Pergamon

Tetrahedron Letters 41 (2000) 10285–10289

TETRAHEDRON LETTERS

A novel synthesis of functionalised tertiary phosphines by palladium catalysed phosphination with triarylphosphines

Fuk Yee Kwong, Chi Wai Lai, Yuan Tian and Kin Shing Chan*

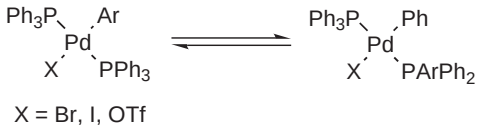
Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong

Received 25 August 2000; revised 13 October 2000; accepted 19 October 2000

Abstract

The palladium catalysed Pd-aryl/P-aryl exchange was applied in the synthesis of various functionalised phosphines from their corresponding substituted aryl triflates using triarylphosphines as the phosphinating agents. This method tolerated many functional groups including ketone, aldehyde, ester, nitrile, methyl ether, pyridyl and chloride groups.

Tertiary phosphines are an important type of ligands in transition metal catalysed reactions.[1] Functional group incorporation is necessary for modified catalysis. However, the synthetic methods available are limited in scope for the synthesis of functionalised phosphines. The preparation of phosphines from the literatures can be divided into two categories. The reaction of halophosphines with organometallic reagents;[2] or transition metal catalysed couplings of primary or secondary phosphines with aryl halides/sulfonate esters.[3–7] The former methodology is not compatible with base-sensitive compounds since organo-lithium/magnesium reagents are used. Easily reducible functional groups such as the aldehyde group are not tolerated in the latter transition-metal catalysed category because reducing zinc metal is used.[4] Although palladium catalysed phosphination using (trimethylsilyl)diphenylphosphine tolerates many functional groups, it is mainly limited to aryl iodides and incompatible with the aldehyde functional group.[5] Besides, the complementary palladium-catalysed phosphination using diphenylphosphine oxide[6] or diphenylphosphine–borane[7] requires subsequent reduction or deprotection steps.

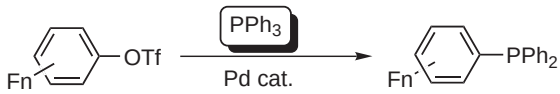


(1)

* Corresponding author.

0040-4039/00/$ - see front matter
PII: S0040-4039(00)01850-5

In order to seek a functional group tolerant phosphination, the interesting aryl–aryl exchange reaction of the palladium bound aryl ring with the phosphorus bound phenyl ring was used (Eq. (1)).[8,9] However, the application of this reaction in synthesis remains limited.[10] Herein, we report the application of the catalytic aryl–aryl exchange for the synthesis of substituted aryl phosphines using economical triarylphosphines as the phosphinating agents (Eq. (2)). This method was found to be compatible with many functional groups such as ketone, aldehyde, ester, nitrile, methoxy and pyridyl groups (Eq. (2)).

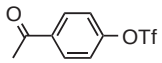
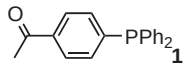
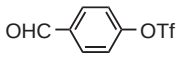
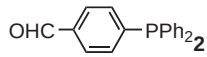
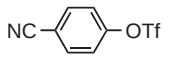
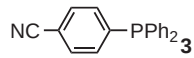
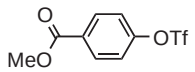
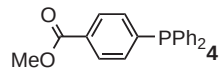
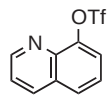
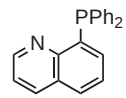
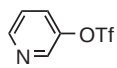
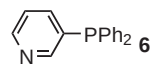
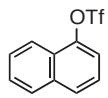
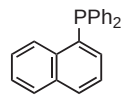
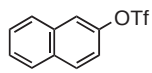
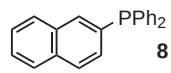
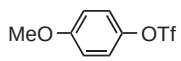
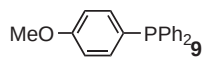
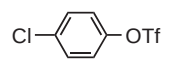
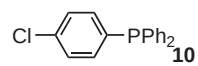
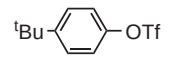
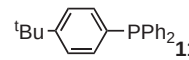


