P(MeNCH$_2$CH$_2$)$_3$N: An Efficient Promoter for the Reduction of Aldehydes and Ketones with Poly(methylhydrosiloxane)

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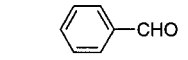
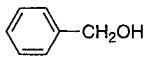
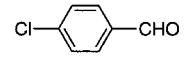
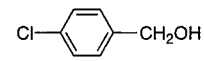
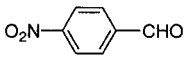
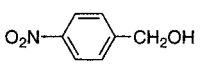
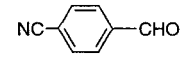
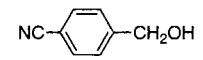
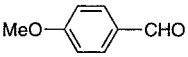
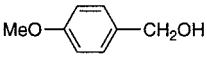
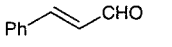
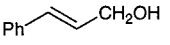
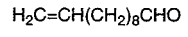
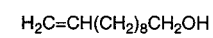
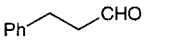
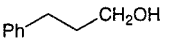
The reduction of carbonyl compounds by hydrosilylation is one of the most effective methods for the synthesis of alcohols.[1] The reactivity of organosilicon reagents, such as trialkoxysilanes and trihalogenated silanes, in these reactions is enhanced by coordination with Lewis bases such as fluoride[2] or DMF.[3] Upon reaction with diols or amino alcohols, these reagents can form pentacoordinate hydrosilicate intermediates[4] that efficiently reduce aldehydes and ketones to the corresponding alcohols.[5] Asymmetric reductions have also been achieved using chiral diols or chiral amino alcohols to give optically active alcohols with good to excellent ee's.[6]

Recently, polymethylhydrosiloxane (PMHS), an inexpensive and stable siloxane polymer has been extensively used in the reduction of imines,[7] azides,[8] and esters[9] in the presence of a catalyst. Although aldehydes and ketones can be reduced by PMHS in the presence of fluoride,[2] bis(dibutylacetoxytin),[10] or $ZnCl_2$,[11] the yields are modest or else rather harsh reaction conditions must be employed. During our ongoing investigation of new synthetic applications of **1**,[12] a commercially available nonionic base (Strem) originally synthesized in our laboratories,[13] we found that **1** promotes the allylation of aromatic aldehydes with allyltrimethylsilane.[14] This prompted us to determine whether **1** can activate Si−H bonds in PMHS to reduce carbonyl compounds. Herein we report that aldehydes and ketones are reduced under mild conditions by PMHS in the presence of catalyst **1**, giving the corresponding alcohols in high yield.

Table 1. Reduction of Aldehydes with PMHS Using 1 as a Promoter[a]

aldehyde	product	yield %[b]
		94
		95
		96
		94
		94
		95
		93
		92

[a] All reactions were conducted at room temperature for 1 h under argon. The THF was freshly distilled over Na and stored over 4 Å molecular sieves. [b] Isolated yield based on the aldehyde.

As seen in Table 1, a variety of aromatic aldehydes were smoothly reduced to the corresponding alcohols in high yields with survival of the aromatic chloro, nitro, cyano, and methoxy substituents. Conjugated as well as isolated double bonds also remained intact during regioselective reduction of the carbonyl groups. Aliphatic aldehydes are reduced to the corresponding alcohols in high yields even though such aldehydes undergo aldol condensation in the presence of catalyst **1**.[15] We assume that under the present reaction conditions equilibrium 1 is rapidly established and lies sufficiently far to the right that aldol condensation via initial deprotonation of the aldehyde by **1** is effectively suppressed.

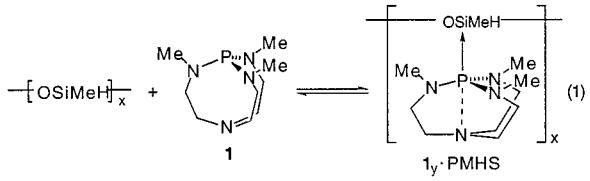


Table 2 shows that aromatic ketones are also efficiently reduced. Although the ester group in the fourth substrate in this table remained intact in the product, the product yield is only modest. This may be due to a partial reduction of the ester functionality. When 4-acetoxyacetophenone (**2**) was subjected to reduction with PMHS

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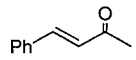
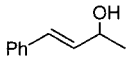
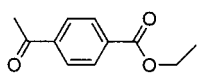
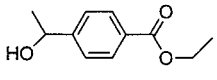
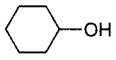
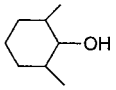
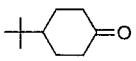
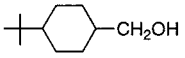
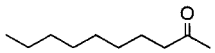
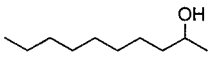
Table 2. Reduction of Ketones with PMHS Using 1 as a Promoter[a]

