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General and Selective Copper-Catalyzed Reduction of Tertiary and Secondary Phosphine Oxides: Convenient Synthesis of Phosphines

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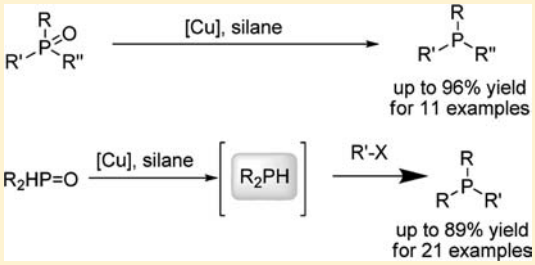
Supporting Information

ABSTRACT: Novel catalytic reductions of tertiary and secondary phosphine oxides to phosphines have been developed. Using tetramethyldisiloxane (TMDS) as a mild reducing agent in the presence of copper complexes, PO bonds are selectively reduced in the presence of other reducible functional groups (FGs) such as ketones, esters, and olefins. Based on this transformation, an efficient one pot reduction/phosphination domino sequence allows for the synthesis of a variety of functionalized aromatic and aliphatic phosphines in good yields.



INTRODUCTION

Phosphines and their derivatives represent an important class of compounds for life sciences and the chemical industry.[1] In general, trivalent phosphines are used in numerous classic organic transformations, such as the Mitsunobu reaction, the Wittig reaction, the Rauhut−Currier reaction, the Appel reaction, and so on. Furthermore, in organometallic chemistry they represent prime ligands to control most transition metal catalyzed reactions due to their excellent metal ligation properties.[2,3] Selected examples of ligands which are or have been applied on an industrial scale in homogeneous catalysis are shown in Figure 1.

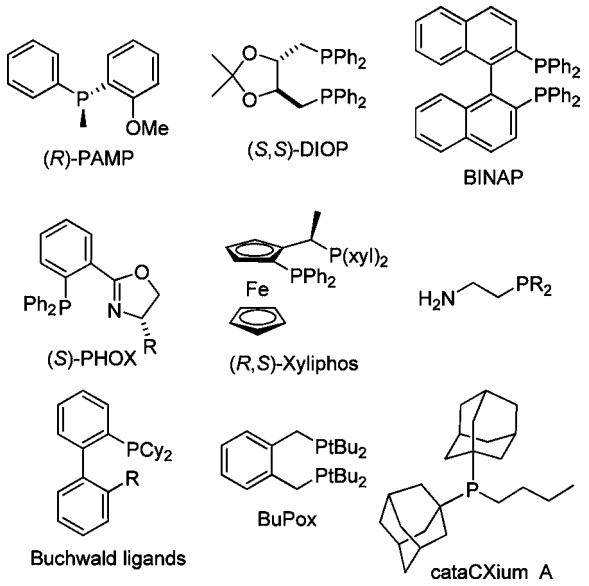


Figure 1. Selected important phosphine ligands for industrially relevant homogeneous catalysis.

Currently, three major methods are used for the synthesis of phosphines: (1) substitution reactions of carbon nucleophiles with P−Cl derivatives or of carbon electrophiles with alkali metal phosphides;[4] (2) phosphination of alkenes, alkynes, or aromatic halids;[5,6] and (3) reduction of phosphine oxides.[7−9] Among these procedures, advantageously the latter strategy makes use of easily available and air-stable substrates. Moreover, phosphine oxides are generated as side products in several industrial reactions. Unfortunately, the known reductions of phosphine oxides make use of an excess of sensitive and/or highly expensive reducing agents, e.g. $LiAlH_4$, DIBAL-H or $HSiCl_3/Et_3N$, and $HSiCl_3/PhSiH_3$. Due to the harsh reaction conditions only poor functional group tolerance is achieved.[7,8]

In order to overcome these limitations, we had the idea to develop a catalytic procedure which should proceed under milder conditions compared to the above-mentioned stoichiometric processes. Furthermore, based on the catalyst it should be possible to tune the selectivity of the reaction. Recently, we[10] and others[11] have demonstrated that catalytic hydrosilylation constitutes a viable option for the reduction of challenging substrates including carboxylic derivatives with excellent chemoselectivity. Surprisingly until today, there is only one method known for the catalytic hydrosilylation of phosphine oxides which used a combination of $Ti(O\text{-}i\text{-}Pr)_4$/silane.[12] This system developed by the Buchwald and Lawrence groups has showed broad substrate scope and air stability except for functional group intolerance toward ketones and esters.

