Organic LETTERS
Letter
pubs.acs.org/OrgLett

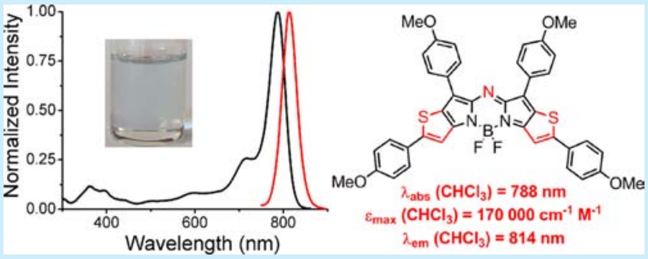
β-Thiophene-Fused BF_2-Azadipyrromethenes as Near-Infrared Dyes

Yayang Wu, Chi Cheng, Lijuan Jiao,* Changjiang Yu, Sufan Wang,* Yun Wei, Xiaolong Mu, and Erhong Hao*

Laboratory of Functional Molecular Solids, Ministry of Education; Anhui Laboratory of Molecule-Based Materials; School of Chemistry and Materials Science, Anhui Normal University, Wuhu, Anhui, China 241000

S Supporting Information

ABSTRACT: A facile synthetic route to a new class of near-IR β-thiophene-fused BF_2-azadipyrromethenes (aza-BDTPs) is presented. Sharp absorption and fluorescence emission bands at around 800 nm were observed for these highly photostable aza-BDTPs, with a large absorption coefficient and very low absorptions in the visible range from 700 to 380 nm.



Near-infrared (NIR) dyes that absorb and/or emit light in the region ranging from 700 to 2000 nm have found diverse applications in medicine and material science, as noninvasive bioimaging,[1] photodynamic, photothermal therapy,[2] photovoltaic, optoelectronics, and laser optical recording.[3] BF_2-azadipyrromethenes (aza-BODIPYs)[4,5] have recently received much attention due to their remarkable photochemical properties, especially their longer wavelength absorption and emission properties in comparison to those of BODIPY analogues.[6−8] For example, the parent aza-BODIPY **A** (Figure 1) absorbs and emits at 650 and 682 nm in chloroform, respectively.

Various elegant approches have been adopted to move the spectra further into the NIR range include the following: (1) the installation of electron-donating groups and/or additional aromatic groups to the 3,5-aryls of the chromophore;[5,9,10] (2) the fusion of aromatic rings onto the 1,2-positions of pyrrolic ring, as demostrated by the *alfa*-benzene-fused aza-BODIPY **B**;[11] and (3) the rigidification of 3,5-aryls via either the installation of a six-member ring onto the 2,3-positions of pyrrolic structure as demostrated by aza-BODIPY **C**[12] or the B−O chelation as demonstrated by aza-BODIPY **D**.[13] By "hybridizing" these approaches, herein, we report a set of β-thiophene-fused aza-BODIPYs (aza-BDTPs), in which the substituted thiophene rings were fused onto the 2,3-positions of the pyrrolic structure of the chromophore. We anticipate these aza-BDTPs as a novel NIR platform would move the absorption bands further to approximately 800 nm.

