

# Palladium-catalyzed, arylation of ethylene (the Heck reaction) under aqueous conditions

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## Abstract

The palladium-catalyzed arylation of ethylene under aqueous or aqueous-organic solvent two-phase conditions has been studied using  $\text{PdCl}_2\text{L}_2$  (L, phosphorus ligand) as the catalyst. Both aqueous  $\text{NaHCO}_3$ -soluble and -insoluble bromoarenes possessing electron withdrawing groups react with ethylene to give the styrenes in good yields by water-soluble catalyst (L,  $(\text{C}_6\text{H}_5)_2\text{P}(m\text{-C}_6\text{H}_4\text{SO}_3\text{Na})$  (tppms)<sup>1</sup>. Bromoarenes possessing electron-donating groups react with difficulty but the reaction takes place with the corresponding iodoarenes to afford the products in moderate yields. The reaction of 3-bromobenzoic acid by water-insoluble (L,  $(\text{C}_6\text{H}_5)_3\text{P}$  (tpp)<sup>2</sup> under two-phase conditions gave the product in a poor yield.

*Keywords:* Aqueous conditions; Arylation; Ethylene; Heck reaction; Olefins

## 1. Introduction

The Heck reaction [1], as well as palladium-catalyzed cross-coupling of haloarenes with organometallic vinyl compounds [2–4], is generally the most useful method for arylation of alkenes. This reaction is applicable to haloarenes and alkenes bearing a variety of functional groups. Recently it has been employed in the synthesis of conductive polymers [5]. In the Heck reaction solvent may be used, but is not often necessary. As the solvent, excess amine is usually seen, as well as acetonitrile, methanol, dimethylformamide and so on.

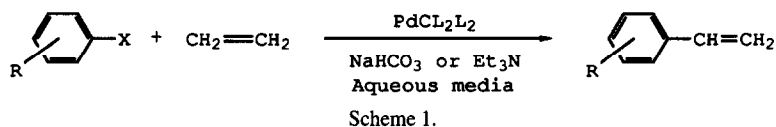
In the past few years we have studied transition metal-catalyzed reactions in aqueous media [6,7].

The use of aqueous media is attractive because of economy and safety. Moreover, its use can simplify catalyst–product separation. Therefore, aqueous/organic solvent two-phase catalysis is finding wide applications [8]. Though aqueous/organic solvent two-phase systems show the characteristic features of water in many organic reactions described above, only a few researches have been devoted to the palladium-catalyzed reactions of alkenes in aqueous media. This fact seems to stem from a conception that water must be completely excluded from the reaction system, otherwise a Wacker-like reaction occurs. In recent years, however, investigations were undertaken to use water as the solvent in palladium-catalyzed reactions of alkenes. A few reports have shown that water can be added in the Heck reaction [9–13]. These researches are concerned with the ary-

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<sup>1</sup> tppms = sodium *m*-(diphenylphosphino)benzenesulfonate

<sup>2</sup> tpp = triphenylphosphine



lations of acrylic acid, acrylonitrile, or cyclic olefins with iodoarenes.

We were interested in the palladium-catalyzed reaction of ethylene in aqueous media, because it appears that ethylene is the most reactive alkene in many transition metal-catalyzed reactions and that often shows different activities from other alkenes. For instance, while cyclohexene or styrene forms a moisture-stable  $[\text{PdCl}_2\text{-alkene}]_2$  complex, which is prepared by the reaction of  $\text{PdCl}_2(\text{C}_6\text{H}_5\text{CN})_2$  with the alkenes [14], the corresponding ethylene complex is extremely sensitive to moisture and instantaneously decomposed on exposure to air. Very recently, it was reported that high-purity vinyl toluenes were obtained by the Heck reaction in a DMF/ $\text{H}_2\text{O}$  two-phase system [15]. In the present study we aimed at searching possible aqueous conditions for the reaction of ethylene with a variety of haloarenes (Scheme 1).

## 2. Results and discussion

There are three combinations to carry out the reaction in an aqueous solution or in a two-phase system under basic conditions: (1) both catalyst and haloarene are water-soluble and present in the aqueous phase, (2) catalyst is water-soluble and haloarene is water-insoluble, and (3) catalyst is water-insoluble and haloarene is water-soluble. Since the catalyst and product are present in different phases in the last two cases, it is expected that the separation of the catalyst from the product would be easy. Initially we employed a water-soluble catalyst and searched for optimal conditions using 3-bromobenzoic acid as the haloarene.

**Reaction of 3-bromobenzoic acid by water-soluble catalyst.** Firstly, palladium acetate combined with water-soluble sodium *m*-(diphenylphosphino)benzenesulfonate ( $(\text{C}_6\text{H}_5)_2\text{P}(\text{m-C}_6\text{H}_4\text{SO}_3\text{Na})$  (tppms), was employed as the

catalyst and a systematic investigation was undertaken with alkaline solution of 3-bromobenzoic acid. The results are shown in Table 1.

