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Graphical Abstract

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Tanay Kesharwani,[a,*] Cory Kornman,[a] Amanda Tonnaer,[a] Amanda Hayes,[a] Seoyoung Kim,[b] Nikesh Dahal,[b] Ralf Romero[a] and Andrew Royappa[a]

[a] *Department of Chemistry, University of West Florida, Pensacola, FL 32514 USA*

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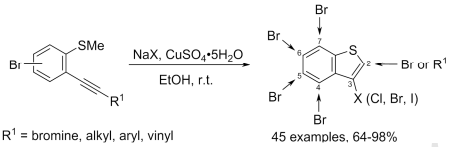

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Sodium halides as the source of electrophilic halogens in green synthesis of 3-halo- and 3,*n*-dihalobenzo[*b*]thiophenes

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ABSTRACT

A convenient methodology for the synthesis of mono- and di-halogenated benzo[*b*]thiophenes is described herein, which utilizes copper(II) sulfate pentahydrate and various sodium halides in the presence of substituted 2-alkynylthioanisoles. The proposed method is facile, uses ethanol as a green solvent, and results in uniquely substituted benzo[*b*]thiophene structures with isolated yields up to 96%. The most useful component of this methodology is the selective introduction of bromine atoms at every available position (2-7) around the benzo[*b*]thiophene ring, while keeping position 3 occupied by a specific halogen atom such as Cl, Br or I. Aromatic halogens are useful reactive handles; therefore, the selective introduction of halogens at specific positions would be valuable in the targeted synthesis of bioactive molecules and complex organic materials via metal-catalyzed cross coupling reactions. This work is a novel approach towards the synthesis of dihalo substituted benzo[*b*]thiophene core structures, which provides a superior alternative to the current methods discussed herein.

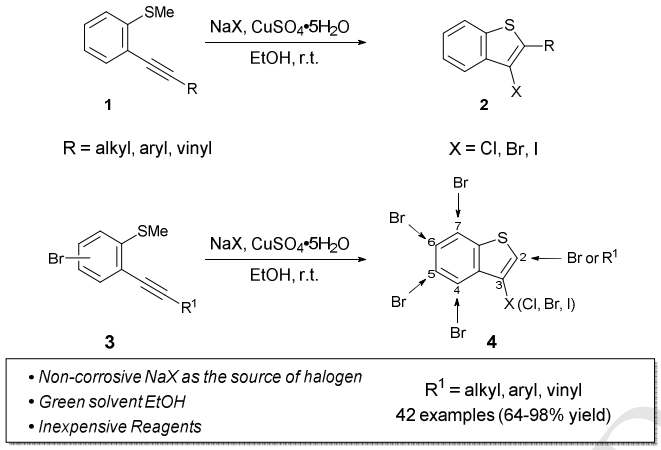
1. Introduction

Substituted benzo[*b*]thiophenes and related chalcogen-containing heterocycles, such as benzofurans and benzoselenophenes, have received much attention in the recent years due to their well-recognized biological1 and materials-related applications.[2] In particular, the molecules containing the benzo[*b*]thiophene core structure have proven to be promising candidates for biomedical applications, including 5-H7R and 5-HTT receptor modulation, i.e., used in the treatment of depression,[3] estrogen receptor-alpha (ERα) and estrogen receptor-beta (ERβ) modulation,[4] breast cancer prevention,[5] immune system regulation via S1P G-protein coupled receptors,[6] and anti-malarial activity.[7] Additional studies have shown that uniquely substituted benzo[*b*]thiophenes may be useful in the treatment of Staphylococcus infections.[8] Organic materials containing the benzothiophene core structure are showcased in devices including novel phosphorescent organic light emitting diodes (PHOLED's) made possible by the low-lying LUMO and high thermal stability associated with aromatic heterocycles;[9] organic thin-film field effect transistors (OFET's) dependent on the high photostability and ionization potential of core-structure organics;[10] and dye-sensitized solar cells (DSSC's).[11]

Given the significant biological and materials applications associated with benzo[*b*]thiophene derivatives, it is no surprise that many synthetic chemists have worked to develop innovative methods for the synthesis of the substituted core structures.[12] Very recently, Reddy and Valetti developed a [4+2] benzannulation between substituted alkenyl thiophenes and various propargyl alcohols to furnish a diverse library of benzo[*b*]thiophene derivatives[13] with the substituents on the 5, 6, and 7 positions. In another report, Yin et al. examined the direct C-H arylation of benzo[*b*]thiophene using catalytic Pd(II) and aryl chlorides to form 2-aryl benzo[*b*]thiophene derivatives.[14] In a similar report, Chen and coworkers utilized a Pd-catalyzed coupling/cyclization reaction of 2-iodothiophenols with terminal alkynes to achieve 2-aryl substituted benzo[*b*]thiophene derivatives in moderate to high yields with fluoro-, chloro- and trifluoromethyl-substituted 5 and 6 positions.[15] Yamauchi and coworkers introduced the multicomponent arylation/cyclization of 2-alkynylthioanisoles to furnish 2,3-diarylated benzo[*b*]thiophene derivatives in a single step using a Pd/phenanthroline catalyst.[16] Cyclization of arylketene dithioacetal monoxides to afford 4, 5, and 6 methoxy-substituted benzo[*b*]thiophenes was reported by Yoshida and coworkers.[17] In the recent literature, it is clear that necessity-driven syntheses have been developed for the production of highly-substituted benzo[*b*]thiophene structures and, when considered in combination, the current methods provide a useful network of strategies to afford variously functionalized structures at many positions. However, to our knowledge, no single report has defined a universal strategy for the selective placement of halogens at any desired position on the benzo[*b*]thiophene ring.

Furthermore, no work to date has addressed the systematic synthesis of dihalogenated benzo[*b*]thiophenes.

Herein, we report a comprehensive method for the synthesis of mono- and dihalogenated benzo[*b*]thiophenes via electrophilic halocyclization of 2-alkynylthioanisoles. We have determined previously that copper(II) sulfate pentahydrate and sodium halide react in the presence of 2-alkynylthioanisoles **1** to afford mono-halogenated benzo[b]thiophene derivatives **2** in isolated yields up to 98% (Scheme 1).[18] In this all-inclusive study, we have expanded upon this foundation through the implementation of new and varied functional groups to test the flexibility of this reaction as well as to demonstrate a scaffold upon which dihalogenated analogues may be achieved. The reaction of bromo-substituted 2-akynylthioanisoles **3** under the same reaction conditions gives dihalogenated benzo[*b*]thiophenes **4** with isolated yields up to 96% (Scheme 1).

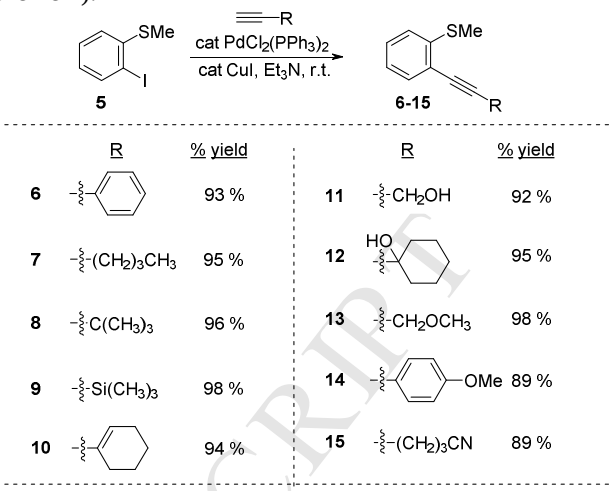


Scheme 1: Synthesis of 3-halobenzo[*b*]thiophenes and systematic synthesis of 3-halo-*n*-bromobenzo[*b*]thiophene

Our approach works at room temperature, tolerates diverse functionalities, and incorporates a green solvent. Additionally, our reaction conditions are not only mild but also tolerant to moisture and air. In addition, this method allows the placement of a bromine reactive handle on positions 2, 4, 5, 6, and 7 around the benzo[*b*]thiophene core ring, while placing chlorine, bromine, or iodine moieties on position 3 depending on which sodium halide (NaCl, NaBr, or NaI) is used for the synthesis. The methods proposed in this report provide an array of easily accessible halogenated compounds with a high potential for functional diversity. The option to install halogens of choice precisely at specific sites opens up many synthetic possibilities due to the well-established halogen selectivity of metal-catalyzed carbon-carbon coupling reactions (I > Br > Cl).

2. Results and Discussion

The desired 2-alkynylthioanisoles **6-15** used for the synthesis of mono-halogenated benzo[*b*]thiophenes were prepared via the Sonogashira coupling of 2-iodothioanisole **5** (1 equiv.) with substituted terminal alkynes (1.2 equiv.) in the presence of catalytic Pd (2 mol %) and catalytic copper (4 mol %) using trimethylamine as solvent (Scheme 2).[18,19] Using these conditions, a variety of functionalized 2-akynylthioanisoles **6-15** were synthesized with isolated yields between 89 and 98% (Scheme 2).



