Chinese Chemical Letters 27 (2016) 631–634

Contents lists available at ScienceDirect

Chinese Chemical Letters

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

Original article

Oxygen-promoted Pd/C-catalyzed Suzuki–Miyaura reaction of potassium aryltrifluoroborates

Chun Liu *, Chao Liu, Xin-Min Li, Zhan-Ming Gao, Zi-Lin Jin

State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian 116024, China

ARTICLE INFO

Article history:
Received 19 October 2015
Received in revised form 14 December 2015
Accepted 23 December 2015
Available online 6 January 2016

Keywords:
Pd/C
Oxygen-promoting effect
Suzuki–Miyaura reaction
Potassium aryltrifluoroborates
Carbazole derivatives

ABSTRACT

A simple and highly efficient protocol has been developed for the Pd/C-catalyzed ligand-free Suzuki–Miyaura reaction of potassium aryltrifluoroborates. In this catalytic system, the results demonstrate that oxygen plays a positive role in the cross-coupling reaction. In addition, this catalytic system could be successfully applied to synthesize biaryl compounds containing a carbazole moiety and the catalyst was recycled seven times without significant loss of catalytic activity.

1. Introduction

In recent years, potassium organotrifluoroborates have been used in the Suzuki–Miyaura reaction, which is one of the most versatile and powerful methods for the carbon–carbon bond formation in the synthesis of biaryl compounds and has been widely developed for its highly efficient and green characteristics [1–4]. Nucleophilic partners of this cross-coupling reaction, the arylboronic acids are not monomeric species, but rather exist as dimeric and cyclic trimeric anhydrides [5]. Moreover, protodeboronation and homocoupling have been prone to competing with the cross-coupling process, particularly for electron-poor arylboronic acids [6,7]. Fortunately, potassium organotrifluoroborate salts offer solutions for these problems. Unlike arylboronic acids, the potassium organotrifluoroborates are monomeric solids, easily prepared from organoboronic acids or esters by the addition of inexpensive potassium hydrogen fluoride (KHF_2) [8]. With very few exceptions, potassium organotrifluoroborates show high stability toward air and water and can be stored indefinitely at room temperature without any precaution [9]. It is an ideal organoboron reagent for organic synthesis.

Significant efforts have been focused on the development of efficient systems for the Suzuki–Miyaura reaction of potassium organotrifluoroborates [10–13], but most of the reported protocols are homogeneous catalytic systems, in which the palladium catalysts are usually not recoverable, and the residual Pd metal in the product could induce serious problems. Therefore, a number of heterogeneous catalysts, which are easily separated and recycled, have come to our attention. Among them, Pd/C is one of the most common heterogeneous catalysts [14,15]. In 2009, LeBlond *et al.* reported the Pd/C-catalyzed cross-coupling of aryl halides with potassium *p*-tolyltrifluoroborate, although longer reaction time and a high loading of catalyst were required [16]. Joucla *et al.* reported a Pd/C-catalyzed approach for the vinylation of aryl halides using potassium vinyltrifluoroborates in *N*-methyl-2-pyrrolidone [17,18].

In the past several years, a series of highly efficient and ligand-free protocols for the Suzuki–Miyaura reaction of aryl boronic acids with aryl halides have been developed by our group [19–22]. In this paper, we describe a simple and efficient approach for the Pd/C-catalyzed ligand-free Suzuki–Miyaura reaction of potassium aryltrifluoroborates with aryl halides in aqueous media. This catalytic system can be successfully applied to synthesize biaryl compounds containing a carbazole moiety, which are important building blocks for the construction of advanced photoelectric materials [23,24]. Importantly, an oxygen-promoting effect was observed in the Pd/C-catalyzed Suzuki–Miyaura reaction of potassium aryltrifluoroborates.

---

* Corresponding author.
E-mail address: cliu@dlut.edu.cn (C. Liu).

http://dx.doi.org/10.1016/j.cclet.2015.12.022

2. Experimental

2.1. General procedure for the Suzuki–Miyaura reaction of potassium aryltrifluoroborates

A mixture of aryl halide (0.5 mmol), potassium aryltrifluoroborate (0.6 mmol), K_2CO_3 (1.0 mmol), Pd/C (0.5 mol%), ethanol (3 mL), and distilled water (1 mL) was stirred at 80 °C in air for the indicated time. The reaction mixture was added to brine (15 mL) and extracted with ethyl acetate (4 × 15 mL). The organic solvent was removed under vacuum, and the product was isolated by short-column chromatography.

