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Organosilane reductions with polymethylhydrosiloxanes

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ABSTRACT *Selective reductions of various organic groups with the inexpensive reducing system, polymethylhydrosylsiloxane, are presented. These include the reduction of olefins, alkyl- and aryl halides, acids, esters, ketones, aldehydes, imines as wellas some highly useful asymmetric reductions.*

INTRODUCTION

The reduction of a comprehensive range of organic functional groups ranging from carboxylic acids to aryl fluorides have been shown to be possible with a variety of organosilanes. A comprehensive review of the ionic and transition metal-catalyzed reductions of organic functional groups has recently appeared (1). Of the organosilanes utilized in these reductions the easily handled triethylsilane (bp 108°C) has been the most popular. It is, however, not the least expensive, nor does it provide the most hydride for the weight. The by-product from a triethylsilane reduction is typically a mixture of triethylsilanol and hexaethyldisiloxane, depending on the reaction and the work-up conditions. The separation of the desired product from these silicon-containing by-products can, in certain cases, be problematic. A number of alternatives to triethylsilane are available. These include diphenylsilane, phenylsilane, triisopropylsilane among others of a similar nature. Indeed, one has the freedom to design the silane reducing agent to fit the needs of a reaction by changing the groups on the silicon to alter the reactivity, the boiling point, and the by-products. Not to be overlooked as an economical and readily available alternative to triethylsilane is the polymethylhydrogensiloxane, PMHS, type materials. The polymethylhydrogen siloxanes cost about 10 percent on a molar Si-H equivalence basis versus triethylsilane. These siloxanes carry considerably more hydride at 1.35 percent on a molar basis than triethylsilane at 0.86 percent. The reaction by-products from the PMHS reductions are polysiloxanes, which typically separate as an insoluble, non-volatile gel. This gel is readily removed from the reaction mixture allowing for a simplified work-up procedure. In this mini-review I will present some of the published organic reductions using the PMHS reducing species.

REDUCTION OF OLEFINS

Although the reduction of olefins can be carried out in an economical fashion with molecular hydrogen this reduction is also possible with silanes and, in particular, with PMHS. The selectivity of the reactions is such that a more substituted double bond will provide a more stable carbocationic intermediate and, therefore, be reduced in preference to a lesser-substituted one. High yields are usually obtained with PMHS and Pd/C or related catalysts (2, 3). β-Chlorostyrene was reduced to β-chloroethylbenzene in good yield with PMHS and palladium nanocomposite catalysis (Eq. 1) (3). The C=C bonds in enones and α,β-unsaturated esters are also nicely reduced with this system.
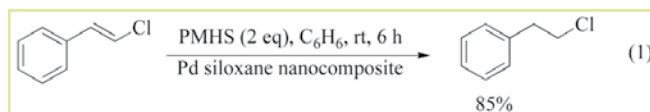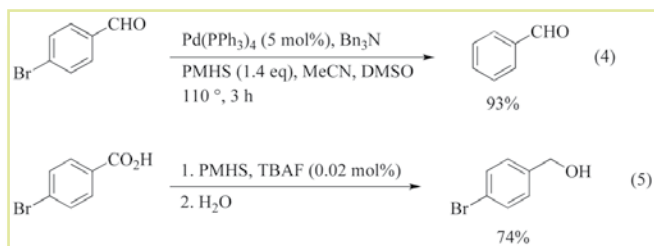