In the usual arylation of ethylene in organic solvent the high ethylene pressure deactivates the catalyst by coordination, probably decreasing the rate of the oxidative addition of haloarene. It has been reported that the modest pressure between 7 and 9 atm looks like a favorable choice for the arylation of ethylene [16]. The reaction was carried out under similar conditions described by Heck, except that organic solvent was replaced by water. Unfortunately, the yield was poor and a large amount of 3-bromobenzoic acid was recovered unchanged. Since the solubility of ethylene into water is very low, we concluded that the difficulty must lie in its low solubility. High pressure was applied, but the yield was still low (Entry 1) in contrast to the Heck reaction under two-phase conditions already reported using cyclic olefins [11]. The addition of tetrahydrofuran as the solvent improved the reaction to some extent (Entry 2).

Another complication of this reaction was the formation of a black precipitate of metallic palladium during the reaction. This fact is attributable to the combined use of  $\text{Pd}(\text{OAc})_2$  and tppms. The reduction of a  $\text{Pd}^{2+}$  species with ethylene in water precedes the coordination of added tppms to it; namely the stabilization of the catalyst by the coordination of tppms does not occur and the precipitate no longer has the activity. This limitation could constitute a major disadvantage when one wishes to extend the Heck reaction to aqueous media. The preformed phosphine palladium complex,  $\text{PdCl}_2(\text{tppms})_2$ , was used as the catalyst. This complex was satisfactory to achieve the Heck reaction in an aqueous phase.

**Reaction of water-insoluble haloarenes by water-soluble catalyst.** Now applications of this reaction under two-phase conditions, where the catalyst and haloarene are present separately in

Table 1. Arylation of Ethylene in Aqueous Media

Entry	Haloarene	$C_2H_4$ , kg/cm <sup>2</sup>	Catalyst	Phase	Base	Yield, % <sup>a)</sup>
1		50	A	H <sub>2</sub> O	(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N	7.6 (5.1) <sup>b)</sup>
2		50	A	H <sub>2</sub> O/THF (1/1)	(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N	34.3 (3.4) <sup>b)</sup>
3		50	B	H <sub>2</sub> O/THF (1/1)	(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N	82.0 (4.2) <sup>b)</sup>
4		50	B	H <sub>2</sub> O/THF (1/1)	NaHCO <sub>3</sub>	75.6
5		50	C	H <sub>2</sub> O/CH <sub>3</sub> CN (1/1)	NaHCO <sub>3</sub>	4
6		50	B	H <sub>2</sub> O/CH <sub>3</sub> CN (1/1)	NaHCO <sub>3</sub>	31.4
7		50	B	H <sub>2</sub> O	NaHCO <sub>3</sub>	63.6
8		50	B	H <sub>2</sub> O/CH <sub>3</sub> CN (1/1)	(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N	78.2
9		50	B	H <sub>2</sub> O/CH <sub>3</sub> CN (1/1)	NaHCO <sub>3</sub>	42.5 (7.7) <sup>c)</sup>
10		50	B	H <sub>2</sub> O/CH <sub>3</sub> CN (1/1)	NaHCO <sub>3</sub>	48.5
11		20	B	H <sub>2</sub> O/CH <sub>3</sub> CN (1/1)	NaHCO <sub>3</sub>	82.3
12		50	B	H <sub>2</sub> O/CH <sub>3</sub> CN (1/1)	NaHCO <sub>3</sub>	55.7
13		50	B	H <sub>2</sub> O/CH <sub>3</sub> CN (1/1)	NaHCO <sub>3</sub>	69.5
14		50	B	H <sub>2</sub> O/CH <sub>3</sub> CN (1/1)	NaHCO <sub>3</sub>	100
15		50	B	H <sub>2</sub> O/CH <sub>3</sub> CN (1/1)	NaHCO <sub>3</sub>	5.3
16		50	B	H <sub>2</sub> O/CH <sub>3</sub> CN (1/1)	NaHCO <sub>3</sub>	45.7
17		20	B	H <sub>2</sub> O/CH <sub>3</sub> CN (1/1)	NaHCO <sub>3</sub>	9.4
18		20	B	H <sub>2</sub> O/(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N (1/1)	-	50.1
19		20	B	H <sub>2</sub> O/GH <sub>3</sub> CN (1/1)	NaHCO <sub>3</sub>	(77.4) <sup>d)</sup>

Conditions: haloarene, 5 mmol; solvent(phase), 16 ml; catalyst (A, Pd(OAc)<sub>2</sub>/2tppms, B, PdCl<sub>2</sub>(tppms)<sub>2</sub>; C, PdCl<sub>2</sub>(tpp)<sub>2</sub>), 1 mol% (Entry 1 and 2, 3 mol%; Entry 3, 6 mol%); base, 5 mmol (Entry 1–5, 15 mmol; Entry 19, 10 mmol); temp, 100 °C; time, 4h. a) GC yield based on the haloarene, b) benzoic acid, c) divinylbenzene, d) 1-(p-hydroxyphenyl)ethanol.

