$PdCl_2$-Catalyzed Reduction of Organic Halides by Triethylsilane

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Summary: The palladium-catalyzed dehalogenation reaction of alkyl or aryl halides with triethylsilane takes place, giving high yields under mild reaction conditions. The efficiency of the reduction is similar for organic chlorides, bromides, or iodides, and the presence of functionalities such as esters or ethers does not interfere with the outcome of the reaction.

Introduction

Despite the large variety of reducing agents available for the removal of halogen substituents from organic halides,[1] new nontoxic, economical, simple, and selective reducing systems are in constant demand. From the various procedures and reagents that have been developed for reductive dehalogenation, the silicon hydrides represent an important family (eq 1).

$$R'{-}X + R_3SiH \rightarrow R'{-}H + R_3SiX \qquad (1)$$

Trialkylsilanes are known to be poor reducing agents, due to their low ability to donate hydrogen atoms[2] or hydrides.[3] To overcome these undesired properties, a variety of modified silanes with weaker Si−H bond strengths and composite reducing systems based on a combination of a silane/transition-metal catalyst have been developed in the last decade. For example, tris(trimethylsilyl)silane has been found to be an effective radical-based reducing agent,[4] while transition-metal complexes insert into the Si−H bond to offer a new transfer agent.[5,6] Thus, appropriate skeletal modification of silanes and/or the judicious selection of a transition-metal transfer agent could provide the opportunity to create suitable reducing systems.

Occasionally, reaction 1 has been applied not to the dehalogenation procedure but to the preparation of organosilicon halides. In fact, Sommer and co-workers[7] introduced reaction 1 as an exchange between triethylsilane and alkyl chlorides in the presence of aluminum iodide. Later, a number of organosilanes were also used as reducing agents for a variety of alkyl halides in the presence of a catalytic amount of aluminum chloride.[8] Organosilicon halides have been prepared by group VIII metal catalyzed reactions using a variety of alkyl halides.[9] In particular, $PdCl_2$ has been employed as a catalyst for the halogenation of the silicon hydride moiety with carbon tetrachloride[10] and with alkyl iodides.[11] Herein, we report the use of the $Et_3SiH/PdCl_2$ system as an extremely efficient method for the dehalogenation of organic chlorides, bromides, and iodides. In addition, some aspects of the reaction mechanism have been tested.

Results and Discussion

Addition of palladium dichloride (5−10 mol %) to a stirred mixture of an appropriate halide and triethylsilane, at room temperature, gave the corresponding dehalogenated product in high yield. A solvent, usually benzene, was required when the alkyl halide and the silane were not mutually soluble or for temperature control when the reaction was exothermic. The dehalogenation of 18 substrates together with the experimental conditions employed are summarized in Table 1. Analysis of the reaction mixture by ^1H NMR and/or by GC/MS showed the unique formation of dehalogenated product and the corresponding triethylsilyl halide. The yields were quantified by using an internal standard and were based on the formation of the reduction product. When possible, the reaction products were isolated either by recrystallization or by chromatography on silica gel. Furthermore, *tert*-butyl iodide, iodomethyl methyl ether, and 1,2-dibromoethane were reduced quantitatively on the basis of the triethylsilyl halide formation. Although reduction proceeded quite rapidly at room temperature, longer reaction times and even heating at 80 °C were necessary in some instances. The reduction of adamantane derivatives better il-

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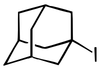
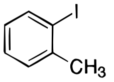
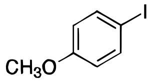
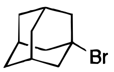
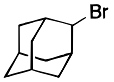
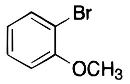
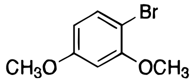
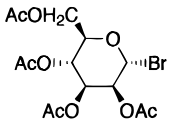
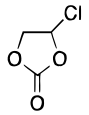
Table 1. Reaction of Organic Halides with Et_3SiH in the Presence of Catalytic Amounts of $PdCl_2$

RX	conditions[a]	yield of RH,[c] %
$C_6H_5CH_2CH_2{-}I$	10 min / r.t.	>95[d]
$CH_3C(O)O(CH_2)_4{-}I$	5 min / r.t.[b]	>95[d]
	2 h / r.t.	78
	10 min / r.t.	>95[d]
	25 min / r.t.[b]	>95[d]
	4 h / 80 °C	84
	6 h / 80 °C	80
$C_6H_5CH_2{-}Br$	2 min / r.t.	>95[d]
$C_6F_5CH_2{-}Br$	5 min / r.t.	>95[d]
$C_6H_5{-}Br$	40 min / r.t.	>95[d]
	2 min / r.t.	>95[d]
	15 min / r.t.	95
	40 min / r.t.	92
$C_6H_5CH_2{-}Cl$	2 min / r.t.	>95[d]
$C_6H_5{-}Cl$	1 h / r.t.	>95[d]
$CH_3OCH_2CH_2OCH_2{-}Cl$	10 min / r.t.	>95[d]
$CH_3OC(O)CH(CH_3){-}Cl$	1 h / r.t.	>95[d]
	24 h / 80 °C	81

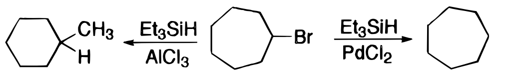
[a] Et_3SiH as solvent and $PdCl_2$ (5 -10 mol %). [b] Anhydrous Et_2O as solvent; Et_3SiI and Et_3SiOEt formed as by-products. [c] Isolated yields or as indicated otherwise. [d] On the basis of product formation in the crude reaction mixture; determined either by ^1H NMR or by GC analysis.

lustrates this picture. 1-Iodoadamantane was reduced in ca. 2 h at room temperature, whereas the *tert*-butyl iodide required only 5 min under the same conditions. The reduction of 1-bromo- and 2-bromoadamantanes was even slower, since heating at 80 °C was necessary. However, in all cases the efficiency of the reduction was high.

