

Synthetic Methods

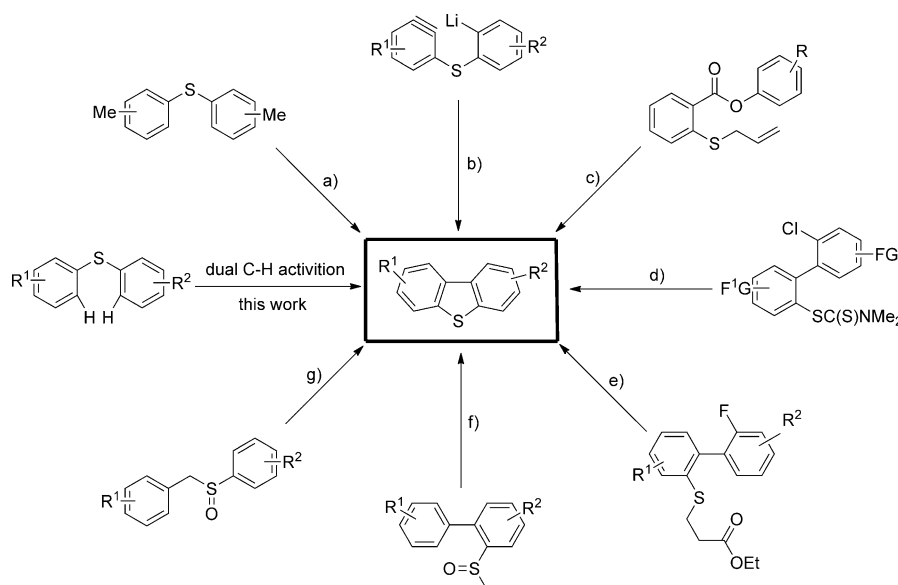
Synthesis of Dibenzothiophenes by Pd-Catalyzed Dual C–H Activation from Diaryl Sulfides

Rui Che,^[a] Zhiqing Wu,^[a] Zhengkai Li,^[a] Haifeng Xiang,^[a] and Xiangge Zhou*^[a, b]

Abstract: Palladium-catalyzed dual C–H functionalization of diaryl sulfides to form dibenzothiophenes (DBTs) by oxidative dehydrogenative cyclization is reported. This protocol afforded various DBTs in moderate to good yields with tolerance of a wide variety of substrates. Benzo[1,2-*b*:4,5-*b'*]bis[*b*]benzothiophene was successfully synthesized by this method, which was used as an organic semiconductor for field-effect transistors.

zenes or 2-haloaryltriflates by using palladium-catalyzed C–C and C–S bond formations was established (route e).^[6] Furthermore, the synthetic method of unsymmetrical DBTs by acid-mediated intramolecular cyclization of biaryl methyl sulfoxides with inorganic reagents, sulfuric acid, and potassium carbonate was also issued (route f).^[7] However, most of these methods are limited by their reliance on necessities of prefunctionalized starting materials or multistep procedures, which are neither atom-economical nor environmentally friendly.

Dibenzothiophenes (DBTs) are usually key core motifs in many important organic compounds including pharmaceuticals, photoactive compounds, dyes, liquid crystals, and conducting polymers.^[1] A number of synthetic methods have been established in recent years. For example, Zeller and co-workers synthesized DBTs bearing dimethyl substituents by using diaryl sulfide with iodine and light under a nitrogen atmosphere in 1975 (Scheme 1, route a).^[2] Fañanás and co-workers disclosed the cyclization of diaryl thioether through a benzyne intermediate (route b).^[3] McNab's group developed a method by using flash vacuum pyrolysis of aryl 2-allylthiobenzoates (route c).^[4] Almost at the same time, Knochel and co-workers reported the successful synthesis of DBTs by a ring-closure procedure starting from functionalized dithiocarbamates (route d).^[5] More recently, a three-step strategy starting from 1-bromo-2-iodoben-



Scheme 1. Strategies toward the synthesis of dibenzothiophenes.