Scheme 2

Using variously substituted 2-alkynylthioanisoles **6-15** as starting materials, a diverse library of 3-halo benzo[*b*]thiophenes **16-45** were synthesized (Table 1). Beginning with a phenyl substituent (entries 1-3), 2-phenyl-3-halogenated benzo[*b*]thiophenes were synthesized. When 2-alkynylthioanisole **6** was subjected to our cyclization conditions using NaCl, 2-phenyl-3-chlorobenzo[*b*]thiophene **16** was formed in excellent 92% yield. When alkyne **6** was subjected to similar reaction conditions, where sodium bromide or iodide was employed instead of sodium chloride, 2-phenyl-3-bromobenzo[*b*]thiophene **17** and 2-phenyl-3-iodobenzo[*b*]thiophene **18** were synthesized in 92% and 83% yields respectively. When an alkyl chain was used instead of a phenyl group on the remote alkyne group the corresponding 2-alkynylthioanisoles, upon chlorocyclization, produced 2-*n*-buyl-3-chlorobenzo[*b*]thiophene **19** in an excellent 86% yield. Once again replacing NaCl with NaBr and NaI, but otherwise using the same reaction conditions, resulted in the bromo- and iodocyclized products **20** and **21** in 83% and 89% yields respectively.

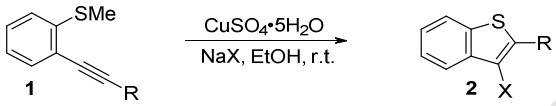
When a sterically hindered *tert*-butyl group was used in place of the linear *n*-butyl group no significant change was observed in reaction yield. The reaction worked equally well furnishing the chloro cyclized product **22** in 82% yield as compared to the 86% yield achieved with the *n*-butyl group (compare entries 22 and 19). Once again NaBr and NaI generated the desired cyclized 2-*tert*-butyl-3-halobenzo[*b*]thiophenes **23** and **24** product in good yields of 89% and 81% respectively. 2-Alkynylthioanisoles with trimethylsilyl substituents (entries 10-12) underwent cyclization to form 3-iodobenzo[*b*]thiophene **27** in excellent 91% yield; however, attempts to synthesize chloro- and bromo- analogues **25** and **26** failed as the reaction yielded a complex, inseparable mixture of products.

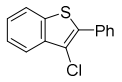
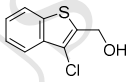
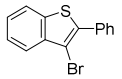
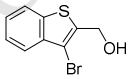
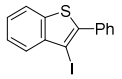
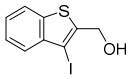
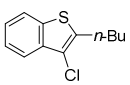
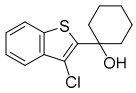
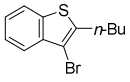
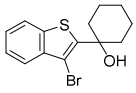
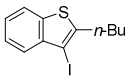
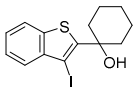
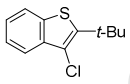
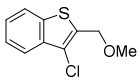
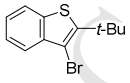
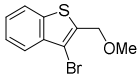
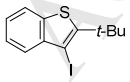
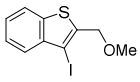
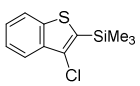
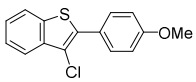
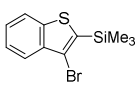
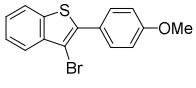
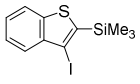
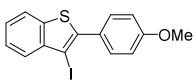
Our reaction tolerates vinyl groups as 2-(1-cyclohexen-1-yl)thioanisole (entries 13-15) cyclized to form 3-chlorobenzo[*b*]thiophene **28** in 82% yield, 3-bromobenzo[*b*]thiophene **29** in high yield of 98%, and 3-iodobenzo[*b*]thiophene **30** in a yield of 81%. We also determined that a primary alcohol works well in our cyclization reaction conditions as the propargyl alcohol **11** (entries 16-18) cyclized in

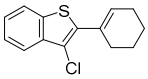
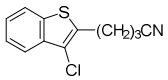
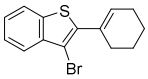
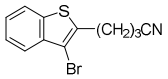
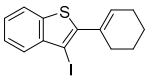
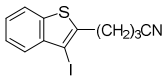
the presence of NaCl to form the desired 3-chlorobenzo[*b*]thiophene **31** in excellent 92% yield. Similarly, alcohol **11** resulted in the formation of 3-bromobenzo[*b*]thiophene **32** in 84% yield, and 3-iodobenzo[*b*]thiophene **33** in 90% yield. Tertiary alcohol substituents attached to the alkyne (entries 19-21) cyclized to form the chloro- and bromo- substituted benzo[*b*]thiophene analogues **34** and **35** in excellent 90% and 96% yields respectively; however, the 2-iodo analogue **36** was formed in a moderate yield of 75%.

The ether functionality was tolerated well in our reaction conditions as alkyne **13** (entries 22-24) bearing a methoxy functionality resulted in the formation 3-chlorobenzo[*b*]thiophene **37**, 3-bromobenzo[*b*]thiophene **38**, and 3-iodobenzo[*b*]thiophene **39** in isolated yields of 97%, 98%, and 97% respectively. Electron-rich alkyne **14** bearing a methoxy group on the remote phenyl ring resulted in excellent yields of 98, 95 and 86% for 3-chlorobenzo[*b*]thiophene **40**, 3-bromobenzo[*b*]thiophene **41**, and 3-iodobenzo[*b*]thiophene **42** respectively (entries 25-27). Hexynenitrile **15** (entries 28-30) works equally well in our cyclization condition resulting in high yields of the desired chloro, bromo and iodo products (**43**, **44** and **45**), once again establishing the superiority of this methodology both in terms of reaction yields and functional group tolerance along with mild reaction conditions.

Table 1. Synthesis of 3-halobenzo[*b*]thiophenes using sodium halides as the source of electrophilic halogens[a]



Entry	Substrate	Product		Lit. Yield[c,d]	Yield[b]	Entry	Substrate	Product		Lit. Yield[c,d]	Yield[b]
1	**6**		**16**	65[d]	92	16	**11**		**31**	-	92
2	**6**		**17**	92[c]	92	17	**11**		**32**	-	84
3	**6**		**18**	100[c]	83	18	**11**		**33**	86[e]	90
4	**7**		**19**	-	86	19	**12**		**34**	-	90
5	**7**		**20**	-	83	20	**12**		**35**	-	96
6	**7**		**21**	93[e]	89	21	**12**		**36**	-	94
7	**8**		**22**	87[d]	82	22	**13**		**37**	-	97
8	**8**		**23**	67[c],10[d]	89	23	**13**		**38**	-	98
9	**8**		**24**	98[c]	81	24	**13**		**39**	97[e]	97
10	**9**		**25**	71[d]	-[f]	25	**14**		**40**	71[d]	98
11	**9**		**26**	0[c],57[d]	-[f]	26	**14**		**41**	87[d]	95
12	**9**		**27**	100[c]	91	27	**14**		**42**	96[c]	86

13	**10**		**28**	-	82	28	**15**		**43**	-	98
14	**10**		**29**	0[c]	98	29	**15**		**44**	79[c]	98
15	**10**		**30**	97[c]	81	30	**15**		**45**	98[c]	82

[a]Reaction conditions: all reactions were performed using 0.30 mmol of thioether, 5.0 equiv of CuSO4•5H2O, and 5.0 equiv NaX (X = Cl, Br, I) in 5 mL of EtOH at room temperature for 24 h.

[b]Isolated yield.

[c]Literature yields reported by Larock and coworkers using I_2 or Br_2 as the electrophile.[12m]

[d]Literature yields reported by Wu and coworkers using $CuCl_2$ or $CuBr_2$ as the electrophile.[12n]

[e]Literature yields reported by our group using $FeCl_3$ and NaI as the electrophile.[19]

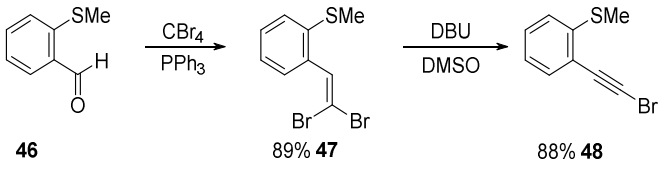
[f]Complex reaction mixture.

