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A highly efficient catalyst for Suzuki coupling of aryl halides and bromoarylphosphine oxides

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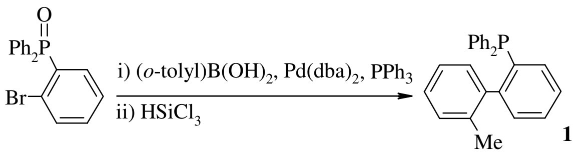
Abstract—The biphenyl-based phosphine, $P(o\text{-}C_6H_4C_6H_4Me)Ph_2$, is a moderately bulky and electron-rich phosphine, which has been successfully applied to the palladium catalyzed Suzuki coupling of activated and deactivated aryl halides as well as bromoarylphosphines and bromoarylphosphine oxides, with low catalyst loading and good to excellent conversions and turnovers.

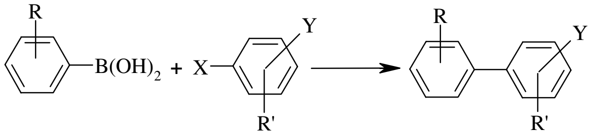
Recently, there has been growing interest in the application of biphenyl-based phosphines in a number of metal-catalyzed reactions such as C–X (X = C, and heteroatoms) coupling reactions as well as hydroformylation, hydrogenation and allylic alkylation.[1–5] In fact, a suitable balance of structural, steric and electronic properties has made biphenyl-based phosphines one of the most effective classes of phosphine ligands identified so far for such reactions.[6–8]

We have recently reported the synthesis of biphenyl-based phosphines by Suzuki coupling of arylboronic acids with haloarylphosphine oxides using $Pd(dba)_2$ and PPh_3 (Scheme 1).[9] This method is of great importance in the synthesis and applications of phosphines. Our initial results showed that some of the phosphine products were more effective than PPh_3 for Suzuki couplings. Therefore, we employed 2-diphenylphosphino-2′-methylbiphenyl **1** for the coupling of aryl halides as well as bromoarylphosphine oxides and a bromoarylphosphine (Scheme 2).[9,10]



Scheme 1. The synthesis of biphenylphosphine **1**.

Optimizations studies led us to employ 0.002 mol % of phosphine **1**, 0.001 mol % of $Pd(OAc)_2$, 2.0 mmol of K_3PO_4, 5 mL of toluene and 1 mL of water for the coupling of 1.0 mmol of 4-bromoacetophenone and 1.5 mmol of $ArB(OH)_2$. The yields and conversions were determined by GC based on acetylbiphenyl and 4-bromoacetophenone, respectively (hexadecane standard). These optimized conditions were used for coupling other aryl halides and arylboronic acids (Table 1). Excellent conversions of aryl chlorides (Table 1, entries 8–9) compared with similar systems indicated that phosphine **1** could potentially be employed in other phosphine assisted catalytic reactions. Indeed, phosphine **1** is efficiently active to convert even deactivated aryl halides. In the case of bifunctional dibromobenzene



R = H, Me; R′ = H, Me, Br, COMe, COPh, OMe, Ph, NO_2;
X = Cl, Br; Y = H, PPh_2, $OPPh_2$

Scheme 2. The Suzuki–Miyaura cross-coupling reaction.

Keywords: Suzuki coupling; Biphenylphosphine; Palladium catalyst.

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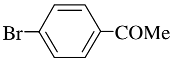
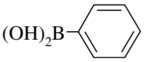
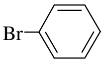
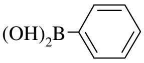
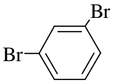
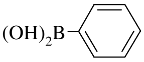
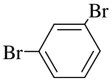
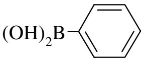
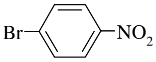
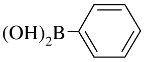
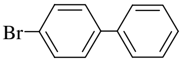
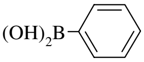
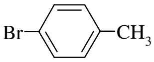
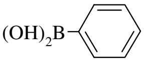
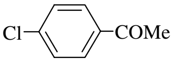
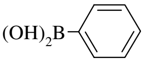
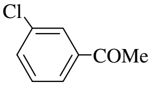
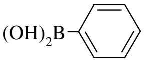
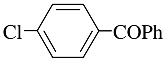
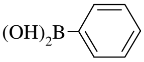
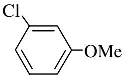
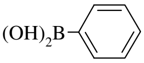
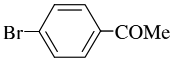
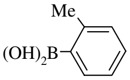
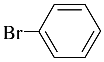
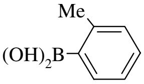
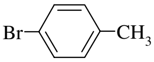
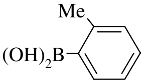
Table 1. Suzuki coupling of aryl halides[a]

