Tetrahedron Letters 57 (2016) 348–350

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Ligand-free palladium catalyzed phosphorylation of aryl iodides

Najmeh Nowrouzi *, Saba Keshtgar, Enayatollah Bahman Jahromi

Department of Chemistry, Faculty of Sciences, Persian Gulf University, Bushehr 75169, Iran

ARTICLE INFO

Article history:
Received 30 June 2015
Revised 26 November 2015
Accepted 3 December 2015
Available online 7 December 2015

Keywords:
Palladium
Phosphorylation
Triarylphosphine
Ligand-free

ABSTRACT

A reusable ligand-free palladium catalyzed phosphorylation of aryl iodides using $PdCl_2$/tetrabutylammonium bromide is described. Functionalized triarylphosphines were obtained in good to excellent yields in the absence of external reductants and supporting ligands.

Phosphines are an important class of organophosphorus compounds. They are often used as ligands in metal complex catalysis and as intermediates in organic synthesis.[1] Ligands play a key role in stabilizing and activating the central metal atom and the presence of functional groups on at least one aryl moiety of a phosphine-ligated metallic center can offer the advantage of optimizing the catalytic properties. The numerous synthetic methods for the preparation of triarylphosphines can be divided into four major categories: Friedel–Crafts reactions,[2] reaction of organometallic reagents with halophosphines,[3] nucleophilic substitution with metallated organophosphines,[4] and catalytic C–P bond formation.[5]

Research in the past years has focused on the catalytic synthesis of phosphines and is still under full development. A significant advancement in the synthesis of triarylphosphines came with the development of transition metal catalysis based on palladium(0) or nickel(0) complexes. In 1987, Tunney and Stille reported the palladium-catalyzed synthesis of several aryldiphenylphosphines by the cross-coupling of aryl halides with (trimethylsilyl) diphenylphosphine or (trimethylstannyl)diphenylphosphine.[6] After this Letter, research efforts have focused on this reaction and remarkable progress has been achieved on improvements of the reaction conditions using palladium.[7] Similarly, nickel(0)-catalyzed protocols have also been employed in the synthesis of several tertiaryphosphines.[8] Cristau et al. were the first to achieve the nickel-catalyzed arylation of diphenylphosphine[8c] and obtained a mixture of triphenylphosphine and tetraphenylphosphonium bromide salt upon reaction of bromobenzene with diphenylphosphine ($HPPh_2$) in the presence of $NiBr_2$. Copper was first used as a co-catalyst in palladium catalyzed phosphorylation reactions.[9] In 2003, copper-catalyzed palladium free phosphorylation methods were developed by Venkataraman and Van Allen[10] and Buchwald and co-workers.[11] However, in contrast to the volume of literature that exists for the formation of aryl–nitrogen and aryl–oxygen bonds using cross-coupling with transition metal catalysts, only a few reports exist for the formation of aryl phosphines.

In continuation of our recent works on palladium catalyzed cross-coupling reactions,[12] herein, we report the reusable ligand-free palladium catalyzed phosphorylation reaction of aryl halides with chlorodiphenylphosphine and dichlorophenylphosphine in tetrabutylammonium bromide.

For optimization of the reaction conditions, we first performed the phosphorylation of iodobenzene with chlorodiphenylphosphine as a model reaction in the presence of catalytic $PdCl_2$ (5 mol %) in tetrabutylammonium bromide (TBAB) and the effects of different parameters were studied. Several bases were screened for this reaction. Initially, sodium hydroxide was utilized as base and the reaction was carried out at 120 °C. Although monitoring by TLC indicated the complete consumption of the starting materials after 30 min, the isolated yield of product was moderate (Table 1, entry 1). Then NaOH was replaced by several different organic and inorganic bases, and NaOH was found to give the best results. Other bases such as Na_2CO_3 and Ca_2CO_3 were inferior, and Bu_3N failed to promote the reaction (Table 1, entries 2–4). In the absence of base, the starting material remained unchanged (Table 1, entry 5). When NaOH was used as base, significant amounts of triphenylphosphine oxide were observed, which accounted for the lower observed yield. We found that the production of triphenylphosphine oxide was minimized when

---

* Corresponding author. Tel.: +98 77 31222341; fax: +98 77 33441494.
E-mail address: nowrouzi@pgu.ac.ir (N. Nowrouzi).

