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Palladium-catalysed direct 3- or 4-arylation of thiophene derivatives using aryl bromides

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ABSTRACT

The palladium-catalysed direct 3- or 4-arylation of 2,5-disubstituted thiophenes using aryl bromides gives a simple access to a variety of 3- or 4-arylthiophene derivatives. Moderate to good yields of 3-arylated thiophenes were obtained using 2,5-dimethylthiophene. In the presence of unsymmetrically disubstituted, 2-acetyl-5-methylthiophene, a regioselective arylation on carbon 4 of thiophene was observed. This reaction provides only HX associated to the base as by-product and reduces the number of steps to prepare these compounds.

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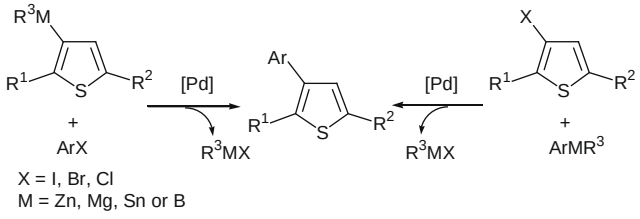
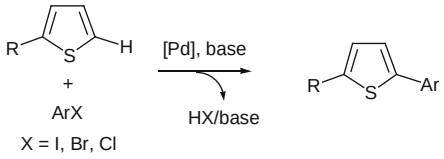
The palladium-catalysed cross-coupling reactions of thiophenes with aryl halides are among the most powerful methods for the preparation of arylthiophenes.[1] The efficiency of palladium-catalysed Stille,[2] Negishi,[3] or Suzuki,[4] cross-coupling for the reaction of aryl halides with thiophene derivatives or of halothiophenes with aryl-metal derivatives has been largely described. However, these reactions require the prior preparation of an organometallic derivative of a heteroaromatic or an aromatic, and provide an organometallic salt (MX) as by-product (Scheme 1).

Since a few years, a new palladium-catalysed procedure for the functionalisation of heteroaromatics has emerged. It consists in directly arylating heteroaromatics via a C–H bond activation of the heteroarenes.[5–8] This procedure proceeds nicely for the coupling of several thiophene derivatives with aryl halides or even triflates.[9–14] For such couplings, no preparation of an organometallic derivative is required. Moreover, this reaction provides only HX associated to a base as by-product, instead of a metallic salt, and therefore is very interesting both in terms of atom-economy and non-toxic wastes. However, so far, most of the results reported for this reaction were obtained with 2-substituted thiophenes and gave 5-arylated thiophenes (Scheme 2).[10]

Some direct 3-arylations of thiophenes via intramolecular cyclisations using 2-substituted thiophenes have been reported.[11] Rare examples of 3- or 4-arylations of thiophenes via palladium-catalysed bimolecular couplings have also been described.[12]



Scheme 1.



Scheme 2.

For example, Lemaire and co-workers have reported in 1998, that the direct arylation of 3-formylthiophene or 3-cyanothiophene gave a mixture of 2-arylthiophenes and 2,4-diarylthiophenes.[12a] In most cases, the 2-arylated thiophenes were formed in high selectivities, and the 2,4-diarylthiophenes were only obtained in low yields. Recently, Miura and co-workers described perarylation reactions of 3-thiophenecarboxylic acid.[13] They examined the preparation of tetraarylthiophenes having two different aryl

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groups at the 2,5- and 3,4-positions. 2,5-Diphenyl- and 2,5-bis(4-methoxyphenyl)-3-thiophenecarboxylates reacted with aryl bromides to give the perarylated thiophenes. To our knowledge, so far, the selective bimolecular palladium-catalysed direct 3- or 4-monoarylation of 2,5-disubstituted thiophenes has not been reported.

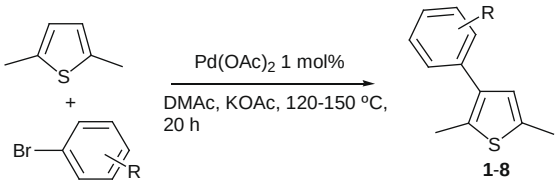
The extension of palladium-catalysed C–H bond activation/functionalisation procedure to a wider diversity of heteroaromatics would be a considerable advantage for sustainable development, because of the lower cost, lower mass and the easier access to reactants, as well as for the treatment of the relatively non-toxic waste. Therefore, the discovery of more effective and selective conditions, for the direct 3- or 4-arylation of thiophenes with aryl halides, is desirable. Here, we wish to report on the palladium-catalysed direct 4-arylation of unsymmetrically 2,5-disubstituted thiophenes and also on the 3-arylation of a symmetrically 2,5-disubstituted thiophene, using aryl bromides.

