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Synthesis of Arylated Perylene Bisimides through C−H Bond Cleavage under Ruthenium Catalysis

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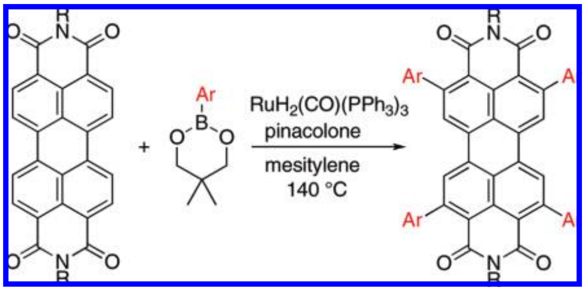
ABSTRACT



Treatment of perylene bisimide (PBI) with various arylboronates in the presence of a ruthenium catalyst provides tetraarylated PBIs at 2,5,8,11-positions in good yields with perfect regioselectivity. The electronic nature of the introduced aryl substituents has a significant impact on their optical and electronic properties. This protocol has been applied to the synthesis of a water-soluble emissive PBI derivative.

Perylene tetracarboxylic acid bisimide (PBI) has received much attention for wide areas of applications toward organic material devices such as organic solar cells, organic light-emitting diodes, field effect transistors, and biomedical sensors.[1]

To gain desirable photophysical and electronic properties, effective chemical syntheses of functional dyes are crucial. However, chemical modification of the perylene moiety of PBIs only relies on halogenation at bay positions, namely, 1,6,7,12-positions and the subsequent transformations, despite their rich material chemistry. This is due to the higher reactivity of the bay positions toward electrophilic substitutions. In addition, substituent effects at the bay positions are substantial due to the large contribution to the HOMO by these positions. On the other hand, substitution at the 2,5,8,11-positions has been believed to be less effective to modify the electronic nature of PBIs, but there has been no experimental proof. Actually, the synthetic procedure of 2,5,8,11-substituted PBIs has been unavailable until our recent report. We have reported that Ru-catalyzed C−H bond activation is effective for alkylation of PBIs at 2,5,8,11-positions.[2] Introduction of alkyl groups at these positions significantly enhances their solid state emission as well as

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(1) (a) Herrmann, A.; Müllen, K. *Chem. Lett.* **2006**, *35*, 978. (b) Würthner, F. *Chem. Commun.* **2004**, 1564. (c) Wasielewski, M. R. *J. Org. Chem.* **2006**, *71*, 5051. (d) Langhals, H. *Helv. Chim. Acta* **2005**, *88*, 1309. (e) Langhals, H. *Heterocycles* **1995**, *40*, 477. (f) Langhals, H. *Molecular Devices. Chiral, Bichromophoric Silicones: Ordering Principles in Complex Molecules in Silicon Based Polymers*; Ganachaud, F.,; Boileau, S.,; Boury, B., Eds.; Springer, 2008; p 51.

(2) Nakazono, S.; Imazaki, Y.; Yoo, H.; Yang, J.; Sasamori, T.; Tokitoh, N.; Cedric, T.; Kageyama, H.; Kim, D.; Shinokubo, H.; Osuka, A. *Chem.−Eur. J.* **2009**, *15*, 7530.

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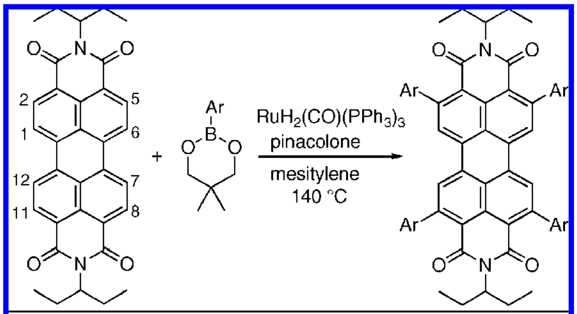
their solubility in organic solvents without causing any serious distortion of the PBI core. To examine the electronic effect of other substituents at 2,5,8,11-positions, we undertook introduction of a variety of aryl groups to PBI.[3] Introduction of aryl groups is quite attractive to modulate the electronic property and aggregation behavior of functional π-systems.[4]

Direct C−H bond functionalization has proven to be a powerful tool in organic synthesis.[5,6] In particular, Kakiuchi and Chatani have established an efficient protocol for direct arylation of aromatic ketones with aryl boronates.[7] Eventually we found that this method is suitable for arylation of PBI at 2,5,8,11-positions.

