Organic LETTERS

Letter

pubs.acs.org/OrgLett

Synthesis of Ultrahighly Electron-Deficient Pyrrolo[3,4-*d*]pyridazine-5,7-dione by Inverse Electron Demand Diels−Alder Reaction and Its Application as Electrochromic Materials

Qun Ye,[†] Wei Teng Neo,[†,§] Ching Mui Cho,[†] Shuo Wang Yang,[‡] Tingting Lin,[†] Hui Zhou,[†] Hong Yan,[†] Xuehong Lu,[∥] Chunyan Chi,[⊥] and Jianwei Xu*,[†,⊥]

[†]Institute of Materials Research and Engineering, A*STAR, 3 Research Link, Singapore 117602, Singapore
[‡]Institute of High Performance Computing, A*STAR, 1 Fusionopolis Way, #16-16 Connexis, Singapore 138632, Singapore
[§]NUS Graduate School for Integrative Sciences and Engineering, National University of Singapore, 28 Medical Drive, Singapore 117456, Singapore
[⊥]Department of Chemistry, National University of Singapore, 3 Science Drive 3, Singapore 117543, Singapore
[∥]School of Materials Science and Engineering, Nanyang Technological University, 50 Nanyang Avenue, Singapore 639798, Singapore

Supporting Information

ABSTRACT: A new electron acceptor 6-alkylpyrrolo[3,4-*d*]pyridazine-5,7-dione (PPD) with a very low LUMO level has been synthesized via a challenging inverse electron demand Diels−Alder reaction between thiophene and furan-decorated tetrazine substrates and an electron-deficient 1-alkyl-1*H*-pyrrole-2,5-dione unit. The PPD monomer has been incorporated into a series of donor−acceptor-type conjugated polymers as electrochromic materials with good optical contrast, fast switching speed, and high coloration efficiency.

Electron-deficient π-conjugated building blocks, which are generally termed as acceptors, have been widely applied for the synthesis of functional dyes and organic electronics materials.[1] The presence of acceptors is essential to tune the energy levels of the frontier orbitals and the absorption of the materials,[1j] and in many cases, the choice of the acceptor is crucial for the high performance of the materials.[1,2] One important attribute of the acceptor is the electron deficiency, and high electron deficiency is of great importance for many applications, such as donor−acceptor dyes with near-infrared absorption and emissions,[3] n-type organic field-effect transistors,[1a,g,k] and light absorption materials in bulk heterojunction blend solar cells.[1d,h]

In our current work, we report an unprecedented pyridazine-fused imide as a novel electron acceptor with ultrahigh electron deficiency. The key synthesis relies on an inverse electron demand Diels−Alder (D−A) reaction on tetrazine. Tetrazine[4] is a known electron-deficient building block and has been studied as a ligand, energetic materials, a fluorescent dye, and an electron acceptor in organic electronics materials. The inverse electron demand D−A reaction on tetrazine has been studied both theoretically[5] and experimentally[6] and applied as a versatile "click" approach for bio-related applications.[7] This reaction works well for electron-rich and strained dienophiles. However, such approach with electron-deficient dienophiles is believed to be challenging and has rarely been reported.[6e] In this study, we challenge the synthesis of 6-alkylpyrrolo[3,4-*d*]pyridazine-5,7-dione (PPD) via an inverse electron demand D−A reaction of functionalized tetrazine with electron-deficient 1-alkyl-1*H*-pyrrole-2,5-dione unit. There are two attributes of the new acceptor which need to be highlighted. The first is the ultrahigh electron deficiency. We compared the lowest unoccupied molecular orbital (LUMO) energy level of the PPD unit with those of some relevant acceptors (Figure 1). Out of the 10 relevant acceptors investigated, only bisbenzothiadiazole has a LUMO energy level lower than the PPD unit. The second is that PPD is designed to undergo convenient side chain engineering and easy incorporation into polymeric materials. The inverse electron demand D−A reaction is also intriguing for discussion. We observed a selective D−A process on thiophene and furan-decorated tetrazine, and only the inverse electron demand D−A pathway was observed. Time-dependent density functional theory (TD-DFT) calculation has been carried out to better understand this process. Finally, we demonstrate the synthesis and characterization of a series of high-performance electrochromic polymers with the newly developed PPD monomer embedded.

