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Catalytic Dehydrogenation of *o*-Alkylated or *o*-Alkoxylated Iodoarenes with Concomitant Hydrogenolysis

Elena Motti[a] and Marta Catellani[a,]*

[a] Dipartimento di Chimica Organica e Industriale and CIRCC, Università di Parma, V.le G. P. Usberti 17A, 43100 Parma, Italy
Fax: (+39)-0521-905472; e-mail: marta.catellani@unipr.it

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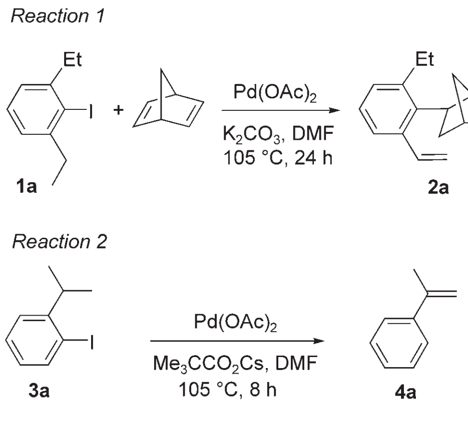
Abstract: Palladium-catalyzed dehydrogenation of suitable chains bonded to an *ortho* position of an iodoarene has been achieved by two methods both involving oxidative addition of the iodoarene to palladium(0) and palladacycle formation under mild conditions.

Keywords: catalysis; C–H activation; dehydrogenation; palladium

In the course of our work on catalyzed C–C coupling *via* palladacycles[1] we came across the catalytic dehydrogenation of a series of primary or secondary *o*-alkyl- or *o*-alkoxyiodoarenes. We observed that saturated chains in an *ortho* position to iodoarenes can be converted catalytically into unsaturated chains by hydrogen transfer to a neighboring C–Pd bond. The result was achieved by the ways shown in Scheme 1 which reports two representative examples.

We shall consider the two reactions of Scheme 1 separately.



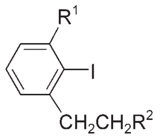
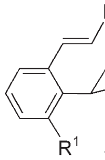
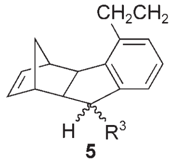
Scheme 1.

Reaction 1: Reaction 1 readily occurs in DMF at 105 °C in the presence of $Pd(OAc)_2$ as catalyst and K_2CO_3 as a base by treatment of *o*,*o*-diethyliodobenzene with norbornadiene. Yields of *exo*-**2a** up to 91% can be attained as shown in Table 1, which reports selected examples. Beside product **2a** another by-product **5a** (*exo*, diasteroisomeric mixture) is formed in a few percent according to Scheme 2.

The presence of triphenylphosphine (TPP) as ligand favors the formation of compound **5a** which increases up to 61% when TPP is used in 4:1 molar ratio to palladium (entries 2 and 3). While no cyclic product is observed using substrate **1b**, only compound **2b** being isolated in 74% yield (entry 4), the presence of a linear chain such as the butyl one leads to both compounds (**2c** and **5c**) in comparable amounts (entry 5). Only the cyclic product of type **5** is formed in high yield if a methyl is present in one *ortho* position (entries 6 and 7).[2]

Scheme 3 depicts the proposed reaction course referred to *o*,*o*-diethyliodobenzene and norbornadiene for simplicity. The reaction starts with the oxidative addition of *o*,*o*-diethyliodobenzene to palladium(0) to form intermediate **A**. Norbornadiene insertion into the resulting arylpalladium bond then gives rise to complex **B**[3] which is stable towards β-hydrogen elimination[4] and readily effects C–H activation of the benzylic CH_2 to give palladacycle **C**.[5] At this point a hydrogen atom is transferred from the methyl of the original ethyl group to the norbornadienylpalladium bond, likely through a palladium hydride species **D**, to give the organic product **2a**, containing the unsaturated chain, and palladium(0). The intermediacy of palladacycle **C** is clearly suggested by the formation of condensed cyclopentene **5a** which must occur from **C** by reductive elimination. Chains longer than ethyl tend to limit hydrogen transfer from the substituted CH_2 and formation of **5** is also favored (Table 1, entry 5). For the aliphatic C–H bond activation that allows the dehydrogenation process, another *ortho*