Scheme 1 illustrates Ru-catalyzed 4-fold arylation of PBI. In the presence of 20 mol % of $RuH_2(CO)(PPh_3)_3$, a mixture of bis(*N*-ethylpropyl)PBI **1** and phenyl boronic acid neopentyl glycol ester was heated in refluxing pinacolone. Despite the insolubility of **1** in pinacolone, the reaction proceeded moderately. After silica gel separation, desirable tetraphenyl PBI **2** was obtained in 57% yield, but triarylated PBI was also detected in the reaction mixture (entry 1). The reaction conditions were slightly modified by the addition of mesitylene as a cosolvent to enable higher reaction temperatures. Then the product was obtained in 83% yield in shorter reaction time (entry 2). A variety of aryl boronates participate in this reaction, and both electron-rich and electron-deficient aryl groups can be introduced. Unfortunately, the reaction with *p*-bromophenyl boronate proceeded sluggishly to provide product **4** in 12% yield along with recovery of 50% of **1** (entry 4). Strongly electron-deficient substrate, *p*-nitrophenyl boronate, could not be used for arylation of **1**.[8]

Scheme 1. Ru-Catalyzed Four-Fold Arylation of PBI **1**



entry	Ar	time (h)	product	yield
1	Ph	40	**2**	57%[b]
2	Ph	21	**2**	83%
3	*p*-MeO(C_6H_4)	42	**3**	83%
4	*p*-Br(C_6H_4)	91	**4**	12%[c]
5	*p*-CF_3(C_6H_4)	47	**5**	75%
6	*p*-Me(C_6H_4)	35	**6**	69%
7	*p*-Me_2N(C_6H_4)	30	**7**	70%

[a] Reaction conditions: Bis(*N*-ethylpropyl)PBI **1** (0.10 mmol), arylboronic acid neopentyl glycol ester, (0.7 mmol), $RuH_2(CO)(PPh_3)_3$ (0.020 mmol), pinacolone (0.5 mL), mesitylene (0.5 mL), 140 °C, 21 h. [b] The reaction was carried out at 110 °C with 11 equiv of arylboronic ester without mesitylene. [c] 50% of **1** was recovered.

All tetraaryl PBIs **2**−**7** were fully characterized by ^1H and ^{13}C NMR analysis as well as high-resolution ESI TOF mass spectroscopy (Supporting Information, SI). Furthermore, the solid-state structures of **4**, **5**, and **7** (Figure 1 and SI) were determined by the X-ray diffraction analysis, elucidating the highly planar structure of the perylene core. This characteristic is in sharp contrast to the modified PBIs at bay areas, of which perylene backbones are considerably twisted.[9,10] The aryl groups are tilted to the perylene core by 50−60°, and the C−C bond lengths between the perylene core and the aryl groups range from 1.480 to 1.499 Å. These structural features imply weak electronic communication between the aryl substituents and the perylene moiety. In crystals, each individual molecule is enough separated because of steric hindrance of aryl groups, indicating the absence of $\pi-\pi$ stacking interaction.

Figure 2 shows UV/vis absorption and fluorescence spectra of **1**, **2**, and **7**. The absorption spectra of arylated PBIs except **7** are well matched with the sum spectra of **1** and aryl substituents, suggesting weak interaction between the perylene core and the substituents in the ground state. In contrast, arylated PBIs at bay positions exhibit substantial bathochromic shifts due to twisting of the perylene core.[4a,b] Introduction of *p*-(*N*,*N*-dimethylamino)phenyl groups, however,

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(3) We have presented these results at the 55th Symposium on Organometallic Chemistry, Japan 2008. Nakazono, S.; Shinokubo, H.; Osuka, A. *Abstracts of the 55th Symposium on Organometallic Chemistry*, Japan 2008; p 199.

