Kobe University Repository : Kernel

PDF issue: 2025-12-05

Synthesis of Thieno[3,2-b]indoles via Halogen Dance and Ligand-Controlled One-Pot Sequential Coupling Reaction

Hayashi, Yuki
Okano, Kentaro
Mori, Atsunori

(Citation)
Organic Letters,20(4):958-961

(Issue Date)
2018-02-16

(Resource Type)
journal article

(Version)
Accepted Manuscript

(Rights)
This document is the Accepted Manuscript version of a Published Work that appeared in final form in Organic Letters, copyright © American Chemical Society after peer review and technical editing by the publisher. To access the final edited and published work see http://dx.doi.org/10.1021/acs.orglett.7b03857

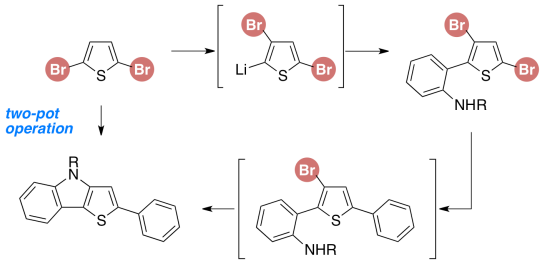
(URL)
https://hdl.handle.net/20.500.14094/90004913

Synthesis of Thieno[3,2-*b*]indoles via Halogen Dance and Ligand-Controlled One-Pot Sequential Coupling Reaction

Yuki Hayashi, Kentaro Okano,* and Atsunori Mori

Department of Chemical Science and Engineering, Kobe University, 1-1 Rokkodai, Nada, Kobe 657-8501, Japan

Supporting Information Placeholder



ABSTRACT: A two-pot synthesis of thieno[3,2-*b*]indole from 2,5-dibromothiophene is described. A halogen dance of 2,5-dibromothiophene was performed with LDA, and subsequent Negishi coupling was performed with 2-iodoaniline derivatives to provide the corresponding coupling products. The resulting two bromo groups have different reactivities, which were utilized for the one-pot Suzuki–Miyaura coupling/intramolecular Buchwald–Hartwig amination to produce thieno[3,2-*b*]indole via an assisted tandem catalysis that involved in situ ligand exchange.

Thiophene-fused indoles are an important class of π-extended functional molecules and medicinal compounds.[1] Among them, thieno[3,2-*b*]indole is often found in numerous reports; substantial efforts have been focused on the development of synthetic methods for these compounds (Figure 1).[1l,1n,2] The reported syntheses of thieno[3,2-*b*]indole are categorized by C–N bond formation as follows: (1) insertion of nitrene via the thermolysis of the azide[3] or reduction of the nitro group[4], (2) amination of thienyl bromide[5], or (3) copper-catalyzed C–H amination.[6] From the perspective of operational safety, functional group compatibility, and further functionalization, we focused on the application of our recent work,[7] which included a one-pot

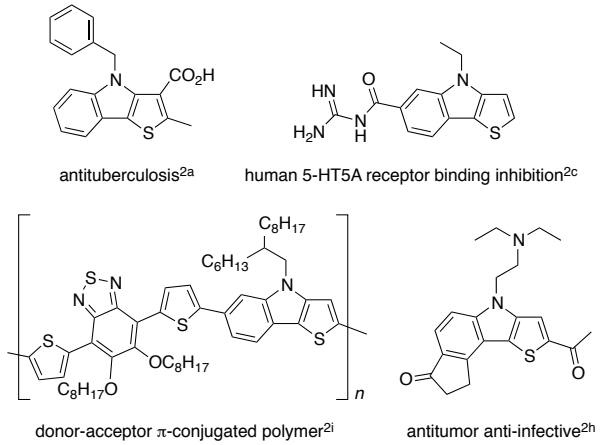
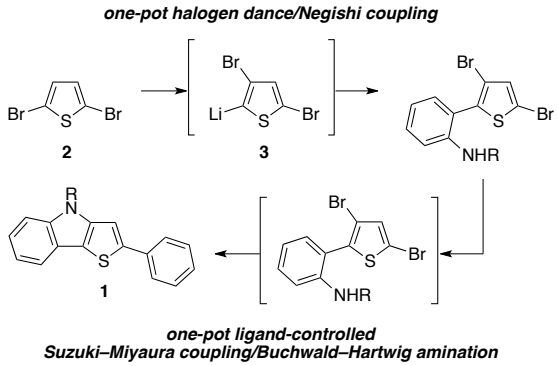


