An efficient and recyclable ligand-free PEG₁₀₀₀-DIL/toluene temperaturedependent biphasic system for palladium catalysed Heck reactions Xiang Liu, Kai Yao, Yu-Lin Hu and Ming Lu*

College of Chemical Engineering, Nanjing University of Science and Technology, 200 Xiaoling Wei, Nanjing 210094, P. R. China

The Heck reaction of aryl halides with terminal olefins was successfully performed by using Pd $(OAc)_2$ as the catalyst in a ligand-free PEG₁₀₀₀-DIL (PEG₁₀₀₀-based dicationic ionic liquid)/toluene system exhibiting temperature-dependent biphasic behavior. In addition, the isolation of the products is readily performed by a simply decantation, and the catalytic system can be recycled and reused without loss of catalytic activity.

Keywords: Heck reaction, Pd (OAc)₂, ligand-free, PEG₁₀₀₀/toluene

The Heck reaction has emerged as an extremely powerful, attractive, and widely utilised method for the construction of carbon-carbon bonds.¹⁻⁷ The reaction normally requires a palladium catalyst to be present, particularly in the reactions of aryl halides with olefins.⁸⁻¹² However, the recovery and reuse of the catalyst is highly difficult. In view of economical and environmental reasons, the development of recyclable catalytic systems is one of the most challenging fields in laboratory and industry. In the past two decades, ionic liquids have attracted increasing attention due to their excellent physicochemical properties, such as reasonable thermal and chemical stability, negligible vapour pressure, and ease of recyclability.13,1 Moreover, carbon-carbon coupling catalysed by a palladium source in ionic liquids (IL) have been employed successfully.¹⁵⁻¹⁷ However, these processes suffer from some limitations: (i) the need for the use of toxic and expensive phosphine or N-heterocyclic carbene ligands, and (ii) the workup complexity, because most ILs show a degree of solubility in commonly used organic solvents, which causes many difficulties for product separation and recovery of the IL, especially in homogeneous catalytic reaction systems. Therefore, the search for new readily available ligand-free catalytic systems for addressing these drawbacks remains an important goal.

Multiphase systems,¹⁸ especially liquid–liquid biphasic systems, have been developed.¹⁹ Currently, some novel temperature-dependent ionic liquid biphasic catalytic systems including organic solvent/ionic liquid and supercritical carbon dioxide/ionic liquid^{20,21} have been reported and it has been found that these catalytic systems have advantages such as high conversions and selectivity, stability at high temperatures, reusability in the reaction, *etc.*, which provide a novel route for separating and recycling of catalysts (Fig. 1). To the best of our knowledge, there is no report on the palladium catalysed Heck reaction in temperature-dependent biphasic systems. Hence,



Fig. 1 Temperature-dependant PEG₁₀₀₀-DIL catalytic system.

* Correspondent. E-mail: Alexwpch@163.com

we now present the first efficient example of a free ligand palladium-catalysed Heck reaction in temperature-dependent organic solvent-ionic liquid biphasic system.

Our group recently demonstrated that a novel PEG₁₀₀₀-based dicationic ionic liquid (PEG₁₀₀₀-DIL, Scheme 1) not only exhibited temperature-dependent phase behavior with toluene, but also performed excellent catalytic activity in some reactions.^{22,23} In continuation of our previous work and to extend our research in developing temperature-dependent biphasic systems and their application in transition-metal-catalysed reactions, we would like to explore the catalysis role of PEG₁₀₀₀-DIL/toluene temperature-dependent biphasic system for Heck coupling in the presence of the cheap and air-stable Pd (OAc)₂.

Initially, investigations were carried out using iodobenzene and methyl acrylate as the reactants for optimising reaction conditions in the PEG₁₀₀₀-DIL/toluene temperature-dependent biphasic system. The effects of base, temperature and the amount of catalyst on the yields in the coupling reactions are summarised in Table 1.