The synthesis of the two building blocks is outlined in Scheme 1. Starting from commercially available 2-cyano furan (**1**) and 2-cyano thiophene (**2**), the tetrazine heterocycle was constructed via established methods,[8] and intermediates **3** and **4** were obtained in 43 and 52% yields, respectively. The following bromination reaction with NBS in hot DMF afforded the dibrominated products **5** and **6** in a good yield. The D−A reaction between tetrazine derivative **6** and an alkylated imide was surveyed under various conditions. According to the general observation that tetrazines with electron-donating substitutions are much less reactive toward an inverse electron demand D−A reaction compared with those with electron-withdrawing groups

Received: October 31, 2014
Published: December 1, 2014

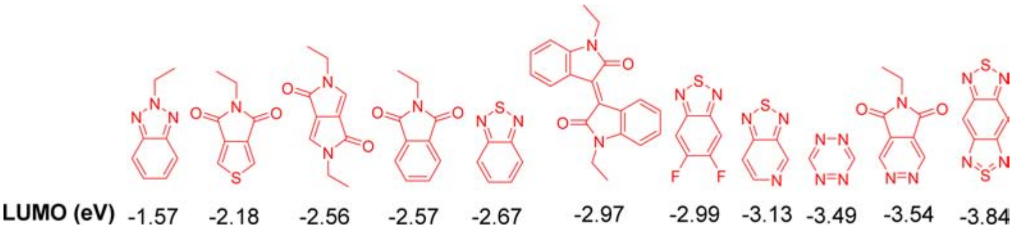
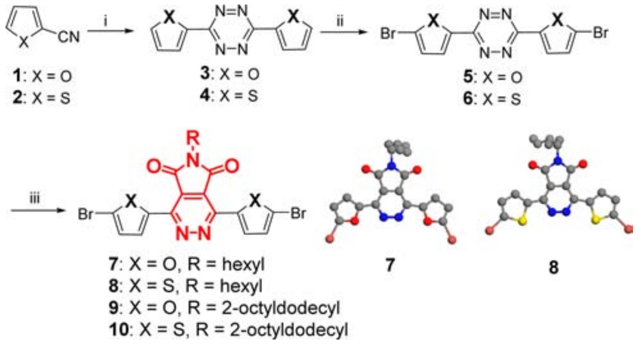


Figure 1. Calculated LUMO energy levels of a series of relevant acceptor monomers. From left to right: benzotriazole, 5-alkylthieno[3,4-*c*]pyrrole-4,6-dione, diketopyrrolopyrrole, 2-alkylisoindole-1,3-dione, benzo[1,2,5]thiadiazole, iso-indigo, 5,6-difluorobenzo[1,2,5]thiadiazole, [1,2,5]thiadiazolo-[3,4-*c*]pyridine, tetrazine, 6-alkylpyrrolo[3,4-*d*]pyridazine-5,7-dione, bisbenzothiadiazole.

Scheme 1. Synthesis of Imide-Fused Pyridazines 7−10[a]



[a]Reaction conditions: (i) hydrazine, sulfur, EtOH; then isoamyl nitrite; (ii) NBS, DMF, 100 °C; (iii) 1-alkyl-1*H*-pyrrole-2,5-dione, diphenyl ether, 160 °C. Insets: single-crystal structures of compounds **7** and **8** with hydrogen atoms omitted for clarity.

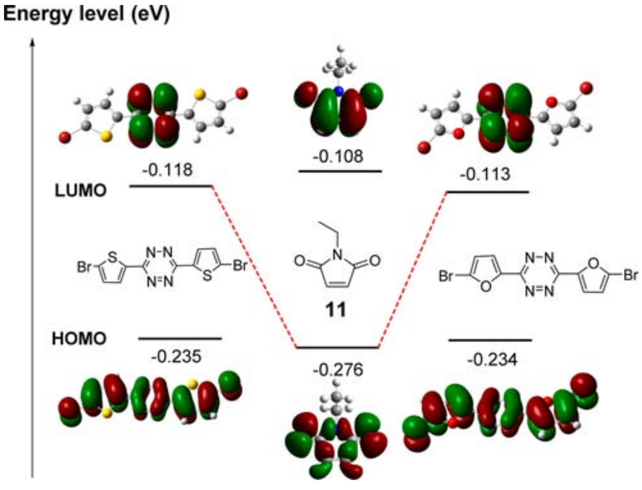


Figure 2. HOMO/LUMO energy profiles and energies (in eV) for compounds **5**, **6**, and **11**. HOMO/LUMO interaction is shown as dotted lines, and the observed pathway is highlighted in red.

