

Facile Synthesis of 2,5-Diarylthiazoles via Palladium-Catalyzed Tandem C–H Substitutions. Design of Tunable Light Emission and Liquid Crystalline Characteristics

Atsunori Mori,* Akitoshi Sekiguchi, Kentaro Masui, Tomohiro Shimada, Masaki Horie, Kohtaro Osakada, Masuki Kawamoto, and Tomiki Ikeda

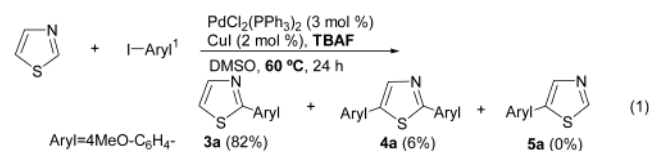
Chemical Resources Laboratory, Tokyo Institute of Technology, 4259 Nagatsuta, Yokohama 226-8503, Japan

Received October 12, 2002; E-mail: amori@res.titech.ac.jp

The transition-metal-catalyzed reaction involving formation of a C–C bond from a specific C–H bond has been a major challenge in organic synthesis. Such a catalytic reaction has been shown to proceed with several late transition metal complexes;^{1,2} however, the major disadvantage of these reactions is that one has to apply a relatively high reaction temperature, higher than 100 °C. In particular, a catalytic substitution reaction of a C–H bond with an organic halide has not been achieved so far at lower temperatures.

Herein, we report that the Pd/Cu-catalyzed C–H bond substitution reaction of thiazole (**1**) in the presence of tetrabutylammonium fluoride (TBAF) as an activator takes place regioselectively under mild conditions. With such a method, a variety of 2,5-diarylthiazole derivatives are synthesized in facile and combinatorial manners. Light-emitting and liquid crystalline characteristics of these molecules are investigated as potential EL materials with polarized light emission.^{3,4}

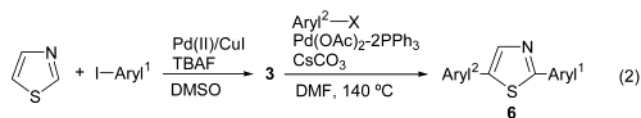
We have been studying a new class of coupling reactions of terminal alkynes and have shown that TBAF serves as a novel and excellent activator for the Pd/Cu-catalyzed reaction to undergo the sp C–H substitution reaction with organic electrophiles.⁵ Hence, we envisaged that sp² C–H substitution would also take place similarly.



Thiazole (**1**), which was a heteroaromatic compound bearing an sp² C–H bond, was chosen as an initial candidate for the coupling, and the Pd/Cu-catalyzed reaction with 4-methoxy-1-iodobenzene (**2a**) was examined in the presence of TBAF. When the reaction was carried out in DMSO at 60 °C, 82% of the product coupled at the 2-position (**3a**) was obtained as shown in eq 1. Worthy of note is the lower reaction temperature, which is remarkably milder among transition-metal-catalyzed C–H substitution with organic electrophiles.^{1c,d} The reaction at a further lower temperature, 40 °C or room temperature, also proceeded, although it took longer reaction periods.⁶ It should also be pointed out that the course of regiochemistry was highly controlled for the reaction to take place at the 2-position. Only 6% of 2,5-diarylated product (**4a**) was obtained, while monosubstituted product at the 5-position (**5a**) was not observed at all. On the other hand, the related coupling reaction catalyzed by palladium in the presence of K₂CO₃ or Cs₂CO₃ was shown by Miura.^{1d} The reaction is reported to proceed at 140 °C, and the regioselectivity is markedly different from our results to give **4** and **5**, while no 2-substituted product **3** is obtained.

Because a facile preparation of 2-arylthiazole **3** is in hand, we envisaged tandem coupling reactions applying the present reaction

and Miura's method leading to the differently substituted 2,5-diarylthiazoles **6**. The method is found to be effective to afford **6** because the alternative reaction site has already been substituted with the preceding reaction. As summarized in Table 1, 2,5-disubstituted derivatives bearing electron-donating and/or -withdrawing substituents were synthesized via the tandem reactions in moderate to excellent yields. The method would be suitable for the combinatorial synthesis of a variety of 2,5-diarylthiazoles.



