Copper- and Phosphane-Free Sonogashira Coupling of Arenediazoniumo-Benzenedisulfonimides

UNIVERSITÀ DEGLI STUDI DI TORINO

Copper and Phosphane free Sonogashira Coupling of Arenediazonium *o*-Benzenedisulfonimides

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Arenediazonium *o*-benzenedisulfonimides can be used as efficient reagents in Sonogashira coupling. In this work, reactions have been carried out in DMSO in very mild conditions (without copper and phosphanes) and gave rise to arylated alkynes in good to excellent yields (25 examples, average yield 83%). All the reactions led to the recovery of *o*-benzenedisulfonimide in yields of greater than 80%, which was recyclable for the preparation of other diazonium salts. Mechanistic insights have allowed us to highlight the fundamental role of DMSO and of the anion of *o*-benzenedisulfonimide in the formation of the catalyst and the importance of the first in the catalytic cycle.

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Introduction

The palladium-catalyzed coupling of terminal alkynes with aryl or alkenyl halides (or triflates), which was described for the first time by Sonogashira *et al.* in 1975,[1a] is one of the most straightforward methods for the preparation of aryl-alkynes and conjugated enynes.[1b-h]

The Sonogashira coupling is generally carried out in mild conditions, in the presence of a catalytic amount of a palladium complex as well as copper iodide and a base (typically an amine) to obtain coupling products in a good yield. The importance of this reaction is made clear by the fact that, over the years, an impressive variety of modifications have been reported.[1e-h] In fact, a search for the term "Sonogashira" in SciFinder, just between 2011 and 2013, provided over 1600 references for journal publications. Interestingly, between these modifications, considerable effort has been directed to the development of effective copper-free processes,[1i-m] providing the opportunity to carry out the Sonogashira reaction under aerobic conditions, because the copper-mediated oxidative homocoupling of alkynes is prevented.

In recent years, arenediazonium salts have been widely used as electrophilic partners in palladium catalyzed cross-coupling reactions,[2] including Mizoroki–Heck reactions, Suzuki–Miyaura and Stille couplings becoming an effective alternative to aryl halides. Typically, there are some important advantages to the use of diazonium salts; first of all, their greater reactivity, due to the fact that the diazonium group is a better nucleofuge than the halide or triflate; they are also easily available from anilines, no base or additional ligands are generally needed; they requires mild reaction conditions and short reaction times and coupling products are generally obtained in high yields.

In spite of these factors, the use of diazonium salts in Sonogashira coupling is scarce.

In 1999, Genet *et al.* reported a Sonogashira reaction between arenediazonium tetrafluoroborates and potassium alkynyltrifluoroborates; however the yields of the coupling products were very low.[3a] More recently, in 2010, Cacchi *et al*. developed an interesting procedure for the Sonogashira coupling of isolated arenediazonium tetrafluoroborates (or, alternatively, generated in situ from anilines) at r.t. using CuI as an additive in the presence of nBu$_4$NI and Et$_2$NH.[3b] In the same year, Sarkar *et al.* reported the coupling of arenediazonium tetrafluoroborate using a palladium–gold dual catalytic system in the presence of 2,6-di-*t*butyl-4-methylpyridine as the ligand.[3c] Finally, in 2011, Beller *et al.* developed a general and convenient palladium-catalyzed Sonogashira reaction of *in situ* generated arenediazonium salts under mild conditions.[3d] In order to obtain alkynones, the same authors also reported a convenient carbonylative Sonogashira coupling.[3e]

Since 1998, some of our research resulted in a new and large family of dry diazonium salts, the arenediazonium o-benzenedisulfonimides **1** (Figure 1).[4a]

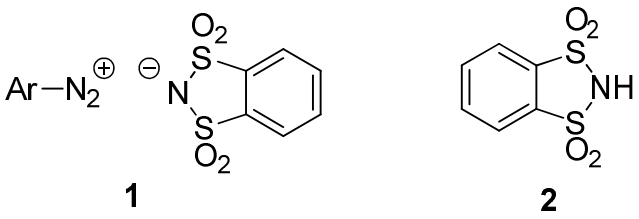
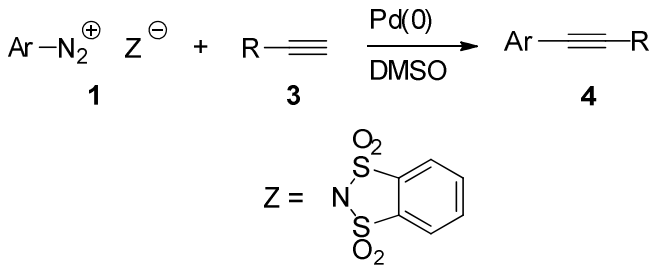


Figure 1. Arenediazonium *o*-benzenedisulfonimides **1** and *o*-benzenedisulfonimide(**2**).

Due to their properties, they have great potential in numerous synthetic applications. These salts are, in fact, easy to prepare and isolate, extremely stable, and can also be stored for an unlimited times. Moreover, they react easily both in water and in organic solvents, and *o*-benzenedisulfonimide[4b] (**2**; Figure 1) can be easily recovered and reused at the end of the reactions.

As part of a broader project aimed at exploring the synthetic potential of these salts, we advantageously employed them in Mizoroki–Heck reactions,[4c] in Stille and Suzuki coupling[4d, 4e] and in the palladium-catalyzed coupling with organoindium derivatives.[4f, 4g]

In the light of these experiments, in this paper we have focused our attention on the reactivity of the said salts **1** as electrophilic partners in Sonogashira coupling reactions (Scheme 1).

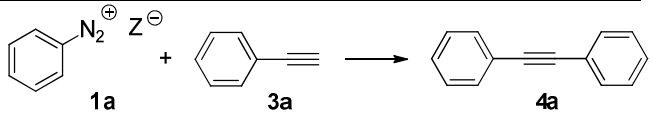


Scheme 1. Sonogashira coupling of salts **1**.

