Synthesis of 4,7-Di(2-thienyl)-2,1,3-benzothiadiazole via Direct Arylation

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Abstract. Owing to its unique electrical and optical properties, 4,7-di(2-thienyl)-2,1,3-benzothiadiazole (DTBT) moiety has become one of the most important building block for the synthesis of high-performance conjugated polymers. DTBT is commonly synthesized by Stille or Suzuki coupling reactions which are costly and time-consuming. In this work, DTBT moiety was prepared via an operationally simple method namely direct arylation. This coupling was performed under mild condition, giving the product in good yield.

1. Introduction

2,1,3-Benzothiadiazole (BT) is an important building block in conjugated polymers owing to its strong electron accepting ability, high values of reduction potential, and good stability, which affords high-performance optoelectronic devices [1] [2]. Adding two electron-rich thiophene units to the BT unit gives 4,7-dithienyl-2,1,3-benzothiadiazole (DTBT) moiety, which is more planar in structure as compared to the original BT moiety. The two thiophene units act as linker groups that advantageously reduces the steric hindrance between the donor unit and the acceptor unit, facilitating intra- or intermolecular interactions, thereby enhancing the delocalization of electrons along the entire polymer chain [3] [4]. The best example comes from the copolymerization of dithienylbenzothiadiazole with alkyl carbazole (PCDTBT), which demonstrates a high $V_{OC}$ of 0.88 V, a decent $J_{SC}$ of 10.6 mA cm$^{-2}$, and an impressive power conversion efficiency (PCE) of over 6% in its bulk heterojunction (BHJ) solar cells [5].

Stille coupling and Suzuki coupling are the most widely used method for synthesizing this thiophene-flanked benzothiadiazole. Despite robust and effective, these classic coupling methods are generally time-consuming as extra synthetic steps are required to install organometallic functional groups (e.g., organotin and organoborane) on the monomers which lead to the generation of highly toxic by-products [6]. Hence, a cleaner and cheaper synthetic procedure would be preferable for the preparation of this moiety. Direct arylation (DA) is an attractive alternative to conventional techniques. DA allows the coupling of simple (hetero)arenes with (hetero)aryl halides, excluding the use of organometallic reagents, thereby reducing the synthetic steps and undesirable metal-containing waste [7-8].

Although there are studies on direct arylation reaction involving benzothiadiazole and thiophene derivatives [9] [10], these reactions tend to use specialised catalyst/ligand systems. Phosphine ligands are the most commonly used directing groups in DA, which displayed high efficiency in the reaction,
yet most of the phosphine-based ligands are air-sensitive and toxic [11]. Therefore, the development of ligand-free direct arylation couplings is highly desirable. Herein, we report an easy and unsophisticated way for the preparation of thiophene-flanked benzothiadiazole under mild reaction conditions.

2. Experimental Study

2.1. Materials and Instruments

All reagents and solvents were obtained commercially and used without further purification. The progress of reactions was checked with thin layer chromatography (TLC) using silica gel 60 F254, and visualization was achieved with Cole-Parmer ultraviolet viewing cabinet. Fourier transform infrared (FTIR) spectra were obtained with PerkinElmer Spectrum 100. The proton ($^1$H) NMR spectra were provided by JEOL ECA 600 (600 MHz) spectrometer using deuterated chloroform (CDCl$_3$) as solvent and tetramethylsilane (TMS) as reference for chemical shifts. UV-VIS absorption spectra were measured in chloroform using an Agilent Cary 60 UV-Vis spectrophotometer.

