



# Synthesis of aryl phosphines by phosphination with triphenylphosphine catalyzed by palladium on charcoal

Chi Wai Lai, Fuk Yee Kwong, Yanchun Wang and Kin Shing Chan\*

Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong

Received 28 March 2001; accepted 24 May 2001

**Abstract**—The palladium-catalyzed phosphination of aryl bromides and triflates by phosphination with triphenylphosphines to yield aryl phosphines was catalyzed by the thermally stable catalyst palladium on charcoal. © 2001 Elsevier Science Ltd. All rights reserved.

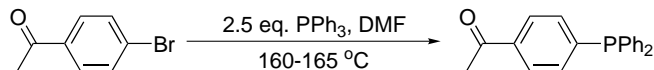
A synthesis of aryl phosphines has been recently reported which involves the phosphination of aryl bromides<sup>1</sup> and triflates<sup>2</sup> with triarylphosphines using 10 mol% of palladium catalysts such as Pd(OAc)<sub>2</sub> and Pd(dba)<sub>2</sub>. This method is direct and applicable to functionalized substrates using air-stable and economical starting materials.<sup>3</sup> However, the use of these homogeneous palladium catalysts suffers from frequent decomposition at elevated temperatures in the course of the reactions to form catalytically inactive palladium black precipitates. No further catalysis proceeds. Since heterogeneous palladium catalysts<sup>4</sup> including palladium on glass,<sup>5</sup> charcoal and even carbon nanofiber<sup>6</sup> have been extensively employed as efficient catalysts in catalysis as well as catalytic hydrogenation, we would like to employ these heterogeneous catalysts in phosphination to improve the efficiency of the process. Palladium on charcoal is particularly attractive since it is commercially available and has been extensively applied in homo-,<sup>7</sup> Sonogashira,<sup>8</sup> Stille,<sup>9</sup> Suzuki,<sup>10</sup> and Negishi<sup>11</sup> cross-couplings as well as in Heck reactions<sup>12</sup> as an air-stable and easily removable catalyst with comparable activity with that of Pd(OAc)<sub>2</sub> and Pd(Ph<sub>3</sub>P)<sub>4</sub>. An added advantage is the easy removal of palladium after the reaction by its simple filtration with Celite and the possibility of its re-use. We now report the use of the Pd/C catalyst in the successful phosphination of aryl bromides and triflates with triphenylphosphine by virtue of its large surface area and thermal stability.

Table 1 shows the effect of Pd/C catalyst loading on the phosphination of 4-bromoacetophenone with 2.5 equiv. of Ph<sub>3</sub>P in DMF at 160°C.<sup>1,2</sup> Amounts of Pd/C catalyst from 1 to 10 mol% had little difference on the rate

and/or yield of the reaction while less than 1 mol% increased the reaction time significantly and lowered the yield slightly. The use of a higher reaction temperature of 160°C allowed a lower catalyst loading of just 1% making this process more attractive compared to the 10 mol% of Pd(OAc)<sub>2</sub> catalyst necessary at 110°C.<sup>1,2</sup>

Table 2 shows the successful phosphination of functionalized aryl bromides, triflates and nonaflate using the optimized conditions. In general, aryl triflates reacted faster than aryl bromides.<sup>1,2b</sup> In some cases (entries 14–17), only the aryl triflates reacted. A variety of functional groups such as ketone, aldehyde, ester, pyridine and cyanide were compatible with the reaction without the need of a protective group as neutral reaction media were employed.<sup>1,2</sup> Electron-deficient substrates (entries 1, 2, 6 and 7) gave higher yields than electron-rich substrates (entries 8 and 9). Presumably, the diphenylarylphosphine products formed from electron-rich substrates may undergo rapid further phosphination.<sup>2b</sup> This is consistent with the observation that

**Table 1.** Effect of Pd/C catalyst loading in phosphination



Entry	Pd/C (mol%)	Time (h)	Yield (%)
1	10	30	45
2	5	32	44
3	1	32	46
4	0.5	96	39
5	0.2	168	37
6	0.1	288	28

\* Corresponding author. E-mail: ksc@cuhk.edu.hk

**Table 2.** Palladium-catalyzed phosphination of aryl bromides, triflates and nonaflate with triphenylphosphine

X = Br, OTf, ONf

Entry	Substrate	X	Product	Time (h)	Yield (%)
1		X = Br		32	46
2		X = OTf		20	39
3		X = Br		No reaction after 9 days	
4		X = OTf		42	20
5		X = ONf		12	35
6		X = Br		73	53
7		X = OTf		47	44
8		X = Br		37	33
9		X = OTf		15	29
10		X = Br		75	31
11		X = OTf		46	20
12		X = Br		52	35
13		X = OTf		20	30
14		X = Br		No reaction after 5 days	
15		X = OTf		26	24
16		X = Br		No reaction after 10 days	
17		X = OTf		168	16
18		X = OTf		33	29

the electron-rich MeO-substituted substrates (entries 8 and 9) reacted faster than electron-poor ones. For sterically hindered 2-substituted aryl bromides and triflates, the phosphination required longer reaction times and lower yields were obtained.

Preliminary experiments showed that Pd/C could be used twice without diminishing its activity by loading the catalyst in a thimble. During the third run, no catalysis occurred. Presumably, the palladium species which dissolved in the course of reaction did not re-deposit on charcoal after the reaction<sup>13</sup> in a sufficient amount, i.e. the leaching rate of the palladium was too fast to allow multiple re-use.