On the other hand, transition-metal-catalyzed oxidative C–H/C–H coupling has emerged as a powerful method for the construction of biaryl scaffolds.^[8] Utilization of two C–H bonds as the coupling partners avoids the steps for installation of pre-activated functional groups and minimizes waste. Over the last few years, considerable efforts have been made to develop catalytic intramolecular dehydrogenative C–C couplings to construct heterocycles, such as carbazoles,^[9] dibenzofurans,^[9b] phenanthridinones,^[10] fluorenes,^[11] and fluorenones.^[12] However, few synthetic methods of sulfur-containing heterocycles were reported by this strategy, which might be caused by the deactivating effect of sulfur on transition-metal catalysts.^[5] Notably, an interesting protocol for the highly regioselective synthesis of polysubstituted DBTs through a palladium-catalyzed cascade reaction by using sulfoxide as a new traceless directing group was demonstrated by the group of Antonchick very

[a] R. Che, Z. Wu, Dr. Z. Li, Dr. H. Xiang, Prof. Dr. X. Zhou
Institute of Homogeneous Catalysis
College of Chemistry, Sichuan University
Chengdu 610064 (P. R. China)
Fax: (+86) 28-8541-2026
E-mail: zhouxiangge@scu.edu.cn

[b] Prof. Dr. X. Zhou
Key Laboratory of Organic Synthesis of Jiangsu Province
College of Chemistry, Chemical Engineering and Materials Science
Soochow University, Suzhou 215123 (P. R. China)

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recently (Scheme 1, route g).^[13] However, this method was limited to products containing a carbonyl group. In light of this, a general and straightforward methodology for the construction of DBTs is still highly desired.

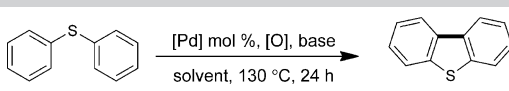
In a continuation of our work on the metal-catalyzed synthesis of sulfur containing compounds^[14,15] and C–H activation,^[16] herein we wish to report an effective method for the synthesis of DBTs from readily available diaryl sulfides by Pd-catalyzed C–H/C–H oxidative cyclization. It has some advantages compared with reported protocols: direct dual C–H activation followed by a C–C coupling reaction avoids the potential pre-functionalization or multiple steps; the reactions can be performed in PivOH without addition of any other solvents; no pretreatment of the chemicals and reaction vessels, as well as mild reaction conditions without an inert atmosphere, made this procedure quite easy to manipulate. Furthermore, the good tolerance of functional groups of substrates makes this protocol useful for further organic synthesis.

We initiated our studies by using diphenyl sulfide (**1a**) as a model substrate, which was treated with Pd(OAc)₂ (10 mol%), O₂ (1 atm.), K₂CO₃ (1 equiv), and PivOH (1 mL) at 130 °C for 24 h. However, no desired product was observed (Table 1, entry 1). Then, some other oxidants were systematically examined. Oxidants, such as Cu(OAc)₂, BQ, oxone, and CF₃SO₃Ag were also ineffective (entries 2–5). Fortunately, when AgOAc was used, a 45% isolated yield of desired product **2a** was obtained (entry 6). The choice of solvent is crucial for this transformation. Other solvents including 1,2-dichloroethane (DCE), toluene, 1,4-dioxane, DMF, DMSO, and acetic acid were not fit for this reaction (entries 7–12). Changing the palladium

source from Pd(OAc)₂ to Pd(tfa)₂ (tfa = trifluoroacetate resulted in a higher yield of 86% (entry 13). Decreasing the loading of silver salt resulted in a lower yield of around 57% (entry 14). Other bases, such as Na₂CO₃ and Cs₂CO₃ were also screened and showed to be less effective for this reaction (entries 15–16). Without any base, the yield was dropped to only 43% (entry 17). When PivOCs was used as the base, the yield was decreased to 65% (entry 18).^[17] Moreover, control experiments confirmed that the reaction did not proceed in the absence of palladium catalyst (entry 19). Therefore, the optimal catalytic system consists of the use of Pd(tfa)₂ (10 mol%), AgOAc (4 equiv), and K₂CO₃ (1 equiv) in PivOH at 130 °C for 24 h.

