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Umpolung of the reactivity of allylsilanes. Palladium(II) catalyzed cyclization of allylsilyl alcohols: a new route to substituted 2-vinyltetrahydrofurans

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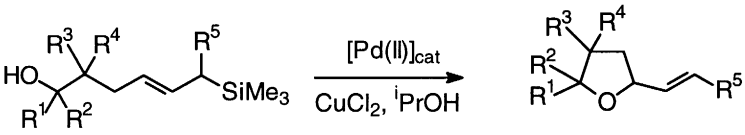
Abstract

Functionalized allylsilanes **1**–**4** undergo palladium(II) catalyzed ring closure to afford 4- and/or 5-substituted 2-vinyltetrahydrofurans (**5**–**8**) under mild conditions. The catalytic reactions proceed through (η^3-allyl)palladium intermediates formed by palladadesilylation of the allylsilane substrates. © 2000 Elsevier Science Ltd. All rights reserved.

Functionalized allylsilanes have proven to be a very useful class of organometallic synthons due to their potential for highly selective transformations by electrophilic reagents.[1a–c] The driving force of the electrophilic attack on allylsilanes is the formation of a β-silicon stabilized carbocation intermediate.[1d] Nucleophilic attack on allylsilanes, however, does not benefit from this type of stabilization. Accordingly, reaction of nucleophiles with allylsilanes requires special reaction conditions, such as an initial metal- or metalloidal attack on the allylsilane substrate[1e–g] or oxidative cleavage of the carbon silicon bond.[1h–i] For example, palladium(II) catalyzed oxidation of allylsilanes with UV light and molecular oxygen has been used to prepare α,β-unsaturated carbonyl compounds.[1j] We have now found that palladium(II) catalysis can also be employed for allylic substitution of the silyl functionality by nucleophiles. Thus, in the presence of catalytic amounts of palladium salts, the hydroxy functionality of 6-trimethylsilyl hexanol derivatives **1**–**4** easily undergo intramolecular nucleophilic attack on the allylic moiety affording 2-vinyltetrahydrofurans (**5**–**8**) in good yields (eq (1), Table 1).



(1)

The allylsilanes (**1**–**4**) could easily be obtained by reduction or Grignard reaction of functionalized allylsilanes **9**–**11** (eq (2)) prepared by a recently reported efficient palladium(0) catalyzed process.[2a] The

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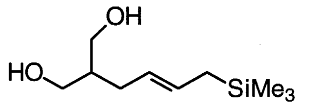
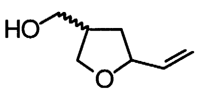
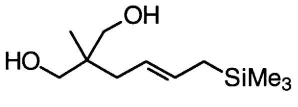
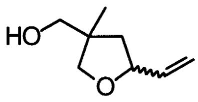
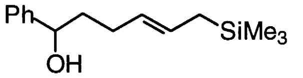
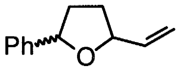
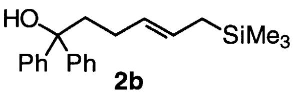
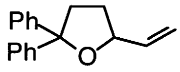
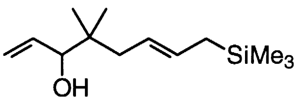
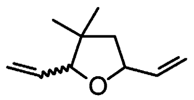
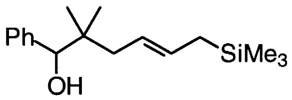
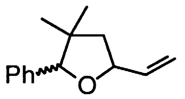
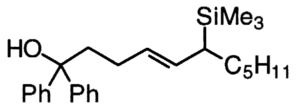
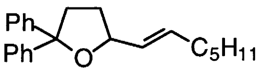
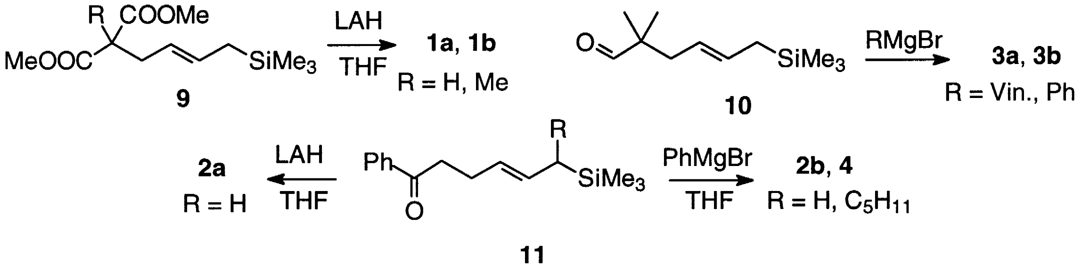
Table 1
Palladium(II) catalyzed cyclization of allylsilanes **1**–**4**[a]