Figure 1. Substituted thienoindoles and related compounds

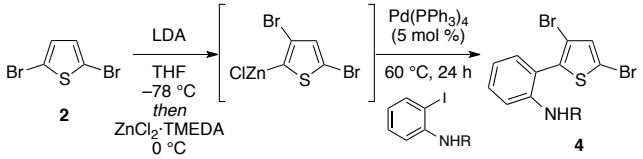
halogen dance/Negishi coupling, which allows regiocontrolled synthesis of multiple arylated thiophenes or furans. Compared with conventional stepwise transformations, the LDA (lithium diisopropylamide)-mediated halogen dance reaction[8] leads to the formation of two chemical bonds in one pot, which reduces a number of reaction pots. Regardless of this synthetic potential, the substrate scope has not been fully investigated, probably owing to the difficulty of controlling the reactivity of transient thienyl anion species. In this study, we further explored the synthetic utility of one-pot halogen dance/Negishi coupling and achieved divergent two-pot synthesis of thieno[3,2-*b*]indoles **1** from 2,5-dibromothiophene (**2**) via a transient thienyl lithium species **3** via the development of one-pot ligand-controlled Suzuki–Miyaura coupling/Buchwald–Hartwig amination that utilize assisted tandem catalysis (Scheme 1).

Scheme 1. Two-pot synthesis of thieno[3,2-*b*]indoles



We first examined the effects of substituents on the nitrogen atom of 2-iodoaniline derivatives for Negishi coupling[9] using the 3,5-dibromothienyl lithium species, which was generated after the halogen dance of 2,5-dibromothiophene (Table 1). In a previous report,[8] halogen dance was performed with LDA[10] at −78 °C. The resulting reaction mixture was treated with $ZnCl_2$·TMEDA[11] at 0 °C, and the thienylzinc species that was generated in situ was subjected to the coupling conditions. In preliminary experiments, Cbz- or Boc-protected 2-iodoaniline derivatives were converted to the corresponding products **4a** and **4b** in low yields (entries 1 and 2). In both cases, the iodoaniline derivatives were recovered, which indicated that the thienylzinc species would be protonated by the relatively acidic carbamate proton. The same reaction with unprotected 2-iodoaniline led to the formation of the desired product **4c** in better yield, which also supported the above postulate (entry 3). In contrast to the electron-withdrawing Cbz and Boc groups, phenyl, butyl, and benzyl groups on the nitrogen resulted in satisfactory yields of products **4d**–**4f** (entries 4–6).

Table 1. Substituent effects in Negishi coupling[a]

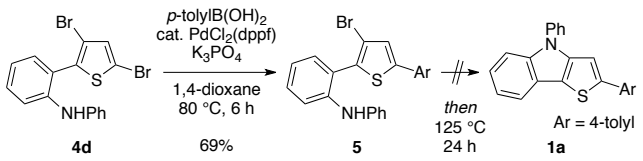


entry	R	product	yield (%)[b]
1	Cbz	**4a**	16
2	Boc	**4b**	23
3	H	**4c**	53
4	Ph	**4d**	69
5	*n*-Bu	**4e**	52
6	Bn	**4f**	58

[a] Reaction conditions: 2,5-dibromothiophene (**2**) (0.70 mmol, 1.4 equiv), LDA (0.65 mmol, 1.3 equiv), THF, −78 °C, 5 min; $ZnCl_2$·TMEDA (0.70 mmol, 1.4 equiv), 0 °C, 15 min; $Pd(PPh_3)_4$ (0.025 mmol, 5 mol %), 2-iodoaniline derivative (0.50 mmol, 1.0 equiv), 60 °C, 24 h. [b] Isolated yield.

