Supporting Information for
Mechanistic studies and optimisation of a Pd-catalysed direct arylation reaction using phosphine-free systems

Junpei Kuwabara,* Masaru Sakai, Qiao Zhang and Takaki Kanbara*

Tsukuba Research Center for Interdisciplinary Materials Science (TIMS), Graduate School of Pure and Applied Sciences, University of Tsukuba, 1-1-1 Tennodai, Tsukuba 305-8573, Japan
*E-mail: kuwabara@ims.tsukuba.ac.jp, kanbara@ims.tsukuba.ac.jp

Materials.
Pd(OAc)$_2$ and 2,2'-bithiophene, 5-hexyl-2,2'-bithiophene, 1-bromo-4-octylbenzene, 2-butylthiophene, and other chemicals were received from commercial suppliers and used without further purification. CDCl$_3$ was purchase from Kanto Chemical. Anhydrous DMAc was purchased from Kanto Chemical and used as a dry solvent. Pd(OPiv)$_2$ was prepared according to the literature method.$^{S1}$

General Methods.
$^1$H and $^{13}$C{$^1$H} NMR spectra were recorded on Bruker AVANCE-400 and Bruker AVANCE-600 NMR spectrometers. $^1$H and $^{13}$C{$^1$H} NMR spectra were measured with tetramethylsilane (TMS) as an internal standard. All manipulations for the reactions were carried out under nitrogen atmosphere using a standard Schlenk technique or a glovebox. Elemental analyses were carried out with a Perkin-Elmer 2400-CHN instrument. Purifications by High Performance Liquid Chromatography (HPLC) were carried out on a JAI LC-9201 using chloroform as an eluent.

Synthesis of quaterthiophene (Scheme 1).$^{S2}$
A mixture of Pd(OAc)$_2$ (44.8 mg, 0.20 mmol), 2,2'-bithiophene (166 mg, 1.0 mmol), and K$_2$CO$_3$ (276 mg, 2.0 mmol) was stirred in anhydrous DMAc (2.0 mL) for 3 h at 100 °C under nitrogen atmosphere. The reaction mixture was cooled to room temperature and diluted with CHCl$_3$. The organic phase was washed with water and brine, and dried over Na$_2$SO$_4$. The product was isolated by column chromatography on silica gel using a mixture of CHCl$_3$ and hexane (1:10) as an eluent. The solvents were removed in vacuo to give quaterthiophene (16.1 mg, 24%). $^1$H NMR (400 MHz, CDCl$_3$): 7.23 (dd, $J = 5.2$ and 1.2 Hz, 2H), 7.18 (dd, $J = 3.6$ and 1.2 Hz, 2H), 7.09 (d, $J = 4.0$ Hz, 2H), 7.08 (d, $J = 4.0$ Hz, 2H), 7.03 (dd, $J = 5.2$ and 3.6 Hz, 2H). $^{13}$C{$^1$H} NMR (100MHz, CDCl$_3$): 137.0, 136.3, 135.8, 127.8, 124.5, 124.3, 124.2, 123.7.
Synthesis of 5,5′′′-dihexylquaterthiophene (Table 1).\textsuperscript{53}

A mixture of Pd(OAc)$_2$ (22.3 mg, 0.10 mmol), 5-hexyl-2,2′-bithiophene (118 µL, 0.50 mmol), and KOPiv (140 mg, 1.0 mmol) was stirred in anhydrous DMAc (2.0 mL) for 3 h at 100 °C under nitrogen atmosphere. The reaction mixture was cooled to room temperature and diluted with CHCl$_3$. The organic phase was washed with water and brine, and dried over Na$_2$SO$_4$. The product was separated by column chromatography on silica gel using a mixture of CHCl$_3$ and hexane (1:13) as an eluent. Purification with HPLC afforded 5,5′′′-dihexylquaterthiophene (35.3 mg, 71%).\textsuperscript{1}H NMR (400 MHz, CDCl$_3$): 7.03 (d, $J = 3.6$ Hz, 2H), 6.99 (d, $J = 4.0$ Hz, 2H), 6.98 (d, $J = 3.6$ Hz, 2H), 6.68 (d, $J = 3.2$ Hz, 2H), 2.79 (t, $J = 7.6$ Hz, 4H), 4.68 (m, 4H), 1.33-1.22 (m, 12H), 0.89 (m, 6H). \textsuperscript{13}C{\textsuperscript{1}H} NMR (100MHz, CDCl$_3$): 145.7, 136.8, 135.4, 134.5, 124.8, 124.0, 123.6, 123.4, 31.6, 31.6, 30.2, 28.8, 22.6, 14.1.

