Organic &
Biomolecular
Chemistry

Cite this: *Org. Biomol. Chem.*, 2012, **10**, 808

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PAPER

# Pd nanoparticle catalysed one-pot sequential Heck and Suzuki couplings of bromo-chloroarenes in ionic liquids and water†‡

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***Received 26th May 2011, Accepted 18th October 2011***
**DOI: 10.1039/c1ob06385e**

Pd nanoparticles generated in green reaction media (*viz.* ionic liquids and water) catalyze the one-pot sequential Heck and Suzuki coupling reactions of bromo-chloroarenes to afford unsymmetrically substituted arenes in good yields.

## Introduction

In the last few decades palladium chemistry has emerged as one of the most powerful tools for the formation of carbon-carbon and carbon-heteroatom bonds. The Pd-catalysed cross-coupling strategy has gained considerable attention as a straightforward method for C(sp$^2$)–C(sp$^2$) bond formation,[1] which opened the access to highly conjugated systems such as polyenes, aryl polyenes, and polyaryls, that are a common structural motif in many natural products[2] and have multiple potential applications as advanced electronic and photonic materials.[3]

In pursuing this objective, several authors have been attracted by the sequential multiple couplings strategy involving the well-known Heck, Suzuki, Stille, Negishi, Hiyama *etc.* reactions, because these processes are usually high-yielding, stereoselective and tolerant towards a wide array of functional groups. This approach has been successful applied for preparing products of practical importance such as N,N-diarylaminostilbenes,[4] arylated heterocycles,[5] multisubstituted olefins[6] and dienes.[7]

Aryl and heteroaryl dihalides have been the privileged substrates due to their lower cost and wider availability, and a number of applications have been reported concerning the synthesis of unsymmetric terphenyls,[8] (tris)-heteroaryls,[9] disubstituted arenes,[10] pyridines,[11] and pyrroles.[12] To achieve high regioselectivity, dihaloarene equivalents like for example bromobenzenesulfonates[13] and bromoarenediazonium tetrafluoroborate[14] have also been explored.

However, in many cases the sequential coupling approach can be very tedious and often suffers several disadvantages: two different catalysts might be required, the intermediate product needs to be isolated, or expensive and not easily available substrates have to be used.[15] Thus, a very attractive and efficient variant would be the one-pot double coupling of commercially available and inexpensive dihaloarenes, with two consecutive couplings performed in the same reaction flask and in the presence of a single metal catalyst. So far, only a few successful examples have been reported.[6,7b,9b,10,11]

To ensure that such a process occurs successfully, the catalyst must be highly efficient and chemoselective toward the first coupling and still maintain its catalytic activity in the subsequent coupling. Of course, the selective displacement of the halogens on a dihaloarene becomes crucial to achieve synthetic utility. In principle, in cases where the halogens are different, the observed selectivity is related to the relative bond dissociation energies of the respective carbon-halogen bonds, the reactivity following the trend C–I > C–Br > C–Cl. The situation is more complicated in the case of cross-coupling reactions of substrates bearing multiple identical halogens.

There are only a handful of reports of such reactions on polyhaloaromatics,[8–12] and in most of them the more reactive iodo/bromoarenes are usually preferred as substrates, while the cheaper and challenging bromo-chloroarenes are unexploited, with few exceptions,[8] due to the hard activation of the C–Cl bond, and this represents a severe limitation from the synthetic standpoint.

Recent reports from these laboratories[16] have demonstrated that Pd colloids can promote the C–Cl bond activation of Heck-, Suzuki-, Stille- and Ullmann-type couplings carried out in tetraalkylammonium ionic liquids (ILs) under aerobic, ligand-free, and relatively mild conditions. The high surface-to-volume ratio and thus the very active superficial atoms of metal nanoparticles, together with the coordination ability of IL anions, enabled our catalyst system to promote the Heck coupling between deactivated electron-rich aryl chlorides and a wide array of complex substituted olefins, allowing combinations of substrates (*e.g.* chloroanisole and cinnamates) that are commonly unreactive with most of the traditional catalysts.[16c]

As a result of our success with simple chloroarenes, we have been interested in examining the application of similar conditions to the aryl dihalides to get unsymmetrically substituted arenes, with

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† Dedicated to Professor Vincenzo Calò on the occasion of his 73rd birthday.

‡ Electronic supplementary information (ESI) available: spectral data of unknown reaction products. See DOI: 10.1039/c1ob06385e

particular attention to those containing unsymmetric 1,2-, 1,3- and 1,4-diethenylphenyl and terphenyl units, due to their practical importance for pharmaceutical and material industries.[4,8,17,18] Here we wish to report our results in the sequential one-pot, two-step process involving Pd colloids-mediated Heck[19] and Suzuki[20] couplings of bromo-chloroaryls in ionic liquids.