Prior to this report the synthesis of 2-chlorobenzo[*b*]thiophenes **19**, **28**, **31**, **34**, **37** and **43** (entries 4, 13, 16, 19, 22 and 28) was not established using electrophilic chlorocyclization. However, the synthesis of **16**, **22**, **25** and **40** was reported by Wu and coworkers[12n] by employing $CuCl_2$ as the electrophile (entries 1, 7, 10 and 25). Our yields were either higher or comparable to Wu's yields for the products containing phenyl, 4-methoxy and *tert*-butyl groups (entries 1, 7 and 25). Additionally, Wu's approach requires a higher temperature, toxic acetonitrile as the solvent and a comparatively expensive copper salt making it less desirable. Our only reaction which was inferior to Wu's method was the cyclization of trimethylsilyl substrate **9** as we could not isolate the cyclized product **25** due to the formation of a complex reaction mixture (entry 10).

Our bromocyclization reaction was also superior to both Wu's and Larock's bromocyclization involving Br_2 and $CuBr_2$ as the electrophiles.[12m] The yield for the cyclization reaction involving phenyl-substituted alkynylthioanisole **6** was identical for both our method and Larock's (entry 2). Interestingly, in exception to our methodology, all other previously reported procedures failed to produce a desired bromocyclized product in high yields when alkyne **8** containing a *tert*-butyl group was employed for the cyclization reaction (entry 8). Our method produced desired 2-*tert*-butyl-3-bromobenzo[*b*]thiophene **23** in a high yield of 89%. The poor yields reported by others were attributed to the formation of an alkyne addition product. Likewise 2-(1-cyclohexane-1-yl)thioanisole **10** resulted in the formation of **29** in 98% yield whereas Larock's approach failed because of the addition of Br_2 to the remote vinyl group (entry 14). As observed earlier with regard to chlorocyclization, our reaction was inferior when trimethylsilyl substrate **9** was subjected to our bromocyclization reaction conditions (entry 11). Bromoyclization of alkyne **14** bearing a methoxy group and hexynenitrile **15** both resulted in much higher yields with our reaction conditions when compared with earlier reported approaches (entries 26 and 29). In addition this is the first report of the synthesis of 2-bromobenzo[*b*]thiophenes **20**, **29**, **32**, **35** and **38** (entries 5, 14, 17, 20, and 23) by electrophilic bromocyclization.

Larock and coworkers reported that yields for the iodocyclization reaction involving I_2 as the electrophile were higher than for our copper-mediated iodocyclization reaction (entries 3, 9, 12, 15, 27 and 30). However, our methodology employs the green solvent ethanol instead of the toxic and carcinogenic solvent DCM. In addition, our methodology also replaces corrosive iodine with relatively benign inorganic salts such as NaI and $CuSO_4$. The yields for the synthesis of 3-iodobenzo[*b*]thiophenes **21**, **33** and **39** (entries 6, 18, and 24) were similar to our previously reported $FeCl_3$/NaI iodocyclization methodology.[19]

After establishing the synthesis of 3-halobenzo[*b*]thiophenes we wanted to extend the scope of our cyclization methodology for the systematic synthesis of *n*-bromo-3-dihalobenzo[*b*]thiophenes (*n* = 2, 4, 5, 6, 7). To achieve this goal we began with developing a strategy for the synthesis of *o*-(2-bromoethynyl)thioanisole **48**, a substrate for the synthesis of 2-bromo-3-halobenzo[*b*]thiophenes. Commercially-available 2-methylthiobenzaldehyde **46**, when subjected to Corey-Fuchs reaction conditions using carbon tetrabromide and triphenylphosphine, produced dibromo alkene **47,** which upon elimination reaction conditions using DBU as a base afforded the desired alkyne **48** in 78% overall yield for the two steps (Scheme 3).

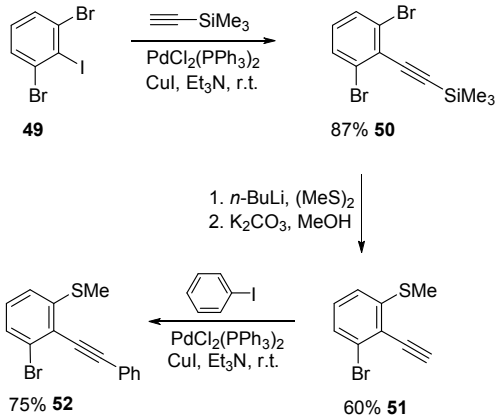


46 89% **47** 88% **48**

Scheme 3

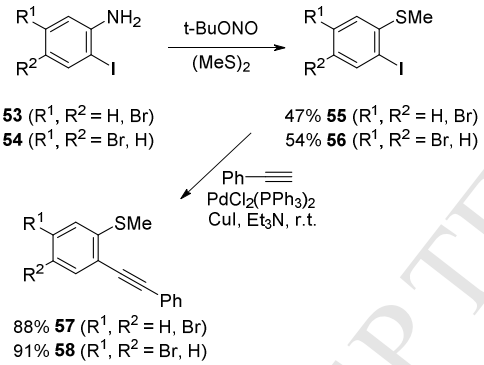
The substrate for the synthesis of 4-bromo-3-halobenzo[*b*]thiophene derivatives was obtained via the selective coupling of commercially-available 2,6-dibromo-iodobenzene **49** with trimethylsilyl acetylene using standard Sonogashira reaction conditions to form the alkynyl-substituted 2,6-dibromobenzene **50** in 87% isolated yield. Subsequent reaction of alkynyl benzene **50** with *n*-butyllithium and dimethyl disulfide, followed by deprotection with potassium carbonate in methanol, furnished the terminal alkynyl thioanisole **51** in 60% isolated yield. In the final step, the terminal alkyne **51** underwent Sonogashira coupling with iodobenzene to afford the final substrate alkyne **52** with the

desired bromine substitution in an isolated yield of 75% (Scheme 4).



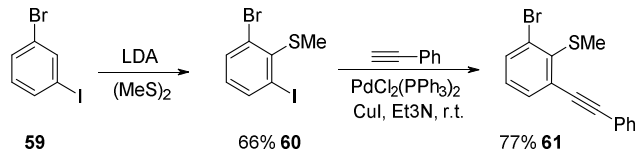
Scheme 4

To obtain 5-bromobenzo[*b*]thiophene and 6-bromobenzo[*b*]thiophene, the analogous bromine-substituted alkynes **57** and **58** were prepared via the reaction of commercially-available 2-iodoanilines **53** and **54** with dimethyl disulfide in the presence of *tert*-butyl nitrite to form the thioanisole intermediates **55** and **56** with yields of 47% and 54% respectively.[20] Following this reaction, an iodine-selective Sonogashira coupling was used to furnish the desired bromine-substituted alkynyl substrates **57** and **58** resulting in isolated yields of 88% and 91% respectively (Scheme 5).



Scheme 5

The starting material used for the synthesis of 7-bromo-3-halobenzo[*b*]thiophenes was obtained via selective lithiation of commercially available *m*-bromoiodobenzene (**59)** using lithium diisopropylamide (LDA) followed by the addition of methyl disulfide in anhydrous THF as the solvent.[21] The resulting di-halogenated thioanisole derivative **60** was obtained in 66% isolated yield. The previous reaction was followed by an iodine-selective Sonogashira coupling with phenylacetylene for the production of 6-bromo-2-alkynylthioanisole **61** with an isolated yield of 77% (Scheme 6).



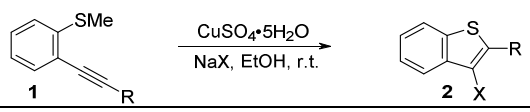
Scheme 6

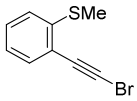
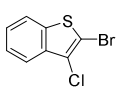
Once the various brominated 2-alkynylthioanisoles were generated via the syntheses outlined above (Schemes 3–7), a variety of dihalogenated benzo[*b*]thiophenes were synthesized using our reaction, with bromines placed at the 2, 3, 4, 5, 6, and 7 positions around the benzo[*b*]thiophene ring (Table 2). We began our substrate study by synthesizing 2-bromo-3-halobenzo[*b*]thiophene derivatives (entries 1-3). The three dihalogenated benzo[*b*]thiophenes **62**, **63** and **64** were obtained from cyclization of o-(2-bromoethynyl)thioanisole **48** with NaCl, NaBr and NaI in the presence of $CuSO_4 \cdot 5H_2O$. 2-bromo-3-iodobenzo[*b*]thiophene **64** resulted in 83% yield, whereas 2,3-dibromobenzo[*b*]thiophene **63** resulted in 80% yield. Our attempts to obtain 2-bromo-3-chlorobenzo[*b*]thiophene **62** in synthetically useful yield failed as the product was only obtained in 17% yield. To our surprise this reaction resulted in multiple products with one product being the 2,3-dichlorobenzo[*b*]thiophene analogue. We believe that the formation of 2,3-dichlorobenzo[*b*]thiophene could be attributed to a halogen exchange reaction of starting bromoalkyne **48** with $CuCl_2$ generated *in situ* via reaction of copper sulfate and sodium halide. However, we did not find any precedent for any such exchange reaction in the literature.

