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Aryliodine (III) Diacetates as Substrates for Pd-Ag Catalyzed Arylation of Alkenes

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Abstract

An unprecedented application of aryliodine (III) diacetates as substrates in Pd-Ag catalyzed arylation of alkenes is described. The mechanistic studies revealed that the binary Pd-Ag catalysis leads to the decomposition of aryliodine (III) diacetates to oxygen and aryl iodides followed by arylation of alkenes forming Heck-type products. Under optimized conditions both electron-rich and electron-deficient alkenes undergo arylation in high yields. Advantageously, the reaction proceeds smoothly in water as a solvent and neither organic ligands nor inert atmosphere are required.

Keywords

Synthesis in Water; Palladium; Cross-coupling; Hypervalent Iodine

The arylation of alkenes using Heck-type transformations is an important method in organic synthesis.¹ The exploration of the scope of this process has revealed a number of possible leaving groups that can be utilized in the aryl electrophile coupling partner (Scheme 1).^{1,2}

Reactions formally involving the use of “H” as a leaving group, so-called dehydrogenative or oxidative Heck transformations, involve Pd(II) catalysis and require an oxidant to regenerate the active Pd(II) species.^{2d,e} The successful oxidizing agents utilized in this process include Cu or Ag salts, benzoquinone, oxygen and peroxides.^{2e} Interestingly, ArI(OAc)₂ reagents, widely used in many palladium-catalyzed oxidative transformations,^{3,4} fail in Heck-type reactions because of their propensity to oxidize olefins^{3,5} and we are unaware of a single example of such chemistry. Herein, we report that such an attempt to use ArI(OAc)₂ reagents in an oxidative Heck process resulted in an unprecedented reaction of ArI(OAc)₂ with alkenes under Pd-Ag binary catalysis (Scheme 2). This finding expands the scope of Heck chemistry by including the formal “I(OAc)₂” leaving group to the existing arsenal of Heck nucleofuges.

When this project was started, a direct arylation of allyl acetate through the functionalization of an aromatic C-H bond was unknown.⁶ In an attempt to accomplish such a transformation, we used PhI(OAc)₂ as an oxidizing agent and electron-rich 2,4-dimethoxybenzene to facilitate the oxidative electrophilic palladination of an aromatic C-H bond. In addition, we

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added one half equivalent of silver carbonate, whose proposed function was to stabilize the intermediate aryl-cationic Pd-complex^{1,7} and to scavenge acetate ions produced during $\text{PhI}(\text{OAc})_2$ reduction. Surprisingly, instead of the expected dimethoxycinnamyl acetate we isolated only unsubstituted cinnamyl acetate (**3a**) in 68% (Scheme 3).

Clearly, allyl acetate underwent cross-coupling with $\text{PhI}(\text{OAc})_2$ ⁸ and not dimethoxybenzene. A search of the literature revealed that this was a new transformation, presumably missed by the previous investigators because $\text{ArI}(\text{OAc})_2$ is not commonly employed as an oxidizing agent in these oxidative Heck transformations. Furthermore, it is known that under acidic conditions $\text{PhI}(\text{OAc})_2$ reacts with arenes and olefins under Pd catalysis to give acetoxyarenes⁹ and vicinal diacetyldiols,¹⁰ respectively. Neither was detected in our experiment conducted under basic conditions. Our optimization experiments are shown Table 1.

It was found (Table 1) that the reaction critically requires both Pd and Ag catalysts; if either is omitted no product is obtained. (*entries 8, 11*). In addition, base is important for the coupling, indeed the highest yields were obtained with 0.5 equiv. of CaCO_3 (*entries 7, 10, 13, 14*). Also, using TEMPO we were able to improve the product yield (*entries 2, 3*). The precise role of TEMPO is not clear at this point, however, this reagent was reported to improve reaction yields in oxidations of allylic alcohols to unsaturated aldehydes by $\text{PhI}(\text{OAc})_2$ ³ and in general is known to facilitate various redox processes.¹¹ Pleasingly, the reaction also proceeded in high yield when water was used as a solvent (*entry 14*).

The effects of electron properties of alkenes were explored next (Table 2). The reactions of electron-deficient alkenes required 10 mol% excess of the alkene and no TEMPO (*entry 5*), whereas the behavior of styrene was similar to that of allyl acetate, requiring 10 mol% of TEMPO (*entry 9*). In addition, the reaction was successful with 4-methoxyphenyliodine (III) diacetate¹² (*entry 10-12*) giving excellent product yields.

Sanford^{13a,b} and Ritter^{13c} have shown that $\text{ArI}(\text{OAc})_2$ are substrates for Pd(II) oxidative insertion into I-O bond, forming Pd(IV) or Pd(III) bimetallic species and aryl iodide as a side product. Thus, we studied the conversion of 4-methoxyphenyliodine (III) diacetate into iodoanisole (Table 3). Indeed, we found that such decomposition¹⁴ is fastest when all our reaction components are present (*entry 7*).

Additionally, we subjected this cross-coupling reaction (Table 1) to a thorough analysis by HPLC-MS and GC-MS. *Trans*-cinnamyl acetate was detected as a major product along with the traces of 3-phenylpropanaldehyde (product of β' -hydride elimination), phenyl iodide (decomposition product), and *cis*-cinnamyl acetate. These findings prompted us to propose a plausible mechanism for the reaction (Scheme 4).

