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# Application of palladium-catalyzed Pd–aryl/P–aryl exchanges: preparation of functionalized aryl phosphines by phosphination of aryl bromides using triarylphosphines

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**Abstract**—Palladium-catalyzed Pd–aryl/P–aryl interchange reaction was applied in the synthesis of various functionalized arylphosphines. This phosphination used inexpensive, readily available and air stable triarylphosphines as the phosphinating agents. Broad functional groups were compatible including keto, aldehyde, ester, nitrile, ether, chloride, pyridyl and thiophenyl groups. Halides were found to be good promoter for the rates and yields of the reaction.

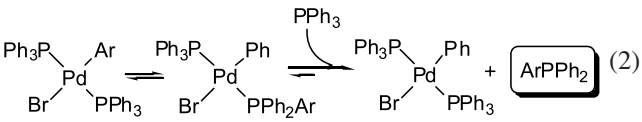

## 1. Introduction

Cross-coupling reactions are important in organic synthesis, especially in pharmaceutical areas. Palladium-catalyzed coupling methodologies are powerful protocols for carbon–carbon and carbon–heteroatom bond formation.[1] However, some of the undesirable side reactions such as Pd–aryl/P–aryl interchanges were observed when arylphosphine ligands were used (Eq. 1).


X = halides, triflate (1)

The Pd–aryl/P–aryl interchange in forming the scrambled side reaction products have been observed in Suzuki–Miyaura coupling,[2] Stille coupling,[3] Heck reaction,[4,5] amination,[6] amidation,[7] ketone-arylation,[8] cyanation,[9] and C–S bond formation reactions,[10,11] polymer synthesis,[12] and etc.[13] (Scheme 1). Consequently, the yields of the reactions suffer and the purification of products becomes more difficult. The unwanted coupled products usually are obtained from 4 to 58% yield in those couplings (Scheme 1). Furthermore, in polymer synthesis, the architecture of the desired polymer may be altered, possibly resulting in poorer properties.[12]

Cheng,[14] Novak[15] and Grushin[16] have demonstrated this aryl exchange reaction is an equilibrium process. The equilibrium is possibly a fine balance of the electronic and steric nature of the phopshine ligands. Mechanistic studies reveal that electron rich arylphosphines facilitate the Pd–aryl/P–aryl interchange reactions,[15] as the electron-donating group may stabilize the developing positive charge from the phosphonium salt intermediate (see Scheme 2, proposed mechanism). From these results, we utilized the aryl–aryl exchange reactions in the preparation of functionalized aryldiphenylphosphine ($ArPPh_2$) from aryl bromides and triphenylphosphine in the presence of palladium catalyst (Eq. 2).




(2)

Synthesis of functionalized aromatic phosphines for the application in fine-tuning catalysis is highly desirable. However synthetic methods available are limited in scope. Traditional methods for the preparation of aromatic phosphines can be classified into two major categories. One method involves the reaction of aryl Grignard or organolithium reagents with chlorophosphines, and is intolerant to a wide variety of functional groups.[17] The second method is the transition metal-catalyzed phosphination. Both nickel- and palladium-catalyzed phosphination of

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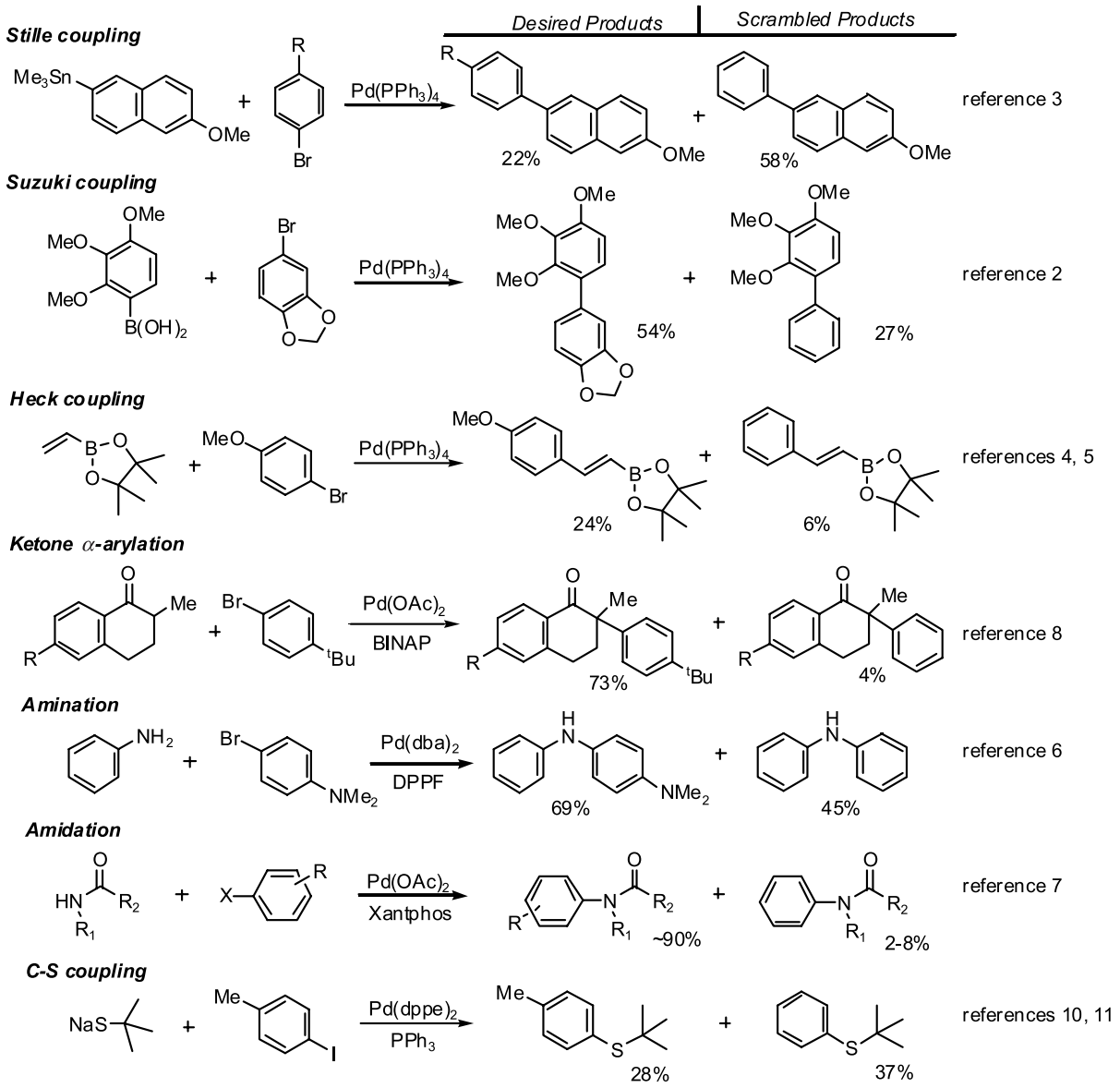