In order to determine the most suitable reaction conditions for this specific arylation, we studied the reactivity of 2,5-dimethylthiophene with 4-bromobenzaldehyde in the presence of 1 mol % $[PdCl(C_3H_5)]_2$ at 120 °C using various bases and solvents (Scheme 3, Table 1). Yields of 21% and 25% in 3-arylation product **1** were obtained using DMF or DMAc as solvents and KOAc as the base (Table 1, entries 1–5). Other solvents such as xylene, DME or NMP were found to give only 0–6% yield of **1**. Employing Cs_2CO_3 or Na_2CO_3 as base in the presence of DMAc, the expected product **1** was not observed (Table 1, entries 6 and 7). Only traces of **1** were detected when K_2CO_3 was used (Table 1, entry 8). $Pd(OAc)_2$ as palladium sources was found to give a slightly higher yield of 31% in **1** (Table 1, entry 9).

Next, we examined the influence of the presence of ligands in the reaction mixture. However, the addition of the phosphine ligands, PPh_3 or dppb was found to be profitless (Table 1, entries 11–14). Finally, we studied the influence of a higher reaction temperature. At 150 °C instead of 120 °C, a better yield of 48% in **1** was obtained (Table 1, entry 15). However, some side-products were also formed.

Then, using the most suitable reaction conditions (DMAc, KOAc, $Pd(OAc)_2$ 1 mol %, 120–150 °C), we examined the scope and limitation of this reaction with a variety of aryl bromides (Scheme 3, Table 2).

First, we examined the reactivity of electron-deficient *para*-substituted aryl bromides. The 3-arylation of 2,5-dimethylthiophene with 4-bromopropiophenone, 4-trifluoromethylbromobenzene or 4-bromobenzonitrile gave **3**–**5** in only 38–50% yields (Table 2, entries 3–5). Unidentified side-products were also formed with these reactants. In the presence of 4-bromobenzophenone or 4-bromonitrobenzene at 120 °C, compounds **2** and **6** were obtained in 61% and 62% yields, respectively (Table 2, entries 2 and 6). With these substrates, the reactions performed at 150 °C gave lower yields due to the formation of side products. Electron-deficient, *ortho*-substituted, 2-bromobenzonitrile reacted at 120 °C gave **7** in 64% yield (Table 2, entry 7). A low yield of 28% was obtained with congested 1-bromonaphthalene due to partial conversion of this aryl bromide (Table 2, entries 8 and 9).



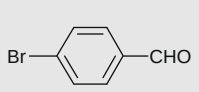
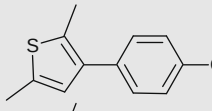
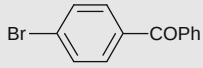
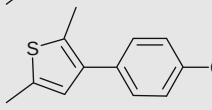
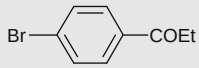
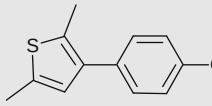
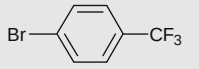
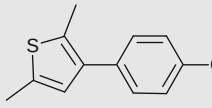
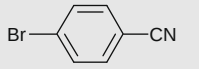
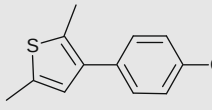
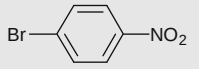
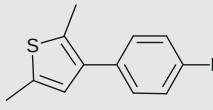
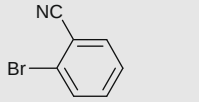
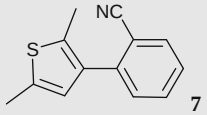
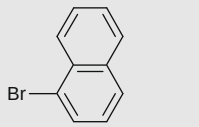
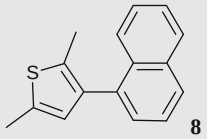
Scheme 3.

