Tetrahedron xxx (2013) 1–5

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

A simple catalytic system based on $PdCl_2(CH_3CN)_2$ in water for cross-coupling reactions using diazonium salts

Ouissam El Bakouri, Martí Fernández, Sandra Brun, Anna Pla-Quintana *, Anna Roglans *

Institut de Química Computacional i Catàlisi (IQCC) and Departament de Química, Universitat de Girona, Campus de Montilivi, 17071 Girona, Spain

ARTICLE INFO

Article history:
Received 19 July 2013
Received in revised form 3 September 2013
Accepted 4 September 2013
Available online xxx

Keywords:
Palladium
Diazonium salts
Cross-coupling reactions
Aqueous medium

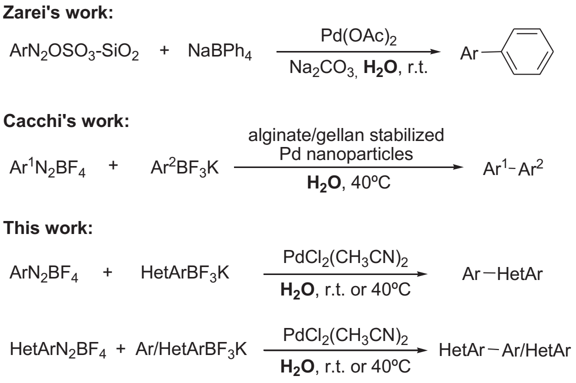
ABSTRACT

Aryl–heteroaryl and heteroaryl–heteroaryl compounds are obtained through the Suzuki–Miyaura cross-coupling reactions between diazonium salts and potassium trifluoroborates using $PdCl_2(CH_3CN)_2$ as the catalyst in water and in the absence of any additive, ligand or base. In addition, the same mild catalytic system is effective for the Matsuda–Heck reaction between several monoolefins with aryldiazonium salts.

1. Introduction

The palladium-catalyzed Suzuki–Miyaura reaction is a widely used method for the construction of C–C bonds.[1] Among the available range of electrophiles, aryldiazonium salts are a particularly good choice since they allow Pd-catalyzed carbon–carbon bond-forming reactions to be run under simple mild conditions.[2] These salts are obtained from readily accessible anilines,[3] which are cheaper than the commonly used aryl halides and triflates, and are highly reactive as electrophiles in the palladium-catalyzed cross-coupling reactions at room temperature even in the absence of a base and added ligands. The potential of these processes would be increased if they were run in an environmentally friendly reaction media, such as water.

Despite the significant advances made in palladium-catalyzed bond-forming reactions using chlorides or triflates in water,[4] only some recent reports have described the use of aryldiazonium salts as electrophiles in Suzuki–Miyaura reactions in water as the only reaction solvent (Scheme 1). Zarei et al. prepared aryldiazonium silica sulfates by supporting the diazonium salts on the surface of silica sulfuric acid for use in Suzuki cross-couplings.[5] These authors described the Suzuki–Miyaura cross-coupling of aryldiazonium silica sulfates with sodium tetraphenylborate. In the presence of $Pd(OAc)_2$ and Na_2CO_3 in heterogeneous conditions, biaryls were afforded in good yields in water media. The authors only used sodium tetraphenylborate as the boron counterpart limiting the number of biphenyls obtained (Scheme 1). In addition, Cacchi et al.[6] used palladium nanoparticles stabilized by an alginate/gellan mixture as a recyclable catalytic system for Suzuki–Miyaura reactions of aryldiazonium tetrafluoroborates with potassium aryltrifluoroborates in water (Scheme 1).



Scheme 1. C–C bond-forming reactions with diazonium salts in water.

None of these previous studies applied the methodology to heteroaromatic substrates in the diazonium electrophile or in the boronic counterpart. This would be highly desirable in view of the widespread appearance of heterocycles in biologically and pharmaceutically active compounds as well as in advanced materials. Hydrogen-bonding between water and heteroatoms has been

---

* Corresponding authors. Tel.: +34 972 418275; fax: +34 972 418150; e-mail address: anna.roglans@udg.edu (A. Roglans).

0040-4020/$ – see front matter © 2013 Published by Elsevier Ltd.
http://dx.doi.org/10.1016/j.tet.2013.09.010

Please cite this article in press as: El Bakouri, O.; et al., Tetrahedron (2013), http://dx.doi.org/10.1016/j.tet.2013.09.010

postulated as minimizing palladium deactivation by the coordination of heterocycles.[7]

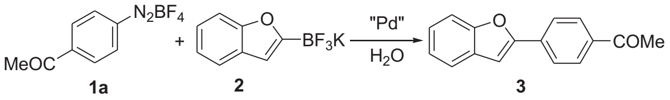
In previous studies in our group, aryl and heteroaryldiazonium salts were shown to be effective partners in palladium-catalyzed C–C bond-forming reactions in aqueous organic medium.[8] In view of the benefits of diazonium salts in palladium chemistry and water as the reaction media for reactions involving heterocycles, we envisioned a simple and effective reaction to involve heterocycles in palladium-catalyzed C–C bond-forming reactions. Here we present our results of the use of aryldiazonium salts in the synthesis of heteroaryl–aryl and biheteroaryl derivatives by Suzuki–Miyaura cross-couplings in water (Scheme 1).

2. Results and discussion

We started the study by attempting the Suzuki–Miyaura cross-coupling to afford heteroaryl–aryl derivatives. It was decided to test potassium organotrifluoroborates[9] as boron counterparts since they are less prone to protodeboronation and have been shown to be highly effective in combination with aryldiazonium salts both by our group[8c,d] and others.[6,10] $PdCl_2$, $Pd(OAc)_2$, $PdCl_2(CH_3CN)_2$, and $Pd(dba)_2$ were chosen from the range of simple, commercially available catalysts. The model reaction chosen was between 4-acetylphenyldiazonium salt **1a** and potassium benzofuran-2-trifluoroborate **2** (Table 1).

