*J. Chem. Research (S)*,
1998, 264–265†

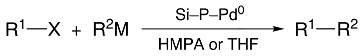
# Silica-supported Phosphine Palladium(0) Complex Catalysed Cross-coupling of Organic Halides with Organotin and Organomagnesium Reagents†

**Ming-Zhong Cai,[a] Cai-Sheng Song[b] and Xian Huang*[a]**

[a]*Department of Chemistry, Hangzhou University, Hangzhou 310028, P.R. China*
[b]*Department of Chemistry, Jiangxi Normal University, Nanchang 330027, P.R. China*

Silica-supported phosphine palladium(0) complex is an efficient catalyst for the cross-coupling of organic halides, except for aliphatic halides, with organotin and organomagnesium reagents; the polymeric catalyst is stable and can be easily separated from a reaction mixture and reused.

The palladium-catalysed cross-coupling reaction has constituted an important method for organic synthesis, and a wide variety of organic electrophiles and organometallic reagents can be used.[1–4] For example, the cross-coupling of organic halides such as acid chlorides,[5] aryl halides[6] and vinyl halides[7] with organotin compounds has been reported to be readily achieved in the presence of a palladium complex in high yields. In most cases, homogeneous catalysts are used, but it is difficult to recover them from products. The development of useful reactions catalysed by soluble transition metals has led to interest in evolving 'insolubilized' versions of these catalysts for ease of recovery and work-up.[8] Hybrid catalysts combining the attributes of conventional homogeneous catalysts with the experimental simplicity of heterogeneous catalysts have been proven to be fruitful subjects for research by both academic and industrial chemists.[9] We have studied the phenylation of acid chlorides and aryl iodides by sodium tetraphenylborate, using a silica-supported phosphine palladium(0) complex ('Si'–P–Pd$^0$').[10] However, to our knowledge, there has been no specific report regarding polymer-bound palladium catalyst for the cross-coupling of organic halides with organotin and organomagnesium reagents. To extend the application of polymeric catalysts ('Si'–P–Pd$^0$') to other organic reactions, we presently wish to report the characteristic features of a polymeric palladium(0) catalyst ('Si'–P–Pd$^0$') for the cross-coupling reactions of organic halides with organotin and organomagnesium reagents (Scheme 1).



$$R^1{-}X + R^2M \xrightarrow[\text{HMPA or THF}]{\text{Si–P–Pd}^0} R^1{-}R^2$$

**Scheme 1** $R^1 = Ar, ArCO$; $X = Cl, Br, I$; $R^2 = Me, Ph$; $M = SnMe_3, MgBr$

Treatment of benzoyl chloride (2 mmol) with tetramethyltin (2,2 mmol) in hexamethylphosphoric triamide (HMPA, 1 ml) at 65 °C for 20 h in the presence of a catalytic amount of 'Si'–P–Pd$^0$ (0.02 mmol, 1 mol%) afforded acetophenone in 85% yield. The catalytic activity of the recovered catalyst was tested for the cross-coupling of benzoyl chloride with tetramethyltin for two recycles and it was found that the yield of acetophenone decreased by 2 and 5% in each recycle, respectively. The cross-coupling reaction can tolerate a number of other functional groups on the acid chlorides, *e.g.* Cl, $NO_2$, $CO_2CH_3$ substituents are not affected. Typical results are summarized in Table 1. As is evident, a variety of substituted acetophenones can successfully be prepared by treating aromatic acid chlorides with tetramethyltin. However, the reactivity of aliphatic acid chlorides was poor and only trace products were obtained. The cross-coupling of methyl 4-iodobenzoate with tetramethyltin also proceeded smoothly at 65 °C in the presence of 'Si'–P–Pd$^0$ without CuI, and methyl 4-methylbenzoate was obtained after 20 h in 88% yield. However, the reactivity of methyl 4-bromobenzoate is obviously lower than that of the corresponding iodide under the same conditions (Table 1).