Results and Discussion

Initially, in order to optimize the reaction conditions, a model reaction between benzenediazonium o-benzenedisulfonimide (**1a**) and phenyl acetylene (**3a**) was studied under different conditions. Firstly, as reported in Table 1, the reaction between **1a** and **3a** in the presence of 2.5 mol-% of $Pd(OAc)_2$ as a pre-catalyst and 2.5 mol-% of two different phosphanes (triphenylphosphane and tris(2-furyl)phosphane) was performed, with or without copper, in various solvents at r.t. The desired coupling product diphenylacetylene (**4a**) was achieved *only in DMSO* and in a very short reaction time (10 min; Table 1, entries 9, 10), whilst no results were obtained with other solvents (Table 1, entries 1–8).

Table 1. Trial reactions between **1a** and **3a**.



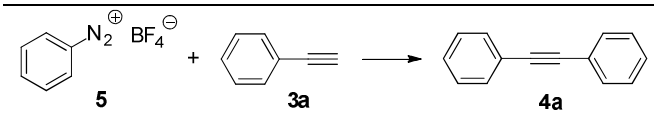
Entry	Solvent	Catalyst	Phosphane	Yield of **4a** (%)[a]
1	THF	$Pd(OAc)_2$	Ph_3P	Traces[b, c]
2	THF	$Pd(OAc)_2$	TFP[d]	Traces[b, c]
3	DMF	$Pd(OAc)_2$	Ph_3P	-[b, c]
4	EtOH	$Pd(OAc)_2$	Ph_3P	-[b, c]
5	1,4-Dioxane	$Pd(OAc)_2$	Ph_3P	-[b, c]
6	H_2O	$Pd(OAc)_2$	Ph_3P	-[b, c]
7	MeCN	$Pd(OAc)_2$	Ph_3P	-[b, c]
8	MeCN	$Pd(OAc)_2$	TFP	-[b, c]
9	DMSO	$Pd(OAc)_2$	Ph_3P	92[e]
10	DMSO	$Pd(OAc)_2$	-	88[e]
11	Anhydrous DMSO	$Pd(OAc)_2$	-	35[f]
12	DMSO	$PdCl_2(Ph_3P)_2$	Ph_3P	-[b, c]
13	DMSO	$Pd_2(dba)_3$	-	25[g]

[a] All the reactions were performed with 2.5 mol-% of catalyst and phosphane (0.05 mmol each) at r.t.; the reactants **1a** and **3a** were in equimolar amounts (2 mmol). [b] No **4a** was obtained, also adding Et_3N and/or CuI and using larger amount of catalysts.[c] The reaction mixture was stirred at r.t. for 8 h. The positive azo-coupling with 2-naphthol confirmed the presence of unreacted **1a**. The heating at 50 °C caused only a decomposition of **1a**. [d] TFP was tris(2-furyl)phosphane.[e] The reaction time was 10 min. Yields refer to the pure and isolated products. The crude residue was purified on a silica gel chromatography column, (petroleum ether /diethyl ether, 9.5:0.5). [f] The reaction was carried out under nitrogen flow and stopped after 10 min even though the azo-coupling test with 2-naphthol was positive.[g] The reaction time was 60 min.

The reaction proceeded without copper, and, interestingly, without phosphanes or other reducing agents (Table 1, entry 10) and bases. It must be stressed that Cacchi[3b] had previously stated that a screen of various solvents (*not DMSO*) afforded no cross-coupled product in the presence or absence of base and/or phosphanes, using various palladium catalysts and a number of temperatures. In order to obtain the coupled products, it was necessary to add *n*Bu_4NI and Et_2NH. On the other hand, Beller[3d] showed that the best results were obtained in DMSO (in the presence of palladium acetate and tris(2-furyl)phospane), while only traces of the desired product were obtained in other organic solvents. We also tested other two palladium catalysts, $Pd_2(dba)_3$ and $Pd(PPh_3)_2Cl_2$ without significant results (Table 1, entries 12,13).

Finally, we performed some reactions using benzenediazonium tetrafluoroborate **5** (Table 2) in order to compare its reactivity with that of **1a.** Without phosphanes**,** the yield of the reaction was very poor (Table 2, entry 3). The simple addition of triphenyl phosphane (Table 2, entry 1) or, better, tris(2-furyl)phosphane[3d] (Table 2, entry 2), meant that the yields were comparable to those obtained with **1a.**

Table 2. Trial reactions between **5** and **3a**.



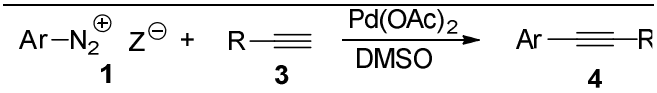
Entry	Catalyst	Phosphane	Yield of **4a** (%)[a,b]
1	$Pd(OAc)_2$	Ph_3P	65
2	$Pd(OAc)_2$	TFP	87
3	$Pd(OAc)_2$	-	15
4	[c]	-	53

[a] All the reactions were performed with 2.5 mol-% of catalyst (0.05 mmol) and phosphane at r.t.; the reactants **3a** and **5** are in equimolar amounts (2 mmol). The solvent was DMSO. [b]Yields refer to the pure and isolated **4a**. The crude residue was purified in a silica gel chromatography column, (petroleum ether /diethyl ether, 9.5:0.5). [c] The catalyst was a mixture of $Pd(OAc)_2$ (0.05 mmol).and **2** (0.1 mmol).

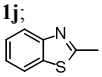
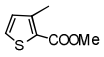
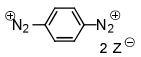
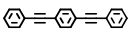
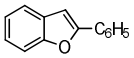
It has been reported that, since phosphanes cause the radical decomposition of diazonium salts, they are not good reducing agents of choice in palladium catalyzed organic reactions.[2a,3c] Despite this, the reaction took place even in the presence of phosphanes.[3d]

The high yield, short reaction time and simplicity of the our procedure, encouraged us to further exploit the generality and the scope of this reaction, using different salts **1** and terminal alkynes **3**. The results are collected in Table 3. We can state that the Sonogashira coupling of various salts **1** and alkynes **3** in DMSO afforded the corresponding arylalkynes **4** in excellent yields (average yield for 25 examples was 83%), in simple and mild

Table 3. Synthesis of arylalkynes **4**.