http://dx.doi.org/10.1016/j.tetlet.2015.12.018

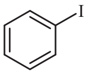
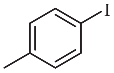
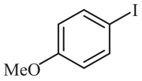
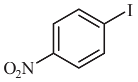
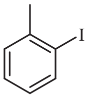
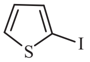
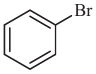
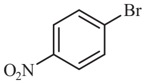
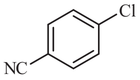
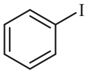
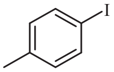
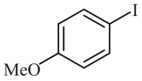
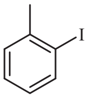
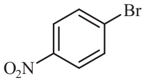
Table 1
Effect of different reaction parameters on the coupling reaction of iodobenzene (1.0 mmol) and chlorodiphenylphosphine (1.0 mmol) in the presence of tetrabutylammonium bromide (0.5 mmol)

Entry	Catalyst (mol %)	Base (2.0 mmol)	T (°C)	Time (h)	Yield[a] (%)
1	5	NaOH	120	0.5	60
2	5	Na_2CO_3	120	24	Trace
3	5	Ca_2CO_3	120	24	Trace
4	5	Bu_3N	120	24	–
5	5	–	120	24	–
6[b]	5	NaOH	120	0.5	93
7[b]	5	NaOH	100	3	80
8[b]	5	NaOH	140	0.5	91
9[b]	3	NaOH	120	0.5	93
10[b]	1	NaOH	120	24	30
11[b]	10	NaOH	120	0.5	91
12[b,c]	3	NaOH	120	24	–

[a] Isolated yield.
[b] The reactions were carried out under an argon atmosphere.
[c] TBAB was removed from the reaction mixture.

Table 2
Phosphorylation of aryl halides with chlorophosphines in the presence of $PdCl_2$ and TBAB

$$\text{ArI} \; + \; \begin{matrix}\text{Ph}_2\text{PCl}\\ \text{or}\\ \text{PhPCl}_2\end{matrix} \xrightarrow[\substack{\text{NaOH}\\ 120\ ^\circ\text{C}}]{\substack{\text{PdCl}_2\\ n\text{-Bu}_4\text{NBr}}} \begin{matrix}\text{Ph}_2\text{PAr}\\ \text{or}\\ \text{PhPAr}_2\end{matrix}$$

Entry	ArX	Ph_nPCl_{3-n}	Time (h)	Yield[c] (%)[Ref.]
1[a]		Ph_2PCl	0.5	93[10]
2[a]		Ph_2PCl	1	90[6]
3[a]		Ph_2PCl	1.2	80[6]
4[a]		Ph_2PCl	1.5	79[13]
5[a]		Ph_2PCl	6	87[10]
6[a]		Ph_2PCl	1	90[6]
7[a]		Ph_2PCl	24	–
8[a]		Ph_2PCl	24	–
9[a]		Ph_2PCl	24	–
10[b]		$PhPCl_2$	3	85[10]
11[b]		$PhPCl_2$	4.5	82[14]
12[b]		$PhPCl_2$	5	75[15]
13[b]		$PhPCl_2$	15	80[16]
14[b]		$PhPCl_2$	24	–

[a] Reaction conditions: aryl halide (1.0 mmol), chlorodiphenylphosphine (1.0 mmol), n-Bu_4NBr (0.5 mmol), $PdCl_2$ (3 mol %), NaOH (2.0 mmol), 120 °C under argon.
[b] Reaction conditions: aryl halide (2.0 mmol), dichlorophenylphosphine (1.0 mmol), n-Bu_4NBr (0.5 mmol), $PdCl_2$ (6 mol %), NaOH (4.0 mmol), 120 °C under argon.
[c] Isolated yield.

the coupling reaction was performed under argon (Table 1, entry 6). A temperature of 120 °C was optimal for this reaction (Table 1, entry 1). When the reaction temperature was lowered to 100 °C, the yield also decreased (Table 1, entry 7). Higher temperatures (Table 1, entry 8) did not improve the conversion and yield of the desired product. Next, the reaction was carried out with different amounts of $PdCl_2$ (1, 3, 10 mol %). As shown in entries 9–11, at 120 °C, 3 mol% of the catalyst was sufficient to catalyze the reaction efficiently. In this case, the corresponding product was obtained in 93% yield within 0.5 h (Table 1, entry 9). Finally, the optimized reaction was performed in the absence of TBAB. However, when TBAB was removed from the reaction mixture, the reaction did not occur (Table 1, entry 12).

