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Abstract: Thieno[3,2-b]thiophene is a structural motif that can be found in many important organic materials. A number of mono-, di- and tetraarylthieno[3,2-b]thiophenes are reported herein.

Key words: cross-coupling reactions, palladium, Suzuki–Miyaura reaction, site selectivity, thieno[3,2-b]thiophene

Thieno[3,2-b]thiophene2 is a structural motif present in a wide range of conducting polymers, p-type organic semiconductors, optoelectronics, nonlinear optics and electroluminescence materials. Thieno[3,2-b]thiophene can be used as a starting material in the synthesis of oligo-functionalized thieno[3,2-b]thiophenes, thienoacenes and helical thienoacenes, which are conducting polymers and chromophores.3b In 2006, McCulloch et al. reported a liquid-crystalline semiconductor polymer (PBT TT) containing thieno[3,2-b]thiophene moieties with a very high charge-carrier mobility (Figure 1).4b Recently, dinaphtho[2,3-b:2′,3′-f]thieno[3,2-b]thiophene (DNTT) and alkylated benzothieno[3,2-b][1]benzothiophene (C13BTBT) were shown to demonstrate a very high thin film mobility of 3.1 cm2/Vs and 17.2 cm2/Vs, respectively, in VD-OFETs.5c Due to intermolecular sulfur–sulfur interactions, materials containing thieno[3,2-b]thiophene may increase the electronic transport between neighboring molecules. The introduction of substituents into the core structure of materials may change electronic properties, solubility as well as molecular packing.6b For tuning electronic properties, heterocycles have been widely functionalized by many methods, especially, by palladium(0)-catalyzed Suzuki reactions.5 Other well-known catalyst systems, such as Pd(PPh3)4 was found to be an efficient catalyst for the current reaction. The Suzuki–Miyaura reactions of 1b in 25–80% yields (Scheme 1 and Table 1). The conditions used were optimized with regard to temperature, solvent, base additive, and water additive. Pd(PPh3)4 was found to be an efficient catalyst for the current reaction. Other well-known catalyst systems, such as Pd(OAc)2/X-Phos, resulted in lower yields of the desired products. All reactions were carried out at 90–110 °C in 4–6 hours.

Scheme 1 Synthesis of 2a–j. Reagents and conditions: (i) 1 (1.0 equiv), Ar1B(OH)2 (1.2 equiv), Pd(PPh3)4 (5 mol%), K3PO4 (2.0 equiv), 110 °C, 4–6 h, solvent (see Table 1).

Figure 1 Some organic materials containing thieno[3,2-b]thiophene and tetrabromofuran,8a based on site-selective palladium(0)-catalyzed Suzuki reactions.

Due to the importance of thieno[3,2-b]thiophene in materials science, we were interested in developing a sequential process for the functionalization of thieno[3,2-b]thiophene via site-selective palladium(0)-catalyzed Suzuki reactions of tetrabromothieno[3,2-b]thiophene with boronic acids. We report herein an efficient synthesis of mono-, di- and tetraarylthieno[3,2-b]thiophene using this strategy.

The Suzuki–Miyaura reactions of 1b (1.0 equiv) with a series of boronic acids (1.2 equiv) resulted in a site-selective formation of 2-aryl-3,5,6-tribromothieno[3,2-b]thiophenes 2a–j in 25–80% yields (Scheme 1 and Table 1). The conditions used were optimized with regard to temperature, solvent, base additive, and water additive. Pd(PPh3)4 was found to be an efficient catalyst for the current reaction. Other well-known catalyst systems, such as Pd(OAc)2/X-Phos, resulted in lower yields of the desired products. All reactions were carried out at 90–110 °C in 4–6 hours.
The structures of the coupling products were established by spectroscopic methods. To confirm the site-selectivity of the Suzuki–Miyaura reactions, the structure of \(2d\) was clearly characterized by X-ray crystal structure and \(^1\)H NMR and \(^{13}\)C NMR analysis (see Figure 2). In agreement with previous reports,\(^7,8,10\) the Suzuki reaction proceeded regioselectively due to the preference of the multibrominated heterocycles to undergo oxidative addition with Pd(0) at the most electron-deficient carbon atoms, for example C2 and/or C5 in the case of 2,3,5,6-tetrabromothieno[3,2-b]thiophene.\(^7a–c\)

