Organic & Biomolecular Chemistry

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DOI: 10.1039/C8OB00235E

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COMMUNICATION

A Pd-Catalyzed Optional Approach for the Synthesis of Dibenzothiophenes

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

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A direct and practical approach for the construction of DBTs was developed via a Pd-catalyzed tandem reaction, in which commercially available *o*-bromo-iodobenzenes combined with benzene thiols or iodobenzenes combined with *o*-bromo-benzene thiol were applied. These two approaches will provide an alternative for the synthesis of DBT derivatives.

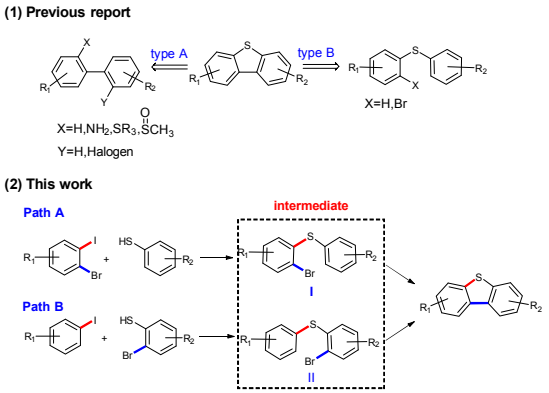
Establishing simple and efficient experimental procedure to access value-added structures is one of the long-lasting goals in organic synthesis. Guided by this goal, the simple multiple bond-forming "one-pot" or tandem-type strategy has attracted much attention, in which multiple chemical transformations are performed sequentially in a single reaction vessel without intermediary purification. Herein, an efficient tandem-type reaction for the synthesis of dibenzothiophene (DBT) derivatives is presented in the presence of palladium catalyst.

DBT derivatives constitute a privileged class of scaffolds with numerous application in pharmaceuticals, agrochemicals, or building blocks for the synthesis of conducting polymers.[1-5] Comparing with thiophene, DBT has enhanced intramolecular π-conjugation which resulted in much more remarkable properties such as more excellent charge transport properties, better thermal stability and so on. Various functionalized DBTs have been extensively used for liquid crystals, super-conductings, OFETs, host materials, organic light-emitting diodes (OLEDs) and so on.[6-12] Moreover, DBT is an electron-donating unit in organic photoconductive materials.[13] However, in the presence of H_2O_2, DBT is converted to dibenzothiophene-*S,S*-dioxide[14], which is used as an electron-withdrawing unit and has been well studied due to its high electron mobility, fluorescence quantum efficiency and thermal stability.[15-18]

Due to the numerous successful applications of fused thiophene scaffolds across a wide range of fields, a number of methods for the efficient synthesis of DBTs have been established in recent years (Scheme 1). However, except that few examples reported by Antonchick[19] and McNab[20] that using aryl benzylsulfoxides and phenyl 2-allythiobenzoates as substrates respectively, most of methods were based on the annulation of biphenyl[21-26] (Scheme 1, type A) or diaryl sulfides (or sulfoxides) derivations (Scheme 1, type B).[27-35] These methods were usually limited by their reliance on necessities of prefunctionalized materials or multistep procedures, which were less atom-economical and less environmentally friendly. Thus, developing novel methods based on simple and commercially available chemicals is of great interest and "one-pot" or tandem-type strategy is appealing.

In our design, C-S and C-C bond of the central five membered ring of DBT are consequently constructed in one synthetic process (Scheme 1). Diphenylsulfides intermediate (Scheme 1, I or II) is firstly produced by C-S coupling reaction, then followed

Scheme 1. Approaches Towards the Synthesis of DBT



by a intramolecular cyclization proceeding through a C-H activation process as a result to afford the desired product. It

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Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

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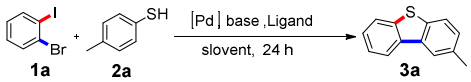
DOI: 10.1039/C8OB00235E

is worth mentioning that there are two approaches for the formation of diphenylsulfides intermediate (Scheme 1, path A and path B) which make the substrates employed more easily accessible and optional.