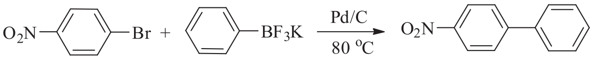
2.2. Recyclability tests of the Pd/C catalyst

For the first run, a mixture of 4-nitrobromobenzene (0.5 mmol), potassium 9-phenylcarbazolyltrifluoroborate (0.6 mmol), K_2CO_3 (1.0 mmol), Pd/C (1.0 mol%), ethanol (3 mL), and distilled water (1 mL) was stirred at 80 °C in air. The reaction was monitored by TLC. At the end of the reaction, the Pd/C catalyst was recovered by simple filtration, washed with chloroform and water, and dried under vacuum for the next run.

3. Results and discussion

Our group has a long standing interest in the effects of different atmospheres on the Suzuki–Miyaura reaction. Since 2007 we have found that oxygen plays a positive role in the palladium-catalyzed ligand-free Suzuki–Miyaura reaction of aryl boronic acids with aryl halides in different solvents, including polyethylene glycol, organic/water mixed solvents and pure water [4,25,26]. These results inspired us to speculate whether oxygen could also promote the Suzuki–Miyaura reaction of potassium phenyltrifluoroborates with aryl halides. Therefore, the Pd/C-catalyzed Suzuki–Miyaura reaction of 4-nitrobromobenzene with potassium phenyltrifluoroborate was performed in the different atmospheres (Table 1). The cross-coupling gave the product in 51% yield in a nitrogen atmosphere (Table 1, entry 2). However, the cross-coupling performed in air provided a 91% yield within the same reaction time, which is much faster than that in nitrogen (Table 1, entry 1). Excitingly, the same cross-coupling reaction carried out in an oxygen atmosphere was completed in 15 min (Table 1, entry 3). It is clear that oxygen promotes the Pd/C-catalyzed Suzuki–Miyaura reaction of potassium phenyltrifluoroborate under aqueous conditions. Consequently, we carried out all the reactions in air for the study.

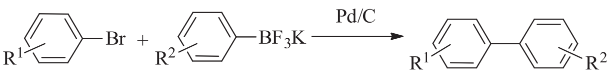
Table 1
The effects of different atmospheres on the Pd/C-catalyzed Suzuki–Miyaura reaction of 4-nitrobromobenzene with potassium aryltrifluoroborate.[a]



Entry	Atmosphere	Time (min)	Yield[b] (%)
1	Air	20	91
2	N_2	20	51[c]
3	O_2	15	98

[a] Reaction conditions: 4-nitrobromobenzene (0.5 mmol), potassium phenyltrifluoroborate (0.6 mmol), Pd/C (0.5 mol%), K_2CO_3 (1.0 mmol), EtOH/H_2O (3 mL/1 mL).
[b] Isolated yield.
[c] The EtOH and H_2O were degassed.

Table 2
The Suzuki–Miyaura reaction of aryl halides with potassium aryltrifluoroborates.[a]



Entry	*R*^{1}	*R*^{2}	Time (min)	Yield (%)[b]
1	4-CN	H	20	91
2	4-NO_2	H	25	95
3	4-CHO	H	25	93
4	4-$COCH_3$	H	30	95
5	4-OCH_3	H	50	78
6	4-OH	H	30	91
7	4-CF_3	4-CH_3	27	95
8	4-CN	4-CH_3	35	96
9	4-CN	4-OCH_3	30	90
10	4-OCH_3	4-OCH_3	60	70
11	4-NO_2	4-CH_3	25	93
12	4-NO_2	3-CH_3	120	79
13	4-NO_2	2-CH_3	120	46
14	2-CN	H	30	94
15	2-CN	4-CH_3	25	97

[a] Reaction conditions: aryl halide (0.5 mmol), potassium aryltrifluoroborate (0.6 mmol), Pd/C (0.5 mol%), K_2CO_3 (1.0 mmol), EtOH/H_2O (3 mL/1 mL), 80 °C, in air. The reaction was monitored by TLC.
[b] Isolated yield.