The mechanism of the phosphination is likely to be similar to our suggested mechanism<sup>1,2</sup> in which palladium, either on the charcoal surface, or in solution,

ligated by phosphines catalyzes the reaction through the formation of phosphonium salts,<sup>14</sup> aryl-Pd/aryl-P exchange and C-P activation.<sup>15,16</sup>

In conclusion, a variety of functionalized phosphines were prepared by the operationally simple phosphination of aryl bromides and triflates using triphenylphosphine and a Pd/C catalyst.

*Experimental:* In a typical experiment, 4-bromoacetophenone (199 mg, 1 mmol), 10% palladium on charcoal (10 mg, 0.01 mmol) and triphenylphosphine (655 mg, 2.5 mmol) were dissolved in DMF (4 ml) in a Teflon screw-capped flask under nitrogen. The reaction mixture was heated to 160°C for 32 h. The reaction was cooled down and dissolved in a minimal amount of dichloromethane, and the product was purified by column chromatography on silica gel using hexane/

ethyl acetate (15/1) as the eluent to obtain the 4-(diphenylphosphino)acetophenone in 46% yield as a white solid.

### Acknowledgements

The authors would like to thank the Direct Grant of the Chinese University of Hong Kong for financial support.

### References

1. Kwong, F. Y.; Chan, K. S. *Chem. Commun.* **2000**, *11*, 1069–1070.
2. (a) Kwong, F. Y.; Chan, K. S. *Organometallics* **2000**, *19*, 2058–2060; (b) Kwong, F. Y.; Lai, C. W.; Tian, Y.; Chan, K. S. *Tetrahedron Lett.* **2000**, *41*, 10285–10289.
3. For the use of air-sensitive and expensive phosphinating reagents, see (a) Cai, D. W.; 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. *Org. Synth., Coll. Vol.* **1999**, *76*, 6–11; (c) Herd, O.; Hessler, A.; Hingst, M.; Machnitzki, P.; Tepper, M.; Stelzer, O. *Catal. Today* **1998**, *42*, 413–420; (d) Ager, D. J.; East, M. B.; Eisenstadt, A.; Laneman, S. A. *Chem. Commun.* **1997**, 2359–2360.
4. (a) Fu, Y.-S.; Yu, S. *Angew. Chem., Int. Ed.* **2001**, *40*, 437–440; (b) Mehnert, C. P.; Weaver, D. W.; Ying, J. Y. *J. Am. Chem. Soc.* **1998**, *120*, 12289–12296; (c) Buchmeyer, M. R. *Chem. Rev.* **2000**, *100*, 1565–1604.
5. Anson, M. S.; Lesse, M. P.; Tonks, L.; Williams, J. M. J. *J. Chem. Soc., Dalton Trans.* **1998**, 3529–3538.
6. Pham-Huu, C.; Keller, N.; Charbonniere, L. J.; Ziessel, R.; Ledoux, M. J. *Chem. Commun.* **2000**, 1871–8172.
7. (a) Venkatraman, S.; Li, C.-J. *Org. Lett.* **1999**, *1*, 1133–1136; (b) Bamfield, P.; Quan, P. M. *Synthesis* **1978**, 537.
8. Bleicher, L.; Cosford, N. D. P. *Synlett* **1995**, 1115–1116.
9. Roth, G. P.; Farina, V.; Liebeskind, L. S.; Peña-Cabrera, E. *Tetrahedron Lett.* **1995**, *36*, 2191–2194.
10. (a) Marck, G.; Villiger, A.; Bucherker, R. *Tetrahedron Lett.* **1994**, *35*, 3277–3280; (b) Ennis, D. S.; McManus, J.; Wood-Kaczmar, W.; Richardson, J.; Smith, G. E.; Carstairs, A. *Org. Process. Res. Dev.* **1999**, *3*, 248–252; (c) Gala, D.; Stamford, A.; Jenkins, J.; Kugelman, M. *Org. Process. Res. Dev.* **1997**, *1*, 163–164; (d) Dyer, U. C.; Shapland, P. D.; Tiffin, P. D. *Tetrahedron Lett.* **2001**, *42*, 1765–1767.
11. Rossi, R.; Bellina, F.; Carpita, A.; Gori, R. *Synlett* **1995**, 344–345.
12. Hallberg, A.; Westfelt, L. *J. Chem. Soc., Perkin Trans. 1* **1984**, 933–935.
13. Jayasree, S.; Seayad, A.; Chaudhari, R. V. *Chem. Commun.* **1999**, 1067–1068.
14. Migita, T.; Nagai, T.; Kiuchi, K.; Kosugi, M. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2869–2870.
15. For mechanistic studies of Pd-aryl/P-aryl exchange using stoichiometric amounts of palladium complexes, see: (a) Kong, K. C.; Cheng, C. H. *J. Am. Chem. Soc.* **1991**, *113*, 6313–6315; (b) Goodson, F. E.; Wallow, T. I.; Novak, B. M. *J. Am. Chem. Soc.* **1997**, *119*, 12441–12453; (c) Grushin, V. V. *Organometallics* **2000**, *19*, 1888–1900.
16. Garrou, P. E. *Chem. Rev.* **1985**, *85*, 171–185.