

Functionalization of a Simple Dithienylethene via Palladium-Catalyzed Regioselective Direct Arylation

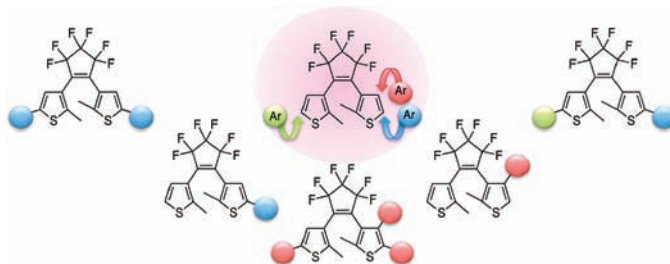
Hiroki Kamiya,[†] Shuichi Yanagisawa,[‡] Satoru Hiroto,[†] Kenichiro Itami,^{*,‡} and Hiroshi Shinokubo^{*,†}

Department of Applied Chemistry, Graduate School of Engineering, Nagoya University, Chikusa-ku, Nagoya 464-8603, Japan, and Department of Chemistry, Graduate School of Science, Nagoya University, Chikusa-ku, Nagoya 464-8602, Japan

hshino@apchem.nagoya-u.ac.jp; itami.kenichiro@a.mbox.nagoya-u.ac.jp

Received October 9, 2011

ABSTRACT



The direct arylation on the thienyl groups of a diarylethene with various aryl iodides efficiently provided arylated dithienylethenes under palladium catalysis. Unsymmetrically substituted dithienylethenes were also synthesized by this protocol. This procedure allows a rapid access to a variety of aryl-substituted dithienylethenes from a single substrate of a simple dithienylethene.

In recent years, organic photochromic compounds have attracted much attention due to the potential applications for photoswitching materials.¹ Among various photochromic systems, diarylethene is one of the most prospective organic molecules owing to their advantageous property over other photochromic compounds in terms of their thermal stability and fatigue resistance as well as their intriguing photochromic behavior.² Diarylethenes often consist of arylated thienyl groups, of which aryl substituents can control the absorption property of the diarylethenes, thus tuning the

color change of the photochromic reaction. However, the synthesis of such aryl-substituted dithienylethenes has been carried out through multistep synthesis, which commenced with the preparation of arylated thiophenes.³

In the past decade, transition-metal-catalyzed direct C–H arylation of aromatic and heteroaromatic compounds has been an active area of research in organic synthesis and organometallic chemistry.^{4,5} In particular, a ligand-controlled regiodivergent direct arylation of thiophenes has been recently reported.⁶ The employment of 2,2′-bipyridyl as a ligand proceeded with α -selectivity to

[†] Department of Applied Chemistry, Graduate School of Engineering.

[‡] Department of Chemistry, Graduate School of Science.

(1) (a) Brown, G. H. *Photochromism*; Wiley-Interscience: New York, NY, 1971. (b) Dürr, H.; Bouas-Laurent, H. *Photochromism: Molecules and Systems*; Elsevier: Amsterdam, 1990. (c) Irie, M. *Photo-reactive Materials for Ultrahigh Density Optical Memory*; Elsevier: Amsterdam, 1994. (d) Raymo, F. M.; Tomasulo, M. *Chem. Soc. Rev.* **2005**, *34*, 327. (e) Gust, D.; Moore, T. A.; Moore, A. L. *Chem. Commun.* **2006**, 1169. (f) Irie, M. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 917.

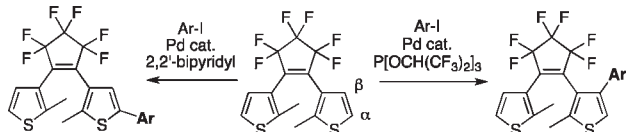
(2) (a) Irie, M. *Chem. Rev.* **2000**, *100*, 1685. (b) Matsuda, K.; Irie, M. *J. Photochem. Photobiol. C* **2004**, *5*, 169. (c) Irie, M.; Uchida, K. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 985. (d) Morimoto, M.; Irie, M. *Chem. Commun.* **2005**, 3895. (e) Tian, H.; Wang, S. *Chem. Commun.* **2007**, 781.