Table 1

Screening of the reaction conditions for Suzuki–Miyaura cross-coupling[a]



Entry	Catalyst (mol %)	Reaction conditions	Yield of **3**[b] (%)
1	$PdCl_2$ (10)	25 °C/5 h	98
2	$Pd(OAc)_2$ (10)	25 °C/2 h	57[c]
3	$PdCl_2(CH_3CN)_2$ (10)	25 °C/3.5 h	98
4	$Pd(dba)_2$ (10)	25 °C/3 h	82[d]
5	$PdCl_2(CH_3CN)_2$ (10)	40 °C/1.5 h	95
6[e]	$PdCl_2(CH_3CN)_2$ (5)	40 °C/1.5 h	99
7[f]	$PdCl_2(CH_3CN)_2$ (1)	40 °C/4 h	70

[a] Unless otherwise noted the reaction conditions used were: diazonium salt **1a** (0.15 mmol), potassium trifluoroborate **2** (0.18 mmol) in water (16 mL).

[b] Isolated yield after column chromatography.

[c] 12% yield of the aryldiazonium homocoupling product was obtained.

[d] 16% yield of the aryldiazonium homocoupling product was obtained.

[e] Reaction run in 8 mL of water as a solvent.

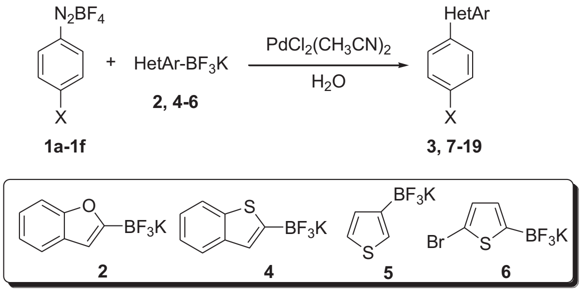
[f] Reaction run in 4 mL of water as a solvent.

When a 10% M of $PdCl_2$ was used at room temperature a 98% yield of the cross-coupled product **3** was obtained after 5 h of reaction (Table 1, entry 1). Using $Pd(OAc)_2$, the yield of **3** dropped to 57% and a 12% yield of homocoupling of the diazonium salt **1a** was also isolated (Table 1, entry 2). $PdCl_2(CH_3CN)_2$ also gave excellent results and in only 3.5 h of reaction (Table 1, entry 3). Using a palladium(0) source, such as $Pd(dba)_2$, the yield of **3** was slightly lower and a 16% yield of aryldiazonium homocoupled product was obtained (Table 1, entry 4). In the following experiments, $PdCl_2(CH_3CN)_2$ was chosen as the best catalyst. Increasing the temperature to 40 °C resulted in a decrease in the reaction time to afford an analogous yield (Table 1, entry 5). The reduction in the catalyst loading was checked at this temperature. As we can see in entry 6 of Table 1, the reaction also worked effectively when the quantity of $PdCl_2(CH_3CN)_2$ was reduced to 5%. However, using a 1 mol % of palladium source, the yield was considerably lower and the reaction time increased (Table 1, entry 7).

To evaluate the scope of the process, a variety of selected heteroaryltrifluoroborates were reacted with aryldiazonium salts with electron-donating and electron-withdrawing groups (Table 2).

Table 2

Suzuki–Miyaura cross-coupling reactions of aryldiazonium salts (**1**) and potassium heteroaryltrifluoroborates **2**, **4**–**6**[a]



Entry	**1** (X)	HetAr-BF_3K	Catalyst (mol %)	Reaction conditions	Product (yield %)[b,c]
1[d]	**1a** (4-COMe)	**2**	10	25 °C/3.5 h	**3** (98)
2	**1a** (4-COMe)	**2**	5	40 °C/4 h	**3** (99)
3	**1b** (4-Me)	**2**	5	40 °C/4 h	**7** (92)
4	**1c** (4-NO_2)	**2**	5	40 °C/4 h	**8** (96)
5	**1f** (2-Me)	**2**	5	40 °C/4 h	**9** (22)[e]
6	**1a** (4-COMe)	**4**	5	40 °C/4 h	**10** (27)
7	**1b** (4-Me)	**4**	5	40 °C/4 h	**11** (61)
8[d]	**1d** (4-OMe)	**4**	10	25 °C/1.5 h	**12** (57)
9	**1d** (4-OMe)	**4**	5	40 °C/4 h	**12** (53)
10	**1a** (4-COMe)	**5**	10	25 °C/1.5 h	**13** (63)
11	**1a** (4-COMe)	**5**	5	40 °C/4 h	**13** (58)
12	**1b** (4-Me)	**5**	5	40 °C/4 h	**14** (45)
13	**1c** (4-NO_2)	**5**	5	40 °C/4 h	**15** (53)
14	**1d** (4-OMe)	**5**	5	40 °C/4 h	**16** (35)
15	**1e** (4-F)	**5**	5	40 °C/4 h	**17** (49)
16	**1b** (4-Me)	**6**	5	40 °C/4 h	**18** (31)[e]
17[d]	**1c** (4-NO_2)	**6**	10	25 °C/6 h	**19** (60)
18	**1c** (4-NO_2)	**6**	5	40 °C/4 h	**19** (61)

[a] Unless otherwise noted the reaction conditions used were: diazonium salt **1a** (0.15 mmol), potassium trifluoroborate **2** (0.18 mmol) in water (8 mL).

[b] Isolated yields after column chromatography.

[c] All crude reaction mixtures were analyzed by GC–MS and, unless otherwise noted, showed only traces of potassium trifluoroborate homocoupling and/or phenol.

[d] Reaction run in 16 mL of water as a solvent and monitored until completion.

[e] Phenol was detected by the GC–MS of the crude reaction mixture.

