Reduction of phosphine oxides to the corresponding phosphine derivatives in Mg/Me₃SiCl/DMI system

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## ARTICLE INFO

ABSTRACT

Direct reductions of phosphine oxides to the corresponding phosphines were performed successfully by using Mg/Me₃SiCl/DMI system. The reduction proceeded under mild conditions and was applicable to a wide range of phosphine oxides; triarylphosphine oxides, alkyldiarylphosphine oxides, and dialkylaryl-phosphine oxides gave the corresponding phosphines in good to excellent yields.

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Phosphines **1** are important reagents. For example, Ph₃P is widely used in Wittig reaction,[1] Mitsunobu reaction,[2] Mukaiyama–Corey lactonization,[3] Appel reaction,[4] and Staudinger reaction.[5] Optically pure phosphine ligands such as BINAP and SEGPHOS are used in asymmetric syntheses.[6] Many methods for preparing **1** have been reported including alkylation of halogenated phosphorus compounds (PCl₃, R₂PCl, etc.) with organometallic reagents,[7] coupling reaction of R₂PH with aryl triflates,[8] and reductive coupling of R₂PCl with aryl triflates in the presence of Zn/NiCl₂(dppe).[9] Reduction of phosphine oxides **2** to **1** would be also a promising way from the view point of recycling of phosphorus resources, since Ph₃P is converted to Ph₃P=O in the before-mentioned reactions and the latter has been discarded as waste. Though chemical reduction of **2** to **1** has been performed with several reductants such as metal hydrides (hydrosilanes,[10] aluminum hydrides,[11] etc.), low valent metal reductants (SmI₂/HMPA,[12] Cp₂TiCl₂/Mg,[13] etc.), and organic reductants (hydrocarbon/activated carbon,[14] hexaethylphosphorus triamide/phosphoryl trichloride,[15] etc.), these procedures are, how-ever, not necessarily suitable since they proceed under harsh condi-tions and require highly reactive and/or explosive reducing agents, and cleavage of C—P bonds also occurred as side reaction. Recently, we reported chemical[16] and electrochemical[17] indirect reduction of Ph₃P=O (**2a**) to Ph₃P (**1a**) via Ph₃PCl₂ (**3a**). We also reported direct
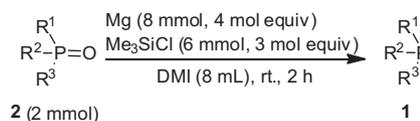
Scheme 1. Mg/Me₃SiCl/DMI promoted reduction of **2** to **1**.

electroreduction of **2a** to **1a** in the presence of trimethylsilyl chloride (Me₃SiCl).[18] In our continuing study on the reduction of **2** to **1**, we found that direct reduction of **2** to **1** proceeded smoothly by using Mg in the presence of Me₃SiCl at room temperature. It is worthy to note that this reduction proceeded in only 1,3-dimethyl-2-imidazolidinone (DMI). In this Letter, we report optimization of the reaction conditions of the reduction of phosphine oxides in the Mg/Me₃SiCl/DMI system as well as the scope and limitation of the reduction (see Scheme 1).

A typical procedure for the reduction of **2a** is as follows. To a mixture of Mg powder (8 mmol, 4 mol equiv), Me₃SiCl (6 mmol, 3 mol equiv), and DMI (8 mL) was added **2a** (2 mmol), and the whole mixture was stirred for 2 h at room temperature. To the reaction mixture was added satd aq (NH₄)₂CO₃, and the mixture was extracted with Et₂O (10 mL × 3). The combined organic layers were washed with satd aq NaCl, dried over Na₂SO₄, and concen-trated under reduced pressure. The resultant was analyzed by ³¹P NMR to find that **1a** and **2a** were obtained in 97:3 ratio. The desired

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Table 1
Mg–Me$_3$SiCl promoted reduction of **2a** to **1a**. Effect of solvents[a]

Entry	Solvent	Ratio[b] (%)	
		1a	**2a**
1	DMI	98 (96)[c]	1
2	MeCN	9 (9)[c]	91
3	DMF	7 (7)[c]	93
4	DMAc	n.d.[d]	100[e]
5	NMP	n.d.[d]	100[e]
6	DMPU	n.d.[d]	100[e]
7	THF	n.d.[d]	100[e]

[a] Compound **2a** (2 mmol), Mg (6 mmol), Me$_3$SiCl (6 mmol), solvent (8 mL), rt, 2 h.
[b] Determined by ^{31}P NMR.
[c] Isolated yields are shown in the parentheses.
[d] Not detected.
[e] No peaks other than **2a** were observed.

