Pergamon

Tetrahedron Letters, Vol. 38, No. 21, pp. 3759-3762, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)00747-8

An Iminophosphine–Palladium Catalyst for Cross-Coupling of Aryl Halides with Organostannanes

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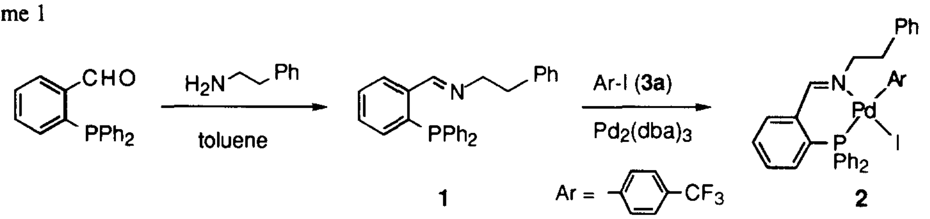
Abstract: A palladium complex bearing iminophosphine ligand, *N*-(2-diphenylphosphinobenzylidene)-2-phenylethylamine (**1**), was found to be more catalytically active than others for the cross-coupling of various types of aryl halides with alkynyl-, alkenyl- and arylstannanes to give the corresponding coupling products in high yields. © 1997 Elsevier Science Ltd.

Because of the availability, stability and low cross-reactivity of organostannanes, the palladium-catalyzed coupling of aryl halides with organostannanes is a powerful tool in organic synthesis.[1,2,3] On the other hand, the low reactivity of organostannanes, which requires rather drastic conditions and thus sometimes causes side reactions, can be a major drawback. Here we report that a palladium complex coordinated with *N*-(2-diphenylphosphinobenzylidene)-2-phenylethylamine (**1**) is an efficient catalyst for the cross-coupling of aryl halides with organostannanes.[4] This catalyst features high rate, wide application and sufficient metal supporting ability. Iminophosphine **1** was readily prepared by condensation of 2-diphenylphosphinobenzaldehyde with 2-phenylethylamine (Scheme 1).[5] Reaction of **1** with $Pd_2(dba)_3$ and (4-trifluoromethyl)iodobenzene (**3a**) gave stable palladium(II) complex **2**, where both phosphorus and nitrogen atoms coordinate to palladium forming a six-membered ring.[6]

Scheme 1



Scheme 2

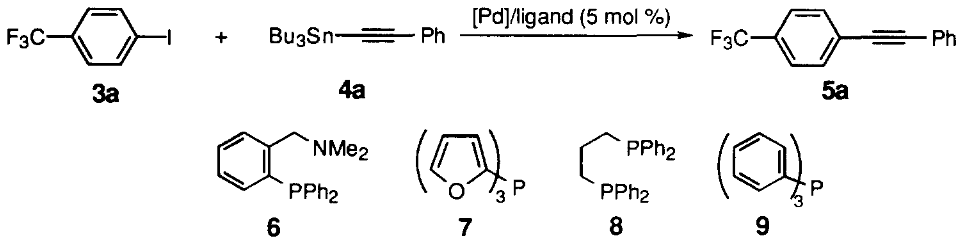


Table 1. Palladium-Catalyzed Coupling of (4-Trifluoromethyl)iodobenzene (**3a**) with Phenylethynyltributyltin (**4a**)[a]

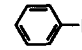
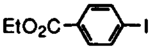
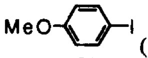
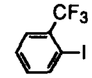
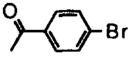
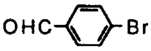
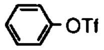
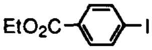
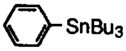
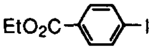
entry	ligand	ligand/Pd	solvent	yield of **5a** (%)[b]
1	**1**[c]	1	THF	90
2	**1**	1	THF	89 (83)[d]
3	**1**	1	toluene	87
4	**1**	1	dioxane	87
5	**1**	1	$CHCl_3$	71
6	**6**	1	THF	79
7	**7** ((2-furyl)$_3$P)	2	THF	57
8	**8** (dppp)	1	THF	34
9	**9** (Ph_3P)	2	THF	1

