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Base-Catalyzed Halogen Dance Reaction and Oxidative Coupling Sequence as a Convenient Method for the Preparation of Dihalo-bisheteroarenes

Yulia A. Getmanenko,*,† Paul Tongwa,‡ Tatiana V. Timofeeva,‡ and Seth R. Marder*,†

Department of Chemistry & Biochemistry and The Center for Organic Photonics and Electronics, Georgia Institute of Technology, 901 Atlantic Drive NW, Atlanta, Georgia 30332-0400, and Department of Chemistry, New Mexico Highlands University, Las Vegas, New Mexico 87701

yulia.getmanenko@chemistry.gatech.edu; seth.marder@chemistry.gatech.edu

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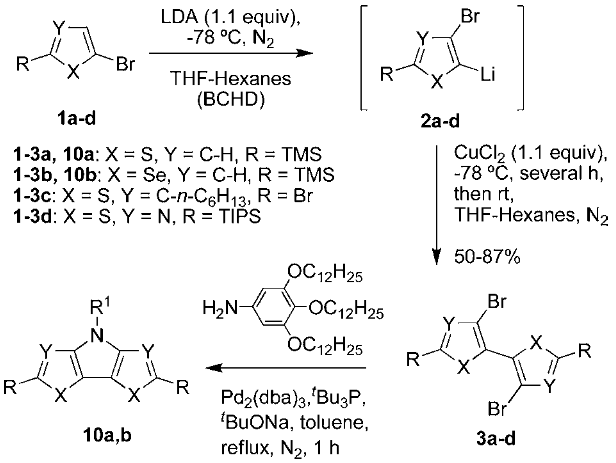
ABSTRACT



A one-pot preparation of the 2,2′-dibromo-1,1′-bisheteroarenes 3a−d from bromo-heteroarenes utilizing the sequence of the base-catalyzed halogen dance (BCHD) reaction and $CuCl_2$-promoted oxidative coupling of the in situ formed α-lithio-*β*-halo-heteroarenes 2a−d provides a convenient access to precursors for the preparation of tricyclic heteroaromatic cores. The structures of 3a,b,d, 6, and 9 were confirmed by single-crystal X-ray analysis, and dibromides 3a and 3b were used for the preparation of dithieno-[2,3-*b*:3′,2′-*d*]-pyrrole 10a and its selenophene analogue 10b, respectively.

Organic materials, which incorporate fused thiophene-based aromatic cores, such as dithieno-[2,3-*b*:3′,2′-*d*]-thiophene (DTT), -pyrrole (DTP), -silole, and -phosphole, find applications as active materials in various electronic and optoelectronic devices.[1−9] 3,3′-Dibromo-2,2′-bithiophene, in some cases substituted at positions 5 and 5′, serves as a key intermediate for the preparation of these aromatic cores as well as dithienoborole.[10] The typical approach to these

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† Georgia Institute of Technology.
‡ New Mexico Highlands University.

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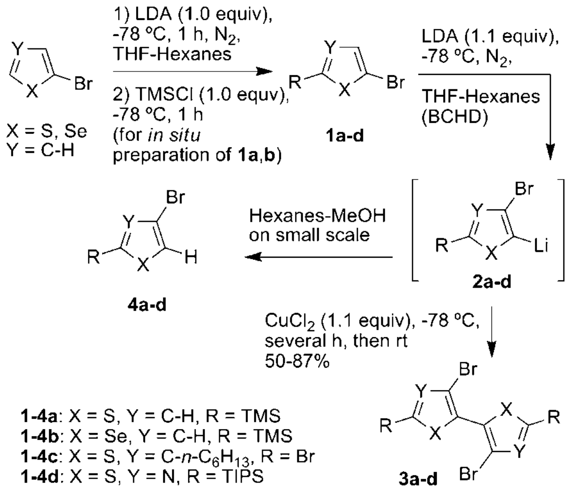
dibromides involves tetrabromination of 2,2′-bithiophene to yield 3,3′,5,5′-tetrabromo-2,2′-bithiophene,[11] which is either reduced by reaction with Zn in acetic acid[12] to obtain 3,3′-dibromo-2,2′-bithiophene or double lithiated followed by trapping with trialkylsilyl chlorides to obtain 5,5′-bistrialkylsilyl-3,3′-dibromo-2,2′-bithiophenes.[6,7,13,14] Decades ago Gronowitz[15] demonstrated that lithiated thiophene derivatives undergo oxidative coupling in the reaction with CuCl$_2$; e.g., 2-lithio-3-bromothiophene, generated by the lithium−halogen exchange from 2,3-dibromothiophene, produced 3,3′-dibromo-2,2′-bithiophene in 50−60% yield. It had also been shown that this so-called base-catalyzed halogen dance (BCHD)[16] reaction can cleanly produce α-lithium-*β*-bromoarenes from α-bromoarenes; for example, 2-lithio-3,5-dibromothiophene was generated from 2,5-dibromothiophene by the reaction with LDA at −78 °C.[17] A variety of heteroaromatic aryl halides were successfully used in the BCHD reaction, and the lithiated species were typically trapped with alcohol to get rearranged aryl halides or with various electrophiles to obtain functionalized materials.[18]

