

## Consecutive Vinylic to Aryl to Allylic Palladium Migration and Multiple C–H Activation Processes\*\*

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The rearrangement of a Pd moiety along a saturated hydrocarbon chain by a sequence involving Pd–H elimination and subsequent readdition has been extensively explored and developed into a very useful synthetic process.<sup>[1]</sup> On the other hand, there are few reports of the “through-space” migration of Pd between remote carbon atoms. The facile 1,4-migration of Pd between a vinylic position and an arene<sup>[2]</sup> and between the *ortho* positions of biaryl compounds<sup>[3]</sup> have recently been reported. Aryl to benzylic<sup>[4]</sup> and alkyl to aryl Pd migrations<sup>[5]</sup> are also known. Herein we report a novel, consecutive vinylic to aryl to allylic Pd migration that involves multiple C–H bond activations, which provides a new route to  $\pi$ -allyl palladium intermediates of great interest in organic synthesis.<sup>[6]</sup>

The reaction of *p*-iodoanisole and 1-phenyl-1-propyne with CsO<sub>2</sub>CCMe<sub>3</sub> as the base provides a 1:1 mixture of (*E*)- and (*Z*)-2-(4-methoxyphenyl)-3-phenyl-2-propenyl pivalate in 20% yield (**1A/B**; Table 1, entry 1). Different aryl halides and alkynes were then used in this reaction, and most combinations give allylic esters in respectable yields. Three isomers are usually obtained when R<sup>2</sup> = *t*Bu, and only two isomers are generated when R<sup>2</sup> = Ph. The ratio of the various isomers is dependent on the reaction time and temperature. It appears that longer reaction times and higher temperatures generally favor the formation of isomer C.

Although these reactions proceed in relatively low yields, the mechanism of this unique transformation is quite interesting. This process appears to involve Pd migration from a vinylic to an aryl to an allylic position and subsequent displacement by a pivalate anion (Scheme 1). Intermediate **5**, generated by oxidative addition of the aryl halide to Pd<sup>0</sup>, adds to the alkyne to produce the vinylic Pd intermediate **6**. Insertion of Pd into the neighboring C–H bond forms palladacycle **7**, and subsequent reductive elimination affords

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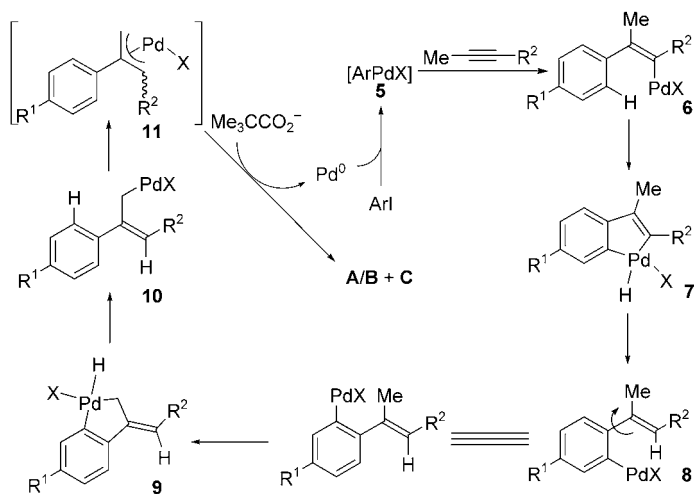
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**Table 1:** Results of the reactions involving multiple Pd migrations.<sup>[a]</sup>

Entry	X	R <sup>1</sup>	R <sup>2</sup>	Products	Yield [%] (A:B:C)
1	I	OMe	Ph	<b>1A/B</b>	20 (1:1:0) <sup>[b]</sup>
2	Br	H	<i>t</i> Bu	<b>2A/B, 2C</b>	35 (1:2:7) <sup>[c]</sup>
3	I	H	<i>t</i> Bu	<b>2A/B, 2C</b>	44 (1:2:12) <sup>[c]</sup>
4	Br	CO <sub>2</sub> Et	<i>t</i> Bu	<b>3A/B, 3C</b>	50 (1:2:18) <sup>[c]</sup>
5	Br	Cl	<i>t</i> Bu	<b>4A/B, 4C</b>	42 (1:2:20) <sup>[c]</sup>

[a] All reactions were conducted on a 0.5-mmol scale for 24 h, and the ratio of ArX to alkyne was 1:1 (sealed vial, under Ar). [b] This reaction was run with 5 mol% Pd(OAc)<sub>2</sub> and 5 mol% dppm at 100°C, along with DMF (10 mL) and CsO<sub>2</sub>CCMe<sub>3</sub> (2 equiv). [c] This reaction was run with 10 mol% Pd(OAc)<sub>2</sub> and 10 mol% dppm at 125°C, as well as *N,N*-dimethylacetamide (DMA, 5 mL) and CsO<sub>2</sub>CCMe<sub>3</sub> (2 equiv).

