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Palladium-Catalyzed Intramolecular Direct Arylation of 2-Bromo-diaryl Sulfoxides via C−H Bond Activation

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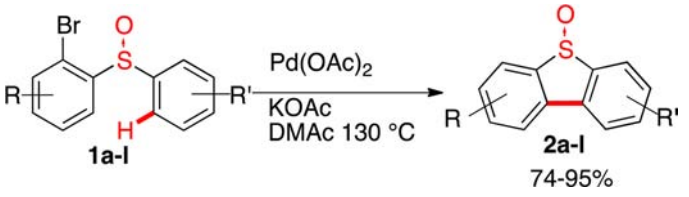
ABSTRACT



Efficient access to dibenzothiophene-*S*-oxides from differently substituted 2-bromo-diarylsulfinyl moieties using ligandless $Pd(OAc)_2$ as the catalyst and KOAc as the base in dimethylacetamide at 130 °C is reported. Various dibenzothiophene-*S*-oxides were obtained in excellent yields.

Biaryl coupling methodologies represent an important tool in modern synthetic organic chemistry. Besides the well-known palladium-catalyzed cross-coupling reactions (Suzuki−Miyaura, Stille, Negishi, Hiyama),[1] transition-metal-catalyzed direct arylation of arenes by C−H bond activation has emerged as an efficient route for the synthesis of complex biaryl molecules.[2] More precisely palladium-catalyzed intramolecular direct arylation, starting from heteroatom- (Z = O, N, Si) tethered 2-halo-diaryl substrates is recognized as a straightforward approach to dibenzofuran, dibenzopyrrole, or silicon-bridged biaryl moieties[3] (Scheme 1). The intramolecular coupling implies activation of C−X and C−H bonds to allow direct C−C bond formation. However the substrate scope of this reaction is currently limited to the presence of nitrogen, oxygen, or silicon as the heteroatom. To the best of our knowledge, the synthesis of dibenzothiophenes by direct arylation of 2-halodiaryl thioethers has never been reported, probably because of the high affinity of sulfur for palladium.

Dibenzothiophenes have numerous applications as bioactive compounds including agrochemicals.[4] Moreover, owing to their optical and redox properties, they are

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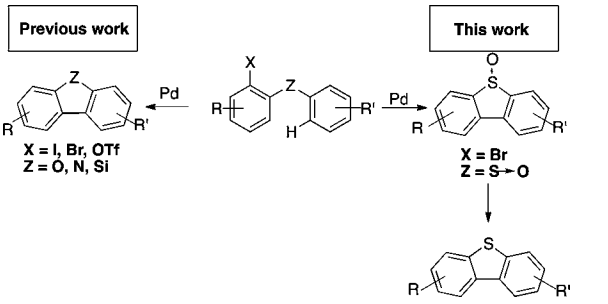
considered as promising scaffolds in the field of organic electronics and materials chemistry.[5] In addition, dibenzothiophene-*S*-oxides[6] are recognized as triplet oxygen precursors by their photochemical deoxygenation.[7] Recently triplet oxygen-mediated cleavage of DNA was demonstrated which raises the interesting potential of triplet oxygen precursors in biological systems.[8] Several straightforward methods to access dibenzothiophenes have been reported, but they often require multistep synthesis.[9] Thus the development of a new strategy to access dibenzothiophene and dibenzothiophene-*S*-oxide scaffolds would be of great interest. Recently Antonchick reported, for the first time, a palladium-catalyzed double C−H activation directed by sulfoxides. The key step of this transformation involved sulfoxide-directed cyclometalation of the aromatic ring, followed by the second, intramolecular C−H bond activation and a Pummerer rearrangement which gave access to dibenzothiophene scaffolds.[10] Taking into account our experience in the use of sulfoxides as chiral auxiliaries in diastereoselective Suzuki−Miyaura cross-coupling reactions,[11] we report herein our results on a new palladium-catalyzed direct arylation, *via* C−H bond activation of easily accessible 2-bromo-diaryl sulfoxides, and its application in the direct synthesis of differently substituted dibenzothiophene-*S*-oxides. The latter can be easily reduced to the corresponding dibenzothiophenes using standard methodologies for the reduction of sulfoxides to thioethers (Scheme 1).[12]