Table 1
Palladium-catalysed direct 3-arylation of 2,5-dimethylthiophene with 4-bromobenzaldehyde (Scheme 3)[15,16]

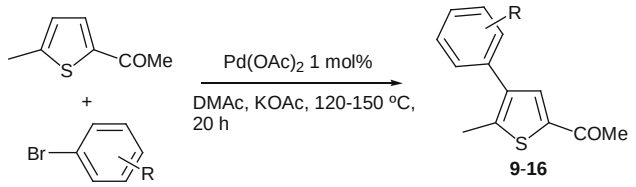
Entry	Catalyst	Solvent	Base	Yield (%)
1	$[PdCl(C_3H_5)]_2$	DMF	KOAc	21
2	$[PdCl(C_3H_5)]_2$	Xylene	KOAc	2
3	$[PdCl(C_3H_5)]_2$	DME	KOAc	0
4	$[PdCl(C_3H_5)]_2$	NMP	KOAc	6
5	$[PdCl(C_3H_5)]_2$	DMAc	KOAc	25
6	$[PdCl(C_3H_5)]_2$	DMAc	Cs_2CO_3	0
7	$[PdCl(C_3H_5)]_2$	DMAc	Na_2CO_3	0
8	$[PdCl(C_3H_5)]_2$	DMAc	K_2CO_3	6
9	$Pd(OAc)_2$	DMAc	KOAc	31
10	$Pd(OAc)_2$	DMAc	KOAc	28[a]
11	$Pd(OAc)_2$/2 PPh_3	DMAc	KOAc	27[b]
12	$[PdCl(C_3H_5)]_2$/4 PPh_3	DMAc	KOAc	27[b]
13	$Pd(OAc)_2$/dppb	DMAc	KOAc	19[c]
14	$[PdCl(C_3H_5)]_2$/2 dppb	DMAc	KOAc	20[c]
15	$Pd(OAc)_2$	DMAc	KOAc	48[d]

Conditions: catalyst $[PdCl(C_3H_5)]_2$ (0.005 equiv) or $Pd(OAc)_2$ (0.01 equiv), 4-bromobenzaldehyde (1 equiv), 2,5-dimethylthiophene (3 equiv), base (2 equiv), 120 °C, 20 h, under argon, isolated yields.
[a] 5 mol % catalyst was employed.
[b] PPh_3: 0.02 equiv.
[c] dppb: 0.01 equiv.
[d] Reaction temperature 150 °C.

Table 2
Palladium-catalysed direct 3-arylations of 2,5-dimethylthiophene with aryl bromides (Scheme 3)[15,16]

Entry	Aryl bromide	Product	Yield (%)
1		 **1**	48
2		 **2**	61[a]
3		 **3**	38[a]
4		 **4**	50
5		 **5**	40
6		 **6**	62[a]
7		 **7**	64[a]
8		 **8**	27[a]
9			28

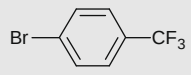
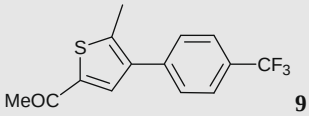
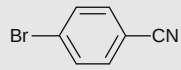
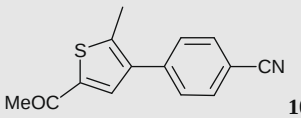
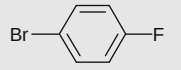
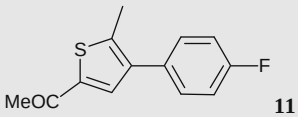
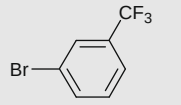
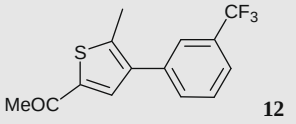
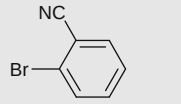
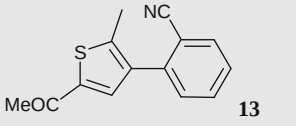
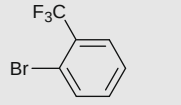
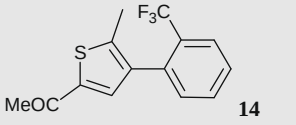
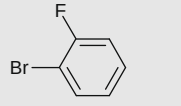
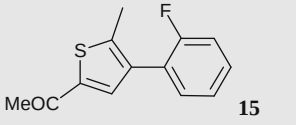
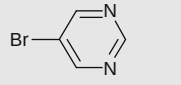
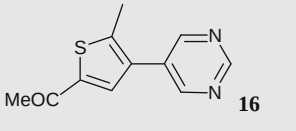
Conditions: catalyst $Pd(OAc)_2$ (0.01 equiv), aryl bromide (1 equiv), 2,5-dimethylthiophene (3 equiv), KOAc (2 equiv), DMAc, 150 °C, 20 h, under argon, isolated yields.
[a] Reaction temperature 120 °C.



