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Controllable Direct Arylation: Fast Route to Symmetrical and Unsymmetrical 4,7-Diaryl-5,6-difluoro-2,1,3-benzothiadiazole Derivatives for Organic Optoelectronic Materials

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Supporting Information

ABSTRACT: Arylation in the 4- and 7-positions of 2,1,3-benzothiadiazole (BT) and its monofluoro- (MFBT) and difluoro- (DFBT) derivatives by (hetero)aryl bromides using Pd-catalyzed C−H activation has been investigated. MFBT and DFBT can be diarylated in moderate to high yields (up to 96% for DFBT) by a variety of aryl bromides. DFBT can be sequentially arylated using two different aryl bromides to give differentially substituted DFBT derivatives. The moderate to high yields of doubly arylated MFBT and DFBT and the ability to obtain differentially substituted products can be applied to a variety of organic photonic and electronic materials.

Electron-poor (hetero)aromatic moieties are key components of many organic materials for opto-electronics, including donor (D)/acceptor (A) polymers for use in bulk heterojunction solar cells,[1] D-A second-order nonlinear optical (NLO) chromophores,[2] D-A, D-A-D, and A-D-A two-photon absorption (2PA) dyes,[3] electron-transport materials,[4] and D-A compounds for dye-sensitized solar cells (DSC).[5]

These electron-poor moieties are very often incorporated into materials via Suzuki or Stille cross couplings using their organometallic or halide (or pseudohalide) derivatives. Generally, electron-poor organometallic coupling partners give poor coupling efficiencies;[6] moreover, in many cases, synthesis of tin and boron derivatives of electron-poor compounds can itself be challenging. In principle, use of electron-poor aryl halide coupling partners tends to increase the effectiveness of the cross coupling; however, this often requires electrophilic halogenation of electron-poor intermediates, which can itself be challenging, typically requiring harsh conditions, and, in some cases, giving mixtures of products. Given the importance of acceptor moieties in organic electronic and photonic materials and the challenges associated with the use and preparation of electron-poor intermediates for Suzuki and Stille cross couplings, development of alternative coupling methodologies for electron-poor (hetero)aromatics may be useful.

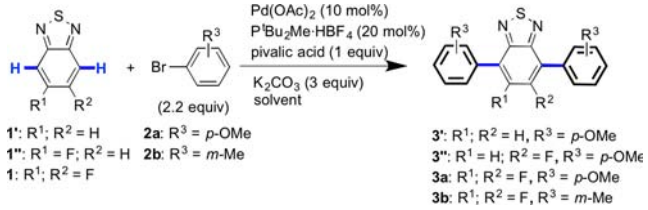
One such methodology is C-H bond activation, which has had an enormous impact on the synthesis of biologically active natural products and pharmacologically relevant substances.[7] More recently, C-H activation has been applied to electron-poor building blocks relevant to optical and electronic materials, such as perylene diimides,[8] naphthalene diimides,[9] thieno[3,4-*c*]pyrrole-4,6-dione,[10] 1,2,4,5-tetrafluorobenzene,[11] and 3,6-dithiophen-2-yl-2,5-dihydro-1,4-diketopyrrolo[3,4-*c*]-pyrroles.[12]

2,1,3-Benzothiadiazole (BT) and its 5-monofluoro- (MFBT) and 5,6-difluoro- (DFBT) derivatives, because of their electron-withdrawing abilities and planar structure, have been widely incorporated into polymers[13] and small molecules[14] for use in solar cells and field-effect transistors,[15] as DSC sensitizers,[16] as 2PA chromophores,[17] and as emitters in organic light-emitting diodes.[18]

However, synthesizing appropriate intermediates for inclusion of BT moieties (especially DFBT) into materials may require several steps[19] and/or harsh conditions, and 4,7-diiodo-DFBT is reportedly unstable.[20] Accordingly, here we report an investigation of the application of C-H activation to BT derivatives.