RESULTS AND DISCUSSION

1. Copper-Catalyzed Hydrosilylation of Phosphine Oxides. Copper complexes have been shown to be active

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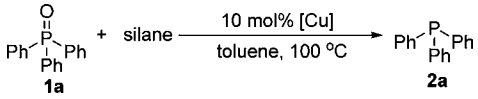
catalysts for the hydrosilylation of olefins,[13] ketones,[14] imines,[15] and more recently also amides.[16] Based on this work and our developments of chemoselective reductions of carboxylic acid derivatives,[10] we became interested in applying copper to the catalytic reduction of phosphine oxides to phosphines. At the start of our investigations, we studied the reduction of uncomplicated triphenylphosphine oxide as a model system. Here, variations of critical reaction parameters were performed applying different copper salts and silanes. In Table 1 selected results are shown.

Table 1. Copper-Catalyzed Reduction of Triphenylphosphine Oxide 1a[a]



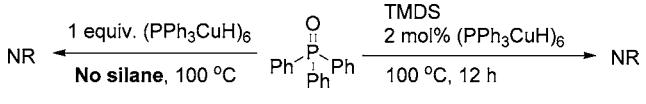
entry	[Cu] (mol %)	silane (equiv)	t (h)	yield (%)[b]
1	–	PMHS (12)	2	NR
2	–	TMDS (12)	2	<1
3	$Cu(OTf)_2$ (5)	PMHS (6)	15	28
4	CuF_2 (5)	PMHS (6)	15	<1
5	$CuCl_2$ (5)	PMHS (6)	15	8
6	$CuBr_2$ (5)	PMHS (6)	15	9
7	CuI (5)	PMHS (6)	15	<1
8	$Cu(OTf)_2$ (10)	PMHS (6)	15	88
9	$Cu(OTf)_2$ (10)	TMDS (3)	15	96
10	$Cu(OTf)_2$ (10)	Ph_2MeSiH (6)	15	NR

[a]Reaction conditions: 0.5 mmol of **1a**, 2 mL of toluene. [b]Determined by GC using *n*-hexadecane as an internal standard.

Even using a large excess of less expensive silanes such as polymethylhydrosiloxane (PMHS) and TMDS as a reductant without a catalyst, basically no product was observed (Table 1, entries 1–2). However, addition of 5 mol % of $Cu(OTf)_2$ in the presence of PMHS afforded the desired triphenylphosphine in 28% yield (Table 1, entry 3). Increasing the catalyst loading to 10 mol % of $Cu(OTf)_2$ led to good to excellent yields (88–96%) of triphenylphosphine (Table 1, entries 8–9). Finally, the best yield was obtained using 3 equiv of TMDS. Notably, under the same conditions, no reaction was observed with Ph_2MeSiH as the reductant (Table 1, entry 10).

In order to understand the origin of the activity of the catalyst system, also stoichiometric experiments with defined copper complexes were performed. However, when $(PPh_3CuH)_6$ (Stryker's reagent) was reacted with 1 equiv of **1a**, no reaction was observed (Scheme 1). This is in agreement

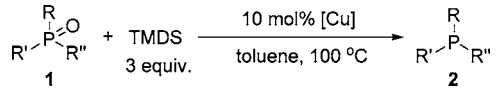
Scheme 1. Reduction with Stryker's Reagent

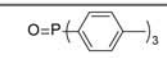
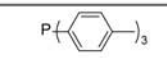
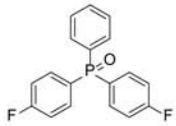
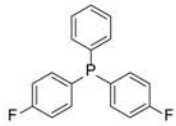
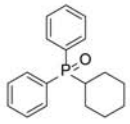
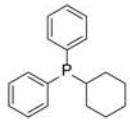
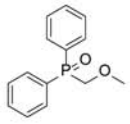
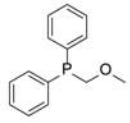
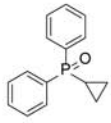
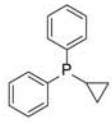
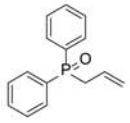
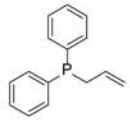
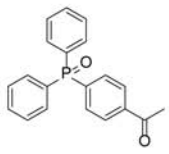
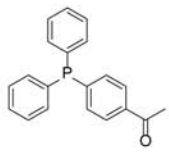
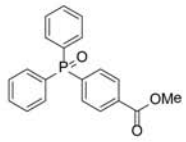
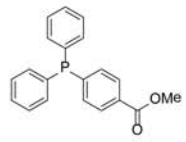
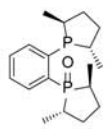
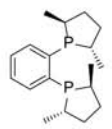
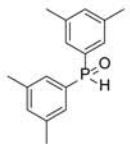
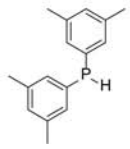


with a recent report which showed that [CuH] is not the active species for hydrosilylation of ketones.[18] Similarly, using a catalyst loading of 2 mol % of $(PPh_3CuH)_6$ no reaction was observed under optimized conditions.