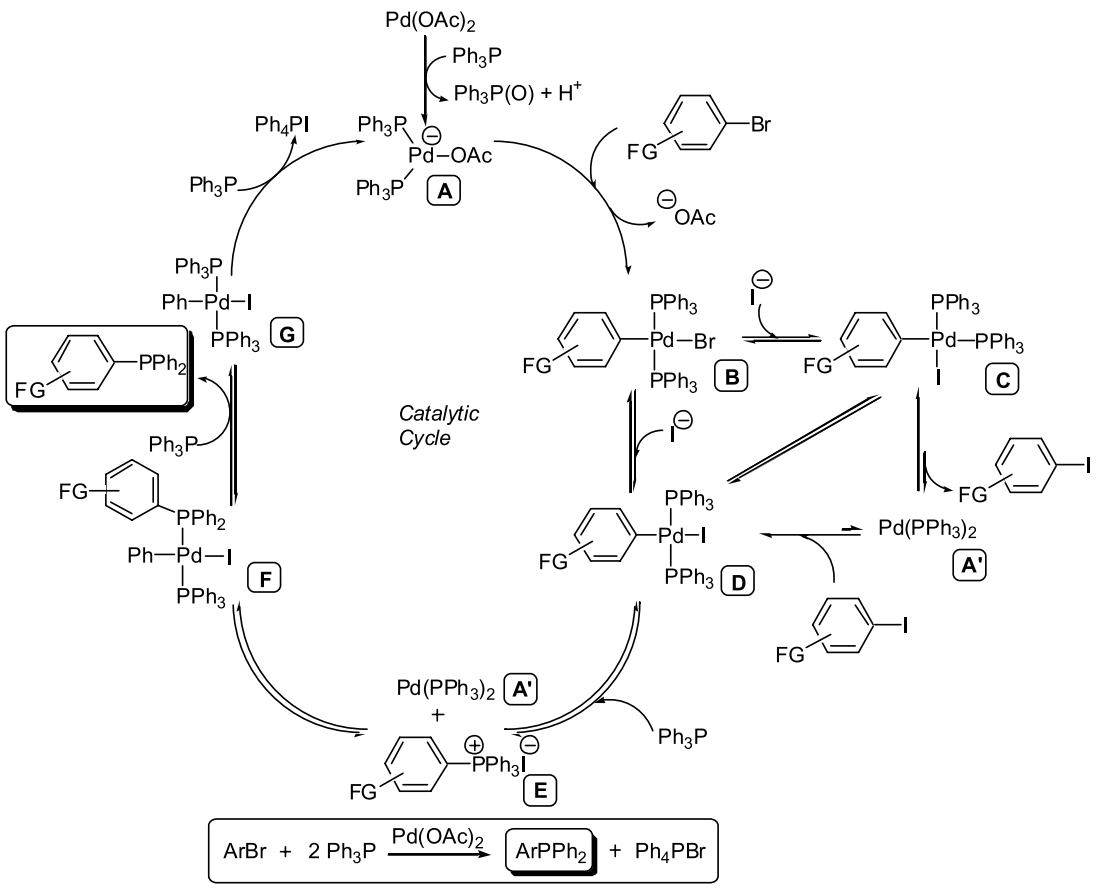

**Scheme 1.** Product scrambling in palladium-catalyzed cross-coupling reactions.

aryl triflates/halides using diphenylphosphine[18,19] ($Ph_2PH$) or chlorodiphenylphosphine[20] ($Ph_2PCl$) were reported recently.[21] The pioneering work of Stille using Pd/$TMSPPh_2$ system showed C–P bond formation from aryl iodides.[22] An alternative two-steps phosphine synthesis using Pd/$Ph_2P(O)H$ protocol requires subsequent reduction.[23] Recently, Lipshutz and co-workers have reported attractive C–P coupling method from aryl sulfonates using Pd/phosphine–borane system.[24] In the meanwhile, both Buchwald and Venkataraman groups disclosed an inexpensive copper-catalyzed phosphination of aryl iodides.[25] Herein, we report the palladium-catalyzed phosphination of functionalized aryl bromides using readily available triarylphosphines as the phosphinating agents to synthesize functionalized aryl phosphines.[26]

## 2. Results and discussion

Our initial discovery that pyridyl aryl triflates underwent successful catalyzed phosphination with triarylphosphines has prompted us to extend the method to aryl halides.[27] 4-Bromoacetophenone was therefore chosen as the prototypical substrate for screening the optimal reaction conditions. Both palladium(II) acetate and tetrakis(triphenylphosphine) palladium(0) complexes catalyzed the phosphination. A lower yield of the reaction was observed when $Pd_2(dba)_3$ complex was used, since dba (*trans*-dibenzylidieneacetone) ligand, has similar chromatographic behavior with the desired products and the purification procedure became more difficult. Therefore, palladium(II) acetate catalyst was preferred. The optimal amounts of triphenylphosphine added to the reaction were found to be 2.3–2.5 equiv. with respect to aryl bromide.[27] The optimized reaction conditions were then applied to the synthesis of other functionalized aryl phosphines (Table 1 and Eq. 3).