and electron-deficient dienophiles are much less prone to undergo D−A reaction with tetrazine,[6] the chemical approach was therefore envisaged to be extremely challenging. In our hands, it was found that the reaction temperature was the crucial parameter to push the reaction forward. As the reaction between **6** and 1-hexyl-1*H*-pyrrole-2,5-dione was tried in refluxing chloroform (60 °C), dioxane (100 °C), and toluene (110 °C), no D−A product was detected at all after 16 h. Once the reaction was heated to 160 °C in diphenyl ether, the inverse electron demand D−A reaction smoothly occurred with the D−A product obtained in 50−70% yield after 16 h. The high reaction temperature (160 °C) was stringent to overcome the energy barrier to let the reaction proceed. One more interesting aspect to highlight is that, even though both thiophene and furan are known to undergo D−A reaction,[9] we did not observe the generation of D−A products on the furan and thiophene units when substrates **5** and **6** were tested under various conditions (25−160 °C). It would thus be intriguing to figure out a selective D−A ligation process on tetrazine rather than on thiophene and furan.

To better elucidate the reactivity of D−A reaction, we carried out TD-DFT calculations at the B3LYP/6-31G level. A normal D−A reaction involves the interaction between the $\mathrm{HOMO}_{\mathrm{diene}}$ and $\mathrm{LUMO}_{\mathrm{dienophile}}$, and the inverse electron demand D−A reaction involves the interaction between the $\mathrm{HOMO}_{\mathrm{dienophile}}$ and $\mathrm{LUMO}_{\mathrm{diene}}$.[10] As the distribution and the energy level of the frontier orbitals are essential for the occurrence of D−A reaction, the HOMO/LUMO profiles and their energy levels of the reacting species are calculated and shown in Figure 2. For substrates **5** and **6**, the HOMO is evenly distributed over the π-system whereas the LUMO is located on the tetrazine unit. Compounds **5** and **6** had similar HOMO and LUMO energy levels. The active double bond of model compound **11** was involved in both the HOMO and LUMO. Given the calculated frontier orbitals, both pathways possibly occur due to the matching phases and similar energy differences of relevant frontier orbitals.

We then calculated the activation energy ($\Delta G^{\ddagger}$) for respective pathways, and the results are summarized in Figure 3. The inverse electron demand D−A reaction between tetrazine moiety and dienophiles is believed to undergo two subsequent steps:

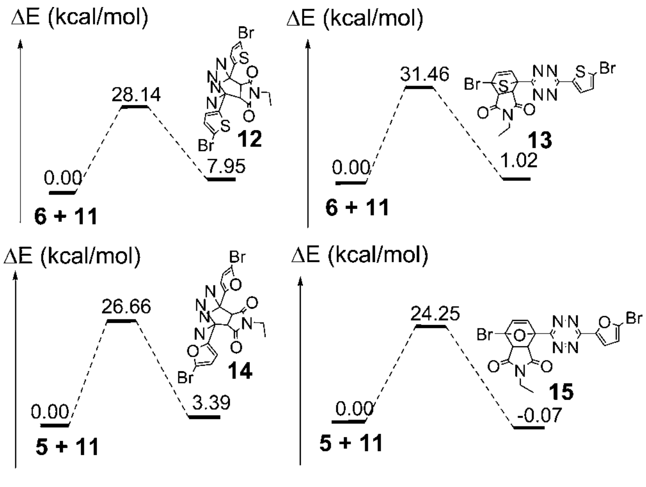
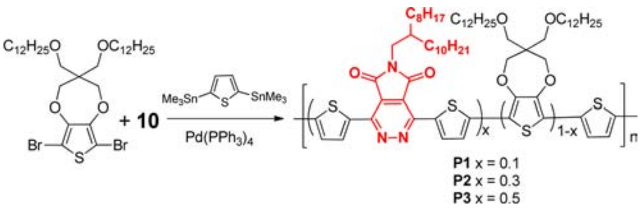


