

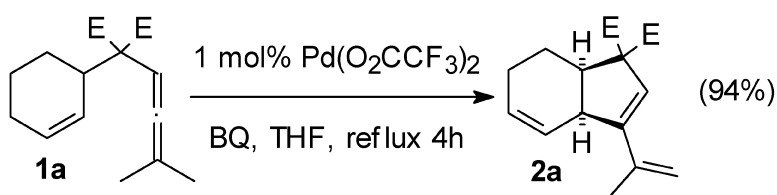
Communication

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Carbon–Carbon Bond Formation in Palladium(II)-Catalyzed Allylic Oxidation: A Novel Oxidative Carbocyclization of Allene-Substituted Olefins

Johan Franzén and Jan-E. Bäckvall*

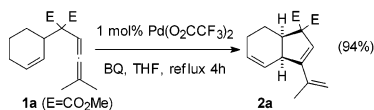
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Functionalizations of C–H bonds are important processes that have attracted considerable attention recently.¹ A special case is the activation of allylic C–H bonds, and there are many reports in the literature on metal-mediated allylic oxidations.^{2–5} Most of these reactions, however, proceed with moderate selectivity and often with the use of stoichiometric amounts of the metal. A few examples of catalytic allylic oxidations are known, and these include palladium- and copper-catalyzed allylic acyloxylation to give allylic esters.^{3,4} Allylic oxidations involving carbon–carbon bond formation are scarce and are only known with the use of stoichiometric amounts of metal.⁶ For example, it is known that palladium(II) complexes can cleave allylic C–H bonds to give (π -allyl)palladium complexes.⁷ Activation of these π -allyl complexes by phosphine ligands and subsequent nucleophilic attack by a stabilized carbanion lead to C–C bond formation in the allylic position.^{6,8} The requirement of stoichiometric amounts of metal limits the synthetic utility of these reactions.

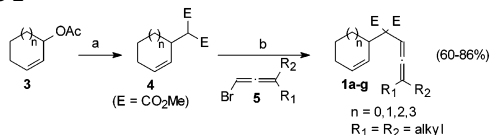
We have recently been involved in palladium-catalyzed reactions with allenes.^{9,10} In the present study, we have found that allene-substituted olefins **1** cyclize oxidatively in the presence of catalytic amounts of Pd(O₂CCF₃)₂ to give **2** (Scheme 1). This is the first example of an allylic oxidation leading to carbon–carbon bond formation employing catalytic amounts of palladium(II).¹¹

Scheme 1



The requisite starting materials **1** were readily obtained from the corresponding allylic acetates **3**. A Pd(0)-catalyzed allylic substitution of the acetate with sodium dimethyl malonate to give **4** followed by reaction with bromoallene **5** furnished **1a–g** (Scheme 2).

Scheme 2^a



^a (a) NaH, (MeO₂C)₂CH₂, Pd(OAc)₂, PPh₃, THF, reflux; (b) NaH, **5**, THF, reflux.

Treatment of allene-substituted olefins **1a–d** with 1 mol % Pd(O₂CCF₃)₂ and 2 equiv of *p*-benzoquinone (BQ) in refluxing THF for 4–6 h gave **2a–d** in good to high yields (entries 1–4, Table 1). The dependence of the substrate ring size on the outcome of the cyclization was investigated (entries 5–7, Table 1). The five-membered ring (**1e**) cyclized to give a mixture of isomers **2e** and **2e'**. The formation of **2e'** can be explained by a Pd(II)-catalyzed isomerization of **2e**.