(4) For selected examples on arylated PBI derivatives at bay areas, see: (a) Qiu, W.; Chen, S.; Sun, X.; Liu, Y.; Zhu, D. *Org. Lett*. **2006**, *8*, 867. (b) Chao, C.-C.; Leung, M.-K.; Su, Y. O.; Chiu, K.-Y.; Lin, T.-H.; Shieh, S.-J.; Lin, S.-C. *J. Org. Chem*. **2005**, *70*, 4323. (c) Sugiyasu, K.; Fujita, N.; Sinkai, S. *Angew. Chem., Int. Ed*. **2004**, *43*, 1229. (d) Ahrens, M. J.; Sinks, L. E.; Rybtchinski, B.; Liu, W.; Jones, B. A.; Giaimo, J. M.; Gusev, A. V.; Goshe, A. J.; Tiede, D. M.; Wasielewski, M. R. *J. Am. Chem. Soc*. **2004**, *126*, 8284. (e) Avlasevich, Y.; Müller, S.; Erk, P.; Müllen, K. *Chem.—Eur. J*. **2007**, *13*, 6555. (f) Kelley, R. F.; Shin, W. S.; Rybtchinski, B.; Sinks, L. E.; Wasielewski, M. R. *J. Am. Chem. Soc*. **2007**, *129*, 3173. (g) Vajiravelu, S.; Ramunas, L.; Juozas Vidas, G.; Valentas, G.; Vygintas, J.; Valiyaveettil, S. *J. Mater. Chem*. **2009**, *19*, 4268. (h) Li, Y.; Zheng, H.; Li, Y.; Wang, S.; Wu, Z.; Liu, P.; Gao, Z.; Liu, H.; Zhu, D. *J. Org. Chem*. **2007**, *72*, 2878.

(5) (a) *Handbook of C-H Transformations*; Dyker, G., Ed.; Wiley-VCH: Weinheim, 2005. (b) Kakiuchi, F.; Chatani, N. *Adv. Synth. Catal*. **2003**, *345*, 1077. (c) Godula, K.; Sames, D. *Science* **2006**, *312*, 67. (d) *Activation of Unreactive Bonds and Organic Synthesis*; Murai, S., Ed.; Springer: Berlin, 1999. (e) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev*. **2007**, *107*, 174.

(6) (a) Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529. (b) Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn*. **1995**, *68*, 62. (c) Kakiuchi, F.; Murai, S. *Acc. Chem. Res*. **2002**, *35*, 826.

(7) (a) Kakiuchi, F.; Kan, S.; Igi, K.; Chatani, N.; Murai, S. *J. Am. Chem. Soc*. **2003**, *125*, 1698. (b) Kakiuchi, F.; Matsuura, Y.; Kan, S.; Chatani, N. *J. Am. Chem. Soc*. **2005**, *127*, 5936. (c) Kitazawa, K.; Kochi, T.; Sato, M.; Kakiuchi, F. *Org. Lett*. **2009**, *11*, 1951.

(8) No reaction proceeded with pentafluorophenyl and 2-thienyl boronates. The use of 1-naphthyl boronate resulted in formation of an inseparable mixture of several atropisomers in 50% yield.

(9) Crystal data for **4**: $C_{60}H_{44}Br_4Cl_6N_2O_4$, M_w = 1389.31, crystal size 0.40 × 0.20 × 0.10 mm, orange prism, monoclinic, space group $P2_1/a$ (No. 14), a = 18.099(4), b = 8.285(3), c = 19.042(5) Å, b = 105.218(9)°, V = 2755.2(13) Å^3, Z = 2, D_{calc} = 1.675 g/cm^3, T = 123(2) K, R = 0.0727 (I > 2.0s(I)), R_w = 0.2335 (all data), GOF = 1.044 (I > 2.0s(I)).