Having the optimized conditions; aryl halide (1.0 mmol), Ph_2PCl (1.0 mmol), NaOH (2.0 mmol), $PdCl_2$ (0.03 mmol) and TBAB (0.5 mmol) at 120 °C under an argon atmosphere (Table 1, entry 9), the phosphorylation reactions proceeded efficiently for iodobenzene and iodobenzenes bearing either an electron-withdrawing or an electron-donating group at the para-position (Table 2, entries 1–4). The methodology was further extended to the coupling of sterically hindered aryl iodides such as 2-iodotoluene (Table 2, entry 5). We found that ortho-substituted iodide also coupled well with this protocol. We also tried to use this method for the coupling of chlorodiphenylphosphine with bromo- and chlorobenzene. Although the cross coupling reaction proceeded efficiently for iodobenzenes, the reactions did not proceed with bromo and chloro derivatives even with an electron-withdrawing group at the *para*-position (Table 2, entries 7–9). These reactions did not proceed even in the presence of PPh_3 as ligand or with increasing the amount of $PdCl_2$ from 3 mol % to 10 mol %.

Instead of chlorodiphenylphosphine, we also examined this method for the coupling of dichlorophenylphosphine with iodobenzenes. The reactions proceeded efficiently and the corresponding products were obtained in high yields (Table 2, entries 10–13).

The role of TBAB in this reaction is crucial. It is well established that the presence of TBAB not only makes the catalytic system stable by preventing the formation of palladium black[17] but also acts both as a reducing agent for the generation of Pd(0)[12b,18] and as an ionic liquid solvent to make the reaction mixture homogeneous.

The recyclability of this system was also examined in the reaction of iodobenzene with chlorodiphenylphosphine. For this purpose, after completion of the reaction and extraction of the product using diethylether, iodobenzene, chlorodiphenylphosphine and base were added to the remaining layer containing Pd (0)/TBAB and the reaction mixture was worked-up after 35 min. Quantitative conversion to the corresponding phosphine was observed for three runs. From the fourth run, a loss of the activity of the system was observed (Table 3).

As shown in Table 1, entry 5, the reaction did not occur in the absence of NaOH. Moreover, in a control experiment, we observed that Ph_2PO^- was produced in the reaction of Ph_2PCl and NaOH under the reaction conditions.

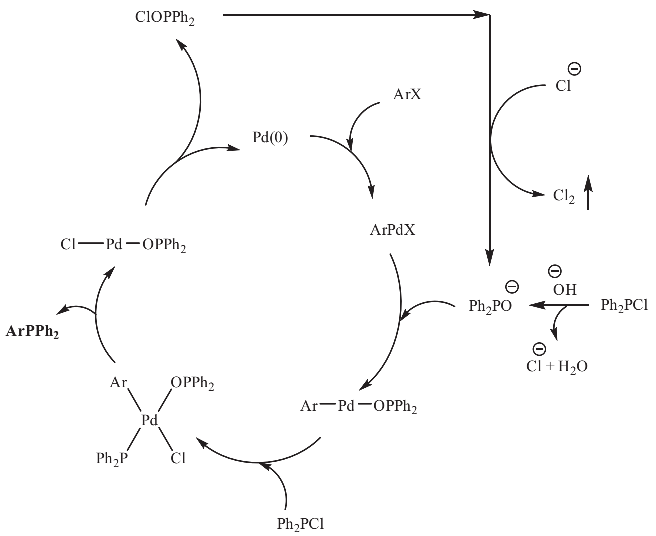
According to the above observations, a proposed mechanism is shown in Scheme 1.

Table 3
Recyclability of Pd(0)/TBAB in the reaction of iodobenzene with chlorodiphenylphosphine[a]

Cycle	Time (min)	Yield[b] (%)
1	30	93
2	35	91
3	45	89
4	70	81
5	90	80

[a] Reaction conditions: iodobenzene (1.0 mmol), chlorodiphenylphosphine (1.0 mmol), PdCl$_2$ (0.03 mmol), n-Bu$_4$NBr (0.5 mmol), NaOH (2.0 mmol), 120 °C, under argon.

[b] Isolated yield.



Scheme 1. A possible mechanism for the palladium catalyzed C–P bond formation.

In conclusion, we have demonstrated several examples of cross coupling reactions between commercially available chlorophosphines and aromatic iodides.[19] Functionalized triarylphosphines, potentially useful as ligands in homogeneous catalysis, were obtained with good to excellent yields by this method in the absence of external reductants and supporting ligands.

Acknowledgment

We thank the Persian Gulf University Research Council for generous partial financial support of this study.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2015.12.018.