The reaction conditions were optimized based on the model transformation of *o*-bromoiodobenzene (**1a**) with 4-methylbenzenethiol (**2a**). Experiments of ligands screening were firstly carried out at 120 °C, together with $PdCl_2$ as the catalyst precursor and CsOPiv as the base in DMA for 24h. As described in Table 1, PPh_3 and PCy_3 (Table 1, entries 1 and 2) were not the suitable ligands for this tandem coupling reaction and only trace or no desired product was observed. Usually, the substrate of thiophenol may lead to the deactivation of transition-metal catalysts. We envisioned that using bidentate ligand to improve the coordination ability may increase the effect of ligand. Fortunately, when the bidentate ligands of dppf (Table 1, entry 3) and bis[2-diphenylphosphino]phenyl]ether (DPEphos) (Table 1, entry 4) were used, 17% and 37% of the desired product **3a** was obtained respectively. Then, several palladium sources were investigated. $Pd(OAc)_2$ provided the comparable result as $PdCl_2$ in 36% yield (Table 1, entries 5). The yield increased to 45% with $Pd(CH_3CN)_2Cl_2$ as catalyst (Table 1, entry 7). However, $Pd(dba)_2$ gave no product (Table 1, entry 6). The choice of base was crucial for this transformation. Switching the base from CsOPiv to Cs_2CO_3 and t-BuOK (Table 1, entries 8-9) identified CsOPiv as the optimal base. Finally, the effect of solvent was studied (Table 1, entries 10-13). The use of DMF and DMSO afforded comparable result as DMA (Table 1, entries 12-13) in 45% and 47% yield respectively, but no desired product was observed in toluene or dioxane (Table 1, entries 10-11). Delightedly, the yield of **3a** was remarkably improved to 70% when the reaction temperature was increased from 120 °C to 140 °C (Table 1, entry 14). Furthermore, increasing the loading of CsOPiv to 5 equivalents resulted in a higher yield of 85% (Table 1, entry 15). Meaningfully, the decrease in the catalyst of $Pd(CH_3CN)_2Cl_2$ loading from 5 mol % to 2.5 mol %, also afforded **3a** in 84% yield (Table 1, entry 16). The optimal reaction conditions thus far being developed employing 1.25 equiv. of *o*-Bromoiodobenzene (**1a**), 1 equiv. of 4-methyl-benzene-thiol (2a), 2.5 mol% of $Pd(CH_3CN)_2Cl_2$, 5 mol % DPEphos, 5.0 equiv. of CsOPiv in DMA at 140 °C for 24 h. This procedure provided 2-methyl-dibenzothiophene (**3a**) in 91% of isolated yield. Replacing o-bromo-iodiobenzene with o-dibromobenzene gave the product **3a** in a lower isolated yield of 84% (Table 1, entry 17).

Table 1. Optimization of Conditions for Palladium Catalyzed Tandem Reaction of *o*-Bromo-iodobenzene with 4-Methylbenzenethiol[a]



1a 2a 3a

entry	catalyst	ligand	base	slovent	yield (%)
1	$PdCl_2$	PPh_3	CsOPiv	DMA	-
2	$PdCl_2$	PCy_3	CsOPiv	DMA	trace
3	$PdCl_2$	dppf	CsOPiv	DMA	17
4	$PdCl_2$	DPEphos	CsOPiv	DMA	37
5	$Pd(OAc)_2$	DPEphos	CsOPiv	DMA	36
6	$Pd(dba)_2$	DPEphos	CsOPiv	DMA	-
7	$Pd(CH_3CN)_2Cl_2$	DPEphos	CsOPiv	DMA	45
8	$Pd(CH_3CN)_2Cl_2$	DPEphos	Cs_2CO_3	DMA	-
9	$Pd(CH_3CN)_2Cl_2$	DPEphos	KO*t*-BU	DMA	-
10	$Pd(CH_3CN)_2Cl_2$	DPEphos	CsOPiv	toluene	-
11	$Pd(CH_3CN)_2Cl_2$	DPEphos	CsOPiv	dioxane	-
12	$Pd(CH_3CN)_2Cl_2$	DPEphos	CsOPiv	DMF	45
13	$Pd(CH_3CN)_2Cl_2$	DPEphos	CsOPiv	DMSO	47
14[b]	$Pd(CH_3CN)_2Cl_2$	DPEphos	CsOPiv	DMA	70
15[b,c]	$Pd(CH_3CN)_2Cl_2$	DPEphos	CsOPiv	DMA	85
16[b,c,d]	$Pd(CH_3CN)_2Cl_2$	DPEphos	CsOPiv	DMA	84/91[e]
17[b,c,d,f]	$Pd(CH_3CN)_2Cl_2$	DPEphos	CsOPiv	DMA	84[e]

[a] Reactions conditions:1a (0.25 mmol), 2a (0.2 mmol), Pd catalyst (0.01mmol), ligand (0.020 mmol), 4 equiv of base , solvent (2 mL) at 120 °C for 24 h. Yields are calculated by GC analysis using biphenyl as an internal standard. [b] The reaction was carried out at 140 °C. [c] CsOPiv (5 equiv) was loaded. [d] Pd catalyst (0.005 mmol) and DPEphos (0.010 mmol) were used. [e] Isolated yield. [f] o-Bromoiodobenzene was replaced by o-dibromobenzene.

