Synthesis, Structure, and Reactivity of 5-(Aryl)dibenzothiophenium Triflates

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Abstract: *A synthetic protocol for the preparation of 5-(aryl)dibenzothiophenium salts starting from inexpensive dibenzothiophene S-oxide and simple arenes is reported. The scope of the method regarding the nature of the arene is evaluated, intermediates along the reaction sequence have been trapped, and side-reactions identified. In addition, the X-ray structures of a complete set of these salts are reported and their reactivities studied. Specifically, chemoselective Suzuki coupling is observed at the dibenzothiophenium in the presence of iodides.*

Introduction

Although the use of sulfonium moieties as linchpins in cross-coupling chemistry,[1] and as source of organic radicals, has been known for more than two decades,[2] it has not been until very recently that the actual synthetic potential of these reagents has been broadly recognized. Variants of the Pd-catalyzed Suzuki–Miyaura,[3] Mizoroki–Heck,[4] Sonogashira,[5] Negishi,[6] Stille,[7] and related reactions, such as Buchwald–Hartwig aminations,[8,9] are now available by employing aryl sulfonium salts as electrophilic partners. Moreover, either by direct reaction with nucleophiles or through photoredox catalyzed processes, the sulfonium moiety can be selectively exchanged with alkyl groups, halogens, or amines under mild reaction conditions.[10,11] Aside from this wide range of applications, additional beneficial attributes are associated with the use of sulfonium salts. Namely, their easy and regioselective preparation from commercially available sulfides[12] or sulfoxides,[13] nonvolatility, and comparatively higher thermal stability than diazonium salts.

Very recently, our group reported on the synthesis of related 5-(cyano)- and 5-(alkynyl) dibenzothiophenium salts by triflic acid anhydride activation of the parent dibenzothiophene S-oxide.[14] Given the synthetic potential of S-(aryl)-

sulfonium salts and the lack of a detailed study on the reaction sequence leading to their formation from the dibenzothiophene S-oxide **1** (see Figure 1), we decided to carefully study this synthetic route, evaluate its scope regarding the nature of the arene, and further explore the reactivity of the sulfonium salts obtained.[15]

Results and Discussion

Trapping of 2 and Characterization of Its Thermally Induced Decomposition Products

We started our investigation by attempting the isolation of compound **2**, the species expected from the activation of **1** with Tf$_2$O (Figure 1). Bistriflates of that general structure
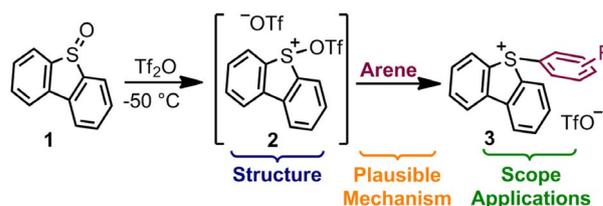
Figure 1. Schematic synthesis of 5-(aryl)dibenzothiophenium triflates.

are usually proposed as the products of activation of sulfoxides when treated with Tf$_2$O. However, no structural characterization of salts with such connectivity has been reported to date. Thus, we slowly added Tf$_2$O to a cooled (−50 °C) dichloromethane solution of **1**, and obtained a red suspension.[14] All our attempts to obtain monocrystals of **2** under these reaction conditions failed. Warming the reaction mixture to −20 °C resulted in the disappearance of the red color and precipitation of a beige solid. Throughout this transformation the sample remained EPR silent. Chromatographic analysis of the reaction mixture allowed the isolation of the salts **4** and **5** in moderate yields, together with a highly insoluble material (Scheme 1a). The formation of **4** and **5** suggests a disproportionation of **2** into the corresponding sulfide and sulfone, followed by reaction of both species with either one or two equivalents of the remaining **2**. The X-ray structure of **4**, in which the sulfonium substituent is *meta* to the SO$_2$ group, evidences that this compound was not formed by oxidation of **6**. In contrast, the necessary intermediate for the formation of **5**, the sulfonium salt **6**, was not observed in this experiment, but it can be obtained in nearly quantitative yield by reaction of **2** with one equivalent of dibenzothio-