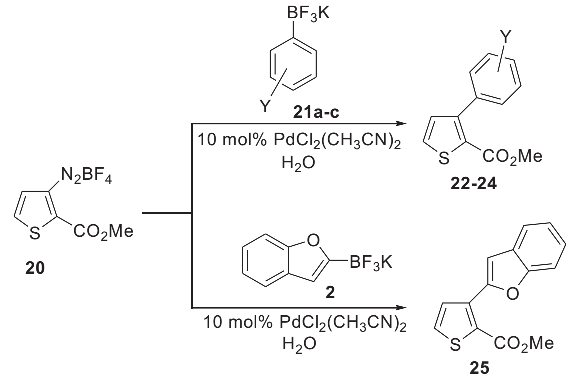
Potassium benzofuran-2-trifluoroborate **2** proved to be efficient in this type of process using several aryldiazonium salts with electron-deficient (Table 2, entries 1, 2, 4) or electron-neutral (Table 2, entry 3) substituents. In all cases, reactions took place with excellent yields at 40 °C in short reaction times. The reaction was seriously affected by steric hindrance and only a 22% yield was obtained when 2-methylphenyl diazonium tetrafluoroborate **1f** was used (Table 2, entry 5). Potassium trifluoroborates based on sulfur heteroatoms, such as benzothiophene **4**, and thiophene derivatives **5** and **6** were then evaluated. Whereas a poor yield was obtained when benzothiophene **4** was reacted with an electron-deficient diazonium salt (Table 2, entry 6), better yields were achieved when electron-neutral (Table 2, entry 7) or electron-rich (Table 2, entries 8 and 9) substituted diazonium salts were involved in the reaction. In the case of the arylation of the 3-position of thiophene (Table 2, entries 10–15), the efficacy of the process was found to be independent from the electronic nature of the aryldiazonium partner. It is notable that a bromide on the thiophene ring, such as in **6** remains intact during the course of the reaction, although electron-deficient substituted diazonium salts need to be used to achieve good yields of the coupling product (compare in Table 2 the entries 16 and 17). Analogous results can be

Please cite this article in press as: El Bakouri, O.; et al., Tetrahedron (2013), http://dx.doi.org/10.1016/j.tet.2013.09.010

obtained with a 10 mol % of catalyst at room temperature and with 5 mol % loading with gentle heating (compare in Table 2, the entries 1 and 2, 8 and 9, and 17 and 18).

The Suzuki–Miyaura cross-coupling when the heteroaromatic framework is in the diazonium electrophile was then studied. The thiophene diazonium salt **20** was successfully coupled with several aryltrifluoroborates **21a**–**c** and potassium benzofurantrifluoroborate **2** using 10 mol % of $PdCl_2(CH_3CN)_2$ at room temperature (Table 3). In the case of potassium 4-fluorophenytrifluoroborate **21c**, gentle heating to 40 °C was needed to achieve a good yield of the cross-coupled product. Finally, the reaction between two heteroaromatic partners was evaluated (Table 3, entry 5). A 65% yield was achieved in 4.5 h for the coupling reaction in water at room temperature.

Table 3
Cross-coupling reactions of heteroaryldiazonium salt **20**[a]



Entry	Reagent	Reaction conditions	Product (yield %)[b]
1	**21a** (Y=3-F)	25 °C/1 h	**22** (45)
2	**21b** (Y=H)	25 °C/1 h	**23** (56)
3	**21c** (Y=4-F)	25 °C/2 h	**24** (26)
4	**21c** (Y=4-F)	40 °C/1 h	**24** (50)
5	**2**	25 °C/4.5 h	**25** (65)[c]

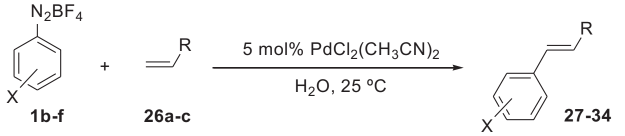
[a] The reaction conditions used were: diazonium salt **1a** (0.15 mmol), potassium trifluoroborate **2** (0.18 mmol) in water (16 mL).

[b] Isolated yields after column chromatography.

[c] 23% yield of the potassium benzofuran-2-trifluoroborate homocoupling product was obtained.

The Matsuda–Heck reaction was first described by Sengupta and Bhattacharya who used diazonium salts in water in an in situ diazotization followed by Heck coupling with ethyl acrylate.[11] The use of water in this reaction has been studied in more detail in the last couple of years. Two papers described the use of palladium nanoparticles as catalysts. Gholinejad used palladium nanoparticles supported on agarose and prepared from $Pd(OAc)_2$ for the coupling of styrene and ethyl acrylate with four aryldiazonium salts,[12] and Pore and Gaikwad described the use of in situ formed Pd nanoparticles from $Pd(OAc)_2$ although with the addition of a surfactant.[13] Two other papers described the reaction by using $Pd(OAc)_2$. Zarei et al. used aryldiazonium silica sulfates for the arylation of methyl acrylate, styrene, and acrylic acid to afford the corresponding disubstituted olefins in good yields.[14] More recently, Sebastián, Vallribera, Nájera et al. applied the methodology to the coupling of the readily available aryldiazonium tetrafluoroborates with a series of monosubstituted olefins.[15] Finally, Correia and Schwalm described the Heck–Matsuda arylation under $Pd(OAc)_2$ catalysis of an N-protected 3-pyrroline with aryldiazonium salt in water as the key step in the concise total synthesis of marinoquinoline derivatives.[16] All the precedents in the literature used $Pd(OAc)_2$ as the pre-catalyst. Having found that $PdCl_2(CH_3CN)_2$ effectively catalyzed Suzuki–Miyaura reactions in water and being aware that Correia et al. recently described the use of this complex as a catalyst in the enantioselective Heck coupling in methanol,[17] we decided to investigate whether it was also effective as a catalyst in the Matsuda–Heck reaction in water. The results are shown in Table 4.

