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Electrochemical Recycling of Benzoquinone in the Pd/Benzoquinone-Catalyzed Heck-Type Reactions from Arenes

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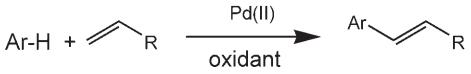
Abstract: Palladium(II) acetate-catalyzed Heck-type reactions have been performed from the arene **1** and alkenes (*n*-butyl acrylate, styrene) in acetic acid at room temperature, in the presence of a catalytic amount of benzoquinone or hydroquinone. The reactions have been made catalytic in benzoquinone [which is used to continuously oxidize the Pd(0) into to the active Pd(II) species able to activate the Ar–H bond] by the electrochemical oxidation of hydroquinone, formed in the reaction, back to benzoquinone.

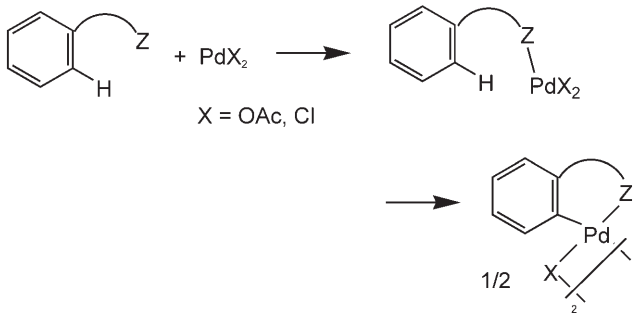
Keywords: arenes; benzoquinone; catalysis; electrochemistry; hydroquinone; palladium

Whereas Pd(0)-catalyzed Heck reactions from *aryl halides* (ArX) have been widely developed,[1] Pd(II)-catalyzed Heck-type reactions from *arenes* (ArH), as pioneered by Fujiwara et al.[2a,b] but working under mild conditions still remain a challenge (Scheme 1).[3]



Scheme 1.

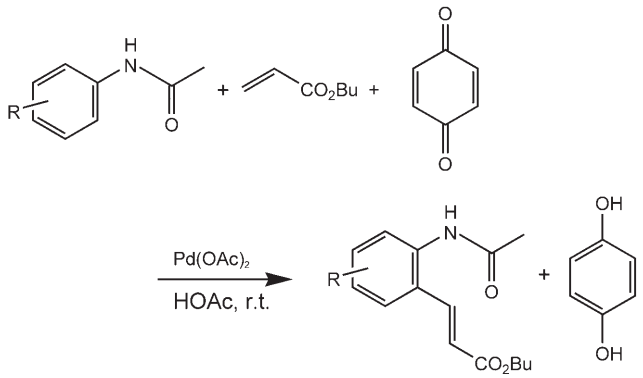
Such reactions are of great interest since arenes are wide-spread and available at low costs. Moreover, no waste is released in the reactions when compared to aryl halides. However, at least two mains challenges must be faced: i) the activation of the Ar–H bond by a Pd(II) species and ii) the recycling of the Pd(0) complex (formed as in all Heck reactions) back to a Pd(II) species by an oxidant. In first approaches, the difficulty of Ar–H bonds activation may be bypassed by attaching a side arm Z on the arene which may behave as a ligand for the Pd(II) catalyst. The intramolecular activation of the (Z)ArH is then facilitated and proceeds at the *ortho* position (orthometallation) (Scheme 2).[4]



Scheme 2.

The second challenge is the recycling of Pd(0) back to a Pd(II) species able to activate the Ar–H bond. This requires an oxidant used in stoichiometric amount. In a recent work, O_2 was used as oxidant assisted by catalytic benzoic acid at 90 °C, the arene being the reaction solvent.[2a] Benzoquinone has also proved to be efficient as oxidant, as reported by de Vries, van Leeuwen et al.[3] Under such conditions, substituted arenes were found to react with *n*-butyl acrylate at room temperature in the presence of a catalytic amount of $Pd(OAc)_2$ and stoichiometric amount of benzoquinone (Scheme 3).