Scheme 4.

Next, we examined the reactivity of 2-acetyl-5-methylthiophene with various aryl bromides (Scheme 4, Table 3). With this unsymmetrically 2,5-disubstituted thiophene, two regioisomers can be obtained in the course of the arylation. We had previously observed, using 2-acetyl-5-methylfuran or 1,5-dimethyl-2-pyrrolecarbonitrile as reactants, that the formation of the 4-arylation products was favoured.[14] In the presence of 2-acetyl-5-methylthiophene, a good selectivity in favour of the 4-arylated compounds was also obtained using $Pd(OAc)_2$ as the catalyst, DMAc as the solvent and KOAc as the base. The 3-arylation products were observed in very low yields with most aryl bromides. In the presence of 4-, 3- or 2-trifluoromethylbromobenzenes, the products **9**, **12** and **14** were obtained in 48–60% yields (Table 3, entries 1, 5, 6 and 8). Relatively similar results were obtained using 4- or 2-bromobenzonitriles. These reactants gave the 4-arylation products **10** and **13** in 63% and 54% yields, respectively (Table 3, entries 3 and 7). Slightly activated 4- or 2-fluorobromobenzenes also led regioselectively to **11** or **15**, but the formation of side products was observed (Table 3, entries 4, 9 and 10). On the other hand, a low yield in **16** was obtained when using 5-bromopyrimidine as the reactant due to the formation of a large amount of by-products (Table 3, entries 11 and 12).

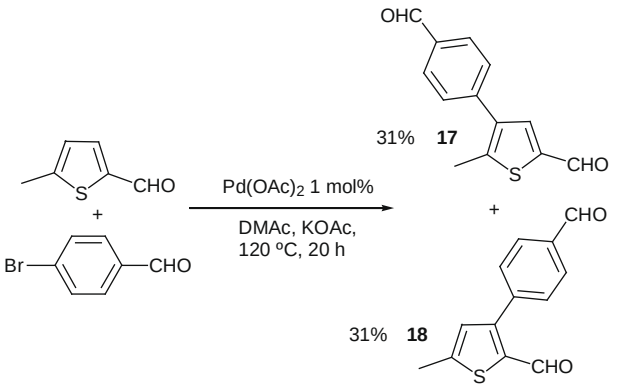
Table 3
Palladium-catalysed direct 4-arylations of 2-acetyl-5-methylthiophene with aryl bromides (Scheme 4)[15,16]

Entry	Aryl bromide	Product	Yield (%)
1		 **9**	32
2			51[a,b]
3		 **10**	63
4		 **11**	40[a,b]
5		 **12**	42
6			48[a,b]
7		 **13**	54[a,b]
8		 **14**	60[a,b]
9		 **15**	50
10			56[a,b]
11		 **16**	15
12			15[a,b]

Conditions: catalyst $Pd(OAc)_2$ (0.01 equiv), aryl bromide (1 equiv), 2-acetyl-5-methylthiophene (3 equiv), KOAc (2 equiv), DMAc, 120 °C, 20 h, under argon, isolated yields.
[a] 2-Acetyl-5-methylthiophene: 2 equiv.
[b] Reaction temperature 150 °C.

Finally, we examined the direct arylation of 2-formyl-5-methylthiophene. Surprisingly, using 4-bromobenzaldehyde as reaction partner, this heteroarene was found to give an equimolar mixture of 3- and 4-arylated thiophenes **17** and **18** in 62% yield (Scheme 5). The arylation of this heteroarene in the presence of other aryl bromides such as 4-bromoacetophenone, 4-bromobenzonitrile or 4-trifluoromethylbromobenzene gave inseparable mixtures of regioisomers. The regioselectivity of the arylations of unsymmetrically 2,5-disubstituted thiophenes appears to be strongly dependent on the nature of the substituents on thiophenes.