Here we report a convenient preparation of heteroaryl dihalides **3** from 2-bromo-5-trialkylsilyl-heteroarenes **1** by the sequence of the BCHD reaction and CuCl$_2$-promoted oxidative coupling of the in situ generated α-lithio-*β*-bromoarenes **2** (Scheme 1).

In the case of 5,5′-bistrimethylsilyl-3,3′-dibromo-2,2′-bithiophene (**3a**) and -selenophene (**3b**), the reaction sequence starts from the corresponding bromide, 2-bromothiophene or 2-bromoselenophene. The first lithiation with 1 equiv of LDA and trapping with TMSCl cleanly produced substrates **1a** and **1b**, which are suitable for the BCHD reaction with halogen at the first α-position and with the second α-position of the heterocycle protected from lithiation by the TMS group. Addition of the second equivalent of LDA to **1a** and **1b** results in a clean and fast rearrangement to form 2-lithio-3-bromo-5-TMS-thiophene **2a** and -selenophene **2b**, respectively (GC/MS and/or ^{1}H NMR analyses of the aryl bromides **4a**,**b** confirmed the clean BCHD reaction). CuCl$_2$-promoted oxidative coupling of **2a** and **2b** produces corresponding dibromides **3a** (60−84% purified yield) and **3b** (50−66% purified yield). This one-pot preparation of **3a** from commercially available 2-bromothiophene is a convenient alternative to the three-step synthesis reported in the literature,[19,11,13] while preparation of **3b** in one pot from 2-bromoselenophene provides an easy access to selenium-containing analogues of DTT, DTP, etc.

Scheme 1. Sequence of the BCHD Reaction and CuCl$_2$ Oxidative Coupling As a Convenient Approach to Aryl Dihalides **3a**−**d**



A different thiophene derivative, 2,5-dibromo-3-*n*-hexylthiophene (**1c**), also underwent a clean BCHD reaction (confirmed by ^{1}H NMR analysis) followed by oxidative coupling, and tetrabromide **3c** was obtained in 80−87% yield.

2-Triisopropylsilyl-5-bromothiazole (**1d**), which was successfully used in the BCHD reaction,[20] produced dibromide **3d** in 60−82% purified yield. Another thiazole bromide, 2-bromo-5-trimethylsilylthiazole (**5**), generated in situ from 2-bromothiazole using Corey's conditions (addition of LDA in the presence of TMSCl)[21] produced 4,4′-dibromo-5,5′-bis(trimethylsilyl)-2,2′-bithiazole (**6**) in 35−50% purified yield, when treated with LDA to induce the BCHD reaction followed by CuCl$_2$ oxidative coupling (Scheme 2). This one-pot preparation of **6** is a valuable alternative to the literature preparation[22] of 4,4′-dibromo-2,2′-bithiazole, which was synthesized from expensive 2,4-dibromothiazole by the monolithiation−oxidative coupling sequence.

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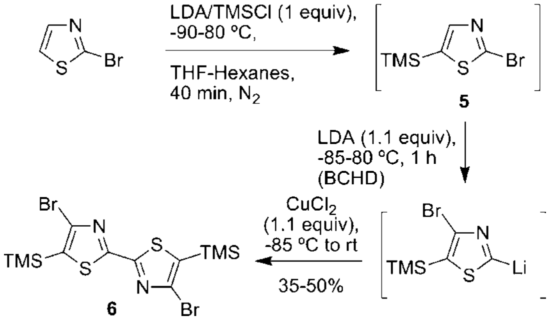
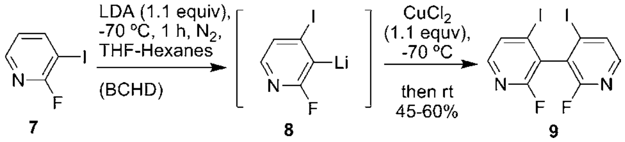
Scheme 2. One-Pot Synthesis of 4,4′-Dibromo-5,5′-bis(trimethylsilyl)-2,2′-bithiazole (**6**)



2-Fluoro-3-iodopyridine (**7**) is another heterocycle, which was reported to undergo a clean BCHD reaction upon treatment with LDA at −75 °C.[23] 2-Fluoro-3-lithio-4-iodopyridine (**8**), generated in situ by the BCHD reaction, underwent CuCl$_2$-promoted oxidative coupling, and 2,2′-difluoro-4,4′-diiodo-3,3′-bipyridine (**9**) was obtained in 45−60% yield (Scheme 3).

