Tetrahedron Letters 57 (2016) 4723–4726

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Synthesis of asymmetrical dibenzothiophene sulfonate esters

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ARTICLE INFO

Article history:
Received 26 July 2016
Revised 30 August 2016
Accepted 7 September 2016
Available online 8 September 2016

Keywords:
Dibenzothiophene
OLED
Lipophilic
Suzuki
Cross-coupling

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.

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(^{3}P)] 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.

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 h. 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 ^{1}HNMR. 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 ^{1}HNMR. 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

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http://dx.doi.org/10.1016/j.tetlet.2016.09.028
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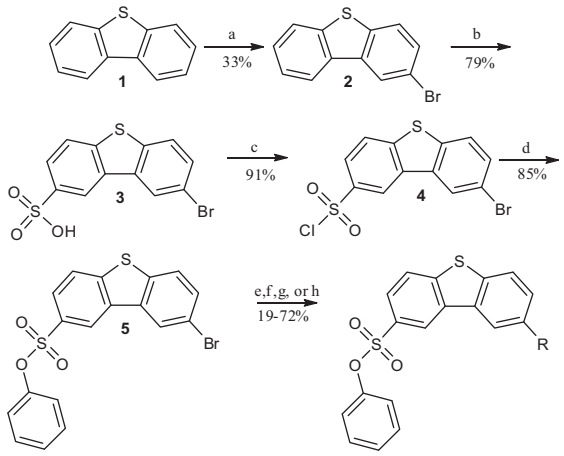
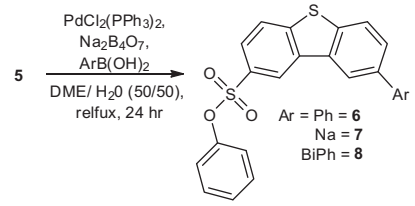
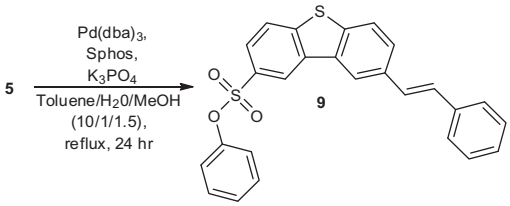


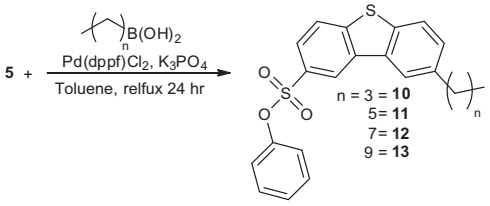
Scheme 1. Reagents and conditions. (a) NBS, DMF, rt. (b) $ClSO_3H$, DCM, −5 °C. (c) $SOCl_2$, DMF (cat), reflux. (d) Phenol, DABCO, DCM, rt. (e) R = Primary Alkyl $RB(OH)_2$, $Pd(dppf)Cl_2$, K_3PO_4, Toluene, reflux. (f) R = Secondary Alkyl $RB(OH)_2$, $PdCl_2(PPh_3)_2$, KF, Toluene, reflux. (g) R =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



Scheme 2. Optimized aromatic coupling conditions.



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



Scheme 4. Optimized primary alkyl coupling conditions. Butyl (**10**) ($n = 3$), hexyl (**11**) ($n = 5$), octyl (**12**) ($n = 7$), decyl (**13**) ($n = 9$).

24 h 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 were 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 [$PdCl_2(PPh_3)_2$], three equivalents of $Na_2B_4O_7$, and 1.2 equiv 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

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%]	$Na_2B_4O_7$	Dioxane/EtOH (5:1)	**6**	0
2	Phenyl	$PdCl_2(PPh_3)_2$ [SPhos]	5% [10%]	K_2CO_3	DME/H_2O (1:1)	**6**	48[a]
3	Phenyl	$Pd(PPh_3)_4$ [SPhos]	3% [10%]	$Na_2B_4O_7$	Dioxane/EtOH (4:1)	**6**	0
4	Phenyl	$Pd(PPh_3)_4$ [SPhos]	10% [10%]	$Na_2B_4O_7$	DME/H_2O (1:1)	**6**	0
5	Phenyl	$Pd(PPh_3)_4$	5%	K_2CO_3	DME/H_2O (1:1)	**6**	18
6	Phenyl	$PdCl_2(PPh_3)_2$	5%	K_2CO_3	DME/H_2O (1:1)	**6**	0[a]
7	Phenyl	$PdCl_2(PPh_3)_2$	5%	$Na_2B_4O_7$	Dioxane/EtOH (5:1)	**6**	0
8	Phenyl	$PdCl_2(PPh_3)_2$	3%	$Na_2B_4O_7$	Dioxane/EtOH (4:1)	**6**	0
9	Phenyl	$PdCl_2(PPh_3)_2$	5%	$Na_2B_4O_7$	DME/H_2O (1:1)	**6**	66[a]
10	Phenyl	$PdCl_2(PPh_3)_2$	5%	$Na_2B_4O_7$	Dioxane/H_2O (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%	$Na_2B_4O_7$	DME/H_2O (1:1)	**6**	71
13	Naphthyl	$PdCl_2(PPh_3)_2$	5%	$Na_2B_4O_7$	DME/H_2O (1:1)	**7**	72
14	Biphenyl	$PdCl_2(PPh_3)_2$	5%	$Na_2B_4O_7$	DME/H_2O (1:1)	**8**	65
15	*trans*-2-Phenylvinyl	$Pd(dba)_3$ [SPhos]	3% [4%]	K_3PO_4	Toluene/H_2O/MeOH (20:2:3)	**9**	31

[a] Yield based on GCMS.