With the dibromothiophenes bearing the 2-aminophenyl moieties in hand, we focused on the one-pot synthesis of p-conjugated thienoindoles by Suzuki–Miyaura coupling[12] and intramolecular Buchwald–Hartwig amination.[13] In the preliminary experiments, the amination of dibromothiophene **4d** led to the formation of a complex mixture. We then attempted arylation at the reactive α- position of thiophene and subsequent amination of the residual β-bromo group

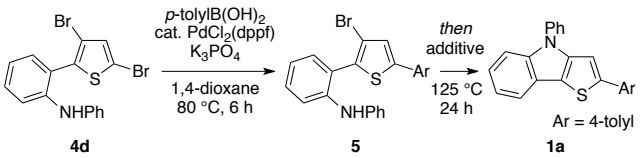
Scheme 2. Initial attempt for one-pot Suzuki–Miyaura coupling/intramolecular Buchwald–Hartwig amination



(Scheme 2). According to our previous report,[7a] we performed Suzuki–Miyaura coupling in the presence of 5 mol % $PdCl_2$(dppf) at 80 °C and obtained compound **5** in 69% yield. Further heating at 125 °C for 24 h did not produce thienoindole **1a**, even with an increased amount of K_2CO_3 (4 equiv).

We then examined additives for achieving the one-pot Suzuki–Miyaura coupling/intramolecular Buchwald–Hartwig amination (Table 2). NaO*t*-Bu proved ineffective in this case, even with a prolonged reaction time (24 h) at 125 °C (entries 1 and 2). Additional monodentate *t*-Bu_3P·HBF_4[13e] (20 mol %) significantly promoted the amination to produce the desired product **1a**, in 69% yield (entry 3). A reduced amount of the phosphorus ligand led to lower yields of thienoindole **1a** with recoveries of arylated intermediate **5** (entries 4 and 5). These results indicate that monodentate *t*-Bu_3P should coordinate to the palladium with bidentate DPPF to generate the active catalyst in situ for the intramolecular amination. The one-pot sequential reaction could be also performed at 125 °C for 5 h via a one-shot addition that includes all the reagents to produce the same thieno[3,2-*b*]indole **1a** in 57% yield (Scheme 3). The established protocol is operationally simple and provides direct access to compounds **5** and **1a** in satisfactory yields.

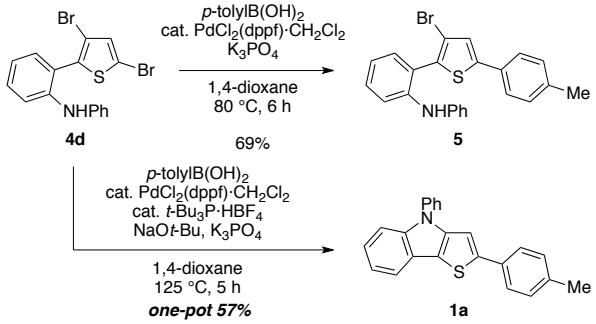
Table 2. One-pot Suzuki–Miyaura coupling/intramolecular Buchwald–Hartwig amination [a]



entry	additive	**1a** (%)[b]
1	none	0
2	NaO*t*-Bu (3 equiv)	0
3	*t*-Bu_3P·HBF_4 (20 mol %), NaO*t*-Bu	69
4	*t*-Bu_3P·HBF_4 (10 mol %), NaO*t*-Bu	40
5	*t*-Bu_3P·HBF_4 (5 mol %), NaO*t*-Bu	19