1 **3** **4**

Entry	Ar	R	Time (min)	Temp. (°C)	Products and Yields (%)
1	**1a**; C_6H_5	**3a**; C_6H_5	10	r.t.	**4a**; 88
2	**1b**; 2-$NO_2C_6H_4$	**3a**; C_6H_5	5	r.t.	**4b**; 95
3	**1c**; 3-$NO_2C_6H_4$	**3a**; C_6H_5	5	r.t.	**4c**; 91
4	**1d**; 4-$NO_2C_6H_4$	**3a**; C_6H_5	5	r.t.	**4d**; 93
5	**1e**; 4-MeC_6H_4	**3a**; C_6H_5	60	35[b]	**4e**; 72
6	**1f**; 4-$MeOC_6H_4$	**3a**; C_6H_5	90	35[b]	**4f**; 69
7	**1g**; 4-BrC_6H_4	**3a**; C_6H_5	5	r.t.	**4g**; 90
8	**1h**; 4-CNC_6H_4	**3a**; C_6H_5	5	r.t.	**4h**; 93
9	**1i**; 2-NO_2-4-$MeOC_6H_4$	**3a**; C_6H_5	5	r.t.	**4i**; 92
10	**1j**; 	**3a**; C_6H_5	5	r.t.	**4j**; 75
11	**1k**; 	**3a**; C_6H_5	5	r.t.	**4k**; 84
12	**1l**; 	**3a**; C_6H_5	5	r.t.	**4l**; 80 
13	**1a**; C_6H_5	**3b**; 4-$NO_2C_6H_4$	5	r.t.	**4d**; 87
14	**1e**; 4-MeC_6H_4	**3b**; 4-$NO_2C_6H_4$	120	35[b]	**4m**; 69
15	**1a**; C_6H_5	**3c**; 4-MeC_6H_4	10	r.t.	**4e**; 87
16	**1h**; 4-CNC_6H_4	**3c**; 4-MeC_6H_4	5	r.t.	**4n**; 93
17	**1f**; 4-$MeOC_6H_4$	**3c**; 4-MeC_6H_4	180	35[b]	**4o**; 64
18	**1d**; 4-$NO_2C_6H_4$	**3c**; 4-MeC_6H_4	5	r.t.	**4m**; 94
19	**1a**; C_6H_5	**3d**; 4-Me OC_6H_4	10	r.t.	**4f**; 88
20	**1e**; 4-MeC_6H_4	**3d**; 4-Me OC_6H_4	120	35[b]	**4o**; 71
21	**1a**; C_6H_5	**3c**; 4-BrC_6H_4	5	r.t.	**4g**; 90
22	**1a**; C_6H_5	**3f**; *n*Bu	10	r.t.	**4p**; 85
23	**1d**; 4-$NO_2C_6H_4$	**3f**; *n*Bu	5	r.t.	**4q**; 90
24	**1f**; 4-$MeOC_6H_4$	**3f**; *n*Bu	120	35[b]	**4r**; 64
25	**1m**; 2-HOC_6H_4	**3a**; C_6H_5	[c]	35[b,d]	**6;** 79 

[a] Yields refer to the pure products isolated by column chromatography, (petroleum ether /diethyl ether , 9.5:0.5). [b] At higher temperatures, a total decomposition of salts **1** were observed.[c] The reaction time was 24 h. [d] On GC-MS analyses, after 30 min two products were detected: 1-(2-hydroxyphenyl)-2-phenylacetylene (**4s**), MS (EI) *m/z* = 194 $[M]^+$ and the cyclization adduct 2-phenylbenzofurane (**6**) MS (EI) *m/z* = 194 $[M]^+$. After 24 hours only **6** was present.

reaction conditions, without additional copper, phosphanes and bases. The reaction is chemoselective; no traces of 1,4-bis(2-phenylethynyl)benzene (**4l**) were detected in the reactions of diazonium salts that bear a bromine atom, which could potentially react as a diazonium group (Table 3, entry 7). Regarding to alkynes **3**, the reaction is not affected by electronic effects; adducts **4** were obtained in satisfactory yields from the reactions of **3** that bear either electron-donating or electron-withdrawing groups. The aliphatic alkyne **3f** also reacted well and good yields of adducts **4p**–**r** were obtained (Table 3, entries 22–24). On the other hand, the electronic effects were clearly important for salts **1**. In fact, adducts **4** were obtained in high yields (generally over 90%) and in very short reaction times at r.t. (about 5-10 min) from salt **1a, 1j, 1l** (Table 3, entries 1, 10, 12, 13, 15, 19, 21, 22) or salts **1b–d, 1h, 1i, 1k** that bear electron-withdrawing groups (Table 3, entries 2–4, 8, 9, 11, 16, 18, 23). The yields were lower for the adducts **4** obtained from salts **1e**–**f, 1m** that bear electron-donating groups. Furthermore, it was necessary to heat the reaction to 35 °C and the reaction times were much longer (Table 3, entries 5, 6, 14, 17, 20, 24, 25). Meta and ortho substituted **1b**–**c**, **1i**, **1k**, **1m** were also coupled satisfactorily with **3a** (Table 3, entries 2, 3, 9, 11, 25). Interestingly, 2-phenylbenzofuran (**6**) was formed from the reaction between **1m** and **3a**, due to the spontaneous cyclization of adduct **4s** (Table 3, entry 25). In all these reactions, the diynes which derives from Glaser coupling of **3** only formed in traces.

Note that, it was possible to recover *o*-benzenedisulfonimide (**2**) in more than 80% yield from all the reactions described above. Sulfonimide **2** could be recycled for the preparation of other salts **1** with economic and ecological benefits.

