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Highly Chemoselective Metal-Free Reduction of Phosphine Oxides to Phosphines

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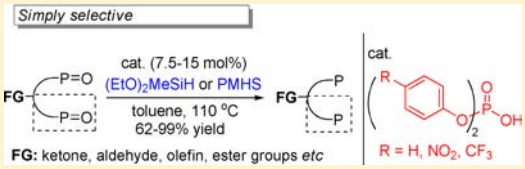
Supporting Information

ABSTRACT: Unprecedented chemoselective reductions of phosphine oxides to phosphines proceed smoothly in the presence of catalytic amounts of specific Brønsted acids. By utilizing inexpensive silanes, e.g., PMHS or $(EtO)_2MeSiH$, other reducible functional groups such as ketones, aldehydes, olefins, nitriles, and esters are well-tolerated under optimized conditions.



INTRODUCTION

Chemoselective reductions of unsaturated compounds constitute an important tool box for more benign organic synthesis.[1b] Although it is an old theme, even today significant efforts are being made to develop highly selective reductions of a specific scaffold in the presence of other reducible functional groups (FG). Notably, such efficient processes are the basic requirement saving protection/deprotection steps and thereby streamlining organic synthesis. In this respect, catalysis not only increases the rate of a given reaction, but also controls its selectivity. Hence, many catalytic methodologies have been established in the past decades to successfully reduce carbonyl, nitro, sulfoxide, and similar compounds.[1] On the other hand, relatively little work is known on the catalytic reduction of related P═O bonds, which are thermodynamically highly stable. With a bond energy of around 502 kJ/mol, they are significantly more stable compared to typical organic functional groups, and the general order of bond energy stability is P−O > C−H > C−O > C−C > C−N.[2,3] Therefore, it is not surprising that highly chemoselective reductions of phosphine oxides until today represent an unsolved problem, although the resulting organophosphines represent valuable intermediates and ligands for transition metal catalysis (Figure 1).[4]

Typical methods for the transformation of phosphine oxides to phosphines rely on the use of an excess of strong reducing agents such as metal hydrides or $HSiCl_3$/additives. Apart from being expensive, these reagents in general have limited functional group tolerance.[5−7] In fact, until recently only the combination of $Ti(O\text{-}i\text{-}Pr)_4$ with hydrosilanes allowed for the selective reduction of a variety of phosphine oxides. Nevertheless, tolerance of esters, ketones, and/or aldehyde groups was not achieved.[8]

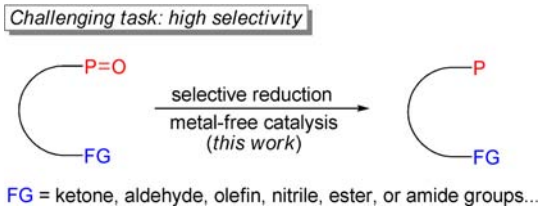


Figure 1. Chemoselective reduction of phosphine oxides.

RESULTS AND DISCUSSION

Recently, we and other groups have shown that catalytic hydrosilylations allow for distinctive chemoselectivity in the reduction of functionalized esters and amides.[9] Based on this work, we discovered a copper-catalyzed hydrosilylation of phosphine oxides and a hydrosilylation-phosphination sequence, too.[10a] While a variety of secondary and tertiary phosphine oxides can be reduced smoothly by this procedure, the preparation of chelating phosphines is more difficult due to the coordination of the product to the metal center.[10b] Interestingly, it is well-known that silanes can also be activated metal-free by applying Lewis acids or Lewis bases.[11] In addition, Brønsted acids were used to activate carbonyl groups and thereby promote the hydrosilylation of ketones and aldehydes.[12] On the other hand, phosphine oxides have been employed as Lewis base catalysts in various transformations.[13] In line with these ideas, herein we report the first metal-free reduction of phosphine oxides to phosphines under mild and convenient conditions. Remarkably, unique chemoselectivity is obtained in the presence of diaryl phosphoric acids as catalyst applying commercially available silanes as reductants.