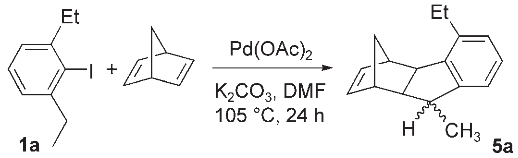
Table 1. Palladium-catalyzed reaction of *o,o*-disubstituted iodoarenes **1** with norbornadiene.[a]

Entry	Substrate	Ligand	Yield [%][b]	Yield [%][b]
		TPP	 **2**	 **5**
1	$R^1 = Et$; $R^2 = H$; **1a**	-	$R^1 = Et$; $R^2 = H$; **2a**, 91[c]	$R^2 = H$; $R^3 = Me$; **5a**, 6
2	**1a**	2	**2a**, 60	**5a**, 36
3	**1a**	4	**2a**, 29	**5a**, 61
4	$R^1 = i$-Pr; $R^2 = Ph$; **1b**	-	$R^1 = i$-Pr; $R^2 = Ph$; **2b**, 74[c]	-
5	$R^1 = n$-Bu; $R^2 = Et$; **1c**	-	$R^1 = n$-Bu; $R^2 = Et$; **2c**, 50	$R^2 = Et$; $R^3 = n$-Pr; **5c**, 44
6	$R^1 = Me$; $R^2 = H$; **1d**	-	-	R^2, $R^3 = H$; **5d**, 94[c]
7	$R^1 = Me$; $R^2 = Ph$; **1e**	-	-	$R^2 = Ph$; $R^3 = H$; **5e**, 92[c]

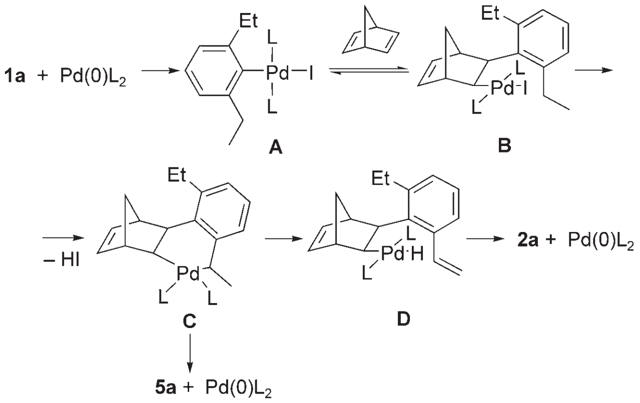
[a] Molar ratio of the reaction components: iodoarene, norbornadiene, K_2CO_3, $Pd(OAc)_2$ 1:1.2:2:0.1; 105 °C, 24 h, DMF as solvent, under nitrogen; 4.4×10^{-3} mmol $Pd(OAc)_2$/mL DMF.

[b] GC yield on the iodoarene.

[c] Isolated yield.



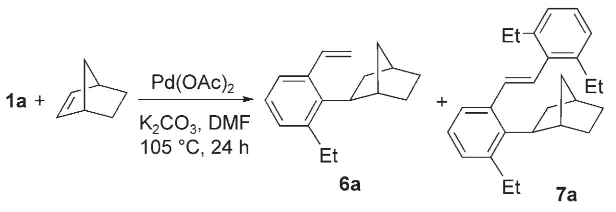
Scheme 2.



Scheme 3. Proposed reaction pathway for the formation of the dehydrogenated and cyclic products (L = TPP, solvent or any coordinating species present in the reaction mixture).

substituent is required, otherwise a four-membered ring closure on the free *ortho* position of the aromatic ring[6] readily occurs, aromatic C–H bond activation being usually preferred to the aliphatic one.[7]

Very subtle factors influence palladacycle formation. With norbornene in place of norbornadiene the overall reaction slows down and the yields of *exo*-**6a** (Scheme 4) are lower. Apparently the process leading to type **C** palladacycle formation occurs more slowly and there is time for the first formed double bond in **6a** to react with a second molecule of iodoarene giving the Heck-type product[8] **7a** (*E*, *exo*). Thus with *o,o*-diethyliodobenzene (**1a**) the reaction carried out in DMF at 105 °C in the presence of $Pd(OAc)_2$ as catalyst and K_2CO_3 as a base for 24 h (Scheme 4) gives 28% of **7a** in addition to 31% of **6a** with 65% conversion of the starting **1a**. By replacing K_2CO_3 with a base such as KOAc, able to favor the steps leading to palladacycle formation (through norbornene insertion),[9] however, it is possible to shift this ratio towards **6a** (64% with 25% **7a** at 99% conversion).