The copious and homogeneous results collected provide a good basis for some comments on the mechanism involved. As previously mentioned, the Sonogashira coupling of salts **1** and alkynes **3** afforded adducts **4** in excellent yields in simple and mild conditions only in DMSO, without copper, phosphanes and bases.

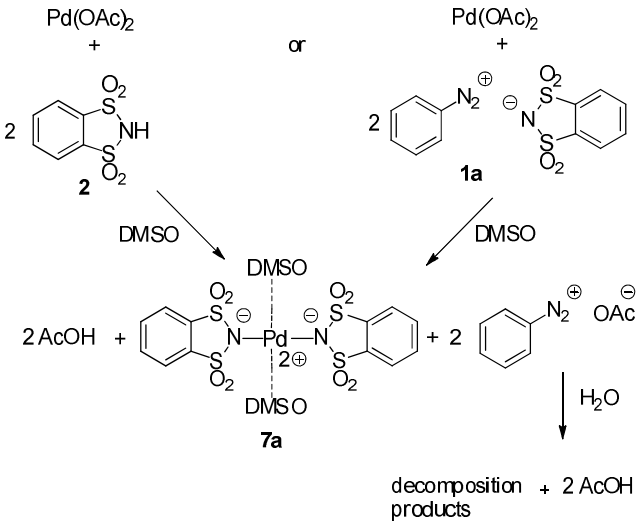
The behaviour of tetrafluoroborate **5** was different: the yield of the reaction carried out without phosphanes was very poor (Table 2; entry 3). The yields were comparable to those obtained with **1a** only adding phosphanes (Table 2; entries 1,2). Interestingly, the reactions of **5** carried out without phosphane, but in the presence of 5 mol% of **2**, afforded **4a** in fairly good yields (Table 2, entry 4). This could

mean that **2** (or better, its anion, the counterion of salts **1**) plays a fundamental role.

In order to demonstrate this, we studied some reactions involving $Pd(OAc)_2$ and respectively **2** and diazonium salt **1a** by NMR (DMSO-d6 was the solvent; see spectra in the Supporting Information). To begin with, we reacted **2** and $Pd(OAc)_2$. We observed, almost immediately, a clear shift in the Me singlet. In fact, this signal, which for Pd(OAc) was seen at 1.71 ppm (spectrum 3), moved to 1.81 ppm after adding **2** (spectrum 4). Moreover, the broad singlet specific of NH (11.57 ppm; spectrum 2) disappeared. The Me singlet of AcOH in DMSO-d6 was precisely at 1.81 ppm. In fact, we observed a sharp increase in the signal at 1.81 ppm, when AcOH was added to the previous mixture (spectrum 5). No changes were observed for the multiplet of aromatic protons of **2** (spectrum 2); in fact they had the same chemical shift (7.72–7.60 ppm). We examined also the IR spectra (registered in DMSO; spectrum I1) of $Pd(OAc)_2$ which showed, among others, two bands at 1620.6 and 1607.3 cm^{-1} respectively, characteristic of the carboxylate anion. The IR spectrum (spectrum I2) of **2** showed, among others, a band at 1266.8 cm-1 due to SO_2 groups. After 15 min, the double band seen previously, moved to 1710.9 and 1624.2 cm^{-1} (spectrum I3). These bands are characteristic of the AcOH carboxylic group. The position of band of SO_2 remained unchanged at 1266.5 cm^{-1}. Interestingly, a band appeared at 475.7 cm^{-1}.

Afterwards, we reacted diazonium salt **1a** (spectrum 1) with $Pd(OAc)_2$. We focused our attention on the Me singlet. After 5 min, we observed the presence of both previously described signals (respectively 1.71 and 1.82 ppm; spectrum 6). After 15 min, only the signal at 1.82 ppm remained (spectrum 7). The multiplet of the anion of **2** was unchanged (7.72-7.59 ppm) and did not appear the signal of NH. On the contrary, the multiplets of benzenic protons of **1a** completely disappeared and two new multiplets, respectively at 7.11–7.03 ppm and 6.70–6.64 ppm, appeared; this points to the decomposition of **1a** (spectrum 7). In both cases, after mixing Pd(OAc)2 with **2** and **1a** respectively, the colour of the DMSO solution immediately turned dark and after about 1 h we observed the precipitation of a black solid that may have been black palladium metal. NMR spectra recorded after the formation of black palladium were identical to the previous ones whereas the band at 475.7 disappeared (Spectrum I4). No reaction occurred between **1a** and $Pd(OAc)_2$ in CD_3CN. No shift of the Me signal was observed; it was only seen a decomposition of **1a** after about 1 hour. Lastly, the NMR spectrum of a solution of $Pd(OAc)_2$ in DMSO-d6 showed that no decomposition of the latter occurred: even after 24 hours the signal of Me is always at 1.71 ppm.

In the light of these results, we assume that the interation between salt **1a** or **2** and $Pd(OAc)_2$ formed (scheme 2) complex **7a**. It was evident that DMSO was essential for its formation and it acted as a S- and/or O-bonded ligand; in fact, its palladium coordination ability is well-known.[5] Unfortunately, attempts to isolate **7a** completely failed.



Scheme 2. Formation of palladium complex **7a**.

Palladium is known to react easily with a number of nitrogen-containing organic compounds, such as amines, imines, nitriles, etc. Such reactions result in the formation of complexes in which nitrogen atoms are co-ordinatively bonded to palladium ions.[6a] Vibrational spectroscopy (IR and Raman) is a suitable tool for the characterization of these compounds[6a] and During *et al.* have found that Pd–N stretching frequency ranges from 528 to 436 cm^{-1}.[6b] On these grounds, the band at 475.7 cm^{-1} (spectrum I3) should be that of Pd–N of **7a**.