2.2. Synthetic Procedures

2.2.1. 4,7-dibromobenzof[c][1,2,5]thiadiazole. A round bottom flask filled with 2,1,3-benzothiadiazole (1 g, 7.34 mmol) and N-bromosuccinimide (NBS) (2.1 equiv., 2.7 g, 15.4 mmol) in 10 mL of concentrated sulphuric acid, H$_2$SO$_4$ (97%) was stirred in a 65 °C oil bath for 3 hours under N$_2$ atmosphere. The reaction flask was cooled to room temperature before transferred to an ice bath. Ice cold distilled water (60 mL) was then added slowly and the resulting white suspension was extracted three times, each with 60 mL of toluene. Subsequently, the combined organic layers were washed with distilled water and brine before dried over anhydrous sodium sulphate, Na$_2$SO$_4$. Solvent was removed under reduced pressure and the product was recrystallized from chloroform/hexane (1:2), giving 2.1 g (97%) of 4,7-dibromo benzof[c][1,2,5]thiadiazole (DBrBT) as off-white needle crystals. Melting point = 188 – 190 °C. $^1$H NMR (600 MHz, CDCl$_3$): δ (ppm) 7.73 (s, 2H). FTIR (ATR): ν (cm$^{-1}$) 3078, 3046, 1654, 1586, 1497, 1475, 1309, 1272, 1183, 1080, 935, 874, 842, 825, 618, 585, 519, 487.

2.2.2. 4,7-di(2-thienyl)-2,1,3-benzothiadiazole. 4,7-dibromobenzof[c][1,2,5]thiadiazole (DBrBT) (70 mg, 0.24 mmol) was placed in a dried two-neck round bottom flask that filled with 20 mL of DMF. An excess of thiophene (Ts) (20 equiv., 0.38 mL, 4.76 mmol) was then added, and the mixture solution was purged with nitrogen gas for 15 minutes before the addition of palladium(II) acetate (Pd(OAc)$_2$) (27 mg, 0.12 mmol), pivalic acid (30 mg, 0.36 mmol) and potassium carbonate K$_2$CO$_3$ (170 mg, 1.2 mmol). The reaction mixture was stirred and heated at 80 °C under nitrogen atmosphere for 24 hours. After being cooled to room temperature, the reaction mixture was diluted with chloroform. The insoluble species were removed by vacuum filtration. The filtrate was subsequently washed with distilled water and brine, before dried over anhydrous Na$_2$SO$_4$. The solvent was then evaporated and the crude orange product was purified by column chromatography with 2% ethyl acetate/hexane as eluent. Recrystallized from hexane yielded 4,7-di(2-thienyl)-2,1,3-benzothiadiazole (DTBT) as bright orange needle-like crystals. Melting point = 120-122 °C. $^1$H NMR (600 MHz, CDCl$_3$): δ (ppm) 8.12 (d, 2H), 7.87 (s, 2H), 7.46 (d, 2H), 7.21 (m, 2H). FTIR (ATR): ν (cm$^{-1}$) 3094, 3012, 1787, 1661, 1577, 1523, 1480, 1421, 1378, 1275, 1215, 1072, 1042, 920, 875, 845, 816, 869, 641, 600, 507.
3. Result and Discussion

The synthetic routes toward 4,7-dibromobenzo[c][1,2,5]thiadiazole (DBrBT) and 4,7-di(2-thienyl)-2,1,3-benzothiadiazole (DTBT) were outlined in Scheme 1. The key monomer DBrBT was synthesized using a procedure that modified from the previously reported methods [12] [13]. A slightly excess of NBS was used in the presence of concentrated H$_2$SO$_4$ to dibrominate 2,1,3-benzothiadiazole. Reactive electrophile, bromine cation (Br$^+$), formed upon the displacement of the bromine atom on NBS by a proton, H$^+$, from the sulphuric acid. These electrophiles replaced the hydrogens of benzothiadiazole successively. Substitution occurs primarily at the meta position as the sulphur and nitrogen atoms of benzothiadiazole tend to donate electrons to the ring by resonance which allow the electron density to be positioned at the meta sites. Since the meta positions are more nucleophilic, electrophiles are more likely to attack these sites. An increase in the reaction temperature (> 65°C) was found to have a detrimental effect on the product yield. This can be rationalized by the fact that bromination is an exothermic reaction which releases heat as the reaction proceeds. The addition of heat will disturb the equilibrium causes the reaction system to respond to the change by restoring a new equilibrium mixture that contains more reactants and fewer products, as Le Chatelier’s principle suggests. The reaction was completed in 3 hours, and the raw product was recrystallized from a mixed solvent of chloroform/ hexane, affording 97% yield of DBrBT as off-white needle-like crystals which subsequently used as the reactant for the preparation of DTBT.