PMHS has been shown to efficiently provide the hydride for the reductive cyclization of α,ω-enynes to exo-methylenecycloalkanes (Eqs. 2, 3) (4). These conversions occur in better yield with PMHS than with triethylsilane.
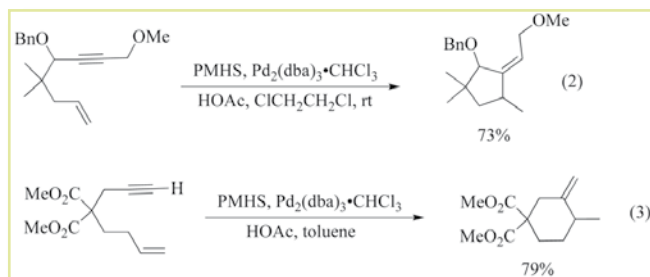
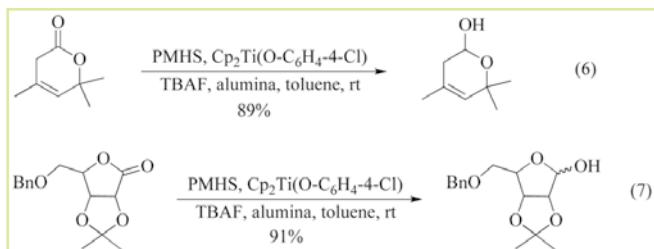## REDUCTION OF AROMATIC AND ALIPHATIC HALIDES

The reduction of aryl halides to the corresponding aromatic hydrocarbon is an important transformation and one that has potential in the destruction of the toxic polyhalogenated aromatics, for example the polybrominated biphenyls among others. Under certain conditions 4-bromobenzaldehyde can be reduced to benzaldehyde in high yield, a novel reduction wherein the very reactive aldehyde group is not reduced (Eq. 4) (5). A number of other aryl bromide reductions in the presence of functional groups are reported in this work. On the other hand, in the presence of fluoride ion in the form of TBAF, 4-bromobenzoic acid is reduced to 4-bromobenzyl alcohol, a case where the difficultly reduced carboxylic acid group is reduced over the aryl bromide (Eq. 5) (6). These two examples

nicely illustrate the potential for the manipulation of the selectivity of organosilane reductions. In other organohalide reductions α-haloketones (5) and vinyl bromides (5) are reduced with PMHS and Pd(0).

(4)

Pd(PPh₃)₄ (5 mol%), Bn₃N
PMHS (1.4 eq), MeCN, DMSO
110 °, 3 h
93%

(5)

1. PMHS, TBAF (0.02 mol%)
2. H₂O
74%

REDUCTION OF CARBOXYLIC ACIDS AND ESTERS

In addition to the example mentioned above, aliphatic carboxylic acids can be reduced to the alcohol under simple conditions with PMHS and a titanate ester catalyst (7). For example, octadecanoic acid is reduced to 1-octadecanol in 86 percent yield. Methyl octadecanoate is reduced under the same conditions to 1-octadecanol in 92 percent yield. The selective reduction of an ester in the presence of an epoxide is possible (8). Of particular utility is the reduction of lactones to hemiacetals. This transformation has been shown to be selective over the reduction of olefins and ketals even though ketals are typically readily reduced by organosilanes (Eqs. 6, 7) (9, 10).

PMHS, Cp₂Ti(O-C₆H₄-4-Cl)
TBAF, alumina, toluene, rt
89%

(6)

PMHS, Cp₂Ti(O-C₆H₄-4-Cl)
TBAF, alumina, toluene, rt
91%

(7)

REDUCTION OF ALDEHYDES AND KETONES

PMHS in the presence of fluoride ion reduces an aldehyde in the presence of a nitro group (6). α-Keto esters can be reduced at the keto functionality in very high yield leaving the ester intact (Eq. 8) (11). Aliphatic ketones with no special ability at the stabilization of an intermediate carbocation, such as those found in acetophenone derivatives, can be reduced to the hydrocarbon under the influence of the strong Lewis acid catalyst, tris(pentafluorophenyl)boron (Eq. 9) (12). The reductive amination of ketones in high yields is also possible (13). Enones are reduced to the saturated ketone with PMHS and a copper carbene catalyst (14). This compares well with the results of this reduction with Wilkinson's catalyst and triethylsilane (15).