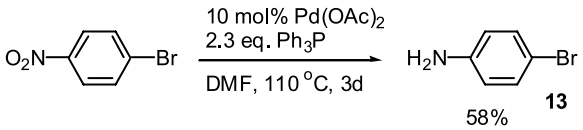
4-Bromobenzaldehyde was directly phosphinated by triphenylphosphine to form 4-(diphenylphosphino)benzaldehyde (Table 1, entry 1). In contrast, the previous preparation




**Scheme 2.** A plausible mechanism for palladium-catalyzed phosphination with added iodides.

of this phosphine, which finds many applications for water-soluble polymers[28] and porphyrins,[29] involved a muti-step synthesis requiring protection/deprotection of the aldehyde group.[30] Other functional groups, such as ester, nitrile, keto, ether and chloride are tolerant to this phosphination reaction (Table 1, entries 2–6). In contrast, previous syntheses of ester and nitrile containing phosphines required a long synthetic pathway.[31] Heterocyclic substrates, 3-bromopyridine and 2-bromothiophene were found to be compatible in this reaction (Table 1, entries 11–12).

Similar rates of reaction were observed for electronically different non-coordinating aryl bromides. The rate of the reaction of coordinating substrates, which contain ester, aldehyde, nitrile, pyridyl and thiophenyl groups required a longer reaction time (Table 1, entries 1, 3, 4, 11 and 12). Presumably strongly coordinating substrates rendered the catalyst complex coordinatively saturated and hence reduced the catalytic efficiency.



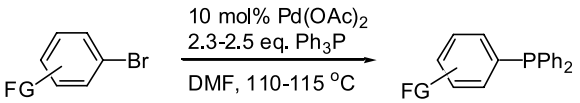

(4)

Some limitations of the substrates used in the palladium-catalyzed phosphination reaction exist. 4-Nitrobromobenzene was found to react quickly within 12 h at 110 °C to give no desired phosphinated-product but the 4-bromoaniline in 58% yield (Eq. 4). Reduction of the nitro-group was therefore very facile.[32] *ortho*-Substituted substrates such as 2-bromoanisole and 2-bromotoluene were found to be ineffective. These starting materials were recovered almost quantitatively after the reaction was heated for 72 h at 110 °C.

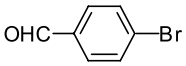
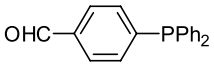
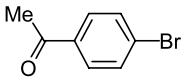
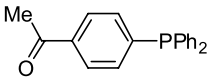
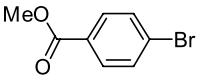
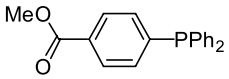
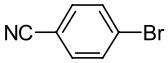
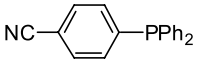
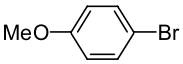
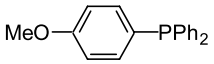
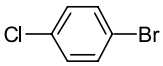
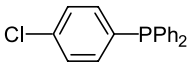
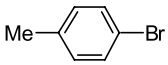
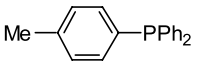
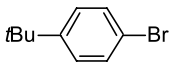
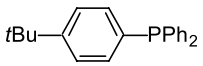
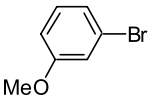
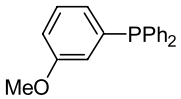
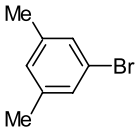
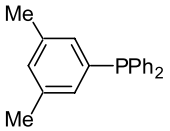
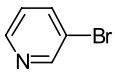
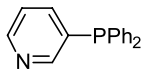
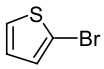
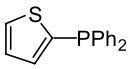
Other triarylphoshphines were found to be efficient diarylphosphinating agents for palladium catalyzed phosphination of aryl bromides (Table 2 and Eq. 5). The *p*-bromoacetophenone was diarylphosphinated by trixylylphosphine, tri(*p*-methoxyphenyl)phosphine and tri(*p*-tolyl)phosphine to yield the corresponding aromatic phosphines in moderate yields with similar rate (Table 2, entries 1–3). Sterically hindered tri(*o*-tolyl)phosphine did not react at all (Table 2, entry 4). These examples demonstrate the generality for diarylphosphination to synthesize various sterically unhindered aryl phosphines.

A user-friendly, economically attractive and environmentally benign phosphination was successfully carried out in solvent-free conditions (Table 3).[33] No significant electronic effect was observed in the solvent-free phosphination since both electron-withdrawing and donating substrates exhibited similar reaction rates (Table 3). *ortho*-Substituted aryl bromides still did not react in solvent-free conditions even at elevated temperature at 140 °C. The rates of the reactions in solvent-free conditions were slower than those in DMF. Presumably, the high viscosity of the reaction mixture was responsible. As $Ph_3P$ melts at 79 °C, at the reaction temperature of 110 °C, triphenylphosphine behaved as the solvent, ligand and phosphinating agent.

**Table 1**. Palladium-catalyzed phosphination of aryl bromides with triphenylphosphine[a]




(3)

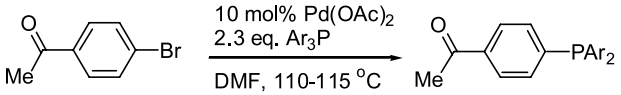
| Entry | Substrate | Product | Time (h) | % Yield[b] |
|---|---|---|---|---|
| 1 |  |  **1** | 64 | 32 |
| 2 |  |  **2** | 20 | 40 |
| 3 |  |  **3** | 36 | 30 |
| 4 |  |  **4** | 48 | 36 |
| 5 |  |  **5** | 24 | 27 |
| 6 |  |  **6** | 20 | 51[c] |
| 7 |  |  **7** | 26 | 58[c] |
| 8 |  |  **8** | 19 | 59[c] |
| 9 |  |  **9** | 18 | 38 |
| 10 |  |  **10** | 18 | 51[c] |
| 11 |  |  **11** | 72 | 25 |
| 12 |  |  **12** | 48 | 54[c] |

[a] Reaction conditions: ArBr (1.0 mmol), $Ph_3P$ (2.3–2.5 mmol), $Pd(OAc)_2$ (10 mol%) in DMF (4.0 mL) at 110–115 °C under nitrogen atmosphere.
[b] Isolated yield.
[c] GC yield in average of 2 runs.