The optimized reaction conditions were applied to examine the generality of this transformation. As shown in Table 2, various substituted *o*-bromoiodobenzenes (**1**) (Table 2, entry 1-10) coupled with 4-methylbenzenethiol (**2a**) were firstly subjected to the reaction. The catalytic system could tolerate a variety of functional substituents on *o*-bromoiodobenzenes including $-CH_3$, -F, $-CF_3$, -Cl and $-NO_2$, which provided further opportunities for functionalization and thus further derivatives. In general, *o*-bromoiodobenzenes bearing electron-deficient substituents (**3c**, **3d**, **3g**, **3h**) worked better than those with electron-rich substituents (**3b**, **3e**) and no product was observed for 4-methoxy-2-bromoiodo-benzene (Table 2, entry 6). It is worth noting that the differences of substituent position also had great effect on the result of reaction. For example, 1-bromo-2-iodo-4-methylbenzene afforded the corresponding products (**3b**) in 81% yield which was higher than that of 2-bromo-1-iodo-4-methylbenzene (**3e**). Moreover, for 2-bromo-4-halo-1-iodobenzenes (table 2, entries 9-10), two isomers were isolated as a mixture in 1:1 ratio in the reaction, which indicated that C-I bond was competitive with C-Br for the C-S coupling. Successively, the scope of various substituted benzenethiol (2) with *o*-bromoiodobenzenes (**1a**) was also examined under the optimized conditions. From Table 2 (entries 11-20), the electronic effects of the substituents on benzenethiol exerted a great influence on the yield of corresponding product which was just contrary to *o*-bromoiodobenzenes derivations. The benzenethiols with electron-withdrawing groups such as -F (**3o**), -Cl (**3p**) gave the corresponding products in moderate yield which were obviously lower than those of electron-donating groups (Table 2, entries 11-14). Benzenethiols bearing strong electron-deficient substituents such as $-CF_3$, $-NO_2$ (Table 2, entries 17 and 18) were less efficient for this reaction. 3-Methylbenzenethiol gave a mixture of **3la** and **3lb** in a 5:1 ratio (Table 2, entry 12) indicating the impact of steric hindrance on regioselectivities. Moreover, α-naphthalenethiol

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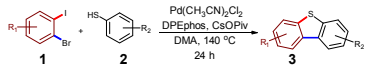
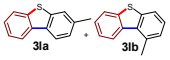
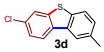
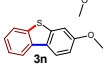
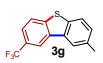
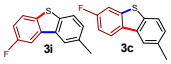
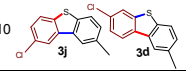
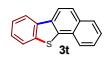
was readily converted to the corresponding products (**3t**) in 92% yield and β- naphthalenethiol furnished a

Table 2. Pd-catalyzed Synthesis of DBTs by *o*-Bromo-iodobenzenes Coupled with Benzenethiols[a]



entry	product	yield(%)	entry	product	yield(%)
1	 3a	91	11	 3k	88
2	 3b	81	12	 3la + 3lb	90[b] 3la : 3lb = 5 : 1
3	 3c	90	13	 3m	72
4	 3d	89	14	 3n	68
5	 3e	66	15	 3o	50
6	 3f	0	16	 3p	66
7	 3g	85	17	 3q	0
8	 3h	91	18	 3y	0
9	 3i 3c	72[b] 3i : 3c = 1 : 1	19	 3r	trace
10	 3j 3d	74[b] 3j : 3d = 1 : 1	20	 3sa 3sb	95[b] 3sa : 3sb = 1 : 1
			21	 3t	92

[a] Reaction was conducted with 2 (0.20 mmol), 1 (0.25 mmol), $Pd(CH_3CN)_2Cl_2$ (0.005 mmol), DPEphos (0.010 mmol), CsOPiv (5.0 equiv.) and DMA (2 mL) at 140 °C for 24 h. Isolated yield. [b] A mixture of two regioisomers obtained (the ratio of products was determined by ^{1}H NMR).

mixture of **3sa** and **3sb** in 1:1 ratio. However, unfortunately, thiophene-2-thiol afforded trace **3r** (Table 2, entry 19) in the reaction.