## Results and discussion

Investigations were started by adapting our previous protocol,[16c] useful to couple the simple chloroarenes, to the one-pot double Heck olefination of 1,2-, 1,3- and 1,4-bromochlorobenzene isomers with an array of olefins. Reaction conditions were calibrated for processing 0.5 mmol of both the dihalide and alkene dissolved in a molten mixture of tetrabutylammonium bromide (TBAB) as the solvent and tetrabutylammonium acetate (TBAA) as base, in the presence of $Pd(OAc)_2$ as the catalyst source (Table 1).

The success of this methodology was obviously dependent on the chemoselectivity of the first olefination. After many experiments, we found that the selective displacement of the two halogens on the benzene ring could be achieved by adjusting the reaction temperature of the two consecutive steps. In the former, by virtue of the efficiency of Pd colloids in the activation of the C–Br bond in these ILs media,[21] the substitution of the bromide occurred at 100 °C with both butyl acrylate and styrene as model olefins, and in all cases quantitative conversions to the corresponding chlorophenyl intermediates were obtained within 0.5–1 h.

Fortunately, the catalyst system exhibited an excellent regioselectivity, allowing the coupling at the bromine site of the dihalide to be completed with the formation of only trace amounts of the symmetric double coupled product. Following the one-pot modality, the second step was initiated immediately after the end of the previous one by the direct addition of the olefin 2 to the reaction mixture without either isolation of the chlorophenyl intermediate or addition of a second catalyst or any other additive, but simply by raising the reaction temperature to 120 °C.

As expected, the second olefination was more difficult as it involves cleavage of the stronger C–Cl bond. As a consequence, reaction times were much longer and yields were dependent on the structure of both the second olefin and the starting bromochloroarene. For sterical reasons, reactions occurring on the less hindered 1,4-bromochlorobenzene were generally faster, giving good to excellent overall yields (Table 1, runs 1–3, 6–8). However, a moderate yield of 52% was observed when a bulky olefin such as ethyl cinnamate was the reaction partner in the second step (Table 1, run 11).

In some cases, unrepeatable results and poor yields during the progress of the second step were obtained, because the formation of insoluble disubstituted arene product prevented an efficient mixing of the reaction mixture.

This problem was surmounted by increasing the reaction temperature of the second step to 140 °C (Table 1, runs 10 and 12). Processes involving 1,2- and 1,3-disubstituted haloarenes were high-yielding but generally required longer reaction times (Table 1, runs 4–5 and 13).

Based on these encouraging results, we decided to explore the one-pot Heck/Suzuki sequential couplings. Optimisation of the reaction conditions was carried out on 4-bromochlorobenzene (Table 2), choosing the Heck coupling in the first step and adopting, in the first instance, the same reaction conditions as in Table 1. After completion of the Heck reaction under the standard conditions (TBAA as the base, at 100 °C), phenyl boronic acid was added to the mixture and heated to 120 °C. At once, TBAA proved to be a suitable base for the Heck reaction but a poor base for the Suzuki coupling (Table 2, runs 1–2).

Searching for the best couple of bases we also investigated the influence of water on the second step, having known[16a,20a] the beneficial effect that this solvent exerts on the Suzuki reaction.[22] Unsatisfactory results were observed by combining TBAA with $K_2CO_3$, $K_3PO_4$ and tetrabutylammonium hydroxide (TBAOH), with or without the presence of water (Table 2, runs 3–5).

Likewise, disappointing results were obtained with $K_2CO_3$ as the sole base for the overall process (Table 2, runs 7–8). High yields could be obtained using potassium carbonate in the first step and cesium carbonate in the second, but in these cases the presence of water proved to be crucial (Table 2, runs 9–11). However, the latter couplings were still unsatisfactory in terms of the reaction times, whereas the couple TBAA/$Cs_2CO_3$ came out definitely better as it successfully afforded a complete conversion in the final product in only 2.5 h (Table 2, run 6).

With such optimized reaction conditions in hand, we carried out the sequential cross-coupling reactions using a combination of typical olefins and phenyl boronic acid with 2-, 3-, or 4-bromochlorobenzene, to get ethenylsubstituted biphenyl derivatives as reported in Table 3.

Next, in order to highlight the synthetic value of these protocols, we attempted to extend their application to a more challenging and intriguing process like the one-pot sequential triple coupling involving a trihaloarene as substrate.