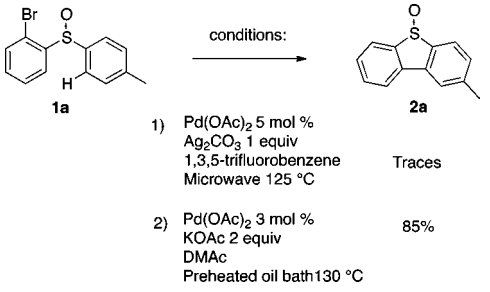
Our preliminary attempts at implementing Scheme 1 were conducted with $Pd(OAc)_2$ (5 mol %) and Ag_2CO_3 (1 equiv) on 1-bromo-2-*p*-tolylsulfinylbenzene **1a**[13] in 1,3,5-trifluorobenzene at 125 °C under microwave irradiation.

Scheme 1. Synthesis of Complex Biarylmolecules from Heteroatom-Tethered 2-Halo-diaryl Substrates



A complex reaction mixture was obtained in 30% yield, and we identified the hydrodehalogenated starting material (*p*-tolylsulfinyl benzene), dibenzothiophene, and the expected product, the dibenzothiophene-*S*-oxide **2a**, in the reaction mixture. Rewardingly, replacing apolar 1,3,5-trifluorobenzene with polar DMAc, substituting the silver base with KOAc, and using 3 mol % $Pd(OAc)_2$ led, in 8 h, to the desired product **2a** in 70% yield, together with traces of the hydrodehalogenated starting material.[14] Noteworthily, reduction of the starting material could be prevented when using a preheated oil bath whereupon **2a** was isolated in an 85% yield (Scheme 2).

Scheme 2. Synthesis of Dibenzothiophene-*S*-oxide **2a** from 1-Bromo-2-*p*-tolylsulfinylbenzene **1a**



Under these optimized reaction conditions, the scope of the reaction was investigated. α-Bromo-diarylsulfoxides **1b**−**l** bearing different substituents on the aryl moieties were synthesized through two known methodologies:[13] (1) S_NAr reaction on 2-fluoro-1-bromoaryls followed by oxidation and (2) by condensation of 2-bromoaryl Grignard reagents on an aryl menthyl sulfinate (Scheme 3).

The 2-bromo-diaryl sulfoxides **1b**−**l** were subjected to the palladium-catalyzed cyclization conditions, and the corresponding dibenzothiophene-*S*-oxides **2b**−**l** were obtained in excellent yields (Table 1). Compound **2b**, bearing only an acetyl group on the dibenzothiophene scaffold, was obtained in an excellent yield of 86%. In addition, various electron-withdrawing and -donating groups in the

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Scheme 3. Synthesis of α-Bromo-diarylsulfoxides **1a**–**l**

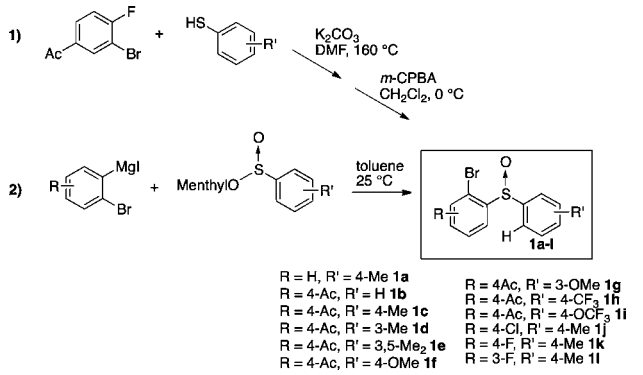
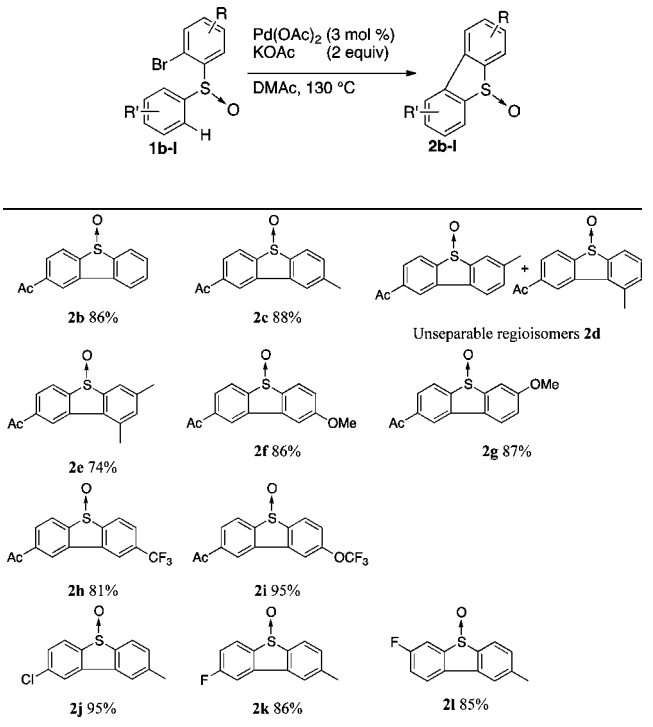


