

Catalytic applications of 1,2,4-diazaphospholide-based ruthenium complexes in the Heck reaction

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Abstract—The palladium-catalyzed Heck reaction was effected with two ruthenium complexes bearing unique heterocyclic 1,2,4-diazaphospholide ligands that contain sp^2 -hybridized phosphorus atoms.

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Tertiary phosphines containing sp^3 hybridized phosphorus atoms have played a key role in organometallic synthesis and catalysis, while compounds based on sp^2 hybridized phosphorous atoms remained a mere curiosity for many years. However, recent studies have clearly demonstrated that such species may be used as ligands for highly active and selective catalysts in different organic transformations.^{1,2} Of particular interest is the heterocyclic phosphorus analogues of the cyclopentadienyl ligand (Cp^-).² These low-coordinate phosphorus compounds have versatile bonding ability and may feature either π - or σ -bonding towards metal centers.³ Recently Mathey and Le Floch synthesized palladium complexes incorporating phospho- and diphosphaferrocenes, which combined a ferrocene backbone and an sp^2 -hybridized phosphorus atom.⁴ The octaethyldiphosphaferrocene complex was found to be a highly efficient ligand in palladium-catalyzed Suzuki cross-coupling reactions.⁵ We are interested in the coordination and application of 1,2,4-diazaphospholides.⁶ Very recently some of us prepared two ruthenium complexes based on bulky 1,2,4-diazaphospholides, $(3,5-R_2dp)RuCp^*$ ($R = tBu, Ph$) (Fig. 1).⁷ The ruthenium complexes are electron-rich, evident of the significant upfield chemical shift of phosphorus compared to the related free ligands (^{31}P NMR $\Delta\delta = -116$ ppm and -125.7 ppm), and bulky with two adjacent *tert*-butyl or phenyl groups

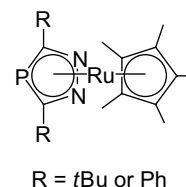


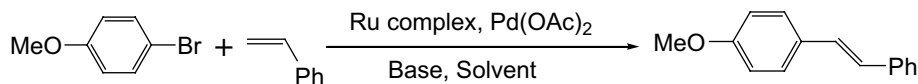
Figure 1.

beside the phosphorus atom (*ortho* to P). They are also thermally robust and can be sublimed under high vacuum at up to 160 °C. The 1,2,4-diazaphospholides may be viewed as phospholyl analogues in which two CH groups are replaced by two nitrogen atoms or as the combination of phospholyl and pyrazolato ions. As the sp^2 hybridized phosphorus atoms in the 1,2,4-diazaphospholide groups have one lone electron pair available for coordination to low-valent transition metal centers, it is thus interesting to evaluate their potential use as ancillary ligands. Here we report our initial work on catalytic applications of the ruthenium complexes in the Heck reaction, which involves the cross-coupling between an aryl halide and an alkene and is one of the most important carbon–carbon bond formation processes.

The factors in the Heck reaction are often complicated so a screening for optimal conditions is necessary.⁸ We chose *p*-bromoanisole, a deactivated bromide and a fairly inert halide, as the aryl halide substrate to couple with styrene, and examined several common solvents and bases.⁹ As seen in Table 1, at 130 °C and under

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Table 1. Solvent and base effect^a

Entry	Solvent	Base	Temperature (°C)	Yield ^b (%)
1	THF	K ₂ CO ₃	100	43
2	Dioxane	K ₂ CO ₃	100	46
3	Toluene	K ₂ CO ₃	130	46
4	DMF	K ₂ CO ₃	130	88
5	DMA	K ₂ CO ₃	130	90
6	DMA	NaOAc	130	52
7	DMA	K ₃ PO ₄	130	89
8	DMA	Cy ₂ NMe	130	56
9	NMP	K ₂ CO ₃	130	94
10	NMP	NaOAc	130	56
11	NMP	K ₃ PO ₄	130	94
12	NMP	Cy ₂ NMe	130	79

^a 1.0 mmol *p*-bromoanisole, 1.5 mmol styrene, 2.0 mmol base, 0.010 mmol Pd(OAc)₂, 0.010 mmol (*t*Bu₂dp)RuCp*, 1 mL solvent, 18 h.

^b GC yields of *trans*-methoxystilbene using

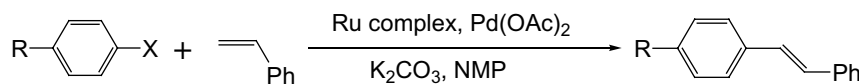
1 mol % Pd(OAc)₂ loading, the yields of *trans*-4-methoxystilbene were excellent in polar aprotic solvents such as dimethylformamide (DMF), dimethylacetamide (DMA) and N-methylpyrrolidone (NMP), with NMP giving the highest yield (entry 9). The yields were much lower in less polar solvents such as toluene, tetrahydrofuran (THF) and dioxane (entries 1–3). For safety concern, the operation temperature was set at 100 °C for the latter two solvents as they have relatively lower boiling points. The bases also affected the yield significantly. In both DMA and NMP, K₂CO₃ and K₃PO₄ gave comparable yields that were better than NaOAc and Cy₂NMe. Thus we decided to use NMP as the solvent and K₂CO₃ as the base for subsequent investigations.