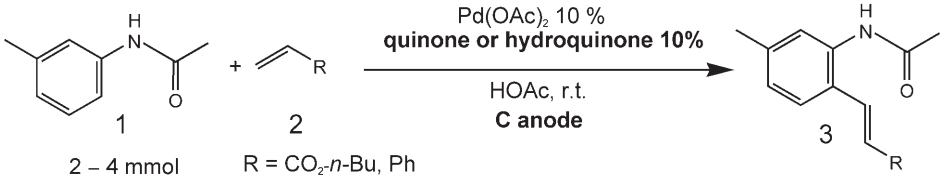
In other Pd(II)-catalyzed Heck-type reactions from arenes, various drastic oxidants have been used in *stoichiometric* amounts such as Ag(I), Cu(II), *t*-BuOOH, $PhCO_3Bu$,[2b,c]. Benzoquinone may be used in catalytic amount but a *stoichiometric* amount of a cooxidant is then required (AgOAc, *t*-BuOOH, etc).[5] In all cases, the expected gain related to the absence of waste upon using arenes is annihilated by the formation of a *stoichiometric* amount of a co-product: hydroquinone (a carcinogenic compound) (Scheme 3)[3] or Ag(0), Cu(I) salts, or products of radicals, etc.[2b,c,5]



Scheme 3.

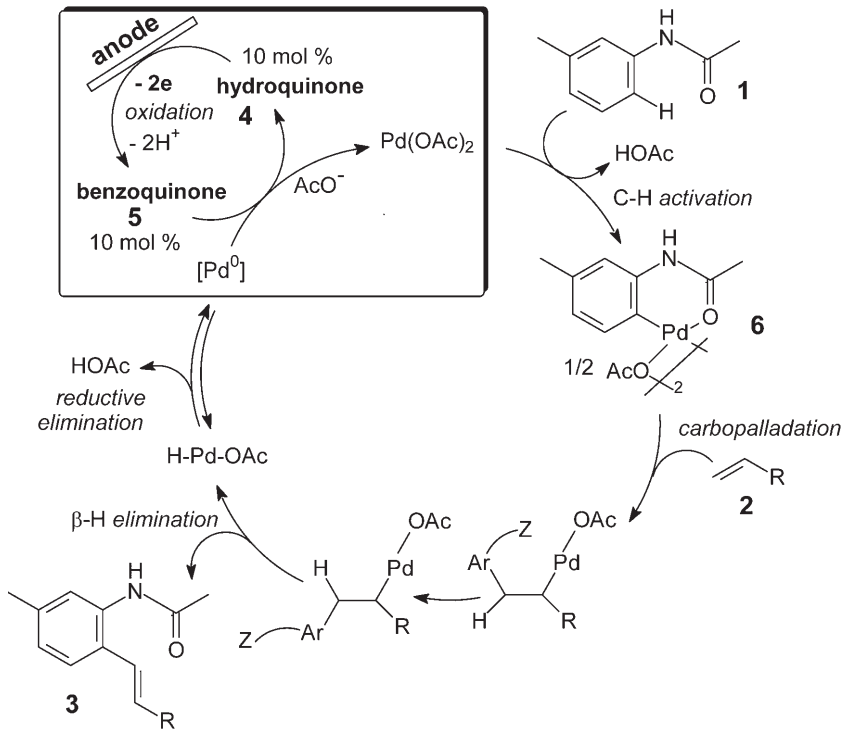
Therefore, we decided to make the reaction of Scheme 3 catalytic in benzoquinone, i.e., to use a catalytic amount of benzoquinone [*viz.* equal to that of the $Pd(OAc)_2$ catalyst] and an anode to oxidize the hydroquinone, formed in each catalytic cycle, back to benzoquinone, the electrons playing then the role of co-oxidant. One may indifferently start with a catalytic amount of hydroquinone since this will be oxidized at the anode into benzoquinone. Such an electrochemical oxidation of hydroquinone back to benzoquinone has proved to be efficient in the Pd(II)-catalyzed diacetoxylation of dienes, as reported by Bäckvall and Gogoll.[6] The reaction was even more efficient when the anode was covered by MnO_2 which acts as a redox catalyst.

We report here preliminary results on the electrochemical Heck-type reactions performed on arenes in the presence of catalytic amounts of $Pd(OAc)_2$ and benzoquinone or hydroquinone (Scheme 4) according to the mechanism proposed in Scheme 5. The arene **1** was selected because it was found to be the most effi-



C anode: oxidation of hydroquinone to benzoquinone
Ni cathode: reduction of H^+ to H_2

Scheme 4.