Entry	Aryl halide	Arylboronic acid	Conversion[b] (%)	10^{-3} TON
1			100	100
2			95	95
3			25 50	75
4[c]			25 (40) 50 (50)	75 (90)
5			20 (90)	20 (90)
6			40	40
7			50	50
8			100	100
9			100	100
10			10	10
11			40 (70)	40 (70)
12			90	90
13			100	100
14			100	100

[a] For a general procedure see Ref. 10; reaction conditions: 1.0 mmol aryl halide, 1.5 mmol $ArB(OH)_2$, 0.001 mol % $Pd(OAc)_2$, 0.002 mol % phosphine **1**, 2.0 mmol K_3PO_4, 5 mL toluene, 1 mL water, 1 h.

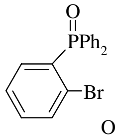
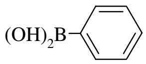
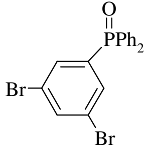
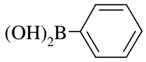
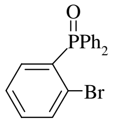
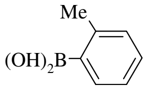
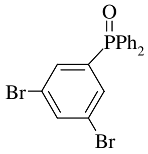
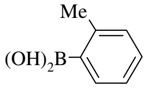
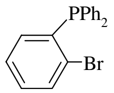
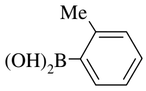
[b] Determined by GC based on aryl halide (hexadecane standard). The numbers in parentheses are from the reaction time 24 h.

[c] 3.0 mmol $ArB(OH)_2$ used.

(Table 1, entry 3), two products, biphenyl and terphenyl, were obtained with 25% and 50% conversion, respectively. Using phenylboronic acid twice as much as before (3 mmol, Table 1, entry 4), had no effect on the conversion after 1 h, but raised it to 90% after 24 h.

We have extended this methodology for the preparation of phosphine oxides. Table 2 summarizes the results obtained. Monobromophosphine oxide was coupled with 1.2 equiv of arylboronic acids (Table 2, entries 1 and 3) to give the corresponding biphenylphosphine oxides. Dibromophosphine oxide was coupled with 2.4 equiv of arylboronic acids (Table 2, entries 2 and 4) to give the corresponding terphenylphosphine oxides. Interestingly, this method is also efficient for coupling arylboronic acids with haloarylphosphines instead of their oxides in the presence of $Pd(OAc)_2$ without an additional phosphine co-catalyst. (2-Bromophenyl)diphenylphosphine [$PPh_2(o\text{-}C_6H_4Br)$] was coupled with *o*-tolylboronic acid (0.04 equiv $Pd(OAc)_2$, 10 h, 100 °C) to give **1** in 75% yield according to ^{31}P NMR (Table 2, entry 5). This method negates a reduction step and

Table 2. Suzuki coupling of bromoarylphosphine oxides and bromoarylphosphine[a]

Entry	Substrate	Arylboronic acid	Yield[b] (%)
1			90
2[c]			82
3			71
4[c]			58
5[d]			75

[a] For a general procedure see Ref. 9; reaction conditions: 1.0 equiv phosphine oxide (or phosphine), 1.2 equiv ArB(OH)$_2$, 0.04 equiv Pd(OAc)$_2$, 0.16 equiv phosphine **1**, 2.0 equiv K_3PO_4, 5 mL toluene, 1 mL water, 5 h.

[b] Isolated yield according to ^{31}P NMR, not optimized.

[c] 2.4 equiv ArB(OH)$_2$ used.

[d] In the absence of phosphine **1**.

if established generally could be an alternative and efficient method for synthesizing a wide variety of phosphines.

In conclusion, we have reported an efficient catalytic system for Suzuki cross-coupling of aryl halides, a bromoarylphosphine and bromoarylphosphine oxides catalyzed by Pd(OAc)$_2$ and the moderately bulky electron-rich 2-diphenylphosphino-2′-methylbiphenyl **1**. Excellent conversions and yields make this system a novel and efficient catalytic system. These reactions take place at low as well as at elevated temperatures although, of course, the reactions require a longer time at a lower temperature. The presence of water and Bu_4NBr led to a very rapid increase in activity.

Acknowledgements

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