In summary, we have demonstrated that using $Pd(OAc)_2$ as the catalyst precursor, the direct 3- or 4-arylation via a C–H bond activation of 2,5-disubstituted thiophenes using aryl bromides proceeds in moderate to good yields. In the presence of the unsymmetrically 2,5-disubstituted thiophene, 2-acetyl-5-methylthiophene, a regioselective arylation in position 4 was observed. This procedure is limited to activated aryl bromides. However, it should be noted that a wide range of functions such as propionyl, benzoyl, formyl, nitro, nitrile, fluoro or trifluoromethyl on the aryl bromide are tolerated. The major by-product is AcOH/KBr instead of metallic salts with classical coupling procedures. Moreover, no preparation of an organometallic derivative is required, reducing the number of steps to prepare these compounds. Despite their interest, most of the products prepared by this method are new, indicating a relatively laborious access to such compounds using more traditional cross-coupling procedures. For these reasons, even if the yields are moderate with some substrates, this procedure should give a simple access to 3- or 4-arylthiophenes.



Scheme 5.

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References and notes

1. Li, J. J.; Gribble, G. W. *Palladium in Heterocyclic Chemistry*; Pergamon: Amsterdam, 2000.
2. (a) Sosabowski, M.; Powell, P. *J. Chem. Res., Synop.* **1995**, 402–403; (b) Lee, B. S.; Lee, J. H.; Chi, D. Y. *J. Org. Chem.* **2002**, *67*, 7884–7886; (c) Derdau, V.; Oekonomopulos, R.; Schubert, G. *J. Org. Chem.* **2003**, *68*, 5168–5173; (d) Su, W.; Urgaonkar, S.; McLaughlin, P. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2004**, *126*, 16433–16439; (e) Pereira, R.; Furst, A.; Iglesias, B.; Germain, P.; Gronemeyer, H.; de Lera, A. R. *Org. Biomol. Chem.* **2006**, *4*, 4514–4525; (f) Zhao, C.; Zhang, Y.; Wang, C.; Rothberg, L.; Ng, M.-K. *Org. Lett.* **2006**, *8*, 1585–1588; (g) Uchiyama, Y.; Ohta, A.; Fujimori, K. *Heterocycles* **2007**, *74*, 251–257.
3. (a) Wu, X.; Rieke, R. D. *J. Org. Chem.* **1995**, *60*, 6658–6659; (b) Rieke, R. D.; Kim, S.-H.; Wu, X. *J. Org. Chem.* **1997**, *62*, 6921–6927; (c) Izmer, V. V.; Lebedev, A. Y.; Nikulin, M. V.; Ryabov, A. N.; Asachenko, A. F.; Lygin, A. V.; Sorokin, D. A.; Voskoboynikov, A. Z. *Organometallics* **2006**, *25*, 1217–1229.
4. (a) Hark, R. R.; Hauze, D. B.; Petrovskaia, O.; Joullie, M. M.; Jaouhari, R.; McComiskey, P. *Tetrahedron Lett.* **1994**, *35*, 7719–7722; (b) Burk, M. J.; Lee, J. R.; Martinez, J. P. *J. Am. Chem. Soc.* **1994**, *116*, 10847–10848; (c) Chamoin, S.; Houldsworth, S.; Kruse, C. G.; Bakker, W. I.; Snieckus, V. *Tetrahedron Lett.* **1998**, *39*, 4179–4182; (d) Pereira, R.; Iglesias, B.; de Lera, A. R. *Tetrahedron* **2001**, *57*, 7871–7881; (e) Feuerstein, M.; Doucet, H.; Santelli, M. *J. Organomet. Chem.