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Palladium-Catalyzed Stereo- and Regiospecific Allylation of Aryl Halides with Homoallyl Alcohols via Retro-Allylation: Selective Generation and Use of σ-Allylpalladium

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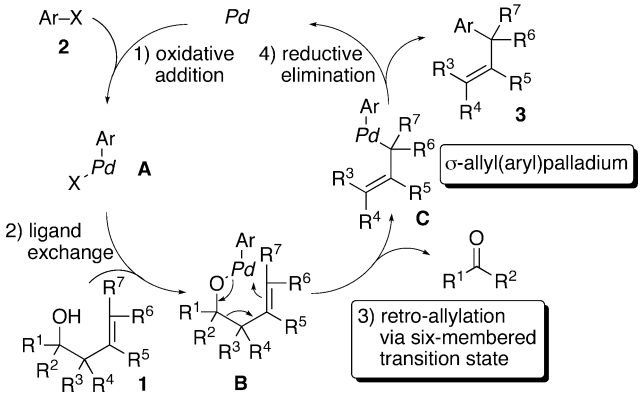
Allylation reactions are not only fundamental but also useful transformations in organic synthesis. Among them, transition-metal-catalyzed cross-coupling allylation of aryl halides with allylmetal reagents ranks as one of the most attractive allylation reactions.[1] In the case of palladium catalysis, allylmetal reagents such as allylstannane and allylmagnesium reagents serve as the allyl sources and effect transmetalation to yield allyl(aryl)palladium intermediates. The intermediate occupies the last place in the catalytic cycle of the cross-coupling allylation reaction, thereby being most responsible for the control of the stereo- and regioselectivity of the allylation reaction when a substituted allyl group is to be introduced. However, such stereo- and regioselective allylations are very difficult processes.[2]

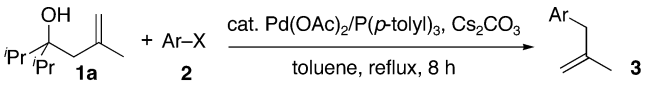
Here we report a new protocol for allylation reaction of aryl halides with homoallyl alcohols as the allyl sources. As outlined in Scheme 1, our strategy relies on retro-allylation reaction[3,4] of intermediate **B** to provide a σ-allyl(aryl)palladium **C**. Given that the retro-allylation would proceed in a concerted fashion via a conformationally regulated six-membered cyclic transition state and that the reductive elimination from **C** is faster than isomerization of **C** to π-allyl(aryl)palladium, the stereo- and regiochemical information of homoallyl alcohol **1** can be transferred to the allylated product **3**.[5]

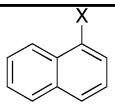
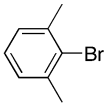
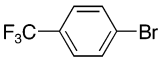
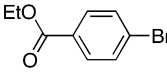
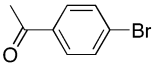
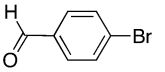
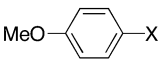
Scheme 1. Working Hypothesis



Treatment of 1-bromonaphthalene (**2a**) with homoallyl alcohol **1a** in the presence of cesium carbonate under palladium catalysis in refluxing toluene provided 1-methallylnaphthalene (**3a**) in good yield (Table 1, entry 1). Sterically demanding **2d** as well as electron-deficient **2e**−**2h** underwent the methallylation reaction. The reaction of electron-rich *p*-bromoanisole (**2i**) resulted in a lower yield of coupling product **3g**. However, use of *p*-iodoanisole (**2j**) provided a satisfactory yield of 59%. Chloronaphthalene remained untouched under the reaction conditions (entry 1). In the reactions of aryl triflates, no significant differences in rate and yield were observed (entries 1 and 7).

Table 1. Palladium-Catalyzed Methallylation of Aryl Halides **2** with Homoallyl Alcohol **1a** via Retro-Allylation[a]



entry	Ar–X **2**		yield /%
1		**2a:** X = Br **2b:** X = Cl **2c:** X = OTf	**3a**, 86 from **2a** **3a**, 6 from **2b** **3a**, 87 from **2c**
2		**2d**	**3b**, 90
3		**2e**	**3c**, 64
4		**2f**	**3d**, 83[b]
5		**2g**	**3e**, 71[c]
6		**2h**	**3f**, 57
7		**2i:** X = Br **2j:** X = I **2k:** X = OTf	**3g**, 29 from **2i** **3g**, 59 from **2j** **3g**, 61 from **2k**

[a] A mixture of $Pd(OAc)_2$ (0.025 mmol), P(*p*-tolyl)$_3$ (0.10 mmol), Cs_2CO_3 (0.72 mmol), **1** (0.60 mmol), and **2** (0.50 mmol) was boiled in toluene (3.0 mL) for 8 h. [b] A catalyst prepared from $Pd(OAc)_2$ (0.013 mmol) and P(*p*-tolyl)$_3$ (0.050 mmol) was used. [c] A catalyst prepared from $Pd(OAc)_2$ (0.013 mmol) and PPh_3 (0.050 mmol) was used.

Homoallyl alcohol **1b** effected allylation of **2a** to yield 1-allylnaphthalene (**3h**) in excellent yield (Scheme 2, Np = 1-naphthyl). As anticipated, high regioselectivity was observed in the reaction of **2a** with homoallyl alcohol **1c** to provide **3i** predominantly. In the reaction of **1d**, the carbon−carbon bond formation also took place at the less substituted carbon to provide linear **3k** selectively. In contrast, homoallyl alcohol **1e**, a butenyl isomer of **1d**, was converted to branched coupling product **3l**. The regiospecificity is highly suggestive of the retro-allylation of **B** followed by rapid reductive elimination (Scheme 1). It is worth noting that alcohol **1f**, the stereoisomer of **1e**, resisted the transformation.