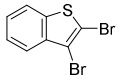
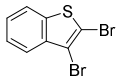
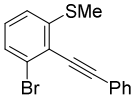
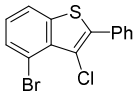
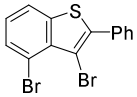
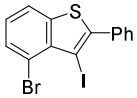
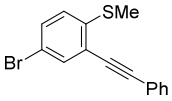
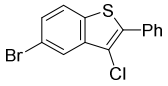
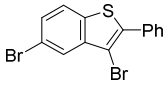
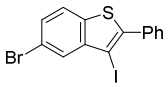
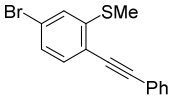
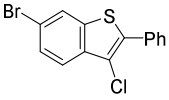
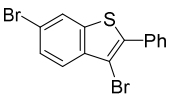
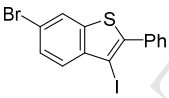
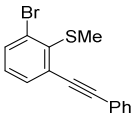
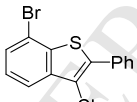
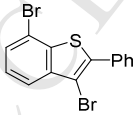
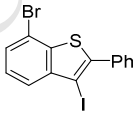
4-bromo-3-halobenzo[*b*]thiophene derivatives (entries 4-6) were made in 78% yield for the chloro-substituted analogue **65**, 66% yield for the bromo-substituted analogue **66**, and 64% yield for the iodo-substituted analogue **67**. The reaction yields were slightly lower, as expected due to steric hindrance from the nearby bromine group interfering with the approach of the electrophile to the alkyne in the cyclization step. This theory was verified by the expected trend of atomic size of the approaching electrophile. The chlorocyclization product was obtained in higher yield as compared to the bromocyclization product, which in turn was obtained in higher yield than the iodocyclization product.

4- and 5-bromo-3-halobenzo[*b*]thiophenes (entries 7-12) were synthesized in high yields. Starting alkynes **57** and **58**, when cyclized using NaCl and $CuSO_4$, resulted in identical yields of 89% for both the cyclized products **68** and **71**. In molecules **57** and **58,** the bromine atoms at both the 4- and 5- positions are too remote to exert a steric effect on the cyclization. The reaction yields were higher and comparable (compare entries 8 and 11; and entries 9 and 12). Therefore it also seems that the electron withdrawing bromine does not have an effect on the cyclization reaction. Therefore, 7-bromo-3-halobenzo[*b*]thiophene derivatives (entries 13-15) were realized in good to excellent yields. Chlorocyclization of alkyne **61** to 7-bromo-3-chlorobenzo[*b*]thiophene **74** resulted in a moderate 73% yield. To our surprise bromo- and iodocyclization of **61** resulted in much higher yields of 92% for 3,7-dibromobenzo[*b*]thiophene **75** and 91% for 7-bromo-3-iodobenzo[*b*]thiophene **76**.

Table 1. Synthesis of 3-halobenzo[*b*]thiophenes using sodium halides as the source of electrophilic halogens[a]



Entry	Substrate		Product		Yield[b]
1		**48**		**62**	17[c]

2		**48**		**63**	80
3		**48**		**64**	83
4		**52**		**65**	78
5		**52**		**66**	66
6		**52**		**67**	64
7		**57**		**68**	89
8		**57**		**69**	91
9		**57**		**70**	94
10		**58**		**71**	89
11		**58**		**72**	86
12		**58**		**73**	96
13		**61**		**74**	73
14		**61**		**75**	92
15		**61**		**76**	91

[a]Reaction conditions A: all reactions were performed using 0.30 mmol of thioether, 5.0 equiv of CuSO4•5H_2O, and 5.0 equiv NaX (X = Cl, Br, I) in 5 mL of EtOH at room temperature for 24 h. Reaction conditions

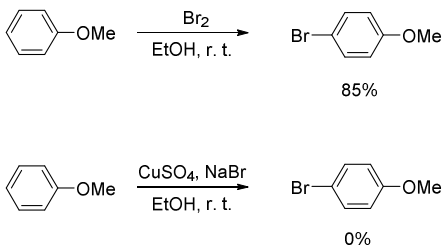
[b]Isolated yield.

[c]NMR yield.

Copper sulfate is the most common, non-toxic and inexpensive copper(II) reagent. $CuSO_4$, when mixed with NaI, is known to form CuI_2 which decomposes readily into CuI and I_2. When iodocyclization reactions were analyzed via TLC, we observed the formation of a purple spot indicative of the formation of molecular iodine in the reaction mixture. Therefore we believe that the iodocyclization proceeds through the well-established mechanism involving I_2 as the electrophile.[22]

$CuSO_4 \cdot 5H_2O$, when mixed with NaCl in ethanol, results in the formation of $CuCl_2$ which is known to rapidly equilibrate between species such as $[CuCl]^+$, $[CuCl_3]^-$, and $[CuCl_4]^{2-}$.[23] We believe that one or more of these electrophilic species are responsible for the reported efficient and high-yielding chlorocyclization reactions. Copper(II) sulfate pentahydrate in ethanol remains as an insoluble blue solid, but upon addition of NaCl to the mixture, the solution changes to a yellow-green color indicative of dissolution and complex ion formation. A similar color change was observed in the reported chlorocyclization reactions. In an analogous reaction $CuSO_4$ and NaBr also results in the formation of $CuBr_2$. In theory, $CuCl_2$ and $CuBr_2$ could decompose to form Cl_2 and Br_2. However, it is well established that the $CuCl_2$ decomposes to CuCl and Cl_2 only at 1000 °C. Therefore cyclization reactions involving Cl_2 as the electrophile are less likely and we believe that the above ionic species are likely to act as the electrophile in these cyclization reactions.

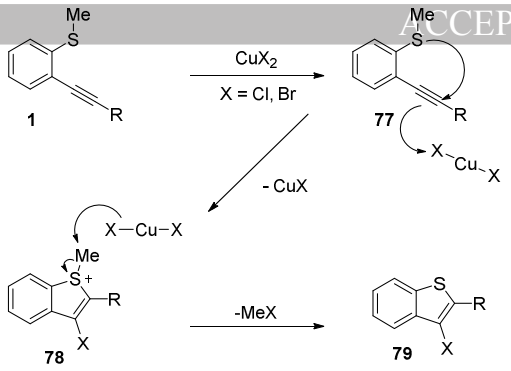
Decomposition of $CuBr_2$ into CuBr and Br_2 occurs at a lower temperature. Therefore, cyclization involving Br_2 is very likely. However, if Br_2 is involved, it would also be more likely to result in the formation of side products involving electrophilic aromatic substitution reactions especially with the electron-rich substrates such as alkyne **14** (Table 1, entry 26). To our surprise, we did not observe any aromatic halogenation as the side products in any of the bromocyclization reactions. In addition, alkyne **10**, which contains a vinyl functionality, did not show any Br_2 addition to the vinyl group, suggesting the absence of Br_2 in the reaction mixture.



Scheme 7

In order to confirm our theory, we subjected the electron-rich anisole to electrophilic bromination in ethanol using Br_2 and $CuSO_4$/NaBr as the electrophiles (Scheme 7). Addition of Br_2 resulted in the formation of 4-bromoanisole in 85% yield, whereas our reaction conditions involving $CuSO_4$/NaBr failed to generate any 4-bromoanisole even after 48 hrs. Therefore we believe that $CuBr_2$ is the electrophilic reagent initiating the cyclization reaction and not Br_2.

The proposed mechanism of the chlorocyclization and bromocyclization reactions are outlined in Scheme 8. Cu(II) can coordinate with the alkyne **1** followed by an anti-attack from a nearby S nucleophile to give the cationic intermediate **77**. The methyl group can be removed subsequently by S_N2 displacement with the help of CuX_2 (X = Cl or Br), eventually forming the desired cyclized product **79**.



Scheme 8

3. Conclusion

A convenient method is introduced for the synthesis of mono-halogenated and di-halogenated benzo[*b*]thiophene derivatives via electrophilic cyclization of 2-alkynylthioanisoles. This method allows selective placement of bromine atoms upon every available position on the benzo[*b*]thiophene ring, i.e., the 2, 3, 4, 5, 6, and 7 positions. The 3 position may be interchanged with iodine or chlorine moieties depending on which sodium halide is used during synthesis. We believe this method stands out among the previously established methods as a new and innovative alternative towards the synthesis of highly functionalized benzo[*b*]thiophene derivatives.

4. Experimental section

Solvents and other starting chemicals were obtained from commercial suppliers and used without any further purification. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker spectrometer at 400 and 100 MHz, respectively. High-resolution mass spectra (HRMS) were recorded on a VG-70S magnetic sector mass spectrometer using direct probe sample introduction and electron ionization (EI). Reaction progress was monitored using thin layer chromatography on glass plates coated with silica gel 60 F_{254}. Short wave UV light was used to visualize the aromatic molecules. Flash column chromatography was performed using silica gel (60−120 mesh) with ACS grade solvents. The alkynes **6-15** and thioanisole **60** were prepared according to literature procedures.[19,21]

General procedure for the synthesis of compounds 16-24, 27-45 and 62-76.

