Convenient and direct preparation of tertiary phosphines *via* nickel-catalysed cross-coupling

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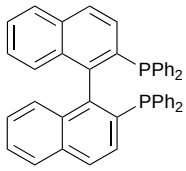
Nickel-catalysed cross-coupling of aryl sulfonates and aryl halides with chlorodiphenylphosphine and a reductant directly affords tertiary phosphines, which have application in a wide variety of asymmetric catalysis.

Tertiary phosphines are extremely useful ancillary ligands in homogeneous catalysis, especially as chiral ligands in asymmetric homogeneous catalysis as exemplified by **1**–**3**.[1–8] The preparations of tertiary phosphines can be divided into four major categories: Friedel–Crafts reactions,[9,10] the reaction of halophosphines with organometallic reagents[11,12] and the reaction of phosphides[13–15] or diarylphosphine compounds[16–18] in the presence of a transition metal catalyst with aryl halides or sulfonate esters. All of the methods have drawbacks ranging from limitations due to incompatabilities with other functional groups, the necessity for a separate step to reduce the phosphine oxide, to the use of pyrophoric reagents. We report here a convenient and direct route to tertiary phosphines by transition metal cross-coupling reaction that eliminates these problems.



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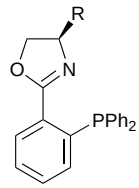

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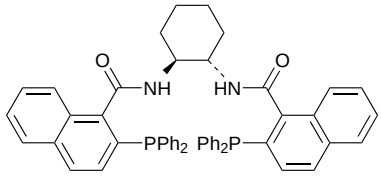

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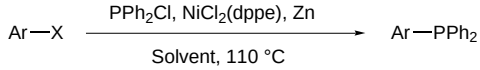
We have determined that tertiary phosphines can be prepared from aryl trifluoromethanesulfonates by nickel-catalysed cross-coupling with Ph_2PCl in the presence of zinc in DMF at 110 °C (Scheme 1). Ph_2PCl has the advantage that it is not pyrophoric, inexpensive and readily available for large scale usage. For example, 2-diphenylphosphinonaphthalene **5** is prepared from **4** *via* nickel-catalysed cross-coupling with Ph_2PCl in 89% yield.† The zinc plays a dual role in the reaction. It reduces Ni^{II} to Ni^0 as well as providing Ph_2PZnCl for transmetallation.

This methodology appears to be quite general for the preparation of other tertiary phosphines (Table 1). The nickel-catalysed cross-coupling procedure successfully produces phosphines in good yields directly from aromatic sulfonates, aromatic halogens, benzylic bromides and vinyl bromides and iodides. Also, the cross-coupling can occur with aromatic



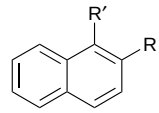
Scheme 1

Table 1 Examples of nickel-catalysed cross couplings

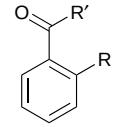
Substrate	Product	Yield (%)
4	**5**	89
6	**5**	78
7	**8**	95
9	**10**	84
11	**10**	46
12	**13**	67
14	**15**	46
16	**17**	90[a]
18	**19**	80
20	**21**	45
22	**1**	52

[a] Isolated as the phosphine oxide by air oxidation during work up.

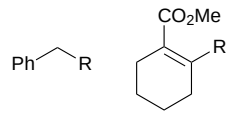
halides and sulfonates that contain *ortho*-substitution. Benzylic halides are extremely active substrates and reactions are completed in minutes. Surprisingly, the coupling reaction tolerates the presence of amides while carboxylic acid inhibit reaction.