Next, the reduction of several different phosphine oxides was studied (Table 2). As shown in Table 2, good to very good yields were achieved for substrates with electron-donating and -withdrawing groups (77–89%; Table 2, entries 1–4). In addition to arylphosphine oxides, also trioctylphosphine oxide was smoothly reduced albeit with a higher catalyst loading (Table 2, entry 5).[19a] Notably, good yields were obtained in the presence of other reducible groups (68–82%; Table 2, entries 6–9). Hence, cyclopropyl-, alkenyl-, ester-, and even ketone-functionalized phosphine oxides were selectively reduced. With respect to asymmetric catalysis it is interesting that bidentate

Table 2. Reduction of Phosphine Oxides[a]



entry	1	2	yield (%)[b]
1			89
2			85
3			86
4			77
5[c,d]	$O=P(Octyl)_3$	$P(Octyl)_3$	70
6			82
7			81
8			68
9			72
10[c]			96
11[c]			82

[a]Reaction conditions: 0.2–0.5 mmol of substrate, 0.6–1.5 mmol of silane, 2 mL of toluene, 10–24 h. [b]Isolated yield. [c]Determined by ^{31}P NMR analysis. [d]20 mol % $Cu(OTf)_2$ was used.

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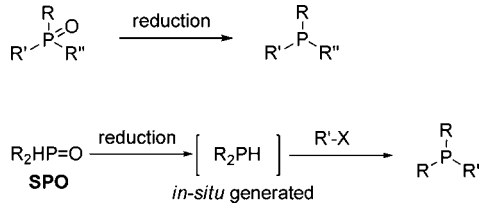
chelating phosphine oxides are reduced in a straightforward manner, too. For example, (*S*,*S*)-Duphos was obtained in excellent yield (96%; Table 2, entry 10).

After the successful copper-catalyzed reduction of a variety of aryl, alkyl, and chelating tertiary phosphine oxides, we asked ourselves whether it would be possible to also reduce secondary phosphine oxides (SPOs). Notably, these substrates have been only scarcely investigated to date. Nevertheless, bis(3,5-dimethylphenyl)phosphine oxide was efficiently reduced with a yield of 82% (Table 2, entry 11).

2. Copper-Catalyzed Domino Reductive Arylation/Alkylation of Secondary Phosphine Oxides. Having a suitable method for the selective reduction of secondary phosphine oxides in hand, we became interested in combining our reduction protocol with subsequent phosphination reactions of the *in situ* generated secondary phosphines with aryl or vinyl halides.[6] In principle, such a domino sequence would allow for the efficient and convergent synthesis of a variety of functionalized phosphines. Ideally, in this approach only one catalyst should be used. To the best of our knowledge such a concept has not been described yet. Notably, as shown in Scheme 2, this reaction sequence also avoids the stoichiometric use of sensitive and toxic secondary phosphines.

Scheme 2. Cu-Catalyzed Reduction of Tertiary Phosphine Oxides and Cu-Catalyzed Reductive Coupling of Secondary Phosphine Oxides with Aryl Halides



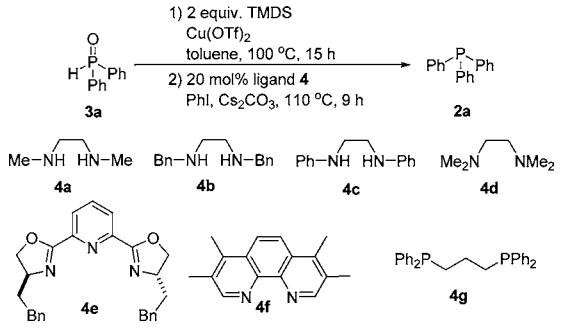
Our initial efforts to find a suitable copper-based system focused on the hydrosilylation of diphenylphosphine oxide (**3a**) in the presence of different precatalysts and silanes (Table S1).[17] Again, in the absence of any catalyst, only a trace amount of diphenylphosphine was formed at high temperature. Though copper halides also catalyzed the reaction with good yields (63–93%; Table S1, entries 5–6), full conversion is only observed for $Cu(OTf)_2$ with TMDS or PMHS as the reductant (Table S1, entries 3–4). With good catalytic activity for the hydrosilylation of **3a** in hand, we explored the possibility of trapping the *in situ* generated secondary phosphine by sequential addition of phenyl iodide.

As shown in Table 3, the use of TMDS and $Cu(OTf)_2$ did not inhibit the subsequent coupling reaction using CuI/*N*,*N*′-dimethylethylenediamine (**4a**) as the catalyst (Table 3, entries 1–2). To our delight, the overall reaction sequence still preceded smoothly giving triphenylphosphine **2a** in 79% yield without the addition of a second Cu source for the coupling step (Table 3, entry 3)!