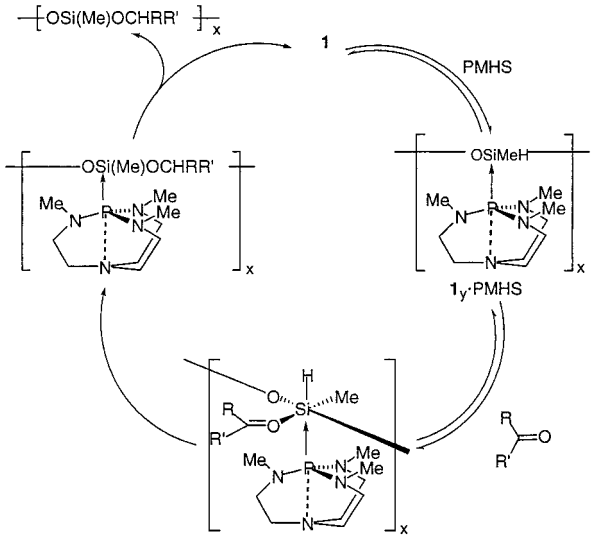
ketones	product	yield %[b]
		92
		95
		90
		79
		74[c]
		23[c]
		72
		64

[a] All reactions were conducted at room temperature for 12 h under argon. THF was freshly distilled over Na and stored over 4 Å molecular sieves. [b] Isolated yield based on the ketone. [c] Determined by GC based on ketone.

followed by acidic workup, up to 25% of 4-hydroxyacetophenone was found in the crude reaction mixture. In a separate experiment it was shown that no hydrolysis of the acetate group of **2** occurred under the acidic conditions employed. When 4-benzoyloxyacetophenone was similarly reduced with PHMS, proton signals of benzyl alcohol as well as of 4-hydroxyacetophenone were detected in the crude reaction product. Incomplete reductions of the carbonyl group were observed in these experiments. No reduction of the carbonyl group in ethyl acetoacetate or of 4-nitro-2-butanone was detected, while only partial reductions were found for 2-(phenylsulfonyl)-acetophenone (20%) and diethyl (2-oxo-2-phenylethyl)-phosphonate (15%). Like the unsaturated aldehydes in Table 1, the unsaturated ketone 4-phenylbut-3-en-2-one (Table 2) underwent chemoselective reduction of the carbonyl group in the presence of the olefinic bond. However 2-decanone, cyclohexanone, and 4-*tert*-butylcyclohexanone gave only moderate yields of product (trans in the case of the last reactant), and the sterically hindered ketone, 2,6-dimethylcyclohexanone, gave the corresponding alcohol in low yield.

That aldehydes are reduced much more rapidly under our conditions than ketones was shown by the reduction of an equimolar mixture of benzaldehyde and acetophenone which gave a corresponding product ratio of 92:8, respectively. Thus chemoselective reduction of an aldehyde group in the presence of a keto functionality can be accomplished.

Scheme 1



The mechanistic rationale proposed in Scheme 1 parallels that put forth earlier for the reduction of carbonyl compounds with hypervalent hydrosilicates.[2−6] The phosphorus atom in **1** initially coordinates with a silicon atom in PMHS to form the corresponding pentacoordinate hydrosilicate $\mathbf{1}_y$·PMHS. The pentacoordinate silicate then further coordinates a carbonyl group to form a hexacoordinate hydrosilicate followed by H transfer to the carbonyl carbon to form the silyl ether linkage. The alcohol is formed during workup in aqueous NaOH or in HF/CH_3CN. The role of **1** as a Lewis base stems from its ability to form a transannular bond between the bridgehead N and P atoms. This bond, which renders the phosphorus electron rich, facilitates phosphorus coordination to the silicon atom to form the pentacoordinate silicate. When $P(NMe_2)_3$, which lacks this electron enrichment mechanism, was employed under the present conditions, no detectable reduction product was observed. The ^{29}Si NMR spectrum of PMHS in the presence of 1 equivalent of **1** also provides evidence for the pathway shown in Scheme 1. Thus the ^{29}Si chemical shifts for PMHS in C_6D_6 (−31.06, −37.34 ppm) disappear and are replaced by two new peaks (−62.23 and −67.20 ppm). These upfield shifts are consistent with an increase in silicon coordination number from four to five[16] and an equilibrium 1 that favors $\mathbf{1}_y$·PMHS.

Although **1** acts catalytically in these reductions, it is actually a promoter inasmuch as **1** is hydrolyzed during the aqueous workup that liberates the alcohol from the silyl ether.

Experimental Section

In a typical procedure for the reactions in Tables 1 and 2, a solution of **1** (0.1 mmol) in THF (1.0 mL) at 0 °C was slowly added to 1.0 mL of a solution of PMHS (0.1 mL, 1.7 mmol) and the aldehyde or ketone (1.0 mmol) in THF (1.0 mL). After the reaction solution was stirred at room temperature (1 h for the aldehydes and 12 h for the ketones) an aqueous solution of NaOH (10%, 5 mL) and ether (10 mL) was added, and the mixture was then stirred at room temperature for another 1 h. Alternatively, for base-sensitive compounds, the crude reaction

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mixture was added to a cooled (0 °C) solution of 48% HF (0.5 mL) in acetonitrile (5 mL). The mixture was stirred at room temperature for 1 h followed by addition of ether (30 mL). The phases were separated, and the water layer was washed with ether (3 × 10 mL). The organic layers were combined, washed with brine (3 × 10 mL), and then dried over $MgSO_4$. The solvent was removed with a rotary evaporator and then under vacuum to give the crude product which was purified by flash chromatography (hexane:ethyl acetate = 10:1) to give the alcohol.

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Supporting Information Available: References containing ^1H and ^{13}C NMR spectral data with which our product spectra compared favorably. This material is available free of charge via the Internet at http://pubs.acs.org.

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