(3) (a) Hanazawa, R.; Sumiya, R.; Horikawa, Y.; Irie, M. *J. Chem. Soc., Chem. Commun.* **1992**, 206. (b) Irie, M.; Sakemura, K.; Okinaka, M.; Uchida, K. *J. Org. Chem.* **1995**, *60*, 8305.

(4) For recent reviews on C–H bond arylation of arenes, see: (a) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792. (b) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2008**, *107*, 174. (c) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev.* **2007**, *36*, 1173. (d) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (e) Kakiuchi, F.; Kochi, T. *Synthesis* **2008**, 3013. (f) Bellina, F.; Rossi, R. *Tetrahedron* **2009**, *65*, 10269. (g) Lei, A.; Liu, W.; Liu, C.; Chen, M. *Dalton Trans.* **2010**, *39*, 10352. (h) Wencel-Delord, J.; Dröge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740. (i) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315. (j) Hirano, K.; Miura, M. *Synlett* **2011**, 294.

afford α -arylated thiophenes,^{6a,c} while the reaction with a $\text{P}[\text{OCH}(\text{CF}_3)_2]_3$ ligand exhibited high β -selectivity in Pd-catalyzed C–H arylation of thiophenes.^{6a,b} This feature is quite useful to construct a diverse list of arylated thiophenes. Here we have applied this synthetic protocol for regioselective functionalization of dithienylethenes. We anticipated that direct arylation on thienyl groups of one single dithienylethene substrate would offer a useful and convenient protocol to access diarylethenes with various aryl-substituted thienyl groups (Scheme 1).

Scheme 1



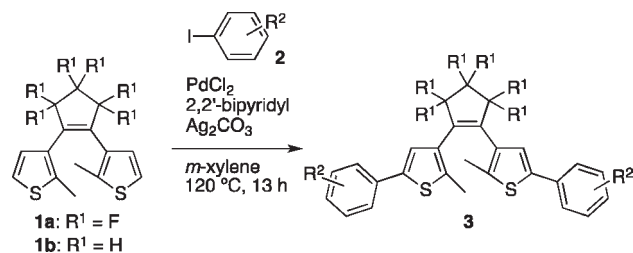
We optimized the reaction conditions for direct arylation of 1,2-di(2-methylthien-3-yl)perfluorocyclopentene (**1a**), since a perfluorocyclopentene unit exhibits the highest reversible durability and photoresponsibility among various platforms for diarylethenes.³ The dithienylethene **1a** was prepared via Suzuki–Miyaura cross-coupling of 1,2-dichlorohexafluorocyclopentene with 2-methyl-3-thienylboronic acid.⁷ The reaction of **1a** with 4-iodoanisole (3.0 equiv), PdCl_2 , 2,2'-bipyridyl, and Ag_2CO_3 in *m*-xylene at 120 °C accomplished α,α' -disubstitution on the thiophene moieties to afford **3a** in 72% yield (Table 1, entry 1). The similar procedure can be applied to various aryl iodides. The reaction with 2- and 3-iodoanisoles provided the corresponding products **3b** and **3c** in 67 and 64% yields, respectively (entries 2 and 3). Utilization of aryl iodides bearing electron-withdrawing groups such as carbonyl and trifluoromethyl substituents was shown to be effective (entries 5 and 6), indicating no noticeable substituent effect. 4-Bromoiodobenzene (**2g**) also participated in this reaction without debromination to furnish the corresponding diarylethene **3g** in 67% yield (entry 7). This feature would be useful for further elaboration of **3g** on the basis of the bromide functionality. A 1-naphthyl group could also be introduced efficiently by the