With the optimized reaction conditions in hand, we next examined the scope of diaryl sulfide substrates. As shown in Table 2, the catalytic system could tolerate a lot of functional substituents including methyl, methoxyl, fluoro, and chloro,

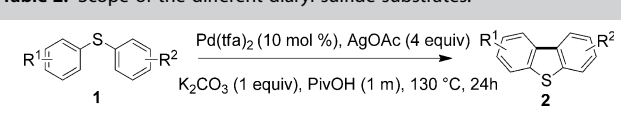
Table 1. Optimization of the reaction conditions.^[a]



Entry	Pd salts	Oxidant	Base	Solvent	Yield [%] ^[b]
1	Pd(OAc) ₂	O ₂ (1 atm.)	K ₂ CO ₃	PivOH	0
2	Pd(OAc) ₂	Cu(OAc) ₂	K ₂ CO ₃	PivOH	0
3	Pd(OAc) ₂	BQ	K ₂ CO ₃	PivOH	0
4	Pd(OAc) ₂	oxone	K ₂ CO ₃	PivOH	0
5	Pd(OAc) ₂	CF ₃ SO ₃ Ag	K ₂ CO ₃	PivOH	0
6	Pd(OAc) ₂	AgOAc	K ₂ CO ₃	PivOH	45
7	Pd(OAc) ₂	AgOAc	K ₂ CO ₃	DCE	0
8	Pd(OAc) ₂	AgOAc	K ₂ CO ₃	toluene	0
9	Pd(OAc) ₂	AgOAc	K ₂ CO ₃	dioxane	0
10	Pd(OAc) ₂	AgOAc	K ₂ CO ₃	DMF	0
11	Pd(OAc) ₂	AgOAc	K ₂ CO ₃	DMSO	0
12	Pd(OAc) ₂	AgOAc	K ₂ CO ₃	HOAc	trace
13	Pd(tfa)₂	AgOAc	K₂CO₃	PivOH	86
14 ^[c]	Pd(tfa) ₂	AgOAc	K ₂ CO ₃	PivOH	57
15	Pd(tfa) ₂	AgOAc	Na ₂ CO ₃	PivOH	50
16	Pd(tfa) ₂	AgOAc	Cs ₂ CO ₃	PivOH	58
17	Pd(tfa) ₂	AgOAc	–	PivOH	43
18	Pd(tfa) ₂	AgOAc	PivOCs	PivOH	65
19	–	AgOAc	K ₂ CO ₃	PivOH	0

[a] All reactions were carried out using diaryl sulfides **1a** (0.5 mmol), Pd salts (10 mol%), base (1 equiv), oxidant (4 equiv), and solvent (1 mL) at 130 °C for 24 h. [b] Yields of isolated product. [c] AgOAc (2 equiv).

Table 2. Scope of the different diaryl sulfide substrates.^[a]



2a , 86%	2b , 79%	2c , 88%	2d , 75%
2e , 87%	2f , 82%	2g , 80%	2h , 81%
2i , 78%	2j , 75%	2k , 79%	2l , 74%
2m , 83%	2n , 77%	2o , 82%	2p , 83%
2q , 68%	2r , 65%	2s , 48%	
2t , 55%	2u , 56%	2v , 58%	
2w , 60%	2x , 51%	2y , 55%	
2z , 57%	2aa , 59%	2ab , 55%	
2ac , 0%	2ad , 0%		

[a] Conditions: diaryl sulfides (0.5 mmol), Pd(tfa)₂ (10 mol%), K₂CO₃ (1 equiv), AgOAc (4 equiv), and PivOH (1 mL) at 130 °C for 24 h; yields of isolated product.