The λ_{max} values of UV–vis absorption spectra of the obtained thiazole derivatives were found to be influenced by the electronic characteristics of the substituent. The peak of **6be** bearing *N,N*-dimethylamino and cyano groups was observed at 398 nm, while that of 2-(4-methoxyphenyl)-5-(4-methylphenyl)thiazole (**6ad**) was at 334 nm. In addition, most of these compounds obtained were found to show light-emitting characteristics. Their wavelength and intensities also depended on the type of substituents, suggesting that the color of emission would be tunable by the electronic property of the functional group. Considerably high photoluminescence quantum yields (Φ) were observed in thiazoles bearing an *N,N*-dimethylamino group such as **6bg** and **6be**.

Although synthesis of 2,5-diarylthiazoles has previously been studied by condensation of (*N*-benzoyl)aminoacetophenone derivatives (Aryl¹COCH₂NHCOAryl²) in the presence of P₂S₅, their yields are generally lower (25–35%).⁷ By contrast, the tandem coupling strategy allows us to afford 2,5-disubstituted thiazole with various substituents in good yields and in a combinatorial manner, which would be potential for the construction of the thiazole library.⁸

It was recently reported that 2,5-diaryl-1,3,4-oxadiazoles exhibit liquid crystalline (LC) as well as light-emitting characteristics.⁹ Similar to those, a number of 2,5-diarylthiazoles synthesized were found to show LC characteristics,⁷ which were evaluated by means of DSC and polarizing microscopy. As summarized in Figure 1, 2,5-diarylthiazoles exhibited the LC phase in remarkably wide ranges of temperature. For example, **6bg** showed an LC phase between 145 and 258 °C. The result markedly contrasts that of oxadiazole **7** bearing the corresponding substituents, which shows an LC phase between 138 and 143 °C.

Redox behaviors of 2,5-diarylthiazoles were also investigated by cyclic voltammetry.^{10,11} It appeared that the electrochemical characteristics were also influenced by a substituent on the aromatic ring. It was found that an electron-donating substituent played an important role for oxidation. The more electron-donating –NMe₂ group was easily oxidized as compared to –OMe. On the other

Table 1. Tandem Coupling of Thiazole and Absorption and Emission Properties of **3**, **4a**, and **6a**

Aryl ¹	% yield of 3	Aryl ² -X	% yield of 6	product	absorption ^b	emission ^b
					λ_{\max} , nm (ϵ , M ⁻¹ cm ⁻¹)	λ_{\max} , nm (Φ) ^c
4-MeOC ₆ H ₄ - (2a)	82	none		3a	300 (10 800)	361 (0.21)
		C ₆ H ₅ I (2c)	69	6ac	333 (28 000)	406 (0.22)
		4-MeC ₆ H ₄ I (2d)	94	6ad	334 (22 800)	408 (0.17)
		4-MeOC ₆ H ₄ I (2a)		4a	339 (22 300)	419 (0.17)
		4-NCC ₆ H ₄ Br (2e)	62	6ae	350 (30 200)	462 (0.27)
4-Me ₂ NC ₆ H ₄ - (2b)	80	none		3b	340 (25 400)	401 (0.19)
		4- ⁿ C ₇ H ₁₃ OC ₆ H ₄ I (2f)	76	6af	339 (27 900)	419 (0.24)
		4-(4- ⁿ C ₇ H ₁₃ C ₆ H ₄)C ₆ H ₄ Br (2g)	39 ^d	6bg	376 (38 200)	462 (0.49)
		2e	26 ^d	6be	398 (26 900)	488 (0.37)

^a A thiazole derivative **3** was prepared with 3 mol % PdCl₂(PPh₃)₂ and 2 mol % CuI (I/I-Aryl¹/TBAF = 2:1:2). Disubstituted thiazole **6** was synthesized with Aryl²-X (2 equiv), CsCO₃ (2 equiv), 10 mol % Pd(OAc)₂, and 20 mol % PPh₃ with stirring for 24–70 h. ^b Absorption spectra and emission spectra were measured as a chloroform solution (1 × 10⁻⁵ and 3 × 10⁻⁶ M, respectively). ^c The quantum yield, Φ , was estimated by comparison of standard 1.0 M quinine sulfate ($\Phi = 0.546$). ^d The yield after recrystallization.