(10) Crystal data for **7**: $C_{34}H_{34.36}Cl_{2.64}N_3O_2$, M_w = 610.58, crystal size 0.40 × 0.20 × 0.05 mm, orange prism, triclinic, space group P-1 (No. 2), a = 9.294(4), b = 10.196(4), c = 18.474(8) Å, a = 85.694(12), b = 83.861(14), g = 66.290(13)°, V = 1592.6(11) Å^3, Z = 2, D_{calc} = 1.273 g/cm^3, T = 123(2) K, R = 0.0880 (I > 2.0s(I)), R_w = 0.2814 (all data), GOF = 1.049 (I > 2.0s(I)).

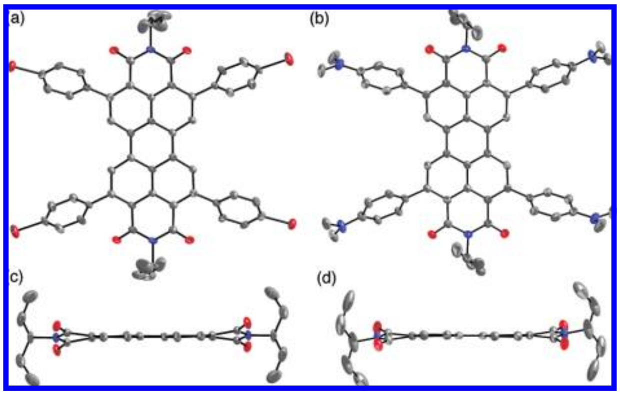


Figure 1. X-ray crystal structures. (a) Top view of **4**, (b) top view of **7**, (c) side view of **4**, and (d) side view of **7**. The thermal ellipsoids were scaled to the 50% probability level. Hydrogen atoms, solvents, and aryl substituents in side views were omitted for clarity.

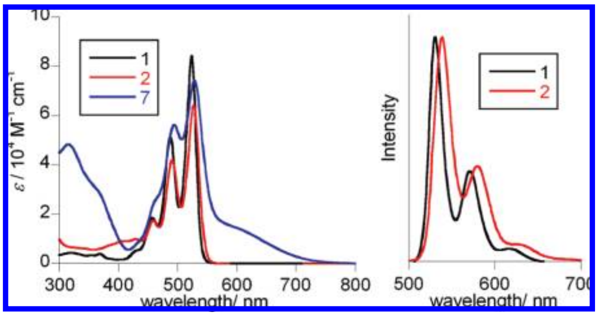


Figure 2. (a) UV/vis absorption spectra of **1**, **2**, and **7** and (b) fluorescence spectra of **1** and **2** measured in CH_2Cl_2.

resulted in dramatic color change to deep violet in CH_2Cl_2. The absorption spectrum of **7** exhibits a broadened band around 600−700 nm, covering the visible light region. Theoretical calculations at the B3LYP/6-31G(d) level indicate that degenerated HOMO and HOMO-1 of **7** are localized on the aryl substituents not on the perylene core (Figure 3c). On the basis of TD-DFT calculations, the absorption of **7** in the low-energy region can be assigned as transitions from HOMO or HOMO-1 to LUMO, which have large charge transfer character.