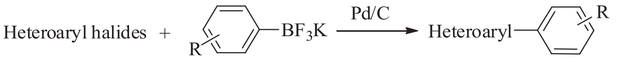
After having optimized the reaction conditions such as solvents, bases and catalysts (see Supporting information), we further investigated the scope and limitations of substrates under the conditions of 75% aqueous ethanol as solvent, K_2CO_3 as base, Pd/C (0.5 mol %) as catalyst at 80 °C in air. As shown in Table 2, in general, most of the reactions gave biaryl derivatives in high yields. The electronic nature of the substituent has some influence on the reactivity of the cross-coupling reactions. It is clear that 4-substituted aryl bromides containing electron-withdrawing groups showed a slightly higher reactivity than those containing electron-donating groups, due to the effect of these substituents on the reactivity of C-Br bond (Table 2, entries 1–6). Either 4-methyl or 4-methoxyl-substituted potassium phenyltrifluoroborates could complete the reactions smoothly (Table 2, entries 7–9). Increasing the steric effect could decrease the reactivity of the substrates (Table 2, entries 12 and 13). Unexpectedly, the *ortho*-substituted substrate, 2-bromobenzonitrile, reacted with potassium phenyltrifluoroborate or potassium *p*-tolyltrifluoroborate, providing the desired products in 94% and 97% yields, respectively (Table 2, entries 14 and 15).

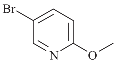
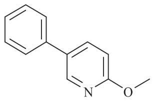
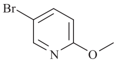
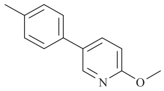
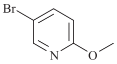
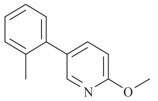
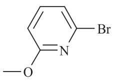
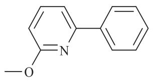
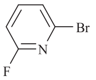
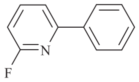
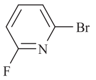
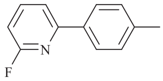
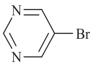
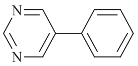
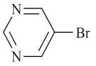
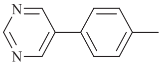
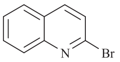
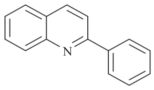
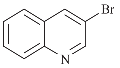
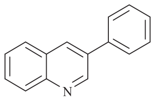
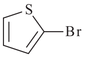
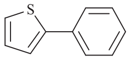
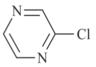
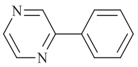
The present protocol was also extended to the synthesis of useful nitrogen-based heterobiaryl compounds. The results are summarized in Table 3. The cross-coupling of 5-bromo-2-methoxypyridine with potassium *p*-tolyltrifluoroborate gave 5-bromo-2-phenylpyridine in a 93% yield (Table 3, entry 2). Using potassium *o*-tolyltrifluoroborate as the nucleophilic partner, the cross-coupling was completed in 120 min, providing an 86% yield (Table 3, entry 3). As for 6-substituted 2-bromopyridines, both 2-bromo-6-methoxypyridine and 2-bromo-6-fluoropyridine provided good to excellent yields of the desired products (Table 3, entries 4–6). Other nitrogen-based heterobiaryls also achieved good results (Table 3, entries 7–10), whereas 2-bromothiophene was less active and generated the product in 44% yield (Table 3, entry 11). In this heterogeneous catalytic system, the reaction between *N*-heteroaryl chloride and potassium phenyltrifluoroborate achieved a moderate yield (Table 3, entry 12).

In recent years, carbazole derivatives have been extensively used as functional building blocks for the synthesis of small molecules, oligomers or polymers, and also as host materials because of their high triplet energy and good hole-transporting ability [27,28]. In this catalytic system, a series of aryl substituted 9-phenylcarbazolyl derivatives have been successfully synthesized *via* the Pd/C-catalyzed Suzuki–Miyaura reaction of aryl bromides with potassium 9-phenylcarbazolyltrifluoroborate. The results presented in Table 4 show that the aryl bromides bearing

Table 3

The Suzuki–Miyaura reaction of heteroaryl halides with potassium aryltrifluoroborates.[a]



Entry	Heteroaryl halide	Product	Time (min)	Yield (%)[b]
1			120	79
2			120	93
3			120	86
4			180	89
5			78	97
6			60	93
7			180	96
8			200	93
9			180	83
10			240	80
11			120	44
12			240	61

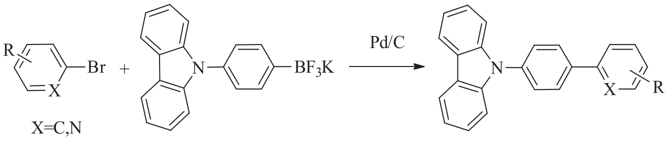
[a] Reaction conditions: heteroaryl halide (0.5 mmol), potassium aryltrifluoroborate (0.6 mmol), Pd/C (0.5 mol%), K_2CO_3 (1.0 mmol), EtOH/H_2O (3 mL/1 mL), 80 °C, in air. The reaction was monitored by TLC.