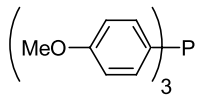
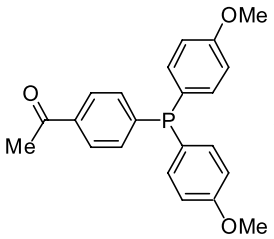
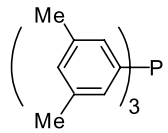
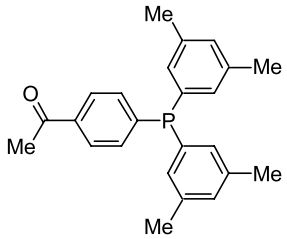
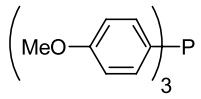
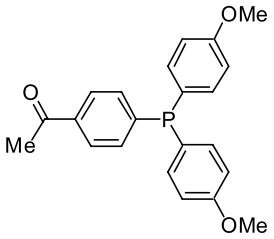
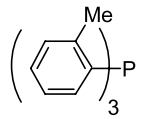
Halides have been discovered to be promoters in many transition metal-catalyzed processes and have become an important aspect of catalysis optimization.[34] To further optimize the phosphination, we had investigated the effect of halides and other anions in palladium-catalyzed phosphination of aryl bromides. Sodium iodide was used as the prototypical salt to examine the salt-effect in this reaction (Table 4). We found that the addition of 2.5 equiv. of NaI to the reaction mixture did enhance the yield. The optimal loading of NaI added was found to be around 5 equiv. (Table 4). A higher loading of 10 equiv. of NaI gave a lower yield of the product.

Other salts were also examined (Table 5). All halides gave

**Table 2**. Palladium-catalyzed phosphination of 4-bromoacetophenone with triarylphosphines[a]



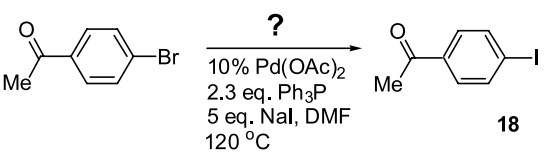

(5)

| Entry | $PAr_3$ | Product | Time (h) | % Yield[b] |
|---|---|---|---|---|
| 1 |  |  **14** | 33 | 39 |
| 2 |  |  **15** | 32 | 34 |
| 3 |  |  **16** | 34 | 33 |
| 4 |  | | 72 | No rxn.[c] |

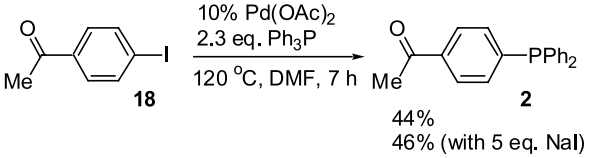
[a] Reaction conditions: 4-bromoacetophenone (1.0 mmol), $Ar_3P$ (2.3 mmol), $Pd(OAc)_2$ (0.1 mmol, 10 mol%) in DMF (4.0 mL) at 110–115 °C under nitrogen atmosphere.
[b] Isolated yield.
[c] Starting material was recovered.

better yields or faster rate of the reaction (Table 5, entry 1 vs. 2–5, 8–10). Among the halides, sodium salts exhibited an equal or better promoting effect than potassium salts (Table 5, entries 3–5, 8–9). Iodide (MI, M=Li, Na, K, $Et_4N$) salts showed faster rate of reaction and higher yield of the product (Table 5, entries 2, 3, 8, 10). Alkali metal iodide generally gave higher yields of reaction compared with ammonium salts (Table 5, entries 1–2, 8 vs. 10). The best result was found to be with the addition of 5 equiv. of NaI, with the isolated yield of 4-(diphenylphosphino)acetophenone obtained in 60%. Non-halide salts such as, $NaBF_4$, $NaPF_6$ and $NH_4PF_6$ were found to be inferior (Table 5, entries 6, 7, 11).

The metal halides likely play several roles in the phosphination. Firstly, the addition of salts to the reaction increased the solvent polarity in the bulk environment, which favors the oxidative addition and formation of phosphonium salt intermediate (Scheme 2). Secondly, the iodide salt may assist the halide exchange for aryl bromide to aryl iodide,[35] and hence provide a lower energy barrier for oxidative addition of carbon–halogen bond with palladium catalyst. The possibility of converting aryl bromides into aryl iodides by the addition of NaI was supported by the observation of a trace amount of 4-iodoacetophenone generated during the course of the phosphination of 4-bromoacetophenone by GC–MS analysis (Eq. 7 and Scheme 2).