To evaluate the efficiency of the ruthenium complexes as ligands, we selected several aryl bromides and chlorides, which are generally harder to couple than corresponding iodides. The choices can be divided into activated, neutral and deactivated bromides and chlorides. First, we studied the coupling of 4'-bromoacetophenone, an activated aryl bromide, and styrene with 0.1 mol % loading of Pd(OAc)₂ and the ruthenium complex. Both ruthenium complexes led to complete conversion of the bromides and excellent yields of *trans*-4-acetylstilbene (Table 2, entries 1 and 2). It was not surprising as in some reports, 4'-bromoacetophenone had been coupled to styrene in the absence of any ligand.¹⁰ Indeed in our test, even without any ruthenium complex, the conversion of this bromide was complete (entry 3). However, when we used bromobenzene, *p*-bromoanisole, 4'-chloroacetophenone and *p*-chloronitrobenzene as the substrate, the systems with the ruthenium complexes gave much higher yields than the ligand free systems, indicating that the ruthenium complexes were essential in the coupling reactions of less reactive aryl halides. For example, with 0.1 mol % Pd(OAc)₂ loading for the coupling of *p*-bromoanisole, the yields were around 70% with the ruthenium complexes and 30% without them (entries 7–9). The difference was more pronounced when aryl chlorides were used as the substrates. In the case of *p*-chloronitrobenzene, at 1 mol %

Pd(OAc)₂ loading, the yield was 99% with the (*t*Bu₂dp)-RuCp* (entry 15), but only 11% without any ruthenium complex (entry 17). While the two ruthenium complexes gave comparable yields for the coupling of aryl bromides, (*t*Bu₂dp)RuCp* was more efficient in the coupling of aryl chlorides than its phenyl analogue. For example, at 1 mol % Pd(OAc)₂ loading, (*t*Bu₂dp)RuCp* gave a complete conversion of *p*-chloronitrobenzene, but (Ph₂dp)RuCp* gave only a 44% yield (entry 16). The better efficiency of the *tert*-butyl complex over its phenyl analogue is likely due to its larger steric bulkiness.

While the palladium complexes based on the ruthenium complex-ligands were effective in the coupling of bromides and selected activated chloride (e.g., *p*-chloronitrobenzene), they were not effective in the coupling of neutral and deactivated chloride such as *p*-chloroanisole (entries 20–23). This is in sharp contrast to PtBu₃, which is highly efficient in the coupling of deactivated aryl chlorides.¹¹ This may be contributed to the steric factor since the planar sp²-phosphorus based 1,2,4-phospholide ligands are not as hindered as the tetrahedral sp³-phosphorus based PtBu₃. As the sp²-phosphorus species are stronger π-acceptors towards low-valent transition metals than tertiary phosphanes,² the ruthenium complexes with sp²-phosphorus atoms may engage in back-bonding with palladium in a fashion similar to phosphites and phosphinites, which have been successfully applied in the Heck reaction.^{12,13}

In summary, we demonstrated that the ruthenium complexes based on η⁵-1,2,4-diazaphospholide groups with an sp²-hybridized phosphorus atoms can act as efficient ligands in the Heck reaction, in which the ruthenium complexes are likely to act as two-electron-donor ligands η¹-bonded to the palladium ion through the phosphorus-atom lone pair.^{4,14} This is the first application of sp²-hybridized phosphorus ligands in the Heck reaction. The results suggest that the metal complexes containing sp²-hybridized phosphorus atoms are viable ligands in organometallic synthesis and catalysis.

Table 2. Heck reaction of selected aryl halides^a

Entry	R	X	Ru complex	Catalyst loading (%)	Yield ^b (%)
1	CH ₃ CO	Br	(<i>t</i> Bu ₂ dp)RuCp*	0.1	96
2	CH ₃ CO	Br	(Ph ₂ dp)RuCp*	0.1	95
3	CH ₃ CO	Br	None	0.1	95
4	H	Br	(<i>t</i> Bu ₂ dp)RuCp*	0.1	52
5	H	Br	(Ph ₂ dp)RuCp*	0.1	42
6	H	Br	None	0.1	19
7	MeO	Br	(<i>t</i> Bu ₂ dp)RuCp*	0.1	68
8	MeO	Br	(Ph ₂ dp)RuCp*	0.1	77
9	MeO	Br	None	0.1	28
10	H	Br	(<i>t</i> Bu ₂ dp)RuCp*	1	80
11	H	Br	(Ph ₂ dp)RuCp*	1	87
10	MeO	Br	(<i>t</i> Bu ₂ dp)RuCp*	1	94
11	MeO	Br	(Ph ₂ dp)RuCp*	1	93
12	NO ₂	Cl	(<i>t</i> Bu ₂ dp)RuCp*	0.1	11
13	NO ₂	Cl	(Ph ₂ dp)RuCp*	0.1	7
14	NO ₂	Cl	None	0.1	4
15	NO ₂	Cl	(<i>t</i> Bu ₂ dp)RuCp*	1	99
16	NO ₂	Cl	(Ph ₂ dp)RuCp*	1	44
17	NO ₂	Cl	None	1	11
18	CH ₃ CO	Cl	(<i>t</i> Bu ₂ dp)RuCp*	1	17
19	CH ₃ CO	Cl	(Ph ₂ dp)RuCp*	1	2
20	H	Cl	(<i>t</i> Bu ₂ dp)RuCp*	1	Trace
21	H	Cl	(Ph ₂ dp)RuCp*	1	—
22	MeO	Cl	(<i>t</i> Bu ₂ dp)RuCp*	1	—
23	MeO	Cl	(Ph ₂ dp)RuCp*	1	—

^a 1.0 mmol aryl halide, 1.5 mmol styrene, 2.0 mmol K₂CO₃, Pd(OAc)₂/(R₂dp)RuCp* = 1:1 molar ratio, 1 mL NMP, 130 °C, 18 h.

^b GC yields of *trans*-stilbenes using undecane as an internal standard.

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