Figure 3. Free energy profiles of normal D−A reaction and inverse electron demand D−A reaction pathways to attach **11** to compounds **5** and **6**. Gibbs free energies are shown in kcal/mol.

formation of the bicyclic intermediates (e.g., **12** and **14**) and formation of the final pyridazine product (**7**−**10**) after loss of one nitrogen gas molecule.[5] Recent theoretical investigations have shown that the second step proceeds with a very low or almost nonexistent energy barrier.[11] Therefore, in our current study, we focus our attention on the first step. For compound **6**, the activation energy barrier ($\Delta G^{\ddagger}$) of inverse electron demand D−A reaction on the tetrazine was 28.14 kcal/mol whereas the activation energy barrier of the D−A reaction at the thiophene position was 31.46 kcal/mol. The higher $\Delta G^{\ddagger}$ of the normal D−A pathway on thiophene unit may account for the observed selectivity. On the contrary, for the furan-attached tetrazine monomer **5**, the activation energy barrier for D−A reaction on the tetrazine is 26.66 and 24.25 kcal/mol for the reaction to occur on the furan unit. The activation energy of the normal D−A reaction on the furan unit of **5** is much higher than that of an alkyl-substituted furan, which has activation energy in the range of 9.6−10 kcal/mol.[12] This was mainly ascribed to the attachment of electron-withdrawing moieties on the furan unit. Kinetically speaking, the D−A reaction on the furan unit would be favored over the tetrazine unit. However, during our survey of the reaction conditions, we did not observe any appreciable amount of D−A products on the furan unit. One reason would be the reversibility of the D−A reaction between furan and imide,[13] and the observed selectivity could be rationalized in the proposed mechanism shown in Figure S1. Due to the dynamic covalent nature of cyclo-adduct **15** between furan and imide, the dissociation occurs at >90 °C.[13] As we did not observe any appreciable amount of furan−imide D−A product from room temperature to 160 °C, we hypothesize that the D−A reaction on furan and tetrazine would occur simultaneously at 160 °C. At this reaction temperature, the dissociation of cyclo-adduct **15** concurrently occurs with the association process. Meanwhile, the inverse electron demand D−A route gradually consumes the starting material in an irreversible way. Hence, any formed **15** was gradually consumed with only the inverse electron demand D−A product obtained.

The frontier orbital energy levels of monomers **9** and **10** were investigated by cyclic voltammetry. The observed LUMO energy levels for compounds **9** and **10** are −3.66 and −3.67 eV, respectively (Figure S33), confirming the strong electron deficiency of the PPD unit.[1j] As the pyridazine imide monomers (**7**−**10**) are designed for convenient side chain engineering and easy incorporation into conjugated functional polymers, such monomers would be of great usefulness as versatile building blocks[1h,k,14] for polymeric organic electronics materials. Herein we demonstrate the preparation of high-performance electrochromic (EC) materials[15] with the pyridazine−imide unit embedded. The random polymers **P1**−**P3** were prepared via Stille coupling reaction according to Scheme 2. Different ratios of acceptor **10** were introduced into the polymer backbone to test its influence on the optical properties and EC performance.

Scheme 2. Synthetic Route of Polymers P1−P3



All three polymers absorbed strongly in the visible region with $\lambda_{max} \sim 530$ nm (Figure S2), which exhibited a purple color at the neutral state. The optical band gap was determined to be 1.77, 1.71, and 1.69 eV for **P1**−**P3**, respectively, and showed a slight decrease after more acceptor was introduced. **P1**−**P3** showed quasi-reversible oxidation upon p-doping (Figure S3), and after more acceptor **10** was incorporated into the polymers (i.e., from **P1** to **P3**), a gradual deepening of the HOMO energy level was observed from −4.92 to −5.00 eV. The spectroelectrochemical study was carried out for **P1**−**P3** on a sandwiched device, and the results are shown in Figures 4, S4 and S5. Upon gradual p-doping, the absorption of the neutral polymer **P1** in the visible range gradually decreased, while the absorption in the near-infrared (NIR) region gradually increased and the residual color of the thin film appeared to be a cyan hue. As more acceptors were introduced in the polymer backbone, an increasing residue absorption in the visible region of the charged species was observed. As a result, **P1** achieved the best optical contrast of 34.1% at 540 nm and 54.2% at 1350 nm.