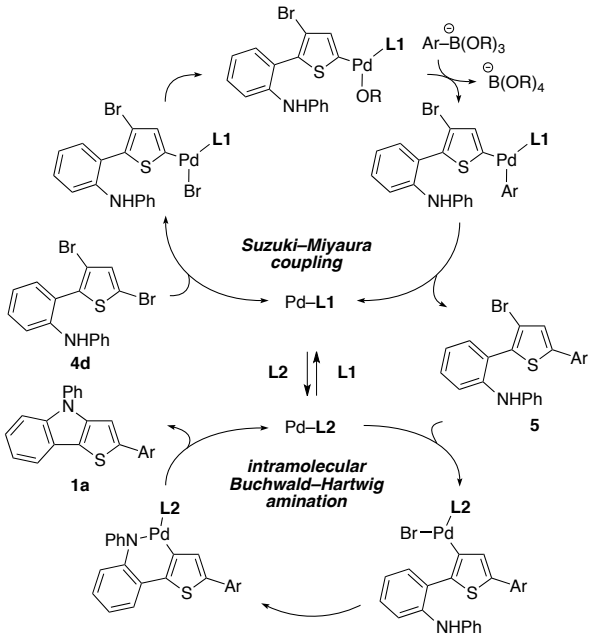
[a] Reaction conditions: dibromothiophene **4d** (0.20 mmol), $ArB(OH)_2$ (0.24 mmol, 1.2 equiv), $PdCl_2$(dppf)·CH_2Cl_2 (0.010 mmol, 5 mol %), K_3PO_4 (0.40 mmol, 2.0 equiv), 1,4-dioxane, 80 °C, 6 h; *t*-Bu_3P·HBF_4 (0.040 mmol, 20 mol %), NaO*t*-Bu (0.60 mmol, 3.0 equiv), 125 °C, 24 h (sealed tube). [b] Isolated yield.

Scheme 3. Ligand-controlled one-pot Suzuki–Miyaura coupling/intramolecular Buchwald–Hartwig amination



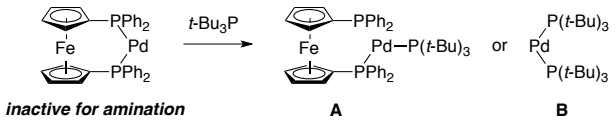
Our proposed one-pot assisted tandem catalytic transformation is illustrated in Scheme 4. The first cross coupling (Suzuki–Miyaura coupling) is catalyzed by the combination of Pd(0) and DPPF (**L1**), which exclusively provides the corresponding arylated thiophene **5**. The second reaction (intramolecular Buchwald–Hartwig amination) is promoted by Pd(0)–*t*-Bu_3P (**L2**), which is generated in situ via ligand exchange. We also performed the one-pot arylation/ intramolecular Buchwald–Hartwig amination using compound **4d** with Pd(*t*-$Bu_3P)_2$ to provide thienoindole **1a** in 16% yield. We observed neither starting dibromothiophene **4d** nor arylated thiophene **5**. These results indicate that both **L1** and **L2** are required for achieving the one-pot reaction and support the assisted tandem catalytic pathway.[14]

Scheme 4. Plausible assisted tandem catalytic pathway for the one-pot Suzuki–Miyaura coupling/intramolecular Buchwald–Hartwig amination



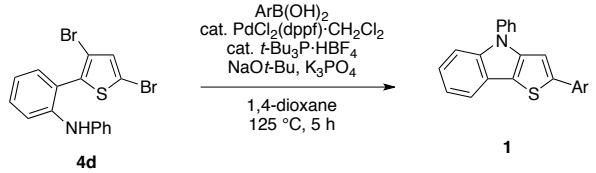
Scheme 3 demonstrates that the Pd–DPPF complex was converted to another catalyst via the addition of the second phosphorus ligand *t*-Bu_3P (Scheme 5). We cannot exclude the possibility that bidentate DPPF was exchanged by two molecules of *t*-Bu_3P. The results in Table 2 indicate that *t*-Bu_3P is crucial for the intramolecular amination. Either **A** or **B**, or both, could catalyze the amination to provide thieno[3,2-*b*]indole **1a**.

