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P′CP′-Pincer palladium complex-catalyzed allylation of *N,N*-dimethylsulfamoyl-protected aldimines

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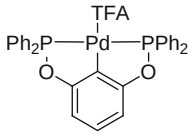
ABSTRACT

The P′CP′-pincer palladium complex-catalyzed allylation of *N,N*-dimethylsulfamoyl-protected aldimines with allyl(tributyl)stannane is investigated for the preparation of *N*-homoallylic sulfamides. The desired *N,N*-dimethylsulfamoyl-protected products are obtained in moderate to high yields in DMF under very mild conditions and a high yielding and convenient deprotection of the *N,N*-dimethylsulfamoyl group is also demonstrated.

The development of novel methods to generate new carbon-carbon bonds is important for the preparation of compounds of interest from pharmaceutical, biological or advanced materials points of view, and belongs to the core of modern organic chemistry.[1] In particular, the allylation of imines has attracted increasing attention because of its importance for the preparation of nitrogen-containing compounds.[2,3]

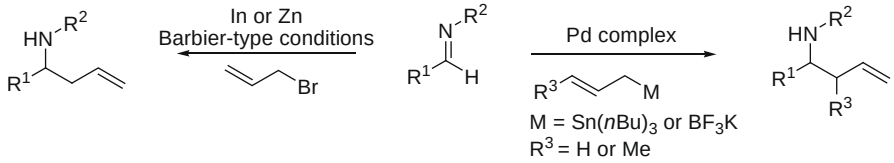


[PdTFA(P'CP')]

Figure 1.

To date, numerous indium- and zinc-mediated allylic additions of imines under typical Barbier-type conditions have been reported (Scheme 1).[4,5] The synthesis often benefits from low toxicity, tolerance towards air and moisture and high yields.

In addition, an alternative procedure involving a palladium-catalyzed reaction in which the η^1-allylpalladium intermediate generated reacts with electrophilic substrates (Scheme 1) has been reported.[6,7] This reaction proceeds via a very different catalytic cycle compared to Barbier-type metal-mediated allylations. First, allylstannanes or trifluoro(allyl)borates undergo a transmetalation reaction with the P′CP′-pincer palladium complex [**PdTFA(P′CP′)**] (Fig. 1).[8,9] Subsequently, the resulting nucleophilic η^1-allylpalladium intermediate reacts with electrophilic aldehydes or aldimines to afford the corresponding allyl product. Szabó and co-workers reported the [**PdTFA(P′CP′)**]-catalyzed allylation of tosylimines in the presence of allylstannane or trifluoro(allyl)borates showing high yields and a wide substrate scope.[6,7] One drawback



Scheme 1.

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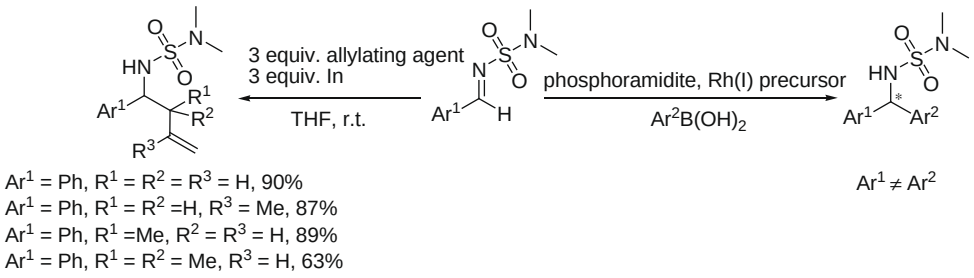
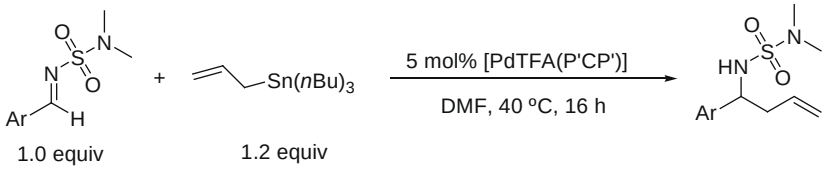


Scheme 2.



