Cross-coupling reactions of aryl and vinyl chlorides catalyzed by a palladium complex derived from an air-stable *H*-phosphonate†

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Received (in Cambridge, UK) 4th January 2006, Accepted 1st February 2006
First published as an Advance Article on the web 21st February 2006
DOI: 10.1039/b518283b

A palladium complex derived from air-stable TADDOLP(O)H catalyzes efficiently Hiyama, Stille, Kumada and Suzuki cross-coupling reactions of aryl and vinyl chlorides.

Transition metal-catalyzed cross-coupling reactions are useful tools for the synthesis of compounds with sp^2–sp^2 linkages, which are valuable building blocks in natural products, liquid crystals, polymers and ligands.[1,2] Iodides and activated bromides can be successfully transformed employing simple metal salts. Aryl chlorides are more useful substrates due to their lower cost and the wider diversity of available compounds. The conversion of aryl chlorides requires recently developed stabilizing ligands. Predominantly, the ligand design focused on electron-rich tertiary phosphines.[3] A notable alternative makes use of alkyl-substituted secondary phosphine oxides[4] as preligands.[5,6] We reported the first use of modular air-stable heteroatom-substituted secondary phosphine oxides as preligands for cross-coupling reactions of aryl chlorides.[7] Diaminophosphine oxides allowed also for efficient nickel-catalyzed C–F bond activation reactions at ambient temperature[8] as well as ruthenium-catalyzed C–H bond arylation reactions using aryl chlorides.[9] Herein, we present the first application of a palladium complex derived from an *H*-phosphonate to cross-coupling reactions between silicon-, tin-, magnesium- or boron-based organometallic species and aryl chlorides.[10]

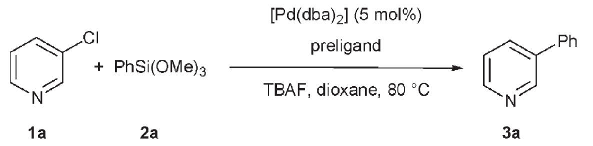
At the outset of our studies, we probed the catalytic activity of palladium complexes derived from different heteroatom-substituted secondary phosphine oxides in Hiyama cross-coupling reactions with aryl chloride **1a** (Table 1). In contrast to our studies on Suzuki coupling reactions,[7] diaminophosphine oxide **4** gave unsatisfactory conversion of chloride **1a** (entry 2). Sterically congested preligand **5**, previously employed in nickel-catalyzed Kumada cross-coupling reactions,[8] gave inferior results (entry 3). However, *H*-phosphonates **7**[11] and **8**[12] enabled isolation of pyridine **3** with good yields (entries 5–8). The influence of Pd/preligand ratio was found to be less pronounced, with an optimal ratio of 1/2 (entry 8).

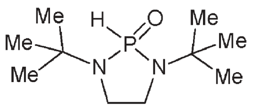
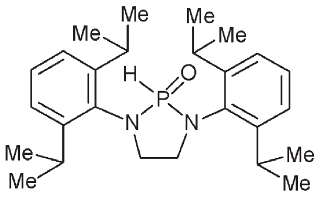
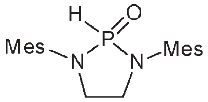
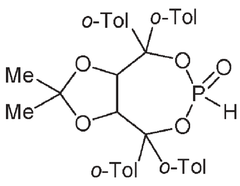
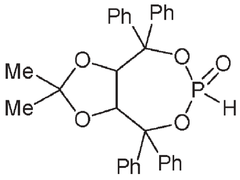
With an optimized catalyst in hand, we probed its application to the conversion of diversely substituted aryl chlorides in Hiyama cross-coupling reactions (Table 2, entries 1–7).‡

Important functional groups, such as an ester (entry 2), a nitro-substituent (entry 4), (enolizable) ketones (entries 5 and 6) and a cyano-group (entry 7) were tolerated.