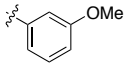
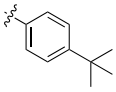
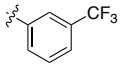
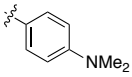
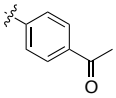
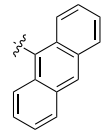
Scheme 5. Mechanistic implications for the active catalyst in the intramolecular Buchwald–Hartwig amination



Subsequently, we investigated the scope and limitations of the one-pot Suzuki–Miyaura coupling/Buchwald–Hartwig amination (Table 3). Phenyl and 4-*tert*-butylphenyl groups were introduced in comparable yields with the *p*-tolyl group, as shown in Scheme 3. The electron-donating 4-dimethylaminophenyl group was introduced to provide the corresponding thienoindole **1d** in 14% yield; however, 4-acetylphenylboronic acid was not reactive and the desired product **1e** was obtained in 29% yield with concomitant generation of unidentified byproducts. A similar tendency was observed for meta-substituted phenylboronic acids. The reaction conditions were not applied to 4-nitrophenylboronic acid due to its low solubility in 1,4-dioxane; alternative reaction conditions B including water as a co-solvent, which proved effective for producing the corresponding product **1h**. The reaction conditions B were also effective for improving the yield of products **1b**, **1e**, **1g**, and **1i**.

Table 3. Scope of the one-pot Suzuki–Miyaura coupling/intramolecular Buchwald–Hartwig amination[a]

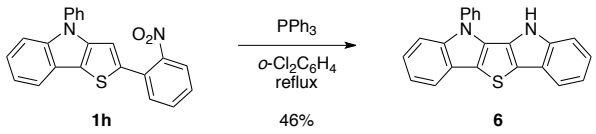


product (Ar)	yield (%)[b]	product (Ar)	yield (%)[b]
1b	34 (89[c])	**1f** 	57
1c 	45	**1g** 	9 (48[c])
1d 	14	**1h**	–[d] (43[c])
1e 	29 (60[c])	**1i** 	28 (45[c])

[a] Reaction conditions A: dibromothiophene **4d** (0.20 mmol), $ArB(OH)_2$ (0.24 mmol, 1.2 equiv), $PdCl_2(dppf)\cdot CH_2Cl_2$ (0.010 mmol, 5 mol %), *t*-$Bu_3P\cdot HBF_4$ (0.040 mmol, 20 mol %), NaO*t*-Bu (0.60 mmol, 3.0 equiv), K_3PO_4 (0.40 mmol, 2.0 equiv), 1,4-dioxane, 125 °C, 5 h (sealed tube). [b] Isolated yield. [c] Reaction conditions B: dibromothiophene **4d** (0.20 mmol), $ArB(OH)_2$ (0.24 mmol, 1.2 equiv), $Pd(PPh_3)_4$ (0.020 mmol, 10 mol %), *t*-$Bu_3P\cdot HBF_4$ (0.080 mmol, 40 mol %), NaO*t*-Bu (0.60 mmol, 3.0 equiv), K_3PO_4 (1.40 mmol, 7.0 equiv), 1,4-dioxane/H_2O (4:1), 125 °C, 22 h (sealed tube). [d] Not detected.

Thienoindole **1h** bearing a 2-nitrophenyl group was confirmed to be a potential synthetic intermediate for an unsymmetrical indolothienoindole (Scheme 6). The nitro group was reduced under heating conditions,[15] and the nitrene intermediate reacted with the proximal thiophene to produce **6**[16] in a moderate yield.

Scheme 6. Synthesis of unsymmetrical indolothienoindole



In conclusion, we described the two-pot synthesis of thieno[3,2-*b*]indole from 2,5-dibromothiophene. Halogen dance and subsequent Negishi coupling with 2-iodoaniline derivatives provided the coupling product, which underwent ligand-controlled one-pot Suzuki–Miyaura coupling/ intramolecular Buchwald–Hartwig amination to produce thieno[3,2-*b*]indoles.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.xxxxxxx. Experimental procedure, compound characterization data, and copies of ^{1}H and ^{13}C-NMR spectra for all new compounds (PDF).