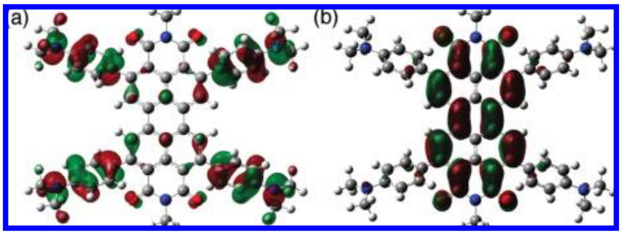
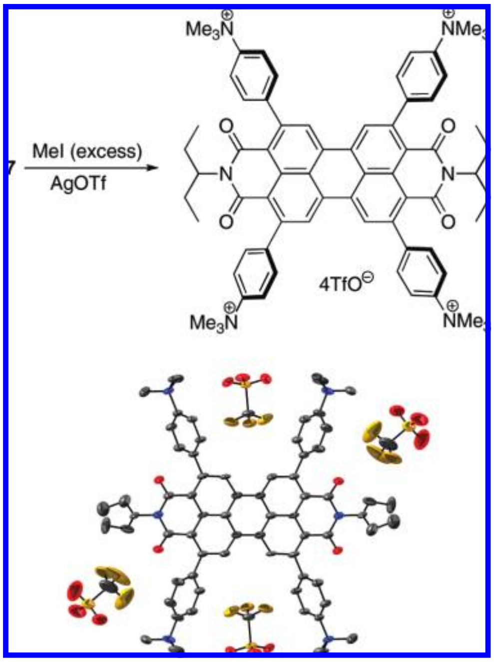


Figure 3. Calculated molecular orbitals at the B3LYP/6-31G(d) level. (a) HOMO and (b) LUMO of **7**.

Introduction of aryl groups also affects their fluorescence properties. In comparison to parent PBI **1** ($\Phi_f = 0.98$), tetraphenyl PBI **2** exhibits much weaker emission ($\Phi_f = 0.16$). Furthermore, fluorescence is perfectly quenched in **3** and **7**, which have strongly donating substituents. On the other hand, the quantum yield of **5** with an electron-withdrawing *p*-(trifluorometyl)phenyl group is higher ($\Phi_f = 0.75$) in solution.

Water-soluble fluorescent labels have been extensively employed for single-molecule tracking in living cells.[11] However, water-soluble PBIs with high fluorescence efficiency are still limited.[12] This is mostly due to fluorescence quenching because of aggregation in aqueous media and interaction with substituents. To gain solubility in water, *N*,*N*-dimethylamino groups of **7** were quaternarized. This conversion would also block off the electron-donating character of the amino group to attain a high fluorescence quantum yield by preventing intramolecular charge transfer interaction. Full methylation was accomplished upon treatment with iodomethane in the presence of AgOTf[13] to cleanly furnish

Scheme 2. Methylation of **7** and X-ray Structure of **8**



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[11] (a) Seisenberger, G.; Ried, M. U.; Endre, T.; Buning, H.; Hallek, M.; Brauchle, C. *Science* **2001**, *294*, 1929. (b) Cotlet, M.; Hofkens, J.; Maus, M.; Gensch, T.; Van der Auweraer, M.; Michiels, J.; Dirix, G.; Van Guyse, M.; Vanderleyden, J.; Visser, A. J. W. G.; De Schryver, F. C. *J. Phys. Chem. B* **2001**, *105*, 4999. (c) Margineanu, A.; Hofkens, J.; Cotlet, M.; Habuchi, S.; Stefan, A.; Qu, J.; Kohl, C.; Müllen, K.; Vercammen, J.; Engelborghs, Y.; Gensch, T.; De Schryver, F. C. *J. Phys. Chem. B* **2004**, *108*, 12242.

[12] (a) Qu, J.; Kohl, C.; Pottek, M.; Müllen, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 1528. (b) Kohl, C.; Weil, T.; Qu, J.; Müllen, K. *Chem.—Eur. J.* **2004**, *10*, 5297. (c) Peneva, K.; Mihov, G.; Nolde, F.; Rocha, S.; Hotta, J.; Braechmans, K.; Hofkens, J.; Uji-i, H; Herromann, A.; Müllen, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 3372.

[13] Ohara, Y.; Akiba, K.; Inamoto, N. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1508.

tetraanilinium salt **8** (Scheme 2). Because of high polarity of **8**, silica gel column chromatography was not suitable for purification. After repeated recrystallization, the desired compound was obtained in 49% yield.[14] Ammonium salt **8** is soluble in polar solvents, such as MeOH, CH_3CN, and water, and achieves high fluorescence quantum yield ($\Phi_f = 0.83$) in water as well as in CH_3CN ($\Phi_f = 0.75$) (Table 1).