Scheme 3. Sequence of BCHD−CuCl$_2$ Oxidative Coupling of 2-Fluoro-3-iodopyridine



Single-Crystal X-ray Structural Analysis of Products. The structures of dibromides **3a**, **3b**, **3d**, **6**, and **9** were confirmed by single-crystal X-ray analysis. 5,5′-Bistrimethylsilyl-3,3′-dibromo-2,2′-bithiophene (**3a**) crystallizes from EtOH in a noncentrosymmetric orthorhombic space group *Pccn* with two independent molecules **A** and **B** in the unit cell, which have similar geometries. Both thiophene rings are planar with mean deviation from planarity 0.027 Å, while the torsion angle between two thiophene rings is −51.6°(4) (**A**) and −60.6°(4) (**B**). The presence of C−Br· · ·S interactions between two thiophene rings allows for the formation of a dimer with a twisted arrangement (Figure 1).

5,5′-Bistrimethylsilyl-3,3′-dibromo-2,2′-biselenophene (**3b**) crystallizes from EtOH in the orthorhomic space group $Pca2_1$ with two independent molecules (**A** and **B**) in the unit cell with TMS groups disordered over two positions with a 0.45: 0.55 occupancy with similar geometries (Supporting Information). Torsion angles Se1A−C3A−C4A−C5A and Se1B−C4B−C5B−C6B are 46.4°(2) and −48.3°(2), respectively. The presence of only one C−Br· ·Se interaction (C−Br bond length 1.802(1) Å; Br· ·Se distance 3.6860(18) Å) results in the transoid confirmation (Figure 2).

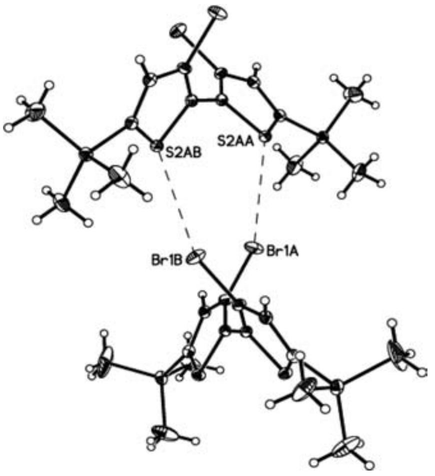


Figure 1. Orientation of the two thiophene rings caused by the presence of intermolecular C−Br· · ·S interactions between the thiophene rings and Br substituents in **3a** (bond length of C3B−Br1B, 1.878(3) Å; intermolecular distance Br1B· · ·S2AB, 3.601(11) Å).

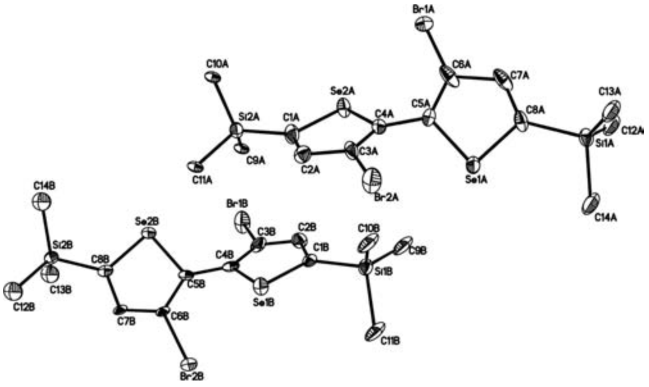


Figure 2. X-ray structure of two symmetrically independent molecules in compound **3b** drawn at 50% probability thermal ellipsoid. H atoms are omitted for clarity.

4,4′-Dibromo-2,2′-bis(triisopropylsilyl)-5,5′-bithiazole (**3d**) crystallizes from EtOH in the triclinic space group P-1; two planar thiazole rings (0.005 Å deviation) have transoid conformation probably due to the absence of the intramolecular C−Br· ·S interactions and the presence of intermolecular Br· ·Br interactions (Figure 3).