* **2003**, *687*, 327–336; (f) Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302–4314; (g) Yam, V. W.-W.; Ko, C.-C.; Zhu, N. *J. Am. Chem. Soc.* **2004**, *126*, 12734–12735; (h) Berthiol, F.; Kondolff, I.; Doucet, H.; Santelli, M. *J. Organomet. Chem.* **2004**, *689*, 2786–2798; (i) Kondolff, I.; Doucet, H.; Santelli, M. *Synlett* **2005**, 2057–2061; (j) Korolev, D. N.; Bumagin, N. A. *Tetrahedron Lett.* **2005**, *46*, 5751–5754; (k) Ko, C.-C.; Kwok, W.-M.; Yam, V. W.-W.; Phillips, D. L. *Chem. Eur. J.* **2006**, *12*, 5840–5848; (l) Arvela, R. K.; Leadbeater, N. E.; Mack, T. L.; Kormos, C. M. *Tetrahedron Lett.* **2006**, *47*, 217–220; (m) Dang, T. T.; Rasool, N.; Dang, T. T.; Reinke, H.; Langer, P. *Tetrahedron Lett.* **2007**, *48*, 845–847; (n) Billingsley, K.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 3358–3366; (o) Kondolff, I.; Doucet, H.; Santelli, M. *J. Het. Chem.* **2008**, *45*, 109–118; (p) Molander, G. A.; Canturk, B.; Kennedy, L. E. *J. Org. Chem.* **2009**, *74*, 973–980.
5. Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174–238.
6. Satoh, T.; Miura, M. *Chem. Lett.* **2007**, *36*, 200–205.
7. Doucet, H.; Hierso, J. C. *Curr. Opin. Drug Discov. Devel.* **2007**, *10*, 672–690.
8. Campeau, L.-C.; Stuart, D. R.; Fagnou, K. *Aldrichim. Acta* **2007**, *40*, 35–41.
9. Roger, J.; Doucet, H. *Org. Biomol. Chem.* **2008**, *6*, 169–174.
10. (a) Ohta, A.; Akita, Y.; Ohkuwa, T.; Chiba, M.; Fukunaga, R.; Miyafuji, A.; Nakata, T.; Tani, N.; Aoyagi, Y. *Heterocycles* **1990**, *31*, 1951–1958; (b) Pivsa-Art, S.; Satoh, T.; Kawamura, Y.; Miura, M.; Nomura, M. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 467–473; (c) Smet, M.; Van Dijk, J.; Dehaen, W. *Synlett* **1999**, 495–497; (d) Battace, A.; Lemhadri, M.; Zair, T.; Doucet, H.; Santelli, M. *Adv. Synth. Catal.* **2007**, *349*, 2507–2516; (e) Derridj, F.; Djebbar, S.; Benali-Baitich, O.; Doucet, H. *J. Organomet. Chem.* **2008**, *693*, 135–144; (f) Pozgan, F.; Roger, J.; Doucet, H. *ChemSusChem* **2008**, *1*, 404–407; (g) Derridj, F.; Roger, J.; Djebbar, S.; Geneste, F.; Doucet, H. *J. Organomet. Chem.* **2009**, *694*, 455–465; (h) Roger, J.; Pozgan, F.; Doucet, H. *Green. Chem.* **2009**, *11*, 425–432.
11. (a) Burwood, M.; Davies, B.; Diaz, I.; Grigg, R.; Molina, P.; Sridharan, V.; Hughes, M. *Tetrahedron Lett.* **1995**, *36*, 9053–9056; (b) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Paladino, G.; Zoni, C. *Eur. J. Org. Chem.* **2005**, 2091–2096; (c) Joucla, L.; Putey, A.; Joseph, B. *Tetrahedron Lett.* **2005**, *46*, 8177–8179; (d) Campeau, L.-C.; Parisien, M.; Jean, A.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128*, 581–590; (e) Putey, A.; Joucla, L.; Picot, L.; Besson, T.; Joseph, B. *Tetrahedron* **2007**, *63*, 867–879; (f) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Sottocornola, S. *Synthesis* **2008**, 136–140.