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a) Isolated species
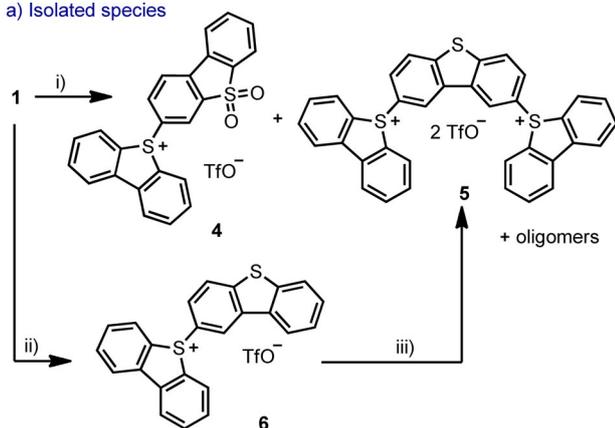
b) X-ray structures of **4** and **6**
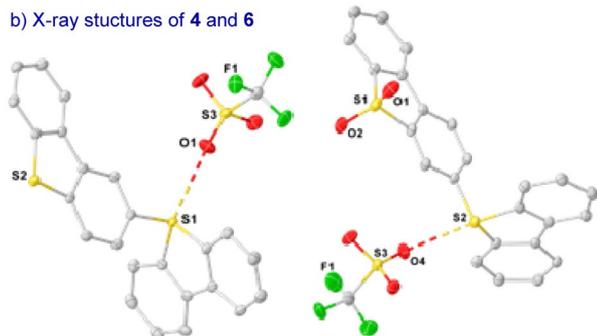
c) Reaction outcome starting from sulfoxide **7**
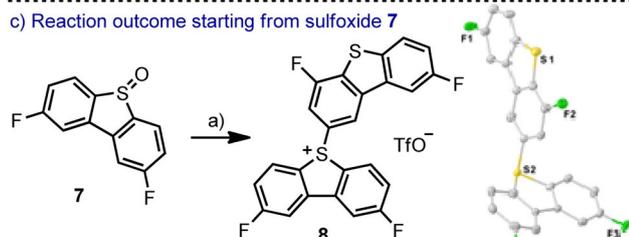
d) Plausible disproportionation mechanism
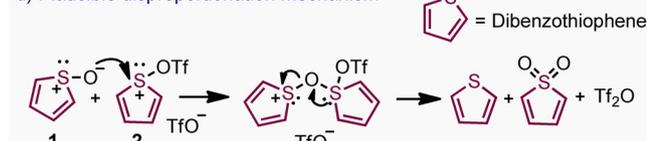
Scheme 1. Thermally induced decomposition products of **2**. Reagents and conditions: i) Tf$_2$O (1.1 equiv), −50°→−20°C, 4 h; **4**, 11%; **5**, 19%; ii) Tf$_2$O (1.1 equiv), −50° and then dibenzothiophene (1.1 equiv), **6**, 95%; iii) Tf$_2$O (1.1 equiv), −50° and then **6**; **5**, 62%. Molecular structures of **4**, **6**, and **8** in the solid state. Anisotropic displacement shown at 50% probability level. Hydrogen atoms and triflate anions omitted for clarity.[16].

phene. Moreover, isolated **6** can further react with a second equivalent of **2** to afford **5** (Scheme 1a). Hence, we believe that the disproportionation of **2** is a slow process compared with the electrophilic aromatic substitution steps leading to **4** and **5**. Finally, MS analysis of the remaining insoluble fraction indicated the formation of highly charged oligomeric species containing four and five dibenzothiophene units, which can be explained by further reaction of **5** with additional **2** (see the Supporting Information). Attempts to inhibit these side reactions by blocking positions 2 and 8 of the dibenzothio-

phene core with fluorine substituents did not improve the reaction outcome, and instead the sulfonium salt **8** was the only product isolated from the complex mixture (Scheme 1c). Further analysis is still necessary to explain the formation of **8**.

Finally, a plausible reaction pathway for the formation of sulfone derivatives is depicted in Scheme 1d. We hypothesize an equilibrium for the formation of **2** from **1** and Tf$_2$O. The attack of **1** onto the sulfur atom in **2**, leads to the formation of an oxygen-bridged disulfonium salt, [17] which presumably rearranges to dibenzothiophene and dibenzothiophene-5,5-dioxide by asymmetric cleavage of the bridge.