The general reaction conditions are shown in Scheme 1 and are based on earlier work using C-H activation on fluorinated

Scheme 1. Direct Arylation of BT Compounds



benzenes.[21] Initial reaction on BT (**1′**) with 1-bromo-4-methoxy benzene (**2a**) in dimethylacetamide (DMAc) at 110 °C gave <10% conversion to the monocoupled product and <5% of the dicoupled product, but MFBT (**1″**) and DFBT (**1**) gave the corresponding diarylated products in 55% and 71% isolated yield, respectively. Given these initial results, we optimized the reaction conditions using DFBT as the C-H

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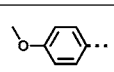
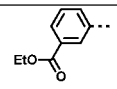
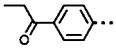
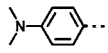
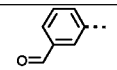
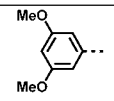
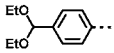
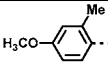
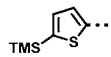
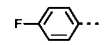
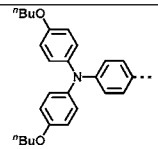
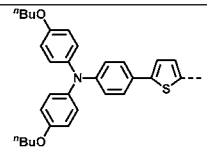
active component and 1-bromo-3-methylbenzene (**2b**) as the arylating reagent.

The optimization study is summarized in Table S1. Reaction with CuI-Phen in place of $Pd(OAc)_2$ and the phosphine gives only a trace of product. Reaction with $Pd(OAc)_2$ in the absence of a phosphine ligand results in very low yield (10%) of the diaryl derivative **3b**. The use of trialkyl phosphines, such as $P^tBu_2Me{\cdot}HBF_4$ and $Ad_2{}^nBuP$, allows much more effective diarylation. However, the different sized phosphine $PCy_3{\cdot}HBF_4$ and bidentate ligand 1,2-bis(dicyclohexylphosphino)ethane (DCPE) only gave 56% and 28% yield, respectively. Modifying the solvent had a dramatic effect on the reaction yields. The most polar solvent used (DMSO) gave no reaction. Other polar solvents—acetonitrile and DMAc—gave moderate to good yields (DMAc has previously been found to be a good solvent for a related palladium-catalyzed coupling between thiophene derivatives and aryl halides);[22] the reactions with DMAc gave unidentified side products immediately after reaching the reaction temperature. Of the solvents tried, toluene gave the highest yield of **3b** (98% by NMR, 96% isolated). Only a slight excess of aryl bromide (1.1 equiv Ar-Br to 1 equiv C-H) was used; thus the high yields seen on a short time scale (3−5 h) are a good indication of the efficiency of the optimized conditions. However, coupling of **2b** with BT and MFBT under these optimized conditions did not give appreciably enhanced results compared to the initial trials, which may indicate that acidity of the C-H activated bond is critical in this reaction (see discussion of the mechanism in the Supporting Information, SI).[21b] Competition experiments (see SI) indicate that **1** reacts with **2a** under the optimized conditions at a rate closely approaching that of the 1,2,4,5-tetrafluorobenzene/**2a** reaction but much more rapidly than the reaction of 1,2-difluorobenzene and **2a**.

Using the optimized conditions with DFBT, we investigated the (hetero)aryl bromide substrate scope of the reaction (Table 1). A variety of aromatic halides were smoothly transformed into the corresponding diarylated DFBT derivatives in moderate to excellent yields. Aryl groups rendered electron rich by strong π-donors were well tolerated (**3a**, **c**-**e**) as were electron-poor groups with π- or σ-electron-withdrawing substituents (**3g**, **i**−**k**). The reaction with 2-bromothiophene was slightly sluggish, most probably due to the formation of oligothiophene by $Pd(OAc)_2$;[23] indeed, blocking of the 5-position with a trimethylsilyl group dramatically improved the yield to 72%. The structure of the 4,7-di(trimethylsilylthienyl) DFBT, **3n**, was confirmed by X-ray crystallography (see SI). 3-Bromopyridine also gave the corresponding product **3o** in satisfactory yield. Sterically congested bromides, such as for **3e** and **3f**, also reacted smoothly to give high yields of diaryl derivatives, which were isolated as a mixture of atropisomers, due to restricted rotation between the *o*-Me group and the DFBT; the rotational barrier was determined to be 17 kcal/mol for **3e** (see SI). Finally, reaction with electron-rich aryl bromides incorporating triarylamines gave **3h** and **3p** in 96% and 57%, respectively; the UV−vis spectra of these compounds exhibit characteristic broad intramolecular charge-transfer bands (see SI). Aryl chlorides also act as arylating reagents using this catalytic combination, although the reaction times are generally longer and yields more modest. For example, reaction between DFBT and 4-chloroanisole yields the diarylated species in 46% yield after 24 h heating. The high isolated yields of diaryl products with many of these substrates suggest that C-H activation may be a viable alternative to incorporating