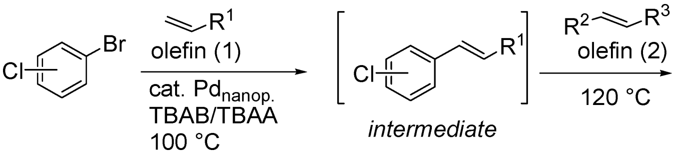
To this end, we coupled 4-bromo-2-chloro-1-iodobenzene with three different nucleophilic partners, in order to get an unsymmetrically trisubstituted arene. In Scheme 1 two representative examples of consecutive triple Heck and Heck/Heck/Suzuki couplings are given, respectively.

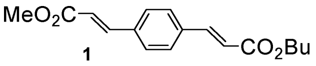
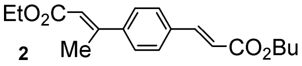
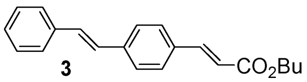
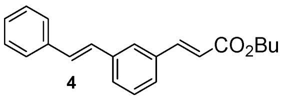
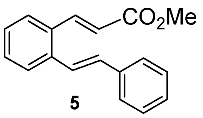
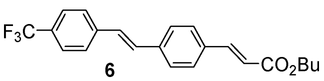
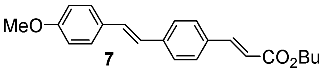
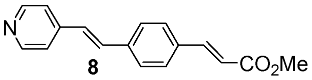
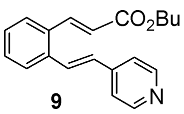
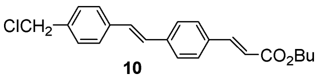
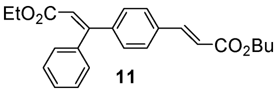
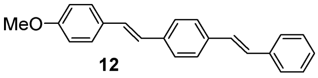
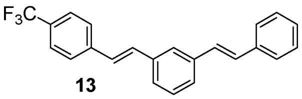
Processes were accomplished under the same conditions as for the double coupling of bromochloroarenes, but carrying out the first step at the temperature of 90 °C to allow the selective activation of the weakest carbon-iodine bond.

Finally, for completing the possible combinations of the coupling processes, we focussed our attempts on the development of a synthetic procedure that enables sequential chemoselective Suzuki reactions of bromo-chlorobenzenes with two different arylboronic acids to get unsymmetrical terphenyls. All the attempts made to carry the double Suzuki coupling using the protocol of the second step in Table 3 (TBAB/$Cs_2CO_3$/$H_2O$) gave rise to disappointing results. Most probably, the prolonged reaction times, due to the additional coupling at the bromine site, along with the high temperature (120 °C) and the aqueous medium, lowered the Pd colloids stability, so that the completion of the first coupling reaction stopped during the second step with precipitation of Pd black.

Based on our recent findings,[16a,23] we exploited tetrabutylammonium hydroxide (TBAOH), a stronger base with respect to $Cs_2CO_3$, that can act also as surfactant and phase transfer agent (PTC), creating a favourable environment for the nanocatalysts and avoiding colloids agglomeration. Indeed, into the emulsioned mixture generated by this surfactant, reactions presumably occur into the special layer surrounding the nanoparticles surface, which

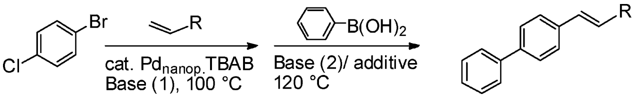
**Table 1** Double Heck one-pot sequential coupling of bromochlorobenzene isomers in ILs[a]



| | Step 1 | | Step 2 | | | | |
|---|---|---|---|---|---|---|---|
| Run | R$^1$ | *t* (h)[b] | R$^2$ | R$^3$ | *t* (h)[c] | Product | Yield (%)[d] |
| 1 | $CO_2Bu$ | 0.5 | $CO_2Me$ | H | 4 |  | 67 |
| 2 | $CO_2Bu$ | 0.5 | $CO_2Et$ | Me | 4 |  | 85 |
| 3 | $CO_2Bu$ | 0.5 | $C_6H_5$ | H | 2 |  | 87 |
| 4 | $CO_2Bu$ | 0.5 | $C_6H_5$ | H | 14 |  | 78 |
| 5 | $CO_2Me$ | 0.5 | $C_6H_5$ | H | 2 |  | 80 |
| 6 | $CO_2Bu$ | 0.5 | 4-$CF_3C_6H_4$ | H | 2 |  | 82 |
| 7 | $CO_2Bu$ | 0.5 | 4-$MeOC_6H_4$ | H | 2 |  | 79 |
| 8 | $CO_2Me$ | 0.5 | 4-Py- | H | 4 |  | 76 |
| 9 | $CO_2Bu$ | 0.5 | 4-Py- | H | 4 |  | 80 |
| 10[e] | $CO_2Bu$ | 0.5 | 4-$ClCH_2C_6H_4$ | H | 5 |  | 65 |
| 11 | $CO_2Bu$ | 0.5 | $CO_2Et$ | $C_6H_5$ | 2 |  | 52 |
| 12[e] | $C_6H_5$ | 1 | 4-$MeOC_6H_4$ | H | 4 |  | 60 |
| 13 | $C_6H_5$ | 1 | 4-$CF_3C_6H_4$ | H | 14 |  | 73 |

