Organic LETTERS

Letter

pubs.acs.org/OrgLett

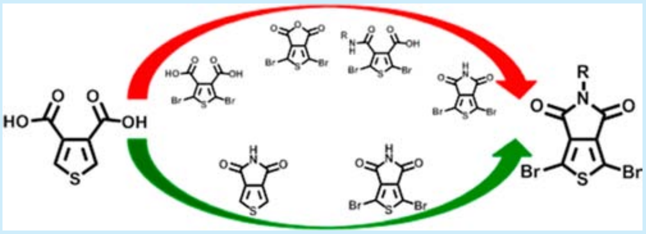
Direct Imide Formation from Thiophene Dicarboxylic Acids Gives Expanded Side-Chain Selection in Thienopyrrolediones

Rylan M. W. Wolfe and John R. Reynolds*

School of Chemistry and Biochemistry, School of Materials Science and Engineering, Center for Organic Photonics and Electronics, Georgia Tech Polymer Network, Georgia Institute of Technology, Atlanta, Georgia 30332, United States

Supporting Information

ABSTRACT: The synthesis of thienopyrroledione (TPD) has been updated to reduce the number of synthetic steps, remove hazardous and toxic reagents, reduce the amount of byproduct waste, and reduce the use of solvents when unnecessary. Diverse functionalization is possible, introducing 16 examples in yields from 34% to 95%. This reaction scheme was shown to be general for thiophene imides, and a more thorough exploration into side chain engineering is presented with TPD acceptors often used in organic electronic applications.



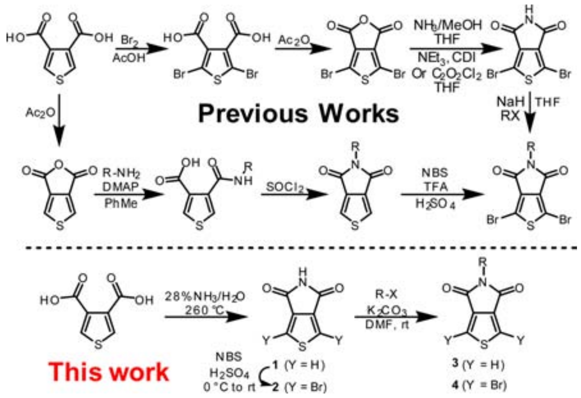
Synthetic chemistry in organic electronics is heavily directed toward the development of new structures for particular properties and applications. Work is focused on obtaining the end product; however, even materials with ideal characteristics have little chance for widespread usage if they cannot be made safely and efficiently. As the field aims for production of molecules at large scales, it is necessary to reevaluate the syntheses. We have implemented five of the 12 Principles of Green Chemistry by (1) preventing waste, (2) maximizing atom economy, (3) using less hazardous reagents and (4) safer solvents, and (5) reducing unnecessary derivatization,[1] while simultaneously expanding the utility of the thienopyrroledione (TPD).

The regiosymmetric nature and ability to append solubilizing chains to repeat units led Pomerantz and Amarasekara,[2] and later Nielsen and Bjørnholm,[3] to investigate TPD as a monomer for conjugated polymers. More recently, TPD has become a common repeat unit in high performance polymers for organic photovoltaic[4,5] and transistor applications.[6] The development of direct arylation polymerization has provided easy access to many TPD-based polymers.[7]

However, while other repeat units have been extensively modified via their side chains,[8] TPD monomers are almost exclusively limited to alkyl chains due to the requirement of an amine precursor in the typical synthesis. Few other chains (oligoether,[9] aryl,[10] and alkoyl substituents[11,12]) have been synthesized. These studies have achieved some success, but the use of TPD is limited with respect to other nitrogen-based acceptors. For example, on diketopyrrolopyrrole[13] and isoindigo,[14] the side chain is installed after core construction allowing for rapid, late-stage modifications.

In a review of common conjugated polymers for organic photovoltaics, Po et al. evaluated the synthetic complexity of repeat units based on the number of synthetic steps, overall yields, purification requirements, and the use of hazardous materials.[15] Thiophene-based imides score remarkably well despite typical syntheses (Scheme 1, top) requiring a number of hazardous reagents.[3,11,16] Their analysis does not take into account the Gabriel synthesis of amine precursors, which may require diisopropylazidodicarboxylate and hydrazine.