(5) For selected papers on C–H arylation of thiophenes with haloaromatics, see: (a) Yanagisawa, S.; Sudo, T.; Noyori, R.; Itami, K. *J. Am. Chem. Soc.* **2006**, *128*, 11748. (b) Join, B.; Yamamoto, T.; Itami, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 3644. (c) Roger, J.; Gottumukkala, A. L.; Doucet, H. *ChemCatChem* **2010**, *2*, 20. (d) Liégault, B.; Lapointe, D.; Caron, L.; Vlassova, A.; Fagnou, K. *J. Org. Chem.* **2009**, *74*, 1826. (e) Kobayashi, K.; Sugie, A.; Takahashi, M.; Masui, K.; Mori, A. *Org. Lett.* **2005**, *7*, 5083. (f) Gozzi, C.; Lavenot, L.; Ilg, K.; Penalva, V.; Lemaire, M. *Tetrahedron Lett.* **1997**, *38*, 8867. (g) Liégault, B.; Petrov, I.; Gorelsky, S. I.; Fagnou, K. *J. Org. Chem.* **2010**, *75*, 1047. (h) Glover, B.; Harvey, K. A.; Liu, B.; Sharp, M. J.; Tymoschenko, M. F. *Org. Lett.* **2003**, *5*, 301.

(6) (a) Yanagisawa, S.; Ueda, K.; Sekizawa, H.; Itami, K. *J. Am. Chem. Soc.* **2009**, *131*, 14622. (b) Ueda, K.; Yanagisawa, S.; Yamaguchi, J.; Itami, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 8946. (c) Yanagisawa, S.; Itami, K. *Tetrahedron* **2011**, *67*, 4425.

(7) Hiroto, S.; Suzuki, K.; Kamiya, H.; Shinokubo, H. *Chem. Commun.* **2011**, *47*, 7149.

Table 1. Direct α -Arylation on the Thiophene Moieties of 1,2-Di-(2-methylthien-3-yl)cyclopentenes **1** with Various Aryl Iodides^a



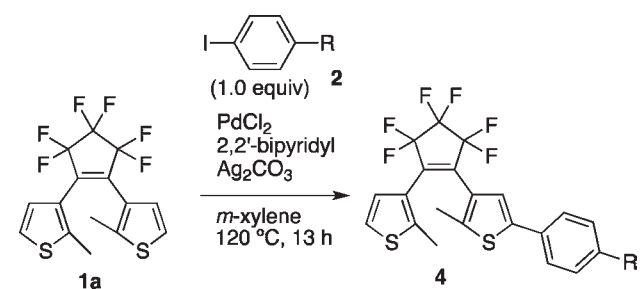
entry	R ¹	aryl iodide	product	yield (%)
1	F		2a → 3a	72 ^b
2	F		2b → 3b	67
3	F		2c → 3c	64
4	F		2d → 3d	74
5	F		2e → 3e	78 ^b
6	F		2f → 3f	63
7	F		2g → 3g	67
8	F		2h → 3h	70
9	H		2a → 3i	44 ^c

^a Reaction conditions: dithienylethene **1** (1.0 equiv), aryl iodide (3.0 equiv), PdCl_2 (30 mol %), 2,2'-bipyridyl (30 mol %), Ag_2CO_3 (3.0 equiv), 120 °C. ^b PdCl_2 (10 mol %) and 2,2'-bipyridyl (10 mol %) were used under otherwise the same reaction conditions. ^c The reaction time was 17 h.

reaction with 1-iodonaphthalene (**2h**) to afford **3h** in good yield (entry 8). The reaction also proceeded with 1,2-dithienylcyclopentene **1b** to produce diarylated product **3i** in 44% yield (entry 9).