Table 4
Matsuda–Heck reactions of aryldiazonium salts (**1**) and olefins **26**[a]



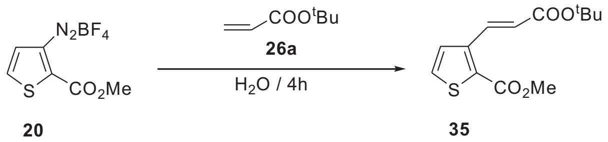
Entry	1 (X)	**26** (R)	Reaction time (h)	Product (yield %)[b]
1	**1b** (4-Me)	**26a** (COO^tBu)	8	**27** (89)
2	**1c** (4-NO_2)	**26a** (COO^tBu)	1.5	**28** (96)
3	**1d** (4-OMe)	**26a** (COO^tBu)	5	**29** (81)
4	**1e** (4-F)	**26a** (COO^tBu)	1.5	**30** (99)
5	**1f** (2-Me)	**26a** (COO^tBu)	7	**31** (69)
6	**1b** (4-Me)	**26b** (Ph)	3	**32** (55)
7	**1e** (4-F)	**26b** (Ph)	7	**33** (28)
8	**1d** (4-OMe)	**26c** ($PO(OEt)_2$)	2	**34** (66)

[a] The reaction conditions used were: diazonium salt **1** (0.18 mmol), alkene **26** (0.30 mmol) in water (8 mL).

[b] Isolated yields after column chromatography.

tert-Butyl acrylate **26a** was arylated in excellent yields with aryldiazonium salts containing both electron-donating and electron-withdrawing substituents (Table 4, entries 1–4). *ortho* Substituents were tolerated and diazonium salt **1f** bearing an *ortho* methyl substituent reacted to give a 69% yield of the arylated product (Table 4, entry 5). Styrene was a poor substrate in this reaction giving only moderate yields of the stilbene derivatives, probably due to the low miscibility of styrene with water (Table 4, entries 6 and 7). Diethyl vinylphosphonate **26c** was also active in the Matsuda–Heck reaction giving a 66% yield of compound **34** (Table 4, entry 8). The arylation of olefins **26a**–**c** only gave products with the (*E*)-configuration, as was confirmed by the large coupling constant values (16–18 Hz) observed between the olefin protons for all compounds **27**–**34**. No residual proton signals from tentative (*Z*)-configuration isomers were observed.

The Matsuda–Heck reaction with the heteroaromatic diazonium salt **20** was also tested. A moderate 33% yield was achieved by reacting **20** with *tert*-butyl acrylate using a 5 mol % catalyst at 25 °C. The yield could be improved to a 74% when increasing both the catalyst loading and the temperature (Scheme 2).



Conditions A: 5 mol% $PdCl_2(CH_3CN)_2$ / 25 °C; 33% yield

Conditions B: 10 mol% $PdCl_2(CH_3CN)_2$ / 40 °C; 74% yield

Scheme 2. Matsuda–Heck reaction with heteroaryldiazonium salt **20**.

3. Conclusions

In summary, we have developed an experimentally simple method for the cross-coupling of aryl and heteroaryldiazonium

Please cite this article in press as: El Bakouri, O.; et al., Tetrahedron (2013), http://dx.doi.org/10.1016/j.tet.2013.09.010

salts with potassium aryl and heteroaryltrifluoroborates using commercially available $PdCl_2(CH_3CN)_2$, water as the only solvent, and running the reactions under mild conditions (room temperature or 40 °C) for short reaction times. The protocol is simple, without the need for a base or ligands, and a wide range of functional groups and heteroaromatic moieties are tolerated. In addition, the catalytic system described has also been tested in Matsuda–Heck reactions in water following an experimentally simple procedure.

4. Experimental section

4.1. General

Reaction mixtures were chromatographed through a silica gel column (230–400 mesh). ^{1}H NMR spectra were measured at 400 MHz and 300 MHz with Bruker instruments. ^{1}H chemical shifts (δ) were referenced to internal solvent resonances and reported relative to $SiMe_4$. GC–MS analyses were performed by an Agilent 7890A gas equipped with an HP-5 capillary column interfaced with an Agilent 5975C mass spectrometer. The electron ionization (EI) source was set at 70 eV.

Commercially available potassium organotrifluoroborates **2**, **4**–**6**, and **21a**–**c**, anilines, and olefins **26a**–**c** were used without purification. Aryldiazonium salts **1a**–**f** and **20** were prepared by treatment of the corresponding aniline with sodium nitrite and HBF_4 in aqueous media following the general method.[3] These salts can be stored for several months at −20 °C.

4.2. General procedure for the Suzuki–Miyaura reactions

Potassium heteroaryltrifluoroborate (0.18 mmol) was added to a solution of aryldiazonium tetrafluoroborate (0.15 mmol) and $PdCl_2(CH_3CN)_2$ (5 mol %, 1.9 mg) in H_2O (8 mL) at 0 °C. The resulting mixture was warmed to room temperature (or heated to 45 °C) and was stirred until the reaction was completed (as observed by the ceasing of the release of N_2) (Tables 1–3). The reaction mixture was extracted with CH_2Cl_2 (3×10 mL), the organic phase was then dried and evaporated, and the crude material was purified by column chromatography on silica gel (hexane/ethyl acetate, gradient) to give the desired compound.

4.2.1. 2-(4-Acetylphenyl)benzo[b]furan (***3***). Colorless solid; mp=170–172 °C (lit.[18] 177–179 °C); δ_H (300 MHz, $CDCl_3$, 25 °C) 2.61 (s, 3H), 7.13 (d, $^4J_{H,H}$=0.8 Hz, 1H), 7.25 (ddd, $^3J_{H,H}$=8.0 Hz, $^3J_{H,H}$=6.8 Hz, $^4J_{H,H}$=1.2 Hz, 1H), 7.32 (ddd, $^3J_{H,H}$=8.0 Hz, $^3J_{H,H}$=6.8 Hz, $^4J_{H,H}$=1.2 Hz, 1H), 7.53 (dd, $^3J_{H,H}$=8.0 Hz, $^4J_{H,H}$=0.8 Hz, 1H), 7.59 (m, 1H), 7.91 (d, $^3J_{H,H}$=8.8 Hz, 2H), 8.00 (d, $^3J_{H,H}$=8.8 Hz, 2H); *m*/*z* (EI) 236 (6, M^+), 221 ($10,\ M-CH_3{}^+$), 44 (100%).

