoxy-2-cyclohexene of $1 : (1 - x_D) : (1 - x_D)$, where x_D is the relative amount of deuterium in the vinylic position of the starting cyclohexene.‡ For a (π-allyl)palladium mechanism the corresponding ratio would be $(2 - x_D)/2 : (1 - x_D) : (2 - x_D)/2$. In calculating the theoretical distributions of the label (Table 1) the presence of mono- and non-deuteriated cyclohexene in addition to dideuteriated material has been accounted for.

¶ Recently, a palladium-mediated allylic amination was reported that most likely proceed *via* a (π-allyl)palladium intermediate: C. H. Heathcock, J. A. Stafford and D. L. Clark, *J. Org. Chem.*, 1992, **57**, 2575.

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