Scheme 3.

Table 1
[PdTFA(P′CP′)]-catalyzed allylation of various aldimines with allyl(tributyl)stannane

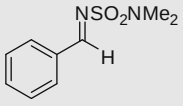
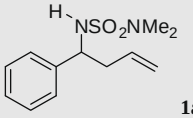
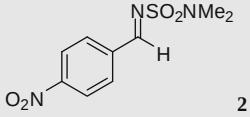
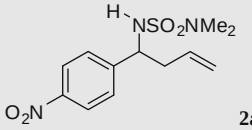
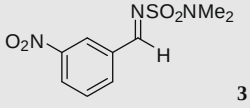
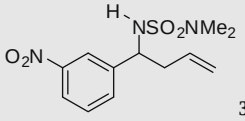
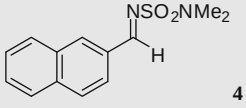
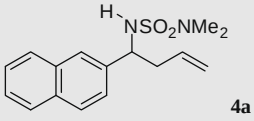
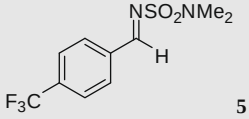
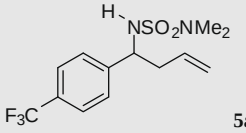
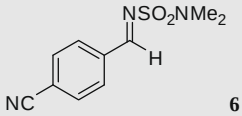
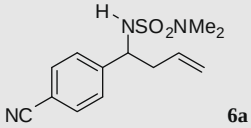
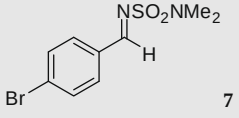
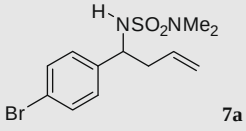
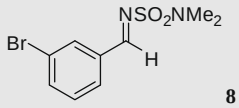
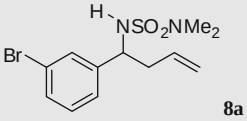
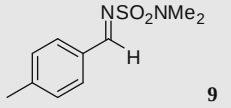
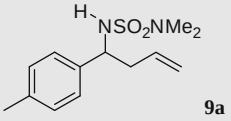
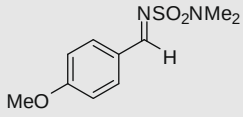
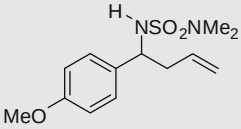
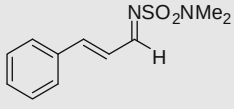
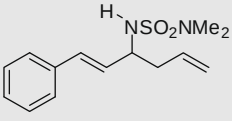
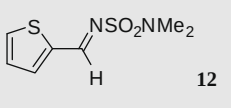
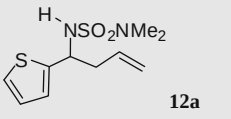
Entry	Substrate	Product	Yield[a] (%)
1	 **1**	 **1a**	81
2	 **2**	 **2a**	85
3	 **3**	 **3a**	93
4	 **4**	 **4a**	85
5	 **5**	 **5a**	80
6	 **6**	 **6a**	80
7	 **7**	 **7a**	96

Table 1 (*continued*)

Entry	Substrate	Product	Yield[a] (%)
8	 **8**	 **8a**	80
9	 **9**	 **9a**	85
10	 **10**	 **10a**	60
11	 **11**	 **11a**	68
12	 **12**	 **12a**	70

Reagents and conditions: 0.1 mmol of aldimine, 0.12 mmol of allyl(tributyl)stannane, 0.005 mmol of [PdTFA(P′CP′)], 0.5 mL of DMF, 4 °C, 16 h.
[a] Isolated yield (average of two runs).

of this protocol is that removal of the tosyl protecting groups is not always straightforward, even under quite harsh conditions (i.e., liq. NH_3/Li or NH_3/Na), and suffers from limited functional group tolerance.[10–12] To overcome this problem and to improve the practicality of the allylation procedure, an easily removable protecting group is highly desirable. In this Letter, the [**PdTFA(P′CP′)**]-catalyzed allylation of *N*,*N*-dimethylsulfamoyl-protected aldimines is described as an alternative.