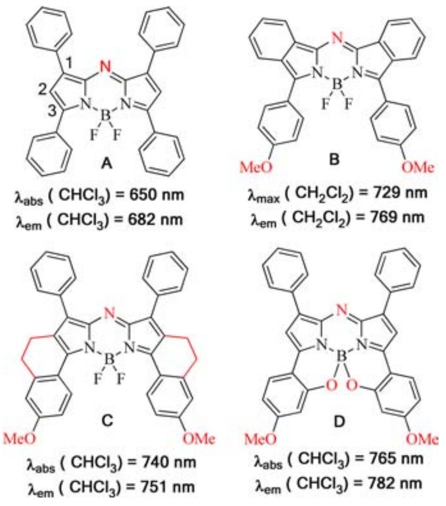


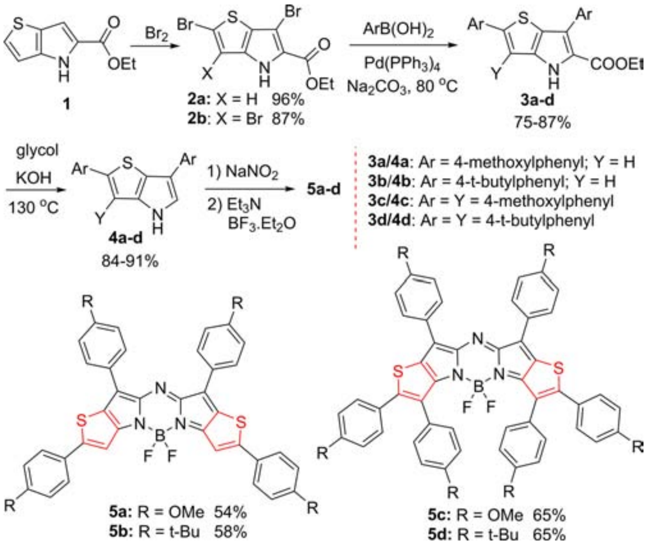
Figure 1. Representative examples to move the absorption and emission bands of aza-BODIPYs further to the NIR spectral range.

These aza-BDTPs were synthesized from thienopyrrole **1** (Scheme 1). Regioselective and stepwise bromination of **1** with a suitable amount of bromine gave the corresponding dibromothienopyrrole **2a** (2 equiv of Br_2) and tribromothienopyrrole **2b** (3.5 equiv of Br_2) in 96% and 87% yields, respectively. This regioselective bromination of **1** was also confirmed by the crystal structures of their subsequent reaction products **3a** and **3c** (Figure S1, Supporting Information), obtained from the Suzuki—Miyaura cross-coupling reactions of **2** and corresponding aryl boronic acids. Upon basic hydrolysis, compounds **3** were smoothly converted to the key synthetic precusors **4a−d** in high yields. Condensation of **4a−d** with sodium nitrite in acetic acid and the subsequent BF_3 complexation using literature methods[12] smoothly generated the target aza-BDTPs **5a−d** in a one-pot fashion in 54−65% yields. These resultant aza-BDTPs were fully characterized by NMR and HRMS.

These aza-BDTPs **5** were prepared without resorting to complicated purification processes such as chromatography separation, except for the Suzuki—Miyaura cross-coupling

Received: November 29, 2013
Published: January 13, 2014

Scheme 1. Syntheses of aza-BDTPs 5a−5d



products which also only need to pass through a short pad of silica gel. For all the other steps, only workup and recrystallization were required to afford compounds pure enough for NMR spectroscopic analysis. It is worth noting that, for the successful condensation of thienopyrrole **4** with with sodium nitrite in acetic acid, the presence of the 4-aryl group on thienopyrrole **4** (1,7-phenyls of the corresponding aza-BDTPs, *Pc* rings) is essential. Our initial attempts to condense both 4-unsubstituted thienopyrrole **4e** and tribromothienopyrrole **7** with sodium nitrite in acetic acid failed (Scheme S1, Supporting Information).

Single crystals of aza-BDTPs **5c** (Figure 2), **5d** (Figure 3) and thienopyrroles **3a**, **3c** (Figure S1, Supporting Information) suitable for X-ray analysis were obtained from the slow evaporation of their corresponding dichloromethane solutions. The planar thienopyrrole planes were observed for all these compounds. An increase of the dihedral angle defined by the substituted phenyl rings ($P_a - P_c$) and the thienopyrrole planes was observed with the installation of additional phenyls (P_b) (Table S1, Supporting Information). For example, the dihedral angle between the phenyl group (P_a) and the thiophene ring is 5.3° in **3a**. This increases to 31.5° in **3c** with the installation of additional phenyls (P_b), which itself has a dihedral angle of 57.6° formed with the thiophene ring. The conversion of **3c** to the target aza-BDTP **5c** has little influence on these dihedral angles. Consequently, similarly large dihedral angles between the phenyls and the thiophene ring were observed in aza-BDTP **5c**. These large dihedral angles combined with the possible steric hindrance effect from *tert*-butyl groups may be responsible for the good solubility of aza-BDTPs **5b** and **5d** in most of the common organic solvents studied.