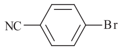
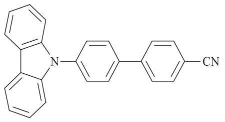
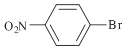
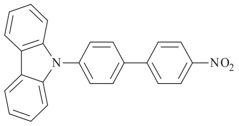
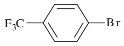
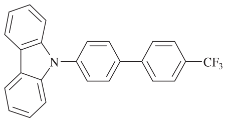
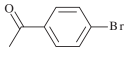
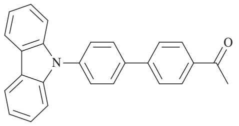
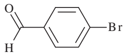
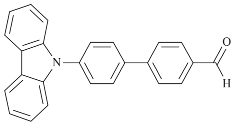
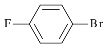
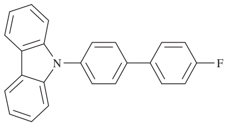
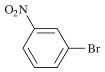
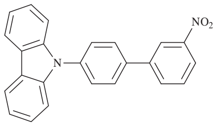
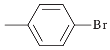
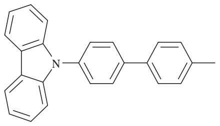
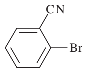
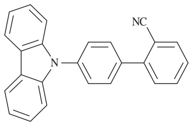
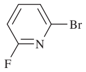
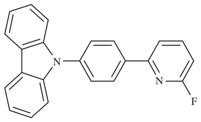
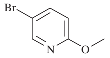
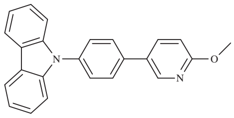
[b] Isolated yield.

electron-withdrawing groups were more effective. Among them, the substrates bearing 4-NO_2, 4-CN, or 4-CF_3, provided the corresponding products in excellent yields within 60 min (Table 4, entries 1–3). Meanwhile, 4-$COCH_3$, 4-CHO and 4-fluoro-substituted aryl bromides were also successfully coupled with 9-phenylcarbazolyltrifluoroborate in good yields (Table 4, entries 4–6). Additionally, an 83% isolated yield was obtained in 120 min in the case of 4-bromotoluene (Table 4, entry 8). It is noteworthy that the cross-coupling reaction between potassium 9-phenylcarbazolyltrifluoroborate and 3-nitrobromobenzene proceeded well, resulting in a 91% yield of the product within 120 min (Table 4, entry 7). To our delight, *ortho*-substituted substrate exhibited almost the same reactivity in terms of rate and yield (Table 4, entry 9). Furthermore, the cross-couplings of 5-bromo-2-methoxypyridine and 6-bromo-2-fluoropyridine also provided good yields of the desired products (Table 4, entries 10 and 11).

Table 4

Synthesis of aryl or heteroaryl substituted 9-phenylcarbazolyl derivatives.[a]



Entry	Aryl halides	Product	Time (min)	Yield (%)[b]
1			60	93
2			60	95
3			60	97
4			90	97
5			100	92
6			83	96
7			120	91
8			120	83
9			60	93
10			80	96
11			240	78

[a] Reaction conditions: aryl or heteroaryl bromides (0.5 mmol), potassium 9-phenylcarbazolyltrifluoroborate (0.6 mmol), Pd/C (0.5 mol%), K_2CO_3 (1.0 mmol), EtOH/H_2O (3 mL/1 mL), 80 °C, in air. The reaction was monitored by TLC.

[b] Isolated yield.

