Synthesis of Alkylated Benzo[2,1-*b*:3,4-*b*′]dithiophenes by Annulative Coupling and Their Direct Arylation under Palladium Catalysis

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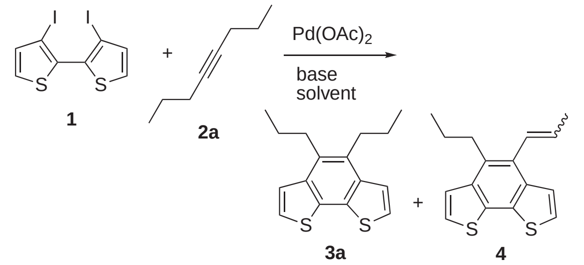
The annulative coupling of 3,3′-diiodo-2,2′-bithiophene with internal alkynes efficiently proceeds in the presence of a palladium catalyst to afford the corresponding benzo[2,1-*b*:3,4-*b*′]dithiophene derivatives. The dithiophenes also undergo palladium-catalyzed direct arylation with aryl bromides at the 2- and 7-positions selectively.

Poly- and oligoaryl compounds involving a thiophene unit have become increasingly important for the organic components of electronic devices, and thus, the synthesis of thiophene-fused aromatic compounds having benzothiophene and thienothiophene skeletons as well as oligothiophenes as the π-conjugated moieties has recently attracted much attention.[1]

On the other hand, the transition-metal-catalyzed annulation of functionalized arenes such as aryl halides with alkynes is now recognized to be a potential tool for preparing condensed aromatics.[2] In the context of our study of catalytic arylation reactions,[3] we have undertaken the annulation of a bithiophene with an aliphatic alkyne, aiming at developing a facile method for constructing an alkylated benzodithiophene unit that has both planarity and solubility. It has been found that 3,3′-diiodo-2,2′-bithiophene (**1**) efficiently couples with internal aliphatic alkynes in a formal [4 + 2] manner by using Pd(OAc)$_2$ and an appropriate tertiary amine as catalyst and base to selectively afford the corresponding annulated benzodithiophenes.[4,5] Furthermore, the catalytic direct arylation of the dithiophenes has been examined.

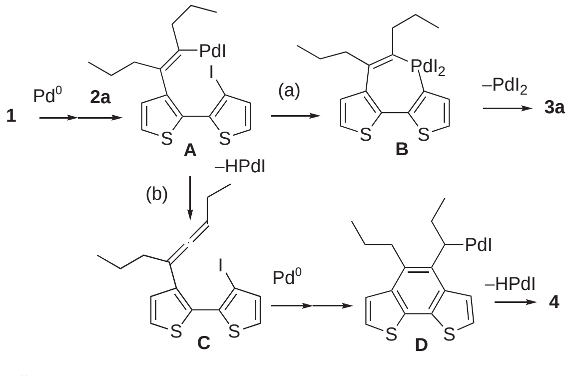
When the diiodide **1** (0.2 mmol) was treated with 4-octyne (**2a**) (0.6 mmol) in the presence of Pd(OAc)$_2$ (0.02 mmol) and Na$_2$CO$_3$ (0.6 mmol) as catalyst and base, respectively, in DMF at 100 °C for 8 h, 4,5-dipropylbenzo[2,1-*b*:3,4-*b*′]dithiophene (**3a**) (48%) was formed along with an inseparable byproduct, 4-propenyl-5-propylbenzo[2,1-*b*:3,4-*b*′]dithiophene (**4**) (5%), the starting material **1** (36%) being recovered (Table 1, Entry 1). The reaction with K$_2$CO$_3$ as base also gave **3a** and **4** (Entry 2).[4a] Use of Ag$_2$CO$_3$ in toluene[4c] unexpectedly led to selective formation of **4**, although the yield was low (Entry 3). It was fortunately found that use of trialkylamines as base in DMF suppressed the formation of **4** and allowed selective synthesis of **3a** with high yield (Entries 4–6). A bulky amine, Cy$_2$NMe (Cy = cyclohexyl) was relatively more effective than Bu$_3$N and the reaction was completed within 2 h at 130 °C even with reduced amounts of Pd(OAc)$_2$ (0.01 mmol) and **2a** (0.24 mmol) (Entry 7). The reaction in *o*-xylene was sluggish (Entry 8). It is noted that the annulation of 3,3′-dibromo-2,2′-bithiophene in place of **1** with **2a** using various phosphine ligands did not proceed.