At the start of our work, we studied the influence of different acids for reduction of triphenylphosphine oxide (**1a**) in the presence of diethoxymethylsilane as reducing agent. As expected, no reaction took place without catalyst (Table 1, entries 1, 16). By using 15 mol % of benzene sulfonic acid or benzoic acid, low yields of triphenylphosphine were obtained (Table 1, entries 5, 8). Surprisingly, the addition of diphenyl phosphoric acid **3a** resulted in 75% yield of PPh_3 (Table 1, entry 2). Using 4 equiv of silane at higher temperature increased the yield to 90% (Table 1, entries 9−10). In order to improve the reactivity of the reductant, different silanes were

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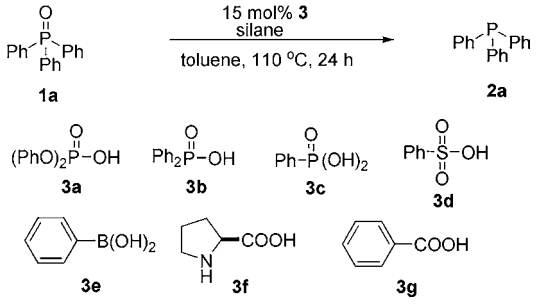
Table 1. Acid-Catalyzed Reduction of Phosphine Oxides[a]



entry	catalyst	silane (equiv.)	T (°C)	yield[b] (%)
1	-	$(EtO)_2MeSiH$ (3)	100	<1
2	**3a**	$(EtO)_2MeSiH$ (3)	100	75
3	**3b**	$(EtO)_2MeSiH$ (3)	100	21
4	**3c**	$(EtO)_2MeSiH$ (3)	100	9
5	**3d**	$(EtO)_2MeSiH$ (3)	100	7
6	**3e**	$(EtO)_2MeSiH$ (3)	100	<1
7	**3f**	$(EtO)_2MeSiH$ (3)	100	<1
8	**3g**	$(EtO)_2MeSiH$ (3)	100	6
9	**3a**	$(EtO)_2MeSiH$ (3)	110	85
10	**3a**	$(EtO)_2MeSiH$ (4)	110	90
11	**3a**	$(EtO)_2MeSiH$ (1)	110	29
12	**3a**	PMHS (4)	110	35
13	**3a**	TMDS (3)	110	62
14	**3a**	$PhSiH_3$ (3)	110	91
15	**3a**	Ph_2SiH_2 (3)	110	56
16	-	Ph_2SiH_2 (3)	110	<1
17[c]	**3a**	$(EtO)_2MeSiH$ (4)	110	35
18[d]	**3a**	$(EtO)_2MeSiH$ (4)	110	69
19[e]	**3a**	$(EtO)_2MeSiH$ (4)	110	91

[a]Reaction conditions: **1a** (0.25 mmol), **3** (0.0375 mmol), toluene (2.0 mL). [b]Determined by GC methods using *n*-hexadecane as an internal standard. [c]THF as the solvent in sealed tube. [d]1,4-Dioxane as the solvent in sealed tube. [e]Solvent: *n*-Bu_2O.

screened. However, the use of other silanes led to lower reactivity except for phenylsilane, which gave comparable 91% yield (Table 1, entries 12–15). The solvent effect reveals that less polar solvents are more suitable and the highest efficiency was obtained in dibutyl ether (35–91% yields, Table 1, entries 17–19).

The unexpected reactivity of the phosphoric acid derivative was mechanistically investigated by ^{31}P NMR. In the 1:1 mixture of $Ph_3P{=}O$ and acid **3a** (Figure 2A), 4 equiv of $(EtO)_2MeSiH$ were added followed by stirring at 95 °C. Immediately after heating, some gas is generated, which was characterized as H_2 by GC. After 6 h, the signals of phosphine oxide **1a** (30.2 ppm) and catalyst **3a** (−10.7 ppm) completely disappeared with the generation of two new signals at −4.8 and −22.0 ppm, respectively, which belong to PPh_3 and the silyl

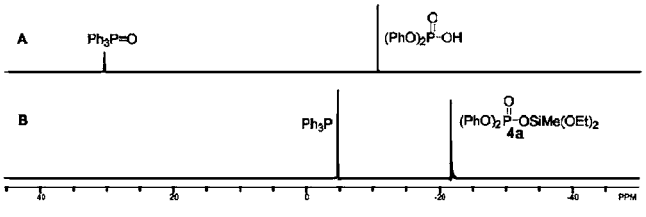
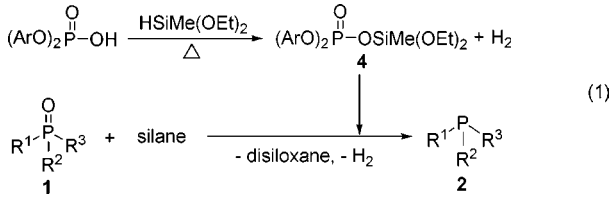


Figure 2. ^{31}P NMR spectra for reduction of **1a**.

ester **4a** (Figure 2B).[14a,b] In order to prove that **4a** is also an active catalyst for the reduction of phosphine oxides, we added to the reaction a mixture of $Ph_3P{=}O$ and $(EtO)_2MeSiH$ (1:2). After stirring at 95 °C for another 6 h, the reaction resulted in full conversion, and the same signals as in spectrum B were observed.