1a was obtained in 96% yield after purification by silica gel column chromatography (hexane/AcOEt = 5:1) (Table 1, entry 1).

Remarkable solvent effect was found: among the solvents examined, DMI was the only solvent to afford **1a** efficiently (Table 1): **1a** was obtained quantitatively in DMI (entry 1), whereas yield of **1a** was less than 10% in acetonitrile (entry 2) and DMF (entry 3), and no **1a** was obtained in DMAc (*N,N*-dimethylacetamide), NMP (*N*-methylpyrrolidone), DMPU (*N,N′*-dimethylpropyleneurea), and THF (entries 4–7).

We investigated metal reductants. Mg powder (4 mol equiv) gave **1a** quantitatively (Table 2, entry 1). Mg turnings (Grignard reaction grade) also gave **1a** in 85% yield (entry 2). The reduction did not occur with activated zinc powder and aluminum chips to recover **2a** unchanged (entries 3 and 4).

A decrease of the amount of Mg powder brought about a decrease of the yield of **1a** to 93% (3 mol equiv), 78% (2 mol equiv), and 45% (1 mol equiv), respectively (entries 5–7).

Me$_3$SiCl was indispensable for the reduction: the reduction did not proceed at all in the absence of Me$_3$SiCl.[19]

From these results, the optimized conditions were as follows: Mg (4 mol equiv), Me$_3$SiCl (3 mol equiv), DMI, room temp. The reduction proceeded in larger scale: to a mixture of Mg powder (45 mmol, 1.5 mol equiv), Me$_3$SiCl (80 mmol, 2.6 mol equiv), and DMI (20 mL) was added **2a** (8.40 g, 30 mmol). After short induction period (ca. 5 min), a heavy exothermic reaction occurred. The whole mixture was stirred for 2 h with cooling by a water bath. After the workup, the reaction mixture was analyzed by ^{31}P NMR to find that **1a** and **2a** were obtained in 94:6 ratio. The desired **1a** (7.08 g, 26 mmol, 87% yield) was obtained after purification by the silica gel column chromatography.

Table 2
Effect of metal reductants[a]

Entry	Metal (mmol)	Ratio[b] (%)	
		1a	**2a**
1	Mg powder (8)	98 (96)[c]	1
2	Mg turnings (8)	85	15
3	Zn powder (8)[d]	n.d.[e]	100[f]
4	Al chips (8)	n.d.[e]	100[f]
5	Mg powder (6)	93	7
6	Mg powder (4)	78	22
7	Mg powder (2)	45	55

[a] Compound **2a** (2 mmol), Metal, Me$_3$SiCl (6 mmol), DMI (8 mL), rt, 2 h.
[b] Determined by ^{31}P NMR.
[c] Isolated yield is shown in the parenthesis.
[d] Zinc was activated by washing with aq dil HCl.
[e] Not detected.
[f] No peaks other than **2a** were observed.

Table 3
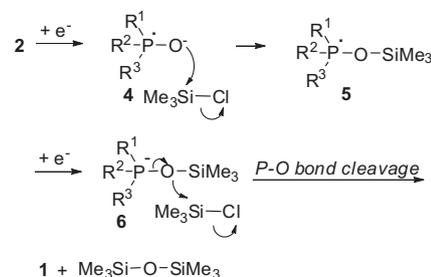Reduction of several types of phosphine oxides

$$\begin{array}{c} R^1 \\ R^1{-}P{=}O \\ R^2 \\ \textbf{2} \ (2 \ \text{mmol}) \end{array} \xrightarrow[\text{DMI (8 mL), Room temp., Time}]{\text{Mg (8 mmol), Me}_3\text{SiCl (6 mmol)}} \begin{array}{c} R^1 \\ R^1{-}P \\ R^2 \\ \textbf{1} \end{array}$$

Entry	R^1	R^2		Time (h)	Ratio[a,b] (%)	
					1	**2**
1	Ph	Ph	**2a**	2	97 (96)	3
2	*o*-Tolyl	*o*-Tolyl	**2b**	4	95 (89)	4
3	*m*-Tolyl	*m*-Tolyl	**2c**	6	91 (84)	7
4	*p*-Tolyl	*p*-Tolyl	**2d**	4	95 (91)	5
5	*p*-Anis	*p*-Anis	**2e**	2	94 (93)	6
6	Ph	*p*-NCC$_6$H$_4$	**2f**	2	Complex	n.d.[d]
7	Ph	^{i}Pr	**2g**	2	37 (54[c])	22
8	Ph	Et	**2h**	2	96 (75[c])	4
9	Et	Ph	**2i**	2	35 (70[c])	57
10	Oct	Oct	**2j**	2	n.d.[d]	98

[a] The ratios of **1** to **2** were determined by ^{31}P NMR.
[b] Yields referred to the isolated **1** are shown in the parentheses.
[c] Yields were evaluated by ^{31}P NMR.[21]
[d] Not detected.