The cross-coupling reaction between aryl halides and phenylmagnesium bromide readily took place in tetrahydrofuran (THF) and in the presence of a catalytic amount of 'Si'–P–Pd$^0$; the results are also summarized in Table 1. Aryl iodides coupled with phenylmagnesium bromide at room temperature for 20 h to give the cross-coupled products almost exclusively, in high yields, whereas 4-methylbromobenzene reacted with phenylmagnesium bromide in refluxing THF to give 4-methyldiphenyl as the main product together with a considerable amount of homocoupled diphenyl.

In conclusion, the silica-supported phosphine palladium(0) complex described here can efficiently catalyse the cross-coupling reaction of organic halides with organotin and organomagnesium reagents; this polymeric palladium catalyst can be reused without noticeable loss of activity. The method presented for preparing ketones and biaryls has the advantages of readily available starting materials, simple and practical procedures, mild reaction conditions and good yields.

## Experimental

Mps were uncorrected. IR spectra were obtained on a Shimadzu IR-435 instrument. The $^1H$ NMR spectra were obtained on a JEOL FX-90Q (90 MHz) instrument with $Me_4Si$ as an internal standard in $CDCl_3$ as solvent. All solvents were dried and distilled before use.

*Preparation of Poly-γ-(diphenylphosphino)propylsiloxane('Si'–P).*—A mixture of fumed silica (6.0 g) and γ-chloropropyltriethoxysilane (5.0 g) in toluene (140 ml) was stirred at 120 °C for 24 h. Distilled water (20 ml) and 10% hydrochloric acid (0.2 ml) were added and the mixture was boiled under reflux for another 48 h. After being cooled to room temperature, the mixture was filtered, washed with distilled water (4 × 50 ml) and dried under vacuum. The resulting white powder was stirred with 1,1,1,3,3,3-hexamethyldisilazane (10 ml) in toluene (80 ml) at 100 °C for 48 h. The mixture was allowed to cool and then filtered, washed with toluene (3 × 20 ml) and acetone (3 × 20 ml) and dried under vacuum to give 7.0 g of poly-γ-chloropropylsiloxane ('Si'–Cl). The chlorine content was 7.24 wt%.

To a 100 ml THF solution of lithiodiphenylphosphine (0.15 mol dm$^{-3}$) was added 'Si'–Cl(6.0 g), and the mixture was boiled under reflux under nitrogen for 30 h. After being cooled to room temperature, 2-chloro-2-methylpropane (2 ml) was added and the mixture was stirred at room temperature for 2 h. The mixture was filtered, washed with ethanol (3 × 30 ml) and distilled water (5 × 40 ml) and dried under vacuum to give 6.5 g of poly-γ-(diphenylphosphino)propylsiloxane ('Si'–P). The phosphine content was 4.37 wt%.

---

*To receive any correspondence.

†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1998, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

**Table 1** Cross-coupling of organic halides with organotin and organomagnesium reagents[a]

| Organic halide | Sn/Mg reagent | Conditions | Product (% yield)[b] |
|---|---|---|---|
| $PhCOCl$ | $SnMe_4$ | HMPA, 65 °C | $PhCOCH_3$(85) |
| 4-$ClC_6H_4COCl$ | $SnMe_4$ | HMPA, 65 °C | 4-$ClC_6H_4COCH_3$(81) |
| 4-$CH_3OC_6H_4COCl$ | $SnMe_4$ | HMPA, 65 °C | 4-$CH_3OC_6COCH_3$(80) |
| 2-$ClC_6H_4COCl$ | $SnMe_4$ | HMPA, 65 °C | 2-$ClC_6H_4COCH_3$(76) |
| 4-$NO_2C_6H_4COCl$ | $SnMe_4$ | HMPA, 65 °C | 4-$NO_2C_6H_4COCH_3$(83) |
| 4-$CH_3OCOC_6H_4I$ | $SnMe_4$ | HMPA, 65 °C | 4-$CH_3C_6H_4CO_2CH_3$(88) |
| 4-$CH_3OCOC_6H_4Br$ | $SnMe_4$ | HMPA, 65 °C | 4-$CH_3C_6H_4CO_2CH_3$(70) |
| $PhI$ | $PhMgBr$ | THF, 30 °C | $Ph_2$(95) |
| 4-$CH_3OC_6H_4I$ | $PhMgBr$ | THF, 30 °C | 4-$CH_3OC_6H_4C_6H_5$(90) |
| $PhBr$ | $PhMgBr$ | THF, 65 °C | $Ph_2$(85) |
| 4-$CH_3C_6H_4Br$ | $PhMgBr$ | THF, 65 °C | 4-$CH_3C_6H_4Ph$(79) |