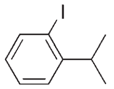
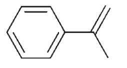
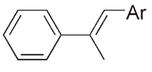
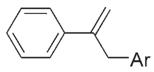
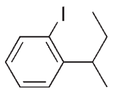
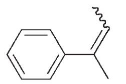
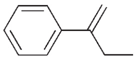
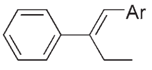
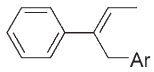
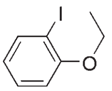
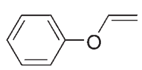
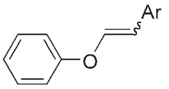
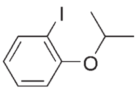
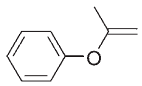
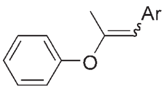
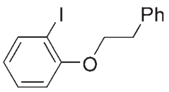
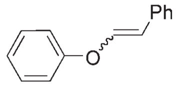


Scheme 4.

Reaction 2: Analogously to reaction 1, reaction 2 (Scheme 1) occurs in DMF at 80–105 °C in the presence of $Pd(OAc)_2$ as catalyst and a base, in particular K_2CO_3 or Me_3CCO_2Cs. In most cases the latter performs better than the former at a substrate to palladium molar ratio of 100.[10] Iodoarenes *o*-substituted by α-branched alkyl chains or by alkoxy chains have been found to be reactive, as shown in Table 2. Linear alkyl chains are inactive.

The styrene derivatives (**4**) thus obtained have a remarkable tendency to give Heck-type products,[8]

Table 2. Palladium-catalyzed reaction of iodoarenes *o*-substituted by α-branched alkyl chains or alkoxy chains (**3**) in the presence of Me$_3$CCO$_2$Cs as a base.[a]

ArI		Dehydrogenation product **4** (yield [%][b])		Heck-type product (yield [%][b,c])	
3a		**4a** (45)		**8a** (25)/**9a** (20)[d]	 
3b		**4b** (15, 10)	 	**8b** (27)/**9b** (15)[e]	 
3c		**4c** (2)		**10** (85 [*E*, 65; *Z*, 20])[f]	
3d		**4d** (15)		**11** (67 [*E*, 60; *Z*, 7])[f]	
3e		**4e** (85 [*E*, 68; *Z*, 17])[g]			

[a] Molar ratio of the reaction components: iodoarene, Me$_3$CCO$_2$Cs, Pd(OAc)$_2$ 1:2:0.01; 105 °C, 8 h, DMF as solvent, under nitrogen; 2.2×10^{-3} mmol Pd(OAc)$_2$/mL DMF.

[b] GC yield.

[c] Products formed by reaction of ArI with the dehydrogenation product.

[d] A 6% of a product resulting from reaction of ArI with **9a** was also isolated and characterized as 1-{2-phenyl-3-[2-(2-propyl)phenyl]prop-2-enyl}-2-(2-propyl)benzene.

[e] Compound **9b** was isolated in a *ca.* 3:1 mixture with an isomer (*ca.* 5%) identified as *E*-2-(2-butyl)-1-(3-phenylbut-1-enyl)benzene.

[f] Another positional isomer not further investigated is present in the reaction mixture in small amount.

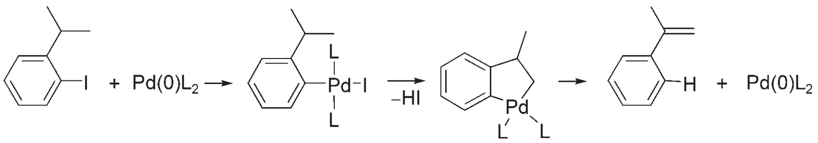
[g] Reaction carried out at 80 °C.

however, by further reaction with the starting iodo derivatives **3**.[11]

The very subtle effects involved in this reaction are clearly evidenced by comparing the reactivity of *o*-ethyliodobenzene and *o*-*n*-propyliodobenzene, which do not form the double bond[12] and *o*-isopropyliodobenzene which does, owing to the presence of an additional methyl group in the alkyl chain able to favor ring formation (Scheme 5).

It is worth noting that if a suitable aromatic C–H bond in the *ortho* chain is available, ring closure on the aromatic carbon[13] is preferred to double bond formation, thus *o*-(1-phenylethoxy)iodobenzene gives 6-methyl-6*H*-benzo[*c*]chromene in 90% yield.