To a vial containing 2-alkynylthioanisole (0.3 mmol) in 5 mL of EtOH was added desired sodium halide (1.5 mmol) and $CuSO_4$•$5H_2O$ (1.5 mmol). The reaction mixture was allowed to stir overnight. The reaction mixture was filtered and absorbed in silica gel before purification via column chromatography using hexanes and ethyl acetate as eluent.

3-Chloro-2-phenylbenzo[*b*]thiophene (16). Product was isolated as a white solid, mp 64-67 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.39-7.51 (m, 5H), 7.79-7.87 (m, 3H), 7.88 (d, *J* = 7.2 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[12n]

3-Bromo-2-phenylbenzo[*b*]thiophene (17). Product was isolated as a white solid, mp 62-64 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.39-7.51 (m, 5H), 7.76-7.78 (m, 2H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[12m]

3-Iodo-2-phenylbenzo[*b*]thiophene (18). Product was isolated as a yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.37 (td, *J* = 7.5, 1.5 Hz, 1H), 7.42-7.50 (m, 4H), 7.66-7.69 (m, 2H), 7.75-7.78 (m, 1H), 7.81-7.84 (m, 1H). Other characterization data are in good agreement with the previous reported data.[12m]

2-*n*-Butyl-3-Chlorobenzo[*b*]thiophene (19). Product was isolated as a colorless oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 0.97 (t, *J* = 7.6 Hz, 3H), 1.40-1.49 (m, 2H), 1.68-1.76 (m, 2H), 2.95 (t, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.2 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 13.9, 22.4, 28.2, 32.6, 117.4, 121.5, 122.5, 124.7, 124.8, 136.5, 137.2, 139.2; IR (neat) 3063.3, 2957.2, 2928.5, 2871.4, 2858.8, 1564.7, 1537.9, 1457.6, 1435.9, 1378.7, 1310.9, 1253.8, 1068.8, 1018.4, 941.3. HRMS (EI+, m/z) calcd for $(C_{12}H_{13}ClS)^+$ 224.0427, found 224.0431.

2-*n*-Butyl-3-Bromobenzo[*b*]thiophene (20). Product was isolated as a pale yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 0.97 (t, *J* = 7.6 Hz, 3H), 1.41-1.50 (m, 2H), 1.69-1.77 (m, 2H), 2.96 (t, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 2H). Other characterization data are in good agreement with the previous reported data.[24]

2-*n*-Butyl-3-Iodobenzo[*b*]thiophene (21). Product was isolated as a yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 0.98 (t, *J* = 7.2 Hz, 3H) 1.40-1.53 (m, 2H) 1.69-1.78 (m, 2H) 2.97 (t, *J* = 7.6 Hz, 2H) 7.31 (t, *J* = 7.6 Hz, 1H) 7.41 (t, *J* = 8.0 Hz, 1H) 7.70 (d, *J* = 8.4 Hz, 1H) 7.72 (d, *J* = 8.0 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[19]

2-*tert*-butyl -3-Chlorobenzo[*b*]thiophene (22). Product was isolated as a yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 1.56 (s, 9H), 7.33 (td, *J* = 8.0, 1.2 Hz, 1H), 7.41 (td, *J* = 7.2, 1.2 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[12n]

3-Bromo-2-*tert*-butylbenzo[*b*]thiophene (23). Product was isolated as a yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 1.59 (s, 9H), 7.33 (t, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[12m]

2-*tert*-butyl-3-Iodobenzo[*b*]thiophene (24). Product was isolated as a yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 1.63 (s, 9H), 7.32 (t, *J* = 8.0 Hz, 1H), 7.41 (t, *J* = 7.2 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[19]

3-Iodo-2-(trimethylsilyl)benzo[*b*]thiophene (27). Product was isolated as a pale yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 0.51 (s, 9H), 7.37 (td, *J* = 8.0, 1.2 Hz, 1H), 7.44 (td, *J* = 7.2, 1.2 Hz, 1H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[12m]

3-Chloro 2-(cyclohex-1-enyl)benzo[*b*]thiophene (28). Product was isolated as an off-white solid: mp 39-41 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 1.69-1.72 (m, 2H), 1.79-1.81 (m, 2H), 2.27 (m, 2H), 2.54 (m, 2H), 6.37 (s, 1H), 7.34 (t, *J* = 8.0 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 21.9, 23.0, 26.0, 29.3, 115.2, 121.9, 122.3, 124.9, 125.1, 130.3, 131.8, 136.0, 138.0, 139.4; IR (neat) 2933.5, 1639.4, 1559.2, 1435.0, 1320.8, 1252.2, 1137.9, 1073.0, 1018.4, 948.7, 888.7, 832.8, 787.2, 752.5, 727.6, 700.6. HRMS (EI+, m/z) calcd for $(C_{14}H_{13}ClS)^+$ 248.0427, found 248.0426.

3-Bromo-2-(cyclohex-1-enyl)benzo[*b*]thiophene (29). Product was isolated as a colorless oil; ^{1}H NMR (400 MHz, chloroform-

d) δ 1.70-1.72 (m, 2H), 1.79-1.83 (m, 2H), 2.26 (m, 2H), 2.52 (m, 2H), 6.32 (s, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[12m]

2-(Cyclohex-1-enyl)-3-idobenzo[*b*]thiophene (30). Product was isolated as a yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 1.68 – 1.76 (m, 2H), 1.77 – 1.85 (m, 2H), 2.22 – 2.30 (m, 2H), 2.42-2.50 (m, 2H), 6.16-6.21 (m, 1H), 7.32 (td, *J* = 8.2, 1.2 Hz, 1H), 7.41 (td, *J* = 8.0, 1.2 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[19]

(3-Chloro-1-benzothiophen-2-yl)methanol (31). Product was isolated as a white solid: mp 91-92 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.02 (s, 1H), 4.98 (d, *J* = 4.0 Hz, 2H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 58.6, 118.0, 122.0, 122.9, 125.1, 125.7, 136.9, 137.3, 137.4; IR (neat) 2928.3, 2851.0, 1627.5, 1561.4, 1456.9, 1219.7, 1014.0, 984.5, 771.9, 757.4, 728.9. HRMS (EI+, m/z) calcd for $(C_9H_7ClOS)^+$ 197.9906, found 197.9906.

(3-bromo-1-benzothiophen-2-yl)methanol (32). Product was isolated as a white solid: mp 92-94 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.00 (bs, 1H), 4.99 (d, *J* = 6.0 Hz, 2H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.80 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 60.1, 105.8, 122.8, 123.1, 125.3, 125.6, 137.9, 138.3, 139.3; IR (neat) 2927.5, 2855.0, 1627.6, 1560.0, 1455.3, 1336.1, 1219.9, 1127.0, 1010.1, 772.2, 757.0, 681.7. HRMS (EI+, m/z) calcd for $(C_9H_7BrOS)^+$ 241.9401, found 241.9407.

(3-iodo-1-benzothiophen-2-yl)methanol (33). The product was obtained as a white solid, mp 97-99 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.05 (s, 1H), 4.97 (d, *J* = 5.8 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 6.8 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 1H), 7.78 (d, *J* = 8.2 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[19]

1-(3-chlorobenzothiophen-2-yl)cyclohexanol (34). Product was isolated as a white solid: mp 50-53 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 1.32-1.42 (m, 1H), 1.71-1.79 (m, 5H), 1.90-2.00 (m, 2H), 2.28-2.36 (m, 2H), 2.43 (s, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.76-7.79 (m, 2H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 21.8, 25.3, 36.4, 73.8, 113.7, 121.5, 122.5, 124.9, 125.0, 135.6, 138.6, 147.4; IR (neat) 3379.7, 2935.8, 2854.0, 1628.1, 1560.2, 1448.2, 1381.0, 1306.7, 1250.4, 1219.7, 1154.9, 1062.7, 1034.8, 1019.0, 966.0, 933.0, 906.6, 870.8, 828.7, 772.2, 755.3, 730.2. HRMS (EI+, m/z) calcd for $(C_{14}H_{15}ClOS)^+$ 266.0532, found 266.0538.