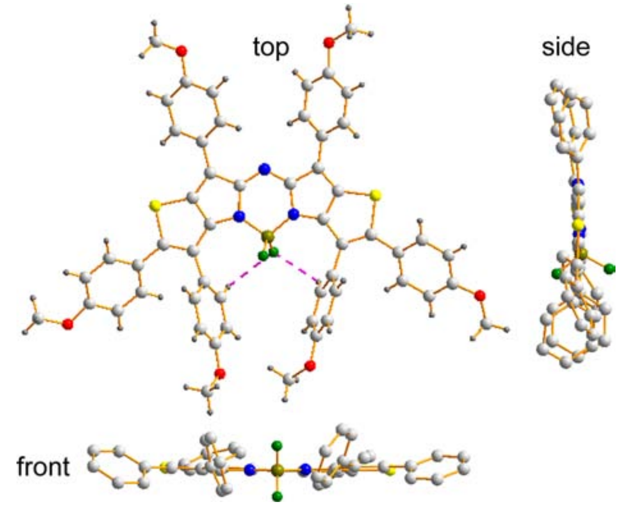


Figure 2. X-ray structures of aza-BDTP **5c**. C, light gray; H, gray; N, blue; B, dark yellow; F, green; S, yellow; O, red. Methoxy groups and hydrogen atoms have been removed in both side and front views for clarity.

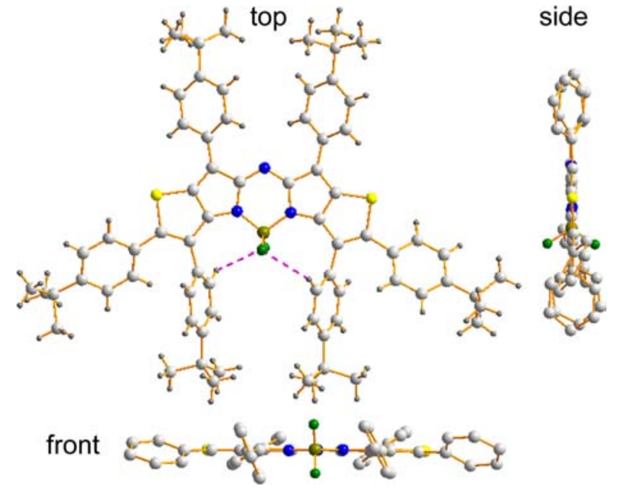


Figure 3. X-ray structures of aza-BDTP **5d**. C, light gray; H, gray; N, blue; B, dark yellow; F, green; S, yellow. *tert*-Butyl groups and hydrogen atoms have been removed in both side and front views for clarity.

Aza-BDTPs **5b** and **5d** have a very small pyrrole−pyrrole dihedral angle (<5.6°) and thiophene−thiophene dihedral angle (<5.2°). This indicates that the installation of thiophenes and the associated substituted phenyls to the aza-BODIPY core cause no structural disruption of the planar core structure. This nearly planar aza-BDTP core results in the the π-conjugation being well extended and is predominantly responsible for the observed optical properties. Multiple intramolecular and intermolecular C−H···F hydrogen bonds between F atoms and various hydrogen atoms are formed due to the strong electron negativity of the F atom. These strong intermolecular hydrogen bondings also help the establishment of the crystal packing structure (Figure S2, Supporting Information) and make these aza-BDTPs nearly parallel to each other in a head-to-tail orientation.

