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Palladium Chloride-Catalyzed Reductive Cleavage of Benzylic Acetal, Ketal and Ether Compounds with Triethylsilane

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Reductive cleavage of benzylic acetal, ketal and ether compounds to the corresponding alkanes using triethylsilane and a catalytic amount of palladium(II) chloride is described. The reductive reaction took place under mild conditions, affording high yields of the corresponding alkane compounds in short reaction times.

Keywords: Reduction, Acetals, Ketals, Ethers, Palladium(II) chloride, Triethylsilane, Alkanes

INTRODUCTION

The development of new methods for the deprotection of functional groups in one-step avoiding the intermediate step of going back to the parent functionality has gained importance in recent years. Aldehydes, ketones and diols are frequently protected as acetals and ketals in organic synthesis, and a number of techniques for their deprotection are known [1-7]. However, some of the reported methods for the deprotection of acetals require high temperatures, long reaction times and most of them involve acidic conditions. It is well known that acidic treatment is often incompatible with the presence of other acid-sensitive functional groups. Thus, milder conditions and safer procedures have been developed for the deprotection of acetals [8-13].

Organosilicon reagents in the presence of small amounts of a catalyst are commonly used for the reduction of functional groups. For example, the combination of chlorodimethylsilane and a catalytic amount of indium trichloride ($InCl_3$) is effective for the deoxygenation of aryl ketones and *sec*-benzylic alcohols to yield the corresponding hydrocarbons [14-15]. Reduction of C-O bonds of primary alcohols or ethers has taken place using triethylsilane (Et_3SiH) and catalytic amounts of $B(C_6F_5)_3$. Gevorgyan *et al.* reported that certain alcohols could be converted to alkanes by using Et_3SiH as reductant, *via* initial formation and reduction of triethylsilyl alkyl ethers [16-17]. Brookhart *et al.* used cationic iridium pincer catalysts for the room temperature cleavage and reduction of a broad range of alkyl ethers with triethylsilane and investigated the mechanistic details governing this catalytic transformation [18]. Similarly, the C-OH bond of benzyl alcohols has been readily reduced to the corresponding C-H bond with triethylsilane in the presence of $Bi(OTf)_3$ catalyst [19]. The reduction of acetals to ethers and orthoesters to acetals with hydrosilane using rhodium catalyst was reported by Ohta *et al.* [20]. The deacetoxylation of propargylic acetates with triethylsilane catalyzed by indium(III) bromide to produce internal alkynes containing a variety of functional groups was demonstrated by Sakai *et al.* [21].

We have previously investigated the efficiency of $Et_3SiH/PdCl_2$ system for various chemical transformations

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*Corresponding author. E-mail: m.mirzaaghayan@ccerci.ac.ir under mild conditions: hydrogenation of 1-alkenes [22,23], selective hydrogenation of the carbon-carbon double bond of α,β-unsaturated ketones to afford the corresponding saturated ketones [24], and reduction of aromatic ketones, aldehydes [25] and alcohols [26,27]. We have also shown the versatility of $R_3SiH/PdCl_2$ system in the chemical transformation of alcohols to silyl ethers and the subsequent deprotection of triethylsilyl ethers to the parent alcohols under mild conditions [28].

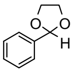
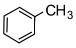
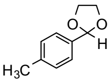
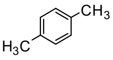
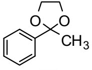
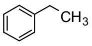
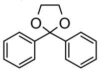
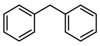
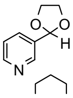
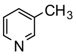
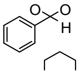
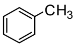
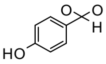
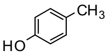
EXPERIMENTAL

All operations were carried out under an argon atmosphere. Ethanol was distilled and stored under argon. GC/MS analysis was performed on a FISON GC 8000 series TRIO 1000 gas chromatograph equipped with a capillary column CP Sil.5 CB, 60 M × 0.25 mm Id.

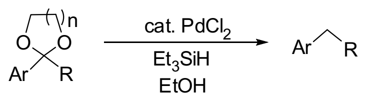
General Procedure for the Reduction

To a solution of an acetal, ketal or ether derivative (1 mmol, 1 equiv.) and triethylsilane (amount indicated in Tables 1 and 2) in ethanol (5 ml) was added a catalytic amount of palladium(II) chloride (10 mol%) under an argon atmosphere. The resulting mixture was stirred for the time indicated in Tables 1 and 2 prior to GC/MS analysis. The reaction mixture was filtered and the filtrate was evaporated. The spectroscopic data of the obtained products were compared with authentic samples [29].

