

Communication

Heck Reaction Catalyzed by Palladacycle in Neat Water[†]

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Cyclopalladated ferrocenylimine has been found to be a type of excellent phosphine-free catalyst for Heck reactions in neat water with both higher yields and turnover numbers than those reported in the literature up to now. Some commercial emulsifying agents, including the commonly used quaternary ammonium salts, have been proved to be excellent additives in the catalysis of the reactions. Not only aromatic iodide, but also aromatic bromide could be coupled with the olefins. All reactions were able to be conducted in air under refluxing condition.

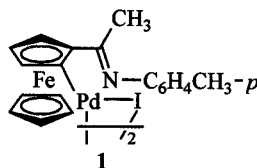
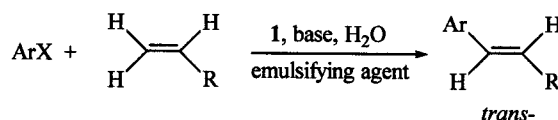
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There is increasing recognition that organic reactions carried out in water may offer advantages over those in organic solvents.¹ Until recently, palladium promoted reactions, especially Heck reactions in aqueous media are not investigated extensively. During the eighties of the last century, in their pioneering work, Beletskaya *et al.* began to use neat water or aqueous organic solvent to conduct Heck reactions.² From then on, one of the interests in Heck reactions in aqueous solution has been scheming and synthesizing a soluble, functional complex of palladium as catalysts.³ There has been scarcely any report of insoluble catalysts in neat water. Most of the recent research indicated that a Pd(0) colloid is the active species which catalyzes the Heck reactions,⁴ there is therefore no difference between soluble and insoluble catalysts in an aqueous reaction process. If an insoluble catalyst could catalyze Heck reactions in aqueous solutions or neat water, it is not necessary to synthesize aqueous soluble palladium complexes modified by functional groups. On the basis of such understanding, we decided to use an aqueous insoluble palladacycle, phosphine-free cyclopalladated ferrocenylimine, which is an excellent catalyst discovered by us recently to catalyze Heck reactions in neat water.

Among all the catalysts employed in Heck reactions, palladacycle is outstanding due to its very high efficiency.⁵ Phosphine-free cyclopalladated ferrocenylimines were em-

ployed in Heck reactions of aromatic halides including iodides, bromides and chlorides with olefins in organic solvents. The turnover numbers achieved were as high as 7.36×10^6 and the high catalytic activity retainable after repeated uses.⁶ Here we report the preliminary results of the Heck reaction in neat water catalyzed by phosphine-free cyclopalladated ferrocenylimine **1** in the presence of base and emulsifying agent (Scheme 1).

Scheme 1



Ar = C₆H₅, *p*-ClC₆H₄, *p*-CH₃C₆H₄, *p*-O₂NC₆H₄, *p*-NCC₆H₄;
 X = I, Br;
 R = CO₂Et, CO₂Bu-*n*, CO₂Me, Ph, CO₂NH₂

Investigation of the arylation of ethyl acrylate by iodobenzene with 2.5×10^{-3} mol% catalyst **1** in the presence of different emulsifying agents is shown in Table 1. Here it can be seen that the emulsifying agents are manifold in assisting Heck reactions. All the quaternary ammonium salts (Entries 1–5) and triton X-100 (Entry 9) used are efficient emulsifying agents that complete the arylation with 2.5×10^{-3} mol% catalyst **1** in 10 or 25 h with moderate to high yields. Tween 60 and 40 (Entries 6, 7) are also efficient, feasible and cheap. The HLB (hydrophile lipophile balance) values of Tween 85, 60 and 40 are 11, 14.9 and 15.6, respectively. The lower efficiency of Tween 85 is attributed to the lower HLB. Higher HLB of about 15 can be appropriate for the emulsification of the reaction mixture. Ethylene glycol and PEGs

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including triethylene glycol and tetraethylene glycol (Entries 10–12) also assist the reaction. The reactivity difference between them is not obvious. From the comparison of five solid oxide powders (Entries 16–20), it could be found that MnO₂ and CuO are the best among them. Turnover numbers obtained with some kinds of feasible emulsifying agents are listed in Table 2.