Table 1. DFBT C-H Activation Scope[a,b]

Ar	Product (yield)	Ar	Product (yield)
	**3a** (71%, 46%[c])		**3i** (85%)
	**3b** (96%)		**3j** (74%)
	**3c** (85%)		**3k** (65%)
	**3d** (88%)		**3l** (89%)
	**3e** (78%)		**3m** (31%)
	**3f** (81%)		**3n** (72%)
	**3g** (91%)		**3o** (70%)
	**3h** (96%)		**3p** (57%)

[a]Conditions: DFBT (0.125 mmol), aryl bromide (2.2 equiv), $Pd(OAc)_2$ (10 mol %), $P^tBu_2Me{\cdot}HBF_4$ (20 mol %), pivalic acid (1.0 equiv), K_2CO_3 (3.0 equiv), toluene (0.5 mL), 120 °C, N_2, 3−5 h. [b]Yield of isolated product. [c]4-Chloroanisole was used instead of 4-bromoanisole, 24 h.

the DFBT group into relevant materials by Suzuki[24] or Stille[25] polycondensation.

To expand the reaction scope, we examined whether it could be controlled to give monoarylated products that could subsequently be C-H activated a second time to give differentially substituted products, which might be relevant to D-A structures for use as DSC or NLO chromophores. After a brief screening of conditions (Table S2), we found that decreasing the concentration of the aryl bromide (**2c**) to 0.5 equiv gave mainly monoarylated product (**4c**, 83% with respect to **2c**) with a small amount of diarylated product (**3c**, 8%). Similarly, as shown in Scheme 2, DFBT reacted with 0.5 equiv of triarylamine **2h** to give mainly monoarylated product, **4**. The monoarylated intermediate could then be further directly arylated by other aryl bromides, as shown in Scheme 2 for the cases of 4-bromobenzaldehyde and 5-bromo-2-thiophenecarbaldehyde.

To further extend the synthetic utility of this strategy, a sequential one-pot diarylation of DFBT was performed as shown in Scheme 3. The treatment of DFBT with 4-bromodimethylaniline (0.8 equiv) for 4 h under standard catalytic conditions mainly gave the monoarylated intermediate. Following the addition of 3-bromotoluene (1.5 equiv) to the

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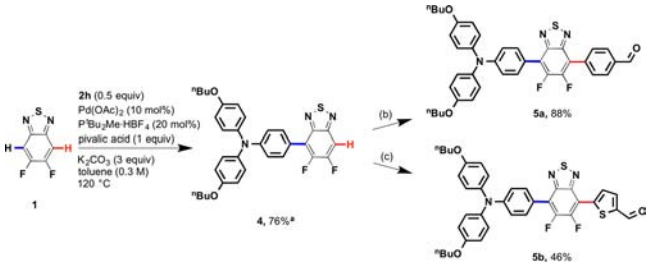
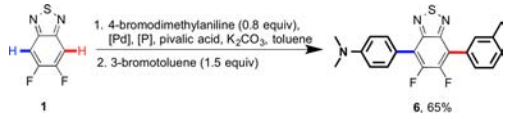
Scheme 2. Synthesis of Unsymmetrical D-A-A Triads



[a]Isolated yield based on the triarylamine. [b]4-Bromobenzaldehyde (1.2 equiv) under standard catalytic condition. [c]5-Bromo-2-thiophenecarbaldehyde (1.2 equiv) under standard catalytic condition.