Additionally, the disiloxane $O[SiMe(OEt)_2]_2$ (formula weight = 282) was detected as the main byproduct of the reduction reactions by GC-MS measurements. Using 1 equiv of silane for the reduction of **1a**, only 28–30% of **2a** is obtained, which indicates that 2–3 Si–H are required for reduction of one P=O as the minimum. Performing catalytic experiments under similar conditions, only replacing the silane by H_2 (80 bar), gave no reduction even at elevated temperatures up to 180 °C. The addition of 15 mol % $(EtO)_2MeSiH$ in the presence of hydrogen also gave only trace amounts of the desired product.

Based on these experimental data and literature reports on the reduction of phosphine oxides and intramolecular Brønsted-acid-catalyzed domino deprotection–hydrosilylations of acetals,[6c,8b,f,12c] we propose that phosphoric silyl ester **4** is formed and acts as the major active species in reduction of phosphine oxides (eq 1).[14c] Concerted activation of both the

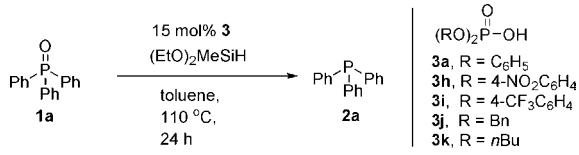


(1)

Lewis acidic silane and the Lewis basic phosphine oxide by bifunctional **4** facilitates the intramolecular deoxygenation to form the phosphine product, disiloxane and H_2.[14d,e] Finally, **4** is released for a new catalytic cycle.

Next, the electronic properties of the phosphate catalyst were varied. Hence, four additional phosphoric acid derivatives were tested under optimized conditions (Table 2). To our delight, a quantitative yield is obtained by using aryl esters substituted with electron-withdrawing groups such as NO_2 or CF_3 (Table 2, entries 2–3). On the other hand, the reactivity is strongly decreased applying alkyl or benzyl esters (low to 3% yield, Table 2, entries 4–5), probably due to the easier hydrolysis of

Table 2. Variation of Different Phosphoric Acid Esters for Reduction of 1a[a]



entry	catalyst (**3**)	yield (%)[b]
1	**3a**	90
2	**3h**	>99
3	**3i**	>99
4	**3j**	16
5	**3k**	3

[a]Reaction conditions: **1a** (0.25 mmol), silane (1.0 mmol), toluene (2.0 mL), 110 °C, 24 h. [b]Determined by GC methods using *n*-hexadecane as an internal standard.

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these esters. In this context, it should be noted that plain phosphoric acid does not promote the desired reduction.

To further understand the role of the phosphoric acid catalyst, kinetic measurements of the three most efficient acids were performed at 100 °C. As shown in Figure 3, the reduction

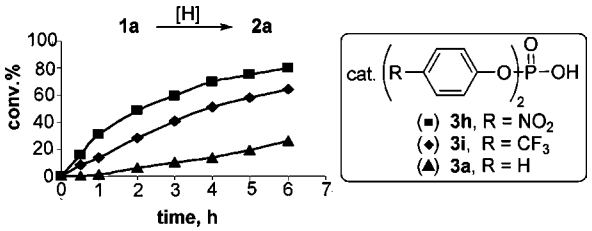


Figure 3. Kinetic study for different catalysts. Reaction conditions: **1a** (0.5 mmol), cat. (0.075 mmol), $(EtO)_2MeSiH$ (2 mmol), toluene (4.0 mL), 100 °C.

of triphenylphosphine oxide (**1a**) proceeds fastest in the presence of aryl phosphates with electron-withdrawing substituents. The best results were observed for the NO_2-substituted phosphate (**3h**) yielding 80% of triphenylphosphine (**2a**) after 6 h. In all three cases, the reaction rates are first-order with respect to the concentration of phosphine oxide ([**1a**]), and a linear relationship between $\ln[\mathbf{1a}]_t$ and reaction time (t/h) was obtained, which indicated an induction period not longer than one hour (Figure S1).[15a]