(2)

Fn = COMe, CHO, COOMe, CN, OMe, Cl, py

In a typical experiment, 4-acetylphenyl triflate was transformed to 4-(diphenylphosphino)acetophenone **1** with 10 mol% of $Pd(OAc)_2$, 2.3 equiv. of triphenylphosphine[11] in DMF for 2 hours at 110°C (Table 1, entry 1). Besides, the 4-formylphenyl triflate underwent smooth

Table 1
Palladium catalysed phosphination of various functionalised aryl triflates using triphenylphosphine

Entry	Substrates	Products	Time/h	%yield[a]
1		 **1**	2	37
2		 **2**	3	31
3		 **3**	3	32
4		 **4**	5	30
5		 **5**	72	45
6		 **6**	24	20 (33)[b]
7		 **7**	16	27[b]
8		 **8**	4	51[b]
9		 **9**	6	20 (25)[b]
10		 **10**	5	45[b]
11		 **11**	6	50[b]

[a] Isolated yield.

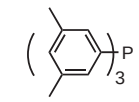
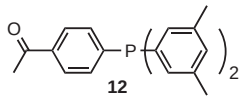
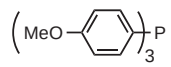
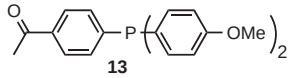
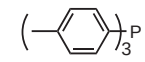
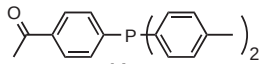
[b] GC yield using anthracene as the internal standard.

reaction to give **2** in 31% yield which showed that this phosphination tolerated a redox sensitive functional group (Table 1, entry 2). In contrast, the previous synthesis of aldehyde phosphine **2** involved an acetal protective pathway.[12] Moreover, the traditional synthesis of 4-(diphenylphosphino)benzonitrile **3** and methyl 4-(diphenylphosphino)benzoate **4** required several steps and the overall yields were approximately 11% and 21%, respectively.[13] In contrast, the phosphines **3** and **4** were obtained in 32% and 30% yield, respectively, in one step (Table 1, entries 3, 4).

The transformation of quinolyl and pyridyl triflates to their corresponding phosphines **5** and **6** required much longer reaction times (Table 1, entries 5 and 6). Presumably, the chelating heteroatom coordinated to the palladium centre and rendered the complex coordinatively saturated,[14] hence the catalytic activity was reduced. The quinolyl phosphine **5** was found to be a useful ligand precursor for asymmetric catalysis.[15] The naphthyl derivatives were successfully phosphinated to yield the naphthyl phosphines **7** and **8** (Table 1, entries 7 and 8). The 1-naphthyl triflate reacted slower than the 2-napthyl substrate probably due to an increase in steric hindrance at the *ortho*-position (Table 1, entries 7 and 8). In fact, this phosphination also tolerated other functional groups such as methoxy and chloride (Table 1, entries 9 and 10). The low yield of the phosphine product **9** was due to the partial oxidation of the product during purification. Although palladium-catalysed phosphination using triphenylphosphine as the reagent tolerated many functional groups, it was found to be incompatible with *p*-nitrophenyl triflate. Initial experiments revealed that the nitro group was reduced to an amino group when the reaction mixture was heated at 110°C for 2 days.[16]

Although both tetrakis(triphenylphosphine) palladium(0) and palladium(II) acetate catalysed phosphination and gave similar yield of the products, $Pd(OAc)_2$ was the catalyst of choice because other triarylphosphines, such as trixylylphosphine, tri(4-methoxyphenyl)phosphine and tri(4-tolyl)phosphine could be used as the phosphinating reagents instead of just PPh_3 only (Table 2, entries 1–3). Therefore, an array of tailor-made phosphines can be prepared easily through this direct methodology in combination with suitable substrates containing different triarylphosphines.

Table 2
Palladium catalysed phosphination of 4-acetylphenyl triflate using triarylphosphines.

Entry	PAr_3	Products	Time/h	%yield[a]
1		 **12**	8	28
2		 **13**	6	24
3		 **14**	8	30

[a] Isolated yield.

