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Pd-catalyzed selective hydrosilylation of aryl ketones and aldehydes

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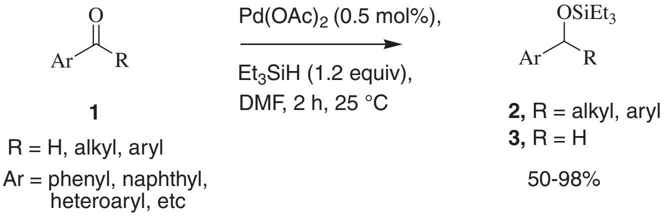
ABSTRACT

Pd salts in combination with triethylsilane as hydride source and DMF as solvent has been found to be excellent catalytic combination that selectively reduces aryl ketones and aldehydes under mild conditions to afford triethylsilyloxy compounds in excellent yields. Product selectivity to the respective benzyl alcohols can however be achieved when the reaction was performed in DMF/H_2O (4:1) as solvent system.

The catalytic reduction of carbon-heteroatom multiple bonds under mild conditions constitutes an important transformation in organic synthesis and pharmaceutical as well as agrochemical industry.[1] Especially, hydrosilylation of C=X (X = N, O) bonds is a promising alternative to other reduction methods such as hydrogenation, transfer hydrogenation as well as reduction with aluminum and boron hydrides, owing to its operational simplicity coupled with high atom-economy.[2] Also it combines reduction of carbonyl functionality with alcohol protection in a single step. Transition metals such as Zn,[3] Fe,[4] Rh,[5] Cu,[6] Re,[7] etc.[8] and their complexes are usually utilized as catalysts for hydrosilylation of carbonyl compounds. Quite recently, the combination of $PdCl_2/Et_3SiH$ has been successfully employed for the reduction of alkyl halides to alkanes,[9a] conversion of alcohols to halides and alkanes[9b] and isomerization of 1-alkenes to 2- and 3-alkenes.[10] The Pd/hydrosilane catalytic system is widely used in the following transformation: hydrosilylation of alkenes[11] and alkynes,[12] reduction of other functional groups such as azides, imines and nitro groups[13] and selective reduction of α,β-unsaturated ketones to saturated ketones.[14] More recently, this catalytic system has been reported for the reduction of aromatic aldehydes, ketones and benzyl alcohols into the corresponding methylene group[15] without much selectivity.

Generally, hydrosilylation of carbonyl compounds with silicon hydride leads to the formation of the corresponding alcohols, but to retain the silyl group as a protecting group is certainly more useful, as they are valuable synthetic intermediates and monomers for the production of organosilane polymers and materials.[16] Chatani and co-workers have observed that the catalytic combination of $Pd(OAc)_2/HSiEt_3$ in DMF at 60 °C results in direct reduction of 2-pyridinyl naphthyl ester to the corresponding silyl ether in 48% yield.[17] Herein we report an efficient catalytic protocol consisting of Pd salts–Et_3SiH–DMF combination that can selectively hydrosilylate various aryl ketones and aldehydes **1**, at ambient condition, to afford the corresponding triethylsilyloxy compounds **2** and **3** in high yields (Scheme 1).

We observed that when acetophenone was subjected to reduction with 1.2 equiv of Et_3SiH and 0.5 mol % $PdCl_2$ as catalyst in dry DMF at 25 °C, the corresponding silyl ether (**2a**) was obtained in 90% yield. In order to study this reaction in a systematic manner, several Pd salts and solvents have been employed and the results are presented in Table 1. Notably, DMF was found to be the best solvent while solvents such as CH_2Cl_2, 1,2-dichloroethane, toluene and benzene have failed. An important feature of this protocol is that product selectivity could be achieved depending upon the choice of solvents used. For instance, when the reaction was conducted in either DMF–water (4:1) or water as solvent, phenyl ethanol was obtained in 85% and 40% yields respectively.[18] Thus, both hydrosilylation and deprotection of the silyl ether were achieved in



Scheme 1. Pd-catalyzed hydrosilylation of aryl ketones and aldehydes.