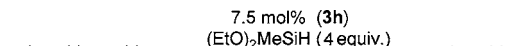
The observed rate (k_{obs}) for **3h**, **3i**, and **3a** was 2.6, 1.8, and 0.53 (10^{-1} h^{-1}), respectively. Apparently, stronger acidity of the Si atom in **4** favors the activation of the P═O bond during its reaction with the silane.[15a]

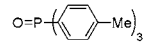
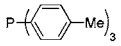
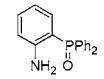
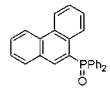
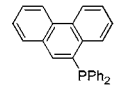
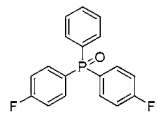
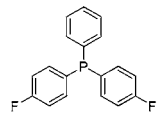
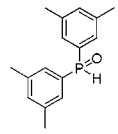
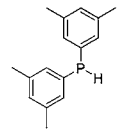
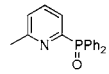
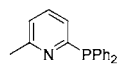
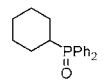
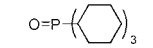
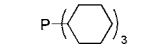
With good catalytic activity in hand, we explored the substrate scope using 7.5 mol % of **3h** as catalyst. As shown in Table 3, various aromatic, heteroaromatic, and aliphatic phosphine oxides were smoothly reduced to the corresponding phosphines with full conversion for most of the substrates. For both tertiary and secondary aromatic phosphine oxides, good reactivity were obtained with isolated yields of 72−87% (Table 3, entries 1−5).[15b] To our delight no negative influence was observed with a heterocyclic substrate (88% yield; Table 3, entry 6). Furthermore, reduction of more sensitive electron-rich alkyl-substituted phosphine oxides gave the products in good isolated yields (70−71%), despite some oxidation of the corresponding products during silica gel chromatography (Table 3, entries 7−8). Sterically hindered diadamantylphosphine oxide and tricyclohexylphosphine oxide can be reduced in excellent yields of 88−99% (Table 3, entries 9−10).

Clearly, most of the reductions shown in Table 3 can be performed with traditional organometallic hydrides or a mixture of $HSiCl_3/Et_3N$, too. However, for organometallic chemistry and catalysis all kinds of functionalized phosphines are important. Hence, the "real" value of a novel reduction protocol for phosphine oxides has to be demonstrated with more challenging substrates. Therefore, acid **3h** was used to catalyze the reduction of phosphine oxides containing other reducible functional groups (Table 4). Indeed, functionalized phosphine oxides were reduced to the corresponding phosphines in good to excellent yields (72−92%). Notably, ester, amide, nitrile, olefin, cyclopropyl and even ketone groups are well-tolerated with a selectivity for the PO bond >99:1!

Since no transition metal being involved, we were interested to test the reduction under air atmosphere. Indeed, the substrate was fully converted to the air-stable phosphine under

Table 3. Phosphoric Acid-Catalyzed Reduction of Phosphine Oxides to Phosphines



entry	1	2	yield (%)[a]
1			84
2			81
3			87
4			72
5[b]			80
6			88
7			71
8			70
9[b]	$O{=}P(Ad)_2H$	$P(Ad)_2H$	99
10[b]			88

[a]Isolated yields. [b]Yields determined by ^{31}P NMR analysis.

air atmosphere, which makes this method very convenient (92% yield, Table 4, entry 1). Using PMHS—one of the most inexpensive silanes—in the presence of 15 mol % **3h** allowed for smooth and selective reduction of a phosphine oxide even in the presence of an aldehyde group (82% yield, Table 4, entry 6). To the best of our knowledge, such selective reductions have not been described before. In fact, protection steps are generally needed for the selective reduction of functional groups in the presence of the more reactive aldehydes.[16]

Having demonstrated the successful reduction of various monophosphine oxides, we finally applied our methodology to the preparation of bisphosphines. As shown in Table 5, six different bisphosphines are obtained without further optimization in 62−96% isolated yields starting from bisphosphine mono- or dioxides. Notably, in the case of the chiral phosphines no racemization is observed. A significant advantage of this metal-free method toward organometallic catalysis is the avoidance of the somewhat problematic substrate/metal complexation.

