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Palladium-catalyzed oxyarylation of olefins using silver carbonate as the base. Probing the mechanism by electrospray ionization mass spectrometry

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ABSTRACT

The $Pd(OAc)_2$-catalyzed oxyarylation of electron-rich (**8** and **12**) and electron-poor (**10**) olefins by *ortho*-iodophenols (**3a**–**d**) was studied using Ag_2CO_3 as the base, in acetone, and in the presence and absence of PPh_3. The corresponding adducts of oxyarylation were obtained in moderate yields. The reaction mechanism was examined by electrospray ionization mass spectrometry (ESI-MS). Cationic arylpalladium intermediate (**14**), formed by the oxidative insertion of Pd(0) into **3a**, and the cationic palladacycles (**15**), obtained by reaction of **14** with olefins **8** and **12**, were intercepted by ESI-MS and characterized by ESI-MS/MS.

1. Introduction

The Heck reaction is one of the most versatile and industrially important palladium-catalyzed carbon-carbon reactions [1,2]. Therefore, this reaction mechanism and several variants have been extensively investigated [3]. Less attention has been given, however, to the oxyarylation (*oxa*-Heck) reaction, and only a few protocols for this interesting transformation have been reported [4–17]. In the first examples of oxyarylation reported by Horino and Inoue [4,5], *cis*-olefins (**1**) were allowed to react with phenylmercury chlorides (**2**, R = HgCl), in the presence of stoichiometric amounts of $PdCl_2$ in acetone–water, yielding stereoselectively compounds of type *trans*-**5** (Fig. 1). A few years latter, they [6] described the same protocol for an intramolecular version, using *ortho*-hydroxyphenylmercury chlorides (**3**, R = HgCl) instead of **2**. Those reactions were, in contrast, found to be *cis*-stereoselective, leading to compounds of type **6**. This approach was also used to prepare several naturally occurring pterocarpans, coumestans and derivatives [13–16]. The reaction of *ortho*-hydroxybenzylmercury chlorides (**4**, R = HgCl) with olefins also showed to be *cis*-stereoselective, leading to compounds type **7** [16].

Catalytic versions of oxyarylations were also reported, using substoichiometric amounts of $Pd(OAc)_2$ and *ortho*-iodophenols (**3**, R = I) to replace the *ortho*-mercuryphenols (**3**, R = HgCl) as the source of organopalladium intermediates [7–12].

We describe herein the $Pd(OAc)_2$-catalyzed oxyarylation of electron-rich (**8** and **12**) and electron-poor (**10**) olefins by *ortho*-iodophenols (**3a**–**d**) using Ag_2CO_3 as the base, in acetone, and in the presence and absence of PPh_3. To investigate the reaction mechanism, the cationic arylpalladium intermediates were intercepted by ESI-MS and characterized by ESI-MS/MS.

2. Results and discussion

Scheme 1 shows the reactions of olefins **8**, **10** and **12** with *ortho*-iodophenols (**3a**–**d**), and Table 1 summarizes major conditions and yields. Using 10 mol% $Pd(OAc)_2$, 20 mol% PPh_3 in acetone or DMF and Na_2CO_3 as the base, none of the desired adducts were formed (data not shown) [9]. However, when Ag_2CO_3 was used as the base in acetone at reflux, and in the presence of PPh_3, reasonable yields of **9a**, **11a** and **13a** were obtained (entries 1, 3 and 5). These

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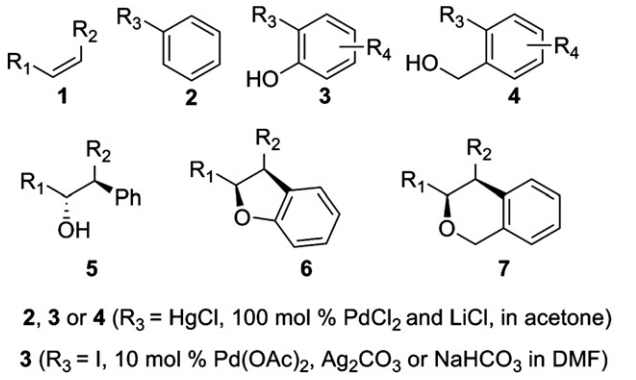
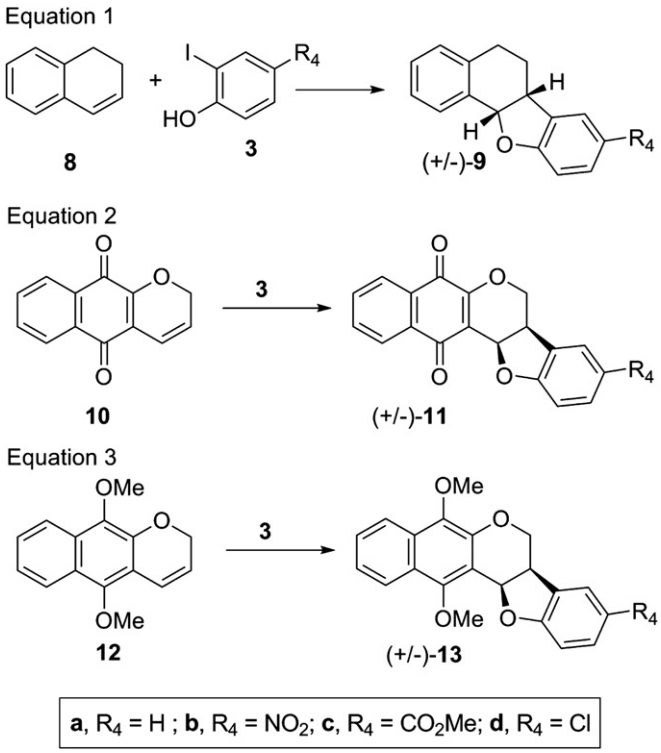