4.2.2. 2-(4-Methylphenyl)benzo[b]furan (***7***). Colorless solid; mp=121–123 °C (lit.[19] 124–125 °C); δ_H (300 MHz, $CDCl_3$, 25 °C) 2.39 (s, 3H), 6.96 (d, $^4J_{H,H}$=0.9 Hz, 1H), 7.16–7.29 (m, 4H), 7.51 (m, 1H), 7.56 (m, 1H), 7.76 (d, $^3J_{H,H}$=8.1 Hz, 2H); *m*/*z* (%) (EI) 209 (22, $M+H^+$), 55 (100).

4.2.3. 2-(4-Nitrophenyl)benzo[b]furan (***8***). Yellow solid; mp=181–183 °C (lit.[20] 184.5–185 °C); δ_H (400 MHz, $CDCl_3$, 25 °C) 7.24 (d, $^4J_{H,H}$=0.8 Hz, 1H), 7.28 (m, 1H), 7.37 (ddd, $^3J_{H,H}$=8.4 Hz, $^3J_{H,H}$=7.2 Hz, $^4J_{H,H}$=1.2 Hz 1H), 7.56 (dd, $^3J_{H,H}$=8.0 Hz, $^4J_{H,H}$=0.8 Hz, 1H), 7.64 (m, 1H), 8.00 (d, $^3J_{H,H}$=8.8 Hz, 2H), 8.30 (d, $^3J_{H,H}$=8.8 Hz, 2H); *m*/*z* (%) (EI) 239 (6, M^+), 44 (100).

4.2.4. 2-(2-Methylphenyl)benzo[b]furan (***9***).[21] Yellow solid; δ_H (300 MHz, $CDCl_3$, 25 °C) 2.61 (s, 3H), 6.92 (d, $^4J_{H,H}$=1.2 Hz, 1H), 7.25–7.35 (m, 5H), 7.54 (m, 1H), 7.63 (m, 1H), 7.88 (m, 1H); *m*/*z* (%) (EI) 208 (100, M^+).

4.2.5. 2-(4-Acetylphenyl)benzo[b]thiophene (***10***). Colorless solid; mp=183–184 °C (lit. 165.2–166.7 °C).[22] δ_H (400 MHz, $CDCl_3$, 25 °C) 2.63 (s, 3H), 7.34–7.39 (m, 2H), 7.66 (d, $^4J_{H,H}$=0.8 Hz, 1H), 7.80 (d, $^3J_{H,H}$=8.8 Hz, 2H), 7.80–7.87 (m, 2H), 8.00 (d, $^3J_{H,H}$=8.8 Hz, 2H); *m*/*z* (%) (EI) 252 (82, M^+), 237 (100), 208 (47).

4.2.6. 2-(4-Methylphenyl)benzo[b]thiophene (***11***). Colorless solid; mp=153–155 °C (lit.[23] 156.9–158.2 °C); δ_H (300 MHz, $CDCl_3$, 25 °C) 2.38 (s, 3H), 7.20–7.24 (m, 2H), 7.16–7.36 (m, 2H), 7.48 (d, $^4J_{H,H}$=0.6 Hz, 1H), 7.60 (d, $^3J_{H,H}$=8.1 Hz, 2H), 7.74 (m, 1H), 7.80 (m, 1H); *m*/*z* (EI) 224 (100, M^+).

4.2.7. 2-(4-Methoxyphenyl)benzo[b]thiophene (***12***).[23] Colorless oil; δ_H (300 MHz, $CDCl_3$, 25 °C) 3.85 (s, 3H), 6.96 (d, $^3J_{H,H}$=8.7 Hz, 2H), 7.25–7.40 (m, 2H), 7.42 (s, 1H), 7.64 (d, $^3J_{H,H}$=8.7 Hz, 2H), 7.75 (m, 1H), 7.80 (m, 1H); *m*/*z* (%) (EI) 240 (100, M^+), 225 (56).

4.2.8. 3-(4-Acetylphenyl)thiophene (***13***).[24] Colorless solid; mp=149–151 °C; δ_H (400 MHz, $CDCl_3$, 25 °C) 2.62 (s, 3H), 7.40–7.45 (m, 2H), 7.57 (dd, $^3J_{H,H}$=2.8 Hz, $^4J_{H,H}$=1.6 Hz, 1H), 7.68 (d, $^3J_{H,H}$=8.4 Hz, 2H), 7.99 (d, $^3J_{H,H}$=8.4 Hz, 2H); *m*/*z* (%) (EI) 202 (60, M^+), 187 (100), 115 (65).

4.2.9. 3-(4-Methylphenyl)thiophene (***14***).[24] Pale yellow solid; mp=97–99 °C; δ_H (300 MHz, $CDCl_3$, 25 °C) 2.36 (s, 3H), 7.19 (d, $^3J_{H,H}$=8.0 Hz, 2H), 7.32–7.40 (m, 3H), 7.47 (d, $^3J_{H,H}$=8.0 Hz, 2H); *m*/*z* (%) (EI) 174 (100, M^+).

4.2.10. 3-(4-Nitrophenyl)thiophene (***15***).[25] Yellow solid; mp=129–130 °C; δ_H (400 MHz, $CDCl_3$, 25 °C) 7.43–7.48 (m, 2H), 7.63 (m, 1H), 7.74 (d, $^3J_{H,H}$=8.8 Hz, 2H), 8.25 (d, $^3J_{H,H}$=8.8 Hz, 2H); *m*/*z* (%) (EI) 205 (98, M^+), 115 (100).