■ SUMMARY

In conclusion, we have demonstrated here for the first time that organocatalytic reductions of phosphine oxides to phosphines are possible.[18,19] Using inexpensive hydrosilanes as the reductant notable features of this metal-free protocol are the broad functional group tolerance and the convenient, air-

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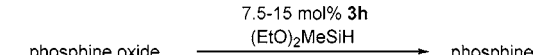
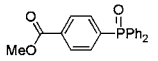
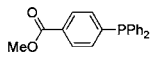
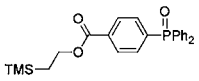
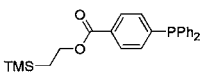
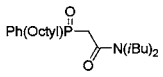
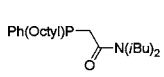
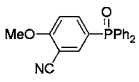
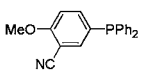
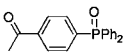
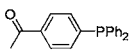
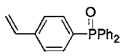
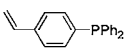
Table 4. Evaluation of the Chemoselectivity in Phosphoric Acid-Catalyzed Reduction of Phosphine Oxides to Phosphines[a]



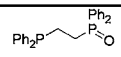
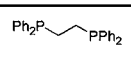
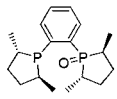
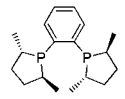
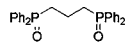
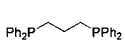
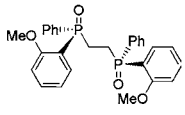
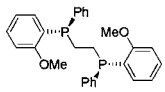
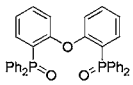
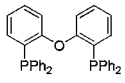
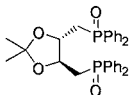
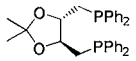
entry	1	2	yield (%)[b]
1[c]			92
2			73
3[d]			86
4			90
5			86
6[d,e]			82
7			89
8			72
9			92

[a]Reaction conditions: **1** (0.5−1.0 mmol), $(EtO)_2MeSiH$ (4 equiv), toluene (2.0−4.0 mL). [b]Isolated yields. [c]Reaction under air atmosphere. [d]Yields determined by ^{31}P NMR analysis. [e]PMHS (4 equiv) as the reductant.

insensitive, and safe reaction conditions. In general, good to very good yields were obtained for the reduction of 25 different aryl, alkyl mono-, and bidentate phosphine oxides. Importantly, excellent chemoselectivity was observed even in the presence of other reducible groups such as aldehyde, ketone, and olefin, which makes this methodology highly applicable for catalytic Wittig reaction, Appel reaction, and Staudinger reaction etc.[7b,20]

Experimental Section. General procedure for hydrosilylation: A 25 mL dried Schlenk tube containing a stirring bar was charged with **3h** (13.0 mg, 0.0375 mmol) and the corresponding phosphine oxide (0.5 mmol). Under Ar flow, dry toluene (2 mL) and $(EtO)_2MeSiH$ (320 μL, 2.0 mmol) were added, and the mixture was stirred at 110 °C for a certain time period. Then, the reaction mixture was cooled to 0 °C and 3N methanolic KOH (5 mL) was added slowly. After the mixture was stirred vigorously for 3 h at room temperature, water (3 mL) was added and the mixture was extracted by ethyl acetate. Then, the organic phase was washed by 1N HCl solution (aq., 5 mL) and saturated $NaHCO_3$ solution (aq., 5 mL). Finally, the organic phase was dried by Na_2SO_4 and concentrated under vacuum. The residue was purified by silica gel column chromatography.

Table 5. Preparation of Bisphosphines through Organo-Catalyzed Reduction of Phosphine Oxides[a]

entry	1	2	yield (%)[b]
1			96 (42)
2[c]			86 (96)
3			82 (25)
4			62 (trace)
5			73 (NR)
6			84 (trace)

[a]Reaction conditions: **1** (0.25−0.5 mmol), **3h** (15 mol % to P═O), $(EtO)_2MeSiH$ (4 equiv, compared to P═O), 110 °C, 8−48 h, toluene (2.0−6.0 mL). [b]Isolated yields, the yields in brackets were obtained by $Cu(OTf)_2$ catalysis (ref 17). [c]Yields determined by ^{31}P NMR analysis.

■ ASSOCIATED CONTENT

Supporting Information

Synthesis and spectroscopic data of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

Notes. The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) *Asymmetric Organocatalysis−From Concepts to Applications in Asymmetric synthesis*; Berkessel, A., Gröger, H., Ed.; Wiley-VCH: New York, 2005. (b) *Modern Reduction Method*; Andersson, P. G., Munslow, I. J., Ed.; Wiley-VCH: New York, 2008. (c) Petersson, M. J.; Loughlin, W. A.; Jenkins, I. D. *Chem. Commun.* **2008**, 4493. (d) Enthaler, S. *ChemCatChem* **2011**, *3*, 666.