As demonstrated in Table 1 (Table 1, entry 4), Et₃N as base gave the desired product with high yield. Those inorganic bases such as KOH, Na₂CO₃ and K₂CO₃ (Table 1, entries 1–3) were worse bases for the coupling due to their poor solubility in the biphasic system. We also optimised the concentration of catalyst and found all the reactions examined led to some degree of conversions but only the use of 2 mmol% palladium acetate gave the best result (Table 1, entries 4, 8, 9). Temperature was an important factor in the range 80–110 °C (Table 1, entries 4–7). The results indicated that the highest yield was obtained at 110 °C. It is noteworthy that PEG₁₀₀₀-DIL/toluene could not be a homogenous phase until the temperature was 80 °C at least.

For practical applications, the separation from reaction product and reusability of the catalyst are very important factors in Heck reactions. Easy catalyst separation and recycling in successive batch operations can greatly increase the efficiency of the reaction. To demonstrate this issue, the recycling experiments were conducted for the coupling reaction of iodobenzene and methyl acrylate. After the product was isolated from the reaction mixture, the residue was washed with toluene three times and the organic layer was decanted. Finally, the ionic layer was concentrated under reduced pressure to remove traces of toluene and the resulting liquid



Scheme 1 Structures of PEG₁₀₀₀-DIL.

 Table 1
 Optimised conditions via the coupling of iodobenzene with methyl acrylate^a

\frown	I + 🦳	COOMe Pd(DAc) ₂ / base 3 ₁₀₀₀₋ DIL/T	e ol.	-COOMe
1a	2	a		3a	
Entry	Base/ mmol	Pd(OAc) ₂ / mmol%	Temp./ °C	Conversion ^b /%	Yield ^c /%
1 2 3 4 5 6 7 8	$\begin{array}{c} KOH\\ Na_2CO_3\\ K_2CO_3\\ Et_3N\\ Et_3N\\ Et_3N\\ Et_3N\\ Et_3N\\ Et_3N\\ Et_3N\end{array}$	2 2 2 2 2 2 2 0.5	110 110 110 110 80 100 120 110	68 75 78 100 88 95 98 55	60 70 73 95 82 88 93 50

^aReaction conditions: iodobenzene (1.0 mmol), acrylate (2.0 mmol), base (2.0 mmol), Pd (OAc)₂, PEG₁₀₀₀-DIL (2.0 g), toluene (3.0 g). ^bDetermined by GC analysis. ^cIsolated yield.

was used for the next cycle under the same conditions. The result in Fig. 2 shows that the catalytic activity is maintained very well even after five cycles.

According to the above optimised conditions, we examined the application of the PEG₁₀₀₀-DIL catalytic system to crosscoupling various aryl iodides and terminal olefins. As shown in Table 2, it was found that there were still electronic effects of substituents on the yields of this reaction; electron-withdrawing or electron-donating substituents reacted with olefins rapidly and generated the coupled products with excellent yields. For the same olefins, aryl iodide with an electronwithdrawing group such as NO₂ (Table 2, entries 11-15) gave a high yield in a shorter time than those cases with electrondonating substituents (Table 2, entries 6-10). It is noteworthy that the reactivity of terminal olefins is also important for Heck reactions. According to the attached functional groups, the activity of terminal olefins was found to be: COOH>Ph> COOMe>COOEt>COOn-Bu, which could be seen from the corresponding yields of desired products. These results are consistent with the well-established trend in traditional Heck reactions using palladium derivatives as catalysts. It should be pointed out that all of the obtained products were transisomers, and were identified by ¹H NMR and melting point.

Encouraged by these results, further investigations were carried out for extending the scope of this catalytic system, the reactivity of substituted aryl bromides and aryl chloride was studied under the same conditions. It is well known that either C–Br or C–Cl is much more difficult compared to C–I activation. Therefore, compared to aryl iodides, it took a longer



Fig. 2 Repeated reactions using recovered $\mathsf{PEG}_{\mathsf{1000}}\text{-}\mathsf{DIL}$ catalytic system.