Table 1 Results of Heck reaction of PhI with CH₂ = CHCO₂Et in neat water catalyzed by 2.5 × 10⁻³ mol% catalyst 1 with different emulsifying agents

Entry ^a	Emulsifying agent ^b	T (h)	Yield ^c (%)
1	Bu ₄ NBr	10	100
2	Me ₄ NI	10	66.4
3	Et ₄ NI	10	73.6
4	Me ₃ PhNI	10	83.1
5	CH ₃ (CH ₂) ₁₄ CH ₂ Me ₃ NBr	10	87.0
6	Tween 60 ^{d,e}	10	78.6
7	Tween 40 ^{d,f}	10	80.3
8	Tween 85 ^{d,g}	25	22.6
9	Triton X-100 ^d	25	82.9
10	Tetraethylene glycol ^d	25	61.8
11	Triethylene glycol ^d	25	71.8
12	Ethylene glycol ^d	25	57.4
13	Gelatin ^d	25	8.6
14	β-CD ^d	25	40.2
15	Dextrin ^d	25	40.1
16	MnO ₂	25	61.9
17	CuO	25	60.6
18	Al ₂ O ₃	25	29.5
19	Al ₂ O ₃ (alkaline)	25	49.5
20	Fe ₃ O ₄	25	24.3

^a Amounts ratio: PhI 5 mmol, CH₂ = CHCO₂Et 6 mmol, Et₃N 6 mmol, water 2 mL, emulsifying agents 5 mmol except Entries 6–15. ^b The concentration of each emulsifying agent used is greater than its critical micellar concentration. ^c Repeated results determined by HPLC based on PhI. ^d Amount: 1 g. ^e Polyoxyethylene sorbitan monostearate. ^f Polyoxyethylene sorbitan monopalmitate. ^g Polyoxyethylene sorbitan trioleate.

Table 2 Turnover numbers obtained with some kinds of feasible emulsifying agents in the reaction of PhI with CH₂ = CHCO₂Et

Entry ^a	Catalyst 1 (mol%)	Emulsifying agent	T (h)	Yield ^b (%)	TON	TOF
1	2.5 × 10 ⁻⁴	Bu ₄ NBr	80	69.5	278000	3475
2	2.5 × 10 ⁻⁴	Tween 60 ^c	80	45.3	181200	2265
3	2.5 × 10 ⁻⁴	Tween 40 ^c	80	61.9	247600	3095
4	2.5 × 10 ⁻⁴	Triton X-100 ^c	80	50.1	200400	2505

^a Amounts ratio: PhI 5 mmol, CH₂ = CHCO₂Et 6 mmol, Et₃N 6 mmol, water 2 mL, emulsifying agents 5 mmol except Entries 2–4.

^b Repeated results determined by HPLC based on PhI. ^c Amount: 1 g.

About twenty kinds of bases used for Heck reactions have been examined. The selected results of effect of bases on Heck reaction in neat water are listed in Table 3. Similar to Heck reactions conducted in organic solvents that have been reported,⁶ Et₃N and NaOAc are the best bases (Entries 1, 2 of Table 3) which are both feasible and cheap. The results of Heck reaction of some different substrates in neat water with Bu₄NBr are listed in Table 4.

Table 3 Selected results of effect of bases on Heck reaction of PhI with CH₂ = CHCO₂Et in neat water with 2.5 × 10⁻³ mol% catalyst 1 and Bu₄NBr

Entry ^a	Base	T (h)	Yield ^b (%)
1	Et ₃ N	10	100
2	NaOAc	25	81.8
3	Na ₂ CO ₃	25	13.7
4	[CH ₃ (CH ₂) ₅] ₃ N	25	47.7
5	[(CH ₃) ₂ CHCH ₂ CH ₂] ₃ N	25	61.2
6	N(CH ₂ CH ₂ OH) ₃	25	52.9
7	<i>p</i> -CH ₃ C ₆ H ₄ NH ₂	25	47.2

^a Amounts ratio: PhI 5 mmol, CH₂ = CHCO₂Et 6 mmol, base 6 mmol, water 2 mL, Bu₄NBr 5 mmol. ^b Repeated results determined by HPLC based on PhI.

The above-mentioned results are summarized to highlight five characteristics: (1) higher efficiency than other catalysts, especially phosphine-free palladium catalysts that have been used in neat water or aqueous organic solvent in the literature reported up to now. The highest turnover number obtained is 278000. (2) The emulsifying agents used are manifold and the emulsions are characterized to be O/W type using dyeing method (Fig. 1 shows the micro-photography of triton X-100 with rhodium B). The concentrations of all the emulsifying agents used are greater than the CMC (critical micellar concentrations). Some commercial reagents, including the commonly used quaternary ammonium salts, have been proved good to excellent. (3) The common and cheap Et₃N and NaOAc can be used as highly efficient bases in this reaction system. (4) The scope of the substrates is broad. Various olefins including acrylates, styrene and acrylamide, and different aryl halides including iodides and bromides could be employed for the reaction. (5) All the reactions were conducted in air under refluxing condition and characterized by freedom from protection of inert gases.