(2) (a) *A Guide to Organophosphorus Chemistry*; Quin, L. D., Ed.; John Wiley & Sons: New York, 2000. (b) *Phosphorus Ligands in Asymmetric Catalysis−Synthesis and Application*; Börner, A., Ed.; Wiley-VCH: Weinheim, 2008.

(3) (a) Hartley, S. B.; Holmes, W. S.; Jacques, J. K.; Mole, M. F.; McCoubrey, J. C. *Quart. Rev.* **1963**, *17*, 204. (b) For electroreduction

of phosphine oxides, see: Kuroboshi, H.; Yano, T.; Kobayashi, K.; Kamenoue, S.; Akagi, T.; Tanaka, H. *Synthesis* **2011**, *24*, 4091.

(4) (a) Tang, W.; Zhang, X. *Chem. Rev.* **2003**, *103*, 3029. (b) Crepy, K. V. L; Imamoto, T. *Top. Curr. Chem.* **2003**, 1−40. (c) Ye, L.; Zhou, J.; Tang, Y. *Chem. Soc. Rev.* **2008**, *37*, 1140. (d) Ding, K.; Han, Z.; Wang, Z. *Chem. Asian J.* **2009**, *4*, 32. (e) Wang, X.; Meng, F.; Wang, Y.; Han, Z.; Chen, Y.-J.; Liu, L.; Wang, Z.; Ding, K. *Angew. Chem., Int. Ed.* **2012**, *51*, 9276.

(5) For the use of metal hydride reducing agents, see: (a) Henson, P. D.; Naumann, K.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 5645. (b) Kobayashi, S.; Suzuki, M.; Saegusa, T. *Polym. Bull.* **1982**, *8*, 417. (c) Imamoto, T.; Takeyama, T.; Kusumoto, T. *Chem. Lett.* **1985**, 1491. (d) Imamoto, T.; Oshiki, T.; Onozawa, T.; Kusumoto, T.; Sato, K. *J. Am. Chem. Soc.* **1990**, *112*, 5244. (e) Imamoto, T.; Kikuchi, S.; Miura, T.; Wada, Y. *Org. Lett.* **2001**, *3*, 87. (f) Stankevic, M.; Pietrusiewicz, K. M. *Synlett* **2003**, 1012. (g) Hiney, R. M.; Higham, L. J.; Muller-Bunz, H.; Gilheany, D. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 7248. (h) Busacca, C. A.; Raju, R.; Grinberg, N.; Haddad, N.; James-Jones, P.; Lee, H.; Lorenz, J. C.; Saha, A.; Senanayake, C. H. *J. Org. Chem.* **2008**, *73*, 1524. (i) Rajendran., K. V.; Gilheany, D. G. *Chem. Commun.* **2012**, *48*, 817.

(6) (a) Horner, L.; Balzer, W. D. *Tetrahedron Lett.* **1965**, *6*, 1157. (b) Cremer, S. E.; Chorvat, R. J. *J. Org. Chem.* **1967**, *32*, 4066. (c) Naumann, K.; Zon, G.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 7012. (d) Marsi, K. L. *J. Org. Chem.* **1974**, *39*, 265. (e) Mckinstry, L.; Livinghouse, T. *Tetrahedron* **1994**, *50*, 6145. (f) Takaya, H.; Akutagawa, S.; Noyori, R. *Org. Synth. VIII* **1993**, 65. (g) Wu, H. C.; Yu, J. Q.; Spencer, J. B. *Org. Lett.* **2004**, *6*, 4675. (h) Berthod, M.; Mignani, G.; Lemaire, M. *Tetrahedron: Asymmetry* **2004**, *15*, 1121. (i) Berthod, M.; Saluzzo, C.; Mignani, G.; Lemaire, M. *Tetrahedron: Asymmetry* **2004**, *15*, 639. (j) A recently reported $InBr_3$/silane system: Pehlivan, L.; Métay, E.; Delbrayelle, D.; Mignani, G.; Lemaire, M. *Tetrahedron* **2012**, *68*, 3151.

(7) (a) Damian, K.; Clarke, M. L.; Cobley, C. J. *J. Mol. Catal., A* **2008**, *284*, 46. (b) O'Brien, C. J.; Tellez, J. L.; Nixon, Z. S.; Kang, L. J.; Carter, A. L.; Kunkel, S. R.; Przeworski, K. C.; Chass, G. A. *Angew. Chem., Int. Ed.* **2009**, *48*, 6836.

