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A *p*-phosphinophenolate ligand for the palladium-catalysed arylation of alkenes†

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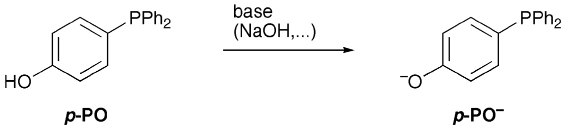
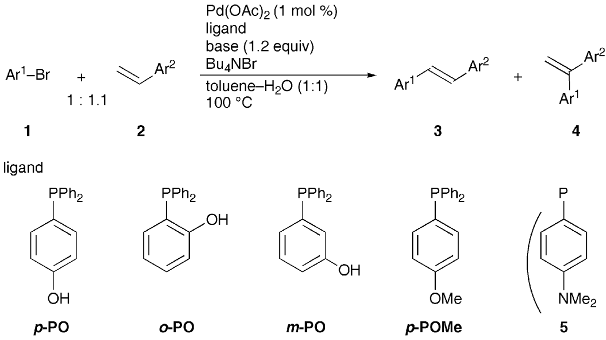
A triphenylphosphine having a strong electron-donating group, an oxyanion, at the *para* position of one of the benzene rings was found to show much higher efficiency compared with other structurally related triarylphosphines in the palladium-catalysed arylation of alkenes.

The choice of an appropriate ligand is one of the most important factors in carrying out transition metal-catalysed reactions successfully.[1] Recently, phosphine ligands having strong σ-donicity induced by electron-donating alkyl substituents are attracting much attention due to their high catalytic activities in combination with transition metals such as palladium.[2] We expected that introduction of an oxyanion on a benzene ring of triarylphosphines would endow triarylphosphines with strong σ-donicity, electrons flowing from the oxyanion to the phosphorous atom with resonance through the benzene ring.[3] Thus, we designed *p*-phosphinophenolate ligand **_p_-PO**$^-$,[4] which can be easily prepared, even *in situ*, from stable *p*-phosphinophenol **_p_-PO**[5,6] by deprotonation with a common base such as NaOH (eqn. (1)), where the problems often encountered in the use of air-sensitive **σ**-donor phosphines having two or three alkyl substituents can be avoided. We chose the palladium-catalysed arylation of alkenes, the Mizoroki–Heck reaction,[7] as a reaction to evaluate **_p_-PO**$^-$ as a **σ**-donor ligand because triphenylphosphines having electron-donating substituents such as dimethylamino or methoxy groups at their *para* positions are reported to be more effective than their parent triphenylphosphine in the Mizoroki–Heck reaction.[8] Here we report that **_p_-PO**$^-$ showed much higher efficiency compared with other structurally related triarylphosphines in the Mizoroki–Heck reaction.



(1)

We first compared phosphinophenolate ligands with other triarylphosphines in terms of efficiency in the palladium-catalysed reaction of 4-bromo(trifluoromethyl)benzene (**1a**) with styrene (**2a**) (eqn. (2) and Table 1). The reaction of **1a** with **2a** in the presence of Pd(OAc)$_2$ (1 mol%), 4-(diphenylphosphino)phenol (**_p_-PO**, 2 mol%), NaOH (1.2 equiv) and Bu$_4$NBr (2 mol%) in toluene–H$_2$O (1 : 1) at 100 °C for 6 h gave a 98 : 2 mixture of (*E*)-4-(trifluoromethyl)stilbene (**3a**) and **α**-[4-(trifluoromethyl)phenyl]styrene (**4a**) in 98% yield (entry 1). Isomeric phosphinophenolate ligands **_o_-PO**$^-$ and **_m_-PO**$^-$ were much less effective than **_p_-PO**$^-$ (entries 2 and 3).[9] Although the oxyanion of **_o_-PO**$^-$ should exert a similar electronic effect as **_p_-PO**$^-$, the coordination of the oxyanion to the palladium may be unfavorable in this case.[4] Removal of the oxyanion functionality resulted in a complete loss of the activity (entries 4 and 5), which was not recovered by addition of 2 mol% of phenol, indicating that an oxyanion has to be located at an appropriate position on the same benzene ring (entry 6). Tris(4-dimethylaminophenyl)phosphine (**5**), a **σ**-donative triarylphosphine, which was reported to be effective for the Mizoroki–Heck reaction,[8] was useless under these conditions (entry 7). The reaction with a weaker base such as tributylamine was much slower (entry 8), probably because a sufficient amount of **_p_-PO**$^-$ could not be generated under these conditions. The lack of Bu$_4$NBr or a ligand also retarded the reaction (entries 9 and 10).



(2)

The Pd–**_p_-PO**$^-$ catalyst in toluene–H$_2$O was successfully applied to the Mizoroki–Heck reaction using various aryl bromides and vinylarenes (eqn. (2) and Table 2). Both electron-rich and -deficient aryl bromides reacted with styrene in good yields (entries 1–4), though a larger amount (up to 8 mol%) of **_p_-PO** was required for the reaction of bromobenzenes having an electron-donating group. Vinylarenes other than styrene underwent the reaction with *p*-tolyl bromide (entries 5 and 6).

