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Palladium-catalyzed protection of alcohols and cleavage of triethylsilyl ethers

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Abstract

The versatility of the palladium (II) chloride/organosilane system has been tested in the transformation of alcohols to the corresponding silyl ethers and the subsequent deprotection of triethylsilyl ethers to the parent alcohols. The reaction takes place under mild conditions and affords high yields.

Keywords: Palladium (II) chloride; Organosilane; Alcohols; Silyl ethers; Deprotection

1. Introduction

Selective protection and deprotection of functional groups is commonly used process in multistep organic synthesis, and the interconversion of one protecting group into another is also an important transformation in synthetic organic chemistry. Thus, the development of new methods for such interconversions in one-step avoiding the intermediate step of going back to the parent functionality has gained importance in recent time [1]. As synthetic targets have become increasingly complex, protection/deprotection protocols using silyl groups have been the most popular methods due to their easy formation and removal, and their stability to a wide range of reagent and reaction conditions [2]. Organosilicon reagents play a prominent role in organic synthesis and are widely applied for functional group transformation [3]. Silicon hydrides have found successful application in reduction, substitution and addition processes in both radical and ionic fashion due to their selectivity, efficiency and low toxicity [4]. Organosilicon chemistry has been applied successfully to alcohols, for the protection as differently substituted silyl ethers [2]. Recently, Baruah et al. have prepared a series of mono and disubstituted silylethers using palladium (II) catalysts. The reaction of different silanes (such as triphenylsilane, triethylsilane, diphenylsilane and methylphenylsilane) and alcohols in the presence of 1 mol% of $Pd(TMEDA)Cl_2$ at temperatures ranging from RT to 60 °C led to the formation of the corresponding silylethers in near quantitative yield [5].

A vast array of acidic, basic, reducing, oxidizing and fluoride-based reagents were developed for the removal of the silyl group [2]. The deprotection of *t*-butyldimethylsilyl ethers using 20 mol% $ZrCl_4$ [6] and the selective deprotection of *t*-butyldimethylsilyl phenols using cesium carbonate [7] in DMF-H_2O were reported. Recently, Hirota and coworkers [8,9] have studied the cleavage of TBDMS ether to form the parent alcohol under mild hydrogenation conditions (ambient H_2 pressure and temperature) using 10% Pd/C in methanol. The same group has also examined the solvent effect on the Pd/C catalyzed cleavage of silyl ethers and olefins under

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the above conditions [10]. A method for selective cleavage of triethylsilyl ethers to the corresponding alcohols in the presence of 10 wt% Pd/C in methanol or ethanol was also described in the literature [11].

The combination of silicon hydrides with palladium dichloride has been reported in few examples, i.e., for the deprotection of aminoacids or peptides [12], for nucleophilic substitutions at silicon atom [13], for the reduction of Schiff bases [14], and for the preparation of halosilanes [15–17]. We have used the system $Et_3SiH/PdCl_2$ for the conversion of organic halides to the corresponding alkanes [18] and for the conversion of alcohols to their corresponding halides and alkanes [19]. More recently, we have demonstrated the high efficiency of $PdCl_2$ and triethylsilane for the carbon–carbon double bond isomerization of 1-alkenes to yield the corresponding 2- and 3-alkenes [20] and for the reduction of alkenes to the corresponding alkanes [21] in the presence of ethanol as solvent, at room temperature.

This paper is a continuation of our previous work on the exploitation of $R_3SiH/PdCl_2$ system for chemical transformation of organic functional groups. Herein we report our preliminary results, which account for the versatility of $PdCl_2/R_3SiH$ couple in the chemical transformation of alcohols to silyl ethers and the subsequent deprotection of triethylsilyl ethers to give the parent alcohols under mild conditions. Direct reaction of different alcohols with silanes in the presence of commercially available palladium dichloride occurs at room temperature to yield the corresponding silyl ethers in high yields. The second aspect of this work consists on the deprotection of triethylsilyl ethers by molecular hydrogen generated in situ by the spontaneous reaction of ethanol and triethylsilane catalyzed by palladium dichloride.