The evolution of oxygen in stoichiometric quantities was confirmed by the indigo carmine and sodium dithionite methods.¹⁵ It is well known that aryl iodine (III) compounds can be obtained by oxidation of aryl iodides with peroxy acids.¹² Thus, the reverse process involves decomposition of $\text{ArI}(\text{OAc})_2$ and generation of AcOOAc and ArI . It is feasible that Pd catalyzes this reaction through the formation of an unstable $\text{PdX}_2(\text{OAc})_2$. Under basic conditions AcOOAc undergoes Ag-catalyzed decomposition with the production of O_2 . The *in-situ* formed aryl iodide reacts with the alkene under these conditions as has been reported previously¹⁶ and shown in a control experiment, in which 0.5 equiv. of each $\text{PhI}(\text{OAc})_2$ and 4-methoxyiodoanisole were used giving the equal amounts of the respective cinnamyl acetates (Scheme 5).

In summary, we discovered a new alkene arylation reaction with $\text{ArI}(\text{OAc})_2$. Since oxidative alkene arylations are commonly achieved with diaryliodonium salts, which are in turn

prepared¹⁷ from $\text{ArI}(\text{OAc})_2$, our process is synthetically more convenient. This reaction does not involve the use of organic ligands or inert atmosphere and can be performed in water as a solvent. Because of the high yields, the purification of the products is advantageously simple and consists only of a short silica gel pad to separate inorganic salts.¹⁸

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18. *General Procedure.* A suspension of 0.023 g of CaCO_3 (0.225 mmol), 0.062 g of Ag_2CO_3 (0.225 mmol), 0.007 g of TEMPO (0.045 mmol), 0.005 g of $\text{Pd}(\text{OAc})_2$ (0.0225 mmol), diacetyliodoarene (0.495 mmol) and 0.049 mL of allyl acetate (0.45 mmol) was stirred in 3 mL of acetonitrile at 70 °C for 8 hours. After that time the solvent was evaporated under reduced pressure, the residue was transferred in 1 mL of CHCl_3 to silica gel column and eluted first with hexanes (40 mL) and then with pure hexanes or EtOAc/hexanes (1/20) to yield pure **3a-f** as oils.

Scheme 1.

Scheme 2.

Scheme 3.

Scheme 4.

Scheme 5.

Table 1

Optimization of Coupling of $\text{ArI}(\text{OAc})_2$ with Allyl Acetate

entry	1a equiv.	2a equiv.	Pd equiv.	Ag₂CO₃ equiv.	TEMPO equiv.	equiv. of base	yield, (%) ^a
1	1	1	0.05	1	0	none	50
2	1.1	1	0.05	1	0	none	52
3	1.1	1	0.05	1	0.1	none	64
4	1.1	1	0.05	1	0.2	none	58
5	1.1	1	0.05	1	0.1	0.5 of K_2CO_3	22
6	1.1	1	0.05	1	0.1	0.5 of Cs_2CO_3	2
7	1.1	1	0.05	1	0.1	0.5 of CaCO_3	88
8	1.1	1	0.05	0	0.1	0.5 of CaCO_3	3
9	1.1	1	0.05	0.1	0.1	0.5 of CaCO_3	28
10	1.1	1	0.05	0.5	0.1	0.5 of CaCO_3	87
11	1.1	1	0	0.5	0.1	0.5 of CaCO_3	0
12	1.1	1	0.01	0.5	0.1	0.5 of CaCO_3	5
13	1.1	1	0.03	0.5	0.1	0.5 of CaCO_3	82
14 ^b	1.1	1	0.03	0.5	0.1	0.5 of CaCO_3	80

^a Isolated by column chromatography.^b Water was used as a solvent

Table 2

Optimization of Coupling of $\text{ArI}(\text{OAc})_2$ with Alkenes

entry	1 (equiv.)	2 (equiv.)	Pd (equiv.)	TEMPO (equiv.)	product	yield, (%) ^a
1	1.1	1	0.05	0.1	3b	68
2	1	1.1	0.05	0.1	3b	75
3	1	1.1	0.03	0.1	3b	72
4	1	1.1	0.03	0	3b	71
5	1	1.1	0.05	0	3b	85
6	1	1.1	0.05	0	3c	69
7	1.1	1.1	0.03	0	3c	31
8	1.1	1	0.03	0.1	3c	73
9	1.1	1	0.05	0.1	3c	88
10	1.1	1	0.05	0.1	3d	89
11	1	1.1	0.05	0.1	3e	87
12	1.1	1	0.05	0	3f	91

^a Isolated by column chromatography.

Table 3
Decomposition of 4-Methoxyphenyl (III) Diacetate to Iodoanisole

entry	catalyst	% of iodoanisole ^a	time for the full conversion, (hours) ^b
1	none	16	78
2	CaCO_3	50	60
3	Ag_2CO_3	57	48
4	$\text{Pd}(\text{OAc})_2$	86	15
5	$\text{Pd}(\text{OAc})_2 + \text{CaCO}_3$	90	13
6	$\text{Pd}(\text{OAc})_2 + \text{Ag}_2\text{CO}_3$	93	12
7	$\text{Pd}(\text{OAc})_2 + \text{CaCO}_3 + \text{Ag}_2\text{CO}_3$	100	5

^a After 8 hours, monitored by NMR.

^b Reactions conducted in sealed NMR tubes.