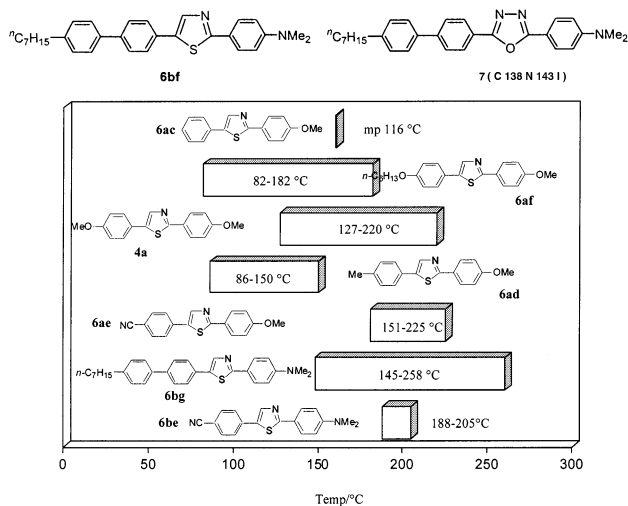


Figure 1. The range of temperature showing liquid crystalline characteristics evaluated with DSC and polarized microscopy. All of the compounds except **6ac** and **6be** showed characteristic texture for nematic phase. The texture of **6be** suggested it was the smectic phase.

hand, a reduction peak was observed at -2.17 V when a cyano group was introduced. Thereby, a thiazole derivative bearing both electron-donating and -withdrawing groups (**6ae** and **6be**) showed oxidation and reduction peaks. These characteristics would suggest both hole- and electron-transporting natures in EL materials.¹²

In summary, a synthetic reaction involving a novel C–H substitution of thiazole with an aromatic compound was demonstrated to be a facile and combinatorial preparation of a variety of light-emitting and liquid crystalline molecules, which would be a highly potential single-layer EL device with polarized light emission, through measurements of UV–vis absorption and emission spectra, LC properties, and CV analyses. With the new preparative methodology in hand, design and synthesis of the related polymer-bound LC and light-emitting thiazole derivatives are in progress and will be described in due course.

Supporting Information Available: Experimental details and analytical data (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