Moreover, some metal complexes of **2** are already known in the literature. Blaschette, Jones *et al.* described complexes with Cd or Cu.[7] For example, the Cd cationic complex **8** (characterized by low-temperature x-ray diffraction) have trans-octahedral coordinations provided by 2 Cd-N bonded anions and 4 water molecules (Figure 2). In the light of these data, we assume that that the **7a** Pd-N bond could be ionic.

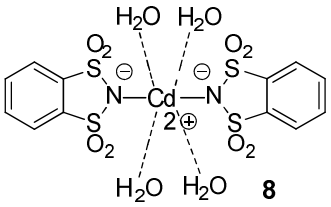


Figure 2. Cd cationic complex of *o*-benzenedisulfonimde **8**.

Interestingly, Pd complexes containing structures similar to **2** had previuosly been used as catalyst. Kalaycioglu *et al.*[8a] prepared a series of neutral-four coordinate palladium(II) complexes **9** (Figure 3) from $Pd(OAc)_2$ and *N*-(2-aminophenyl)arylsulfonamides in DMSO. These complexes were used as catalysts in some oxidation reactions.

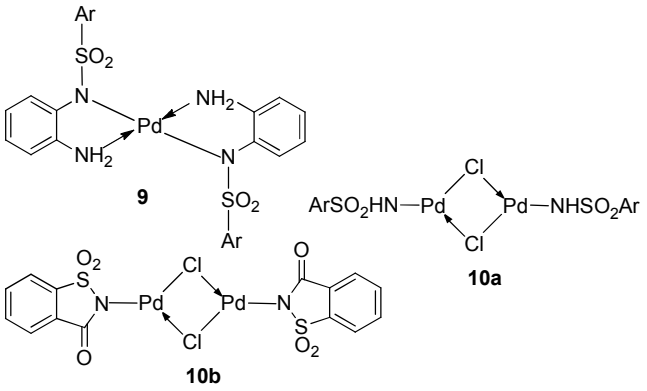
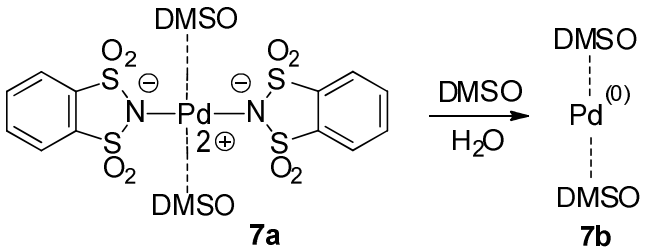


Figure 3. Pd(II) complexes of sulfonamides and saccharin.

Sudalai *et al*.[8b] synthesized a novel family of sulfonamide **10a** or saccharin-based Pd complexes **10b** (Figure 2) from $PdCl_2$. These pre-catalysts have shown excellent activity in several cross-coupling arylation including Suzuki, Heck, and Sonogashira reactions. In particular, **10b** was very effective in Sonogashira coupling in totally copper-free conditions. Pd(0) nanoparticles formed from its decomposition, in the presence of tetrabutylammonium salts. These are the real catalyst.

On these grounds, we assume that Pd(II) complex **7a** is the actual pre-catalysts for this Sonogashira coupling; **7a**, as mentioned above, was rather unstable and decomposed. This was confirmed by IR analyses: the absorption band of Pd–N (identified at 475.7 cm^{-1}) disappeared in the long run (after 1h; spectrum I4). Consequently, a palladium(0) species could form from its decomposition (Scheme 3).

It is not at all easy to explain how this may happen in the absence of phosphanes or other reducing agents. In the literature, it is reported that *is possible* to use Pd(II) complexes as a pre-catalyst without a phosphanes. The decomposition of the latter formed some kind of colloidal or soluble Pd(0) species *in situ* (eventually protected with tetralkylammonium salts). These are the catalysts for Heck and Suzuki coupling, especially in reactions of active substrates such as aryl iodides and diazonium salts.[1c] Recently, Amini *et al*.[9a] affirmed that $Pd(OAc)_2$ in DMSO, or better in 2:1 mixture H_2O/DMSO, afforded Pd(0) species which are active catalysts for Heck reaction.



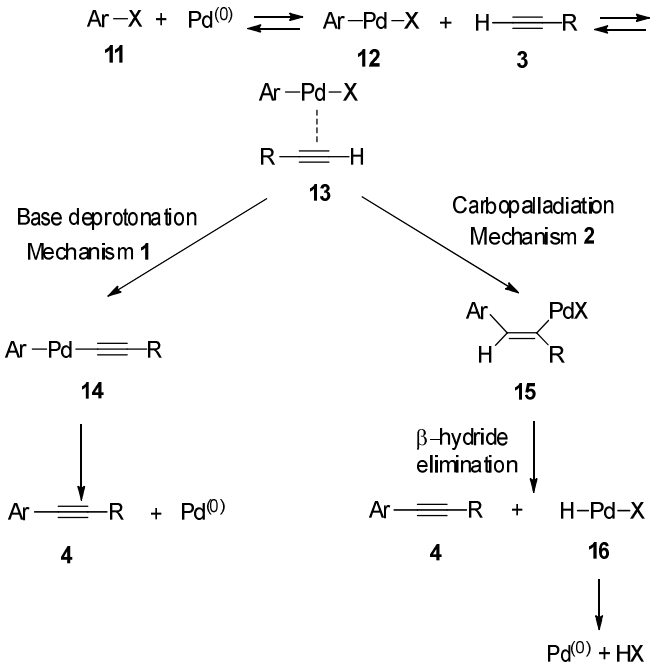
Scheme 3. Formation of Pd(0) catalyst.

Moreover, it was shown that the Pd(0) nanoparticles can be obtained from $[PdCl_2(CNCH_3)_2]$ in solvent solution both as a reducing agent and as a stabilizer.[9b] Five solvents were tested, including DMSO. It was a very good stabilizer, avoiding nanoparticles agglomeration and protecting them from oxidation. However, it did not work, differently from ethylene glycol or H_2O, as a reducing agents.