Scheme 1. Synthetic Route to Functionalized TPDs

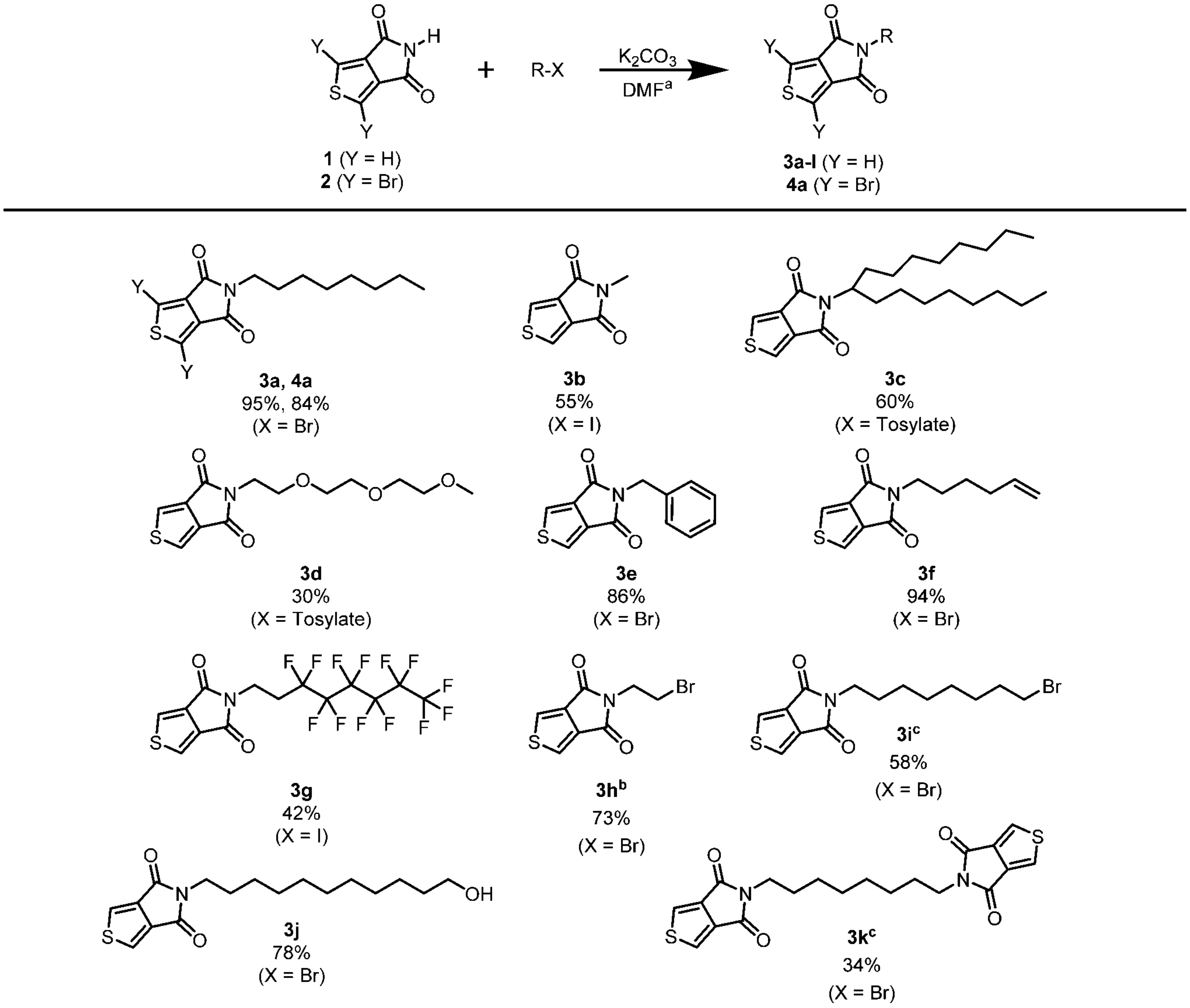


For example, Nielsen and Bjørnholm's synthesis[3] for TPD (Scheme 1, top) uses acetic anhydride (approximately 100 equiv) and thionyl chloride (OPCW Schedule III Chemical,[17] approximately 150 equiv) as reagents, resulting in large excesses that must be quenched or recovered. The installed side chain must then withstand harsh bromination conditions (sulfuric acid and trifluoroacetic acid, a persistent environmental chemical). Scheme 1 also shows routes others have developed to the unfunctionalized, brominated imide.[12,16] No effort has yet been reported to capitalize on this work, possible because these methods still require acetic anhydride, oxalyl chloride or