Remarkably, TADDOL derivative **8** allowed for cross-coupling reactions between aryl chlorides and various organometallic species as pronucleophiles. Thus, Stille (entry 8), Kumada (entries

Table 1 Performance of palladium catalysts derived from secondary phosphine oxides



Nr	Preligand			Yield[a] (%)
1	—		—	—
2		**4**	10 mol%	(18)[b]
3		**5**	10 mol%	—
4		**6**	10 mol%	(25)[b]
5		**7**	10 mol%	(51)[b]
6		**8**	20 mol%	(57)[b]
7			5 mol%	61
8			10 mol%	63

[a] **1a** (1.00 mmol), **2a** (2.00 mmol), TBAF (2.00 mmol), [Pd(dba)$_2$] (5.0 mol%), dioxane (2 mL), 80 °C, 17 h, isolated yields. [b] By GC analysis *versus* *n*-decane as internal standard.

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† Electronic supplementary information (ESI) available: Experimental section. See DOI: 10.1039/b518283b

Table 2 Palladium-catalyzed cross-coupling reactions with aryl and vinyl chlorides **1** (see Scheme 1)[a]

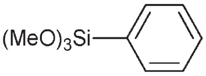
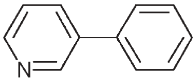
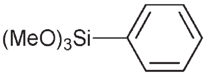
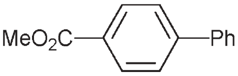
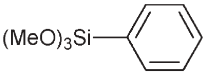
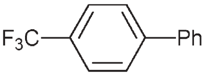
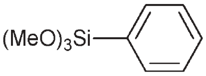
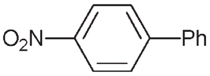
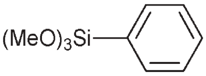
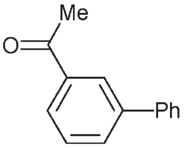
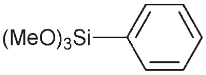
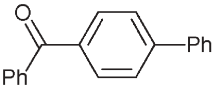
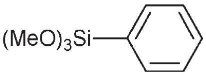
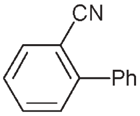
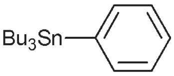
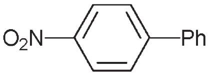
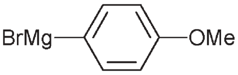
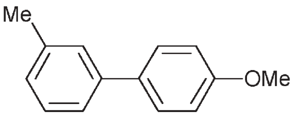
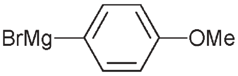
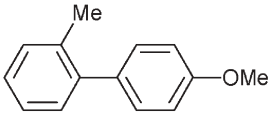
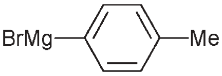
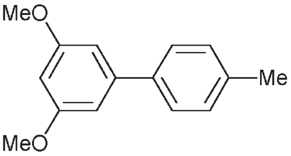
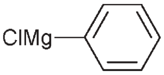
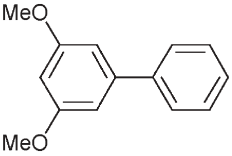
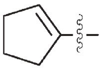
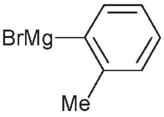
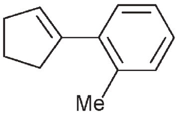
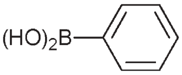
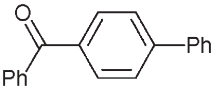
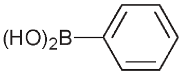
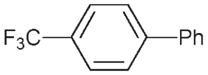
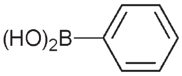
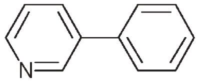
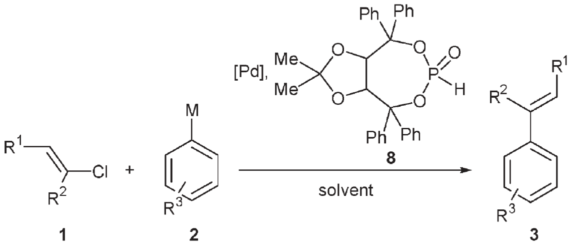
Nr	R	Pronucleophile	Product		Yield (%)
1	3-py			**3a**	63
2	4-$MeO_2CC_6H_4$			**3b**	68
3	4-$F_3CC_6H_4$			**3c**	62
4	4-$O_2NC_6H_4$			**3d**	79
5	3-AcC_6H_4			**3e**	71
6	4-$PhC(O)C_6H_4$			**3f**	65
7	2-NCC_6H_4			**3g**	60[b]
8	4-$O_2NC_6H_4$			**3d**	72[b]
9	3-MeC_6H_4			**3h**	73
10	2-MeC_6H_4			**3i**	61
11	3,5-$(MeO)_2C_6H_3$			**3j**	86
12	3,5-$(MeO)_2C_6H_3$			**3k**	95
13				**3l**	85
14	4-$PhC(O)C_6H_4$			**3f**	74