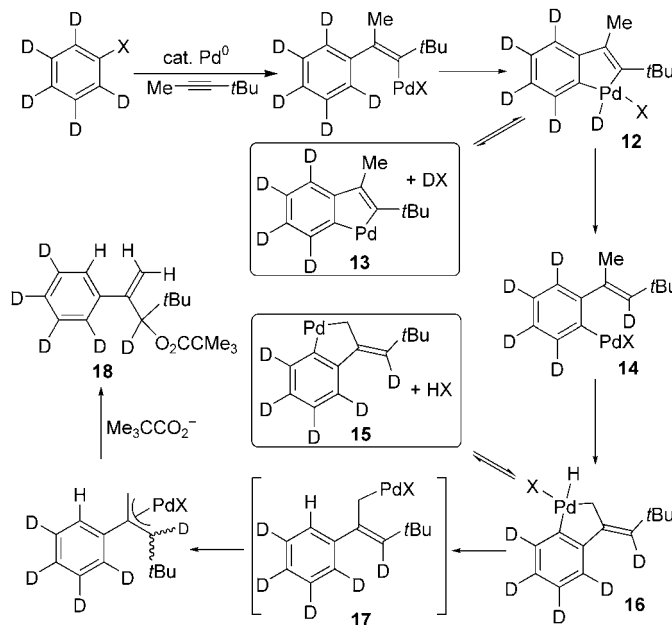

**Scheme 1.** Proposed mechanism of the Pd migration.

**8.** This results in Pd migration from a vinylic to an aryl position by C–H bond activation, a process we have reported earlier.<sup>[2]</sup>

To initiate a second C–H bond activation, the Pd moiety apparently rotates into the vicinity of the methyl group. Insertion of Pd into the neighboring C–H bond affords palladacycle **9**, which undergoes reductive elimination with transfer of the Pd moiety to the allylic position. This unprecedented migration generates Pd intermediate **10**, which rapidly isomerizes to the corresponding  $\pi$ -allyl palladium species **11**. This unusual process provides a new route for preparing  $\pi$ -allyl palladium compounds, which have proven very versatile as intermediates in organic synthesis.<sup>[6]</sup> The three isomeric ester products are presumed to arise by attack of the pivalate anion on the Pd intermediate **11**.

This proposed mechanism indicates that the migration of Pd is always accompanied by a simultaneous migration of hydrogen in the opposite direction. Thus, the observation of a hydrogen or deuterium shift should provide convincing evidence for the Pd migration. [D<sub>5</sub>]Bromobenzene (99%

deuterium) and 4,4-dimethyl-2-pentyne were allowed to react with Pd(OAc)<sub>2</sub> (10 mol%), dppm (1,2-bis-(diphenylphosphino)methane; 10 mol%), and CsO<sub>2</sub>CCMe<sub>3</sub> (2 equiv) in DMA at 125°C (Scheme 2). The *E* and *Z* isomers

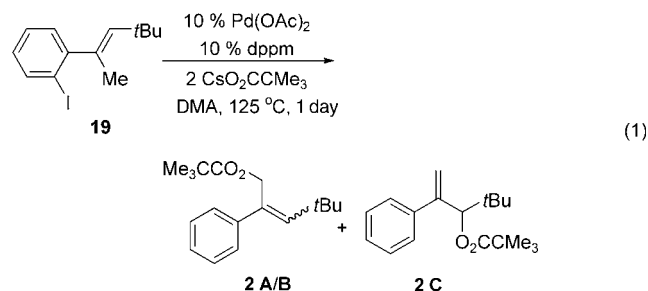

**Scheme 2.** Proposed formation of the deuterium-labeled product.

of 4,4-dimethyl-2-phenylpent-2-enyl pivalate and 1-*tert*-butyl-2-phenyl-2-propenyl pivalate (**18**) were obtained in a ratio of 1:2:7. Ester **18** was isolated in 20% yield and found to contain 40% deuterium in the allylic position and 95% hydrogen in one of the two *ortho* positions of the phenyl moiety (GC–MS data indicate that hydrogen is only incorporated at one of the two *ortho* positions). This result, except for the relatively low allylic deuterium content, is consistent with the proposed mechanism. However, the deuterium content can be increased by adding 10 equivalents of D<sub>2</sub>O to the reaction mixture. The three products were again obtained in a similar ratio, and the resulting ester **18** contained 55% hydrogen in one *ortho* position of the arene and 75% deuterium in the allylic position.