[a] General reaction conditions: TBAB (1 g), TBAA (1.5 mmol), bromochlorobenzene (0.5 mmol), olefin 1 (0.5 mmol), olefin 2 (0.5 mmol); *T* (step 1) 100 °C, *T* (step 2) 120 °C; stirred under air. [b] Reaction times needed for the complete conversion of the starting reagents into the intermediate (determined by GC-MS) [c] Time of the maximum conversion of the intermediate into the final product. [d] Overall isolated yields. [e] Temperature of the second step 140 °C.

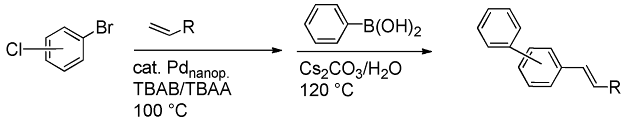
**Table 2** Optimisation of the reaction conditions in the one-pot Heck/Suzuki sequential coupling on 4-bromochlorobenzene[a]

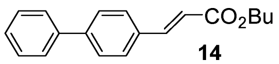
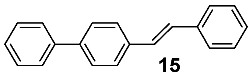
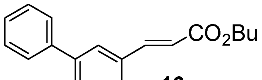
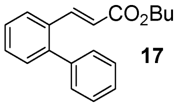
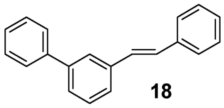


| | Step 1 | | | | Step 2 | | | |
|---|---|---|---|---|---|---|---|---|
| Run | R | Base (1) | *t* (h) | Conv. (%) | Base (2) | Additive[d] | *t* (h) | Yield (%)[e] |
| 1[b] | $CO_2Bu$ | TBAA | 0.5 | 99 | TBAA | — | 14 | 0 |
| 2[b] | $CO_2Bu$ | TBAA | 0.5 | 99 | TBAA | $H_2O$ | 14 | 0 |
| 3[c] | $CO_2Bu$ | TBAA | 0.5 | 99 | $K_2CO_3$ | $H_2O$ | 14 | 0 |
| 4[c] | $CO_2Bu$ | TBAA | 0.5 | 99 | $K_3PO_4$ | $H_2O$ | 14 | 50 |
| 5[c] | $CO_2Bu$ | TBAA | 0.5 | 99 | TBAOH | $H_2O$ | 14 | 10 |
| 6[c] | $CO_2Bu$ | TBAA | 0.5 | 99 | $Cs_2CO_3$ | $H_2O$ | 2 | 95 |
| 7[b] | $CO_2Bu$ | $K_2CO_3$ | 1 | 90 | $K_2CO_3$ | — | 14 | 0 |
| 8[b] | $CO_2Bu$ | $K_2CO_3$ | 1 | 90 | $K_2CO_3$ | $H_2O$ | 14 | 20 |
| 9[c] | $CO_2Bu$ | $K_2CO_3$ | 1 | 90 | $Cs_2CO_3$ | — | 14 | 0 |
| 10[c] | $CO_2Bu$ | $K_2CO_3$ | 1 | 90 | $Cs_2CO_3$ | $H_2O$ | 14 | 77 |
| 11[c] | Ph | $K_2CO_3$ | 1 | 80 | $Cs_2CO_3$ | $H_2O$ | 14 | 90 |

[a] General reaction conditions: TBAB (1 g), 4-bromoclorobenzene (0.5 mmol), olefin (0.5 mmol), boronic acid (0.75 mmol); *T* (step 1) 100 °C, *T* (step 2) 120 °C; under stirring and under air. [b] Base (1) (1.5 mmol) added only in step 1. [c] Base (1) (0.75 mmol) and base (2) (1 mmol). [d] Added before starting the second step. [e] GLC overall yields.