**Table 1** Synthesis of 2-Aryl-3,5,6-tribromothieno[3,2-b]thiophene 2a-j

<table>
<thead>
<tr>
<th>2</th>
<th>Ar(^1)B(OH)(_2) used</th>
<th>Solvent/H(_2)O (4:1)</th>
<th>Yield(^a) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>PhB(OH)(_2)</td>
<td>toluene</td>
<td>51</td>
</tr>
<tr>
<td>b</td>
<td>4-MeC(_6)H(_4)B(OH)(_2)</td>
<td>toluene</td>
<td>50</td>
</tr>
<tr>
<td>c</td>
<td>3,5-Me(_2)C(_6)H(_4)B(OH)(_2)</td>
<td>toluene</td>
<td>80</td>
</tr>
<tr>
<td>d</td>
<td>4-t-BuC(_6)H(_4)B(OH)(_2)</td>
<td>toluene</td>
<td>55</td>
</tr>
<tr>
<td>e</td>
<td>4-MeOC(_6)H(_4)B(OH)(_2)</td>
<td>1,4-dioxane(^b)</td>
<td>25</td>
</tr>
<tr>
<td>f</td>
<td>(\beta)-NaphthylB(OH)(_2)</td>
<td>toluene</td>
<td>42</td>
</tr>
<tr>
<td>g</td>
<td>3-EtOC(_6)H(_4)B(OH)(_2)</td>
<td>toluene</td>
<td>55</td>
</tr>
<tr>
<td>h</td>
<td>4-F(_3)CC(_6)H(_4)B(OH)(_2)</td>
<td>toluene</td>
<td>68</td>
</tr>
<tr>
<td>i</td>
<td>acenaphthene-5-boronic acid</td>
<td>toluene</td>
<td>52</td>
</tr>
<tr>
<td>j</td>
<td>3-Me-4-MeOC(_6)H(_4)B(OH)(_2)</td>
<td>toluene</td>
<td>50</td>
</tr>
</tbody>
</table>

\(^a\) Isolated yields.
\(^b\) See refs. 7b and 11.

![Figure 2](image_url) **Figure 2** X-ray crystal structure of 2d

The Suzuki–Miyaura reactions of \(1\) (1.0 equiv) with 2.2 equivalents of arylboronic acids afforded symmetrical 2,5-diaryl-3,6-dibromothieno[3,2-b]thiophenes 3a–d\(^{11}\) in 30–70\% yield (Scheme 2 and Table 2). The reactions again proceeded with very good site-selectivity as confirmed by \(^1\)H NMR and \(^{13}\)C NMR.

Similarly, the unsymmetrically disubstituted 2,5-diaryl-3,6-dibromothieno[3,2-b]thiophenes 4a–c could also be synthesized by our method with predictable selectivity (Scheme 3 and Table 3).\(^{12}\)

![Scheme 2](image_url) **Scheme 2** Synthesis of 3a–d. Reagents and conditions: (i) 1 (1.0 equiv), Ar\(^1\)B(OH)\(_2\) (2.2 equiv), Pd(Ph\(_3\)P)\(_4\) (10 mol%), K\(_2\)PO\(_4\) (4.0 equiv), toluene-H\(_2\)O (4:1), 110 °C, 4–6 h.

<table>
<thead>
<tr>
<th>3</th>
<th>Ar(^1)B(OH)(_2) used</th>
<th>Yield(^a) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>PhB(OH)(_2)</td>
<td>58</td>
</tr>
<tr>
<td>b</td>
<td>4-MeC(_6)H(_4)B(OH)(_2)</td>
<td>70</td>
</tr>
<tr>
<td>c</td>
<td>3,5-Me(_2)C(_6)H(_4)B(OH)(_2)</td>
<td>42</td>
</tr>
<tr>
<td>d</td>
<td>4-t-BuC(_6)H(_4)B(OH)(_2)</td>
<td>30</td>
</tr>
</tbody>
</table>

\(^a\) Isolated yields.

![Scheme 3](image_url) **Scheme 3** Synthesis of 4a–c. Reagents and conditions: (i) 2 (1.0 equiv), Ar\(^1\)B(OH)\(_2\) (1.2 equiv), Pd(Ph\(_3\)P)\(_4\) (10 mol%), K\(_2\)PO\(_4\) (2.0 equiv), toluene-H\(_2\)O (4:1), 110 °C, 4–6 h.