There are two approaches for the formation of 2-bromo-phenyl phenyl sulfide. In addition to the above strategy, the alternative one is to use iodobenzene and 2-bromobenzenethiol as the substrates. However, under the previous optimized conditions, most substrate of 2-bromobenzenethiol was converted into thianthrene **6** in the yield of 76% (Scheme 2). Delightfully, upon further optimization of the reaction conditions, the desired product of **3u** was achieved in 85% (Table3, entry 1) yield when increasing the amount of DPEphos ligand from 5 mol% to 10 mol%. With the new optimized reaction conditions in hand, a variety of substituted iodobenzenes were tested. The results were shown in Table 3. Most of employed iodobenzene derivations reacted smoothly with 2-bromobenzenethiol under the standard conditions to afford the corresponding products in moderate to excellent yields. It was worth noting that the strong electron donating (-OCH_3) (Table 3, entry 7) and electron withdrawing (-NO_2) (Table 3, entry 11) substitutions on iodobenzene partner gave the corresponding products of **3m** and **3y** in low yields. No product was achieved with 4-iodoaniline. Interestingly, the yield of **3y** was increased to 75% if replacing 4-nitro-iodobenzene with 4-nitro-bromobenzene. Moreover, electronic

Scheme 2. Selectivity for the Pd-Catalyzed Reaction of Iodobenzene with *o*-Bromo-benzenethiol

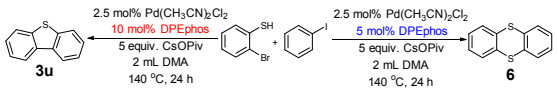
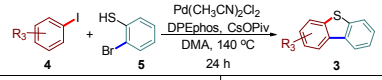
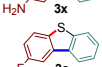
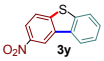
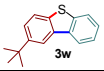
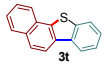


Table 3. Pd-catalyzed Synthesis of DBTs by Iodobenzenes Coupled with *o*-Bromobenzenethiol[a]



entry	product	yield(%)	entry	product	yield (%)
1	 3u	85	7	 3m	60[c]
2	 3k	trace	8	 3x	0
3	 3v	70	9	 3o	81
4	 3la 3lb	85[b] 3la:3lb = 5 : 1	10	 3p	90
5	 3a	88	11	 3y	40/75[d]
6	 3w	84	12	 3t	30

[a] Reaction was conducted with **5** (0.20 mmol), **4** (0.25mmol), $Pd(CH_3CN)_2Cl_2$ (0.005 mmol), DPEphos (0.020 mmol), CsOPiv (5.0 equiv) and DMA (2.0 mL) at 140 °C for 24 h. Isolated yield. [b] A mixture of two regioisomers (the ratio of products was determined by ^{1}H NMR). [c] CsOPiv (6 equiv.) was loaded. [d] The substrate was *p*-nitrobromobenzene.

effect and steric hindrance of methyl group at 2-position of iodobenzene had a great influence on the reaction and only trace of product was obtained (Table 3, entry 2). In the case of 1-iodonaphthalene, 30% yield of desired product **3t** was obtained (Table 3, entry 12).

A putative reaction mechanism was depicted in Scheme 3. The C-S coupling of aryl C-I bond with benzene thiol occurred firstly to generate intermediate **A**, followed by an oxidative addition of C-Br bond to form intermediate **B**. Finally, intermediate **B** underwent a cyclization through a C-H activation process to form intermediate **C** and then afforded the desired product **3** by reductive elimination. According this proposal, the

Scheme 4. The proposed Reaction

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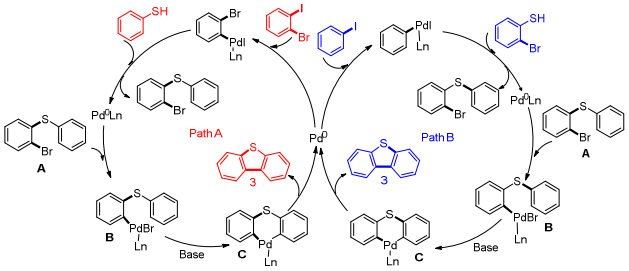
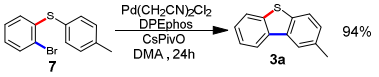


Scheme 5. Reaction of **7** Under Standard



formation of intermediate **A** was a matter of prime importance. To gain a preliminary insight into this tandem reaction, (2-bromophenyl)(p-tolyl)sulfane **7** (Scheme 4) was synthesized according to the literature method,[36] which was then heated under standard conditions leading to the formation of **3a** in 94% yield (Scheme 4).

In conclusion, we have developed a direct and highly efficient approach for the construction of DBTs via a Pd-catalyzed tandem reaction, using simple and commercially available *o*-bromoiodobenzenes combined with benzenethiols or iodobenzenes combined with *o*-bromo-benzenethiol as substrates. These two alternatives for the combination of substrates will certainly make this method more flexible and attract the attention of organic chemists interested in this class of compounds.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (21673261, 21603245, 21703265 and 21573111), Key Laboratory of Organic Synthesis of Jiangsu Province (KJS1747), the Funding from Nanjing University of Posts and Telecommunications (NY217072, NY215016, NY215079).

Conflicts of interest

There are no conflicts to declare".

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