**Table 3** One-pot Heck/Suzuki sequential couplings in ILs[a]



| Run | Reagents | *t* (h) | Product | Yield (%)[b] |
|---|---|---|---|---|
| 1 | R = $CO_2Bu$ | 2 |  **14** | 92 |
| 2 | R = $C_6H_5$ | 4 |  **15** | 90 |
| 3 | R = $CO_2Bu$ | 6 |  **16** | 68 |
| 4 | R = $CO_2Bu$ | 14 |  **17** | 67 |
| 5 | R = $C_6H_5$ | 14 |  **18** | 60 |

[a] General reaction conditions: TBAB (1 g), TBAA (0.75 mmol), bromochlorobenzene (0.5 mmol), olefin (0.5 mmol), $Cs_2CO_3$ (1 mmol), boronic acid (0.75 mmol); *T* (I step) 100 °C, *T* (II step) 120 °C; under stirring and under air. [b] Overall isolated yields.

contains the organic species, $Bu_4N^+$ cations and the anionic counterpart. In addition, TBAOH would facilitate solvation of the low polar aryl dihalide in neat water avoiding the use of an organic co-solvent.

Under these conditions the one-pot double Suzuki coupling of bromochloroarenes with a number of arylboronic acids could be smoothly accomplished by performing the first step (the C–Br activation) at 60 °C; whereas the second step, occurring on the chlorobiaryl intermediate, required at least 100 °C to be completed (Table 4). It was gratifying to find that these reactions proceeded equally well for 1,4- (Table 4, runs 1–3), 1,3- (Table 4, runs 4–6) and 1,2- (Table 4, run 7) bromochlorobenzene isomers, affording o-, m- and p-terphenyl in good to excellent yields.

This method can compete with the one recently reported by Hii,[8a] in which the first coupling was achieved at room temperature using a ligandless palladium catalyst, but the second step required isolation of the chlorobiaryl intermediate, a minimum temperature of 60 °C and the presence of a SPhos ligand.

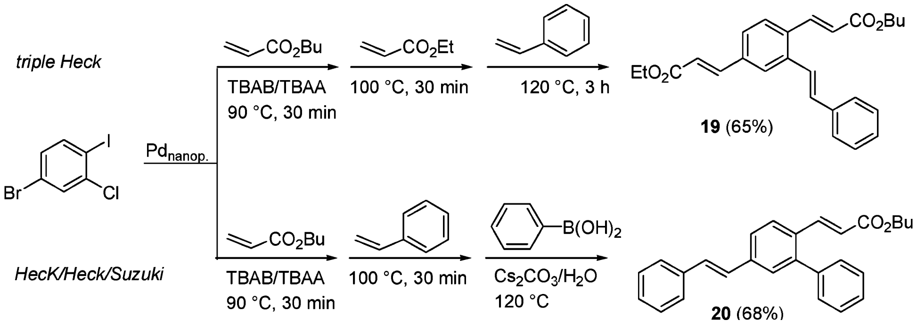
## Conclusions

In summary, we have disclosed a series of reactions which constitute a powerful methodology for the synthesis of extended π-systems having a multisubstituted unsymmetrical arene as the basic skeleton.

This protocol, based on an appropriate combination of Heck and Suzuki cross coupling, complements existing strategies[10] broadening their scope with more challenging substrates (bromochloroarenes), and can be particularly intriguing due to the practical importance of extended conjugated systems in material science, particularly in the optoelectronic field.[6a,17]

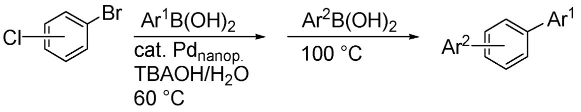
The practical benefits include readily-available and inexpensive starting materials, substrate versatility, experimentally straightforward procedures and good product yields. In addition, the method is highly sustainable because it employs green solvents (ionic liquids or water), is ligand-free (no toxic or expensive phospane ligands) and has relatively mild conditions (*T* = 60–120 °C).

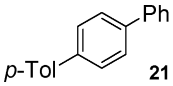
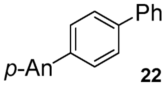
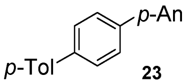
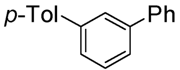
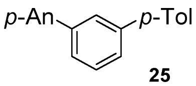
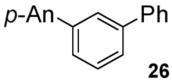
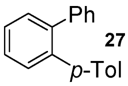
To the best of our knowledge, for the first time in the literature the one-pot sequential coupling strategy involving the Heck reaction is applied to bromochloroarenes and simultaneously to a wide range of alkenes, including some deactivated olefins, such as cinnamic esters (see Table 1, run 11).