Intense and sharp absorption bands were observed for aza-BDTPs **5** (Figure 4a). For example, in chloroform, aza-BDTP **5a** has a strong absorption at 788 nm with a large absorption coefficient (ε = 170 000 cm^{-1} M^{-1}) and a full width at half-maximum (fwhm) of 45 nm (Table 1). In comparison with that of simple aza-BODIPY **A**, there is a 138 nm bathochromic shift and a nearly 2-fold increase in the absorption coefficient. In comparison with those reported for NIR aza-BODIPYs **B**, **C**, and **D**, aza-BDTP **5a** also shows a 69, 48, and 23 nm red shift of the absorption maximum, respectively. This strong absorption band close to 800 nm and very low absorptions in the visible light region ranging in wavelength from 700 to 380 nm indicate that aza-BDTP **5a** may be used as a selective NIR absorber,[14]

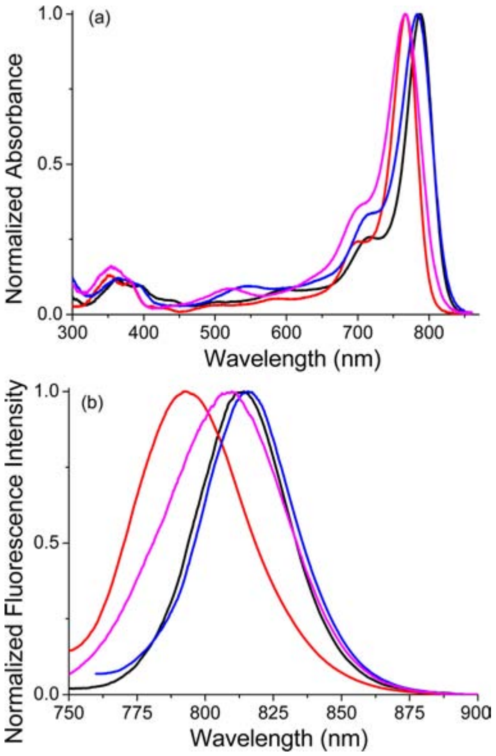


Figure 4. Normalized UV−vis (a) and fluorescence (b) spectra of aza-BDTPs **5a** (black), **5b** (red), **5c** (blue), **5d** (magenta) in chloroform.

Table 1. Photophyscial Properties of aza-BDTPs 5 at Room Temperature in Chloroform

dyes	λ_{abs}^{max} (fwhm)^a/ nm	λ_{em}^{max} (fwhm)^b/ nm	ε (cm^{-1} M^{-1})	ϕ^c	τ^d (ns)	K_f/K_{nr}^e (10^9s^{-1})
5a	788 (45)	814 (40)	170000	0.10	1.69	0.06/0.53
5b	767 (42)	793 (48)	223900	0.12	1.69	0.07/0.52
5c	784 (57)	816 (40)	182000	0.04	1.53	0.03/0.63
5d	767 (59)	807 (53)	144500	0.05	1.18	0.04/0.81
A^f	650	682	76600	0.34		

[a] Full width at half-maximum height. [b] Excited at 730 nm. [c] Fluorescence quantum yield was obtained using Indocyanine Green as reference compound ($\phi = 0.12$ in DMSO); the standard errors are less than 5%. [d] Fluorescence lifetime; standard derviations are less than 0.04 ns. [e] $K_f = \phi/\tau$, $K_{nr} = (1 - \phi)/\tau$. [f] Data reported in ref 4a.

finding great applications in the NIR laser welding of transparent polymers.