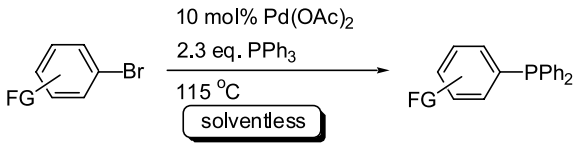

(7)

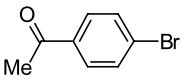
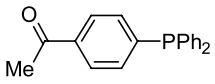
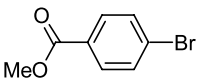
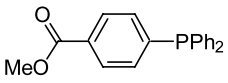
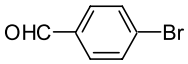
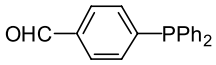
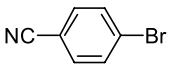
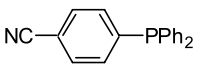
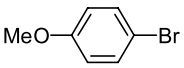
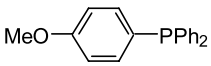
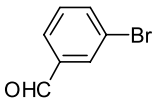
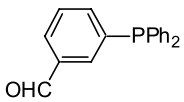
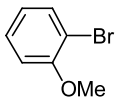
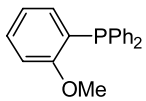
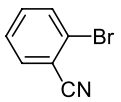
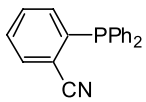



(8)

The more reactive 4-iodoacetophenone likely undergoes fast oxidative addition with palladium catalyst in the

**Table 3**. Solvent-free palladium-catalyzed phosphination of aryl bromides[a]

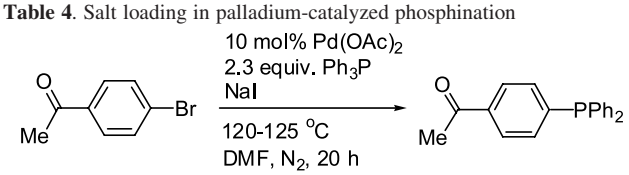



| Entry | Substrate | Product | Time (h) | % Yield[b] |
|---|---|---|---|---|
| 1 |  |  **2** | 1.5 | 44 |
| 2 |  |  **3** | 2.5 | 40 |
| 3 |  |  **1** | 2.5 | 40 |
| 4 |  |  **4** | 2.5 | 38 |
| 5 |  |  **5** | 1.0 | 33 |
| 6 |  |  **17** | 2.5 | 34 |
| 7 |  |  | 7 | No rxn.[c] |
| 8 |  |  | 7 | No rxn.[c] |

[a] Reaction conditions: ArBr (1.0 mmol), $Ph_3P$ (2.3 mmol), and $Pd(OAc)_2$ (0.1 mmol, 10 mol%) at 110–115 °C under nitrogen atmosphere.
[b] Isolated yield.
[c] Reaction temperature (140 °C).

catalytic cycles (Scheme 2). Indeed, 4-iodoacetophenone reacted about three times faster than 4-bromoacetophenone (Eq. 8). Similar metal iodide acceleration phenomenon in the cross-coupling reactions have been observed.[36] Moreover, as iodide anion is less coordinating, therefore it dissociates more rapidly than bromides and chlorides,[34] and the concentration of coordinatively unsaturated palladium species would increase. Pd–aryl/P–aryl exchanges would be more facile as reported by Grushin on the addition step.[16] Hence a faster rate of reaction was observed (Table 5, entries 2, 3, 8, 10). The possibility of iodide anion in forming a new pentacoordinated anionic palladium species,[37] which facilitates the subsequent reductive elimination, could not be excluded.

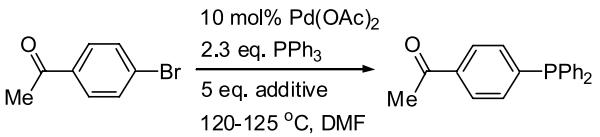
**Table 4**. Salt loading in palladium-catalyzed phosphination




| Entry | NaI (equiv). | % GC yield |
|---|---|---|
| 1 | 0 | 44 |
| 2 | 2.5 | 56 |
| 3 | 5 | 68 |
| 4 | 10 | 56 |

Scheme 2 illustrates a plausible mechanism for the reaction involving Pd(0)/Pd(II) cycles. Palladium(II) acetate is in situ reduced by triphenylphosphine to form acetate ligated complex **A**, $PdL_2(OAc)^-$ (L=triphenylphosphine).[38,39] This active anionic palladium complex **A** then undergoes oxidative addition with an aryl bromide to afford palladium complex **B** (Scheme 2).[40] Halide exchange by the addition of iodide ion (from NaI or KI) generated complexes **C** and **D**.[37] As we have observed that a trace amount of 4-iodoacetophenone formed during the course of the reaction by GC–MS analysis,[41] the ligand substitution

**Table 5**. Salt effects in palladium-catalyzed phosphination of aryl bromide[a]




(6)

| Entry | Additive | Time (h) | % Yield[b] |
|---|---|---|---|
| 1 | / | 20 | 40[c] |
| 2 | LiI | 6 | 51 |
| 3 | NaI | 20 | 68 (60)[c] |
| 4 | NaBr | 23 | 65 |
| 5 | NaCl | 23 | 51 |
| 6 | $NaBF_4$ | 22 | 34 |
| 7 | $NaPF_6$ | 20 | 0 |
| 8 | KI | 10 | 67 |
| 9 | KBr | 10 | 40 |
| 10 | $Et_4NI$ | 2 | 49 |
| 11 | $NH_4PF_6$ | 20 | 0 |

[a] Reaction conditions: ArBr (1.0 mmol), $Ph_3P$ (2.3 mmol), additive (5.0 mmol) and $Pd(OAc)_2$ (0.1 mmol, 10 mol%) in DMF (4.0 mL) at 120–125 °C under nitrogen atmosphere.
[b] GC yield.
[c] Isolated yield.

product from **B** to **C** is feasible. A new equilibrium from **C**–**A′**–**D** would be established (Scheme 2). The *trans*-complex **D** subsequently undergoes iodide dissociation and reductive elimination with triphenylphosphine to produce a phosphonium salt **E** and palladium complex **A′**. Such Pd-catalyzed phosphonium salt formation for *meta*- and *para*- but not *ortho*-substituted aryl bromides has been reported.[42] Grushin *et al.* also reported that the iodide can facilitate the Pd–aryl/P–aryl interchange through the phosphonium salt pathway in the $ArPdX(PPh_3)_2$ complex.[43]

The anionic palladium complex **A** or **A′** undergoes oxidative addition by carbon–phosphorus bond activation of the phosphonium salt **E** to generate the coordinated $ArPPh_2$ Pd-complex (Scheme 2).[44,45] Finally, ligand substitution by triphenylphosphine to Pd(II) complex **F** gives $ArPPh_2$ and Pd–phenyl complex **G**. The $PdL_2I^-$ species is regenerated by reductive elimination of triphenylphosphine and Pd bound phenyl group to yield the tetraphenylphosphonium iodide co-product (Scheme 2). The formation of tetraphenylphosphonium co-product was detected by $^{31}P$ NMR ($\delta$=24.0 ppm)[46] in the reaction mixture. Therefore, two equivalents of $PPh_3$ were required. The first one serves as the diphenylphosphinating agent and the second one yields the phosphonium salt co-product.