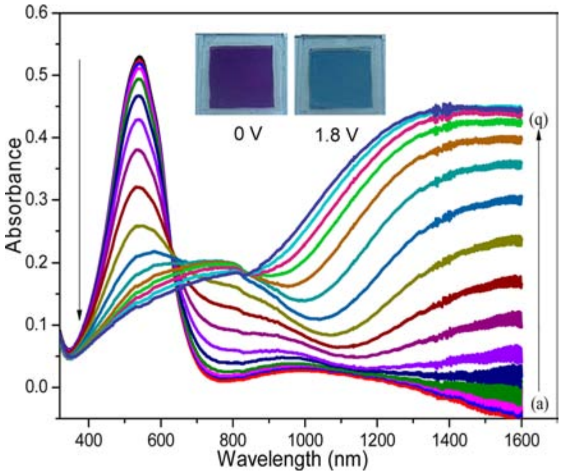


Figure 4. UV−vis−NIR absorptions of **P1** at various applied potentials (V): (a) 0.0, (b) 0.2, (c) 0.4, (d) 0.5, (e) 0.6, (f) 0.7, (g) 0.8, (h) 0.9, (i) 1.0, (j) 1.1, (k) 1.2, (l) 1.3, (m) 1.4, (n) 1.5, (o) 1.6, (p) 1.7, (q) 1.8 V.

The switching properties of the EC polymers **P1**−**P3** were investigated by chronoamperometry to monitor the changes in transmittance as a function of time while sweeping the potentials between 1.5 and −1.5 V at local absorption maxima, and the results are shown in Figures 5, S6, and S7 and summarized in Table S2. All three polymers exhibited fast switching with coloration time in the visible region at 1−2 s and bleaching time at 7−8 s. The amount of acceptor in the polymer did not significantly influence the switch time of the EC polymers. **P1** showed the most promising coloration efficiency of 436 cm^2/C in the visible region (542 nm) and 457 cm^2/C in the NIR region (1350 nm).

In summary, we have successfully synthesized a unique PPD building block with ultrahigh electron deficiency by an inverse electron demand D−A reaction. Different side chains can be conveniently attached on the PPD monomer, and conjugated polymers can be prepared via palladium-catalyzed cross-coupling reactions. Hence, it would be very useful for the preparation of donor−acceptor-type conjugated polymers. We also noticed an intriguing selective D−A process on the thiophene and furan-ligated tetrazine. This process has been investigated by TD-DFT calculations, and we hypothesized that the high activation energy

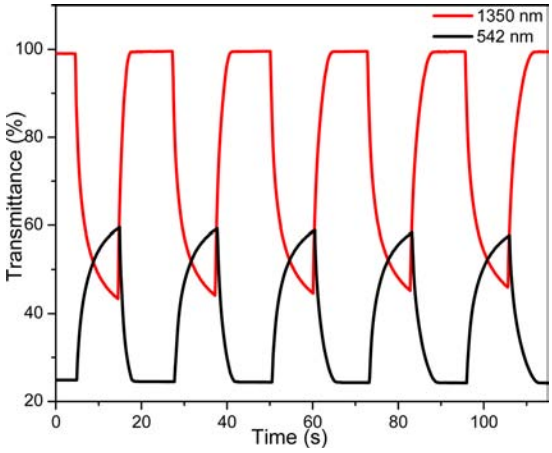


Figure 5. Square-wave potential step absorptiometry of **P1** monitored at 542 and 1350 nm between 1.5 V and −1.5 V with a switch time of 10 s.

of the thiophene−imide interaction and the dynamic covalent nature of the furan−imide cyclo-adduct would be the reason for the observed selectivity. We also demonstrated the incorporation of this novel monomer into electrochromic materials. Stable EC polymers have been prepared with good optical contrast, fast switching speed, and high coloration efficiency. We are currently seeking to synthesize more novel monomers based on the D−A reaction on tetrazine and to apply these building blocks for organic electronics materials.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Synthetic procedures and characterization data for all new compounds, DFT calculation details, X-ray crystallographic data, and more electrochromic characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: jw-xu@imre.a-star.edu.sg.