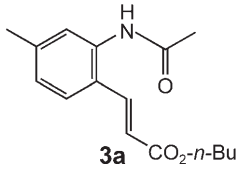
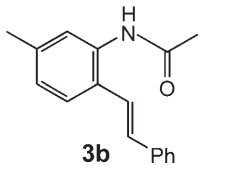
Scheme 5.

cient one in the arylation of *n*-butyl acrylate (91% yield) by de Vries, van Leeuwen et al. (Scheme 3).[3]

From the results collected in Table 1, one observes that benzoquinone (**5a**) or hydroquinone (**4a**) has been used in a catalytic amount [10% as for $Pd(OAc)_2$]. The electrochemical recycling of benzoquinone performed in a divided cell allowed the synthesis of the desired product **3a** when *n*-butyl acrylate was used (entries 1–3, 5). The electrolyses were performed in acetic acid, at room temperature at a carbon woven anode in the scale of 2.2–4.4 mmol of **1**. Electrolyses at constant potential (entries 1, 2, 5) or constant current (entry 3) provided similar yields. The reaction was performed with the less reactive styrene. The reaction was indeed slower and afforded the desired new product **3b** in a more moderate yield (entry 10). Yet this stems from the fact that the carbopalladation of styrene was less favored than that of *n*-butyl acrylate with, as a consequence, a lower hydroquinone turnover. The reaction of styrene is indeed not reported in the process involving stoichiometric amount of benzoquinone.[3] The reaction of an electron rich-alkene such as CH_2=CHO-*i*-Bu was not successful, yet the chemical reaction performed in the presence of a stoichiometric amount of benzoquinone did not work either. This evidences that the limiting step is not the electrochemical recycling of the benzoquinone but most probably the carbopalladation step (Scheme 5).

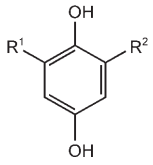
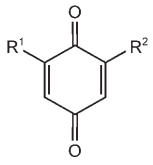
The use of an undivided cell requires that the quinone was not reduced at the cathode. From the reduction peak potentials of quinones determined in acetic acid at a gold disk electrode, it appears that quinones **5a–c** were reduced before the protons of the medium whose reduction started at *ca* −0.6 V *vs.* SCE (Table 2). A nickel foam cathode was thus selected so that the reduction of protons took place at a less negative potential. The electrolyses performed in an undivided cell using a catalytic amount of **5a** did not work (entries 4, 6). The starting arene **1** was fully recovered despite the large amount of electricity passed through the cell. This shows that under electrolytic conditions, the benzoquinone **5a** was more easily reduced than the protons of acetic acid, despite the use of a nickel cathode. The less easily reduced quinone **5c** (Table 2) was thus selected with the hope that pro-

Table 1. $Pd(OAc)_2$-catalyzed arylation of alkenes by ArH **1** (Scheme 4) in the presence of a catalytic amount of benzoquinone (BQ) or hydroquinone (HQ) with electrochemical recycling of the benzoquinone in acetic acid [D = divided cell; UD = undivided cell; F = Faraday (theoretical F = 2)].

Entry	Cell	E (V *vs.* SCE)	I [mA]	BQ or HQ (10 mol%)	Alkene **2**	Product **3**	Yield of **3** [%][c]	F	**1** (recovered [%])
1[a]	D	+0.8		**5a**	CH_2=CH−CO_2-*n*-Bu	 **3a**	78 (100)[d]	1.43	11
2[b]	D	+0.9		**5a**	idem	idem	75	2.1	4
3[b]	D		220	**5a**	idem	idem	82	5.4	Traces
4[b]	UD	+0.9		**5a**	idem	idem	0	5.2	100
5[b]	D	+1.1		**4a**	idem	idem	75	3.7	0
6[b]	UD	+1.1		**4a**	idem	idem	0	5.3	100
7[b]	D	+0.7		**5c**	idem	idem	61	4	27
8[b]	D		230	**5c**	idem	idem	51	6.3	25
9[b]	UD	+0.7		**5c**	idem	idem	0	5.3	40
10[b]	D	+0.9		**5a**	CH_2=CH−Ph	 **3b**	36	1.9	n.d.
11	D	+0.8		no	CH_2=CH−CO_2-*n*-Bu	**3a**	30	4	traces

[a] 4.4 mmol of **1** and 4.8 mmol of **2**.
[b] 2.2 mmol of **1** and 2.6 mmol of **2**. In all cases: $Pd(OAc)_2$: 10% mol in acetic acid (9 mL).
[c] Yields are related to the initial ArH and were determined after work-up by ^{1}H NMR using $Cl_2CHCHCl_2$ as an internal standard.
[d] Yield in parenthesis is related to the charge which was less than the expected one due to the interruption of the electrolysis.