(8) (a) Berk, S. C.; Buchwald, S. L. *J. Org. Chem.* **1992**, *57*, 3751. (b) Coumbe, T.; Lawrence, N. J.; Muhammad, F. *Tetrahedron Lett.* **1994**, *35*, 625. (c) Lawrence, N. J.; Drew, M. D.; Bushell, S. M. *J. Chem. Soc. Perkin Trans. 1* **1999**, 3381. (d) Allen, A., Jr.; Ma, L.; Lin, W. *Tetrahedron Lett.* **2002**, *43*, 3707. (e) Berthod, M.; Favre-Réguillon, A.; Mohamad, J.; Mignani, G.; Docherty, G.; Lemaire, M. *Synlett* **2007**, 1545. (f) Petit, C.; Favre-Réguillon, A.; Albela, B.; Bonneviot, L.; Mignani, G.; Lemaire, M. *Organometallics* **2009**, *28*, 6379. (g) Petit, C.; Favre-Réguillon, A.; Mignani, G.; Lemaire, M. *Green Chem.* **2010**, *12*, 326.

(9) (a) Matsubara, K.; Iura, T.; Maki, T.; Nagashima, H. *J. Org. Chem.* **2002**, *67*, 4985. (b) Zhou, S.; Junge, K.; Addis, D.; Das, S.; Beller, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 9507. (c) Sunada, Y.; Kawakami, H.; Imaoka, T.; Motoyama, Y.; Nagashima, H. *Angew. Chem., Int. Ed.* **2009**, *48*, 9511. (d) Das, S.; Zhou, S.; Addis, D.; Junge, K.; Enthaler, S.; Beller, M. *Top. Catal.* **2010**, *53*, 979. (e) Das, S.; Addis, D.; Zhou, S.; Junge, K.; Beller, M. *J. Am. Chem. Soc.* **2010**, *132*, 1770. (f) Addis, D.; Das, S.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 6004. (g) Das, S.; Möller, K.; Junge, K.; Beller, M. *Chem.—Eur. J.* **2011**, *17*, 7414. (h) Das, S.; Addis, D.; Knöpke, L. R.; Bentrup, U.; Brückner, A.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 9180. (i) Das, S.; Addis, D.; Junge, K.; Beller, M. *Chem.—Eur. J.* **2011**, *43*, 12186.

(10) (a) Li, Y.; Das, S.; Zhou, S.; Junge, K.; Beller, M. *J. Am. Chem. Soc.* **2012**, *134*, 9727. (b) If bisphosphine oxides were the substrates in $Cu(OTf)_2$/TMDS system, the colour of reaction solution became dark brown in stead of being colourless for monophosphine oxides (also see the results in Table 5).

(11) For activation of silanes by Lewis bases or acids, see: (a) Parks, D. J.; Blachwell, J. M.; Piers, W. E. *J. Org. Chem.* **2000**, *65*, 3090. (b) Malkov, A. V.; Liddon, A. J. P. S.; Ramírez-López, P.; Bendova, L.; Haigh, D.; Kočovský, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 1432. (c) Tan, M.; Zhang, Y.; Ying, J. Y. *Adv. Synth. Catal.* **2009**, *351*, 1390. (d) Rendler, S.; Oestreich, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 5997.

(12) (a) Doyle, M. P.; DeBruyn, D. J.; Kooistra, D. A. *J. Am. Chem. Soc.* **1972**, *94*, 3659. (b) West, C. T.; Donnelly, S. J.; Kooistra, D. A.; Doyle, M. P. *J. Org. Chem.* **1973**, *38*, 2675. (c) Gellert, B. A.; Kahlcke, N.; Feurer, M.; Roth, S. *Chem.—Eur. J.* **2011**, *17*, 12203. (d) Chem, X.; Deng, Y.; Jiang, K.; Lai, G.; Ni, Y.; Yang, K.; Jiang, J.; Xu, L. *Eur. J. Org. Chem.* **2011**, 1736.

(13) For use of phosphine oxide as organocatalysts, see: (a) Ogawa, C.; Konishi, H.; Sugiura, M.; Kobayashi, S. *Org. Biomol. Chem.* **2004**, *2*, 446. (b) Kobayashi, S.; Sugiura, M.; Ogawa, C. *Adv. Synth. Catal.* **2004**, *346*, 1023. (c) Kotani, S.; Shimoda, Y.; Suguiura, M.; Nakajima, M. *Tetrahedron Lett.* **2009**, *50*, 4602. (d) Benaglia, M.; Rossi, S. *Org. Biomol. Chem.* **2010**, *8*, 3824.