AUTHOR INFORMATION

Corresponding Author

*E-mail: okano@harbor.kobe-u.ac.jp

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

This work was financially supported by JSPS KAKENHI, Grant Numbers JP16K05774 in Scientific Research (C), JP16H01153 in the Middle Molecular Strategy, Creation of Innovation Centers for Advanced Interdisciplinary Research Areas (Innovative Bioproduction Kobe), and Kawanishi Memorial ShinMaywa Education Foundation. This work was performed under the Cooperative Research Program of "Network Joint Research Center for Materials and Devices."

REFERENCES

(1) Thieno[2,3-*b*]indoles, see: (a) Kobayashi, G.; Furukawa, S.; Matsuda, Y.; Natsuki, R. *Yakugaku Zasshi* **1969**, *89*, 58. (b) Binder, D.; Noe, C. R.; Prager, B. C. *Arch. Pharm.* **1981**, *314*, 751. (c) Kanbe, K.; Naganawa, H.; Nakamura, K. T.; Okami, Y.; Takeuchi, T. *Biosci. Biotechnol. Biochem.* **1993**, *57*, 636. (d) Olesen, P. H.; Hansen, J. B.; Engelstoft, M. *J. Heterocycl. Chem.* **1995**, *32*, 1641. (e) Engqvist, R.; Javaid, A.; Bergman, J. *Eur. J. Org. Chem.* **2004**, 2589. (f) Butin, A. V.; Tsiunchik, F. A.; Abaev, V. T.; Zavodnik, V. E. *Synlett* **2008**, 1145. (g) Moghaddam, F. M.; Saeidian, H.; Mirjafary, Z.; Taheri, S.; Kheirjou, S. *Synlett* **2009**, 1047. (h) Boeini, H. Z. *Helv. Chim. Acta* **2009**, *92*, 1268. (i) Singh, P. P.; Yadav, A. K.; Ila, H.; Junjappa, H. *Eur. J. Org. Chem.* **2011**, 4001. (j) Acharya, A.; Kumar, S. V.; Ila, H. *Chem. Eur. J.* **2015**, *21*, 17116. (k) Egorov, D. I. *Chem. Heterocycl. Compd.* **2016**, *52*, 779. (l) Irgashev, R. A.; Karmatsky, A. A.; Rusinov, G. L.; Charushin, V. N. *Org. Lett.* **2016**, *18*, 804. Thieno[3,4-*b*]indoles, see: (m) Shafiee, A.; Sattari, S. *J. Heterocycl. Chem.* **1982**, *19*, 227. (n) Pham, N. N.; Parpart, S.; Grigoryan, S.; Ngo, T. N.; Dang, T. T.; Ghochikyan, T. V.; Saghyan, A. S.; Ehlers, P.; Langer, P. *Eur. J. Org. Chem.* **2017**, 538.