[a] The reaction was carried out in 5 mL of solvent at 25 °C for 24 h using 0.437 mmol of (4-trifluoromethyl)iodobenzene (**3a**), 0.481 mmol of phenylethynyltributyltin (**4a**), 0.0109 mmol of $[PdCl(\pi\text{-}C_3H_5)]_2$ and a ligand. [b] Determined by ^{19}F NMR. [c] Palladium complex **2** was used. [d] Isolated yield is given in the parenthesis.

The catalytic activity of the iminophosphine **1**–palladium complex and some other palladium catalysts was examined for the reaction of (4-trifluoromethyl)iodobenzene (**3a**) with phenylethynyltributyltin (**4a**) (Scheme 2). The conversion was readily monitored by ^{19}F NMR studies of the reaction mixture.[7] Yields of 1-phenyl-2-(4-trifluoromethyl)phenylethyne (**5a**) obtained in the reaction carried out for 24 h are summarized in Table 1. It was found that iminophosphine–palladium complex **2** shows higher reaction rate than any other palladium complexes examined. Thus, the reaction of **3a** with **4a** in THF in the presence of 5 mol % of palladium complex **2** at 25 °C gave 90% yield of cross-coupling product **5a** (entry 1). A palladium catalyst generated in situ from iminophosphine **1** and $[PdCl(\pi\text{-}C_3H_5)]_2$ (ligand/Pd = 1/1) was as effective as the preformed palladium catalyst (entry 2). In toluene or dioxane, the cross-coupling of **3a** with **4a** proceeded as well as in THF by use of **1** as a ligand of palladium (entries 3-5). A palladium complex coordinated with aminophosphine **6**, where the imino moiety in **1** is replaced by an amino group, was a little less catalytically active, giving 79% of **5a** (entry 6). Under the same reaction conditions, the palladium complex of tri(2-furyl)phosphine (**7**) (ligand/Pd = 2) gave only 57% yield (entry 7).

It is noteworthy that P–N ligands **1** and **6** are more effective than tri(2-furyl)phosphine (**7**), which has been reported by Farina and co-workers to be the best phosphine ligand in the coupling of iodobenzene with vinyltributyltin.[3,8] Their studies on the effect of phosphine ligands on the reaction rate show that the dissociation of a ligand from the palladium(II) intermediate to make a vacant coordination site for vinyltin is responsible for the high catalytic activity. In the reaction with iminophosphine ligand **1**, the catalytic cycle involves complex **2** where both phosphino and imino groups coordinate to palladium forming a chelate. The dissociation of either phosphorus or nitrogen atom on **2** is unlikely because of the chelate coordination.[9,10] Nevertheless, the iminophosphine is more effective than the monodentate phosphine **7** in the present cross-coupling, suggesting that the vacant coordination site proposed by Farina is not always necessary for the high reaction rate. Contrary to the high yields observed with P–N ligands **1** and **6**, the yield of **5a** was low (34%)

Table 2. Cross-Coupling of Aryl Halides with Organostannanes Catalyzed by Iminophosphine (**1**)–Palladium[a]

entry	RSnR'3	Ar–X	solvent	temp (°C)	time (h)	yield of **5**[b] (%)
1	$Ph{-}{\equiv}{-}SnBu_3$ (**4a**)	 (**3b**)	THF	50	24	93
2		 (**3c**)	THF	50	18	86
3		 (**3d**)	THF	50	29	91
4		 (**3e**)	toluene	80	32	92
5		 (**3f**)	toluene	90	72	90
6		 (**3g**)	toluene	90	48	84
7[c]		 (**3h**)	toluene	80	48	93
8[d]	 (**4b**)	 (**3c**)	toluene	90	43	90
9[e]	 (**4c**)	 (**3c**)	toluene	90	140	84