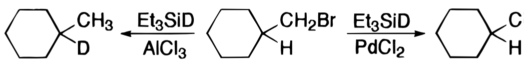
Generally, chlorides, bromides, and iodides behave similarly, although they tend to display an increasing reactivity in the order RI > RBr > RCl, which may be envisaged from their overall behavior in Table 1. For a particular halogen atom, aryl halides behave like alkyl halides and no substantial difference is observed between primary, secondary, and tertiary substituents. However, in some cases, the molecular arrangement plays an important role, although this is difficult to evaluate at present. The presence of functionalities such as ester or ether groups in the starting materials did not interfere with the outcome of the reaction.

The efficiency and the experimental simplicity of the present methodology can be appreciated in comparison with the methodologies previously employed for the debromination of 2,3,4,6-tetra-*O*-acetyl-α-glucopyranosyl bromide. The expected products were obtained in 80% and 100% yields using hydrogenolysis over Raney nickel (1000 psi at 50 °C in 2 h)[12] or tributyltin hydride (5 equiv at 80 °C in 15 min),[13,14] respectively, whereas the $Et_3SiH/PdCl_2$ method gave a yield of 92% in less than 40 min at room temperature.

In order to obtain some information about the mechanism operating in this reaction, we first performed some experiments to exclude the intermediacy of carbenium ions. It is well documented that the reactions with $AlCl_3$ as catalyst proceed *via* a carbenium ion, since structural rearrangements are observed during the reductions of bromocycloheptane with Et_3SiH (eq 2) and cyclohexylmethyl bromide with Et_3SiD (eq 3).[8] Replacing $AlCl_3$ with $PdCl_2$, we observed the expected debrominated products without structural rearrangements (eqs 2 and 3), indicating that the two catalysts behaved differently.



(2)



(3)

The intermediacy of free radicals in palladium chemistry has been demonstrated in some cases.[15] Therefore, in order to assess the importance of free radicals in the $PdCl_2/Et_3SiH$ system we attempted the free-radical-clock methodology.[16] Bromides **1**−**3** were chosen as the precursors of carbon-centered radicals, since their rearrangements have been studied in detail. In fact, neo-

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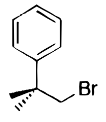

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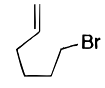

2

3

phyl, 5-hexenyl, and *trans*-(2-phenylcyclopropyl)carbinyl radicals undergo skeletal rearrangements with rate constants of 1×10^3, 2×10^5, and 3×10^{11} s^{-1}, respectively, at room temperature.[16] The reaction of neophyl bromide (**1**) under normal conditions, in 15 min, yielded only *tert*-butylbenzene, suggesting either that no radicals were involved in this reaction or that their lifetimes were shorter than the neophyl rearrangement. Bromides **2** and **3** resulted in a mixture of a variety of products (GC/MS analysis), which have not all been identified in detail. However, the two expected products from the radical rearrangements derived from bromides **2** and **3**, i.e. methylcyclopentane and 4-phenyl-1-butene, were found to be present in ca. 10% yield (retention times identical with those of authentic samples). These results indicate that we cannot exclude, at least in part, the involvement of free radicals.

The above observations together with (i) the identification by GC/MS of small amounts of Et_3SiCl in the reduction of bromide or iodide derivatives along with the corresponding triethylsilyl halides and (ii) the formation of metallic Pd during the reaction allowed us to suggest the following: The reaction of an alkyl halide with metallic palladium, generated *via* reaction 4,

$$2Et_3SiH + PdCl_2 \rightarrow 2Et_3SiCl + Pd + H_2 \qquad (4)$$

should result in a palladium complex. This oxidative addition may involve radical intermediacy.[17] Triethylsilane could transfer the H atom to palladium in exchange for the halide. The remaining step is the reductive elimination, which would produce the desired product and regenerate the palladium catalyst. An alternative proposed mechanism,[11] in which the silane first adds oxidatively to the palladium catalyst followed by exchange between the silyl and alkyl groups, cannot be ruled out at present. Further work on the stereochemical aspects of these reductions in order to assess their potential applications and to obtain further mechanistic information is in progress in our laboratory.

Experimental Section

Materials. Neophyl bromide was obtained by an exchange reaction from neophyl chloride.[18] Bromide **3** was prepared as follows: Commercially available *trans*-2-phenyl-1-cyclopropanecarboxylic acid was first reduced by $LiAlH_4$ to the corresponding alcohol and then brominated with PBr_3. A nonseparable mixture of *trans*-2-phenyl-1-(bromomethyl)cyclopropane and 4-bromo-4-phenyl-1-butene was obtained and was then epoxidized with 3-chloroperbenzoic acid. After chromatography on silica gel, *trans*-2-phenyl-1-(bromomethyl)cyclopropane was isolated as pure material.

All other materials were commercially available and, where necessary, were purified by standard methods.

Typical Procedure. To a stirred solution of 1-bromo-2,5-dimethoxybenzene (0.52 g, 2.4 mmol) and triethylsilane (0.39 g, 3.35 mmol) was added a catalytic amount of palladium dichloride (40 mg) under argon at room temperature. An exothermic reaction took place and was complete in 15 min. The residue was purified by chromatography on silica gel using a mixture of pentane/ether (80/20) as eluent to yield 311 mg of 1,4-dimethoxybenzene (95%).

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