Rhodium-catalysed direct *ortho* arylation of 2-arylpyridines with arylstannanes *via* C–H activation

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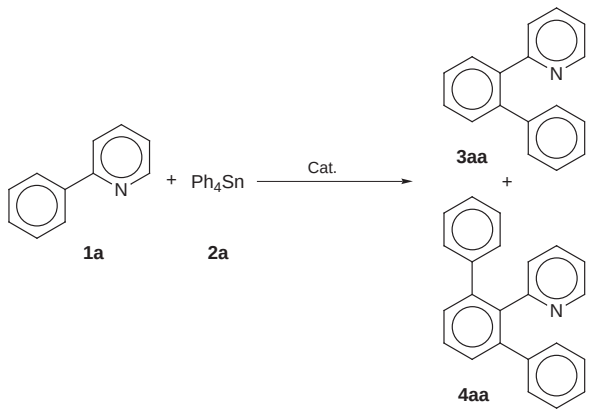
The *ortho* position of the aromatic ring of pyridyl group-substituted aromatic compounds was directly arylated with tetraarylstannanes in the presence of a catalytic amount of a rhodium(I)–phosphine complex.

Transition metal-catalysed cross-coupling reactions of aromatic compounds with arylated typical metal compounds such as Mg, Zn, B, Si and Sn are useful synthetic routes to biaryl compounds.[1] A variety of aromatic compounds such as ArI (Cl, Br), ArOTf, ArOMs, $ArOP(O)(OR)_2$, ArOR, ArSR and ArN_2BF_4 have been used for the cross-coupling reactions with typical arylated metal compounds. These reactions involve C–X bond cleavage [X = halide, OTf, OMs, $OP(O)(OR)_2$, OR, SR and N_2BF_4] *via* the oxidative addition of a low valent transition metal (M) complexes and subsequent transmetalation between the resultant C–M–X species and arylated metal compounds. There has, however, been no report of the cross-coupling reaction between the aromatic C–H bond and organometal compounds. In 1993, Murai *et al*. reported ruthenium-catalysed *ortho* alkylation of acetophenones with terminal alkenes, which represented the first effective catalytic C–C bond formation involving the cleavage of an aryl C–H bond.[2] It is thought that chelation of the acetyl group of acetophenone directs the ruthenium complex to cleave the *ortho* C–H bond. The pyridyl group has also been known to direct transition metal-catalysed C–H bond cleavage of an aromatic ring as in the rhodium-catalysed *ortho* alkylation of pyridylbenzenes with terminal alkenes[3] and ruthenium-catalysed carbonylation with CO and terminal alkenes.[4] We report herein our finding that the *ortho* position of pyridylbenzenes is directly arylated with tetra-arylstannanes in the presence of a catalytic amount of a rhodium(I)–phosphine complex.

Initial work was centered on the reaction of 2-phenylpyridine **1a** with tetraphenylstannane **2a** in the presence of a catalytic amount of various transition metal complexes (Scheme 1). The results are summarized in Table 1. The $[RhCl(C_8H_{14})_2]_2$–PPh_3 catalytic system produced singly phenylated product **3aa** in 24% yield (entry 1). Other phosphine ligands such as PCy_3, $P(OPh)_3$ and dppe were less effective, giving **3aa** in lower yields (entries 2–4). The highest yield was obtained using



Scheme 1

Table 1 Reaction of **1a** with **2a** in the presence of a catalytic amount of various transition metal complexes[a]

Entry	Catalyst	Yield (%)[b]
1	$[RhCl(C_8H_{14})_2]_2 + 4PPh_3$	24
2	$[RhCl(C_8H_{14})_2]_2 + 4PCy_3$	10
3	$[RhCl(C_8H_{14})_2]_2 + 4P(OPh)_3$	6
4	$[RhCl(C_8H_{14})_2]_2$ + 2dppe	7
5	$RhCl(PPh_3)_3$	29
6	$RhCl(CO)(PPh_3)_2$	5
7	$Pd_2(dba)_3{\cdot}CHCl_3 + 4PPh_3$	0
8	$Pt_2(dba)_3{\cdot}CHCl_3 + 4PPh_3$	0
9	$[IrCl(cod)]_2 + 4PPh_3$	0
10	$Ru_3(CO)_{12} + 6PPh_3$	0