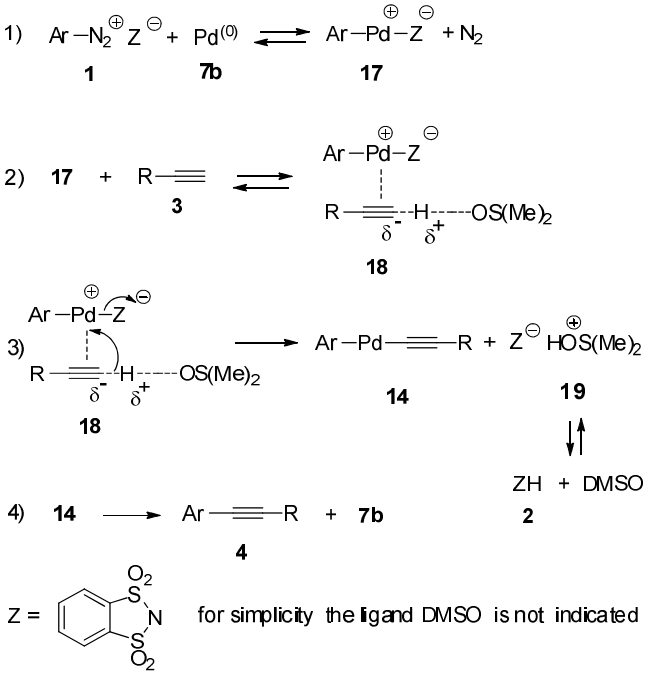
In the light of these results, we assume that the reductive decomposition of **7a** afforded Pd(0) species **7b**, which was highly stabilized by DMSO (Scheme 3). The reducing agent could be the small amount of H_2O[9b] dissolved in DMSO. In fact the reactions were carried out in an aerobic atmosphere and we did not use anhydrous DMSO. On the other hand, in anhydrous enviroment the yields of **4a** was significantly lower (Table 1; entry 11). However, a possible active role for DMSO (associated with its Pd-coordination ability) in the reduction of **7a** cannot be excluded. Therefore, the Pd[0] nanoparticles **7b** stabilized by DMSO could be the effective catalyst for this Sonogashira coupling.

Two principal mechanisms are hypothesized[1c,10a] for the copper-free Sonogashira coupling. They both required an oxidative addition between the electrophilic partner **11** and the Pd[0] complex (for simplicity, in the Scheme 4 the ligands are not indicated) and a subsequent alkyne **3** coordination of the adduct **12**, with the formation of complex **13**. Alternatively, it is also reported [1k, 10b-c] that oxidative addition of Pd(0) on alkyne **3** affords a hydridoalkynylpalladate complex by insertion of Pd in the carbon-hydrogen bond.The interaction between **12** and this complex, in the presence of a base, leads to the formation of **14.** Then, the first one continues by subsequent base deprotonation and reductive elimination. Two alternatives have been suggested for the deprotonation step[10,11a]: for electron-rich alkynes a "cationic pathway" is hypothesized where the slow formation of a cationic Pd-alkyne complex takes place via a nucleofuge X-base exchange; for electron-poor alkynes a proton-transfer from an uncharged complex occurs to produce a palladium-acetylide intermediate. The second hypothesized mechanism involves a carbopalladation first and then a β-hydride elimination. (Scheme 4). The current literature shows only one evidence for this carbopalladiation mechanism.[11b] In fact, Tsuji[1c] states that it is generally believed that the β-elimination from specie **15** (that should form alkyne **4**) is not possible. Moreover DFT calculations recently performed by Najera, Lledos and Ujaque *et al*.[11b] clearly demonstrate that carbopalladiation pathway can be discarded.

In order to explain the mechanism of the Sonogashira coupling catalyzed by **7b**, we can use the mechanism hypothesized by Beller as a model (Scheme 5).[3d] This is broadly the first mechanism described above.



Scheme 4. Proposed mechanism for copper free Sonogashira reactions.



Scheme 5. Hypothesized mechanism.

Firstly, the oxidative addition of diazonium salt **1** to species **7b** formed arylPd(II) intermediate **17** (step 1) which produced adduct **18** by interaction with **3** (step 2). Beller[3d] states that a base (acetate, the counterion of diazonium salt)-assisted deprotonation of **3** afforded the corresponding aryl(alkenyl)Pd(II) adduct **14**. However**,** the anion of **2** is a weaker base than acetate; AcOH pK_a in DMSO is 12.6[12] while **1** pK_a is -4.2 (determined using the same method we described to calculate its pK_a in butanone[13]) and it is unthinkable that it can deprotonate the very weak acid **3.** We suppose that the formation of a hydrogen bond between **3** and the highly basic solvent DMSO weakens the alkynil C-H bond and make the carbon nucleophilic enough to form a new C-Pd bond. The formation of this bond may be also favoured by the fact that Pd-N is a ionic bond, the very weak base Z^- is a good leaving group and that DMSO is poor at solvating anions (step 3). Finally, in the step 4, **14** afforded the final product **4** and regenerated catalyst **7b**. In this way, we can explain why the reaction proceeded *only* in DMSO; the other solvents tested are not able to sufficiently weaken the alkynil C-H bond. Moreover, as mentioned above, salts **1** bearing electron-donating groups coupled with greater difficulty. Evidently, the presence of electron-donating groups on the aromatic ring (the one that comes from **1**) of adduct **18** make Pd less available to nucleophilic attack.

Conclusions

The importance and the synthetic utility of the Sonogashira coupling between arenediazonium *o*-benzenedisulfonimides and terminal alkynes as a powerful method for the formation of arylated alkynes is largely due to the mildness of the reaction, to the easy preparation and high stability of arenediazonium *o*-benzenedisulfonimides, to the high yields and the cleanness of the reactions (there are no side reactions that may complicate the isolation and purification of the arylated alkynes). Moreover, it must be highlighted that the actual pre-catalyst should be an *o*-benzenedisulfonimide based Pd(II) complex that generates the Pd(0) catalyst. Interestingly, no copper, phosphanes, bases or co-catalysts are needed. For this reason, the fundamental role that DMSO and anion of *o*-benzenedisulfonimide play in the formation of the actual pre-catalyst of this Sonogashira coupling must be highlighted. Moreover, DMSO also plays a fundamental role in the catalytic cycle, increasing the reactivity of alkyne.

