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Heck reactions in monoglyme and diglyme using BmimCl as pre-ligand

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Heck reactions between iodobenzene and methyl acrylate were carried out in monoglyme and diglyme as solvents, using different ligands and palladium sources, and good to high yields were obtained in the production of (*E*)-substituted olefins. The ionic liquid BmimCl was successfully utilized as pre-ligand to substitute triphenylphosphine. Copyright © 2008 John Wiley & Sons, Ltd.

Keywords: Heck reaction; monoglyme; diglyme; BmimCl

Introduction

In recent years there has been much focus and emphasis on the Heck reaction for the construction of carbon–carbon bonds involving palladium-catalyzed coupling of haloarenes (or haloalkenes) with alkenes.[1,2] A variety of substituted and functionalized alkenes have been successfully arylated or alkenylated via the Heck reaction to synthetically produce useful molecules.[3–6] The Heck reaction is usually carried out in polar solvents such as DMF,[7–11] MeCN,[12–14] water,[15–19] ionic liquids,[20–25] PEGs,[26–30] supercritical carbon dioxide[31–34] and others.[35–38]

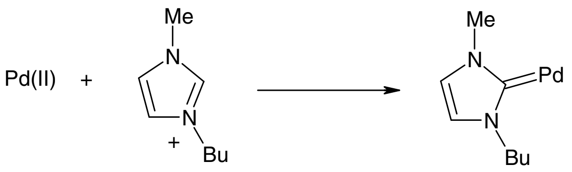
However, as environmentally unfriendly phosphines are generally used, there is a continuous need to improve these processes.[39–45] Catalyst development has led to a variety of different ligand systems, including palladacycles.[46–49] As ligands, bulky and electron-rich monodentate phosphines,[50–52] and carbon donors like N-heterocyclic carbenes (NHCs)[53–56] should be mentioned here owing to the high activities of the derived Pd(0) catalysts. NHCs and their transition metal complexes are currently the focus of intense research in organometallic chemistry. NHCs have become increasingly popular in the last few years as an attractive alternative to tertiary phosphines in homogeneous catalysis.

In our search in to develop new processes in cross-coupling reactions,[57–59] we describe herein a study on the Heck reaction in two different solvents, monoglyme and diglyme. We used two palladium sources, palladium acetate [$Pd(OAc)_2$] and tris(dibenzylideneacetone)dipalladium [$Pd_2(dba)_3$], PPh_3 and BmimCl (butyl-methyl imidazolium chloride) as precursors of the corresponding carbene ligands (Scheme 1). We verified that the system derived from $Pd(OAc)_2$ and BmimCl in monoglyme as a highly efficient catalyst system for the Heck reaction. In all cases, (*E*)-products were selectively obtained.

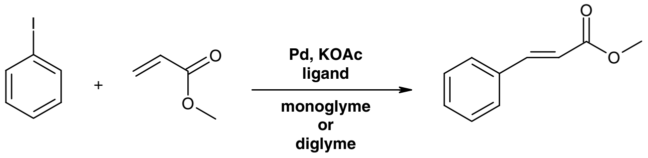
Table 1. Effect of different ligands and palladium sources in the Heck reaction[a]

Entry	Solvent	Catalyst	Ligand	Conversion[b,c] (%)
1	Monoglyme	$Pd(OAc)_2$	PPh_3	100
2	Monoglyme	$Pd_2(dba)_3$	PPh_3	98
3	Monoglyme	$Pd(OAc)_2$	BmimCl	100
4	Monoglyme	$Pd_2(dba)_3$	BmimCl	32
5[d]	Monoglyme	$Pd(OAc)_2$	none	35
6[d]	Monoglyme	$Pd_2(dba)_3$	none	30
7	Diglyme	$Pd(OAc)_2$	PPh_3	27
8	Diglyme	$Pd_2(dba)_3$	PPh_3	32
9	Diglyme	$Pd(OAc)_2$	BmimCl	97
10	Diglyme	$Pd_2(dba)_3$	BmimCl	74
11[d]	Diglyme	$Pd(OAc)_2$	None	31
12[d]	Diglyme	$Pd_2(dba)_3$	None	25

[a] 1.0 mmol iodobenzene, 1.1 mmol methyl acrylate, 3 mmol KOAc, 3 mL solvent, 10 mol% ligand and 5 mol% Pd at 80 °C for 18 h. [b] Determined by GC-MS. [c] Only (*E*)-olefins were obtained. [d] Ligand-free system.



