JOC *Note*

Halide-Free Dehydrative Allylation Using Allylic Alcohols Promoted by a Palladium−Triphenyl Phosphite Catalyst

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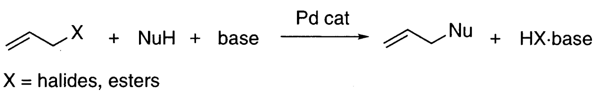
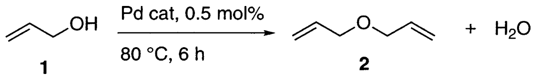
Abstract: The triphenyl phosphite−palladium complex was found to effect catalytic substitution reactions of allylic alcohols via a direct C−O bond cleavage. The dehydrative etherification proceeded efficiently without any cocatalysts and bases to give allylic ethers in good to excellent yields.

Palladium-catalyzed transformations of allylic compounds represent powerful and well-established synthetic procedures for carbon−carbon and carbon−heteroatom bond formation, with high chemo-, regio-, and stereoselectivities.[1] Acetates, carbonates, and related derivatives of allylic alcohols have normally been used as substrates, because the parent alcohols do not undergo the allylic transformation due to the difficulty of the allylic C−O bond cleavage by Pd catalysts. While it is inevitable for the reaction of allyl halides and esters under basic conditions to form the corresponding salt wastes, direct utilization of allylic alcohols without any additional promoters potentially provides economical, technical, and environmental advantages because of the formation of water as a coproduct derived from the leaving OH group (Scheme 1). As an approach for promoting Pd-catalyzed transformations of allylic alcohols, several researchers have demonstrated that additives such as $P(C_6H_5)_3$−DEAD,[2] As_2O_3,[3] B_2O_3,[4] $BF_3 \cdot Et_2O$,[5] BEt_3,[6] $B(C_6H_5)_3$,[7] $SnCl_2$,[8] $Ti(O^iPr)_4$,[9] and CO_2[10] can activate and/or convert the OH moiety into more labile leaving groups.[11] Successful application of a halide-free process involving the C−O bond cleavage of allylic alcohols without any activating reagents has been more limited.[12,13] In a recent work reported by Ozawa and Yoshifuji, η^3-allylpalladium complexes bearing the unique bidentate sp^2-hybridized phosphorus ligand, diphosphinidenecyclobutene, proved to be capable of catalyzing C- and N-allylations using allylic alcohols without OH-activators.[14] However, the addition of pyridine as a base was required for the C-allylation of active methylene compounds to enhance their nucleophilicity. Herein, we will describe a highly efficient Pd−$P(OC_6H_5)_3$ catalyst for substitution reactions of allylic alcohols via direct C−O bond cleavage without cocatalysts and bases, affording allylic ethers in excellent yields.

SCHEME 1



SCHEME 2



We first examined the reactivity of 2-propene-1-ol (**1**, 10 mmol) with Pd catalysts (0.05 mmol) in the absence of solvent or additives. The screening test of the Pd catalysts revealed that a combined catalyst, $Pd_2(dba)_3 \cdot CHCl_3$ and $P(OC_6H_5)_3$, provided the best catalyst performance with the dehydrative etherification of **1** at 80 °C under neutral conditions (Scheme 2). As shown in Table 1, the aryl phosphite ligand $P(OC_6H_5)_3$, with electron-withdrawing character, gave a satisfactory result in the formation of diallyl ether (**2**). Use of 4 equiv of the phosphite ligand with respect to Pd was required to give an optimum yield (entries 2−4). The use of $P(CH_2CH_2CH_2CH_3)_3$ and DPPB[12a,c] ligands led to moderate yields of **2**, while other phosphorus ligands were ineffective. An isolable Pd(0) complex $[Pd\{P(OC_6H_5)_3\}_4]$ (**3**)[15] was also suitable for the dehydrative etherification with a similar catalyst activity, whereas a Pd(II) complex, [PdCl$_2$-

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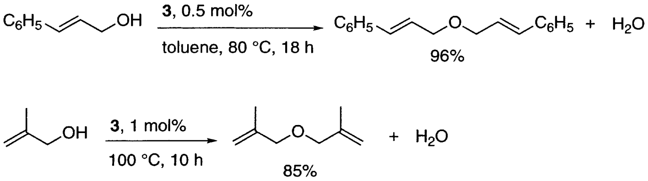
TABLE 1. Ligand Effect on the Pd-Catalyzed O-Allylation of 1[a]

entry	ligand	P/Pd	conversion[b] (%)	yield **2**[b] (%)
1		0	0	0
2	$P(OC_6H_5)_3$	1	44	39
3	$P(OC_6H_5)_3$	2	82	80
4	$P(OC_6H_5)_3$	4	91	85
5	$P(^nC_4H_9)_3$	4	71	68
6	$P(C_6H_5)_3$	4	7	3
7	DPPE	4	10	6
8	DPPP	4	17	16
9	DPPB	4	58	56
10	$P(OC_2H_5)_3$	4	17	13
11[c]	$P(OC_6H_5)_3$	4	86	84
12[d]	$P(OC_6H_5)_3$	2	11	3

[a] Reaction conditions: **1** (10 mmol), Pd catalyst (5.0×10^{-2} mmol/Pd) at 80 °C for 6 h without solvent under an argon atmosphere. [b] Determined by ^1H NMR. [c] $[Pd\{P(OC_6H_5)_3\}_4]$ **3** was used as a catalyst. [d] $[PdCl_2\{P(OC_6H_5)_3\}_2]$ was used as a catalyst. [e] DPPE = 1,2-bis(diphenylphosphino)ethane; DPPP = 1,3-bis(diphenylphosphino)propane; DPPB = 1,4-bis(diphenylphosphino)butane.