Being aware of the difficulty that the isolation of **2** entails, we decided to chemically trap it. It was hypothesized that the use of a monodentate neutral ligand, able to engage in strong σ-donation to the S^{IV} center of **2**, might provide sufficient stabilization to allow the isolation of the corresponding adduct before side-reactions take place. Hence, one equivalent of DMAP was added to a freshly prepared suspension of **2** at −50°C. This addition causes the slow formation of an orange/yellow solid (**9**), which was obtained in analytically pure form after washing with dry dichloromethane (Scheme 2a). X-ray diffraction analysis of the monocrystals obtained by cooling a saturated dichloromethane solution confirmed the formation of the expected Lewis adduct **9**. In the solid state, **9** adopts a dimeric structure in which the geometry around each dibenzothiophene S-atom can be defined as distorted octahedral. Two vertices are occupied

a)

b)
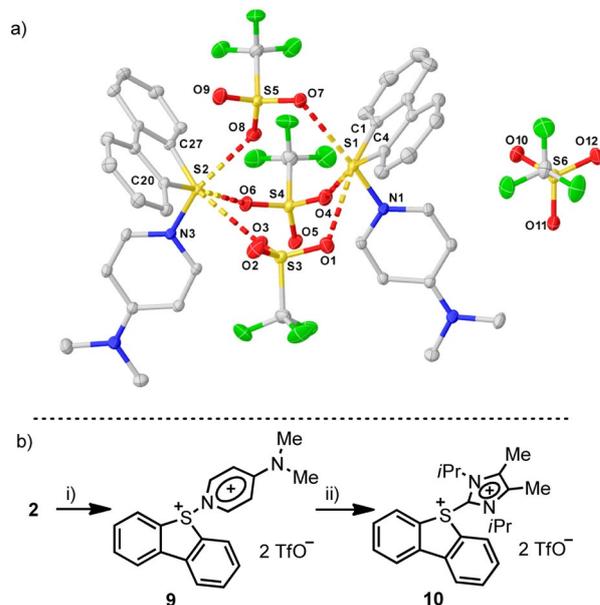
Scheme 2. Coordination of Lewis bases to **2**. Reagents and conditions: i) DMAP (1 equiv), −50°C→RT, DCM, **9**, 37%; ii) 1,3-Diisopropyl-4,5-dimethyl-imidazol-2-ylidene (1.0 equiv), THF **10**, 20%. Molecular structure of compound **9**. Anisotropic displacement shown at 50% probability level. Hydrogen atoms, non-coordinating triflate anion and solvent omitted for clarity. Selected bond lengths [Å]: C1–S1 1.773(2), C4–S1 1.777(2), S1–N1 1.734(1), S1⋯O1 2.991(1), S1⋯O4 3.821(1), S1⋯O7 2.769(1), S1⋯O8 3.232(1), S2–C20 1.778(2), S2–C27 1.781(1), S2–N3 1.735(1), S2⋯O3 2.986(1), S2⋯O6 2.963(1), S2⋯O8 2.534(1).[16]

by the aryl rests of the dibenzothiophene moiety, while the pyridine ligand is positioned at a third vertex, adopting a *cis* relationship with both arene substituents. The other three vertices of the octahedron are each occupied by one triflate anion, which additionally act as a bridge to a second S center. Five from the six S–O contacts [S1···O1, 2.991(1); S1···O4, 3.821(1); S1···O7, 2.769(1); S2···O3, 2.986(1); S2···O6, 2.963-(1); S2···O8, 2.534(1)] are significantly shorter than the sum of the van der Waals radii of the corresponding elements (3.32 Å), evidence of a significant Lewis acid character at the S atom. The isolation of **9** unequivocally demonstrates that the primary product of activation of **1** with Tf$_2$O is a dicationic S^{IV} species. Moreover, **9** is still electrophilic and upon treatment with one equivalent of a stronger σ-donor, such as 1,3-diisopropyl-4,5-dimethyl-imidazol-2-ylidene, ligand exchange takes place to afford the carbene adduct **10** (Scheme 2b).[18]