Further prolongation of reaction time for the second step to 12 h gave a higher yield which implies that the catalyst active in the reduction step exists for the whole procedure (Table 3, entry 4).

Next, the influence of different nitrogen ligands **4b–g** on the arylation step was tested. Compared to **4a**, all other ligands gave lower yields for the desired product (Table 3, entries 8–13). It should be noted that the use of PMHS as the reductant

Table 3. Copper-Catalyzed Domino Reduction–Phosphination Reaction Sequence: Optimization of Reaction Conditions[a]



	[Cu] (mol %)			
entry	1st step	2nd step	**4**	yield (%)[b]
1	$Cu(OTf)_2$ (10)	CuI (5)	–	46
2	$Cu(OTf)_2$ (10)	CuI (5)	**4a**	87
3	$Cu(OTf)_2$ (10)	–	**4a**	79
4[c]	$Cu(OTf)_2$ (10)	–	**4a**	83
5	$Cu(OTf)_2$ (15)	–	**4a**	85
6	$Cu(OTf)_2$ (5)	–	**4a**	62
7	$Cu(OTf)_2$ (2.5)	–	**4a**	32
8	$Cu(OTf)_2$ (10)	–	**4b**	35
9	$Cu(OTf)_2$ (10)	–	**4c**	47
10	$Cu(OTf)_2$ (10)	–	**4d**	49
11	$Cu(OTf)_2$ (10)	–	**4e**	45
12	$Cu(OTf)_2$ (10)	–	**4f**	61
13	$Cu(OTf)_2$ (10)	–	**4g**	22
14[d]	$Cu(OTf)_2$ (10)	–	**4a**	23
15[e]	$Cu(OTf)_2$ (10)	–	**4a**	68
16[f]	$Cu(OTf)_2$ (10)	–	**4a**	69

[a]Reaction conditions: 0.25 mmol of **3a**, 0.25 mmol of phenyl iodide, 0.5 mmol of Cs_2CO_3, 2 mL of toluene. [b]Determined by GC method using *n*-hexadecane as an internal standard. [c]12 h for 2nd step. [d]1.0 mmol of PMHS used as reductant. [e]0.5 mmol of K_2CO_3 used as base. [f]0.5 mmol of K_3PO_4 used as base.

or the use of K_2CO_3 or K_3PO_4 as the base lowered the efficiency (Table 3, entries 14–16).

After successful demonstration of our concept in a model reaction, we were interested in exploring the generality of this novel domino reduction–phosphination sequence. As shown in Table 4, a broad tolerance for several functional groups is observed. Thus, the reduction and subsequent coupling can be performed in the presence of amino, ether, and halide substituents. Furthermore, electron-donating and -withdrawing substituents on the aromatic rings of the aryl iodide are well tolerated except for the nitro-substituted arene (58–83% yield; Table 4, entries 1–9). Gratifyingly, sterically hindered and heteroaromatic aryl halides as well as vinyl iodides gave the corresponding phosphines in moderate to excellent yields (Table 4, entries 8, 10–12).[19b]

Due to the importance of alkyl-substituted phosphines in organometallic catalysis, alkylphosphine oxides were investigated as substrates, too. By application of the sterically hindered di-*tert*-butylphosphine oxide, phenyl-di-*tert*-butylphosphine was obtained in 56% yield (Table 4, entry 13). Notably, in a previous report the coupling reaction of aryl iodides with isolated *tert*-Bu_2PH did not work at all,[6a] which means that the slight excess of silane may play a positive role in the second coupling reaction in our work. On the other hand, the

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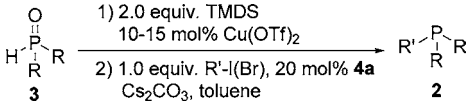
Table 4. Copper-Catalyzed Domino Reduction–Phosphination Reaction Sequence: Substrate Scope and Limitations[a]



entry	R	R' X	2	yield (%)[b]
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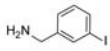
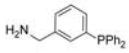
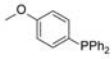
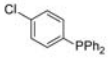
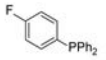
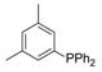
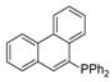
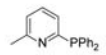
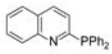
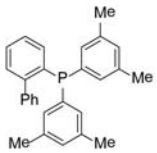
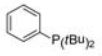
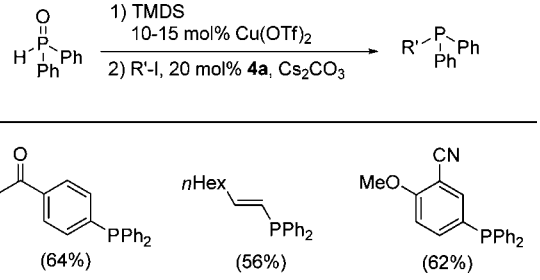
2	Ph			71
3	Ph			58
4	Ph			79
5	Ph			77
6	Ph			79
7	Ph			83
8	Ph			73
9	Ph			77
10	Ph			89
11	Ph			82
12	3,5-Xylyl			83
13[c]	*t*Bu			56
14[c]	Et			70