Received: December 22, 2016
Published: February 20, 2017

DOI: 10.1021/acs.orglett.6b03830
Org. Lett. 2017, 19, 996−999

Scheme 2. Scope of Side Chains Available via Nucleophilic Substitution on Different Electrophiles



[a] Isolated yields are shown. Unoptimized reaction conditions: Imide (1.0 equiv), R–X (1.5 equiv), K_2CO_3 (2.0 equiv), DMF (0.1 M), rt. [b] Formation of dimer not observed. [c] 1.0 equiv of octyldibromide used. 92% overall conversion of **1** to products **3i** and **3k**.

thionyl chloride, dimethylaminopyridine (DMAP), sodium hydride, ammonia, and carbonyl diimidazole (CDI).

Here, we report a new synthetic route (Scheme 1, bottom) from the dicarboxylic acid to TPD with enhanced atom economy and mild functionalization conditions that allow for a diverse class of molecules (see Scheme 2). We accomplish atom economy through the elimination of reaction steps and of reactants used in severe excess. The only solvents required are aqueous ammonia, sulfuric acid, and DMF. Overall yields are comparable to previously reported syntheses. The unbrominated and dibromo derivatives are ready for direct arylation polymerization, and the dibromo species can be polymerized via Stille, Suzuki, and other coupling routes. We also show this method is applicable to other thiophene imides as exemplified by the synthesis of 2,2′-bithiophene-3,3′-dicarboximide.

Our synthetic route was inspired by the original synthesis of unfunctionalized TPD using ammonium hydroxide with thiophene-3,4-dicarboxylic anhydride.[18] This reaction was well-known for the synthesis of phthalimide.[19] We have shown the imide can be generated directly from commercially available 3,4-thiophene dicarboxylic acid. The diacid was fully dissolved in minimal concentrated aqueous ammonia. Excess ammonia and water were removed by gentle heating to give a white solid. Complete conversion to the diammonium salt was confirmed by NMR. The solid was then heated, neat, to 260–280 °C, at which temperature the reaction mixture became a homogeneous melt. The crude product (**1**) slowly sublimed from the reaction and was conveniently collected in this way. Starting material and amide intermediates were present as impurities in the crude product. The starting material was removed via trituration with water, and pure **1** was obtained through Kugelrohr sublimation or recrystallization from acetonitrile.

The brominated derivative (**2**) was desired for use in cross-coupling reactions. To avoid optimizing the reaction for each side chain, or exposing side chains to harsh brominating agents, we developed new conditions for brominating the unfunctionalized imide. NBS (4 equiv) in cold concentrated sulfuric acid gave sufficiently pure product after quenching over ice.

The literature procedure for functionalizing TPD using NaH in THF[11] was unsuccessful in our hands on both **1** and **2**. Seeking milder general conditions potentially useful for all TPD derivatives, we employed potassium carbonate in DMF (Scheme 2, top). DMF readily solubilized the TPD imides and all side chain precursors used in this study. Reactions were completed at room temperature with overnight stirring.

To prove the widespread applicability of this approach, we first repeated the synthesis of primary and secondary alkyl chains. These were synthesized using halides (1-bromooctane, **3**, **4a**) or tosylates (9-tosylheptadecane, **3c**) as leaving groups, eliminating the need for an amine synthesis, as is required for 5-(2-hexyldecyl)thienopyrrole-4,6-dione using the commercially available 2-hexadecan-1-ol.[20] This especially simplified the synthesis of the methyl derivative (**3b**). Whereas methyl iodide is an easily handled liquid, methylamine is a gas at room temperature and is a DEA List I chemical.[21]