A plausible mechanism for this phosphination starts with in situ reduction of palladium(II) acetate by triphenylphosphine to palladium(0) (Fig. 1).[17] The substituted aryl triflate undergoes oxidative addition with Pd(0) to afford an aryl palladium(II) species. The facile aryl–aryl

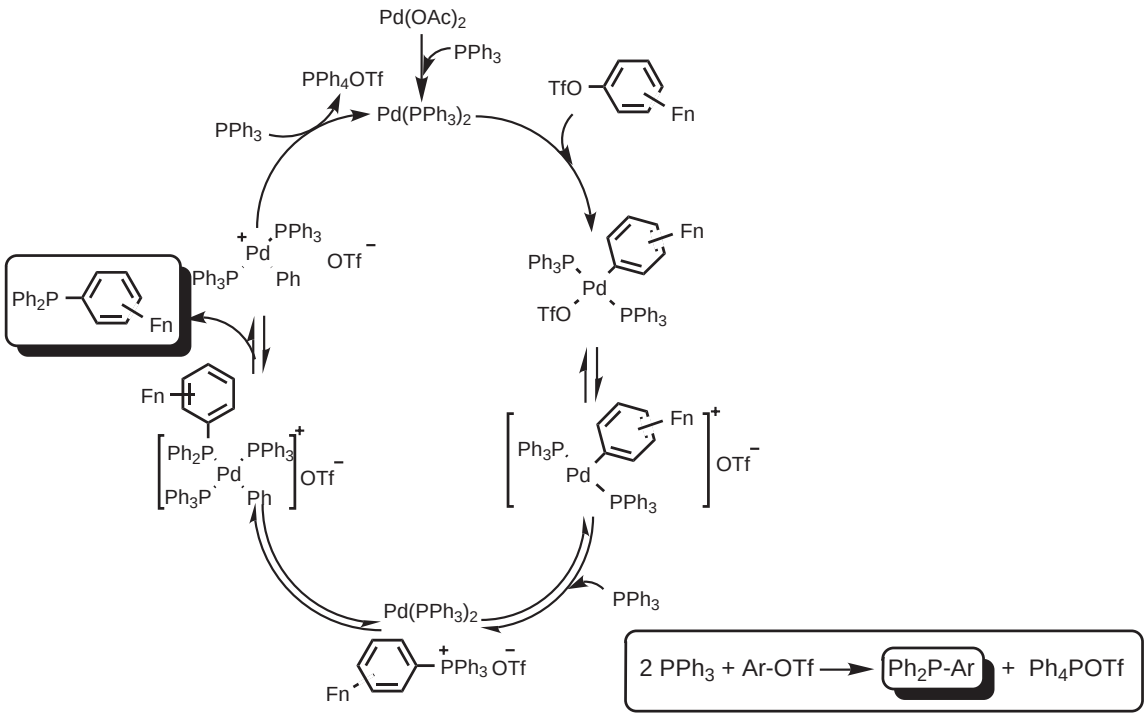


Figure 1. Suggested mechanism for palladium catalysed phosphination

exchange occurs by reductive elimination between Pd–Ar with triphenylphosphine to give a phosphonium salt,[18] which subsequently undergoes C–P bond oxidative addition with Pd(0) to generate the coordinated phosphine product, and phenyl–palladium species. Finally, ligand substitution affords the functionalised phosphine and reductive elimination of palladium bound phenyl group with triphenylphosphine regenerates the catalytic active Pd(0) species and Ph_4POTf which was isolated in 72% yield (Fig. 1). In fact, the aryldiphenylphosphine was observed as the major product and only a trace amount of diarylphenylphosphine was detected by GC–MS analysis with extended reaction time. Therefore, arylphenylphosphination by further exchange is very slow.

In conclusion, a variety of functionalised phosphines were prepared by palladium catalysed phosphination of aryl triflates using economical triarylphosphines as the phosphinating agent. This methodology tolerated many functional groups including ketone, aldehyde, ester, nitrile, methoxy and pyridyl groups.

Acknowledgements

We thank the Research Grants Council of Hong Kong (MF/rgcgrant/rgccav/564/98) for financial support.