Table 2 Heck reactions of aryl lodides with terminal olefins^a

R ₁	≻-I + <u>—</u>	R ₂ Pd(OAc PEG ₁₀₀₀)₂/ Et₃N 」_DIL/Tol. R		
1а–с 2а–е			3a–o		
Entry	R1	R2	Time / h	Yield ^ь / %	
1	1a , H	2a , COOMe	4	3a , 95	
2	1a, H	2b, COOEt	4	3b , 94	
3	1a, H	2c , COOn-Bu	4	3c , 91	
4	1a , H	2d, COOH	4	3d , 98	
5	1a , H	2e , Ph	4	3e , 96	
6	1b , 4-OMe	2a , COOMe	6	3f , 94	
7	1b , 4-OMe	2b, COOEt	6	3g , 92	
8	1b , 4-OMe	2c , COOn-Bu	6	3h , 91	
9	1b , 4-OMe	2d, COOH	6	3i , 95	
10	1b , 4-OMe	2e , Ph	6	3j , 95	
11	1c, 4-NO ₂	2a , COOMe	2.5	3k , 99	
12	1c , 4-NO ₂	2b, COOEt	2.5	3I , 96	
13	1c , 4-NO ₂	2c , COOn-Bu	2.5	3m , 95	
14	1c , 4-NO ₂	2d, COOH	2.5	3n , 99	
15	1c , 4-NO ₂	2e , Ph	2.5	3o , 99	

^aReaction conditions: aryl iodides (1.0 mmol), terminal olefins (2.0 mmol), Et₃N (2.0 mmol), Pd(OAc)₂ (2 mmol%), PEG₁₀₀₀-DIL (2.0 g), toluene (3.0 g), 110 °C, the reaction was monitored by TLC.

^b Isolated yield.

reaction time for completing the Heck reaction of aryl bromides and aryl chloride with methyl acrylate. The results in Table 3 also show the electronic nature of the aryl bromides has a clear effect on the coupling reactions. For example, the coupling reaction of electron-rich 4-methyl-bromobenzene with methyl acrylate provided a 68% isolated yield (Table 3, entry 4), but for electron-deficient 4-nitro-bromobenzene, the desired coupled product was obtained in 80% isolated yield (Table 3, entry 2). However, it was unfortunate that poor yields were obtained for an aryl chloride even if possessing electrondrawing groups such as nitro (Table 3, entries 5–6).

In conclusion, we have disclosed an efficient and recyclable ligand-free PEG_{1000} -DIL/toluene catalytic system for the Heck reaction of aryl halides with terminal olefins, especial aryl iodides. It is worth noting that the present work is the first example of a Heck reaction catalysed by $Pd(OAc)_2$ in a temperature-dependent biphasic system. Moreover, the desired products were isolated by a simple decantation, and the catalytic system can be recycled and reused without evident

 Table 3
 Heck reactions of aryl bromides and aryl chloride with methyl acrylate^a

+OMe -	Pd(OAc) ₂ / PEG ₁₀₀₀₋ D	[/] Et ₃ N DIL/Tol. R ₁	OMe
2a			3a, 3k,3p,3q
R1	Х	Time / h	Yield ^b /%
H 4-NO ₂ 2,4-NO ₂ 4-CH ₃ 2,4-NO ₂ 4-NO ₂	1d, Br 1e, Br 1f, Br 1g, Br 1h, Cl 1i, Cl	36 30 24 48 48 48	3a, 75 3k, 80 3p, 90 3q, 68 3p, 46 3k, 38
	+OMe - 2a R1 H 4-NO ₂ 2,4-NO ₂ 4-CH ₃ 2,4-NO ₂ 4-NO ₂	$\begin{array}{c} + = \underbrace{\bigcirc}_{OMe} & \underbrace{\Pr(OAc)_{2'}}_{PEG_{1000},E} \\ \hline \\ 2a & & \\ \hline \\ R1 & X \\ \hline \\ H & 1d, Br \\ 4-NO_2 & 1e, Br \\ 2,4-NO_2 & 1f, Br \\ 4-CH_3 & 1g, Br \\ 2,4-NO_2 & 1h, Cl \\ 4-NO_2 & 1i, Cl \\ \hline \end{array}$	$\begin{array}{c} + & \underbrace{ \begin{array}{c} O \\ OMe \end{array} } \underbrace{ \begin{array}{c} Pd(OAc)_2/ \ Et_3N \\ PEG_{1000}. DIL/Tol. \end{array} } \\ \hline R1 \\ \hline R1 \\ H \\ 1d, \ Br \\ 4-NO_2 \\ 1e, \ Br \\ 30 \\ 2,4-NO_2 \\ 1f, \ Br \\ 24 \\ 4-CH_3 \\ 1g, \ Br \\ 48 \\ 2,4-NO_2 \\ 1h, \ Cl \\ 48 \\ 4-NO_2 \\ 1i, \ Cl \\ 48 \\ \end{array} } \begin{array}{c} \\ \end{array} $