Table 2. Oxidation and reduction peak potentials of hydroquinones[a] and quinones[a] in acetic acid at 20 °C.

	E^p_{Ox} (V *vs.* SCE)[b]		E^p_{Red} (V *vs.* SCE)[b]
$R^1=R^2=H$ (**4a**)	+1.13	$R^1=R^2=H$ (**5a**)	−0.08
$R^1=H$, $R^2=OCH_3$ (**4b**)	+0.99	$R^1=H$, $R^2=OCH_3$ (**5b**)	−0.13[c]
$R^1=R^2=CH_3$ (**4c**)	+0.53[d]	$R^1=R^2=CH_3$ (**5c**)	−0.15

[a] 2 mM in acetic acid containing *n*-Bu_4NBF_4 (0.3 M).
[b] At a gold disk electrode ($d=0.5$ mm), at the scan rate of 0.5 $V\cdot s^{-1}$.
[c] Reduction peak potential of **5b** formed in the electrochemical oxidation of **4b**.
[d] Oxidation peak potential of **4c** formed in the electrochemical reduction of **5c**.

tons will be reduced before **5c**. Although the electrochemical reaction worked at controlled potential or current in a divided cell (Table 1, entries 7, 8), the reaction performed in an undivided cell was not successful (entry 9), establishing that the quinones investigated in this work were definitively reduced at potential less negative than that of protons, a fact which prevented the use of an undivided cell.

The mechanism of the $Pd(OAc)_2$/benzoquinone-catalyzed Heck-type reaction from the arene **1** is proposed in Scheme 5. The assumed intermediate dimeric complex **6** formed in the first step of the catalytic cycle, by activation of the Ar–H bond of **1**, has indeed been isolated by Horino and Inoue and found to react with alkene (R = COMe) to give the arylated alkene.[7] One notices that the coordination of the Pd(II) center by the oxygen of the carbonyl group in complex **6** is sufficiently weak to allow the carbopalladation step to proceed. It has been indeed shown by Brown, Ricci et al. that the formation of too stable palladacycles prevents the carbopalladation from proceeding.[8] The complex formed in the carbopalladation step is probably not ligated by the carbonyl group since, in the present case, an 8-membered palladacycle would be formed. This should favor the internal rotation around the C–C bond and consequently the β-H elimination (Scheme 5). A strong coordination as in a palladacycle would have indeed blocked the latter reactions. The Pd(0)-catalyzed Heck reactions performed from ArX require a base which is supposed to favor the reductive elimination from H–Pd–XL_2 complexes.[1,9] The Pd(II)-catalyzed Heck-type reactions from arenes reported by de Vries, van Leeuwen et al.[3] and the Pd(II)/benzoquinone-catalyzed version presented in this work proceed in acetic acid in the absence of any base. This is due to a reversible reductive elimination from H–Pd–OAc. We have indeed reported that the oxidative addition of the $Pd(0)L_4$ ($L=PPh_3$) complex with acetic acid was reversible (equilibrium constant $K=0.5\cdot10^{-3}$ M in DMF, 20 °C).[10] The benzoquinone acts as a ligand[11] for the Pd(0) species formed in the reductive elimination and as an oxidant. Both factors favor the reductive elimination by shifting the equilibrium towards the transient Pd(0) species. Consequently, no base is required in such reactions.

An alternative process would consist in recycling the active Pd(II) salt by the direct electrochemical oxidation of Pd(0) in the absence of benzoquinone. A preliminary experiment (Table 1, entry 11) did work but gave compound **3a** with a lower yield of 30%.

In conclusion, it has been established that a catalytic amount of benzoquinone or hydroquinone may be used in the $Pd(OAc)_2$-catalyzed reaction of an ArH (**1**) with alkenes without any co-oxidant, in a friendly environmentally process. The benzoquinone could be made catalytic because of its continuous recycling by the electrochemical oxidation of hydroquinone at an anode. Work is in progress to extend the scope of this reaction and to optimize the direct electrochemical oxidation of the Pd(0) to the active Pd(II) in the absence of benzoquinone.

Experimental Section

General Methods

^1H NMR spectra were recorded at 400 MHz or 250 MHz (TMS as internal reference). ^{13}C NMR spectra were recorded at 62.9 MHz (TMS as internal reference). All reactions were performed under argon in vessels connected to a Schlenk line.