[a]Reaction conditions: 0.25–0.5 mmol of substrate, 0.5–1.0 mmol of Cs_2CO_3, 2 mL of toluene; 100 °C and 10–24 h for the 1st step, 110 °C and 7–48 h for the 2nd step. [b]Isolated yield. [c]Yield determined by ^{31}P NMR analysis.

corresponding diethylphenylphosphine was attained in 70% overall yield (Table 4, entry 14) without further optimization. For lower chain alkyl phosphines such as the latter diethyl-substituted phosphine the advantages of our protocol compared to previously known methods are obvious: The direct use and/or the protection of an extremely sensitive dialkylphosphine are avoided.[20] Here, no special handling and precautions are needed. It should be noted that this methodology could also be applied for reactions which involve primary phosphines.[21]

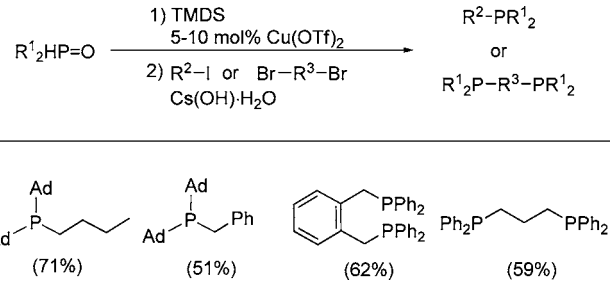
Advantageously, substrates with other reducible functional groups, such as olefin, nitrile, and even ketone, are successfully transformed to the corresponding phosphines, too. Especially, tolerance of the carbonyl group makes this methodology interesting, as the corresponding phosphine can be easily derivatized further on (Scheme 3). It should be noted that no other known reduction protocol of phosphine oxides shows similar chemoselectivity!

Scheme 3. Chemoselective Domino Synthesis of Phosphines (Yields Are Given in Brackets)



Encouraged by all these results, finally we studied the extension of our sequential method toward the use of ubiquitous available alkyl halides (Scheme 4). In this case the

Scheme 4. Domino Synthesis of Alkyl-Substituted Phosphines (Yields Are Given in Brackets)



second phosphination step should occur under basic conditions and may lead to trialkylphosphines or mixed alkylarylphosphines. Indeed, after *in situ* generation of di-1-adamantylphosphine or diphenylphosphine, these secondary phosphines are efficiently deprotonated by an excess of base and successfully coupled with four different alkyl halides. As shown in Scheme 4, not only mono- but also chelating bisphosphines are obtained with good to excellent yields (51–71%).

SUMMARY

In summary, we have demonstrated for the first time that copper-catalyzed reduction of secondary and tertiary phosphine oxides using inexpensive TMDS as a reductant is possible. Combining this novel reduction with a subsequent copper-catalyzed phosphination reaction allows the synthesis of triaryl-, alkyldiaryl-, aryldialkyl-, and trialkylphosphines to be possible in good yields. Furthermore, chelating phosphines can be prepared in a straightforward manner. Notable features of our methodology and its application to domino phosphination are the functional group tolerance and the convenient reaction conditions.

EXPERIMENTAL SECTION

General procedure for hydrosilylation–phosphination reaction: A 10-mL dried Schlenk tube containing a stirring bar was charged with $Cu(OTf)_2$ (13.5 mg, 0.0375 mmol) and the corresponding secondary phosphine oxide (0.25 mmol). Under Ar flow dry toluene (2 mL) and TMDS (90 μL, 0.5 mmol) were added, and the mixture was stirred at

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100 °C for 10 h. Then, the reaction mixture was cooled to room temperature and *N,N′*-dimethylethylenediamine (5.2 μL, 0.05 mmol), Cs_2CO_3 (164 mg, 0.5 mmol), and the respective halide compound (0.25 mmol) were added under Ar flow. The suspension was allowed to heat to 110 °C and stirred overnight. Then, the reaction mixture was cooled to 0 °C and 3 N methanolic KOH was added slowly. After the mixture was stirred vigorously for 5 h at room temperature, water (3 mL) was added and the mixture was extracted with ethyl acetate which was washed by 1 N HCl solution (aq., 5 mL) and saturated $NaHCO_3$ solution (aq., 5 mL). Then, the organic phase was dried by Na_2SO_4 and concentrated under vacuum. The residue was purified by silica gel column chromatography.