Fig. 1. Olefins (**1**), organopalladium species (**2**, **3** and **4**), reaction conditions and the corresponding products of oxyarylation (**5**, **6** and **7**).

reactions were also successfully carried out essentially in the same yields in the absence of PPh_3 (entries 2, 4 and 6). Since PPh_3 failed to improve the yields, we decided to use phosphine free experiments in the reactions of **8**, **10** and **12** with *ortho*-iodophenols **3b**, **3c** and **3d.** When **3b** was allowed to react with these olefins, adducts **9b**, **11b** and **13b** were respectively obtained in 10–50% yields (entries 7–9), whereas *ortho*-iodophenol **3c** led to products **9c**, **11c** and **13c** in 32–52% yields (entries 10–12). Only olefin **8** was allowed to react with *ortho*-iodophenol **3d**, and the adduct **9d** was obtained in a 68% yield.

Considering that electron-rich olefins react faster than electron-poor olefins under conditions favoring the cationic mechanism [17–19], competitive experiments were performed for the reaction of select olefin pairs (1 equiv. of each) with **3a** (1 equiv.) in the presence of Ag_2CO_3 as the base (Table 2). Olefin **8** was more reactive than **10**, and adduct **9a** was the main product formed in this experiment (entry 1). Olefin **12** was also more reactive than **10**, and adduct **13a** was the main product formed under the same conditions (entry 2). These results are in agreement with HOMO values (Table 3) since this orbital in **10** is lower in energy than those of **8** and **12**. However, **8** was slightly more reactive than **12**, in spite of the fact that the HOMO value in **12** is higher in energy. Steric hindrance between the methoxy group near the double bound in **12** and the incoming arylpalladium intermediate may be responsible for the lower reactivity of this olefin.



Scheme 1. Oxyarylation of olefins **8**, **10** and **12** by *ortho*-iodophenol **3a**–**d**.

Table 1
Yields and major conditions for the reactions outlined in Scheme 2 and performed in acetone, in the presence of 10 mol% of $Pd(OAc)_2$ and 3 equiv. of Ag_2CO_3 under reflux.

Entry	Olefin	3	Adduct	PPh_3	Yield (%)
1	**8**	**a**	**9a**	0.2 equiv.	45
2	**8**	**a**	**9a**	–	50
3	**10**	**a**	**11a**	0.2 equiv.	36
4	**10**	**a**	**11a**	–	40
5	**12**	**a**	**13a**	0.2 equiv.	50
6	**12**	**a**	**13a**	–	45
7	**8**	**b**	**9b**	–	50
8	**10**	**b**	**11b**	–	<10
9	**12**	**b**	**13b**	–	26
10	**8**	**c**	**9c**	–	52
11	**10**	**c**	**11c**	–	35
12	**12**	**c**	**13c**	–	43
13	**8**	**d**	**9d**	–	68

Table 2
Competitive experiments of selected olefins toward **3a**: 1 equiv. of each olefin, 1 equiv. of **3a**, 20 mol% $Pd(OAc)_2$, 20 mol% of PPh_3, 3 equiv. of Ag_2CO_3, acetone and reflux.

Entry	Olefin	Olefin	Products[c]
1[a]	**8**	**10**	**9** (45%) + **11** (4%)
2[a]	**12**	**10**	**13** (41%) + **11** (3%)
3[b]	**8**	**12**	**9** (25%) + **13** (15%)

[a] Reflux for 20 h.
[b] Reflux for 8 h.
[c] Product distribution measured by GC.

Table 3
HOMO values of olefins **8**, **10** and **12**.

Entry	Olefin/HOMO	HOMO (eV)
1	**8**	−7.95
2	**10**	−8.64
3	**12**	−7.43

HOMO in eV (*ab initio* HF 3-21G (*)).

To gain mechanistic information, we monitored the reaction of **8**, **10** and **12** with **3a** via direct infusion ESI-MS and its tandem version (ESI-MS/MS) in the positive ion mode hoping to intercept and characterized key cationic intermediates. ESI-MS has been recently incorporated in the set of techniques that are suitable for mechanistic studies in organic and inorganic chemistry, owing to its outstanding ability to "fish", with high sensitivity, speed and gentleness, ionic or ionized intermediates directly from reaction solutions in the gas phase [20]. Owing to these characteristics, ESI-MS is able to provide continuous snapshots of the changing composition of reaction solutions [21–28].

2.1. Oxa-Heck Pd(II) intermediates

We first studied the reaction of **3a** with **8** in acetone and in the presence of 10 mol% of $Pd(OAc)_2$, 20 mol% of PPh_3 and 3 equiv. of Ag_2CO_3, in acetone. Interestingly, ESI-MS provides the first mechanistic data for this reaction by intercepting the cationic Pd(II) species **14a** of *m*/*z* 723, formed in the oxidative addition step of Pd