In contrast to the five- and six-membered ring substrates **1a–e**, which all gave the *cis*-fused ring systems, the seven-membered ring substrate **1f** afforded the *trans*-fused ring system **2f** as a single

Table 1. Palladium(II)-Catalyzed Oxidative Carbocyclization of Allene-Substituted Olefins **1^a**

Entry	Starting material	Product	Yield (%) / ratio
1			94
2			84 ^b
3			76 2c : 2c' = 1:1 <i>E/Z</i> = 4/1
4			96 2d : 2d' = 1:1
5			80 ^c 2e : 2e' = 52:48
6			82
7			73
8			64
9			78 ^d

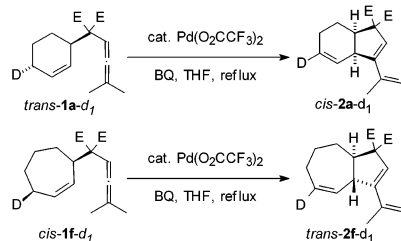
^a Unless otherwise noted, **1**, Pd(O₂CCF₃)₂ (1 mol %), and BQ (2 equiv) were dissolved in THF (5 mL/mmol) and refluxed for 4 h. ^b 6 h of reflux was required for full conversion. ^c 12 h of reflux was required for full conversion. ^d Refluxing toluene and Pd(OAc)₂ (2 mol %) were used.

isomer in 82% yield. The stereochemistry of **2f** was unambiguously assigned by NOE measurements. When the ring size was further increased to an eight-membered ring **1g**, the *cis*-fused ring system was again obtained as the only product. The acyclic substrate **1h** gave triene **2h**. Interestingly, allylic pivalate *trans*-**1i**, in which the allenic moiety and the ester function are *trans* to one another, underwent oxidative cyclization in refluxing toluene with Pd(OAc)₂ as the catalyst to give vinylic pivalate **2i**.¹² On the other hand, the isomeric substrate *cis*-**1i**, with the pivalate and the allenic moiety *cis* to one another, cyclized to give **2a**. The latter reaction is not an oxidation reaction but formally an elimination of pivalic acid with cyclization.

If an additional olefin was placed in the allenic side chain, or if two methyl groups were placed in the allylic position, the cyclization was completely inhibited under the present reaction conditions.

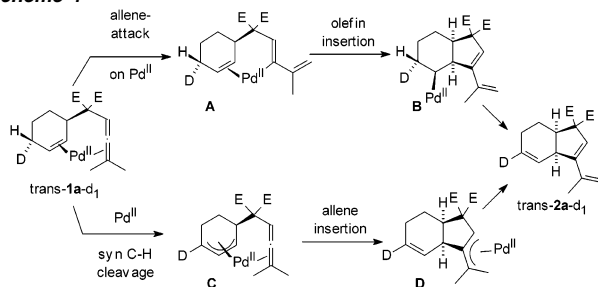
To gain further insight into the mechanism of the cyclization of **1** to **2**, deuterated compounds *trans*-**1a-d**₁ and *cis*-**1f-d**₁ were prepared.¹³ Oxidation of *trans*-**1a-d**₁ and *cis*-**1f-d**₁ by BQ in the presence of catalytic amounts of Pd(O₂CCF₃)₂ gave *cis*-**2a-d**₁ and *trans*-**2f-d**₁, respectively, with complete retention of deuterium (Scheme 3).

Scheme 3



At least two mechanisms can be considered for these palladium-catalyzed oxidative carbon–carbon bond forming reactions. A mechanism via a (π -cyclohexenyl)palladium complex (*trans*-**1a-d**₁, Scheme 4) with palladium syn to the pending allene followed by nucleophilic attack on palladium by the allene¹⁴ (**A**) and subsequent insertion would give **B**. Subsequent syn β -hydride elimination would give *trans*-**2a-d**₁. Also, formation of a (η^3 -cyclohexenyl)palladium complex from the top side of the ring (**C**) followed by insertion of the allene into the allyl–palladium bond¹⁵ (**D**), and subsequent β -hydride elimination, would account for the retention of deuterium. A Pd(II)/Pd(IV) cycloaddition path seems less likely but cannot be excluded.¹⁶

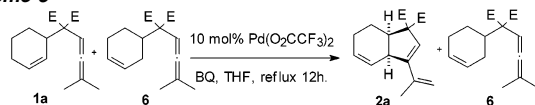
Scheme 4



The seven-membered ring analogue *cis*-**1f-d**₁ would follow analogous mechanisms but with palladium on the opposite side of the ring as the pendant allene.