Recently, Minnaard and co-workers presented the *N,N*-dimethylsulfamoyl group as an inexpensive, low-molecular-weight protecting/activating group for Rh(I)-catalyzed asymmetric arylation of aldimines and described an efficient method for its removal using a microwave-assisted procedure.[13] Encouraged by these results, we extended this research to the Barbier-type allylation for the preparation of *N*-homoallylic sulfamides in high yields with different allyl bromides in THF as the optimal solvent (Scheme 2).[14] Interestingly, Minnaard found that even by using simple conventional heating, the *N*-homoallylic sulfamides could be deprotected. So far, the latter procedure has been applied to only one substrate.

In the present study we demonstrate how the scope of this reaction can be extended by using the [**PdTFA(P′CP′)**]-catalyzed allylation of a series of *N,N*-dimethylsulfamoyl-protected aldimines.

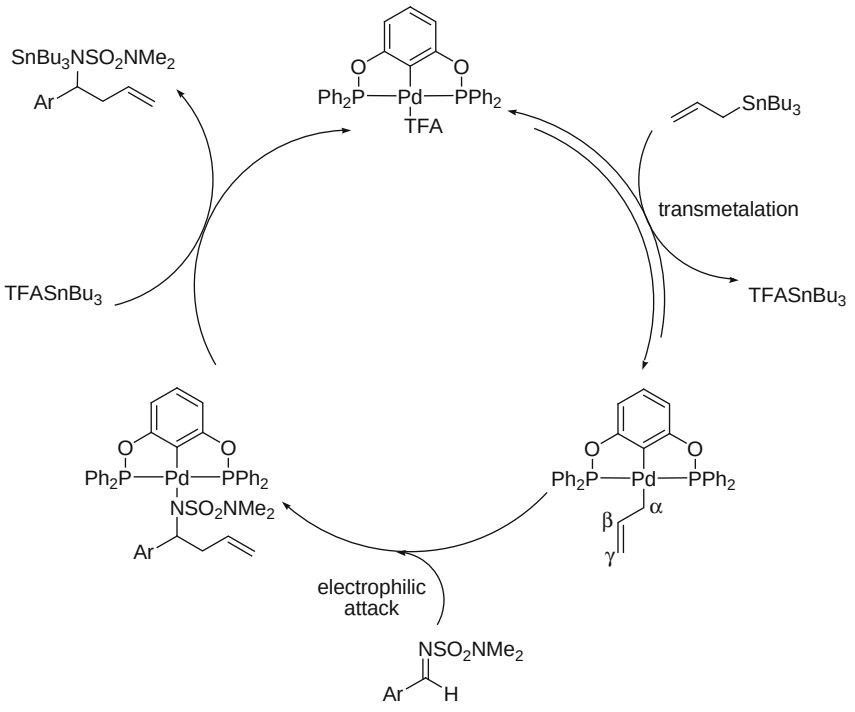
Using the typical reaction conditions reported by Szabó and coworkers,[7] 1 equiv of aldimine was reacted with 1.2 equiv of allylstannane in the presence of 5 mol % of [**PdTFA(P′CP′)**] at 40 °C in DMF for 16 h (Scheme 3). After completion, the reaction mixture was quenched with saturated aqueous KF solution (1 mL) and the resulting mixture was stirred at room temperature (16 h) to remove toxic organic tin residues.[15] The products were extracted from the solution with ethyl acetate (3 × 2 mL) and were subjected to flash column chromatography to isolate analytically pure products.[16]

