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ABSTRACT

Asymmetrical dibenzothiophene sulfonate esters are key intermediates in the production of site specific dibenzothiophene-S-oxide (DBTO) analogs and are potentially efficacious in the production of organic light-emitting diodes (OLEDs). The synthesis of these asymmetrical DBTs requires a less direct, yet efficient, pathway utilizing Suzuki coupling to add primary alkyl, secondary alkyl, aromatic, and vinylic substituents to the DBT sulfonate ester. The coupling reactions produce a small library of asymmetrical dibenzothiophene sulfonate esters ranging from low to good yield.

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Introduction

Asymmetrical dibenzothiophene sulfonate esters are key intermediates in the production of photoactive dibenzothiophene-S-oxide (DBTO) analogs. Dibenzothiophene-S-oxide derivatives are believed to release ground state atomic oxygen [$O(^3P)$] and are useful in creating organic light-emitting diodes (OLEDs).¹ Dibenzothiophene (DBT) derivatives in their oxidized form as DBTO or dibenzothiophene-S-dioxide (DBTOO) have displayed a history of varied photochemistry with the addition of a variety of substituents and different degrees of oxidation about the thiophene sulfur.² Various symmetrical DBTO derivatives have shown intriguing oxidative capabilities with small organic molecules, and more recently, with biomolecules.^{3–8} Symmetrical DBTO derivatives have shown limited lipophilicity, which prompted the development of unsymmetrical dibenzothiophene derivatives. Converting the sulfonate ester of an asymmetrical DBT to the sodium sulfonate salt predictably elicits strong water solubility for an otherwise nonpolar molecule. Previous attempts to prepare various dibenzothiophene sulfonic acids without protection of the acid group were troublesome as the sensitivities of common carbon-carbon coupling reactions force a less direct synthetic pathway.

Phenyl sulfonate esters withstand a variety of reaction conditions while not interfering with other chemical reactions.⁹ The phenyl sulfonate analog of 2-bromodibenzothiophene (**5**) provides a platform by which alkyl, aryl, and vinylic substituents may be coupled to the DBT by virtue of Suzuki coupling. Coupling aromatic and aliphatic groups to DBTs has much value in the exploration of OLEDs, as large DBT analogs are produced for their high triplet energy.¹⁰ This growing field hosts tremendous potential in utilizing unsymmetrical DBT

derivatives.^{10–13} Asymmetrical DBT derivatives boast untapped potential for use in OLEDs and selective biomolecule oxidation. Their synthesis is henceforth detailed.

Results and Discussion

The general synthetic route to the unsymmetrical dibenzothiophene sulfonate esters is shown in Scheme 1. This method allowed the preparation of aryl, vinyl, primary and secondary alkyl substituted dibenzothiophene sulfonate esters.

(a) NBS, DMF, rt. (b) $ClSO_3H$, DCM, $-5^\circ C$. (c) $SOCl_2$, DMF (cat), reflux. (d) Phenol, DABCO, DCM, rt. (e) R=Primary Alkyl $RB(OH)_2$, $Pd(dppf)Cl_2$, K_3PO_4 , Toluene, reflux. (f) R=Secondary Alkyl $RB(OH)_2$, $PdCl_2(PPh_3)_2$, KF, Toluene, reflux. (g) R=Aromatic $ArB(OH)_2$, $PdCl_2(PPh_3)_2$, NaB_4O_7 , DME/ H_2O (1:1), reflux. (h) R=*trans*-2-Phenylvinyl $IB(OH)_2$, $Pd_2(dba)_3$, SPhos, K_3PO_4 , Toluene/ $H_2O/MeOH$ (20:2:3), reflux.

Scheme 1. Reagents and conditions.