SCHEME 3



$\{P(OC_6H_5)_3\}_2]$, did not effectively promote the reaction (entries 11 and 12).

The $P(OC_6H_5)_3$-coordinated Pd(0) complex also effects the activation of other allylic alcohols. The dehydrative etherification of cinnamyl alcohol proceeded successfully in toluene under otherwise identical conditions to give the corresponding ether in 96% yield. Reaction of 2-methallyl alcohol afforded the corresponding ether in 85% yield at 100 °C and at higher concentrations of the catalyst **3** (1 mol %) (Scheme 3). However, the reaction of crotyl alcohol at 80 °C provided a mixture of isomers of ethers and 1,3-butadiene, which was possibly formed by simultaneous β-H elimination from η^3-crotylpalladium intermediate.

Valuable information for the reaction mechanism was provided by separate experiments. The time-course of the conversion of **1** into **2** in the presence of **3** (0.5 mol %) at 80 °C indicated that the yield of **2** reached ca. 90% within 2 h. However, complete conversion was not obtained even after longer reaction times, and formation of a trace amount of propionaldehyde was observed as an isomerization product from **1**.[16] These results suggest that allyl alcohol **1** should be in equilibrium with **2** and water under the reaction conditions. In fact, a 1:1 mixture of **2** and H_2O in the presence of the catalyst **3** at the same temperature provided a mixture of **2** (90%), **1** (9%), and propionaldehyde (1%) after 18 h of reaction. Screening experiments using several drying agents such as molecular sieves in the dehydrative etherification revealed that addition of Na_2SO_4 (140 mg) led to a maximum yield of **2** (95%). These data, as well as the previously reported results on the stoichiometric reaction of **1** with Pd(0) complex, giving a η^3-allyl(hydroxo)palladium complex,[17] imply that the Pd−phosphite catalyst effectively promotes C−O bond cleavage of allylic alcohols to provide η^3-allylpalladium intermediates. These would be further attacked by another equivalent of **1** or other alcohols leading to the allylated products. The cleaved OH group with strong basicity not only facilitates the nucleophilic attack of the alcohols on the η^3-allyl ligand to give allylation products but also sometimes promotes the β-H elimination[18] of the putative η^3-allylpalladium intermediate with the liberation of water.

TABLE 2. Dehydrative Allylation of Alcohols[a]

entry	ROH	time (h)	yield **4**[b] (%)
1	CH_3OH	6	83
2	C_2H_5OH	6	83
3	$(CH_3)_2CHOH$	6	46
4	$(CH_3)_3COH$	42	19
5	cyclohexanol	14	(54)
6	$(CH_3)_2CHCH_2OH$	14	73
7	$(CH_3)_3CCH_2OH$	14	79 (74)
8	$C_6H_5CH_2OH$	14	(60)
9	furfuryl alcohol	14	56 (55)
10	3-butene-1-ol	14	60
11	3-butyne-1-ol	6	trace

[a] Reaction conditions: ROH (5 mmol), **1** (10 mmol), **3** (5.0×10^{-2} mmol) at 80 °C without solvent. [b] Determined by ^1H NMR. Isolated yields are given in parentheses.

Cross etherification using **1** and other alcohols can be attained to give unsymmetrical allyl ethers (**4**) along with the formation of **2**. When the Pd catalyst **3** (0.024 mmol) was added to the mixture of **1** (4.7 mmol) and methanol-d_4 (4.7 mmol) in a NMR tube, the homo- and cross-etherifications took place smoothly at 80 °C as shown in Figure 1. The ^1H NMR experiment revealed that the yields of **2** and allyl methyl ether-d_3 (**4a**) were 28 and 56%, respectively, after 5 h, and the molar ratio was not changed through further reaction. It should be noted that hydrolysis of allyl ethyl ether with an equimolar amount of water in the presence of **3** (1 mol %) at 80 °C for 18 h formed ethanol in 30% yield. This result, in addition to the reaction of **2** with H_2O mentioned above, strongly suggested that the reaction of **1** to **2** or allyl alkyl ether **4** proceeded reversibly to produce an equilibrium mixture. The yields of **4** were improved by increasing the ratio of **1** to the added alcohols. The results of the allylic etherification of 2 equiv of **1** with an aliphatic alcohol in the presence of the Pd catalyst **3** (1 mol %) at 80 °C are summarized in Table 2. The structures of the alcohols were found to influence the outcome of the reaction. While a wide variety of primary alcohols was convertible to the desired products in moderate to good yields, allylation of bulkier tertiary alcohols, i.e., *tert*-butyl alcohol, gave an unsatisfactory result (entry 4). The reaction can be applied to 2-furfuryl alcohol and 3-butene-1-ol, whereas the result of 3-butyne-1-ol was unsuccessful, possibly due to a catalyst deactivation caused by replacement of the $P(OC_6H_5)_3$ ligand with the substrate alkyne (entries 9−11).