Synthesis of 5-(aryl)Dibezothiophenium Triflates: Scope and Limitations

The next step in our investigation was the study of the reaction between **2** and aromatic substrates. Hence, a series of functionalized arenes were carefully added to freshly prepared suspensions of **2** at −50°C, and the mixture was warmed to −20°C and stirred for a 12 hours. Under these reaction conditions, deleterious side-reactions were minimized and a remarkable scope of sulfonium salts (**3a–r**) was obtained (Scheme 3). This synthetic route allows access to the desired compounds without the use of I^{III} reagents.[19] Ideal substrates for this transformation are moderate electron-rich arenes and heteroarenes such as anisole derivatives, alkyl- or aryl-substituted benzenes, haloarenes, and thiophenes. In most of the cases the reaction proceeded in good to excellent yields and satisfactory *para*/*ortho* ratios. In addition, it is tolerant to halogens, ethers, esters, and heteroaromatic skeletons. The reactivity of **2** and **9** is similar in terms of conversion into **3a** when benzene is used as substrate. For this range of aromatic compounds we have no evidence against the formation of sulfonium salts **3** by electrophilic aromatic substitution, even the cyclopropane ring of **3h** survives. However, single-electron oxidation of the substrate by **2** followed by immediate recombination of the two radicals cannot be excluded (Scheme 4).[20]

Figure 2 depicts the molecular diagrams of the salts **3m** and **3o** in the solid state (see the Supporting Information for the crystallographic structures of **3b–l**). It worth noting that interactions between the S atom and the triflate counteranion, reminiscent of the ones observed in **9**, are again detected along the complete series. The S1···O1 distances [2.990(1) Å for **3m** and 3.057(2) Å for **3o**] are shorter than the sum of the van der Waals radii, revealing the still remarkable electrophilic character at that position.

Electron-poor rings such as 1,2-dichlorobenzene are still able to render the corresponding sulfonium salt (**3k**) by reaction with **2**, albeit in moderate to low yields. Careful column chromatography is necessary to separate **3k** from the side-products **4** and **5**, which are formed in considerable
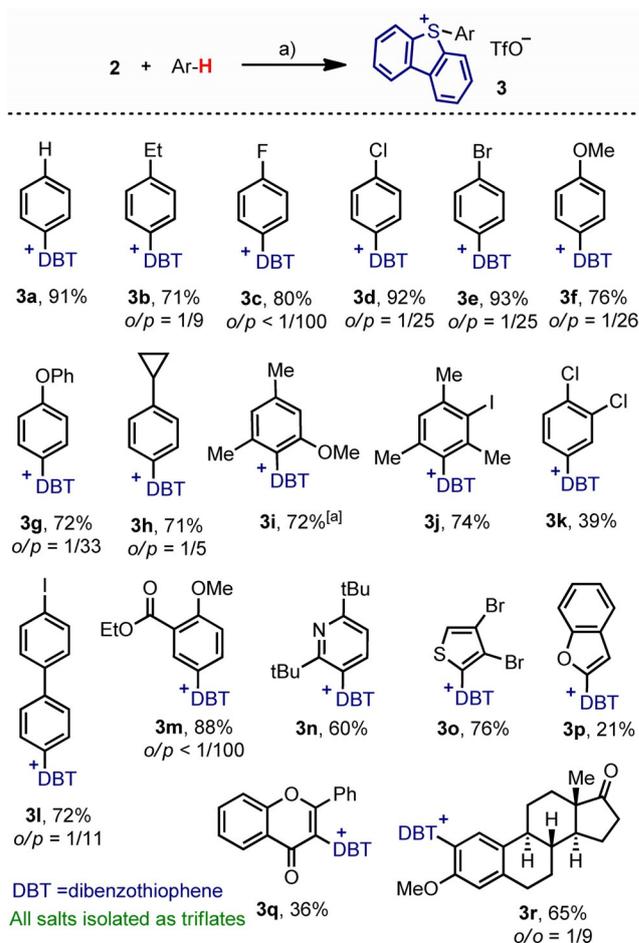
Scheme 3. Synthesis of 5-(aryl)dibenzothiophenium triflates. If not indicated, only one regioisomer was detected. Reagents and conditions: a) Arene (1.1 equiv) −50°→-20°C, 15 h. [a] Isolated as a 1:2 mixture of rotamers.
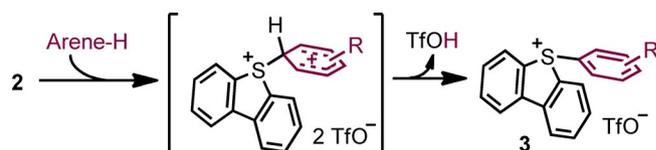
Scheme 4. Proposed mechanism for the sulfonium salt formation when using substrates of moderate electron richness.

amounts. Electron poorer substrates such as 1,4-difluorobenzene or trifluoromethylbenzene are inert to the attack of **2**. In these essays only decomposition products **4** and **5** together with polycationic dibenzothiophene oligomers are observed.