2. Results and discussion

Two different protocols were used in order to obtain the desired product. **Protocol 1**: addition at room temperature of palladium dichloride (2 mol%) to a stirred mixture of an alcohol and a silane in 1:1.4 ratio gave the corresponding silyl ether in good yield (Table 1). When the two reagents were not mutually soluble, as in the case of Ph_3SiH, benzene was used as solvent (see Scheme 1). **Protocol 2**: addition of $PdCl_2$ (2 mol%) to a stirred mixture of a triethylsilyl ether and Et_3SiH in dry ethanol (10 ml) at 80 °C for 8 h led to the deprotection of the silyl ether to give the parent alcohol (Table 2) (see Scheme 2).

The data in Table 1 indicate the formation of silyl ethers in good yields starting from benzyl, primary and secondary alcohols. It is worth noting that this methodology allows for the protection of alcohols with differently substituted silyl groups through the employment of the corresponding silicon hydrides, which are sometimes more available and more stable than the corresponding halides. The reaction of alcohols with triethylsilane takes place spontaneously, accompanied with hydrogen evolution. The formation of triethylsilyl ethers is fast independently of the nature of the alcohol structure (primary, secondary or benzylic). In the case of triphenylsilane, benzene was required to solubilize the reagents. The use of a solvent has a pronounced effect on the reaction rate (the reaction becomes slower).

The mechanism proposed for the palladium-catalyzed transformation of alcohols to their corresponding silyl ethers stipulates the generation of molecular hydrogen. This assumption is based on our previous study on olefin hydrogenation. We have used molecular hydrogen generated by a simple and spontaneous reaction of

Table 1
Conversion of alcohols to silyl ethers[a]

ROH[b]	R'_3SiH[b]	Time (h)	$ROSiR'_3$ Yield,[c] (%)
$PhCH_2OH$	Et_3SiH	0.25	98
	t-$Bu(Me)_2SiH$	2	95[d]
	Ph_3SiH	6	90[e]
2-Octanol	Et_3SiH	0.25	78
	t-$Bu(Me)_2SiH$	24	71[d]
	Ph_3SiH	24	64[d,e]
1-Decanol	Et_3SiH	0.30	98
	t-$Bu(Me)_2SiH$	0.45	76
	Ph_3SiH	7	84[e]

[a] $PdCl_2$ (2 mol%).
[b] $ROH:R'_3SiH = 1:1.4$.
[c] Isolated yields after passage through a florisil column.
[d] Determined by GC analysis on the basis of product formation in the crude reaction mixture.
[e] In benzene as solvent.

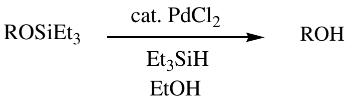
$$ROH \xrightarrow[R'_3SiH]{\text{cat. } PdCl_2} RCH_2\text{–}OSiR'_3$$

Scheme 1.

Table 2
Conversion of silyl ethers to alcohols[a]

Starting material	Product	Yield[b] (%)
$CH_3CH_2CH_2OSiEt_3$	1-Propanol	81
$CH_3CH_2CH_2CH_2OSiEt_3$	1-Butanol	98
$CH_3CH_2CH_2(OSiEt_3)CH_3$	2-Butanol	98
$CH_3(CH_3)C(OSiEt_3)(CH_3)$	*tert*-Butanol	95
$CH_3CH_2CH_2CH_2CH_2OSiEt_3$	1-Pentanol	98
$CH_3CH_2CH_2CH(OSiEt_3)CH_3$	2-Pentanol	98
$CH_3CH_2CH_2CH_2CH_2CH_2OSiEt_3$	1-Hexanol	98
$CH_3CH_2CH_2CH_2CH_2CH_2CH_2OSiEt_3$	1-Heptanol	88
$CH_3CH(OSiEt_3)CH_2CH_2(OSiEt_3)$	1,3-Butanediol	98
$CH_3CH_2CH(OSiEt_3)CH_2(OSiEt_3)$	1,2-Butanediol	98

[a] $PdCl_2$ (2 mol%)/Et_3SiH/RO–$SiEt_3$ (1 eq.) in reflux of EtOH after 8 h.
[b] Determined by GC/mass analysis.



$$ROSiEt_3 \xrightarrow[\substack{Et_3SiH\\EtOH}]{\text{cat. } PdCl_2} ROH$$

Scheme 2.