Table 1. Optical Properties of Tetraaryl PBIs

PBI	ε ($M^{-1}cm^{-1}$)	λ_{max} (nm)[a]	λ_{em} (nm)[b]	Φ_f (solution)[c]
1	84000	524	531	0.98
2[d]	64000	527	541	0.16
3	49000	532	-	-
4	80000	528	539	0.15
5	74000	525	536	0.75
6	67000	529	543	0.02
7	59000	528	-	-
8[e]	58000	537	555	0.83
8[f]	80000	525	538	0.75

[a] The longest absorption maxima. [b] Excited at the longest absorption maxima. [c] Absolute quantum yield determined by a calibrated integrating sphere system within ± 3% errors. [d] Measured in toluene. [e] Measured in water. [f] Masured in CH_3CN.

The electrochemical properties of arylated PBIs have been measured in CH_2Cl_2 by cyclic voltammetry (Table 2). For **5**, one oxidation at 1.300 V and two reduction potentials at −0.988 and −1.244 were observed as reversible waves versus ferrocene/ferrocenium. No reversible oxidation waves could be observed for **3** and **7**. In comparison to the parent PBI **1**, positive shifts of oxidation and reduction potentials were detected for **4** and **5**, whereas electron-donating aryl groups lead to negative shifts for **3** and **6**. These results clarify that HOMO and LUMO levels are substantially influenced by the aryl substituents at 2,5,8,11-positions.

Table 2. Electrochemical Properties of Tetraaryl PBIs[a]

PBI	Ar	E^2_{red} (V)	E^1_{red} (V)	E^1_{ox} (V)
5	p-$CF_3(C_6H_4)$	−1.244	−0.988	1.300
4	p-$Br(C_6H_4)$	−1.281	−1.044	1.289
1	–	−1.309	−1.107	1.191
2	Ph	−1.332	−1.124	1.140
6	p-$Me(C_6H_4)$	−1.338	−1.156	1.196
3	p-$MeO(C_6H_4)$	−1.352	−1.154	–
7	p-$Me_2N(C_6H_4)$	−1.414	−1.314	-
8[b]	p-$Me_3N(C_6H_4)$	−1.190	−0.989	-

[a] Conditions: Potentials versus ferrocene/ferrocenium ion couple. Working electrode: Pt. Counter electrode: Pt. Reference electrode: Ag/$AgClO_4$. Scan rate: 100 mV/s. Electrolyte: Bu_4NPF_6. Solvent: CH_2Cl_2. [b] Solvent: CH_3CN.

In summary, we have accomplished regioselective 4-fold direct arylation of PBI at 2,5,8,11-positions of the perylene core via Ru-catalyzed C−H bond functionalization. Both electron-rich and electron-deficient aryl groups can be installed to PBI. The electronic nature of aryl substituents has a significant impact on their optical and electrochemical properties. In addition, we have applied the present protocol to the synthesis of highly emissive water-soluble PBI **8**. Further direct functionalization of PBIs including introduction of heteroatoms is currently underway in our group.

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Supporting Information Available: General procedures, spectral data for compounds, absorption and fluorescence spectra. CIF file for the X-ray analysis of **4**, **5**, **7**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) Crystal data for **8**: $C_{76}H_{86}F_{12}N_6O_{18}S_4$, $M_w = 1727.75$, crystal size 0.20 × 0.10 × 0.05 mm, red prism, triclinic, space group P-1 (No. 2), $a = 6.815(4)$, $b = 14.674(10)$, $c = 20.572(10)$ Å, $a = 70.543(19)$, $b = 80.424(18)$, $g = 84.60(2)°$, $V = 1910.9(19)$ Å^3, $Z = 1$, $D_{calc} = 1.501$ g/cm^3, $T = 123(2)$ K, $R = 0.0956$ ($I > 2.0s(I)$), $R_w = 0.2600$ (all data), GOF = 1.174 ($I > 2.0s(I)$).