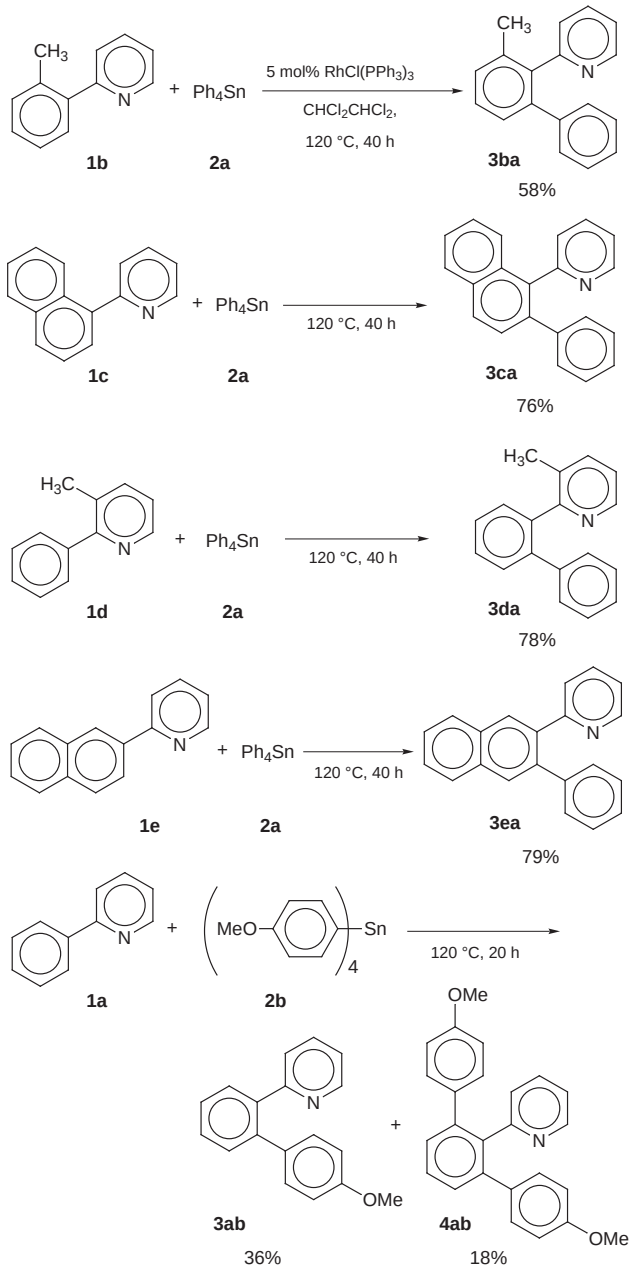
[a] A mixture of **1a** (0.5 mmol), **2a** (0.75 mmol) and metal complexes (10 mol% of **1a**, based on metal) in THF (1.5 ml) was stirred in a sealed vial under N_2 at 120 °C for 20 h. Product was **3aa**. [b] Determined by GLC.

$RhCl(PPh_3)_3$, affording **3aa** in 29% yield (entry 5), while the use of $RhCl(CO)(PPh_3)_2$ gave **3aa** in only 5% yield (entry 6). In these cases, only a trace amount of doubly phenylated product **4aa** was observed. Other low valent transition metal complexes of Pd, Pt, Ir and Ru did not show any catalytic activity (entries 7–10). The reaction of **1a** with **2a** was then carried out in various solvents in the presence of 5 mol% of $RhCl(PPh_3)_3$. The results are summarized in Table 2. The reactions in toluene, THF and MeCN afforded the product **3aa** in low yields of 14, 16 and 12%, respectively, together with a trace amount of **4aa** (entries 1–3). The yield of the products slightly increased using chlorinated alkanes such as $CHCl_3$, 1,2-dichloroethane and 1,1,1-trichloroethane as solvent, affording **3aa** in 32, 37 and 27%, respectively. Surprisingly, 1,1,2,2-tetrachloroethane exhibited a dramatic effect, giving **3aa** and **4aa** in good yields of 65 and 20%, respectively. In this case, trichloroethylene originating from the solvent *via* dehydrochlorination was detected by GLC after the reaction. In order to study the effects of this olefin on the reaction, a small amount (0.25 mmol) of trichloroethylene was added to the reaction of **1a** and **2a** using THF as solvent. This experiment afforded **3aa** and **4aa** in improved yields of 42 and 3%, respectively, compared to the