As shown in Scheme 1, DBrBT was coupled with thiophenes (Ts) through Pd(OAc)$_2$-catalysed direct arylation coupling under phosphine-free condition. The mole ratio between DBrBT and Ts was found to affect the reaction notably. When the feed ratio of Ts to DBrBT is 5, a lot of unreacted starting material and partially soluble purple byproducts were observed, giving an isolated yield of 45%. The purple byproducts, which were believed to be the oligomers or even polymers of thiophene-BT, had found to diminish as the feed ratio of Ts/DBrBT increased. This observation suggested that an increase of thiophene amount could most probably suppress the formation of oligomeric byproducts. A decrease of side reaction naturally increases the yield of product. Thus, the product yield had improved to 66% as the feed ratio increased to 20 (Table 1).
Table 1: Direct-arylation of 4,7-dibromobenzothiadiazole (DBrBT) and thiophene (Ts) under different mole ratio.

| Entry | Ts/DBrBT (mmol/mmol) | Temperature (°C) [time (h)] | Yielda (%) |
|-------|----------------------|----------------------------|------------|
| 1     | 5                    | 80 [24]                    | 45         |
| 2     | 10                   | 80 [24]                    | 64         |
| 3     | 20                   | 80 [24]                    | 66         |

a Isolated yield.

Black precipitates, which were believed to be palladium (Pd) black, were filtered out at the end of the reaction. The arise of Pd black is most likely due to a high concentration of active catalyst species, Pd(0), which tends to agglomerate under ligand-free condition since ligands are catalyst’s stabilizer. The amount of Pd black was found to decrease as the feed ratio of Ts/DBrBT increase, implying that most of the generated Pd(0) species had been used in the coupling reaction instead of forming Pd black. This observation also explained the increase of product yield at high feed ratio of Ts/DBrBT.

The obtained products were characterized by $^1$H NMR spectroscopy (Figure 1). It can be seen that the bands are concentrated in a region of 7.0 – 8.2 ppm as aromatic protons are highly deshielded by the diamagnetic anisotropy of the ring. DBrBT moiety only has two chemically equivalent protons and thus give a single NMR absorption peak (7.73 ppm) on the spectrum. The addition of thiophene units renders DTBT moiety four distinct sets of protons. The peak at the highest chemical shift (8.12 ppm) is assigned to the hydrogen on carbon 1 (H1) of thiophene, considering the deshielding effect of the adjacent electronegative sulphur atom. The deshielding effect of sulphur atom diminishes with increasing distance, giving H2 a chemical shift of 7.21 ppm. Signals for H1 and H3 are split into doublets by H2.

Figure 1: $^1$H NMR (600 MHz) spectra of DTBT (top) and DBrBT (bottom) in CDCl$_3$. 
Figure 2 shows the UV-VIS absorption spectra of DBrBT and DTBT in chloroform. Notice that the spectra of DBrBT and DTBT are almost similar at least in the peak shapes, suggesting a great similarity in their nature of chromophore. The absorption spectrum of DTBT moiety possess two characteristic bands (310 nm and 445 nm). The absorption band that lies at shorter wavelength can be assigned to $\pi-\pi^*$ transitions, while the band that appears at longer wavelength corresponded to the intramolecular charge transfer (ICT) between thiophenes and BT. A bathochromic shift was observed for the secondary band (445 nm) in the spectrum of DTBT as compared to 355 nm in the spectrum of DBrBT. This is most probably due to the addition of thiophene rings which increases the extent of conjugation in DTBT moiety, thereby decreases the energy required for electronic excitation, giving longer wavelength. Absorption of 445 nm light renders DTBT moiety yellow in colour (Figure 3). Under UV light (365 nm) irradiation, both DBrBT and DTBT moieties show vivid colour, indicating their fluorescence nature (Figure 3).