4.2.11. 3-(4-Methoxyphenyl)thiophene (***16***).[26] Colorless solid; mp=124–126 °C; δ_H (400 MHz, $CDCl_3$, 25 °C) 3.83 (s, 3H), 6.93 (d, $^3J_{H,H}$=8.8 Hz, 2H), 7.30–7.38 (m, 3H), 7.52 (d, $^3J_{H,H}$=8.8 Hz, 2H); *m*/*z* (%) (EI) 190 (100, M^+), 147 (50).

4.2.12. 3-(4-Fluorophenyl)thiophene (***17***).[26] Pale yellow oil; δ_H (300 MHz, $CDCl_3$, 25 °C) 7.07 (t, $^3J_{H,H}$=$^3J_{H,F}$=8.8 Hz, 2H), 7.30–7.39 (m, 3H), 7.54 (dd, $^3J_{H,H}$=8.8 Hz, $^4J_{H,F}$=5.2 Hz, 2H); *m*/*z* (%) (EI) 178 (100, M^+).

4.2.13. 2-Bromo-5-(4-methylphenyl)thiophene (***18***).[27] Pale yellow wax; δ_H (300 MHz, $CDCl_3$, 25 °C) 2.35 (s, 3H), 6.99 (br s, 2H), 7.15–7.19 (m, 2H), 7.40 (d, $^3J_{H,H}$=8.1 Hz, 2H); *m*/*z* (%) (EI) 252–254 (100, M^+), 129 (77).

4.2.14. 2-Bromo-5-(4-nitrophenyl)thiophene (***19***). Yellow solid; mp=134–135 °C (lit.[28] 124–125 °C); δ_H (300 MHz, $CDCl_3$, 25 °C) 7.13 (d, $^3J_{H,H}$=3.0 Hz, 1H), 7.24 (d, $^3J_{H,H}$=3.0 Hz, 1H), 7.66 (d, $^3J_{H,H}$=9.0 Hz, 2H), 8.26 (d, $^3J_{H,H}$=9.0 Hz, 2H); *m*/*z* (%) (EI) 283–285 (50, M^+), 158 (100).

4.2.15. Methyl 3-(3-fluorophenyl)thiophene-2-carboxylate (***22***)*, methyl 3-phenylthiophene-2-carboxylate* (***23***)*, and methyl 3-(4-fluorophenyl)thiophene-2-carboxylate* (***24***). Compounds (**22**)–(**24**) were previously described by us.[8d]

4.2.16. Methyl 3-(2-benzo[b]furan)-thiophene-2-carboxylate (***25***). Pale yellow solid; mp=71–73 °C; δ_H (300 MHz, $CDCl_3$, 25 °C) 3.95 (s, 3H), 7.25 (m, 1H), 7.33 (m, 1H), 7.50 (m, 1H), 7.53 (d, $^3J_{H,H}=5.4$ Hz, 1H), 7.65 (m, 1H), 7.73 (d, $^3J_{H,H}=5.4$ Hz, 1H), 7.94 (d, $^4J_{H,H}=0.9$ Hz, 1H); *m*/*z* (%) (EI) 258 (100, M^+), 227 (56).

4.3. General procedure for the Matsuda–Heck reactions

Olefin (0.30 mmol) was added to a solution of aryldiazonium tetrafluoroborate (0.18 mmol) and $PdCl_2(CH_3CN)_2$ (5 mol %, 2.3 mg) in H_2O (8 mL) at 0 °C. The resulting mixture was warmed to room temperature and stirred until the reaction was completed (as observed by the ceasing of the release of N_2) (Table 4 and Scheme 2). The reaction mixture was extracted with CH_2Cl_2 (3×10 mL), the organic phase was then dried and evaporated and the crude material was purified by column chromatography on silica gel (hexane/ethyl acetate, gradient) to give the desired compound.

*4.3.1. tert-Butyl (E)-4-methylcinnamate (**27**).*[29] Pale yellow oil; δ_H (400 MHz, $CDCl_3$, 25 °C) 1.53 (s, 9H), 2.36 (s, 3H), 6.31 (d, $^3J_{H,H}=16.0$ Hz, 1H), 7.16 (d, $^3J_{H,H}=8.0$ Hz, 2H), 7.39 (d, $^3J_{H,H}=8.0$ Hz, 2H), 7.55 (d, $^3J_{H,H}=16.0$ Hz, 1H); *m*/*z* (%) (EI) 218 (8, M^+), 162 (67, $[M-{}^tBu]^+$), 32 (100).

*4.3.2. tert-Butyl (E)-4-nitrocinnamate (**28**).* Pale yellow solid; mp=148–150 °C (lit.[29] 155–157 °C); δ_H (400 MHz, $CDCl_3$, 25 °C) 1.55 (s, 9H), 6.49 (d, $^3J_{H,H}=16.2$ Hz, 1H), 7.61 (d, $^3J_{H,H}=16.2$ Hz, 1H), 7.65 (d, $^3J_{H,H}=8.8$ Hz, 2H), 8.23 (d, $^3J_{H,H}=8.8$ Hz, 2H); *m*/*z* (%) (EI) 234 (5, $[M-Me]^+$), 194 (28), 176 (30), 32 (100).

*4.3.3. tert-Butyl (E)-4-methoxycinnamate (**29**).* Pale yellow oil (lit.[30] 34–35 °C); δ_H (400 MHz, $CDCl_3$, 25 °C) 1.53 (s, 9H), 3.84 (s, 3H), 6.24 (d, $^3J_{H,H}=15.9$ Hz, 1H), 6.89 (d, $^3J_{H,H}=8.7$ Hz, 2H), 7.46 (d, $^3J_{H,H}=8.7$ Hz, 2H), 7.54 (d, $^3J_{H,H}=15.9$ Hz, 1H); *m*/*z* (%) (EI) 234 (10, M^+), 178 (64, $[M-{}^tBu]^+$), 32 (100).