Importantly, the employment of 1.0 equiv of aryl iodides resulted in α -arylation on one of the two thienyl groups under otherwise identical reaction conditions. The reaction of 4-iodoanisole, ethyl 4-iodobenzoate, and iodobenzene afforded the corresponding monoarylated dithienylethenes **4a–4c** predominantly in moderate yields (Table 2). In each case, diarylated product **3** was also formed in ca. 10% yield to reduce the yield of the desired

Table 2. Selective α -Monoarylation on the Thiophene Moiety of 1,2-Dithienylcyclopentene **1a**^a

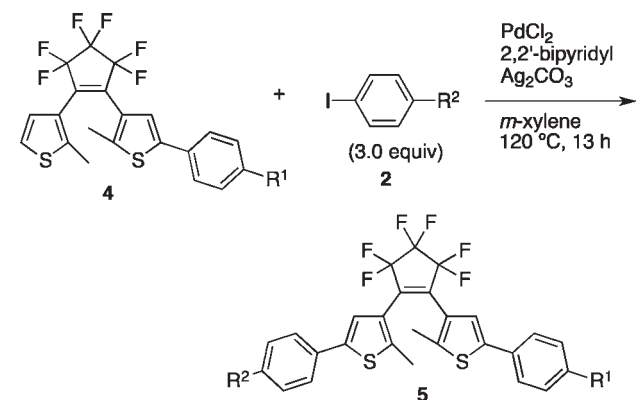


entry	R	product	yield (%)
1	OMe	2a 4a	32
2	CO ₂ Et	2e 4b	36 ^b
3	H	2d 4c	36

^a Reaction conditions: dithienylethene **1a** (1.0 equiv), aryl iodide (1.0 equiv), PdCl₂ (30 mol %), 2,2'-bipyridyl (30 mol %), Ag₂CO₃ (1.0 equiv), *m*-xylene, 120 °C, 13 h. ^b PdCl₂ (10 mol %) and 2,2'-bipyridyl (10 mol %) were used under otherwise the same reaction conditions.

compound **4**. The monoarylated products **4** are useful for the construction of unsymmetrically substituted dithienylethenes (Table 3). For example, the direct arylation of **4a** with ethyl 4-iodobenzoate provided unsymmetrically substituted dithienylethene **5a** with 4-methoxyphenyl and 4-ethoxycarbonylphenyl groups in 40% yield.

Table 3. Synthesis of Unsymmetrically Substituted Dithienylethene **5**

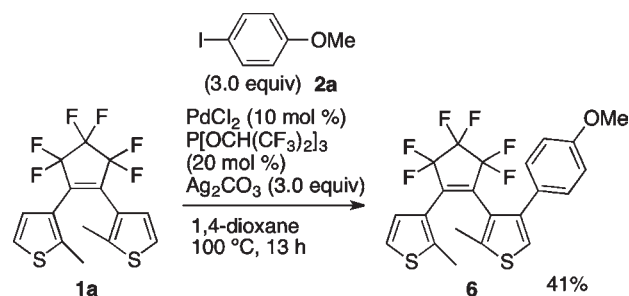


entry	R ¹	R ²	product	yield (%)
1	OMe	4a CO ₂ Et	2e 5a	40 ^a
2	H	4c OMe	2a 5b	40 ^b
3	H	4c CO ₂ Me	2i 5c	37 ^b

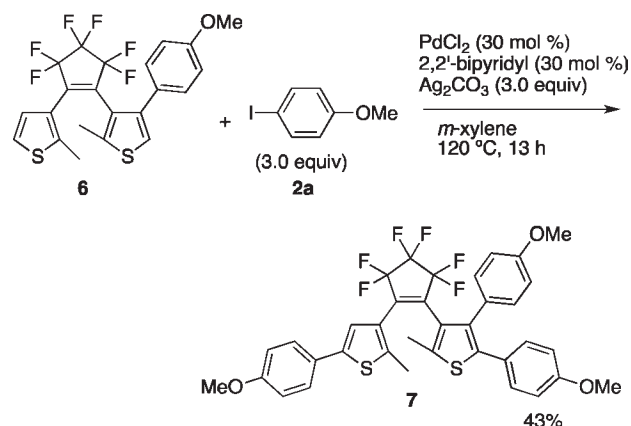
^a Reaction conditions: diarylethene **4** (1.0 equiv), aryl iodide **2e** (3.9 equiv), PdCl₂ (39 mol %), 2,2'-bipyridyl (39 mol %), Ag₂CO₃ (3.9 equiv), *m*-xylene (0.30 mL), 120 °C, 13 h. ^b Aryl iodide **2** (3.0 equiv), PdCl₂ (30 mol %), and 2,2'-bipyridyl (30 mol %) were used under otherwise the same reaction conditions.