**Scheme 1** Two examples of triple one-pot sequential couplings.

**Table 4** Synthesis of unsymmetrical terphenyls by one-pot double Suzuki coupling of bromochloroarenes[a]



| Run | Boronic acids | $t$ (h)[b] | Product | Yield (%)[c] |
|---|---|---|---|---|
| 1 | Ar$^1$ = $C_6H_5$ Ar$^2$ = 4-$MeC_6H_4$ | 1.5 |  **21** | 85 |
| 2 | Ar$^1$ = $C_6H_5$ Ar$^2$ = 4-$MeOC_6H_4$ | 2.5 |  **22** | 86 |
| 3 | Ar$^1$ = 4-$MeOC_6H_4$ Ar$^2$ = 4-$MeC_6H_4$ | 7 |  **23** | 70 |
| 4 | Ar$^1$ = $C_6H_5$ Ar$^2$ = 4-$MeC_6H_4$ | 2 |  **24** | 90 |
| 5 | Ar$^1$ = 4-$MeC_6H_4$ Ar$^2$ = 4-$MeOC_6H_4$ | 4 |  **25** | 80 |
| 6 | Ar$^1$ = $C_6H_5$ Ar$^2$ = 4-$MeOC_6H_4$ | 3 |  **26** | 60 |
| 7 | Ar$^1$ = $C_6H_5$ Ar$^2$ = 4-$MeC_6H_4$ | 8 |  **27** | 62 |

[a] Reaction conditions. 1st step: TBAOH 1.5 M (1 ml), bromochloroarene (0.5 mmol), Pd acetate (1 mol%), boronic acid (R$^1$, 0.6 mmol), $T$ = 60 °C. 2nd step: boronic acid (R$^2$, 0.6 mmol), $T$ = 100 °C. [b] Total reaction times. [c] Isolated yields determined over the two steps.

## Experimental section

### Representative procedure for sequential one-pot double Heck couplings

In a 10 ml vial, equipped with a screw cap and a magnetic bar, tetrabutylammonium bromide (TBAB, 1 g), tetrabutylammonium acetate (TBAA, 0.45 g, 1.5 mmol), $Pd(OAc)_2$, (1.7 mg, 0.0075 mmol, 1.5 mol%), olefin 1 (0.5 mmol), and bromochlorobenzene (0.5 mmol) were placed. The solution was heated to 100 °C under air until the disappearance of the first olefin monitored by GC-MS. Olefin 2 (0.5 mmol) was then added and the reaction mixture was heated to 120 °C for the proper reaction time (see Tables 1). Monitoring of the reaction mixture by GLC and GC-MS provided reagents conversion. After completion of the reaction, the mixture was added to 20 mL of water and extracted with dichloromethane (3 × 20 mL). The combined organic layers were washed with water (2 × 20 mL), dried with anhydrous $MgSO_4$ and concentrated in vacuo. The residue was purified by chromatography on silica gel to give the desired product. Unknown compounds were identified by NMR analysis (see ESI‡).

### Representative procedure for sequential one-pot Heck/Suzuki couplings

In a 10 ml vial, equipped with a screw cap and a magnetic bar, TBAB (1 g), 4-bromoclorobenzene (0.5 mmol), olefin (0.5 mmol), TBAA (0.75 mmol), and $Pd(OAc)_2$, (1.7 mg, 0.0075 mmol, 1.5 mol%) were placed. The mixture was heated to 100 °C and stirred under air. The reaction was monitored by GC-MS until the completion of the Heck coupling. Then, boronic acid (0.75 mmol) and $Cs_2CO_3$ (1 mmol) and 150 μl of $H_2O$ were added and the temperature was raised to 120 °C. Monitoring of the reaction mixture by GLC and GC-MS provided reagents conversion (see Table 3). After completion of the reaction, both yields and products identification were carried out after extraction of the mixture followed by column chromatography as reported in the previous procedure.

### Representative procedure for sequential one-pot double Suzuki couplings

In a 10 ml vial, equipped with a screw cap and a magnetic bar, a solution of TBAOH 1.5 M (1 ml, 1.5 mmol), bromochloroarene (0.5 mmol), Pd acetate (1 mol%), boronic acid ($R^1$, 0.6 mmol) were placed. The reaction mixture was heated to 60 °C and stirred under air until the completion of the first step. Then, a boronic acid ($R^2$, 0.6 mmol) was added and the reaction temperature was raised to 100 °C for the proper time (see Table 4). Monitoring of the reaction mixture by GLC and GC-MS provided reagents conversion. After completion of the reaction, both yields and products identification were carried out after extraction of the mixture followed by column chromatography as reported in the previous procedure.

## Acknowledgements

Partial financial support of this work by the Ministry of University and Scientific Research of Italy (MIUR) and by University of Bari is gratefully acknowledged.