*4.3.4. tert-Butyl (E)-4-fluorocinnamate (**30**).* Colorless solid; mp=47.5–48.5 °C (lit.[29] 44–46 °C); δ_H (400 MHz, $CDCl_3$, 25 °C) 1.53 (s, 9H), 6.29 (d, $^3J_{H,H}=16.0$ Hz, 1H), 7.02–7.09 (m, 2H), 7.46–7.51 (m, 2H), 7.54 (d, $^3J_{H,H}=16.0$ Hz, 1H); *m*/*z* (%) (EI) 222 (2, M^+), 166 (12, $[M-{}^tBu]^+$), 32 (100).

*4.3.5. tert-Butyl (E)-2-methylcinnamate (**31**).*[31] Pale yellow oil; δ_H (300 MHz, $CDCl_3$, 25 °C) 1.54 (s, 9H), 2.42 (s, 3H), 6.29 (d, $^3J_{H,H}=15.7$ Hz, 1H), 7.15–7.28 (m, 3H), 7.53 (m, 1H), 7.89 (d, $^3J_{H,H}=15.7$ Hz, 1H); *m*/*z* (%) (EI) 218 (10, M^+), 32 (100).

*4.3.6. (E)-4-Methylstilbene (**32**).* Colorless solid; mp=117–119 °C (lit.[32] 118.5–119 °C); δ_H (300 MHz, $CDCl_3$, 25 °C) 2.35 (s, 3H), 7.03 (d, $^3J_{H,H}=16.6$ Hz, 1H), 7.09 (d, $^3J_{H,H}=16.6$ Hz, 1H), 7.16 (d, $^3J_{H,H}=8.1$ Hz, 2H), 7.23 (tt, $^3J_{H,H}=7.3$ Hz, $^4J_{H,H}=1.2$ Hz, 1H), 7.30–7.37 (m, 2H), 7.40 (d, $^3J_{H,H}=8.1$ Hz, 2H), 7.47–7.51 (m, 2H); *m*/*z* (%) (EI) 195 (11, $M+H^+$), 55 (100).

*4.3.7. (E)-4-Fluorostilbene (**33**).*[33] Colorless solid; mp=123–125 °C; δ_H (300 MHz, $CDCl_3$, 25 °C) 7.00 (d, $^3J_{H,H}=16.6$ Hz, 1H), 7.07 (d, $^3J_{H,H}=16.6$ Hz, 1H), 7.01–7.71 (m, 2H), 7.25 (m, 1H), 7.32–7.38 (m, 2H), 7.44–7.51 (m, 4H); *m*/*z* (%) (EI) 198 (100, M^+), 183 (65), 177 (45), 98 (55).

*4.3.8. Diethyl (E)-2-(4methoxycarbonylphenyl)vinylphosphonate (**34**).*[34] Colorless oil; δ_H (400 MHz, $CDCl_3$, 25 °C) 1.35 (t, $^3J_{H,H}=7.2$ Hz, 6H), 3.83 (s, 3H), 4.07–4.17 (m, 4H), 6.09 (dd, $^2J_{H,P}=18.0$ Hz, $^3J_{H,H}=17.6$ Hz, 1H), 6.90 (d, $^3J_{H,H}=8.8$ Hz, 2H), 7.45 (d, $^3J_{H,H}=8.8$ Hz, 2H), 7.46 (dd, $^3J_{H,P}=22.8$ Hz, $^3J_{H,H}=17.6$ Hz, 1H); *m*/*z* (%) (EI) 270 (8, M^+), 161 (25), 44 (100).

*4.3.9. Methyl 3[(E)-2-(tert-butoxycarbonyl)vinyl]thiophene-2-carboxylate (**35**).* Compound (**35**) was previously described by us.[8d]

Acknowledgements

Financial support from MICINN (CTQ2011-23121) of Spain and 'Generalitat de Catalunya' (2009SGR637) is acknowledged. S.B. thanks the University of Girona for a predoctoral grant.