PMHS, Sn(OTf)₂
MeOH, rt, 12-14 h
(10 mol%)
98%

(8)

PMHS, (C₆F₅)₃B
CH₂Cl₂, rt
88%

(9)
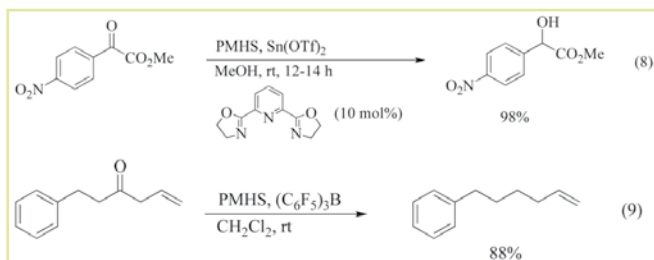
REDUCTION OF IMINES

Imines are readily reduced to secondary amines by PMHS. The yields are good to excellent (16). In a related and

highly useful reaction hydroxylimines can be reduced and simultaneously converted to their t-Boc-protected derivatives in a single step (Eq. 10) (17). Another approach to the t-Boc-protected amines is via the single-step reduction of organic azides with PMHS in the presence of t-Boc anhydride (Eq. 11) (18).

PMHS, Pd/C
Boc₂O, EtOH
90%

(10)

PMHS, Pd/C
Boc₂O, EtOH
88%

(11)
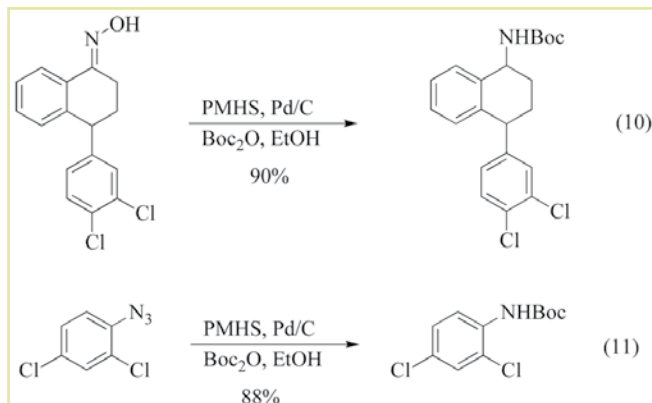
REDUCTIVE DEALLYLATION REACTIONS

PMHS in the presence of zinc chloride and Pd(0) readily reductively eliminates propylene from allyl ethers, allyl amines, and allyl esters. These transformations represent the deprotection of various allyl substituted organic functionalities. They can be carried out in the presence of several functional groups including halides, esters, nitro groups and ketals (Eq. 12) (19).

PMHS, ZnCl₂, Pd(PPh₃)₄
THF, rt
85%

(12)
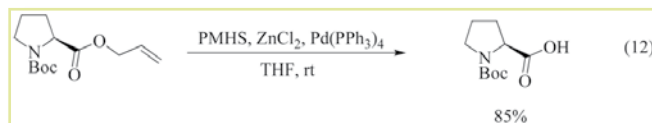
ASYMMETRIC REDUCTIONS OF PROCHIRAL KETONES

A bis(tetrahydroindenyl)titanium catalyst activated with phenylsilane can be used in the enantioselective PMHS hydrosilylation of arylalkyl ketones (Eq. 13). The reactions occur in good to excellent yields and very high ee's. For example, acetophenone is enantioselctively reduced in 73 percent yield and 97 percent ee. PMHS gives improved results in both yields and ee's versus those of phenylsilane. The reduction of prochiral dialkyl ketones does not occur with high ee's under the same conditions with even the sterically-biased tert-butylmethyl ketone giving only 53 percent ee (20, 21).