(2) (a) Grinev, A. N.; Trofimkin, Y. I.; Lomanova, E. V.; Pershin, G. N.; Polukhina, L. M.; Nikolaeva, I. S.; Pushkina, T. V.; Filitis, L. N.; Golovanova, E. A.; Okinshevich, O. V. *Khim.-Farm. Zh.***1982**, *16*, 1332. (b) Mezlova, M.; Aaron, J. J.; Svoboda, J.; Adenier, A.; Maurel, F.; Chane-Ching, K. *J. Electroanal. Chem.* **2005**, *581*, 93. (c) Kinoyama, I.; Miyamoto, S.; Hoshii, H.; Miyazaki, T.; Yamazaki, M. WO2008096791A1, 2008. (d) Karthikeyan, S. V.; Perumal, S.; Shetty, K. A.; Yogeeswari, P.; Sriram, D. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3006. (e) Zhang, X. H.; Cui, Y.; Katoh, R.; Koumura, N.; Hara, K. *J. Phys. Chem. C* **2010**, *114*, 18283. (f) Al-Trawneh, S. A.; El-Abadelah, M. M.; Zahra, J. A.; Al-Taweel, S. A.; Zani, F.; Incerti, M.; Cavazzoni, A.; Vicini, P. *Biorg. Med. Chem.* **2011**, *19*, 2541. (g) Kamimoto, N.; Schollmeyer, D.; Mitsudo, K.; Suga, S.; Waldvogel, S. R. *Chem. Eur. J.* **2015**, *21*, 8257. (h) Gurova, K.; Rydkina, E. B.; Wade, W. WO2015050472A1, 2015. (i) Huang, H.; Li, Q.; Qiu, M.; Wang, Z.; Zhang, X.; Liu, S.; Fu, N.; Zhao, B.; Yang, R.; Huang, W. *RSC Advances* **2016**, *6*, 45873. (j) Eom, Y. K.; Kang, S. H.; Choi, I. T.; Yoo, Y. J.; Kim, J. H.; Kim, H. K. *J. Mater. Chem. A* **2017**, *5*, 2297. (k) Acharya, A.; Gautam, V.; Ila, H. *J. Org. Chem.* **2017**, *82*, 7920. (l) Zhang, T.; Han, H.; Zou, Y.; Lee, Y.-C.; Oshima, H.; Wong, K.-T.; Holmes, R. J. *ACS Appl. Mater. Interfaces* **2017**, *9*, 25418.

(3) (a) Smith, P. A. S.; Boyer, J. H. *J. Am. Chem. Soc.* **1951**, *73*, 2626. (b) Pudlo, M.; Csanyi, D.; Moreau, F.; Hajos, G.; Riedl, Z.; Sapi, J. *Tetrahedron* **2007**, *63*, 10320. (c) Jana, N.; Nguyen, Q.; Driver, T. G. *J. Org. Chem.* **2014**, *79*, 2781. (d) Alt, I. T.; Plietker, B. *Angew. Chem. Int. Ed.* **2016**, *55*, 1519.

(4) (a) Kaszynski, P.; Dougherty, D. A. *J. Org. Chem.* **1993**, *58*, 5209. (b) Appukkuttan, P.; Van der Eycken, E.; Dehaen, W. *Synlett* **2005**, 127. (c) Koumura, N.; Hara, K. *Heterocycles* **2013**, *87*, 275. (d) Huang, H.; Qiu, M.; Li, Q.; Liu, S.; Zhang, X.; Wang, Z.; Fu, N.; Zhao, B.; Yang, R.; Huang, W. *J. Mater. Chem. C* **2016**, *4*, 5448. (e) Srour, H.; Doan, T.-H.; Silva, E. D.; Whitby, R. J.; Witulski, B. *J. Mater. Chem. C* **2016**, *4*, 6270.

(5) Huang, Y.; Wu, D.; Huang, J.; Guo, Q.; Li, J.; You, J. *Angew. Chem., Int. Ed.* **2014**, *53*, 12158.

(6) Takamatsu, K.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2014**, *16*, 2892.

(7) (a) Okano, K.; Sunahara, K.; Yamane, Y.; Hayashi, Y.; Mori, A. *Chem. Eur. J.* **2016**, *22*, 16450. (b) Miyagawa, N.; Murase, Y.; Okano, K.; Mori, A. *Synlett* **2017**, *28*, 1106.