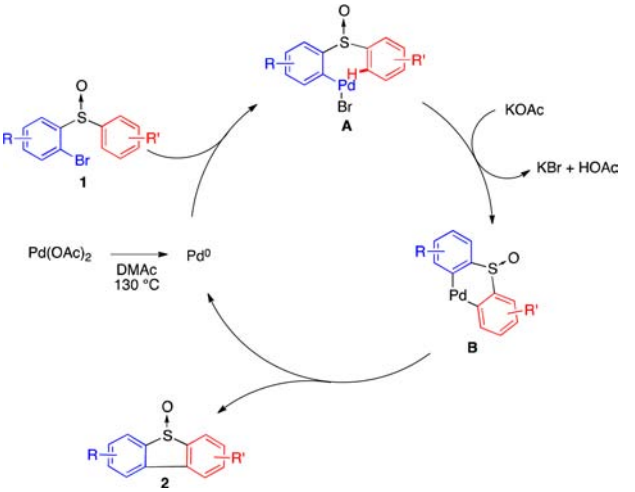
Table 1. Palladium-Catalyzed Intramolecular Coupling of **1b**–**l**[a]



[a] Reaction conditions: **1b**–**l** (1 mmol), KOAc (2 mmol), $Pd(OAc)_2$ (0.03 mmol), and DMAc (6 mL) at 130 °C for 8 h.

ortho-, *meta*-, or *para*-position of the diaryl sulfoxide were well tolerated. An acetyl group at the *meta*-position of the bromo aryl unit and electron-donating groups such as methyl- or methoxy- at the *para*-position of the second aryl unit gave the dibenzothiophene-*S*-oxides **2c** and **2f** in excellent yield. In contrast, in the presence of a methyl group at the *meta*-position, the formation of two unseparable regioisomers **2d** in 30% yield was observed. This can be explained by the presence of two sites for C–H activation *ortho* to the sulfinyl group. Consequently, dibenzothiophene-*S*-oxide **2e** with two methyl groups

Scheme 4. Plausible Mechanism



at the *meta*-positions was obtained in satisfactory yield (74%). However with a methoxy group at the *meta*-position, only **2g** was detected and isolated in 87% yield without any trace of the other regioisomer. Direct arylation of the bromo-diaryl sulfoxides **1h** and **1i**, bearing the acetyl group and electron-withdrawing substituents such as $-CF_3$ or $-OCF_3$, was performed in excellent yields of 81% and 95%, respectively. Moreover, with fluorine or chlorine at the *meta*- or *para*-position of the bromo aryl unit, we were pleased to obtain in excellent yield the corresponding chloro- or fluoro-dibenzothiophene-*S*-oxides **2j**–**2l** (Table 1).

During the course of the reaction, a rapid color change of the reaction medium occurred from orange to black suggesting a reduction of $Pd(OAc)_2$ to Pd(0) by DMAc at 130 °C.[15] Therefore, mechanistically, we assume that the first step is an oxidative addition of the α-bromo-diaryl sulfoxide **1** by insertion of the Pd(0) into the C–Br bond to give the arylpalladium bromide intermediate **A**. This Pd(II) species allows the C–H activation process to produce the more stable six-membered palladacycle **B**, which undergoes reductive elimination to afford the desired dibenzothiophene-*S*-oxide **2** and regenerate the Pd(0)-catalyst (Scheme 4).

In conclusion a new strategy to access dibenzothiophene derivatives via intramolecular direct arylation is reported. Due to both the easily accessible bromo-diaryl sulfoxides as starting materials and the versatility of such an approach, this reaction provides a practical method to build up highly valuable dibenzothiophene-based scaffolds.

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Supporting Information Available. Experimental protocols and characterization data for new compounds, copies of ^{1}H, ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.