Independent of which mechanism that operates, the results of the deuterium experiment require that palladium binds to the six-membered ring syn to the pending allene because both allylic C–H bond cleavage and β -elimination are syn-selective processes. Analogously, Pd(II) must bind anti to the side chain for the seven-membered ring. However, formation of **2h** from **1h** is only consistent with the first proposal, involving intermediates **A** and **B**. Furthermore, when **1a** and **6** were allowed to react in a competitive reaction, only **1a** was converted to **2a**, whereas **6** remained unreacted (Scheme 5).¹⁷ This suggests that a pathway

Scheme 5



via (π -allyl)palladium intermediate **C** (Scheme 4) is less likely. However, another interpretation is that the cyclohexene double bond is not forming a favorable chelate in **6** required to give (π -allyl)palladium intermediate **C** (cf. *trans*-**1a-d**₁ \rightarrow **C**, Scheme 4).

In summary, we have found that allene-substituted olefins undergo an oxidative cyclization, in good to excellent yields, in the presence of Pd(O₂CCF₃)₂ as catalyst and *p*-benzoquinone as the stoichiometric oxidant. The fact that the catalyst loading can be as low as 1 mol % and that the starting materials are readily accessible makes this oxidation attractive in organic synthesis.

Acknowledgment. Financial support from the Swedish Research Council and the Swedish Foundation for Strategic Research is gratefully acknowledged.

Supporting Information Available: Experimental procedures and characterizations for products **1a**, **2a**, deuterated compounds *trans*-**1a-d**₁, *cis*-**2a-d**₁, *cis*-**1f-d**₁, *trans*-**2f-d**₁, and spectral data for all new compounds (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- To our knowledge, there are only a few examples of Pd(II)-catalyzed oxidative alkylation of olefins known. For example, olefinic silyl enol ethers undergo Pd(II)-catalyzed cyclizations via silyl enol attack on the olefin.^{11a,b} Also, intramolecular attack by carbon nucleophiles on cyclic 1,3-dienes occurs in Pd(II)-catalyzed oxidations.^{11c,d} (a) Toyota, M.; Rudyanto, M.; Masataka, I. *J. Org. Chem.* **2002**, *67*, 3374–3386. (b) Ito, Y.; Aoyama, H.; Hirao, T.; Mochizuki, A.; Saegusa, T. *J. Am. Chem. Soc.* **1979**, *101*, 494–496. (c) Rönn, M.; Andersson, P. G.; Bäckvall, J. E. *Tetrahedron Lett.* **1997**, *38*, 3603–3606. (d) Castaño, A. M.; Persson, B. A.; Bäckvall, J. E. *Chem.-Eur. J.* **1997**, *3*, 482–490.
- Attempts to cyclize **1i** with Pd(O₂CCF₃)₂/BQ in refluxing THF gave no reaction, and the starting material was recovered. Attempts to cyclize **1i** with Pd(O₂CCF₃)₂/BQ in refluxing toluene resulted in a complex mixture of unidentified products.
- Deuterated compounds *trans*-**1a-d**₁ and *cis*-**1f-d**₁ were prepared via Pd(0)-catalyzed NaBD₄ reduction of the corresponding allylic trifluoroacetate (see Supporting Information).
- Formation of the vinylidene-palladium intermediate **A** is believed to involve a nucleophilic attack on the palladium atom to give a carbocationic intermediate followed by elimination of a proton, rather than an oxidative allylic C–H abstraction. However, both pathways would lead to the same intermediate **A**.
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- Compounds **1a** and **6** would be able to form the same (π -allyl)palladium intermediate and should in that case both cyclize to give **2a**.

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