^aReaction conditions: ArX (1.0 mmol), methyl acrylate (2.0 mmol), Et_3N (2.0 mmol), Pd (OAc)₂ (2 mmol%), PEG₁₀₀₀-DIL (2.0 g), toluene (3.0 g), 110 °C, the reaction was monitored by TLC. ^bIsolated yield.

decrease in activity. Further efforts to extend the application of the system in other Pd-catalysed reactions are in progress in our laboratory.

Experimental

All the chemicals were from commercial sources without any pretreatment. All reagents were of analytical grade. The ionic liquids were synthesised according to the literature procedure.23 ¹H NMR spectra were recorded on a Bruker 500-MHz spectrometer with tetramethylsilane (TMS) as an internal standard. Melting points were recorded on a Buchi R-535 apparatus and are uncorrected. Gas chromatography (GC) analysis was performed on an Agilent GC-6820 equipped with a 30 m \times 0.32 mm \times 0.5 µm HP-Innowax capillary column and a flame ionisation detector. GC-MS analyses were performed on a Saturn 2000 GC/MS instrument.

Palladium acetate catalysed Heck cross-coupling reaction of aryl halides with terminal olefins in a PEG₁₀₀₀-DIL/toluene temperaturedependent biphasic system; general procedure

Under an air atmosphere, a flask was charged with aryl halides (1.0 mmol), terminal olefins (2.0 mmol), Et₃N (2 mmol), PEG₁₀₀₀-DIL/toluene (2.0 g/3.0 g) and Pd(OAc)₂ (2 mmol%). The mixture was heated to 110 °C for the indicated time and the reaction progress was monitored by TLC. After the reaction the solution was cooled to room temperature, the organic phase was separated by decantation, and then rinsed with water $(3 \times 10 \text{ mL})$. The organic phase was dried with anhydrous sodium sulfate, filtered, and the solvent was removed under reduced pressure. The residue was purified by column chromatography to afford the desired product. All products are known compounds and the identities of some representative compounds were confirmed by comparison with literature spectroscopic data.

 (\vec{E}) -Methyl cinnamate $(\mathbf{3a})$:²⁴ Rf = 0.4 (petroleum ether/ethyl acetate = 100:1, v/v). Chromatography solvent petroleum ether/ethyl acetate = 150/1, v/v). ¹H NMR (500 MHz, CDCl₃): δ = 7.73 (d, J = 16.0 Hz, 1H), 7.28-7.55 (m, 5H), 6.45 (d, J = 16.0 Hz, 1H),3.83 (s, 3H); GC-MS: m/z (%) = 162 (44) [M⁺], 131 (100), 103 (67), 77 (36), 51 (20).

(*E*)-*Ethyl cinnamate* (**3b**):²⁵ Rf = 0.5 (petroleum ether/ethyl acetate = 100:1, v/v). Chromatography solvent petroleum ether/ethyl acetate = 150/1, v/v) ¹H NMR (500 MHz, CDCl₃): δ = 7.72 (d, J=16.1 Hz, 1H), 7.379-7.55 (m, 5H), 6.44-6.47 (m, 1H), 4.26-4.30 (m, 2H) 1.34–1.37 (m, 3H); GC-MS: m/z (%) = 176 (23) [M⁺], 131 (100), 103 (57), 77 (34).

(*E*)-*Butyl cinnamate* (**3c**):²⁵ Rf = 0.4 (petroleum ether/ethyl acetate = 100:1, v/v). Chromatography solvent petroleum ether/ethyl acetate

= 150/1, v/v). ¹H NMR (500 MHz, CDCl₃): δ = 7.69 (d, J = 16.0 Hz, 1H), 7.51–7.54 (m, 2H), 7.37–7.39 (m, 3H), 6.45 (d, J = 16.0 Hz, 1H), 4.21 (t, J = 6.7 Hz, 2H), 1.65–1.74 (m, 2H), 1.38–1.50 (m, 2H), 0.97 (t, J = 7.3 Hz, 3H); GC-MS: m/z (%) = 204 (18) [M⁺], 148 (74), 131 (100), 103 (45), 77 (24).