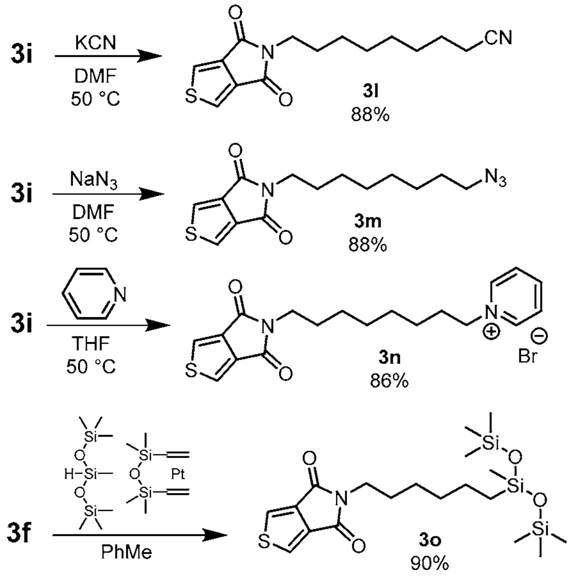
Sterics of the electrophile affected the end product. Reactions at primary, secondary, and benzylic (**3e**) carbons proceeded without issue. When using 1,8-dibromooctane as an electrophile, the stoichiometry was set to allow both mono- (**3i**) and disubstitution (**3k**). Interestingly, dimer formation was not seen when using 1,2-dibromoethane as an electrophile, even when **3h** was reacted with excess **1**. We were unable to extend these conditions to a tertiary electrophile, *tert*-butyl bromide. Heating at 50 or 100 °C overnight did not promote product formation.

The choice of side chain has a dramatic impact on the final properties and uses of the TPD derivatives, which were focused on in Scheme 2. Oligoether chains (**3d**) have been investigated previously to produce amphiphilic materials, but the ether chains are particularly susceptible to bromination. They are postulated to affect the dielectric constant in conjugated polymers[22,23] and have been used in Langmuir–Blodgett deposition techniques.[9] The yield of (**3d**) was reduced by difficulty in chromatographic separation from the tosylate electrophile. Treating the reaction with excess lithium bromide is recommended (see Supporting Information procedure for **3c**). Perfluoroalkyl chains are popular for improving n-type mobilities[24] and for their solubility in perfluorinated solvents.[25] To avoid special conditions often required for attaching perfluoroalkyl chains, electron-deficient 1*H*,1*H*,2*H*,2*H*-perfluorooctyl chains were used in this study to give **3g** in satisfactory yield.

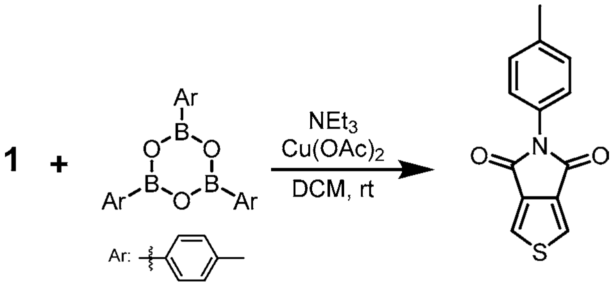
Scheme 3 presents latent functionality end groups that are useful for post-polymerization functionalization or for diversifying monomer units. The bromine terminated octyl chain (**3i**) served as an electrophile and was functionalized to the nitrile derivative (**3l**), which is useful for increasing the dielectric constant,[26] to the azido derivative (**3m**), useful for cross-linking to make thermally stable, solvent resistant films,[27] and to a pyridyl group (**3n**), useful for creating conjugated polyelectrolytes for fluorescence sensing systems,[28] electrochromic films,[29] interlayers in OPV,[30] and for thermoelectrics.[31] Alternatively, the hydroxyl terminated chain (**3j**) is primed for a reaction with an acyl chloride. Hydrosilylation with Karstedt's catalyst gave a siloxy terminated alkyl chain (**3o**) that has been shown to reduce $\pi-\pi$ stacking distances and increase mobility in solution cast films of isoindigo-based molecules.[32]

Aryl *N*-functionalization of TPD is challenging due to the lower solubility and the need to purchase or synthesize custom anilines as precursors. By using Chan–Lam couplings, as shown in Scheme 4, completed with boroxines (dehydrated boronic acid rings), we arrived at arylated TPD (**3p**) without the need for anilines.