The reaction course appears to be clear in the case of α-branched alkyls exemplified by the reaction depicted in Scheme 5. Oxidative addition of the iodoarene to palladium is the first step. This is followed by formation of a palladacycle which must be five-membered when the *o*-isopropyl chain is involved (in contrast to the previously shown type 1 reaction, where the intermediate palladacycle is likely to be six-membered).[2] The formation of six-membered palladacycles, however, cannot be excluded at present for other substrates. Five- or six-membered palladacycles have been proposed by Baudoin and co-workers to be intermediates in the case of dehydrogenation of substrates containing benzylic *gem*-alkyl groups.[14] These authors also achieved a Heck-type reaction on the dehydrogenated product, adding a second molecule of a different aryl halide.[14c]



Scheme 5. Reaction course proposal for the dehydrogenation of *o*-isopropyliodobenzene (L = solvent or any coordinating species present in the reaction mixture).

That palladacycles are involved in the hydrogen transfer reactions leading to double bond formation is further supported by the findings by Dyker[15] who used iodoarenes containing an *o*-*tert*-butyl or an *o*-methoxy group not allowing β-hydrogen elimination to obtain the products resulting from their further reaction with a second molecule of the iodoarene and by Carmona[16] and Echavarren[17] who isolated the corresponding metallacycles. A recent paper by Fagnou also is worth mentioning.[18] In most cases, however, to gain unequivocal evidence for the intermediacy of five- or six-membered palladacycles an accurate mechanistic investigation is required.

In conclusion, *o*-paraffinic chains in iodoarenes can be transformed into the corresponding olefinic ones through oxidative addition of the iodide to palladium(0), palladacycle formation either with the help of a suitable olefin or directly from alkyl chains of appropriate conformation, and hydrogen transfer to an sp^3 C–Pd bond (Scheme 1). Since the dehydrogenation products belong to the classes of styrenes and phenyl vinyl ethers practical applications can be expected, particularly in the area of polymerization, as already known for α-methylstyrene. Further work is in progress to clarify the reaction scope and the nature of the intermediates involved.

Experimental Section

General Procedure for the Reaction of 2,6-Disubstituted Aryl Iodides with Rigid and Strained Cyclolefins

A DMF solution (12 mL) of the 2,6-disubstituted aryl iodide (0.54 mmol) and the strained cyclolefin (0.64 mmol) was introduced under nitrogen into a Schlenk-type flask containing $Pd(OAc)_2$ (12 mg, 0.054 mmol) and the base (K_2CO_3, 1.1 mmol or KOAc, 2.2 mmol). The resulting mixture was heated at 105 °C under stirring for 24 h. After cooling to room temperature, the mixture was diluted with CH_2Cl_2 (50 mL), washed with a 5% solution of H_2SO_4 (2 × 30 mL) and dried over Na_2SO_4. The crude material was analyzed by GC and the products were isolated by flash chromatography using hexane as eluent.

General Procedure for the Reaction of 2-Alkyl- or 2-Alkoxy-Substituted Aryl Iodides

A DMF solution (8 mL) of the desired aryl iodide (1.8 mmol) was introduced under nitrogen into a Schlenk-type flask containing $Pd(OAc)_2$ (4 mg, 0.018 mmol) and Me_3CCO_2Cs (842 mg, 3.6 mmol). The resulting mixture was heated at 80–105 °C under stirring for 8 h. After cooling to room temperature, the mixture was diluted with CH_2Cl_2 (40 mL), washed first with a 5% solution of H_2SO_4 (30 mL), then with water (30 mL) and dried over Na_2SO_4. In the case of 2-ethoxyiodobenzene and 2-isopropoxyiodobenzene the reaction mixture was washed four times only with water (4 × 20 mL). The crude material was analyzed by GC and ^1H NMR. The products were separated by flash chromatography using hexane or mixture hexane-ethyl acetate as eluents.

Acknowledgements

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[11] To our knowledge compounds of type **10** and **11** have not been prepared so far under the conditions of a conventional Heck reaction from aryl vinyl ethers, probably owing to the instability of the latter.

[12] Analogously, no double bond formation was obtained under our conditions with substituents offering steric hindrance or unsuitable conformation such as for example *o*,*o*-diethyl and *o*,*o*-diisopropyl.

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