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Heterogeneous Heck reaction catalyzed by Pd/C in ionic liquid

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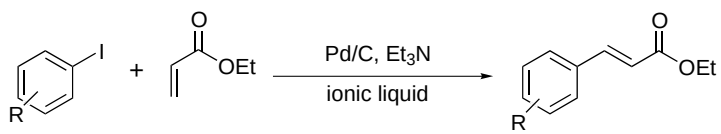
Abstract—Pd/C-catalyzed Heck reactions of aryl halides with olefins proceeded in moderate to satisfactory yields in ionic liquid [bmim]PF_6. The ionic liquid involving a catalyst was easily recycled.

Palladium-catalyzed carbon–carbon bond forming reactions have contributed remarkably to synthetic organic chemistry.[1] Among these reactions, Heck and its related reactions have been extensively utilized in preparing a wide variety of olefinic compounds.[2] One major transformation in the Heck reaction is the synthesis of cinnamic acid and its derivatives, which are very versatile compounds as flavour substances or UV absorbents and so on. Especially in the case where preparation of some substituted aryl aldehydes was difficult, the Heck reaction has great synthetic value. In view of the economy of the reaction, the recovery as well as recycling of the expensive Pd catalyst is required. However, a homogeneous Pd catalyst usually precipitated from the solution and recycling or recovery of an active Pd catalyst was difficult. Heterogeneous catalysts would be much better from such a viewpoint. Reetz and Lohmer developed colloidal Pd clusters generated electrochemically.[3] Recently, Ying et al. reported Pd-grafted molecular sieves that effectively catalyze heterogeneous Heck reactions.[4] Pd/C is a recoverable heterogeneous catalyst and is stable and relatively inexpensive, although its catalytic activity was undeveloped[5] except in catalytic hydrogenation. Scattered precedents of Pd/C-catalyzed carbon–carbon bond forming reactions[6] exemplify its catalytic reactivity. Attention was then focused on the Heck reaction in an ionic liquid, which has attracted growing interest as an environmentally benign re-usable solvent.[7–10] Especially, the highly polar nature of ionic liquid is expected to work as an activating and stabilizing solvent for Pd/C-catalyzed Heck reactions.

Recent results on the Heck reaction in an ionic liquid,[10] as well as our current interests in the selectivity in Pd-catalyzed arylation leading to aromatized ionone natural products,[11] prompted us to report an expedient Pd/C-catalyzed Heck reaction in an ionic liquid (Scheme 1).

The reaction was carried out simply by heating a solution of aryl substrate, olefin and base in ionic liquid with 3 mol% of 10% Pd/C. As the ionic liquid, [bmim]PF_6[12] was employed because of its air and moisture stability, easy availability and higher utility in several organic reactions.[7–10] Pd/C dispersed well in [bmim]PF_6. After the reaction, the product was



1 2 3

Scheme 1.

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extracted simply by stirring with *n*-hexane or diethyl ether several times followed by decantation of the upper organic layer. Isolation of products from the ionic liquid was complete according to GLC analysis of the remaining ionic liquid. No aqueous work-up was required.[10a,c] The Pd/C was kept and suspended completely in the ionic liquid layer after the extraction.

Some representative results are compiled in Table 1. As shown in entries 1 and 2, ethyl cinnamate was obtained in high yield. Aryl iodides having electron-donating or -accepting substituents gave the corresponding cinnamates in moderate to acceptable yields (Table 1, entries 4–6). Among the bases investigated, triethylamine gave the best result. An inorganic base such as sodium hydrogencarbonate[11] provided poor yields (entry 3). Bromobenzene also gave ethyl cinnamates and the results are listed in Table 2. However, aryl triflates were recovered completely even at 140°C with or without a phosphine ligand.

Under conventional reaction conditions, a homogeneous Pd catalyst deteriorated and a Pd black deposited after the reaction. Recovery of the Pd catalyst is usually not realistic, thus eliminating the possibility of recycling the Pd catalyst. On the other hand, since Pd/C remained only in the ionic liquid, the ionic liquid containing Pd/C can be re-used as a catalyst system itself, as shown in Table 3. Although a certain decrease in yields was observed after the second re-use, probably due to accumulation of triethylammonium iodide (Table 3, entries 3–5), washing the ionic liquid layer with water[10c] recovered the catalytic activity to the same level as in a fresh system (Table 3, entry 6).

The present reaction conditions were applicable to a combination of other substrates and olefins (Scheme 2, Table 4 and Fig. 1). Acrylonitrile, styrene (Table 4, entries 1–5) and methyl methacrylate (Fig. 1) afforded

Table 1. Pd/C-catalyzed Heck reactions with ethyl acrylate in ionic liquid

Entry[a]	Aryl iodide	Time (h)	Yield (%)[c]
1	R = H	1	92
2	R = H	12	95
3[b]	R = H	12	(19)[d]
4	R = 4-Me	12	53
5	R = 4-OMe	12	69
6	R = 4-COMe	24	65

[a] See Ref. 13.
[b] Sodium hydrogencarbonate was used.
[c] Only *E*-isomers were obtained.
[d] Yield in parentheses was obtained by GLC analysis.