(2,6-Dimethylphenyl)diphenylphosphine.[6b] Yield: 73%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34−7.09 (m, 11 H), 6.97 (dd, J_1 = 2.70 Hz; J_2 = 7.5 Hz, 2 H), 2.12 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.6 (d, *J* = 15.9 Hz), 136.4 (d, *J* = 14.0 Hz), 131.8, 131.6, 130.2, 128.1, 128.5, 127.7, 23.9 (d, *J* = 18.1 Hz); ^{31}P NMR (121 MHz, $CDCl_3$): δ −14.9; MS (EI): *m*/*z* 290.

■ 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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Author Contributions

†Y.L. and S.D. contributed equally.

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) *A Guide to Organophosphorus Chemistry*; Quin, L. D., Ed.; John Wiely & Sons: New York, 2000.

(2) (a) *Phosphorus Ligands in Asymmetric Catalysis−Synthesis and Application*; Börner, A., Ed.; Wiley-VCH: Weinheim, 2008. (b) Tang, W.; Zhang, X. *Chem. Rev.* **2003**, *103*, 3029. (c) Crepy, K. V. L; Imamoto, T. *Top. Curr. Chem.* **2003**, 1−40.

(3) For the use of phosphines in organocatalysis, see: (a) Ye, L.; Zhou, J.; Tang, Y. *Chem. Soc. Rev.* **2008**, *37*, 1140. (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.

(4) For selected examples, see: (a) Zapf, A.; Ehrentraut, A.; Beller, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 4153. (b) Ehrentraut, A.; Zapf, A.; Beller, M. *J. Mol. Catal. A: Chem.* **2002**, 515. (c) Junge, K.; Oehme, G.; Monsees, A.; Riermeier, T.; Dingerdissen, U.; Beller, M. *Tetrahedron Lett.* **2002**, *43*, 4977. (d) Honaker, M. T.; Sandefur, B. J.; Hargett, J. L.; McDaniel, A. L.; Salvatore, R. N. *Tetrahedron. Lett.* **2003**, *44*, 8373. (e) Korff, C.; Helmchen, G. *Chem. Commun.* **2004**, 530. (f) Rataboul, F.; Zapf, A.; Jackstell, R.; Harkal, S.; Riermeier, T.; Monsees, A.; Dingerdissen, U.; Beller, M. *Chem.—Eur. J.* **2004**, *10*, 2983. (g) Junge, K.; Hagemann, B.; Enthaler, S; Spannenberg, A.; Michalik, M.; Oehme, G.; Monsees, A.; Riermeier, T.; Beller, M. *Tetrahedron: Asymmetry* **2004**, *15*, 2621. (h) Zapf, A.; Jackstell, R.; Rataboul, F.; Riermeier, T.; Monsees, A.; Fuhrmann, C.; Shaikh, N.; Dingerdissen, U.; Beller, M. *Chem. Commun.* **2004**, 38. (i) Hagemann, B.; Junge, K.; Enthaler, S.; Michalik, M.; Riermeier, T.; Monsees, A.; Beller, M. *Adv. Synth. Catal.* **2005**, *347*, 1978. (j) Harkal, S.; Kumar, K.; Michalik, D.; Zapf, A.; Jackstell, R.; Rataboul, F.; Riermeier, T.; Monsees, A.; Beller, M. *Tetrahedron Lett.* **2005**, *46*, 3237. (k) Liu, D.; Gao, W.; Dai, Q.; Zhang, X. *Org. Lett.* **2005**, *7*, 4907. (l) Zhang, W.; Chi, Y.; Zhang, X. *Acc. Chem. Res.* **2007**, *40*, 1278. (m) Han, Z.; Wang, Z.; Zhang, X.; Ding, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 5345. (n) Dumrath, A.; Wu, X.-F.; Neumann, H.; Spannenberg, A.; Jackstell, R.; Beller, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 8988. (o) Liu, Z.; Du, H. *Org. Lett.* **2010**, *12*, 3054. (p) Morikawa, S.; Michigami, K.; Amii, H. *Org. Lett.* **2010**, *12*, 2520. (q) de la Fuente, V.; Waugh, M.; Eastham, G. R.; Castillón, S.; Claver, C. *Chem.—Eur. J.* **2010**, *16*, 6919. (r) Wang, X.; Han, Z.; Wang, Z.; Ding, K. *Angew. Chem., Int. Ed.* **2011**, *51*, 936.