Scheme 3. Scope of Side Chains through Latent Functionality for Pre- and Post-polymerization Processing



Scheme 4. Chan–Lam Coupling of Aryl Boronic Acids to Imides

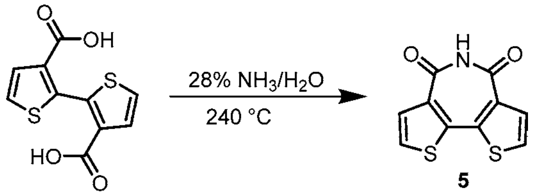


3r
86%

We have extended our conditions to the synthesis of unfunctionalized dithieno[3,2-*c*:2′,3′-*e*]azepine-4,6-dione (commonly known as 2,2′-bithiophene-3,3′-dicarboximide or BTI) (**5**) as illustrated in Scheme 5. Although polymers of BTI have given remarkably high fill factors in OPV devices,[4] the synthesis suffers the same drawbacks of TPD preparation.

With these new conditions, significant reduction in waste during synthesis is achieved without sacrificing yield. The mild conditions for functionalization have permitted an expanded selection of TPD molecules. With these available, new

Scheme 5. Imide Formation from Bithiophene Dicarboxylic Acid



5
52%

DOI: 10.1021/acs.orglett.6b03830
Org. Lett. 2017, 19, 996–999

explorations into advanced materials incorporating TPD and other thiophene imides are possible.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b03830.

Experimental procedures, characterization, and spectral data (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: reynolds@chemistry.gatech.edu.

ORCID

Rylan M. W. Wolfe: 0000-0003-4653-1483
John R. Reynolds: 0000-0002-7417-4869

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research was conducted with Government support under and awarded by DoD, Air Force Office of Scientific Research, National Defense Science and Engineering Graduate (NDSEG) Fellowship, 32 CFR 168a. Work was supported by the Department of the Navy, Office of Naval Research Award Nos. N00014-14-1-0580 and N00014-14-1-0173.

■ REFERENCES

(1) Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: New York, 1998.

(2) Pomerantz, M.; Amarasekara, A. S. *Synth. Met.* **2003**, *135–136*, 257–258.

(3) Nielsen, C. B.; Bjørnholm, T. *Org. Lett.* **2004**, *6* (19), 3381–3384.

(4) Guo, X.; Zhou, N.; Lou, S. J.; Smith, J.; Tice, D. B.; Hennek, J. W.; Ortiz, R. P.; Navarrete, J. T. L.; Li, S.; Strzalka, J.; Chen, L. X.; Chang, R. P. H.; Facchetti, A.; Marks, T. J. *Nat. Photonics* **2013**, *7* (10), 825–833.

(5) Small, C. E.; Chen, S.; Subbiah, J.; Amb, C. M.; Tsang, S.; Lai, T.; Reynolds, J. R.; So, F. *Nat. Photonics* **2011**, *6* (2), 115–120.

(6) Guo, X.; Ortiz, R. P.; Zheng, Y.; Kim, M.; Zhang, S.; Hu, Y.; Lu, G.; Facchetti, A.; Marks, T. J. *J. Am. Chem. Soc.* **2011**, *133* (34), 13685–13697.

(7) Berrouard, P.; Najari, A.; Pron, A.; Gendron, D.; Morin, P.-O.; Pouliot, J.-R.; Veilleux, J.; Leclerc, M. *Angew. Chem., Int. Ed.* **2012**, *51* (9), 2068–2071.

(8) Mei, J.; Bao, Z. *Chem. Mater.* **2014**, *26* (1), 604–615.

(9) Ouattara, M. P.; Lenfant, S.; Vuillaume, D.; Pézolet, M.; Rioux-Dubé, J.-F.; Brisson, J.; Leclerc, M. *Macromolecules* **2013**, *46* (16), 6408–6418.

(10) Kim, B.-G.; Ma, X.; Chen, C.; Ie, Y.; Coir, E. W.; Hashemi, H.; Aso, Y.; Green, P. F.; Kieffer, J.; Kim, J. *Adv. Funct. Mater.* **2013**, *23* (4), 439–445.

(11) Warnan, J.; Cabanetos, C.; Bude, R.; El Labban, A.; Li, L.; Beaujuge, P. M. *Chem. Mater.* **2014**, *26* (9), 2829–2835.