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(16) Formation of propionaldehyde by competitive isomerization of **1** was confirmed after 10 h (3% yield).

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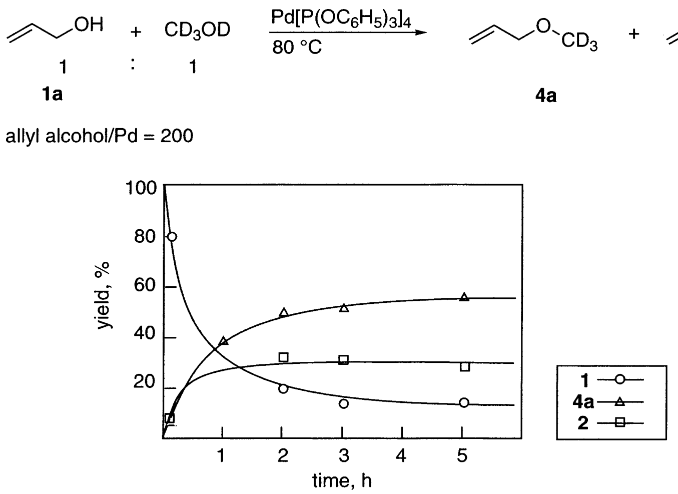
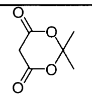
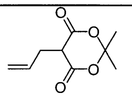
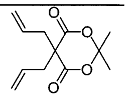
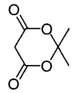
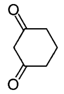
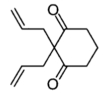
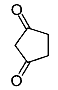
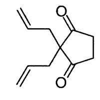
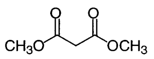
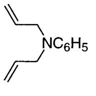


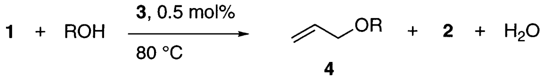
FIGURE 1. Time curves for conversion of **1** into **2** and **4a**.

TABLE 3. C- and N-Allylation by Use of 1

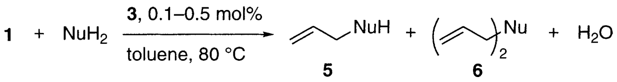
Entry	NuH_2	**1**/NuH_2	Time (h)	Product Yield[a] (%)	
				5	6
1[b]		1	2	 17	 66
2[b]		2	2	0	96
3[b]		2	2	0	 92
4[b]		2	2	0	 94
5[c]		2	25	0	0
6[c]	$C_6H_5NH_2$	2	4	0	 84

[a] Yields with respect to **1**. [b] Reaction conditions: **1** (5 mmol), NuH_2 (2.5 or 5 mmol), **3** (1.0×10^{-2} mmol) at 80 °C in toluene (2.5 mL) under an argon atmosphere. [c] Reaction conditions: **1** (3.5 mmol), NuH_2 (1.75 mmol), **3** (1.75×10^{-2} mmol) at 80 °C in toluene (2.5 mL) under an argon atmosphere.

SCHEME 4



SCHEME 5



The allylation reaction using catalyst **3** was successfully extended to other C- and N-nucleophiles (NuH_2) (Scheme 5). When an equimolar amount of **1** was treated with 2,2-dimethyl-1,3-dioxane-4,6-dione in the presence of 0.2 mol % of **3** at 80 °C in toluene, mono- and diallylated products (**5** and **6**, respectively) were obtained even under neutral conditions, but with poor selectivity (entry 1 in Table 3). The allylation reaction performed with 0.5 equiv of NuH_2 with respect to **1** under otherwise identical conditions predominantly afforded the diallylated product **6** in 96% yield (entry 2). Other cyclic compounds, including five- and six-membered diketones and aniline, were effectively converted into diallylated products (entries 3, 4, and 6). The fact that dimethyl malonate did not participate in the allylation suggests a facile coordination of acyclic 1,3-dicarbonyl compounds to the Pd center, leading to inhibition of the catalysis induced by the $P(OC_6H_5)_3$ ligand (entry 5).

In summary, we have shown that the easily handled Pd−$P(OC_6H_5)_3$ catalyst system provides convenient halide-free allylation reactions by directly using allylic alcohols. The reaction, even with low catalyst loading (0.2−1 mol %), smoothly proceeds to give the corresponding allylic ethers and the related C−C and C−N bond-forming products. Cocatalysts and bases are not required in the allylations, which is thus of great promise for achieving environmentally benign processes. Further studies are still in progress to elucidate how allylic alcohols react with Pd−$P(OC_6H_5)_3$ species and to develop other catalytic transformations of allylic alcohols.

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Supporting Information Available: Experimental details for the synthesis and NMR data of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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