Electron-rich (hetero)aromatic rings are problematic as well, but for different reasons. For example, reaction of **2** with *N*-methylindole (**11**) afforded a complex mixture of products from which dibenzothiophene is the main product. The sulfonium salts **6** and **3s**, and bis(indole) **12** were isolated as well (Scheme 5a). Additionally, tri- and tetraindolic structures were detected by MS analysis. This outcome suggests, as reported by Kita et al. for the treatment of pyrroles with hypervalent I^{III} reagents,[21] that single-electron oxidation of methylindole by **2** takes place, yielding an indole radical
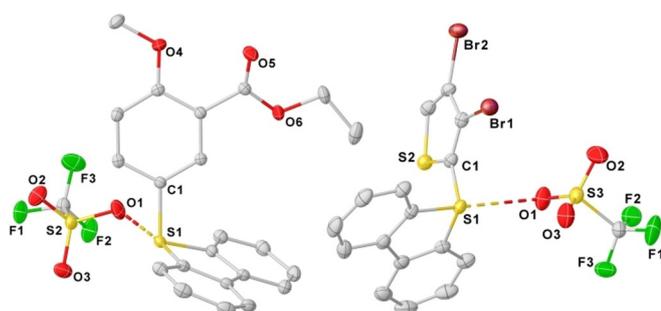
Figure 2. Molecular structures of **3m** (left) and **3o** (right) in the solid state. Anisotropic displacement shown at 50% probability level. Hydrogen atoms omitted for clarity. Selected bond lengths [Å] and angles [deg]: **3m**, C1–S1 1.776(1), S1···O1 2.990(1); C1-S1-O1 80.8(1); **3o**, C1–S1 1.763 (3), S1···O1 3.057(2); C1-S1-O1 77.1(1).[16]

taking place readily.[22] We rationalized at this stage that aniline-substituted sulfonium salts might be obtained in a two-step sequence starting from the fluorobenzene derivative **3c**. In this salt the fluoride is expected to be activated towards nucleophilic aromatic substitution because of the strong electron-withdrawing nature of the sulfonium moiety at the *para* position. Should that substitution be feasible, reaction of **3c** with amines may deliver the desired aniline-derived sulfonium salts. Actually, it was found that a variety of secondary amines were suitable for the reaction, leading to a set of sulfonium salts (**14a–e**) containing structurally differentiated aniline substituents (Scheme 6). The chlorobenzene derivative **3d** is unable to deliver the products **14a–e** under identical reaction conditions.

Scheme 5. a) Reaction of **2** with 1-methylindole (**11**). b) Reaction of **2** with TEMPO. Reagents and conditions: i) 1-methylindole (1.1 equiv), CH₂Cl₂, −50→−20°C. ii) CH₂Cl₂, −50→−20°C.
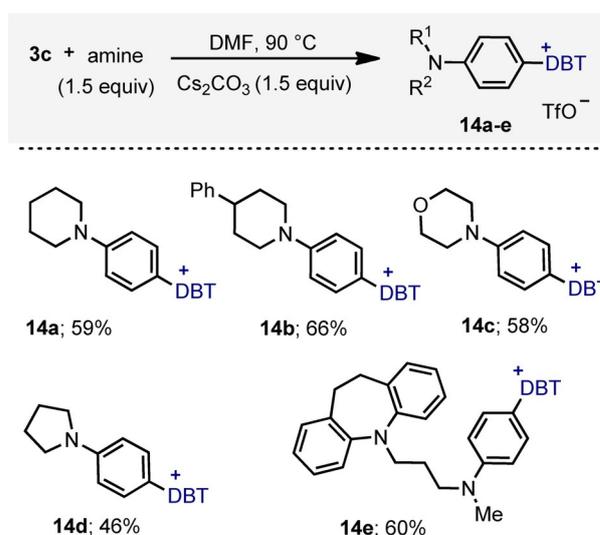
Scheme 6. Synthesis of aniline-substituted dibenzothiophenium triflates by nucleophilic aromatic substitution.

cation, which oxidatively couples with more indole producing **12** and indole oligomers. Simultaneously, the dibenzothiophene being formed partially reacts with **2** to afford **6**. Additional evidence of the feasibility of a radical mechanism when easy to oxidize substrates are employed derives from the reaction of **2** with stoichiometric amounts of TEMPO. This essay affords a clean mixture of **6** (75% yield of isolated product) and the TEMPO oxoamonium triflate **13** (Scheme 5b).