Entry	Substrate	Conditions [°C, h]	Product	Yield[b] [%]
1	 **1a**	25, 1.5	 **5a**	86
2[c]	**1a**	25, 14, BQ/H^+	**5a**	40
3	 **1b**	25, 2.5	 **5b**	62
4	 **2a**	40, 1.5	 **6a**	69
5	 **2b**	40, 2.5[d]	 **6b**	60
6	 **3a**	20, 15	 **7a**	50[e]
7	 **3b**	20, 14	 **7b**	53
8	 **4**	20, 4[d]	 **8**	66[f]

[a] Unless otherwise stated the reactions were conducted in ^{i}PrOH using 5 mol% $Li_2[PdCl_4]$ and 2.5 equiv. of $CuCl_2$. [b] Isolated yield. [c] 5 mol% $Pd(OAc)_2$, 2.2 equiv. of BQ and 27 mol% H_3PO_4 in CH_2Cl_2/MeOH 10:1. [d] The substrate was added by syringe pump (for 0.5 h and 3 h for **2b** and **4** respectively) whereupon the reaction mixture was stirred. [e] According to the GC analysis, this reaction gives **7a** quantitatively. Lowering of the yield can be ascribed to the volatility of the product. [f] About 15% of the *cis*-isomer was also formed.

choice of solvent is of great importance for the successful accomplishment of the cyclization reaction. We found that the cyclization is very fast and proceeds with good yield in a number of alcoholic solvents (ROH, R=Me, Et, ^{i}Pr and ^{t}Bu). However, in other solvents, such as acetonitrile, THF, DMSO, CH_2Cl_2 and DMF, a slow reaction with a very low conversion occurred.

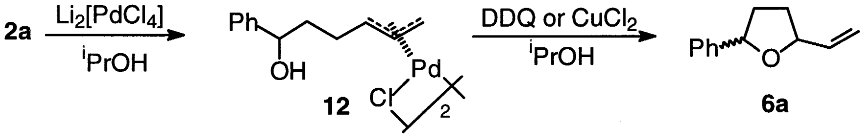
Since the palladium(II) catalyst is reduced to palladium(0) in the nucleophilic attack, a reoxidant has to be applied to regenerate the palladium(II) catalyst source. For cyclization of allylsilanes, copper(II) chloride proved to be the most efficient reoxidant for palladium (entries 1 and 3–8). We have also tried other reoxidants, such as benzoquinone (BQ) and its derivatives, which are commonly used in palladium(II) catalyzed allylic oxidation of alkenes and 1,4-oxidation of conjugated dienes.[2b,c] Employment of BQ as the oxidant requires acidic reaction conditions[2b] since a protonation step is involved in the reduction of BQ to hydroquinone. However, using acidic conditions and BQ as the reoxidant leads to a very slow reaction with a low yield. The catalyst was usually deactivated before the starting material was fully converted. The best results (entry 2) with BQ as a reoxidant were achieved by employing 27 mol% phosphoric acid in a CH_2Cl_2/MeOH solvent mixture (10:1).