We also attempted direct arylation of the thieryl group at the β -position.⁸ The reaction of **1** with 3.0 equiv of 4-iodoanisole, PdCl₂, P[OCH(CF₃)₂]₃, and Ag₂CO₃ in *m*-xylene at 100 °C afforded none of the desired products. After several trials, we eventually found that the use of 1,4-dioxane as the reaction solvent effected β -arylation on only one of the two thieryl groups to provide dithienylethene **6** in 41% yield with high regioselectivity (Scheme 2). Interestingly, β,β' -diarylation was not observed even with the use of an increased amount of 4-iodoanisole. Unfortunately, the use of other iodoarenes such as iodobenzene resulted in quite low yields under the optimized reaction conditions. However, this type of reaction is promising because a diarylethene bearing β -arylated thieryl groups is difficult to synthesize through conventional protocols.⁹

Scheme 2. Direct β -Arylation on the Thiophene Moiety of 1,2-Dithienylcyclopentene **1a**



Scheme 3



(8) For examples of β -arylation of thiophenes, see: (a) Okazawa, T.; Satoh, T.; Miura, M.; Nomura, M. *J. Am. Chem. Soc.* **2002**, *124*, 5286. (b) Vogler, T.; Studer, A. *Org. Lett.* **2008**, *10*, 129. (c) Nakano, M.; Tsurugi, H.; Satoh, T.; Miura, M. *Org. Lett.* **2008**, *10*, 1851. (d) Kirchberg, S.; Tani, S.; Ueda, K.; Yamaguchi, J.; Studer, A.; Itami, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 2387.

(9) Diarylethenes with methyl substituents at β -positions of the thiophene moieties have been synthesized. (a) de Meijere, A.; Zhao, L.; Belov, V. N.; Bossi, M.; Noltemeyer, M.; Hell, S. W. *Chem.—Eur. J.* **2007**, *13*, 2503. (b) Kobatake, S.; Muto, H.; Irie, M. *Chem. Lett.* **2006**, *35*, 102.

The β -arylated product **6** can be subjected to further arylation of the remaining C–H bonds on the thiophene moieties. Treatment of **6** with 3.0 equiv of 4-iodoanisole under the standard α -arylation conditions induced α,α' -disubstitution to afford diarylethene **7** in 43% yield (Scheme 3). The product was assigned by its ^1H NMR spectrum and high-resolution mass spectrum observed at $m/z = 686.1371$ (calcd for $(\text{C}_{36}\text{H}_{28}\text{F}_6\text{O}_3\text{S}_2)^+ = 686.1379$). This is the first example of a diarylethene with an α,β -diarylated thienyl group.

In conclusion, we have demonstrated versatile functionalization of a simple dithienylethene at the α - and β -positions of the thiophene moieties through a Pd-catalyzed direct C–H arylation strategy. The regioselectivity of arylation can be controlled by the proper choice of ligands. The present protocol would be useful for the construction

of diverse diarylethenes including unsymmetrically substituted dithienylethenes.

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research in Priority Areas “New Frontiers in Photochromism (No. 471)” from the Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan and the Global COE program in Chemistry of Nagoya University. H.S. acknowledges Asahi Glass Foundation for financial support.

Supporting Information Available. General procedures and spectral data for new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.