Author Contributions

W.T.N. and C.M.C contributed equally to this paper.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We would like to acknowledge the financial support from the Agency for Science, Technology and Research (A*STAR), and Singapore Ministry of National Development (MND) (Grant No. 1321760011).

■ REFERENCES

(1) (a) Zhan, X.; Facchetti, A.; Barlow, S.; Marks, T. J.; Ratner, M. A.; Wasielewski, M. R.; Marder, S. R. *Adv. Mater.* **2011**, *23*, 268. (b) Facchetti, A. *Chem. Mater.* **2011**, *23*, 733. (c) Balan, A.; Baran, D.; Toppare, L. *Polym. Chem.* **2011**, *2*, 1029. (d) Duan, C.; Huang, F.; Cao, Y. *J. Mater. Chem.* **2012**, *22*, 10416. (e) Biniek, L.; Schroeder, B. C.; Nielsen, C. B.; McCulloch, I. *J. Mater. Chem.* **2012**, *22*, 14803. (f) Robb, M. J.; Ku, S.-Y.; Brunetti, F. G.; Hawker, C. J. *J. Polym. Sci., Part A: Polym. Chem.* **2013**, *51*, 1263. (g) Zhao, Y.; Guo, Y.; Liu, Y. *Adv. Mater.* **2013**, *25*, 5372. (h) Pron, A.; Leclerc, M. *Prog. Polym. Sci.* **2013**, *38*, 1815. (i) Goetz, K. P.; Vermeulen, D.; Payne, M. E.; Kloc, C.; McNeil, L. E.; Jurchescu, O. D. *J. Mater. Chem. C* **2014**, *2*, 3065. (j) Takimiya, K.; Osaka, I.; Nakano, M. *Chem. Mater.* **2014**, *26*, 587. (k) Guo, X.; Facchetti, A.; Marks, T. J. *Chem. Rev.* **2014**, *114*, 8943.

(2) (a) Zhang, Y.; Zou, J.; Cheuh, C.-C.; Yip, H.-L.; Jen, A. K.-Y. *Macromolecules* **2012**, *45*, 5427. (b) Stuart, A. C.; Tumbleston, J. R.; Zhou, H.; Li, W.; Liu, S.; Ade, H.; You, W. *J. Am. Chem. Soc.* **2013**, *135*, 1806.

(3) (a) Qian, G.; Wang, Z. Y. *Chem.—Asian J.* **2010**, *5*, 1006. (b) Ellinger, S.; Graham, K. R.; Shi, P.; Farley, R. T.; Steckler, T. T.; Brookins, R. N.; Taranekar, P.; Mei, J.; Padilha, L. A.; Ensley, T. R.; Hu, H.; Webster, S.; Hagan, D. J.; Stryland, E. W. V.; Schanze, K. S.; Reynolds, J. R. *Chem. Mater.* **2011**, *23*, 3805.

(4) (a) Kaim, W. *Coord. Chem. Rev.* **2002**, *230*, 127. (b) Saracoglu, N. *Tetrahedron* **2007**, *63*, 4199. (c) Clavier, G.; Audebert, P. *Chem. Rev.* **2010**, *110*, 3299. (d) Kozhevnikov, D. N.; Prokhorov, A. M. Triazines and Tetrazines. In *Progress in Heterocyclic Chemistry*; Gribble, G. W., Joule, J. A., Eds.; Elsevier: Amsterdam, 2011; Vol. 23, pp 449−462.