Table 1

Coupling of Aromatic and Vinyl Groups

Entry	B(OH) ₂	Catalyst [Co-ligand]	Loading (mol %)	Base	Solvent System	Product	Yield
1	phenyl	PdCl ₂ (PPh ₃) ₂ [SPhos]	5% [10%]	Na ₂ B ₄ O ₇	Dioxane/EtOH (5:1)	6	0%
2	phenyl	PdCl ₂ (PPh ₃) ₂ [SPhos]	5% [10%]	K ₂ CO ₃	DME/ H ₂ O (1:1)	6	48% ^a
3	phenyl	Pd(PPh ₃) ₄ [SPhos]	3% [10%]	Na ₂ B ₄ O ₇	Dioxane/EtOH (4:1)	6	0%
4	phenyl	Pd(PPh ₃) ₄ [SPhos]	10% [10%]	Na ₂ B ₄ O ₇	DME/ H ₂ O (1:1)	6	0%
5	phenyl	Pd(PPh ₃) ₄	5%	K ₂ CO ₃	DME/ H ₂ O (1:1)	6	18%
6	phenyl	PdCl ₂ (PPh ₃) ₂	5%	K ₂ CO ₃	DME/ H ₂ O (1:1)	6	0% ^a
7	phenyl	PdCl ₂ (PPh ₃) ₂	5%	Na ₂ B ₄ O ₇	Dioxane/EtOH (5:1)	6	0%
8	phenyl	PdCl ₂ (PPh ₃) ₂	3%	Na ₂ B ₄ O ₇	Dioxane/EtOH (4:1)	6	0%
9	phenyl	PdCl ₂ (PPh ₃) ₂	5%	Na ₂ B ₄ O ₇	DME/ H ₂ O (1:1)	6	66% ^a
10	phenyl	PdCl ₂ (PPh ₃) ₂	5%	Na ₂ B ₄ O ₇	Dioxane/ H ₂ O (5:1)	6	69% ^a
11	phenyl	PdCl ₂ (PPh ₃) ₂	5%	KF	Toluene	6	45% ^a
12	phenyl	PdCl ₂ (PPh ₃) ₂	5%	Na ₂ B ₄ O ₇	DME/ H ₂ O (1:1)	6	71%
13	naphthyl	PdCl ₂ (PPh ₃) ₂	5%	Na ₂ B ₄ O ₇	DME/ H ₂ O (1:1)	7	72%
14	biphenyl	PdCl ₂ (PPh ₃) ₂	5%	Na ₂ B ₄ O ₇	DME/ H ₂ O (1:1)	8	65%
15	<i>trans</i> -2-phenylvinyl	Pd(dba) ₃ [SPhos]	3% [4%]	K ₃ PO ₄	Toluene/H ₂ O/MeOH (20:2:3)	9	31%

^a Yield based on GCMS

The approach shown in Scheme 1, begins with the addition of bromine to the 2 position of (**1**). This was achieved through a slow addition of N-Bromosuccinimide (NBS) in DMF to a solution of DBT in DMF, which was stirred for 24 hours. A white powder resulted from 5 recrystallizations in ethanol yielding (**2**) in 33% yield and 95% purity. The obtained 2-Bromodibenzothiophene (**2**) was dissolved in DCM and cooled to -5°C when one equivalent of chlorosulfonic acid in DCM was added dropwise to the chilled solution. This resulted in a white precipitate which was filtered over a glass frit and washed with a liberal amount of chilled DCM. This produced (**3**) in 79% yield and greater than 90% purity as confirmed by ¹HNMR. The sulfonic acid was converted to a sulfonyl chloride (**4**) by reflux in thionyl chloride accelerated by a small amount of DMF. A white solid was isolated after quenching the reflux with ice followed by a normal phase column. This produced a 91% yield with 99% purity as shown by ¹HNMR. The sulfonate ester (**5**) was produced by the addition of phenol and DABCO to a solution of (**4**) in DCM at room temperature. The solution was stirred for 24 hours followed by concentration under reduced pressure, and purification by normal phase flash chromatography. Compound **5** was isolated at an 85% yield.

Alternate approaches to synthesize unsymmetrical DBTs did not produce isomerically pure product. Adding the hydrocarbon substituent to **1**, followed by the addition of the sulfonic acid produced an unsymmetrical DBT; however, during the addition of the sulfonic acid there were multiple sites of addition about the DBT. These isomers cannot be easily separated on a preparative scale. The coupling of **5** to different hydrocarbon substituents was achieved by the quintessential Suzuki coupling reaction. This reaction was optimized for primary alkyl, secondary alkyl, aryl, and vinylic substituents. No single set of reaction conditions was capable of providing optimized yields for the different substituents. Each substituent required a particular set of reaction conditions to achieve the optimal yield. Thus, reaction optimization was required for each substituent.