References

- (1) (a) Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529. (b) Weissman, H.; Song, X.; Milstein, D. *J. Am. Chem. Soc.* **2001**, *123*, 337. (c) Oi, S.; Fukita, S.; Hirata, N.; Watanuki, N.; Miyano, S.; Inoue, Y. *Org. Lett.* **2001**, *3*, 2579. (d) Pivsa-Art, S.; Satoh, T.; Kawamura, Y.; Miura, M.; Nomura, M. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 467. (e) Jia, C.; Piao, D.; Oyamada, J.; Lu, W.; Kitamura, T.; Fujiwara, Y. *Science* **2000**, *287*, 1992. (f) Satoh, T.; Kawamura, Y.; Miura, M.; Nomura, M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1740. (g) Oguma, K.; Miura, M.; Satoh, T.; Nomura, M. *J. Am. Chem. Soc.* **2000**, *122*, 10464. (h) Chen, H.; Schlecht, S.; Sempke, T. C.; Hartwig, J. F. *Science* **2000**, *287*, 1995. (i) Waltz, K. M.; Hartwig, J. F. *Science* **1997**, *277*, 211. (j) Cho, J.-Y.; Tse, M. K.; Holmes, D.; Maleczka, R. E., Jr.; Smith, M. R., III. *Science* **2002**, *295*, 305.
- (2) For reviews: (a) Dyker, G. *Angew. Chem., Int. Ed.* **1999**, *38*, 1698. (b) Jia, C.; Kitamura, T.; Fujiwara, Y. *Acc. Chem. Res.* **2001**, *34*, 633.
- (3) For reviews: (a) Kraft, A.; Grimsdale, A. C.; Holmes, A. B. *Angew. Chem., Int. Ed.* **1998**, *37*, 402–428. (b) Friend, R. H.; Gymer, R. W.; Holmes, A. B.; Burroughes, J. H.; Marks, R. N.; Taliani, C.; Bradley, D. D. C.; Dos Santos, D. A.; Brédas, J. L.; Löglund, M.; Salaneck, W. R. *Nature* **1999**, *397*, 121–128. (c) Shirota, Y. *J. Mater. Chem.* **2000**, *10*, 1–25. (d) Kim, D. Y.; Cho, H. N.; Kim, C. Y. *Prog. Polym. Sci.* **2000**, *25*, 1089–1139. (e) Mitschke, U.; Bäuerle, P. *J. Mater. Chem.* **2000**, *10*, 1471–1507.
- (4) (a) Demus, D.; Goodby, J. W.; Gray, G. W.; Spiess, H.-W. *Handbook of Liquid Crystals*; Wiley: Germany, 1998. (b) Bahadur, B. *Liquid Crystals—Applications and Uses*; World Scientific: Singapore, 1990.
- (5) (a) Mori, A.; Shimada, T.; Kondo, T.; Sekiguchi, A. *Synlett* **2001**, 649. (b) Mori, A.; Kawashima, J.; Shimada, T.; Suguro, M.; Hirabayashi, K.; Nishihara, Y. *Org. Lett.* **2000**, *2*, 2935. (c) Mori, A.; Kondo, T.; Kato, T.; Nishihara, Y. *Chem. Lett.* **2001**, 286.
- (6) The reaction at 40 °C for 96 h afforded 61% of **3a** (**3a/4a** = 9:1) and at room temperature for 96 h, 35% (**3a/4a** = 20:1).
- (7) Dölling, K.; Zäschke, H.; Schubert, H. *J. Prakt. Chem.* **1979**, *321*, 643.
- (8) An example of library construction for light-emitting materials: Shiedel, M.-S.; Briehn, C. A.; Bäuerle, P. *Angew. Chem., Int. Ed.* **2001**, *40*, 4677.
- (9) Mochizuki, H.; Hasui, T.; Kawamoto, M.; Shiono, T.; Ikeda, T.; Adachi, C.; Taniguchi, Y.; Shirota, T. *Chem. Commun.* **2000**, 1923.
- (10) Kaifer, A. E.; Gómez-Kaifer, M. *Supramolecular Electrochemistry*; Wiley-VCH: Weinheim, 1999.
- (11) Tables of peak potential values for **3** and **6**: See the Supporting Information.
- (12) (a) Kido, J.; Kohda, M.; Okuyama, K.; Nagai, K. *Appl. Phys. Lett.* **1992**, *61*, 761–763. (b) Zhang, C.; von Seggern, H.; Kraabel, B.; Schmidt, H.-W.; Heeger, A. J. *Synth. Met.* **1995**, *72*, 185–188. (c) Kido, J.; Shionoya, H.; Nagai, K. *Appl. Phys. Lett.* **1995**, *67*, 2281–2283. (d) Birgersson, J.; Kaeriyama, K.; Barta, P.; Bröms, P.; Fahlman, M.; Granlund, T.; Salaneck, W. R. *Adv. Mater.* **1996**, *8*, 982–985. (e) Wu, C. C.; Sturm, J. C.; Register, R. A.; Tian, J.; Dana, E. P.; Thompson, M. E. *IEEE Trans. Electron Devices* **1997**, *44*, 1269–1281.

JA0289189