[a] Coupling reactions of organic halides with organotin reagent were carried out at 65 °C with 2 mmol of acid chloride or aryl halide, 2.2 mmol of tetramethyltin and 0.02 mmol of palladium catalyst in 1 ml of HMPA for 20 h; coupling reactions of aryl halides with organomagnesium reagent were carried out at 30 or 65 °C with 1 mmol of aryl halide, 1.5 mmol of phenylmagnesium bromide and 0.01 mmol of palladium catalyst in 5 ml THF for 20 h. [b] Yields are of isolated, pure product and based on the organic halides.

*Preparation of 'Si'–P–Pd$^0$*.—To a solution of $PdCl_2$ (0.15 g) in acetone (40 ml) was added 'Si'–P (2.05 g). The mixture was refluxed under nitrogen for 48 h. The yellow solid produced was filtered off, washed with acetone (3 × 30 ml), then stirred with hydrazine hydrate (1.50 g, 30 mmol) and EtOH (20 ml) at 30 °C under nitrogen for 3 h. The resulting product was filtered off, washed with EtOH (4 × 30 ml) and $Et_2O$ (2 × 30 ml and dried under vacuum to give 1.86 g of the dark-green polymeric palladium(0) complex. The palladium content was 3.20 wt% and the phosphine content was 3.45 wt%.

*Typical Procedure for the Cross-coupling of Organic Halides with Tetramethyltin*.—A mixture of $SnMe_4$ (0.393 g, 2.2 mmol), benzoyl chloride (0.282 g, 2 mmol) and 'Si'–P–Pd$^0$ (0.070 g, 0.02 mmol) in HMPA (1 ml) was stirred under nitrogen at 65 °C for 20 h. The reaction mixture was cooled, dissolved in diethyl ether (50 ml). The 'Si'–P–Pd$^0$ was separated from the mixture by filtration, washed with diethyl ether (3 × 30 ml), dried *in vacuo* and reused in the next run. The ethereal solution was washed with distilled water (5 × 30 ml, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was purified by preparative TLC on silica gel (light petroleum–ethyl acetate = 7:1) to afford acetophenone (0.204 g, 85%).

Acetophenone.[5] $\nu_{max}$ (film)/cm$^{-1}$ 3050, 2940, 1680, 1600, 1450, 1360, 760, 690; $\delta_H$ ($CDCl_3$) 2.53 (3 H, s), 7.22–7.60 (3 H, m), 7.75–7.98 (2 H, m).

4′-Chloroacetophenone:[5] $\nu_{max}$ (film)/cm$^{-1}$ 3060, 2920, 1680, 1590, 1490, 1360, 820; $\delta_H$ ($CDCl_3$) 2.80 (3 H, s), 7.73 (2 H, d, $J$ 9.0 Hz), 8.20 (2 H, d, $J$ 9.0 Hz).

4′-Methoxyacetophenone:[5] $\nu_{max}$ (film)/cm$^{-1}$ 3040, 2920, 1675, 1600, 1360, 1255, 1170, 835; $\delta_H$ ($CDCl_3$) 2.70 (3 H, s), 4.08 (3 H, s), 7.05 (2 H, d, $J$ 9.0 Hz), 8.04 (2 H, d, $J$ 9.0 Hz).

2′-Chloroacetophenone:[11] $\nu_{max}$ (film)/cm$^{-1}$ 3050, 2920, 1690, 1590, 1430, 1360, 960, 755; $\delta_H$ ($CDCl_3$) 2.56 (3 H, s), 7.23 (4 H, s).

4′-Nitroacetophenone: Mp 78–79 °C (lit.[12] 79–80 °C); $\nu_{max}$ (KBr)/cm$^{-1}$ 2930, 1690, 1605, 1520, 1340, 870; $\delta_H$ ($CDCl_3$ 2.70 (3 H, s), 8.05 (2 H, d, $J$ 9.0 Hz), 8.26 (2 H, d, $J$ 9.0 Hz).