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Table 1
Pd-catalyzed hydrosilylation of acetophenone: effect of solvent and catalyst[a]

Entry	Catalyst	Solvent	Yield (%)
1	$Pd(OAc)_2$	CH_3CN	60
		DMF	98
		Water	40[b]
		DMF–water (4:1)	85[b]
2	$PdCl_2$	DMF	90
3	$Pd(PhCN)_2Cl_2$	DMF	94
4	$Pd(dba)_2$	DMF	60
5	$Pd(Ph_3P)_4$	DMF	95
6	Sulflimine palladacycle[19]	DMF	96
7	Saccharin palladium complex[20]	DMF	95
8	10%Pd/C	DMF	89
9	Pd [(*R*,*R*)-BINAP]Cl_2	DMF	80[c]
10	Pd[(−)-sparteine]$(OAc)_2$	DMF	82[c]

Reagents and conditions:
[a] Acetophenone (1 mmol), $Pd(OAc)_2$ (0.5 mol %), Et_3SiH (1.2 mmol), solvent (2 ml), 25 °C, 1 h.
[b] Phenyl ethanol was obtained.
[c] No optical induction observed.

a single step with Pd salts in catalytic amount. Moreover, all the Pd catalysts gave excellent yields of hydrosilylated products; the highest yield of silylether was obtained with $Pd(OAc)_2$ (98%) while $Pd(dba)_2$ gave the lowest yield (60%). Sulfilimine palladacycle[19] and Pd–saccharin complex[20] also gave high yields of silyl ether. We also attempted to induce chirality in the molecule using different chiral Pd catalysts (entries 9 and 10) but with no asymmetric induction. With $Pd(OAc)_2$ as catalyst, other hydrosilanes such as Ph_2SiH_2 and polymethylhydrosiloxane (PMHS) were examined and found to be unreactive. In order to understand the scope and generality of the reaction, a wide range of aryl ketones were subjected to hydrosilylation under this reaction condition.[21] As can be seen from Table 2, the method worked exceedingly well in all the aryl ketones. Substrates containing bulky groups, such as tetralone, 9-fluorenone and 2-methyl-1-phenylpropan-1-one were readily converted to the corresponding silyl ethers in excellent yields. However, in case of chloro substituted aryl ketone (entry g), dehaloganated silyl ether was obtained in moderate yield (50%).

In order to extend the scope of the Pd-catalyzed hydrosilylation, a wide range of functionalized aromatic aldehydes including indole-3-carboxaldehyde were subjected to the optimized conditions (Table 3).[21] Indeed, the protocol gave excellent yields of the respective hydrosilylated products (entries a–n). The method has shown high tolerance for other sensitive functional groups such as ester, fluoro, hydroxyl, amine, imine, olefin and alkyne present either on aromatic nucleus or aliphatic system. In case of chloro substituted aryl aldehydes, the corresponding dehaloganated silyl ether was obtained in 51–54% yield along with 10% of dechlorinated benzaldehyde (entry f). For bromobenzaldehydes, the exclusive product obtained was the debrominated benzaldehyde (entry g).

Table 2
Pd-catalyzed hydrosilylation of aryl ketones[a]

Entry	Substrate	Product (**2**)	Yield[b,c] (%)
a	Acetophenone	1-Phenylethoxy-triethylsilane	98 (85)
b	4-Methylacetophenone	1-*p*-Tolylethoxy-triethylsilane	96 (80)
c	4-Methoxyaceto-phenone	1-(4-Methoxyphenyl)-ethoxytriethylsilane	80
d	Propiophenone	1-Phenylpropoxy-triethylsilane	96
e	2-Methyl-1-phenyl-propan-1-one	2-Methyl-1-phenylprop-oxytriethylsilane	96 (79)
f	Benzophenone	Diphenylmethoxy-triethylsilane	95 (86)
g	4-Chlorobenzo-phenone	Diphenylmethoxy-triethylsilane	50[d]
h	1-Tetralone	1,2,3,4-Tetrahydro-naphthalen-1-yloxy-triethylsilane	91
i	2-Acetylnaphthalene	1-Naphthalen-2-ylethoxy-triethylsilane	96 (84)
j	1-Indanone	2,3-Dihydro-1*H*-inden-1-yloxytriethylsilane	95
k	9-Fluorenone	9*H*-Fluoren-9-yloxy-triethylsilane	95

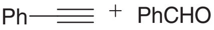
Reagents and conditions:
[a] Ketones (1 mmol), $Pd(OAc)_2$ (0.5 mol %), Et_3SiH (1.2 mmol), dry DMF (2 ml), 25 °C, 1 h.
[b] Isolated yield.
[c] The number in the parenthesis refers to isolated yield of the corresponding benzyl alcohol when DMF–water (4:1) was employed.
[d] ~12% Of the corresponding unsubstituted acetophenone was obtained.