Table 1. Reaction of 3,3′-diiodo-2,2′-bithiophene (**1**) with 4-octyne (**2a**)[a]



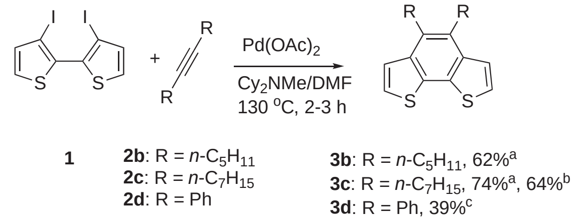
Entry	Base	Solvent	Time/h	Yield[b]/%	
				3a	**4**
1	Na$_2$CO$_3$	DMF	8	48	5
2	K$_2$CO$_3$	DMF	8	54	11
3	Ag$_2$CO$_3$	toluene	8		29[c]
4	Bu$_3$N	DMF	8	>95	
5	CyNMe$_2$	DMF	8	92	
6	Cy$_2$NMe	DMF	4	>95 (84)	
7[d]	Cy$_2$NMe	DMF	2	>95	
8	Cy$_2$NMe	*o*-xylene	8	32	

[a]Reaction conditions: [**1**]:[**2a**]:[Pd(OAc)$_2$]:[base] = 0.2:0.6:0.02:0.6 (in mmol), at 100 °C under N$_2$. [b]GC yield based on the amount of **1** used. Value in parentheses is isolated yield. [c]E/Z = 12:1. [d][**1**]:[**2a**]:[Pd(OAc)$_2$]:[base] = 0.2:0.24:0.01:0.48 (in mmol), at 130 °C.

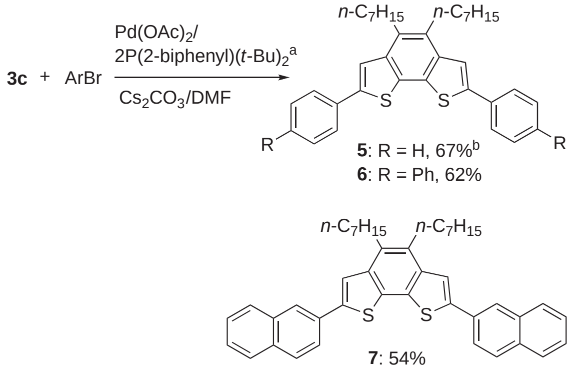


Scheme 1. Proposed mechanism leading to **3a** and **4**.

A plausible mechanism for the reaction of **1** with **2a** leading to **3a** and **4** is illustrated in Scheme 1. The first step involves oxidative addition of **1** to Pd^0 generated in the reaction medium, which is followed by insertion of **2a** to produce vinylpalladium **A**. The subsequent formation of palladacycle **B** (path a) and reductive elimination affords **3a** together with PdI$_2$. The reduction of PdI$_2$ to catalytically active Pd^0 may be enhanced by an amine added.[6] In an alternative pathway from **A**, β-H elimination gives allene **C** (path b).[7] The reaction of **C** with Pd^0 leading to benzylpalladium **D** and β-H elimination in **D** give **4**.[7] Use of an amine base is considered to suppress path b, whereas an inorganic



Scheme 2. Reaction of 3,3′-diiodo-2,2′-bithiophene (**1**) with alkynes **2b**–**2d**. [**1**]:[**2**]:[Pd]:[Cy_2NMe] = [a]0.2:0.24:0.01:0.48, [b]1:1.2:0.01:2.4, [c]1:1.2:0.05:2.4 (in mmol).



Scheme 3. Reaction of **3c** with ArBr. [a][ArBr]:[**3c**]:[$Pd(OAc)_2$]:[Cs_2CO_3] = 0.55:0.25:0.025:0.55 (in mmol), in DMF at 150 °C for 24–48 h. [b][PhBr] = 1.0.

carbonate base induces the undesirable β-H elimination.

The reaction of **1** with 1.2 equiv. of 6-dodecyne (**2b**) and 8-hexadecyne (**2c**) in the presence of 0.01–0.05 equiv. of $Pd(OAc)_2$ for 2–3 h afforded benzodithiophenes **3b** and **3c** in 62–74% isolated yields (Scheme 2). Diphenylacetylene also reacted to produce compound **3d**.

Meanwhile, the catalytic direct arylation of five-membered heteroarenes including thiophenes with aryl halides via C–H bond cleavage as a useful, straightforward method for preparing arylated heteroarenes has recently been a subject of intensive study.[8] While the dithiophene **3** has a condensed resonance structure, it was found to effectively undergo arylation at the 2- and 7-positions on treatment with aryl bromides under similar conditions to those used for the reaction of 2,2′-bithiophene itself in our recent report.[9] Thus, **3c** reacted with bromobenzene, 4-bromobiphenyl, and 2-bromonaphthalene in the presence of $Pd(OAc)_2/P(biphenyl\text{-}2\text{-}yl)(t\text{-}Bu)_2$ and Cs_2CO_3 as catalyst and base, respectively, in DMF to give the corresponding diarylated products **5**–**7**[10] with substantial yields, albeit the conditions were not optimized (Scheme 3).

In summary, we have shown an effective annulative coupling under palladium catalysis to produce 4,5-disubstituted benzo[2,1-*b*:3,4-*b*′]dithiophenes. Not only the compounds are useful scaffolds for constructing soluble π-conjugated systems,[11,12] but also the protocol may provide valuable information for designing related new catalytic cycles.

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10 λ_{abs} (nm, in CH_2Cl_2) **5**: 356; **6**: 377; **7**: 378. λ_{emis} (nm, in CH_2Cl_2) **5**: 396, 416; **6**: 424, 446; **7**: 419, 441.

11 It is worth noting that treatment of compound **3c** with NBS in DMF selectively gave its 2,7-dibromo derivative in 97% yield, which may be a useful substrate for various cross-couplings.

12 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

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