A sharp fluorescence emission maximum (fwhm = 40 nm) of aza-BDTP **5a** appears at 814 nm (Figure 4b) with an acceptable fluorescence quantum yield ($\phi = 0.10$ in chloroform), comparable to that of commercial available ICG. The increases of the absorption fwhm and the decreases of the fluorescence quantum yields were observed from **5a**, **5b** to **5c**, **5d** respectively (Table 1), correlated with the further installation of phenyls (P_b) to the thiophene ring. Spectral shifts were observed for aza-BDTPs **5** with the variation of solvent polarities. For example, the absorption and emssion bands for aza-BDTP **5c** were red-shifted from 785 and 813 nm to 799 and 827 nm respectively, when the solvent was changed from toluene to DMSO (Table S2, Supporting Information). A small solvent dependence of the Stokes shifts (Table S4, Supporting Information) and an unsatisfactory correlation coefficient in the Lippert−Mataga plot of aza-BDTP **5c** in 12 solvents (Figure S6, Supporting Information) were observed, which may indicate that the permanent dipole moments for **5c** are similar in the ground and excited states.[15]

The molecular orbital calculations for these compounds on the density functional theory (DFT) level using a B3LYP/6-31G basis set were performed on **5c**. The LUMO distribution of **5c** was donated by all atomic orbitals in the aromatic rings except two phenyls (P_b), while contributions to the HOMO distribution were mainly from the aza-BODIPY core (Table S6, Supporting Information). Intramolecular charge transfer (ICT) from the aza-BODIPY core to the orbitals of four phenyls (P_a and P_c) was possible in **5c**, which could partly explain their low fluorescence quantum yields, but the intramolecular C−Ar (P_a, P_b, and P_c rings) rotations and the heavy-atom effects from sulfur atoms may also be possible. The fluorescence decay histograms of aza-BDTPs **5** all fitted with a single exponential function (Figures S8−S11, Supporting Information) with the fluorescence lifetimes τ vary between 1.18 and 1.69 ns in chloroform (Table 1). Nevertheless, the nonradiative deactivation processes are favored for **5** with the values of k_{nr} ranging from 0.52×10^9 s^{-1} to 0.81×10^9 s^{-1} in chloroform.

The photostabilities of aza-BDTPs **5a−d** in toluene were measured by continuous irradiation with a Xe lamp (500 W). In comparison with a well-known commercial NIR dye ICG in DMSO, these aza-BDTPs **5** show excellent photostability (Figure 5) during the period of strong irradiation (26 min): more than 98% of the amount of aza-BDTP **5b** remained, while only 83% of ICG remained under the same conditions.

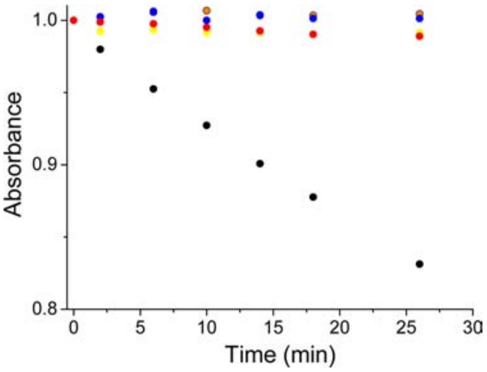


Figure 5. Comparison of the photostabilities of aza-BDTPs (5×10^{-6} M) **5a** (organe), **5b** (yellow), **5c** (blue), **5d** (red) in toluene and ICG (3×10^{-5} M, balck) in DMSO under continuous irradiation with a 500 W Xe lamp; 28 mW cm^{-2}; 20 °C.

In conclusion, we have synthesized a set of aza-BDTPs with strong and sharp absorption at around 800 nm, very low absorptions in the visible light region ranging from 700 to 380 nm, and a comparable fluorescence yield to that of comercial available ICG, without resorting to complicated purification processes. The highly favorable photophysical properties and efficient synthesis warrant further applications of these dyes in biotechnology and material science.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details, NMR, additional photophysical data, and CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Authors

*E-mail: jiao421@mail.ahnu.edu.cn.
*E-mail: sfwang@mail.ahnu.edu.cn.
*E-mail: haoehong@mail.ahnu.edu.cn.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work is supported by the National Nature Science Foundation of China (Grants Nos. 21072005, 21272007, and 21372011) and National Science Foundation of Anhui Province (1208085MB29).