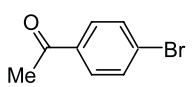
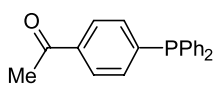
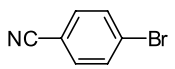
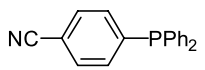
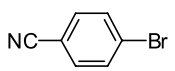
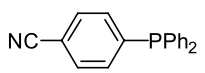
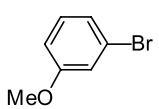
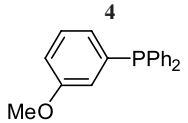
The iodide promoting effect in the phosphination was found to be general for aryl bromides and the results are listed in Table 6. Both the rates and about 10–20% increase in product yields were observed.

## 3. Conclusion

In conclusion, a catalytic user-friendly palladium-catalyzed phosphination using triarylphosphines as the phosphinating reagents was developed and optimized. This carbon–phosphorus bond formation was compatible with a number of functional groups, including aldehyde, keto, ester, nitrile, ether, pyridyl and thiothenyl group. This phosphination utilizes the air-stable triphenylphosphine as the phosphinating reagent and the reaction were carried out in neutral media. This process has a great potential to tailor a variety of substituted phosphines by using different triarylphopshines with various functionalized aryl bromides.

**Table 6**. Palladium-catalyzed phosphination of aryl bromides with iodide salts[a]


(9)

| Entry | Substrate | Product | Salt | Time (h) | % Yield[b] |
|---|---|---|---|---|---|
| 1 |  |  **2** | KI | 10 | 60 |
| 2 |  |  **4** | NaI | 48 | 52 |
| 3 |  |  **4** | KI | 16 | 49 |
| 4 |  |  **9** | KI | 12 | 42 |

[a] Reaction conditions: ArBr (1.0 mmol), $Ph_3P$ (2.3 mmol), $Pd(OAc)_2$ (0.1 mmol, 10 mol%) and salt (5.0 mmol) in DMF (4.0 mL) under nitrogen atmosphere at 120–125 °C
[b] Isolated yield.

## 4. Experimental

### 4.1. General considerations

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. Hexane for chromatography was distilled from anhydrous calcium chloride. *N*,*N*-Dimethylformamide was distilled from magnesium sulfate under reduced pressure.[47] Thin layer chromatography was performed on Merck precoated silica gel 60 $F_{254}$ plates. Silica gel (Merck, 70–230 and 230–400 mesh) was used for column chromatography. $^1$H NMR spectra were recorded on a Brüker DPX 300 (300 MHz) spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ ($\delta$ 7.26 ppm), or with tetramethylsilane (TMS, $\delta$ 0.00 ppm) as the internal standard. Chemical shifts ($\delta$) were reported as part per million (ppm) in $\delta$ scale downfield from TMS. $^{13}$C NMR spectra were recorded on a Brüker DPX 300 (75 MHz) spectrometer and referenced to $CDCl_3$ ($\delta$ 77.00 ppm). $^{31}$P NMR spectra were recorded on a Varian 400 (162 MHz) and referenced to 85% $H_3PO_4$ externally. Coupling constants ($J$) were reported in Hertz (Hz). Mass spectra (EIMS and FABMS) were recorded on a HP 5989B Mass Spectrometer. High resolution mass spectra (HRMS) were obtained on a Brüker APEX 47e FT-ICR mass spectrometer (ESIMS). GC–MS analysis was conducted on a HP G1800C GCD system using a HP5MS column (30 m×0.25 mm). The products described in GC yield according to the authentic samples/anthracene calibration curve.

*General procedure A: palladium-catalyzed phosphination of aryl bromides in DMF*. Aryl bromides (1.0 mmol), triphenylphosphine (655 mg, 2.5 mmol) and $Pd(OAc)_2$ (22.4 mg, 0.1 mmol, 10 mol%) were charged to a Teflon screw-capped Schlenk flask. Evacuated and backfilled with nitrogen three times. The Schenk flask was then added dry DMF (4.0 mL) under nitrogen. The solution was heated to 110–115 °C for a specified time in Table 1 and generally the color of the solution changed from yellow to red. The reaction was cooled down and DMF was removed under reduced pressure. The residue was purified by column chromatography on silica gel eluting with hexane/ethyl acetate to obtain the pure product.

*General procedure B: palladium-catalyzed phosphination of aryl bromides under solventless conditions*. Aryl bromides (1.0 mmol), triphenylphosphine (603 mg, 2.3 mmol) and $Pd(OAc)_2$ (22.4 mg, 0.1 mmol, 10 mol%) were charged to a Teflon screw-capped Schlenk flask. Evacuated and backfilled with nitrogen three cycles. The solution was heated to 115 °C for a specified time in Table 3. The reaction was cooled down and dichloromethane was added. The residue was purified by column chromatography on silica gel eluting with hexane/ethyl acetate to obtain the pure product.

*General procedure C: palladium-catalyzed phosphination of aryl bromides in the presence of salts*. Aryl bromides (1.0 mmol), triphenylphosphine (603 mg, 2.3 mmol), $Pd(OAc)_2$ (22.4 mg, 0.1 mmol, 10 mol%) and salt (5.0 mmol) were charged to a Teflon screw-capped Schlenk flask. Evacuated and backfilled with nitrogen three times. The Schenk flask was then added dry DMF (4.0 mL) under nitrogen. The solution was heated to 120–125 °C for a specified time in Tables 4 and 5. The reaction was cooled down and DMF was removed under reduced pressure. The residue was purified by column chromatography on silica gel eluting with hexane/ethyl acetate to obtain the pure product.