References and notes

1. For monographies, see: (a) Negishi, E. *Handbook of Organopalladium Chemistry for Organic Synthesis*; Wiley-Interscience: New York, NY; (b) de Meijere, A.; Diederich, F. *Metal-catalyzed Cross-coupling Reactions*; Wiley-VCH: Weinheim, Germany.
2. For reviews, see: (a) Roglans, A.; Pla-Quintana, A.; Moreno-Mañas, M. *Chem. Rev.* **2006**, *106*, 4622–4643; (b) Felpin, F.-X.; Nassar-Hardy, L.; Le Callonnec, F.; Fouquet, E. *Tetrahedron* **2011**, *67*, 2815–2831; (c) Taylor, J. G.; Moro, A. V.; Correia, C. R. D. *Eur. J. Org. Chem.* **2011**, 1403–1428.
3. (a) Roe, A. *Org. React.* **1949**, *5*, 193–228; (b) Doyle, M. P.; Bryker, W. J. *J. Org. Chem.* **1979**, *44*, 1572–1574.
4. For a recent review about cross-couplings using water as solvent, see: Alonso, D. A.; Nájera, C. In *Science of Synthesis. Water in Organic Synthesis*; Kobayashi, S., Ed.; George Thieme: Stuttgart, 2012; Vol. 2011/7, pp 535–578.
5. Zarei, A.; Khazdooz, L.; Hajipour, A. R.; Rafiee, F.; Azizi, G.; Abrishami, F. *Tetrahedron Lett.* **2012**, *53*, 406–408.
6. Cacchi, S.; Caponetti, E.; Casadei, M. A.; Giulio, A. D.; Fabrizi, G.; Forte, G.; Goggiamani, A.; Moreno, S.; Paolicelli, P.; Petrucci, F.; Prastaro, A.; Saladino, M. L. *Green Chem.* **2012**, *14*, 317–320.
7. Fleckenstein, C. A.; Plenio, H. *Chem. Soc. Rev.* **2010**, *39*, 694–711.
8. (a) Masllorens, J.; Moreno-Mañas, M.; Pla-Quintana, A.; Roglans, A. *Org. Lett.* **2003**, *5*, 1559–1561; (b) Masllorens, J.; Bouquillon, S.; Roglans, A.; Hénin, F.; Muzart, J. *J. Organomet. Chem.* **2005**, *690*, 3822–3826; (c) Masllorens, J.; González, I.; Roglans, A. *Eur. J. Org. Chem.* **2007**, 158–166; (d) Raduán, M.; Padrosa, J.; Pla-Quintana, A.; Parella, T.; Roglans, A. *Adv. Synth. Catal.* **2011**, *353*, 2003–2012.
9. (a) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007**, *40*, 275–286; (b) Darses, S.; Genêt, J.-P. *Chem. Rev.* **2008**, *108*, 288–305; (c) Molander, G. A.; Canturk, B.; Kennedy, L. E. *J. Org. Chem.* **2009**, *74*, 973–980.
10. Selected references: (a) Darses, S.; Jeffery, T.; Brayer, J. L.; Demoute, J. P.; Genêt, J. P. *Bull. Soc. Chim. Fr.* **1996**, *133*, 1095–1102; (b) Darses, S.; Genêt, J. P.; Brayer, J. L.; Demoute, J. P. *Tetrahedron Lett.* **1997**, *38*, 4393–4396; (c) Darses, S.; Michaud, G.; Genêt, J. P. *Tetrahedron Lett.* **1998**, *39*, 5045–5048; (d) Darses, S.; Michaud, G.; Genêt, J. P. *Eur. J. Org. Chem.* **1999**, 1875–1883; (e) Frohn, H.-J.; Adonin, N. Y.; Bardin, V. V.; Starichenko, V. F. *J. Fluorine Chem.* **2002**, *117*, 115–120; (f) Gallo, V.; Mastrorilli, P.; Nobile, C. F.; Paolillo, R.; Taccardi, N. *Eur. J. Inorg. Chem.* **2005**, 582–588; (g) Varnedoe, L. S.; Angel, B. D.; McClellan, J. L.; Hanna, J. M., Jr. *Lett. Org. Chem.* **2010**, *7*, 1–6; (h) Schmidt, B.; Hölter, F. *Org. Biomol. Chem.* **2011**, *9*, 4914–4920; (i) Peters, M.; Trobe, M.; Tan, H.; Kleineweischede, R.; Breinbauer, R. *Chem.—Eur. J.* **2013**, *19*, 2442–2449.
11. Sengupta, S.; Bhattacharya, S. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1943–1944.
12. Gholinejad, M. *Appl. Organomet. Chem.* **2013**, *27*, 19–22.
13. Gaikwad, D. S.; Pore, D. M. *Synlett* **2012**, 2631–2634.
14. Zarei, A.; Khazdooz, L.; Pirisedigh, A.; Hajipour, A. R.; Seyedjamali, H.; Aghaei, H. *Tetrahedron Lett.* **2011**, *52*, 4554–4557.
15. Salabert, J.; Sebastián, R. M.; Vallribera, A.; Cívicos, J. F.; Nájera, C. *Tetrahedron* **2013**, *69*, 2655–2659.
16. Schwalm, C. S.; Correia, C. R. D. *Tetrahedron Lett.* **2012**, *53*, 4836–4840.
17. Correia, C. R. D.; Oliveira, C. C.; Salles, A. G., Jr.; Santos, E. A. F. *Tetrahedron Lett.* **2012**, *53*, 3325–3328.
18. Kitamura, Y.; Sako, S.; Udzu, T.; Tsutsui, A.; Maegawa, T.; Monguchi, Y.; Sajiki, H. *Chem. Commun.* **2007**, 5069–5071.
19. Jaseer, E. A.; Prasad, D. J. C.; Sekar, G. *Tetrahedron* **2010**, *66*, 2077–2082.
20. Takeda, N.; Miyata, O.; Naito, T. *Eur. J. Org. Chem.* **2007**, 1491–1509.
21. Kondolff, I.; Doucet, H.; Santelli, M. *J. Heterocycl. Chem.* **2008**, *45*, 109–118.
22. Sun, L.-L.; Deng, C.-L.; Tang, R.-Y.; Zhang, X.-G. *J. Org. Chem.* **2011**, *76*, 7546–7550.
23. Tamba, S.; Okubo, Y.; Tanaka, S.; Monguchi, D.; Mori, A. *J. Org. Chem.* **2010**, *75*, 6998–7001.
24. Wu, X.; Rieke, R. D. *J. Org. Chem.* **1995**, *60*, 6658–6659.
25. Rieke, R. D.; Kim, S.-H.; Wu, X. *J. Org. Chem.* **1997**, *62*, 6921–6927.
26. Feuerstein, M.; Doucet, H.; Santelli, M. *J. Organomet. Chem.* **2003**, *687*, 327–336.
27. Mohapatra, S.; Holmes, B. T.; Newman, C. R.; Prendergast, C. F.; Frisbie, C. D.; Ward, M. D. *Adv. Funct. Mater.* **2004**, *14*, 605–609.
28. Latassa, D.; Prim, D.; Kirsch, G. *Heterocycl. Commun.* **1998**, *4*, 81–94.
29. Gillespie, K. M.; Sanders, C. J.; O'Shaughnessy, P.; Westmoreland, I.; Thickitt, C. P.; Scott, P. *J. Org. Chem.* **2002**, *67*, 3450–3458.
30. Imashiro, R.; Seki, M. *J. Org. Chem.* **2004**, *69*, 4216–4226.
31. De Vries, A. H. M.; De Vries, J. G.; DSM N. V., Neth. PCT Int. Appl. NL 1017138, 2001.
32. Artuso, E.; Barbero, M.; Degani, I.; Dughera, S.; Fochi, R. *Tetrahedron* **2006**, *62*, 3146–3157.
33. Buckley, B. R.; Neary, S. P. *Adv. Synth. Catal.* **2009**, *351*, 71–77.
34. Brunner, H.; Le Cousturier de Courcy, N.; Genêt, J. P. *Synlett* **2000**, 201–204.

Please cite this article in press as: El Bakouri, O.; et al., Tetrahedron (2013), http://dx.doi.org/10.1016/j.tet.2013.09.010