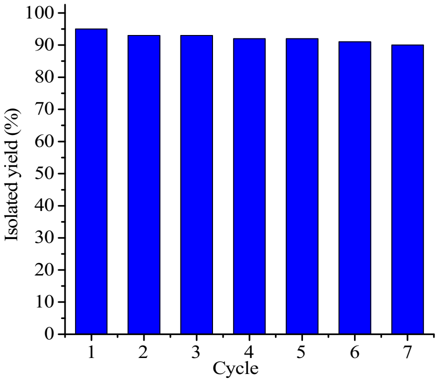


Fig. 1. Reusability of the Pd/C catalyst in the cross-coupling of 4-nitrobromobenzene with potassium 9-phenylcarbazolyltrifluoroborate. Reaction conditions: 4-nitrobromobenzene (0.5 mmol), potassium 9-phenylcarbazolyltrifluoroborate (0.6 mmol), Pd/C (1.0 mol%), K_2CO_3 (1.0 mmol), 80 °C, in air. 1.0 h for the first to forth runs, 1.5 h for the fifth and seventh runs. The reactions were monitored by TLC.

Thus, this work provides an efficient and practical method for the synthesis of aryl or heteroaryl substituted 9-phenylcarbazolyl derivatives.

In order to demonstrate the recovery and reusability of the catalyst, the coupling reaction between potassium 9-phenylcarbazolyltrifluoroborate and 4-nitrobromobenzene was chosen as model reaction for the recyclability tests. The results are shown in Fig. 1. In accordance with this post-processing method, the former fourth reaction cycles could give the product up to 93% yield within 60 min. In the fifth reaction cycle, a 93% yield of product was obtained after prolonging the reaction time to 90 min, and the catalytic system could be run for at least seven times without significant loss in activity. Obviously, the present protocol demonstrates high efficiency for the synthesis of biaryl compounds containing a carbazole moiety.

4. Conclusion

In summary, we have developed a simple, efficient and ligand-free protocol for the Suzuki–Miyaura reaction of aryl bromides or heteroaryl halides with potassium aryltrifluoroborate catalyzed by the Pd/C in 75% ethanol. This protocol could be used for the synthesis of aryl substituted 9-phenylcarbazolyl derivatives and the catalyst could be recycled for at least seven times with high activity. In addition, an oxygen-promoting effect was observed in the Pd/C-catalyzed Suzuki–Miyaura reaction of potassium aryltrifluoroborates.

Acknowledgments

The authors thank the financial support from the National Natural Science Foundation of China (Nos. 21276043, 21421005). Z. Jin acknowledges the Research Foundation of Dalian University of Technology for Retired Professors (No. DUTTX2015102).

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.cclet.2015.12.022.