References

1. Kosolapoff, G. M.; Maier, L. *Organic Phosphorus Compounds*, *Vol. 1*, Wiley-Interscience: New York, 1972.
2. (a) Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayaashi, H.; Taketomi, T.; Akutagawa, S.; Noyori, R. J. *Org. Chem.* **1986**, *51*, 629–631. (b) Takaya, H.; Akutagawa, S.; Noyori, R. *Org. Synth. Coll. Vol. VIII* **1993**, 57–62.
3. (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.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *Org. Synth.*, *Coll. Vol. 76*, **1999**, 6–11. (c) Herd, O.; Hebler, A.; Machnitzki, P.; Tepper, M.; Stelzer, O. *Catalysis Today* **1998**, *42*, 413–420.
4. Ager, D. J.; East, M. B.; Eisenstadt, A.; Laneman, S. *Chem. Commun.* **1997**, 2359–2360.
5. Tunney, B. H.; Stille, J. K. *J. Org. Chem.* **1987**, *52*, 748–753.
6. For recent references, see: (a) Gelpke, A. E. S.; Kooijman, H.; Spek, A. L.; Hiemstra, H. *Chem. Eur. J.* **1999**, *5*, 2472–2482. (b) Ding, K.; Wang, Y.; Yun, H.; Liu, J.; Wu, Y.; Terada, M.; Okubo, Y.; Mikami, K. *Chem. Eur. J.* **1999**, *5*, 1734–1737. (c) Vyskocil, S.; Smrcina, M.; Hanus, V.; Polasek, M.; Kocovsky, P. *J. Org. Chem.* **1998**, *63*, 7738–7748. (d) Martorell, G.; Garcias, X.; Janura, M.; Saá, J. M. *J. Org. Chem.* **1998**, *63*, 3463–3467. (e) Bringmann, G.; Wuzik, A.; Vedder, C.; Pfeiffer, M.; Stalke, D. *Chem. Commun.* **1998**, 1211–1212.
7. Lipshutz, B. H.; Buzard, D. H.; Yun, C. S. *Tetrahedron Lett.* **1999**, *40*, 201–204.
8. Garrou, P. E. *Chem. Rev.* **1985**, *85*, 171–185.
9. For mechanistic studies of Pd–aryl/P-aryl exchange using stoichiometric amount 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.
10. For the first synthetic application, see: (a) Kwong, F. Y.; Chan, K. S. *Organometallics* **2000**, *19*, 2058–2060. (b) Kwong, F. Y.; Chan, K. S. *Chem. Commun.* **2000**, 1069–1070.
11. Triphenylphosphine was used as received and without recrystallisation.
12. (a) Hoots, J. E.; Rauchfuss, T. B.; Wrobleski, D. A. *Inorg. Synth.* **1982**, *21*, 175–177. (b) Schiemenz, G. P.; Kaack, H. *Leibigs. Ann. Chem.* **1973**, 1494–1497.
13. (a) Chou, W. N.; Pomerantz, M. *J. Org. Chem.* **1991**, *56*, 2762–2769. (b) Schiemenz, G. P.; Siebeneich, H. U. *Chem. Ber.* **1969**, *102*, 1883–1886. (c) Aexandrovich, P. S.; DeMejo, L. P.; Jadwin, T. A.; Wilson, J. C. US Patent 4,837,394.
14. Hu, W. H.; Chen, C. C.; Xue, G. P.; Chan, A. S. C. *Tetrahedron*: *Asymmetry* **1998**, *9*, 4183–4192.
15. Francio, G.; Faraone, F.; Leitner, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 1428–1430.
16. Unpublished results.
17. Amatore, C.; Jutand, A.; M'Barki, M. A. *Organometallics* **1992**, *11*, 3009–3013.
18. (a) Hinkle, R. J.; Stang, P. J.; Kowalalski, M. H. *J. Org. Chem.* **1990**, *55*, 5033–5036. (b) Kowalalski, M. H.; Hinkle, R. J.; Stang, P. J. *J. Org. Chem.* **1989**, *54*, 2783–2784. (c) Migita, T.; Nagai, T.; Kiuchi, K.; Kosugi, M. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2869–2870.