Table 1 provides a list of conditions used for the optimization of coupling aryl substituents to **5**. Initial reaction probes were carried out using a modified literature procedure using SPhos as a co-ligand.¹⁴ It was employed after the failure of Entry 5, which had previously been employed successfully on 2-bromodibenzothiophene. Entries 1-4 showed little success except with the second reaction, which produced a 48% yield according to GCMS. Thereafter, the catalyst loading and solvent system was manipulated until a satisfactory result was obtained.

For the coupling of aryl groups to **5** as shown in Scheme 2, the ideal reaction conditions were met by loading 5% mol of bis(triphenylphosphine)-palladium(II) dichloride [PdCl₂(PPh₃)₂], three equivalents of Na₂B₄O₇, and 1.2 equivalents of phenyl boronic acid in DME and distilled water (1:1). This set of reaction conditions initially produced a 66% yield by GCMS analysis (Entry 9). Entry 10 provided a better yield with 69%; however, the reaction mixture contained residual starting material (**5**), which proved to be difficult to separate from **6**. The selected conditions, which were only analyzed by GCMS, were then repeated on a gram scale giving a 71% yield. The reaction was then carried out with naphthyl boronic acid and biphenyl boronic acid producing **7** and **8** in yields of 35% and 65%, respectively.

Scheme 2. Optimized aromatic coupling conditions.

Coupling of DBT to a vinylic group (Scheme 3) was also achieved using reaction conditions utilized in a parallel project within the group. *Trans*-2-phenylvinyl boronic acid in a solution with Pd(dba)₃, SPhos, K₃PO₄ in Toluene:H₂O:MeOH (10:2:3). This produced 99% pure product in 31% yield. Carbons that are sp² hybridized have shown retarded coupling under standard

Table 2: Coupling of Primary Alkyl Groups

Entry	B(OH) ₂	Catalyst	Loading (mol %)	Base	Solvent System	Product	Yield
1	butyl	PdCl ₂ (PPh ₃) ₂	5%	Na ₂ B ₄ O ₇	DME:H ₂ O (1:1)	10	0%
2	butyl	Pd(dppf)Cl ₂	20%	K ₃ PO ₄	Toluene	10 ^a	57% ^a
3	butyl	Pd(dppf)Cl ₂	20%	K ₃ PO ₄	Toluene	10	60%
4	hexyl	Pd(dppf)Cl ₂	20%	K ₃ PO ₄	Toluene	11	48%
5	octyl	Pd(dppf)Cl ₂	20%	K ₃ PO ₄	Toluene	12	32%
6	decyl	Pd(dppf)Cl ₂	20%	K ₃ PO ₄	Toluene	13	20%

^a Yield based on GCMS

Suzuki coupling conditions. The yield, though not ideal, is acceptable as Suzuki coupling with DBTs has also shown hindered reactivity.¹³

Scheme 3: Optimized vinylic coupling conditions for *trans*-2-phenylvinyl (**9**)

As shown in Scheme 4, the next series of reactions probed were aimed to couple primary alkyl chains to **5**. Products were not obtained when the best conditions from aromatic coupling were applied. The literature was then used to overcome this challenge by working with reaction conditions used for successful alkyl coupling.¹⁵ As shown in Table 2, 20% mol loading of [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium (II) [Pd(dppf)Cl₂] with three equivalents of K₃PO₄ combined with 1.2 equivalents of butyl boronic acid in toluene provided a 57% yield per GCMS analysis after 24 hours of reflux (Table 2, Entry 2). The reaction, scaled to one gram, provided a 60% isolated yield of phenyl 8-butylidibenzo[b,d]thiophene-2-sulfonate. As the length of the alkyl boronic acid increased, the isolated yield decreased from 60% to 19% (Table 2, Entry 3-6), which suggested increased steric hindrance associated with alkyl boronic acid was responsible for the decreased yields.