Further coupling of 3b or 4c with 2.4 equivalents of arylboronic acids afforded tetraarylated thieno[3,2-b]thiophenes 5a–c containing four identical aryl groups (Scheme 4 and Table 4). Of note, attempts to prepare triarylated thieno[3,2-b]thiophenes from the dissymmetrical 2,5-diaryl-3,6-dibromothieno[3,2-b]thiophenes 4a–c resulted in an inseparable mixture of 2,3,5- and 2,5,6-triarylated thieno[3,2-b]thiophenes.

Interestingly, 1 could also undergo site-selective Heck coupling with 4-methylstyrene,\(^{13}\) and Sonogashira reaction with 4-methylphenylethylene (Scheme 5).\(^{14}\)
In conclusion, we have showed that the Suzuki–Miyaura reactions of polybromothieno[3,2-b]thiophene can proceed with predictable site-selectivity, preferably at C2 and C5.15 Controlled synthesis of 2-aryl-3,5,6-tribromothieno[3,2-b]thiophenes, 2,5-diaryl-3,6-dibromothieno[3,2-b]thiophenes, and tetraarylated thieno[3,2-b]thiophenes could thus be achieved. Similar regioselectivity was observed for the Heck and Sonogashira couplings of 2,3,5,6-tetrabromothieno[3,2-b]thiophenes. Applications of this coupling strategy in the synthesis of materials incorporating thieno[3,2-b]thiophene moieties are now underway in our laboratory, and will be reported in due course.

References and Notes

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(11) General Procedure for the Synthesis of 2-Aryl-3,5,6-
tribromothieno[3,2-b]thiophene 2a-j: Toluene was
degassed by exchanging between vacuum and a stream of
argon (3 ×). 2,3,5,6-Tetramethoxymethoxythieno[3,2-b]thiophene
(1.0 equiv) and Pd(PPh3)4 (0.05–0.10 equiv) were dissolved in
this degassed toluene (4 mL) at 60–70 °C. To the obtained
solution H2O (1 mL), K2PO4 (2.0 equiv), and aryloboronic
acid (1.2 equiv) were added. The reaction was vigorously
stirred under argon atmosphere at 110 °C until TLC (100% hexane)
showed the complete consumption of the starting
material. The reaction mixture was filtered to remove
insoluble particles. The filtrate was washed several times
with H2O, dried over Na2SO4 and concentrated under
reduced pressure by rotary evaporation. The residue was
purified by SiO2 column chromatography (100% hexane) to
give the product as a white solid. In case of alkoxypyphenyl
boronic acid (ref. 2b). In fact, toluene–H2O gave the same result.
2,3,6-Tribromothieno[3,2-b]thiophene (0.57 mg, 0.125 mmol, 1.0 equiv), Na2CO3
(79.5 mg, 0.75 mmol, 6.0 equiv) and 4-methylstyrene (295.5 mg,
12.5 mmol, 10.0 equiv) were added to the solution of the
catalyst under a stream of argon. The reaction solution was
heated at 90 °C in 5.5 h under argon atmosphere. The
progress of the reaction was monitored by TLC (100% hexane).
Besides the monoalkenyl substituted derivative, small amounts of di- and trialkenyl-substituted derivatives
were also observed. When the starting material was
completely consumed as indicated by TLC, the brownish
mixture was allowed to cool to r.t., filtered through Celite to
remove the brown precipitate. The filtrate was extracted
several times with EtOAc, washed with H2O (3 ×) and dried
over anhydrous Na2SO4. The solvent was removed under
reduced pressure by rotary evaporation and the residue
was purified by SiO2 column chromatography to
give the monobrominated 2,3,5,6-tetramethoxymethoxythieno[3,2-b]
thiophene as a yellow solid (76.1 mg, 42%); mp 126–127
°C. 1H NMR (500 MHz, CDCl3); δ = 7.40 (d, J = 8.0 Hz, 2 H,
Ar), 7.20 (d, J = 16.5 Hz, 1 H), 7.17 (d, J = 8.5 Hz, 2 H,
Ar), 6.98 (d, J = 16.0 Hz, 1 H), 2.36 (s, 3 H, Me). 13C NMR
(500 MHz, CDCl3); δ = 139.4, 139.1, 138.7, 135.1, 133.4,
131.2, 129.6, 126.7, 118.9, 112.5, 107.2, 102.5, 21.4.