Chemicals

Acetic acid was a commercial product and used as obtained. The arene **1**, *n*-butyl acrylate, styrene, benzoquinones (**5a–c**) hydroquinones (**4a–c**) and $Pd(OAc)_2$ were commercial products.

Electrochemical Set-up and Electrochemical Procedure for Cyclic Voltammetry

Cyclic voltammetry was performed with a home-made potentiostat and a wave-form generator, PAR Model 175. The cyclic voltammograms were recorded on a Nicolet 3091 digital oscilloscope. Experiments were carried out in a three-electrode cell connected to a Schlenk line. The cyclic voltammetry was performed at a steady gold disk electrode ($d=0.5$ mm) with a scan rate of 0.5 $V \cdot s^{-1}$. The counter electrode was a platinum wire of *ca.* 1 cm^2 apparent surface area; the reference was a saturated calomel electrode separated from the solution by a bridge filled with 3 mL of acetic acid containing *n*-Bu_4NBF_4 (0.3 M). 10 mL of acetic acid containing *n*-Bu_4NBF_4 (0.3 M) were poured into the cell.

General Procedure for Cyclic Voltammetry

2.2 mg (0.02 mmol) of benzoquinone (**5a**) were added into the cell and the cyclic voltammetry was performed in reduction first. In other experiments, 2.2 mg (0.02 mmol) of hydroquinone (**4a**) were added to the cell and the cyclic voltammetry was performed in oxidation first.

General Procedure for Preparative Electrolyses: Synthesis of 3a

Preparative electrolyses were carried out at room temperature in a two-compartment air-tight three-electrode cell. The two compartments were separated by a sintered glass disk (porosity 4). The anode was a carbon cloth (*ca.* 4 cm^2 surface area). The cathode was a nickel foam (*ca.* 1 cm^2 surface area). The reference was a saturated calomel electrode separated from the solution by a bridge filled with a solution of *n*-Bu_4NBF_4 (0.3 M) in acetic acid (3 mL). The anodic and cathodic compartments were respectively filled with 9 and 1 mL of acetic acid containing *n*-Bu_4NBF_4 (0.3 M). 328 mg (2.2 mmol) of the arene **1** were added to the cell, followed by 409 μL (2.86 mmol) of *n*-butyl acrylate and 24 mg (0.22 mmol) of sublimed benzoquinone (**5a**) or 24 mg (0.22 mmol) of hydroquinone (**4a**) and finally 49 mg (0.22 mmol) of $Pd(OAc)_2$. The electrolysis was conducted at a controlled potential (or controlled current) using a Tacussel PJT 35–2 potentiostat. The electrolysis was stopped after passage of the desired charge (i.e., after 4 h). The anodic compartment was diluted with 15 mL of diethyl ether and hydrolyzed with aqueous NaOH (2.5 M) until pH 7. After extraction with diethyl ether, the organic phase was dried on $MgSO_4$ and evaporated. The yields of **3a** and recovered **1** were determined on the crude mixture by ^1H NMR (250 MHz) spectroscopy using $CHCl_2CHCl_2$ as internal standard and by comparison with the authentic sample.[3] The product was isolated by flash chromatography (eluent: heptane/ethyl acetate). The ^1H NMR and mass spectroscopy data were similar to those of an authentic sample.[3]

Synthesis of 3b by Reaction of 1 with Styrene

The reaction was performed as above using 2.86 mmol of styrene. Product **3b** was isolated by flash chromatography (heptane/ethyl acetate: 60/40) as a pale brown solid. ^1H NMR (400 MHz, $CDCl_3$): $\delta=7.61$ (s, 1H), 7.52 (d, $J=7.4$ Hz, 1H), 7.46 (d, $J=7.9$ Hz, 1H), 7.40 (t, $J=7.5$ Hz, 1H), 7.32 (t, $J=7.5$ Hz, 1H), 7.14 (d, $J=16$ Hz, 1H), 7.03 (d, $J=7.9$ Hz, 1H), 6.98 (d, $J=16$ Hz, 1H), 2.37 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (62.9 MHz): $\delta=167.73$, 138.54, 137.22, 135.67, 134.55, 131.57, 128.76, 128.63, 127.96, 126.62, 124.93, 123.56, 116.14, 24.27, 21.27; HR-MS (CI, CH_4): $m/z=252$ $(M+H)^+$ (100%), calcd for $C_{17}H_{18}ON$ $(M+H)^+$: 252.1388; found: 252.1386.

Acknowledgements

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