![Figure 2: UV-VIS absorption spectra of DBrBT (solid blue) and DTBT (dot red) in CHCl₃.](image-url)

![Figure 3: Solution colour of (a) DBrBT under ambient condition in CHCl₃; (b) DBrBT under 365 nm UV light; (c) DTBT under ambient condition in CHCl₃; and DTBT under 365 nm UV light.](image-url)
4. Conclusions

In summary, 4,7-di(2-thienyl)-2,1,3-benzothiadiazole (DTBT) moiety has been successfully synthesized via a phosphine-free direct arylation coupling. Product yield was found to increase as the mole ratio of Ts/DBrBT increased. The ease of product’s purification owing to the absence of toxic phosphine by-products makes this ligand-free procedure attractive in terms of ecology and economy.

5. References

[1] Medlej H, Awada H, Abbas M, Wantz G, Bousquet A, Grelet E, Hariri K, Hamieh T, Hiorns RC, and Dagron-Lartigau C 2013 Effect of spacer insertion in a commonly used dithienosilole/benzothiadiazole-based low band gap copolymer for polymer solar cells. *Eur. Polym. J.* **49** 4176–4188.

[2] Abbas A, Pillai J J, Sreekumar K, Joseph R and Kartha C S 2018 Photophysical and photoconductive aspects of donor-acceptor low band gap conjugated copolymer. *Opt. Mater.* **84** 813–820.

[3] Wu F, Chen S, Chen L and Chen Y 2015 Tuning joint sequence for donor-acceptor polymers based on fluorinated benzothiadiazole with thiophene/furan bridgeds. *Polym.* **78** 154–160.

[4] Zhou H, Yang L and You W 2012 Rational Design of High Performance Conjugated Polymers for Organic Solar Cells. *Macromol.* **45** 607–632.

[5] Park S H, Roy A, Beuapré S, Cho S, Coates N, Moon J S, Moses D, Leclerc M, Lee K and Heeger A J 2009 Bulk heterojunction solar cells with internal quantum efficiency approaching 100%. *Nat. Photonics.* **3** 297–303.

[6] Bura T, Blaskovits J T and Leclerc M 2016 Direct (Hetero)arylation Polymerization: Trends and Perspectives. *J. Am. Chem. Soc.* **138** 10056–10071.

[7] Pouliot J R, Grenier F, Blaskovits J T, Beuapré S and Leclerc M 2016 Direct (Hetero)arylation Polymerization: Simplicity for Conjugated Polymer Synthesis. *Chem Rev.* **116** 14225–74.

[8] Gobalasingham N S and Thompson B C 2018 Direct arylation polymerization: A guide to optimal conditions for effective conjugated polymers. *Prog. Polym. Sci.* **83** 135–201.

[9] Matsidik R, Martin J, Schmidt S, Obermayer J, Lombeck F, Nübling F, Komber H, Fazzi D and Sommer M 2015 C-H arylation of unsubstituted furan and thiophene with acceptor bromides: Access to donor-acceptor-donor-type building blocks for organic electronics. *J. Org. Chem.* **80** 980–987.

[10] Wang X, Wang K and Wang M 2015 Synthesis of conjugated polymers via an exclusive direct-arylation coupling reaction: A facile and straightforward way to synthesize thiophene-flanked benzothiadiazole derivatives and their copolymers. *Polym. Chem.* **6** 1846–1855.

[11] He X X, Li Y F, Huang J, Shen D S and Liu F S 2016 A convenient phosphine-free palladium-catalyzed direct arylation of thiazole under mild aerobic conditions. *J. Organomet. Chem.* **803** 58–66.

[12] Heiskanen J P, Vivo P, Saari N M, Hukka T I, Kastinen T, Kaunisto K, Lemmetyinen H J and Hormi O E O 2016 Synthesis of Benzothiadiazole Derivatives by Applying C-C Cross-Couplings. *J. Org. Chem.* **81** 1535–1546.
[13] Nguyen H T, Nguyen L T T, Nguyen T T, Luu A T and Van L T 2014 Synthesis of hyperbranched conjugated polymers based on 3-hexylthiophene, triphenylamine and benzo [c] [1,2,5] thiadiazole moieties: convenient synthesis through suzuki polymerization and impact of structures on optical properties. *J. Polym. Res.* **21** 552—563.

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