**4.1.1. 4-(Diphenylphosphino)benzaldehyde (1).**[48] General procedure A was followed. $R_f$=0.6 (hexane/ethyl acetate=10:1). Mp 75.5–77 °C (lit. 69–71 °C).[49] $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.32–7.43 (m, 12H), 7.80 (dd, 2H, $J$=8.1, 1.5 Hz), 10.00 (s, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 128.8 (d, $J_{CP}$=7.2 Hz), 129.3, 133.5 (d, $J_{CP}$=18.3 Hz), 134.0 (d, $J_{CP}$=20.0 Hz), 135.7 (d, $J_{CP}$=10.4 Hz), 136.0, 146.5 (d, $J_{CP}$=15.5 Hz), 191.9; $^{31}$P (162 MHz, $CDCl_3$) $\delta$ −3.41; MS (EI): *m*/*z* (relative intensity) 290 ($M^+$, 100), 261 (8), 211 (9), 183 (95), 165 (12), 152 (20).

**4.1.2. 4-(Diphenylphosphino)acetophenone (2).**[50] General procedure A was followed. $R_f$=0.2 (hexane/ethyl acetate=20:1). Mp 118–120 °C (lit. 119–120 °C).[50] $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 2.57 (s, 3H), 7.29–7.38 (m, 12H), 7.88 (dd, 2H, $J$=8.3, 1.3 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 26.6, 127.9 (d, $J_{CP}$=6.2 Hz), 128.6 (d, $J_{CP}$=7.2 Hz), 129.1, 133.2 (d, $J_{CP}$=18.5 Hz), 133.9 (d, $J_{CP}$=19.9 Hz), 135.9 (d, $J_{CP}$=10.4 Hz), 136.7, 144.3 (d, $J_{CP}$=14.2 Hz), 197.8; MS (EI): *m*/*z* (relative intensity) 304 ($M^+$, 100), 289 (10), 261 (12), 227 (11), 183 (90), 152 (30).

**4.1.3. Methyl 4-(diphenylphosphino)benzoate (3).**[51] General procedure A was followed. $R_f$=0.6 (hexane/ethyl acetate=10:1). Mp 103–105 °C (lit. 99–100 °C).[49] $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.28–7.38 (m, 12H), 7.97 (dd, 2H, $J$=8.4, 1.5 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 52.2, 128.7 (d, $J_{CP}$=7.1 Hz), 129.1, 129.3 (d, $J_{CP}$=6.4 Hz), 133.0, 133.1 (d, $J_{CP}$=18.5), 133.9 (d, $J_{CP}$=19.9 Hz), 136.1 (d, $J_{CP}$=10.5 Hz), 144.0 (d, $J_{CP}$=14.0 Hz), 166.9; MS (EI): *m*/*z* (relative intensity) 320 ($M^+$, 100), 289 (8), 261 (7), 207 (9), 183 (70), 166 (12).

**4.1.4. 4-(Diphenylphosphino)benzonitrile (4).**[52] General procedure A was followed. $R_f$=0.6 (hexane/ethyl acetate = 10:1). Mp 86–87 °C (lit. 86–87 °C).[49] $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.28–7.39 (m, 12H), 7.57 (dd, 2H, $J$=8.4, 1.2 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 111.8, 118.9, 128.8 (d, $J_{CP}$=7.4 Hz), 129.5, 131.7 (d, $J_{CP}$=5.9 Hz), 133.4 (d, $J_{CP}$=18.4 Hz), 134.0 (d, $J_{CP}$=20.2 Hz), 135.3 (d, $J_{CP}$=10.3 Hz), 145.1 (d, $J_{CP}$=16.5 Hz); MS (EI): *m*/*z* (relative intensity) 287 ($M^+$, 100), 208 (55), 195 (8), 183 (62), 177 (12).

**4.1.5. 4-(Diphenylphosphino)anisole (5).**[53] General procedure A was followed. Mp 64.5–65.5 °C (lit. 63–65 °C).[50b] $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.69 (s, 3H), 7.10 (dd, 2H, $J$=8.1, 4.0 Hz), 7.24–7.59 (m, 12H); MS (EI): *m*/*z* (relative intensity) 292 ($M^+$, 100), 277 (12), 259 (10), 215 (30), 183 (48).

**4.1.6. 3-(Diphenylphosphino)anisole (9).**[54] General procedure A was followed. $R_f$=0.4 (hexane/ethyl acetate = 20:1); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.71 (s, 3H),

6.83–6.90 (m, 3H), 7.22–7.34 (m, 11H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 55.1, 114.3, 118.9 (d, $J_{CP}$=21.1 Hz), 126.0 (d, $J_{CP}$=18.8 Hz), 128.5 (d, $J_{CP}$=6.8 Hz), 128.7, 129.5 (d, $J_{CP}$=7.7 Hz), 133.7 (d, $J_{CP}$=19.4 Hz), 137.0 (d, $J_{CP}$=10.6 Hz), 138.7 (d, $J_{CP}$=11.0 Hz), 159.5 (d, $J_{CP}$=8.3 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ −3.81; MS (EI): *m/z* (relative intensity) 292 ($M^+$, 100), 213 (22), 199 (20), 183 (48).

**4.1.7. 3-(Diphenylphosphino)pyridine (11).**[55] General procedure A was followed. $R_f$=0.8 (hexane/ethyl acetate=5:1); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.34 (d, 1H, *J*=1.4 Hz), 8.30 (d, 1H, *J*=8.3 Hz), 7.92 (t, 1H, *J*=8.2 Hz), 7.27–7.69 (m, 11H); MS (EI): *m/z* (relative intensity) 263 ($M^+$, 100), 186 (20).