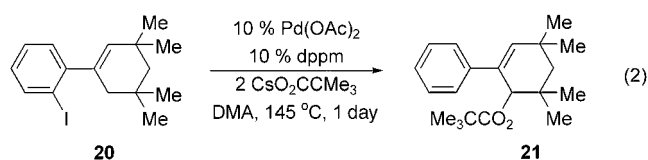
The loss of deuterium in the allylic position probably arises by deuterium/hydrogen exchange through an equilibrium between organopalladium(IV) intermediate **12** and palladacycle **13** or direct exchange of the metal hydride/deuteride in intermediate **12**. Incorporation of deuterium in the allylic position is dependant on the competition between H/D exchange and Pd migration, and it appears that neither is dominant in this case. This reaction was repeated in the presence of 10 equivalents of H<sub>2</sub>O, and the three esters obtained incorporate approximately the same ratio of allylic deuterium as the reaction conducted in the absence of H<sub>2</sub>O. A similar exchange of hydrogen and deuterium has been observed in aryl norbornyl palladacycles.<sup>[7]</sup> When nondeuterated bromobenzene and 4,4-dimethyl-2-pentyne were allowed to react in the presence of 10 equivalents of D<sub>2</sub>O, the ester **18** that was obtained had incorporated 40%

deuterium in one of the *ortho* positions of the arene and 40 % deuterium in the allylic position. Although the experimental data is consistent with the proposed mechanism, an alternative mechanism involving an organopalladium(II) palladacycle<sup>[8]</sup> and a Pd- $\pi$ -arene complex<sup>[9]</sup> is also possible. Further studies to better understand the mechanism of this process are underway.

We also carried out a Pd migration reaction with the aryl iodide **19**, which would be expected to generate intermediate **8** directly [Eq. (1)]. This species might then undergo Pd



migration to produce the same mixture of pivalate esters formed by the consecutive rearrangement. Under the same reaction conditions, we obtained the anticipated product mixture (**2A**:**2B**:**2C** = 1:2:20) in 65 % yield. Although the ratio of the regioisomer **2C** to **2A/B** is a little higher than in the consecutive migration process, the results are still consistent with our proposed mechanism. We also examined the reaction of aryl iodide **20** under the usual reaction conditions, but at 145 °C [Eq. (2)]. This reaction affords the allylic pivalate **21** in 45 % yield. Thus, it appears that the aryl palladium intermediate corresponding to **20** is able to undergo migration to a secondary allylic position.



In terms of mechanism, an intermediate such as **17** could also be generated by carbopalladation of the allene 4,4-dimethyl-1,2-pentadiene, which might arise by isomerization of 4,4-dimethyl-2-pentyne. However, when carried out with [D<sub>5</sub>]bromobenzene, this process would not introduce a hydrogen atom into the *ortho* position of the arene or a deuterium atom into the allylic position of the final ester product, unless the Pd moiety could reversibly migrate from the allylic to the aryl to the vinylic position. Only then could we observe a hydrogen atom in the *ortho* position of the arene and a deuterium atom in the vinylic position, as well as deuterium incorporation into the allylic position. To better understand this process, the reaction shown in Equation (1) was conducted in the presence of 10 equivalents of D<sub>2</sub>O. The isolated product **2C** contained 40 % deuterium in one of the *ortho* positions of the arene (according to GC-MS analysis,

see Supporting Information), but no deuterium in the vinylic or allylic positions. This suggests that the vinylic to aryl migration is not a reversible process. Because no deuterium incorporation in the methylene or allylic positions was observed, we can also rule out reversible Pd migration from the allylic to the aryl position.

In conclusion, we have discovered a novel consecutive vinylic to aryl to allylic Pd migration, which affords a unique way to generate  $\pi$ -allyl palladium complexes. This migration process appears to involve an equilibrium between organopalladium(IV) hydrides and organopalladium(II) intermediates, which undergo facile exchange with a hydrogen source in the solution. However, we cannot rule out direct exchange of the Pd<sup>IV</sup> hydride. We are continuing to study this process in order to better understand the mechanism and its synthetic potential.

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