REFERENCES

(1) (a) Yuan, L.; Lin, W.; Zheng, K.; He, L.; Huang, W. *Chem. Soc. Rev.* **2013**, *42*, 622. (b) Kiyose, K.; Kojima, H.; Nagano, T. *Chem.—Asian J.* **2008**, *3*, 506. (c) Yuan, L.; Lin, W.; Zhao, S.; Gao, W.; Chen, B.; He, L.; Zhu, S. *J. Am. Chem. Soc.* **2012**, *134*, 13510. (d) Zhang, Z.; Xu, B.; Su, J.; Shen, L.; Xie, Y.; Tian, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 11654.

(2) (a) Qian, G.; Wang, Z. Y. *Chem.—Asian J.* **2010**, *5*, 1006. (b) Huang, L.; Yu, X.; Wu, W.; Zhao, J. *Org. Lett.* **2012**, *14*, 2594.

(3) (a) Law, K. Y. *Chem. Rev.* **1993**, *93*, 449. (b) Pansare, V. J.; Hejazi, S.; Faenza, W. J.; Prud'homme, R. K. *Chem. Mater.* **2012**, *24*, 812.

(4) (a) Killoran, J.; Allen, L.; Gallagher, J. F.; Gallagher, W. M.; O'Shea, D. F. *Chem. Commun.* **2002**, 1862. (b) McDonnell, S. O.; Hall, M. J.; Allen, L. T.; Byrne, A.; Gallagher, W. M.; O'Shea, D. F. *J. Am. Chem. Soc.* **2005**, *127*, 16360. (c) McDonnell, S. O.; O'Shea, D. F. *Org. Lett.* **2006**, *8*, 3493. (d) Wu, D.; O'Shea, D. F. *Org. Lett.* **2013**, *15*, 3392.

(5) (a) Tasior, M.; O'Shea, D. F. *Bioconjugate Chem.* **2010**, *21*, 1130. (b) Murtagh, J.; Frimannsson, D. O.; O'Shea, D. F. *Org. Lett.* **2009**, *11*, 5386. (c) Tasior, M.; Murtagh, J.; Frimannsson, D. O.; McDonnell, S. O.; O'Shea, D. F. *Org. Biomol. Chem.* **2010**, *8*, 522. (d) Bhuniya, S.; Lee, M. H.; Jeon, H. M.; Han, J. H.; Lee, J. H.; Park, N.; Maiti, S.; Kang, C.; Kim, J. S. *Chem. Commun.* **2013**, *49*, 7141. (e) Coskun, A.; Yilmaz, M. D.; Akkaya, E. U. *Org. Lett.* **2007**, *9*, 607. (f) Adarsh, N.; Avirah, R. R.; Ramaiah, D. *Org. Lett.* **2010**, *12*, 5720.

(6) (a) Loudet, A.; Burgess, K. *Chem. Rev.* **2007**, *107*, 4891. (b) Ulrich, G.; Ziessel, R.; Harriman, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 1184. (c) Ziessel, R.; Ulrich, G.; Harriman, A. *New J. Chem.* **2007**, *31*, 496. (d) Boens, N.; Leen, V.; Dehaen, W. *Chem. Soc. Rev.* **2012**, *41*, 1130.