(14) (a) Similarly to the structure of **4a**, chemical shift for $(PhO)_2P(O)(OTMS)$ in ^{31}P NMR is assigned as −20.8 ppm, see: Chojnowski, J.; Cypryk, M.; Michalski, J.; Woźniak, L. *J. Organomet. Chem.* **1985**, *288*, 275. (b) EI-MS (**4a**): m/z = 382 (M^+; 70 eV; 40%), 367 (8%), 337 (100%), 309 (32%), 291 (26%), 277 (11%), 261 (44%), 233 (31%), 215 (61%), 201 (9%), 170 (8%), 151 (9%), 123 (15%), 105 (3%), 91 (4%), 77 (26%), 51 (4%). Intermediate **4a** is sensitive to moisture and temperature. Although many attempts were carried out to isolate **4a** by silica gel chromatography and high-vacuum distillation under Ar, color change was always observed and $(EtO)_3SiMe$ was the major compound obtained through decomposition of **4a**. (c) The formation of phosphoric silyl esters from phosphoric acids and hydrosilanes is supported by the formation of silyl ethers from alcohols and hydrosilanes in the presence of Lewis aicds, see: Sridhar, M.; Raveendra, J.; Ramanaiah, B. C.; Narsaiah, C. *Tetrahedron Lett.* **2011**, *52*, 5980. (d) Both Lewis basic 'P═O' and Lewis acidic 'Si' sites in intermediates **4** are believed to be the key for its unique reactivity for reduction of phosphine oxides compared to other acids. (e) For silyl esters, such as TMSOTf as Lewis acid catalyst, see: Vorbrüggen, H.; Krolikiewicz, K.; Bennua, B. *Chem. Ber.* **1981**, *114*, 1234.

(15) (a) For details, see the Supporting Information. (b) Under the same conditions, no reactivity was observed for reduction of [4-(N,N-dimethylamino)phenyl]diphenylphosphine oxide.

(16) For selective reduction of ketones and esters in the presence of aldehydes, see: Bastug, G.; Dierick, S.; Lebreux, F.; Markó, I. E. *Org. Lett.* **2012**, *14*, 1306.

(17) Conditions for $Cu(OTf)_2$ catalyzed reduction of phosphine oxide: 0.25 mol of the substrate, 10 mol % of $Cu(OTf)_2$ and 300 mol % of tertramethyldisiloxane (TMDS) compared to each P═O, 100 °C, 24 h, toluene (2−6 mL).

(18) (a) Performing a Scifinder search using the key words "phosphine oxide reduction" gave about 250 publications since year 2000 which demonstrates the general interest in this area.

(19) For the use of phosphines with reducible groups, such as ketone, aldehyde, imine, olefin groups, see: (a) Mikami, K.; Wakabayashi, K.; Aikawa, K. *Org. Lett.* **2006**, *8*, 1517. (b) Jing, Q.; Sandoval, C. A.; Yamaguchi, Y.; Kato, K.; Ding, K. *Chin. J. Chem.* **2007**, *25*, 1163. (c) Yeh, W.-Y.; Lin, C.-S. *Organometallics* **2004**, *23*, 917. (d) Garralda, M. A.; Hernández, R.; Ibarlucea, L.; Pinilla, E.; Torres, M. R.; Zarandona, M. *Organometallics* **2007**, *26*, 1031. (e) Guan, Z.; Marshall, W. J. *Organometallics* **2002**, *21*, 3580. (f) Sun, Y.-W.; Jiang, J.-J.; Zhao, M.-X.; Wang, F.-J.; Shi, M. *J. Organomet. Chem.* **2011**, 2850. (g) Shintani, R.; Duan, W.; Nagano, T.; Okada, A.; Hayashi, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 4611. (h) Douglas, T. M.; Le Nôtre, J.; Brayshaw, S. K.; Frost, C. G.; Weller, A. S. *Chem. Commun.* **2006**, 3408.

(20) (a) van Kalkeren, H. A.; Leenders, S. H. A. M.; Hommersom, C. R. A.; Rutjes, F. P. J. T.; van Delft, F. L. *Chem.—Eur. J.* **2011**, *17*, 11290. (b) van Kalkeren, H. A.; Bruins, J. J.; Rutjes, F. P. J. T.; van Delft, F. L. *Adv. Synth. Catal.* **2012**, *354*, 1417.