(E)-Methyl 3-(4-nitrophenyl) acrylate (3k):²⁶ Rf = 0.4 (petroleum ether/ethyl acetate = 20:1, v/v). Chromatography solvent petroleum ether/ethyl acetate = 50/1, v/v). White solid; Mp. 137.5–138.7 °C; ¹H NMR (500 MHz, CDCl₃): $\delta = 8.23 - 8.25$ (m, 2H), 7.66–7.73 (m, 3H), 6.55 (d, J = 16.1 Hz, 1H), 3.83 (s, 3H); GC-MS: m/z (%)= 207 (48) [M⁺], 176 (100), 146 (88), 130 (78), 118 (63), 102 (69), 90 (41), 76 (40), 51 (30).

Received 29 October 2011; accepted 28 November 2011 Paper 1100960 doi: 10.3184/003685011X13238914941786 Published online: 27 December 2011

References

- 1 S. Dinesh, W. Yogesh, B. Kushal and B.Bhalchandra, Tetrahedron Lett., 2011. 52. 2390-2393.
- 2 I.P. Beletskaya and A.V. Cheprakov, Chem. Rev., 2000, 100, 3009.
- 3 U. Christmann and R. Vilar, Angew. Chem. Int. Ed., 2005, 44, 366.
- 4 A. Zapf and M. Beller, Chem. Commun., 2005, 431.
- J.P. Genet and M. Savignac, J. Organomet. Chem., 1999, 576, 305.
- 6 I.P. Beletskaya and A.V. Cheprakov, Chem. Rev., 2000, 100, 3009.
- C. Amatore and A. Jutand, J. Organomet. Chem., 1999, 576, 254.
- 8 S. Oi, K. Sakai and Y. Inoue, Org. Lett., 2005, 7, 4009.
- 9 J. Yorke, L. Wan, A. Xia and W. Zheng, Tetrahedron Lett., 2007, 48, 8843.
- 10 O. Akba and S. Özkar, J. Organomet. Chem., 2009, 694, 731.
- 11 Y.D. Wang and M. Lin, Tetrahedron., 2009, 65, 57.
- X.R. Wang and F. Chen, J. Chem. Res., 2010, 714. 12
- 13 S.B. Park and H. Alper, Org. Lett., 2003, 5, 3209.
- 14 H. Hagiwara, Y. Sugawara and K. Isobe, Org. Lett., 2004, 6, 2325.
- 15 S. Bouquillon, B. Ganchegui and B. Estrine, Organomet. Chem., 2001, 634. 153.
- 16 Y.Q. Cai and G.H. Gao, Catal Lett., 2007, 119, 154.
- R. Wang and J.M. Shreeve, J. Org. Chem., 2006, 71, 426. 17
- 18 Y.H. Wang and Z.L. Jin, J. Mol. Catal. A: Chem., 2003, 195, 133.
- 19 S. Sunitha and B.N. Rachapudi, Tetrahedron Lett., 2007, 48, 6962.
- 20 Y. Leng and L. Shen, Angew. Chem. Int. Ed., 2009, 8, 168.
- 21 B. Tan and Z.L. Jin, Appl. Organomet. Chem., 2008, 22, 620.
- 22 H.Z. Zhi and J. Luo, Chem. Commun., 2009, 3, 1.
- 23 Y.L. Hu and M. Lu, ChemCatChem., 2010, 2, 392.
- 24 B.R. Buckley and S.P. Neary, Adv. Synth. Catal., 2009, 71.
- 25 S.H. Huang and F.Y. Tsai, Molecules, 2010, 315
- 26 S. Sawoo and A. Sarkar, Tetrahedron, 2009, 65, 4367.

Copyright of Journal of Chemical Research is the property of Science Reviews 2000 Ltd. and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.