Butyl (**10**) (n=3), hexyl (**11**) (n=5), octyl (**12**) (n=7), decyl (**13**) (n=9).

Scheme 4. Optimized primary alkyl coupling conditions

As shown in Scheme 5, the coupling of secondary alkyl boronic acids to **5** was the least efficient coupling. Initially, the coupling of isopropyl boronic acid and **5** to yield **14** was investigated; however, only a 24% yield was achieved as listed in Table 3 (Entry 2). This low yield was complicated by an unidentified byproduct possessing the same m/z as the product. The unidentified byproduct was suspected of being the n-propyl analog; however the byproduct could not be separated from the target molecule on a preparative scale.

Scheme 5. General conditions and products for Table 3 Entries 1-10.

In addition to isopropyl boronic acid, cycloalkyl boronic acids

Table 3
Coupling of Secondary Alkyl Groups

Entry	B(OH) ₂	Catalyst	Loading (mol %)	Base	Solvent System	Product	Yield
1	isopropyl	PdCl ₂ (PPh ₃) ₂	10%	KF	Toluene	14	0%
2	isopropyl	Pd(dppf)Cl ₂	20%	K ₃ PO ₄	Toluene	14	24% ^a
3	cyclohexyl	PdCl ₂ (PPh ₃) ₂	10%	KF	Toluene	16	0%
4	cyclohexyl	C ₂₄ H ₅₄ P ₂ Pd ^b	5%	K ₃ PO ₄	Toluene	16	0%
5	cyclohexyl	C ₂₄ H ₅₄ P ₂ Pd ^b	5%	Na ₂ B ₄ O ₇	DME:H ₂ O (1:1)	16	0%
6	cyclohexyl	C ₂₄ H ₅₄ P ₂ Pd ^b	5%	Na ₂ B ₄ O ₇	Dioxane ^c	16	0%
7	cyclohexyl	C ₂₄ H ₅₄ P ₂ Pd ^b	5%	KF	Dioxane ^c	16	0%
8	cyclohexyl	C ₂₄ H ₅₄ P ₂ Pd ^b	5%	KF	Dioxane ^c	16	0%
9	cyclopentyl	PdCl ₂ (PPh ₃) ₂	10%	KF	Toluene	17	0%
10	cyclopentyl	Pd(dppf)Cl ₂	20%	K ₃ PO ₄	Toluene	17	0%
11	cyclopropyl	Pd(dppf)Cl ₂	20%	K ₃ PO ₄	Toluene	15	25% ^a
12	cyclopropyl	PdCl ₂ (PPh ₃) ₂	10%	K ₃ PO ₄	Toluene	15	66% ^d
13	cyclopropyl	PdCl ₂ (PPh ₃) ₂	10%	KF	Toluene	15	65% ^e

^a Yield based on GCMS. ^b Bis(tri-tert butylphosphine)palladium (0). ^c Solvent underwent freeze, pump, thaw. ^d Yield based on GCMS, contains excessive side product. Reaction ran for 36 hours

were investigated as shown in Scheme 5. Despite attempting a variety of conditions with cyclohexyl boronic acid and cyclopentyl boronic acid, no coupled product was obtained (Table 3, Entry 3-10). For cyclopropyl boronic acid, two sets of conditions displayed good coupling. The conditions noted in Table 3 Entry 12 provided a 66% yield; however, the crude product mixture contained unreacted and dehalogenated **5** as indicated by GCMS analysis. The presence of unreacted and dehalogenated **5** was eliminated by using KF which produced a 65% yield without any of the byproducts which had previously stalled purification (Table 3, Entry 13) as shown in

Scheme 6. Optimized secondary alkyl coupling conditions for (**15**)

In summary, a versatile method to couple a variety of hydrocarbon groups to unsymmetrical dibenzothiophenes has been catalogued. This work provides conditions to couple aromatic, vinylic, primary alkyl and secondary alkyl groups using Suzuki coupling reactions. This protocol possesses the ability to aide in the OLED tuning and synthesis of lipophilic **DBTO** derivatives, which will be the primary aim of future work.

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