**4.1.8. 4-(Di(4-tolyl)phosphino)acetophenone (14).** General procedure A was followed. 4-Bromoacetophenone (199 mg, 1.0 mmol), palladium(II) acetate (22.4 mg, 0.1 mmol), tri(4-tolyl)phosphine (699 mg, 2.3 mmol) and dry DMF (4 mL) were used to obtain 4-(di(4-tolyl)phosphino)acetophenone (**14**) (129 mg, 39%) as light yellow solid after purified by column chromatography on silica gel using a solvent mixture (hexane/ethyl acetate=10:1) as the eluent. $R_f$=0.4 (hexane/ethyl acetate=10:1). Mp 58–60 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 2.35 (s, 6H), 2.57 (s, 3H), 7.15–7.25 (m, 8H), 7.36 (dd, 2H, *J*=8.4, 1.5 Hz), 7.86 (dd, 2H, *J*=8.4, 1.5 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 21.3, 26.6, 127.9 (d, $J_{CP}$=6.0 Hz), 129.5 (d, $J_{CP}$=7.5 Hz), 132.7 (d, $J_{CP}$=9.0 Hz), 133.0 (d, $J_{CP}$=18.2 Hz), 134.0 (d, $J_{CP}$=20.3 Hz), 136.5, 139.2, 145.3 (d, $J_{CP}$=14.3 Hz), 197.8; $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ −12.60; MS (EI): *m/z* (relative intensity) 332 ($M^+$, 100), 317 (5), 289 (10), 281 (7), 241 (8), 211 (30), 197 (28); HRMS (ESIMS) calcd for $C_{22}H_{21}OPH^+$ 333.1408, found 333.1385.

**4.1.9. 4-(Bis(3,5-dimethylphenyl)phosphino)acetophenone (15).** General procedure A was followed. 4-Bromoacetophenone (199 mg, 1.0 mmol), palladium(II) acetate (22.4 mg, 0.1 mmol), trixylylphosphine (796 mg, 2.3 mmol) and dry DMF (4 mL) were used to yield 4-(bis(3,5-dimethyl)phosphino)acetophenone (**15**) (122 mg, 34%) as pale yellow solid after purified by column chromatography on silica gel using a solvent mixture (hexane/ethyl acetate=10:1) as the eluent. $R_f$=0.6 (hexane/ethyl acetate = 10:1). Mp 56–58 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 2.27 (s, 12H), 2.59 (s, 3H), 6.93 (s, 2H), 6.96 (s, 2H), 7.00 (s, 2H), 7.34 (dd, 2H, *J*=8.3, 1.4 Hz), 7.87 (dd, 2H, *J*=8.3, 1.4 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 21.3, 26.6, 127.9 (d, $J_{CP}$=6.2 Hz), 131.0, 131.7 (d, $J_{CP}$=20.2 Hz), 133.2 (d, $J_{CP}$=18.2 Hz), 135.7 (d, $J_{CP}$=9.5 Hz), 136.5, 138.1 (d, $J_{CP}$=7.9 Hz), 145.1 (d, $J_{CP}$=14.8 Hz), 198.0; $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ −12.88; MS (EI): *m/z* (relative intensity) 360 ($M^+$, 100), 345 (8), 317 (12), 253 (8), 241 (15), 225 (13), 211 (22), 193 (16); HRMS (ESIMS) calcd for $C_{24}H_{25}OPH^+$ 361.1721, found 361.1709.

**4.1.10. 4-(Di(4-methoxyphenyl)phosphino)acetophenone (16).** General procedure A was followed. 4-Bromoacetophenone (199 mg, 1.0 mmol), palladium(II) acetate (22.4 mg, 0.1 mmol), tri(4-methoxyphenyl)phosphine (810 mg, 2.3 mmol) and dry DMF (4 mL) were used to yield 4-(di(4-methoxyphenyl)phosphino)acetophenone (**16**) (120 mg, 33%) as pale yellow solid after purified by column chromatography on silica gel using a solvent mixture (hexane/ethyl acetate=10:1) as the eluent. $R_f$=0.2 (hexane/ethyl acetate=10:1). Mp 54–56 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 2.57 (s, 3H), 3.81 (s, 6H), 6.90 (dd, 4H, *J*=6.0, 2.1 Hz), 7.25–7.32 (m, 6H), 7.85 (dd, 2H, *J*=8.4, 1.5 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 26.6, 55.2, 114.3 (d, $J_{CP}$=8.3 Hz), 127.1 (d, $J_{CP}$=7.4 Hz), 127.8 (d, $J_{CP}$=5.8 Hz), 132.6 (d, $J_{CP}$=17.7 Hz), 135.5 (d, $J_{CP}$=21.5 Hz), 136.3, 146.1 (d, $J_{CP}$=13.9 Hz), 160.5, 197.8; $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ −13.03; MS (EI): *m/z* (relative intensity) 364 ($M^+$, 100), 349 (10), 281 (9), 257 (10), 245 (30), 229 (8), 214 (40), 199 (18); HRMS (ESIMS) calcd for $C_{22}H_{21}O_3PH^+$ 365.1307, found 365.1289.

**4.1.11. 3-(Diphenylphosphino)benzaldehyde (17).**[56] General procedure B was followed. $R_f$=0.6 (hexane/ethyl acetate=10:1); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.32–7.43 (m, 12H), 7.80 (dd, 2H, *J*=8.1, 1.5 Hz), 10.00 (s, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 128.8 (d, $J_{CP}$=7.2 Hz), 129.3, 133.5 (d, $J_{CP}$=18.3 Hz), 134.0 (d, $J_{CP}$=20.0 Hz), 135.7 (d, $J_{CP}$=10.4 Hz), 136.0, 146.5 (d, $J_{CP}$=15.5 Hz), 191.9; $^{31}$P (162 MHz, $CDCl_3$) $\delta$ −3.41; MS (EI): *m/z* (relative intensity) 290 ($M^+$, 100), 261 (8), 211 (9), 183 (95), 165 (12), 152 (20).

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