(7) (a) Zhang, X.; Xiao, Y.; Qi, J.; Qu, J.; Kim, B.; Yue, X.; Belfield, K. D. *J. Org. Chem.* **2013**, *78*, 9153. (b) Marsico, F.; Turshatov, A.; Weber, K.; Wurm, F. R. *Org. Lett.* **2012**, *15*, 3844. (c) Jiao, C.; Huwang, K.-W.; Wu, J. *Org. Lett.* **2011**, *13*, 632. (d) Porrel, A.; De Nicola, A.; Ziessel, R. *Org. Lett.* **2012**, *14*, 5696. (e) Jiang, X.; Zhang, J.; Furuyama, T.; Zhao, W. *Org. Lett.* **2012**, *14*, 248. (f) Uppal, T.; Hu, X.; Fronczek, F. R.; Maschek, S.; Bobadova-Parvanova, P.; Vicente, M. G. H. *Chem.—Eur. J.* **2012**, *18*, 3893. (g) Yu, C.; Xu, Y.; Jiao, L.; Zhou, J.; Wang, Z.; Hao, E. *Chem.—Eur. J.* **2012**, *18*, 6437.

(8) (a) Yang, Y.; Guo, Q.; Chen, H.; Zhou, Z.; Guo, Z.; Shen, Z. *Chem. Commun.* **2013**, *49*, 10620. (b) Awuah, S. G.; Polreis, J.; Biradar, V.; You, Y. *Org. Lett.* **2011**, *13*, 3884. (c) Umezawa, K.; Nakamura, Y.; Makino, H.; Citterio, D.; Suzuki, K. *J. Am. Chem. Soc.* **2008**, *130*, 1550.

(9) Bellier, Q.; Pegaz, S.; Aronica, C.; Guennic, B. L.; Andraud, C.; Maury, O. *Org. Lett.* **2011**, *13*, 22.

(10) (a) Zhang, X.; Yu, H.; Xiao, Y. *J. Org. Chem.* **2012**, *77*, 669. (b) Gresser, G.; Hartmann, H. M.; Wrackmeyer, K. L.; Riede, M. *Tetrahedron* **2011**, *67*, 7148. (c) Bellier, Q.; Dalier, F.; Jeanneau, E.; Maury, O.; Andraud, C. *New J. Chem.* **2012**, *36*, 768.

(11) (a) Lu, H.; Shimizu, S.; Mack, J.; Shen, Z.; Kobayashi, N. *Chem.—Asian J.* **2011**, *6*, 1026. (b) Gresser, G.; Hummert, M.; Hartmann, H.; Leo, K.; Riede, M. *Chem.—Eur. J.* **2011**, *17*, 2939. (c) Liu, H.; Mack, J.; Fuo, Q.; Lu, H.; Kobayashi, N.; Shen, Z. *Chem. Commun.* **2011**, *47*, 12092.

(12) (a) Zhao, W.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1677. (b) Zhao, W.; Carreira, E. M. *Chem.—Eur. J.* **2006**, *12*, 7254.

(13) (a) Loudet, A.; Bandichhor, R.; Burgess, K.; Palma, A.; McDonnell, S. O.; Hall, M. J.; O'Shea, D. F. *Org. Lett.* **2008**, *10*, 4771. (b) Kovtun, Y. P.; Yakubovskiy, V. P.; Shandura, M. P. *Chem. Heterocycl. Compd.* **2008**, *44*, 1298.

(14) (a) Nakamura, M.; Tahara, H.; Takahashi, K.; Nagata, T.; Uoyama, H.; Kuzuhara, D.; Mori, S.; Okujima, T.; Yamada, H.; Uno, H. *Org. Biomol. Chem.* **2012**, *10*, 6840. (b) Wakamiya, A.; Murakami, T.; Yamaguchi, S. *Chem. Sci.* **2013**, *4*, 1002.

(15) (a) Qin, W.; Leen, V.; Dehaen, W.; Cui, J.; Xu, C.; Tang, X.; Liu, W.; Rohand, T.; Beljonne, D.; Van Averbeke, B. *J. Phys. Chem. C* **2009**, *113*, 11731. (b) Filarowski, A.; Kluba, M.; Cieślik-Boczula, K.; Koll, A.; Kochel, A.; Pandey, L.; De Borggraeve, W. M.; Van der Auweraer, M.; Catalán, J.; Noens, N. *Photochem. Photobiol. Sci.* **2010**, *9*, 996.