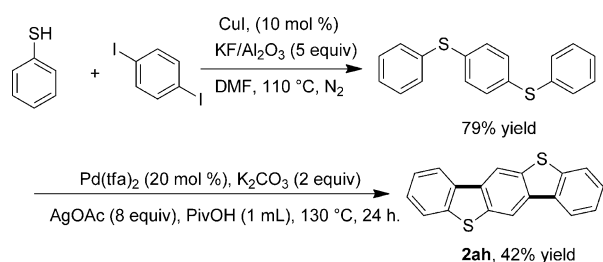
which provided further opportunities for functionalization and thus further derivatives. In general, diaryl sulfides bearing electron-rich substituents worked better than those with electron-deficient substituents. For example, 4-methoxydiphenyl sulfide and 4-fluorodiphenyl sulfide resulted in the desired products **2k** and **2s** in 79 and 48% yields, respectively (**2k** and **2s** in Table 2). Remarkably, both sterically hindered 4,4'-dimethyldiphenyl sulfide and 4,4'-dimethoxydiphenyl sulfide could afford the desired products in good yields of around 85% (**2e** and **2m** in Table 2). Furthermore, 1- or 2-naphthyl phenyl sulfides were also reacted smoothly and transformed to the corresponding products (**2u–2x**, **2y–2ab**) under the standard reaction conditions in moderate yields ranging from 51 to 60%. For the 2-naphthyl phenyl sulfides, reactions selectively occurred at the less sterically hindered site. Unfortunately, diaryl sulfides bearing strong electron-deficient substituents were inactive for this reaction (**2ac–2ad**).

The regioselectivity of this reaction was then studied with 3-substituted diphenyl sulfide as a model substrate. As shown in Table 3, diphenyl sulfide containing electron-donating groups, such as methyl or methoxyl, afforded better total yields than

Table 3. Selectivity of the cyclization.		
Substrates	Yield [%] ^[a]	Products 2/2' ^[b]
1 ae , R = MeO	76	2 ae/2 ae' 4.9:1
1 af , R = Me	78	2 af/2 af' 2:1
1 ag , R = F	45	2 ag/2 ag' 1.1:1
[a] Isolated yield of 2 and 2' . [b] Ratio was determined by GCMS.		

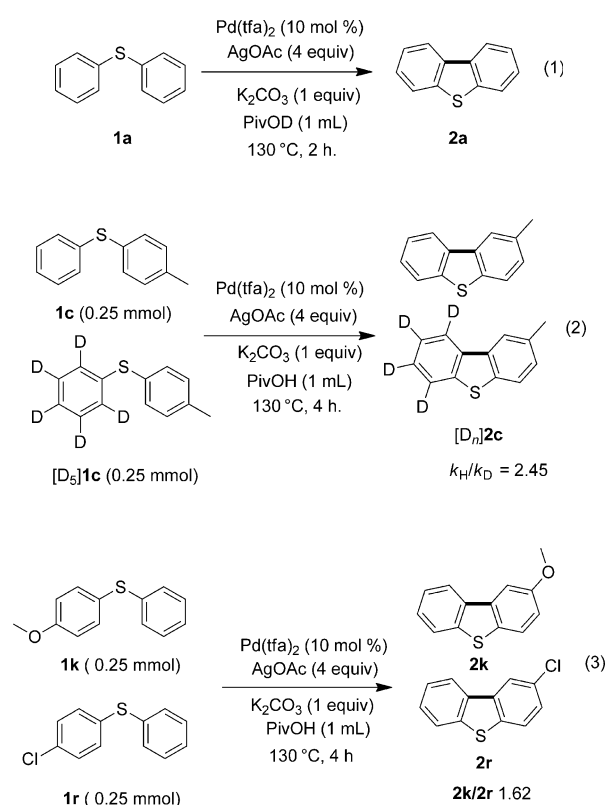
that containing a fluoro group, as expected. Moreover, steric hindrance showed strong effects on the regioselectivities. Thus, 3-methoxydiphenyl sulfide gave two different products in a ratio of 4.9:1, whereas 1.1:1 was obtained in the case of the fluoro-substituted substrate.

At last, by using this strategy, we succeeded in constructing the benzo[1,2-*b*:4,5-*b'*]bis[*b*]benzothiophene **2ah** as shown in Scheme 2, which can be used as an organic semiconductor for field-effect transistors.^[18]

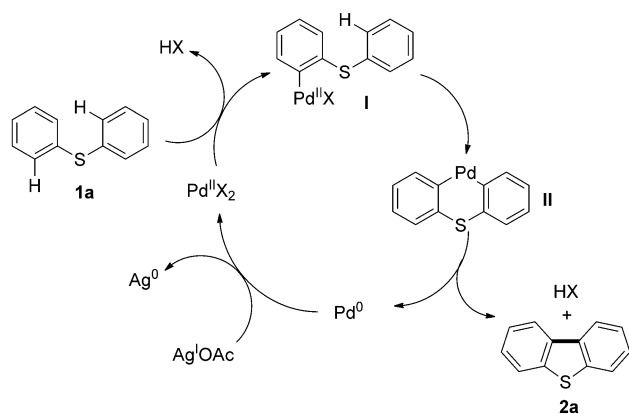


Scheme 2. Synthesis of benzo[1,2-*b*:4,5-*b'*]bis[*b*]benzothiophene.