Table 3
Pd-catalyzed hydrosilylation of aryl aldehydes[a]

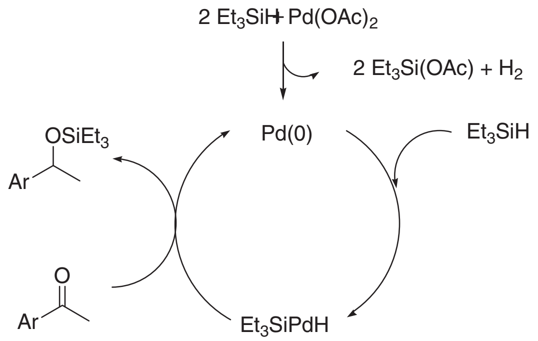
Entry	Substrates	Product (**3**)	Yield[b,c] (%)
a	Benzaldehyde	Benzyloxytriethylsilane	93 (87)
b	4-Methylbenzaldehyde	4-Methylbenzyloxy-triethylsilane	93
c	4-Methoxy-benzaldehyde	4-Methoxybenzyloxy-triethylsilane	96 (90)
d	4-(Methylthio)-benzaldehyde	4-(Methylthio)benzyloxy-triethylsilane	75
e	3,4-(Methylenedioxy)-benzaldehyde	3,4-(Methylenedioxy)benzyloxy-triethylsilane	96 (90)
f	2-, 3- or 4-Chloro-benzaldehyde	Benzyloxytriethylsilane	51–54[d]
g	2-, 3- or 4-Bromo-benzaldehyde	Benzaldehyde	87–88
h	4-Fluorobenzaldehyde	4-Fluorobenzyloxytriethylsilane	81
i	4-(Trifluoromethyl)-benzaldehyde	4-(Trifluoromethyl)benzyloxy-triethylsilane	90
j	Methyl 2-formyl 3,5-dimethoxybenzoate	Methyl 3,5-dimethoxy-2-((triethylsilyloxy)methyl)benzoate	92
k	4-Hydroxy-3-methoxy-benzaldehyde	4-Hydroxy-3-methoxybenzyl-oxytriethylsilane	81
l	Indole-3-carboxaldehyde	3-(((Triethylsilyl)oxy)-methyl)-indole	87
m	Methyl 3-(4-formyl-phenyl)acrylate	Methyl 3-(4-(((triethylsilyl)-oxy)methyl)phenyl)acrylate	86
n	Methyl 3-(4-formyl-phenyl)propanoate	Methyl 3-(4-(((triethylsilyl)oxy)methyl)phenyl)propanoate	85

Reagents and conditions:
[a] Aldehyde (1 mmol), $Pd(OAc)_2$ (0.5 mol %), Et_3SiH (1.2 mmol), dry DMF (2 ml), 25 °C, 1 h.
[b] Isolated yield.
[c] The number in the parenthesis refers to isolated yield of the corresponding benzyl alcohol when DMF–water (4:1) was employed.
[d] ~10% Of the corresponding unsubstituted benzaldehyde was obtained.

Table 4
Pd-catalyzed hydrosilylation of carbonyl compounds: competitive experiments[a]

Entry	Substrates	Product	Yield[b,c] (%)
a	$PhCH_2CH_2COCH_3$ + $PhCOCH_3$	$PhCH(OSiEt_3)CH_3$	96
b	$PhCH_2CH_2COCH_3$ + PhCHO	$PhCH_2OSiEt_3$	91
c	$PhCH_2$CH2$COCH_3$ + $PhCOCH_3$	$PhCH(OSiEt_3)$CH3	94
d	$PhCH_2$CH2CHO + PhCHO	$PhCH_2OSiEt_3$	88
e	PhCHO + $PhCOCH_3$	$PhCH_2OSiEt_3$	84
f	4-CF_3 PhCHO + 4-CH_3 PhCHO	4-CF_3 $PhCH_2OSiEt_3$ + 4-CH_3 $PhCH_2OSiEt_3$	90 (2.5:1)
g		$PhCH_2OSiEt_3$	91
h		$PhCH_2OSiEt_3$	83

Reagents and conditions:
[a] 1:1 Molar equivalents of substrates (5 mmol each), $Pd(OAc)_2$ (0.5 mol %), Et_3SiH (6 mmol), dry DMF (10 ml), 25 °C, 1 h.
[b] Isolated yield.
[c] ^{1}H NMR spectrum of the crude sample indicates no reaction for other substrate.