Scheme 1. NHC complex.



Scheme 2. Heck reaction between iodobenzene and methyl acrylate.

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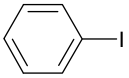
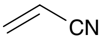
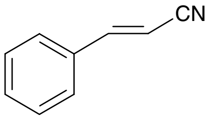
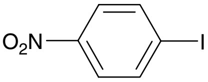
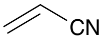
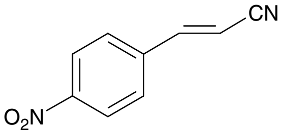
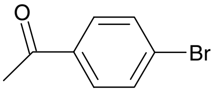
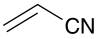
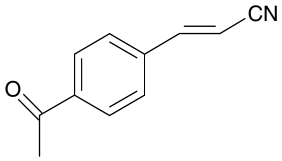
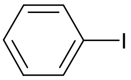
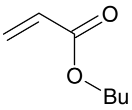
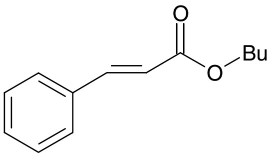
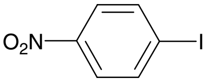
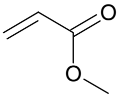
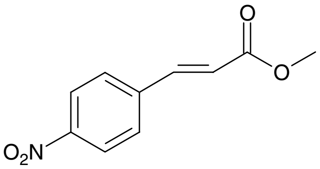
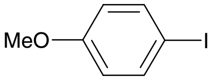
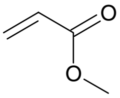
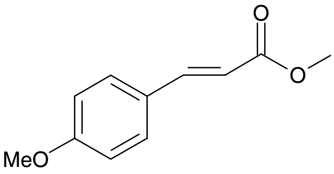
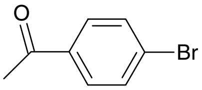
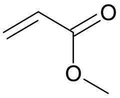
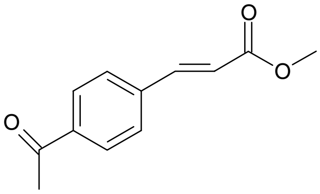
Table 2. Heck reaction of different aryl halides and olefins in monoglyme[a,b]

Entry	Aryl halides	Olefin	Product	Conversion[c] (%)
1				96
2				94
3				92
4				98
5				100
6				93
7				94

[a] 1.0 mmol aryl halide, 1.1 mmol olefin, 3 mmol KOAc, 10 mol% BmimCl and 5 mol% $Pd(OAc)_2$, 5 mL monoglyme at 80 °C for 18 h.
[b] Only (*E*)-olefins were obtained.
[c] Determined by GC-MS.

Results and Discussion

Our initial investigation started with the cross-coupling reaction of iodobenzene and methyl acrylate as a model system (Scheme 2). The reaction was carried out in the presence of 5 mol% Pd(0) in monoglyme (monoethylene glycol di-methyl ether) or in diglyme (diethylene glycol di-methyl ether) as solvent at 80 °C for 18 h. With the $Pd(OAc)_2$ as Pd(II) source and $Pd_2(dba)_3$ as Pd(0) source, two ligands (PPh_3 and BmimCl) were tested and moderate to high yields were obtained. The results are described in Table 1.