Evaluation of a Pd(0) formation (Table 1, Figure S1).

A general procedure was as follow (Entry 2). A mixture of Pd(OAc)$_2$ (22.3 mg, 0.10 mmol), 5-hexyl-2,2′-bithiophene (118 µL, 0.50 mmol), KOPiv (140 mg, 1.0 mmol), and ferrocene (90 mg, 0.50 mmol) was stirred in anhydrous DMAc (2.0 mL) at 100 °C under nitrogen atmosphere. A portion of a reaction mixture (ca. 20 µL) was taken out at 1 and 3 h. The NMR yield at each reaction time was obtained from the integral values of the signal for 5,5′′′-dihexylquaterthiophene at 7.03 ppm on the basis of the internal standard (ferrocene).

Sub-stoichiometric reaction (Scheme 3).

A mixture of Pd(OAc)$_2$ (154 mg, 0.50 mmol), 2-butylthiophene (147 µL, 1.0 mmol), 1-bromo-4-octylbenzene (118 µL, 0.50 mmol) and K$_2$CO$_3$ (207 mg, 1.5 mmol) was stirred in anhydrous DMAc (4 mL) for 24 h at 100 °C under nitrogen atmosphere. The reaction mixture was cooled to room temperature and diluted with CHCl$_3$. The organic phase was washed with water and brine, and dried over Na$_2$SO$_4$. The products were separated by column chromatography on silica gel using a mixture of CHCl$_3$ and hexane (1:10) and a following HPLC separation. The following three compounds were isolated as major products: 2-butyl-5-(4-octylphenyl)thiophene (23.5 mg, 0.072 mmol), 5,5′-dibutyl-2,2′-bithiophene (21.5 mg, 0.077 mmol), and 4,4′-dioctyl-1,1′-biphenyl (23.6 mg, 0.062 mmol).

5,5′-dibutyl-2,2′-bithiophene (21.5 mg, 0.077 mmol)\textsuperscript{84} \textsuperscript{1}H NMR (400 MHz, CDCl$_3$): 6.89 (d, $J = 3.2$ Hz, 2H), 6.64 (d, $J = 3.6$ Hz, 2H), 2.78 (t, $J = 7.6$ Hz, 4H), 1.66 (m, 4H), 1.40 (m, 4H), 0.94 (t, $J = 7.6$ Hz, 6H). \textsuperscript{13}C{\textsuperscript{1}H} NMR (100 MHz, CDCl$_3$): 144.8, 135.5, 124.7, 122.7, 33.9, 30.0, 22.3, 14.0. GC-MS: m/z = 278 (Calcd. for [M]$^+$: 278).

4,4′-dioctyl-1,1′-biphenyl
**Evaluation of the catalytic reactions. (Table 2)**

A general procedure was as follow (Entry 2). A mixture of Pd(OAc)$_2$ (2.2 mg, 0.010 mmol), pivalic acid (17 μL, 0.15 mmol), 2-butylthiophene (74 μL, 0.50 mmol), 1-bromo-4-octylbenzene (118 μL, 0.50 mmol), K$_2$CO$_3$ (172 mg, 1.3 mmol) and ferrocene (90 mg, 0.50 mmol) was stirred in anhydrous DMAc (2.0 mL) at 100 °C under nitrogen atmosphere. A portion of a reaction mixture (ca. 20 μL) was taken out at 0, 1, 3, 6, 9, 12, and 24 h. The NMR yield at each reaction time was obtained from the average integral values of the signal for the product at 7.43 and 6.73 ppm on the basis of the internal standard (ferrocene).