To gain some preliminary insight into the reaction mechanism, we carried out some control experiments [see Eq. (1–3)].^[19] Treatment of **1a** with a catalytic amount of Pd(tfa)₂, AgOAc, and K₂CO₃ in PivOD at 130 °C for 2 h resulted in no deuterated product **2a** [see Eq. (1) and the Supporting Information for details], which indicates that the C–H bond activation step is irreversible under the reaction conditions. A primary kinetic isotopic effect (KIE) of 2.45 was observed for the competition reaction between **1c** and [D₅]**1c** [Eq. (2)], which revealed that the C–H bond cleavage might be involved in the rate-determining step.^[8b,20] In addition, the competition reactions between electronically differentiated **1k** and **1r** afforded **2k** and **2r** in a ratio of 1.62 [Eq. (3)].



Higher reactivity of the electron-rich substrates suggests that electrophilic aromatic substitution (SEAr) would be responsible for C–H activation, rather than concerted metalation–deprotonation (CMD).^[21] Furthermore, in all of the catalytic reactions, a shining argentate silver mirror was observed on the glass wall of the reaction vessel (see Figure 1 of the Supporting Information), which revealed Ag^I as an oxidant during the reaction. Based on the above observations and the literature, a plausible mechanistic pathway is proposed as shown in Scheme 3. The reaction is initiated by fast electrophilic palladation of **1a** with PdX₂ to generate intermediate I. Further intramolecular C–H cleavage takes place to generate intermediate II, which was considered as the rate-determining step.^[8b,20] The following reductive elimination affords product dibenzothiophene **2a** and generates a Pd⁰ species, which is oxidized by Ag^IOAc to regenerate a Pd^{II} species to finish the catalytic cycle.



Scheme 3. Possible mechanistic pathways.

In summary, we have developed an efficient approach to the synthesis of dibenzothiophenes by a Pd-catalyzed intramolecular oxidative C–H/C–H coupling of diaryl sulfides. A broad range of functional groups were well tolerated under the simple reaction conditions, and a series of dibenzothiophenes with substituents at different positions were obtained in moderate to good yields. It is worth mentioning that the substrates diaryl sulfides weren't oxidated under our standard conditions. Further extension of the current method and application of the obtained sulfur heterocycles as photoelectric materials will be pursued.

Experimental Section

General procedure for the synthesis of dibenzothiophenes

Under an air atmosphere, diaryl sulfides (0.5 mmol), Pd(tfa)₂ (0.05 mmol), AgOAc (2 mmol), K₂CO₃ (0.5 mmol), and PivOH (1 mL) were added into a Schlenk tube. The plunger was then closed after CO₂ completely released in about 10 min. After the mixture had been stirred at 130 °C for 24 h, the reaction mixture was cooled to room temperature, filtered through a short Celite pad, and washed with dichloromethane. The combined filtrate was then concentrated and separated on a silica gel column by using petroleum ether/EtOAc as the eluent, giving the corresponding pure dibenzothiophene products.

Acknowledgements

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Keywords: C–H arylation • cyclization • dibenzothiophenes • diphenyl sulfides • palladium

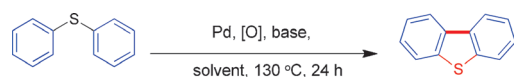
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Oxidative cyclization: Dibenzothiophenes can be prepared from readily available diaryl sulfides by Pd-catalyzed C–H/C–H oxidative cyclization. A wide

scope of substrates was applied with moderate to good yields of up to 88% (see scheme).

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Synthesis of Dibenzothiophenes by Pd-Catalyzed Dual C–H Activation from Diaryl Sulfides

