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# $PdCl_2$-catalyzed hydrosulfonamidation of homo allylic alcohols: an efficient synthesis of allylic sulfonamides

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ABSTRACT

A new protocol for the palladium chloride-catalyzed direct hydrosulfonamidation of homoallylic alcohols with migration of the double bond is described. This method requires no preactivation of alcohols and the reaction is environmentally benign with water as the only by-product. Various homoallylic alcohols on hydrosulfonamidation with sulfonamides gave the corresponding products in good yields.

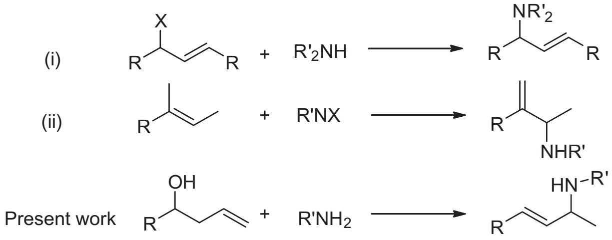
Amines and their derivatives are of fundamental importance as natural products, pharmacological agents, fine chemicals, and dyes.[1] Furthermore, a plethora of naturally bioactive compounds such as, alkaloids, amino acids, and nucleotides contain amine groups. Despite numerous known procedures, the development of improved methods for the synthesis of amines continues to be a highly challenging and active area of research.[2] In this respect hydroamination,[3] the addition of an N–H bond across carbon–carbon unsaturation, offers an efficient, atom-economical route to nitrogen-containing molecules that are important for fine chemicals, pharmaceuticals, or useful chiral building blocks. Although several efficient catalysts for the hydroamination of alkynes,[4] vinylarenes,[5] dienes,[6] and electron-deficient alkenes[7] have recently been discovered, general systems for intermolecular hydroaminations of unactivated olefins remain elusive.[8]

Allylamines are ubiquitous in various biologically active compounds and their synthesis is an important industrial and synthetic goal. The allylamine fragment can be encountered in natural products, but often the allylamine is transformed to a range of products by reduction, oxidation, or other functionalization of the double bond. Thus allylamines have been used as starting materials for the synthesis of numerous compounds such as, α- and β-amino acids,[9] different alkaloids[10], and carbohydrate derivatives.[11]

The synthesis of allylic amines can, in principle, be divided into two groups of reactions, which are outlined in Scheme 1. The first type (i) constitutes allylic amines synthesized by nucleophilic allylic substitution and the second (ii) is the direct allylic amination of simple alkenes.[12]

A transition metal-catalyzed substitution reaction of activated allylic alcohol derivatives with nitrogen nucleophiles is one of the most powerful and reliable methods for the synthesis of allylic amines.[13] However, they usually require preactivation of the parent allylic alcohol to the corresponding allylic halides, carboxylates, carbonates, phosphates, and related compounds. The reaction proceeds through π-allyl metal intermediates, generated by the oxidative addition of allylic substrates to a low-valence metal center, and the following nucleophilic addition gives allylic amines as a consequence of new C–N bond formation. In terms of atom-economy[14] and environmental concerns, however, these catalyses still have much room for improvement.

The current study was motivated by our recent finding that hydroazidation of homoallyl alcohols to the corresponding allylic azides using $PdCl_2$ as a catalyst and $TMSN_3$ as an azide source, which appears to involve the nucleophilic attack of an azide onto



**Scheme 1.** Protocols for the synthesis of allylic amines.

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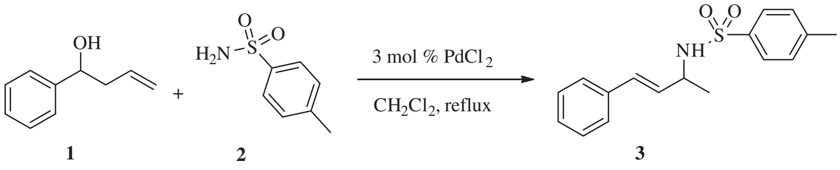
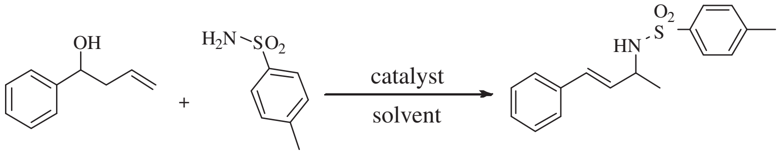