Table 2. Pd/C-catalyzed Heck reactions of aryl bromide

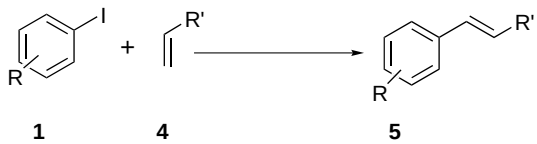
Entry[a]	Aryl bromide	Time (h)	Yield (%)[c]
1	R = H	12	40
2	R = H[b]	12	45
3	R = 4-NO_2	12	85
4	R = 3-Cl	12	52
5	R = 4-OMe	12	25

[a] All reactions were carried out in the same manner as in Table 1 at 140°C.
[b] Triphenylphosphine (0.04 equiv.) was added.
[c] Only *E*-isomers were obtained.

Table 3. Recycle of catalyst system

Entry[a]	Recycle	Yield (%)
1	0	92
2	1	93
3	2	84
4	3	81
5	4	80
6[b]	5	95

[a] Reaction was carried out as described in Table 1 for 12 h.
[b] Catalyst system in entry 6 was washed with water before use.



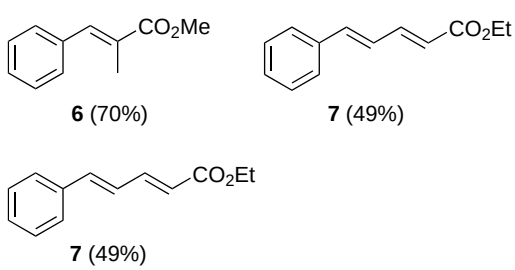
1 **4** **5**

Scheme 2.

Table 4. Pd/C-catalyzed Heck reactions with olefins in ionic liquid

Entry[a]	Aryl iodide **1**	Olefin **4**	Time (h)	Yield (%)[b]
1	R = H	R′ = CN	12	92[c]
2	R = 4-OMe	R′ = CN	12	88[d]
3	R = 4-Me	R′ = Ph	24	59
4	R = 4-OMe	R′ = Ph	24	59
5	R = 4-COMe	R′ = Ph	24	29
6	R = H	R′ = COMe	12	32[e]
7	R = H	R′ = COMe	12	26[f]
8	R = H	R′ = COEt	12	16

[a] Reaction was carried out in the same manner as in Table 1.
[b] Only *E*-isomers were obtained except entries 1 and 2.
[c] The ratio of *E*/*Z* isomer was 4:1.
[d] The ratio of *E*/*Z* isomer was 3.6:1.
[e] 4-Phenyl-2-pentanone (15%) was accompanied along with recovered iodobenzene.
[f] Sodium hydrogencarbonate was used.



6 (70%) **7** (49%)

7 (49%)

Figure 1.

the Heck products in acceptable yields. In the reactions with vinylketones (Table 4, entries 6–8), yields were low probably due to instability of both olefins and products. Reaction of bromostyrene and ethyl acrylate also provided the desired product **7** (Fig. 1).

In all cases, reactions were clean and the only side products were arylhalides. Conversion yields could not be obtained because of the high volatility of the arylhalides recovered.

Dupont et al.[8b] and, subsequently, Xiao et al.[8d] reported the isolation and identification of a Pd complex formed from $Pd(OAc)_2$ or $PdCl_2$ with ionic liquid. Dissolution of Pd black over 100°C was proposed by Earle et al.[10c] We investigated the presence of the Pd species in an ionic liquid before and after the present Heck reaction by ICP emission spectroscopy. After filtration of the suspending Pd/C, ICP analysis revealed that the concentration of Pd in the ionic liquid was negligible. This important observation implies that the Pd/C catalyzes the Heck reaction on the surface of Pd held on the carbon.[3]

Thus, we have offered an expedient protocol for Heck arylation reactions by using Pd/C as an inexpensive and stable catalyst in ionic liquid. One major advantage of the present protocol is that the catalyst system was easily re-usable without loss of catalytic activity, thereby multiplying catalyst turn-over. Another advantage is that the reaction proceeded without phosphine ligands, which are expensive, toxic and contaminants of products. Green character of the ionic liquid as well as easy operation make the present Heck reaction attractive.

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13. Typical experimental procedure: To a stirred slurry of 10% Pd/C (33 mg, 0.031 mmol) in [bmim]PF_6 (1 ml) was added iodobenzene (204 mg, 1 mmol), triethylamine (210 μl, 1.5 mmol) and ethyl acrylate (163 ml, 1.5 mmol). The resulting slurry was heated at 100°C under a nitrogen atmosphere for 12 h under a rubber septum. After cooling to rt, the product was extracted six times with *n*-hexane by vigorous stirring followed by decantation of the upper *n*-hexane layer. Evaporation of the combined organic layer and subsequent medium-pressure LC purification of the residue (eluent: AcOEt:*n*-hexane = 1:3) afforded *E*-ethyl cinnamate (151 mg, 86%).