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Allenes as Carbon Nucleophiles in Palladium-Catalyzed Reactions: Observation of Anti Attack of Allenes on (π-Allyl)palladium Complexes

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Nucleophilic attack on (π-allyl)palladium complexes is one of the most studied organometallic steps in catalytic palladium chemistry.[1,2] In catalytic reactions a (π-allyl)palladium intermediate can be generated from an allylic carboxylate,[2,3] a conjugated diene,[4,5] or an allene.[6,7] Various carbon and heteroatom nucleophiles are known to react with the (π-allyl)palladium intermediates in these reactions.[1,8] Recently, also enantioselective catalytic reactions involving nucleophilic attack to (π-allyl)palladium complex have been reported.[9−11]

Examples on the use of π-nucleophiles, for instance, C−C double bonds, in (π-allyl)palladium chemistry are scarce.[12] Some of the few examples include the use of an allylstannane or an allylsilane as nucleophiles in palladium-catalyzed substitution of an allylic acetate.[12d,13] Attack by an unactivated carbon−carbon double bond on a (π-allyl)palladium complex has been inferred as a mechanistic possibility in catalytic carbon−carbon bond-forming reactions,[14−16] but thus far no stereochemical evidence has been provided. In this communication we report on the first established example of trans attack by an allene double bond on a (π-allyl)palladium complex. It is shown that the allene acts as a nucleophile and has attacked the π-allyl complex on the face opposite to that of palladium.

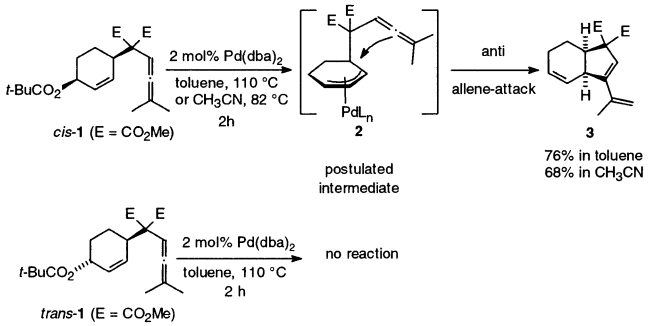
In connection with our studies on palladium-catalyzed intramolecular carbon−carbon bond-forming reactions,[17−19] we observed that allenic allylic pivalate *cis*-**1**[20] underwent a smooth cyclization in the presence of catalytic amounts of $Pd(dba)_2$ in toluene or acetonitrile to give product **3**. Attempted reaction with *trans*-**1** in toluene under the same reaction conditions gave no cyclization product, and the starting material was recovered (Scheme 1).

These observations led us to postulate that (π-allyl)palladium complex **2,** generated from *cis*-**1** by anti oxidative addition, could be the intermediate. Attack by the allene on the π-allyl group on the face opposite to that of palladium would give the cyclized product **3**.[21] Attempts to detect intermediate **2** by ^{1}H NMR during the palladium-catalyzed reaction of *cis*-**1** in toluene-d_8 were unsuccessful, and only starting material and product could be observed. We argued that this may be due to a slow oxidative addition of the allylic pivalate to $Pd(dba)_2$ followed by a fast nucleophilic attack by the allene.

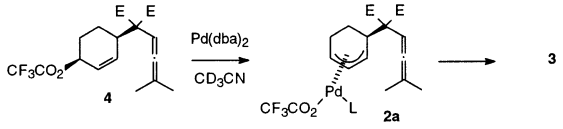
We therefore prepared the trifluoroacetate analogue **4**,[22] which is expected to rapidly generate the postulated intermediate at a much lower temperature than that required for *cis*-**1**.[23] The reaction of **4** with $Pd(dba)_2$ in CD_3CN at room temperature was monitored by ^{1}H NMR spectroscopy (Scheme 2).

In this case a (π-allyl)palladium complex was observed which on prolonged reaction time and slightly elevated temperatures[24] afforded the cyclized product **3**. The ^{1}H NMR of the π-allyl complex is consistent with the postulated intermediate in Scheme 1. Since oxidative addition of allylic carboxylates to Pd(0) is known

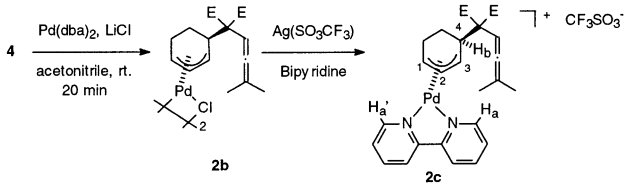
Scheme 1



Scheme 2



Scheme 3



to take place with inversion of configuration[1,2] we have assigned it as **2a**, where palladium is trans to the allenic side chain.

To obtain further evidence for the stereochemistry assigned for (π-allyl)palladium complex **2a**, and rule out any type of isomerization,[23b] we isolated the latter complex as the chloride dimer **2b** and transformed it to the bipyridyl complex **2c** (Scheme 3). Bipyridyl ligands have been previously employed as reporter ligands to assign the stereochemistry of various (π-allyl)palladium complexes.[25−27] In these assignments the 2,2′ protons, which usually exchange with one another in an apparent π-allyl rotation,[28] are used as reporter protons.