Scheme 3. One-Pot Synthesis of an Unsymmetrical Triad



reaction vessel as a second arylating reagent, the diarylated product, **6**, was obtained in 65% overall yield and was easily purified from byproducts by column chromatography. Future studies will determine whether this one-pot reaction is applicable to a broader range of differentially substituted products.

In conclusion, we have developed an efficient palladium-catalyzed method for the direct mono- and diarylation of DFBT with aryl bromides. These conditions are somewhat less effective for MFBT and much less so for BT; further work is needed to develop efficient C-H activations for those substrates, perhaps involving the use of stronger bases. However, in the case of DFBT the approach is general and effective for a variety of electron-rich and electron-poor aryl halide coupling partners, and excellent yields are generally obtained. These conditions can be applied to the synthesis of a wide variety of symmetrical and unsymmetrical new conjugated materials based on the DFBT core, either through isolation and purification of monoarylated intermediates or in an one-pot procedure.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Henson, Z. B.; Müllen, K.; Bazan, G. C. *Nat. Chem.* **2012**, *4*, 699. (b) Li, G.; Zhu, R.; Yang, Y. *Nat. Photonics* **2012**, *6*, 153.

(2) (a) Barlow, S.; Marder, S. R. In *Functional Organic Materials*; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, 2007, p 393. (b) Dalton, L. R.; Sullivan, P. A.; Bale, D. *Chem. Rev.* **2010**, *110*, 25.

(3) (a) Kim, H.-M.; Cho, B. R. *Chem. Commun.* **2009**, 153. (b) Pawlicki, M.; Collins, H. A.; Denning, R. G.; Anderson, H. L. *Angew. Chem., Int. Ed.* **2009**, *48*, 3244.

(4) Anthony, J. E.; Facchetti, A.; Heeney, M.; Marder, S. R.; Zhan, X. *Adv. Mater.* **2010**, *22*, 3876.

(5) Hagfeldt, A.; Boschloo, G.; Sun, L.; Kloo, L.; Pettersson, H. *Chem. Rev.* **2010**, *110*, 6595.

(6) (a) Suzuki, A. *Chem. Commun.* **2005**, 4759. (b) Espinet, P.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4704.

(7) (a) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2011**, *45*, 788. (b) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792. (c) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (d) Mkhalid, I. A.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890. (e) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624.

(8) (a) Battagliarin, G.; Li, C.; Enkelmann, V.; Müllen, K. *Org. Lett.* **2011**, *13*, 3012. (b) Teraoka, T.; Hiroto, S.; Shinokubo, H. *Org. Lett.* **2011**, *13*, 2532. (c) Zhang, J.; Singh, S.; Hwang, D. K.; Barlow, S.; Kippelen, B.; Marder, S. R. *J. Mater. Chem. C* **2013**, *1*, 5093.

(9) (a) Yue, W.; Lv, A.; Gao, J.; Jiang, W.; Hao, L.; Li, C.; Li, Y.; Polander, L. E.; Barlow, S.; Hu, W.; Di Motta, S.; Negri, F.; Marder, S. R.; Wang, Z. *J. Am. Chem. Soc.* **2012**, *134*, 5770. (b) Suraru, S.-L.; Zschieschang, U.; Klauk, H.; Würthner, F. *Chem. Commun.* **2011**, *47*, 11504.

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

(11) Lu, W.; Kuwabara, J.; Iijima, T.; Higashimura, H.; Hayashi, H.; Kanbara, T. *Macromolecules* **2012**, *45*, 4128.

(12) (a) Zhang, J.; Kang, D.-Y.; Barlow, S.; Marder, S. R. *J. Mater. Chem.* **2012**, *22*, 21392. (b) Liu, S.-Y.; Shi, M.-M.; Huang, J.-C.; Jin, Z.-N.; Hu, X.-L.; Pan, J.-Y.; Li, H.-Y.; Jen, A. K. Y.; Chen, H.-Z. *J. Mater. Chem. A* **2013**, *1*, 2795. (c) Guo, Q.; Dong, J.; Wan, D.; Wu, D.; You, J. *Macromol. Rapid Commun.* **2013**, *34*, 522.