These experiments show that *N,N*-dimethylsulfamoyl-protected aldimines can be allylated smoothly under mild conditions in moderate to excellent yields (data shown are those of the isolated, purified products) and show good functional group tolerance (Table 1). For benchmark substrate **1**, the corresponding homoallylic product **1a** was obtained in a good yield of 81%. Similarly, substrates **2**, **3**, **5** and **6** bearing various electron-withdrawing *para*-substituents were converted into the corresponding homoallylic products in 80–93% yield. The presence of weakly electron-donating functional groups in substrates **4** and **9** did not result in any loss of reactivity and both afforded the respective products **4a** and **9a** in 85% yield. In contrast, the yield was considerably lower for substrate **10** bearing the stronger electron-donating methoxy group. Remarkably, halogenated substrates **7** and **8** gave the desired products in good yields without loss of the bromine atoms, that is, no products from palladium-catalyzed C–Br activation were observed. Undoubtedly, this is an attractive feature of this approach allowing further modification, that is, tandem reactions[17] via cross-coupling reactions using a different metal catalyst. Furthermore, successful transformation of the halogenated substrates strongly indicates that no Pd leaching from [**PdTFA(P′CP′)**] occurs, for example, by decomposition, as otherwise, the formed active Pd(0) species could insert oxidatively into the C–Br bond affording undesired by-products. Moreover, cinnamylaldimine **11** and 2-thienylaldimine **12** were also converted into the corresponding homoallylic products (entries 11 and 12).

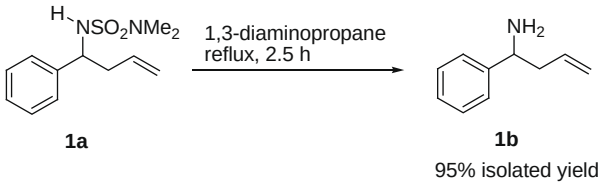
It is worth mentioning that the isolated yields obtained in this study are generally 10–15% lower than those of the tosyl-protected aldimines.[7] This is most likely due to the presence of the strongly electron-donating Me_2N group instead of the *p*-tolyl group which decreases the electrophilicity of the corresponding aldimine. In particular, for the electron-enriched substrates (entries 10 and 11), both conversion and yield were lower in comparison with the corresponding tosyl-protected aldimines.

On the basis of the catalytic cycle proposed by Szabó and Yao,[6,9,15] the [**PdTFA(P′CP′)**]-catalyzed allylation of *N,N*-dimethylsulfamoyl aldimines can be depicted stepwise as shown in Scheme 4: (1) Transmetalation of tri(*n*-butyl)allyltin with [**PdTFA(P′CP′)**] and formation of an η^1-allyl-palladium complex; (2) electrophilic attack on the γ-position of the η^1-allyl moiety by the aldimine and formation of the Pd-coordinated homoallylic amide and (3) product exchange with the organotin salt and regeneration of the catalyst.

As a proof of concept, deprotection of *N*-homoallylic sulfamide **1a** was carried out in refluxing 1,3-diaminopropane by conventional heating in an oil bath (Scheme 5).[14] The conversion was monitored by TLC. The reaction was found to go to completion



Scheme 4.



Scheme 5.

(95% yield) within 2.5 h. This result is in full agreement with previous reports[13,14] and confirms the efficiency and reliability of this deprotection procedure.

In conclusion, [**PdTFA(P′CP′)**] is shown to be an excellent homogeneous catalyst for the allylation of *N,N*-dimethylsulfamoyl-protected aldimines, affording the corresponding homoallylic products which are easily deprotected to homoallylic primary amines. The ease of deprotection and wide functional group tolerance of the C–C coupling reaction demonstrate the synthetic potential of this procedure.

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.02.187.

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16. *General catalysis procedure*: Aldimine 1–12 (0.1 mmol), allylstannane (0.12 mmol) and [PdTFA(P′CP′)] (0.005 mmol) in DMF (0.5 mL) were stirred for 16 h at 40 °C. The reaction was then quenched by addition of 1 mL saturated aqueous KF solution and was stirred overnight at room temperature, followed by extraction with EtOAc (3 × 2 mL). The combined organic layers were washed with brine (1 × 5 mL), then dried over $MgSO_4$ and concentrated under vacuum. The crude products were immediately subjected to silica gel column chromatography using hexanes/EtOAc (7:3) as eluent. ^{1}H and ^{13}C NMR spectral data of products **1a–12a** are available in the Supplementary data.
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