References and notes

1. (a) Methot, J. L.; Roush, W. R. *Adv. Synth. Catal.* **2004**, *346*, 1035–1050; (b) Xu, K.; Yang, F.; Zhang, G.; Wu, Y. *Green Chem.* **2013**, *15*, 1055; (c) Glueck, D. S. *Top. Organomet. Chem.* **2010**, *31*, 65; (d) Demmer, C. S.; Larsen, N. K.; Bunch, L. *Chem. Rev.* **2011**, *111*, 7981.
2. (a) Ude, W.; Besecke, S.; Riemann, A.; Schroeder, G. *Ger. Offen.* **1986**. DE 3425282 A1; (b) Wan, I. Y.; McGrath, J. E.; Kashiwagi, T. *ACS Symp. Ser.* **1995**, *599*, 29.
3. (a) Rabinowitz, R.; Pellon, J. *J. Org. Chem.* **1961**, *26*, 4623–4626; (b) Peer, M.; de Jong, J. C.; Kiefer, M.; Langer, T.; Rieck, H.; Schell, H.; Sennhenn, P.; Sprinz, J.; Steinhagen, H.; Wiese, B.; Helmchen, G. *Tetrahedron* **1996**, *52*, 7547–7583; (c) Bélanger, E.; Pouliot, M. F.; Paquin, J. F. *Org. Lett.* **2009**, *11*, 2201–2204; (d) Veits, Yu. A.; Neganova, E. G.; Vinogradova, O. S. *Russ. J. Gen. Chem.* **2005**, *75*, 1060–1068; (e) Grelaud, G.; Argouarch, G.; Paul, F. *Tetrahedron Lett.* **2010**, *51*, 3786–3788; (f) Stefani, H. A.; Silva, N. C. S.; Vasconcelos, S. N. S.; Manarin, F.; Souza, F. B. *Tetrahedron Lett.* **2013**, *54*, 2809–2812; (g) Saha, D.; Ghosh, R.; Sarkar, A. *Tetrahedron* **2013**, *69*, 3951–3960; (h) Buchner, B.; Lockhart, L. B., Jr. *J. Am. Chem. Soc.* **1951**, *73*, 755–756; (i) Kaesz, H. D.; Stone, F. G. A. *J. Org. Chem.* **1959**, *24*, 635–637.
4. (a) Seipel, K. R.; Platt, Z. H.; Nguyen, M.; Holland, A. W. *J. Org. Chem.* **2008**, *73*, 4291–4294; (b) Hayashi, M.; Yamasaki, T.; Kobayashi, Y.; Imai, Y.; Watanabe, Y. *Eur. J. Org. Chem.* **2009**, 4956–4962.
5. Liancheng, Y.; Xiangyang, Q.; Longhe, X. *Prog. Chem.* **2011**, *23*, 893–902.
6. Tunney, S. E.; Stille, J. K. *J. Org. Chem.* **1987**, *52*, 748–753.
7. (a) Martín, S. E.; Bonaterra, M.; Rossi, R. A. *J. Organomet. Chem.* **2002**, *664*, 223–227; (b) Bonaterra, M.; Rossi, R. A.; Martín, S. E. *Organometallics* **2009**, *28*, 933–936; (c) Herd, O.; Hessler, A.; Hingst, M.; Tepper, M.; Stelzer, O. *J. Organomet. Chem.* **1996**, *522*, 69–76; (d) Herd, O.; Hessler, A.; Hingst, M.; Machnitzki, P.; Tepper, M.; Stelzer, O. *Catal. Today* **1998**, *42*, 413–420; (e) Brauer, D. J.; Hingst, M.; Kottsieper, K. W.; Liek, C.; Nickel, T.; Tepper, M.; Stelzer, O.; Sheldrick, W. S. *J. Organomet. Chem.* **2002**, *645*, 14–26; (f) Kwong, F. Y.; Chan, K. S. *Chem. Commun.* **2000**, 1069–1070; (g) Kwong, F. Y.; Lai, C. W.; Tian, Y.; Chan, K. S. *Tetrahedron Lett.* **2000**, *41*, 10285–10289; (h) Kwong, F. Y.; Lai, C. W.; Yu, M.; Tian, Y.; Chan, K. S. *Tetrahedron* **2003**, *59*, 10295–10305; (i) Kwong, F. Y.; Lai, C. W.; Yu, M.; Chan, K. S. *Tetrahedron* **2004**, *60*, 5635–5645; (j) Kwong, F. Y.; Chan, K. S. *Organometallics* **2000**, *19*, 2058–2060; (k) Kwong, F. Y.; Chan, K. S. *Organometallics* **2001**, *20*, 2570–2578; (l) Kwong, F. Y.; Lai, C. W.; Chan, K. S. *Tetrahedron Lett.* **2002**, *43*, 3537–3539; (m) Lai, C. W.; Kwong, F. Y.; Wang, Y.; Chan, K. S. *Tetrahedron Lett.* **2001**, *42*, 4883–4885; (n) Wang, Y.; Lai, C. W.; Kwong, F. Y.; Jia, W.; Chan, K. S. *Tetrahedron* **2004**, *60*, 9433–9439.