Table 2 Reaction of **1a** with **2a** in the presence of a catalytic amount of $RhCl(PPh_3)_3$ in various solvents[a]

		Yield (%)[b]	
Entry	Solvent	**3aa**	**4aa**
1	Toluene	14	0
2	THF	16	1
3	MeCN	12	0
4	$CHCl_3$	32	2
5	$ClCH_2CH_2Cl$	37	1
6	$MeCCl_3$	27	1
7	$Cl_2CHCHCl_2$	65 (56)	20 (20)

[a] A mixture of **1a** (0.5 mmol), **2a** (0.5 mmol) and $RhCl(PPh_3)_3$ (5 mol%) in solvent (1.5 ml) was stirred in a sealed vial under N_2 at 120 °C for 20 h. [b] Determined by GLC. Yields in parentheses are for isolated compounds.



Scheme 2

original yields of 16 and 1% (see Table2, entry 2). Thus the trichloroethylene generated *in situ* during the reaction may partly be responsible for the remarkable effect of 1,1,2,2-tetrachloroethane.

Results for the reactions of other pyridyl-substituted aromatic compounds **1** with arylstannanes **2** in the presence of 5 mol% of $RhCl(PPh_3)_3$ in 1,1,2,2-tetrachloroethane are shown in Scheme 2.†‡ The reactions of **2a** with 2-(2-methylphenyl)pyridine **1b** and 2-(1-naphthyl)pyridine **1c** having only one *ortho* C–H bond on the aromatic ring gave singly phenylated products **3ba** and **3ca**. in good yields. 3-Methyl-2-phenylpyridine **1d** containing two possible reactive *ortho* C–H bonds gave singly phenylated product **3da** in 78% yield selectively. As was described in ref. 3 and 4, the steric interaction between the phenyl group and the methyl group in **3da** prevented the second phenylation. 2-(2-Naphthyl)pyridine **1e** was also phenylated only at the 3-position of the naphthalene ring, affording singly phenylated product **3ea** in 79% yield selectively. In this case, the steric hindrance of the 8-position of the naphthalene ring would prevent phenylation at the 1-position. Tetra(*p*-methoxyphenyl)-stannane **2b** reacted with **1a** affording **3ab** and **4ab** in 36 and 18% yield, respectively.

Although the mechanism of the present reaction is not yet clear, a reaction pathway involving the N atom-directed oxidative addition of the low valent rhodium complex to the *ortho* C–H bond of the phenyl ring followed by phenylation with tetraphenylstannane may be possible.

The reaction reported herein represents the first example of the cross-coupling reaction between aromatic C–H bonds and organometal compounds, and provides a new method for direct arylation of the *ortho* position of pyridyl-substituted aromatic compounds. Further work is now in progress to determine the full scope of this reaction.

Notes and references

† The structures of the compounds **3aa**, **3ba**, **3ca**, **3da**, **3ea**, **3ab**, **4aa** and **4ab** were in a complete accord with the obtained IR, MS, ^1H and ^{13}C NMR and elemental analysis data. The assignment of signals in ^1H and ^{13}C NMR spectra was confirmed by ^1H–^1H COSY and ^1H–^{13}C HMQC spectra.

‡ Typical experimental procedure: A mixture of **1a** (74.2 mg, 0.478 mmol), **2a** (213.5 mg, 0.500 mmol) and $RhCl(PPh_3)_3$ (23.1 mg, 0.025 mmol) in 1,1,2,2-tetrachloroethane (1.5 ml) was stirred in a sealed vial under N_2 at 120 °C for 20 h. The reaction mixture was taken up in $CHCl_3$ and washed with diluted aqueous ammonia and water. After the $CHCl_3$ layer was dried over K_2CO_3, the solvent was evaporated, and then the residue was purified by medium-pressure preparative liquid chromatography (Yamazen Corp., Ultra Pack column, silica gel, 40 μm, 60 Å, 26 × 300 mm) eluting with 3% acetone in $CHCl_3$ to give **3aa** (62.5 mg, 56%) and **4aa** (28.8 mg, 20%). Yields shown in Scheme 2 are for isolated compounds.

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