1-(3-bromobenzothiophen-2-yl)cyclohexanol (35). Product was isolated as a white solid: mp 79-81 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 1.32-1.42 (m, 1H), 1.73-1.79 (m, 5H), 1.90-2.00 (m, 2H), 2.34-2.42 (m, 2H), 2.48 (s, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.78 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 21.8, 25.2, 36.5, 74.1, 101.1, 122.3, 122.8, 125.0, 125.1, 136.3, 139.9, 149.0; IR (neat) 2932.9, 1627.3, 1557.8, 1452.7, 1380.9, 1335.5, 1219.8, 1063.9, 965.1, 818.7, 772.3, 729.1, 675.0. HRMS (EI+, m/z) calcd for $(C_{14}H_{15}BrOS)^+$ 310.0027, found 310.0019.

1-(3-iodobenzothiophen-2-yl)cyclohexanol (36). Product was isolated as an off-white solid: mp 117-119 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 1.35-1.45 (m, 1H), 1.75-1.85 (m, 5H), 1.90-2.00 (m, 2H), 2.39-2.46 (m, 3H), 7.34 (t, *J* = 8.0 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 21.9, 25.2, 36.8, 73.5, 74.3, 122.2, 125.2, 125.3, 125.5, 137.0, 142.8, 152.0; IR (neat) 3397.4, 2933.2, 2858.9, 1639.0, 1556.3, 1450.4, 1433.3, 1384.4, 1242.8, 1219.7, 1150.1, 1063.0, 1019.9, 964.7, 904.9, 811.6, 770.3, 751.3, 727.8, 616.8. HRMS (EI+, m/z) calcd for $(C_{14}H_{15}IOS)^+$ 357.9888, found 357.9897.

(3-chloro-1-benzothiophen-2-yl)methyl methyl ether (37). Product was isolated as a yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 3.45 (s, 3H), 4.78 (s, 2H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 58.5, 67.4, 119.0, 122.0, 122.8, 125.0, 125.6, 135.0, 136.7, 137.6; IR (neat) 3060.68, 2989.0, 2927.3, 2822.2, 1727.3, 1672.0, 1510.4, 1435.2, 1368.4, 1312.1, 1254.4, 1234.9, 1094.9, 1020.9, 941.6, 753.7, 727.7. HRMS (EI+, m/z) calcd for $(C_{10}H_9ClOS)^+$ 212.0063, found 212.0061.

(3-bromo-1-benzothiophen-2-yl)methyl methyl ether (38). Product was isolated as a yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 3.46 (s, 3H), 4.78 (s, 2H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 58.6, 69.0, 106.8, 122.7, 123.2, 125.2, 125.6, 125.8, 137.1, 138.2; IR (neat) 3059.1, 2988.3, 2926.8, 2821.4, 1728.3, 1671.2, 1504.6, 1456.1, 1434.5, 1366.1, 1304.8, 1251.1, 1193.7, 1096.1, 1020.3, 920.2, 753.0, 726.7. HRMS (EI+, m/z) calcd for $(C_{10}H_9BrOS)^+$ 255.9557, found 255.9564.

(3-iodo-1-benzothiophen-2-yl)methyl methyl ether (39). Product was obtained as a yellow liquid; ^{1}H NMR (400 MHz, chloroform-*d*) δ 3.47(s, 3H), 4.77 (s, 2H), 7.37 (td, *J* = 7.2, 1.2 Hz, 1H), 7.43 (td, *J* = 7.2, 1.2 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[19]

4-(3-chloro-1-benzothiophen-2-yl)phenyl methyl ether (40). Product was isolated as an off-white solid: mp 100-101 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 3.87 (s, 3H), 7.01 (d, *J* = 8.4 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 8.8 Hz, 2H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[12n]

4-(3-bromo-1-benzothiophen-2-yl)phenyl methyl ether (41). Product was isolated as an off-white solid: mp 86-88 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 3.87 (s, 3H), 7.01 (d, *J* = 8.4 Hz, 2H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.71 (d, *J* = 8.8 Hz, 2H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[12n,25]

4-(3-iodo-1-benzothiophen-2-yl)phenyl methyl ether (42). Product was obtained as a white solid, mp 84-86 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 3.80 (s, 3H), 6.95 (d, *J* = 8.6 Hz, 2H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.41 (t, *J* = 7.8 Hz, 1H), 7.59 (d, *J* = 8.7 Hz, 2H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[26]

4-(3-Chlorobenzo[*b*]thiophene-2-yl)butanenitrile (43). Product was isolated as a colorless oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.08-2.15 (m, 2H), 2.43 (t, *J* = 7.2 Hz, 2H), 3.12 (t, *J* = 7.2 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 16.6, 26.2, 27.1, 118.9, 119.1, 121.8, 122.6, 125.2, 125.4, 135.4, 136.6, 137.0; IR (neat) 3061.5, 2931.5, 2248.1, 1565.0, 1538.0, 1432.1, 1313.6, 1254.2, 1160.5, 1068.1, 1017.7, 941.1, 752.8, 727.0, 667.5. HRMS (EI+, m/z) calcd for $(C_{12}H_{10}ClNS)^+$ 235.0222, found 235.0220.

4-(3-Bromobenzo[*b*]thiophene-2-yl)butanenitrile (44). Product was isolated as a colorless oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.09-2.16 (m, 2H), 2.44 (t, *J* = 7.2 Hz, 2H), 3.13 (t, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 7.2 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 2H). Other characterization data are in good agreement with the previous reported data.[12m]

4-(3-Iodobenzo[*b*]thiophene-2-yl)butanenitrile (45). Product was isolated as a yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.07-2.17 (m, 2H), 2.44 (t, *J* = 7.2 Hz, 2H), 3.13 (t, *J* = 7.2 Hz, 2H), 7.35 (td, *J* = 8.2, 1.2 Hz, 1H), 7.42 (td, *J* = 8.0, 1.2 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[19]

2,3-dibromobenzothiophene (63). Product was isolated as a colorless oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.38 (t, *J* = 6.4 Hz, 1H), 7.43 (t, *J* = 6.4 Hz, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[12m,27]

2-bromo-3-iodo-benzothiophene (64). Product was isolated as a colorless oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.37 (t, *J* = 8.0 Hz, 1H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.65-7.71 (m, 2H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 87.3, 119.8, 122.1, 126.0, 126.1, 126.4, 140.5, 141.2. IR (neat) 2926.9, 1485.7, 1451.6, 1425.4, 1416.7, 1243.3, 1219.8, 1019.7, 980.9, 882.9, 772.5, 748.5, 720.9, 706.7. HRMS (EI+, m/z) calcd for $(C_8H_4BrIS)^+$ 337.8262, found 337.8269.

4-bromo-3-chloro-2-phenyl-benzothiophene (65). Product was isolated as a white solid: mp 90-92 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.20 (t, *J* = 8.0 Hz, 1H), 7.42-7.51 (m, 3H), 7.66-7.71 (m, 3H), 7.77 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 116.6, 117.3, 122.1, 125.8, 128.8, 129.1, 129.9, 131.6, 132.4, 133.4, 139.0, 139.6; IR (neat) 3055.2, 2926.7, 2854.5, 1543.1, 1483.2, 1446.0, 1397.6, 1310.9, 1187.2, 1093.2, 906.8, 771.4, 749.9, 726.7, 693.9. HRMS (EI+, m/z) calcd for $(C_{14}H_8BrClS)^+$ 321.9219, found 321.9212.

4-bromo-3-bromo-2-phenyl-benzothiophene (66). Product was isolated as a white solid: mp 111-114 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.20 (t, *J* = 7.6 Hz, 1H), 7.45-7.50 (m, 3H), 7.65 (d, *J* = 6.4 Hz, 2H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 104.4, 117.2, 122.0, 122.2, 123.7, 125.2, 125.5, 128.5, 128.6, 128.8, 129.0, 129.7, 130.2, 131.7, 133.4, 133.9, 140.2, 140.9; IR (neat) 3020.6, 2926.2, 2854.5, 1539.8, 1475.8, 1444.9, 1395.1, 1257.8, 1185.1, 1090.1, 890.7, 803.2, 760.7, 747.4, 725.3, 695.4. HRMS (EI+, m/z) calcd for $(C_{14}H_8Br_2S)^+$ 365.8713, found 365.8716.

4-bromo-3-iodo-2-phenyl-benzothiophene (67). Product was isolated as a white solid: mp 131-134 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.19 (t, *J* = 8.0 Hz; 1H), 7.47-7.49 (m, 3H), 7.53-7.55 (m, 2H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.84 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 118.4, 122.3, 125.3, 128.6, 129.3, 130.2, 130.7, 131.8, 135.3, 135.9, 141.3, 145.5; IR (neat) 2925.8, 2854.5, 1537.6, 1471.8, 1434.6, 1394.1, 1181.6, 1091.0, 878.2, 794.4, 761.6, 741.4, 722.2, 693.8. HRMS (EI+, m/z) calcd for $(C_{14}H_8BrIS)^+$ 413.8575, found 413.8587.