Several phosphine oxides **2** were reduced under the optimized conditions (Table 3). Triarylphosphine oxides **2a**–**2e** gave the corresponding triarylphosphine **1a**–**1e** in quantitative yields (entries 1–5), whereas triarylphosphine oxide having an electron-withdrawing group such as (4-cyanophenyl)diphenylphosphine oxide (**2f**) gave only a complex mixture.[20] Alkyldiarylphosphine oxides **2g** and **2h** (entries 7 and 8) and dialkylarylphosphine oxide **2i** (entry 9) were also reduced with the Mg–Me$_3$SiCl–DMI system to afford the corresponding phosphine derivatives, **1g**, **1h**, and **1i**, in good yields.[21] On the other hand, reduction of trialkylphosphine oxide **2j** did not proceed at all to recover **2j** quantitatively.

A plausible mechanism is shown in Scheme 2.[18] At the initial stage of the reaction, one-electron reduction of **2** with Mg would occur to afford the corresponding anion radical **4**. The anion radical **4** would be trapped immediately with Me$_3$SiCl to afford silylated radical **5**. Further one-electron reduction of **5** followed by elimination of hexamethyldisiloxane would occur to afford **1**.

In conclusion, a direct reduction of phosphine oxides **2** to the corresponding phosphines **1** was performed successfully by using Mg–Me$_3$SiCl–DMI system. Though DMI was a special solvent to promote the reduction, detail of the effect of DMI is still not clear at present and will be discussed in near future.[22–25] The reduction could be applicable to simple phosphine oxides as well as more complicated phosphine oxides. Since Mg is stable and easy to handle, and not so expensive, the present method gives a way to recycle use of expensive phosphine reagents in organic syntheses.

$$\textbf{2} \xrightarrow{+ \ e^-} \begin{array}{c} R^1 \\ R^2{-}\overset{\cdot}{P}{-}O^- \\ R^3 \quad \text{Me}_3\text{Si}{-}\text{Cl} \\ \textbf{4} \end{array} \longrightarrow \begin{array}{c} R^1 \\ R^2{-}\overset{\cdot}{P}{-}O{-}\text{SiMe}_3 \\ R^3 \\ \textbf{5} \end{array}$$

$$\xrightarrow{+ \ e^-} \begin{array}{c} R^1 \\ R^2{-}\overset{-}{P}{-}O{-}\text{SiMe}_3 \\ R^3 \quad \text{Me}_3\text{Si}{-}\text{Cl} \\ \textbf{6} \end{array} \xrightarrow{\underline{P\text{-}O \ bond \ cleavage}}$$

$$\textbf{1} \ + \ \text{Me}_3\text{Si}{-}\text{O}{-}\text{SiMe}_3$$

Scheme 2. A plausible mechanism of reduction of **2** to **1** by using Mg–Me$_3$SiCl–DMI system.

Acknowledgments

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19. In electroreduction of **2a** without Me₃SiCl, cleavage of C—P bond occurred to give diphenylphosphine oxide (Ph₂PH=O).
20. Though several peaks were observed from −3.64 to −6.12 ppm (attributable to P(III) species) by analysis of the crude product by ^{31}P NMR, **2f** was not detected.
21. Since **1g**, **1h**, and **1i** were easily oxidized under air, the yields of these products were estimated by ^{31}P NMR of the reaction mixture.
22. In the initial stage of the reaction, Mg would react with Me₃SiCl (and a small amount of water included in the solvent) to afford a small amount of MgCl₂.
23. DMI itself is not so highly polar solvent since donor number (DN) and acceptor number (AN) of DMI (DN/AN 27/19) is similar to those of MeCN (14/20), DMF (29/21), and THF (20/8). However, DN and AN of DMI (62/52) and DMF (78/48) increased remarkably by addition of a small amount of MgCl₂ (0.1 M). The electron transfer from Mg to **2** and/or **5** would only occur in such highly polar environment. DN and AN were determined by solvatochromism. DN: Soukup, R. W.; Sone, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 2286; AN: Reichardt, C. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 29.
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