**Synthesis of 2,4-dimethyl-5-(4-methylphenyl)-1,3-thiazole (Table 3).** S5

A mixture of Pd(OPiv)$_2$ (3.1 mg, 0.010 mmol), pivalic acid (34 μL, 0.30 mmol), 2,4-dimethyl-1,3-thiazole (107 μL, 1.0 mmol), 1-bromo-4-methylbenzene (171 mg, 1.0 mmol), K$_2$CO$_3$ (345 mg, 2.5 mmol) was stirred in anhydrous DMAc (4.0 mL) at 100 °C for 24 h under nitrogen atmosphere. After cooling to room temperature, organic materials were extracted with a mixture of ethyl acetate and hexane (1:1), and washed with water and brine. The organic phase was dried under Na$_2$SO$_4$ and purified by column chromatography (silica gel) using ethyl acetate and hexane (1:20) as an eluent. 2,4-Dimethyl-5-(4-methylphenyl)-1,3-thiazole was obtained as light brown oil (188.8 mg, 92%).

$^1$H NMR (400 MHz, CDCl$_3$): 7.30 (d, $J = 8.4$ Hz, 2H), 7.21 (d, $J = 8.0$ Hz, 2H), 2.68 (s, 3H), 2.44 (s, 3H), 2.38 (s, 3H). $^{13}$C{${^1}$H} NMR (100 MHz, CDCl$_3$): 162.8, 146.7, 137.4, 131.4, 129.4, 129.3, 129.0, 21.2, 19.1, 16.0.

**Synthesis of 2-(4-methylphenyl)-benzo[b]thiophene.** S6

A mixture of Pd(OPiv)$_2$ (3.1 mg, 0.010 mmol), pivalic acid (34 μL, 0.30 mmol), benzo[b]thiophene (134 mg, 1.0 mmol), 1-bromo-4-methylbenzene (171 mg, 1.0 mmol), K$_2$CO$_3$ (345 mg, 2.5 mmol) was stirred in anhydrous DMAc (4.0 mL) at 100 °C for 24 h under nitrogen atmosphere. After cooling to room temperature, organic materials were extracted with a mixture of ethyl acetate and hexane (1:1), and washed with water and brine. The organic phase was dried under Na$_2$SO$_4$ and purified by column chromatography (silica gel) using ethyl acetate and hexane (1:20) as an eluent. 2-(4-Methylphenyl)benzo[b]thiophene was obtained as white solid (189.1 mg, 84%).
Synthesis of 5,7-bis(4-(trifluoromethyl)phenyl)-2,3-dihydrothieno[3,4-b][1,4]dioxine.  
A mixture of Pd(OPiv)$_2$ (3.1 mg, 0.010 mmol), pivalic acid (34 μL, 0.30 mmol), 3,4-ethylenedioxythiophene (106 μL, 1.0 mmol), 1-bromo-4-trifluoromethylbenzene (276 μL, 2.0 mmol), K$_2$CO$_3$ (345 mg, 2.5 mmol) was stirred in anhydrous DMAc (4.0 mL) at 100 °C for 24 h under nitrogen atmosphere. After cooling to room temperature, organic materials were extracted with a mixture of ethyl acetate and hexane (1:1), and washed with water and brine. The organic phase was dried under Na$_2$SO$_4$ and purified by column chromatography (silica gel) using ethyl acetate and hexane (1:20) as an eluent. 5,7-bis(4-(trifluoromethyl)phenyl)-2,3-dihydrothieno[3,4-b][1,4]dioxine was obtained as white solid (417 mg, 97%).