References

[1] N. Miyaura, A. Suzuki, Palladium-catalyzed cross-coupling reactions of organoboron compounds, Chem. Rev. 95 (1995) 2457–2483.
[2] A. Suzuki, Recent advances in the cross-coupling reactions of organoboron derivatives with organic electrophiles, 1995–1998, J. Organomet. Chem. 576 (1999) 147–168.
[3] A.F. Littke, G.C. Fu, Palladium-catalyzed coupling reactions of aryl chlorides, Angew. Chem. Int. Ed. 41 (2002) 4176–4211.
[4] C. Liu, Y. Zhang, N. Liu, J. Qiu, A simple and efficient approach for the palladium-catalyzed ligand-free Suzuki reaction in water, Green Chem. 14 (2012) 2999–3003.
[5] D.G. Hall, Structure, Properties, and Preparation of Boronic Acid Derivatives. Overview of Their Reactions and Applications, John Wiley & Sons, Weinheim, Germany, 2005.
[6] M.S. Wong, X.L. Zhang, Ligand promoted palladium-catalyzed homo-coupling of arylboronic acids, Tetrahedron Lett. 42 (2001) 4087–4089.
[7] H.G. Kuivila, K.V. Nahabedian, Electrophilic displacement reactions. X. General acid catalysis in the protodeboronation of areneboronic acids, J. Am. Chem. Soc. 83 (1961) 2159–2163.
[8] E. Vedejs, R.W. Chapman, S.C. Fields, S. Lin, M.R. Schrimpf, Conversion of arylboronic acids into potassium aryltrifluoroborates: convenient precursors of arylboron difluoride Lewis acids, J. Org. Chem. 60 (1995) 3020–3027.
[9] S. Darses, J.P. Genet, Potassium organotrifluoroborates: new perspectives in organic synthesis, Chem. Rev. 108 (2008) 288–325.
[10] G.A. Molander, B. Canturk, Organotrifluoroborates and monocoordinated palladium complexes as catalysts—A perfect combination for Suzuki–Miyaura coupling, Angew. Chem. Int. Ed. 48 (2009) 9240–9261.
[11] S. Darses, J.P. Genêt, J.L. Brayer, J.P. Demoute, Cross-coupling reactions of arenediazonium tetrafluoroborates with potassium aryl- or alkenyltrifluoroborates catalyzed by palladium, Tetrahedron Lett. 38 (1997) 4393–4396.
[12] L. Liu, Y. Dong, N. Tang, A highly efficient and recyclable ligand-free protocol for the Suzuki coupling reaction of potassium aryltrifluoroborates in water, Green Chem. 16 (2014) 2185–2189.
[13] L. Liu, Y. Dong, B. Pang, J. Ma, [Bmim] PF_6-promoted ligandless Suzuki–Miyaura coupling reaction of potassium aryltrifluoroborates in water, J. Org. Chem. 79 (2014) 7193–7198.
[14] Y. Kitamura, S. Sako, T. Udzu, et al., Ligand-free Pd/C-catalyzed Suzuki–Miyaura coupling reaction for the synthesis of heterobiaryl derivatives, Chem. Commun. (2007) 5069–5071.
[15] F.X. Felpin, Ten years of adventures with Pd/C catalysts: from reductive processes to coupling reactions, Synlett 25 (2014) 1055–1067.
[16] C.R. LeBlond, K.M. Butler, M.W. Ferrington, M.A. Browe, Palladium on carbon-catalyzed cross-coupling of aryl halides with potassium *p*-tolyltrifluoroborate in air, Synth. Commun. 39 (2009) 636–640.
[17] L. Joucla, G. Cusati, C. Pinel, L. Djakovitch, Efficient heterogeneous vinylation of aryl halides using potassium vinyltrifluoroborate, Tetrahedron Lett. 49 (2008) 4738–4741.
[18] L. Joucla, G. Cusati, C. Pinel, L. Djakovitch, Heterogeneously Pd/C catalysed procedure for the vinylation of aryl bromides, Appl. Catal., A: Gen. 360 (2009) 145–153.
[19] W. Han, C. Liu, Z.L. Jin, In situ generation of palladium nanoparticles: a simple and highly active protocol for oxygen-promoted ligand-free Suzuki coupling reaction of aryl chlorides, Org. Lett. 9 (2007) 4005–4007.
[20] X. Rao, C. Liu, Y. Xing, et al., Oxygen-promoted palladium-on-carbon-catalyzed ligand-free Suzuki reaction for the synthesis of heterobiaryls in aqueous media, Asian J. Org. Chem. 2 (2013) 514–518.
[21] C. Liu, W. Yang, A fast and oxygen-promoted protocol for the ligand-free Suzuki reaction of 2-halogenated pyridines in aqueous media, Chem. Commun. (2009) 6267–6269.
[22] W. Yang, C. Liu, J. Qiu, In situ formation of *N*,*O*-bidentate ligand via the hydrogen bond for highly efficient Suzuki reaction of aryl chlorides, Chem. Commun. 46 (2010) 2659–2661.
[23] Z.S. Wang, N. Koumura, Y. Cui, et al., Hexylthiophene-functionalized carbazole dyes for efficient molecular photovoltaics: tuning of solar-cell performance by structural modification, Chem. Mater. 20 (2008) 3993–4003.
[24] E.M. Barea, C. Zafer, B. Gultekin, et al., Quantification of the effects of recombination and injection in the performance of dye-sensitized solar cells based on *N*-substituted carbazole dyes, J. Phys. Chem. C 114 (2010) 19840–19848.
[25] W. Han, C. Liu, Z. Jin, Aerobic ligand-free Suzuki coupling reaction of aryl chlorides catalyzed by in situ generated palladium nanoparticles at room temperature, Adv. Synth. Catal. 350 (2008) 501–508.
[26] C. Liu, Q. Ni, F. Bao, J. Qiu, A simple and efficient protocol for a palladium-catalyzed ligand-free Suzuki reaction at room temperature in aqueous DMF, Green Chem. 13 (2011) 1260–1266.
[27] M.H. Tsai, H.W. Lin, H.C. Su, et al., Highly efficient organic blue electrophosphorescent devices based on 3,6-bis(triphenylsilyl)carbazole as the host material, Adv. Mater. 18 (2006) 1216–1220.
[28] P. Moonsin, N. Prachumrak, R. Rattanawan, et al., Carbazole dendronised triphenylamines as solution processed high T_g amorphous hole-transporting materials for organic electroluminescent devices, Chem. Commun. 48 (2012) 3382–3384.