8. (a) Cai, D.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *J. Org. Chem.* **1994**, *59*, 7180–7181; (b) Cai, D. W.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *J. Org. Synth.* **1999**, *76*, 6–11; (c) Cristau, H. J.; Chêne, A.; Christol, H. *J. Organomet. Chem.* **1980**, *185*, 283–295; (d) Zhao, Y. L.; Wu, G. J.; Li, Y.; Gao, L. X.; Han, F. S. *Chem. Eur. J.* **2012**, *18*, 9622–9627; (e) Ager, D. J.; Laneman, S. A. *Chem. Commun.* **1997**, 2359–2360.
9. Al-Masum, M.; Livinghouse, T. *Tetrahedron Lett.* **1999**, *40*, 7731–7734.
10. Van Allen, D.; Venkataraman, D. *J. Org. Chem.* **2003**, *68*, 4590–4593.
11. Gelman, D.; Jiang, L.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 2315–2318.
12. (a) Nowrouzi, N.; Tarokh, D.; Motevalli, S. *J. Mol. Catal. A: Chem.* **2014**, *385*, 13–17; (b) Nowrouzi, N.; Motevalli, S.; Tarokh, D. *J. Mol. Catal. A: Chem.* **2015**, *396*, 224–230; (c) Nowrouzi, N.; Tarokh, D. *J. Iran. Chem. Soc.* **2015**, *12*, 1623–1628.
13. Schiemenz, G. P.; Nielsen, P. *Phosphorus, Sulfur Silicon Relat. Elem.* **1985**, *21*, 259–266.
14. (a) Keglevich, G.; Ovacs, T. K.; Satlos, F. C. *Heteroat. Chem.* **2015**, *26*, 199–205; (b) Williams, D. B. G.; Kotze, P. D. R.; Ferreira, A. C.; Holzapfel, C. W. *J. Iran. Chem. Soc.* **2011**, *8*, 240–246.
15. Russell, M. G.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **2000**, 505–513.
16. Segall, Y.; Granoth, I. *J. Am. Chem. Soc.* **1978**, *100*, 5130–5134.
17. (a) Li, J. H.; Liu, W. J.; Xie, Y. X. *J. Org. Chem.* **2005**, *70*, 5409–5412; (b) Beller, M.; Fischer, H.; Kiihlein, K.; Reisinger, C. P.; Herrmarn, W. A. *J. Organomet. Chem.* **1996**, *520*, 257–259; (c) Liu, W. J.; Xie, Y. X.; Liang, Y.; Li, J. H. *Synthesis* **2006**, *5*, 860–864.
18. Iranpoor, N.; Firouzabadi, H.; Rajabi Moghadam, K. H.; Motavalli, S. *RSC Adv.* **2014**, *4*, 55732–55737.
19. *Typical procedure for the reaction of iodobenzene and chlorodiphenylphosphine:* A mixture of iodobenzene (1.0 mmol, 0.11 mL), chlorodiphenylphosphine (1.0 mmol, 0.18 mL), PdCl$_2$ (0.03 mmol, 0.0053 g) and NaOH (2.0 mmol, 0.08 g) were added to a flask containing tetrabutylammonium bromide (0.5 mmol, 0.15 g) under an argon atmosphere. The mixture was heated in an oil bath at 120 °C with stirring and the reaction was followed by TLC analysis. When the reaction was complete (0.5 h), the solution was cooled to room temperature and the product was extracted with diethyl ether (3 × 3 mL). The solvent was then removed and pure triphenylphosphine was obtained as a white solid in 93% yield (0.243 g). Mp 80–82 °C (lit. 81–82 °C);[14a] ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 7.40 (s, 15H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 137.46, 137.36, 134.07, 133.88, 128.96, 128.78, 128.71; ^{31}P NMR (162 MHz, CDCl$_3$) δ ppm: −5.5.[20] MS (EI) m/z = 262 [M$^+$].
20. (a) Nomiya, K.; Noguchi, R.; Ohsawa, K.; Tsuda, K.; Oda, M. *J. Inorg. Biochem.* **2000**, *78*, 363–370; (b) Amatore, C.; Jutand, A.; M'Barki, M. A. *Organometallics* **1992**, *11*, 3009–3013; (c) Balema, V. P.; Wiench, J. W.; Pruski, M.; Pecharsky, V. K. *Chem. Commun.* **2002**, 724–725.