(12) General Procedure for the Synthesis of 2,5-Diaryl-3,6-
dibromothieno[3,2-b]thiophenes 4a–c: Toluene was
degassed by exchanging between vacuum and a stream of
argon (3 ×). 2-Ar1-3,5,6-tribromothieno[3,2-b]thiophene 2a: Starting from
1 (230 mg, 0.5 mmol) and phenylboronic acid (74 mg,
0.6 mmol), 2a was isolated (191 mg, 51%) as white crystals;
mp 132–133 °C. 1H NMR (500 MHz, CDCl3): δ = 7.68 (m, 2 H,
Ar), 7.45 (m, 3 H, Ar), 1.36 (m), 2870 (m), 1653 (m), 1598 (m), 746 (m) cm–1. HRMS (EI,
\( \text{M}^+ \)) calcd for C20H14Br2S2: 475.8904; found: 475.8916.

(13) Synthesis of 2-(4-Methylstyryl)-3,5,6-
tribromothieno[3,2-b]thiophene (6): DMF (4 mL)
was saturated with argon by exchanging between vacuum and a
stream of argon (3 ×). Pd(OAc)2 (2.8 mg, 0.0125 mmol, 0.1 equiv) and P(Cy)3 (7.0 mg, 0.025mmol, 0.2 equiv) were
dissolved in this argon-saturated solvent. The brownish
yellow solution was stirred at r.t. for further 30 min to
produce the catalyst. 2,3,5,6-Tetramethoxymethoxythieno[3,2-
b]thiophene (0.57 mg, 0.125 mmol, 1.0 equiv), Na2CO3
(79.5 mg, 0.75 mmol, 6.0 equiv) and 4-methylstyrene (295.5 mg,
12.5 mmol, 10.0 equiv) were added to the solution of the
catalyst under a stream of argon. The reaction solution was
heated at 90 °C in 5.5 h under argon atmosphere. The
progress of the reaction was monitored by TLC (100% hexane).
Besides the monoalkenyl substituted derivative, small amounts of di- and trialkenyl-substituted derivatives
were also observed. When the starting material was
completely consumed as indicated by TLC, the brownish
mixture was allowed to cool to r.t., filtered through Celite to
remove the brown precipitate. The filtrate was extracted
several times with EtOAc, washed with H2O (3 ×) and dried
over anhydrous Na2SO4. The solvent was removed under
reduced pressure by rotary evaporation and the residue
was purified by SiO2 column chromatography (100% hexane) to
give the product as a white solid. In case of alkoxypyphenyl
boronic acid (ref. 2b). In fact, toluene–H2O gave the same result.
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(79.5 mg, 0.75 mmol, 6.0 equiv) and 4-methylstyrene (295.5 mg,
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catalyst under a stream of argon. The reaction solution was
heated at 90 °C in 5.5 h under argon atmosphere. The
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remove the brown precipitate. The filtrate was extracted
several times with EtOAc, washed with H2O (3 ×) and dried
over anhydrous Na2SO4. The solvent was removed under
reduced pressure by rotary evaporation and the residue
was purified by SiO2 column chromatography (100% hexane) to

(14) General Procedure for the Synthesis of 2-Alkynyl-3,5,6-
tribromothieno[3,2-b]thiophene 7: A mixture (1:1) of
dissopropylamine and THF was saturated with argon by exchanging
between vacuum and a stream of argon (3 ×). 2,3,5,6-Tetramethoxymethoxythieno[3,2-b]
thiophene (1.0 equiv), Pd(OAc)2 (0.1 equiv), Pd(PPh3)4 (0.2 equiv) and Cul (0.2 equiv) were
added to this argon-saturated solution. The suspension was
heated to 75 °C while vigorously stirred until it became homogeneous.
To the obtained pale yellow mixture, a solution of arylacetylene (1.2 equiv) in argon-saturated THF
(1.0 mL) was added dropwise in 30 min. The reaction
mixture was heated at 75 °C for 3–6 h. The pale yellow
reaction mixture turned reddish brown when the reaction
completed as indicated by TLC (100% hexane). The reaction mixture was adsorbed on silica gel, dried under reduced
pressure and purified by SiO2 column chromatography to
furnish the monooalkynylated derivative. Besides the desired
product, a significant amount of the symmetric diynes
resulting from the homocoupling reaction of the alkynes
was separated. All attempts to reduce this by-product were not
successful.

(15) CCDC 971825 contains the supplementary crystallographic
data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via
www.ccdc.cam.ac.uk/data_request/cif.