## Notes and references

1 For reviews of metal-catalysed cross-coupling reactions, see:(*a*) Cross-Coupling Reactions: A Practical Guide: *Top. Curr. Chem.* 2002, 219; (*b*) *Handbook of Organopalladium Chemistry for Organic Synthesis*, (Ed.: E.-i. Negishi), Wiley Interscience, New York, 2002; (*c*) A. F. Littke and G. C. Fu, *Angew. Chem., Int. Ed.*, 2002, **41**, 4176; (*d*) J. Hassan, M. Sevignon, C. Gozzi, E. Schulz and M. Lemaire, *Chem. Rev.*, 2002, **102**, 1359.

2 C. Thirsk and A. J. Whiting, *J. Chem. Soc., Perkin Trans. 1*, 2002, 999–1023.

3 For properties and applications of conjugated polymers in optoelectronics see: (*a*) the special issue of *Chem. Phys.*, 1999, p. 245; (*b*) R. H. Friend, R. W. Gymer, A. B. Holmes, J. H. Burroughes, R. N. Marks, C. Taliani, D. D. C. Bradley, D. A. Dos Santos, J. L. Brédas, M. Lögdlund and W. R. Salaneck, *Nature*, 1999, **397**, 121; (*c*) A. Kraft, A. C. Grimsdale and A. B. Holmes, *Angew. Chem., Int. Ed.*, 1998, **37**, 402; (*d*) R. E. Martin and F. Diederich, *Angew. Chem., Int. Ed.*, 1999, **38**, 1350; (*e*) J. L. Segura and N. J. Martìn, *J. Mater. Chem.*, 2000, **10**, 2403; (*f*) H. Meier, *Angew. Chem., Int. Ed. Engl.*, 1992, **21**, 1399.

4 M. V. Nandakumar and J. G. Verkade, *Angew. Chem., Int. Ed.*, 2005, **44**, 3115.

5 (*a*) A. F. Khan, M. Schnürch, M. D. Mihovilovic and P. Stanetty, *Lett. Org. Chem.*, 2009, **6**, 171–174; (*b*) T. Y. H. Wu, P. Schultz and G. S. Ding, *Org. Lett.*, 2003, **5**, 3587–3590.

6 (*a*) K. Itami, K. Tonogaki, Y. Ohashi and J. Yoshida, *Org. Lett.*, 2004, **6**, 4093–4096; (*b*) K. Itami, T. Nokami, Y. Ishimura, K. Mitsudo, T. Kamei and J.-I Yoshida, *J. Am. Chem. Soc.*, 2001, **123**, 11577–11585.

7 (*a*) G. A. Molander and Y. J. Yokoyama, *J. Org. Chem.*, 2006, **71**, 2493–2498; (*b*) S. E. Denmark and S. A. Tymonko, *J. Am. Chem. Soc.*, 2005, **127**, 8004–8005.

8 (*a*) J. M. A. Miguez, L. A. Adrio, A. Sousa-Pedrares, J. M. Vila and K. K. Hii, *J. Org. Chem.*, 2007, **72**, 7771; (*b*) A. K. Sahoo, T. Oda, Y. Nakao and T. Hiyama, *Adv. Synth. Catal.*, 2004, **346**, 1715–1727.

9 (*a*) J. S. Siddle, A. S. Batsanov and M. R. Bryce, *Eur. J. Org. Chem.*, 2008, 2746–2750; (*b*) T. Jensen, H. Pedersen, B. Bang-Andersen, R. Madsen and M. Jørgensen, *Angew. Chem., Int. Ed.*, 2008, **47**, 888–890.

10 X. Zhang, A. Liu and W. Chen, *Org. Lett.*, 2008, **10**, 3849–3852.

11 S. T. Handy, T. Wilson and A. J. Muth, *J. Org. Chem.*, 2007, **72**, 8496–8500.

12 S. T. Handy and J. J. Sabatini, *Org. Lett.*, 2006, **8**, 1537–1539.

13 C.-H. Cho, I.-S. Kim and K. Park, *Tetrahedron*, 2004, **60**, 4589.

14 R. H. Taylor and F.-X. Felpin, *Org. Lett.*, 2007, **9**, 2911.

15 (*a*) Y. A. Getmanenko and R. J. Twieg, *J. Org. Chem.*, 2008, **73**, 830; (*b*) R. S. Coleman and M. C. Walczak, *Org. Lett.*, 2005, **7**, 2289–2291; (*c*) J. Chae, J. Yun and S. L. Buchwald, *Org. Lett.*, 2004, **6**, 4809–4812; (*d*) R. Ferraccioli, D. Carenzi, O. Rombolà and M. Catellani, *Org. Lett.*, 2004, **6**, 4759–4762; (*e*) M. J. Mio, L. C. Kopel, J. B. Braun, T. L. Gadzikwa, K. L. Hull, R. G. Brisbois, C. J. Markworth and P. A. Grieco, *Org. Lett.*, 2002, **4**, 3199–3202; (*f*) T. Kawasaki and Y. Yamamoto, *J. Org. Chem.*, 2002, **67**, 5138–5141.