It is important to emphazise that the system $Pd_3(dba)_2$ and PPh_3 would produce directly the active catalyst $[Pd(PPh_3)_3]$, while Pd(II) would be reduced in the presence of PPh_3 and small amounts of water to Pd(0), thus generating the catalyst $[Pd(PPh_3)_3]$ along with H^+ production.[60–63] Finally, Pd(II) upon reduction with $Bmim^+$ would generate the corresponding carbene Pd(0) complex and H^+.[64] $Pd_2(dba)_3$ in the presence of $Bmim^+$ is not expected to generate carbene since Pd is already in the reduced form. Rather, in this case BmimCl would act simply to increase ionic strength. Solvatation with monoglyme and diglyme is expected to be very effective due to the presence of the vicinal hydroxy groups. In addition, both solvents can act as reductive agents to Pd(II).

Results showed that Heck reactions using monoglyme as solvent furnished moderate to high yields. Excellent results were obtained with $Pd(OAc)_2$ and $Pd_3(dba)_2$ and PPh_3 as ligand (entries 1 and 2). When we used $Pd(OAc)_2$ employing BmimCl as ligand (entry 3), the yield was the same as that obtained with PPh_3, thus justifying substitution of PPh_3 by $Bmim^+$. As expected, $Pd_2(dba)_3$ in the presence of BmimCl resulted in a poor reaction yield (entry 4). Ligand-free reactions were also carried out in monoglyme but poor yields were obtained (entries 5 and 6) and, in these cases, we observed the formation of Pd black, so ligands are needed to stabilize the Pd(0).

Diglyme was also tested as solvent and poor yields were obtained when PPh_3 was used (entries 7 and 8) or in the absence of ligands (entries 11 and 12), where again we observed the formation of Pd black. However, quite surprisingly, good yields were obtained in the presence of BmimCl (entries 9 and 10), even using $Pd_3(dba)_2$.

Owing to the high toxicity of PPh_3, BmimCl would be a better choice as pre-ligand as it is more environmentally safe. The formation of an NHC complex[53–56] justifies the activity of the catalyst.

To generalize the method, other activated and deactivated halides, and different olefins, in the presence of BmimCl as pre-ligand and $Pd(OAc)_2$ in monoglyme were tested, and high yields were obtained. The results are summarized in Table 2.

All cross-coupling reactions (entries 1–7) yielded substituted-aryl olefins with high yields independently of the electron-withdrawing or -donating substituents, showing that the reaction medium was satisfatory for these different functional groups. The products could be easily separated from the catalyst by extraction with chloroform. It should be noted that in all cases only (*E*)-olefins were obtained selectively as confirmed by GC-MS and ^1H NMR, and compared with the literature.[65–68]

Experimental

General procedure for Heck reaction in monoglyme

In a 25 ml reaction flask, iodobenzene (1 mmol), methyl acrylate (1 mmol), $Pd(OAc)_2$ (0.05 mmol), KOAc (3 mmol) and BmimCl (0.1 mmol) were suspended in monoglyme (3 ml) at 80 °C for 18 h. The reaction mixture was extracted with chloroform. The organic phase was washed with water and brine and dried over anhydrous magnesium sulfate. The solution was filtered under celite®, the solvent evaporated and the crude product analyzed by GC-MS and ^1H NMR. (*E*)-Methyl cinnamate: white solid. ^1H NMR ($CDCl_3$, 300 MHz, ppm): δ 7.69 (d, $J = 16.1$ Hz, 1 H), 7.50–7.53 (m, 2 H), 7.39–7.37 (m, 3 H), 6.44 (d, $J = 16.1$ Hz, 1 H), 3.80 (s, 3 H). GC-MS: 166 *m/z*, 135 *m/z*, 107 *m/z*, 77 *m/z*.

Conclusion

In summary, the $Pd(OAc)_2$–BmimCl–monoglyme system proved to be a suitable system for the Heck reactions. Therefore BmimCl can advantageously be used as pre-ligand to substitute PPh_3. It is cheaper, safer and more environmentally friendly. Using the present protocol only *E*-olefins were obtained.

Acknowledgments

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