Experimental Section

General: Analytical grade reagents and solvents were used and reactions were monitored by GC and GC-MS. Column chromatography and TLC were performed on Merck silica gel 60 (70-230 mesh ASTM) and GF 254, respectively. Petroleum ether refers to the fraction boiling in the range 40–70 °C. R.t. is 20 °C. Mass spectra were recorded on an HP 5989B mass selective detector connected to an HP 5890 GC, cross-linked methyl silicone capillary column. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Brucker Avance 200 spectrometer at 200 and 50 MHz respectively. IR spectra were recorded on a Perkin Elmer Spectrum BX FT-IR spectrometer as solutions in DMSO. Dry arenediazonium o-benzenedisulfonimides **1** were prepared as described previously by us.[4a] The crude salts were virtually pure (by ^{1}H NMR spectroscopy) and were used in subsequent reactions with alkynes **3** without further crystallization. Benzenediazonium tetrafluoroborate (**5**) was prepared as described in the literature.[14] All the other reagents were purchased by Sigma-Aldrich or Alfa-Aesar. Structures and purity of all the products obtained in this research were confirmed by their spectral (NMR

and MS) data.Yields of the pure (GC, GC-MS, TLC and NMR) isolated arylalkynes **4** are reported in Table 3. NMR data and spectra of **4** are reported in Supporting Information.

Diphenylacetylene (4a). **Typical procedure**

To a stirring mixture of phenylacetylene (**3a**, 2 mmol, 0.21 g), $Pd(OAc)_2$ (0.05 mmol; 11.2 mg) in DMSO (5 ml), benzenediazonium o-benzenedisulfonimides **1a** (2 mmol, 0.65 g) were added. Immediately, the color of the solution turned black. The mixture was stirred at r.t. for 10 min; the completion of the reaction was confirmed by the absence of azo coupling with 2-naphthol. Then, the reaction mixture was poured into diethyl ether/water (100 mL, 1:1). The aqueous layer was separated and extracted with diethyl ether (50 mL). The combined organic extracts were washed with water (50 mL), dried with Na_2SO_4 and evaporated under reduced pressure. GC-MS analyses of the crude residue showed diphenylacetilene (**4a**, MS (EI): *m/z* = 178 $[M]^+$) as the major product, besides traces of 1,4-diphenylbutadiyne (MS (EI) *m/z* = 202 $[M]^+$). The crude residue was chromatographed on a short column, eluting with petroleum ether/diethyl ether (9.5:0.5). The only eluted product was title compound (**4a**, 0.32 g, 88% yield). The aqueous layer and aqueous washings were collected and evaporated under reduced pressure. The tarry residue was passed through a column of Dowex 50x8 ion exchange resin (1.6 g/1 g of product), eluting with water (about 50 mL). After removal of water under reduced pressure, virtually pure (^{1}H NMR) *o*-benzenedisulfonimide (**2**) was recovered (0.36 g, 82% yield). All the arylalkynes **4** reported in entries of Table 2 were prepared according to the above procedure.

Diphenylacetylene (4a): white solid**;** 0.32 g (yield 88%); m.p. 60–61 °C (EtOH; Lit.[15] 60–61 °C). NMR data identical to that reported in the literature.[3c] MS (EI): *m/z* = 178 $[M^+]$.

1-Nitro-2-(2-phenylethynyl)benzene (4b): waxy solid; 0.43 g (yield 95%); Lit.[16] m.p. 37–40 °C NMR data identical to that reported in the literature.[16] MS (EI): *m/z* = 223 $[M^+]$.

1-Nitro-3-(2-phenylethynyl)benzene (4c): pale yellow solid; 0.41 g (yield 90%); m.p. 69–70 °C (EtOH; Lit.[17] 71–72 °C). NMR data identical to that reported in the literature.[17] MS (EI): *m/z* = 223 $[M^+]$.

1-Nitro-4-(2-phenylethynyl)benzene (4d): pale yellow solid. From **1c** and **3a** 0.42 g (yield 93%); from **1a** and **3b** 0.39 g (yield 87%); m.p. 120–121 °C (EtOH; Lit.[18] 120–121 °C). NMR data identical to that reported in the literature.[3d] MS (EI): *m/z* = 223 $[M^+]$.

1-Methyl-4-(2-phenylethynyl)benzene (4e): white solid. From **1e** and **3a** 0.28 g (yield 72%); from **1a** and **3c** 0.33 g (yield 87%); m.p. 71–72 °C (EtOH; Lit.[8b] 71 °C). NMR data identical to that reported in the literature.[3d] MS (EI): *m/z* = 192 $[M^+]$.

1-Methoxy-4-(2-phenylethynyl)benzene (4f): white solid. From **1f** and **3a** 0.29 g (yield 69%); from **1a** and **3d** 0.37 g (yield 88%); m.p. 60–61 °C (EtOH; Lit.[17] 59–60 °C). NMR data identical to that reported in the literature.[3b] MS (EI): *m/z* = 208 $[M^+]$.

1-Bromo-4-(2-phenylethynyl)benzene (4g): white solid. From **1g** and **3a** 0.46 g (yield 90%); From **1a** and **3e** 0.46 g (yield 90%); m.p. 83–84°C (EtOH; Lit.[19] 83–83.5 °C). NMR data identical to that reported in the literature.[3b] MS (EI): *m/z* = 256, 258 $[M^+]$.