Post-Synthetic Modification of Sulfonium Salts by Nucleophilic Aromatic Substitution and Synthetic Applications

Given their electron richness, aniline substrates are not well-tolerated by the protocol just described. However, sulfonium salts containing these substituents might be synthetically useful compounds because haloanilines are not always easy to obtain. In fact, classical Friedel–Crafts aniline halogenation is difficult to control, with polyhalogenation

Finally, it was recently reported that thianthrenium cations participate in site-selective coupling reactions over typical linchpins such as C−Br and C−OTf bonds.[11b] We rationalized that with the DBT unit being more electron-poor than the thianthrenium one, the insertion of Pd along the C−DBT bond should be even more favored. Hence, we decided to challenge the well-established C−I site selectivity in the Suzuki coupling versus the C−DBT.[23] Specifically, the salt **3l** was chosen as a substrate because the iodo and dibenzothiophenium units are in identical stereoelectronic environments but on independent rings. One equivalent of 4-(trifluoromethyl)phenyl boronic acid was used for this experiment (Scheme 7). From this assay, carried out at 35°C and employing only 0.5 mol% of Pd(AcO)₂ as catalyst, the product of selective arylation at the C−DBT bond (**15**) was isolated in 90% yield. By MS we detected traces of the thioether **16**, which derives from initial insertion of Pd into one of the internal C−S bonds of the dibenzothiophene moiety, and traces of the product resulting from coupling at the C−I site. This result demonstrates intrinsic chemoselectivity for C−DBT over C−I in the Suzuki reaction. Given the mild reaction conditions and simple catalyst employed to promote the
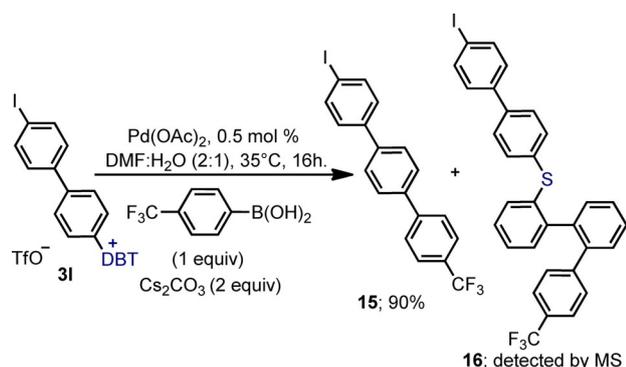
Scheme 7. Chemoselective Suzuki coupling at C–DBT over C–I bonds.

coupling, as well as the exquisite site selectivity observed, we envision the use of DBT units as a promising linchpin to enable rapid access to densely functionalized polyarenes through coupling reactions.

Conclusion

In summary, we report herein a straightforward method for the synthesis 5-(aryl)dibenzothiophenium triflates by metal-free sulfenylation of C–H bonds. Preliminary mechanistic studies based on trapping intermediates, and the careful isolation of decomposition products, suggests that an electrophilic aromatic substitution is operative for the sulfenylation of electron-neutral or moderately-rich arenes. The generation of radicals by single-electron transfer between **2** and the substrate is more conceivable for more electron-rich aromatics, leading to complex reaction mixtures. Comparison of the reactivity of the DBT linchpin with that of C–I bonds in a model Suzuki reaction reveals full selectivity for the DBT moiety over the competing C–I coupling site. Hence, we anticipate a widespread range of applications for 5-(aryl)dibenzothiophenium triflates in Pd chemistry, in particular for the execution of sequential biaryl couplings leading to the construction of polyarenes.

Acknowledgements

Conflict of interest

The authors declare no conflict of interest.

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[15] 5-(aryl)dibenzothiophenium salts have been very recently prepared in situ, and directly used as substrates in photoredox catalyzed C–H/C–H coupling reactions; their systematic characterization is not reported in that article (Ref. [11c]).

[16] CCDC 1946820, 1946822, 1946823, 1946824, 1946825, 1946826, 1946827, 1946828, 1946829, 1946830, 1946831, 1946832, 1946833, 1946834, 1946835 and 1946836 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

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