**Scheme 2.**

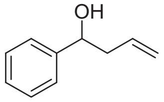
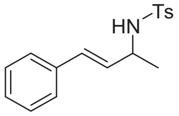
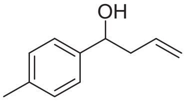
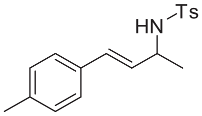
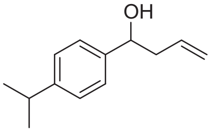
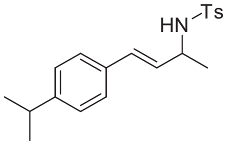
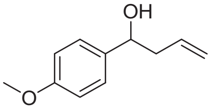
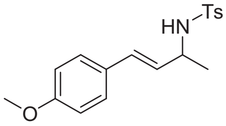
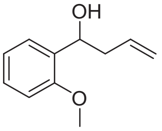
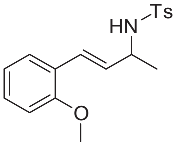
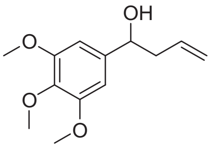
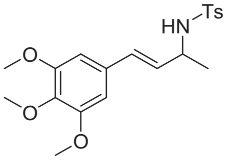
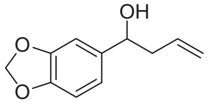
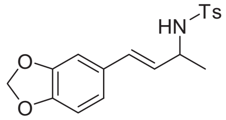
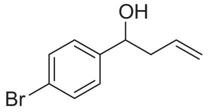
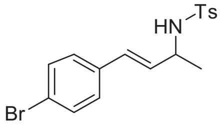
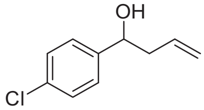
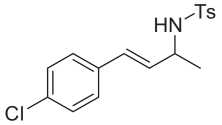
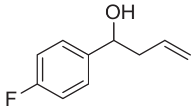
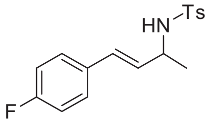
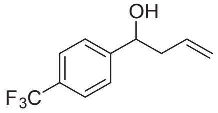
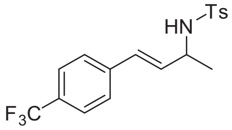
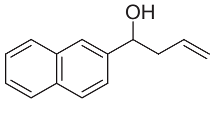
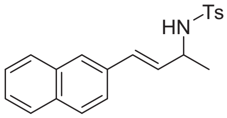
**Table 1**
Screening of various solvents and catalysts for reaction of allylic amines from homoallylic alcohols[a]



| Entry | Catalyst | Solvent | Temp (°C)/time (h) | Yield (%) |
|---|---|---|---|---|
| 1 | $PdCl_2$ | $CH_2Cl_2$ | 40/8 | 90 |
| 2 | $Pd(OAc)_2$ | $CH_2Cl_2$ | 40/8 | 0 |
| 3 | $Pd(PPh_3)_4$ | $CH_2Cl_2$ | 40/8 | 0 |
| 4 | Pd/C | $CH_2Cl_2$ | 40/8 | 0 |
| 5 | $Pd(dba)_2$ | $CH_2Cl_2$ | 40/8 | 0 |
| 6 | $Pd(dppf)Cl_2$ | $CH_2Cl_2$ | 40/8 | 0 |
| 7 | $Pd(PPh_3)_2Cl_2$ | $CH_2Cl_2$ | 40/8 | 27 |
| 8 | $Pd(CH_3CN)_2Cl_2$ | $CH_2Cl_2$ | 40/8 | 42 |
| 9 | $PdCl_2$ | THF | 60/12 | 30 |
| 10 | $PdCl_2$ | 1,4-Dioxane | 100/12 | 40 |
| 11 | $PdCl_2$ | DCE | 80/12 | Trace |
| 12 | $PdCl_2$ | DMF, DMSO, $CH_3NO_2$, $H_2O$ | 100/12 | 0 |
| 13 | $PdCl_2$ | Toluene, xylene | 100/12 | 0 |

[a] Reaction conditions: homoallylic alcohol (1 mmol), tosylamide (1.2 mmol), catalyst (3 mol %) solvent (3 mL).

**Table 2**
Direct hydrosulfonamidation of different homoallylic alcohols with *p*-toluenesulfonamide using $PdCl_2$ for the synthesis of allylic amines[a]

| Entry | Homoallyl alcohol | Product | Yield (%) |
|---|---|---|---|
| 1 |  |  | 90 |
| 2 |  |  | 91 |
| 3 |  |  | 90 |
| 4 |  |  | 84 |
| 5 |  |  | 79[b] |
| 6 |  |  | 84 |
| 7 |  |  | 87 |
| 8 |  |  | 75 |
| 9 |  |  | 75 |
| 10 |  |  | 70 |
| 11 |  |  | 70 |
| 12 |  |  | 82 |

[a] Reaction conditions as exemplified in typical experimental procedure.[22]

[b] Yield of the *E* isomer.