Table 2 Palladium-catalyzed cross-coupling reactions with aryl and vinyl chlorides **1** (see Scheme 1)[a] (*Continued*)

Nr	R	Pronucleophile	Product		Yield (%)
15	4-$F_3CC_6H_4$			**3c**	92
16	3-py			**3a**	95

[a] General reaction conditions: Hiyama and Stille reaction: **1** (1.00 mmol), **2** (2.00 mmol), TBAF (2.00 mmol), [Pd(dba)$_2$] (5.0 mol%), **8** (10.0 mol%), dioxane (2 mL), 80 °C. Kumada reaction: **1** (1.00 mmol), **2** (1.50 mmol), [Pd(OAc)$_2$] (2.0 mol%), **8** (4.0 mol%), THF (2 mL), 60 °C. Suzuki reaction: **1** (1.00 mmol), **2** (1.50 mmol), [Pd(dba)$_2$] (2.0 mol%), **8** (4.0 mol%), KO*t*-Bu (3.00 mmol), THF (5 mL), 60 °C. Isolated yields. [b] By GC analysis *versus* *n*-decane as internal standard.



Scheme 1 Cross-coupling reactions with a palladium complex derived from TADDOLP(O)H (**8**) (see Table 2).

9–13) and Suzuki (entries 14–16) reactions were efficiently catalyzed. Functionalized aryl chlorides gave rise to the corresponding biphenyls in good yields of isolated product (entries 8 and 14). Furthermore, the air-stable catalyst was applicable to the use of heterocyclic (entries 1 and 16) as well as vinylic chlorides (entry 13). Importantly, the protocol was not limited to electron-poor substrates, but allowed also for the use of electron-rich, thereby electronically deactivated, aryl chlorides (entries 9–12).

In conclusion, we present the application of an efficient palladium catalyst derived from *H*-phosphonate TADDOLP(O)H (**8**) to cross-coupling reactions between aryl and vinyl chlorides and various organometallic species. The results reported herein represent the first use of an air-stable heteroatom-substituted secondary phosphine oxide in Hiyama and Stille as well as palladium-catalyzed Kumada cross-coupling reactions.

Support by the Fonds der Chemischen Industrie, the Ludwig-Maximilians-Universität, and Professor P. Knochel is acknowledged. We thank the DFG for substantial financial support within the Emmy Noether-Program.

Notes and references

‡ Representative procedure for palladium-catalyzed Hiyama cross-coupling reactions of aryl chlorides (Table 2, entry 4): A solution of [Pd(dba)$_2$] (29 mg, 0.05 mmol, 5.0 mol%) and **8** (51 mg, 0.10 mmol, 10.0 mol%), 4-chloronitrobenzene (0.158 g, 1.00 mmol), phenyltrimethoxysilane (**2a**) (0.397 g, 2.00 mmol) and TBAF (0.631 g, 2.00 mmol) in dry dioxane (2 mL) was stirred for 17 h at 80 °C. Et_2O (50 mL) and H_2O (50 mL) were added to the reaction mixture. The separated aqueous phase was extracted with Et_2O (2 × 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The remaining residue was purified by column chromatography on silica gel (*n*-pentane/Et_2O = 50/1→30/1) to yield **3d** (0.157 g, 79%) as a light yellow solid.

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