(2)

Using 5 mol% $Li_2[PdCl_4]$ catalyst and $CuCl_2$ as the reoxidant in ^{i}PrOH **1**–**4** smoothly undergo at rt or at a slightly elevated temperature (40°C).[3] The reaction is fast with primary (**1a**–**b**) and simple secondary alcohols (**2a**), and, even sterically hindered tertiary alcohols (**2b**, **4**) are cyclized in 2–4 h at rt. The relatively short reaction time is important for cyclization of **2b** and **4** since these compounds can easily undergo dehydration even under mild reaction conditions. A longer reaction time is required in the presence of methyl substituents at the three position of the substrate (**3a**–**b**). The regio- and chemoselectivity of the reaction is excellent. The ring closure reaction provides exclusively five membered rings with the formation of seven membered rings not being observed. The employed solvent (^{i}PrOH) is also a secondary alcohol, and therefore it is a potential nucleophile. However, products arising from an external nucleophilic attack by the solvent have not been observed, suggesting that the internal nucleophilic attack is much faster than the external one. The stereoselectivity of the ring closure is usually rather poor, as seen by the fact that the two diastereomers of **5**, **6a** and **7** are formed in approximately the same ratio.

Mechanism. It is well documented that allylsilanes react with Pd(II) salts affording (η^3-allyl)palladium complexes.[4] We could also isolate the intermediary allylpalladium complex of the cyclization reaction (eq (3)). We have found that the palladadesilylation process is facilitated by alcoholic solvents and chloride salts, while addition of bases hindered the reaction. (η^3-Allyl)palladium complex **12** is an air-stable species, which does not undergo spontaneous cyclization. Therefore, complex **12** has to be activated to allow a nucleophilic attack by the hydroxy group. This activation can be achieved by addition of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) or $CuCl_2$ to the ^{i}PrOH solution of **12**. It is interesting to note that cyclization does not occur in the presence of BQ. This is probably due to the fact that BQ is less able to activate nucleophilic attack on (η^3-allyl)palladium complexes than DDQ, especially in the presence of chloride ligands.[5] Therefore it is important to perform the BQ mediated catalytic reaction under chloride free conditions (entry 2). We have also found that an increase in the acidity slows down the rate of the nucleophilic attack. This can easily be explained by the fact that the ring closure involves deprotonation of the OH group, which is hindered in the presence of acids.



(3)

The above results show that the basicity of the reaction medium has opposite effects on the palladadesilylation and on the nucleophilic attack of the OH group. Accordingly, neutral conditions are expected to give the best results, which can be ensured when $CuCl_2$ is used as the reoxidant and activator of the nucleophilic attack. Using alcoholic solvents is beneficial for both processes of eq (3). The alcoholic solvents facilitate the elimination of the silyl group under the palladadesilylation through the formation of stable alkyl-siloxanes, and hindering the silyl migration to the OH group of the substrate. Furthermore, in the nucleophilic attack the solvent molecules may also act as weak bases providing assistance in the deprotonation of the hydroxy group.

In summary, we have shown that under mild conditions allyl–silyl alcohols undergo a nucleophilic substitution reaction in the presence of catalytic amounts of palladium salts and $CuCl_2$. As far as we know, this is the first example of palladium catalyzed allylic substitution of the silyl functionality by nucleophiles. In addition, employment of a silyl leaving group offers an interesting alternative to acetate and carbonate functionalities, which are commonly used in palladium catalyzed allylic substitution reactions.

Acknowledgements

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3. General procedure: The ^{i}PrOH (5 ml) solution of the allylsilane (0.5 mmol), Li_2PdCl_4 (0.025 mmol, 5 mol%, 0.007 g) and $CuCl_2$ (1.25 mmol, 0.168 g) was stirred under argon for the temperatures and times listed in Table 1. After the reaction was complete, the reaction mixture was diluted with ether, washed with brine, then dried over anhydrous $MgSO_4$. Removal of the solvent in vacuo and purification of the residual oil by chromatography in pentane/ether afforded the corresponding product.
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