16 (*a*) A. Monopoli, V. Calò, F. Ciminale, P. Cotugno, C. Angelici, N. Cioffi and A. Nacci, *J. Org. Chem.*, 2010, **75**, 3908–3911; (*b*) V. Calò, A. Nacci, A. Monopoli and P. Cotugno, *Chem.–Eur. J.*, 2009, **15**, 1272–1279; (*c*) V. Calò, A. Nacci, A. Monopoli and P. Cotugno, *Angew. Chem., Int. Ed.*, 2009, **48**, 6101–6103; (*d*) V. Calò, A. Nacci, A. Monopoli and F. Montingelli, *J. Org. Chem.*, 2005, **70**, 6040–6044. For a review on the previous papers of the group on this topic see also; V. Calò, A. Nacci and A. Monopoli, *Eur. J. Org. Chem.*, 2006, 3791–3802.

17 For selected examples of photochemical properties and applications of diethenylphenyl aromatic derivatives in material science see: (*a*) H. Meng, F. Sun, M. B. Goldfinger, F. Gao, D. J. Londono, D. J. Marshal, G. S. Blackman, K. D. Dobbs and D. E. Keys, *J. Am. Chem. Soc.*, 2006, **128**, 9304–9305; (*b*) H. Meier, *Angew. Chem., Int. Ed. Engl.*, 1992, **31**, 1399–1420, and references cited therein.

18 For reviews and practical applications of terphenyls in material science and medicinal chemistry see: (*a*) J.-K. Liu, *Chem. Rev.*, 2006, **106**, 2209–2223; (*b*) P. Karastatiris, J. A. Mikroyannidis, I. K. Spiliopoulos, M. Fakis and P. Persephonis, *J. Polym. Sci., Part A: Polym. Chem.*, 2004, **42**, 2214–2224; (*c*) B. Chen, U. Baumeister, G. Pelzl, M. K. Das, X. Zeng, G. Ungar and C. Tschierske, *J. Am. Chem. Soc.*, 2005, **127**, 16578–16591; (*d*) A. A. Kiryanov, P. Sampson and A. J. Seed, *J. Mater. Chem.*, 2001, **11**, 3068–3077; (*e*) M. Roberti, D. Pizzirani, M. Recanatini, D. Simoni, S. Grimaudo, A. Di Cristina, V. Abbadessa, N. Gebbia and M. Tolomeo, *J. Med. Chem.*, 2006, **49**, 3012–3018; (*f*) D. Simoni, G. Giannini, M. Roberti, R. Rondanin, R. Baruchello, M. Rossi, G. Grisolia, F. P. Invidiata, S. Aiello, S. Marino, S. Cavallini, A. Siniscalchi, N. Gebbia, L. Crosta, S. Grimaudo, V. Abbadessa, A. Di Cristina and M. Tolomeo, *J. Med. Chem.*, 2005, **48**, 4293–4299; (*g*) J. Ohkanda, J. W. Lockman, M. A. Kothare, Y. Qian, M. A. Blaskovich, S. M. Sebti and A. D. Hamilton, *J. Med. Chem.*, 2002, **45**, 177–188.

19 For general reviews on the Heck reaction see: (*a*) N. T. S. Phan, M. Van Der Sluys and C. W. Jones, *Adv. Synth. Catal.*, 2006, **348**, 609–679; (*b*) F. Alonso, I. P. Beletskaya and M. Yus, *Tetrahedron*, 2005, **61**, 11771–11835; (*c*) I. P. Beletskaya and A. V. Cheprakov, *Chem. Rev.*, 2000, **100**, 3009.

20 Reviews on the Suzuki coupling reaction (*a*) J. Hassan, M. Sévignon, C. Gozzi, E. Schulz and M. Lemaire, *Chem. Rev.*, 2002, **102**, 1359; (*b*) N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457.

21 V. Calò, A. Nacci, A. Monopoli, S. Laera and N. Cioffi, *J. Org. Chem.*, 2003, **68**, 2929–2933.

22 The beneficial effect of water is probably twofold: from one hand it is due to the formation of the hydroxyl anions which are responsible for the activation of the boronic acid, from the other the favorable action of water is related to the possibility of dissolving and removing ionic by-products (*e.g.* halide ions and boric acid salts) from the catalytic active sites of Pd catalyst.

23 A. Monopoli, A. Nacci, V. Calò, F. Ciminale, P. Cotugno, A. Mangone, L. C. Giannossa, P. Azzone and N. Cioffi, *Molecules*, 2010, **15**, 4511–4525.