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

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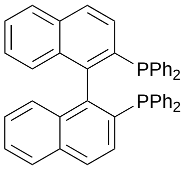
Nickel-catalysed cross-coupling of aryl sulfonates and aryl halides with chlorodiphenylphosphine and a reductant directly affords tertiary phosphines, which have application in a wide variety of asymmetric catalysis.

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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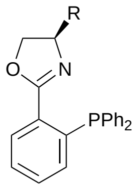

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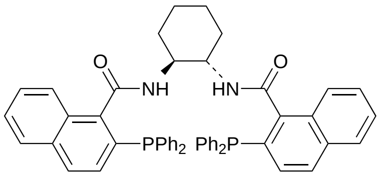

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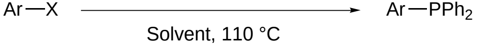
We have determined that tertiary phosphines can be prepared from aryl trifluoromethanesulfonates by nickel-catalysed cross-coupling with Ph_2PCl in the presence of zinc in DMF at 110 °C (Scheme 1). Ph_2PCl has the advantage that it is not pyrophoric, inexpensive and readily available for large scale 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 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.



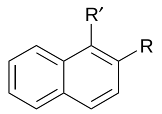
$$\mathrm{Ar{-}X} \xrightarrow[\text{Solvent, 110 °C}]{\mathrm{PPh_2Cl,\ NiCl_2(dppe),\ Zn}} \mathrm{Ar{-}PPh_2}$$

Scheme 1

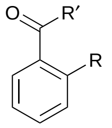
Table 1 Examples of nickel-catalysed cross couplings

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

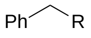
[a] Isolated as the phosphine oxide by air oxidation during work up.



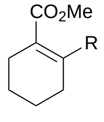
4 R = OTf, R′ = H
5 R = PPh_2, R′ = H
6 R = Br, R′ = H
7 R = OTf, R′ = CO_2Me
8 R = PPh_2, R′ = CO_2Me



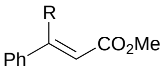
9 R = OTf, R′ = OMe
10 R = PPh_2, R′ = OMe
11 R = Br, R′ = OMe
12 R = OTf, R′ = NHBn
13 R = PPh_2, R′ = NHBn
14 R = Br, R′ = (*S*)-NHCHMePh
15 R = PPh_2, R′ = (*S*)-NHCHMePh



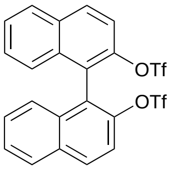
16 R = Br
17 R = PPh_2



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.

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