The ^{1}H NMR spectrum of **2c** in acetonitrile at room temperature showed that the exchange rate between H_a and H_a' was close to coalescence and these protons were hardly visible at room temperature. At lower temperature two separated peaks emerged, and at −23 °C there were two broad doublets at 8.8 ppm (H_a) and 9.3 ppm (H_a'), respectively, integrating for one proton each. On irradiation at 8.8 ppm the peak at 9.3 ppm was saturated because of the exchange, and a significant NOE was observed for two of the allyl hydrogens (at C-1 and C-3) and for H_b (at C-4). Analogously, irradiation at H_b gave NOE at H_a and H_a'. These NMR experiments establish that the palladium and H_b are on the same face of the ring and that the side chain with the allene is trans to palladium.

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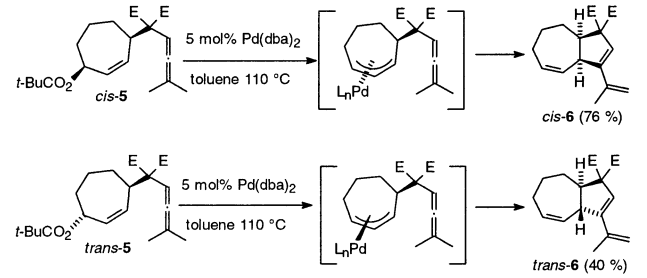
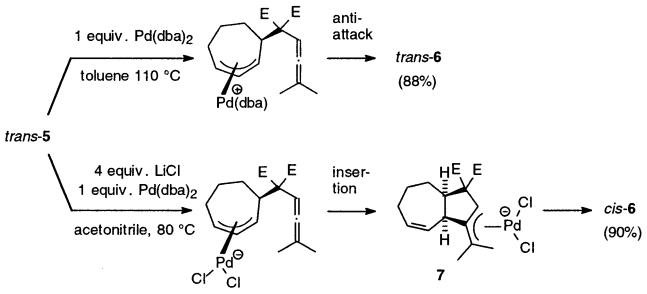
Scheme 4



Scheme 5



The stereoselectivity of the allene attack was further demonstrated by the catalytic reaction of *cis*-**5** and *trans*-**5**,[29] which afforded *cis*-**6** and *trans*-**6**,[21] respectively, via the π-allyl intermediate indicated (Scheme 4). In both cases the stereoselectivity was >98% according to ^{1}H NMR and GC. These catalytic reactions also show the synthetic potential of this new carbon−carbon bond-forming reaction.

Apparently, electron-withdrawing ligands (e.g., dba) on palladium are necessary for the olefinic double bond to attack the π-allyl group. This increases the electrophilicity of the allyl group and makes it susceptible toward attack by the electron-rich double bond. In a stoichiometric reaction it was demonstrated that the pathway via external double bond attack was blocked upon addition of LiCl in acetonitrile (Scheme 5). Thus, with chloride ligands on palladium in the (π-allyl)palladium complex, double bond insertion of the allene into the allyl−palladium bond occurs[14,30] to give *cis*-**6** via π-allyl complex **7**. In toluene without LiCl anti attack by the allene to yield *trans*-**6** takes place. In this way a dual stereocontrol was obtained in the reaction of *trans*-**5** via its corresponding π-allyl complex (Scheme 5).

When *trans*-**1** was allowed to react in acetonitrile in the presence of LiCl, **3** was obtained in 80% yield, which is consistent with anti oxidative addition followed by insertion.

In conclusion, we have demonstrated that an allene can act as a nucleophile in palladium chemistry by attacking a (π-allyl)palladium complex with electron-withdrawing ligands from the face opposite to that of palladium.[31] The stereoselectivity of the allene attack should be of importance in organic transformations, and work is in progress to study the synthetic potential of this new reaction.

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Supporting Information Available: Experimental procedures and characterizations for products **1**, **3**, **4**, and **5** and complexes **2b** and **2c** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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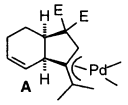
(20) *cis*-**1** and *trans*-**1** are readily available via the chloroacyloxylation approach.[4,5a] Cis chloropivalation of 1,3-cyclohexadiene and subsequent substitution of the chloride with either retention (Pd^0) or inversion (heat) afforded the starting material **1** (see Supporting Information).
(21) The stereochemistry was established by ^{1}H NMR (NOE, coupling constants).
(22) The trifluoroacetate esters **4** was prepared via ester hydrolysis of the corresponding pivalate esters *cis*-**1**, yielding the corresponding alcohols which were treated with trifluoroacetic anhydride.
(23) Allylic trifluoroacetates are known to undergo fast oxidative addition: Granberg, K. L.; Bäckvall, J. E. *J. Am. Chem. Soc*. **1992,** *114*, 6858.
(24) One minute after addition of Pd(dba)$_2$ at room temperature a mixture of starting material (**4**), **2a**, and **A** was observed. After 30 min at room-temperature all **4** was consumed, and the major compound obtained was **A** together with **2a**. Compound **A** is presumably formed via trapping of the tertiary carbocation by Pd(0). Heating **A** to 70−80 °C for 2 h gave **3**.



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(31) One reviewer suggested that Pd(0) is assisting in the nucleophilic attack by coordinating to the allene. This is a possible pathway that we cannot exclude.

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