12. (a) Lavenot, L.; Gozzi, C.; Ilg, K.; Orlova, I.; Penalva, V.; Lemaire, M. *J. Organomet. Chem.* **1998**, *567*, 49–55; (b) Okazawa, T.; Satoh, T.; Miura, M.; Nomura, M. *J. Am. Chem. Soc.* **2002**, *124*, 5286–5287.
13. Nakano, M.; Tsurugi, H.; Satoh, T.; Miura, M. *Org. Lett.* **2008**, *10*, 1851–1854.
14. (a) Gottumukkala, A. L.; Doucet, H. *Adv. Synth. Catal.* **2008**, *350*, 2183–2188; (b) Fall, Y.; Doucet, H.; Santelli, M. *ChemSusChem.* **2009**, *2*, 153–157.
15. As a typical experiment (Table 3, entry 3), the reaction of 2-acetyl-5-methylthiophene (0.420 g, 3 mmol), 4-bromobenzonitrile (0.182 g, 1 mmol) and KOAc (0.196 g, 2 mmol) at 120 °C over 20 h in dry DMAc (5 mL) in the presence of $Pd(OAc)_2$ (0.01 mmol) under argon affords the corresponding product **10** after evaporation and filtration on silica gel in 63% (0.152 g) isolated yield.
16. All compounds gave satisfactory ^1H, ^{13}C and elementary analysis. ^1H NMR (200 MHz, $CDCl_3$) of new compounds: **1**: δ 10.0 (s, 1H), 7.93 (d, J = 8.5 Hz, 2H), 7.55 (d, J = 8.5 Hz, 2H), 6.77 (s, 1H), 2.48 (s, 6H); **2**: δ 7.95–7.80 (m, 4H), 7.70–7.40 (m, 5H), 6.78 (s, 1H), 2.51 (s, 3H), 2.49 (s, 3H); **3**: δ 8.02 (d, J = 8.5 Hz, 2H), 7.47 (d, J = 8.5 Hz, 2H), 6.75 (s, 1H), 3.05 (q, J = 7.5 Hz, 2H), 2.48 (s, 6H), 1.27 (t, J = 7.5 Hz, 3H); **4**: δ 7.67 (d, J = 8.5 Hz, 2H), 7.51 (d, J = 8.5 Hz, 2H), 6.73 (s, 1H), 2.47 (s, 6H); **5**: δ 7.69 (d, J = 8.5 Hz, 2H), 7.48 (d, J = 8.5 Hz, 2H), 6.72 (s, 1H), 2.47 (s, 6H); **6**: δ 8.27 (d, J = 8.5 Hz, 2H), 7.53 (d, J = 8.5 Hz, 2H), 6.76 (s, 1H), 2.49 (s, 6H); **7**: δ 7.77 (d, J = 7.6 Hz, 1H), 7.60 (d, J = 7.6 Hz, 1H), 7.50–7.30 (m, 2H), 6.69 (s, 1H), 2.50 (s, 3H), 2.43 (s, 3H); **8**: δ 8.00–7.65 (m, 3H), 7.58–7.27 (m, 4H), 6.69 (s, 1H), 2.52 (s, 3H), 2.22 (s, 3H); **9**: δ 7.72 (d, J = 8.1 Hz, 2H), 7.71 (s, 1H), 7.52 (d, J = 8.1 Hz, 2H), 2.57 (s, 6H); **10:** δ 7.78 (d, J = 8.3 Hz, 2H), 7.61 (s, 1H), 7.50 (d, J = 8.3 Hz, 2H), 2.52 (s, 6H); **11**: δ 7.61 (s, 1H), 7.30 (dd, J = 8.0 and 4.5 Hz, 2H), 7.12 (t, J = 8.0 Hz, 2H), 2.52 (s, 3H), 2.50 (s, 3H); **12**: δ 7.69–7.60 (m, 5H), 2.57 (s, 3H), 2.56 (s, 3H); **13:** δ 7.77 (d, J = 8.3 Hz, 1H), 7.72 (m, 1H), 7.68 (s, 1H), 7.55–7.25 (m, 2H), 2.53 (s, 3H), 2.46 (s, 3H); **14**: δ 7.80 (d, J = 8.1 Hz, 1H), 7.70–7.45 (m, 3H), 7.25 (d, J = 8.1 Hz, 1H), 2.54 (s, 3H), 2.30 (s, 3H); **15:** δ 7.61 (s, 1H), 7.45–7.05 (m, 4H), 2.54 (s, 3H), 2.45 (s, 3H); **16**: δ 9.21 (s, 1H), 8.80 (s, 2H), 7.63 (s, 1H), 2.52 (s, 6H); **17**: δ 10.10 (s, 1H), 9.89 (s, 1H), 7.99 (d, J = 8.5 Hz, 2H), 7.76 (s, 1H), 7.58 (d, J = 8.5 Hz, 2H), 2.63 (s, 3H); **18**: δ 10.10 (s, 1H), 9.79 (s, 1H), 7.99 (d, J = 8.5 Hz, 2H), 7.65 (d, J = 8.5 Hz, 2H), 6.98 (s, 1H), 2.62 (s, 3H).