Scheme 2. Catalytic cycle for Pd-catalyzed hydrosilylation of aromatic ketones and aldehydes.

On the other hand, *p*-fluorobenzaldehyde underwent the reaction smoothly to give the corresponding hydrosilylated product without the fluoro group being affected.[23] However, the reaction failed in the case of aliphatic ketones and aldehydes, which is a limitation of this protocol. This catalytic system can be unique in selectively hydrosilylating aromatic ketones or aldehydes in the presence of aliphatic ketones or aldehydes. This was substantiated by carrying out the competitive experiments involving 1:1 molar equivalents of aliphatic ketones/aldehydes and aromatic ketones/aldehydes, results of which are presented in Table 4. As can be seen from Table 4, acetylene and imine groups were not affected in the presence of aromatic aldehyde. For 4-phenylbut-3-en-2-one and cinnamaldehyde, the corresponding saturated 4-phenyl-2-butanone and hydrocinnamaldehyde were obtained in 78% and 69% yields respectively. The catalytic cycle for the Pd-catalytic hydrosilylation process is shown in Scheme 2. The first step involves the reaction of $Pd(OAc)_2$ with Et_3SiH to give the active metallic Pd(0) species. The oxidative addition of Et_3SiH with Pd(0) then leads to the formation of highly reactive intermediate Et_3SiPdH complex,[22] which transfers hydride to aromatic carbonyl compounds followed by reductive elimination affording aryloxy silylated compounds along with the liberation of Pd(0).

In conclusion, we have shown that Pd salts are highly effective catalysts for selective hydrosilylation of aryl ketones and aldehydes, when carried out in DMF as solvent at 25 °C and triethylsilane as hydride source. The corresponding benzylic alcohols could however be obtained in excellent yields when the reaction was performed in DMF/H_2O (4:1) as solvent system.

Acknowledgments

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21. *General experimental procedure for the hydrosilylation of aryl ketones and aldehydes*:
    To a stirred solution of palladium catalyst (0.5 mol %) in dry DMF (2.0 mL) was added aryl ketones or aryl aldehydes (1.0 mmol) followed by the addition of triethylsilane (1.2 mmol). The resulting solution was then stirred for 1 h. After completion of the reaction, it was subsequently loaded directly onto the column (silica gel 60–120 mesh) for purification using petroleum ether as eluents to afford pure **2** or **3**, respectively.
    *Spectral data for compound **2f***: *Yield*: 91%; colorless liquid; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.60 (q, J = 8.1 Hz, 6H), 0.93 (t, J = 8.0 Hz, 9H), 1.58–2.01 (m, 4H), 2.57–2.82 (m, 2H), 4.72 (t, J = 4.3 Hz, 1H) 6.92–7.07 (m, 3H), 7.26–7.29 (m, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 5.4, 7.0, 19.5, 29.1, 33.1, 69.2, 125.1, 126.9, 127.9, 128.5, 136.6, 139.8; Anal. Calcd for $C_{16}H_{26}$Osi: C, 73.22; H, 9.98. Found: C, 73.28; H, 9.82.
    *Spectral data for compound **3e***: 96%; colorless liquid; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.61 (q, J = 8.0 Hz, 6H), 0.93 (t, J = 8.3 Hz, 9H), 4.61 (s, 2H), 5.93 (s, 2H), 6.74 (d, J = 1.0 Hz, 2H), 6.82 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 4.4, 6.7, 64.5, 100.6, 107.1, 107.8, 119.3, 135.2 146.4, 147.5; Anal. Calcd for $C_{14}H_{22}O_3Si$: C, 63.12; H, 8.32. Found: C, 63.28; H, 8.20.
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