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Palladium Pincer-Complex Catalyzed Allylation of Tosylimines by Potassium Trifluoro(allyl)borates

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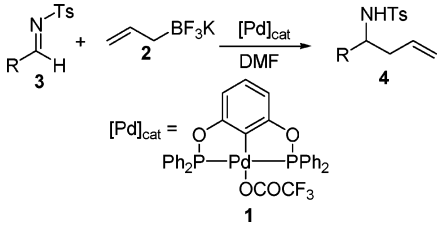
ABSTRACT



Palladium pincer complex 1 catalyzes the reaction of trifluoro(allyl)borate 2 with a wide range of tosylimines (3) under mild and neutral reaction conditions. This catalytic transformation affords homoallylic amines (4) in good to excellent yield. Mechanistic studies suggest that a transmetalation reaction between complex 1 and the borate salt 2 provides an η^1-allylpalladium complex, which subsequently reacts with the imine substrate.

Allylpalladium chemistry is one of the most successful areas in transition-metal catalysis. In the most common application of this methodology, an allylpalladium intermediate is generated, which subsequently reacts with nucleophiles.[1] Recently, however, possibilities to extend allylpalladium chemistry to electrophilic substrates have attracted much attention, as certain allylpalladium species[2,3] have been shown to react with electrophiles. In these catalytic reactions, the active allylpalladium species are usually generated in a transmetalation reaction between an allylstannane and a palladium complex. Because of the toxicity of organo-tin reagents, and the tedious separation of the tin-containing byproducts,[4] it would be desirable to replace the allylstannane component of the reaction with other allylmetal species.[5] We have now found that in palladium-catalyzed electrophilic substitution reactions allylstannanes can be replaced by potassium trifluoro(allyl)borate **2**.[6] Thus, palladium pincer complex **1** catalyzes the allylation of tosylimines **3** with the borate salt **2** (Scheme 1). A wide range of tosylimines (**3a**−**i**) can be allylated by this procedure in good to excellent yields (Table 1).

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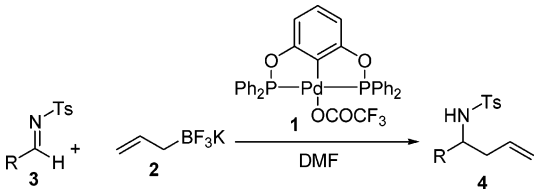
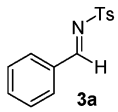
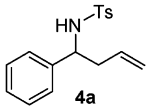
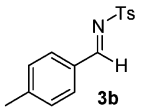
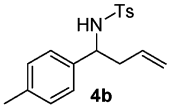
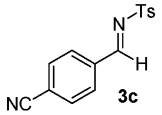
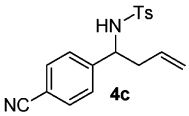
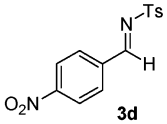
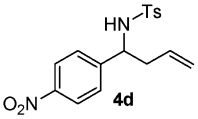
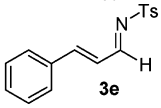
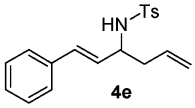
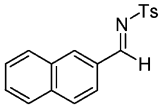
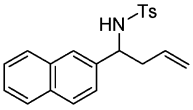
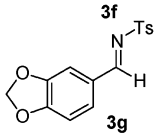
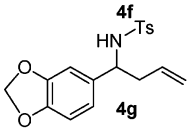
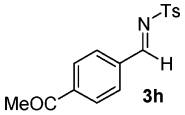
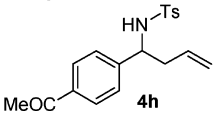
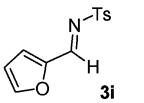
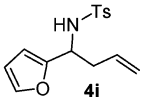
Scheme 1. Allylation of Tosylimines by Pincer-Complex Catalyst **1**



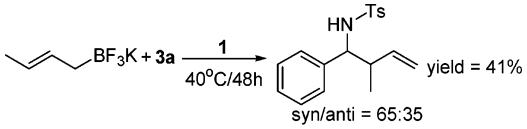
In a typical procedure, the imine **3** (0.10 mmol), borate salt **2** (0.11 mmol) and pincer complex **1** (0.005 mmol, 5 mol %) in DMF (300 μL) were reacted for 24 h at 25−50 °C. After workup, the crude product was purified by column chromatography. The reactions were typically carried out at 40 °C (entries 1−6); however, bulky (**3f**, entry 7) or deactivated (**3g**, entry 8) imines required 50 °C reaction temperature, while activated imines **3h** (entry 9) and **3i** (entry 10) could be allylated at 25 °C. The mild and neutral reaction conditions are compatible with many functional groups, such as MeCO, NO_2, acetals, and CN. In this regard, the imine functionality of **3c** and **3h** could be selectively allylated in the presence of the cyano and keto groups. To assess the stereochemistry of the catalytic allylation reaction we reacted **3a** with (*E*)-crotyltrifluoroborate[6b] (Scheme 2). This reaction, however, proceeds with a poor yield and stereoselectivity.