(5) For hydrophosphination of alkenes or alkynes, see: (a) Douglass, M. R.; Stern, C. L.; Marks, T. J. *J. Am. Chem. Soc.* **2001**, *123*, 10221. (b) Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 2368. (c) Kondoh, A.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2007**, *129*, 4099. (d) Carlone, A.; Bartoli, G.; Bosco, M.; Sambri, L.; Melchiorre, P. *Angew. Chem., Int. Ed.* **2007**, *46*, 4504. (e) Hayashi, M. *Chem. Rec.* **2009**, *9*, 236. (f) Feng, J.; Chen, X.; Shi, M.; Duan, W. *J. Am. Chem. Soc.* **2010**, *132*, 5562. (g) Huang, Y.; Chew, R. J.; Li, Y.; Pullarkat, S. A.; Leung, P. *Org. Lett.* **2011**, *13*, 5862.

(6) Ullmann type C-P coupling: (a) Gelman, D.; Jiang, L.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 2315. (b) Allen, D. V.; Venkataraman, D. *J. Org. Chem.* **2003**, *68*, 4590. (c) Murata, M.; Buchwald, S. L. *Tetrahedron* **2004**, *60*, 7397. Recent Ullmann C−N/O coupling: (d) Kwong, F. Y.; Klapars, A.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 581. (e) Fang, Y.; Li, C. *J. Am. Chem. Soc.* **2007**, *129*, 8092. (f) Altman, R. A.; Shafir, A.; Choi, A.; Lichtor, P. A.; Buchwald, S. L. *J. Org. Chem.* **2008**, *73*, 284. (g) Jiao, J.; Zhang, X.; Chang, N.; Wang, J.; Wei, J.; Shi, X.; Chen, Z. *J. Org. Chem.* **2011**, *76*, 1180.

(7) For the use of metal hydride reductants, 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) Wang, Y.; Li, X.; Ding, K. *Tetrahedron: Asymmetry* **2002**, *13*, 1291.

(8) For the use of silane reductants, see: (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) Takaya, H.; Akutagawa, S.; Noyori, R. *Org. Synth. VIII* **1993**, 65−69. (f) Mckinstry, L.; Livinghouse, T. *Tetrahedron* **1994**, *50*, 6145. (g) Ding, K.; Wang, Y.; Yun, H.; Liu, J.; Wu, Y.; Terada, M.; Okubo, Y.; Mikami, K. *Chem.—Eur. J.* **1999**, *5*, 1734. (h) Wu, H. C.; Yu, J. Q.; Spencer, J. B. *Org. Lett.* **2004**, *6*, 4675. (i) Berthod, M.; Mignani, G.; Lemaire, M. *Tetrahydron: Asymmetry* **2004**, *15*, 1121. (j) Berthod, M.; Saluzzo, C.; Mignani, G.; Lemaire, M. *Tetrahydron: Asymmetry* **2004**, *15*, 639. (k) Tani, K.; Behenna, D. C.; McFadden, R. M.; Stoltz, B. M. *Org. Lett.* **2007**, *9*, 2529.

(9) For the reduction of SPO, see: (a) Stankevic, M.; Pietrusiewicz, K. M. *Synlett* **2003**, 1012. (b) 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. (c) Petit, C.; Favre-Réguillon, A.; Mignani, G.; Lemaire, M. *Green Chem.* **2010**, *12*, 326.

(10) (a) Zhou, S.; Junge, K.; Addis, D.; Das, S.; Beller, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 9507. (b) Das, S.; Zhou, S.; Addis, D.; Junge, K.; Enthaler, S.; Beller, M. *Top. Catal.* **2010**, *53*, 979. (c) Das, S.; Addis, D.; Zhou, S.; Junge, K.; Beller, M. *J. Am. Chem. Soc.* **2010**, *132*, 1770. (d) Addis, D.; Das, S.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 6004. (e) Das, S.; Möller, K.; Junge, K.; Beller, M. *Chem.—Eur. J.* **2011**, *17*, 7414. (f) Das, S.; Addis, D.; Knöpke, L. R.; Bentrup, U.; Brückner, A.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 9180. (g) Das, S.; Addis, D.; Junge, K.; Beller, M. *Chem.—Eur. J.* **2011**, *43*, 12186. (h) Das, S.; Wendt, B.; Möller, K.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 1662.

(11) (a) Mao, Z.; Gregg, B. T.; Cutler, A. R. *J. Am. Chem. Soc.* **1995**, *117*, 10139. (b) Parks, D. J.; Piers, W. E. *J. Am. Chem. Soc.* **1996**, *118*, 9440. (c) Parks, D. J.; Blackwell, J. M.; Piers, W. E. *J. Org. Chem.* **2000**, *65*, 3090. (d) Matsubara, K.; Iura, T.; Maki, T.; Nagashima, H. *J. Org.*

Chem. **2002**, *67*, 4985. (e) Motoyama, Y.; Mitsui, K.; Ishida, T.; Nagashima, H. *J. Am. Chem. Soc.* **2005**, *127*, 13150. (f) Nakanishi, J.; Tatamidani, H.; Fukumoto, Y.; Chatani, N. *Synlett* **2006**, 869. (g) Hanada, S.; Motayama, Y.; Nagashima, H. *Tetrahedron Lett.* **2006**, *47*, 6173. (h) Hanada, S.; Tsutsumi, E.; Motoyama, Y.; Nagashima, H. *J. Am. Chem. Soc.* **2009**, *131*, 15032. (i) Sunada, Y.; Kawakami, H.; Imaoka, T.; Motoyama, Y.; Nagashima, H. *Angew. Chem., Int. Ed.* **2009**, *48*, 9511.