$^1$H NMR (400 MHz, CDCl$_3$): 7.83 (d, $J = 8.0$ Hz, 4H), 7.59 (d, $J = 8.0$ Hz, 4H), 4.36 (s, 4H). $^{13}$C $^1$H NMR (100 MHz, CDCl$_3$): 139.8, 136.1 (d, $J = 1.5$ Hz), 128.4 (q, $J = 32$ Hz), 126.0, 125.6 (q, $J = 3.6$ Hz), 122.9, 115.2, 64.6.
Scheme S1 Another proposed reaction mechanism for formation of Pd(0) via CMD and disproportionation mechanism.

Scheme S2

Scheme S3 A proposed mechanism for a formation of a biphenyl derivative.
Fig. S1. Time courses for the yields of 5,5''''-dihexylquaterthiophene in the reactions of Table 1.

Fig. S2. ¹H NMR spectra of the reaction mixture and separated products of the reaction in Scheme 2 (CDCl₃, 400 MHz).
Fig. S3. Time-dependent changes of $^1$H NMR spectra in the reaction of Entry 2 in Table 2 (CDCl$_3$, 400 MHz).

Fig. S4. $^1$H NMR spectra of the reaction mixture at 24 h in Figure 2 (a) reaction with 2.0 mol% Pd(OPiv)$_2$ and (b) 1.0 mol% Pd(OPiv)$_2$ (CDCl$_3$, 600 MHz).
Fig. S5 Time courses for the yields of 2-butyl-5-(4-octylphenyl)thiophene with different amount of Pd(OPiv)$_2$. The reaction conditions are shown in Table 2.
Fig. S6 $^1$H NMR spectrum of 2-butyl-5-(4-octylphenyl)thiophene (CDCl$_3$, 400 MHz).

Fig. S7 $^{13}$C($^1$H) NMR spectrum of 2-butyl-5-(4-octylphenyl)thiophene (CDCl$_3$, 100 MHz).
Fig. S8 $^1$H NMR spectrum of 4,4′-dioctyl-1,1′-biphenyl (CDCl$_3$, 400 MHz).

Figure S9 $^{13}$C{$(^1$H}) NMR spectrum of 4,4′-dioctyl-1,1′-biphenyl (CDCl$_3$, 100 MHz).
Fig. S10 $^1$H NMR spectrum of quaterthiophene (CDCl$_3$, 400 MHz).

Fig. S11 $^{13}$C($^1$H) NMR spectrum of quaterthiophene (CDCl$_3$, 100 MHz).
Fig. S12 $^1$H NMR spectrum of 5,5''-dihexylquaterthiophene (CDCl$_3$, 400 MHz).

Fig. S13 $^{13}$C{$^1$H} NMR spectrum of 5,5''-dihexylquaterthiophene (CDCl$_3$, 100 MHz).
Fig. S14 $^1$H NMR spectrum of 5,5'-dibutyl-2,2'-bithiophene (CDCl$_3$, 400 MHz).

Fig. S15 $^{13}$C{$^1$H} NMR spectrum of 5,5'-dibutyl-2,2'-bithiophene (CDCl$_3$, 100 MHz).
Fig. S16 $^1$H NMR spectrum of 2,4-dimethyl-5-(4-methylphenyl)-1,3-thiazole (CDCl$_3$, 400 MHz).

Fig. S17 $^{13}$C$^1$H} NMR spectrum of 2,4-dimethyl-5-(4-methylphenyl)-1,3-thiazole (CDCl$_3$, 100 MHz).
Fig. S18 $^1$H NMR spectrum of (4-methylphenyl)-benzo[b]thiophene (CDCl$_3$, 400 MHz).

Fig. S19 $^{13}$C{$^1$H} NMR spectrum of 2-(4-methylphenyl)-benzo[b]thiophene (CDCl$_3$, 100 MHz).
Fig. S20 $^1$H NMR spectrum of 5,7-bis(4-(trifluoromethyl)phenyl)-2,3-dihydrothieno[3,4-b][1,4]dioxine (CDCl$_3$, 400 MHz).

Fig. S21 $^1$H NMR spectrum of 5,7-bis(4-(trifluoromethyl)phenyl)-2,3-dihydrothieno[3,4-b][1,4]dioxine (CDCl$_3$, 100 MHz).
References