(8) (a) Gronowitz, S. *Recent advances in the chemistry of thiophenes*; Academic Press: Cambridge, England, 1963; Vol. 1. (b) Fröhlich, J. In *Prog. Heterocycl. Chem.*; Padwa, A., Ed.; Pergamon Press: 1994; Vol. 6, p 1. (c) Iddon, B. *Heterocycles* **1995**, *41*, 533. (d) Gronowitz, S.; Holm, B. *Acta Chem. Scand.* **1969**, *23*, 2207. (e) Kano, S.; Yuasa, Y.; Yokomatsu, T.; Shibuya, S. *Heterocycles* **1983**, *20*, 2035. (f) Sauter, F.; Fröhlich, H.; Kalt, W. *Synthesis* **1989**, 771. (g) Froehlich, H.; Kalt, W. *J. Org. Chem.* **1990**, *55*, 2993. (h) Peyron, C.; Navarre, J.-M.; Van Craynest, N.; Benhida, R. *Tetrahedron Lett.* **2005**, *46*, 3315. (i) Getmanenko, Y. A.; Tongwa, P.; Timofeeva, T. V.; Marder, S. R. *Org. Lett.* **2010**, *12*, 2136. (j) Duan, X.-F.; Zhang, Z.-B. *Heterocycles* **2005**, *65*, 2005. (k) Shono, K.; Sumino, Y.; Tanaka, S.; Tamba, S.; Mori, A. *Org. Chem. Front.* **2014**, *1*, 678. (l) Schnurch, M.; Spina, M.; Khan, A. F.; Mihovilovic, M. D.; Stanetty, P. *Chem. Soc. Rev.* **2007**, *36*, 1046.

(9) (a) Negishi, E.-I.; King, A. O.; Okukado, N. *J. Org. Chem.* **1977**, *42*, 1821. (b) Negishi, E.-I. *Acc. Chem. Res.* **1982**, *15*, 340. (c) Negishi, E. I. *Angew. Chem. Int. Ed.* **2011**, *50*, 6738.

(10) (a) Hamell, M.; Levine, R. *J. Org. Chem.* **1950**, *15*, 162. (b) Levine, R.; Fernelius, W. C. *Chem. Rev.* **1954**, *54*, 449.

(11) (a) Isobe, M.; Kondo, S.; Nagasawa, N.; Goto, T. *Chem. Lett.* **1977**, *6*, 679. (b) Snégaroff, K.; Komagawa, S.; Chevallier, F.; Gros, P. C.; Golhen, S.; Roisnel, T.; Uchiyama, M.; Mongin, F. *Chem. Eur. J.* **2010**, *16*, 8191.

(12) (a) Miyaura, N.; Yanagi, T.; Suzuki, A. *Synth. Commun.* **1981**, *11*, 513. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

(13) (a) Paul, F.; Patt, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1994**, *116*, 5969. (b) Guram, A. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 7901. (c) Hamann, B. C.; Hartwig, J. F. *J. Am. Chem. Soc.* **1998**, *120*, 7369. (d) Old, D. W.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 9722. (e) Hartwig, J. F.; Kawatsura, M.; Hauck, S. I.; Shaughnessy, K. H.; Alcazar-Roman, L. M. *J. Org. Chem.* **1999**, *64*, 5575.

(14) (a) Fogg, D. E.; dos Santos, E. N. *Coord. Chem. Rev.* **2004**, *248*, 2365–2379. (b) Shindoh, N.; Takemoto, Y.; Takasu, K. *Chem. Eur. J.* **2009**, *15*, 12168. (c) Kato, H.; Ishigame, T.; Oshima, N.; Hoshiya, N.; Shimawaki, K.; Arisawa, M.; Shuto, S. *Adv. Synth. Catal.* **2011**, *353*, 2676. (d) Schmidt, B.; Krehl, S.; Hauke, S. *J. Org. Chem.* **2013**, *78*, 5427.

(15) Liu, S.-G.; Su, W.-Y.; Pan, R.-K.; Zhou, X.-P.; Wen, X.-L.; Chen, Y.-Z.; Wang, S.; Shi, X.-B. *Spectrochim. Acta, Part A* **2013**, *103*, 417.

(16) Ahn, H. C.; Cho, Y. J.; Kwon, H. J.; Kim, B. O.; Kim, S. M. WO2011132865A1, 2011.