Methyl 4-methylbenzoate:[13] $\nu_{max}$ (film)/cm$^{-1}$ 2940, 1715, 1610, 1435, 1100, 840; $\delta_H$ ($CDCl_3$) 2.53 (3 H, s), 3.95 (3 H, s), 7.23 (2 H, d, $J$ 9.0 Hz), 7.95 (2 H, d, $J$ 9.0 Hz).

*Typical Procedure for the Cross-coupling of Aryl Halides with Phenylmagnesium*.—A mixture of phenylmagnesium bromide (1.5 mmol), iodobenzene (1 mmol) and 'Si'–P–Pd$^0$ (0.01 mmol) in THF (5 ml) was stirred under nitrogen at 30 °C for 20 h. Then a saturated aqueous $NH_4Cl$ solution (30 ml) was added and the mixture was stirred at 30 °C for 10 min, and extracted with diethyl ether (2 × 30 ml. The ethereal solution was washed with distilled water (2 × 20 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was purified by preparative TLC on silica gel (light petroleum) to give diphenyl (0.146 g, 95%).

Diphenyl: Mp 69–70 °C (lit.[17] 70 °C); $\nu_{max}$ (KBr)/cm$^{-1}$ 3040, 1600, 1480, 730, 695; $\delta_H$ ($CDCl_3$) 6.95–7.55 (10 H, m).

4-Methoxydiphenyl: Mp 87–88 °C (lit.[15] 90–91 °C); $\nu_{max}$ (KBr)/cm$^{-1}$, 3030, 1600, 1485, 1440, 1250, 1035, 830, 760; $\delta_H$ ($CDCl_3$ 3.72 (3 H, s), 6.81 (2 H, d, $J$ 9.0 Hz), 7.05–7.70 (7 H, m).

4-Methyldiphenyl: Mp 46–47 °C (lit.[16] 47.5 °C); $\nu_{max}$ (KBr)/cm$^{-1}$ 3050, 1485, 820, 750, 690; $\delta_H$ ($CDCl_3$) 2.32 (3 H, s), 6.95–7.62 (9 H, m).

This work was supported by the Natural Science Foundation of Jiangxi Province in China.

*Received, 6th October 1997; Accepted, 20th January 1998*
*Paper E/7/07180I*

## References

1 M. Kumada, *Pure Appl. Chem*., 1980, **52**, 669.
2 E. Negishi, *Acc. Chem. Res*., 1982, **15**, 340.
3 J. K. Stille, *Angew. Chem., Int. Ed. Engl*., 1986, **25**, 508.
4 J. M. Brown and N. A. Cooley, *Chem. Rev*., 1988, **88**, 1031.
5 D. Milstein and J. K. Stille, *J. Org. Chem*., 1979, **44**, 1613.
6 R. J. P. Corriu, B. Geng and J. J. E. Moreau, *J. Org. Chem*., 1993, **58**, 1443.
7 J. K. Stille and B. L. Groh, *J. Am. Chem. Soc*., 1987, **109**, 813.
8 C. G. Overberger and K. N. Sannes, *Angew. Chem., Int. Ed. Engl*., 1974, **13**, 99.
9 D. C. Bailey and S. H. Langer, *Chem. Rev*., 1981, **81**, 109.
10 M. Z. Cai, C. S. Song and X. Huang, *Synth. Commun*., in the press.
11 M. A. Thorold Rogers, *J. Chem. Soc*., 1956, 2784.
12 A. H. Ford-Moore and H. N. Rydon, *J. Chem. Soc*., 1946, 679.
13 P. S. Manchand, J. M. Townsend, P. S. Belica and H. S. Wong, *Synthesis*, 1980, 409.
14 J. Forrest, *J. Chem. Soc*., 1960, 574.
15 Y. Tamura, M. W. Chun, K. Inoue and J. Minamikawa, *Synthesis*, 1978, 822.
16 I. R. Sherwood, W. F. Short and R. Stansfield, *J. Chem. Soc*., 1932, 1832.