Compound **6** crystallizes in the tetragonal space group *P*4(2)/*n* with two independent molecules per unit cell. The molecules form chains with short Br· ·Br intermolecular contacts and perpendicular relative orientations (Supporting Information, Figure 5).

Dibromides **3a** and **3b** were examined in the cyclization reaction with aryl amine, and dithieno- and diselenopheno-

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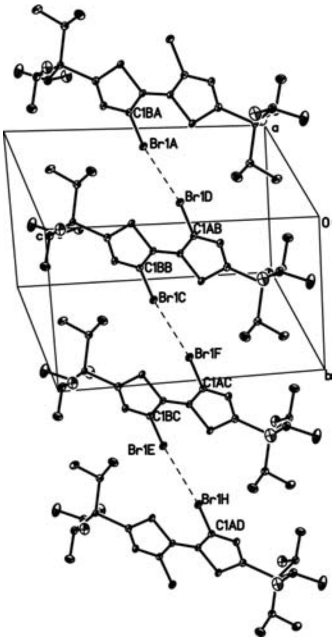
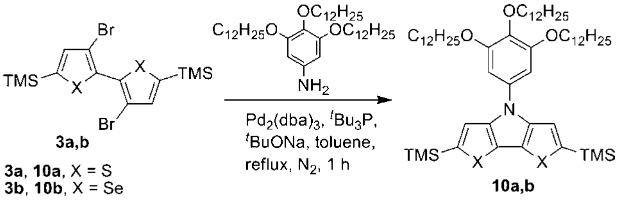


Figure 3. Transoid orientation in **3d** formed by the presence of Br•••Br interactions in a ribbon-like molecular arrangement in the unit cell.

[3,2-*b*:2′,3′-*d*]pyrrole derivatives **10a** and **10b** were obtained in 53% and 51−81% yields, respectively, using slightly modified literature conditions (Scheme 4).[4]

Scheme 4. Examples of the Preparation of Tricyclic Cores from Dihalides **3a** and **3b**



Electrochemical properties of the tricyclic aromatic cores **10a**,**b** were examined by cyclic voltammetry (Figure 4, Table 1). 2,6-Bis-TMS-dithieno- and 2,6-bis-TMS-diselenopheno-[3,2-*b*:2′,3′-*d*]pyrroles **10a** and **10b** showed reversible oxidation waves at similar potentials with a slightly lower oxidation potential for selenophene derivatives.

The UV−vis absorption spectra of the DTP derivative and its selenium analogue showed a similar band structure with a slight red shift observed for a heavier chalcogenophene derivative. A similar bathochromical shift (15 nm) and negative shift of the reduction potential (−0.06 V) were observed for benzo[1,2-*b*:4,5-*b*′]dichalcogenophenes upon substitution of S with Se.[24]

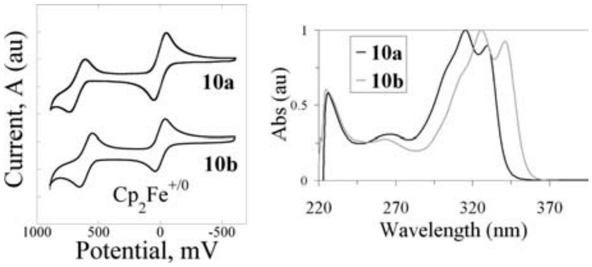


Figure 4. Cyclic voltammograms (0.1 M ^{n}Bu$_4$NPF$_6$ in THF, Cp$_2$Fe internal standard at 0 V, 50 mV•s^{-1} scan rate) and UV−vis absorption spectra of **10a** and **10b**.

Table 1. Optical and Electrochemical Properties of Dithieno- and Diselenopheno-[3,2-*b*:2′,3′-*d*]pyrroles **10a** and **10b**

compound	λ_{max}, nm (CH_2Cl_2)	$E_{1/2}^{0/+1}$, V
10a	226, 266, 315, 329	+0.67
10b	225, 263, 326, 341	+0.61

Oxidative coupling of the halo-lithio-arenes generated in situ by the BCHD reaction resulted in a formation of aryl dihalides, which can be used for the preparation of various tricyclic aromatic cores. This method was successfully tested on different heterocycles, such as thiophenyl-, thiazolyl-, selenophenyl-, and pyridinyl-halides, and can be potentially extended to a variety of haloarenes, which undergo a clean BCHD reaction.

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Supporting Information Available: The detailed synthetic procedures, copies of the spectral analyses, and crystallographic data for **3a**,**b**,**d**, **6**, and **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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