[a] The reaction was carried out in 5 mL of solvent using 0.437 mmol of aryl halide (**3**), 0.481 mmol of organostannane (**4**), 0.0109 mmol of $[PdCl(\pi\text{-}C_3H_5)]_2$ and 0.0219 mmol of the iminophosphine **1**. [b] Isolated yield based on aryl halide. [c] The reaction was carried out in the presence of 1.31 mmol of tetrabutylammonium bromide using 0.656 mmol of phenylethynyltributyltin. [d] Vinyltributyltin (0.656 mmol) was used. [e] Phenyltributyltin (0.874 mmol) was used.

Scheme 3

$$\underset{\mathbf{4a\text{-}c}}{R{-}SnBu_3} + \underset{\mathbf{3b\text{-}h}}{X{-}Ar} \xrightarrow{\mathbf{1}\ +\ [PdCl(\pi\text{-}C_3H_5)]_2} \underset{\mathbf{5}}{R{-}Ar}$$

with the bisphosphine ligand, 1,3-bis(diphenylphosphino)propane (**8**) (entry 8), which forms a six-membered ring on coordination to a metal in a similar manner as P–N ligand **1**. It follows that the coordination of nitrogen atom is essential for high catalytic activity, though its role in the reaction is not clear at present.

High catalytic activity of the palladium complex coordinated with iminophosphine **1** was also demonstrated in the cross-coupling of a variety of aryl halides **3b-h** with organostannanes **4a-c** (Scheme 3). The reaction of aryl iodides **3b-e** with **4a** in the presence of 5 mol % of the catalyst gave over 86% yields of the corresponding ethynylation products, irrespective of the electron-withdrawing or electron-donating characters of the substituents on the phenyl (entries 1-4 in Table 2). Aryl bromides **3f,g** and triflate **3h** also underwent the cross-coupling, though a prolonged reaction time is required (entries 5-7). Acetyl and formyl substituents were tolerated. Vinylation and phenylation of aryl iodide **3c** were also successful by use of vinyltributyltin (**4b**) and phenyltributyltin (**4c**), respectively, in the presence of the iminophosphine–palladium catalyst (entries 8-9).

Acknowledgment:

We thank Professor Tamio Hayashi (Kyoto University) for helpful discussions.

References and Notes:

† Deceased on October 4, 1995.

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5 A mixture of 881 mg (3.03 mmol) of 2-diphenylphosphinobenzaldehyde and 386 mg (3.19 mmol) of 2-phenylethylamine in 35 mL of toluene was stirred under reflux for 6 h. After concentration under a reduced pressure, 20 mL of hexane was added to the residue. Filtration of the resulting light-yellow solid gave 1.07 g of *N*-(2-diphenylphosphinobenzylidene)-2-phenylethylamine (**1**) (89%): mp 87-89 °C; ^{1}H NMR ($CDCl_3$) δ 2.75 (t, J = 7.8 Hz, 2 H), 3.70 (t, J = 7.8 Hz, 2 H), 6.85-6.91 (m, 1 H), 7.11-7.42 (m, 17 H), 7.92-7.98 (m, 1 H), 8.82 (d, J = 4.6 Hz, 1 H); $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ -13.2; Anal. Calcd for $C_{27}H_{24}NP$: C, 82.42; H, 6.15; N, 3.56. Found: C, 82.25; H, 6.19; N, 3.56. For the preparation of 2-diphenylphosphinobenzaldehyde, see: Rauchfuss, T. B.; Wrobleski, D. A. *Inorg. Synth.* **1982**, *21*, 175-179.

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7 ^{19}F NMR ($CDCl_3$, CF_3COOH as external standard) for **3a**: δ 12.64; **5a**: δ 12.85.

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(*Received in Japan* 26 *March* 1997; *revised* 17 *April* 1997; *accepted* 18 *April* 1997)