The reaction of **1d** afforded the linear coupling product **3k**. However, **3k** comprised a 1:1 mixture of (*E*)- and (*Z*)-isomers. Gratifyingly, the use of diastereomerically pure **1g**, having *tert*-butyl and methyl groups at the oxygenated carbon, allowed

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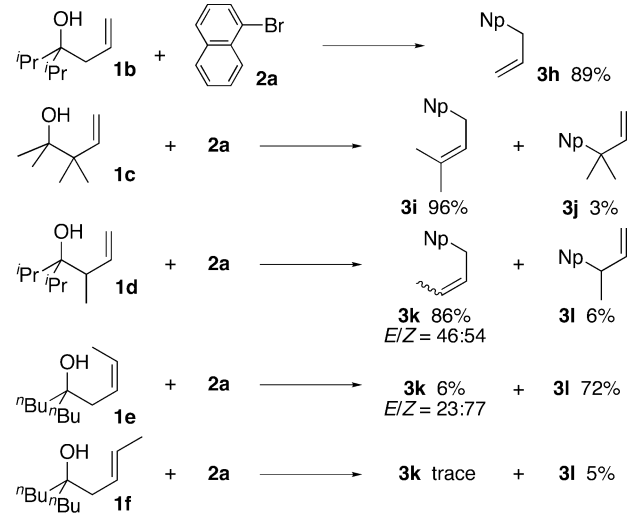
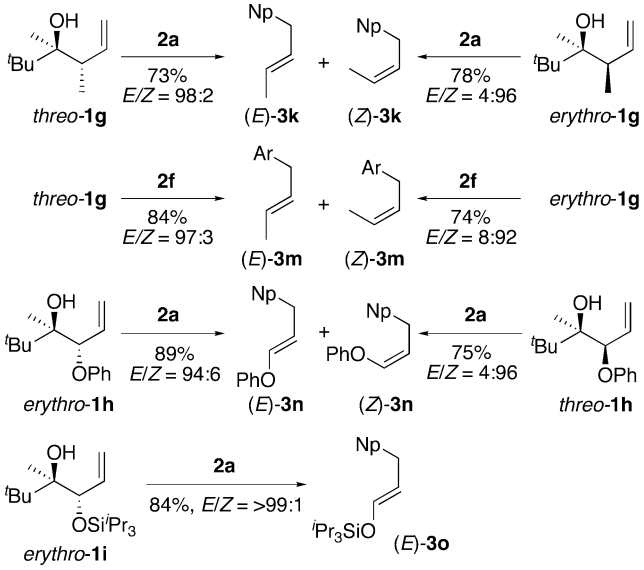
Scheme 2. Allylation of **2a** with Various Homoallyl Alcohols[a]



[a] The reaction conditions are the same as those in Table 1, except for the reaction of **1e** (2 equiv of **1e** and 2.4 equiv of Cs_2CO_3 were used).

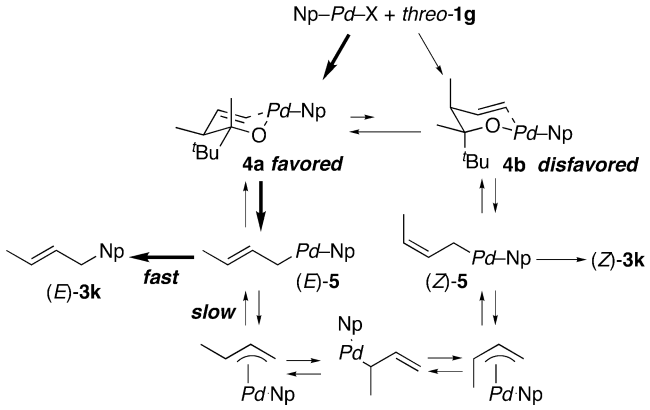
Scheme 3. Regio- and Stereospecific Allylation with Diastereomerically Pure Homoallyl Alcohols



stereospecific synthesis of (*E*)- and (*Z*)-**3k** (Scheme 3). Treatment of **2a** with *threo*-**1g**[6] under the palladium catalysis afforded (*E*)-**3k** stereoselectively. On the other hand, formation of (*Z*)-**3k** was more favored over that of (*E*)-**3k** in the reaction of *erythro*-**1g**.[6] The allylation controlled by the relative stereochemistry of **1** was applicable to stereospecific synthesis of vinyl ether **3n** starting from diastereomerically pure **1h**. Highly stereoselective synthesis of silyl enolate **3o** also underscores the utility of the retro-allylation strategy.

We are tempted to rationalize the stereospecificity controlled by starting homoallyl alcohols as follows (Scheme 4). Upon the retro-allylation reaction of *threo*-**1g**, a chair transition state **4a** would be the most stable, because of steric reasons, compared to other possible transition states including another chair transition state **4b** and twist-boat transition states. Formation of (*E*)-crotyl(naphthyl)-palladium (*E*)-**5** is thus favored. The intermediate probably undergoes reductive elimination so rapidly that its isomerization into π-allylpalladium and any other isomers is negligible.

Scheme 4



Taking advantage of retro-allylation as a bond-cleavage strategy, we have devised a new method for the preparation of σ-allylpalladium, which is difficult to generate in a stereo- and regioselective manner. Coupled with immediate use of the σ-allylpalladium, the retro-allylation realizes stereo- and regiospecific allylations of aryl halides. The retro-allylation system will be applicable to other transformations catalyzed by other transition metals.

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Supporting Information Available: Experimental details, characterization data for new compounds, and stereochemical assignment of **1h** (PDF, CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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