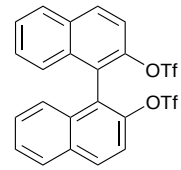
4 R = OTf, R′ = H
5 R = PPh_2, R′ = H
6 R = Br, R′ = H
7 R = OTf, R′ = CO_2Me
8 R = PPh_2, R′ = CO_2Me



9 R = OTf, R′ = OMe
10 R = PPh_2, R′ = OMe
11 R = Br, R′ = OMe
12 R = OTf, R′ = NHBn
13 R = PPh_2, R′ = NHBn
14 R = Br, R′ = (*S*)-NHCHMePh
15 R = PPh_2, R′ = (*S*)-NHCHMePh



16 R = Br
17 R = PPh_2
18 R = OTf
19 R = PPh_2
20 R = Br
21 R = PPh_2



22
(Tf = CF_3SO_2)

Trifluoromethanesulfonate substrates give higher yields compared to the corresponding bromide substrate due to hydrodehalogenation side reaction. Double cross-coupling of the *S*-isomer of the bis(trifluoromethanesulfonate) **22** can be achieved to form *S*-BINAP **1** without any racemisation of the axial chirality.‡

This methodology is a convenient procedure to prepare a wide variety of tertiary phosphines. The use of a cheap phosphorus reagent coupled with the tolerance of the reaction to a wide variety of functional groups as well as direct access to phosphorus(III) products makes this a useful, versatile approach to phosphorus ligands.

Footnotes and References

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† *Typical reaction procedure*: to a solution of **4** (10.6 g, 40 mmol), $NiCl_2$(dppe) [dppe = ethylenebis(diphenylphosphine)] (0.315 g, 0.60 mmol) and Ph_2PCl (8.85 g, 40 mmol) in anhydrous DMF (25 ml) was added Zn (4.10 g, 63 mmol) portionwise at 5–10 °C. The mixture was heated to 100–110 °C and monitored by GC. The reaction mixture was cooled to 80 °C, filtered and rinsed with a minimal amount of DMF. The combined filtrate was cooled to 5 °C and the product crystallised overnight. The solids were filtered, rinsed with MeOH and dried at room temp. under vacuum to give 11.21 g (89%) of **5** as an off-white solid. Satisfactory ^1H and ^{31}P NMR and mass spectral data were obtained on all the products.

‡ Optical purities of substrates and products were determined by optical rotation.

1 D. J. Ager and M. B. East, *Asymmetric Synthetic Methodology*, CRC Press, Boca Raton, FL, 1995.
2 P. von Matt and A. Pfaltz, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 566.
3 P. von Matt, O. Loiseleur, G. Koch, A. Pfaltz, C. Lefeber, T. Feucht and G. Helmchen, *Tetrahedron: Asymmetry*, 1994, **5**, 573.
4 B. M. Trost and R. C. Bunt, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 99.
5 S. Akutagawa, *Appl. Catal. A*, 1995, **128**, 171.
6 R. Noyori, *Science*, 1990, **248**, 1194.
7 R. Noyori and H. Takaya, *Acc. Chem. Res.*, 1990, **23**, 345.
8 H. Takaya, T. Ohta and R. Noyori, in *Asymmetric Hydrogenation*, ed. I. Ojima, New York, NY, 1993.
9 W. Ude, S. Besecke, A. Riemann and G. Schroeder, *Ger. Offen.*, 1986, DE 3425282 A1.
10 I.-Y. Wan, J. E. McGrath and T. Kashiwagi, *ACS Symp. Ser.*, 1995, **599**, 29.
11 E. P. Kyba, M. C. Kerby and S. P. Rines, *Organometallics*, 1986, **5**, 1189.
12 F. Langer, K. Puntener, R. Sturmer and P. Knochel, *Tetrahedron: Asymmetry*, 1997, **8**, 715.
13 S. J. Coote, G.J. Dawson, C. G. Frost and J. M. J. Williams, *Synlett*, 1993, 509.
14 M. D. Fryzuk and B. Bosnich, *J. Am. Chem. Soc.*, 1977, **99**, 6262.
15 M. D. Fryzuk and B. Bosnich, *J. Am. Chem. Soc.*, 1978, **100**, 5491.
16 D. Cai, J. F. Payack, D. R. Bender, D. L. Hughes, T. R. Verhoeven and P. J. Reider, *J. Org. Chem.*, 1994, **59**, 7180.
17 S. E. Tunney and J. K. Stille, *J. Org. Chem.*, 1987, **52**, 748.
18 S. R. Gilbertson and G. W. Starkey, *J. Org. Chem.*, 1996, **61**, 2922.

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