(12) Beaupré, S.; Najari, A.; Leclerc, M. *Synth. Met.* **2013**, *182*, 9–12.

(13) Grzybowski, M.; Gryko, D. T. *Adv. Opt. Mater.* **2015**, *3* (3), 280–320.

(14) Wang, E.; Mammo, W.; Andersson, M. R. *Adv. Mater.* **2014**, *26* (12), 1801–1826.

(15) Po, R.; Bianchi, G.; Carbonera, C.; Pellegrino, A. *Macromolecules* **2015**, *48* (3), 453–461.

(16) Griffini, G.; Douglas, J. D.; Piliego, C.; Holcombe, T. W.; Turri, S.; Fréchet, J. M. J.; Mynar, J. L. *Adv. Mater.* **2011**, *23* (14), 1660–1664.

(17) Organisation for the Prohibition of Chemical Weapons. *Convention on the Prohibition of the Development, Production, Stockpiling, and Use of Chemical Weapons and on their Destruction*; 2005.

(18) Sice, J. *J. Org. Chem.* **1954**, *19* (1), 70–73.

(19) Noyes, W. A.; Porter, P. K. *Org. Synth.* **1922**, *2*, 75.

(20) Van Pruissen, G. W. P.; Gholamrezaie, F.; Wienk, M. M.; Janssen, R. A. J. *J. Mater. Chem.* **2012**, *22* (38), 20387.

(21) *Crime Control Act of 1990. Pub. L. 101–647. 104 Stat. 4789. 29 November 1990.*

(22) Torabi, S.; Jahani, F.; Van Severen, I.; Kanimozhi, C.; Patil, S.; Havenith, R. W. A.; Chiechi, R. C.; Lutsen, L.; Vanderzande, D. J. M.; Cleij, T. J.; Hummelen, J. C.; Koster, L. J. A. *Adv. Funct. Mater.* **2015**, *25* (1), 150–157.

(23) Jahani, F.; Torabi, S.; Chiechi, R. C.; Koster, L. J. A.; Hummelen, J. C. *Chem. Commun.* **2014**, *50* (73), 10645–10647.

(24) Jung, B. J.; Tremblay, N. J.; Yeh, M.-L.; Katz, H. E. *Chem. Mater.* **2011**, *23* (3), 568–582.

(25) Takeda, Y.; Andrew, T. L.; Lobez, J. M.; Mork, A. J.; Swager, T. M. *Angew. Chem., Int. Ed.* **2012**, *51* (36), 9042–9046.

(26) Cho, N.; Schlenker, C. W.; Knesting, K. M.; Koelsch, P.; Yip, H.-L.; Ginger, D. S.; Jen, A. K.-Y. *Adv. Energy Mater.* **2014**, *4* (10), 1301857.

(27) Kim, H. J.; Han, A. R.; Cho, C. H.; Kang, H.; Cho, H. H.; Lee, M. Y.; Fréchet, J. M. J.; Oh, J. H.; Kim, B. J. *Chem. Mater.* **2012**, *24* (1), 215–221.

(28) Jiang, H.; Taranekar, P.; Reynolds, J. R.; Schanze, K. S. *Angew. Chem., Int. Ed.* **2009**, *48* (24), 4300–4316.

(29) Cutler, C. A.; Bouguettaya, M.; Reynolds, J. R. *Adv. Mater.* **2002**, *14* (9), 684–688.

(30) Zhou, H.; Zhang, Y.; Mai, C.-K.; Collins, S. D.; Nguyen, T.-Q.; Bazan, G. C.; Heeger, A. J. *Adv. Mater.* **2014**, *26* (5), 780–785.

(31) Mai, C.-K.; Russ, B.; Fronk, S. L.; Hu, N.; Chan-Park, M. B.; Urban, J. J.; Segalman, R. A.; Chabinyc, M. L.; Bazan, G. C. *Energy Environ. Sci.* **2015**, *8* (8), 2341–2346.

(32) Mei, J.; Kim, D. H.; Ayzner, A. L.; Toney, M. F.; Bao, Z. *J. Am. Chem. Soc.* **2011**, *133* (50), 20130–20133.