(5) (a) Gomez-Bengoa, E.; Helm, M. D.; Plant, A.; Harrity, J. P. A. *J. Am. Chem. Soc.* **2007**, *129*, 2691. (b) Hayden, A. E.; Houk, K. N. *J. Am. Chem. Soc.* **2009**, *131*, 4084. (c) Domingo, L. R.; Picher, M. T.; Sáez, J. A. *J. Org. Chem.* **2009**, *74*, 2726. (d) Liu, F.; Paton, R. S.; Kim, S.; Liang, Y.; Houk, K. N. *J. Am. Chem. Soc.* **2013**, *135*, 15642. (e) Liu, F.; Liang, Y.; Houk, K. N. *J. Am. Chem. Soc.* **2014**, *136*, 11483.

(6) (a) Boger, D. L.; Sakya, S. M. *J. Org. Chem.* **1988**, *53*, 1415. (b) Sauer, J.; Heldmann, D. K.; Hetzenegger, J.; Krauthan, J.; Sichert, H.; Schuster, J. *Eur. J. Org. Chem.* **1998**, 2885. (c) Sauer, J.; Heldmann, D. K. *Tetrahedron* **1998**, *54*, 4297. (d) Girardot, M.; Nomak, R.; Snyder, J. K. *J. Org. Chem.* **1998**, *63*, 10063. (e) Miller, G. P.; Tetreau, M. C. *Org. Lett.* **2000**, *2*, 3091.

(7) (a) Blackman, M. L.; Royzen, M.; Fox, J. M. *J. Am. Chem. Soc.* **2008**, *130*, 13518. (b) Devaraj, N. K.; Hilderbrand, S.; Upadhyay, R.; Mazitschek, R.; Weissleder, R. *Angew. Chem., Int. Ed.* **2010**, *49*, 2869. (c) Taylor, M. T.; Blackman, M. L.; Dmitrenko, O.; Fox, J. M. *J. Am. Chem. Soc.* **2011**, *133*, 9646. (d) Versteegen, R. M.; Rossin, R.; Hoeve, W.; Janssen, H. M.; Robillard, M. S. *Angew. Chem., Int. Ed.* **2013**, *52*, 14112. (e) Denk, C.; Svatunek, D.; Filip, T.; Wanek, T.; Lumpi, D.; Fröhlich, J.; Kuntner, C.; Mikula, H. *Angew. Chem., Int. Ed.* **2014**, *53*, 9655. (f) Lang, K.; Chin, J. W. *Chem. Rev.* **2014**, *114*, 4764.

(8) (a) Li, Z.; Ding, J. *Macromol. Chem. Phys.* **2011**, *212*, 2260. (b) Wen, S.; Dong, Q.; Cheng, W.; Li, P.; Xu, B.; Tian, W. *Sol. Energy Mater. Sol. Cells* **2012**, *100*, 239. (c) Hwang, D. K.; Dasari, R. R.; Fenoll, M.; Alain-Rizzo, V.; Dindar, A.; Shim, J. W.; Deb, N.; Fuentes-Hernandez, C.; Barlow, S.; Bucknall, D. G.; Audebert, P.; Marder, S. R.; Kippelen, B. *Adv. Mater.* **2012**, *24*, 4445.

(9) Fringuelli, F.; Taticchi, A. *The Diels−Alder Reaction: Selected Practical Methods*; John Wiley & Sons: New York, 2002.

(10) Fleming, I. Thermal Pericyclic Reactions. In *Molecular Orbitals and Organic Chemical Reactions: Reference Edition*; Wiley: New York, 2010; pp 185−274.

(11) Sadasivam, D. V.; Prasad, E.; Flowers, R. A., II; Birney, D. M. *J. Phys. Chem. A* **2006**, *110*, 1288.

(12) (a) Gandini, A.; Coelho, D.; Silvestre, A. J. D. *Eur. Polym. J.* **2008**, *44*, 4029. (b) Liu, X.; Du, P.; Liu, L.; Zheng, Z.; Wang, X.; Joncheray, T.; Zhang, Y. *Polym. Bull.* **2013**, *70*, 2319.

(13) Bergman, S. D.; Wudl, F. *J. Mater. Chem.* **2008**, *18*, 41.

(14) Guo, X.; Baumgarten, M.; Müllen, K. *Prog. Polym. Sci.* **2013**, *38*, 1832.

(15) (a) Beaujuge, P. M.; Reynolds, J. R. *Chem. Rev.* **2010**, *110*, 268. (b) Sonmez, G. *Chem. Commun.* **2005**, 5251.