Table 1. Palladium-Catalyzed Allylation of Tosylimines[a]

Entry	Imine	Temp. [°C]	Product	Yield[b]
1	 **3a**	40	 **4a**	95
2	**3a**	40	**4a**	66[c]
3	 **3b**	40	 **4b**	95
4	 **3c**	40	 **4c**	88
5	 **3d**	40	 **4d**	86
6	 **3e**	40	 **4e**	90
7	 **3f**	50	 **4f**	95
8	 **3g**	50	 **4g**	95
9	 **3h**	25	 **4h**	79
10	 **3i**	25	 **4i**	95

[a] Unless otherwise stated, the reactions were conducted in DMF for 24 h using 5 mol % of complex **1** as catalyst and 1.1 equiv of borate salt **2**. [b] Isolated yield. [c] 5 mol % of $Pd(OAc)_2$ and 5 mol % of PPh_3 were used as catalyst.

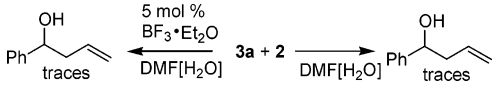
Scheme 2. Catalytic Allylation Using (*E*)-Crotyltrifluoroborate Substrate



We also tested $Pd(OAc)_2$ as catalyst anticipating the formation of a bis-allylpalladium intermediate, which would be able to allylate imine **3a**.[2j] Using 5 mol % $Pd(OAc)_2$ and 5 mol % PPh_3, imine **3a** was allylated in 66% yield (entry 2). Use of PPh_3 proved to be indispensable to get an acceptable yield, as $Pd(OAc)_2$ alone or other phosphine free catalysts (such as $[Pd(allyl)Cl]_2$) gave a low conversion of **3a**.

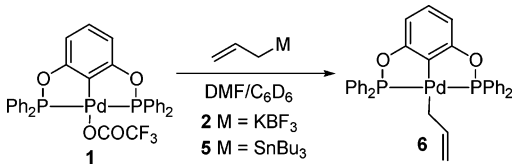
We have also performed a control experiment using the reaction conditions given in entry 1 without adding palladium catalyst (Scheme 3). In this experiment, homoallylic amine **4a** was not formed at all. The only product observed in this reaction was a trace of homoallyl alcohol. This product is probably formed by the reaction of benzaldehyde (resulted from partial hydrolysis of the imine) and **2**.

Scheme 3. Reactions in the Absence of Palladium Catalyst **1**



Mechanistic Aspects. Batey and Sze-Wan[6d] showed that tosylimines are allylated in excellent yield by two equivalents of borate salt **2** in CH_2Cl_2 using 5 mol % of $BF_3{\cdot}Et_2O$ as Lewis acid catalyst. We have attempted to perform this Lewis acid-catalyzed reaction with **3a** and **2** in DMF (Scheme 3); however, we did not observe any formation of the desired homoallylamine product (**4a**). This probably can be explained by the deactivation of the employed Lewis acid ($BF_3{\cdot}Et_2O$) by the DMF solvent. A clear advantage of using **1** as catalyst is that application of 1.1 equiv. of **2** is sufficient to obtain high yields, while employment of Lewis acid catalyst $BF_3{\cdot}$

Scheme 4. Stoichiometric Reactions with Pincer Complex **1** and Allylmetal Reagents **2** and **5**



Et_2O requires the use of 2 equiv of the allylic substrate (**2**). On the other hand, Batey's conditions give higher yield and stereoselectivity with crotyltrifluoroborate, than the pincer-complex catalyzed reaction (Scheme 2).

To gain more mechanistic insights into the above catalytic process (Scheme 1), we monitored the stoichiometric reaction of **1** and **2** by ^{31}P NMR spectroscopy. Complex **1**, dissolved in a mixture of DMF/C_6D_6 (10:1), was reacted with **2** at room temperature (Scheme 4). Addition of **2** led to a decrease of the ^{31}P NMR peak of **1** at δ 146.0 ppm, while a new peak appeared at δ 148.4 ppm clearly indicating a reaction between the palladium complex (**1**) and the allylic substrate (**2**). To clarify the nature of this reaction we performed a similar stoichiometric experiment using allylstannane (**5**) in place of **2** (Scheme 4). In this process we observed again a downfield shift by δ 2.4 ppm of the ^{31}P NMR shift of complex **1**. In a recent study we have shown[3b] that pincer complex **1** reacts with allylstannanes to form η^1-allylpalladium complex **6**. Therefore, the fact that either of allylstannane **5** or borate salt **2** gives the same product when reacted with complex **1** strongly indicates that **2** also undergoes a transmetalation reaction[7] with complex **1** resulting in (η^1-allyl)palladium complex **6** (Scheme 4). Complex **6** subsequently undergoes electrophilic attack by tosylimine **3**[3] affording homoallylic amines **4**.

In summary, we have developed a palladium pincer-complex catalyzed allylation reaction, where tosylimines were allylated with borate salt **2**. This reaction is assumed to proceed via (η^1-allyl)palladium intermediate (**6**). Application of this procedure eliminates the use of toxic tin compounds, thereby extending the synthetic utility of the palladium catalyzed electrophilic substitution reaction.

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Supporting Information Available: Experimental procedures, NMR data, as well as ^1H and ^{13}C NMR spectra of products **4a**−**j**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) For studies on the transmetalation reaction between palladium complexes and potassium trifluoro(organo)borates, see: (a) Molander, G. A.; Bialatto, B. *J. Org. Chem.* **2003**, *68*, 4302. (b) Darses, S.; Genet, J.-P. *Eur. J. Org. Chem.* **2003**, 4313.