4-(2-Phenylethynyl)benzonitrile (4h): white solid; 0.38 g (yield 90%); m.p. 107–108°C (EtOH; Lit.[20] 106–108 °C). NMR data identical to that reported in the literature.[3d] MS (EI): *m/z* = 203 $[M^+]$.

4-Methoxy-2-nitro-1-(2-phenylethynyl)benzene (4i): is known in the literature,[21] but no physical and spectral data are reported. Pale yellow solid; 0.47 g (yield 92%); m.p. 67 °C (EtOH). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 7.58–7.49 (m, 4H), 7.32–7.28 (m, 3H), 7.11–7.05 (m, 1H), 3.84 (s, 3H) ppm, ^{13}C NMR (50 MHz, $CDCl_3$, 25°C): δ = 159.6, 150.6, 135.7, 132.0, 129.0, 128.6, 122.9, 119.9, 110.9, 109.6, 95.4, 85.1, 56.1 ppm. MS (EI): *m/z* = 253 (25) $[M^+]$, 236 (15), 176 (30), 163 (35), 105 (100), 77 (70).

2-(2-Phenylethynyl)benzothiazole (4j): yellow viscous oil[22]; 0.35 g (yield 75%); NMR data identical to that reported in the literature.[22] MS (EI): *m/z* = 235 $[M^+]$.

Methyl 3-(2-phenylethynyl)thiophene-2-carboxylate (4k): yellow viscous oil[23]; 0.41 g (yield 84%); NMR data identical to that reported in the literature.[23] MS (EI): *m/z* = 242 $[M^+]$.

1,4-Bis(2-phenylethynyl)benzene (4l): white solid; 0.45 g (yield 80%); m.p. 183–184°C (EtOH; Lit.[24] 153–154 °C). NMR data identical to that reported in the literature.[24] MS (EI): *m/z* = 278 $[M^+]$.

1-Methyl-4-[2-(4-nitrophenyl)ethynyl]benzene (4m): pale yellow solid. From **1e** and **3b** 0.33 g (yield 69%); from **1d** and **3c** 0.45 g (yield 94%); m.p. 156–157°C (EtOH; Lit.[25] 156–157 °C). NMR data identical to that reported in the literature.[25] MS (EI): *m/z* = 237 $[M^+]$.

4-[2-(4-Methylphenyl)ethynyl]benzonitrile (4n): white solid; 0.40 g (yield 93%); m.p. 162–163°C (EtOH; Lit.[26] 162–164 °C). NMR data identical to that reported in the literature.[26] MS (EI): *m/z* = 217 $[M^+]$.

1-Methoxy-4-[2-(4-methylphenyl)ethynyl]benzene (4o): white solid. From **1f** and **3c** 0.28 g (yield 64%); from **1e** and **3d** 0.31 g (yield 71%); m.p. 126–127°C (EtOH; Lit.[24] 126–130 °C). NMR data identical to that reported in the literature.[24] MS (EI): *m/z* = 222 $[M^+]$.

1-Phenyl-1-hexyne (4p): yellow viscous oil[27]; 0.27 g (yield 85%); NMR data identical to that reported in the literature.[3d] MS (EI): *m/z* = 158 $[M^+]$.

1-(4-Nitrophenyl)-1-hexyne (4q): yellow viscous oil;[18] 0.37 g (yield 90%); NMR data identical to that reported in the literature.[18] MS (EI): *m/z* = 203 $[M^+]$.

1-(4-Methoxyphenyl)-1-hexyne (4r): yellow viscous oil;[28] 0.24 g (yield 64%); NMR data identical to that reported in the literature.[28] MS (EI): *m/z* = 188 $[M^+]$.

2-Phenylbenzofuran (6): white solid; 0.31 g (yield 79%); m.p. 121–122°C (EtOH; Lit.[29] 120–121 °C). NMR data identical to that reported in the literature.[30] MS (EI): *m/z* = 194 $[M^+]$.

Reactions of 1a or 2 with $Pd(OAc)_2$

a) In a NMR tube, $Pd(OAc)_2$ (0.1 mmol, 22.4 mg), **1a** (0.2 mmol, 64.6 mg) and DMSO-d6 (2 ml) was added. Immediately, the color of the solution turned dark. As it has been described above, the progress of the reaction was followed on NMR. After 15 min, we observed a formation of decomposition products of **1a,** 7.53–7.45 and 7.12–7.05 ppm (2m) and the formation of AcOH, 1.82 ppm (s, 3H). The signals of the anion of **2** remained unchanged at 7.72-7.60 ppm (m, 4H). We observed also, after about 1 hour, the formation of a black powder.

b) In a NMR tube, $Pd(OAc)_2$ (0.1 mmol, 22.4 mg), **1a** (0.2 mmol, 64.6 mg) and CD_3CN (2 ml) was added. No change in color was noted. The progress of the reaction was followed on NMR. After 1 h, we observed unchanged **1a:** 8.46-8.41 (m, 2H), 8.22-8.13 (m, 1H), 7.88-7.80 (m, 2H), 7.69-7.58 (m, 4H) ppm. Also the singlet of Me of Pd(OAc) remained unchanged at 1.85 ppm; in fact, recording the spectrum of $Pd(OAc)_2$ in CD_3CN, a singlet at 1.85 ppm was observed. After 8 hours we observed a formation of a decomposition product of **1a** (various multiplet between 7.88 and 7.00 ppm) and the singlet at 1.85 ppm due to $Pd(OAc)_2$.

c) In a NMR tube, $Pd(OAc)_2$ (0.1 mmol, 22.4 mg), **2** (0.2 mmol, 48.2 mg) and DMSO-d6 (2 ml) was added. Immediately, the color of the solution turned dark As described above, the progress of the reaction was followed on NMR. After 5 min, we observed a formation of AcOH, 1.82 ppm (s, 3H). The signals of **2** remained unchanged at 7.72-7.60 ppm (m, 4H). After about 1 hour, we observed also the formation of a black powder.

Supporting Information (see footnote on the first page of this article): …

Acknowledgments

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