In conclusion, an insoluble phosphine-free palladacycle has been successfully applied to catalyze Heck reactions in neat water. From the high yields and turnover numbers, it is suggested that the catalyst in neat water should not be confined to soluble type. The high diversity of substrates, excellent efficiency and convenience of operation of insoluble palladacycle make it an excellent kind of practical catalyst for Heck coupling reaction in neat water.

Table 4 Heck reaction of some different substrates in neat water with Bu₄NBr

Entry ^a	ArX	R	Catalyst 1 (mol%)	T (h)	Yield (%)	TON	TOF
1	C ₆ H ₅ I	CO ₂ Bu	2.5 × 10 ⁻³	10	100 ^b	40000	4000
2	C ₆ H ₅ I	CO ₂ Me	2.5 × 10 ⁻³	10	94.7 ^c	37880	3788
3	C ₆ H ₅ I	C ₆ H ₅	2.5 × 10 ⁻³	10	92.1 ^b	36840	3684
4	C ₆ H ₅ I	CONH ₂	2.5 × 10 ⁻³	10	74.5 ^c	29800	2980
5	<i>p</i> -ClC ₆ H ₄ I	CO ₂ Bu	2.5 × 10 ⁻³	10	100 ^b	40000	4000
6	<i>p</i> -ClC ₆ H ₄ I	CO ₂ Et	2.5 × 10 ⁻³	10	100 ^b	40000	4000
7	<i>p</i> -ClC ₆ H ₄ I	CO ₂ Me	2.5 × 10 ⁻³	10	93.1 ^c	37240	3724
8	<i>p</i> -ClC ₆ H ₄ I	C ₆ H ₅	2.5 × 10 ⁻³	20	94.2 ^c	37680	1884
9	<i>p</i> -CH ₃ C ₆ H ₄ I	CO ₂ Bu	2.5 × 10 ⁻³	10	97.0 ^c	38800	3880
10	<i>p</i> -CH ₃ C ₆ H ₄ I	CO ₂ Et	2.5 × 10 ⁻³	10	91.8 ^c	36720	3672
11	<i>p</i> -CH ₃ C ₆ H ₄ I	CO ₂ Me	2.5 × 10 ⁻³	10	88.1 ^c	35240	3524
12	<i>p</i> -CH ₃ C ₆ H ₄ I	C ₆ H ₅	2.5 × 10 ⁻³	20	89.7 ^c	35880	1794
13	<i>p</i> -O ₂ NC ₆ H ₄ Br	CO ₂ Et	2.5 × 10 ⁻²	20	99.0 ^b	3960	198
14	<i>p</i> -O ₂ NC ₆ H ₄ Br	CO ₂ Et	2.5 × 10 ⁻³	80	68.5 ^b	27400	343
15	<i>p</i> -NCC ₆ H ₄ Br	CO ₂ Et	2.5 × 10 ⁻²	20	90.5 ^c	3620	181
16	<i>p</i> -NCC ₆ H ₄ Br	CO ₂ Et	2.5 × 10 ⁻³	80	60.5 ^c	24200	303

^a Amounts ratio: ArX 5 mmol, CH₂ = CHR 6 mmol, Et₃N 6 mmol, Bu₄NBr 5 mmol, water 2 mL. ^b Determined by HPLC based on ArX.

^c Isolated yields based on ArX.

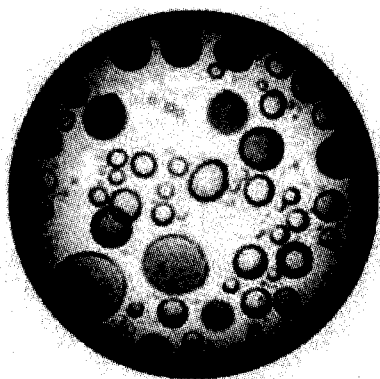


Fig. 1 Micro-photography of triton X-100 with rhodium B.

Experimental

Cyclopalladated ferrocenylimine **1** was synthesized according to the reported method.⁶

Typical procedure for Scheme 1: ArX (5 mmol), olefin (6 mmol), base (6 mmol), emulsifying agent (5 mmol or 1 g), water (2 mL) and catalyst were added in a flask with an condenser, then the mixer was stirred in air at about 100 °C in oil bath. The yields of *trans*-products were determined by HPLC or thin layer chromatography based on ArX.

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