1. (R,R)'(EBTHI)TiF₂
PhSiH₃, pyrrolidine, MeOH
60°, THF
2. PMHS, MeOH, 15°
3. NaOH aq
80%; >98% ee

(13)
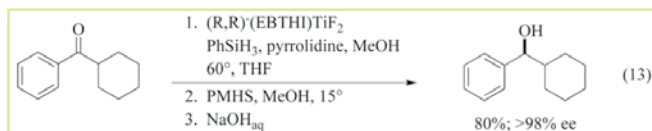
A copper hydride asymmetric reduction of aryl and heteroaryl ketones is possible wherein the copper hydride reducing species is generated 'in-situ' from PMHS (22, 23). The keys to this reaction are the use of the inexpensive PMHS as the hydride source. The higher reactivity of the PMHS over other silanes such as tetramethyldisiloxane (much slower) and triethylsilane (<3 percent yield) and phenylsilane (no reduction) is another advantage. With concentrations as low as 0.0009 mol% the di-tert-butylmethoxy-SEGPHOS, R-(-)-DTBM-SEGPHOS, ligand proved to be the most effective.

ASYMMETRIC REDUCTION OF ENONES

The enantioselective PMHS/CuH reduction of β-substituted cyclic enones has been reported. These reactions make use of the (S)-p-tol-BINAP chiral ligand as the source of the enantioselectivity. The reductions occur equally well with cyclopentenones, cyclohexenones and cycloheptenones with typical yields of 80 to 90 percent and ee values of >92 percent (24). The highly selective and active DTBM-SEGPHOS ligand in combination with PMHS and catalytic (Ph₃P)CuH can be used in the enantioselective conjugate reduction of β-substituted cyclic enones as well. With this system the yields are greater than 90 percent and the ee values in excess of 96 percent (Eq. 14) (25).
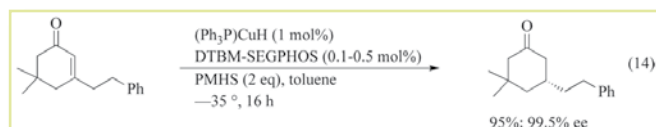

ASYMMETRIC REDUCTION OF α,β-UNSATURATED ESTERS AND LACTONES

The DTBM-SEGPHOS ligand together with PMHS and CuH works well in the conjugate reduction of α,β-unsaturated esters and lactones. The reaction conditions and workup procedure are straightforward. This reaction works well for the acyclic esters as well as the lactones (Eq. 15, 16). The chiral-PPF-P(t-Bu)₂ ligands also work well in this transformation (26). A similar approach with PMHS, CuH, and (S)-p-tol-BINAP gives products with slightly lower ee's (27).
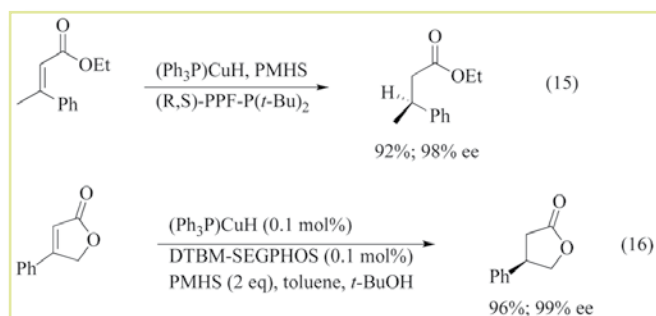
ASYMMETRIC REDUCTION OF IMINES

The titanium precatalyst, (EBTHI)TiF₂, can be activated with phenylsilane and then used in the PMHS enantioselective reduction of N-aryl imines from dialkyl ketones to chiral amines in excellent yields and extremely high ee's (28). The results from N-aryl imines of arylalkyl ketones gives lower yields and much lower ee's than those of the dialkyl systems. It has been shown that the addition of isobutylamine to the reaction greatly increases the yield and ee values in the reduction of arylalkyl imines (17) (29).
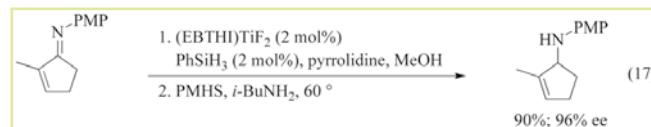
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