Et_3SiH and EtOH in the presence of $PdCl_2$ catalyst. The reduction reaction took place at room temperature in high yields. The absence of products resulting from hydrosilylation and dehydrosilylation reactions is in agreement with the generation of molecular hydrogen that reacts efficiently with the carbon–carbon double bond. Furthermore, we have noticed during the preparation of silyl ethers (in this work) that prolonged reaction times at room temperature led to the incomplete transformation of the alcohols to the corresponding triethylsilyl ethers even when operating in the presence of an excess of triethylsilane. Based on previous reports on deprotection reaction of triethylsilyl ethers under hydrogen pressure catalyzed by Pd/C [8,9], we do believe that molecular hydrogen generated during the silyl ether formation and adsorbed on the palladium catalyst is responsible of the low yield obtained. This result prompted us to investigate the effects of molecular hydrogen (generated in situ by the reaction of Et_3SiH and ethanol in the presence of $PdCl_2$) on the cleavage of triethylsilyl ethers. The cleavage of triethylsilyl ethers to the corresponding alcohols is outlined in Scheme 2.

Reaction of a triethylsilyl ether with triethylsilane (at least one equivalent) in EtOH at 80 °C in the presence of catalytic amounts of $PdCl_2$ leads to the formation of the parent alcohol. GC/MS analysis shows that the reaction is quantitative for primary, secondary and tertiary alcohols after 8 h (Table 2). The method has the advantage to work under mild conditions and avoid the use of high pressures of hydrogen.

In conclusion, these results account for the efficiency and flexibility of the palladium catalyzed transformation of alcohols in the presence of organosilicon hydrides. $Et_3SiH/PdCl_2$ system provides a mild and efficient catalytic system for the protection of alcohols and subsequent removal of the triethylsilyl protecting group. We have shown that the reaction of $Et_3SiH/PdCl_2$ system with alcohols gives the triethylsilyl ethers after 30 min in high yield. We have also developed a novel and efficient method for the cleavage of triethylsilyl ethers to the corresponding alcohols in the presence of a catalytic amount of $PdCl_2$, triethylsilane and ethanol as solvent. The ready availability of the catalyst, the high yields and the simplicity of the procedure render this methodology advantageous for work involving triethylsilyl ether manipulation. Further work in our laboratory is aimed at studying the selective deprotection of triethylsilyl group over other silyl groups present in the same molecule.

3. Experimental

All manipulations were carried under an argon atmosphere. Benzene, hexane and ethanol were distilled and stored under argon. The reported yields are based on GC/MS analysis using a FISON GC 8000 series TRIO 1000 gas chromatography equipped with a column capillary CP Sil.5 CB, 60 M × 0.25 mm Id.

3.1. General procedure for the preparation of silylethers

To a solution of alcohol (one equivalent) and a silane (1.4 equivalent) was added a catalytic amount of palladium (II) chloride (2 mol%) at room temperature under an argon atmosphere. When the two reagents were not mutually soluble, as in the case of Ph_3SiH, benzene was used as solvent. The resulting mixture was stirred for indicated time at room temperature (see Table 1) and then 10 ml of hexane was added to the solution. The residue was filtered over Florisil column (to remove the palladium salts) and the filtrate was evaporated.

3.2. General procedure for the preparation of alcohols from silylethers

To a solution of a triethylsilyl ether (one equivalent) and Et_3SiH (one equivalent) in dry ethanol was added a catalytic amount of palladium (II) chloride (2 mol%). The resulting mixture was stirred for 8 h at 80 °C (see Table 2) and then 10 ml of hexane was added to the solution. The residue was filtered over silica gel (to remove the palladium salts) and the filtrate was evaporated. The crude product was analyzed by GC/MS.

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