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

Hiroyuki Watanabe, Jun Kumagai, Hayato Tsurugi, Tetsuya Satoh, and Masahiro Miura* Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565-0871

(Received August 27, 2007; CL-070914; E-mail: miura@chem.eng.osaka-u.ac.jp)

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 Na₂CO₃ (0.6 mmol) as catalyst and base, respectively, in DMF at 100 °C for 8h, 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_2CO_3 as base also gave 3a and 4 (Entry 2).^{4a} Use of Ag₂CO₃ 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_2NMe (Cy = cyclohexyl) was relatively more effective than Bu₃N 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.

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,

Table 1. Reaction of 3,3'-diiodo-2,2'-bithiophene (1) with 4-octyne $(2a)^a$



Entry	Base	Solvent	Time/h	Yield ^b /%	
				3 a	4
1	Na ₂ CO ₃	DMF	8	48	5
2	K_2CO_3	DMF	8	54	11
3	Ag_2CO_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	

^aReaction conditions: [1]:[2a]:[Pd(OAc)₂]:[base] = 0.2:0.6: 0.02:0.6 (in mmol), at 100 °C under N₂. ^bGC yield based on the amount of 1 used. Value in parentheses is isolated yield. ^cE/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.

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 PdI₂. The reduction of PdI₂ to catalytically active Pd⁰ 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 Pd⁰ 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]:[Cy₂NMe] = ^a0.2:0.24:0.01:0.48, ^b1:1.2:0.01:2.4, ^c1:1.2:0.05:2.4 (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-2-yl)(*t*-Bu)₂ and Cs₂CO₃ 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.

This work was supported, in part, by Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology, Japan and by the Cooperative Research with Sumitomo Chemical Co., Ltd.

References and Notes

- a) J. Roncali, *Chem. Rev.* **1997**, *97*, 173. b) U. Mitschke, P. Bäuerle, J. Mater. Chem. **2000**, *10*, 1471. c) H. E. Katz, Z. Bao, S. L. Gilat, *Acc. Chem. Res.* **2001**, *34*, 359. d) Y. Sun, Y. Liu, D. Zhu, J. Mater. Chem. **2005**, *15*, 53. e) I. F. Perepichka, D. F. Perepichka, H. Meng, F. Wudl, *Adv. Mater.* **2005**, *17*, 2281. f) K. Takimiya, Y. Kunugi, T. Otsubo, *Chem. Lett.* **2007**, *36*, 578.
- 2 a) R. C. Larock, *Top. Organomet. Chem.*, **2005**, Vol. 14, p. 147. b) J. Tsuji, *Palladium Reagents and Catalysts*, 2nd ed., John Wiley & Sons, Chichester, UK, **2004**, pp. 231–265.
- 3 Selected reports on catalytic annulation of alkynes from our laboratory: a) T. Yasukawa, T. Satoh, M. Miura, M. Nomura, *J. Am. Chem. Soc.* 2002, *124*, 12680. b) S. Kawasaki, T. Satoh, M. Miura, M. Nomura, *J. Org. Chem.* 2003, *68*, 6836. c) K. Ueura, T. Satoh, M. Miura, *J. Org. Chem.* 2007, *72*, 5362.
- 4 a) The related Pd-catalyzed annulation of 1,8-diiodonaphthalene with alkynes was reported. It was described that the reaction with 2a in the presence of Pd(OAc)₂ and K₂CO₃–Bu₄NBr gave the expected acenaphthylene derivative in a moderate yield with contamination of an isomer (13%) bearing one exo-cyclic double bond. It would have a similar structure to that of 4: G. Dyker, *J. Org. Chem.* 1993, 58, 234. b) Cr-Promoted reaction of 2,2'-dibromo-1,1'-biphenyl with alkynes: K. Kanno, Y. Liu, A. Iesato, K. Nakajima, T. Takahashi, *Org. Lett.* 2005, 7, 5453. c) Pd-Catalyzed 1:2 coupling of 1,2-diiodobenzene with alkynes: W. Huang, X. Zhou, K. Kanno, T. Takahashi, *Org. Lett.* 2004, 6, 2429.
- 5 a) Dialkoxynaphtho[2,1-b:3,4-b']dithiophene: J. D. Tovar, A. Rose, T. M. Swager, J. Am. Chem. Soc. 2002, 124, 7762. b) Dialkylbenzo[1,2-b;4,3-b']dithiophene: Y. Nishide, Y. Inagaki, H. Ogura, K. Tanaka, Phosphorus, Sulfur Silicon Relat. Elem. 2005, 180, 1479. c) K. Tanaka, H. Osuga, N. Tsujiuchi, M. Hisamoto, Y. Sakaki, Bull. Chem. Soc. Jpn. 2002, 75, 551.
- 6 F. R. S. Clark, R. O. C. Norman, C. B. Thomas, J. Chem. Soc., Perkin Trans. 1 1975, 121.
- 7 Pd-Catalyzed reaction of aryl bromides with internal aliphatic alkynes to give arylallenes: S. Pivsa-Art, T. Satoh, M. Miura, M. Nomura, *Chem. Lett.* **1997**, 823.
- 8 a) M. Miura, M. Nomura, *Topics in Current Chemistry*, 2002, Vol. 219, p. 211. b) J. Hassan, M. Sévignon, C. Gozzi, E. Schulz, M. Lemaire, *Chem. Rev.* 2002, *102*, 1359. c) M. Miura, T. Satoh, *Top. Organomet. Chem.*, 2005, Vol. 14, p. 55. d) L.-C. Campeau, K. Fagnou, *Chem. Commun.* 2006, 1253. e) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* 2007, *107*, 174. f) T. Satoh, M. Miura, *Chem. Lett.* 2007, *36*, 200.
- 9 A. Yokooji, T. Satoh, M. Miura, M. Nomura, *Tetrahedron* 2004, 60, 6757.
- 10 λ_{abs} (nm, in CH₂Cl₂) **5**: 356; **6**: 377; **7**: 378. λ_{emis} (nm, in CH₂Cl₂) **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 crosscouplings.
- 12 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/ index.html.