different phases, were explored. Bromobenzene gave styrene in only a small amount without organic solvent, or in benzene–or THF–water system. Prolongation of the reaction time increased the yield to some extent. To transfer bromobenzene into the aqueous phase,  $\beta$ - or  $\gamma$ -cyclodextrin, which includes bromobenzene in its cavity, was added as a phase transfer agent [17]. But they had no influence on the reaction. Changing the solvent to acetonitrile (Entry 6) or triethylamine improved the reaction and resulted in moderate yield. These results reveal that acetonitrile or triethylamine, which can coordinate to metals, can stabilize the catalyst until bromobenzene adds oxidatively to the water-soluble catalyst and the next catalytic cycle starts. Unlike bromobenzene, however, iodobenzene gave styrene with or without organic solvent in 60–80% yield (Entries 7 and 8). In the usual organic solvent systems iodo- and bromoarenes undergo reaction comparably in most instances, with iodoarenes usually being a little more reactive. The Heck reaction of iodoarenes in aqueous media gives the products in high yields. It seems probable that in the present arylation of ethylene iodoarenes are more reactive than bromoarenes under two-phase conditions.

The reaction was extended to a variety of substrates. Bromoarenes with electron-withdrawing groups reacted smoothly to afford the products in high yields (Entries 12–15). It is noteworthy that methyl *p*-bromobenzoate gave the expected product in ca. 70% yield without appreciable amount of *p*-vinyl benzoic acid. Its yield was lower than 5%. Namely, the ester group remained intact in an alkaline solution during the reaction under two-phase conditions.

In contrast, bromoarenes with electron-donating groups such as *p*-bromophenol, *p*-bromoanisole, and *p*-bromoaniline, reacted with difficulty under these conditions (Entry 15). The use of the iodo derivatives improved the reaction and the products were obtained in modest yields under 20–50 atm of ethylene (Entries 16–18). In this manner we succeeded in achieving the reaction using water-miscible tetrahydrofuran or acetonitrile as the organic phase. After the reaction, the

solution separated into aqueous and organic phases. Therefore, at the end of the reaction the catalyst can be removed very easily from the product through a simple phase separation.

The reaction of *p*-iodophenol, in which  $\text{NaHCO}_3$  is substituted for triethylamine and a mixture of acetonitrile and water are used as solvent, is worthy of note. The reaction of *p*-iodophenol with ethylene took place in a triethylamine–water two-phase system smoothly and *p*-hydroxystyrene was obtained in a 50.1% yield (Entry 18). In an acetonitrile–water two-phase system containing 2 equiv. of  $\text{NaHCO}_3$  as the base (Entry 19), almost all of the *p*-iodophenol was consumed. The system recovered was not of two-phase but a homogeneous one. After acidifying the solution, the product was extracted with ether. The NMR spectrum of the product, showed a different spectrum from that of *p*-hydroxystyrene. The product was identified as 1-(*p*-hydroxyphenyl)ethanol, the hydration product of *p*-hydroxystyrene.

*Reaction of 3-bromobenzoic acid by water-insoluble catalyst.* The other example of the reaction system, in which the catalyst and haloarene are present separately in different phases, is made up by the combination of an alkaline solution of bromobenzoic acid,  $\text{PdCl}_2(\text{tpp})_2$ , and organic solvent. Use of acetonitrile or tetrahydrofuran as the organic solvent resulted in low yields (ca. 4%) (Entry 5). This low yield is attributable to the incomplete transfer of both the benzoic acid or sodium salt and catalyst into the other phases. In the water-soluble tppms-based catalysis described above, however, the catalyst itself functions as both phase transfer agent and metal catalyst and a favorable two-phase system can be realized.

### 3. Experimental

NMR and IR spectra were recorded using JEOL PMX60SI and Perkin Elmer 1600 FT-IR, respectively. CG analysis was carried out on a column Silicon DC 550 2 m, at 150–200°C. All solvents

were degassed and stored under an argon atmosphere after distillation. Tppms was prepared according to be literature method [18]. Catalyst  $\text{PdCl}_2(\text{tppms})_2$  was synthesized by a method similar to that reported by Kharasch [14], by addition of a benzene solution of  $\text{PdCl}_2(\text{C}_6\text{H}_5\text{CN})_2$  to an ethanol solution of tppms.

*Reaction of m-bromobenzoic acid and p-iodophenol (Entry 19).* In a 50 ml stainless steel autoclave were placed the catalyst, the alkaline solution of bromobenzoic acid, the organic solvent (if used), and a stirring bar. Air was purged with ethylene and then the system was charged with ethylene. The reaction was conducted with magnetically stirring (reaction conditions, see Table 1.). After the reaction the autoclave was washed with aqueous NaOH. The collected aqueous phase was acidified with diluted HCl and extracted with ether. The extract was subjected to NMR analysis to confirm whether polymeric products were formed or not. The product of *m*-bromobenzoic acid was dissolved in benzene and then esterified with *N,N*-dimethylformamide dimethyl acetal. The yield of arylation was gas chromatographically determined as the methyl ester.

*Reactions of other haloarenes.* The reaction was conducted similarly as described above. The aqueous layer was extracted with ether. The ethereal solution was combined with the organic layer

and subjected to GC analysis. The structure of the product was based on the NMR spectrum.

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