5-bromo-3-chloro-2-phenyl-benzothiophene (68). Product was isolated as a white solid: mp 118-119 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.43-7.49 (m, 4H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 2H), 8.02 (s, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 115.9, 119.4, 123.8, 125.1, 128.7, 128.9, 129.2, 129.4, 132.0, 135.5, 138.3, 139.6; IR (neat) 1581.5, 1486.0, 1437.1, 1264.5, 1220.0, 1058.4, 993.6, 796.5, 772.4, 735.8, 752.9, 735.8, 690.7. HRMS (EI+, m/z) calcd for $(C_{14}H_8ClIS)^+$ 321.9219, found 321.9216.

3,5-dibromo-2-phenyl-benzothiophene (69). Product was isolated as a white solid: mp 131-133 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.42-7.51 (m, 4H), 7.68 (d, *J* = 8.8 Hz, 1H), 7.75 (d, *J* = 7.2 Hz, 2H), 8.02 (s, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 104.0, 119.5, 123.6, 126.5, 128.7, 128.8, 129.2, 129.7, 132.7, 136.4, 140.2, 140.9; IR (neat) 1578.6, 1485.8, 1435.9, 1260.5, 1071.6, 1059.8, 977.9, 902.9, 808.0, 795.7, 750.1. HRMS (EI+, m/z) calcd for $(C_{14}H_8Br_2S)^+$ 365.8713, found 365.8712.

5-bromo-3-iodo-2-phenyl-benzothiophene (70). Product was isolated as a white solid: mp 117-119 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.46-7.50 (m, 4H), 7.64-7.68 (m, 3H), 7.99 (s, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 78.2, 119.7, 123.6, 128.7, 128.7, 129.2, 129.3, 130.1, 134.3, 137.8, 143.8, 144.2; IR (neat) 1432.1, 1219.8, 1070.6, 970.1, 896.9, 860.2, 787.5, 772.5, 751.6, 727.5, 694.4. HRMS (EI+, m/z) calcd for $(C_{14}H_8BrIS)^+$ 413.8575, found 413.8562.

6-bromo-3-chloro-2-phenyl-benzothiophene (71). Product was isolated as a white solid: mp 120-122 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.41 -7.52 (m, 3H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.78 (d, *J* = 7.2 Hz, 2H), 7.96 (s, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 116.6, 119.6, 123.6, 124.9, 128.7, 128.9, 129.1, 129.3, 132.0, 136.9, 137.0, 138.2; IR (neat) 2927.0, 1585.5, 1556.4, 1486.3, 1449.9, 1385.7, 1317.1, 1220.0, 1089.5, 1052.2, 898.4, 851.8, 799.9, 772.2, 762.2, 688.5. HRMS (EI+, m/z) calcd for $(C_{14}H_8BrClS)^+$ 321.9219, found 321.9219.

3,6-dibromo-2-phenyl-benzothiophene (72). Product was isolated as a white solid: mp 125-127 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.41-7.52 (m, 3H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.70-7.76 (m, 3H), 7.96 (s, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 104.8, 119.6, 124.8, 125.0, 128.8, 128.9, 129.2, 129.7, 132.8, 138.2, 139.0, 139.1; IR (neat) 2926.6, 1584.3, 1550.9, 1484.7, 1446.4, 1384.9, 1296.4, 1219.8, 1088.3, 1052.0, 888.1, 798.3, 772.3, 759.2, 740.9, 688.1. HRMS (EI+, m/z) calcd for $(C_{14}H_8Br_2S)^+$ 365.8713, found 365.8717.

6-bromo-3-iodo-2-phenyl-benzothiophene (73). Product was isolated as a yellow solid: mp 115-116 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.46-7.52 (m, 3H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 3H), 7.94 (s, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 78.9, 119.6, 124.6, 127.5, 128.7, 129.0, 129.3, 130.1, 134.3, 140.2, 141.0, 142.9; IR (neat) 2926.3, 1443.4, 1384.2, 1219.7, 1088.1, 872.5, 852.9, 797.7, 772.3, 735.6, 693.7. HRMS (EI+, m/z) calcd for $(C_{14}H_8BrIS)^+$ 413.8575, found 413.8583.

7-bromo-3-chloro-2-phenyl-benzothiophene (74). Product was isolated as a white solid: mp 87-89 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.36 (t, *J* = 7.6 Hz, 1H), 7.45-7.50 (m, 3H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.82 (t, *J* = 8.8 Hz, 3H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 115.7, 117.2, 121.3, 126.4, 128.2, 128.8, 129.0, 129.3, 131.9, 137.8, 138.4, 138.9; IR (neat) 3685.2, 3620.9, 3020.0, 2977.5, 2400.6, 1522.1, 1477.3, 1423.7, 1215.4, 1046.7, 929.0, 771.1, 669.4. HRMS (EI+, m/z) calcd for $(C_{14}H_8BrClS)^+$ 321.9219, found 321.9217.

3,7-dibromo-2-phenyl-benzothiophene (75). Product was isolated as a white solid: mp 77-78 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.36 (t, *J* = 8.0 Hz, 1H), 7.43-7.52 (m, 3H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 6.8 Hz, 2H), 7.83 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 105.4, 115.5, 122.7, 126.5, 128.1, 128.7, 129.1, 129.6, 132.6, 139.3, 139.7, 140.1; IR (neat) 3686.2, 3617.6, 3020.0, 2400.6, 1524.1, 1478.5, 1423.9,

1393.4, 1215.6, 1047.3, 929.0, 770.8, 669.4, 627.1. HRMS (EI+, m/z) calcd for $(C_{14}H_8Br_2S)^+$ 365.8713, found 365.8707.

7-bromo-3-iodo-2-phenyl-benzothiophene (76). Product was isolated as a white solid: mp 98-99 °C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.36 (t, *J* = 8.0 Hz, 1H), 7.45-7.51 (m, 3H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 7.2, 2H), 7.79 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 79.6, 115.2, 125.3, 126.5, 128.0, 128.6, 129.2, 130.0, 134. 2, 140.6, 142.7, 143.4; IR (neat) 3020.2, 2400.7, 1216.8, 929.1, 770.8, 669.3. HRMS (EI+, m/z) calcd for $(C_{14}H_8BrIS)^+$ 413.8575, found 413.8578.

Synthesis of 1-(2,2-dibromovinyl)-2-methylsulfanyl-benzene (47).

A vial containing CBr_4 (3.0 mmol) and aldehyde (3.0 mmol) in 8 mL of DCM was cooled to 0 °C. A mixutre of PPh_3 (6.0 mmol) in 4 mL DCM was added dropwise to the reaction mixture with stirring. The mixture was allowed to warm to room temperature. The mixture was concentrated under vacuum, adsorbed onto silica gel, and purified via column chromatography using hexanes as an eluent. Product was isolated as an off-white solid: mp 49-50 °C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.48 (s, 3H) 7.21 (t, *J* = 7.6 Hz, 1H) 7.28-7.37 (m, 2H) 7.52 (d, *J* = 7.6 Hz, 1H) 7.58 (s, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 16.2, 92.6, 125.1, 126.3, 129.1, 129.3, 134.9, 135.5, 137.7; IR (neat) 1585.9, 1458.7, 1435.0, 1220.0, 1069.8, 1046.0, 953.4, 937.7, 874.5, 836.7, 790.6, 772.4, 737.1. HRMS (EI+, m/z) calcd for $(C_9H_8Br_2S)^+$ 305.8713, found 305.8707.[28]

Synthesis of 1-(2-bromoethynyl)-2-methylsulfanyl-benzene (48).

A vial containing 1-(2,2-dibromovinyl)-2-methylsulfanyl-benzene (0.27 mmol) in 1 mL of DMSO was cooled to 15 °C. A mixture of DBU (0.27 mmol) in 1 mL of DMSO was added dropwise to the reaction mixture. The mixture was extracted with water, concentrated under vacuum, and purifed via column chromatography using hexanes as an eluent. Product was isolated as a yellow liquid; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.48 (s, 3H), 7.07 (t, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 15.5, 56.4, 78.1, 121.3, 124.6, 129.5, 133.3, 142.5; IR (neat) 2919.5, 2193.5, 1995.7, 1582.3, 1460.1, 1434.7, 1070.4, 1038.4, 749.5. HRMS (EI+, m/z) calcd for $(C_9H_7BrS)^+$ 225.9452, found 225.9450.

Synthesis of 2-(2,6-dibromophenyl)ethynyl trimethylsilane (50).

Under anhydrous conditions, a 50 mL RBF containing 1,3-dibromo-2-iodobenzene (2.0 mmol), $Pd(PPh_3)_4$ (0.10 mmol), and CuI (0.10 mmol) in 10 mL of triethylamine was equipped with a reflux condenser. TMS-acetylene (2.0 mmol) was added dropwise to the mixture. The reaction mixture was heated to 70 °C and was allowed to stir overnight. The mixture was concentrated under vacuum, adsorbed onto silica gel, and purifed via column chromatography using hexanes as an eluent. Product was isolated as a yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 0.301 (s, 9H), 6.99 (t, *J* = 8.4 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 2H). Other characterization data are in good agreement with the previous reported data.[29]

Synthesis of 1-bromo-2-ethynyl-3-methylsulfanyl-benzene (51).