(13) (a) Zhang, Y.; Zou, J. Y.; Cheuh, C. C.; Yip, H. L.; Jen, A. K. Y. *Macromolecules* **2012**, *45*, 5427. (b) Zhou, H.; Yang, L.; Stuart, A. C.; Price, S. C.; Liu, S.; You, W. *Angew. Chem., Int. Ed.* **2011**, *50*, 2995. (c) You, J.; Dou, L.; Yoshimura, K.; Kato, T.; Ohya, K.; Moriarty, T.; Emery, K.; Chen, C.-C.; Gao, J.; Li, G.; Yang, Y. *Nat. Commun.* **2013**, *4*, 1446.

(14) (a) Lin, L. Y.; Chen, Y. H.; Huang, Z. Y.; Lin, H. W.; Chou, S. H.; Lin, F.; Chen, C. W.; Liu, Y. H.; Wong, K. T. *J. Am. Chem. Soc.* **2011**, *133*, 15822. (b) van der Poll, T. S.; Love, J. A.; Nguyen, T. Q.; Bazan, G. C. *Adv. Mater.* **2012**, *24*, 3646.

(15) (a) Zhang, W.; Smith, J.; Watkins, S. E.; Gysel, R.; McGehee, M.; Salleo, A.; Kirkpatrick, J.; Ashraf, S.; Anthopoulos, T.; Heeney, M.; McCulloch, I. *J. Am. Chem. Soc.* **2010**, *132*, 11437. (b) Tsao, H. N.; Cho, D. M.; Park, I.; Hansen, M. R.; Mavrinsky, A.; Yoon, D. Y.; Graf, R.; Pisula, W.; Spiess, H. W.; Müllen, K. *J. Am. Chem. Soc.* **2011**, *133*, 2605.

(16) (a) Velusamy, M.; Thomas, K. R. J.; Lin, J. T.; Hsu, Y.-C.; Ho, K.-C. *Org. Lett.* **2005**, *7*, 1899. (b) Zhu, W.; Wu, Y.; Wang, S.; Li, W.; Li, X.; Chen, J.; Wang, Z.-S.; Tian, H. *Adv. Funct. Mater.* **2011**, *21*, 756.

(17) (a) Kato, S.-I.; Matsumoto, T.; Shigeiwa, M.; Gorohmaru, H.; Maeda, A.; Ishi-i, T.; Mataka, S. *Chem.—Eur. J.* **2006**, *12*, 2303. (b) Cheng, J.-Z.; Lin, C.-C.; Chou, P.-T.; Chaskar, A.; Wong, K. T. *Tetrahedron* **2011**, *67*, 734.

(18) (a) Liu, J.; Zhou, Q.; Cheng, Y.; Geng, Y.; Wang, L.; Ma, D.; Jing, X.; Wang, F. *Adv. Mater.* **2005**, *17*, 2974. (b) Chen, L.; Zhang, B.; Cheng, Y.; Xie, Z.; Wang, L.; Jing, X.; Wang, F. *Adv. Funct. Mater.* **2010**, *20*, 3143.

(19) Zhang, Y.; Chien, S. C.; Chen, K. S.; Yip, H. L.; Sun, Y.; Davies, J. A.; Chen, F. C.; Jen, A. K. *Chem. Commun.* **2011**, *47*, 11026.

(20) You, W., WO Patent WO/2011/156,478, 2011.

(21) (a) Do, H.-Q.; Daugulis, O. *J. Am. Chem. Soc.* **2008**, *130*, 1128. (b) Lafrance, M.; Rowley, C. N.; Woo, T. K.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128*, 8754.
(22) Derridj, F.; Roger, J.; Djebbar, S.; Doucet, H. *Org. Lett.* **2010**, *12*, 4320.
(23) Schipper, D. J.; Fagnou, K. *Chem. Mater.* **2011**, *23*, 1594.
(24) Sakamoto, J.; Rehan, M.; Wegner, G.; Schluter, A. D. *Macromol. Rapid Commun.* **2009**, *30*, 653.
(25) Carsten, B.; He, F.; Son, H. J.; Xu, T.; Yu, L. *Chem. Rev.* **2011**, *111*, 1493.