Table 1. $PdCl_2$-Catalyzed Reductive Cleavage of Benzylic Acetal and Ketal Compounds to the Corresponding Alkanes with Et_3SiH in Ethanol

entry	Substrate		Ar⌒R	Substrate/ Et_3SiH	Time min	Yield[a]%
1		**1a**		1/2	30	96
2		**1b**		1/2 1/2	30 60	70 82
3		**1c**		1/2	30	95
4		**1d**		1/10 1/13	60[b] 60[b]	75 81
5		**1e**		1/6	60[b]	78
6		**1f**		1/2	30	96
7		**1g**		1/2	30	90

[a]Determined by GC/Ms analysis. [b]The reaction was conducted in refluxing ethanol.



1a-g **2a-g**

Scheme 1

$$\underset{\textbf{3a-k}}{\text{ROR'}} \xrightarrow[\text{Et}_3\text{SiH}\ \text{EtOH}]{\text{cat. PdCl}_2} \underset{\textbf{4a-k}}{\text{R''H}}$$

Scheme 2

RESULTS AND DISCUSSION

The present work was aimed at exploring the efficiency of molecular hydrogen, generated *in situ* by the reaction of Et_3SiH with EtOH in the presence of a catalytic amount of $PdCl_2$, for the reductive cleavage of benzylic acetal, ketal and ether compounds to the corresponding alkanes. The reduction of various benzylic acetal, ketal and ether compounds with Et_3SiH in the presence of palladium dichloride in ethanol occurred at room temperature to give the corresponding aryl alkane products in high yields (Schemes 1 and 2). The hydrogenation reaction requires the use of an inert atmosphere and anhydrous solvent. In a typical experiment, $PdCl_2$ (10 mol%) was added at room temperature to a stirred mixture of acetal, ketal or ether derivative (1 equiv.) and Et_3SiH (2 equiv.) in dry ethanol (5 ml). An exothermic reaction occurred during the first five minutes and then the temperature decreased to room temperature. The resulting mixture was stirred for the time indicated in Tables 1 and 2 prior to GC/MS analysis.

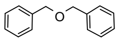
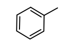
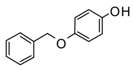
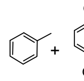
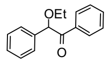
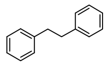
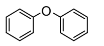
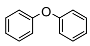
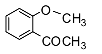
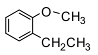
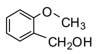
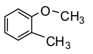
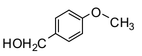
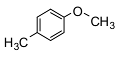
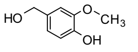
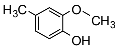
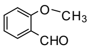
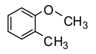
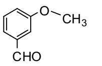
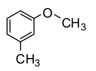
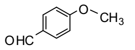
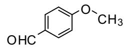
The reductive cleavage of benzylic acetals and ketals took place in high yields (entries 1-7, Table 1). For example, the reaction of 1 equiv. of 2-phenyl-1,3-dioxolane (entry 1, Table

1, **1a**) with $Et_3SiH/PdCl_2$ (2 equiv./10 mol%) in ethanol (5 ml) for 30 min at room temperature led to the formation of toluene in 96% yield. Similarly, the reaction of 2-*p*-tolyl-1,3-dioxolane (entry 2, Table 1, **1b**) or 2-methyl-2-phenyl-1,3-dioxolane (entry 3, Table 1, **1c**) gave *p*-xylene or ethylbenzene in 82 and 95% yield after 60 and 30 min, respectively. It should be noted that for certain compounds, an excess of triethylsilane or longer reaction times were required to drive the reaction to completion. For example, the reaction of 2,2-diphenyl-1,3-dioxolane (entry 4, Table 1, **1d**) with Et_3SiH (substrate/Et_3SiH: 1/10 or 1/13) produced diphenylmethane in 75 and 81% yield, respectively, after 60 min refluxing. The reaction of 3-(1,3-dioxolan-2-yl)pyridine (entry 5, Table 1, **1e**) with 6 equiv. Et_3SiH produced 3-methylpyridine in 78% yield after 60 min in ethanol refluxing. 2-Phenyl-1,3-dioxane (entry 6, Table 1, **1f**) and 4-(1,3-dioxan-2-yl)phenol (entry 7, Table 1, **1g**) were successfully reduced to the corresponding toluene and *p*-cresol in 82 and 95% yield after 30 min, respectively.