Under anhydrous conditions, a mixutre of 2-(2,6-dibromophenyl)ethynyl trimethylsilane (2.12 mmol) and 10 mL of THF was cooled to -78 °C. *n*-butyllithium (2.33 mmol) was added dropwise to the mixture. The reaction mixture was allowed to stir at -78 °C for one hour. Dimethyl disulfide (4.24 mmol) was added dropwise to the mixture. The mixture was allowed to warm to room temperature over night with stirring. The mixture was concentrated under vacuum and the resulting concentrate was dissolved in 4 mL MeOH. K_2CO_3 (3.50 mmol) was added to the mixture. The mixture was allowed to stir at room temperature overnight. The reaction mixture was concentrated under vacuum, adsorbed onto silica gel, and purified via column chromatography using hexanes as the eluent. Product was isolated as a colorless oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.49 (s, 3H), 3.79 (s, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.154 (t, *J* = 7.2 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 15.6, 79.6, 83.6, 88.8, 122.7, 126.8, 128.3, 129.8, 145.1; IR (neat) 3273.5, 2920.5, 2851.0, 1568.3, 1544.9, 1429.6, 1195.5, 1080.4, 969.9, 957.0, 762.3, 722.1, 705.0. HRMS (EI+, m/z) calcd for $(C_9H_7BrS)^+$ 225.9452, found 225.9443.

Synthesis of 1-bromo-3-methylsulfanyl-2-(2-phenylethynyl)benzene (52).

To a vial containing a 1-bromo-3-methylsulfanyl-2-(2-phenylethynyl)benzene (0.634 mmol) and iodobenzene (1.90 mmol) in 5 mL of Et_3N, $PdCl_2(PPh_3)_2$ (0.032 mmol) and CuI (0.032 mmol) were added. The mixture was allowed to stir at room temperature overnight. The reaction mixture was concentrated under vacuum, adsorbed to silica gel, and purified via column chromatography using hexanes as the eluent. Product was isolated as a yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.50 (s, 3H), 7.09-7.15 (m, 2H), 7.37-7.40 (m, 4H), 7.62-7.65 (m, 2H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 15.6, 86.0, 100.9, 122.6, 122.8, 123.0, 126.4, 128.2, 128.5, 128.9, 129.2, 131.9, 144.5; IR (neat) 3019.9, 2400.5, 1598.8, 1571.6, 1543.8, 1491.0, 1440.1, 1396.9, 1216.0, 1098.1, 929.0, 871.8, 849.8, 756.8, 690.3, 669.09. HRMS (EI+, m/z) calcd for $(C_{15}H_{11}BrS)^+$ 301.9765, found 301.9767.

General procedure for the synthesis of thioanisoles 55 and 56.[21]

A 50 mL RBF containing 4(5)-bromo-2-iodoaniline (1.0 mmol) and dimethyl disulfide (1.0 mmol) in 3 mL CH_3CN was heated to reflux with stirring. *Tert*-butyl nitrite (1.0 mmol) was added dropwise to the reaction mixture. The mixture was allowed to reflux for one hour and was monitored to completion via TLC. The reaction mixture was concentrated under vacuum, adsorbed onto silica gel, and purified via column chromatography using hexanes as the eluent.

4-bromo-2-iodo-1-methylsulfanyl-benzene (55). Product was isolated as an orange liquid; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.44 (s, 3H), 6.94 (d, *J* = 8.4 Hz, 1H), 7.45 (d, *J* = 8.8 Hz, 1H), 7.91 (s, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 17.3, 97.6, 118.1, 125.9, 131.7, 141.1, 142.6; IR (neat) 2982.6, 2916.8, 2849.4, 1639.8, 1554.5, 1537.7, 1430.0, 1356.6, 1246.9, 1109.4, 1085.5, 1011.7, 869.6, 799.6, 751.2. HRMS (EI+, m/z) calcd for $(C_7H_6BrIS)^+$ 327.8418, found 327.8419.

4-bromo-1-iodo-2-methylsulfanyl-benzene (56). Product was isolated as an orange solid: mp 53-55 °C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.46 (s, 3H), 6.96 (d, *J* = 8.0 Hz, 1H), 7.15 (s, 1H), 7.59 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 17.1, 94.9, 123.3, 127.3, 129.0, 140.4, 145.8; IR (neat) 1553.8, 1435.2, 1356.5, 1246.6, 1219.9, 1089.9, 1072.9, 1002.2, 845.9, 800.4, 768.1. HRMS (EI+, m/z) calcd for $(C_7H_6BrIS)^+$ 327.8418, found 327.8422.

Synthesis of 1-bromo-3-iodo-2-methylsulfanyl-benzene (60).

A solution of 1-bromo-3-iodobenzene (2.56 mL, 10.0 mmol) in anhydrous THF (20 mL) was cooled to -78 °C using acetone-dry ice bath. To this solution LDA (20 mL, 1.5 M in THF, 30.0 mmol) was added dropwise. After stirring for 1h, methyldisulfide (2.88 mL, 32.0 mmol) was added dropwise, and the mixture was allowed to come to room temperature and stirred overnight. After workup with a saturated NH_4Cl solution, the mixture was extracted with dichloromethane. The organic layer was separated, dried over $MgSO_4$, concentrated under vacuum and purified via column chromatography. The product was isolated as a yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.43 (s, 1H) 6.78 (t, *J* = 7.6 Hz, 1H) 7.64 (d, *J* = 8.0 Hz, 1H) 7.88 (d, *J* = 8.0 Hz, 1H). Other characterization data are in good agreement with the previous reported data.[21]

General Procedure for the synthesis of alkyne 57, 58 and 61.

To a vial containing 1-bromo-3-iodo-2-methylsulfanyl-benzene (0.658 mmol) in 4 mL of Et_3N, phenylacetylene (0.790 mmol), $PdCl_2(PPh_3)_2$ (0.013 mmol), and CuI (0.026 mmol) were added. The reaction mixture was allowed to stir at room temperature overnight. The reaction mixture was concentrated under vacuum, adsorbed onto silica gel, and purified via column chromatography using hexanes as an eluent.

4-bromo-1-methylsulfanyl-2-(2-phenylethynyl)benzene (57). Product was isolated as a yellow solid: mp 44-46 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.50 (s, 3H), 7.03 (d, *J* = 8.8 Hz, 1H), 7.35-7.42 (m, 4H), 7.56-7.62 (m, 4H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 15.4, 85.7, 97.2, 117.6, 122.9, 123.4, 125.8, 128.5, 128.9, 131.7, 131.8, 134.7, 141.1; IR (neat) 1597.3, 1571.0, 1490.8, 1442.1, 1431.3, 1387.3, 1251.0, 1219.8, 1089.0, 1059.3, 877.7, 806.1, 772.2, 757.4, 686.4. HRMS (EI+, m/z) calcd for $(C_{15}H_{11}BrS)^+$ 301.9765 found 301.9760.

4-bromo-2-methylsulfanyl-1-(2-phenylethynyl)benzene (58). Product was isolated as a yellow solid: mp 75-77 ^{o}C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.45 (s, 3H), 7.14-7.22 (m, 2H), 7.25-7.32 (m, 4H), 7.50-7.53 (m, 2H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 15.2, 86.1, 97.1, 120.1, 123.0, 123.1, 126.6, 127.4, 128.5, 128.7, 131.7, 133.3, 144.2; IR (neat) 1569.9, 1488.63, 1458.0, 1439.8, 1375.9, 1219.84, 1084.9, 1067.2, 850.8, 816.1, 772.3, 753.0, 690.2. HRMS (EI+, m/z) calcd for $(C_{15}H_{11}BrS)^+$ 301.9765, found 301.9757.

1-bromo-2-methylsulfanyl-3-(2-phenylethynyl)benzene (61). Product was isolated as a yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.58 (s, 3H), 7.12 (t, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 3.6 Hz, 3H), 7.52-7.61 (m, 4H); ^{13}C NMR (100 MHz, chloroform-*d*) δ 19.2, 88.4, 94.9, 123.2, 128.7, 128.9, 129.2, 130.4, 130.6, 131.9, 132.6, 133.4, 139.5; IR (neat) 3019.9, 2400.5, 1598.8, 1571.6, 1543.8, 1491.0, 1440.1, 1396.9, 1216.0, 1098.1, 929.0, 871.8, 849.8, 756.8, 690.3, 669.09. HRMS (EI+, m/z) calcd for $(C_{15}H_{11}BrS)^+$ 301.9765, found 301.9760.

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