Because of the triarylphosphine framework, **_p_-PO**$^-$ should show π-acceptive character and should nicely support low valent transition metal complexes such as palladium(0) complexes.[1] We

Table 1 Palladium-catalysed arylation of styrene with 4-bromo(trifluoromethyl)benzene[a]

Entry	Ligand	Base	Bu$_4$NBr (mol%)	Yield (%)[b]	**3a** : **4a**[b]
1	**_p_-PO**	NaOH	2	98	98 : 2
2	**_o_-PO**	NaOH	2	2	50 : 50
3	**_m_-PO**	NaOH	2	31	94 : 6
4	**_p_-POMe**	NaOH	2	<1	—
5	Ph$_3$P	NaOH	2	<1	—
6	Ph$_3$P + PhOH[c]	NaOH	2	1	>99 : 1
7	**5**	NaOH	2	<1	—
8	**_p_-PO**	Bu$_3$N	2	<1	—
9	**_p_-PO**	NaOH	0	22	86 : 14
10	none	NaOH	2	1	71 : 29

[a] The reaction was carried out in toluene–H$_2$O (1 : 1, 2.0 mL) at 100 °C for 6 h using **1a** (0.40 mmol), **2a** (0.44 mmol) and a base (0.48 mmol) in the presence of Pd(OAc)$_2$ (4.0 μmol), a ligand (8.0 μmol) and Bu$_4$NBr. [b] Determined by GC. [c] With Ph$_3$P (2 mol%) and PhOH (2 mol%).

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† Electronic supplementary information (ESI) available: general procedure. See http://www.rsc.org/suppdata/cc/b4/b411125g/

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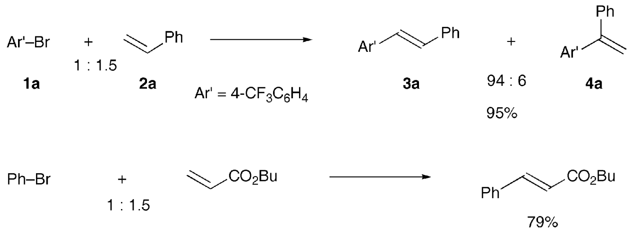
Table 2 Palladium-catalysed arylation of vinylarenes with aryl bromides[a]

Entry	Ar^1	Ar^2	***p*-PO** (mol%)	Time/h	Yield of **3** (%)[b]
1	4-MeC_6H_4	Ph	4	6	89[c]
2	4-$MeOC_6H_4$	Ph	8	76	67
3	4-AcC_6H_4	Ph	2	24	89
4	3-AcC_6H_4	Ph	2	11	76
5	4-MeC_6H_4	4-$MeOC_6H_4$	4	48	92
6	4-MeC_6H_4	4-$CF_3C_6H_4$	4	24	96

[a] The reaction was carried out in toluene–H_2O (1 : 1, 2.0 mL) at 100 °C using an aryl bromide (0.40 mmol), a vinylarene (0.44 mmol) and NaOH (0.48 mmol) in the presence of $Pd(OAc)_2$ (4.0 μmol), ***p*-PO** and Bu_4NBr (8.0 μmol). [b] Isolated yield based on the aryl bromide. [c] Determined by GC.



Scheme 1 *Reagents and conditions*: $Pd(OAc)_2$ (0.001 mol%), ***p*-PO** (0.002 mol%), NaOAc (1.1 equiv), Bu_4NBr (2 mol%), DMA, 130 °C, 72 h.

expected that this character should increase the longevity of the Pd–***p*-PO**$^-$ catalyst by preventing the palladium(0) complexes from aggregation and performed the arylation of styrene and butyl acrylate using a much reduced amount (substrate/catalyst = 100,000) of the catalyst. Although the conditions in eqn. (2) (toluene–H_2O, NaOH, 100 °C) as they stand could not be applied to the reaction, higher temperature in conjunction with use of less volatile DMA as a solvent and sodium acetate as a base enabled high yields with low loading of the catalyst (Scheme 1). Thus, the treatment of **1a** with styrene in the presence of $Pd(OAc)_2$ (0.001 mol%), ***p*-PO** (0.002 mol%), NaOAc (1.1 equiv) and Bu_4NBr (2 mol%) in DMA at 130 °C for 72 h gave a mixture of **3a** and **4a** in 95% yield, where the turnover number reached 95,000. The reaction conditions were applied also to the arylation of butyl acrylate, which afforded the corresponding cinnamate (Scheme 1).

In conclusion, we have demonstrated that a phosphinophenolate ligand is effective for the palladium-catalysed arylation of alkenes in terms of both the catalytic activity and the longevity of the catalyst. Further studies on application of the catalyst system to other transition metal-catalysed reactions as well as elucidation of the role of the oxyanion is in progress.

Notes and references

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8 M. Qadir, T. Möchel and K. K. Hii, *Tetrahedron*, 2000, **56**, 7975–7979.

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