(12) (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.; 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.

(13) (a) Lipshutz, B. H.; Servesko, J. M.; Taft, B. R. *J. Am. Chem. Soc.* **2004**, *126*, 8352. (b) Lee, D.; Kim, D.; Yun, S. *Angew. Chem., Int. Ed.* **2006**, *45*, 2785. (c) Lee, D.; Yang, Y.; Yun, J. *Org. Lett.* **2007**, *9*, 2749. (d) Baker, B. A.; Bošković, Ž. V.; Lipshutz, B. H. *Org. Lett.* **2008**, *10*, 289. (e) Deutsch, C.; Krause, N.; Lipshutz, B. H. *Chem. Rev.* **2008**, *108*, 2916. (f) Huang, S.; Voigtritter, K. R.; Unger, H. B.; Lipshutz, B. H. *Synlett* **2010**, 2041.

(14) (a) Díez-González, S.; Kaur, K.; Zinn, F. K.; Stevens, E. D.; Nolan, S. P. *J. Org. Chem.* **2005**, *70*, 4784. (b) Deschamp, J.; Chuzel, O.; Hannedouche, J.; Riant, O. *Angew. Chem., Int. Ed.* **2006**, *45*, 1292. (c) Lee, C. T.; Lipshutz, B. H. *Org. Lett.* **2008**, *10*, 4187. (d) Moser, M.; Bošković, Ž. V.; Crowe, C. S.; Lipshutz, B. H. *J. Am. Chem. Soc.* **2010**, *132*, 7852.

(15) Lipshutz, B. H.; Shimizu, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 2228.

(16) Das, S.; Join, B.; Junge, K.; Beller, M. *Chem. Commun.* **2012**, *48*, 2683.

(17) For details, see the Supporting Information.

(18) Shirobokov, O. G.; Kuzmina, L. G.; Nikonov, G. I. *J. Am. Chem. Soc.* **2011**, *133*, 6487.

(19) (a) If the mixture of $Cu(OTf)_2$ and TMDS was stirred for 30 min before the addition of tricyclohexylphosphine oxide, a much higher yield was obtained as 98% under the same conditions. (b) When 4-trifluoromethylbenzene bromide was used, (4-trifluoromethylphenyl)diphenylphosphine was produced with a yield of 35%.

(20) (a) Gatineau, D.; Giordano, L.; Buono, G. *J. Am. Chem. Soc.* **2011**, *133*, 10728. (b) Bernoud, E.; Alayrac, C.; Delacroix, O.; Gaumont, A. *Chem. Commun.* **2011**, *47*, 3239. (c) Rajendran, K. V.; Gilheany, D. G. *Chem. Commun.* **2012**, *48*, 817.

(21) For use of primary phosphine and PH_3, see: (a) Semenzin, D.; Etemad-Moghadam, G.; Albouy, D.; Koenig, M. *Tetrahedron Lett.* **1994**, *35*, 3297. (b) Chatterjee, S.; George, M. D.; Salem, G.; Willis, A. C. *J. Chem. Soc., Dalton Trans.* **2001**, 1890. (c) Herrbach, A.; Marinetti, A.; Baudoin, O.; Guénard, D.; Guéritte, F. *J. Org. Chem.* **2003**, *68*, 4897. (d) Brauer, D. J.; Kottsieper, K. W.; Roßenbach, S.; Stelzer, O. *Eur. J. Inorg. Chem.* **2003**, 1748. (e) Reiter, S. A.; Nogai, S. D.; Schmidbaur, H. *Dalton Trans.* **2005**, 247. (f) Xie, J.; Huang, J.; Zhu, N.; Zhou, Z.; Che, C. *Chem.—Eur. J.* **2005**, *11*, 2405. (g) Vlád, G.; Richter, F. U.; Horváth, I. T. *Tetrahedron Lett.* **2005**, *46*, 8605. (h) Hiney, R. M.; Higham, L. J.; Muller-Bunz, H.; Gilheany, D. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 7248. (i) Hall, J. W.; Yang, X.; Jones, R. A. *Chem. Commun.* **2010**, *46*, 6168.