The results showed that benzylic acetal and ketal compounds are readily cleaved with Et_3SiH in the presence of 10 mol% of palladium(II) chloride to yield aryl methane and mono and/or disilylated diols. Indeed, both mono and disilylated diols were observed in the GC/MS spectra. The formation of monosilylated diol is most likely due to the partial hydrogenation of the disilylated diol. In fact, we have previously demonstrated that triethylsilyl ethers can be easily cleaved to the corresponding alcohols by $Et_3SiH/EtOH$ system in the presence of $PdCl_2$ catalyst [28]. The formation of benzyl alcohol as an intermediate during the reductive cleavage of acetals is not excluded. Its subsequent reduction to the corresponding methylene compounds takes place in very short reaction time [27].

We have also examined the reduction of ether compounds (Table 2). The results indicate that benzylic ethers can be readily converted to the corresponding alkanes in excellent yields. For example, the reaction of 1 equiv. of dibenzylether (entry 1, Table 2, **3a**) with $Et_3SiH/PdCl_2$ (3 equiv./10 mol%) in ethanol (5 ml) for 30 min at room temperature led to the formation of toluene in 99% yield. The formation of toluene is most likely a stepwise process. We believe that the cleavage of dibenzylether with Et_3SiH in the presence of palladium catalyst yields aryl methane compound (toluene) and benzyl alcohol. The latter is then reduced to toluene [27]. However, it should be noted that Gevorgyan *et al*. reported no reaction for the reduction of similar ether. Indeed, (2-(benzyloxy)propan-2-yl)benzene compound did not undergo the reduction using 4 equiv. Et_3SiH and $B(C_6H_5)_3$ or $B(C_6F_5)_3$ system as reductant [16,17]. The reaction of 4-(benzyloxy)phenol (entry 2, Table 2, **3b**) with 4 equiv. of Et_3SiH for 30 min produced toluene in 99% yield. We also observed the presence of hydroquinone and its mono and/or disilylated form. However, for the reduction of *O*-ethylbenzoine, an excess of triethylsilane and longer reaction times in refluxing ethanol was required. Indeed, the reaction of 1 equiv. of *O*-ethylbenzoine (entry 3, Table 2, **3c**) with $Et_3SiH/PdCl_2$ (15 equiv./10 mol%) for 60 min in ethanol refluxing (5 ml) led to the formation of dibenzyl in 59% yield. In this case, an increase of the reaction time did not have any effect on the reaction yield.

Table 2. $PdCl_2$-Catalyzed Reductive Cleavage of Ether Compounds to the Corresponding Alkanes with Et_3SiH in Ethanol

entry	ROR'		R"H	Substrate/ Et_3SiH	Time min	Yield^a%
1		**3a**		1/3	30	99
2		**3b**		1/4	30	99
3		**3c**		1/15 1/15	60^b 120^b	59 61
4		**3d**		1/10	60	no reaction
5		**3e**		1/4	60^b	99
6		**3f**		1/2	10	98
7		**3g**		1/2	10	100
8		**3h**		1/2	10	96
9		**3i**		1/2	30	100
10		**3j**		1/2	30	86
11		**3k**		1/2	30	100

^{a}Determined by GC/Ms analysis. ^{b}The reaction was conducted in refluxing ethanol.

This method of reduction appears to be limited to benzylic ether compounds. In fact, when the reaction conditions described above were applied to diphenylether, only the starting material was recovered after 60 min reaction even with 10 equiv. Et_3SiH in ethanol at room temperature (entry 4, Table 2, **3d**). Furthermore, for the reaction of 2-methoxyacetophenone (entry 5, Table 2, **3e**), 2- and 4-methoxybenzylalcohol (entries 6-7, Table 2, **3f-g**) or 4-hydroxy-3-methoxybenzylalcohol (entry 8, Table 2, **3h**) with $Et_3SiH/PdCl_2$, only a reduction of the ketone or alcohol function was observed while the ether function remained intact [25,27]. Moreover, the reaction of 2- or 4-methoxybenzylalcohol led to the formation of *o*- or *p*-methylanisole. Similarly, we observed only the reduction of the aldehyde function of 2-, 3- or 4-methoxybenzaldehyde (entries 9-11, Table 2, **3i-k**) under similar conditions to give *o*-, *m*- or *p*-methylanisole, respectively. It should be noted that in the case of 4-methoxybenzaldehyde, only *p*-methylanisole was recovered after 60 min reaction even with 10 equiv. of Et_3SiH in ethanol at room temperature.

In conclusion, we have developed a simple and efficient method for the reduction of acetal, ketal and ether compounds to the corresponding aryl alkanes using $Et_3SiH/PdCl_2$ system in ethanol. The proposed procedure has several advantages including the ready availability of the catalyst and simple workup. The adoption of this simple technique will be an attractive addition to the range of procedures already known for this general transformation.

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